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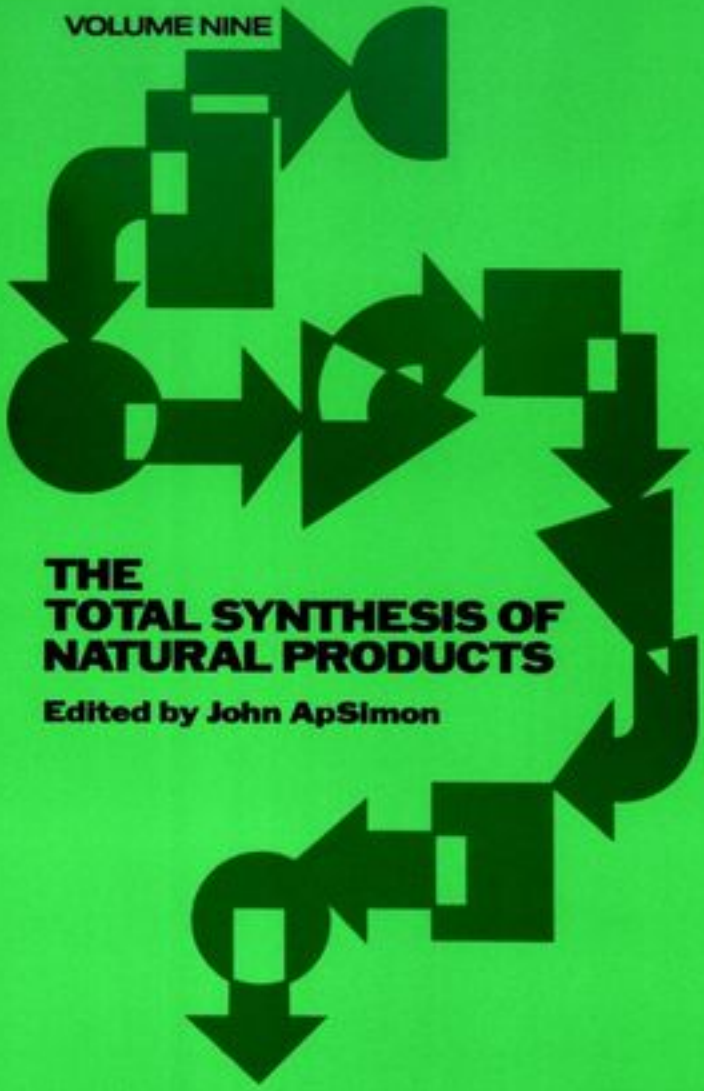

THE TOTAL SYNTHESIS OF NATURAL PRODUCTS

Edited by John ApSimon

THE TOTAL SYNTHESIS OF NATURAL PRODUCTS

The Total Synthesis of Natural Products

VOLUME 9

Edited by

John ApSimon

Ottawa-Carleton Institute for Research and Graduate Studies in Chemistry

and

Department of Chemistry
Carleton University, Ottawa

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Preface

This volume is a single author effort covering the massive amount of synthetic work associated with Insect Pheromone Chemistry for the period 1979 to 1990. Professor Mori has, once more, demonstrated in a masterful way his key position in this field.

I have been editor of this series since its inception in 1973 and, although I am convinced of its value to the discipline of organic synthesis, other responsibilities and interests have slowly intruded, to the state where I must regretfully pass on the onerous task of keeping the initiative alive to another editor. Over the past 18 years, I have had the honor of working with many outstanding authors and scientists. I thank you personally for this collaboration, friendship, and support.

JOHN APSIMON

Ottawa, Canada
November 1991

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The Total Synthesis of Natural Products, Volume 9
Edited by John ApSimon

The Synthesis of Insect Pheromones, 1979–1989

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1. INTRODUCTION

Since the appearance of the first edition of this chapter in Volume Four of this series,[1] a tremendous amount of work has been published in the field of pheromone synthesis. Simple but unique structures that can frequently be seen among pheromone molecules became favorite targets of synthetic chemists to test their methodology and strategy in pursuit of simplicity, selectivity, and efficiency. It is therefore very difficult to write a comprehensive review on pheromone synthesis. However, it is the aim of this chapter to summarize almost all of the notable syntheses in the pheromone area published between April 1979 to February 1990. Thus, this chapter will be of service to those chemists who want a quick view of the existing synthetic methods for each of the individual pheromones.

The pheromones described in this chapter are classified according to the structural type, as in the first edition. Because the synthesis of optically active pheromones is now a common practice, enantioselective synthesis has been included in each section instead of being made into an independent section. The relationships between absolute configuration and pheromone activity are briefly summarized at the end of this chapter.

There are a number of recent monographs and reviews on pheromones. The following brief listing highlights the focus of literature published within the time frame of this chapter.

A monograph on all aspects of pheromone research—including isolation, structure determination, synthesis, and estimation of enantiomeric purity—was published in 1984.[2]

Synthetic methodologies useful in preparing chiral pheromones were thoroughly reviewed.[3]

The present status of pheromone biochemistry was compiled as a monograph.[4]

Three general reviews on insect pheromones become available.[5-7]

Ritter reviewed steric factors in pheromonal pest control;[8] he also reviewed his own applied research on semiochemicals.[9]

A concise review on chiral insect pheromones was published in Czech.[10]

Schneider reviewed the problem of insect olfaction.[11]

A comprehensive review became available on structure determination of pheromones by combined microchemical and gas chromatographic methods.[12]

The following additional reviews were published:

a short review[13]

an account of the background of pheromone research and its application in insect pest control[14,15]

a thorough review covering the literature published in 1982 and 1983[16]

a review on isoprenoid pheromones (in Russian)[17]

a pedagogical review on chirality in insect communication[18]

an account of the pheromone metabolism in insects[19]

2. GENERAL METHODS

Some useful methods for the synthesis and analysis of pheromones are listed below.

A. Useful Synthetic Methods

(1) Alkylation of Acetylides in DMSO

In addition to the existing procedures for the alkylation of 1-alkynes,[1] Chong and Wong proposed a method employing methyllithium (base) and DMSO (solvent).[20] As shown in Eq. 1, terminal acetylenes afford disubstituted acetylenes in good yield.

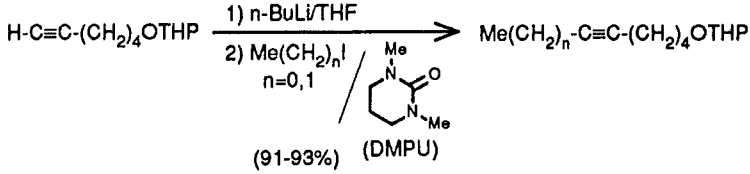
$$\text{H-C}\equiv\text{C-R} \xrightarrow[\text{2) R'X/DMSO}]{\text{1) MeLi·LiBr/Et}_2\text{O-THF}} \text{R'-C}\equiv\text{C-R} \qquad (1)$$

(77-87% yield)

R=CH_2OTHP, CH_2OCH_2Ph, Ph, $CH(OEt)_2$
R'=n-C_6H_{13}, n-$C_{10}H_{21}$, Me_2CHCH_2
X-Cl, Br, I

(2) Alkylation of Acetylides in the Presence of DMPU

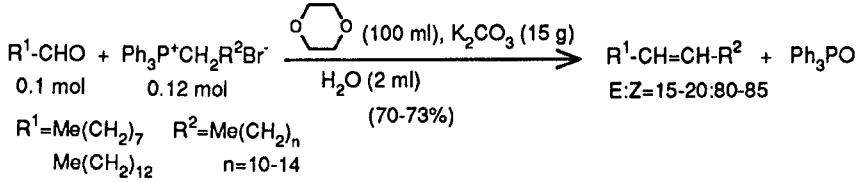
Bengtsson and Liljefors employed DMPU (1,3-dimethyl-2-oxohexahydropyrimidine) as a good substitute for the carcinogenic HMPA in the alkylation of lithium acetylides (Eq. 2).[21]



(2)

(3) Wittig Reaction in a Heterogeneous Medium

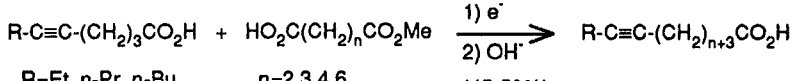
The Wittig reaction can be carried out in a solid-liquid medium under mild conditions in good yield as shown in Eq. 3.[22] Wittig chemistry as used in pheromone synthesis was reviewed by Bestmann and Vostrowsky.[23]



(3)

(4) Kolbe Synthesis of Unsaturated Pheromones

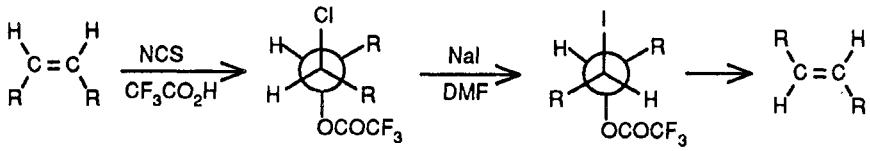
Kolbe electrolysis was used for the coupling of 5-alkynic acids and half esters to give alkynic acids, which could be converted into unsaturated pheromones (Eq. 4).[24]



(4)

(5) Olefin Inversion

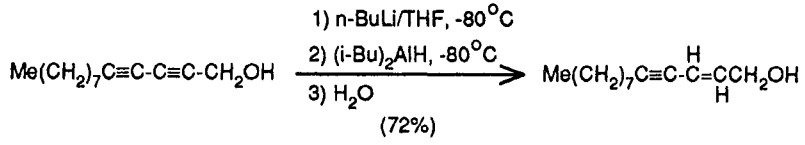
Inversion of the geometry of alkenes is a useful method in pheromone synthesis.[25] Treatment of alkenes with N-chlorosuccinimide in trifluoroacetic acid results in *anti*-addition of the element of trifluoroacetyl hypochlorite. Heating the *vic*-chlorohydrin trifluoroacetate with sodium iodide in DMF produced alkenes with inversion of the geometry (Eq. 5).[26]



(5)

(6) Reduction of Diynols to Enynols

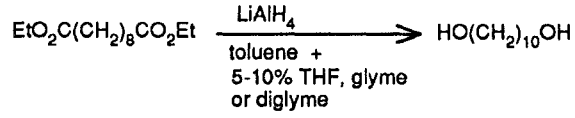
2,4-Diyn-1-ols can be reduced to (2*E*)-en-4-yn-1-ols by treating the corresponding lithium alcoholates with diisobutylaluminum hydride (Eq. 6).[27]



(6)

(7) Reduction of Diesters to Diols

Aksenov et al. reported that the preparation of α,ω-diols from diesters by reduction with lithium aluminum hydride was made possible in toluene by the addition of 5–10% of THF, glyme, or diglyme (Eq. 7).[28]



(7)

(8) Preparation of ω-Bromo-α-alkanols from α,ω-Diols

Pure ω-bromo-α-alkanols were prepared in good yields by refluxing a mixture of α,ω-diols, 48% hydrobromic acid and benzene using a Dean-Stark water separator (Eq. 8).[29]

$$HO(CH_2)_nOH \xrightarrow[\text{reflux } (-H_2O)]{48\%\ HBr/C_6H_6} Br(CH_2)_nOH \qquad (8)$$

$n = 2 \sim 12$; (40-90%)

(9) Preparation of ω-Acetoxy-α-alkanols from α,ω-Diols

Monoacetylation of α,ω-diols was achieved in high yield by the use of continuous extraction of the reaction mixture consisting of α,ω-diols, acetic acid, water, and sulfuric acid (Eq. 9).[30]

$$HO(CH_2)_nOH \xrightarrow[\text{Continuous extraction with hexane, cyclohexane or cyclohexane-}CCl_4]{AcOH\text{-}H_2O,\ H_2SO_4} AcO(CH_2)_nOH \qquad (9)$$

$n = 8, 10, 12$; (75-94%)

(10) Preparation of ω-t-Butyldimethylsilyloxy-α-alkanols from α,ω-Diols

McDougal et al. silylated the monosodium alkoxide salt of α,ω-diols with one equivalent of *t*-butyldimethylsilyl chloride to furnish monosilylated material in good yield (Eq. 10).[31] A polymer-supported organosilyl protecting group was also used in pheromone synthesis.[32]

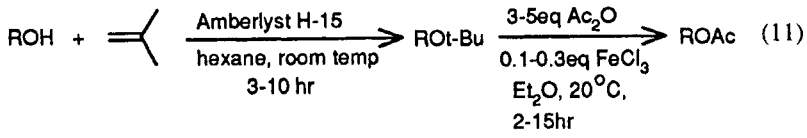
$$HO(CH_2)_nOH \xrightarrow[\text{2) t-BuSiMe}_2\text{Cl}]{\text{1) 1eq NaH/THF}} HO(CH_2)_nO\overset{\overset{Me}{|}}{\underset{\underset{Me}{|}}{Si}}\text{t-Bu} \qquad (10)$$

$n = 2 \sim 10$; (77-97%)

(11) Mild Protection and Deprotection of Alcohols as t-Butyl Ethers

t-Butyl ether was found to be the most appropriate protection for ω-hydroxyalkyl halides when they were to be converted into organolithium or Grignard reagents. ω-*t*-Butoxy organolithium and Grignard reagents can be prepared in ether, exactly like the nonfunctionalized ones, and their reactivity is normal.[33]

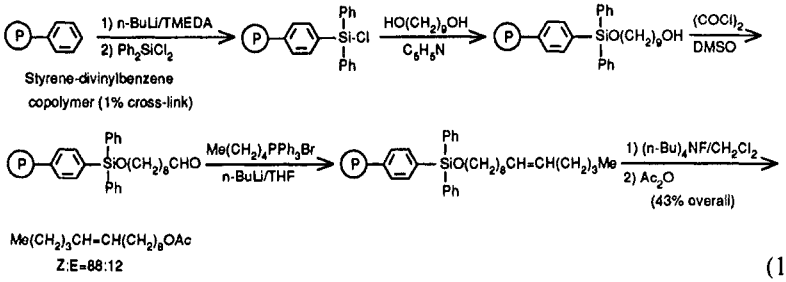
The protection and deprotection of alcohols as *t*-butyl ethers can be achieved under the mild conditions exemplified in Eq. 11.[34]



(11)

(12) Solid Phase Synthesis

A method different from that developed by Leznoff[35] was devised by Chan and Huang.[32] They prepared polymer-anchored diphenylchlorosilane and used it for the protection of the hydroxy group. Equation 12 illustrates its use in the synthesis of (*Z*)-9-tetradecenyl acetate (fall armyworm moth pheromone).



(12)

Other synthetically useful methods are: (1) vitamin B_{12}-mediated electrochemical reactions;[36] (2) carbocupration reactions;[37] (3) stereodirected synthesis with α-haloboronic esters;[38,39] (4) heteroatom-assisted substitution of acyclic secondary tosylates with lithium dialkylcuprates;[40] and (5) semi-hydrogenation of acetylenes using homogeneous catalysis with $(dba)_2Pd_2 \cdot CHCl_3 \cdot Ar_3P$, although the *Z*/*E* selectivity was poor.[41]

B. Useful Analytical Methods

Reverse-phase TLC and HPLC were shown to be useful for the separation of pheromones.[42] ^{13}C NMR spectroscopy was employed for the assignment of the geometry of carbon-carbon double bond(s) of olefinic pheromones.[43,44]

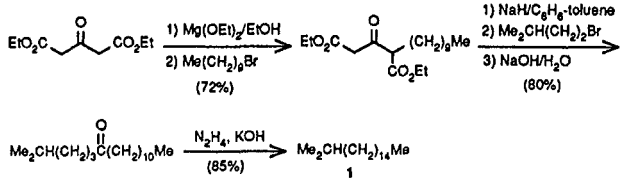
Methods were reviewed for determining the enantiomeric purity of pheromones.[3,45] Slessor et al. described a method for determining the enantiomeric composition of chiral alcohols, lactones, and hydroxy acids in quantities rang-

ing from 25 ng to 10 μg.[46] Derivatization of the substance with enantiomerically pure acetyllactyl chloride, followed by GLC analysis enables enantiomeric estimation.

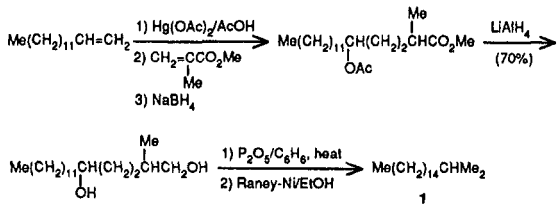
3. ALKANES AS PHEROMONES

A. 2-Methylheptadecane 1 ($C_{18}H_{38}$)

The title hydrocarbon is the sex pheromone of the tiger moth (*Holomelina aurantiaca; Arctiidae* species). This achiral alkane was synthesized by Naoshima employing diethyl 3-oxoglutarate as the starting material (Scheme 1).[47] Another synthesis was reported by Bhalerao (Scheme 2).[48]



Scheme 1

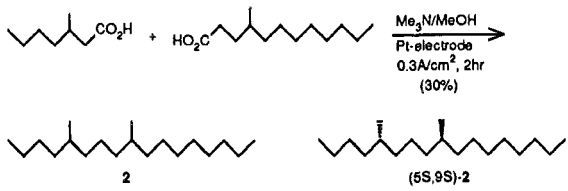


Scheme 2

B. (5*S*,9*S*)-5,9-Dimethylheptadecane 2 ($C_{19}H_{40}$)

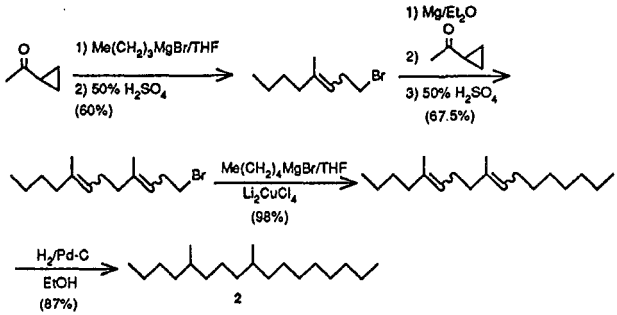
The mountain-ash bentwing (*Leucoptera scitella*) is a pest in the apple orchards in Hungary. Its female-produced sex pheromone was identified by Francke et al. as 5,9-dimethylheptadecane **(2).**[49] A synthesis of a diastereomeric mixture of **2** was achieved by the mixed Koble electrolysis of (±)-3-methylheptanoic acid and (±)-4-methyldodecanoic acid (Scheme 3).[49]

Helmchen's synthesis of the four stereoisomers of **2** was followed by their bioassay to reveal (5*S*,9*S*)-**2**, $[\alpha]_D$ + 2.1° ($CHCl_3$) as the natural pheromone.[50]



Scheme 3

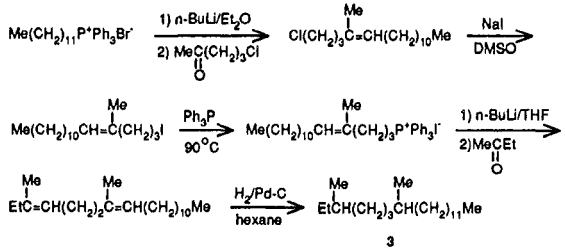
Other stereoisomers neither synergize nor inhibit catches with (5*S*,9*S*)-**2**, and, therefore, a diastereomeric mixture is practically useful.[49,50] Another multigram synthesis of a diastereomeric mixture of **2** was reported by Rama and Capuzzi (Scheme 4).[51]



Scheme 4

C. 3,7-Dimethylnonadecane 3 ($C_{21}H_{44}$)

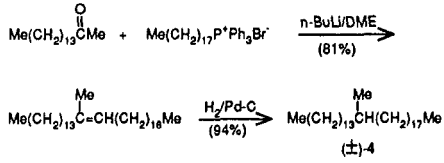
The female-produced sex pheromone of the alfalfa blotch leafminer (*Agromyza frontella*) was identified as 3,7-dimethylnonadecane (**3**).[52] A diastereomeric mixture of **3** was synthesized, as shown in Scheme 5, and shown to be bioactive.[52]



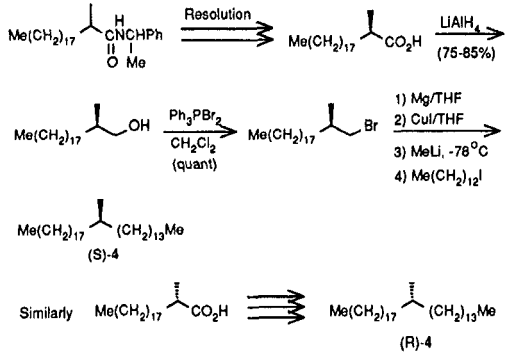
Scheme 5

D. 15-Methyltritriacontane 4 ($C_{34}H_{70}$)

This is the female-produced sex-stimulant pheromone of the stable fly (*Stomoxys calcitrans*). A synthesis of (±)-**4** is shown in Scheme 6.[53]



Scheme 6



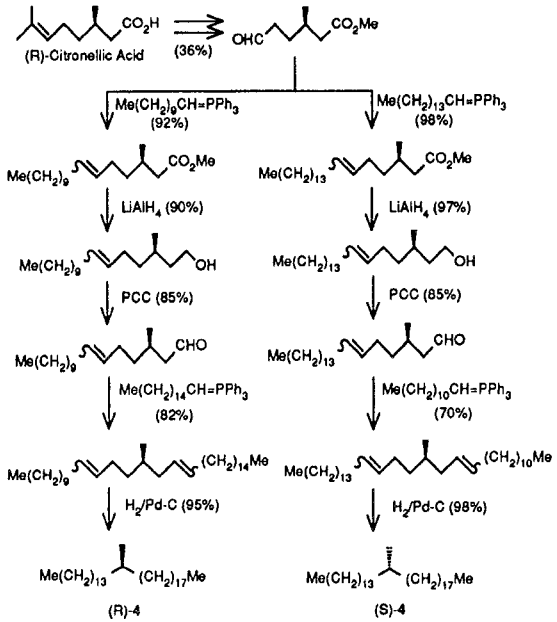
Scheme 7

Two syntheses were reported for the enantiomers of **4**. Scheme 7 shows the synthesis reported by Sonnet.[54] The chiral part of the molecule was synthesized via optical resolution. The enantiomeric bromides were then converted to the cuprates and coupled with tridecyl iodide to give the enantiomers of **4**. Their bioassay results are not yet published.

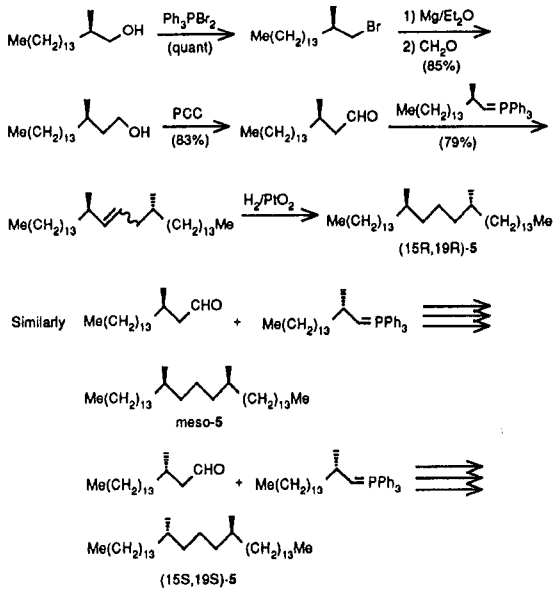
Naoshima and Mukaidani synthesized the pure enantiomers of **4** in good overall yield, starting from (*R*)-(+)-citronellic acid (Scheme 8).[53]

E. 15,19-Dimethyltritriacontane 5 ($C_{35}H_{72}$)

This alkane is also the mating-stimulant pheromone isolated from female stable flies (*Stomoxys calcitrans*). Sonnet prepared (15*R*,19*R*)-, (15*S*,19*S*)-, and *meso*-**5** (Scheme 9).[54] The starting chiral alcohol was obtained by resolution in the same manner as shown in Scheme 7.



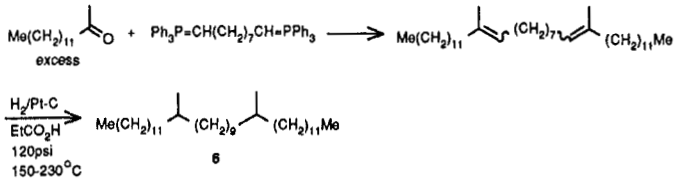
Scheme 8



Scheme 9

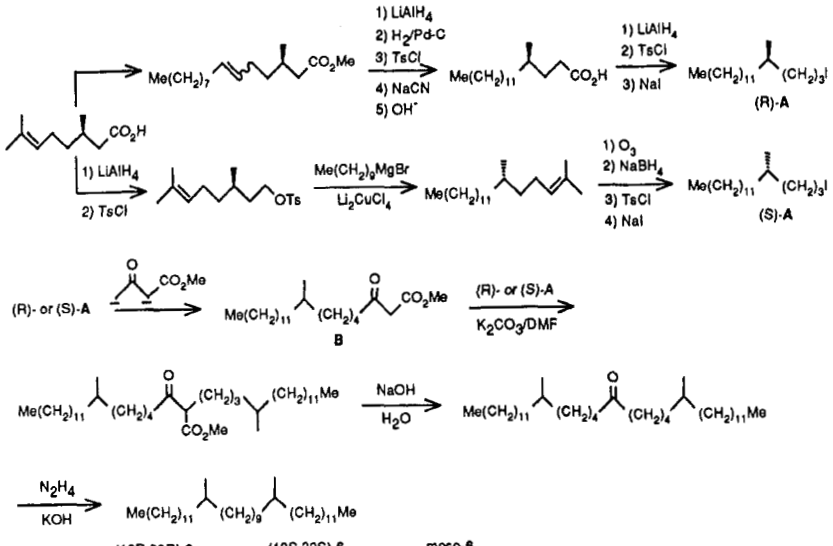
F. *meso*-15,23-Dimethylpentatriacontane 6 ($C_{37}H_{76}$)

The title compound is the sex-stimulant pheromone of the female tsetse fly (*Glossina pallidipes*). A simple synthesis of a diastereomeric mixture of **6** was reported by Carlson et al. (Scheme 10).[55] Both the enantiomers of **6**, as well as



Scheme 10

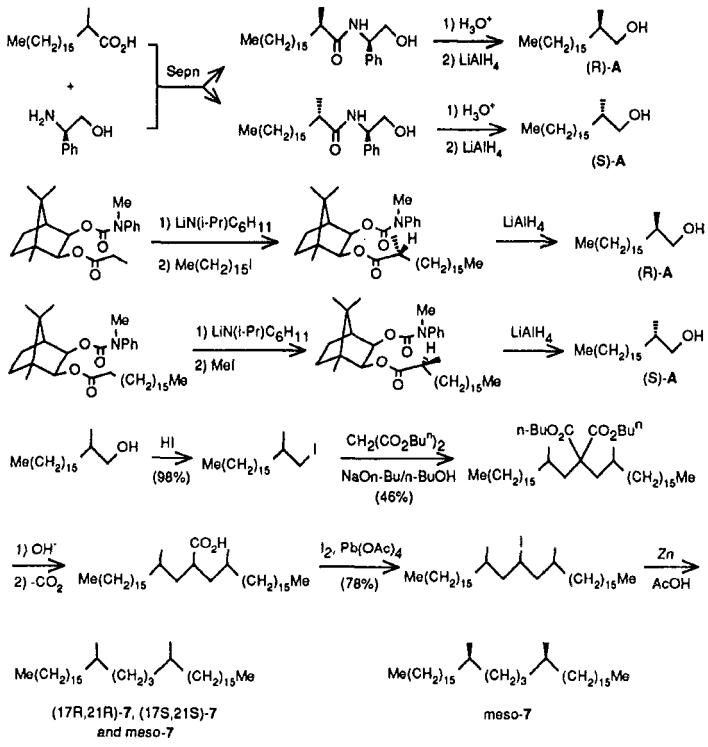
meso-**6**, were synthesized from (*R*)-(+)-citronellic acid, employing the alkylation of the dianion derived from methyl acetoacetate as the key-step (Scheme 11).[56] Only *meso*-**6** was shown to be bioactive.[57]



Scheme 11

G. *meso*-17,21-Dimethylheptatriacontane 7 ($C_{39}H_{80}$)

This is the female-produced sex-stimulant pheromone of the tsetse fly (*Glossina morsitans morsitans*). All of the three possible stereoisomers were synthesized by Helmchen (Scheme 12).[58] The enantiomers of **A** were synthesized either by



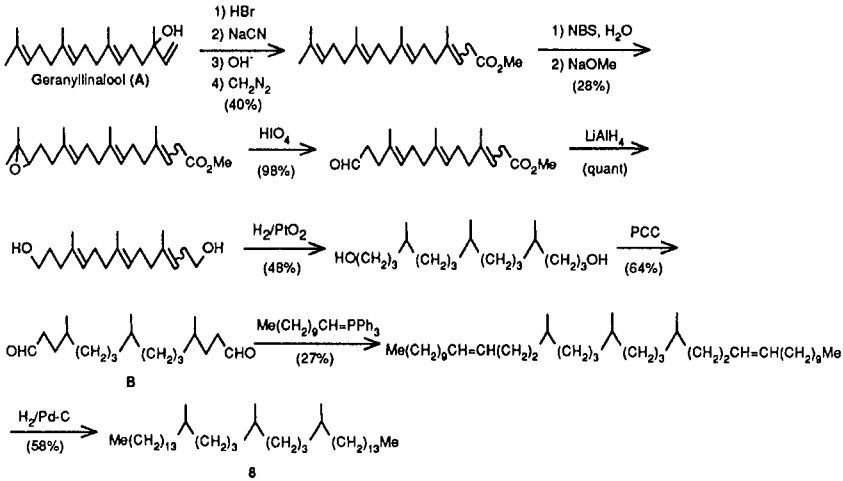
Scheme 12

optical resolution or by asymmetric alkylation. By combining the enantiomers of **A**, (17*R*,21*R*)-, (17*S*,21*S*)-, and *meso*-**7** were prepared. Only the *meso*-isomer was shown to be bioactive.[59]

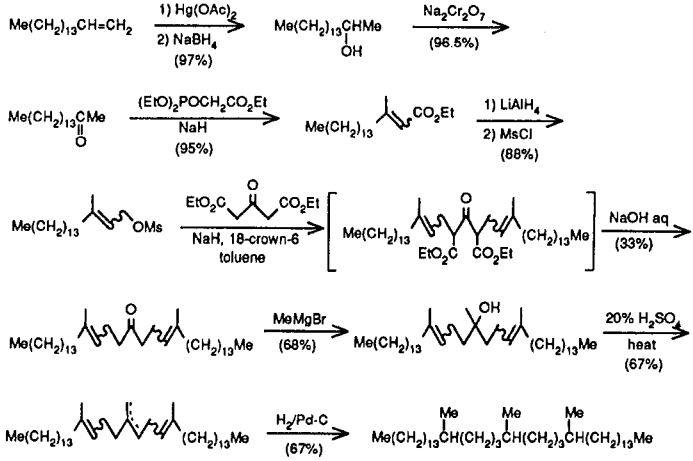
H. 15,19,23-Trimethylheptatriacontane 8 ($C_{40}H_{82}$)

The title compound is also the sex-stimulant pheromone isolated from the female tsetse fly (*Glossina morsitans morsitans*). Two new syntheses of its dias-

tereomeric mixture were published.[60,61] In the earlier synthesis, geranyllinalool **(A)** was converted to a symmetrical intermediate **B,** the chain elongation of which by a Wittig reaction completed the construction of the carbon skeleton (Scheme 13).[60] Naoshima et al. utilized diethyl 3-oxoglutarate as their symmetrical building block to obtain a diastereomeric mixture of **8** (Scheme 14).[61]



Scheme 13

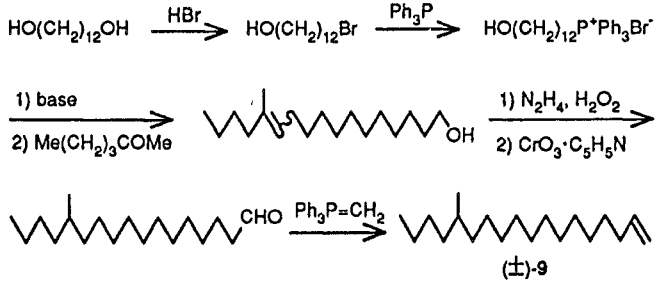


Scheme 14

4. PHEROMONE HYDROCARBON WITH A TERMINAL DOUBLE BOND

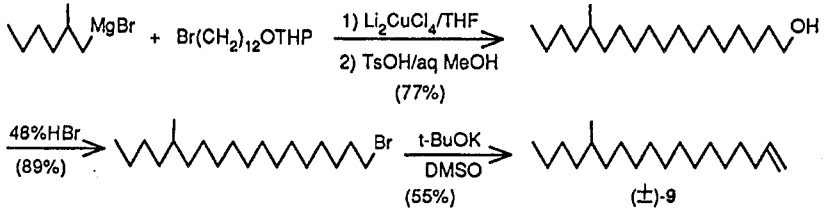
A. (*S*)-14-Methyl-1-octadecene **9** ($C_{19}H_{38}$)

The title compound **9** was isolated and identified as the sex pheromone of the peach miner moth (*Lyonetia clerkella*), which is one of the destructive pests in the peach orchards of Japan. The first synthesis of (±)-**9** was executed at the time of its isolation for the purpose of identification.[62] That synthesis is lengthy and inefficient (Scheme 15).[62] Two more efficient syntheses of (±)-**9** were pub-



Scheme 15

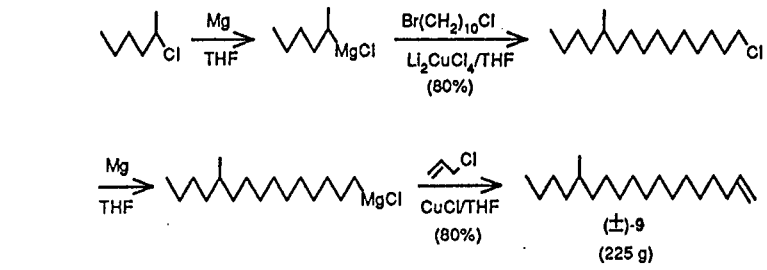
lished later by chemists in industry. Manabe et al. introduced the double bond of (±)-**9** at the final stage of their synthesis (Scheme 16),[63] while Yamamoto



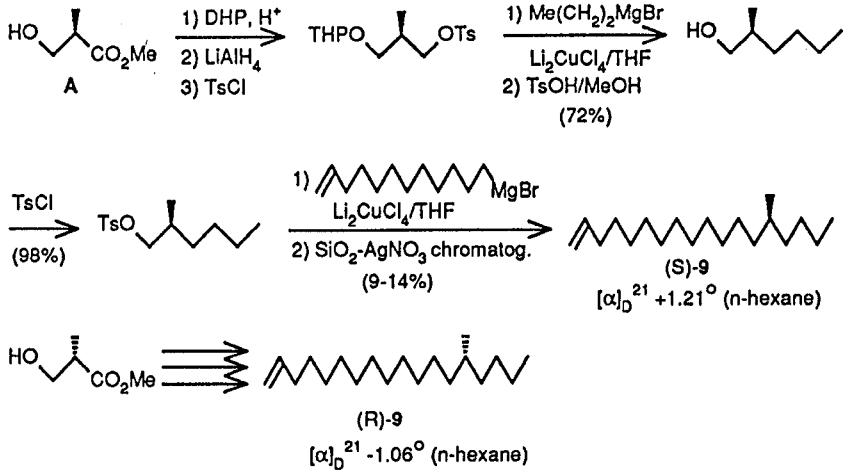
Scheme 16

and Fukumoto used allyl chloride as one of their starting materials (Scheme 17).[64]

Four different syntheses of optically active **9** were reported. In Mori's first synthesis, the enantiomers of methyl β-hydroxyisobutyrate (**A**) were employed as the chiral building blocks (Scheme 18).[65] **A** is of microbial origin and com-



Scheme 17



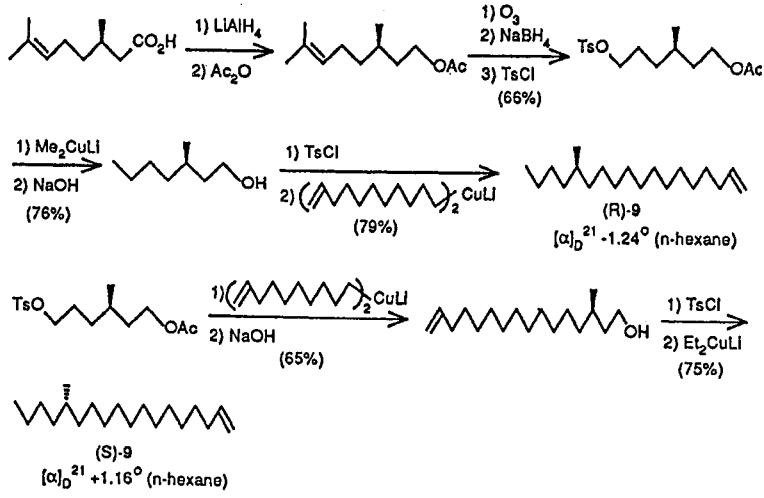
Scheme 18

mercially available. In the final step of the synthesis, however, the yield was quite modest due to the difficulty in separating **9** from other hydrocarbons generated as byproducts.

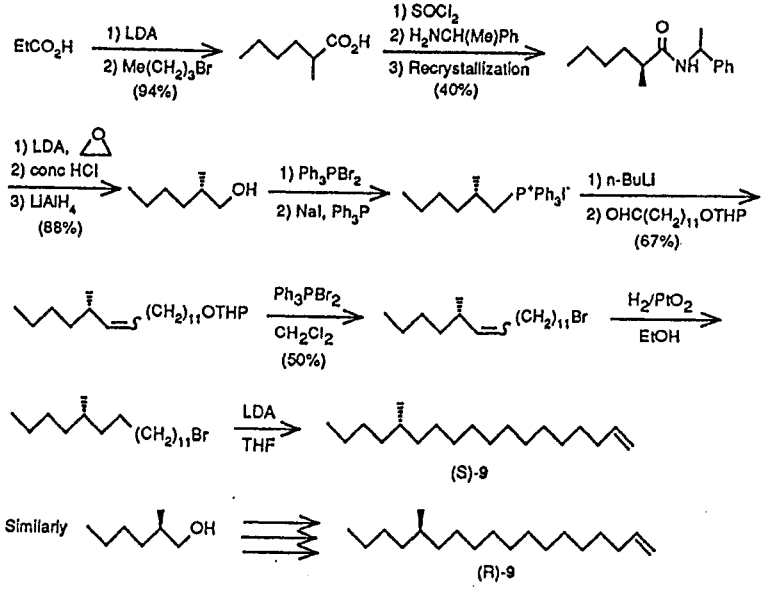
(*R*)-(+)-Citronellic acid was used as the starting material in the second synthesis of (*R*)-**9** and (*S*)-**9** (Scheme 19).[66] Only (*S*)-**9** exhibited the pheromone activity, although (±)-**9** was also active.[67]

The third synthesis by Sonnet et al. was based on the optical resolution of an intermediate (Scheme 20).[68]

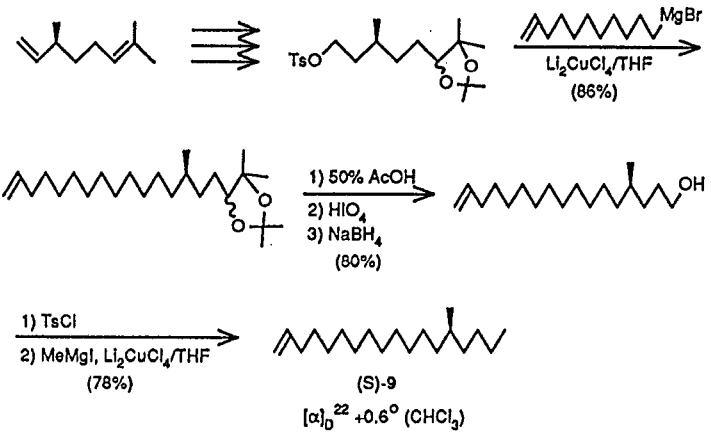
Serebryakov converted (*S*)-(+)-3,7-dimethyl-1,6-octadiene into (*S*)-**9** (Scheme 21).[69]



Scheme 19



Scheme 20



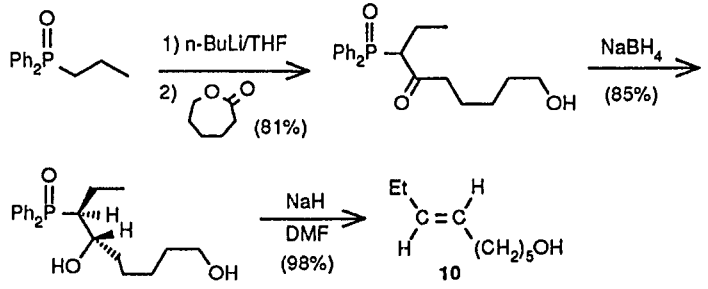
Scheme 21

5. PHEROMONE ALCOHOLS AND ACETATES WITH AN *E*-DOUBLE BOND

A. (*E*)-6-Nonen-1-ol **10** ($C_9H_{18}O$) and (*E*)-6-Nonenyl Acetate **11** ($C_{11}H_{20}O_2$)

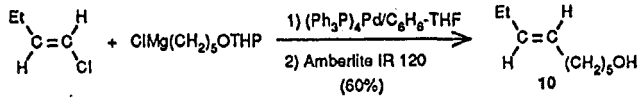
Males of the Mediterranean fruit fly (*Ceratitis capitata*) produce (*E*)-6-nonen-1-ol **10** as the sex pheromone. The corresponding acetate **11** is the attractant for the female melon fly (*Dacus cucurbitae*).

A Wittig-Horner reaction was employed to furnish **10** (Scheme 22).[70,71]



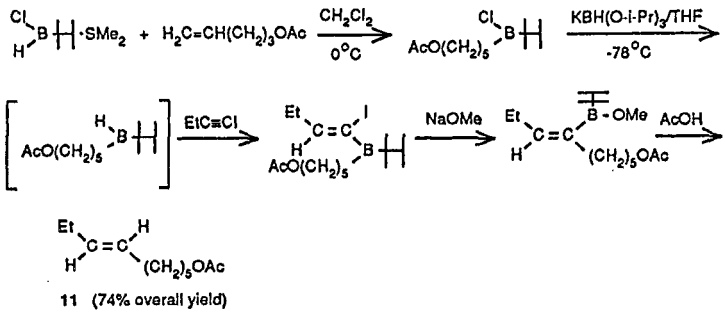
Scheme 22

A synthesis of **10** was also achieved by the palladium-catalyzed reaction of (*E*)-1-chloro-1-butene with a Grignard reagent (Scheme 23).[72]



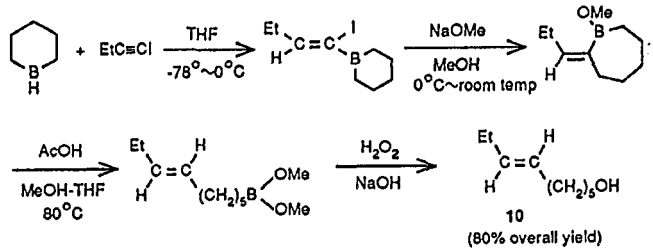
Scheme 23

Vinylic organoboranes were shown to be useful in the synthesis of (*E*)-alkenes.[73-76] (*E*)-6-Nonenyl acetate **11** was synthesized via thexylchloroborane-dimethyl sulfide (Scheme 24).[75] This procedure affords the (*E*)-pheromones of >97% chemical purity essentially in a one-pot synthesis.



Scheme 24

Another one-pot synthetic method for (*E*)-pheromones utilizes monohydroboration of 1-alkynes with borinane as the first step (Scheme 25).[73,75] The re-



Scheme 25

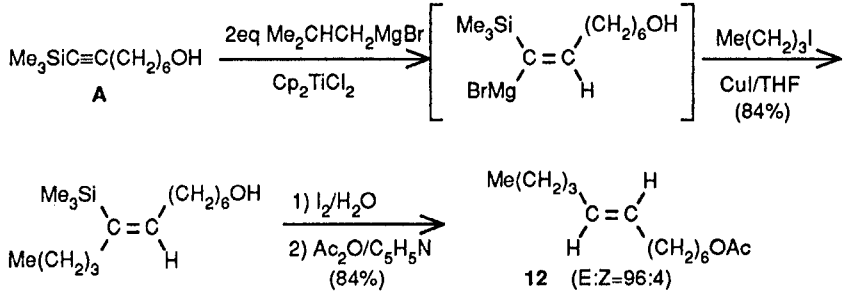
sulting *B*-(*E*)-1-alkenylborinanes, when treated with sodium methoxide, furnish intermediates containing the seven-membered borepane moiety, which yield (*E*)-pheromones upon protonolysis and oxidation. The products are of ≥ 99% chemical purity.

A synthesis of **11** was executed by the deoxygenation of the corresponding epoxide with diphosphorus tetraiodide.[77] The pure epoxide was obtained by chromatographic (SiO_2) purification of the mixture of epoxide isomers.

B. (*E*)-7-Dodecenyl Acetate 12 ($C_{14}H_{26}O_2$)

This is the sex pheromone of the false codling moth (*Cryptophlevia leucotreta*). Three different syntheses of **12**, by means of transition metal catalysis, were reported recently.[78–80]

In Sato's synthesis (Scheme 26), hydromagnesiation of **A** with isobutylmag-

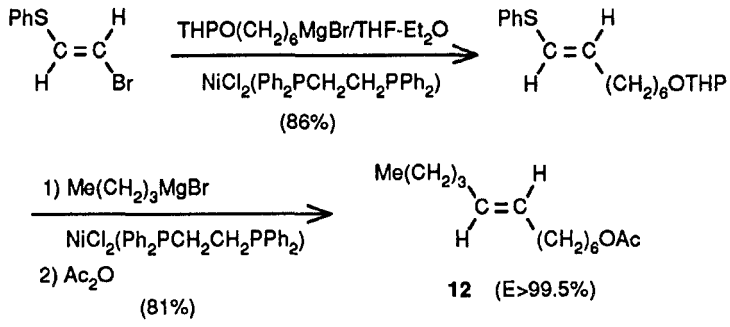


Scheme 26

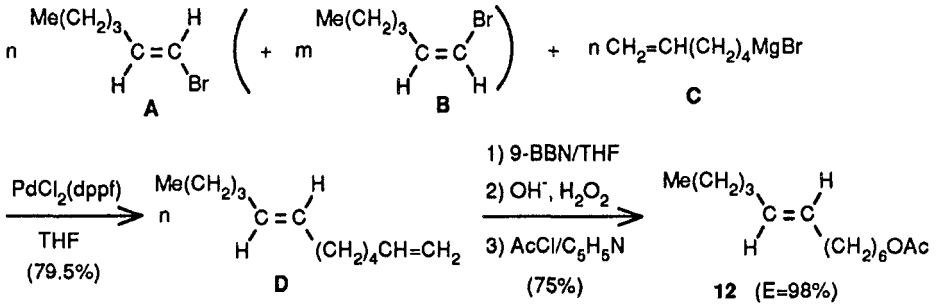
nesium bromide in the presence of titanocene dichloride was followed by treatment of the resulting Grignard reagent with alkyl iodide to yield a vinylsilane, which was desilylated and acetylated to give **12**.[78]

Naso and his co-workers developed a general method for the synthesis of (*E*)-pheromones employing a nickel catalyst (Scheme 27).[79] Starting from (*E*)-1-bromo-2-phenylthioethene, two cross-coupling reactions of the Grignard reagents in the presence of a nickel catalyst yielded **12** of high chemical purity. Many (*E*)-pheromones were synthesized by this method.

Rossi and Carpita prepared **12** by the cross-coupling of an alkenyl bromide with a Grignard reagent in the presence of dichloro [1,1′-*bis*(diphenylphosphino)ferrocene]palladium [= $PdCl_2$(dppf)].[80] The reactivity of **A** (Scheme 28) was higher than **B** in this coupling reaction. A mixture of **A**



Scheme 27



Scheme 28

and **B** (molar ratio = n : m) therefore reacted with n/(m + n) eq of **C** to give only the desired product **D** (Scheme 28).

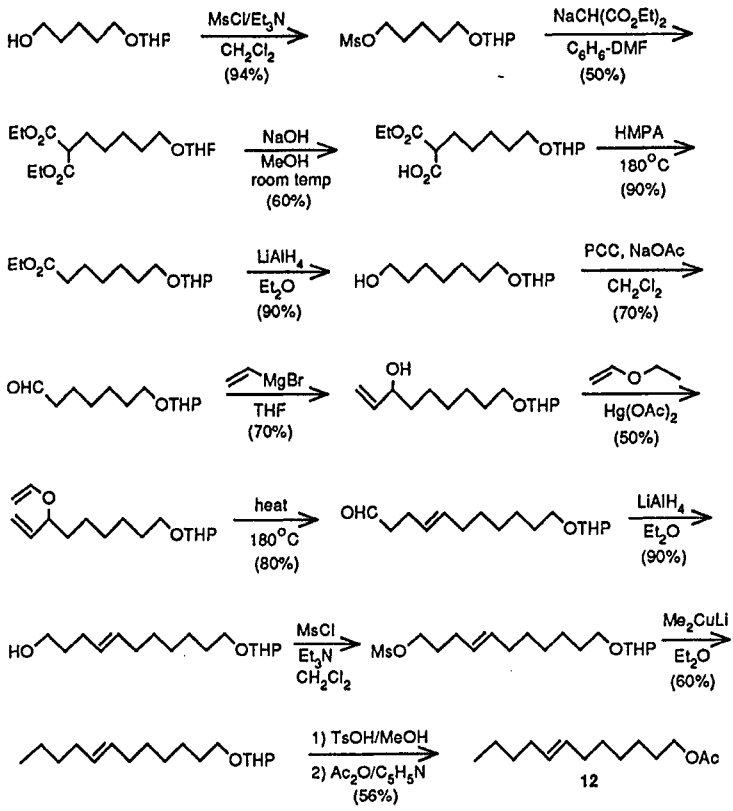
This pheromone **12** was also synthesized by other methods, which have already been summarized.[72,75]

Quite a lengthy and classical synthesis of **12** by Vig et al. (Scheme 29)[81] contrasts the brevity of the aforementioned syntheses of **12** by modern methods.

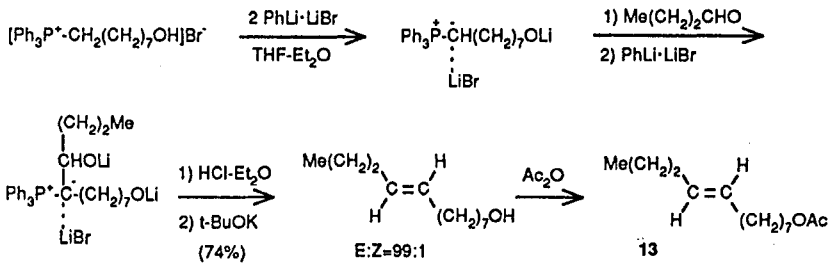
C. (*E*)-8-Dodecenyl Acetate 13 ($C_{14}H_{26}O_2$)

This is the minor component of the pheromone of the oriental fruit moth (*Grapholita molesta*).

A synthesis of **13** employing classical acetylenic chemistry was reported by Mithran and Mandapur.[82] A more interesting synthesis by Schlosser et al. utilized (*E*)-selective variant of the Wittig reaction (Scheme 30).[83] This betaine-



Scheme 29

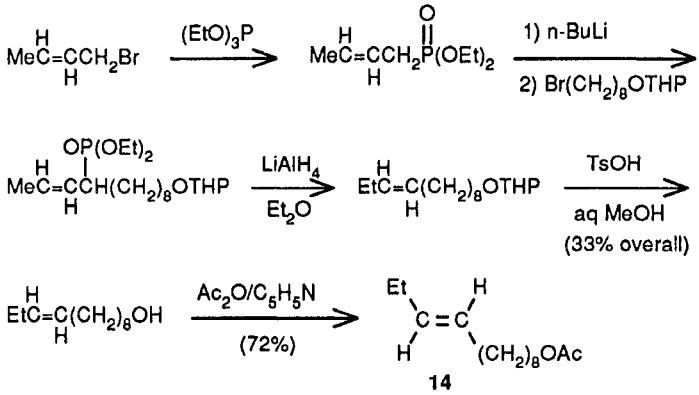


Scheme 30

ylide modification of the Wittig reaction allows the synthesis of (*E*)-alkenes with an isomeric purity of 99%.

D. (*E*)-9-Dodecenyl Acetate **14** ($C_{14}H_{26}O_2$)

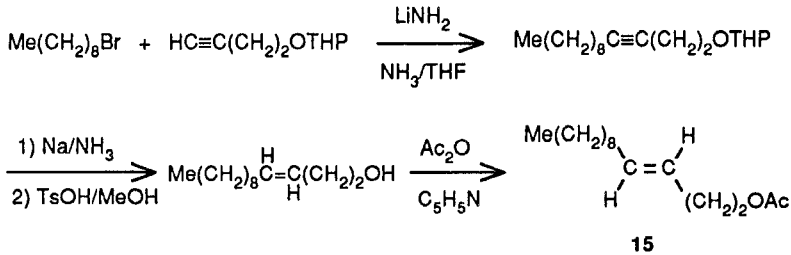
This is the pheromone component of the red bollworm moth (*Diparopsis castanea*) and the cereal tortrix moth (*Cnephasia pumicana*). The European pine shoot moth (*Rhyacionia buoliana*) also uses **14** as its pheromone. Bestmann et al. synthesized **14** as shown in Scheme 31.[84]



Scheme 31

E. (*E*)-3-Tridecenyl Acetate **15** ($C_{15}H_{28}O_2$)

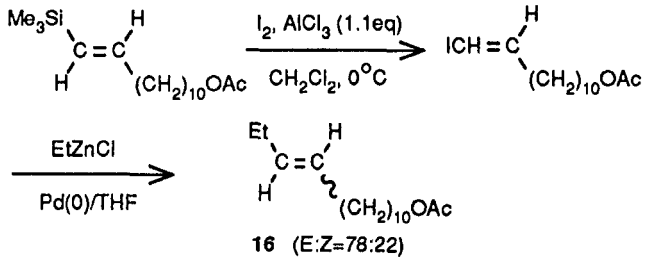
The female-produced sex pheromone of the tobacco stem borer (*Scrobipalpa heliopa*) was shown to be (*E*)-3-tridecenyl acetate **15.** It was synthesized by means of classical acetylenic chemistry (Scheme 32).[85]



Scheme 32

F. (*E*)-11-Tetradecenyl Acetate **16** ($C_{16}H_{30}O_2$)

This, together with its (*Z*)-isomer, is the sex pheromone of oak leafroller moth (*Archips semiferanus*) and the omniferous leafroller moth (*Platynota stultana*). Chan and Koumaglo synthesized a mixture of **16** and its (*Z*)-isomer in a 78 : 22 ratio, corresponding to that found in the case of the natural pheromone.[86] Their "tunable stereoselective alkene synthesis" is based on the variation of the stereoselectivity of iododesilylation of terminal (*E*)-vinylsilanes with a changing amount of Lewis acid (Scheme 33).[86]

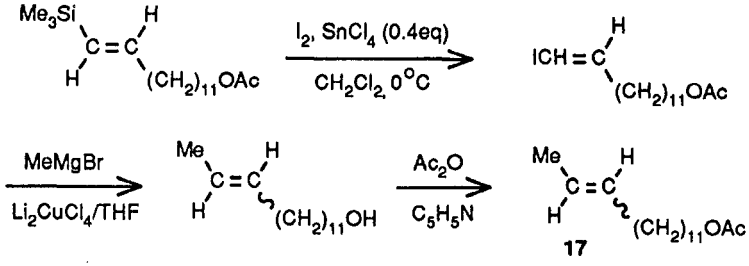


Scheme 33

A conventional acetylenic route was also employed to prepare **16** and its (*Z*)-isomer, involving the Birch reduction and semi-hydrogenation.[87] Other methods, already discussed, were also employed for the synthesis of **16**.[72,75,88]

G. (*E*)-12-Tetradecenyl Acetate **17** ($C_{16}H_{30}O_2$)

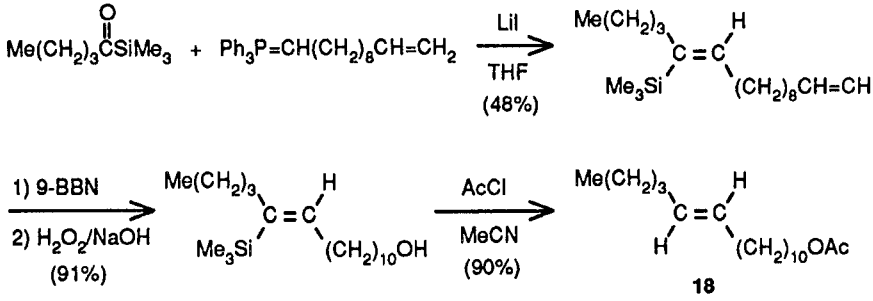
In combination with its (*Z*)-isomer, **17** is the pheromone of the Asian corn borer moth (*Ostrina furnacalis*). Kang et al. synthesized **17** starting from 12-tetradecyn-1-ol THP ether by the Birch reduction of the triple bond, while its semi-hydrogenation gave the (*Z*)-isomer of **17**.[89] Chan and Koumaglo prepared a 1 : 1 mixture of **17** and its (*Z*)-isomer (Scheme 34).[86]



Scheme 34

H. (*E*)-11-Hexadecenyl Acetate **18** ($C_{18}H_{34}O_2$)

This is the pheromone component of the sweet potato leaf folder moth (*Brachmia macroscopa*) and some other species such as the cabbage moth (*Mamestra brassicae*) and *Sceliodes cordalis*. Sonderquist and Anderson reported a highly stereoselective synthesis of **18** by their acylsilane-ylide chemistry (Scheme 35).[90]



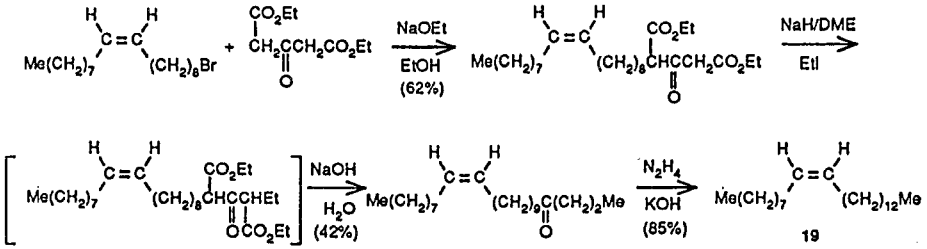
Scheme 35

6. PHEROMONE HYDROCARBONS AND ACETATES WITH A Z-DOUBLE BOND

A. Muscalure, (Z)-9-Tricosene **19** ($C_{23}H_{46}$)

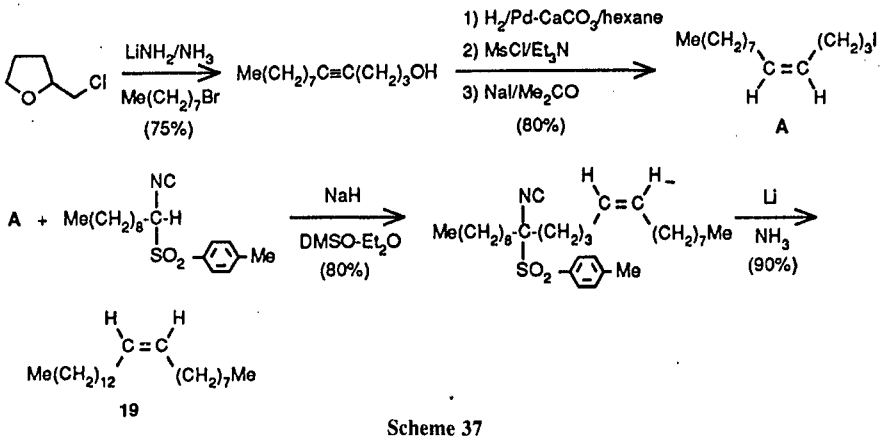
This is the female-produced sex pheromone of the house fly (*Musca domestica*). Many new syntheses of **19** have been published based on carbanion chemistry, organotransition metal chemistry, organoborane chemistry, etc.

Naoshima et al. synthesized **19** by alkylating diethyl 3-oxoglutarate with oleyl bromide and ethyl iodide (Scheme 36).[91]

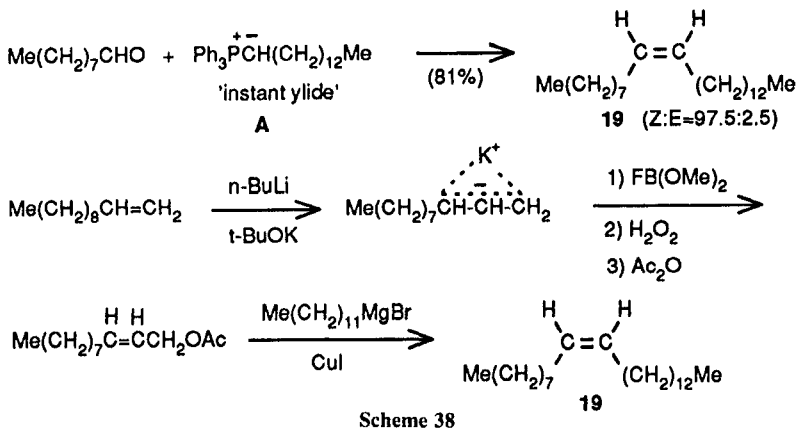


Scheme 36

Yadav et al. dialkylated tosylmethyl isocyanide, and the product was reduced with lithium in liquid ammonia to give **19** (Scheme 37).[92,93]



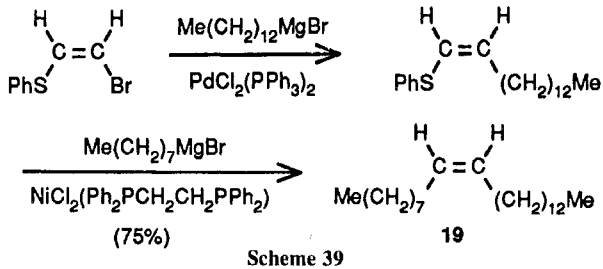
Scheme 37



Scheme 38

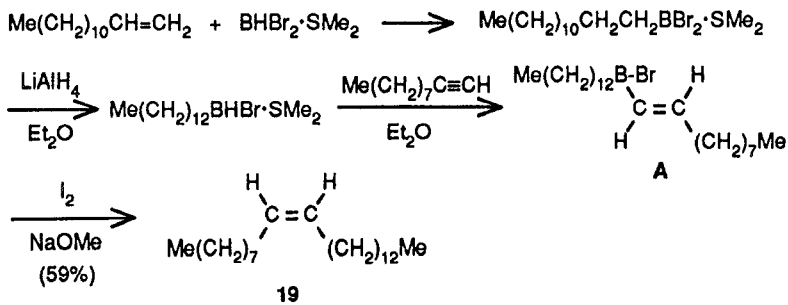
Scheme 38 illustrates the synthesis of **19** by Schlosser's group.[94] The first approach is the use of "instant ylide," which is a mixture of sodium amide and the phosphonium salt. By the addition of ether or THF, ylide can be generated instantly. Reaction of ylide **A** with nonanal furnished **19** in 81% yield with $E:Z$ ratio of 2.5:97.5. Their second approach was the coupling of dodecylmagnesium bromide with (*Z*)-2-undecyl acetate to give **19** of ca. 97.5% purity.[94]

Fiandanese's synthesis of (*E*)-alkenes (Scheme 27) could be modified to give (*Z*)-alkenes.[79] Muscalure **19** of ≥98.3% chemical purity was obtained as shown in Scheme 39.[79]



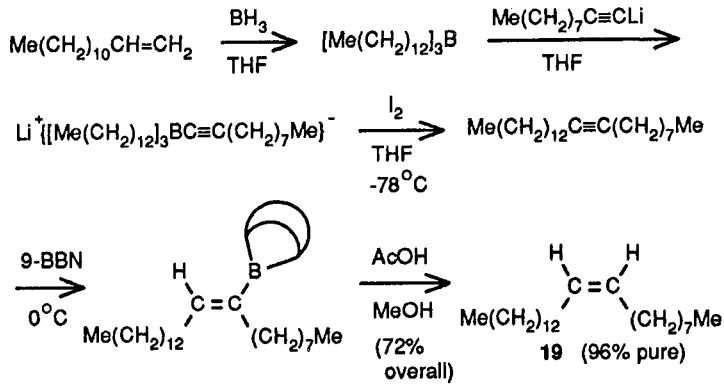
Scheme 39

Organoborane chemistry was extensively used for the synthesis of **19.** In Brown's first synthesis of **19,** base-induced iodination of a vinylborane **A** provided **19** (Scheme 40).[95,96] The second synthesis of **19** by Brown et al. utilized



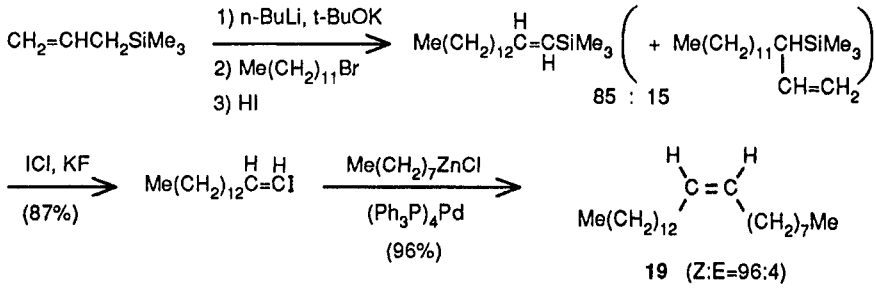
Scheme 40

their improved procedures for the protonolysis of alkenyldialkylboranes to give (Z)-alkenes of high purity.[97] Thus, muscalure **19** was synthesized by hydroboration-protonolysis of 9-tridecyne, which was prepared by iodination of lithium (1-decynyl)tri-tridecylborate (Scheme 41).[98]



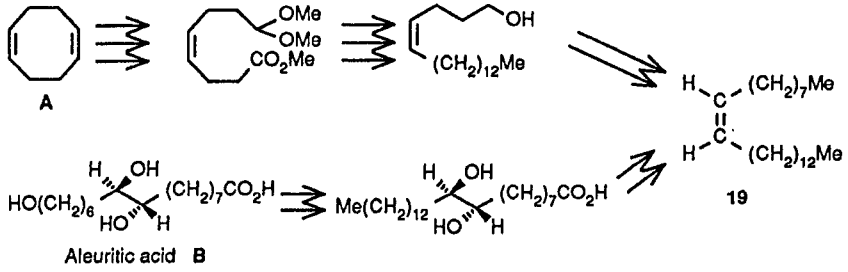
Scheme 41

Chan's organosilicon approach for the synthesis of **19** is shown in Scheme 42.[99]



Scheme 42

One of the (Z)-double bonds of 1,5-cyclooctadiene **A** (Scheme 43) served as the (Z)-double bond of **19.**[100] Conversion of an Indian natural product, aleuritic acid **B,** to **19** was also reported.[101,102]

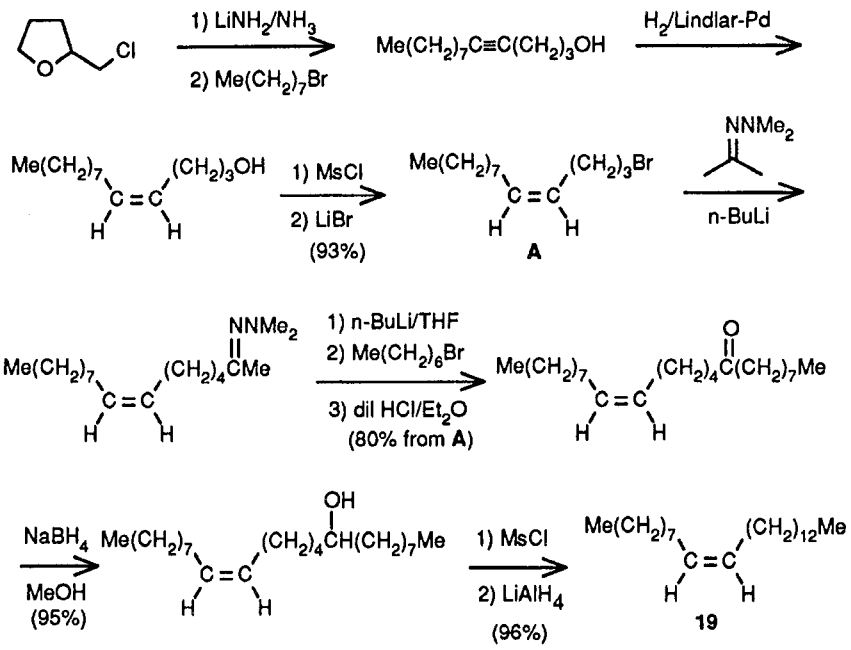


Scheme 43

Another synthesis of **19** is based on the connection of the alkenyl and alkyl chains by using acetone N,N-dimethylhydrazone as the connective synthon (Scheme 44).[103]

B. (Z)-5-Decenyl Acetate 20 ($C_{12}H_{22}O_2$)

This is the pheromone component of the turnip moth (*Agrotis segetum*), and was synthesized from 1-hexyne and 4-bromo-1-butanol THP ether. The resulting alkynyl THP ether was hydrogenated over Lindlar catalyst to give (Z)-5-

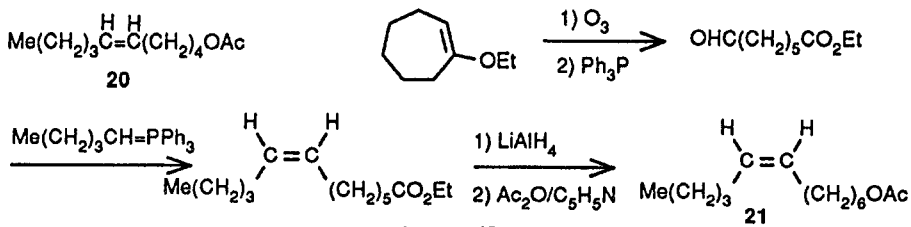


Scheme 44

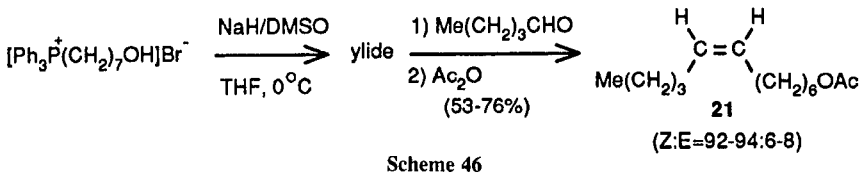
decen-1-ol THP ether. It was then converted to **20** by acetyl chloride in acetic acid.[104] Liljefors et al. published structure-activity studies on **20** and related compounds using molecular mechanics.[105,106]

C. (Z)-7-Dodecenyl Acetate 21 ($C_{14}H_{26}O_2$)

The cabbage looper (*Trichoplusia ni*) uses this acetate **21** as its pheromone. Bestmann et al. synthesized **21** by the Wittig reaction employing the ylide prepared by treating a phosphonium salt with sodium hexamethyldisilazide (Scheme 45).[107] Horiike and Hirano also synthesized **21** by a Wittig route employing

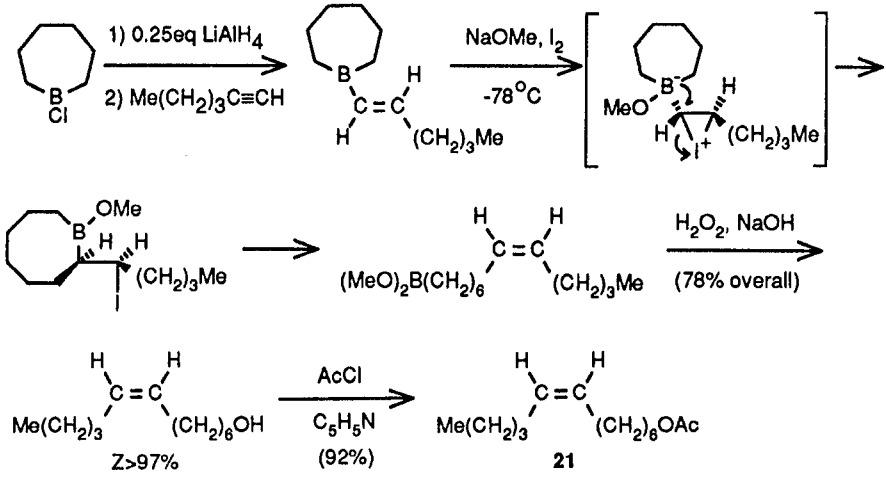


Scheme 45



Scheme 46

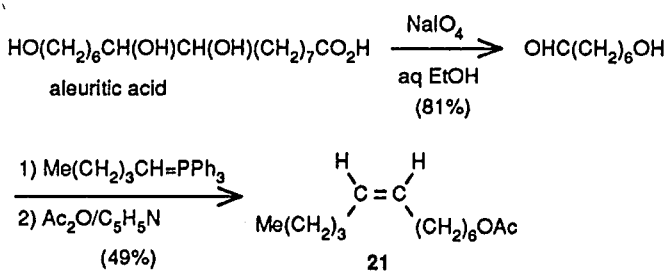
sodium hydride and DMSO as the base (Scheme 46).[108] Fiandanese's synthetic method for (*E*)-alkenes (cf. Scheme 27) was modified to give **21**.[79]



Scheme 47

Organoborane chemistry was useful in preparing **21** (Scheme 47).[76,109] Another synthesis of **21** was achieved via lithium (1-alkynyl)borate (cf. Scheme 41).[98]

Aleuritic acid, an easily accessible (in India) component of shellac, was employed as the starting material for the synthesis of **21** (Scheme 48).[110] The pres-

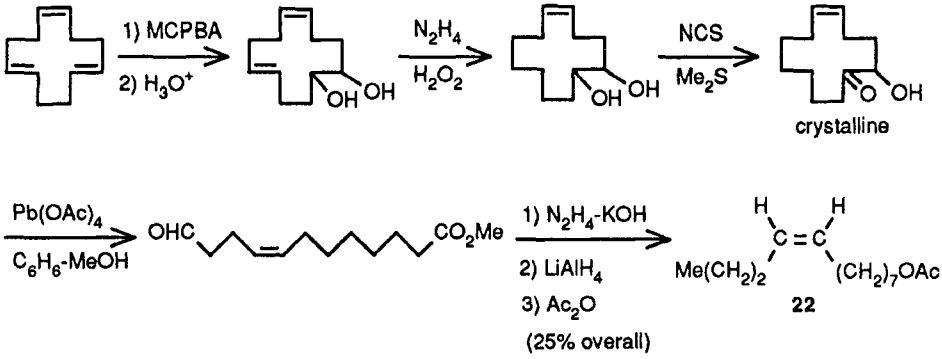


Scheme 48

ence of all parts of the acetate group was found to be very important for the expression of the pheromone activity of **21**.[111]

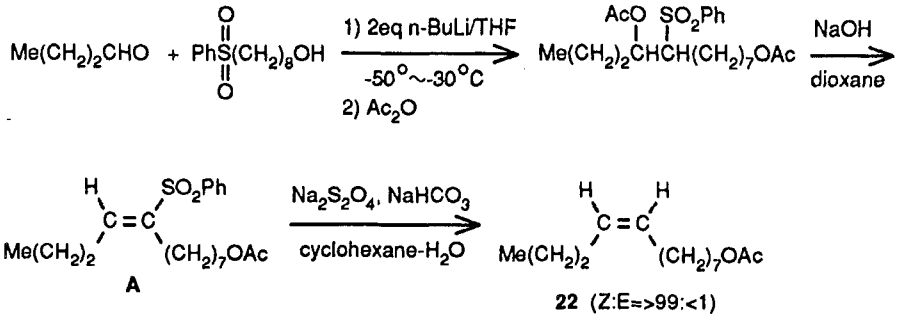
D. (Z)-8-Dodecenyl Acetate 22 ($C_{14}H_{26}O_2$)

This is the sex pheromone of the oriental fruit moth (*Grapholitha molesta*). Skattebøl employed 1,5,9-cyclododecatriene as the starting material for the synthesis of **22** (Scheme 49).[112]



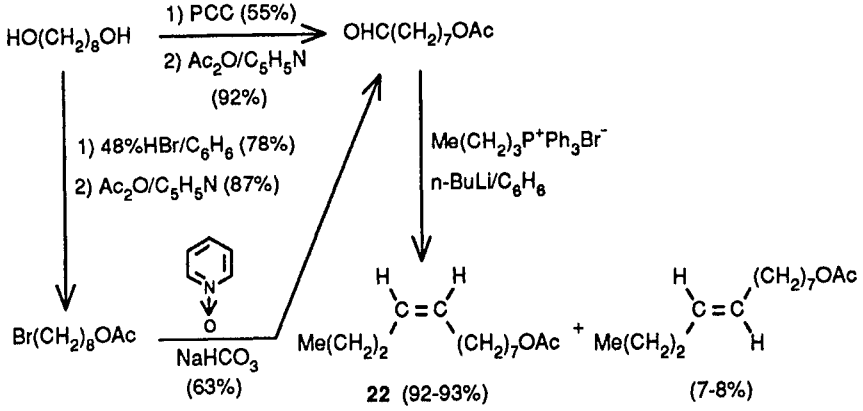
Scheme 49

Julia and Stacino synthesized **22** as shown in Scheme 50.[113] The notable step in this synthesis is the stereoselective hydrogenolysis of the sulfonyl group of **A**.



Scheme 50

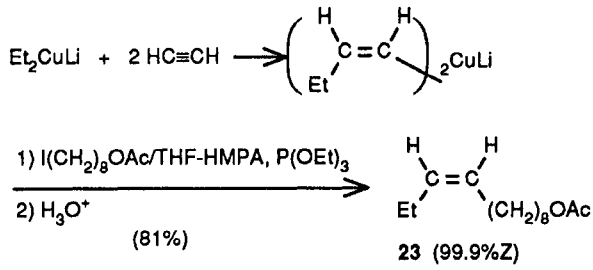
Kang et al. employed the Wittig chemistry as shown in Scheme 51 to prepare a 92–93 : 7–8 mixture of **22** and its (*E*)-isomer.[114] The mixture with this ratio was found to be quite attractive against the oriental fruit moth.



Scheme 51

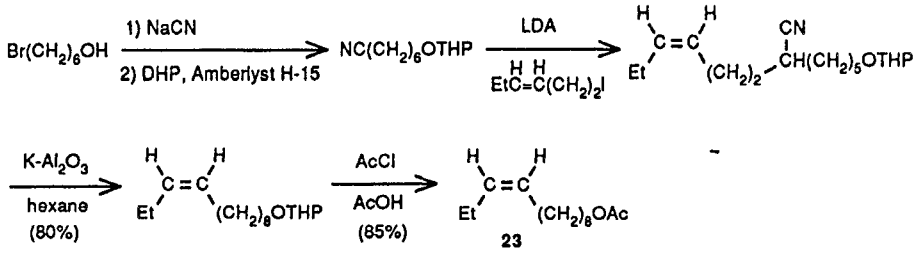
E. (Z)-9-Dodecenyl Acetate 23 ($C_{14}H_{26}O_2$)

The pheromone of the European grape berry moth (*Eupoecilia (Clysia) ambiguella*) is (*Z*)-9-dodecenyl acetate **23** of high purity, and even 1% of its (*E*)-isomer has an almost total inhibiting effect on its bioactivity. Normant and co-workers prepared pure **23** employing organocopper chemistry as shown in Scheme 52.[115]



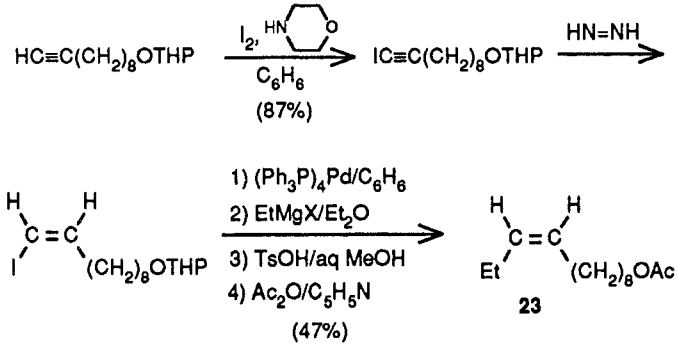
Scheme 52

The female-produced sex pheromone of the grape berry moth (*Paralobesia viteana*) is also **23.** Julia synthesized **23** by his sulfone method (cf. Scheme 50).[113] Reductive decyanation of alkyl nitriles with potassium on alumina (Scheme 53) was the key-step of Savoia's synthesis of **23.**[116] Michelot's syn-



Scheme 53

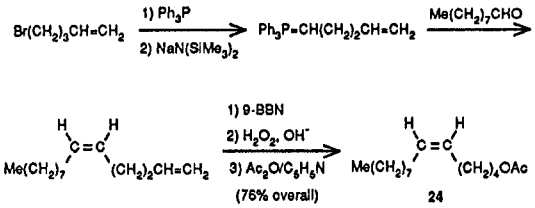
thesis of **23** employed tetrakis(triphenylphosphine) palladium as the catalyst for the cross-coupling (Scheme 54).[117]



Scheme 54

F. (Z)-5-Tetradecenyl Acetate 24 ($C_{16}H_{30}O_2$)

The heart and dart moth (*Scotia exclamationis*) employs a 95 : 5 mixture of (*Z*)-5-tetradecenyl acetate **24** and (*Z*)-9-tetradecenyl acetate **26** as its pheromone. Bestmann et al. synthesized **24** by a Wittig route (Scheme 55).[118] The New



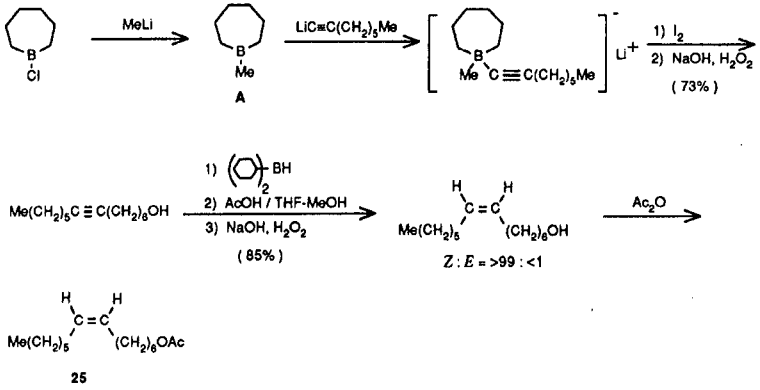
Scheme 55

Zealand leafroller moth (*Planotortrix excessana*) also uses a mixture of **24** and (Z)-7-tetradecenyl acetate **25** as the pheromone. Interestingly, the ratio of **24** to **25** was found to vary continuously from 3 : 97 to 71 : 29 in individual female moths in New Zealand.[119]

G. (Z)-7-Tetradecenyl Acetate 25 ($C_{16}H_{30}O_2$)

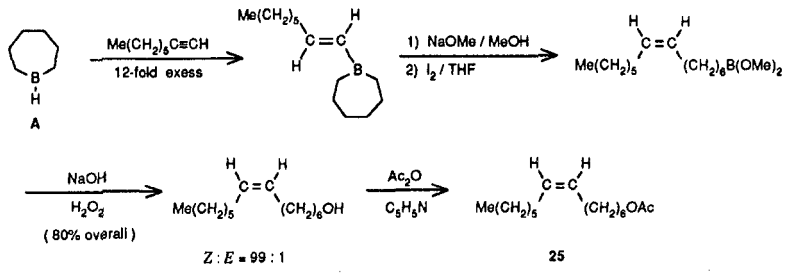
This is the pheromone of the spotted cutworm moth (*Amathes c-nigrum*). A full paper of its synthesis appeared (cf. Scheme 38, Ref. 1).[107]

A synthesis of (Z)-7-tetradecen-1-ol by means of organoborane chemistry via *B*-methylborepane **A** was reported by Brown et al. (Scheme 56).[120] The



Scheme 56

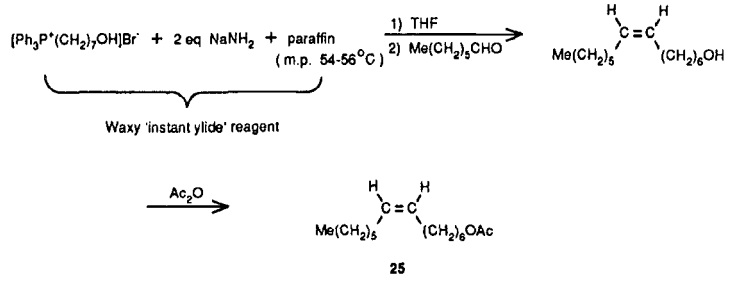
procedure used for the synthesis of (Z)-7-dodecenyl acetate **21** was also applied to prepare **25** (cf. Scheme 45).[109] In another borane-mediated synthesis of **25**, Brown employed borepane **A** as the starting material (Scheme 57).[76] The method



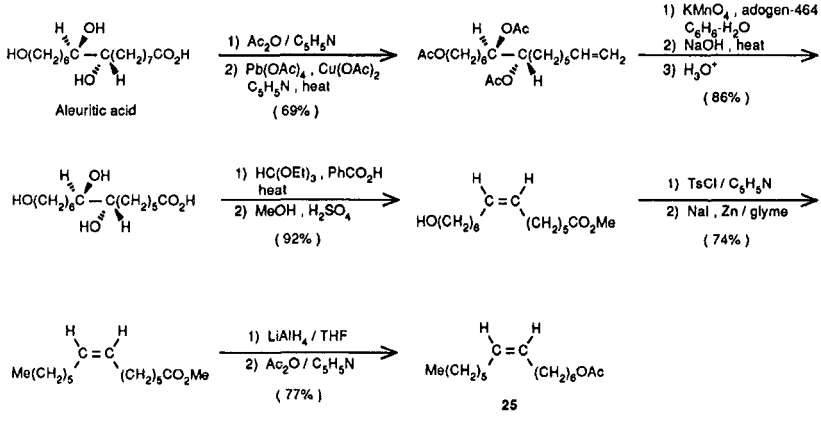
Scheme 57

used for the synthesis of (*Z*)-9-tricosene **19** (cf. Scheme 41) was also used for the synthesis of **25**.[98]

Schlosser's "instant ylide" was used to prepare **25** (Scheme 58).[121] Subramanian and Sharma converted aleuritic acid to **25** (Scheme 59).[122]



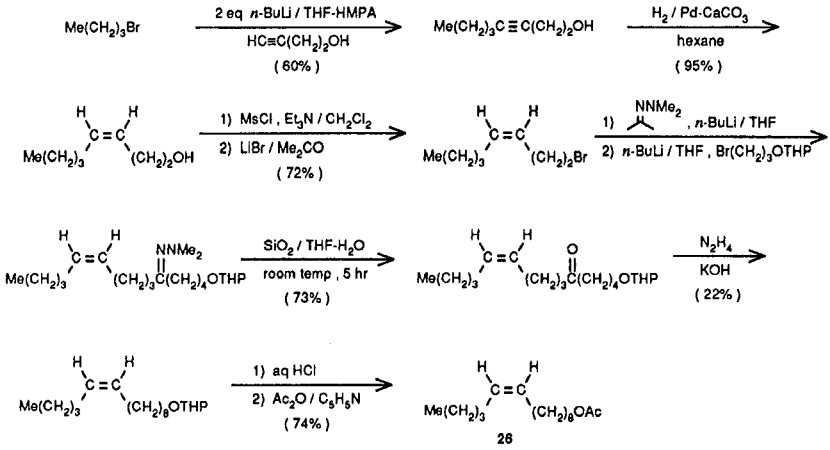
Scheme 58



Scheme 59

H. (Z)-9-Tetradecenyl Acetate **26** ($C_{16}H_{30}O_2$)

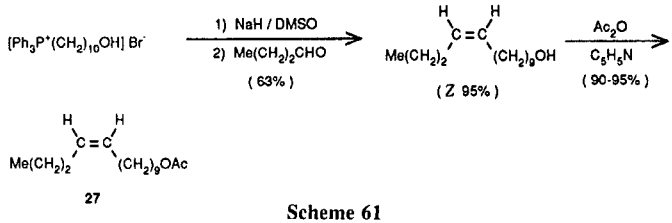
This is the pheromone of the fall armyworm (*Spodoptera frugiperda*), the smaller tea tortrix (*Adoxophyes fasciata*), and some other insects such as the summerfruit tortrix moth (*Adoxophyes orana*) and the heart and dart moth (*Scotia exclamationis*). Several syntheses of **26** were reported such as Bestmann's Wittig route,[118] Julia's sulfone route,[113] and Michelot's palladium-catalyzed coupling route.[117] An acetylenic route was also recorded by Kang.[114] Mitra and Reddy prepared **26** starting from acetone dimethylhydrazone (Scheme 60).[123]



Scheme 60

I. (Z)-10-Tetradecenyl Acetate **27** ($C_{16}H_{30}O_2$)

The sex pheromone of the apple leafminer moth (*Phyllonorycter ringoniella*) was suggested to be a mixture of **27** and (4*E*,10*Z*)-4,10-tetradecadienyl acetate.[124] Horiike et al. prepared **27** and related (Z)-alkenyl acetates by the Wittig reaction (Scheme 61).[125]



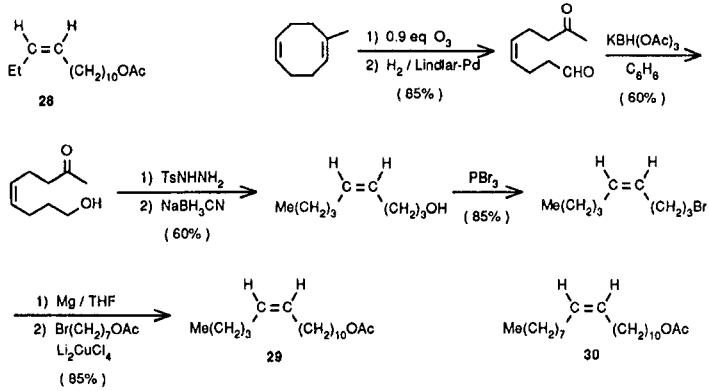
Scheme 61

J. (Z)-11-Tetradecenyl Acetate 28 ($C_{16}H_{30}O_2$)

This is the pheromone component of the oak leafroller moth (*Archips semiferanus*). This was synthesized by the palladium-catalyzed Grignard-coupling reaction according to Linstrumelle (cf. Scheme 23).[72] A synthesis via acetylenic route was also reported.[114]

K. (Z)-11-Hexadecenyl Acetate 29 ($C_{18}H_{34}O_2$)

This is the pheromone of the purple stem borer (*Sesamia inferens*), the diamond back moth (*Plutella xylostella*), and the cabbage moth (*Momestra brassicae*). Several syntheses of **29** were achieved by means of Wittig chemistry,[121] organoborane chemistry,[95,120] organotransition metal chemistry,[79] and acetylenic chemistry.[126] A synthesis of **29** was reported by Tolstikov et al. starting from 1-methyl-1,5-cyclooctadiene (Scheme 62).[127]



Scheme 62

L. (Z)-11-Icosenyl Acetate 30 ($C_{22}H_{42}O_2$)

This was identified as the aggregation pheromone in a fly (*Drosophila malerkotliana*). This was not attractive alone, but was synergistic with fermenting food or with acetone.[128]

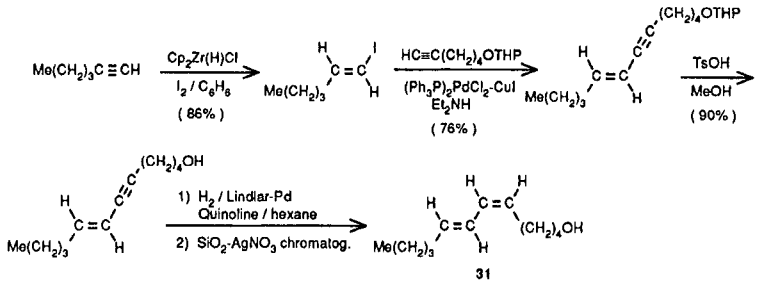
7. PHEROMONE ALCOHOLS AND ACETATES WITH A CONJUGATED DIENE AND CONJUGATED ENYNE SYSTEMS

Conjugated dien-1-ols and their acetates are frequently encountered among pheromones. Bestmann et al. reported a general synthesis of such conjugated

dienes with (*E*,*E*)-, (*Z*,*Z*)-, (*Z*,*E*)-, and (*E*,*Z*)- geometries essentially by means of Wittig chemistry.[129]

A. (5*Z*,7*E*)-5,7-Dodecadien-1-ol 31 ($C_{12}H_{22}O$)

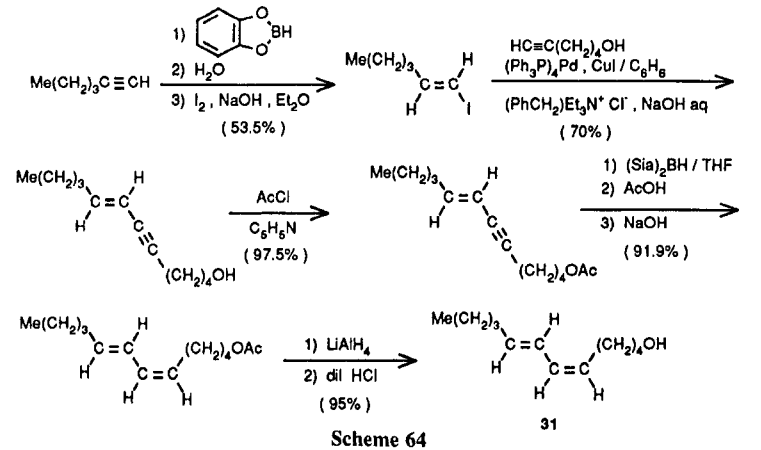
This is the female-produced pheromone of the pine moth (*Dendrolimus spectabilis*) and the forest tent caterpillar (*Malacosoma disstria*). The acetate of **31** is the pheromone of *D. punctatus*. A synthesis of **31** reported by Ando et al. utilized organozirconium chemistry to generate the (*E*)-double bond (Scheme 63).[130] The final semi-hydrogenation, however, was not sufficiently selective



Scheme 63

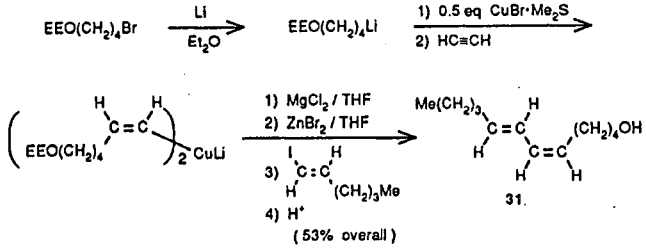
to give a mixture of the starting enyne (5%), the over-reduced monoenes (24%), and the desired diene (71%). These were separated by chromatography.

Rossi and Carpita synthesized **31** by the combination of organoborane chemistry and organopalladium chemistry (Scheme 64).[131] Application of organo-



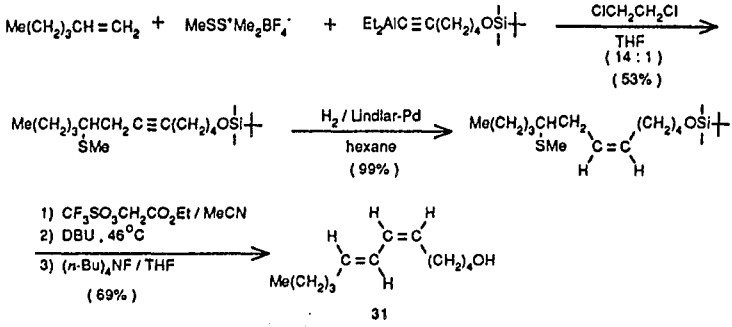
Scheme 64

copper chemistry by Normant et al. led to an efficient synthesis of **31** (Scheme 65).[132]



Scheme 65

A synthesis of **31** by Trost and Martin was an application of their alkynylsulfenylation reaction of olefins (Scheme 66).[133]

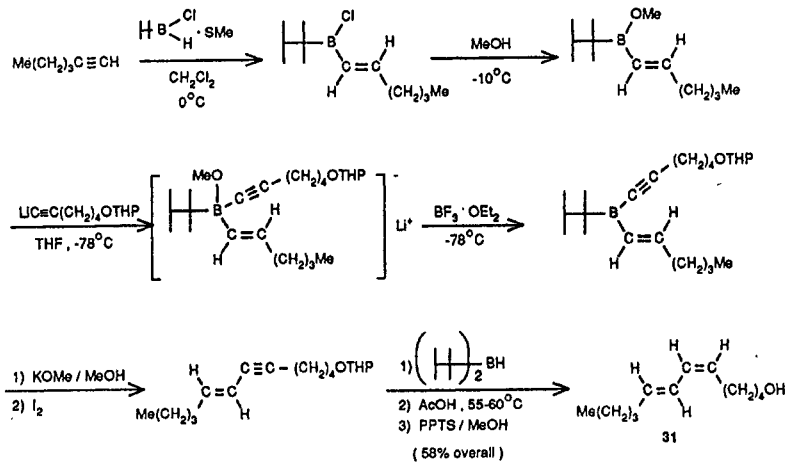


Scheme 66

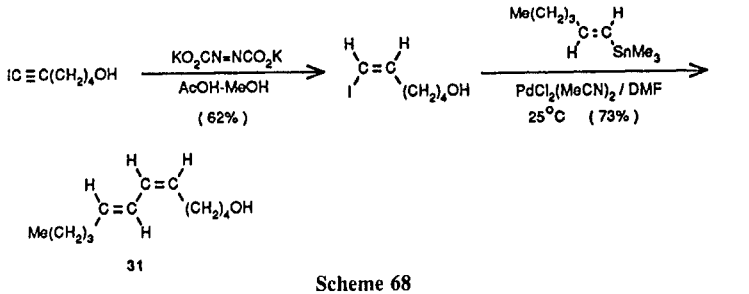
Organoborane chemistry as applied by Brown to the synthesis of **31** proved to be highly successful (Scheme 67).[134]

Stille and Groh prepared **31** by means of the palladium-catalyzed cross-coupling reaction of a vinyl iodide with a vinylstannane (Scheme 68).[135] Another synthesis of **31** by Stille and Simpson utilized a palladium-catalyzed coupling of vinyl iodides with acetylenic tin reagents (Scheme 69).[136]

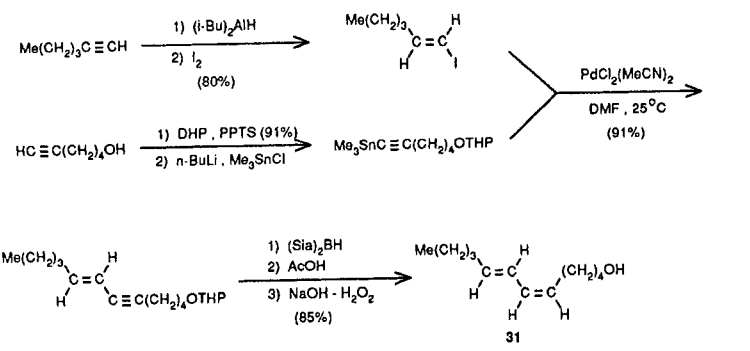
Scheme 70 illustrates Huang's synthesis of **31**.[137] This formylolefination of aldehydes by means of (formylmethyl)triphenylarsonium bromide in the presence of potassium carbonate gave (*E*)-α,β-unsaturated aldehydes (>98% E) in excellent yields.



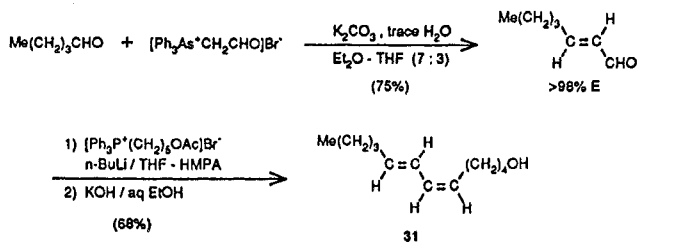
Scheme 67



Scheme 68

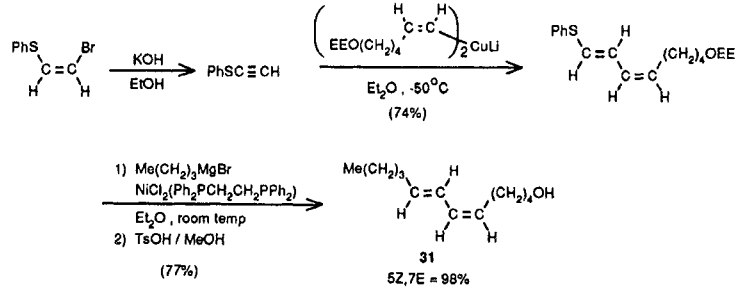


Scheme 69



Scheme 70

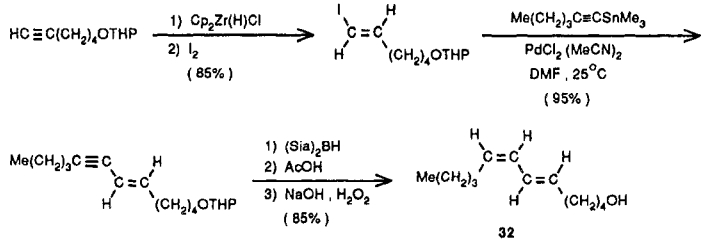
Recently Naso and co-workers published an efficient synthesis of **31** by combination of organocopper and organopalladium chemistries, starting from phenylthioacetylene (Scheme 71).[138]



Scheme 71

B. (5*E*,7*Z*)-5,7-Dodecadien-1-ol 32 ($C_{12}H_{22}O$)

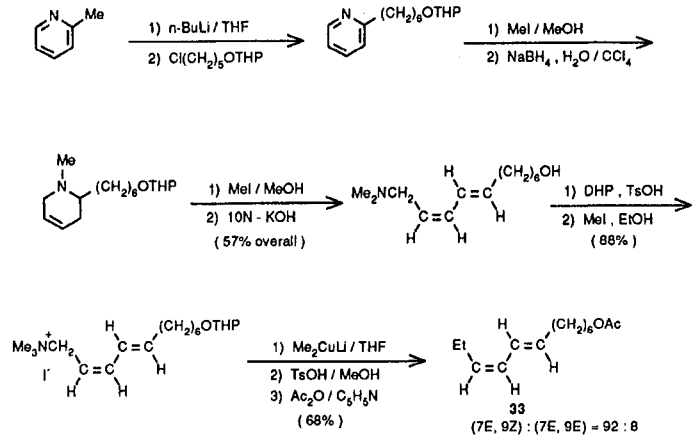
This is the pheromone of the pine moth (*Dendrolinus spectrobilis*). Stille's organotin chemistry with the aid of palladium catalysis yielded **32**, as shown in Scheme 72.[136]



Scheme 72

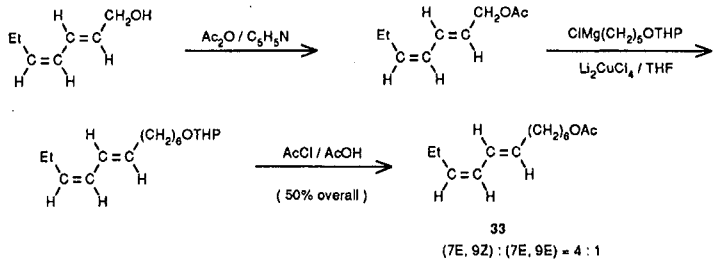
C. (7*E*,9*Z*)-7,9-Dodecadienyl Acetate **33** ($C_{14}H_{24}O_2$)

This is the sex pheromone of the grape vine moth (*Lobesia botrana*). Langlois's synthesis of **33** started from 2-picoline (Scheme 73).[139]



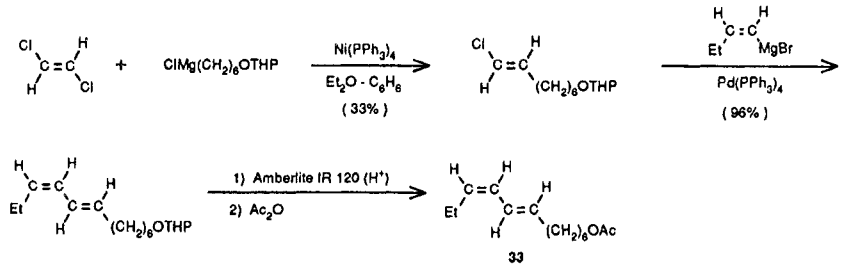
Scheme 73

A Grignard coupling reaction was employed for the synthesis of **33** (Scheme 74).[140] Preparation of (2*E*,4*Z*)-2,4-heptadien-1-ol, the starting material, had previously been reported.[141]



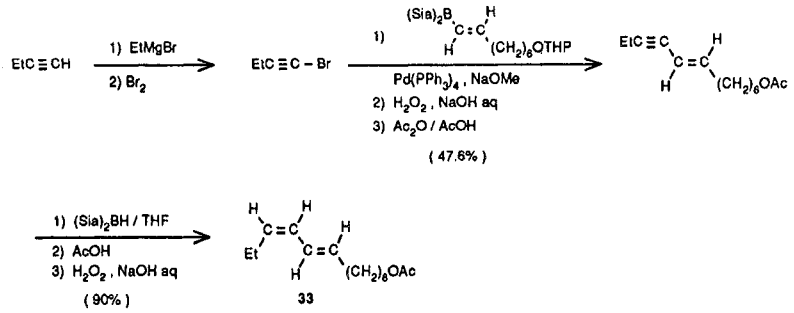
Scheme 74

Linstrumelle prepared **33** by nickel- and palladium-catalyzed coupling reactions of Grignard reagents with vinyl chlorides (Scheme 75).[142]



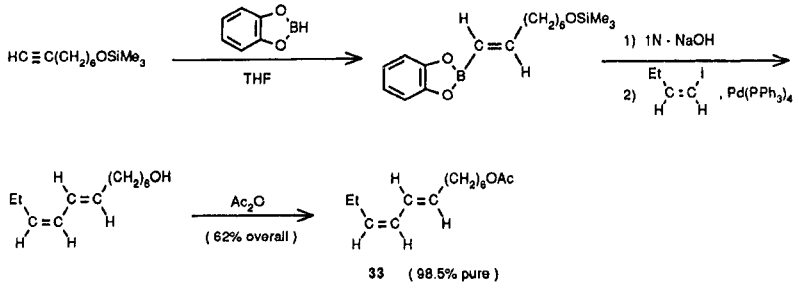
Scheme 75

Rossi et al. employed the palladium-catalyzed coupling reaction of 1-alkenylborane with 1-bromoalkyne in their synthesis of **33** (Scheme 76).[143]



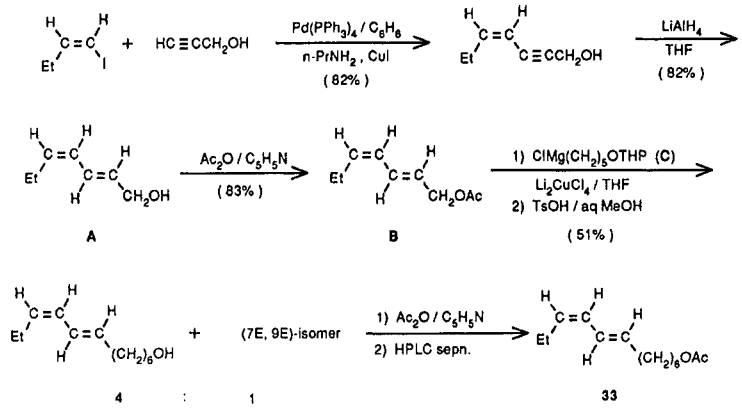
Scheme 76

A similar palladium-catalyzed coupling reaction of 1-alkenylborane with (*Z*)-1-iodo-1-butene was used by Cassani et al. to prepare **33** (Scheme 77).[144]



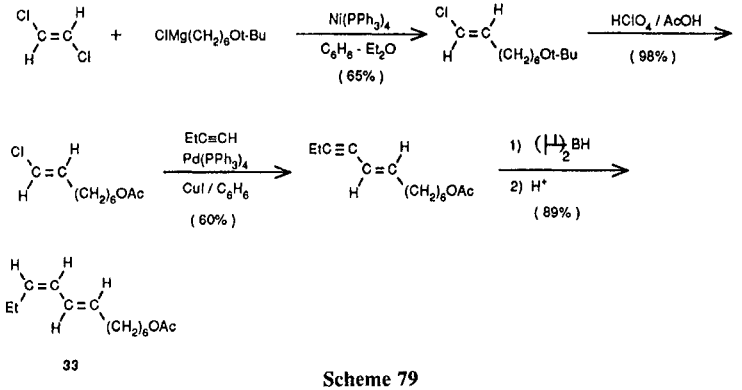
Scheme 77

Descoins et al. reported two syntheses of **33** employing organotransition metal chemistry.[145] In their first synthesis, coupling of (Z)-1-iodo-1-butene and propargyl alcohol was followed by reduction to selectively give **A** (Scheme 78).[145] However, the Grignard coupling of **B** and **C** caused isomerization at C_9.



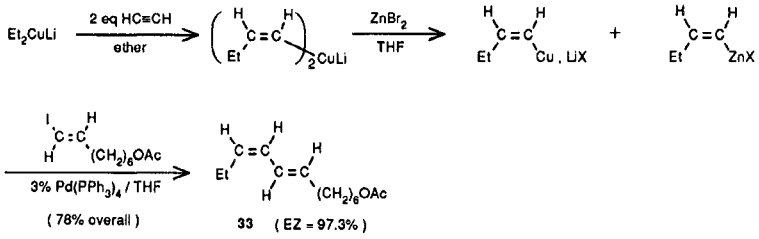
Scheme 78

The product was a 4 : 1 mixture of **33** and its (7*E*,9*E*)-isomer, which had to be separated by preparative HPLC. The second route (Scheme 79) was more selective than the first.[145]

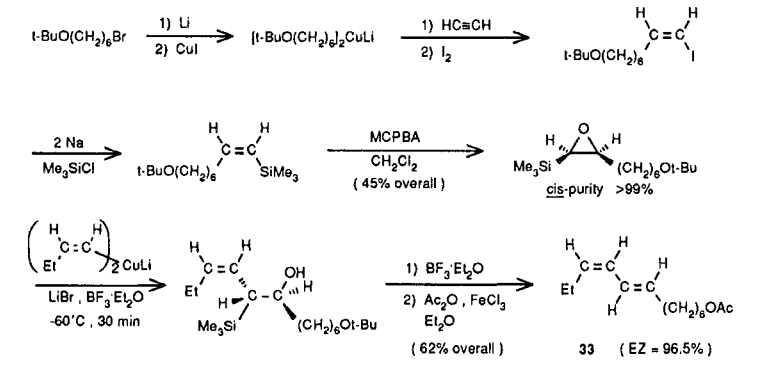


Scheme 79

Normant's organocopper chemistry was used for the synthesis of **33** and proved to be quite efficient (Scheme 80).[132] Alexakis and Jachiet also employed organocopper chemistry to prepare **33** (Scheme 81).[146,147] Alexakis developed

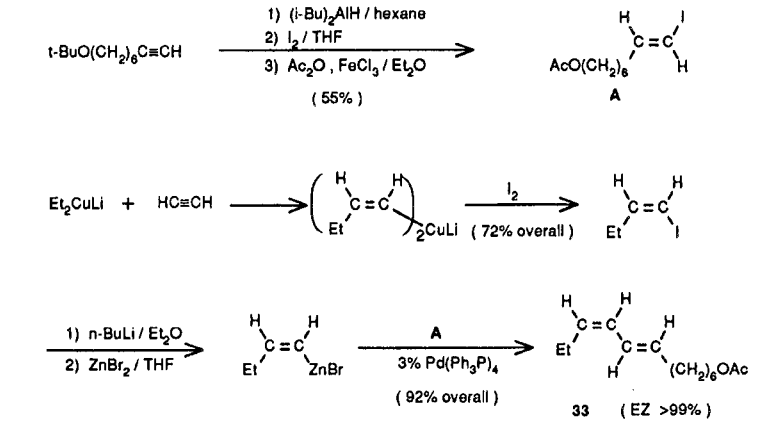


Scheme 80

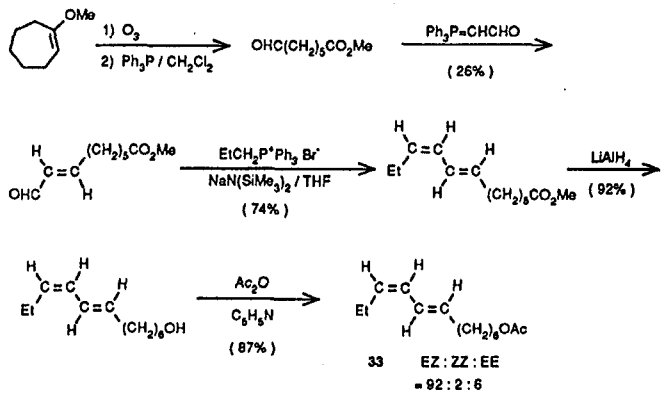


Scheme 81

a new method for the preparation of ω-hydroxyalkenyl iodides via hydroalumination-iodination of ω-*t*-butoxyalkynes, and used the method for the synthesis of **33** (Scheme 82).[148]

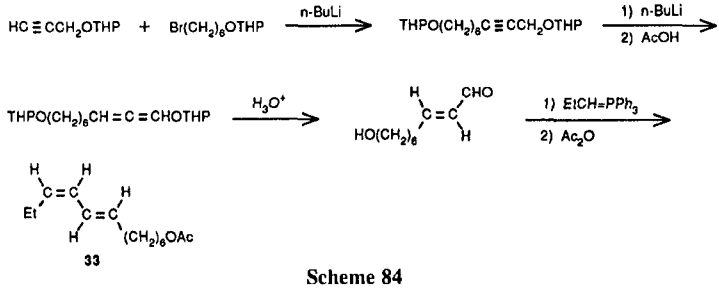


Scheme 82



Scheme 83

Bestmann et al. synthesized **33** by Wittig chemistry (Scheme 83).[149] A synthesis of **33** by a Wittig route was also reported in connection with the effect of isomeric purity on pheromone activity (Scheme 84).[150] A combination of ace-

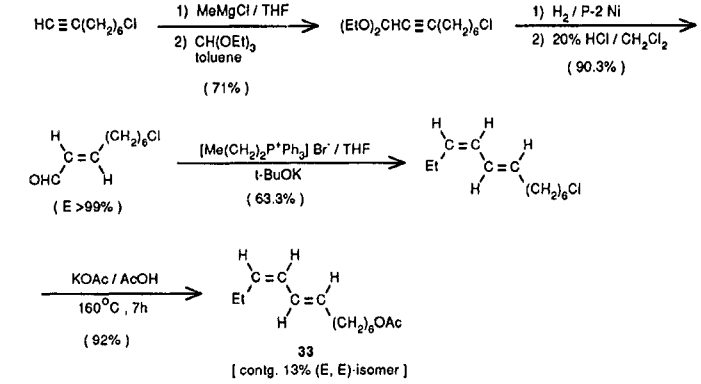


Scheme 84

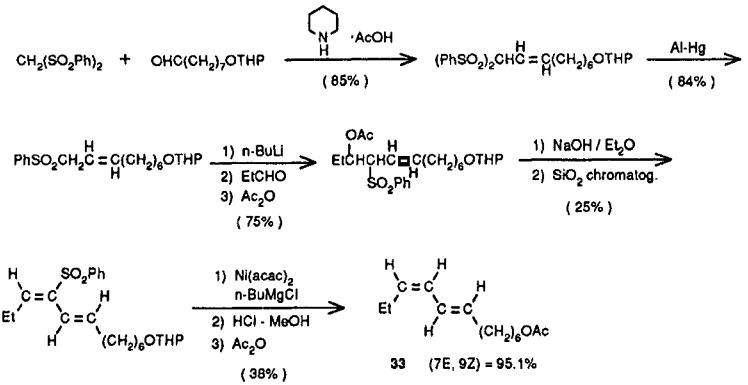
tylenic and Wittig chemistries allowed a large-scale preparation of **33** (Scheme 85).[151]

Julia's sulfone chemistry was applied to the synthesis of **33,** although the overall yield was modest (Scheme 86).[152] Phenylthioacetylene was found to be a good starting material for the synthesis of **33** (Scheme 87).[138]

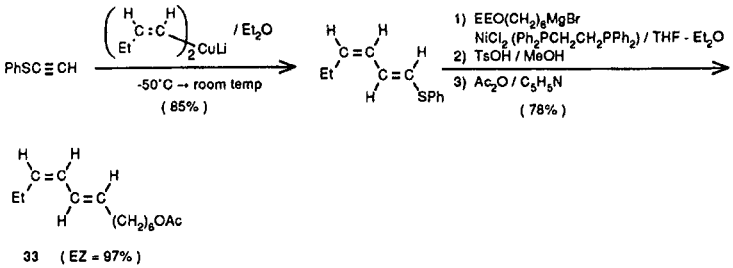
The ultraviolet absorber, 2-hydroxy-4-methoxybenzophenone, and the antioxidants, BHT and BHA, were found to be effective in solution as the chemical protectors of pheromones with the conjugated double-bond system from isomerization and oxidation.[153]



Scheme 85



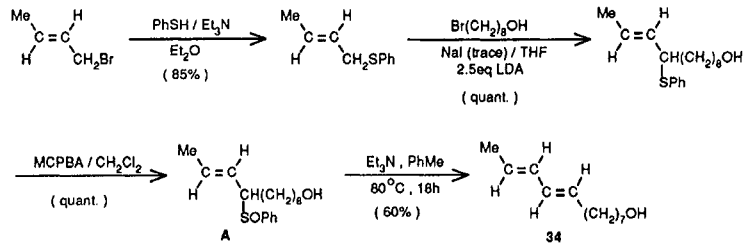
Scheme 86



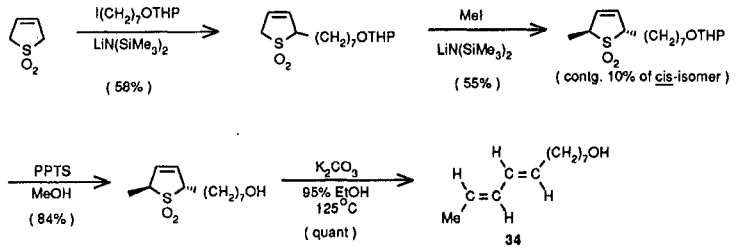
Scheme 87

D. (8*E*,10*E*)-8,10-Dodecadien-1-ol 34 ($C_{12}H_{22}O$)

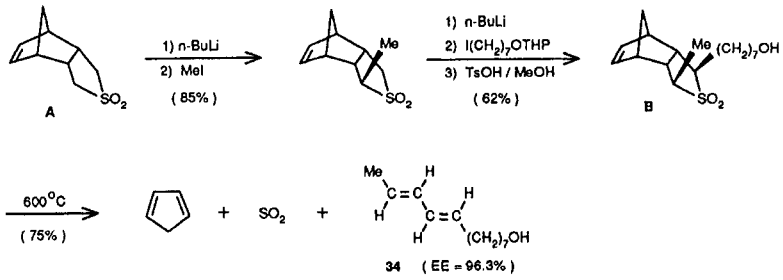
This is the sex pheromone of codling moth (*Laspeyresia pomonella*). Organosulfur chemistry was utilized for the synthesis of **34** by four groups. Thermolysis of allylic sulfoxide **A** to **34** was reported by Babler and Haack (Scheme 88).[154] Alkylation of 3-sulfolenes was the key reaction in Yamada's synthesis of **34** (Scheme 89).[155,156] Double alkylation of sulfone **A** to give **B** was followed by its thermolysis to give **34** (Scheme 90).[157] Julia used his sulfone chemistry for the synthesis of **34** (Scheme 91).[158]



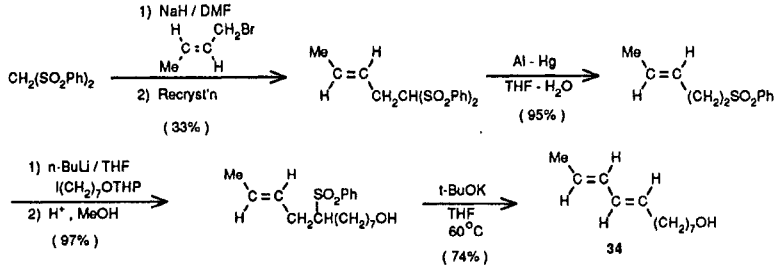
Scheme 88



Scheme 89

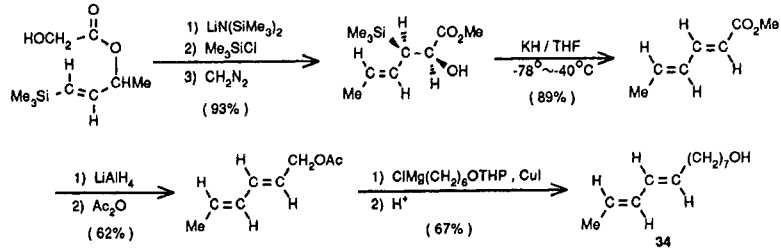


Scheme 90



Scheme 91

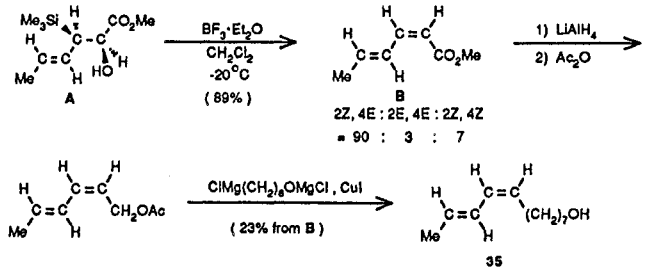
Sato et al. synthesized **34** employing the ester enolate Claisen rearrangement of (*E*)-1-methyl-3-trimethylsilyl-2-propenyl glycolate followed by the Peterson reaction (Scheme 92).[159]



Scheme 92

E. (8*Z*,10*E*)-8,10-Dodecadien-1-ol 35 ($C_{12}H_{22}O$)

Hedya ochroleucana employs this dienol **35** as its pheromone. A synthesis of **35** by Sato et al. started from **A** (Scheme 93), which was prepared as shown in



Scheme 93

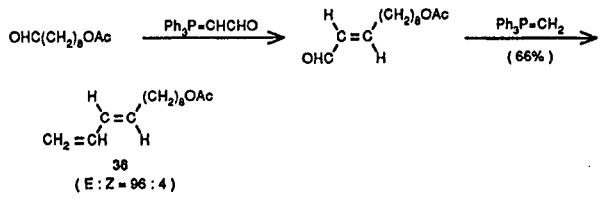
Scheme 92.[159] The selectivity to generate (2Z,4E)-**B,** however, was not satisfactory.

A synthesis of (8Z,10Z)-8,10-dodecadienyl acetate by palladium-catalyzed coupling of an organozinc compound and 1-iodo-1-alkene was reported by Björkling et al.[160]

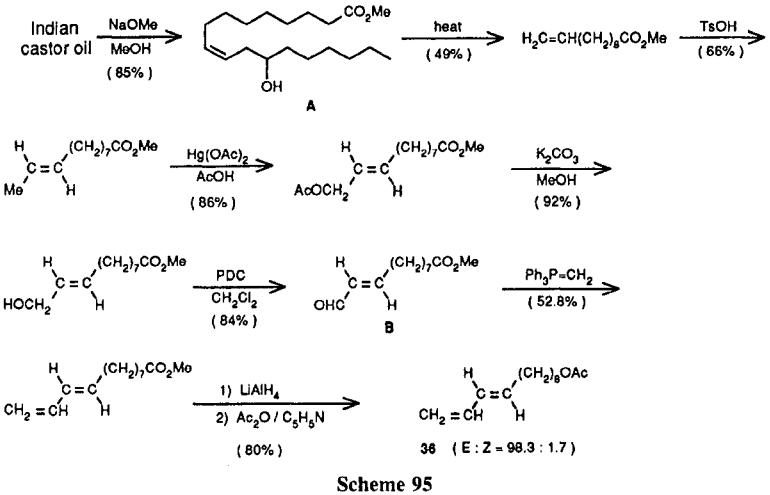
F. (*E*)-9,11-Dodecadienyl Acetate 36 ($C_{14}H_{24}O_2$)

The female-produced sex pheromone of the red-bollworm moth (*Diparopsis castanea*) is a mixture of 9,11-dodecadienyl acetate (*E*:*Z* = 80:20), (*E*)-9-dodecenyl acetate, 11-dodecenyl acetate, and dodecyl acetate.

Two syntheses of **36** were based on Wittig chemistry. Bestmann et al. prepared **36** as shown in Scheme 94.[149] Ranganathan et al. synthesized **36** starting from Indian castor oil (Scheme 95).[161] Methyl ricinoleate **A,** prepared from



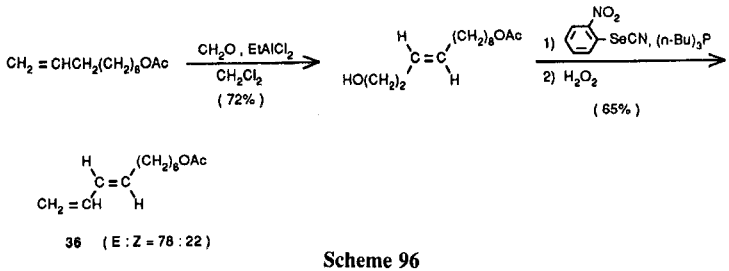
Scheme 94



Scheme 95

castor oil, was converted to the key-intermediate **B**,[cf. 162] and then to the pheromone **36** in 11.6% overall yield from castor oil.[161]

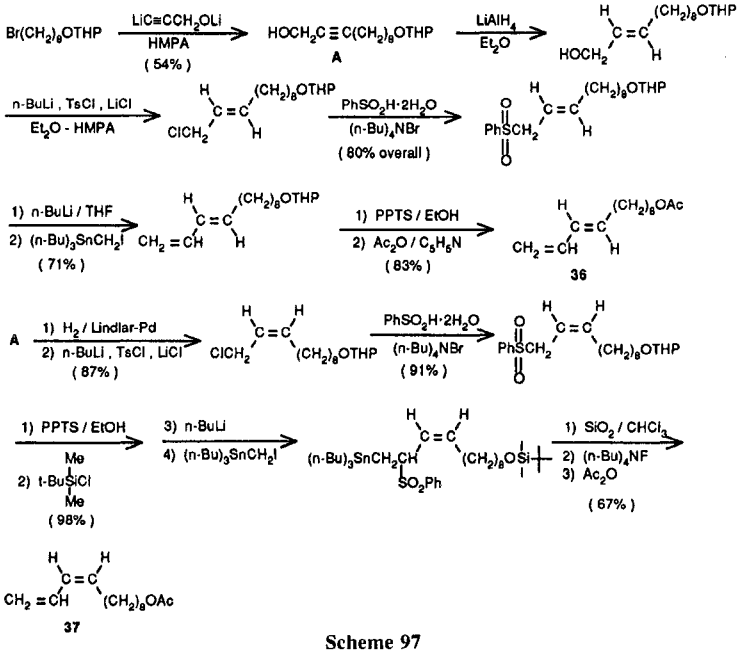
Snider and Phillips used an ethylaluminum dichloride-catalyzed ene reaction of formaldehyde with 10-undecenyl acetate for the synthesis of **36** (Scheme 96).[163]



Scheme 96

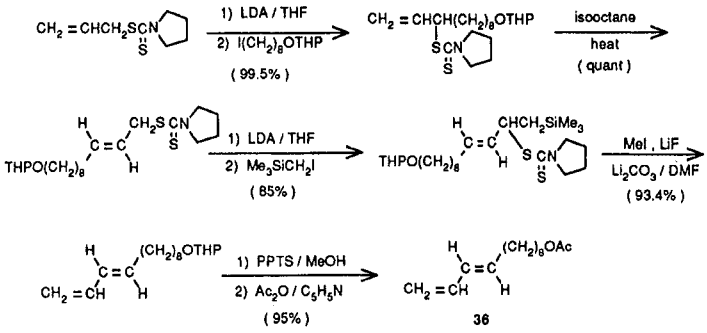
Several syntheses of **36** were based on sulfur chemistry as follows. A synthesis of **36** was accomplished in 44% overall yield from 3-sulfolene in the same manner as for the synthesis of **34** (cf. Scheme 89).[155,156]

Ochiai et al. synthesized both (*E*)- and (*Z*)-9,11-dodecadienyl acetates via phenylsulfones by lengthy routes (Scheme 97).[164]



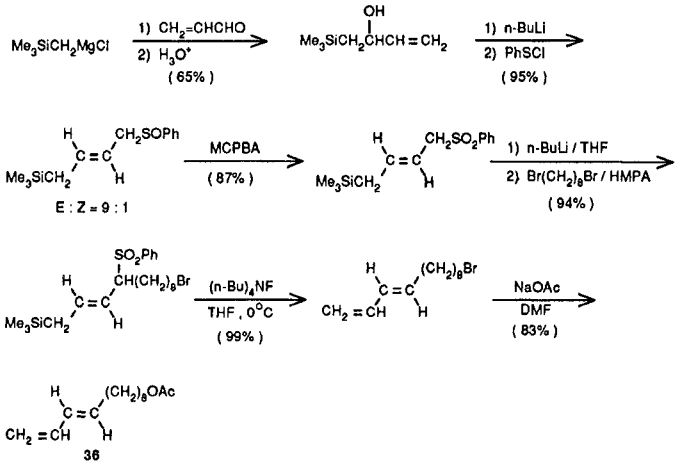
Scheme 97

Hayashi et al. prepared pure **36** starting from allyl dithiocarbamate (Scheme 98).[165]



Scheme 98

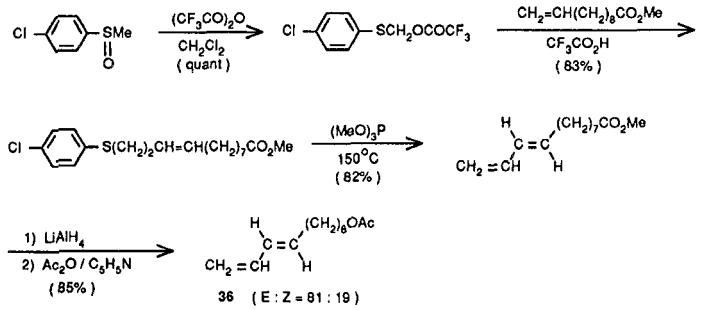
Schechter employed (*E*)-1-benzenesulfonyl-4-trimethylsilyl-2-butene for the construction of the (*E*)-1,3-butadienyl part of **36** (Scheme 99).[166]



Scheme 99

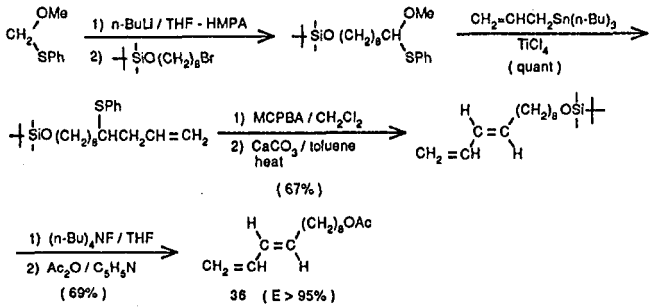
The "ene" reaction of methyl 10-undecenoate with *p*-chlorophenylthiomethyl trifluoroacetate was the key-step in Ishibashi's synthesis of **36** (Scheme 100).[167]

Julia's sulfone chemistry (Scheme 91) was also used for the synthesis of (*E*)-9,11-dodecadien-1-ol.[158]



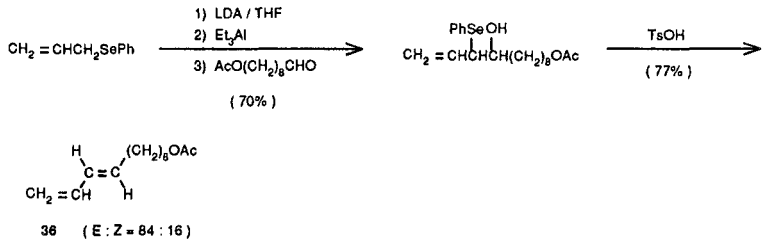
Scheme 100

Otera and his co-workers synthesized **36** employing methoxy(phenylthio)methane as the initial building block (Scheme 101).[168]



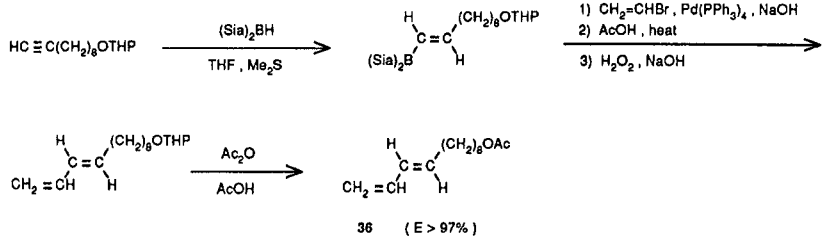
Scheme 101

Organoselenium intermediates were used by Yamamoto et al. to prepare **36** (Scheme 102).[169]



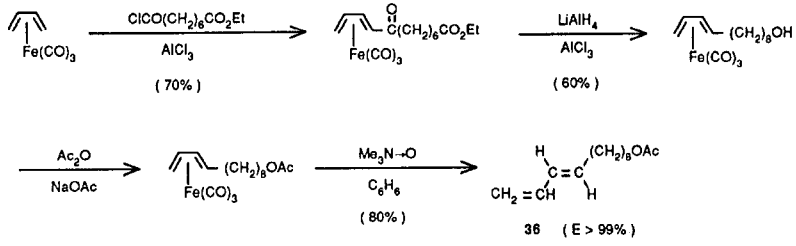
Scheme 102

Rossi et al. reported a palladium-catalyzed synthesis of (*E*)-**36** (Scheme 103).[143] Diene-iron carbonyl complex was used for the synthesis of **36** by Knox



Scheme 103

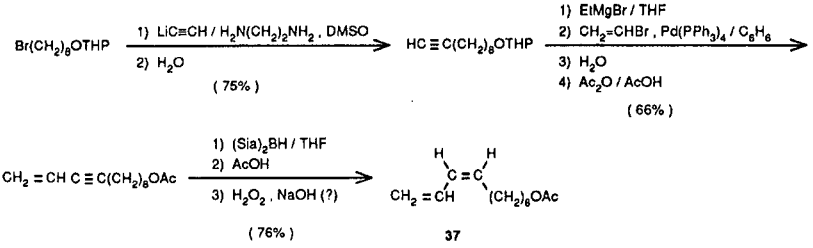
and Thom (Scheme 104).[170] Several other pheromones such as **35** were also synthesized by this method.



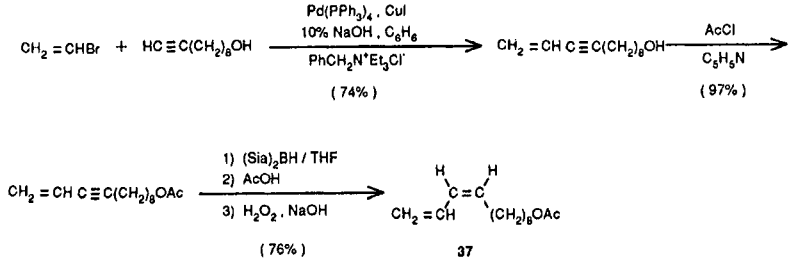
Scheme 104

G. (Z)-9,11-Dodecadienyl Acetate 37 ($C_{14}H_{24}O_2$)

Ochiai et al. prepared **37** by means of organosulfur chemistry (Scheme 97).[164] Palladium-catalyzed reactions were used by Rossi et al. for the synthesis of **37** (Scheme 105[171] and Scheme 106[172]). Michelot also prepared **37** by a similar coupling reaction.[117]



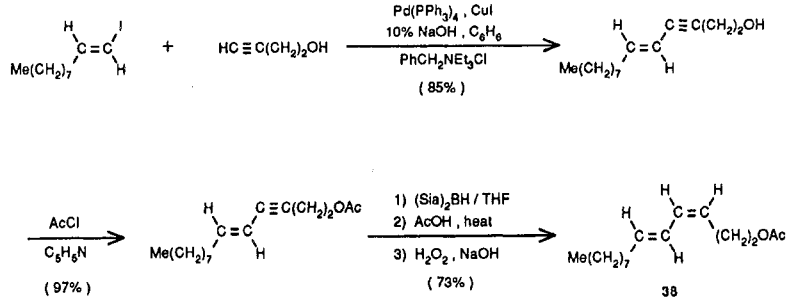
Scheme 105



Scheme 106

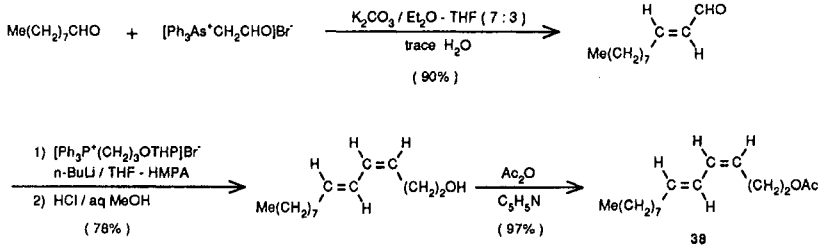
H. (3*Z*,5*E*)-3,5-Tetradecadienyl Acetate **38** ($C_{16}H_{28}O_2$)

This is the sex pheromone of the carpenter worm moth (*Prinoxystus robiniae*). Rossi et al. synthesized **38** by a palladium-catalyzed reaction (Scheme 107).[172]



Scheme 107

By employing their stereoselective formylolefination method with triphenylarsonium ylide, Huang et al. synthesized **38** (Scheme 108).[137] Preparation of

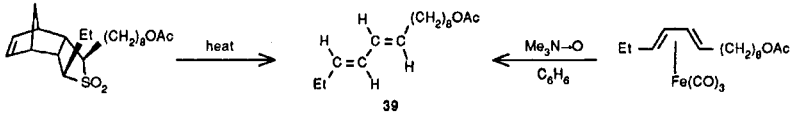


Scheme 108

(3Z,5Z)-5-fluoro-3,5-tetradecadienyl acetate, which enhances the pheromone activity of **38**, was reported by Camps et al.[173,174]

I. (9*E*,11*E*)-9,11-Tetradecadienyl Acetate 39 ($C_{16}H_{28}O_2$)

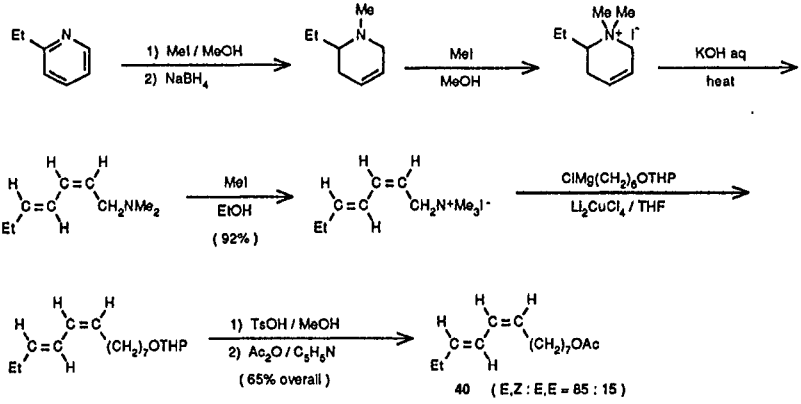
The light-brown apple moth (*Epiphyas postwittana*) uses **39** as its pheromone component. This was synthesized by the sulfone alkylation-thermolysis route (Scheme 109),[157] and also by employing a 1,3-diene-iron carbonyl complex (Scheme 109).[170]



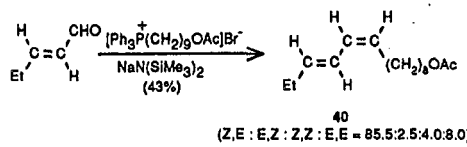
Scheme 109

J. (9Z,11*E*)-9,11-Tetradecadienyl Acetate 40 ($C_{16}H_{28}O_2$)

This is the pheromone of the cotton leafworm (*Spodoptera litura*) and the Egyptian cotton leafworm (*S. littoralis*). Langlois's synthesis of 85% pure **40** started from 2-ethylpyridine (Scheme 110).[175] Bestmann's Wittig chemistry also led to the preparation of 85% pure **40** (Scheme 111).[149]

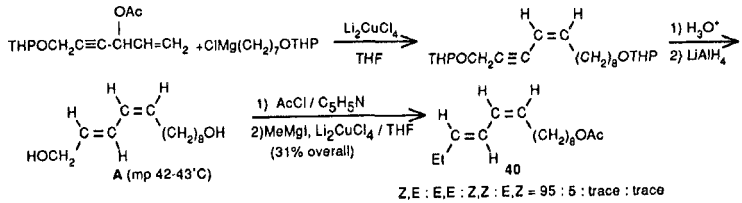


Scheme 110



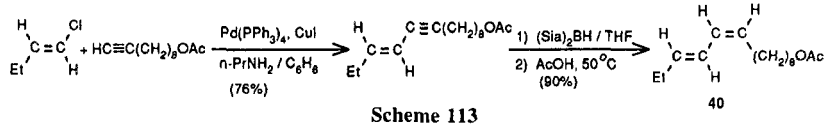
Scheme 111

In the synthesis of **40** by Cassani et al., the intermediate **A** could be purified by recrystallization, and 95% pure **40** could be prepared (Scheme 112).[140]

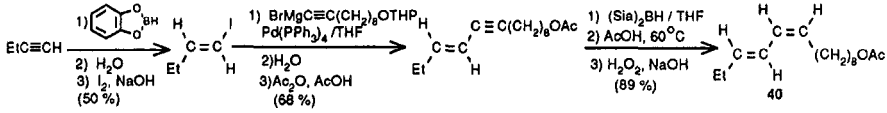


Scheme 112

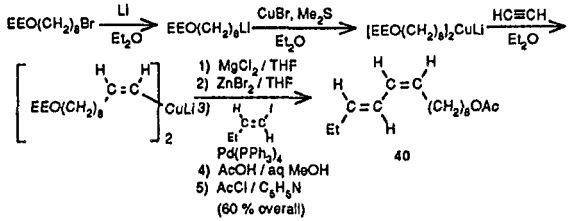
Palladium-catalyzed syntheses of **40** were reported by Linstrumelle (Scheme 113),[176] Rossi (Scheme 114),[143] Normant (Scheme 115),[132] and Norin (Scheme 116).[177]



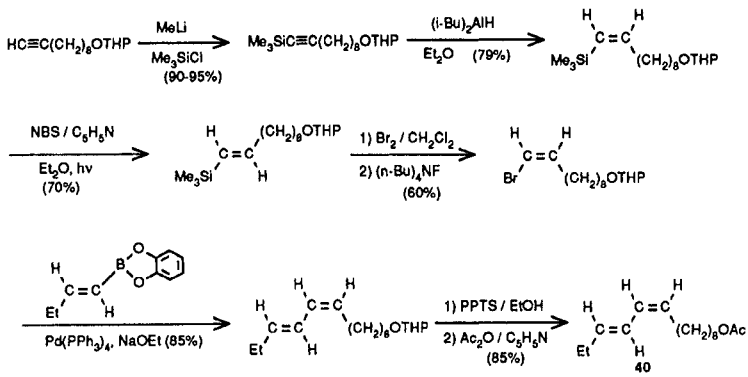
Scheme 113



Scheme 114

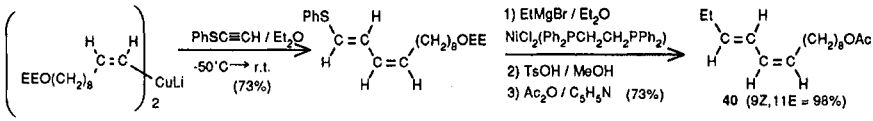


Scheme 115



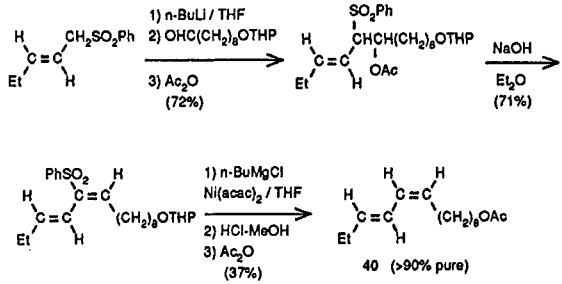
Scheme 116

A nickel-catalyzed reaction was used by Naso and his co-workers for the synthesis of **40** (Scheme 117).[138]

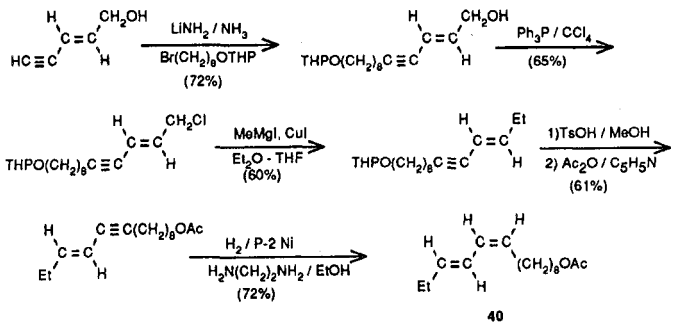


Scheme 117

Julia's synthesis of **40** was based on his sulfone chemistry (Scheme 118).[152,178] Yadav et al. prepared **40** via an acetylenic route (Scheme 119).[179]



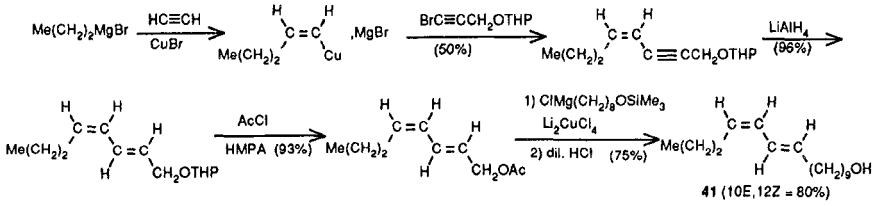
Scheme 118



Scheme 119

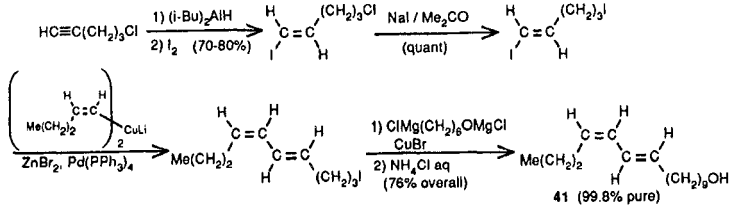
K. Bombykol [(10*E*,12*Z*)-10,12-Hexadecadien-1-ol] 41 ($C_{16}H_{30}O$)

This is the well-known sex pheromone of the silkworm moth (*Bombyx mori*). Normant reported an organocopper-based synthesis of **41** (Scheme 120).[180] The

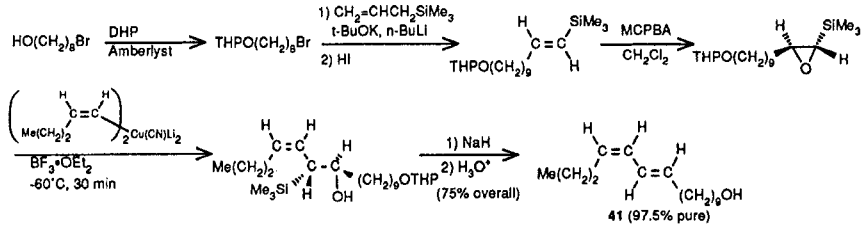


Scheme 120

second organocopper-based synthesis with concomitant use of palladium-catalysis was also reported by Normant (Scheme 121).[132] The third organocopper-

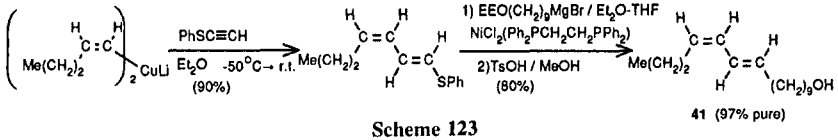


Scheme 121



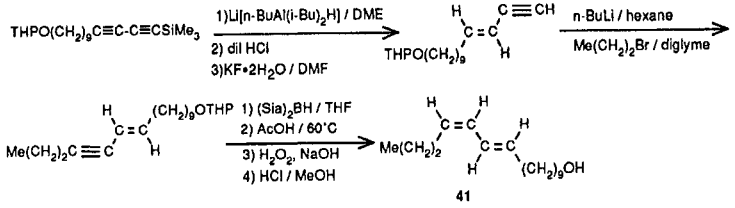
Scheme 122

based synthesis was reported by Alexakis and Jachiet (Scheme 122).[146,147] Naso's combination of organocopper and organotransition metal chemistries resulted in an efficient synthesis of **41** (Scheme 123).[138]



Scheme 123

Hydroalumination of 1-(trimethylsilyl)-1,3-diyne was employed to construct the (*E*)-olefinic system of **41** (Scheme 124).[181]

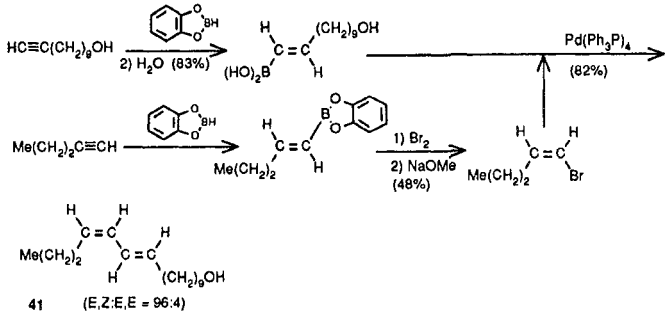


Scheme 124

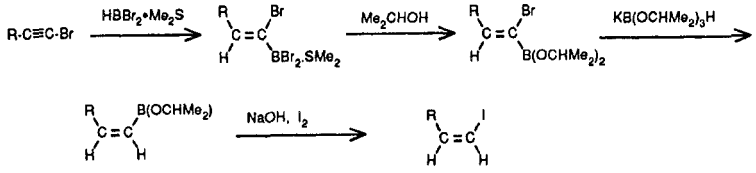
Bombykol (**41**) was also synthesized by means of organoborane chemistry. Suzuki and his co-workers used their palladium-catalyzed cross-coupling reaction between alkenylboranes and 1-bromoalkene to prepare **41** (Scheme 125).[182,183] (*Z*)-1-Iodo-1-alkenes can be conveniently prepared as shown in Scheme 126.[184] (*Z*)-1-Iodo-1-pentene can be a precursor to **41.** Bombykol (**41**) could be prepared by a palladium-catalyzed cross-coupling reaction between an alkenylboronate and 1-iodo-1-alkene (Scheme 127).[185]

Trost's palladium-catalyzed decarboxylative elimination reaction yielded bombykol of about 90% purity (Scheme 128).[186]

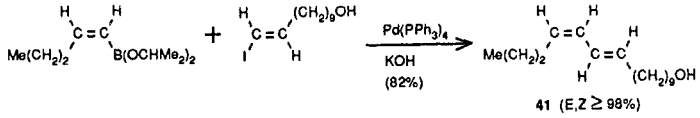
Ishibashi's "ene"-type reaction previously yielded a thioether **A** (Scheme 129; cf. Scheme 100), which was converted to **41.**[187]



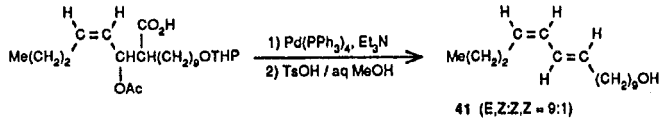
Scheme 125



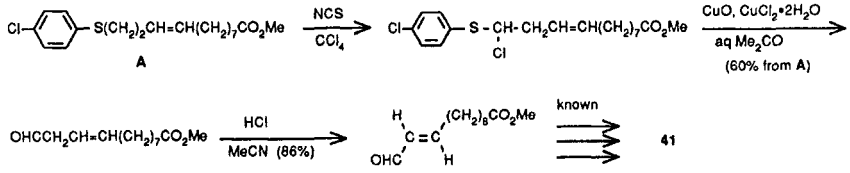
Scheme 126



Scheme 127

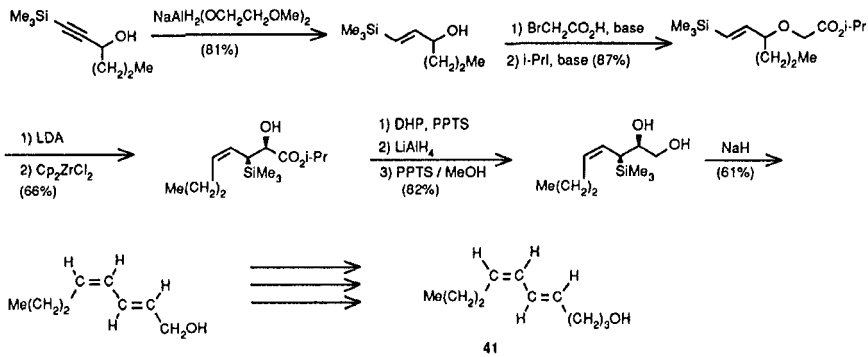


Scheme 128



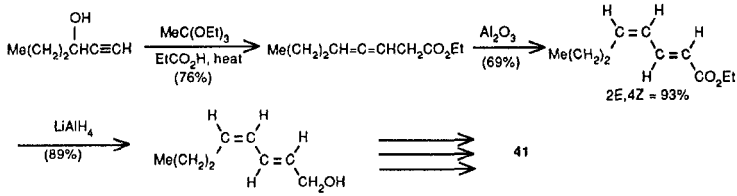
Scheme 129

A combination of zirconium-mediated [2,3] Wittig rearrangement and Peterson reaction allowed Kuroda et al. to prepare the key (*E*,*Z*)-diene system of **41** (Scheme 130).[188]



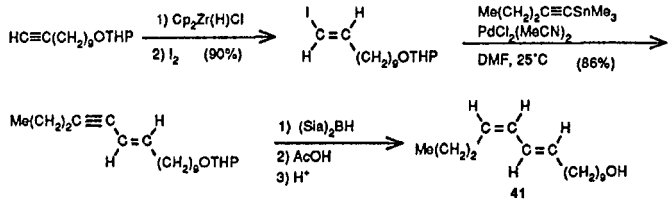
Scheme 130

Tsuboi et al. discovered a rearrangement of allenic esters to (2*E*,4*Z*)-dienoic esters with alumina catalyst, and used that reaction for the synthesis of the (*E*,*Z*)-diene portion of **41** (Scheme 131).[189,190]



Scheme 131

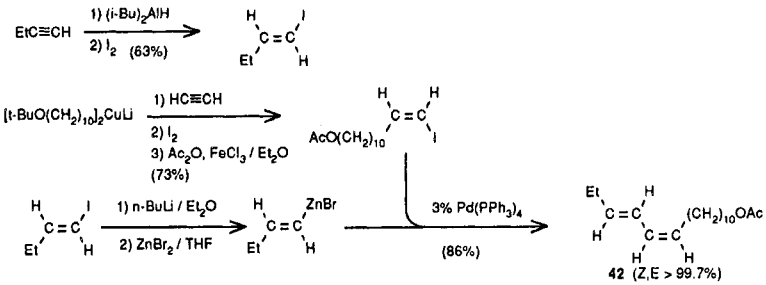
A synthesis reported by Stille and Simpson employed their palladium-catalyzed reaction of a vinyl iodide with an acetylenic tin reagent (Scheme 132).[191]



Scheme 132

L. (11Z,13E)-11,13-Hexadecadienyl Acetate 42 ($C_{18}H_{32}O_2$)

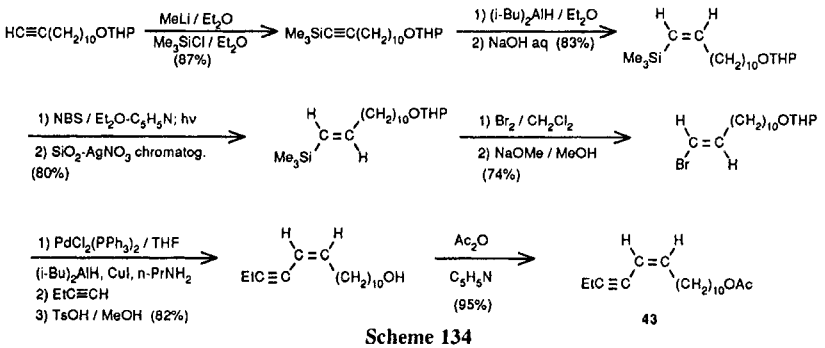
This is a potent pheromone component in some processionary moth species. Alexakis and Duffault synthesized **42** by coupling (*E*)-1-butenylzinc bromide with a (*Z*)-1-iodo-1-alkene (Scheme 133).[148]



Scheme 133

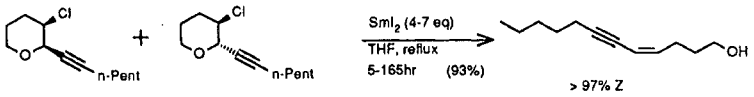
M. (Z)-11-Hexadecen-13-ynyl Acetate 43 ($C_{18}H_{30}O_2$)

This is a plausible component of the sex pheromone of the oak processionary moth (*Thaumetopoea processionea*). Camps et al. reported a synthesis of **43** by means of organopalladium chemistry (Scheme 134).[192] A new method to con-



Scheme 134

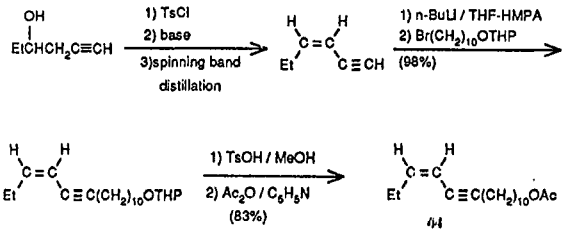
struct the (*Z*)-1-en-3-yne system of **43** by ring cleavage of a β-halogeno ether with samarium iodide was reported by Crombie and Rainbow (Scheme 135).[193]



Scheme 135

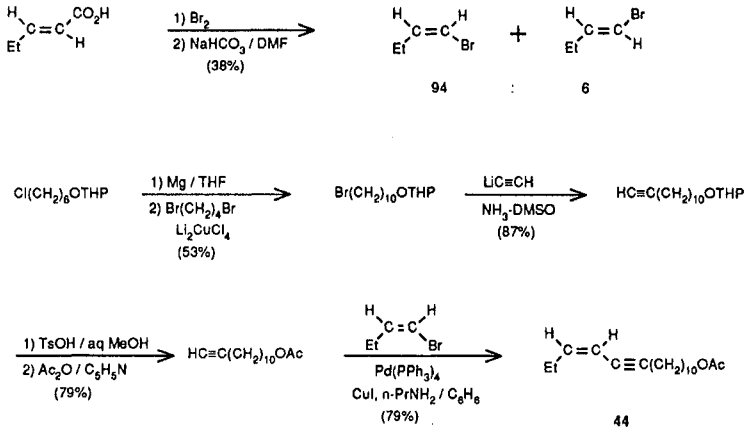
N. (Z)-13-Hexadecen-11-ynyl Acetate 44 ($C_{18}H_{30}O_2$)

This is the female-produced sex pheromone of the processionary moth (*Thaumetopoea pityocampa*), a major defoliator of pine trees in Mediterranean countries. The first synthesis of **44** was achieved by Camps et al. as shown in Scheme 136.[194]

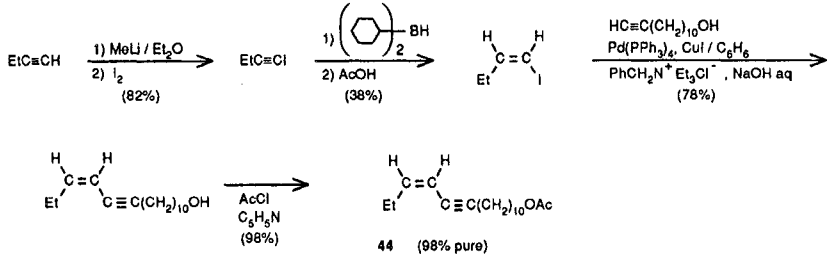


Scheme 136

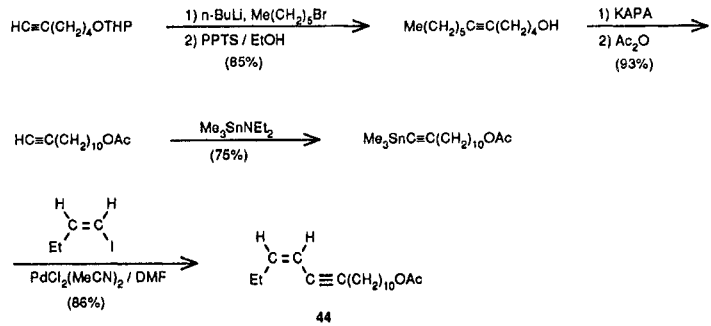
Michelot et al. reported a palladium-catalyzed synthesis of **44** (Scheme 137).[195] Scheme 138 illustrates the second palladium-mediated synthesis by Rossi and Carpita.[196] Stille's third palladium-mediated synthesis utilized an organotin intermediate (Scheme 139).[191]



Scheme 137

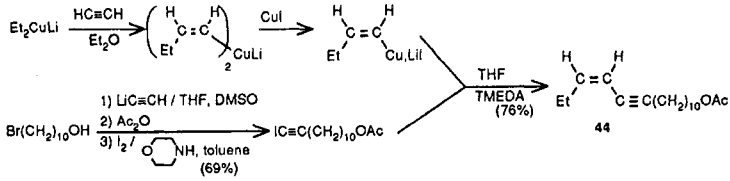


Scheme 138



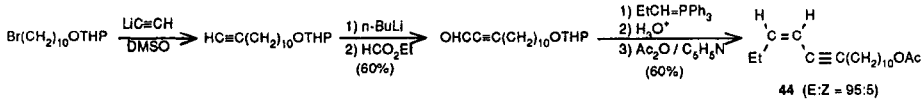
Scheme 139

Normant's organocopper chemistry was successfully applied to synthesize **44** (Scheme 140).[197]



Scheme 140

Shani et al.[198] and Camps et al.[199] synthesized **44** via almost similar routes, by employing acetylenic intermediates followed by Wittig olefination, Scheme 141 shows the synthesis by Camps.[199]



Scheme 141

8. PHEROMONE HYDROCARBONS, ALCOHOLS, AND ACETATES WITH A NONCONJUGATED DIENE SYSTEM

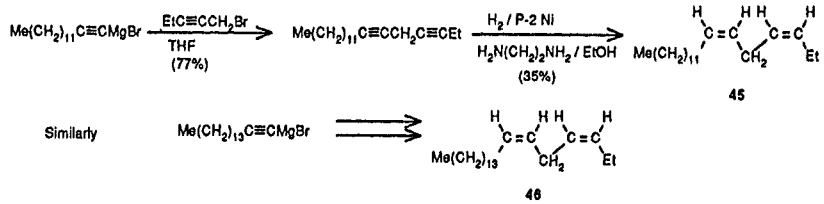
General synthetic methods for 1,4-, 1,5-, and 1,6-alkadiene pheromones were reported by Bestmann et al., based essentially on Wittig chemistry.[200,201]

A. (3Z,6Z)-3,6-Nonadecadiene 45 ($C_{19}H_{36}$)

This is a pheromone component of geometrid moths (*Geometriidae*). Nikolaev and Kovalev synthesized **45** as shown in Scheme 142.[202]

B. (3Z,6Z)-3,6-Henicosadiene 46 ($C_{21}H_{40}$)

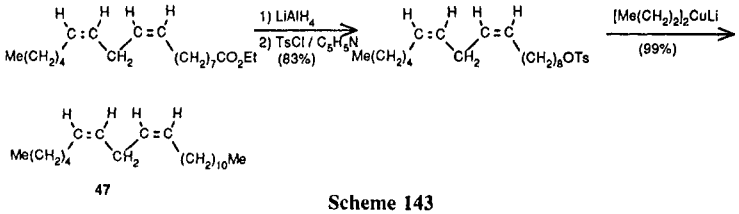
This is a pheromone component of tiger moths and allies (*Arctiidae*) and was synthesized by Nikolaev and Kovalev in the same manner as for **45** (Scheme 142).[202]



Scheme 142

C. (6Z,9Z)-6,9-Henicosadiene 47 ($C_{21}H_{40}$)

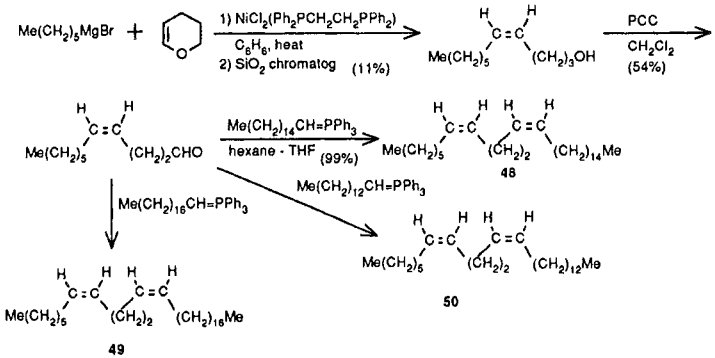
This is the EAG active diene found in the sex-attractant secretion of an Arctiid moth (*Utetheisa ornatrix*). Meinwald et al. synthesized **47,** starting from ethyl linoleate (Scheme 143).[203]



Scheme 143

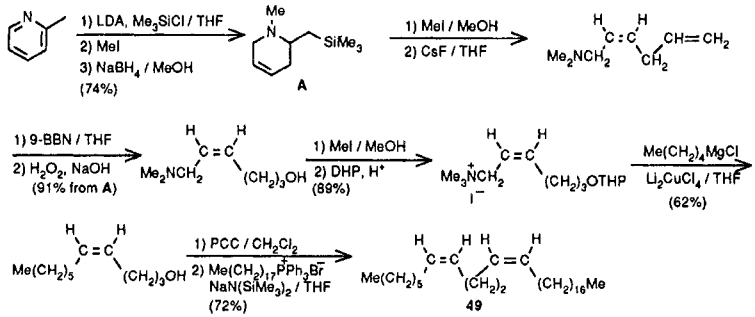
D. (7Z,11Z)-7,11-Heptacosadiene 48 ($C_{27}H_{52}$), (7Z,11Z)-7,11-Nonacosadiene 49 ($C_{29}H_{56}$), and (7Z,11Z)-7,11-Pentacosadiene 50 ($C_{25}H_{48}$)

The major sex pheromone of the fruit fly (*Drosophila melanogaster*) was identified as **48.** The minor biological activity was associated with **49** and **50.** Davis and Carlson synthesized **48, 49,** and **50** employing the coupling reaction of dihydropyran and Grignard reagents under nickel catalysis as the key-step (Scheme 144).[204]



Scheme 144

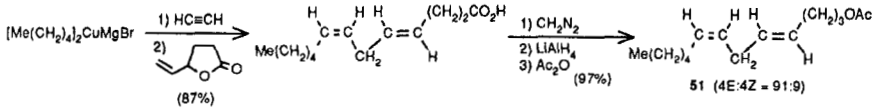
Langlois achieved a synthesis of **49** by utilizing a silicon-induced fragmentation, a coupling reaction with a Grignard reagent, and a Wittig reaction (Scheme 145).[205]



Scheme 145

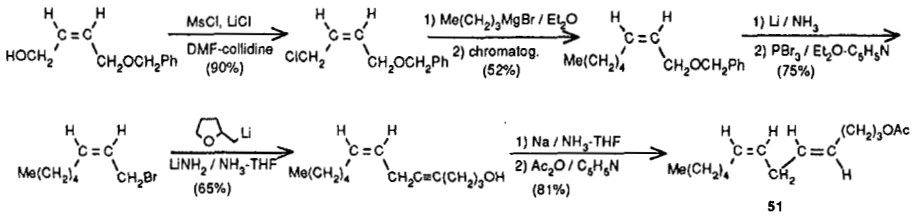
E. (4*E*,7*Z*)-4,7-Tridecadienyl Acetate **51** ($C_{15}H_{26}O_2$)

The potato tuberworm moth (*Phthorimaea operculella*) uses **51** as the female-produced sex pheromone. S_N2'-type reaction of γ-vinyl-γ-butyrolactone with an organocopper reagent was employed by Fujisawa et al. for the synthesis of **51** (Scheme 146).[206]



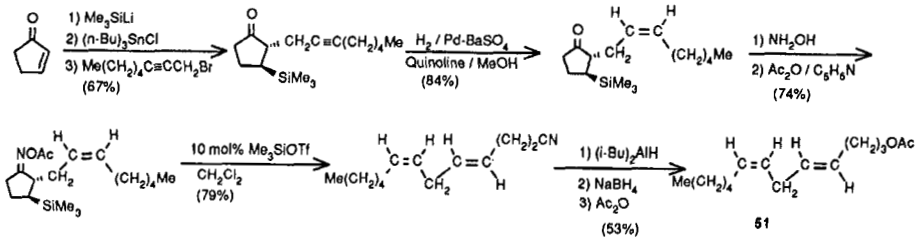
Scheme 146

In Yadav's synthesis, a Grignard coupling was followed by alkylation of an acetylenic alcohol to give **51** (Scheme 147).[207]



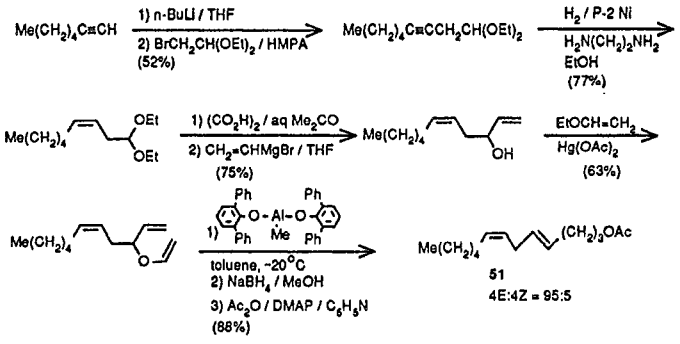
Scheme 147

Nishiyama et al. employed a Beckmann fragmentation of a cyclopentanone oxime to prepare **51** (Scheme 148).[208]



Scheme 148

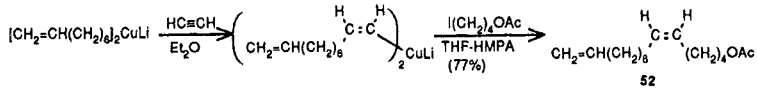
H. Yamamoto and co-workers synthesized **51** by highly stereocontrolled Claisen rearrangement using an organoaluminum reagent (Scheme 149).[209,210]



Scheme 149

F. (Z)-5,13-Tetradecadienyl Acetate 52 ($C_{16}H_{28}O_2$)

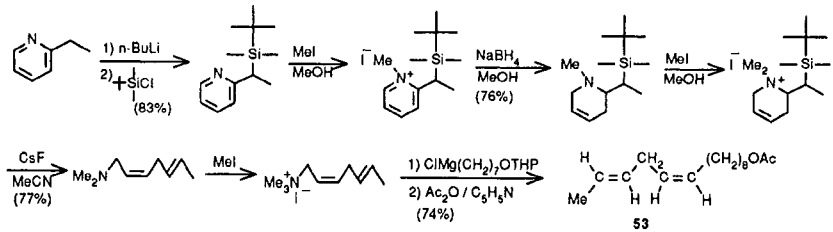
This is the pheromone of the European goat moth (*Cossus cossus*). **52** was synthesized by Normant et al. by alkylation of an organocopper reagent (Scheme 150).[115]



Scheme 150

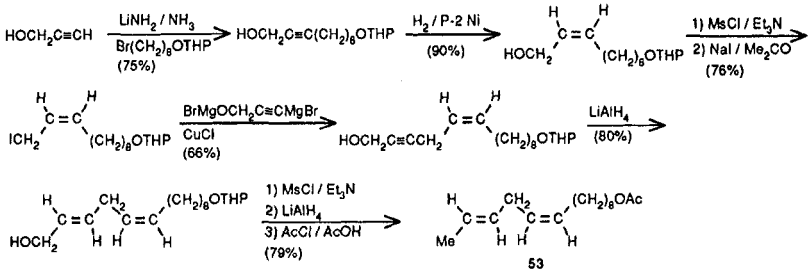
G. (9Z,12*E*)-9,12-Tetradecadienyl Acetate 53 ($C_{16}H_{28}O_2$)

This is the pheromone of the southern armyworm moth (*Spodoptera eridiana*), the almond moth (*Cedra cautella*), the Indian meal moth (*Plodia interpunctella*), and several other Lepidopteran insects. A synthesis of **53** by Bac and Langlois employed a fluoride ion induced silicon fragmentation of a tetrahydropyridinium salt (Scheme 151).[211]



Scheme 151

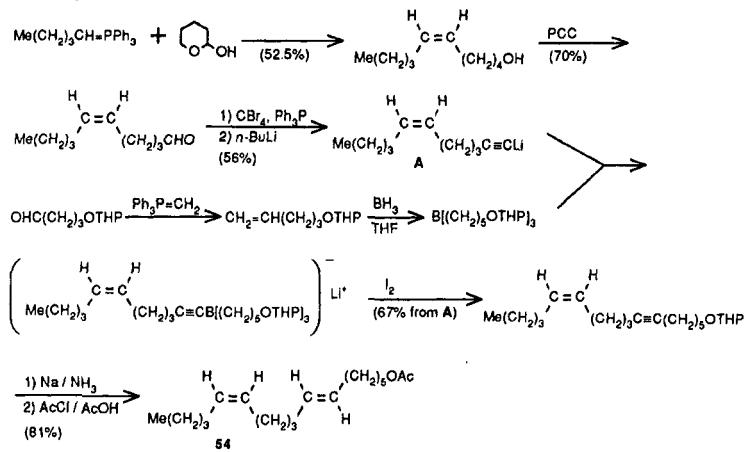
Mandapur prepared **53** by means of classical acetylenic chemistry (Scheme 152).[212]



Scheme 152

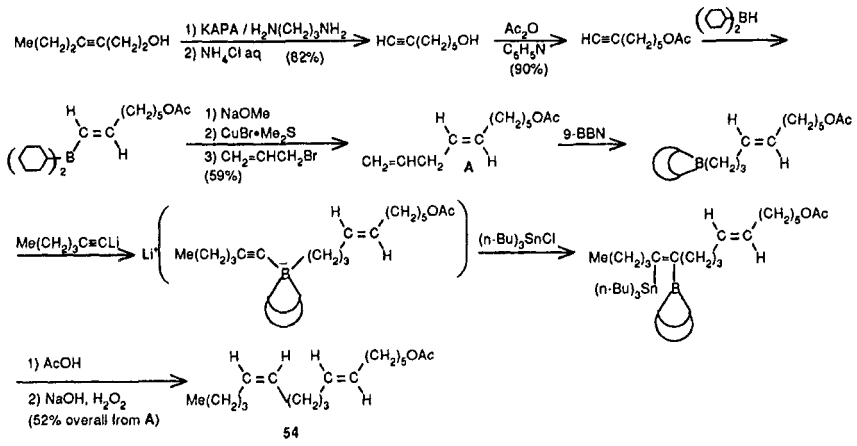
H. (6*E*,11*Z*)-6,11-Hexadecadienyl Acetate **54** ($C_{18}H_{32}O_2$)

This acetate **54** and (6*E*,11*Z*)-6,11-hexadecadienal were isolated as the pheromone of the wild silk moth (*Antheraea polyphemus*). Bestmann and Li synthesized **54** by a combination of Wittig chemistry and organoborane chemistry (Scheme 153).[213] Another synthesis of **54** as reported by Wang and Chu utilized



Scheme 153

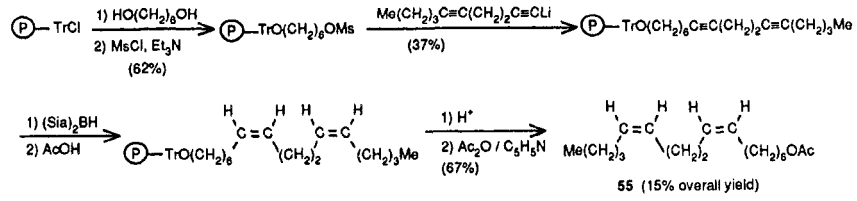
an intramolecular transfer reaction of lithium 1-hexynyltrialkylborate as induced by tri(*n*-butyl)tin chloride (Scheme 154).[214]



Scheme 154

I. Gossyplure, a Mixture of (7Z,11Z)-7,11-Hexadecadienyl Acetate 55 and Its (7Z,11*E*)-Isomer 56 ($C_{18}H_{32}O_2$)

Six new syntheses of **55** and **56** were reported since mid-1979. Leznoff's solid-phase synthesis was applied to the preparation of **55** (Scheme 155).[215] The

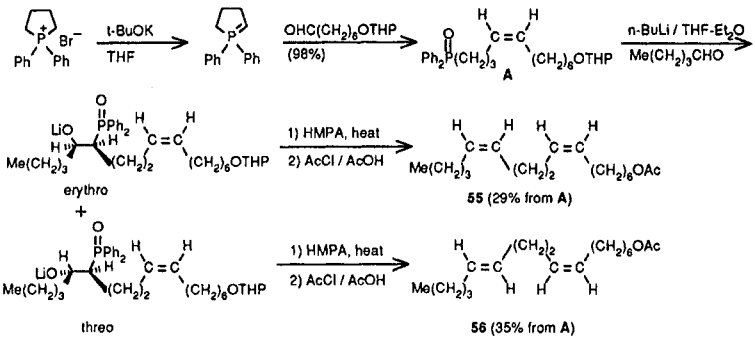


Scheme 155

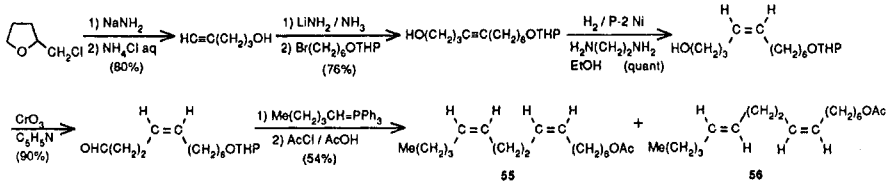
polymer support employed was 1% or 2% styrene-divinylbenzene co-polymer containing trityl chloride groups. This unique synthesis of **55**, however, was not very efficient.

A cyclic phosphonium ylide was used to prepare a mixture of **55** and **56** (Scheme 156).[216] By carrying out the Horner reaction in a 1 : 1 mixture of THF and ether, it was possible to obtain the desired ca. 1 : 1 mixture of **55** and **56**, which is active as the pheromone of the pink bollworm moth (*Pectinophora gossypiella*).

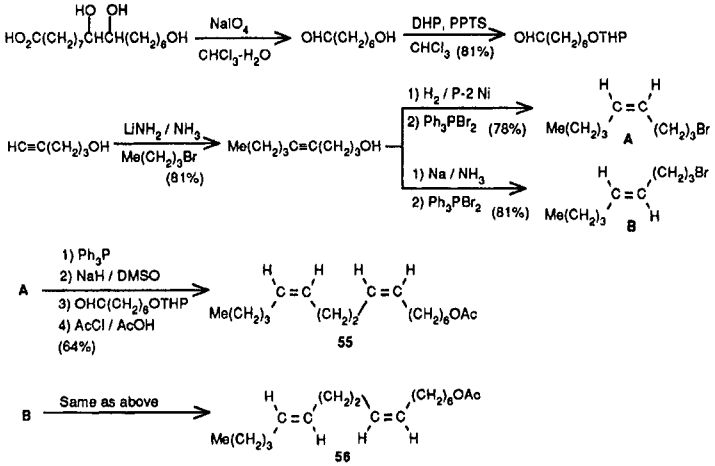
Joshi et al. synthesized gossyplure by a combination of an acetylenic route and Wittig chemistry (Scheme 157).[217] They also prepared **55** and **56** separately, employing aleuritic acid as the starting material (Scheme 158).[217]



Scheme 156



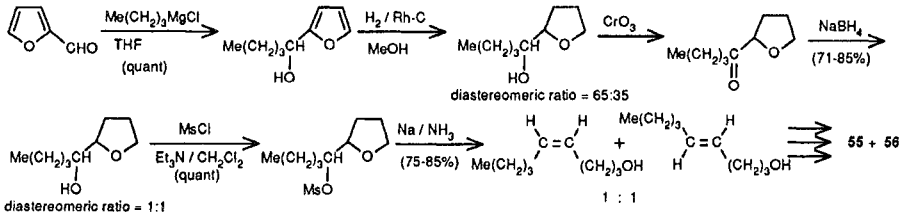
Scheme 157



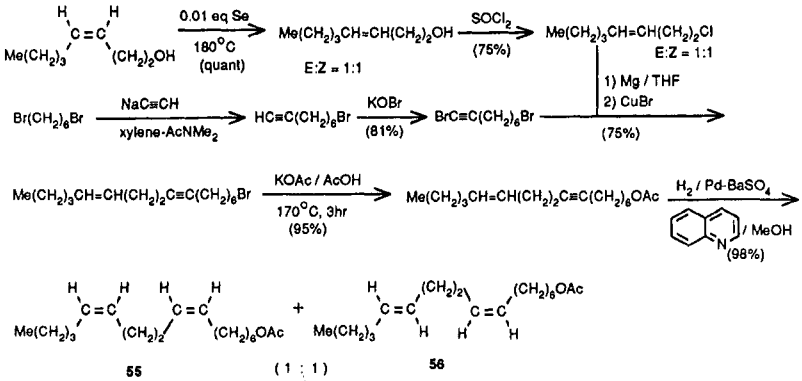
Scheme 158

Fernández and Hernández developed a simple method for the preparation of a 1:1 mixture of (*Z*)- and (*E*)-4-nonen-1-ol starting from furfural (Scheme 159).[218]

Ishihara and Yamamoto's synthesis (Scheme 160) was based on acetylenic



Scheme 159

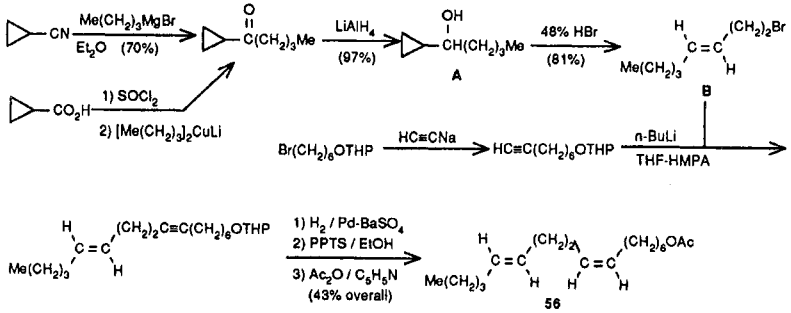


Scheme 160

chemistry and furnished a 1 : 1 mixture of **53** and **56**.[219] Their process is employed by Shin-Etsu Chemical Co. for the production of gossyplure.

Michelot synthesized **55** by organopalladium-catalyzed cross-coupling reaction (cf. Scheme 54).[117]

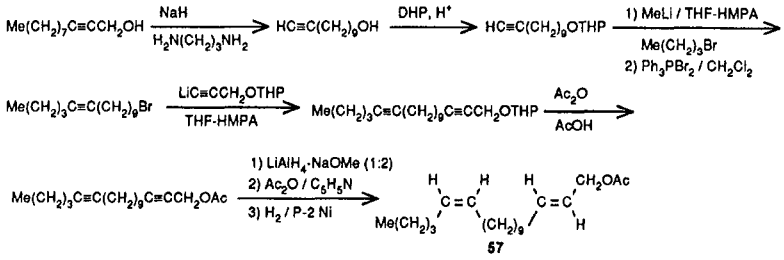
(7Z,11*E*)-7,11-Hexadecadienyl acetate **(56)** is the sex pheromone of the Angoumois grain moth (*Sitotroga cerealella*). Kang's synthesis of **56** employed the Julia cleavage (**A** → **B**) as the key-step to generate the (*E*)-double bond (Scheme 161).[220]



Scheme 161

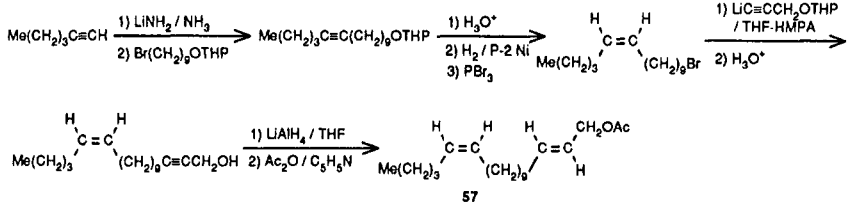
J. (2*E*,13*Z*)-2,13-Octadecadienyl Acetate **57** ($C_{20}H_{36}O_2$)

Isolation of the sex pheromone of the grape root borer (*Vitacea polistiformis*) was carried out by Schwarz et al. using only seven female insects. The pheromone was identified as **57** and synthesized as shown in Scheme 162.[221]



Scheme 162

The leopard moth (*Zeuzera pyrina*) also secretes **57** as its pheromone, which was synthesized by the acetylenic route (Scheme 163).[222] Descoins also synthesized **57** by a combination of an organopalladium-catalyzed process and acetylenic chemistry (Scheme 164).[223]

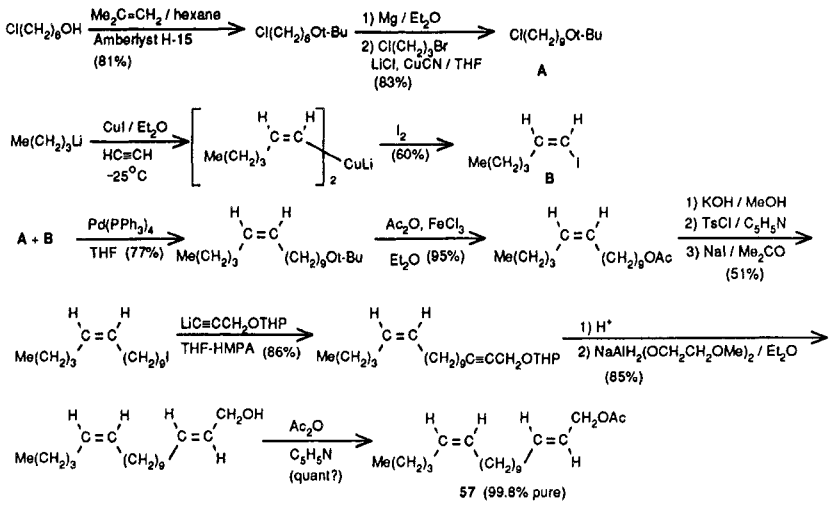


Scheme 163

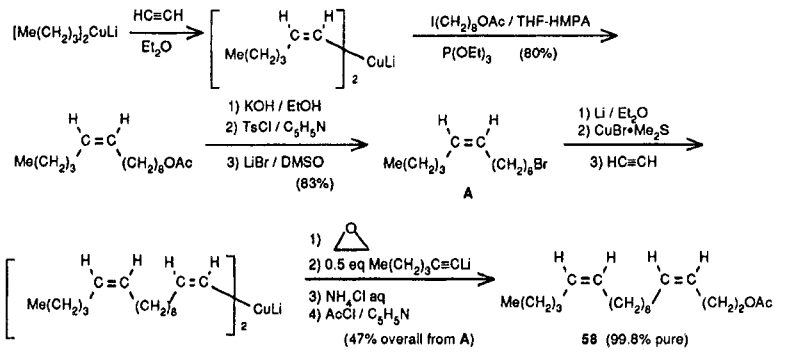
Both a clearwing moth, *Synanthedon acerrubri*, a pest of maples in the northeastern U.S.A., and the squash vine borer (*Melittia satyriniformis*) were attracted by **57**.

K. (3*Z*,13*Z*)-3,13-Octadecadienyl Acetate **58** ($C_{20}H_{36}O_2$)

This is the main component of the sex pheromone of the smaller clearwing moth (*Synanthedon tenuis*). Application of Normant's carbocupration method led to a new and efficient synthesis of **58** (Scheme 165).[224]



Scheme 164



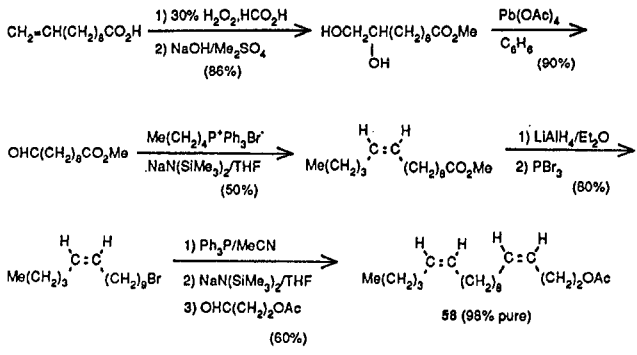
Scheme 165

Szántay and co-workers synthesized **58** by Wittig chemistry (Scheme 166).[225]

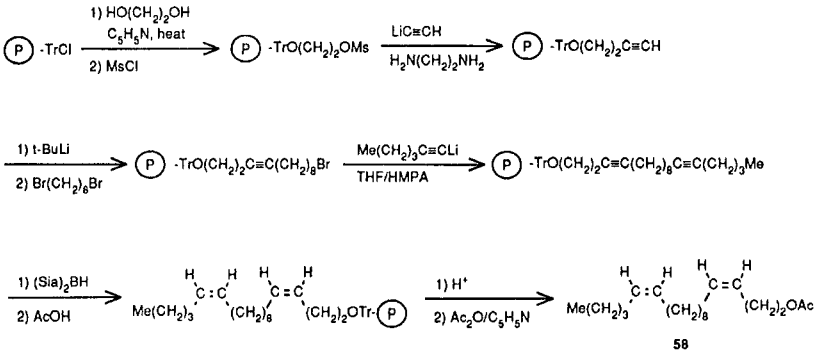
Leznoff's polymer-support synthesis of **58** employed a 2% cross-linked styrene-divinylbenzene co-polymer containing pendant trityl chloride groups (Scheme 167).[215]

The synthesis of **58** and its (3*E*)-isomer **60,** the pheromone of the lesser peachtree borer (*Synanthedon pictipes*) and the peachtree borer (*S. exitiosa*), by the U.S.D.A. group was published as a full paper (Scheme 95, Ref. 1).[226]

An efficient synthesis of **58** and **60** was reported by Yamamoto et al. by an



Scheme 166

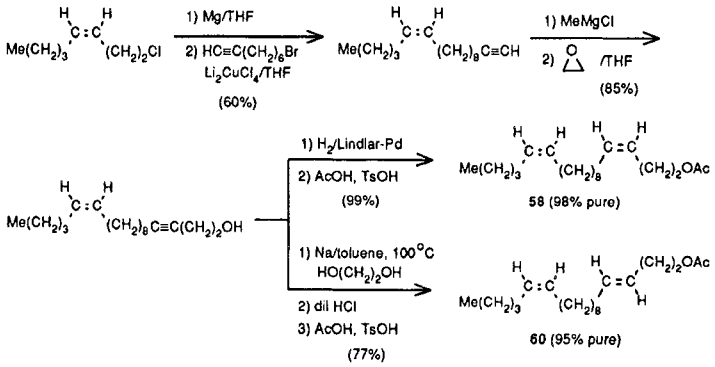


Scheme 167

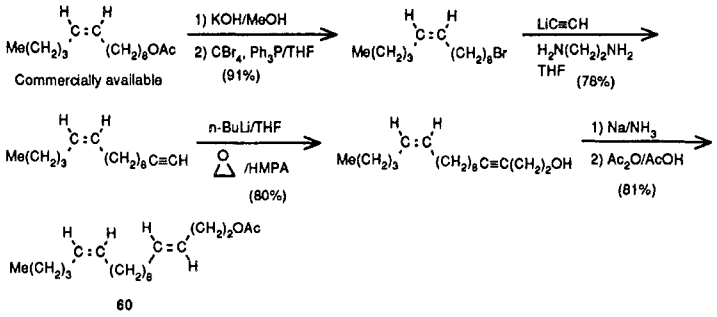
acetylenic route (Scheme 168).[227] Noteworthy is the reduction of the triple bond to (*E*)-double bond with sodium in toluene instead of the Birch process.

L. (3*E*,13*Z*)-3,13-Octadecadien-1-ol 59 ($C_{18}H_{34}O$) and (3*E*,13*Z*)-3,13-Octadecadienyl Acetate 60 ($C_{20}H_{36}O_2$)

The poplar twig clearwing moth (*Paranthrene tabaniformis*) secretes **59** as its pheromone. Synthesis of **60** from commercially available (*Z*)-9-tetradecenyl acetate was reported by Voerman employing an acetylenic route (Scheme 169).[228]

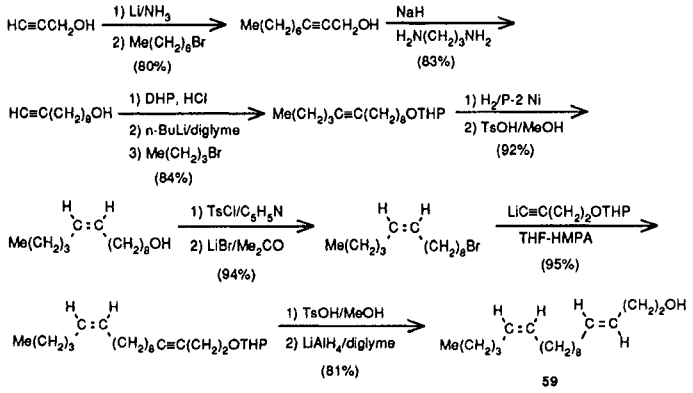


Scheme 168



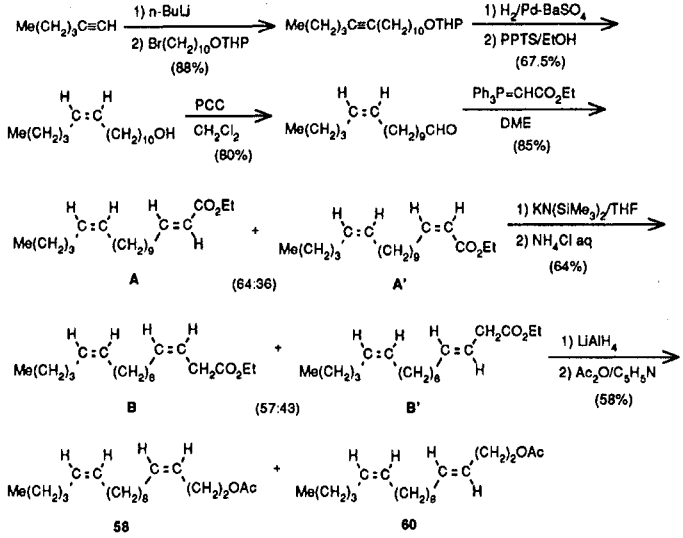
Scheme 169

Zhang et al. reported a synthesis of **59**, based on acetylenic chemistry involving the acetylene zipper reaction (Scheme 170).[229] They also synthesized other three isomers in a similar fashion.



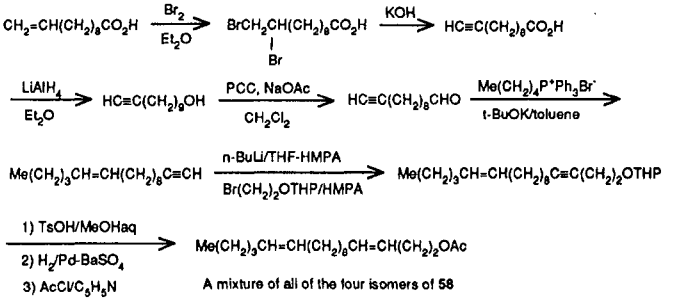
Scheme 170

A mixture of **58** and **60,** which attracts the cherrytree borer (*Synanthedon hector*), was synthesized by deconjugating the α,β-unsaturated esters **A** + **A′** to the β,γ-unsaturated esters **B** + **B′** (Scheme 171).[230] The apple clearwing



Scheme 171

moth (*S. myopaeformis*) secretes a mixture of all of the four isomers of 3,13-octadecadienyl acetate (*Z*/*E* = 97/3 at C-3, and *Z*/*E* = 98/2 at C-13) as its pheromone. This mixture was synthesized by a combination of the Wittig and acetylene routes (Scheme 172).[231]



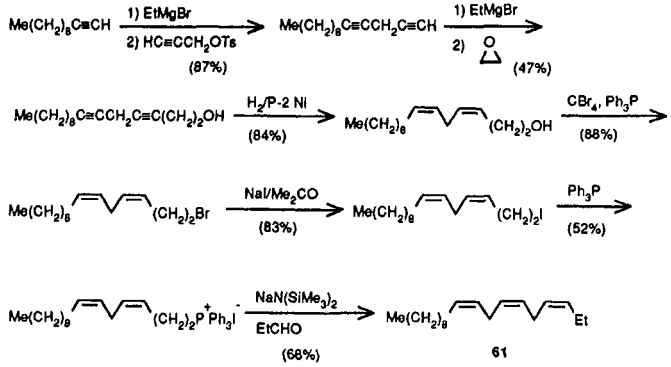
Scheme 172

9. PHEROMONE HYDROCARBONS, ALCOHOLS, AND ACETATES WITH A TRIENE OR TETRAENE SYSTEM

A. (3Z,6Z,9Z)-3,6,9-Nonadecatriene 61 ($C_{19}H_{34}$)

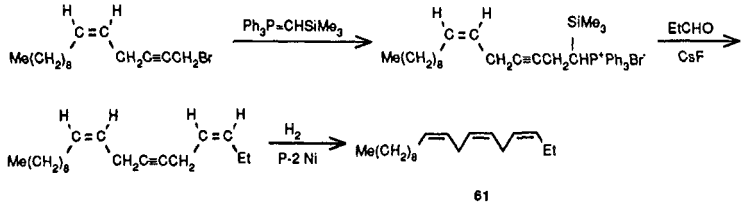
This is the pheromone component of the giant looper (*Boarmia selenaria*).[232] It was also found as a pheromone component of the fall cankerworm moth (*Alsophila pometaria*),[233] *Creatonotos transiens*, and *C. gangis*.[234]

The synthesis of **61** by Becker et al. (Scheme 173) was based on acetylenic and Wittig chemistry.[232]



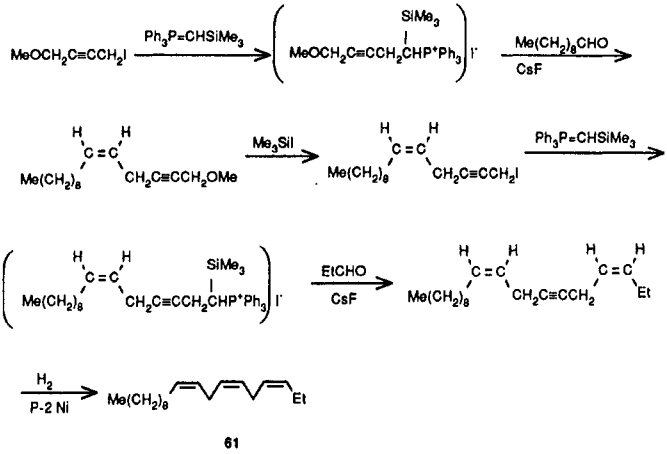
Scheme 173

Employing a silylated phosphorus ylide, Bestmann et al. synthesized **61** via desilylation-Wittig reaction (Schemes 174 and 175).[235]

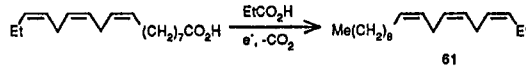


Scheme 174

Syntheses of **61** and related methylene-interblocked Lepidopteran pheromones by acetylenic chemistry, Wittig reactions, and Kolbe electrolysis were reported by Bestmann et al. (Scheme 176).[236]

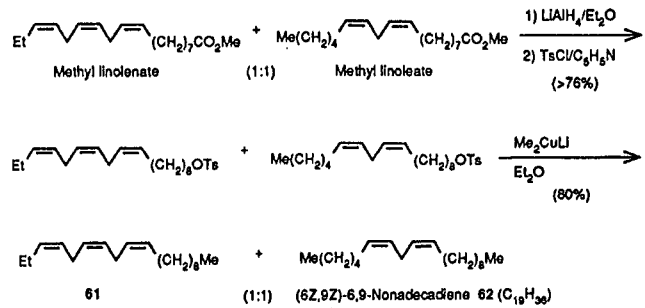


Scheme 175



Scheme 176

The pheromone bouquet of the geometrid moth (*Alsophila quadripunctata*) consists of (6Z,9Z)-6,9-nonadecadiene **62** ($C_{19}H_{36}$) and **61.** A blend containing **61** and **62** in a ratio of 1 : 1 was most effective in attracting male moths in the field. Mangold and his co-workers prepared this blend starting from a 1 : 1 mixture of methyl linolenate and methyl linoleate (Scheme 177).[237]

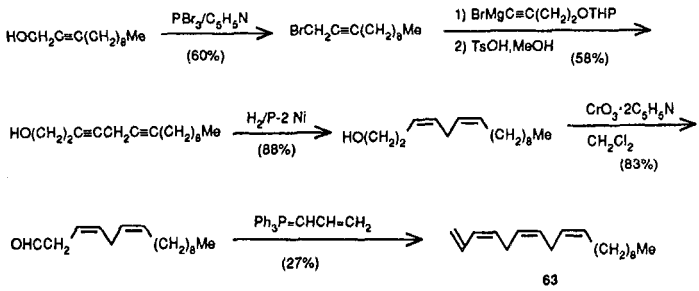


Scheme 177

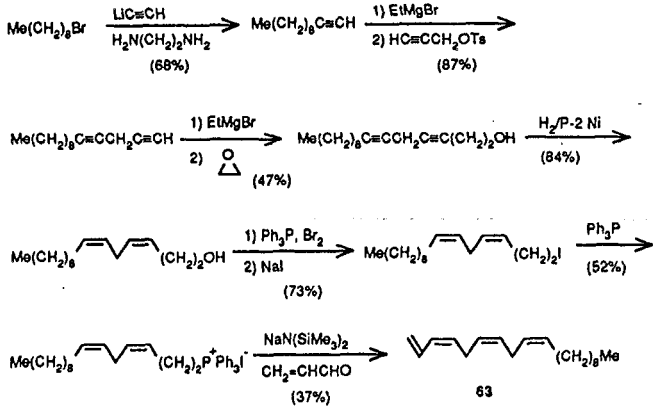
B. (3Z,6Z,9Z)-1,3,6,9-Nonadecatetraene 63 ($C_{19}H_{32}$)

This is the sex pheromone of the winter moth (*Operophthera brumata*).[238,239]

Meinwald synthesized **63** by a combined acetylene-Wittig route (Scheme 178).[238,240] Bestmann et al. also synthesized **63** (Scheme 179).[239]



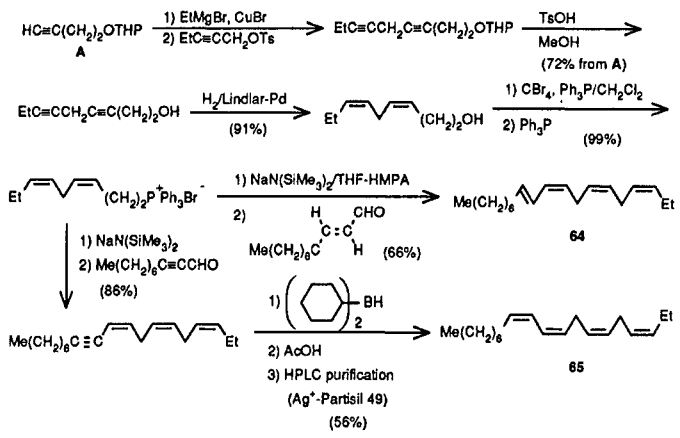
Scheme 178



Scheme 179

C. (3Z,6Z,9Z,11*E*)-3,6,9,11-Nonadecatetraene 64 ($C_{19}H_{32}$) and Its (3Z,6Z,9Z,11Z)-Isomer 65 ($C_{19}H_{32}$)

These two hydrocarbons, together with **61**, constitute the sex pheromone of the fall cankerworm moth (*Alsophila pometaria*). Wong et al. synthesized both **64** and **65** (Scheme 180).[233] Meinwald and his co-workers also prepared **64**.[241]

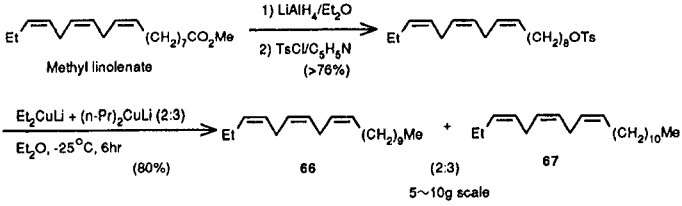


Scheme 180

D. (3Z,6Z,9Z)-3,6,9-Icosatriene 66 ($C_{20}H_{36}$) and (3Z,6Z,9Z)-3,6,9-Henicosatriene 67 ($C_{21}H_{38}$)

The female-produced pheromone of the velvetbean caterpillar moth (*Anticarsia gemmatalis*) is a mixture of **66** and **67.** A blend containing **66** and **67** in a ratio of 2 : 3 is most effective in attracting male moths in the field. Heath et al. prepared **66** and **67** from linolenic acid [(9Z,12Z,15Z)-octadecatrienoic acid] by homologating the tosylate of the corresponding alcohol with either lithium diethylcuprate or lithium di-*n*-propylcuprate.[242]

Yu and Mangold prepared a 2 : 3 mixture of **66** and **67** from methyl linolenate (Scheme 181).[243]

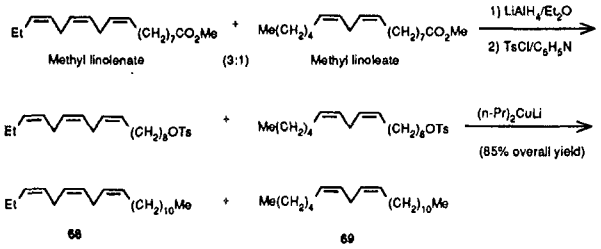


Scheme 181

E. (3Z,6Z,9Z)-3,6,9-Henicosatriene 68 ($C_{21}H_{38}$)

The pheromone bouquet of the tropical pest *Mocis latipes* is a mixture of **68** and (6Z,9Z)-6,9-henicosadiene **69** ($C_{21}H_{40}$). A blend containing **68** and **69** in

a ratio of 3 : 1 is the most effective attractant in the field. This mixture was prepared from a 3 : 1 mixture of methyl linolenate and methyl linoleate (Scheme 182).[237]

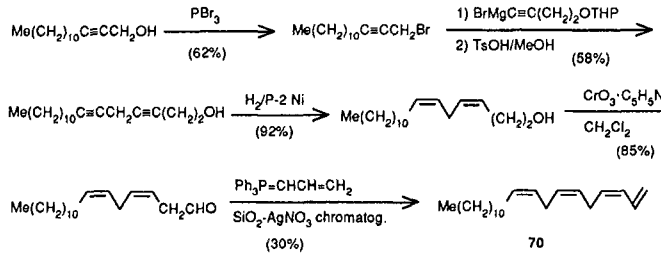


Scheme 182

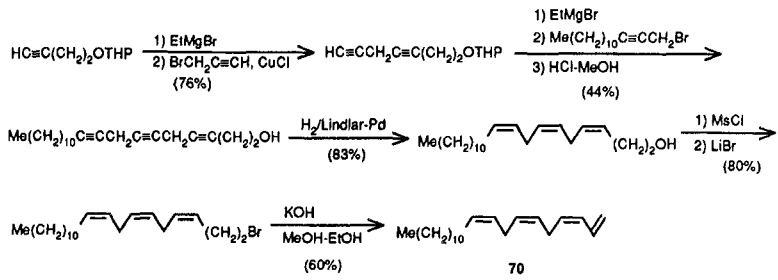
F. (3Z,6Z,9Z)-1,3,6,9-Henicosatetraene 70 ($C_{21}H_{36}$)

The tetraene **70** is the major component of the female-produced sex pheromone of an Arctiid moth (*Ultetheisa ornatrix*). Meinwald and co-workers published two different syntheses of **70.**[203,241]

A Wittig reaction was used in the first synthesis for the construction of the terminal conjugated diene system (Scheme 183),[203] while in the second, that system was constructed by an elimination reaction (Scheme 184).[241]



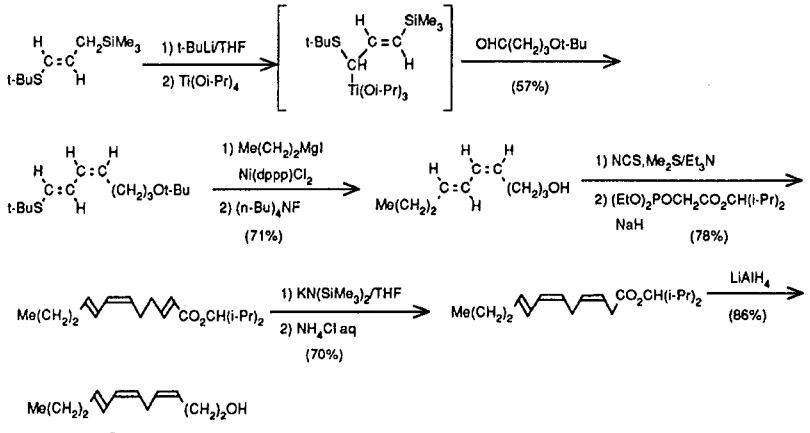
Scheme 183



Scheme 184

G. (3Z,6Z,8E)-3,6,8-Dodecatrien-1-ol 71 ($C_{12}H_{20}O$)

This is the trail pheromone of both the subterranean termite (*Reticulitermes virginicus*) and the eastern subterranean termite (*R. flavipes*). Yamamoto's new synthesis of **71** is based on his observation that deconjugative protonation of dienolates from (*E*)-2-alkenoate using potassium disilazide as the base gives (*Z*)-3-alkenoate predominantly (Scheme 185).[245,246]



71

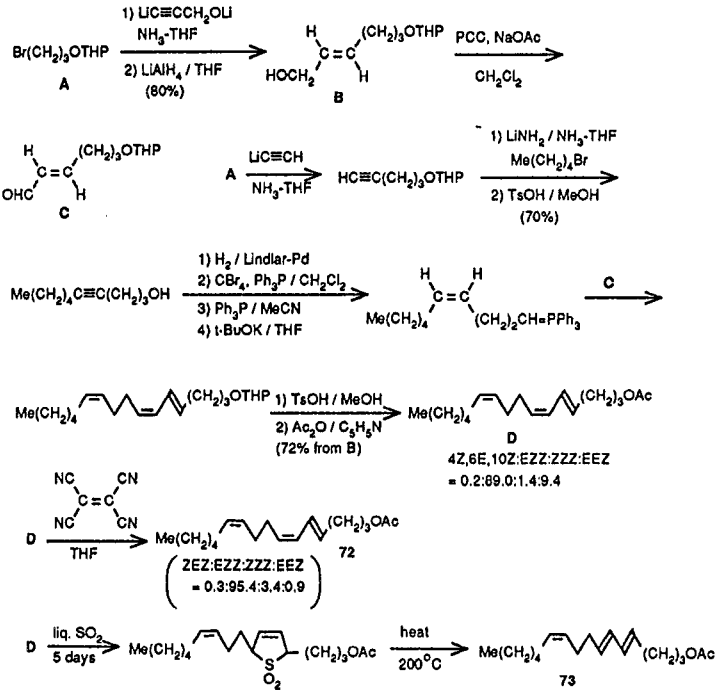
Scheme 185

H. (4E,6Z,10Z)-4,6,10-Hexadecatrienyl Acetate 72 ($C_{18}H_{30}O$) and Its (6E)-Isomer 73

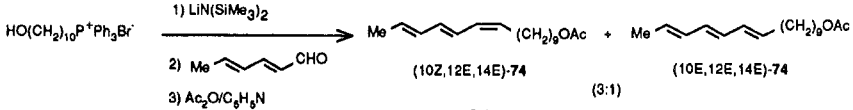
The cocoa pod borer (*Conopomorpha cramerella*) secretes as its female-produced sex pheromone a mixture of **72, 73,** their corresponding alcohols, and 1-hexadecanol. A mixture of 40 : 60 : 4 : 6 : 10 ratio of the above five components was found to be a potent attractant. The synthesis of **72** and **73** was achieved (Scheme 186), using the appropriate sequences of acetylenic chemistry and Wittig reactions.[247]

I. 10,12,14-Hexadecatrienyl Acetate 74 ($C_{18}H_{30}O$)

This is the female-produced sex pheromone of the mulberry pyralid (*Glyphodes pyloalis*).[248] Eight geometrical isomers of **74** were synthesized by six nonselective routes leading to a mixture of (10*Z*,12*E*,14*E*)-**74** and (10*E*,12*E*,14*E*)-**74** (Scheme 187).[249] The geometry of the natural pheromone has not yet been elucidated.



Scheme 186



Scheme 187

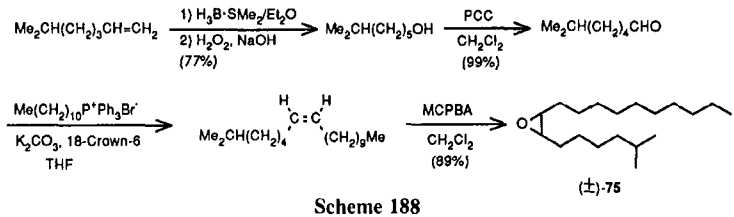
10. PHEROMONES WITH AN EPOXY RING

A. Disparlure, (7*R*,8*S*)-(+)-7,8-Epoxy-2-methyloctadecane 75 ($C_{19}H_{38}O$)

This is the pheromone of the gypsy moth (*Lymantria dispar*).

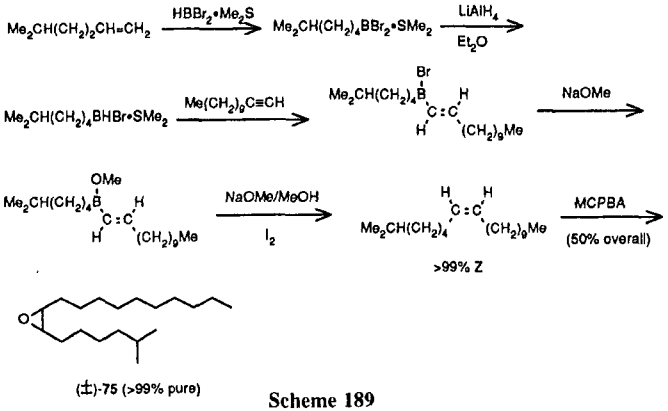
(1) Syntheses of (±)-75

Four new syntheses of (±)-disparlure **(75)** have been published since 1979. Markgraf et al. employed Wittig olefination in the presence of 18-crown-6 followed by epoxidation to prepare (±)-**75** (Scheme 188).[250] Brown's organobor-



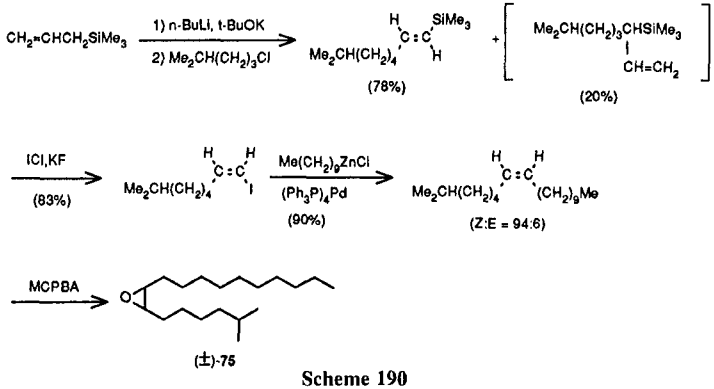
Scheme 188

ane chemistry was used to achieve an efficient synthesis of (±)-**75** (Scheme 189).[251]



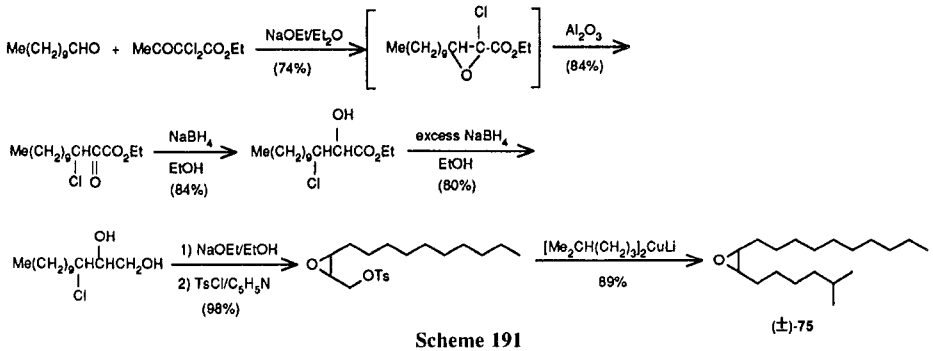
Scheme 189

Chan's synthesis of **75** is based on the stereoselective iodination of an (*E*)-alkenylsilane to give a (*Z*)-alkenyl iodide. Palladium-catalyzed coupling of the iodoalkene with an organozinc reagent yielded the desired (*Z*)-alkene, which was epoxidized to (±)-**75** (Scheme 190).[99] Tsuboi et al. reported a synthesis of



Scheme 190

(±)-**75** without recourse to 2-methyl-7-octadecene as the key-intermediate (Scheme 191).[252]

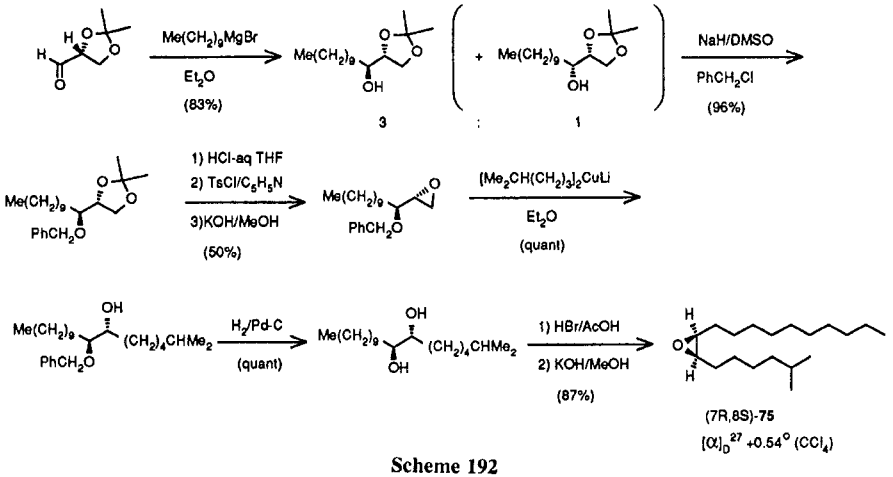


Scheme 191

(2) Syntheses of (7R,8S)-(+)-75

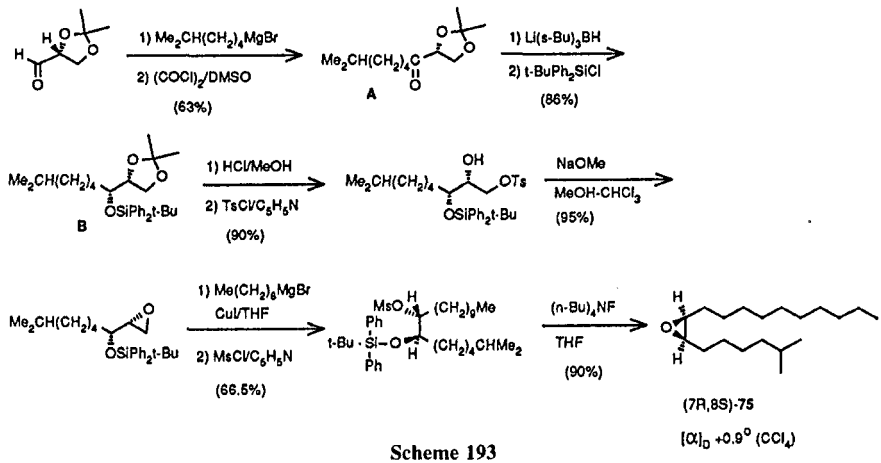
Fourteen different syntheses of the bioactive (+)-enantiomer of disparlure (**75**) have been recorded since 1979.

A. Syntheses Starting from Chiral Building Blocks. (+)-Glyceraldehyde acetonide was employed by two groups for the synthesis of (+)-**75.** Lin et al. prepared all of the four stereoisomers of **75** starting from (+)-glyceraldehyde acetonide (Scheme 192).[253] Its treatment with decylmagnesium bromide, how-



Scheme 192

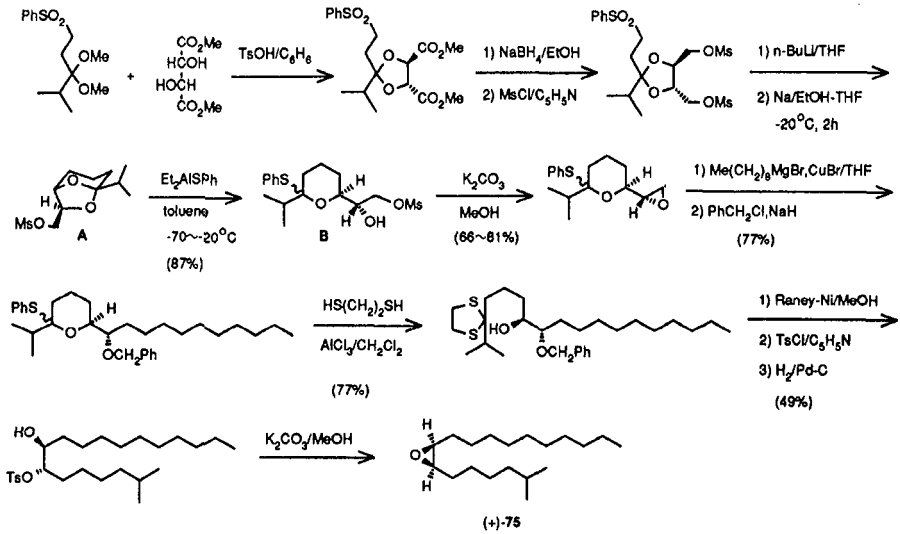
ever, yielded a considerable amount of the undesired stereoisomer. Jurczak et al. also used (+)-glyceraldehyde acetonide to prepare (+)-**75** (Scheme 193).[254]



Scheme 193

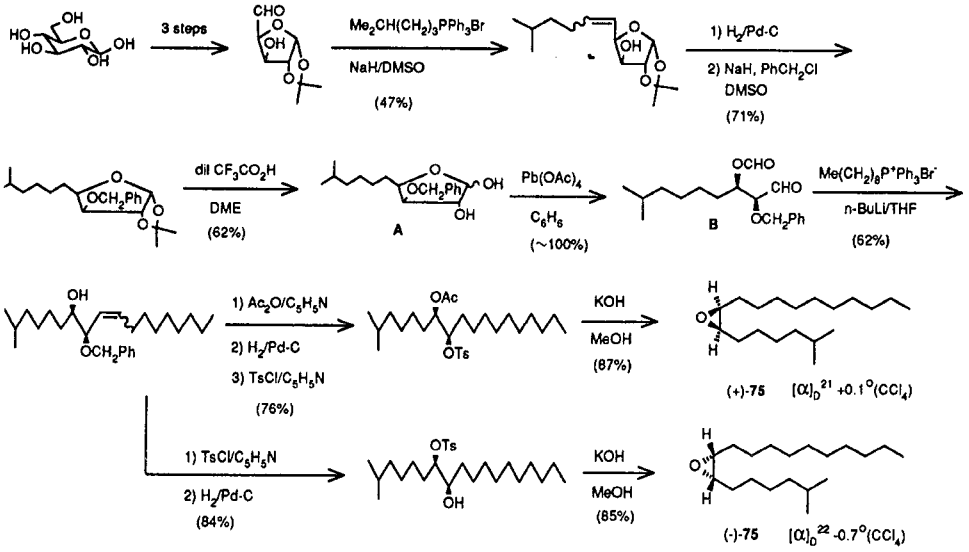
In their case, the Grignard product was first oxidized to a ketone **A**, which was reduced with L-selectride® to give the desired isomer **B** after silylation in more favorable selectivity of 9 : 1.

Masaki et al. synthesized (+)-**75** starting from (+)-tartaric acid (Scheme 194).[255] They utilized a cleavage reaction of an intramolecular acetal **A** with an organoaluminum reagent to give **B.**



Scheme 194

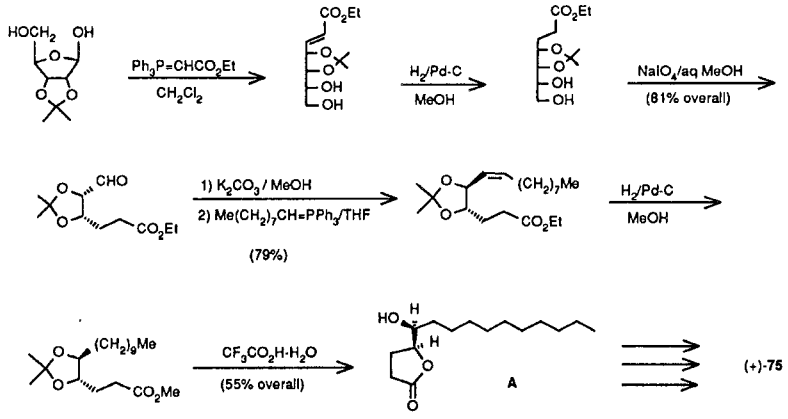
Achmatowicz et al. achieved a synthesis of (+)- and (−)-**75** from D-glucose (Scheme 195).[256] Two out of the four chiral centers of D-glucose were utilized,



Scheme 195

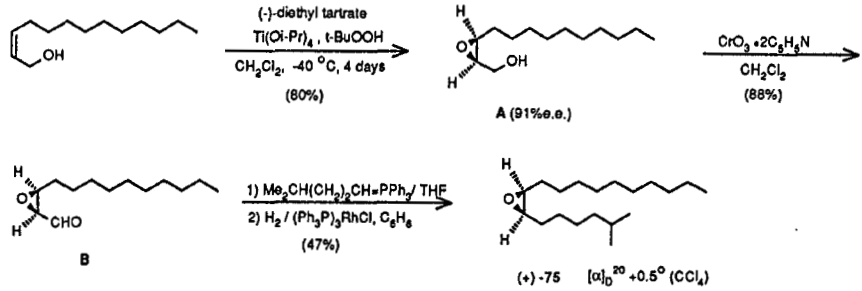
and the unwanted two chiral centers were removed by the glycol cleavage reaction **(A → B).**

D-Ribose served as the starting material in Wightman's synthesis of the lactone **A** (Scheme 196),[257] which was the key intermediate in Marumo's synthesis of (+)-**75.**[258]



Scheme 196

A synthesis of (+)-**75** was reported by Tolstikov et al., which consists in the conversion of D-galactinal triacetate to (2*R*,3*S*)-2,3-epoxy-1-tridecanol (**A** in Scheme 197).[259]

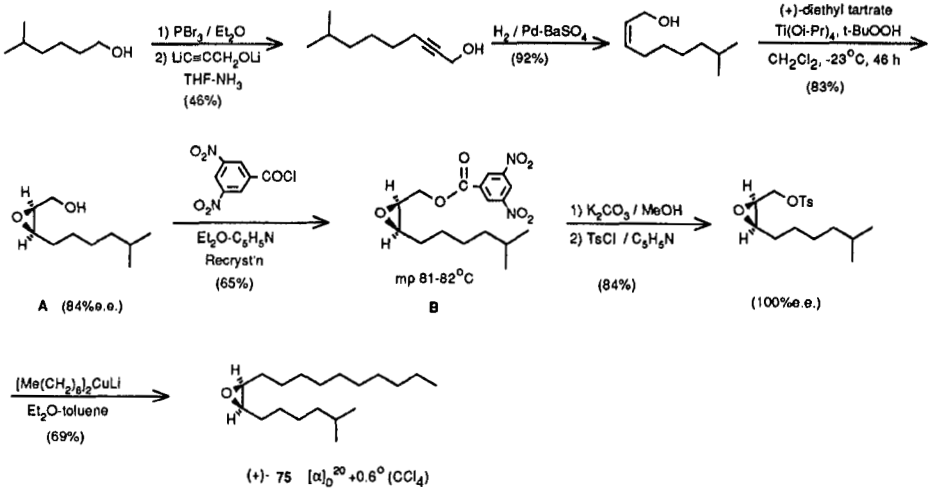


Scheme 197

B. Syntheses Based on Chemical Asymmetric Reactions. Four papers have appeared reporting the application of the Sharpless asymmetric epoxidation to disparlure synthesis.

Sharpless et al. converted the epoxy alcohol **A** (Scheme 197) to the corresponding aldehyde **B**, to which the remaining carbon chain was attached by a Wittig reaction.[260]

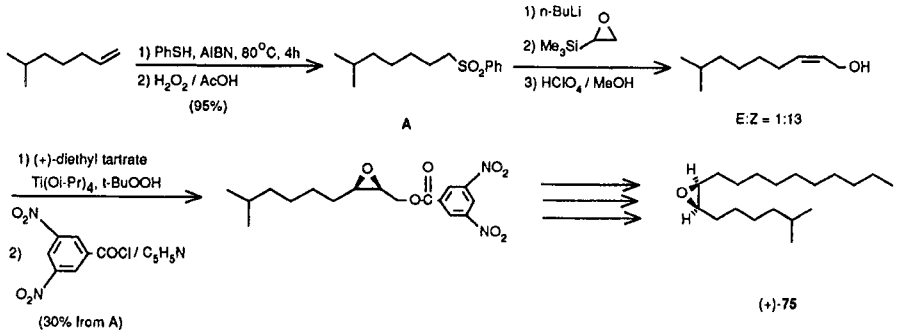
Mori and Ebata prepared optically pure (+)-**75** as shown in Scheme 198.[261,262] Optically impure epoxy alcohol **A**, which was prepared by asym-



Scheme 198

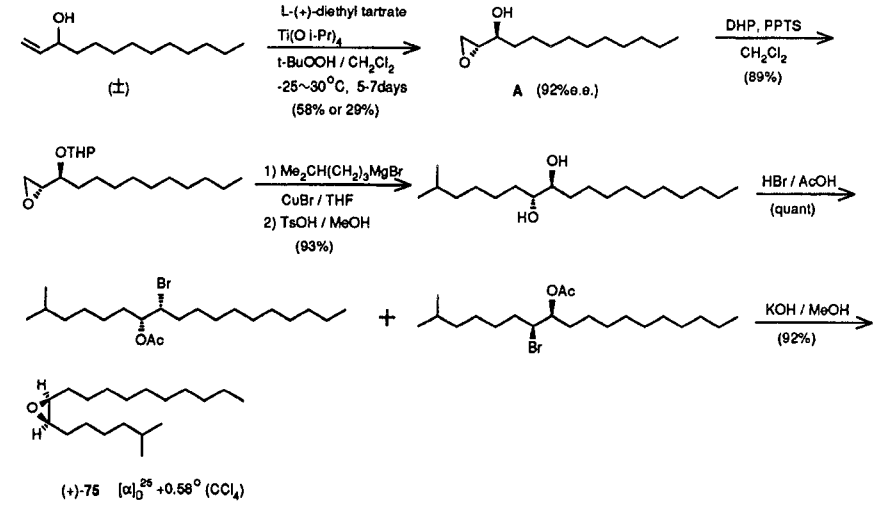
metric epoxidation, was purified by recrystallizing the corresponding 3,5-dinitrobenzoate **B** to give, after hydrolysis, optically pure **A.** The corresponding epoxy tosylate was treated with lithium di(*n*-nonyl)cuprate to give (+)-disparlure **75.**

Wicha and his co-workers developed a new method for the preparation of allylic alcohols from alkyl phenyl sulfone and trimethylsilylethylene oxide, and used it for the synthesis of Mori's epoxy alcohol (Scheme 199).[263] A full report of this work appeared recently.[1090]



Scheme 199

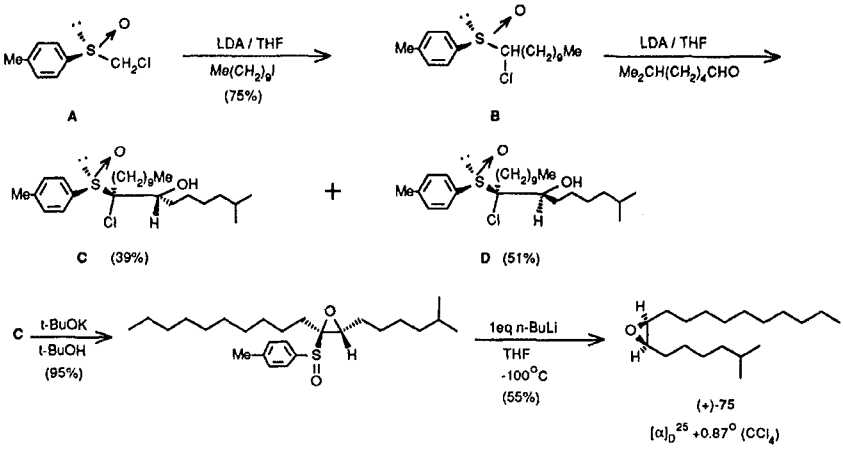
Lin et al. prepared an epoxy alcohol **A** through the kinetic resolution of (±)-1-tridecen-3-ol by Sharplress asymmetric epoxidation (Scheme 200).[264] (+)-Disparlure **(75)** was synthesized from **A** in five steps in 60% overall yield.



Scheme 200

Kametani et al. achieved a formal synthesis of (+)-**75** from an optically active 2-furylcarbinol prepared by the kinetic resolution according to Sharpless.[1227, 1228]

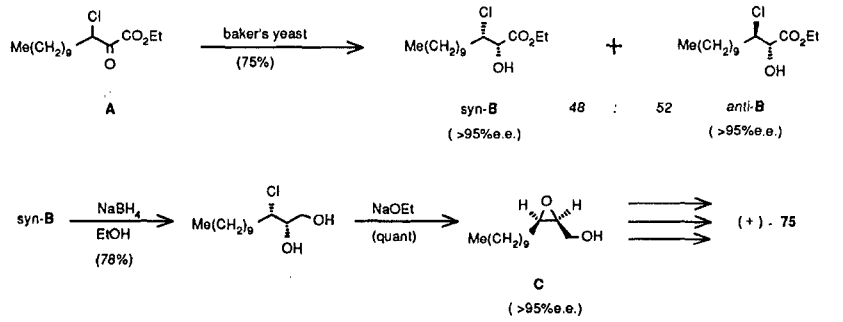
Alkylation of an optically active sulfoxide was used in Yamakawa's synthesis of (+)-**75** (Scheme 201).[265, 266] Alkylation of **A** with decyl iodide to give **B**



Scheme 201

was followed by aldol reaction of **B** with 6-methylheptanal to give a separable mixture of **C** and **D.** The former gave (+)-**75,** while the latter gave (−)-*trans*-isomer of **75.**

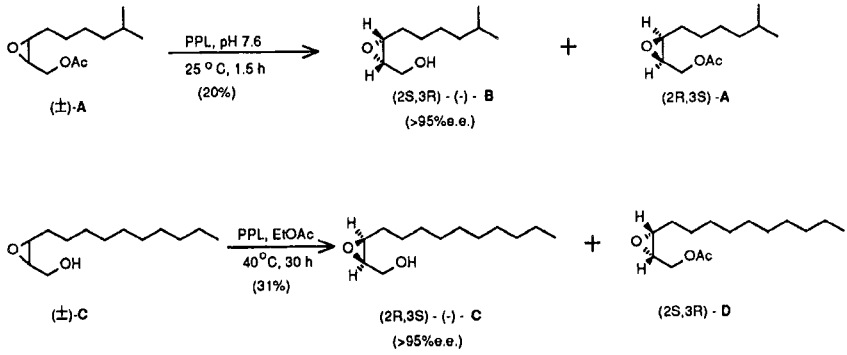
C. Syntheses Based on Biochemical Asymmetric Reactions. Tsuboi et al. prepared the epoxy alcohol **C,** which was used by Sharpless as the key-intermediate leading to (+)-**75,** employing the yeast reduction (Scheme 202).[267] Re-



Scheme 202

duction of an α-keto ester **A** yielded a separable mixture of hydroxy esters, *syn*- and *anti*-**B.** Further transformation of *syn*-**B** yielded the epoxy alcohol **C.**

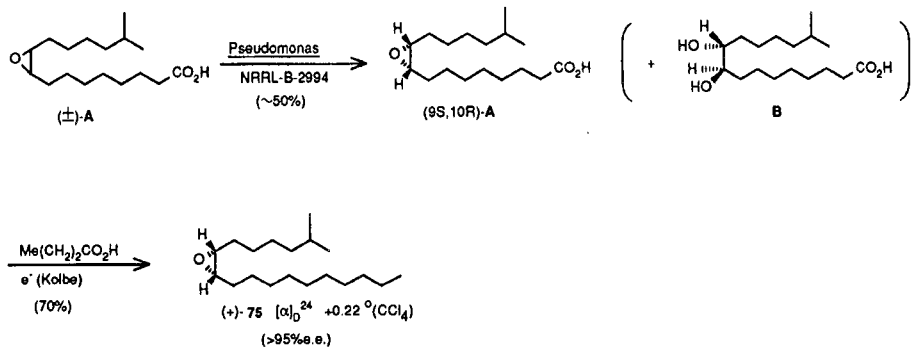
Bianchi et al. used porcine pancreatic lipase (PPL) for the asymmetric hydrolysis of (±)-**A** (Scheme 203)[268] to yield (2*S*,3*R*)-**B,** which was an interme-



Scheme 203

diate in Mori's synthesis of (+)-**75.**[262] Similarly, asymmetric transesterification of (±)-**C** with ethyl acetate in the presence of PPL yielded (2*R*,3*S*)-**C,** the Sharpless intermediate.

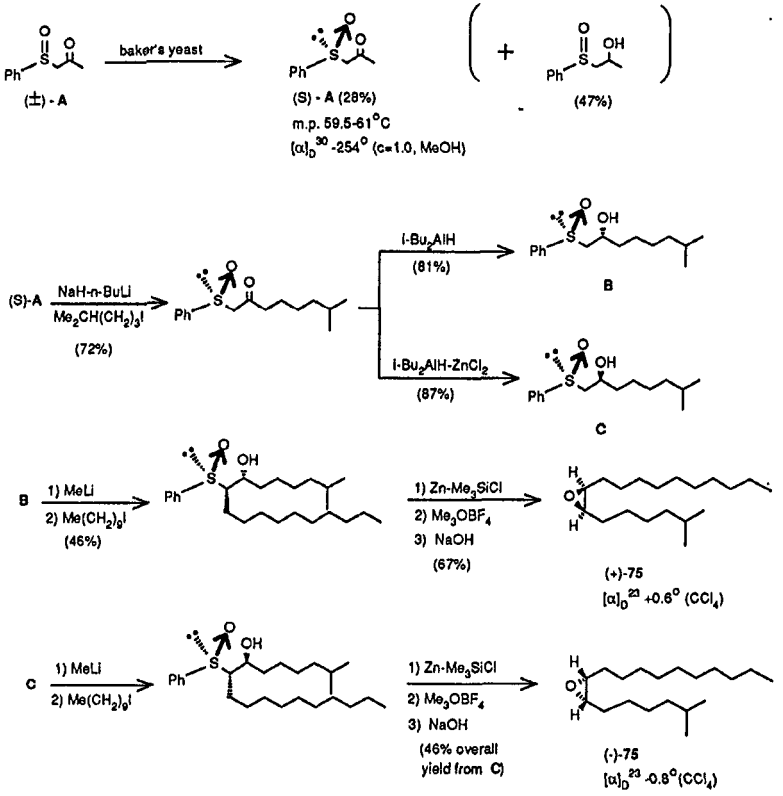
Otto et al. treated (±)-epoxy acid **A** with *Pseudomonas* NRRL-B-2994 and obtained (9*S*,10*R*)-**A.** Kolbe electrolysis of this with *n*-butyric acid gave (+)-**75** (Scheme 204).[269]



Scheme 204

Over a decade ago, Iriuchijima reduced (±)-phenylsulfinylacetone **A** with baker's yeast to give in 28% yield optically pure (*S*)-**A.**[270] Starting from (*S*)-**A,**

Fujisawa and his co-workers accomplished the synthesis of (+)- and (−)-**75**, demonstrating the utility of the chiral sulfoxide **A** (Scheme 205).[271]



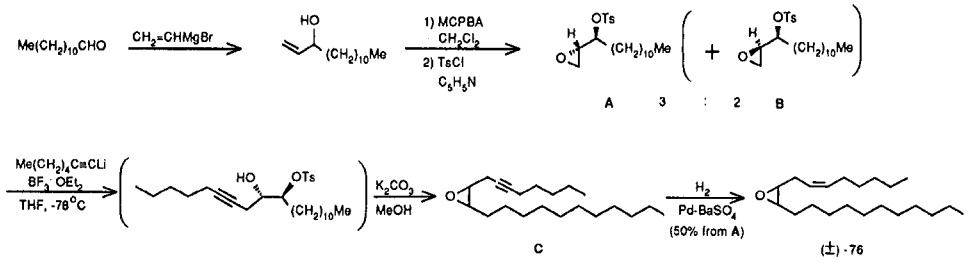
Scheme 205

B. (6*Z*,9*S*,10*R*)-9,10-Epoxy-6-henicosene **76** ($C_{21}H_{40}O$)

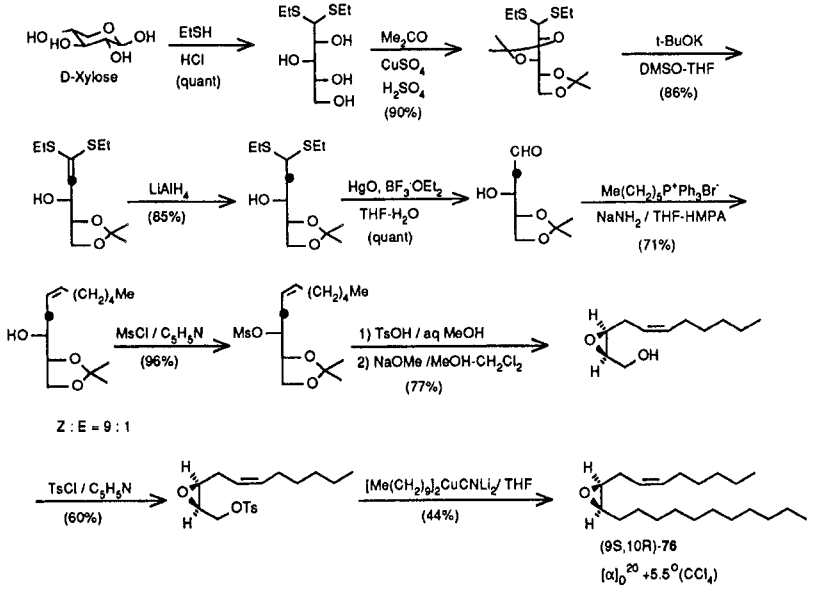
This is a pheromone component of the ruby tiger moth (*Phragmatobia fuliginosa*). A synthesis of (±)-**76** by Bell and Clacclo employed alkylation of tosyloxy epoxide **A** to give **C** (Scheme 206).[272]

D-Xylose was converted to (9*S*,10*R*)-**76** by Rollin and Pougny (Scheme 207).[273] Their product, however, was contaminated with 10% of its (*E*)-isomer.

Another synthesis of both the enantiomers of **76** was recently achieved by Ebata and Mori (Scheme 208).[274] Two chiral centers of **76** were introduced by Sharpless epoxidation to give **B** from **A**. Recrystallization of **B** gave pure **B**



Scheme 206

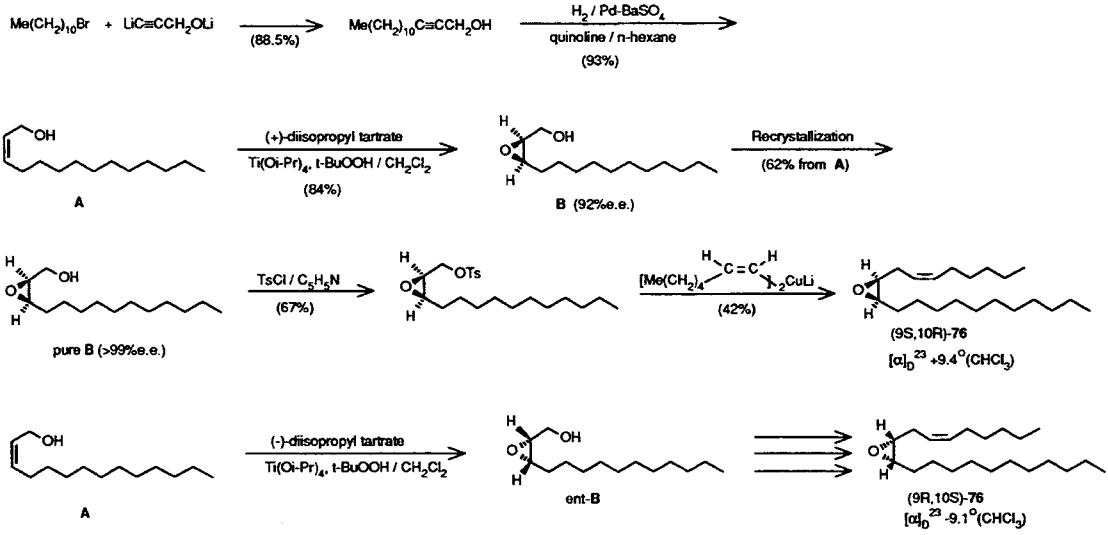


Scheme 207

with > 99% e.e. Normant's carbocupration method was used for the chain-elongation of the tosylate **C** to give **76.** This process was quite efficient to give **76** in five steps from propargyl alcohol in 14% overall yield.

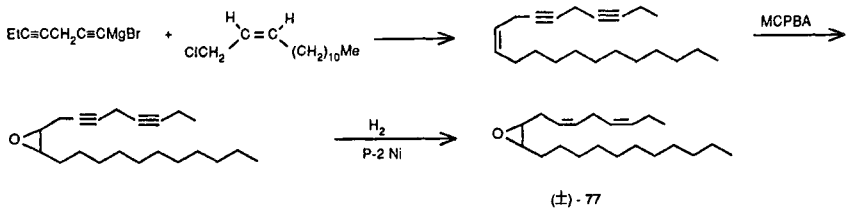
C. (3*Z*,6*Z*,9*S*,10*R*)-9,10-Epoxy-3,6-henicosadiene 77 ($C_{21}H_{38}O$)

This is a pheromone component of the salt marsh caterpillar moth (*Estigmene acrea*), the fall webworm moth (*Hyphantria cunea*), and two Asian moths (*Creatonotos transiens* and *C. gangis*).


Me(CH2)10Br + LiC≡CCH2OLi
(88.5%)
Me(CH2)10C≡CCH2OH
H2 / Pd-BaSO4
quinoline / n-hexane
(93%)
A
(+)-diisopropyl tartrate
Ti(Oi-Pr)4, t-BuOOH / CH2Cl2
(84%)
B (92%e.e.)
Recrystallization
(62% from A)
pure B (>99%e.e.)
TsCl / C5H5N
(67%)
[Me(CH2)4
2CuLi
(42%)
(9S,10R)-76
[α]D23 +9.4°(CHCl3)
(-)-diisopropyl tartrate
Ti(Oi-Pr)4, t-BuOOH / CH2Cl2
ent-B
(9R,10S)-76
[α]D23 -9.1°(CHCl3)

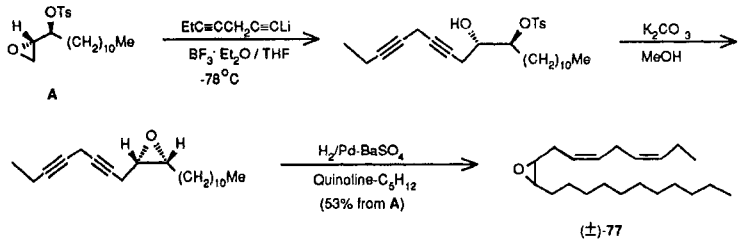
Scheme 208

Nikolaeva and Kovalev reported a synthesis of (±)-**77** (Scheme 209).[275]



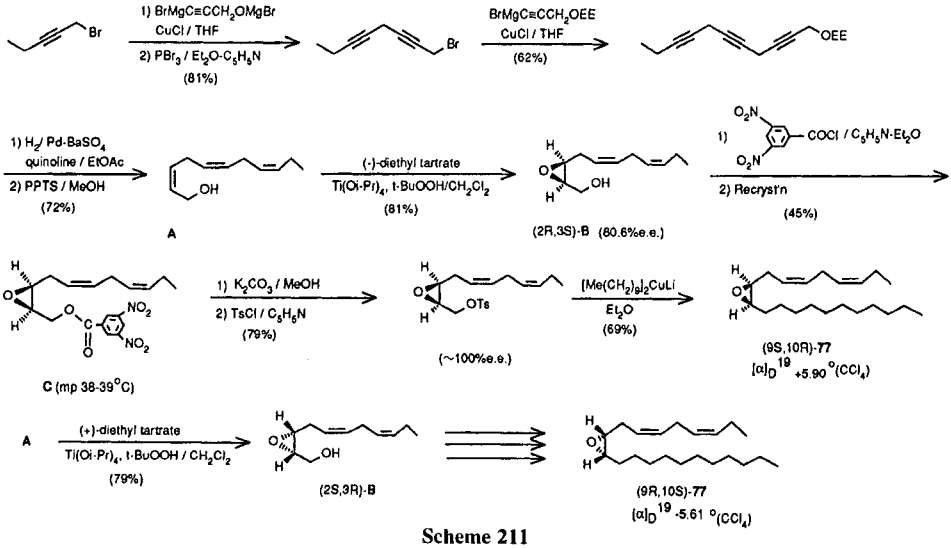
Scheme 209

Another synthesis of (±)-**77** was reported by Bell and Clacclo by the same method as used for the synthesis of (±)-**76** (Scheme 210).[272]



Scheme 210

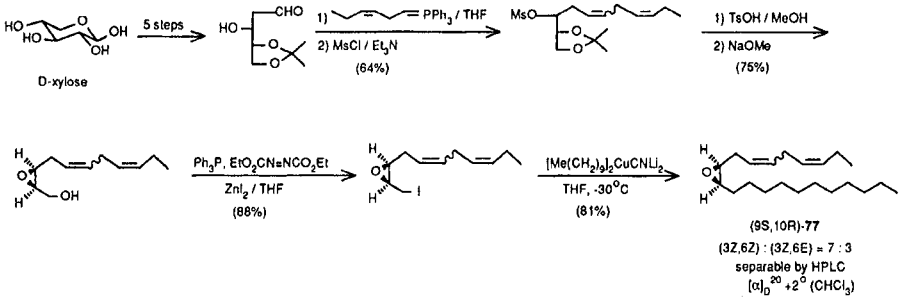
Mori and Ebata synthesized both the enantiomers of **77** employing the Sharpless asymmetric epoxidation (Scheme 211).[261,262] Epoxidation of trienol **A** in



Scheme 211

the presence of (−)-diethyl tartrate gave (2*R*,3*S*)-**B**, while the use of (+)-diethyl tartrate afforded (2*S*,3*R*)-**B**. Purification of **B** was achieved by recrystallization of **C** to give optically pure **B**, the tosylate of which was treated with lithium didecylcuprate to furnish (9*S*,10*R*)-(+)-**77**. Similarly, (−)-**77** was also synthesized. Only (9*S*,10*R*)-**77** was bioactive when tested by EAG.

Pougny and Rollin reported a synthesis of (+)-**77** starting from D-xylose (Scheme 212)[276] in a manner similar to their synthesis of **76** (Scheme 207).[273]



Scheme 212

A synthesis of related chiral *bis*-homoallylic epoxides was achieved employing asymmetric epoxidation.[277]

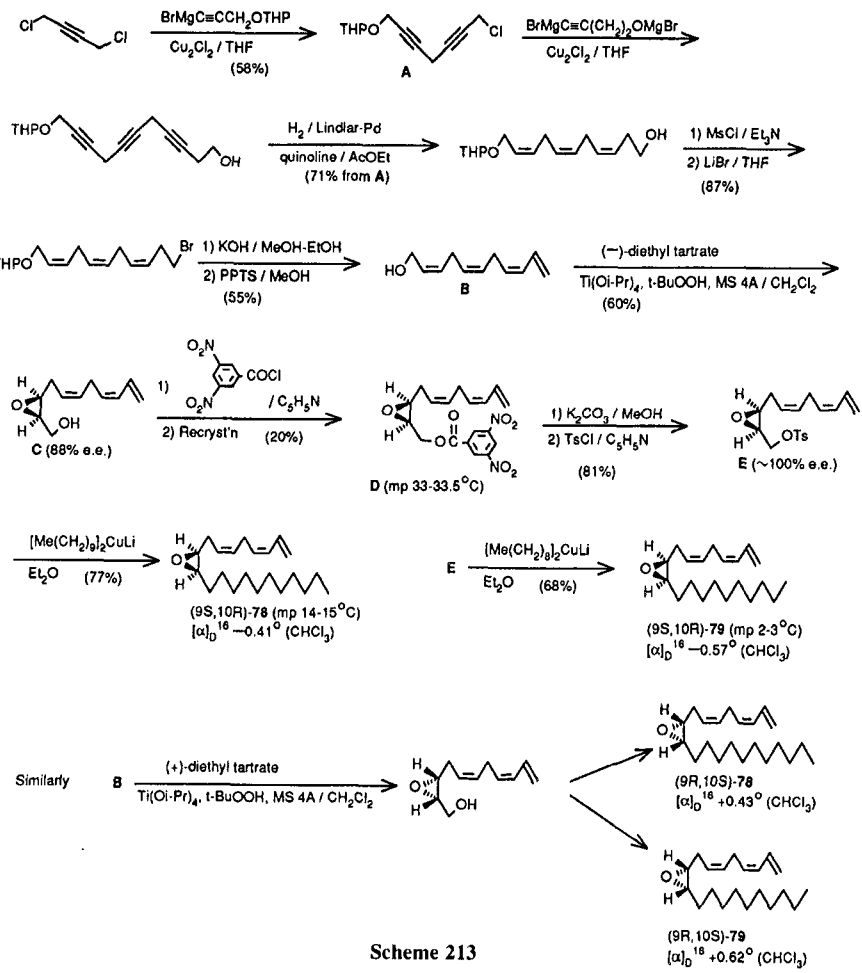
D. (3*Z*,6*Z*,9*S*,10*R*)-9,10-Epoxy-1,3,6-icosatriene **78** ($C_{20}H_{34}O$) and (3*Z*,6*Z*,9*S*,10*R*)-9,10-Epoxy-1,3,6-henicosatriene **79** ($C_{21}H_{36}O$)

These are the pheromone components of the fall webworm moth (*Hyphantria cunea*). A mixture of (3*Z*,6*Z*,9*S*,10*R*)-**77**, (9*Z*,12*Z*)-9,12-octadecadienal, (9*Z*,12*Z*,15*Z*)-9,12,15-octadecatrienal, **78**, and **79** attracted male fall webworm moths into traps.

Both the enantiomers of **78** and **79** were synthesized employing the Sharpless asymmetric epoxidation in the manner similar to the synthesis of **77** (Scheme 213).[278,279]

11. CHIRAL ALCOHOLS AND THEIR ESTERS AS PHEROMONES

Many chiral alcohols and their esters serve as insect pheromones. In this section, individual pheromones are arranged in increasing order of the length of the main carbon-chain of alcohols or the alcohol part of esters. Use of organ-



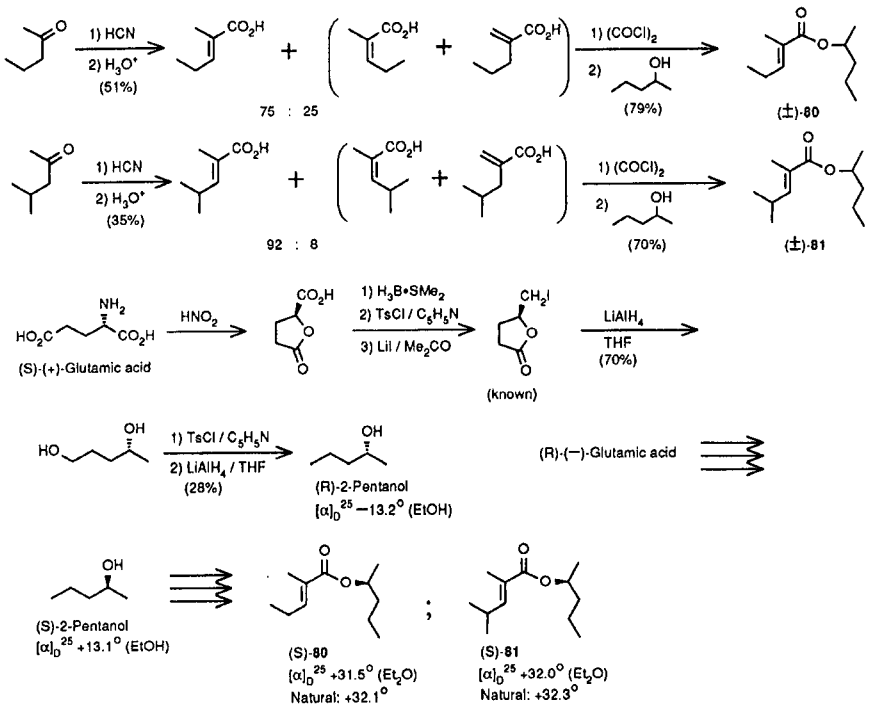
Scheme 213

oboranes in enantioselective syntheses of alcohols was recently reviewed.[280–282]

A. Dominicalure 1 [(*S*)-1-Methylbutyl (*E*)-2-Methyl-2-pentenoate] 80 ($C_{11}H_{20}O_2$) and Dominicalure 2 [(*S*)-1-Methylbutyl (*E*)-2,4-Dimethyl-2-pentenoate] 81 ($C_{12}H_{22}O_2$)

Dominicalure 1 **(80)** and 2 **(81)** are the male-produced aggregation pheromones of the lesser grain borer (*Rhyzopertha dominica*). They are attractive to both sexes of that insect.

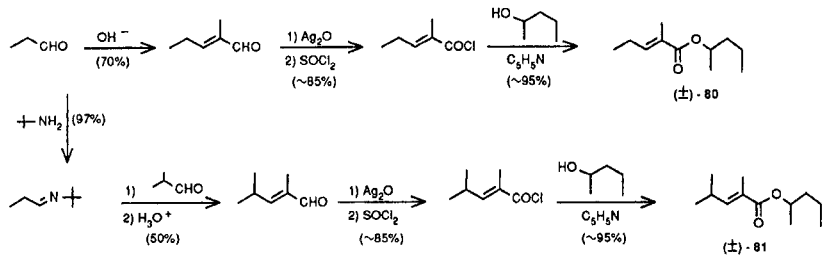
The racemates and the enantiomers of **80** and **81** were synthesized (Scheme 214).[283] The enantiomers of 2-pentanol were prepared from the enantiomers of



Scheme 214

glutamic acid. The natural **80** and **81** were shown to be enantiomerically pure (+)-isomers, as revealed by the $[\alpha]_D$ measurement and NMR study. The natural (*S*)-(+)-**80** and **81** were about twice as active as the unnatural (*R*)-(−)-**80** and **81** as assayed by their field test.

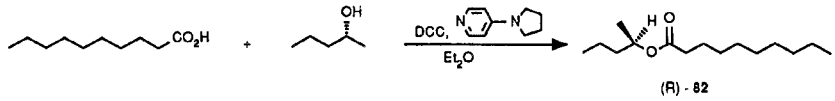
Moiseenkov and his co-workers also synthesized (±)-**80** and (±)-**81** (Scheme 215).[284]



Scheme 215

B. (*R*)-1-Methylbutyl Decanoate 82 ($C_{15}H_{30}O_2$)

This is the pheromone of the bagworm moth (*Thyridopteryx ephemeraeformis*).[285] Both (*R*)-**82** and (*S*)-**82** were synthesized and bioassayed (Scheme 216).[285] Only (*R*)-**82** was active. The (*S*)-enantiomer was inactive without any inhibitory effect against (*R*)-**82.**

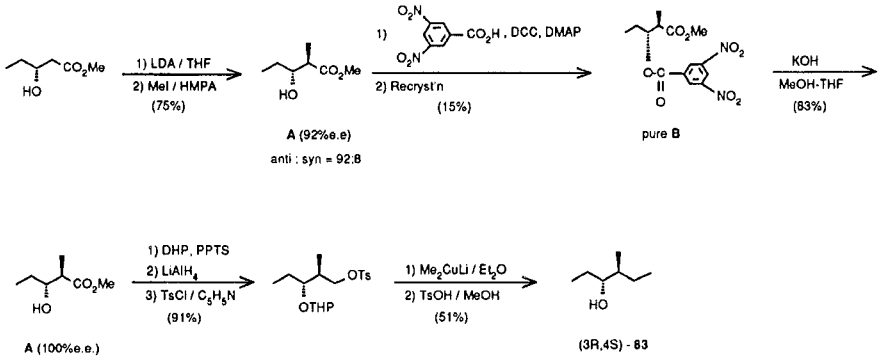


Scheme 216

C. (3*R*,4*S*)-4-Methyl-3-hexanol 83 ($C_7H_{16}O$)

Pasteels et al. identified **83** as a pheromone by extracting the heads of all adult castes of the ant (*Tetramorium impurum*).[286]

Kato and Mori synthesized **83** starting from methyl (*R*)-3-hydroxypentanoate (Scheme 217).[287] Because of the unsatisfactory enantiomeric purity (92% e.e.)



Scheme 217

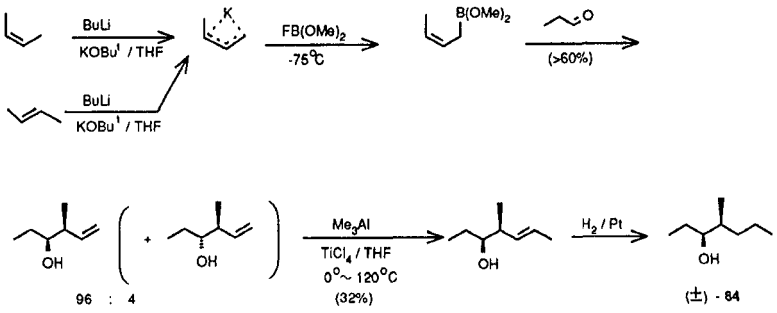
of the starting material, the intermediate **A** was purified as its 3,5-dinitrobenzoate **B** to make it both diastereomerically and enantiomerically pure.

D. (3*S*,4*S*)-4-Methyl-3-heptanol 84 ($C_8H_{18}O$)

This is a component of the aggregation pheromone of the smaller European elm bark beetle (*Scolytus multistriatus*).[288,289] Recently, its (3*R*,4*S*)-isomer was identified as the trail pheromone of the ant (*Leptogenys diminuta*).[290]

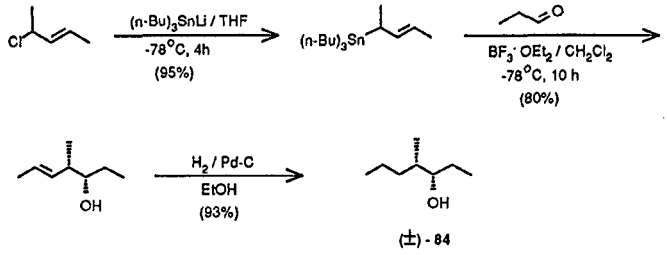
(1) Syntheses of (±)-84

Three syntheses of (3*R**,4*R**)-(±)-**84** were reported. Schlosser and Fujita synthesized (±)-**84** by the addition of dimethyl (*Z*)-2-butenylboronate to propanal, followed by the transfer of a methyl group of trimethylaluminum to the double bond in the presence of titanium tetrachloride (Scheme 218).[291]



Scheme 218

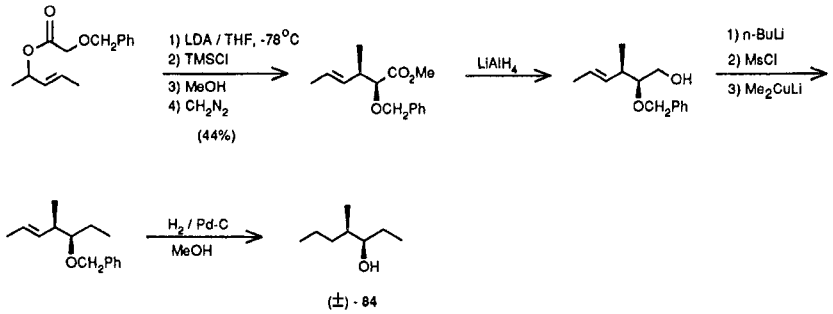
Koreeda and Tanaka employed the Lewis acid-catalyzed addition of tri-*n*-butyl-1-methyl-2-butenyltin to propanal for the synthesis of (±)-**84** (Scheme 219).[292]



Scheme 219

Kallmerten and Gould prepared (±)-**84** by the enolate Claisen rearrangement of *O*-benzylated 1-methyl-(*E*)-2-butenyl glycolate to give an acyclic product with *syn*-stereochemistry (Scheme 220).[293]

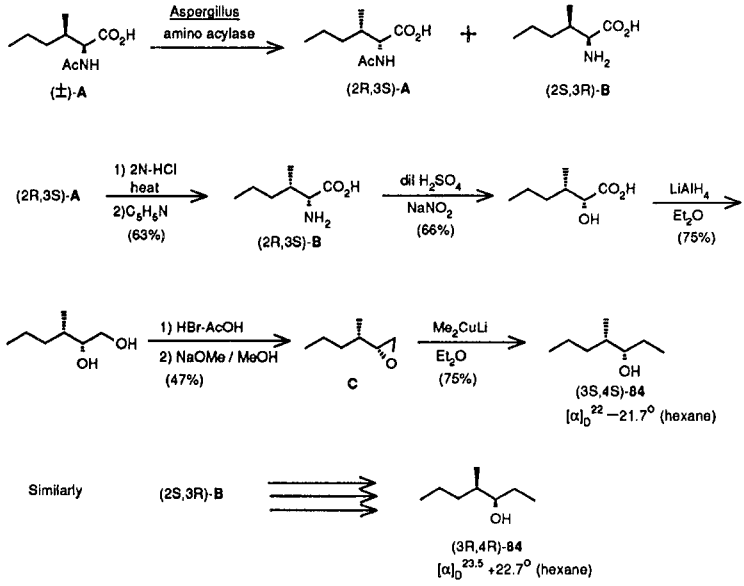
Optical resolution of (±)-**84** was reported by Blight et al.[294]



Scheme 220

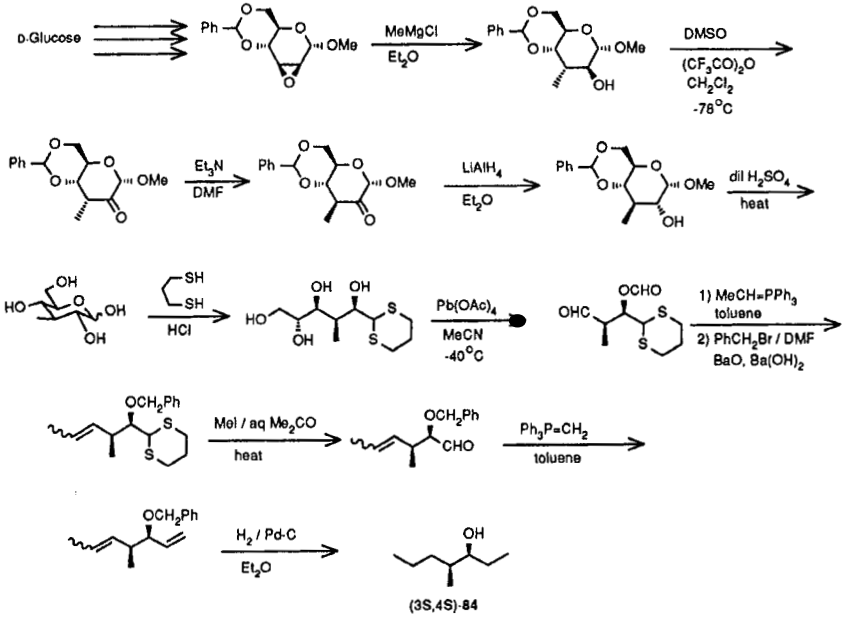
(2) Syntheses of Optically Active 84 Starting from Chiral Building Blocks

Mori and Iwasawa's first success in synthesizing the natural (3*S*,4*S*)-**84** in 1980 was based on the enzymatic resolution of (±)-*threo*-2-acetamino-3-methylhexanoic acid **A** (Scheme 221).[295] The amino acid (2*R*,3*S*)-**B** was converted to epoxide **C**, which was treated with lithium dimethylcuprate to give (3*S*,4*S*)-**84.**



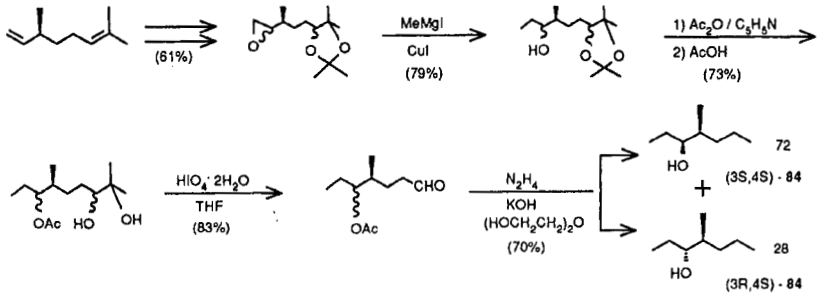
Scheme 221

Pougny and Sinaÿ synthesized, in 35% overall yield, the natural and bioactive (3*S*,4*S*)-**84** starting from D-glucose (Scheme 222).[296]



Scheme 222

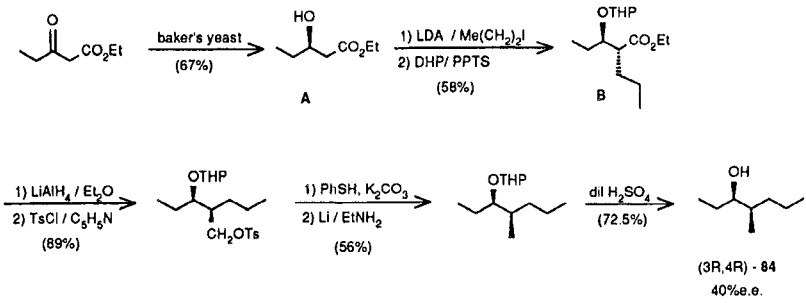
A synthesis of (−)-**84** from (+)-3,7-dimethyl-1,6-octadiene was reported by Serebryakov and his co-workers (Scheme 223).[297]



Scheme 223

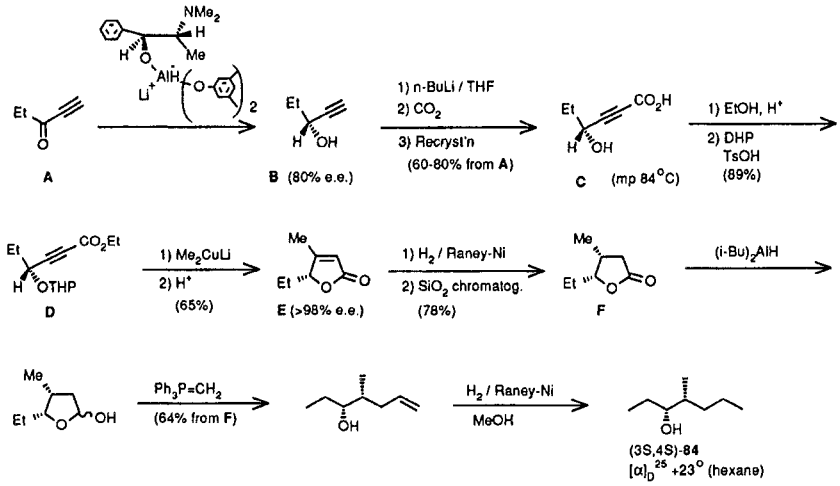
(3) Syntheses of Optically Active 84 by Asymmetric Reactions

In Fráter's synthesis of (3*R*,4*R*)-**84,** partially enantioselective reduction of ethyl 3-oxopentanoate to (*R*)-**A** with baker's yeast was followed by its diastereoselective alkylation to produce **B,** which eventually furnished (3*R*,4*R*)-**84** of 40% e.e. (Scheme 224).[298]



Scheme 224

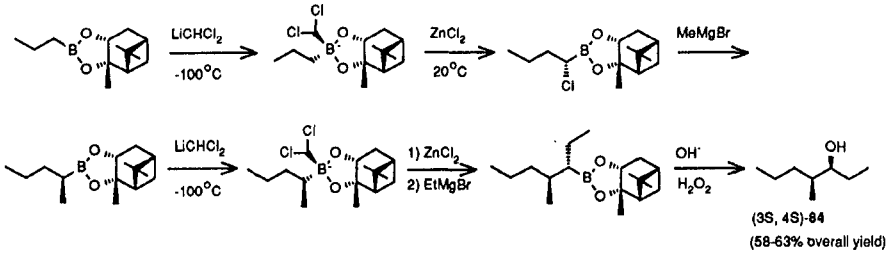
Vigneron et al. synthesized pure (3*S*,4*S*)-**84** by employing their asymmetric reduction of acetylenic ketones (Scheme 225).[299,300] Their asymmetric reduction of **A** afforded **B** (80% e.e.). The acid **C** prepared from **B** could be recrystallized to give **C** of high e.e., which afforded unsaturated lactone **E** with



Scheme 225

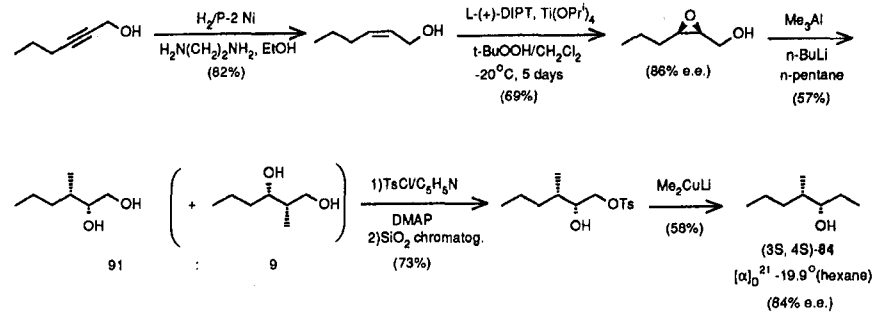
>98% e.e.[300] Its hydrogenation was fairly selective to give the *cis*-lactone **F** as the major product. The lactone **F** was further manipulated to give (3*S*,4*S*)-**84.**

Matteson's enantioselective synthesis via pinanediol boronic esters yielded (3*S*,4*S*)-**84** of high e.e. (Scheme 226).[301,302]



Scheme 226

Nakagawa and Mori synthesized (3*S*,4*S*)-**84** employing asymmetric epoxidation coupled with regioselective cleavage of the epoxy ring with trimethylaluminum (Scheme 227).[303]

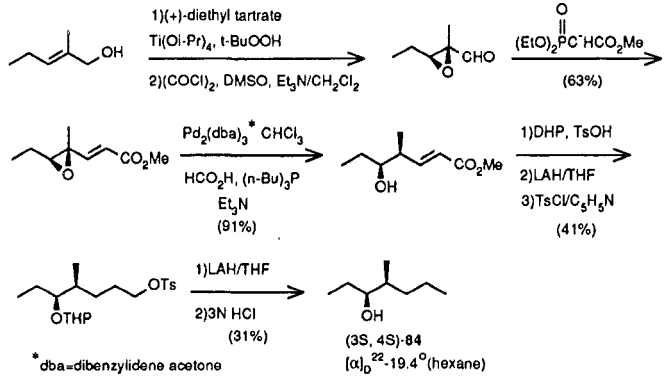


Scheme 227

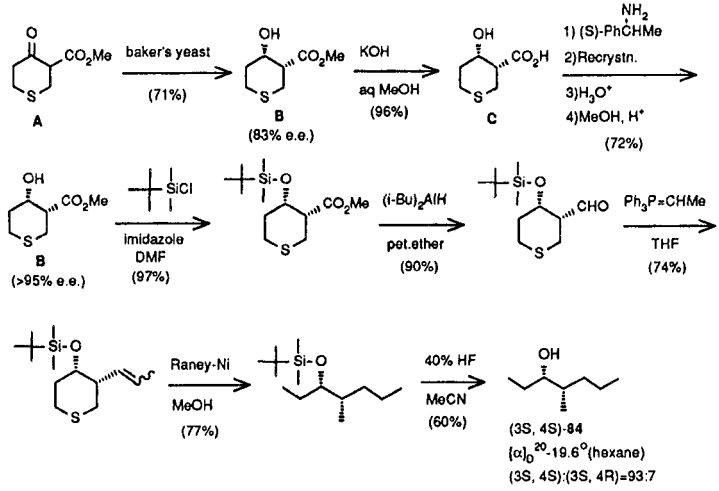
Shimizu and co-workers prepared (3*S*,4*S*)-**84** (92% e.e.) by means of the Sharpless epoxidation and palladium-catalyzed selective hydrogenolysis of the derived alkenyl epoxide with formic acid (Scheme 228).[304]

Hoffmann et al. reduced cyclic β-keto ester **A** (Scheme 229) to give hydroxy ester **B** (83% e.e.), which was purified by recrystallizing the amine salt of the corresponding acid **C.**[305] Starting from the pure ester **B,** (3*S*,4*S*)-**84** was synthesized.

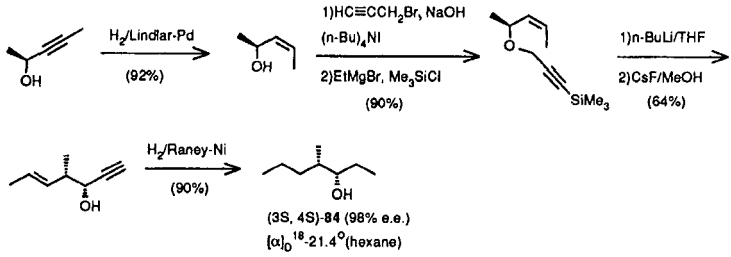
Nakai and co-workers employed asymmetric [2.3]-Wittig rearrangement for the synthesis of (3*S*,4*S*)-**84** (Scheme 230).[306] The starting alkynol was obtained by optical resolution.



Scheme 228

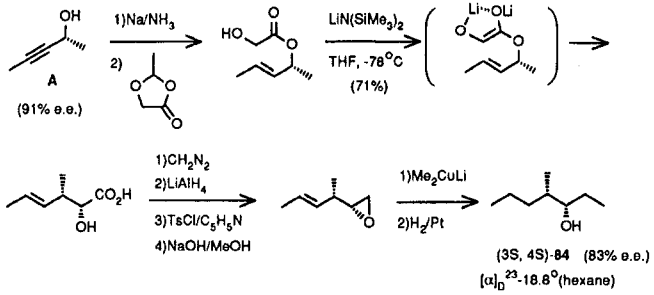


Scheme 229



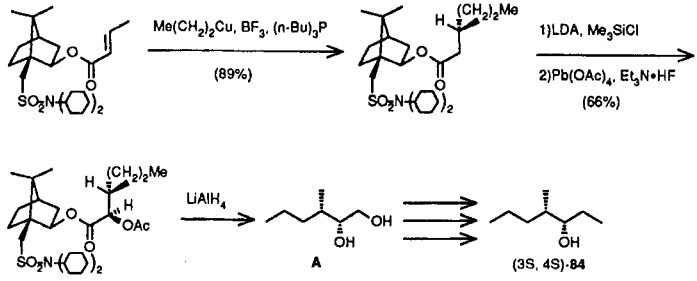
Scheme 230

Fujisawa et al. prepared (3*S*,4*S*)-**84** employing chirality transfer in the ester enolate Claisen rearrangement of (2*E*,1*R*)-1-methyl-2-butenyl glycolate as the key-step (Scheme 231).[307]



Scheme 231

Oppolzer and Dudfield employed asymmetric α-acetoxylation of a carboxylic ester for the preparation of glycol **A** (Scheme 232),[308] which was the key-intermediate in several other syntheses of (3*S*,4*S*)-**84.**

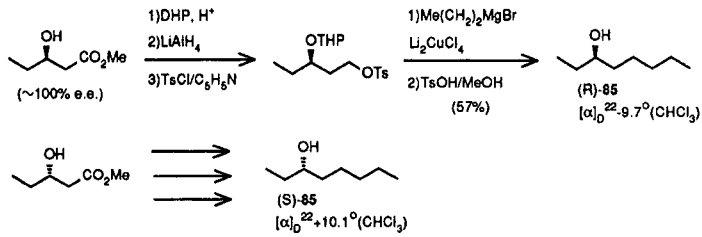


Scheme 232

E. 3-Octanol 85 ($C_8H_{18}O$)

The mandibular glands of *Myrmica* ants contain 3-octanol **85.** *Myrmica scabrinodis* and *M. rubra* were attracted by (*R*)-**85.**[309] In the case of *M. scabrinodis*, the naturally occurring mixture of (*R*)-**85** and (*S*)-**85** (9 : 1) is more active than (*R*)-**85.**[309] Other ants like *Crematogaster castanea* and *C. liengmei* seem to use (*S*)-**85** as their pheromone.[310]

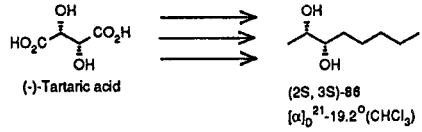
Pure enantiomers of **85** were synthesized from pure enantiomers of methyl 3-hydroxypentanoate (Scheme 233) by conventional chain-elongation.[311]



Scheme 233

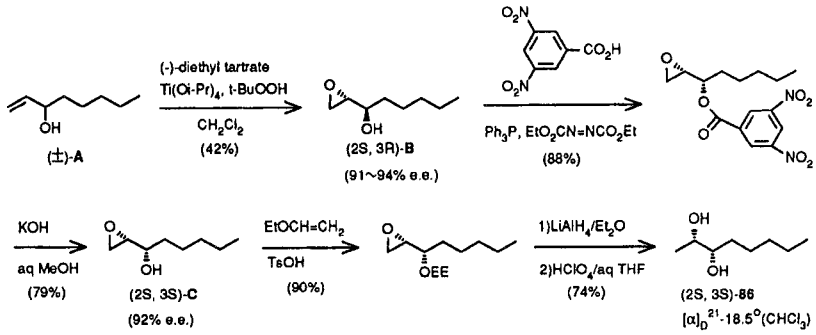
F. (2*S*,3*S*)-2,3-Octanediol **86** ($C_8H_{18}O_2$)

The grape borer (*Xylotrechus pyrrhoderus*) is a major pest of grapevines in Japan. The male-produced sex pheromone is a mixture of (2*S*,3*S*)-2,3-octanediol **86** and (*S*)-2-hydroxy-3-octanone **137** in a ratio of 80:20–95:5. Sakai et al. prepared both the enantiomers of **86** from tartaric acid (Scheme 234; details of the synthesis are not reported).[312]



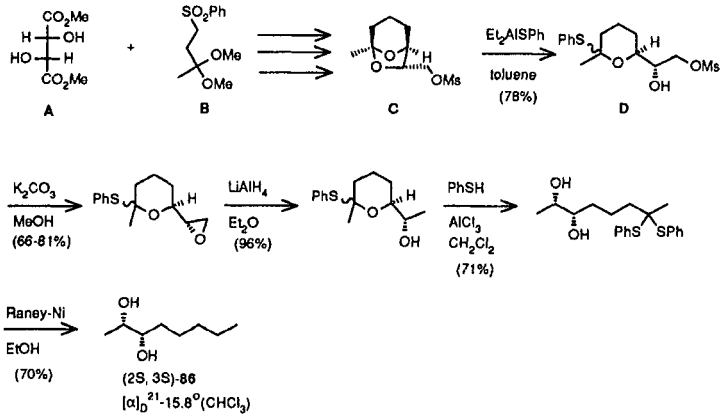
Scheme 234

Mori and Otsuka synthesized (2*S*,3*S*)-**86** from (±)-1-octen-3-ol employing the Sharpless asymmetric epoxidation as the initial step (Scheme 235).[313] The overall yield of (2*S*,3*S*)-**86** from (±)-**A** was 19% in six steps.



Scheme 235

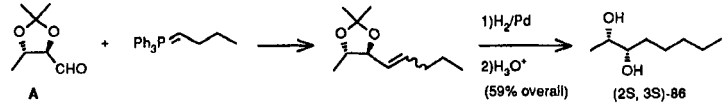
Masaki's synthesis of (2*S*,3*S*)-**86** utilized (+)-tartaric acid as the starting material (Scheme 236).[255] By the route which had been employed in their syn-



Scheme 236

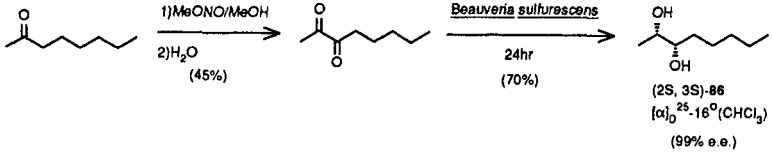
thesis of (+)-*exo*-brevicomin, (+)-dimethyl tartrate **A** and the sulfone **B** were converted to **C.** Cleavage of the bicyclic acetal **C** to yield **D** was followed by further transformation to generate (2*S*,3*S*)-**86.**

Servi and his co-workers also prepared (2*S*,3*S*)-**86** (Scheme 237).[314] The starting material **A** was prepared by employing baker's yeast in the key-reduction step.[315]



Scheme 237

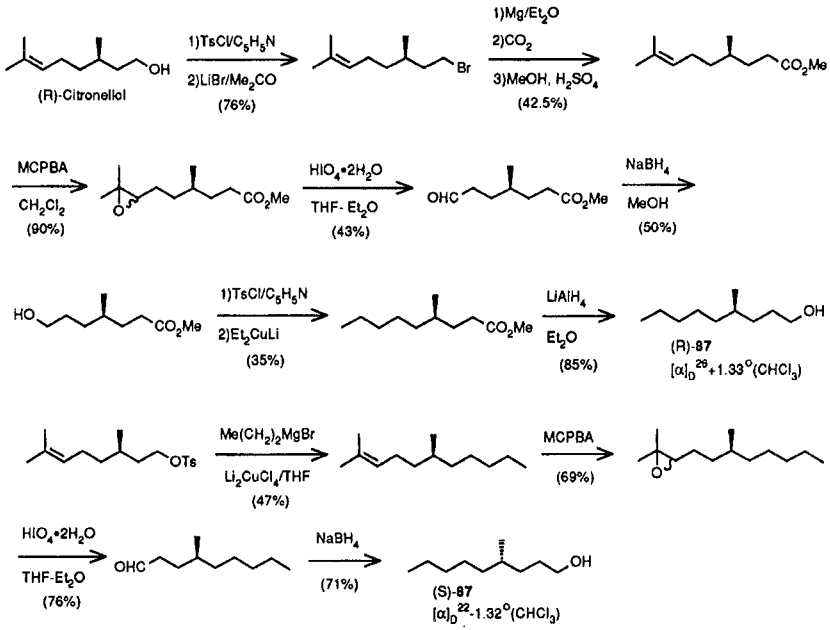
Veschambre reduced 2,3-octanedione with a fungus, *Beauveria sulfurescens*, to give (2*S*,3*S*)-**86** (Scheme 238).[316]



Scheme 238

G. (*R*)-4-Methyl-1-nonanol **87** ($C_{10}H_{22}O$)

This is the sex pheromone of the yellow mealworm (*Tenebrio molitor*). By synthesizing both the enantiomers of **87** from (*R*)-citronellol, Tanaka et al. determined the absolute configuration of the natural **87** as *R* (Scheme 239).[317]



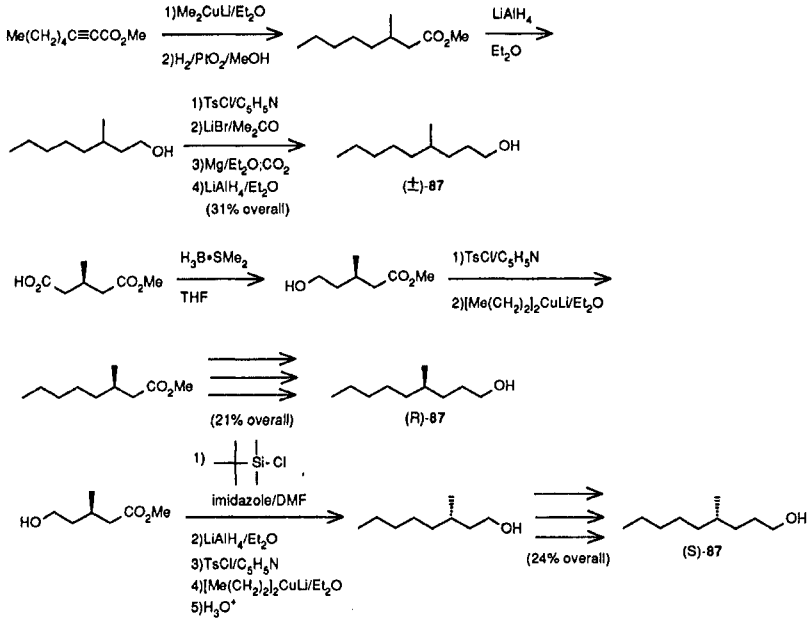
Scheme 239

Their synthetic (*R*)-**87** was as active as the natural **87**. (*S*)-**87** did not show any synergistic or antagonistic activity.

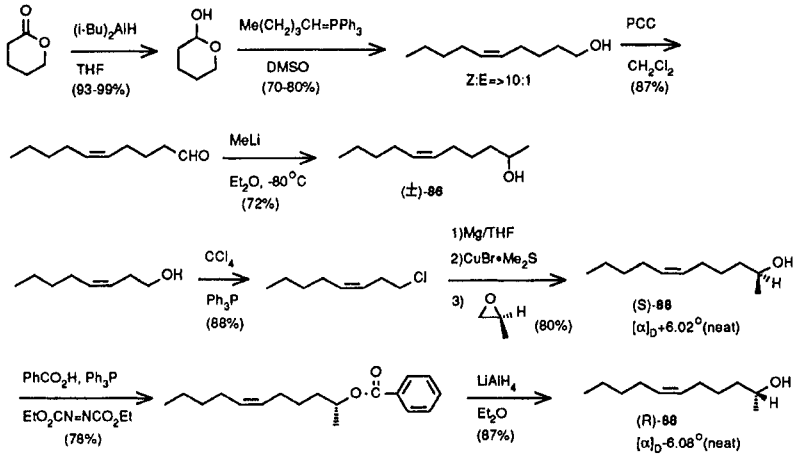
Carpita et al. synthesized (±)-**87** and the two enantiomers of **87** (Scheme 240).[318]

H. (*R*)-Nostrenol [(*Z*)-6-Undecen-2-ol] **88** ($C_{11}H_{22}O$)

This is the volatile signal of ant-lions (*Euroleon nostras* and *Grocus bore*). Baeckström et al. synthesized (±)-**88** and the two enantiomers of **88** (Scheme 241).[319] The natural compound was shown to be enantiomerically pure (*R*)-**88** (> 99.9% e.e.).[319]



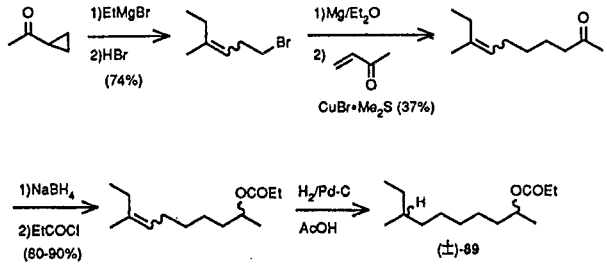
Scheme 240



Scheme 241

I. 1,7-Dimethylnonyl Propanoate 89 ($C_{14}H_{28}O_2$)

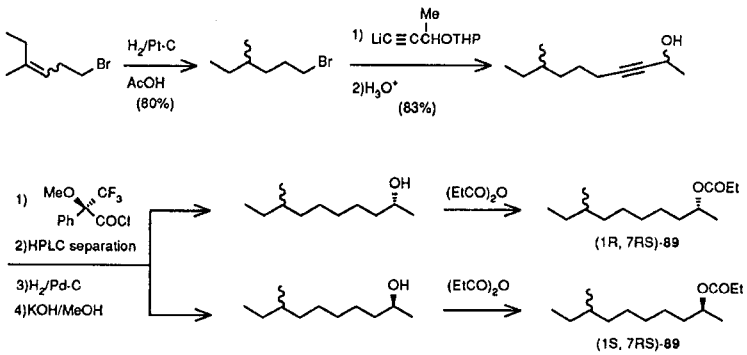
Guss et al. isolated 10 μg of the female-produced sex pheromone of the western corn rootworm (*Diabrotica virgifera virgifera*) and identified it as 1,7-dimethylnonyl propanoate **89**.[320] A diastereomeric mixture of all of the four isomers of **89** was synthesized (Scheme 242) and shown to be attractive against



Scheme 242

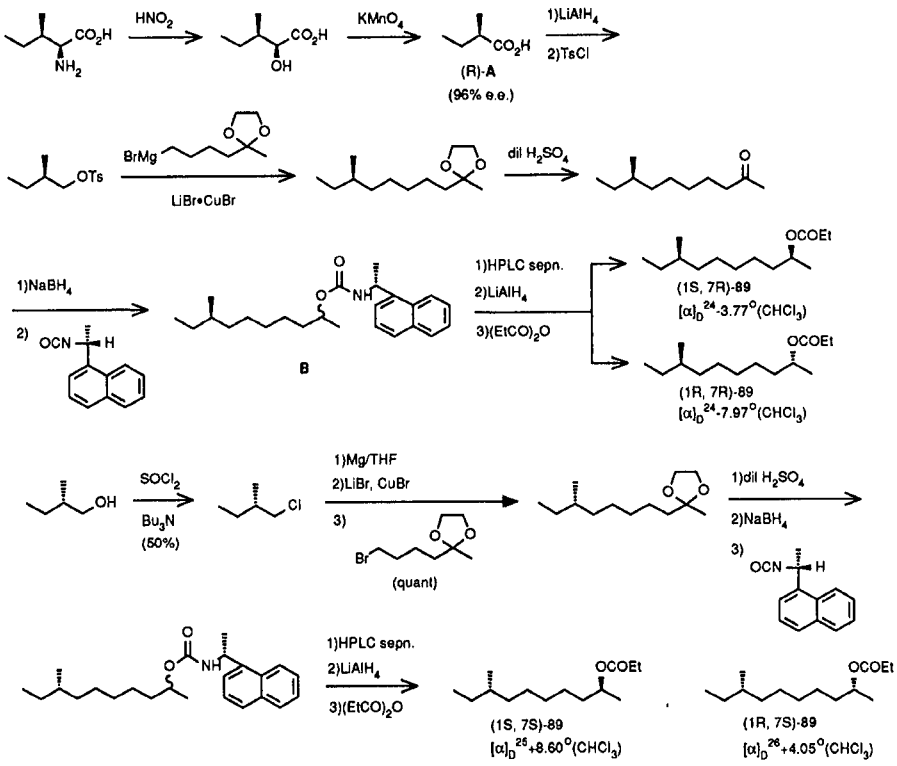
the males of the western corn rootworm.[320] It was also attractive against *D. virgifera zeae*, Mexican corn rootworm (*D. longicornis*), *D. porracea*, and northern corn rootworm (*D. barberi*).[320]

All of the four possible stereoisomers of **89** was prepared by Sonnet et al. via optical resolution of the intermediates.[321] They first synthesized (1*R*,7*RS*)-**89** and (1*S*,7*RS*)-**89** (Scheme 243).[321] This synthesis involved the HPLC separa-



Scheme 243

tion of the diastereomers employing (*R*)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) as the derivatizing agent. Subsequently, they synthesized all of the four isomers by HPLC separation of the intermediates (Scheme 244).[322] For the preparation of (1*S*,7*S*)-**89** and (1*R*,7*S*)-**89,** commercially avail-



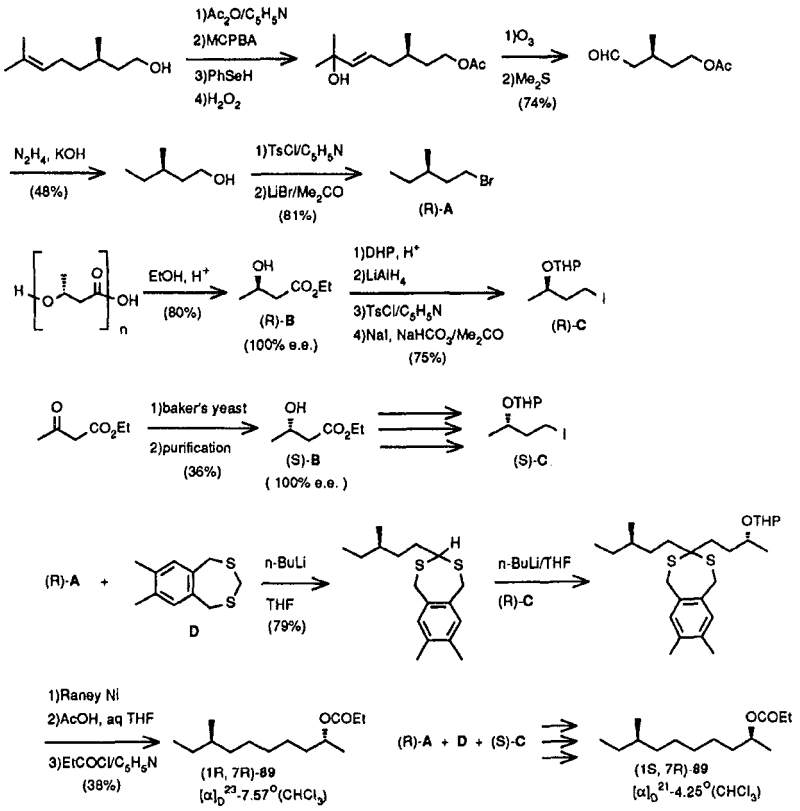
Scheme 244

able (*S*)-2-methyl-1-butanol (99.2–99.5% e.e.) was employed as a starting material, while for the synthesis of (1*S*,7*R*)-**89** and (1*R*,7*R*)-**89,** D-isoleucine was employed. The key-step was the HPLC separation of the diastereomeric carbamates **B** derived from the corresponding alcohols and (*R*)-1-(1-naphthyl)ethyl isocyanate.

Biotests of the four synthetic isomers of **89** revealed the following stereochemistry-bioactivity relationships.[322–324] Males of *D. virgifera virgifera* and *D. virgifera zeae* responded strongly to the (1*R*,7*R*)-isomer and secondarily to (1*S*,7*R*)-**89,** while *D. porracea* responded exclusively to (1*S*,7*R*)-**89.** The (1*S*,7*S*)- and (1*R*,7*S*)-isomers were inactive in all tests. Synergism or inhibition

was not detected when mixtures of isomers were tested against *D. virgifera virgifera.*[323] Only the (1*R*,7*R*)-isomer was attractive to the northern corn rootworm (*D. barberi*).[324] Inhibition of *D. barberi* response to (1*R*,7*R*)-**89** took place when either the (1*S*,7*R*)- or (1*S*,7*S*)-isomers were in the testing sample. (1*S*,7*S*)-**89** was inactive against *D. barberi*. Thus, the propanoates attractive to rootworm species were (1*R*,7*R*)-**89** and (1*S*,7*R*)-**89.**

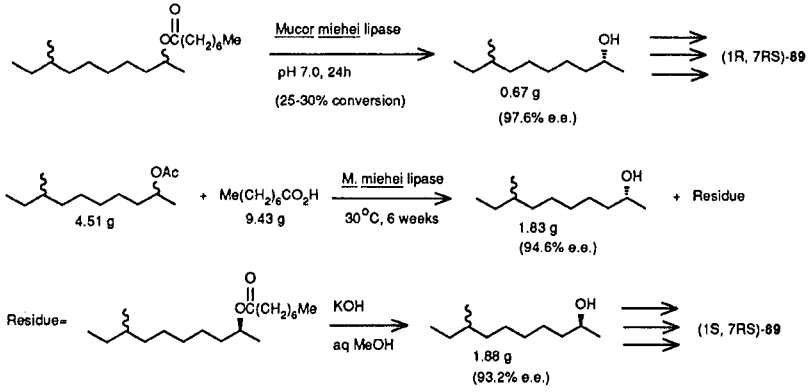
Mori and Watanabe accomplished the enantioselective synthesis of bioactive (1*R*,7*R*)-**89** and (1*S*,7*R*)-**89,** starting from chiral building blocks as shown in Scheme 245.[325] Building block (*R*)-**A** was prepared from enantiomerically pure



Scheme 245

(*R*)-citronellol, while the enantiomers of another building block **C** was derived from the pure enantiomers of ethyl 3-hydroxybutanoate **B.** Connection of **A** with **B** employing **D** as the pivot generated the carbon framework of **89,** which finally yielded (1*R*,7*R*)-**89** and (1*S*,7*R*)-**89.**

By employing *Mucor miehei* lipase as the resolving agent, (1*R*,7*RS*)-**89** and (1*S*,7*RS*)-**89** were prepared by Sonnet and Baillargeon (Scheme 246).[326]



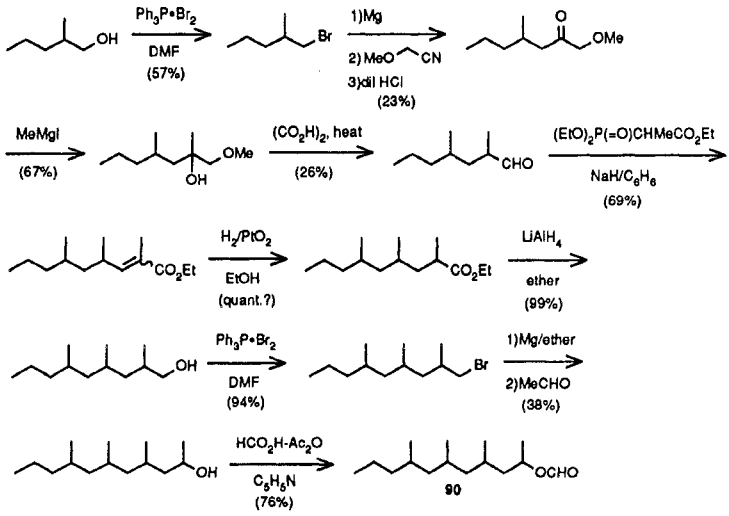
Scheme 246

A synthesis of (1*RS*,7*R*)-**89** was achieved starting from (*S*)-(+)-3,7-dimethyl-1,6-octadiene.[327]

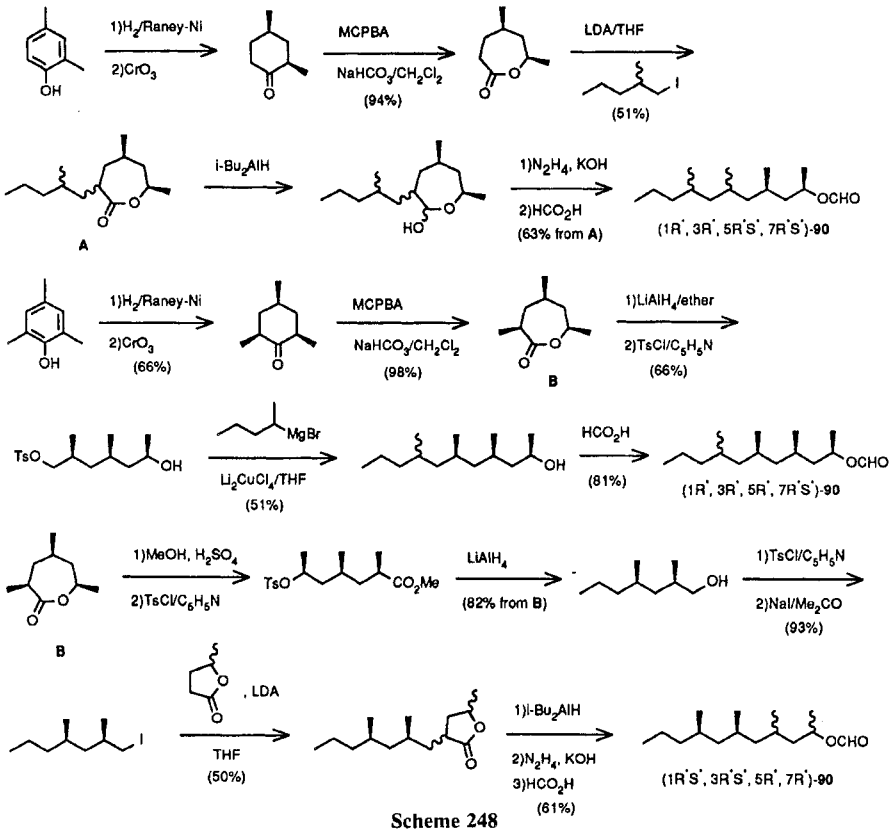
J. Lardolure [(1*R*,3*R*,5*R*,7*R*)-1,3,5,7-Tetramethyldecyl Formate] 90 ($C_{15}H_{30}O_2$)

Lardolure **90** was isolated by Y. Kuwahara et al. as the aggregation pheromone of the acarid mite (*Lardoglyphus konoi*). This mite is a primary pest for stored products such as dried meat and fresh meal. Y. Kuwahara et al. identified the pheromone as 1,3,5,7-tetramethyldecyl formate (**90**) by synthesizing its diastereomeric mixture, which was found to be bioactive. Their synthetic route is shown in Scheme 247.[328] The synthetic mixture consisting of the eight diastereomers of **90** showed seven peaks when analyzed by capillary GLC, and the peak exhibiting the shortest retention time coincided with that of the natural **90.** Y. Kuwahara et al. assigned (*R*)-configuration to C-1 of the natural **90** by comparing both the NMR spectral and chiroptical properties of the natural **90** with (*S*)-1-methylheptyl formate.[328]

In order to establish the stereochemistry of **90,** Mori and S. Kuwahara carried out three different syntheses of **90** (Scheme 248).[329] By these routes, 1,3-*syn*-**90,** 1,3,5-*syn*-**90,** and 5,7-*syn*-**90** were prepared and analyzed by capillary GLC to reveal the fact that all of them exhibited the peak due to the natural **90.** The natural pheromone was therefore thought to have a 1*R*,3*R*,5*R*,7*R* configuration.

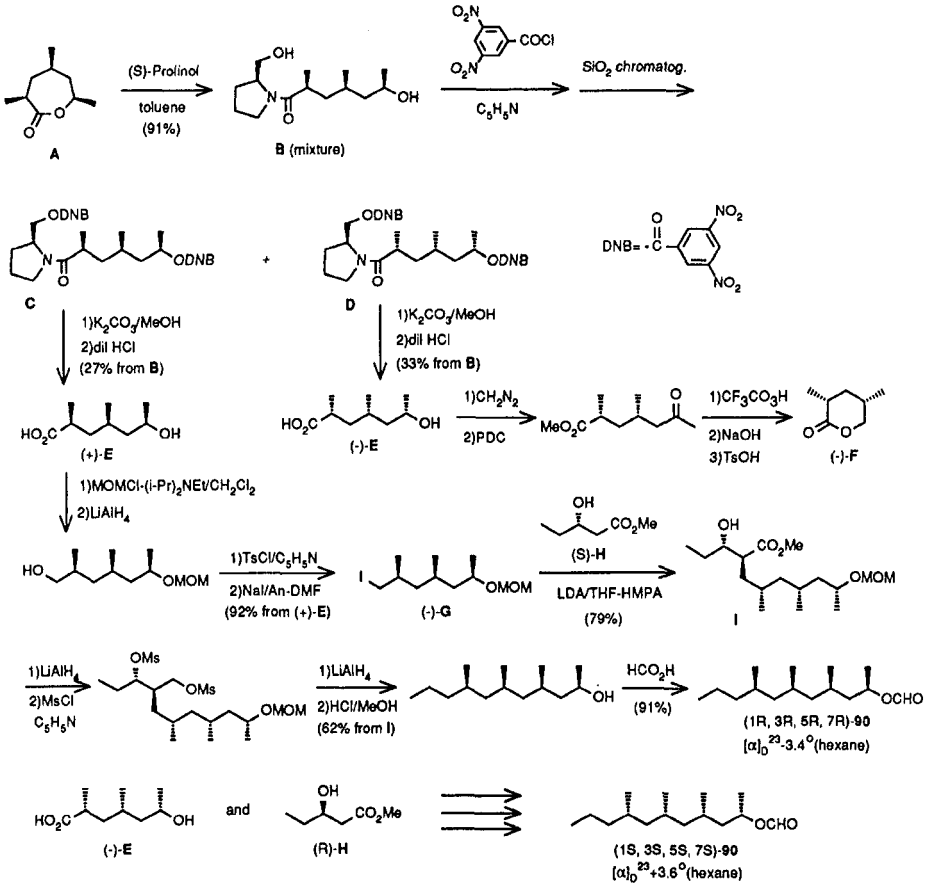


Scheme 247



Scheme 248

Mori and S. Kuwahara then accomplished the synthesis of (1*R*,3*R*,5*R*,7*R*)-**90** and its antipode (Scheme 249).[330] Optical resolution of the lactone **A** yielded



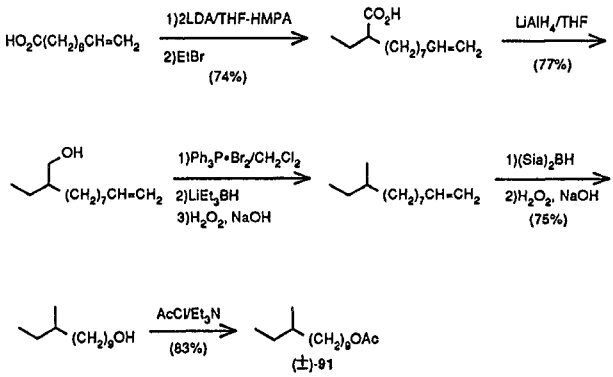
Scheme 249

(+)-**E** and (−)-**E**. The absolute configuration of (−)-**E** as depicted in Scheme 249 was proved by its conversion to the known (−)-**F**. The key building block (−)-**G** was prepared from (+)-**E**. Alkylation of methyl (*S*)-3-hydroxypentanoate (**H**) with (−)-**G** gave the *anti*-alkylation product **I**, which was converted to (1*R*,3*R*,5*R*,7*R*)-**90**. Similarly, (−)-**E** and (*R*)-**H** furnished (1*S*,3*S*,5*S*,7*S*)-**90**. Only (1*R*,3*R*,5*R*,7*R*)-**90** was attractive against the mite.

K. 10-Methyldodecyl Acetate 91 ($C_{15}H_{30}O_2$)

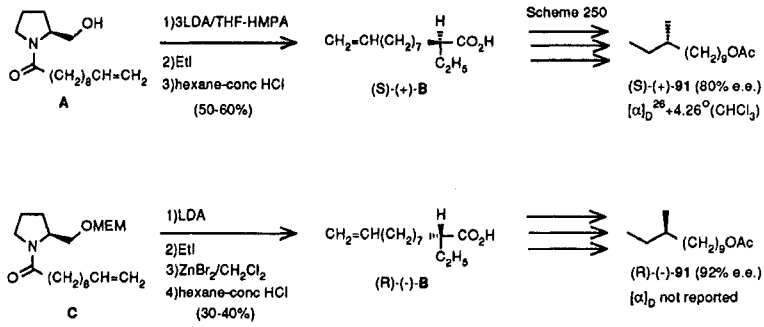
This is a minor component of the pheromone bouquet of the smaller tea tortrix moth (*Adoxophyes* species).[331,332] (*R*)-**91** was found to be slightly more bioactive than (*S*)-**91**.[333] Further field tests suggested that there is an optimum *R*:*S* ratio of 95:5 for trapping of males.[334]

A synthesis of (±)-**91** was reported by Sonnet and Heath (Scheme 250).[335]



Scheme 250

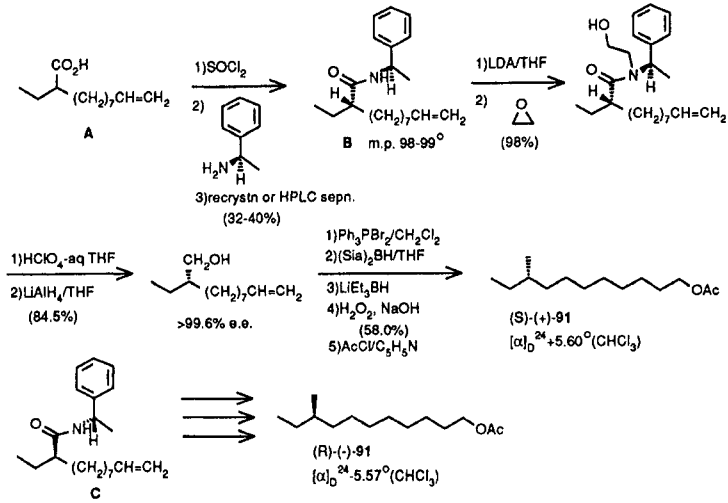
They also achieved an enantioselective synthesis of both the enantiomers of **91**, employing (*S*)-prolinol as the chiral auxiliary (Scheme 251).[336] Alkylation of



Scheme 251

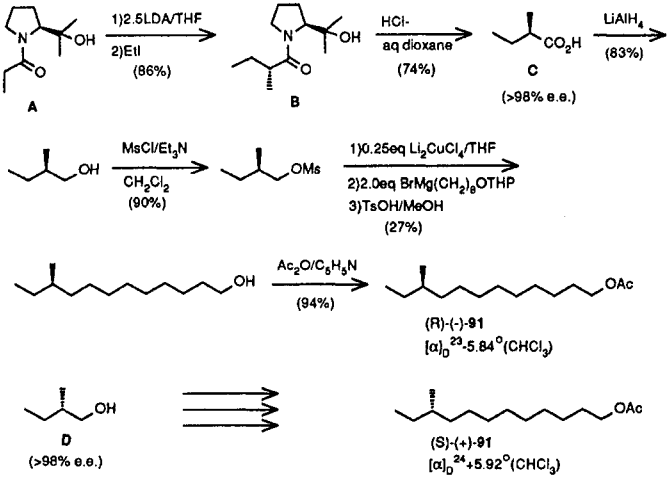
the dianion of **A** gave (*S*)-(+)-**B**, while that of the anion of **C** yielded (*R*)-(−)-**B**.

Sonnet's other synthesis employed optical resolution of the acid **A** via amides **B** and **C** as the key-step (Scheme 252).[336]



Scheme 252

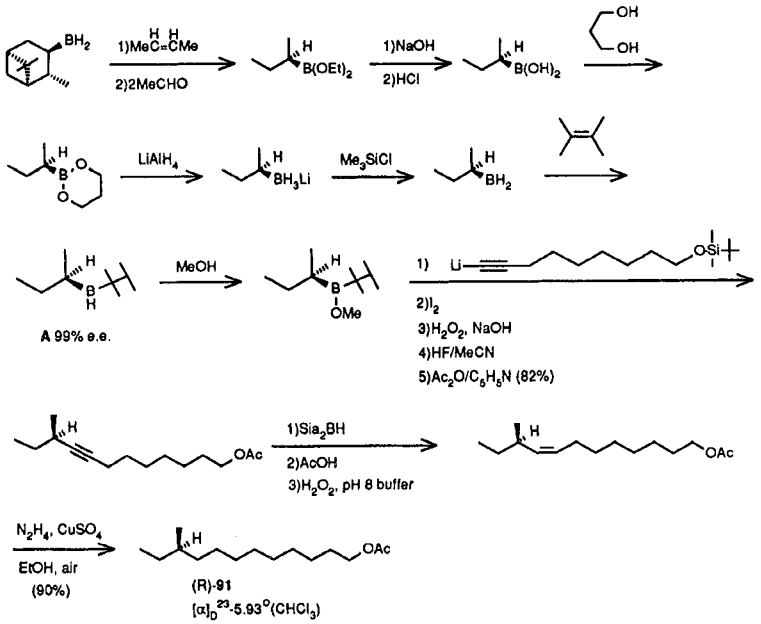
Hjalmarsson and Högberg also achieved a synthesis of the enantiomers of **91** (Scheme 253).[337] Their first step in preparing (*R*)-**91** was the asymmetric



Scheme 253

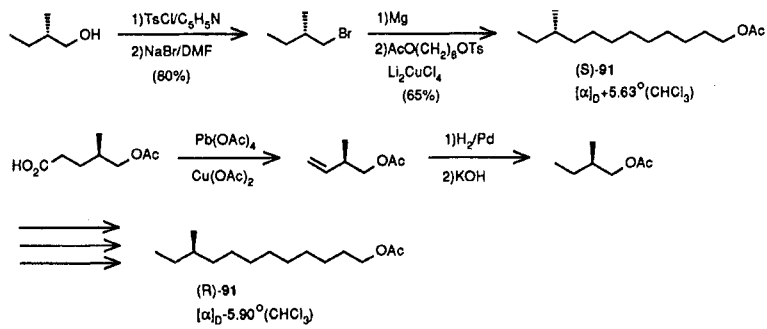
ethylation of the amide **A** to prepare (*R*)-2-methylbutanoic acid (**C**) via **B**. For the preparation of (*S*)-**91**, (*S*)-2-methyl-1-butanol (**D**) was employed as the starting material.

Brown et al. synthesized (*R*)-**91** starting from (*R*)-2-butylthexylborane (**A**) (Scheme 254).[338]

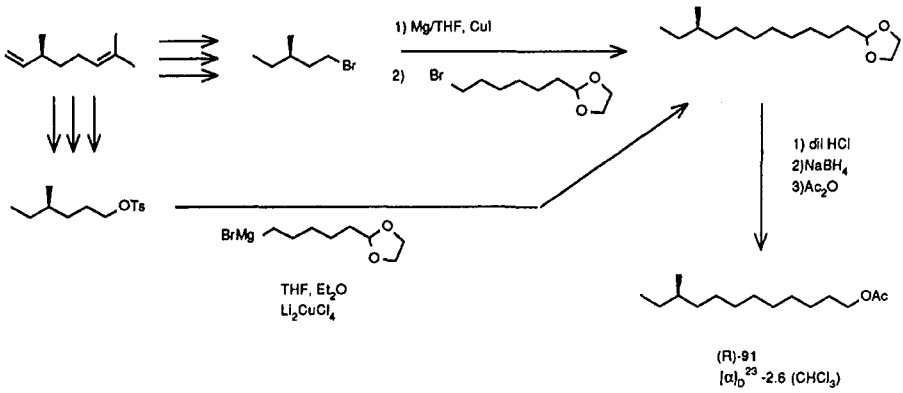


Scheme 254

Ceskis and Moiseenkov synthesized both the enantiomers of **91** (Scheme 255).[339] Serebryakov's synthesis of (*R*)-**91** is summarized in Scheme 256.[340]

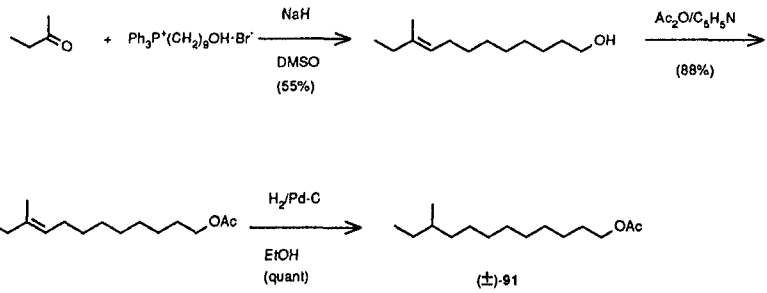


Scheme 255



Scheme 256

A simple synthesis of (±)-**91** was reported by Horiike et al. (Scheme 257).[341]



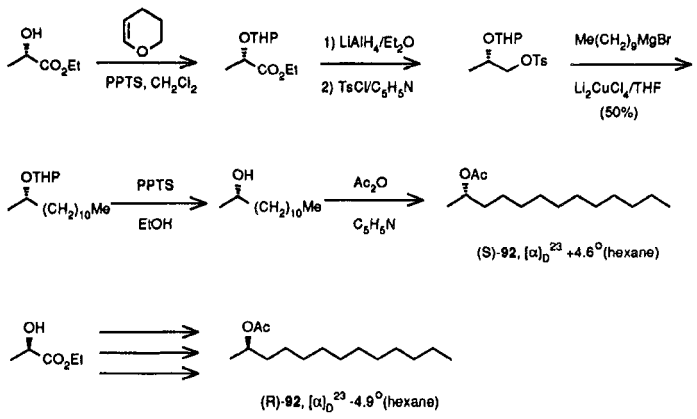
Scheme 257

L. (*S*)-1-Methyldodecyl Acetate **92** ($C_{15}H_{30}O_2$)

Aggregation pheromone components of *Drosophila mulleri* are (*S*)-(+)-1-methyldodecyl acetate (**92**) and (*Z*)-10-heptadecen-2-one.[342] Both the enantiomers of **92** were synthesized from the enantiomers of ethyl lactate (Scheme 258).[342]

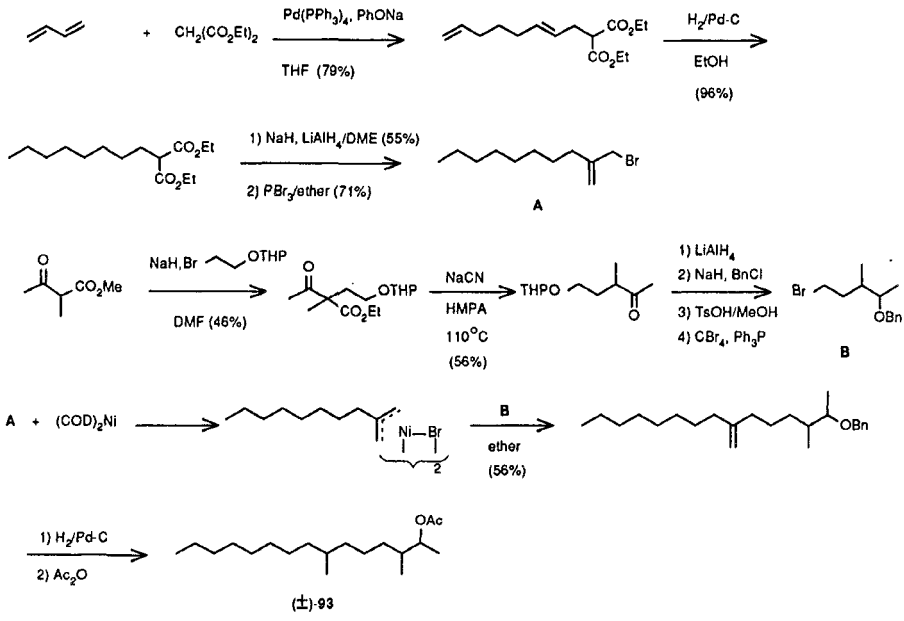
M. 1,2,6-Trimethyltetradecyl Acetate **93** ($C_{19}H_{38}O_2$) and 1,2,6-Trimethyltetradecyl Propanoate **94** ($C_{20}H_{40}O_2$)

Pine sawflies belonging to two genera (*Diprion* and *Neodiprion*) employ the acetate **93** or propanoate **94** of 3,7-dimethyl-2-pentadecanol as their sex-attractant pheromone.[343,344]

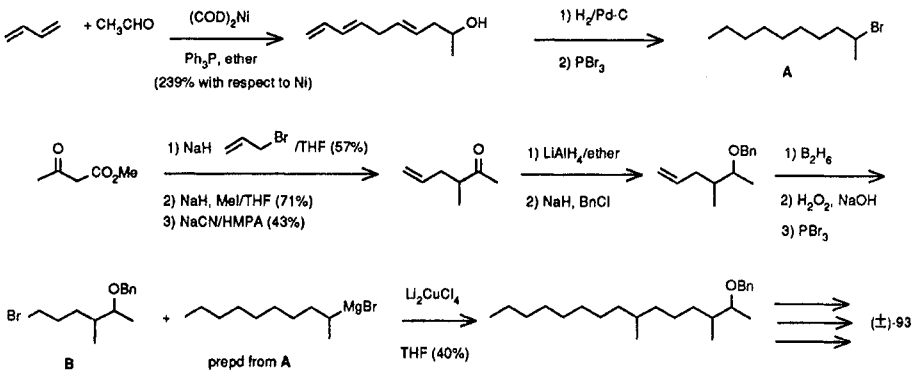


Scheme 258

Baker et al. reported two syntheses of a diastereomeric mixture of (±)-3,7-dimethyl-2-pentadecanol by utilizing the product of the palladium-catalyzed reaction of 1,3-butadiene with diethyl malonate and that of the nickel-catalyzed reaction of 1,3-butadiene with acetaldehyde (Schemes 259 and 260).[345]

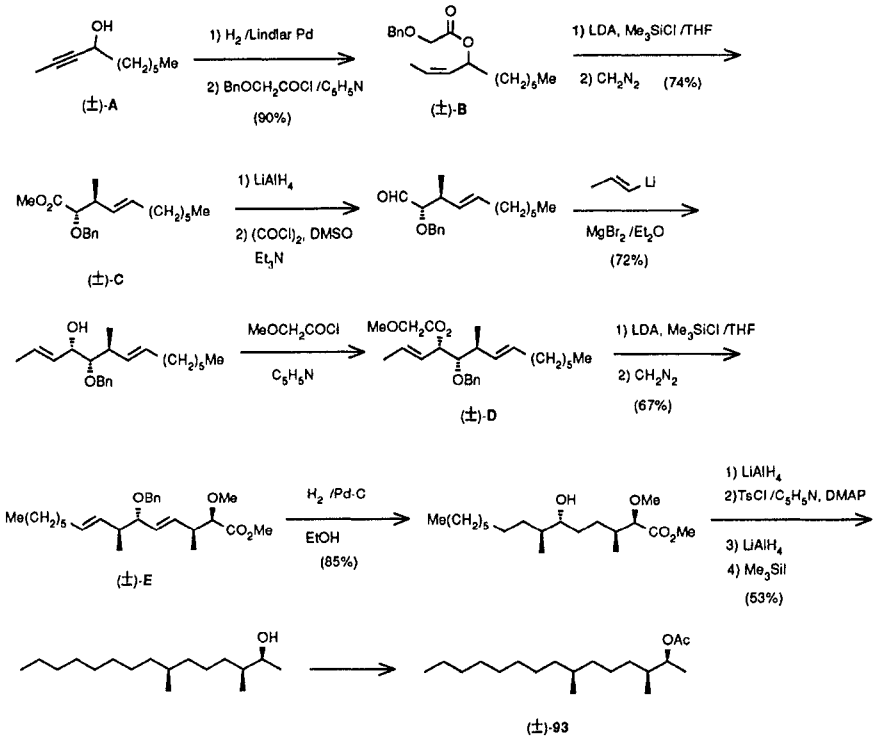


Scheme 259



Scheme 260

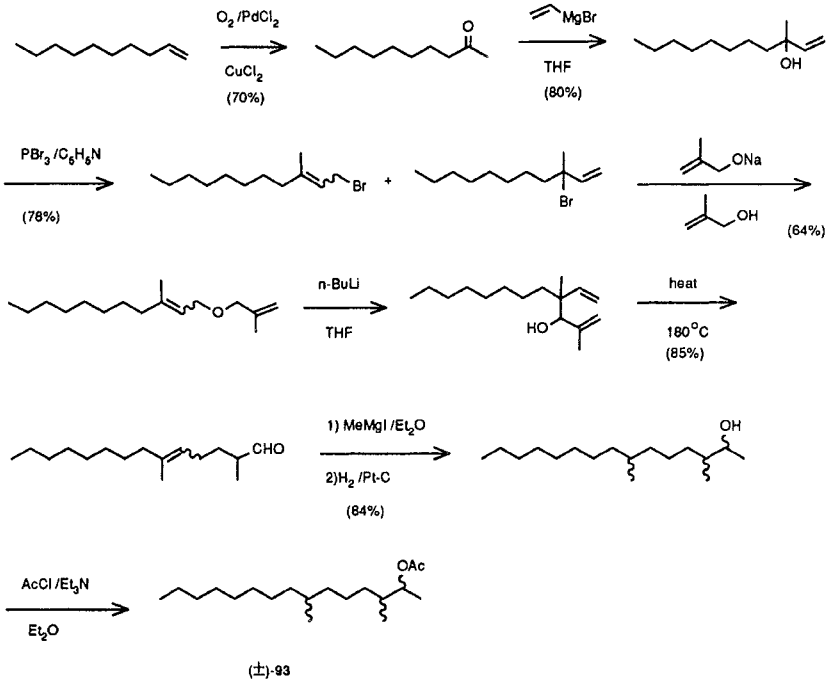
Another synthesis of (±)-3,7-dimethyl-2-pentadecanol was reported by Kallmerten and Balestra by the enolate Claisen rearrangement of allylic glycolates (Scheme 261).[346] Thus, the rearrangement of (±)-**B** (prepared from **A**) pro-



Scheme 261

duced (±)-**C** stereoselectively. Similarly, **D** yielded **E** after the rearrangement, which was finally converted to the target alcohol.

A synthesis reported by Serebryakov also used a rearrangement reaction (Scheme 262).[347] Serebryakov reported another synthesis of (1*RS*,2*S*,6*RS*)-**93** (Scheme 263-1).[348]

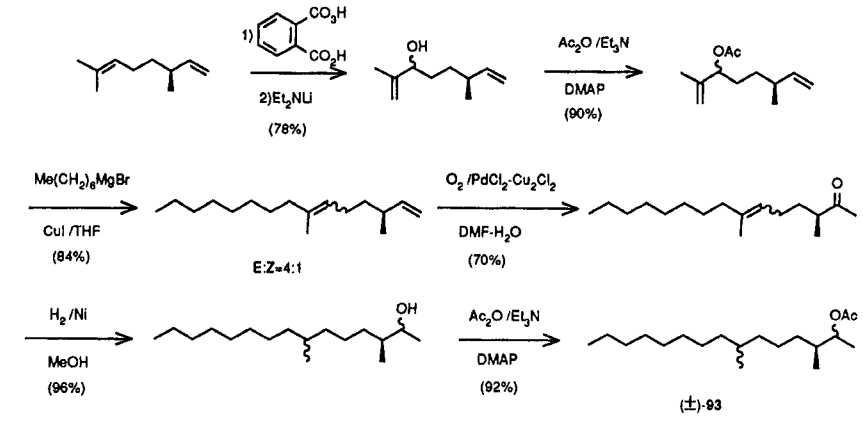


Scheme 262

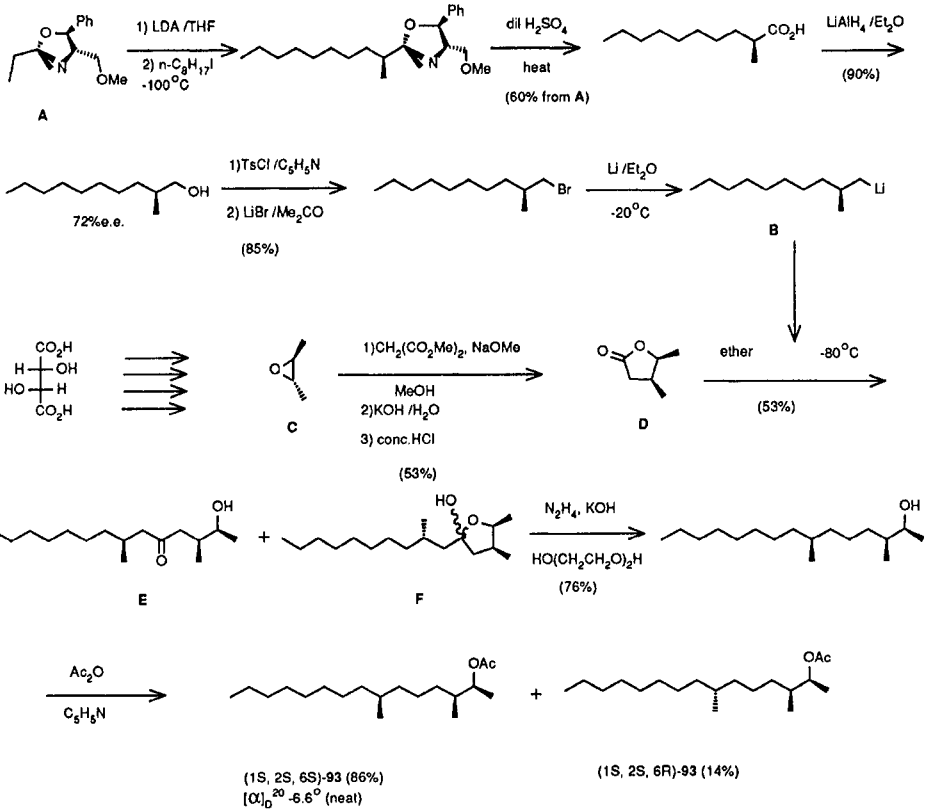
A new synthesis of (1*S*,2*S*,6*S*)-**93** and **94** was reported by Norin et al. (Scheme 263-2).[349] The chiral center at C-6 was provided by an asymmetric synthesis. Two other chiral centers originated from (+)-tartaric acid. Addition of **B** to **D** was the key-step, creating a mixture of **E** and **F.**

A full account of Tai's earlier synthesis of (1*S*,2*S*,6*RS*)- and (1*R*,2*R*,6*RS*)-**94** was published.[350] Tai's new synthesis of (1*S*,2*R*,6*R*)- and (1*S*,2*R*,6*S*)-**93** and **94** employed two chiral parts, **A** and **B,** for the coupling reaction (Scheme 264).[351] Ethyl (*R*)-citronellate was used to prepare **A,** while **B** was derived from (2*S*,3*S*)-2-methyl-3-hydroxybutanoic acid.

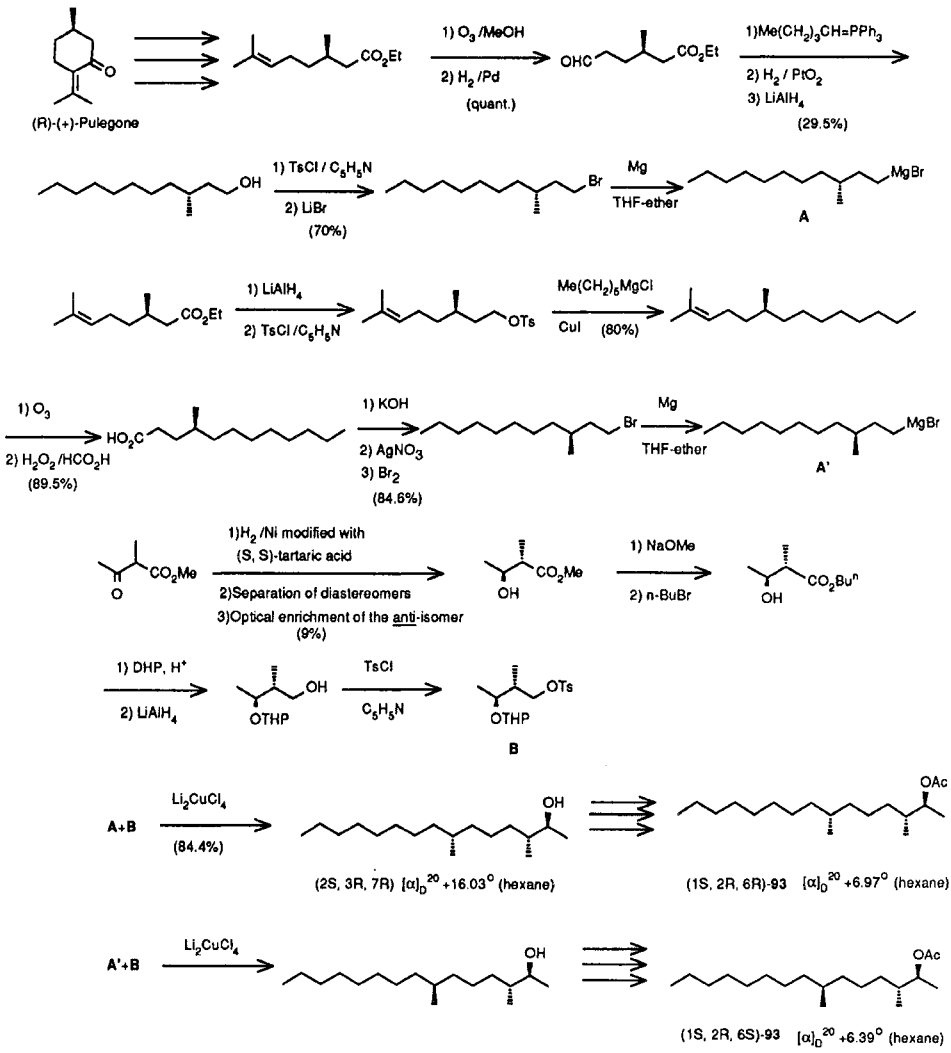
Fujisawa and co-workers synthesized (1*S*,2*S*,6*S*)-**93,** starting from sulfur-containing β-hydroxy esters obtained by the yeast reduction of the corresponding β-keto esters (Scheme 265).[352,353]



Scheme 263-1

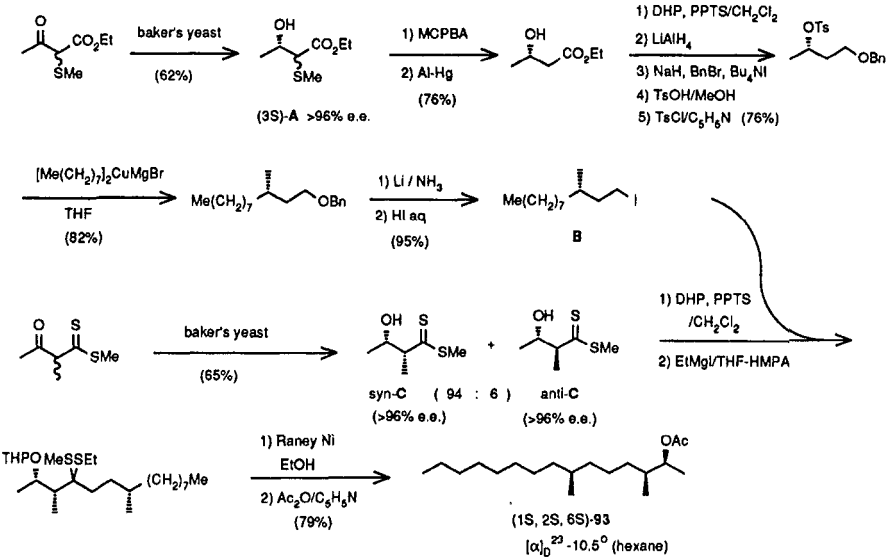


Scheme 263-2



Scheme 264

Larchevêque et al. reported the synthesis of (1*S*,2*S*,6*S*)- and (1*S*,2*R*,6*R*)-**93**, starting from ethyl (*R*)-3-hydroxybutanoate, D-serine, ethyl (2*S*,3*S*)-2-methyl-3-hydroxybutanoate, and D-threonine (Scheme 266).[354] Biochemical methods were employed for the preparation of the chiral hydroxy esters. Utilization of serine[355] and threonine[356] is also noteworthy in this synthesis.

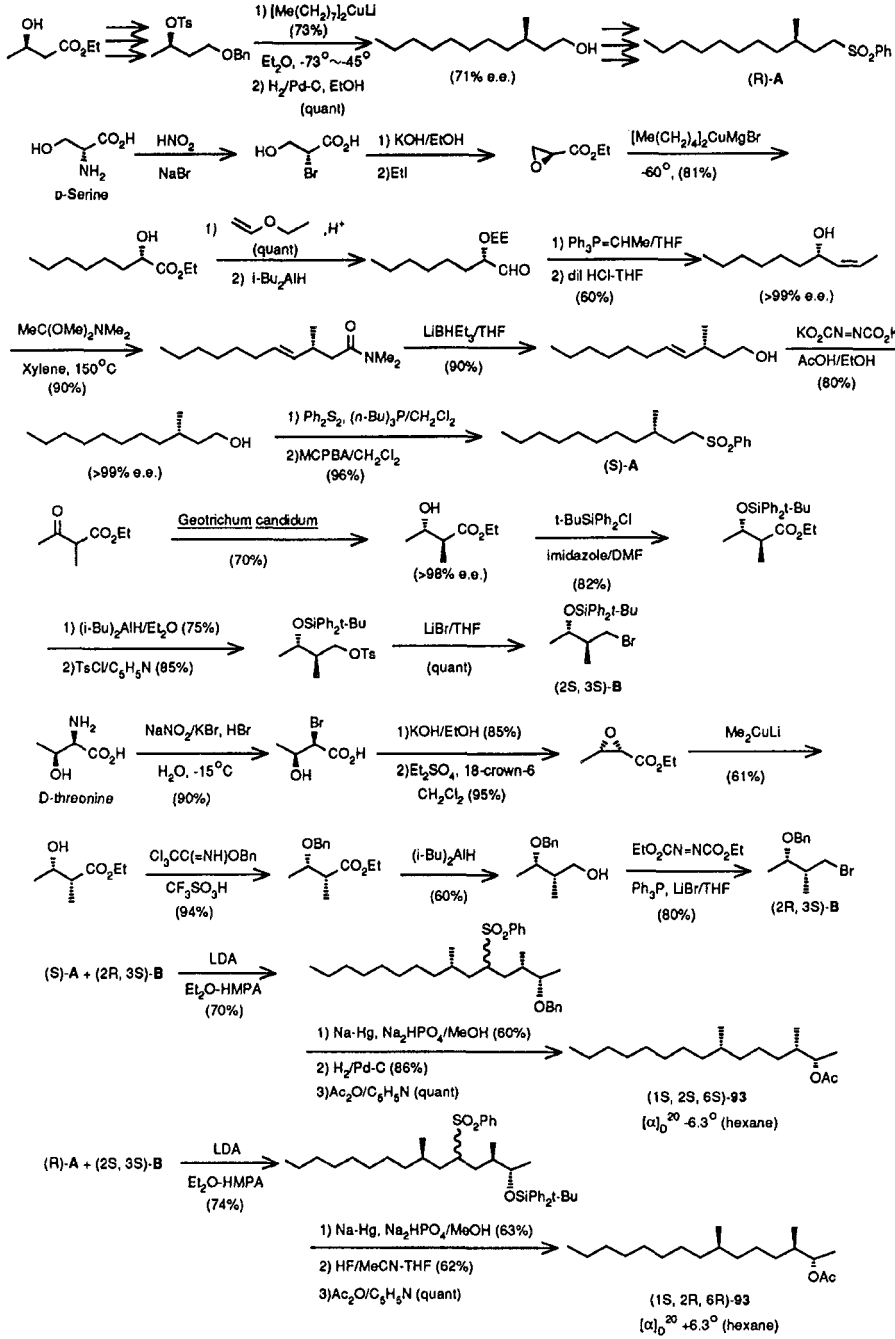


Scheme 265

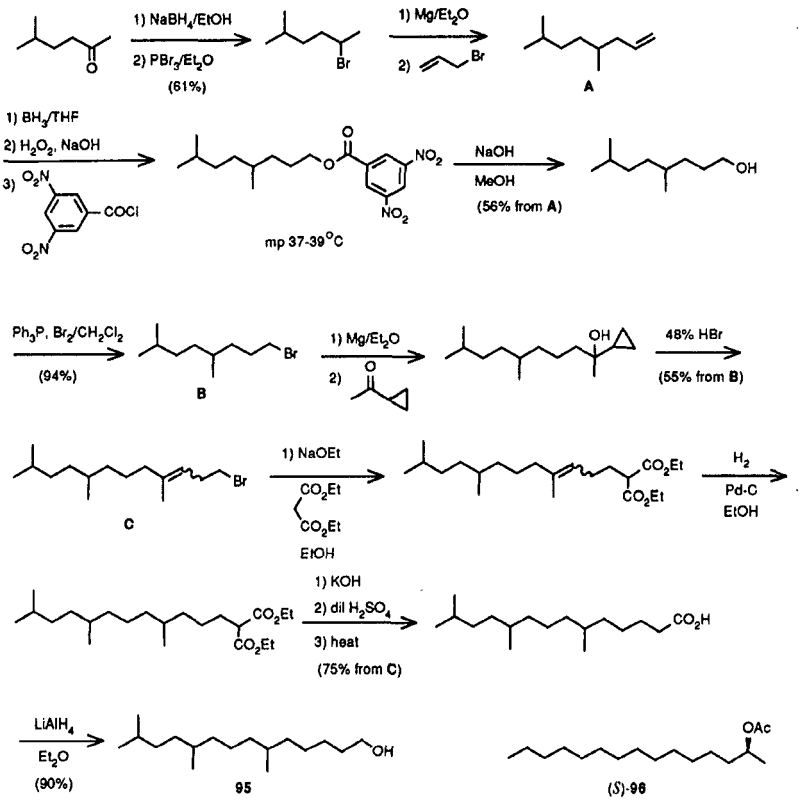
Among pine sawflies, species recognition is made possible by their use of different stereoisomers of **93** and **94.** The white pine sawfly (*Neodiprion pinetum*) employs (1*S*,2*S*,6*S*)-**93** as its major pheromone.[357] To the red-headed pine sawfly (*Neodiprion lecontei*), (1*S*,2*S*,6*S*)-**93** was again the active isomer.[358] In the case of *N. pinetum*, the minor component (1*S*,2*R*,6*R*)-**93** was found to be a synergist.[359] On the other hand, the introduced pine sawfly in the U.S.A. (*Diprion similis*) utilizes (1*S*,2*R*,6*R*)-**94** as the major component and (1*S*,2*S*,6*S*)-**94** as a synergist.[360] The European pine sawfly (*Neodiprion sertifer*) employs (1*S*,2*S*,6*S*)-**93** as the major pheromone, also employing (1*S*,2*R*,6*R*)-**93** as the synergist.[360] Against *Diprion similis* in the U.K., both (1*R*,2*R*,6*R*)-**94** and its antipode were active.[361]

N. 6,10,13-Trimethyl-1-Tetradecanol 95 ($C_{17}H_{36}O$)

This is the aggregation pheromone produced by male stink bugs (*Stiretrus anchorago*).[362] A diastereomeric mixture of all the possible stereoisomers of **95** was synthesized in 4% overall yield over 13 steps (Scheme 267) and shown to be bioactive.[362]



Scheme 266



Scheme 267

O. (*S*)-1-Methltetradecyl Acetate **96** ($C_{17}H_{34}O_2$)

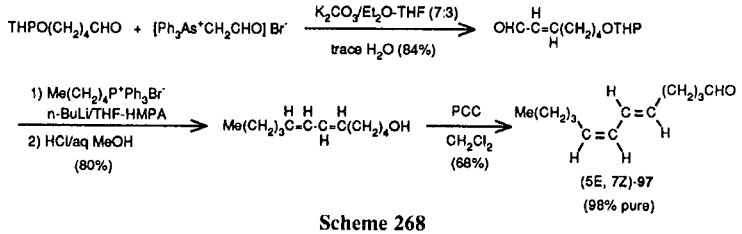
This acetate **96** and 2-pentadecanone were identified as the major aggregation pheromone components in *Drosophila busckii*.[363] 2-Pentadecanone and (*S*)-**96** were each active alone. The flies responded to (±)-**96** but not to the pure (*R*)-**96**. The synthesis of **96** was achieved in the same manner as reported for **92** (cf. Scheme 258).[342]

12. PHEROMONE ALDEHYDES

Many aldehydes are employed as insect pheromones. The syntheses of achiral olefinic aldehydes are discussed first, followed by the syntheses of three chiral aldehydes.

A. (5*E*,7*Z*)-5,7-Dodecadienal **97** ($C_{12}H_{20}O$)

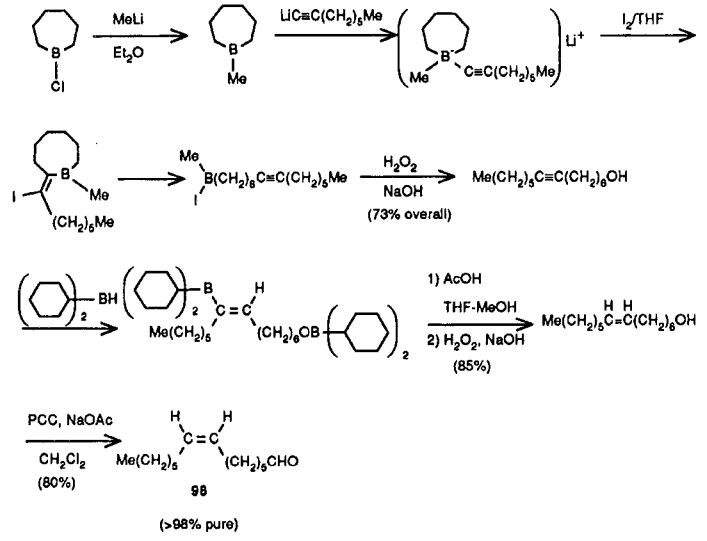
This is the pheromone of the western tent caterpillar (*Melacosoma californicum*).[364] A unique synthesis of **97** utilizing (formylmethyl)triphenylarsonium bromide as one of the starting materials was recently reported by Huang et al. (Scheme 268).[365]



Scheme 268

B. (*Z*)-7-Tetradecenal **98** ($C_{14}H_{26}O$)

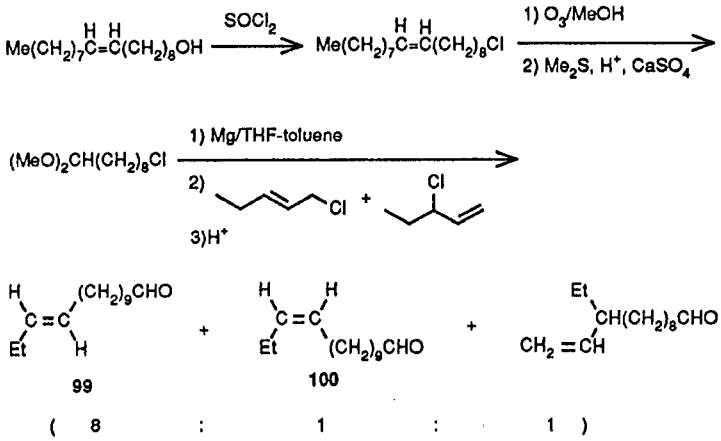
The citrus flower moth (*Prays citri*) employs **98** as its pheromone. Brown's synthesis of **98** via boracyclanes is shown in Scheme 269.[120]



Scheme 269

C. (*E*)- and (*Z*)-11-Tetradecenal 99 and 100 ($C_{14}H_{26}O$)

The sex pheromone of the eastern spruce budworm is a 95 : 5 mixture of **99** and **100.** A simple and economical synthesis of **99** and **100** as an 8 : 1 mixture was reported by Wiesner and Tan (Scheme 270) starting from oleyl alcohol.[366]



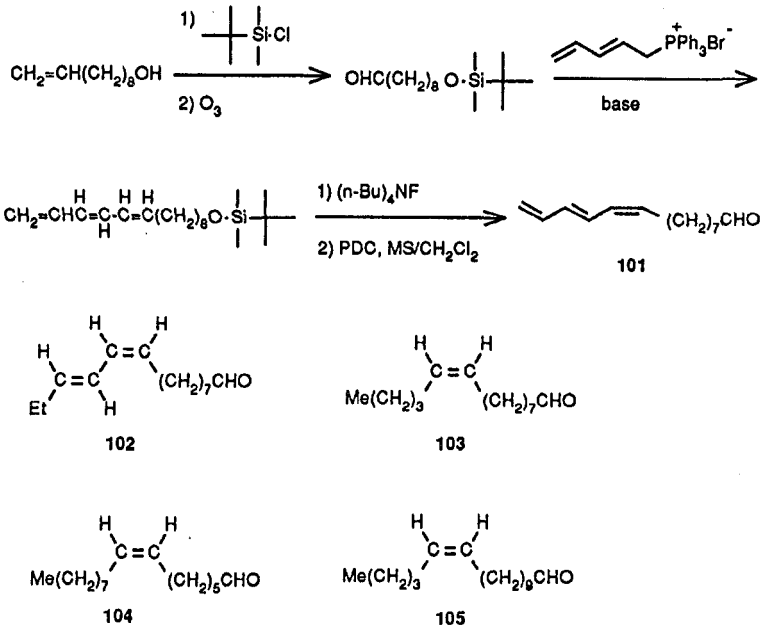
Scheme 270

D. (9*Z*,11*E*)-9,11,13-Tetradecatrienal 101 ($C_{14}H_{22}O$), (9*Z*,11*E*)-9,11-Tetradecadienal 102 ($C_{14}H_{24}O$), and (*Z*)-9-Tetradecenal 103 ($C_{14}H_{26}O$)

The sex pheromone of female of the carob moth (*Ectomyelois ceratoniae*) is a mixture of **101, 102,** and **103** in the ratio of 10 : 1 : 1.[367] Baker et al. synthesized **101** (Scheme 271).[367] PDC oxidation of (9*Z*,11*E*)-9,11-tetradecadien-1-ol yielded **102.**

E. (*Z*)-7-Hexadecenal 104 ($C_{16}H_{30}O$)

This is the trail pheromone of the Argentine ant (*Iridomyrmex humilis*). Brown et al. synthesized **104** via boracyclanes in the same manner as shown in Scheme 269 for the synthesis of **98.**[120] In the present case, 1-decyne was used in the second step instead of 1-octyne.



Scheme 271

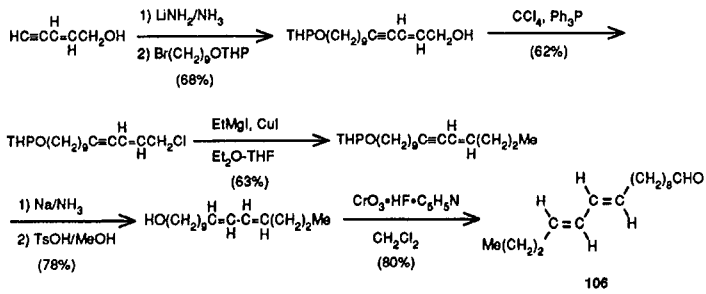
F. (Z)-11-Hexadecenal 105 ($C_{16}H_{30}O$)

This is a common component of the sex pheromones of *Lepidoptera*, such as the rice stem borer (*Chilo suppressalis*), the cotton bollworm (*Heliothis armigera*), the tobacco budworm (*Heliothis virescens*), the iris borer (*Macronoctua onusta*), the diamond back moth (*Plutella xylostella*), and *Leucania separata.* Liu et al. prepared **105** by using the coupling reaction between 6-(tetrahydropyranyloxy)hexylmagnesium bromide with (*Z*)-5-decenyl tosylate.[368] (*E*)-10-Hexadecenal was identified as the sex pheromone of the yellow peach moth (*Dichocrocis punctiferalis*).[244]

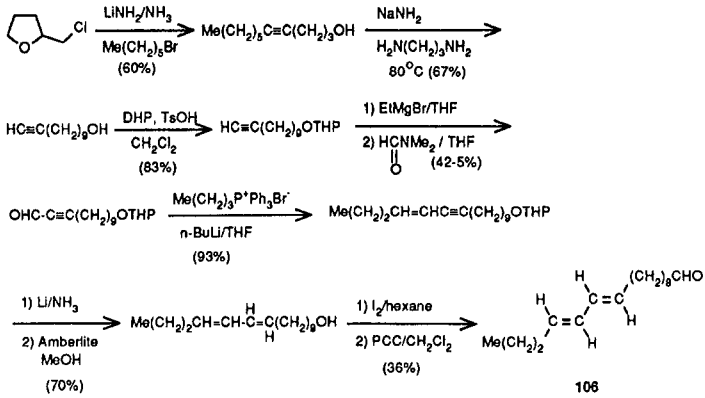
G. (10*E*,12*E*)-10,12-Hexadecadienal 106 ($C_{16}H_{28}O$)

This is the major component of the female produced sex pheromone of the spiny bollworm (*Earias insulana*).[369]

Yadav et al. synthesized **106** by an acetylenic route (Scheme 272).[179] Scheme 273 reports another synthesis of **106**.[370]



Scheme 272



Scheme 273

H. (11*E*,13*E*)-11,13-Hexadecadienal **107** ($C_{16}H_{28}O$)

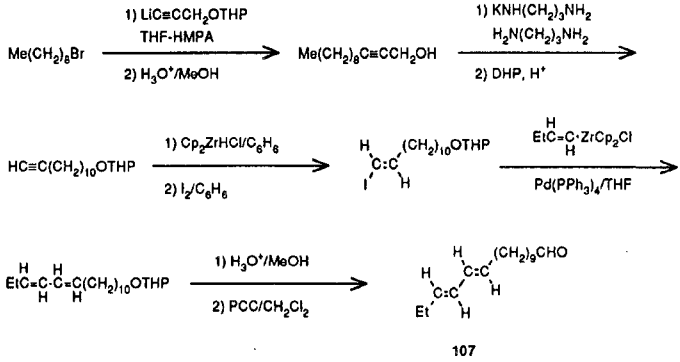
The cabbage webworm (*Hellula undalis*) employs **107** as the female-produced sex pheromone.[371] Its synthesis was achieved by Arai et al.[371] by means of hydrozirconation reaction (Scheme 274).[372]

Lo and Shiao synthesized **107** in a simpler manner by a Wittig route (Scheme 275).[373] The dienol isomers **A** and **B** were separable by chromatography over silica gel impregnated with silver nitrate.

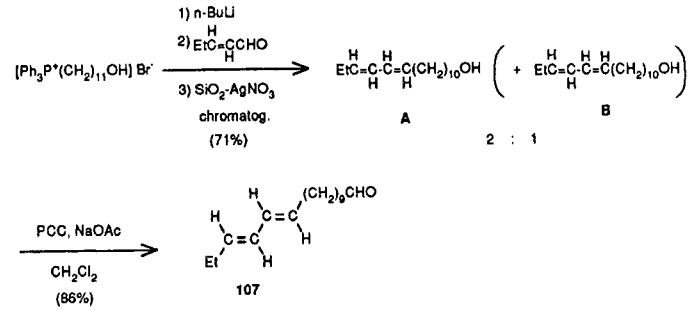
Another synthesis of **107** by Yamada et al. employed alkylation of a sulfone as the key reaction (Scheme 276).[156]

I. (11*Z*,13*Z*)-11,13-Hexadecadienal **108** ($C_{16}H_{28}O$)

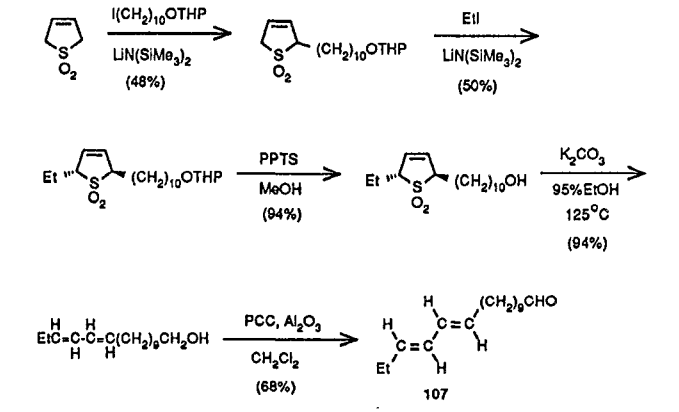
The sex pheromone of the naval orangeworm (*Amyelois transitella*) was obtained from ether rinses of the sex pheromone gland of calling females, and



Scheme 274

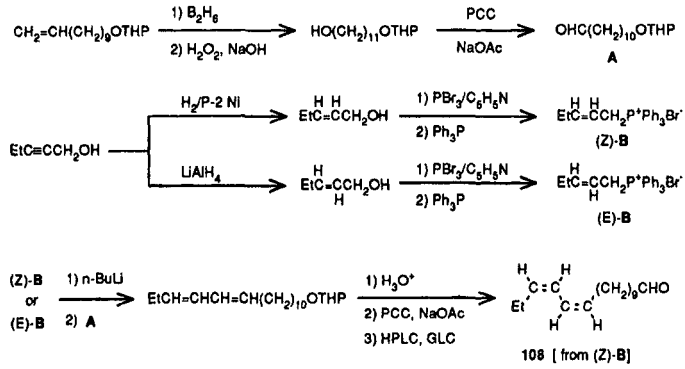


Scheme 275



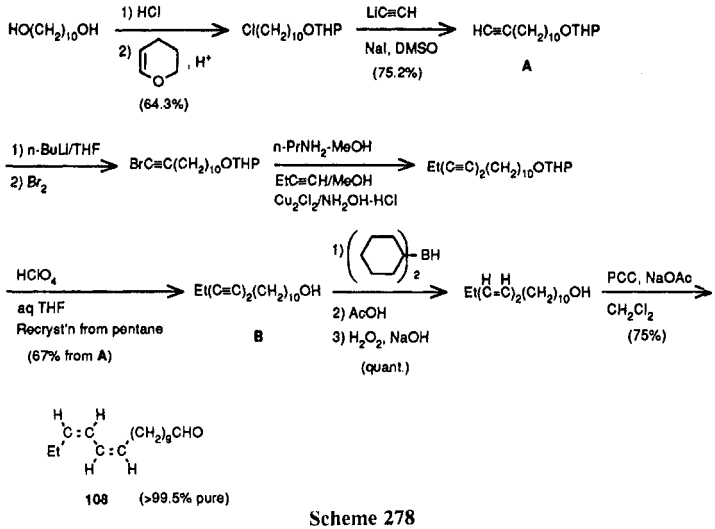
Scheme 276

was identified as **108**.[374] Coffelt et al. synthesized all of the four possible isomers of **108** by a nonstereoselective route followed by HPLC and GLC separation (Scheme 277).[374]



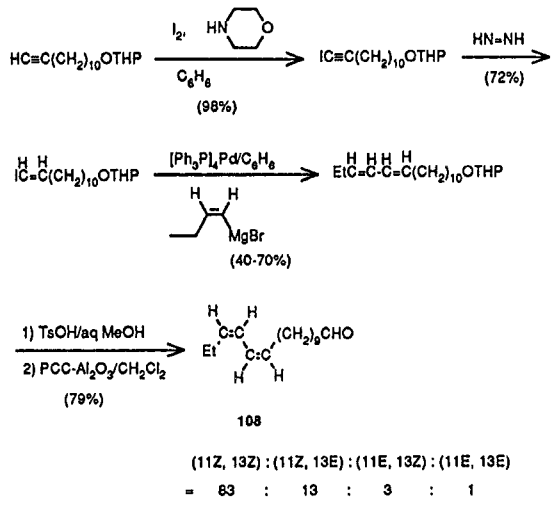
Scheme 277

Soon afterwards, Sonnet and Heath published a stereoselective synthesis of **108** via an acetylene route (Scheme 278).[375] They purified the diynol **B** by recrystallization.



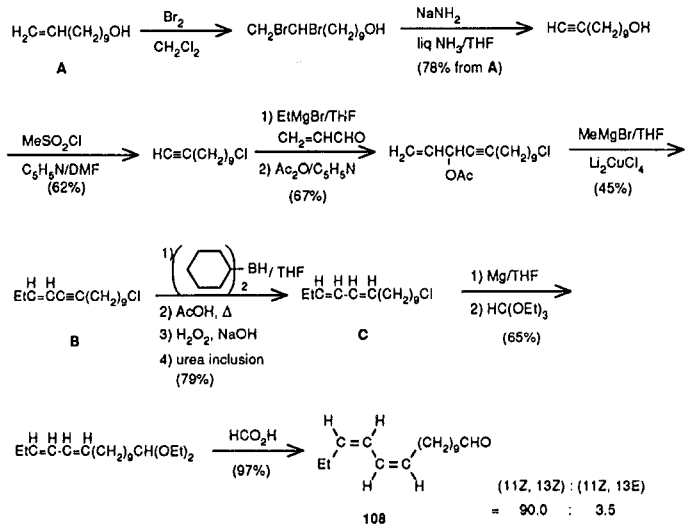
Scheme 278

Michelot's synthesis of **108** employed tetrakis[triphenylphosphine]palladium as a catalyst for cross-coupling (Scheme 279).[117]



Scheme 279

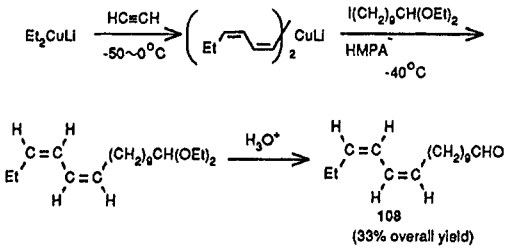
Bishop and Morrow reported a large-scale synthetic process of **108** (Scheme 280), by which they prepared 2.8 kg of **108.**[376] A noteworthy step in the present



Scheme 280

synthesis was the selective inclusion of **C** by urea as the mild purification method of a labile diene such as **C**. Although the chlorodiene **C** was readily convertible to a Grignard reagent, the chloroenyne **B** proved to be inert toward magnesium even by entrainment techniques.

Taylor and his co-workers employed the Normant reaction (acetylene carbocupration followed by electrophilic trapping of the resulting cuprate) for the synthesis of **108** (Scheme 281)[377] by a short and relatively efficient route. Their



Scheme 281

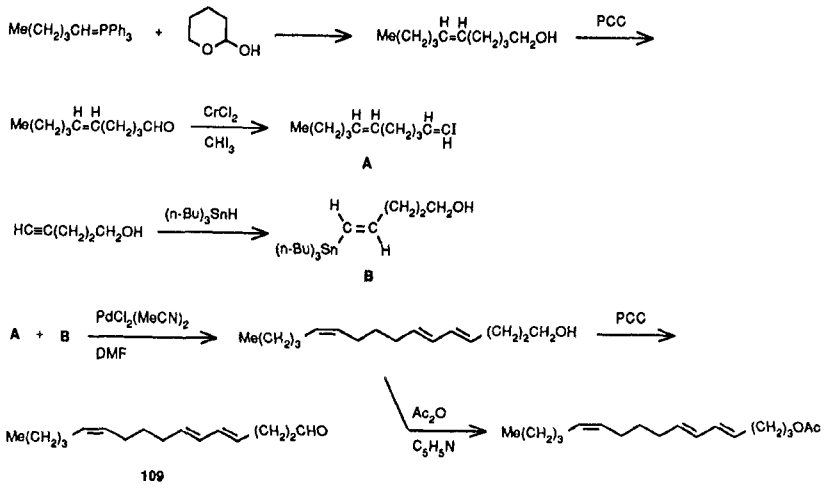
detailed experimental procedure, including the apparatus used for double acetylene carbocupration, has also been published.[378]

J. (4*E*,6*E*,11*Z*)-4,6,11-Hexadecatrienal 109 ($C_{16}H_{26}O$)

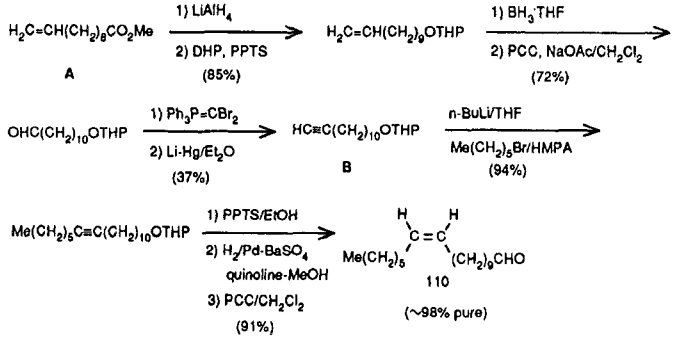
This aldehyde and (4*E*,6*E*,11*Z*)-4,6,11-hexadecatrienyl acetate were the major components of the female-produced sex pheromone of the eri silkworm (*Samia cynthia ricini*).[379] Bestmann et al. synthesized these two compounds by a palladium-catalyzed cross-coupling reaction of vinyl halides with vinylstannanes (Scheme 282).[379]

K. (*Z*)-11-Octadecenal 110 ($C_{18}H_{34}O$)

A species of the wax moth (*Achroia grisella*) employs **110** as its sex pheromone. It is also the minor component of the pheromone system of the spotted bollworm (*Earias vittella*), in which **106** is the major component. Ranganathan's synthesis of **110** (Scheme 283) started from methyl 10-undecenoate **A**, which can be prepared from castor oil.[380] The intermediate **B** was also con-



Scheme 282



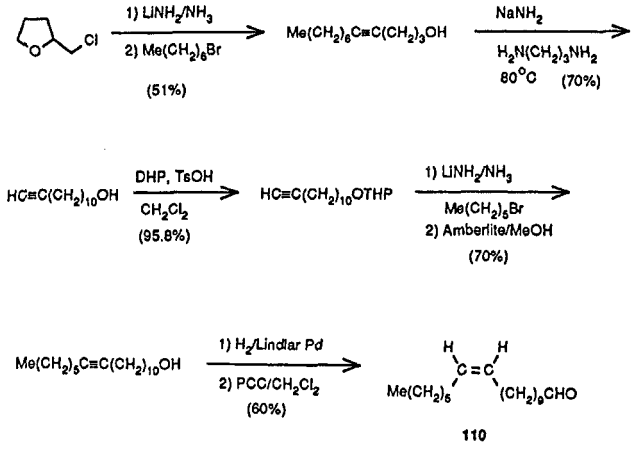
Scheme 283

verted to several other pheromones, such as that of the Egyptian cotton leafworm (*Spodoptera littoralis*).

Yadav et al. prepared **110** by a conventional acetylene route (Scheme 284).[370]

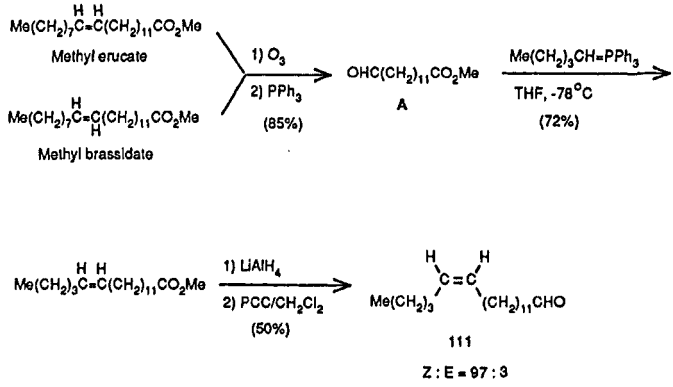
L. (Z)-13-Octadecenal 111 ($C_{18}H_{34}O$)

The rice stem borer (*Chilo suppressalis*) is a serious pest of rice in Asian countries. Its female-produced sex pheromone is a 5 : 1 mixture of **105** and **111.**



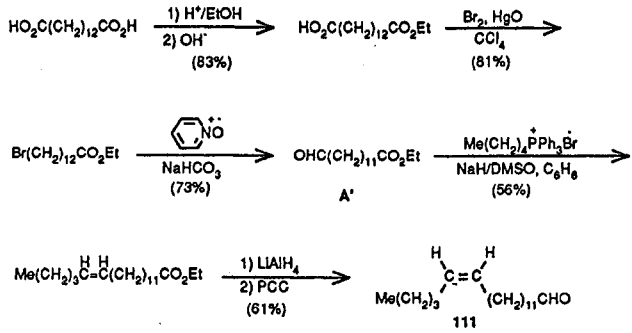
Scheme 284

Bestmann et al. synthesized **111** by a Wittig route (Scheme 285).[381] Their starting material was either methyl erucate or methyl brassidate.



Scheme 285

Kang et al. reported a different synthesis of Bestmann's intermediate, the aldo ester **A'** (Et instead of Me), starting from tetradecanedioic acid (Scheme 286).[382]

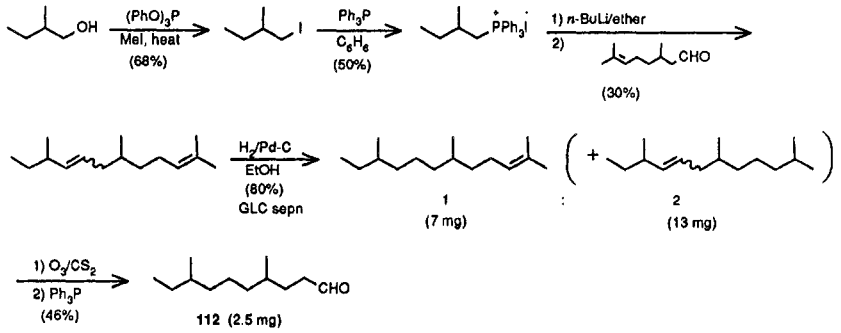


Scheme 286

M. (4*R*,8*R*)-4,8-Dimethyldecanal (Tribolure) 112 ($C_{12}H_{24}O$)

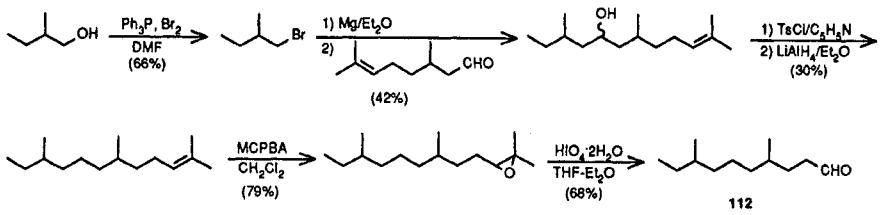
Suzuki isolated and identified the male-produced aggregation pheromone of the red-flour beetle (*Tribolium castaneum*) as 4,8-dimethyldecanal.[383,384] The confused flour beetle, (*Tribolium confusum*) also employs **112** as the aggregation pheromone. Recently, Suzuki et al. identified the aggregation pheromone of *T. freemani* as **112**, and named it "tribolure."[385]

To confirm the proposed structure, Suzuki synthesized a mixture of all the possible stereoisomers of **112** (Scheme 287).[384] His synthetic sample was about 10 times less active than the natural **112**.



Scheme 287

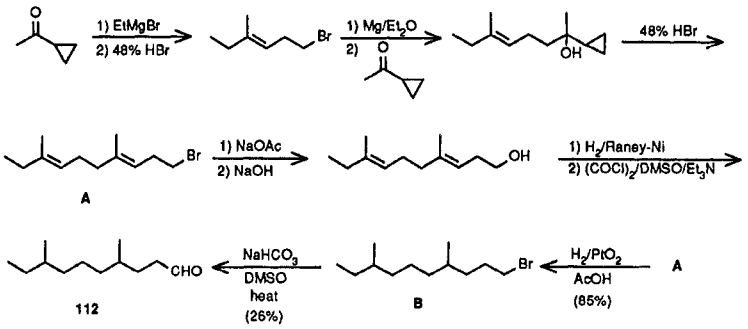
Another synthesis of a stereoisomeric mixture of **112** was also reported by Suzuki (Scheme 288).[386] He prepared not only **112** but also its several analogs, and found only **112** to be attractive against both *Tribolium castaneum* and *T.*



Scheme 288

confusum at the dose of 100 ng per disk.[386] Later, however, Mori et al. found 2,6-dimethyloctyl formate to be almost as active as the stereoisomeric mixture of **112**.[387]

A simple synthesis of a stereoisomeric mixture of **112** was achieved by Breuer et al. (Scheme 289).[388] They utilized the Julia cleavage of cyclopropyl alcohols



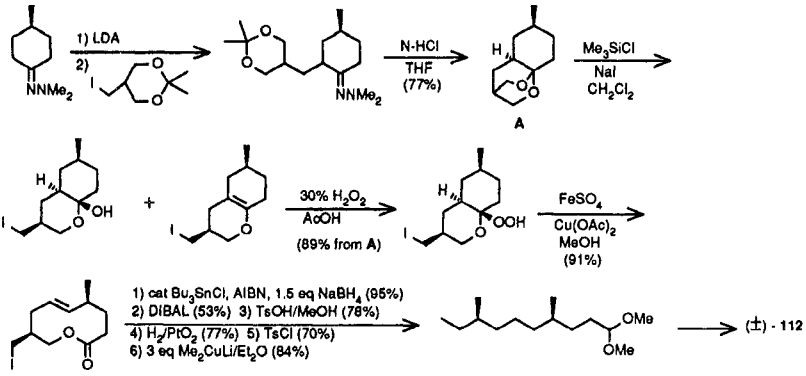
Scheme 289

as the key reaction to produce **A**. A slightly shorter synthesis of **112** from **A** via **B** was later reported.[387]

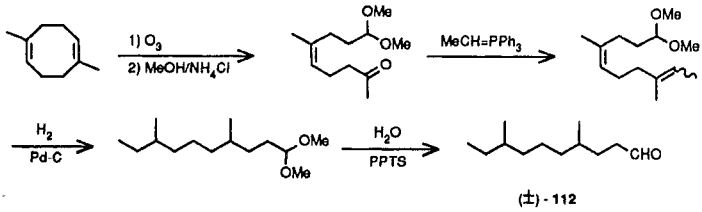
A unique and selective synthesis of (±)-*syn*-**112** was reported by Schreiber and Hulin (Scheme 290).[389] A group-selective dealkylation reaction of a bridged acetal **A** with trimethylsilyl iodide served to control stereochemistry at the chiral centers that are separated from each other.

A synthesis of a diastereomeric mixture of **112** was reported by Odinokov et al. starting from 1,5-dimethyl-1,5-cyclooctadiene (Scheme 291).[390]

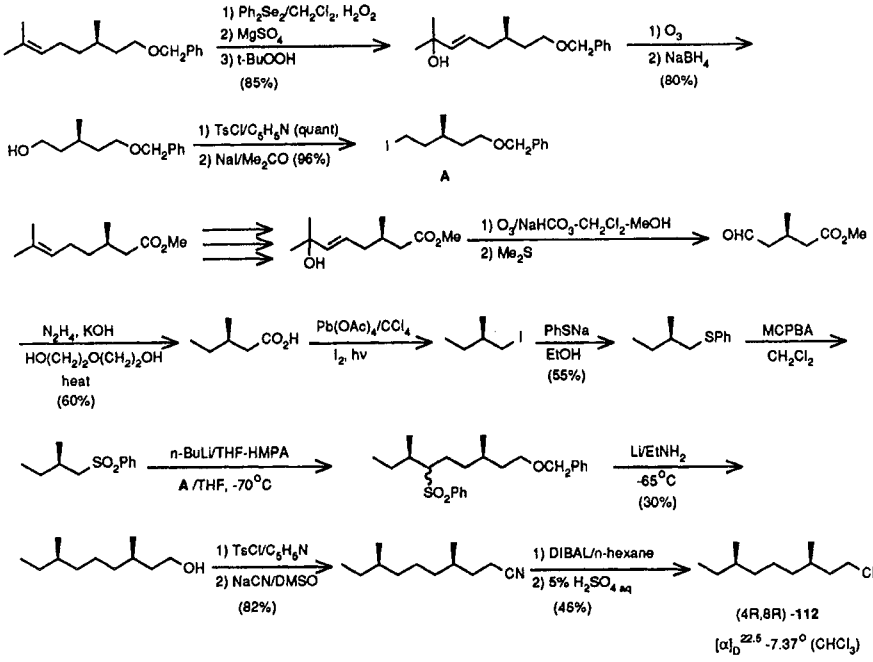
Mori et al. achieved a synthesis of all of the four possible stereoisomers of **112** (Schemes 292–294).[391] Their strategy was to couple two chiral building blocks by sulfone alkylation, Grignard coupling, or mixed Kolbe electrolysis. Bioassay of the stereoisomers of **112** revealed (4*R*,8*R*)-**112** to be as potent as the natural pheromone.[392,393] Suzuki et al. later found that a mixture of (4*R*,8*R*)-**112** and (4*R*,8*S*)-**112** in a ratio of 8 : 2 was about 10 times more active than (4*R*,8*R*)-**112** alone.[394]



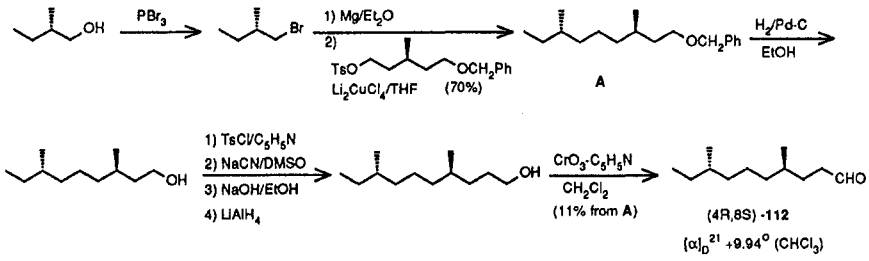
Scheme 290



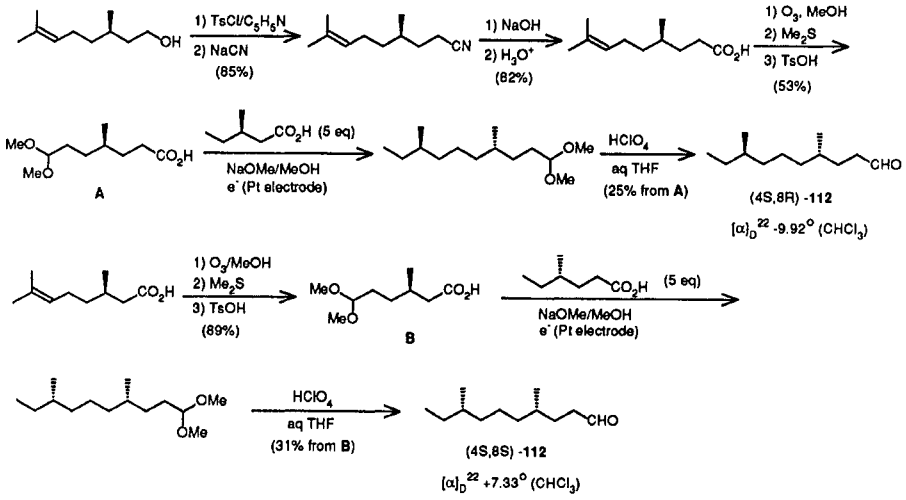
Scheme 291



Scheme 292



Scheme 293



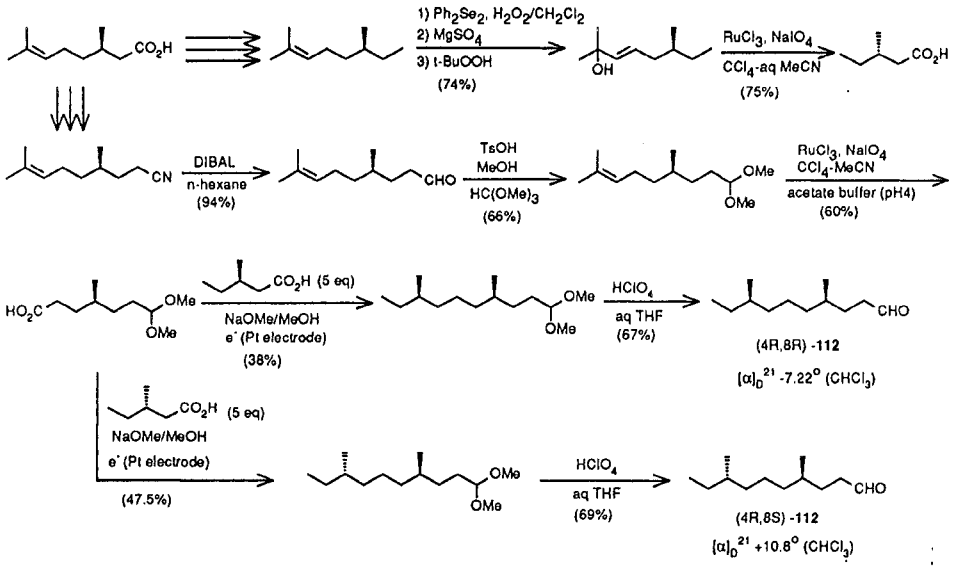
Scheme 294

In order to supply an additional amount of (4*R*,8*R*)-**112** and (4*R*,8*S*)-**112**, Mori et al. developed another synthetic route via mixed Kolbé electrolysis (Scheme 295).[395] The overall yield of (4*R*,8*R*)-**112** from (*R*)-citronellic acid by this process was 8%.

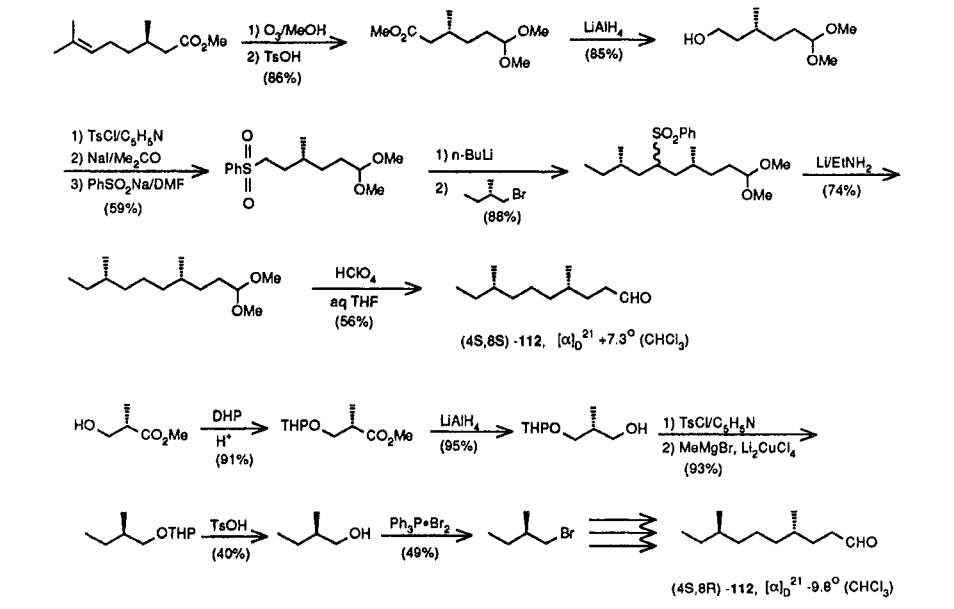
A further need of (4*S*,8*S*)-**112** and (4*S*,8*R*)-**112** for biological studies motivated Mori et al. to prepare them via sulfones (Scheme 296).[396] This route produced (4*S*,8*S*)-**112** and (4*S*,8*R*)-**112** in a 14–17% overall yield from (*R*)-citronellic acid.

Another synthesis of (4*R*,8*R*)-**112** by Fuganti et al. (Scheme 297) started from (*S*)-3-(2-furyl)-2-methyl-1-propanol, which is a bifunctional chiral C_5 building block prepared by means of yeast reduction.[397]

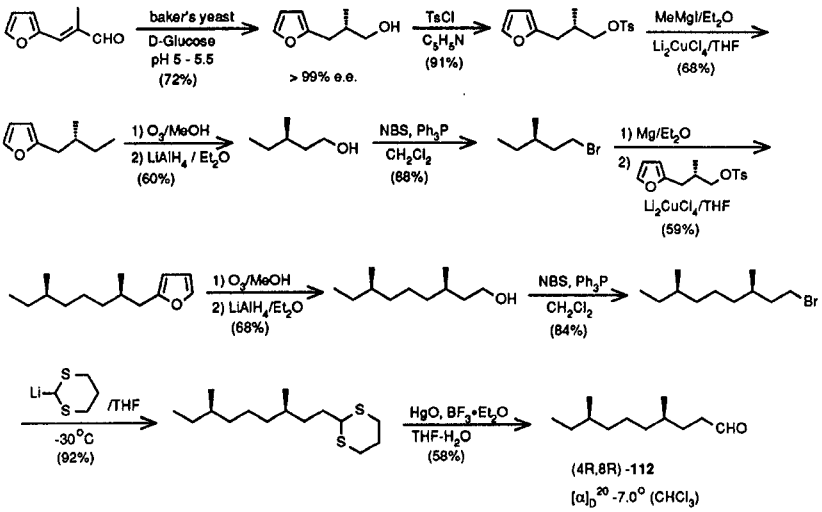
Moiseenkov and his co-workers prepared (4*R*,8*R*)-**112** and its (4*R*,8*S*)-isomer by connecting two chiral building blocks (Scheme 298).[398,399]



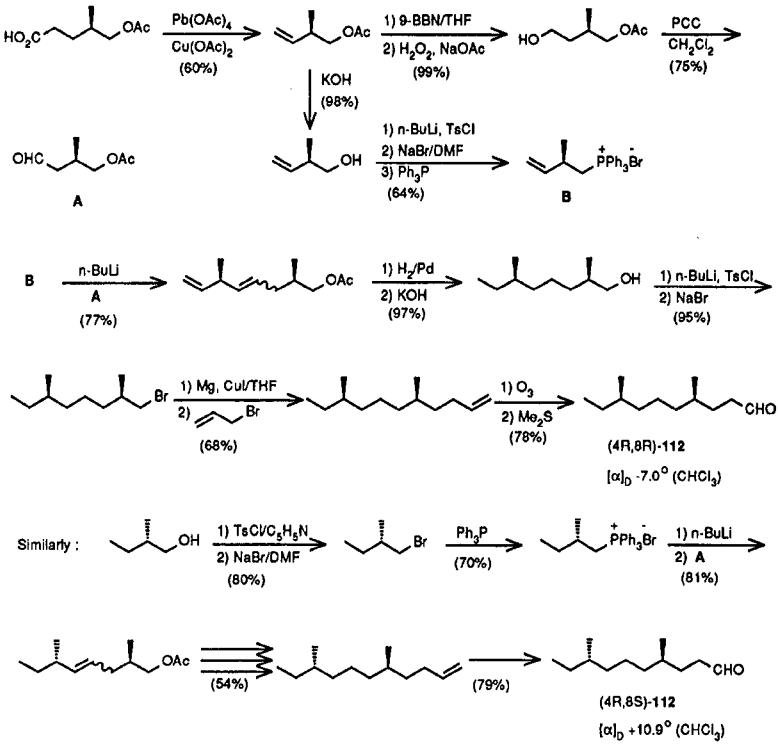
Scheme 295



Scheme 296

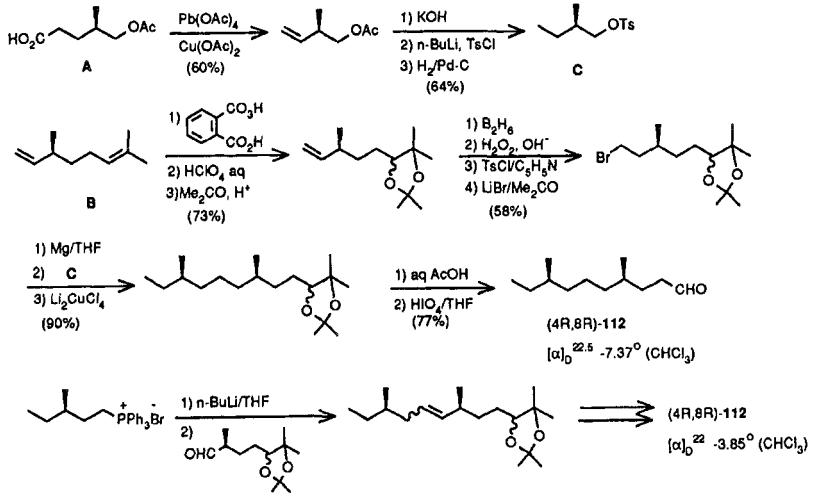


Scheme 297



Scheme 298

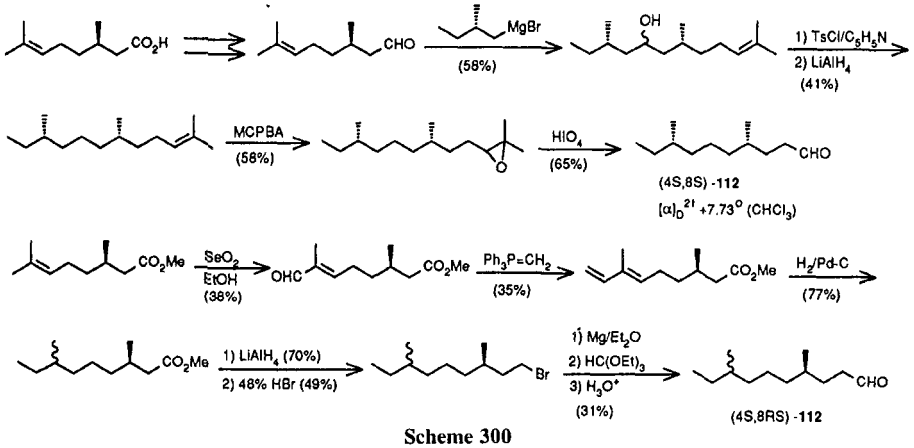
Starting from (*R*)-5-acetoxy-4-methylpentanoic acid **(A)** and (*S*)-3,7-dimethyl-1,6-octadiene **(B),** Serebryakov and his co-workers achieved a synthesis of (4*R*,8*R*)-**112** (Scheme 299).[400] They also reported another route to



Scheme 299

(4*R*,8*R*)-**112** with 52% e.e., starting from enantiomerically impure (*S*)-3,7-dimethyl-1,6-octadiene.[401] Their synthetic **112** and analogs were tested against *T. confusum*, and (4*R*,8*R*)-**112** was confirmed to be the most potent attractant.[402] Recently, Serebryakov reported a modification of his earlier synthesis of (4*R*,8*R*)-**112** by using the Wittig reaction for the connection (Scheme 299).[403]

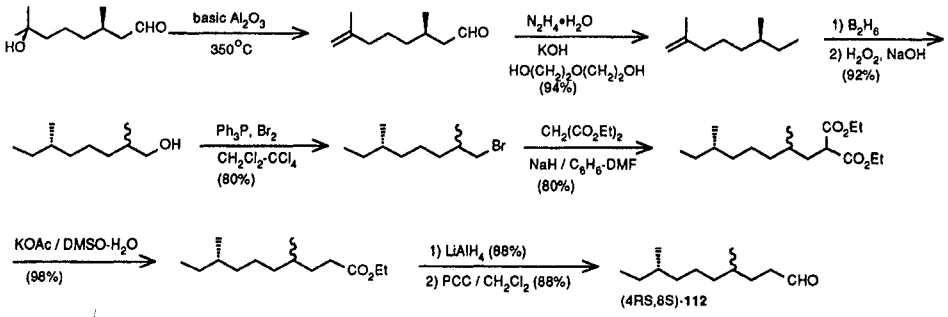
Suzuki et al. reported a synthesis of (4*S*,8*S*)-**112** as shown in Scheme 300.[404]



Scheme 300

They also synthesized (4*R*,8*RS*)-**112** and several analogs of **112**, and assayed them to confirm the strongest attractivity of (4*R*,8*R*)-**112**.[404]

Randad and Kulkarni described a synthesis of (4*RS*,8*S*)-**112** starting from (*R*)-7-hydroxycitronellal (Scheme 301).[405]



Scheme 301

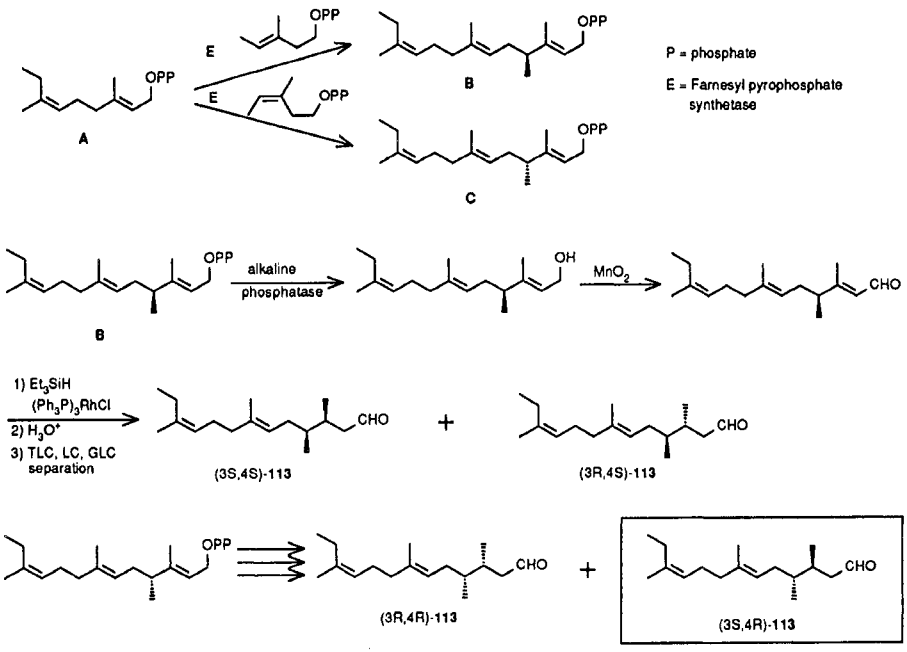
N. Faranal [(3*S*,4*R*,6*E*,10*Z*)-3,4,7,11-Tetramethyl-6,10-tridecadienal] 113 ($C_{17}H_{30}O$)

Ritter et al. isolated and identified faranal (**113**) as the trail-following pheromone of the worker Pharaoh's ant (*Monomorium pharaonis*).[406] Its detection threshold is ca. 1 pg/cm of a trail.

Kobayashi et al. synthesized all of the four possible stereoisomers of (6*E*,10*Z*)-**113** (Scheme 302).[407] The unique feature of their synthesis was in the use of farnesyl pyrophosphate synthetase for the construction of the chiral center at C-4. Another chiral center at C-3 was generated nonselectively, but the isomers were separable by chromatographic means. Bioassay of the isomers indicated (3*S*,4*R*,6*E*,10*Z*)-**113** to be the natural pheromone.

Mori and Ueda carried out the synthesis of both (3*S*,4*R*,6*E*,10*Z*)-**113** and its (3*R*,4*S*)-isomer (Scheme 303), and found (3*S*,4*R*)-**113** to be bioactive.[408,409] Both the chemical and enantiomeric purities of the products obtained by this synthesis was ca. 90%, and the final purification of **113** was carried out by preparative GLC to secure purer samples. This defect was due to the incomplete resolution of the hydroxy acid **A** to give lactone enantiomers **B** of ca. 90% e.e., and also due to the contamination with the (*Z*)-isomer of **C**. An asymmetric synthesis of (3*R*,4*R*)-lactone **B** was later reported by Enders (Scheme 304).[410]

Two syntheses of faranal **113** by strategies slightly similar to those of Mori and Ueda, but resulting in the preparation of its racemate, were reported inde-

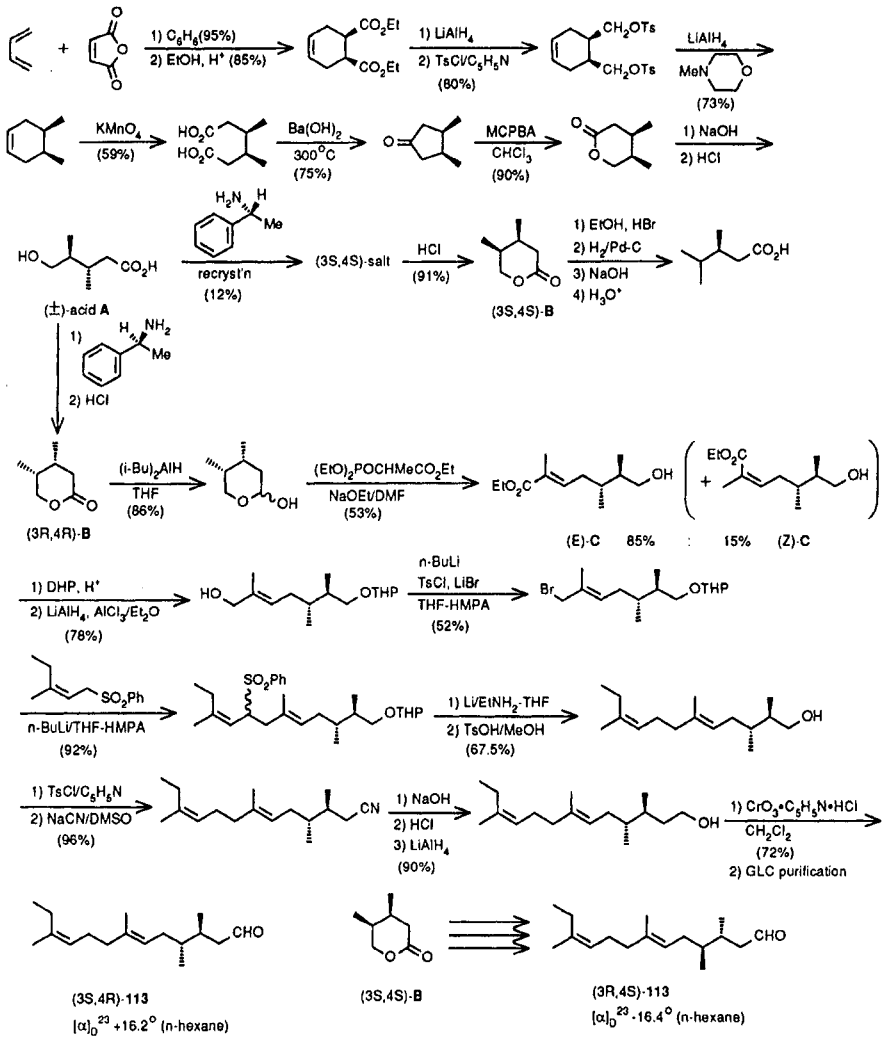


Scheme 302

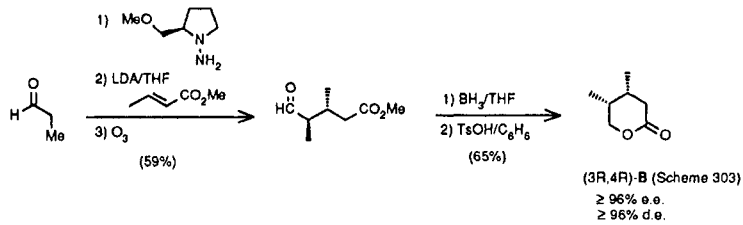
pendently by British groups. Baker et al. synthesized (±)-**113** as shown in Scheme 305.[411,412] In their synthesis, the *E*-double bond at C-6 was constructed stereoselectively by alkylation of the alkenyllithium derived from **A** with bromide (±)-**C,** which was prepared from Mori's intermediate (±)-**B.**

Knight and Ojhara employed the Wittig reaction for the construction of the C-6 double bond (Scheme 306).[413,414] Starting from Mori's intermediate (±)-**B,** phosphonium salt (±)-**D** was prepared via half ester (±)-**C.** The Wittig reaction between **A** and the phosphorane derived from **D** produced a mixture of stereoisomers (*E*:*Z* = 46:54). Separation of (±)-**113** from its (6*Z*)-isomer was finally achieved by preparative GLC.

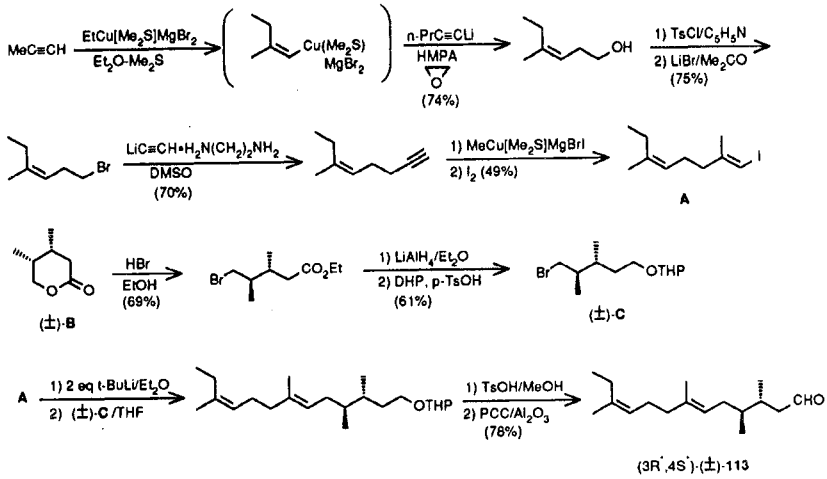
Szántay's synthesis provided geometrically and enantiomerically pure **113** for the first time (Scheme 307).[415,416] The key building blocks in this synthesis were (6*Z*)-homogeranyl bromide **(A)** and (*S*)-3-methyl-5-pentanolide **(B).** The latter was prepared by enzymatic production of a chiral half ester (methyl hydrogen 3-methylglutarate) from a prochiral diester (dimethyl 3-methylglutarate). As shown in Scheme 307, the synthesis was convergent, and proceeded in 1.9% overall yield from geraniol.



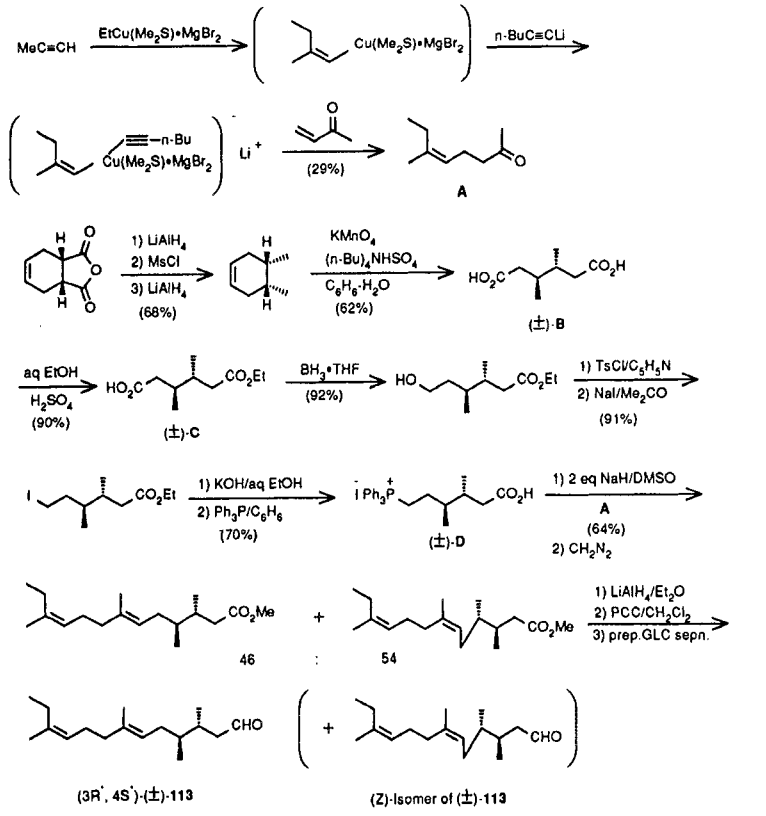
Scheme 303



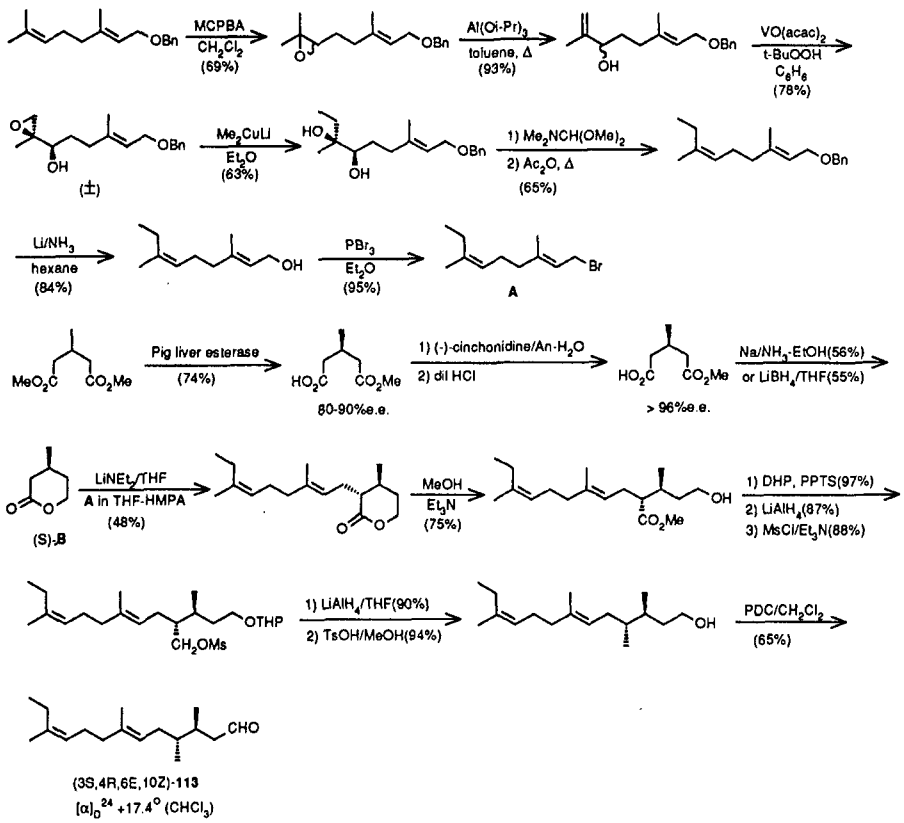
Scheme 304



Scheme 305



Scheme 306

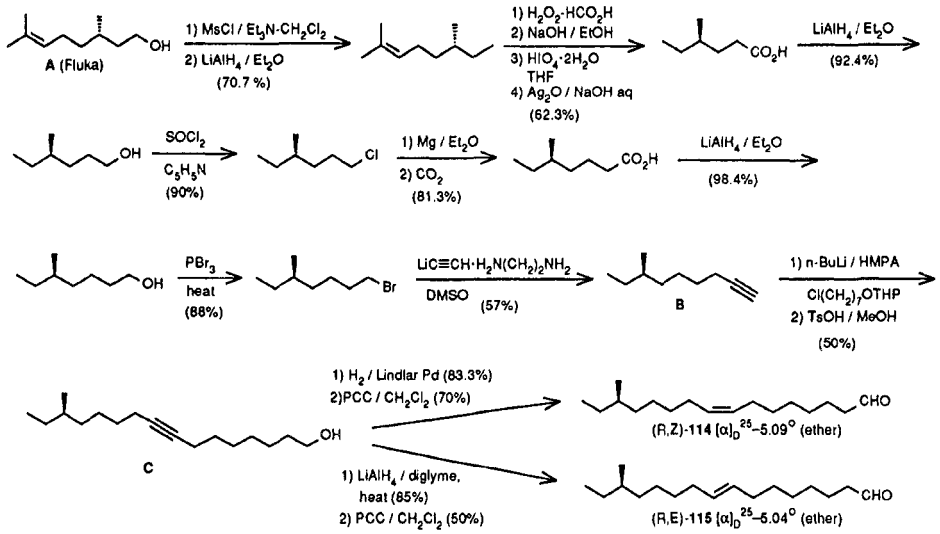


Scheme 307

O. (*R*,*Z*)-Trogodermal 114 and (*R*,*E*)-Trogodermal 115 [14-Methyl-8-hexadecenal] ($C_{17}H_{32}O$)

Dermestid beetles (*Trogoderma* species) and khapra beetle (*Trogoderma granarium*) employ trogodermals **114** and **115** as the female-produced sex pheromone. (*R*)-Trogodermal is the bioactive enantiomer,[417–419] although Rossi et al. claimed the (*S*)-isomer to be more bioactive.[420,421]

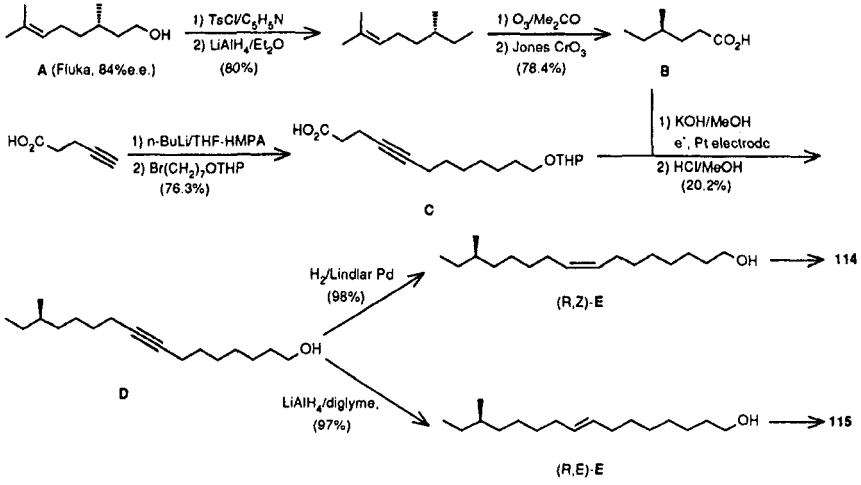
Synthesis of both **114** and **115** by Rossi et al. is shown in Scheme 308.[421] They started from (*S*)-(−)-citronellol (**A**) and employed the known alkyne **C**[cf. 422,423] as the key-intermediate. They claimed their (*R*)-**114** to be less bioactive than (*S*)-**114**, which had previously been synthesized by them.[424] Their (*S*)-**114** was reported to be active against the male khapra beetle at the dose of



Scheme 308

10^{-8}–10^{-9} μg, while (*R*)-**114** was active at 2×10^{-1} μg. This biological result was later disproved by Levinson.[419]

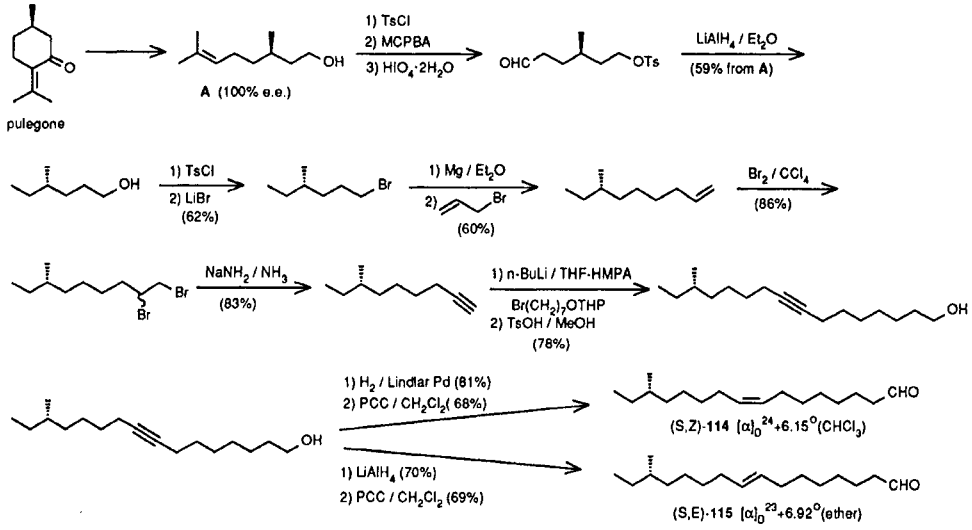
Mixed Kolbé electrolysis was employed as the key reaction in the synthesis of (*E*)- and (*Z*)-isomers of (*R*)-14-methyl-8-hexadecen-1-ol (**E**) by Jensen and Schäfer (Scheme 309).[425] Starting from (*S*)-citronellol (**A**), the acid **B** was pre-



Scheme 309

pared, which was then coupled with **C** to give **D** after deprotection. Reduction of **D** gave the alkenols **E**, which had already been converted (Rossi et al.[421]) to **114** and **115** respectively.

Mori et al. synthesized enantiomerically pure (*S*)-**114** and (*S*)-**115** to precisely determine their biological activity. (*R*)-Pulegone was converted to the enantiomerically pure (*R*)-citronellol, which was converted to the target molecules shown in Scheme 310.[426] By employing these samples, pure (*S*)-**114** was

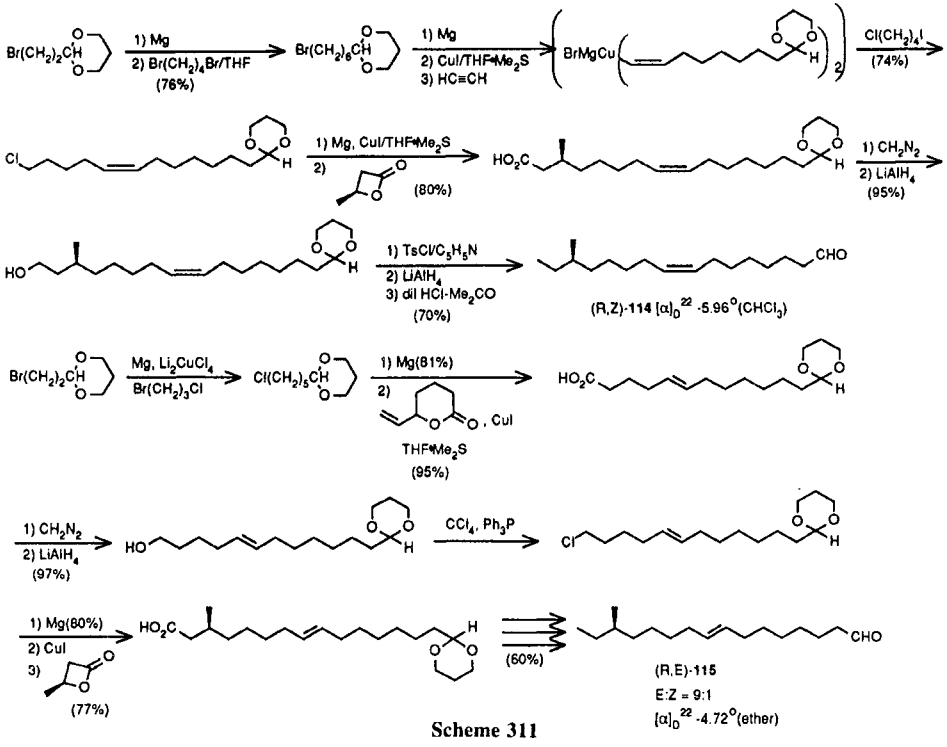


Scheme 310

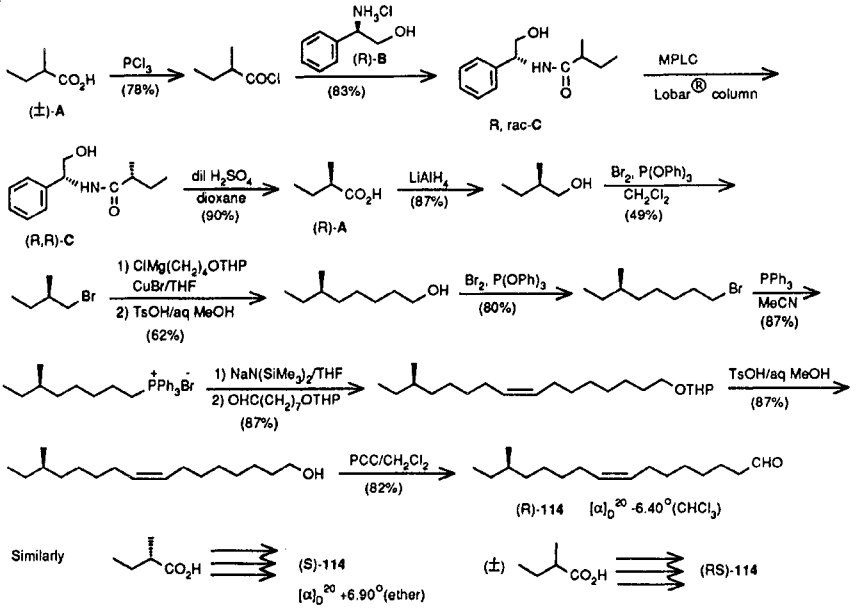
found to be 10^{-3} times less active than (*R*)-**114.** Similarly, (*R*)-**115** was 0.5×10^3 times more active than (*S*)-**115.** It should be added that (*S*)-**114** and (*S*)-**115** induced very low but definite receptor potentials when recorded from the antennae of male khapra beetles.

Sato et al. employed (*S*)-3-butanolide as the key chiral building block in their synthesis of **114** and **115** (Scheme 311).[427]

Bestmann et al. synthesized both (*R*)-**114** and (*S*)-**114** via optical resolution of 2-methylbutanoic acid **(A)** (Scheme 312).[428] The amide **C** prepared from **A** and (*R*)-phenylglycinol **(B)** could be separated by MPLC with a Lobar® column. The resolved acids, (*R*)-**A** and (*S*)-**A,** were converted to (*R*)-**114** and (*S*)-**114.** Bioassay of their samples on *T. granarium* confirmed the previous result: (*R*)-**114** was 10^2–10^3 times more active than (*S*)-**114.** It should be added that (*R*)-2-methyl-1-butanol, the key-intermediate in the synthesis of (*R*)-**114** and **115,** was synthesized by Brown et al. by their organoborane chemistry.[429]

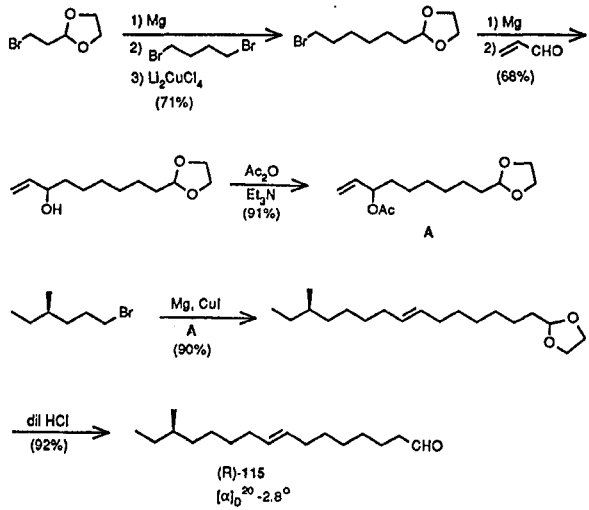


Scheme 311

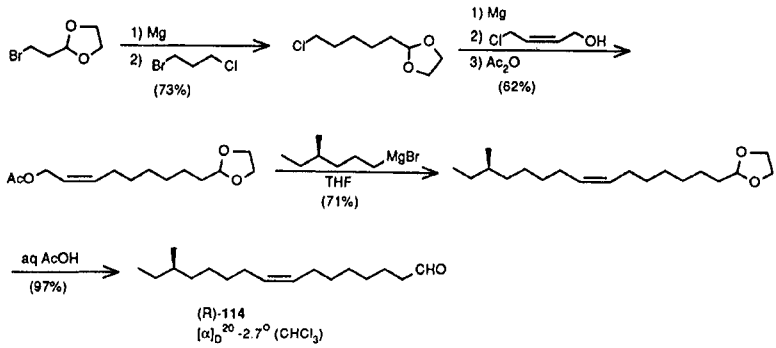


Scheme 312

Serebryakov and co-workers synthesized both (*R*)-**115** (Scheme 313)[430] and (*R*)-**114** (Scheme 314)[431] starting from (*R*)-4-methylhexyl bromide.

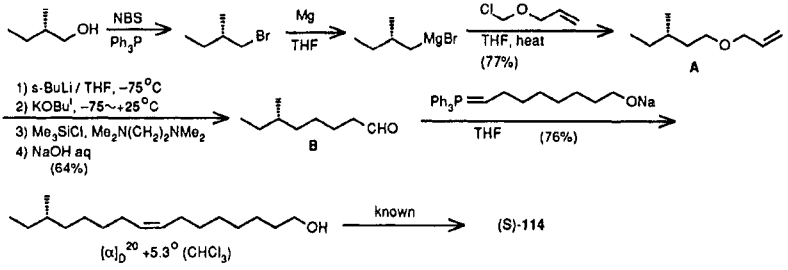


Scheme 313



Scheme 314

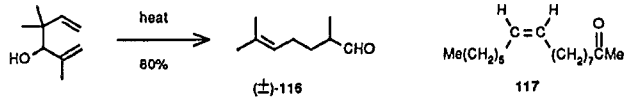
Schlosser and Strunk employed the Wittig rearrangement of allyl ether **A** to aldehyde **B** as the key-step in their synthesis of (*S*)-**114** (Scheme 315).[432]



Scheme 315

P. 2,6-Dimethyl-5-heptenal 116 ($C_9H_{16}O$)

This is the alarm pheromone of yellow ants (*Acanthomyops* species). Serebryakov and Gamalevich prepared (±)-**116** by means a Cope rearrangement (Scheme 316).[433]



Scheme 316

13. PHEROMONE KETONES

Many ketones are employed as pheromones. In this section, achiral ketones will be discussed first, followed by branched-chain chiral ketones and hydroxy ketones.

A. (Z)-5-Undecen-2-one ($C_{11}H_{20}O$)

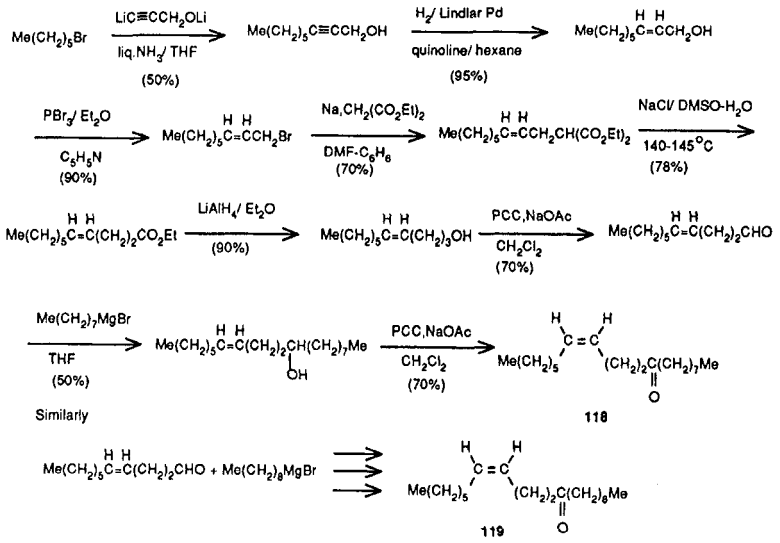
This was isolated as the principal volatile component contained in the pedal gland exudate of the bontebok (*Damaliscus dorcas dorcas*). A number of syntheses have been reported.[434-440] Because this is not an insect pheromone but a mammalian pheromone, these syntheses will not be detailed here.

B. (*Z*)-10-Heptadecen-2-one **117** ($C_{17}H_{32}O$)

Drosophila mulleri employs **117** as a component of its aggregation pheromone. This was prepared by treatment of (*Z*)-9-hexadecenoic acid with methyllithium.[342]

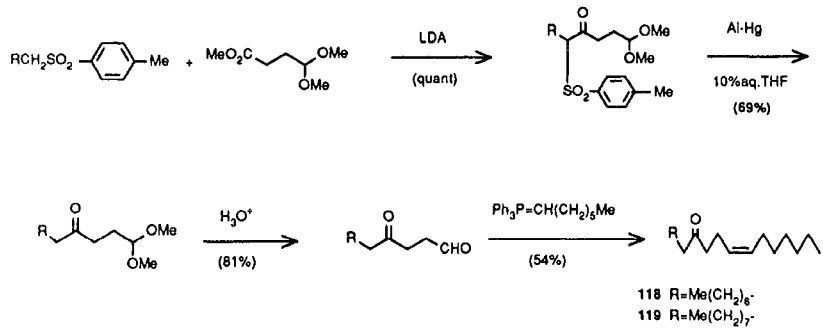
C. (*Z*)-12-Nonadecen-9-one **118** ($C_{19}H_{36}O$) and (*Z*)-13-Icosen-10-one **119** ($C_{20}H_{38}O$)

As two unsaturated ketones, **118** and **119** are the female-produced sex pheromone of the peach fruit moth (*Carposia niponensis*), which is the major economic pest of apples, peaches, and other fruits in Japan.[441] Since 1979 many new syntheses of **118** and **119** have been reported. Synthesis of both **118** and **119** by Vig et al. utilized the acetylene route (Scheme 317).[442]

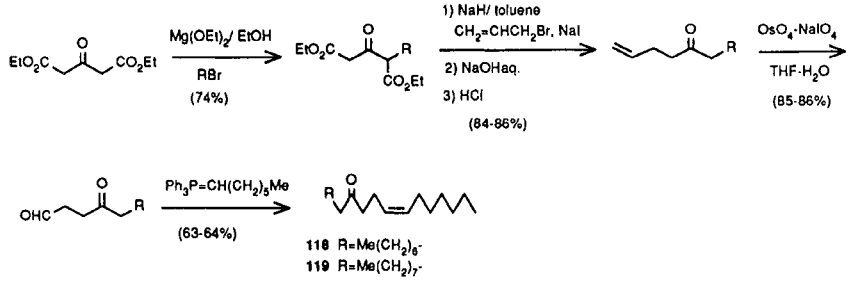


Scheme 317

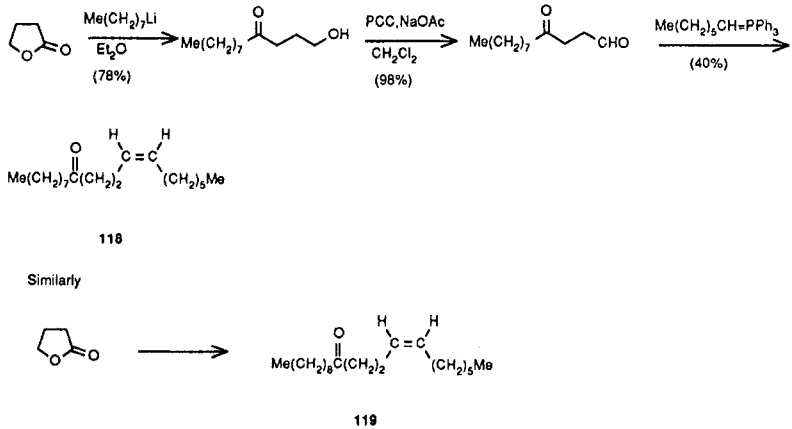
Yoshida and Saito prepared **118** and **119** employing acylation of a *p*-tolylsulfone as the key-step (Scheme 318), followed by the Wittig reaction.[443] Naoshima et al. also utilized the Wittig reaction to prepare **118** and **119** (Scheme 319).[444] The Wittig reaction was again employed by Hernández et al. in the synthesis of **118** and **119** (Scheme 320).[445]



Scheme 318

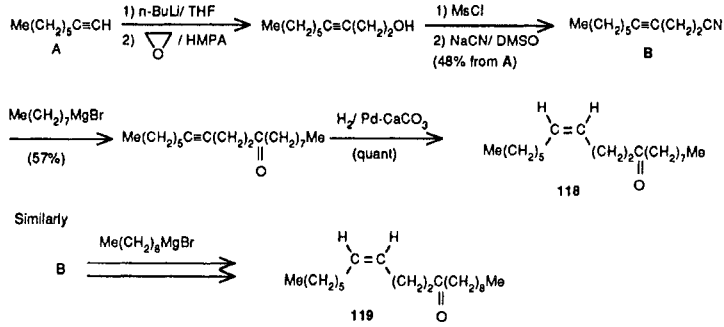


Scheme 319



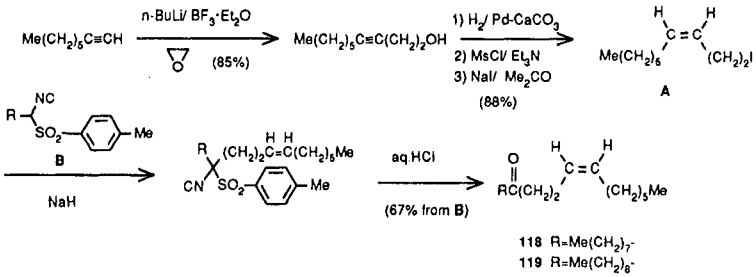
Scheme 320

Sonnet reported one-pot conversion of alkynes to cyanoethylated alkynes and applied the method to the preparation of **118** and **119** (Scheme 321).[446]



Scheme 321

Yadagiri and Yadav synthesized **118** and **119** by two successive alkylations on tosylmethyl isocyanide with appropriate alkyl groups, followed by hydrolysis of the resulting products to the ketones (Scheme 322).[447]



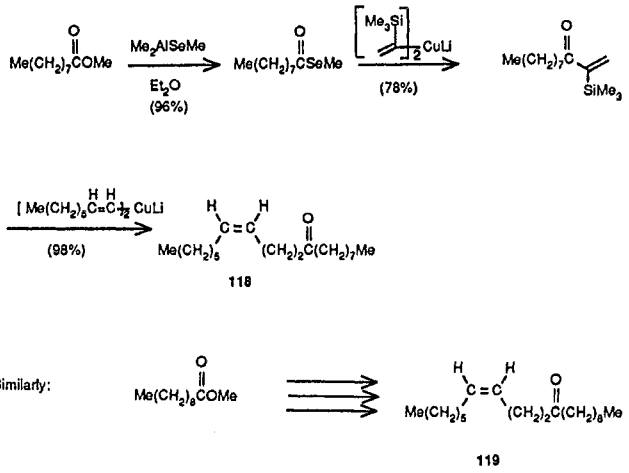
Scheme 322

Kochetkov and his co-workers achieved a short synthesis of **118** and **119** by the reaction of alkenylcopper(I) reagents with seleno esters (Scheme 323).[448]

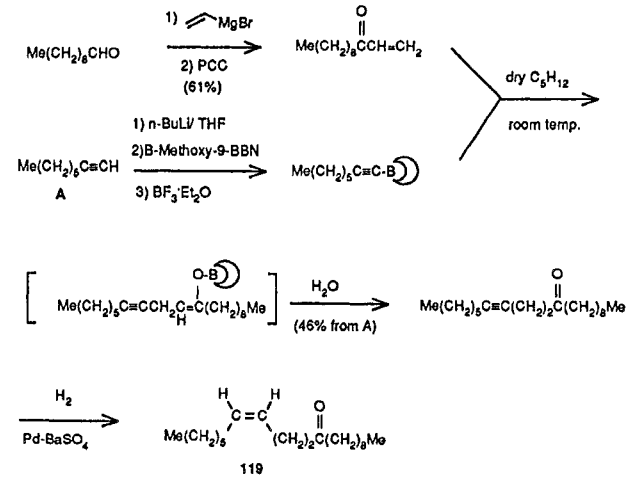
A synthesis of **119** by Kang and Cho was based on organoborane chemistry (Scheme 324).[449] Kang explored three other routes for the synthesis of **119** (Schemes 325–327).[450]

Wenkert et al. prepared the (*Z*)-alkene part of **118** by the nickel-catalyzed Grignard reaction with dihydropyran (Scheme 328).[451] By this method of (*Z*)-alkene preparation, they also synthesized muscalure (**19**) and (*Z*)-5-decenyl iso-

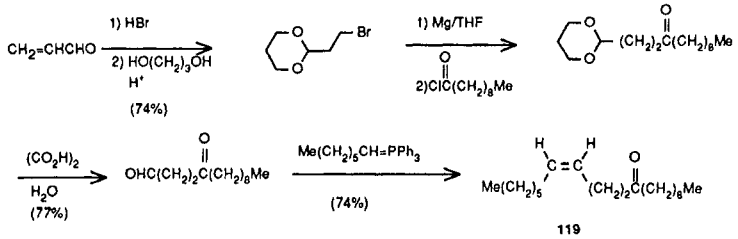
valerate, the female-produced sex pheromone of the pine emperor moth (*Nudaurelia cytherea cytherea*).[451]



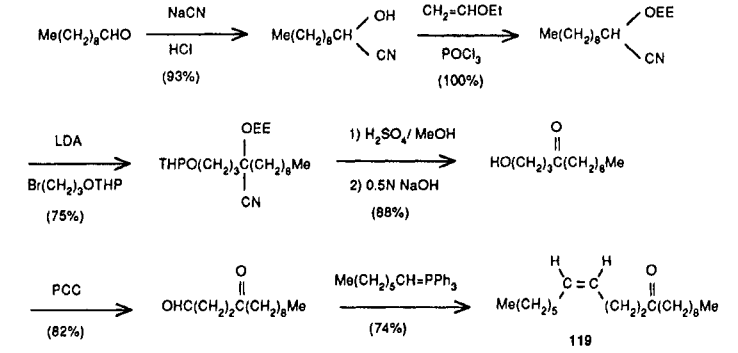
Scheme 323



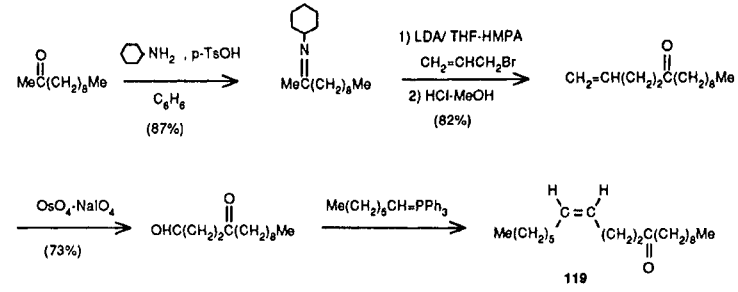
Scheme 324



Scheme 325



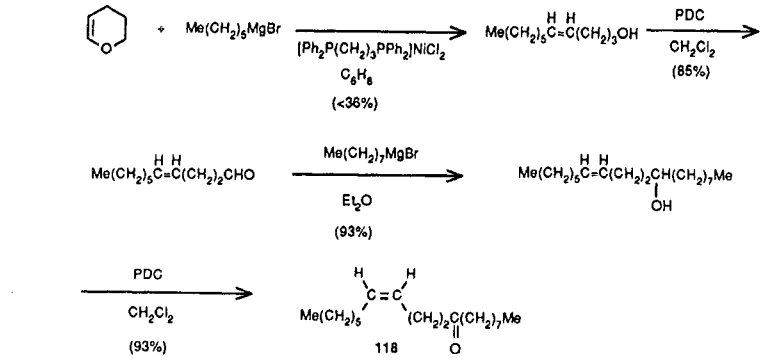
Scheme 326



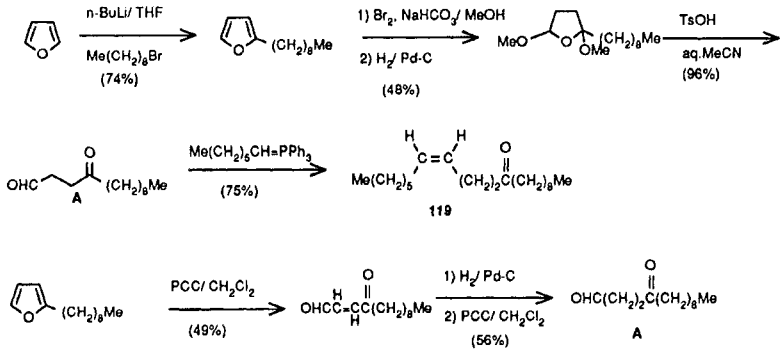
Scheme 327

In Kang's 1987 synthesis, 2-nonylfuran was employed as the precursor to provide keto aldehyde **A** necessary for the construction of **119** by the Wittig reaction (Scheme 329).[452] The same keto aldehyde was prepared in a different manner as shown by Bhalerao and his co-workers (Scheme 330).[453]

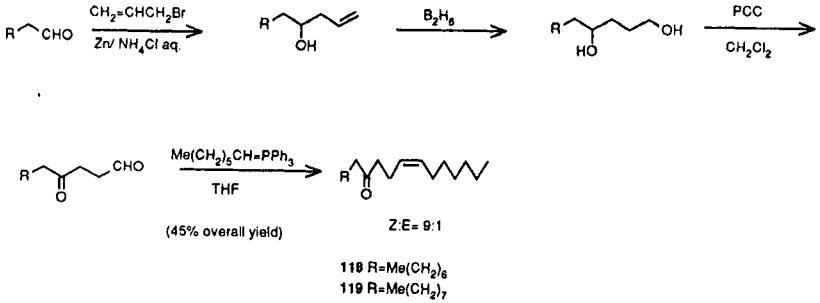
Trehan et al. synthesized **118** and **119** by alkylation of appropriate metallo-



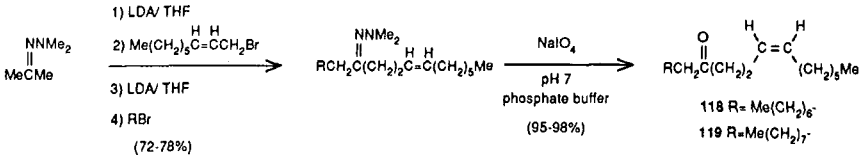
Scheme 328



Scheme 329



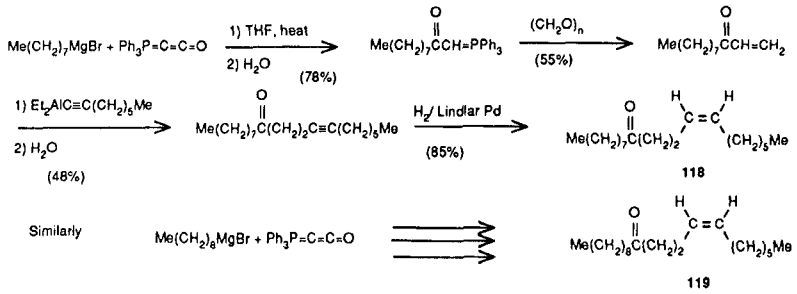
Scheme 330



Scheme 331

hydrazones followed by hydrolysis (Scheme 331).[454] Independently, Yamashita et al. prepared **118** and **119** by the same method.[455]

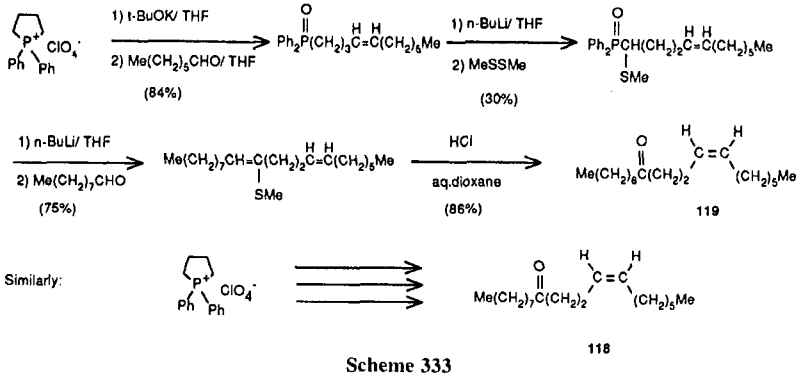
Bestmann and Schmidt developed an interesting route to **118** and **119** by using a reaction between Grignard reagents and ketenylidene triphenylphosphorane (Scheme 332).[456]



Scheme 332

A synthesis of **118** and **119** from furfural was reported.[457] Both **118** and **119** were prepared in four steps from 1-decyne and 1-undecyne, respectively.[458]

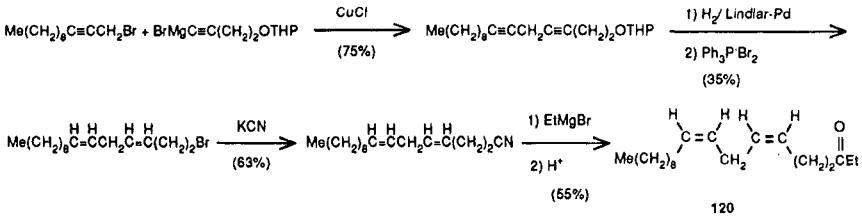
Yamamoto et al. prepared both **118** and **119** from 1,1-diphenyl-phosphoranium perchlorate (Scheme 333).[459]



Scheme 333

D. (6Z,9Z)-6,9-Nonadecadien-3-one 120 ($C_{19}H_{34}O$)

(3Z,6Z,9Z)-3,6,9-Nonadecatriene **(61)** and (6Z,9Z)-6,9-nonadecadien-3-one **(120)** are the female-produced sex pheromones of *Peribatodes rhomboidaria*, which is a pest in vineyards.[460] Buser et al. synthesized **120** in a manner similar to the synthesis of the peach fruit moth (*Carposina*) pheromones **118** and **119** (Scheme 334).[460]

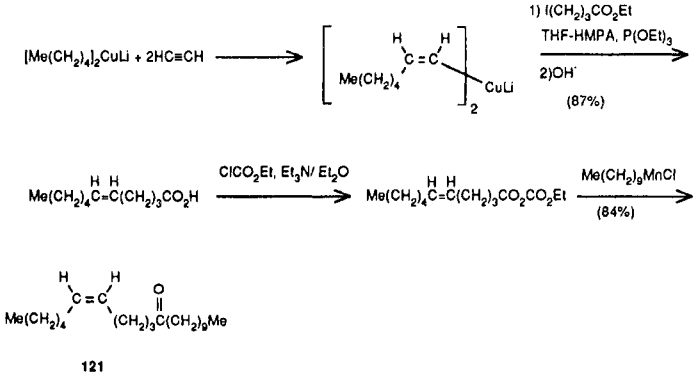


Scheme 334

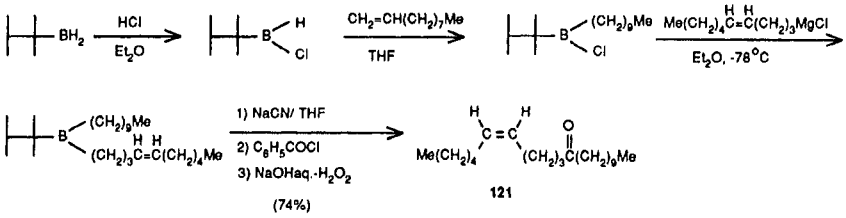
E. (Z)-6-Henicosen-11-one 121 ($C_{21}H_{40}O$) and (Z)-1,6-Henicosadien-11-one 122 ($C_{21}H_{38}O$)

These are the principal **(121)** and the minor **(122)** male-produced sex pheromone components of the Douglas-fir tussock moth (*Orgyia pseudotsugata*). Many new syntheses of **121** and **122** have been reported since 1979.

Normant and his co-workers used organocopper and organomanganese chemistry to prepare **121** (Scheme 335).[115] Thexylchloroborane was employed by Zweifel and Pearson for the synthesis of **121** (Scheme 336).[461]

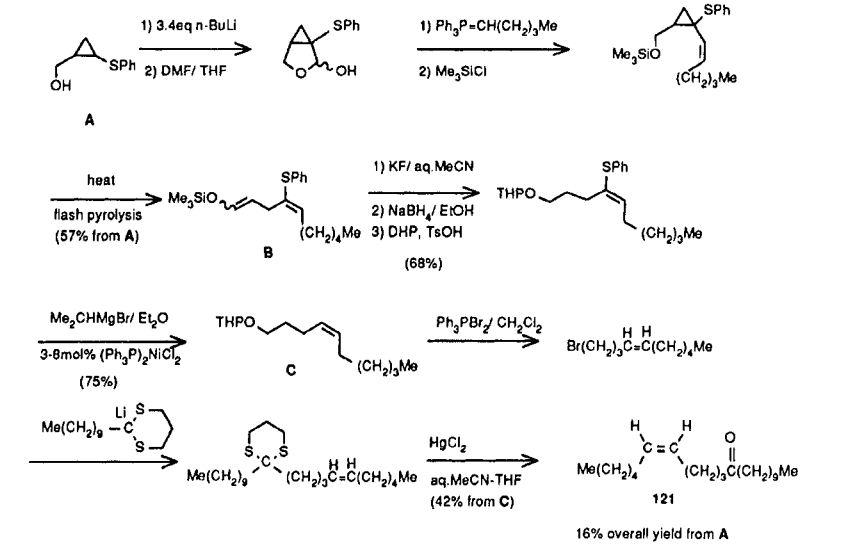


Scheme 335



Scheme 336

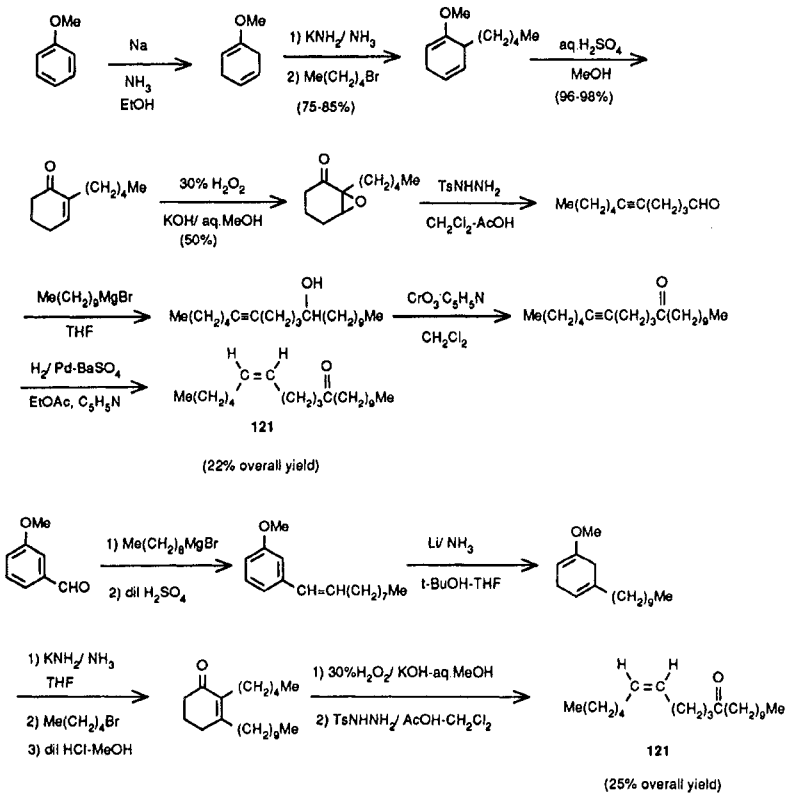
Trost's synthesis of **121** is based on his finding that isopropylmagnesium bromide in the presence of bis-(triphenylphosphino)nickel(II) chloride reduces vinyl sulfides to the corresponding olefins without overreduction; this 11-step synthesis provided **121** in 16% overall yield from **A** (Scheme 337).[462]



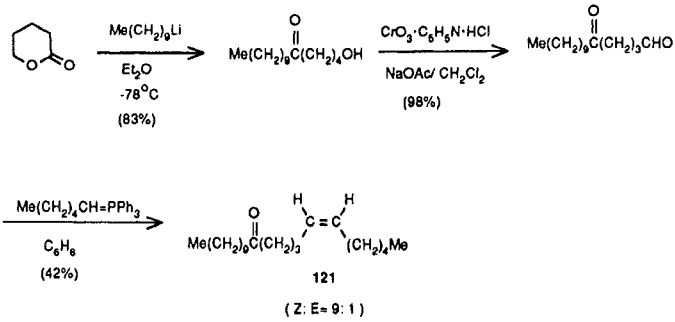
Scheme 337

Subba Rao et al. employed the Birch reduction and Eschenmoser cleavage as the key-steps in their two different syntheses of **121** (Scheme 338),[463] which proved to be quite efficient.

A very short synthesis of **121** (Scheme 339) was reported by Fernández et al., although the geometrical purity of **121** was $Z:E = 9:1$.[445]

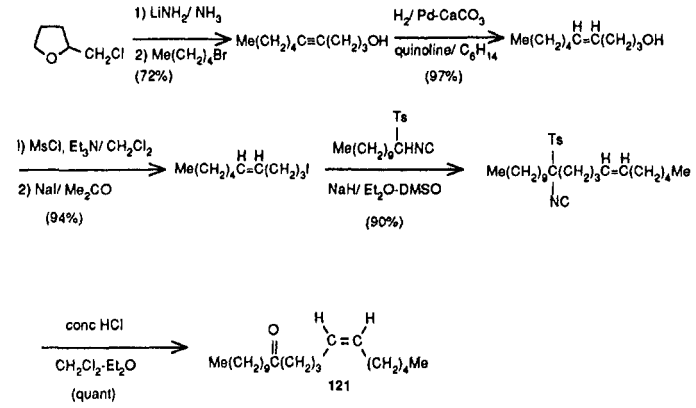


Scheme 338



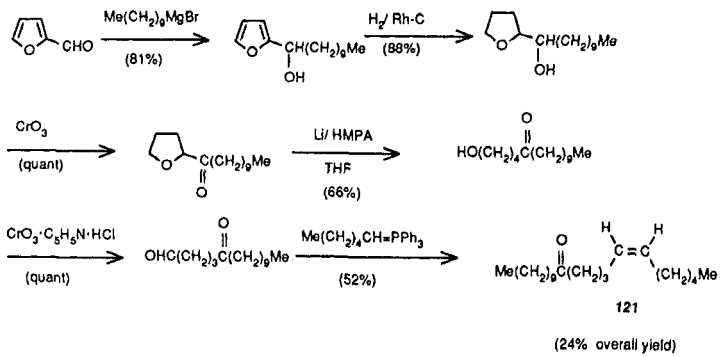
Scheme 339

Yadav's synthesis of **121** involved alkylation of tosylmethylisocyanide followed by acid hydrolysis (Scheme 340).[464]



Scheme 340

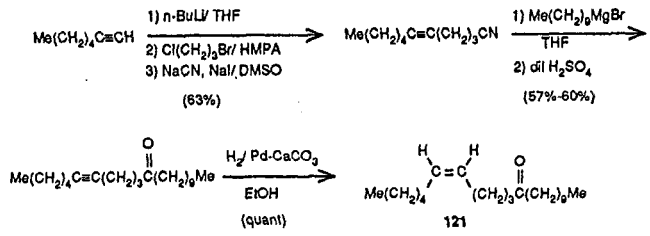
Fernández reported another synthesis of **121** starting from furfural (Scheme 341).[465]



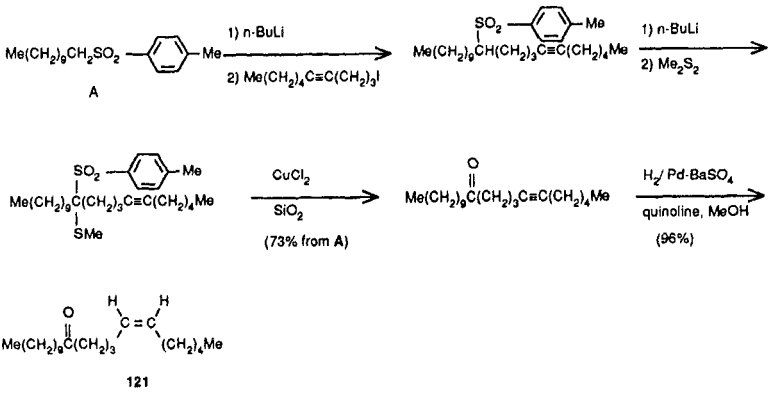
Scheme 341

Sonnet's method of one-pot conversion of an alkyne to a 5-alkynenitrile was applied to the synthesis of **121** (Scheme 342), and gave it in > 30% overall yield.[446]

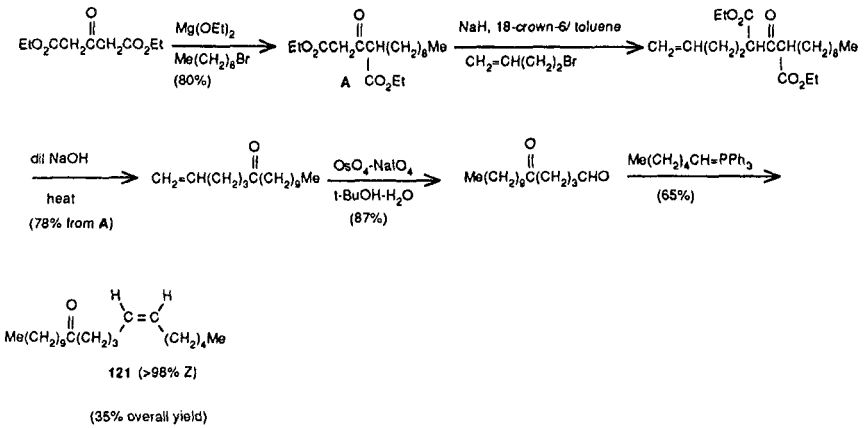
Murata et al. reported a synthesis of **121** starting from tosylsulfone **A** (Scheme 343).[466] Naoshima's synthesis began with diethyl 3-oxoglutarate and gave **121** in 35% overall yield (Scheme 344).[467]



Scheme 342

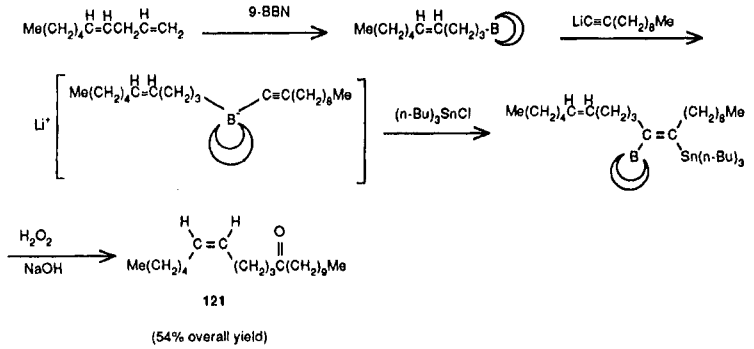


Scheme 343



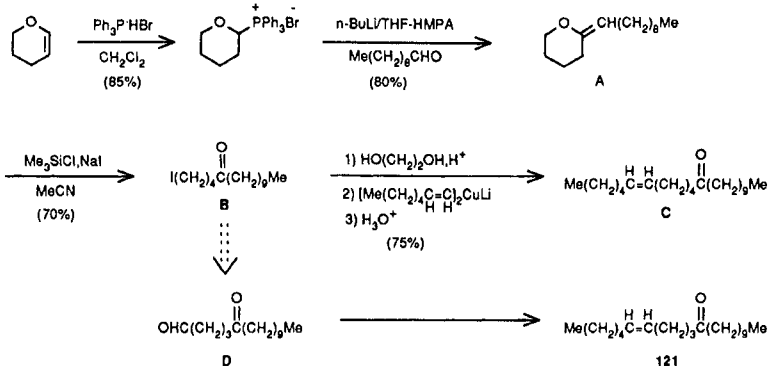
Scheme 344

Wang and Chu reported a highly efficient synthesis of **121** by tri-*n*-butyltin chloride-induced intramolecular transfer reaction of lithium 1-alkynyltrialkylborate (Scheme 345).[214]



Scheme 345

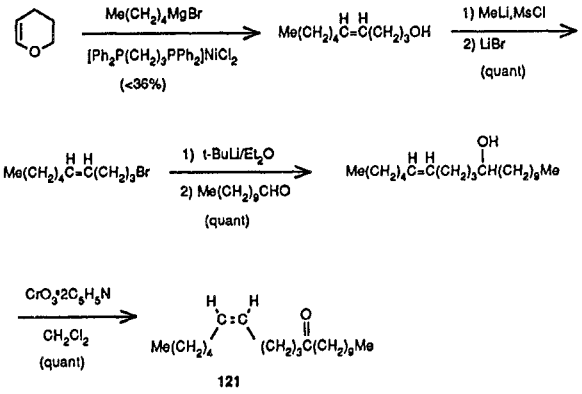
Ousset et al. claimed that they prepared **121** by an interesting route via an enol ether **A** (Scheme 346).[468] What they actually synthesized, however, was



Scheme 346

not **121** but **C**. Conversion of their intermediate **B** to **D** will complete the synthesis of **121** from **A**, because **D** is a popular intermediate for the synthesis of **121** (*vide supra*).

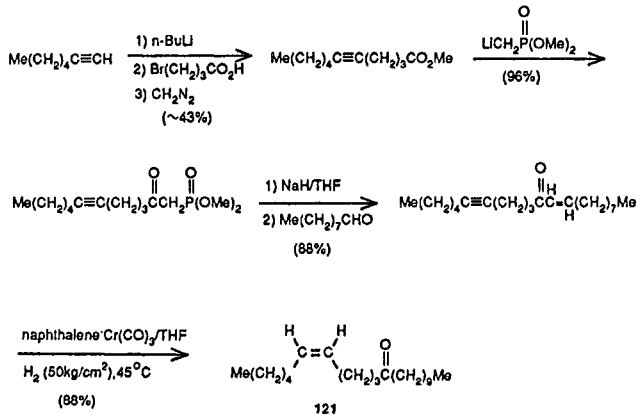
Wenkert employed the nickel-catalyzed Grignard reaction with dihydropyran for the construction of the *Z*-double bond of **121** (Scheme 347).[451]



Scheme 347

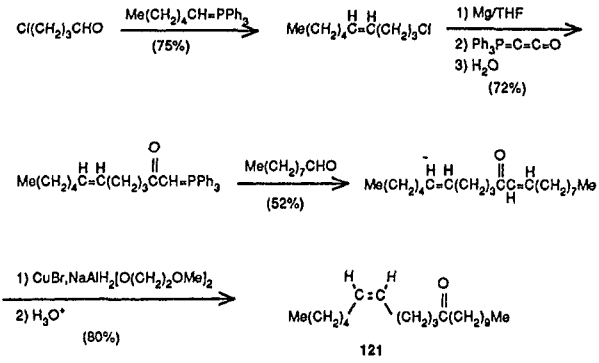
Sodeoka and Shibasaki found a new hydrogenation procedure for alkynes to give (*Z*)-alkenes and α,β-unsaturated ketones to yield saturated ketones using (naphthalene)tricarbonylchromium(0) catalyst, and employed this reaction for the synthesis of **121** (Scheme 348).[469]

Bestmann and Schmidt reported a unique four-step synthesis of both **121**

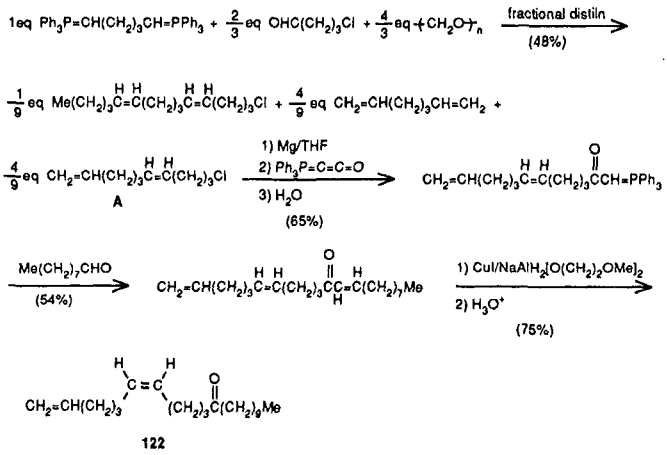


Scheme 348

(Scheme 349) and **122** (Scheme 350) using the reaction of Grignard reagents with ketenylidene triphenylphosphorane as the key-step.[456]

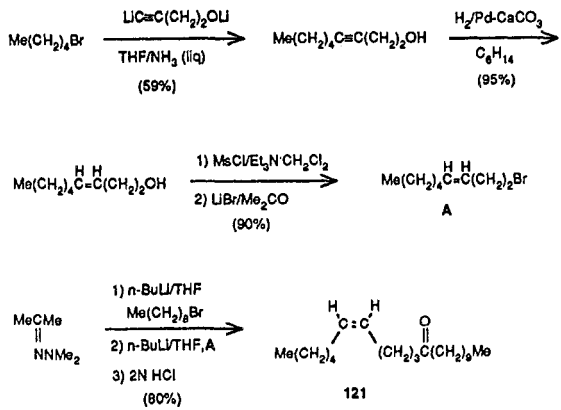


Scheme 349

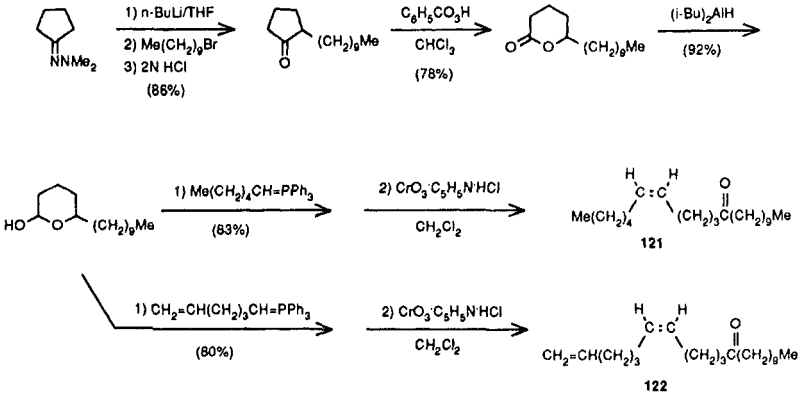


Scheme 350

Bis-alkylation of acetone *N,N*-dimethylhydrazone yielded **121** (Scheme 351) as reported by Reddy and Mitra.[470] They then described an improved route to both **121** and **122** starting from cyclopentanone *N,N*-dimethylhydrazone (Scheme 352).[471]



Scheme 351

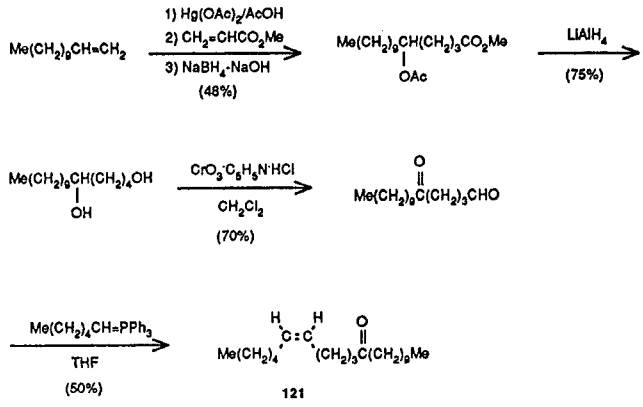


Scheme 352

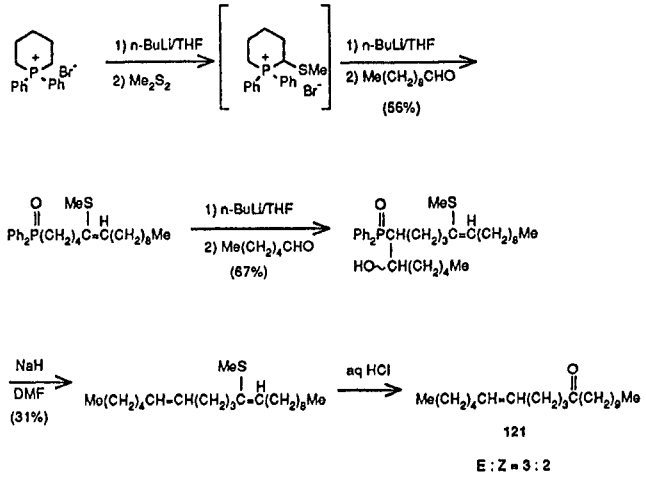
Bhalerao and Dasaradhi prepared **121** as shown in Scheme 353.[48] The key-step was the solvomercuration of 1-dodecene and reductive carbon-carbon bond formation with methyl acrylate in the presence of sodium borohydride to give methyl 5-acetoxypentadecanoate.[48]

Yamamoto et al. prepared a mixture of **121** and its (*E*)-isomer from a cyclic phosphonium salt (Scheme 354).[472]

Mitra and Reddy achieved a simple synthesis of both **121** and **122** in two



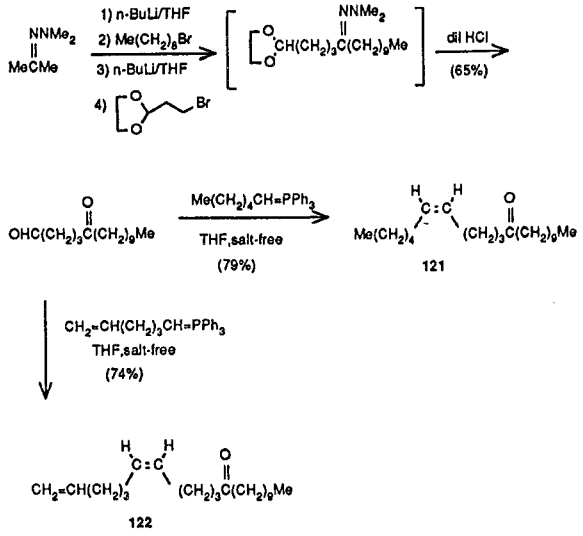
Scheme 353



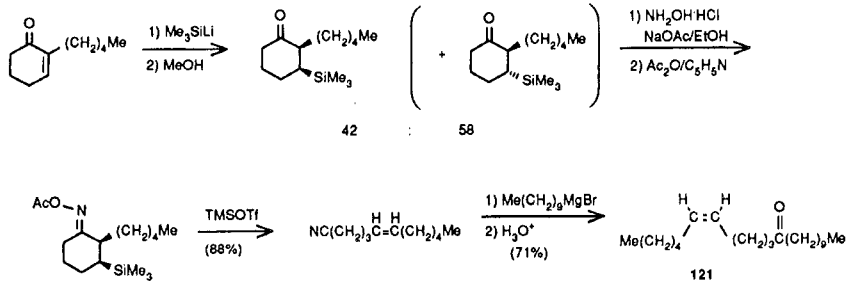
Scheme 354

steps using acetone dimethylhydrazone as the key starting material (Scheme 355).[473]

Nishiyama's synthesis of **121** started from a cyclohexenone and utilized silicon-directed Beckmann fragmentation (Scheme 356).[208]



Scheme 355



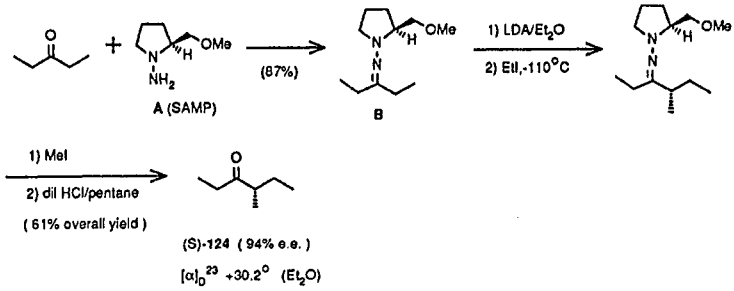
Scheme 356

F. (Z)-24-Tritriaconten-2-one 123 ($C_{33}H_{64}O$)

This, together with 2-hentriacontanone and some other homologs, is the female-produced sex-attractant pheromone of the Canadian red-sided garter snake (*Thamnophis sirtalis parietalis*), which is not an insect; therefore, its pheromone chemistry will not be discussed here.

G. (*S*)-4-Methyl-3-hexanone 124 ($C_7H_{14}O$)

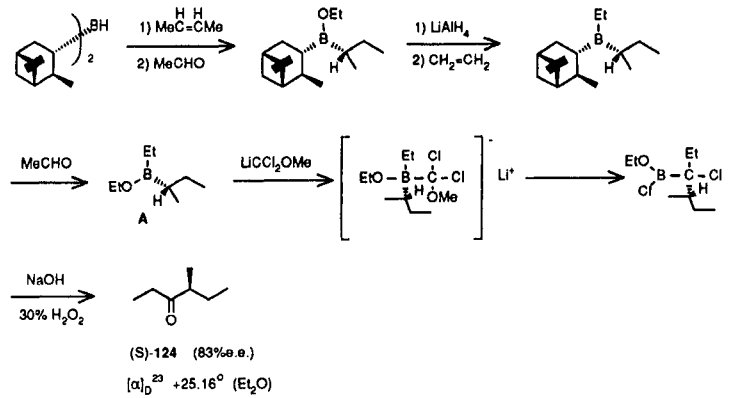
The ant *Manica mutica* uses (*S*)-(+)-4-methyl-3-hexanone (**124**) as its alarm pheromone. Enders et al. reported an asymmetric synthesis of **124** by alkylation of a metallated chiral hydrazone (Scheme 357).[474,475] Reaction of diethyl ketone



Scheme 357

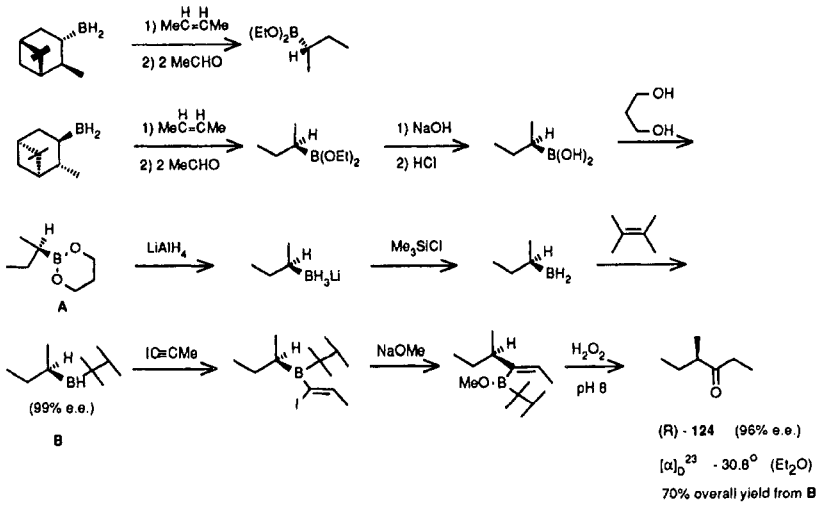
with (*S*)-1-amino-2-methoxymethylpyrrolidine (**A**, SAMP) yielded a chiral hydrazone **B**, of which alkylation was found to be highly enantioselective.[474,475]

Brown et al. synthesized **124** (83% e.e.) by carbenoidation of a chiral borinic ester **A** (Scheme 358).[476] Another asymmetric synthesis of the antipodal (*R*)-**124**



Scheme 358

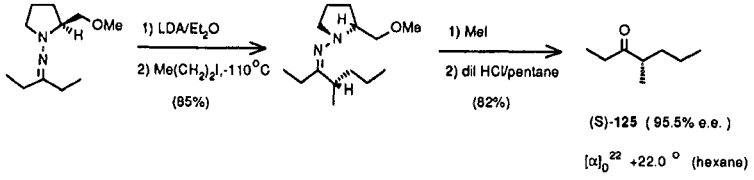
(96% e.e.) was also achieved by Brown et al. by employing a chiral boronic ester **A** as the key-intermediate (Scheme 359).[338] Optically active monoalkylthexylboranes such as **B** (> 99% e.e.) are useful chiral building blocks in synthesizing a variety of optically active compounds.



Scheme 359

H. (*S*)-4-Methyl-3-heptanone 125 ($C_8H_{16}O$)

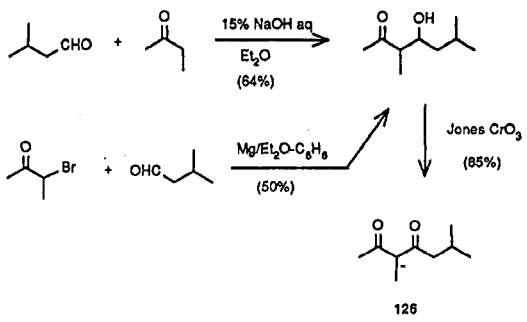
The leaf-cutting ant (*Atta texana*) employs (*S*)-**125** as its principal alarm pheromone. Enders synthesized **125** (99.5% e.e.) by his SAMP-hydrazone alkylation method (Scheme 360).[474,475]



Scheme 360

I. 3,6-Dimethyl-2,4-heptanedione 126 ($C_9H_{16}O_2$)

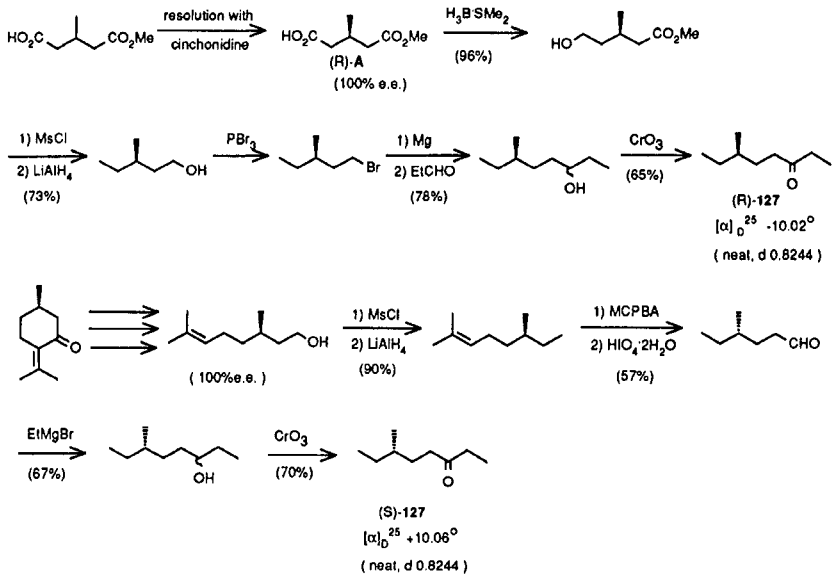
This is the female-produced pheromone of the mushroom fly (*Megaselia halterata*). Starting from 4,000 female flies, 30 μg of **126** was obtained. This pheromone exists as a mixture of the keto-enol tautomers in a 3 : 1 ratio; therefore, the chirality at C-3 is interchangeable. The synthesis of **126** by Baker et al. is shown in Scheme 361.[477]



Scheme 361

J. 6-Methyl-3-octanone 127 ($C_9H_{18}O$)

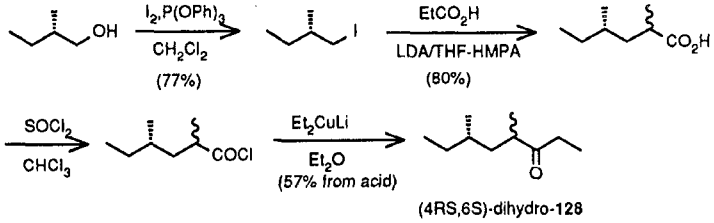
This was identified as the alarm pheromone of ants in the genus *Crematogaster*. Naoshima et al. synthesized both the enantiomers of **127** (Scheme 362).[478] The overall yield of (*R*)-**127** from (*R*)-**A** was 26%, while that of (*S*)-**127** from (*R*)-pulegone was 14%.



Scheme 362

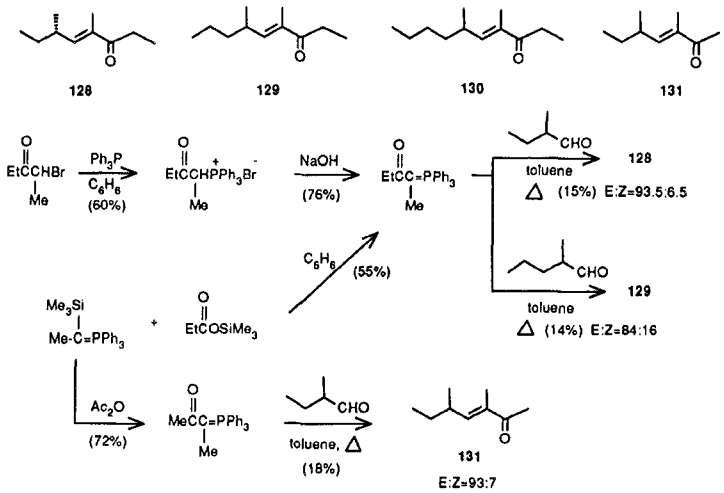
K. (*S*)-Manicone [(4*E*,6*S*)-4,6-Dimethyl-4-octen-3-one] 128 ($C_{10}H_{18}O$), Homomanicone 129 ($C_{11}H_{20}O$), Bishomomanicone 130 ($C_{12}H_{22}O$), and Normanicone 131 ($C_9H_{16}O$)

Manicone **(128)** is the alarm pheromone constituent of the mandibular glands in two North American species of ants, *Manica mutica* and *M. bradleyi*. It is also the main pheromone of *M. rubida*. Its absolute configuration was recently assigned as *S* by comparing dihydromanicone with synthetic (4*RS*,6*S*)-4,6-dimethyl-3-octanone employing the complexation GLC method.[479,480] The synthesis of (4*RS*,6*S*)-dihydromanicone is shown in Scheme 363.[480] In addition to



Scheme 363

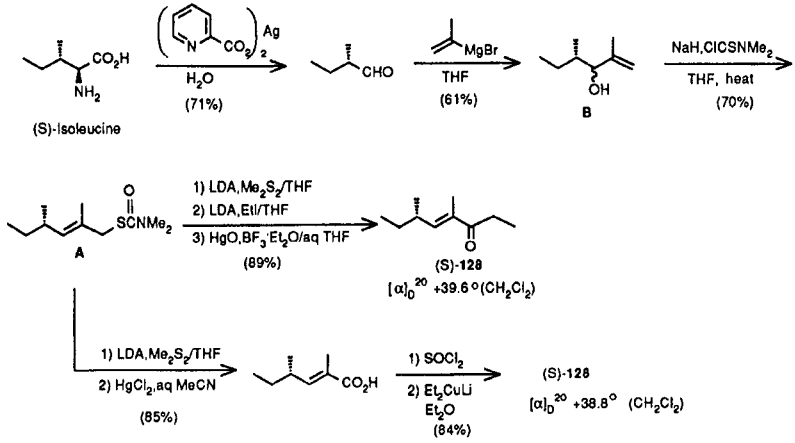
manicone **(128)**, Bestmann et al. also isolated **129**, **130**, and **131** (**128**:**129**:**130**:**131** = 100:6:0.3:2.7) in the mandibular gland secretion of *M. rubida*.[480] Bestmann's synthesis of (±)-**128**, (±)-**129**, and (±)-**131** is shown in Scheme 364.[480] The Wittig reaction was fairly selective in giving (*E*)-**128**



Scheme 364

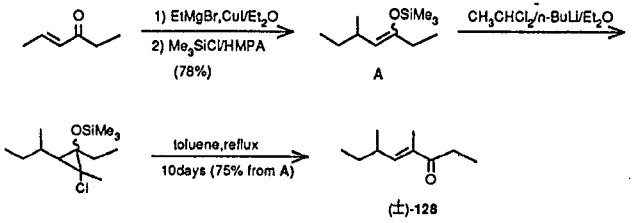
and its higher (**129**) or lower (**131**) homologs, although the yield was rather poor.

Nakai and co-workers prepared **128** starting from (*S*)-isoleucine (Scheme 365).[481] Their key-intermediate was allylic thiocarbamate **A** readily derived from allylic alcohol **B** via the [3,3]sigmatropic rearrangement.



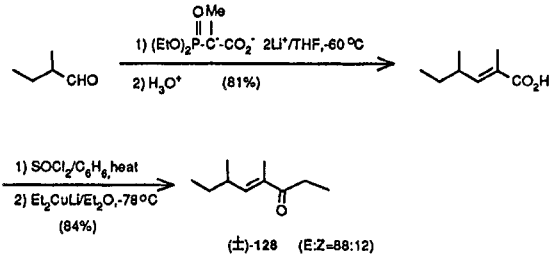
Scheme 365

Three other syntheses of (±)-**128** were reported. Conia et al. synthesized (±)-**128** by the addition of chloromethylcarbene to trimethylsilyl enol ether and subsequent thermolysis of the addition product (Scheme 366).[482] Coutrot and



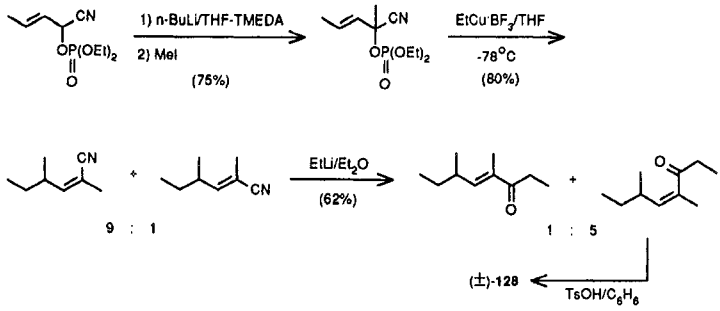
Scheme 366

Ghribi prepared (±)-**128** using the Horner reaction with 2-diethoxyphosphonopropanoic acid dianion (Scheme 367).[483] A synthesis of (±)-**128** by Yoneda et



Scheme 367

al. utilized their finding that enone cyanohydrin diethyl phosphates react regioselectively and stereoselectively with a variety of organocopper reagents to give (*Z*)-predominant 2-alkenenitriles as γ-coupling products. Thus, the (*Z*)-isomer of (±)-**128** was obtained as the major product (Scheme 368), which could be isomerized to (±)-**128** by treatment with acid.[484]

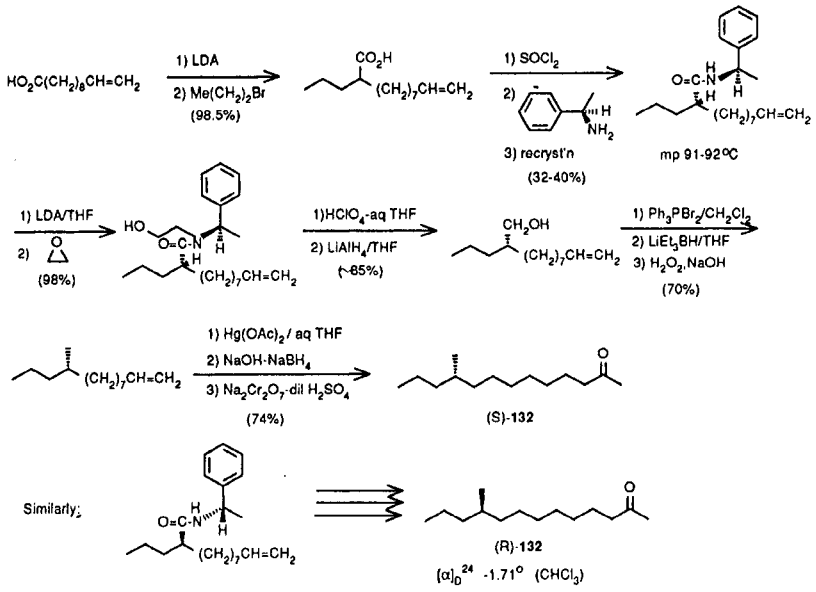


Scheme 368

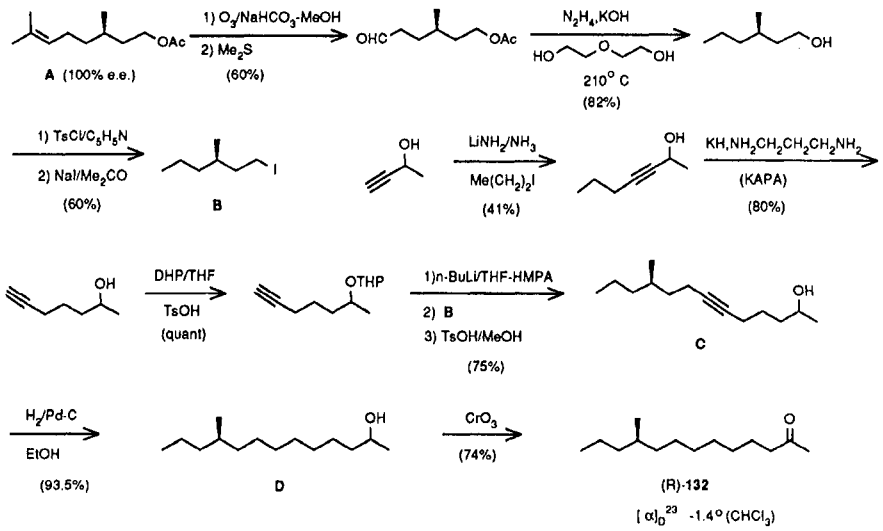
L. (*R*)-10-Methyl-2-tridecanone 132 ($C_{14}H_{28}O$)

This is the sex pheromone of the southern corn rootworm (*Diabrotica undecimpunctata howardi*). Sonnet synthesized both the enantiomers of **132** starting from 10-undecenoic acid involving the optical resolution of an intermediate (Scheme 369).[336] Male southern corn rootworms preferred (*R*)-**132**.[485]

Senda and Mori synthesized (*R*)-**132** starting from (*R*)-citronellyl acetate (**A**) (Scheme 370).[486] Although their starting material **A** was of 100% e.e., partial racemization might have taken place to a small extent at the stage of hydrogen-



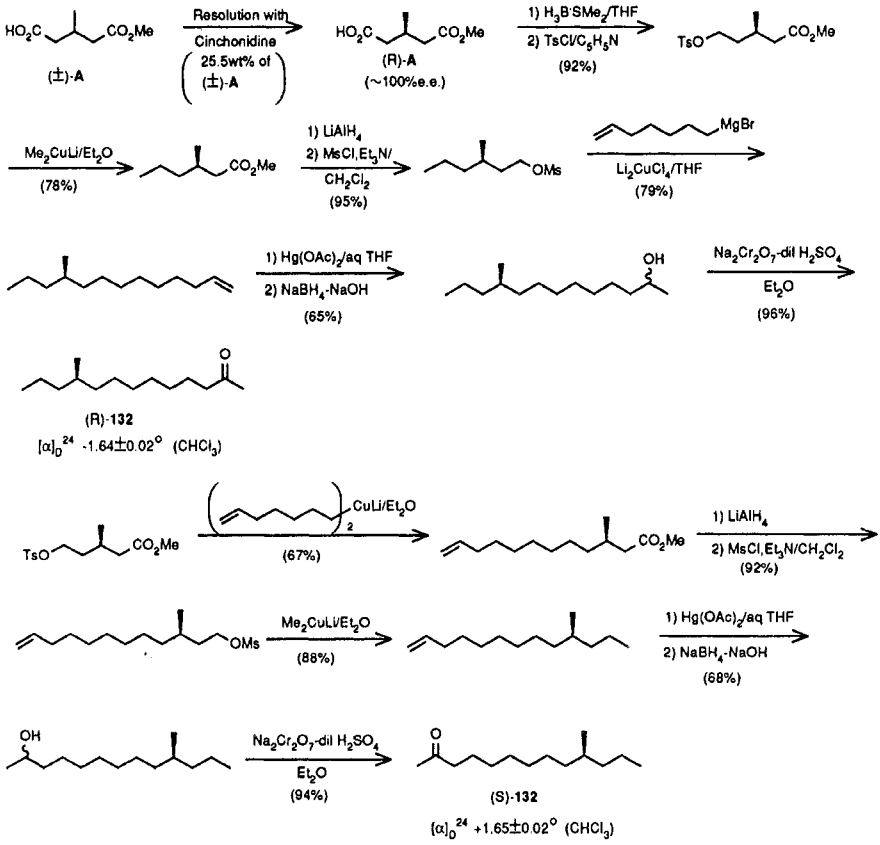
Scheme 369



Scheme 370

ation of alkyne **C** to alkane **D** on palladium-charcoal. This possible racemization was later pointed out by Oppolzer.[487]

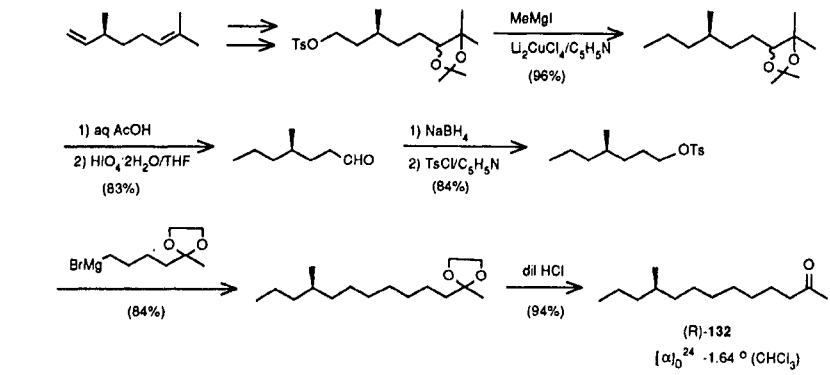
Rossi's synthesis of the enantiomers of **132** started from methyl hydrogen (*R*)-3-methylglutarate **(A)** (Scheme 371), and furnished enantiomerically pure



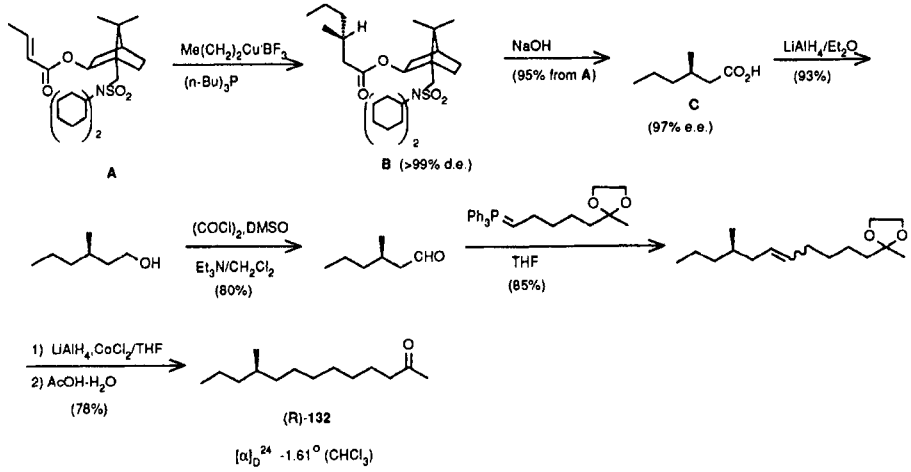
Scheme 371

(*R*)- and (*S*)-**132**.[488] Serebryakov et al. synthesized (*R*)-**132** from (*S*)-3,7-dimethyl-1,6-octadiene with an overall yield of 24–26% (Scheme 372).[489]

The key-step in Oppolzer's synthesis of (*R*)-**132** was the asymmetric 1,4-addition of propylcopper to the camphorsulfonamide-shielded crotonate ester (Scheme 373).[487] They avoided the racemization in the course of saturation of



Scheme 372



Scheme 373

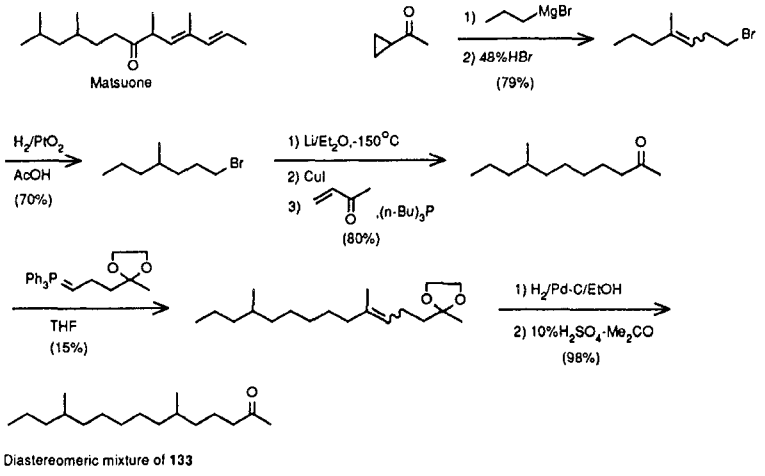
the double bond by using lithium aluminum hydride in the presence of cobalt (II) chloride as the reducing agent.

M. Matsuone [(2*E*,4*E*)-4,6,10,12-Tetramethyl-2,4-tridecadien-7-one] ($C_{17}H_{30}O$)

The pine bast scales (*Matsucoccus resinosae*, *M. matsumurae*, and *M. thunbergianae*) use this compound as the primary component of their sex-attractant pheromones.[490] A synthesis of this ketone has been accomplished,[490] but the details are not yet available (March 1990).

N. (6*R*,12*R*)-6,12-Dimethyl-2-pentadecanone 133 ($C_{17}H_{34}O$)

The female-produced sex pheromone of the banded cucumber beetle (*Diabrotica balteata*) was isolated and identified as 6,12-dimethyl-2-pentadecanone **(133).**[491] Chuman et al. synthesized a diastereomeric mixture of **133,** and the product was proved to be bioactive (Scheme 374).[491]

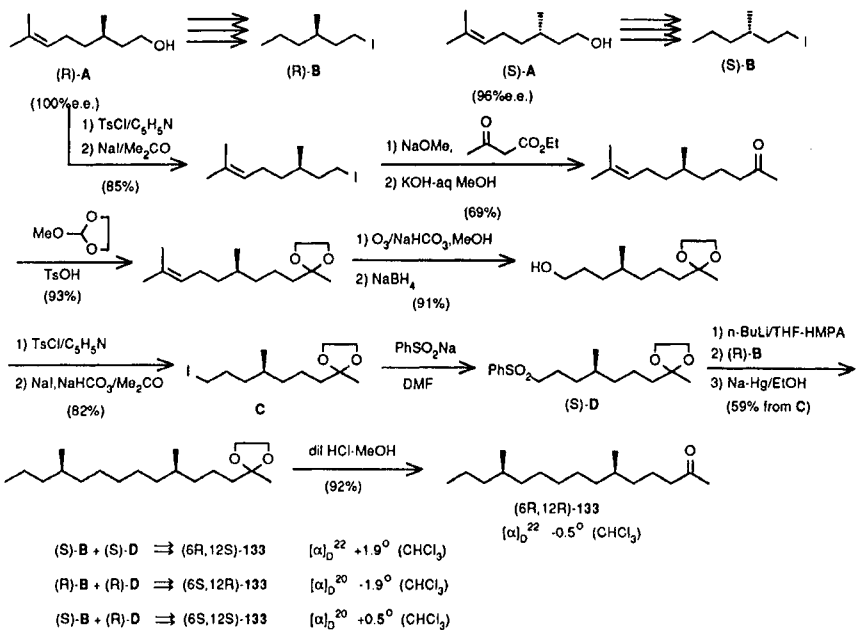


Scheme 374

All of the four possible stereoisomers of **133** were then synthesized by Mori and Igarashi starting from the enantiomers of citronellol **(A).**[492] The terminal building block **B** was prepared from **A** by the known method (Scheme 375).[486] Another building block was the phenylsulfone **D,** which was also prepared from **A** via **C.** The scheme shows the four possible combinations of the enantiomers of **B** and **D** that furnished all of the isomers of **133.** Bioassay showed (6*R*,12*R*)-**133** to be highly active, while (6*S*,12*S*)-**133** was inactive. Both (6*R*,12*S*)-**133** and (6*S*,12*R*)-**133** were only marginally active.[493]

O. (3*S*,11*S*)-3,11-Dimethyl-2-nonacosanone 134 ($C_{21}H_{42}O$) and (3*S*,11*S*)-29-Hydroxy-3,11-dimethyl-2-nonacosanone 135 ($C_{21}H_{42}O_2$)

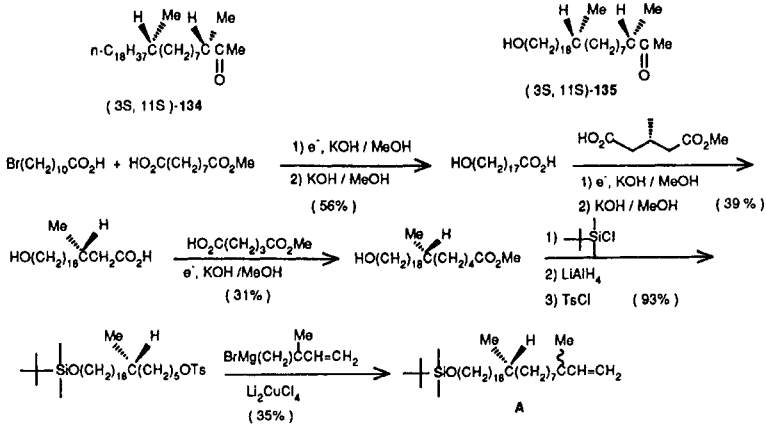
These two ketones **(134** and **135)** are the female-produced wing-raising pheromones of the German cockroach (*Blattella germanica*). A full report of the synthesis (Schemes 249–252, Ref. 1) of all of the possible isomers of **134** and



Scheme 375

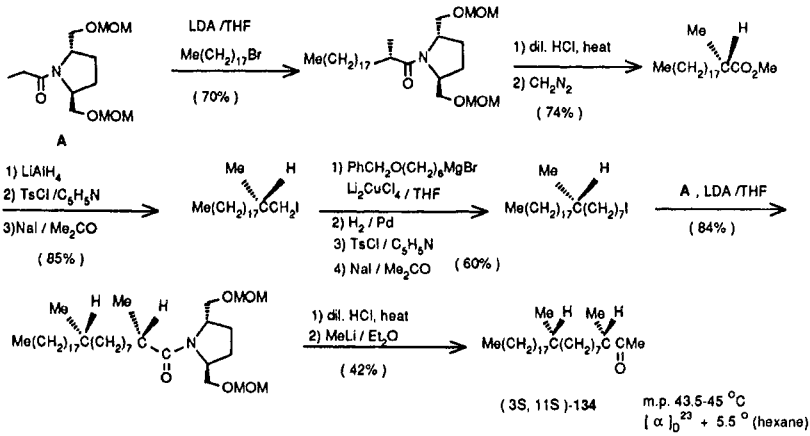
135 was published by Mori et al.[494] Bioassay of the isomers was carried out by Nishida and Fukami, who found even the unnatural isomers were as active as the natural (3*S*,11*S*)-**134** and (3*S*,11*S*)-**135**.[495]

Jensen-Korte and Schäfer employed the Kolbe electrolysis to construct the carbon skeleton of **135** (Scheme 376).[496] Their synthesis, however, did not ex-



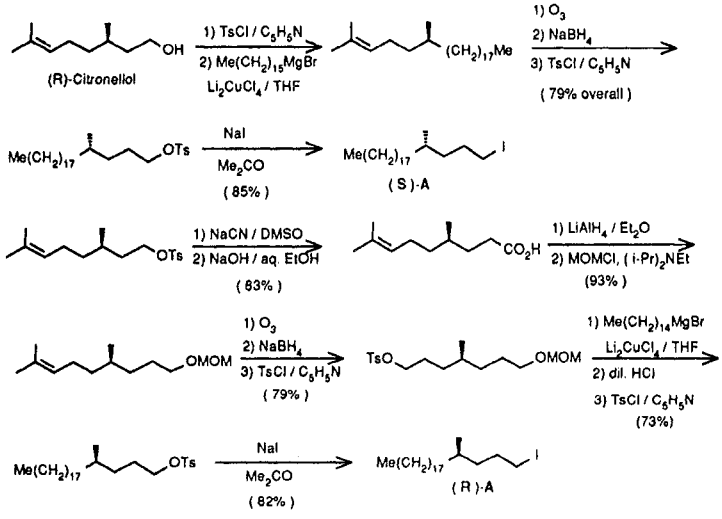
Scheme 376

tend to **135,** but was abandoned at the stage of (3*RS*,11*S*)-**A.** Katsuki and Yamaguchi achieved an asymmetric synthesis of (3*S*,11*S*)-**134** by using their chiral auxiliary **A** twice (Scheme 377).[497]

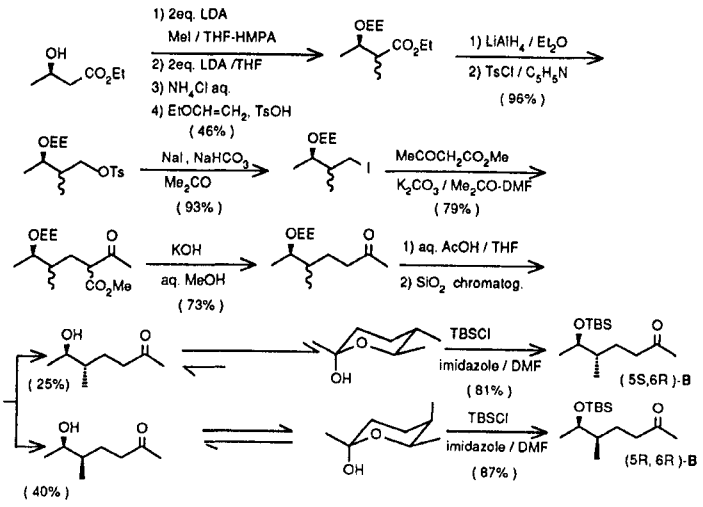


Scheme 377

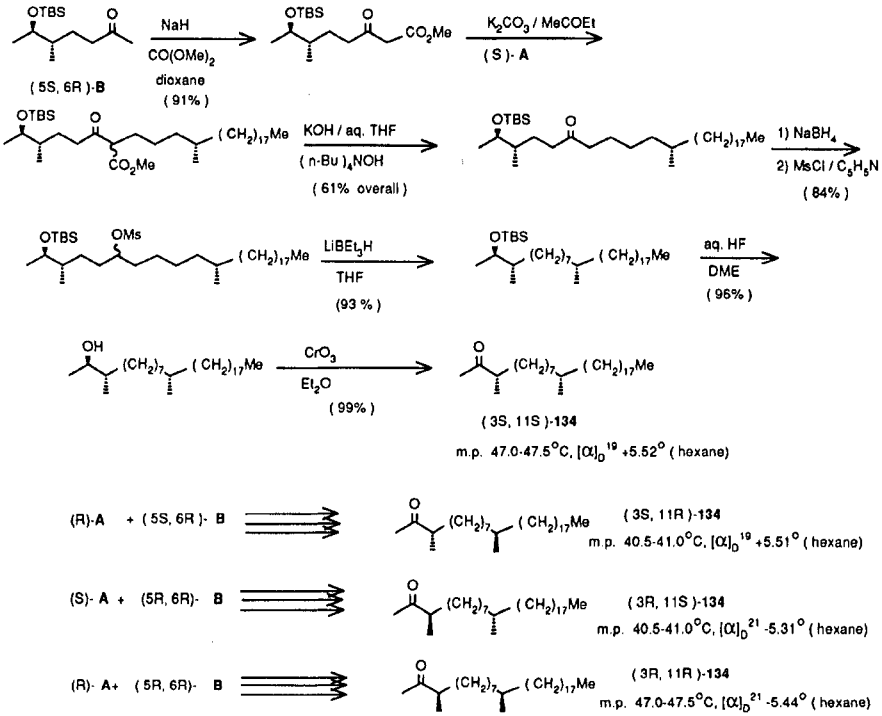
Mori and Takikawa developed a new synthesis of all of the four isomers of **134** starting from (*R*)-citronellol (~ 100% e.e.) and ethyl (*R*)-3-hydroxybutanoate (~ 100% e.e.) (Schemes 378–380).[498] The key-step (Scheme 379) was



Scheme 378



Scheme 379

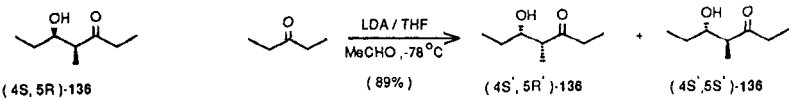


Scheme 380

the chromatographic separation of (5*RS*,6*R*)-6-hydroxy-5-methyl-2-heptanone to give pure (5*R*,6*R*)- and (5*S*,6*R*)-isomers. All of the four isomers of **134** were confirmed to be bioactive.

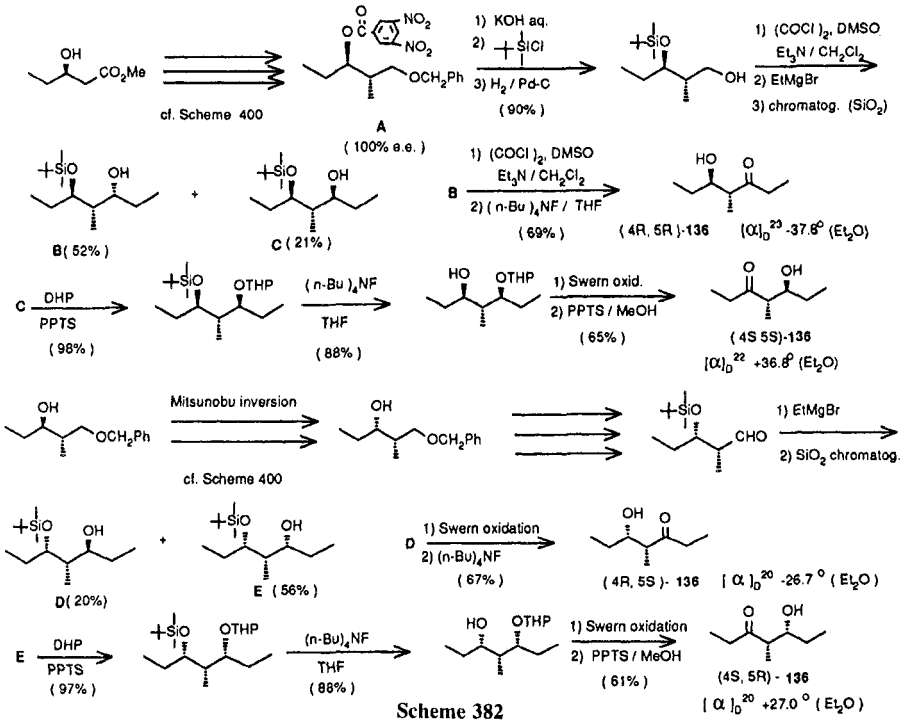
P. Sitophilure [(4*S*,5*R*)-5-Hydroxy-4-methyl-3-heptanone] 136 ($C_8H_{16}O_2$)

Burkholder et al. isolated 7.5 μg of **136** as the aggregation pheromone of the rice weevil (*Sitophilus oryzae*) and the maize weevil (*Sitophilus zeamais*).[499,500] Its *syn*-(4*S**,5*R**)-stereochemistry was deduced by a synthesis of (±)-**136** according to Smith (Scheme 381).[501] The diastereomers (4*S**,5*R**)-**136** and (4*S**,5*S**)-**136** were separated by preparative GLC.[499,500]



Scheme 381

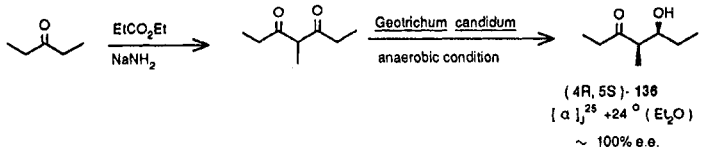
Mori and Ebata synthesized all of the four stereoisomers of **136,** starting from a single chiral building block **A** (Scheme 382).[502] Comparison of the ace-



Scheme 382

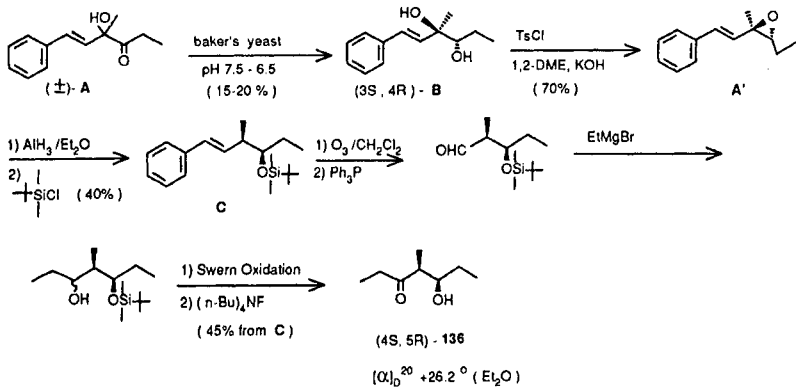
tyl lactate derivatives of the natural and synthetic samples revealed the pheromone of the maize weevils to be > 98% 4*S*,5*R*, while that of the rice weevils was at least 92% 4*S*,5*R*.[503] Bioassay also indicated (4*S*,5*R*)-**136** to be the major component of the pheromone of both *S. zeamais* and *S. oryzae*.[503]

Four other syntheses of **136** have been published since then. Fauve and Veschambre reduced 4-methyl-3,5-heptanedione with a fungus (*Geotrichum candidum*) under anaerobic conditions and obtained the antipode of sitophilure [(4*R*,5*S*)-**136**] in unspecified yield (Scheme 383).[504] Fuganti's synthesis of the



Scheme 383

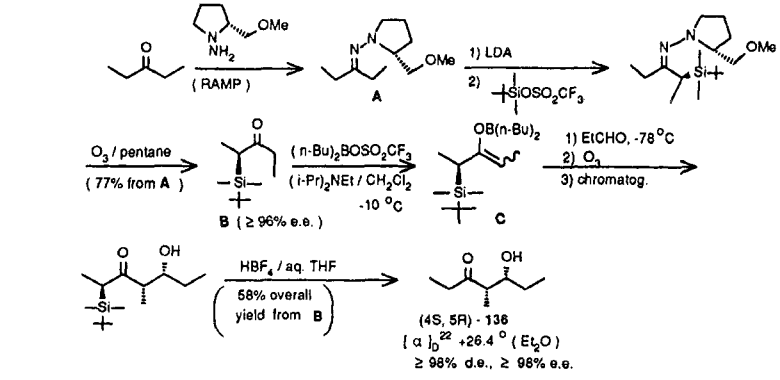
natural (4*S*,5*R*)-**136** is unique (Scheme 384),[505] employing the biotransformation of (±)-**A** to (3*S*,4*R*)-**B** with baker's yeast.[506]



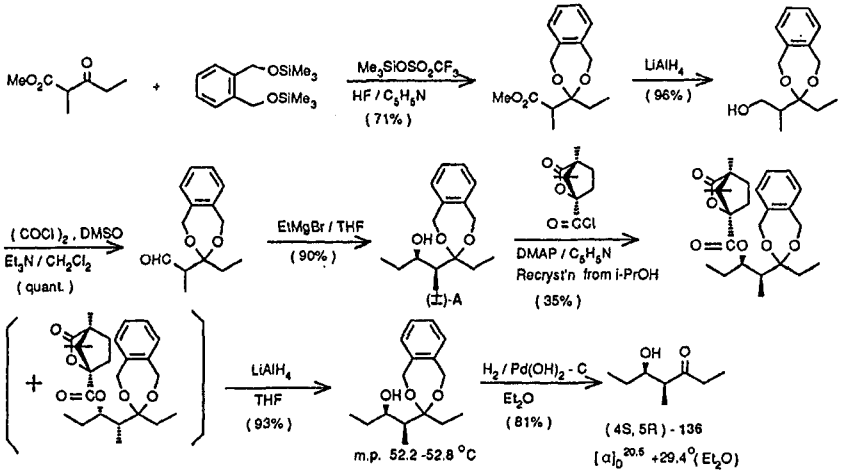
Scheme 384

An interesting asymmetric synthesis of (4*S*,5*R*)-**136** was reported by Enders and Lohray (Scheme 385).[507] They first prepared (*S*)-α-silylketone **B** starting from the RAMP-hydrazone **A** of diethyl ketone.[508] Subsequent diastereoselective and enantioselective aldol reaction between propanal and the boron enolate **C** yielded (4*S*,5*R*)-**136** with satisfactory purity.

Mori et al. reported a synthesis of 2.2 g of (4*S*,5*R*)-**136** by resolving (±)-**A** (Scheme 386) with (−)-ω-camphanyl chloride.[509] The overall yield of this synthesis was 19%, and all of the intermediates were crystalline.



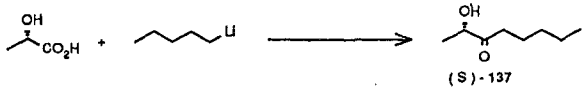
Scheme 385



Scheme 386

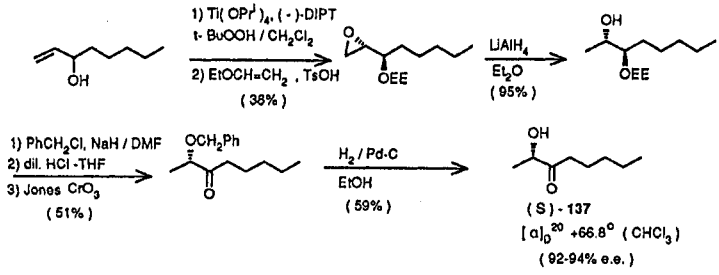
Q. (*S*)-2-Hydroxy-3-octanone 137 ($C_8H_{16}O_2$)

This hydroxyketone **137** and (2*S*,3*S*)-2,3-octanediol **(86)** were isolated and identified by Sakai et al. as the male-produced sex pheromone of the grape borer (*Xylotrechus pyrrhoderus*).[312] They synthesized (*S*)-**137** by treatment of (*S*)-lactic acid with pentyllithium (Scheme 387).[312] Mori and Otsuka prepared



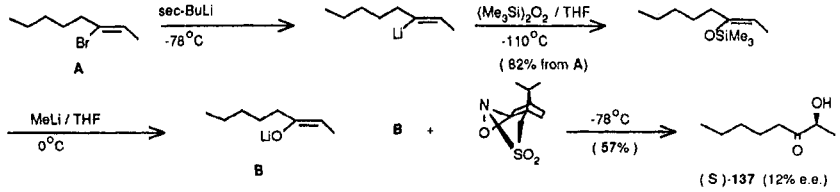
Scheme 387

(*S*)-**137** employing the Sharpless asymmetric epoxidation as the key-step (Scheme 388).[313]



Scheme 388

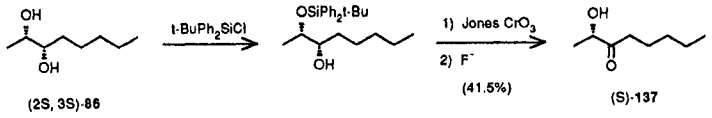
Davis et al. reported an asymmetric synthesis of (*S*)-**137** (12% e.e.) by asymmetric oxidation of a lithioenolate **B**, which was prepared from bromoalkene **A** in a selective manner (Scheme 389).[510] Servi achieved selective oxi-



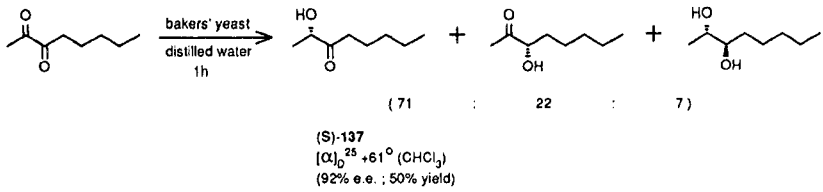
Scheme 389

dation of the hydroxy group at C-3 of (2*S*,3*S*)-**86** after protecting its less hindered hydroxy group at C-2 with 1 eq of *t*-butyldiphenylsilyl chloride. The monoprotected diol was oxidized and deprotected to give (*S*)-**137** (Scheme 390).[314] Veschambre and his co-workers reduced octane-2,3-dione with baker's yeast to produce (*S*)-**137** in 71% yield (Scheme 391).[316]

The biological study on the synthetic materials revealed (*R*)-**137** to be a pheromone inhibitor.[511]



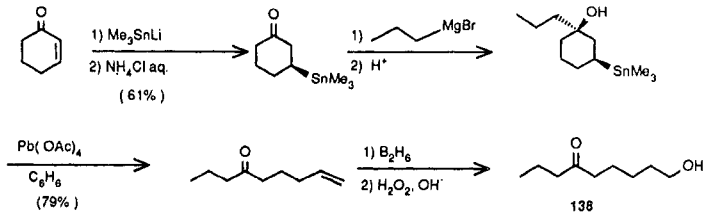
Scheme 390



Scheme 391

R. 6-Oxo-1-nonanol 138 ($C_9H_{18}O_2$)

This is the rectal gland secretion of the fruit flies (*Dacus occipitalis* and (*D. halfordiae*). O'Shea and Kitching synthesized **138** by means of organotin chemistry (Scheme 392).[512]



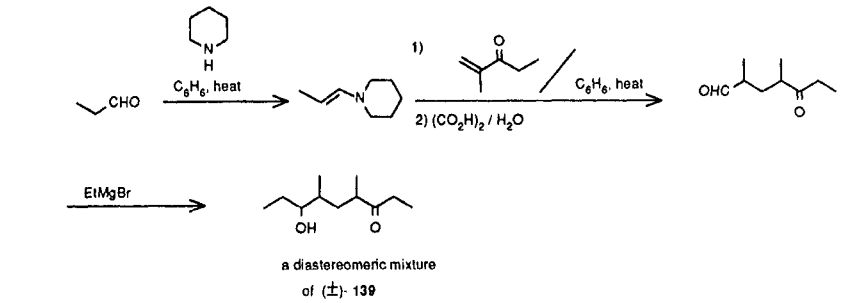
Scheme 392

S. Serricornin [(4*S*,6*S*,7*S*)-7-Hydroxy-4,6-dimethyl-3-nonanone] 139 ($C_{11}H_{22}O_2$)

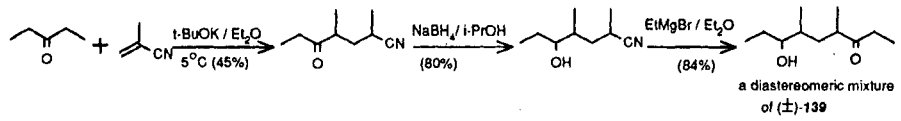
Serricornin (**139**) is the female-produced sex pheromone of the cigarette beetle (*Lasioderma serricorne*).[513,514] The chemistry and biology of **139** was extensively studied by Chuman et al.[514-516] Assignment of the absolute configuration to the three chiral centers of **139** was achieved as a result of the synthetic works to prepare several of the possible stereoisomers of **139** undertaken cooperatively by Chuman and Mori.[514]

Soon after the isolation of **139,** Chuman et al. achieved a synthesis of a diastereomeric mixture of **139** (Scheme 393).[517] The synthetic product was bioactive at a dose of 1 ng. Ono et al. then developed a more efficient synthesis of the diastereomeric mixture of **139** (Scheme 394), which could be executed on a large scale for production of the pheromone traps.[518]

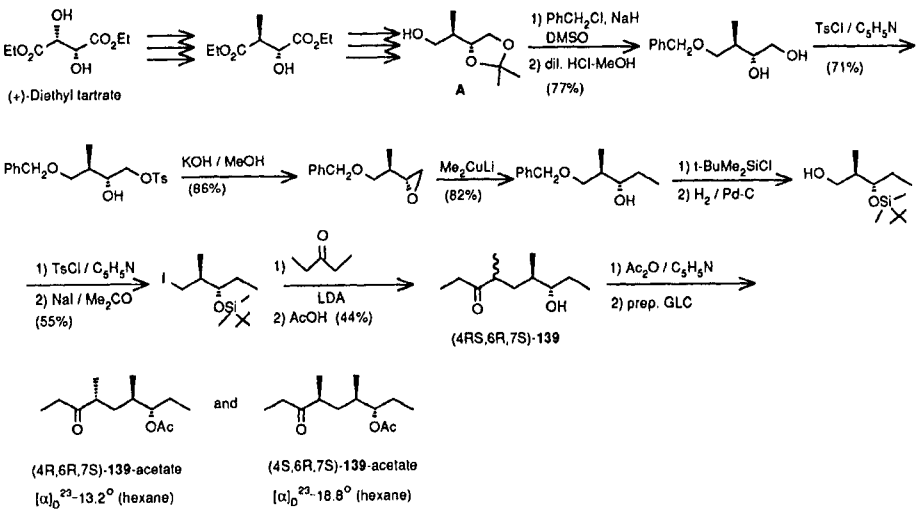
As the first step to clarify the absolute configuration of **139,** (4*RS*,6*R*,7*S*)-**139** was synthesized from (+)-tartaric acid (Scheme 395).[519] Conversion of (+)-tartaric acid to **A** was a known process.[520] After acetylation, the acetates of



Scheme 393

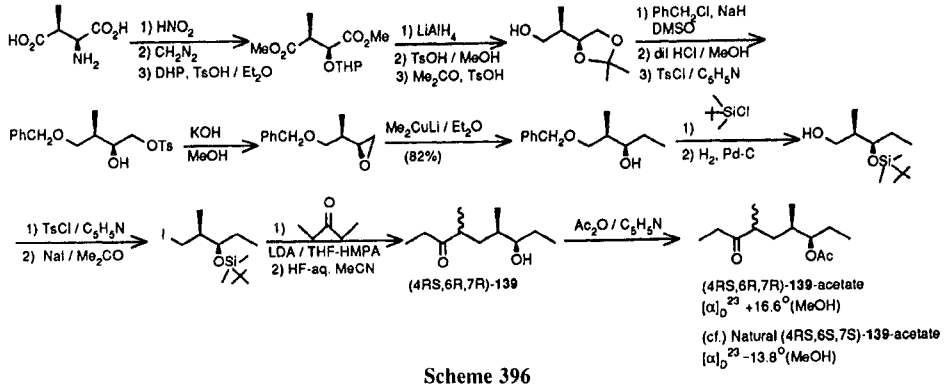


Scheme 394



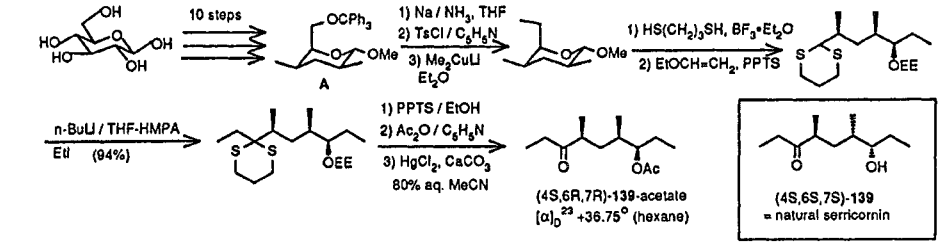
Scheme 395

(4*R*,6*R*,7*S*)-**139** and (4*S*,6*R*,7*S*)-**139** were separable by preparative GLC. Neither of them, however, was identical to the acetate of the natural **139.** The configuration of C-6 and C-7 was therefore thought to be either (6*R*,7*R*) or (6*S*,7*S*). Then (4*RS*,6*R*,7*R*)-**139** was synthesized from (2*S*,3*S*)-(+)-β-methyl-



Scheme 396

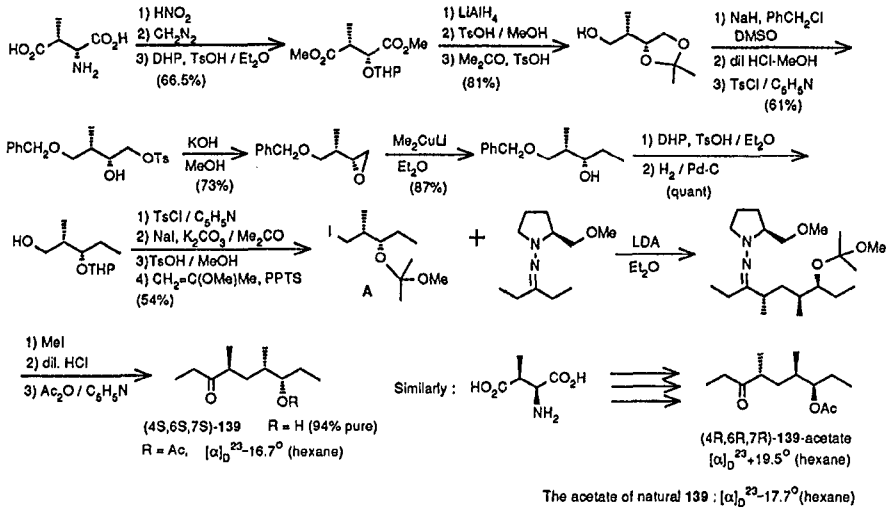
aspartic acid (Scheme 396).[521] The synthetic (4*RS*,6*R*,7*R*)-(+)-acetate of **139** was carefully compared (GLC and ^{13}C NMR) with the (−)-acetate derived from the natural **139,** and the absolute configuration at C-6 and C-7 of the natural **139** was concluded to be 6*S*,7*S*.[521] The next, and the conclusive, work was the synthesis of (4*S*,6*R*,7*R*)-**139** from D-glucose (Scheme 397).[522] Conversion of



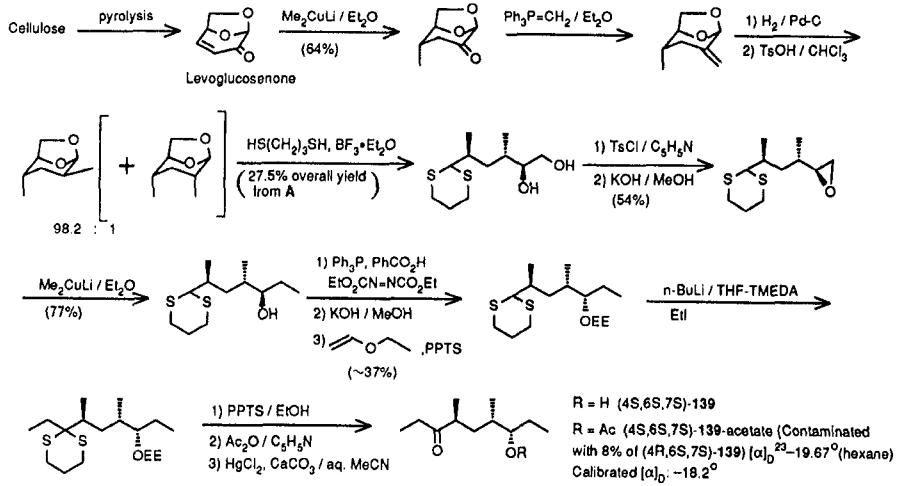
Scheme 397

D-glucose to **A** was a known process in connection with the synthesis of α-multistriatin **234.**[523] Because the synthetic (4*S*,6*R*,7*R*)-**139**-acetate was different from the acetate of the natural pheromone on the basis of GLC and ^{13}C NMR comparison, serricornin was concluded to be (4*S*,6*S*,7*S*)-**139.**[522]

Two different syntheses of (4*S*,6*S*,7*S*)-**139,** the natural pheromone itself, were reported in 1982. In the first synthesis, the key-step was the asymmetric alkylation of SAMP-hydrazone of diethyl ketone with iodide **A** (Scheme 398).[524] Starting from (2*R*,3*R*)-β-methylaspartic acid, (4*S*,6*S*,7*S*)-**139** was synthesized. Similarly, the antipode (4*R*,6*R*,7*R*)-**139** was also prepared from (2*S*,3*S*)-β-methylaspartic acid. Only the natural (4*S*,6*S*,7*S*)-**139** was biologically active. The second synthesis started from cellulose (Scheme 399) to give (4*S*,6*S*,7*S*)-**139** in a manner similar to that shown in Scheme 397.[525]

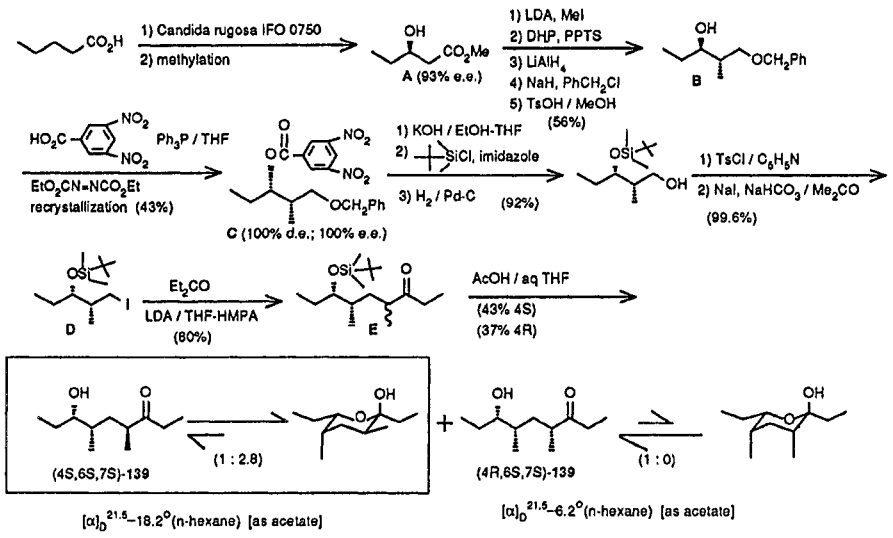


Scheme 398



Scheme 399

A synthesis of **139** by Mori and Watanabe (Scheme 400)[526] was based on the fact that **139** exists as an equilibrium mixture of the cyclic hemiacetal form and open-chain form.[526,527] The starting material was methyl (*R*)-3-hydroxypentanoate (**A**), which was prepared by microbial β-oxidation of pentanoic acid. Conversion of **A** to **B** was followed by Mitsunobu inversion at the secondary



Scheme 400

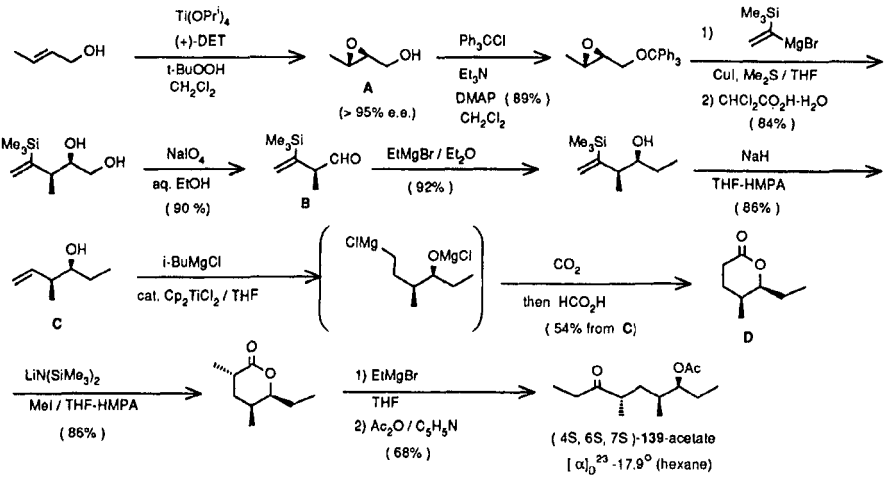
hydroxy group to give crystalline **C**. After recrystallization, **C** was further converted to iodide **D**. Alkylation of diethyl ketone with **D** yielded a diastereomeric mixture **E**. After deprotection, serricornin was readily separated from its (4*R*,6*S*,7*S*)-isomer, because the latter remained as the acyclic and polar form. Serricornin [(4*S*,6*S*,7*S*)-**139**] possesses only one axial methyl group in its hemiacetal form, while (4*R*,6*S*,7*S*)-**139** must have two axial methyl groups upon cyclization. The latter, therefore, did not cyclize at all. The overall yield of serricornin by this route was 7.6% from **A**.[526]

Another synthesis of **139** by Sato and his co-workers was based on the diastereoselective addition of ethylmagnesium bromide to an optically active α-alkenyl-β-trimethylsilyl-β,γ-unsaturated carbonyl compound **B** (Scheme 401).[528,529] Preparation of **B** was achieved by employing **A**, which in turn was obtained by the Sharpless epoxidation. Hydromagnesiation of **C** was followed by carbonation to give lactone **D**, which finally yielded serricornin acetate.

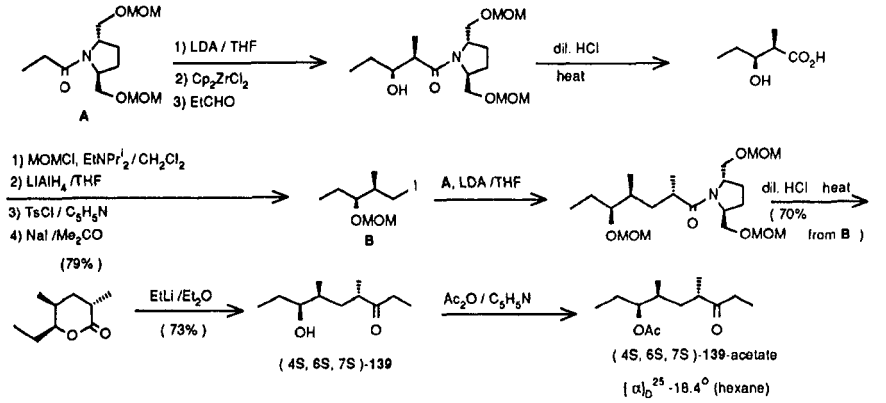
Katsuki and Yamaguchi synthesized **139** by using their own asymmetric aldol and alkylation reactions (Scheme 402).[497]

Hoffmann's synthesis of (4*RS*,6*S*,7*S*)-**139** utilized yeast reduction of methyl tetrahydro-4-oxo-2*H*-thiopyran-3-carboxylate (**A**) to give optically active hydroxy ester **B** with 98% d.e. and 83% e.e. This was purified by recrystallization of the (*S*)-α-phenylethylammonium salt of the corresponding acid **C** and used in the synthesis (Scheme 403).[305,530]

Baker and Devlin employed Masamune's asymmetric aldol reaction with the

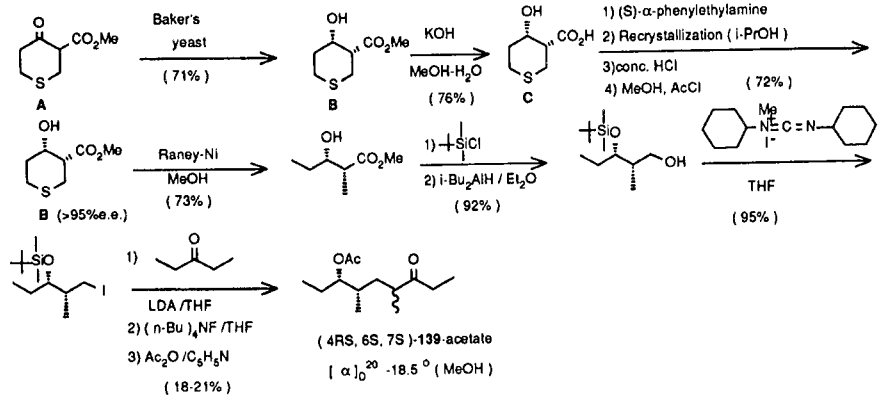


Scheme 401

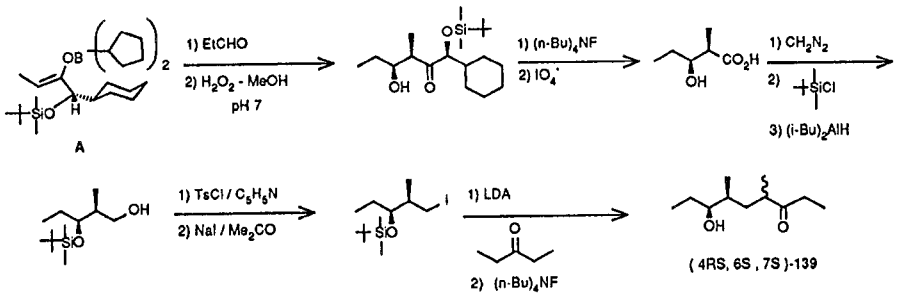


Scheme 402

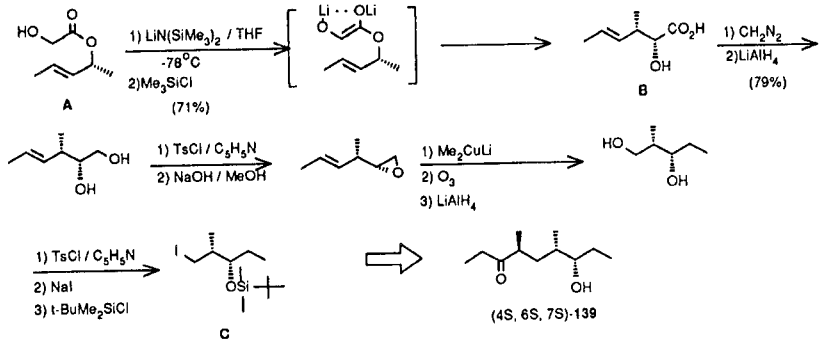
boron enolate **A** in their synthesis of **139** (Scheme 404).[531] Fujisawa et al. employed ester enolate Claisen rearrangement (**A** → **B**, Scheme 405) as the key-step in their synthesis of iodide **C**, an intermediate in the previous synthesis of **139**.[307] Redlich et al. started from D-glucose, and prepared lactone **B** (Scheme 406), which had been converted to **139** by others.[532] The same lactone **B** was also synthesized by Takano et al. starting from (*S*)-*O*-benzylglycidol.[533] Serebryakov and his co-workers employed (*S*)-3,7-dimethyl-1,6-octadiene to prepare the lactone **B**.[534]



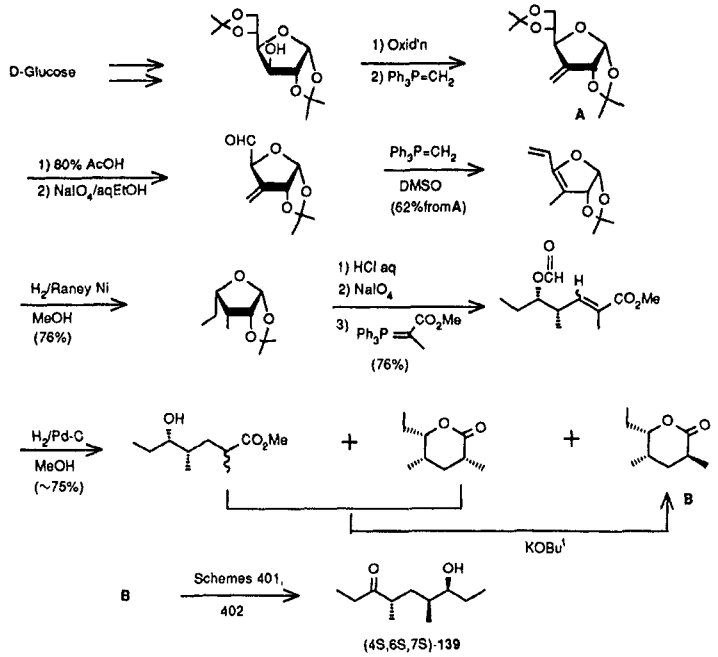
Scheme 403



Scheme 404



Scheme 405



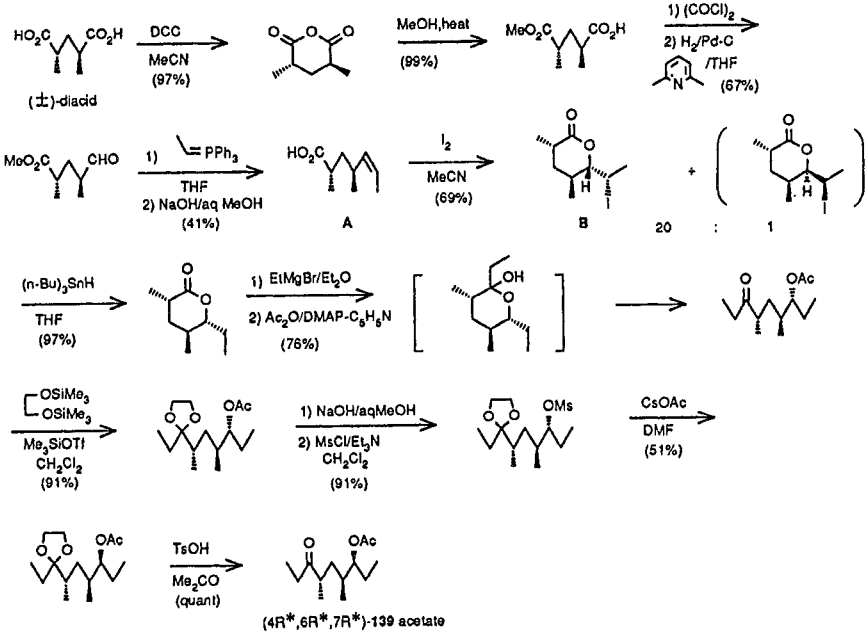
Scheme 406

Two stereoselective syntheses of (±)-serricornin **(139)** are worthy of note. First, Bartlett et al. employed stereocontrolled iodolactonization reaction (**A** → **B**) to prepare the acetate of (±)-**139** (Scheme 407).[535] Pilli and Murta synthesized (±)-**139** by using Heathcock's *syn*-selective aldol reaction (Scheme 408).[536] An interesting feature of this work is the preparation of the lactone **A** (> 98% pure by capillary GC) with proper stereochemistry by equilibration at C-1.

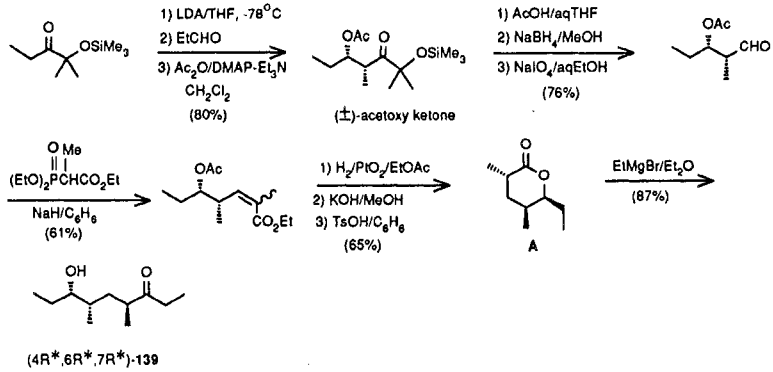
Extensive biological works were done concerning **139**.[514,537] Only (4*S*,6*S*,7*S*)-**139** showed pheromone activity. (4*S*,6*S*,7*R*)-Isomer of serricornin was inhibitory against the action of (4*S*,6*S*,7*S*)-**139**.[538] Pheromone activity of the stereoisomers of **139** was studied carefully in order to develop pheromone traps.[539–541]

14. ACIDS AND ESTERS AS PHEROMONES

Perhaps the best-known compound in this group of pheromones is (*E*)-9-oxo-2-decenoic acid, the queen substance of the honeybee. Compounds in this group will be discussed according to the increasing order of the carbon chain length.



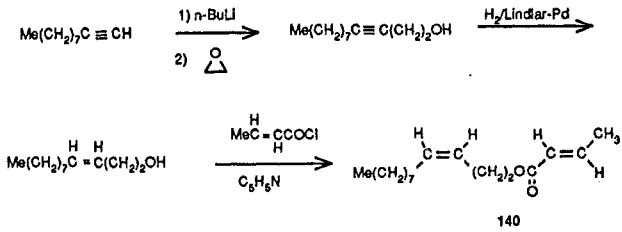
Scheme 407



Scheme 408

A. (Z)-3-Dodecenyl (*E*)-2-Butenoate 140 ($C_{16}H_{28}O_2$)

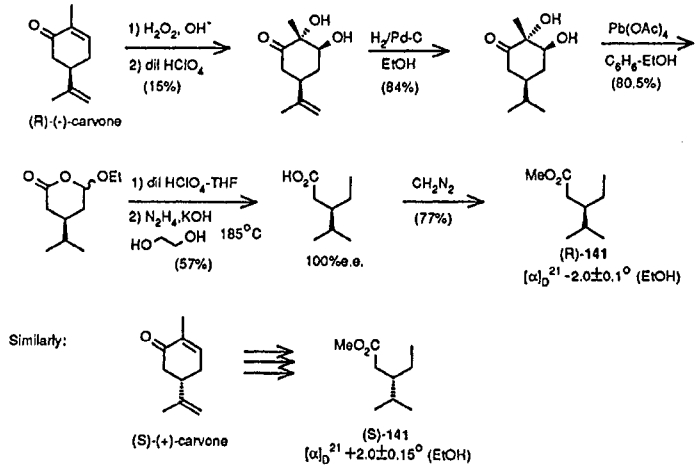
This is the female-produced sex pheromone of the sweet potato weevil (*Cylas formicarius elegantulus*). Acylation of (*Z*)-3-dodecen-1-ol with (*E*)-2-butenoyl chloride provided **140** (Scheme 409).[542]



Scheme 409

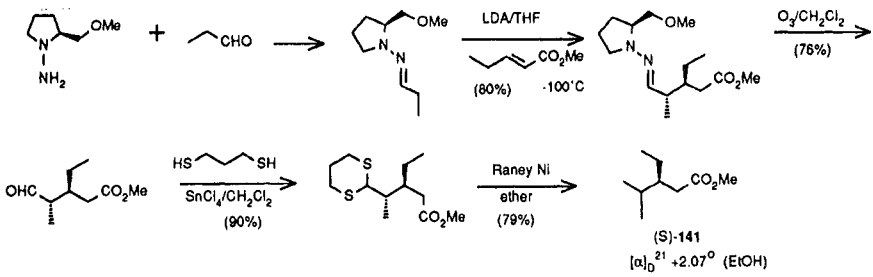
B. Methyl 3-Isopropylpentanoate 141 ($C_9H_{18}O_2$)

This ester was identified from ants: the red wood ant (*Formica rufa*) and the small forest ant (*Formica polyctena*).[543] In the case of the latter, **141** was identified from the heads of workers, as well as from heads of old queens.[544] In laboratory bioassays, **141** showed a strong aggregation-inhibiting effect.[544] Both (*R*)- and (*S*)-**141** were synthesized by Tanida and Mori, starting from the enantiomers of carvone (Scheme 410).[545] An asymmetric synthesis of (*S*)-**141** was



Scheme 410

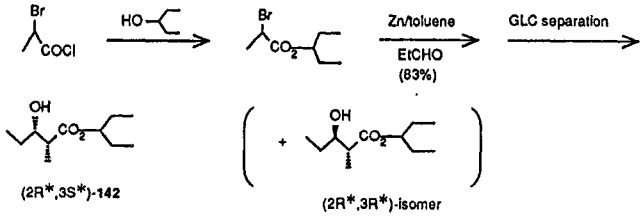
reported by Enders and Rendenbach.[546] The key-step was the asymmetric Michael addition of lithiated propanal-SAMP-hydrazone to methyl (*E*)-2-pentenoate (Scheme 411).[546]



Scheme 411

C. Sitophilate [1-Ethylpropyl (2*S*,3*R*)-2-Methyl-3-hydroxypentanoate] 142 ($C_{10}H_{22}O_3$)

The male-produced aggregation pheromone of the granary weevil (*Sitophilus granarius*) was isolated by Burkholder et al. and identified as **142.**[547] They also accomplished the synthesis of (±)-**142** (Scheme 412).[547]

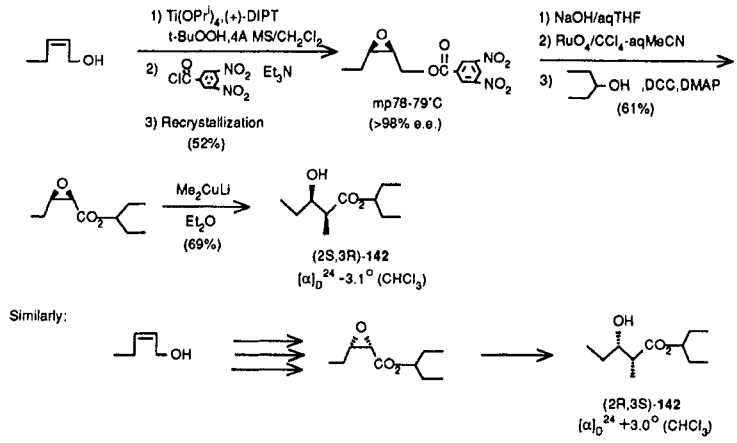


Scheme 412

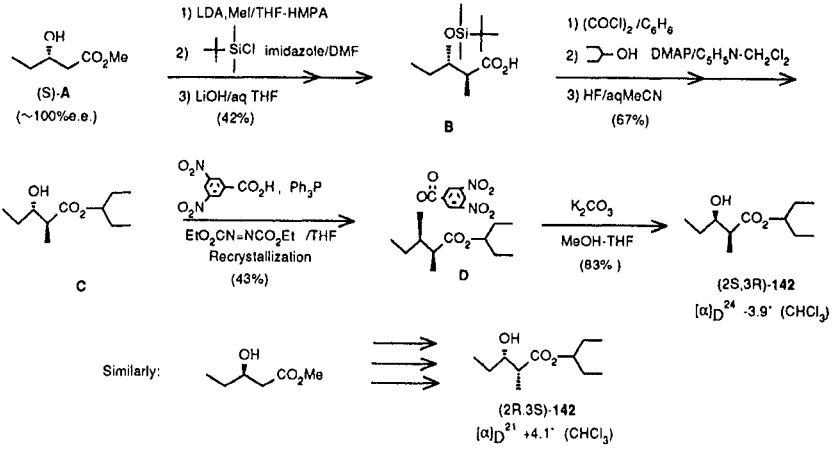
Chong synthesized both the enantiomers of **142** by the Sharpless epoxidation and organocopper chemistry (Scheme 413).[548] Mori and Ishikura also synthesized the enantiomers of **142,** starting from the pure enantiomers of methyl 3-hydroxypentanoate **(A)** (Scheme 414).[549] The key-steps of this synthesis were the dianion alkylation **(A → B)** and the Mitsunobu inversion **(C → D).** Bioassay of the synthetic samples revealed (2*S*,3*R*)-**142** to be the natural pheromone.[550]

D. (*E*)-9-Hydroxy-2-decenoic Acid 143 ($C_{10}H_{18}O_3$)

Queen honeybees produce (*E*)-9-hydroxy-2-decenoic acid **(143)** in their mandibular glands as a component of the swarm-setting pheromone. Both the en-



Scheme 413

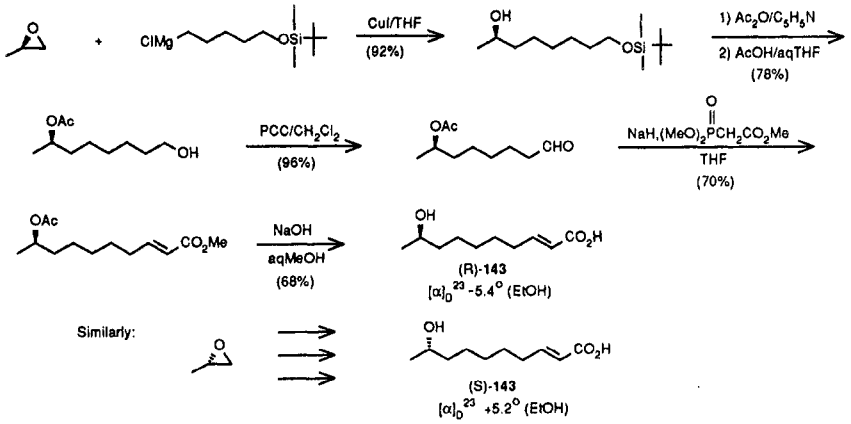


Scheme 414

antiomers of **143** were prepared from the enantiomers of propylene oxide (Scheme 415).[551] The more bioactive isomer was (*R*)-**143**.[551]

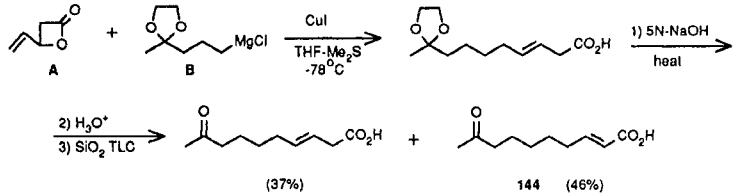
E. (*E*)-9-Oxo-2-decenoic Acid **144** ($C_{10}H_{16}O_3$)

This keto acid **144** is known as the Queen substance of the honeybee and inhibits ovary development in workers. It influences worker bee behavior by inhibiting Queen rearing.



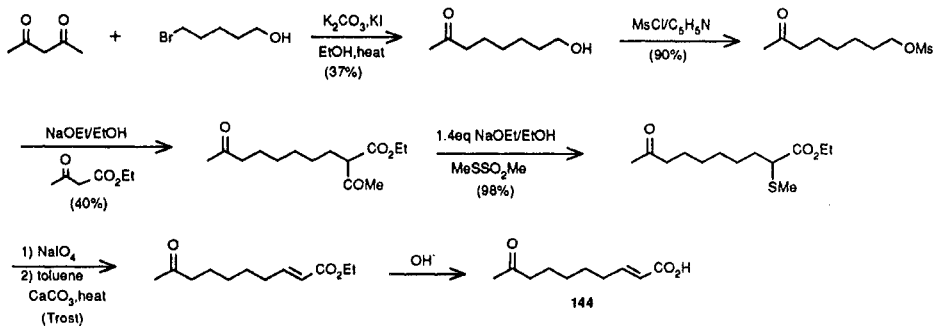
Scheme 415

Fujisawa et al. developed a synthesis of **144,** employing as the key-step the reaction of β-vinyl-β-propiolactone **(A)** with a Grignard reagent **B** in the presence of cuprous iodide (Scheme 416).[552] Ogura et al. improved the Trost syn-



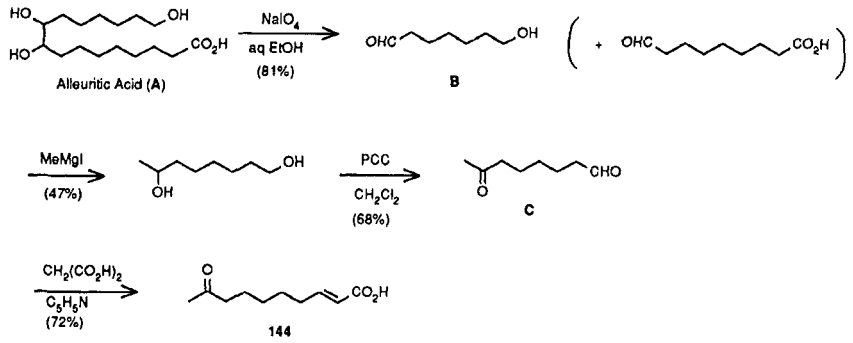
Scheme 416

thesis (Scheme 211, Ref. 1) of **144** by using their novel method for preparation of 2-(methylthio)alkanoic ester (Scheme 417).[553]



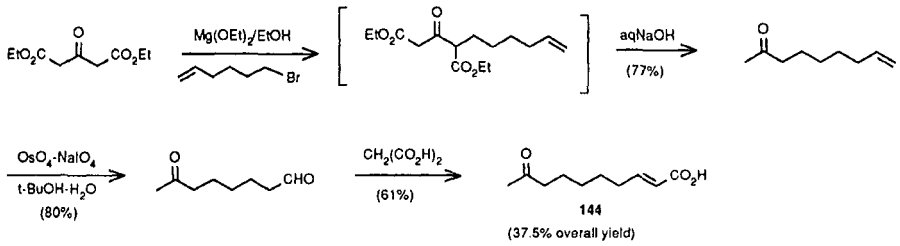
Scheme 417

Chadha and co-workers prepared **144** starting from aleuritic acid, a readily accessible component of shellac (Scheme 418).[554] The acid **A** was cleaved with sodium periodate to give **B**, which was converted to the key keto aldehyde **C**.



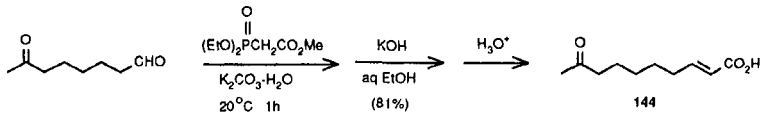
Scheme 418

Diethyl 3-oxoglutarate was the starting material of Naoshima's efficient synthesis of **144** (Scheme 419).[467] Villiéras et al. found that liquid-liquid hetero-

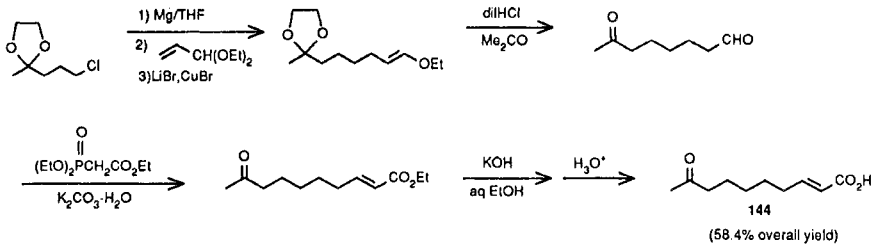


Scheme 419

geneous media of low basicity such as potassium carbonate solution allow the Wittig-Horner reaction of fragile aldehydes in good yield, and they applied this method to the synthesis of **144** (Scheme 420).[555] Villiéras's synthesis of **144** was quite efficient (Scheme 421).[556]

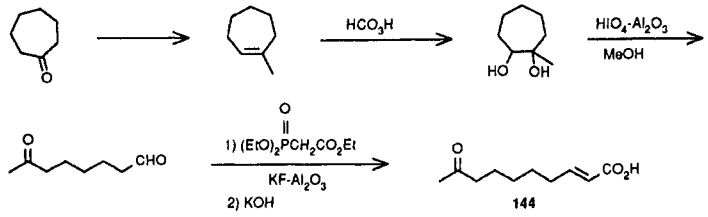


Scheme 420



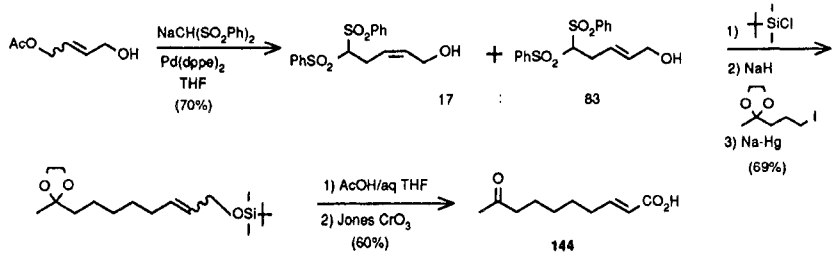
Scheme 421

A slight modification of Barbier's synthesis (Scheme 208, Ref. 1) was reported by Villemin (Scheme 422), in which reagents supported on alumina were



Scheme 422

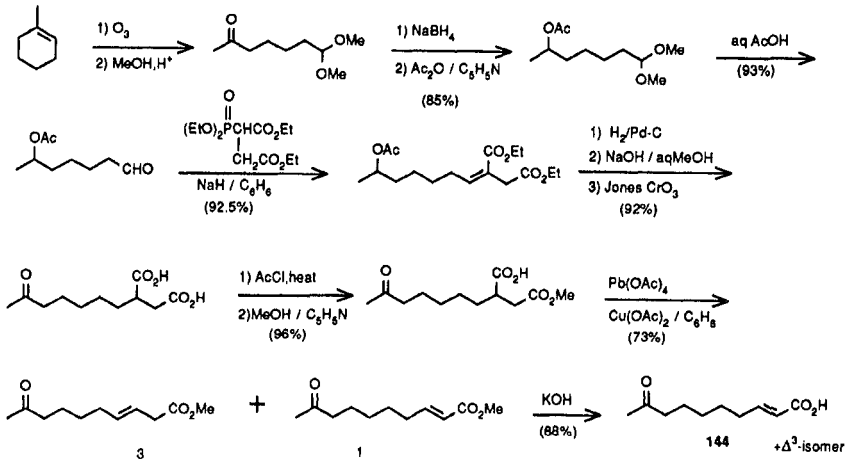
employed.[557] Ferroud et al. synthesized **144** (Scheme 423) by using



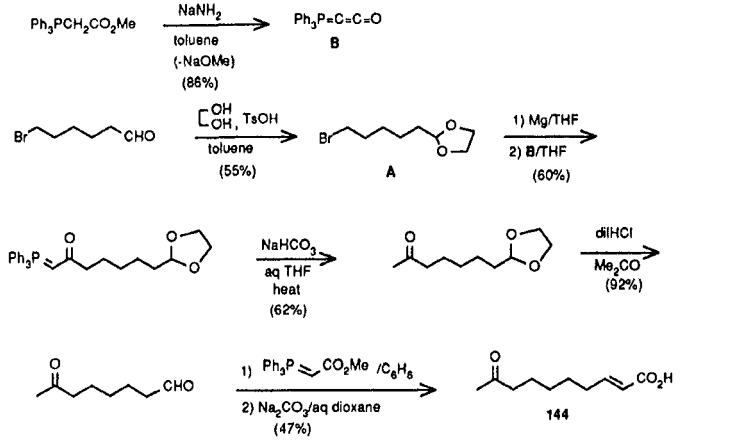
Scheme 423

bis(phenylsulfonyl)methane as the pivotal building block.[558] A synthesis of **144** was achieved by a three-carbon elongation method (Scheme 424).[559] This synthesis, however, is lengthy and inefficient.

Bestmann et al. reported a unique synthesis of **144** by chain-lengthening of a Grignard reagent derived from **A** with ketenylidenetriphenylphosphorane **(B)** (Scheme 425).[560] Another synthesis of **144** was reported, in which 7-oxooctanal



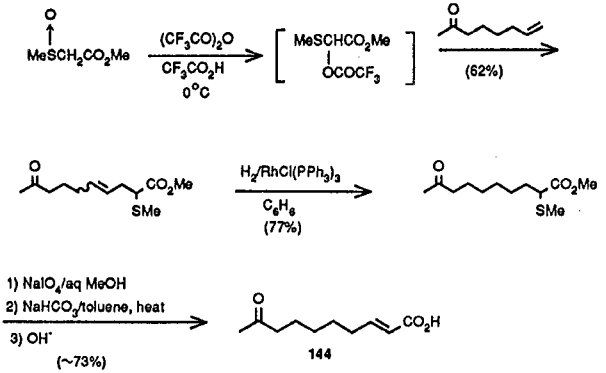
Scheme 424



Scheme 425

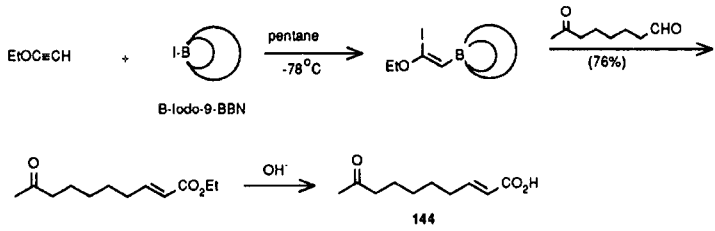
was employed as the key-intermediate.[561] Webster and Prestwich prepared carrier-free tritium labeled Queenbee pheromone **144.**[562]

Ishibashi's application of sulfur chemistry resulted in a new synthesis of **144** (Scheme 426).[563] Suzuki's synthesis of **144** was based on his new synthetic



Scheme 426

method for (*E*)-α,β-unsaturated esters by the highly chemoselective reaction of *B*-iodo-9-BBN-ethoxyethylene adduct with aldehydes (Scheme 427).[564]

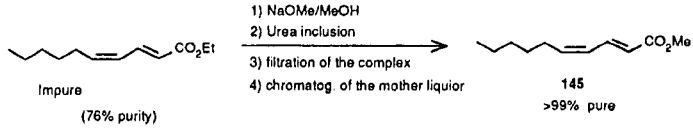


Scheme 427

F. Methyl (2*E*,4*Z*)-2,4-Decadienoate 145 ($C_{11}H_{18}O_2$)

This is a pheromone component of the forest pest six-spined spruce bark beetle (*Pityogenes chalcographus*) together with chalcogran **238.** Strong synergism was observed between **145** and chalcogran **238** in attracting *P. chalcographus*. The mixture caught 34 times more beetles than chalcogran alone, while **145** had no activity at all.[565] References to all of the existing 19 different syntheses of **145** are cited in Baeckström's paper.[566] Baeckström et al. prepared **145** by transesterification of the commercially available ethyl (2*E*,4*Z*)-2,4-decadienoate (76% purity) with sodium methoxide in methanol.[566] Crude **145** was

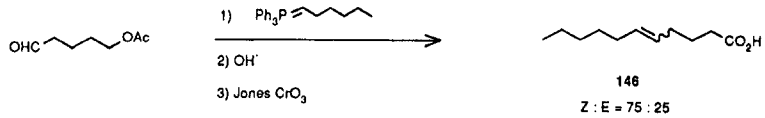
further purified by removing the (2*E*,4*E*)-isomer as urea inclusion complex. The purified (2*E*,4*Z*)-**145** was > 99% pure (Scheme 428).[566]



Scheme 428

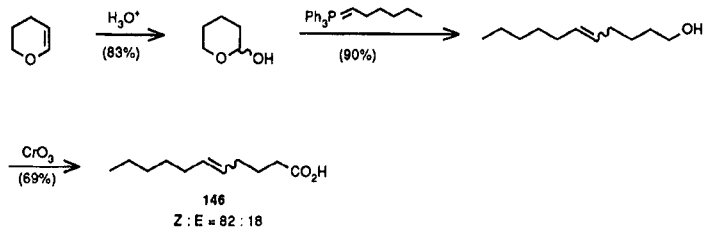
G. (*Z*)- and (*E*)-5-Undecenoic Acid **146** ($C_{11}H_{20}O_2$)

The female-produced sex pheromone of the varied carpet beetle (*Anthrenus verbasci*) was identified by Kuwahara and Nakamura as an 85 : 15 mixture of (*Z*)-5-undecenoic acid **(146)** and its *E*-isomer.[567] They synthesized a 75 : 25 mixture of (*Z*)- and (*E*)-**146,** starting from 5-acetoxypentanal (Scheme 429).[567] Harada



Scheme 429

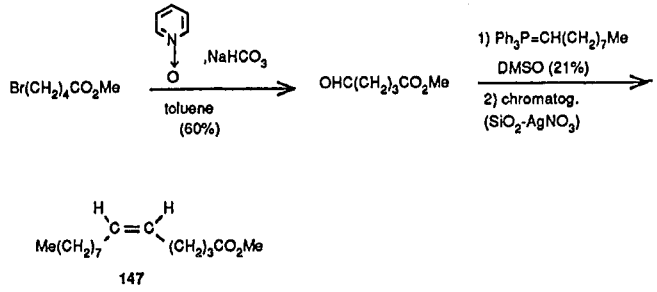
and Mori synthesized an 82 : 18 mixture of (*Z*)- and (*E*)-**146** in a simple manner starting from dihydropyran (Scheme 430).[568]



Scheme 430

H. Methyl (*Z*)-5-Tetradecenoate **147** ($C_{15}H_{28}O_2$)

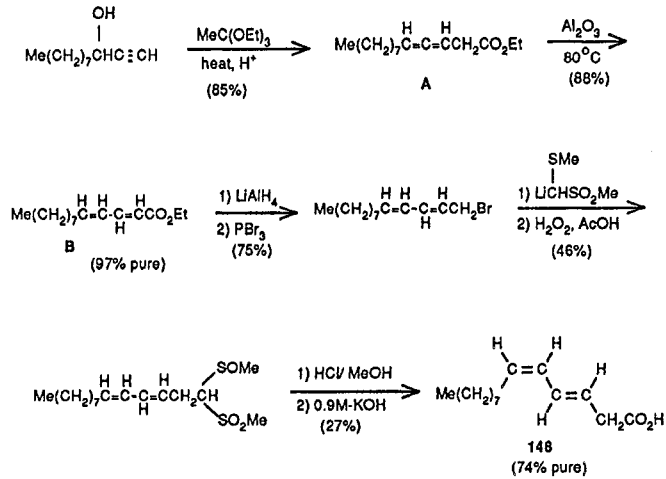
The female-produced sex pheromone of the soybean beetle (*Anomala rufocuprea*) was identified by Tamaki et al. as **147.**[569] They synthesized it by the Wittig reaction followed by chromatographic purification (Scheme 431).[569]



Scheme 431

I. Megatomoic Acid [(3*E*,5*Z*)-3,5-Tetradecadienoic Acid] 148 ($C_{14}H_{24}O_2$)

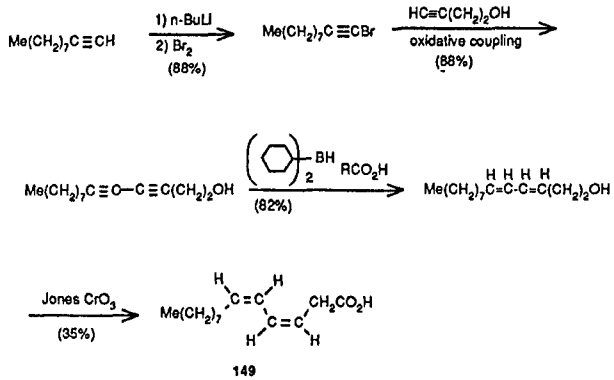
This is the pheromone of the black carpet beetle (*Attagenus megatoma*). Tsuboi et al. prepared **148** stereoselectively by the rearrangement of an allenic ester **A** to (2*E*,4*Z*)-dienic ester **B** (Scheme 432).[570]



Scheme 432

J. (3Z,5Z)-3,5-Tetradecadienoic Acid 149 ($C_{14}H_{24}O_2$)

Attagenus elongatulus employs this acid **149** as a pheromone component. DeJarlais and Emken reported a synthesis of **149** by employing classical acetylenic chemistry followed by hydroboration-protonolysis (Scheme 433).[571]

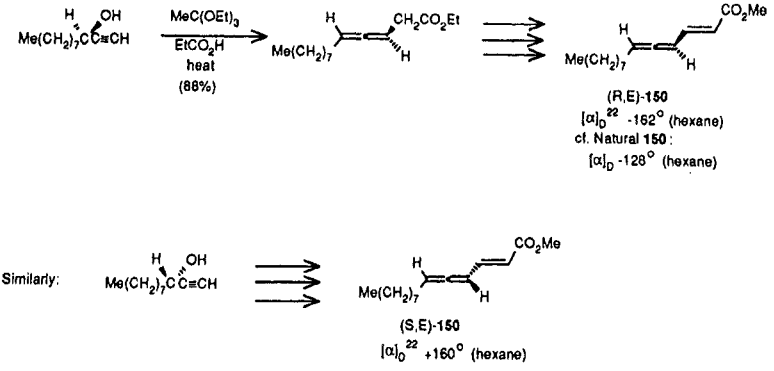


Scheme 433

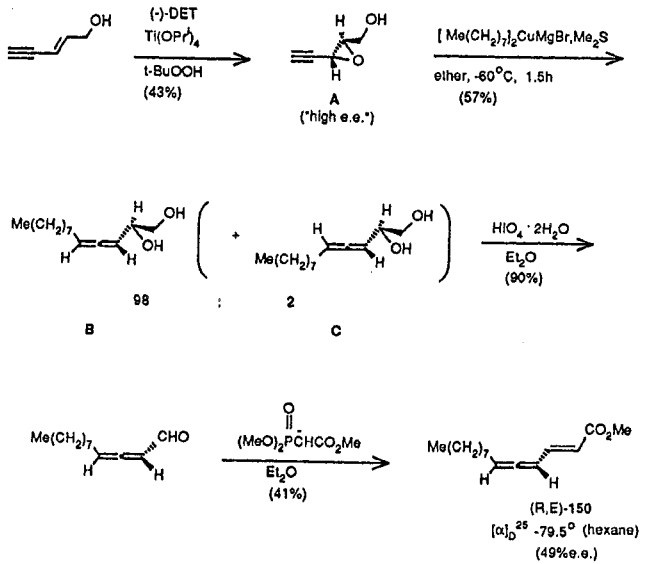
Rossi et al. prepared (3Z,5Z)-3,5-tetradecadienyl acetate, which can be a useful precursor for the synthesis of **149.**[172]

K. Methyl (*R*,*E*)-2,4,5-Tetradecatrienoate 150 ($C_{15}H_{24}O_2$)

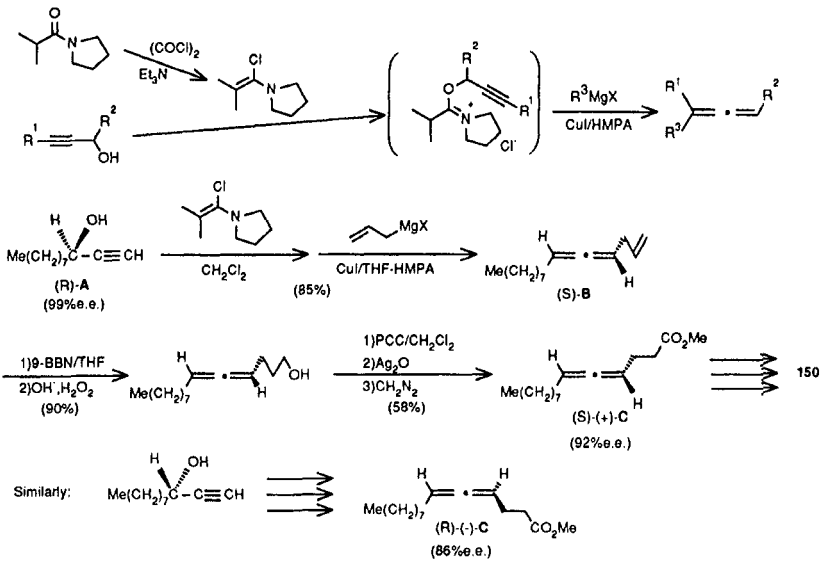
This is the male-produced pheromone of the dried bean beetle (*Acanthoscelides obtectus*). Mori's synthesis of both (*R*)- and (*S*)-**150** was published in full detail (summarized in Scheme 434).[572] Two additional syntheses of optically active **150** have been reported. Oehlschlager and Czyzewska applied the Sharpless asymmetric epoxidation to the synthesis of **150** (Scheme 435).[573] Reaction of dioctylmagnesium cuprate with alkenyl epoxy alcohol **A** gave dihydroxyallenes **B** and **C** in a ratio of 98:2 when the reaction was carried out in the presence of dimethyl sulfide. Their synthetic (*R*)-**150,** however, was of only 49% e.e. based on the maximum $[\alpha]_D$ value reported for **150.**[572] Fujisawa et al. synthesized **150** by the reaction of propargyl alcohol **A** with allyl Grignard reagent using 1-chloro-2-methyl-*N*,*N*-tetramethylenepropenylamine to give (*S*)-**B** via a



Scheme 434



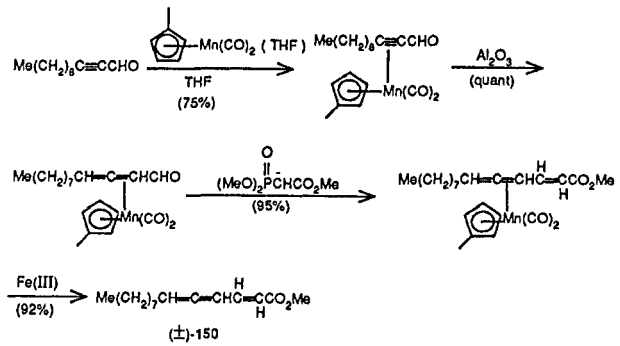
Scheme 435



Scheme 436

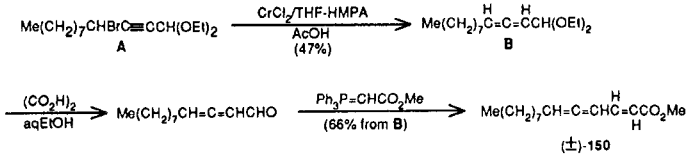
syn-type of S_N2' reaction (Scheme 436).[574] They obtained both (*R*)- and (*S*)-**C**, which were previously converted by Mori et al. to the enantiomers of **150**.[572]

Five syntheses of (±)-**150** were reported in the period between 1979 and 1989. Franck-Neumann and Brion synthesized (±)-**150** via allenemanganese complexes (Scheme 437).[575] Reduction of γ-bromo-α-acetylenic acetal **A** to



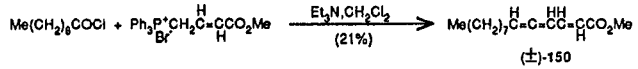
Scheme 437

α-allenic acetal **B** with chromous ion was used by Ledoussal et al. in their synthesis of (±)-**150** (Scheme 438).[576] Lang et al. synthesized (±)-**150** by the

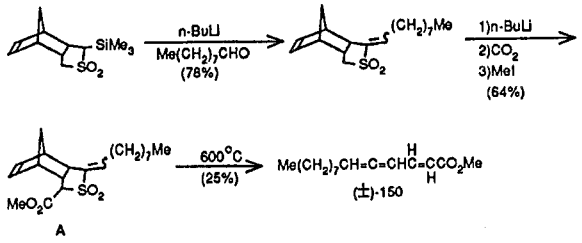


Scheme 438

Wittig reaction (Scheme 439).[577] In a synthesis of (±)-**150** (Scheme 440), Bloch

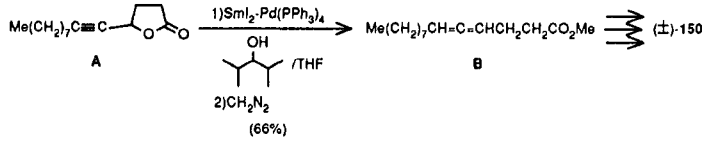


Scheme 439



Scheme 440

et al. employed extrusion of sulfur dioxide from **A** as the key-step.[578] As shown in Scheme 441, Yamaguchi and his co-workers reduced propargylic lactone **A** with samarium iodide and zero-valent palladium in the presence of 2,4-dimethyl-3-pentanol to produce allenic ester **B** after methylation.[579]



Scheme 441

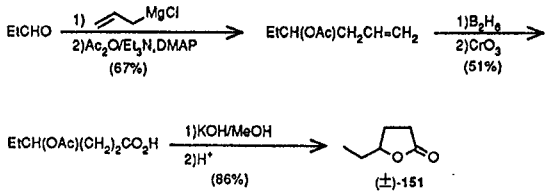
15. PHEROMONE LACTONES

Many lactones have been isolated as insect pheromones. In this section, γ- and δ-lactones with alkyl side chain will be discussed in order of the increasing length of the main carbon chain. Macrolides will then be discussed. Terpenoidal lactones are discussed in Section 18.

A. 4-Hexanolide 151 ($C_6H_{10}O_2$)

This γ-lactone **151** was isolated as a pheromone component of the dermestid beetle (*Trogoderma glabrum*). The khapra beetle (*Trogoderma granarium*) was reported to respond to (*R*)-**151**, but to neither (*S*)-**151** nor (±)-**151**.[580] Bioassay of both the enantiomers of **151** as prepared by Mori[581] was found to be inactive against *T. glabrum* when assayed by Levinson.[582] Neither of the enantiomers of **151** was synergistic to the action of (*R*,*Z*)-trogodermal (**114**), the major pheromone of *T. glabrum*.

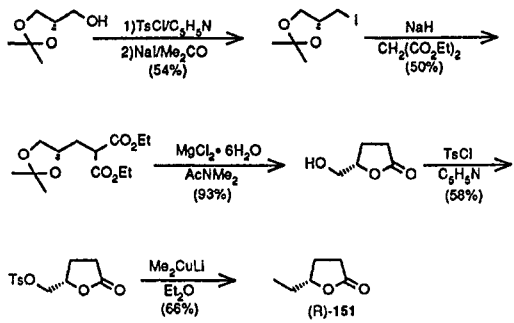
Optical resolution of (±)-**151** on a column of cellulose triacetate (crystallographic form I) was reported, which enabled the resolution in a preparative scale.[583] Serebryakov and his co-workers prepared (±)-**151** as shown in Scheme 442.[584]



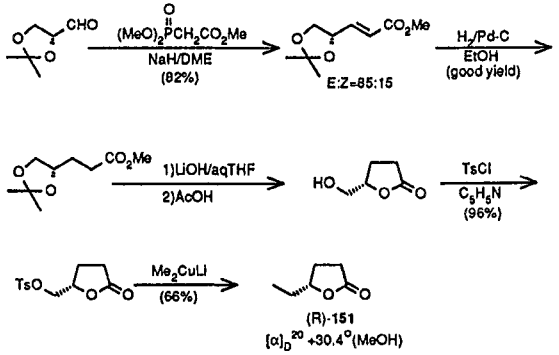
Scheme 442

(1) Syntheses Starting from Chiral Building Blocks

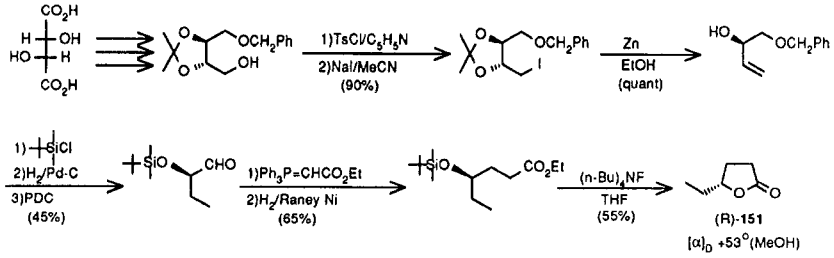
Five syntheses of optically active **151** were achieved starting from optically active natural products. Serebryakov prepared (*R*)-**151** from (*S*)-glycerol acetonide (Scheme 443).[585] Kang and Shin began with (*R*)-glyceraldehyde acetonide to prepare (*R*)-**151** (Scheme 444).[586] L-(+)-Tartaric acid was also converted to (*R*)-**151** in two different manners (Schemes 445 and 446).[587,588] Gurjar and Patil published a lengthy synthesis of (*R*)-**151** from D-glucose (Scheme 447).[589]



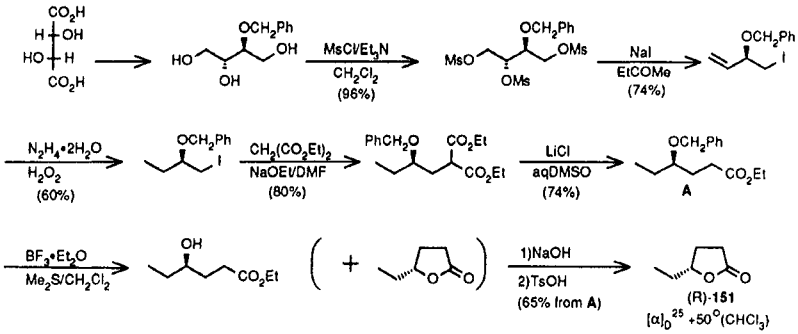
Scheme 443



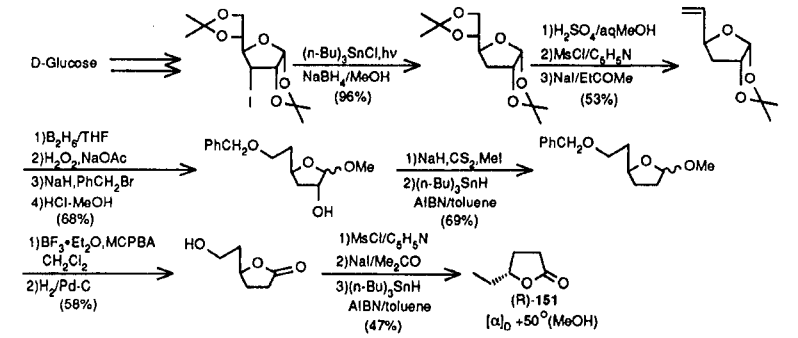
Scheme 444



Scheme 445



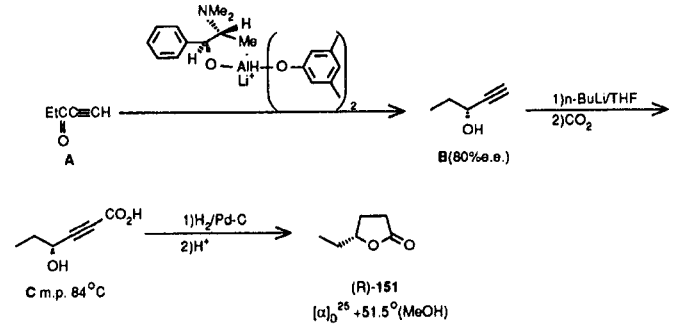
Scheme 446



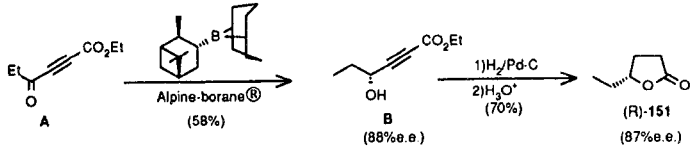
Scheme 447

(2) Syntheses Based on Chemical Asymmetric Reactions

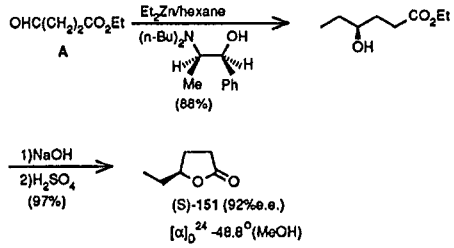
Three chemical asymmetric syntheses of **151** have been reported to date. Vigneron and Bloy employed lithium aluminum hydride modified with *N*-methylephedrine and 3,5-dimethylphenol to reduce α-acetylenic ketone **A** to optically active propargylic alcohol **B** (Scheme 448).[590] Because acid **C** was crystalline, pure (*R*)-**151** could be obtained.[590] Midland and Tramontano reduced acetylenic keto ester **A** (Scheme 449) with *B*-3-pinanyl-9-BBN to give **B**, which was converted to (*R*)-**151**.[591] Chemoselective alkylation of formyl ester **A** with dialkylzinc using *N*,*N*-dibutylnorephedrine enabled Soai et al. to prepare (*S*)-**151** of 92% e.e. (Scheme 450).[592]



Scheme 448



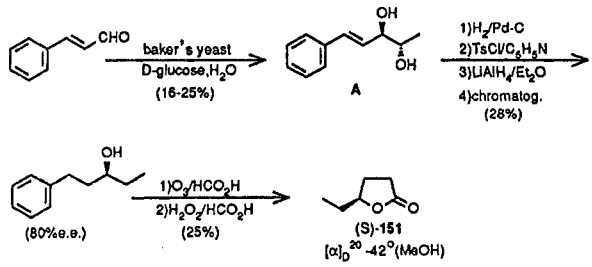
Scheme 449



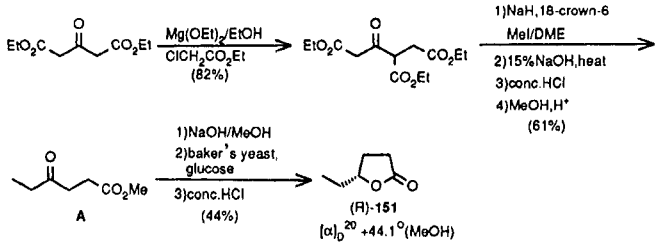
Scheme 450

(3) Syntheses Based on Biochemical Asymmetric Reactions

Six syntheses of **151** used biochemical asymmetric processes. Fuganti and his co-workers employed **A** (Scheme 451) as the starting material, which could be prepared by fermentation of cinnamaldehyde with baker's yeast and glucose.[593] Naoshima et al. reduced keto ester **A** (Scheme 452) with baker's yeast to give



Scheme 451



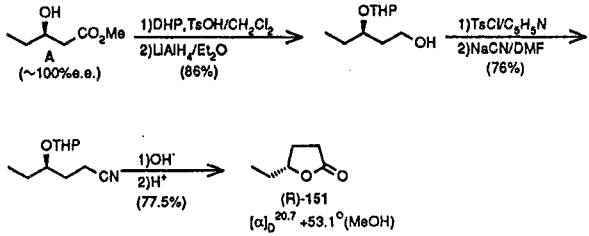
Scheme 452

(*R*)-**151**.[594] Mori et al. employed the enantiomers of 3-hydroxypentanoic esters **A** and **B** to prepare **151** (Scheme 453).[581] The (*R*)-enantiomer **A** was commercially available and could be purified to an optically pure state by recrystallization of the corresponding 3,5-dinitrobenzoate. The (*S*)-enantiomer **B** was obtained by yeast reduction of **C**.[581] Kozikowski et al. reduced a phenylsulfone **A** with baker's yeast to give **B**, which finally afforded (*S*)-**151** of 60% e.e. (Scheme 454).[595] Fujisawa and his co-workers reduced β-keto sulfone **A** with baker's yeast to give **B**, which was converted to (*R*)-**151** (Scheme 455).[596] Blanco et al. achieved the kinetic optical resolution of (±)-**151** to give (*R*)-**151** of 75% e.e. (Scheme 456).[597]

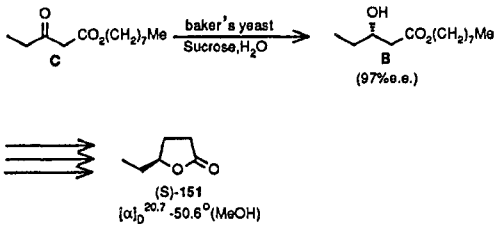
B. *cis*-2-Methyl-5-hexanolide **152** ($C_7H_{12}O_2$)

This was isolated as the major volatile component of the pheromonal blend of the carpenter bee (*Xylocopa hirsutissima*).

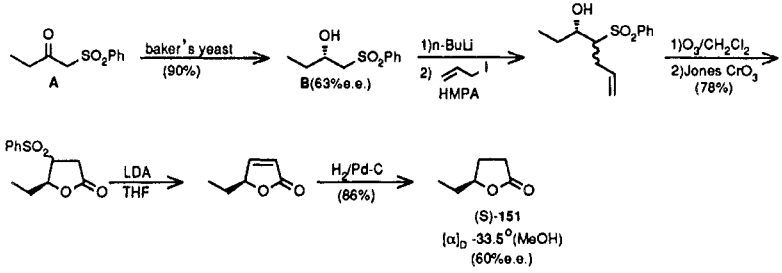
Five new syntheses of (±)-**152** have been reported since 1979. Bacardit and Moreno-Mañas converted dehydroacetic acid (**A**) to (±)-**152** (Scheme



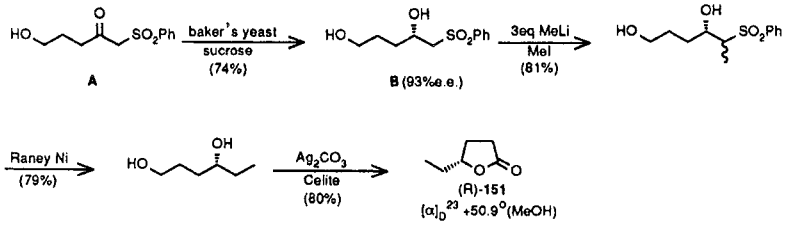
Similarly:



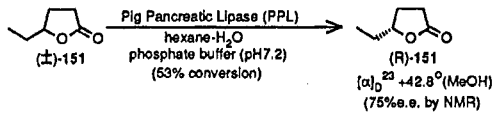
Scheme 453



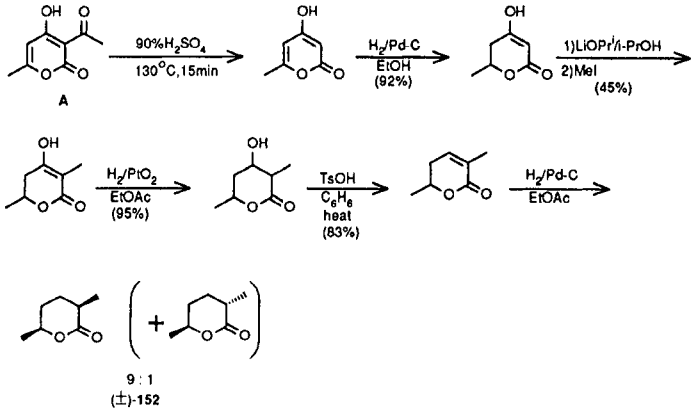
Scheme 454



Scheme 455

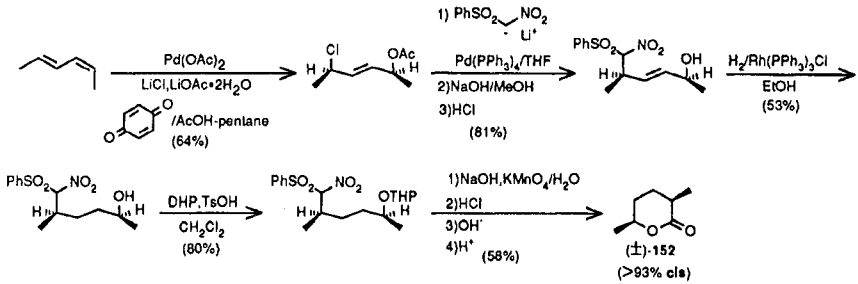


Scheme 456



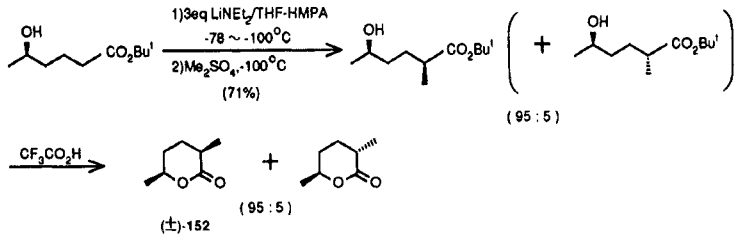
Scheme 457

457).[598,599] The first and key step of Bäckvall's synthesis of (±)-**152** was the stereocontrolled 1,4-addition to a conjugated diene catalyzed by palladium (Scheme 458).[600] Narasaka and Ukaji synthesized (±)-**152** by a highly stereo-

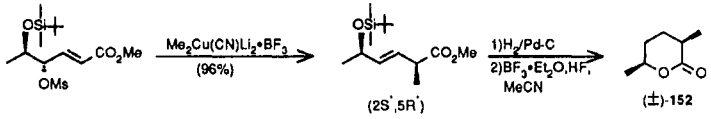


Scheme 458

selective alkylation reaction of an ester enolate generated from *t*-butyl 5-hydroxyhexanoate (Scheme 459).[601] A synthesis of (±)-**152** by Ibuka et al. employed organocopper-Lewis acid-mediated 1,3-chirality transfer of acyclic γ,δ-

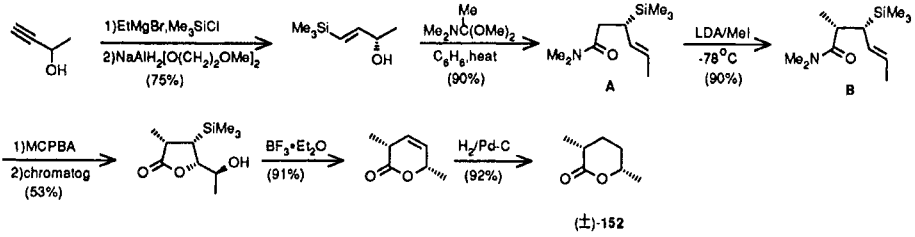


Scheme 459



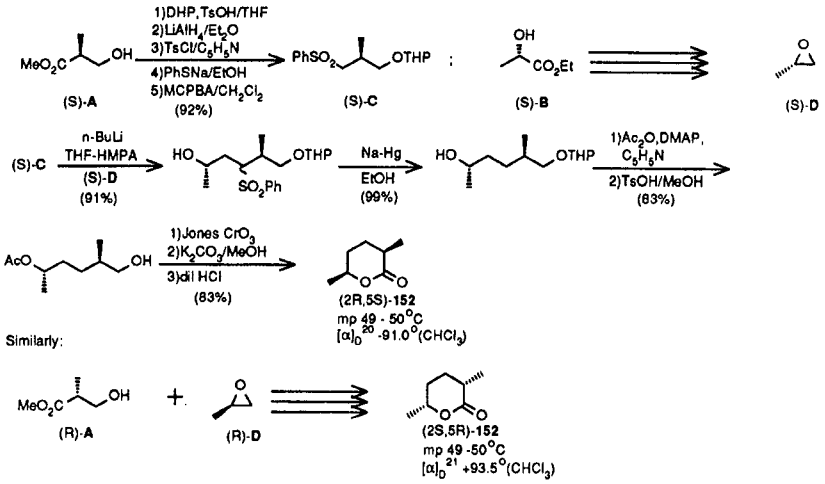
Scheme 460

dioxygenated (*E*)-α,β-unsaturated ester (Scheme 460).[602] Another synthesis of (±)-**152** utilized organosilicon chemistry, especially stereoselective alkylation of **A** to **B** (Scheme 461).[603]

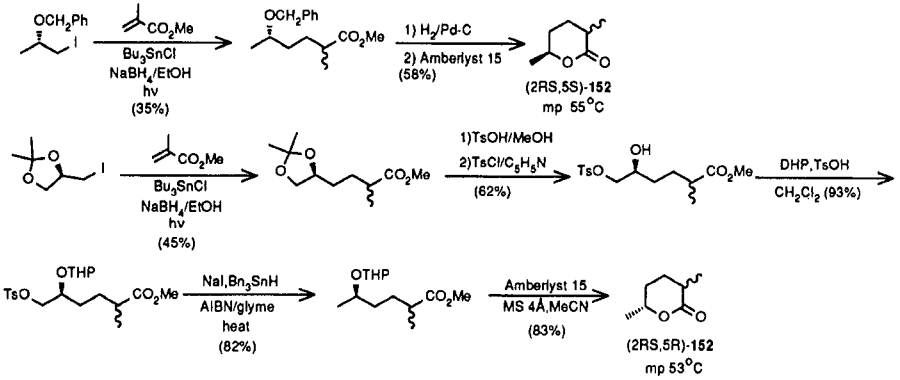


Scheme 461

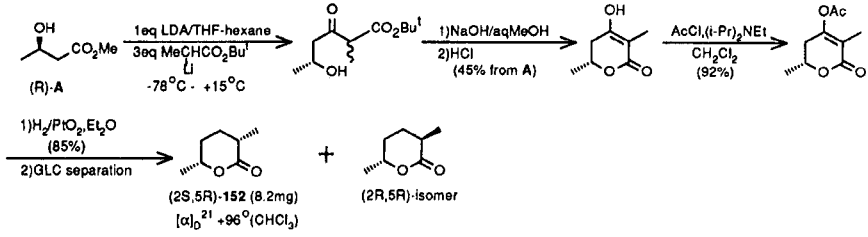
Four syntheses of optically active **152** have been published based on the chiral building block approach. Mori and Senda synthesized both (2*R*,5*S*)-**152** and (2*S*,5*R*)-**152,** starting from the enantiomers of methyl 3-hydroxy-2-methylpropanoate **(A)** and ethyl (*S*)-lactate **(B)** (Scheme 462).[604] This approach enabled them to prepare enantiomerically pure **152.** Gerth and Giese synthesized (2*RS*,5*S*)-**152** and (2*RS*,5*R*)-**152** by using chiral radical precursors to achieve radical-mediated C-C bond formation (Scheme 463).[605] Brandänge et al. prepared (2*S*,5*R*)-**152** in a concise manner from methyl (*R*)-3-hydroxybutanoate **A** (Scheme 464).[606] Bernardi and Ghiringhelli synthesized the enantiomers of **152** starting from a dithiane alcohol **A** (Scheme 465).[607] A synthesis of (2*R*,5*R*)-**152,**



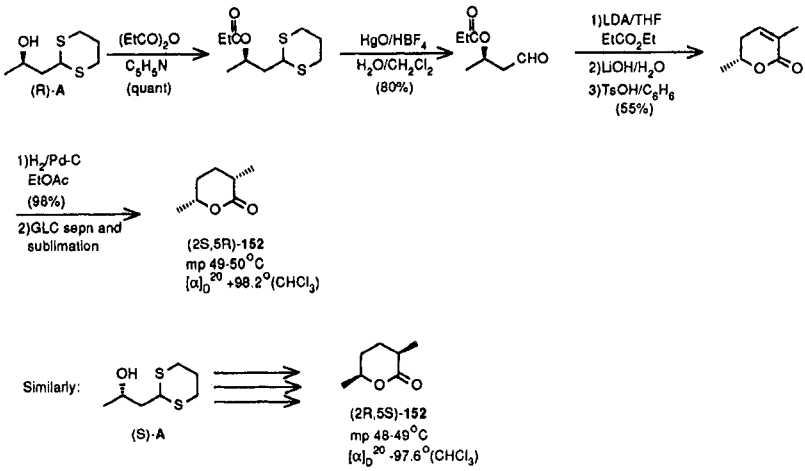
Scheme 462



Scheme 463



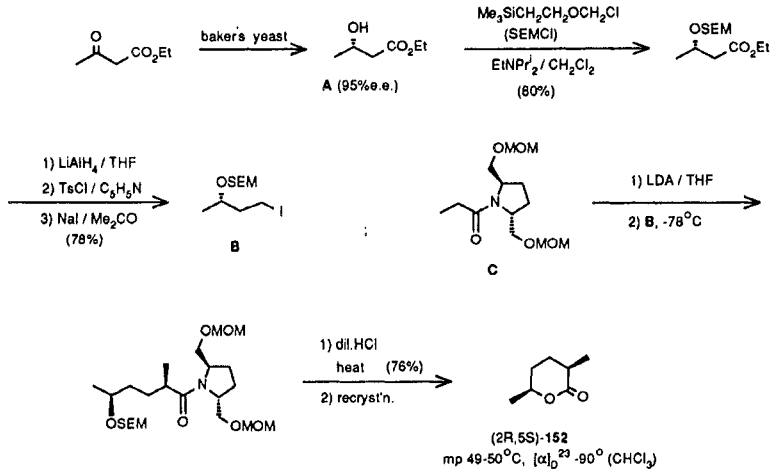
Scheme 464



Scheme 465

a stereoisomer of the pheromone, was reported by Hanessian et al. starting from a sugar.[608]

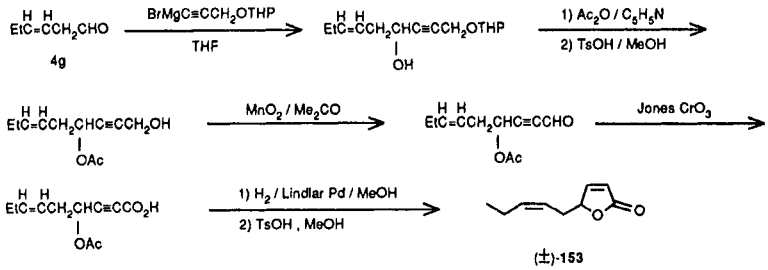
Only one asymmetric synthesis of **152** has been reported by Katsuki and Yamaguchi (Scheme 466).[497] Their synthesis was a combination of yeast reduction and alkylation of the amide enolate derived from **C** with **B.**



Scheme 466

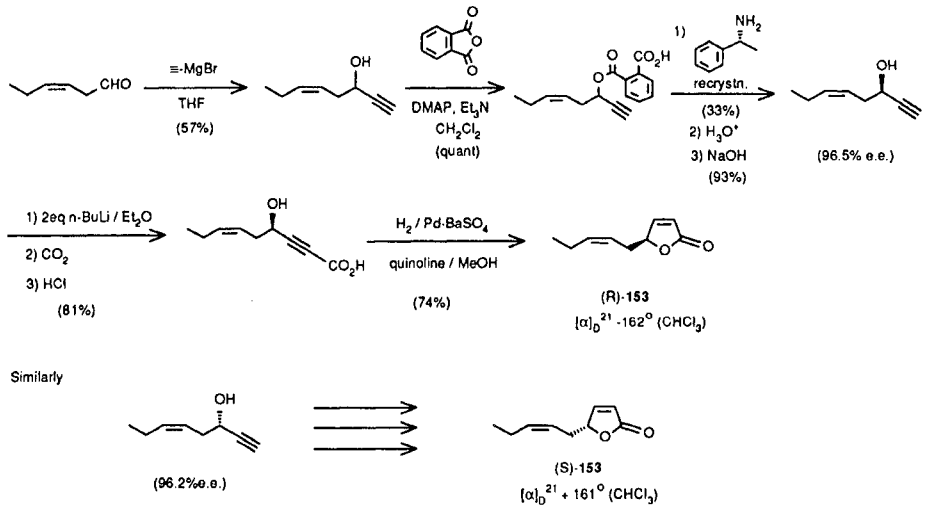
C. (2Z,6Z)-2,6-Nonadien-4-olide 153 ($C_9H_{12}O_2$)

This lactone, together with β-phenylethyl alcohol, was isolated by Kuwahara as the possible male-produced sex pheromone of a pyralid moth (*Aphomia gularis*). He synthesized (±)-**153** (Scheme 467), but it was behaviorally inactive



Scheme 467

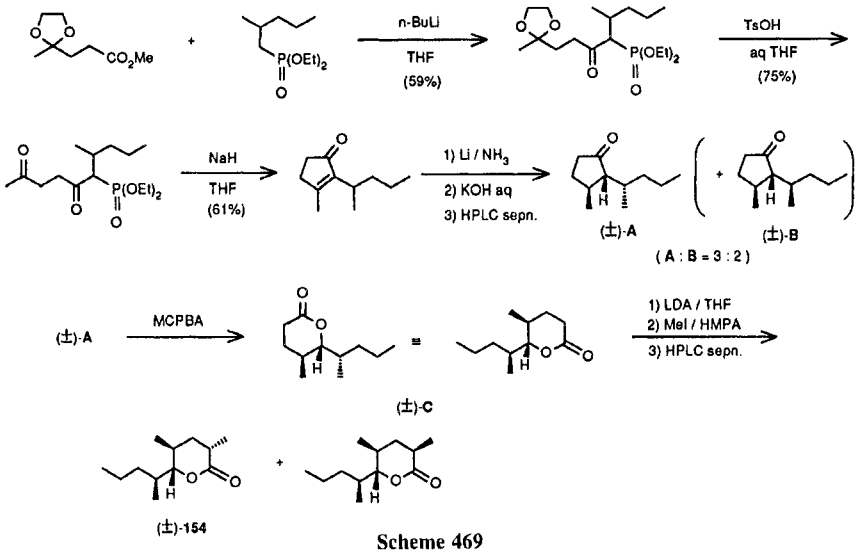
against the female moth.[609] Miyashita and Mori synthesized the enantiomers of **153** by resolving an intermediate (Scheme 468).[610] The synthetic enantiomers of **153,** however, were biologically inactive.[610] Further studies are necessary to clarify this matter.



Scheme 468

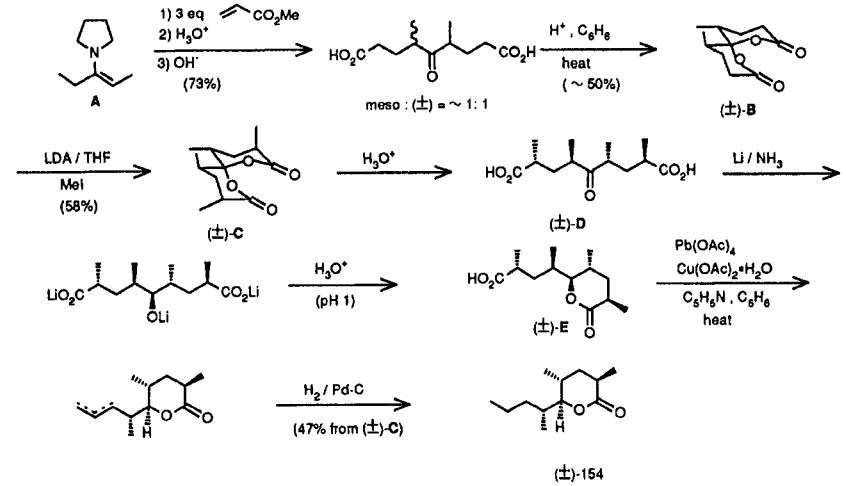
D. Invictolide [(3*R*,5*R*,6*S*,1′*R*)-3,5-Dimethyl-6-(1′-methylbutyl)-tetrahydro-2H-pyran-2-one] 154 ($C_{12}H_{22}O_2$)

Invictolide **(154)** is one of the three lactones **(154, 155,** and **210)** isolated from the red imported fire ant (*Solenopsis invicta*) as the Queen recognition pheromone.[611,612] Rocca et al. synthesized (±)-**154** as proof of their proposed structure (Scheme 469).[612] Their synthesis was nonselective, and they had to separate the unwanted isomers two times.

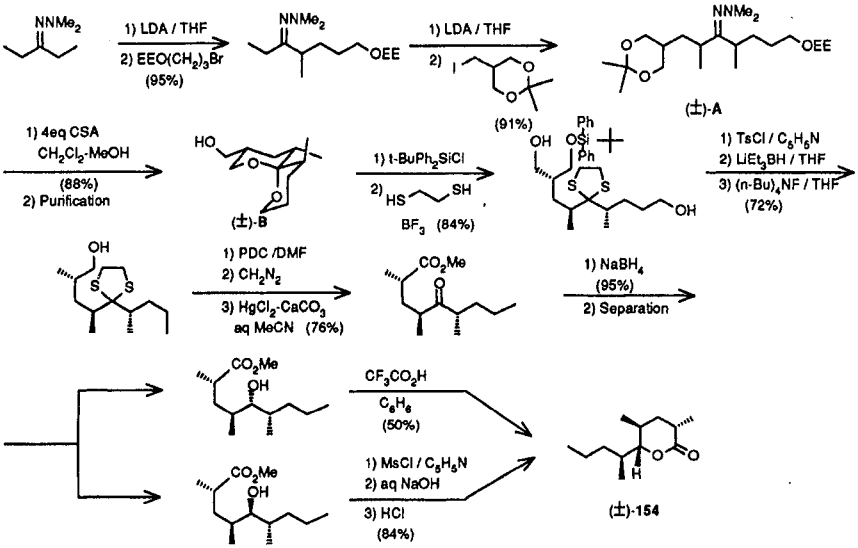


Scheme 469

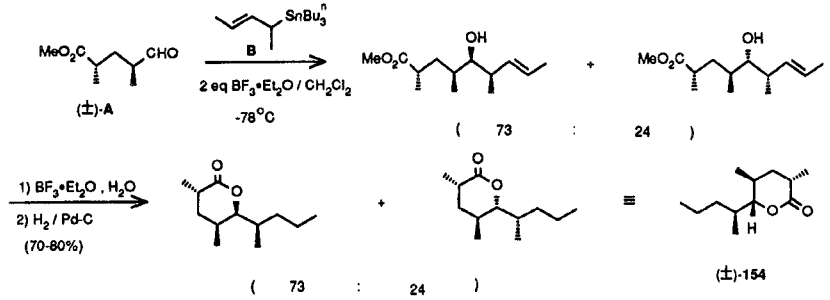
Four additional syntheses of (±)-**154** have been reported. Hoye et al. devised an interesting synthesis of (±)-**154** (Scheme 470).[613] They stereoselectively methylated spiro-dilactone (±)-**B,** which was prepared from **A,** to give (±)-**C.**[614] After hydrolysis, (±)-**C** gave (±)-**D.** Its lithium-ammonia reduction was followed by thermodynamically controlled lactonization to give (±)-**E**[(±)-**E**: its isomer = 14.6 : 1].[613] Further conversion (as shown in the Scheme) furnished (±)-**154.** Schreiber and Wang synthesized (±)-**154** by stereoselective formation of a spiroacetal (±)-**B** from (±)-**A** (Scheme 471).[615] That spiroacetalization established the three chiral centers out of four in the invictolide molecule. Y. Yamamoto et al. employed the Lewis acid-mediated reaction of (±)-**A** with an allyltin **B** as the key-step (Scheme 472) and obtained (±)-**154** as a minor product.[616] Stereoselective cyclization of enyne (±)-**A** mediated by zirconocene (Scheme 473) yielded (±)-ketone **B,** which was an intermediate in a previous synthesis of (±)-**154.**[617]



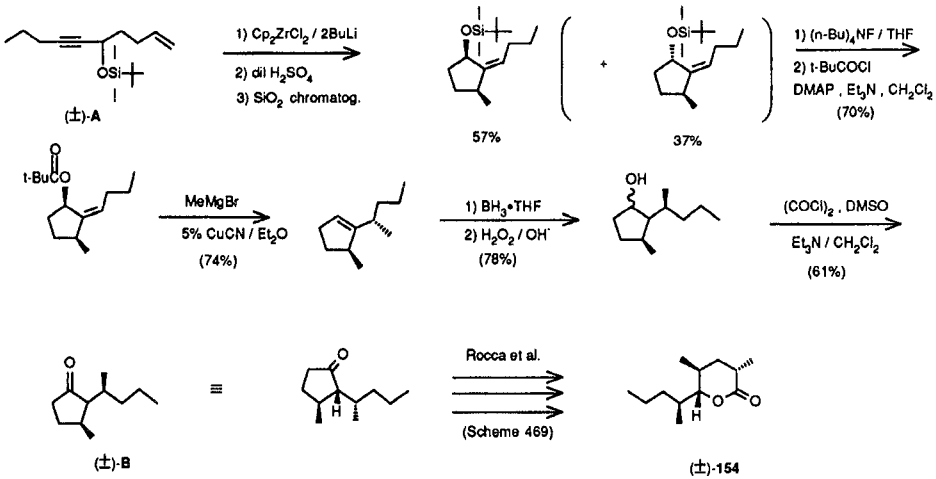
Scheme 470



Scheme 471



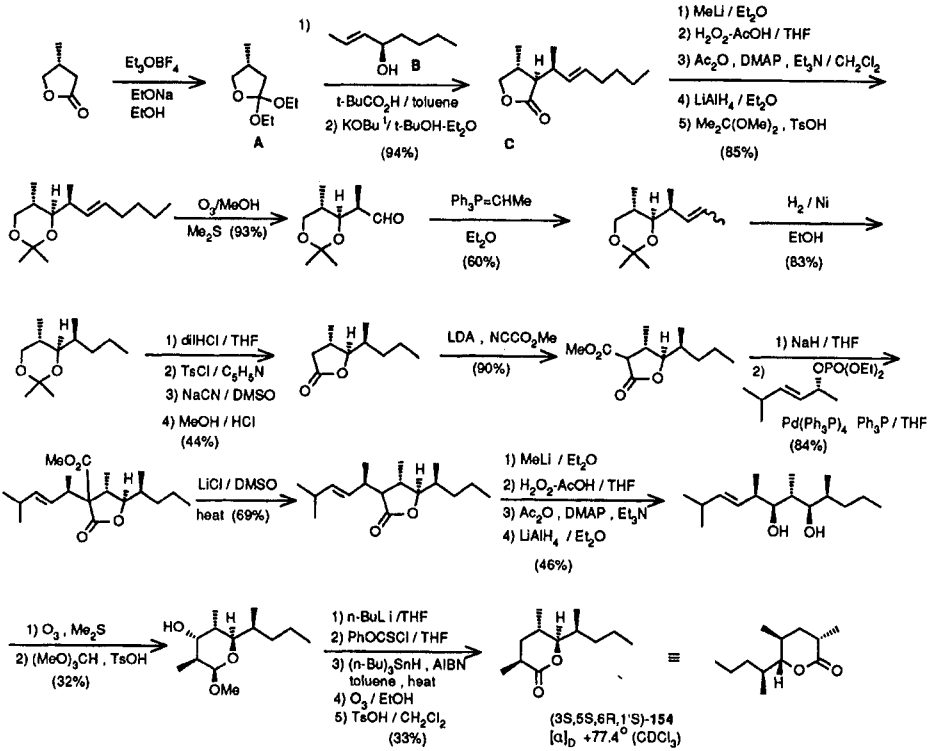
Scheme 472



Scheme 473

Five syntheses of optically active **154** have been published. Ziegler et al. synthesized unnatural (+)-**154** (Scheme 474),[618,619] starting from (*R*)-3-methyl-4-butanolide.[620] The key Claisen rearrangement (**A** + **B** → **C**) was highly stereoselective after equilibration at C-2 to give **C** of 95% d.e. and > 99% e.e. After a lengthy sequence of reactions, **C** yielded (±)-**154.** Zieglaer et al. also prepared (±)-**154** by the same route, starting from (±)-3-methyl-4-butanolide[618] and found (±)-**154** to be bioactive, while (+)-**154** was inactive.

Shortly afterwards, Mori and Nakazono prepared both the enantiomers of **154**[621] and (−)-**154** was indeed bioactive.[622] In this synthesis, the four chiral centers of **154** were constructed by means of the Sharpless asymmetric epoxidation of allylic alcohol **A,** diastereoselective methylation of β-hydroxy ester



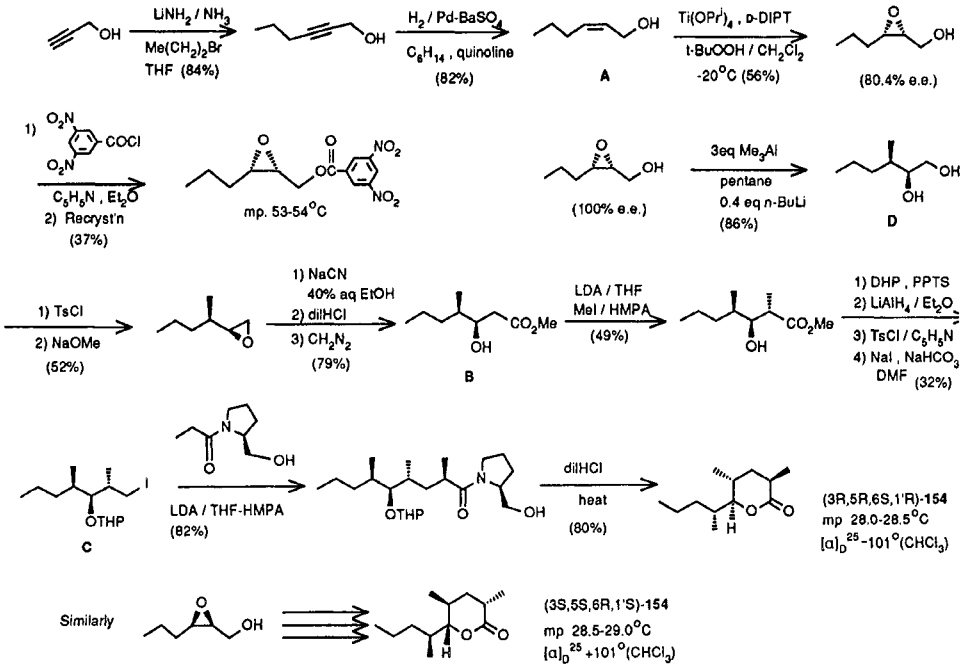
Scheme 474

B, and the Evans asymmetric alkylation with alkylating agent **C** (Scheme 475).[621] Instead of asymmetric epoxidation, enzymatic resolution of the *N*-chloroacetylamino acid **A** (Scheme 476) was also employed for the preparation of diol **D**, the key-intermediate in the synthesis shown in Scheme 475.[623]

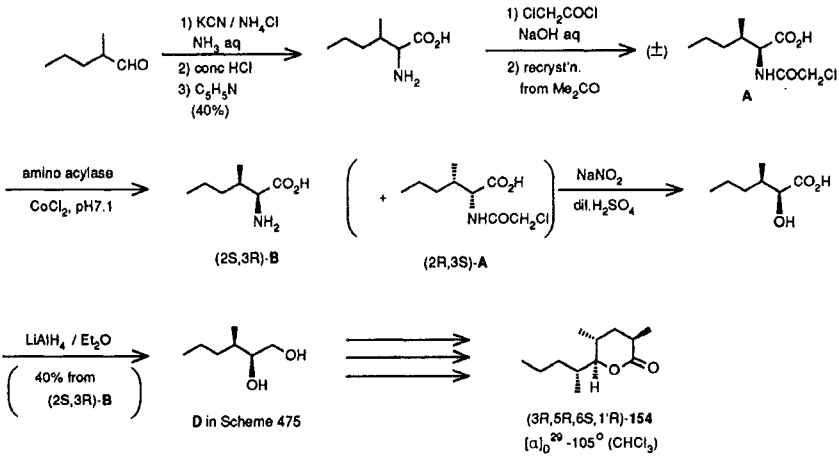
Wakamatsu et al. started from levoglucosan and obtained a 74:26 mixture of (−)-**154** and its 3*S*-isomer (Scheme 477).[624] Balestra and Kallmerten synthesized (−)-**154** by using diastereoselective [2.3] Wittig rearrangement of a tertiary α-lithio ether as the key reaction (Scheme 478).[625]

E. (2*Z*,4*Z*,6*E*)-2,4,6-Decatrien-5-olide [(*E*)-6-(1-Pentenyl)-2H-pyran-2-one] 155 ($C_{10}H_{12}O_2$)

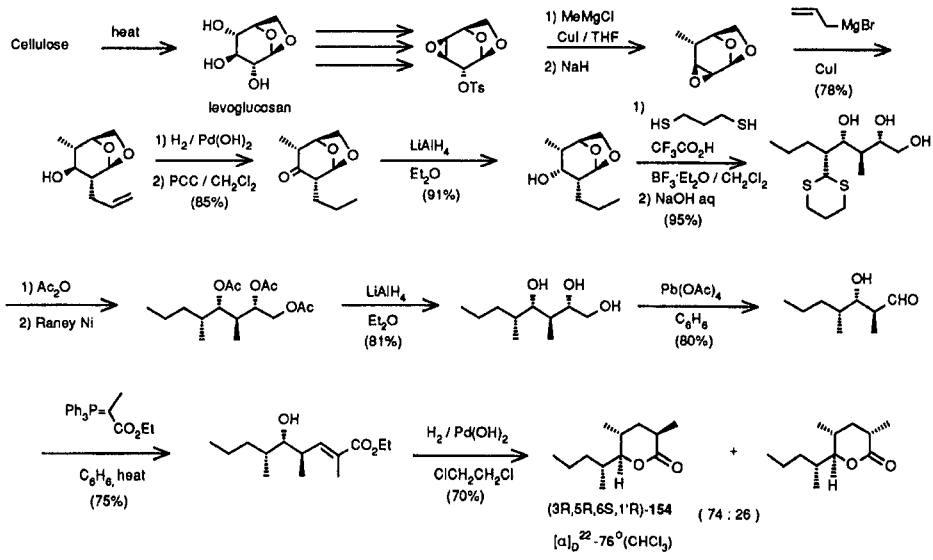
Together with **154**, this is a component of the Queen recognition pheromone for *Solenopsis invicta*, which attracts worker ants and causes them to move



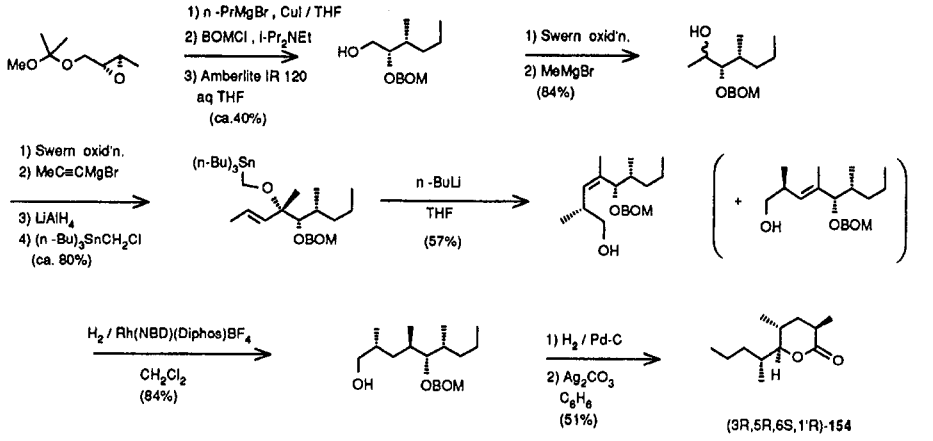
Scheme 475



Scheme 476

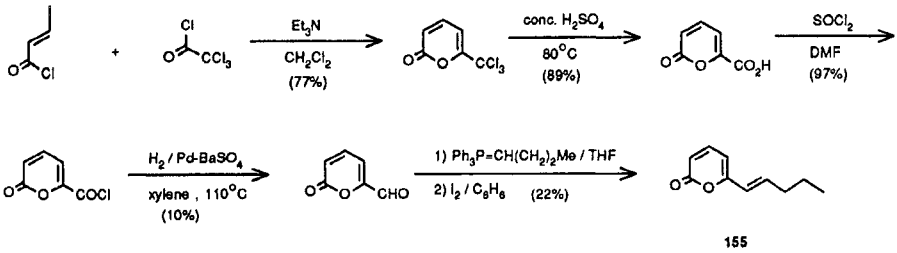


Scheme 477

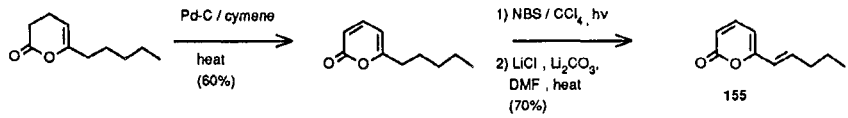


Scheme 478

inanimate objects treated with Queen extracts into their nests as if they were real Queens. Rocca et al. synthesized **155** as shown in Scheme 479.[611] The same lactone **155** was identified as a component of the male mandibular gland secretion of carpenter ants (*Camponotus pennsylvanicus, C. herculeanus*, and *C. noveboracensis*).[626] Jones and Fales synthesized **155** in a straightforward manner (Scheme 480).[626]



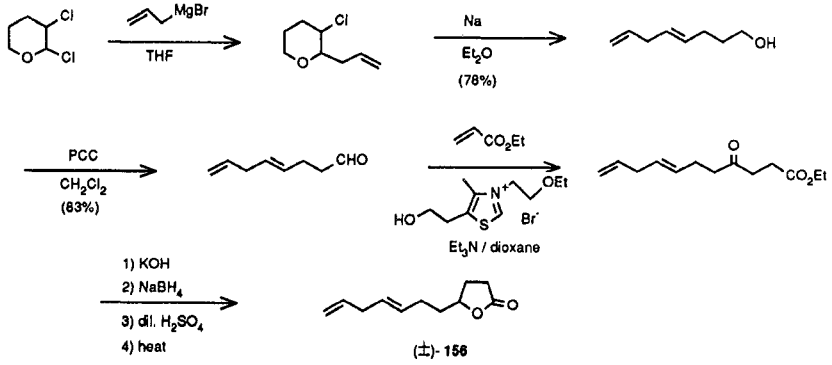
Scheme 479



Scheme 480

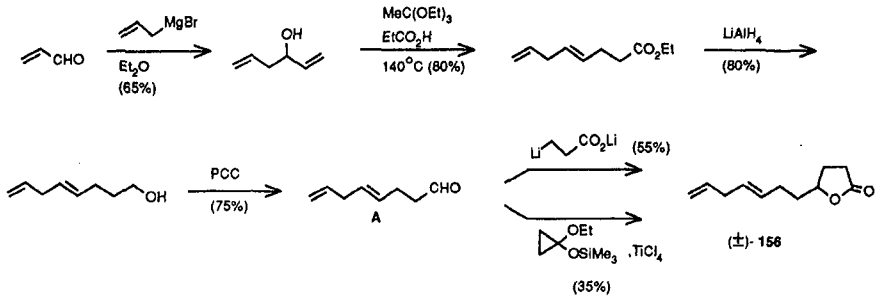
F. (*E*)-7,10-Undecadien-4-olide [5-(3*E*,6-Heptadienyl)-dihydro-2(3H)-furanone] 156 ($C_{11}H_{16}O_2$)

This lactone **156** is a component of the smoke-emitted pheromone of male melon flies (*Dacus cucurbitae*), and it was synthesized by Voaden as shown in Scheme 481.[627] Mamdapur's synthesis of **156** was based on three-carbon elongation of

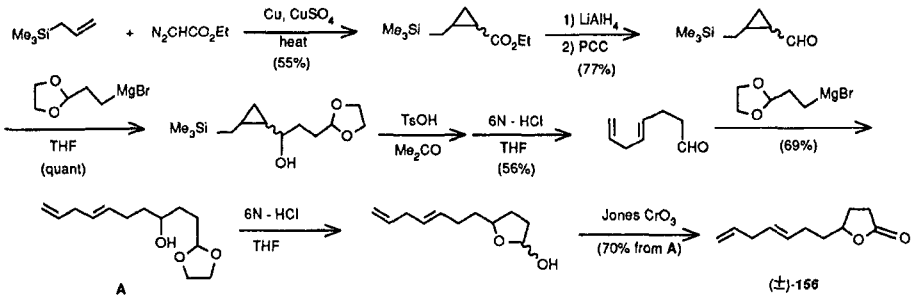


Scheme 481

aldehyde **A** by two different methods (Scheme 482).[628] Wilson and Zucker devised a new method for the synthesis of skipped dienes via organosilicon intermediates (Scheme 483).[629]



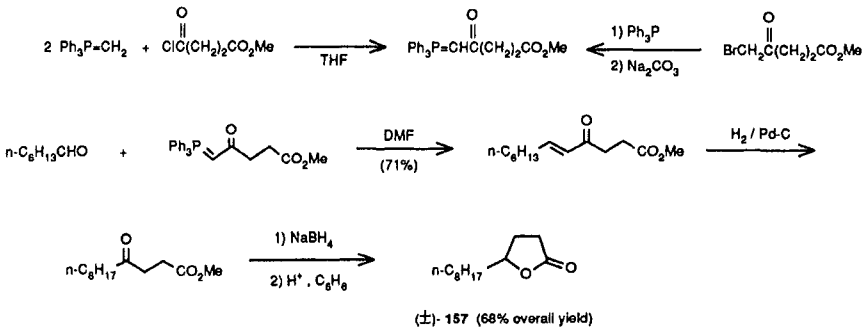
Scheme 482



Scheme 483

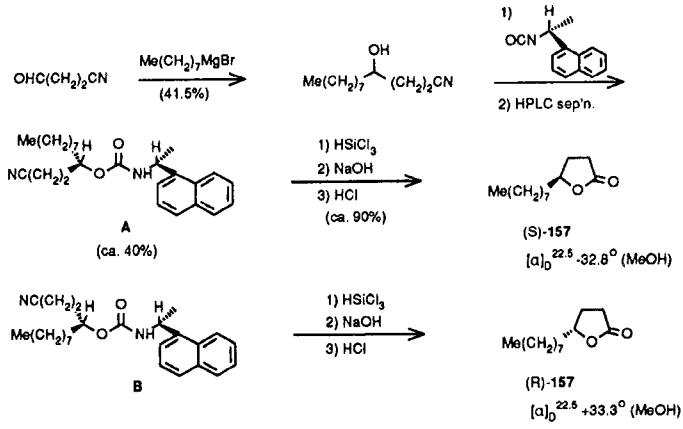
G. 4-Dodecanolide 157 ($C_{12}H_{22}O_2$)

This lactone **157** is a defensive secretion of rove beetles (*Bredius mandibularis*). An efficient synthesis of (±)-**157** was achieved via five-carbon homologation by the Wittig reaction (Scheme 484).[630]



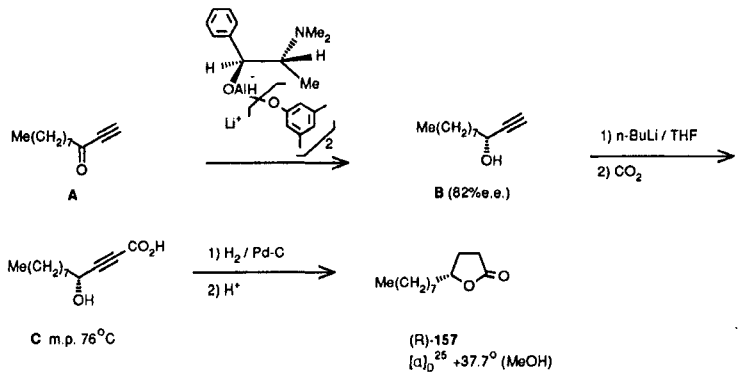
Scheme 484

Both the enantiomers of **157** were prepared by Pirkle and Adams by separating the diastereomeric carbamates **A** and **B** (Scheme 485) by HPLC.[631] Their assignment of *R*-configuration to (−)-**157** was in error.



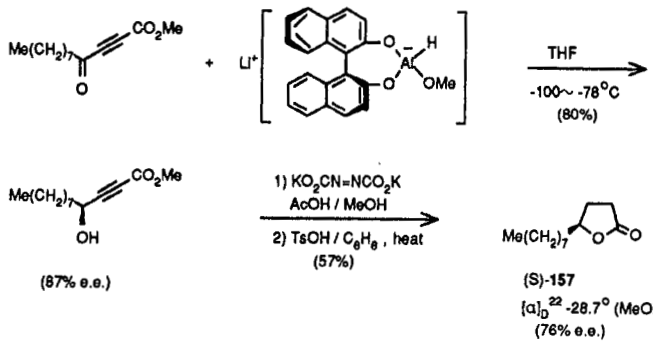
Scheme 485

Four different chemical asymmetric syntheses of **157** have been recorded. First, Vigneron and Bloy employed a chiral hydride reagent to reduce **A** to **B** (Scheme 486), which was converted to (*R*)-**157**.[590] Noyori et al. employed bi-

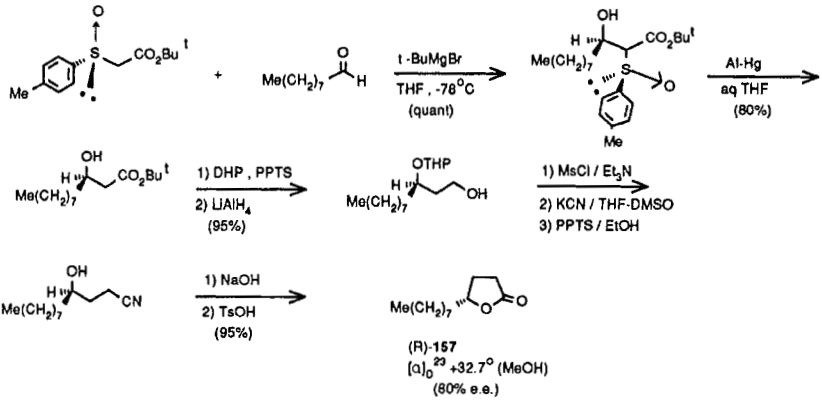


Scheme 486

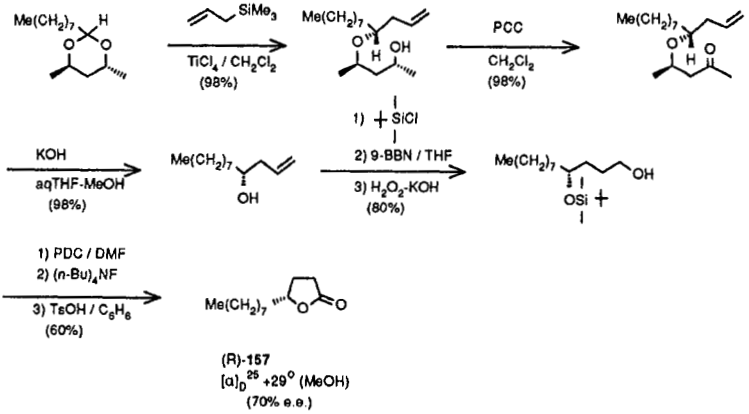
naphthol-modified lithium aluminum hydride for the synthesis of (*S*)-**157** (Scheme 487).[632,633] Starting from a chiral sulfoxide, Solladié prepared (*R*)-**157** (Scheme 488).[634] Bartlett et al. employed a chiral acetal as the starting material to synthesize (*R*)-**157** (Scheme 489).[635]



Scheme 487

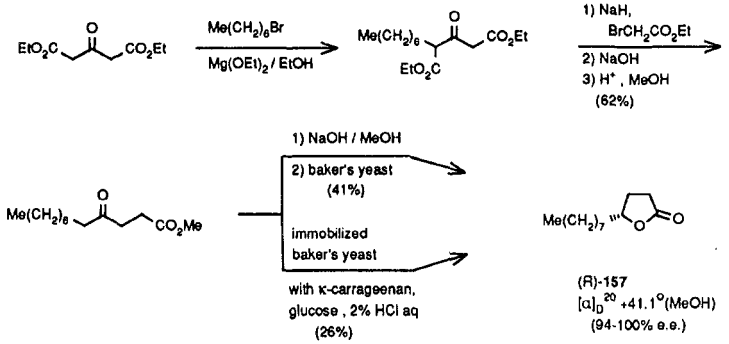


Scheme 488



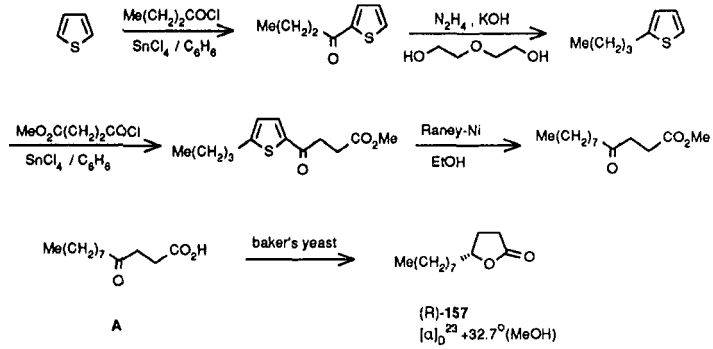
Scheme 489

Three chiral syntheses of **157** were executed by reduction with baker's yeast. Naoshima et al. reduced the sodium salt of 4-oxododecanoic acid to give (*R*)-**157** of 94–100% e.e. (Scheme 490).[636] They also employed baker's yeast immo-



Scheme 490

bilized with carrageenan.[636] Utaka et al. carefully examined the reduction condition with baker's yeast and obtained (*R*)-**157** [> 98% e.e.; $[\alpha]_D$ + 42.4° (MeOH)] in 71% yield by reducing the potassium salt of the keto acid.[637] A new synthesis of the intermediate keto acid **A** was achieved by Rao et al., using thiophene as a chain extender (Scheme 491).[638] By reducing **A** with baker's

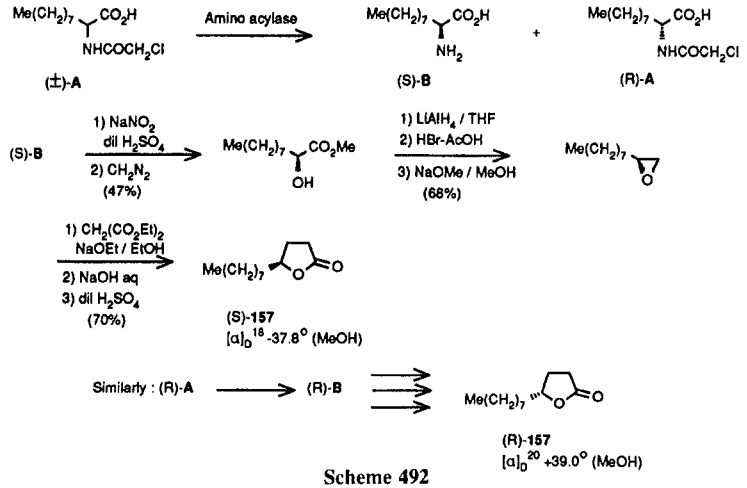


Scheme 491

yeast, they obtained (*R*)-**157**, although they erroneously depicted their product as (*S*)-**157**.

Sugai and Mori synthesized the enantiomers of **157**, starting from the en-

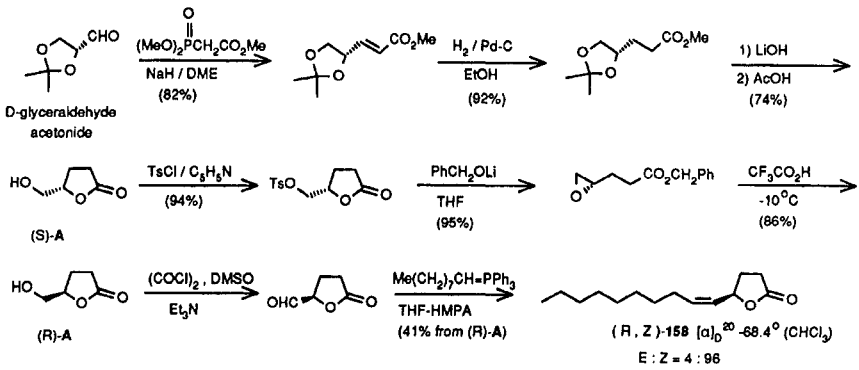
antiomers of 2-aminodecanoic acid **B**, which was prepared by resolving (±)-**A** with an amino acylase of fungal (*Aspergillus*) origin (Scheme 492).[639]



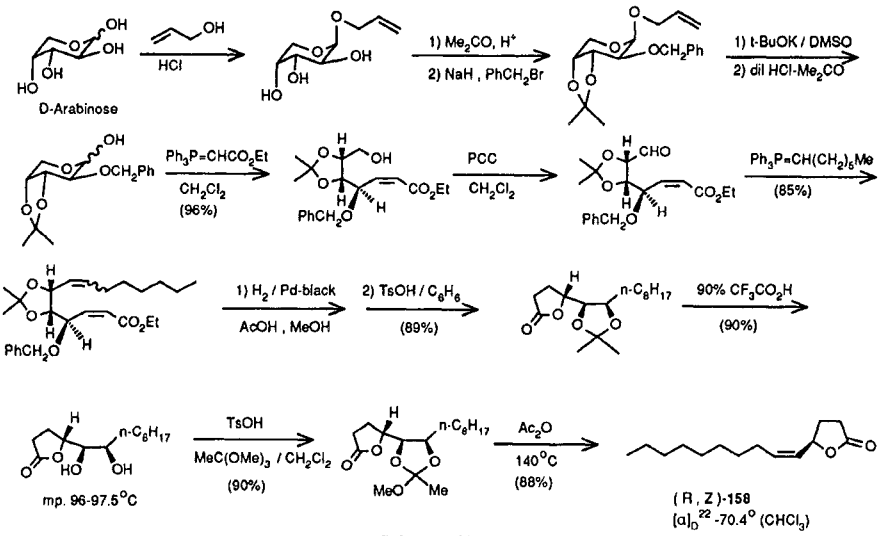
Scheme 492

H. (*R*,*Z*)-5-Tetradecen-4-olide 158 ($C_{14}H_{24}O_2$)

This is the female-produced sex pheromone of the Japanese beetle (*Popillia japonica*). A full paper of the synthesis of the enantiomers of **158** from glutamic acid was published by Doolittle et al. (cf. Scheme 259, Ref. 1).[640] Two other syntheses of **158** were reported starting from optically active natural products. Kang et al. employed D-glyceraldehyde acetonide as the starting material to prepare (*S*)-**A** first, which was epimerized to (*R*)-**A** and converted to (*R*,*Z*)-**158** (Scheme 493).[641] D-Arabinose was the starting material in Nishida's synthesis of (*R*,*Z*)-**158** (Scheme 494).[642]

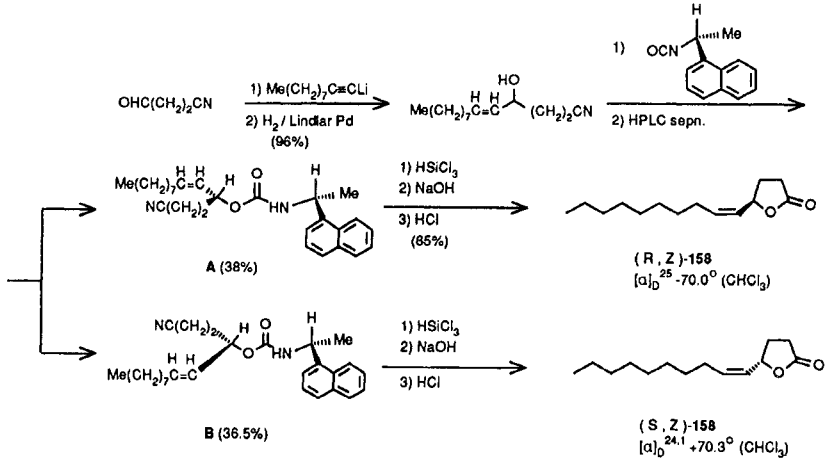


Scheme 493



Scheme 494

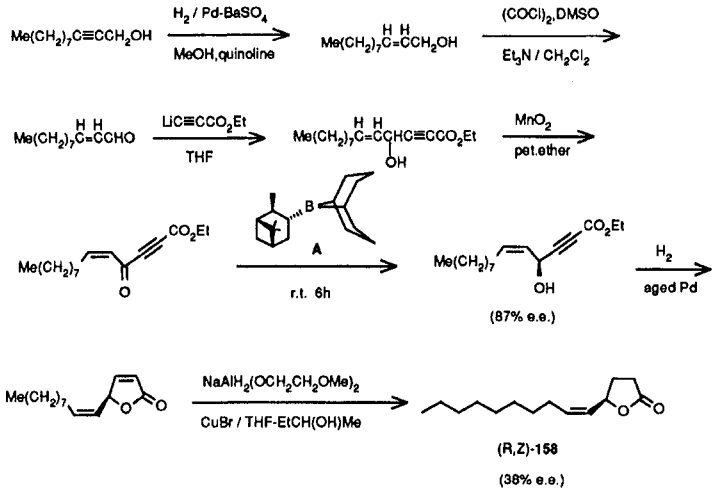
Pirkle and Adams reported a synthesis of **158** by HPLC separation of the diastereomeric carbamates (**A** and **B**) (Scheme 495).[631]



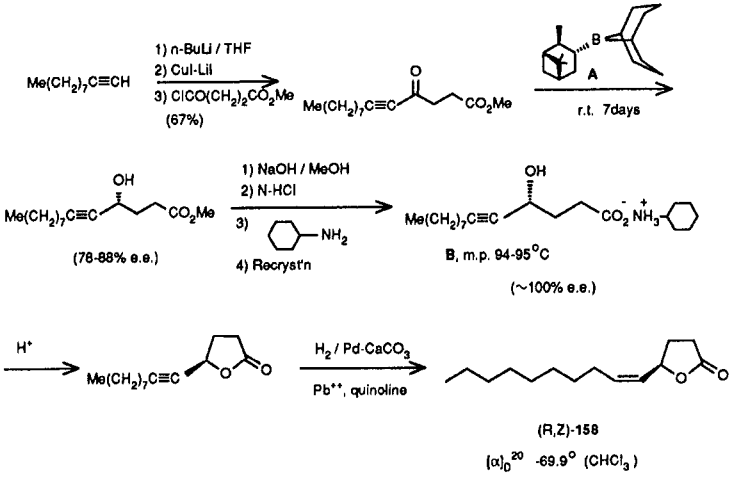
Scheme 495

Four different groups of workers employed chemical asymmetric reduction for the synthesis of (*R*,*Z*)-**158.** By using the asymmetric reducing agent *B*-3-pinanyl-9-borabicyclo[3.3.1]nonane (**A,** Alpine borane®), Midland et al. syn-

thesized **158** in two different ways (Schemes 496 and 497).[591,643] The latter

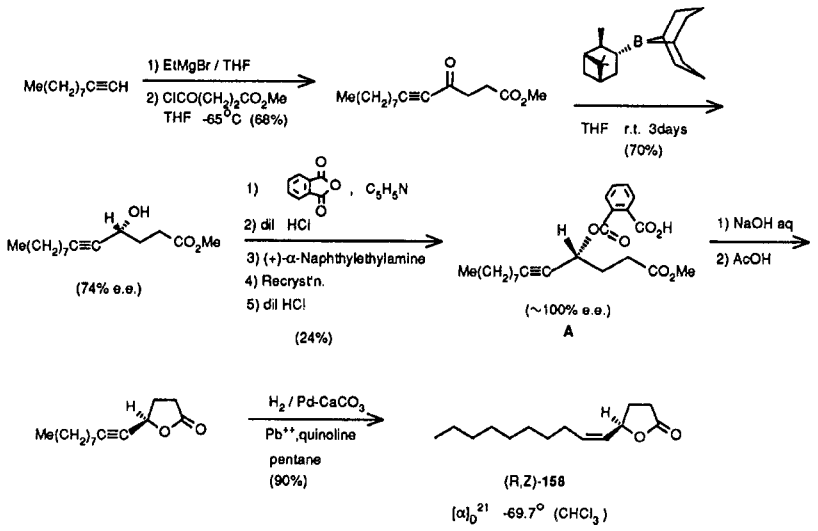


Scheme 496



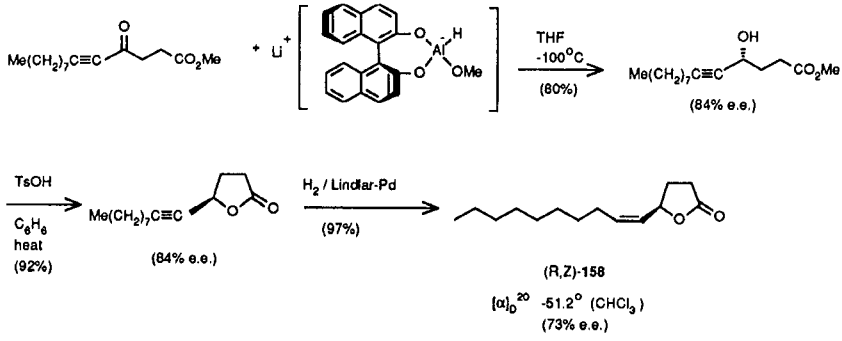
Scheme 497

process yielded pure (*R*,*Z*)-**158** because it was possible to purify the intermediate **B** by recrystallization. Baker and Rao also used Alpine borane® for their synthesis of (*R*,*Z*)-**158** (Scheme 498).[644] They purified an amine salt of the phthalic half ester **A** by recrystallization and obtained pure (*R*,*Z*)-**158.** Noyori's



Scheme 498

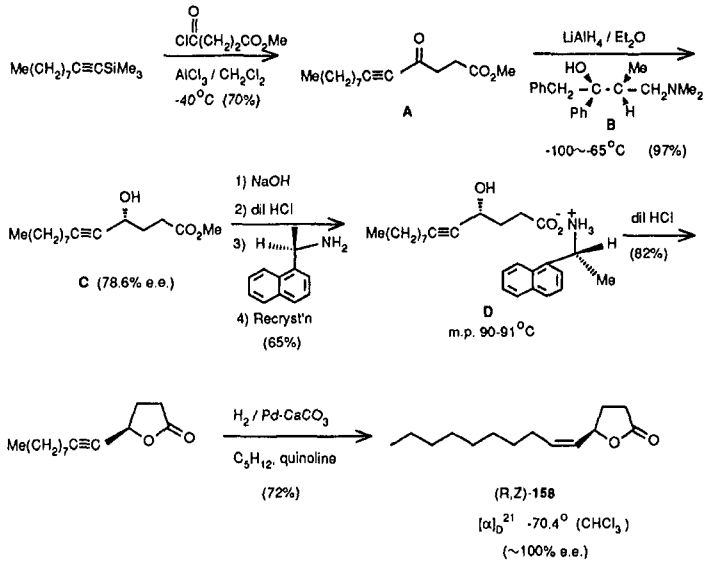
binaphthol-modified lithium aluminum hydride was also used to prepare **158** (Scheme 499).[632,633] Senda and Mori reduced keto ester **A** with lithium alu-



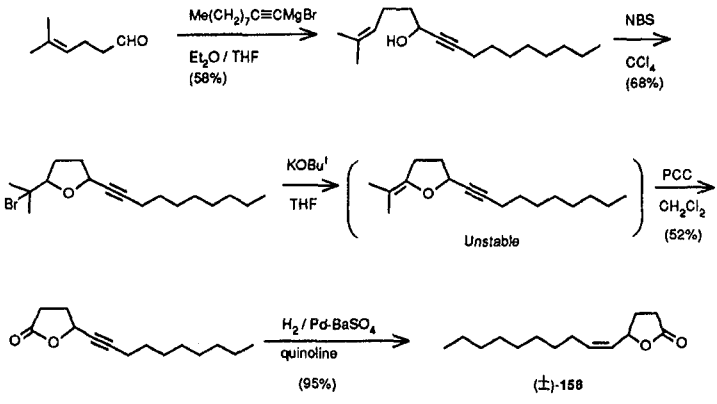
Scheme 499

minum hydride-Darvon alcohol (Chirald®) **B** to give **C** of 79–85% e.e. (Scheme 500).[645] This ester **C** was hydrolyzed, and the resulting acid was found to give crystalline salt **D.** Its recrystallization yielded pure material, which finally furnished enantiomerically pure **(*R*,*Z*)-158.** This process was employed, with a small modification, for the multi-kg synthesis of **(*R*,*Z*)-158.**

Chandrasekaran and his co-workers published a synthesis of (±)-**158** (Scheme 501).[646] However, (±)-**158** is biologically inactive.[640]



Scheme 500

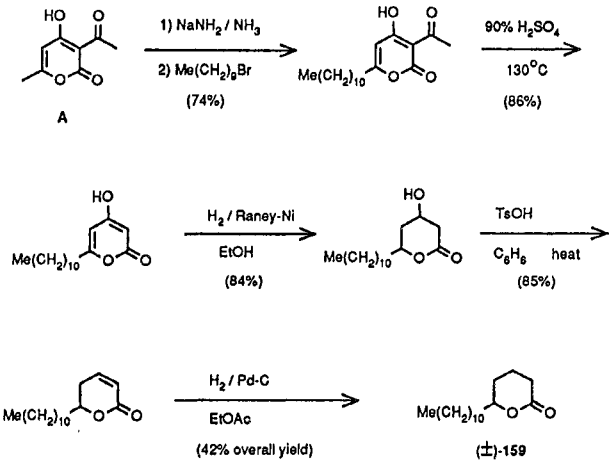


Scheme 501

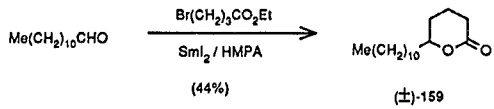
I. (*R*)-5-Hexadecanolide 159 ($C_{16}H_{30}O_2$)

This δ-lactone **159** was isolated from heads of the Queens of the oriental hornet (*Vespa orientalis*) as a pheromone for the workers to stimulate the construction of Queen cells. Bioassay of Mori's synthetic enantiomers of **159** by Ishay proved only (*R*)-**159** to be bioactive.[647]

Two new syntheses of (±)-**159** have been reported. Bacardit and Moreno-Mañas prepared (±)-**159** starting from dehydroacetic acid **A** (Scheme 502).[599,648] Samarium(II) iodide-induced Barbier-type reaction was employed by Otsubo et al. for the preparation of (±)-**159** (Scheme 503).[649]



Scheme 502

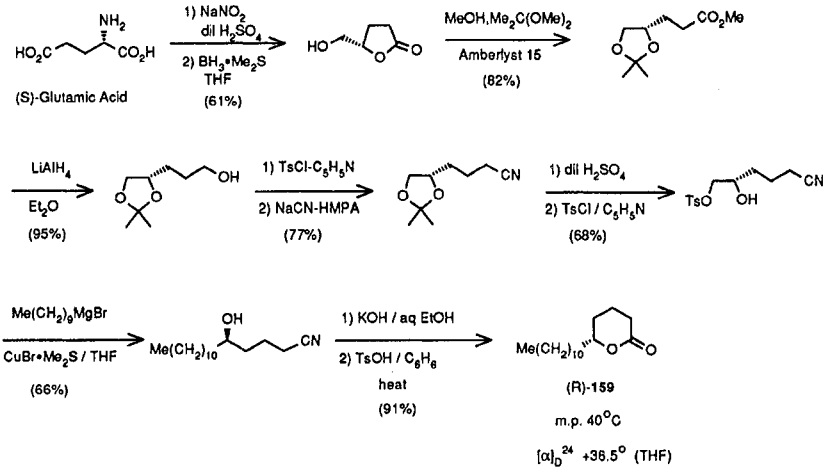


Scheme 503

Nineteen different syntheses of optically active **159** have been reported as detailed below.

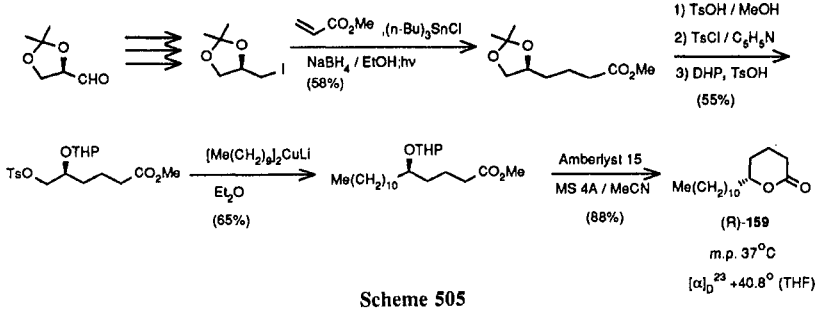
(1) Syntheses Starting from Chiral Building Blocks

Larchevêque and Laland prepared (*R*)-**159** starting from (*S*)-glutamic acid (Scheme 504).[650] Gerth and Giese synthesized (*R*)-**159** by radical carbon-carbon



Scheme 504

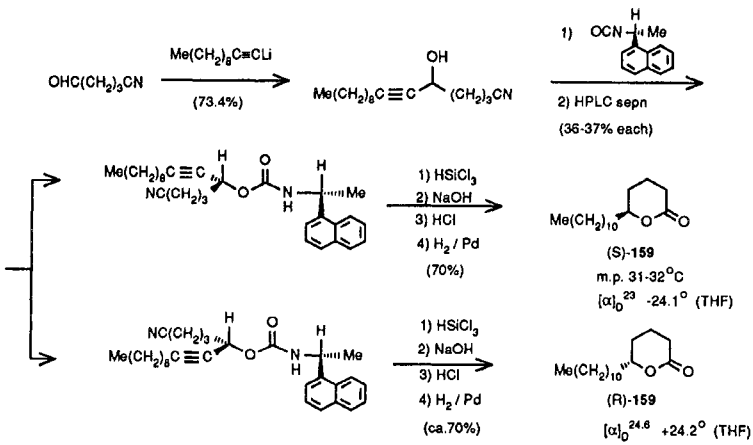
bond formation using a chiral radical precursor prepared from (*R*)-glyceraldehyde acetonide (Scheme 505).[605]



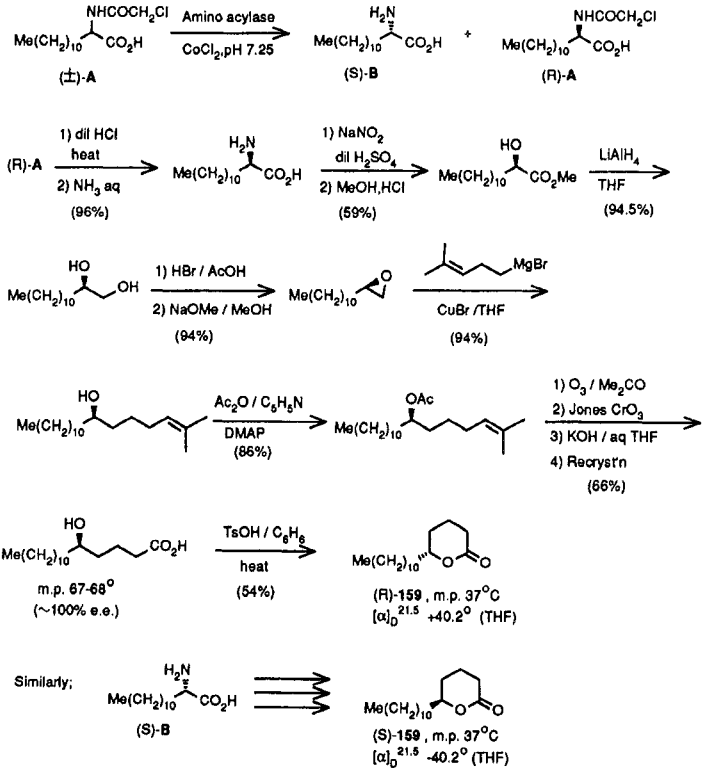
Scheme 505

(2) Syntheses by Means of Optical Resolutions

Pirkle and Adams prepared the enantiomers of **159** by HPLC separation of the diastereomeric carbamate (Scheme 506).[631] The specific rotations of their products, however, were smaller than those reported by others. Mori and Otsuka also employed resolution of the intermediate for the preparation of the enantiomers of **159**.[651] In this case, the starting (±)-2-chloroacetaminotridecanoic acid **(A)** was resolved with amino acylase to give (*S*)-2-aminotridecanoic acid **(B)** and (*R*)-**A** (Scheme 507). The synthetic enantiomers of **159** were tested by Ishay against the oriental hornet and (*R*)-**159** was found to be bioactive.[647]



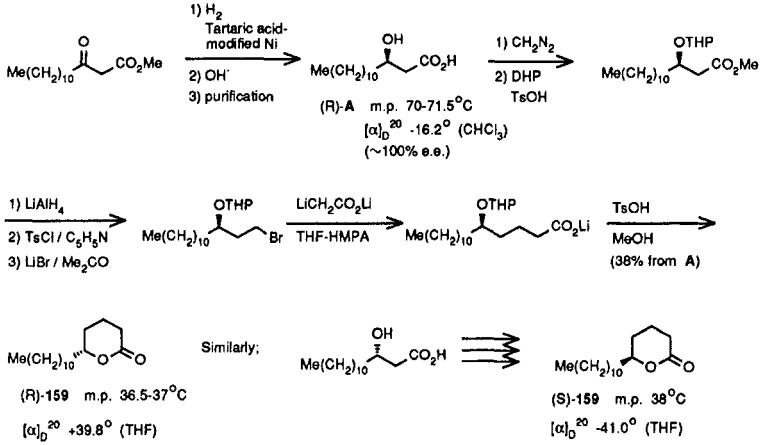
Scheme 506



Scheme 507

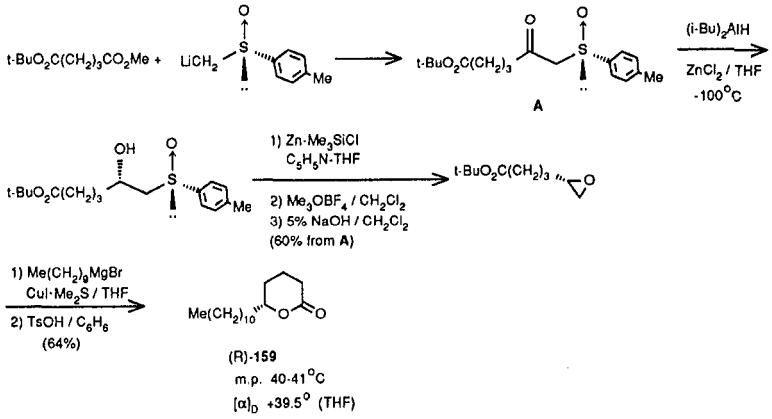
(3) Syntheses Based on Chemical Asymmetric Reactions

Three enantioselective syntheses of **159** have been reported based on the chemical asymmetric reduction of a carbonyl function. Kikukawa and Tai employed catalytic hydrogenation over tartaric acid-modified nickel[652] for the reduction of the carbonyl group, and secured pure enantiomers of **159** in high overall yield (Scheme 508).[653] Kosugi et al. synthesized (*R*)-**159** by means of highly



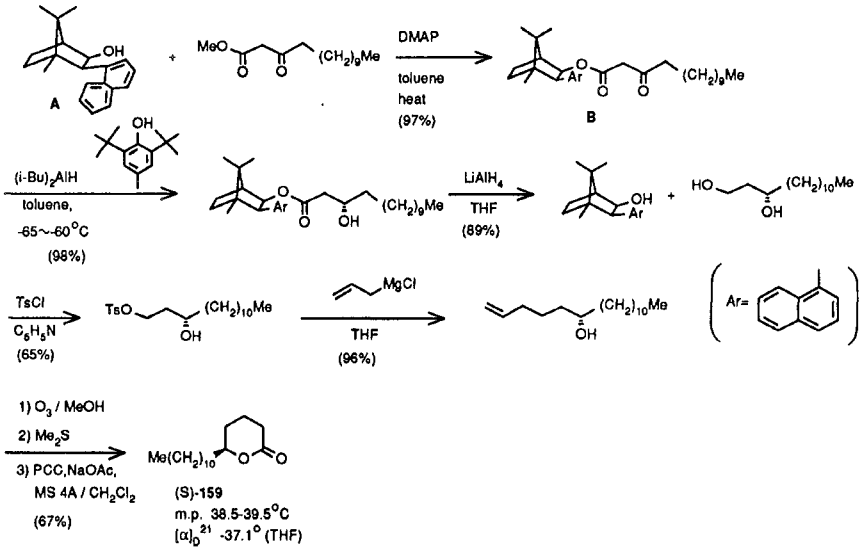
Scheme 508

diastereoselective reduction of chiral β-ketosulfoxides under chelation control (Scheme 509).[654] Taber et al. employed a chiral alcohol **A**, which was designed



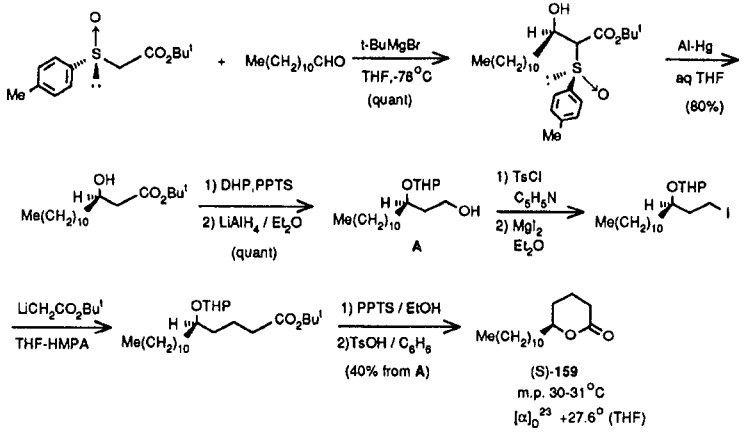
Scheme 509

to block one face of the carbonyl group of the keto ester **B**, as the chiral auxiliary to achieve highly enantioselective synthesis of (*S*)-**159** (Scheme 510).[655]



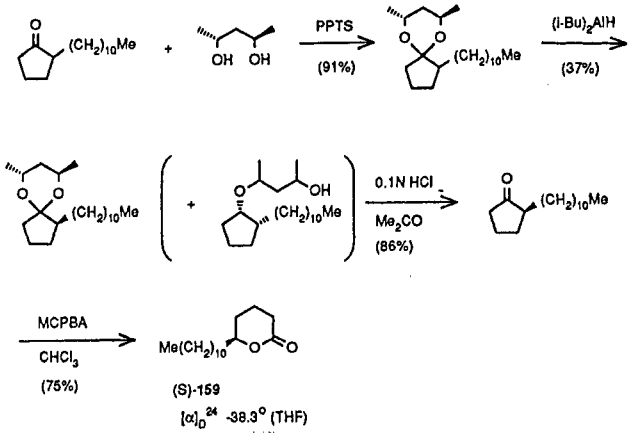
Scheme 510

Four chiral syntheses of **159**, as detailed below, were based on chemical asymmetric reactions other than carbonyl reduction. Solladié and Matloubi-Moghadam employed aldol-type reaction between a chiral sulfoxide and an aldehyde for the synthesis of (*S*)-**159** (Scheme 511).[634] By resolving 2-undecyl-



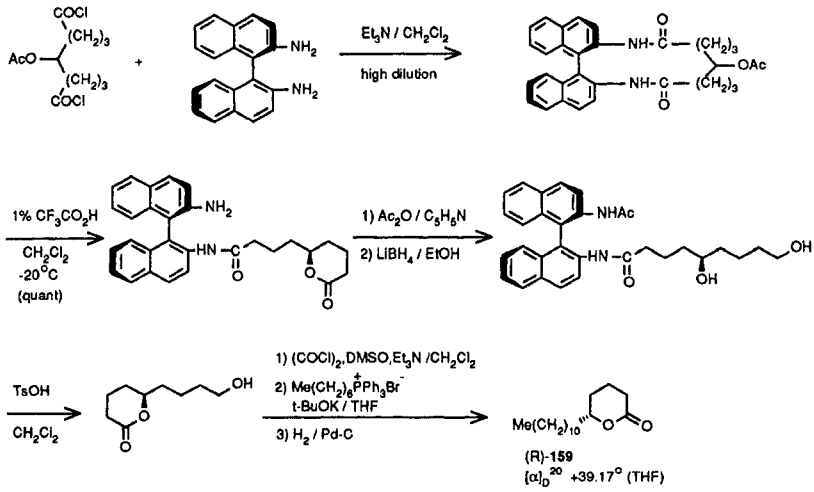
Scheme 511

cyclopentanone via its acetal with (2*R*,4*R*)-2,4-pentanediol, Yamamoto et al. synthesized (*S*)-**159** (Scheme 512).[656] Another unique synthesis of (*R*)-**159** by



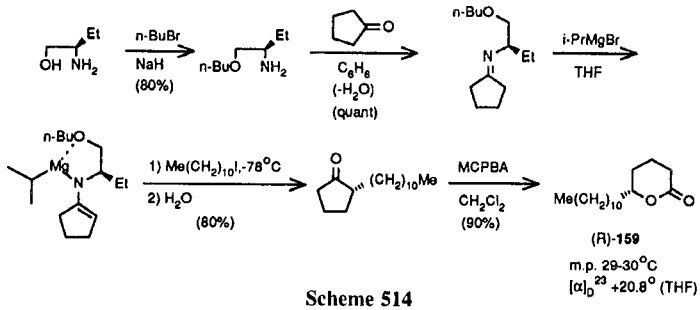
Scheme 512

Oda et al. employed a new asymmetric lactonization reaction using a C_2-chiral auxiliary (Scheme 513).[657] Kapadi prepared (*R*)-**159** of low enantiomeric purity



Scheme 513

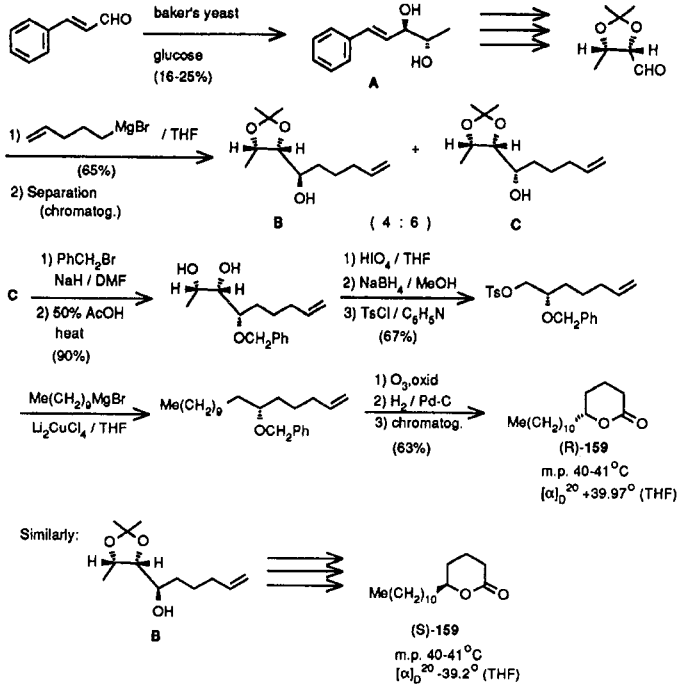
by alkylation of an asymmetric enamine followed by the Baeyer-Villiger oxidation of the resulting optically active ketone (Scheme 514).[658]



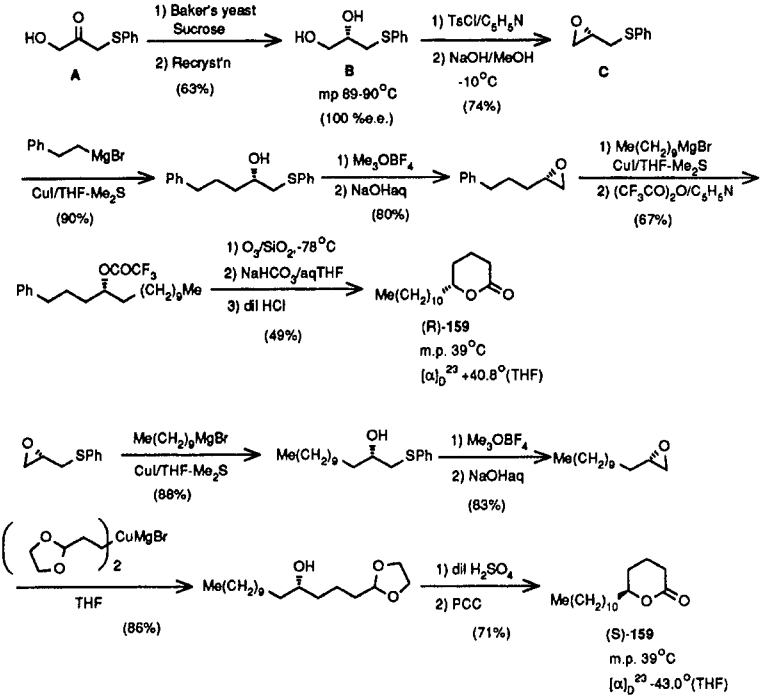
Scheme 514

(4) Syntheses Based on Biochemical Asymmetric Reactions

Eight chiral syntheses of **159** were based on biochemical asymmetric reactions. Servi synthesized the pure enantiomers of **159** starting from the diol **A** (Scheme 515), which was prepared by the reduction of cinnamaldehyde with baker's

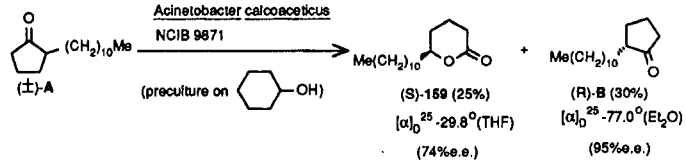


Scheme 515



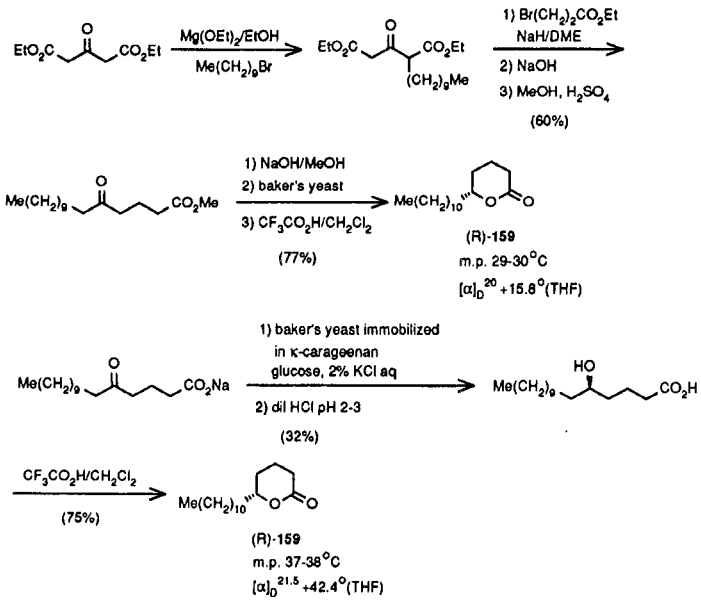
Scheme 516

yeast.[659] Fujisawa et al. prepared a chiral epoxide **C** (Scheme 516) starting from **A**, the reduction of which with baker's yeast furnished optically active alcohol **B**.[660] The epoxide **C** was converted to the enantiomers of **159** (Scheme 516).[660] Furstoss and his co-workers achieved an enantioselective microbial Baeyer-Villiger oxidation (Scheme 517).[661] By this method, (*S*)-**159** and (*R*)-**B** were obtained. Chemical Baeyer-Villiger oxidation of (*R*)-**B** would give (*R*)-**159**.[cf. 656]



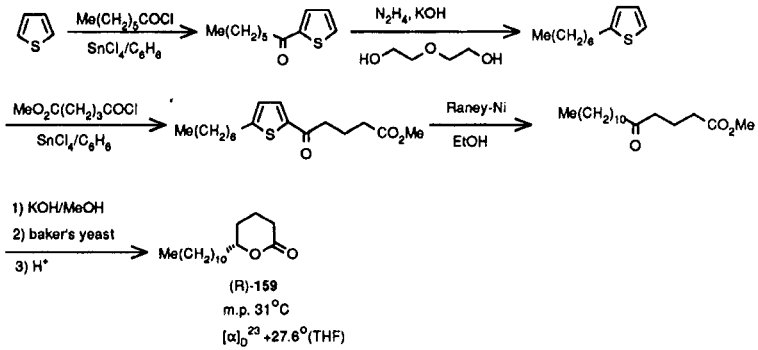
Scheme 517

Five papers reported the enantioselective reduction of 5-oxohexadecanoic acid with baker's yeast. Naoshima et al. prepared (*R*)-**159** (ca. 40% e.e.) by yeast reduction of the keto acid (Scheme 518).[594] They could later improve their



Scheme 518

method to obtain pure (*R*)-**159** (ca. 100% e.e.) by employing baker's yeast immobilized in carrageenan and reducing the sodium salt of the keto acid (Scheme 518).[636] Reduction of potassium 5-oxohexadecanoate with baker's yeast was also highly enantioselective to give (*R*)-**159**, m.p. 37.5–38°C, $[\alpha]_D^{23}$ + 39.5° (THF), in 40% yield.[637,662] Bhalerao et al. reported a new synthesis of 5-oxohexadecanoic acid using thiophene as a chain extender (Scheme 519).[638]



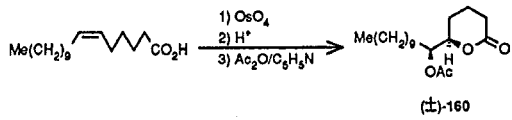
Scheme 519

J. (5*R*,6*S*)-6-Acetoxy-5-hexadecanolide 160 ($C_{16}H_{32}O_4$)

The major component of the oviposition attractant pheromone from the apical droplet of eggs of the Southern house mosquito (*Culex pipiens fatigans*) was shown by Laurence and Pickett to be *erythro*-6-acetoxy-5-hexadecanolide **160.**[663] The natural pheromone was later shown to be (5*R*,6*S*)-**160,** by comparing Mori's synthetic enantiomers with the natural pheromone.[664]

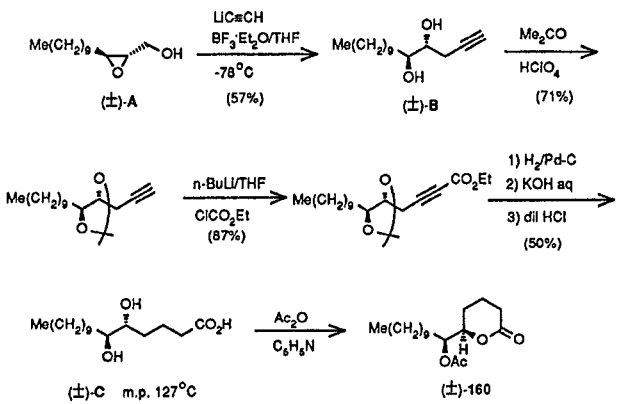
(1) Syntheses of (±)-160

Seven syntheses of (±)-**160** have been reported. Laurence and Pickett were the first to synthesize (±)-**160** by *cis*-hydroxylation of (*Z*)-5-hexadecenoic acid as the key-step (Scheme 520).[663] Yamaguchi and Hirao used their new alkynyla-



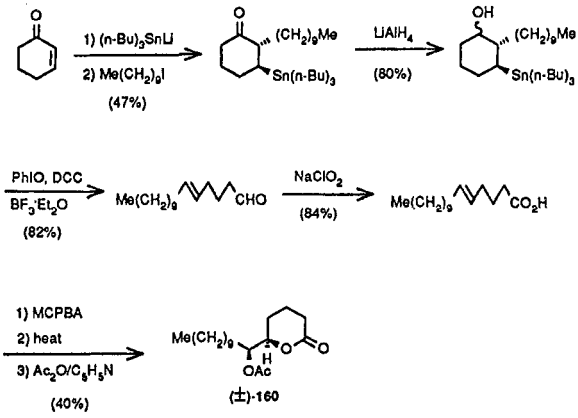
Scheme 520

tion reaction of epoxy alcohols derived from (*E*)-allylic alcohols for the synthesis of (±)-**160** (Scheme 521).[665] Thus, lithium acetylide in the presence of



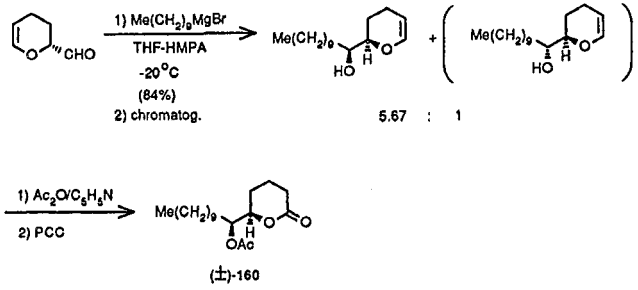
Scheme 521

boron trifluoride etherate reacted with epoxy alcohol (±)-**A** to give *erythro*-glycol (±)-**B**, which was converted to (±)-**160** via (±)-**C**. Ochiai et al. prepared (±)-**160** by using oxidative 1,4-fragmentation of γ-stannyl alcohol with iodosylbenzene as the key-step (Scheme 522).[666,667] The stereocontrolled ad-



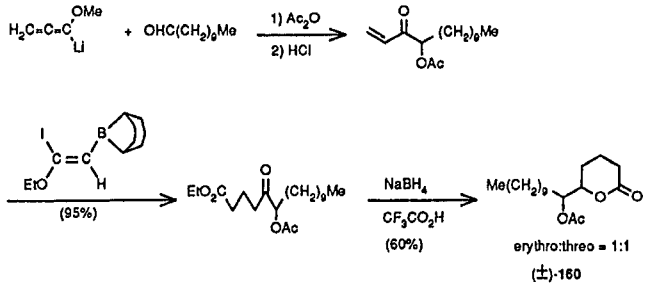
Scheme 522

dition of decylmagnesium bromide to acrolein dimer was the key-step of Jefford's short and efficient synthesis of (±)-**160** (Scheme 523).[668] Suzuki and his



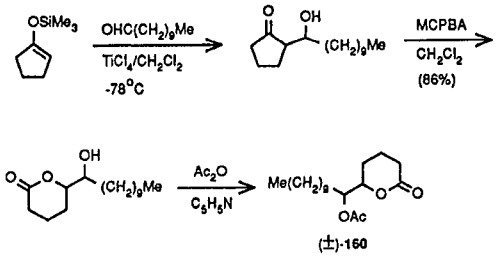
Scheme 523

co-workers employed the Michael-type reaction of *B*-iodo-9-BBN/ethoxyacetylene adduct to α,β-unsaturated ketone to prepare a 1 : 1 mixture of (±)-**160** and its *threo*-isomer (Scheme 524).[669] Dawson et al. published a simple syn-



Scheme 524

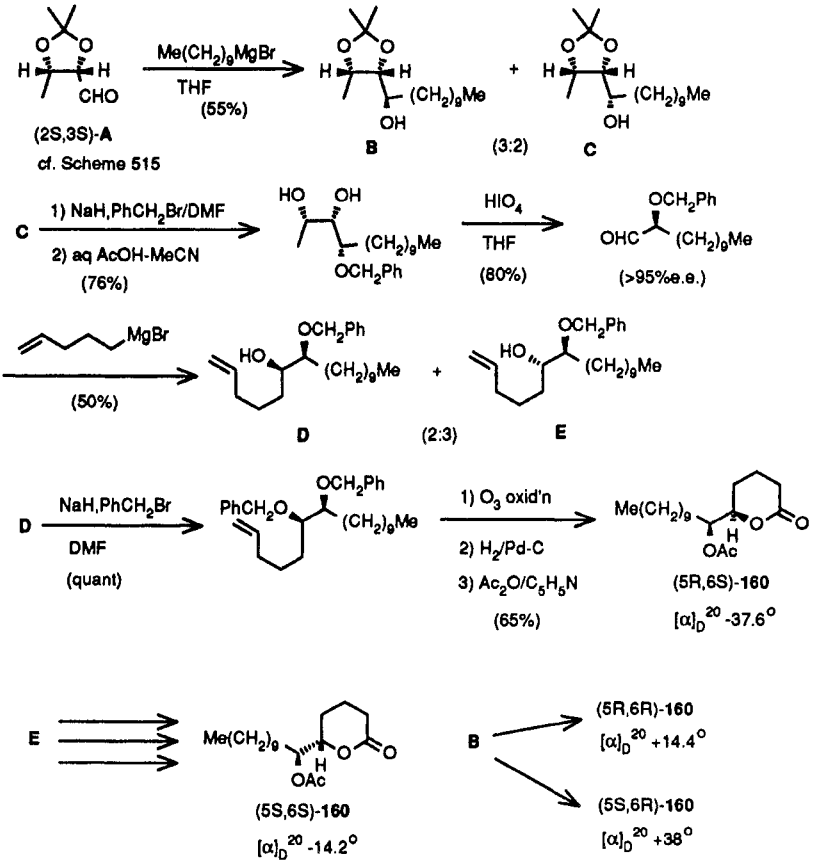
thesis of an isomeric mixture of (±)-**160** and its *threo*-isomer by means of aldol reaction, followed by Baeyer-Villiger oxidation and acetylation (Scheme 525).[670]



Scheme 525

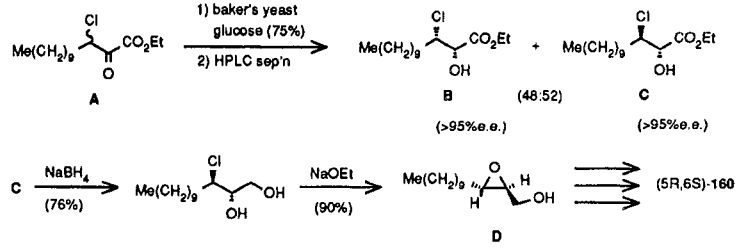
(2) Syntheses Based on Biochemical Asymmetric Reactions

Biochemical asymmetric reactions were used in three syntheses of optically active **160.** The first synthesis by Fuganti et al. employed chiral aldehyde **A** (Scheme 526) as the starting material, which was prepared from cinnamaldehyde by yeast reduction.[671] Their synthesis provided all of the four possible



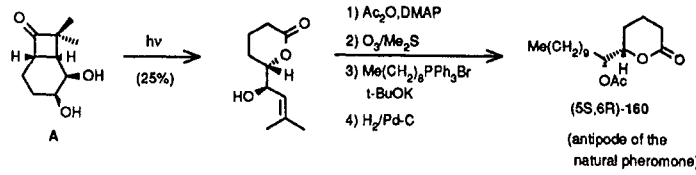
Scheme 526

stereoisomers of **160.** Tsuboi et al. reduced (±)-chloroketo ester **A** (Scheme 527) with baker's yeast and obtained **B** and **C** after HPLC separation of the



Scheme 527

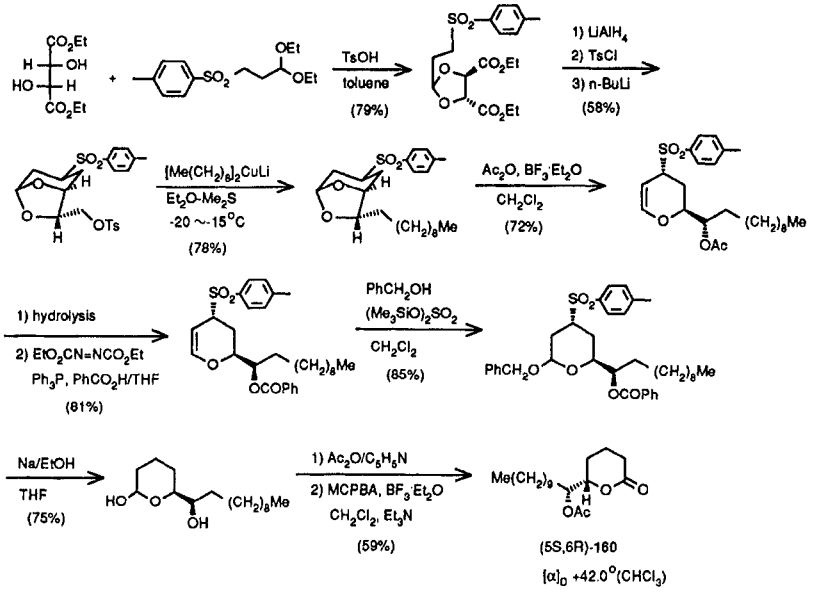
mixture.[672] The hydroxy ester **C** could be converted to the epoxide **D**. Because **D** was converted by others to (5*R*,6*S*)-**160** (*vide infra*), the present preparation of **D** implied a formal synthesis of it. Rahman et al. prepared the antipode of the natural pheromone by the photochemical method (Scheme 528).[673] The chiral starting material **A** was prepared biochemically.



Scheme 528

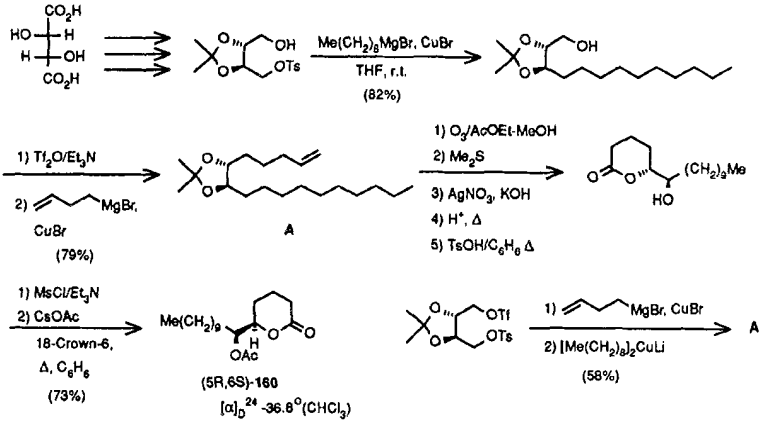
(3) Syntheses Starting from Chiral Building Blocks

Eight different syntheses of optically active **160** were achieved starting from chiral natural products. Masaki et al. employed (+)-diethyl tartrate as the starting material (Scheme 529), providing the antipode [(5*S*,6*R*)-**160**] of the natural



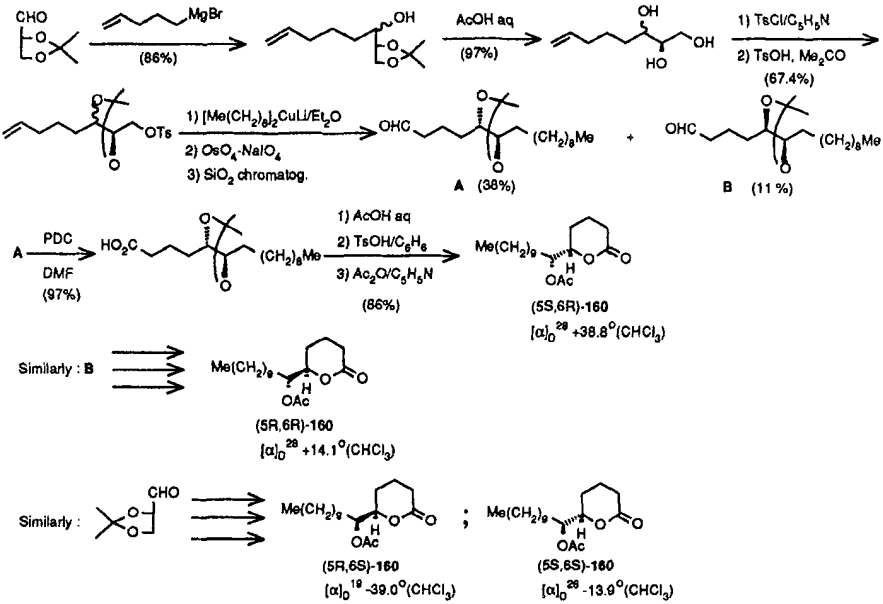
Scheme 529

pheromone.[674] Kotsuki et al. prepared (5*R*,6*S*)-**160** from (−)-tartaric acid (Scheme 530).[675] Machiya et al. started from the enantiomers of glyceraldehyde



Scheme 530

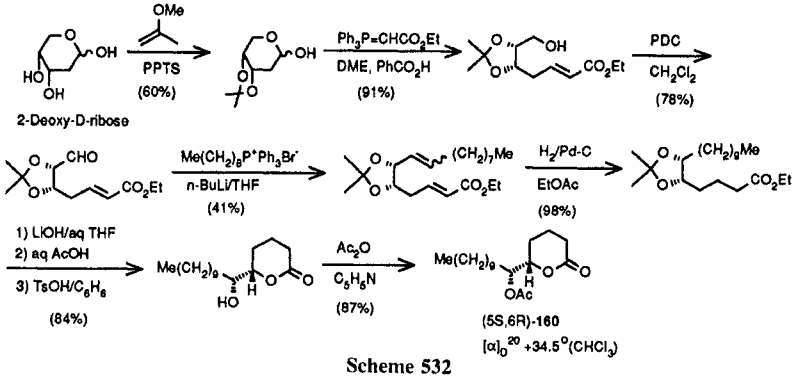
acetonide to synthesize all of the four isomers of **160** (Scheme 531).[676] Bioassay



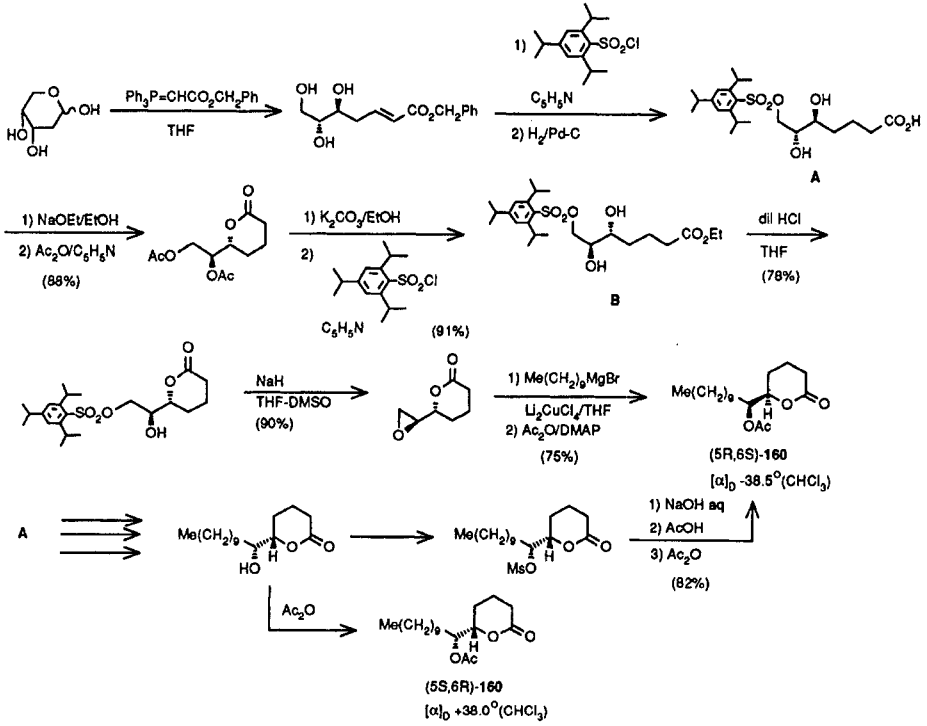
Scheme 531

of their four isomers on *C. pipiens molestus* showed (5*R*,6*S*)-**160** to be the most active attractant.[676]

Kang and Shin synthesized the antipode [(5*S*,6*R*)-**160**] of the natural pheromone starting from 2-deoxy-D-ribose (Scheme 532).[677] Rokach et al. prepared the enantiomers of **160** also from 2-deoxy-D-ribose (Scheme 533).[678,679] The

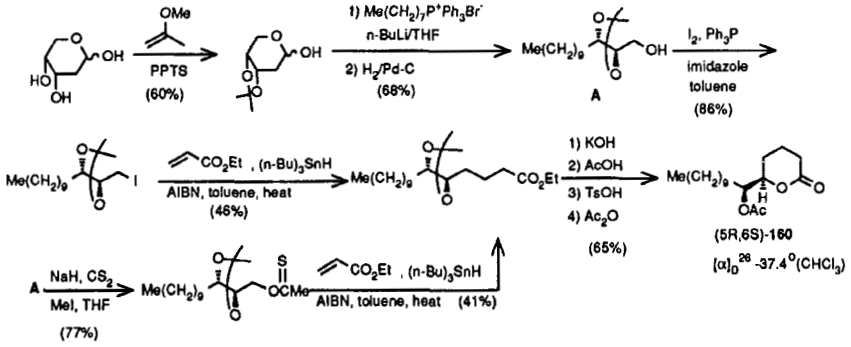


Scheme 532



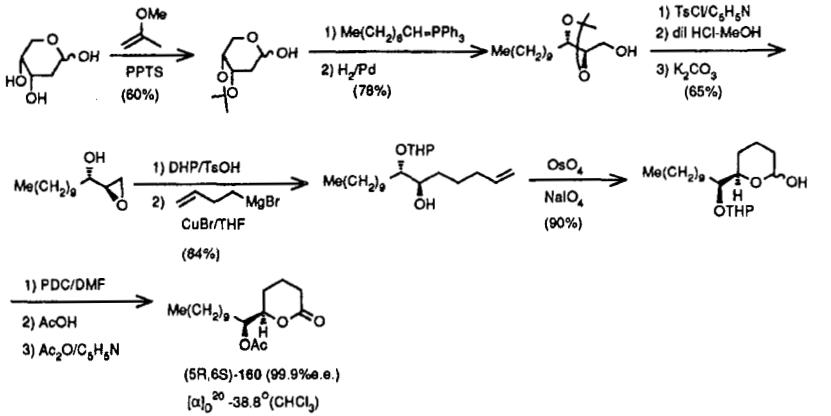
Scheme 533

notable feature of their synthesis is the inversion of configuration of the contiguous carbinol centers by means of the Payne rearrangement (**A** → **B**).[678] Kang and Cho employed a radical carbon-carbon bond formation for the synthesis of (5*R*,6*S*)-**160** from 2-deoxy-D-ribose (Scheme 534).[680] Ichimoto et al. synthe-



Scheme 534

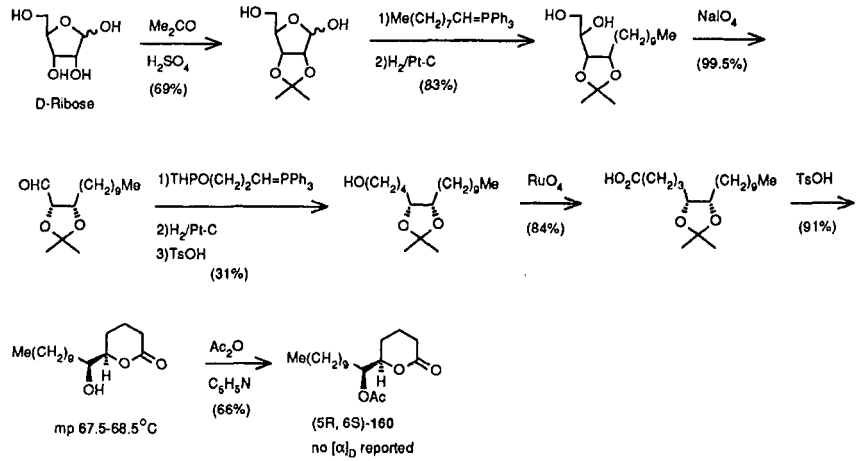
sized (5*R*,6*S*)-**160** in 12.7% overall yield from 2-deoxy-D-ribose (Scheme 535).[681] Kamikawa et al. used D-ribose as their starting material, and prepared (5*R*,6*S*)-**160** in 9.1% overall yield in 10 steps (Scheme 536).[682]



Scheme 535

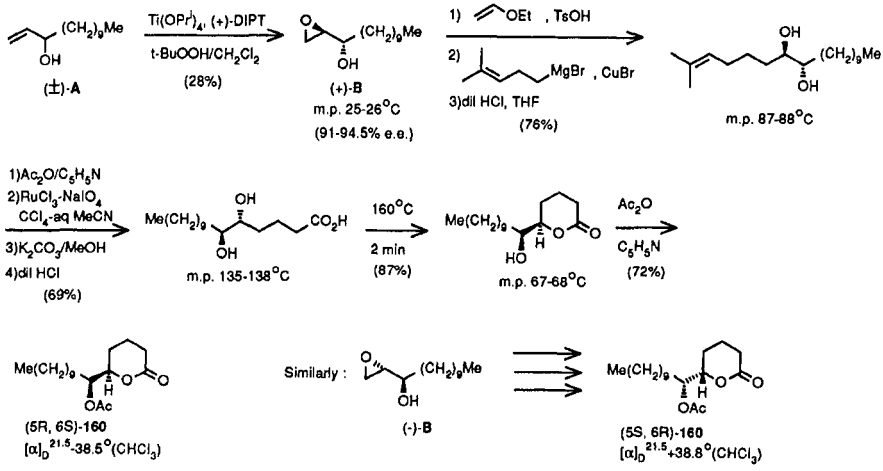
(4) Syntheses Based on Chemical Asymmetric Reactions

The Sharpless asymmetric epoxidation was applied in four syntheses of (5*R*,6*S*)-**160.** Mori and Otsuka synthesized both (5*R*,6*S*)-**160** and (5*S*,6*R*)-**160** by asymmetric epoxidation of (±)-**A** to give either (+)-**B** or (−)-**B** (Scheme

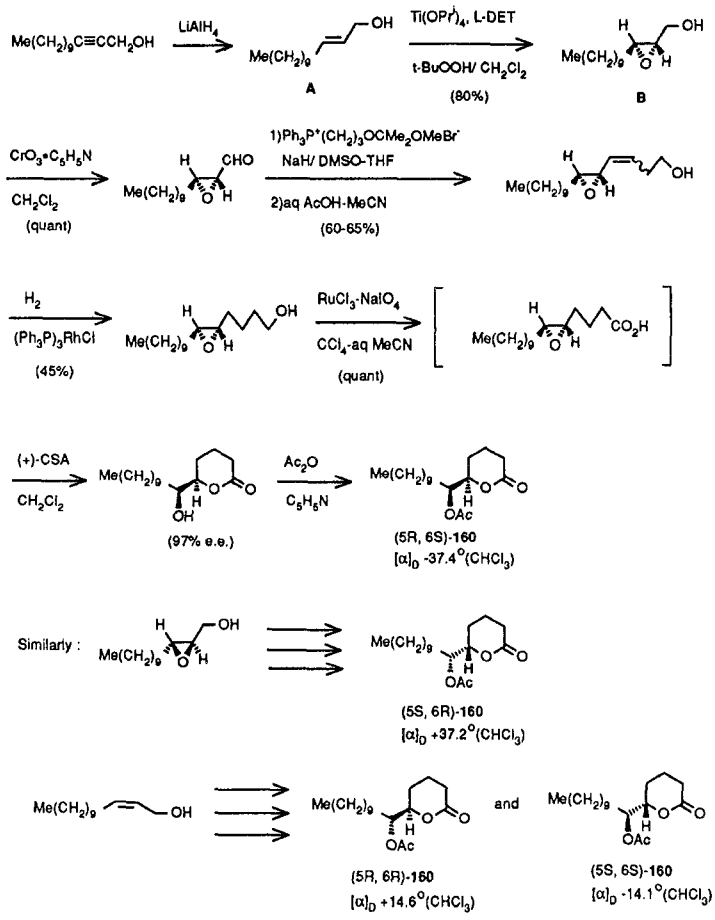


Scheme 536

537).[683] Lin et al. prepared all of the four stereoisomers of **160** by asymmetric epoxidation (Scheme 538).[684] A very short synthesis of the enantiomers of **160** was reported by Barua and Schmidt (Scheme 539).[685] Optically active epoxide **B** as prepared from (±)-**A** by the Sharpless procedure was acetylated to give **C**, which was treated with β-lithiated β-ethylthioacrylate to give lactone **D.** This was reduced with Raney nickel to furnish **160.**[685] In Kametani's synthesis of (5*R*,6*S*)-**160,** the beginning step was the kinetic resolution of 1-(2-furyl)-1-



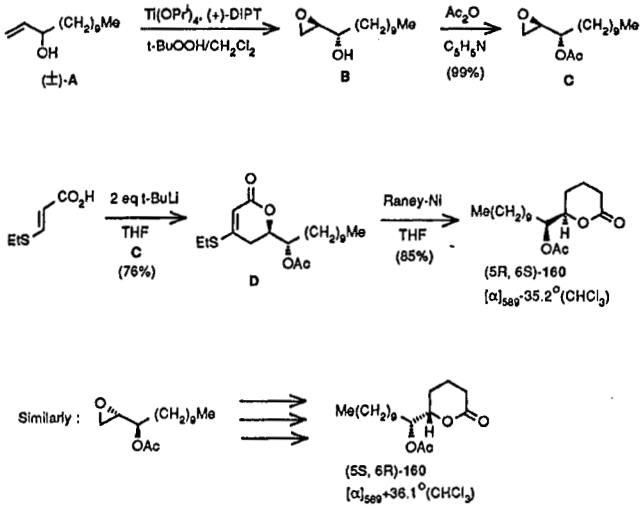
Scheme 537



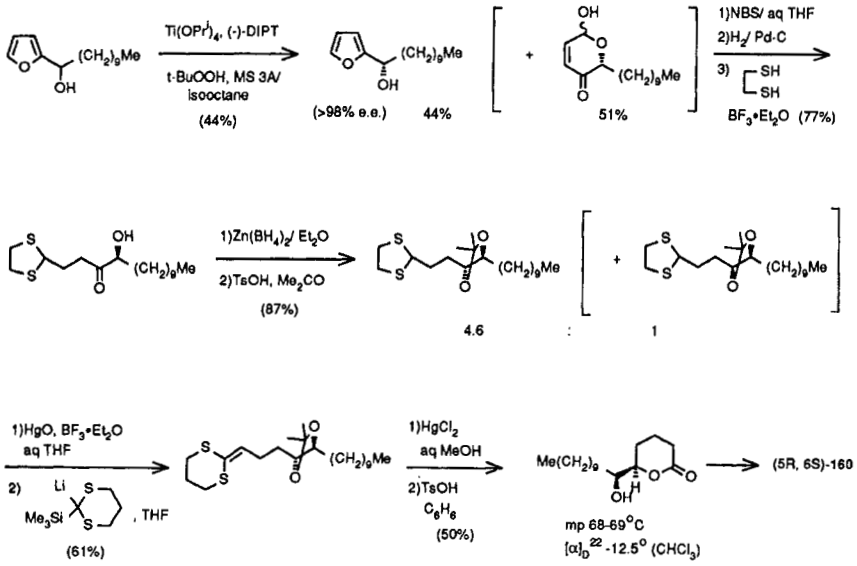
Scheme 538

undecanol by the Sharpless protocol (Scheme 540).[686, 1228] They, however, did not prepare the pheromone itself, but interrupted their synthesis at the stage of the hydroxy lactone. Wang et al. prepared (5*R*,6*S*)-**160** and (5*S*,6*S*)-**160** starting from cyclohexane-1,2-diol (Scheme 541).[687] The key-step was the kinetic resolution of (±)-**B** to give (*S*)-**B.**

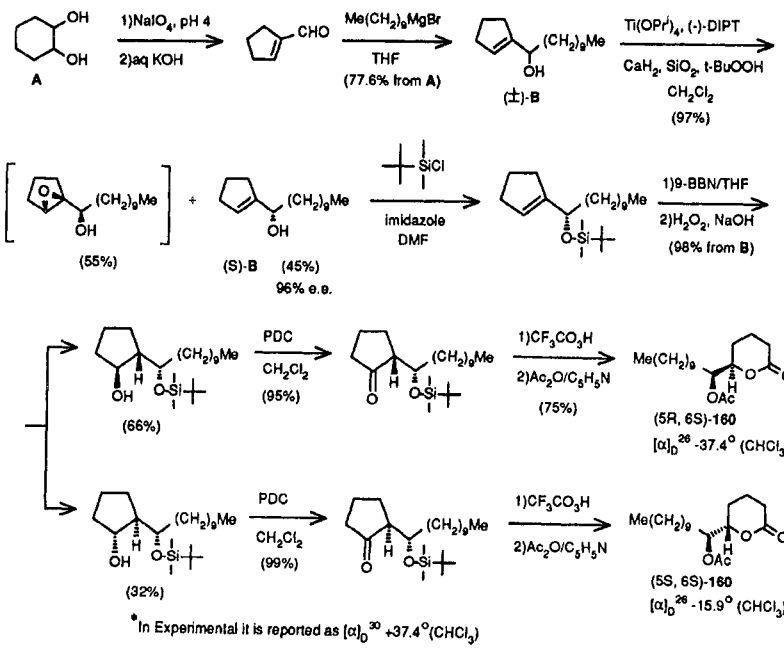
Other asymmetric chemical reactions were employed in the following three works. Asymmetric reduction of 2-cyclohexen-1-one with the chiral reducing agent (Scheme 542) to give (*S*)-2-cyclohexen-1-ol was the starting step in Fujisawa's synthesis of both (5*R*,6*S*)-**160** and (5*S*,6*R*)-**160.**[688] In the synthesis by Ko and Eliel, reduction of oxathiane **A** yielded **B,** which was converted to



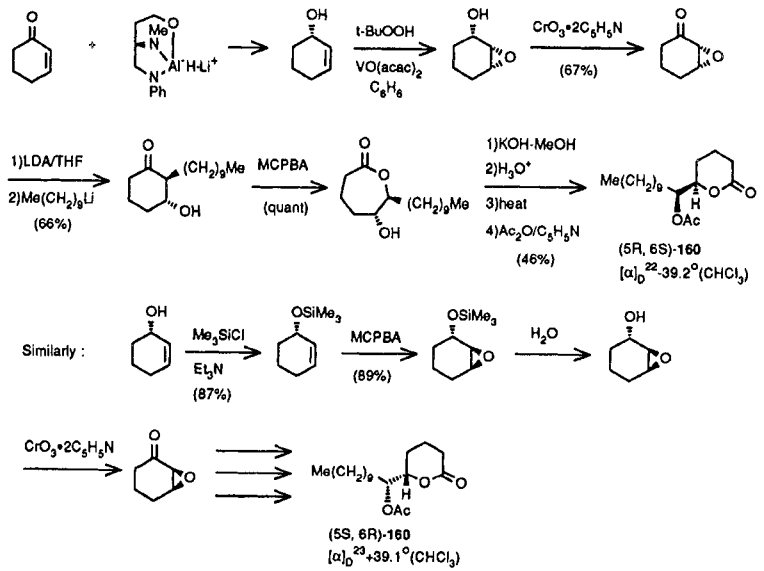
Scheme 539



Scheme 540

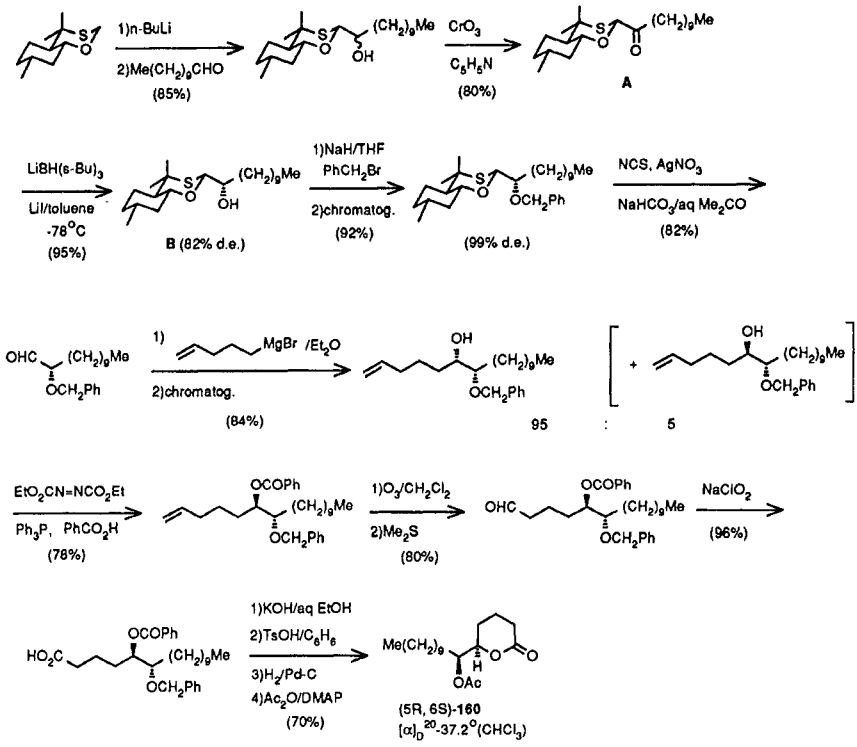


Scheme 541



Scheme 542

(5*R*,6*S*)-**160** through a lengthy route that included inversion of configuration at C-5 (Scheme 543).[689] Zhou et al. prepared (5*R*,6*S*)-**160** and (5*S*,6*R*)-**160** by



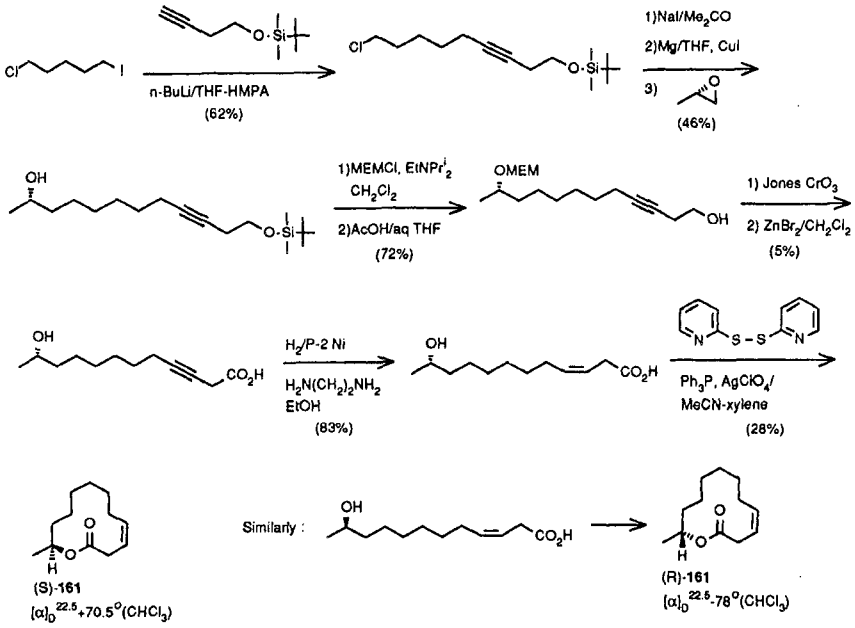
Similarly (5R, 6R)-160, $[\alpha]_D^{20}$+14.4°($CHCl_3$), and (5S, 6R)-160, $[\alpha]_D^{20}$+37.2°($CHCl_3$), were prepared.

Scheme 543

employing asymmetric addition of a chiral sulfoxide (*p*-TolSOCH$_2$CO$_2$Bu^t) to (*R*)-(+)-2-benzyloxydodecanal.[690] The efficacy of (5*R*,6*S*)-**160** as the mosquito attractant was demonstrated in western Kenya, and the possibility of using this material in combination with a safe insecticide was confirmed.[691] The pheromone (5*R*,6*S*)-**160** was active against not only the southern house mosquito [*C. pipiens fatigans* (= *C. quinquefasciatus*)] but also *C. tarsalis*, while it was inactive against the yellowfever mosquito (*Aedes aegypti*) and the common malaria mosquito (*Anopheles quadrimaculatus*).[692] Substitution of the acetyl group of (5*R*,6*S*)-**160** by fluoroacetyl resulted in the preparation of a strong oviposition attractant against the southern house mosquito (*C. pipiens fatigans*).[693]

K. Ferrulactone II [(3*Z*,11*S*)-3-Dodecen-11-olide] **161** ($C_{12}H_{20}O_2$)

This is a component of the aggregation pheromone of the rusty grain beetles (*Cryptolestes ferrugineus*).[694] Oehlschlager et al. prepared (±)-**161**, (*R*)-**161**, and (*S*)-**161** employing propylene oxide as the chiral source (Scheme 544).[695]

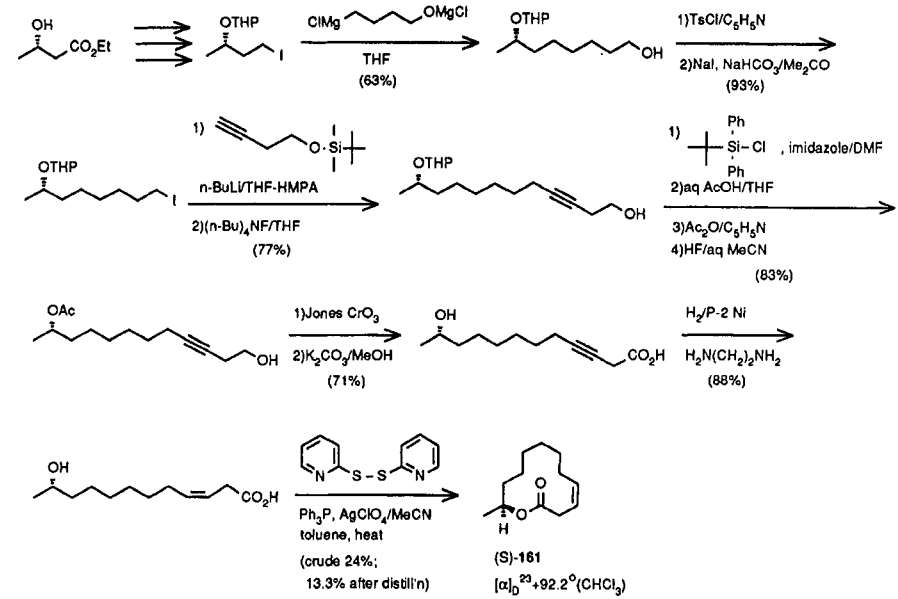


Scheme 544

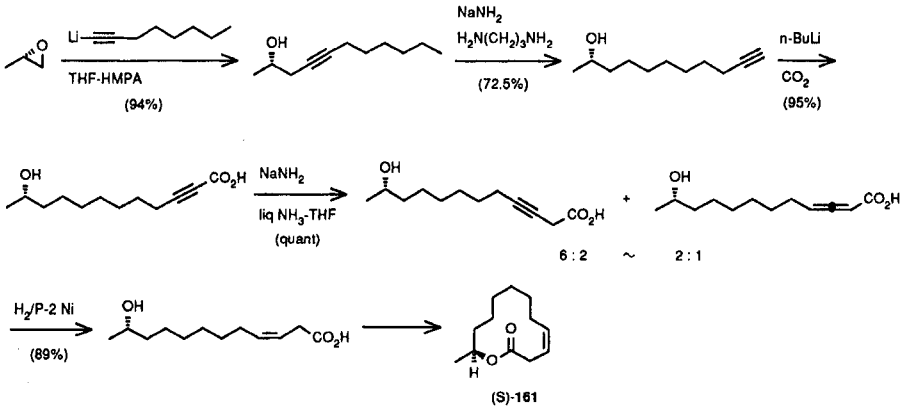
Mori et al. employed ethyl (*S*)-3-hydroxybutanoate as the chiral source and prepared (*S*)-**161** (Scheme 545).[696] Oehlschlager et al. subsequently reported an improved synthesis of the seco-acid (Scheme 546).[697] It was later found that enantiomerically pure (*S*)-**161** is produced by *C. ferrugineus*, while (*R*)-**161** is produced by the merchant grain beetle (*Oryzaephilus mercator*).[698]

L. (*Z*)-3-Dodecen-12-olide **162** ($C_{12}H_{20}O_2$)

The flat grain beetle (*Cryptolestes pusillus*) is a worldwide pest of stored products. Millar et al. isolated and identified three macrolides as its aggregation pheromone.[699] (*Z*)-3-Dodecen-12-olide (**162**) was the major volatile and was



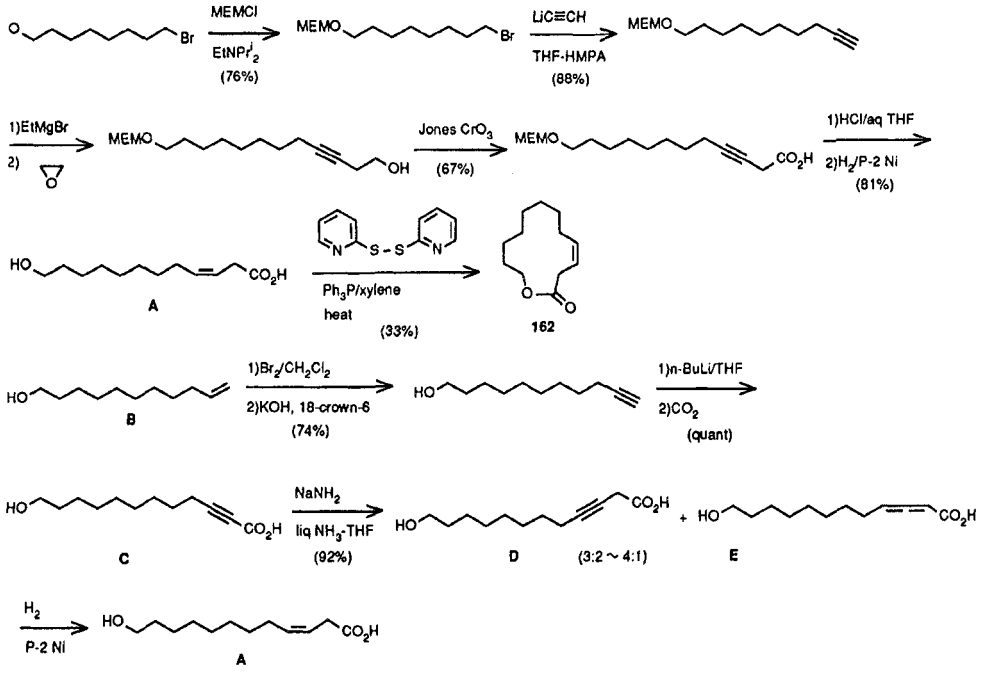
Scheme 545



Scheme 546

active alone. (5*Z*,13*S*)-5-Tetradecen-13-olide **(165)** was not active alone, but synergized the response to **162.** (3*Z*,6*Z*)-3,6-Dodecadien-12-olide **(163)** was active alone at higher concentrations, but did not significantly increase the response when added to the most active mixture of **162** and **165.** Millar et al. synthesized **162** by means of acetylenic chemistry followed by the Corey ma-

crolactonization (Scheme 547).[700] The seco-acid **A** was later prepared in a more

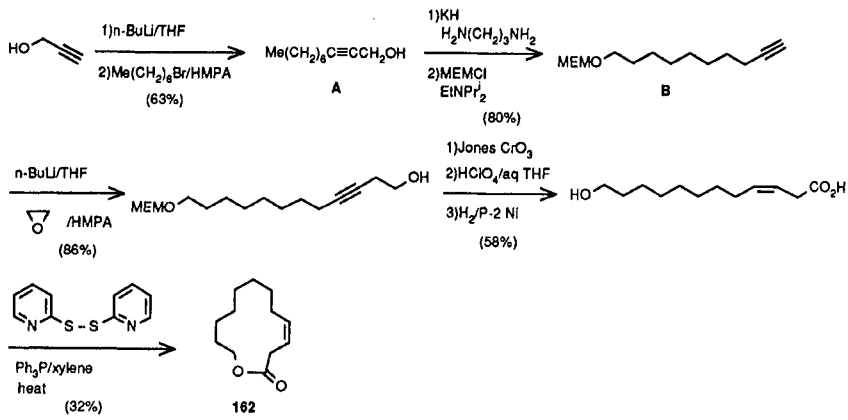


Scheme 547

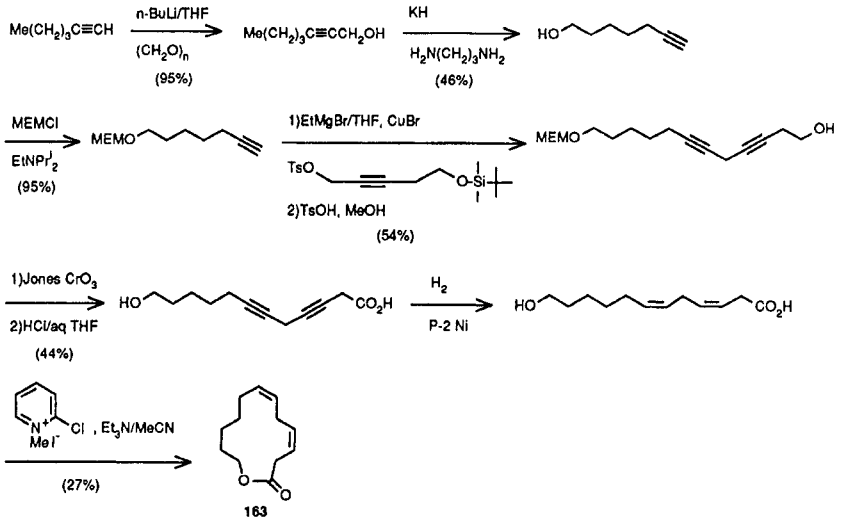
efficient manner starting from 10-undecen-1-ol **(B).**[697] The key-step was the deconjugation of α,β-alkynoic acid **C** to a mixture of β,γ-alkynoic acid **D** and allenic acid **E,** which was semi-hydrogenated to **A** (Scheme 547). Mori et al. employed the acetylene zipper reaction for the preparation of the 1-alkyne **B** from **A** (Scheme 548).[701]

M. (3Z,6Z)-3,6-Dodecadien-12-olide 163 ($C_{12}H_{18}O_2$)

The sawtoothed grain beetle (*Oryzaephillus surinamensis*) produces as its aggregation pheromone (3Z,6Z)-3,6-dodecadien-12-olide **(163),** (3Z,6Z,11*R*)-3,6-dodecadien-11-olide **(164),** and (5Z,8Z,13*R*)-5,8-tetradecadien-13-olide **(166).**[698,702] Millar and Oehlschlager prepared **163** by the standard acetylene chemistry followed by the Mukaiyama cyclization (Scheme 549).[703] They later reported an alternative and more efficient synthesis (Scheme 550).[697]



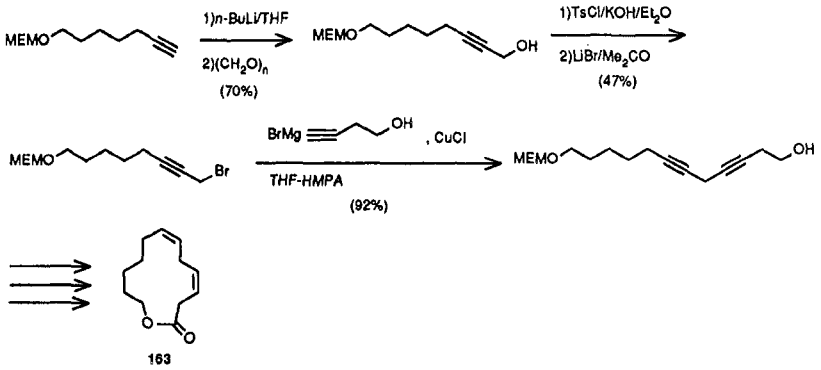
Scheme 548



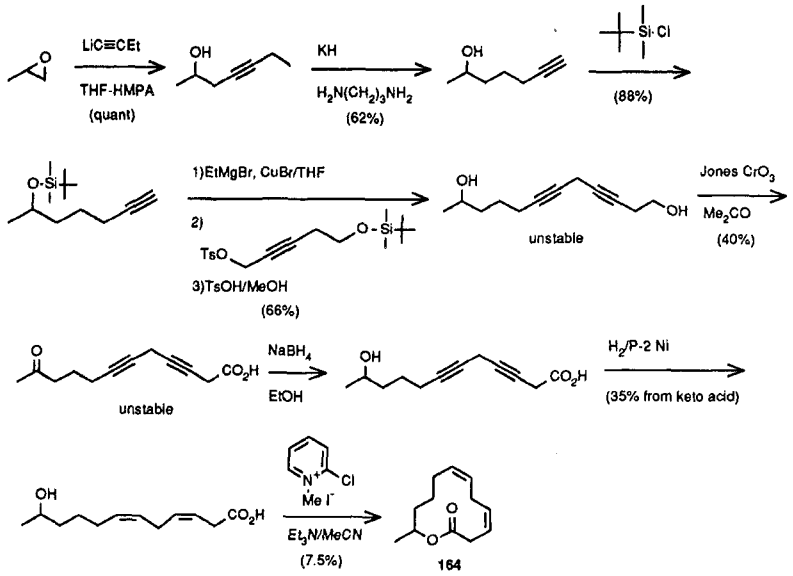
Scheme 549

N. (3*Z*,6*Z*,11*R*)-3,6-Dodecadien-11-olide 164 ($C_{12}H_{18}O_2$)

This is the aggregation pheromone of *Oryzaephillus surinamensis* and *O. mercator*.[702,704] Millar and Oehlschlager synthesized (±)-**164** as shown in Scheme 551.[703] By slightly modifying the procedure, they also synthesized (*S*)-**164**, which was inactive as the pheromone.[704] The natural pheromone was pure (*R*)-**164**.[698,704] Oehlschlager et al. reported an alternative synthesis of **164**



Scheme 550

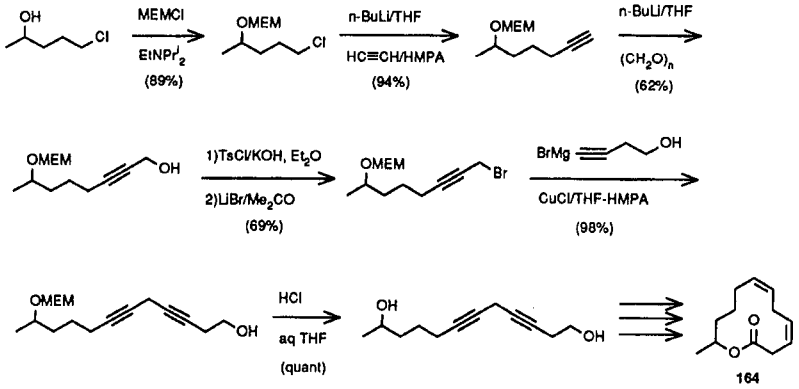


Scheme 551

(Scheme 552).[697] Due to the unstable nature of the diyne intermediates, neither of the two routes was efficient enough.

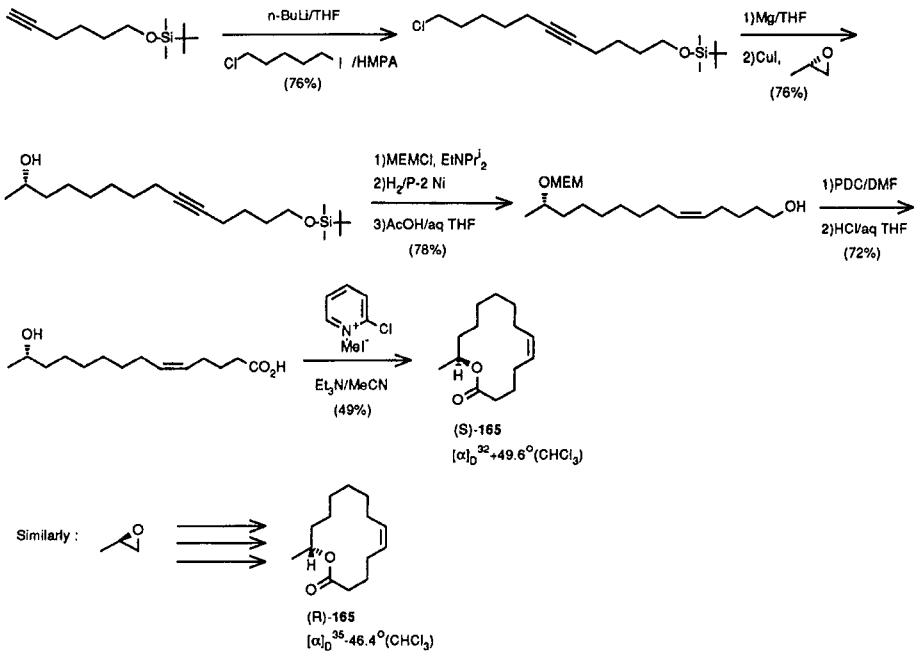
O. (5*Z*,13*S*)-5-Tetradecen-13-olide 165 ($C_{14}H_{22}O_2$)

In Millar's synthesis of both (*R*)-**165** and (*S*)-**165,** the enantiomers of propylene oxide were employed as the chiral building blocks, and the final lactonization



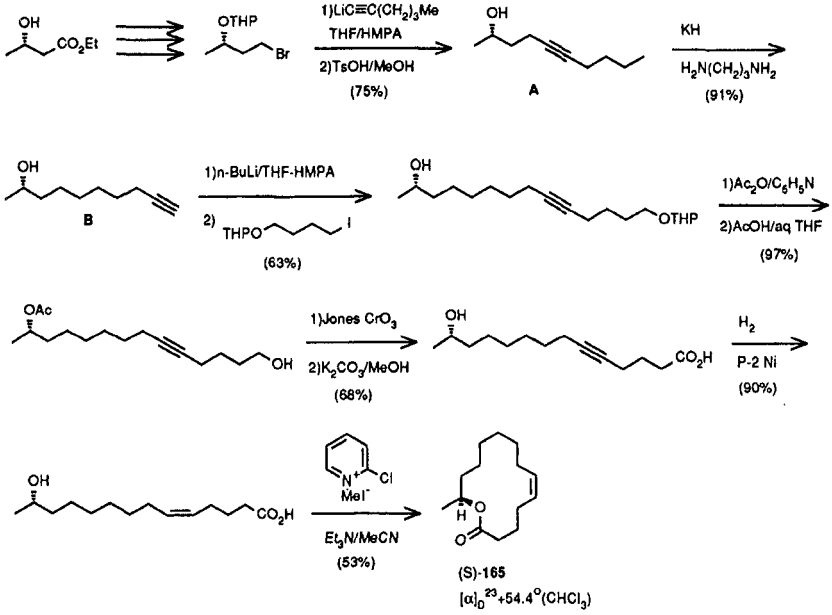
Scheme 552

was carried out by the Mukaiyama procedure (Scheme 553).[700] Only (*S*)-**165** was found to be produced by the flat grain beetle (*C. pusillus*), while the grain beetle (*C. turcicus*) produces a 33 : 67 mixture of the *R*- and *S*-isomers.[698] In



Scheme 553

C. turcicus, **165** functions as a synergist of (5*Z*,8*Z*,13*R*)-5,8-tetradecadien-13-olide (**166**).[705] Mori et al. employed ethyl (*S*)-3-hydroxybutanoate as the starting material for the synthesis of (*S*)-**165**.[701] In their synthesis, acetylene-zipper reaction (**A** → **B**, Scheme 554) was the key-reaction.[701] Naoshima et al. syn-

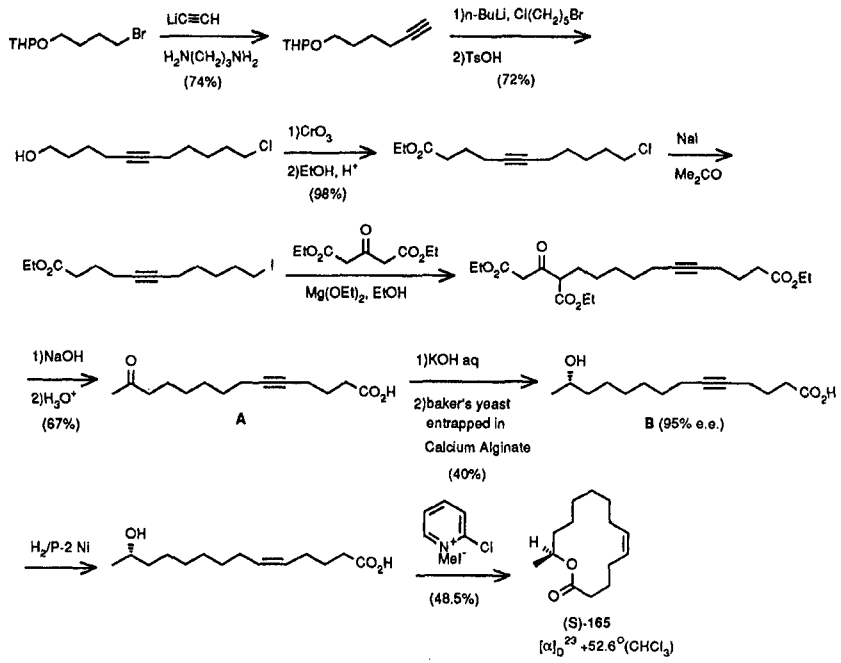


Scheme 554

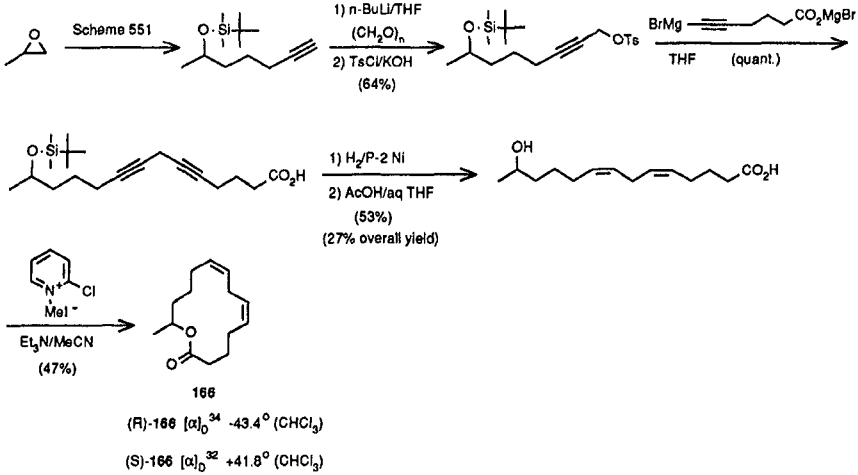
thesized (*S*)-**165** by reducing keto acid **A** to hydroxy acid **B** with immobilized baker's yeast (Scheme 555).[706] A full paper of this work has been published.[1089]

P. (5*Z*,8*Z*,13*R*)-5,8-Tetradecadien-13-olide 166 ($C_{14}H_{20}O_2$)

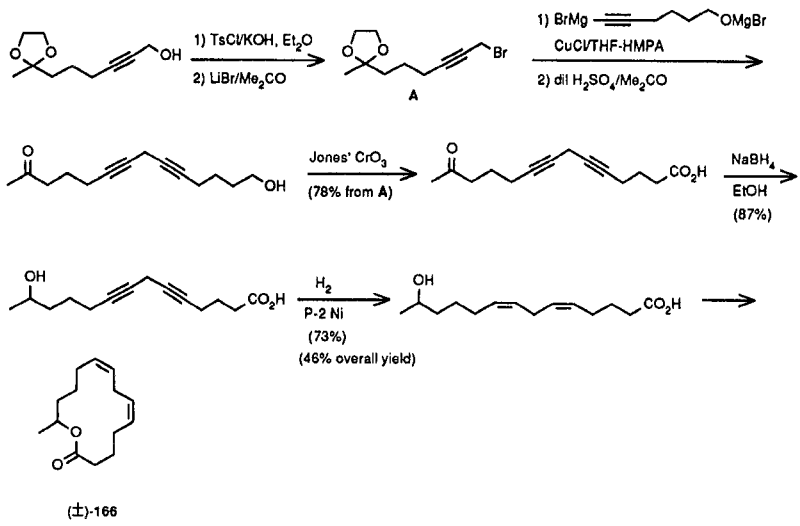
This is the aggregation pheromone of the grain beetle (*Cryptolestes turcicus*).[707] The natural **166** is a mixture of *R*- and *S*-isomers in a ratio of 85 : 15.[698] It was active alone and synergized by **165**, which is inactive by itself.[707] *Oryzaephillus surinamensis* also employs (*R*)-**166** as the synergist.[702,704] Millar and Oehlschlager synthesized (±)-**166**, (*R*)-**166**, and (*S*)-**166** (Scheme 556).[703] An improved synthesis of (±)-**166** was later recorded by Oehlschlager et al. (Scheme 557).[697] Pure (*R*)-**166** and (*S*)-**166** were inactive against *C. turcicus*, but mixtures of (*R*)-**166** and (*S*)-**166** were active.[707]



Scheme 555



Scheme 556



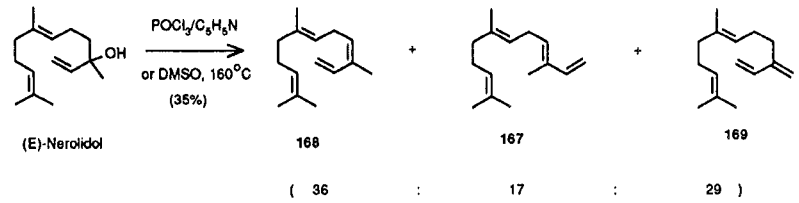
Scheme 557

Chirality of these macrolide pheromones of Cucujidae grain beetles and its implications for species specificity were discussed by Oehlschlager et al.[698,704,708]

16. ISOPRENOID HYDROCARBONS AS PHEROMONES

A. (*E*,*E*)-α-Farnesene 167 and (*Z*,*E*)-α-Farnesene 168 [(3*E*,6*E*)- and (3*Z*,6*E*)-3,7,11-Trimethyl-1,3,6,10-dodecatetraene] ($C_{15}H_{24}$)

These are the terpenoid trail pheromone components isolated from whole worker extracts of the red imported fire ant (*Solenopsis invicta*).[709] Vander Meer et al. synthesized the farnesenes by dehydrating (*E*)-nerolidol (Scheme 558).[709] The

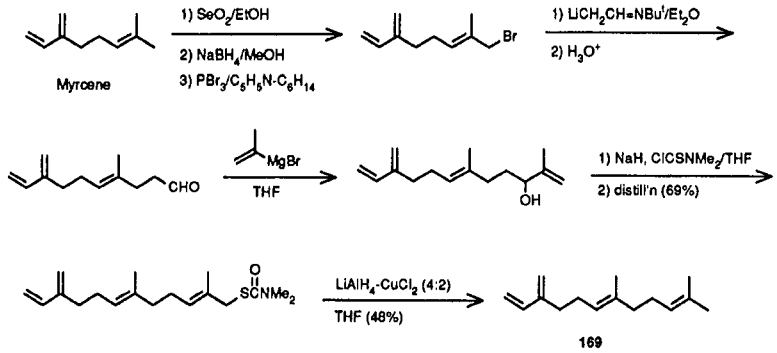


Scheme 558

isomers were separated by Florisil chromatography. (*E,E*)-α-Farnesene **(167)** was highly active at the dose of ca. 10^{-12} g/cm against the ants. Significant trail-following activity was shown by (*Z,E*)-α-farnesene **(168)** at 10^{-13} g/cm.[709]

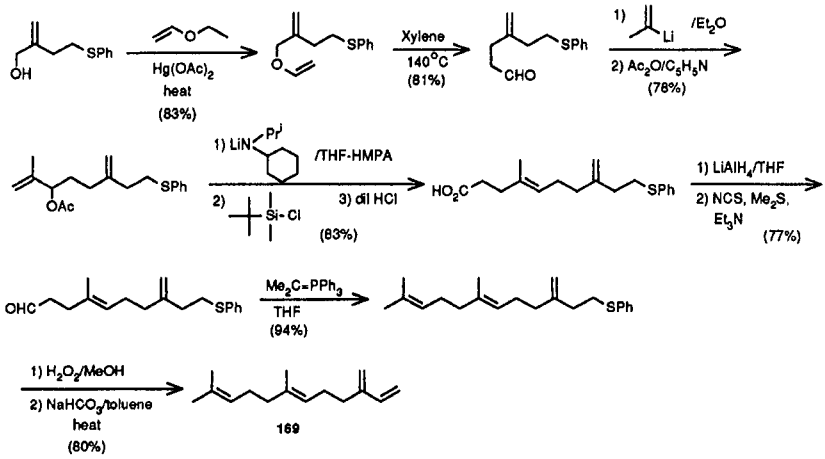
B. (*E*)-β-Farnesene [(*E*)-7,11-Dimethyl-3-methylene-1,6,10-dodecatriene] 169 ($C_{15}H_{24}$)

This is the alarm pheromone of the cotton aphid (*Aphis gossypii*).[710] Nakai and his co-workers prepared **169** from myrcene employing an allylic carbamate as an intermediate (Scheme 559).[481] Starting from 2-(hydroxymethyl)-4-(phenyl-



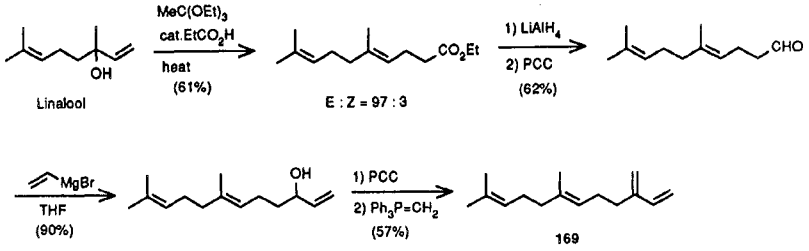
Scheme 559

thio)-1-butene, Mandai et al. synthesized **169** (Scheme 560).[711] Kang's synthe-



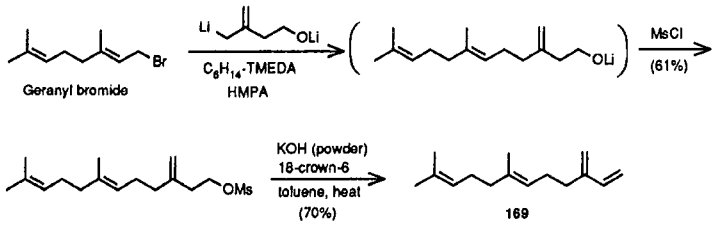
Scheme 560

sis of **169** started from linalool (Scheme 561).[712] Szántay's synthesis of **169**



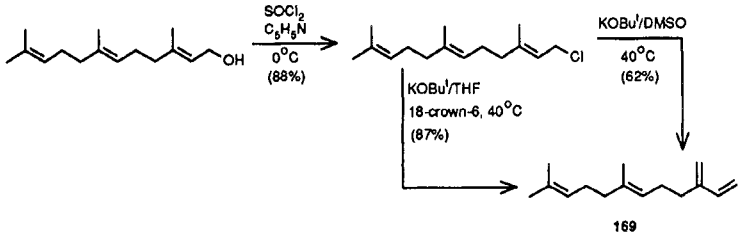
Scheme 561

(Scheme 562) was simple and efficient, starting from geranyl bromide.[713] Far-



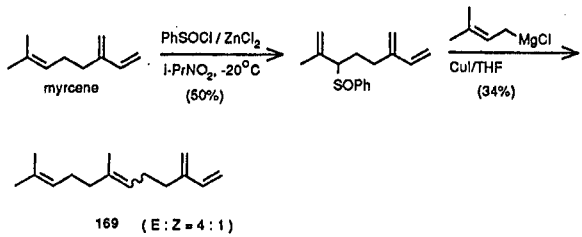
Scheme 562

nesol was converted to **169** in two steps by Kang et al (Scheme 563).[714] Mo-

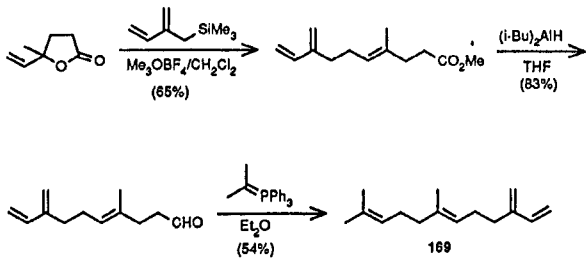


Scheme 563

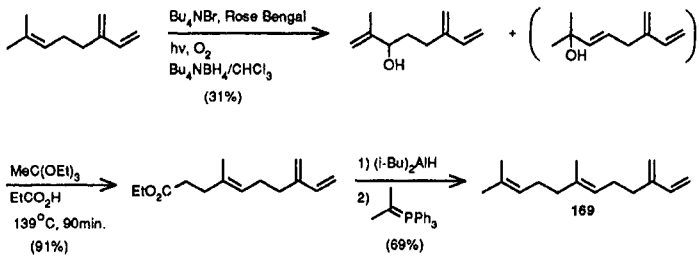
iseenkov and his co-workers achieved a two-step synthesis of 80% pure **169** from myrcene (Scheme 564).[715] Kawashima and Fujisawa's synthesis of **169** used an unsaturated lactone as the starting material (Scheme 565).[716] Baeckström et al. converted myrcene into **169** in 19.5% overall yield (Scheme 566).[717]



Scheme 564



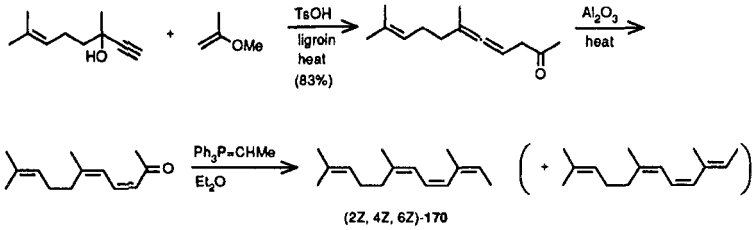
Scheme 565



Scheme 566

C. (Z,Z,Z)-Allofarnesene [(2Z,4Z,6Z)-3,7,11-Trimethyl-2,4,6,10-dodecatetraene] 170 ($C_{15}H_{24}$)

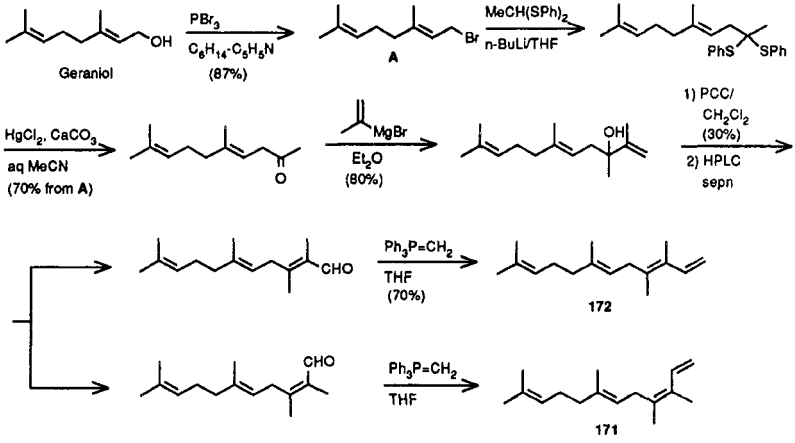
This is a component of the trail pheromone of the red imported fire ant (*Solenopsis invicta*).[718] Williams et al. prepared **170** as shown in Scheme 567.[718]



Scheme 567

D. (*Z*,*E*)-Homofarnesene and (*E*,*E*)-Homofarnesene [(3*Z*,6*E*)- and (3*E*,6*E*)-3,4,7,11-Tetramethyl-1,3,6,10-dodecatetraene] 171 and 172 ($C_{15}H_{26}$)

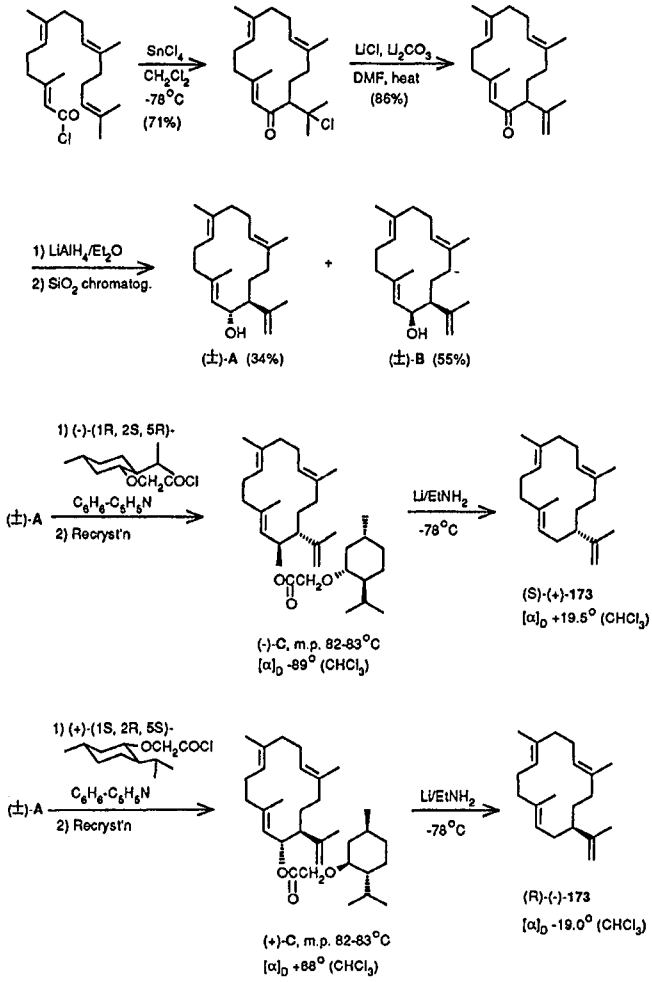
These are the trail pheromone components of the red imported fire ant (*Solenopsis invicta*).[719] Alvarez et al. synthesized a mixture of **171** and **172** (Scheme 568).[719] Synthetic **171** and **172** had trail pheromone activity comparable to that of the natural pheromones (ca. 40 pg/cm).[719]



Scheme 568

E. (*E*,*E*,*E*)-Neocembrene 173 ($C_{20}H_{32}$)

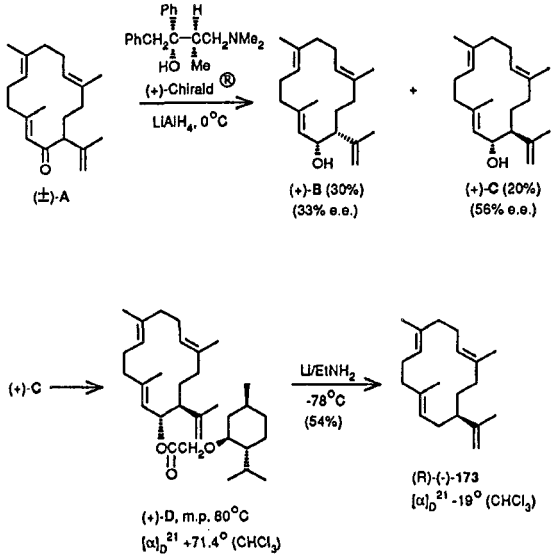
This macrocyclic diterpene hydrocarbon is a termite trail pheromone of *Nasutitermes exitosus*, *N. walkeri*, and *N. graveolus*.[720] It is also produced in the


SnCl4
CH2Cl2
-78°C
(71%)
LiCl, Li2CO3
DMF, heat
(86%)
1) LiAlH4/Et2O
2) SiO2 chromatog.
(±)-A (34%)
(±)-B (55%)
1) (-)-(1R, 2S, 5R)-
OCH2COCl
C6H6-C5H5N
2) Recryst'n
(±)-A
(-)-C, m.p. 82-83°C
[α]D -89° (CHCl3)
Li/EtNH2
-78°C
(S)-(+)-173
[α]D +19.5° (CHCl3)
1) (+)-(1S, 2R, 5S)-
OCH2COCl
C6H6-C5H5N
2) Recryst'n
(±)-A
(+)-C, m.p. 82-83°C
[α]D +88° (CHCl3)
Li/EtNH2
-78°C
(R)-(-)-173
[α]D -19.0° (CHCl3)

Scheme 569

Dufour's gland of fertile Queens of the Pharaoh's ant (*Monomorium pharaonis*), and it may serve as a Queen recognition pheromone.[721]

Kato et al. synthesized both the enantiomers of **173** by optical resolution of an intermediate (Scheme 569).[722] They employed menthoxyacetyl chloride as the resolving agent for (±)-**A.** (Incidentally, the absolute configuration given for menthoxyacetic acid in Ref. 722 is in error.) The resolved (+)-**173** and (−)-**173** showed pheromone activity of a high order, and they could not be differentiated from each other or from the racemic mixture in the bioassay. The activity recorded was of the same order as that of the natural pheromone. (*R*)-(−)-(*E,E,E*)-neocembrene **(173)** was also synthesized by the asymmetric reduction of the ketone (±)-**A** with (+)-Chirald®-lithium aluminum hydride complex to give (+)-**B** and (+)-**C,** the latter of which was further purified via **D** and deoxygenated, giving (*R*)-(−)-**173** (Scheme 570).[723]



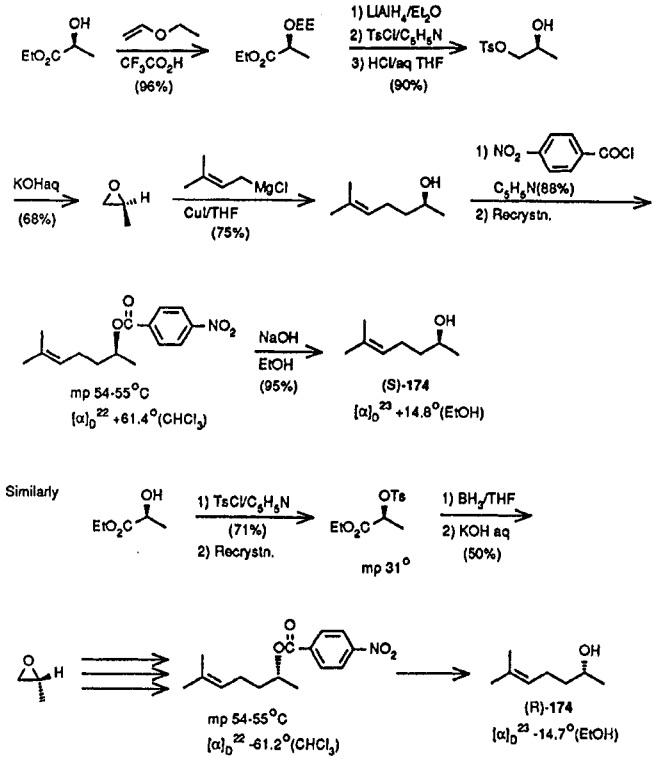
Scheme 570

17. ISOPRENOID ALCOHOLS, FORMATE, ACETATES, PROPANOATES, AND EPOXIDE AS PHEROMONES

A. Sulcatol (6-Methyl-5-hepten-2-ol) 174 ($C_8H_{16}O$)

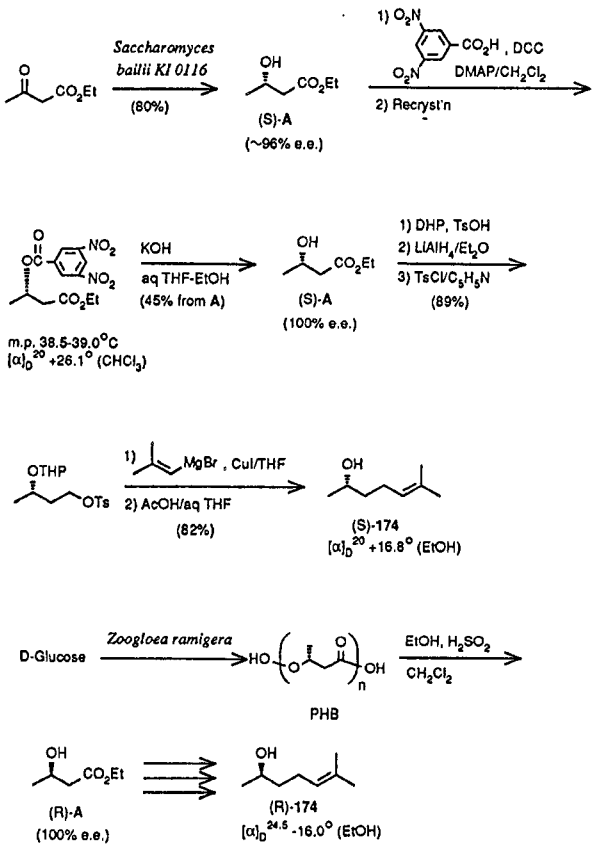
This is the aggregation pheromone produced by the males of an ambrosia beetle (*Gnathotrichus sulcatus*) as a 65 : 35 mixture of (*S*)- and (*R*)-isomers.[724] In laboratory and field bioassays, *G. sulcatus* responded to sulcatol only when both enantiomers were present.[725]

Johnston and Slessor reported a synthesis of the enantiomers of **174,** starting from the enantiomers of propylene oxide (Scheme 571).[726] They purified **174** as its crystalline *p*-nitrobenzoate.



Scheme 571

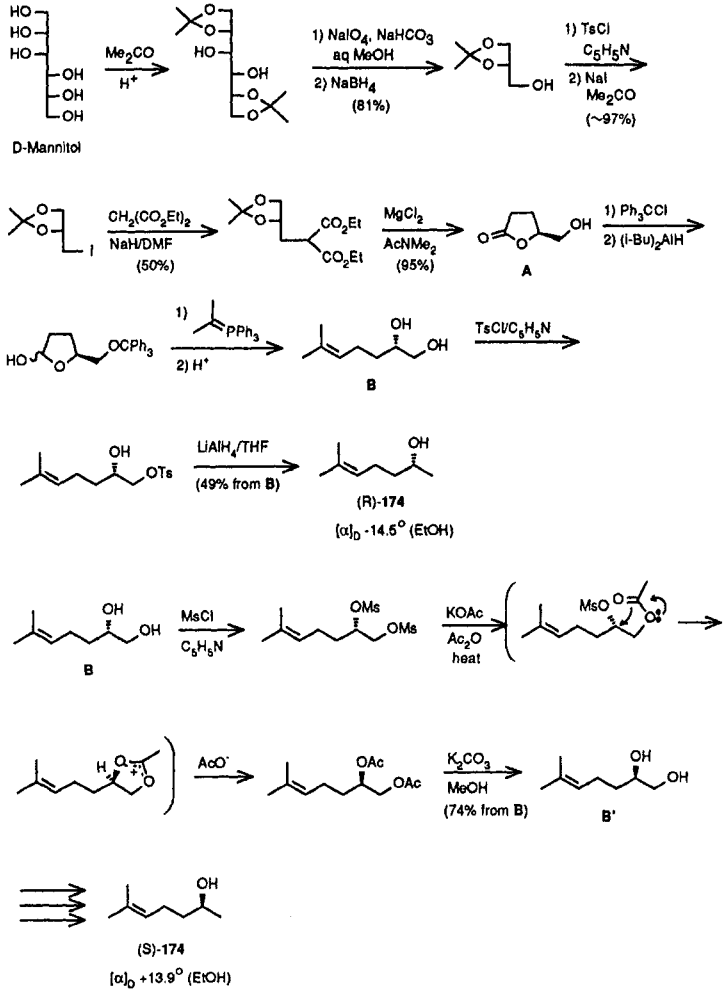
Mori et al. employed biochemical methods for the preparation of (*R*)-**174** and (*S*)-**174** (Scheme 572).[727,728] In the first approach, (*S*)-**A** was produced by



Scheme 572

the reduction of ethyl acetoacetate with baker's yeast, the enantiomeric purity of which was 87% e.e.[727] They then devised methods to provide the pure enantiomers of **A** by employing *Saccharomyces bailii* (yeast) and *Zoogloea ramigera* (bacteria).[325,729] Starting from the pure enantiomers of **A**, the pure enantiomers of sulcatol were synthesized.[728]

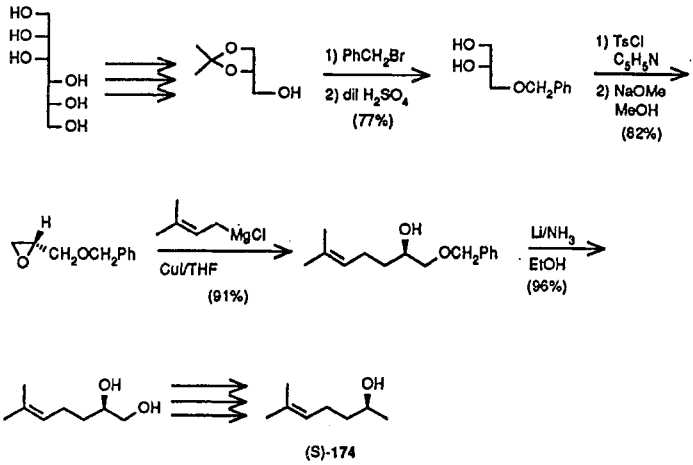
Takano et al. started from D-mannitol[730] and prepared the enantiomers of **174** via lactone **A** and the diol enantiomers **B** and **B′** (Scheme 573).[731] They



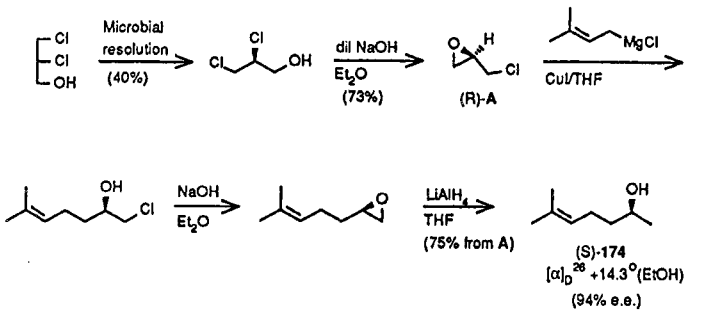
Scheme 573

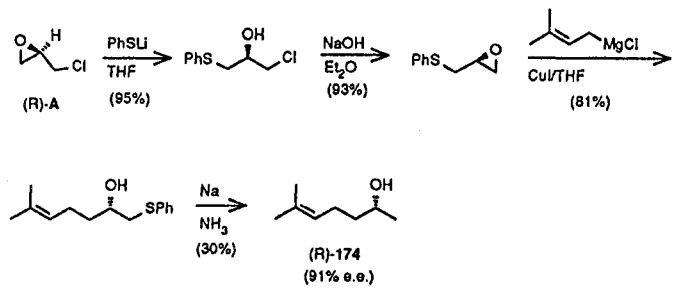
developed another conversion of D-mannitol to (*S*)-sulcatol **(174)** (Scheme 574).[732] In Takano's third synthesis of **174,** microbial resolution of (±)-2,3-dichloro-1-propanol was employed (Scheme 575).[733]

Biochemical methods were also employed for the synthesis of **174.** Veschambre and his co-workers reduced 6-methyl-5-hepten-2-one with various mi-

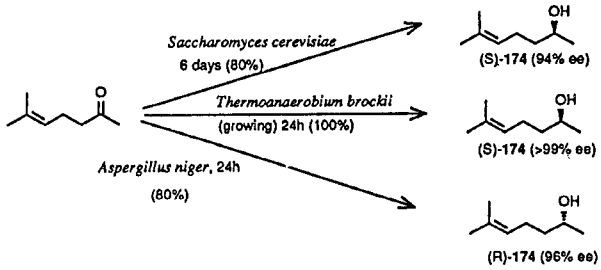


Scheme 574



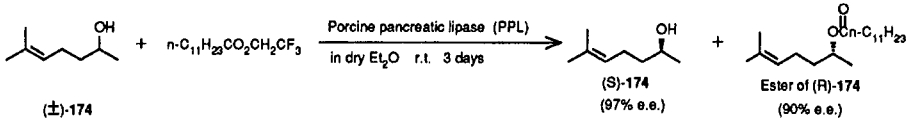


Scheme 575



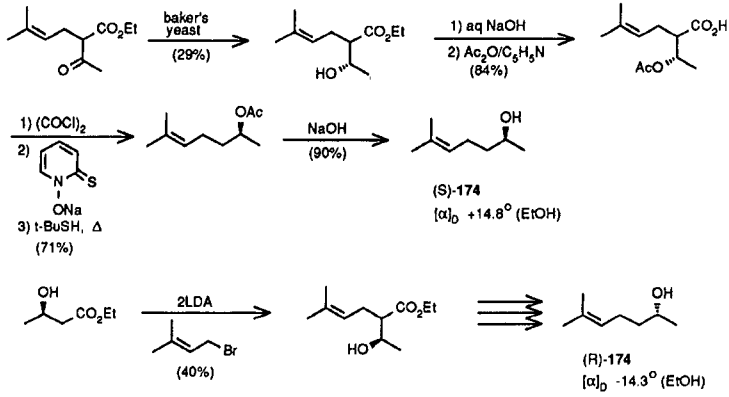
Scheme 576

croorganisms (Scheme 576).[734] *Saccharomyces cerevisiae* and *Thermoanaerobium brockii* reduced the ketone to (*S*)-**174,** while *Aspergillus niger* gave (*R*)-**174.**[734] Stokes and Oehlschlager resolved (±)-sulcatol **(174)** with porcine pancreatic lipase and 2,2,2-trifluoroethyl laurate in ether (Scheme 577).[735] Wong



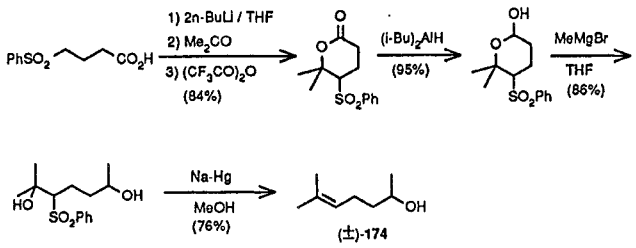
Scheme 577

et al. also resolved (±)-**174** with porcine pancreatic lipase and vinyl acetate.[736] Maycock and his co-workers achieved a synthesis of (*R*)-**174** and (*S*)-**174** by using biochemical asymmetric reduction and the Barton decarboxylation reaction (Scheme 578).[737]



Scheme 578

(±)-Sulcatol (**174**) was prepared from 4-phenylsulfonylbutanoic acid as shown in Scheme 579.[738]

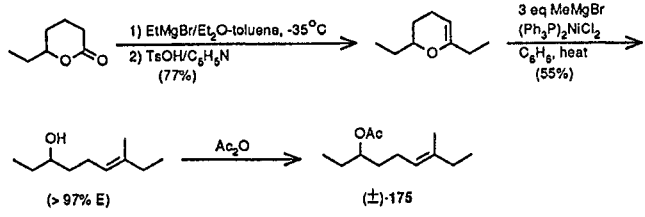


Scheme 579

B. Quadrilure [(3*R*,6*E*)-3-Acetoxy-7-methyl-6-nonene] 175 ($C_{12}H_{22}O_2$)

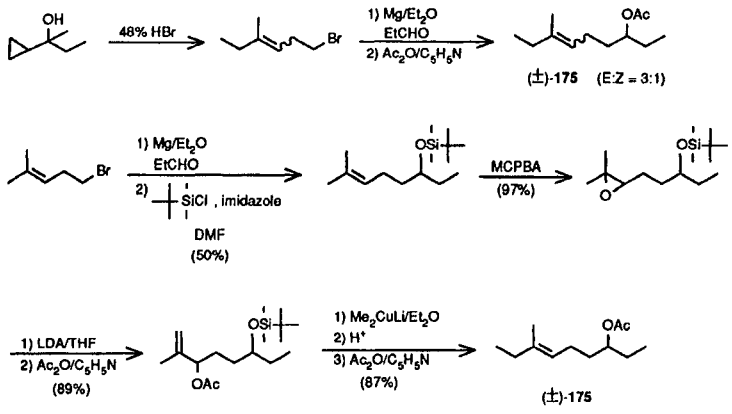
Male square-necked grain beetles (*Cathartus quadricollis*) produce the aggregation pheromone **175,** which is highly attractive to both sexes.[739] Only (*R*)-**175** was biologically active.[739]

Kocieński et al. announced a synthesis of (±)-**175** using the nickel-catalyzed coupling of methylmagnesium bromide with 2,6-diethyl-3,4-dihydro-2H-pyran (Scheme 580).[740] Johnston and Oehlschlager first prepared an (*E*,*Z*)-mixture of

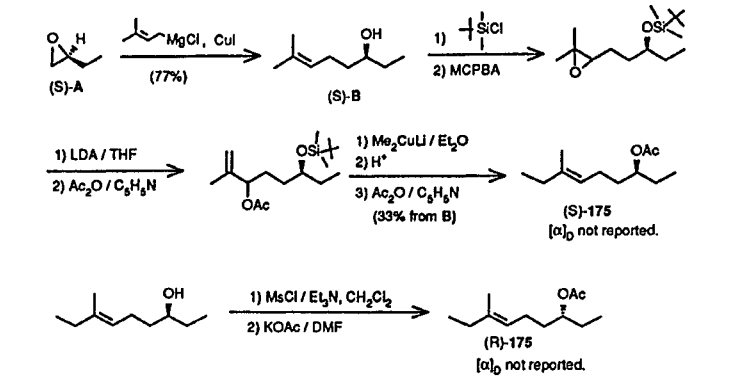


Scheme 580

(±)-**175,** and then compared it with the natural pheromone by GLC as well as ^{1}H NMR to confirm the *E*-geometry of the natural pheromone (Scheme 581).[741] They then prepared (±)-**175** by the standard chain-extension reaction, treating an allylic acetate with an organocopper reagent (Scheme 581).[741] Finally, both the enantiomers of **175** were synthesized by them from (*S*)-ethyloxirane (Scheme 582).[741] The natural pheromone was shown to be (*R*)-**175.** Mori and Puapoom-



Scheme 581

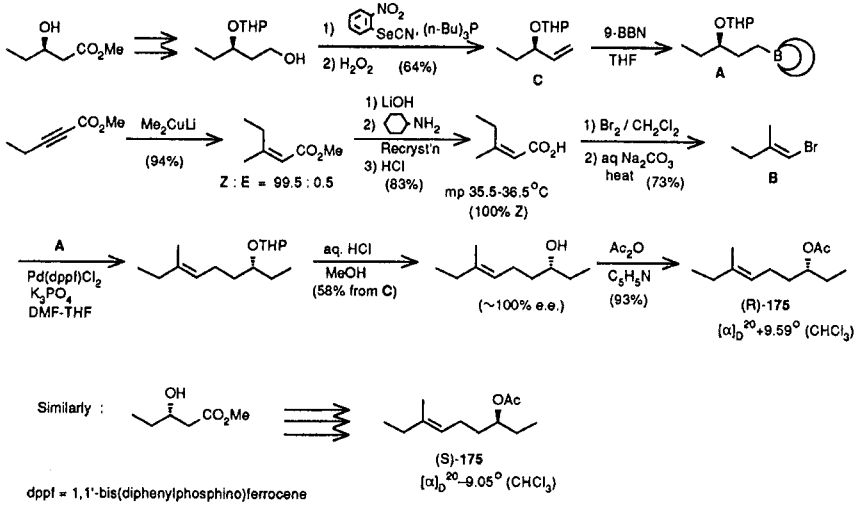


Scheme 582

chareon efficiently synthesized (*R*)-**175** and (*S*)-**175** starting from the enantiomers of methyl 3-hydroxypentanoate (Scheme 583).[742] The key reaction was the cross-coupling between *B*-alkyl-9-BBN **(A)** and (*E*)-1-bromo-2-methyl-1-butene **(B)** according to Suzuki,[743] and **175** was obtained in 34–35% overall yield in 8 steps.

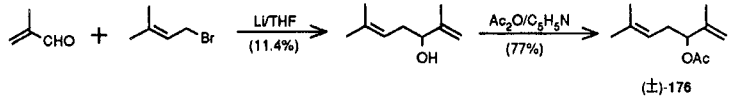
C. (*R*)-3-Acetoxy-2,6-dimethyl-1,5-heptadiene 176 ($C_{11}H_{18}O_2$)

This is the female-produced sex pheromone of the comstock mealybug (*Pseudococcus comstocki*) as isolated independently by Negishi et al.[744] and Bierl-



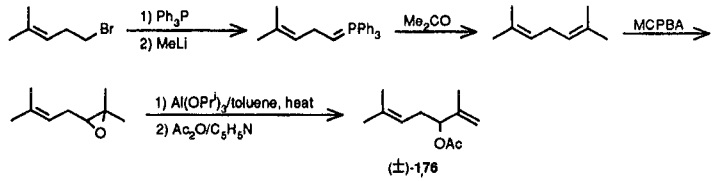
Scheme 583

Leonhardt et al.[745] To confirm the proposed structure, Uchida et al. prepared (±)-**176** as shown in Scheme 584.[746] Bierl-Leonhardt et al. also synthesized



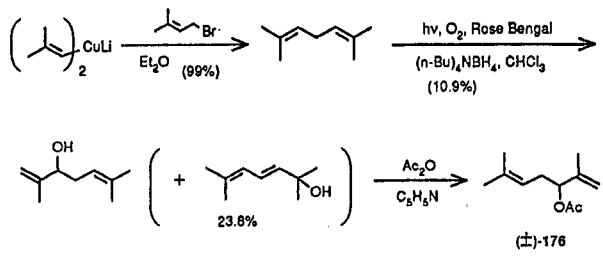
Scheme 584

(±)-**176** (Scheme 585).[745] Baeckström et al. prepared (±)-**176** via photooxi-

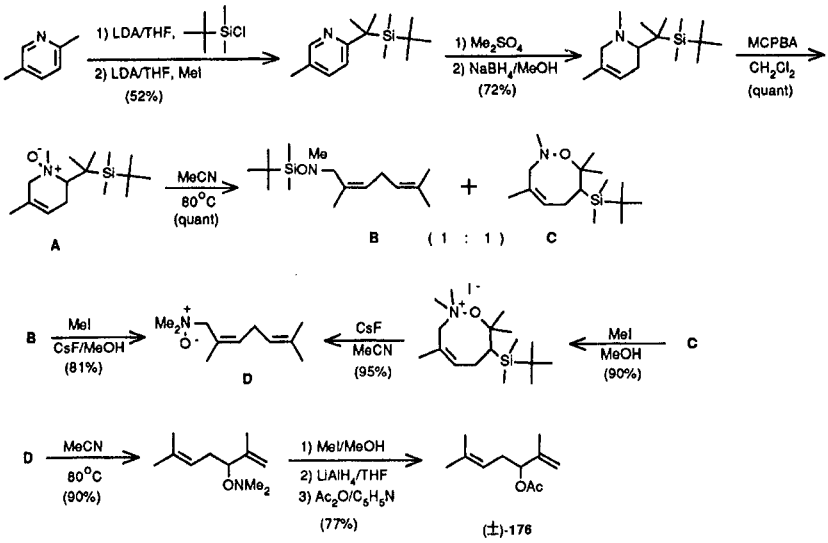


Scheme 585

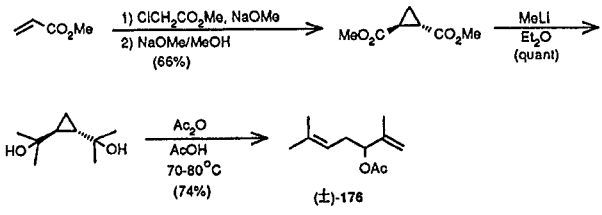
dation of 2,6-dimethyl-2,5-heptadiene, which was obtained by cross-coupling of lithium *bis*(2-methylpropenyl)cuprate with 3-methyl-1-bromo-2-butene (Scheme 586).[747] Langlois and his co-workers achieved a synthesis of (±)-**176** via a sila-Cope elimination (Scheme 587).[748] The overall yield was 20%. Skattebøl and Stenstrøm synthesized (±)-**176** in three steps from methyl chloroacetate and methyl acrylate (Scheme 588).[749] Scheme 589 illustrates the synthesis



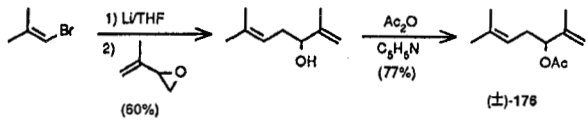
Scheme 586



Scheme 587

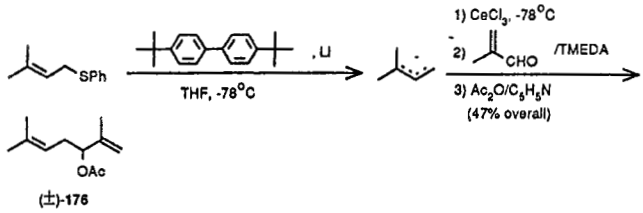


Scheme 588



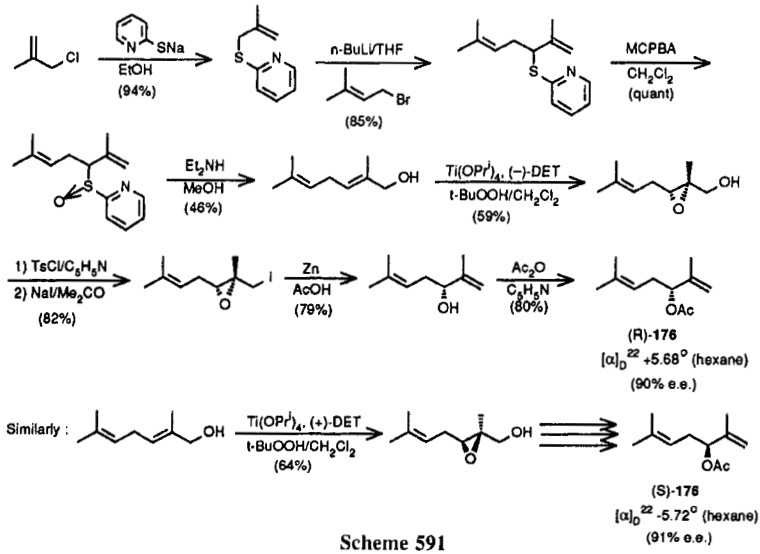
Scheme 589

of (±)-**176** by Ishchenko et al.[750] Cohen's synthesis of (±)-**176** (Scheme 590) proceeded in 47% overall yield.[751]



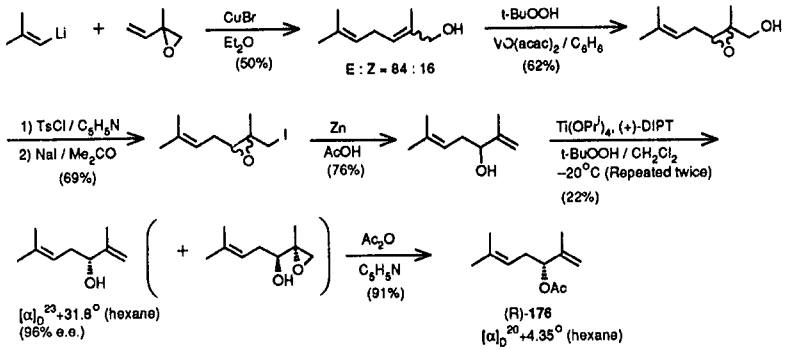
Scheme 590

The dextrorotatory [$[\alpha]_D$ + 6.2° (hexane)] natural pheromone[745] was shown to be with *R*-configuration by the synthesis of (*R*)-**176** and (*S*)-**176** by Mori and Ueda (Scheme 591).[752] The Sharpless asymmetric epoxidation was used for the



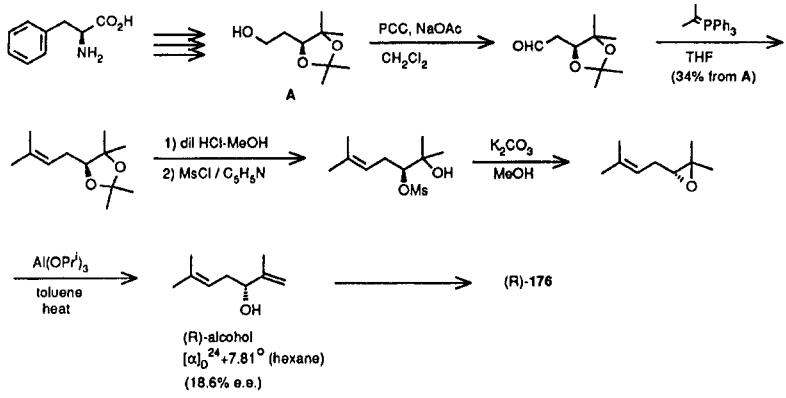
Scheme 591

introduction of asymmetry to prepare (*R*)-**176** and (*S*)-**176**[752] or (*R*)-**176** (Scheme 592).[753] The *R*-configuration of the natural pheromone was confirmed by its



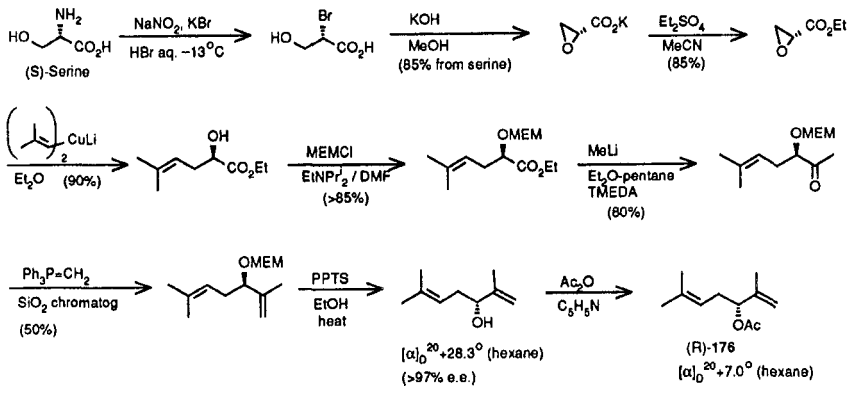
Scheme 592

derivation from (*S*)-phenylalanine (Scheme 593).[753] The key-intermediate **A** in



Scheme 593

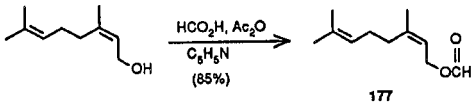
this conversion was prepared from (*S*)-phenylalanine in six steps according to the method of Terashima et al.[754] Partial racemization took place in the course of the conversion to yield (*R*)-**176** of rather low enantiomeric purity. Larchevêque and Petit achieved a synthesis of (*R*)-**176** starting from (*S*)-serine (Scheme 594).[755]



Scheme 594

D. Neryl Formate [(*Z*)-3,7-Dimethyl-2,6-octadienyl Formate] 177 ($C_{11}H_{18}O_2$)

This is the alarm pheromone of the mold mite (*Tyrophagus putrescentiae*) and was synthesized by treating nerol with acetic formic anhydride (Scheme 595).[756]

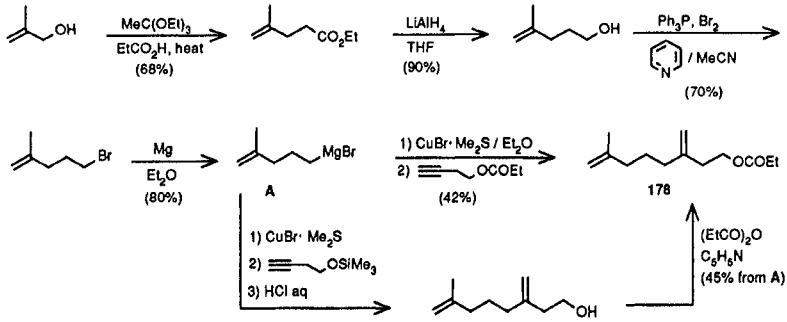


177

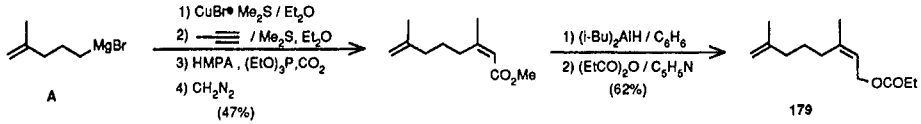
Scheme 595

E. 7-Methyl-3-methylene-7-octenyl Propanoate 178 ($C_{13}H_{22}O_2$), (*Z*)-3,7-Dimethyl-2,7-octadienyl Propanoate 179 ($C_{13}H_{22}O_2$), and (*E*)-3,7-Dimethyl-2,7-octadienyl Propanoate 180 ($C_{13}H_{22}O_2$)

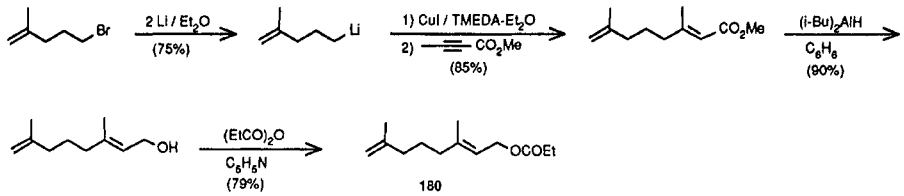
The San Jose scale (*Quadraspidiotus perniciosus*) is a major and widespread orchard pest. Its female-produced sex pheromone is a mixture of **178** (48.5%), **179** (46.7%), and **180** (4.8%).[757,758] Anderson et al. synthesized both **178** (Scheme 596) and **179** (Scheme 597) by the application of organocopper chemistry.[759] Each synthetic component (**178** or **179**) was independently attractive to male San Jose scale. Synthesis of **180** was also achieved by Anderson et al. again by means of organocopper chemistry (Scheme 598).[758] This component



Scheme 596

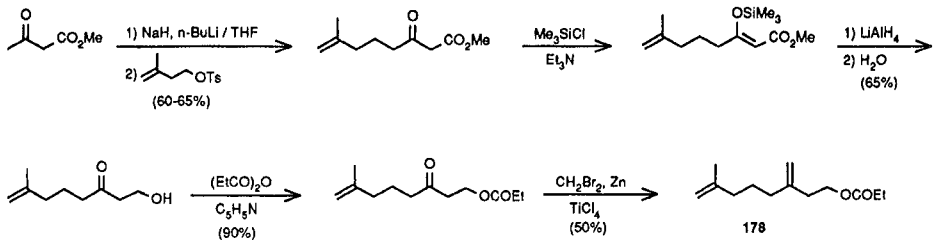


Scheme 597

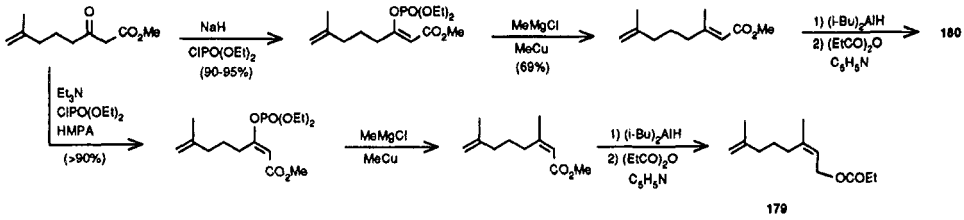


Scheme 598

(180) was individually attractive like the other two, and there did not appear to be a synergistic effect on trap catch when a mixture of components was used as a lure.[758] In Weiler's synthesis of **178** (Scheme 599), **179,** and **180** (Scheme

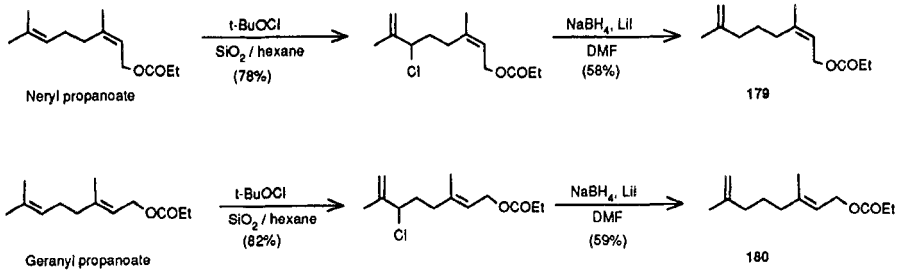


Scheme 599



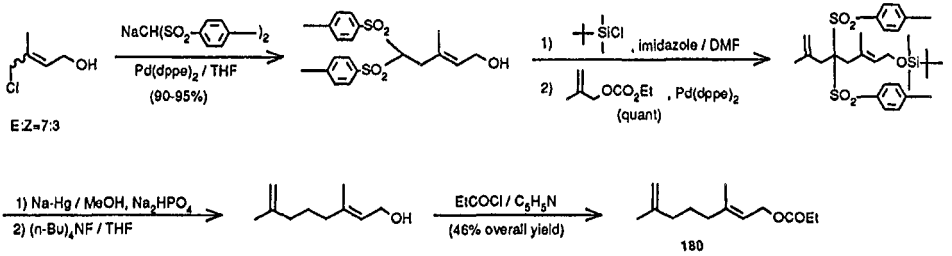
Scheme 600

600), a β-keto ester served as the common intermediate.[760] Szántay and co-workers developed a concise synthesis of both **179** and **180** (Scheme 601), start-



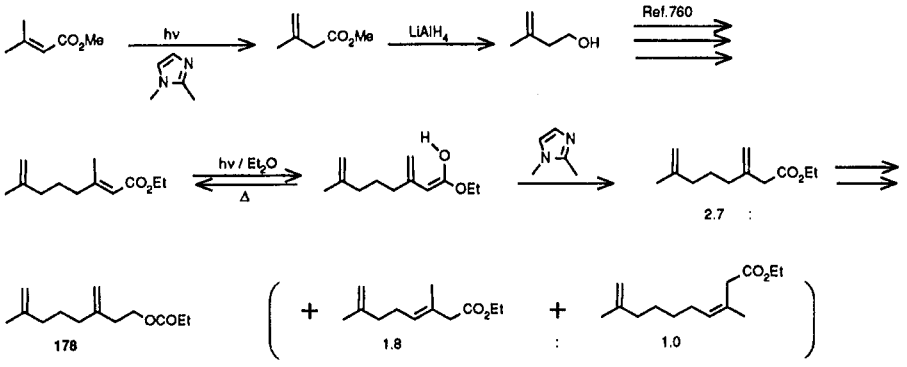
Scheme 601

ing from the commercially available monoterpenes, nerol and geraniol.[761] Ferroud et al. prepared **180** by employing *bis*(*p*-tolylsulfonyl)methane as the building block (Scheme 602).[558] Lombardo and Weedon prepared **178** by a

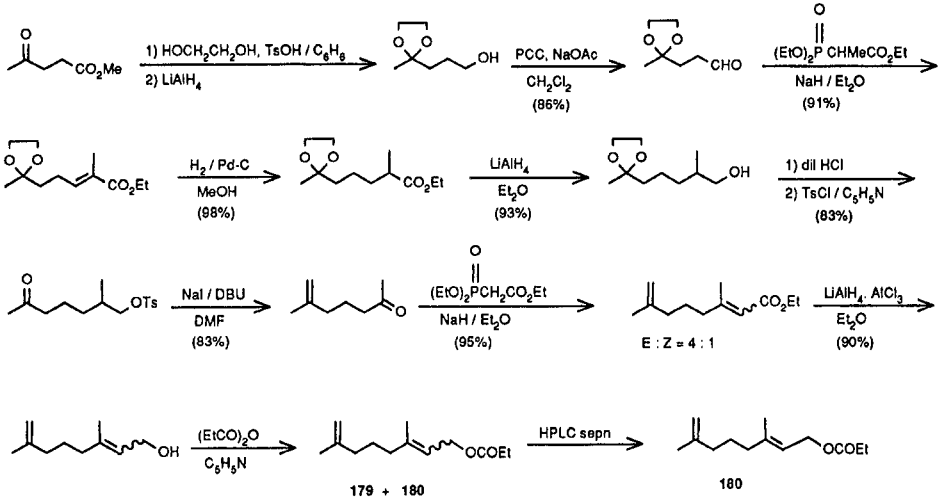


Scheme 602

photochemical deconjugation reaction (Scheme 603) as a mixture with two other products.[762] A lengthy synthesis of **180** was reported by Dhokte and Rao (Scheme 604) starting from methyl levulinate.[763] Odinokov et al. synthesized



Scheme 603

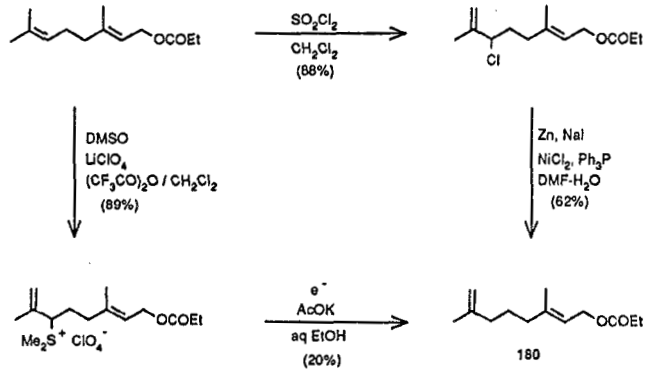


Scheme 604

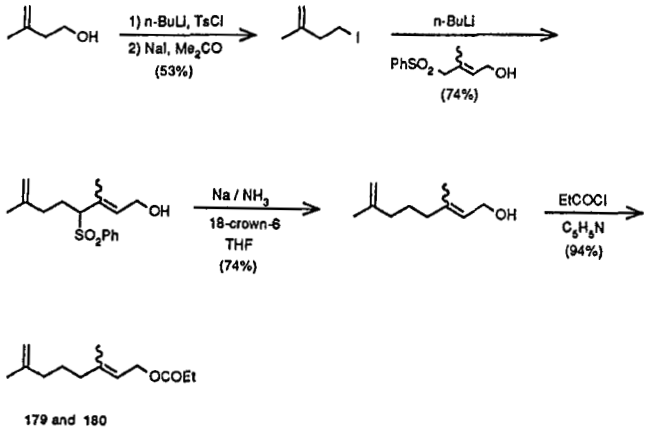
180 from geranyl propanoate (Scheme 605).[764] Moiseenkov et al. also prepared **179** and **180** (Scheme 606).[765]

F. Ipsenol (2-Methyl-6-methylene-7-octen-4-ol) 181 ($C_{10}H_{18}O$) and Ipsdienol (2-Methyl-6-methylene-2,7-octadien-4-ol) 182 ($C_{10}H_{16}O$)

(*S*)-(−)-Ipsenol **(181)** and (*S*)-(+)-ipsdienol **(182)** were first isolated as the pheromone components of the California fivespined ips (*Ips paraconfusus*). In



Scheme 605

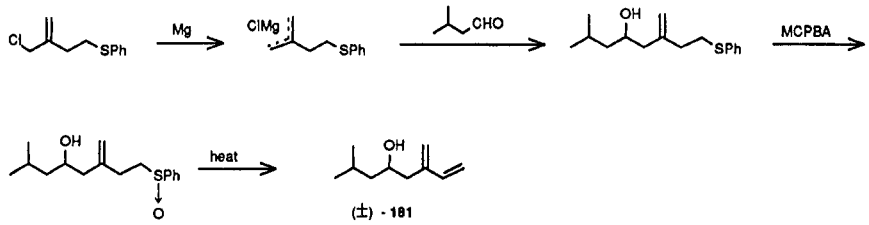


Scheme 606

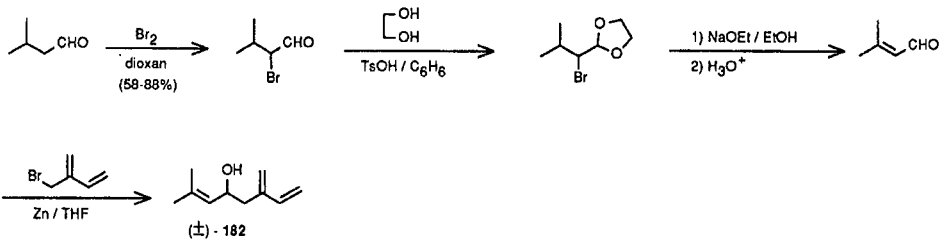
California, the male pine engraver (*Ips pini*) produces (*R*)-(−)-**182** as the major aggregation pheromone, and this enantiomer was found to inhibit the attractive pheromone response in *I. paraconfusus*.[766] (*S*)-(+)-Ipsdienol **(182)** interrupted the response of the Californian *I. pini* to (*R*)-(−)-**182.**[767] On the East coast of

the U.S.A., *I. pini* reacts to (*S*)-(+)-**182.** This interesting phenomenon was studied at the receptor cell level by electrophysiological method to reveal the existence of two distinct types of receptor cells: one keyed to (+)-**182** and the other keyed to (−)-**182.**[768] Further detailed study on interpopulation and intrapopulation variation of the enantiomeric purity of **182** in *I. pini* was reported by Miller et al.[769] A mixture of verbenone and ipsenol inhibits the attraction to the aggregation pheromone as emitted by eight-toothed engraver beetle (spruce bark beetle, *I. typographus*), while that of verbenone and ipsdienol attracts the insects.[770]

Over 10 different syntheses of (±)-**181** and/or (±)-**182** have been reported since 1979. Cazes et al. synthesized (±)-**181** in 52% overall yield (Scheme 607).[771] A synthesis of (±)-**182** was reported by Cheskis et al. (Scheme 608).[772]

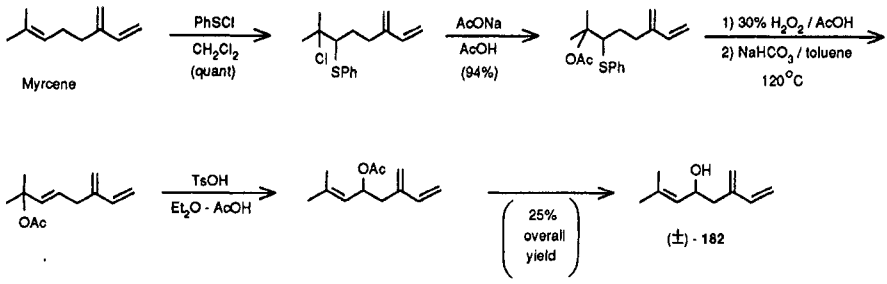


Scheme 607

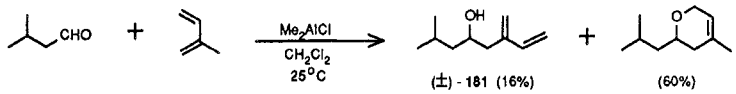


Scheme 608

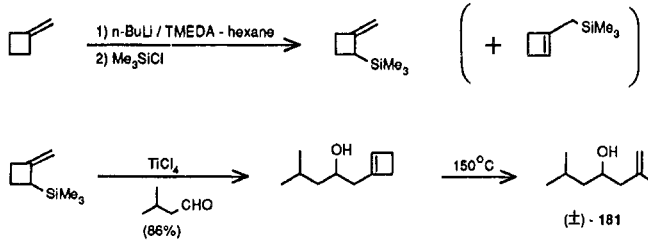
Masaki et al. converted myrcene to (±)-**182** via the addition of benzenesulfenyl chloride (Scheme 609).[773,774] Snider and Rodini prepared (±)-**181** in a single step from isoprene and 3-methylbutanal by an ene reaction (Scheme 610).[775] The major product of this reaction, however, was the Diel-Alder adduct, and (±)-**181** was a minor product. (±)-Ipsenol **(181)** was synthesized by Wilson et al., employing 2-trimethylsilylmethylenecyclobutane as an isoprene equivalent (Scheme 611).[776] Halazy and Krief prepared (±)-**181** by using α-selenocyclobutyllithium as a 2-lithio-1,3-diene equivalent (Scheme 612).[777] Sakurai et al. synthesized (±)-**181** and (±)-**182** starting from 2-trimethylsilylmethyl-1,3-bu-



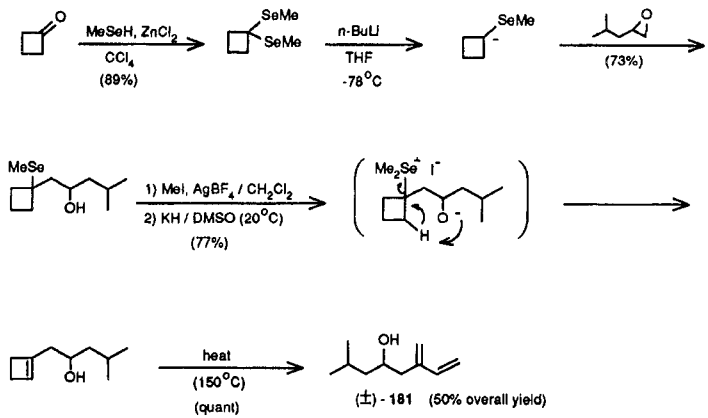
Scheme 609



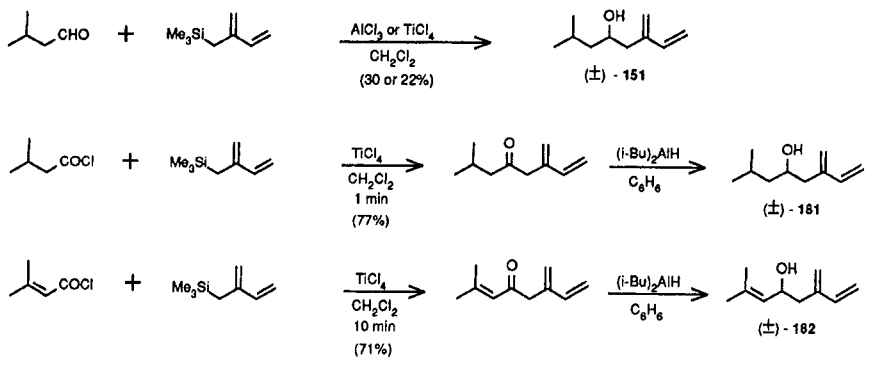
Scheme 610



Scheme 611

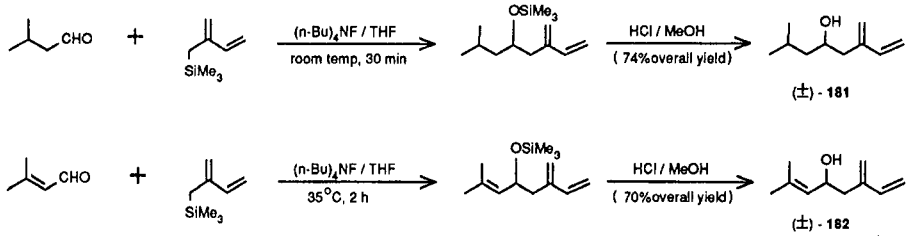


Scheme 612



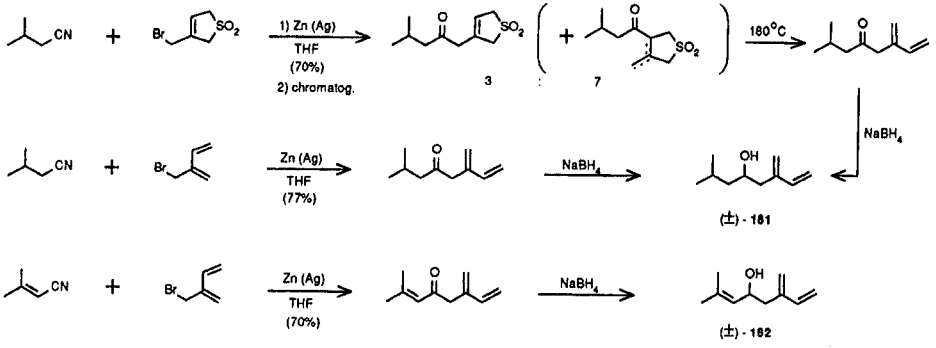
Scheme 613

tadiene (Scheme 613).[778] The same silyldiene, when treated with tetra-*n*-butylammonium fluoride, efficiently isoprenylated aldehydes to give (±)-**181** and (±)-**182** (Scheme 614).[779] Rousseau and Drouin used allylic organozinc com-



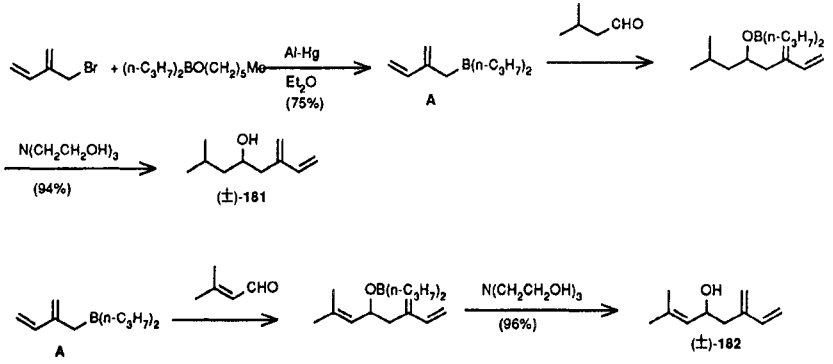
Scheme 614

pounds for the conversion of the nitriles to the ketones corresponding to (±)-**181** and (±)-**182** (Scheme 615).[780] A dienylborane **A** was prepared by Bubnov and



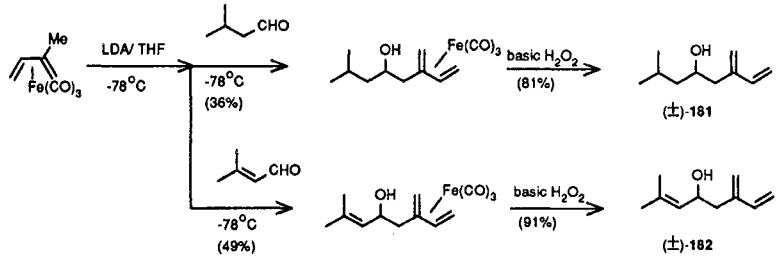
Scheme 615

Etinger, and was used for isoprenylation of the aldehydes to produce (±)-**181** and (±)-**182** quite efficiently (Scheme 616).[781] Semmelhack and Fewkes used



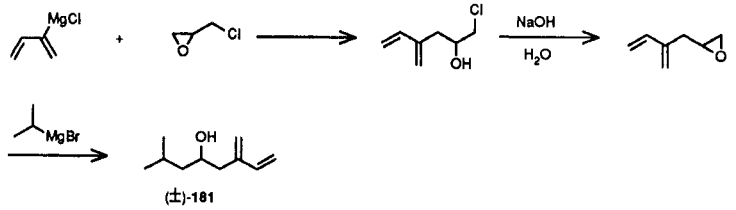
Scheme 616

(η^4-isoprene)iron tricarbonyl as the isoprene equivalent and synthesized (±)-**181** and (±)-**182** (Scheme 617).[782] Vorskanyan et al. published an additional syn-



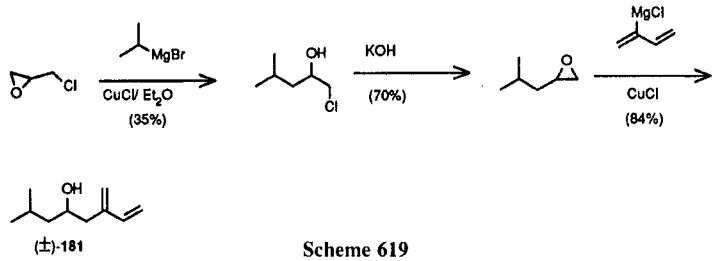
Scheme 617

thesis of (±)-**181** (Scheme 618),[783] which is a variant of the previous synthesis



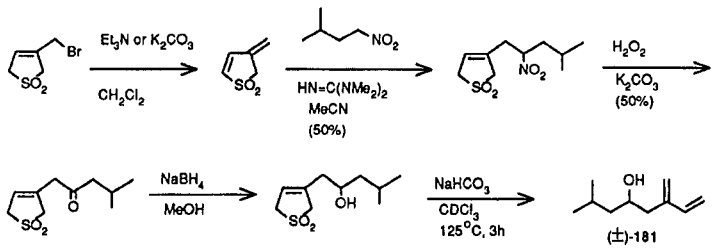
Scheme 618

by Cheskis and Moiseenkov (Scheme 619).[784] A new route to (±)-**181** was



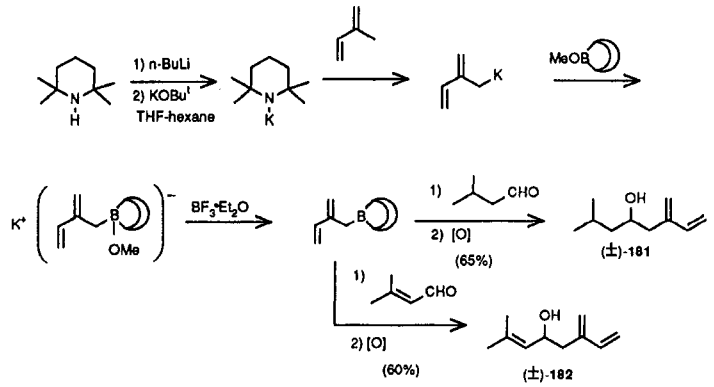
Scheme 619

developed using 3-methylene-2,3-dihydrothiophene S,S-dioxide as an allylic sulfone and Michael acceptor (Scheme 620).[785] Brown and Randad synthesized



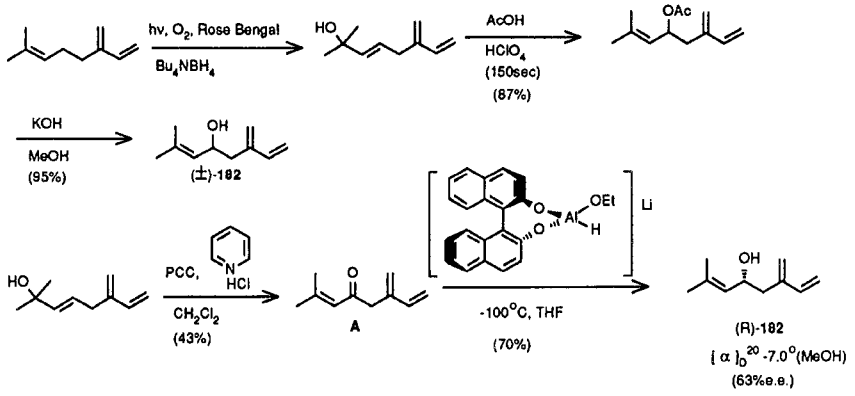
Scheme 620

(±)-**181** and (±)-**182** by using *B*-isoprenyl-9-BBN in a manner similar to Bubnov[781] (Scheme 621).[786]



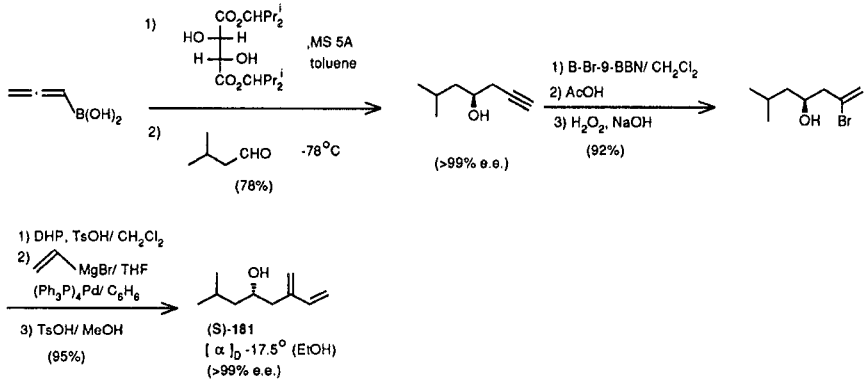
Scheme 621

Six new papers have appeared since 1979 on the preparation of the enantiomers of **181** and **182.** Baeckström et al. employed myrcene as the starting material, prepared (±)-**182** first (Scheme 622), and then obtained (*R*)-(−)-**182**



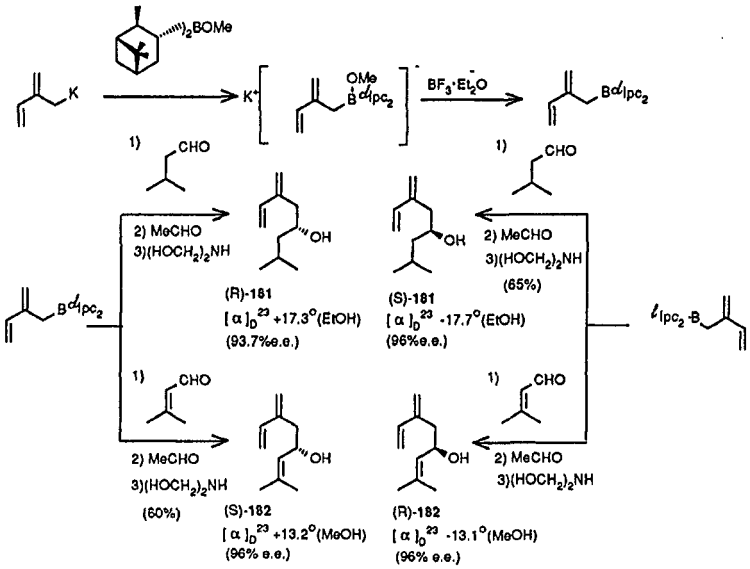
Scheme 622

(63% e.e.) by Noyori's asymmetric reduction of the corresponding ketone **A.**[787] Kubo et al. carried out the optical resolution of (±)-**181** and (±)-**182** after their derivatization with (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid (MTPA) to the corresponding MTPA esters, followed by HPLC separation of the diastereomers.[788] H. Yamamoto and co-workers prepared (*S*)-**181** of > 99% e.e. by their new asymmetric reaction using chiral allenyl boronic ester (Scheme 623).[789]



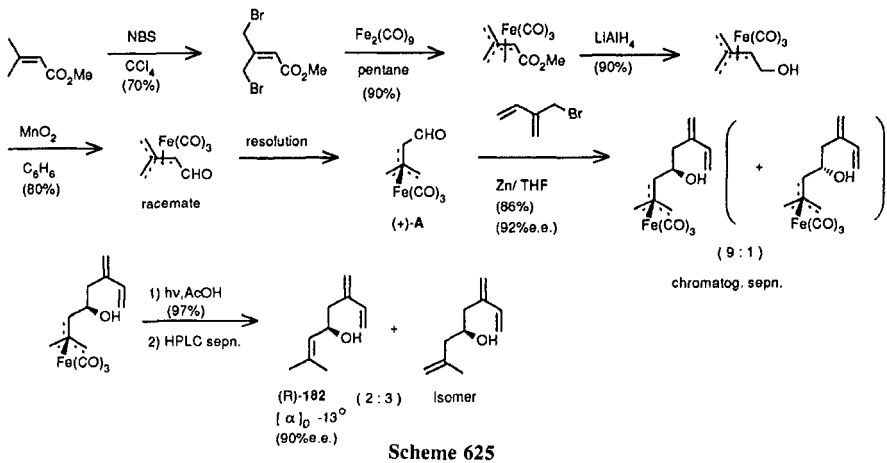
Scheme 623

Brown and Randad employed *B*-isoprenyldiisopinocampheylborane to prepare the enantiomers of both **181** and **182** (Scheme 624).[786,790] Bubnov modi-



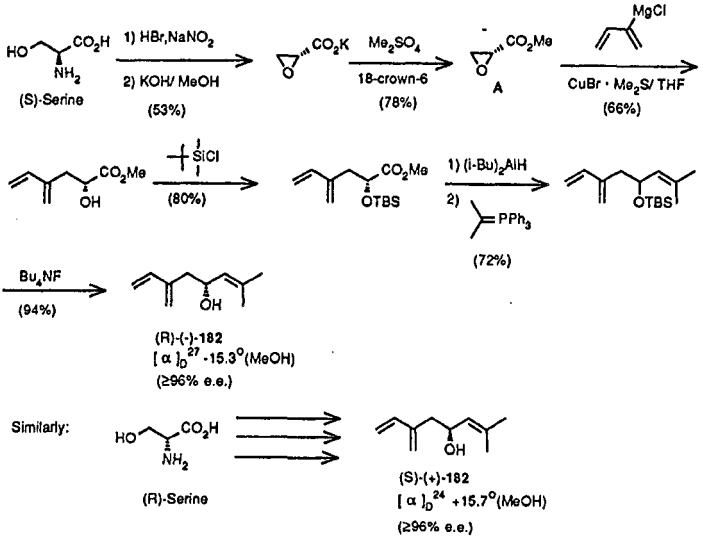
Scheme 624

fied his synthesis of (±)-**181** and (±)-**182** via organoboron intermediates to prepare the enantiomers of both **181** and **182.**[791] A unique synthesis of (*R*)-**182** was reported by Franck-Neumann et al., who used an optically active iron complex **A** as the key-intermediate (Scheme 625).[792] However, (*R*)-**182** was the minor product of this synthesis.



Scheme 625

Mori and Takikawa prepared both the enantiomers of ipsdienol **(182)** starting from the enantiomers of serine (Scheme 626).[793] The key-step was the epoxide opening of **A** with a Grignard reagent prepared from chloroprene.

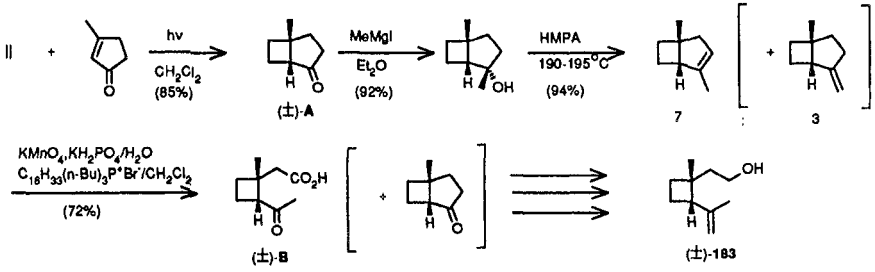


Scheme 626

G. Grandisol (*cis*-2-Isopropenyl-1-methylcyclobutaneethanol) 183 ($C_{10}H_{18}O$)

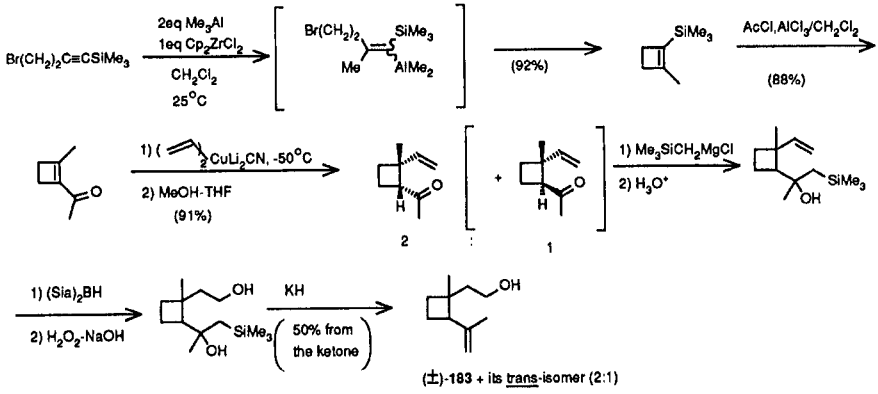
(1*R*,2*S*)-(+)-Grandisol **(183)** was first identified as a pheromone component of the male cotton boll weevil (*Anthonomus grandis*). It was also shown to be a pheromone component of the bark beetle (*Pityophthorus pityographus*).[794]

Over a dozen syntheses of (±)-**183** or (+)-**183** have been recorded since 1979, in addition to 15 syntheses reviewed in Ref. 1. Rosini et al. reported a short synthesis of keto acid **B** from the known bicyclic ketone **A** (Scheme 627).[795] The acid **B** had previously been converted to (±)-**183.** Negishi's syn-



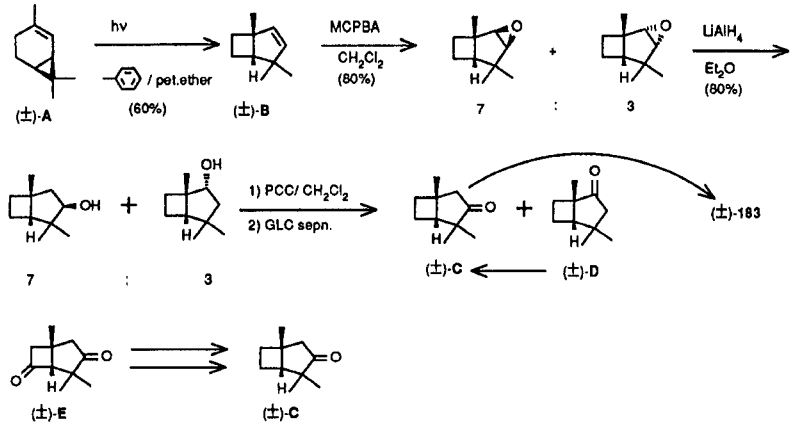
Scheme 627

thesis of (±)-**183** was achieved by using his silicon-promoted cyclization reaction of ω-haloalkenylaluminum as catalyzed by zirconocene (Scheme 628).[796,797] The final product of this synthesis was a mixture of (±)-**183** and



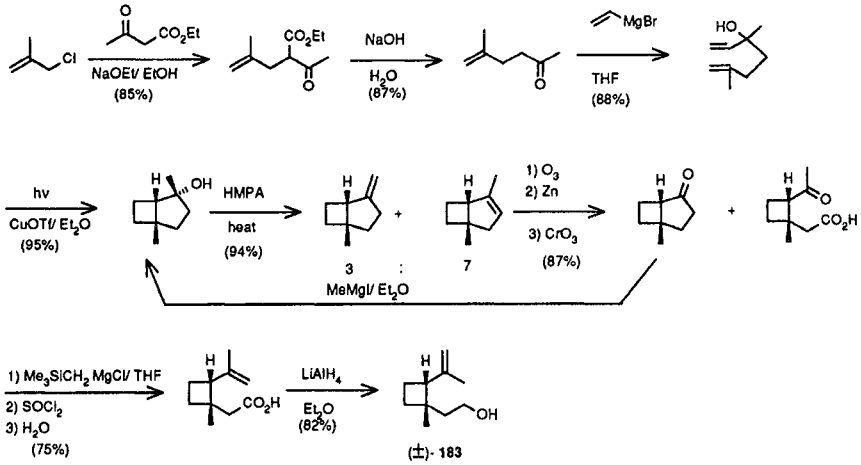
Scheme 628

its *trans*-isomer. Photo-induced rearrangement of (+)-Δ^2-carene (**A**) to a bicyclo[3.2.0]heptene **B** was used by Sonawane et al. (Scheme 629)[798] for the



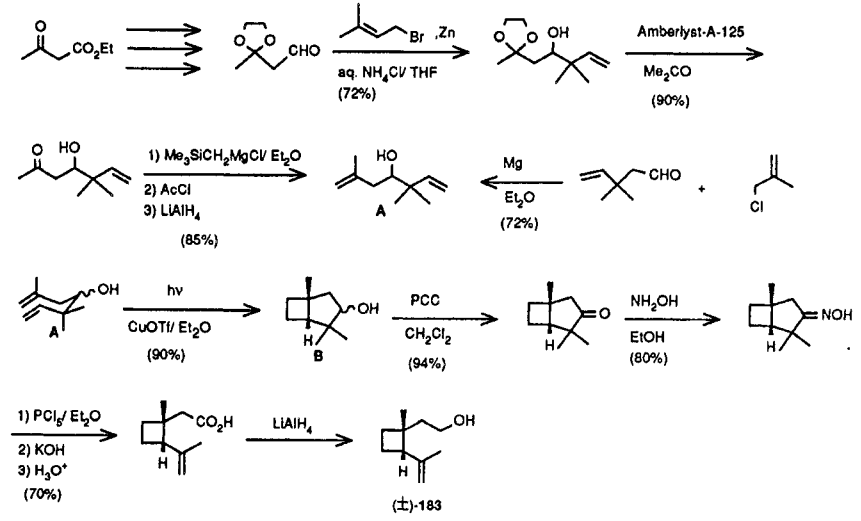
Scheme 629

preparation of ketone **C**, which had been used by others in the synthesis of (±)-**183**. Another inefficient synthesis of the ketone **C** from **E** was reported by Rømming et al.[799] In Rosini's synthesis of (±)-**183** (Scheme 630), the key-step



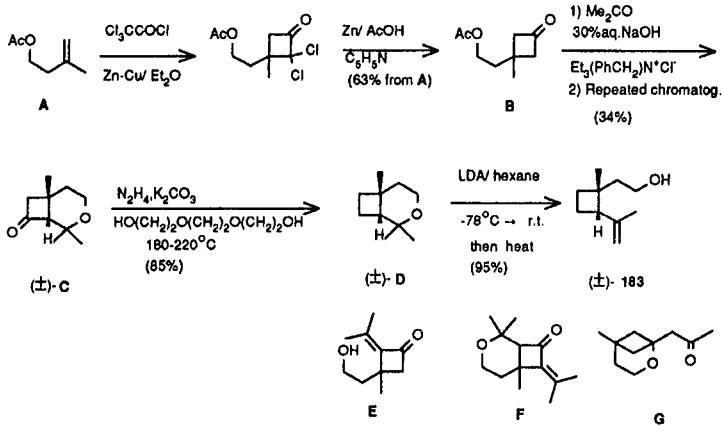
Scheme 630

was the photocyclization of 3,6-dimethyl-1,6-heptadien-3-ol.[800] The overall yield of (±)-**183** by this synthesis was 31% from methallyl chloride. Rosini et al. further improved their photocyclization route (Scheme 631).[801] In this case, too, the photocyclization step (**A** → **B**) resulted in an excellent yield.



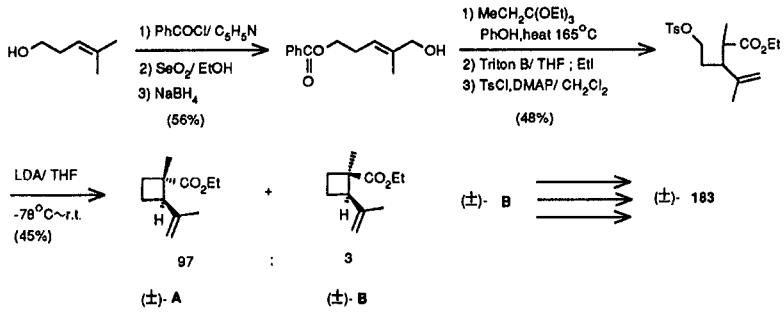
Scheme 631

A very short synthesis of (±)-**183** by Dreiding et al. utilized [2 + 2]cycloaddition of dichloroketene to construct the cyclobutane ring (Scheme 632).[802] There is a drawback at step **C** → **D** because other byproducts (**E, F,**



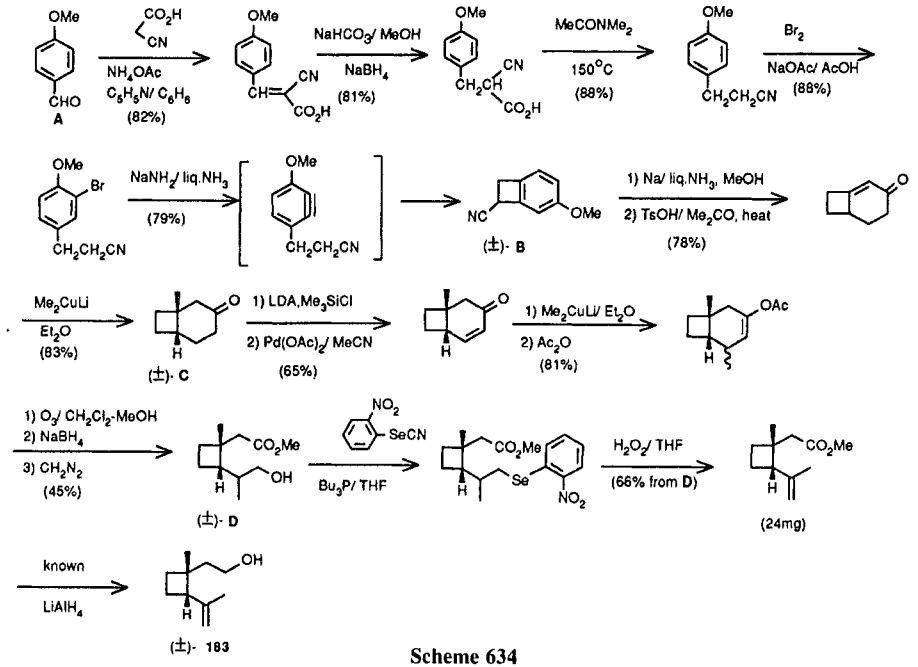
Scheme 632

and **G**) had to be removed by repeated chromatography. Kim et al. used intramolecular alkylation to build up the cyclobutane ring (Scheme 633).[803] This

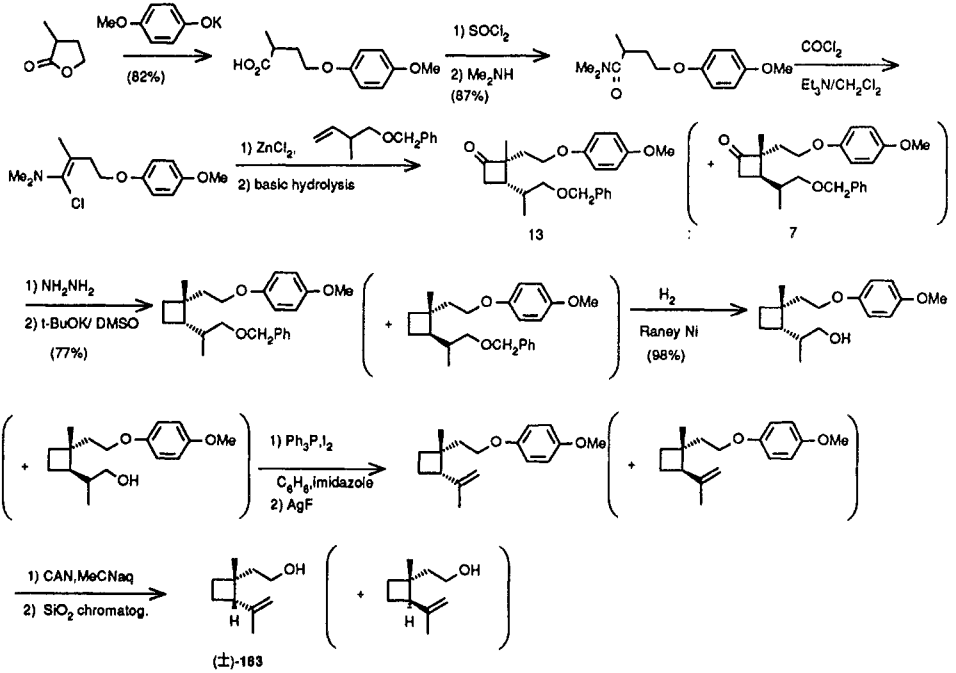


Scheme 633

reaction unfortunately furnished the unwanted *trans*-compound **A** as the major product, while the desired ester **B** was the minor product. Kametani et al. employed benzobutane **B,** which was prepared from *p*-methoxybenzaldehyde,[804] as the starting material for the synthesis of (±)-**183** (Scheme 634).[805] Conversion of **B** to **C** was the crucial feature of this route which, however, was too lengthy. Grandguillot and Rouessac prepared (±)-**183** by a ketiminium [2 + 2]cycloaddition (Scheme 635).[806]

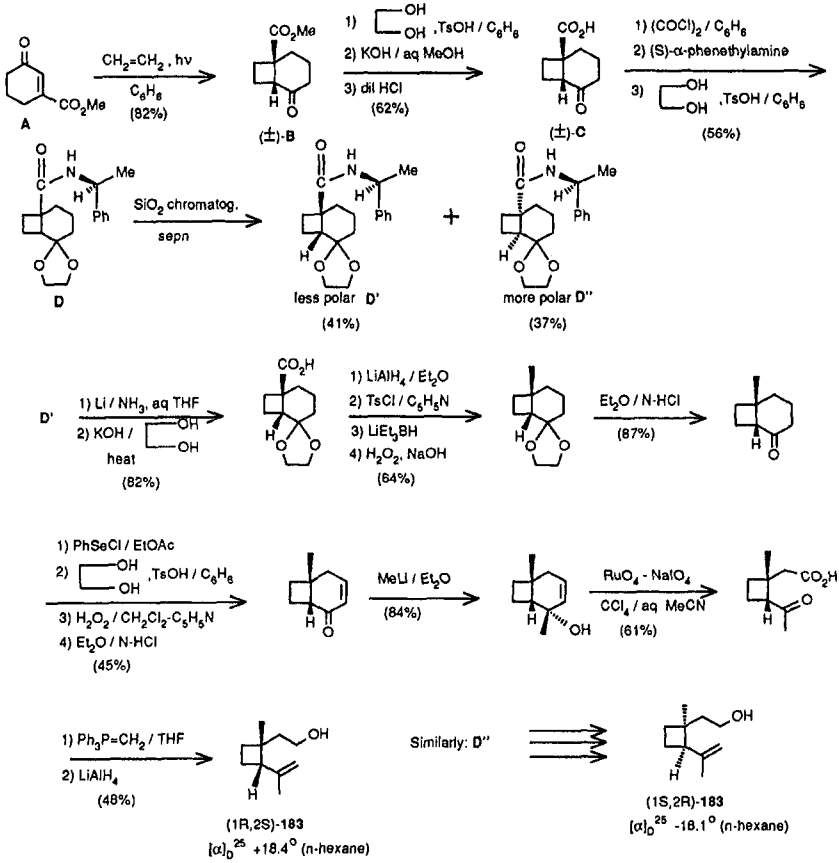


Scheme 634



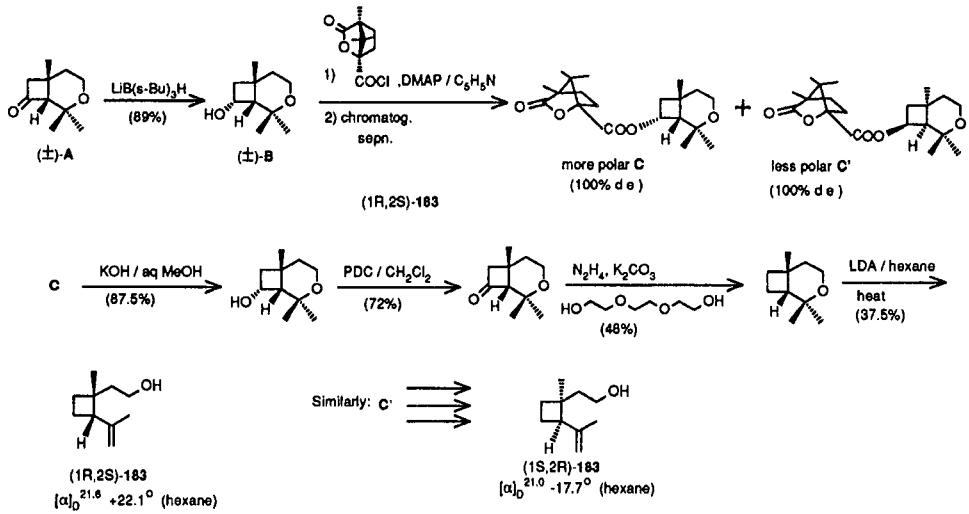
Scheme 635

Six new syntheses of the enantiomers of **183** have been published since 1979; two by optical resolution, two by biochemical asymmetric synthesis, and two by chemical asymmetric synthesis. Webster and Silverstein resolved a bicyclo[4.2.0]octanecarboxylic acid **C** (Scheme 636) in analogy with Mori's 1978 work, in which a similar bicyclo[3.2.1]heptanecarboxylic acid was resolved (Scheme 233a, Ref. 1).[807] For the cleavage of the amide bond of **D′** and **D″**, they developed a new procedure as shown in Scheme 636.[cf. 808] No direct proof



Scheme 636

was given in this paper to support the claimed > 99% enantiomeric purity of the enantiomers of **183.** Mori and Nagano modified the Dreiding synthesis of (±)-**183** (Scheme 632) to furnish both the enantiomers as shown in Scheme 637.[809] They resolved alcohol (±)-**B** by acylating it with (−)-ω-camphanyl

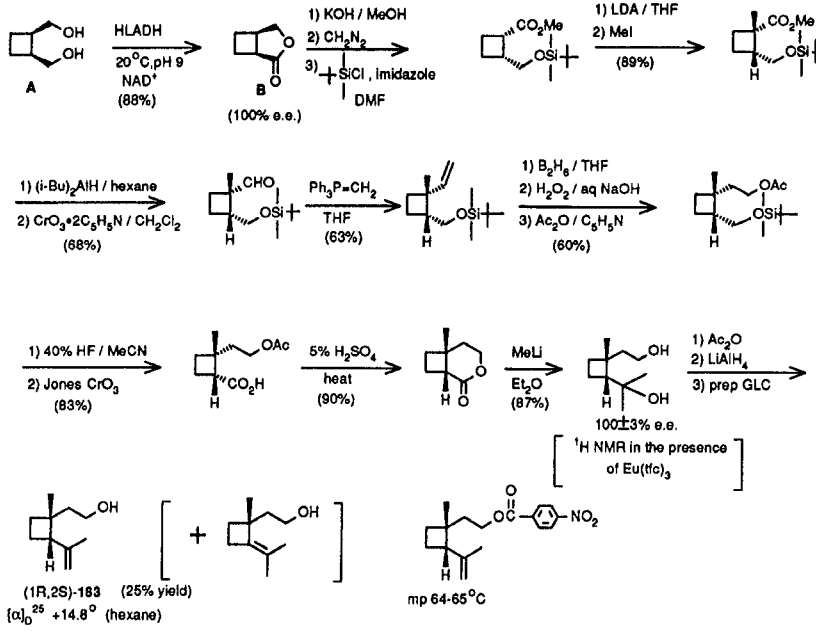


Scheme 637

chloride. The resulting diastereomers **C** and **C'** were separable by chromatography. In spite of the small discrepancy between the $[\alpha]_D$ value of their (+)-**183** and that of (−)-**183,** their enantiomers proved to be enantiomerically pure by examining the ^{1}H NMR spectra (400 MHz) of their MTPA esters.[cf. 811] The rotation value is not always a good criterion to judge optical purity.

Chiral building blocks generated by biochemical means were used by two groups to prepare **183.** Jones et al. obtained lactone **B** by oxidizing *meso*-diol **A** with horse liver alcohol dehydrogenase (HLADH) and converted **B** to (+)-**183** (Scheme 638).[810] The enantiomeric purity of their (+)-**183** was estimated to be ca. 100% by ^{1}H NMR examination (100 MHz) of its MTPA ester in the presence of Eu(fod)$_3$. The final step of their synthesis, however, was not selective, and GLC separation of the products was necessary to secure pure **183.**

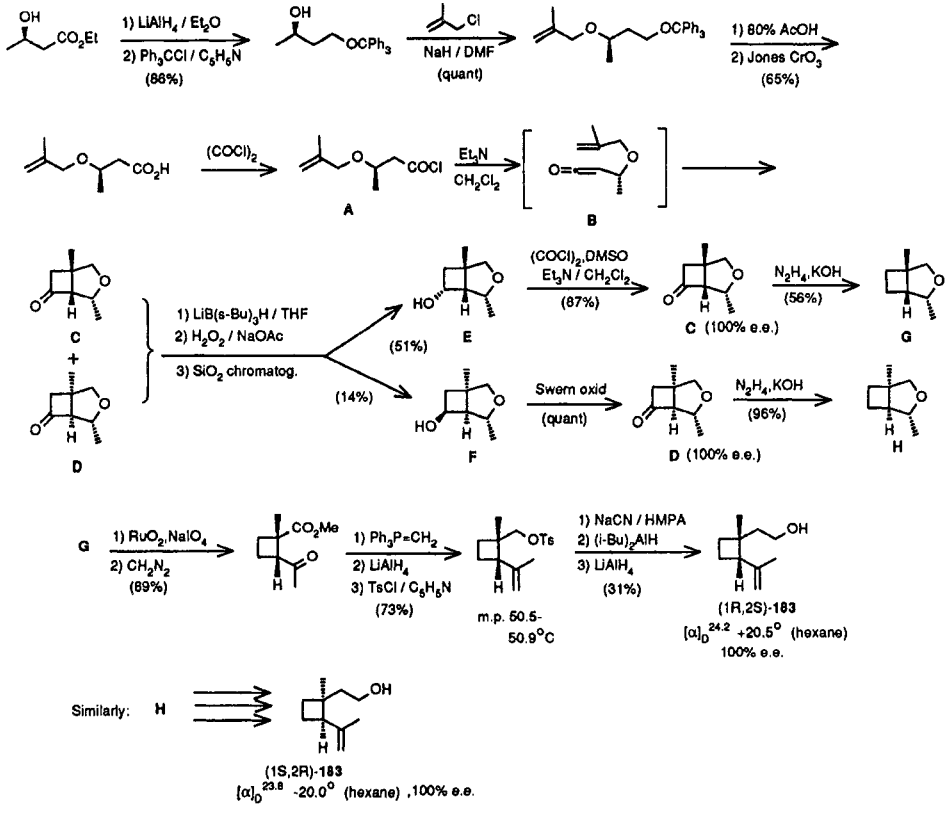
Mori and Miyake synthesized the enantiomers of grandisol (Scheme 639) starting from ethyl (*R*)-3-hydroxybutanoate.[811] The starting material could readily be prepared by ethanolysis of PHB (poly-β-hydroxybutyrate) of microbial origin. The key-step was the intramolecular cycloaddition of the acyl chloride **A** to give a diastereomeric mixture of **C** and **D** via ketene **B.** Separation of the mixture was successful after reduction to give pure **E** and **F.** These were converted to (+)-**183** and (−)-**183** via **G** and **H.** Careful estimation of the enantiomeric purity was executed at the stage of the ketones **C** and **D,** and also with the final products. ^{1}H NMR studies on the MTPA esters of (+)-**183** and (−)-**183** at 400 MHz proved their 100% enantiomeric purities. The enantiomers of **183** synthesized by Mori and Miyake were assayed by Dickens against the boll wee-



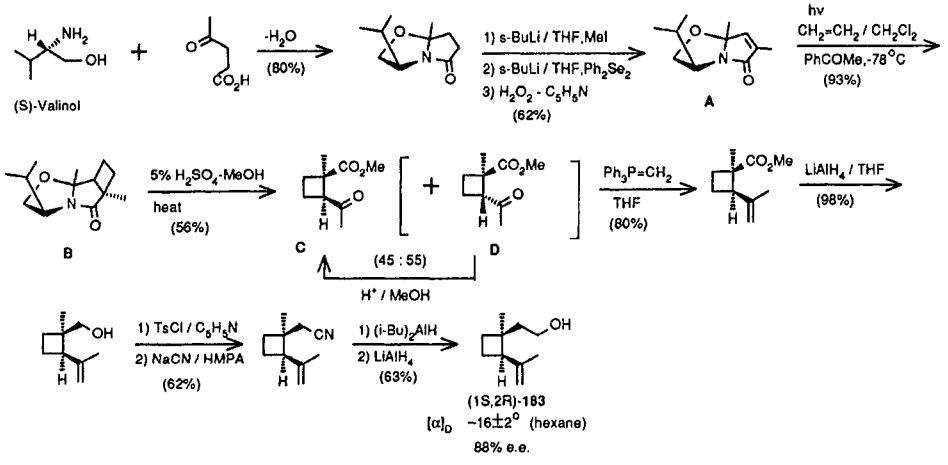
Scheme 638

vil. He found only (1*R*,2*S*)-(+)-**183** to be bioactive by EAG studies and field tests.[812] This was not in accord with the old data, which show both (+)-**183** and (−)-**183** to be bioactive in laboratory bioassay against the boll weevil.[813] In the old experiments, (+)-**183** of 80% e.e. and (−)-**183** of 91% e.e. were used. This rather low enantiomeric purity of the samples and/or the design of the bioassay must have been the origin of the previous erratic result.

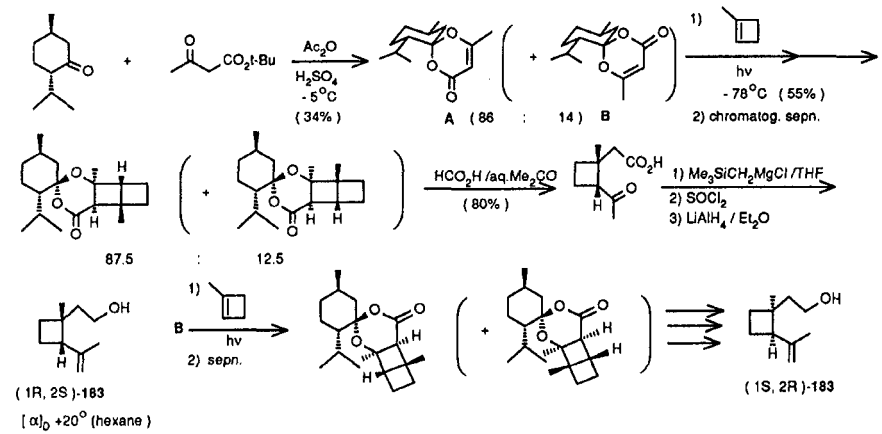
The following two asymmetric syntheses of **183** employed, as the key-steps, intramolecular photocycloaddition of alkenes to chiral α,β-unsaturated carbonyl compounds. First, Meyers and Fleming developed asymmetric [2 + 2] photocycloaddition of ethylene to α,β-unsaturated lactam **A** to give **B** (Scheme 640).[814] The lactam **A** was prepared from (*S*)-valinol and levulinic acid. The product **B** was contaminated with ca. 7–8% of its *endo*-cyclobutane-fused isomer. Because the photocycloaddition mixture was further processed without separation, the resulting (−)-grandisol **(183)** was enantiomerically impure (ca. 88% e.e.). Second, Demuth et al. prepared both (+)-**183** and (−)-**183** by asymmetric photocycloaddition of 2-methylcyclobutene to optically pure spirocyclic enone **A** (Scheme 641).[815] The spirocyclic enone **A** could be prepared from (−)-menthone and *t*-butyl acetoacetate. This is the shortest enantioselective synthesis of grandisol enantiomers.



Scheme 639



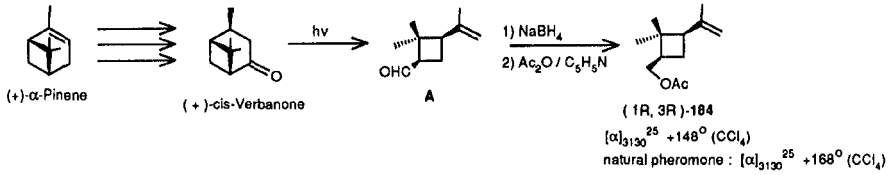
Scheme 640



Scheme 641

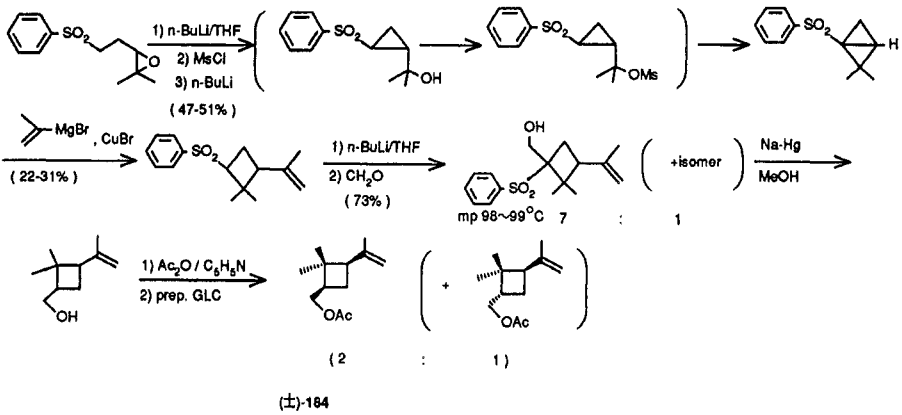
H. (1*R*,3*R*)-3-Isopropenyl-2,2-dimethylcyclobutanemethyl Acetate 184 ($C_{12}H_{20}O_2$)

The female-produced sex pheromone of the citrus mealybug (*Planococcus citri*) was identified as **184** by Bierl-Leonhardt et al.[816] Their synthesis of **184** (Scheme 642) was achieved by the photolysis of (+)-*cis*-verbanone to give olefinic al-

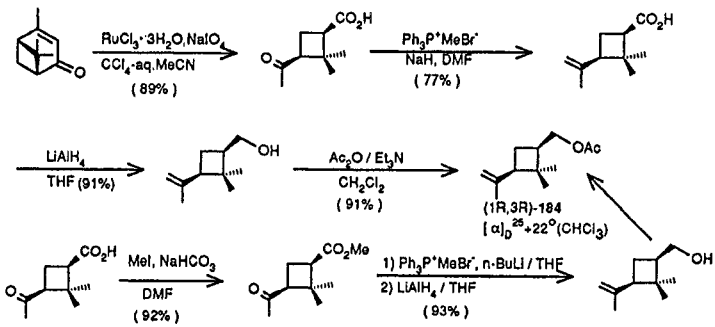


Scheme 642

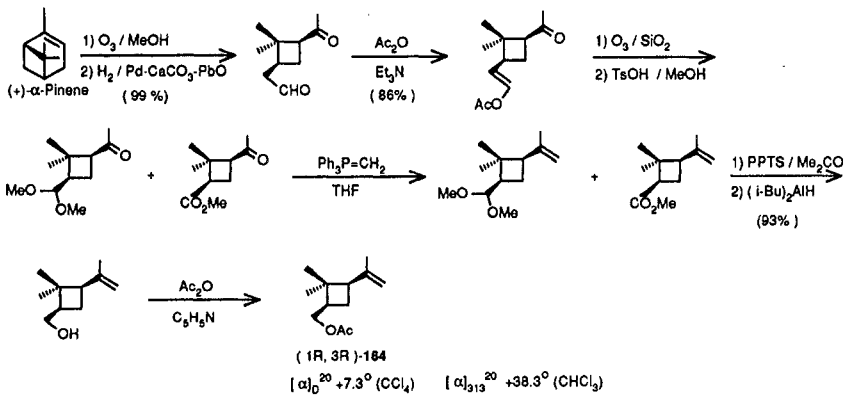
dehyde **A**, reduction and acetylation of which furnished the pheromone.[816] (1*S*,3*S*)-Isomer of **184** as well as the *trans*-isomer and the alcohol precursor of **184** were far less active than (1*R*,3*R*)-**184**.[816] Gaoni synthesized (±)-**184** by conjugate addition of isopropenylmagnesium bromide in the presence of copper(I) bromide to 1-benzenesulfonyl-2,2-dimethylbicyclobutane (Scheme 643).[817] The bicyclobutane was prepared from a γ,δ-epoxysulfone.[818] The final purification of (±)-**184** was carried out by preparative GLC. Carlsen and Odden's synthesis of **184** started from (+)-verbenone, which was oxidized with ruthenium tetroxide (Scheme 644).[819] Starting from (+)-α-pinene, Odinkov et al. synthesized **184** as shown in Scheme 645.[820] A four-step synthesis of **184**



Scheme 643

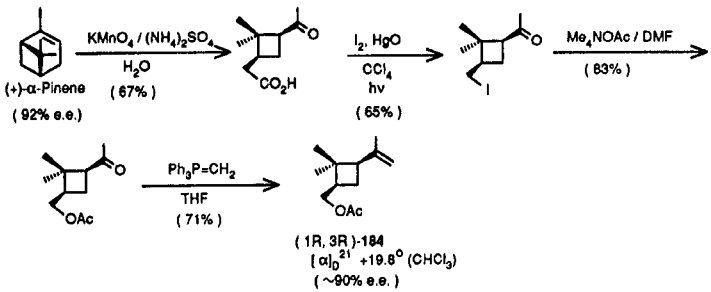


Scheme 644



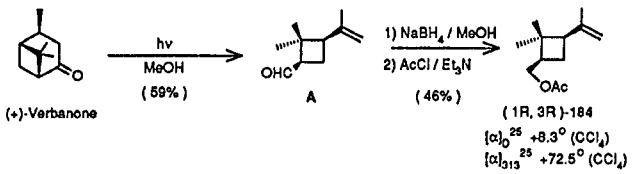
Scheme 645

was reported by Wolk et al. starting from (+)-α-pinene (Scheme 646).[821] Out



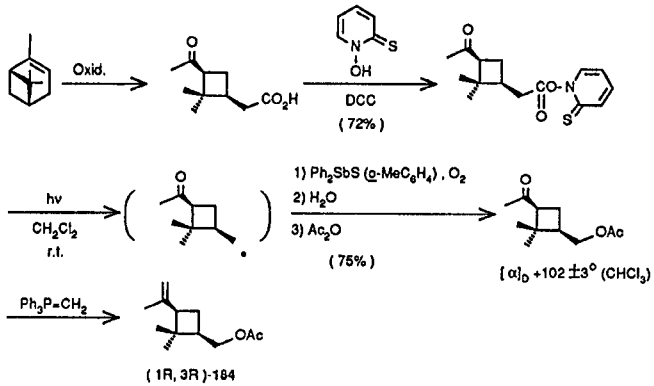
Scheme 646

of eight analogs of **184,** only (1*R*,3*R*)-3-isopropenyl-2,2-dimethylcyclobutaneethyl acetate was bioactive, showing that all functional groups of **184** are essential for optimal biological activity.[822] Serebryakov et al. prepared **184** essentially in the same manner as employed by Bierl-Leonhardt (Scheme 647).[823]



Scheme 647

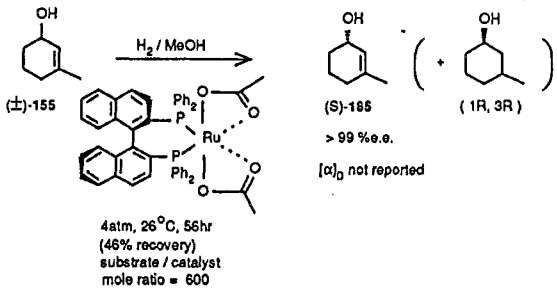
Barton employed his radical decarboxylation reaction to prepare **184** as shown in Scheme 648.[824]



Scheme 648

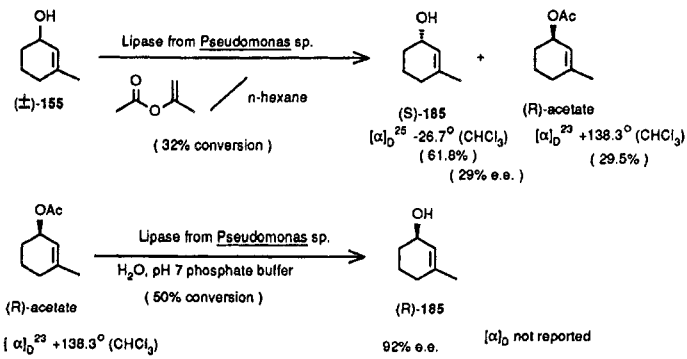
I. Seudenol (3-Methyl-2-cyclohexen-1-ol) 185 ($C_7H_{12}O$)

This is a component of the aggregation pheromone produced by the female Douglas-fir beetle (*Dendroctonus pseudotsugae*). Since Mori's synthesis of the enantiomers of **185** (Scheme 235, Ref. 1), three papers have appeared on the enantioselective synthesis of **185.** Noyori and his co-workers developed a new method for kinetic resolution of racemic allylic alcohols by BINAP-ruthenium(II)-catalyzed hydrogenation and obtained (*S*)-**185** (Scheme 649).[825] Two

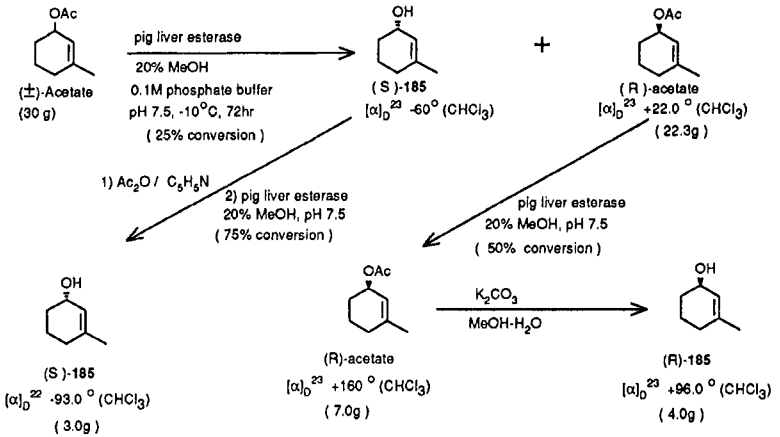


Scheme 649

papers on the synthesis of optically active **185** were reported based on enzymatic resolution. Wong et al. employed lipase of the *Pseudomonas* species (Scheme 650),[736] while Mori and Ogoche employed pig liver esterase (Scheme 651).[826]



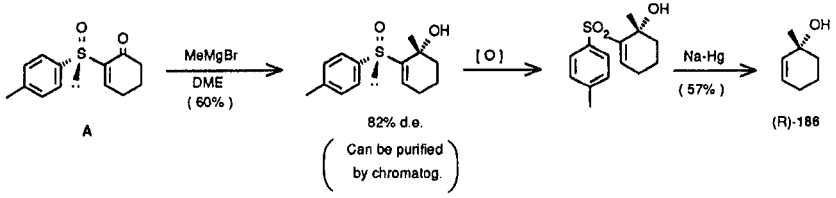
Scheme 650



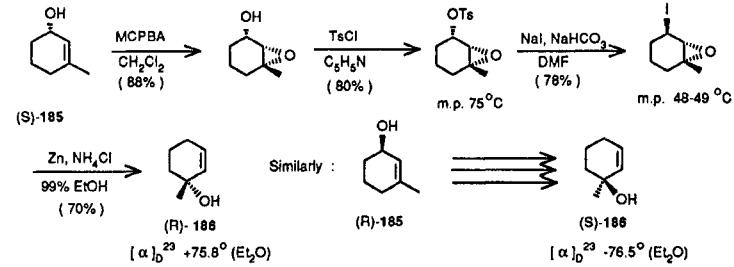
Scheme 651

J. 1-Methyl-2-cyclohexen-1-ol 186 ($C_7H_{12}O$)

This is the component of the female-produced aggregation pheromone of the Douglas-fir beetle (*Dendroctonus pseudotsugae*) that attracts both sexes, males predominantly.[827] Optically active **186** was synthesized by two groups. Posner's synthesis started from chiral sulfoxide **A** (Scheme 652),[828] while Mori et al. converted optically active seudenol **(185)** to **186** (Scheme 653).[826,829] Both of the syntheses were based on the intramolecular transfer of chirality.



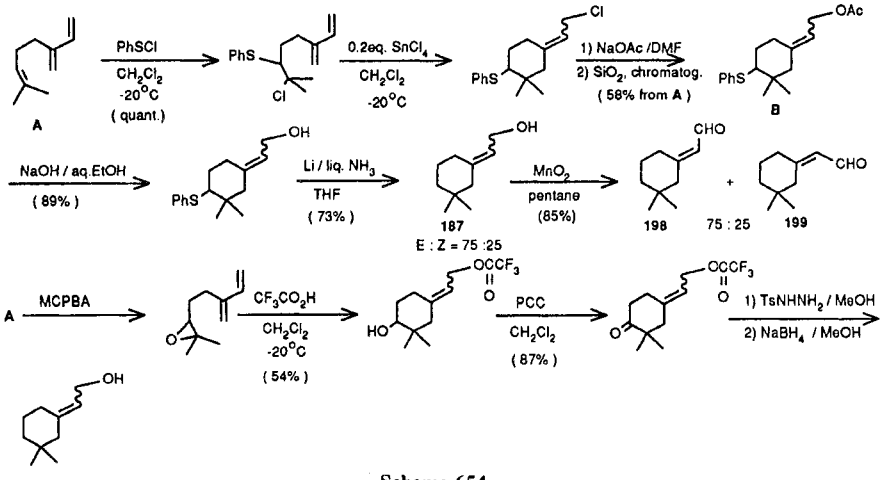
Scheme 652



Scheme 653

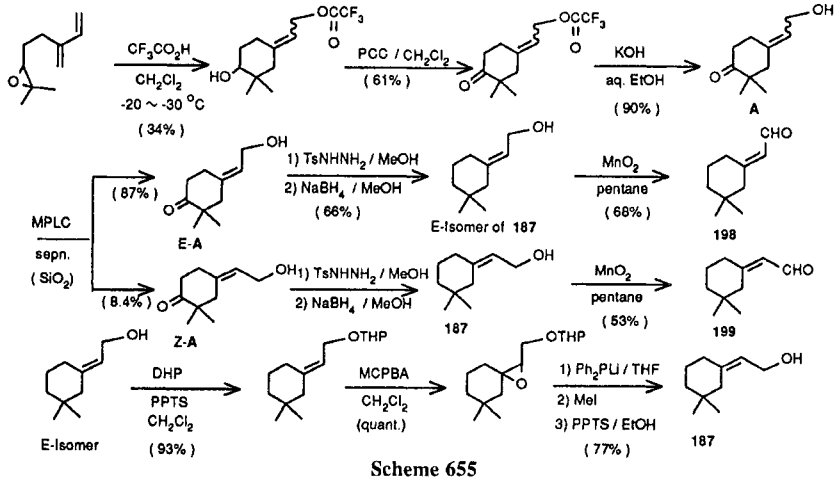
K. (Z)-2-Ochtoden-1-ol [(Z)-3,3-Dimethyl-$\Delta^{1,\beta}$-cyclohexaneethanol] **187** ($C_{10}H_{18}O$)

This is a component of the male-produced sex pheromone of the boll weevil (*Anthonomus grandis*). Masaki et al. examined the acid-catalyzed cyclization of the terminally functionalized myrcene derivatives (Scheme 654) and obtained



Scheme 654

187.[830,831] The major product, however, was the *E*-isomer of **187**. Mori and Itou modified Masaki's procedure to prepare geometrically pure **187** (Scheme 655).[832] Thus, purification of **A** by medium pressure liquid chromatography



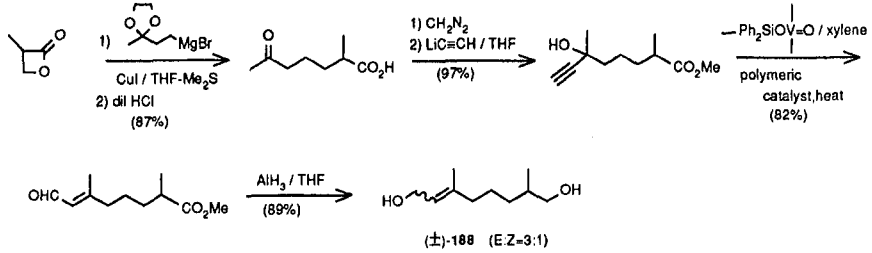
Scheme 655

resulted in the separation of (*E*)-**A** and (*Z*)-**A**, the latter being converted to **187**. Because (*Z*)-**A** was the minor product, conversion of the *E*-isomer to **187** was executed by the olefin inversion (Scheme 655).[832]

L. (*E*)-3,7-Dimethyl-2-octene-1,8-diol 188 ($C_{10}H_{20}O_2$)

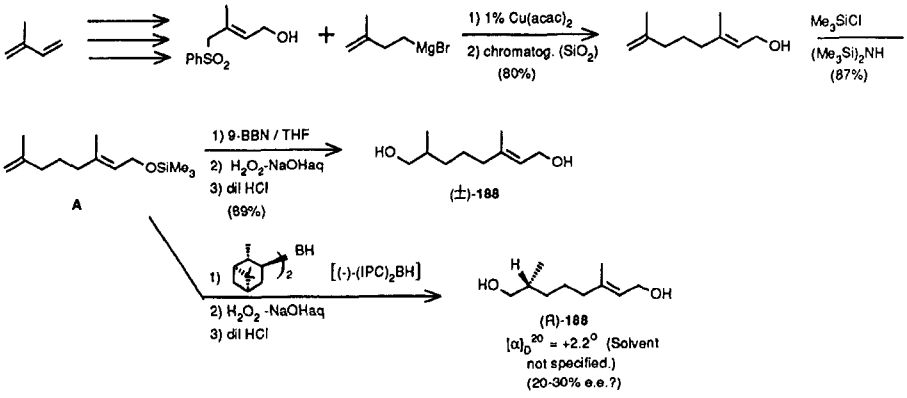
This is one of the components of the hairpencil secretion of the African monarch butterfly (*Danaus chrysippus*). Since 1979, four syntheses of (±)-**188** and a synthesis of (*S*)-**188**, as well as that of (*R*)-**188** of low e.e., have been reported. The absolute configuration of the natural **188** has yet to be determined.

Fujisawa's synthesis of (±)-**188** employed the ring-opening reaction of α-methyl-β-propiolactone as the key-step (Scheme 656).[833] The final product



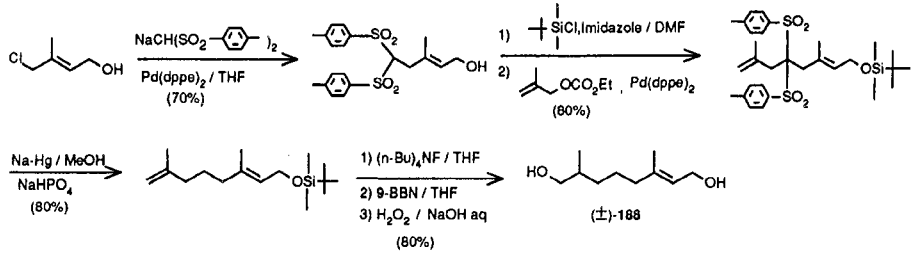
Scheme 656

by this synthesis was a mixture of **188** and its *Z*-isomer. Copper-catalyzed substitution of an allylic phenylsulfone with a Grignard reagent was the key-step in Julia's synthesis of (±)-**188** (Scheme 657).[834] Julia also prepared optically



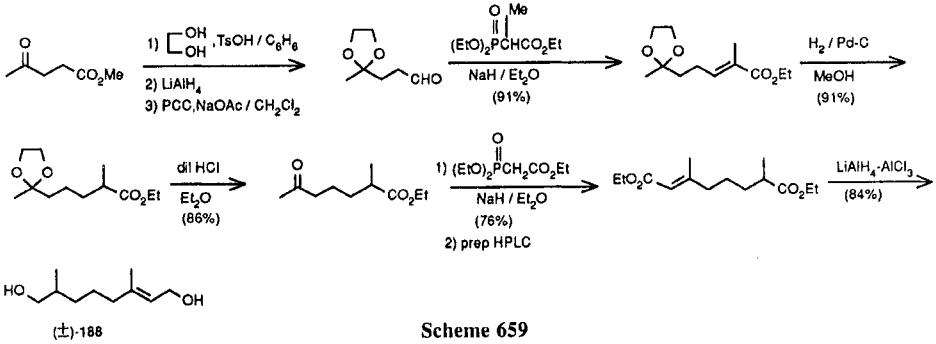
Scheme 657

active **188** by asymmetric hydroboration of the olefinic intermediate **A**.[834] Ferroud et al. synthesized (±)-**188** by employing *bis*(*p*-tolylsulfonyl)methane as an initial building block (Scheme 658).[558] Dhokte and Rao's synthesis of

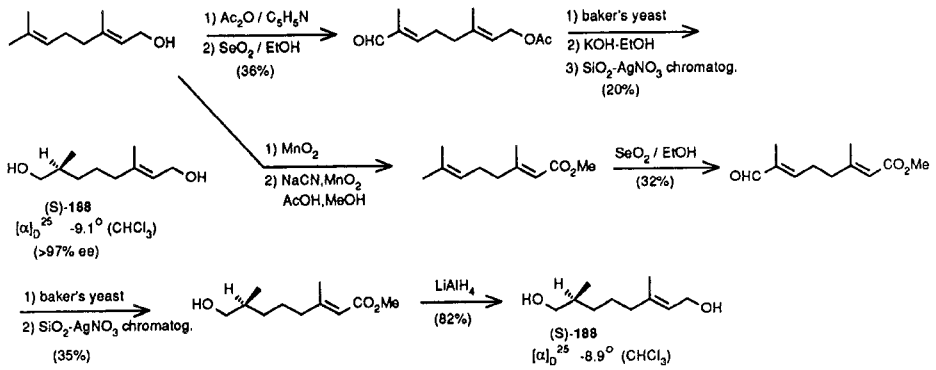


Scheme 658

(±)-**188** started from methyl levulinate and proceeded in the conventional manner (Scheme 659).[763] Gramatica et al. used baker's yeast to prepare (*S*)-**188** of high enantiomeric purity (Scheme 660).[835]



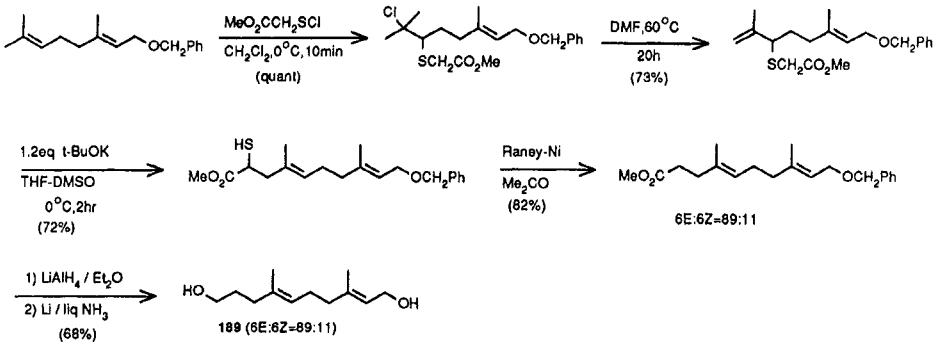
Scheme 659



Scheme 660

M. (2*E*,6*E*)-3,7-Dimethyl-2,6-decadiene-1,10-diol **189** ($C_{12}H_{22}O_2$)

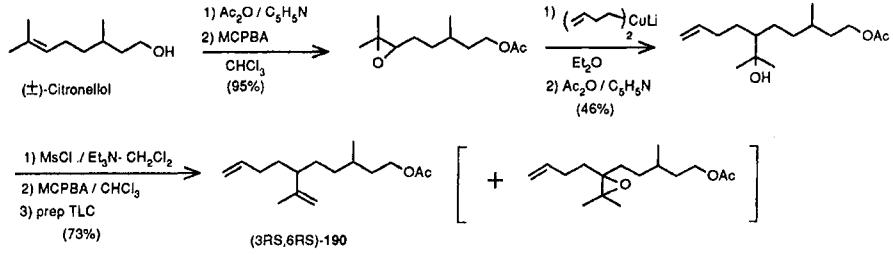
This is one of the components of the hairpencil secretion of the male Queen butterfly (*Danaus gilippus berenice*). Masaki et al. synthesized **189** (contaminated with 11% of its 6*Z*-isomer), starting from geraniol (Scheme 661).[836]



Scheme 661

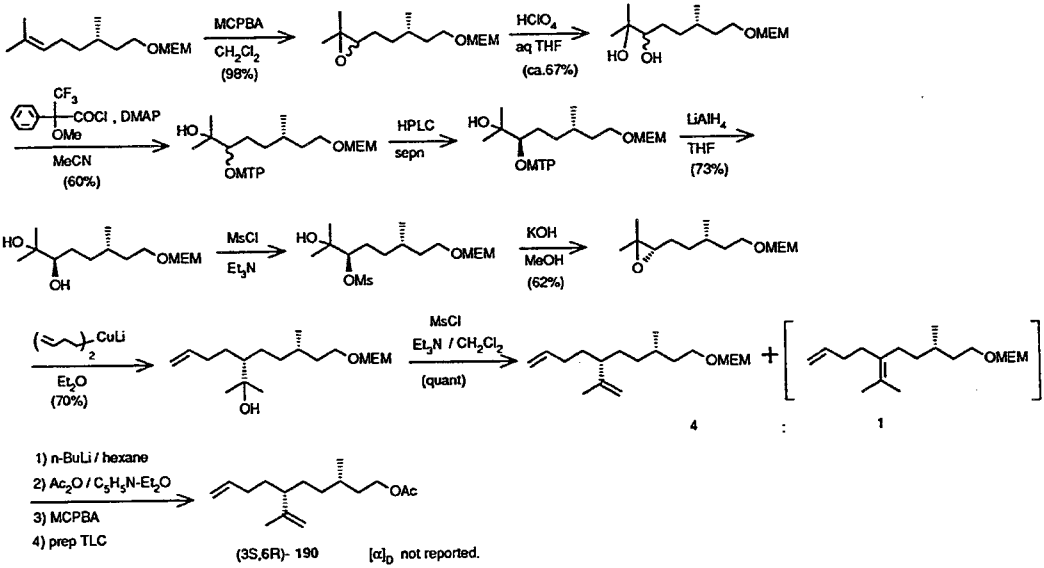
N. (3*S*,6*R*)-3-Methyl-6-isopropenyl-9-decenyl Acetate **190** ($C_{16}H_{28}O_2$) and (*R*,*Z*)-3-Methyl-6-isopropenyl-3,9-decadienyl Acetate **191** ($C_{16}H_{26}O_2$)

These are the pheromone components of the female California red scale (*Aonidiella aurantii*). Anderson et al. determined the absolute configuration of **190** as 3*S*,6*R* in the following manner.[837] First, a mixture of all four diastereomers of **190** was prepared from (±)-citronellol in four steps (Scheme 662);



Scheme 662

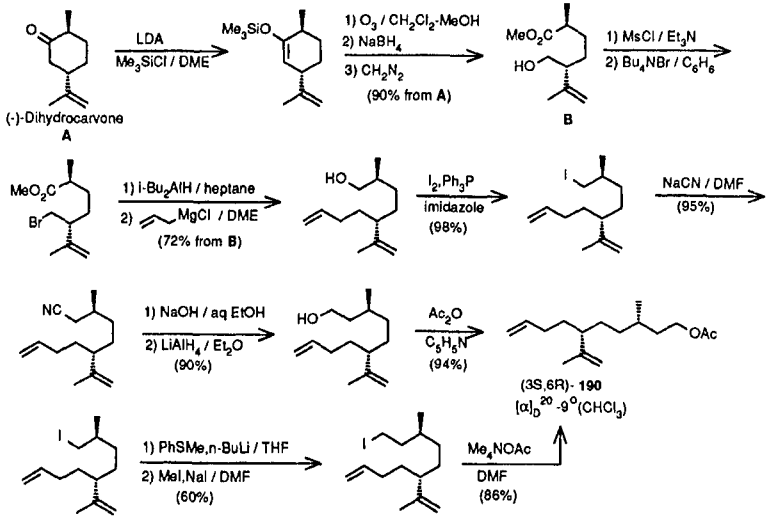
this mixture was bioactive. Then, (3*S*,6*RS*)- **190** and (3*R*,6*RS*)-**190** were synthesized by the same method as shown in Scheme 663, starting from (*S*)- and


MCPBA
CH_2Cl_2
(98%)
$HClO_4$
aq THF
(ca.67%)
OMEM
HO OH
CF_3
COCl , DMAP
OMe
MeCN
(60%)
OMTP
HPLC
sepn
$LiAlH_4$
THF
(73%)
MsCl
Et_3N
OMs
KOH
MeOH
(62%)
CuLi
Et_2O
(70%)
OH
MsCl
Et_3N / CH_2Cl_2
(quant)
4 : 1
1) n-BuLi / hexane
2) Ac_2O / C_5H_5N-Et_2O
3) MCPBA
4) prep TLC
OAc
(3S,6R)- 190
$[\alpha]_D$ not reported.

Scheme 663

(*R*)-citronellol, respectively. Only (3*S*,6*RS*)-**190** was bioactive. Finally, starting from (*S*)-citronellol, both (3*S*,6*R*)-**190** and (3*S*,6*S*)-**190** were synthesized (Scheme 663), and the former was shown to be more active than the latter. The natural pheromone was identical to (3*S*,6*R*)-**190** by capillary GLC. The by-product with a tetrasubstituted double bond was removed by epoxidation, followed by preparative TLC.[837]

(−)-Dihydrocarvone was converted to (3*S*,6*R*)-**190** by Baudouy and Maliverney (Scheme 664).[838] In this synthesis, the two chiral centers of the starting

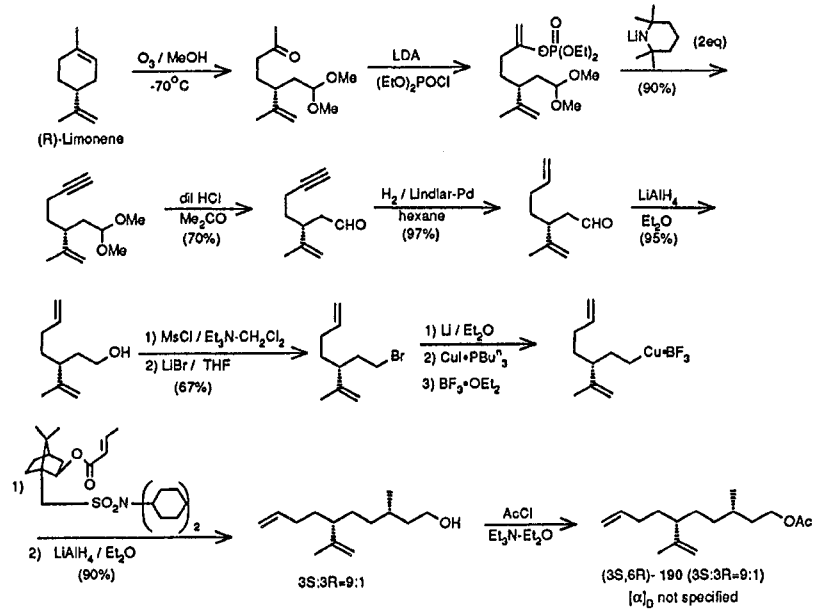


Scheme 664

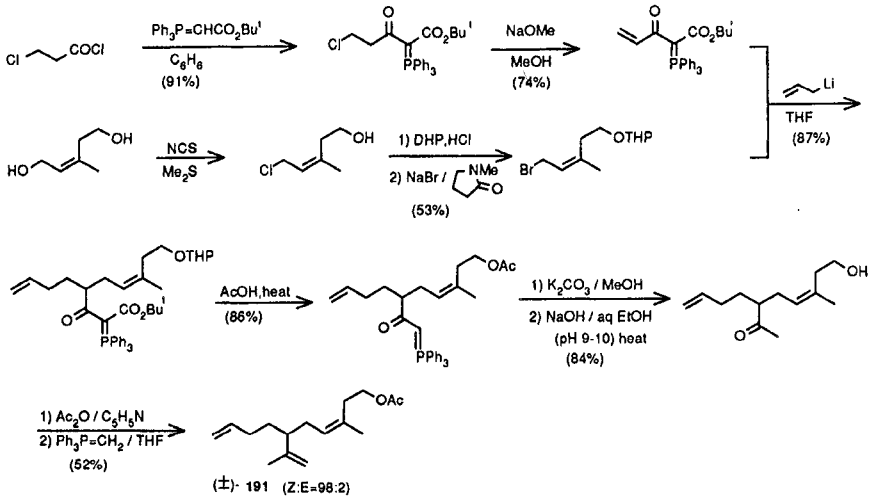
material were brought into the final product, thus eliminating the tedious separation problem in the course of the synthesis. Becker and Sahali started from (*R*)-limonene and prepared (3*S*,6*R*)-**190** (Scheme 665).[839] The asymmetric Michael reaction yielded the adduct with 80% d.e., which gave (3*S*,6*R*)-**190** of 90% purity. Dragan et al. also reported a synthesis of **190**.[840]

Since 1979, nine new syntheses of (±)-**191** or (*R*)-**191** have been reported. Cooke and Burman prepared (±)-**191** by using an unsaturated acylphosphorane (Scheme 666).[841] A very short synthesis of (±)-**191** was reported by Celebuski and Rosenblum employing an organoiron reagent (Scheme 667).[842]

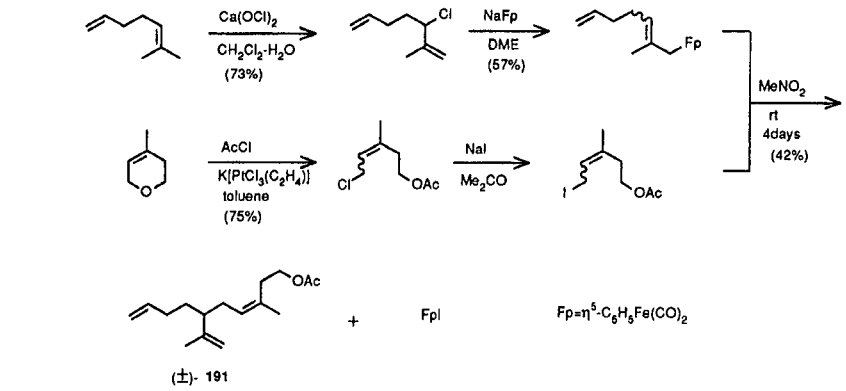
Four out of the seven enantioselective syntheses of (*R*,*Z*)-**191** employed optically active monoterpenes as the starting materials. (*S*)-(+)-Carvone was converted to (*R*,*Z*)-**191** by Caine and Crews as shown in Scheme 668.[843] Hutch-



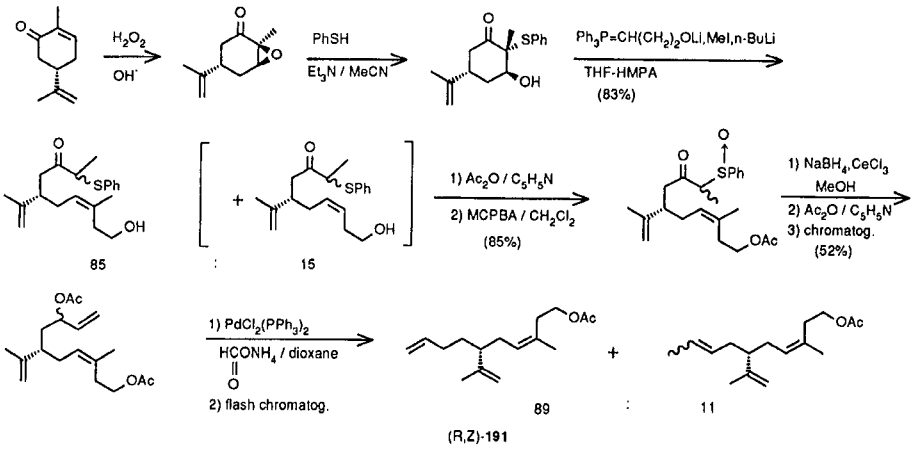
Scheme 665



Scheme 666



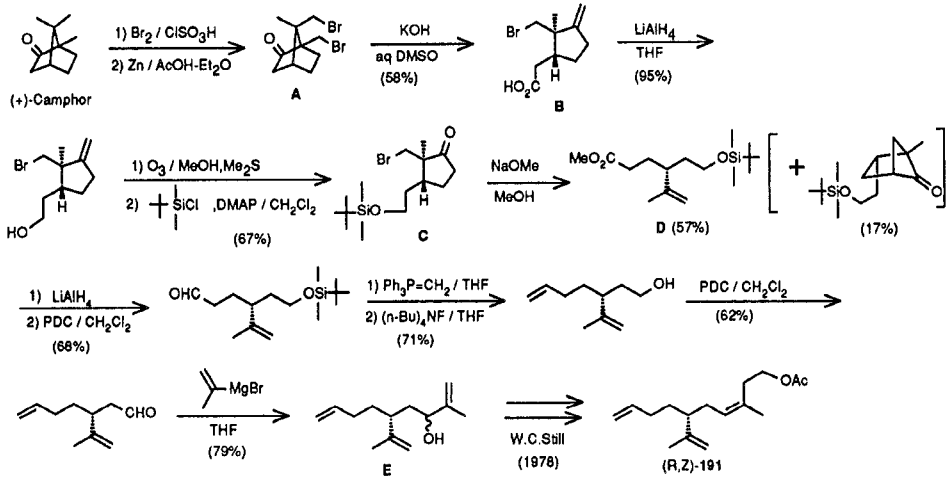
Scheme 667



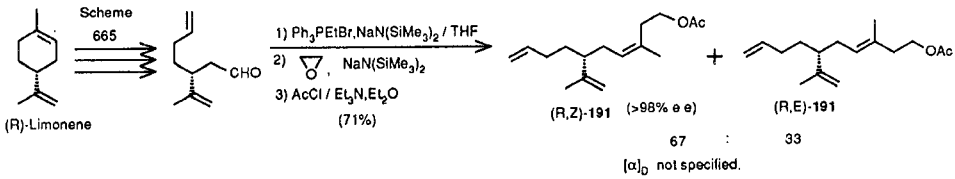
Scheme 668

inson and Money started from (+)-camphor, and an acyclic intermediate **D** was obtained after two-ring cleavage reactions (Scheme 669, **A** → **B** and **C** → **D**).[844] Their synthesis was completed at the stage of **E**, which had been converted to **191** previously (Scheme 193, Ref. 1). By employing (*R*)-limonene as the starting material, Becker and Sahali synthesized a 67:33 mixture of (*R*,*Z*)-**191** and (*R*,*E*)-**191** (Scheme 670).[839] (*R*)-Limonene was converted by Baudouy and Prince to (*R*,*Z*)-**191** in 25% overall yield (Scheme 671).[845] Their synthesis afforded a final product of high purity. Especially noteworthy is the stereoselective elaboration of the (*Z*)-trisubstituted double bond of **191**.

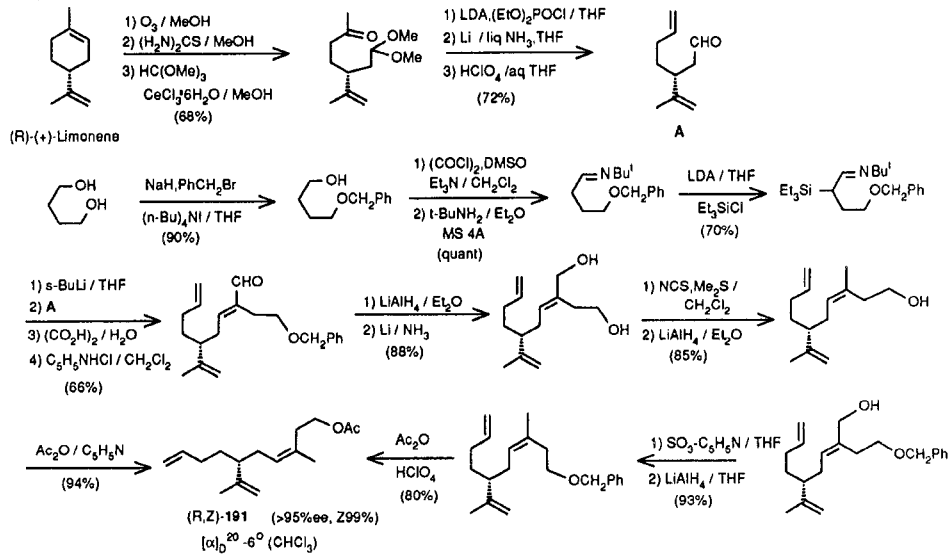
Three papers have appeared on the chemical asymmetric syntheses of



Scheme 669

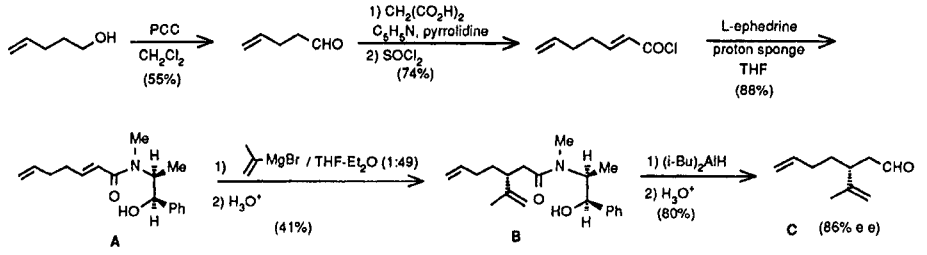


Scheme 670

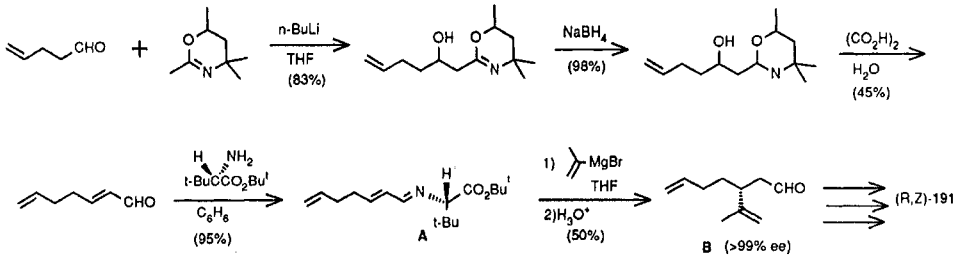


Scheme 671

(*R*,*Z*)-**191.** In the synthesis by Leznoff et al., an aldehyde (**C** in Scheme 672 and **B** in Scheme 673) was chosen as the key intermediate.[846] Mukaiyama's



Scheme 672

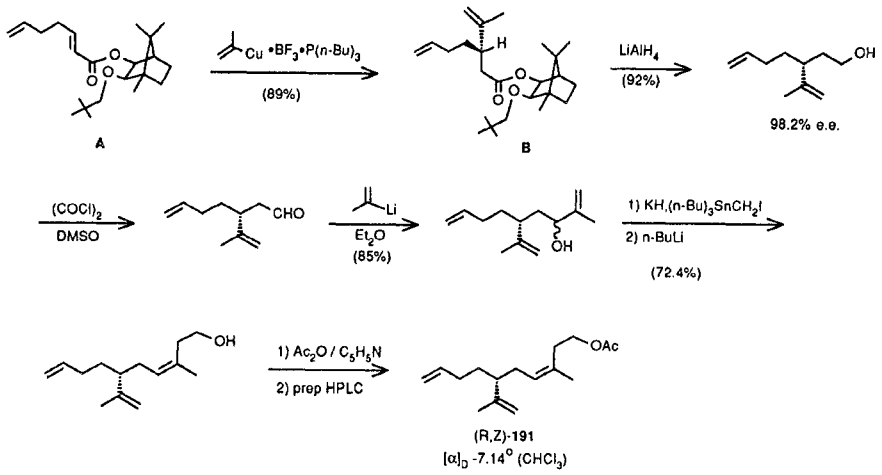


Scheme 673

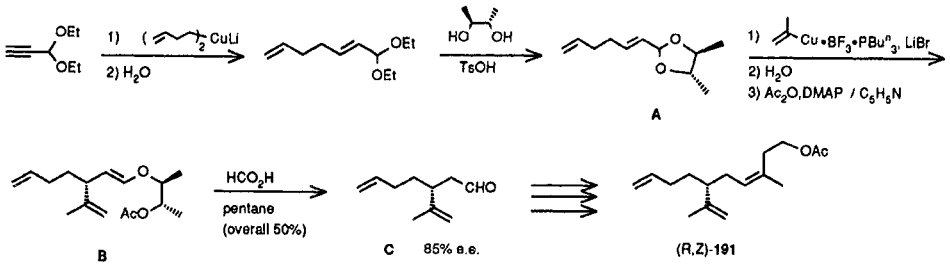
asymmetric Michael addition using (−)-ephedrine as the chiral auxiliary was first tried in yielding (*R*)-aldehyde of 86% e.e. (Scheme 672).[846] The key-step was the Michael addition of isopropenylmagnesium bromide to **A** yielding **B,** which was hydrolyzed to **C.** Then Koga's method for the Michael addition by using the aldimine **A** was tested, giving (*R*)-aldehyde of > 99% e.e. (Scheme 673).[846] Conversion of the aldehyde to **191** was known. Oppolzer and Stevenson synthesized (*R*,*Z*)-**191** by asymmetric 1,4-addition of isopropenylcopper to a chiral enoate **A** to give **B** as the key-step (Scheme 674).[847] Addition of isopropenylcopper to chiral α,β-unsaturated acetal **A** to give **B** was the key-step of the synthesis of aldehyde **C** by Mangeney et al. (Scheme 675).[848] A new synthesis of (±)-**191** was briefly discussed by Cohen.[849]

O. (*S*,*E*)-3,9-Dimethyl-6-isopropyl-5,8-decadienyl Acetate 192 ($C_{17}H_{30}O_2$)

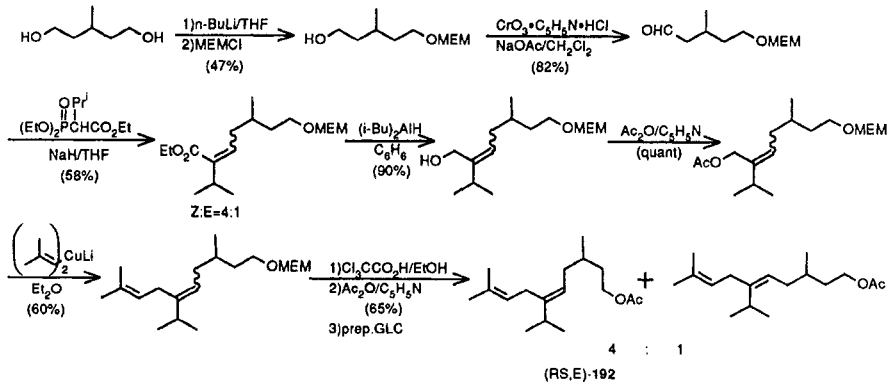
This is the sex pheromone of the yellow scale (*Aonidiella citrina*). The first synthesis of (±)-**192** was reported by Anderson and Henrick (Scheme 676).[850]



Scheme 674



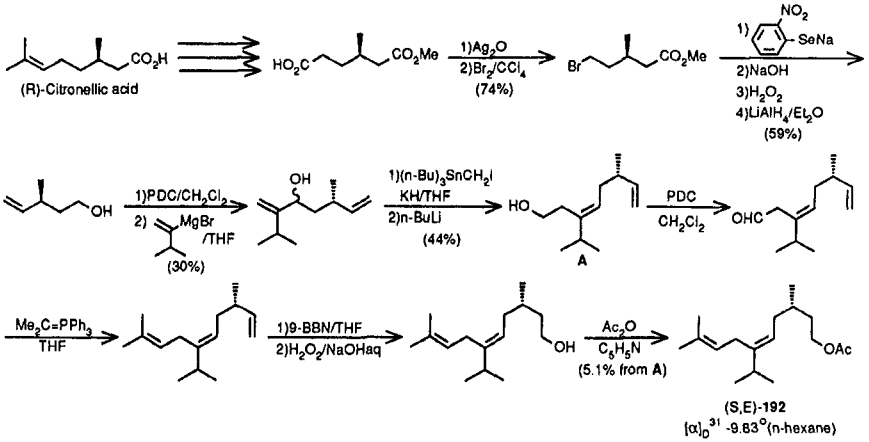
Scheme 675



Scheme 676

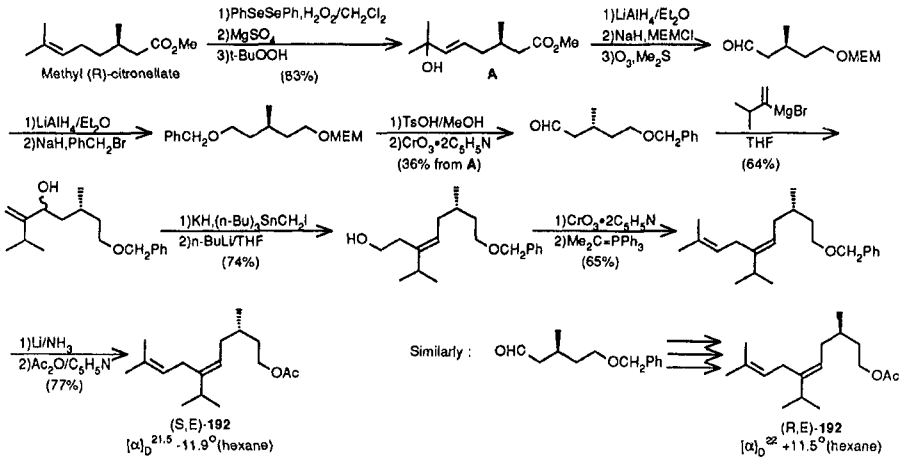
GLC purification of the final product was followed by bioassay to prove (*RS*,*E*)-**192** as bioactive.[850] A synthesis of (*RS*,*E*)-**192** and (*RS*,*Z*)-**192** (Scheme 194, Ref. 1) was published in full detail.[851]

Three enantioselective syntheses of (*S*,*E*)-**192** have been reported. Mori's first synthesis began with (*R*)-citronellic acid and employed Still's [2.3]Wittig rearrangement as the key-step to generate the *E*-double bond (Scheme 677).[852]



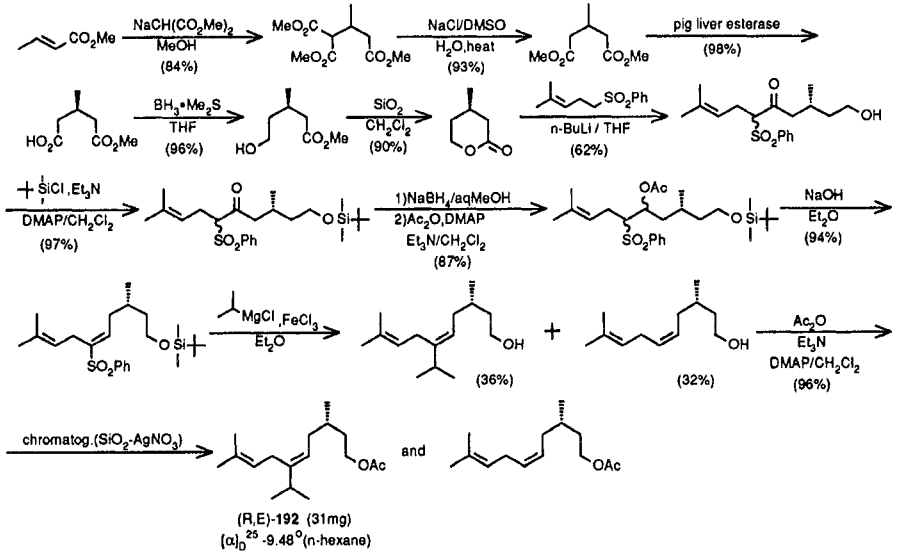
Scheme 677

The overall yield of this synthesis, however, was poor. The second and improved synthesis of **191** by Mori and Kuwahara (Scheme 678) was more effi-



Scheme 678

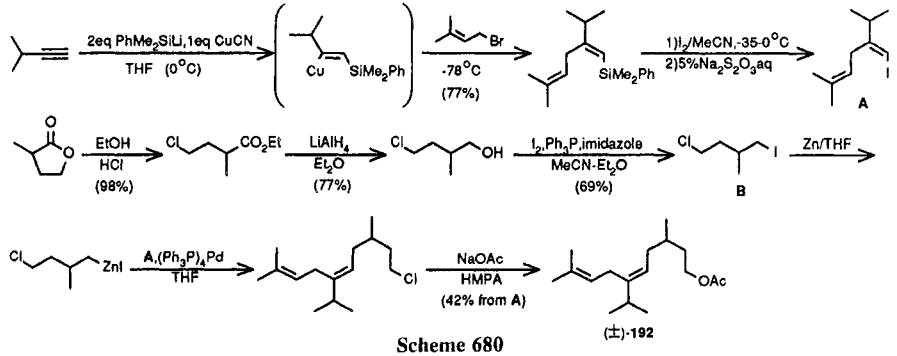
cient, and furnished (*R*,*E*)-**192** and (*S*,*E*)-**192** in 10% and 7% overall yield, respectively, from methyl (*R*)-citronellate.[853] The enantiomers of **192** were tested on the yellow scale and only the *S*-enantiomer was shown to be bioactive.[854] In Julia's synthesis of (*R*,*E*)-**192** (Scheme 679), the key-step was the



Scheme 679

introduction of the isopropyl group by the stereoselective cross-coupling reaction of the diene sulfone with isopropylmagnesium chloride in the presence of ferric chloride.[855]

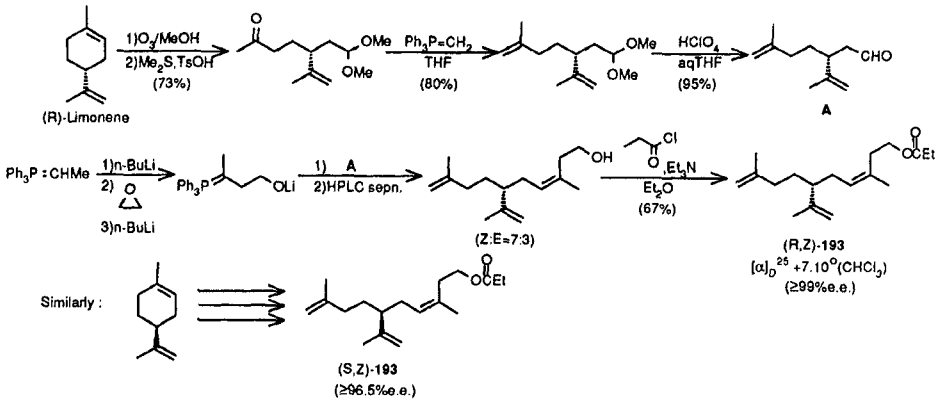
A new synthesis of (*RS*,*E*)-**192** was recently reported by Millar using silylcupration of an alkyne as the beginning step to construct the trisubstituted double bond (Scheme 680).[856]



Scheme 680

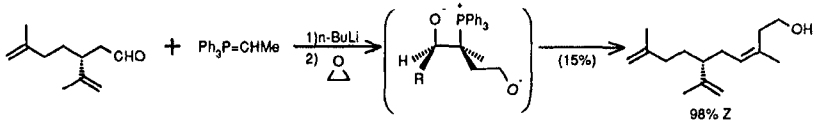
P. (*R*,*Z*)-3,9-Dimethyl-6-isopropenyl-3,9-decadienyl Propanoate 193 ($C_{18}H_{30}O_2$)

This is the female-produced sex pheromone of the white peach scale (*Pseudaulacaspis pentagona*).[857] Starting from the enantiomers of limonene, Heath et al. synthesized all of the stereoisomers of **193** (Scheme 681) and found (*R*,*Z*)-**193**



Scheme 681

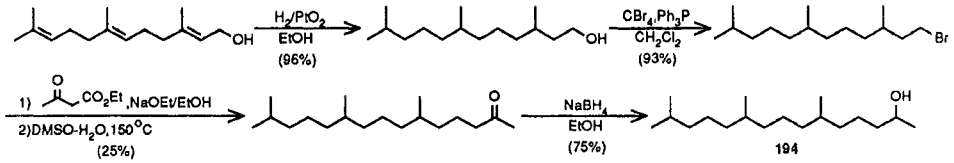
to be bioactive.[857,858] They also achieved the selective construction of the trisubstituted (*Z*)-double bond (Scheme 682).[858]



Scheme 682

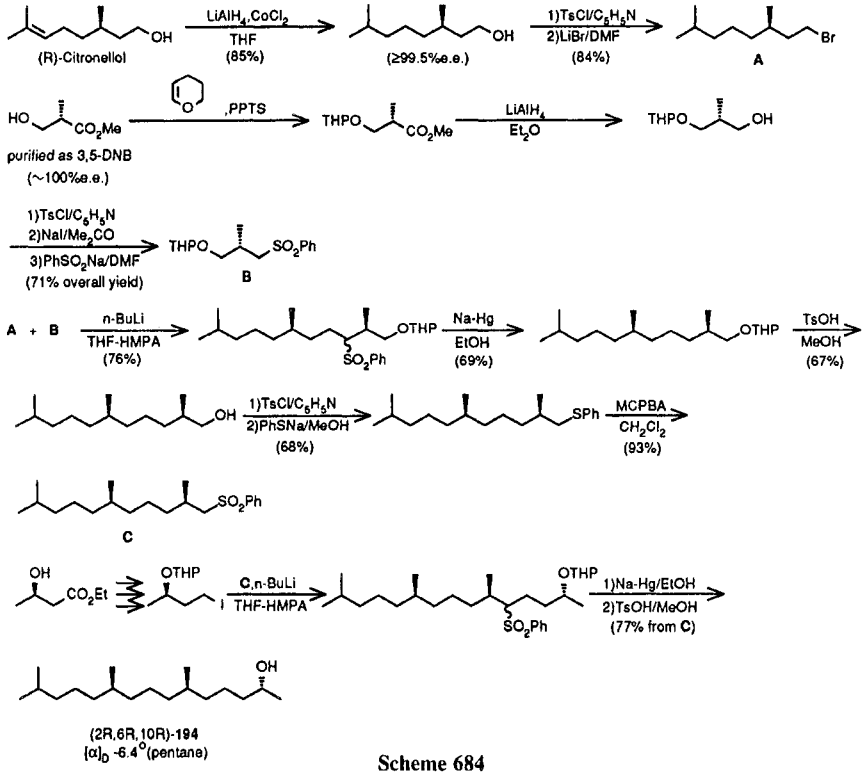
Q. 6,10,14-Trimethyl-2-pentadecanol 194 ($C_{18}H_{38}O$)

This is the female-produced sex pheromone of the rice moth (*Corcyra cephalonica*).[859] A synthesis of **194,** which resulted in the preparation of a mixture of all of the eight possible stereoisomers, was achieved by Hall et al. (Scheme 683).[859] The synthetic stereoisomeric mixture of **194** significantly attracted the male moths at 2 ng level. The enantioselective synthesis of four out of the eight stereoisomers of **194** was carried out by Mori et al. employing (*R*)-citronellol, methyl (*R*)- or (*S*)-3-hydroxy-2-methylpropanoate, and ethyl (*R*)- or (*S*)-3-hy-



Scheme 683

droxybutanoate as the chiral building blocks.[860] Scheme 684 illustrates the synthesis of (2*R*,6*R*,10*R*)-**194**, which is as active as the natural pheromone.[860]

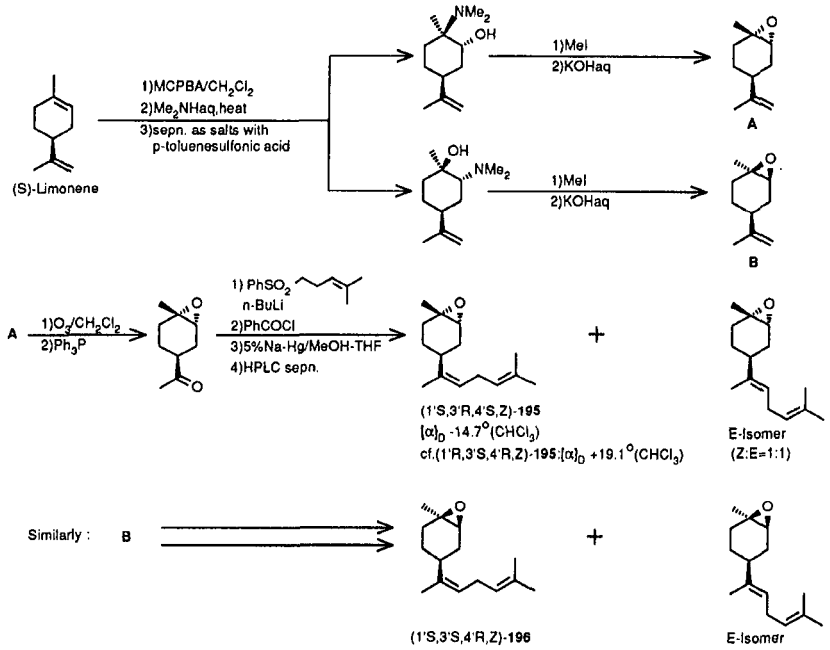


Scheme 684

R. (1′*S*,3′*R*,4′*S*,*Z*)-2-(3′,4′-Epoxy-4′-methylcyclohexyl)-6-methylhepta-2,5-diene 195 ($C_{15}H_{24}O$) and Its (3′*S*,4′*R*)-Isomer 196

This is the male-produced sex pheromone of the green stink bug (*Nezara viridula*).[861,862] The Brazilian population of *N. viridula* employs *trans*-epoxide **195**

as its pheromone,[861] while the ratio of **195** to **196** from the Japanese *N. viridula* was essentially 1 : 1, as compared to the 3 : 1 ratio for the U.S. *N. viridula*.[862] Synthesis of the eight possible stereoisomers of **195** by Baker et al. was followed by their bioassay against the Brazilian population of the stink bug to demonstrate the natural pheromone as **195**.[861] Baker's synthesis of **195** and **196** is shown in Scheme 685.[861] Marron and Nicolaou also prepared the enantiomers



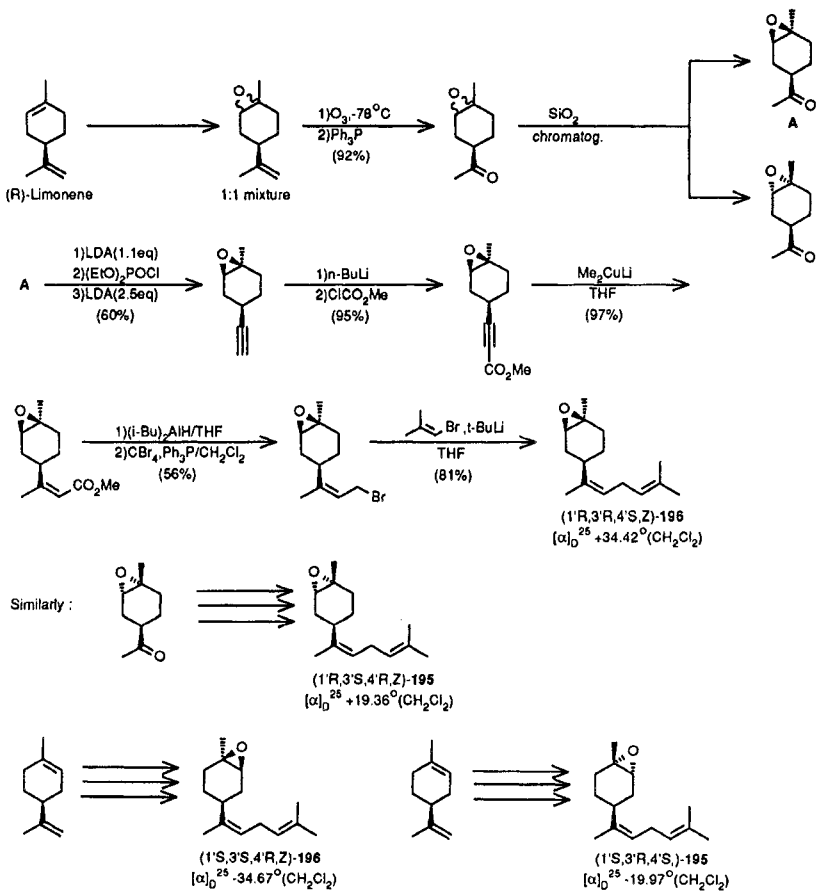
Scheme 685

of both **195** and **196** starting from the enantiomers of limonene oxide (Scheme 686).[863]

18. ISOPRENOID ALDEHYDES, KETONES, ACIDS, ESTERS, AND LACTONES AS PHEROMONES

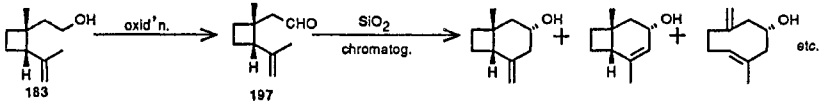
A. Grandisal (*cis*-1-Isopropenyl-1-methylcyclobutaneethanal) 197 ($C_{10}H_{16}O$)

This is a component of the male-produced aggregation pheromone of the northern pine weevil (*Pissodes approximatus*),[864] Engelmann spruce weevil (*P.*



Scheme 686

strobi),[864] and deodar weevil (*P. nemorensis*),[865] together with grandisol **(183).** Grandisol **(183)** can be oxidized to grandisal **(197),** but the attempted purification of (±)-**197** by silica gel chromatography resulted in severe decomposition (Scheme 687).[866]

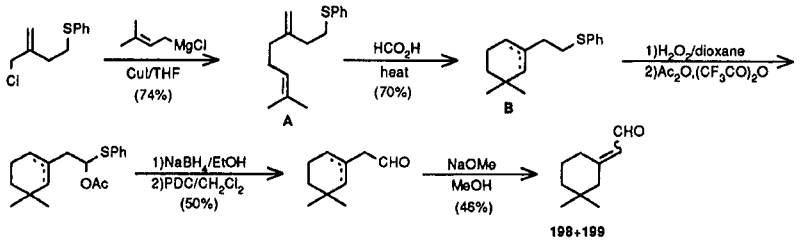


Scheme 687

B. (*E*)-2-Ochtoden-1-al [(*E*)-3,3-Dimetyl-$\Delta^{1,\beta}$-cyclohexaneethanal] **198** ($C_{10}H_{16}O$) and (*Z*)-2-Ochtoden-1-al **199** ($C_{10}H_{16}O$)

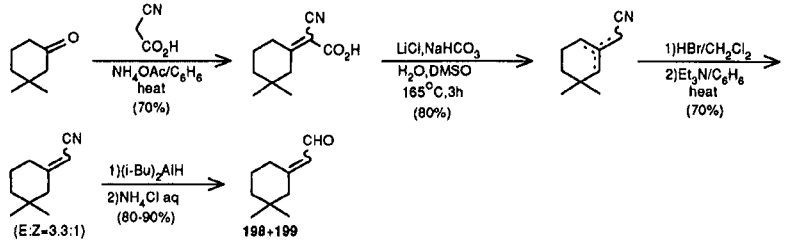
These two are the components of the male-produced sex pheromone of the boll weevil (*Anthonomus grandis*). Recently, Dickens and Prestwich suggested that **199** is not essential for attraction of the boll weevil.[867]

Several new syntheses of **198** and **199** have been published since 1979. Masaki et al. prepared a 75:25 mixture of **198** and **199** by oxidizing the corresponding alcohol mixture **(187)** with manganese dioxide (Scheme 654).[830,831] The key-step of Mandai's synthesis of a mixture of **198** and **199** was the cyclization of sulfide **A** to **B** (Scheme 688).[868] Ghosh et al. synthesized a mixture



Scheme 688

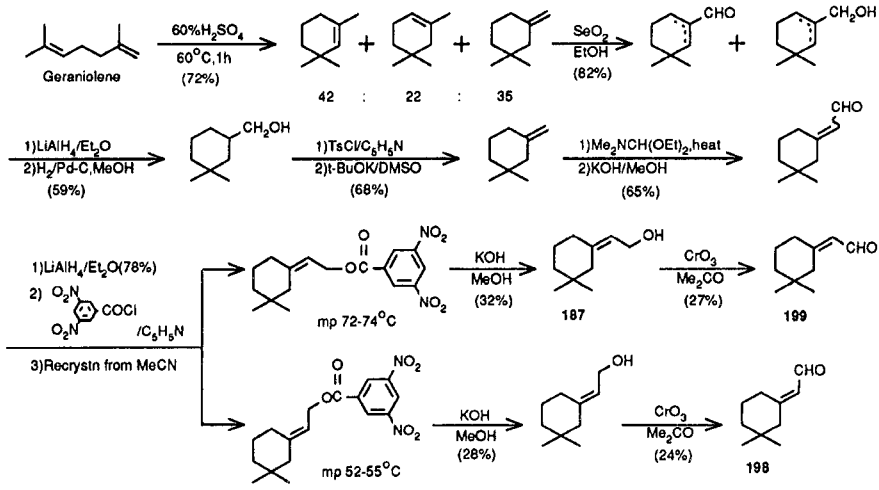
of **198** and **199** starting from 3,3-dimethylcyclohexanone (Scheme 689).[869] Ger-



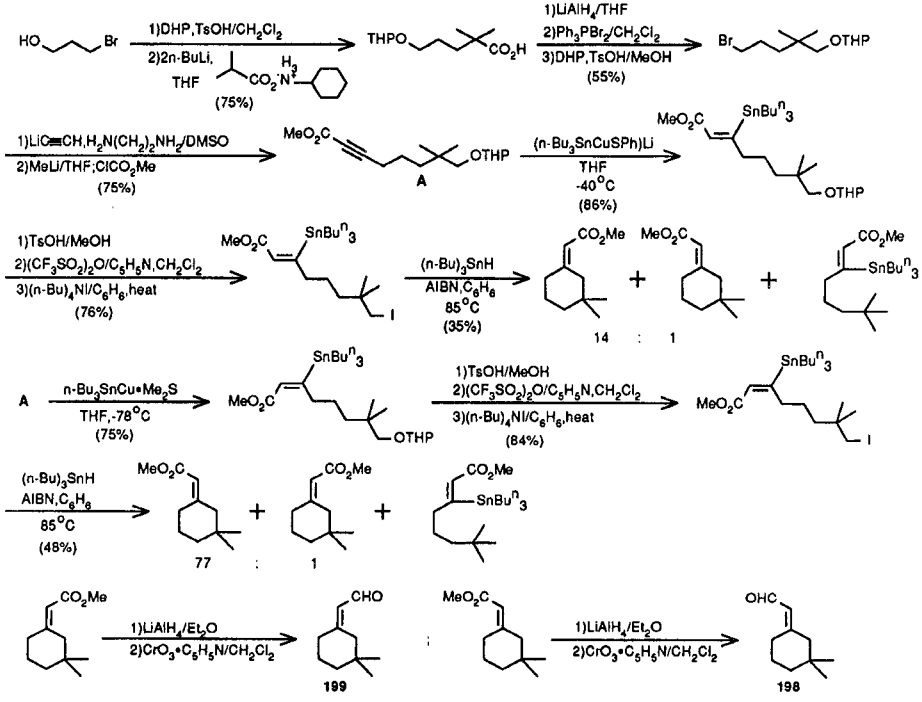
Scheme 689

aniolene was the starting material for Nomura and Fujihara's synthesis of **198** and **199** (Scheme 690).[870] They found it possible to separate the 3,5-dinitrobenzoates of **187** and its *E*-isomer by recrystallization, and therefore, they were able to prepare pure **198** and **199.** Mori and Itou prepared pure **198** and **199** by oxidizing (*E*)-**187** and (*Z*)-**187** as shown in Scheme 655.[832]

A stereoselective synthesis of these aldehydes was reported by Harris and Weiler by means of a radical cyclization-elimination reaction to selectively generate exocyclic alkenes (Scheme 691).[871] Negishi et al. treated 7-bromo-2-io-

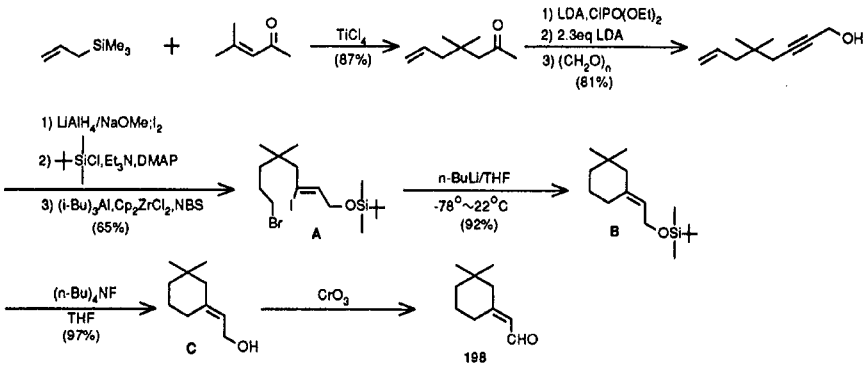


Scheme 690



Scheme 691

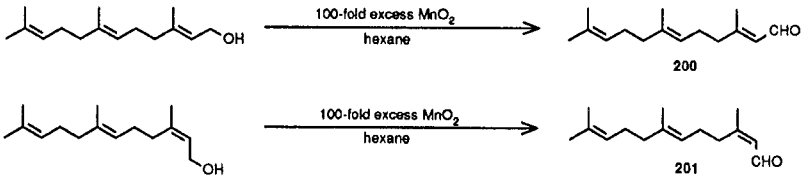
doalkene **A** with *n*-butyllithium to effect the stereoselective cyclialkylation reaction yielding **B**, which was converted to (*E*)-alcohol **C** (Scheme 692).[872]



Scheme 692

C. (*E*,*E*)-Farnesal [(2*E*,6*E*)-3,7,11-Trimethyldodeca-2,6,10-trienal] **200** ($C_{15}H_{24}O$) and Its (2*Z*,6*E*)-Isomer **201**

A blend of **200** and **201** was isolated as a male wing-gland pheromone of the rice moth (*Corcyra cephalonica*), which induces the attraction of female moths.[873] Both **200** and **201** were prepared by oxidation of (*E*,*E*)-farnesol and its (*Z*,*E*)-isomer (Scheme 693).[873] (*Z*,*E*)-Farnesal **(201)** readily isomerizes to **200.**



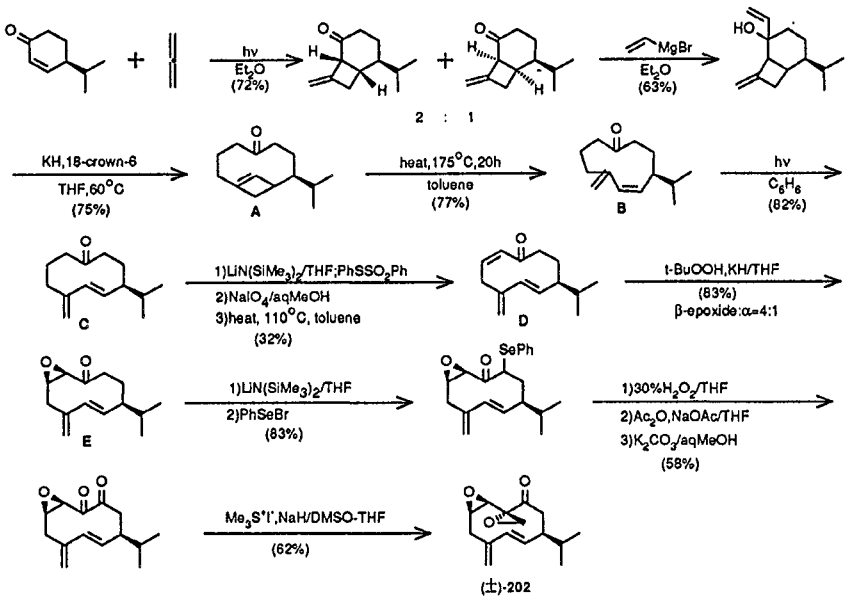
Scheme 693

D. (−)-Periplanone-B **202** ($C_{15}H_{20}O_3$)

This is one of the two major pheromone components produced by female American cockroaches (*Periplaneta americana*). Since the first synthesis of **202** by W.C. Still in 1979 (Scheme 281, Ref. 1), four syntheses of (±)-**202** and two syntheses of the natural enantiomer (−)-**202** have been published.

(1) Syntheses of (±)-Periplanone-B

The cyclobutene-bridgehead olefin route (Scheme 694) was developed by Schreiber and Santini.[874] In this synthesis, cyclobutene-bridgehead olefin **A** was

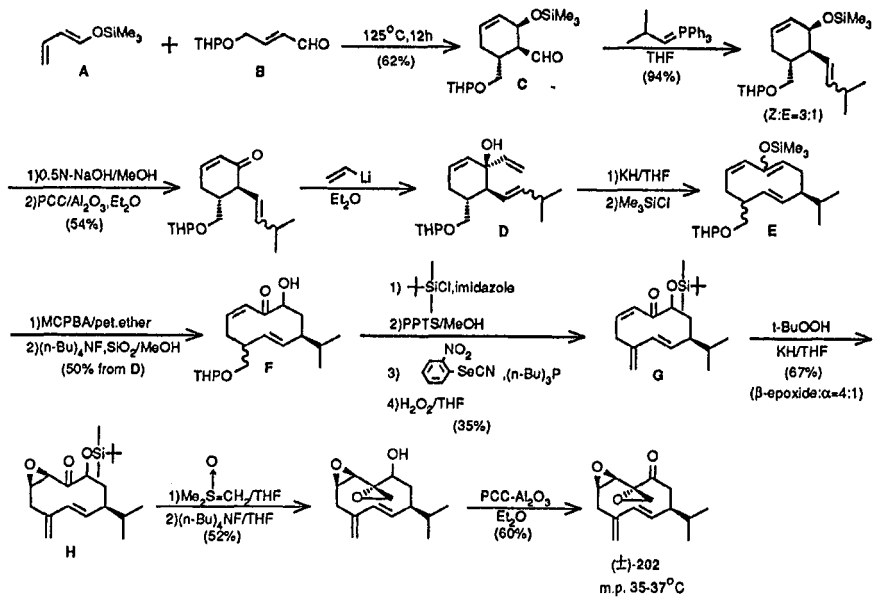


Scheme 694

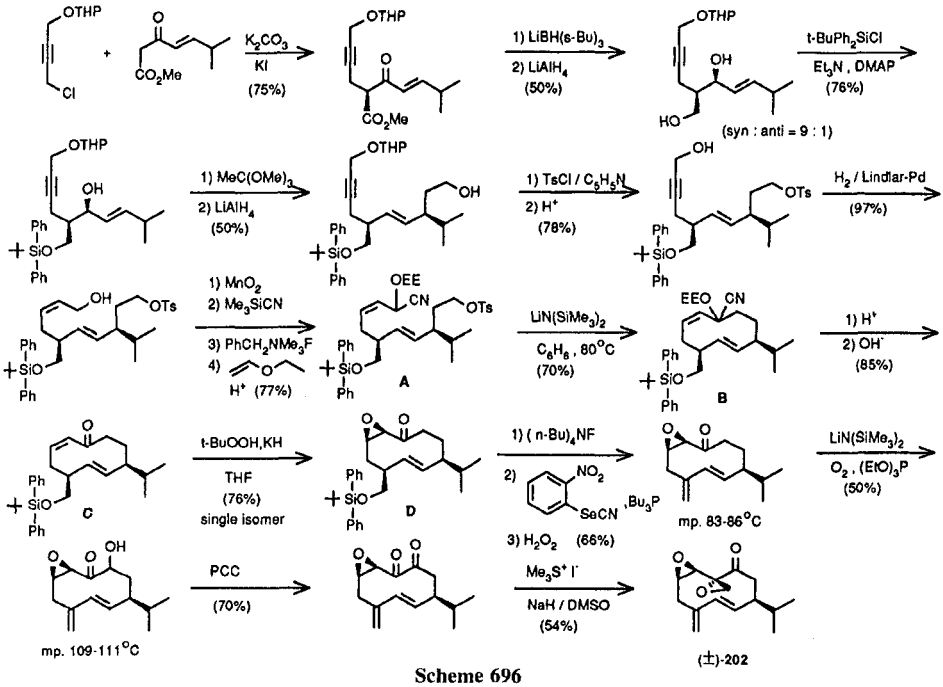
thermolyzed to *cis*-diene **B**, photoisomerization of which yielded *trans*-dienone **C**. The dienone **C** was further functionalized to give (±)-**202**. The overall yield of (±)-**202** by the Schreiber 13-step synthesis was 1.7%.[874]

Hauptmann et al. improved Still's first synthesis of **202** by the Diels-Alder synthesis (**A** + **B** → **C**) of **C**, from which the key-intermediate **D** for the oxy-Cope rearrangement (**D** → **E** → **F**) was prepared as shown in Scheme 695.[875] In this synthesis, (±)-**202** was obtained as crystals, and, therefore, it was possible to carry out its X-ray analysis. The overall yield of (±)-**202** by this route was 1% in 16 steps. In these two syntheses, the epoxidation of the α,β-unsaturated ketone (**D** → **E** in Scheme 694 and **G** → **H** in Scheme 695) was not highly selective, and yielded ca. 20% of the undesired α-epoxide.

Without recourse to the oxy-Cope rearrangement, Takahashi et al. constructed the 10-membered ring by the intramolecular alkylation (**A** → **B** in Scheme 696).[876] In their synthesis, the epoxidation step (**C** → **D**) was selective



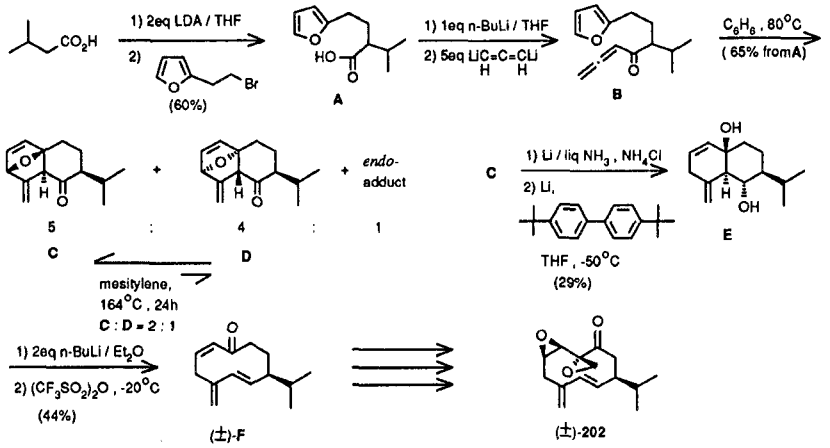
Scheme 695



Scheme 696

to give only the desired β-epoxide. The overall yield of (±)-**202** by the Takahashi 23-step synthesis was 0.5%.

Cauwberghs and De Clercq developed a formal synthesis of (±)-**202** via trienone **F**, which had been employed by Schreiber as the key-intermediate (Scheme 697).[877] Addition of dilithiated allene to **A** gave **B**, which was heated



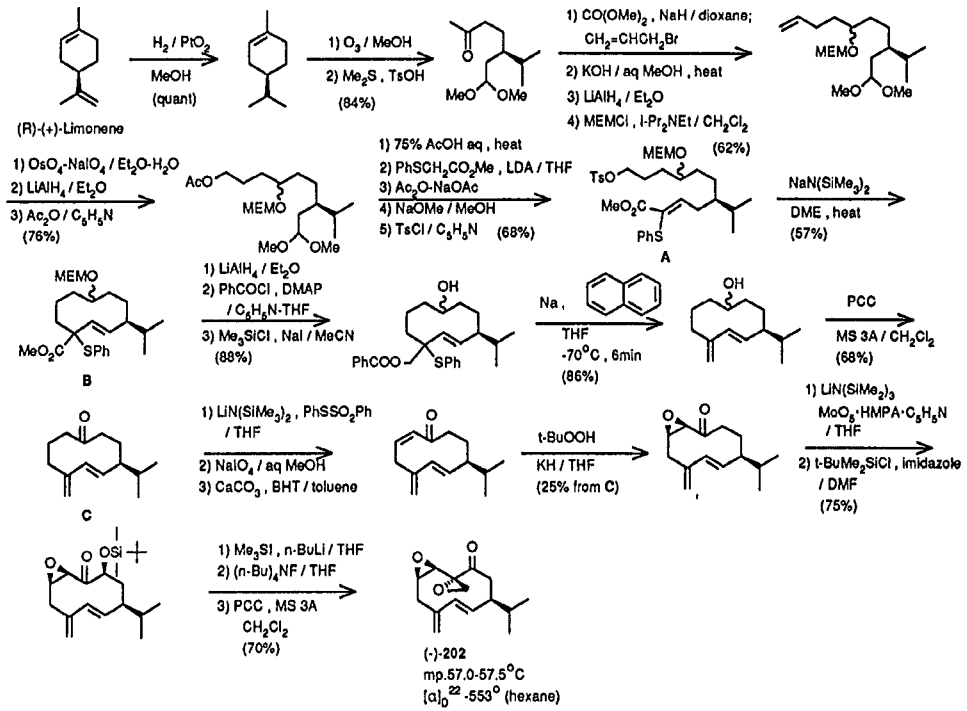
Scheme 697

to effect the intramolecular Diels-Alder reaction to give two *exo*-adducts, **C** and **D**. Subsequently, **C** was first reduced and then reductively cleaved to furnish **E**. The Grob fragmentation of **E** gave (±)-**F** in 4.2% overall yield. Schreiber and Santini converted (±)-**F** to (±)-**202** in 24.8% yield.[874] Therefore, the formal overall yield of (±)-**202** by the De Clercq synthesis was 1%.

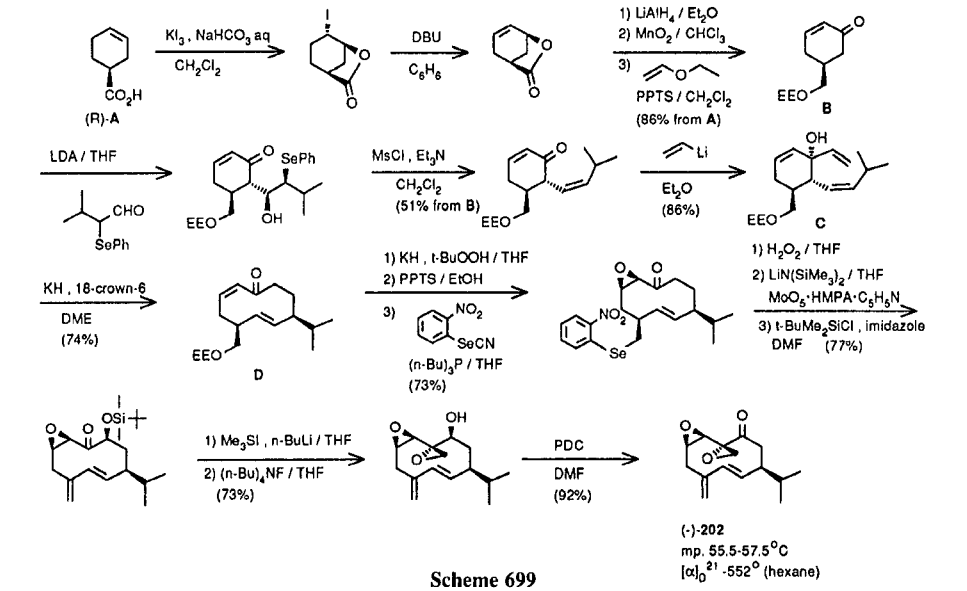
(2) Syntheses of (−)-Periplanone-B

Two different enantioselective syntheses of (−)-periplanone-**B** (**202** = naturally occurring enantiomer) were reported by Mori's group. In the first synthesis, (*R*)-(+)-limonene was chosen as the starting material, and the 10-membered ring was constructed by the intramolecular alkylation (**A** → **B**) as shown in Scheme 698.[878,879] **B** was then converted to ketone **C**, the (−)-enantiomer of the Schreiber intermediate, which finally furnished crystalline (−)-**202** in 0.5% overall yield via 29 steps from (*R*)-(+)-limonene.

In the second enantioselective synthesis, (−)-periplanone-B (**202**) was synthesized from (*S*)-(−)-3-cyclohexene-1-carboxylic acid (**A**) through 18 steps in 11% overall yield (Scheme 699).[880,881] The key-step was the oxy-Cope rear-



Scheme 698

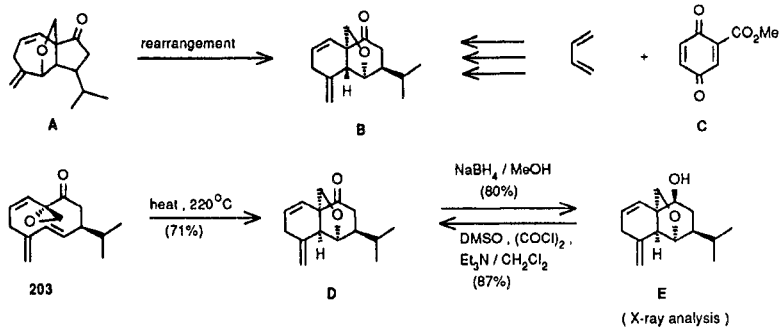


Scheme 699

rangement of **C** to give **D.** This efficient synthesis of (−)-**202** allowed the preparation of a substantial quantity of the crystalline pheromone.

E. (−)-Periplanone-A 203 ($C_{15}H_{20}O_2$)

This name was first given to a compound isolated by Persoons et al. for the pheromone component produced by female American cockroaches (*Periplaneta americana*). They proposed structure **A** for it (Scheme 700), and demonstrated its facile rearrangement to a stable and biologically inactive compound **B.**[882,883]

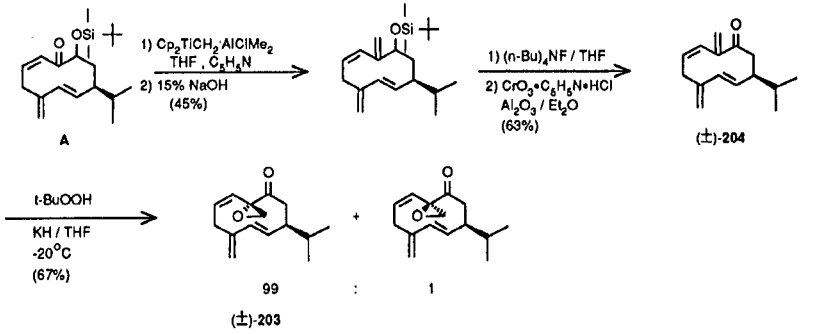


Scheme 700

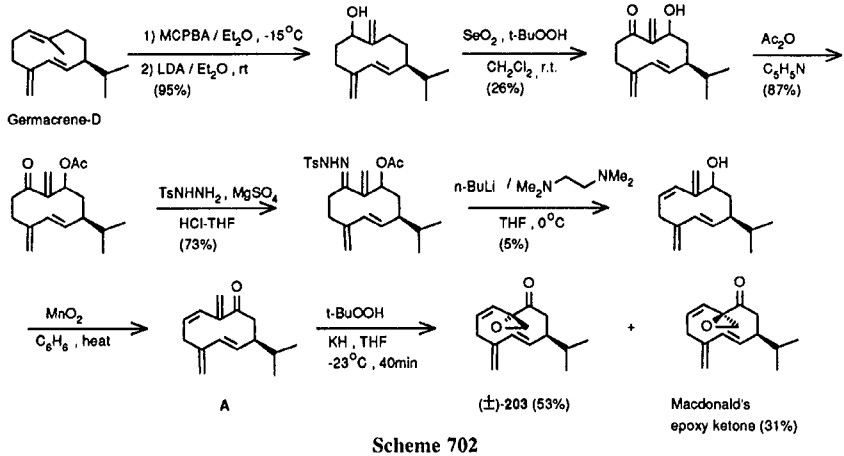
The structure **B** was supported by a synthesis of its racemate from **C** and 1,3-butadiene by Mori and Igarashi.[884] The true structure of Persoons's compound was shown to be not **A** but **D,** which was the thermal decomposition product of the genuine pheromone **203.**[885,1229] An X-ray analysis of **E** was the key in solving the problem.[885] The compound isolated by Persoons turned out to be biologically inactive, and, therefore, **D** was given the name isoperiplanone-A.[886] A concise review on this structural problem was described by Mori et al.[887]

In 1986, Hauptmann et al. isolated **203** from the American cockroach, named it periplanone-A, synthesized (±)-**203,** and found it to be bioactive.[888] Their synthesis started from the trienone **A** (Scheme 701),[888] which had served as an intermediate in Still's first synthesis of periplanone-B.[875,889]

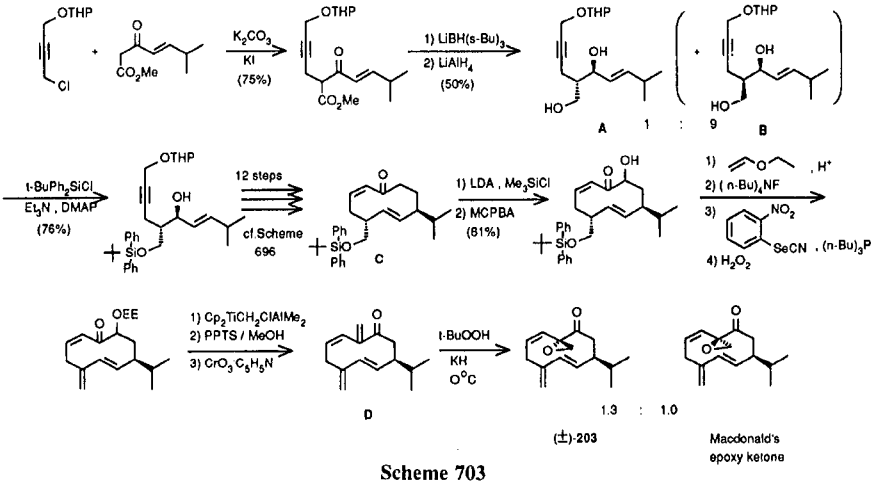
Two other syntheses of (±)-**203** have been reported. Shizuri et al. converted germacrene-D to tetraenone **A,** and epoxidized **A** as shown in Scheme 702.[890] In Shizuri's case, (±)-**203** and its epimer were obtained in a ratio of 1.7 : 1.0, while Hauptmann et al. reported a ratio of 99 : 1. Another synthesis of (±)-**203** was achieved by Takahashi et al. (Scheme 703).[891] In Takahashi's periplanone-B synthesis,[876] diol **B** was used as the intermediate. Its *anti*-isomer **A** was also



Scheme 701

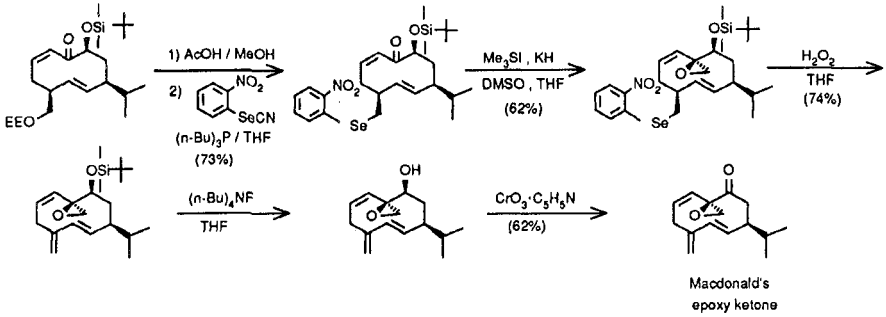


Scheme 702



Scheme 703

obtained as the minor product. This isomer **A** was converted to ketone **C** in the same manner as in the case of the synthesis of (±)-periplanone-B. The ketone **C** was further manipulated to give tetraenone **D,** the intermediate common to others.[888,890] Epoxidation of **D** yielded a 1.3:1.0 mixture of (±)-**203** and its epimer, which is in accord with Shizuri's result.[890] The epimer of (±)-**203** was first synthesized by Macdonald et al., starting from Still's intermediate (Scheme 704).[892] The epimer, which was called Macdonald's epoxy ketone, was biologically inactive.



Scheme 704

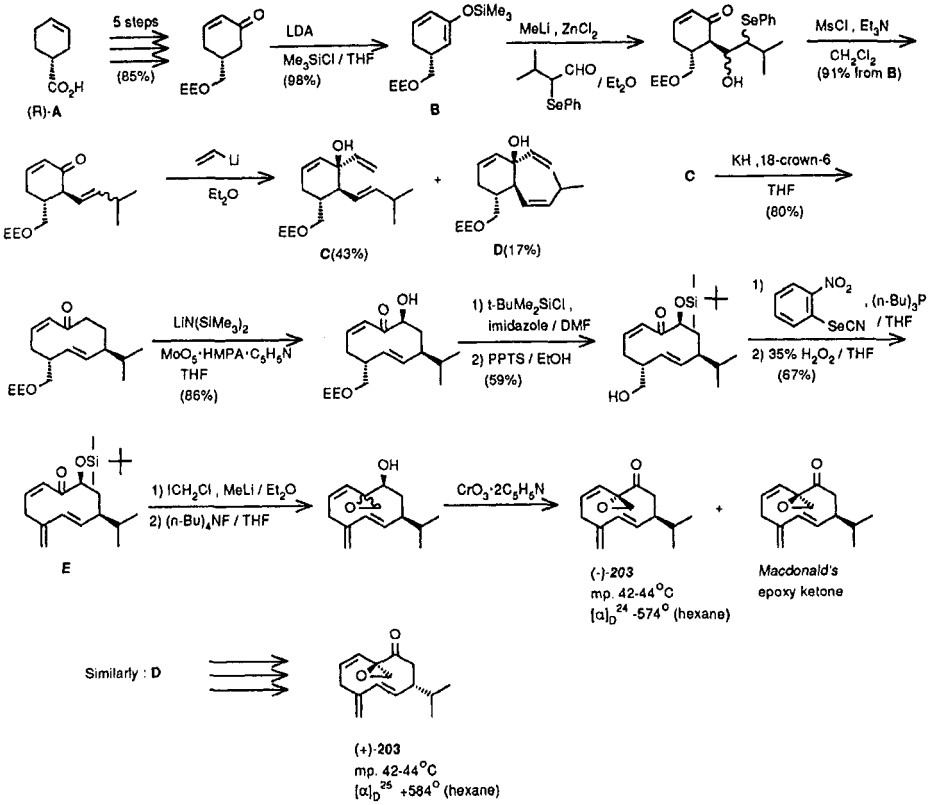
Kuwahara and Mori achieved an enantioselective synthesis of both the enantiomers of periplanone-A **(203)** and proved only (−)-**203** to be bioactive.[887,1229] Their synthesis (Scheme 705) furnished both the enantiomers of **203** as crystals.

Nishino et al. showed that periplanone-A[(−)-**203**] and periplanone-B[(−)-**202**] participate specifically with the corresponding sex pheromone receptors.[893]

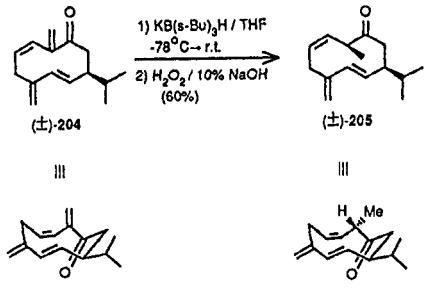
F. Periplanone-C 204 ($C_{15}H_{20}O$) and Periplanone-D 205 ($C_{15}H_{22}O$)

These two compounds are minor and less bioactive components of the female-produced sex pheromone of the American cockroach (*Periplaneta americana*). These were originally called periplanone-D_1 and periplanone-D_2, respectively,[894] but were later given their present names.[886]

(±)-Periplanone-C **(204)** was an intermediate of Hauptmann's synthesis of (±)-periplanone-A **(203,** (Scheme 701).[888] Reduction of (±)-**204** yielded (±)-periplanone-D **(205,** Scheme 706).[894]



Scheme 705

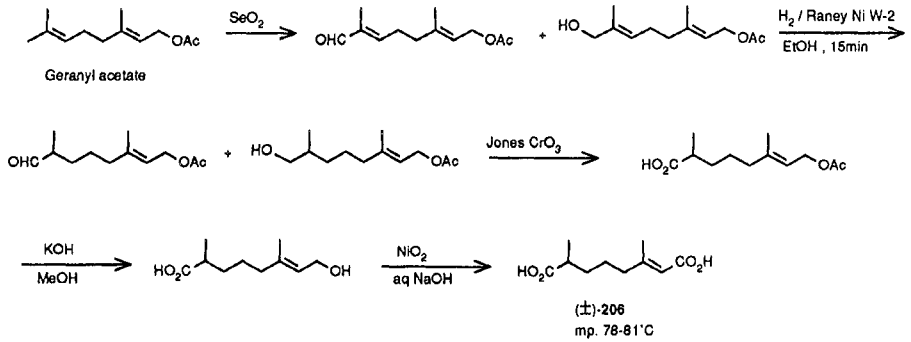


Scheme 706

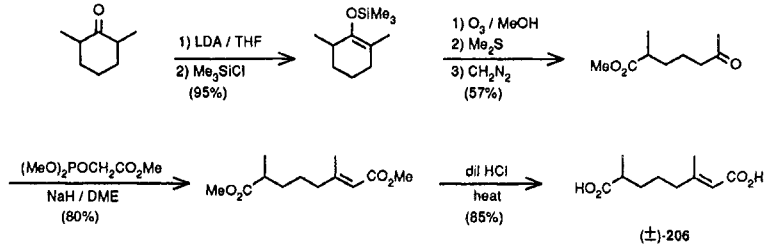
G. Callosobruchusic Acid [(*E*)-3,7-Dimethyl-2-octene-1,8-dioic Acid] 206 ($C_{10}H_{16}O_4$)

In 1981 Yamamoto and his co-workers isolated and identified the copulation release pheromone of the azuki bean weevil (*Callosobruchus chinensis*), which induces the male to extrude his genital organ and attempt copulation.[895] They named it erectin and found it to consist of two synergistically acting fractions. One was a mixture of methyl-branched hydrocarbons such as 11,15-dimethyltritriacontane. The other was callosobruchusic acid **(206).**[895]

Two syntheses of (±)-**206** have been reported. Tanaka et al. converted geranyl acetate into (±)-**206** as shown in Scheme 707.[896] Kang and Lee synthesized (±)-**206** starting from 2,6-dimethylcyclohexanone (Scheme 708).[897]

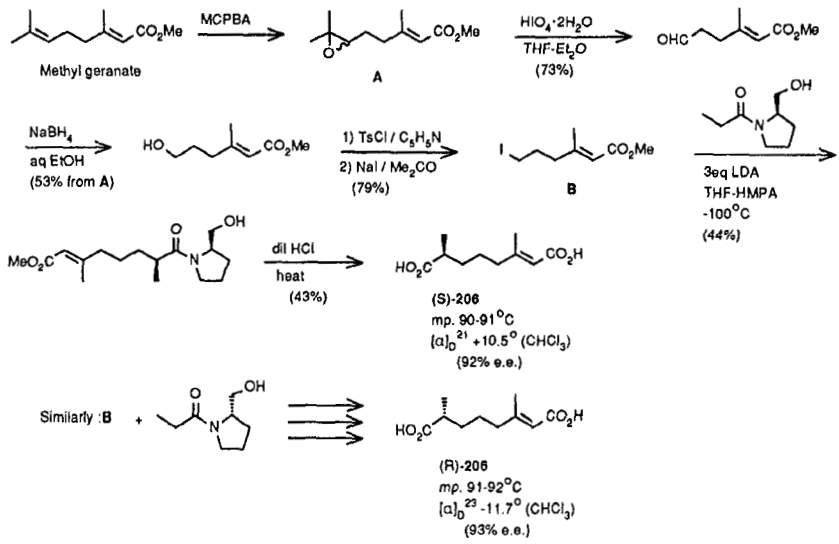


Scheme 707



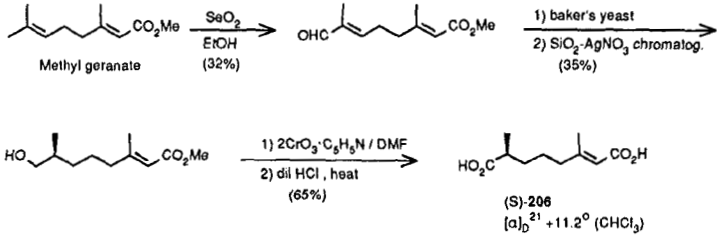
Scheme 708

Mori et al. prepared both the enantiomers of **206** by employing the asymmetric alkylation procedure developed by Evans (Scheme 709).[898] Starting from methyl 6,7-epoxygeranate **(A),** iodide **B** was synthesized, and it was used for the asymmetric alkylation of prolinol propanamide. Although (*S*)-**206** was about twice as active as (*R*)-**206,** both the enantiomers were bioactive.[898] Gramatica



Scheme 709

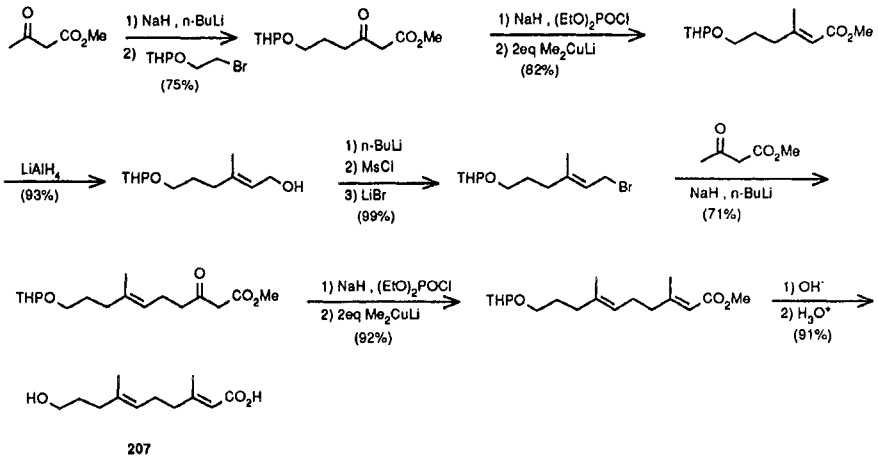
et al. prepared (*S*)-**206** by means of asymmetric reduction with baker's yeast (Scheme 710).[835]



Scheme 710

H. (2*E*,6*E*)-10-Hydroxy-3,7-dimethyl-2,6-decadienoic Acid 207 ($C_{12}H_{20}O_3$)

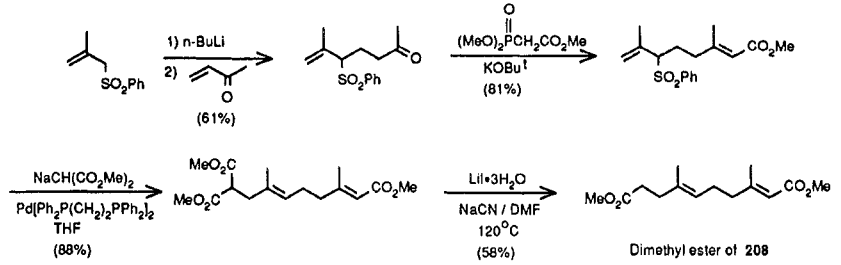
This is the major component in the hairpencil secretion of the male monarch butterfly (*Danaus plexippus*). Sum and Weiler published a full paper of their synthesis of **207** (Scheme 711).[899]



Scheme 711

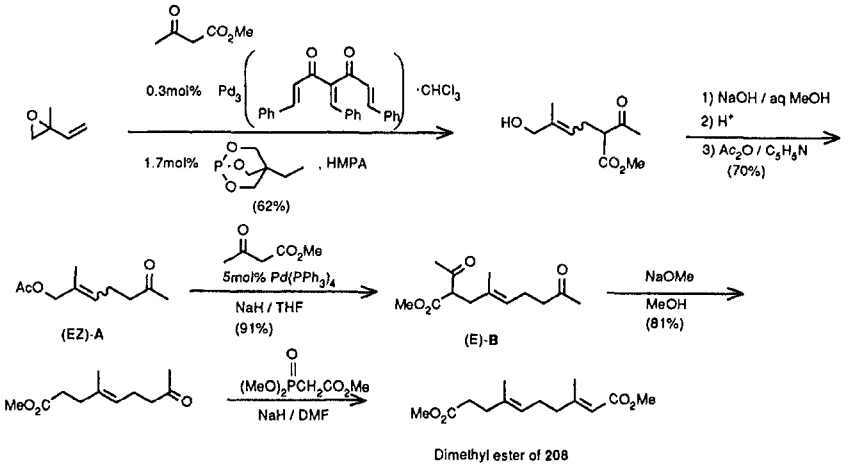
I. (2*E*,6*E*)-3,7-Dimethyl-2,6-decadiene-1,10-dioic Acid 208 ($C_{12}H_{18}O_2$)

This is also a component in the hairpencil secretion of the male monarch butterfly (*Danaus plexippus*). Trost et al. developed a synthesis of the dimethyl ester of **208,** starting from methallyl phenyl sulfone by means of palladium-catalyzed carbon-carbon bond formation (Scheme 712).[900] Another synthesis of



Scheme 712

the dimethyl ester of **208** by Tsuji et al. also resulted from the application of organopalladium chemistry as shown in Scheme 713.[901] It should be noted that the reaction of **A** with methyl acetoacetate in the presence of the palladium catalyst yielded pure (*E*)-**B.**



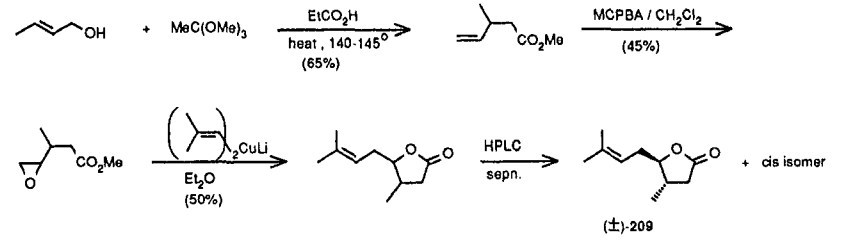
Scheme 713

J. Eldanolide [(3*S*,4*R*)-3,7-Dimethyl-6-octen-4-olide] 209 ($C_{10}H_{16}O_2$)

This is the male-produced sex attractant pheromone isolated from the wing glands of the African sugarcane borer (*Eldana saccharina*).[902,903]

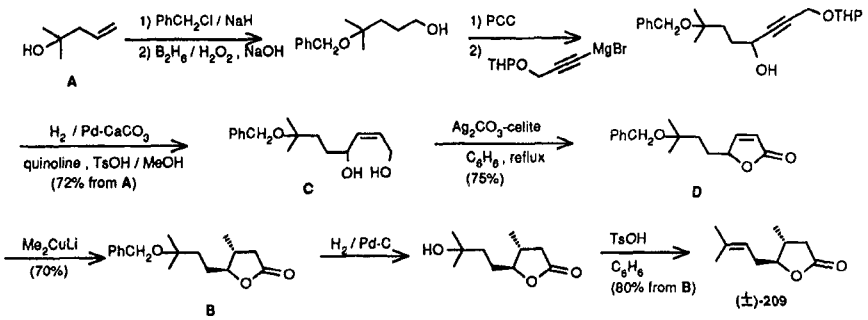
(1) Syntheses of (±)-Eldanolide

Ten different syntheses of (±)-**209** have been reported. Kunesch et al. synthesized (±)-**209** and confirmed their structural proposal by a route involving organocopper chemistry (Scheme 714).[902,903] Chakraborty and Chandrasekaran



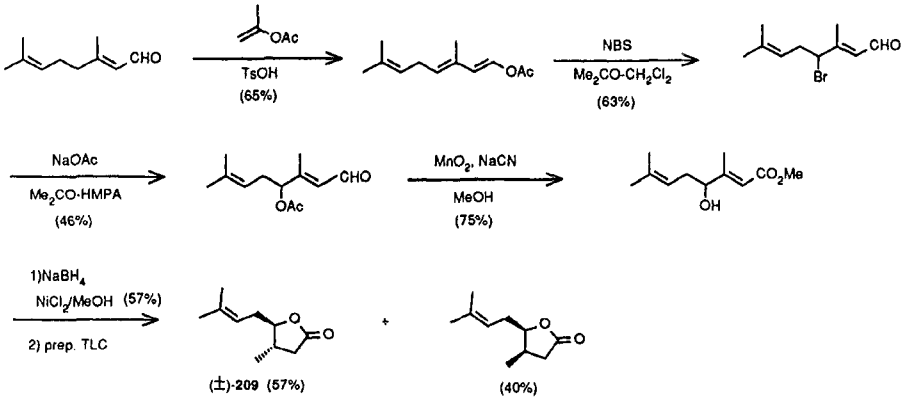
Scheme 714

prepared (±)-**209** as shown in Scheme 715.[904] The key-step there was the oxidation of diol **C** to lactone **D.** Iriye et al. converted citral to (±)-**209** and its



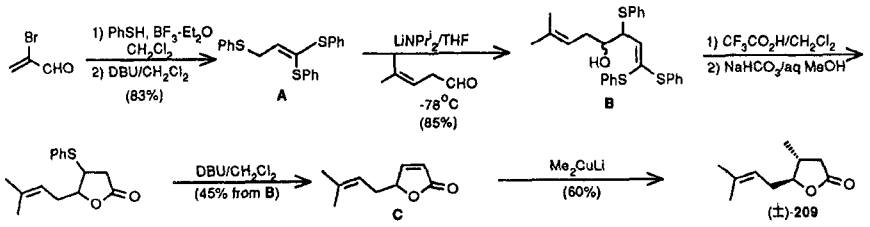
Scheme 715

cis isomer (Scheme 716).[905,906] Dziadulewicz and Gallagher employed γ-addition of 4-methyl-3-pentanal to ketene dithioacetal **A** to give **B** as the key-step

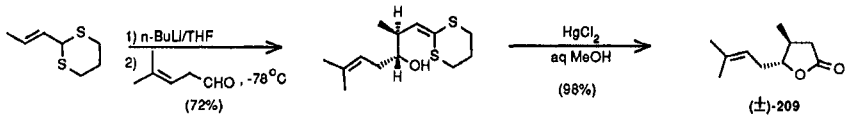


Scheme 716

in their synthesis of (±)-**209** (Scheme 717).[907,908] Another synthesis via ketene dithioacetal was published by Fang and Hong (Scheme 718).[909]

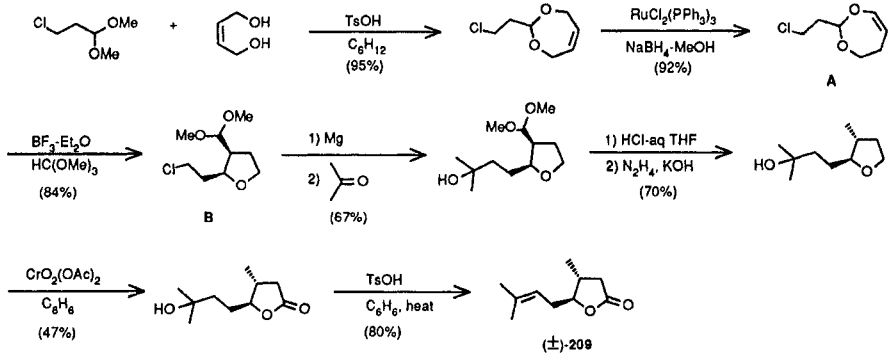


Scheme 717



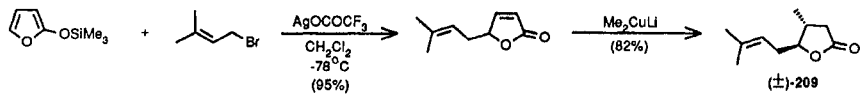
Scheme 718

Acid-catalyzed rearrangement of 4,5-dihydro-1,3-dioxepin **A** to 2,3-substituted tetrahydrofuran **B** was the key-step in the synthesis of (±)-**209** by Frauenrath and Philipps (Scheme 719).[910] This synthesis is suitable for a large-scale



Scheme 719

preparation, and 26.8 g of (±)-**209** was obtained. Jefford's synthesis provided (±)-**209** in only two steps from a commercially available starting material by prenylation of a silyl 1,3-dienol ether (Scheme 720).[911] Barua and Schmidt used

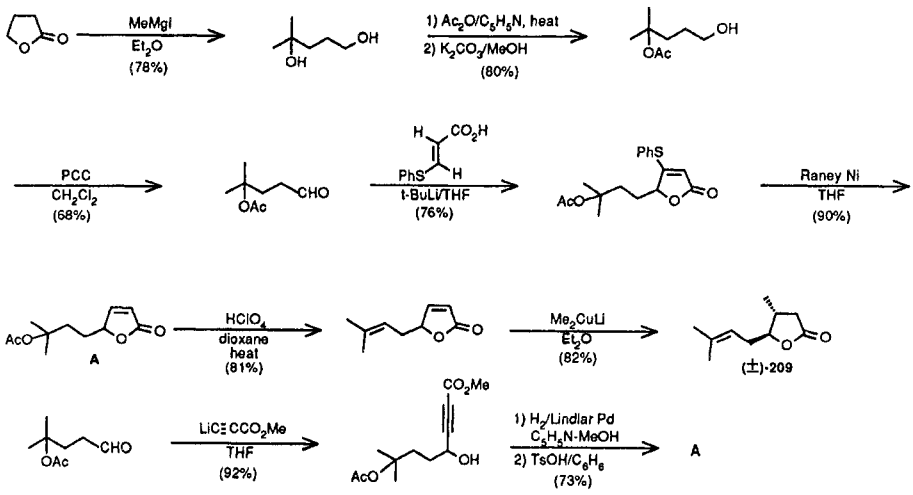


Scheme 720

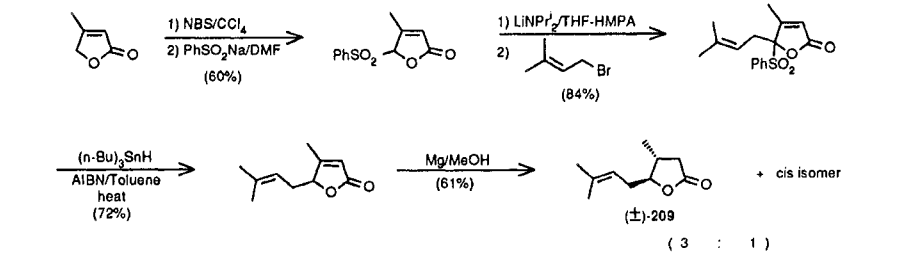
β-phenylthioacrylic acid and methyl propiolate as the C_3 building block for the synthesis of (±)-**209** (Scheme 721).[912] Yoda et al. synthesized a mixture of (±)-**209** and its *cis* isomer as shown in Scheme 722.[913]

(2) Syntheses of Optically Active Eldanolide

The natural (3*S*,4*R*)-**209** was first synthesized by Mori et al. in 1982 as an intermediate in the synthesis of a marine diterpenoid aplidiasphingosine.[914] The



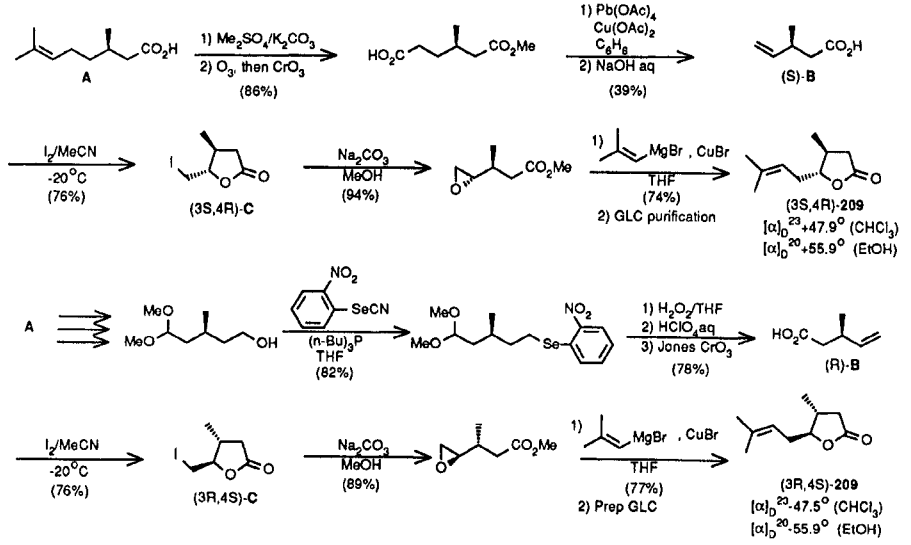
Scheme 721



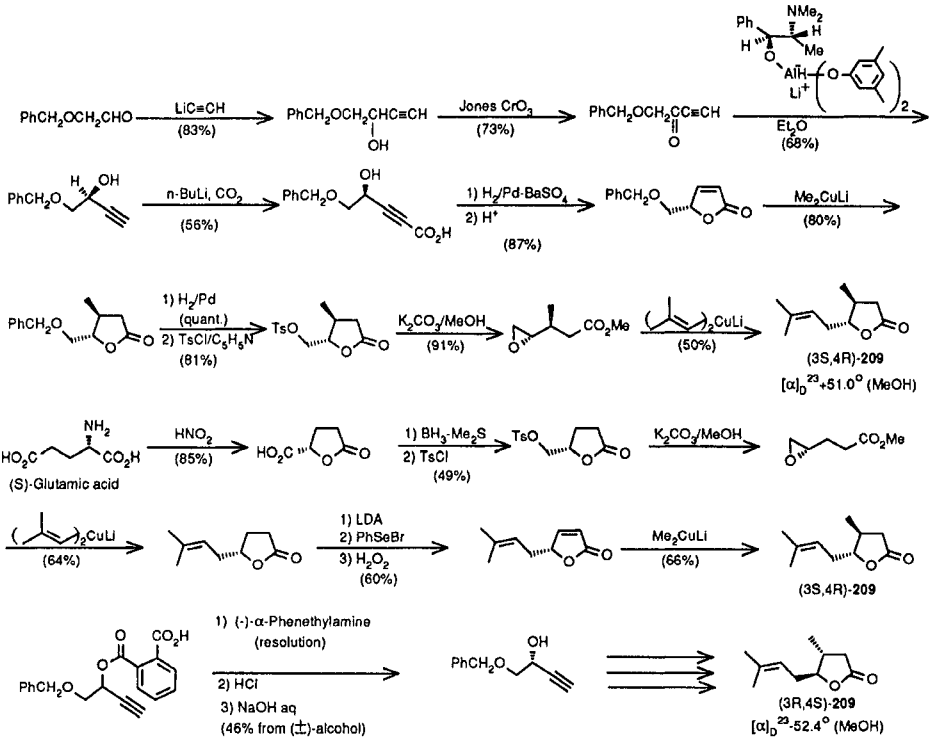
Scheme 722

details of the synthesis, together with preparation of (3*R*,4*S*)-**209**, were published in 1983.[915] As shown in Scheme 723, the synthesis led to the pure enantiomers of **209** starting from pure (*R*)-citronellic acid (**A**). The key-step was the iodolactonization of **B** to give **C**.[915] In late 1982 Vigneron et al. also reported the synthesis of both the enantiomers of **209** (Scheme 724).[903,916] They prepared the enantiomers from glutamic acid, or by optical resolution or asymmetric reduction. Like Mori's synthesis, they also employed an epoxy ester as the key-intermediate. By comparison of the CD spectrum of the natural **209** with the synthetic enantiomers, the absolute configuration of the natural eldanolide was shown to be 3*S*,4*R*. The natural enantiomer was biologically more active than its antipode by EAG test.[903]

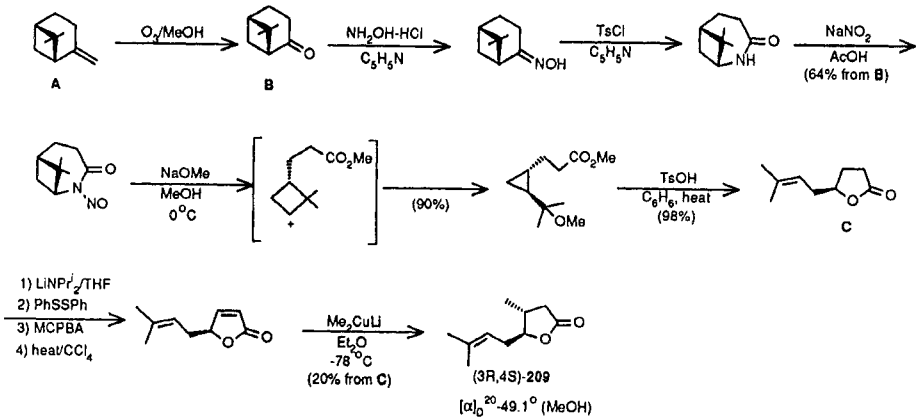
Four other syntheses of optically active **209** started from natural products. Yokoyama et al. employed (−)-β-pinene (**A**) as the starting material and pre-



Scheme 723

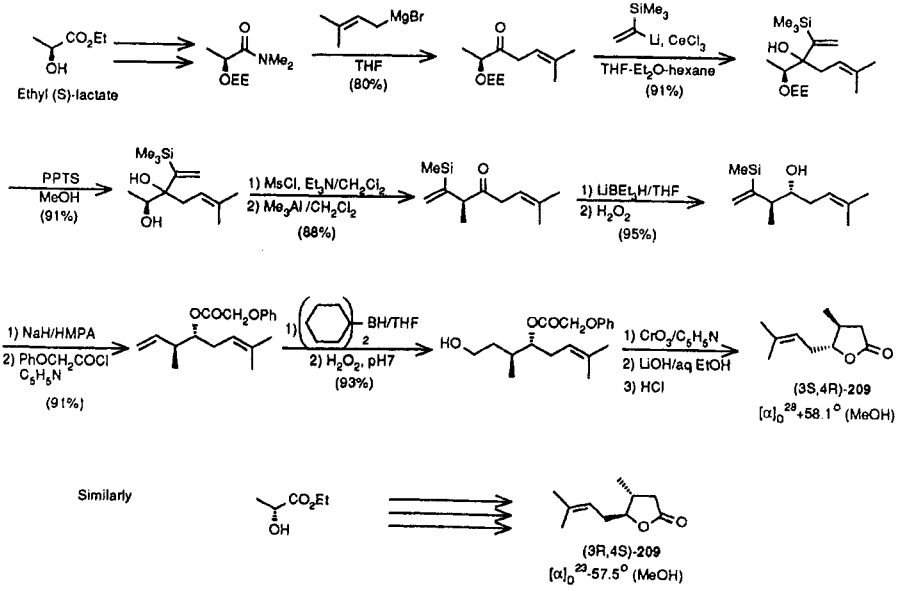


Scheme 724



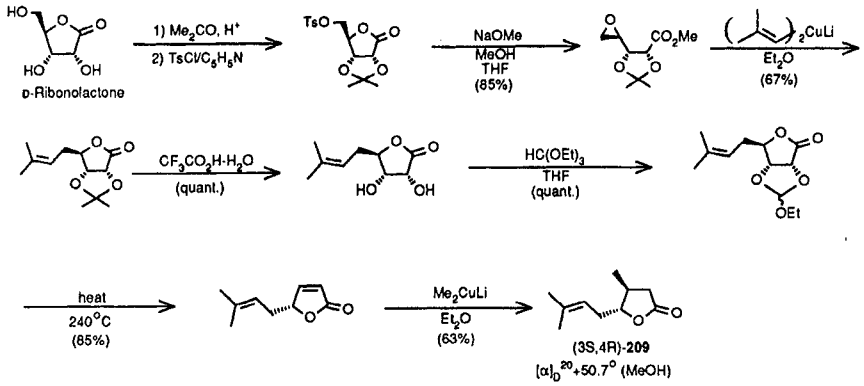
Scheme 725

pared the antipode of the natural **209** (Scheme 725).[917] Suzuki et al. synthesized the enantiomers of **209** from ethyl lactate, using their asymmetric pinacol-type rearrangement (Scheme 726).[918] Font and his co-workers converted D-ribono-

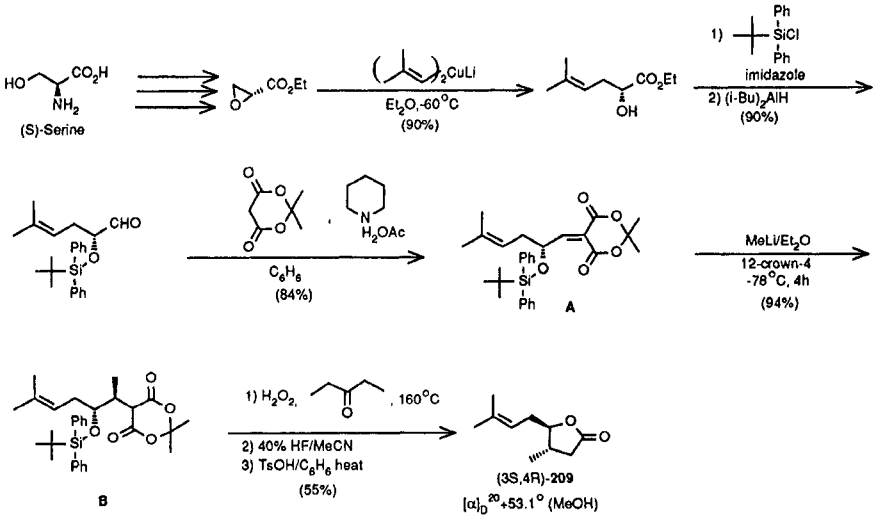


Scheme 726

lactone into (3*S*,4*R*)-**209** (Scheme 727).[919,920] Starting from (*S*)-serine, Larchevêque et al. synthesized (3*S*,4*R*)-**209** (Scheme 728).[921] The key-step was the conjugate addition of methyllithium to **A** to give **B.**

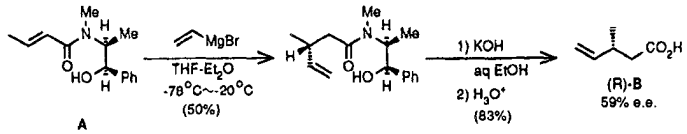


Scheme 727



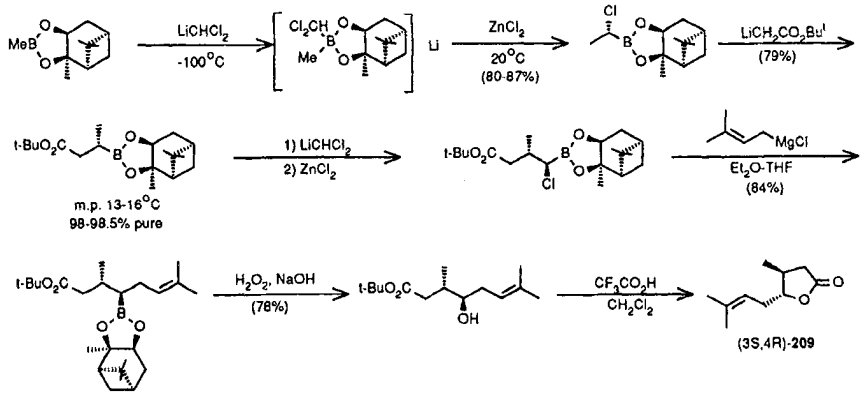
Scheme 728

Four asymmetric syntheses of **209** have been recorded. Whittaker reported an application of Mukaiyama's asymmetric Michael addition to the synthesis of (*R*)-**B** (Scheme 729),[922] which was used by Mori et al. for the synthesis of (3*R*,4*S*)-**209.**[915] The optical yield of the asymmetric reaction, however, was not



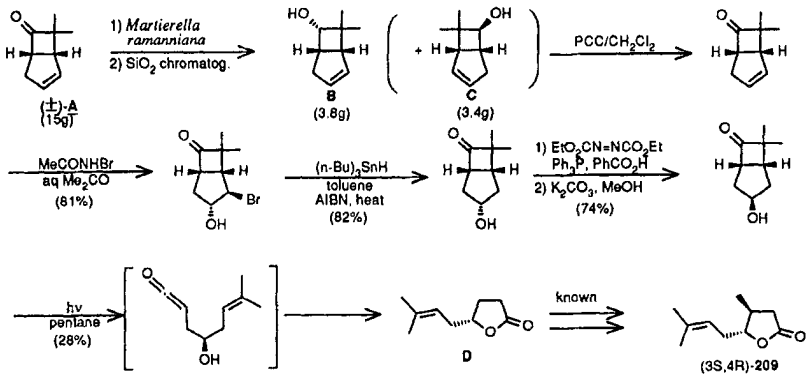
Scheme 729

as high (59% e.e.). Matteson's highly successful asymmetric synthesis of (3*S*,4*R*)-**209**, the antipode of the natural pheromone, was achieved via pinanediol boronic esters (Scheme 730).[302] Biochemical reduction of a bicyclic ketone



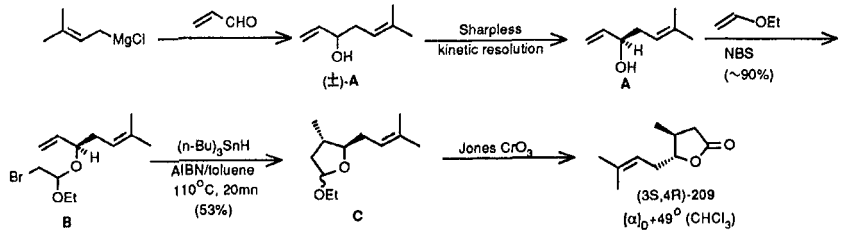
Scheme 730

(±)-**A** with a fungus (*Mortierella remanniana*) was the first step of Roberts's synthesis of (3*S*,4*R*)-**209** (Scheme 731).[923,924] The synthesis, however, ended



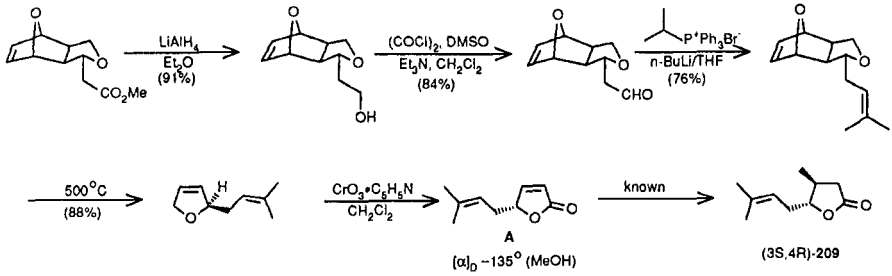
Scheme 731

up at the stage of lactone **D.** Yadav and Gadgil synthesized (3*S*,4*R*)-**209** starting from an optically active allylic alcohol **A,** which was prepared by Sharpless kinetic resolution (Scheme 732).[925] The key-step was the radical-induced cy-



Scheme 732

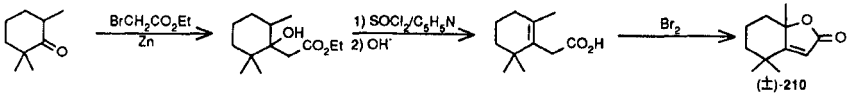
clization of bromoacetal **B** to give **C.** Bloch and Seck reported a synthesis of **A,** the immediate precursor of (3*S*,4*R*)-**209** (Scheme 733).[926]



Scheme 733

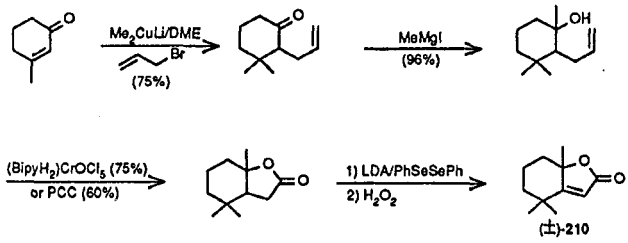
K. (*R*)-Dihydroactinidiolide (2-Oxo-4,4,7a-trimethyl-2,4,5,6,7,7a-hexahydrobenzofuran) 210 ($C_{11}H_{16}O_2$)

This is a component of the Queen recognition pheromone of the red imported fire ant (*Solenopsis invicta*), together with two other lactones **(154** and **155).**[611] (*S*)-(+)-Dihydroactinidiolide **(210)** was first isolated from the essential oil of a Japanese plant "matatabi" (*Actinidia polygama*) as an attractant against *Felidae* animals such as cats and lions.[927] Sakan et al. carried out the first synthesis of (±)-**210** as shown in Scheme 734.[927] Since then, numerous syntheses of (±)-**210**



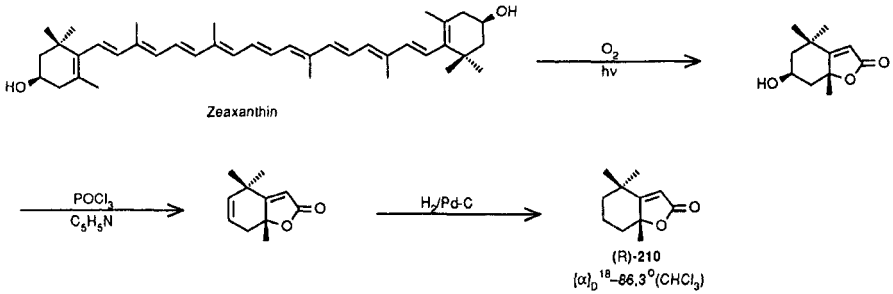
Scheme 734

have been reported (see Refs. 10–22 of Ref. 1053). For example, Chakraborty and Chandrasekaran prepared (±)-**210** as shown in Scheme 735.[928]



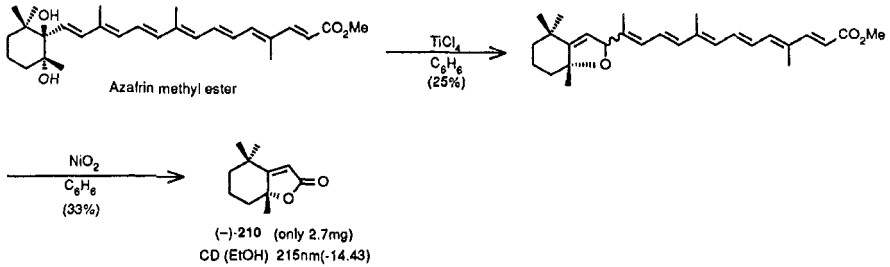
Scheme 735

The absolute configuration of (−)-dihydroactinidiolide (**210**) was determined as *R* by its derivation from zeaxanthin (Scheme 736).[929] Eugster and his



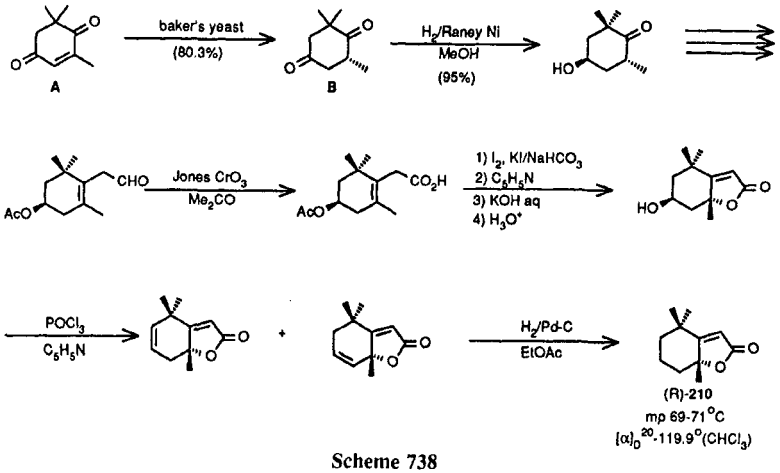
Scheme 736

co-workers also showed (−)-**210** to be *R* by converting azafrin methyl ester to (−)-**210** (Scheme 737).[930]

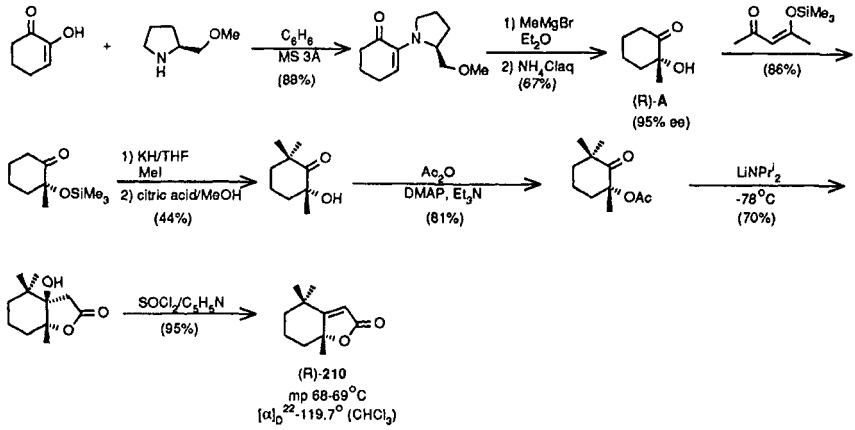


Scheme 737

Four syntheses of (*R*)-**210** have been achieved since then. First, Kienzle et al. synthesized (*R*)-**210** (Scheme 738),[931] employing baker's yeast for the asymmetric reduction of **A** to **B**.[932] Sato's synthesis (Scheme 739) was accomplished

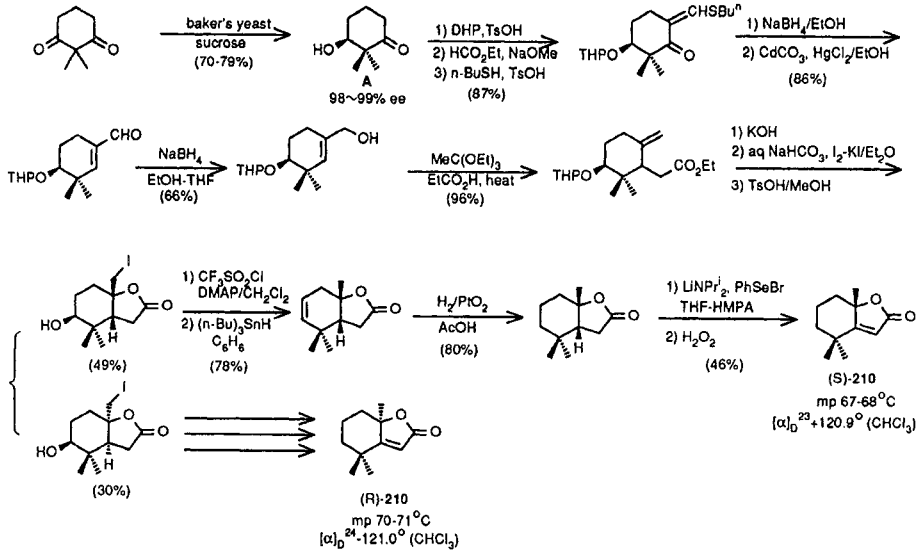


Scheme 738



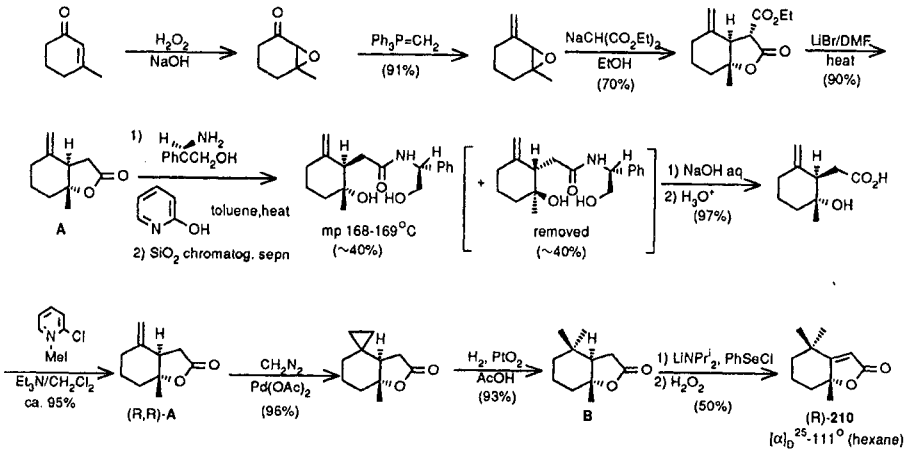
Scheme 739

by means of asymmetric synthesis of 2-hydroxy-2-methylcyclohexanone (**A**) using (*S*)-prolinol methyl ether as the chiral auxiliary.[933] Mori and Nakazono synthesized both (*R*)-**210** and (*S*)-**210** starting from (*S*)-3-hydroxy-2,2-dimethylcyclohexanone (**A**) (Scheme 740).[934] The enantiomers of **210** prepared



Scheme 740

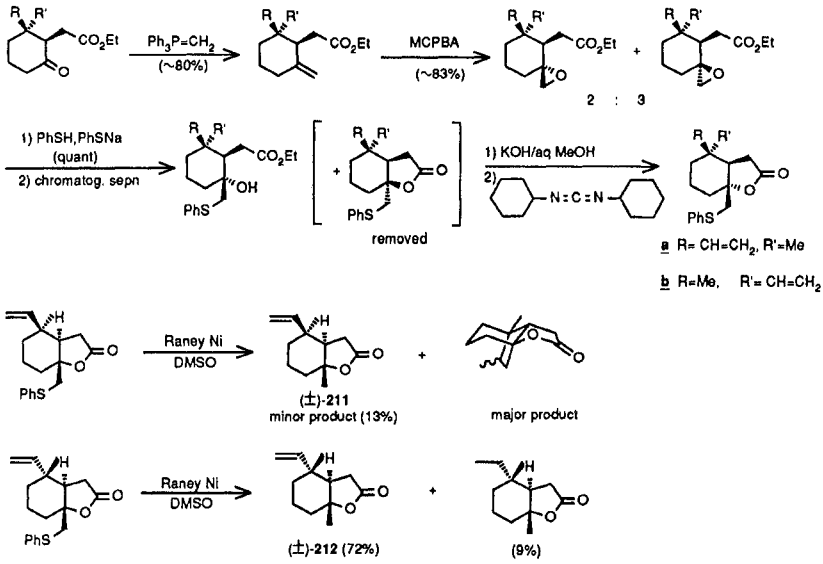
by this route were bioassayed by Tumlinson to reveal (*R*)-(−)-**210** as active.[622] Battiste and his co-workers prepared (*R*)-**210** by resolving a racemic methylene lactone **A** (Scheme 741).[935] The resolved (*R,R*)-**A** yielded (*R*)-**210** via tetrahydroactinidiolide **B.**



Scheme 741

L. Anastrephin (2-Oxo-4-ethenyl-4,7a-dimethyl-2,4,5,6,7,7a-hexahydrobenzofuran) 211 ($C_{12}H_{18}O_2$) and Epianastrephin 212 ($C_{12}H_{18}O_2$)

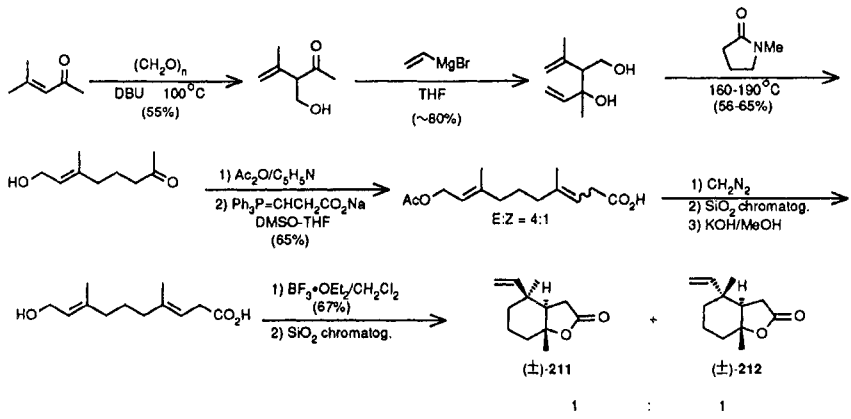
These are major components of the male-produced sex pheromone of both Caribbean (*Anastrepha suspensa*) and Mexican (*Anastrepha ludens*) fruit flies.[936,937] The natural products isolated from *A. suspensa* were mixtures of two enantiomers [(−)-isomers : (+)-isomers = 55 ± 3 : 45 ± 3].[936] To confirm their structural proposal, Battiste and his co-workers synthesized (±)-**211** and (±)-**212** (Scheme 742)[936] by employing their spirooxirane route to *trans*-fused



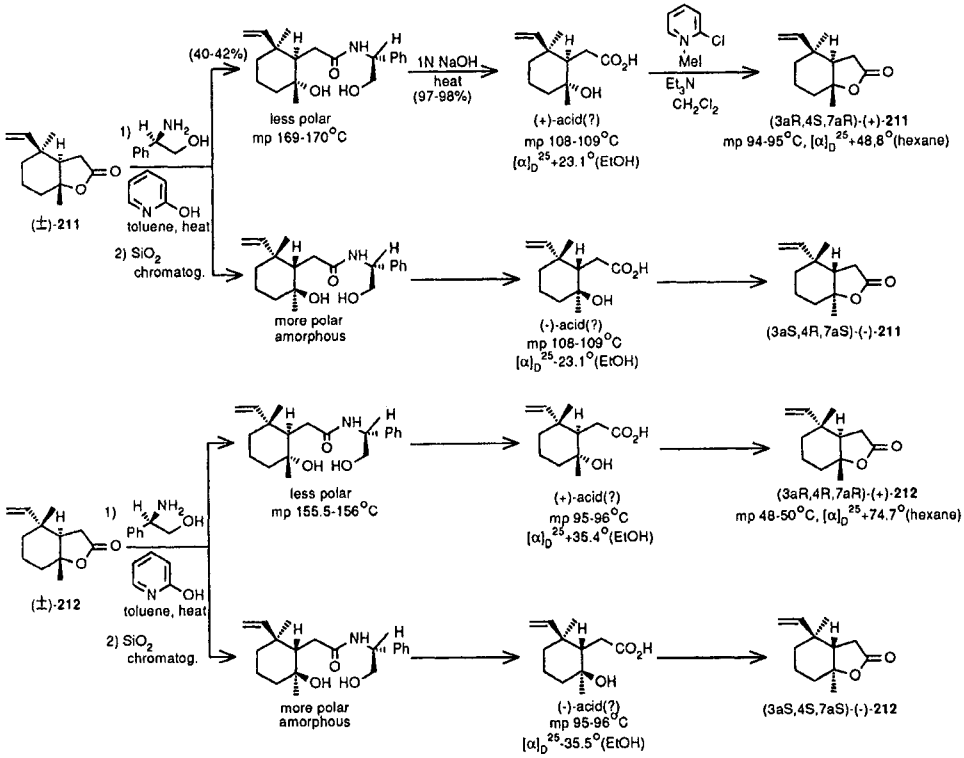
Scheme 742

γ-lactones.[938] Far more efficient synthesis of a 1 : 1 mixture of (±)-**211** and (±)-**212** was reported by Saito et al., based on the cationic cyclization of (3*E*,8*E*)-10-hydroxy-4,8-dimethyl-3,8-decadienoic acid (Scheme 743).[939]

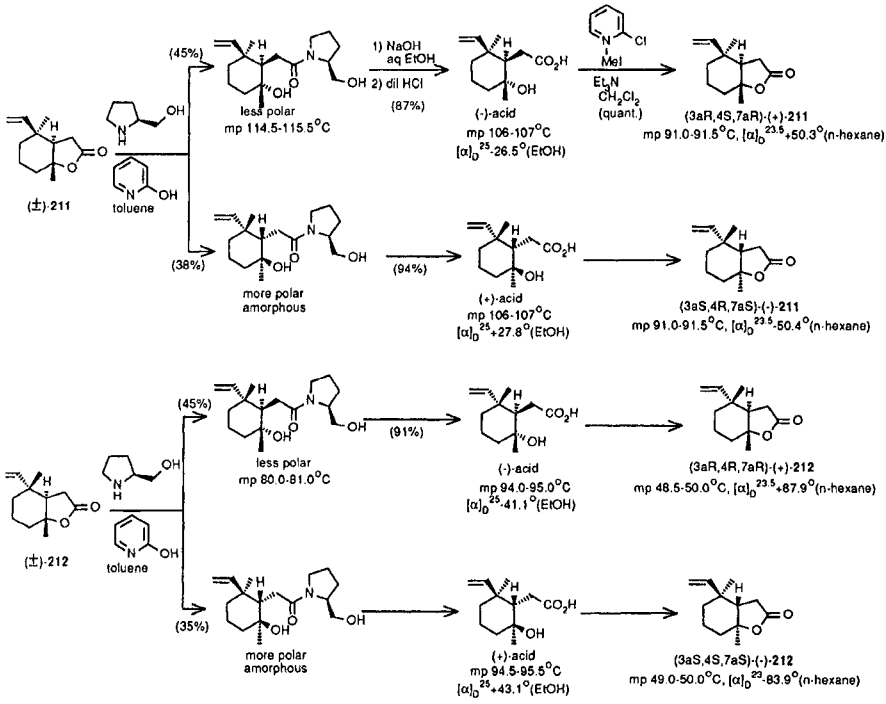
Two syntheses of the enantiomers of **211** and **212** have been published, both by means of the optical resolution of the racemates. Battiste and his co-workers used (*R*)-(−)-phenylglycinol as the resolving agent and separated the diastereomeric amides by silica gel chromatography (Scheme 744).[935] The amides were converted to the enantiomers of the lactones, **211** and **212.** Mori and Nak-



Scheme 743



Scheme 744



Scheme 745

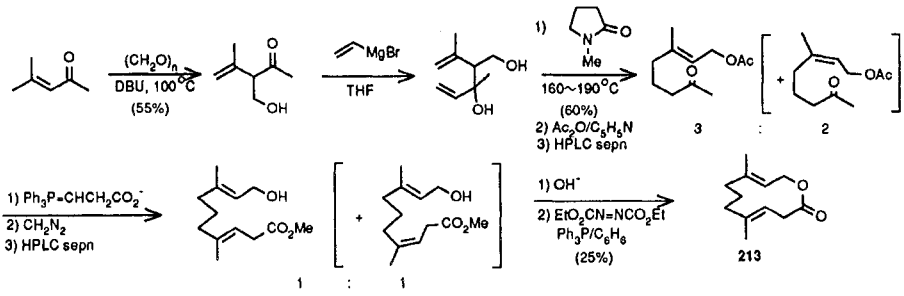
azono employed (*S*)-(+)-prolinol as the resolving agent (Scheme 745).[940] Mori et al. observed the formation of (+)-**211** and (+)-**212** from the corresponding (−)-acids, while Battiste et al. reported the formation of (+)-**211** and (+)-**212** from (+)-acids.

Robacker found that only treatments containing at least (*Z*)-3-nonen-1-ol and/or (3*Z*,6*Z*)-3,6-nonadien-1-ol in combination with (3a*S*,4*S*,7a*S*)-epianastrephin **(212)** elicited strong behavioral responses of virgin female Mexican fruit flies (*A. ludens*).[941,942]

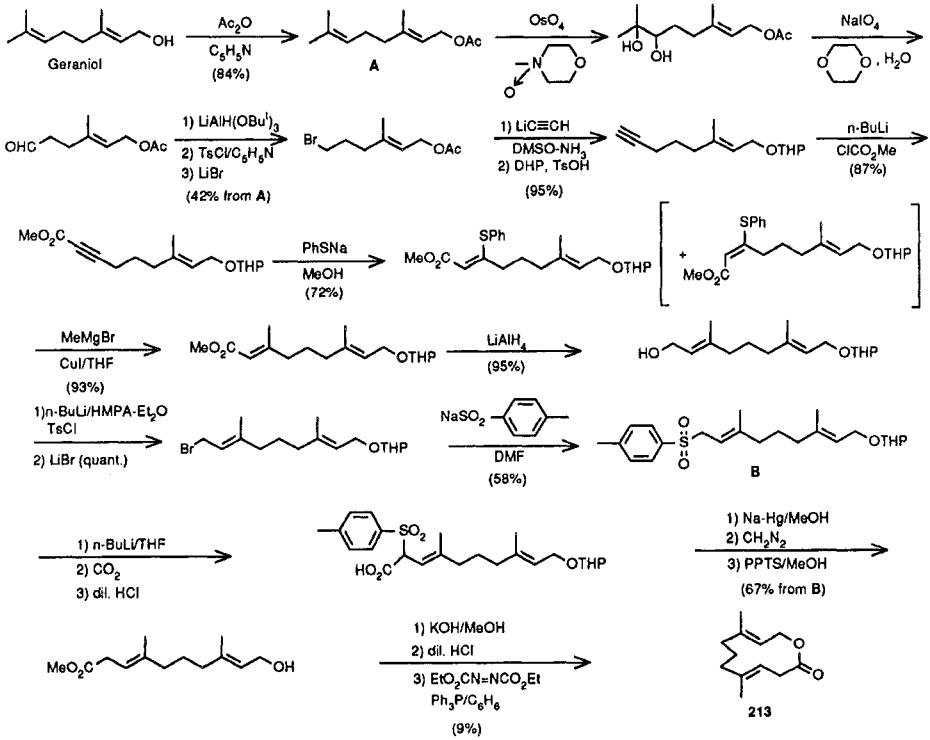
M. Suspensolide [(3*E*,8*E*)-4,8-Dimethyl-3,8-decadien-10-olide] 213 ($C_{12}H_{18}O_2$)

The Caribbean fruit fly (*Anastrepha suspensa*) is a pest of citrus, guava, and other fruits in Central and North America. The male pheromone consists of (*Z*)-3-nonen-1-ol, (3*Z*,6*Z*)-3,6-nonadien-1-ol, suspensolide **213,** anastrephin **211,** and epianastrephin **212.**[943]

Battiste et al. synthesized **213** without any stereocontrol (Scheme 746).[944] A stereocontroled synthesis of **213** by Mori and Nakazono, however, was lengthy and inefficient (Scheme 747),[940] with the yield of the final lactonization reaction particularly requiring improvement.



Scheme 746

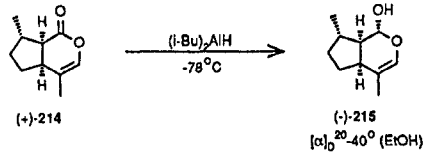


Scheme 747

N. (4a*S*,7*S*,7a*R*)-Nepetalactone 214 ($C_{10}H_{14}O_2$) and (1*R*,4a*S*,7*S*,7a*R*)-Nepetalactol 215 ($C_{10}H_{16}O_2$)

The sex pheromone of the vetch aphid (*Megoura viciae*) is a synergistic mixture of nepetalactone **(214)** and nepetalactol **(215).**[945,946] Nepetalactol **(215)** also works as the sex pheromone of the green bug (*Schizaphis graminum*).[947] (4a*S*,7*S*,7a*R*)-(+)-Nepetalactone **(214)** was first isolated from catnip (catmint, *Nepeta cataria*) in 1941 as a unique monoterpene highly attractive against cats.[948] The existing syntheses of nepetalactone and its relatives were reviewed by Thomas.[949] Therefore, only the recent syntheses, those that appeared after the isolation of **214** as the aphid pheromone, will be reviewed here.

Dawson et al. reduced **214** (isolated from *N. cataria*) with diisobutylaluminum hydride to give **215,**[945] whose stereochemistry was determined by the X-ray diffraction study of the crystalline 3,5-dinitrobenzoate of **215** (Scheme 748).[946] According to the method developed by Schreiber et al.,[950] Sakurai et

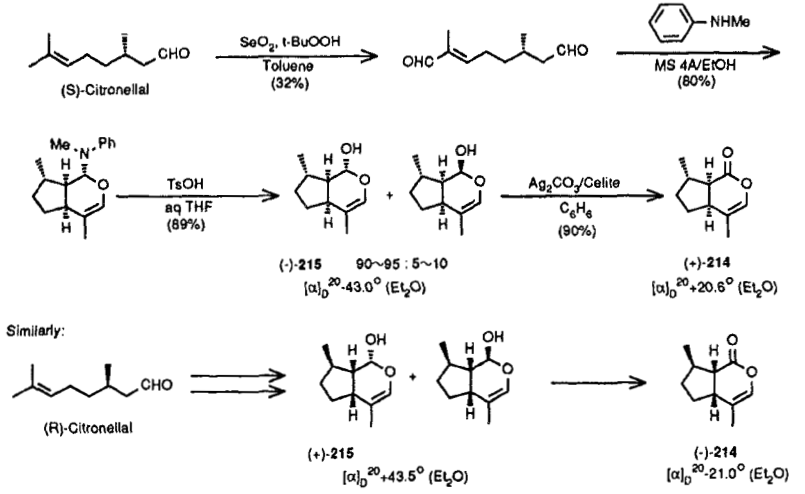


Scheme 748

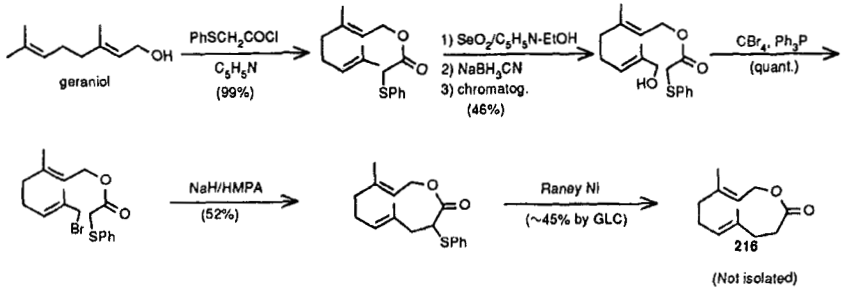
al. synthesized the enantiomers of **214** and **215,** starting from the enantiomers of citronellal (Scheme 749).[951] Interestingly, to the aphid only the natural enantiomer is active,[946] but to cats both the enantiomers of **215** are powerful attractants.[951]

O. Ferrulactone I [(4*E*,8*E*)-4,8-Dimethyl-4,8-decadien-10-olide] 216 ($C_{12}H_{18}O_2$)

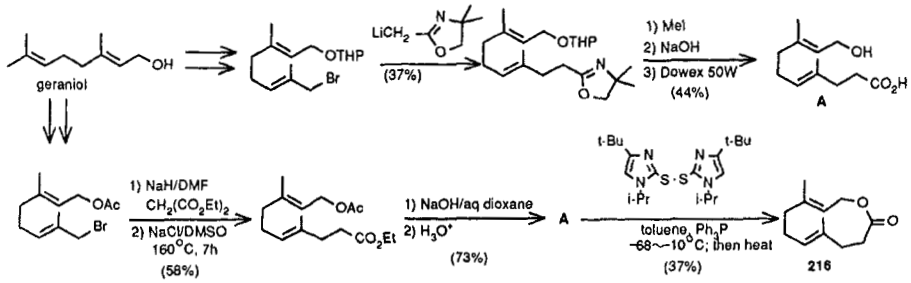
This is a macrolide aggregation pheromone produced by the male rusty grain beetle (*Cryptolestes ferrugineus*) and was isolated from their frass together with ferrulactone II **(161).**[694] Geraniol was converted to **216** by Oehlschlager et al. as shown in Scheme 750.[695] The yield at the final step was estimated by GLC analysis of the reaction mixture, and **216** could not be isolated. They then developed a better route (Scheme 751), employing Corey's macrolactonization method for the cyclization of **A** to yield ca. 100 ng of **216.**[695] Sakai and Mori



Scheme 749

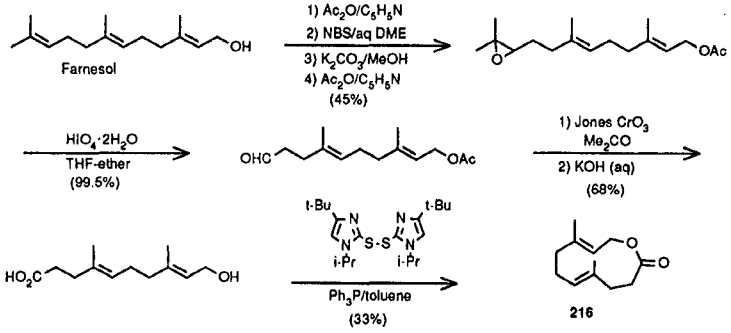


Scheme 750



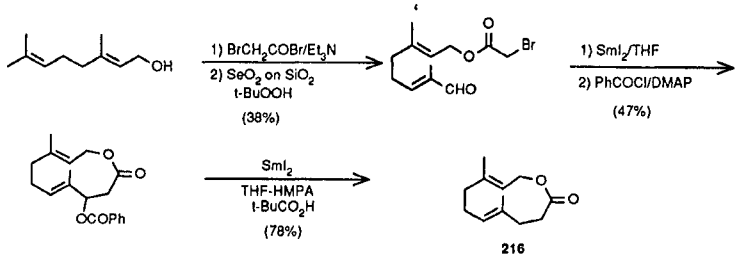
Scheme 751

developed another synthesis of **216,** starting from (2*E*,6*E*)-farnesol (Scheme 752).[696] The overall yield of **216** from farnesol was 10.4% in seven steps. A



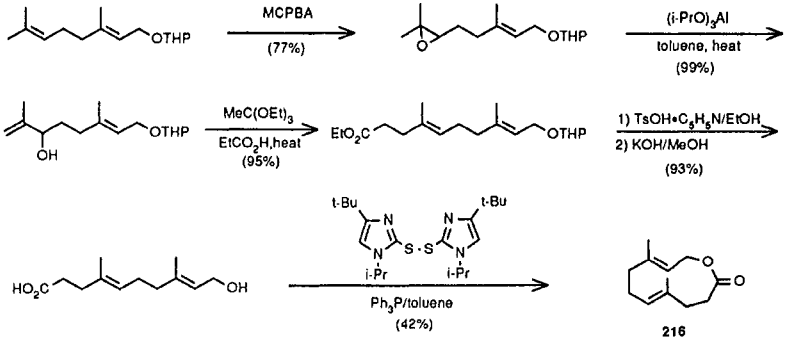
Scheme 752

short synthesis of **216** was published by Inanaga et al. employing intramolecular Reformatsky reaction as the key-step (Scheme 753).[952] Use of samarium(II)



Scheme 753

iodide was the special feature of their synthesis. Cheskis et al. prepared **216** beginning with geraniol (Scheme 754).[953]



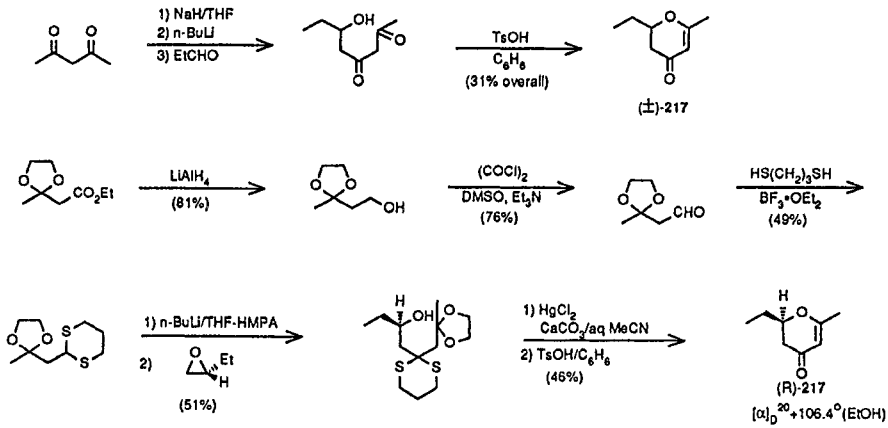
Scheme 754

19. OXYGEN HETEROCYCLES (EXCLUDING EPOXIDES, LACTONES, HEMIACETALS, AND ACETALS) AS PHEROMONES

A. Hepialone [(*R*)-2-Ethyl-6-methyl-2,3-dihydro-4H-pyran-4-one] 217 ($C_8H_{12}O_2$)

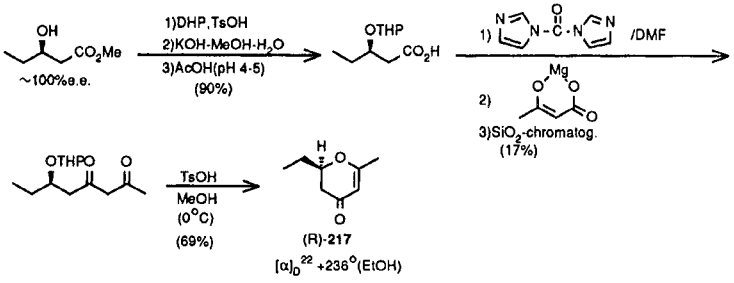
This is a sex-pheromonal component produced by the male moth (*Hepialus californicus*). Kubo et al. isolated **217** from the sex scales or hairpencils of the males. The CD spectrum of **217** suggested its *R*-configuration.[954]

Uchino et al. synthesized both (±)-**217** and (*R*)-**217** as shown in Scheme 755.[955] The known (*R*)-ethyloxirane, which was prepared from (+)-malic acid,



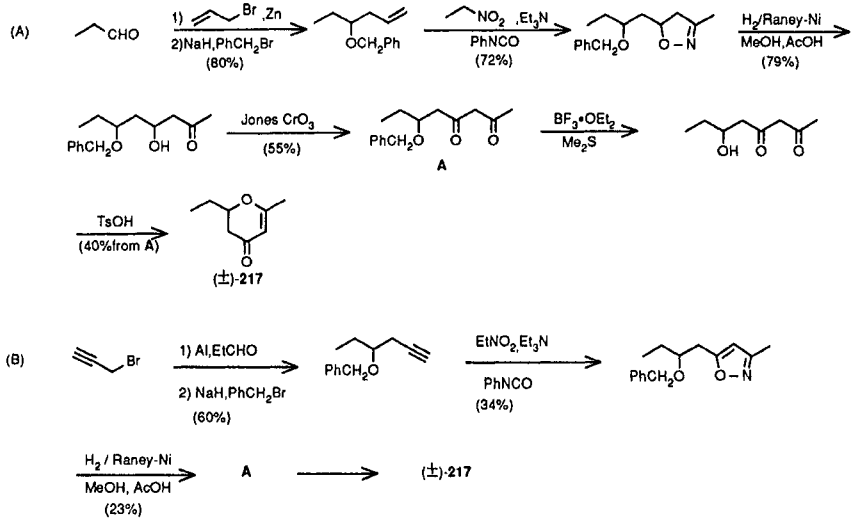
Scheme 755

was the chiral building block in Uchino's synthesis. Hayashi and Mori achieved another synthesis of (*R*)-**217**, starting from methyl (*R*)-3-hydroxypentanoate (Scheme 756).[956] Enantiomerically pure (*R*)-**217** was obtained through this route



Scheme 756

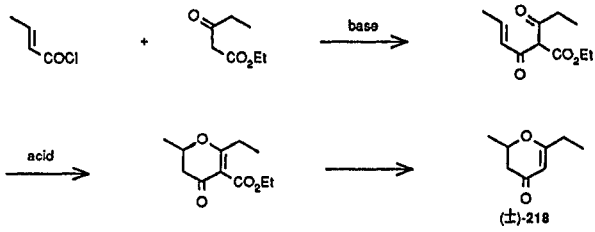
by carefully avoiding the racemization at the final stage of cyclization.[956] Yadav and Rao reported a synthesis of (±)-**217** by employing a 1,3-dipolar cycloaddition as a key step (Scheme 757).[957] Their route (A) was more efficient than route (B).



Scheme 757

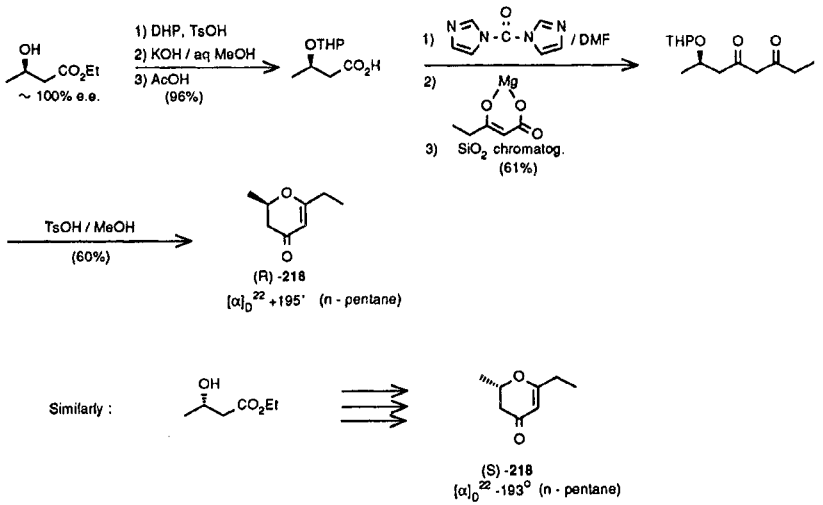
B. (*R*)-6-Ethyl-2-methyl-2,3-dihydro-4H-pyran-4-one 218 ($C_8H_{12}O_2$)

This is one of the three major components of the pheromone blend of the male swift moth (*Hepialus hecta*).[958] Francke's synthesis of (±)-**218** is summarized in Scheme 758.[958] Mori and Kisida synthesized both the enantiomers of **218**,

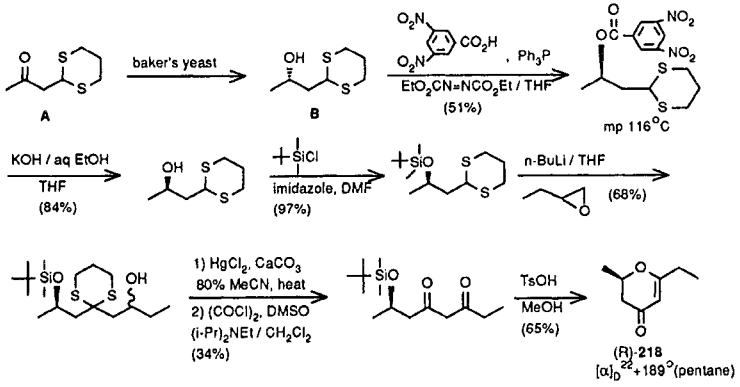


Scheme 758

starting from the enantiomers of ethyl 3-hydroxybutanoate (Scheme 759a).[959] The natural pheromone was identical with (*R*)-**218.** Another synthesis of (*R*)-**218** was achieved by Jacot-Guillarmod and his co-workers as shown in Scheme 759b.[1086] Their synthesis started from the known dithiane alcohol **B,** which was



Scheme 759a

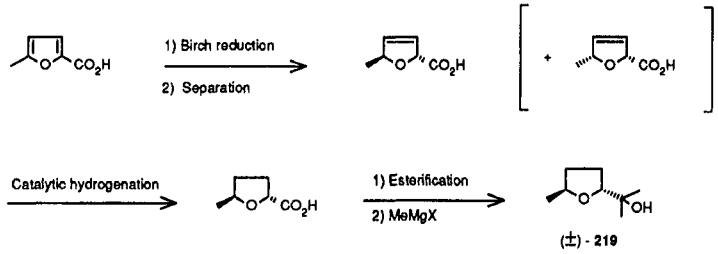


Scheme 759b

obtained by the reduction of **A** with baker's yeast.[1087] Bianchi also reported a synthesis of **218.**[1088]

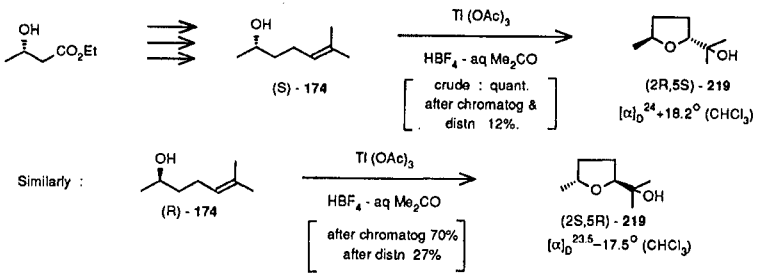
C. (2*R*,5*S*)-*trans*-Pityol [*trans*-2-(1-Hydroxy-1-methylethyl)-5-methyltetrahydrofuran] 219 ($C_8H_{16}O_2$)

This is a male-produced pheromone component of the bark beetle (*Pityophthorus pityographus*).[794] A synthesis of (±)-**219** by Francke et al. (Scheme 760)[794]



Scheme 760

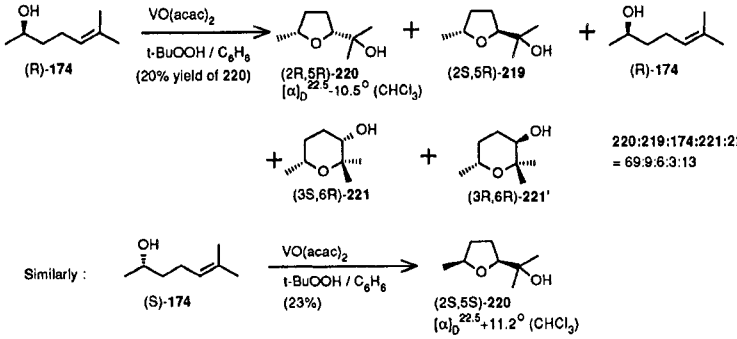
was followed by the synthesis of both the enantiomers of **219** by Mori and Puapoomchareon by thallium(III)-catalyzed cyclization of the enantiomers of sulcatol **174** (Scheme 761).[728] The natural pheromone was shown to be (2*R*,5*S*)-**219** by GLC analysis and bioassay.[794]



Scheme 761

D. *cis*-Pityol [*cis*-2-(1-Hydroxy-1-methylethyl)-5-methyltetrahydrofuran] 220 ($C_8H_{16}O_2$)

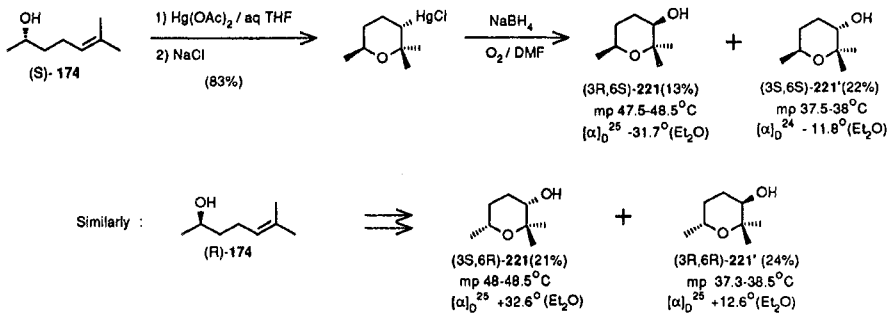
This was isolated by Francke as a volatile compound from the elm bark beetle (*Pteleobius vittatus*).[960] Vanadyl acetylacetonate-catalyzed oxidation of the enantiomers of sulcatol afforded the enantiomers of **220** as the major products (Scheme 762).[961]



Scheme 762

E. (3*R*,6*S*)-*cis*-Tetrahydro-2,2,6-trimethyl-2H-pyran-3-ol 221 ($C_8H_{16}O_2$)

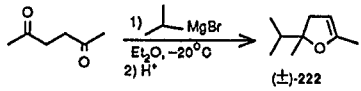
This is a pheromone component of the bark beetle (*P. vittatus*).[794,962] Two enantiomers of **221**, together with the enantiomers of the *trans*-isomer **221'**, were synthesized by oxymercuration-oxygenation of the enantiomers of sulcatol (Scheme 763).[963] By testing all of these isomers against *P. vittatus*, (3*R*,6*S*)-**221** was shown to be the natural pheromone.[962]



Scheme 763

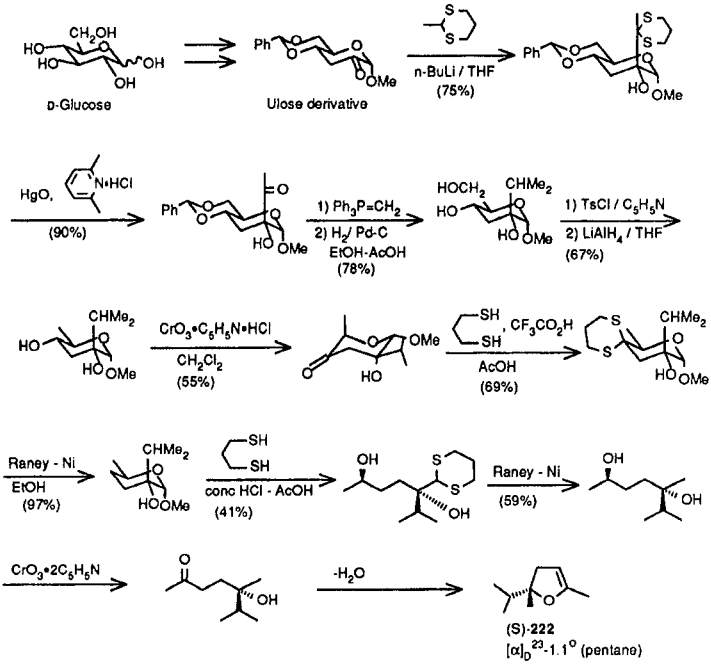
F. 2,3-Dihydro-2-isopropyl-2,5-dimethylfuran 222 ($C_9H_{16}O$)

This is a sex-specific compound in females of the polyphagous beetle (*Hylecoetus dermestoides*).[964] A single-step synthesis of (±)-**222** was reported by



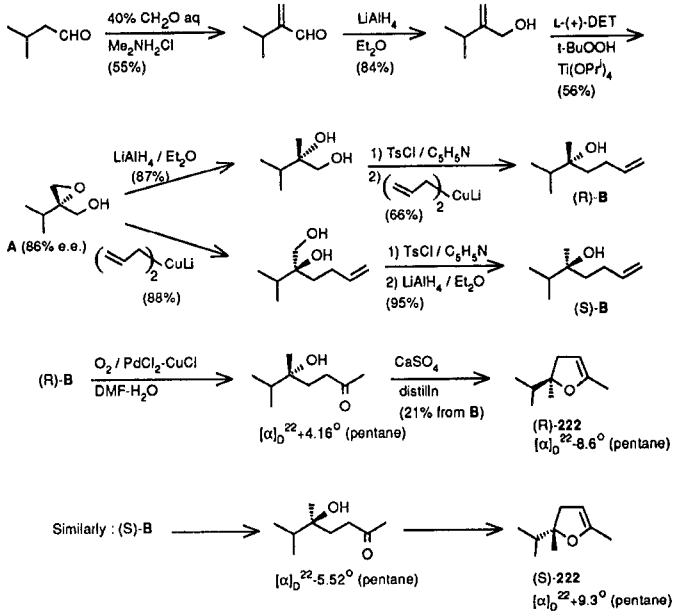
Scheme 764

Redlich et al. by a Grignard reaction followed by acidification (Scheme 764).[965] Redlich's synthesis of (*S*)-**222** started from D-glucose (Scheme 765).[965,966] The



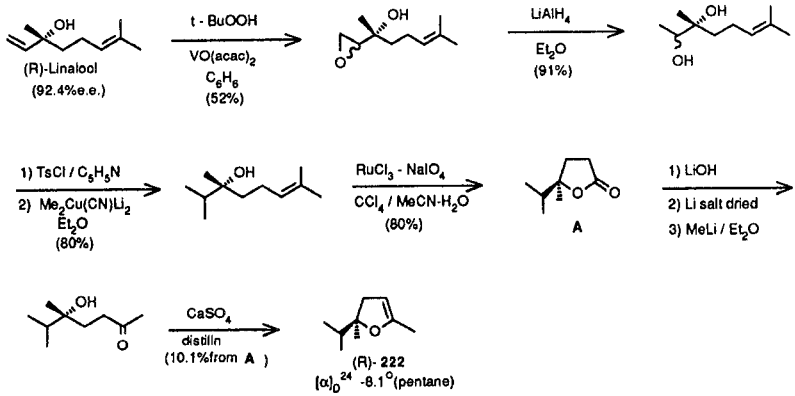
Scheme 765

synthetic (*S*)-**222** was reported to show $[\alpha]_D^{23}$ −1.1° (pentane).[965,966] Mori et al. synthesized both (*R*)-**222** and (*S*)-**222**, starting from (*S*)-2,3-epoxy-2-isopropyl-1-propanol **A**, which was prepared by the Sharpless asymmetric epoxidation (Scheme 766).[967] Their (*R*)-**222** and (*S*)-**222** showed $[\alpha]_D$ values of −8.6° and +9.3°, respectively, in pentane. These values were different from that reported for (*S*)-**222** (−1.1°) by Redlich.[965,966] Mori et al. then converted (*R*)-linalool to (*R*)-**222** to confirm the levorotatory nature of (*R*)-**222** (Scheme



Scheme 766

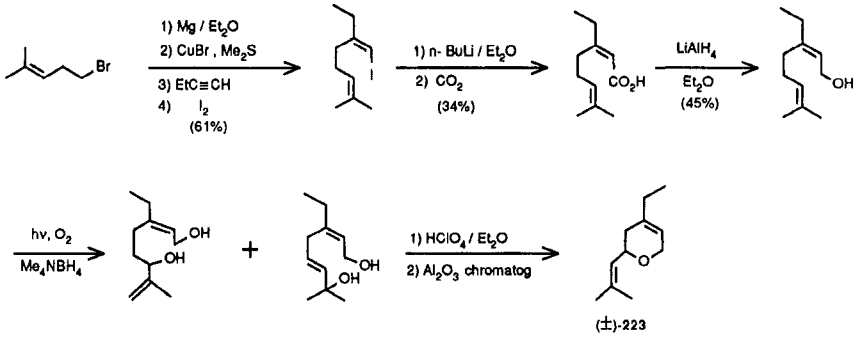
767).[967] The product thus obtained showed $[\alpha]_D^{24}$ −8.1° (pentane). Therefore, the specific rotation values reported by Mori should be regarded as the correct ones.



Scheme 767

G. 10-Homonerol Oxide 223 ($C_{11}H_{18}O$)

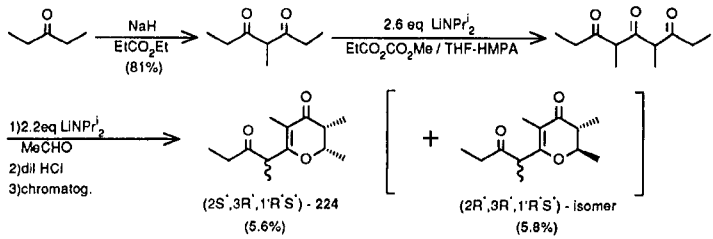
This is a volatile signal from an ant-lion (*Grocus bore*). Baeckström et al. synthesized (±)-**223** and found the natural product to be racemic.[319] Their synthetic route is shown in Scheme 768.[319]



Scheme 768

H. (2*S*,3*R*,1′*R*)-Stegobinone [2,3-Dihydro-2,3,5-trimethyl-6-(1′-methyl-2-oxobutyl)-4H-pyran-4-one] 224 ($C_{13}H_{20}O_3$)

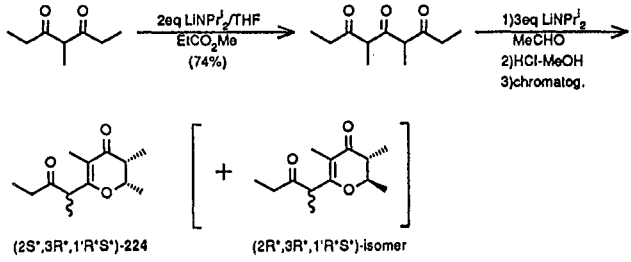
This is one of the two sex pheromone components of the female drugstore beetle (*Stegobium paniceum*).[968] One year after Kuwahara's structural proposal, two groups independently announced the biomimetic synthesis of a diastereomeric mixture of **224**.[969-971] Scheme 769 illustrates Mori's synthetic route.[969,971] Has-



Scheme 769

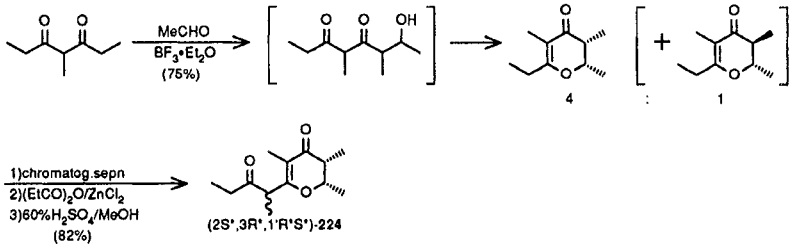
sner's route (Scheme 770) is almost the same as Mori's.[970] The synthetic (2*S**,3*R**,1′*R***S**)-**224** was bioactive, but the threshold amount was $\sim 10^{-4}$

μg, while the natural pheromone was active even at doses of 3×10^{-7} μg.[970,971]



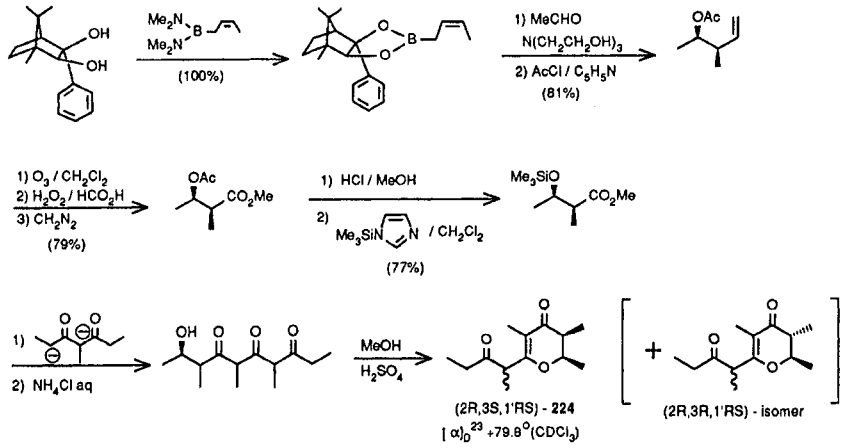
Scheme 770

Ono's improved synthesis of (2*S**,3*R**,1′*R***S**)-**224** (Scheme 771) was far more efficient than the biomimetic syntheses.[972]

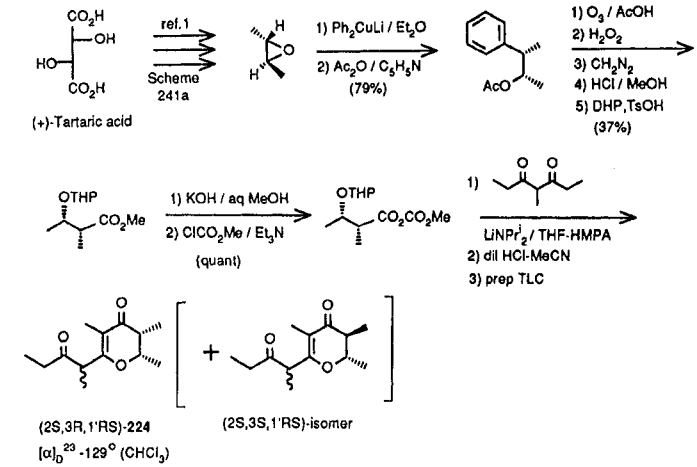


Scheme 771

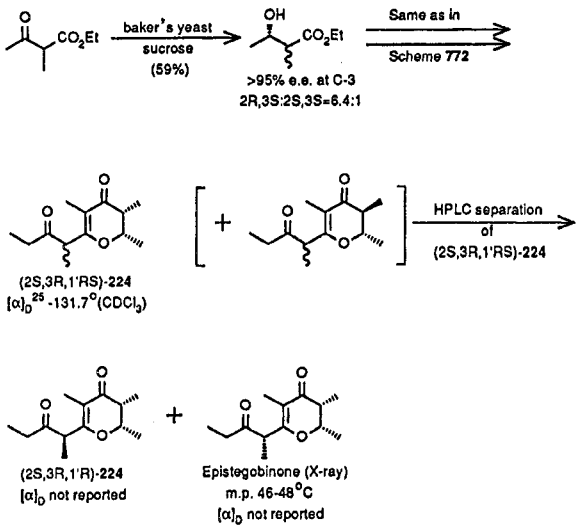
To clarify the absolute configuration of the natural stegobinone, both Hoffmann et al. and Mori et al. worked on the synthesis of **224.** The first stage was to determine the absolute configuration of **224** at C-2 and C-3. Both groups adopted the same strategy on the basis of the above-mentioned biomimetic synthesis of **224.** It was to acylate 4-methylheptane-3,5-dione with (2*R*,3*S*)- and/or methyl (2*S*,3*R*)-3-hydroxy-2-methylbutanoate, or its equivalent. Hoffmann et al. prepared the required hydroxy ester by the asymmetric synthetic method employing (*Z*)-crotylboronate (Scheme 772).[973,974] By comparing the CD spectrum of the synthetic (2*R*,3*S*,1′*RS*)-**224,** especially in the 350 nm region, with that of the natural stegobinone, the latter was concluded to possess 2*S*,3*R*-absolute configuration.[973,974] Starting from the enantiomers of tartaric acid, Mori et al. synthesized both (2*S*,3*R*,1′*RS*)-**224** and (2*R*,3*S*,1′*RS*)-**224** (Scheme



Scheme 772



Scheme 773

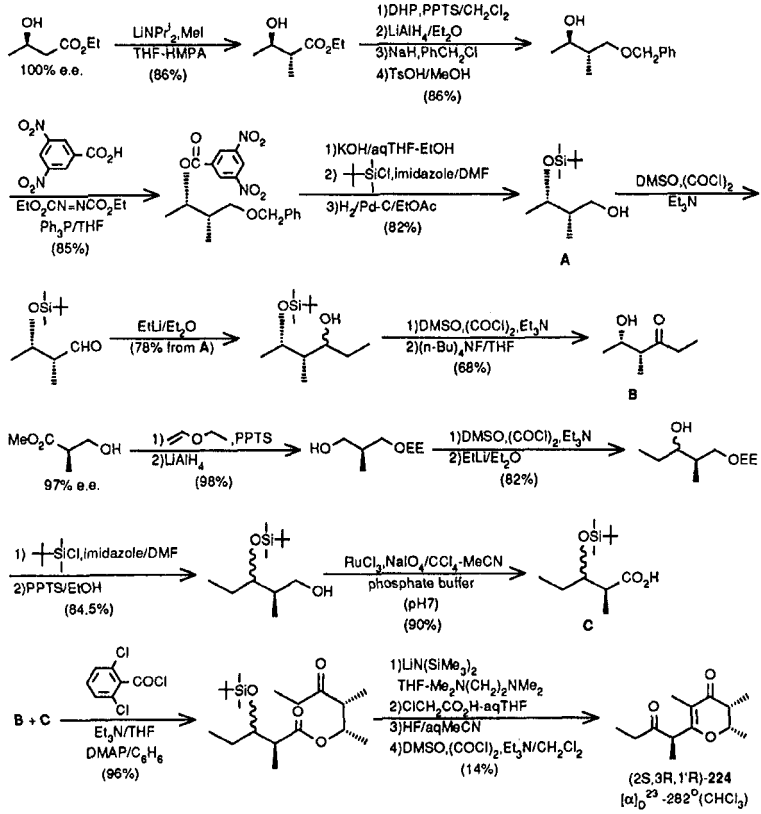


Scheme 774

773).[971] Mori's synthetic (2*S*,3*R*,1′*RS*)-**224** was still less bioactive than the natural pheromone itself.

The first synthesis of the natural (2*S*,3*R*,1′*R*)-stegobinone **224** was achieved by Hoffmann et al. (Scheme 774).[974] Introduction of *S*-configuration at C-2 was executed by the yeast reduction of a β-keto ester, and (2*S*,3*R*,1′*RS*)-**224** could be separated by preparative HPLC to produce stegobinone and epistegobinone. Because epistegobinone was crystalline, its structure could be solved by X-ray analysis as 2*S*,3*R*,1′*S*. The absolute configuration of the natural stegobinone was therefore determined as 2*S*,3*R*,1′*R*.[974]

The second synthesis of (2*S*,3*R*,1′*R*)-**224** was executed by Mori and Ebata with stereocontrol at C-2 and C-1′ (Scheme 775).[975] Starting from two optically active β-hydroxy esters of microbial origin, two building blocks **B** and **C** were prepared and combined. Subsequent intramolecular acylation was followed by cyclization and oxidation to give (2*S*,3*R*,1′*R*)-**224.** This synthetic material was more bioactive than (2*S*,3*R*,1′*RS*)-**224,** although it was less active than the extract of the female drugstore beetle.[975] It was later shown that the addition of (2*S*,3*R*,1′*S*)-epistegobinone to stegobinone significantly reduces the response of male drugstore beetle.[976] Stegobinone is also used as the female sex pheromone of the common furniture beetle (*Anobium punctatum*).[977]

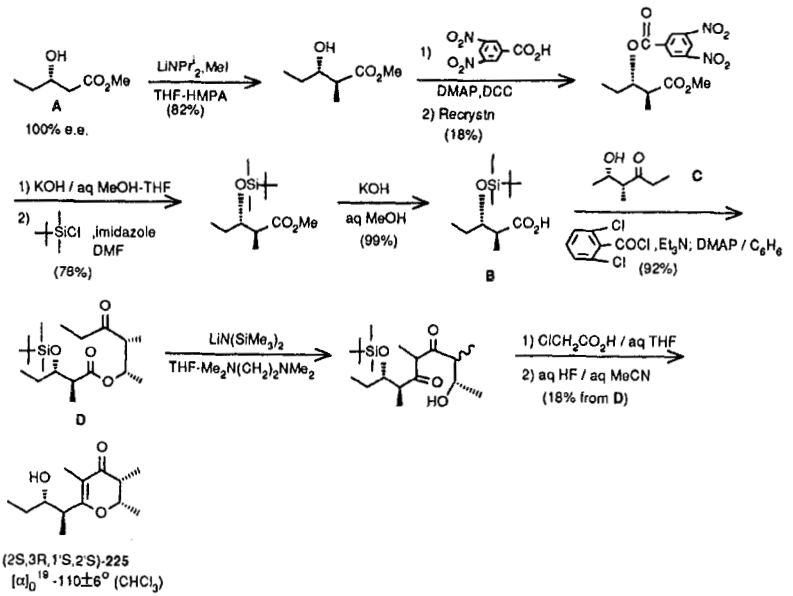


Scheme 775

I. (2*S*,3*R*,1′*S*,2′*S*)-Stegobiol [2,3-Dihydro-2,3,5-trimethyl-6-(2′-hydroxy-1′-methylbutyl)-4H-pyran-4-one] 225 ($C_{13}H_{22}O_3$)

This is another component of the female-produced sex pheromone of the drugstore beetle (*Stegobium paniceum*).[978]

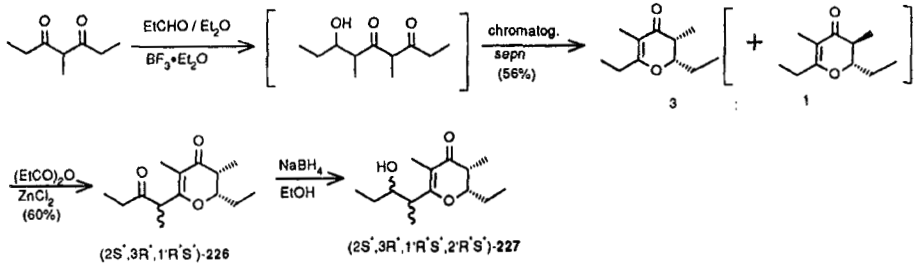
Mori and Ebata synthesized **225** by the route similar to that employed for the synthesis of stegobinone.[979] As shown in Scheme 776, methyl (*S*)-3-hydroxypentanoate **A** was one of the starting materials. The ester **A** was converted to **B** and coupled with the known hydroxy ketone **C**[975] to produce an ester **D.** This ester **D** was submitted to intramolecular acylation, cyclization, and deprotection to give **225,** which was identical with the natural product.[979]



Scheme 776

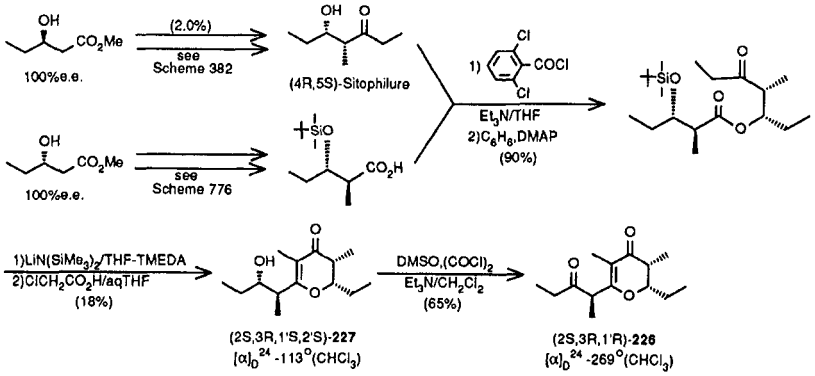
J. (2*S*,3*R*,1′*R*)-Serricorone [2,3-Dihydro-2-ethyl-3,5-dimethyl-6-(1′-methyl-2′-oxobutyl)-4H-pyran-4-one] 226 ($C_{14}H_{22}O_3$)

This is a female produced sex pheromone component of the cigarette beetle (*Lasioderma serricorne*).[980,981] Its synthesis was accomplished in the same manner as stegobinone. A diastereomeric mixture of the racemates was prepared by Chuman et al. (Scheme 777).[980,981] The natural serricorone was shown



Scheme 777

to be (2*S*,3*R*,1′*R*)-**226**, by a synthesis starting from the enantiomers of methyl 3-hydroxypentanoate (Scheme 778).[982]



Scheme 778

K. (2*S*,3*R*,1′*S*,2′*S*)-Serricorole [2,3-Dihydro-3,5-dimethyl-2-ethyl-6-(1′-methyl-2′-hydroxybutyl)-4H-pyran-4-one] 227 ($C_{14}H_{24}O_3$)

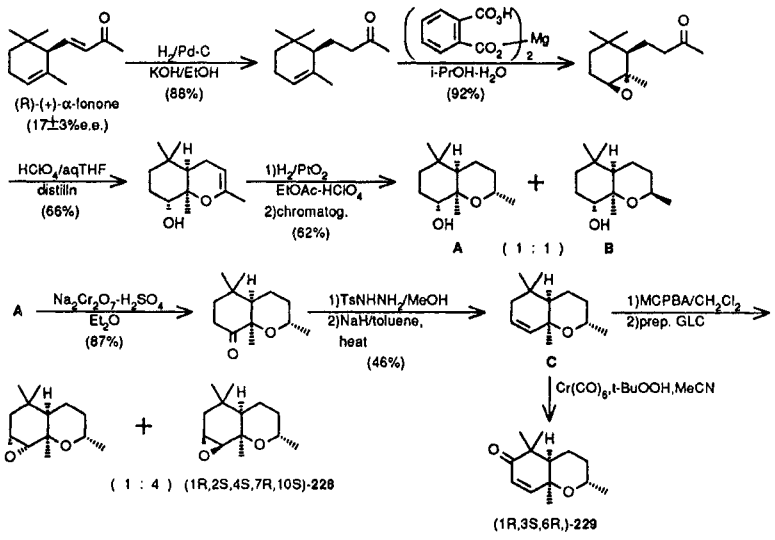
This is also a female-produced sex pheromone component of the cigarette beetle (*Lasioderma serricorne*).[980,981] A diastereomeric mixture of the racemates was synthesized by Chuman et al. (Scheme 777),[980,981] and the natural (2*S*,3*R*,1′*S*,2′*S*)-isomer was synthesized by Ebata and Mori (Scheme 778).[982]

L. (1*R*,2*S*,4*S*,7*R*,10*S*)-9,10-Epoxytetrahydroedulan (1,6,6,10-Tetramethyl-3,11-dioxatricyclo[5.4.0.$0^{2,4}$]undecane) 228 ($C_{13}H_{22}O_2$)

This is the main component among the volatiles from hairpencils of male monarch butterflies of the genus *Euploea* such as *E. klugii*, *E. boisduvalii*, *E. leucostictos*, *E. tulliolus*, *E. mulciber*, and *E. eusipites*. Enantiomerically enriched α-ionone was converted to **228** of 19 ± 3% e.e. by Francke et al. (Scheme 779).[983]

M. (1*R**,3*S**,6*R**)-1,3,7,7-Tetramethyl-2-oxabicyclo[4.4.0]dec-9-en-8-one 229 ($C_{13}H_{20}O_2$)

This was found in hairpencil extracts of the monarch butterfly (*Danaus plexippus*). Francke et al. synthesized enantiomerically enriched **229** as shown in Scheme 779.[983]



Scheme 779

20. ACETALS AS PHEROMONES

Many acetals have been isolated as pheromones. Bicyclic acetals with bridged-ring systems will be treated first, followed by a discussion of tricyclic acetals. The NMR and mass spectral data of several 6,8-dioxabicyclo[3.2.1]octanes were recorded by Mundy et al.[984]

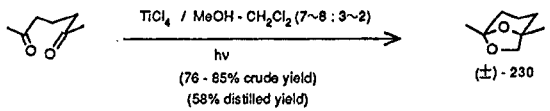
A. (1*S*,5*R*)-Frontalin (1,5-Dimethyl-6,8-dioxabicyclo[3.2.1]octane) 230 ($C_8H_{14}O_2$)

This is the female-produced pheromone of the southern pine beetle (*Dendroctonus frontalis*), and the male-produced pheromone of the western pine beetle (*Dendroctonus brevicomis*). The Douglas-fir beetle (*Dendroctonus pseudotsugae*) also uses **230** as a pheromone component. *D. frontalis* and *D. pseudotsugae* seem to possess enantioselective acceptors on their pheromone receptor cells.[985,986]

(1) Syntheses of (±)-Frontalin

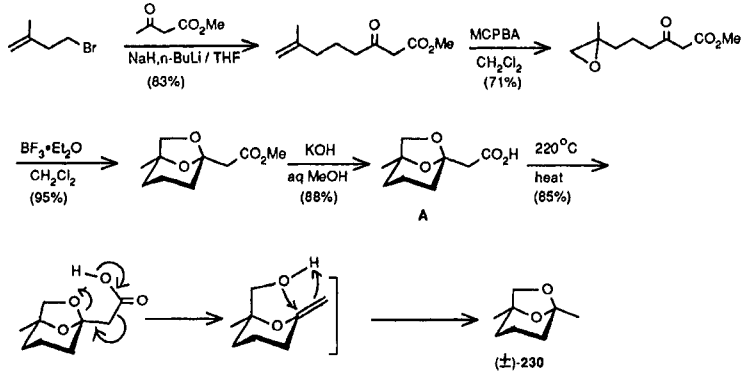
Nine additional syntheses of (±)-**230** have appeared since 1979. A full paper was published describing Sato's synthesis of (±)-**230** by irradiation of heptane-

2,6-dione in methanol with quartz-filtered light in the presence of titanium(IV) chloride (Scheme 780).[987] Sum and Weiler used their dianion alkylation method



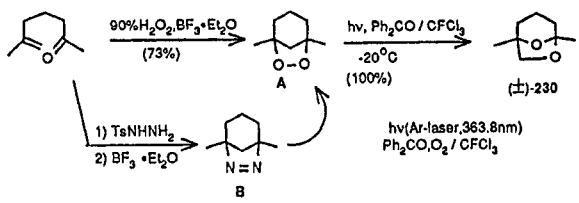
Scheme 780

to develop an efficient synthesis of (±)-**230** (Scheme 781).[988] Noteworthy is



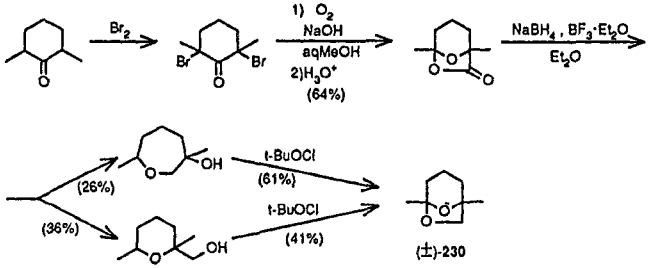
Scheme 781

the facile thermal decarboxylation of **A** to give (±)-**230.** An interesting synthesis of (±)-**230** was achieved by photo-induced decomposition of bicyclo[3.2.1]endoperoxide **A,** which could be prepared in two different manners (Scheme 782).[989] This synthetic work was followed by bioassay of the endo-



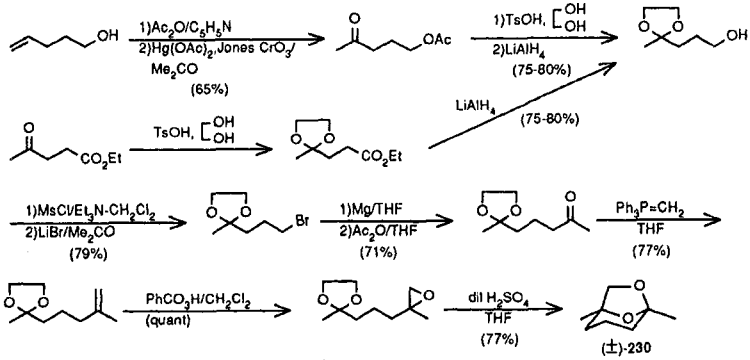
Scheme 782

peroxide **A** and azoalkane **B**. Electroantennogram (EAG) studies of **A** and **B** revealed them to be bioactive against *D. brevicomis*, as is (±)-**230** itself.[989] Utaka et al. converted 2,6-dimethylcyclohexanone to (±)-**230** (Scheme 783).[990]

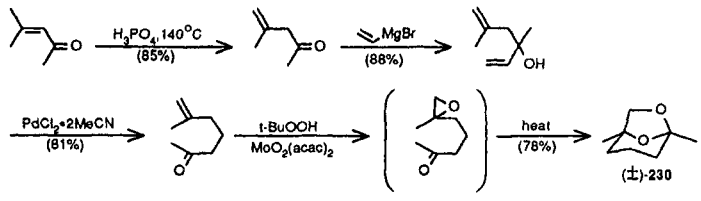


Scheme 783

Joshi's synthesis of (±)-**230** started from ethyl levulinate or 4-penten-1-ol (Scheme 784),[991] while Serebryakov prepared (±)-**230** from mesityl oxide (Scheme 785).[992] Imamoto's simple synthesis of (±)-**230** was based on the

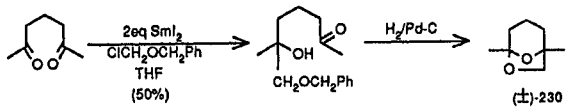


Scheme 784



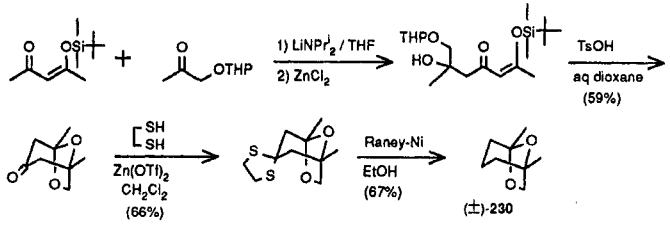
Scheme 785

hydroxymethylation method using samarium(II) iodide (Scheme 786).[993] The



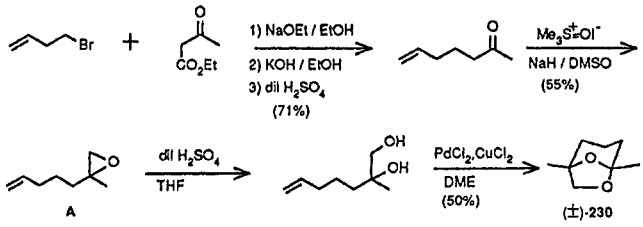
Scheme 786

synthesis of (±)-**230** by Hagiwara and Uda (Scheme 787) used the cross-aldol



Scheme 787

condensation of the lithio-enolate of 4-(*t*-butyldimethylsilyloxy)-3-penten-2-one with a protected α-ketol.[994] Kongkathip et al. synthesized (±)-**230** from ethyl acetoacetate in five steps involving cyclization with palladium catalyst (Scheme 788).[995]

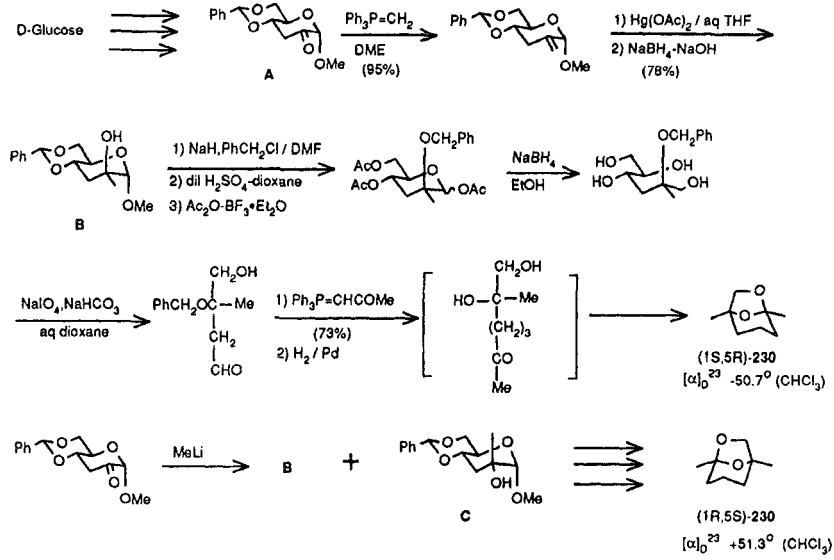


Scheme 788

(2) Syntheses of the Enantiomers of Frontalin

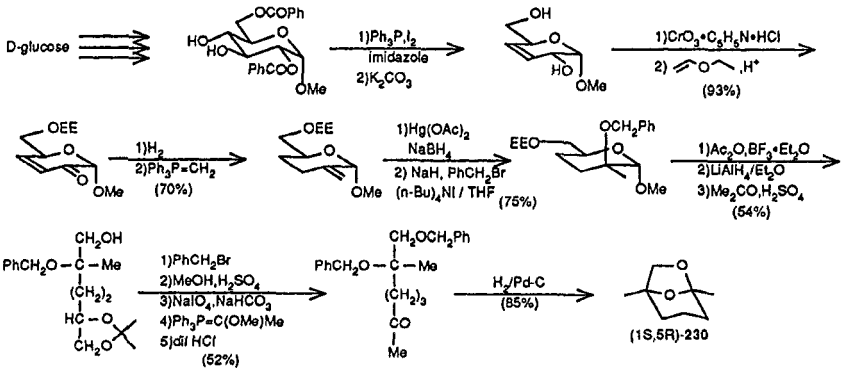
Since 1975 when Mori synthesized the enantiomers of **230** for the first time, many enantioselective syntheses of **230** have been reported. Fifteen different syntheses of the enantiomers of **230** have appeared since 1979.

In five syntheses, sugars and α-hydroxy acids were employed as the chiral building blocks. A full paper of the synthesis of the enantiomers of **230** from D-glucose was published by Fraser-Reid and his co-workers.[996] As shown in Scheme 789, they prepared **A** from D-glucose, from which the diastereomeric



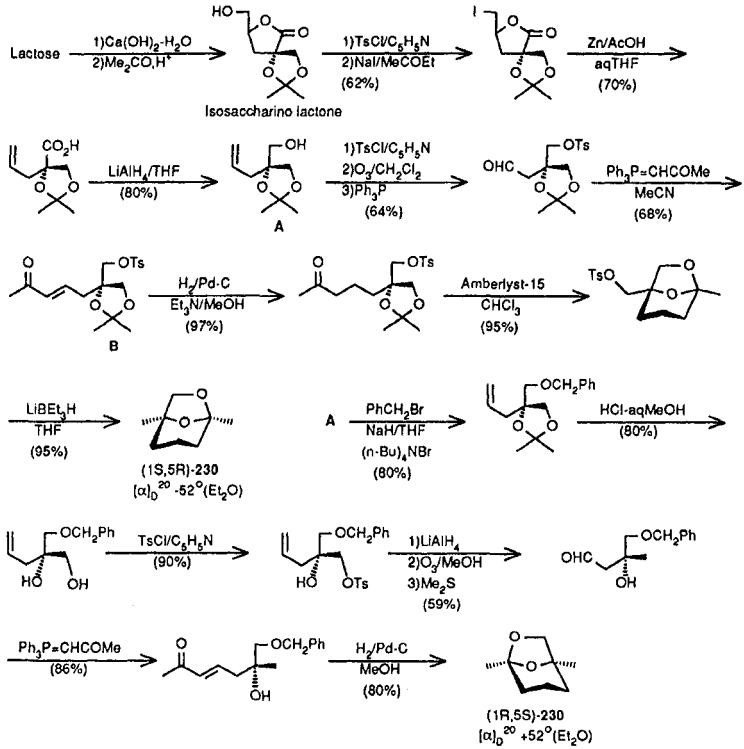
Scheme 789

tertiary alcohols **B** and **C** were synthesized. Subsequently, **B** yielded (1*S*,5*R*)-**230**, and **C** furnished the (1*R*,5*S*)-isomer. They also recorded an alternative and a more efficient synthesis of (1*S*,5*R*)-frontalin (Scheme 790).[996]



Scheme 790

Monneret and co-workers started from lactose (Scheme 791) and synthesized

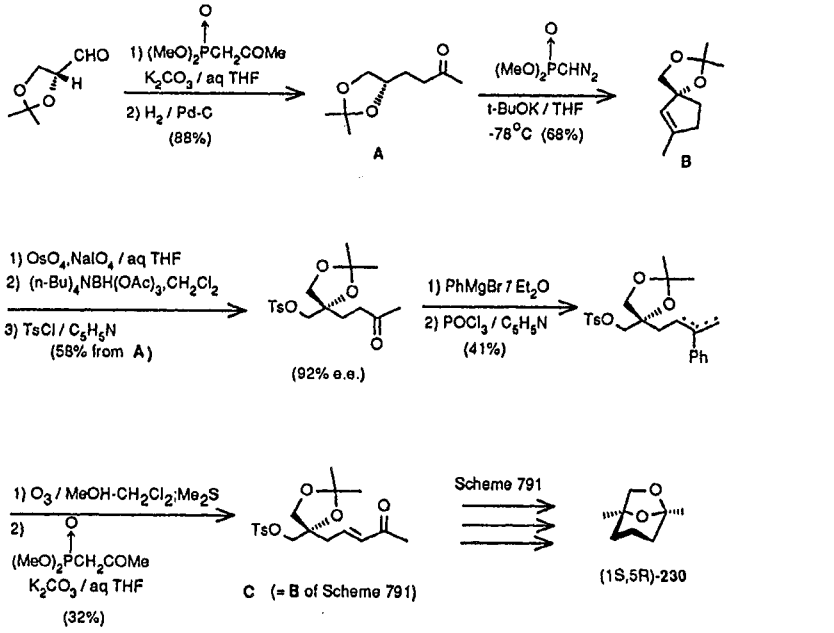


Scheme 791

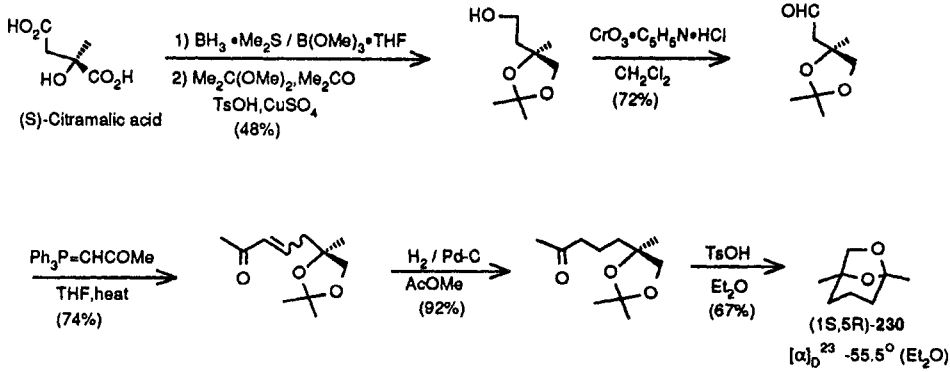
both the enantiomers of **230.**[997,998] However, these syntheses starting from sugars are too lengthy. Monneret's intermediate **B** (Scheme 791) was later synthesized by Ohira et al. from D-glyceraldehyde acetonide (Scheme 792).[999] The key-step was the intramolecular insertion of carbene into the C-H bond adjacent to the protected secondary hydroxy group **(A → B).**

Barner and Hübscher employed (*S*)-citramalic acid as their starting material and synthesized (1*S*,5*R*)-**230** (Scheme 793).[1000] Naef and Seebach began with the enantiomers of lactic acid and efficiently synthesized both enantiomers of **230** by applying their principle of "self-reproduction of chirality" (Scheme 794).[1001]

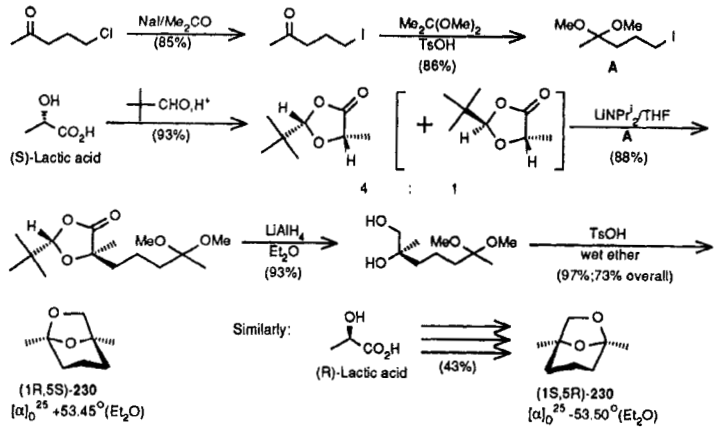
Out of seven chemical asymmetric syntheses of **230,** three utilized asymmetric carbon-carbon bond formation reactions. Sakito and Mukaiyama synthesized the enantiomers of frontalin by an asymmetric Grignard reaction employ-



Scheme 792

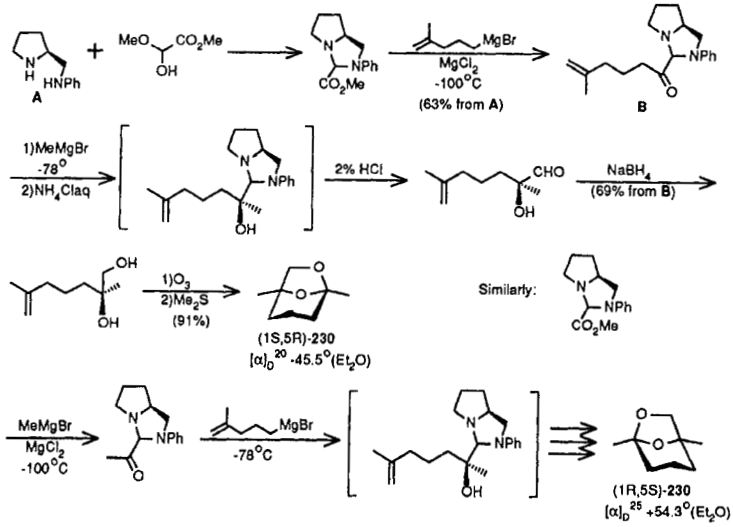


Scheme 793



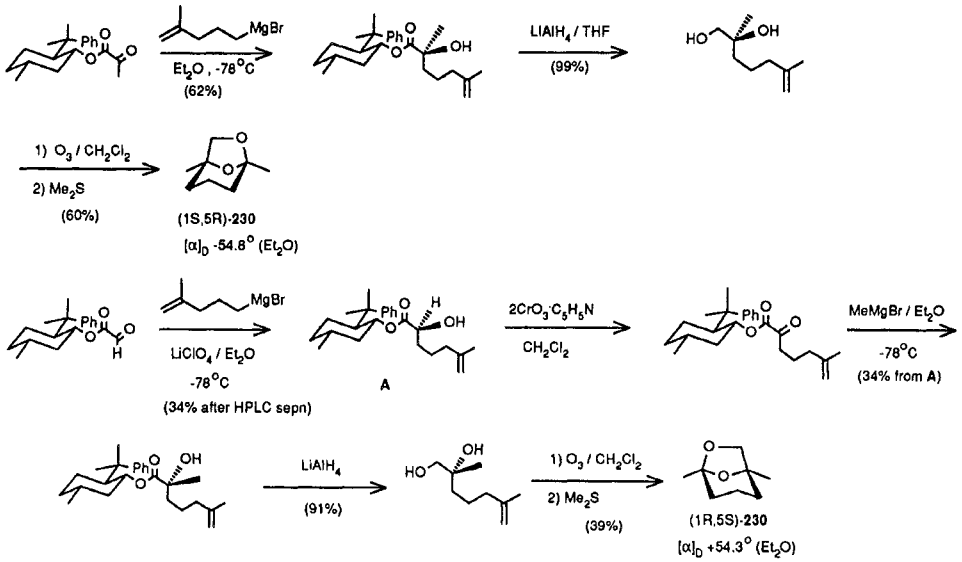
Scheme 794

ing (*S*)-2-(anilinomethyl)pyrrolidine as the chiral auxiliary (Scheme 795).[1002]



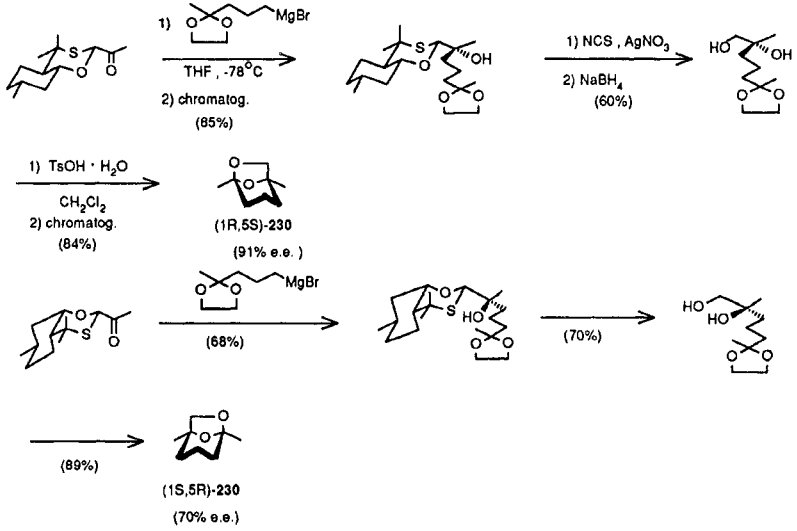
Scheme 795

By using (*R*)-8-phenylmenthol as the chiral auxiliary, Whitesell and Buchanan prepared both the enantiomers of **230** (Scheme 796).[1003] Ohwa and Eliel reported two asymmetric syntheses of **230,** the shorter one consisting of four steps and the longer of seven, employing chiral 1,3-oxathiane precursors (Schemes

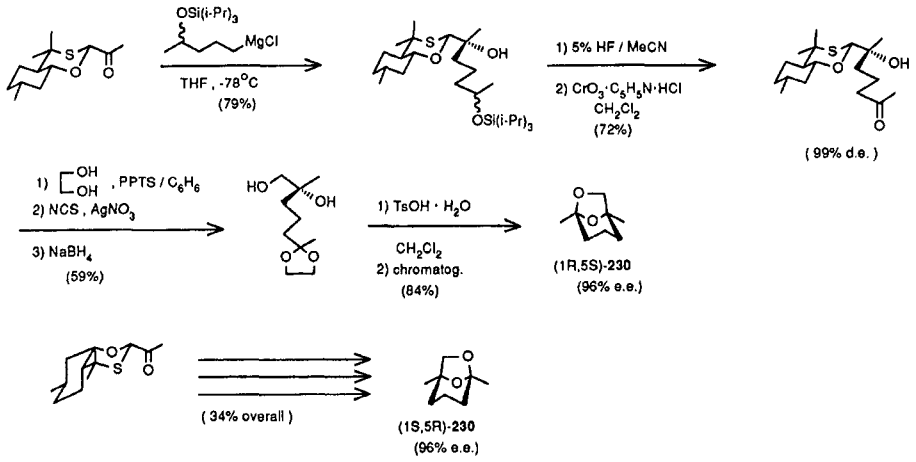


Scheme 796

797 and 798).[1004] The lengthy route yielded products of higher e.e. (96%) than the shorter one [(−)-**230**: 70% e.e.].

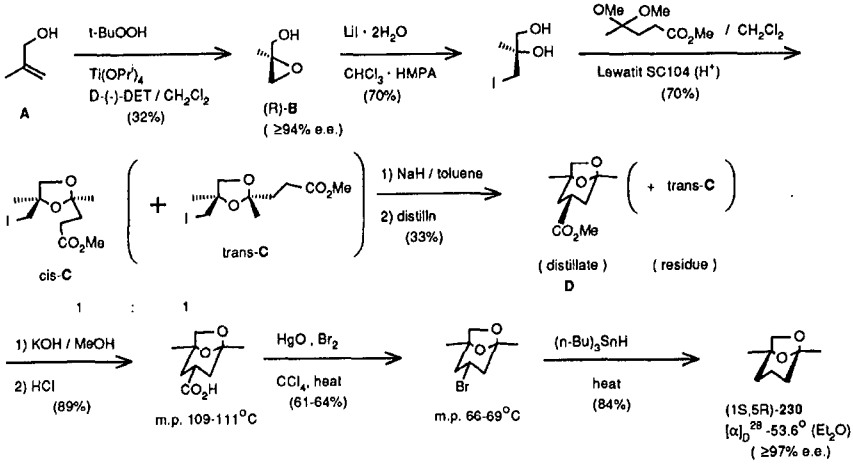


Scheme 797



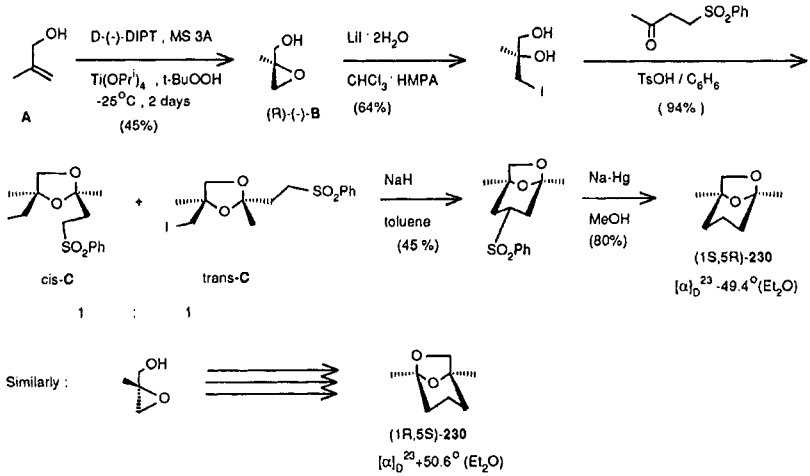
Scheme 798

The Sharpless asymmetric epoxidation was applied in the four enantioselective syntheses of frontalin. Meister and Scharf epoxidized methallyl alcohol **A** to (*R*)-**B** (Scheme 799).[1005] The unique feature of their synthesis was the carbon-



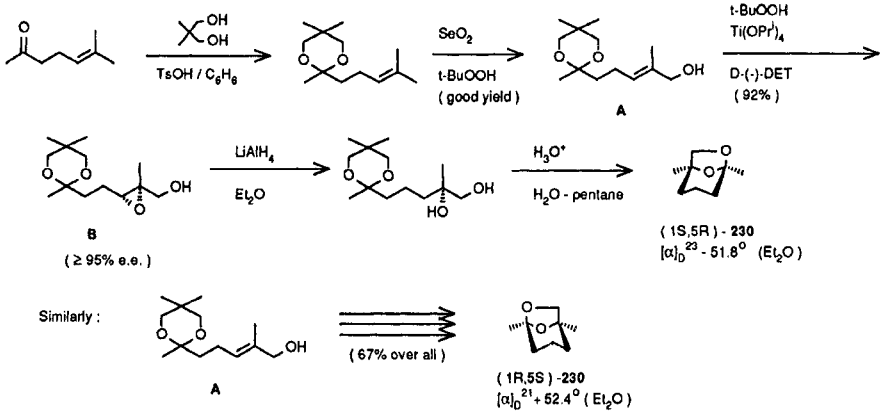
Scheme 799

carbon bond formation (*cis*-**C** → **D**) *after* the formation of the acetal ring. Scharf and his co-workers later reported an improved synthesis along this line using phenylsulfone as the readily removable activator (Scheme 800).[1006] Lee pre-



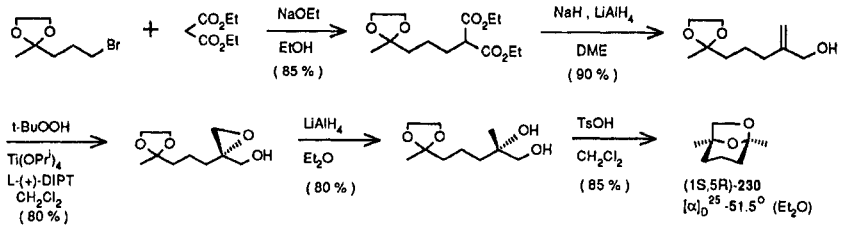
Scheme 800

pared both the enantiomers of **230** by epoxidizing **A** to give **B** (Scheme 801),[1007]

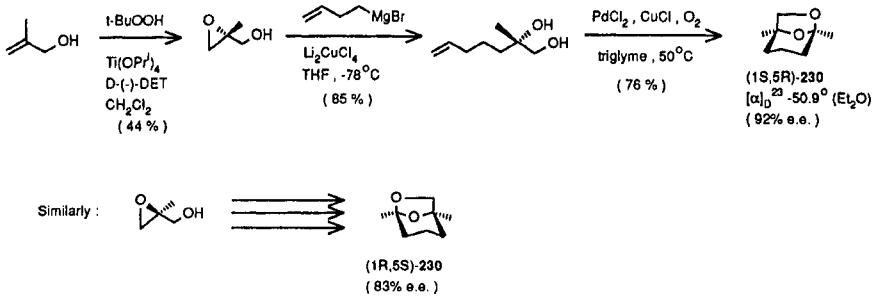


Scheme 801

in which the use of a bulky acetal group was necessary. If the corresponding ethylene acetal was epoxidized, both the chemical and asymmetric yield dropped remarkably.[1007] Yadav et al. (Scheme 802),[1008] as well as Murahashi and co-workers (Scheme 803),[1009] employed the asymmetric epoxidation to prepare **230.** In Murahashi's synthesis, the palladium-catalyzed intramolecular acetalization was also worthy of note.[1009]

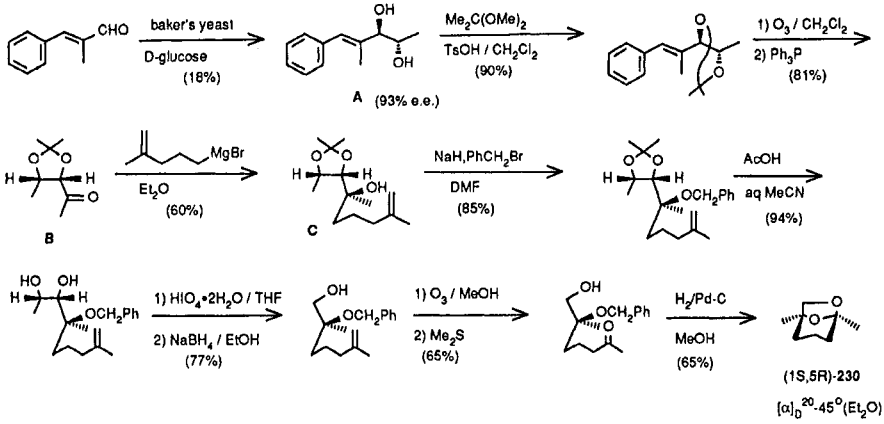


Scheme 802



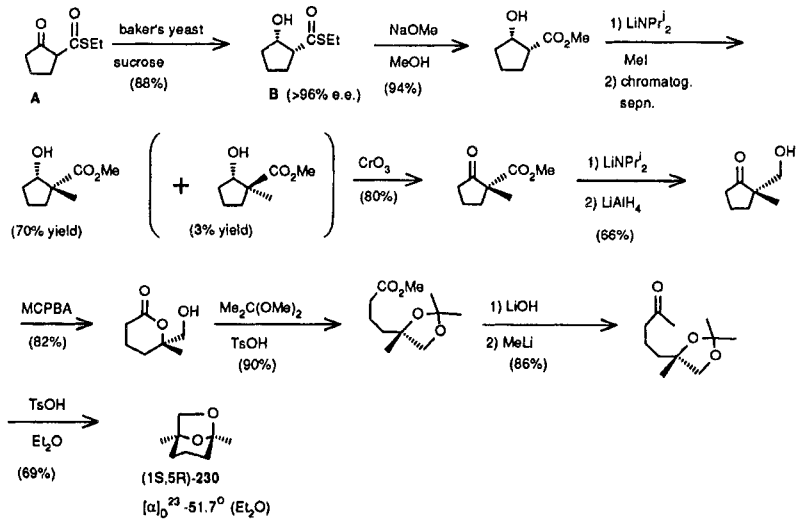
Scheme 803

Biochemical reactions were used by three groups for the preparation of the enantiomers of **230.** Fuganti et al. reduced α-methylcinnanaldehyde with baker's yeast to give **A.** This was converted to **B,** to which was added a Grignard reagent to selectively produce **C** (Scheme 804).[1010] Conversion of **C** to (−)-**230**



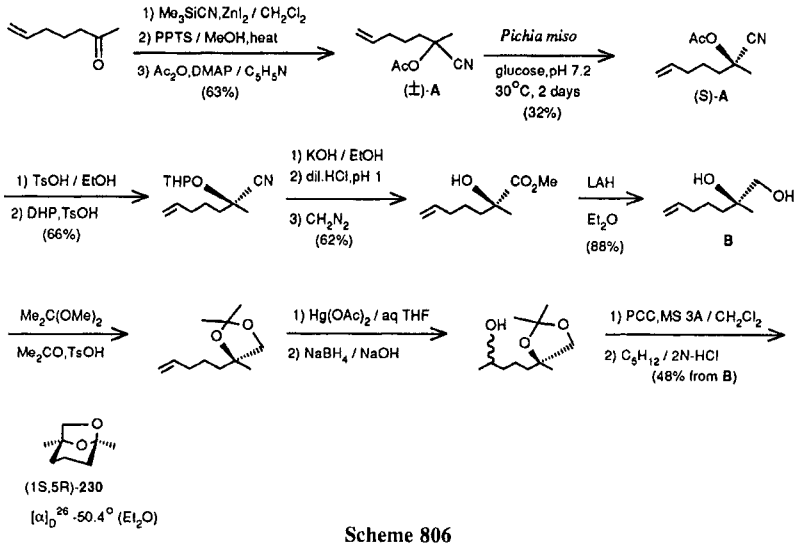
Scheme 804

was a routine process. Sato et al. reduced β-keto thiol ester **A** to give a hydroxy ester **B**, which was converted to (−)-**230** (Scheme 805).[1011] Ohta et al. achieved



Scheme 805

kinetic resolution of (±)-**A** on incubation with *Pichia miso* (yeast) to give (*S*)-**A**, which was converted to (−)-**230** (Scheme 806).[1012]



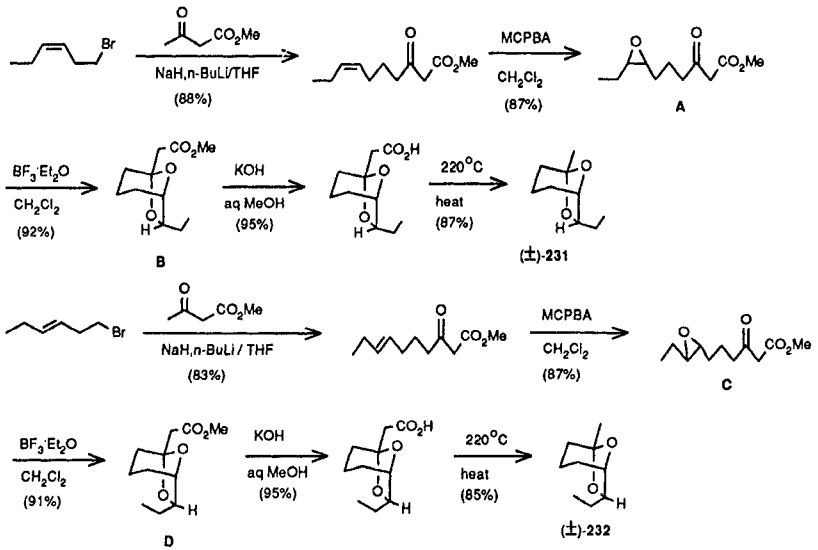
Scheme 806

B. (1*R*,5*S*,7*R*)-*exo*-Brevicomin (*exo*-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]octane) 231 ($C_9H_{16}O_2$) and (1*R*,5*S*,7*S*)-*endo*-Brevicomin (*endo*-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1] octane 232 ($C_9H_{16}O_2$)

exo-Brevicomin **231** is the aggregation pheromone of the western pine beetle (*Dendroctonus brevicomis*) and the western balsam bark beetle (*Dryocetes confusus*), while *endo*-brevicomin **232** is the pheromone of the southern pine beetle (*Dendroctonus frontalis*) and *Dryocetes autographus*. The aggregation response of *D. frontalis* to entrap when baited with frontalin can be enhanced by (1*R*,5*S*,7*S*)-(+)-**232**, while (1*S*,5*R*,7*R*)-(−)-**232** significantly reduces the beetle response to frontalin.[1013] Due to the presence of contiguous chiral centers at C-1 and C-7, both **231** and **232** are the favorite targets for chemists engaged in stereoselective synthesis, and, therefore, over 50 syntheses of **231** and **232** have been published since 1979.

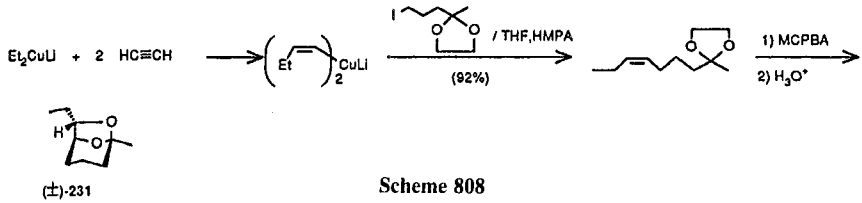
(1) Syntheses of Racemic Brevicomins

The classical strategy to control the relative stereochemistry between C-1 and C-7 is to introduce the diol system by stereospecific epoxidation or hydroxylation of the *E*- or *Z*-double bond. Accordingly, the preparation of the geometrically pure olefinic ketone (or its equivalent) has been pursued. Sum and Weiler synthesized both (±)-**231** and (±)-**232** (Scheme 807), employing the dianion



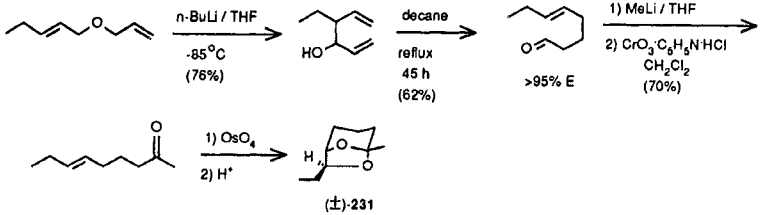
Scheme 807

alkylation as the key chain-elongation reaction.[988] Noteworthy is the cyclization step (**A** → **B** and **C** → **D**) because it was totally stereospecific in these two cases. A number of earlier syntheses of (±)-**231** and (±)-**232** involved a thermal or acid-catalyzed cyclization of an epoxy ketone to generate the acetal, often as an *exo-endo* mixture. Normant's organocopper chemistry was employed for the synthesis of (±)-**231** (Scheme 808).[115] Mikami and Nakai syn-



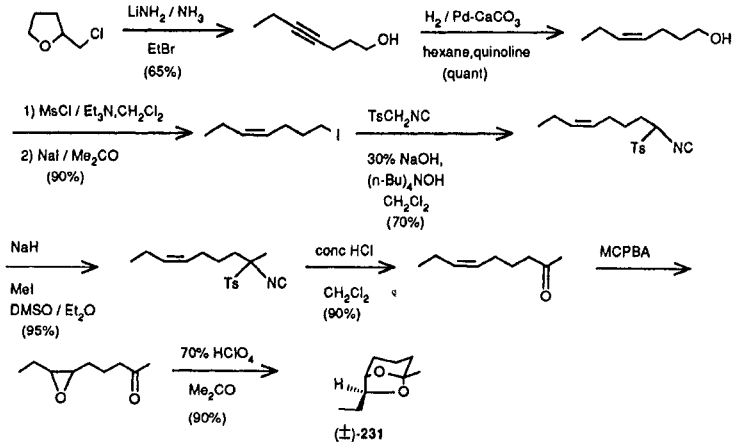
Scheme 808

thesized (±)-**231** by the application of the tandem [2.3]Wittig-oxy Cope rearrangement (Scheme 809).[1014] Classical acetylene chemistry coupled with the



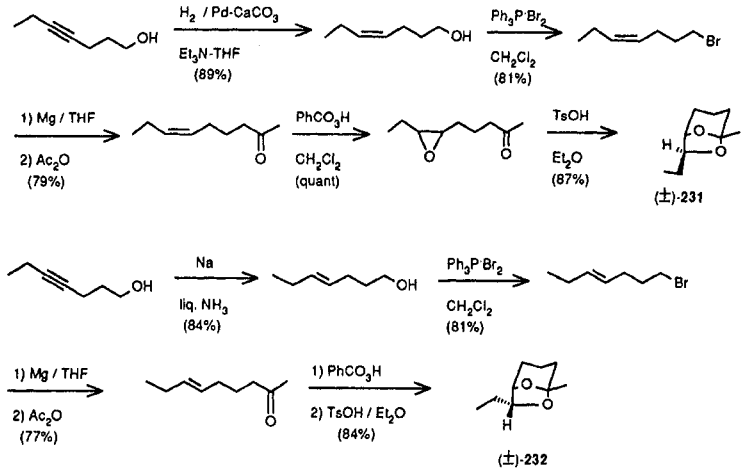
Scheme 809

use of tosylmethyl isocyanide enabled Yadav and co-workers to prepare (±)-**231** (Scheme 810).[1015] Application of the well-established acetylene chemistry en-



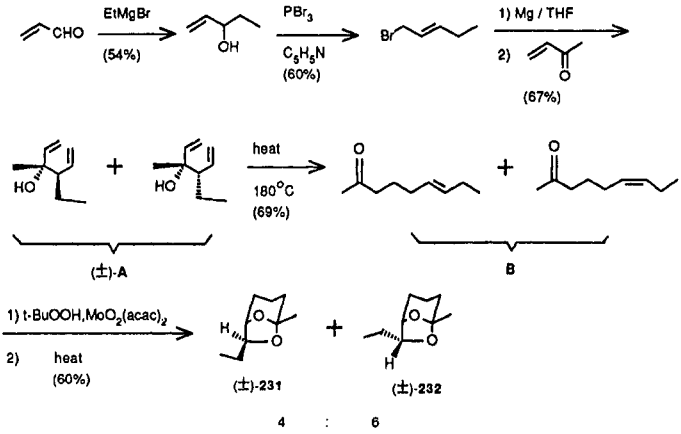
Scheme 810

abled Joshi et al. to synthesize both (±)-**231** and (±)-**232** (Scheme 811).[991]



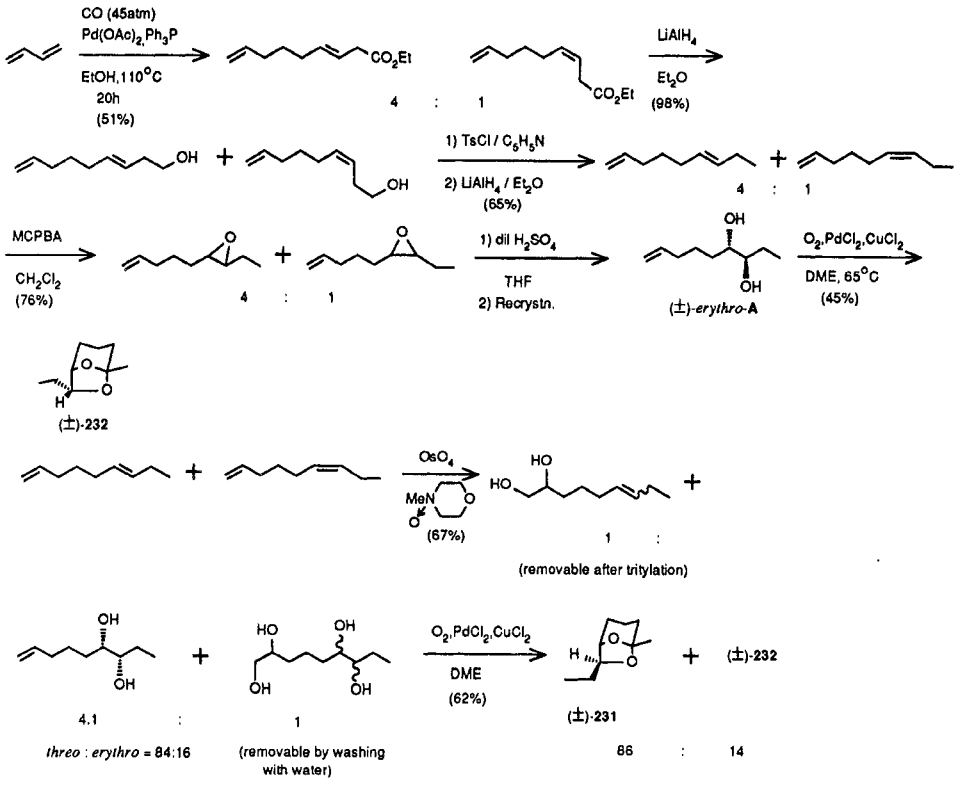
Scheme 811

Oxy-Cope rearrangement (**A** → **B**, Scheme 812) was the key-step in Serebry-



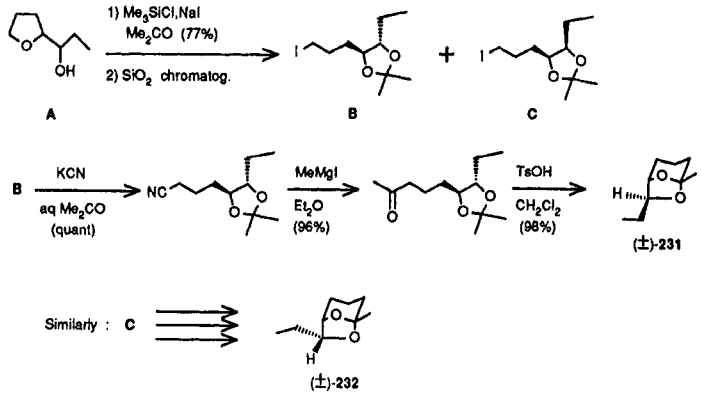
Scheme 812

akov's synthesis of (±)-**231** and (±)-**232**.[1016] Grigg and his co-workers were the first to apply the intramolecular Wacker-type reaction in the synthesis of intramolecular acetals, and their full paper on the synthesis of (±)-**231** and (±)-**232** has been published (Scheme 813),[1017] in which the 400 MHz ^{1}H nmr

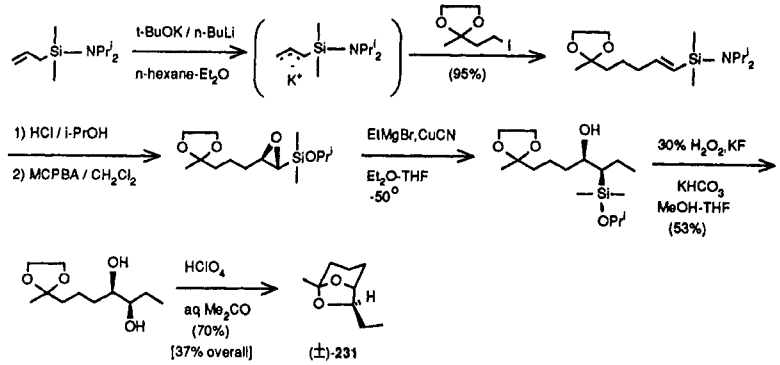


Scheme 813

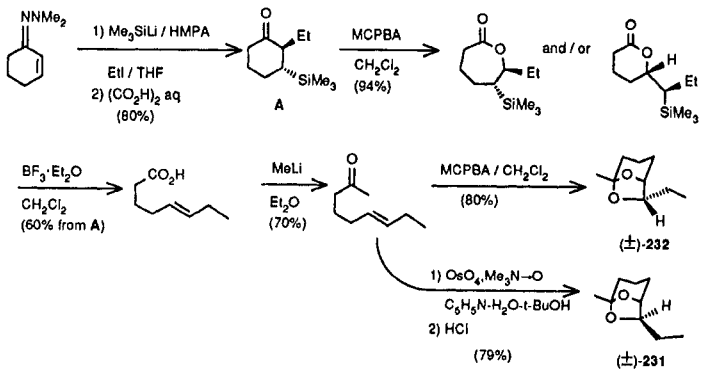
spectra of (±)-**231** and (±)-**232** are listed. As shown in the Scheme, Grigg's palladium-catalyzed reaction of butadiene with carbon monoxide and ethanol was of low stereoselectivity (4 : 1), and this fact complicated the synthesis. Jatczak et al. devised a new method for the cleavage of a tetrahydrofuran derivative **A** (Scheme 814) to give a mixture of **B** and **C**, which were separately converted to (±)-**231** and (±)-**232**, respectively.[1018] (*E*)-1-Silyl-1-alkene was found to give *threo*-1,2-diol stereoselectively, and Tamao et al. prepared (±)-**231** (Scheme 815).[1019] Another silicon-mediated synthesis of both (±)-**231** and (±)-**232** was published by Hudrlik et al. (Scheme 816).[1020] Organosulfur chemistry was also useful in providing (±)-brevicomins, and Ishibashi et al. prepared (±)-**231** and (±)-**232** starting from *p*-chlorophenyl methyl sulfoxide (Scheme 817).[1021] Oxidative Grob fragmentation of γ-tributylstannyl alcohol **A** to olefinic ketone **B** was the key step in Ochiai's synthesis of (±)-**232** (Scheme 818).[667]



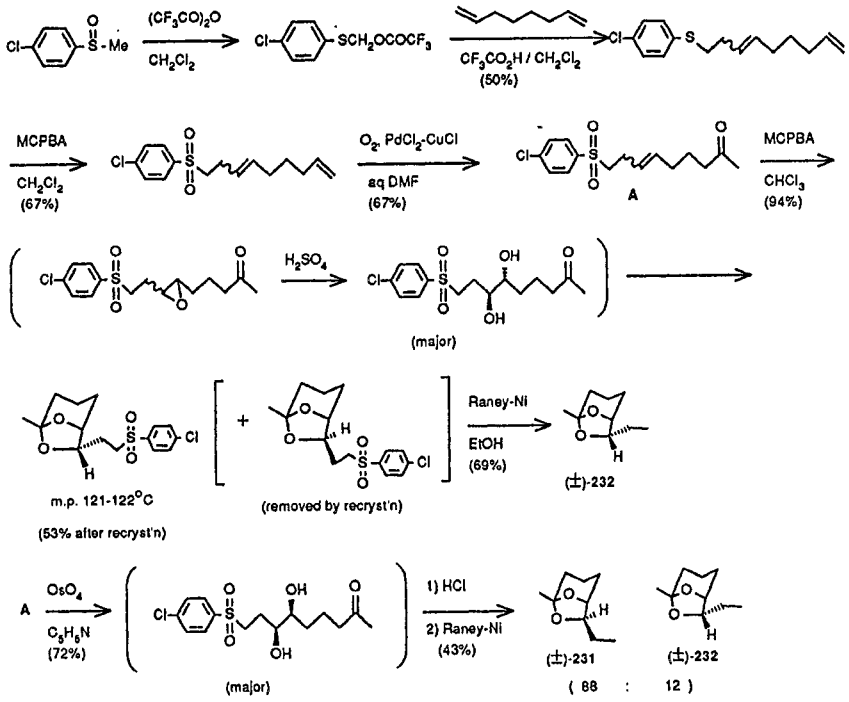
Scheme 814



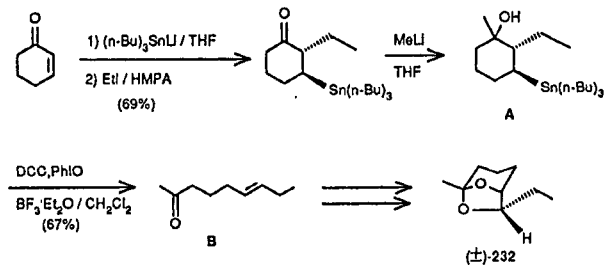
Scheme 815



Scheme 816

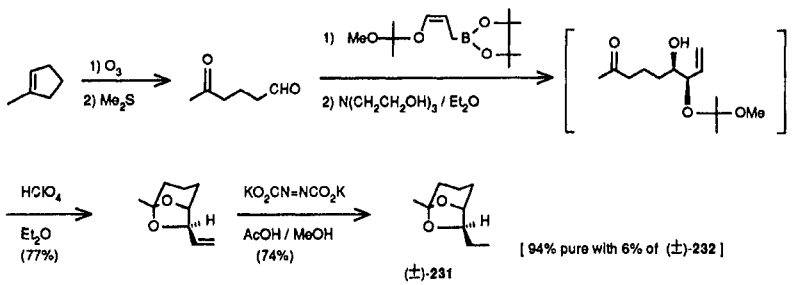


Scheme 817



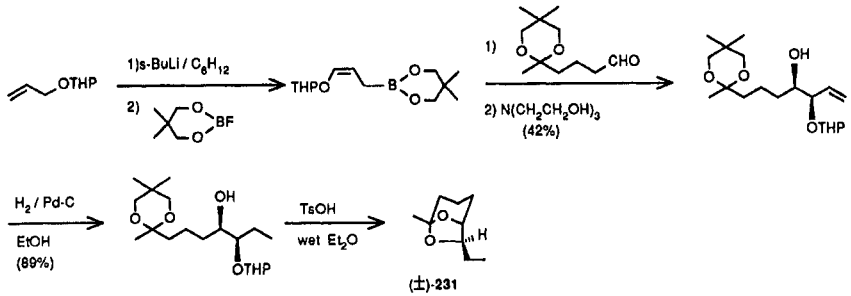
Scheme 818

Diastereoselective formation of the 1,2-diol system, the key feature of brevicomin precursors, was attempted by nucleophilic addition of an appropriate carbanion to an aldehyde intermediate. Hoffmann et al. studied the addition of γ-alkoxy-(Z)-allylboronates to aldehydes and synthesized (±)-**231** (Scheme



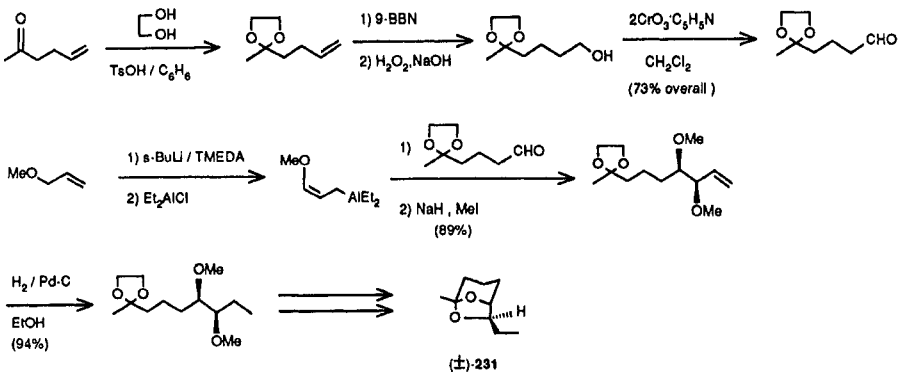
Scheme 819

819).[1022, 1023] Similarly but independently, Wuts and Bigelow also synthesized (±)-**231** by the same methodology (Scheme 820).[1024] A γ-methoxyallylalu-



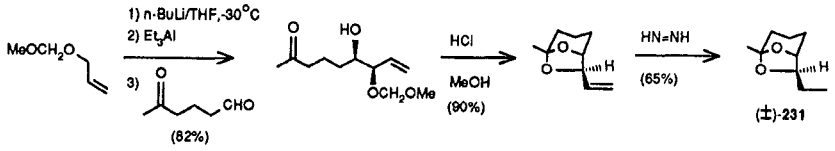
Scheme 820

minum compound and an aldehyde were chosen by Koreeda and Tanaka as the starting materials for the synthesis of (±)-**231** (Scheme 821).[1025] Similarly, the



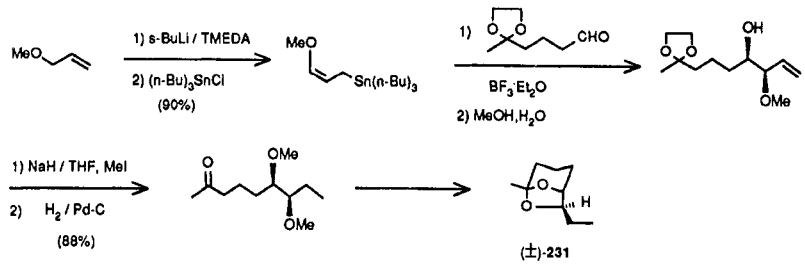
Scheme 821

addition of a heterosubstituted allylic carbanion to an aldehyde was employed by Y. Yamamoto et al. to prepare (±)-**231** (Scheme 822).[1026] (*Z*)-Methoxy-



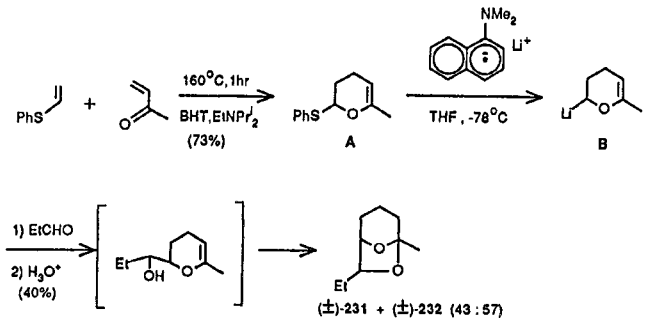
Scheme 822

allylstannane was used by Koreeda and Tanaka to prepare (±)-**231** (Scheme 823).[1027]



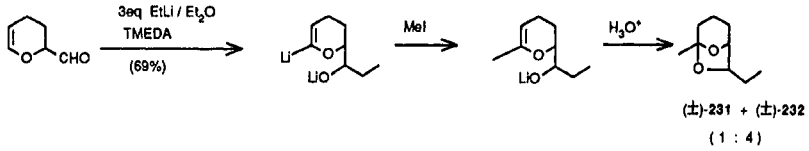
Scheme 823

The third approach to *exo*- and *endo*-brevicomin was the ring formation by hetero-Diels-Alder reactions. Cohen and Matz prepared a dihydropyran **A** (Scheme 824), which was converted to a mixture of (±)-**231** and (±)-**232** via



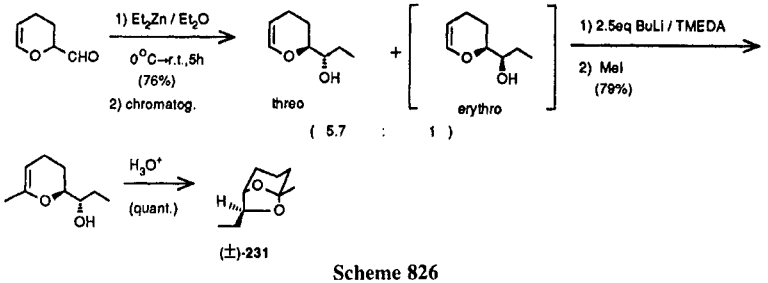
Scheme 824

α-lithioether (±)-**B**.[1028] Cohen and Bhupathy then reported a more efficient and simple one-flask synthesis of a mixture of (±)-**231** and (±)-**232** (1:4) from acrolein dimer in 69% yield (Scheme 825).[1029] Stereoselective addition of ethyl-



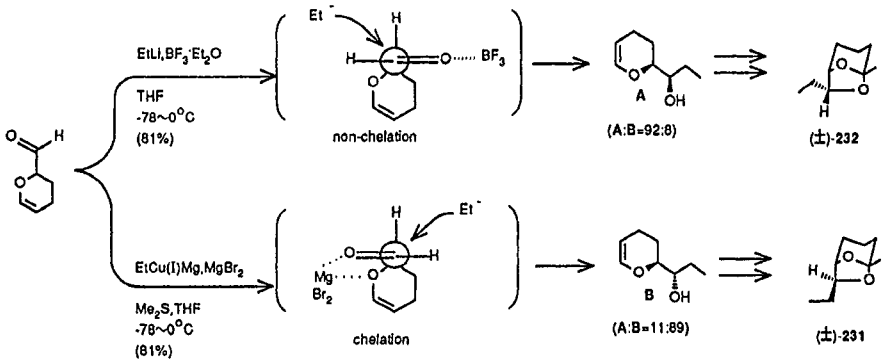
Scheme 825

metallic reagents to acrolein dimer was subsequently achieved by Cohen to produce (±)-**231** as the major product (Scheme 826).[1030] Singh and Oehl-



Scheme 826

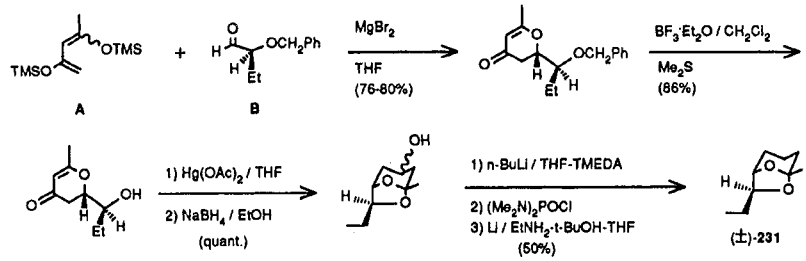
schlager further studied the chelation versus nonchelation control in addition reactions of ethylmetallic reagents to acrolein dimer (Scheme 827).[1031] When



Scheme 827

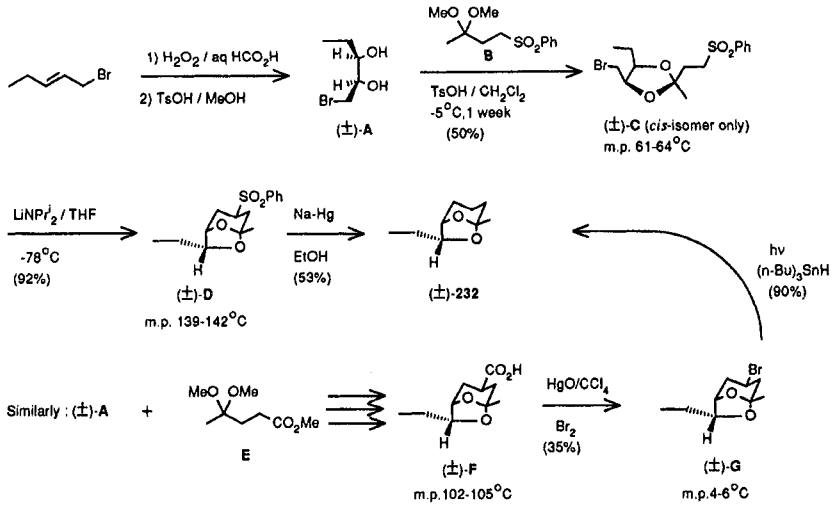
ethyllithium was used in the presence of boron trifluoride etherate, high selectivity (92:8) was observed for nonchelation-controlled addition, yielding the

erythro-product leading to (±)-**232.** Ethylcopper reagents in the presence of magnesium salts were found to give the *threo*-product generated by chelation control.[1031] Chelation-controlled facially selective cyclocondensation between diene **A** and α-benzyloxyaldehyde **B** as catalyzed by magnesium bromide in THF was employed by Danishefsky et al. for their stereoselective synthesis of (±)-**231** (Scheme 828).[1032] Scharf and co-workers found that the transacetal-



Scheme 828

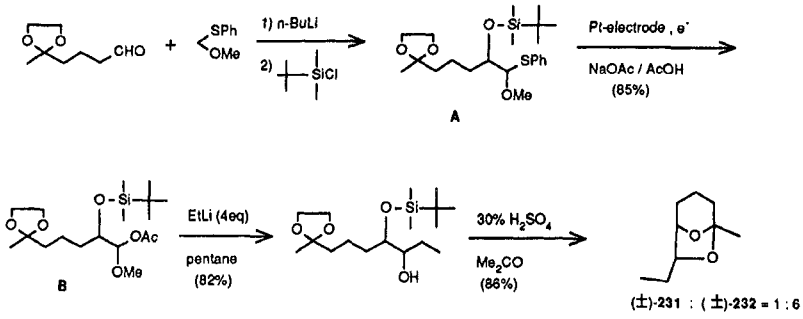
ization between (±)-**A** and **B** under kinetic control results in (±)-**C.** This acetal **C** was treated with a base to produce the brevicomin skeleton **D,** which furnished (±)-**232** (Scheme 829).[1033] Another route starting from (±)- **A** and **E** was also developed via (±)-**F** and (±)-**G** to generate (±)-**232.**[1033]



Scheme 829

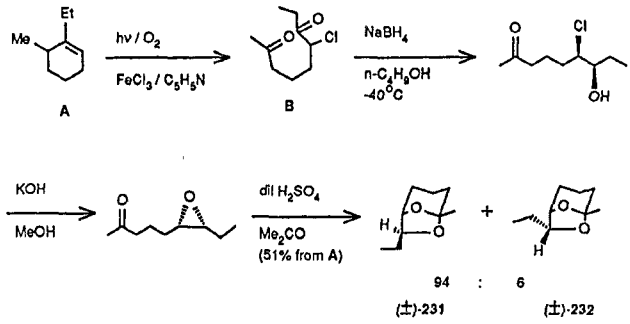
Several other syntheses of (±)-**231** and/or (±)-**232** have been reported. By employing methoxy(phenylthio)methane as a homologation reagent, Otera et

al. prepared a mixture of (±)-**231** and (±)-**232** (Scheme 830).[1034] Electrolysis



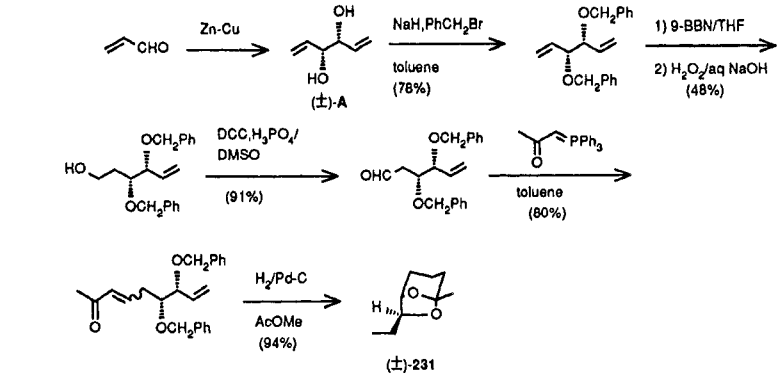
Scheme 830

of hemithioacetal **A** yielded mixed acetal **B,** to which ethyllithium was added to construct the brevicomin skeleton. A unique and efficient synthesis of (±)-**231** was reported by Sato et al. (Scheme 831), which employed a photochemical

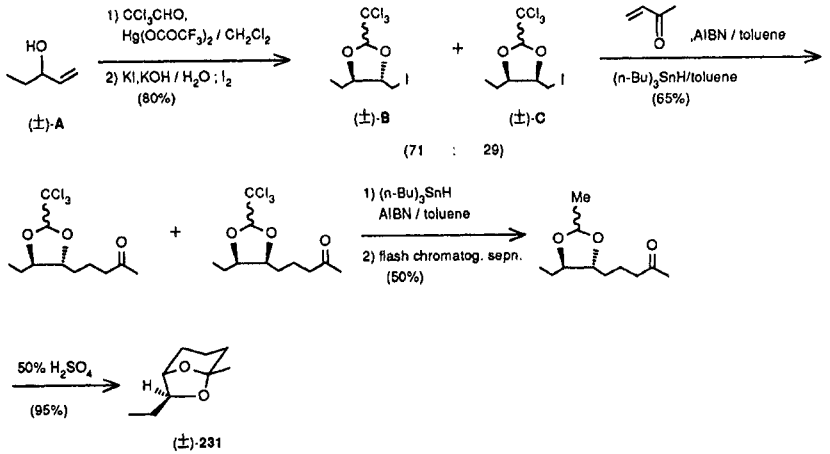


Scheme 831

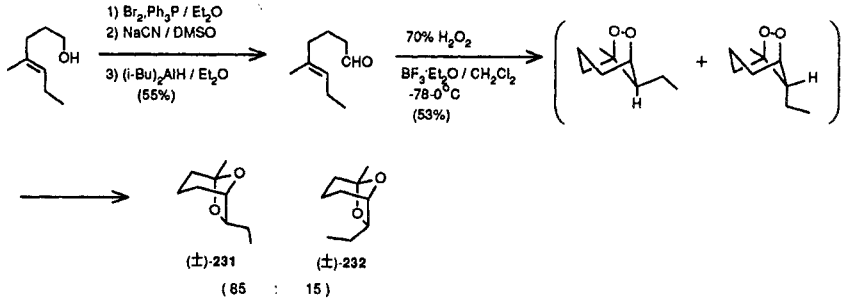
reaction (**A** → **B**) and diastereoselective reduction of chloroketone **B.**[1035] (±)-1,2-Divinylglycol **A,** a product of the reductive dimerization of acrolein with zinc-copper couple, was converted to (±)-**231** (Scheme 832).[1036] As shown in Scheme 833, Giese et al. used a radical reaction to construct the carbon skeleton of (±)-**231.**[1037] An interesting chain-carbonyl transposition strategy was adopted by Wilson et al. to realize a unique synthesis of (±)-**231,** contaminated with a small amount of (±)-**232** (Scheme 834).[1038] Another novel and



Scheme 832

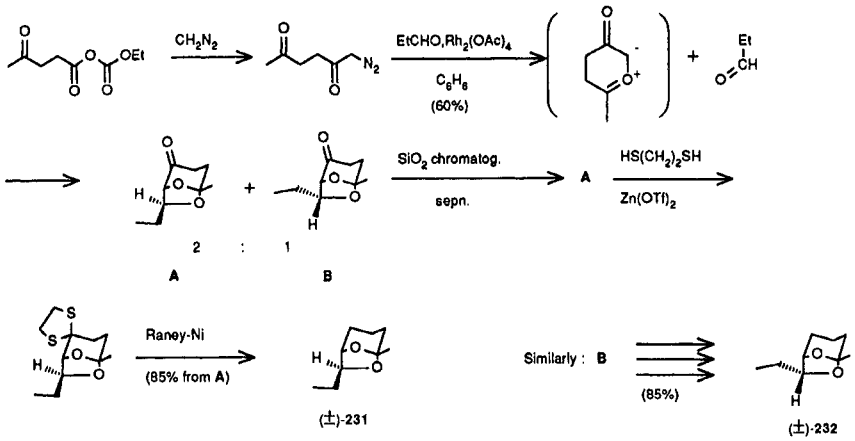


Scheme 833



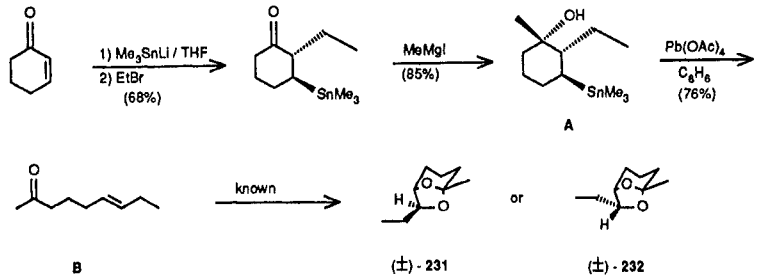
Scheme 834

noteworthy construction of the intramolecular acetal system, as reported by Padwa et al., employed the rhodium-catalyzed cycloaddition reaction of 1-diazo-2,5-hexanedione to propanal (Scheme 835).[1039, 1040] Oxidative fragmentation of



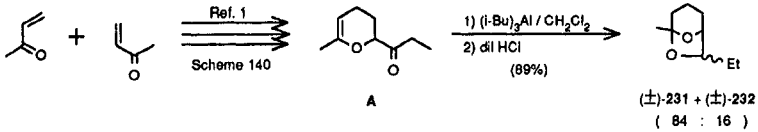
Scheme 835

γ-hydroxystannane **A** to give the known enone **B** was the key-step of Kitching's synthesis of (±)-**231** or (±)-**232** (Scheme 836).[512] Bartelt and Mundy reduced



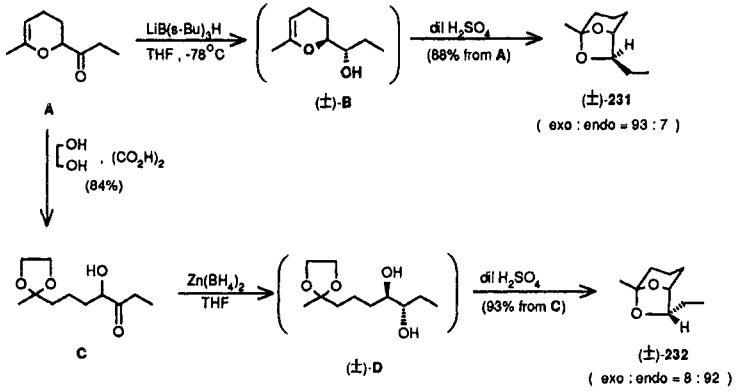
Scheme 836

A with triisobutylaluminum to create a mixture of (±)-**231** and (±)-**232** (Scheme 837).[1041] A thorough investigation of this type of reduction of a carbonyl group



Scheme 837

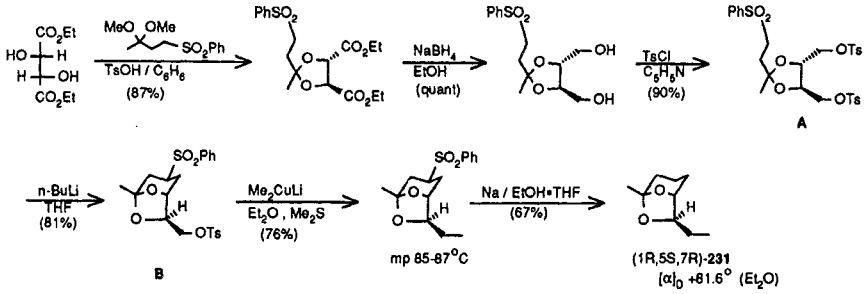
with various reducing agents was made by Ramaswamy and Oehlschlager.[1042] As shown in Scheme 838, they achieved an efficient synthesis of (±)-**231** and (±)-**232** by this approach.[1042]



Scheme 838

(2) Synthesis of Optically Active Brevicomins

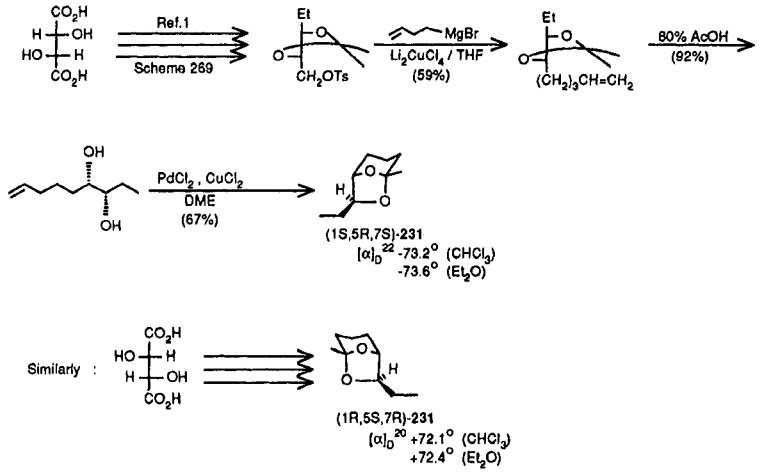
A. From Tartaric Acid. Mori's first synthesis in 1974 of the enantiomers of *exo*-brevicomin **231** started from tartaric acid (Scheme 268, Ref. 1). Since 1979, seven new syntheses of optically active brevicomins have been achieved beginning with tartaric acid. Diethyl D-tartrate was converted by Masaki et al. to (1*R*,5*S*,7*R*)-(+)-**231**, the bioactive enantiomer (Scheme 839).[1043] They were



Scheme 839

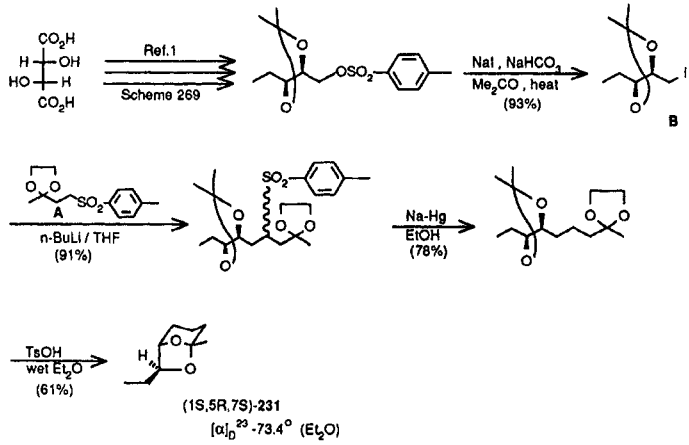
the first to employ the acetal intermediates in earlier stages to execute the final ring-closure by carbon-carbon bond formation in a later stage (**A** → **B**). Mori and Seu employed the palladium-catalyzed Wacker reaction for the 11-step syn-

thesis (4.5% overall yield) of (+)-**232** and (−)-**232** from the enantiomers of tartaric acid (Scheme 840).[1044] In another synthesis, Seu and Mori constructed



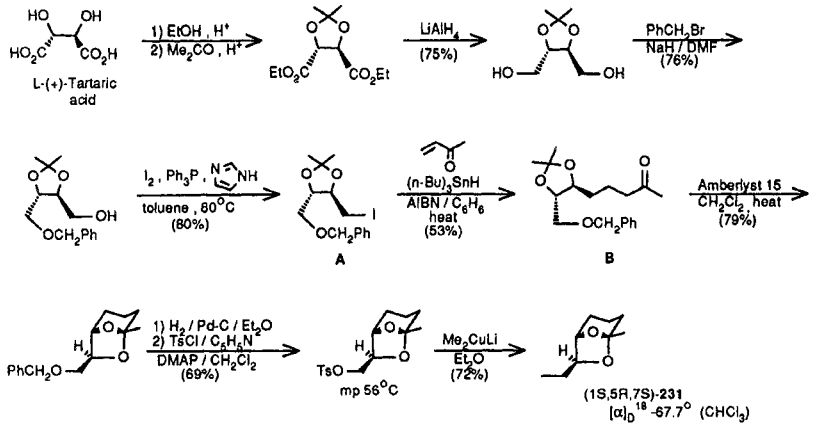
Scheme 840

the carbon skeleton of (−)-**231** by alkylating a sulfone **A** with **B** (Scheme 841).[1045] A radical carbon-carbon bond formation reaction (**A** → **B**) was the



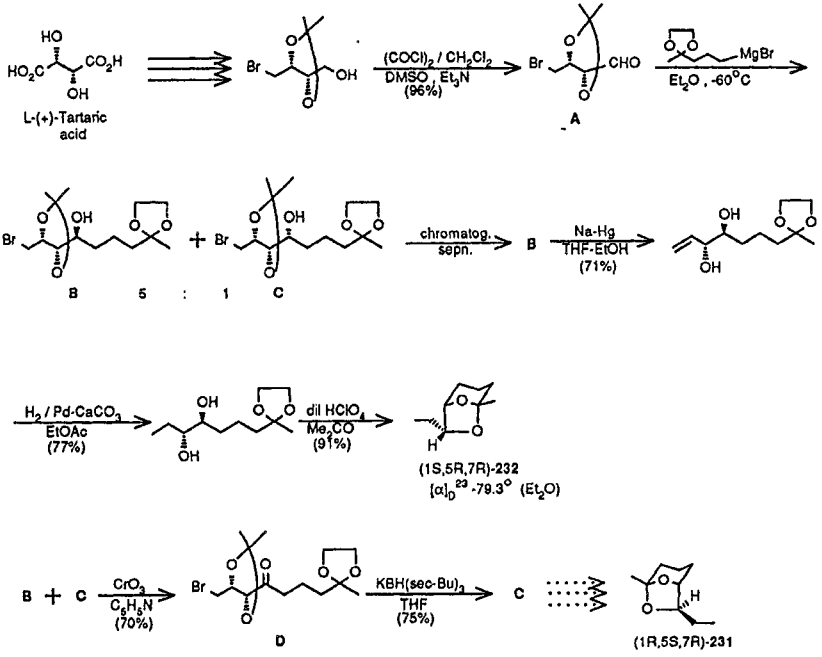
Scheme 841

key reaction in Giese's synthesis of (−)-**231** (Scheme 842).[1046] The overall yield in Giese's synthesis was as high as 17%. Achmatowicz and Wicha de-



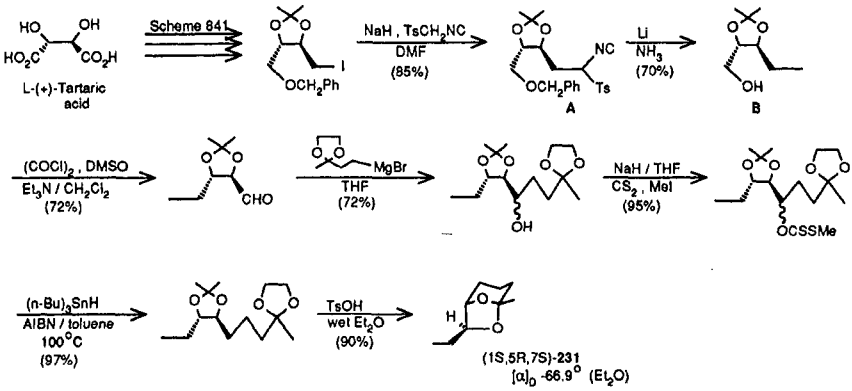
Scheme 842

veloped an interesting synthesis of (−)-*endo*-brevicomin **(232)** from (+)-tartaric acid by using a diastereoselective Grignard reaction with **A** to give **B** predominantly (Scheme 843).[1047] Because **B** could be converted into **C** by



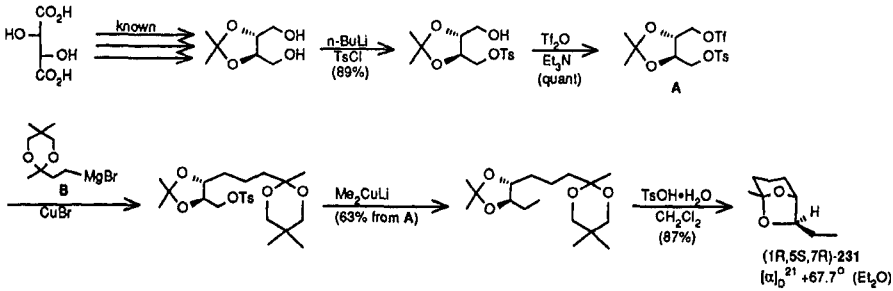
Scheme 843

oxidation-reduction via **D**, this procedure also constitutes a formal synthesis of (−)-*exo*-brevicomin **(231).** Yadav's synthesis of (−)-**231** was based on the reduction of a dialkylated tosylmethyl isocyanide with lithium in liquid ammonia to the corresponding hydrocarbon **(A → B)** (Scheme 844).[93] Kotsuki et al. pre-



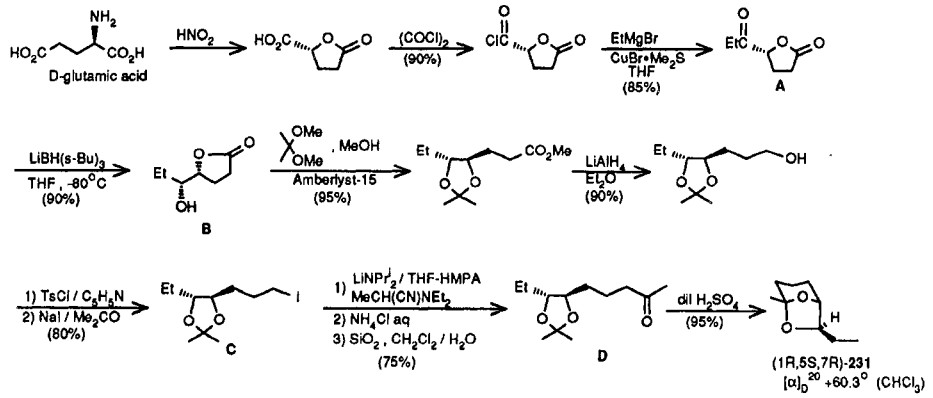
Scheme 844

pared (+)-**231** by a coupling reaction between the triflate **A** and the Grignard reagent **B** in the presence of cuprous bromide (Scheme 845).[1048] It should be noted that the tosylate in **A** was less reactive than the triflate.



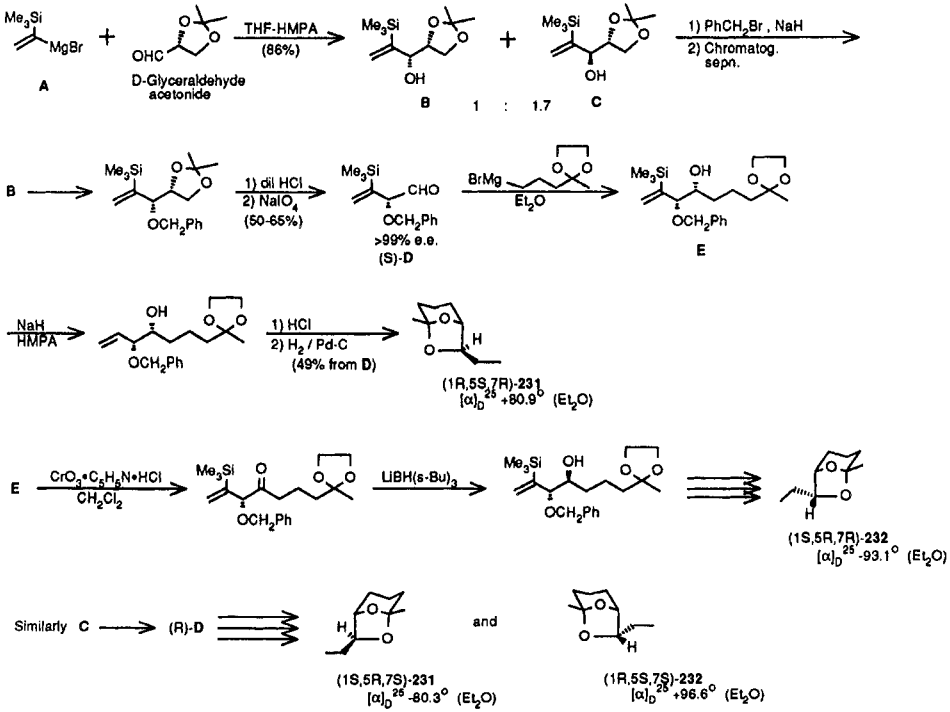
Scheme 845

B. From Glutamic Acid. Larchevêque and Lalande synthesized (+)-*exo*-brevicomin **(231)** starting from D-glutamic acid (Scheme 846).[1049, 1050] Notable features of their synthesis are the stereoselective reduction of ketone **A** to alcohol **B** and the two-carbon elongation reaction **(C → D)** with a new reagent $MeCH(CN)NEt_2$.

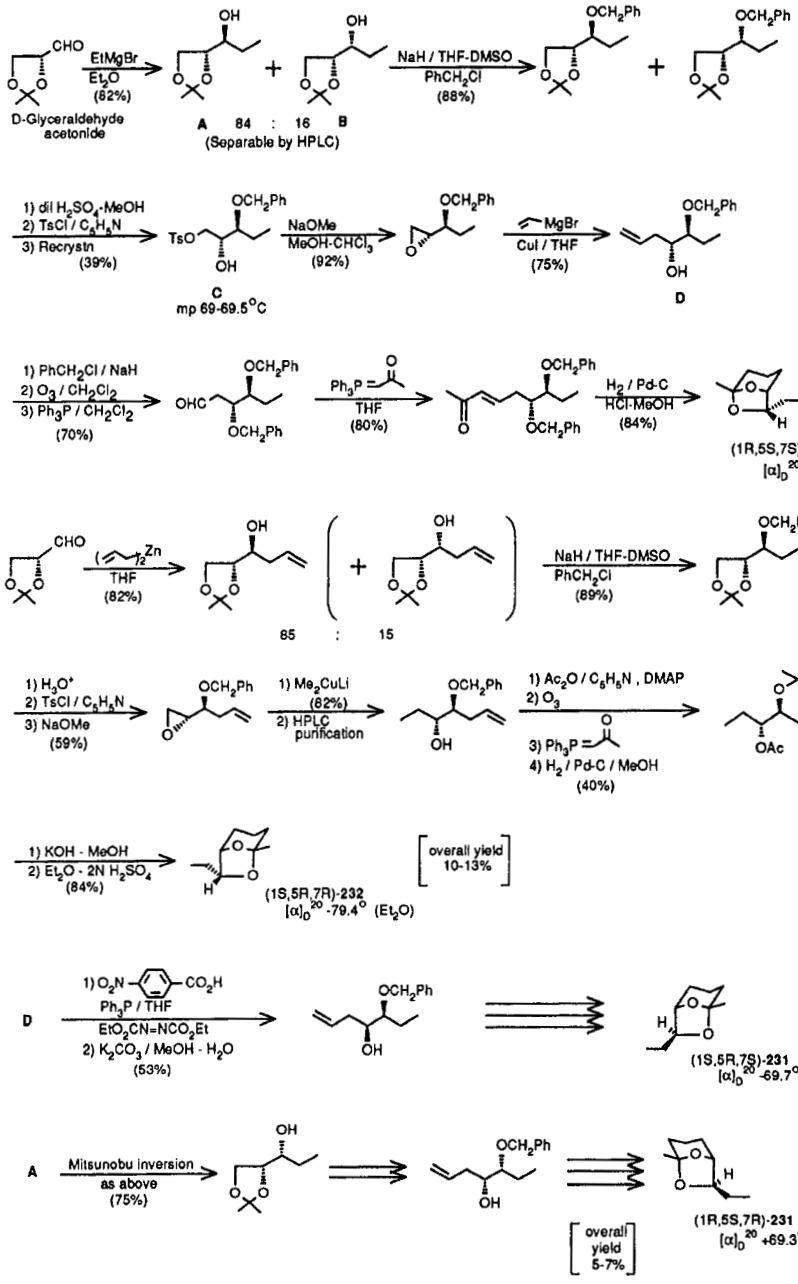


Scheme 846

C. From Glyceraldehyde Acetonide. Sato et al. synthesized the enantiomers of **231** and **232** starting from D-glyceraldehyde acetonide (Scheme 847).[1051] The

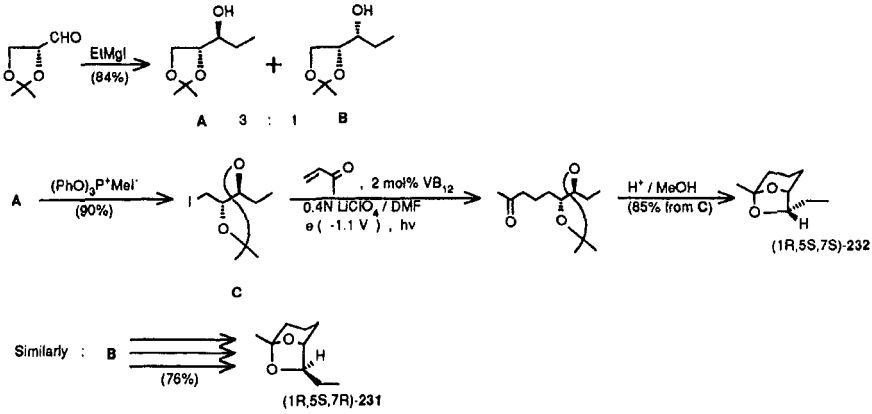


Scheme 847


D-Glyceraldehyde acetonide
EtMgBr
Et2O
(62%)
A 84 : 16 B
(Separable by HPLC)
NaH / THF-DMSO
PhCH2Cl
(88%)
1) dil H2SO4-MeOH
2) TsCl / C5H5N
3) Recrystn
(39%)
mp 69-69.5°C
NaOMe
MeOH-CHCl3
(92%)
MgBr
CuI / THF
(75%)
1) PhCH2Cl / NaH
2) O3 / CH2Cl2
3) Ph3P / CH2Cl2
(70%)
THF
(80%)
H2 / Pd-C
HCl-MeOH
(84%)
(1R,5S,7S)-232 (>98% e.e.)
[α]D20 +80.0° (Et2O)
THF
(82%)
85 : 15
1) H3O+
2) TsCl / C5H5N
3) NaOMe
(59%)
1) Me2CuLi
(82%)
2) HPLC purification
1) Ac2O / C5H5N , DMAP
2) O3
3) Ph3P=O
4) H2 / Pd-C / MeOH
(40%)
1) KOH - MeOH
2) Et2O - 2N H2SO4
(84%)
overall yield 10-13%
(1S,5R,7R)-232
[α]D20 -79.4° (Et2O)
D
1) O2N-C6H4-CO2H
Ph3P / THF
EtO2CN=NCO2Et
2) K2CO3 / MeOH - H2O
(53%)
(1S,5R,7S)-231
[α]D20 -69.7° (Et2O)
A
Mitsunobu inversion
as above
(75%)
overall yield 5-7%
(1R,5S,7R)-231
[α]D20 +69.3° (Et2O)

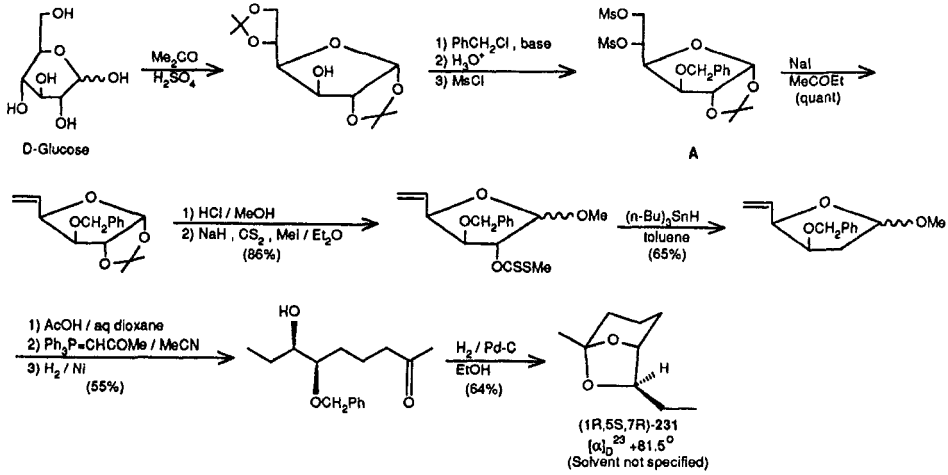
Scheme 848

key-step was the stereoselective Grignard reaction with α-benzyloxy-β-trimethylsilyl-3-butenal **D.** Mulzer et al. also prepared the enantiomers of **231** and **232** from D-glyceraldehyde acetonide (Scheme 848).[1052] The Mitsunobu inversion played an important role in their synthesis. A remarkably simple synthesis of (+)-*exo*- and *endo*-brevicomins was achieved by Scheffold et al. (Scheme 849) by employing vitamin B_{12}-catalyzed carbon-carbon bond formation.[36, 1054]



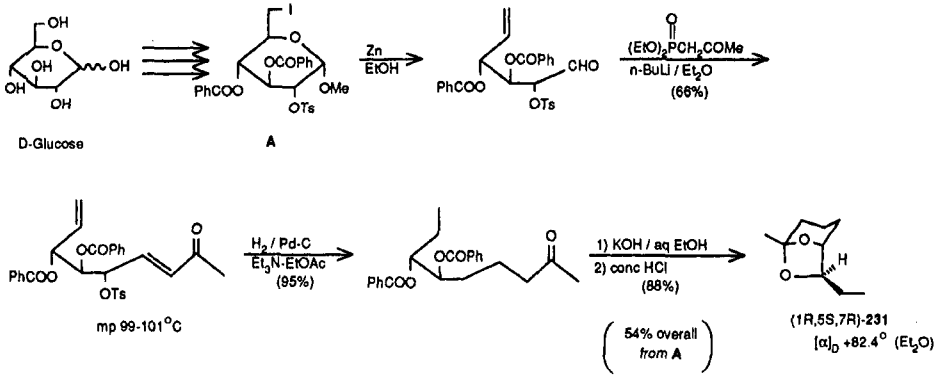
Scheme 849

D. From D-*Glucose and Other Sugars.* Sherk and Fraser-Reid seven step synthesis of (+)-*exo*-brevicomin **231** from D-glucose via dimesylate **A** yielded overall 21% from **A** (Scheme 850).[1055] (+)-*exo*-Brevicomin **231** was prepared



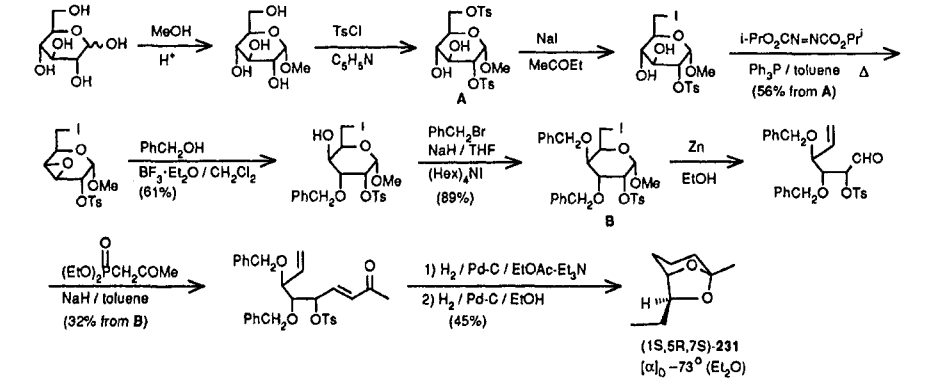
Scheme 850

in a more efficient manner by Ferrier and Prasit (Scheme 851).[1056] Ferrier et al.



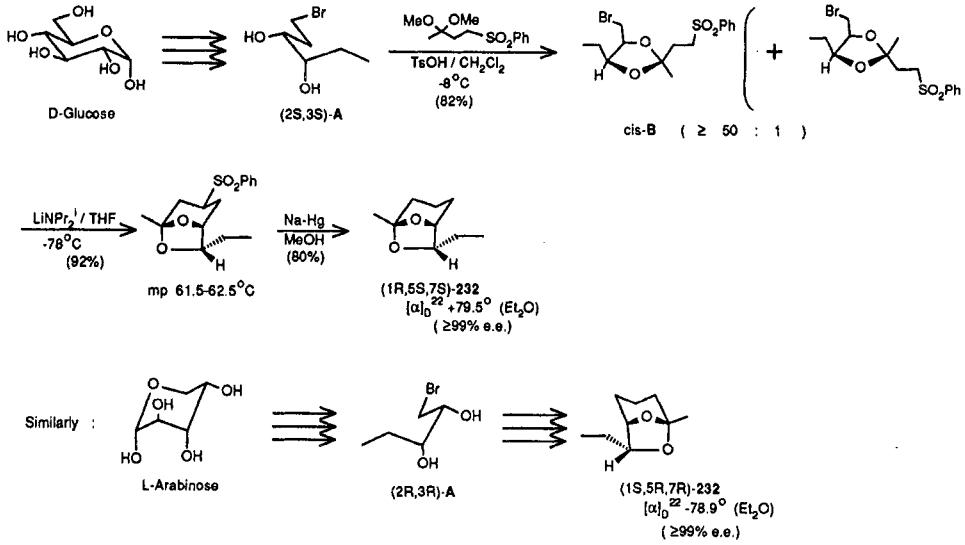
Scheme 851

also synthesized (−)-**231** from D-glucose as shown in Scheme 852.[1057] Thus,



Scheme 852

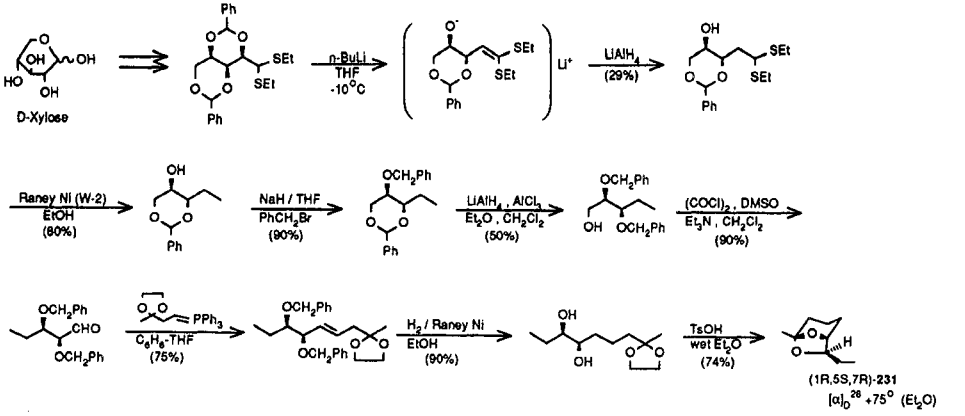
they were able to prepare both the enantiomers of **231** from D-glucose. Both the enantiomers of **232** were synthesized by Scharf and his co-workers by the route similar to that used for the synthesis of (±)-**232** (Scheme 853; cf. Scheme 829).[1058] The key cycloacetalization under kinetic control yielded *cis*-**B** as the major product. D-Xylose was converted to (+)-**231** by Yadav et al. (Scheme 854).[1059] Redlich's synthesis of (+)-**232** and (−)-**232** started from D-ribose (Scheme 855).[1060] In Redlich's paper, biological activities of **231** and **232** are summarized concisely. In most cases, syntheses of brevicomins from carbo-



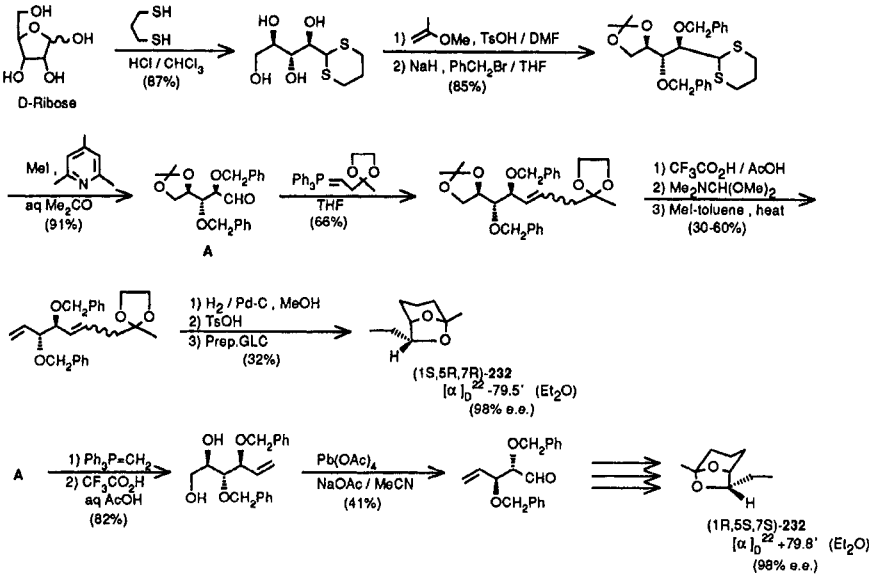
Scheme 853

hydrates are rather lengthy processes due to the necessity of removing the extraneous chiral centers of the starting materials.

E. By Asymmetric Epoxidation. The invention of asymmetric epoxidation by Sharpless et al. greatly facilitated the brevicomin synthesis. Seven different syntheses of **231** and/or **232** employed this reaction. Johnston and Oehlschlager

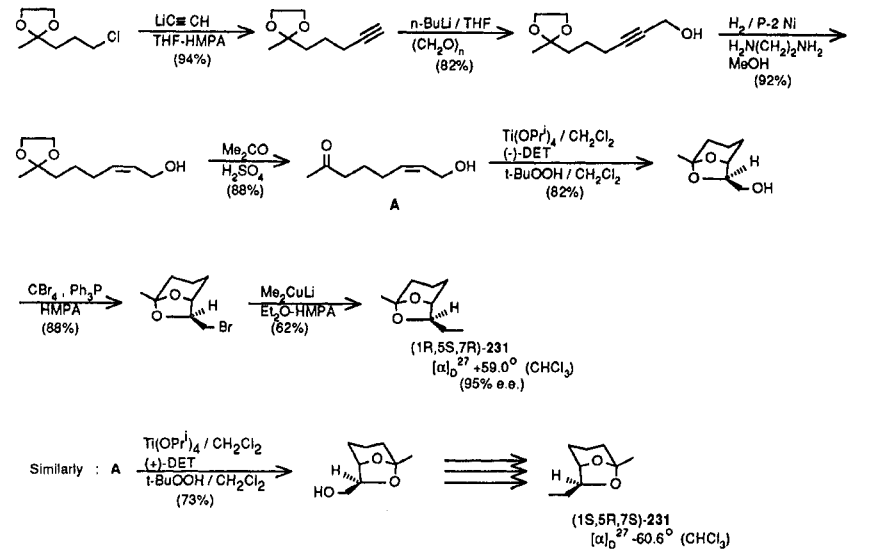


Scheme 854



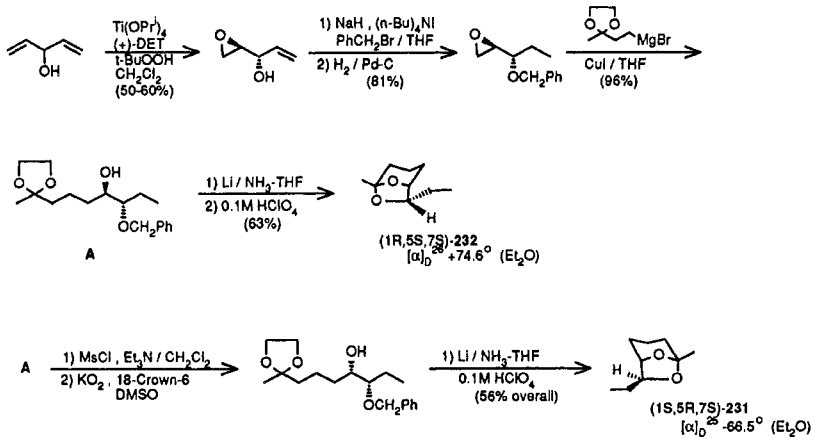
Scheme 855

prepared the enantiomers of **231** in 30–40% overall yield as shown in Scheme 856.[1061] Starting from divinylcarbinol, Takano and his co-workers synthesized



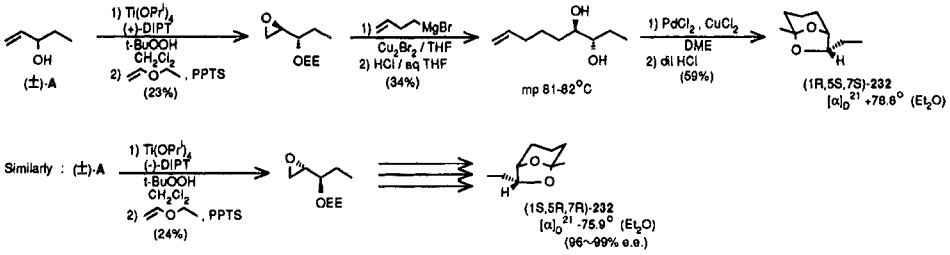
Scheme 856

(−)-**231** and (+)-**232** (Scheme 857).[1062] In Takano's process, the selectivity of



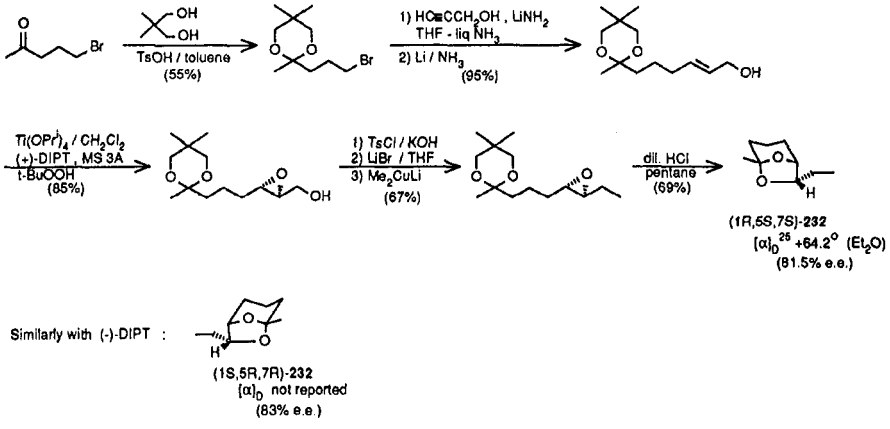
Scheme 857

the epoxidation step was 90 : 10 enantioselectivity and 93 : 3 *threo-erythro* selectivity.[1062] Mori and Seu synthesized the enantiomers of **232** by the Sharpless epoxidation, followed by chain elongation and the Wacker oxidation (Scheme 858).[1063] The enantiomers of *endo*-brevicomin **232** were also prepared by

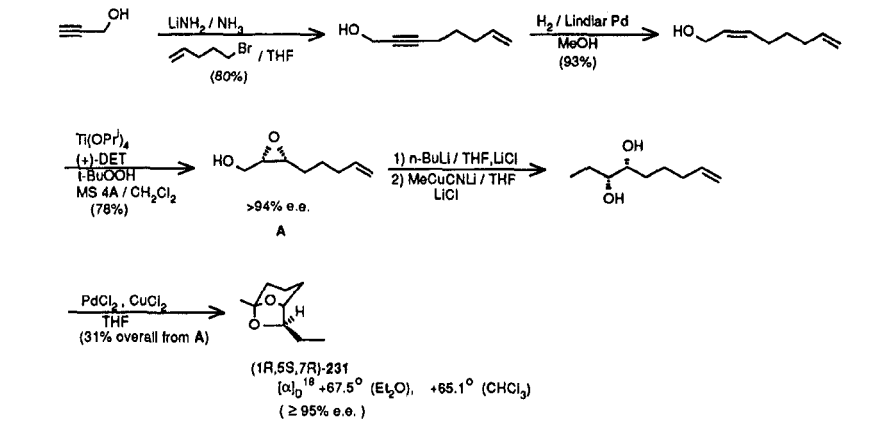


Scheme 858

Oehlschlager and Johnston (Scheme 859).[1064] Sutherland and his co-workers employed Payne rearrangement in THF of 2,3-epoxy alcohol in their five-step synthesis of (+)-**231** (Scheme 860).[1065] Scharf et al. synthesized the enantiomers of **231** and **232** by combination of the Sharpless epoxidation and sulfone alkylation (Scheme 861).[1006] They also prepared the analogs of **231** and **232** with a vinyl group instead of the ethyl group at C-7 by using Sharpless epoxidation and sulfone alkylation.[1066] Yadav et al. synthesized (−)-**232** as shown in Scheme 862.[1067]

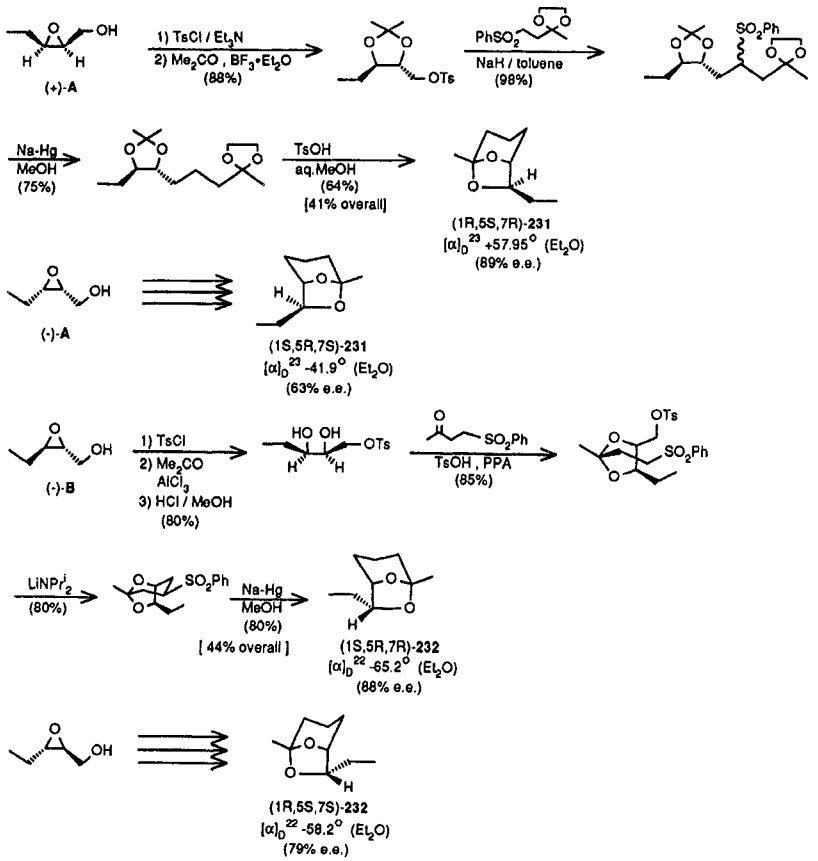


Scheme 859

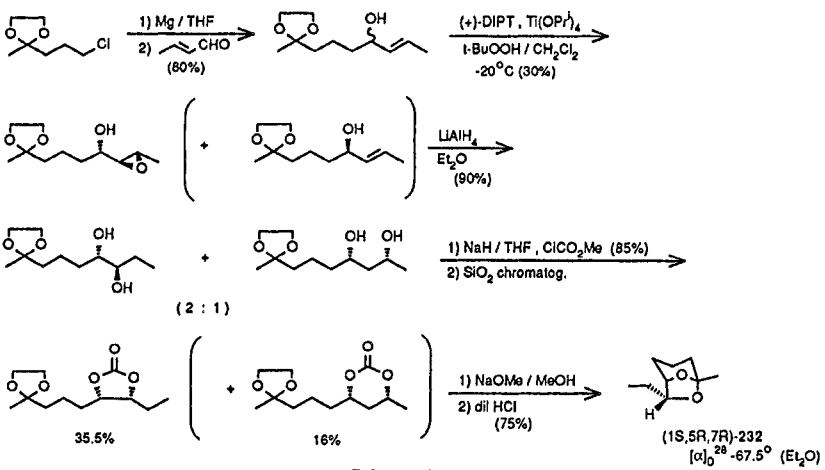


Scheme 860

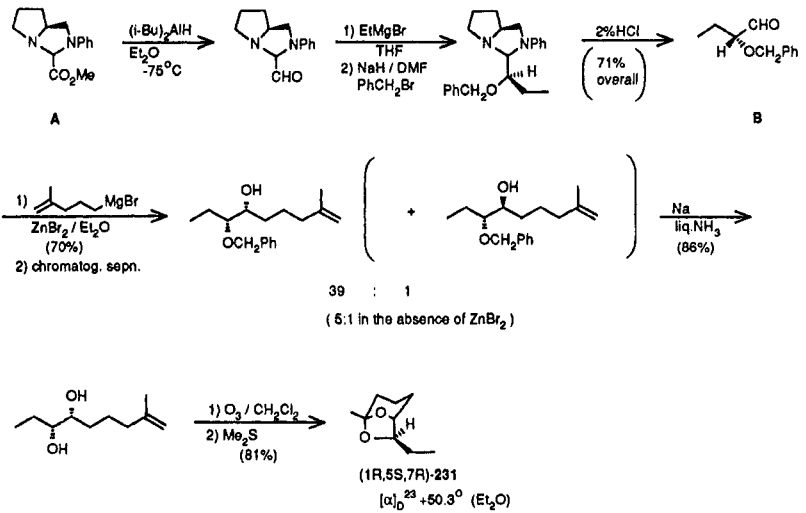
F. By Chemical Asymmetric Reactions Other than Asymmetric Epoxidation. In a synthesis of (+)-**231** by Asami and Mukaiyama, ester **A** was prepared from (*S*)-2-(anilinomethyl)pyrrolidine, from which **B** was derived (Scheme 863).[1068] Their (+)-**231** was found to be of moderate optical purity. (*R*)-Carvone was used by Wuts et al. to prepare a chiral boronate **A,** which was treated with aldehyde **B** to yield **C** and then (−)-**231** (Scheme 864).[1069] The homologation of chiral boronic esters **A** and **B** with dichloromethyllithium was employed by Matteson et al. in the synthesis of (+)-**231** (Scheme 865).[301,302] Chong and Mar employed chiral α-alkoxyorganostannane (*R*)-**B,** which was



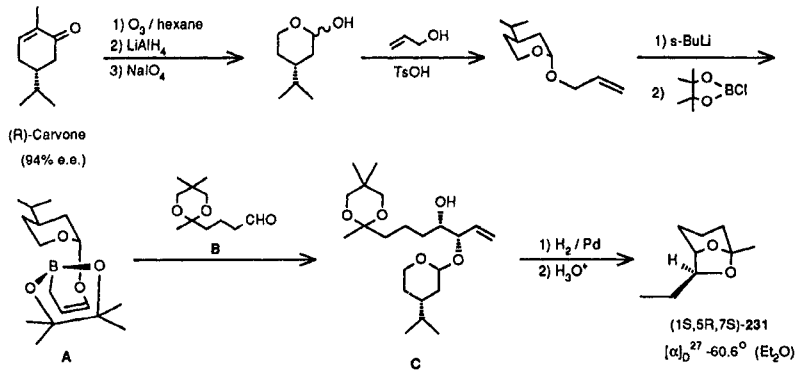
Scheme 861



Scheme 862



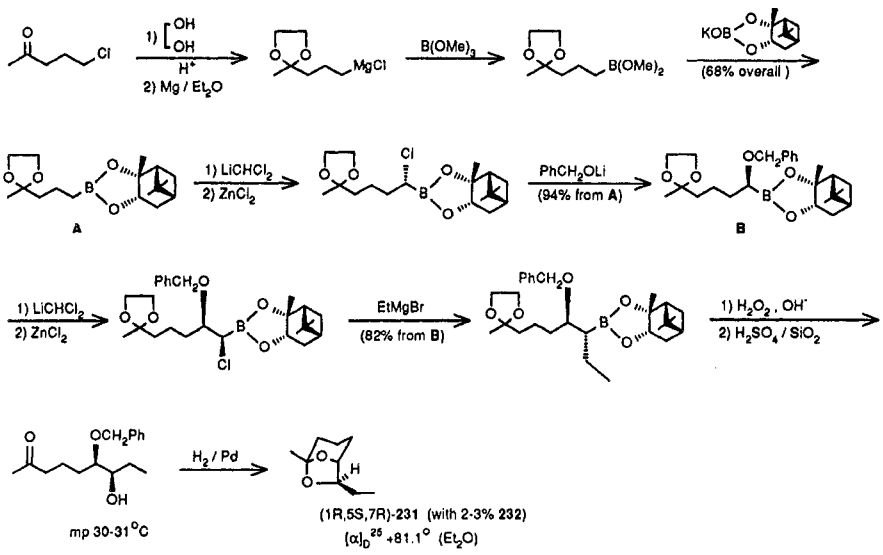
Scheme 863



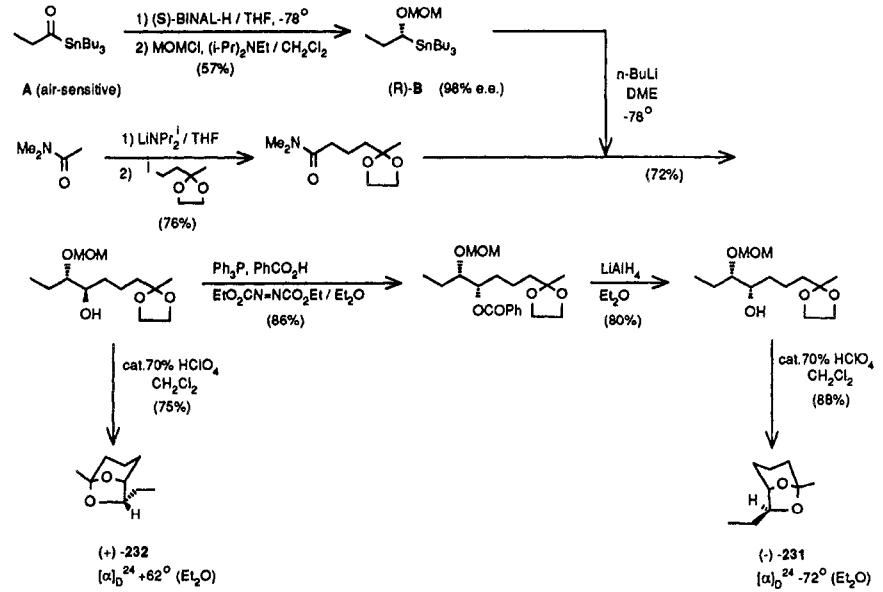
Scheme 864

prepared by reducing **A** with 2,2′-dihydroxy-1,1′-binaphthyl-modified lithium aluminum hydride (BINAL-H), for the synthesis of (−)-**231** and (+)-**232** (Scheme 866).[1070] Koga and his co-workers achieved asymmetric dihydroxylation of **A** to give (+)-**231** (Scheme 867),[1071] which is the most direct synthesis of (+)-**231**.

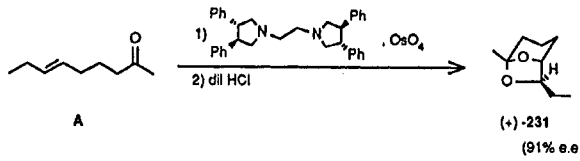
G. By Biochemical Asymmetric Reactions. Biochemical asymmetric reactions, such as reduction and aldol formation, were used for the synthesis of brevicomins.



Scheme 865

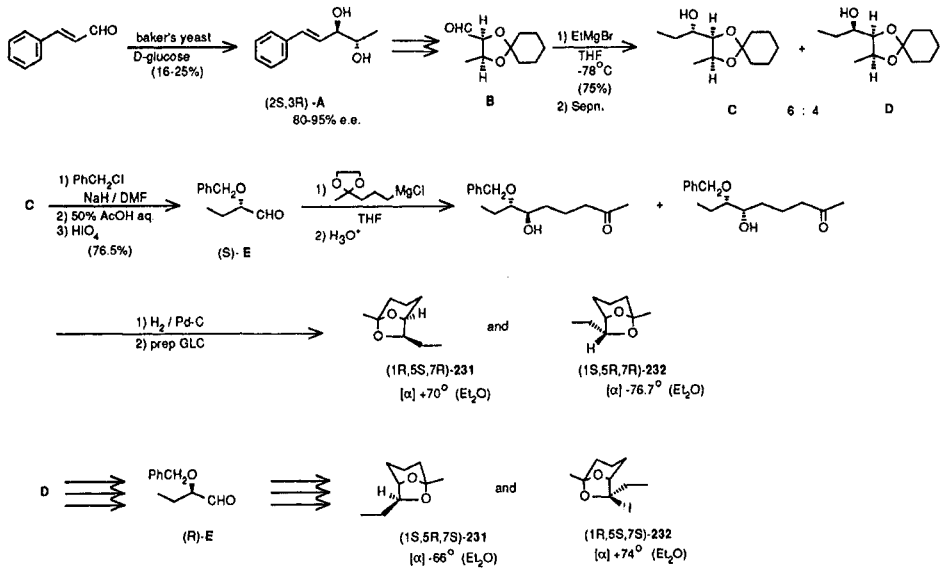


Scheme 866



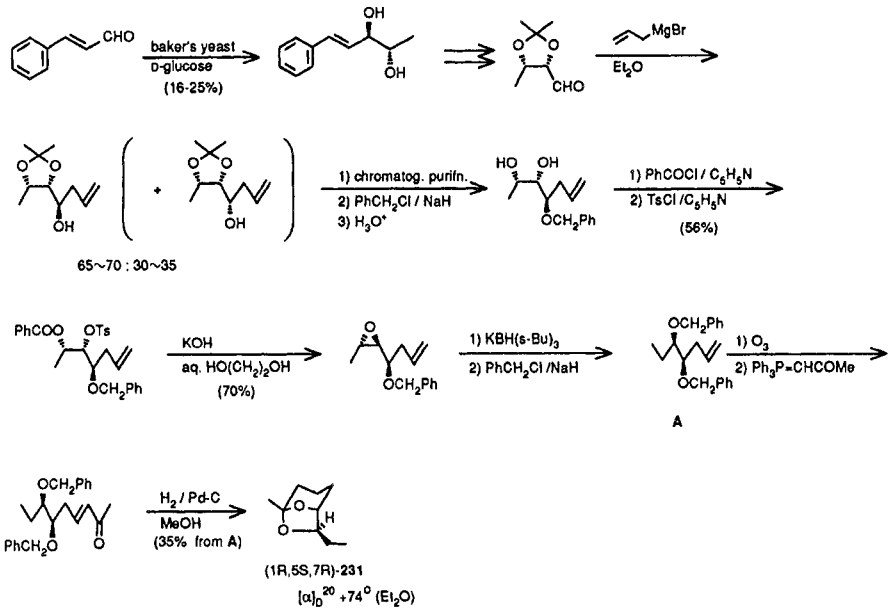
Scheme 867

Treatment of cinnamaldehyde with baker's yeast and D-glucose produces diol **A** (Scheme 868). Fuganti and co-workers converted **A** to **B.** When **B** was

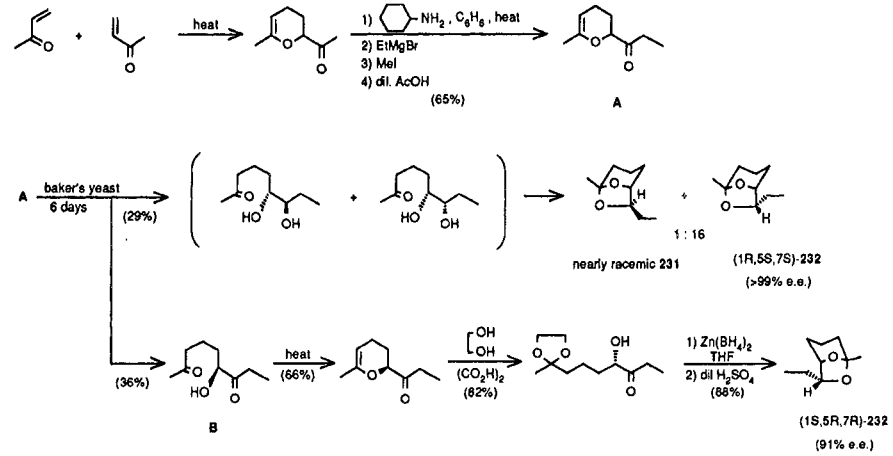


Scheme 868

treated with ethylmagnesium bromide, a separable mixture of **C** and **D** was obtained. (*S*)-Aldehyde **E**, derived from **C**, yielded (+)-**231** and (−)-**232**, while (*R*)-**E**, derived from **D**, furnished (−)-**231** and (+)-**232** in a nonstereoselective manner (Scheme 868).[1072] Later Fuganti et al. reported another synthesis of (+)-**231** as shown in Scheme 869.[1073] This synthesis was again nonstereoselective. A unique preparation of the enantiomers of **232** by Ramaswamy and Oehlschlager was based on the yeast reduction of **A** to generate **B**, (±)-**231**, and (+)-**232** (Scheme 870).[1074] The reduction process is an example of kinetic

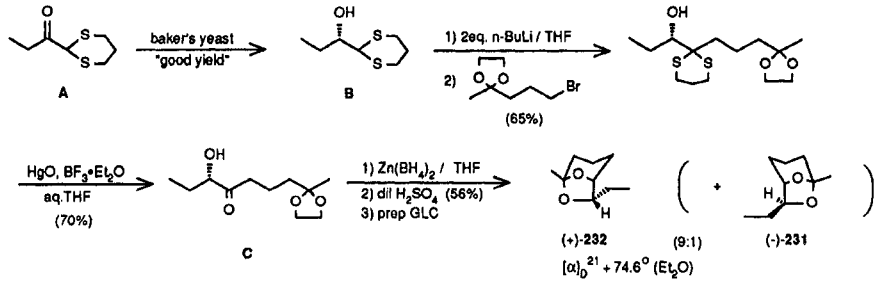


Scheme 869



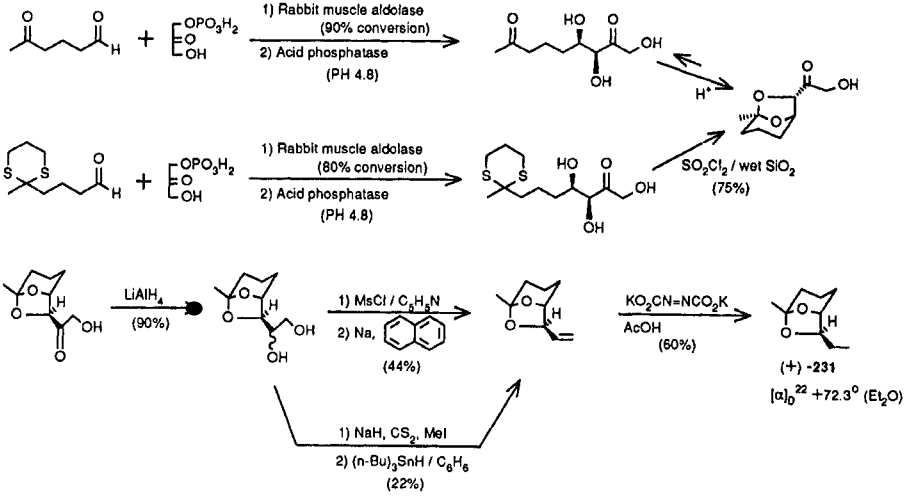
Scheme 870

resolution by baker's yeast. Noda and Kikuchi reduced **A** with baker's yeast to give **B**, which was converted to (+)-**232** via diastereoselective reduction of hydroxyketone **C** (Scheme 871).[1075]



Scheme 871

A unique chemoenzymatic synthesis of (+)-**231** by Schultz et al. utilized highly stereoselective carbon-carbon bond formation with rabbit muscle fructose-1,6-diphosphate aldolase (Scheme 872).[1076]

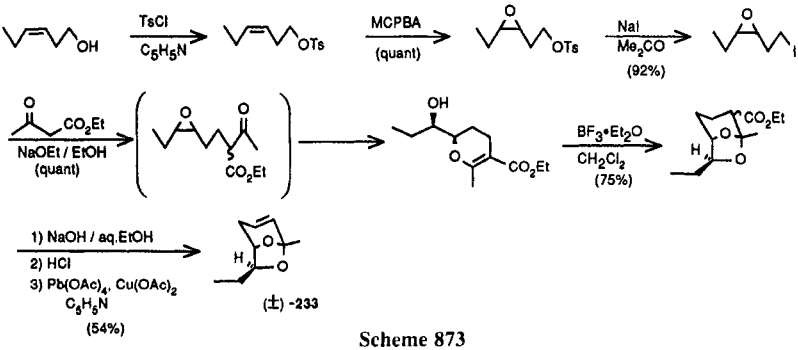


Scheme 872

C. *exo*-7-Ethyl-5-methyl-6,8-dioxabicyclo[3.2.1]oct-3-ene 233 ($C_9H_{14}O_2$)

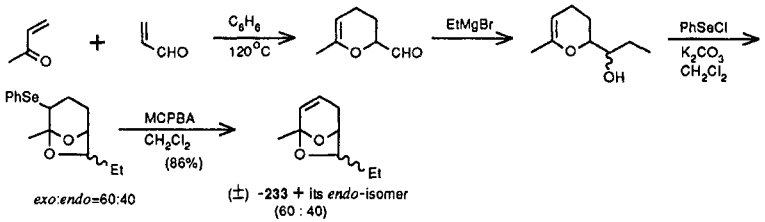
Although **233** is not an insect pheromone but a mammalian pheromone, its syntheses will be reviewed here due to its close structural resemblance to **231.**

This olefinic acetal **233** is a chemical signal of the male state and a potential multipurpose pheromone of the house mouse (*Mus musculus*).[1077, 1078] This compound (±)-**233** had been synthesized, even before its discovery as a natural product, as an intermediate of Kossanyi's synthesis of (±)-*exo*-brevicomin **231** (Scheme 140, Ref. 1).[1079] Wiesler et al. synthesized (±)-**233** starting from (*Z*)-3-hexen-1-ol and introducing the C-3 double bond at the final stage (Scheme 873).[1077] Mundy and Bornmann prepared a mixture of (±)-**233** and its *endo*-



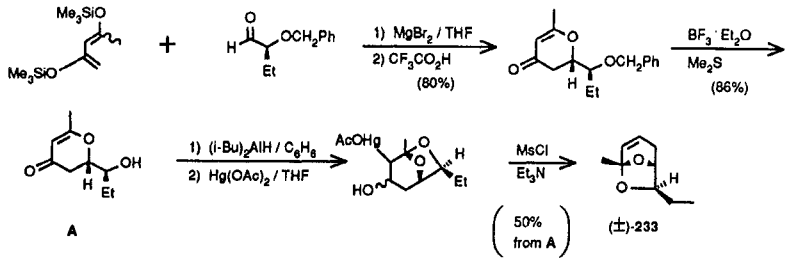
Scheme 873

isomer by using organoselenium chemistry (Scheme 874).[1080] Diastereofacial



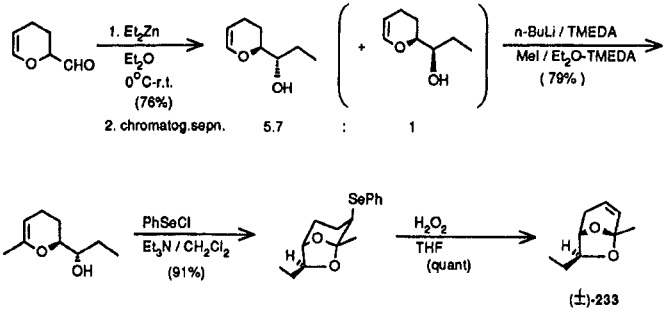
Scheme 874

control in the cyclocondensation reaction was the key to Danishefsky's synthesis of (±)-**233** (Scheme 875).[1032, 1081] The cyclocondensation was followed by



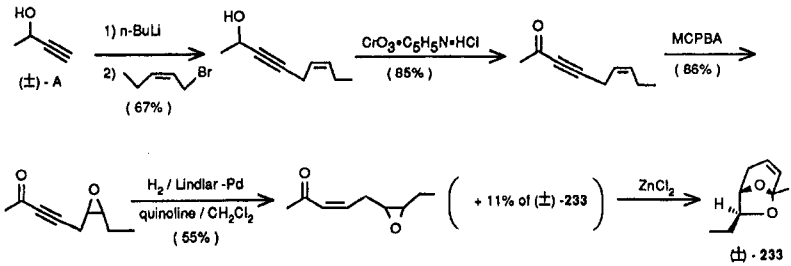
Scheme 875

mercuric-ion-initiated acetal formation, and the resultant α-mercuriocarbinol was treated with methanesulfonyl chloride in triethylamine to effect olefin formation. Bhupathy and Cohen prepared (±)-**233** by means of organoselenium chemistry (Scheme 876).[1030] Acid-catalyzed intramolecular opening of an epox-



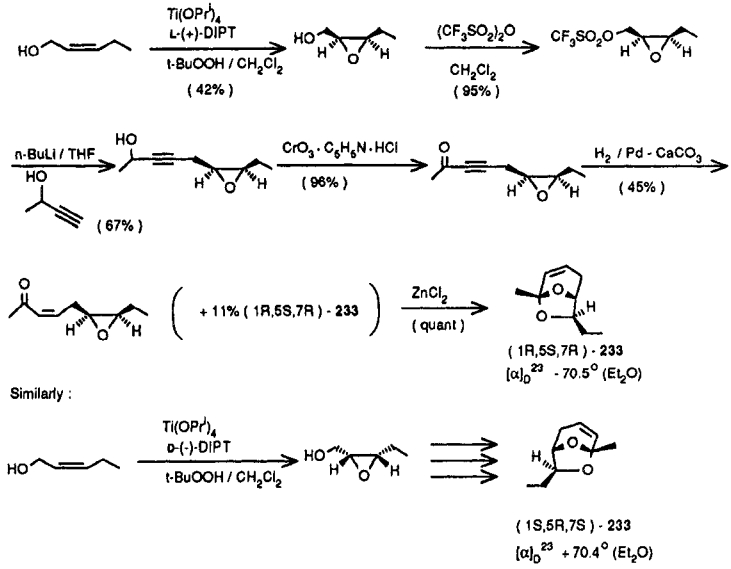
Scheme 876

ide by a carbonyl group was the key reaction of Wasserman's synthesis of (±)-**233** (Scheme 877).[1082]

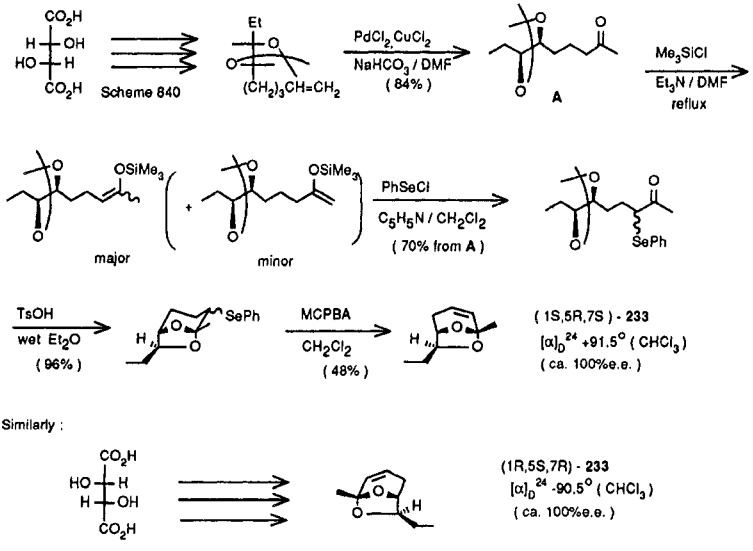


Scheme 877

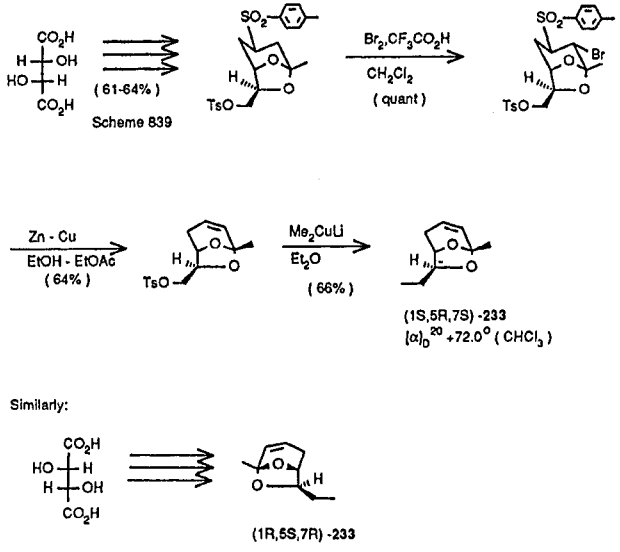
Three different syntheses of the enantiomers of **233** were reported. The relationship between bioactivity and absolute configuration of **233** is not yet known. In Wasserman's synthesis, the Sharpless asymmetric epoxidation was employed (Scheme 878).[1083] Mori and Seu started from tartaric acid and employed organoselenium chemistry for the introduction of the double bond (Scheme 879).[1084] Masaki et al. also synthesized the enantiomers of **233** by beginning with the enantiomers of tartaric acid (Scheme 880).[1085]



Scheme 878



Scheme 879

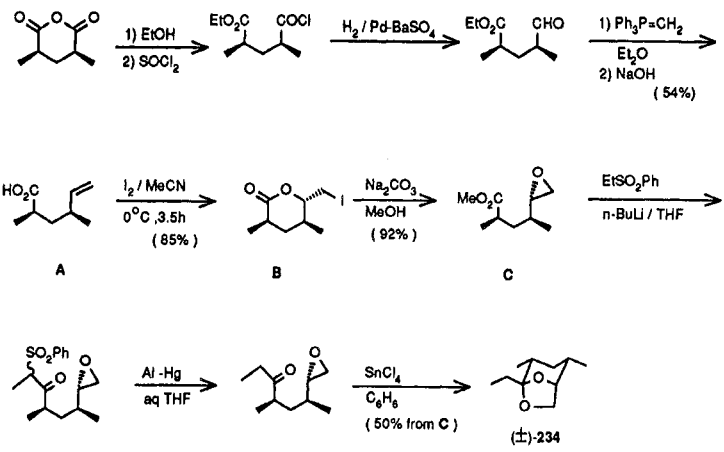


Scheme 880

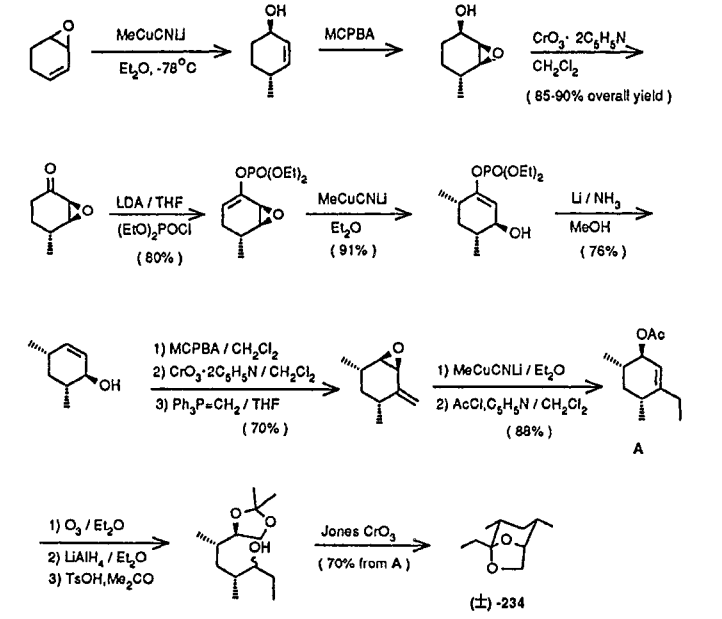
D. (1*S*,2*R*,4*S*,5*R*)-α-Multistriatin (2,4-Dimethyl-5-ethyl-6,8-dioxabicyclo[3.2.1]octane 234 ($C_{10}H_{18}O_2$)

This is the pheromone of the smaller European elm bark beetle (*Scolytus multistriatus*). Since 1979 several new syntheses of (±)-**234** have been published. Bartlett and Myerson's synthesis of (±)-**234** started from *meso*-2,4-dimethylglutaric anhydride, and utilized a highly stereoselective iodolactonization reaction (**A** → **B**) to fix the relative stereochemistry of the third chiral center (Scheme 881).[1091] Marino's organocopper chemistry enabled him to prepare (±)-**234** stereoselectively (Scheme 882).[1092] The noteworthy step in the synthesis of (±)-**234** by Walba and Wand was the diastereoselective (> 95%) addition of lithiothioformaldine to aldehyde **A** to create **B** (Scheme 883).[1093] In connection with a synthesis of (±)-**234**, **C** (Scheme 883) was reported to be bioactive as an analog of α-multistriatin.[1094] Serebryakov et al. reported a synthesis of a mixture of multistriatin isomers as shown in Scheme 884.[1095]

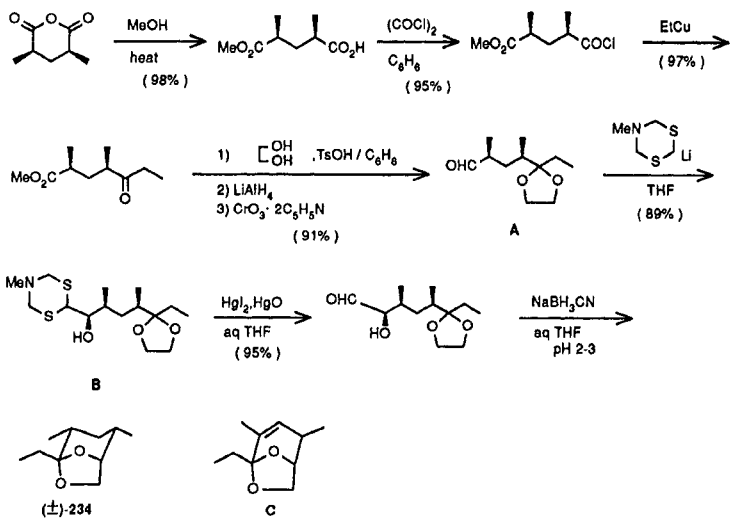
Eight new enantioselective syntheses of **234** or its isomer have been reported since 1979. Four of them were initiated by chiral building blocks, and the others



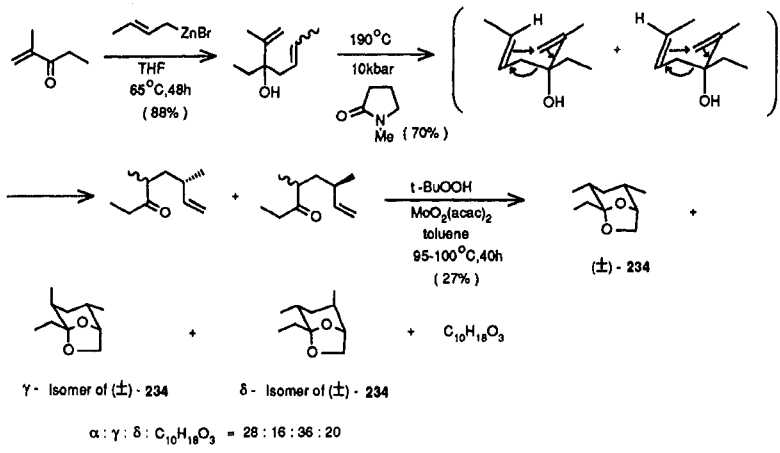
Scheme 881



Scheme 882

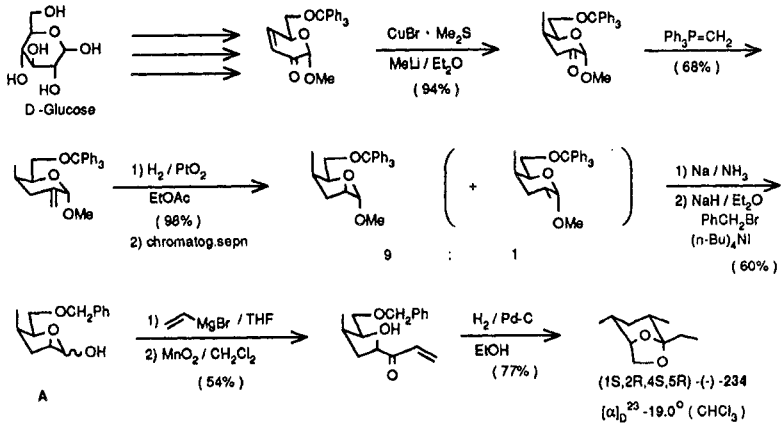


Scheme 883

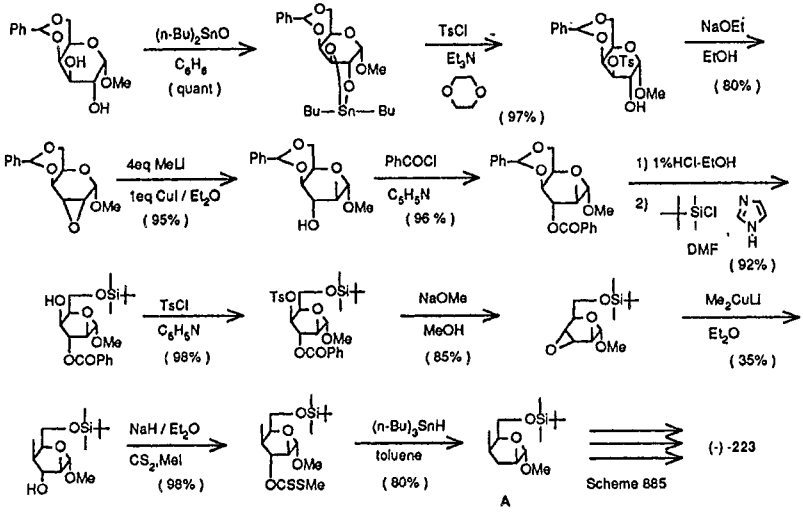


Scheme 884

employed chemical asymmetric reactions. Details of the conversion of D-glucose to **234** (Scheme 277a, Ref. 1) by Sum and Weiler appeared as a full paper.[1096] Fraser-Reid et al. also employed D-glucose as their starting material and prepared **234** as shown in Scheme 885.[1097,1098] A compound **(A)** which is equivalent to the key-intermediate **A** of the Fraser-Reid synthesis was also prepared from D-galactose (Scheme 886).[1099] Levoglucosenone, which is obtain-

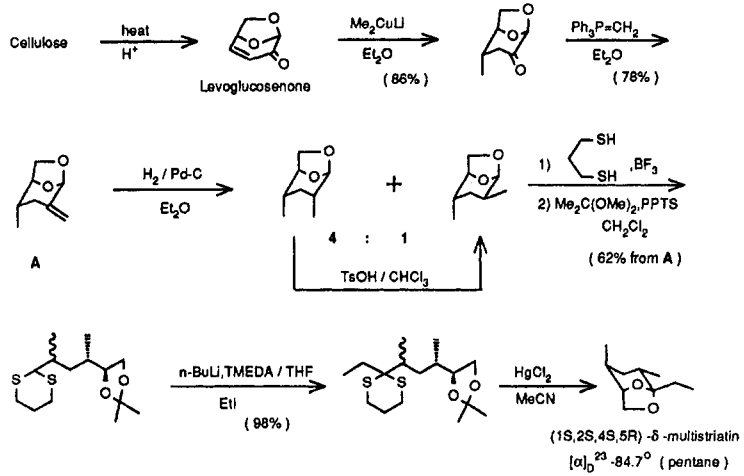


Scheme 885

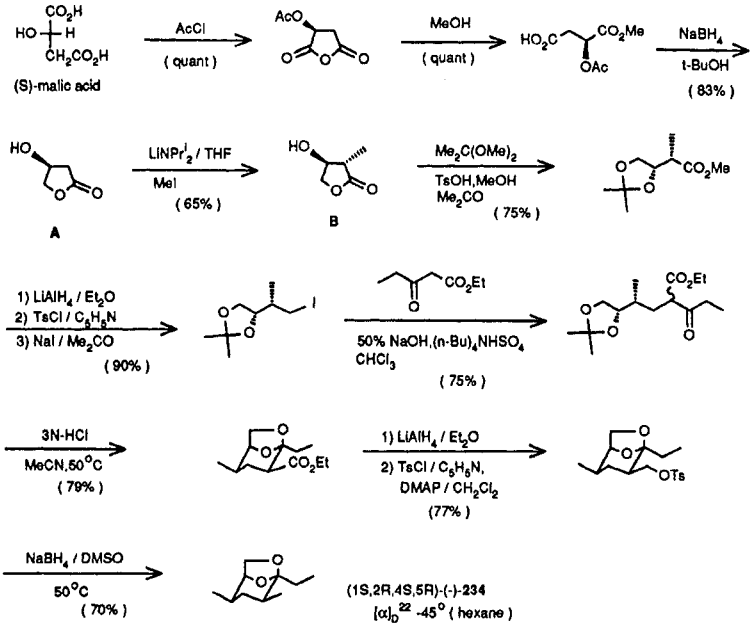


Scheme 886

able by acid-catalyzed pyrolysis of cellulose, was converted to (−)-δ-multistriatin by M. Mori et al. (Scheme 887).[525,1100] A formal synthesis of the enantiomers of δ-multistriatin was reported by Mulzer et al.[1101] Larchevêque and Henrot converted (*S*)-malic acid to **234** (Scheme 888), employing the stereoselective alkylation of hydroxylactone **A** to **B**.[1102] D-Glyceraldehyde acetonide was converted to a mixture of **234** and its β-,γ-, and δ-isomers by means

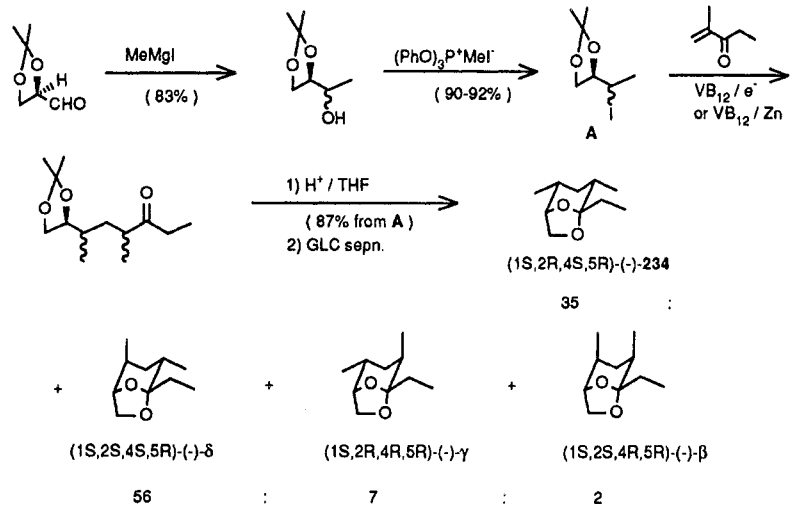


Scheme 887



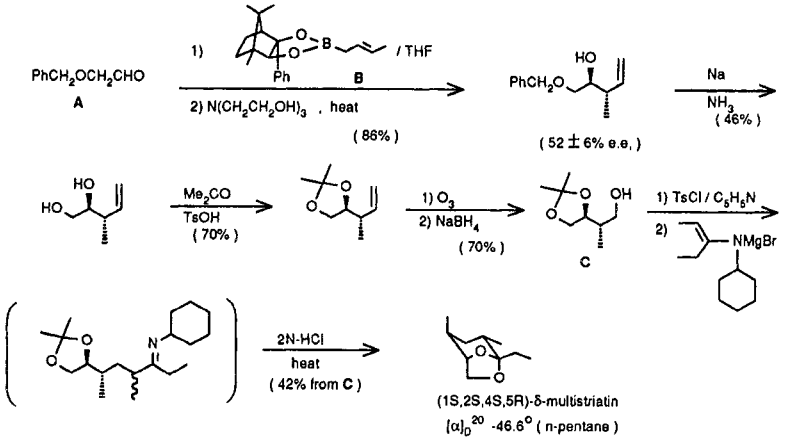
Scheme 888

of vitamin B_{12}-mediated electrochemical reaction to elongate the carbon chain (Scheme 889).[36]

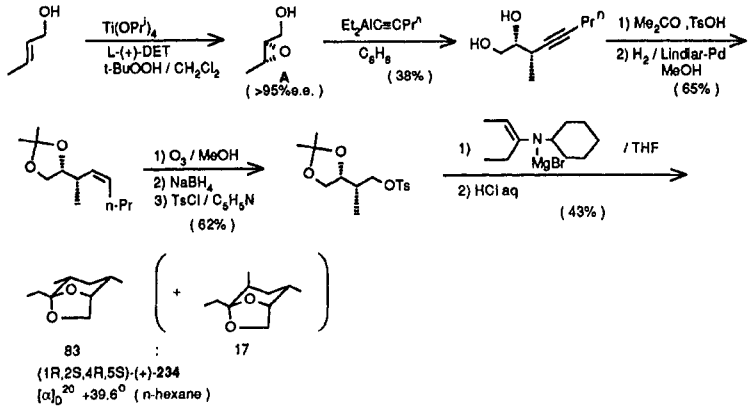


Scheme 889

A synthesis of (−)-δ-multistriatin by Hoffmann and Helbig used the diastereoselective reaction between benzyloxyacetaldehyde **A** and the chiral boronate **B**, and yielded the product of 52% e.e. (Scheme 890).[1103] Helbig converted

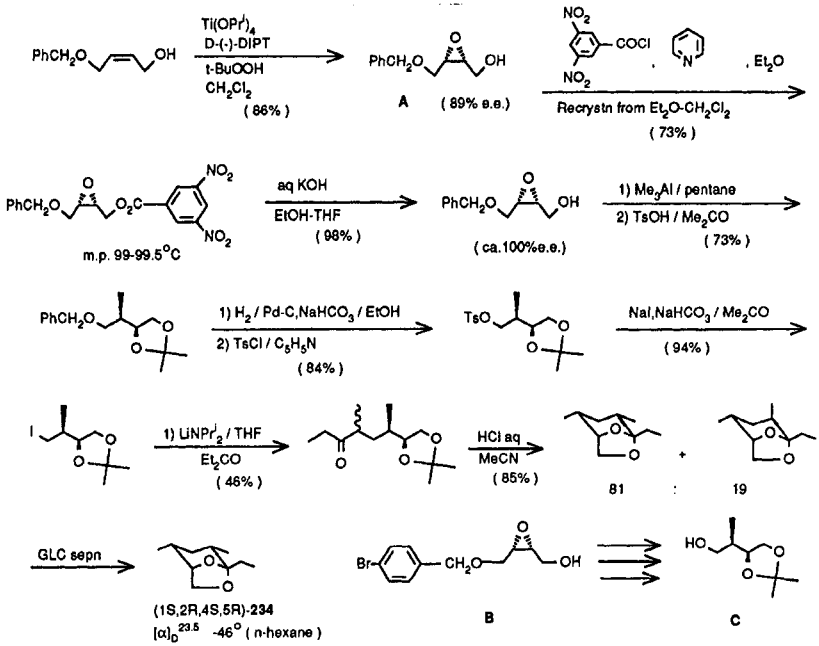


Scheme 890



Scheme 891

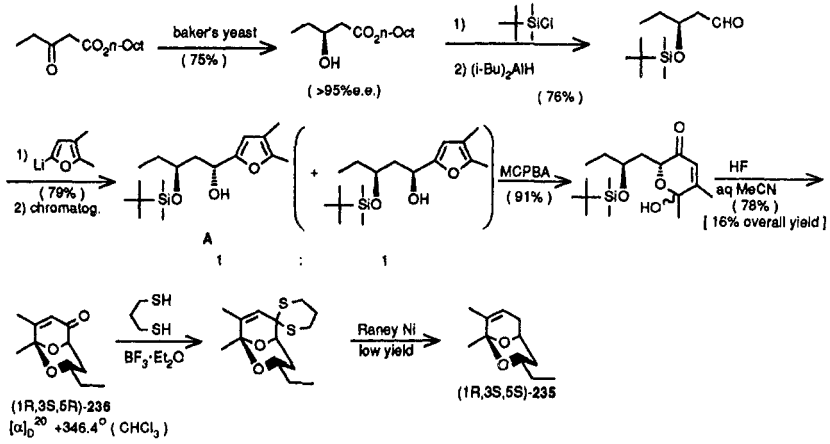
epoxy alcohol **A** (Scheme 891), which was obtained by the Sharpless epoxidation, to (+)-**234.**[1104] Mori and Seu also employed the Sharpless asymmetric epoxidation for the synthesis of (−)-α-multistriatin **234** as shown in Scheme 892.[1105] By using the Sharpless asymmetric epoxidation, Chong and Wong prepared the key-intermediate **C** via **B.**[1106]



Scheme 892

E. (1*R*,3*S*,5*S*)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-ene **235** ($C_{11}H_{18}O_2$) and (1*R*,3*S*,5*R*)-1,8-Dimethyl-3-ethyl-2,9-dioxabicyclo[3.3.1]non-7-en-6-one **236** ($C_{11}H_{16}O_3$)

These are the male-produced pheromone components (together with **218**) of the swift moth (*Hepialus hecta*).[1107] Two independent but similar syntheses of **235** and **236** were published in 1986. De Shong et al. synthesized **236** via a furan precursor **A** (Scheme 893).[1108] The olefinic acetal **235** was obtained in low yield

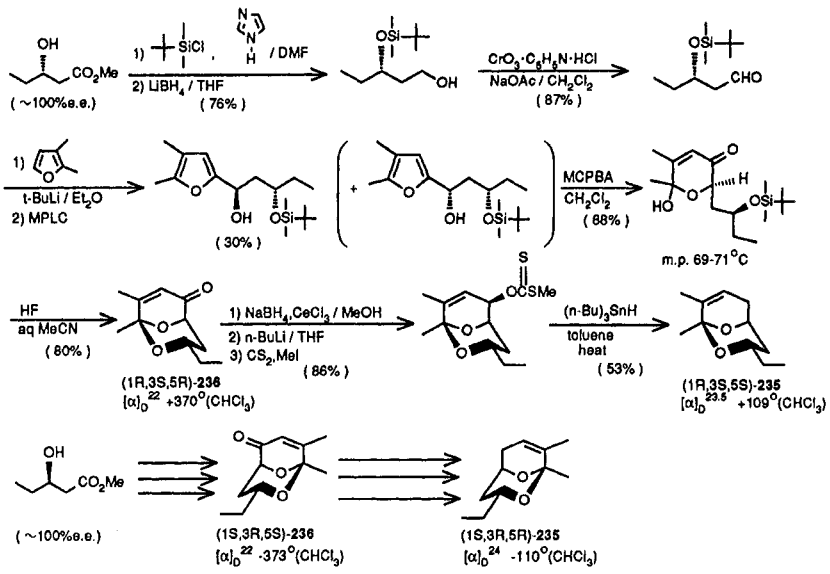


Scheme 893

by this De Shong protocol.[1108] Mori and Kisida synthesized both the enantiomers of **235** and **236** in enantiomerically pure state as shown in Scheme 894.[959] By using the synthetic enantiomers, the absolute configuration of the natural pheromone was determined as (1*R*,3*S*,5*S*)-**235** and (1*R*,3*S*,5*R*)-**236** by GLC comparison of the synthetic and natural samples on a chiral stationary phase.[959,1109]

F. 1,3-Dimethyl-2,9-dioxabicyclo[3.3.1]nonane ($C_9H_{16}O_2$)

This is not a pheromone but a compound occurring specifically in the Norway spruce infested by the striped ambrosia beetle (*Trypodendron lineatum*).[1110] (The genuine pheromone of *T. lineatum* is lineatin **237**.) However, a number of syntheses of this compound have been reported. Some authors stated 1,3-dimethyl-2,9-dioxabicyclo[3.3.1]nonane to be bioactive, when, actually, it is biologically inactive. Those who are interested in the syntheses of this bicyclic acetal are directed to Refs. 1111–1119.



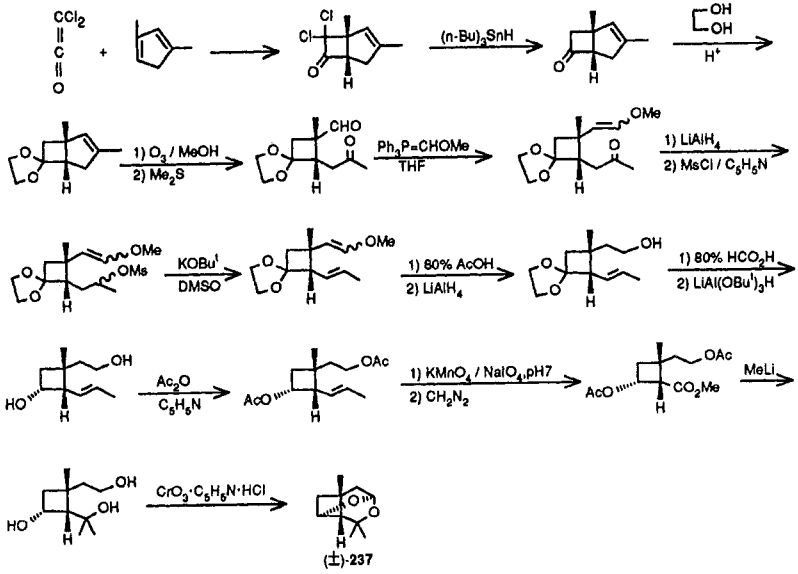
Scheme 894

G. (1*R*,4*S*,5*R*,7*R*)-Lineatin (3,3,7-Trimethyl-2,9-dioxatricyclo[3.3.1.$0^{4,7}$]nonane) 237 ($C_{10}H_{16}O_2$)

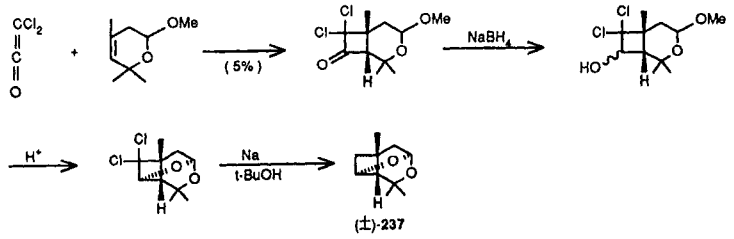
This is the female-produced aggregation pheromone of the striped ambrosia beetle (*Trypodendron lineatum*). Since 1979, six new syntheses of (±)-**237** and four syntheses of optically active **237** have been reported.

(1) Syntheses of (±)-Lineatin

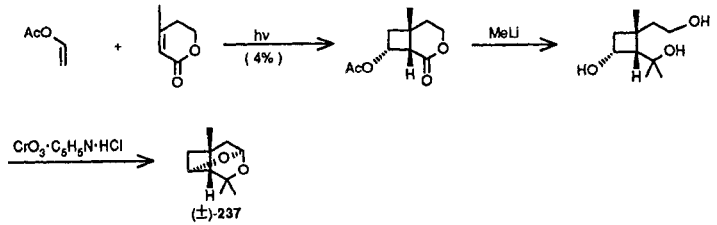
In most cases, [2 + 2]cycloaddition reactions were employed to construct the cyclobutane ring. Borden et al. reported, without experimental details, four syntheses of (±)-**237** (Schemes 895–898).[1120] Cycloaddition of dichloroketene to olefins or photocycloaddition of vinyl acetate to α,β-unsaturated carbonyl compounds were the key-steps in these four syntheses. Weiler and his co-workers executed the photocycloaddition of allene to unsaturated lactone **A** to give a mixture of **B** and **C**. The mixture was further processed to finally produce a mixture of (±)-**237** and its isomer, which were separable by chromatography (Scheme 899).[1121] [2 + 2]Cycloaddition of acetylene to lactone **A** to yield **B** was the key-step of White's synthesis of (±)-**237** (Scheme 900).[1122] Smooth cycloaddition occurred only when **A** in acetonitrile saturated with a stream of



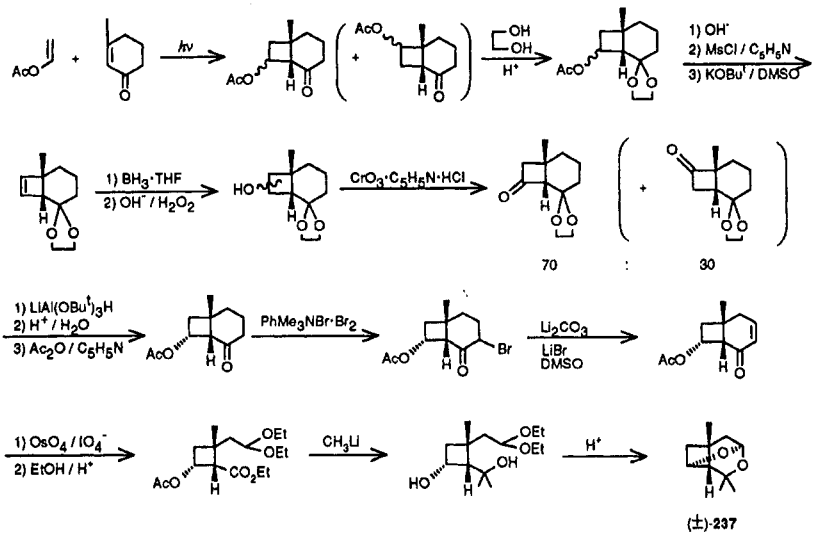
Scheme 895



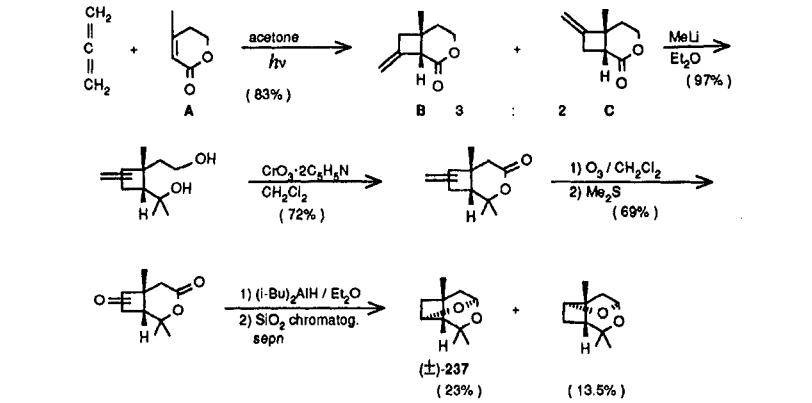
Scheme 896



Scheme 897



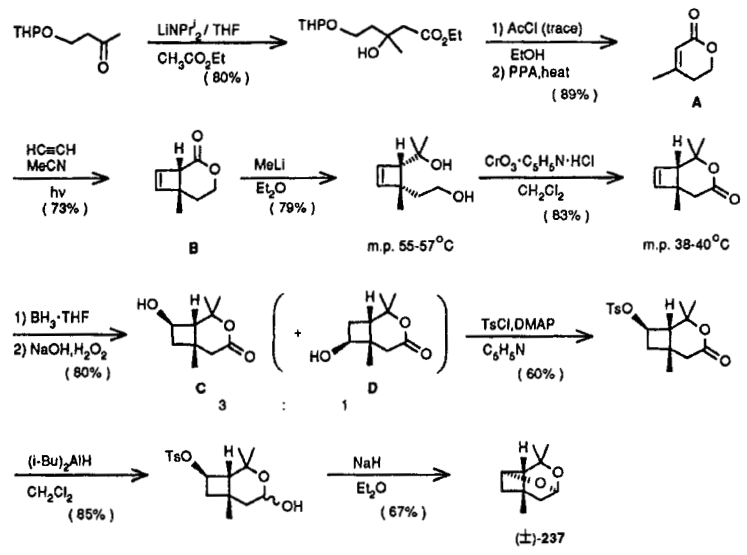
Scheme 898



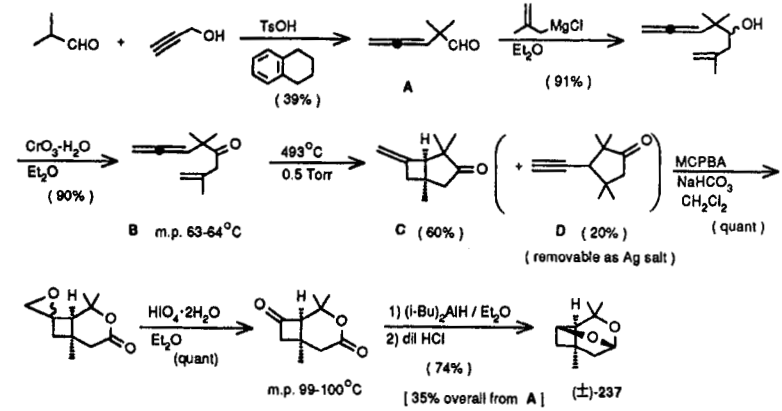
Scheme 899

acetylene was irradiated through Vycor glass. Tosylation of a mixture of **C** and **D** only resulted in the tosylate of **C**, leaving unreacted **D**, which was removable by chromatography.[1122]

Two syntheses of (±)-**237** (Schemes 901 and 902) by Skattebøl were highly efficient by virtue of the straightforward construction of the carbon skeleton by thermally induced intramolecular [2 + 2] cycloaddition (**B** → **C**).[1123,1124] In the route shown in Scheme 901, the separation of **C** and **D** was troublesome,



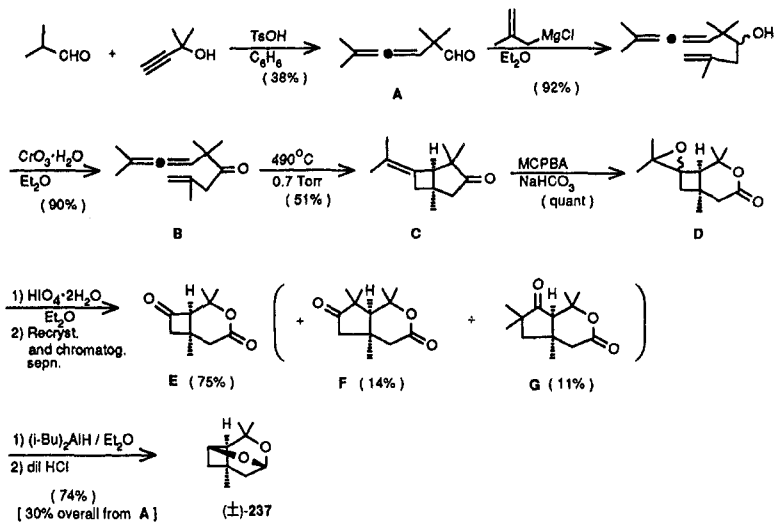
Scheme 900



Scheme 901

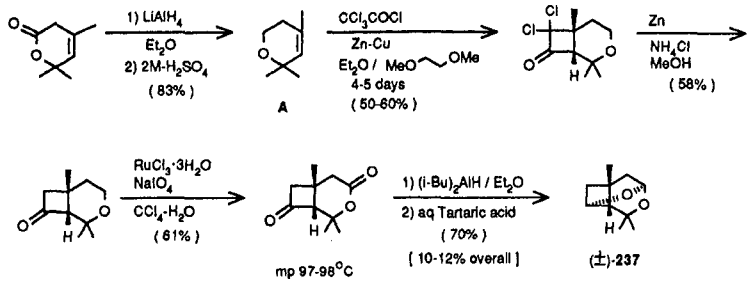
while in the other route (Scheme 902), cleavage of the epoxide **D** with periodic acid gave a separable mixture of **E, F,** and **G,** the latter two being the rearrangement products. The process shown in Scheme 902 was industrialized to produce (±)-**237** in 30% overall yield from **A.**

[2 + 2] Cycloaddition of dichloroketene with a cyclic allyl ether **A** was the



Scheme 902

key step of the Oehlschlager synthesis (Scheme 903).[1125] Dreiding and his co-

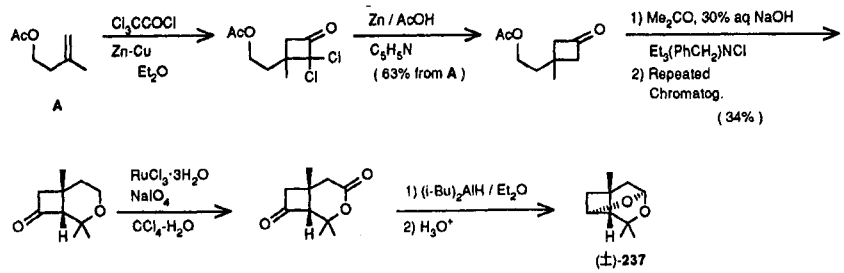


Scheme 903

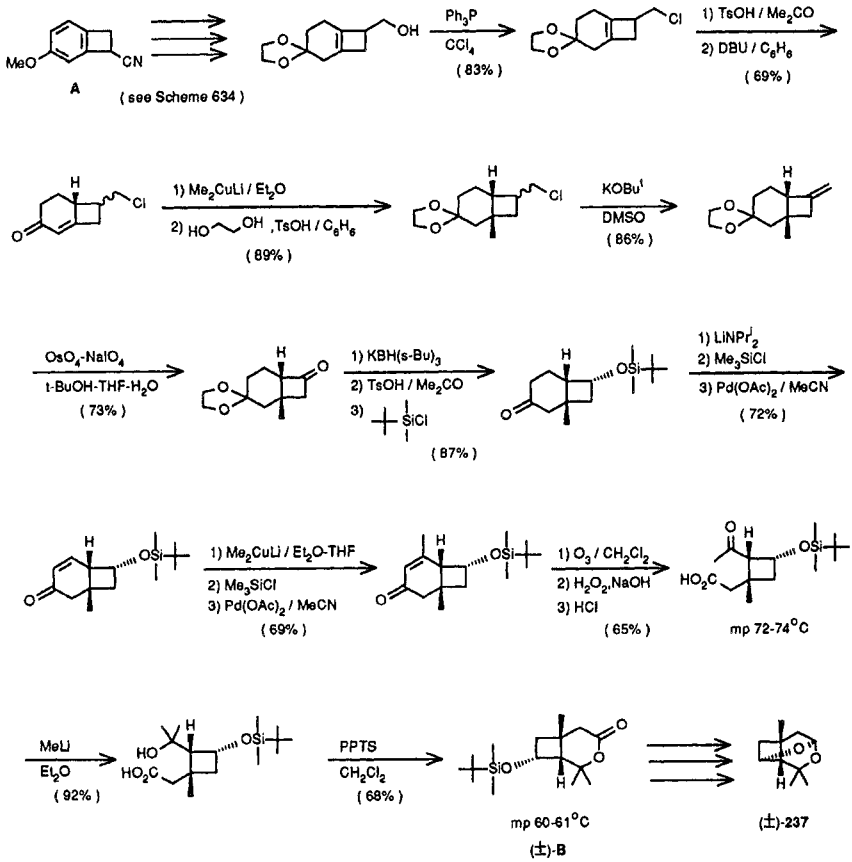
workers also employed the addition of dichloroketene in their synthesis of (±)-**237** (Scheme 904).[802] A lengthy route to (±)-**237** from a benzocyclobutene **A** was reported by Kametani et al. (Scheme 905),[805] which produced (±)-**B.**

(2) Syntheses of Optically Active Lineatin

Five syntheses of optically active lineatin have been reported since 1979; four by resolution of intermediates and one starting from a sugar. The first step of

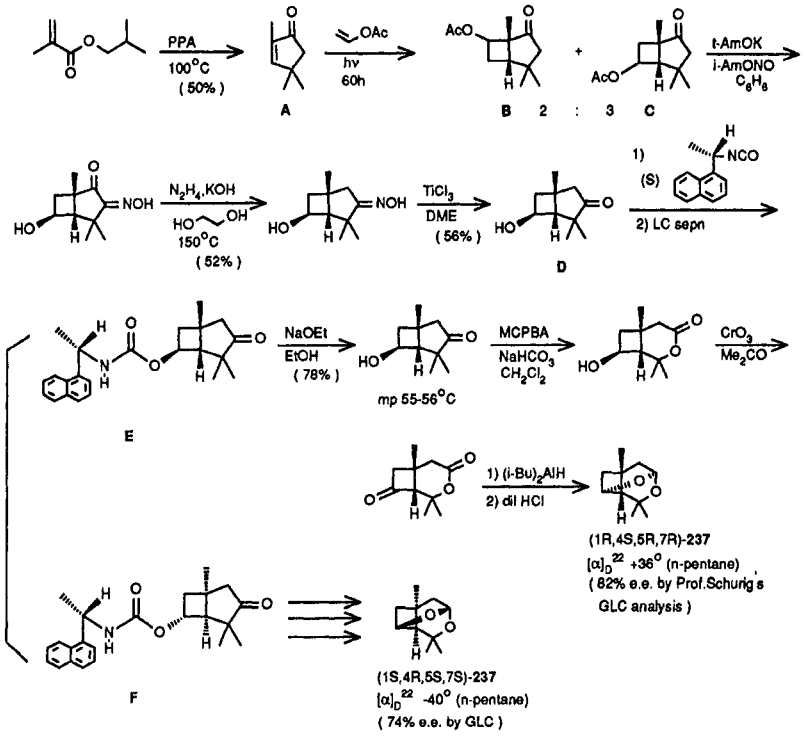


Scheme 904



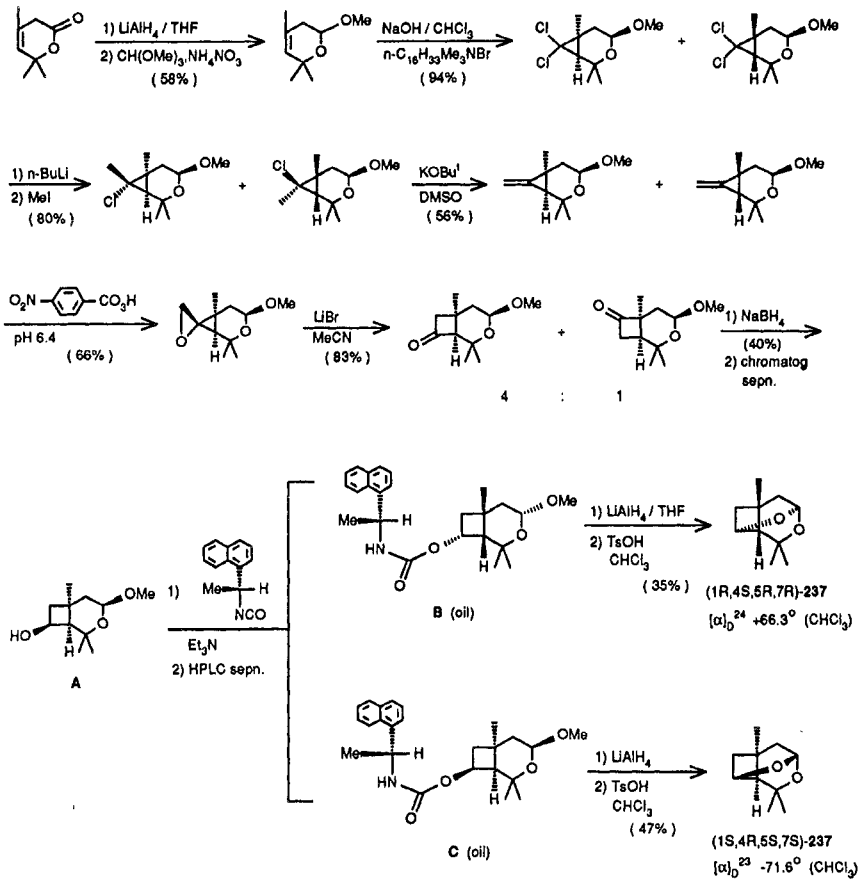
Scheme 905

Mori-Sasaki synthesis was the photo-cycloaddition of **A** with vinyl acetate to give a mixture of **B** and **C** (Scheme 906).[1126] The unwanted isomer **B** was



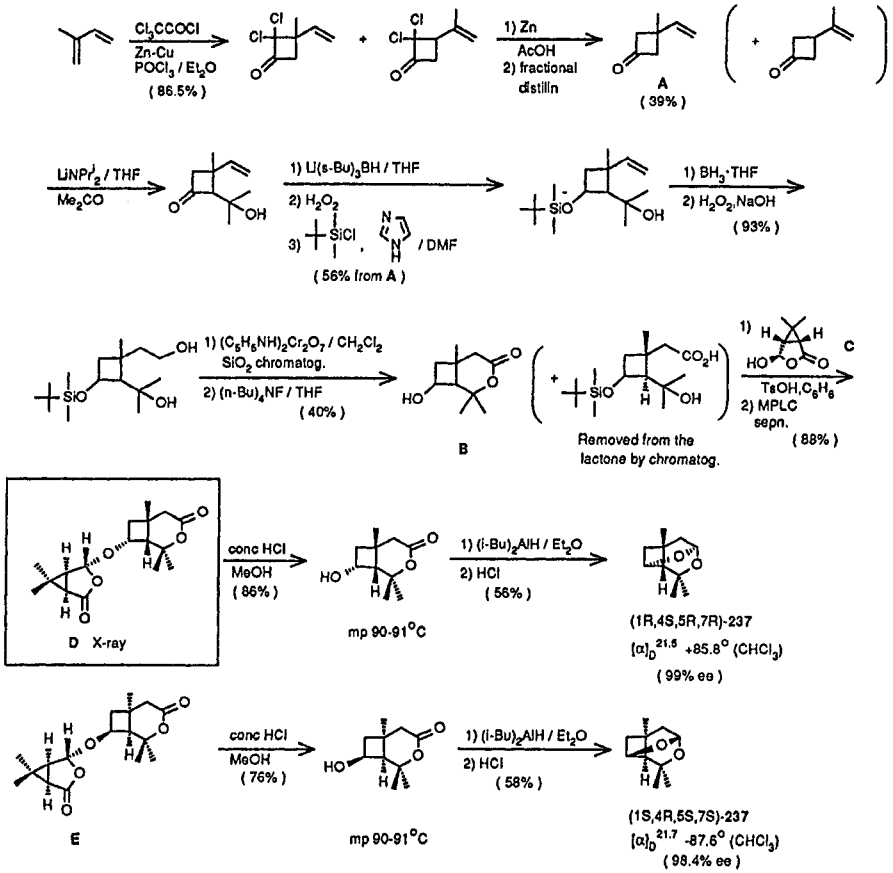
Scheme 906

destroyed by retro-aldol reaction in the course of the next conversion. Resolution of **D** as its carbamate diastereomers **E** and **F** was partially successful by chromatography to produce (+)-lineatin and its antipode of moderate e.e. In this work Mori misassigned the absolute configuration of the final products on the basis of misinterpretation of their ORD/CD data. Slessor and Oehlschlager et al. constructed the cyclobutane ring of **237** in a unique manner and resolved hydroxyacetal **A** via a mixture of carbamate diastereomers **B** and **C** (Scheme 907).[1127] They were able to assign (1*R*,4*S*,5*R*,7*R*)-configuration to the bioactive (+)-**237** on the basis of chromatographic and ^{1}H NMR properties of **B** and **C**, as well as by comparing the chiroptical properties of **237** with those of other pheromone acetals. By the improved route as shown in Scheme 908, Mori et al. were able to secure the pure enantiomers of **237** and unambiguously establish



Scheme 907

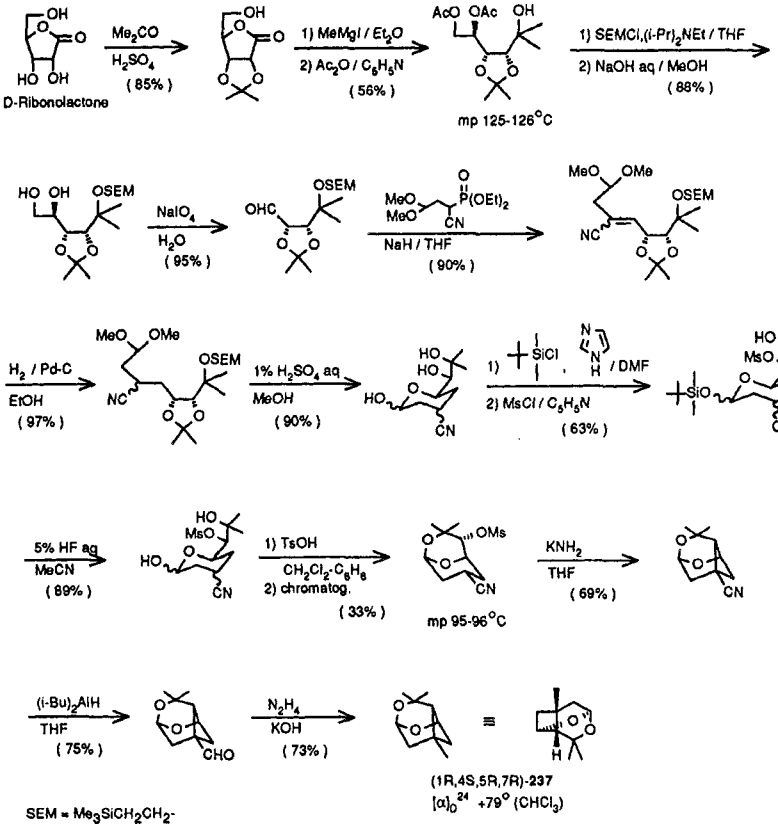
their absolute configuration as shown in the Scheme.[1128,1129] In this synthesis, (±)-lactone **B** was resolved by using derivative **C** of chrysanthemic acid as the resolving agent. The resulting diastereomers **D** and **E** were readily separable by MPLC, and the structure of **D** was determined by X-ray crystallographic analysis. The enantiomeric purity of (+)-**237** as well as that of its antipode were carefully estimated by GLC and NMR analyses.[1129] Kandil and Slessor employed D-ribonolactone as the starting material and synthesized (+)-**237**, confirming its (1*R*,4*S*,5*R*,7*R*)-stereochemistry (Scheme 909).[1130] This 16-step synthesis chemically established the absolute configuration of (+)-**237** and provided it in 2.7% overall yield.



Scheme 908

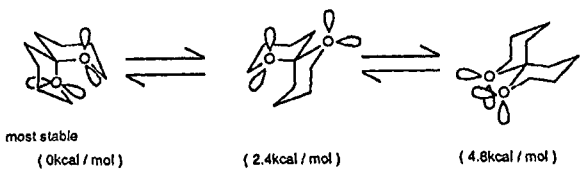
21. SPIROACETALS AS PHEROMONES

Since 1977 many spiroacetals have been isolated and identified as insect pheromones or secretions, mainly by W. Francke and his co-workers. Among them 1,7-dioxaspiro[5.5]undecanes exist not only as insect pheromones but also as antibiotics such as avermectins and milbemycins. Synthetic chemistry of 1,7-dioxaspiro[5.5]undecanes was reviewed by Kluge.[1131] A comprehensive review of the chemistry of spiroacetals appeared in 1989.[1132] ^{1}H- and ^{13}C-NMR spectra of spiroacetals were measured and analyzed.[1133, 1134] Mass spectra of alkyl-1,6-dioxaspiro[4.5]decanes were discussed by Francke et al.[1135] Stereoelectronic



Scheme 909

effects in spiroacetals (especially 1,7-dioxaspiro[5.5]undecanes) were studied by Deslongchamps et al. to deduce the stable conformers (Scheme 910).[1136]



Scheme 910

A. Chalcogran (2-Ethyl-1,6-dioxaspiro[4.4]nonane) 238 ($C_9H_{16}O_2$)

This is the major component of the aggregation pheromone of the six-spined spruce bark beetle (*Pityogenes chalcographus*), as first discovered by Francke et al. in 1979.[1137] Another component of the pheromone is methyl (2*E*,4*Z*)-2,4-decadienoate **145.**[1137] There are four stereoisomers of chalcogran **238** (Scheme 911). Hindguts of the male beetle contain the most active (2*S*,5*R*)-**238** and least

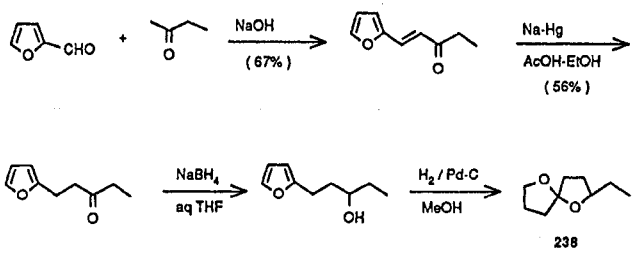
Stereoisomers of chalcogran 238

Scheme 911

active (2*S*,5*S*)-**238.**[1137] Two unnatural isomers, (2*R*,5*R*)-**238** and (2*R*,5*S*)-**238,** had intermediate activities.[1137] A mixture of **145** and **238** is marketed as a trap lure for *P. chalcographus*.[1137]

(1) Syntheses of a Stereoisomeric Mixture of Chalcogran

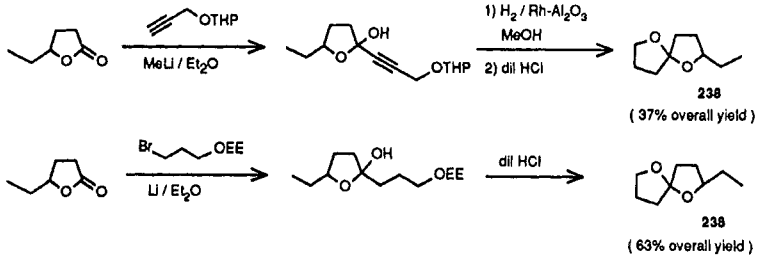
There are several reports on the synthesis of a mixture of all of the isomers of **238.** Francke and Reith prepared an isomeric mixture of **238** (Scheme 912),



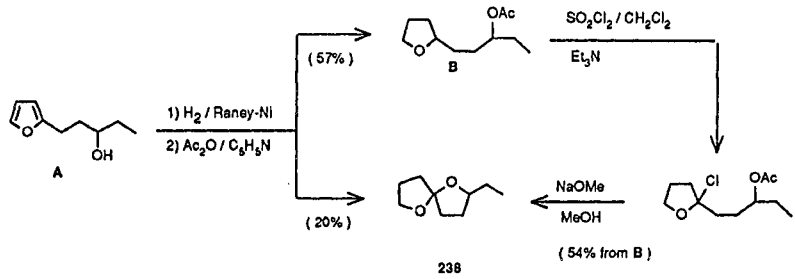
Scheme 912

starting from furfural and butanone.[1138] Other alkyl-1,6-dioxaspiro[4.4]nonanes were also synthesized and their mass spectra discussed.[1138] Smith and his co-

workers started from (±)-4-hexanolide and prepared **238** in 37% or 63% overall yield (Scheme 913).[1139,1140] Torgov's synthesis of **238** (Scheme 914) is a mod-

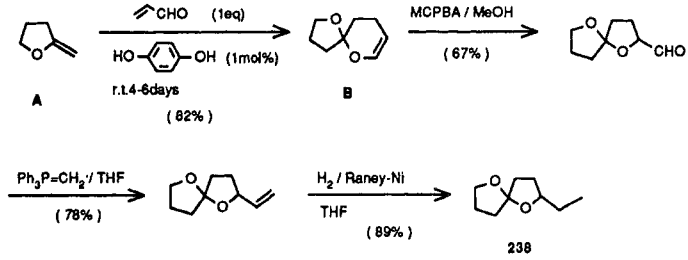


Scheme 913



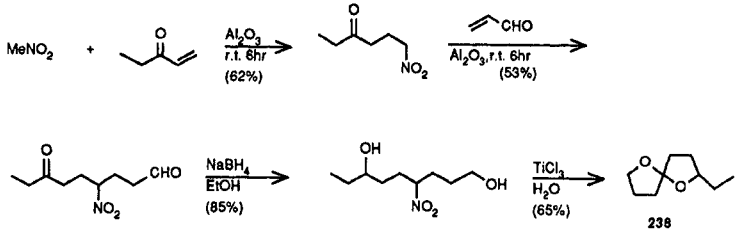
Scheme 914

ification of the Francke synthesis (Scheme 912), producing **238** in 51% yield from the furan compound **A**.[1141] Ireland and Häbich employed the hetero-Diels-Alder reaction between furanoid exocyclic vinyl ether **A** with acrolein to give **B**, which was converted to **238** (Scheme 915).[1142,1143]



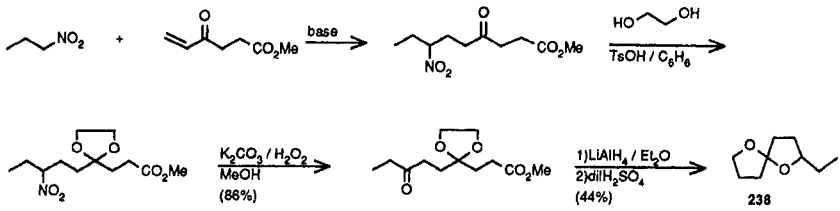
Scheme 915

Nitromethane, ethyl vinyl ketone, and acrolein were the starting materials in Rosini's synthesis of **238** (Scheme 916).[1144] Reissig and his co-workers em-



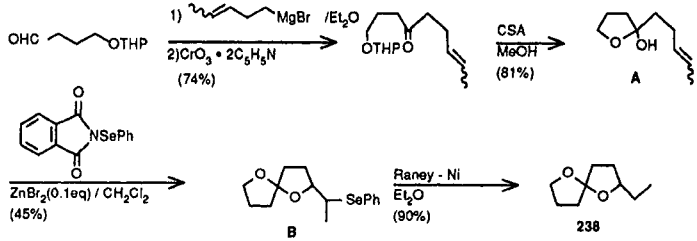
Scheme 916

ployed nitropropane for the synthesis of **238** (Scheme 917).[1145] The key-step of



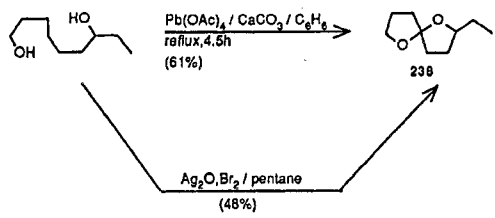
Scheme 917

Ley's synthesis of **238** was the cyclization of hemiacetal **A** with N-phenylselenophthalimide and zinc bromide to create **B** (Scheme 918).[1146] 1,7-Nonane-



Scheme 918

diol was converted to **238** by alkoxy radical process with either lead tetraacetate or silver oxide-bromine (Scheme 919).[1147]



Scheme 919

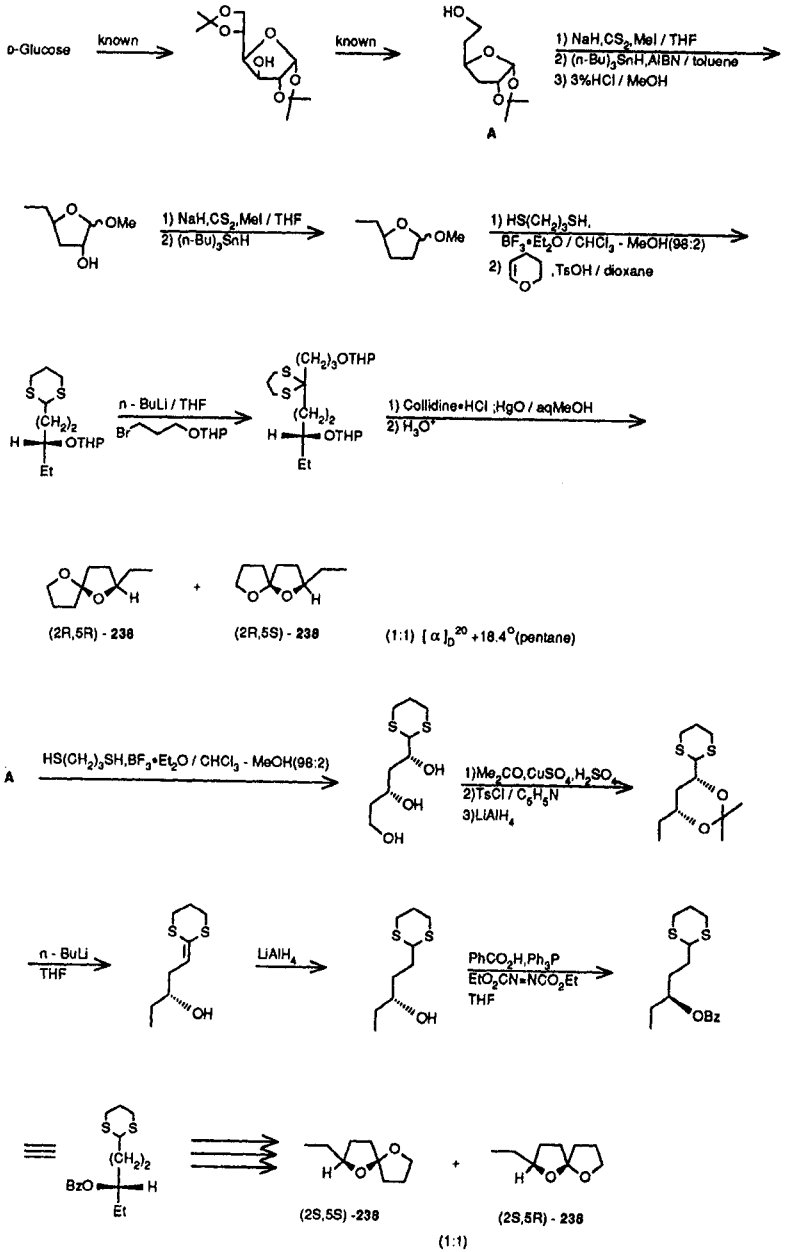
(2) Syntheses of Optically Active Chalcogran

Schurig's complexation GC method can be used for the estimation of the enantiomeric excess of the enantiomeric pairs (cf. Scheme 911) of chalcogran by using an optically active nickel complex as the stationary phase.[1148] Starting from D-glucose, Redlich synthesized (2*R*,5*RS*)-**238** and (2*S*,5*RS*)-**238** as shown in Scheme 920.[1149,1150] (2*R*,5*RS*)-Chalcogran **238** was also synthesized by Seebach and his co-workers, by employing (*S*)-malic acid (Scheme 921).[1151] Enders used acetone dimethylhydrazone and epoxides as starting materials to prepare (2*S*,5*RS*)-**238** (Scheme 922).[1152]

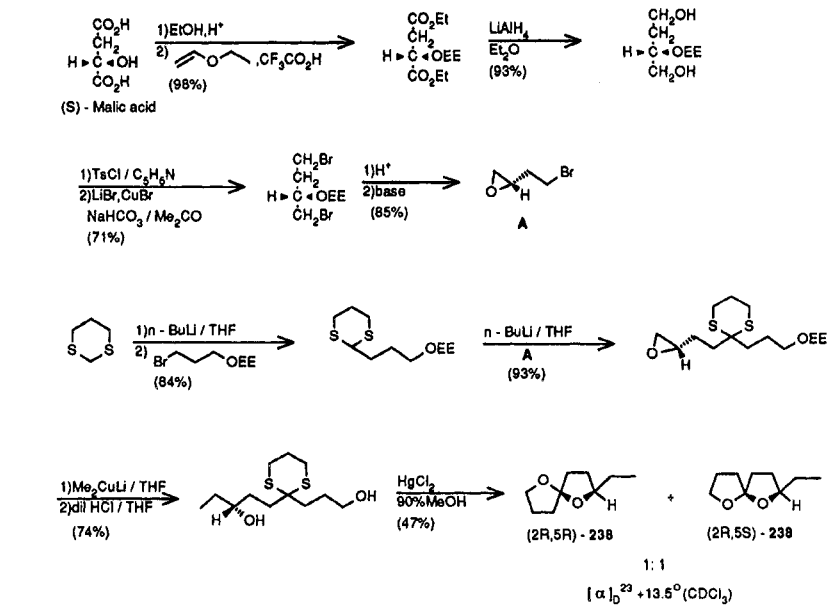
In a recent synthesis by Högberg et al., all the stereoisomers of **238** were secured for bioassay purpose.[1153] As shown in Scheme 923, their synthesis was a modification of Smith's route (Scheme 913). Their starting materials were the enantiomers of 4-hexanolide **A**, which were prepared by chromatographic resolution of (±)-**A**. (2*R*,5*RS*)-Chalcogran could be separated by careful chromatography on silica gel to produce (2*R*,5*R*)-**238** and (2*R*,5*S*)-**238.** Similarly, (2*S*,5*S*)-**238** and (2*S*,5*R*)-**238** were also prepared. Their purities were estimated by capillary GLC analysis on a chiral stationary phase, Ni(II) *bis*(3-heptafluorobutyryl-1-(*R*)-camphorate, in SE-54 (Scheme 923).

B. 1,7-Diethyl-1,6-dioxaspiro[4.4]nonane 239 ($C_{11}H_{20}O_2$) and 1,7-Dipropyl-1,6-dioxaspiro[4.4]nonane 240 ($C_{13}H_{24}O_2$)

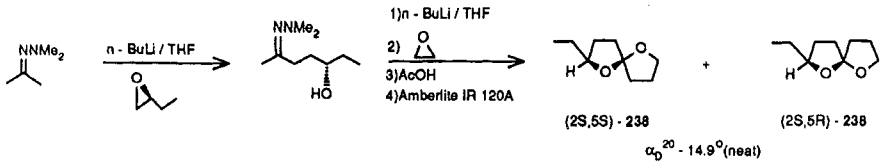
These are the components of the pheromone bouquets of *Andrena* bees. The palaearctic bee (*Andrena wilkella*) produces **239,**[1154] and *A. haemorrhoa* produces **240.**[1155] Enders prepared **239** and **240** both as a stereoisomeric mixture, by alkylating acetone dimethylhydrazone with epoxides (Scheme 924).[1152]


D-Glucose
known
known
1) NaH,CS2,MeI / THF
2) (n-Bu)3SnH,AIBN / toluene
3) 3%HCl / MeOH
A
1) NaH,CS2,MeI / THF
2) (n-Bu)3SnH
1) HS(CH2)3SH,
BF3•Et2O / CHCl3 - MeOH(98:2)
2) ,TsOH / dioxane
n - BuLi / THF
1) Collidine•HCl ;HgO / aqMeOH
2) H3O+
(2R,5R) - 238
(2R,5S) - 238
(1:1) [α]D20 +18.4°(pentane)
HS(CH2)3SH,BF3•Et2O / CHCl3 - MeOH(98:2)
1)Me2CO,CuSO4,H2SO4
2)TsCl / C5H5N
3)LiAlH4
n - BuLi
THF
LiAlH4
PhCO2H,Ph3P
EtO2CN=NCO2Et
THF
(2S,5S) -238
(2S,5R) - 238
(1:1)

Scheme 920



Scheme 921



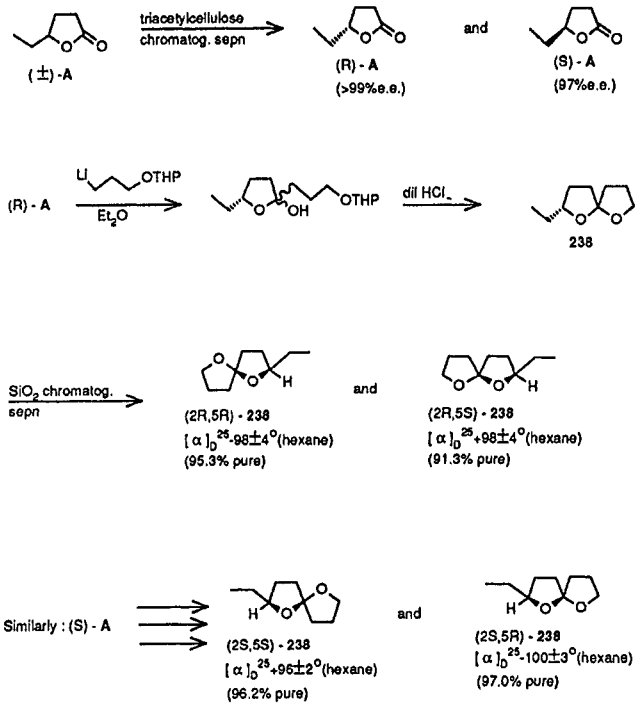
Scheme 922

C. 2-Methyl-1,6-dioxaspiro[4.5]decane 241 ($C_9H_{16}O_2$)

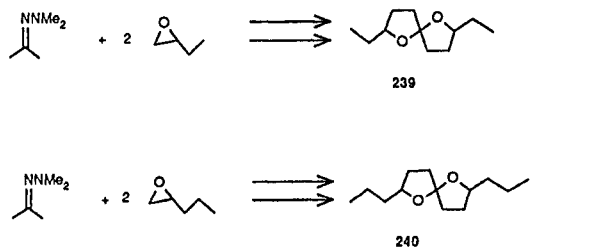
This is a pheromone component of the common wasp (*Paravespula vulgaris*).[1156] The absolute configuration of the natural product is still unknown.

(1) Syntheses of a Stereoisomeric Mixture of 241

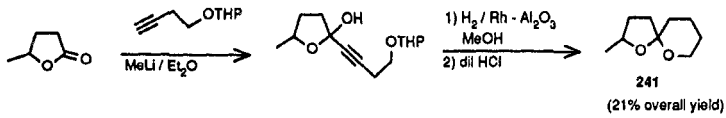
Several syntheses of a stereoisomeric mixture of **241** were reported by the same methods as those used for the synthesis of **238.** Starting from (±)-4-pentanolide, Smith and his co-workers synthesized (±)-**241** (Scheme 925).[1139] Ireland's hetero-Diels-Alder route was used to synthesize **B** from **A** (Scheme 926), and



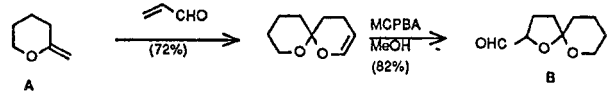
Scheme 923



Scheme 924

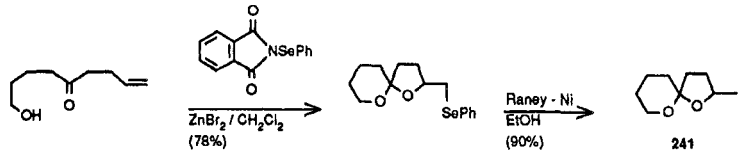


Scheme 925



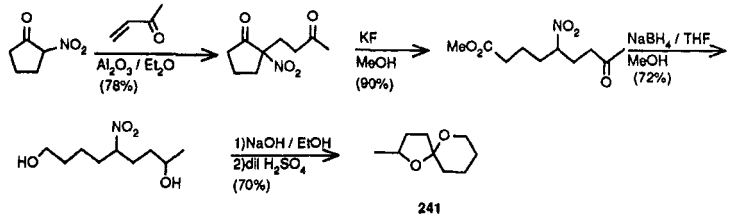
Scheme 926

B can be a precursor to **241.**[1142] Ley's organoselenium-mediated cyclization was applied to the synthesis of **241** (Scheme 927).[1146, 1157] In Rosini's synthesis

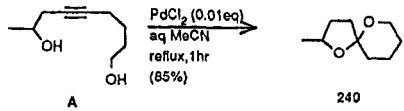


Scheme 927

of **241,** 2-nitrocyclopentanone was used as the starting material (Scheme 928).[1158] Utimoto prepared **241** in a simple manner by a regioselective acetalization of acetylene diol **A** (Scheme 929).[1159]



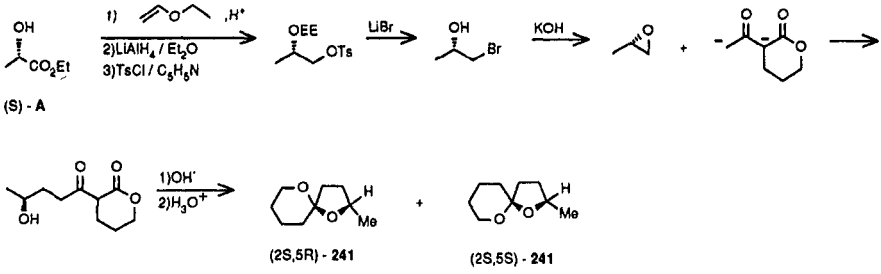
Scheme 928



Scheme 929

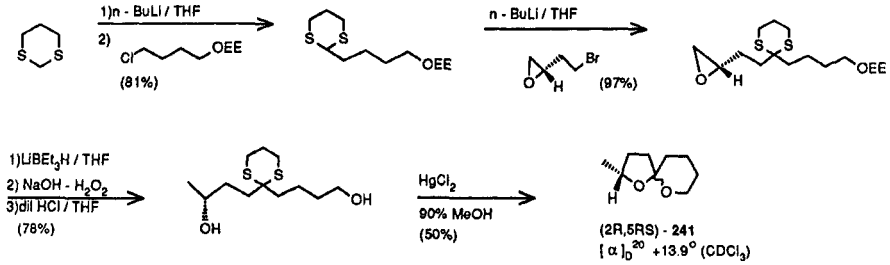
(2) *Syntheses of Optically Active* 241

The first synthesis of (2*S*,5*RS*)-**241** was reported by Schurig and his co-workers starting from ethyl (*S*)-lactate **A** (Scheme 930).[1160] The enantiomeric purity of



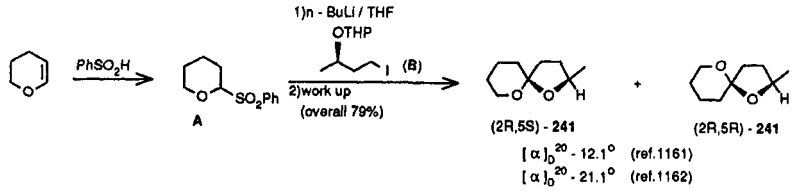
Scheme 930

the product could be checked by GLC on manganese-*bis*-3-heptafluorobutyryl-(*R*)-camphorate.[1160] Seebach et al. synthesized (2*R*,5*RS*)-**241** starting from (*S*)-malic acid (Scheme 931).[1151] Ley's synthesis of (2*R*,5*RS*)-**241** was achieved by



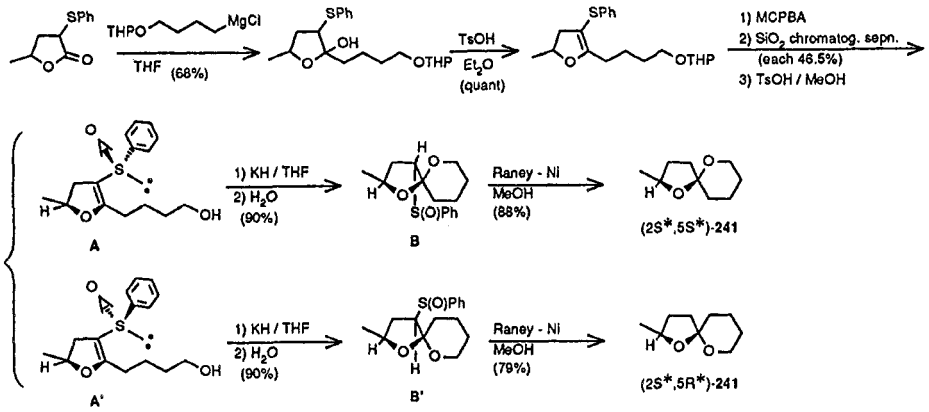
Scheme 931

alkylation of 2-benzenensulfonyltetrahydropyran **A** with chiral iodide **B** (Scheme 932).[1161,1162]



Scheme 932

Stereocontrol of the chirality at the spirocenter of **241** was achieved by Iwata et al. by intramolecular Michael addition of the hydroxy group to the α,β-unsaturated sulfoxide moiety of **A** to produce **B** (Scheme 933), yielding dias-



Scheme 933

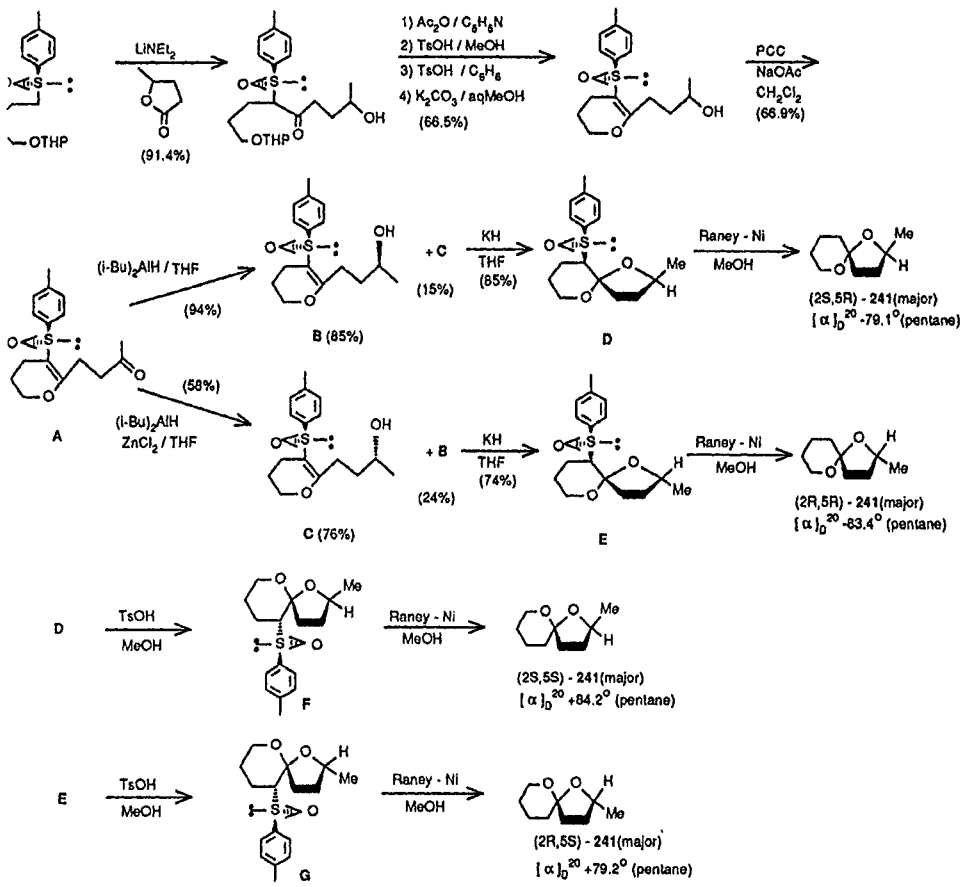
tereomerically pure (2*S*,*5*S**)-**241** and (2*S**,5*R**)-**241**.[1163] Iwata further improved this strategy to synthesize all of the four stereoisomers of **241** (Scheme 934).[1164,1165] Three steps in Scheme 934 are noteworthy: (i) stereoselective reduction of **A** to create either **B** or **C** as the major product by changing the reducing agent; (ii) kinetically controled cyclization of **B** and **C** to produce **D** and **E**, respectively; and (iii) conversion of **D** and **E** to thermodynamically more stable **F** and **G** by acid treatment.

D. 7-Methyl-1,6-dioxaspiro[4.5]decane 242 ($C_9H_{16}O_2$)

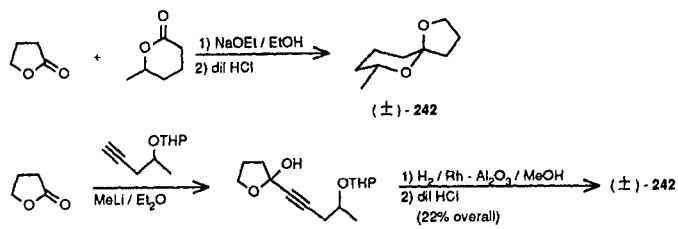
Together with **241**, this is a pheromone component of the common wasp (*Paravespula vulgaris*).[1156] The absolute configuration of the natural product isolated from an American bark beetle (*Conophthorus* sp.) was shown to be (5*S*,7*S*)-**242**.[1166]

(1) Syntheses of (±)-242

Francke et al. prepared (±)-**242** starting from γ-butyrolactone and δ-caprolactone (Scheme 935).[1133] Only a single diastereomer was obtained due to the

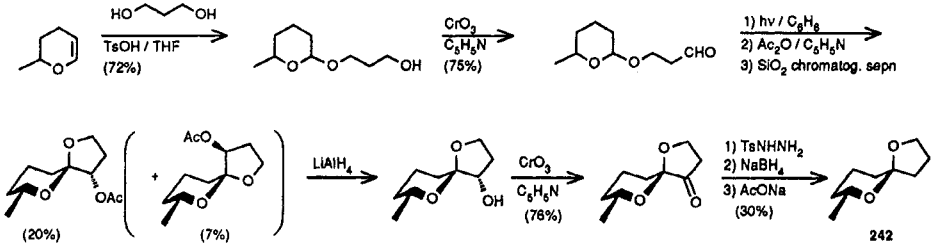


Scheme 934



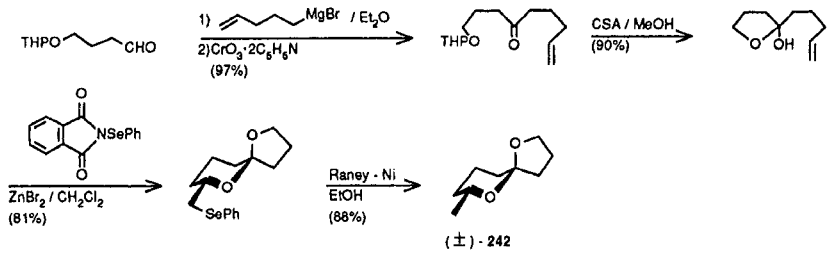
Scheme 935

oxygen anomeric effect.[1133] Smith et al. also started from γ-butyrolactone (Scheme 935, lower line).[1139] Koźluk et al. started from 6-methyldihydropyran and employed a photochemical reaction for spiroacetal formation (Scheme 936).[1167] Ley used organoselenium-mediated cyclization to prepare (±)-**242**



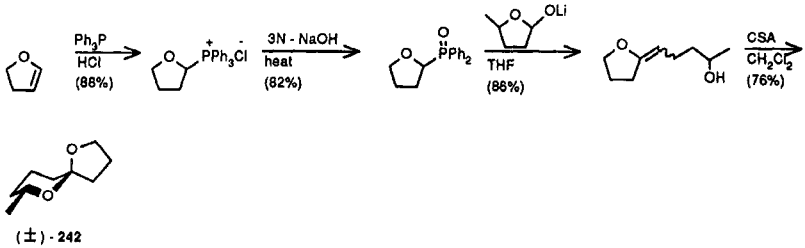
Scheme 936

(Scheme 937).[1146,1157] Ley's other method was the Horner-Wittig reaction



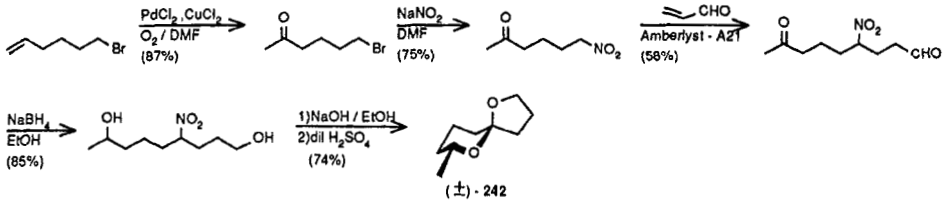
Scheme 937

of 2-diphenylphosphinoxytetrahydropyran with γ-valerolactol (Scheme 938).[1168,1169] Functionalized nitroalkanes were the intermediates in Rosini's

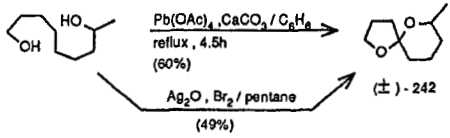


Scheme 938

synthesis of (±)-**242** (Scheme 939).[1158] The alkoxy radical route was also successful in providing (±)-**242** (Scheme 940).[1147]



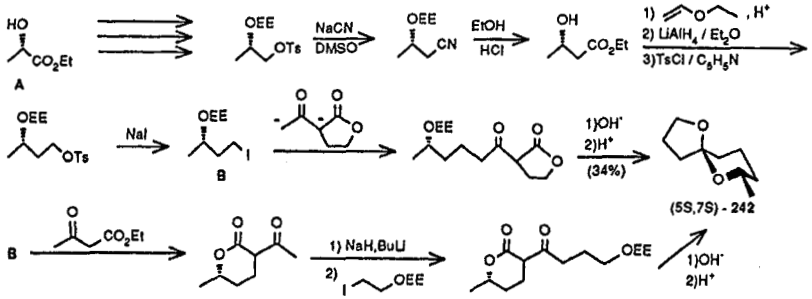
Scheme 939



Scheme 940

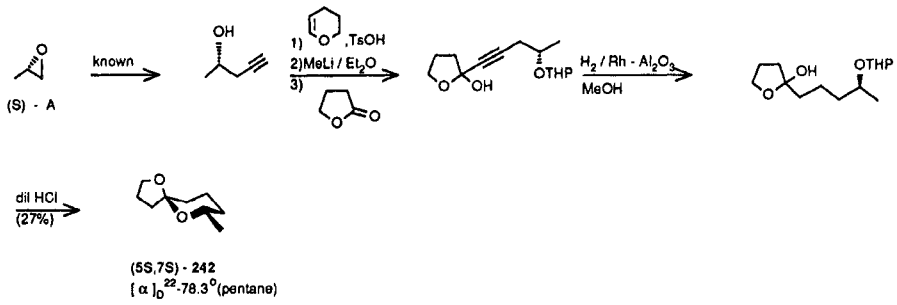
(2) *Syntheses of (5S,7S)-242*

Schurig and his co-workers synthesized (5*S*,7*S*)-**242** from ethyl (*S*)-lactate **A** (Scheme 941).[1160] In this paper, complexation GLC analysis of **242** is discussed



Scheme 941

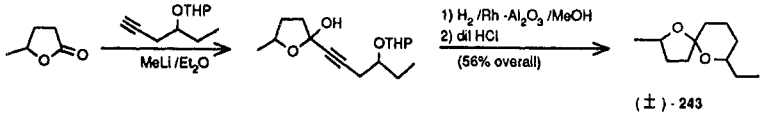
in detail. The key-step of the Schurig synthesis was the alkylation of the dianion, which was derived from α-acetyl-γ-butyrolactone as developed by Mori et al.[1170] Smith and his co-workers converted (*S*)-propylene oxide into (5*S*,7*S*)-**242** (Scheme 942).[1140]



Scheme 942

E. 7-Ethyl-2-methyl-1,6-dioxaspiro[4.5]decane 243 ($C_{11}H_{20}O_2$)

The two diastereomers of **243** were first found in the workers of *P. vulgaris*, and serve as the constituents of their anti-aggregation pheromones.[1171] These diastereomers were also found in the volatile secretion from the mandibular glands of the bee pollinator, *Andrena haemorrhoa*.[1172] An isomeric mixture of **243** was synthesized by Smith and his co-workers (Scheme 943) starting from

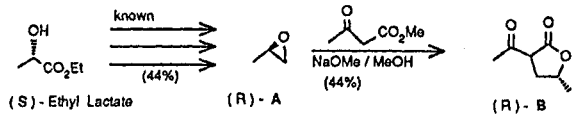


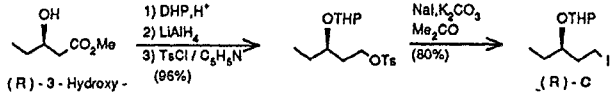
Scheme 943

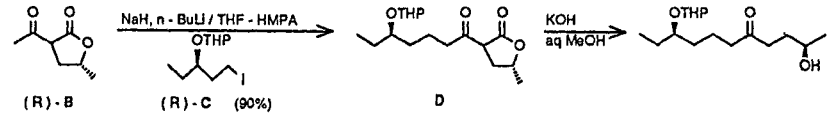
(±)-4-pentanolide.[1140] All of the four energetically possible stereoisomers of **243** were synthesized by Mori and Ikunaka by employing dianion alkylation as the key-step (Scheme 944).[1173] The starting chiral building blocks were ethyl (*S*)-lactate, dimethyl (*S*)-malate, and methyl (*R*)-3-hydroxypentanoate. Lactone **B**, which was prepared from propylene oxide **A**, was connected with **C** to produce **D**, which finally yielded **243**. By changing the partner of the connection, all of the four thermodynamically stable isomers of **243** were synthesized.[1173]

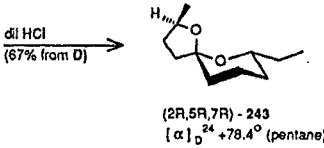
F. 2-Ethyl-7-methyl-1,6-dioxaspiro[4.5]decane 244 ($C_{11}H_{20}O_2$)

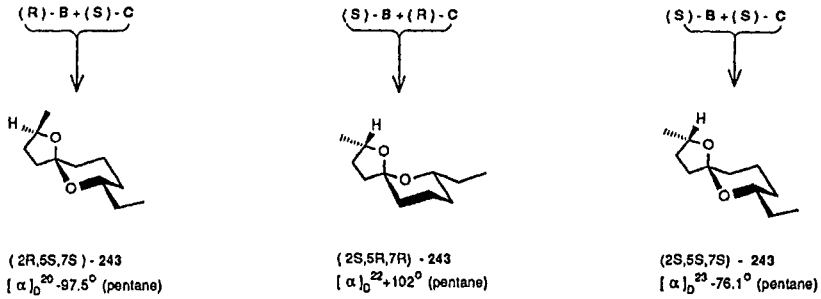
This is a pheromone component of *P. vulgaris*[1171] and *Andrena haemorrhoa*.[1155] The parasitoid wasp (*Megarhyssa nortoni nortoni*)[1174] and the cucumber fly (*Dacus cucumis*)[1175,1176] also produce **244**. An isomeric mixture of **244** was prepared by Smith and his co-workers as shown in Scheme 945.[1140]



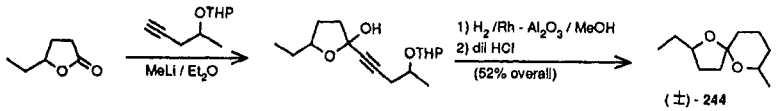








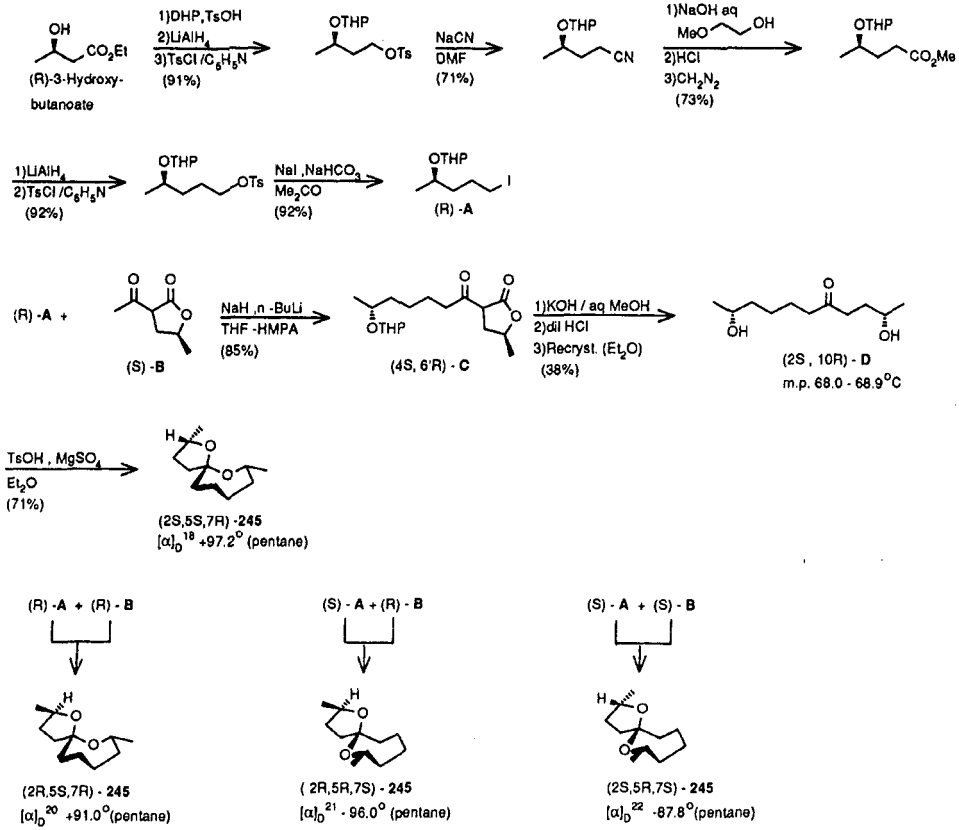
Scheme 944



Scheme 945

G. 2,7-Dimethyl-1,6-dioxaspiro[4.6]undecane 245 ($C_{11}H_{20}O_2$)

This is a component of the volatile secretion from the mandibular glands of *A. haemorrhoa*.[1155] Mori et al. synthesized four thermodynamically stable isomers of **245** in a manner similar to that used for the synthesis of **243** (Scheme 946).[1177]



Scheme 946

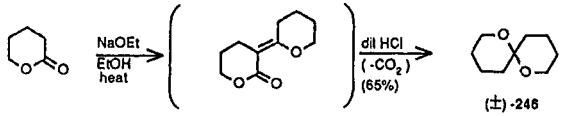
Alkylation of **B**[1173] with **A** gave **C**, which was hydrolyzed and decarboxylated. In this case, keto diol **D** could be isolated due to the unfavorable nature of the cyclization leading to a seven-membered ring. Under the forcing condition that employs magnesium sulfate as the dehydrating agent, **D** yielded **245.** In this paper, $[\alpha]_D$ values as well as the ^{13}C NMR data of various spiroacetals are compared and discussed.[1177]

H. 1,7-Dioxaspiro[5.5]undecane 246 ($C_9H_{16}O_2$), 3-Hydroxy-1,7-dioxaspiro[5.5]undecane 247 ($C_9H_{16}O_3$), and 4-Hydroxy-1,7-dioxaspiro[5.5]undecane 248 ($C_9H_{16}O_3$)

The major component of the sex pheromone produced by the female olive fruit fly (*Dacus oleae*) was shown to be 1,7-dioxaspiro[5.5]undecane (olean) **246** by Baker, Francke, and their co-workers in 1980.[1178,1179] Two hydroxyspiroacetals **247** and **248** are the minor components of the pheromone.[1179,1180] In the field test, (±)-**246** was proved to be active.[1178,1179,1181]

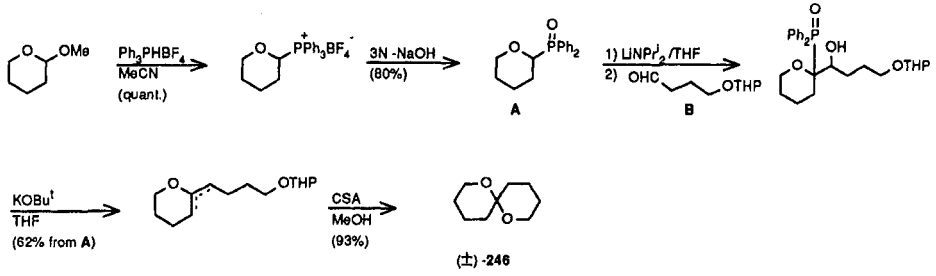
(1) Syntheses of the Racemates of 246, 247, and 248

Baker et al. synthesized (±)-**246** from δ-valerolactone (Scheme 947).[1178,1179]



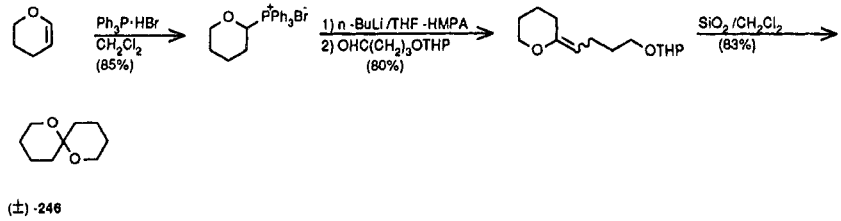
Scheme 947

The Horner-Wittig reaction of aldehyde **B** with 2-diphenylphosphinoxytetrahydropyran **A** was the key-step in Ley's synthesis of (±)-**246** (Scheme 948).[1168,1169] Ousset et al. also employed the Wittig reaction to prepare (±)-**246**



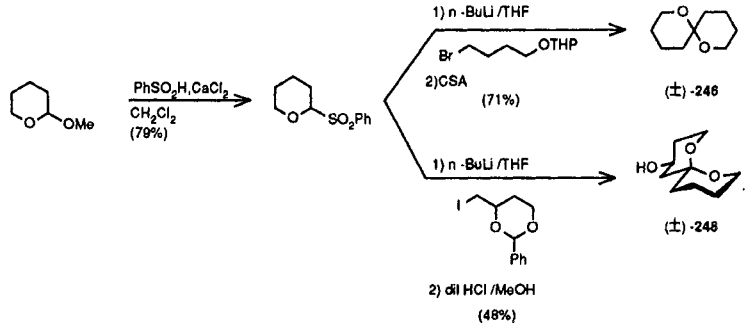
Scheme 948

(Scheme 949).[468] Ley's second synthesis of (±)-**246** was based on the alkylation of 2-benzenesulfonyltetrahydropyran (Scheme 950);[1161,1162] (±)-**248** was also synthesized by the same method (Scheme 950).[1161] A unique synthesis of (±)-**246** by Brinker et al. was achieved by a carbene insertion reaction (Scheme 951).[1182] In this synthesis, however, two byproducts were also obtained. Reddy

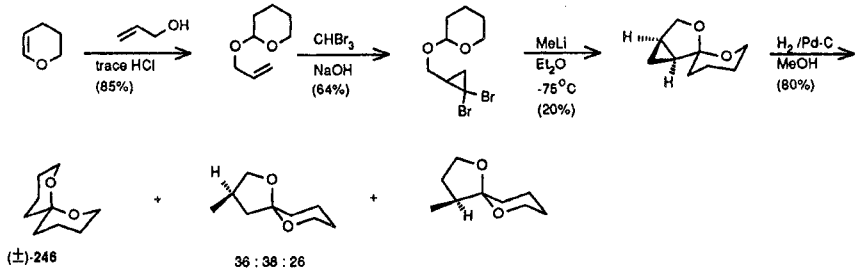


(±)-246

Scheme 949



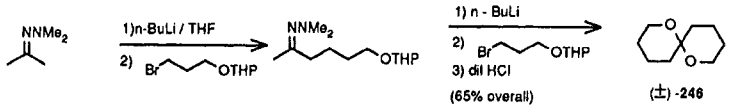
Scheme 950



(±)-246 + + 36 : 38 : 26

Scheme 951

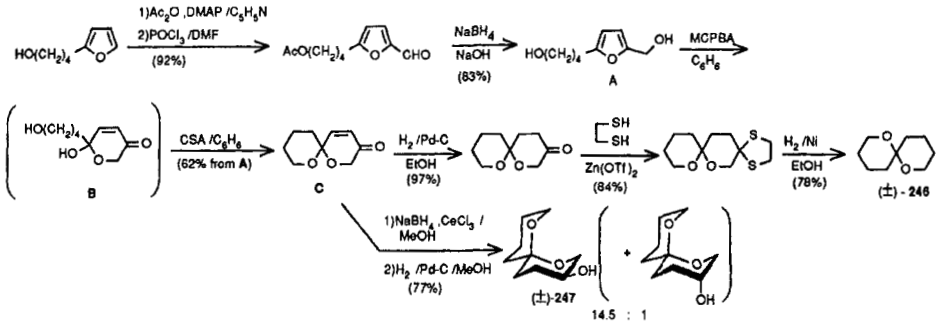
and Mitra prepared (±)-**246** by *bis*-alkylation of acetone dimethylhydrazone (Scheme 952).[470] The key-step in DeShong's synthesis of (±)-**246** and (±)-**247**



(±)-246

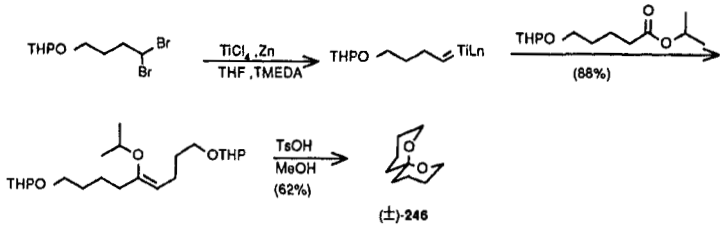
Scheme 952

was MCPBA oxidation of furan **A** to produce pyranone **C** via **B** (Scheme 953).[1183] Kocieński synthesized (±)-**246** by alkylidenation of ester carbonyl



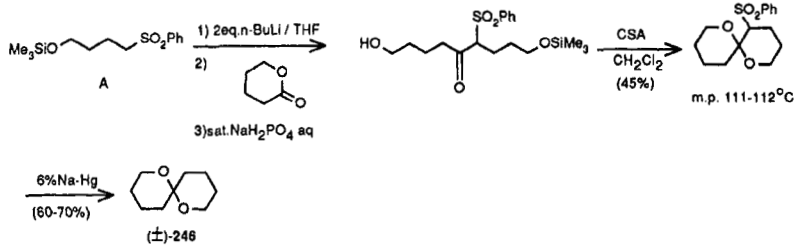
Scheme 953

with a metal carbene complex (Scheme 954).[1184] Brimble et al. prepared (±)-**246**



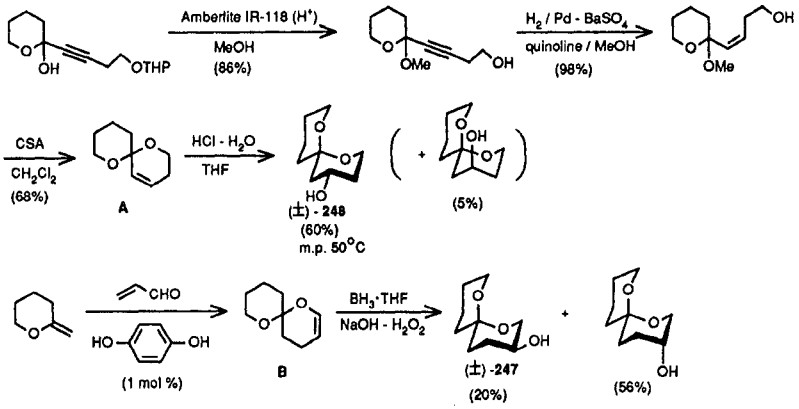
Scheme 954

from phenylsulfone **A** and δ-valerolactone (Scheme 955).[1185] Baker's synthesis



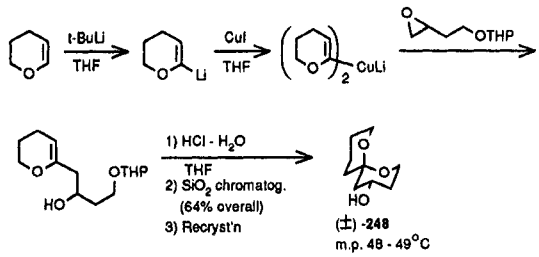
Scheme 955

of hydroxyspiroacetals (±)-**247** and (±)-**248** (Scheme 956) was achieved by hydration or hydroboration-oxidation of unsaturated spiroacetals **A** or **B**.[1179,1180]



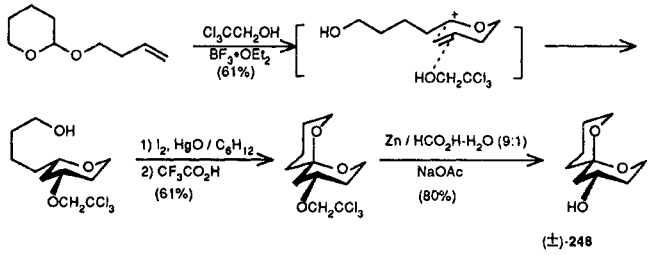
Scheme 956

Kocieński and Yeates synthesized (±)-**248**, employing the organocuprate derived from 6-lithio-3,4-dihydro-2(H)-pyran (Scheme 957).[1186] A cation-olefin

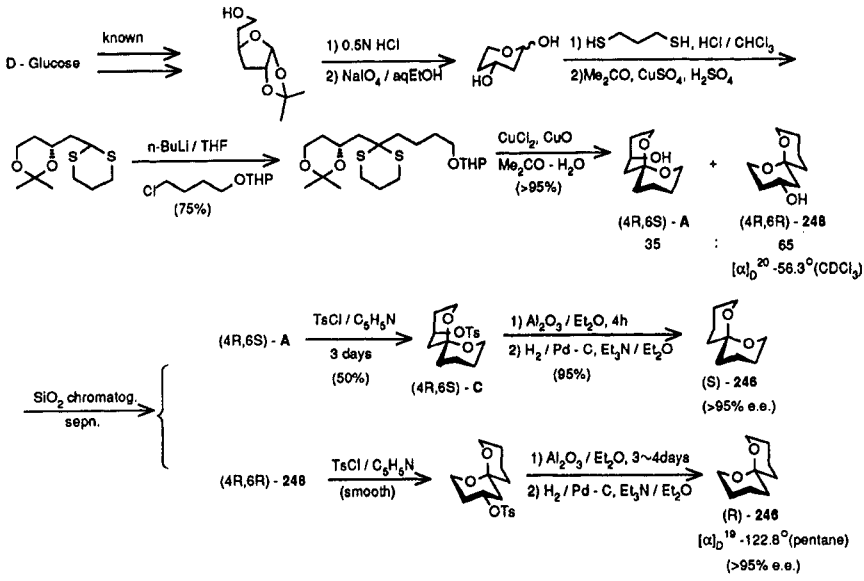


Scheme 957

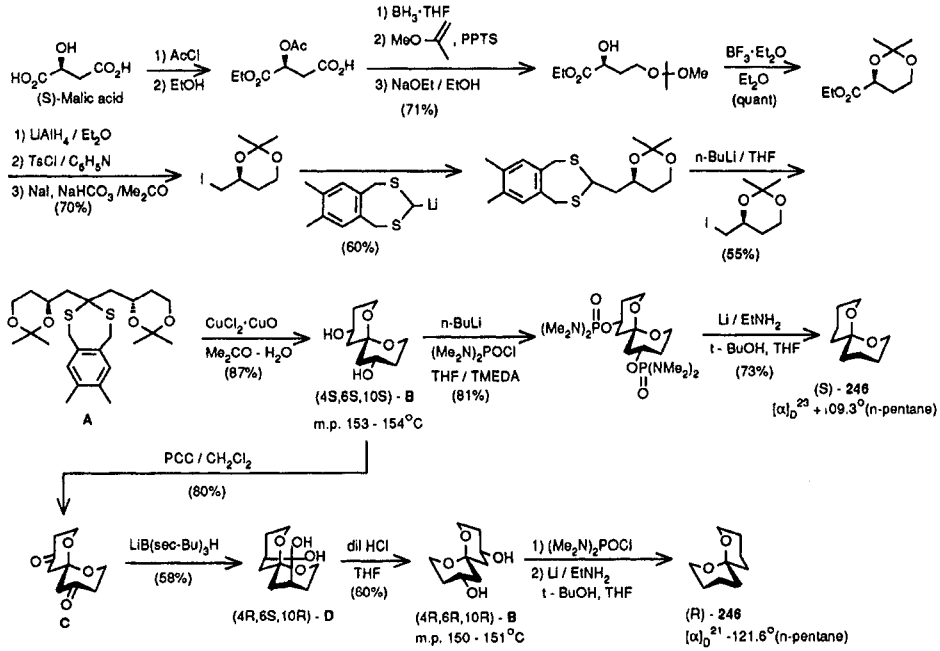
cyclization reaction was used by Kay and Williams to prepare (±)-**248** (Scheme 958).[1187]



Scheme 958



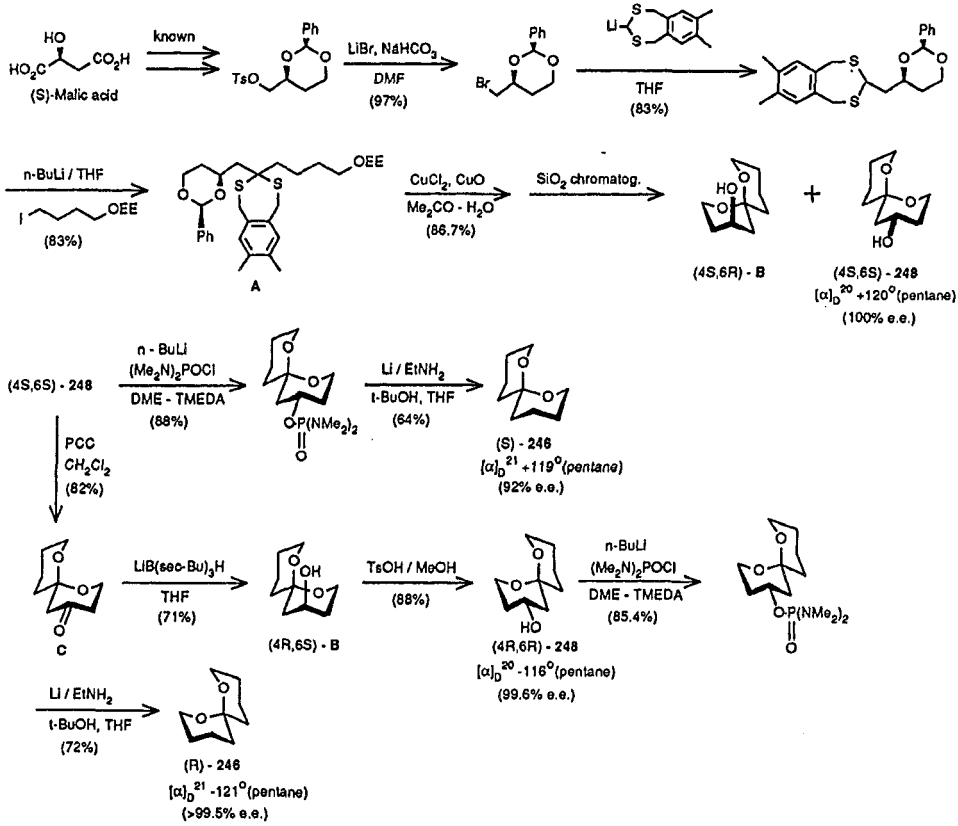
Scheme 959



Scheme 960

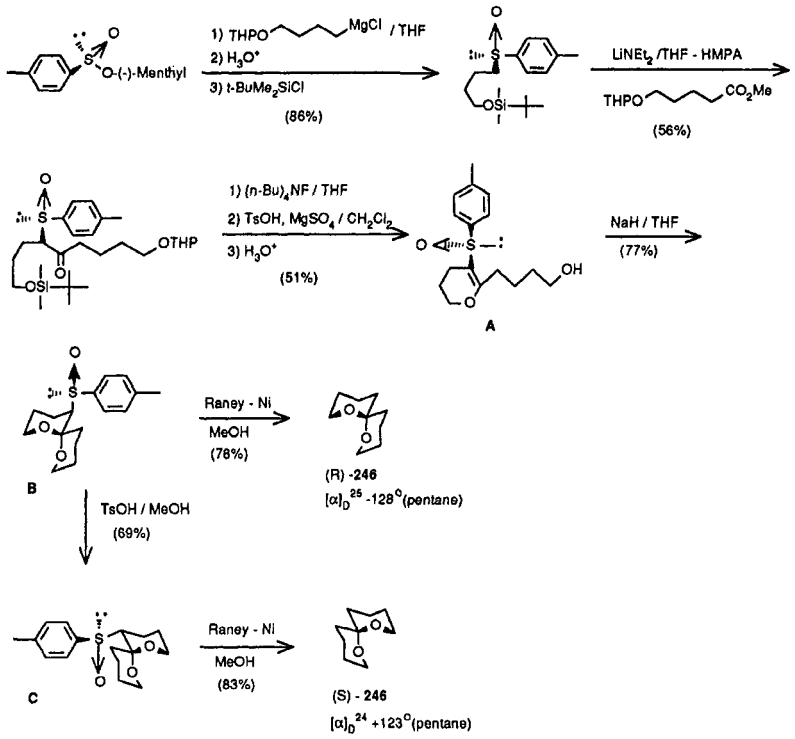
(2) Syntheses of the Enantiomers of 246, 247, and 248

Four different syntheses of the enantiomers of 1,7-dioxaspiro[5.5]undecane **246** have been reported. Redlich and Francke began with D-glucose and prepared both the enantiomers of **246** and (4*R*,6*R*)-**248** (Scheme 959).[1188] Mori's first synthesis (Scheme 960) used two molecules of (*S*)-malic acid to construct a molecule of **246.**[1189,1190] Deprotection of **A** yielded (4*S*,6*S*,10*S*)-**B** with two equatorial hydroxy groups. This was oxidized to **C,** the reduction of which with L-selectride® produced diaxial diol **D.** When **D** was treated with acid, it isomerized to (4*R*,6*R*,10*R*)-**B** with two equatorial hydroxy groups. Thus, the hydroxy groups were used as the handle to fix the conformation of spiroacetals.[1190] In Mori's second synthesis, only one molecule of (*S*)-malic acid was incorporated into **246** (Scheme 961).[1189,1191] Conversion of (4*S*,6*S*)-**248** to (4*R*,6*R*)-**248**



Scheme 961

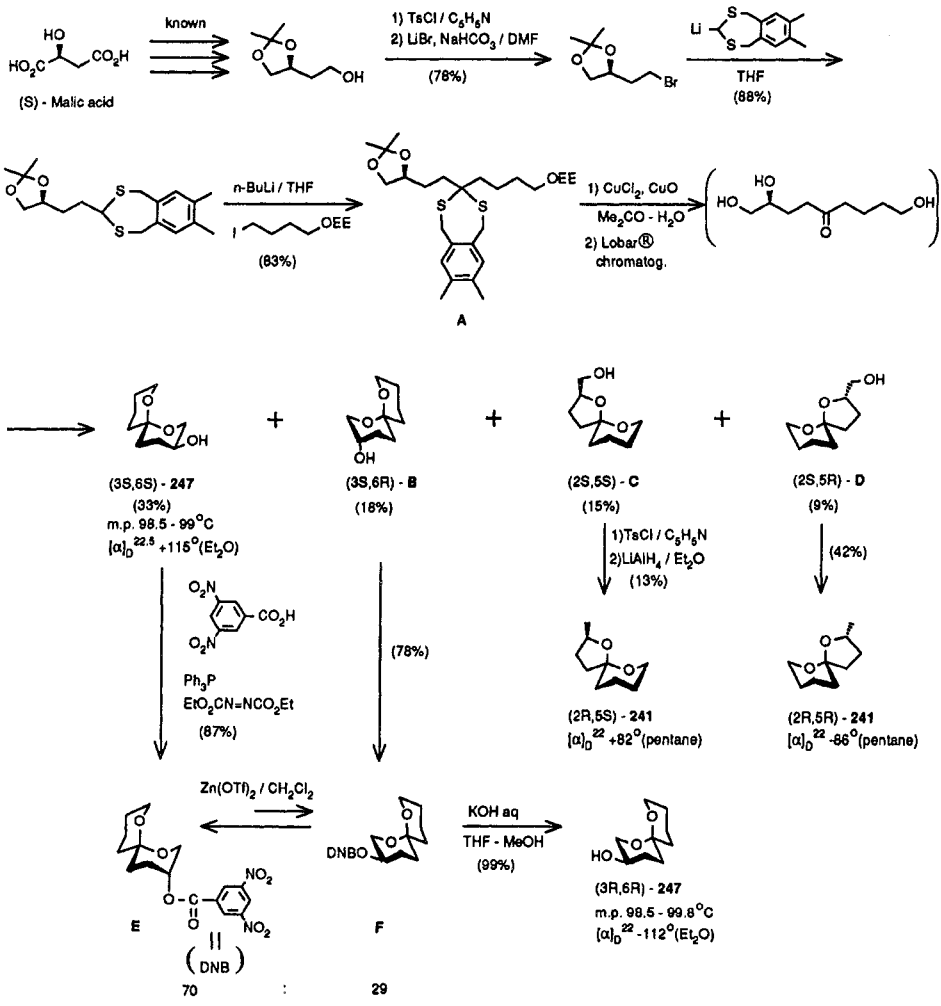
via **C** and (4*R*,6*S*)-**B** was the key transformation in this synthesis. The enantiomeric purity of (*R*)-**246** and (*S*)-**246** was determined by complexation GLC.[1191] Iwata et al. synthesized both (*R*)-**246** and (*S*)-**246** starting from (−)-menthyl (*S*)-*p*-toluenesulfinate (Scheme 962).[1192,1193] The key-step of their syn-



Scheme 962

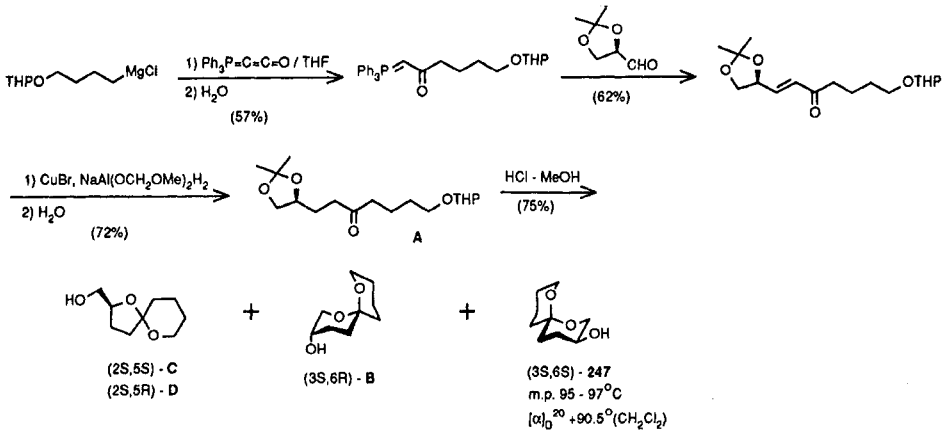
thesis was the diastereoselective intramolecular Michael addition of the hydroxy group of **A**, which provided spiroacetal **B** as the kinetically controlled product with the axial sulfinyl group. Treatment of **B** with acid effected its isomerization to the stabler isomer **C**. Desulfurization of **B** and **C** produced (*R*)-**246** and (*S*)-**246**, respectively.

Both the enantiomers of 3-hydroxy-1,7-dioxaspiro[5.5]undecane **247** were synthesized by Mori et al., starting from (*S*)-malic acid (Scheme 963).[1191,1194] In this particular case, deprotection of **A** yielded all of the four possible isomers of the spiroacetals, (3*S*,6*S*)-**247**, **B**, **C**, and **D**. Another noteworthy finding was the stabler nature of the axially substituted spiroacetal **E** in comparison with its



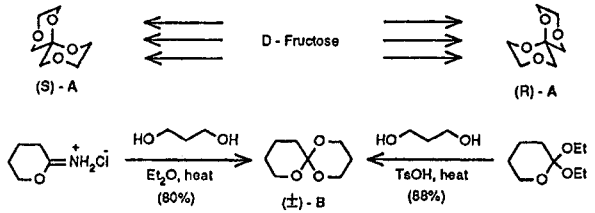
Scheme 963

isomer **F** with an equatorial substituent. Both (2*R*,5*S*)-**241** and (2*R*,5*R*)-**241** were also obtained by derivation from **C** and **D**, respectively. Bestmann and Schmidt synthesized (3*S*,6*S*)-**247** starting from D-glyceraldehyde acetonide.[1195] They executed the cyclization of the same keto triol as previously reported by Mori et al.[1191] As shown in Scheme 964, Bestmann also obtained a mixture of all of four possible spiroacetals, one of which was (3*S*,6*S*)-**247**. However, the exact ratio of the products was not reported.



Scheme 964

Both the enantiomers of spirobi-1,4-dioxane **A** were prepared from D-fructose (Scheme 965), although their bioactivity was not studied.[1196,1197] Hani-

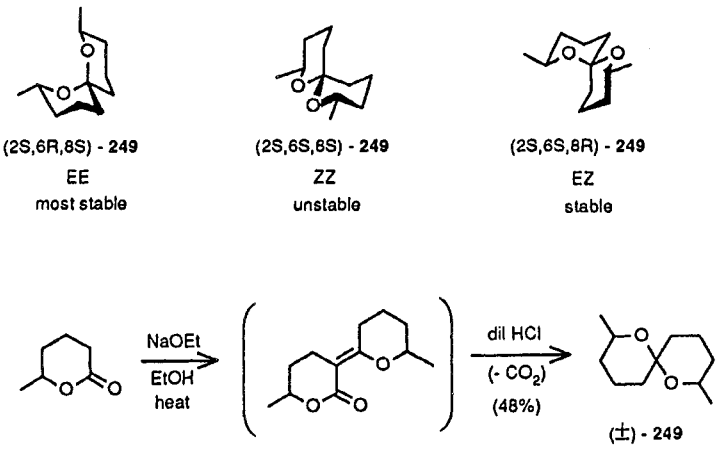


Scheme 965

otakis et al. synthesized (±)-1,5,7-trioxaspiro[5.5]undecane **B** (Scheme 965), and found it to be highly bioactive against the olive fruit fly (*Dacus oleae*).[1198] It must be mentioned that (*R*)-**246** was active on the male *D. oleae*, while (*S*)-**246** was active on females.[1199] The natural pheromone produced by the female *D. oleae* is (±)-**246**.[1199] An Australian fruit fly, *D. cacuminatus*, also produces (±)-**246**.[1175]

I. (2*S*,6*R*,8*S*)-2,8-Dimethyl-1,7-dioxaspiro[5.5]undecane 249 ($C_{11}H_{20}O_2$)

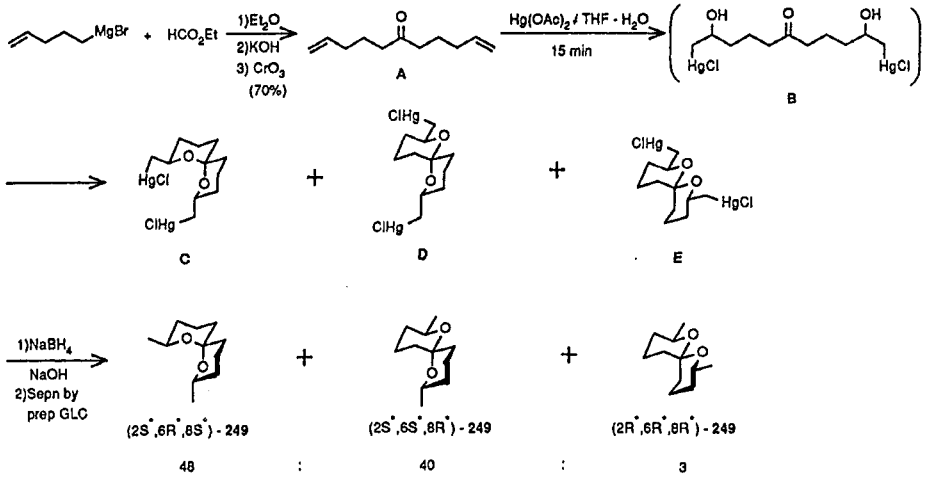
2,8-Dimethyl-1,7-dioxaspiro[5.5]undecane **249** can exist as three diastereomeric pairs (total six) of the enantiomers (Scheme 966).[1133] The (2*S**,6*R**,8*S**)-



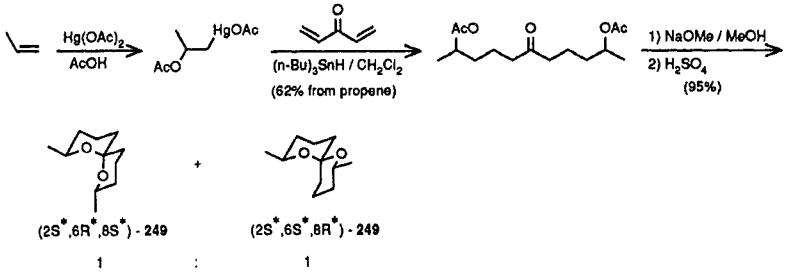
Scheme 966

isomer of **249** is the major component of the cephalic secretion of *Andrena wilkella*.[1154] In this bee secretion, a small amount of (2*S**,6*S**,8*R**)-**249** was also present. Tengö et al. showed (2*S*,6*R*,8*S*)-**249** to be the bioactive isomer in attracting patroling male bees in the field.[1200] The (2*R*,6*S*,8*R*)-isomer was behaviorally inactive, and in a racemic mixture it did not inhibit the response of the bees. The diastereomers of **249** other than the (2*S*,6*R*,8*S*)-isomer were almost inactive. The (2*S*,6*R*,8*S*)-isomer was later identified as the major component of the rectal gland secretion of the male cucumber fly (*Dacus cucumis*) and *D. halfordiae*.[1175,1176] In the former fly, the (2*S**,6*S**,8*S**)- and (2*S**,6*S**,8*R**)-isomers were also found as the minor components of the secretion.[1175,1176] The parasitoid wasp (*Megarhyssa nortoni nortoni*) also secretes **249**.[1174]

(2*S**,6*R**,8*S**)-2,8-Dimethyl-1,7-dioxaspiro[5.5]undecane (±)-**249** was first synthesized by Francke et al. starting from 5-hexanolide (Scheme 966).[1133] Its (2*S**,6*S**,8*R**)-isomer was also characterized, and the NMR spectra of both the isomers were analyzed.[1133] Kitching et al. was able to characterize all three isomers, (2*S**,6*R**,8*S**)-, (2*S**,6*S**,8*R**)-, and (2*R**,6*R**,8*R**)-**249**, by synthesizing them from dienone **A** via mercury(II)-catalyzed cyclization reaction (Scheme 967).[1176,1201] Their 400 MHz ^{1}H-NMR spectra were also recorded.[1176] The noteworthy feature of this synthesis was the isolation of even the least stable (2*R**,6*R**,8*R**)-isomer, which readily isomerized with acid to the stablest (2*S**,6*R**,8*S**)-**249**.[1176] Giese's synthesis of a mixture of (2*S**,6*R**,8*S**)-**249** and (2*S** ,6*S**,8*R**)-**249** was based on the radical carbon-carbon bond formation (Scheme 968).[1037]

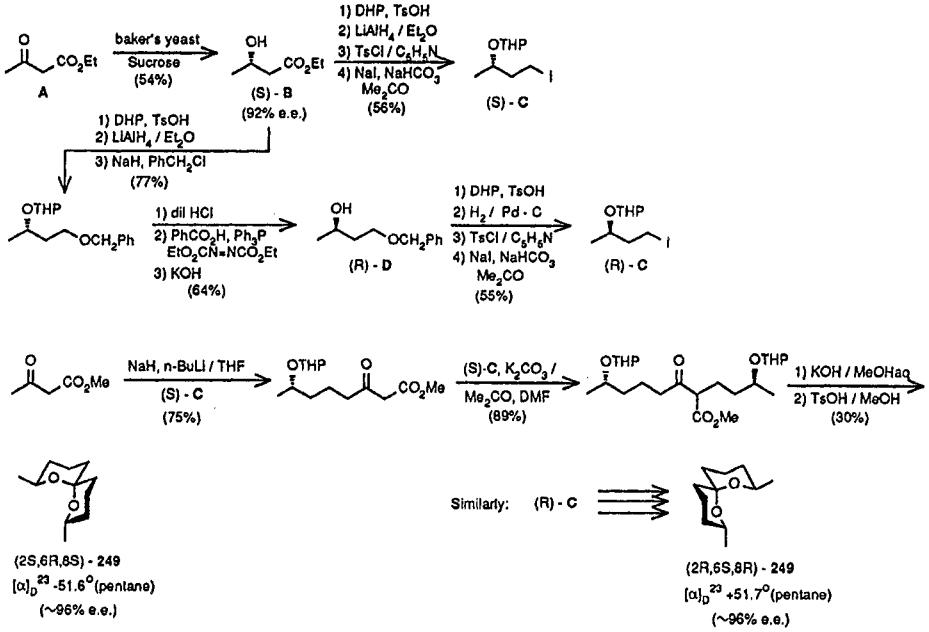


Scheme 967



Scheme 968

Mori and Tanida synthesized both (2*S*,6*R*,8*S*)-**249** and its antipode, starting from ethyl acetoacetate **A** (Scheme 969).[1202,1203] Reduction of **A** with baker's yeast produced (*S*)-**B**, which was converted to (2*S*,6*R*,8*S*)-**249** via (*S*)-**C**. On the other hand, (*R*)-**D** was prepared from (*S*)-**B** via Mitsunobu inversion and converted to (2*R*,6*S*,8*R*)-**249**. This 1981 synthesis was later improved by Mori and Watanabe.[1204] By using the pure enantiomers of ethyl 3-hydroxybutanoate as the chiral building blocks, they secured pure (2*S*,6*R*,8*S*)-**249** and (2*R*,6*S*,8*R*)-**249** (Scheme 970).[1204] Moreover, they clarified how it was possible to prepare (2*S*,6*R*,8*S*)-**249** of 98.7% e.e. starting from ethyl (*S*)-3-hydroxybutanoate of 85% e.e. (Scheme 970).[1204] Employing (*S*)-malic acid as one of the starting materials, (2*R*,6*S*,8*R*)-**249** and (2*R*,6*R*,8*S*)-**249** were synthesized by Mori and Watanabe (Scheme 971).[1204] In this synthesis, the enantiomeric



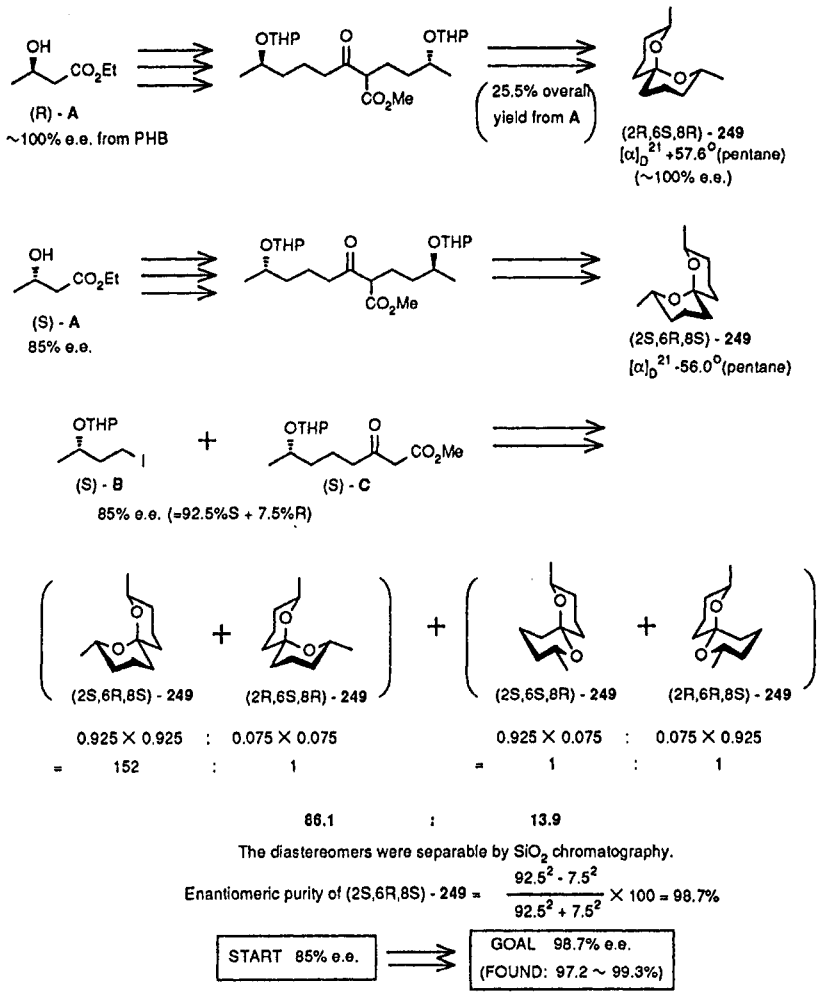
Scheme 969

purity of **C** could be determined by the ^{1}H-NMR analysis of its MTPA ester. It should be noted that **E** could be isomerized to **D** because the 3,5-dinitrobenzoate of **D** was crystalline, while that of **E** was an oil. Thus 3,5-dinitrobenzoate of **E** was isomerized with acid, and the crystalline 3,5-dinitrobenzoate of **D** could be separated.

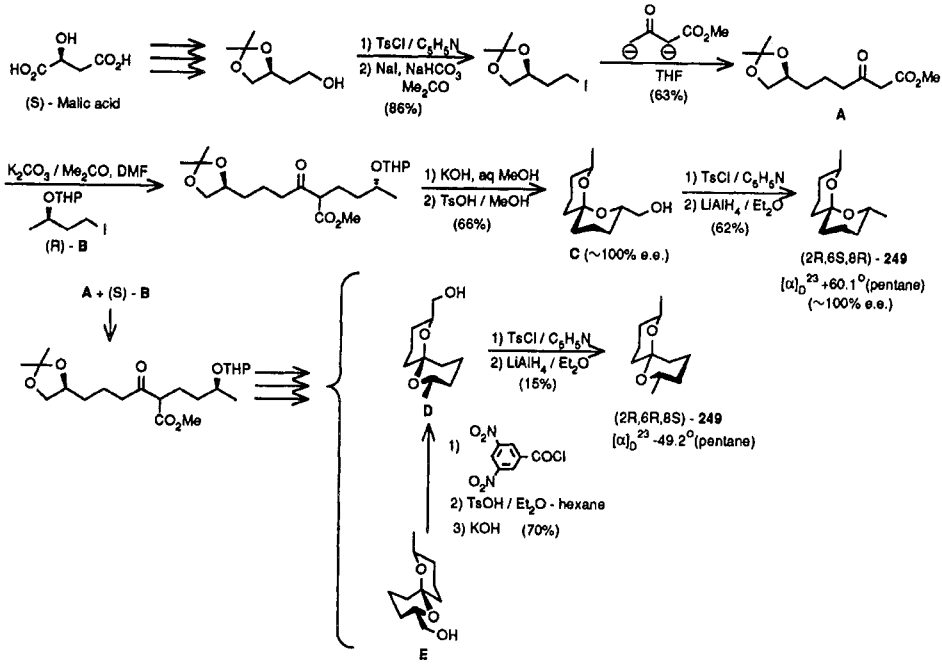
Isaksson et al. reported the preparative separation of the enantiomers of (2*R**,6*S**,8*R**)-**249** and (2*R**,6*R**,8*S**)-**249** by chromatography on microcrystalline triacetylcellulose.[1205] With this technique, they could prepare all four energetically stable isomers of **249.**

J. 2-Ethyl-8-methyl-1,7-dioxaspiro[5.5]undecane 250 ($C_{12}H_{22}O_2$)

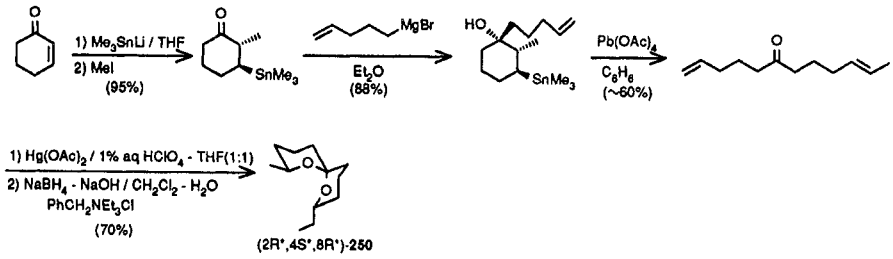
This is the unusual even-carbon-membered spiroacetal found in the rectal gland secretion of an Australian fruit fly (*Dacus occipitalis*).[1175] Kitching et al. synthesized (2*R*,4*S*,8*R*)-**250** by means of organotin chemistry coupled with oxymercuration-cyclization (Scheme 972).[512] This spiroacetal was also found in the oriental fruit fly (*D. dorsalis*) and *D. latifrons*.[1175]


OH
CO2Et
(R) - A
~100% e.e. from PHB
OTHP
O
OTHP
CO2Me
25.5% overall yield from A
(2R,6S,8R) - 249
[α]D21 +57.6° (pentane)
(~100% e.e.)
OH
CO2Et
(S) - A
85% e.e.
OTHP
O
OTHP
CO2Me
(2S,6R,8S) - 249
[α]D21 -56.0° (pentane)
OTHP
I
(S) - B
OTHP
O
CO2Me
(S) - C
85% e.e. (=92.5%S + 7.5%R)
(2S,6R,8S) - 249
(2R,6S,8R) - 249
(2S,6S,8R) - 249
(2R,6R,8S) - 249
0.925 × 0.925 : 0.075 × 0.075
= 152 : 1
0.925 × 0.075 : 0.075 × 0.925
= 1 : 1
66.1 : 13.9
The diastereomers were separable by SiO2 chromatography.
Enantiomeric purity of (2S,6R,8S) - 249 = (92.5² - 7.5²) / (92.5² + 7.5²) × 100 = 98.7%
START 85% e.e.
GOAL 98.7% e.e.
(FOUND: 97.2 ~ 99.3%)

Scheme 970



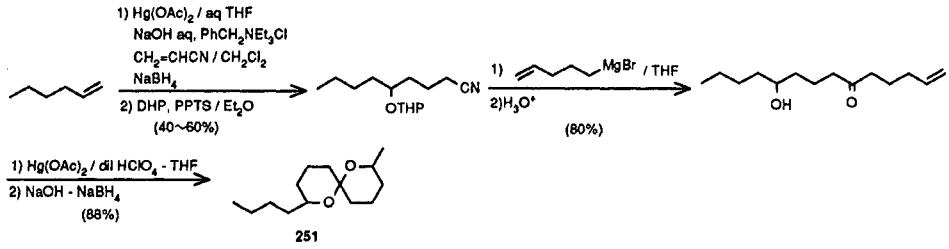
Scheme 971



Scheme 972

K. 2-Butyl-8-methyl-1,7-dioxaspiro[5.5]undecane 251 ($C_{14}H_{26}O_2$)

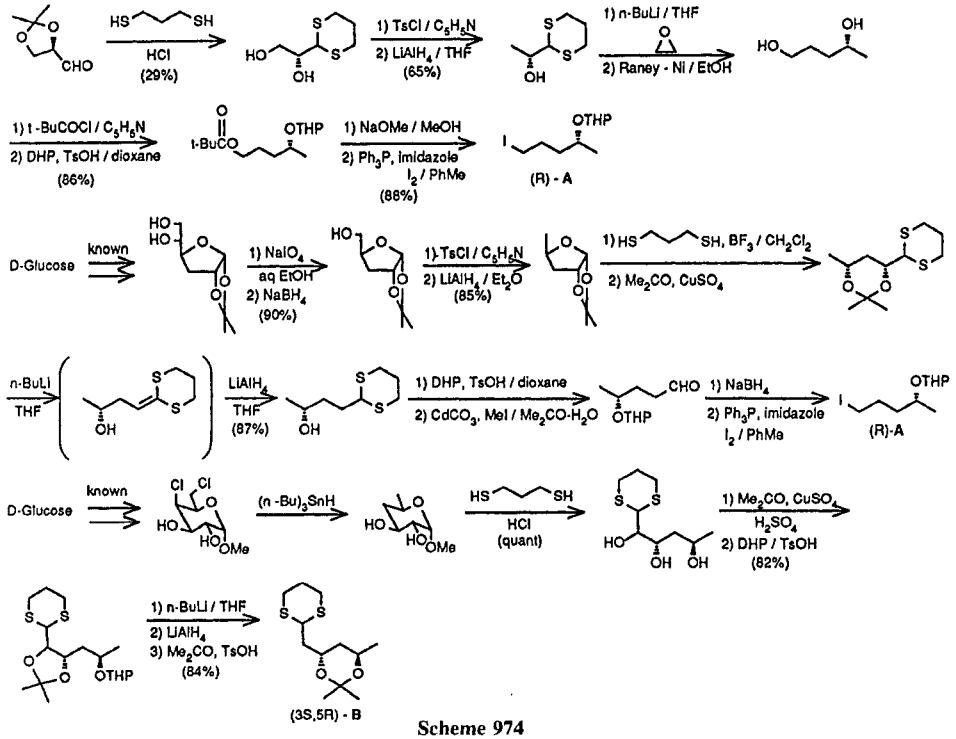
This unusual even-carbon membered spiroacetal was found as a minor component of the rectal gland secretion of the fruit fly species (*D. latifrons*) found in Southeast Asia and Hawaii.[1175] O'Shea and Kitching synthesized **251** by the oxymercuration-cyclization route (Scheme 973).[512]



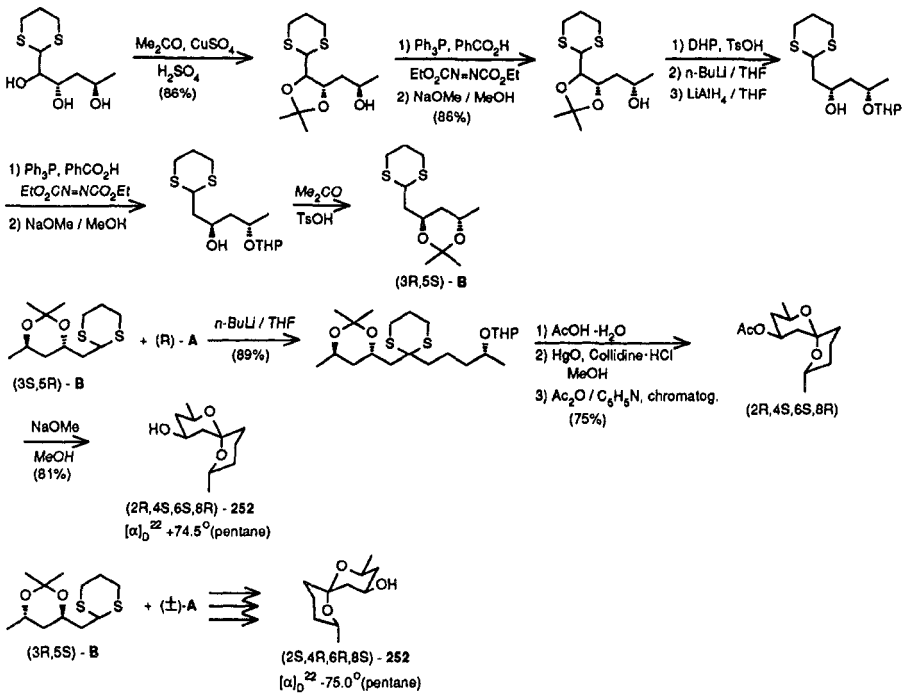
Scheme 973

L. 2,8-Dimethyl-1,7-dioxaspiro[5.5]undecan-4-ol 252 ($C_{11}H_{20}O_3$)

This is a minor component of the mandibular gland secretion of *Andrena wilkella*.[1172] The absolute configuration of the natural product has not yet been determined. Both (2*R*,4*S*,6*S*,8*R*)-**252** and its antipode were synthesized starting from chiral building blocks of carbohydrate origin by Redlich and Schneider (Scheme 974).[1206] Coupling of the building blocks **A** with **B**[1207] yielded the enantiomers of **252.** This synthesis is selective, but lengthy.



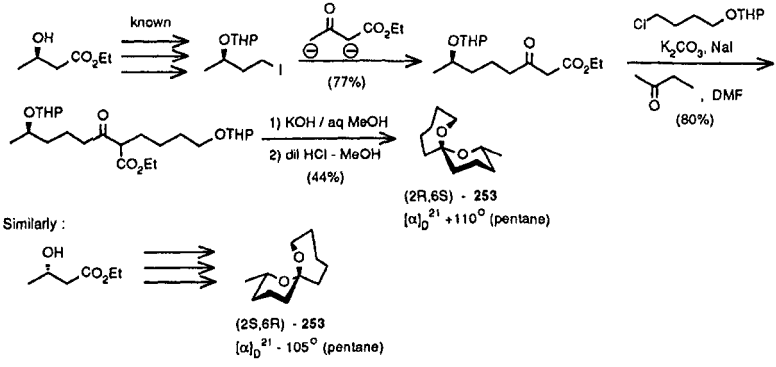
Scheme 974



Scheme 974 (*Continued*)

M. 2-Methyl-1,7-dioxaspiro[5.6]dodecane 253 ($C_{11}H_{20}O_2$)

This is a component of the volatile secretion from the mandibular glands of a bee (*Andrena haemorrhoa*).[1155] Both (2*R*,6*S*)-**253** and (2*S*,6*R*)-**253** were synthesized by Mori and Katsurada (Scheme 975), starting from the enantiomers



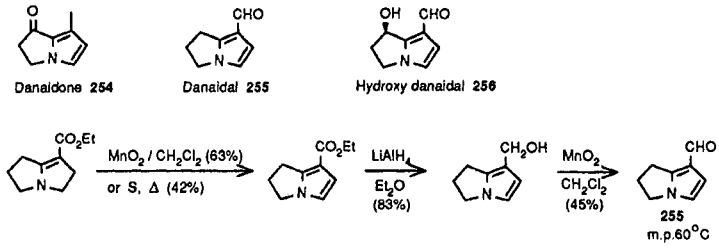
Scheme 975

of ethyl 3-hydroxybutanoate.[1208] Due to the oxygen anomeric effect, **253** was obtained as a single isomer.

22. NITROGEN HETEROCYCLES AND SULFUR-CONTAINING COMPOUNDS AS PHEROMONES

A. Danaidone (2,3-Dihydro-7-methyl-1H-pyrrolizin-1-one) 254 (C_8H_9ON), Danaidal (1-Formyl-6,7-dihydro-5H-pyrrolizine) 255 (C_8H_9ON), and Hydroxydanaidal (1-Formyl-6,7-dihydro-5H-pyrrolizin-7-ol) 256 ($C_8H_9O_2N$)

These are pheromones secreted by several male butterflies and moths such as the African monarch (*Danaus chrysippus*), the queen butterfly (*D. gilippus berenice*), *Creatonotos gangis*, and *C. transiens* (Scheme 976).[1209,1210] They are biosynthesized from pyrrolizine alkaloids in plants ingested by them.[1209,1210] A synthesis of danaidal **255** was reported by Röder et al. (Scheme 976).[1211] An



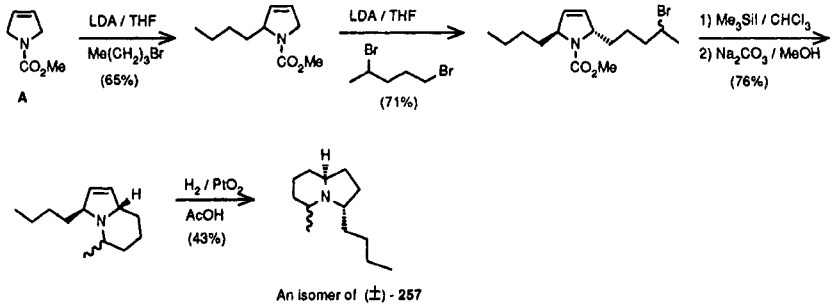
Scheme 976

Arctiid moth (*Cisseps fulvicollis*) was attracted by both (*R*)-**256** and (*S*)-**256.**[1212] *Cisseps*, *Ctenucha*, and *Halysidota* moths were all attracted by both the enantiomers of **256,** the (*S*)-isomer having been the more attractive.[1212]

B. (3*R*,5*S*,9*S*)-Monomorine I (5-Methyl-3-butyloctahydroindolizine) 257 ($C_{13}H_{25}N$)

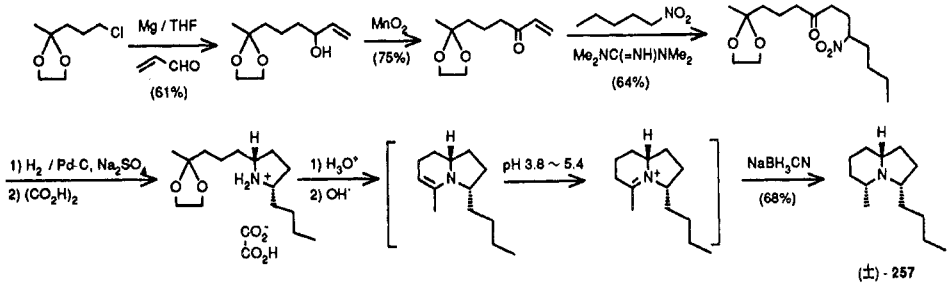
This is a trail pheromone of the Pharaoh's ant (*Monomorium pharaonis*).[1213] The natural (+)-**257** was shown to possess the 3*R*,5*S*,9*S*-configuration by the synthesis of (3*S*,5*R*,9*R*)-(−)-**257** by Royer and Husson.[1214]

Macdonald synthesized an isomer of **257** starting from pyrroline urethane **A** (Scheme 977).[1215] A biomimetic synthesis by Stevens and Lee yielded (±)-**257**



Scheme 977

stereoselectively (Scheme 978).[1216] Kibayashi and his co-workers synthesized

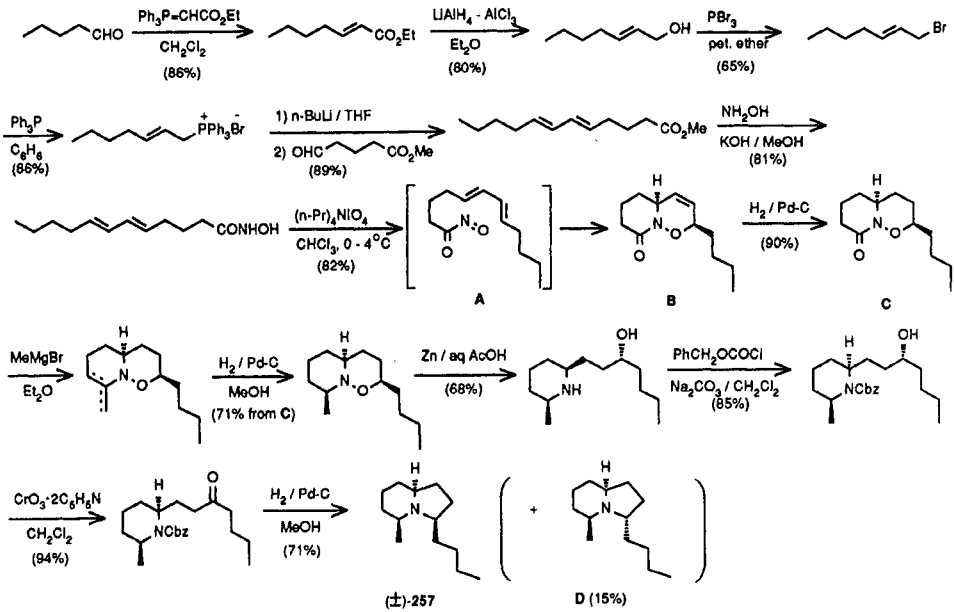


Scheme 978

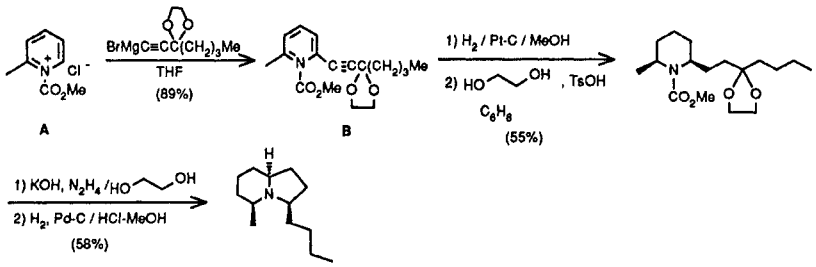
(±)-**257** by intramolecular nitroso-Diels-Alder reaction (**A** → **B**) (Scheme 979).[1217,1218] Their final step was unfortunately not selective, and the epimer **D** was also obtained as the minor product.

A short synthesis of (±)-**257** was reported by Kawanishi and his co-workers by using their highly regioselective α-alkynylation reaction of 1-methoxycarbonyl-2-methylpyridinium chloride with a Grignard reagent (**A** → **B**) as shown in Scheme 980.[1219] Another short synthesis by Jefford et al. delivered (±)-**257** in only six steps in an overall yield of 26% (Scheme 981).[1220] The key features were the regiospecific one-step assembly of the ring system from a suitably substituted pyrrole and its subsequent reduction to all-*cis*-substituted octahydroindolizine intermediate.

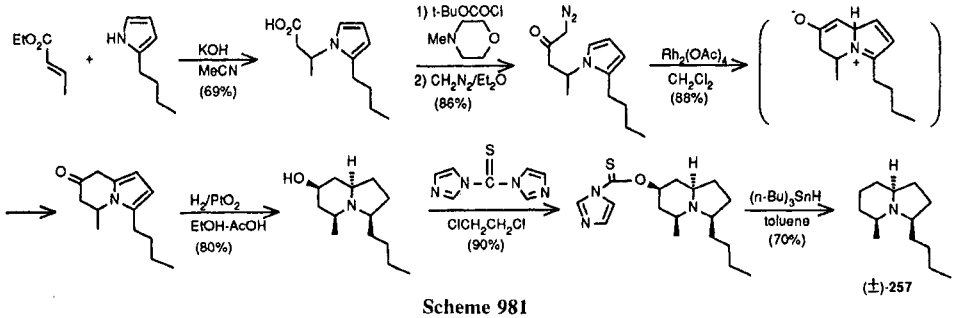
The first enantioselective synthesis of the antipode [(3*S*,5*R*,9*R*)-(-)-**257**] of monomorine I was reported by Royer and Husson (Scheme 982).[1214] They used (*R*)-(-)-phenylglycinol as the chiral building block. The natural (+)-monomorine I **257** was synthesized from diethyl L-(+)-tartrate by Yamazaki and Kibayashi as shown in Scheme 983.[1221]



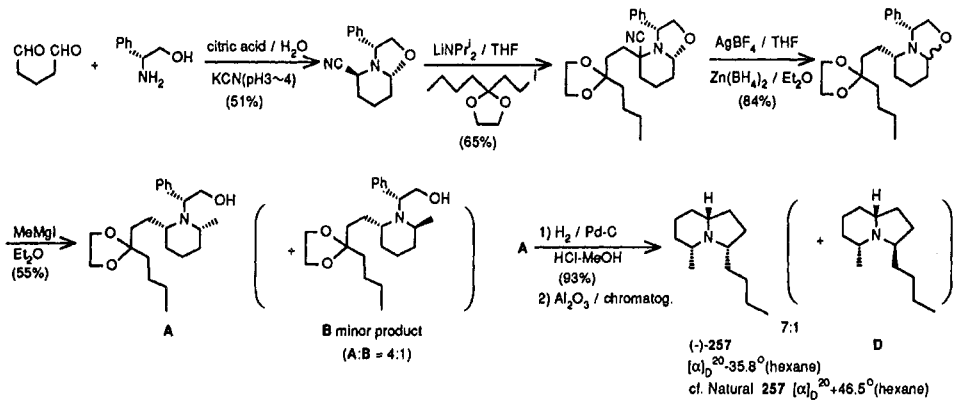
Scheme 979



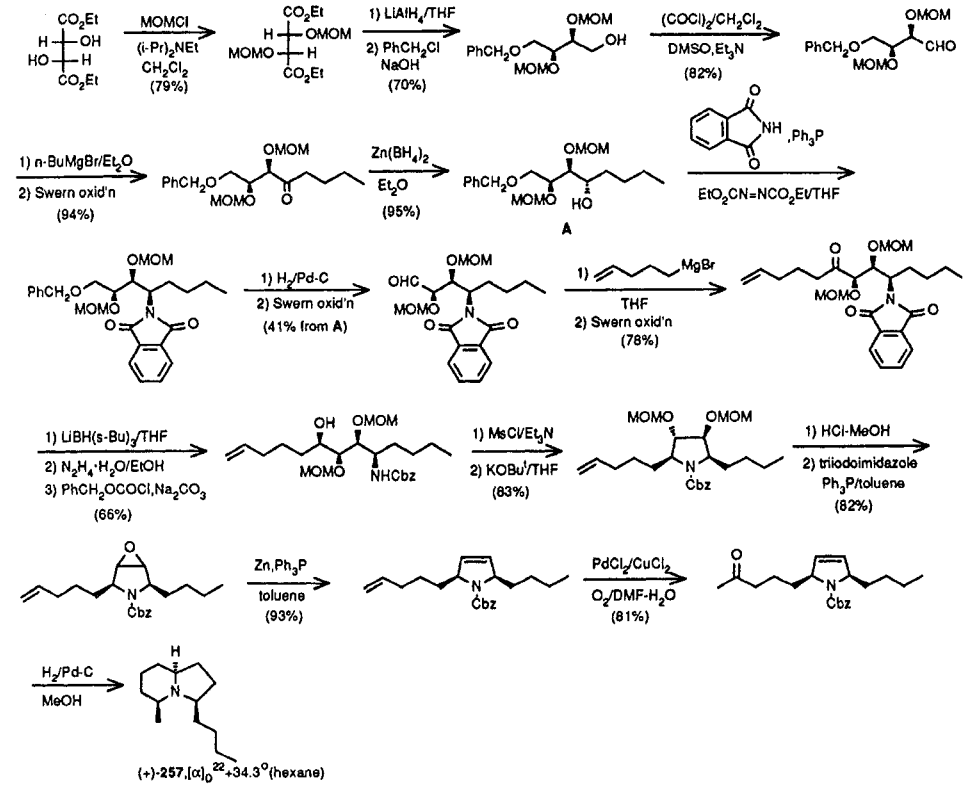
Scheme 980



Scheme 981



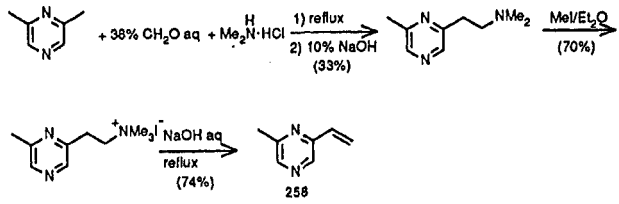
Scheme 982



Scheme 983

C. 2-Methyl-6-vinylpyrazine 258 ($C_7H_8N_2$)

This is the male-produced sex pheromone of the papaya fruit fly, *Toxotrypana curvicauda*.[1222] Chuman et al. synthesized **258** as shown in Scheme 984, start-

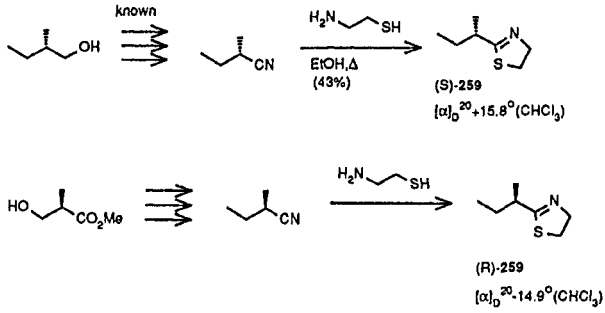


Scheme 984

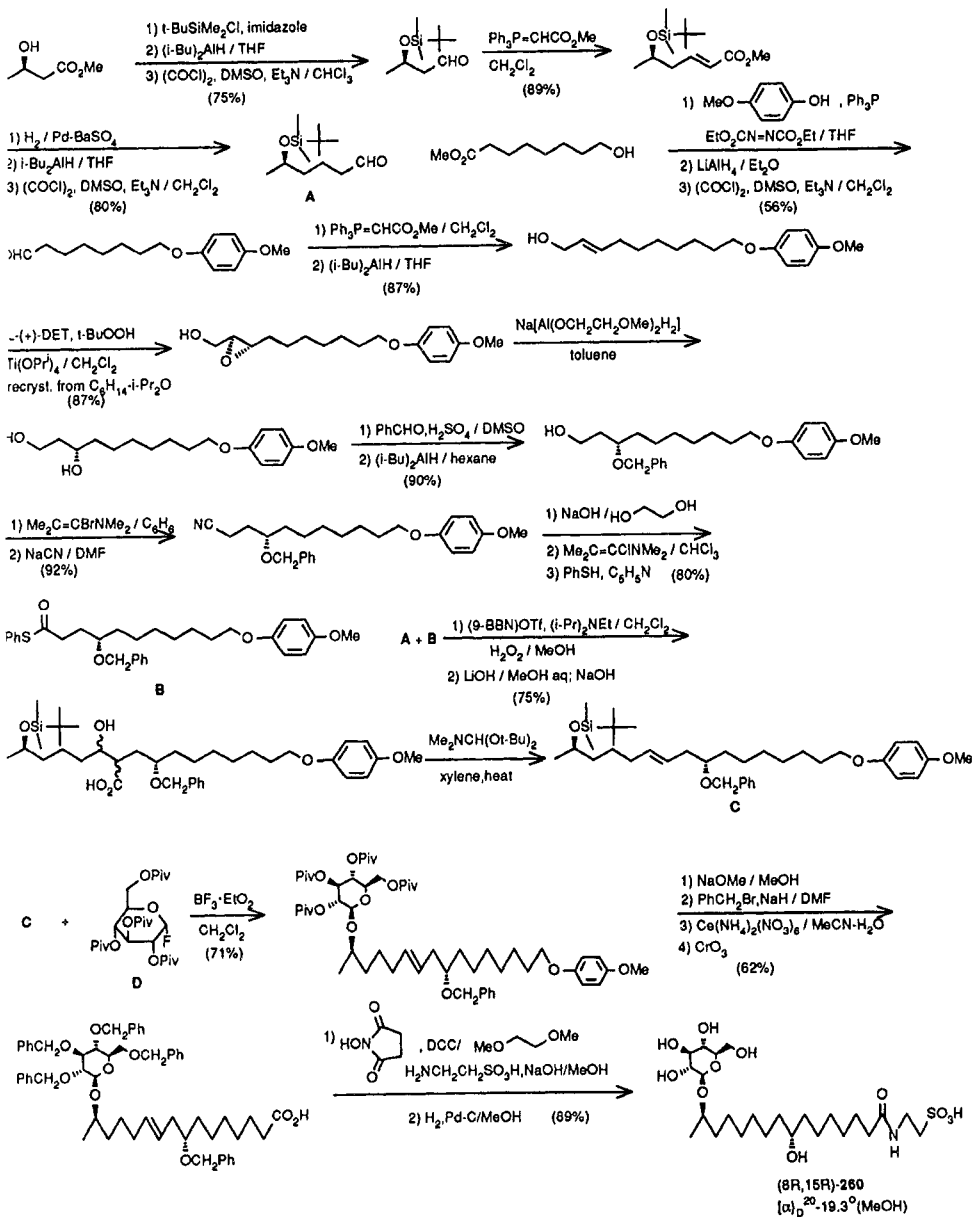
ing from 2,6-dimethylpyrazine.[1222] It should be added that 2,5-dimethylpyrazine and 3-ethyl-2,5-dimethyl-pyrazine were identified as trail pheromones of ants.[1223]

D. 2-sec-Butyl-4,5-dihydrothiazole 259 ($C_7H_{13}NS$)

In combination with *exo*-7-ethyl-6,8-dioxabicyclo[3.2.1]oct-3-ene **233**, this functions as a chemical signal of the male state and a potential multi-purpose pheromone of the house mouse (*Mus musculus*).[1078] Both the enantiomers of **259** were synthesized by Masaki et al. (Scheme 985).[1224] The absolute configuration of the natural compound has yet to be established.



Scheme 985


1) t-BuSiMe2Cl, imidazole
2) (i-Bu)2AlH / THF
3) (COCl)2, DMSO, Et3N / CHCl3
(75%)
Ph3P=CHCO2Me
CH2Cl2
(89%)
1) MeO-C6H4-OH, Ph3P
EtO2CN=NCO2Et / THF
2) LiAlH4 / Et2O
3) (COCl)2, DMSO, Et3N / CH2Cl2
(56%)
1) H2 / Pd-BaSO4
2) i-Bu2AlH / THF
3) (COCl)2, DMSO, Et3N / CH2Cl2
(80%)
A
1) Ph3P=CHCO2Me / CH2Cl2
2) (i-Bu)2AlH / THF
(87%)
(+)-DET, t-BuOOH
Ti(OPr-i)4 / CH2Cl2
recryst. from C6H14-i-Pr2O
(87%)
Na[Al(OCH2CH2OMe)2H2]
toluene
1) PhCHO, H2SO4 / DMSO
2) (i-Bu)2AlH / hexane
(90%)
1) Me2C=CBrNMe2 / C6H6
2) NaCN / DMF
(92%)
1) NaOH / HO-CH2CH2-OH
2) Me2C=CClNMe2 / CHCl3
3) PhSH, C5H5N (80%)
B
A + B
1) (9-BBN)OTf, (i-Pr)2NEt / CH2Cl2
H2O2 / MeOH
2) LiOH / MeOH aq; NaOH
(75%)
Me2NCH(Ot-Bu)2
xylene, heat
C
BF3·EtO2
CH2Cl2
(71%)
D
1) NaOMe / MeOH
2) PhCH2Br, NaH / DMF
3) Ce(NH4)2(NO3)6 / MeCN-H2O
4) CrO3
(62%)
1) DCC / MeO-CH2CH2-OMe
H2NCH2CH2SO3H, NaOH/MeOH
2) H2, Pd-C/MeOH (69%)
(8R,15R)-260
[α]D20 -19.3° (MeOH)

Scheme 986

E. (15*R*)-2-{[15-(β-D-Glucopyranosyl)oxy]-8-hydroxyhexadecanoyl]amino}ethanesulfonic Acid 260 ($C_{24}H_{47}O_{11}NS$)

This is the oviposition-deterring pheromone secreted by females of the European cherry fruit fly (*Rhagoletis cerasi*), each of which lays one single egg into half-ripe cherries.[1225] Ernst and Wagner synthesized the four stereoisomers: (8*R*,15*R*)-, (8*S*,15*R*)-, (8*R*,15*S*)-, and (8*S*,15*S*)-**260.**[1226] By comparing the ^{1}H-NMR spectra of the synthetic four isomers with that of the natural **260,** the configuration at C-15 was determined as *R*. Scheme 986 illustrates the synthesis of (8*R*,15*R*)-**260.**[1226] Other isomers were prepared in the same manner.

23. CONCLUSION

The synthesis of 260 pheromones (in Ref. 1, 96 pheromones were discussed) have been reviewed in this book. The survey of literature encompasses the period April 1979 to the end of February 1990. If I have overlooked any works, I apologize to any chemists in this area whose research and work have been inadvertently omitted.

The most notable advance achieved in this decade has been a clearer understanding of the significance of chirality in pheromone perception. Scheme 987 summarizes the results obtained thus far. As can be seen from the Scheme, stereochemistry-pheromone activity relationships are quite complicated.

Like other bioactive and chiral natural products, many of the chiral pheromones belong to category **A** of Scheme 987. In this group of pheromones, only one enantiomer is bioactive and no inhibitory action can be observed with the inactive antipode. However, other unusual cases exist, as shown in categories **B** through **H.**

In group **B,** only one enantiomer is bioactive and the inactive antipode inhibits the action of the correct enantiomer. Especially in the case of the Japanese beetle pheromone as studied by Tumlinson, its racemate lacks biological activity due to the strong inhibition caused by the wrong enantiomer.

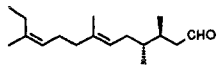
In the case of the pheromones in group **C,** insects do not distinguish the stereoisomers. Thus, every stereoisomer of the German cockroach pheromone evokes the response of the male.

Ipsdienol is the pheromone belonging to group **D.** Different species of *Ips* bark beetles use different enantiomers, and the chirality of the pheromone is quite important in establishing and maintaining a particular *Ips* species.

Sulcatol is the pheromone in Group **E,** which requires both enantiomers for pheromone activity, as exemplified by the ambrosia beetle (*Gnathotrichus sulcatus*).

A. Only one enantiomer is bioactive, and the antipode does not inhibit the action of the pheromone.

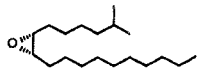
western pine beetle (exo-brevicomin)



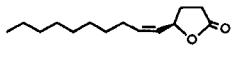
pharaoh's ant (faranal)

etc.

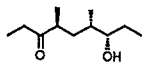
B. Only one enantiomer is bioactive, but the antipode or diastereomer inhibits the action of the pheromone.



gypsy moth (disparlure)



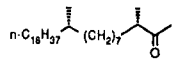
Japanese beetle



cigarette beetle (sericomin)

etc.

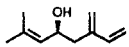
C. All the stereoisomers are bioactive.



German cockroach

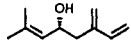
etc.

D. Even in the same genus different species use different enantiomers.



Ips paraconfusus

[(+)-ipsdienol]



Ips calligraphus

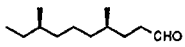
[(-)-ipsdienol]

E. Both the enantiomers are required for bioactivity.

Gnathotrichus sulcatus

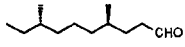
[(+)-sulcatol] [(-)-sulcatol]

F. Only one enantiomer is as active as the natural pheromone, but its activity can be enhanced by the addition of a less active stereoisomer.



(natural pheromone)

red flour beetle



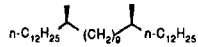
(unnatural and less active)

G. One enantiomer is active on male insects, while the other is active on females.

(R) ♂ (S) ♀

olive fruit fly

H. Only the meso-isomer is active.



tsetse fly (Glossina pallidipes)

etc.

Scheme 987

Groups **F, G,** and **H** are also interesting, especially in the case of the olive fruit fly pheromone, whose *R*-isomer is active on males, while the other is active on females. Only the *meso*-isomer of the tsetse fly pheromone was bioactive.

As summarized above, the relationships between stereochemistry and pheromone activity are complicated. The precise meaning of this diversity may be clarified only after more extensive investigation of the nature of pheromone perception by insects.

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REFERENCES

1. Mori, K. In *The Total Synthesis of Natural Products*, ApSimon, J., Ed., John Wiley: New York, 1981, Vol. 4.
2. Hummel, H. E.; Miller, T. A. Ed., *Techniques in Pheromone Research*, Springer-Verlag: New York, 1984.
3. Mori, K. *Tetrahedron.* **1989,** *45,* 3233.
4. Prestwich, G. D.; Blomquist, G. J., Ed., *Pheromone Biochemistry*, Academic Press: Orlando, 1987.
5. Brand, J. M.; Young, J. C.; Silverstein, R. M. In *Progress in the Chemistry of Organic Natural Products*, Herz, W.; Griesebach, H. and Kirby, G. W., Ed., Springer-Verlag: Vienna, 1979, Vol. 37.
6. Bestmann, H. J.; Vostrowsky, O. In *Chemie der Pflanzenschutz- und Schädlingsbekämpfungsmittel*, Wegler, R., Ed., Springer-Verlag: Berlin, 1980, Band 6.
7. Bestmann, H. J.; Vostrowsky, O. *Seifen, Öle, Fette, Wachse,* **1988,** *114,* 612.
8. Ritter, F. J. In *Stereoselectivity of Pesticides; Biological and Chemical Problems*, Ariëns, E. J., van Rensen, J. J. S., and Welling, W., Ed., Elsevier: Amsterdam, 1988.
9. Ritter, F. J. *Agriculture, Ecosystems and Environment.* **1988,** *21,* 3.
10. Körblová, E.; Romaňuk, M. *Chem. Listy.* **1987,** *81,* 819.
11. Schneider, D. In *Foundations of Sensory Science*, Dawson, W. W., and Enoch, J. M., Ed., Springer-Verlag: Berlin, 1984.
12. Attygalle, A. B.; Morgan, E. D. *Angew. Chem., Int. Ed. Engl.* **1988,** *27,* 460.
13. Baker, R.; Evans, D. A. *Chem. Brit.* **1980,** *16,* 412.
14. Silverstein, R. M. *Science.* **1981,** *213,* 1326.
15. Silverstein, R. M. *Pure Appl. Chem.* **1982,** *54,* 2479.
16. Baker, R.; Herbert, R. H. *Natural Products Report.* **1984,** 299.
17. Moiseenkov, A. M.; Levedeva, K. V.; Cheskus, V. A. *Usp. Khim.* **1984,** *53,* 1709.
18. Silverstein, R. M. *J. Chem. Ecol.* **1988,** *14,* 1981.
19. Prestwich, G. D. *Science.* **1987,** *237,* 999.
20. Chong, J. M.; Wong, S. *Tetrahedron Lett.* **1986,** *27,* 5445.
21. Bengtsson, M.; Liljefors, T. *Synthesis.* **1988,** 250.
22. LeBigot, Y.; Delmas, M.; Gaset, A. *J. Agric. Food Chem.* **1983,** *31,* 1096.
23. Bestmann, H. J.; Vostrowsky, O. *Chem. Phys. Lipid.* **1979,** *24,* 335.
24. Seidel, W.; Schäfer, H. J. *Chem. Ber.* **1980,** *113,* 3898.
25. Sonnet, P. E. *Tetrahedron.* **1980,** *36,* 557.
26. Sonnet, P. E. *J. Org. Chem.* **1980,** *45,* 154.
27. Doolittle, R. E. *Synthesis.* **1984,** 730.

28. Aksenov, V. S.; Khushvakhtova, S.; Vakher, P. L.; Parismoa, R.; Numanov, I. U.; Shadrina, I. V. *Dokl. Akad. Nauk Tadzh. S.S.R.* **1986,** *29,* 602; *Chem. Abstr.* **1987,** *107,* 236026s.
29. Kang, S.-K.; Kim, W.-S.; Moon, B.-H. *Synthesis.* **1985,** 1161.
30. Babler, J. H.; Coghlan, M. J. *Tetrahedron Lett.* **1979,** 1971.
31. McDougal, P. G.; Rico, J. G.; Oh, Y.-I.; Condor, B. D. *J. Org. Chem.* **1986,** *51,* 3388.
32. Chan, T.-H.; Huang, W.-Q. *J. Chem. Soc., Chem. Commun.* **1985,** 909.
33. Gardette, M.; Alexakis, A.; Normant, J. F. *Tetrahedron.* **1985,** *41,* 5887.
34. Alexakis, A.; Gardette, M.; Colin, S. *Tetrahedron Lett.* **1988,** *29,* 2951.
35. Ref. 1, p. 14, Eq. 33.
36. Scheffold, R.; Abrecht, S.; Orlinski, R.; Ruf, H.-R.; Stamouli, P.; Tinembart, O.; Walder, L.; Weymuth, C. *Pure Appl. Chem.* **1987,** *59,* 363.
37. Alexakis, A. *L'Actualité Chimique.* **1987,** 203.
38. Matteson, D. S. *Chem. Rev.* **1989,** *89,* 1535.
39. Matteson, D. S. *Tetrahedron.* **1989,** *45,* 1859.
40. Hanessian, S.; Thavonekham, B.; DeHoff, B. *J. Org. Chem.* **1989,** *54,* 5831.
41. Trost, B. M.; Braslan, R. *Tetrahedron Lett.* **1989,** *30,* 4657.
42. Ando, T.; Hasegawa, Y.; Uchiyama, M. *Agric. Biol. Chem.* **1986,** *50,* 2935.
43. Rossi, R.; Carpita, A.; Quirici, M. G.; Veracini, C. A. *Tetrahedron.* **1982,** *38,* 639.
44. Ando, T.; Kusa, K.; Uchiyama, M.; Yoshida, S.; Takahashi, N. *Agric. Biol. Chem.* **1983,** *47,* 2849.
45. Mori, K. in Ref. 2, Chapter 12.
46. Slessor, K. N.; King, G. G. S.; Miller, D. R.; Winston, M. L.; Cutforth, T. L. *J. Chem. Ecol.* **1985,** *11,* 1659.
47. Naoshima, Y.; Yamamoto, T.; Wakabayashi, S.; Hayashi, S. *Agric. Biol. Chem.* **1980,** *44,* 2231.
48. Dasaradhi, L.; Bhalerao, U. T. *Synth. Commun.* **1987,** *17,* 1845.
49. Francke, W.; Francke, S.; Tóth, M.; Szöcs, G.; Guerin, P.; Arn, H. *Naturwissenschaften.* **1987,** *74,* 143.
50. Tóth, M.; Helmchen, G.; Leikauf, U.; Sziráki, G.; Szöcs, G. *J. Chem. Ecol.* **1989,** *15,* 1535 [Synthetic details are not reported].
51. Rama, F.; Capuzzi, L. *Synth. Commun.* **1989,** *19,* 1051.
52. Carrière, Y.; Millar, J. G.; McNeil, J. N.; Miller, D.; Underhill, E. W. *J. Chem. Ecol.* **1988,** *14,* 947.
53. Naoshima, Y.; Mukaidani, H. *J. Chem. Ecol.* **1987,** *13,* 325.
54. Sonnet, P. E. *J. Chem. Ecol.* **1984,** *10,* 771.
55. Carlson, D. A.; Nelson, D. R.; Langley, P. A.; Coates, T. W.; Davis, T. L.; Laegwatervan der Linden, M. E. *J. Chem. Ecol.* **1984,** *10,* 429.
56. Kuwahara, S.; Mori, K. *Agric. Biol. Chem.* **1983,** *47,* 2599.
57. McDowell, P. G.; Hassanali, A.; Dransfield, R. *Physiol. Entomol.* **1985,** *10,* 183.
58. Ade, E.; Helmchen, G.; Heiligenmann, G. *Tetrahedron Lett.* **1980,** *21,* 1137.
59. Coates, T. W.; Langley, P. A. *Overseas Development Administration and University of Bristol, Tsetse Research Lab., Annual Report,* **1980** pp. 20–21.
60. Hoshino, C.; Mori, K. *Agric. Biol. Chem.* **1980,** *44,* 3007.
61. Naoshima, Y.; Mukaidani, H.; Shibayama, S.; Murata, T. *J. Chem. Ecol.* **1986,** *12,* 127.

62. Sugie, H.; Tamaki, Y.; Sato, R.; Kumakura, M. *Appl. Entomol. Zool.* **1984,** *19,* 323.
63. Manabe, Y.; Minamikawa, J.; Otsubo, J.; Tamaki, Y. *Agric. Biol. Chem.* **1985,** *49,* 1205.
64. Yamamoto, A.; Fukumoto, T. *Agric. Biol. Chem.* **1989,** *53,* 1183.
65. Kato, M.; Mori, K. *Agric. Biol. Chem.* **1985,** *49,* 2479.
66. Mori, K.; Kato, M. *Liebigs Ann. Chem.* **1985,** 2083.
67. Sato, R.; Abe, N.; Sugie, H.; Kato, M.; Mori, K.; Tamaki, Y. *Appl. Entomol. Zool.* **1986,** *21,* 478.
68. Sonnet, P. E.; Proveaux, A. T.; Adamek, E.; Sugie, H.; Sato, R.; Tamaki, Y. *J. Chem. Ecol.* **1987,** *13,* 547.
69. Nguyen Cong Hao, Mavrov, M. V.; Serebryakov, E. P. *Bioorg. Khim,* **1988,** *14,* 250.
70. Buss, A. D.; Warren, S. *J. Chem. Soc., Chem. Commun.* **1981,** 100.
71. Buss, A. D.; Greeves, N.; Levin, D.; Wallace, P.; Warren, S. *Tetrahedron Lett.* **1984,** *25,* 357.
72. Ratovelomanana, V.; Linstrumelle, G. *Synth. Commun.* **1984,** *14,* 179.
73. Brown, H. C.; Basavaiah, D.; Singh, S. M. *Synthesis,* **1984,** 920.
74. Brown, H. C.; Basavaiah, D.; Kulkarni, S. U.; Lee, H. D.; Negishi, E.; Katz, J.-J. *J. Org. Chem.* **1986,** *51,* 5270.
75. Brown, H. C.; Lee, H. D.; Kulkarni, S. U. *J. Org. Chem.* **1986,** *51,* 5282.
76. Brown, H. C.; Basavaiah, D.; Singh, S. M.; Bhat, N. G. *J. Org. Chem.* **1988,** *53,* 246.
77. Martinez, A. G.; Oliver Ruiz, M. *Synthesis.* **1983,** 663.
78. Sato, F.; Watanabe, H.; Tanaka, Y.; Yamaji, T.; Sato, M. *Tetrahedron Lett.* **1983,** *24,* 1041.
79. Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *J. Chem. Soc., Perkin Trans. 1.* **1985,** 1115.
80. Rossi, R.; Carpita, A. *Tetrahedron Lett.* **1986,** *27,* 2529.
81. Vig, O. P.; Sharma, M. L.; Verma, N. K.; Malik, N. *Indian J. Chem.* **1981,** *20B,* 860.
82. Mithran, S.; Mandapur, V. R. *Chem. and Ind.* **1986,** 711.
83. Schlosser, M.; Tuong, H. B.; Schaub, B. *Tetrahedron Lett.* **1985,** *26,* 311.
84. Canevet, C.; Röder, T.; Vostrowsky, O.; Bestmann, H. J. *Chem. Ber.* **1980,** *113,* 1115.
85. Baker, R.; Herbert, R. H.; Neequaye, N. N.; Rao, K. N. *J. Chem. Ecol.* **1985,** *11,* 989.
86. Chan, T. H.; Koumaglo, K. *Tetrahedron Lett.* **1986,** *27,* 883.
87. Kang, S.-K.; Ku, M.-S.; No, K.; Lee, J.-O. *J. Korean Chem. Soc.* **1987,** *31,* 576.
88. Basavaiah, D. *Heterocycles.* **1982,** *18,* 153.
89. Kang, S.-K.; Park, J.-M.; Huang, K.-L.; Lee, J.-U.; Goh, H.-G. *Bull. Korean Chem. Soc.* **1985,** *6,* 15.
90. Sonderquist, J. A.; Anderson, C. L. *Tetrahedron Lett.* **1988,** *29,* 2777.
91. Naoshima, Y.; Ozawa, H.; Takenami, Y.; Wakabayashi, S.; Hayashi, S. *Agric. Biol. Chem.* **1981,** *45,* 1723.
92. Yadav, J. S.; Reddy, P. S. *Tetrahedron Lett.* **1984,** *25,* 4025.
93. Yadav, J. S.; Reddy, P. S.; Joshi, B. V. *Tetrahedron.* **1988,** *44,* 7243.
94. Moiseenkov, A. M.; Schaub, B.; Margot, C.; Schlosser, M. *Tetrahedron Lett.* **1985,** *26,* 305.
95. Brown, H. C.; Basavaiah, D. *J. Org. Chem.* **1982,** *47,* 3806.

96. Brown, H. C.; Basavaiah, D.; Kulkarni, S. U.; Bhat, N. G.; Vera Prasad, J. V. N. *J. Org. Chem.* **1988,** *53,* 239.
97. Brown, H. C.; Molander, G. A. *J. Org. Chem.* **1986,** *51,* 4512.
98. Brown, H. C.; Wang, K. K. *J. Org. Chem.* **1986,** *51,* 4514.
99. Koumaglo, K.; Chan, T. H. *Tetrahedron Lett.* **1984,** *25,* 717.
100. Odinokov, V. N.; Tolstikov, G. A.; Galeyeva, R. I.; Kargapoltseva, T. A. *Tetrahedron Lett.* **1982,** *23,* 1371.
101. Subramanian, G. B. V.; Michael, G. *Chem. and Ind.* **1986,** 749.
102. Subramanian, G. B. V.; Mehrotra, A.; Mehrotra, K. *Tetrahedron.* **1986,** *42,* 3967.
103. Kelkar, S. V.; Joshi, G. S.; Reddy, G. B.; Kulkarni, G. H. *Synth. Commun.* **1989,** *19,* 1369.
104. Olsson, A.-M.; Jönsson, J. Å; Thelin, B.; Liljefors, T. *J. Chem. Ecol.* **1983,** *9,* 375.
105. Liljefors, T.; Thelin, B.; van der Pers, J. N. C.; Löfstedt, C. *J. Chem. Soc., Perkin Trans. 2.* **1985,** 1957.
106. Liljefors, T.; Bengtsson, M.; Hansson, B. S. *J. Chem. Ecol.* **1987,** *13,* 2023.
107. Bestmann, H. J.; Koschatsky, K. H.; Vostrowsky, O. *Chem. Ber.* **1979,** *112,* 1923.
108. Horiike, M.; Hirano, C. *Agric. Biol. Chem.* **1980,** *44,* 2229.
109. Basavaiah, D.; Brown, H. C. *J. Org. Chem.* **1982,** *47,* 1792.
110. Chattopadhyay, A.; Mandapur, V. R.; Chadha, M. S., *Indian J. Chem.* **1983,** *22B,* 158.
111. Liljefors, T.; Thelin, B.; van der Pers, J. N. C. *J. Chem. Ecol.* **1984,** *10,* 1661.
112. Aukrust, A.; Rongved, P.; Skattebøl, L. *Acta Chem. Scand.* **1985,** *B39,* 267.
113. Julia, M.; Stacino, J.-P. *Tetrahedron.* **1986,** *42,* 2469.
114. Kang, S.-K.; Ahn, S. S.; Kim, J. H.; Lee, J.-O. *J. Korean Chem. Soc.* **1988,** *32,* 65.
115. Cahiez, G.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1980,** *21,* 1433.
116. Savoia, D.; Tagliavini, E.; Trombini, C.; Umani-Ronchi, A. *J. Org. Chem.* **1980,** *45,* 3227.
117. Michelot, D. *Synthesis,* **1983,** 130.
118. Bestmann, H. J.; Brosche, T.; Koschatzky, K. H.; Michaelis, K.; Platz, H.; Vostrowsky, O.; Knauf, W. *Tetrahedron Lett.* **1980,** *21,* 747.
119. Foster, S. P.; Clearwater, J. R.; Muggleston, S. J. *J. Chem. Ecol.* **1989,** *15,* 457.
120. Brown, H. C.; Basavaiah, D.; Bhat, N. G. *J. Org. Chem.* **1986,** *51,* 4518.
121. Schaub, B.; Blaser, G.; Schlosser, M. *Tetrahedron Lett.* **1985,** *26,* 307.
122. Subramanian, G. B. V.; Sharma, R. *Synth. Commun.* **1989,** *19,* 1197.
123. Mitra, R. B.; Reddy, G. B. *Synthesis.* **1989,** 694.
124. Sugie, H.; Tamaki, Y.; Kawasaki, K.; Wakou, M.; Oku, T.; Hirano, C.; Horiike, M. *Appl. Entomol. Zool.* **1986,** *21,* 578.
125. Horiike, M.; Tanouchi, M.; Hirano, C. *Agric. Biol. Chem.* **1980,** *44,* 257.
126. Kang, J.-K.; Lee, C.-H.; Kim, J. H.; Lee, J.-O. *J. Korean Chem. Soc.* **1988,** *32,* 60.
127. Tolstikov, G. A.; Odinokov, V. N.; Galeeva, R. I.; Bakeeva, R. S.; Akhunova, V. R. *Tetrahedron Lett.* **1979,**4851.
128. Shaner, A. M.; Jackson, L. L.; Graham, K. J.; Leu, R. D. *J. Chem. Ecol.* **1989,** *15,* 265.
129. Bestmann, H. J.; Süss, J.; Vostrowsky, O. *Liebigs Ann. Chem.* **1981,** 2117.
130. Ando, T.; Vu, M. H.; Yoshida, S.; Takahashi, N. *Agric. Biol. Chem.* **1982,** *46,* 717.

131. Rossi, R.; Carpita, A. *Tetrahedron.* **1983,** *39,* 287.
132. Gardette, M.; Jabri, N.; Alexakis, A.; Normant, J. F. *Tetrahedron.* **1984,** *40,* 2741.
133. Trost, B. M.; Martin, S. J. *J. Am. Chem. Soc.* **1984,** *106,* 4263.
134. Brown, H. C.; Bhat, N. G.; Basavaiah, D. *Synthesis.* **1986,** 674.
135. Stille, J. K.; Groh, B. L. *J. Am. Chem. Soc.* **1987,** *109,* 813.
136. Stille, J. K.; Simpson, J. H. *J. Am. Chem. Soc.* **1987,** *109,* 2138.
137. Huang, Y.-Z.; Shi, L.; Yang, J.; Cai, Z. *J. Org. Chem.* **1987,** *52,* 3558.
138. Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L.; Rotunno, D. *Tetrahedron Lett.* **1989,** *30,* 243.
139. Dressaire, G.; Langlois, Y. *Tetrahedron Lett.* **1980,** *21,* 67.
140. Cassani, G.; Massardo, P.; Piccardi, P. *Tetrahedron Lett.* **1980,** *21,* 3497.
141. Cassani, G.; Massardo, P.; Piccardi, P. *Tetrahedron Lett.* **1979,** 633; Ref. 1, p. 33.
142. Ratovelomanana, V.; Linstrumelle, G. *Tetrahedron Lett.* **1981,** *22,* 315.
143. Rossi, R.; Carpita, A.; Quirici, M. G. *Tetrahedron.* **1981,** *37,* 2617.
144. Cassani, G.; Massardo, P.; Piccardi, P. *Tetrahedron Lett.* **1983,** *24,* 2513.
145. Descoins, C.; Lettere, M.; Linstrumelle, G.; Michelot, D.; Ratovelomanana, V. *Synth. Commun.* **1984,** *14,* 761.
146. Alexakis, A.; Jachiet, D. *Tetrahedron Lett.* **1988,** *29,* 217.
147. Alexakis, A.; Jachiet, D. *Tetrahedron.* **1989,** *45,* 381.
148. Alexakis, A.; Duffault, J. M. *Tetrahedron Lett.* **1988,** *29,* 6243.
149. Bestmann, H. J.; Süss, J.; Vostrowsky, O. *Tetrahedron Lett.* **1979,** 2467.
150. Ideses, R.; Klug, J. T.; Shani, A.; Gothilf, S.; Gurevitz, E. *J. Chem. Ecol.* **1982,** *8,*195.
151. Yamamoto, A.; Fukumoto, T. *Agric. Biol. Chem.* **1989,** *53,* 2521.
152. Cuvigny, T.; Hervé du Penhoat, C.; Julia, M. *Tetrahedron.* **1987,** *43,* 859.
153. Ideses, R.; Shani, A. *J. Chem. Ecol.* **1988,** *14,* 1657.
154. Babler, J. H.; Haack, R. A. *J. Org. Chem.* **1982,** *47,* 4801.
155. Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *Chem. Lett.* **1983,** 1003.
156. Yamada, S.; Ohsawa, H.; Suzuki, T.; Takayama, H. *J. Org. Chem.* **1986,** *51,* 4934.
157. Bloch, R.; Abecassis, J. *Tetrahedron Lett.* **1983,** *24,* 1247.
158. Hervé du Penhoat, C.; Julia, M. *Tetrahedron.* **1986,** *42,* 4807.
159. Sato, T.; Tsunekawa, H.; Kohama, H.; Fujisawa, T. *Chem. Lett.* **1986,** 1553.
160. Björkling, F.; Norin, T.; Unelius, R. *Synth. Commun.* **1985,** *15,* 463.
161. Ranganathan, S.; Kumar, R.; Maniktala, V. *Synth. Commun.* **1982,** *12,* 921.
162. Ranganathan, D.; Ranganathan, S.; Mehrotra, M. M. *Tetrahedron.* **1980,** *36,* 1869.
163. Snider, B. B.; Phillips, G. B. *J. Org. Chem.* **1983,** *48,* 464.
164. Ochiai, M.; Ukita, T.; Fujita, E. *Chem. Pharm. Bull.* **1983,** *31,* 1641.
165. Hayashi, T.; Yanagida, M.; Matsuda, Y.; Oishi, T. *Tetrahedron Lett.* **1983,** *24,* 2665.
166. Hsiao, C.-N.; Schechter, H. *Tetrahedron Lett.* **1984,** *25,* 1219.
167. Ishibashi, H.; Komatsu, H.; Maruyama, K.; Ikeda, M. *Tetrahedron Lett.* **1985,** *26,* 5791.
168. Sato, T.; Okura, S.; Otera, J.; Nozaki, H. *Tetrahedron Lett.* **1987,** *28,* 6299.
169. Yamamoto, Y.; Saito, Y.; Maruyama, K. *Tetrahedron Lett.* **1982,** *23,* 4597.
170. Knox, G. R.; Thom, I. G. *J. Chem. Soc., Chem. Commun.* **1981,** 373.

171. Rossi, R.; Carpita, A.; Gaudenzi, M. L. *Synthesis*, **1981,** 359.
172. Rossi, R.; Carpita, A.; Quirici, M. G.; Gaudenzi, M. L. *Tetrahedron.* **1982,** *38,* 631.
173. Camps, F.; Coll, J.; Fabrias, G.; Guerrero, A. *Tetrahedron.* **1984,** *40,* 2871.
174. Alcazar, A.; Camps, F.; Coll, J.; Fabrias, G.; Guerrero, A. *Synth. Commun.* **1985,** *15,* 819.
175. DeCodts, G.; Dressaire, G.; Langlois, Y. *Synthesis.* **1979,** 510.
176. Ratovelomana V.; Linstrumelle, G. *Synth. Commun.* **1981,** *11,* 917.
177. Björkling, F.; Norin, T.; Unelius, C. R.; Miller, R. B. *J. Org. Chem.* **1987,** *52,* 292.
178. Cuvigny, T.; Fabre, J. L.; Hervé, du Penhoat, C.; Julia, M. *Tetrahedron Lett.* **1983,** *24,* 4319.
179. Yadav, J. S.; Deshpande, P. K.; Reddy, E. R. *Synth. Commun.* **1989,** *19,* 125.
180. Commerçon, A.; Normant, J. F.; Villieras, J. *Tetrahedron.* **1980,** *36,* 1215.
181. Miller, J. A.; Zweifel, G. *J. Am. Chem. Soc.* **1983,** *105,* 1383.
182. Miyaura, N.; Suginome, H.; Suzuki, A. *Tetrahedron Lett.* **1983,** *24,* 1527.
183. Miyaura, N.; Suginome, H.; Suzuki, A. *Tetrahedron.* **1983,** *39,* 3271.
184. Brown, H. C.; Somayaji, V. *Synthesis.* **1984,** 919.
185. Miyaura, N.; Satoh, M.; Suzuki, A. *Tetrahedron Lett.* **1986,** *27,* 3745.
186. Trost, B. M.; Fortunak, J. M. *J. Am. Chem. Soc.* **1980,** *102,* 2841.
187. Ishibashi, H.; Komatsu, H.; Ikeda, M. *J. Chem. Res. (S).* **1987,** 296.
188. Kuroda, S.; Katsuki, T.; Yamaguchi, M.; *Tetrahedron Lett.* **1987,** *28,* 803.
189. Tsuboi, S.; Masuda, T.; Makino, H.; Takeda, A. *Tetrahedron Lett.* **1982,** *23,* 209.
190. Tsuboi, S.; Masuda, T.; Takeda, A. *J. Org. Chem.* **1982,** *47,* 4478.
191. Stille, J. K.; Simpson, J. H. *J. Am. Chem. Soc.* **1987,** *109,* 2138.
192. Camps, F.; Chamorro, E.; Gasol, V.; Guerrero, A. *Synth. Commun.* **1989,** *19,* 3211.
193. Crombie, L.; Rainbow, L. J. *Tetrahedron Lett.* **1988,** *29,* 6517.
194. Camps, F.; Coll, J.; Canela, R.; Guerrero, A.; Riba, M. *Chem. Lett.* **1981,** 703.
195. Michelot, D.; Guerrero, A.; Ratovelomanna, V. *J. Chem. Res. (S).* **1982,** 93.
196. Rossi, R.; Carpita, A. *Tetrahedron.* **1983,** *39,* 287.
197. Gardette, M.; Alexakis, A.; Normant, J. F. *J. Chem. Ecol.* **1983,** *9,* 219.
198. Shani, A.; Klug, J. T.; Skorka, J. *J. Chem. Ecol.* **1983,** *9,* 863.
199. Camps, F.; Coll, J.; Guerrero, A.; Riba, M. *J. Chem. Ecol.* **1983,** *9,* 869.
200. Bestmann, H. J.; Koschatzky, K.-H.; Plenchette, P.; Süss, J.; Vostrowsky, O. *Liebigs Ann. Chem.* **1982,** 536.
201. Bestmann, H. J.; Koschatzky, K.-H.; Vostrowsky, O. *Liebigs Ann. Chem.* **1982,** 1478.
202. Nikolaev, L. A.; Kovalev, B. G. *Zh. Org. Khim.* **1988,** *24,* 1835.
203. Jain, S. C.; Dussourd, D. E.; Conner, W. E.; Eisner, T.; Guerrero, A.; Meinwald, J. *J. Org. Chem.* **1983,** *48,* 2266.
204. Davis, T. L.; Carlson, D. A. *Synthesis.* **1989,** 936.
205. Bac, N. V.; Fall, Y.; Langlois, Y. *Tetrahedron Lett.* **1986,** *27,* 841.
206. Fujisawa, T.; Sato, T.; Kawashima, M.; Naruse, K.; Tamai, K. *Tetrahedron Lett.* **1982,** *23,* 3383.
207. Yadav, J. S.; Reddy, P. S. *Synth. Commun.* **1986,** *16,* 1119.

208. Nishiyama, H.; Sakuta, K.; Osaka, N.; Arai, H.; Matsumoto, M.; Itoh, K. *Tetrahedron.* **1988,** *44,* 2413.

209. Maruoka, K.; Nonoshita, K.; Banno, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1988,** *110,* 7922.

210. Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990,** *112,* 316.

211. Bac, N. V.; Langlois, Y. *J. Am. Chem. Soc.* **1982,** *104,* 7666.

212. Chattopadhyay, A.; Mandapur, V. R. *Indian J. Chem.* **1987,** *26B,* 868.

213. Bestmann, H. J.; Li, K. *Tetrahedron Lett.* **1981,** *22,* 4941.

214. Wang, K. K.; Chu, K.-H. *J. Org. Chem.* **1984,** *49,* 5175.

215. Svirskaya, P. J.; Leznoff, C. C. *J. Chem. Ecol.* **1984,** *10,* 321.

216. Muchowski, J. M.; Venuti, M. C. *J. Org. Chem.* **1981,** *46,* 459.

217. Joshi, N. N.; Mandapur, V. R.; Chadha, M. S. *Tetrahedron.* **1984,** *40,* 3285.

218. Fernández, S.; Hernández, E. *Synth. Commun.* **1982,** *12,* 915.

219. Ishihara, T.; Yamamoto, A. *Agric. Biol. Chem.* **1984,** *48,* 211.

220. Kang, S.-K.; Yao, K.-O.; Moon, H. S. *Bull. Korean Chem. Soc.* **1987,** *8,* 235.

221. Schwarz, M.; Klun, J. A.; Leonhardt, B. A.; Johnson, D. T. *Tetrahedron Lett.* **1983,** *24,* 1007.

222. Tonini, C.; Cassani, G.; Massardo, P.; Guglielmetti, G.; Castellari, P. L. *J. Chem. Ecol.* **1986,** *12,* 1545.

223. Ramiandrasoa, F.; Descoins, C. *Synth. Commun.* **1989,** *19,* 2703.

224. Gardette, M.; Alexakis, A.; Normant, J. F. *J. Chem. Ecol.* **1983,** *9,* 225.

225. Vinczer, P.; Baán, G.; Novák, L.; Szántay, Cs. *Tetrahedron Lett.* **1984,** *25,* 2701.

226. Doolittle, R. E.; Proveaux, A. T.; Heath, R. R. *J. Chem. Ecol.* **1980,** *6,* 271.

227. Yamamoto, A.; Ishihara, T.; Fukumoto, T. *Agric. Biol. Chem.* **1989,** *53,* 285.

228. Voerman, S. *J. Chem. Ecol.* **1979,** *5,* 759.

229. Zhang Xue-Hai; Guo Guang-Zhong; Lin Guo-Quiang; Wu Yuan-Wei; Wu Pei-Heng; Li Zhen-Yu; Wei Kang-Mian. *J. Chem. Ecol.* **1986,** *12,* 1263.

230. Kang, S.-K.; Park, S.-K. *Bull. Korean Chem. Soc.* **1988,** *9,* 149.

231. Vinczer, P.; Béan, G.; Juvancz, Z.; Novák, L.; Szántay, Cs. *Synth. Commun.* **1985,** *15,* 1257.

232. Becker, D.; Kimmel, T.; Cyjon, R.; Moore, I.; Wysoki, M.; Bestmann, H. J.; Platz, H.; Roth, K.; Vostrowsky, O. *Tetrahedron Lett.* **1983,** *24,* 5505.

233. Wong, J. W.; Palaniswamy, P.; Underhill, E. W.; Steck, W. T.; Chisholm, M. D. *J. Chem. Ecol.* **1984,** *10,* 463.

234. Wunderer, H.; Hansen, K.; Bell, T. W.; Schneider, D.; Meinwald, J. *Exp. Biol.* **1986,** *46,* 11.

235. Bestmann, H. J.; Dötzer, R.; Manero-Alvarez, J.; *Tetrahedron Lett.* **1985,** *26,* 2769.

236. Bestmann, H. J.; Roth, K.; Michaelis, K.; Vostrowsky, O.; Schäfer, H.-J.; Michaelis, R. *Liebigs Ann. Chem.* **1987,** 417.

237. Yu, H.-M.; Becker, H.; Mangold, H. K. *Chem. and Ind.* **1989,** 39.

238. Roelofs, W. L.; Hill, A. S.; Linn, C. E.; Meinwald, J.; Jain, S. C.; Herbert, H. J.; Smith, R. F. *Science.* **1982,** *217,* 657.

239. Bestmann, H. J.; Brosche, T.; Koschatzky, K. H.; Knauf, W. *Tetrahedron Lett.* **1982,** *23,* 4007.

240. Jain, S. C.; Roelofs, W. L.; Meinwald, J. *J. Org. Chem.* **1983,** *48,* 2274.

241. Huang, W.; Pulaski, S. P.; Meinwald, J. *J. Org. Chem.* **1983,** *48,* 2270.

242. Heath, R. R.; Tumlinson, J. H.; Leppla, N. C.; McLaughlin, J. R.; Dueben, B.; Dundulis, E.; Guy, R. H. *J. Chem. Ecol.* **1983,** *9,* 645.

243. Yu, H.-M.; Mangold, H. K. *Chem. and Ind.* **1988,** 787.

244. Konno, Y.; Arai, K.; Sekiguchi, K.; Matsumoto, Y. *Appl. Entomol. Zool.* **1982,** *17,* 207.

245. Ikeda, Y.; Ukai, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron Lett.* **1984,** *25,* 5177.

246. Ikeda, Y.; Ukai, J.; Ikeda, N.; Yamamoto, H. *Tetrahedron.* **1987,** *43,* 743.

247. Beevor, P. S.; Cork, A.; Hall, D. R.; Nesbitt, B. F.; Day, R. K.; Mumford, J. D. *J. Chem. Ecol.* **1986,** *12,* 1.

248. Seol, K. Y.; Honda, H.; Usui, K.; Ando, T.; Matsumoto, Y. *Agric. Biol. Chem.* **1987,** *51,* 2285.

249. Ando, T.; Ogura, Y.; Koyama, M.; Kurane, M.; Uchiyama, M.; Seol, K. Y. *Agric. Biol. Chem.* **1988,** *52,* 2459.

250. Markgraf, J. H.; Lusskin, S. I.; McDonald, E. C.; Volpp, B. D. *J. Chem. Ecol.* **1983,** *9,* 211.

251. Brown, H. C.; Basavaiah, D. *Synthesis.* **1983,** 283.

252. Tsuboi, S.; Furutani, H.; Takeda, A.; Kawazoe, K.; Sato, S. *Bull. Chem. Soc. Japan.* **1987,** *60,* 2475.

253. Lin, G.-Q.; Wu, B.-C.; Liu, L.-Y.; Xian, X.-Q.; Zhou, W.-S. *Acta Chem. Sinica.* **1984,** 74.

254. Pikul, S.; Kozlowska, M.; Jurczak, J. *Tetrahedron Lett.* **1987,** *28,* 2627.

255. Masaki, Y.; Serizawa, Y.; Nagata, K.; Oda, H.; Nagashima, H.; Kaji, K. *Tetrahedron Lett.* **1986,** *27,* 231.

256. Achmatowicz, Jr., O.; Sadownik, A.; Bielski, R. *Polish J. Chem.* **1985,** *59,* 553.

257. Jigajimmi, V. B.; Wightman, R. H. *Carbohydrate Res.* **1986,** *147,* 145.

258. Iwaki, S.; Marumo, S.; Saito, T.; Yamada, M.; Katagiri, K. *J. Am. Chem. Soc.* **1974,** *96,* 7842.

259. Tolstikov, A. G.; Khakhalina, N. V.; Odinokov, V. N. *Zhur. Org. Khim.* **1987,** *23,* 2469. See also *Zhur. Org. Khim.* **1989,** *25,* 296.

260. Rossiter, R. E.; Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981,** *103,* 464.

261. Mori, K.; Ebata, T. *Tetrahedron Lett.* **1981,** *22,* 4281.

262. Mori, K.; Ebata, T. *Tetrahedron.* **1986,** *42,* 3471.

263. Marczak, S.; Masnyk, M.; Wicha, J. *Tetrahedron Lett.* **1989,** *30,* 2845.

264. Lin, G.-Q.; Jiang, Y.-Y.; Zhou, W.-S. *Acta Chem. Sinica.* **1985,** 257.

265. Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *Tetrahedron Lett.* **1988,** *29,* 313.

266. Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *J. Org. Chem.* **1989,** *54,* 3130.

267. Tsuboi, S.; Furutani, H.; Utaka, M.; Takeda, A. *Tetrahedron Lett.* **1987,** *28,* 2709.

268. Bianchi, D.; Cabri, W.; Cesti, P.; Francalanci, F.; Rama, F. *Tetrahedron Lett.* **1988,** *29,* 2455.

269. Otto, P. P. J. H. L.; Stein, F.; van der Willigen, C. A. *Agric. Ecosyst. Environ.* **1988,** *21,* 121.

270. Iriuchijima, S.; Kojima, N. *Agric. Biol. Chem.* **1978,** *42,* 451.
271. Sato, T.; Itoh, T.; Fujisawa, T. *Tetrahedron Lett.* **1987,** *28,* 5677.
272. Bell, T. W.; Claccio, J. A. *Tetrahedron Lett.* **1988,** *29,* 865.
273. Rollin, P.; Pougny, J.-R. *Tetrahedron.* **1986,** *42,* 3479.
274. Ebata, T.; Mori, K. *Agric. Biol. Chem.* **1989,** *53,* 801.
275. Nikolaeva, L. N.; Kovalev, B. G. *Zhur. Org. Khim.* **1985,** *21,* 746.
276. Pougny, J.-R.; Rollin, P. *Tetrahedron Lett.* **1987,** *28,* 2977.
277. Millar, J. G.; Underhill, E. W. *J. Org. Chem.* **1986,** *51,* 4726.
278. Tóth, M.; Buser, H. R.; Peña, A.; Arn, H.; Mori, K.; Takeuchi, T.; Nikolaeva, L. N.; Kovalev, B. G. *Tetrahedron Lett.* **1989,** *30,* 3405.
279. Mori, K.; Takeuchi, T. *Liebigs Ann. Chem.* **1989,** 453.
280. Brown, H. C.; Singaram, B. *Acc. Chem. Res.* **1988,** *21,* 287.
281. Matteson, D. S. *Synthesis.* **1986,** 973.
282. Matteson, D. S. *Acc. Chem. Res.* **1988,** *21,* 294.
283. Williams, H. J.; Silverstein, R. M.; Burkholder, W. E.; Khorramshahi, A. *J. Chem. Ecol.* **1981,** *7,* 759.
284. Ceskis, B. A.; Yartitz, A. P.; Levedeva, K. V.; Moiseenkov, A. M. *Khim. Prir. Soedin.* **1985,** 107.
285. Leonhardt, B. A.; Neal, Jr., J. W.; Klun, J. A.; Schwarz, M.; Plimmer, J. R. *Science.* **1983,** *219,* 314.
286. Pasteels, J. M.; Verhaeghe, J. C.; Ottinger, R.; Braekman, J. C.; Daloze, D. *Insect Biochem.* **1981,** *11,* 675.
287. Kato, M.; Mori, K. *Agric. Biol. Chem.* **1985,** *49,* 3073.
288. Mori, K. *Tetrahedron.* **1977,** *33,* 289.
289. Wadhams, L. J.; Angst, M. E.; Blight, M. M. *J. Chem. Ecol.* **1982,** *8,* 477.
290. Attygalle, A. B.; Vostrowsky, O.; Bestmann, H. J.; Steghaus-Kovac, S.; Maschwitz, U. *Naturwissenschaften* **1988,** *75,* 315.
291. Schlosser, M.; Fujita, K. *Angew. Chem. Int. Ed. Engl.* **1982,** *21,* 309.
292. Koreeda, M.; Tanaka, Y. *Chem. Lett.* **1982,** 1297.
293. Kallmerten, J.; Gould, T. J. *Tetrahedron Lett.* **1983,** *24,* 5177.
294. Blight, M. M.; Wadhams, L. J.; Wenham, M. J. *Insect Biochem.* **1979,** *9,* 525.
295. Mori, K.; Iwasawa, H. *Tetrahedron.* **1980,** *36,* 2209.
296. Pougny, J.-R.; Sinaÿ, P. *J. Chem. Res. (S).* **1982,** 1; *ibid.*, *(M)* **1982,** 0186-0196.
297. Hao, N. C.; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 1792.
298. Fráter, G. *Helv. Chim. Acta.* **1979,** *62,* 2829.
299. Vigneron, J. P.; Méric, R.; Dhaenens, M. *Tetrahedron Lett.* **1980,** *21,* 2057.
300. Vigneron, J. P.; Bloy, V. *Tetrahedron Lett.* **1980,** *21,* 1735.
301. Matteson, D. S.; Sadhu, K. M. *J. Am. Chem. Soc.* **1983,** *105,* 2077.
302. Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986,** *108,* 810.
303. Nakagawa, M.; Mori, K. *Agric. Biol. Chem.* **1984,** *48,* 2505.
304. Oshima, M.; Yamazaki, H.; Shimizu, I.; Nisar, M.; Tsuji, J. *J. Am. Chem. Soc.* **1989,** *111,* 6280.

305. Hoffmann, R. W.; Ladner, W.; Helbig, W. *Liebigs Ann. Chem.* **1984,** 1170.
306. Sayo, N.; Azuma, K.; Mikami, K.; Nakai, T. *Tetrahedron Lett.* **1984,** *25,* 565.
307. Fujisawa, T.; Tajima, K.; Sato, T. *Chem. Lett.* **1984,** 1669.
308. Oppolzer, W.; Dudfield, P. *Helv. Chim. Acta.* **1985,** *68,* 216.
309. Cammaerts, M.-C.; Mori, K. *Physiol. Entomol.* **1987,** *12,* 381.
310. Brand, J. M. *J. Chem. Ecol.* **1985,** *11,* 177.
311. Fujiwhara, M.; Mori, K. *Agric. Biol. Chem.* **1986,** *50,* 2925.
312. Sakai, T.; Nakagawa, Y.; Takahashi, J.; Iwabuchi, K.; Ishii, K. *Chem. Lett.* **1984,** 263.
313. Mori, K.; Otsuka, T. *Tetrahedron.* **1985,** *41,* 553.
314. Pedrocchi-Fantoni, G.; Servi, S. *J. Chem. Res. (S).* **1986,** 199.
315. Fuganti, C.; Grasselli, P. In *Enzymes in Organic Synthesis* (CIBA Foundation Symposium 111). Pitman: London, **1985,** 112–127.
316. Bel-Rhlid, R.; Fauve, A.; Veschambre, H. *J. Org. Chem.* **1989,** *54,* 3221.
317. Tanaka, Y.; Honda, H.; Ohsawa, K.; Yamamoto, I.; *J. Pesticide Sci.* **1989,** *14,* 197.
318. Carpita, A.; De Magistris, E.; Rossi, R. *Gazz. Chim. Ital.* **1989,** *119,* 99.
319. Baeckström, P.; Bergström, G.; Björkling, F.; He Hui-Zhu; Högberg, H.-E.; Jacobsson, U.; Lin Guo-Quiang; Löfqvist, J.; Norin, T.; Wassgren, A.-B. *J. Chem. Ecol.* **1989,** *15,* 61.
320. Guss, P. L.; Tumlinson, J. H.; Sonnet, P. E.; Proveaux, A. T. *J. Chem. Ecol.* **1982,** *8,* 545.
321. Sonnet, P. E.; Carney, R. L.; Henrick, C. *J. Chem. Ecol.* **1985,** *11,* 1371.
322. Tumlinson, J. H.; In *Les Médiateurs Chimiques Agissant sur le Comportement des Insectes* (Les colloques de l'INRA, No. 7). Paris: Institut National de la Recherche Agronomique, **1982,** 193–201.
323. Guss, P. L.; Sonnet, P. E.; Carney, R. L.; Branson, T. F.; Tumlinson, J. H. *J. Chem. Ecol.* **1984,** *10,* 1123.
324. Guss, P. L.; Sonnet, P. E.; Carney, R. L.; Tumlinson, J. H.; Wilkin, P. J. *J. Chem. Ecol.* **1985,** *11,* 21.
325. Mori, K.; Watanabe, H. *Tetrahedron.* **1984,** *40,* 299.
326. Sonnet, P. E.; Baillargeon, M. W. *J. Chem. Ecol.* **1987,** *13,* 1279.
327. Nguyen Cong Hao;, Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 2080.
328. Kuwahara, Y.; Yen, L. T. M.; Tominaga, Y.; Matsumoto, K.; Wada, Y. *Agric. Biol. Chem.* **1982,** *46,* 2283.
329. Mori, K.; Kuwahara, S. *Tetrahedron.* **1986,** *42,* 5545.
330. Mori, K.; Kuwahara, S. *Tetrahedron.* **1986,** *42,* 5539.
331. Tamaki, Y.; Noguchi, H.; Sugie, H.; Sato, R.; Kariya, A. *Appl. Entomol. Zool.* **1979,** *14,* 101.
332. Suguro, T.; Mori, K. *Agric. Biol. Chem.* **1979,** *43,* 869.
333. Tamaki, Y.; Sugie, H.; Kariya, A.; Arai, S.; Ohba, M.; Terada, T.; Suguro, T.; Mori, K. *Japan. J. Appl. Entomol. Zool.* **1980,** *24,* 221.
334. Tamaki, Y.; Sugie, H.; Osakabe, M.; Sonnet, P. E. *Appl. Entomol. Zool.* **1983,** *18,* 292.
335. Sonnet, P. E.; Heath, R. R. *J. Chem. Ecol.* **1982,** *8,* 41.
336. Sonnet, P. E. *J. Org. Chem.* **1982,** *47,* 3793.

337. Hjalmarsson, M.; Högberg, H.-E. *Acta Chem. Scand.* **1985,** *B39,* 793.
338. Brown, H. C.; Bakshi, R. K.; Singaram, B. *J. Am. Chem. Soc.* **1988,** *110,* 1529.
339. Ceskis, B.; Moiseenkov, A. M. *Zh. Org. Khim.* **1988,** *24,* 103.
340. Nguyen Cong Hao; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1988,** 690.
341. Horiike, M.; Hirano, C.; Tamaki, Y. *Agric. Biol. Chem.* **1982,** *46,* 1925.
342. Bartelt, R. J.; Schaner, A. M.; Jackson, L. L. *J. Chem. Ecol.* **1989,** *15,* 399.
343. Jewett, D. M.; Matsumura, F.; Coppel, H. C. *Science.* **1976,** *192,* 51.
344. Mori, K.; Tamada, S. *Tetrahedron.* **1979,** *35,* 1279.
345. Baker, R.; Winton, P. M.; Turner, R. W. *Tetrahedron Lett.* **1980,** *21,* 1175.
346. Kallmerten, J.; Balestra, M. *J. Org. Chem.* **1986,** *51,* 2855.
347. Serebryakov, E. P.; Gamalevich, G. D. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 114.
348. Nguyen Cong Hao; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1988,** 1142.
349. Byström, S.; Högberg, H.-E.; Norin, T. *Tetrahedron.* **1981,** *37,* 2249.
350. Matsumura, F.; Tai, A.; Coppel, H. C.; Imaida, M. *J. Chem. Ecol.* **1979,** *5,* 237.
351. Kikukawa, T.; Imaida, M.; Tai, A. *Chem. Lett.* **1982,** 1799.
352. Itoh, T.; Yonekawa, Y.; Sato, T.; Fujisawa, T. *Tetrahedron Lett.* **1986,** *27,* 5405.
353. Itoh, T.; Sato, T.; Fujisawa, T. *Nippon Kagaku Kaishi.* **1987,** 1414.
354. Larchevêque, M.; Sanner, C.; Azerad, R.; Buisson, D. *Tetrahedron.* **1988,** *44,* 6407.
355. Larchevêque, M.; Petit, Y. *Tetrahedron Lett.* **1987,** *28,* 1993.
356. Petit, Y.; Sanner, C.; Larchevêque, M. *Synthesis.* **1988,** 538.
357. Kraemer, M.; Coppel, H. C.; Matsumura, F.; Kikukawa, T.; Mori, K. *Environ. Entomol.* **1979,** *8,* 519.
358. Kraemer, M. E.; Coppel, H. C.; Matsumura, F.; Wilkinson, R. C.; Kikukawa, T. *J. Chem. Ecol.* **1981,** *7,* 1063.
359. Olaifa, J. I.; Matsumura, F.; Kikukawa, T.; Coppel, H. C. *J. Chem. Ecol.* **1988,** *14,* 1131.
360. Kikukawa, T.; Matsumura, F.; Olaifa, J.; Kraemer, M.; Coppel, H. C.; Tai, A. *J. Chem. Ecol.* **1983,** *9,* 673.
361. Longhurst, C.; Baker, R.; Mori, K. *Experientia.* **1980,** *36,* 946.
362. Kochansky, J.; Aldrich, J. R.; Lusby, W. R. *J. Chem. Ecol.* **1989,** *15,* 1717.
363. Shaner, A. M.; Tanico-Hogan, L. D.; Jackson, L. L. *J. Chem. Ecol.* **1989,** *15,* 2577.
364. Underhill, E. W.; Chisholm, M. D.; Steck, W. *Can. Entomol.* **1980,** *112,* 629.
365. Huang, Y.-Z.; Shi, L.; Yang, J.; Cai, Z. *J. Org. Chem.* **1987,** *52,* 3558.
366. Wiesner, C. J.; Tan, S.-H. *Chem. and Ind.* **1980,** 627.
367. Baker, T. C.; Francke, W.; Löfstedt, C.; Hanson, B. S.; Du, J.-W.; Phelan, P. L.; Vetter, R. S.; Youngman, R. *Tetrahedron Lett.* **1989,** *30,* 2901.
368. Liu, T.-L.; Xu, B.-Y.; Li, Z.-M. *Youji Huaxue.* **1988,** 156. [*Chem. Abstr.* **1988,** *110,* 23583w].
369. Hall, D. R.; Beevor, P. S.; Lester, R.; Nesbitt, B. F. *Experientia.* **1980,** *36,* 152.
370. Yadav, J. S.; Balakrishnan, K.; Sivadasan, L. *Indian J. Chem.* **1989,** *28B,* 297.
371. Arai, K.; Ando, T.; Sakurai, A.; Yamada, H.; Koshihara, T.; Takahashi, N. *Agric. Biol. Chem.* **1982,** *46,* 2395.

372. Hart, D. W.; Blackburn, T. F.; Schwartz, J. *J. Am. Chem. Soc.* **1975,** *97,* 679.
373. Lo, V. M.; Shiao, M.-J. *Synth. Commun.* **1986,** *16,* 1647.
374. Coffelt, J. A.; Vick, K. W.; Sonnet, P. E.; Doolittle, R. E. *J. Chem. Ecol.* **1979,** *5,* 955.
375. Sonnet, P. E.; Heath, R. R. *J. Chem. Ecol.* **1980,** *6,* 221.
376. Bishop, C. E.; Morrow, G. W. *J. Org. Chem.* **1983,** *48,* 657.
377. Furber, M.; Taylor, R. J. K.; Burford, S. C. *Tetrahedron Lett.* **1985,** *26,* 3285.
378. Furber, M.; Taylor, R. J. K.; Burford, S. C. *J. Chem. Soc., Perkin Trans. 1.* **1986,** 1809.
379. Bestmann, H. J.; Attygalle, A. B.; Schwarz, J.; Garbe, W.; Vostrowsky, O.; Tomida, I. *Tetrahedron Lett.* **1989,** *30,* 2911.
380. Ranganathan, S.; Maniktala, V.; Kumar, R. *Synth. Commun.* **1982,** *12,* 959.
381. Bestmann, H. J.; Wax, R.; Vostrowsky, O. *Chem. Ber.* **1979,** *112,* 3740.
382. Kang, S.-K.; Yoo, K.-O.; Kim, J.-H. *J. Korean Chem. Soc.* **1985,** *29,* 452.
383. Suzuki, T. *Agric. Biol. Chem.* **1980,** *44,* 2519.
384. Suzuki, T. *Agric. Biol. Chem.* **1981,** *45,* 1357.
385. Suzuki, T.; Nakakita, H.; Kuwahara, Y. *Appl. Entomol. Zool.* **1987,** *22,* 340.
386. Suzuki, T. *Agric. Biol. Chem.* **1981,** *45,* 2641.
387. Mori, K.; Kuwahara, S.; Fujiwhara, M. *Proc. Indian Acad. Sci. (Chem. Sci.).* **1988,** *100,* 113.
388. Breuer, E.; Deutsch, J.; Lazarovici, P. *Chem. and Ind.* **1982,** 907.
389. Schreiber, S. L.; Hulin, B. *Tetrahedron Lett.* **1986,** *27,* 4561.
390. Odinokov, V. N.; Ahmetova, V. R.; Ceskis, B. A.; Moiseenkov, A. M.; Tolstikov, G. A. *Zh. Org. Khim.* **1986,** *22,* 281.
391. Mori, K.; Kuwahara, S.; Ueda, H. *Tetrahedron.* **1983,** *39,* 2439.
392. Levinson, H. Z.; Mori, K. *Naturwissenschaften.* **1983,** *70,* 190.
393. Suzuki, T.; Mori, K. *Appl. Entomol. Zool.* **1983,** *18,* 134.
394. Suzuki, T.; Kozaki, J.; Sugawara, R.; Mori, K. *Appl. Entomol. Zool.* **1984,** *19,* 15.
395. Mori, K.; Kato, M.; Kuwahara, S. *Liebigs Ann. Chem.* **1985,** 861.
396. Mori, K.; Takikawa, H. *Liebigs Ann. Chem.* **1991,** 497.
397. Fuganti, C.; Grasselli, P.; Servi, S.; Högberg, H.-E. *J. Chem. Soc., Perkin Trans. 1.* **1988,** 3061.
398. Moiseenkov, A. M.; Ceskis, B. A. *Dokl. Akad. Nauk SSSR.* **1986,** *290,* 1379.
399. Ceskis, B. A.; Lebedeva, K. V.; Moiseenkov, A. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1988,** 865.
400. Nguyen, C. H.; Ceskis, B. A.; Mavrov, M. V.; Moiseenkov, A. M.; Serebryakov, E. P. *Zh. Org. Khim.* **1987,** *23,* 498.
401. Nguyen, C. H.; Mavrov, M. V.; Serebryakov, E. P. *Zh. Org. Khim.* **1987,** *23,* 1649.
402. Akhaev, N. S.; Zakladnoy, G. A.; Mavrov, M. V.; Moiseenkov, A. M.; Nguyen, C. H.; Serebryakov, E. P.; Ceskis, B. A. *Bioorg. Khim.* **1988,** *14,* 243.
403. Mavrov, M. V.; Hao, N. C.; Serebryakov, E. P. *Bioorg. Khim.* **1989,** *15,* 123.
404. Suzuki, T.; Ozaki, J.; Sugawara, R. *Agric. Biol. Chem.* **1983,** *47,* 869.
405. Randad, R. S.; Kulkarni, G. H. *Indian J. Chem.* **1986,** *25B,* 296.
406. Ritter, F. J.; Brüggemann-Rotgans, I. E. M.; Verwiel, P. E. J.; Persoons, C. J.; Talman, E. *Tetrahedron Lett.* **1977,** 2617.

407. Kobayashi, M.; Koyama, T.; Ogura, K.; Seto, S.; Ritter, F. J.; Brüggemann-Rotgans, I. E. M. *J. Am. Chem. Soc.* **1980,** *102,* 6602.
408. Mori, K.; Ueda, H. *Tetrahedron Lett.* **1981,** *22,* 461.
409. Mori, K.; Ueda, H. *Tetrahedron.* **1982,** *38,* 1227.
410. Enders, D. presented at *6th IUPAC Congress on Pesticide Chemistry.* Ottawa, **1986.**
411. Baker, R.; Billington, D. C.; Ekanayake, N. *J. Chem. Soc., Chem. Commun.* **1981,** 1234.
412. Baker, R.; Billington, D. C.; Ekanayake, N. *J. Chem. Soc., Perkin Trans. 1.* **1983,** 1387.
413. Knight, D. W.; Ojhara, B. *Tetrahedron Lett.* **1981,** *22,* 5101.
414. Knight, D. W.; Ojhara, B. *J. Chem. Soc., Perkin Trans. 1.* **1983,** 955.
415. Poppe, L.; Novák, L.; Kolonits, P.; Bata, A.; Szántay, Cs. *Tetrahedron Lett.* **1986,** *27,* 5769.
416. Poppe, L.; Novák, L.; Kolonits, P.; Bata, A.; Szántay, Cs. *Tetrahedron.* **1988,** *44,* 1477.
417. Levinson, H. Z.; Mori, K. *Naturwissenschaften.* **1980,** *67,* 148.
418. Silverstein, R. M.; Cassidy R. F.; Burkholder, W. E.; Shapas, T. J.; Levinson, H. Z.; Levinson, A. R.; Mori, K. *J. Chem. Ecol.* **1980,** *6,* 911.
419. Levinson, H. Z.; Levinson, A. R.; Mori, K. *Naturwissenschaften.* **1981,** *67,* 480.
420. Rossi, R.; Niccoli, A. *Naturwissenschaften.* **1978,** *65,* 259.
421. Rossi, R.; Salvadori, P. A.; Carpita, A.; Niccoli, A. *Tetrahedron.* **1979,** *35,* 2039.
422. Mori, K.; *Tetrahedron.* **1974,** *30,* 3817.
423. Mori, K.; Suguro, T.; Uchida, M. *Tetrahedron.* **1978,** *34,* 3119.
424. Rossi, R.; Carpita, A. *Tetrahedron.* **1977,** *33,* 2447.
425. Jensen, U.; Schäfer, H.-J. *Chem. Ber.* **1981,** *114,* 292.
426. Mori, K.; Kuwahara, S.; Levinson, H. Z.; Levinson, A. R. *Tetrahedron.* **1982,** *38,* 2291.
427. Sato, T.; Naruse, K.; Fujisawa, T. *Tetrahedron Lett.* **1982,** *23,* 3587.
428. Bestmann, H. J.; Frighetto, R. T. S.; Frighetto, N.; Vostrowsky, O. *Liebigs Ann. Chem.* **1988,** 877.
429. Brown, H. C.; Naik, R. G.; Bakahi, R. K.; Pyun, C.; Singaram, B. *J. Org. Chem.* **1985,** *50,* 5586.
430. Nguyen, C. H.; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 903.
431. Nguyen, C. H.; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 906.
432. Schlosser, M.; Strunk, S. *Tetrahedron.* **1989,** *45,* 2649.
433. Serebryakov, E. P.; Gamalevich, G. D. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 132.
434. Burger, B. V.; leRoux, M.; Garbers, C. F.; Spies, H. S. C.; Bigalke, R. G.; Pachler, K. G. R.; Wessels, P. L.; Christ, V.; Maurer, K. H. *Z. Naturforsch.* **1976,** *31c,* 21.
435. Mori, K.; Ara, T.; Matsui, M. *Agric. Biol. Chem.* **1977,** *41,* 2295.
436. Brown, H. C.; Racherla, U. S.; Basavaiah, D. *Synthesis.* **1984,** 303.
437. Reddy, P. B.; Yadav, J. S. *Synth. Commun.* **1984,** *14,* 327.
438. Rosini, G.; Ballini, R.; Petrini, M. *Synthesis.* **1986,** 46.
439. Kuchin, A. V.; Andreeva, N. I.; Tolshkov, G. A. *J. Org. Chem.* (*USSR, Engl. Trans.*). **1987,** *23,* 403.
440. Fujii, M.; Nakamura, K.; Mekata, H.; Oka, S.; Ohno, A. *Bull. Chem. Soc. Japan.* **1988,** *61,* 495.

441. Tamaki, Y.; Honma, H.; Kawasaki, K. *Appl. Entomol. Zool.* **1977,** *12,* 60.
442. Vig, O. P.; Sharma, M. L.; Taneja, K. C.; Malik, N. *Indian J. Chem.* **1981,** *20B,* 863.
443. Yoshida, T.; Saito, S. *Bull. Chem. Soc. Japan.* **1982,** *55,* 3047.
444. Naoshima, Y.; Kawakubo, M.; Wakabayashi, S.; Hayashi, S. *Agric. Biol. Chem.* **1981,** *45,* 439.
445. Hernández, J. E.; Cisneros, A.; Fernández, S. *Synth. Commun.* **1983,** *13,* 191.
446. Sonnet, P. E. *J. Chem. Ecol.* **1983,** *9,* 551.
447. Yadagiri, P.; Yadav, J. S. *Synth. Commun.* **1983,** *13,* 1067.
448. Sviridov, A. F.; Ermolenko, M. S.; Yashunsky, D. V.; Kochetkov, N. K. *Tetrahedron Lett.* **1983,** *24,* 4359.
449. Kang, S.-K.; Cho, H.-S. *Bull. Korean Chem. Soc.* **1984,** *5,* 130.
450. Kang, S.-K.; Park, J.-M.; Yoo, K.-O.; Lee, J.-O.; Goh, H. G. *Bull. Korean Chem. Soc.* **1985,** *6,* 86.
451. Wenkert, E.; Ferreira, V. F.; Michelotti, E. L.; Tingoli, M. *J. Org. Chem.* **1985,** *50,* 719.
452. Kang, S.-K.; Park, D. C.; No, K. *Bull. Korean Chem. Soc.* **1987,** *8,* 485.
453. Dasaradhi, L.; Rao, S. J.; Bhalerao, U. T. *Indian J. Chem.* **1988,** *27B,* 167.
454. Trehan, I. R.; Singh, L.; Ohri, H. K.; Kad, G. L. *Indian J. Chem.* **1988,** *27B,* 350.
455. Yamashita, M.; Matsumiya, K.; Murakami, K.; Suemitsu, R. *Bull. Chem. Soc. Japan.* **1988,** *61,* 3368.
456. Bestmann, H. J.; Schmidt, M. *Tetrahedron Lett.* **1985,** *26,* 6171.
457. Sorochinskaya, A. M.; Kovalev, B. G.; Avdeeva, L. A. *Zh. Org. Khim.* **1988,** *24,* 316.
458. Kovalev, B. G.; Sorochinskaya, A. M.; Avdeeva, L. A. *Khim. Prirod Soedin.* **1988,** 123.
459. Yamamoto, I.; Tanaka, S.; Fujimoto, T.; Ohta, K. *J. Org. Chem.* **1989,** *54,* 747.
460. Buser, H. R.; Guerin, P. M.; Tóth, M.; Szöcs, G.; Schmid, A.; Francke, W.; Arn, H. *Tetrahedron Lett.* **1985,** *26,* 403.
461. Zweifel, G.; Pearson, N. R. *J. Am. Chem. Soc.* **1980,** *102,* 5919.
462. Trost, B. M.; Ornstein, P. L. *Tetrahedron Lett.* **1981,** *22,* 3463.
463. Pramod, K.; Ramanathan, H.; Subba Rao, G. S. R. *J. Chem. Soc., Perkin Trans. 1.* **1983,** 7.
464. Reddy, P. S.; Sahasrabudhe, A. B.; Yadav, J. S. *Synth. Commun.* **1983,** *13,* 379.
465. Fernández, S.; Quintanilla, R.; Hernández, J. E. *Synth. Commun.* **1983,** *13,* 621.
466. Murata, Y.; Inomata, K.; Kinoshita, H.; Kotake, H. *Bull. Chem. Soc. Japan.* **1983,** *56,* 2539.
467. Naoshima, Y.; Ike, H.; Ogawa, T.; Nakayama, T.; Kondo, H. *Agric. Biol. Chem.* **1984,** *48,* 2151.
468. Ousset, J. B.; Mioskowski, C.; Yang, Y.-L.; Falck, J. R. *Tetrahedron Lett.* **1984,** *25,* 5903.
469. Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1985,** *50,* 1147.
470. Reddy, G. B.; Mitra, R. B. *Synth. Commun.* **1986,** *16,* 1723.
471. Reddy, G. B.; Mitra, R. B. *Synth. Commun.* **1987,** *17,* 893.
472. Yamamoto, I.; Tanaka, S.; Fujimoto, T.; Ohta, K.; Matsuzaki, K. *Nippon Kagaku Kaishi* (*J. Chem. Soc. Japan*). **1987,** 1227.
473. Mitra, R. B.; Reddy, G. B. *Indian J. Chem.* **1988,** *27B,* 691.
474. Enders, D.; Eichenauer, H. *Angew. Chem. Int. Ed. Engl.* **1979,** *18,* 397.

475. Enders, D.; Eichenauer, H.; Baus, U.; Schubert, H.; Kremer, K. A. M. *Tetrahedron.* **1984,** *40,* 1345.

476. Brown, H. C.; Jadhav, P. K.; Desai, M. C. *Tetrahedron.* **1984,** *40,* 1325.

477. Baker, R.; Parton, A. H.; Rao, V. B.; Rao, V. J. *Tetrahedron Lett.* **1982,** *23,* 3103.

478. Naoshima, Y.; Hayashi, D.; Ochi, M. *Agric. Biol. Chem.* **1988,** *52,* 1605.

479. Bestmann, H. J.; Attygalle, A. B.; Glasbrenner, J.; Riemer, R.; Vostrowsky, O. *Angew. Chem. Int. Ed. Engl.* **1987,** *26,* 784.

480. Bestmann, H. J.; Attygale, A. B.; Glasbrenner, J.; Riemer, R.; Vostrowsky, O.; Constantino, M. C.; Malikian, G.; Morgan, E. D. *Liebigs Ann. Chem.* **1988,** 55.

481. Mimura, T.; Kimura, Y.; Nakai, T. *Chem. Lett.* **1979,** 1361.

482. Blanco, L.; Slouqui, N.; Rousseau, G.; Conia, J. M.; *Tetrahedron Lett.* **1981,** *22,* 645.

483. Coutrot, P.; Ghribi, A. *Synthesis.* **1986,** 790.

484. Yoneda, R.; Harusawa, S.; Kurihara, T. *J. Chem. Soc., Perkin Trans. 1.* **1988,** 3163.

485. Guss, P. L.; Tumlinson, J. H.; Sonnet, P. E.; McLaughlin, J. R. *J. Chem. Ecol.* **1983,** *9,* 744.

486. Senda, S.; Mori, K. *Agric. Biol. Chem.* **1983,** *47,* 795.

487. Oppolzer, W.; Dudfield, P.; Stephenson, T.; Godel, T. *Helv. Chim. Acta.* **1985,** *68,* 212.

488. Rossi, R.; Carpita, A.; Chini, M. *Tetrahedron.* **1985,** *41,* 627.

489. Nguyen Cong Hao; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 2083.

490. Lanier, G. N.; Qi, Y.-T.; West, J. R.; Park, S. C.; Webster, F. X.; Silverstein, R. M. *J. Chem. Ecol.* **1989,** *15,* 1645.

491. Chuman, T.; Guss, P. L.; Doolittle, R. E.; McLaughlin, J. R.; Krysan, J. L.; Schalk, J. M.; Tumlinson, J. H. *J. Chem. Ecol.* **1987,** *13,* 1601.

492. Mori, K.; Igarashi, Y. *Liebigs Ann. Chem.* **1988,** 717.

493. McLaughlin, J. R.; Tumlinson, J. H.; Mori, K. *J. Econ. Entomol.* **1991,** *84,* 99.

494. Mori, K.; Masuda, S.; Suguro, T. *Tetrahedron.* **1981,** *37,* 1329.

495. Nishida, R.; Fukami, H. *Mem. Coll. Agric. Kyoto Univ.* **1983,** *No. 122,* 1.

496. Jensen-Korte, U.; Schäfer, H.-J. *Liebigs. Ann. Chem.* **1982,** 1532.

497. Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1987,** *28,* 651.

498. Mori, K.; Takikawa, H. *Tetrahedron.* **1990,** *46,* 4473.

499. Schmuff, N. R.; Phillips, J. K.; Burkholder, W. E.; Fales, H. M.; Chen, C.-W.; Roller, P. P.; Ma, M. *Tetrahedron Lett.* **1984,** *25,* 1533.

500. Phillips, J. K.; Walgenbach, C. A.; Klein, J. A.; Burkholder, W. E.; Schmuff, N. R.; Fales, H. M. *J. Chem. Ecol.* **1985,** *11,* 1263.

501. Smith III, A. B.; Levenberg, P. A. *Synthesis.* **1981,** 567.

502. Mori, K.; Ebata, T. *Tetrahedron.* **1986,** *42,* 4421.

503. Walgenbach, C. A.; Phillips, J. K.; Burkholder, W. E.; King, G. G. S.; Slessor, K. N.; Mori, K. *J. Chem. Ecol.* **1987,** *13,* 2159.

504. Fauve, A.; Veschambre, H. *Tetrahedron Lett.* **1987,** *28,* 5037.

505. Fronza, G.; Fuganti, C.; Högberg, H.-E.; Pedrocchi-Fantoni, G.; Servi, S. *Chem. Lett.* **1988,** 385.

506. Fuganti, C.; Grasselli, P.; Servi, S.; Spreafico, F.; Zirotti, C. *J. Org. Chem.* **1984,** *49,* 4087.

507. Enders, D.; Lohray, B. B. *Angew. Chem. Int. Ed. Engl.* **1988,** *27,* 581.

508. Enders, D.; Lohray, B. B. *Angew. Chem. Int. Ed. Engl.* **1987,** *26,* 351.

509. Mori, K.; Yoshimura, T.; Sugai, T. *Liebigs Ann. Chem.* **1988,** 899. In this reference, the formula depicted for (−)-ω-camphanyl chloride was in error, showing its antipode as registered in the Aldrich Catalog of that day [cf. *Aldrichim. Acta.* **1988,** *21,* 16].

510. Davis, F. A.; Lal, G. S.; Wei, J. *Tetrahedron Lett.* **1988,** *29,* 4269.

511. Iwabuchi, K.; Takahashi, J.; Nakagawa, Y.; Sakai, T. *Appl. Entomol. Zool.* **1986,** *21,* 21.

512. O'Shea, M. G.; Kitching, W. *Tetrahedron.* **1989,** *45,* 1177.

513. Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M. *Tetrahedron Lett.* **1979,** 2361.

514. Chuman, T.; Mochizuki, K.; Mori, M.; Kohno, M.; Kato, K.; Noguchi, M. *J. Chem. Ecol.* **1985,** *11,* 417.

515. Chuman, T. *Nippon Nogeikagaku Kaishi* (*J. Agric. Chem. Soc. Japan*). **1984,** *58,* 1135.

516. Yang, K.-K.; Kim, K.-S.; Shin, S.-C. *J. Korean Agric. Chem. Soc.* **1989,** *32,* 57.

517. Chuman, T.; Kato, K.; Noguchi, M. *Agric. Biol. Chem.* **1979,** *43,* 2005.

518. Ono, M.; Ōnishi, I.; Chuman, T.; Kohno, M.; Kato, K. *Agric. Biol. Chem.* **1980,** *44,* 2259.

519. Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M.; Nomi, H.; Mori, K. *Agric. Biol. Chem.* **1981,** *45,* 2019.

520. Mori, K.; Iwasawa, H. *Tetrahedron.* **1980,** *36,* 87.

521. Mori, K.; Nomi, H.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M. *Tetrahedron Lett.* **1981,** *22,* 1127.

522. Mori, M.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M.; Nomi, H.; Mori, K. *Tetrahedron Lett.* **1982,** *23,* 667.

523. Sum, P.-E.; Weiler, L. *Can. J. Chem.* **1978,** *56,* 2700.

524. Mori, K.; Nomi, H.; Chuman, T.; Kohno, M.; Kato, K.; Noguchi, M. *Tetrahedron.* **1982,** *38,* 3705.

525. Mori, M.; Chuman, T.; Kato, K.; Mori, K. *Tetrahedron Lett.* **1982,** *23,* 4593.

526. Mori, K.; Watanabe, H. *Tetrahedron.* **1985,** *41,* 3423.

527. Mori, M.; Chuman, T.; Kato, K. *Tetrahedron Lett.* **1984,** *25,* 2553.

528. Takeda, Y.; Kobayashi, Y.; Sato, F. *Chem. Lett.* **1985,** 471.

529. Kobayashi, Y.; Kitano, Y.; Takeda, Y.; Sato, F. *Tetrahedron.* **1986,** *42,* 2937.

530. Hoffmann, R. W.; Helbig, W.; Ladner, W. *Tetrahedron Lett.* **1982,** *23,* 3479.

531. Baker, R.; Devlin, J. A.; *J. Chem. Soc., Chem. Commun.* **1983,** 147.

532. Redlich, H.; Samm, K.; Lenfers, J.-B.; Bruns, W. *Carbohyd. Res.* **1988,** *174,* 341.

533. Takano, S.; Sekiguchi, Y.; Ogasawara, K. *Heterocycles.* **1989,** *29,* 445.

534. Nguyen, C. H.; Mavrov, M. V.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989,** 1361.

535. Bartlett, P. A.; Richardson, D. P.; Myerson, J. *Tetrahedron.* **1984,** *40,* 2317.

536. Pilli, R. A.; Murta, M. M. *Synth. Commun.* **1988,** *18,* 981.

537. Levinson, H. Z.; Levinson, A. R. *Z. Angew. Entomol.* **1987,** *103,* 217.

538. Mori, M.; Mochizuki, K.; Kohno, M.; Chuman, T.; Ohnishi, A.; Watanabe, H.; Mori, K. *J. Chem. Ecol.* **1986,** *12,* 83.

539. Chuman, T.; Mochizuki, K.; Mori, M.; Kohno, M.; Ono, M.; Ōnishi, I.; Kato, K. *Agric. Biol. Chem.* **1982,** *46,* 593.

540. Chuman, T.; Mochizuki, K.; Mori, M.; Kohno, M.; Kato, K.; Nomi, H.; Mori, K. *Agric. Biol. Chem.* **1982,** *46,* 3109.
541. Mochizuki, K.; Chuman, T.; Mori, M.; Kohno, M.; Kato, K.; Mori, K. *Agric. Biol. Chem.* **1984,** *48,* 2833.
542. Heath, R. R.; Coffelt, J. A.; Sonnet, P. E.; Proshold, F. I.; Dueben, B.; Tumlinson, J. H. *J. Chem. Ecol.* **1986,** *12,* 1489.
543. Bühring, M.; Francke, W.; Heemann, V. *Z. Naturforsch.* **1976,** *31c,* 748.
544. Francke, W.; Bühring, M.; Horstmann, K. *Z. Naturforsch.* **1980,** *35c,* 829.
545. Tanida, K.; Mori, K. *Nippon Kagaku Kaishi* (*J. Chem. Soc. Japan*). **1981,** 635.
546. Enders, D.; Rendenbach, B. E. M. *Tetrahedron.* **1986,** *42,* 2235.
547. Phillips, J. K.; Miller, S. P. F.; Andersen, J. F.; Fales, H. M.; Burkholder, W. E. *Tetrahedron Lett.* **1987,** *28,* 6145.
548. Chong, J. M. *Tetrahedron.* **1989,** *45,* 623.
549. Mori, K.; Ishikura, M. *Liebigs Ann. Chem.* **1989,** 1263.
550. a) Burkholder, W. E. personal communication; b) Chambers, J. personal communication; c) Levinson, H. Z.; Levinson, A.; Ren, Z.; Mori, K. *J. Appl. Entomol.* **1990,** *110,* 203.
551. Kandil, A. A.; Slessor, K. N. *Can. J. Chem.* **1983,** *61,* 1166.
552. Fujisawa, T.; Sato, T.; Itoh, T. *Chem. Lett.* **1982,** 219.
553. Ogura, K.; Sanada, K.; Takahashi, K.; Iida, H. *Tetrahedron Lett.* **1982,** *23,* 4035.
554. Chattopadhyay, A.; Mandapur, V. R.; Chadha, M. S. *Indian J. Chem.* **1983,** *22B,* 158.
555. Villiéras, J.; Rambaud, M.; Graff, M. *Tetrahedron Lett.* **1985,** *26,* 53.
556. Villiéras, J.; Rambaud, M.; Graff, M. *Synth. Commun.* **1985,** *15,* 569.
557. Villemin, D. *Chem. and Ind.* **1986,** 69.
558. Ferroud, D.; Gaudin, J. M.; Genet, J. P. *Tetrahedron Lett.* **1986,** *27,* 845.
559. Dhokte, U. P.; Rao, A. S. *Synth. Commun.* **1987,** *17,* 355.
560. Bestmann, H. J.; Schmidt, M.; Schobert, R. *Synthesis.* **1988,** 49.
561. Nomura, M.; Fujiwara, Y. *Yukagaku.* **1988,** *37,* 453.
562. Webster, F. X.; Prestwich, G. D. *J. Chem. Ecol.* **1988,** *14,* 957.
563. Ishibashi, H.; Ohnishi, M.; Senda, T.; Ikeda, M. *Synth. Commun.* **1989,** *19,* 857.
564. Satoh, Y.; Tayano, T.; Hara, S.; Suzuki, A. *Tetrahedron Lett.* **1989,** *30,* 5153.
565. Byers, J. A.; Biergersson, G.; Loefkvist, J.; Bergstroem, G. *Naturwissenschaften.* **1988,** *75,* 153.
566. Baeckström, P.; Jacobsson, U.; Norin, T.; Unelius, C. R. *Tetrahedron.* **1988,** *44,* 2541.
567. Kuwahara, Y.; Nakamura, S. *Appl. Entomol. Zool.* **1985,** *20,* 354.
568. Harada, H.; Mori, K. *Agric. Biol. Chem.* **1989,** *53,* 1439.
569. Tamaki, Y.; Sugie, H.; Noguchi, H. *Appl. Entomol. Zool.* **1985,** *20,* 359.
570. Tsuboi, S.; Masuda, T.; Takeda, A. *Bull. Chem. Soc. Japan.* **1983,** *56,* 3521.
571. De Jarlais, W. J.; Emken, E. A. *J. Chem. Ecol.* **1987,** *13,* 179.
572. Mori, K.; Nukada, T.; Ebata, T. *Tetrahedron.* **1981,** *37,* 1343.
573. Oehlschlager, A. C.; Czyzewska, E. *Tetrahedron Lett.* **1983,** *24,* 5587.
574. Fujisawa, T.; Iida, S.; Sato, T. *Tetrahedron Lett.* **1984,** *25,* 4007.
575. Franck-Neumann, M.; Brion, F. *Angew. Chem., Int. Ed. Engl.* **1979,** *18,* 688.
576. Ledoussal, B.; Gorgues, A.; LeCoq, A. *Tetrahedron Lett.* **1985,** *26,* 51.

577. Lang, R. W.; Kohl-Mines, E.; Hansen, H.-J. *Helv. Chim. Acta.* **1985,** *68,* 2249.
578. Bloch, R.; Hassan-Gonzales, D. *Tetrahedron.* **1986,** *42,* 4975.
579. Tabuchi, T.; Inanaga, J.; Yamaguchi, M.*Tetrahedron Lett.* **1986,** *27,* 5237.
580. Ravid, U.; Silverstein, R. M.; Smith, L.-R. *Tetrahedron.* **1978,** *34,* 1449.
581. Mori, K.; Mori, H.; Sugai, T. *Tetrahedron.* **1985,** *41,* 919.
582. Levinson, H. Z. personal communication to K. M. dated October 22, 1984.
583. Francotte, E.; Lohmann, D. *Helv. Chim. Acta.* **1987,** *70,* 1569.
584. Nguyen Cong Hao; Mavrov, M. V.; Cherelashvili, Z. G.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1988,** 1184.
585. Zhdankina, G. M.; Serebryakov, E. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985,** 2605.
586. Kang, S.-K.; Shin, D.-S. *Bull. Korean Chem. Soc.* **1987,** *8,* 215.
587. Rama Rao, A. V.; Reddy, E. R.; Joshi, B. V.; Yadav, J. S. *Tetrahedron Lett.* **1987,** *28,* 6497.
588. Yadav, J. S.; Sreenivasa Rao, E.; Rao, V. S. *Synth. Commun.* **1989,** *19,* 705.
589. Gurjar, M. K.; Patil, V. J. *Indian J. Chem.* **1986,** *25B,* 596.
590. Vigneron, J. P.; Bloy, V. *Tetrahedron Lett.* **1980,** *21,* 1735.
591. Midland, M. M.; Tramontano, A. *Tetrahedron Lett.* **1980,** *21,* 3549.
592. Soai, K.; Yokoyama, S.; Hayasaka, T.; Ebihara, K. *Chem. Lett.* **1988,** 843.
593. Bernardi, R.; Fuganti, C.; Grasselli, P.; Masinoni, G. *Synthesis.* **1980,** 50.
594. Naoshima, Y.; Ozawa, H.; Kondo, H.; Hayashi, S. *Agric. Biol. Chem.* **1983,** *47,* 1431.
595. Kozikowski, A. P.; Mugrage, B. B.; Li, C. S.; Felder, L. *Tetrahedron Lett.* **1986,** *27,* 4817.
596. Sato, T.; Okumura, Y.; Itai, J.; Fujisawa, T. *Chem. Lett.* **1988,** 1537.
597. Blanco, L.; Guibé-Jampel, E.; Rousseau, G. *Tetrahedron Lett.* **1988,** *29,* 1915.
598. Bacardit, R.; Moreno-Mañas, M. *Tetrahedron Lett.* **1980,** *21,* 551.
599. Bacardit, R.; Moreno-Mañas, M. *J. Chem. Ecol.* **1983,** *9,* 703.
600. Bäckvall, J. E.; Byström, S. E.; Nyström, J. E. *Tetrahedron.* **1985,** *41,* 5761.
601. Narasaka, K.; Ukaji, Y. *Chem. Lett.* **1986,** 81.
602. Ibuka, T.; Nakao, T.; Nishii, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **1986,** *108,* 7420.
603. Russell, A. T.; Procter, G. *Tetrahedron Lett.* **1987,** *28,* 2041.
604. Mori, K.; Senda, S. *Tetrahedron.* **1985,** *41,* 541.
605. Gerth, D. B.; Giese, B. *J. Org. Chem.* **1986,** *51,* 3726.
606. Brandänge, S.; Leijonmarck, H.; Ölund, J. *Acta Chem. Scand.* **1989,** *43,* 193.
607. Bernardi, R.; Ghiringhelli, D. *Synthesis.* **1989,** 939.
608. Hanessian, S.; Demailly, G.; Chapleur, Y.; Leger, S. *J. Chem. Soc., Chem. Commun.* **1981,** 1125.
609. Kuwahara, Y. *Appl. Entomol. Zool.* **1980,** *15,* 478.
610. Miyashita, Y.; Mori, K. *Agric. Biol. Chem.* **1981,** *45,* 2521.
611. Rocca, J. R.; Tumlinson, J. H.; Glancey, B. M.; Lofgren, C. S. *Tetrahedron Lett.* **1983,** *24,* 1889.
612. Rocca, J. R.; Tumlinson, J. H.; Glancey, B. M.; Lofgren, C. S. *Tetrahedron Lett.* **1983,** *24,* 1893.
613. Hoye, T. R.; Peck, D. R.; Swanson, T. A. *J. Am. Chem. Soc.* **1984,** *106,* 2738.

614. Hoye, T. R.; Peck, D. R.; Trumper, P. K. *J. Am. Chem. Soc.* **1981,** *103,* 5618.
615. Schreiber, S. L.; Wang, Z. *J. Am. Chem. Soc.* **1985,** *107,* 5303.
616. Yamamoto, Y.; Taniguchi, K.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1985,** 1429.
617. Rajan Babu, T. V.; Nugent, W. A.; Taber, D. F.; Fagan, P. J. *J. Am. Chem. Soc.* **1988,** *110,* 7128.
618. Ziegler, F. E.; Stirchak, E. P.; Wester, R. T. *Tetrahedron Lett.* **1986,** *27,* 1229.
619. Ziegler, F. E.; Cain, W. T.; Kneisley, A.; Stirchak, E. P.; Wester, R. T. *J. Am. Chem. Soc.* **1988,** *110,* 5442.
620. Mori, K. *Tetrahedron.* **1983,** *39,* 3107.
621. Mori, K.; Nakazono, Y. *Tetrahedron.* **1986,** *42,* 6459.
622. Tumlinson, J. H. personal communication dated October 30, 1986.
623. Senda, S.; Mori, K. *Agric. Biol. Chem.* **1987,** *51,* 1379.
624. Wakamatsu, T.; Nishikimi, Y.; Kikuiri, H.; Nakamura, H.; Ban, Y. *Heterocycles.* **1987,** *26,* 1761.
625. Balestra, M.; Kallmerten, J. *Tetrahedron Lett.* **1988,** *29,* 6901.
626. Jones, T. H.; Fales, H. M. *Tetrahedron Lett.* **1983,** *24,* 5439.
627. Voaden, D. J. *Synth. Commun.* **1984,** *14,* 53.
628. Chattopadhyay, A.; Mamdapur, V. R. *Indian J. Chem.* **1988,** *27B,* 169.
629. Wilson, S. R.; Zucker, P. A. *J. Org. Chem.* **1988,** *53,* 4682.
630. Ronald, R. C.; Wheeler, C. J. *J. Org. Chem.* **1983,** *48,* 139.
631. Pirkle, W. H.; Adams, P. E. *J. Org. Chem.* **1979,** *44,* 2169.
632. Nishizawa, M.; Yamada, M.; Noyori, R. *Tetrahedron Lett.* **1981,** *22,* 247.
633. Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984,** *106,* 6717.
634. Solladié, G.; Matloubi-Moghadam, F. *J. Org. Chem.* **1982,** *47,* 91.
635. Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* **1983,** *105,* 2088.
636. Naoshima, Y.; Hasegawa, H.; Saeki, T. *Agric. Biol. Chem.* **1987,** *51,* 3417.
637. Utaka, M.; Watabu, H.; Takeda, A. *J. Org. Chem.* **1987,** *52,* 4363.
638. Rao, S. J.; Bhalerao, U. T.; Tilak, B. D. *Indian J. Chem.* **1988,** *27B,* 257.
639. Sugai, T.; Mori, K. *Agric. Biol. Chem.* **1984,** *48,* 2497.
640. Doolittle, R. E.; Tumlinson, J. H.; Proveaux, A. T.; Heath, R. R. *J. Chem. Ecol.* **1980,** *6,* 473.
641. Kang, S.-K.; Shin, D.-S.; Lee, J.-O.; Goh, H.-G. *Bull. Korean Chem. Soc.* **1986,** *7,* 444.
642. Nishida, Y.; Konno, M.; Hori, H.; Ohrui, H.; Meguro, H. *Agric. Biol. Chem.* **1987,** *51,* 635.
643. Midland, M. M.; Nguyen, N. H. *J. Org. Chem.* **1981,** *46,* 4107.
644. Baker, R.; Rao, V. B. *J. Chem. Soc., Perkin Trans. 1.* **1982,** 69.
645. Senda, S.; Mori, K. *Agric. Biol. Chem.* **1983,** *47,* 2595.
646. Baskaran, S.; Islam, I.; Chandrasekaran, S. *J. Org. Chem.* **1990,** *55,* 891.
647. Ishay, J. (Tel Aviv University), personal communication to K. M.
648. Bacardit, R.; Moreno-Mañas, M. *Chem. Lett.* **1982,** 5.
649. Otsubo, K.; Kawamura, K.; Inanaga, J.; Yamaguchi, M. *Chem. Lett.* **1987,** 1487.
650. Larchevêque, M.; Lalande, J. *Tetrahedron.* **1984,** *40,* 1061.
651. Mori, K.; Otsuka, T. *Tetrahedron.* **1985,** *41,* 547.

652. Nakahata, M.; Imaida, M.; Ozaki, H.; Harada, T.; Tai, A. *Bull. Chem. Soc. Japan.* **1982,** *55,* 2186.

653. Kikukawa, T.; Tai, A. *Chem. Lett.* **1984,** 1935.

654. Kosugi, H.; Konta, H.; Uda, H. *J. Chem. Soc., Chem. Commun.* **1985,** 211.

655. Taber, D. F.; Deker, P. B.; Gaul, M. D. *J. Am. Chem. Soc.* **1987,** *109,* 7488.

656. Mori, A.; Yamamoto, H. *J. Org. Chem.* **1985,** *50,* 5444.

657. Sakamoto, A.; Yamamoto, Y.; Oda, J. *J. Am. Chem. Soc.* **1987,** *109,* 7188.

658. Gadkari, R. G.; Kapadi, A. H. *Indian J. Chem.* **1987,** *26B,* 814.

659. Servi, S. *Tetrahedron Lett.* **1983,** *24,* 2023.

660. Fujisawa, T.; Itoh, T.; Nakai, M.; Sato, T. *Tetrahedron Lett.* **1985,** *26,* 771.

661. Alphand, V.; Archelas, A.; Furstoss, R. *J. Org. Chem.* **1990,** *55,* 347.

662. Utaka, M.; Watabu, H.; Takeda, A. *Chem. Lett.* **1985,** 1475.

663. Laurence, B. R.; Pickett, J. A. *J. Chem. Soc., Chem. Commun.* **1982,** 59.

664. Laurence, B. R.; Mori, K.; Otsuka, T.; Pickett, J. A.; Wadhams, L. J. *J. Chem. Ecol.* **1985,** *11,* 643.

665. Yamaguchi, M.; Hirao, I. *J. Chem. Soc., Chem. Commun.* **1984,** 202.

666. Ochiai, M.; Ukita, T.; Nagao, Y.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1985,** 637.

667. Ochiai, M.; Ukita, T.; Iwaki, S.; Nagao, Y.; Fujita, E. *J. Org. Chem.* **1989,** *54,* 4832.

668. Jefford, C. W.; Jaggi, D.; Boukouvalas, J. *Tetrahedron Lett.* **1986,** *27,* 4011.

669. Kawamura, F.; Tayano, T.; Satoh, Y.; Hara, S.; Suzuki, A. *Chem. Lett.* **1989,** 1723.

670. Dawson, G. W.; Mudd, A.; Pickett, J. A.; Pile, M. M.; Wadhams, L. J. *J. Chem. Ecol.* **1990,** *16,* 1779.

671. Fuganti, C.; Grasselli, P.; Servi, S. *J. Chem. Soc., Chem. Commun.* **1982,** 1285.

672. Tsuboi, S.; Furutani, H.; Utaka, M.; Takeda, A. *Tetrahedron Lett.* **1987,** *28,* 2709.

673. Rahman, S. S.; Wakefield, B. J.; Roberts, S. M.; Dowle, M. D. *J. Chem. Soc., Chem. Commun.* **1989,** 303.

674. Masaki, Y.; Nagata, K.; Kaji, K. *Chem. Lett.* **1983,** 1835.

675. Kotsuki, H.; Kadota, I.; Ochi, M. In *31st Symposium on the Chemistry of Natural Products, Symposium Papers:* Nagoya 1989; 494.

676. Machiya, K.; Ichimoto, I.; Kirihata, M.; Ueda, H. *Agric. Biol. Chem,.* **1985,** *49,* 693.

677. Kang, S.-K.; Shin, D.-S. *Bull. Korean Chem. Soc.* **1986,** *7,* 308.

678. Prasit, P.; Rokach, J. *J. Org. Chem.* **1988,** *53,* 4421.

679. Rokach, J.; Zamboni, R.; Lau, C.-K.; Guindon, Y. *Tetrahedron Lett.* **1981,** *22,* 2579.

680. Kang, S.-K.; Cho, I.-H. *Tetrahedron Lett.* **1989,** *30,* 743.

681. Ichimoto, I.; Yoshizawa, T.; Machiya, K.; Kirihata, M.; Ueda, H. *Chem. Express.* **1988,** *3,* 687.

682. Kamikawa, T.; Yamagiwa, Y.; Katsui, T. *Kinki Daigaku Rikogakubu Kenkyu Hokoku.* **1987,** *23,* 79.

683. Mori, K.; Otsuka, T. *Tetrahedron.* **1983,** *39,* 3267.

684. Lin Guo-qiang; Xu Hai-jian; Wu Bi-chi; Guo Guong-zhong; Zhou Wei-shan; *Tetrahedron Lett.* **1985,** *26,* 1233.

685. Barua, N. C.; Schmidt, R. R.; *Tetrahedron.* **1986,** *42,* 4471.

686. Kametani, T.; Tsubuki, M.; Tatsuzaki, Y.; Honda, T. *Heterocycles.* **1988,** *27,* 2107.

687. Wang, Z.-M.; Qian, X.-H.; Zhou, W.-S. *Tetrahedron.* **1990,** *46,* 1191.

688. Sato, T.; Watanabe, M.; Honda, N.; Fujisawa, T. *Chem. Lett.* **1984,** 1175.

689. Ko, K.-Y.; Eliel, E. L.; *J. Org. Chem.* **1986,** *51,* 5353.

690. Zhou, W.; Cheng, J.; Lin, G. *Huaxue Xnebao.* **1988,** *46,* 274.

691. Otieno, W. A.; Onyango, T. O.; Pile, M. M.; Laurence, B. R.; Dawson, G. W.; Wadhams, L. J.; Pickett, J. A. *Bull. Entomol. Res.* **1988,** *78,* 463.

692. Hwang, Y.-S.; Mulla, M. S.; Chaney, J. D.; Lin, G.-Q.; Xu, H.-J. *J. Chem. Ecol.* **1987,** *13,* 245.

693. Briggs, G. G.; Cayley, G. R.; Laurence, B. R.; Pickett, J. A. *PCT Int. Appl. WO* 8604897 [*Chem. Abstr.* **1987,** *106,* 133826c].

694. Wong, J. W.; Verigin, V.; Oehlschlager, A. C.; Borden, J. H.; Pierce, Jr., H. D.; Pierce, A. M.; Chong, L. *J. Chem. Ecol.* **1983,** *9,* 451.

695. Oehlschlager, A. C.; Wong, J. W.; Verigin, V. G.; Pierce, Jr., H. D. *J. Org. Chem.* **1983,** *48,* 5009.

696. Sakai, T.; Mori, K. *Agric. Biol. Chem.* **1986,** *50,* 177.

697. Oehlschlager, A. C.; Czyzewska, E.; Aksela, R.; Pierce, Jr., H. D. *Can. J. Chem.* **1986,** *64,* 1407.

698. Oehlschlager, A. C.; King, G. G. S.; Pierce, Jr., H. D.; Pierce, A. M.; Slessor, K. N.; Millar, J. G.; Borden, J. H.; *J. Chem. Ecol.* **1987,** *13,* 1543.

699. Millar, J. G.; Pierce, Jr., H. D.; Pierce, A. M.; Oehlschlager, A. C.; Borden, J. H.; Barak, A. V. *J. Chem. Ecol.* **1985,** *11,* 1053.

700. Millar, J. G.; Oehlschlager, A. C.; Wong, J. W. *J. Org. Chem.* **1983,** *48,* 4404.

701. Sakai, T.; Hamamoto, H.; Mori, K. *Agric. Biol. Chem.* **1986,** *50,* 1621.

702. Pierce, A. M.; Pierce, Jr., H. D.; Oehlschlager, A. C.; Borden, J. H. *J. Agric. Food Chem.* **1985,** *33,* 848.

703. Millar, J. G.; Oehlschlager, A. C. *J. Org. Chem.* **1984,** *49,* 2332.

704. Pierce, A. M.; Pierce, Jr., H. D.; Oehlschlager, A. C.; Czyzewska, E.; Borden, J. H. *J. Chem. Ecol.* **1987,** *13,* 1525.

705. Millar, J. G.; Pierce, Jr., H. D.; Pierce, A. M.; Oehlschlager, A. C.; Borden, J. H. *J. Chem. Ecol.* **1985,** *11,* 1071.

706. Naoshima, Y.; Nakamura, A.; Nishiyama, T.; Haramaki, T.; Mende, M.; Munakata, Y. *Chem. Lett.* **1989,** 1023.

707. Millar, J. G.; Pierce, Jr., H. D.; Pierce, A. M.; Oehlschlager, A. C.; Borden, J. H. *J. Chem. Ecol.* **1985,** *11,* 1071.

708. Oehlschlager, A. C.; Pierce, A. M.; Pierce, Jr., H. D.; Borden, J. H. *J. Chem. Ecol.* **1988,** *14,* 2071.

709. Vander Meer, R. K.; Williams, F. D.; Lofgren, C. S. *Tetrahedron Lett.* **1981,** *22,* 1651.

710. Bowers, W. S.; Nault, L. R.; Webb, R. E.; Dutky, S. R. *Science.* **1972,** *177,* 1121.

711. Mandai, T.; Kawada, M.; Otera, J. *J. Org. Chem.* **1983,** *48,* 5183.

712. Kang, S.-K.; Kim, S.-G. *Bull. Korean Chem. Soc.* **1986,** *7,* 157.

713. Poppe, L.; Novák, L.; Szántay, Cs.; *Synth. Commun.* **1987,** *17,* 173.

714. Kang, S.-K.; Chung, G.-Y.; Lee, D.-H. *Bull. Korean Chem. Soc.* **1987,** *8,* 351.

715. Vesyelovsky, V. V.; Dragan, V. A.; Moiseenkov, A. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1987,** 2787.

716. Kawashima, M.; Fujisawa, T. *Bull. Chem. Soc. Japan.* **1988,** *61,* 4051.
717. Baeckström, P.; Li, L.; Wickramaratne, M.; Norin, T. *Synth. Commun.* **1990,** *20,* 423.
718. Williams, H. J.; Strand, M. R.; Vinson, S. B. *Tetrahedron.* **1981,** *37,* 2763.
719. Alvarez, F. M.; Vander Meer, R. K.; Lofgren, C. S. *Tetrahedron.* **1987,** *43,* 2897.
720. Birch, A. J.; Brown, W. V.; Corrie, J. E. T.; Moore, B. P. *J. Chem. Soc., Perkin Trans. 1.* **1972,** 2653.
721. Edwards, J. P.; Chambers, J. *J. Chem. Ecol.* **1984,** *10,* 1731.
722. Kato, T.; Suzuki, M.; Kobayashi, T.; Moore, B. P. *J. Org. Chem.* **1980,** *45,* 1126.
723. Aoki, M.; Uyehara, T.; Kato, T.; Kabuto, K.; Yamaguchi, S. *Chem. Lett.* **1983,** 1121.
724. Byrne, K. J.; Swingar, A. A.; Silverstein, R. M.; Borden, J. H.; Stokkink, E. *J. Insect Physiol.* **1974,** *20,* 1895.
725. Borden, J. H.; Chong, L.; McLean, J. A.; Slessor, K. N.; Mori, K. *Science.* **1976,** *192,* 894.
726. Johnston, B. D.; Slessor, K. N. *Can. J. Chem.* **1979,** *57,* 233.
727. Mori, K. *Tetrahedron.* **1981,** *37,* 1341.
728. Mori, K.; Puapoomchareon, P. *Liebigs Ann. Chem.* **1987,** 271.
729. Sugai, T.; Fujita, M.; Mori, K. *Nippon Kagaku Kaishi* (*J. Chem. Soc. Japan*). **1983,** 1315.
730. Takano, S.; Goto, E.; Hirama, M.; Ogasawara, K. *Heterocycles.* **1981,** *16,* 951.
731. Takano, S.; Goto, E.; Ogasawara, K. *Chem. Lett.* **1982,** 1913.
732. Takano, S.; Hirama, M.; Ogasawara, K. *Heterocycles.* **1983,** *20,* 1363.
733. Takano, S.; Yanase, M.; Takahashi, M.; Ogasawara, K. *Chem. Lett.* **1987,** 2017.
734. Belan, A.; Bolte, J.; Fauve, A.; Gourcy, J. G.; Veschambre, H. *J. Org. Chem.* **1987,** *52,* 256.
735. Stokes, T. M.; Oehlschlager, A. C. *Tetrahedron Lett.* **1987,** *28,* 2091.
736. Wang, Y.-F.; Lalonde, J. J.; Momongan, M.; Bergbreiten, D. E.; Wong, C.-H. *J. Am. Chem. Soc.* **1988,** *110,* 7200.
737. Afonso, C. M.; Teresa Barros, M.; Godinho, L.; Maycock, C. D. *Tetrahedron Lett.* **1989,** *30,* 2707.
738. Thompson, C. M.; Frick, J. A.; Woytowicz, C. E. *Synth. Commun.* **1988,** *18,* 889.
739. Pierce, Jr., H. D.; Pierce, A. M.; Johnston, B. D.; Oehlschlager, A. C.; Borden, J. H. *J. Chem. Ecol.* **1988,** *14,* 2169.
740. Kocieński, P.; Dixon, N. J.; Wadman, S. *Tetrahedron Lett.* **1987,** *28,* 2091.
741. Johnston, B. D.; Oehlschlager, A. C. *J. Org. Chem.* **1986,** *51,* 760.
742. Mori, K.; Puapoomchareon, P. *Liebigs Ann. Chem.* **1990,** 159.
743. Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Satoh, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989,** *111,* 314.
744. Negishi, T.; Uchida, M.; Tamaki, Y.; Mori, K.; Ishiwatari, T.; Asano, G.; Nakagawa, K. *Appl. Entomol. Zool.* **1980,** *15,* 328.
745. Bierl-Leonhardt, B. A.; Moreno, D. S.; Schwarz, M.; Forster, H. S.; Plimmer, J. R.; DeVilbiss, E. D. *J. Chem. Ecol.* **1982,** *8,* 689.
746. Uchida, M.; Nakagawa, K.; Negishi, T.; Asano, S.; Mori, K. *Agric. Biol. Chem.* **1981,** *45,* 369.
747. Baeckström, P.; Björkling, F.; Högberg, H.-E.; Norin, T. *Acta Chem. Scand.* **1984,** *B38,* 779.

748. Fall, Y.; Bac, N. V.; Langlois, Y. *Tetrahedron Lett.* **1986,** *27,* 3611.
749. Skattebøl, L.; Stenstrøm, Y. *Acta Chem. Scand.* **1989,** *43,* 93.
750. Ishchenko, R. E.; Veshelovskii, V. V.; Moiseenkov, A. M.; Cheskis, B. A.; Kovalev, V. G. *Khim. Prirod. Soed.* **1989,** 132.
751. Cohen, T.; Bhupathy, M. *Acc. Chem. Res.* **1989,** *22,* 152.
752. Mori, K.; Ueda, H. *Tetrahedron.* **1981,** *37,* 2581.
753. Nakagawa, N.; Mori, K. *Agric. Biol. Chem.* **1984,** *48,* 2799.
754. Terashima, S.; Tseng, C. C.; Hayashi, M.; Koga, K. *Chem. Pharm. Bull.* **1979,** *27,* 758.
755. Larchevêque, Petit, Y. *Bull. Soc. Chim. Frane.* **1989,** 130.
756. Kuwahara, Y.; Sakuma, L. *Agric. Biol. Chem.* **1982,** *46,* 1855.
757. Gieselmann, M. J.; Rice, R. E.; Jones, R. A.; Roelofs, W. L.; *J. Chem. Ecol.* **1979,** *5,* 89.
758. Anderson, R. J.; Gieselmann, M. J.; Chinn, H. R.; Adams, K. G.; Henrick, C. A.; Rice, R. E.; Roelofs, W. L.; *J. Chem. Ecol.* **1981,** *7,* 695.
759. Anderson, R. J.; Chinn, H. R.; Gill, K.; Henrick, C. A.; *J. Chem. Ecol.* **1979,** *5,* 919.
760. Alderdice, M.; Spino, C.; Weiler, L. *Tetrahedron Lett.* **1984,** *25,* 1643.
761. Novák, L.; Poppe, L.; Szántay, Cs.; Szabó, E. *Synthesis.* **1985,** 939.
762. Lombardo, D. A.; Weedon, A. C. *Tetrahedron Lett.* **1986,** *27,* 5555.
763. Dhokte, U. P.; Rao, A. S. *Synth. Commun.* **1988,** *18,* 811.
764. Odinokov, V. N.; Kookovinich, O. S.; Zaynoollin, R. A.; Tzigleetzeva, E. Yu.; Sultanmooratova, V. R.; Vesyelovskii, V. V.; Dragan, B. A.; Rubinskaya, T.Ya.; Cheskis, B.A.; Moiseenkov, A. M.; Tolstikov, G. A. *Khim. Prirod. Soed.* **1989,** 419.
765. Moiseenkov, A. M.; Ishchenko, R. E.; Vesyelovskii, V. V.; Odynokov, V. N.; Poloonin, E. V.; Cheskis, B. A.; Tolstikov, G. A. *Khim. Prirod. Soed.* **1989,** 422.
766. Light, D. M.; Birch, M. C. *Naturwissenschaften.* **1979,** *66,* 159.
767. Birch, M. C.; Light, D. M.; Wood, D. L.; Browne, L. E.; Silverstein, R. M.; Bergot, B. J.; Ohloff, G.; West, J. R.; Young, J. C. *J. Chem. Ecol.* **1980,** *6,* 703.
768. Mustaparta, H.; Tømmerås, B. Å.; Lanier, G. N.; *J. Chem. Ecol.* **1985,** *11,* 999.
769. Miller, D. R.; Borden, J. H.; Slessor, K. N. *J. Chem. Ecol.* **1989,** *15,* 233.
770. Schlyter, F.; Birgersson, G.; Leufven, A. *J. Chem. Ecol.* **1989,** *15,* 2263.
771. Cazes, B.; Guittet, E.; Julia, S.; Ruel, O.*J. Organometal. Chem.* **1979,** *177,* 67.
772. Cheskis, B. A.; Lebedeva, K. V.; Koroleva, T. I.; Kondratev, Y. A.; *Khemoretseptsia Nasekomykh.* **1979,** *4,* 129.
773. Masaki, Y.; Hashimoto, K.; Sakuma, K.; Kaji, K. *J. Chem. Soc., Chem. Commun.* **1979,** 855.
774. Masaki, Y.; Hashimoto, K.; Sakuma, K.; Kaji, K. *J. Chem. Soc. Perkin Trans. 1.* **1984,** 1289.
775. Snider, B. B.; Rodini, D. J. *Tetrahedron Lett.* **1980,** *21,* 1815.
776. Wilson, S. R.; Phillips, L. R.; Natalie, Jr., K. J.; *J. Am. Chem. Soc.,* **1979,** *101,* 3340.
777. Halazy, S.; Krief, A. *Tetrahedron Lett.* **1980,** *21,* 1997.
778. Sakurai, H.; Hosomi, A.; Saito, M.; Sasaki, K.; Iguchi, H.; Sasaki, J.; Araki, Y. *Tetrahedron.* **1983,** *39,* 883.
779. Hosomi, A.; Araki, Y.; Sakurai, H. *J. Org. Chem.* **1983,** *48,* 3122.
780. Rousseau, G.; Drouin, J. *Tetrahedron.* **1983,** *39,* 2307.
781. Bubnov, Y. N.; Etinger, M. Yu. *Tetrahedron Lett.* **1985,** *26,* 2797.

782. Semmelhack, M. F.; Fewkes, E. J. *Tetrahedron Lett.* **1987,** *28,* 1497.
783. Vorskanyan, S. A.; Fobanyan, Zh. A.; Badaryan, Sh. O. *Arm. Khim. Zh.* **1987,** *40,* 181.
784. Cheskis B. A.; Moiseenkov, A. M. *Dokl. Akad. Nauk SSSR.* **1982,** *265,* 1410.
785. Nomoto, T.; Takayama, H. *J. Chem. Soc., Chem. Commun.* **1989,** 295.
786. Brown, H. C.; Randad, R. S. *Tetrahedron.* **1990,** *46,* 4463.
787. Baeckström, P.; Björkling, F.; Högberg, H.-E.; Norin, T. *Acta Chem. Scand.* **1983,** *B37,* 1.
788. Kubo, I.; Komatsu, S.; Iwagawa, T.; Wood, D. L. *J. Chromatog.* **1986,** *363,* 309.
789. Ikeda, N.; Arai, I.; Yamamoto, H. *J. Am. Chem. Soc.* **1986,** *108,* 483.
790. Brown, H. C.; Randall, R. S. *Tetrahedron Lett.* **1990,** *31,* 455.
791. Bubnov, Y. N.; Etinger, M. Yu.; *Izv. Akad. Nauk SSSR, Ser. Khim.* **1988,** 1687.
792. Franck-Neumann, M.; Martina, D.; Heitz, M.-P. *Tetrahedron Lett.* **1989,** *30,* 6679.
793. Mori, K.; Takikawa, H. *Tetrahedron.* **1991,** *47,* 2163.
794. Francke, W.; Pan, M.-L.; König, W. A.; Mori, K.; Puapoomchareon, P.; Heuer, H.; Vité, J. P. *Naturwissenschaften.* **1987,** *74,* 343.
795. Rosini, G.; Salomoni, A.; Squarcia, F. *Synthesis.* **1979,** 942.
796. Negishi, E.; Boardman, L. D.; Tour, J. M.; Sawada, H.; Rand, C. L. *J. Am. Chem. Soc.* **1983,** *105,* 6344.
797. Negishi, E.; Boardman, L. D.; Sawada, H.; Bagheri, V.; Stoll, A. T.; Tour, J. M.; Rand, C. L. *J. Am. Chem. Soc.* **1988,** *110,* 5383.
798. Sonawane, H. R.; Nanjundiah, B. S.; Kumar, M. U. *Tetrahedron Lett.* **1984,** *25,* 2245.
799. Rømming, C.; Skattebøl, L.; Stenstrøm, Y. *Acta Chem. Scand.* **1986,** *40B,* 434.
800. Rosini, G.; Marotta, E.; Petrini, M.; Ballini, R. *Tetrahedron.* **1985,** *41,* 4633.
801. Rosini, G.; Geier, M.; Marotta, E.; Petrini, M.; Ballini, R. *Tetrahedron.* **1986,** *42,* 6027.
802. Aljancic-Solaja, I.; Rey, M.; Dreiding, A. S. *Helv. Chim. Acta.* **1987,** *70,* 1302.
803. Kim, D.; Jang, Y. M.; Kim, I. O.; Park, S. W. *J. Chem. Soc., Chem. Commun.* **1988,** 760.
804. Kametani, T.; Kajiwara, M.; Fukumoto, K. *Tetrahedron.* **1974,** *30,* 1053.
805. Kametani, T.; Toya, T.; Ueda, K.; Tsubuki, M.; Honda, T. *J. Chem. Soc., Perkin Trans. 1.* **1988,** 2433.
806. Grandquillot, J.-C.; Rouessac, F. *Chemica Scripta.* **1989,** *29,* 99.
807. Webster, F. X.; Silverstein, R. M. *J. Org. Chem.* **1986,** *51,* 5226.
808. Webster, F. X.; Millar, J. G.; Silverstein, R. M. *Tetrahedron Lett.* **1986,** *27,* 4941.
809. Mori, K.; Nagano, E. *Liebigs Ann. Chem.* **1991,** 341.
810. Jones, J. B.; Finch, M. A. W.; Jakovac, I. J.; *Can. J. Chem.* **1982,** *60,* 2007.
811. Mori, K.; Miyake, M. *Tetrahedron.* **1987,** *43,* 2229.
812. Dickens, J. C.; Mori, K. *J. Chem. Ecol.* **1989,** *15,* 517.
813. Mori, K.; Tamada, S.; Hedin, P. A. *Naturwissenschaften.* **1978,** *65,* 653.
814. Meyers, A. I.; Fleming, S. A. *J. Am. Chem. Soc.* **1986,** *108,* 306.
815. Demuth, M.; Polomer, A.; Sluma, H.-D.; Dey, A. K.; Krüger, C.; Tsay, Y.-H.; *Angew. Chem. Int. Ed. Engl.* **1986,** *25,* 1117.
816. Bierl-Leonhardt, B. A.; Moreno, D. S.; Schwarz, M.; Fargerlund, J.; Plimmer, J. R. *Tetrahedron Lett.* **1981,** *22,* 389.

817. Gaoni, Y. *Tetrahedron Lett.* **1982,** *23,* 5215.
818. Gaoni, Y. *Tetrahedron Lett.* **1981,** *22,* 4339.
819. Carlsen, P. H. J.; Odden, W. *Acta Chem. Scand.* **1984,** *B38,* 501.
820. Odinkov, V. N.; Kukovinets, O. S.; Isakova, L. A.; Zainulin, R. A.; Moiseenkov, A. M.; Tolstikov, G. A. *Dokl Akad. Nauk SSSR.* **1984,** *279,* 398.
821. Wolk, J. L.; Goldschmidt, Z.; Dunkelblum, E. *Synthesis.* **1986,** 347.
822. Dunkelblum, E.; Ben-Dov, Y.; Goldschmidt, Z.; Wolk, J. L.; Somekh, L. *J. Chem. Ecol.* **1987,** *13,* 863.
823. Serebryakov, E. P.; Sooslova, L. M.; Moiseenkov, A. M.; Shavirin, S. V. Zaikuna, N. V.; Sorotzinskaya, A. M.; Kovalev, B. G. *Isv. Akad. Nauk SSSR, Ser. Khim.* **1986,** 1603.
824. Barton, D. H. R.; Ozbalik, N.; Schmitt, M. *Tetrahedron Lett.* **1989,** *30,* 3263.
825. Kitamura, M.; Kasahara, I.; Manabe, K.; Noyori, R.; Takaya, H. *J. Org. Chem.* **1988,** *53,* 708.
826. Mori, K.; Ogoche, J. I. J. *Liebigs Ann. Chem.* **1988,** 903.
827. Libby, L. M.; Oehlschlager, A. C.; Ryker, L. C. *J. Chem. Ecol.* **1983,** *9,* 1533.
828. Posner, G. H. *Acc. Chem. Res.* **1987,** *20,* 70.
829. Mori, K.; Hazra, B. G.; Pfeiffer, R. J.; Gupta, A. K.; Lindgren, B. S. *Tetrahedron.* **1987,** *43,* 2249.
830. Masaki, Y.; Hashimoto, K.; Sakuma, K.; Kaji, K. *Tetrahedron Lett.* **1982,** *23,* 1481.
831. Masaki, Y.; Hashimoto, K.; Sakuma, K.; Kaji, K. *Bull. Chem. Soc. Japan.* **1984,** *57,* 3466.
832. Mori, K.; Itou, M. *Liebigs Ann. Chem.* **1989,** 969.
833. Fujisawa, T.; Sato, T.; Kawara, T.; Noda, A. *Tetrahedron Lett.* **1982,** *23,* 3193.
834. Julia, M.; Verpeaux, J.-N. *Tetrahedron.* **1983,** *39,* 3289.
835. Gramatica, P.; Gardina, G.; Speranza, G.; Manitto, P. *Chem. Lett.* **1985,** 1395.
836. Masaki, Y.; Sakuma, K.; Kaji, K. *Chem. Lett.* **1980,** 1061.
837. Anderson, R. J.; Adams, K. G.; Chinn, H. R.; Henrick, C. A. *J. Org. Chem.* **1980,** *45,* 2229.
838. Baudouy, R.; Maliverney, C. *Tetrahedron.* **1988,** *44,* 471.
839. Becker, D.; Sahali, Y. *Tetrahedron.* **1988,** *44,* 4541.
840. Dragan, V. A.; Veselovskii, V. V.; Moiseenkov, A. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1989,** 1143.
841. Cooke, Jr., M. P.; Burman, D. L. *J. Org. Chem.* **1982,** *47,* 4955.
842. Celebuski, J.; Rosenblum, M. *Tetrahedron.* **1985,** *41,* 5741.
843. Caine, D.; Crews, E. *Tetrahedron Lett.* **1984,** *25,* 5359.
844. Hutchinson, J. H.; Money, T. *Can. J. Chem.* **1985,** *63,* 3182.
845. Baudouy, R.; Prince, P. *Tetrahedron.* **1989,** *45,* 2067.
846. Whittaker, M.; McArthur, C. R.; Leznoff, C. C. *Can. J. Chem.* **1985,** *63,* 2844.
847. Oppolzer, W.; Stevenson, T. *Tetrahedron Lett.* **1986,** *27,* 1139.
848. Mangeney, P.; Alexakis, A.; Normant, J. F. *Tetrahedron Lett.* **1987,** *28,* 2363.
849. Cohen, T.; Piccolino, E.; McCullough, D. W.; cited as Ref. 87 of Ref. 751.
850. Anderson, R. J.; Henrick, C. A. *J. Chem. Ecol.* **1979,** *5,* 773.
851. Suguro, T.; Roelofs, W. L.; Mori, K. *Agric. Biol. Chem.* **1981,***45,* 2509.
852. Masuda, S.; Kuwahara, S.; Suguro, T.; Mori, K. *Agric. Biol. Chem.* **1981,** *45,* 2515.

853. Mori, K.; Kuwahara, S. *Tetrahedron.* **1982,** *38,* 521.

854. Roelofs, W. L.; Gieselmann, M. J.; Mori, K.; Moreno, D. S.; *Naturwissenschaften.* **1982,** *69,* 348.

855. Alvarez, E.; Cuvigny, T.; Harvé du Penhoat, C.; Julia, M. *Tetrahedron.* **1988,** *44,* 119.

856. Millar, J. G. *Tetrahedron Lett.* **1989,** *30,* 4913.

857. Heath, R. R.; McLaughlin, J. R.; Tumlinson, J. H.; Ashley, T. R.; Doolittle, R. E. *J. Chem. Ecol.* **1979,** *5,* 941.

858. Heath, R. R.; Doolittle, R. E.; Sonnet, P. E.; Tumlinson, J. H. *J. Org. Chem.* **1980,** *45,* 2910.

859. Hall, D. R.; Cork, A.; Lester, R.; Nesbitt, B. F.; Zagatti, P. *J. Chem. Ecol.* **1987,** *13,* 1575.

860. Mori, K.; Harada, H.; Zagatti, P.; Cork, A.; Hall, D. R. *Liebigs Ann. Chem.* **1991,** 259.

861. Baker, R.; Borges, M.; Cooke, N. G.; Herbert, R. H. *J. Chem. Soc., Chem. Commun.* **1987,** 414.

862. Aldrich, J. R.; Lusby, W. R.; Marron, B. E.; Nicolaou, K. C.; Hoffmann, M. P.; Wilson, L. T. *Naturwissenschaften.* **1989,** *76,* 173.

863. Marron, B. E.; Nicolaou, K. C. *Synthesis.* **1989,** 537.

864. Booth, D. C.; Phillips, T. W.; Claesson, A.; Silverstein, R. M.; Lanier, G. N.; West, J. R.; *J. Chem. Ecol.* **1983,** *9,* 1.

865. Phillips, T. W.; West, J. R.; Foltz, J. L.; Silverstein, R. M.; Lanier, G. N. *J. Chem. Ecol.* **1984,** *10,* 1417.

866. Webster, F. X.; Zeng, X.-N.; Silverstein, R. M. *J. Chem. Ecol.* **1987,** *13,* 1725.

867. Dickens, J. C.; Prestwich, G. D. *J. Chem. Ecol.* **1989,** *15,* 529.

868. Mandai, T.; Mizobuchi, K.; Kawada, M.; Otera, J. *J. Org. Chem.* **1984,** *49,* 3403.

869. Ghosh, A.; Banerjee, U. K.; Venkateswaran, R. V. *J. Chem. Res.* (*S*). **1986,** 148.

870. Nomura, M.; Fujihara, Y. *Yukagaku.* **1987,** *36,* 515.

871. Harris, F. L.; Weiler, L. *Tetrahedron Lett.* **1987,** *28,* 2941.

872. Negishi, E.; Zhang, Y.; Bagheri, V. *Tetrahedron Lett.* **1987,** *28,* 5793.

873. Zagatti, P.; Kunesch, G.; Ramiandrasoa, F.; Malosse, C.; Hall, D. R.; Lester, R.; Nesbitt, B. F. *J. Chem. Ecol.* **1987,** *13,* 1561.

874. Schreiber, S. L.; Santini, C. *J. Am. Chem. Soc.* **1984,** *106,* 4038.

875. Hauptmann, H.; Mühlbauer, G.; Walker, N. P. C. *Tetrahedron Lett.* **1986,** *27,* 1315.

876. Takahashi, T.; Kanda, Y.; Nemoto, H.; Kitamura, K.; Tsuji, J.; Fukazawa, Y. *J. Org. Chem.* **1986,** *51,* 3393.

877. Cauwberghs, S. G.; De Clercq, P. J. *Tetrahedron Lett.* **1988,** *29,* 6501.

878. Kitahara, T.; Mori, M.; Koseki, K.; Mori, K. *Tetrahedron Lett.* **1986,** *27,* 1343.

879. Kitahara, T.; Mori, M.; Mori, K. *Tetrahedron.* **1987,** *43,* 2689.

880. Kuwahara, S.; Mori, K. *Heterocycles.* **1989,** *28,* 167.

881. Kuwahara, S.; Mori, K. *Tetrahedron.* **1990,** *46,* 8075.

882. Talman, E.; Verwiel, P. E. J.; Ritter, F. J.; Persoons, C. J. *Isr. J. Chem.* **1978,** *17,* 227.

883. Persoons, C. J.; Verwiel, P. E. J.; Ritter, F. J.; Nooyen, W. J. *J. Chem. Ecol.* **1982,** *8,* 439.

884. Mori, K.; Igarashi, Y. *Tetrahedron.* **1990,** *46,* 5101.

885. Kuwahara, S.; Mori, K. *Tetrahedron Lett.* **1989,** *30,* 7447.

886. Persoons, C. J.; Ritter, F. J.; Verwiel, P. E. J.; Hauptmann, H.; Mori, K. *Tetrahedron Lett.* **1990,** *31,* 1747.
887. Mori, K.; Kuwahara, S.; Igarashi, Y. *Pure Appl. Chem.* **1990,** *62,* 1307.
888. Hauptmann, H.; Mühlbauer, G.; Sass, H. *Tetrahedron Lett.* **1986,** *27,* 6189.
889. Still, W. C. *J. Am. Chem. Soc.* **1979,** *101,* 2493.
890. Shizuri, Y.; Matsunaga, K.; Tamaki, K.; Yamaguchi, S.; Yamamura, S. *Tetrahedron Lett.* **1988,** *29,* 1971.
891. Takahashi, T.; Yamashita, Y.; Doi, T.; Tsuji, J.; Fukazawa, Y. *30th Symposium on the Chemistry of Natural Products, Fukuoka, Symposium Papers.* **1988,** 410.
892. Macdonald, T. L.; Delahunty, C. M.; Sawyer, J. S. *Heterocycles.* **1987,** *25,* 305.
893. Nishino, C.; Kobayashi, K.; Fukushima, M. *Comp. Biochem. Physiol.* **1989,** *92C,* 193.
894. Biendl, M.; Hauptmann, H.; Sass, H. *Tetrahedron Lett.* **1989,** *30,* 2367.
895. Tanaka, K.; Ohsawa, K.; Honda, H.; Yamamoto, I. *J. Pesticide Sci.* **1981,** *6,* 75.
896. Tanaka, K.; Ohsawa, K.; Honda, H.; Yamamoto, I. *J. Pesticide Sci.* **1982,** *7,* 535.
897. Kang, S.-K.; Lee, D.-H. *Bull. Korean Chem. Soc.* **1987,** *8,* 487.
898. Mori, K.; Ito, T.; Tanaka, K.; Honda, H.; Yamamoto, I. *Tetrahedron.* **1983,** *39,* 2303.
899. Sum, F. W.; Weiler, L. *Tetrahedron. 37,* Supplement No. 9, **1981,** 303.
900. Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980,** *102,* 5979.
901. Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981,** *22,* 2575.
902. Kunesch, G.; Zagatti, P.; Lallemand, J. Y.; Debal, A.; Vigneron, J. P. *Tetrahedron Lett.* **1981,** *22,* 5271.
903. Vigneron, J. P.; Méric, R.; Larchevêque, M.; Debal, A.; Lallemande, J. Y.; Kunesch, G.; Zagatti, P.; Gallois, M. *Tetrahedron.* **1984,** *40,* 3521.
904. Chakraborty, T. K.; Chandrasekaran, S. *Tetrahedron Lett.* **1984,** *25,* 2891.
905. Iriye, R.; Yoshifuji, T.; Takeda, N.; Tatematsu, A. *Agric. Biol. Chem.* **1984,** *48,* 2923.
906. Iriye, R. *Agric. Biol. Chem.* **1985,** *49,* 2775.
907. Dziadulewicz, E.; Gallagher, T. *Tetrahedron Lett.* **1985,** *26,* 4547.
908. Dziadulewicz, E.; Hodgson, D.; Gallagher, T. *J. Chem. Soc., Perkin Trans. 1.* **1988,** 3367.
909. Fang, J.-M.; Hong, B.-C. *Synth. Commun.* **1986,** *16,* 523.
910. Frauenrath, H.; Philipps, T. *Tetrahedron.* **1986,** *42,* 1135.
911. Jefford, C. W.; Sledeski, A. W.; Boukouvalas, J. *Tetrahedron Lett.* **1987,** *28,* 949.
912. Barua, N. C.; Schmidt, R. R. *Synthesis.* **1986,** 891.
913. Yoda, H.; Shirakawa, K.; Takabe, K. *Chem. Lett.* **1989,** 1391.
914. Mori, K.; Umemura, T. *Tetrahedron Lett.* **1982,** *23,* 3391.
915. Uematsu, T.; Umemura, T.; Mori, K. *Agric. Biol. Chem.* **1983,** *47,* 597.
916. Vigneron, J. P.; Méric, R.; Larchevêque, M.; Debal, A.; Kunesch, G.; Zagatti, P.; Gallois, M. *Tetrahedron Lett.* **1982,** *23,* 5051.
917. Yokoyama, Y.; Yunokihara, M. *Chem. Lett.* **1983,** 1245.
918. Suzuki, K.; Ohkuma, T.; Tsuchihashi, G. *Tetrahedron Lett.* **1985,** *26,* 861.
919. Ortuño, R. M.; Mercé, R.; Font, J. *Tetrahedron Lett.* **1986,** *27,* 2519.
920. Ortunño, R. M.; Mercé, R.; Font, J. *Tetrahedron.* **1987,** *43,* 4497.
921. Larchevêque, M.; Tamagnan, G.; Petit, Y. *J. Chem. Soc., Chem. Commun.* **1989,** 31.
922. Whittaker, M. *Chem. and Ind.* **1986,** 463.

923. Davies, H. G.; Roberts, S. M.; Wakefield, B. J.; Winders, J. A. *J. Chem. Soc., Chem. Commun.* **1985,** 1166.

924. Butt, S.; Davies, H. G.; Dawson, M. J.; Lawrence, G. C.; Leaver, J.; Roberts, S. M.; Turner, M. K.; Wakefield, B. J.; Wall, W. F.; Winders, J. A. *J. Chem. Soc., Perkin Trans. 1.* **1987,** 903.

925. Yadav, J. S.; Gadgil, V. R. *J. Chem. Soc., Chem. Commun.* **1989,** 1824.

926. Bloch, R.; Seck, M. *Tetrahedron.* **1989,** *45,* 3731.

927. Sakan, T.; Isoe, S.; Hyeon, S. B. *Tetrahedron Lett.* **1967,** 1623.

928. Chakraborty, T. K.; Chandrasekaran, S. *Tetrahedron Lett.* **1984,** *25,* 2895.

929. Isoe, S.; Hyeon, S. B.; Katsumura, S.; Sakan, T. *Tetrahedron Lett.* **1972,** 2517.

930. Eschenmoser, W.; Uebelhart, P.; Eugster, C. H. *Helv. Chim. Acta.* **1982,** *65,* 353.

931. Kienzle, F.; Mayer, H.; Minder, R. E.; Thommen, H. *Helv. Chim. Acta.* **1978,** *61,* 2616.

932. Leuenberger, H. G. W.; Boguth, W.; Widmer, E.; Zell, R. *Helv. Chim. Acta.* **1976,** *59,* 1832.

933. Sato, T.; Funabora, M.; Watanabe, M.; Fujisawa, T. *Chem. Lett.* **1985,** 1391.

934. Mori, K.; Nakazono, Y. *Tetrahedron.* **1986,** *42,* 283.

935. Strekowski, L.; Visnick, M.; Battiste, M. A. *J. Org. Chem.* **1986,** *51,* 4836.

936. Battiste, M. A.; Strekowski, L.; Vanderbilt, D. P.; Visnick, M.; King, R. W.; Nation, J. L. *Tetrahedron Lett.* **1983,** *24,* 2611.

937. Stokes, J. B.; Uebel, E. C.; Warthen, Jr., J. D.; Jacobson, M.; Flippen-Anderson, J. L.; Gilardi, R.; Spishakoff, L. M.; Wilzer, K. R. *J. Agric. Food Chem.* **1983,** *31,* 1962.

938. Strekowski, L.; Battiste, M. A. *Tetrahedron Lett.* **1981,** *22,* 279.

939. Saito, A.; Matsushita, H.; Kaneko, H. *Chem. Lett.* **1984,** 729.

940. Mori, K.; Nakazono, Y. *Liebigs Ann. Chem.* **1988,** 167.

941. Robacker, D. C.; Hart, W. G. *Entomol. Exp. Appl.* **1985,** *39,* 103.

942. Robacker, D. C. *J. Chem. Ecol.* **1988,** *14,* 1715.

943. Chuman, T.; Sivinski, J.; Heath, R. R.; Galkins, C. O.; Tumlinson, J. H.; Battiste, M. A.; Wydra, R. L.; Strekowski, L.; Nation, J. L. *Tetrahedron Lett.* **1988,** *29,* 6561.

944. Battiste, M. A.; Rocca, J. R.; Wydra, R. L.; Tumlinson, J. H.; Chuman, T. *Tetrahedron Lett.* **1988,** *29,* 6565.

945. Dawson, G. W.; Griffiths, D. C.; Janes, N. F.; Mudd, A.; Pickett, J. A.; Wadhams, L. J.; Woodcock, C. M. *Nature.* **1987,** *325,* 614.

946. Dawson, G. W.; Janes, N. F.; Mudd, A.; Pickett, J. A.; Slawin, A. M. Z.; Wadhams, L. J.; Williams, D. J. *Pure Appl. Chem.* **1989,** *61,* 555.

947. Dawson, G. W.; Griffiths, D. C.; Merritt, L. A.; Mudd, A.; Pickett, J. A.; Wadhams, L. J.; Woodcock, C. M. *Entomol. Exp. Appl.* **1988,** *48,* 91.

948. McElvain, S. M.; Bright, R. D.; Johnson, P. R. *J. Am. Chem. Soc.* **1941,** *63,* 1558.

949. Thomas, A. F. In *The Total Synthesis of Natural Products;* John Wiley, New York; Ap-Simon, J. Ed.; **1973,** *2,* 69; *Ibid.* **1981,** *4,* 496; *Ibid.* **1988,** *7,* 339.

950. Schreiber, S. L.; Meyers, H. V.; Wiberg, K. B. *J. Am. Chem. Soc.* **1986,** *108,* 8274.

951. Sakurai, K.; Ikeda, K.; Mori, K. *Agric. Biol. Chem.* **1988,** *52,* 2369.

952. Moriya, T.; Honda, Y.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1988,** *29,* 6947.

953. Cheskis, B. A.; Shapiro, N. A.; Moiseenkov, A. M. *Dokl. Akad. Nauk SSSR.* **1988,** *303,* 1387.

954. Kubo, I.; Matsumoto, T.; Wagner, D. L.; Shoolery, J. M. *Tetrahedron Lett.* **1985,** *26,* 563.

955. Uchino, K.; Yamagiwa, Y.; Kamikawa, T.; Kubo, I. *Tetrahedron Lett.* **1985,** *26,* 1319.

956. Hayashi, S.; Mori, K. *Agric. Biol. Chem.* **1986,** *50,* 3209.

957. Yadav, J. S.; Rao, E. S. *Synth. Commun.* **1988,** *18,* 2315.

958. Francke, W.; Mackenroth, W.; Schröder, W.; Schulz, S.; Tengö, J.; Engels, E.; Engels, W.; Kuttmann, R.; Schneider, D. *Z. Naturforsch.* **1985,** *40c,* 145.

959. Mori, K.; Kisida, H. *Tetrahedron.* **1986,** *42,* 5281.

960. Francke, W. *Pure Appl. Chem.* **1989,** *61,* 539.

961. Mori, K.; Puapoomchareon, P. *Liebigs Ann. Chem.* **1989,** 1261.

962. Klimetzek, P.; Bartels, J.; Francke, W. *J. Appl. Entomol.* **1989,** *107,* 518.

963. Mori, K.; Puapoomchareon, P. *Liebigs Ann. Chem.* **1988,** 175.

964. Francke, W.; Mackenroth, W.; Schröder, W.; Levinson, A. R. *Les Colloques de l'INRA.* **1982,** *7,* (Les Médiateurs Chimiques), 85.

965. Redlich, H.; Jiang Xiang-jun; Paulsen, H.; Francke, W. *Tetrahedron Lett.* **1981,** *22,* 5043.

966. Redlich, H.; Jiang Xiang-jun, *Liebigs Ann. Chem.* **1982,** 717.

967. Mori, K.; Ebata, T.; Takechi, S. *Tetrahedron.* **1984,** *40,* 1761.

968. Kuwahara, Y.; Fukami, H.; Howard, R.; Ishii, S.; Matsumura, F.; Burkholder, W. E. *Tetrahedron.* **1978,** *34,* 1769.

969. Sakakibara, M.; Mori, K. *Tetrahedron Lett.* **1979,** 2401.

970. Ansell, J. M.; Hassner, A. *Tetrahedron Lett.* **1979,** 2497.

971. Mori, K.; Ebata, T.; Sakakibara, M. *Tetrahedron.* **1981,** *37,* 709.

972. Ono, M.; Onishi, I.; Kuwahara, Y.; Chuman, T.; Kato, K. *Agric. Biol. Chem.* **1983,** *47,* 1933.

973. Hoffmann, R. W.; Ladner, W. *Tetrahedron Lett.* **1979,** 4653.

974. Hoffmann, R. W.; Ladner, W.; Steinbach, K.; Massa, W.; Schmidt, R.; Snatzke, G. *Chem. Ber.* **1981,** *114,* 2786.

975. Mori, K.; Ebata, T. *Tetrahedron.* **1986,** *42,* 4413.

976. Kodama, H.; Ono, M.; Kohno, M.; Ohnishi, A. *J. Chem. Ecol.* **1987,** *13,* 1859.

977. White, P. R.; Birch, M. C. *J. Chem. Ecol.* **1987,** *13,* 1695.

978. Kodama, H.; Ono, M.; Kohno, M.; Ohnishi, A. *J. Chem. Ecol.* **1987,** *13,* 1871.

979. Mori, K.; Ebata, T. *Tetrahedron.* **1986,** *42,* 4685.

980. Chuman, T.; Mochizuki, K.; Kato, K.; Ono, M.; Okubo, A. *Agric. Biol. Chem.* **1983,** *47,* 1413.

981. Chuman, T.; Mochizuki, K.; Mori, M.; Kohno, M.; Kato, K.; Noguchi, M. *J. Chem. Ecol.* **1985,** *11,* 417.

982. Ebata, T.; Mori, K. *Agric. Biol. Chem.* **1987,** *51,* 2925.

983. Francke, W.; Schulz, S.; Sinnwell, V.; König, W. A.; Roisin, Y. *Liebigs Ann. Chem.* **1989,** 1195.

984. Mundy, B. P.; Dirks, G. W.; Larter, R. M.; Craig, A. C.; Lipkowitz, K. B.; Carter, J. *J. Org. Chem.* **1981,** *46,* 4005.

985. Payne, T. L.; Richerson, J. V.; Dickens, J. C.; West, J. R.; Mori, K.; Berisford, C. W.; Hedden, R. L.; Vité, J. P.; Blum, M. S. *J. Chem. Ecol.* **1982,** *11,* 1359.

986. Dickens, J. C.; Payne, T. L.; Ryker, L. C.; Rudinsky, J. A. *J. Chem. Ecol.* **1982,** *8,* 873.

987. Sato, T.; Kaneko, H.; Yamaguchi, S. *J. Org. Chem.* **1980,** *45,* 3778.
988. Sum, P.-E.; Weiler, L. *Can. J. Chem.* **1979,** *57,* 1475.
989. Wilson, R. M.; Rekers, J. W. *J. Am. Chem. Soc.* **1981,** *103,* 206.
990. Utaka, M.; Makino, H.; Oota, Y.; Tsuboi, S.; Takeda, A. *Tetrahedron Lett.* **1983,** *24,* 2567.
991. Joshi, N. N.; Mandapur, V. R.; Chadha, M. S. *J. Chem. Soc., Perkin Trans. 1.* **1983,** 2963.
992. Serebryakov, E. P.; Gamalevich, G. D. *Izv. Akad. Nauk SSSR. Ser. Khim.* **1985,** 1890.
993. Imamoto, T.; Takeyama, T.; Yokoyama, M. *Tetrahedron Lett.* **1984,** *25,* 3225.
994. Hagiwara, H.; Uda, H. *J. Chem. Soc., Perkin Trans. 1.* **1985,** 283.
995. Kongkathip, B.; Sookkho, R.; Kongkathip, N. *Chem. Lett.* **1985,** 1849.
996. Jarosz, S.; Hicks, D. R.; Fraser-Reid, B. *J. Org. Chem.* **1982,** *47,* 935.
997. Trinh, M.-C.; Florent, J.-C.; Monneret, C. *J. Chem. Soc., Chem. Commun.* **1987,** 615.
998. Trinh, M.-C.; Florent, J.-C.; Monneret, C. *Tetrahedron.* **1988,** *44,* 6633.
999. Ohira, S.; Ishi, S.; Shinohara, K.; Nozaki, H. *Tetrahedron Lett.* **1990,** *31,* 1039.
1000. Barner, R.; Hübscher, J. *Helv. Chim. Acta.* **1983,** *66,* 880.
1001. Naef, R.; Seebach, D. *Liebigs Ann. Chem.* **1983,** 1930.
1002. Sakito, Y.; Mukaiyama, T. *Chem. Lett.* **1979,** 1027.
1003. Whitesell, J. K.; Buchanan, C. M. *J. Org. Chem.* **1986,** *51,* 5443.
1004. Ohwa, M.; Eliel, E. L. *Chem. Lett.* **1987,** 41.
1005. Meister, C.; Scharf, H.-D. *Liebigs Ann. Chem.* **1983,** 913.
1006. Wershofen, S.; Classen, A.; Scharf, H.-D. *Liebigs Ann. Chem.* **1989,** 9.
1007. Lee, A. W. M. *J. Chem. Soc., Chem. Commun.* **1984,** 578.
1008. Yadav, J. S.; Joshi, B. V.; Sahasrabudhe, A. B. *Synth. Commun.* **1985,** *15,* 797.
1009. Hosokawa, T.; Makabe, Y.; Shinohara, T.; Murahashi, S.-I. *Chem. Lett.* **1985,** 1529.
1010. Fuganti, C.; Grasselli, P.; Servi, S. *J. Chem. Soc., Perkin Trans. 1.* **1983,** 241.
1011. Sato, T.; Maeno, H.; Noro, T.; Fujisawa, T. *Chem. Lett.* **1988,** 1739.
1012. Ohta, H.; Kimura, Y.; Sugano, Y.; Sugai, T. *Tetrahedron.* **1989,** *45,* 5469.
1013. Vité, J. P.; Billings, R. F.; Ware, C. W.; Mori, K. *Naturwissenschaften.* **1985,** *72,* 99.
1014. Mikami, K.; Nakai, T. *Chem. Lett.* **1982,** 1349.
1015. Reddy, P. S.; Vidyasagar, V.; Yadav, J. S. *Synth. Commun.* **1984,** *14,* 197.
1016. Serebryakov, E. P.; Gamalevich, G. D.; Shechtman, R. I. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985,** 1887.
1017. Byrom, N. T.; Grigg, R.; Kongkathip, B.; Reimer, G.; Wade, A. R. *J. Chem. Soc., Perkin Trans. 1.* **1984,** 1643.
1018. Jatczak, M.; Amouroux, R.; Chastrette, M. *Tetrahedron Lett.* **1985,** *26,* 2315.
1019. Tamao, K.; Nakajo, E.; Ito, Y. *J. Org. Chem.* **1987,** *52,* 4412.
1020. Hudrlik, P. R.; Hudrlik, A. M.; Yimenu, T.; Waugh, M. A.; Nagendrappa, G. *Tetrahedron.* **1988,** *44,* 3791.
1021. Ishibashi, H.; Uehara, C.; Komatsu, H.; Ikeda, M. *Chem. Pharm. Bull.* **1987,** *35,* 2750.
1022. Hoffmann, R. W.; Kemper, B. *Tetrahedron Lett.* **1982,** *23,* 845.
1023. Hoffmann, R. W.; Kemper, B.; Metternich, R.; Lehmeier, T. *Liebigs Ann. Chem.* **1985,** 2246.

1024. Wuts, P. G. M.; Bigelow, S. S. *Synth. Commun.* **1982,** *12,* 779.
1025. Koreeda, M.; Tanaka, Y. *J. Chem. Soc., Chem. Commun.* **1982,** 845.
1026. Yamamoto, Y.; Saito, Y.; Maruyama, K. *Tetrahedron Lett.* **1982,** *23,* 4959.
1027. Koreeda, M.; Tanaka, Y. *Tetrahedron Lett.* **1987,** *28,* 143.
1028. Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980,** *102,* 6900.
1029. Cohen, T.; Bhupathy, M. *Tetrahedron Lett.* **1983,** *24,* 4163.
1030. Bhupathy, M.; Cohen, T. *Tetrahedron Lett.* **1985,** *26,* 2619.
1031. Singh, S. M.; Oehlschlager, A. C. *Can. J. Chem.* **1988,** *66,* 209.
1032. Danishefsky, S. J.; Pearson, W. H.; Harvey, D. F.; Maring, C. J.; Springer, J. P. *J. Am. Chem. Soc.* **1985,** *107,* 1256.
1033. Meister, C.; Shen, Z.-P.; Scharf, H.-D. *Liebigs Ann. Chem.* **1984,** 147.
1034. Mandai, T.; Irei, H.; Kawada, M.; Otera, J. *Tetrahedron Lett.* **1984,** *25,* 2371.
1035. Sato, T.; Oikawa, T.; Kobayashi, K. *J. Org. Chem.* **1985,** *50,* 1646.
1036. Küfner, U.; Schmidt, R. R. *Synthesis.* **1985,** 1060.
1037. Giese, B.; Bartmann, D.; Hasskerl, T. *Liebigs Ann. Chem.* **1987,** 427.
1038. Wilson, R. M.; Goudar, J. S.; Sidenstick, J. E. *J. Am. Chem. Soc.* **1987,** *109,* 6895.
1039. Padwa, A.; Chinn, R. L.; Zhi, L. *Tetrahedron Lett.* **1989,** *30,* 1491.
1040. Padwa, A.; Fryxell, G. E.; Zhi, L. *J. Am. Chem. Soc.* **1990,** *112,* 3100.
1041. Bartelt, K. E.; Mundy, B. P. *Synth. Commun.* **1989,** *19,* 2915.
1042. Ramaswamy, S.; Oehlschlager, A. C. *Can. J. Chem.* **1989,** *67,* 794.
1043. Masaki, Y.; Nagata, K.; Serizawa, Y.; Kaji, K. *Tetrahedron Lett.* **1982,** *23,* 5553.
1044. Mori, K.; Seu, Y.-B. *Liebigs Ann. Chem.* **1986,** 205.
1045. Seu, Y.-B.; Mori, K. *Agric. Biol. Chem.* **1986,** *50,* 2923.
1046. Giese, B.; Rupaner, R. *Synthesis.* **1988,** 219.
1047. Achmatowicz, B.; Wicha, J. *Liebigs Ann. Chem.* **1988,** 1135.
1048. Kotsuki, H.; Kadota, I.; Ochi, N. *Tetrahedron Lett.* **1989,** *30,* 3999.
1049. Larchevêque, M.; Lalande, J. *J. Chem. Soc., Chem. Commun.* **1985,** 83.
1050. Larchevêque, M.; Lalande, J. *Bull. Soc. Chim. France.* **1987,** 116.
1051. Sato, F.; Takahashi, O.; Kato, T.; Kobayashi, Y. *J. Chem. Soc., Chem. Commun.* **1985,** 1638.
1052. Mulzer, J.; Angermann, A.; Münch, W. *Liebigs Ann. Chem.* **1986,** 825.
1053. Thomas, A. F.; Bessiere, Y. In *The Total Synthesis of Natural Products;* ApSimon, J., Ed.; John Wiley; New York, **1988;** Vol. 7.
1054. Scheffold, R. *Nachr. Chem. Tech. Lab.* **1988,** *36,* 261.
1055. Sherk, A. E.; Fraser-Reid, B. *J. Org. Chem.* **1982,** *47,* 932.
1056. Ferrier, R. J.; Prasit, P. *J. Chem. Soc., Perkin Trans. 1.* **1983,** 1645.
1057. Ferrier, R. J.; Schmidt, P.; Tyler, P. C. *J. Chem. Soc., Perkin Trans. 1.* **1985,** 301.
1058. Yusufoğlu, A.; Antons, S.; Scharf, H.-D. *J. Org. Chem.* **1986,** *51,* 3485.
1059. Yadav, J. S.; Vidyasagar, V.; Reddy, P. S. *Carbohyd. Res.* **1986,** *156,* 236.
1060. Redlich, H.; Bruns, W.; Francke, W.; Schurig, V.; Payne, T. L.; Vité, J. P. *Tetrahedron.* **1987,** *43,* 2029.
1061. Johnston, B. D.; Oehlschlager, A. C. *J. Org. Chem.* **1982,** *47,* 5384.
1062. Hatakeyama, S.; Sakurai, K.; Takano, S. *J. Chem. Soc., Chem. Commun.* **1985,** 1759.

1063. Mori, K.; Seu, Y.-B. *Tetrahedron.* **1985,** *41,* 3429.
1064. Oehlschlager, A. C.; Johnston, B. D. *J. Org. Chem.* **1987,** *52,* 940.
1065. Page, P. C. B.; Rayner, C. M.; Sutherland, I. O. *J. Chem. Soc., Chem. Commun.* **1988,** 356.
1066. Wershofen, S.; Scharf, H.-D. *Synthesis.* **1988,** 854.
1067. Yadav, J. S.; Vidyasagar, V.; Rao, E. S. *Synth. Commun.* **1989,** *19,* 605.
1068. Asami, M.; Mukaiyama, T. *Chem. Lett.* **1983,** 93.
1069. Wuts, P. G. M.; Bigelow, S. S. *J. Chem. Soc., Chem. Commun.* **1984,** 736.
1070. Chong, J. M.; Mar, E. K. *Tetrahedron.* **1989,** *45,* 7709.
1071. Nakajima, M.; Tomioka, K.; Koga, K. *Yukigoseikagaku (J. Synth. Org. Chem. Japan).* **1989,** *47,* 882.
1072. Bernardi, R.; Fuganti, C.; Graselli, P. *Tetrahedron Lett.* **1981,** *22,* 4021.
1073. Fuganti, C.; Grasselli, P.; Pedrocchi-Fantoni, G.; Servi, S.; Zirotti, C. *Tetrahedron Lett.* **1983,** *24,* 3753.
1074. Ramaswamy, S.; Oehlschlager, A. C. *J. Org. Chem.* **1989,** *54,* 255.
1075. Noda, Y.; Kikuchi, M. *Chem. Lett.* **1989,** 1755.
1076. Schultz, M.; Waldmann, H.; Vogt, W.; Kunz, H. *Tetrahedron Lett.* **1990,** *31,* 867.
1077. Wiesler, D. P.; Schwende, F. J.; Carmack, M.; Novotny, M. *J. Org. Chem.* **1984,** *49,* 882.
1078. Schwende, F. J.; Wiesler, D.; Jorgenson, J. W.; Carmack, M.; Novotny, M. *J. Chem. Ecol.* **1986,** *12,* 277.
1079. Chaquin, P.; Morizur, J.-P.; Kossanyi, J. *J. Am. Chem. Soc.* **1977,** *99,* 903.
1080. Mundy, B. P.; Bommann, W. G. *J. Org. Chem.* **1984,** *49,* 5264.
1081. Danishefsky, S. J.; Pearson, W. H.; Harvey, D. F. *J. Am. Chem. Soc.* **1984,** *106,* 2455.
1082. Wasserman, H. H.; Wolff, S.; Oku, T. *Tetrahedron Lett.* **1986,** *27,* 4909.
1083. Wasserman, H. H.; Oku, T. *Tetrahedron Lett.* **1986,** *27,* 4913.
1084. Mori, K.; Seu, Y.-B. *Tetrahedron.* **1986,** *42,* 5901.
1085. Masaki, Y.; Iwata, I.; Imaeda, T.; Oda, H.; Nagashima, H. *Chem. Pharm. Bull.* **1988,** *36,* 1241.
1086. Deschenaux, P.-F.; Kallimopoulos, T.; Jacot-Guillarmod, A. *Helv. Chim. Acta.* **1989,** *72,* 1259.
1087. Ghiringhelli, D. *Tetrahedron Lett.* **1983,** *24,* 287.
1088. Bianchi, G. *Gazz. Chim. Ital.* **1988,** *118,* 699.
1089. Naoshima, Y.; Nakamura, A.; Munakata, Y.; Kamezawa, M.; Tachibana, A. *Bull. Chem. Soc. Japan.* **1990,** *63,* 1263.
1090. Marczak, S.; Masnyk, M.; Wicha, J. *Liebigs Ann. Chem.* **1990,** 345.
1091. Bartlett, P. A.; Myerson, J. *J. Org. Chem.* **1979,** *44,* 1625.
1092. Marino, J. P.; Abe, H. *J. Org. Chem.* **1981,** *46,* 5379.
1093. Walba, D. M.; Wand, M. D. *Tetrahedron Lett.* **1982,** *23,* 4995.
1094. Cowling, A. P.; Mann, J.; Usmani, A. A. *J. Chem. Soc., Perkin Trans. 1.* **1981,** 2116.
1095. Serebryakov, E. P.; Gamlevich, G. D.; Smasheena, G. A.; Zoolin, V. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1985,** 2776.
1096. Sum, P.-E.; Weiler, L. *Can. J. Chem.* **1982,** *60,* 327.
1097. Fitzsimmons, B. J.; Plaumann, D. E.; Fraser-Reid, B. *Tetrahedron Lett.* **1975,** 3925.

1098. Plaumann, D. E.; Fitzsimmons, B. J.; Ritchie, B. M.; Fraser-Reid, B. *J. Org. Chem.* **1982,** *47,* 941.

1099. Lagrange, A.; Olesker, A.; Costa, S.; Lukacs, G.; Thang, T. T. *Carbohyd. Res.* **1982,** *110,* 159.

1100. Mori, M.; Chuman, T.; Kato, K. *Carbohyd. Res.* **1984,** *129,* 73.

1101. Mulzer, J.; de Lasalle, P.; Freissler, A. *Liebigs Ann. Chem.* **1986,** 1152.

1102. Larchevêque, M.; Henrot, S. *Tetrahedron.* **1987,** *43,* 2303.

1103. Hoffmann, R. W.; Helbig, W. *Chem. Ber.* **1981,** *114,* 2802.

1104. Helbig, W. *Liebigs Ann. Chem.* **1984,** 1165.

1105. Mori, K.; Seu, Y.-B. *Tetrahedron.* **1988,** *44,* 1035.

1106. Chong, J. M.; Wong, S. *J. Org. Chem.* **1987,** *52,* 2596.

1107. Sinnwell, V.; Schulz, S.; Francke, W.; Kittmann, R.; Schneider, D. *Tetrahedron Lett.* **1985,** *26,* 1707.

1108. De Shong, P.; Lin, M.-T.; Perez, J. J. *Tetrahedron Lett.* **1986,** *27,* 2091.

1109. Schulz, S.; Francke, W.; König, W. A.; Schurig, V.; Mori, K.; Kittmann, R.; Schneider, D. *J. Chem. Ecol.* **1990,** *16,* 3511.

1110. Heemann, V.; Francke, W. *Naturwissenschaften.* **1976,** *63,* 344.

1111. Redlich, H.; Schneider, B.; Francke, W. *Tetrahedron Lett.* **1980,** *21,* 3009.

1112. Redlich, H.; Schneider, B.; Francke, W. *Tetrahedron Lett.* **1980,** *21,* 3013.

1113. Redlich, H.; Schneider, B.; Hoffmann, R. W.; Geueke, K.-J. *Liebigs Ann. Chem.* **1983,** 393.

1114. Sato, T.; Itoh, T.; Hattori, C.; Fujisawa, T. *Chem. Lett.* **1983,** 1391.

1115. Kongkathip, B.; Kongkathip, N. *Tetrahedron Lett.* **1984,** *25,* 2175.

1116. Guindon, Y.; St. Denis, Y.; Daigneault, S.; Morton, H. E. *Tetrahedron Lett.* **1986,** *27,* 1237.

1117. Page, P. C. B.; Rayner, C. M.; Sutherland, I. O. *Tetrahedron Lett.* **1986,** *27,* 3535.

1118. Mohr, P.; Tamm, C. *Tetrahedron Lett.* **1987,** *28,* 395.

1119. Adams, J.; Frenette, R. *Tetrahedron Lett.* **1987,** *28,* 4773.

1120. Borden, J. H.; Handley, J. R.; Johnston, B. D.; MacConnell, J. G.; Silverstein, R. M.; Slessor, K. N.; Swigar, A. A.; Wong, D. T. W. *J. Chem. Ecol.* **1979,** *5,* 681.

1121. McKay, W. R.; Ounsworth, J.; Sum, P.-E.; Weiler, L. *Can. J. Chem.* **1982,** *60,* 872.

1122. White, J. D.; Avery, M. A.; Carter, J. P. *J. Am. Chem. Soc.* **1982,** *104,* 5486.

1123. Skattebøl, L.; Stenstrøm, Y. *Tetrahedron Lett.* **1983,** *24,* 3021.

1124. Skattebøl, L.; Stenstrøm, Y. *Acta Chem. Scand.* **1985,** *B39,* 291.

1125. Johnston, B. D.; Slessor, K. N.; Ochlschlager, A. C. *J. Org. Chem.* **1985,** *50,* 114.

1126. Mori, K.; Sasaki, M. *Tetrahedron.* **1980,** *36,* 2193.

1127. Slessor, K. N.; Oehlschlager, A. C.; Johnston, B. D.; Pierce, Jr.; H. D.; Grewal, S. K.; Wickremesinghe, K. G. *J. Org. Chem.* **1980,** *45,* 2290.

1128. Mori, K.; Uematsu, T.; Minobe, M.; Yanagi, K. *Tetrahedron Lett.* **1982,** *23,* 1921.

1129. Mori, K.; Uematsu, T.; Minobe, M.; Yanagi, K. *Tetrahedron.* **1983,** *39,* 1735.

1130. Kandil, A. A.; Slessor, K. N. *J. Org. Chem.* **1985,** *50,* 5649.

1131. Kluge, A. F. *Heterocycles.* **1986,** *24,* 1699.

1132. Perron, F.; Albizati, K. F. *Chem. Rev.* **1989,** *89,* 1617.

1133. Francke, W.; Reith, W.; Sinnwell, V. *Chem. Ber.* **1980,** *113,* 2686.

1134. Pothier, N.; Rowan, D. D.; Deslongchamps, P.; Saunders, J. K. *Can. J. Chem.* **1981,** *59,* 1132.

1135. Francke, W.; Hindorf, G.; Reith, W. *Naturwissenschaften.* **1979,** *66,* 619.

1136. Deslongchamps, P.; Rowan, D. D.; Pothier, N.; Sauvé, T.; Saunders, J. K. *Can. J. Chem.* **1981,** *59,* 1105.

1137. Byers, J. A.; Högberg, H.-E.; Unelius, C. R.; Birgesson, G.; Löfqvist, J. *J. Chem. Ecol.* **1989,** *15,* 685 (and refs. therein).

1138. Francke, W.; Reith, W. *Liebigs Ann. Chem.* **1979,** 1.

1139. Phillips, C.; Jacobson, R.; Abrahams, B.; Williams, H. J.; Smith, L. R. *J. Org. Chem.* **1980,** *45,* 1920.

1140. Jacobson, R.; Taylor, R. J.; Williams, H. J.; Smith, L. R. *J. Org. Chem.* **1982,** *47,* 3140.

1141. Kozhich, O. A.; Segal, G. M.; Torgov, I. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1982,** 325.

1142. Ireland, R. E.; Häbich, D. *Tetrahedron Lett.* **1980,** *21,* 1389.

1143. Ireland, R. E.; Häbich, D. *Chem. Ber.* **1981,** *114,* 1418.

1144. Rosini, G.; Ballini, R.; Petrini, M.; Marotta, E. *Angew Chem., Int. Ed. Engl.* **1986,** *25,* 941.

1145. Zschiesche, R.; Hafner, T.; Reissig, H.-U. *Liebigs Ann. Chem.* **1988,** 1169.

1146. Doherty, A. M.; Ley, S. V.; Lygo, B.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1.* **1984,** 1371.

1147. Cekovic, Z.; Bosnjak, J. *Croat. Chim. Acta.* **1985,** *58,* 671.

1148. Koppenhofer, B.; Hinzer, K.; Weber, R.; Schurig, V. *Angew. Chem. Int. Ed. Engl.* **1980,** *19,* 471.

1149. Redlich, H.; Francke, W. *Angew. Chem. Int. Ed. Engl.* **1980,** *19,* 630.

1150. Redlich, H. *Liebigs Ann. Chem.* **1982,** 708.

1151. Hungerbühler, E.; Naef, R.; Wasmuth, D.; Seebach, D.; Loosli, H.-R.; Wehrli, A. *Helv. Chim. Acta.* **1980,** *63,* 1960.

1152. Enders, D.; Dahmen, W.; Dederichs, E.; Weuster, P. *Synth. Commun.* **1983,** *13,* 1235.

1153. Högberg, H.-E.; Hedenström, E.; Isaksson, R.; Wassgren, A.-B. *Acta Chem. Scand.* **1987,** *B41,* 694.

1154. Francke, W.; Reith, W.; Bergström, G.; Tengö, J. *Naturwissenschaften.* **1980,** *67,* 149.

1155. Francke, W.; Reith, W.; Bergström, G.; Tengö, J. *Z. Naturforsch.* **1981,** *36c,* 928.

1156. Francke, W.; Hindorf, G.; Reith, W. *Angew. Chem., Int. Ed. Engl.* **1978,** *17,* 862.

1157. Ley, S. V.; Lygo, B. *Tetrahedron Lett.* **1982,** *23,* 4625.

1158. Rosini, G.; Ballini, R.; Marotta, E. *Tetrahedron.* **1989,** *45,* 5935.

1159. Utimoto, K. *Pure Appl. Chem.* **1983,** *55,* 1845.

1160. Hinzer, K.; Weber, R.; Schurig, V. *Tetrahedron Lett.* **1981,** *22,* 55.

1161. Ley, S. V.; Lygo, B.; Wonnacott, A. *Tetrahedron Lett.* **1985,** *26,* 535.

1162. Ley, S. V.; Lygo, B.; Sternfeld, F.; Wonnacott, A. *Tetrahedron.* **1986,** *42,* 4333.

1163. Iwata, C.; Hattori, K.; Uchida, S.; Imanishi, T. *Tetrahedron Lett.* **1984,** *25,* 2995.

1164. Iwata, C.; Moritani, Y.; Sugiyama, K.; Fujita, M.; Imanishi, T. *Tetrahedron Lett.* **1987,** *28,* 2255.

1165. Iwata, C.; Moritani, Y.; Sugiyama, K.; Izaki, H.; Kuroki, T.; Imanishi, T. *Chem. Pharm. Bull.* **1988,** *36,* 4785.

1166. Francke, W. personal communication dated February 25, 1990.

1167. Koźluk, T.; Cottier, L.; Descotes, G. *Tetrahedron.* **1981,** *37,* 1875.
1168. Ley, S. V.; Lygo, B. *Tetrahedron Lett.* **1984,** *25,* 113.
1169. Ley, S. V.; Lygo, B.; Organ, H. M.; Wonnacott, A. *Tetrahedron.* **1985,** *41,* 3825.
1170. Mori, K.; Sasaki, M.; Tamada, S.; Suguro, T.; Masuda, S. *Tetrahedron.* **1979,** *35,* 1601.
1171. Francke, W.; Hindorf, G.; Reith, W. *Naturwissenschaften.* **1979,** *66,* 618.
1172. Bergström, G.; Tengö, J.; Reith, W.; Francke, W. *Z. Naturforsch.* **1982,** *37c,* 1124.
1173. Mori, K.; Ikunaka, M. *Tetrahedron.* **1984,** *40,* 3471.
1174. Davies, N. W.; Madden, J. L. *J. Chem. Ecol.* **1985,** *11,* 1115.
1175. Kitching, W.; Lewis, J. A.; Fletcher, M. T.; Drew, R. A. I.; Moore, C. J.; Francke, W. *J. Chem. Soc., Chem. Commun.* **1986,** 853.
1176. Kitching, W.; Lewis, J. A.; Perkins, M. V.; Drew, R.; Moore, C. J.; Schurig, V.; König, W. A.; Francke, W. *J. Org. Chem.* **1989,** *54,* 3893.
1177. Mori, K.; Soga, H.; Ikunaka, M. *Liebigs Ann. Chem.* **1985,** 2194.
1178. Baker, R.; Herbert, R.; Howse, P. E.; Jones, O. T.; Francke, W.; Reith, W. *J. Chem. Soc., Chem. Commun.* **1980,** 52.
1179. Baker, R.; Herbert, R. H. *J. Chem. Soc., Perkin Trans. 1.* **1987,** 1123.
1180. Baker, R.; Herbert, R. H.; Parton, A. H. *J. Chem. Soc., Chem. Commun.* **1982,** 601.
1181. Mazomenos, B. E.; Haniotakis, G. E. *J. Chem. Ecol.* **1985,** *11,* 397.
1182. Brinker, U. H.; Haghani, A.; Gomann, K. *Angew. Chem. Int. Ed. Engl.* **1985,** *24,* 230.
1183. De Shong, P.; Waltermire, R. E.; Ammon, H. L. *J. Am. Chem. Soc.* **1988,** *110,* 1901.
1184. Mortimore, M.; Kocieński, P. *Tetrahedron Lett.* **1988,** *29,* 3357.
1185. Brimble, M. A.; Officer, D. L.; Williams, G. M. *Tetrahedron Lett.* **1988,** *29,* 3609.
1186. Kocieński, P.; Yeates, C. *Tetrahedron Lett.* **1983,** *24,* 3905.
1187. Kay, I. T.; Williams, E. C. *Tetrahedron Lett.* **1983,** *24,* 5915.
1188. Redlich, H.; Francke, W. *Angew. Chem., Int. Ed. Engl.* **1984,** *23,* 519.
1189. Mori, K.; Uematsu, T.; Watanabe, H.; Yanagi, K.; Minobe, M. *Tetrahedron Lett.* **1984,** *25,* 3875.
1190. Mori, K.; Uematsu, T.; Yanagi, K.; Minobe, M. *Tetrahedron.* **1985,** *41,* 2751.
1191. Mori, K.; Watanabe, H.; Yanagi, K.; Minobe, M. *Tetrahedron.* **1985,** *41,* 3663.
1192. Iwata, C.; Fujita, M.; Hattori, K.; Uchida, S.; Imanishi, T. *Tetrahedron Lett.* **1985,** *26,* 2221.
1193. Iwata, C.; Fujita, M.; Kuroi, T.; Hattori, K.; Uchida, S.; Imanishi, T. *Chem. Pharm. Bull.* **1988,** *36,* 3257.
1194. Mori, K.; Watanabe, H. *Tetrahedron Lett.* **1984,** *25,* 6025.
1195. Bestmann, H. J.; Schmidt, M. *Tetrahedron Lett.* **1986,** *27,* 1999.
1196. Chen, J. Y. C.; Hough, L.; Richardson, A. C. *J. Chem. Soc., Chem. Commun.* **1982,** 1152.
1197. Chen, J. Y. C.; Hough, L.; Richardson, A. C. *J. Chem. Soc., Perkin Trans. 1.* **1985,** 1457.
1198. Haniotakis, G.; Mavraganis, V. G.; Ragoussis, V. *J. Chem. Ecol.* **1989,** *15,* 1057.
1199. Haniotakis, G.; Francke, W.; Mori, K.; Redlich, H.; Schurig, V. *J. Chem. Ecol.* **1986,** *12,* 1559.
1200. Tengö, J.; Agren, L.; Baur, B.; Isaksson, R.; Liljefors, T.; Mori, K.; König, W.; Francke, W. *J. Chem. Ecol.* **1990,** *16,* 429.

1201. Kitching, W.; Lewis, J. A.; Fletcher, M. T.; De Voss, J. J.; Drew, R. A. I.; Moore, C. J. *J. Chem. Soc., Chem. Commun.* **1986,** 855.

1202. Mori, K.; Tanida, K. *Heterocycles.* **1981,** *15,* 1171.

1203. Mori, K.; Tanida, K. *Tetrahedron.* **1981,** *37,* 3221.

1204. Mori, K.; Watanabe, H. *Tetrahedron.* **1986,** *42,* 295.

1205. Isaksson, R.; Liljefors, T.; Reinholdsson, P. *J. Chem. Soc., Chem. Commun.* **1984,** 137.

1206. Redlich, H.; Schneider, B. *Liebigs Ann. Chem.* **1983,** 412.

1207. Redlich, H.; Schneider, B.; Hoffmann, R. W.; Geueke, K.-J. *Liebigs Ann. Chem.* **1983,** 393.

1208. Mori, K.; Katsurada, M. *Liebigs Ann. Chem.* **1984,** 157.

1209. Bell, T. W.; Boppré, M.; Schneider, D.; Meinwald, J. *Experientia.* **1984,** *40,* 713.

1210. Boppré, M.; Schneider, D. *J. Comp. Physiol. A.* **1985,** *157,* 569.

1211. Röder, E.; Wiedenfeld, H.; Bourauel, T. *Liebigs Ann. Chem.* **1986,** 1645.

1212. Krasnoff, S. B.; Dussourd, D. E. *J. Chem. Ecol.* **1989,** *15,* 47.

1213. Talman, E.; Ritter, F. J.; Verwiel, P. E. J.; In *Mass Spectrometry in Biochemistry and Medicine*; Frigerio, A., and Castagnoli, N. Eds. Raven Press: New York, 1974, 197-217.

1214. Royer, J.; Husson, H.-P. *J. Org. Chem.* **1985,** *50,* 670.

1215. Macdonald, T. L. *J. Org. Chem.* **1980,** *45,* 193.

1216. Stevens, R. V.; Lee, A. W. M. *J. Chem. Soc., Chem. Commun.* **1982,** 102.

1217. Iida, H.; Watanabe, Y.; Kibayashi, C. *Tetrahedron Lett.* **1986,** *27,* 5513.

1218. Watanabe, Y.; Iida, H.; Kibayashi, C. *J. Org. Chem.* **1989,** *54,* 4088.

1219. Yamaguchi, R.; Hata, E.; Matsuki, T.; Kawanishi, M. *J. Org. Chem.* **1987,** *52,* 2094.

1220. Jefford, C. W.; Tang, Qian, Zaslona, A. *Helv. Chim. Acta.* **1989,** *72,* 1749.

1221. Yamazaki, N.; Kibayashi, C. *Tetrahedron Lett.* **1988,** *29,* 5767.

1222. Chuman, T.; Landolt, P. J.; Heath, R. R.; Tumlinson, J. H. *J. Chem. Ecol.* **1987,** *13,* 1979.

1223. Attygale, A. B.; Morgan, E. D. *J. Chem. Ecol.* **1984,** *10,* 1453.

1224. Masaki, Y.; Iwata, I.; Imaeda, T.; Oda, H.; Nagashima, H. In *Abstracts of Papers, 16th International Symposium on the Chemistry of Natural Products (IUPAC).* Kyoto, Japan, 1988, PB 102 (p. 348).

1225. Hurter, J.; Boller, E. F.; Stadler, E.; Blattmann, B.; Buser, H.-R.; Bosshard, M. U.; Damm, L.; Kozlowski, M. W.; Schöni, R.; Raschdorf, F.; Dahinden, R.; Schlumpf, E.; Fritz, H.; Richter, W. J.; Schreiber, J. *Experientia.* **1987,** *43,* 157.

1226. Ernst, B.; Wagner, B. *Helv. Chim. Acta.* **1989,** *72,* 165.

1227. Kametani, T.; Tsubuki, M.; Honda, T. *Chem. Pharm. Bull.* **1988,** *36,* 3706.

1228. Kametani, T.; Tsubuki, M.; Tatsuzaki, Y.; Honda, T. *J. Chem. Soc., Perkin Trans. 1.* **1990,** 639.

1229. Kuwahara, S.; Mori, K. *Tetrahedron.* **1990,** *46,* 8083.

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