

Zinc(II) Reagents

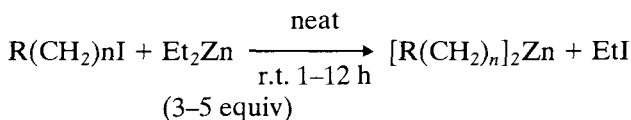
NOBUKI OGUNI

1. Introduction

There are two kinds of organozinc compounds: Grignard-type reagents and dialkylzincs. Organozinc reagents have been used for the carbon-carbon bond-forming reactions, for example, Reformatsky and Simmons-Smith reactions. Nevertheless dialkylzinc compounds have been little used for organic reactions except organometallic component of Ziegler catalyst. After our first report of the discovery in 1883 on the enantioselective addition of diethylzinc to benzaldehyde catalyzed by chiral β -aminoalcohols, this field of asymmetric carbon-carbon bond forming catalytic reaction was developed largely by many researchers. Also the asymmetric amplification, that is extreme amplification in enantioselectivity was found in this reaction and gave the extensive effect for all enantioselective catalytic reactions.¹⁻⁴

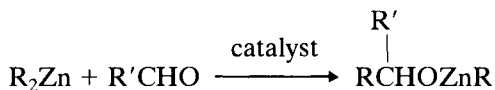
2. Scope and limitations

Dialkylzincs can be prepared easily by transmetallation from alkylaluminiums and alkylboranes. Particularly, diethylzinc and dimethylzinc among many dialkylzincs are commercially available in most countries. Therefore the synthetic method of non-commercially available organozinc compounds using diethylzinc will be convenient and advantageous in comparison with other methods.^{3,4}



Dialkylzincs have been known to be unreactive to aldehydes, esters, imines, and so on, in polar solvents at room temperature. This characteristic of

organozincs is quite different from alkyl-lithium and dialkylmagnesium which react easily on mixing with aldehydes, ketones, and other functionalized compounds even at low temperature. Dialkylzinc only reacts with aldehydes to give addition products in the presence of basic catalysts such as trialkyl amines. The reaction products are monoalkylzinc alkoxides which easily associate to afford cubic tetramers co-ordinated with oxygen atoms of alkoxides. The alkyl group of alkylzinc alkoxide does not react with aldehydes.

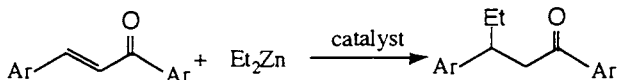


Dialkylzincs also react with β -aminoalcohols or β -thioalcohols to give 2-valence 3-co-ordinated alkylzinc compounds which also associate to form dimers. When aldehydes and excess dialkylzincs are present in the media, dimer easily dissociate to catalyse the addition reaction of dialkylzincs to aldehydes. There have been reports of the use of chiral β -aminoalcohols⁵⁻⁵⁰ containing β -diamines, β -aminothiols,⁶⁸⁻⁷² hydroxy-pyridines⁵¹⁻⁵⁷ and amino-alcohol derivatives of ferrocene⁵⁸⁻⁶³ and benzene-chrom complexes⁶⁴⁻⁷² in the reaction media of dialkylzincs with aldehydes to afford optically active products. Generally the chirality of the carbon bonded with a hydroxy group affects predominantly the chirality of the product rather than one with an amino group. In general aromatic and α,β -unsaturated aldehydes give high enantioselective products in reactions using β -difunctionalized chiral auxiliaries. In enantioselective addition of dialkylzincs to aldehydes, asymmetric amplification was found, even if a small amount of β -aminoalcohols bearing low optical purity was used as a catalyst, very high enantiomeric products were obtained. Investigations of the mechanism of this curious reaction estimated that the monomeric zincaminoalkoxide is the real active catalyst, and its racemic dimer associate cannot dissociate in reaction media.⁷³⁻⁷⁶ When the chemical constitution and absolute configuration of the product are exactly the same with chiral auxiliary used, the product itself can also catalyse the reaction to produce the same compound. This reaction was realized in isopropylation of pyridinecarbaldehydes with di-isopropylzinc, by a reaction called autocatalysis.⁷⁷⁻⁸²

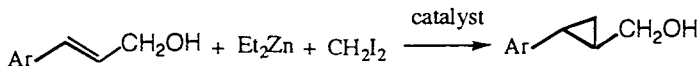
Chiral Lewis acid-catalysed alkylation of aldehydes with dialkylzincs gave highly enantioselective products. Two outstanding catalysts are the titanium-chiral TADDOL and titanium-chiral disulfonamido systems.⁸³⁻¹⁰⁵ Both catalysts give the very high enantiomeric products from all kinds of aldehydes, both aliphatic and alicyclic. However, in the former catalyst system an equimolar amount of titanium alkoxides to aldehydes is needed to obtain addition products in high yield.

Highly enantioselective 1,4-addition of diethylzinc to α,β -unsaturated ketones was attained using nickel or copper complexes of β -aminoalcohols.¹⁰⁶⁻¹¹⁰ Also the catalytic enantioselective cyclopropanation of allylic alcohols with

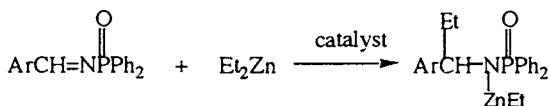
5: Zinc(II) Reagents



diethylzinc- CH_2I_2 was found using chiral titanium-disulfonamido complexes as catalyst.^{111–124}



Dialkylzinc can add to imino groups by catalysis of chiral titanium complexes to give chiral amine derivatives, followed by hydrolysis to afford optical active primary amines.^{125–129}

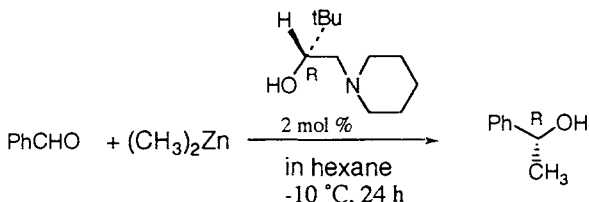


Cautions: Dialkylzincs are highly flammable liquids, which induce spontaneous ignition in air, and react violently with water and alcohols. Therefore, dialkylzincs should be kept under an inert atmosphere.

Protocol 1.

Chiral β -aminoalcohol-mediated asymmetric addition of diethylzinc to benzaldehyde⁸ (Scheme 5.1)

Alkylation, particularly ethylation of aromatic compounds has been investigated with many kinds of β -aminoalcohols and highly enantioselective reactions also reported.



Scheme 5.1

Equipment

- Two-necked, round-bottomed flask (500 mL) fitted with rubber septum and a Teflon-coated magnetic stirring bar
- Three-way stopcock fitted to the top of flask and connected to a vacuum/argon (or dry nitrogen) source
- Magnetic stirrer
- All-glass syringe with a needle-lock Luer and medium-gauge needle
- Water-jacketed short-path distillation apparatus
- Separating funnel (500 mL)
- Rotary evaporator

Protocol 1. Continued**Materials**

- Dry toluene
- Benzaldehyde
- Diethylzinc
- (*R*)-1-*t*-Butyl-2-piperidinoethanol
- Technical ether for extraction

explosive on contact to air**flammable**

1. Flame dry the reaction vessel and place with a stirrer bar *in vacuo*. Fill the flask with argon and maintain a slightly positive argon pressure throughout this reaction.
2. Assemble the syringe and needle while hot and flush the syringe with argon.
3. Support the flask using clamp and a stand with a heavy base.
4. Charge the flask with toluene (200 mL) using a syringe by piercing the septum on the reaction flask.
5. Keep the flask at -40°C with a dry ice/acetone bath.
6. Add benzaldehyde (10 g, 94.2 mmol) and (*R*)-1-*t*-butyl-2-piperidinoethanol (0.37 g, 2.0 mmol) using syringes under stirring.
7. Add diethylzinc (10.5 mL, 102 mmol) dropwise from the syringe through the septum on the reaction flask to the mixture in the flask with vigorous stirring.
8. Allow the temperature of the flask to rise from -40°C to -10°C with an ice/NaCl bath, and keep the mixture at -10°C for 24 h.
9. Quench the mixture by dropping 2M HCl (100 mL) with stirring at 0°C .
10. Transfer the mixture to a separating funnel and separate the two layers. Extract the water layer with ether (2×50 mL).
11. Transfer the organic layer to a 500 mL flask. Dry the organic layer over Na_2SO_4 , and filter through a filter paper. Concentrate the filtrate under reduced pressure using a rotary evaporator ($30^{\circ}\text{C}/30$ mm Hg).
12. Transfer the oily residue to a water-jacketed, short path distillation apparatus equipped with a thermometer. Distil the crude product under reduced pressure to obtain 1-phenyl-1-propanol(b.p. $103\text{--}104^{\circ}\text{C}$ 14 mm Hg; 12.6 g, 98% yield) as a colourless oil.
13. Determine the absolute configuration and enantiomeric excess(*ee*) of the product. The absolute configuration can be determined by the sign of $[\alpha]_{\text{D}}$ $[\alpha]_{\text{D}} -45.4$.(*c* 2.0, $\text{C}_2\text{H}_5\text{OH}$) indicated a (*S*)-configuration. *Ee* ($>98\%$) was determined by HPLC analysis (column, Daicel CHIRALCEL OB; 100/0.2 hexane/2-propanol; t_{R} of (*S*)-isomer, 12 min; t_{R} of (*R*)-isomer, 13 min.

(*R*)-1-Dialkylamino-3-3-dimethylbutan-2-ol was prepared by the reaction of (*R*)-*t*-butyl-ethylene oxide^a with bromomagnesium dialkylamide as follows.

To a solution of ethylmagnesium bromide (5.0 mmol) in tetrahydrofuran (THF)(10 mL) was added a solution of a secondary amine (5.0 mmol) in THF(5

mL). After the mixture has been stirred at 35°C for 1 h, (*R*)-*t*-butylethylene oxide (500 mg, 5 mmol) was added to the solution, which was then stirred for 6 h at room temperature before being poured into saturated aq.NH₄Cl. The aqueous solution was acidified with 1 mol dm⁻³ HCl (20 ml), extracted with ethyl acetate (30 mL × 2), and then made alkaline by 10% aq. NaOH and extracted with ethyl acetate (20 mL × 2). The combined organic layer was washed with brine (20 mL × 2), dried over Na₂SO₄, and distilled or recrystallized to give the corresponding (*R*)-1-dialkylamino-3,3-dimethylbutan-2-ol in good yield. The enantiomeric excess of the β-aminoalcohol thus obtained was determined as over 99% by HPLC analysis of the corresponding 3,5-dinitrophenyl carbamate, using a chiral stationary phase(column, Sumitomo Chemical Co. Sumipax OA 4000).

(*R*)-3,3-Dimethyl-1-piperidinobutan-2-ol (**1**) was obtained from the reaction of piperidine (425 mg, 5 mmol) and (*R*)-*t*-butylethylene oxide (500 mg, 5 mmol) in yield of 743 mg (80%), b.p. 59–61°C/1 mmHg). [α]_D²⁵ –72.4 (C 1.8, CHCl₃).

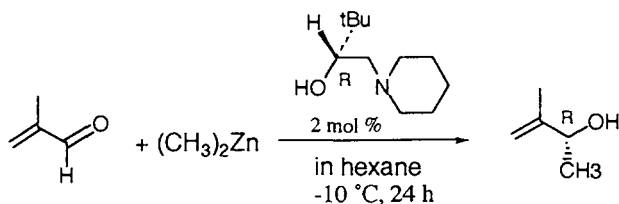
(*R*)-1-(3-Azabicyclo[3.2.2]nonan-3-yl)-3-dimethylbutan-2-ol was obtained from the reaction of 3-azabicyclo[3.3.3]nonane (630 mg, 5 mmol) and (*R*)-*t*-butylethylene oxide (500 mg, 5 mmol) in yield of 1.12 g (88%), m.p.105–108°C). [α]_D²² –64.2° (C 1.0, CHCl₃).

^a Leven, P. A.; Walti, A. Organic Synthesis **1943**, Coll. Vol. 2, 5–9. Hurst, S. J.; Bruce, J. M. *J. Chem. Soc.* **1963**, 147.

Protocol 2.

Chiral β-aminoalcohol mediated asymmetric addition of dimethylzinc to methylacrylaldehyde²⁹ (Scheme 5.2)

Methylation of aldehydes has been investigated less frequently, because dimethylzinc has a very low boiling point like diethyl ether. However, it can be handled easily as a toluene solution.



Scheme 5.2

Equipment

- Two-necked, round-bottomed flask (500 mL) fitted with rubber septum and a Teflon-coated magnetic stirring bar
- Three-way stopcock fitted to the top of the flask and connected to a vacuum/argon (or dry nitrogen) source
- Magnetic stirrer
- All-glass syringe with a needle-lock Luer and medium-gauge needle
- Water-jacketed short-path distillation apparatus
- Separating funnel (500 mL).

Protocol 2. Continued**Materials**

- Dry ether and hexane
- Methylacrylaldehyde
- Dimethylzinc
- (*R*)-1-*t*-Butyl-2-piperidinoethanol
- Technical ether for extraction

explosive on contact with air**flammable**

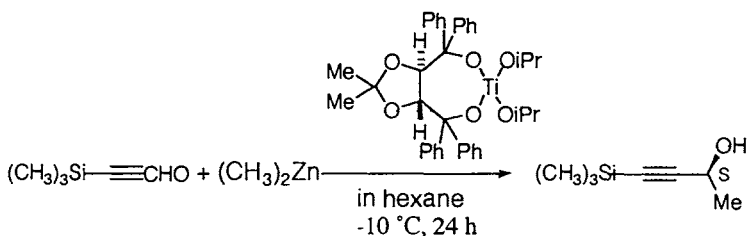
1. Flame dry the reaction vessel and place with a stirrer bar *in vacuo*. Fill the flask with argon and maintain a slightly positive argon pressure throughout the reaction.
2. Assemble the syringe and needle while hot and flush the syringe with argon.
3. Support the flask using clamp and a stand with a heavy base.
4. Charge the flask with hexane (100 mL) and there (100 mL) using a syringe by piercing the septum on reaction flask.
5. Keep the flask at -40°C with a dry ice/acetone bath.
6. Charge methylacrylaldehyde (6.6 g, 94.2 mmol) and (*R*)-1-*t*-butyl-2-piperidinoethanol (0.37 g, 2.0 mmol) with syringes under stirring.
7. Remove dimethylzinc in a syringe from the cylinder of dimethylzinc stored at -10°C under argon pressure.
8. Add dimethylzinc (10.5 mL, 102 mmol) dropwise from the syringe through the septum on the reaction flask to the mixture in the flask with vigorous stirring.
9. Allow the temperature of the flask to rise from -40°C to 15°C and keep the mixture at this temperature for 96 h.
10. Quench the mixture by adding 2 M HCl (100 mL) dropwise with stirring at 0°C .
11. Transfer the mixture to a separating funnel and separate into two layers. Extract the water layer with ether (2×50 mL).
12. Transfer the organic layer to a 500 mL flask. Dry the organic layer over Na_2SO_4 , and filter through a filter paper. Concentrate the filtrate by distillation under ordinal pressure.
13. Transfer the oily residue to a water-jacketed, short path distillation apparatus equipped with a thermometer. Distill the crude product under reduced pressure to obtain 3-methylbut-3-en-2-ol (b.p. $106\text{--}108^{\circ}\text{C}/760$ mm Hg; 6.8 g, 70% yield) as a colourless oil. The product is .99% pure by $^1\text{H-NMR}$; $\text{d}(\text{CDCl}_3)$ 1.29 (3H,d, J 6.7Hz), 1.60(1H,s), 1.75(3H,s), 4.25(1H,q, J 6.7Hz), 4.80(1H,s), and 4.96(1H,s).
14. Determine the absolute configuration of the product from the sign of $[\alpha]_D$. $[\alpha]_D -5.6$ (c 8.0, CHCl_3) showed it to be (*S*)-configurational product.

15. Enantiomeric excess(ee) (>95%) was determined by HPLC analysis of the 3,5-dinitrophenyl carbamate^a (column, Sumitomo Chemical Co. SUMIPAX OA 4000) in hexane/ethanol 100:1.5; t_R of (*R*)-isomer, 41 min; t_R of (*S*)-isomer, 36 min.

^a React 3-methylbut-3-en-2-ol (8.6 mg, 1.0 mmol) with 3,5-dinitrophenylisocyanide (21 mg, 1.0 mmol) in toluene (2.0 mL) at room temperature for 1 h with stirring. This mixture is used directly for HPLC.

Protocol 3.

Chiral Taddolated catalysed asymmetric addition of dimethylzinc to trimethylsilylpropynal¹⁰⁵ (Scheme 5.3)



Scheme 5.3

Equipment

- Two-necked, round-bottomed flask (500 mL) fitted with rubber septum and a teflon-coated magnetic stirring bar
- Three-way stopcock fitted to the top of the flask and connected to a vacuum/argon (or dry nitrogen) source
- Magnetic stirrer
- All-glass syringe with a needle-lock Luer and medium-gauge needle
- Water-jacketed short-path distillation apparatus
- Separatory funnel (500 mL)

Materials

- Dry toluene
- 3-Trimethylsilylpropynal
- Dimethylzinc
- (4*R*,5*R*)-2,2'-dimethyl- $\alpha,\alpha',\alpha',\alpha'$ -Tetraphenyl-1,3-dioxolane-4,5-dimethanol(TADDOL)
- Technical ether for extraction

explosive on contact with air

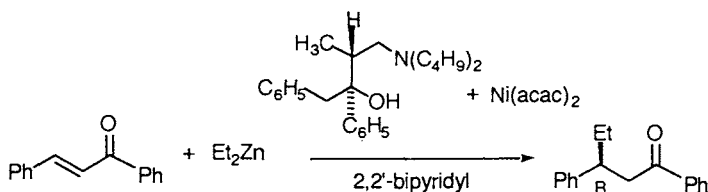
flammable

1. Flame dry the reaction vessel and place with a stirrer bar *in vacuo*. Fill the flask with argon and maintain a slightly positive argon pressure throughout the reaction.
2. Assemble the syringe and needle while hot and flush the syringe with argon.
3. Support the flask using clamp and a stand with a heavy base.

Protocol 3. Continued

4. Charge the flask with TADDOL (15.1 g, 20 mmol) and toluene (100 mL) using a syringe by piercing the septum on reaction flask.
5. Add titanium tetraisopropoxide (6 mL, 20 mmol) to the above mixture at room temperature and stir the resulting solution for 10 h.
6. Remove toluene and isopropanol produced under reduced pressure with stirring.
7. Dissolve the residue in *t*-butylmethyl ether (100 mL) solution containing titanium tetraisopropoxide (35 mL, 120 mmol).
8. Transfer dimethylzinc in a syringe from the cylinder of dimethylzinc stored at -10°C under an argon pressure.
9. Add dimethylzinc (12 mL, 180 mmol) dropwise from the syringe through the septum on the reaction flask to the mixture in the flask with vigorous stirring.
10. Add 3-trimethylsilylpropynal (16 g, 100 mmol) with a syringe with stirring at -20°C .
11. Allow the temperature of the flask to rise from -20°C to 0°C and keep the mixture at this temperature for 48 h.
12. Quench the mixture by adding 2M HCl(100 mL) dropwise with stirring at 0°C .
13. Transfer the mixture to a separating funnel and separate into two layers. Extract the water layer with ether (2×50 mL).
14. Transfer the organic layer to a 500 mL flask. Dry the organic layer over Na_2SO_4 , and filter through a filter paper. Concentrate the filtrate under reduced pressure using a rotary evaporator ($25^{\circ}\text{C}/50$ mm Hg).
15. Transfer the oily residue to a water-jacketed, short-path distillation apparatus equipped with a thermometer. Distil the crude product under reduced pressure to obtain 4-trimethylsilyl-3-butyn-2-ol (b.p. $77^{\circ}\text{C}/20$ mm Hg; 14.7 g, 98% yield) as a colourless oil. The product is 99% pure by ^1H NMR; $\delta(\text{CDCl}_3)$ 0.15(9H,s), 1.42 (3H,d, J 4.6 Hz), 1.85 (1H, d, J 3.8 Hz), and 4.50 (1H, m).
16. Determine the absolute configuration of the product from the sign of $[\alpha]_{\text{D}}$. $[\alpha]_{\text{D}} -24.2$ (c 2.0, CHCl_3) showed it to be (*S*)-configurational product.
17. Enantiomeric excess(ee) (96%) was determined by HPLC analysis of the 3,5-dinitrobenzoate^a (column, Daicel, CHIRAPAK AD in volume ratio of hexane/2-propanol (100:1); t_{R} of (*R*)-isomer, 30 min; t_{R} of (*S*)-isomer, 40 min.

^aReact 3-trimethylsilylbut-3-yn-2-ol (14.2 mg, 0.1 mmol) with 3,5-dinitrobenzoyl chloride (23 mg, 0.1 mmol) in toluene (2.0 mL) in the presence of triethylamine (1 mL) at room temperature for 1 h with stirring. Remove Et_3NHCl by filtration and use the filtrate directly for HPLC.

Protocol 4.**Asymmetric 1,4-conjugate addition of diethylzinc to chalcone catalysed by chiral nickel complex¹⁰⁶ (Scheme 5.4)****Scheme 5.4****Equipment**

- Two-necked, round-bottomed flask (300 mL) fitted with a rubber septum and a Teflon-coated magnetic stirring bar
- Three-way stopcock fitted to the top of flask and connected to a vacuum/argon (or dry nitrogen) source
- Magnetic stirrer
- All-glass syringe with a needle-lock Luer and medium-gauge needle
- Water-jacketed short-path distillation apparatus
- Separating funnel (300 mL)
- Rotary evaporator
- Chiralcel OK for HPLC

Materials

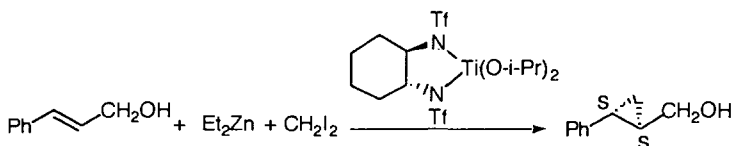
- Dry toluene
- Bis(acetylacetonato)nickel(II)
- *R*-(–)-(1*S*,2*R*)-*N,N*-Dibutylnorephedrine (DBNE)
- 2,2'-Bipyridyl
- Chalcone
- Diethylzinc
- Acetonitrile
- Hexane
- Technical ether for extraction

explosive on exposure to air**flammable**

1. Flame dry the reaction vessel and place with a stirrer bar *in vacuo*. Fill the flask with argon and maintain a slightly positive argon pressure throughout this reaction.
2. Assemble the syringe and needle while hot and flush the syringe with argon.
3. Support the flask using clamp and a stand with a heavy base.
4. Place bis(acetylacetonato)nickel(ii) (3.6 g, 14 mmol) in the flask.
5. Add (1*S*,2*R*)-(–)-DBNE (0.896 g, 34 mmol) to the flask in CH₃CN (20 mL) using a syringe by piercing the septum on reaction flask. Stir the mixture at 80°C for 1 h.
6. Remove the acetylacetone liberated and CH₃CN under reduced pressure.
7. Add 2,2'-bipyridyl (0.22 g, 14 mmol) in CH₃CN (20 mL) to the flask and stir at 80°C for 1 h.

Protocol 4. Continued

8. Cool the resulting green solution to room temperature.
9. Charge chalcone (4.16 g, 0.2 mol) in CH_3CN (100 mL) to above mixture followed by stirring for 20 min at room temperature.
10. Cool to -30°C this solution and add diethylzinc (1.0M toluene solution, 240 mL, 0.24 mol) dropwise from the syringe through the septum on the reaction flask and stir for 12 h at this temperature.
11. Quench the mixture by dropping 1M HCl (100 mL) with stirring at 0°C .
12. Transfer the mixture to a separating funnel and allow the two layers to separate. Extract the aqueous layer with ether (4×20 mL), and dry over anhydrous Na_2SO_4 .
13. Transfer the organic layer to a 300 mL round-bottomed flask and concentrate under reduced pressure using a rotary evaporator ($30^\circ\text{C}/30$ mm Hg).
14. Purify the residue by silica gel chromatography (eluent, hexane/chloroform, 1:1, v/v) to obtain (*R*)-(-)-1,3-diphenylpentan-1-one (2.26 g, 47% yield), which displays the appropriate ^1H NMR in CDCl_3 .
15. Determine the absolute configuration and enantiomeric excess (ee) of the product. The absolute configuration is determined from the sign of $[\alpha]_D$. $[\alpha]_D -4.7$ (c 2.5, EtOH) indicated (*R*)-configuration. Ee (90%) was determined by HPLC analysis (column, Daicel CHIRALCEL OD; hexane/2-propanol, 100:0.2, flow rate 0.5 mL/min; t_R of (*S*)-isomer, 40.1 min; t_R of (*R*)-isomer, 44.8 min).

Protocol 5.**Chiral disulfonamide-titanate catalysed asymmetric cyclopropanation of cinnamyl alcohol¹²⁴ (Scheme 5.5)****Scheme 5.5****Equipment**

- Two-necked, round-bottomed flask (500 mL) fitted with a rubber septum and a Teflon-coated magnetic stirring bar
- Three-way stopcock fitted to the top of the flask and connected to a vacuum/argon (or dry nitrogen) source
- Magnetic stirrer
- All-glass syringe with a needle-lock Luer and medium-gauge needle
- Water-jacketed short-path distillation apparatus
- Separating funnel (500 mL)

Materials

- Dry dichloromethane
- Di-iodomethane
- Diethylzinc
- (4*R*,5*R*)-2,2'-Dimethyl- $\alpha,\alpha',\alpha',\alpha'$ -tetraphenyl-1,3-dioxolane-4,5-dimethanol(TADDOL)
- Ti (OiPr)₄
- Technical ether for extraction
- Molecular sieve 4A and Ti(OiPr)₄

explosive on exposure to air**flammable****flammable**

1. Flame dry the reaction vessel and place with a stirrer bar *in vacuo*. Fill the flask with argon and maintain a slightly positive argon pressure throughout the section.
2. Assemble the syringe and needle while hot and flush the syringe with argon.
3. Support the flask using clamp and a stand with a heavy base.
4. Charge the flask with CH₂I₂ (1.6 mL, 20 mmol) and CH₂Cl₂ (50 mL) using a syringe by piercing the septum on reaction flask.
5. Remove diethylzinc in a syringe from the cylinder of diethylzinc stored under argon pressure.
6. Add diethylzinc (1 mL, 10 mmol) dropwise to the flask at 0°C and stir the resulting solution for 15 min. A white precipitate is formed (solution **A**).
7. Mix (4*R*,5*R*)-TADDOL (1.4 g, 2.9 mmol) and molecular sieve 4A (10 g) in CH₂Cl₂ (5 mL), and add Ti(OiPr)₄ (0.74 mL, 2.5 mmol) with stirring. Stir for 1.5 h at room temperature.
8. Remove the solvent and isopropanol produced by the reaction under reduced pressure and leave the residue under high vacuum. Dissolve the residue into CH₂Cl₂ (50 mL) (solution **B**).
9. Mix solutions **A** and **B** in the flask at -40°C and add immediately cinnamyl alcohol (1.4 g, 10.4 mmol) to the mixture with stirring.
10. Stir the mixture at 0°C for 90 min and add TiCl₄ (0.16 mL, 1.5 mmol).
11. Cool the solution to -40°C and quench the reaction by pouring the mixture into saturated aq. NH₄Cl solution (300 mL).
12. Transfer the mixture to a separating funnel and allow the two layers to separate. Extract the water layer with ethyl acetate (50 mL).
13. Wash the organic layer with saturated aqueous NH₄Cl, and brine, then dry over MgSO₄ and concentrate under reduced pressure (25°C/30 mm Hg).
14. Purify the crude product by flash chromatography (EtOAc/hexane, 80:20) to obtain (1.2 g, 80% yield) as a colourless oil. The product is .99% pure by ¹H NMR.
15. Determine the absolute configuration of the product from the sign of [α]_D. [α]_D + 84 (*c* 1.3, EtOH) indicated a (2*SS*,3*SS*)- configurational product.
16. Enantiomeric excess(ee) (90%) was determined by GC analysis of the tri-fluoroacetate derivative on a chiral stationary phase: Cyclodex GT-A column, 0.32 mm \times 30 m (25 psi, 110°C), *t*_r 11.5 min (minor), 12.0 (major).

References

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