

Lanthanide(III) Reagents

TAKESHI NAKAI and KATSUHIKO TOMOOKA

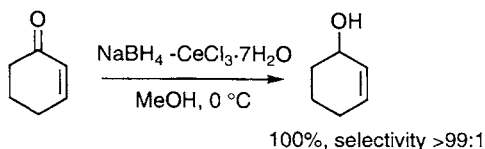
1 Introduction

The lanthanide group consists of the 15 elements from lanthanum to lutetium in the periodic table. In the past two decades the synthetic uses of a variety of lanthanide complexes, in terms of the kind of central lanthanides, the oxidation state (+2–+4), and the kind of ligands, have been developed.¹ This chapter focuses primarily on the four classes of the most popular trivalent lanthanides, namely, cerium(III) complexes (CeL_3), europium(III) complexes (EuL_3), ytterbium complexes (YbL_3), and lanthanum(III) complexes (LaL_3). Note that many synthetic applications have been found not only of divalent samarium reagents such as SmI_2^{2-4} and tetravalent cerium reagents such as cerium ammonium nitrate (CAN)⁵ but also of lanthanide metals such as Ce, Sm, and Yb, which are, however, beyond the scope of this chapter.

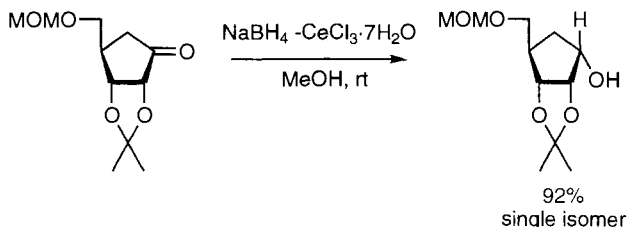
The trivalent state is the most common oxidation state for lanthanides. Generally speaking, lanthanide(III) complexes (except for the alkoxides) are hard Lewis acids and hence they have a strong affinity toward hard bases such as oxygen donor ligands. This strong oxophilicity is one of the most important characteristics of lanthanide(III) reagents and provides the principal basis for their unique synthetic applications.

2. Cerium(III) reagents

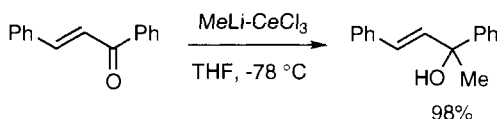
Cerium(III) salts, particularly CeCl_3 , have found many synthetic applications as inexpensive, unique reagents (stoichiometric use). Of the most widespread use are the NaBH_4 – CeCl_3 system that allows the regioselective reductions of α,β -enones (Scheme 12.1)^{6,7} and the stereoselective reduction of ketones



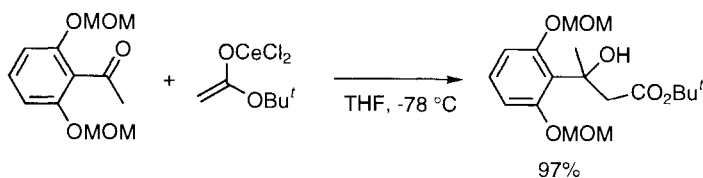
Scheme 12.1

**Scheme 12.2**

(Scheme 12.2),⁸ and the organocerium reagents (RCeCl_2), generated *in situ* from organolithiums or Grignard reagents and CeCl_3 , which can smoothly undergo the normal 1,2-addition reactions to carbonyl compounds including α,β -enones (Scheme 12.3).⁹ Particularly notable is that the use of CeCl_3 as an additive in these reactions significantly suppresses unfavourable side reactions (enolization, reduction, conjugate addition, etc.) which are often encountered with the use of organolithiums or Grignard reagents alone. In addition, a higher stereoselectivity is often observed by virtue of the chelating ability of the cerium reagents involved.

**Scheme 12.3**

In a similar manner, treatment of lithium enolates with CeCl_3 generates the cerium enolates which undergo aldol reactions usually in a higher yield than with lithium enolates alone,^{10,11} particularly when sterically hindered and/or easily enolizable carbonyl partners are used (Scheme 12.4).¹¹ The stereoselectivity of Ce -enolate reactions is essentially the same as that of Li -enolate reactions, since both reactions proceed through a cyclic transition state.

**Scheme 12.4**

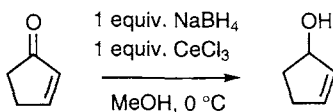
Furthermore, cerium halides are also useful as promoters for the reductive coupling of α -haloketones with carbonyl compounds. The use of CeI_3 affords

the α,β -unsaturated carbonyl compounds, whereas the $\text{CeCl}_3\text{-NaI}$ or $\text{CeCl}_3\text{-SnCl}_2$ systems produce the aldols.¹²

Protocol 1.

Reduction of 2-cyclopentenone by $\text{NaBH}_4\text{-CeCl}_3$ ^{6,7} (Scheme 12.5).

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.



Scheme 12.5

Equipment

- An Erlenmeyer flask (300 mL) equipped with a stirring bar.

Materials

- Cerium chloride heptahydrate (FW 372.6), 19.0 g, 50 mmol
- 2-Cyclopentenone (FW 82.10), 4.1 g, 50 mmol
- Methanol, 120 mL
- Sodium borohydride (FW 37.83), 1.9 g, 50 mmol

irritant, hygroscopic

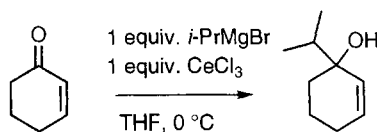
flammable, toxic

flammable, corrosive

1. Add cerium chloride heptahydrate (50 mmol), 2-cyclopentenone (50 mmol), methanol (120 mL) and stirring bar to the flask. Stir the mixture until the cerium chloride is completely dissolved.
2. Immerse the flask in an ice bath, add sodium borohydride (50 mmol) in portions over 5 min. Hydrogen is evolved vigorously with elevation of temperature to 15–20°C.
3. Stir the mixture for an additional 10 min, and then concentrate the resulting white suspension to about 30 mL under reduced pressure.
4. Add water (100 mL) to dissolve inorganic salts and extract the mixture with ether (3×50 mL). Dry the combined extracts over MgSO_4 and concentrate to a volume of c. 10 mL. Distil the residue under ordinary pressure to collect 2-cyclopenten-1-ol (3.7 g, 88%) with 96% purity.

Protocol 2.**Preparation of organocerium reagents and reaction with carbonyl compounds: reaction of *i*-propylcerium reagent with 2-cyclohexene-1-one⁹ (Scheme 12.6)**

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.

**Scheme 12.6****Equipment**

- A two-necked, round-bottomed flask (500 mL) fitted with a septum, a three-way stopcock, and a magnetic stirring bar. The three-way stopcock is connected to a vacuum/argon source.
- Vacuum/argon source.
- Syringes
- Mortar
- Oil bath

Materials

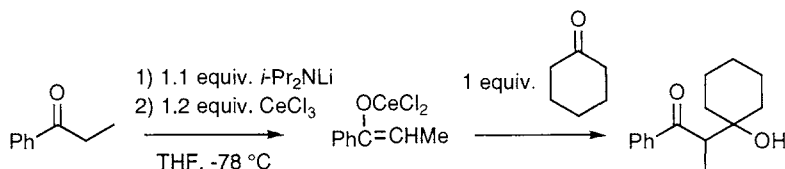
- Cerium chloride heptahydrate (FW 372.6), 18.0 g, 48 mmol
- *i*-Propylmagnesium bromide (FW 147.3), 1.8 M solution in THF, 27 mL, 48 mmol
- 2-Cyclohexene-1-one (FW 96.13), 3.85 g, 40 mmol
- Dry THF

irritant, hygroscopic**flammable, moisture sensitive****highly toxic****flammable corrosive**

1. Quickly finely grind cerium chloride heptahydrate to a powder in a mortar and place it in a two-necked round-bottomed flask. Immerse the flask in an oil bath and heat gradually to 135–140°C with evacuation (<0.5 mmHg). After 1 h at this temperature, completely dry the cerium chloride *in vacuo* by stirring at the same temperature for an additional hour. While the flask is still hot, introduce argon gas and cool the flask in an ice bath. Add dry THF (200 mL) all at once with vigorous stirring. Remove the ice bath and stir the suspension overnight under argon at room temperature.
2. Add a THF (27 mL) solution of *i*-PrMgBr (48 mmol) at 0°C, and stir the mixture at that temperature for 1.5 h.
3. Add a THF (10 mL) solution of 2-cyclohexene-1-one (40 mmol) dropwise over 10 min.
4. After 30 min at 0°C, add an aqueous solution of acetic acid (3%, 150 mL) and extract with ether (3 × 50 mL). Wash the combined extracts with brine, a solution of NaHCO₃, and brine. Dry the extract over MgSO₄ and concentrate under reduced pressure. Distil the desired product (4.5 g, 80%) as a fraction boiling at 83–85°C at 15 mmHg. This sample may contain 3% of 1,4-addition product as determined by capillary GLC analysis (Silicon OV-17).

Protocol 3.**Aldol reaction with cerium enolate: synthesis of 2-(1-hydroxycyclohexyl)-1-phenyl-1-propanone^{10,11} (Scheme 12.7)**

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.

**Scheme 12.7****Equipment**

- A two-necked, round-bottomed flask (200 mL) fitted with a septum, a three-way stopcock, and a magnetic stirring bar. The three-way stopcock is connected to a vacuum/argon source
- Vacuum/argon source
- Syringes

Materials

- Di-isopropylamine (FW 101.2), 1.5 mL **flammable, corrosive**
- *n*-BuLi (FW 64.06), 1.53 M solution in hexane, 7.2 mL, 11 mmol **pyrophoric, moisture-sensitive**
- Propiophenone (FW 134.2), 1.34 g, 10 mmol
- Cerium chloride, anhydrous (FW 246.5) suspension in THF (see Protocol 2) **irritant, hygroscopic**
- Cyclohexanone (FW 98.15), 0.982 g, 11 mmol **corrosive, toxic**
- Dry THF **flammable, corrosive**

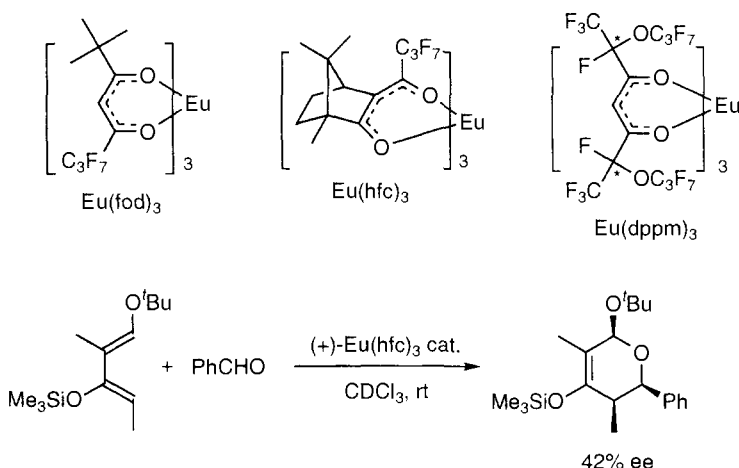
1. Flame dry the reaction vessel under dry argon. Quickly add a stirring bar while the flask is hot, and then refill the flask with argon through several vacuum cycles. Maintain a slightly positive argon pressure throughout this reaction.
2. Add THF (15 mL) and di-isopropylamine (1.5 mL) and cool the mixture to -78°C with a dry ice-acetone bath. Add dropwise a hexane solution of *n*-BuLi (11 mmol) with stirring. After stirring for 10 min, add a THF (5 mL) solution of propiophenone (10 mmol).
3. After stirring for 1 h, add a THF (50 mL) suspension of anhydrous cerium chloride (12 mmol) (see Protocol 2) via a syringe and stir the mixture for 30 min at that temperature.
4. Add a THF (2 mL) solution of cyclohexanone (10 mmol).
5. Stirring for 30 min, then pour the mixture into an aqueous solution of acetic acid (3%, 50 mL). Extract with ether (3 × 50 mL), and then wash the combined extracts with brine, a solution of NaHCO₃, and brine. Dry the extract

Protocol 3. Continued

over MgSO_4 and concentrate under reduced pressure. Purify the crude product by flash chromatography (silica gel, hexane–ethylacetate, 5:1) to give 2-(1-hydroxycyclohexyl)-1-phenyl-1-propane (1.67 g, 72%), $[\alpha]^{20}_{\text{D}} -5.3^\circ$ (c 1.2, EtOH).

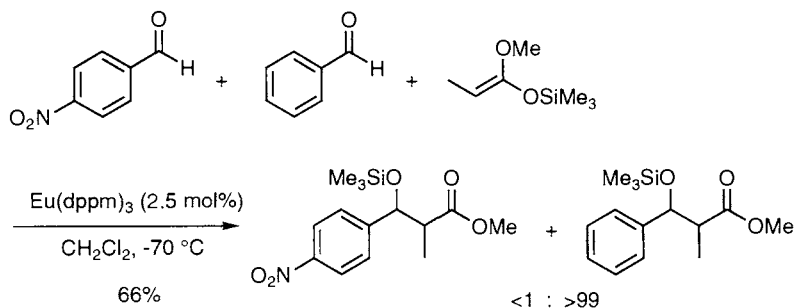
3. Europium(III) reagents

Although Eu(III) complexes such as $\text{Eu}(\text{fod})_3$ are familiar to organic chemists as NMR shift agents, the use of Eu complexes as synthetic reagents is a rather recent event. In 1983 Danishefsky *et al.* demonstrated the usefulness of (+)- $\text{Eu}(\text{hfc})_3$ as an asymmetric catalyst for the hetero Diels–Alder reaction (Scheme 12.8). Since then, a variety of Eu(III) complexes, including EuCl_3 and $\text{Eu}(\text{dppm})_3$, have been used as unique catalysts for different synthetic transformations.

**Scheme 12.8**

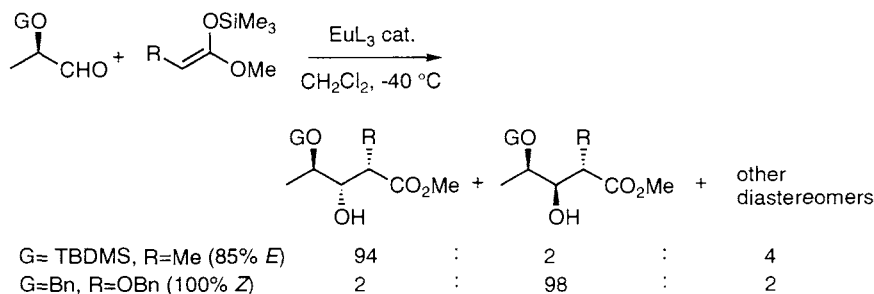
To date, europium(III) complexes have found many applications as efficient Lewis acid catalysts for Diels–Alder reactions,^{14,15} hetero Diels–Alder reactions,^{14,16–18} aldol reactions with ketene silyl acetals (KSA),^{19–25} Michael reactions of α,β -enones with KSA,²⁶ and cyanosilylation of aldehydes with silyl cyanides.²⁷ Compared with conventional Lewis acids such as TiCl_4 , SnCl_4 , and $\text{BF}_3 \cdot \text{OEt}_2$ (stoichiometric use), the europium catalyses are often quite unique in chemo- and stereoselectivities. For instance, $\text{Eu}(\text{dppm})_3$ is effective as the catalyst for aldol reactions between aldehydes and KSA, but not effective for the reactions between aldehydes and ketone-derived enol silyl ethers.²¹

Scheme 12.9 illustrates the unique ability of $\text{Eu}(\text{dppm})_3$ to discriminate the aldehydes, where *p*-nitrobenzaldehyde is less reactive than benzaldehyde. This reversal of reactivity is ascribed to preferential activation of benzaldehyde over *p*-nitrobenzaldehyde by the Eu catalyst. A similar molecular discrimination by $\text{Eu}(\text{fod})_3$ is achieved between ketones and α,β -enones in the reactions with KSA in which the Eu catalyst preferentially activates the latter in preference to the former.²²

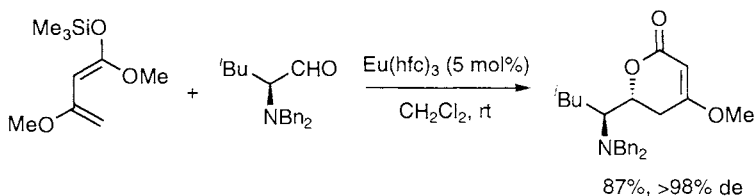


Scheme 12.9

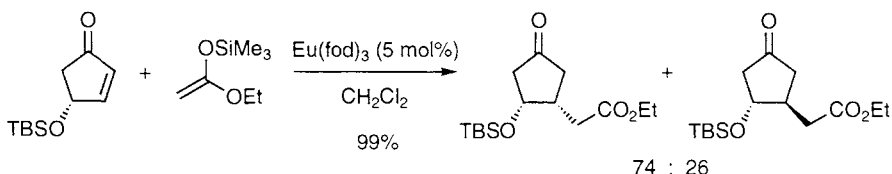
Of more significance is the unique stereocontrolling ability of the Eu-catalysts. For example, the $\text{Eu}(\text{fod})_3$ -catalysed aldol reactions of chiral α -alkoxy aldehydes with KSA provides high levels of diastereofacial selection and simple diastereoselections, where the stereochemistry of the major product is effectively modulated by changing the protecting group (G) through the molecular recognition (chelation vs. non-chelation) by the Eu catalyst (Scheme 12.10).^{23–25} A similar stereomodulation by the Eu catalyst is attained in the hetero Diels–Alder reactions of α -amino and α -alkoxy aldehydes (Scheme 12.11).^{28,29} Interestingly, the Michael addition of the 4-siloxy cyclopentenone with the acetate-derived KSA is shown to proceed with the sterically less favourable *syn* diastereofacial selectivity (Scheme 12.12).³⁰



Scheme 12.10



Scheme 12.11



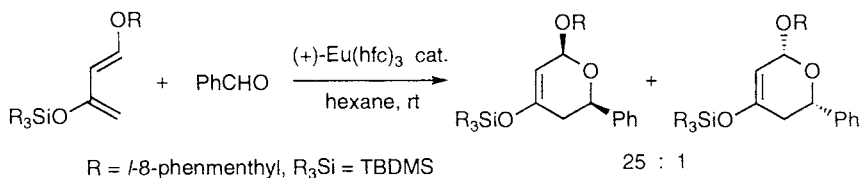
Scheme 12.12

As far as asymmetric catalysis by chiral europium complexes is concerned, modest enantioselectivities (up to 42% ee) are observed in the (+)-Eu(hfc)₃ catalysed hetero Diels–Alder reactions (Scheme 12.8),¹³ whereas almost no asymmetric inductions (up to 10% ee) are observed in the (–)-Eu(dppm)₃-catalysed aldol reactions.²¹ More recently, the chiral europium complex, prepared *in situ* from Eu(OTf)₃ and the disodium salt of a chiral diamine, has been reported to provide *c.* 40% ee in the aldol reactions of benzaldehyde with KSA.³¹ Thus, the development of asymmetric catalysis by chiral Eu complexes remains a challenge.

Protocol 4.

Diels–Alder reaction¹⁷ (Scheme 12.13)

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.



Scheme 12.13

Equipment

- A two-necked, round-bottomed flask fitted with a septum, a three-way stopcock, and a magnetic stirring bar. A three-way stopcock is connected to a vacuum/argon source
- Vacuum/argon source
- Syringes

Materials

- Benzaldehyde (FW 106.12), 234 mg, 2.20 mmol
- *l*-8-Phenmethoxy diene (FW 414.71), 912 mg, 2.20 mmol
- (+)-Eu(hfc)₃ (FW 1193.73), 131 mg, 0.11 mmol
- Dry Hexane, 12 mL
- Triethylamine (FW 101.19), 8 mL
- Methanol 4 mL

highly toxic, cancer suspect agent

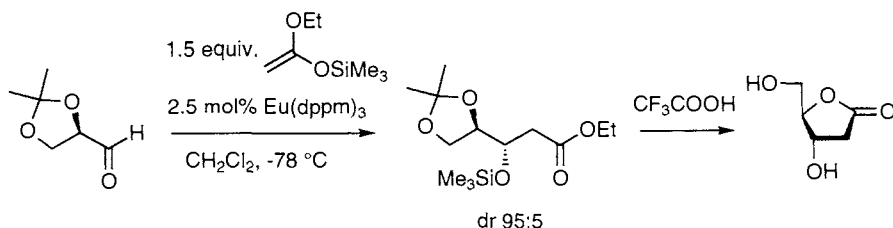
hygroscopic
flammable, irritant
flammable, corrosive
flammable, toxic

1. Add a solution of benzaldehyde (2.20 mmol) and *l*-8-phenmethoxy diene (2.20 mmol) in hexane (12 mL) to the flask. Cool the mixture to -20°C and add (+)-Eu(hfc)₃ (0.11 mmol). Keep the reaction mixture at between -10 and -20°C for 60 h.^a
2. Add triethylamine (8 mL) and methanol (4 mL) and allow the mixture to warm to room temperature. Remove the volatiles *in vacuo*, and pass the crude material through a plug of silica gel. Wash the plug with ethyl acetate. Concentrate the organics under reduced pressure to give enol silyl ether (1.10 g, 95%, dr 25:1). Crystallize this material from ethanol and recrystallize this residue from the mother liquors to give optically pure compound as white crystals (0.69 g, 60%); m.p. $59.5\text{--}60.8^{\circ}\text{C}$, $[\alpha]^{23}_{\text{D}} +47.3^{\circ}$ (c 1.1, CHCl_3).

^a After which time NMR analysis showed that no starting aldehyde or diene remained.

Protocol 5.
Eu(fod)₃-catalysed aldol reaction: preparation of optically pure 2-deoxy-D-ribonolactone²³ (Scheme 12.14)

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.

**Scheme 12.14****Equipment**

- A two-necked, round-bottomed flask (30 mL) fitted with a septum, a three-way stopcock, and a magnetic stirring bar. The three-way stopcock is connected to a vacuum/argon source
- A round-bottomed flask (30 mL) fitted with a stirring bar
- Vacuum/argon source.
- Syringes

Protocol 5. Continued**Materials**

- D-Glyceraldehyde acetonide (FW 130.1), 130 mg, 1.0 mmol
- 1-Ethoxy-1-trimethylsiloxyethene (FW 160.3), 240 mg, 1.5 mmol
- (–)-Eu(dppm)₃ (FW 2072), 30 w/v% solution in CF₂ClCFCFCl₂,^a 172 μL, 0.025 mmol
- Dry CH₂Cl₂

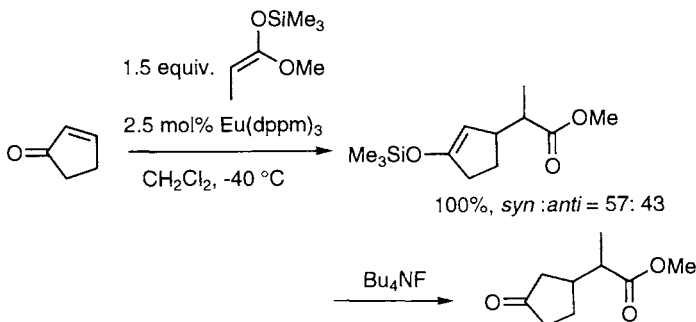
toxic, irritant

1. Flame dry the reaction vessel under dry argon. Quickly add a stirring bar while the flask is hot, and then refill the flask with argon through several vacuum cycles. Maintain a slightly positive argon pressure throughout this reaction.
2. Add a solution of D-glyceraldehyde acetonide (1 mmol) and 1-ethoxy-1-trimethylsiloxyethene (1.5 mmol) in CH₂Cl₂ (4 mL) to the flask with the aid of a syringe through the septum and then cool it to –78°C. Add a solution of (–)-Eu(dppm)₃ in CF₂ClCFCFCl₂ (172 μL, 0.025 mmol) and then stir the mixture for 2 h at the same temperature.
3. Add saturated aqueous NH₄Cl solution and extract with ethyl acetate (3 × 20 mL). Wash the combined extracts with brine, dry over MgSO₄, and concentrate the crude product under reduced pressure (diastereomer ratio; *anti/syn* = 95:5).
4. Dissolve a crude product in THF (2 mL) and to this add trifluoroacetic acid (0.5 mL) and one drop of water.
5. After stirring for 1 day, add aqueous NaHCO₃ solution and extract with ethyl acetate (5 × 30 mL). Wash the combined extracts with brine and concentrate under reduced pressure. Purify the crude product by flash chromatography (silica gel; hexane–ethylacetate, 5:1) to give optically pure 2-deoxy-D-ribonolactone (0.118 g, 90%), [α]_D²⁰ 25.3° (c 1.2, EtOH).

^a Purchased from Dai-ichi Kagaku Yakuin.

Protocol 6.**(+)-Eu(dppm)₃-catalysed Michael reaction: reaction of a ketenesilylacetal with 2-cyclopentenone.²⁶ (Scheme 12.15)**

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.

**Scheme 12.15****Equipment**

- A two-necked, round-bottomed flask (30 mL) fitted with a septum, a three-way stopcock, and a magnetic stirring bar. The three-way stopcock is connected to a vacuum/argon source
- Vacuum/argon source
- Syringes

Materials

- 2-Cyclopentenone (FW 82.10), 41 mg, 0.5 mmol
- (E)-1-[(trimethylsilyl)oxy]-1-methoxy-1-propene
- (+)-Eu(dppm)₃, 30 w/v% solution in CF₂ClCFCFCl₂^a
- Dry CH₂Cl₂
- Tetrabutylammonium fluoride (FW 261.5), 1.0 M solution in THF
- Dry THF

toxic, irritant
flammable, irritant
flammable, corrosive

1. Flame dry the reaction vessel under dry argon. Quickly add a stirring bar while the flask is hot, and then refill the flask with argon through several vacuum cycles. Maintain a slightly positive argon pressure throughout this reaction.
2. Add a solution of 2-cyclopentenone (0.5 mmol) in CH₂Cl₂ (1.5 mL) and a 30 w/v% solution of (+)-Eu(dppm)₃ (0.0125 mmol) in CF₂ClCFCFCl₂ to the flask with the aid of a syringe through the septum and then cool it to -40 °C. Add (E)-1-[(trimethylsilyl)oxy]-1-methoxy-1-propene (0.75 mmol) to the stirred solution.
3. After stirring for 1 h, pour the mixture into a aqueous saturated solution of NaHCO₃. Extract with ethyl acetate (3 × 30 mL). Wash the combined extracts with brine, dry over MgSO₄, and concentrate the crude product under reduced pressure.

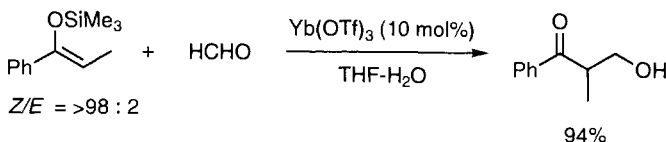
Protocol 6. Continued

4. Dissolve a crude product in THF (1 mL) and to this add a 1.0 M THF solution of Bu₄NF (1 mL) at room temperature. After stirring for several hours and monitor the disappearance of the silyl enol ether by TLC.
5. Pour the mixture into a water (20 mL) and extract with ethyl acetate (5 × 30 mL). Wash the combined extracts with brine and concentrate under reduced pressure. The crude product was purified by flash chromatography (silica gel, hexane–ethyl acetate) to give 3-[(1'-carbomethoxy)ethyl]-1-cyclopentanone (78 mg, 100%) as a diastereomer mixture (*syn:anti* = 57:43).

^a Purchased from Dai-ichi Kagaku Yakuhin.

4. Ytterbium(III) reagents

The most important of these reagents is ytterbium triflate, Yb(OTf)₃, which has found wide application as a catalyst for several C–C bond-forming reactions. The most notable is the Yb(OTf)₃-catalysed aldol reaction of aldehydes (or acetals) with enol silyl ethers which proceeds smoothly in dichloromethane and, more significantly, even in aqueous media (Scheme 12.16).^{32–36} It should be noted that a similar catalytic activity is also observed with Nd(OTf)₃, Gd(OTf)₃, and Lu(OTf)₃.

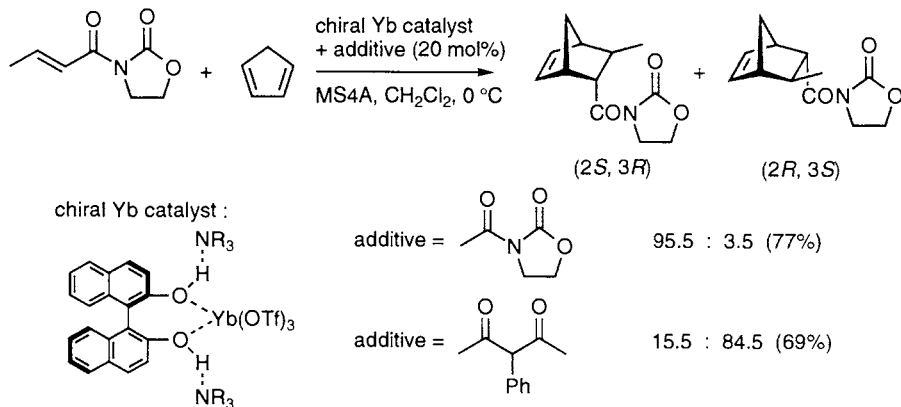


Scheme 12.16

In addition, Yb(OTf)₃ is also effective as a catalyst for the Michael reactions of α,β-enones with enol silyl ethers,³⁷ the Friedel–Crafts acylations with acid anhydrides,^{38,39} and the Diels–Alder reactions, wherein Yb(OTf)₃ is, however, often less active than Sc(OTf)₃. A major merit of the Yb-catalysed reactions is that the catalyst is stable in water and hence can be easily recovered from the aqueous layer and reused.³⁵

More significantly, the chiral Yb triflate, prepared *in situ* from Yb(OTf)₃, (*R*)-binaphthol, and a tertiary amine, is shown to serve as an efficient asymmetric catalyst for the Diels–Alder reaction (Scheme 12.17).⁴⁰ The most striking feature of the asymmetric catalysis is that the chiral Yb catalyst, when combined with 3-phenylacetylacetone as an additive (another achiral ligand), shows the opposite sense of enantioselection to that observed in the cases where the substrate itself or 3-acetyl-1,3-oxazolin-2-one acts as another ligand

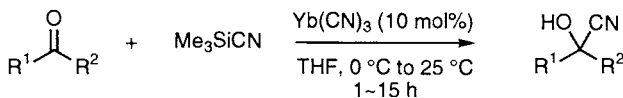
12: Lanthanide(III) Reagents



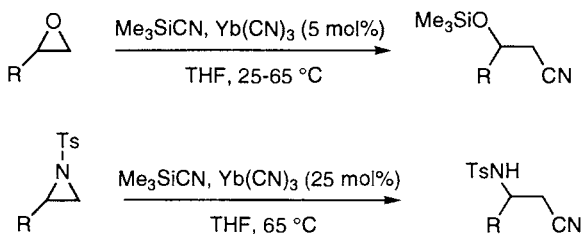
Scheme 12.17

as depicted in Scheme 12.17. The remarkable enantiocontrol by a proper choice of achiral ligands is explained in terms of the significant difference in complexation mode between the chiral catalytic species involved and the imide dienophile. A similar phenomenon is observed when other lanthanide triflates such as Lu(OTf)₃, Tm(OTf)₃, and Ho(OTf)₃ are used in place of Yb(OTf)₃.

Further notable ytterbium reagents are Yb(fod)₃ as an efficient catalyst for the ene-type reaction of aldehydes with vinylic ethers,⁴¹ and Yb(CN)₃ as an active catalyst for the cyanosilylation of carbonyls, including enolizable ketones and α,β -enones (Scheme 12.18),⁴² and for the regioselective ring opening of oxiranes and aziridines with Me₃SiCN (Scheme 12.19).^{43,44}

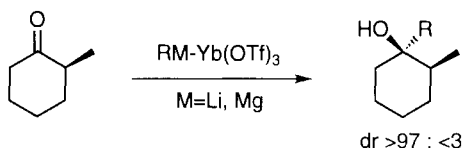


Scheme 12.18



Scheme 12.19

Ytterbium complexes have also found stoichiometric uses in organic synthesis. The alkylytterbium complex, generated *in situ* from $\text{Yb}(\text{OTf})_3$ or YbCl_3 and an alkyl-lithium or Grignard reagent, provides a unique and high stereoselectivities in the additions to ketones (Scheme 12.20).^{45,46}

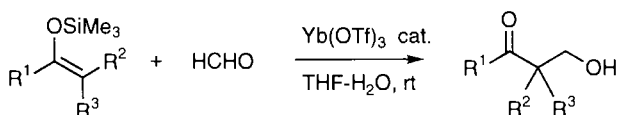


Scheme 12.20

Protocol 7.

$\text{Yb}(\text{OTf})_3$ -catalysed aldol reaction: reaction of an enol trimethylsilyl ether with formaldehyde. General procedure³⁶ (Scheme 12.21)

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.



Scheme 12.21

Equipment

- A round-bottomed flask fitted with a stirring bar

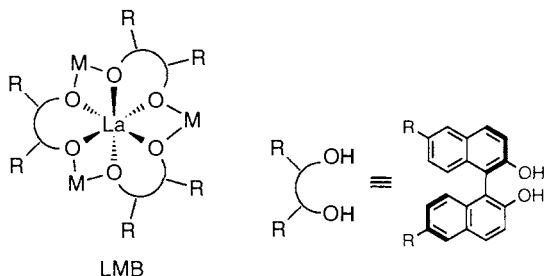
Materials

- Formaldehyde (FW 30.03), 40 wt. % solution in water, 1 mL **highly toxic, cancer-suspect agent**
- Enol silyl ether, 0.4 mmol
- $\text{Yb}(\text{OTf})_3$ (FW 620.3), 25 mg, 0.04 mmol **irritant, hygroscopic**
- THF **flammable, corrosive**

1. Add commercial formaldehyde solution (40% water solution, 1 mL) and THF (3 mL) to the flask.
2. Add $\text{Yb}(\text{OTf})_3$ (0.04 mmol, 10 mol%) and a THF (1 mL) solution of enol silyl ether (0.4 mmol) at room temperature, and then stir the mixture for 24 h at this temperature.
3. Remove the THF under reduced pressure. Add water and extract the product with CH_2Cl_2 . After the usual work-up, chromatograph the crude product on silica gel to yield the aldol product. $\text{Yb}(\text{OTf})_3$ was almost quantitatively recovered from the aqueous layer after removing water and could be reused.

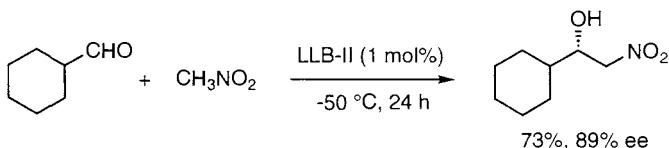
5. Lanthanum(III) reagents

Recently $\text{La}_3(\text{O}^t\text{Bu})_9$ has been found to serve as an efficient Lewis base catalyst for C–C bond-forming reactions such as the aldol reaction of α -chloro ketones with aldehydes, the nitroaldol (Henry) reactions of aldehydes with nitroalkanes, and the intramolecular aldol reactions of 1,5-diketones.⁴⁷ Based on these findings, Shibasaki's group has developed several (*R*)- or (*S*)-binaphthol (BINOL)-based chiral bimetallic lanthanum complexes, $\text{LaM}_3\text{tris}(\text{binaphthoxide})$ LMB ($\text{M} = \text{Li}, \text{Na}, \text{K}$) (Scheme 12.22), which serve as excellent asymmetric catalysts for the nitroaldol reaction, the hydrophosphonylation of aldehydes and imines, the Diels–Alder reaction, and the Michael reaction.⁴⁸



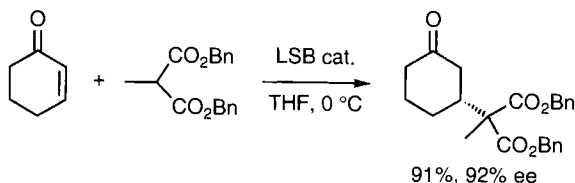
Scheme 12.22

Of special value is the enantioselective nitroaldol reaction catalysed by (*R*)-LLB, prepared *in situ* from either $\text{LaCl}_3 \cdot 7\text{H}_2\text{O}$, the dilithium salt of (*R*)-BINOL, and NaO^tBu or from $\text{La}(\text{O}^i\text{Pr})_3$ and (*R*)-BINOL, and *n*-BuLi, and then H_2O , which affords the nitroaldol in a high % ee (Scheme 12.23).^{49,50} Interestingly, the use of either the second generation LLB-II catalyst (LLB + LiOH) or the 6,6'-disubstituted BINOL-based LLB provides a higher % de and % ee in the reactions leading to a diastereomeric mixture of the nitroaldols.



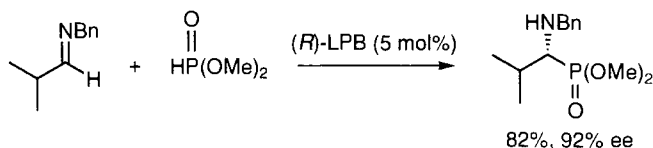
Scheme 12.23

LLB also serves as an efficient asymmetric catalyst for the Diels–Alder reaction⁴⁹ and the hydrophosphonylation of aldehydes,^{51–53} but not for the Michael reaction and the hydrophosphonylation of imines. Significantly, however, LSB and LPB are shown to work as an excellent asymmetric catalyst for the Michael reaction (Scheme 12.24)^{54,55} and the hydrophosphonylation of



Scheme 12.24

imines (Scheme 12.25),⁵⁶ respectively. It should be noted that similar chiral bimetallic complexes derived from other lanthanides such as EuMB, GdMB, and PrMB ($M = \text{Li, Na, K}$) often show a comparably high catalytic activity, but provides a much lower % ee in general.

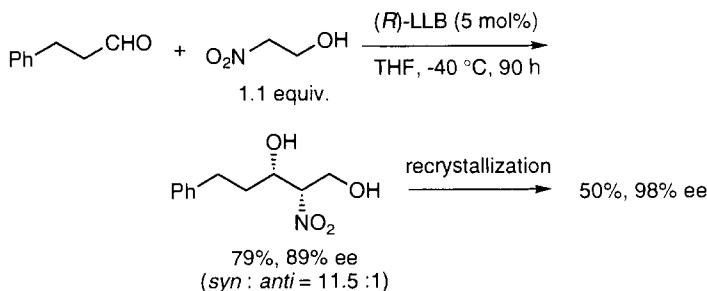


Scheme 12.25

Protocol 8.

Catalytic asymmetric nitroaldol reaction⁵⁰

Caution! Carry out all procedures in a well-ventilated hood, and wear disposable vinyl or latex gloves and chemical-resistant safety goggles.



Scheme 12.26

Equipment

- A two-necked, round-bottomed flask fitted with a septum, a three-way stopcock, and a magnetic stirring bar. A three-way stopcock is connected to a vacuum/argon source
- Vacuum/argon source
- Syringes

Materials

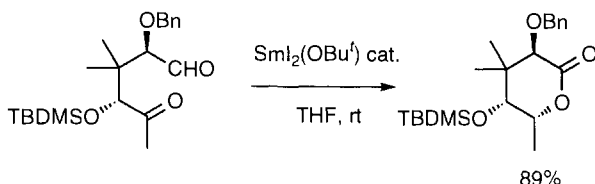
- (*R*)-(+)-1,1'-Bi-2-naphthol (FW 286.33), 6.5 g, 22.7 mmol irritant
- *n*-Butyllithium (FW 64.06), 1.60 M solution in hexanes, 28.4 mL, 45.4 mmol flammable, moisture sensitive
- $\text{LaCl}_3 \cdot 7\text{H}_2\text{O}$ (FW 371.38), 3.12 g, 8.40 mmol irritant, hygroscopic
- $\text{NaO}-t\text{-Bu}$ (FW 96.11), 242 mg, 2.52 mmol flammable, corrosive
- 2-Nitroethanol (FW 91.07), 19.1 mg, 0.21 mmol irritant
- Hydrocinnamaldehyde (FW 134.18), 25.5 mg, 0.19 mmol irritant
- Dry THF flammable, corrosive

1. Add (*R*)-(+)-1,1'-Bi-2-naphthol (22.7 mmol) to the flask. Dry at 50°C for 2 h under reduced pressure. Add dry THF (119 mL) under Ar,
2. Add a hexanes solution of *n*-BuLi (1.60 N, 28.4 mL, 45.4 mmol) at 0°C.
3. Charge a suspension of $\text{LaCl}_3 \cdot 7\text{H}_2\text{O}$ (8.40 mmol) in THF (100 mL) to the different flask. Sonicate for 30 min at room temperature. To this suspension, add the above-prepared solution of dilithium binaphthoxide and a THF solution of $\text{NaO}-t\text{-Bu}$ (0.52 N, 4.85 mL, 2.52 mmol), dropwise at room temperature.
4. Vigorously stir the mixture overnight at room temperature, and then for 48 h at 50°C. Stand the mixture at room temperature. The resulting supernatant may contain an optically active LLB complex (0.03 M).
5. Charge a THF solution of optically active LLB complex (0.03 M, 209 μL , 0.00627 mmol) to the flask. Add THF (500 μL) and cool the mixture to -40°C and stir for 30 min.
6. Add a THF (200 μL) solution of 2-nitroethanol (15 μL , 0.21 mmol), and stir the mixture for 30 min at the same temperature.
7. Add hydrocinnamaldehyde (25 μL , 0.19 mmol), and then stir the mixture for 90 h at -40°C).
8. Add a 1N HCl and then extract with AcOEt (30 mL); wash the organic layer with brine. Dry the extract over Na_2SO_4 and concentrate under reduced pressure. Purify the crude product by chromatography (Lobar Lichropep RI-8 prepacked column, $\text{CH}_3\text{CN}-\text{H}_2\text{O}$ 1:1), to give (2*S*,3*S*)-2-nitro-5-phenyl-1,3-pentanediol (70%, *syn:anti* = 11:1, 91% ee). Determine the enantiomeric excess HPLC analysis using DAISEL CHIRALPAK AD (hexane: *i*-PrOH 9:1).

6. Other lanthanide(III) reagents

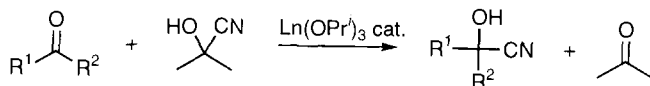
So far, the synthetic utilities of the four important classes of trivalent lanthanide reagents have been described. Outlined below are selected examples of the synthetic uses of other trivalent lanthanide complexes as catalysts.

A series of lanthanide isopropoxides, including $\text{La}(\text{OPr}^i)_3$, $\text{Ce}(\text{OPr}^i)_3$, $\text{Sm}(\text{OPr}^i)_3$, $\text{Gd}(\text{OPr}^i)_3$, have been found to exhibit an efficient catalytic activity in the Meerwein-Ponndorof-Verley (MPV) reductions. These catalysts



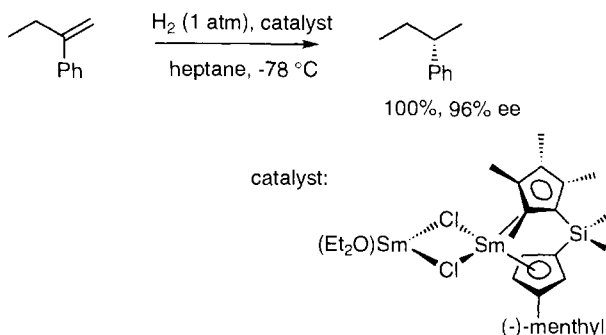
Scheme 12.27

are far more active than the existing catalysts such as $\text{Al}(\text{OPr}^i)_3$. Interestingly, $\text{Sm}(\text{OBu}^t)_2$, prepared *in situ* from SmI_2 and di-*t*-butylperoxide, works well as a catalyst for MPV reduction^{57–60} and also for the intramolecular Tishchenko reaction (Scheme 12.27).⁶¹ These lanthanide alkoxides also serve as an efficient catalyst for the transhydrocyanation of acetone cyanohydrin to aldehydes or ketones (Scheme 12.28).⁶²



Scheme 12.28

$\text{Lu}(\text{III})$ and $\text{Sm}(\text{III})$ hydride complexes having pentamethylcyclopentadienyl (Cp') ligands work as an extremely active homogeneous catalyst for the hydrogenation of terminal olefins in particular.^{63,64} Of special value is the asymmetric hydrogenation using a chiral samarium catalyst with a chiral auxiliary on the Cp ring (Scheme 12.29).⁶⁵



Scheme 12.29

Finally, some lanthanide complexes such as $(\text{Cp}'_2 \text{LnR})_2$ ($\text{Ln} = \text{La}, \text{Sm}, \text{Yb}, \text{Nd}, \text{Lu}$; $\text{R} = \text{H}, \text{Me}$) have been shown to be extremely active homogeneous catalysts for the polymerization of ethylene (not propylene), methyl metha-

crylate (MMA), ϵ -caprolactam, and δ -valerolactone.^{66,67} Of interest is the lanthanide-catalyzed polymerization of MMA which proceeds in a living polymerization fashion to produce polymers of high molecular weight ($>5 \times 10^5$) with a narrow polydispersity ($M_w/M_n = 1.02\text{--}1.03$) and a high syndiotacticity ($>95\%$).^{68,69}

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12: Lanthanide(III) Reagents

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