

Scandium(III) and yttrium(III)

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1. Introduction

According to the inorganic chemistry text book written by Cotton and Wilkinson,¹ scandium is not truly a rare earth element but yttrium and lanthanides are rare earth elements. The stable oxidation state of scandium is trivalent and the ionic radius of scandium (III) is significantly smaller (0.89 \AA) than those for any of the rare earth elements ($1.0\text{--}1.17 \text{ \AA}$). Chemical behaviour is intermediate between aluminium and that of lanthanides. Yttrium has a trivalent oxidation state similar to scandium and lanthanide elements and the ionic radius of yttrium (III) (1.04 \AA) is close to those of erbium (1.03 \AA) and holmium (1.04 \AA). Yttrium resembles lanthanide elements in its chemical properties.

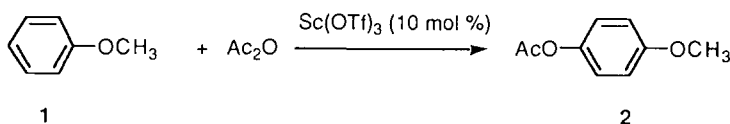
2. Scandium(III) triflate

Among scandium(III) compounds, scandium(III) trifluoromethanesulfonate (triflate) $[\text{Sc}(\text{OTf})_3]$ is the most attractive reagent and has been intensively studied in organic synthesis because it has a stronger Lewis acidity than that of other scandium (III) compounds.² Compared to even yttrium(III) and lanthanide(III) triflates, $\text{Sc}(\text{OTf})_3$ has a stronger Lewis acidity and catalyses certain reactions which are not mediated by yttrium(III) and lanthanide(III) triflates. The stronger Lewis acidity of $\text{Sc}(\text{OTf})_3$ is probably due to its smaller ionic radius than those of lanthanides. $\text{Sc}(\text{OTf})_3$ is commercially available or readily prepared by the reaction of scandium oxide and trifluoromethanesulfonic acid in water.³ Characteristic features of scandium triflate are as follows. It can be used as a catalyst in the presence of water and catalyses certain reactions and maintains catalytic activity. It can be recovered from the aqueous layer after reaction and reused in further reactions. As it is stable in water and air, it is easy to handle and the catalysed reaction can be carried out by a simple procedure.

2.1 Friedel–Crafts reaction

$\text{Sc}(\text{OTf})_3$ catalyses Friedel–Crafts acylation reaction of arenes effectively.⁴ It mediates the reaction more efficiently than $\text{Yb}(\text{OTf})_3$ and $\text{Y}(\text{OTf})_3$. Acylation

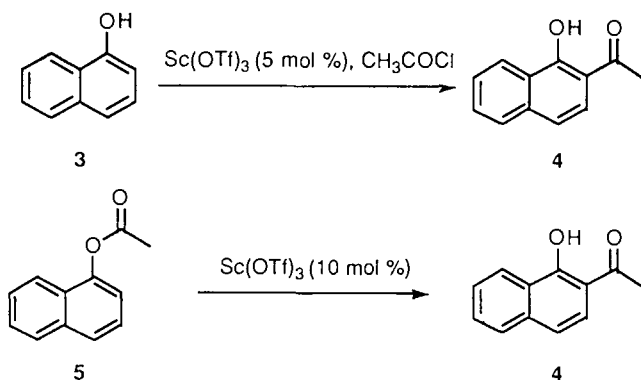
of benzene and toluene does not proceed, but reaction with more electron-rich arenes gives acylated products. Reaction with anisole, thioanisole, *o*- and *m*-dimethoxybenzene gives the corresponding single acylated product in excellent yields, respectively (Scheme 11.1).



Scheme 11.1

The advantages of the process are as follows. First, a catalytic amount (1 mol %) of $\text{Sc}(\text{OTf})_3$ is enough to promote the reaction in contrast to the conventional acylation reaction which requires a stoichiometric amount of Lewis acid. Second, evolution of hydrogen halide during quenching of Lewis acid, such as AlCl_3 , is avoided. Third, $\text{Sc}(\text{OTf})_3$ can be recovered from the aqueous layer and re-used as a catalyst, whereas disposal of a considerable amount of aluminium hydroxide which results from the work-up process is a severe environmental problem in the conventional Friedel–Crafts process.

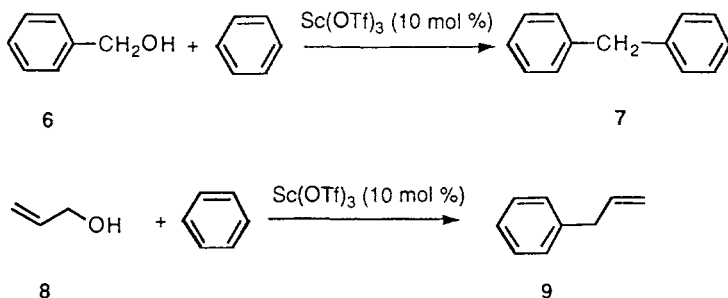
$\text{Sc}(\text{OTf})_3$ has been shown to catalyse *ortho*-selective acylation of phenol and naphthol derivatives with acyl halides to yield the corresponding ketones in high yields.⁵ The hydroxynaphthyl ketones (**4**) can also be obtained by $\text{Sc}(\text{OTf})_3$ -catalysed Fries rearrangement of acyloxy naphthalenes (Scheme 11.2).⁶



Scheme 11.2

$\text{Sc}(\text{OTf})_3$ catalyses Friedel–Crafts benzylation and allylation reactions with arenes using benzyl alcohol (**6**) and allylic alcohols (**8**) as electrophiles to give diarylmethanes (**7**) and allylarenes (**9**), respectively (Scheme 11.3).⁵ Water,

11: Scandium(III) and yttrium(III)



Scheme 11.3

produced during the reaction, does not spoil catalytic activity of Sc(OTf)_3 and a catalytic amount (10 mol %) of Sc(OTf)_3 is enough for the reaction. In contrast to conventional Friedel–Crafts benzylation and allylation using organic halides as electrophiles which produces troublesome hydrogen halides as by-products, this process only produces water. Considering the advantages of Sc(OTf)_3 in the Friedel–Crafts reaction, it may solve some severe environmental problems induced by conventional Lewis acid-promoted reactions in industry.

Protocol 1.

Preparation of *p*-methoxyacetophenone⁴

Equipment

- Three-necked round-bottomed flask (50 mL)
- Magnetic stirrer
- Thermostatted oil bath
- Reflux condenser
- Three-way stopcock
- Stopcocks
- Thermometer (100°C)
- Drying tube (calcium chloride)
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3)
- Erlenmeyer flask (200 mL)
- Teflon-coated magnetic stirrer bar (2.0 × 0.7 cm)

Materials

- Distilled (CaH₂ nitromethane (FW 61.04), 10 mL
- Anisole (FW 108.14), 1.08 g, 10.0 mmol
- Distilled acetic anhydride (FW 102.09), 1.02 g, 10.0 mmol
- Sc(OTf)_3 (FW 492.16), 0.98 g, 2.0 mmol
- Diethyl ether for extraction, 60 mL
- Anhydrous magnesium sulfate

flammable
irritant, hygroscopic
corrosive, lachrymator
irritant, hygroscopic
flammable, toxic
hygroscopic

1. Place Sc(OTf)_3 (0.98 g, 2.0 mmol) and a magnetic stirrer bar in a three-necked round-bottomed flask (50 mL) connected with two stopcocks and a three-way stopcock.
2. Heat a flask in an oil bath at 180°C under vacuum (1 mm Hg) for 1 h.
3. When the flask has cooled to room temperature, connect a reflux condenser, a thermometer and a drying tube.

Protocol 1. Continued

4. Add nitromethane (10 mL) to the flask and stir for 10 min, and then add anisole (1.08 g, 10.0 mmol) and acetic anhydride (1.02 g, 10.0 mmol).
5. Heat the solution to 50°C in an oil bath equipped with a temperature controller (bath temperature, 70°C).
6. Keep the temperature at 50°C with stirring and monitor the disappearance of anisole by TLC (visualized with UV). It takes 4 h to complete the reaction.
7. Add water (30 mL) to the solution. Separate the organic layer with the aid of separating funnel (100 mL). Extract the aqueous layer with three portions of diethyl ether (20 mL). Wash the combined organic layers with brine (30 mL). Transfer the solution to an Erlenmeyer flask and dry the solution over anhydrous magnesium sulfate.
8. Filter the dried solution through a sintered-glass filter funnel and remove the solvent on a rotary evaporator to leave a pale-yellow residue. Distill the residue by Kugelrohr at 0.4 mmHg to collect 1.22 g (7.4 mmol, 74%) of the product (oven temperature, 110°C). The compound was characterized by ¹H NMR and elemental analysis. The product comprises only *p*-acetoxyanisole; no *o*- and *m*-isomers were detected by capillary GC analysis (capillary column coated with (5%-phenyl)methylpolysiloxane).

Protocol 2.**Reaction of benzylalcohol with benzene⁷***Equipment*

- Three-necked round-bottomed flask (200 mL)
- Magnetic stirrer
- Thermostatted oil bath
- Reflux condenser
- Three-way stopcock
- Drying tube (calcium chloride)
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3).
- Erlenmeyer flask (200 mL)
- Teflon-coated magnetic stirrer bar (2.0 × 0.7 cm)

Materials

- Benzene (FW 78.11), 100 mL, 1.11 mol
- Distilled benzyl alcohol (FW 108.14) 2.16 g, 20.0 mmol
- Sc(OTf)₃^a (FW 492.16), 0.98 g, 2.0 mmol
- Diethyl ether for extraction, 50 mL
- Anhydrous magnesium sulfate

cancer-suspect agent, flammable
irritant, hygroscopic
irritant, hygroscopic
flammable, irritant
hygroscopic

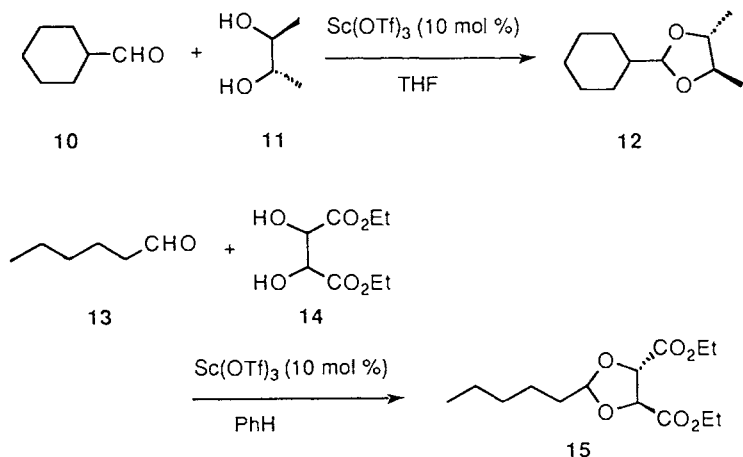
1. Assemble a three-neck round-bottomed flask, a magnetic stirrer bar, a reflux condenser, and a drying tube.
2. Add Sc(OTf)₃ (0.98 g, 2.0 mmol), benzene (100 mL) and benzyl alcohol (2.16 g, 20.0 mmol) to the flask and heat the solution at refluxing temperature with stirring.
3. After stirring for 8 h under reflux, cool the flask to room temperature.

4. Add water (50 mL) to the solution. Separate the organic layer with the aid of separating funnel (300 mL). Extract the aqueous layer with diethyl ether (50 ml). Wash the combined organic layers with brine (30 ml). Transfer the organic layer to an Erlenmeyer flask and dry the solution over anhydrous magnesium sulfate.
5. Filter the dried solution through a sintered-glass filter funnel and remove the solvent on a rotary evaporator. Distil the residue at 3.0 mmHg to collect 2.7 g (16.2 mmol, 81%) of the product boiling at 97°C. The compound was characterized by GC/MS, ^1H NMR and elemental analysis.
6. Concentrate the aqueous layer with a rotary evaporator and heat the crystalline residue $[\text{Sc}(\text{OTf})_3]$ at 180°C under vacuum for 20 h. The recovered $\text{Sc}(\text{OTf})_3$ can be used in the next Friedel–Crafts benzylation and allylation reactions.

^a Commercial $\text{Sc}(\text{OTf})_3$ retains moisture. Dry $\text{Sc}(\text{OTf})_3$ by heating in a flask using an oil bath at 180°C under vacuum (1 mm Hg) for more than 1 h (see Protocol 1).

2.2 Acetalization

Chiral acetals are particularly important precursors for the synthesis of enantiomerically pure compounds.⁸ Chiral dioxane and dioxolane are prepared by the direct reaction of aldehydes or ketones with chiral 1,3-diols and 1,2-diols in the presence of a catalytic amount of $\text{Sc}(\text{OTf})_3$ at room temperature (Scheme 11.4).⁹ Chiral 2,4-pentandiol, 2,3-butandiol, and diethyl tartarate are used as chiral diols. Considering that the chiral acetals derived from diethyl tartarate have only been prepared by trans-acetalization under acidic conditions,^{10,11} this method is convenient and practical. It is worth noting that removal of water which results from the acetalization is not necessary.



Scheme 11.4

Protocol 3.**Scandium(III) triflate catalysed acetalization of aldehyde⁹***Equipment*

- Three-necked round-bottomed flask (100 mL)
- Magnetic stirrer
- Three-way stopcock
- Stopcocks
- Drying tube (calcium chloride)
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3)
- Erlenmeyer flask (200 mL)
- Teflon-coated magnetic stirrer bar (2.0 × 0.7 cm)

Materials

- Dry distilled benzene (P₂O₅) (FW 78.11), 30 mL
 - Distilled hexanal (FW 100.16), 1.00 g, 10.0 mmol
 - L-(+)-Diethyl tartarate (FW 206.19), 2.50 g, 12.1 mmol
 - Sc(OTf)₃^a (FW 492.16), 0.98 g, 2.0 mmol
 - Diethyl ether for extraction, 50 mL
 - Anhydrous magnesium sulfate
- cancer-suspect agent, flammable
flammable, irritant
irritant, hygroscopic
flammable, irritant
hygroscopic

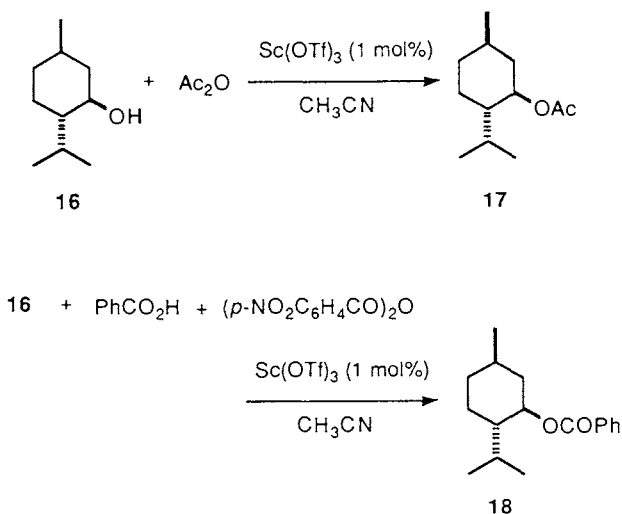
1. Assemble a three-neck round-bottomed flask (100 mL), a magnetic stirrer bar, a stopcock, a three-way stopcock and a drying tube.
2. Add Sc(OTf)₃ (0.98 g, 2.0 mmol) and benzene (15 mL) into a flask and stir the suspension for 10 min at room temperature.
3. Add (1*R*, 2*R*)-(+)-diethyl tartarate (2.50 g, 12.1 mmol) and stir the mixture at room temperature for 5 min until the mixture becomes homogeneous. Then, add hexanal (1.0 g, 10.0 mmol) and stir the solution at room temperature.
4. Monitor the production of the acetal by GC. After stirring for 48 h, add water (50 mL) to the solution. Separate the organic layer with the aid of a separating funnel (300 mL). Extract the aqueous layer with diethyl ether (50 mL). Wash the combined organic layers with brine (30 mL). Transfer the organic layer to a Erlenmeyer flask (200 mL) and then dry them over anhydrous magnesium sulfate.
5. Filter the dried solution through a sintered-glass filter funnel and remove the solvent on a rotary evaporator. Distil the residue at 0.3 mmHg to collect 1.98 g (6.9 mmol, 69%) of the product boiling at 97–100°C. The compound was characterized by GC/MS, ¹H NMR and elemental analysis.

^aCommercial Sc(OTf)₃ retains moisture. Dry Sc(OTf)₃ by heating in a flask using oil bath at 180°C under vacuum (1 mm HG) for more than 1 h (see Protocol 1).

2.3 Acetylation and esterification of alcohol

Acylation of alcohol is often required in organic synthesis, e.g. protection of a hydroxy group. The base-catalysed acylation by acid anhydride or acyl chloride is usually performed with a tertiary amine such as pyridine and its derivatives.¹² Acid-catalysed acylation of alcohols with acid anhydride is an

alternative acylation method which requires mild conditions. $\text{Sc}(\text{OTf})_3$ is an efficient catalyst for acylation of alcohols by acid anhydrides (Scheme 11.5).^{13,14} It also effectively catalyses the esterification of alcohols with carboxylic acid in the presence of *p*-nitrobenzoic anhydride.



Scheme 11.5

Protocol 4.

Preparation of L-acetyl menthol (17)^{13,14}

Equipment

- Three-necked round-bottomed flask (100 mL)
- Magnetic stirrer
- Three-way stopcock
- Stopcocks
- Drying tube (calcium chloride)
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3)
- All-glass syringe with a needle-lock luer (volume appropriate for quantity of solution to be transferred)
- Erlenmeyer flask (200 mL)
- Teflon-coated magnetic stirrer bar (2.0×0.7 cm)
- Glass column (2.5 cm \times 50 cm) packed with silica gel

Materials

- Dry distilled acetonitrile (CaH_2) (FW 41.05), 30 mL
- Distilled acetic anhydride (FW 102.09), 1.0 mL, 10.6 mmol
- L-(-)-Menthol (FW 156.27), 1.56 g, 10.0 mmol
- $\text{Sc}(\text{OTf})_3^a$ (FW 492.16), 0.05 g, 0.1 mmol
- Diethyl ether for extraction, 150 mL
- n-Hexane for column chromatography
- Ethyl acetate for column chromatography
- Anhydrous magnesium sulfate

flammable, toxic
corrosive, lachrymator
irritant
irritant, hygroscopic
flammable, irritant
flammable, irritant
irritant
hygroscopic

Protocol 4. Continued

1. Assemble a three-necked round-bottomed flask (100 mL), drying tube, a three-way stopcock, and a stopcock.
2. Add L-menthol (1.56 g, 10.0 mmol), acetic anhydride (1.53 g, 15.0 mmol), and acetonitrile (29 mL) to the flask and stir the solution for 10 min at room temperature.
3. Add dropwise a acetonitrile solution (1.0 mL) of $\text{Sc}(\text{OTf})_3$ (49.6 mg, 0.10 mmol) with the aid of a syringe (2.0 ml) through the three-way stopcock.
4. After stirring for 1 h, add a saturated aqueous sodium hydrogen carbonate solution (50 mL) to the solution. Transfer the mixture to a separating funnel (300 mL) and extract the aqueous layer with three portions of diethyl ether (50 mL) and separate the organic layer. Wash the combined organic layers with brine (30 mL), then dry over anhydrous magnesium sulfate. Capillary GC analysis (capillary column coated with 100% dimethylpolysiloxane) of the organic solution shows that L-menthol is converted into the acylated product quantitatively.
5. Filter the dried solution through a sintered-glass filter funnel and remove the solvent on a rotary evaporator. Prepare a column (2.5 cm \times 50 cm) for chromatography using silica gel (Merck Silica Gel 60) and *n*-hexane as the eluant. Dissolve the residue in a minimum volume (2 mL) of *n*-hexane and elute the column with *n*-hexane–ethyl acetate (5:1). Evaporate the eluate on a rotary evaporator to yield a colourless residue (2.00 g, 10.0 mmol, 100%). GC/MS and ^1H NMR spectra of the products display the suitable structure.

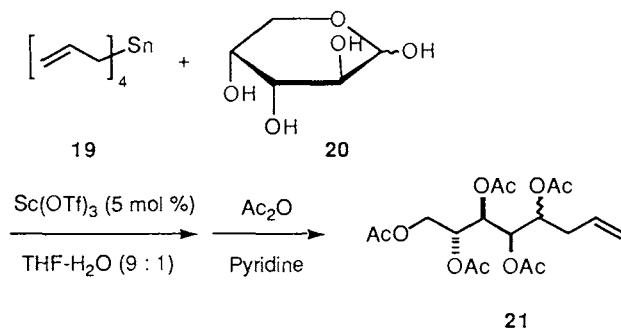
^a Commercial $\text{Sc}(\text{OTf})_3$ retains moisture. Dry $\text{Sc}(\text{OTf})_3$ by heating in a flask using an oil bath at 180°C under vacuum (1 mm Hg) for more than 1 h (see Protocol 1).

2.4 Allylation of carbonyl compounds with tetra-allyltin catalysed by scandium(III) triflate

Allylation of carbonyl compounds has been recognized as an important process to produce synthetically useful homoallylic alcohols.¹⁵ Tetra-allyltin is a good allyl transfer agent and itself reacts with ketones and aldehydes in the presence of an acid catalyst under mild conditions.¹⁶ Water-tolerant $\text{Sc}(\text{OTf})_3$ is an efficient catalyst for the allylation of carbonyl compounds with tetra-allyltin in aqueous media.¹⁷ The allylation reaction of ketones and aldehydes proceeds smoothly in the presence of catalytic amounts of $\text{Sc}(\text{OTf})_3$ to produce homoallylic alcohols in good yields under mild conditions. For example, monosaccharides such as D-arabinose (**20**) is easily allylated in aqueous media (Scheme 11.6).

The allylated adducts of saccharides are intermediates for the synthesis of higher saccharides.

11: Scandium(III) and yttrium(III)



Scheme 11.6

Protocol 5.

Scandium(III) triflate catalysed allylation of D-arabinose¹⁷

Equipment

- Three-necked round-bottomed flask (200 mL)
- Single-necked round-bottomed flask (300 mL)
- Magnetic stirrer
- Three-way stopcock
- Drying tube (calcium chloride)
- Pressure equalizing dropping funnel (50 mL)
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3)
- Erlenmeyer flask (200 mL)
- Teflon-coated magnetic stirrer bar (2.0 × 0.7 cm)
- Glass column (2.5 cm × 50 cm) packed with silica gel

Materials

- Dry distilled acetonitrile (CaH_2) (FW 41.05), 90 mL
 - Distilled water (FW 18.02), 10 mL
 - D-(+)-Arabinose (FW 151.12), 1.51 g, 10.0 mmol
 - Tetra-allyltin^a (FW 282.98), 1.41 g, 5.0 mmol
 - $\text{Sc}(\text{OTf})_3$ ^b (FW 492.16), 0.25 g, 0.5 mmol
 - Distilled pyridine (CaH_2) (FW 79.10), 25 mL
 - Acetic anhydride (FW 102.09), 10 mL, 0.13 mmol
 - Diethyl ether for extraction, 150 mL
 - Ethyl acetate for column chromatography
 - Anhydrous magnesium sulfate
- flammable, toxic**

toxic
irritant, hygroscopic
flammable, toxic
corrosive, lachrymator
flammable, irritant
flammable, irritant
hygroscopic

1. Assemble a three-necked round-bottomed flask (200 mL), drying tube, a three-way stopcock, and a dropping funnel.
2. Add $\text{Sc}(\text{OTf})_3$ (0.25 g, 0.50 mmol) and acetonitrile (40 mL)–water (10 mL) solution of D-arabinose (1.51 g, 10.0 mmol) to the flask.
3. Add acetonitrile (50 mL) solution of tetra-allyltin (1.41 g, 5.0 mmol) dropwise from a dropping funnel at room temperature and stir the solution at the same temperature for 60 h.
4. Transfer the solution into single-necked round-bottomed flask (300 mL) and remove the solvents on a rotary evaporator to leave a white residue.

Protocol 5. Continued

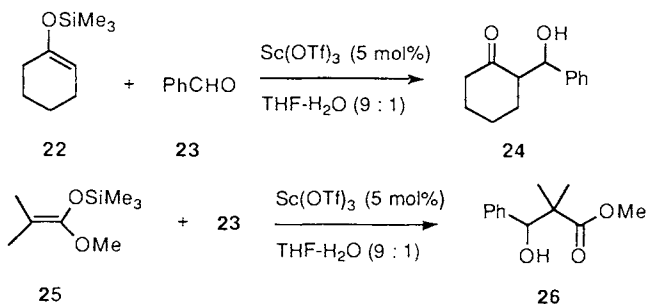
- Cool the flask with a ice-bath and add pyridine (25 mL) and Ac_2O (10 mL, 0.13 mol) with stirring. After 30 min warm the flask to room temperature and stir for 5 h.
- Transfer the solution into single-necked round-bottomed-flask (200 mL) and remove 70–80% volume of pyridine and excess of Ac_2O using a rotary evaporator under reduced pressure (10 mm Hg, temp 70°C). Treat the residue with cold 1M HCl (100 mL) and transfer the mixture to a separating funnel (300 mL). Extract the water layer with three portions of diethyl ether (50 ml) and wash the combined organic layer with a saturated aqueous solution of NaHCO_3 (50 mL). Transfer the organic layer to an erlenmeyer flask and dry the solution over anhydrous magnesium sulfate.
- Remove the solvent on a rotary evaporator to leave a pale-yellow viscous residue. Prepare a column (2.5 cm \times 50 cm) for chromatography using silica gel (Merck Silica Gel 60) and hexane as the eluant. Dissolve the residue in a minimum volume (5 mL) of chloroform and elute the column with ethyl acetate. Evaporate the ethyl acetate eluate on a rotary evaporator to yield a colourless residue (2.78 g, 6.9 mmol, 69%). Capillary GC analysis (Capillary column coated with 100% dimethypolysiloxane) of the residue shows that the product is a mixture of diastereomers (*anti:syn* 5 65:35). ^1H NMR spectra of the products display suitable structures.

^a Tetra-allyltin is prepared by the reaction of allylmagnesium chloride with tin(IV) chloride.^{18,19}

^b Commercial $\text{Sc}(\text{OTf})_3$ retains moisture. Dry $\text{Sc}(\text{OTf})_3$ by heating in a flask using oil bath at 180°C under vacuum (1 mm Hg) for more than 1 h (see Protocol 1).

2.5 Scandium(III) triflate-catalysed Mukaiyama aldol reaction

Although a wide variety of Lewis acid catalysts has been proposed for the Mukaiyama aldol reaction,²⁰ $\text{Sc}(\text{OTf})_3$ is a promising alternative catalyst for the reaction from the viewpoint that it can be used in aqueous media and recovered and reused (Scheme 11.7).²¹ Most Lewis acids usually decompose



Scheme 11.7

in the presence of even a small amount of water but $\text{Sc}(\text{OTf})_3$ works as a catalyst in aqueous media. A catalytic amount of $\text{Sc}(\text{OTf})_3$ (5 mol%) effectively catalyses the reaction of silyl enol ethers with aldehyde or acetals to yield the corresponding aldol adducts in H_2O –THF (1:9) solvent.

Protocol 6.

$\text{Sc}(\text{OTf})_3$ -catalysed reaction of 1-trimethylsiloxy-1-cyclohexene (22) with benzaldehyde (23) in aqueous media²¹

Equipment

- Three-necked round-bottomed flask (100 mL)
- Magnetic stirrer
- Three-way stopcock
- Stopcocks
- Septum
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3)
- All-glass syringe with a needle-lock luer (volume appropriate for quantity of solution to be transferred)
- Erlenmeyer flask (100 mL)
- Teflon-coated magnetic stirrer bar (2.0×0.7 cm)
- Glass column (2.5 cm \times 50 cm) packed with silica gel

Materials

- | | |
|---|-----------------------------|
| • Distilled dry tetrahydrofuran (THF) (FW 80.17), 25 mL | flammable, irritant |
| • 1-Trimethylsiloxy-cyclohexene ^a (FW 170.33), 1.70 g, 10.0 mmol | moisture sensitive irritant |
| • Distilled benzaldehyde (FW 106.12), 1.06 g, 10.0 mmol | cancer suspect |
| • $\text{Sc}(\text{OTf})_3$ (FW 492.16), ^b 0.25 g, 0.5 mmol | irritant, hygroscopic |
| • Diethyl ether for extraction, 150 mL | flammable, irritant |
| • <i>n</i> -Hexane for column chromatography | flammable, irritant |
| • Ethyl acetate for column chromatography | flammable, irritant |
| • Anhydrous magnesium sulfate | hygroscopic |

1. Assemble a three-necked round-bottomed flask (100 mL), a three-way stopcock and stopcocks under argon while the apparatus is still hot.
2. Assemble a syringe (20 mL) and needle (30 cm) while hot and allow the assembled syringe to cool to room temperature in a desiccator. Flush the syringe with argon.
3. When the flask has cooled to room temperature, add $\text{Sc}(\text{OTf})_3$ (0.246 g, 0.50 mmol). Then, add THF (8.0 mL) and H_2O (2.0 mL) to the flask using the syringe through the septum on the three-way stopcock.
4. Add THF (10.0 mL) solution of benzaldehyde (1.06 g, 10.0 mmol) and 1-trimethylsiloxy-1-cyclohexene (1.72 g, 10.0 mmol) using a syringe (20 mL) through the septum on the three-way stopcock at room temperature. Stir the mixture and monitor the reaction by a silica gel TLC (Merck Silica Gel 60 PF₂₅₄).
5. After 7 days, add water (50 mL) to the solution. Transfer the mixture to a separating funnel (300 mL) and extract the aqueous layer with three portions of diethyl ether (50 mL). Wash the combined organic layers with brine (30 mL), then dry over anhydrous magnesium sulfate. Capillary GC analysis

Protocol 6. Continued

(capillary column coated with (5%-phenyl)methylpolysiloxane) of the organic solution shows the presence of a diastereomeric mixture of the product (*syn:anti* = 75:25).

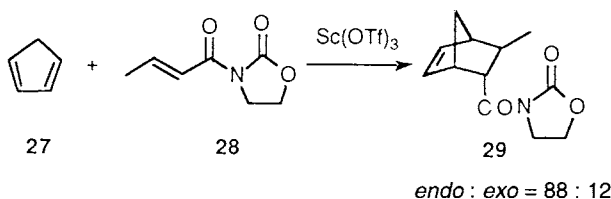
6. Filter the dried solution through a sintered-glass filter funnel and remove the solvent on a rotary evaporator. Prepare a column (2.5 cm × 50 cm) for chromatography using silica gel (Merck Silica Gel 60) and *n*-hexane as the eluant. Dissolve the residue in a minimum volume (2 mL) of *n*-hexane and elute the column with *n*-hexane–ethyl acetate (5:1). Evaporate the eluate on a rotary evaporator to yield a white solid (1.28 g, 6.3 mmol, 63%). GC/MS and ¹H NMR spectra of the products display the suitable structure.

^a Commercially available.

^b Commercial Sc(OTf)₃ retains moisture. Dry Sc(OTf)₃ by heating in a flask using an oil bath at 180 °C under vacuum (1 mm Hg) for more than 1 h (see Protocol 1).

2.6 Diels–Alder reaction

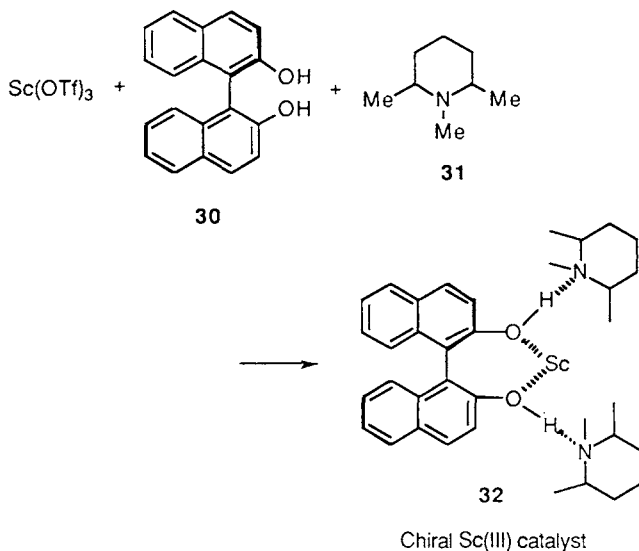
Although Lewis acid-catalysed Diels–Alder reactions have been shown to proceed under mild conditions, they are often accompanied by a diene polymerization.²² They frequently need excess amounts of the catalyst in the carbonyl-containing dienophiles. Sc(OTf)₃ is an efficient catalyst for Diels–Alder reactions of carbonyl-containing dienophiles with cyclopentadiene.²³ Thus, 3-crotonoyl-1,3-oxazolidin-2-one (**28**) reacts with cyclopentadiene (**27**) to give a mixture of corresponding adduct (**29**), in the ratio of *endo:exo* = 87:13, in a good yield (Scheme 11.8).



Scheme 11.8

Asymmetric version of this reaction can be achieved using chiral binaphthol (**30**), *cis*-1,2,3-trimethylpiperidine (**31**), and molecular sieve 4A together with Sc(OTf)₃ (Scheme 11.9).²⁴ The *endo* adduct (*endo:exo* = 86:14–89:11) of the reaction of **28** with **27** is obtained in up to 96% ee. It must be noted that the enantioselectivity of the reaction decreases in accordance with ageing time and temperature of the preparation of the chiral catalyst (**32**).²⁵ 3-Acetyl-1,3-oxazolidin-2-one is found to be effective for preventing the ageing effect.

11: Scandium(III) and yttrium(III)



Scheme 11.9

Protocol 7.

Asymmetric Diels–Alder reaction of cyclopentadiene (27) with 3-crotonoyl-1,3-oxazolidin-2-one (28)²⁴

Equipment

- Three-necked round-bottomed flask (100 mL)
- Magnetic stirrer
- Three-way stopcock
- Stopcocks
- Septum
- All-glass syringe with a needle-lock luer (volume appropriate for quantity of solution to be transferred)
- Dry ice–methanol bath
- Separating funnel (300 mL)
- Sintered-glass filter funnel (porosity 3)
- Erlenmeyer flask (100 mL)
- Glass column (2.5 cm × 50 cm) packed with silica gel
- Vacuum/inert gas source and inlet

Materials

- Distilled (P₂O₅) dichloromethane (FW 84.93), 25 mL toxic, irritant
- 3-Crotonoyl-1,3-oxazolidin-2-one^a (FW 155.15), 1.55 g, 10 mmol
- Freshly distilled cyclopentadiene^b (FW 66.10), 1.98 g, 30.0 mmol flammable
- Powder molecular sieve 4A (activated)^c 1.0 g
- (*R*)-Binaphthol^d (FW 286.33), 0.34 g, 1.18 mmol irritant
- *cis*-1,2,3-Trimethylpiperidine^e (FW 127.22), 0.31 g, 2.4 mmol
- Sc(OTf)₃ (FW 492.16), 0.49 g, 1.0 mmol irritant, hygroscopic
- Diethyl ether for extraction, 150 mL flammable, toxic
- *n*-Hexane for column chromatography flammable, irritant
- Ethyl acetate for column chromatography flammable, irritant
- Anhydrous magnesium sulfate hygroscopic

Protocol 7. Continued

1. Place $\text{Sc}(\text{OTf})_3$ (0.49 g, 1.0 mmol) and powder molecular sieves 4A (activated) (1.0 g) in a three-necked round-bottomed flask (100 mL) connected with a three-way stopcock and stopcocks.
2. Heat a flask by oil bath at 190°C under vacuum (1 mm Hg) for 5 h.
3. Flush the flask with argon through several vacuum cycles while the apparatus is still hot.
4. After cooling the flask to room temperature, add (*R*)-binaphthol (0.34 g, 1.2 mmol) to the flask.
5. Assemble a syringe (20 mL) and needle (30 cm) while hot and allow the assembled syringe to cool to room temperature in a desiccator. Flush the syringe with argon.
6. Add dichloromethane (10 mL) using the syringe through the septum on the three-way cock and cool the flask with dry ice-ethanol bath to -78°C under a slight pressure of argon.
7. Add *cis*-1,2,3-trimethylpiperidine (0.31 g, 2.4 mmol) using a syringe (1 mL) through the septum on the three-way stopcock into the flask at -78°C . Stir the mixture at this temperature for 30 min.
8. Add dichloromethane (15.0 mL) solution of 3-crotonoyl-1,3-oxazolidin-2-one (1.55 g, 10 mmol) and freshly distilled cyclopentadiene (1.98 g, 30 mmol) using a syringe (10 mL) through the septum on the three-way stopcock.
9. Stir the mixture at -78°C for 4 h and then warm it slowly to 0°C over a period of 10 h. Monitor the reaction by a silica gel TLC (Merck Silica Gel 60 PF₂₅₄).
10. Add water (50 mL) to the solution and transfer the mixture to a separating funnel (300 mL) and separate the organic layer. Extract the aqueous layer with two portions of diethyl ether (50 mL). Wash the combined organic layers with brine (30 mL), then dry them over anhydrous magnesium sulfate. Capillary GC analysis (capillary column coated with (5%-phenyl)methylpolysiloxane) of the organic solution shows the presence of a diastereomeric mixture of the product (*endo:exo* = 88:12).
11. Filter the dried solution through a sintered-glass filter funnel and remove the solvent on a rotary evaporator. Prepare a column (2.5 cm \times 50 cm) for chromatography using silica gel (Merck Silica Gel 60) and *n*-hexane as the eluant. Dissolve the residue in a minimum volume (2 mL) of *n*-hexane and elute the column with *n*-hexane-ethyl acetate (10:1). Evaporate the eluate on a rotary evaporator to yield a colourless residue (1.40 g, 7.0 mmol, 70%). GC/MS and ^1H NMR spectra of the products display the suitable structure.

12. The enantiomeric excess of the *endo* adduct is determined to be 86% ee by HPLC analysis (Daicel Ciralpak AD; *n*-hexane-*i*-PrOH, 80:20; 0.5 ml/min).

^a 3-Crotonoyl-1,3-oxazolidin-2-one is prepared by the reaction of crotonoyl chloride with 2-oxazolidinone in THF in the presence of *n*-butyllithium.²⁶

^b Cyclopentadiene is freshly distilled by thermolysis of commercial dicyclopentadiene at 180°C just prior to use.

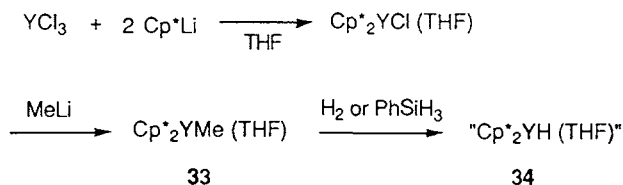
^c Obtained from Aldrich.

^d Commercially available.

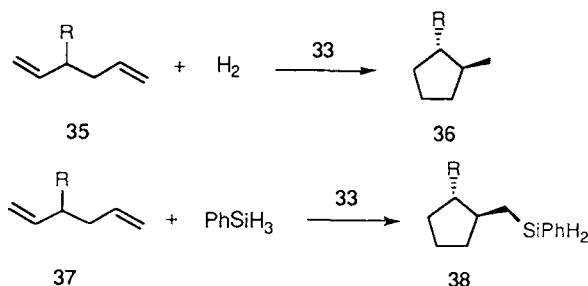
^e *cis*-1,2,3-trimethylpiperidine is prepared by *N*-methylation of commercial *cis*-1,3-dimethylpiperidine by formaldehyde and formic acid.²⁷

3. Cyclopentadienyl yttrium hydride

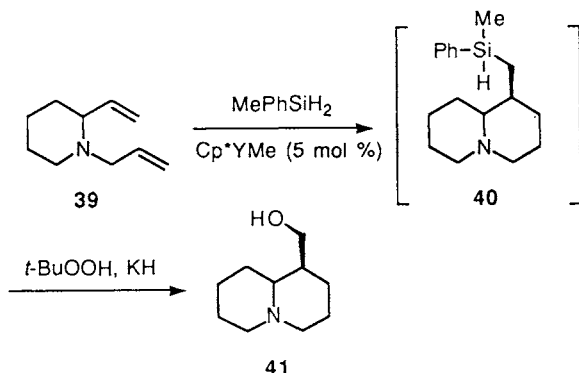
Since inorganic yttrium (III) compounds are less Lewis acidic than the corresponding scandium(III) compounds, they are seldom used as Lewis acid catalysts. Cyclopentadienyl derivatives of yttrium(III) hydrides have been studied in organic synthesis and found to catalyse hydrosilylation of alkenes²⁸ and cyclization of dienes.²⁹ The high regioselectivities and stereoselectivities of these reactions are worthy of note. Cyclopentadienyl yttrium hydride [$(\eta^5\text{-C}_5\text{Me}_5)_2\text{YH}(\text{THF})$] (**34**) is conveniently prepared *in situ* in the reaction of ciscyclopentadienylalkyl yttrium [$(\eta^5\text{-C}_5\text{Me}_5)_2\text{YCH}_3(\text{THF})$] (**33**) with hydrogen or phenylsilane and can be used for the catalytic reactions (Scheme 11.10). Thus, $(\eta^5\text{-C}_5\text{Me}_5)_2\text{YCH}_3(\text{THF})$ catalyses the cyclization/hydrosilylation of dienes with phenylsilane smoothly to afford the cyclized organosilane (**38**) (Scheme 11.11).³⁰ Cyclization reaction of dienes has been applied to the synthesis of epilupine, one of the lupin alkaloids (**41**) (Scheme 11.12).³¹



Scheme 11.10



Scheme 11.11



Scheme 11.12

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