TCIMAIL
number 107

TCI

CONTENTS

CHEMICALS NOTE

Carbon-Carbon Bond-Forming Reactions
Using a New Lewis Acid

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Introduction

Lewis acids are employed in many carbon-carbon bond-forming reactions and play important roles in organic syntheses including accelerated reactions rates, improved selectivities and reactions under mild conditions. Reactions using Lewis acids are widely used in industry. However, reactions should be carried out under strictly anhydrous conditions as most Lewis acids decompose or are deactivated in the presence of water. Furthermore, for the reactions involving nitrogen-containing compounds such as imines, Lewis acids are trapped by the nitrogen atoms resulting in deactivation of the catalyst. The reactions may not proceed satisfactorily or an excess of Lewis acid may be required for the reaction to proceed. Therefore, even though traditional Lewis acids are widely utilized for a variety of reactions, they present some unfavorable problems as well.

Recently, S. Kobayashi and co-workers have developed new types of Lewis acids to overcome these problems. The new catalysts are pre-period transition metal triflates, which are formed upon coordination of triflate, (a strong electron-withdrawing group) to metals in Group III or Group IV such as, Lanthanides and Hafnium.

In this paper, carbon-carbon bond forming reactions using new Lewis acids, developed by S. Kobayashi and co-workers, are described. For details, please refer to the related literatures at the end of this paper.
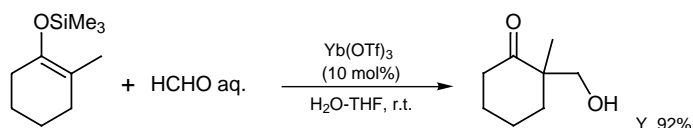
Aldol Reactions

Strict anhydrous conditions are absolutely essential when aldol reaction between silyl enol ethers and aldehydes are carried out using general Lewis acid catalysts such as $TiCl_4$, $SnCl_4$, $BF_3 \cdot OEt_2$, *etc*. Therefore, it is impossible to use commercially available aqueous formaldehyde solution as a reaction substrate. Because $TiCl_4$, $SnCl_4$, $BF_3 \cdot OEt_2$, *etc*. react more quickly with water rather than with the formaldehyde in aqueous formaldehyde solution and they decompose or are deactivated. To get avert this problem, dry gaseous formaldehyde is used in many cases. However, gaseous formaldehyde has some disadvantages because it must be generated before use from solid polymeric paraformaldehyde by thermal depolymerization. Gaseous formaldehyde also tends to self-polymerize.

The use of Lanthanide triflate [$Ln(OTf)_3$] and Scandium triflate [$Sc(OTf)_3$], both of which are stable in water, as Lewis acid catalysts has made possible for aldol reactions with silyl enol ethers and commercial formaldehyde solution.[1-3] Even in the presence of water, the reaction quickly proceeds with a catalytic amounts of Lewis acid and gives the corresponding desired hydroxymethylated adducts in high yields.
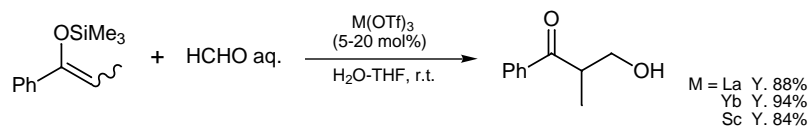
Good results were obtained in commercial formaldehyde solution-THF media with 5-10 mol% $Yb(OTf)_3$.[1] These reactions proceed in good yields under mild conditions even with the sterically hindered silyl enol ethers. Furthermore, di-and poly-hydroxymethylated products, which are often produced as side products under general basic conditions, were not observed, and no side products by double bond migration of the silyl enol ether were produced.


The versatility of these catalyst is futher demonstrated by the fact the Aldol reaction can be performed in a wide variety of conditions. Aldol adducts are obtained in good yields, not only in aqueous formaldehyde solution, but also in a variety of other aldehydes including water-soluble aldehydes.[2-5] The catalysts can be employed for aldol reactions without dehydration of hydrates. They can be employed in aldehydes having a free hydroxyl group, which reacts with metal enolates or usual Lewis acids. The catalysts can also be employed in aldehydes having a nitrogen atom, which coordinates to the Lewis acids resulting in the deactivation of the acids. Furthermore, good results were also obtained in the solvent system, H_2O–EtOH–Toluene.
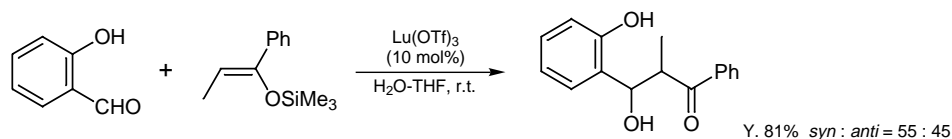
The aldol-type reaction of ketene silyl acetals with aldehydes should be carried out in the presence of organic solvents because ketene silyl acetal is so sensitive to water that its hydrolysis precedes the desired aldol reaction in aqueous media. $Ln(OTf)_3$ and $Sc(OTf)_3$ serve as superb Lewis acids in not only aqueous media but also organic solvents to afford the corresponding aldol-type adducts in good yields.[2,6]
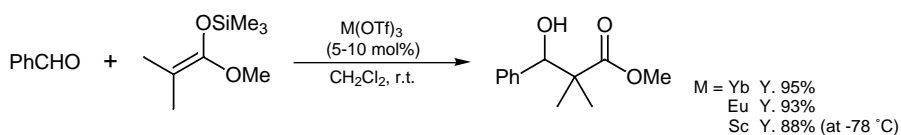
The presence of a small quantity of a surfactant makes aldol reactions possible in water without using organic solvents.[7] In this catalyzed aldol reaction in micellar systems, specific use of $Sc(OTf)_3$ as a Lewis acid catalyst is preferable. Even ketene silyl acetal, which easily reacts with water, reacts with aldehydes in the presence of sodium dodecylsulfate (SDS) in aqueous media, to produce the corresponding aldol adduct in a high yield. This method is an excellent reaction which can be carried out in aqueous media requiring no organic solvents.
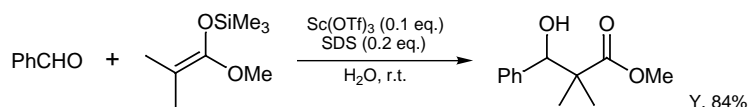
Diels-Alder Reaction

The Diels-Alder reaction is one of the most important reactions for the construction of cyclohexene derivatives and is promoted through the use of Lewis acid catalysts, which allow the reaction to proceed under relatively mild conditions. However, they are often accompanied by diene polymerization and require excess amounts of the catalyst when using carbonyl containing dienophiles.

$Ln(OTf)_3$ and $Sc(OTf)_3$ function as an excellent Lewis acid catalysts in the Diels-Alder reaction of a dienophile having a carbonyl group with a diene.[8,9] $Sc(OTf)_3$ is especially excellent, having generality for a wide scope of substrates giving the corresponding adducts in good yield with high endo-selectivity.


Y. 93% *endo* : *exo* = 100 : 0
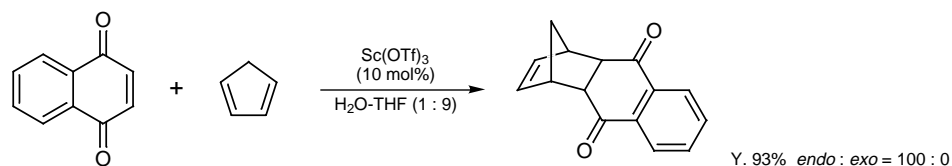
Furthermore, chiral Yb or Sc catalysts, prepared from $Yb(OTf)_3$ or $Sc(OTf)_3$, (*R*)-(+)-1,1′-bi-2-naphthol (BINOL) and a tertiary amine, act as useful catalysts for the asymmetric Diels-Alder reactions.[10]

Friedel-Crafts Reaction

The Friedel-Crafts reaction is a fundamental reaction for organic syntheses and an important reaction widely applied in industrial processes.

$AlCl_3$ is used as a general Lewis acid in the Friedel-Crafts acylation. However, a stoichiometric amount of $AlCl_3$ is required because the Lewis acid is consumed by coordination with the formed aromatic ketones. Use of $Ln(OTf)_3$, $Sc(OTf)_3$ and $Hf(OTf)_4$ as Lewis acid catalyst permits Friedel-Crafts reactions to occur with a catalytic amount.[11] Nitromethane is a suitable solvent in place of halogenated hydrocarbons, which cause environmental problems. Furthermore, addition of $LiClO_4$ improves the yield of the product. Aromatic ketones are obtained in high yields from reactions between a variety of aromatic compounds (except benzene) and acid anhydrides.

quant.
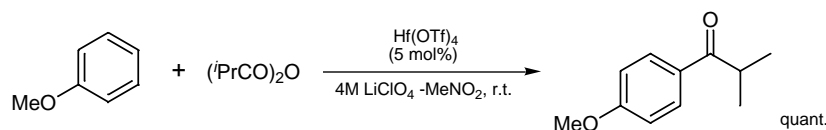
The most extensively utilized Friedel-Crafts alkylation conditions employ an alkyl halide and a catalytic amount of Lewis acid such as $AlCl_3$. However, this process is accompanied by the generation of hydrogen halide which causes side reactions. Even the use of alcohols instead of alkyl halides produces water which causes $AlCl_3$ to decompose and generate hydrogen halides, thus necessitating a considerably large quantity of $AlCl_3$ to be employed. Utilization of $Sc(OTf)_3$ as a Lewis acid makes it possible to use allyl and aromatic alcohols or aromatic aldehydes and acetals as alkylating agents without generating hydrogen halide.[12] Moreover, the reaction proceeds with a catalytic amount of $Sc(OTf)_3$ to produce allylbenzene and diarylmethane derivatives highly selectively.

Y. 91%
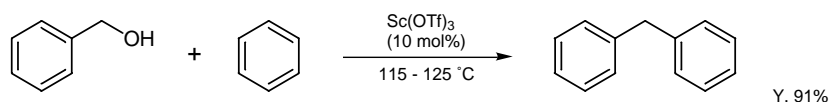
Mannich-Type Reactions

Classical Mannich reactions occasionally involve side reactions such as deaminations, so a variety of improvements have been made to the reaction process. The reaction between imines and silyl enolates is a useful method to synthesize a β-aminocarbonyl compound. However, as Lewis acids are often deactivated, the reactions of imines using Lewis acids are sometimes unsuccessful, or if the reactions proceed, more than stoichiometric amounts of Lewis acids are needed.

Use of Ln(OTf)$_3$, Sc(OTf)$_3$, Zr(OTf)$_4$ and Hf(OTf)$_4$ in a catalytic amount allows syntheses of β-aminocarbonyl compounds in high yields from reactions of imines and silyl enolates.[13,14]


$$M = Yb \quad Y. 97\% \text{ (in } CH_2Cl_2)$$
$$Zr \quad Y. 85\%$$
$$Hf \quad Y. 97\% \text{ (at 0 °C to r.t.)}$$
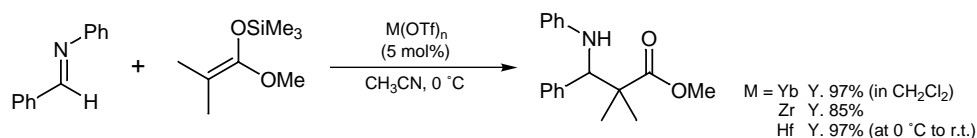
Ln(OTf)$_3$, Sc(OTf)$_3$, Zr(OTf)$_4$ and Hf(OTf)$_4$ act effectively as Lewis acid catalysts in a one-pot reaction in which an imine generated from an aldehyde and an amine immediately followed by reaction with a silyl enolate produces β-aminocarbonyl compounds.[14] In the presence of a catalytic amount of Yb(OTf)$_3$ and a dehydrating agent, a reaction between an aldehyde and an amine followed by an addition of silyl enolate leads to the production of a β-aminocarbonyl compound in high yields without the formation of an aldol adduct. Generally, whereas use of aliphatic aldehydes involves side reactions because unstable imines having active protons at the α-position are formed, use of Yb(OTf)$_3$ leads to the formation of β-aminocarbonyl compounds in high yields.

Y. 81%
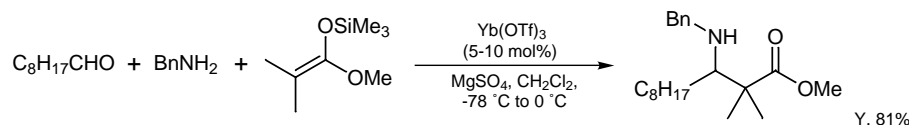
Yb(OTf)$_3$ and Sc(OTf)$_3$ perform as an excellent Lewis acid catalyst in micellar systems, where three-component Mannich-type reactions, in the presence of SDS, in aqueous media use a vinyl ether as an enolate component.[15] Further, they are also effective for Mannich-type reactions using acylhydrazone as electrophiles.[16]

Other Carbon-Carbon Bond-Forming Reactions

The reactions using Group III and IV pre-period transition metal triflates as shown here constitute only a part of their usefulness. A variety of other reactions have been reported such as the Michael Reactions,[2,8] allylation reactions,[5,14,16,17] Fries rearrangements,[18] aza Diels-Alder reactions,[19] asymmetric aza Diels-Alder reactions,[20] 1,3-Dipolar Cycloadditions,[21] asymmetric 1,3-Dipolar Cycloadditions,[22] and Strecker-type reactions.[23] Further they are used as effective Lewis acid catalysts for the construction of libraries in combinatorial chemistry.[24]
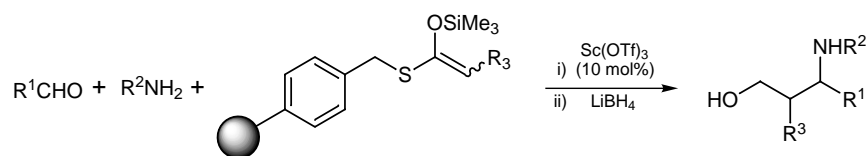
Recoverable and Reusable Lewis Acid Catalysts

The disposal of aluminum hydroxide produced from the treatment of $AlCl_3$ in the industrial Friedel-Crafts reactions, is a problem. However, the new Lewis acid catalysts introduced in this paper are capable of continuous use and are recoverable and reusable upon completion of the reactions. Where a solvent system of H_2O–EtOH–Toluene (1:7:4) is used toluene is added to the aqueous phase reaction solution to make two phases upon completion of the reaction, and the separated aqueous layer in which the catalyst is dissolved, is used directly in the next reaction without removing water.[5] Even reuse will not decrease the yield of the product. Further, in reactions using organic solvents, the catalyst can be recovered by distilling away water after addition of water to stop the reaction, followed by extraction of the product.[6] Use of the recovered catalyst in a reaction has shown the same good results as the initial reaction. Recovery and reuse can be made in a variety of reactions including Aldol reactions, Diels-Alder reactions, Friedel-Crafts reactions, *etc*.

1st run 86% (*syn* : *anti* = 38 : 62)   3rd run 90% (*syn* : *anti* = 38 : 62)
2nd run 82% (*syn* : *anti* = 38 : 62)   4th run 82% (*syn* : *anti* = 39 : 61)
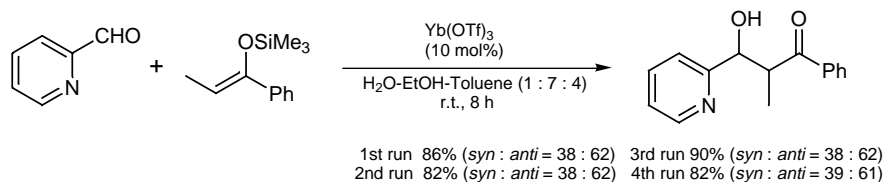
Much attention has been focused on environmental problems. Harmful benzene and halogenated solvents have become strictly regulated, calling for chemical processes which do not use harmful organic solvents. The new Lewis acid catalysts developed by S. Kobayashi and co-workers are stable in aqueous medium. They can be excellent catalysts as they are friendly to global-wide environments. They not only make organic reactions possible in aqueous media, but they are also recoverable and reusable after the completion of chemical reactions.

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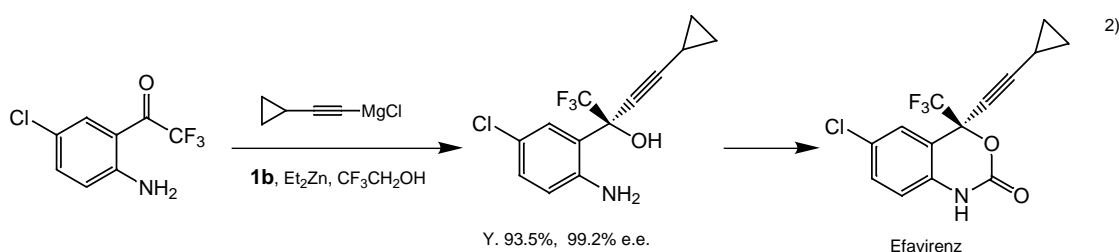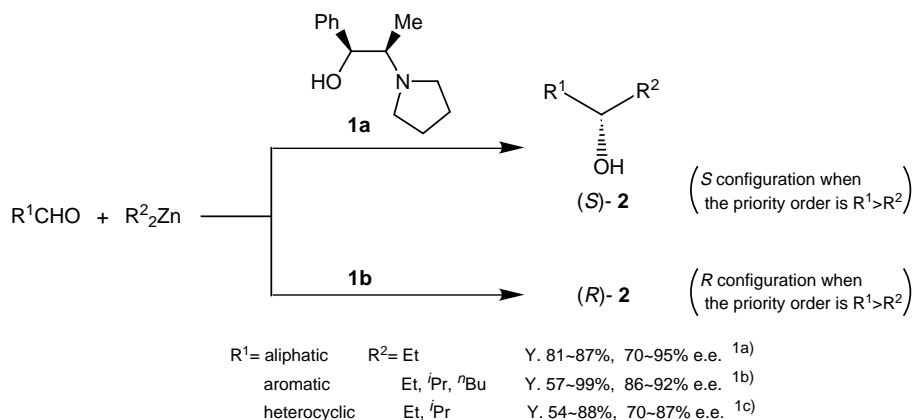

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Related Compounds

$(CF_3SO_3)_3La$ — Trifluoromethanesulfonic Acid Lanthanum(III) Salt — 25g 5g [T1293]

$(CF_3SO_3)_3Yb \cdot xH_2O$ — Trifluoromethanesulfonic Acid Ytterbium(III) Salt, Hydrate — 25g 5g [T1610]

$(CF_3SO_3)_3Sc$ — Trifluoromethanesulfonic Acid Scandium(III) Salt — 1g [T1663]

CHIRAL β-AMINO ALCOHOL

P1375 **(1S,2R)-1-Phenyl-2-(1-pyrrolidinyl)propan-1-ol** **(1a)** **1g**

P1374 **(1R,2S)-1-Phenyl-2-(1-pyrrolidinyl)propan-1-ol** **(1b)** **1g**

R^1= aliphatic $\quad$ R^2= Et $\quad$ Y. 81~87%, 70~95% e.e. [1a]

$\quad\quad\quad$ aromatic $\quad\quad$ Et, ^{i}Pr, ^{n}Bu $\quad$ Y. 57~99%, 86~92% e.e. [1b]

$\quad\quad\quad$ heterocyclic $\quad$ Et, ^{i}Pr $\quad$ Y. 54~88%, 70~87% e.e. [1c]

Y. 93.5%, 99.2% e.e.

Efavirenz

Chiral β-amino alcohols **1a** and **1b**, developed by K. Soai and co-workers, are useful chiral catalysts for enantioselective addition of dialkylzinc compounds to aliphatic,[1a] aromatic[1b] and five-membered heterocyclic[1c] aldehydes. This addition method with **1** affords secondary alcohols **2** with high optical purity.[1] Moreover, **1b** as a chiral ligand was applied to the enantioselective ketone alkynylation reaction, which is a key step in synthesis of Efavirenz.[2] Efavirenz is HIV reverse transcriptase inhibitor.

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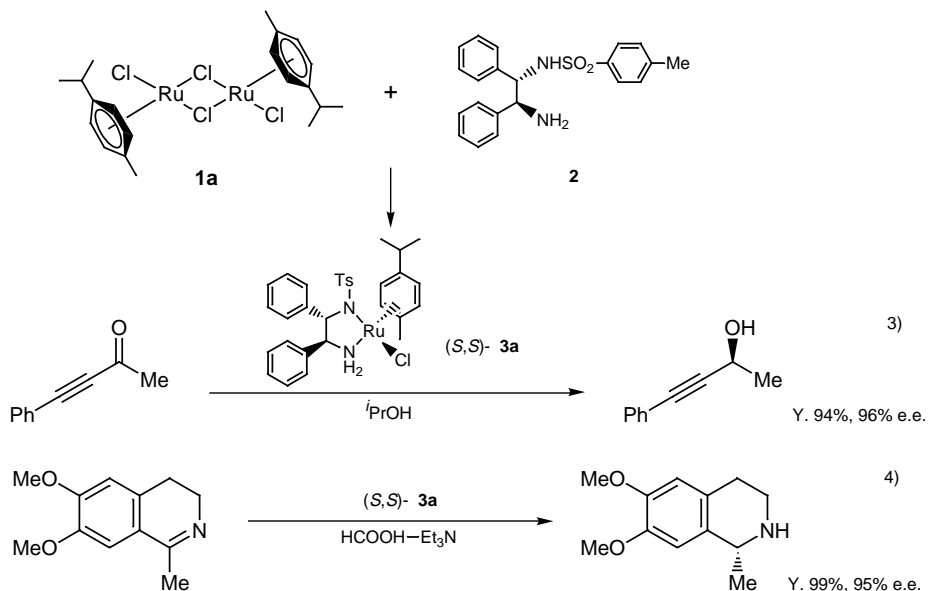
Related Products

D2128	(1R,2S)-2-Di-n-butylamino-1-phenyl-1-propanol	5g	1g
D2129	(1S,2R)-2-Di-n-butylamino-1-phenyl-1-propanol		1g
H0784	(R)-(-)-2-[Hydroxy(diphenyl)methyl]-1-methylpyrrolidine		100mg
H0768	(S)-(+)-2-[Hydroxy(diphenyl)methyl]-1-methylpyrrolidine		100mg

TCIMAIL

D2751	Dichloro(*p*-cymene)ruthenium(II) Dimer	(1a)	5g	1g
B1902	Benzeneruthenium(II) Chloride Dimer	(1b)		1g

Arene Ru(II) complexes **1** are stable precursor for the preparation of asymmetric catalysts. For example, BINAP-Ru(II) and Pybox-Ru(II) are prepared from **1** and these catalysts are useful for asymmetric hydrogenation of ketones[1] and asymmetric cyclopropanation of olefins,[2] respectively. Recently, R. Noyori and co-workers have found that Ru(II) catalyst **3**, which is prepared from **1** and chiral amine **2**, is extremely effective for asymmetric hydrogenation. The asymmetric transfer hydrogenation of ketones and imines using chiral Ru(II) catalyst **3** affords chiral alcohols[3] and chiral amines,[4] respectively, in good yield and high enantiomeric purity.

Currently, there are two standard methods for hydrogenation of ketones and imines: catalytic reduction with hydrogen and transfer hydrogenation with alcohols or formic acid as hydrogen donors. The latter method is attractive because of its operational simplicity in that it requires no high pressure autoclave in the chemical procedures.
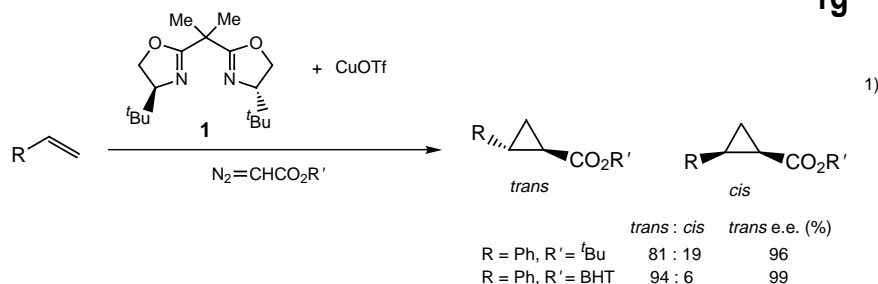
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Related Product
A1548   (*R,R*)-*N*-(*p*-Toluenesulfonyl)-1,2-diphenylethylenediamine   1g
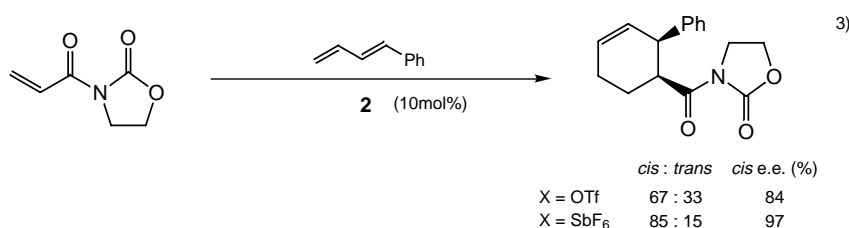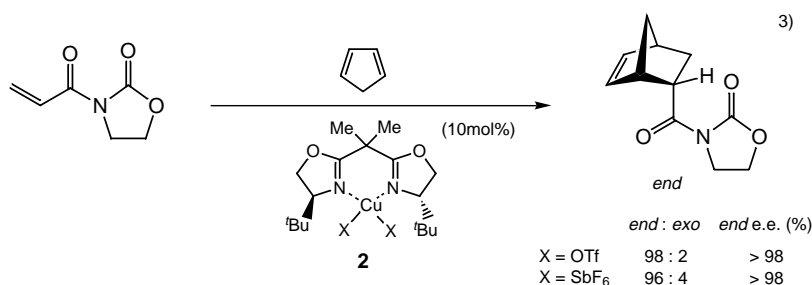
I0567 (S,S)-(-)-2,2'-Isopropylidenebis(4-tert-butyl-2-oxazoline) (1)

1g 100mg

1)

Me Me
+ CuOTf

1

$N_2=CHCO_2R'$

R, trans, CO_2R'
R, cis, CO_2R'

trans

cis

		trans : cis	trans e.e. (%)
R = Ph, R' = ^tBu		81 : 19	96
R = Ph, R' = BHT		94 : 6	99

BHT : 2,6-Di-tert-butyl-4-methylphenyl

C_2-Symmetric bisoxazoline **1** is a useful chiral ligand for enantiocontrol of metal-catalyzed reactions. For example, the chiral Cu(I) complex, which is generated from **1** and copper(I) triflate, is applied to asymmetric cyclopropanation of olefins and affords *trans*-diastereomers with high enantioselectivity.[1] The reaction was used for total syntheses of (+)- and (-)-Scopadulcic acid A.[2]

3)

Me Me
(10mol%)

O O

^tBu X X ^tBu

2

end

		end : exo	end e.e. (%)
X = OTf		98 : 2	> 98
X = SbF$_6$		96 : 4	> 98

3)

Ph

Ph

2 (10mol%)

		cis : trans	cis e.e. (%)
X = OTf		67 : 33	84
X = SbF$_6$		85 : 15	97

Recently, Cu(II) complex of **1** have been successfully employed as enantioselective Lewis acid catalyst in Diels-Alder reactions,[3] Aldol additions,[4] and Michael additions.[5]

References
1) **Bis(oxazolines) as chiral ligand**
Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.*, **1991**, *113*, 726.
2) **Total syntheses of (+)-and (-)-Scopadulcic Acid A**
Fox, M. E.; Li, C.; Marino, J. P., Jr.; Overman, L. E. *J. Am. Chem. Soc.*, **1999**, *121*, 5467.
3) **Enantioselective Diels-Alder Reactions**
Evans, D.A.; Miller, S. J.; Lectka, T.; von Matt, P. *J. Am. Chem. Soc.*, **1999**, *121*, 7559.
Evans, D.A.; Barnes, D. M.; Johnson, J. S.; Lectka, T.; von Matt, P.; Miller,S. J.; Murry, J. A.; Norcross, R. D.; Shaughnessy, E.A.; Campos, K. R. *J. Am. Chem. Soc.*, **1999**, *121*, 7582.
4) **Enantioselective aldol additions of enolsilanes**
Evans, D. A.; Kozlowski, M. C.; Murry, J. A.; Burgey, C. S.; Campos, K. R.; Connell, B. T.; Staples, R. J. *J. Am. Chem. Soc.*, **1999**, *121*, 669.
Evans, D. A.; Burgey, C. S.; Kozlowski, M. C.; Tregay, S.W. *J. Am. Chem. Soc.*, **1999**, *121*, 686.
5) **Enantioselective Michael Additions of enolsilanes to unsaturated ester derivatives**
Evans, D.A.; Willis, M. C.; Johnston, J. N. *Org. Lett.*, **1999**, *1*, 865.

The application of rhenium compounds to synthetic organic reactions has progressed rapidly in 1990's while a variety of transition metal compounds, such as Pd, Ru and Ni complexes *etc.*, which have been utilized since the 1950's. Characteristics of the organorhenium reactions are being discovered and applications for rhenium compounds such as **1** and **2**[1] are being developed.

M1296   Methyltrioxorhenium(VII) (MTO)   (1)   100mg

$$CH_3ReO_3$$

[2a]

1   (1mol%) , H_2O_2

^tBuOH, r.t.

Y.90%
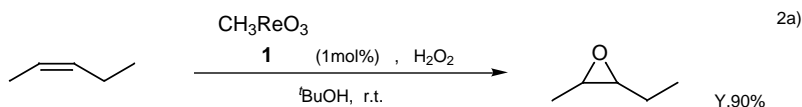
The rhenium reagent **1** is used with hydrogen peroxide for catalytic oxidation reactions. For example, oxidation of olefins using a catalytic amount of **1** proceeds smoothly at room temperature and affords the corresponding epoxides in high yields.[2a] It is also applied to oxidizing phenols to quinones,[2b] benzaldehydes to phenols,[2c] sulfide to sulfoxides[2d] and tertiary carbon to tertiary alcohols.[2d]

T1803   Tetra-*n*-butylammonium Perrhenate   (2)   5g   1g

[3]

$^nBu_4NReO_4$

2   (10mol%)

p-TsOH • H_2O , CH_2Cl_2 , r.t.
(10mol%)

Y.83%
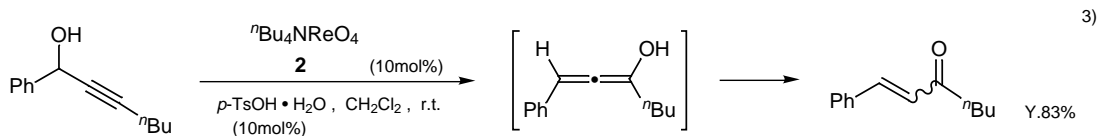
The rhenium reagent **2**, which is different from the homologous premanganates, is not capable of oxidizing alcohols nor olefins. However, 1,3-rearrangement of allylic and propargylic alcohols occurs in the presence of a catalytic amount of **2** and *p*-toluenesulfonic acid.[3] Furthermore, the combined use of **2** and a protic acid is quite effective catalyzing the Beckmann Rearrangement.[4]

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1) Review
 Kusama, H.; Narasaka, K. *Yuki Gosei Kagaku Kyokai Shi (J. Synth. Org. Chem. Japan)*, **1996**, *54*, 644.
2) Catalytic oxidation with MTO and H_2O_2
 a) Hermann, W. A.; Fischer, R.W.; Marz, D.W.; *Angew. Chem. Int. Ed. Engl.*, **1991**, *30*, 1638.
 b) Adam, W.; Hermann, W. A.; Lin, J.; Saha-Moller, C. R. *J. Org. Chem.*, **1994**, *59*, 8281.
 c) Yamazaki, S. *Chem. Lett.*, **1995**, 127.
 d) Adam, W.; Mitchell, C. M.; Saha-Moller, C. R. *Tetrahedron*, **1994**, *50*, 13121.
 e) Murray, R. W.; Iyanar, K.; Chen, J.; Wearing, J. T. *Tetrahedron Lett.*, **1995**, *36*, 6415.
3) 1,3-Rearrangement of allylic and propargylic alcohols with $^nBu_4NReO_4$ and *p*-TsOH
 Narasaka, K.;Kusama, H.; Hayashi, Y. *Chem. Lett.*, **1991**, 1413.
4) Beckmann rearrangement with $^nBu_4NreO_4$ and CF_3SO_3H
 Narasaka, K.; Kusama, H.; Yamashita, Y.; Sato, H. *Chem. Lett.*, **1993**, 489.
 Kusama, H.; Yamashita, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.*, **1995**, *68*, 373.

MILD AND SELECTIIVE REAGENTS FOR CLEAVAGE OF PROTECTING GROUPS

| B2132 | *B*-Bromocatecholborane | (1a) | 5g |
| B1669 | *B*-Chlorocatecholborane | (1b) | 5g |

Y. 82%

Y.quant.

Y. 53%
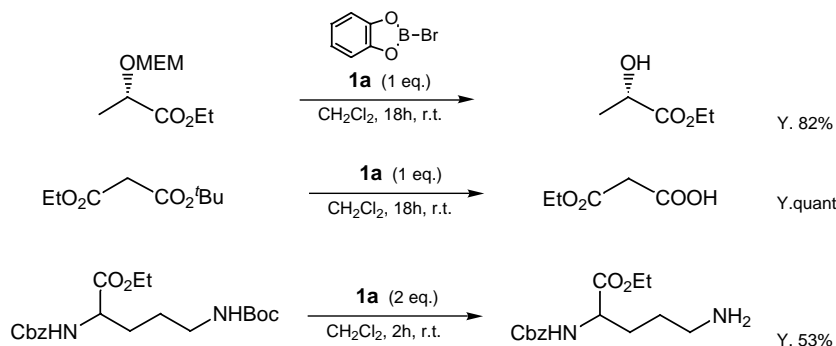
The reagents **1**, which are Lewis acids, selectively cleave certain ether, ester and carbamate protecting groups under mild conditions.[1] The relative reactivity of common protecting groups towards **1** was reported:[1a] MOMOR, MEMOR > BOC > CBZ, ^{t}BuOR > PhCH$_2$OR > CH$_2$=CHCH$_2$OR > ^{t}BuO$_2$CR, secondary alkylOR > PhCH$_2$O$_2$CR, primary alkylOR >> alkylO$_2$CR. The reagent **1b**, which has lower reactivity than **1a**, may be advisable when higher selectivity is required, for example, synthesis of natural products. Additionally, TBDMS, TBDPS and PMB ethers are not affected by **1**.[2]

MOM = Methoxymethyl, MEM = 2-Methoxyethoxymethyl, Boc = *tert*-Butoxycarbonyl, Cbz = Benzyloxycarbonyl, TBDMS = *tert*-Butyldimethylsilyl, TBDPS = *tert*-Butyldiphenylsilyl, PMB = *p*-Methoxybenzyl

References
1) **Mild and selective reagents for cleavage of ether, ester, and carbamate protecting groups**
   a) Boeckman, R. K., Jr., Potenza, J. C. *Tetrahedron Lett.*, **1985**, *26*, 1411.
   b) King, P. F.; Stroud, S. G. *Tetrahedron Lett.*, **1985**, *26*, 1415.
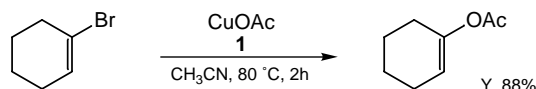2) **Synthesis of prostaglandin F$_{2\alpha}$ photoaffinity probes**
   Golinski, M.; Heine, M.; Watt, D.S.; *Tetrahedron Lett.*, **1991**, *32*, 1553.
3) **Synthetic studies on spinosyn A.**
   Paquette, L. A.; Gao, Z.; Ni, Z.; Smith, G. F. *Tetrahedron Lett.*, **1997**, *38*, 1271.

ACETOXYLATION OF VINYL BROMIDE

| A1540 | **Copper (I) Acetate** | (1) | 5g |

Y. 88%

Generally, the synthesis of vinyl acetates is difficult when vinyl halides are used as starting materials. However, the use of **1** allows the reaction to produce vinyl acetate relatively easily.[1] For example, heating an acetonitrile solution of 1-bromocyclohexene with excess of **1** provides a mild and simple means for convertion into 1-acetoxycyclohexene.[1a]

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1) **Vinyl Acetates from vinyl bromides**
   a) Klumpp, G. W.; Bos. H.; Schakel, M.; Schmitz, R. F.; Vrielink, J. J. *Tetrahedron Lett.*, **1975**, 3429.
   b) Commercon, A.; Normant, J.; Villieras, J. *J. Organomet. Chem.*, **1975**, *93*, 415.

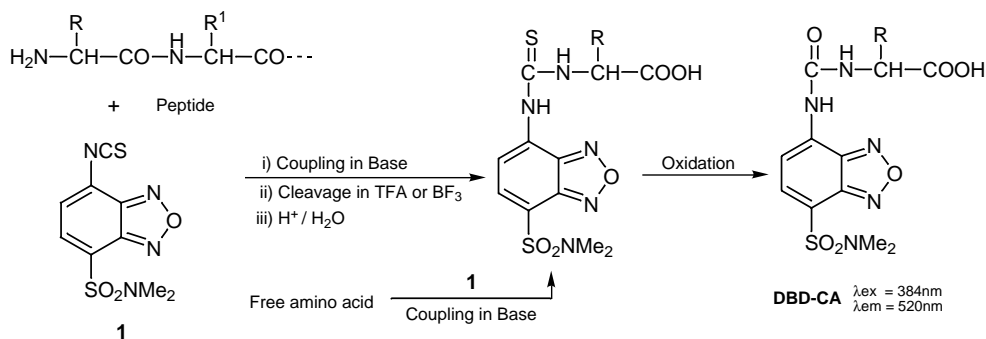### Other Metal Complexes
| R0069 | Rhodium(II) Acetate Dimer | 100mg |
| A1424 | Palladium(II) Acetate | 1g |

A5575 DBD-NCS   100mg

[4-(N,N-Dimethylaminosulfonyl)-7-isothiocyanato-2,1,3-benzoxadiazole]

The Edman degradation method has been widely used for sequence analysis of peptides and proteins. For this reason, it has been a very important tool in the field of biochemistry and biomedical science. Although phenyl isothiocyanate is generally employed for the Edman degradation method, more sensitive the Edman reagents were needed. Recently, K. Imai and co-workers have developed a novel fluorogenic Edman reagent **1**[1,2] which has the following advantages;

(1) Stable and non-fluorescent prior to derivatization.

(2) DBD-carbamoyl(CA) amino acids are stable and have strong fluorescence intensity.

(3) DBD-CA amino acids are separated on a reversed-phase HPLC column and detected at the sub-picomole level.

(4) Used for the determination of the amino acid sequence and the D/L-amino acid configuration.

(5) Used as a fluorogenic labeling reagent for amino groups.

#### References
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   Imai, K.; Uzu, S.; Nakashima, K.; Akiyama, S. *Biomet. Chromatogr.*, **1993**, *7*, 56.
2) **Development of an efficient amino acid sequencing method using DBD-NCS**
   Matsunaga, H.; Santa, T.; Hagiwara, K.; Homma, H.; Imai, K.; Uzu, S.; Nakashima, K.; Akiyama, S. *Anal. Chem.*, **1995**, *67*, 4276.
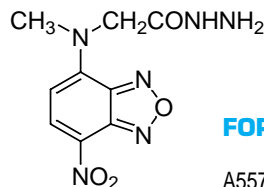   Huang, Y.; Matsunaga, H.; Toriba, A.; Santa, T.; Fukushiam, T.; Imai, K. *Anal. Biochem.*, **1999**, *270*, 257.
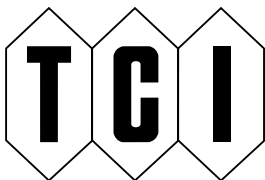
LABELING REAGENTS FOR HPLC
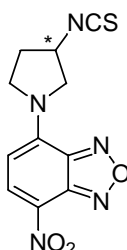
FOR AMINO GROUPS

A5577   (R)-(-)-NBD-Py-NCS   100mg
A5578   (S)-(+)-NBD-Py-NCS   100mg

FOR CARBONYL GROUPS

A5573   NBD-CO-Hz   100mg

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