SYNTHESIS ALERTS

Synthesis Alerts is a new monthly feature to help readers of Synthesis keep abreast of new reagents, catalysts, ligands, chiral auxiliaries, and protecting groups which have appeared in the recent literature. Emphasis is placed on new developments but established reagents, catalysts etc are also covered if they are used in novel and useful reactions. In each abstract, a specific example of a transformation is given in a concise format designed to aid visual retrieval of information.

Synthesis Alerts is a personal selection by Paul Blakemore, Brian Dymock, Philip Hall, Philip Kocienski, J.-Y. Le Brazidec and Alessandro Pontiroli of the University of Southampton. The journals regularly covered by the abstractors are: Angewandte Chemie International Edition, Bulletin de la Societe Chimie de France, Bulletin of the Chemical Society of Japan, Chemische Berichte, Chemistry Letters, Helvetica Chimica Acta, Journal of Organic Chemistry, Journal of Organometallic Chemistry, Journal of the American Chemical Society, Liebigs Annalen, Tetrahedron Letters.

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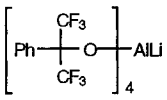
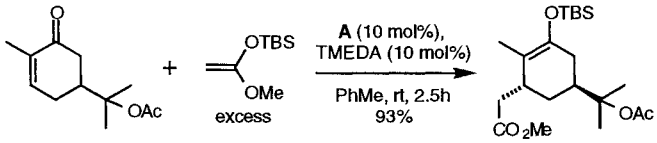
Lithium Tetrakis{[bis(trifluoromethyl)phenyl]methoxy}aluminate — ***Catalyst***

The title compound catalyses the1,4- addition of silyl ketene acetals to enones.



A



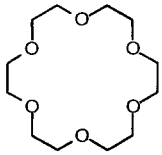
5 examples:- yields > 81%

A also catalyses the S_N2 displacement of allylic acetates.

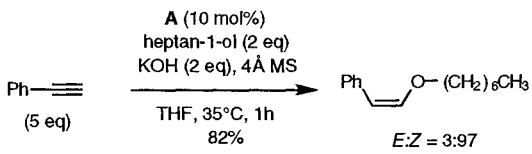
T. J. Barbarich, S. T. Handy, S. M. Miller, O. P. Anderson, P. A. Grieco, S. H. Strauss *Organometallics*, **1996**, *15*, 3776.

18-Crown-6 — ***Catalyst***

The title compound was used to synthesise vinyl ethers under phase transfer conditions.



A



10 examples; yields typically >75%

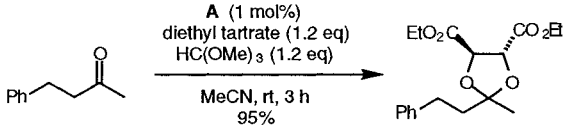
G. Bellucci, C. Chiappe, G. L. Moro *Synlett*, **1996**, 880.

Scandium Trifluoromethanesulfonate — ***Catalyst***

The title compound is a highly active acetalisation catalyst. For its use as a Friedel-Crafts catalyst see *Synlett*, **1996**, 871.

$Sc(OTf)_3$

A



4 examples:- yields >87%

The title compound was also useful for the preparation of 1,3-dioxolanones and -dioxanones with α- and β-hydroxy acids.

K. Ishihara, Y. Karumi, M. Kubota, H. Yamamoto *Synlett*, **1996**, 839.

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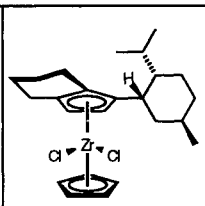
(1-Neomenthyl-4,5,6,7-tetrahydroindenyl)(cyclopentadienyl)zirconium Dichloride — *Catalyst*

Catalyst for the asymmetric carbomagnesiation of unactivated alkenes. The catalyst is easily recoverable.



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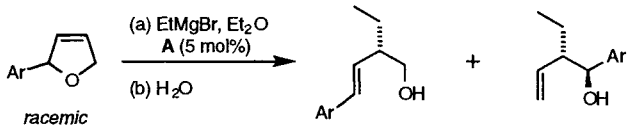


6 examples: yields 31-95%

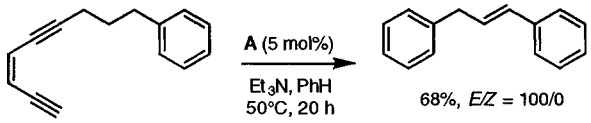
L. Bell, R. J. Whitby, R. V. H. Jones, M. C. H. Standen *Tetrahedron Lett.*, **1996**, *37*, 7139.

Bis(tri*iso*propylphosphine)rhodium(I) Chloride — *Catalyst*

The title complex catalyses the cycloaromatisation of various enediynes via a proposed vinylidene-rhodium intermediate.

$RhCl(^iPr_3P)_2$

A



Six examples (yields 10-68%, usually highly *E* selective).

K. Ohe, M. Kojima, K. Yonehara, S. Uemura *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 1823.

Benzylidenebis(tricyclohexylphosphine)ruthenium(IV) Dichloride — *Catalyst*

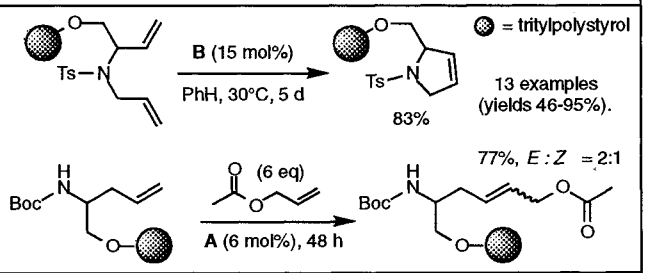
The title compound **A**, and its analogue **B**, respectively catalyse cross metathesis and ring-closing reactions of polymer bound nitrogeneous alkene.

$Cl_2(PCy_3)_2Ru{=}CHPh$

A

$Cl_2(PCy_3)_2Ru{=}CH{-}CH{=}CPh_2$

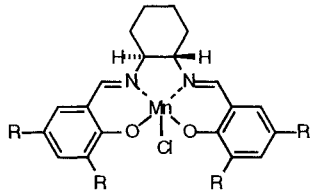
B



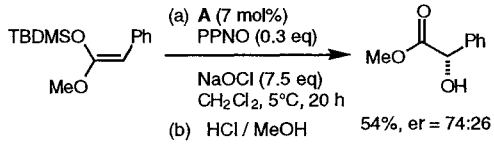
M. Schuster, J. Pernerstorfer, S. Blechert *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 1979.

(Salen)-Manganese(III) Complex — *Catalyst*

The title complex catalyses the asymmetric α-hydroxylation of silyl enol ethers and silyl ketene acetals.



A (R = *t*-Bu)



Four different substrates oxidised under a variety of conditions (yields 8-99%, %ee 9-81%). Nature of additive, oxidant and pH have a profound effect on outcome of reaction.

PPNO = 4-phenylpyridine *N*-oxide

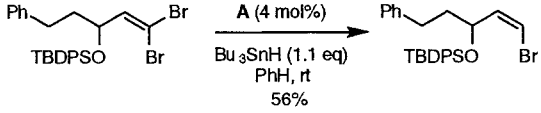
W. Adam, R. T. Fell, C. Mock-Knoblauch, C. R. Saha-Möller *Tetrahedron Lett.*, **1996**, *37*, 6531.

Tetrakis(triphenylphosphine)palladium(0) — *Catalyst*

The title compound catalyses the hydrogenolysis of 1,1-dibromoalk-1-enes by tributyltin hydride to yield the corresponding (*Z*)-1-bromoalk-1-enes stereoselectively.

$Pd(PPh_3)_4$

A



13 examples (yields 56-90%); in all cases >98% (*Z*).

J. Uenishi, R. Kawahama, Y. Shiga, O. Yonemitsu *Tetrahedron Lett.*, **1996**, *37*, 6759.

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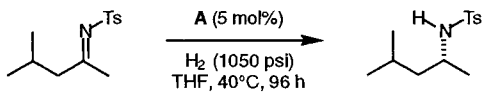
Ruthenium(II) Acetate (*R*)-BINAP Complex — *Catalyst*

The title complex catalyses the asymmetric hydrogenation of tosyl imines.

A. B. Charette, A. Giroux *Tetrahedron Lett.*, **1996**, *37*, 6669.

(*R*)-Ru(OAc)$_2$BINAP

A



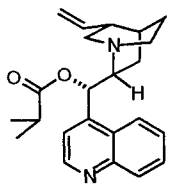
48%, er = 74:26

Seven examples including acetophenone (yields 48-82%, %ee 17-84%). Lower yields with bulkier substrates.

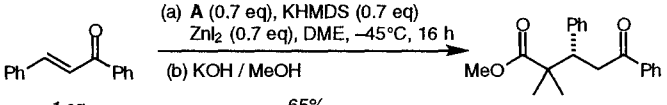
Cinchonine — *Chiral Auxilliary*

The isobutyl ester **A** of the title compound undergoes diastereoselective Michael reactions.

M. Shimizu, Y. Onogawa, T. Fujisawa *Synlett*, **1996**, 827.



A



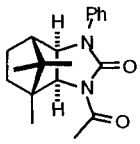
er = 96:4

Twelve examples. Using LDA as the base and Me_4Sn as the Lewis acid reverses the stereochemistry of the reaction.

(1*R*,2*S*,6*R*,7*S*)-3-Ethanoyl-1,10,10-trimethyl-5-phenyl-3,5-diazatricyclo[5.2.1.0^{2,6}]decan-4-one — *Chiral Auxiliary*

Lithium and titanium enolates prepared from the title compound react with aldehydes with opposite diastereoselectivity.

C. Palomo, M. Oiarbide, A. González, J. M. García, F. Berrée, A. Linden *Tetrahedron Lett.*, **1996**, *37*, 6931.



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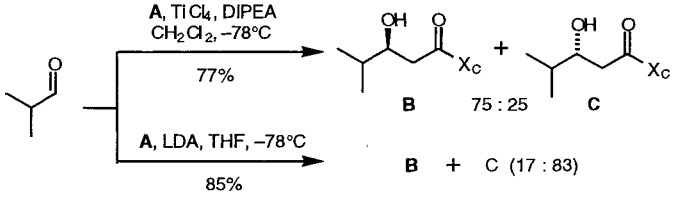


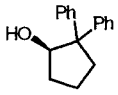
Nine aldehydes devoid of proximate stereogenic centres examined.

(*R*)-2,2-Diphenylcyclopentanol — *Chiral Auxiliary*

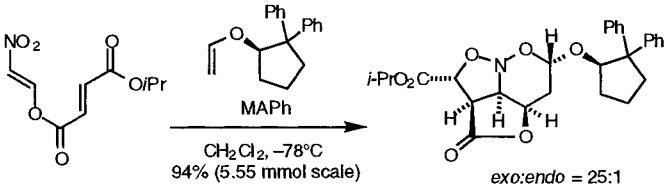
The vinyl ether prepared from the title compound participates in tandem [4+2]/[3+2] cycloadditions with nitroalkenes using Lewis acid catalysis.

Preparation: S. E. Denmark, et al. *J. Org. Chem.*, **1995**, *60*, 3205.

S. E. Denmark, A. Thorarensen, D. S. Middleton *J. Am. Chem. Soc.*, **1996**, *118*, 8255.



A



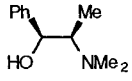
exo:endo = 25:1

MAPh = methylaluminium bis(2,6-diphenylphenoxide)
The reaction illustrated is a key step in the synthesis of Rosmarinecine.

(1*S*, 2*R*)-*N*-Methylephedrine — *Ligand*

The title compound promotes the enantioselective Reformatsky reaction to form α,α -difluoro-β-hydroxy esters.

J. M. Andrés, M. A. Martínes, R. Pedrosa, A. Péres-Encabo *Synthesis*, **1996**, 1070.



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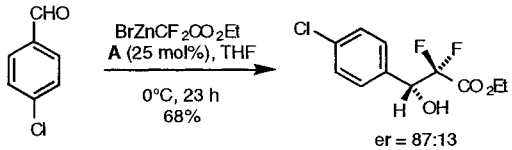

er = 87:13

Examples with 5 similar aldehydes and 2 other ephedrine derived catalysts are reported with 34-68 % yields and er = 60:40 to 91:9.

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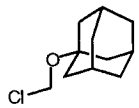
[(1-Adamantyl)oxy]methyl Chloride — *Protecting Group*

The title compound is a histidine protecting group. The 1-adamantyloxymethyl group is cleaved with trifluoroacetic acid.

Y. Okada, J. Wang, T. Yamamoto, Y. Mu, T. Yokoi *J. Chem. Soc., Perkin Trans. 1*, **1996**, 2139.



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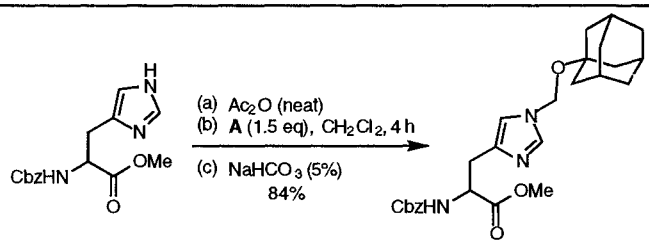
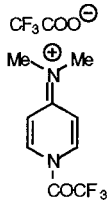


4-Dimethylamino-1-trifluoroacetylpyridinium Trifluoroacetate — *Reagent*

Aryltrifluoromethyl ketones are obtained upon treatment of aromatic compounds with the title iminium salt in presence of aluminium chloride.

G. Simchen, A. Schmidt *Synthesis*, **1996**, 1093.



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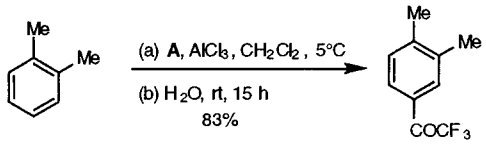


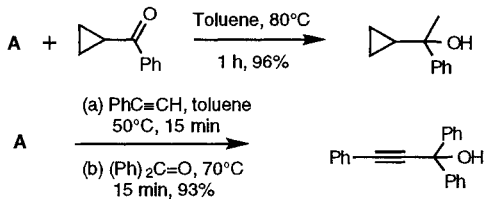
A is stable and easy to handle.

[(3-Dimethylamino)propyl]dimethylaluminium — *Reagent*

The title complex effects methylation and ethynylation of carbonyl compounds in high yields.

W. Baidossi, A. Rosenfeld, B. C. Wassermann, S. Schutte, H. Schumann, J. Blum *Synthesis*, **1996**, 1127.

A



α, β-Unsaturated carbonyl compounds undergo 1,4 addition of methyl or ethynyl groups.

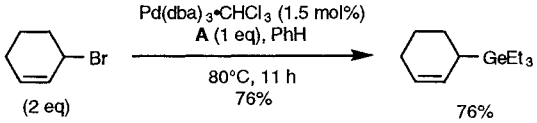
(Triethylgermyl)tributylstannane — *Reagent*

The title compound gives allylic germanes on reaction with allylic bromides in the presence of Pd(0).

T. Nakano, K. Ono, T. Migita *Chem. Lett.* **1996**, 697.

$Et_3GeSnBu_3$

A

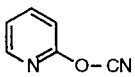


Eight examples; yields 20-92%

2-Pyridyl Cyanate — *Reagent*

The title compound reacts with Grignard reagents to give nitriles.

J. S. Koo, J. I. Lee *Synth. Commun.* **1996**, *26*, 3709.



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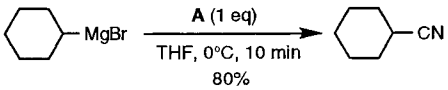

Ten examples; yields 72-97%.

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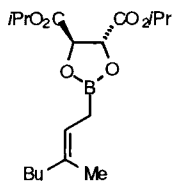
(*S,S*)-4,5-Di(isopropoxycarbonyl)-2-[(*E*)-3-methylhept-2-enyl]-2-bora-1,3-dioxolane — *Reagent*

The title compound undergoes enantioselective addition to aldehydes with the generation of a quaternary centre.



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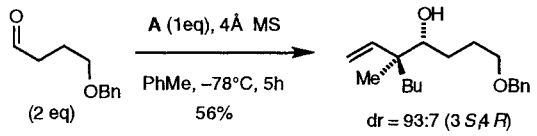
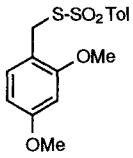


Yields are generally >75% when the aldehyde contains unfunctionalised side chains.

Y. Yamamoto, S. Hara, A. Suzuki *Synlett*, **1996**, 883.

2,4-Dimethoxybenzylthio Methylphenylsulfonate — *Reagent*

The title compound is an electrophilic sulfenylating agent for the preparation of thiols bearing the acid-labile 2,4-dimethoxybenzyl protecting group.



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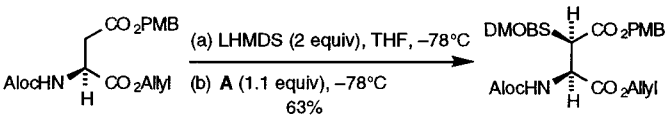
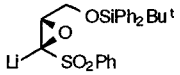


The 2,4-dimethoxybenzyl (DMOB) protecting group can be removed using mercury(II) trifluoroacetate, the free thiol being liberated by treatment of the resulting mercury(II) salt with hydrogen sulfide

N. Shibata, J. E. Baldwin, A. Jacobs, M. E. Wood *Tetrahedron*, **1996**, *52*, 12839.

(1*R*,2*S*)-1-Lithio-1-phenylsulfonyl-2-({[(tert-butyldiphenyl)silyl]oxy}methyl)oxirane — *Reagent*

The presence of the sulfone moiety in the title compound ensures a 6- *endo* cyclisation which has been applied to the synthesis of polycyclic *trans*-fused tetrahydropyrans.



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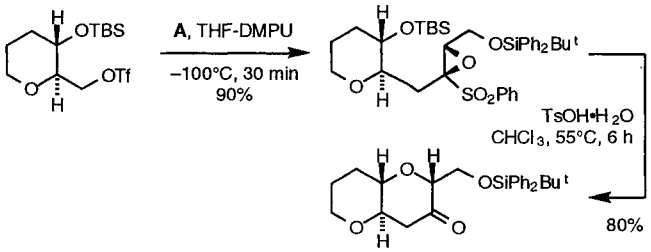
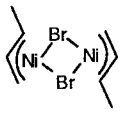


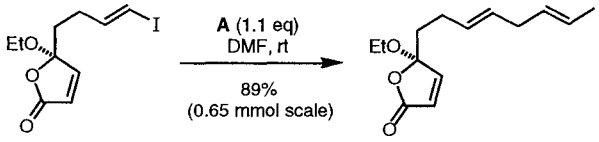
Y. Mori, K. Yaegashi, H. Furukawa *J. Am. Chem. Soc.*, **1996**, *118*, 8158.

Bis(π-crotyl)nickel Bromide — *Reagent*

The title compound undergoes coupling with alkenyl iodides to give 1,4-dienes. Unlike most crotyl metal reagents, it reacts preponderantly at the less hindered terminus.



A

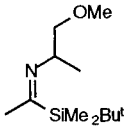


Single example taken from a synthesis of (+)-Cerulenin

T. E. Kedar, M. W. Miller, L. S. Hegedus *J. Org. Chem.*, **1996**, *61*, 6121.

1-[(*tert*-Butyldimethyl)silyl]-1-[*N*-(2-methoxy-1-methylethyl)imino]ethane — *Reagent*

The azaenolate derived from treating the title compound with LDA undergoes alkylation to give products which hydrolyse to acyl *tert*-butyldimethylsilanes.



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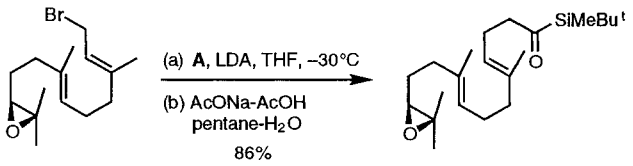

The example illustrated is a key step in the synthesis of Dammarenediol II

E. J. Corey, S. Lin *J. Am. Chem. Soc.*, **1996**, *118*, 8765.

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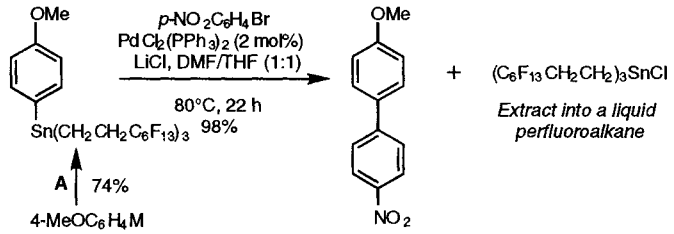
Bromotri(perfluorohexylethyl)stannane — *Reagent*

Arylstannanes prepared from the title compound undergo Stille coupling reactions. The tin byproducts are separated by simple extraction into a perfluoroalkane phase which is immiscible with water and organic solvents.

D. P. Curran, M. Hoshino *J. Org. Chem.*, **1996**, 61, 6480.

$(C_6F_{13}CH_2CH_2)_3SnBr$

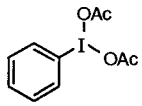
A



Iodosobenzene Diacetate — *Reagent*

The title compound together with trimethylsilyl halides haloacetoxylates 1,4-dimethoxynaphthalenes.

P. A. Evans, T. A. Brandt *Tetrahedron Lett.*, **1996**, *37*, 6443.



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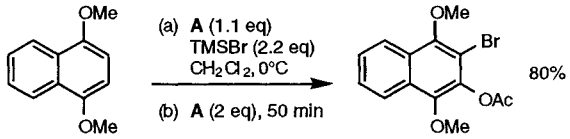
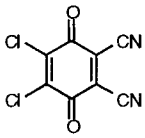


By control of stoichiometry and subtle changes in reaction conditions mono- and dibromo derivatives can also be procured. Nine examples (yields 71-75%).

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone — *Reagent*

The title compound selectively deprotects primary allyl ethers.

J. S. Yadav, S. Chandrasekhar, G. Sumithra, R. Kache *Tetrahedron Lett.*, **1996**, *37*, 6603.



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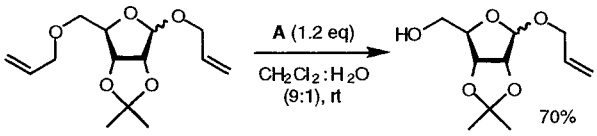
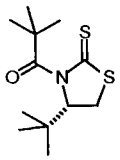


Total of 11 well-chosen examples (yields 70-92%).

(*S*)-4-*tert*-Butyl-3-pivaloyl-1,3-thiazolidine-2-thione — *Reagent*

Kinetic resolution of *sec*-alcohols is achieved via pivaloylation with the thiazolidinethione **A**.

S. Yamada, T. Ohe *Tetrahedron Lett.*, **1996**, *37*, 6777.



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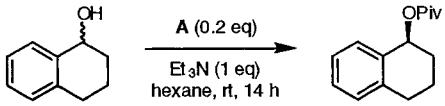


87%, er = 92:8

Twenty examples of kinetic resolution of benzylic *sec*-alcohols. Includes the use of some slightly different thiazolidines and oxazolidines (yields 49-99%, %ee 19-84%).

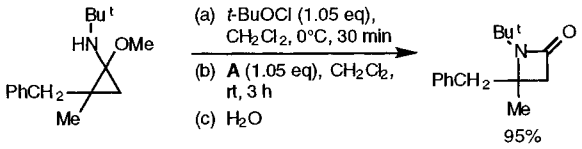
Silver Tetrafluoroborate — *Reagent*

Silver induced ring expansion of cyclopropyl *N*-chloroaminal derivatives gives β-lactams.

N. De Kimpe, K. A. Tehrani, G. Fonck *J. Org. Chem.*, **1996**, *61*, 6500.

$AgBF_4$

A



Six examples (yields 41-95%)

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