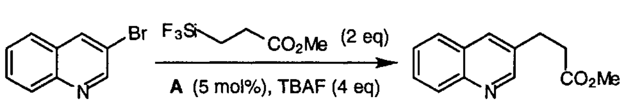
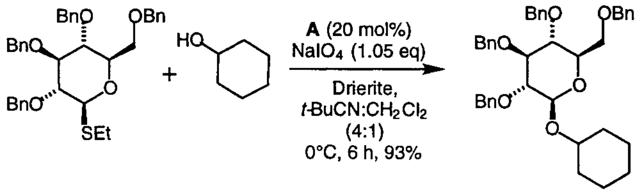
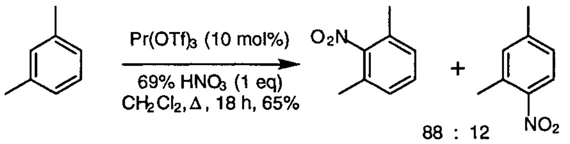
SYNTHESIS ALERTS

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 Glasgow. 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.

Tetrakis(triphenylphosphine)palladium		***Catalyst***
A cross-coupling reaction of alkyltrifluorosilanes with aryl halides was achieved using the title catalyst with excess tetrabutylammonium fluoride. H. Matsuhashi, S. Asai, K. Hirabayashi, Y. Hatanaka, A. Mori, T. Hiyama *Bull. Chem. Soc. Jpn.*, **1997**, *70*, 437.	$Pd(PPh_3)_4$ **A**	 30 examples with 6 different trifluorosilanes and 14 aryl bromides and iodides. Yields generally 60-80%.

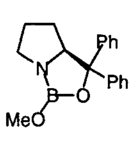
Trityl Tetrakis(pentafluorophenyl)borate		***Catalyst***
Catalytic stereoselective synthesis of several glycosides from thioglycosides is achieved by this catalyst with sodium periodate. H. Uchiro, T. Mukaiyama *Chem. Lett.*, **1997**, 121.	$TrB(C_6F_5)_4$ **A**	 10 examples; yields all >90%. α:β = 8:92

Lanthanide(III) Triflates		***Catalyst***
These triflates (1-10 mol%) catalyse the nitration of simple arenes using *stoichiometric* quantities of 69% nitric acid. F. J. Waller, A. G. M. Barrett, D. C. Braddock, D. Ramprasad *Chem. Commun.*, **1997**, 613.	$Ln(OSO_2CF_3)_3$ **A**	 5 different catalysts with *m*-xylene (Ln = La, Eu, Pr, Sc, Yb). The only byproduct is water and the catalyst may be recycled by evaporation.

Chiral Amino Alcohol–Trimethyl Borate Complex *Catalyst*

Asymmetric borane reduction of prochiral ketones with this reagent prepared *in situ* gives high enantioselectivity.

M Masui, T. Shioiri *Synlett* **1997**, 273.



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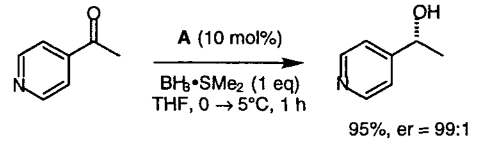
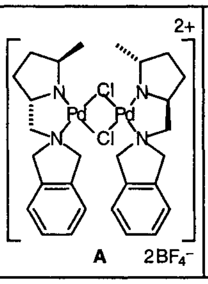


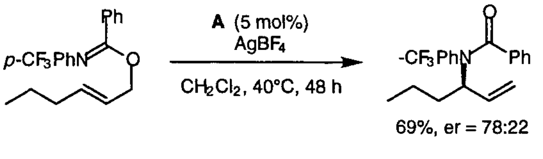
6 examples of ketones; yields >95%, ee's generally >95%. The catalyst is made from the amino alcohol (1.0 eq) and trimethylborate (1.2 eq). The methoxy group enhances the Lewis acidity of the boron.

Dichloro[(*S*)-2-isoindolinylmethyl)- *N*-methylpyrrolidine]palladium(II) *Catalyst*

Treatment of the title compound with silver tetrafluoroborate gives a compound which catalyses the asymmetric rearrangement of allylic amidates to allyl amides.

M. Calter, T.K. Hollis, L.E. Overman, J. Ziller, G.G. Zipp *J. Org. Chem.*, **1997**, *62*, 1449.

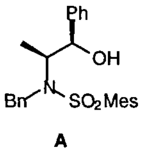




(1*S*,2*R*)-*N*-Benzyl-*N*-mesitylsulfonylnorephedrine *Chiral Auxiliary*

Esters prepared from the title compound undergo *anti* selective boron-mediated asymmetric aldol reaction.

A. Abiko, J.-F. Liu, S. Masamune *J. Am. Chem. Soc.* **1997**, *119*, 2586.



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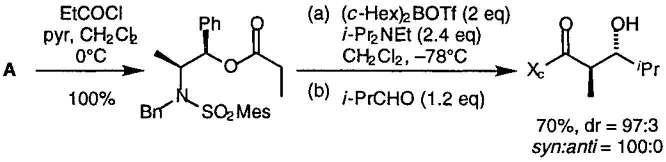
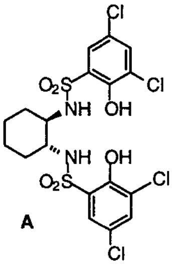
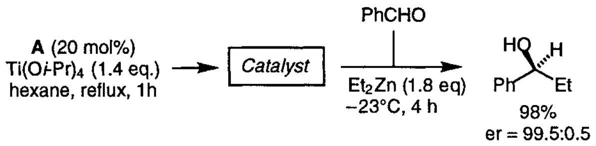


(1*R*, 2*R*)-(+)-1,2-(3,3′,5,5′-tetrachloro-2,2′-dihydroxydibenzenesulfonamido)cyclohexane *Ligand*

Addition of diethyl zinc to benzaldehyde in the presence of the title catalyst proceeds with excellent yield and er.

C. Guo, J. Qiu, X. Zhang, D. Verdugo, M. L. Larter, R. Christie, P. Kennedy, P. J. Walsh *Tetrahedron* **1997**, *53*, 4145.



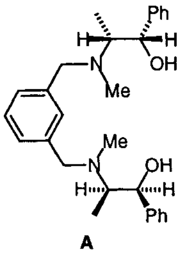


10 analogous catalysts were tested with yields = 10-100% and er up to 96 : 4. Detailed preparations of the catalysts are also presented.

(+)-(1*R*, 2*S*)-Bis[*N*-methyl- *N*-(2-hydroxy-2-phenyl-1-methyl)ethyl]-3-xylylenediamine *Ligand*

Asymmetric Reformatsky reactions of *tert*-butyl bromoacetate and various carbonyl compounds in the presence of the title amino alcohol proceed in moderate to good yield and good stereoselectivity.

J. M. Andrés, Y. Martín, R. Pedrosa, A. Pérez-Encabo *Tetrahedron* **1997**, *53*, 3787.



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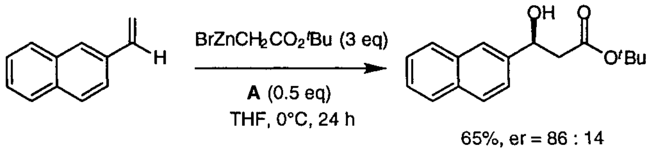
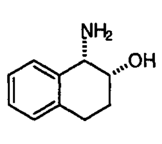


9 other examples reported, yields 35-90%, %ee 34-78%. 11 other catalysts were screened with inferior yields and enantioselectivities.

(1*S*,2*R*)-1-Amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene — *Ligand*

The title compound is a homochiral ligand for the enantioselective reduction of prochiral ketones.

C. M. Belluci, A. Bergamini, P. G. Cozzi, A. Papa, E. Tagliavini, A. Umani-Ronchi *Tetrahedron: asymmetry* **1997**, *8*, 895.



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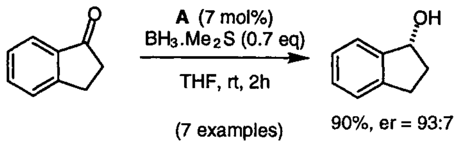


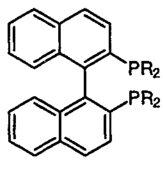
The *N*,*N*-dibutyl amino derivative of **A** has been used for the addition of Et_2Zn to benzaldehyde (er = 72:28).

2,2′-Bis(di-*p*-tolylphosphino)-1,1′-binaphthyl (Tol-BINAP) — *Ligand*

Tol-BINAP is one third the cost of BINAP and is equally effective in the Pd-catalysed coupling of alkylamines with aryl triflates.

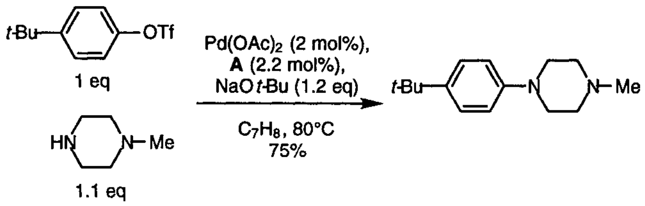
J.P. Wolfe, S.L. Buchwald *J. Org.Chem.*, **1997**, *62*, 1264.

See also:-
J. Louie, M.S. Driver, B.C. Hamann, J.F. Hartwig *J. Org.Chem.*, **1997**, *62*, 1268.



R = *p* -tolyl

A

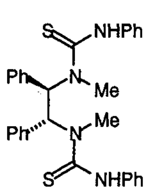


Slow addition of the triflate may be required for good yields in some cases.

Homochiral Bisthiourea Ligand — *Ligand*

The complex derived from $(RuCl_2C_6H_6)_2$ (**A**) and chiral bis-thiourea ligand **B**, catalyses the asymmetric hydride transfer reduction of prochiral ketones.

F. Touchard, P. Gamez, F. Fache, M. Lemaire *Tetrahedron Lett.*, **1997**, *38*, 2275.



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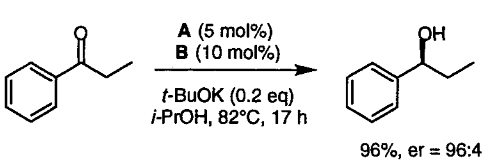
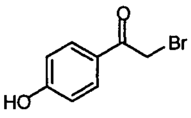


4 examples of reduction of simple phenyl ketones (yields 92-98%, %ee 85-94%). Extended reaction times (>12 h) are required for high conversions.

4-Hydroxyphenacyl Bromide — *Protecting Group*

The title compound can be used to protect phosphates. The 4-hydroxyphenacyl protecting group is cleaved photochemically.

C.-H. Park, R. S. Givens *J. Am. Chem. Soc.* **1997**, *119*, 2453.



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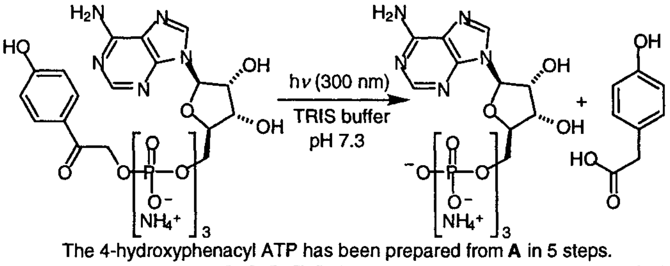
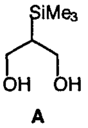


The 4-hydroxyphenacyl ATP has been prepared from **A** in 5 steps.

2-Trimethylsilylpropane-1,3-diol — *Protecting Group*

The formation of cyclic acetals from carbonyl compounds and diol **A** provides '*cyclo*-SEM' protection. The resulting 5-trimethylsilyl-1,3-dioxanes are easily cleaved by treatment with $LiBF_4$ in THF.

B. H. Lipshutz, P. Mollard, C. Lindsley, V. Chang *Tetrahedron Lett.*, **1997**, *38*, 1873.



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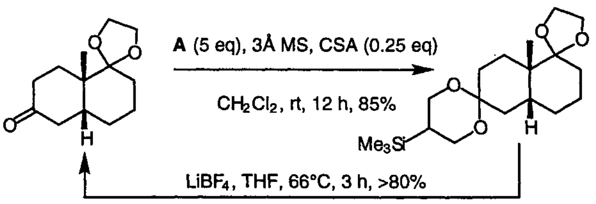


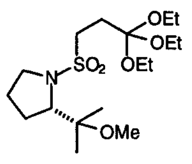
7 other simpler examples
(yields protection 45, 65-97%; yields deprotection 79-93%).

(*S*)-1-(3-Triethoxy propyl)sulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine

Reagent

Asymmetric cyclopentannulation of cyclic enones is accomplished with high enantioselectivity after reaction with the anion of the title sulfonamide.

C. Huart, L. Ghosez *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 634.



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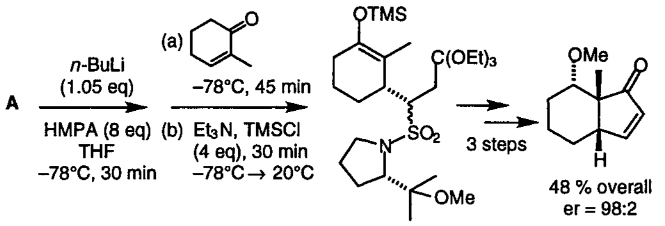


3 other examples are reported, yields 33-48%, %ee 92-98%.

Tetrabutylammonium Halides

Reagent

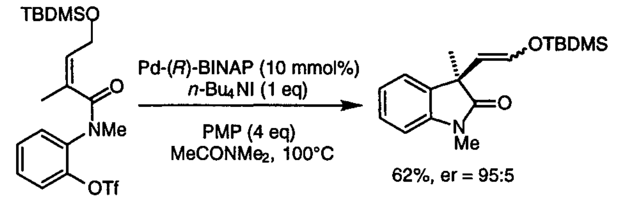
Intramolecular Heck reactions in the presence of the title salts and BINAP display enhanced enantioselectivity.

L. E. Overman, D. J. Poon *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 518.

$n\text{-}Bu_4NX$

X = I, Br, Cl

A



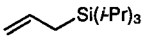
Hydrohalide salts of 1,2,2,6,6-pentamethylpiperidine (PMP) also promote the reaction with comparable yields and enantioselectivity (6 examples).

Allyltri isopropylsilane

Reagent

[3+2] Cycloaddition of the title silane and 1-acetylcycloalkenes in the presence of $TiCl_4$ provides exclusively silylbicycloalkanes in good yields instead of the Hosomi-Sakurai reaction products.

H.-J. Knölker, N. Foitzik, H. Goesmann, R. Graf, P. G. Jones, G. Wanzl *Chem. Eur. J.* **1997**, *3*, 538.



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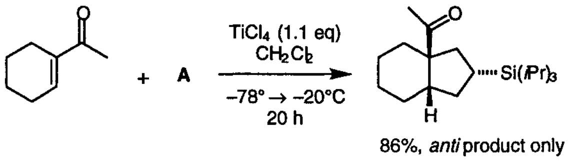


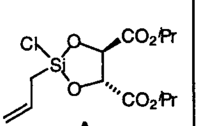
Various examples reported with different substrates and allylsilanes with lower yields (25 - 82%) and good to excellent *anti:syn* selectivity (5:1 to 100% *anti*).

Tartrate Ester Modified Allylsilanes

Reagent

These allylsilanes were found to serve as useful reagents for regiospecific and stereoselective allylation of aldehydes *without any catalyst*.

L. C. Zhang, H. Sakurai, M. Kira *Chem. Lett.*, **1997**, 129.



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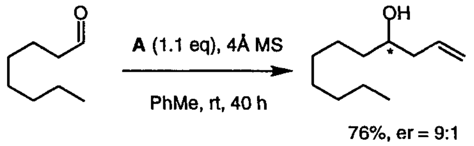


Yields 45-93%, %ee 20-80%.

Tin(II) Triflate

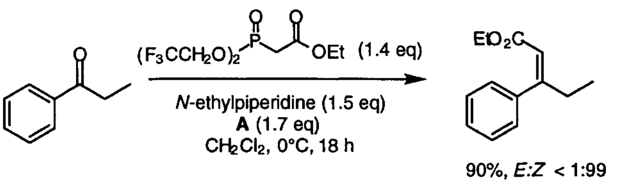
Reagent

Good *Z* or selectivity is obtained in the Horner-Wadsworth-Emmons reactions of methyl bis(trifluoroethyl) phosphonoacetate with aryl ketones using the title reagent in the presence of *N*-ethylpiperidine.

S. Sano, K. Yokoyama, M. Fukushima, T. Yagi, Y. Nagao *Chem. Commun.*, **1997**, 559.

$Sn(OSO_2CF_3)_2$

A



7 examples of ketones or aldehydes in THF or CH_2Cl_2 and comparison with NaH mediated reactions.

Sodium on Solid Support

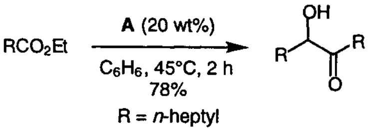
Reagent

5-20 wt% of sodium on NaCl, glass powder, poly(ethylene) or poly(propylene) gave good yields for the acylation reaction of carboxylic acids.

M. Makosza, K. Grela *Synlett* **1997**, 267.

Na/support

A



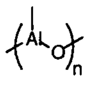
8 examples with mostly NaCl as the solid support. Yields 60-70%. The reagent may be prepared *via* low temperature (−33°C) deposition of sodium from its solution in liquid ammonia.

Methylalumoxane

Reagent

This extremely strong Lewis acid is a useful reagent for organic reactions such as the Diels-Alder reaction and amidation of esters.

M. Akakura, H. Yamamoto *Synlett* **1997**, 277.



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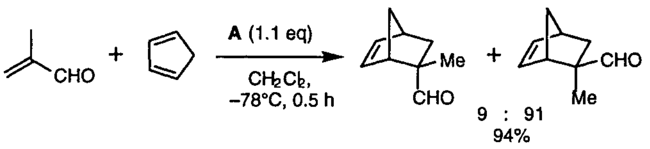


7 examples of the Diels-Alder reaction; yields generally >85%.

Diisopropylzinc-Magnesium Bromide Complex

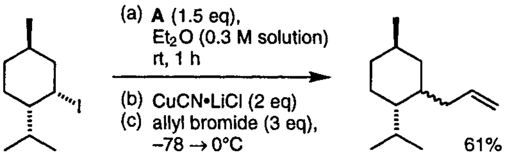
Reagent

i-Pr$_2$Zn, generated *in situ* from *i*-Pr$_2$MgBr (2 eq) and ZnBr$_2$ (1 eq), leads to a smooth iodine–zinc exchange in secondary alkyl iodides.

L. Micouin, P. Knochel *Synlett* **1997**, 327.

i-Pr$_2$Zn•MgBr$_2$

A



8 examples, yields 60-80%. Racemisation occurs with chiral alkyl iodides.

Tetrachlorosilane

Reagent

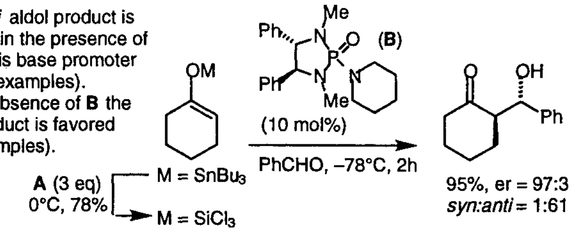
Trichlorosilyl ethers prepared from trimethylsilyl ethers and the title compound undergo highly selective asymmetric aldol reactions.

S. E. Denmark, K.-T. Wong, R. A. Stavenger *J. Am. Chem. Soc.* **1997**, *119*, 2333.

SiCl$_4$

A

The *anti* aldol product is favored in the presence of the Lewis base promoter (**B**) (11 examples).
In the absence of **B** the *syn* product is favored (15 examples).



95%, er = 97:3
syn:*anti* = 1:61

Lithium Tri- *tert*-butylzincate

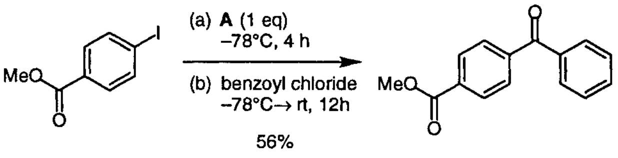
Reagent

The title compound metallates alkyl and aryl iodides to the corresponding mixed zincates which react with electrophiles *without transfer of the tert-butyl group.*

Y. Kondo, M. Fujinami, M. Uchiyama, T. Sakamoto *J. Chem. Soc, Perkin Trans. I*, **1997**, 799.

(*t*-Bu)$_3$ZnLi

A

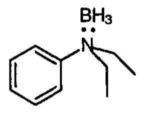


N,N-Diethylaniline•Borane (DEANB) Complex — *Reagent*

The commercially available complex **A** effectively reduces a variety of functional groups, including: aldehydes, ketones, carboxylic acids, amides and lactams.

See following paper for use of DEANB (**A**) as borane source in CBS reduction reactions.

A. M. Salunkhe, E. R. Burkhardt *Tetrahedron Lett.*, **1997**, *38*, 1519.



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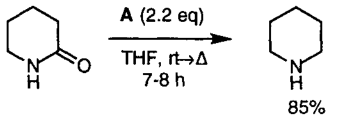
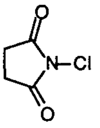


11 varied examples (yields 51, 85-94%). **A** is also an effective hydroboration reagent, showing good regioselectivity.

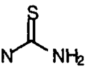
N-Chlorosuccinimide / Thiourea — *Reagent*

Successive treatment of aldoximes with NCS (**A**), followed by thiourea (**B**) and triethylamine, produces the corresponding isothiocyanates in excellent yield.

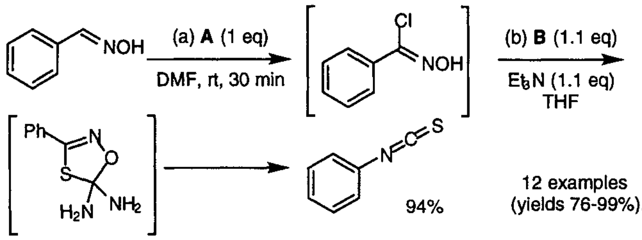
J. N. Kim, K. S. Jung, H. J. Lee, J. S. Son *Tetrahedron Lett.*, **1997**, *38*, 1597.



A



B

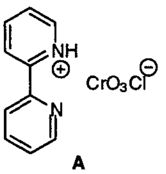


12 examples (yields 76-99%).

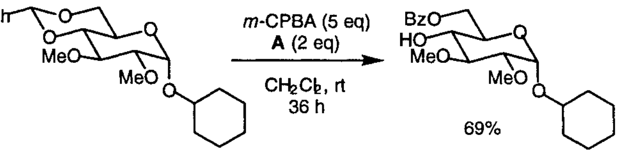
2,2′-Bipyridinium Chlorochromate / 3-Chloroperoxybenzoic Acid — *Reagent*

Oxidative cleavage of benzylidene acetals to hydroxy esters is effected by the title reagent pair. Possible oxidation of the released hydroxyl function is negligible.

F. A. Luzzio, R. A. Bobb *Tetrahedron Lett.*, **1997**, *38*, 1733.



A

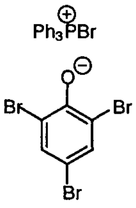


10 examples (yields 48, 69-79%).

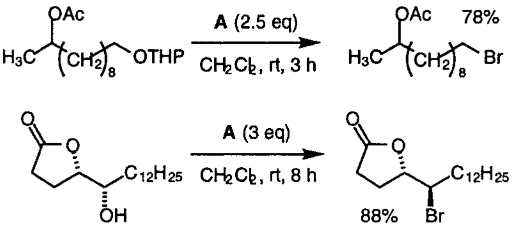
Bromotriphenylphosphonium 2,4,6-Tribromophenoxide — *Reagent*

Primary and secondary alcohols are smoothly converted to the corresponding bromides under mild conditions by treatment with **A**. THP ethers can also be directly transformed to bromides with **A**.

A. Tanaka, T. Oritani *Tetrahedron Lett*, **1997**, *38*, 1955.



A



7 examples (yields 78-99%).

Zinc Amalgam — *Reagent*

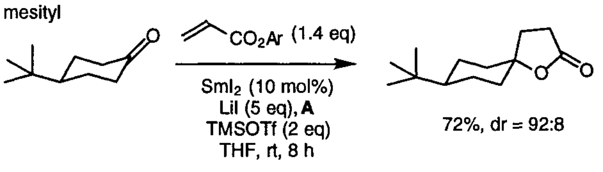
A complex system of **A**, LiI and TMSOTf allows for the *in situ* regeneration of SmI_2 from Sm(III) species. Thus SmI_2 mediated reactions can be made catalytic in samarium.

E. J. Corey, G. Z. Zheng *Tetrahedron Lett.*, **1997**, *38*, 2045.

Zn•Hg

A

Ar = mesityl



5 examples of spiroannulation of ketones with mesityl acrylate (yields 70-84%). Also demonstrated: deoxygenation of styrene oxide (67% yield), and cyclisation of 6-iodo-1-phenylhex-1-yne (82% yield).