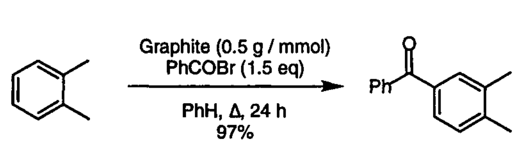
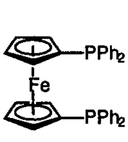
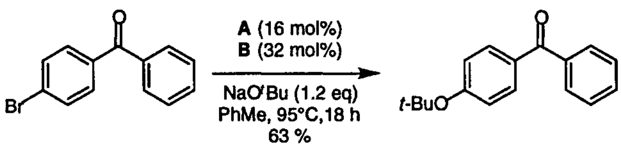
SYNTHESIS ALERTS

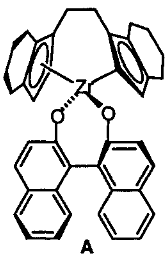
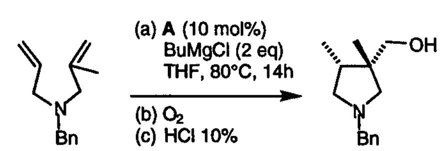
Synthesis Alerts is a monthly feature to help readers of Synthesis keep abreast of new reagents, catalysts, ligands, chiral auxiliaries, and protecting groups which have appeared in the recent literature. Emphasis is placed on new developments but established reagents, catalysts etc are also covered 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, John Christopher, Louise Lea, Philip Kocienski, J.-Y. Le Brazidec, Robert Narquizian and Christopher Smith 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.

Georg Thieme Verlag does not accept responsibility for the accuracy, content, or selection of the data.

Graphite		***Catalyst***
Graphite promotes Friedel-Crafts acylation of aromatic compounds with acyl halides. M. Kodomari, Y. Suzuki, K. Yoshida *Chem. Comm.* **1997**, *16*, 1567.	Graphite	 10 examples (yields 70-97%).

Bis(1,5-cyclooctadiene) Nickel(0) / 1, 1'-Bis(diphenylphosphino)ferrocene (dppf)		***Catalyst***
A combination of title reagents **A** and **B** catalyses the formation of alkyl and silyl ethers from aryl halides and sodium alkoxides or siloxides. G. Mann, J. F. Hartwig *J. Org. Chem.* **1997**, *62*, 5413.	$Ni(COD)_2$ **A**  **B**	 12 examples (yields 53-98%) of ether formation from electron deficient aryl halides. Sodium counterion was found to be crucial.

[Ethylene-1,2-bis(η^5-4,5,6,7-tetrahydro-1-indenyl)]](R)-1,1'-bi-2-naphthoxy]zirconium(II)		***Catalyst***
Synthesis of heterocycles using zirconium catalyzed asymmetric diene cyclization. Y. Yamaura, M. Hyakutake, M. Mori *J. Am. Chem. Soc.* **1997**, *119*, 7615.	 **A**	 72%, er = 86:14 6 examples (yields 24-79%, %ee 44-86%). Other five- and six-membered rings were also prepared with moderate yields and good stereocontrol.

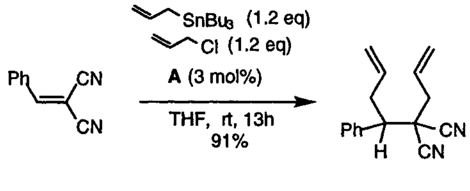
Bis(triphenylphosphine)palladium(II) Dichloride — *Catalyst*

Catalyses the amphiphilic double allylation of activated olefins.

H. Nakamura, J.-G. Shim, Y. Yamamoto *J. Am. Chem. Soc.* **1997**, *119*, 8113.

$PdCl_2(PPh_3)_2$

A

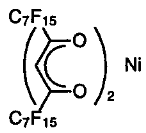


12 examples (yields 0, 43-91%).

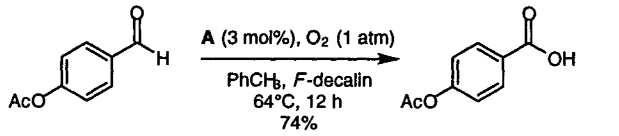
Fluorinated Bis(8,10-heptadecanedionato)Nickel(II) — *Catalyst*

A new method for the biphasic oxidation of aldehydes, sulfides and olefins to carboxylic acids, sulfoxides or sulfones, and epoxides respectively, using transition metal catalysts (Ni, Ru) bearing perfluorinated ligands.

I. Klement, H. Lütgens, P. Knochel *Angew. Chem Int. Ed. Engl.* **1997**, *36*, 1454.



A

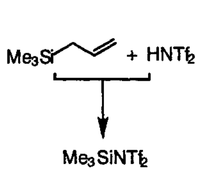


5 examples of oxidation of aldehydes (yields 71-87%); 9 examples of oxidation of sulfides (yields 60-91%); 7 examples of oxidation of olefins (yields 71-85%).

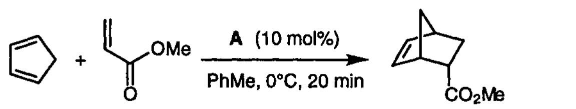
N-Trimethylsilylbis(trifluoromethanesulfonyl)imide — *Catalyst*

The title reagent **A** complexes carbonyl compounds more effectively than TMSOTf (**B**). The use of **A** to catalyse Diels-Alder reactions is investigated.

B. Mathieu, L. Ghosez *Tetrahedron Lett.* **1997**, *38*, 5497.



A



cat. = **A**, 83%, dr = 96:4
B, <5%, dr = 93:7

5 examples of Diels-Alder reactions (yields 74-92%, dr (*endo*) > 67:33).

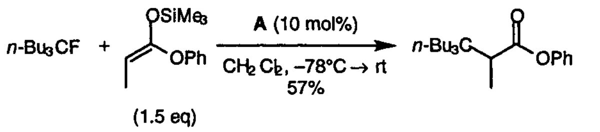
Trimethylaluminium — *Catalyst*

Catalyses the alkylation of a variety of nucleophiles by *tert*-alkyl fluorides.

T. Ooi, D. Uraguchi, N. Kagoshima, K. Maruoka *Tetrahedron Lett.* **1997**, *38*, 5679.

Me_3Al

A



11 examples (yields 38, 60-76%).

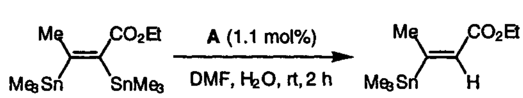
Copper(I) Chloride — *Catalyst*

Treatment of alkyl (*Z*)-2,3-bis(trimethylstannyl)-2-alkenoates with a catalytic amount of copper(I) chloride in wet DMF effects chemo- and stereoselective removal of a 2-trimethylstannyl group.

E. Piers, E. J. McEachern, M. A. Romero *J. Org. Chem.* **1997**, *62*, 6034.

CuCl

A



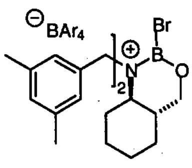
91%, *E*:*Z* > 93:7

7 examples (yields 75-94%, *E*:*Z* > 91:9). The *Z* alkenoate products are available by treatment of alkyl (*Z*)- or (*E*)-2,3-bis(trimethylstannyl)-2-alkenoates with dilute hydrochloric acid in DMF. 12 examples (yields 74-95%, *Z*:*E* > 79:21).

Diels-Alder Catalyst ***Catalyst***

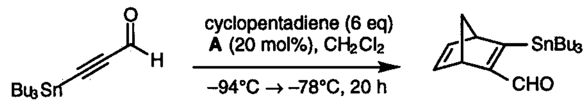
The title compound catalyses the asymmetric Diels-Alder reaction of cyclopentadiene with *α,β*-acetylenic aldehydes.

E. J. Corey, T. W. Lee *Tetrahedron Lett.* **1997**, *38*, 5755.



A

Ar = 3,5-$(CF_3)_2C_6H_3$



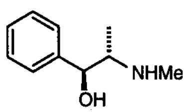
83%, er = 90:10

4 examples of the above process with varying *β*-substituent (silyl or stannyl) of the ynal (yields 37-83%, %ee 90-87%).

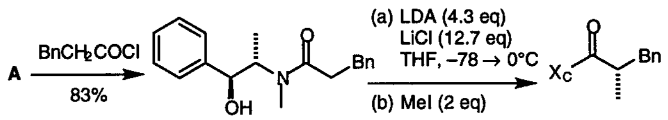
(1*S*,2*S*)-2-*N*-methylamino-1-phenylpropan-1-ol ***Chiral Auxiliary***

Pseudoephedrine as a practical chiral auxiliary for the synthesis of higly enantiomerically enriched carboxylic acids, alcohols, aldehydes, and ketones.

A. G. Myers, B. H. Yang, H. Chen, L. McKinstry, D. J. Kopecky, J. L. Gleason *J. Am. Chem. Soc.* **1997**, *119*, 6496.



A



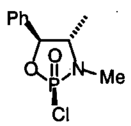
99%, dr = 97:3

Full detailed paper describing the employment of pseudoephedrine as a general chiral auxiliary for the synthesis of highly enantioenriched functionalised derivatives (34 examples).

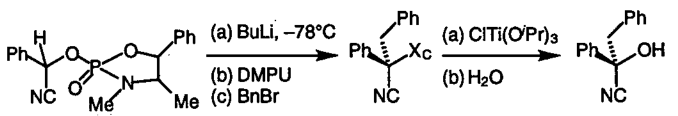
(2*R*,4*S*,5*R*)-3-Benzyl-2-chloro-4-methyl-5-phenyl-1,3,2-oxazaphospholidin-2-one ***Chiral Auxiliary***

Enantioselective synthesis of tertiary cyanohydrins, *via* stereoselective umpolung reactions with metallated *P*-chiral cyanohydrin phosphates.

T. Schrader *Chem. Eur. J.* **1997**, *3*, 1273.



A



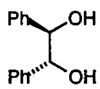
58%, dr = 91:9 85%, er > 98:2 (recrystallisation)

11 examples of tertiary cyanohydrin phosphate (yields 38-69%, %de 48-94).
7 examples of tertiary cyanohydrins (yields 44-92%, %ee > 96).

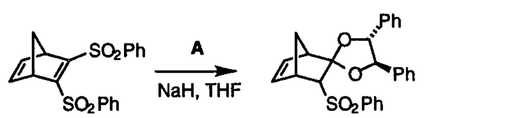
(*R,R*)-(+)-1,2-Diphenylethane-1,2-diol ***Chiral Auxiliary***

A novel enantiotopic discrimination between the carbon atoms of a double bond to afford diastereo- and enantiopure ketones.

S. Cossu, O. De Lucchi, P. Pasetto *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1504.



A



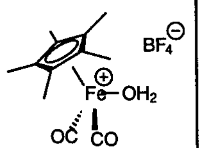
88%, er > 99:1, dr > 99:1

5 examples of various chiral auxiliaries and 3 examples of bisphenylsulfonyl alkenes (yields 72-97%, %de 0-100%).

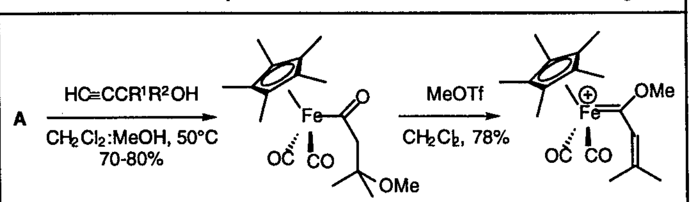
η*^{5}–Pentamethylcyclopentadienyl(dicarbonyl)hydroxo Iron(II) Tetrafluoroborate Complex** ***Reagent

The title compound provides a novel route to new *α,β*-unsaturated acyl iron complexes *via* direct activation of alk-2-yn-1-ol, which can then be converted to the corresponding (alkenyl)carbene complexes.

G. Poignant, F. Martin, V. Guerchais *Synlett* **1997** 913.



A



6 examples forming both the *s-cis* and *s-trans* alkenylcarbene complexes.

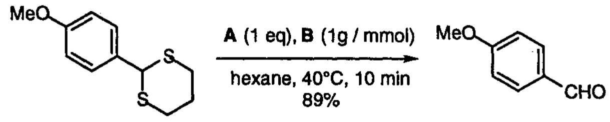
Iron(III) Nitrate / Montmorillonite K10 — *Reagent*

Deprotection of 1,3-dithiolanes and 1,3-dithianes was achieved in high yield using $Fe(NO_3)_3$ and Montmorillonite K10. The anhydrous conditions described allow hydrolytically labile substrates to be deprotected.

M. Hirano, K. Ukawa, S. Yakabe, J. H. Clarke, T. Morimoto *Synthesis* **1997**, 858.

$Fe(NO_3)_3$
A

Montmorillonite K10
B

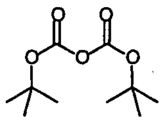


21 examples (yields 81-100%).

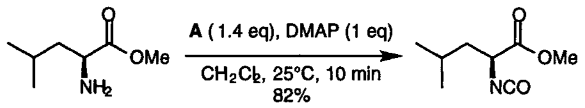
Di-*tert*-butyldicarbonate (Boc_2O) — *Reagent*

The title coumpound is used during a phosgene-free synthesis of enantiopure α-*iso*cyanato carboxylic acid esters.

H. Knölker and T. Braxmeier *Synlett*, **1997**, 925.



A



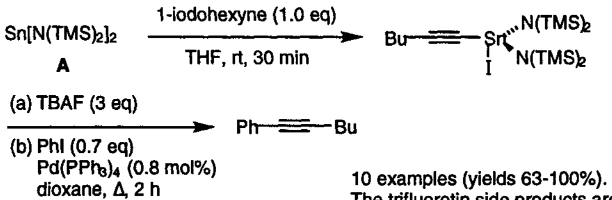
7 examples (yields 49-95%). Isocyanates were converted to their corresponding ureas, Cbz- and Aloc-protected amino acid esters.

Bis[bis(trimethylsilyl)amido]tin(II) — *Reagent*

Monoorganostannanes are available from reagent **A** and the corresponding organic halide in quantitative yields. Addition of TBAF forms a hypervalent fluorinated organotin species which undergoes palladium(0) catalysed coupling with aryl and vinyl iodides in good yields.

E. Fouquet, M. Pereyre, A. L. Rodriguez *J. Org. Chem.* **1997**, *62*, 5242.

$Sn[N(TMS)_2]_2$
A



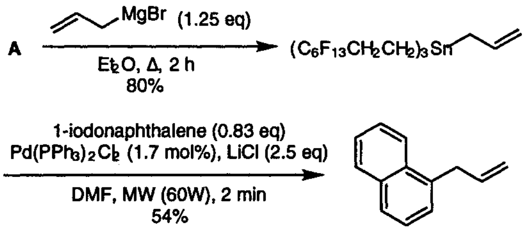
10 examples (yields 63-100%). The trifluorotin side products are easily removed.

Tris(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)tin Bromide — *Reagent*

A series of fluorinated aryltin, heteroaryltin and allyltin reagents synthesised from **A** underwent palladium-catalysed fluorous Stille cross-coupling reactions. The reactions required less than 2 minutes for completion when conducted under microwave irradiation.

M. Larhed, M. Hoshino, S. Hadida, D. P. Curran, A. Hallberg *J. Org. Chem* **1997**, *62*, 5583.

$(C_6F_{13}CH_2CH_2)_3SnBr$
A



16 examples (yields 39-96%)

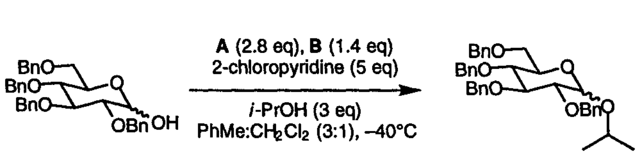
Diphenylsulfoxide / Trifluoromethanesulfonic Anhydride — *Reagent*

Direct glycosylations with 1-hydroxy glycosyl donors using trifluoromethanesulfonic anhydride and diphenyl sulfoxide.

B. A. Garcia, J. L. Poole, D. Y. Gin *J. Am. Chem. Soc.* **1997**, *119*, 7597.

Ph_2SO
A

Tf_2O
B



86%, α:β = 27:73

Oxygen, nitrogen, sulfur and carbon nucleophiles were all found to be suitable glycosyl acceptors using this procedure (9 examples).

Triisopropyloxytitanium(IV) Chloride / Cyclopentylmagnesium Chloride — *Reagent*

The title reagent pair effect the cyclisation of a variety of substituted succinimides possessing a pendant olefin function. This represents a new method for the synthesis of functionalised pyrrolizidine, indolizidine, and mitomycin alkaloids.

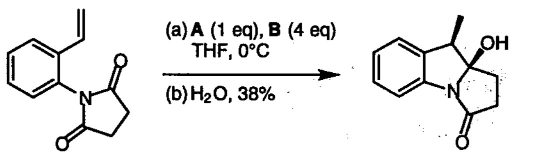
J. Lee, J. D. Ha, J. K. Cha *J. Am. Chem. Soc.* **1997**, *119*, 8127.

ClTi(O-*i*-Pr)$_3$

A

c-C_5H_9MgCl

B

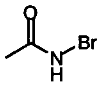


9 examples (yields 38-68%). The intermediate oxatitanacycles have been either hydrolysed or oxidised in a study directed toward mitomycins.

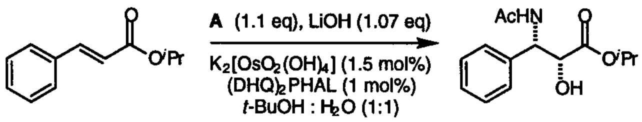
N-Bromoacetamide — *Reagent*

N-Bromoacetamide is used as a new nitrogen source for the catalytic asymmetric aminohydroxylation of olefins.

M. Bruncko, G. Schlingloff, K. B. Sharpless *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1483.



A



81%, er = 96:4

5 examples (yields 46-81%, %ee 89-99).

Bis(trimethylsilylmethyl) Zinc — *Reagent*

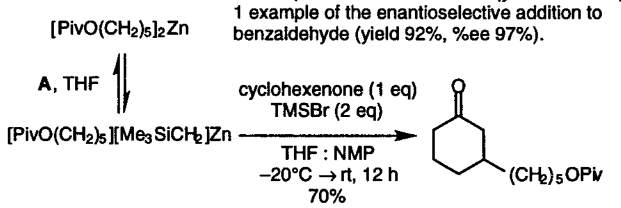
Preparation and reactions of *β*-silyl diorganozinc compounds, a new class of zinc reagents. As with cuprates, the trimethylsilylmethyl group acts as a dummy ligand and is not transferred.

S. Berger, F. Langer, C. Lutz, P. Knochel, A. Mobley, C. K. Reddy, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1496.

$(Me_3SiCH_2)_2Zn$

A

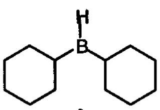
7 examples of Michael addition (yields 49-87%). 1 example of the enantioselective addition to benzaldehyde (yield 92%, %ee 97%).



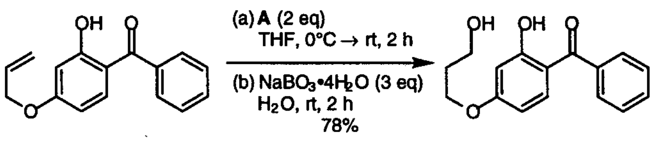
Dicyclohexylborane — *Reagent*

The title reagent selectively hydroborates terminal olefins in the presence of aldehydes and ketones.

G. W. Kabalka, S. Yu, N.-S. Li *Tetrahedron Lett.* **1997**, *38*, 5455.



A

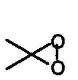


7 examples (yields 50, 68-80%).

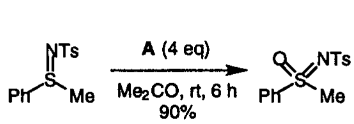
Dimethyl Dioxirane — *Reagent*

Enables the direct conversion of sulfilimines to sulfoximines.

N. Gaggero, L. D'Accolti, S. Colonna, R. Curci *Tetrahedron Lett.* **1997**, *38*, 5559.



A

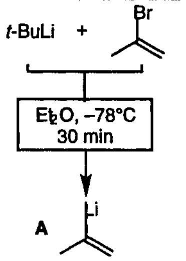


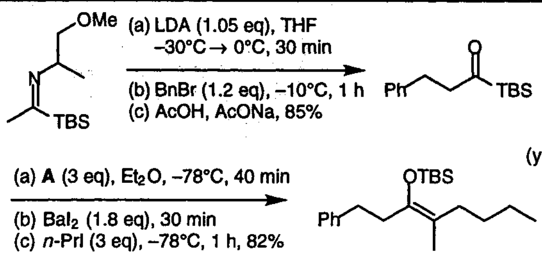
7 examples (yields 90-92%). Negligible *N*-oxidation was observed.

2-Propenyllithium — *Reagent*

A three component coupling process for the stereospecific synthesis of tetrasubstituted *Z*-enol silyl ethers is described.

E. J. Corey, S. Lin, G. Luo *Tetrahedron Lett.* **1997**, *38*, 5771.



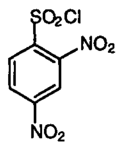


4 examples (yields 72-82%).

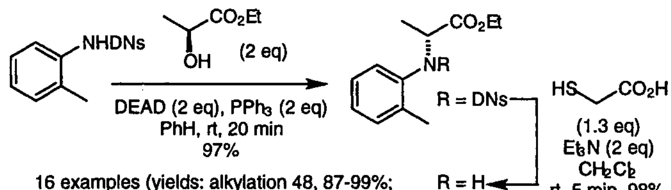
2,4-Dinitrobenzenesulfonyl Chloride — *Reagent*

Secondary sulfonamides derived from the title reagent can be easily *N*-alkylated *via* classical or Mitsunobu conditions and the resultant tertiary sulfonamides 'deprotected' to yield secondary amines.

T. Fukuyama, M. Cheung, C.-K. Jow, Y. Hidai, T. Kan *Tetrahedron Lett.* **1997**, *38*, 5831.



A



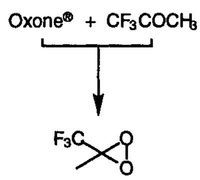
16 examples (yields: alkylation 48, 87-99%; deprotection 91-98%).

DNs = 2,4-dinitrobenzenesulfonyl

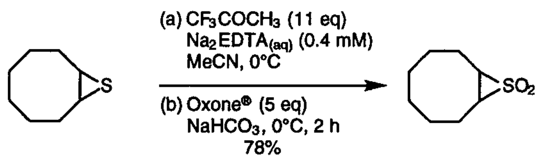
Methyl(trifluoromethyl) Dioxirane (TFDO) — *Reagent*

Effects the oxidation of episulfides to the corrsponding episulfones in good yield.

P. Johnson, R. J. K. Taylor *Tetrahedron Lett.* **1997**, *38*, 5873.



A



6 examples (yields 32-95%).

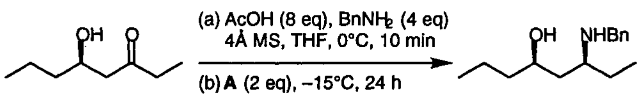
Sodium Cyanoborohydride — *Reagent*

The title reagent effects the diastereoselective reduction of 3-hydroxyimines (generated *in situ* from 3-hydroxy ketones) to yield *syn*-1,3-amino alcohols with good control.

M. Haddad, J. Dorbais, M. Larchevêque *Tetrahedron Lett.* **1997**, *38*, 5981.

$NaBH_3CN$

A



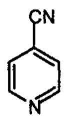
76%, *syn*:*anti* = 87:13

7 examples (yields 75-79%, %de 62-90%).

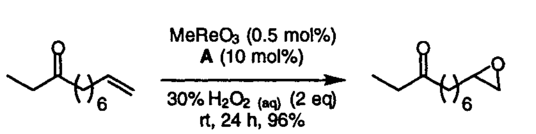
3-Cyanopyridine — *Ligand*

Enhances the methyltrioxorhenium catalysed epoxidation of terminal olefins.

C. Copéret, H. Adolfsson. K. B. Sharpless *Chem. Comm.* **1997**, *16*, 1565.



A



14 examples (yields 85-96%). An improved yield of the acid sensitive epoxide, styrene oxide, can be obtained by employing a mixture of pyridine and cyanopyridine.