SYNTHESIS ALERTS

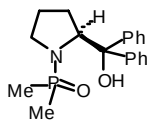
Synthesis Alerts is a monthly feature to help readers of Synthesis keep abreast of new reagents, catalysts, ligands, chiral auxiliaries, and protecting groups which have appeared in the recent literature. Emphasis is placed on new developments but established reagents, catalysts etc are also covered 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, Stephen Brand, John Christopher, Emma Guthrie, Philip Kocienski, Louise Lea, Graham McAllister, Russell McDonald and Robert Narquizian of Glasgow University. The journals regularly covered by the abstractors are: Angewandte Chemie International Edition, Bulletin of the Chemical Society of Japan, Chemistry A European Journal, Chemistry Letters, European Journal of Organic Chemistry, Helvetica Chimica Acta, Heterocycles, Journal of Organic Chemistry, Journal of the American Chemical Society, Organometallics, Synlett, Synthesis, Tetrahedron, Tetrahedron Asymmetry and Tetrahedron Letters.

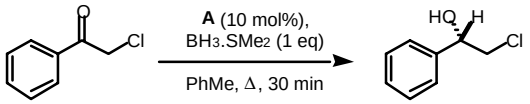
Georg Thieme Verlag does not accept responsibility for the accuracy, content, or selection of the data.

(*S*)-*N*-(Dimethylphosphoryl)- α,α-diphenylpyrrolidine-2-methanol — ***Catalyst***

The title phosphinamide catalyses the asymmetric reduction of ketones by borane.



A



81%, er = 96:4

2 examples (yields 81 and 90%, %ee 92 and 62%).

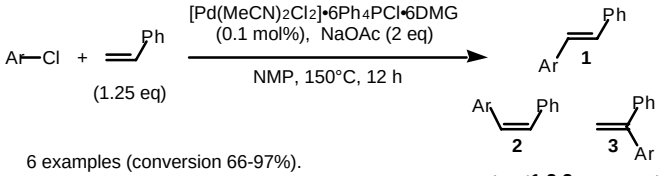
B. Burns, N. P. King, H. Tye, J. R. Studley, M. Gamble, M. Wills *J. Chem. Soc., Perkin Trans 1* **1998**, 1027.

Tetraphenylphosphonium Chloride — ***Catalyst***

The combination of a Pd(II) catalyst and **A** in the presence of small amounts of *N,N*-dimethylglycine (DMG) currently represents the most active and selective catalyst system for Heck reactions of normally unreactive halides.

Ph_4PCl

A



6 examples (conversion 66-97%).

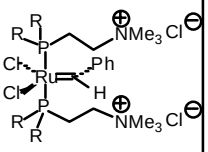
NMP = *N*-methylpyrrolidinone
Ar = *p*-benzaldehyde

98% conversion (**1**:**2**:**3** = 98:<1:2), only 1% of undesired scrambling products

M. T. Reetz, G. Lohmer, R. Schwickardi *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 481.

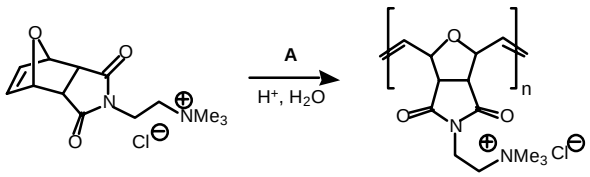
Water-Soluble Ruthenium Metathesis Catalyst — ***Catalyst***

The title reagent, in the presence of a Brønsted acid, catalyses living ring opening metathesis polymerisation (ROMP) in aqueous media.



A

R = cyclohexyl



The presence of acid not only serves to remove small concentrations of hydroxide ions (which cause significant catalyst decomposition), but also accelerates polymerisation and yields a true living system.

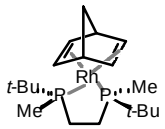
D. M. Lynn, B. Mohr, R. H. Grubbs *J. Am. Chem. Soc.* **1998**, *120*, 1627.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

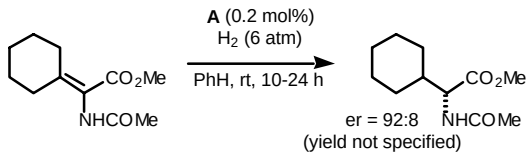
1,2-Bis(*tert*-butylmethylphosphino)ethane Rhodium(I) Norbornadiene Complex — *Catalyst*

The synthesis of a new class of P-chiral phosphine ligands and their application to the rhodium(I) catalysed asymmetric hydrogenation of α-(acylamino)- arylates is described.

T. Imamoto, J. Watanabe, Y. Wada, H. Masuda, H. Yamada, H. Tsuruta, S. Matsukawa, K. Yamaguchi *J. Am. Chem. Soc.* **1998**, *120*, 1635.



A



er = 92:8
(yield not specified)

10 examples employing **A** (%ee 55-99.9%); 11 other examples employing analogous catalysts.

(Dibenzylideneacetone)palladium(0) — *Catalyst*

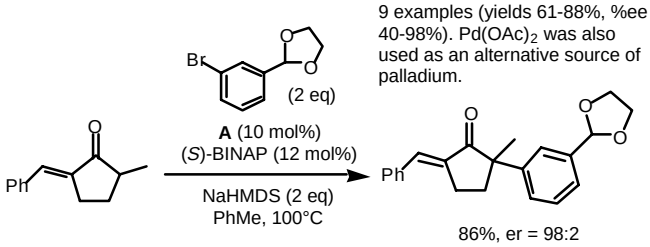
The title reagent in the presence of (*S*)-BINAP catalyses the enantioselective arylation of ketone enolates to afford quaternary stereogenic centres.

J. Åhman, J. P. Wolfe, M. V. Troutman, M. Palucki, S. L. Buchwald *J. Am. Chem. Soc.* **1998**, *120*, 1918.

$Pd_2(dba)_3$

A

9 examples (yields 61-88%, %ee 40-98%). $Pd(OAc)_2$ was also used as an alternative source of palladium.



86%, er = 98:2

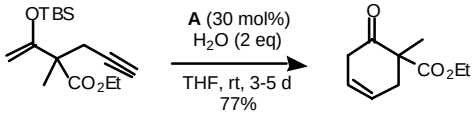
Tungsten Pentacarbonyl Tetrahydrofuran Complex — *Catalyst*

The title reagent catalyses the *endo-dig* cyclisation of ω-acetylenic silyl enol ethers.

K. Maeyama, N. Iwasawa *J. Am. Chem. Soc.* **1998**, *120*, 1928.

$W(CO)_5$•THF

A



6 examples (yields 73-93%). The process is only successful for terminal acetylenes.

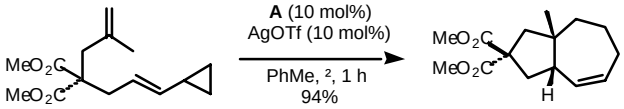
Tris(triphenylphosphine)rhodium(I) Chloride — *Catalyst*

The title reagent catalyses the intramolecular [5+2] cycloaddition of alkenes to tethered vinyl cyclopropanes.

P. A. Wender, C. O. Husfeld, E. Langkopf, J. A. Love *J. Am. Chem. Soc.* **1998**, *120*, 1940.

$RhCl(PPh_3)_3$

A



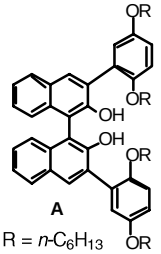
6 examples (yields 77-94%). All substrates possessing a 3-carbon tether between olefins yielded *cis* 5,7-ring systems, those with a 4-carbon tether yielded *trans* 6,7-ring systems.

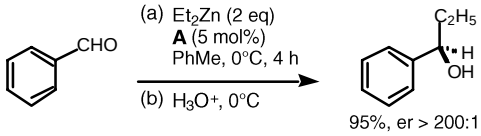
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

(*R*)-3,3′-Bis(2″,5″-dihexyloxyphenyl)-1,1′-binapthol — *Catalyst*

A catalyses the enantioselective addition of diethylzinc to aldehydes.

W.-S. Huang, Q.-S. Hu, L. Pu *J. Org. Chem.* **1998**, *63*, 1364.



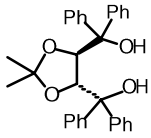


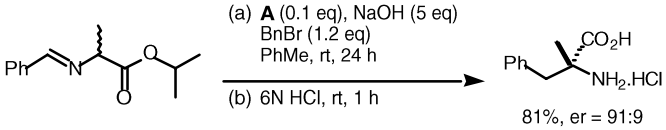
23 examples of aromatic, aliphatic and aryl or alkyl substituted α,β-unsaturated aldehydes (yields 62-97%, %ee 90->99%).

(4*R*,5*R*)-2,2-Dimethyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol [(R,R)-TADDOL] — *Catalyst*

A catalyses the *C*-alkylation of aldimine Schiff's bases of alanine esters under phase-transfer conditions.

Y. N. Belokon, K. A. Kochetkov, T. D. Churkina, N. S. Ikonnikov, A. A. Chesnokov, O. V. Larionov, V. S. Parmár, R. Kumar, H. B. Kagan *Tetrahedron: Asymmetry* **1998**, *9*, 851.



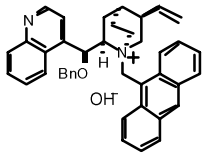


5 examples (crude yields 45-95%, %ee 20-75%).

N-Anthracenylmethyl Cinchodinium Hydroxide — *Catalyst*

The title catalyst mediates the enantioselective epoxidation of α,β-unsaturated ketones under phase transfer conditions.

B. Lygo, P. G. Wainright *Tetrahedron Lett.* **1998**, *39*, 1599.

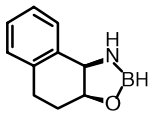


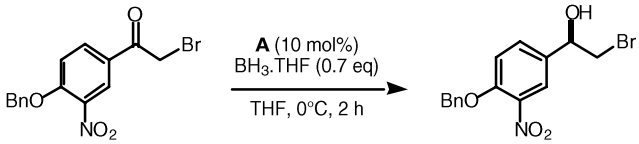
8 examples (yields 42-93%, %ee 69-87%). The *pseudo* enantiomer of **A** gives comparable but opposite enantioselectivity in these epoxidations.

Homochiral Oxazaborolidine — *Catalyst*

The title catalyst mediates the enantioselective reduction of an α-bromo ketone with BH_3.

R. Hett, C. H. Senanayake, S. A. Wald *Tetrahedron Lett.* **1998**, *39*, 1705.





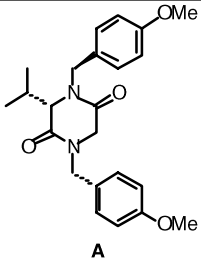
er = 98:2

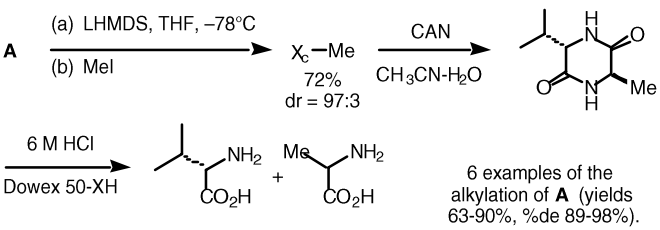
Yield unspecified. 11 other related catalysts were used in the above reduction (%ee 12-96%).

(3*S*)-*N*,*N*′-Bis(*p*-methoxybenzyl)-3-isopropylpiperazine-2,5-dione — *Chiral Auxiliary*

Chiral auxiliary **A** employs a chiral relay network for the synthesis of enantiomerically pure α-amino acids. Non-stereogenic *N*-benzyl protecting groups enhance diastereocontrol during enolate alkylation.

S. D. Bull, S. G. Davies, S. W. Epstein, J. V. A. Ouzman *Chem. Commun.* **1998**, 659.



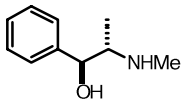


6 examples of the alkylation of **A** (yields 63-90%, %de 89-98%).

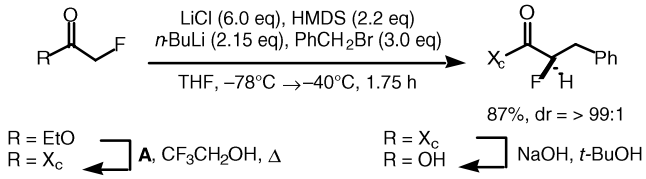
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

Pseudoephedrine — *Chiral Auxilliary*

The title chiral auxilliary mediates the diastereoselective alkylation of its α-fluoroacetamide derivatives.



A

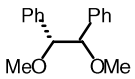


6 examples (yields 29-97%, de 93->99%) are described.

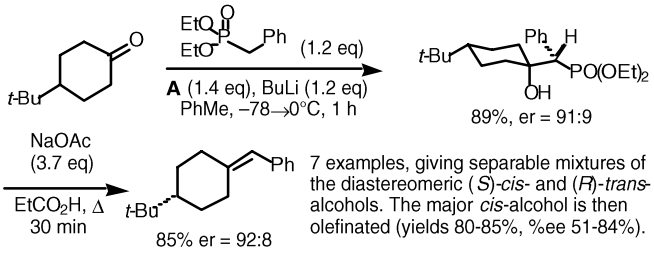
A. G. Myers, L. McKinstry, J. K. Barbay, J. L. Gleason *Tetrahedron Lett.* **1998**, *39*, 1335.

(1*S*,2*S*)-1,2-Dimethoxy-1,2-diphenylethane — *Ligand*

An asymmetric Horner-Wadsworth-Emmons reaction mediated by ligand **A** is described.



A

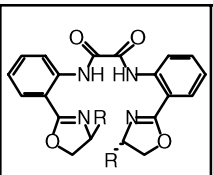


7 examples, giving separable mixtures of the diastereomeric (*S*)-*cis*- and (*R*)-*trans*-alcohols. The major *cis*-alcohol is then olefinated (yields 80-85%, %ee 51-84%).

M. Mizuno, K. Fujii, K. Tomioka *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 515.

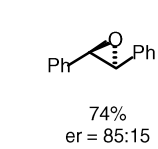
Bis[(*R*)-dihydro-5-isopropyloxazolylphenyl]oxalamide — *Ligand*

Enantioselective epoxidation catalysed by ruthenium complexes with ligand **A** is reported. The catalyst is treated with $NaIO_4$ oxidant prior to addition of the substrate in order to minimise production of benzaldehyde and improve ee.



R = *i*-Pr

A

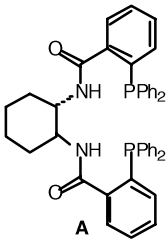


3 examples (yields 50-74%, %ee 25-69%)

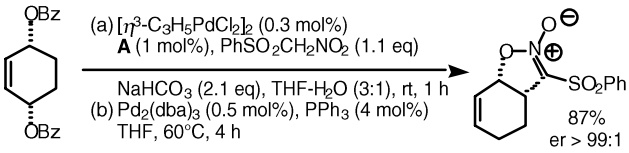
N. End, A. Pfaltz *Chem. Commun.* **1998**, 589.

(–)-(1*S*,2*S*,)-Bis[(diphenylphosphino)benzamido]cyclohexane — *Ligand*

A palladium catalyst derived from the title ligand effected the asymmetric alkylation of a *meso* allylic dibenzoate by (phenylsulfonyl)-nitromethane. The resultant product was utilised in a total synthesis of (+)-valienamine.



A



The achiral palladium catalyst was added after the first alkylation was complete to enhance the rate of the subsequent annulating substitution reaction.

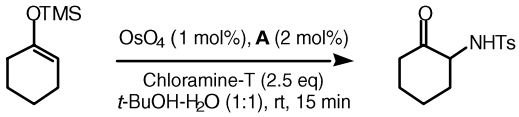
B. M. Trost, L. S. Chupak, T. Lübbers *J. Am. Chem. Soc.* **1998**, *120*, 1732.

Dihydroquinidine- *p*-chlorobenzoate [(DHQD)$_2$-CLB] — *Ligand*

Osmium tetroxide and the title ligand catalyse the asymmetric aminohydroxylation of silyl enol ethers.

(DHQD)$_2$-CLB

A



35%, er = 96:4

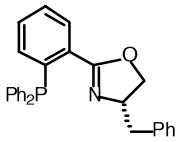
7 examples (yields 28-45%, %ee 70-92%) including two using the alternative ligand dihydroquinidine-pyrimidine.

P. Phukan, A. Sudalai *Tetrahedron: Asymmetry* **1998**, *9*, 1001.

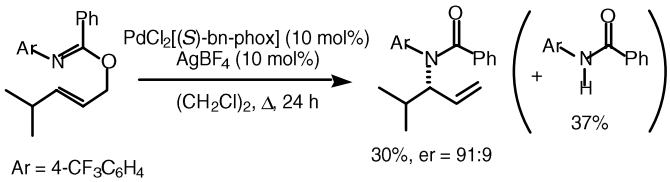
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

(*S*)-(+)-2-[2-(Diphenylphosphino)phenyl]-4-(benzyl)oxazoline [(S)-bn-phox] — *Ligand*

The asymmetric aza-Claisen rearrangement of allyl imidates catalysed by homochiral palladium(II) complexes is reported.



A

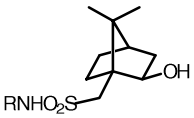


4 examples (yields 30-88%, %ee 28-81%).

Y. Uozumi, K. Kato, T. Hayashi *Tetrahedron: Asymmetry* **1998**, *9*, 1065.

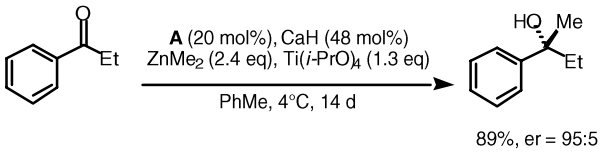
10-*N*-[(Naphthylmethyl)sulfonyl]borneol — *Ligand*

The title compound mediates the enantioselective alkylation of ketones with diethyl- and dimethyl- zinc.



A

R = 1-naphthylmethyl

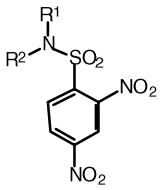


14 examples (yields 3-95%, %ee 0, 34-86%) are described

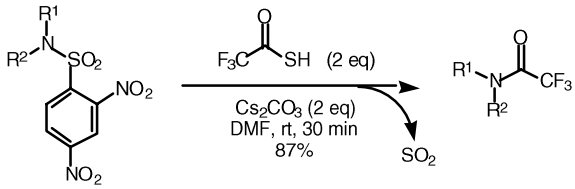
D. J. Ramón, M. Yus *Tetrahedron Lett.* **1998**, *39*, 1239.

2,4-Dinitrobenzenesulfonamide — *Protecting Group*

The 2,4-dinitrobenzenesulfonamide protecting group for amines can be removed with thioacids to give the corresponding amide.



A



R^1 = *p*-methoxybenzyl
R^2 = $CH_2CH{=}CH_2$

8 examples (yields 81-96%) are described.

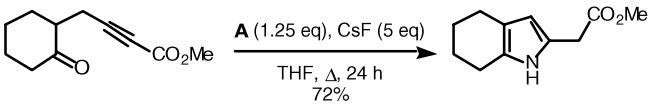
T. Messeri, D. D. Sternbach, N. C. O. Tomkinson *Tetrahedron Lett.* **1998**, *39*, 1669.

Titanium Isopropoxide — *Reagent*

A new titanium reagent **A** prepared from the reaction of titanium isopropoxide with lithium in the presence of TMSCl, is utilised in the synthesis of heterocycles with dry air or pure nitrogen as the nitrogen source.

Ti(O*i*Pr)$_4$-Li-TMSCl

A



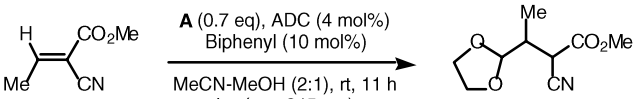
5 examples (yields 37-72% in dry air, 51-90% in pure nitrogen). The methodology is applied to a formal total synthesis of (±)-lycopodine. Preparation of **A** is described.

M. Mori, K. Hori, M. Akashi, M. Hori, Y. Sato, M. Nishida *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 636.

2-Trimethylsilyl-1,3-dioxolane — *Reagent*

A new method is described for the generation of hydroxymethyl anion equivalents by photo-induced electron transfer catalysis (PET catalysis) starting from α-silyl ethers.

A



10 examples of photoinduced radical additions of α-silyl ethers to electron poor alkenes (yields 15-64%, %de 28-72%).

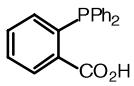
ADC = 9,10-Anthracenedicarbonitrile

G. Gutenberger, E. Steckhan, S. Blechert *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 660.

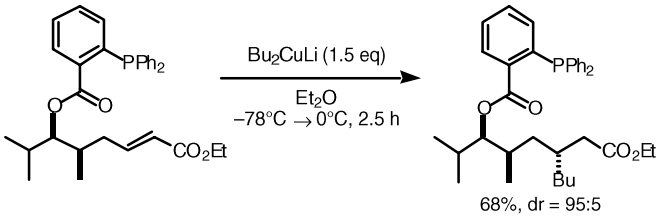
This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

o-Diphenylphosphanylbenzoic Acid — *Reagent*

ortho-Diphenylphosphanylbenzoyl esters direct diastereoselective addition of Gilman cuprates to α,β-unsaturated enoates.



A



7 examples (yields 60-93%, %de 60-90%).

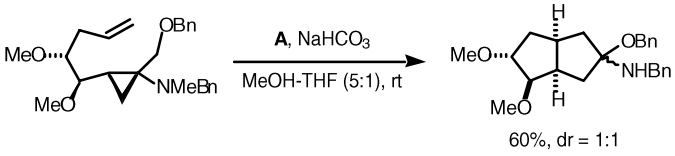
B. Breit *Angew. Chem. Int. Ed. Engl.* **1998**, *37*, 525.

Cerium(IV) Ammonium Nitrate — *Reagent*

A novel tandem [3 + 2]-type cycloaddition using a CAN-mediated ring-opening reaction of cyclopropylamines is reported. The previously unreported accelerative effect of the *N*-benzyl group for oxidative ring opening is also described.

$Ce(NH_4)_2(NO_3)_6$

A



6 examples (yields 42-77%).

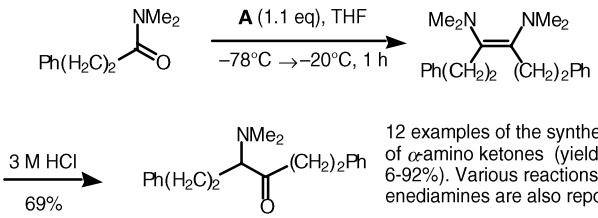
Y. Takemoto, S. Yamagata, S. Furuse, H. Hayase, T. Echigo, C. Iwata *Chem. Commun.* **1998**, 651.

Dimethylphenylsilyllithium — *Reagent*

A reacts with tertiary amides to give enediamines, which can be isolated in good yield when the α-carbon is branched. The enediamines can be hydrolysed to α-amino ketones.

$PhMe_2SiLi$

A

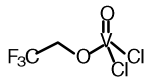


12 examples of the synthesis of α-amino ketones (yields 6-92%). Various reactions of enediamines are also reported.

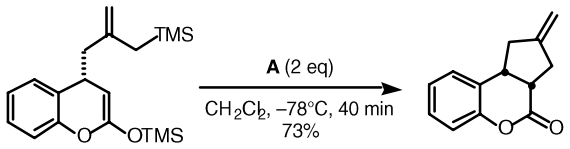
I. Fleming, U. Ghosh, S. R. Mack, B. P. Clark *Chem. Commun.* **1998**, 711.

Dichloro(2,2,2-trifluoroethoxy)oxovanadium(V) — *Reagent*

The title reagent promotes the one-electron oxidative cyclisation of silyl enol ethers onto allyl silanes. The unsymmetrical coupling of silyl enol ethers can also be achieved employing the title reagent.



A

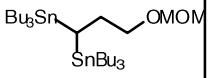


5 examples of oxidative cyclisation (yields 71-83%).

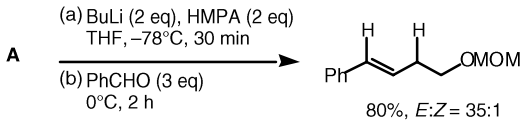
K. Ryter, T. Livinghouse *J. Am. Chem. Soc.* **1998**, *120*, 2658.

1,1-Bis(tributylstannyl)-3-[(methoxymethyl)oxy]propane — *Reagent*

A novel method of three-carbon elongation using the title reagent is reported.



A



13 examples of the reaction of **A** with aldehyde, ketone, ester or alkyl halide electrophiles (yields 48-85%).

N. Isono, M. Mori *J. Org. Chem.* **1998**, *63*, 1773

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.

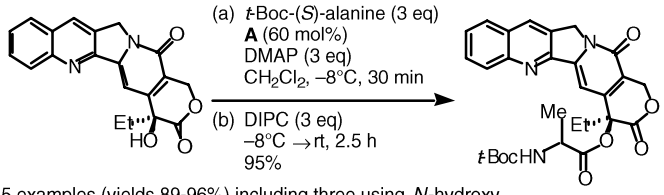
Scandium Triflate — *Reagent*

Esterification of the hindered tertiary alcohol 20-(*S*)-camptothecin is performed using the title reagent in combination with DMAP.

R. B. Greenwald, A. Pendri, H. Zhao *Tetrahedron: Asymmetry* **1998**, *9*, 915.

$Sc(OTf)_3$

A



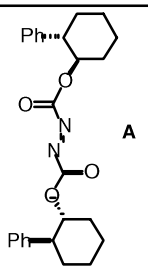
5 examples (yields 89-96%) including three using *N*-hydroxy succinimide esters without DIPC. Epimerisation was minimal (<2%) in all cases.

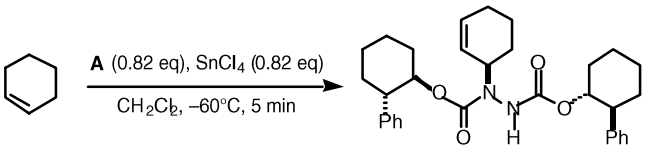
94%, er = 99:1

Di-(-)-(1 *R*,2*S*)-2-phenyl-1-cyclohexyl Diazenedicarboxylate — *Reagent*

Asymmetric azo-ene reactions using the title reagent are described.

M. A. Brimble, C. K. Y. Lee *Tetrahedron: Asymmetry* **1998**, *9*, 873.





80%, dr = 97:3

5 examples (yields 57-92%, %de 72-94%)

Diphenyl Cyanomethylenephosphonate — *Reagent*

The title reagent effects the synthesis of *cis*-1-alkenenitriles from aldehydes.

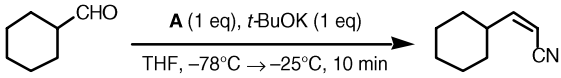
T. Y. Zhang, J. C. O'Toole, J. M. Dunigan *Tetrahedron Lett.* **1998**, *39*, 1461.

CH_3CN

(a) LDA
(b) $(PhO)_2P(O)Cl$
(c) HCl

$(PhO)_2P(O)CH_2CN$

A



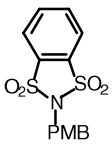
93%, *Z*:*E* = 64:36

7 examples (yields 68-100%, *Z*:*E* 64:6-100:0) are described.

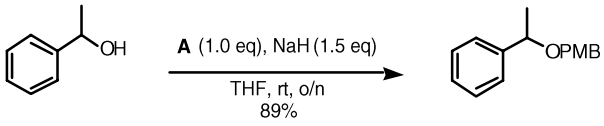
N-(4-Methoxybenzyl)- *o*-benzenedisulfonimide — *Reagent*

The title reagent mediates the conversion of alcohols and phenols to the corresponding 4-methoxybenzyl (PMB) ethers.

P. H. J. Carlsen *Tetrahedron Lett.* **1998**, *39*, 1799.



A



3 examples (yields 57-78%) are described. Treatment of **A** with aqueous KOH in DMF yields 4-methoxy benzyl alcohol thus constituting a mild procedure for deaminating amines.

Samarium Diiodide / Iodoform — *Reagent*

The title reagent pair mediates the diiodomethylation of aldehydes and ketones.

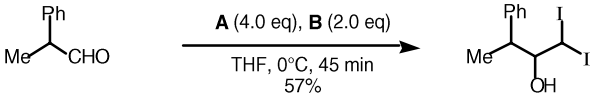
J. M. Concellón, P. L. Bernad, J. A. Pérez-Andrés *Tetrahedron Lett.* **1998**, *39*, 1409.

SmI_2

A

CHI_3

B



erythro:*threo* > 99:1

15 examples (yields 0, 23-61%) are described. Transformation of the α-diiodoalcohols to the corresponding α-hydroxy acids and α-iodoaldehydes is also reported.

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.