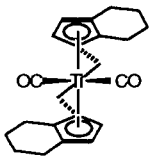
SYNTHESIS ALERTS

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.

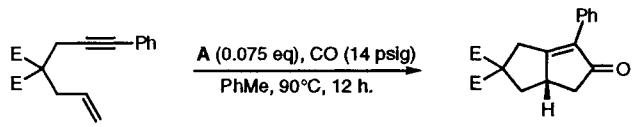
Synthesis Alerts is a personal selection by Paul Blakemore, Brian Dymock, Philip Hall, Philip Kocienski, J.-Y. Le Brazidec and Alessandro Pontiroli of the University of Glasgow. The journals regularly covered by the abstractors are: Angewandte Chemie International Edition, Bulletin de la Societe Chimie 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.

(*S,S*)-Ethanobis(tetrahydroindene)dicarbonyl Titanium(II) — ***Catalyst***

First catalytic asymmetric Pauson-Khand type cyclization.



A

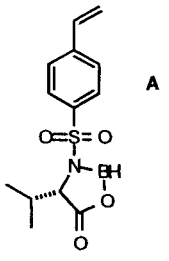


E = CO_2Bu^t — 8 examples using 5-20% catalyst. — 92% (er = 97/3)

F. A. Hicks, S. L. Buchwald *J. Am. Chem. Soc.*, **1996**, *118*, 11688.

Polymeric Oxazoborolidinone Catalyst — ***Catalyst***

Crosslinked polymers prepared from the monomer **A** catalyse the asymmetric Diels-Alder reaction between methacrolein and cyclopentadiene.



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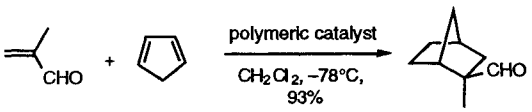


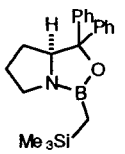
exo:endo = 99:1
er = 96:4

The nature of the other monomers that make up the cross-linked polymer have a significant effect on the outcome of the reaction. Five catalyst systems examined.

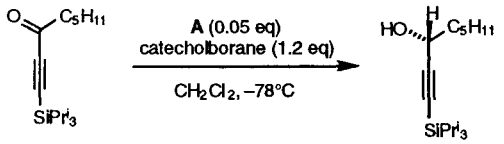
K. Kamahori, S. Itsuno *J. Org. Chem.*, **1996**, *61*, 8321.

(*S*)-3,3-Diphenyl-1-[(trimethylsilyl)methyl]tetrahydro-1*H*,3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborole — ***Catalyst***

The title compound catalyses the enantioselective reduction of α,β-ynones using catecholborane as the stoichiometric reductant. Enantioselectivity is dependent on the size of the boron substituent.



A



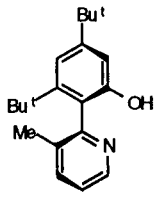
12 examples; yields ≥ 90%; er = 4:1 to 66:1 — 98% (er = 66:1)

C. J. Helal, P. A. Magriotis, E. J. Corey *J. Am. Chem. Soc.*, **1996**, *118*, 10938.

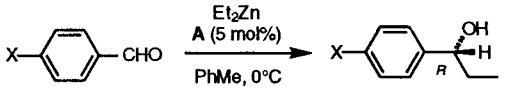
(*R*)-(+)-3,5-Di-*tert*-butyl-2-(3-methyl-2-pyridyl)phenol — *Catalyst*

The title compound catalyses the asymmetric addition of diethylzinc to *p*-substituted aromatic aldehydes. The er increases as X becomes more electron demanding.

H. Zhang, F. Xue, T. C. W. Mak, K. S. Chan *J. Org. Chem.*, **1996**, *61*, 8002.



A



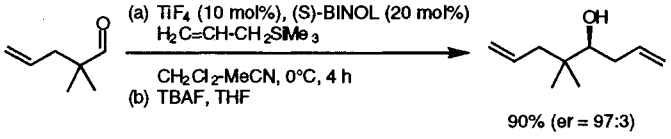
X = Me_2N, MeO, H, Cl, CN (yields 88-97%; er = 7:3 to 95:5)

Titanium Tetrafluoride — *Catalyst*

The complexes derived from TiF_4 and (*R*)- or (*S*)-1,1′-bi-2-naphthol catalyse the enantioselective addition of allyltrimethylsilane to aldehydes.

D. R. Gauthier, E. M. Carreira *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 2363.

TiF_4



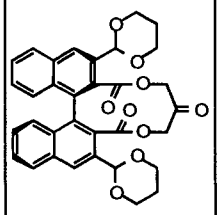
90% (er = 97:3)

8 examples: 69-93% yield; er = 80:20 to 97:3

(*R*)-2,3:4,5-Bis[3-(1,3-dioxan-2-yl)-[2,1-*a*]-naphtho]-7,11-dioxa-1,6,9-trioxoundecane — *Catalyst*

A dioxirane generated *in situ* from the title C_2-symmetric binaphthalene derivative epoxidises stilbene enantioselectively.

D. Yang, X.-C. Wang, M.-K. Wong, Y.-C. Yip, M.-W. Tang *J. Am. Chem. Soc.*, **1996**, *118*, 11309.



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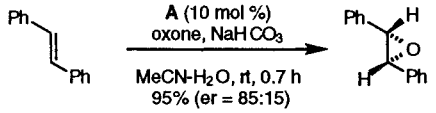


Eight catalysts with varying substitution at C-3 of the naphthalene ring were examined. Stilbene was the only substrate. Catalyst **A** was the most reactive.

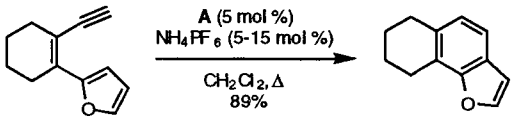
(*p*-Cymene)(triphenylphosphine)ruthenium Dichloride — *Catalyst*

The title compound, together with ammonium hexafluorophosphate, catalyses the 6π-electrocyclisation of dienylalkynes to aromatic rings via vinylidene intermediates.

C. A. Merlic, M. A. Pauly *J. Am. Chem. Soc.*, **1996**, *118*, 11319.

$RuCl_2$(*p*-cymene)(PPh_3)

A

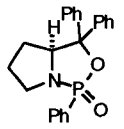


8 examples; yields 0-89%. The reaction works best when the terminal alkene is incorporated in a heterocyclic ring (furan, thiophene, benzofuran) though N-methylindole gave a poor yield (18%). The alkyne must be terminal.

(5*S*)-2-Oxo-3-oxa-1-aza-2-phospha-2,4,4-triphenylbicyclo[3.3.0]octane — *Catalyst*

Easily prepared stable catalyst for the asymmetric reduction of ketones with borane.

V. Peper, J. Martens *Tetrahedron Lett.*, **1996**, *37*, 8351.



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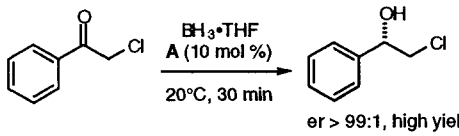
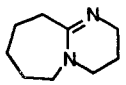


er > 99:1, high yield

Acetophenone was the only other ketone examined but a range of oxazaphospholidine catalysts were tested under various conditions. For the illustrated reaction 0.5 mol % of **A** still gives high asymmetric induction (er = 94:6)

1,8-Diazabicyclo[5.4.0]undec-7-ene / Copper (II) Triflate — *Catalyst*

A complex derived from $Cu(OTf)_2$ and DBU (or DBN) catalyses the allylic oxidation of alkenes by *tert*-butyl perbenzoate.



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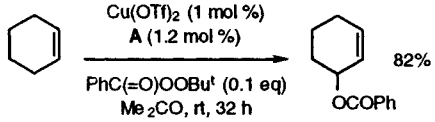
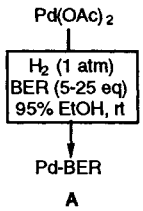


18 examples of the oxidation of a variety of simple alkenic hydrocarbons (yields 26-80%). In the absence of DBU or DBN very little if any reaction occurs.

G. Sekar, A. DattaGupta, V. K. Singh *Tetrahedron Lett.*, **1996**, *37*, 8435.

Palladium on Borohydride Exchange Resin (BER) — *Catalyst*

Pd-BER (**A**) in the presence of CsI acts as a semihydrogenation catalyst for acetylenes.



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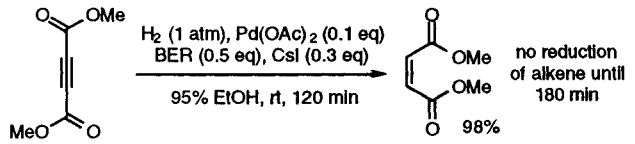


9 well chosen varied examples (yields 97-100%). Terminal acetylenes can be semihydrogenated with only 1 mol % $Pd(OAc)_2$ / 0.25 eq BER. In each case any reduction of the product alkene commences well after the completion of acetylene semihydrogenation.

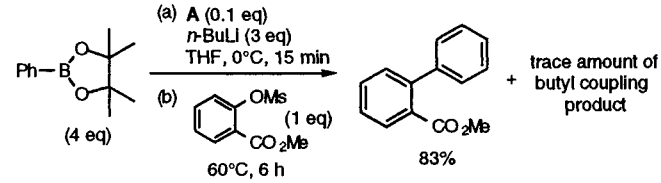
N. M. Yoon, K. B. Park, H. J. Lee, J. Choi *Tetrahedron Lett.*, **1996**, *37*, 8527.

Bis(triphenylphosphine)nickel(II) Chloride — *Catalyst*

The title compound catalyses coupling of aryl mesylates with lithium aryborates.

$NiCl_2(PPh_3)_2$

A



8 examples (yields 80-95%). In each case the aryl mesylate has an electron withdrawing substituent.

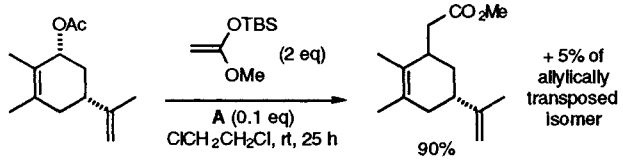
Y. Kobayashi, R. Mizojiri *Tetrahedron Lett.*, **1996**, *37*, 8531.

Lithium Cobalt-Bisdicarbollide — *Catalyst*

Superior catalyst for the nucleophilic substitution of allylic acetates.

$LiCo(B_9C_2H_{11})_2$

A

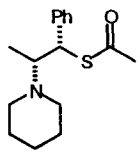


12 examples (yields 71-99%).

P. A. Grieco, W. J. DuBay, L. J. Todd *Tetrahedron Lett.*, **1996**, *37*, 8707.

(1*S*,2*R*)-2-(*N*-Piperidinyl)-1-phenylpropane-1-thiol Acetate — *Catalyst*

The title cmpound [prepared from (+)-norephedrine] catalyses the asymmetric addition of diethylzinc to aldehydes.



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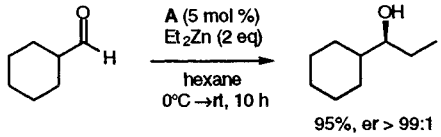
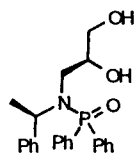


5 examples (yields 95-100%, er > 99:1).

M.-J. Jin, S.-J. Ahn, K.-S. Lee *Tetrahedron Lett.*, **1996**, *37*, 8767.

(2S)-1-Amino-N-[(R)-methylbenzyl)]-N-(diphenylphosphoryl)propane-2,3-diol — Ligand

A borane reagent prepared from the title compound catalyses the asymmetric reduction of ketones.



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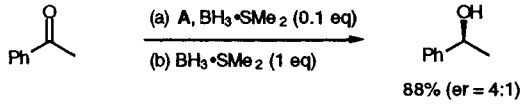
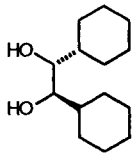


M. P. Gamble, J. R. Studley, M. Wills *Tetrahedron: Asymmetry*, **1996**, *7*, 3071.

(R,R)-1,2-Dicyclohexylethane-1,2-diol — Ligand

A reliable and efficient moderate scale synthesis of the title compound from homochiral 1,2-diphenylethane-1,2-diol is reported. **A** is a chiral director for the insertion of a chloromethyl group into boronic esters. Both enantiomers of **A** are readily available.



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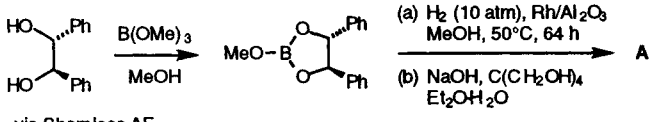
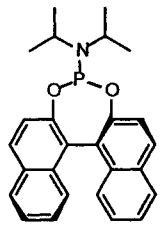


W. C. Hiscox, D. S. Matteson *J. Org. Chem.*, **1996**, *61*, 8315.

Chiral Phosphoramidites — Ligand

Complexes derived from homochiral phosphoramidite **A** and $Cu(OTf)_2$ catalyse asymmetric conjugate addition of dialkylzincs to enones. The catalyst is probably a Cu(I) species generated *in situ*.



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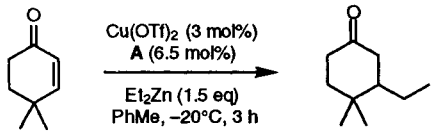
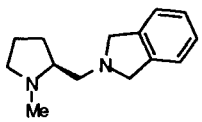


7 examples: 68-88% yield; er = 85:15 to 95:5.

A. H. M. de Vries, A. Meetsma, B. L. Feringa *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 2374.

N-{[(S)-N-Methyl-2-pyrrolidinyl]methyl}isoindoline — Ligand

A complex derived from homochiral diamine **A** and $SnBr_2$ catalyses the enantioselective acylation of racemic 2° alcohols with benzoyl bromide.



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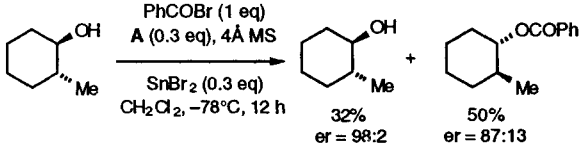


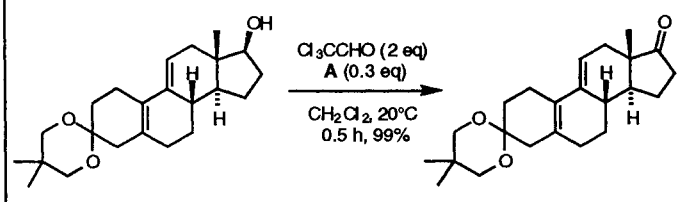
8 examples (alcohol yields 40-49%, %ee 51-96%; ester yields 34-50%, %ee 55-97%). The kinetic resolution procedure described works best for cyclic alcohols.

T. Oriyama, Y. Hori, K. Imai, R. Sasaki *Tetrahedron Lett.*, **1996**, *37*, 8543.

Zirconium(IV) tert-Butoxide / Chloral — Reagent

A new variety of the Oppenhauer oxidation with chloral as the hydride acceptor gives ketones from alcohols in high yields under mild conditions.

$Zr(OBu^t)_4$
Cl_3CCHO
A



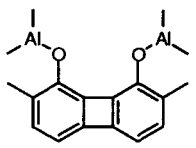
Oxidation with chloral and the heterogeneous catalyst $SiO_2/Zr(OPr^n)_x$ is also reported (yields = 42-96%).

K. Krohn, B. Knauer, J. Küpke, D. Seebach, A. K. Beck, M. Hayakawa *Synthesis* **1996**, 1341.

(2,7-Dimethyl-1,8-biphenylenedioxy)bis(dimethylaluminum) — *Reagent*

Directed aldol reactions of enol silanes, conjugate addition reactions of silyl ketene acetals, reduction reactions using Bu_3SnH, and Claisen rearrangements of allyl vinyl ethers are induced using the title bidentate Lewis acid.

T. Ooi, M. Takahashi, K. Maruoka *J. Am. Chem. Soc.*, **1996**, *118*, 11307.



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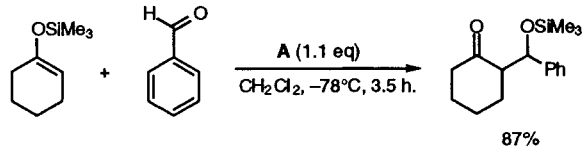


87%

[(Trimethylsilyl)methyl]copper(I) — *Reagent*

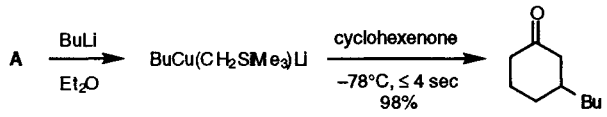
Reaction of organolithium reagents with the title compound gives mixed organocuprates which are highly reactive, thermally stable, and efficient in the transfer of the alkyl group. The byproduct on workup is tetramethylsilane.

Preparation: J. A. J. Jarvis, R. Pearce, M. F. Lappert *J. Chem. Soc., Dalton Trans.*, **1977**, 999.

S. H. Bertz, M. Ericksson, G. Miao, J. P. Snyder *J. Am. Chem. Soc.*, **1996**, *118*, 10906.

Me_3SiCH_2Cu

A

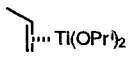


Good rate and stability also observed for the β-silyl organocuprates of the type $RCu[N(SiMe_3)_2]Li$ and $RCu(SSiMe_3)Li$.

Diisopropoxy(η^2-propene)titanium — *Reagent*

The title compound, prepared by reaction of $Ti(OPr^i)_4$ with 2 Pr^iMgCl, reacts with alka-3,4-dienyl carbonates via an intramolecular nucleophilic acyl substitution reaction to afford alkenyltitanium compounds.

Y. Yoshida, S. Okamoto, F. Sato *J. Org. Chem.*, **1996**, *61*, 7826.



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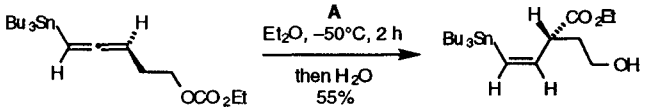
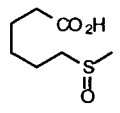


9 examples; yields 49-88%. 3 examples failed.

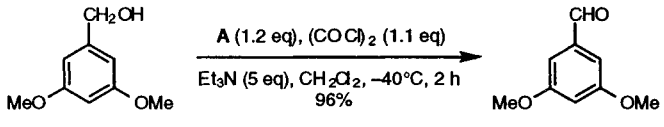
6-(Methylsulfinyl)hexanoic Acid — *Reagent*

The title compound serves as a substitute for DMSO in Swern oxidations. The resultant thioether is odourless and can be recovered. The carboxyl group can be used to tether the reagent to a solid support.

Y. Liu, J. C. Vederas *J. Org. Chem.*, **1996**, *61*, 7856.



A

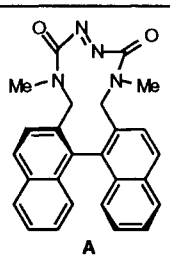


6 examples; yields 31-94%.

(*R*)-4,9-Dimethyl-4,5,9,10-tetrahydro-3*H*,8*H*-naphtho[2.1-f:1′2′-h]-1,2,4,11-tetraazacyclododecine-5,8-dione — *Reagent*

The homochiral azodicarboxamide **A** reacts with achiral oxazolidinone enolates to give α-hydrazino acid derivatives with high stereoselectivity.

J. M. Harris, R. McDonald, J. C. Vederas *J. Chem. Soc., Perkin Trans.1*, **1996**, 2669.



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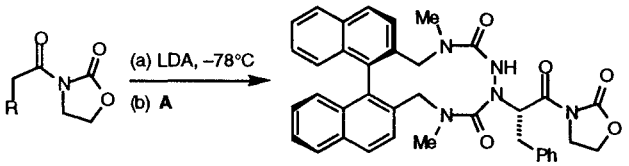


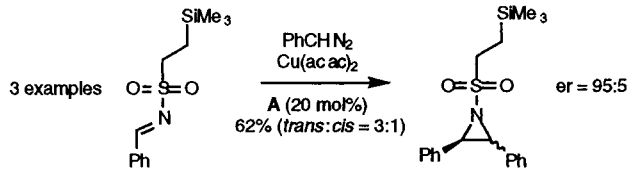
Two examples

R = Me (85%; dr>95:5)
R = CH_2Ph (92%; dr>95:5))

4,11,11-Trimethyl-5-oxa-3-thiatricyclo[6.2.1.0^{1,6}]undecane — *Reagent*

The sulfur ylide generated from the title compound, together with $Cu(acac)_2$ and phenyldiazomethane, accomplishes an asymmetric aziridination of N-SES aldimines. The source and purity of the $Cu(acac)_2$ is important.

A

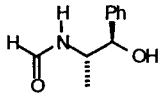


For a related asymmetric epoxidation of aldehydes see: V. K. Aggarwal, J. G. Ford, A. Thompson, R. V. H. Jones, M. C. H. Syanden *J. Am. Chem. Soc.*, **1996**, *118*, 7004.

V. K. Aggarwal, A. Thompson, R. V. H. Jones, M. C. H. Standen *J. Org. Chem.*, **1996**, *61*, 8368.

(–)-(1*R*,2*S*)-*N*-Formylnorephedrine — *Reagent*

The title compound undergoes enantioselective addition to nitroalkenes. The adducts can be converted to vicinal amino alcohols.



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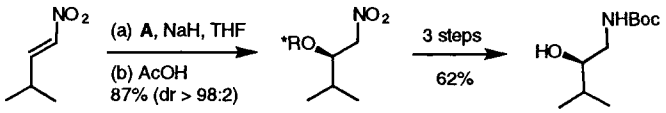
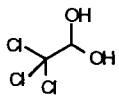


5 examples: 34-53% yield overall (4 steps)

D. Enders, A. Hartwig, G. Raaba, and J. Runsink *Angew. Chem. Int. Ed. Engl.*, **1996**, *35*, 2388.

Chloral Hydrate / Hydrogen Peroxide — *Reagent*

The combination of the two title reagents effects a highly regio- and stereoselective epoxidation of alkenes.



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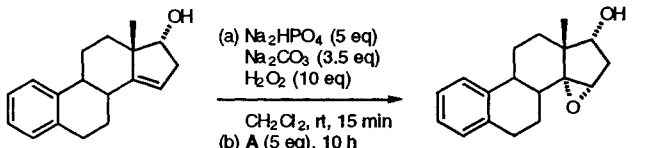


95% (no β-epoxide isolated)

3 other steroidal substrates were epoxidised in near quantitative yield. The presence of a proximate free hydroxyl is essential for good facial control (*e.g.*, the α-acetate gives 1:1 α:β epoxides).

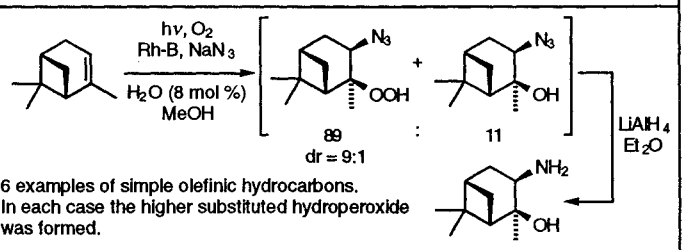
H. Kasch *Tetrahedron Lett.*, **1996**, *37*, 8349.

Sodium Azide — *Reagent*

1,2-Azidohydroperoxides are accessible from alkenes when irradiated in the presence of **A**, oxygen and an appropriate sensitiser.

NaN_3

A



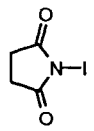
6 examples of simple olefinic hydrocarbons. In each case the higher substituted hydroperoxide was formed.

Rh-B = Rhodamine B

A. G. Griesbeck, T. Hundertmark, J. Steinwascher *Tetrahedron Lett.*, **1996**, *37*, 8367.

N-Iodosuccinimide — *Reagent*

Iodoalkenes can be procured under mild conditions from alkenylsilanes by the action of **A** in CH_3CN / $ClCH_2CN$.



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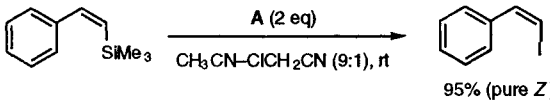

95% (pure *Z*)

22 well chosen varied examples (yields typically 60-95%). Retention of olefin geometry is diminished for substrates with less bulky allylic substituents. The presence of allylic oxygen functionality favours the *E*-olefin regardless of the alkenylsilane geometry.

D. P. Stamos, A. G. Taylor, Y. Kishi *Tetrahedron Lett.*, **1996**, *37*, 8647.