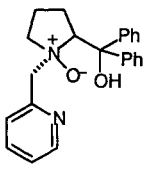
SYNTHESIS ALERTS

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.

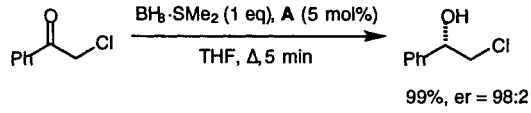
Synthesis Alerts is a personal selection by Paul Blakemore, John Christopher, Louise Lea, Philip Kocienski, J.-Y. Le Brazidec, Robert Narquizian and Christopher Smith of the University of Glasgow. The journals regularly covered by the abstractors are: Angewandte Chemie International Edition, Bulletin 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.

(*S*)-*N*-(2-Pyridylmethyl)-2-(diphenylhydroxymethyl)pyrrolidine ***N*-Oxide** ***Catalyst***

The homochiral *N*-oxide **A** catalyses the enantioselective borane reduction of simple phenyl ketones.



A

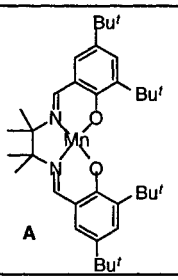


The reduction of ethyl phenyl ketone and α-methoxyacetophenone is also examined (yields 99%, %ee 68% (*R*) and 48%(*R*) respectively).

I. A. O'Neil, C. D. Turner, S. B. Kalindjiam *Synlett* **1997**, 777.

Achiral Manganese Salen Complex ***Catalyst***

Asymmetric epoxidation has been achieved using the achiral Mn-salen complex **A** with homochiral (–)-sparteine ligand.



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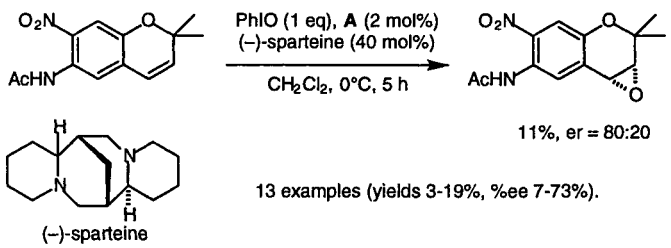
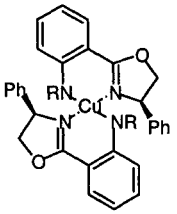


13 examples (yields 3-19%, %ee 7-73%).

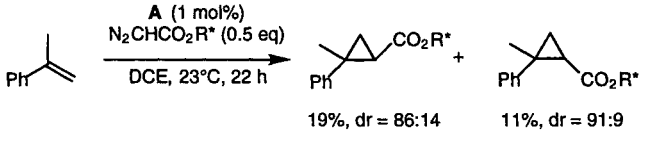
T. Hashikayata, Y. Ito, T. Katsuki *Tetrahedron*, **1997**, 9541.

Bis[(4*R*)-2-(2-toluenesulfonylamino)phenyl-4-phenyl-1,3-oxazolinate]copper(II) ***Catalyst***

The title reagent **A** was found to be an effective catalyst for the enantioselective cyclopropanation of olefins.



A, R = SO_2Tol



4 examples (yields 27-51%, *trans:cis* > 63:37, %ee 52-82%).

R* = *d*-menthyl, DCE = 1,2-dichloroethane

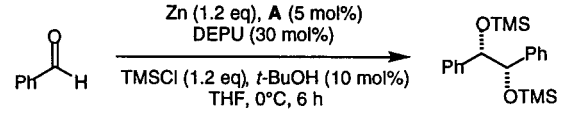
T. Ichiyanagi, M. Shimizu, T. Fujisawa *Tetrahedron*, **1997**, 9599.

Trichlorotris(tetrahydrofuran)titanium(III) — *Catalyst*

Good diastereoselectivity in the reductive coupling of aldehydes and ketones is achieved in a catalytic system derived from the title reagent.

$TiCl_3(THF)_3$

A



89%, dr = 88:12

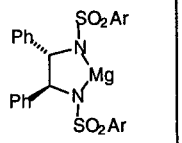
5 examples of aromatic aldehydes (yields 83-94%, %de 66-82%). Similar yields but lower selectivities (%de 10-66%) are observed for 7 aldehyde and ketone examples in the absence of DEPU.

DEPU = 1,3-diethyl-1,3-diphenylurea

T. A. Lipski, M. A. Hilfiker, S. G. Nelson *J. Org. Chem.* **1997**, *62*, 4566.

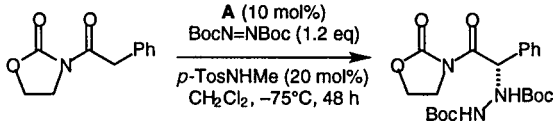
(4*S*,5*S*)-1,3-Bis(2,4-dimethylphenylsulfonyl)-2-magnesio-4,5-diphenylimidazoline — *Catalyst*

Chiral magnesium bis(sulfonamide) complexes as catalysts for the merged enolization and enantioselective amination of *N*-acyloxazolidinones.



Ar = 2,4-dimethylphenyl

A



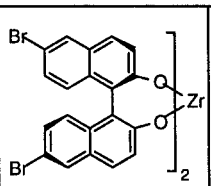
92%, er = 93:7

6 examples (yields 84-97%, %ee 80-90%).

D. A. Evans, S. G. Nelson *J. Am. Chem. Soc.* **1997**, *119*, 6452.

Bis[(*S*)-6,6′-dibromo-1,1′-bi-2-naphthoxy]zirconium(IV) — *Catalyst*

Catalytic enantioselective Mannich-type reactions using a novel chiral zirconium catalyst.



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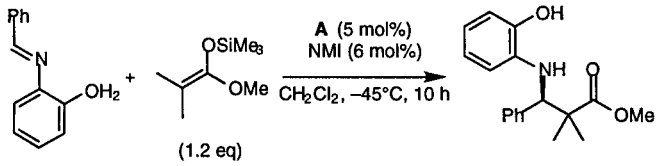


(1.2 eq)

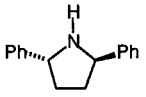
70%, er = 94:6

8 examples (yields 56-100%, %ee 80-98%).

H. Ishitani, M. Ueno, S. Kobayashi *J. Am. Chem. Soc.* **1997**, *119*, 7153.

(*R*,*R*)-*trans*-2,5-Diphenylpyrrolidine — *Chiral Auxiliary*

Asymmetric Diels-Alder reactions of chiral 1-amino-3-siloxybuta-1,3-diene: application to the enantioselective synthesis of (–)-α-elemene.



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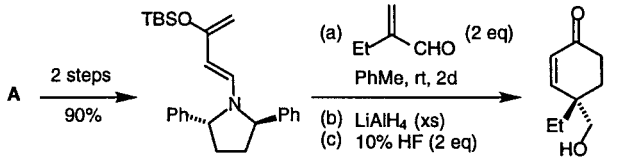


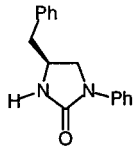
75%, er = 93:7

6 examples (yields 64-82%, %ee 86-93%).

S. A. Kozmin, V. H. Rawal *J. Am. Chem. Soc.* **1997**, *119*, 7165.

(*S*)-4-Benzyl-1-phenylimidazolidin-2-one — *Chiral Auxiliary*

N-Acylimidazolidin-2-ones: new chiral auxiliaries for carboxylic acid alkylation.



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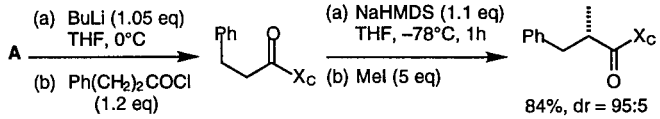


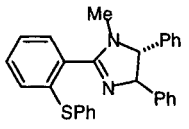
84%, dr = 95:5

6 examples (yields 54-92%, %de 72-98%).

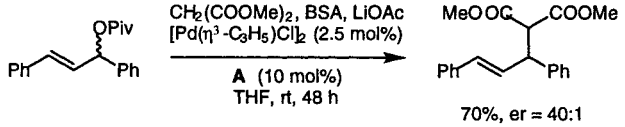
K. Königsberger, K. Prasad, O. Repic, T. J. Blacklock *Tetrahedron: Asymmetry* **1997**, *8*, 2347.

(4*S*,5*S*)-1-Methyl-2-(2-phenylthiophenyl)- *trans*-4,5-diphenyl-4,5-dihydroimidazole — *Ligand*

The palladium complex of the title compound has been used for the asymmetric allylic substitution of 1,3-diphenylprop-2-enyl pivalate.



A



70%, er = 40:1

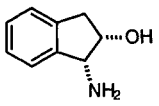
7 examples (yields 19-91%, %ee 48-96%).

BSA = *N*,*O*-bis(trimethylsilyl)acetimide.

T. Morimoto, K. Tachibana, K. Achiwa *Synlett* **1997**, 783.

(1*R*,2*S*)-(+)-*cis*-1-Aminoindan-2-ol — *Ligand*

Stereochemically rigid amino alcohol **A** is an effective ligand for the control of asymmetric ruthenium-catalyzed transfer hydrogenation of ketones.



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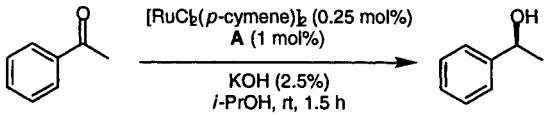


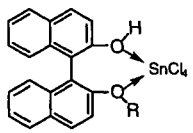
70%, er = 96 : 4

9 examples (yields 40-94%, %ee 7-98%). The requirement of an aromatic system in the substrate is demonstrated by the low enantioselectiviy for the reduction of a nonaromatic ketone example.

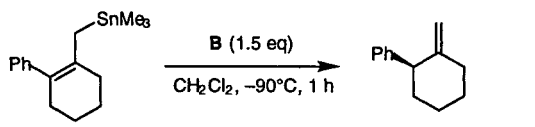
M. Palmer, T. Walsgrove, M. Wills *J. Org. Chem.* **1997**, *62*, 5226.

Homochiral Bronsted Acid — *Reagent*

The title reagent **B** effects the enantioselective protonation of prochiral allyltrimethyltins.



A R = H
B R = Me



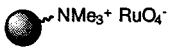
> 95%, er = 84:16

Experimental conditions optimised on a simple system utilising **A**. 4 useful examples employing **B** (yields >95%, %ee 31-89%). Use of safer tributyl- and triphenyltin derivatives results in reduced enantioselectivity.

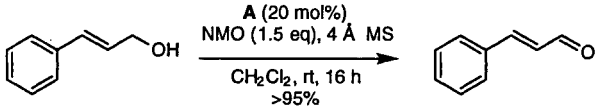
K. Ishihara, Y. Ishida, S. Nakamura, H. Yamamoto *Synlett* **1997**, 758.

Polymer-Supported Perruthenate — *Reagent*

A polymer supported perruthenate reagent has been developed for the oxidation of primary and secondary alcohols, affording pure products without the need for a conventional workup procedure.



A

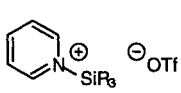


10 examples (yields 54-95%). Reagent **A** has been effectively used stoichiometrically as well as catalytically by the addition of co-oxidants, trimethylamine *N*-oxide (TMAO) or *N*-methylmorpholine *N*-oxide (NMO).

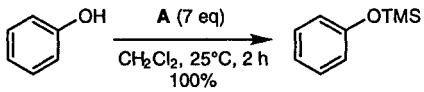
B. Hinzen, S. V. Ley *J. Chem. Soc., Perkin Trans. 1* **1997**, *13*, 1909.

N-Trimethylsilylpyridinium Triflate — *Reagent*

Effects the trimethylsilylation of alcohols in high yield without the need for an aqueous workup.



A R = Me
B R = Pr^i
C R = Ph



5 examples (yields 80-93%). Reaction of **B** and **C** with 1-octanol is also reported (yields 78% and 84% respectively).

G. A. Olah, D. A. Klumpp *Synthesis* **1997**, 774.

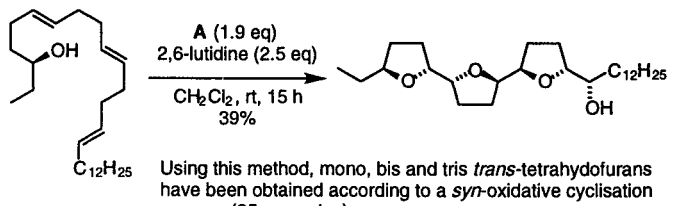
Trifluoroacetylperrhenate — *Reagent*

syn-Oxidative polycyclisations of hydoxy-polyenes: stereoselective and potentially biomimetic syntheses of all *trans*-polytetra-hydrofurans.

T. B. Towne, F. E. McDonald *J. Am. Chem. Soc.* **1997**, *119*, 6022.

$(CF_3CO_2)ReO_3$

A

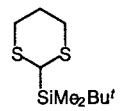


Using this method, mono, bis and tris *trans*-tetrahydofurans have been obtained according to a *syn*-oxidative cyclisation process (25 examples).

2-*tert*-Butyldimethylsilyl-1,3-dithiane — *Reagent*

Multicomponent linchpin couplings of silyl dithianes via solvent-controlled Brook rearrangement.

A. B. Smith III, A. M. Boldi *J. Am. Chem. Soc.* **1997**, *119*, 6925.



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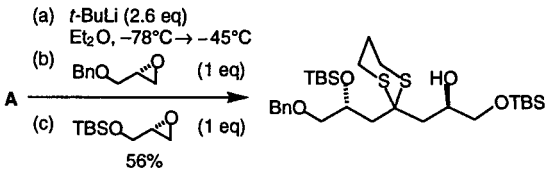
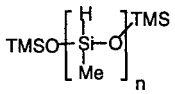


6 examples (yields 56-74%). The methodology has been extended to the synthesis of C23-C31 fragment of roflamicoin.

Polymethylhydrosiloxane — *Reagent*

The title reagent is a stoichiometric reductant for the Barton-McCombie deoxygenation of alcohols. Using this methodology tributyltin hydride needs only be present in a catalytic quantity (generated *in situ* from $(Bu_3Sn)_2O$).

R. M. Lopez, D. S. Hays, G. C. Fu *J. Am. Chem. Soc.* **1997**, *119*, 6949.



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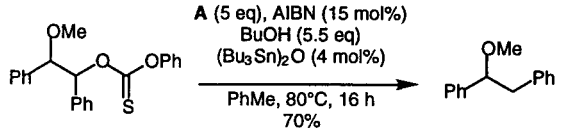


6 multifunctional examples (yields 66-75%). In each case the yield is comparable with the analogous reaction carried out using a stoichiometric quantity of Bu_3SnH.

Gallium(III) Chloride / Trimethylsilylacetylene — *Reagent*

Gallium(III) chloride promotes the C_2-olefination of aromatic hydrocarbons with silylacetylene *via* novel organogallium intermediates.

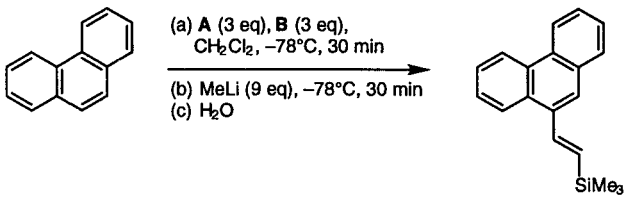
M. Yamaguchi, Y. Kido, A. Hayashi, M. Hirama *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1313.

$GaCl_3$

A

$HC{\equiv}CSiMe_3$

B

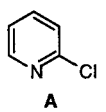


12 examples of Friedel-Crafts type (*E*)-β-silylvinylation (yields 41-76%).

2-Chloropyridine — *Reagent*

2-Chloropyridine is a highly economical alternative to 2,6-di-*tert*-butylpyridine in the triflation of the quinolone shown. The authors speculate that it will find application in other transformations as well. 2-Chloropyridine is 1/100th the cost of 2,6-di-*tert*-butylpyridine.

A. G. Myers, N. J. Thom, M. E. Fraley, S. B. Cohen, D. J. Madar *J. Am. Chem. Soc.*, **1997**, *119*, 6072.



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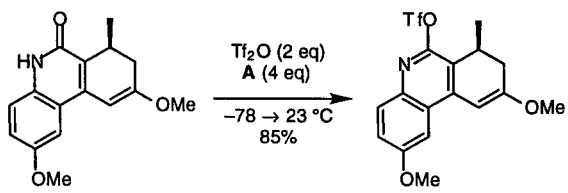
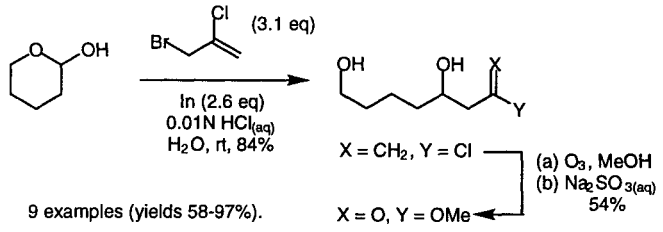


Indium

Reagent

Indium metal (**A**) mediates the reaction of 3-bromo-2-chloroprop-1-ene with aldehydes in an aqueous medium. The resultant β-hydroxy-vinylchlorides are precursors to useful β-hydroxy esters.

In



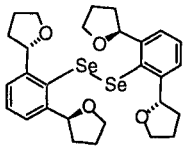
9 examples (yields 58-97%).

X.-H. Yi, Y. Meng, C.-J. Li *Tetrahedron Lett.* **1997**, *38*, 4731.

2,6-Bis[(2 *S*)-tetrahydrofuran-2-yl]phenyl Diselenide

Reagent

The selenotriflate prepared *in situ* from chiral diselenide **A** exhibits high facial selectivity in the selenomethoxylation of alkenes. Ring closures of hydroxy- and carboxyalkenes are also effected with good stereocontrol.



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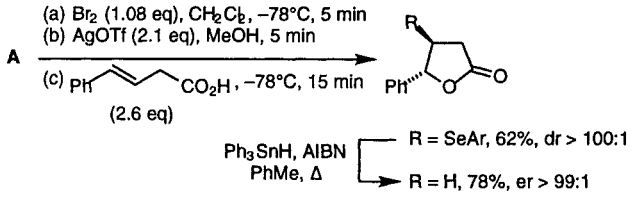


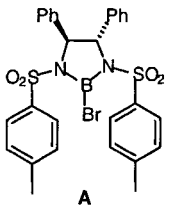
6 examples of selenomethoxylation (yields 67-81%, %de 33-99%), 3 examples of ring closure (yields 61-84%, %de 81-99%).

R. Déziel, E. Malenfant, C. Thibault, S. Fréchette, M. Gravel *Tetrahedron Lett.* **1997**, *38*, 4753.

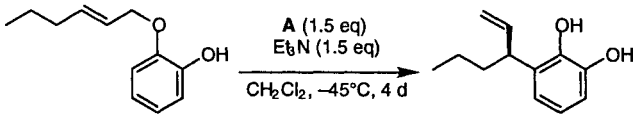
(*R,R*)-1-Bromo-3,4-diphenyl-2,5-di(*p*-toluenesulfonyl)-1-boraimidazoline

Reagent

The known organoboron reagent **A** promotes the first enantioselective aromatic Claisen rearrangement of allylic catechol monoethers. The proximal free hydroxyl function is essential for reaction.



A



89%, er = 97:3

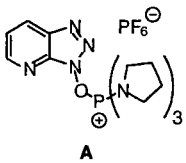
6 examples (yields 51-97%, %ee 57, 86-95%). The above example conducted with the *cis* isomer yields the enantiomeric product with comparable selectivity.

H. Ito, A. Sato, T. Taguchi *Tetrahedron Lett.* **1997**, *38*, 4815.

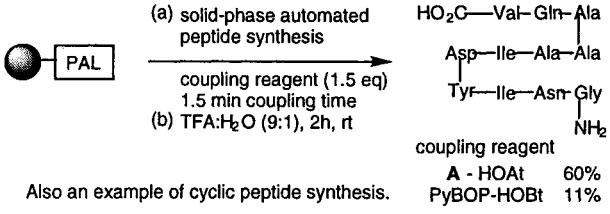
7-Azabenzotriazol-1-yloxytris(pyrrolidino)phosphonium Hexafluorophosphate (PyAOP)

Reagent

A new dehydrative coupling reagent for solid phase peptide synthesis. Unlike uronium salts (*eg* HATU), excess PyAOP (**A**) does not undergo detrimental side-reaction at the amino terminus.



A



Also an example of cyclic peptide synthesis.

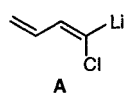
= polyethylene glycol - polystyrene graft

F. Albericio, M. Cases, J. Alsina, S. A. Triolo, L. A. Carpino, S. A. Kates *Tetrahedron Lett.* **1997**, *38*, 4853.

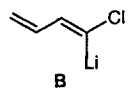
1-Lithio-1-chlorobutadienes

Reagent

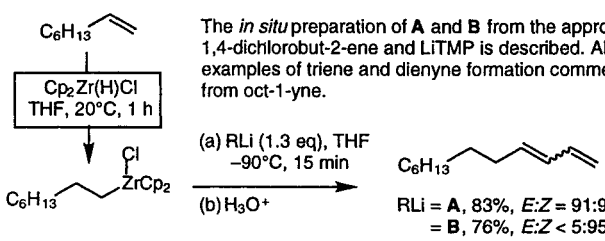
Treatment of alkyl, vinyl or alkynyl zirconocenes with carbenoid **A** yields the corresponding terminal *trans* diene, triene or dienyne respectively. Use of the isomer **B** leads to analogous products homologated with a *cis* terminal diene moiety.



A



B



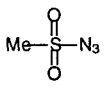
The *in situ* preparation of **A** and **B** from the appropriate 1,4-dichlorobut-2-ene and LiTMP is described. Also examples of triene and dienyne formation commencing from oct-1-yne.

RLi = **A**, 83%, *E:Z* = 91:9
= **B**, 76%, *E:Z* < 5:95

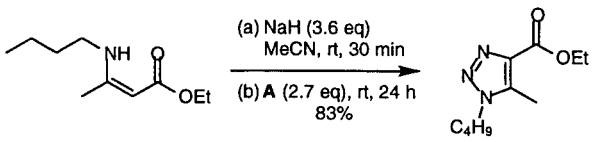
A. Kasatkin, R. J. Whitby *Tetrahedron Lett.* **1997**, *38*, 4857.

Mesyl Azide — *Reagent*

1,2,3-Triazoles are accessible by diazo transfer from **A** to β-amino-α,β-unsaturated ketones or esters.



A

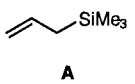


7 examples (yields 20, 37, 72-97%). Low yields are experienced with aryl enamines.

G. A. Romeiro, L. O. R. Pereira, M. C. B. V. de Souza, V. F. Ferreira, A. C. Cunha *Tetrahedron Lett.* **1997**, *38*, 5103.

Allyltrimethylsilane / Titanium Tetrachloride — *Reagent*

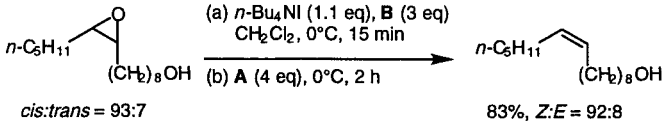
The title reagent pair effect the *anti* elimination of iodohydrin derivatives to yield alkenes. When used in conjunction with tetrabutylammonium iodide the stereoretentive deoxygenation of epoxides is achievable.



A

$TiCl_4$

B



cis:trans = 93:7

83%, *Z:E* = 92:8

5 examples (yields 36, 62-83%).

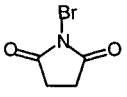
K. Yachi, K. Maeda, H. Shinokubo, K. Oshima *Tetrahedron Lett.* **1997**, *38*, 5161.

Triphenylphosphine / *N*-Bromosuccinimide (NBS) — *Reagent*

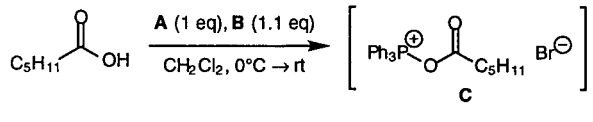
Acyloxytriphenylphosphonium salts (*eg* **C**), prepared *in situ* by the reaction of carboxylic acids with triphenylphosphine (**A**) - NBS (**B**) complex, selectively *N*-acylate a variety of amino phenols.

PPh_3

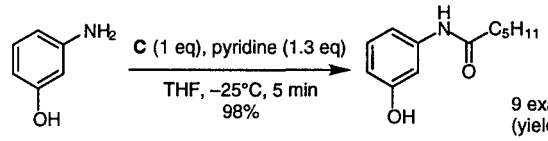
A



B



C

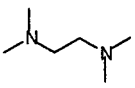


9 examples (yields 54, 81-99%).

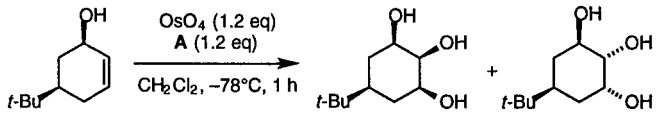
P. Frøyen *Tetrahedron Lett.* **1997**, *38*, 5359.

Tetramethylethylenediamine (TMEDA) — *Reagent*

The addition of TMEDA (**A**) to osmium tetroxide in dichloromethane effects the directed dihydroxylation of both acyclic and cyclic allylic alcohols.



A



87% 4%

4 examples of cyclic allylic alcohols (yields 54-91%, *syn:anti* > 6:1). If 'Upjohn' conditions are employed for the illustrated example *syn:anti* = 1:7. For acyclic allylic polyenes dihydroxylation occurs predominantly at the allylic site and not at remote electron rich double bonds, 4 examples (yields 68-74%).

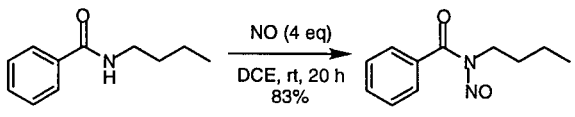
T. J. Donohoe, P. R. Moore, M. J. Waring *Tetrahedron Lett.* **1997**, *38*, 5027.

Nitric Oxide — *Reagent*

Gaseous nitric oxide (**A**) effects the nitrosation of amides in aprotic non-oxygenated solvents.

NO

A



13 examples (yields 0-95%). Reaction is retarded by bulky substituents.

DCE = 1,2-dichloroethane

T. Itoh, K. Nagata, Y. Matsuya, M. Miyazaki, A. Ohsawa *Tetrahedron Lett.* **1997**, *38*, 5017.