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:

Stephen Brand, John Christopher, Emma Guthrie, Philip Kocienski, Louise Lea, Russell McDonald, Graeme McAllister and Robert Narquizian of Glasgow University.

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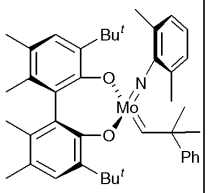
The journals regularly covered by the abstractors are:

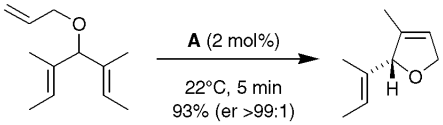
Angewandte Chemie International Edition
Bulletin of the Chemical Society of Japan
Chemical Communications
Chemistry A European Journal
Chemistry Letters
European Journal of Organic Chemistry
Helvetica Chimica Acta
Heterocycles
Journal of the American Chemical Society
Journal of Organic Chemistry
Organometallics
Perkin Transactions 1
Synlett
Synthesis
Tetrahedron
Tetrahedron Asymmetry and Tetrahedron Letters

Chiral molybdenum metathesis catalyst ***Catalyst***

Complex A accomplishes an asymmetric synthesis of dihydrofurans *via* catalytic kinetic resolution or enantioselective desymmetrisation of diallyl ethers.



A

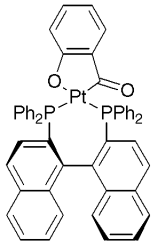


4 examples of kinetic resolution in which *unreacted* diallyl ether is obtained in 75, 92-98% ee ; 6 examples of desymmetrisation (yields 28, 83-91%; ee 10, 73-99%). Reactions are run neat.

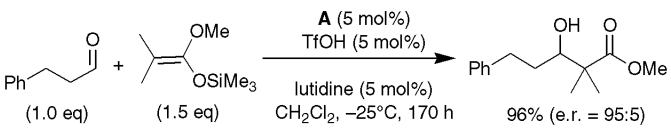
D. S. La, J. B. Alexander, D. R. Cefalo, D. D. Graf, A. H. Hoveyda, R. R. Schrock *J. Am. Chem. Soc.* **1998**, *120*, 9720.

Pt(OC$_6$H$_4$CO)[(R)-BINAP] ***Catalyst***

The title compound catalyses the asymmetric aldol addition of methyl trimethylsilyl dimethylketene acetal to aldehydes.



A



7 aldehyde substrates tried. *t*-BuCHO does not work at all; c-C$_6$H$_5$CHO gives low yields. Unhindered aldehyde gives 66-99% yield and 10-91% ee

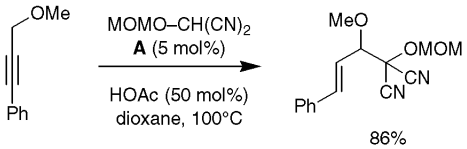
O. Fujimura *J. Am. Chem. Soc.* **1998**, *120*, 10032.

Tetrakis(triphenylphosphine)palladium(0) ***Catalyst***

Symmetrical dialkyl alkynes and phenyl alkyl alkynes react with pronucleophiles in the presence of Pd(0) and acetic acid to give allylation products.

Pd[PPh$_3$)$_4$

A



10 examples involving 6 alkynes and 5 pronucleophiles gave 64-99% yield allylated products. 3 examples of intramolecular allylation (84-93%) are also reported.

I. Kadota, A. Shibuya, Y. S. Gyoung, Y. Yamamoto *J. Am. Chem. Soc.* **1998**, *120*, 10262.

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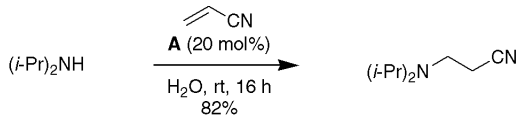
Indium(III) Chloride — *Catalyst*

The title reagent catalyses the Michael reaction between primary or secondary amines and α,β-ethylenic compounds in water under mild conditions. **A** can be recovered and re-used without loss of activity.

$InCl_3$

A



22 examples (yields 6-98%).

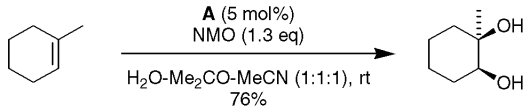
T.-P. Loh and L.-L. Wei *Synlett* **1998**, 975.

Microencapsulated Osmium Tetraoxide (MC OsO_4) — *Catalyst*

Preparation and use of **A** for the dihydroxylation of olefins is reported. The catalyst can be recovered and re-used without loss of activity.

MC OsO_4

A



11 examples (yields 68-89%) are reported.

S. Nagayama, M. Endo, S. Kobayashi *J. Org. Chem.* **1998**, *63*, 6094.

Bis(cyclopentadienyl)zirconium dichloride — *Catalyst*

The zirconium-catalysed reactions of alkynyl halides with EtMgBr are reported. The reaction proceeds *via* a zirconocene-ethylene complex and a zirconacycle to yield cyclobutene derivatives.

Cp_2ZrCl_2

A

4 examples (yields 50-61%).

K. Kasai, Y. Liu, R. Hara, T. Takahashi *Chem. Commun.* **1998**, 1989.

Tetrabutylammonium Bromide / Tetrabutylammonium Iodide — *Catalyst*

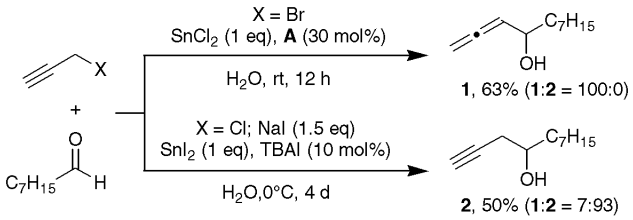
Tetrabutylammonium halides promote carbonyl propargylation or allenylation. Selectivity between propargylation and allenylation depends on the halide.

Bu_4NBr

A

Bu_4NI

B

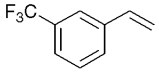


6 examples of propargylations (yields 48-77%, selectivity 100%) and 6 examples of allenylations (yields 50-80%, selectivity 80-98%) are reported.

Y. Masuyama, A. Ito, M. Fukuzawa, K. Terada, Y. Kurusu *Chem. Commun.* **1998**, 2025.

m-Trifluoromethylstyrene — *Catalyst*

A is a cocatalyst in the cross coupling of organozinc species and organic halides.



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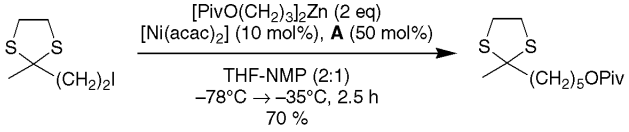

8 examples (yields 66-78%).

R. Giovannini, T. Stüdemann, G. Dussin, P. Knochel *Angew. Chem. Int. Ed.* **1998**, *37*, 2387.

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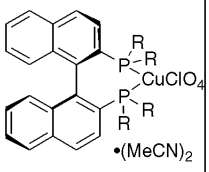
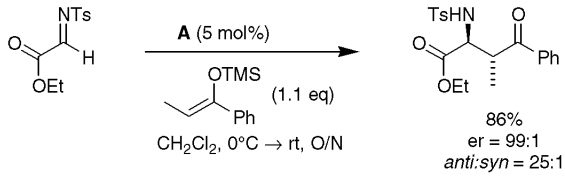
(*R*)-Tol-BINAP-$CuClO_4$•$(MeCN)_2$ — *Catalyst*

A catalyses the diastereo- and enantioselective alkylation of α-imino esters with enol silanes.



A

R = 4-MeC_6H_4

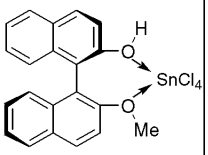


7 examples (yields 71-86%, %ee 46-98%, 3:1 ≤ *anti:syn* ≤ 25:1)

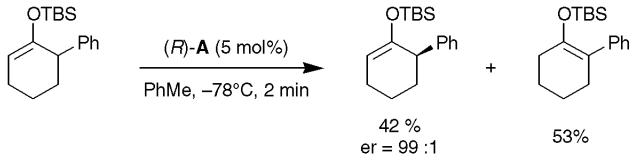
D. Ferraris, B. Young, C. Cox, W. J. Drury III, T. Dudding, T. Lectka *J. Org. Chem* **1998**, *63*, 6090.

(BINOL-Me)-tin tetrachloride complex — *Catalyst*

The title Lewis acid-assisted Brønsted acid (LBA) catalyses highly regio- and stereoselective isomerisation of "kinetic" silyl enol ethers to "thermodynamic" silyl enol ethers. The catalytic system is applied to the enantiomer-selective isomerisation of a racemic enol ether.



A



12 examples of isomerisation (yields 78-97%, thermodynamic : kinetic ratio ≥ 72:28) and the above example of enantiomer-selective isomerisation are reported.

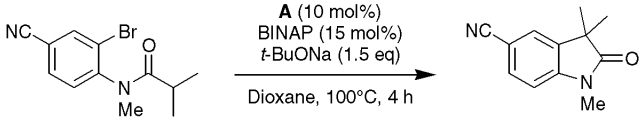
K. Ishihara, H. Nakamura, S. Nakamura, H. Yamamoto *J. Org. Chem.* **1998**, *63*, 6444.

Bis(dibenzylideneacetone)palladium(0) — *Catalyst*

A catalyses inter- and intramolecular α-arylation of amides. Intramolecular amide arylation of 2-haloanilides represents a versatile methodology for preparing substituted oxindoles. The intramolecular reaction is significantly more tolerant of electronic and steric substrate modifications than the intermolecular reaction.

$Pd(dba)_2$

A

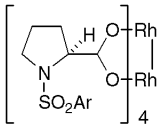


9 examples of intermolecular reactions (yields 16-72%), and 9 examples of intramolecular reactions (yields 52-83%) are described.

K. H. Shaughnessy, B. C. Hamann, J. F. Hartwig *J. Org. Chem.* **1998**, *63*, 6546.

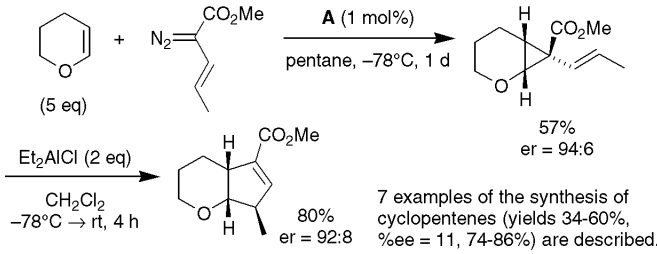
Rhodium *N*-(dodecylbenzenesulfonyl)prolinate [$(Rh_2(S\text{-}DOSP)_4)$] — *Catalyst*

A is utilised in the asymmetric synthesis of cyclopentenes by [3+2] annulations between vinylcarbenoids and vinyl ethers.



A

Ar = 4-$C_{12}H_{25}$Ph



7 examples of the synthesis of cyclopentenes (yields 34-60%, %ee = 11, 74-86%) are described.

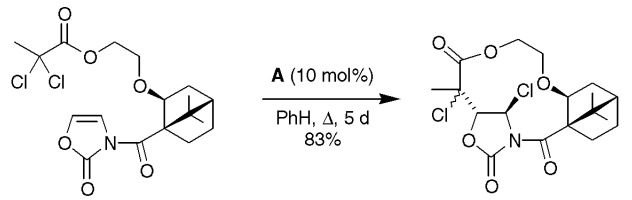
H. M. L. Davies, N. Kong, M. R. Churchill *J. Org. Chem.* **1998**, *63*, 6586.

Bis-(Triphenylphosphine)Ruthenium(II) Dichloride — *Catalyst*

The title catalyst mediates the intramolecular addition of a chiral *gem*-dichloroacyl moiety to a 2-oxazolone. The methodology is utilised in the synthesis of 2-amino alcohols containing three contiguous stereocentres.

$RuCl_2(PPh_3)_3$

A



Two examples (yields 75%, 83%) are described.

T. Morita, H. Matsunaga, E. Sugiyama, T. Ishizuka, T. Kunieda *Tetrahedron Lett.* **1998**, *39*, 7131.

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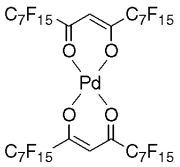
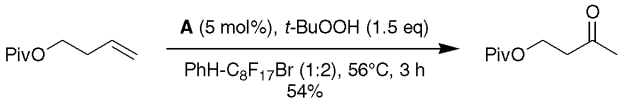
Palladium(0) Catalyst — *Catalyst*

The title catalyst mediates the Wacker oxidation of alkenes in a perfluorooctane-benzene biphasic system.



A

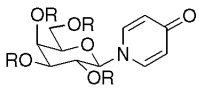


B. Betzemeier, F. Lhermitte, P. Knochel *Tetrahedron Lett.* **1998**, *39*, 6667.

15 examples (yields 54-95%). **A** can be recovered from the fluorous phase and reused, though progressively longer reaction times are required.

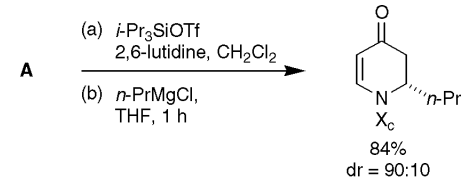
N-(2,3,4,6-Tetra-*O*-pivaloyl-β-D-galactopyranosyl)pyrid-4-one — *Chiral Auxiliary*

The title compound reacts with Grignard reagents to give 2-substituted 5,6-dehydropiperidin-4-ones with good to high stereoselectivity.



A

R = Piv

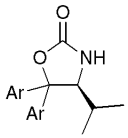


M. Follmann and H. Kunz *Synlett* **1998**, 989.

3 examples (yields 74–84%, dr [(*S*):(*R*)] = 90:10 - 0:100).

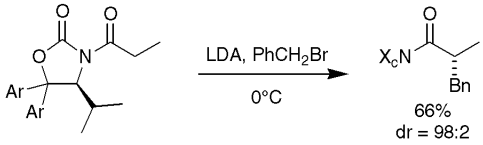
5,5-Ditolyl-(4*S*)-isopropyl oxazolidin-2-one — *Chiral Auxiliary*

The title auxiliary directs the diastereoselective methylation, benzylation and azidation of its *N*-acylated derivatives. Furthermore, it is readily cleaved by LiOH.



A

Ar = 4-MeC_6H_4

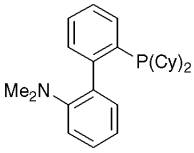


C. L. Gibson, K. Gillon, S. Cook *Tetrahedron Lett.* **1998**, *39*, 6733.

2 examples (yields 52, 66%, %de 94, 96%). Similar use of 2 other auxiliaries (R = 2-naphthyl, Ph) is described.

2-Dimethylamino-2′-(dicyclohexylphosphino)biphenyl — *Ligand*

The title ligand together with $Pd_2(dba)_3$ is a very active catalyst which mediates a variety of coupling reactions such as the amination of aryl bromides and chlorides, Suzuki couplings, and arylation of ketone enolates—all at room temperature.



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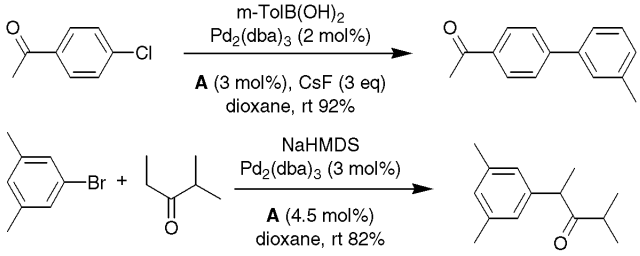
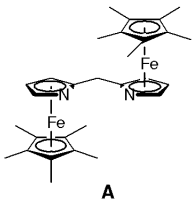


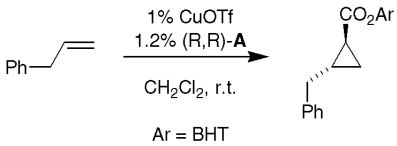
D. W. Old, J. P. Wolfe, S. L. Buchwald *J. Am. Chem. Soc.* **1998**, *120*, 9722.

C_2-Symmetric Bisazaferrocene — *Ligand*

The title compound represents a new class of planar-chiral ligands which, together with CuOTf, catalyses the enantioselective cyclopropanation of alkenes.



A



M. M.-C. Lo, G. C. Fu *J. Am. Chem. Soc.* **1998**, *120*, 10270.

6 examples or aryl-, alkyl- and silyl-substituted *terminal* alkenes: 64-90% yield; 87-96% ee; trans:cis = 93:7–96:4

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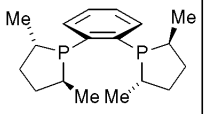
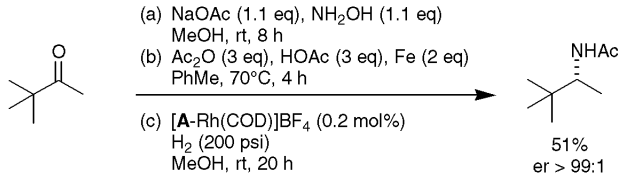
(*S,S*)-1,2-Bis(2,5-dimethylphospholano)benzene (Me-DuPHOS) — *Ligand*

A rhodium catalyst derived from the title ligand is utilised in a three-step procedure for the asymmetric catalytic reductive amination of ketones.



A

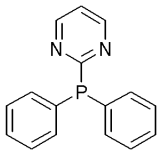


2 examples of reductive amidation using **A** and (*R,R*)-**A** are reported (yields 32, 51%, ee > 99:1).

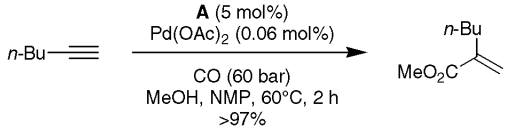
M. J. Burk, G. Casy, N. B. Johnson *J. Org. Chem.* **1998**, *63*, 6084.

2-Pyrimidyldiphenylphosphine — *Ligand*

The title ligand mediates the palladium(II)-catalysed carbonylation of terminal and internal alkynes.



A

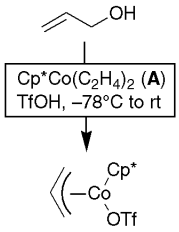


6 examples (yields 25, 48->97%) are described. *Bis*- or *tris*- 2-pyridyl substituted phosphines resulted in significantly longer reaction times.

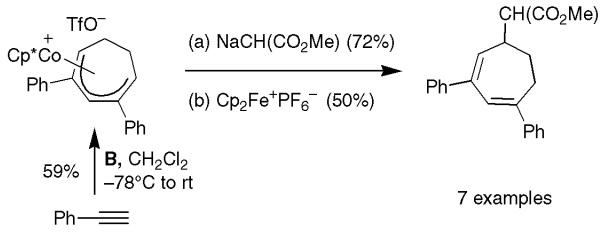
M. T. Reetz, R. Demuth, R. Goddard *Tetrahedron Lett.* **1998**, *39*, 7089.

Cp*Co(C_2H_4)$_2$ — *Reagent*

Complexes **B** derived from the title compound **A** undergo intermolecular allyl/alkyne [3+2+2] cycloaddition reactions to give cationic η^5-cycloheptadienyl complexes which can alkylate soft nucleophiles.



B



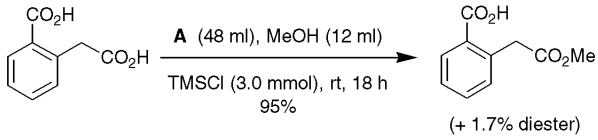
7 examples

N. Etkin, T. L. Dzwiniel, K. E. Schweibert, J. M. Stryker *J. Am. Chem. Soc.* **1998**, *120*, 9707.

2,2-Dimethoxypropane — *Reagent*

The title compound, methanol and a catalytic amount of HCl selectively esterifies aliphatic carboxylic acids in the presence of aromatic carboxylic acids. The reaction gives high yields and takes place at room temperature.

A



(+ 1.7% diester)

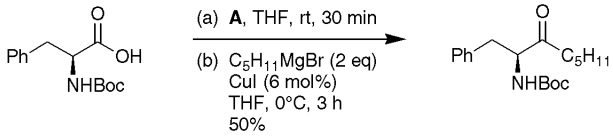
6 examples of substrates with both aliphatic and aromatic carboxylic acids (>95% yield); 16 examples of aliphatic carboxylic acids (usually 100% yield). Even in the presence of 20 mol% TMSCl, aromatic carboxylic acids give very low yields of the ester (typically <3%).

A. Rodriguez, M. Nomen, B. W. Spur, J. J. Godfroid *Tetrahedron Lett.* **1998**, *39*, 8563.

N,N-Carbonyldiimidazole — *Reagent*

A is utilised in a convenient conversion of α-aminoacids into NH-Boc protected α-aminoketones *via* imidazolides.

A



9 examples (yields 30-68%).

B. F. Bonini, M. Comes-Franchini, M. Fochi, G. Mazzanti, A. Ricci, G. Varchi *Synlett* **1998**, 1013.

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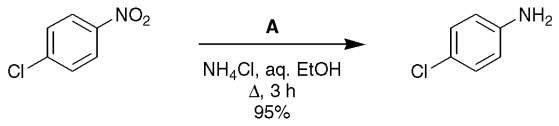
Indium

Reagent

Treatment of a range of aromatic nitro compounds with **A** and aqueous ethanolic ammonium chloride results in selective reduction of the nitro groups; ester, nitrile, amide and halide substituents are unaffected.

In

A



11 examples (yields 60-99%).

C. J. Moody and M. R. Pitts *Synlett* **1998**, 1028.

Samarium(II) Iodide / Nickel(II) Iodide

Reagent

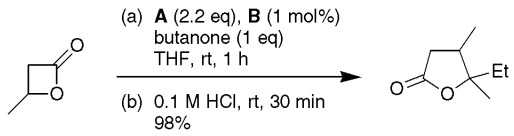
In the presence of the title reagent pair, β-lactones react with aldehydes, ketones and imines to afford tetrahydrofuranones and pyrrolidinones in good to high yield.

SmI_2

A

NiI_2

B



17 examples of coupling with aldehydes and ketones (yields 0, 74-98%) and 7 examples of coupling with imines (yields 70-93%) are reported.

F. Machrouhi, J.-L. Namy *Tetrahedron* **1998**, *54*, 11111.

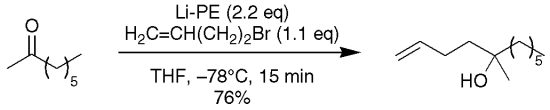
Metals on polyethylene solid support

Reagent

Convenient preparation of "high-surface alkali metals" deposited on solid-supports and subsequent use in a variety of reactions is reported. The metals can be stored as stable suspensions in inert solvents if protected against oxygen. Preparation of Zn on solid-support is also reported.

M / Polyethylene (PE)

M = Li, Na, K, Zn



36 examples in total of the use of Na-PE in the acyloin reaction, formation of organolithium species using Li-PE and trapping with electrophiles, an intramolecular Dieckmann cyclisation utilising K-PE and Reformatsky and Barbier-type reactions using Zn-PE are reported. Yields are good to excellent.

M. Makosza, P. Nieczypor, K. Grela *Tetrahedron* **1998**, *54*, 10827.

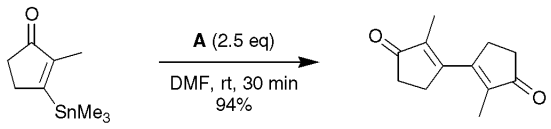
Copper(I) Chloride

Reagent

The title reagent mediates the intermolecular homocoupling of alkenyltrimethylstannanes, to afford functionalised conjugated dienes and tetraenes in good to high yield.

CuCl

A



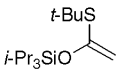
17 examples (yields 18-91%) are reported.

E. Piers, P. L. Gladstone, J. G. K. Yee, E. J. McEachern *Tetrahedron* **1998**, *54*, 10609.

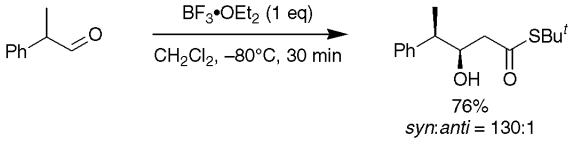
1-(Triisopropylsilyloxy)-1-(*tert*-butylthio)ethene

Reagent

Exceptional Cram-type selectivites in Mukaiyama aldol reactions of **A** are reported. The level of 1,2-asymmetric induction is promoted by the bulk of the silyl group.



A



3 examples (yields 76-78%, 5:1 ≤ *syn*:*anti* ≤ 130:1) are described.

A. P. Davis, S. J. Plunkett, J. E. Muir *Chem. Commun.* **1998**, 1797.

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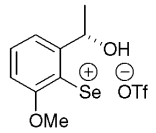
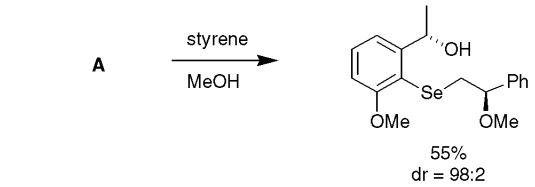
(*R*)-2-Methoxy-6-(1-hydroxyethyl)phenylselenyl triflate — *Reagent*

The asymmetric methoxyselenenylation of styrene derivatives using **A** is reported.



A

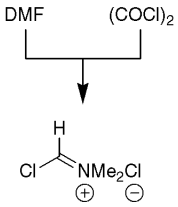


6 examples (yields 42-66%, %de = 20-96%).

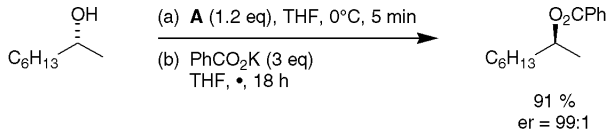
G. Fragale, M. Neuburger, T. Wirth *Chem. Commun.* **1998**, 1867.

(Chloromethylene)dimethylammonium chloride — *Reagent*

The title compound (generated *in situ* from DMF and oxalyl chloride) reacts with secondary alcohols to form imidate esters. Reaction with potassium carboxylates or potassium phthalimide gives products with clean inversion of stereochemistry.



A

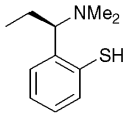


17 examples of ester formation (yields 15-91%, %ee = 51->95%) and 9 examples of formation of phthalimido derivatives (yields 25-98%, %ee = 0, 72-96%) are reported.

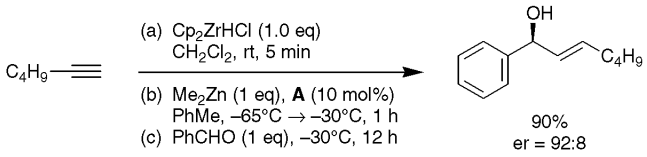
A. G. M. Barrett, D. C. Braddock, R. A. James, N. Koike, P. A. Procopiou *J. Org. Chem.* **1998**, *63*, 6273.

2-(*R*)-1-[(Dimethylamino)propyl]thiophenol — *Reagent*

In situ hydrozirconation of alkynes, transmetallation to zinc, and addition to aldehydes catalysed by **A** provides an efficient protocol for the asymmetric preparation of (*E*)-allylic alcohols.



A



10 examples (yields 63-90%, %ee 63-99)

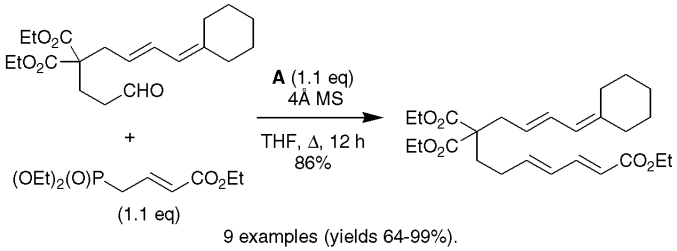
P. Wipf, S. Ribe *J. Org. Chem.* **1998**, *63*, 6454.

Lithium Hydroxide — *Reagent*

A promotes Horner-Wadsworth-Emmons dienylation of aldehydes and ketones.

LiOH

A



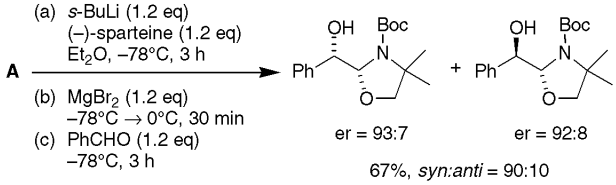
9 examples (yields 64-99%).

J. M. Takacs, M. R. Jaber, F. Clement, C. Walters *J. Org. Chem.* **1998**, *63*, 6757.

N-Boc-4,4-dimethyl-1,3-oxazolidine — *Reagent*

Formation and reaction of the 2-metallated title reagent in the presence of (–)-sparteine is described representing a new chiral formyl anion equivalent. The two diastereoisomers are formed with high enantioselectivity although little diastereoselectivity is observed in the absence of $MgBr_2$.

A



1 example is reported.

N. Kise, T. Urai, J. Yoshida *Tetrahedron: Asymmetry* **1998**, *9*, 3125.

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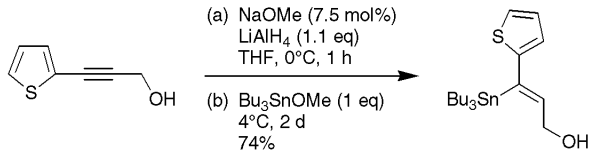
Tributyltin Methoxide — *Reagent*

A facilitates transmetallation from aluminium to tin in a preparation of tributylstannylprop-2-en-1-ols.

Bu_3SnOMe

A



M. Havránek, D. Dvorák *Synthesis* **1998**, *9*, 1264.

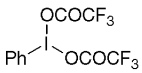
12 examples (yields 13-74%).

Iodine / Bis-(trifluoroacetoxy)iodobenzene — *Reagent*

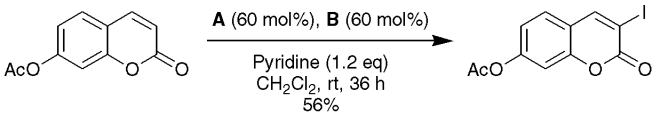
The title reagent pair effects the iodination of a variety of functionalised olefins.

I_2

A



B

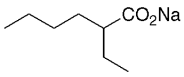


R. Benhida, P. Blanchard, J.-L. Fourrey *Tetrahedron Lett.* **1998**, *39*, 6849.

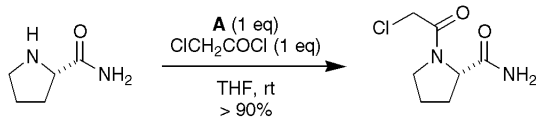
10 examples (yields 23, 56-96%) are described.

Sodium 2-Ethylhexanoate — *Reagent*

The title reagent, which is soluble in common organic solvents, mediates the practical acylation of amines.



A



J. Fitt, K. Prasad, O. Repic, T. J. Blacklock *Tetrahedron Lett.* **1998**, *39*, 6991.

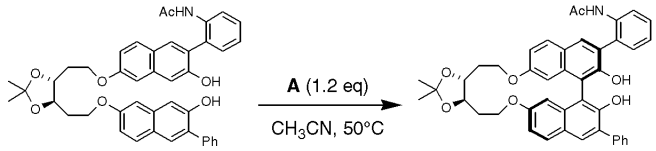
4 examples (yields 80->90%) are described. The reaction does not proceed *via* a mixed anhydride and therefore gives single acylation products.

Manganese *tris*(acetylacetonate) — *Reagent*

The title catalyst mediates the diastereoselective oxidative coupling of *seco*-biaryl compounds to give symmetrical and unsymmetrical BINOL-derivatives.

$Mn(acac)_3$

A



75%, dr = 95:5

B. H. Lipshutz, Y.-J. Shin *Tetrahedron Lett.* **1998**, *39*, 7017.

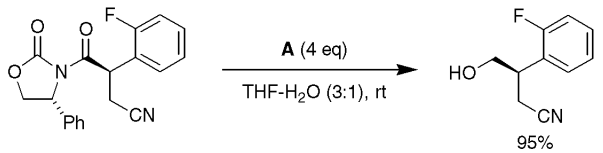
9 examples (yields 69-89%, %de 84–97%) are described.

Sodium Borohydride — *Reagent*

The title reagent in aqueous THF mediates the reductive cleavage of *N*-acyloxazolidinones.

$NaBH_4$

A



95%
er >99:1

M. Prashad, D. Har, H.-Y. Kim, O. Repic *Tetrahedron Lett.* **1998**, *39*, 7067.

13 examples (yields 75-95%, %ee >99%) are described. In contrast, use of $LiBH_4$ resulted in ~10% racemisation.

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