

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:

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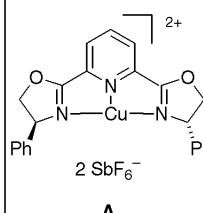
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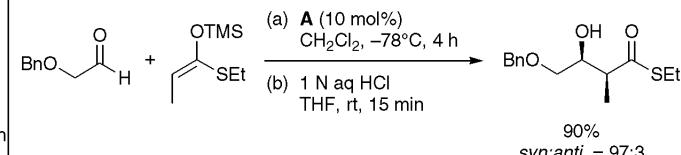
Copper[(*S,S*)-phenylbis(oxazolinyl)pyridine]dihexafluoroantimonate

Catalyst

A mediates Mukaiyama aldol reactions between benzyloxyacetaldehyde and a range of silylketene acetals.



D. A. Evans, M. C. Kozlowski, J. A. Murry, C. S. Burgey, K. R. Campos, B. T. Connell, R. S. Staples *J. Am. Chem. Soc.* **1999**, *121*, 669.

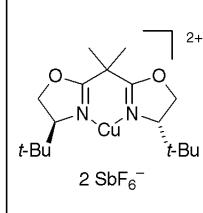


12 examples (yields 11-90%, diastereofacial selectivity ≥74:26, %ee ≥63%).

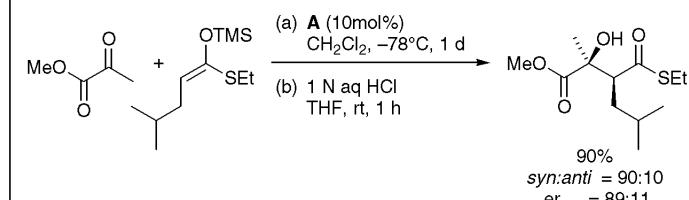
Copper[(*S,S*)-*tert*-butylbis(oxazolinyl)propane]dihexafluoroantimonate

Catalyst

Bisoxazolidine **A** catalyses the aldol addition of a variety of enolsilanes to pyruvate esters.



D. A. Evans, C. S. Burgey, M. C. Kozlowski, S. W. Tregay *J. Am. Chem. Soc.* **1999**, *121*, 686.

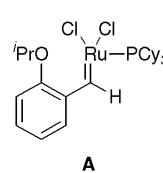


24 examples (yields 53-97%, diastereofacial selectivity ≥90:10, %ee ≥22%).

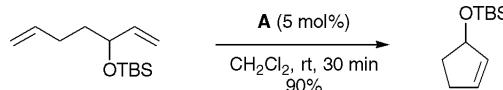
Dichlorotricyclohexylphosphino-(2-*iso*-propyloxy)benzylidene ruthenium(II)

Catalyst

The use of **A** as a recyclable ring closing metathesis catalyst is described.



J. S. Kingsbury, J. P. A. Harrity, P. J. Bonitatebus, Jr., A. H. Hoveyda *J. Am. Chem. Soc.* **1999**, *121*, 791.

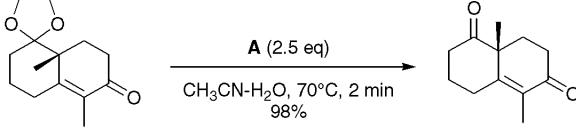
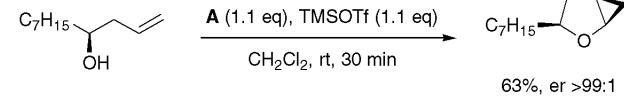
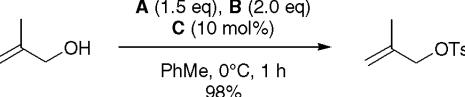
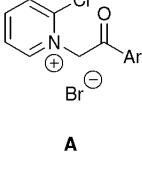
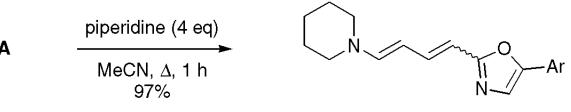
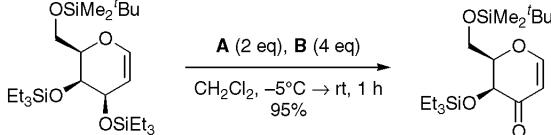


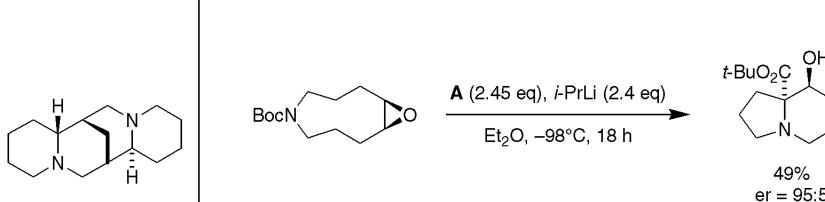
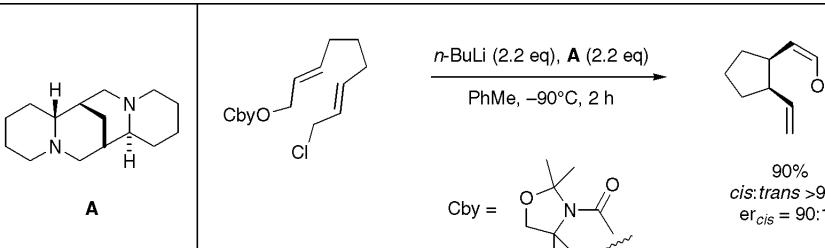
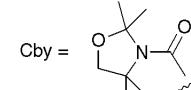
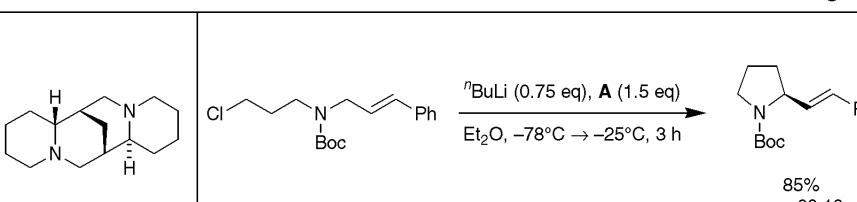
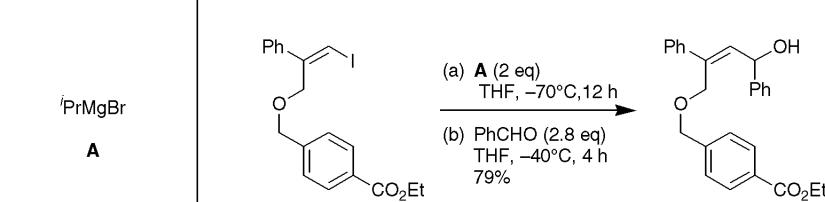
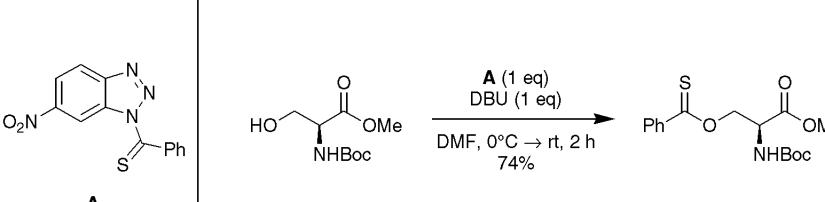
9 examples (yields 67-99%).

(R)-2,2'-Binaphthol-Silver Triflate Complex			Catalyst
A catalyses the enantioselective aldol addition of trialkyltin enol ethers with benzaldehyde. The required enol ethers are prepared <i>in-situ</i> from the corresponding enol trichloroacetate.			<p>PhCHO, A (10 mol%) Bu₃SnOMe (10 mol%) MeOH (2 eq) -20°C → rt, 18 h 94% anti:syn = 92:8 er_{anti} = 90:10</p>
A. Yanagisawa, Y. Matsumoto, K. Asakawa, H. Yamamoto <i>J. Am. Chem. Soc.</i> 1999 , <i>121</i> , 892.			3 examples (yields 59–94%, 78:22 ≤ anti:syn ≤ 92:8, %ee _{anti} = 84–95%) are reported.
Lithium Perchlorate			Catalyst
The title reagent is used together with 1,4-diazabicyclo[2.2.2]octane (DABCO) to catalyse the coupling of α,β -unsaturated carbonyl compounds with aldehydes in the Baylis-Hillman reaction.			<p>PhCHO (1 eq) A (70 mol%) DABCO (15 mol%) Et₂O, -20°C → 0°C, 20 h 75%</p>
M. Kawamura, S. Kobayashi <i>Tetrahedron Lett.</i> 1999 , <i>40</i> , 1539.			12 examples (yields 35–85%) are reported.
Bis(acetoacetonato)nickel(II)			Catalyst
Et ₂ Zn/A and Et ₃ B/A catalysts promote the homoallylation of carbonyl compounds. With both catalytic systems isoprene reacts with aldehydes to provide 1,3- <i>anti</i> -isomers with excellent selectivity.			<p>t-BuCHO A (10 mol%), isoprene (4 eq) Et₂Zn (2.4 eq) THF, rt, 1 h 66% anti:syn = 15:1</p>
M. Kimura, H. Fujimatsu, A. Ezoe, K. Shibata, M. Shimizu, S. Matsumoto, Y. Tamaru <i>Angew. Chem. Int. Ed.</i> 1999 , <i>38</i> , 397.			16 examples (yields 0, 16–90%, 1:5 ≤ anti:syn ≤ 20:1).
[1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium			Catalyst
A catalyses the synthesis of enantioenriched homopropargylic alcohols <i>via</i> addition to aldehydes of transient chiral allenylindium reagents derived from enantioenriched propargylic mesylates.			<p>C₆H₁₁CHO (0.9 eq) A (5 mol%), InI (1.4 eq) THF-HMPA (3:1), rt, 16 h 76% anti:syn = 95:5 er_{anti} = 98:2</p>
J. A. Marshall, C. M. Grant <i>J. Org. Chem.</i> 1999 , <i>64</i> , 696.			6 examples (yields 62–88%, 45:55 ≤ anti:syn ≤ 95:5, %ee _{anti} = 92–96%).
(S,S)-2,2''-Bis[(diethylphosphino)methyl]-1,1''-biferrocene			Ligand
The optically active diphosphine A is utilised in the rhodium-catalysed asymmetric hydrosilylation of ketones.		<p>(a) H₂Si(<i>m</i>-FC₆H₄)₂ (1.5 eq) [Rh(COD)]₂BF₄ (1.0 mol%) A (1.1 mol%), THF (b) K₂CO₃, MeOH 90%, er = 95:5</p>	
R. Kuwano, T. Uemura, M. Saitoh, Y. Ito <i>Tetrahedron Lett.</i> 1999 , <i>40</i> , 1327.			8 examples (yields 82–99%, %ee = 77–94%).

[(R)-α-(2-Naphthyl)aminomethyl]ferrocene			Ligand
A novel copper(I) catalysed substitution of unsymmetrical allyl chlorides with diorganozinc compounds utilising A is reported.			R = neopentyl
F. Dübner, P. Knochel <i>Angew. Chem. Int. Ed.</i> 1999 , <i>38</i> , 379.	11 examples (yields 45-72%, 90:10 ≤ $S_{N2}':S_{N2}$ ≤ 99:1, %ee = 37-87%).		
(R,S,R,S)-P,P'-1,2-Phenylenabis(endo-2,5-dimethyl-7-phosphabicyclo[2.2.1]heptane)			Ligand
A highly enantioselective hydrogenation of enol acetates catalysed by a Rh-(ligand A) complex is reported.			100% conversion er = 93:7
Q. Jiang, D. Xiao, Z. Zhang, P. Cao, X. Zhang <i>Angew. Chem. Int. Ed.</i> 1999 , <i>38</i> , 516.	13 examples (conversions 100%, %ee = 66->99%).		
(αR,α'R)-2,2'-Bis-(α-N,N'-dimethylaminobenzyl)-(S,S)-1,1'-bis(diphenylphosphino)ferrocene			Ligand
The use of a series of C_2 -symmetric diamino FERRIPHOS ligands, including the title compound, in the enantioselective preparation of chiral α -amino acids is described.			er = 98:2
J. J. Almena Perea, M. Lotz, P. Knochel <i>Tetrahedron: Asymmetry</i> 1999 , <i>10</i> , 375.	11 examples (%ee = 95->99%) are reported.		
Propargyl Chloroformate			Protecting Group
The title reagent is used to introduce the propargyloxycarbonyl (Proc) group for the novel protection of amino and hydroxy functions. Similarly, protection of carboxy functions as the propargyl ester is reported.			3 examples of protection (yields 100%) and 2 examples of cleavage (yields 88-100%) are reported.
Y. Fukase, K. Fukase, S. Kusumoto <i>Tetrahedron Lett.</i> 1999 , <i>40</i> , 1169.			
Zirconium Tetrachloride			Protecting Group
Zirconium tetrachloride catalyses the <i>in-situ</i> transacetalisation of carbonyl compounds under mild conditions. The reaction is selective for aldehydes in the presence of ketones but the selectivity diminishes when the ketone is cyclic. Thus competition experiments show that benzaldehyde and cyclohexanone give nearly a 1:1 mixture of 1,3-dioxanes. The method can also be used for the formation of thioacetals.			90%
H. Firouzabadi, N. Iranpoor, B. Karimi <i>Synlett</i> 1999 , <i>321</i> .	20 examples. In the absence of the diol, the diethyl acetal is formed instead.		

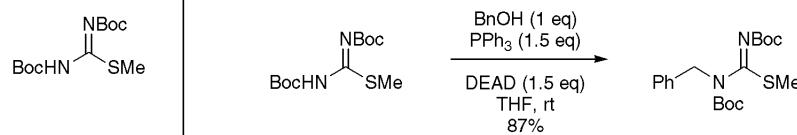
Iodine Monobromide		Protecting Group
<p><i>tert</i>-Butyldimethylsilyl ethers of simple alcohols, carbohydrates and nucleosides cleave on treatment with iodine monobromide (1.5 equiv.) in MeOH at room temperature. Acetals, PMB ethers, TBDPS ethers, esters and amides survive unscathed.</p>	I-Br	
K. P. Ravindranathan Kartha and R. A. Field <i>Synlett</i> , 1999, 311.		8 non-trivial examples; yields 80-96%
Iron(III) Chloride		Reagent
<p>A promotes the tandem Nazarov-type electrophilic closure of a 1,4-dien-3-one, followed by intramolecular [4+3]-cycloaddition of the resulting oxyallyl cation with a pendant 1,3-diene.</p>	FeCl ₃ A	
Y. Wang, A. M. Arif, F. G. West <i>J. Am. Chem. Soc.</i> , 1999, 121, 876.		4 examples (yields 53-75%).
Palladium(II) Chloride / Copper(II) Chloride		Reagent
The title reagent pair catalyse the reaction of hydroxy alkenes with CO and MeOH to give tetrahydropyrans.	PdCl ₂ A CuCl ₂ B	
J. D. White, J. Hong, L. A. Robarge <i>Tetrahedron Lett.</i> 1999, 40, 1463.		5 examples (yields 0, 20-61%) are reported.
Silver Tetrafluoroborate		Reagent
<p>A promotes the rapid transformation of 2-(trimethylsilyl)ethyl sulfides into thioesters under mild conditions. The reagent is not suitable for substrates with acid sensitive functionalities.</p>	AgBF ₄ A	
H. Grundberg, M. Andergran, U. J. Nilsson <i>Tetrahedron Lett.</i> 1999, 40, 1811.		10 examples (yields <5-100%).
Magnesium		Reagent
The title reagent is used in the coupling of ketones or aldehydes with trimethylsilyl chloride giving silyl enol ethers. The reaction is highly Z-selective and is applicable to both cyclic and acyclic carbonyl compounds.	Mg A	
Y. Ishino, Y. Kita, H. Maekawa, T. Ohno, Y. Yamasaki, T. Miyata, I. Nishiguchi <i>Tetrahedron Lett.</i> 1999, 40, 1349.		11 examples (yields 15-100 %, 60:40 ≤ E:Z ≤ 2:98).

Cerium Ammonium Nitrate			Reagent
The title reagent effects the rapid deprotection of cyclic ketals and acetals. A wide variety of functional and protecting groups are tolerated and the method is suitable for acid-labile substrates.	(NH ₄) ₂ Ce(NO ₃) ₆ A		
A. Ates, A. Gautier, B. Leroy, J.-M. Plancher, Y. Quesnel, I. E. Markó <i>Tetrahedron Lett.</i> 1999 , <i>40</i> , 1799.			10 examples (yields 6-98%).
(Diethoxymethyl)tributylstannane			Reagent
Reaction of A with olefinic alcohols in the presence of acid results in facile transacetalisation followed by intramolecular cyclopropanation.	Bu ₃ SnCH(OEt) ₂ A		
M. Sugawara, J. Yoshida <i>Tetrahedron Lett.</i> 1999 , <i>40</i> , 1717.			9 examples (yields 43-93%, %ee 84->99%).
p-Toluenesulfonyl Chloride / Triethylamine / Trimethylamine Hydrochloride			Reagent
The sulfonylation of a range of alcohols has been achieved using the title reagent combination. The system represents an alternative to the traditional use of pyridine, and the problematic chloride forming side-reaction is circumvented.	TsCl A Et ₃ N B Me ₃ N•HCl C		
Y. Yoshida, Y. Sakakura, N. Aso, S. Okada, Y. Tanabe <i>Tetrahedron</i> 1999 , <i>55</i> , 2183.			49 examples (yields 28-98%).
2-Chloro-N-(p-nitrophenacyl)pyridinium Bromide			Reagent
Reaction of the title reagent with aliphatic secondary amines provides a one-pot route to 1-amino-4-(5-aryloxazol-2-yl)buta-1,3-dienes.	 A Ar = p-nitrophenyl		
E. V. Babaev, A. A. Tsisevich <i>J. Chem. Soc., Perkin Trans. 1</i> 1999 , 399.			5 examples (yields 83-97%). A clear predominance of the (1E,3E) isomer (85-90%) over the (1E,3Z) isomer is observed.
(Diacetoxyiodo)benzene / Trimethylsilyl Azide			Reagent
The title reagent pair promotes the allylic oxidation of O-silylated glycals. Reactions with the reported system proceed in higher yield than with the traditional PhI(OH)OTs reagent. Use of this complex in the allylic O-benzyl deblocking of glycals is also discussed.	PhI(OAc) ₂ A TMSN ₃ B		
A. Kirschning, U. Hary, C. Plumeier, M. Ries, L. Rose <i>J. Chem. Soc., Perkin Trans. 1</i> 1999 , 519.			6 examples (yields 43-95%).

(-)-Sparteine	Reagent
A new and enantioselective indolizidine synthesis by <i>meso</i> -epoxide α -deprotonation and transannular N–C insertion in the presence of chiral base A is reported. D. M. Hodgson, L. A. Robinson <i>Chem. Commun.</i> 1999, 309.	 <p style="text-align: center;">A</p> <p style="text-align: center;">Et₂O, -98°C, 18 h</p> <p style="text-align: right;">49% er = 95:5</p>
	1 example is reported.
(-)-Sparteine	Reagent
Sparteine-mediated chiral induction by an elimination-coupled lithium-ene reaction in the synthesis of (+)-(3 <i>R</i> ,4 <i>R</i>)-1,2-dihydromultifidene is reported. A. Deiters, D. Hoppe <i>Angew. Chem. Int. Ed.</i> 1999, 38, 546.	 <p style="text-align: center;">A</p> <p style="text-align: center;">n-BuLi (2.2 eq), A (2.2 eq) PhMe, -90°C, 2 h</p> <p style="text-align: right;">90% cis:trans >99:1 er_{cis} = 90:10</p> <p>Cby = </p>
(-)-Sparteine	Reagent
Asymmetric syntheses of <i>N</i> -Boc 2-substituted pyrrolidines and piperidines by intramolecular cyclization in the presence of A are reported. C. Serino, N. Stehle, Y. S. Park, S. Florio, P. Beak <i>J. Org. Chem.</i> 1999, 64, 1160.	 <p style="text-align: center;">A</p> <p style="text-align: center;">n-BuLi (0.75 eq), A (1.5 eq) Et₂O, -78°C → -25°C, 3 h</p> <p style="text-align: right;">85% er = 90:10</p> <p>8 examples (yields 29-93%, %ee = 30-94%).</p>
Isopropylmagnesium Bromide	Reagent
Using A or i Pr ₂ Mg, highly functionalised alkenylmagnesium halides can be prepared at low temperature <i>via</i> an iodine-magnesium exchange with retention of configuration of the double bond. Under these conditions functional groups such as cyanide, carbamate or ethyl ester are tolerated. M. Rottländer, L. Boymond, G. Cahiez, P. Knochel <i>J. Org. Chem.</i> 1999, 64, 1080.	 <p style="text-align: center;">A</p> <p style="text-align: center;">(a) A (2 eq) THF, -70°C, 12 h</p> <p style="text-align: center;">(b) PhCHO (2.8 eq) THF, -40°C, 4 h 79%</p> <p style="text-align: right;">11 examples (yields 60-95%).</p>
1-Thiobenzoyl-6-nitrobenzotriazole	Reagent
Thionoacyl nitrobenzotriazoles including A are utilised in an efficient synthesis of thionoesters. M. A. Shalaby, H. Rapoport <i>J. Org. Chem.</i> 1999, 64, 1065.	 <p style="text-align: center;">A</p> <p style="text-align: center;">DMF, 0°C → rt, 2 h 74%</p> <p style="text-align: right;">14 examples using 8 different thionoacyl nitrobenzotriazoles (yields 53-89%).</p>

1,3-bis-Boc-2-methyl-2-thiopseudourea**Reagent**

A synthetic route towards disubstituted guanidines is described. A series of primary and secondary alcohols were guanylated under Mitsunobu conditions and subsequent reaction with amines affords disubstituted guanidines.

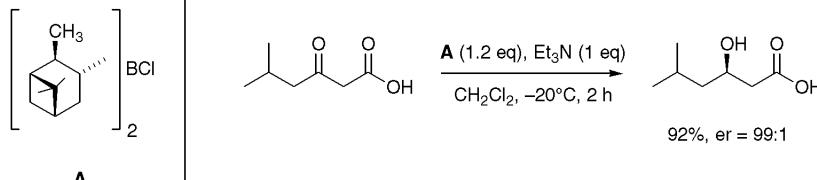


H.-O Kim, F. Mathew, C. Ogbu *Synlett* 1999, 193.

10 examples (yields 32-100%) are reported.

B-Chlorodiisopinocampheylborane**Reagent**

The title reagent is used in the enantioselective synthesis of β -hydroxy carboxylic acids.

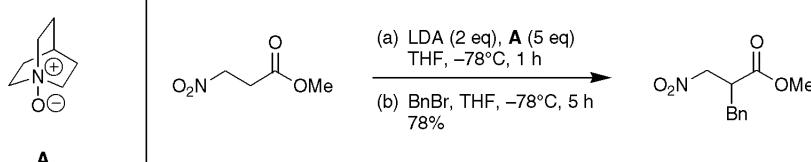


Z. Wang, C. Zhao, M. E. Pierce, J. M. Fortunak *Tetrahedron: Asymmetry* 1999, 10, 225.

8 examples (yields 87-92%, %ee = 91->98%).

Quinuclidine N-oxide**Reagent**

The use of **A** as a replacement for HMPA in a range of reactions is reported.

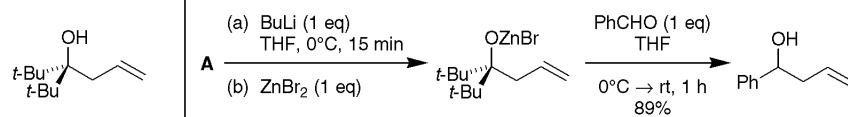


I. A. O'Neil, J. Y. Q. Lai, D. Wynn *Chem. Commun.* 1999, 59.

4 examples (yields 78-90%) are described.

3-Tert-butyl-2,2-dimethylhex-5-en-3-ol**Reagent**

A novel fragmentation-allylation reaction of **A** generates an allylic zinc reagent *in situ*, which reacts with a range of electrophiles.

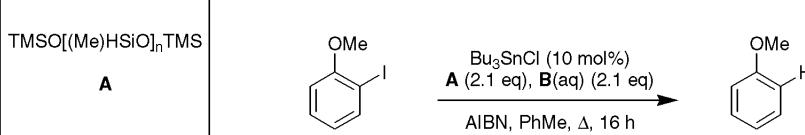


P. Jones, P. Knochel *J. Org. Chem.* 1999, 64, 186.

12 reactions with aldehydes, ketones and imines (yields 63-99%). Similar reactions of γ -substituted homoallylic alcohols are also reported.

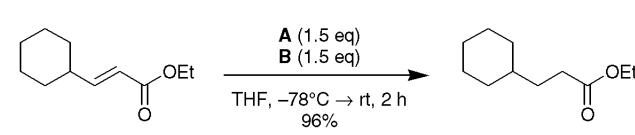
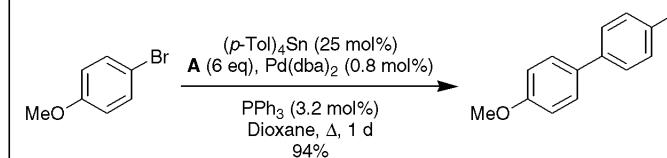
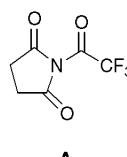
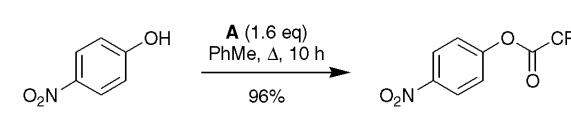
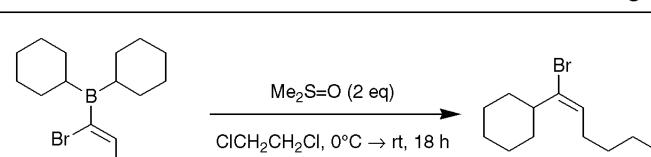
Polymethylhydrosiloxane (PHMS) / Potassium Fluoride**Reagent**

The title reagent pair catalyses the *in situ* generation of tributyltin hydride from tributyltin chloride. The technique can be applied to reactions catalytic in tin.



I. Terstiege, R. E. Maleczka Jr. *J. Org. Chem.* 1999, 64, 342.

10 examples (yields 21-96%) of a variety of tin-mediated reactions are reported.

Bis(acetylacetonato)cobalt(II) / Diisobutylaluminium Hydride			Reagent
The title reagents are used in the selective 1,4-reduction of α,β -unsaturated carbonyl compounds.	$\text{Co}(\text{acac})_2$ A		
T. Ikeno, T. Kimura, Y. Ohtsuka, T. Yamada <i>Synlett</i> 1999 , 96.			15 examples (yields 60-100%).
Tetrabutylammonium Fluoride			Reagent
Palladium-catalysed cross-coupling reactions between organostannanes and organic halides facilitated by A are reported. All four substituents on tin can take part in carbon-carbon bond formation.	Bu_4NF A		
K. Fugami, S. Ohnuma, M. Kameyama, T. Saotome, M. Kosugi <i>Synlett</i> 1999 , 63.			5 examples (yields 0, 27-95%).
N-(Trifluoroacetyl)succinimide			Reagent
The trifluoroacetylation of alcohols, phenols and amines is conveniently achieved using A .	 A		
A. R. Katritzky, B. Jang, G. Qiu, Z. Zhang <i>Synthesis</i> 1999 , 55.			14 examples (yields 83-99%) are described.
Dimethyl Sulfoxide			Reagent
Reaction of (<i>Z</i>)-1-bromoalk-1-enyldialkylboranes with DMSO results in 1,2-migration of an alkyl group from the boron to the α -carbon without elimination of bromine to give internal (<i>E</i>)-alkenyl bromides.	$\text{Me}_2\text{S}=\text{O}$		
M. Hoshi, H. Kazuya, S. Arase, A. Arase <i>Chem. Commun.</i> 1999 , 627.			9 examples (yields 28-73%); isomeric purity generally 99%.