

# 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.

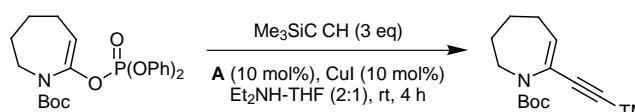
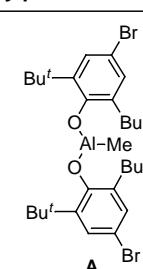
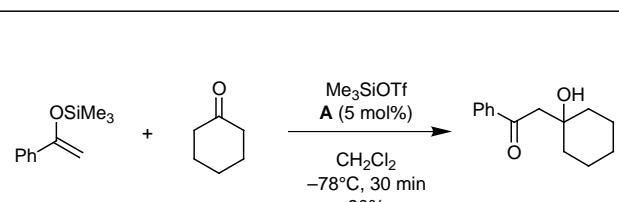
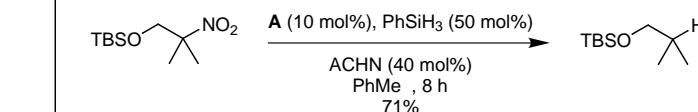
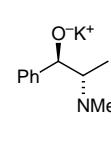
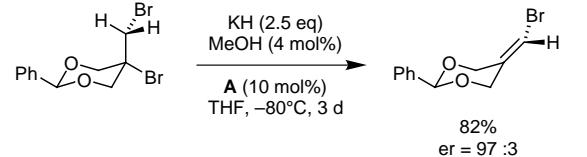
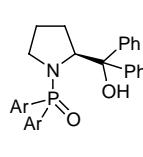
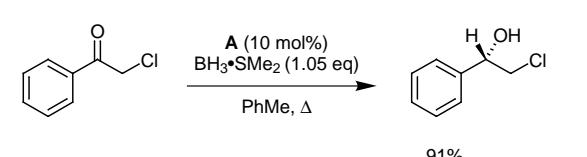
**Synthesis Alerts** is a personal selection by Stephen Brand, John Christopher, Emma Guthrie, Philip Kocienski, Louise Lea, Alastair McDonald, Graeme McAllister and Robert Narquian of Glasgow University. The journals regularly covered by the abstractors are: *Angewandte Chemie International Edition*, *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*.

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Zinc	Catalyst
<p>Synthesis of thiol esters from acyl chlorides and thiols in the presence of activated zinc is described. <b>A</b> can be recovered and reused after reactivation.</p> <p>H. M. Meshram, G. S. Reddy, K. H. Bindu, J. S. Yadav <i>Synlett</i> <b>1998</b>, 877.</p>	<p><b>Zn</b></p> <p><b>A</b></p> <p>PhSH (1 eq) A (1 eq) PhMe, rt, 5 h 90%</p> <p>18 examples (yields 89-91%).</p>

Homochiral Phosphoramido Lewis Base	Catalyst
<p>The title phosphoramido catalyses an asymmetric aldol reaction between a range of trichlorosilyl enolates and aromatic aldehydes, with high anti-diastereoselectivity and moderate to high enantioselectivity.</p> <p>S. E. Denmark, R. A. Stavenger, K.-T. Wong <i>Tetrahedron</i> <b>1998</b>, 54, 10389.</p>	<p>A (10 mol%) ArCHO (1eq) CH<sub>2</sub>Cl<sub>2</sub>, -78°C, 30 min Ar = <i>p</i>-MeO(C<sub>6</sub>H<sub>5</sub>)</p> <p>97%, anti:syn = 35:1 er<sub>anti</sub> = 96:4</p> <p>5 examples (yields 91-97%, 15:1 ≤ anti:syn ≤ 35:1).</p>

Vanadyl Acetylacetone	Catalyst
<p>Tertiary cyclopropanol systems react with a catalytic amount of <b>A</b> under an oxygen atmosphere to afford β-hydroxyketones and β-diketones.</p> <p>M. Kirihara, M. Ichinose, S. Takizawa, T. Momose <i>Chem. Commun.</i> <b>1998</b>, 1691.</p>	<p>VO(acac)<sub>2</sub> <b>A</b></p> <p>O<sub>2</sub>, EtOH, rt</p> <p>60% (1:1)</p> <p>9 examples (combined yields 46-85%).</p>

<b>Tetrakis(triphenylphosphine)palladium(0)</b>			<b>Catalyst</b>
A variety of <i>N</i> -heterocycles are synthesized from lactams via Pd(0)-catalysed couplings of their corresponding enol phosphates.	Pd(PPh <sub>3</sub> ) <sub>4</sub> <b>A</b>		
K. C. Nicolaou, G.-Q. Shi, K. Namato, F. Bernal <i>Chem. Commun.</i> <b>1998</b> , 1757.			8 examples (yields 72-93%).
<b>Methylaluminium bis(4-bromo-2,6-di-<i>tert</i>-butylphenoxide</b>			<b>Catalyst</b>
As little as 5 mol% of the title reagent enhances the catalytic activity of trialkylsilyl sulfonates in the Mukaiyama directed aldol condensation.	 <b>A</b>		The title reagent acts as a cocatalyst stabilising a silyl counteranion. 8 examples involving aldehydes and ketones. Yields 60-91%.
<b>Tributyltin Hydride</b>			<b>Reagent</b>
The catalytic reduction of nitroalkanes to alkanes with <b>A</b> is reported.	BU <sub>3</sub> SnH <b>A</b>		7 examples (yields 61-76%). ACHN = 1,1'-Azobis(cyclohexanecarbonitrile)
J. Tormo, D. S. Hays, G. C. Fu <i>J. Org. Chem.</i> <b>1998</b> , 63, 5296.			
<b>Potassium Ephedrinate</b>			<b>Catalyst</b>
The title compound allows the synthesis of axially dissymmetric 1,3-dioxanes via highly enantioselective dehydrohalogenation reactions.	 <b>A</b>		8 examples (yields 70-86%, %ee ≤ 65%).
M. Amadji, J. Vadecard, D. Cahard, L. Duhamel, P. Duhamel, J.-C. Plaquevent <i>J. Org. Chem.</i> <b>1998</b> , 63, 5541.			
<b>N-(Di-p-anisylphosphoryl)-(S)-<math>\alpha,\alpha</math>-diphenyl-2-pyrrolidinemethanol</b>			<b>Catalyst</b>
The title compound catalyses the asymmetric reduction of ketones by borane.	 <b>A</b> Ar = p-MeO(C <sub>6</sub> H <sub>4</sub> )		16 examples (yields 65-91%, %ee 56-95%).
M. P. Gamble, A. R. C. Smith, M. Wills <i>J. Org. Chem.</i> <b>1998</b> , 63, 6068.			

<b>Cobalt(II) Acetylacetone</b>		<b>Catalyst</b>
The title catalyst mediates the coupling of vinylic halides with organomagnesium reagents.	$\text{Co}(\text{acac})_2$ <b>A</b>	<p style="text-align: center;"><math>\text{A}</math> (3 mol%), NMP (4 eq) <math>n\text{-BuMgCl}</math> (1.5 eq) THF, <math>-5^\circ\text{C}</math>, 15 min 63%</p>
G. Cahiez, H. Avedissian <i>Tetrahedron Lett.</i> <b>1998</b> , 39, 6159.	13 examples (yields 36-90%). Importantly no isomerisation of secondary alkyl groups is observed. The reaction is less efficient for the introduction of tertiary alkyl groups.	

<b>Cobalt (II) Acetylacetone</b>		<b>Catalyst</b>
The title catalyst mediates the coupling of vinylic halides with organozinc reagents, with retention of alkene stereochemistry.	$\text{Co}(\text{acac})_2$ <b>A</b>	<p style="text-align: center;"><math>\text{A}</math> (25 mol%) <math>\text{AcO}(\text{CH}_2)_4\text{ZnI}</math> (3 eq) THF-NMP (5:2), <math>55^\circ\text{C}</math>, 4 h 77%</p>
H. Avedissian, L. Bérillon, G. Cahiez, P. Knochel <i>Tetrahedron Lett.</i> <b>1998</b> , 39, 6163.	7 examples (yields 50-77%) are described.	

<b>Palladium(II) Acetate</b>		<b>Catalyst</b>
The title reagent mediates the catalytic oxidation of primary and secondary alcohols, using oxygen, to their corresponding aldehydes and ketones.	$\text{Pd}(\text{OAc})_2$ <b>A</b>	<p style="text-align: center;"><math>\text{A}</math> (5 mol%), Pyridine (4 eq) <math>\text{O}_2</math> (1 atm), 3 Å MS PhMe, <math>80^\circ\text{C}</math>, 2 h 94%</p>
T. Nishimura, T. Onoue, K. Ohe, S. Uemura <i>Tetrahedron Lett.</i> <b>1998</b> , 39, 6011.	9 examples (yields 58-96%) are described.	

<b>(3S)-<i>N,N</i>-Bis(<i>p</i>-methoxybenzyl)-3-isopropylpiperazine-2,5-dione</b>		<b>Chiral Auxiliary</b>
The title auxiliary is used in the asymmetric synthesis of $\alpha$ -amino acids in high yield and with excellent diastereoselectivity.		<p style="text-align: center;">(a) LHMDS (1.1 eq) THF, <math>-78^\circ\text{C}</math>, 1 h (b) <math>\text{BnBr}</math> (2 eq) <math>-78^\circ\text{C}</math>, 3 h 88%, dr = 99:1 6 examples (yields 64-88%, %de 89-98%).</p>

<b>4-(<i>N</i>-Carbohydroxamic acid)-10,10-dimethyl-5-thia-4-azatricyclo[5.2.1.0]decane-5,5-Dioxide</b>		<b>Chiral Auxiliary</b>
The acylnitroso compound derived from <b>A</b> undergoes [4+2] cycloaddition with a range of dienes in high yield and with excellent diastereoselectivity.		<p style="text-align: center;"><math>\text{A}</math> <math>\xrightarrow[\text{CH}_2\text{Cl}_2, 0^\circ\text{C}, 15 \text{ min}]{\text{Et}_4\text{N}^+\text{IO}_4^-}</math> <math>\xrightarrow{(10 \text{ eq})}</math> 94%, dr &gt; 99:1 3 examples (yields 75-94%, %de &gt; 98%).</p>

<b>(+)-(5<i>R</i>,6<i>S</i>)-4-(Benzylloxycarbonyl)-5,6-diphenyl-2,3,5,6-tetrahydro-4<i>H</i>-1,4-oxazine-2-one</b>		<b>Chiral Auxiliary</b>
The acetoxy-oxazine derived from <b>A</b> is utilised in a Lewis acid-promoted coupling with allyltrimethylsilane in good yield and with good-excellent selectivity. The methodology is used to prepare hydroxymethylene and hydroxyethylene peptide isosteres.	<p><b>A</b></p>	<p>98%, single isomer</p> <p>3 examples (yields 22-99%).</p>
Y. Aoyagi, R. M. Williams <i>Tetrahedron</i> <b>1998</b> , <i>54</i> , 10419.		

<b>Homochiral phosphine</b>		<b>Ligand</b>
The title ligand is utilised in the palladium catalysed allylic alkylation of 2-cyclopentyl chloride with acetoxy malonate. The methodology is used in the construction of lactone <b>B</b> , a building block for several natural products.	<p><b>A</b></p>	<p>2 examples (yields 94, 96%, %ee &gt; 98%).</p> <p><b>B</b></p>
S. Kudis, G. Helmchen <i>Tetrahedron</i> <b>1998</b> , <i>54</i> , 10449.		

<b>2,2-Bis[2-((4<i>S</i>)-4,5-dihydro-4-(tert-butyl)oxazolyl)]-propane</b>		<b>Ligand</b>
A copper(I) complex derived from the title ligand catalyses the asymmetric cyclopropanation of silyl enol ethers with diazoacetates. Cyclopropane ring cleavage affords γ-ketocarboxylates in excellent yield and high stereoselectivity.	<p><b>A</b></p>	<p>5 examples (yields 46-82%, %ee = 11-96%).</p>
A. Ebinger, T. Heinz, G. Umbricht, A. Pfaltz <i>Tetrahedron</i> <b>1998</b> , <i>54</i> , 10469.		

<b>2,2-Bis[2-((4<i>S</i>)-4,5-dihydro-4-(tert-butyl)oxazolyl)]-propane</b>		<b>Ligand</b>
Copper(II) bisoxazolines prepared from the title ligand are potent catalysts for the asymmetric hetero-Diels-Alder reactions pyruvate esters and 1,2-diketones.	<p><b>A</b></p>	<p>96% (er &gt; 99:1)</p> <p>12 examples, yields 42-96% (ee 37, 77, 91-99%). Catalyst loading as little as 0.05% works in some cases.</p>
S. Yao, M. Johannsen, H. Andrain, R. G. Hazell, and K. A. Jørgensen, <i>J. Am. Chem. Soc.</i> , <b>1998</b> , <i>120</i> , 8599.		

<b>(1<i>R</i>,2<i>S</i>)-(−)-Ephedrine</b>		<b>Ligand</b>
The first example of a thermodynamically controlled enantioselective aldol reaction is reported. The chelating chiral ligand <b>A</b> mediates the addition of arylacetonitriles to aldehydes in the asymmetric, <i>anti</i> -selective synthesis of β-hydroxynitriles.	<p><b>A</b></p>	<p>86% er = 70:30</p> <p>2 examples (yields 86, 61%, %ee = 40, 77%).</p>
P. R. Carlier, W. W.-F. Lam, N. C. Wan, I. D. Williams <i>Angew. Chem. Int. Ed.</i> <b>1998</b> , <i>37</i> , 2252.		

<b>2-Methyl-6-[(1<i>S</i>,2<i>S</i>)-1,3,3-trimethyl-2-(benzylsulfanyl)-bicyclo[2.2.1]hept-2-yl]methyl]pyridine</b>		<b>Ligand</b>
The title ligand is utilised in a highly enantioselective palladium-catalysed allylic substitution.		<p>1 example is reported. BSA = Bis(trimethylsilyl)acetamide.</p>
B. Koning, A. Meetsma, R. M. Kellogg <i>J. Org. Chem.</i> <b>1998</b> , 63, 5533.		

<b>8,10-Methano-11-butyl-9,9-dimethyl-8,9,10,11-tetrahydrobenzo[b] [1,10] phenanthroline</b>		<b>Ligand</b>
Five new chiral 1,10-phenanthrolines including the title compound have been synthesised and evaluated in an enantioselective palladium catalysed allylic substitution reaction.		<p>5 examples (yields 88-95%, %ee = 4-84%). BSA = Bis(trimethylsilyl)acetamide.</p>
G. Chelucci, A. Saba <i>Tetrahedron: Asymmetry</i> <b>1998</b> , 9, 2575.		

<b>8-Diphenylphosphino-8'-methoxy-1,1'-binaphthyl</b>		<b>Ligand</b>
The title ligand mediates the enantioselective palladium-catalysed reduction of allylic esters to the corresponding olefins.		<p>6 examples (yields 41-80%, %ee 41-86%) are described. NMP = 1-Methyl-2-pyrrolidone.</p>
K. Fuji, M. Sakurai, T. Kinoshita, T. Kawabata <i>Tetrahedron Lett.</i> <b>1998</b> , 39, 6323.		

<b>Tetrabutylammonium Hydrogen Peroxide (TBAH)</b>		<b>Reagent</b>
A mild and efficient removal of camphorsultam using <b>A</b> is reported.		<p>13 examples (yields &lt;5-75%). 5 examples of the hydrolysis of hindered esters and amides using dry TBAH are also reported (yields 41-100%).</p>
T. Hasegawa, H. Yamamoto <i>Synlett</i> <b>1998</b> , 882		

<b>n-Butyllithium / Dibutylmagnesium</b>		<b>Reagent</b>
The title reagent pair metallates 2-substituted-1,3-dithianes. Results are superior to those obtained with <i>n</i> -BuLi alone.		<p>2 examples (yields 71, 85%).</p>
M. Ide, M. Yasuda, M. Nakata <i>Synlett</i> <b>1998</b> , 936.		

<b>Tetrathiafulvalene</b>		<b>Reagent</b>
<p>The radical cation of the title reagent is generated <i>in situ</i> and used in the stereoselective synthesis of the tetracyclic core of <i>Aspidosperma</i> alkaloids. Cyclisation proceeds <i>via</i> a one-pot 'radical-polar crossover'.</p> <p>R. Fletcher, M. Kizil, C. Lampard, J. A. Murphy, S. J. Roome <i>J. Chem. Soc., Perkin Trans. 1</i> <b>1998</b>, 2341.</p>		
		75%, single isomer 4 examples (yields 27-75%).

<b>Samarium(II) Iodide</b>		<b>Reagent</b>
<p>The title reagent is used in the synthesis of 6- and 7-membered rings <i>via</i> sequential ketyl-olefin coupling / intramolecular nucleophilic acyl substitution.</p> <p>G. A. Molander, M. Sono <i>Tetrahedron</i> <b>1998</b>, 54, 9289.</p>		
		18 examples (yields 0, 54-74%).

<b>Tri[(S)-2-hydroxy-1-propyl]amine</b>		<b>Reagent</b>
<p>A pre-catalyst made from the title reagent and zirconium tetra-<i>t</i>-butoxide effects enantioselective cleavage of meso epoxides using azidotrimethylsilane and allyl bromide to give O-silyl bromohydrins.</p> <p>W. A. Nugent <i>J. Am. Chem. Soc.</i> <b>1998</b>, 120, 7139.</p>		
		7 examples including 5-, 6-, 7- and 8-membered ring meso epoxides. Yields 81-92%; ee 84-96%.

<b>Toluene-<i>p</i>-sulfonylhydrazine</b>		<b>Reagent</b>
<p><i>N</i>-<i>tert</i>-Butyldimethylsilyl aldehyde tosylhydrazone prepared from the title reagent react with alkylolithium reagents to give adducts that extrude nitrogen in a free radical process</p> <p>A. G. Myers, M. Movassaghi, <i>J. Am. Chem. Soc.</i> <b>1998</b>, 120, 8891.</p>		
		16 examples. yields 78-96%. The reaction involves addition of the lithium reagent and protonation of the adduct followed by elimination of <i>p</i> -toluenesulfuric acid, protodesilylation, and loss of nitrogen. Lithium acetylides or Grignard reagents add slowly or not at all. The reaction works well with complex substrates.

<b>Tris(dimethylamino)sulfonium difluorotrimethylsilicate (TAS-F)</b>		<b>Reagent</b>
<p>The title reagent is a useful replacement for TBAF in the deprotection of TBS, TES, and TBDPS ethers, 2-(trimethylsilyl)ethyl esters and 2-(trimethylsilyl)ethyl carbamates. Base-catalysed dehydration reactions attending deprotections with TBAF are not observed.</p> <p>K. A. Scheidt, H. Chen, B. C. Follows, S. B. Chemler, D. S. Coffey, W. R. Roush <i>J. Org. Chem.</i> <b>1998</b>, 63, 6436.</p>		
		10 examples; yields 75-95%. TAS-F in DMF offers the mildest conditions reported to date for the deprotection of primary TBDPS ethers.

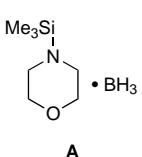
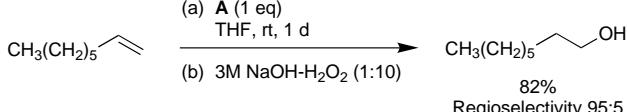
Zinc/acetyl chloride	Reagent
<p>Reduction of sulfonyl chlorides with zinc in the presence of acetyl chloride provides an efficient and cheap source of symmetrical thiosulfonic S-esters which are more reactive than disulfides as sulfenylating agents and more stable than the alternative sulphenyl chlorides.</p> <p>F. Chemla, <i>Synlett</i>, 1998, 894</p>	<p>Zn AcCl</p> <p>8 examples (yields 34-90%) including both alkyl and aryl sulfonyl chlorides. The yields are lower with alkylsulfonyl chlorides. Disulfones (<math>\text{RSO}_2\text{SO}_2\text{R}</math>) are minor byproducts in all cases and the major product in the case of <i>p</i>-iodobenzenesulfonyl chloride.</p>

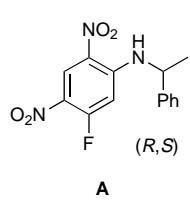
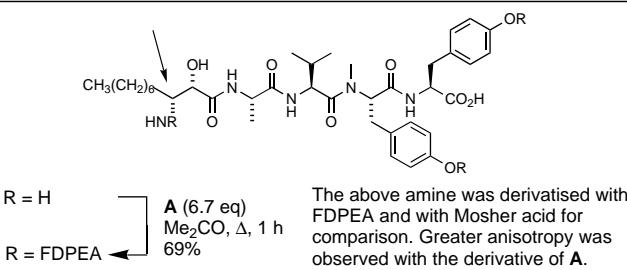
Allyldimethyltritylsilane (ADTS)	Reagent
<p>The title compound gives a variety of cyclopentanols via Lewis acid mediated annulation to electron deficient olefins.</p> <p>M. D. Groening, G. P. Brengel, A. I. Meyers <i>J. Org. Chem.</i> 1998, 63, 5517.</p>	<p><b>A</b></p>

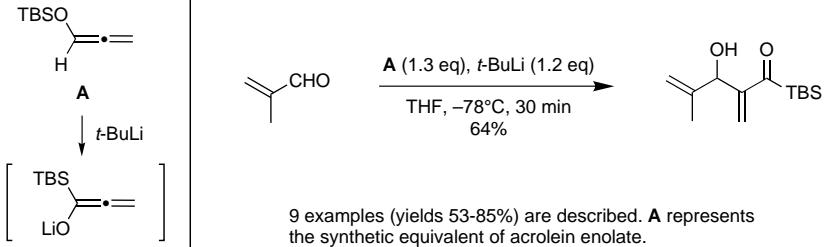
S-(1-Oxido-2-pyridinyl)-1,1,3,3-tetramethylthiouronium hexafluorophosphate	Reagent
<p>The title compound is utilised in the preparation of hindered Barton esters.</p> <p>P. Garner, J. T. Anderson, S. Dey <i>J. Org. Chem.</i> 1998, 63, 5732.</p>	

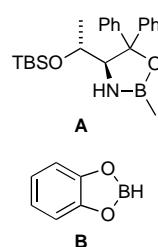
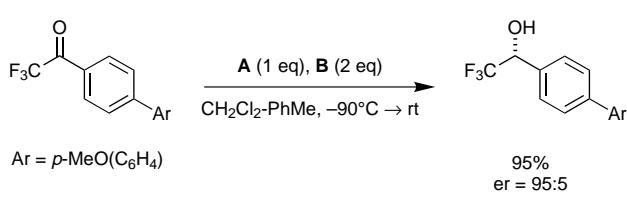
Sodium Bromate / Sodium Hydrogensulfite	Reagent
<p>The title reagent pair mediate the selective bromination of alkylbenzenes.</p> <p>D. Kikuchi, S. Sakaguchi, Y. Ishii <i>J. Org. Chem.</i> 1998, 63, 6023.</p>	<p>NaBrO<sub>3</sub> <b>A</b></p> <p>NaHSO<sub>3</sub> <b>B</b></p>

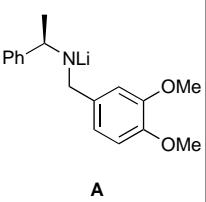
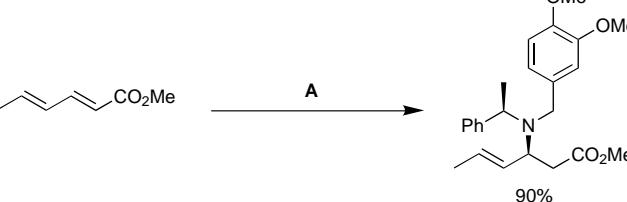
Tributylstannylidiodomethane	Reagent
<p>The title reagent is used to convert aliphatic aldehydes to their corresponding <i>E</i>-alkenyl tributylstannanes.</p> <p>D. M. Hodgson, A. M. Foley, P. J. Lovell <i>Tetrahedron Lett.</i> 1998, 39, 6419.</p>	<p>Bu<sub>3</sub>SnCH<sub>2</sub>I <b>A</b></p>

<b>Borane-N-trimethylsilyl-morpholine complex</b>			<b>Reagent</b>
The title reagent is an air-stable crystalline material which mediates the hydroboration of alkenes.			
J. A. Soderquist, J. R. Medina, R. Huertas <i>Tetrahedron Lett.</i> <b>1998</b> , <i>39</i> , 6119.	1 example is described. <b>A</b> provides a convenient alternative to other borane complexes due to its stability. Furthermore, upon aqueous work-up, <b>A</b> yields volatile or water-soluble by-products.		

<b>1-Fluoro-2,4-dinitrophenyl-5-(R,S)-phenylethylamine (FDPEA)</b>			<b>Reagent</b>
The title reagent can be used for the determination of absolute configuration of $\alpha$ -chiral primary amines. Candidates are derivatised by the displacement of fluorine in <b>A</b> .			The above amine was derivatised with FDPEA and with Mosher acid for comparison. Greater anisotropy was observed with the derivative of <b>A</b> .

<b>(t-Butyldimethylsilyloxy)allene</b>			<b>Reagent</b>
Alpha-deprotonation of the title reagent (followed by <i>O</i> to <i>C</i> silicon migration) generates a nucleophile which adds to aldehydes to give $\alpha,\beta$ -unsaturated acylsilanes.			9 examples (yields 53-85%) are described. <b>A</b> represents the synthetic equivalent of acrolein enolate.

<b>Homochiral Oxazaborolidine / Catecholborane</b>			<b>Reagent</b>
The title reagent pair mediates the enantioselective reduction of a variety of aryltrifluoromethyl ketones.			5 examples (yields 73-95%, %ee 72-90%) are described. Slightly lower enantioselectivity is observed using 10 mol% of <b>A</b> .

<b>Lithium (<math>\alpha</math>-methylbenzyl)(3,4-dimethoxybenzyl)amide</b>			<b>Reagent</b>
The title reagent behaves as a chiral differentially protected ammonia equivalent which undergoes stereoselective conjugate addition.			1 example is described.