

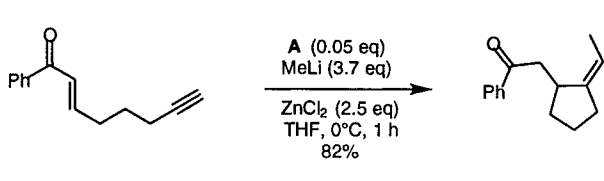
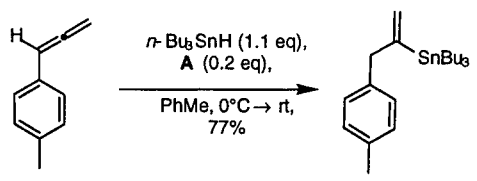
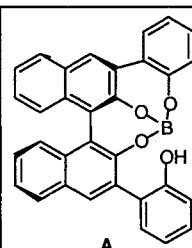
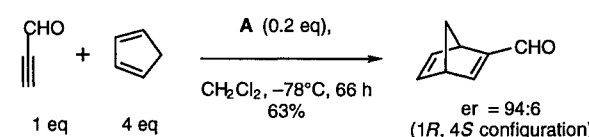
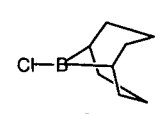
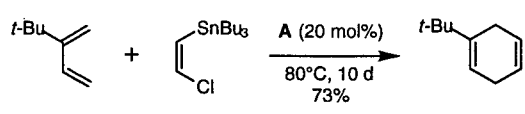
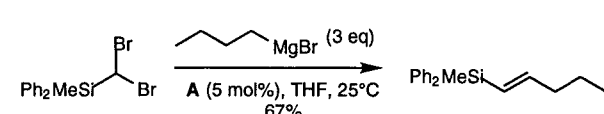
SYNTHESIS ALERTS

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, Brian Dymock, Philip Hall, Philip Kocienski, J.-Y. Le Brazidec and Alessandro Pontiroli of the University of Glasgow. The journals regularly covered by the abstractors are: *Angewandte Chemie International Edition*, *Bulletin de la Societe Chimie de France*, *Bulletin of the Chemical Society of Japan*, *Chemische Berichte*, *Chemistry Letters*, *Helvetica Chimica Acta*, *Journal of Organic Chemistry*, *Journal of Organometallic Chemistry*, *Journal of the American Chemical Society*, *Liebigs Annalen*, *Tetrahedron Letters*.

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Sodium Tungstate / Aminomethyl Phosphoric Acid / Methyl(trioctylammonium)hydrogensulfate		Catalyst
<p>The title catalysts effect the epoxidation of olefins with 30% H₂O₂ under halide free conditions with good yields. This method is operationally simple, environmentally benign, economical and may be conducted on a large scale.</p> <p>K. Sato, M. Aoki, M. Ogawa, F. Hashimoto, D. Panyella, R. Noyori <i>Bull. Chem. Soc. Jpn.</i> 1997, <i>70</i>, 905.</p>	$\begin{matrix} \text{Na}_2\text{WO}_4 \cdot 2\text{H}_2\text{O} \\ \text{H}_2\text{NCH}_2\text{PO}_3\text{H}_2 \\ [\text{CH}_3(\text{n-C}_8\text{H}_{17})_3\text{N}]\text{HSO}_4 \\ (2:1:1) \end{matrix}$ <p>A</p>	<p>Yields are generally >85%.</p> <p>This full paper contains examples with various substrates including terminal olefins, 1,1-di-, 1,2-di-, tri- and tetra- substituted olefins, cyclic olefins, allylic alcohols and esters, α,β-unsaturated ketones and ethers.</p>
Titanocene Dicarboxyl		Catalyst
<p>Titanocene-catalyzed cyclocarbonylation of <i>o</i>-allyl aryl ketones to γ-butyrolactones.</p> <p>N. M. Kablaoui, F. A. Hicks, S. L. Buchwald <i>J. Am. Chem. Soc.</i> 1997, <i>119</i>, 4424.</p>	$\text{Cp}_2\text{Ti}(\text{CO})_2$ <p>A</p>	<p>(10 examples)</p>
Gallium Lithium Bis(binaphthoxide) Complex		Catalyst
<p>A highly enantioselective ring opening of epoxides with thiols catalyzed by a gallium lithium bis(binaphthoxide) complex.</p> <p>T. Iida, N. Yamamoto, H. Sasai, M. Shibasaki <i>J. Am. Chem. Soc.</i> 1997, <i>119</i>, 4783.</p>	<p>A</p>	<p>Molecular sieves dramatically increased the efficiency of this reaction (8 examples).</p>

Bis(cyclooctadiene)nickel(0)		Catalyst
Nickel-catalyzed organozinc-promoted carbocyclizations of electron deficient alkenes with tethered unsaturation.	$\text{Ni}(\text{COD})_2$ A	 <p>A (0.05 eq) MeLi (3.7 eq) ZnCl₂ (2.5 eq) THF, 0°C, 1 h 82% (17 examples)</p>
J. Montgomery, E. Oblinger, A. V. Savchenko <i>J. Am. Chem. Soc.</i> 1997 , <i>119</i> , 4911.		
Tris(pentafluorophenyl)borane		Catalyst
Catalyses the hydrostannylation of allenes in a highly regioselective manner to give vinylstannanes, whereby the tin atom becomes attached to the central carbon of the allene system.	$\text{B}(\text{C}_6\text{F}_5)_3$ A	 <p><i>n</i>-Bu₃SnH (1.1 eq), A (0.2 eq), PhMe, 0°C → rt, 77%</p> <p>Catalysis by Pd(PPh₃)₄ resulted in attachment of tin to the distal terminus of the allene. 8 examples given.</p>
V. Gevorgyan, J.-X. Liu, Y. Yamamoto, <i>J. Org. Chem.</i> 1997 , <i>62</i> , 2963.		
(R)-3,3'-Bis(2-hydroxyphenyl)-2,2'-dihydroxy-1, 1'-binaphthylborate		Catalyst
Catalyst for the asymmetric Diels-Alder reaction between acetylenic aldehydes and dienes.	 A	 <p>A (0.2 eq), CH₂Cl₂, -78°C, 66 h 63% er = 94:6 (1<i>R</i>, 4<i>S</i> configuration) 5 examples using different substrates and 3 different catalysts.</p>
K. Ishihara, S. Kondo, H. Kurihara, H. Yamamoto <i>J. Org. Chem.</i> , 1997 , <i>62</i> , 3026.		
B-Chloro-9-borobicyclo[3.3.1]nonane		Catalyst
Catalyses the Diels-Alder reaction between <i>cis</i> -2-chlorovinyltributylstannane and simple dienes <i>via</i> temporary covalent activation of the dienophile.	 A	 <p>A (20 mol%) 80°C, 10 d 73%</p> <p>3 other examples employing borane catalysts (yields 71-78%). An alternative hydroboration-DA-dehydroboration sequence is also examined.</p>
D. A. Singleton, S.-W. Leung, J. P. Martinez, Y.-K. Lee <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 3163.		
Manganese(II) Chloride		Catalyst
Treatment of dibromomethyltrialkylsilanes with alkyl Grignard reagents in the presence of A provides <i>E</i> -vinylsilanes in good yield with excellent stereoselectivity.	MnCl_2 A	 <p>MgBr (3 eq) A (5 mol%), THF, 25°C 67%</p> <p>A preformed stoichiometric manganese reagent, R₃MnMgBr, can also be utilised. 15 examples (yields 62-96%). In each case no trace of the <i>cis</i> isomer was detected.</p>
H. Kakiya, R. Inoue, H. Shinokubo, K. Oshima <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 3275.		

Hexabutylguanidinium Chloride		Catalyst
The title reagent catalyses the decomposition of alkyl chloroformates to afford the corresponding alkyl chlorides. The reaction occurs with clean inversion of configuration.		
F. Foulon, B. Fixari, D. Picq, P. Le Perchec <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 3387.		Significant racemisation occurs if the above reaction is conducted in a polar solvent. Primary chloroformates react rapidly in PhCl at 100°C (3 examples, yields 100%).
[1,1'-Bis(diphenylphosphino)ferrocene]nickel(II) Chloride		Catalyst
The title reagent is an effective catalyst for the Suzuki cross-coupling of aryl chlorides with aryl boronic acids.		
A. F. Indolese <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 3513.		15 examples (yields 0, 26-95%). dppf = 1,1'-bis(diphenylphosphino)ferrocene
(S)-3-(Cyclohexylamino)-N-benzylpyrrolidine		Chiral Auxiliary
3-Aminopyrrolidine lithium amide in enantioselective addition of organolithium compounds onto aromatic aldehydes.		
A. Corruble, J.-Y. Valnot, J. Maddaluno, P. Duhamel <i>Tetrahedron: Asymmetry</i> 1997 , <i>8</i> , 1519.		The effect of the alkyl group on the 3-amino functional group was studied (8 examples) and several aldehydes were tested (3 examples).
(1R,5S,8S)-8-Isopropyl-4,4-dimethyl-7-(4-toluenesulfonyl)-3-oxa-1,7-diazabicyclo[3.3.0]octane		Chiral Auxiliary
The easily prepared isoxazolidine A is readily acylated under mild conditions. The derived amides undergo highly diastereoselective alkylation and aldol reactions.		
A. Abiko, J.-F. Liu, G. Wang, S. Masamune <i>Tetrahedron Lett.</i> 1997 , <i>38</i> , 3261.		6 examples of aldol reactions (yields 90-93%, <i>syn:anti</i> > 98:2, %de > 92%) and 7 examples of alkylation (yields 90-97%, %de = 92%). Products can be easily converted to alcohols, aldehydes or ketones <i>via</i> one-step procedures.
(S)-(+)-4-(2-Methylpropyl)-2-(2-pyridyl)-2-oxazoline		Ligand
Homoallylic alcohols may be prepared with good <i>anti</i> -diastereoselectivity and moderate enantioselectivity from condensation of aromatic aldehydes with (<i>E</i>)-but-2-enyltrichlorosilane in the presence of the title ligand.		
R. M. Angell, A. G. M. Barrett, D. C. Braddock, S. Swallow, B. D. Vickery <i>Chem. Commun.</i> 1997 , 919.		6 examples; yields 66-91%; %ee = 36-74%.

Ligand		
(S)-5,5',6,6',7,7',8,8'-Octahydro-1,1'-bi-2-naphthol		
Novel asymmetric alkylation of aromatic aldehydes with triethylaluminum catalyzed by BINOL and H ₈ -BINOL.		 100%, er = 98.2:1.8
A. S. C. Chan, F.-Y. Zhang, C.-W. Yip <i>J. Am. Chem. Soc.</i> 1997 , <i>119</i> , 4080.		Good enantioselectivities were obtained starting from aromatic aldehydes (9 examples) but are lower using AlMe ₃ as alkylating reagent.
Ligand		
(S,S)-2,2'-Bis[4-(isopropyl)oxazolyl]-1,1'-binaphthyl		
Catalytic asymmetric Wacker-type cyclization.		 (5 examples) 75%, er = 98:2
Y. Uozumi, K. Kato, T. Hayashi <i>J. Am. Chem. Soc.</i> 1997 , <i>119</i> , 5063.		
Ligand		
(2S,5R)-5-Isopropyl-3-phenyl-2-pyridin-2-ylthiazolidin-4-one		
Diastereoselective synthesis of pyridyl substituted thiazolidin-4-ones: new ligands for the Cu(I) catalyzed asymmetric conjugate addition of diethylzinc to enones.		 95%, er = 81:19
A. H. M. de Vries, R. P. Hof, D. Staal, R. M. Kellogg, B. L. Feringa <i>Tetrahedron: Asymmetry</i> 1997 , <i>8</i> , 1539.		This asymmetric conjugate addition was carried out using ligands with different substitution patterns (4 examples).
Ligand		
(1S,2R)-2-(cis-2,6-dimethyl-1-piperidino)indan-1-ol		
Synthesis of new indane-derived amino alcohols as chiral ligands: application to the enantioselective addition of diethylzinc to aldehydes.		 93%, er = 90:10
L. Solà, A. Vidal-Ferran, A. Moyano, M. A. Pericàs, A. Riera <i>Tetrahedron: Asymmetry</i> 1997 , <i>8</i> , 1559.		The substitution of the amino functional group was studied and several aldehydes tested (8 examples).
Reagent		
(2R)-N-(Acryloyl)bornane-10,2-sultam		
The Asymmetric Baylis-Hillman reaction: application to the synthesis of tulipalin B.		 98%, er = 99.5:0.5
L. J. Brzezinski, S. Rafel, J. W. Leahy <i>J. Am. Chem. Soc.</i> 1997 , <i>119</i> , 4317.		Excellent enantioselectivities were obtained from several aldehydes (7 examples) but this reaction did not work using benzaldehyde.

(S)-1-(Benzyloxy)ethyl Acetate		Reagent
Synthesis and Lewis acid catalyzed nucleophilic substitution of chiral 1-alkoxyalkyl carboxylates.		$\text{A} \xrightarrow[\text{Ether/hexane, } -78^\circ\text{C, 0.5 h}]{\text{(Bu)}_2\text{CuLi (3 eq), BF}_3\cdot\text{OEt}_2 \text{ (3 eq)}} \text{BnO-CH(CH}_3\text{)-Bu}$ <p>53%, er = 93:7</p> <p>1-Alkoxyalkyl carboxylate A was prepared by a Baeyer-Villiger oxidation of the corresponding α-alkoxy ketone (12 examples).</p>
H. Matsutani, S. Ichikawa, J. Yaruva, T. Kusumoto, T. Hiyama <i>J. Am. Chem. Soc.</i> 1997 , <i>119</i> , 4541.		
(1R,2R)-(Dicarbonyl-η^5-cyclopentadienyliron){η^2-1-[(<i>p</i>-methoxybenzyl)oxy]propene} Tetrafluoroborate		Reagent
Reaction with copper enolates leads to optically active 3-hydroxy-2-methyl-5-oxo esters, after redox-promoted alkoxy carbonylation		$\text{2.2 eq} \xrightarrow[\text{THF, } -78^\circ\text{C, 30 min}]{\text{A (1 eq)}} \text{Intermediate} \xrightarrow[\text{THF, } -78^\circ\text{C}]{\text{CAN (5 eq), NaOMe (5 eq), CO}}$ <p>Overall yield = 40%</p> <p>Several examples given illustrating the versatility of this reagent.</p>
W. Zhen, K.-H. Chu, M. Rosenblum <i>J. Org. Chem.</i> , 1997 , <i>62</i> , 3344.		
4-Phenyl-1,3-oxazolidinone		Reagent
Treatment of either <i>R</i> or <i>S</i> forms of the oxazolidinones with strong base generates stabilised nitrogen anions capable of undergoing diastereoselective Michael addition to nitroolefins.		$\text{A} \xrightarrow[\text{THF, } 0^\circ\text{C, 1 h}]{t\text{-BuOK (1 eq), 18-C-6 (1 eq)}} \text{Intermediate} \xrightarrow[\text{THF, } -78^\circ\text{C, 15 min}]{\text{Nitroolefin}}$ <p>87%, dr >99:1</p>
D. Lucet, L. Toupet, T. Le Gall, C. Mioskowski, <i>J. Org. Chem.</i> 1997 , <i>62</i> , 2682.		
1,4-Diazabicyclo[2.2.2]octane		Reagent
Used in the palladium catalysed coupling of <i>o</i> -haloanilines with ketones to give indoles.		$\text{1 eq} \xrightarrow[\text{DMF, } 105^\circ\text{C, 3 h}]{\text{Pd(OAc)}_2 \text{ (0.05 eq), A (3 eq)}} \text{Indole}$ <p>72%</p> <p>11 examples: acyclic ketones are less effective in the coupling though acylsilanes and pyruvic acid also couple efficiently.</p>
C. Chen., D. R. Lieberman, R. D. Larsen, T. R. Verhoeven, P. J. Reider <i>J. Org. Chem.</i> 1997 , <i>62</i> , 2676.		
Allyl(2-chloroethyl)dimethylsilane		Reagent
Treatment with magnesium generates the corresponding Grignard reagent. Following nucleophilic attack, the silyl group may be oxidatively transposed to an alcohol. Hence the title reagent can be considered as a synthon for the β -hydroxyethyl group.		$\text{A} \xrightarrow[\text{(b) PhCHO, } 0^\circ\text{C}]{\text{(a) Mg, THF}} \text{Intermediate} \xrightarrow[\text{(b) NaHCO}_3, \text{H}_2\text{O}_2]{\text{(a) KHF}_2, \text{TFA, CHCl}_3}$ <p>65% (to intermediate), 78% (to final product)</p> <p>10 examples of nucleophilic reactions with aldehydes, ketones and epoxides.</p>
A.M. Klos, G.R. Heintzelman, S.M. Weinreb <i>J. Org. Chem.</i> 1997 , <i>62</i> , 3758.		

Methoxytrimethylsilane		Reagent
<p>Glycosidic spiro-orthoesters are prepared from sugar lactones and diols by treatment with A in the presence of a catalytic amount of trimethylsilyl triflate.</p> <p>H. Ohtake, T. Iimori, S. Ikegami <i>Tetrahedron Lett.</i> 1997, <i>38</i>, 3413.</p>	<p>MeOSiMe₃</p> <p>A</p>	<p>A (10 eq) TMSOTf (2 mol%) PhMe rt, 1.5 h 77%</p> <p>3 examples (yields 77-87%).</p>
Lithium Aluminium Hydride / Aluminium Chloride		Reagent
<p>The title reagent pair effect the highly regio-selective reductive cleavage of glycosidic spiro-orthoesters to yield β-glycosides.</p> <p>Together with the preceding paper this work constitutes a novel glycosylation protocol.</p> <p>T. Iimori, H. Ohtake, S. Ikegami <i>Tetrahedron Lett.</i> 1997, <i>38</i>, 3415.</p>	<p>LiAlH₄</p> <p>A</p> <p>AlCl₃</p> <p>B</p>	<p>A (2 eq) B (2 eq) CH₂Cl₂ - Et₂O rt, 2 h 98%</p> <p>3 examples (yields 92-98%).</p>
<i>t</i>-Butyl isocyanide / <i>n</i>-Butyl isocyanate		Reagent
<p>Primary nitro compounds are transformed into nitriles by treatment with the title reagents.</p> <p>L. E. Kaim, A. Gacon <i>Tetrahedron Lett.</i> 1997, <i>38</i>, 3391.</p>	<p>A</p> <p>B</p>	<p>A (2.2 eq) B (3 eq), Et₃N (1 eq) PhMe, 80°C, 3 d 70%</p> <p>6 examples (yields 57-86%). α,β-Unsaturated nitriles are formed more rapidly (2-3 h).</p>
Bis(pinacolato)diboron		Reagent
<p>The title reagent participates in cross-coupling reactions with aryl triflates under Pd(0) catalysis to yield useful aryl boronates.</p> <p>T. Ishiyama, Y. Itoh, T. Kitano, N. Miyaura <i>Tetrahedron Lett.</i> 1997, <i>38</i>, 3447.</p>	<p>A</p>	<p>A (1.1 eq) PdCl₂(dppf) (3 mol%) dppf (3 mol%) KOAc (3 eq) dioxane, 80°C, 1 d 81%</p> <p>11 examples (yields 64-93%). As expected electron-deficient aryl triflates show enhanced reactivity.</p> <p>dppf = 1,1'-bis(diphenylphosphino)ferrocene</p>
Dimethylphosgeniminium Chloride		Reagent
<p>Efficiently converts THP-protected alcohols into alkyl chlorides.</p> <p>T. Schlama, V. Gouvernour, C. Mioskowski <i>Tetrahedron Lett.</i> 1997, <i>38</i>, 3517.</p>	<p>A</p>	<p>A (1.05 eq) CH₂Cl₂, 0°C 95%</p> <p>8 examples (yields 30-95%). Addition of tetrabutylammonium bromide to the reaction mixture yields the corresponding alkyl bromides.</p>