

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, Stephen Brand, John Christopher, Emma Guthrie, Philip Kocienski, Louise Lea, Graham McAllister, Russell McDonald 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, Chemistry A European Journal, Chemistry Letters, European Journal of Organic Chemistry, Helvetica Chimica Acta, Heterocycles, Journal of Organic Chemistry, Journal of the American Chemical Society, Organometallics, Synlett, Synthesis, Tetrahedron, Tetrahedron Asymmetry and Tetrahedron Letters.

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Scandium(III) Trifluoromethanesulfonate			Catalyst
A catalyses the Friedel-Crafts alkylation of a range of aromatic compounds with methanesulfonates derived from secondary alcohols.	Sc(OTf) ₃ A		A (10 mol%) Mesitylene, 80°C, 2 h 93%

H. Kotsuki, T. Oshisi, M. Inoue *Synlett* **1998**, 255.

11 examples (yields 36-98%). The catalyst can be reused without a significant loss of activity.

Chiral (Salen) Mn(III) Complex / Ammonium Acetate			Catalyst
The title reagent pair catalyse the asymmetric epoxidation of various unfunctionalised olefins by hydrogen peroxide.	 A : R = t-Bu, Mn complex with a chiral salen ligand. B : NH ₄ OAc		A (5 mol%), B (20 mol%) H ₂ O ₂ (3 eq) CH ₂ Cl ₂ -MeOH (1:1), 2°C, 1.25 h (+) 90%, er = 96:4

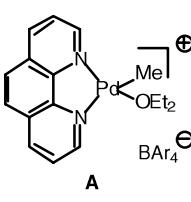
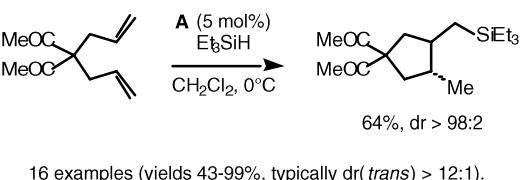
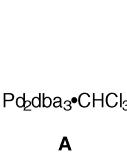
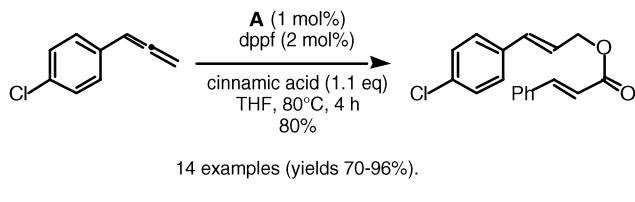
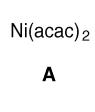
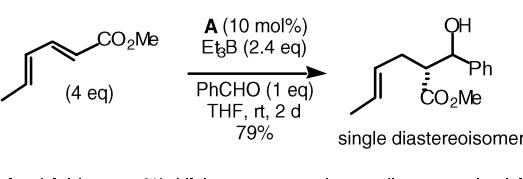
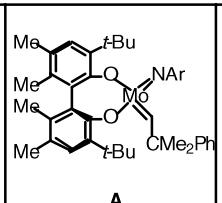
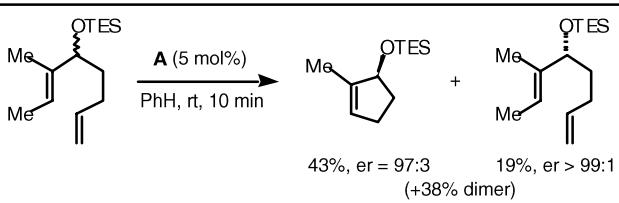
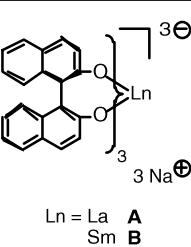
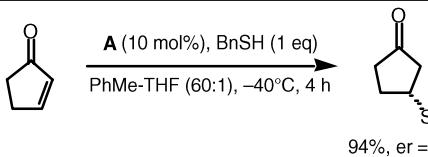
P. Pietikäinen *Tetrahedron* **1998**, 54, 4319.

3 examples given (yields 71-90%, %ee 84-96%).

Microencapsulated Scandium(III) Trifluoromethanesulfonate			Catalyst
Polystyrene microcapsules (MC) of scandium(III) triflate were found to catalyse a wide variety of reactions (e.g. imino aldol, aldol, Mannich, Michael, Friedel-Crafts acylation). The microencapsulated form of the Lewis acid was found to be more active than monomeric material and could be recovered via simple filtration.	MC Sc(OTf) ₃ A		1st use of A , 92% 2nd use of A , 97% 3rd use of A , 95%

S. Kobayashi, S. Nagayama *J. Am. Chem. Soc.* **1998**, 120, 2985.

Various reactions are illustrated (yields >76%). In each case no decrease in activity was noted when the catalyst was re-used in subsequent transformations. The simple preparation of the catalyst is described.

1,10-Phenanthroline-Palladium(I) Complex		Catalyst
The title reagent catalyses the tandem cyclisation/hydrosilylation of functionalised 1,6-dienes to afford the corresponding <i>trans</i> cyclopentanes. R. A. Widenhoefer, M. A. DeCarli <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 3805	 <p>A Ar = 3,5-bis(trifluoromethyl)phenyl</p>	 <p>16 examples (yields 43-99%, typically dr(<i>trans</i>) > 12:1).</p>
Tris(dibenzylideneacetone)dipalladium(0)-Chloroform Adduct		Catalyst
The title reagent catalyses the regio- and stereoselective hydrocarboxylation of arylallenenes. M. Al-Masum, Y. Yamamoto <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 3809.	 <p>A</p>	 <p>dppf = 1,1'-bis(diphenylphosphino)ferrocene 14 examples (yields 70-96%).</p>
Nickel(II) Acetylacetone		Catalyst
The title reagent catalyses the homoallylation of benzaldehyde with 1,3-dienes. M. Kimura, A. Ezoe, K. Shibata, Y. Tamari <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 4033.	 <p>A</p>	 <p>single diastereoisomer 10 examples (yields 55-95%). High 1,2-, 1,3- and 1,2,3-diastereoselectivities are typically obtained (1,3-anti:syn > 15:1, 1:15 < 1,2-anti:syn < 5.2:1).</p>
Molybdenum Metathesis Catalyst		Catalyst
The title reagent catalyses the asymmetric ring-closing metathesis (ARCM) of racemic 1,6-dienes. J. B. Alexander, D. S. La, D. R. Cefalo, A. H. Hoveyda, R. R. Schrock <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 4041.	 <p>A Ar = 2,5-diisopropylphenyl</p>	 <p>43%, er = 97:3 19%, er > 99:1 (+38% dimer) 8 examples (product yields <5, 40-55%, %ee <5, 45-93%; recovered diene 17-50%, %ee <5, 57, 91-99%).</p>
Sodium Lanthanum Tris(binaphthoxide)		Catalyst
The title reagent catalyses the enantioselective Michael addition of thiols to cycloalkenones. Analogous complex B catalyses enantioselective protonation in the Michael addition of thiols to acyclic thioenoates. E. Emori, T. Arai, H. Sasai, M. Shibusaki <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 4043.	 <p>A Ln = La B Sm</p>	 <p>94%, er = 78:22 6 examples of enantioselective conjugate addition employing A (yields 56-94%, %ee 56-90%). 5 examples of asymmetric protonation in Michael reactions employing B (yields 50-98%, %ee 75-93%).</p>

Butylstannonic Acid		Catalyst
The title catalyst mediates the transesterification of esters under mild conditions.		<p>12 examples (yields 0, 46–100%) are described. The use of A in the acetylation / deacetylation of alcohols is also described.</p>
R. L. E. Furlán, E. G. Mata, O. A. Mascaretti <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 2257.		
N-(1,2,3,4,6,7,8,9-Octahydroanthracenesulfonyl)ephedrine		Chiral Auxiliary
The title auxiliary mediates the stereoselective aldol reaction of propionate derivatives.		<p>For: R = <i>n</i>-Bu, <i>i</i>-Pr2NEt, 95% <i>syn:anti</i> = 93:7 <i>dr</i> = 97:3</p> <p>For: R = <i>c</i>-hex, NEt3, 95% <i>anti,syn</i> = 98:2 <i>dr</i> = 86:14</p>
J.-F. Liu, A. Abiko, Z. Pei, D. C. Buske, S. Masamune <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 1873.		
17-Diphenylphosphino-2,5,8,11,14-pentaoxabicyclo[13.4.0]nonadeca-15,17,19-triene		[PPh₂(bc-5)] Ligand
A Palladium(0) complex derived from the title ligand catalyses the cyanation of aryl halides with sodium cyanide.		<p>6 examples (yields 85–93%).</p>
T. Okano, M. Iwahara, J. Kiji <i>Synlett</i> 1998 , 243.		
N-[2-(Diphenylphosphino)benzylidene]-2-phenylethylamine		Ligand
A palladium(0) complex derived from the title ligand effects the <i>syn</i> selective carbostannylation of acetylenes by alkynyl stannanes.		<p>10 examples (yields 52–82%). Addition is always exclusively <i>syn</i> although regioselectivity is highly substrate dependent.</p>
E. Shirakawa, H. Yoshida, T. Kurahashi, Y. Nakao, T. Hiyama <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 2975.		
(R,R)-4,6-Dibenzofurandiyl-2,2'-bis(4-phenyloxazoline) (DBFOX/Ph)		Ligand
Various cationic aqua complexes derived from the title ligand and transition metal(II) perchlorates catalyse highly enantioselective Diels-Alder reactions. The catalytic species are reasonably robust and can exhibit extreme chiral amplification.		<p>The above reaction is extensively investigated in all regards (Mg, Mn, Fe, Cu, Zn, Co, Cr, Ga metal complexes are all studied). All yields and enantioselectivities are excellent in optimised cases (comparable to the illustrated example).</p>
S. Kanemasa, Y. Oderaotoshi, S. Sakaguchi, H. Yamamoto, J. Tanaka, E. Wada, D. P. Curran <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 3074.		

Bis(dihydroquininyl)anthraquinone		Ligand
<p>The title ligands mediate the regioselective aminoxylation of cinnamates to phenyl serines with high enantioselectivity.</p> <p>B. Tao, G. Schlingloff, K. B. Sharpless <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 2507.</p>	<p>A Alk* = dihydroquininyl B Alk* = quinidinyl</p>	<p>X (4 mol%) $K_2[OsO_4(OH)_4]$ (4 mol%) <i>t</i>-BuOCl (3.1 eq) BnOC(=O)NH₂ (3.1 eq) <i>n</i>-PrOH, rt, 1.5 h</p> <p>X = A: 58% (2<i>R</i>,3<i>S</i>) er = 98:2</p> <p>X = B: 62% (2<i>S</i>,3<i>R</i>) er = 96:4</p> <p>8 enantiocomplementary examples (yields 40–68%, %ee 87–96) are described.</p>

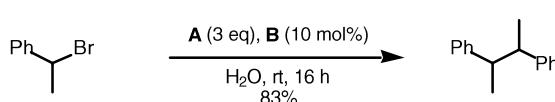
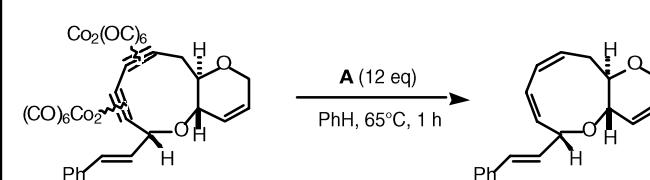
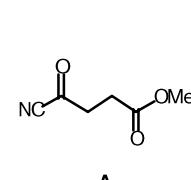
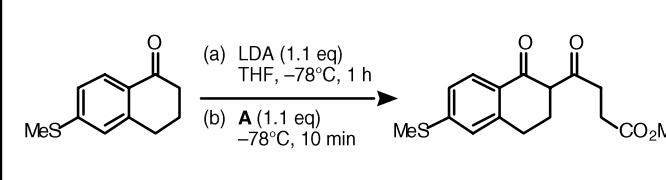
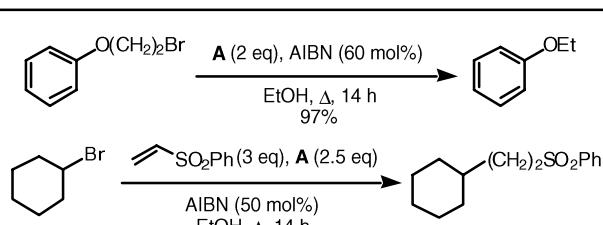
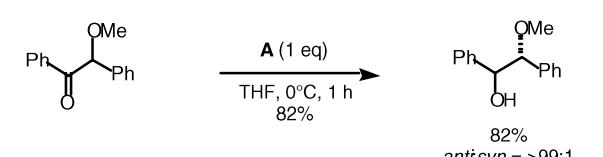
Phenyldimethylsilyllithium		Reagent
<p>Lithium enolates are prepared from silyl enol ethers using the title reagent.</p> <p>I. Fleming, R. S. Roberts, S. C. Smith <i>J. Chem. Soc., Perkin Trans 1</i> 1998, 1209.</p>	<p>A</p>	<p>PhMe₂SiLi A (11 eq) THF, -78°C 10 min → PhC(=O)Li PhC(=O)Li + MeI (11 eq) THF, -78°C → rt 77%</p> <p>2 examples (yields 74, 77%).</p>

Phenyldimethylsilyllithium		Reagent
<p>Toluene-<i>p</i>-sulfonamides of secondary amines and indoles are cleaved by the title reagent in good yield.</p> <p>I. Fleming, J. Frackenpohl, H. Ila <i>J. Chem. Soc., Perkin Trans 1</i> 1998, 1229.</p>	<p>A</p>	<p>PhMe₂SiLi A (3 eq) THF, 0°C, 6 h 91%</p> <p>7 examples (yields 72–91%). Aziridine toluene-<i>p</i>-sulfonamides are opened by A to give β-silylethyl sulfonamides.</p> <p>Ts = <i>p</i>-toluenesulfonyl</p>

(Trifluoromethyl)trimethylsilane		Reagent
<p>A novel nucleophilic trifluoromethylation of esters with A is reported. The ester functionality is converted into the trifluoromethylcarbonyl group without formation of double addition products and the reaction is applicable to both enolisable and non-enolisable esters.</p> <p>J. Wiedemann, T. Heiner, G. Mloston, G. K. S. Prakash, G. A. Olah <i>Angew. Chem. Int. Ed.</i> 1998, <i>37</i>, 820.</p>	<p>A</p>	<p>Me₃SiCF₃ A (1.25 eq) TBAF (2.5 mol%) Pentane, -78°C → rt, 24 h 85%</p> <p>8 examples (yields 0, 68–95%).</p>

Titanocene Dichloride		Reagent
<p>A 3-step synthesis of indoles is described. Pivotal aryl alkyl dibromide intermediates are realised via regioselective insertion of an olefin into a titanocene benzyne complex.</p> <p>K. Aoki, A. J. Peat, S. L. Buchwald <i>J. Am. Chem. Soc.</i> 1998, <i>120</i>, 3068.</p>	<p>A</p>	<p>(a) A (0.9 eq) PhMe, rt, 1 h (b) CH₂=CHBu (2 eq) MeMgBr (1 eq) 50°C, 4 h (c) Br₂ (2 eq) CH₂Cl₂, -78°C</p> <p>Subsequent annulation with BnNH₂ under Pd(0) catalysis, followed by deprotection/oxidation affords indole products. 10 examples (yields (3–4 steps) 18–54%).</p>

2,2'-Azobisisobutyronitrile (AIBN) / Tributyltin Hydride			Reagent
Tin(IV) radical enolates formed by the action of $\text{Bu}_3\text{Sn}^\bullet$ on α -allyloxy enones undergo facile [3,3]-sigmatropic rearrangement.			6 examples (yields 51-74%).
E. J. Enholm, K. M. Moran, P. E. Whitley, M. A. Battiste <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 3807.			
Lithium Diisopropylamide (LDA)			Reagent
Ortho metallation of arenes with A utilising a neopentyl ester as a directing group is reported.			8 examples (yields 52-93%).
S. Caron, J. M. Hawkins <i>J. Org. Chem.</i> 1998 , <i>63</i> , 2054.			
(+)-N-Fluoro-2,10-(3,3-dichlorocamphorsultam)			Reagent
The title compound mediates the electrophilic asymmetric fluorination of enolates.			6 examples (yields <5-95%, %ee 0-76%).
F. A. Davis, P. Zhou, C. K. Murphy, G. Sundarababu, H. Qi, W. Han, R. M. Przeslawski, B.-C. Chen, P. J. Carroll <i>J. Org. Chem.</i> 1998 , <i>63</i> , 2273.			
Samarium(II) Iodide / Tetrakis(triphenylphosphine) Palladium			Reagent
The title reagent pair mediates the ring contraction of methyl 5-vinylpyranosides to 2-vinyl cyclopentanols with moderate <i>trans</i> selectivity.			54% dr = 96:4 24% dr = 68:32
J. M. Aurrecoechea, B. López <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 2857.			
Iodine			Reagent
Iodine in methanol mediates the selective cleavage of alkyl silyl ethers in the presence of aryl silyl ethers.			97%
B. H. Lipshutz, J. Keith <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 2495.			

Manganese / Copper(II) Chloride			Reagent
The title reagent pair mediates the homo- and cross-coupling of alkyl halides in aqueous media.	Mn A CuCl ₂ B		A (3 eq), B (10 mol%) H ₂ O, rt, 16 h 83%
J. Ma, T.-K. Chan <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 2499.			8 examples of homo-coupling (yields 52-100%) and 2 examples of cross-coupling with an allyl bromide (yields 62, 79%) are described.
Tributyltin Hydride			Reagent
The title reagent mediates the reductive decomplexation of acetylene biscobalhexacarbonyl complexes to form the corresponding <i>cis</i> alkenes.	<i>n</i> -Bu ₃ SnH A		A (12 eq) PhH, 65°C, 1 h
S. Hosokawa, M. Isobe <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 2609.			8 examples (yields 35-82%) are described. A similar decomplexation using triethylsilane gives <i>cis</i> -vinylsilanes.
Carbomethoxypropionyl Cyanide			Reagent
The title reagent reacts regioselectively with ketone enolates to form 1,3-dicarbonyl compounds.			(a) LDA (1.1 eq) THF, -78°C, 1 h (b) A (1.1 eq) -78°C, 10 min
Q. Tang, S. E. Sen <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 2249.			6 examples (yields 73-95%) of <i>C</i> -acylation under kinetic and thermodynamic conditions are described.
1,1,2,2-Tetraphenyldisilane			Reagent
The title reagent participates in the reduction of alkyl bromides, addition to alkenes and alkylation of heterocyclic bases.	Ph ₂ Hsi-SiHPh ₂ A		A (2 eq), AIBN (60 mol%) EtOH, Δ, 14 h 97% PhSO ₂ Ph (3 eq), A (2.5 eq) AIBN (50 mol%) EtOH, Δ, 14 h 78%
O. Yamazaki, H. Togo, S. Matsubayashi, M. Yokoyama <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 1921.			26 examples are described.
Dichloroiridium Hydride			Reagent
Dichloroiridium hydride mediates the reduction of aldehydes, ketones and alkyl halides.	InCl ₃ $\xrightarrow[n\text{-}Bu_3\text{SnH}]{\text{THF}, -78^\circ\text{C}}$ Cl ₂ InH A		A (1 eq) THF, 0°C, 1 h 82% anti:syn = >99:1
T. Miyai, K. Inoue, M. Yasuda, I. Shibata, A. Baba <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 1929.			16 examples (yields 23-99%) are described. Nitro, cyano and ester groups are unreactive.