

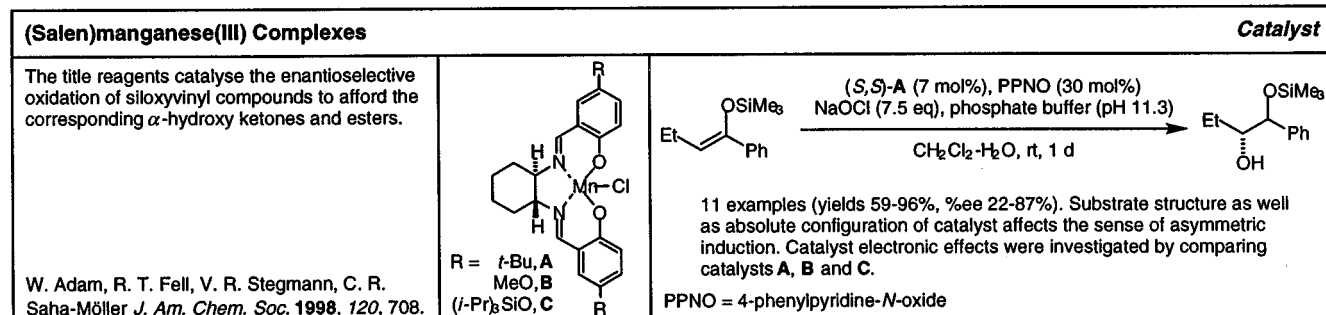
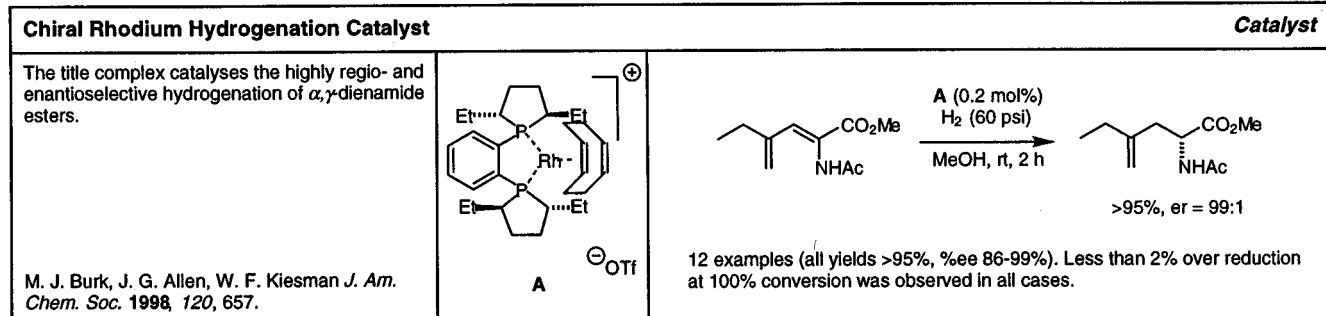
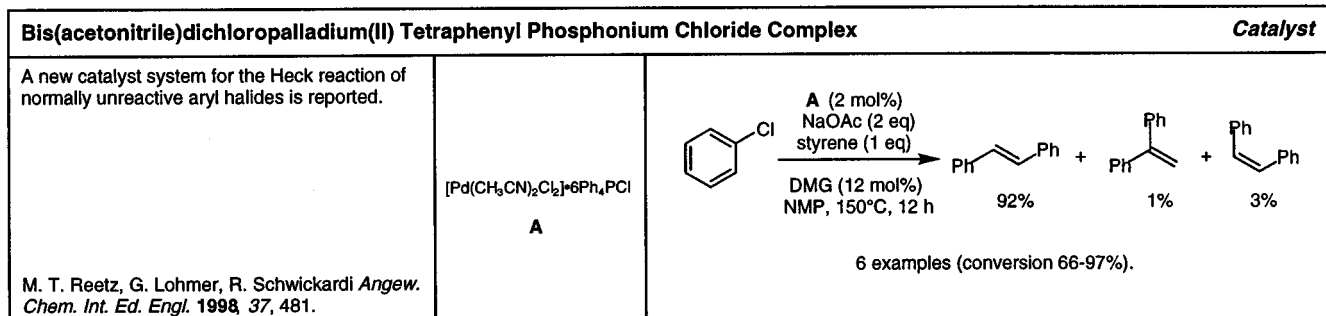
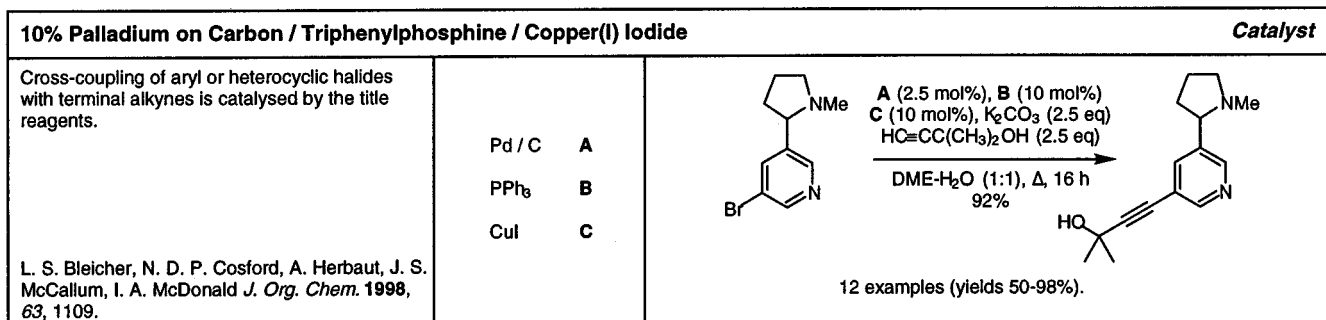
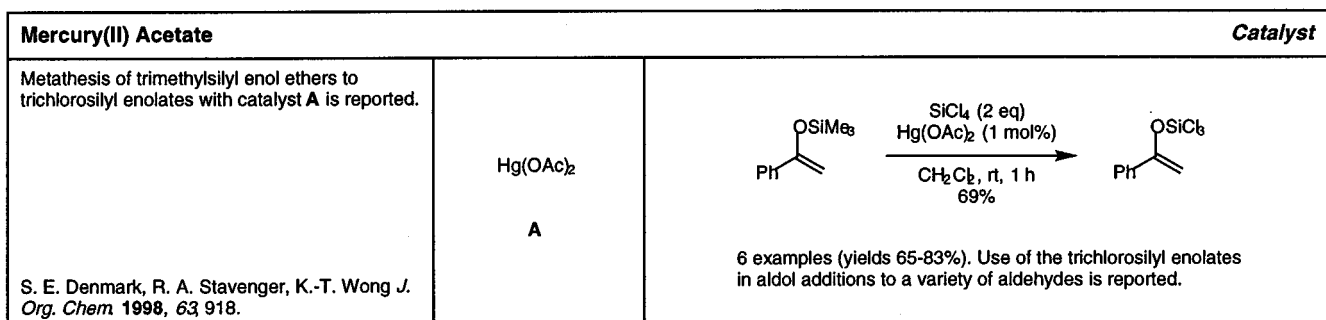
SYNTHESIS ALERTS

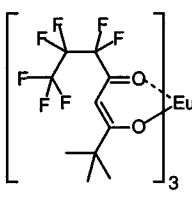
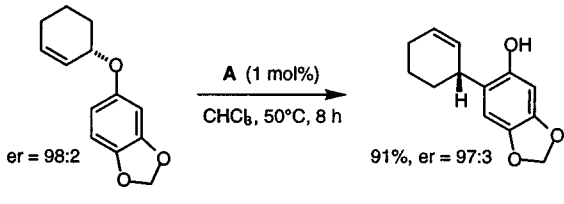
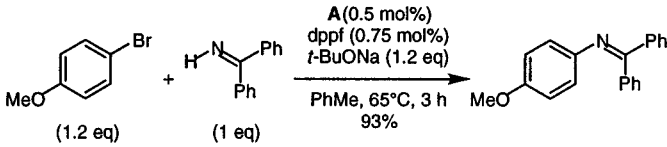
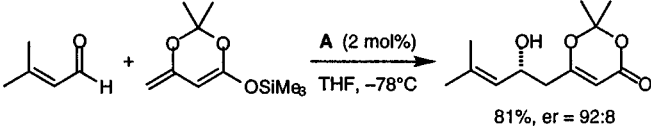
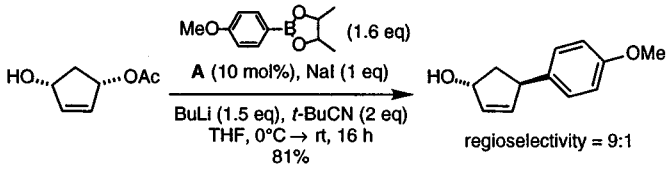
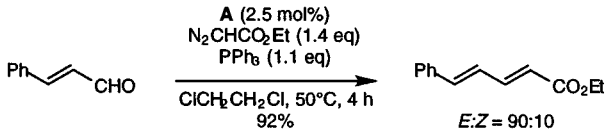
Synthesis Alerts is a monthly feature to help readers of Synthesis keep abreast of new reagents, catalysts, ligands, chiral auxiliaries, and protecting groups which have appeared in the recent literature. Emphasis is placed on new developments but established reagents, catalysts etc are also covered 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 Narquizian 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*.

Georg Thieme Verlag does not accept responsibility for the accuracy, content, or selection of the data.

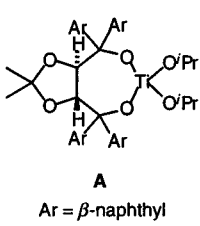
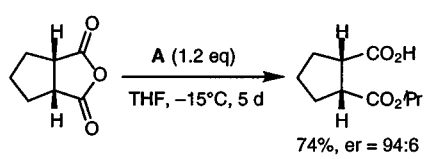
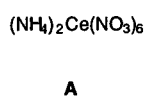
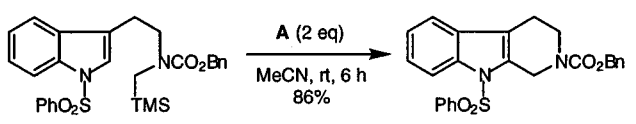

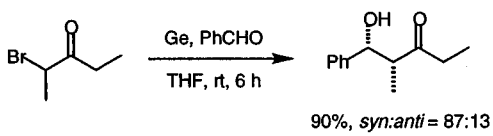
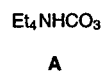
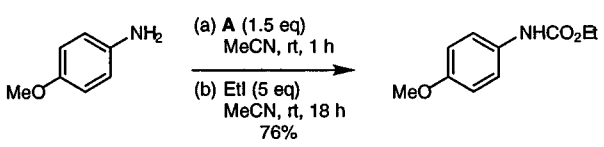
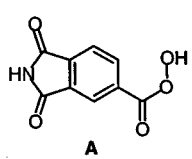
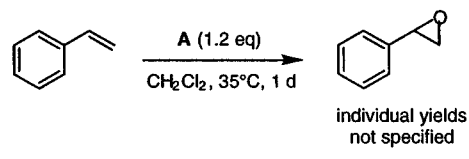
Bis(triphenylphosphine)nickel(II) Chloride		Catalyst
<p>The title reagent catalyses the cross-coupling of lithium alkenylborates with sterically congested <i>cis</i>-vinyl bromides.</p>	<p style="text-align: center;">$\text{NiCl}_2(\text{PPh}_3)_2$</p> <p style="text-align: center;">A</p>	<p style="text-align: right;">90%, single isomer</p> <p style="text-align: center;">9 examples (yields 0, 56-90%).</p>
<p>Y. Kobayashi, Y. Nakayama, R. Mizojiri <i>Tetrahedron</i> 1998, <i>54</i>, 1053.</p>		
Bis(triphenylphosphine)nickel(0)		Catalyst
<p>The title reagent catalyses the cross-coupling reaction between chloromethylated para-quinones and vinylalanes. The protocol described allows for an expeditious route to the vitamins K₁ and K₂.</p>	<p style="text-align: center;">$\text{NiCl}_2 + \text{PPh}_3$</p> <p style="text-align: center;">↓ BuLi, THF, rt</p> <p style="text-align: center;">$(\text{Ph}_3\text{P})_2\text{Ni}$</p> <p style="text-align: center;">A</p>	<p style="text-align: right;">88%</p> <p style="text-align: right;">9 examples (yields 67-86%).</p>
<p>B. H. Lipshutz, S. Kim, P. Mollard, K. L. Stevens <i>Tetrahedron</i> 1998, <i>54</i>, 1241.</p>		
Bis(cyclooctadiene)nickel(0)		Catalyst
<p>Nickel catalysed [4+2] cycloadditions proceed in cases in which the corresponding Diels-Alder cycloaddition either fails or requires forcing conditions. A study on the stereochemistry and electronic effects using nickel was also conducted.</p>	<p style="text-align: center;">$\text{Ni}(\text{COD})_2$</p> <p style="text-align: center;">A</p> <p style="text-align: center;">$\text{P}[\text{OCH}(\text{CF}_3)_2]_3$</p> <p style="text-align: center;">B</p>	<p style="text-align: right;">90%, single isomer</p>
<p>P. A. Wender, T. E. Smith <i>Tetrahedron</i> 1998, <i>54</i>, 1255.</p>		



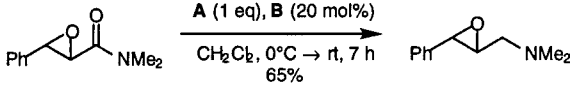
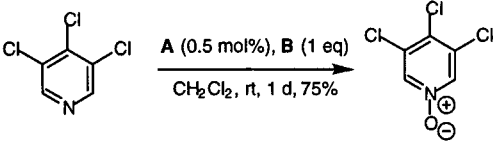
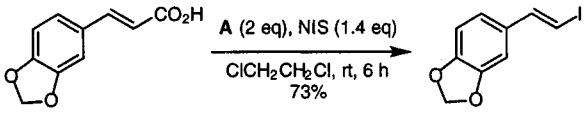
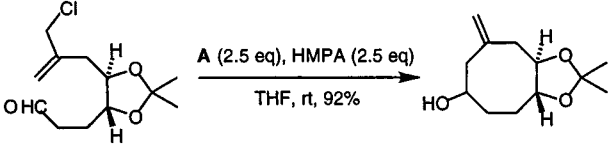
Europium Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyloctane-3,5-dionate) (Eu(fod)3)		Catalyst
<p>The title reagent catalyses the aromatic Claisen rearrangement of allylic phenols with excellent chirality transfer. Synthesis of the requisite aryl ethers is also described by the palladium catalysed asymmetric <i>O</i>-alkylation of phenols by allylic carbonates.</p>	 <p style="text-align: center;">A</p>	 <p style="text-align: center;">er = 98:2</p> <p style="text-align: center;">91%, er = 97:3</p> <p style="text-align: center;">12 examples (yields 79-97%, Δ(%ee) ≈ -1%).</p>
<p>B. M. Trost, F. D. Toste <i>J. Am. Chem. Soc.</i> 1998, <i>120</i>, 815.</p>		
Palladium(II) Acetate		Catalyst
<p>The title reagent is a pre-catalyst for the <i>N</i>-arylation of azoles and imines.</p>	<p>Pd(OAc)₂</p> <p style="text-align: center;">A</p>	 <p style="text-align: center;">(1.2 eq) (1 eq)</p> <p style="text-align: center;">93%</p> <p style="text-align: center;">15 examples (yields 76-97%). More sluggish reaction rates were found with pyrrole derivatives.</p> <p style="text-align: center;">dppf = 1,1'-bis(diphenylphosphino)ferrocene</p>
<p>G. Mann, J. F. Hartwig, M. S. Driver, C. Fernández-Rivas <i>J. Am. Chem. Soc.</i> 1998, <i>120</i>, 827.</p>		
(S)-Tol-BINAP Copper(II) Fluoride Complex		Catalyst
<p>The <i>in situ</i> generated title reagent catalyses the enantioselective addition of a silyl dienolate to aldehydes. The protocol described represents a relatively new paradigm for asymmetric carbonyl addition chemistry whereby chiral enolates are catalytically regenerated.</p>	<p>(Bu₄N)Ph₃SiF₂ Cu(OTf)₂ + (S)-Tol-BINAP ↓ (S)-Tol-BINAP•CuF₂</p> <p style="text-align: center;">A</p>	 <p style="text-align: center;">81%, er = 92:8</p> <p style="text-align: center;">10 examples (yields 48, 74-98%, %ee 65-95%).</p>
<p>J. Krüger, E. M. Carreira <i>J. Am. Chem. Soc.</i> 1998, <i>120</i>, 837.</p>		
Bis(triphenylphosphine)nickel(II) Chloride		Catalyst
<p>The title catalyst mediates the coupling of arylborates with an allylic acetate.</p>	<p>Ni(PPh₃)₂Cl₂</p> <p style="text-align: center;">A</p>	 <p style="text-align: center;">(1.6 eq)</p> <p style="text-align: center;">A (10 mol%), NaI (1 eq)</p> <p style="text-align: center;">BuLi (1.5 eq), t-BuCN (2 eq)</p> <p style="text-align: center;">THF, 0°C → rt, 16 h</p> <p style="text-align: center;">81%</p> <p style="text-align: center;">regioselectivity = 9:1</p> <p style="text-align: center;">8 examples (yields 63-98%). The use of NaI and t-BuCN as additives significantly enhances 1,3-selectivity.</p>
<p>Y. Kobayashi, E. Takahisha, S.B. Usmani <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 597.</p>		
Bis(triphenylphosphine)ruthenium(II) Chloride		Catalyst
<p>The title reagent catalyses the olefination of aldehydes with ethyl diazoacetate.</p>	<p>Ru(PPh₃)₂Cl₂</p> <p style="text-align: center;">A</p>	 <p style="text-align: center;">A (2.5 mol%)</p> <p style="text-align: center;">N₂CHCO₂Et (1.4 eq)</p> <p style="text-align: center;">PPh₃ (1.1 eq)</p> <p style="text-align: center;">ClCH₂CH₂Cl, 50°C, 4 h</p> <p style="text-align: center;">92%</p> <p style="text-align: center;">E:Z = 90:10</p> <p style="text-align: center;">6 examples (yields 82-92%, E:Z ≥ 90:10).</p>
<p>O. Fujimura, T. Honma <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 625.</p>		

(<i>R</i>)-Methylaluminum-β-binaphthoxide		Catalyst
The title reagent catalyses the enantioselective alkylation of aldehydes with 5-alkoxy oxazoles.		<p>92%, er (<i>cis</i>) = 94:6 <i>cis:trans</i> = 83:7</p> <p>20 examples (yields 51-92%, %ee (<i>cis</i>) 64-90%, <i>cis:trans</i> 43:57 to 97:3).</p> <p>Ar = <i>o</i>-anisyl</p>
H. Suga, K. Ikal, T. Iyata <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 869.	A	
<i>trans</i>-4,5-Diphenylimidazoline		Chiral Auxiliary
Dianions derived from C ₂ symmetric chiral imidazolines provide excellent stereocontrol in alkylation reactions affording quaternary benzylic centres.		<p>79%, dr = >98:2</p> <p>5 examples (yields 75-86%, %de 80->95%). Alkylation of monoanions derived from <i>N</i>-substituted imidazolines is also described and gives complementary diastereoselectivity.</p>
P. I. Dalko, Y. Langlois <i>Chem. Commun.</i> 1998 , 331.	A	
(-)-Sparteine		Ligand
Metallation of <i>N</i> -methylisoindoline-borane complexes with <i>s</i> -BuLi in the presence of the title ligand allows for subsequent diastereo- and enantioselective alkylation.		<p>55%, er = 94:6 18%</p> <p>5 examples (yields 66-79%, %de 33-96%, %ee(major) = 64-89%).</p>
A. J. Blake, M. R. Ebdon, D. N. A. Fox, W. Li, N. S. Simpkins <i>Synlett</i> 1998 , 189.	A	
Chiral P,N Ligand		Ligand
A new chiral P,N ligand is described which gives practically useful enantio- and regioselectivities in palladium catalysed allylic alkylations.		<p>91%, er = 98:2 (+4% regioisomer)</p> <p>Ar = 1-naphthyl BSA = <i>N,O</i>-bis(trimethylsilyl)acetamide</p>
R. Prétot, A. Pfaltz <i>Angew. Chem. Int. Ed. Engl.</i> 1998 , <i>37</i> , 323.	A	
(<i>S,S</i>)-1,2-Diphenylethylenediamine [(<i>S,S</i>)-DPEN]		Ligand
Addition of the title chiral ligand to a racemic ruthenium(II) complex selectively activates one enantiomer to catalyse the asymmetric hydrogenation of simple ketones.		<p>100%, er = 98:2</p> <p>2 examples (yields quantitative, %ee 90, 95%).</p>
T. Ohkuma, H. Doucet, T. Pham, K. Mikami, T. Korenaga, M. Terada, R. Noyori <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 1086.	A	

(<i>R,R</i>)-1,2-Di(pyridine-2-carboxamido)cyclohexane		Ligand
<p>A molybdenum complex derived from the title ligand effects the asymmetric substitution of allylic acetates and carbonates. Products resulting from attack at the most substituted terminus predominate.</p> <p>B. M. Trost, I. Hachiya <i>J. Am. Chem. Soc.</i> 1998, <i>120</i>, 1104.</p>	<p style="text-align: center;">A</p>	<p style="text-align: center;">14 examples (yields 50-88%, regioselectivity >5:1, %ee 75-98%).</p>
Tris[3-(<i>N,N</i>-dimethylguanidino)phenyl]phosphine		Ligand
<p>The title ligand mediates the palladium catalysed (Sonogashira) coupling of iodoarenes and terminal alkynes in water.</p> <p>H. Dibowski, F.P. Schmidtchen <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 525.</p>	<p style="text-align: center;">A</p>	<p style="text-align: center;">2 examples (yields 60-86%).</p>
Diethyl Zinc		Reagent
<p>Treatment of various 5-iodoketones with the title reagent (A) in the presence of nickel catalyst B produces cyclopentanols.</p> <p>T. Stüdemann, M. Ibrahim-Ouali, G. Cahiez, P. Knochel <i>Synlett</i>, 1998, 143.</p>	<p>A</p> <p>B</p>	<p style="text-align: center;">11 examples (64-82%, %de 90-98%). The method only allows for the preparation of 5 membered rings. Ester functionality is tolerated by the reaction conditions.</p>
(3-Carboethoxy-1-propyl)(trimethylsilylmethyl)zinc		Reagent
<p>Functionalised mixed alkyl(trimethylsilylmethyl)-zinc reagents add efficiently to a variety of Michael acceptors with exclusive 1,4-regioselectivity with no need for transition metal catalysis. The trimethylsilylmethyl group acts as a perfect dummy ligand.</p> <p>P. Jones, C. K. Reddy, P. Knochel <i>Tetrahedron</i>, 1998, <i>54</i>, 1471.</p>	<p style="text-align: center;">A</p>	<p style="text-align: center;">The mixed zinc reagent can also add to αβ-unsaturated aldehydes without the need for HMPA.</p>
Dilithium tetrachlorocuprate		Reagent
<p>The title reagent catalyses the carbonylative cyclization of iodoarenes bearing a proximal enolate precursor to provide cyclic ketones or lactones.</p> <p>E. Negishi, H. Makabe, I. Shimoyama, G. Wu, Y. Z. Zhang <i>Tetrahedron</i>, 1998, <i>54</i>, 1095.</p>	<p>A</p>	<p style="text-align: center;">2 examples employing A (yields 20, 98%).</p>

Di-isopropoxytitanium TADDOLate		Reagent
<p>The title reagent effects the highly enantioselective ring opening of cyclic <i>meso</i>-anhydrides to afford the corresponding isopropyl hemiesters.</p> <p>G. Jaeschke, D. Seebach <i>J. Org. Chem.</i> 1998, <i>63</i>, 1190.</p>	 <p style="text-align: center;">A Ar = β-naphthyl</p>	 <p>14 examples (yields 59-99%, %ee 0, 50-98%). The use of sub-stoichiometric A in the presence of stoichiometric amounts of $\text{Al}(\text{O}^i\text{Pr})_3$ is also reported.</p>
Ceric Ammonium Nitrate (CAN)		Reagent
<p>The title reagent promotes Pictet-Spengler cyclizations of α-silylamides.</p> <p>H. J. Kim, U. C. Yoon, Y.-S. Jung, N. S. Park, E. M. Cederstrom, P. S. Mariano <i>J. Org. Chem.</i> 1998, <i>63</i>, 860.</p>	 <p style="text-align: center;">A</p>	 <p>11 examples (yields 7-86%).</p>
Germanium		Reagent
<p>The title reagent (prepared <i>in situ</i> from germanium(II) iodide and potassium metal) is an effective promoter of the Reformatsky reaction. Good <i>syn</i> diastereoselectivity is observed.</p> <p>H. Kagoshima, Y. Hashimoto, D. Oguro, K. Saigo <i>J. Org. Chem.</i> 1998, <i>63</i>, 691.</p>	 <p style="text-align: center;">A</p>	 <p>13 examples of the reaction of α-bromo carbonyl compounds or enantiomerically pure oxazolidinone derivatives with aldehydes (yields 0, 32-98%, <i>syn:anti</i> 78:22 to 99:1).</p>
Tetraethylammonium Hydrogen Carbonate		Reagent
<p>The preparation of carbamates from amines, alkyl halides and A is described.</p> <p>A. Inesi, V. Mucclante, L. Rossi <i>J. Org. Chem.</i> 1998, <i>63</i>, 1337.</p>	 <p style="text-align: center;">A</p>	 <p>14 examples (yields 0, 53-98%).</p>
5-Hydroperoxycarbonylphthalimide		Reagent
<p>The cheap title reagent effects the epoxidation of alkenes. The by-product carboxylic acid is highly insoluble in the reaction media and acid catalysed side-reactions of the product epoxides are minimal.</p> <p>A. P. James, R. A. W. Johnstone, M. McCarron, J. P. Sankey, B. Trenbith <i>Chem. Commun.</i> 1998, 429.</p>	 <p style="text-align: center;">A</p>	 <p>16 examples (all yields 98-100%). The preparation of A is described.</p>

S-Methyl N-Phenyl Methaneimidothioate		Reagent
2-Nitroenamines are prepared by condensation of substituted nitromethanes with S-methyl methaneimidothioates in the absence of solvent.		
K. A. Tumer <i>Synthesis</i> , 1998, 139.		10 examples (yields 38, 75-100%).
Aluminum Tris(2,6-diphenylphenoxide)		Reagent
Precomplexation of a conjugated aldehyde with the title reagent promotes subsequent deprotonation at the most distal enolisable site. This allows for the controlled mixed aldol reaction between conjugated and non-conjugated (or non-enolisable) aldehydes.		
S. Saito, M. Shiozawa, M. Ito, H. Yamamoto <i>J. Am. Chem. Soc.</i> 1998, 120, 813.		18 examples of mixed aldols between aldehyde pairs (yields 26, 55-99%). Also 8 examples between conjugated ketones and aldehydes (yields 38, 68-99%). In all cases the conjugated carbonyl component acts as the nucleophile, reacting at the extremity of its unsaturation.
(-)-Chlorobis(isopinocampheyl)borane (DIP-chloride) / (-)-Sparteine		Reagent
The title pair of reagents effect the enantioselective enolborination of meso ketones.		
D. E. Ward, W.-L. Lu <i>J. Am. Chem. Soc.</i> 1998, 120, 1098.		65%, dr = 96:4
		5 examples (yields 15-85%, %de 90-92%). The method is also effective for the kinetic resolution of racemic non-symmetric ketones.
Sodium N-Chloro-O-benzylcarbamate		Reagent
The title reagent A (or the closely related Boc derivative B) acts as a nitrogen source and stoichiometric oxidant in the asymmetric aminohydroxylation of olefins. Using this system the aminohydroxylation of styrenes with excellent enantioselectivity is possible for the first time.		
K. L. Reddy, K. B. Sharpless <i>J. Am. Chem. Soc.</i> 1998, 120, 1207.	R = Bn, A t-Bu, B	67%, er = 96:4 (+14% regioisomer)
		23 examples of styrenes employing A and B (yields 35-98%, regioselectivity 50:50 to 91:9 in favour of the benzylamine, %ee 74-99%). In general slightly higher enantioselectivities are achieved using B.
1-[N-(Benzyloxycarbonyl)aminomethyl]benzotriazole		Reagent
The title reagent is used as an electrophilic aminomethyl equivalent in asymmetric Mannich reactions with Evans oxazolidinones. The Cbz-group survives the conditions necessary for auxiliary removal and is itself cleaved by catalytic hydrogenolysis under mild conditions.		
E. Arvanitis, H. Ernst, A. A. Ludwig, A. J. Robinson, P. B. Wyatt <i>J. Chem. Soc., Perkin Trans. 1</i> 1998, 521.		65%, dr = 96:4
		3 examples (yields 58-65%, %de 86-92%).

Hydridotris(triphenylphosphine)rhodium(I) Carbonyl / Diphenylsilane		Reagent
<p>The title reagent pair mediates the reduction of tertiary amides to tertiary amines. The reaction can be performed in the presence of hydride sensitive functionalities.</p>	<p>RhH(CO)(PPh₃)₃ A Ph₂SiH₂ B</p>	 <p>12 examples (yields 65-94%). Epoxides and esters are not reduced under the reaction conditions.</p>
<p>R. Kuwano, M. Takahashi, Y. Ito <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 1017.</p>		
Perrhenic acid / Bis(trimethylsilyl)peroxide (BTSP)		Reagent
<p>The title reagent pair mediates the <i>N</i>-oxidation of pyridines. Both electron deficient and electron rich pyridines can be successfully employed as substrates.</p>	<p>HReO₄ A Me₃SiOOSiMe₃ B</p>	 <p>16 examples (yields 11-98%). The turnover frequency is sensitive to water content, thus A was used as a 65-70% aqueous solution.</p>
<p>C. Coperet, H. Adolfsson, J. P. Chiang, A.K. Yudin, K.B. Sharpless <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 761.</p>		
Tetrabutylammonium Trifluoroacetate (TBATFA)		Reagent
<p>The title reagent mediates the conversion of α,β-unsaturated carboxylic acids to the corresponding halides by <i>N</i>-halosuccinimides, thus constituting a metal-free Hunsdiecker reaction.</p>	<p>$n\text{-Bu}_4\text{N}^+$ $\text{O}^- \text{C}(=\text{O}) \text{CF}_3$ A</p>	 <p>18 examples (yields 18-97%), including chloro- and bromo-decarboxylation reactions.</p>
<p>D. Naskar, S. Chowdhury, S. Roy <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 699.</p>		
Samarium(II) Iodide		Reagent
<p>The title reagent mediates the intramolecular reductive cyclisation of allyl chlorides with aldehydes.</p>	<p>SmI₂ A</p>	 <p>6 examples of the formation of 8 and 9-membered rings (yields 80-97%).</p>
<p>H. Arimoto, I. Hayakawa, M. Kuramoto, D. Uemura <i>Tetrahedron Lett.</i> 1998, <i>39</i>, 863.</p>		