

SYNTHESIS ALERTS

Synthesis Alerts is a new 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.

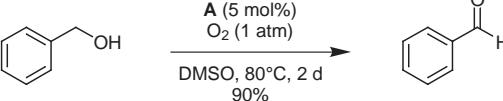
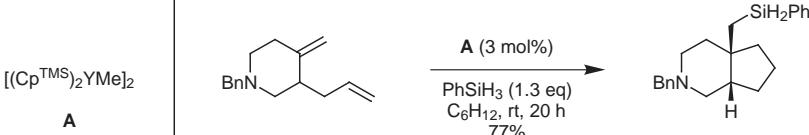
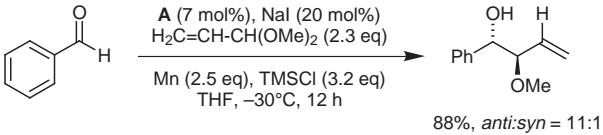
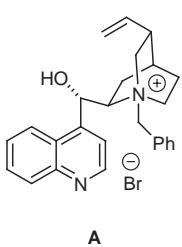
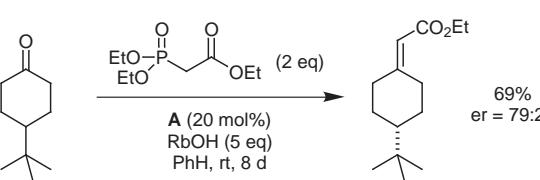
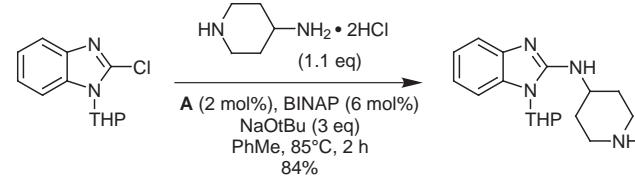
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Tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)ytterbium			Catalyst
Ketene acetals derived from mannopyranose and glucopyranose serve as electron-rich dienophiles in facially selective, Lewis acid-catalysed inverse electron demand hetero-Diels-Alder reactions. S. C. Johnson, C. Crasto, S. M. Hecht <i>Chem. Commun.</i> 1998 , 1019.	Yb(fod) ₃ A	<p style="text-align: center;">$X_c = \begin{array}{c} \text{---} \\ \\ \text{---} \end{array} \text{---} \begin{array}{c} \text{---} \\ \\ \text{---} \end{array} \text{---} \begin{array}{c} \text{---} \\ \\ \text{---} \end{array}$</p>	<p style="text-align: center;">A (5 mol%) PhH, Δ</p> <p style="text-align: right;">81% dr = 84:16</p> <p>4 examples (yields 50-97%, 1:1 \leq endo:exo \leq 32:1).</p>

Scandium(III) Trifluoromethanesulfonate			Catalyst
A catalyses the Strecker-type reaction of aldehydes, amines and tributyltin cyanide to afford α -amino nitriles in high yields. The reactions proceed smoothly in both organic and aqueous solutions and complete recovery of both the catalyst and all tin compounds is achieved. S. Kobayashi, T. Busujima, S. Nagayama <i>Chem. Commun.</i> 1998 , 981.	Sc(OTf) ₃ A	<p style="text-align: center;">A (10 mol%), Ph₂CHNH₂ (1 eq) Bu₃SnCN (1.5 eq) H₂O, rt, 20 h 89%</p>	<p style="text-align: center;">6 examples (yields 79-94%).</p>

<i>(S,S)</i> -Ethylene-1,2-bis(η^5 -4,5,6,7-tetrahydro-1-indenyl)titanium difluoride			Catalyst
A highly enantioselective titanium-catalysed hydrosilylation of imines to give secondary amines is described. The slow addition of primary amine additives greatly expands the scope of the reaction, isobutylamine giving the best results with high reaction rate and enantioselectivity. X. Verdaguer, U. E. W. Lange, S. L. Buchwald <i>Angew. Chem. Int. Ed. Engl.</i> 1998 , 37, 1103.	<p style="text-align: center;">(a) A (1 mol%) PhSiH₃ (3 mol%) piperidine-MeOH (1:1) 60°C, 20 min</p> <p style="text-align: center;">(b) PMHS (9 eq) <i>i</i>-BuNH₂ (2 eq) THF, 65°C, 2.5 h</p> <p style="text-align: right;">96%, er = 96:4</p> <p>9 examples (yields 73-97%, %ee 69, 91-99%). Enantioselectivity is not limited by the <i>E:Z</i> ratio of the imine. PMHS = polymethylhydrosiloxane</p>	<p style="text-align: center;">A</p>	

Poly-L-leucine			Catalyst
A new procedure for the Julia-Colonna asymmetric epoxidation is described in the synthesis of (+)-clausenamide. A is mixed with the oxidant and immobilised on cross-linked aminomethylpolystyrene to furnish a fixed bed reactor convenient for continuous flow synthesis of optically active epoxides.			
M. W. Cappi, W.-P. Chen, R. W. Flood, Y.-W. Liao, S. M. Roberts, J. Skidmore, J. A. Smith, N. M. Williamson <i>Chem. Commun.</i> 1998 , 1159.	3 examples of oxidation using polyleucine catalysts (conversion 66-89%, %ee 83-89%).		
Tungsten(0) Pentacarbonyl Tetrahydrofuran Complex			Catalyst
The title reagent promotes the cycloisomerisation of γ -hydroxyalkynes. The resultant glycals are a source of 2,3,6-trideoxyhexoses. Glycosylation with an acyclic alkynyl alcohol allows for reiterative application of the cycloisomerisation reaction and to oligosaccharide synthesis.			
F. E. McDonald, H. Y. H. Zhu <i>J. Am. Chem. Soc.</i> 1998 , 120, 4246.	6 examples of ring closure (yields 23-47%). A sensitive trisaccharide unit of the natural product PI-080 is synthesised via iteration of the methodology.		
Chiral Copper(I) Lewis Acid			Catalyst
A catalyses the enantioselective alkylation of α -imino esters by enol silanes.			
D. Ferraris, B. Young, T. Dudding, T. Lectka <i>J. Am. Chem. Soc.</i> 1998 , 120, 4548.	8 examples (yields 65-95%, %ee 89-98%). Products are often solids and can be recrystallised to near optical purity.		
Hexahydro-6-oxo-1,1,4,4-tetramethyl-1<i>H</i>-1,4-diazepinium bis(trifluoromethanesulfonate)			Catalyst
The title compound is a general and efficient catalyst for the epoxidation of olefins.			
S. E. Denmark, Z. Wu <i>J. Org. Chem.</i> 1998 , 63, 2810.	11 examples (yields 33, 74-94%).		
Planar-chiral DMAP derivative			Catalyst
The title compound catalyses the deracemisation/ring opening of azlactones affording protected α -amino acids.			
J. Liang, J. C. Ruble, G. C. Fu <i>J. Org. Chem.</i> 1998 , 63, 3154.	9 examples (yields 94-98%, %ee 44-78%).		

Palladium(II) Acetate			Catalyst
The title compound catalyses the oxidation of primary and secondary allylic and benzylic alcohols.	$\text{Pd}(\text{OAc})_2$ A		
K. P. Peterson, R. C. Larock <i>J. Org. Chem.</i> 1998 , 63, 3185.			17 examples (yields 42-96%). The reaction is effective on a 100 mmol scale with no decrease in reactivity or yield.
Yttrium complex			Catalyst
Complex A catalyses the cyclisation/silylation of dienes containing 1,1-disubstituted olefins.	$[(\text{Cp}^{\text{TMS}})_2\text{YMe}]_2$ A		
G. A. Molander, E. D. Dowdy, H. Schumann <i>J. Org. Chem.</i> 1998 , 63, 3386.			12 examples (yields 49-98%).
Chromium(II) Chloride			Catalyst
The title compound catalyses a variant of the Takai-Utimoto reaction of acrolein acetals with aldehydes.	CrCl_2 A		
R. K. Boeckman, R. A. Hudack <i>J. Org. Chem.</i> 1998 , 63, 3524.			12 examples (yields 46-94%, 1:1.5 ≤ anti:syn ≤ 20:1).
N-Benzylchinchoninium Bromide			Catalyst
The title catalyst mediates the enantioselective Horner-Wadsworth-Emmons olefination of a variety of symmetrical cyclohexanones, under phase transfer conditions.			
S. Arai, S. Hamaguchi, T. Shioiri, <i>Tetrahedron Lett.</i> 1998 , 39, 2997.			5 examples (yields 15-89%, %ee 7-57%) are described. A variety of phase-transfer catalysts are investigated.
Tris(dibenzylideneacetone)dipalladium(0)			Catalyst
The title catalyst mediates selective amination by a primary amine in the presence of a secondary amine.	$\text{Pd}_2(\text{dba})_3$ A		
Y. Hong, C. H. Senanayake, T. Xiang, C. P. Vandenbossche, G. J. Tanoury, R. P. Bakale, S. A. Wald <i>Tetrahedron Lett.</i> 1998 , 39, 3121.			12 examples (yields 58-95%) are described. Selectivity for the primary amine ranges from 9:1 to >99:1.

Bis(triphenylphosphine)palladium(II) Dichloride			Catalyst
The title catalyst mediates the coupling of thiol esters with organozinc reagents, to give ketones.			
$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ A		$\text{iZn}-\text{CH}_2-\text{CH}_2-\text{CO}_2\text{Et}$ (2 eq) A (10 mol%) PhMe , rt, 40 min 88%	
H. Tokuyama, S. Yokoshima, T. Yamashita, T. Fukuyama <i>Tetrahedron Lett.</i> 1998 , 39, 3189.			28 examples (yields 50-99%) are described.

N-Trimethylsilyl-bistrifluoromethanesulfonimide			Catalyst
The title catalyst (prepared <i>in situ</i>) mediates the conjugate allylation of enones and enoates.			
		A (10 mol%) CH_2Cl_2 , $-78^\circ\text{C} \rightarrow \text{rt}$, 1 h 97%	 97% dr > 99:1
N. Kuhnert, J. Peverley, J. Robertson <i>Tetrahedron Lett.</i> 1998 , 39, 3215.			8 examples (yields 55-97%) are described.

Chloro-<i>p</i>-cymene-(<i>N</i>-<i>p</i>-toluenesulfonyl-1,3-diaminopropane)ruthenium(II)			Catalyst
The title catalyst mediates the efficient cyclopropanation of olefins with alkyl diazoacetates.			
		A (0.5 mol%) 60°C , 4 h 94% <i>cis:trans</i> = 63:37	
F. Simal, A. Demonceau, A.F. Noels <i>Tetrahedron Lett.</i> 1998 , 39, 3493.			2 examples (yields 89 and 94%) are described. The use of 5 other monotosylated diamine ligands is also described.

(Anthraquinone-1,8-dioxy)bis(triisopropoxy-titanium)			Catalyst
The title bidentate catalyst activates carbonyl groups and epoxides in nucleophilic reactions.			
		A (10 mol%), HNBn_2 (1.1 eq) CH_2Cl_2 , 0°C , 9 h 73%	 4 examples (yields 54-99%) are described. A is a stronger Lewis acid than $\text{Ti}(\text{O}^{\prime}\text{Pr})_4$.

Rh(acac)[(S)-binap]			Catalyst
Aryl- and alkenyl-boronic acids undergo enantioselective 1,4-addition to enones in the presence of a chiral phosphine-rhodium catalyst.			
		A (3 mol%) dioxane/ H_2O 100°C 93% (er > 49:1)	 Arylboronic acids substituted with electron donating or electron withdrawing groups worked equally well. 12 examples: yields typically 51-99%; ee ≥ 91%

2-[2-Methylamino-4-chloro-1-phenyl]-1,2,3,4-tetrahydroisoquinoline		Catalyst
The title compound catalyses the asymmetric protonation of amide enolates.	<p>A</p>	
E. Vedejs, A. W. Kruger <i>J. Org. Chem.</i> 1998 , <i>63</i> , 2792.		

Planar-chiral DMAP derivative		Catalyst
The title compound catalyses the kinetic resolution of arylalkylcarbinols.	<p>A</p>	
J. C. Ruble, J. Tweddel, G. C. Fu <i>J. Org. Chem.</i> 1998 , <i>63</i> , 2794.		

Bis(dicyclopentadienyl)vanadium Dichloride		Catalyst
The title compound catalyses the pinacol coupling of secondary aliphatic aldehydes with excellent diastereoselection. The chlorosilane additive plays an important role in the construction of catalytic systems and also assists the stereoselection.	<p>A</p>	
T. Hirao, M. Asahara, Y. Muguruma, A. Ogawa <i>J. Org. Chem.</i> 1998 , <i>63</i> , 2812.		

(1S,2S)-Pseudoephedrine		Chiral Auxiliary
Aryllithium reagents react rapidly and efficiently with β -aryl- α , β -unsaturated <i>tert</i> -butyl esters bearing a chiral oxazolidine (derived from the title compound) to give 1,4-addition products in high yields and optical purity.	<p>A</p>	
L. F. Frey, R. D. Tillyer, A.-S. Caille, D. M. Tschaen, U.-H. Dolling, E. J. J. Grabowski, P. J. Reider <i>J. Org. Chem.</i> 1998 , <i>63</i> , 3120.		

2-Hydroxypinan-3-one		Chiral Auxiliary
The diastereoselective protonation of potassium enolates of chiral Schiff bases derived from the title compound and racemic α -amino esters is reported.	<p>A</p>	
M. Tabcheh, C. Guibourdenche, L. Pappalardo, M.-L. Roumestant, P. Viallefond <i>Tetrahedron: Asymmetry</i> , 1998 , <i>9</i> , 1493.		

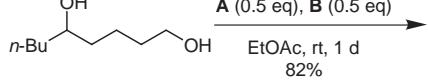
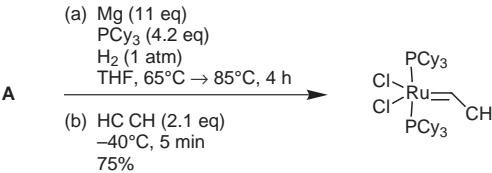
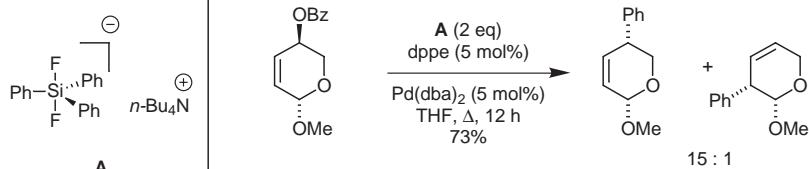
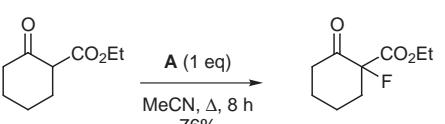
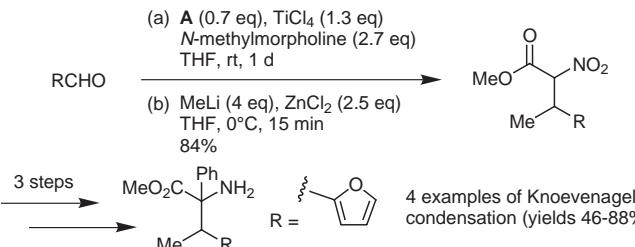
(S,S)-1,2-Bis(2,5-diethylphospholano)benzene (Et-DuPHOS)		Ligand
A cationic rhodium(I) complex derived from the title ligand catalyses the asymmetric hydrogenation of α -acyloxy acrylates. The resultant products are easily hydrolysed to α -hydroxyesters or reduced to yield 1,2-diols.		<p>$Rh(I)^* = [(cod)Rh(S,S)-Et-DuPHOS]OTf$</p> <p>14 examples (all full conversions, %ee >93%). The E:Z ratio of the enol ester had little effect on the enantioselectivity of the reduction.</p>
M. J. Burk, C. S. Kalberg, A. Pizzano <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 4345.		

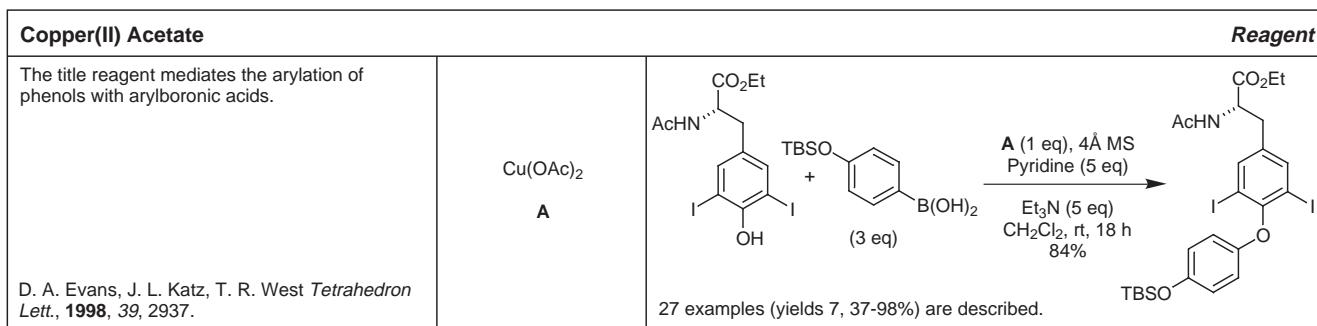
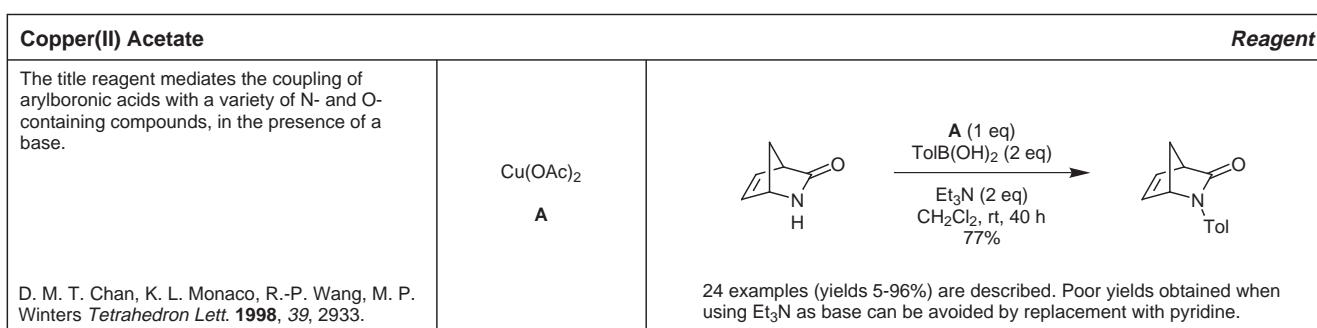
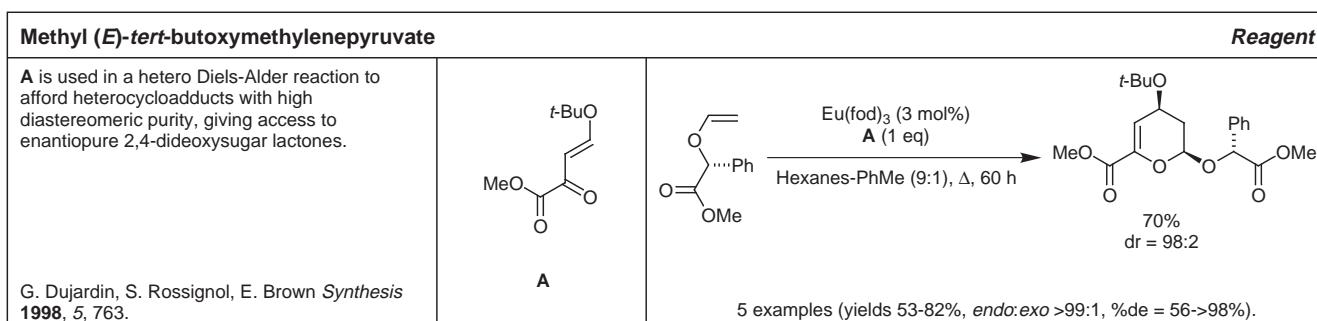
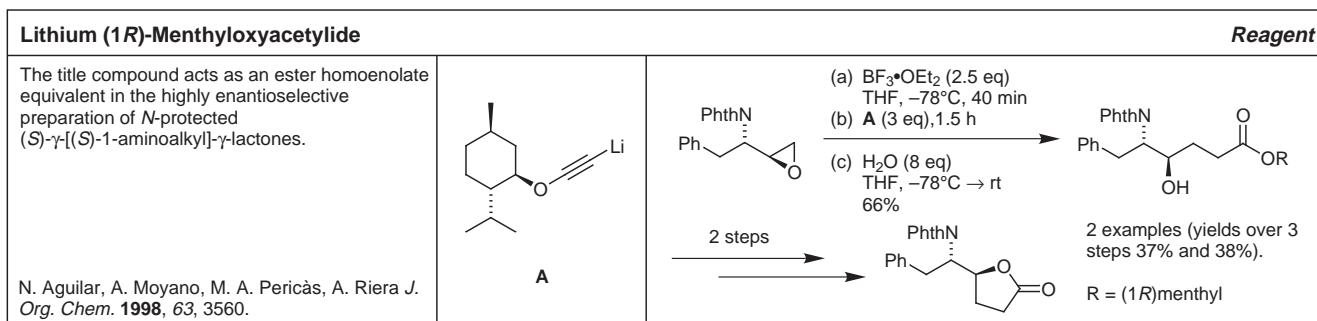
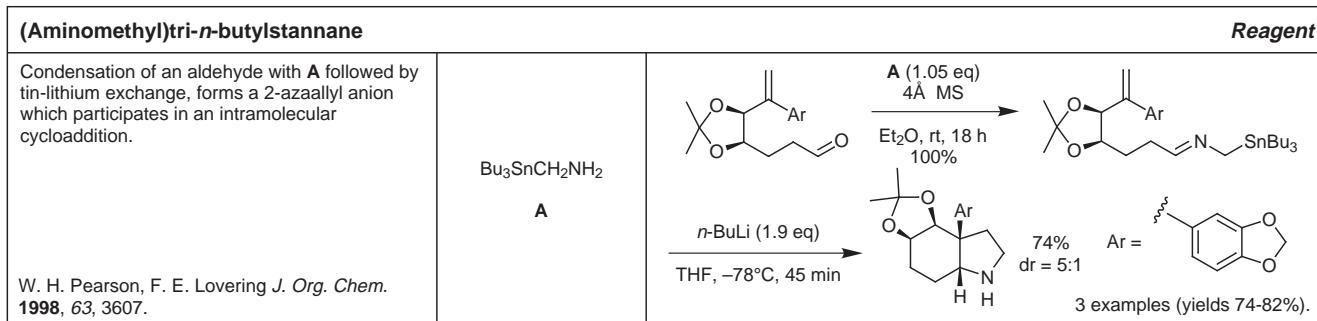
N,N',N''-Trimethyl-1,4,7-triazacyclonone (Cn^+)		Ligand
A ruthenium catalyst derived from the title ligand catalyses the oxidation of alcohols to aldehydes and ketones.		<p>15 examples (yields 83-95%).</p>

(2<i>S</i>,2<i>S</i>)-Bis(diphenylphosphinoxy)-(1<i>R</i>,1<i>R</i>)-dicyclopentane (BICPO)		Ligand
A cationic rhodium(I) complex derived from the title ligand catalyses the enantioselective hydrogenation of dehydroamino acids.		<p>11 examples (quantitative yields, %ee 46-95%).</p>

(Z)-4-Iodo-1-(tributylstannylyl)but-1-ene		Reagent
The bifunctional title compound is employed as an alkylating agent in a novel cyclohexenone annulation procedure.		<p>6 examples (alkylation yields 54-92%).</p>

Vanadium(V) Oxytrinitrate		Reagent
Nitration of a range of substituted aromatic compounds with A under mild conditions is reported.		<p>12 examples with a variety of aromatic substitution (yields 0, 54->99%).</p>

Triphenylphosphine / Carbon Tetrabromide			Reagent
In the presence of ethyl acetate, the title reagent pair selectively acetylates primary alcohols in high yield.	A PPh ₃ B CBr ₄		
H. Hagiwara, K. Morohashi, H. Sakai, T. Suzuki, M. Ando <i>Tetrahedron</i> 1998 , <i>54</i> , 5845.			25 examples including 12 examples of formylation using ethyl formate as the solvent (yields 5, 19-100%).
Ruthenium(III) Chloride Hydrate			Reagent
The title reagent is utilised in a convenient preparation of ruthenium carbene complexes.	A RuCl ₃ ·3H ₂ O		
J. Wolf, W. Stür, C. Grünwald, H. Werner, P. Schwab, M. Schulz <i>Angew. Chem. Int. Ed. Engl.</i> 1998 , <i>37</i> , 1124.	2 examples (yields 75% and 76%).		
Tetrabutylammonium Triphenyldifluorosilicate (TBAT)			Reagent
The title compound is an effective phenylation reagent in palladium-catalysed coupling reactions.	A Ph ₃ Si(F) ₂ ⁻ n-Bu ₄ N ⁺		
M.-R. Brescia, P. DeShong <i>J. Org. Chem.</i> 1998 , <i>63</i> , 3156.	5 examples with complete inversion of configuration (yields 60-75%).		
N,N'-Difluoro-2,2'-bipyridinium bis(tetrafluoroborate)			Reagent
The title reagent is a highly reactive and easy-to-handle electrophilic fluorinating agent with high effective fluorine content.	A [2,2'-bipyridinium] ²⁺ OTf ⁻		
T. Umemoto, M. Nagayoshi, K. Adachi, G. Tomizawa <i>J. Org. Chem.</i> 1998 , <i>63</i> , 3379.	13 examples (yields 28-82%).		
Methyl Nitroacetate			Reagent
Knoevenagel condensation of the title compound with aldehydes gives α -nitro enoate esters which undergo easy conjugate addition of zinc reagents. The sequence is a versatile synthesis of α -amino acid derivatives.	A H ₃ CO-C(=O)-CH ₂ -NO ₂		
R. S. Fornicola, E. Oblinger, J. Montgomery <i>J. Org. Chem.</i> 1998 , <i>63</i> , 3528.	4 examples of Knoevenagel condensation (yields 46-88%).		



Tris(pentafluorophenyl)borane			Reagent
Stereoselective addition of weak nucleophiles to α - and β -alkoxy ketones is mediated by pentacoordinate complexes generated <i>in situ</i> using the commercially available title compound or Me_3Al .	$\text{B}(\text{C}_6\text{F}_5)_3$ A		
T. Ooi, D. Uraguchi, N. Kagoshima, K. Maruoka <i>J. Am. Chem. Soc.</i> , 1998 , <i>120</i> , 5327.			
[β-(Trimethylsilyl)acryloyl]-<i>tert</i>-butyldimethylsilane			Reagent
Reaction of the <i>E</i> and <i>Z</i> isomers of the title compound with lithium enolates of α,β -unsaturated methyl ketones afford cis-5,6- and trans-5,6-disubstituted 3-cycloheptenones respectively. The reaction involves a Brook rearrangement followed by a divinylcyclopropane rearrangement.	$\text{O}=\text{SiMe}_2\text{Bu}^t$ A		
K. Takeda, A. Nakajima, M. Takeda, Y. Okamoto, T. Sato, E. Yoshii, T. Koizumi, M. Shiro <i>J. Am. Chem. Soc.</i> , 1998 , <i>120</i> , 4947.			6 examples; yields 67-84%
Diethylzinc			Reagent
A new easy route to dialkylzinc reagents is based on the irradiation of iodoalkanes with diethylzinc in dichloromethane at rt at $\lambda \geq 280$ nm. A simple GE sunlamp suffices.	Et_2Zn		
A. B. Charette, A. Beauchemin, J.-F. Marcoux <i>J. Am. Chem. Soc.</i> , 1998 , <i>120</i> , 5114.			21 examples; yields generally 80-95%. EtZnI can be used in place of Et2Zn.
Ethoxyoxovanadium(V) Dichloride			Reagent
Alanes and alanates undergo oxidative coupling using the title reagent.	VO(OEt)Cl_2 A		
T. Ishikawa, A. Ogawa, T. Hirao, <i>J. Am. Chem. Soc.</i> , 1998 , <i>120</i> , 5124.			5 examples; yields 65-76%. 9 examples; yields 24-91%. Some biaryl product is formed.
Fluoroform			Reagent
The title reagent is a trifluoromethylating agent when deprotonated in DMF with a base.	CHF_3 A		
B. Folléas, I. Marek, J.-F. Normant, L.S. Jalmes <i>Tetrahedron Lett.</i> , 1998 , <i>39</i> , 2973.			6 examples (yields 20-60%) are described.

Copper(II) Toluenesulfonate		Reagent
The title reagent mediates the α -sulfonyloxylation of unsymmetrical ketones.	$\begin{array}{c} \text{CuO} \\ \downarrow \\ \text{Cu}(\text{OTs})_2 \\ \text{A} \end{array}$	<p style="text-align: center;">A (1.5 eq) MeCN, rt, 14 h 62%</p>
J. C. Lee, Y. Choi <i>Tetrahedron Lett.</i> 1998 , 39, 3171.		15 examples (yields 62-84%) using methanesulfonic, <i>p</i> -toluenesulfonic and <i>p</i> -nitrobenzenesulfonic acid are described.

Benzotriazol-1-yloxytris(dimethylamino)phosphonium Hexafluorophosphate (BOP)		Reagent
Hydroxybenzotriazolyl esters, formed <i>in situ</i> from carboxylic acids and the above reagent undergo reduction, under relatively mild conditions, with sodium borohydride.	$\begin{array}{c} \text{N} \\ \parallel \\ \text{C}_6\text{H}_4-\text{N}=\text{N}-\text{C}_6\text{H}_4-\text{O}^+-(\text{Me}_2\text{N})_3\text{P}^-\text{PF}_6^- \\ \text{A} \end{array}$	<p style="text-align: center;">(a) A (1.1 eq), DIPEA (1.2 eq) THF, rt, 5 min (b) NaBH4 (1 eq), THF, rt, o/n 96%</p>

Bis(cyclopentadienyl)titanium-bis(triethylphosphite)		Reagent
The title reagent mediates the desulfurisation of thioacetals in the presence of trialkylsilanes to give the corresponding tetraalkylsilanes.	$\begin{array}{c} \text{Cp}_2\text{TiCl}_2 \quad \text{P(OEt)}_3 \\ \downarrow \quad \downarrow \\ \text{Mg} \quad (\text{1.2 eq}) \\ \downarrow \\ \text{Cp}_2\text{Ti[P(OEt)}_3]_2 \\ \text{A} \end{array}$	<p style="text-align: center;">THF, rt, 1.5 h 58%</p>

Bis(cyclopentadienyl)titanium-bis(triethylphosphite)		Reagent
The title reagent mediates the conversion of carbonyl compounds to allylsilanes with 1,1-bis(phenylthio)-2-triorganosilylethanes.	$\begin{array}{c} \text{Cp}_2\text{TiCl}_2 \quad \text{P(OEt)}_3 \\ \downarrow \quad \downarrow \\ \text{Mg} \quad (\text{1.2 eq}) \\ \downarrow \\ \text{Cp}_2\text{Ti[P(OEt)}_3]_2 \\ \text{A} \end{array}$	<p style="text-align: center;">THF, rt, 2 h 79% E:Z = 44:56</p>

N-Chloro-N-sodio-2-trimethylsilylethyl Carbamate		Reagent
The title reagent is a new nitrogen source for the asymmetric aminohydroxylation of olefins.	$\begin{array}{c} \text{Me}_3\text{Si}-\text{CH}_2-\text{CO}_2\text{iPr} \\ \text{Na}^+ \quad \text{Cl}^- \\ \text{A} \end{array}$	<p style="text-align: center;">A (3.1 eq) NaOH (2.9 eq) t-butylhypochlorite (3.1 eq) K₂OsO₂(OH)₄ (4 mol%) n-PrOH-H₂O (1:1), rt, 45 min 70%</p> <p style="text-align: center;">(DHQD)₂PHAL (5 mol%) (DHQD)₂PHAL (5 mol%)</p>