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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, John Christopher, Louise Lea, Philip Kocienski, J.-Y. Le Brazidec, Robert Narquizian and Christopher Smith 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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Tris(dibenzylmethido) Iron(III)		Catalyst
The title reagent catalyses the dimethylation of gem-dichlorocyclopropanes by MeMgBr in the presence of 4-methylanisole.	Fe(dbm) _s A	OBn MeMgBr (3 eq), A (5 mol%) 4-methylanisole (1.1 eq) THF, rt, 3 h 66% Me Me
Y. Nishi, K. Wakasugi, Y. Tanabe <i>Synlett</i> 1998 , 67.		8 examples (yields 37-73%).

Chiral (Salen)Chromium(III) Complexes		Catalyst
Dihydropyranones are obtained in good yields and enantioselectivities <i>via</i> Diels-Alder reactions catalysed by A or B .	R—WHAN NAME OF THE PROPERTY OF	(a) (1 eq) TMSO OMe A (2 mol%), 4Å MS TBME, -40°C, 24 h (b) TFA (cat.) CH ₂ Cl ₂ , rt, 10 min 86%, er = 92:8
S. E. Schaus, J. Branalt, E. N. Jacobsen <i>J. Org. Chem.</i> 1998 , <i>63</i> , 403.	R = OMe B	7 examples (yields 65-98%, %ee = 62-93%). TBME = <i>tert</i> -butylmethylether

Scandium(III) Trifluoromethanesulfonate			Catalyst
A 3-component reaction between aldehydes, amines and allyltributyl stannane, catalysed by A is reported. The reactions proceed in water, in the absence of organic solvents, to afford homoallylic amines in high yield.	Sc(OTf) ₈	CHO	NHPh PH
S. Kobayashi, T. Busujima, S. Nagayama <i>Chem. Commun.</i> 1998 , 19.		12 examples (yields 66-90%). SDS = sodium dodecylsulfate	

Iron(III) 2-Ethylhexanoate			Catalyst
The title reagent is used as a novel, mild Lewis acid catalyst for the stereoselective Diels-Alder reaction of ethyl (<i>E</i>)-4-oxobutenoate with alkyl vinyl ethers to give <i>cis</i> -2,4-disubstituted pyrans with high diastereomeric excesses.	Fe(BuEtCHCO ₂) ₃	EO ₂ C (6 eq)	CO ₂ Et 80%, dr = 99:1
D. B. Gorman, I. A. Tomlinson <i>Chem. Commun.</i> 1998, 25.		3 examples (yields 78-80%, %de 98%). O also reported, with shorter reaction times and concentration of catalyst.	possible at elevated temperature

Tris(pentafluorophenyl) Boron		Catalyst
The title reagent catalyses the hydrostannation of C-C multiple bonds. V. Gevorgyan, JX. Liu, Y. Yamamoto Chem. Commun. 1998, 37.	B(C ₆ F ₅) ₃ A	A (10 mol%) Bu ₈ SnCl (1.5 eq) Et ₃ SiH (1 eq) PhMe, 0°C → rt, 4 h 85%, ZE = 95:5 8 examples (yields 70-90%). Hydrostannation of an allene and an alkene is also described.

Titanium(IV) Chloride		Catalyst
The title reagent catalyses the regioselective aldol reaction between aldehydes and ketones with addition occuring to the more encumbered α -site of the ketone.	TICL A	A (10 mol%) PhMe, rt, 16 h 66%, syn:anti = 83:17 6%
R. Mahrwald, B. Gündogan <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 413.		12 examples (yields 62-91%, regioselectivity ≥ 86:14).

(Bromobinol)zinc complex			Catalyst
The title complex catalyses the asymmetric addition of α -alkoxy silyl ketene acetals to 2-aminophenol imines to afford the corresponding β -aminoalcohols. By simple variation of substrate and solvent both syn and $anti$ adducts can be selectively realised.	Br O DM Pr	1	O'Pr OTBS o, er = 98:2 anti = 96:4
S. Kobayashi, H. Ishitani, M. Veno <i>J. Am. Chem. Soc.</i> 1998 , <i>120</i> , 431.	A DMI = 1,2-dimethyl- imidazole	4 examples of <i>syn</i> adducts (yields 65-100%, %ee 91-98%, <i>syn:anti</i> 7 examples of <i>anti</i> adducts (yields 41-100%, %ee 76-96%, 57:42 ≤ 94:6) Ar = 2-hydroxyphenyl, PMP = 4-met	anti:syn ≤

The title reagent in the presence of sodium tent-butoxide catalyses the highly enantioselective 1,4-addition of trimethylphosphonoacetate to enones. T. Arai, H. Sasai, K. Yamaguchi, M. Shibasaki J. Am. Chem. Soc. 1998, 120, 441. Catalyst Catalyst A (10 mol%) A (10 mol%) NaO'Bu (9 mol%) A (10 mol%) NaO'Bu (9 mol%) F(OMe)₂ 64%, er(*) = 99:1 In both cases no 1,2-addition product was found.

Dichloroethoxyoxyvanadium α-Hydroxy ketones are cleaved chemoselectively by the title catalyst under an oxygen atmosphere. VO(OEt)Cb A 11 examples (yields 55-87%).

Homochiral Oxazaborolidine		Catal
Oxazaborolidine A together with borane catalyses highly enantioselective reduction of ketones.	Q N B Me H	Ph A (10 mol%), BH ₃ •THF (1 eq) Ph OH THF, 0°C, 5 min OH 84%, er = 99:1 5 examples (yields 68-100%, %ee 66-99%).
N. Hashimoto, T. Ishizuka, T. Kunieda Heterocycles 1997, 46, 189.		

Dirhodium(II) Tetrakis[N-phthaloyl-(S)-	tert-leucinate]	Catalyst
The title catalyst mediates the enantioselective intramolecular CH-insertion of α -methoxycarbonyl- α -diazo acetamides.	Bu, A	MeO ₂ C PNP CI CH ₂ Cb, rt, 6 h 83%, er = 91:9
M. Anada, S-I. Hashimoto <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 79.	A	6 examples (yields 72-84%, %ee 33-74%). PNP = 4-nitrophenyl

Indium Trichloride		Catalyst
The title catalyst mediates the Mannich-type reaction between aldehydes, amines and silyl enol ethers, in water, to give β-amino ketones and esters. TP. Loh, LL. Wei <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 323.	InCb A	NH ₂ + Ph A (20 mol%) HCHO _(aq) HCHO _(aq) H ₂ O, rt, 1 d 91% 18 examples (yields 21-91%). The Lewis acid catalyst is recoverable and reusable. Yields using aliphatic enolisable imines are poor.

C ₂ -Symmetric bis-sulfoxide			C	hiral Auxiliary
The use of the title C ₂ -symmetric bis-sulfoxide A for the desymmetrisation of a <i>meso</i> -cyclopentitol is described. N. Maezaki, A. Sakamoto, T. Tanaka, C. Iwata <i>Tetrahedron: Asymmetry</i> 1998 , <i>9</i> , 179.	- ₀ ⁺ S ⁺ ₀ -	BnO., OBn (a) KHMDS 18-crowr THF, -78 (b) BnBr	- \ /	OBn BnO OH 91%, er = 98:2

Ligand

Ligand

Ligand

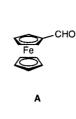
Ligand

Chiral Auxiliary

Ferrocenecarbaldehyde

The ferrocenyl N-pivaloyl N, O-acetal derived from alanine and the title reagent (preparation described) undergoes alkylation with complete retention of configuration (cf Seebach's self-reproduction of chirality).

F. Alonso, S.G. Davies, A. S. Elend, J.L. Haggitt J. Chem. Soc., Perkin Trans. 1 1998, 2, 257.



LDA, BnBr THF, -78°C → rt, 18 h 90%, dr > 99:1 R = Rr

8 examples with different bromides (yields 71-95%, %de 92->98%).

(2S,3S,7R)-NORPHOS-7-NEt 2

A new chiral bisphosphine ligand, NORPHOS-7-NEt₂ (A) has been prepared. It has been applied to the palladium catalysed asymmetric allylic alkylation of racemic (E)-diphenyl-2-propenyl pivalate.

I. Achiwa, A. Yamazaki, K. Achiwa Synlett, 1998, 45



MeO₂C ∠CO₂Me CO₂Me [Pd/π-C₃H₅)Cl₂ (2.5 mol%) QСО′Ви A (10 mol%), BSA, LiOAc CH₂Ck, rt, 2 d 90%, er > 99:1

BSA = N, O-bis(trimethylsily!)acetamide

(5S)-1,3-Diaza-3-phenyl-2-phospha-2-[(quinolin-8-yl)oxy]bicyclo[3.3.0]octane

A palladium complex derived from the title ligand catalyses asymmetric allylic amination reactions with good enantioselectivity.

13 examples (yields 36-100%, ee% 73-94). 3 other ligands were also investigated.

T. Constantieux, J. Brunel, A. Labande, G. Buono Synlett 1998, 49.

A palladium complex of the title ligand catalyses the asymmetric substitution reaction of allylic

2-[2-(Diphenylphosphino)phenyl]-4,5-(3,4,6-tri-

A (1.2 mol%)

O-pivaloyl-3-deoxy- α -D-glucopyrano)-4,5-dihydrooxazole

[Pd(C₃H₅)Cl₂ (0.5 mol%) dimethyl malonate (3 eq)

KOAc (0.5 mol%), BSA (3 eq) CH₂Cl₂, rt, 2 h

CQ₂Me

90%, er = 87:13

100%, er = 92:8

5 examples (yields 77-94%, %ee 69-98%).

BSA = N, O- bis(trimethylsilyl)acetamide

B. Gläser, H. Kunz Synlett 1998, 53.

acetates with malonate nucleophiles.

(R,R)-2,2 "-Bis[(S)-1-(dialkylphosphino)ethyl]-1,1 "-biferrocene

Rhodium(I) complexes of the title trans-chelating ligand catalyse the asymmetric aldol reaction of 2-cyanopropionates.

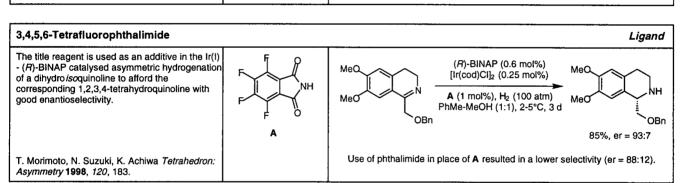
67%, er = 93:7anti:syn = 81:19

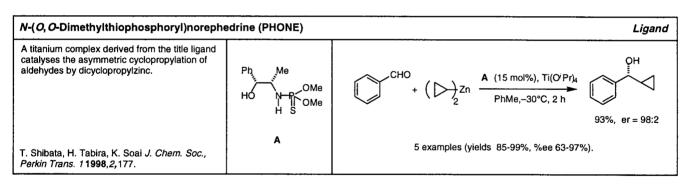
15 examples (yields 44-88%, %ee 3-93%).

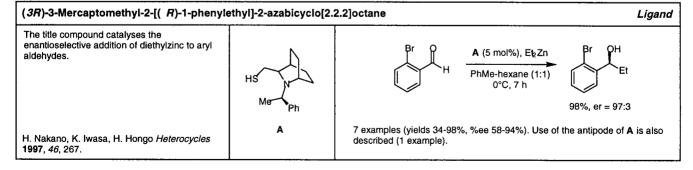
R. Kuwano, H. Miyazaki, Y. Ito Chem. Commun. 1998, 71.

120, 445.

3-exo-(Dimethylamino) isoborneol (DAIB) The title reagent catalyses the asymmetric addition of diphenylzinc to ketones to afford chiral 3° alcohols. A (15 mol%) ZnPh₂ (3.5 eq) PhMe, rt, 48 h 76%, er = 88:12 P. I. Dosa, G. C. Fu J. Am. Chem. Soc. 1998,







2-(2-Aminophenyl)acetaldehyde Dimethyl Acetal **Protecting Group** The title amine has been employed as a base-stable carboxylic acid protecting group. The carboxylic acid is regenerated *via* the corresponding indolylamide intermediate. CH(OMe)₂ PPTS (5 mol%) A, pyridine RCOCI rt, 1 h, 77% PhH, Δ, 5 h CH(OMe)₂ 84% LiOH, H₂O₂ THF-H₂O, 2.5 h 87% 13 examples (deprotection yields 75-100%). Five different deprotection conditions are described. E. Arai, H. Tokuyama, M. S. Linsell, T. Fukuyama *Tetrahedron Lett.* **1998**, *39*, 71. RCO₂H R = 2-furyl

1-Phenyl-1 H-tetrazole-5-thiol		Reagent
Condensation of metallated sulfones derived from the title reagent with aldehydes yields trans-1,2-disubstituted olefins with excellent stereoselectivity.	¥ N Ph	(a) KHMDS (1.1 eq) $ DME, -55^{\circ}C, 70 \text{ min} $ (b) $c\text{-}C_6H_{11}CHO (1.5 eq)$ $-55^{\circ}C \rightarrow \text{rt}, 18 \text{ h} $ 71%, $E:Z > 99:1$
P. R. Blakemore, W. J. Cole, P. J. Kocienski, A. Morely <i>Synlett</i> 1998, 26.	A	4 examples under optimised conditions (yields 22, 59-81%, <i>E:Z</i> ≥ 94:6). The effects of base and solvent on the reaction were investigated. DME = 1,2-dimethoxyethane

Oxone [®]				Reagent
The title reagent oxidises aliphatic and electron-deficient aryl aldehydes to the corresponding acids under buffered conditions. In the former case the presence of acetone in the reaction manifold was found to be advantageous.	2KHSO₅•KHSO₄•K₂SO₄	Ph = CHO -	Oxone® (0.9 eq) acetone, EDTA (pH 7-7.5) MeCN, 2°C, 3.5 h 73%	Ph CO₂H
K. S. Webb, S. J. Ruszkay <i>Tetrahedron</i> 1998, 401.	A	In the absence of acetone th examples of aliphatic aldehy 40-86%) and 5 examples of 73-94% in the absence of ac	de oxidation in the presence electron-deficient aryl aldeh	of acetone (yields 24,

2-(Diethoxymethyl)tributylstannane Reag		
The title reagent was used to prepare a 2-(tributyIstannyI)-1,3-dioxolane. B. J. Mellor, P. E. Murray, E. J. Thomas Tetrahedron 1998, 243.	EtO SnBu ₃	BzOOHOBz A (2 eq), CSA (8 mol%) PhH, Δ, 4 h, 80% BzOOSNBu ₈ Attempts to directly cross couple the product with vinylic halides failed; however, transmetallation of the di-TBS derivative by BuLi followed by addition to aldehydes was successful.

Chemical Manganese Dioxide (CMD)		Reagent
Chemical manganese dioxide, produced for dry battery manufacture, efficiently oxidises benzylic and allylic alcohols to the corresponding aldehydes and ketones under mild conditions.	MnO ₂	OH CO ₂ B A (10 eq) CO ₂ B CO ₂ B 80%
T. Aoyama, N. Sonoda, M. Yamanchi, K. Toriyama, M. Anzai, A. Ando, T. Shloiri <i>Synlett</i> 1998, 35.	A	12 examples (yields 50-95%).

Di-n-butylphosphine Oxide		Reagent
S-Methyl xanthates are readily deoxygenated by the action of the title reagent and a radical initiator. The procedure removes the need for toxic organotin hydrides and can be carried out with the complete exclusion of water.	BU H Bu	A (3 eq), AIBN (0.75 eq) dioxane, Δ, 1 d 93%
D. O. Jang, D.H. Cho, D. H. R. Barton <i>Synlett</i> 1998 , 39.		10 examples (yields 11-97%).

Silica Gel / Zinc Borohydride			Reagent
The title reagents effect the one-pot reductive amination of conjugated aldehydes and ketones. B. C. Ranu, A. Majee, A. Sarkar <i>J. Org. Chem.</i> 1998, <i>63</i> , 370.	SiO₂ A Zn(BH₄)₂ B	(a) c-C ₆ H ₁₁ NH ₂ (1 eq) A, rt, 4 h (b) B (1 eq) DME, 5°C, 50 min 85% 16 examples (yields 75-90%).	

(N,O)-Bis(trimethylsilyl)acetamide (BSA)		
Enamines are prepared from ketones and secondary amines with the title reagent and a catalytic amount of methyl iodide.	Me₃SiN— Me	(a) Mel (2.5 mol%) petroleum ether 40°C, 30 min (b) cyclopentanone (0.8 eq) A (0.8 eq), 70°C, 1 h 89%
Y. Yamamoto, C. Matui <i>J. Org. Chem.</i> 1998 , <i>63</i> , 377.		13 examples (yields 0, 80-93%).

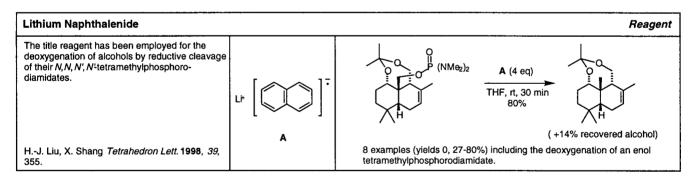
Di-n-butyltin Dihydride / Di- n-butyltin Did	chloride / Hexa	amethy	/lphosphoramide (HMPA) Reagent
Imines are reduced in the presence of carbonyl groups to provide secondary amines. The <i>in situ</i> prepared reductant is the highly coordinated tin hydride Bt ₂ SnClH-HMPA I. Shibata, T. Morluchi-Kawakami, D. Tanizawa, T. Suwa, E. Sugiyama, H. Matsuda, A. Baba <i>J. Org. Chem.</i> 1998 , <i>63</i> , 383.	Bu₂SnH₂ Bu₂SnCl₂ (Me₂N)₃PO	A B C	Ph Ph A (1 eq), B (1 eq), C (2 eq) Ph Ph THF, rt, 20 h 73% 4 examples (yields 54-78%). The preparation of unsymmetrical tertiary amines from the tin amides resulting from hydrostannation of imines is also reported.

Di-n-butyltin Dihydride / Di- n-butyltin Dichloride / Hexamethylphosphoramide (HMPA) Imines are reduced in the presence of carbonyl groups to provide secondary amines. The in situ prepared reductant is the highly coordinated tin hydride Bu2SnClH-HMPA Bu2SnCl2 B (Me2N)3PO C 4 examples (yields 54-78%). The preparation of unsymmetrical tertiary amines from the tin amides resulting from hydrostannation of imines is also reported.

Phenylsulfenyl Triflate The title reagent (prepared in situ from PhSCI and AgOTf) mediates the direct formation of hindered glycosides from thioglycosides. Phonology (a) A (2.5 eq), DTBMP (3 eq) CH_2CI_2 , $-78^{\circ}C$, 10 min (b) OBN CH_2CI_2 , $-78^{\circ}C$ OBN OHA 0 min OH OH

The title amine mediates the desymmetrisation of *meso*-1,2-diols by asymmetric benzoylation. To riyama, K. Imai, T. Hosoya, T. Sano Tetrahedron Lett. 1998, 39, 397. The title amine mediates the desymmetrisation of meso-1,2-diols by asymmetric benzoylation. A (1 eq), BzCl (1.5 eq) A (1 eq), BzCl (1.5 eq) A (1 eq), BzCl (1.5 eq) A Desymmetrisation of five substrates was examined in CH₂Cl₂ and EtCN (yields 62-89%, %ee 48-96%).

Borane / Dibutylboron Trifluoromethanesulfonate			Reagent
The title reagent pair reductively cleaves benzylidene and isopropylidene acetals of a variety of hexopyranosides with a high degree of regioselectivity. L. Jiang, TH. Chan Tetrahedron Lett. 1998, 39, 355.	BH₃•THF A Bu₂BOTf B	\\ _SPh	



Triphenylphosphine / 1,1-Di(tert-butylpe	roxy)cyclohexane	Reagent
The title pair of reagents mediate the desulfurisation of 2-methylene-3-thioalkyl-propionates to 2-methylene alkanoates.	PPh ₃ A 'BuO ₂ O ₂ 'Bu	OAc OAc OAc OAc OAc OAc OAc OAc OAc OAc
HS. Dang, KM. Kim, B.P. Roberts Tetrahedron Lett. 1998, 39, 501.	В	4 examples (yields 51-71%). The use of di- <i>tert</i> -butyl peroxide (20 mol%) in place of B gave lower yields of desulfurised product.