# 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 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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Tetrakis(triphenylphosphine)palladium		Catalyst
A cross-coupling reaction of alkyltrifluorosilanes with aryl halides was achieved using the title catalyst with excess tetrabutylammonium fluoride.  H. Matsuhashi, S. Asai, K. Hirabayashi, Y. Hatanaka, A. Mori, T. Hiyama Bull. Chem. Soc. Jpn., 1997, 70, 437.	Pd(PPh <sub>3</sub> ) <sub>4</sub> A	Br F <sub>3</sub> S CO <sub>2</sub> Me (2 eq)  A (5 mol%), TBAF (4 eq) THF, Δ, 8 h, 65%  30 examples with 6 different trifluorosilanes and 14 aryl bromides and iodides. Yields generally 60-80%.

Trityl Tetrakis(pentafluorophenyl)borate			Catalyst
Catalytic stereoselective synthesis of several glycosides from thioglycosides is achieved by this catalyst with sodium periodate.	TrB(C <sub>6</sub> F <sub>5</sub> ) <sub>4</sub> <b>A</b>	BnO OBn HO NalO <sub>4</sub> (1.05 eq)  BnO SEt (4:1)  O°C, 6 h, 93%	BnO OBn BnO
H. Uchiro, T. Mukaiyama <i>Chem. Lett.</i> , <b>1997</b> , 121.		10 examples; yields all >90%	$\alpha\beta = 8:92$

Lanthanide(III) Triflates		Catalyst
These triflates (1-10 mol%) catalyse the nitration of simple arenes using <i>stoichiometric</i> quantities of 69% nitric acid.	Ln(OSO <sub>2</sub> CF <sub>3</sub> ) <sub>3</sub>	Pr(OTf) <sub>3</sub> (10 mol%) O <sub>2</sub> N + + + + + + + + + + + + + + + + + + +
F. J. Waller, A. G. M. Barrett, D. C. Braddock, D. Ramprasad <i>Chem. Commun.</i> , <b>1997</b> , 613.		5 different catalysts with m-xylene (Ln = La, Eu, Pr, Sc, Yb).  The only byproduct is water and the catalyst may be recycled by evaporation.

Catalyst

Catalyst

#### Chiral Amino Alcohol-Trimethyl Borate Complex

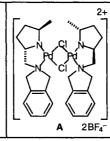
Asymmetric borane reduction of prochiral ketones with this reagent prepared in situ gives high enantioselectivity.

6 examples of ketones; yields >95%, ee's generally >95%. The catalyst is made from the amino alcohol (1.0 eq) and trimethylborate (1.2 eq). The methoxy group enhances the Lewis acidity of the boron.

M Masui, T. Shioiri Synlett, 1997, 273.

#### Dichloro[(S)-2-isoindolinylmethyl)- N-methylpyrrolidine]palladium(II)

Treatment of the title compound with silver tetrafluoroborate gives a compound which catalyses the asymmetric rearrangement of allylic amidates to allyl amides.



M. Calter, T.K. Hollis, L.E. Overman, J. Ziller, G.G. Zipp J. Org. Chem., 1997, 62, 1449.

#### (1S,2R)-N-Benzyl-N-mesitylsulfonylnorephedrine

Esters prepared from the title compound undergo anti selective boron-mediated asymmetric aldol reaction.

A. Abiko, J.-F. Liu, S. Masamune J. Am. Chem. Soc. 1997,119, 2586.

### (1R, 2R)-(+)-1,2-(3,3',5,5'-tetrachloro-2,2'-dihydroxydibenzenesulfonamido)cyclohexane

Ligand

Ligand

Chiral Auxiliary

Addition of diethyl zinc to benzaldehyde in the presence of the title catalyst proceeds with excellent yield and er.

**PhCHO** A (20 mol%) Catalyst Ti(O+Pr)4 (1.4 eq.) Et<sub>2</sub>Zn (1.8 eq) `Et hexane, reflux, 1h -23°C, 4 h 98% er = 99.5:0.5

10 analogous catalysts were tested with yields = 10-100% and er up to 96: 4. Detailed preparations of the catalysts are also presented.

#### C. Guo, J. Qiu, X. Zhang, D. Verdugo, M. L. Larter, R. Christie, P. Kennedy, P. J. Walsh Tetrahedron 1997, 53, 4145.

## (+)-(1 R, 2S)-Bis[N-methyl- N-(2-hydroxy-2-phenyl-1-methyl)ethyl]-3-xylylenediamine

Asymmetric Reformatsky reactions of tert-butyl bromoacetate and various carbonyl compounds in the presence of the title amino alcohol proceed in moderate to good yield and good stereoselectivity.

9 other examples reported, yields 35-90%, %ee 34-78%. 11 other catalysts were screened with inferior yields and enantioselectivities.

Ligand

Ligand

Ligand

**Protecting Group** 

**Protecting Group** 

# (1S,2R)-1-Amino-2-hydroxy-1,2,3,4-tetrahydronaphthalene

The title compound is a homochiral ligand for the enantioselective reduction of prochiral ketones.

A (7 mol%)
BH<sub>3</sub>.Me<sub>2</sub>S (0.7 eq)
THF, rt, 2h

(7 examples) 90%, er = 93

C. M. Belluci, A. Bergamini, P. G. Cozzi, A. Papa, E. Tagliavini, A. Umani-Ronchi *Tetrahedron:* asymmetry **1997**, *8*, 895.

The N,N-dibutyl amino derivative of  $\bf A$  has been used for the addition of EbZn to benzaldehyde (er = 72:28).

# 2,2'-Bis(di-p-tolylphosphino)-1,1 '-binaphthyl (Tol-BINAP)

Tol-BINAP is one third the cost of BINAP and is equally effective in the Pd-catalysed coupling of alkylamines with anyl triflates.

J.P. Wolfe, S.L. Buchwald *J. Org. Chem.*, **1997**, *62*, 1264.

See also:

J. Louie, M.S. Driver, B.C. Hamann, J.F. Hartwig J. Org. Chem., 1997, 62, 1268.

$$PR_2$$

$$PR_2$$

$$R = p - \text{tolyl}$$

Pd(OAc)<sub>2</sub> (2 mol%),
A (2.2 mol%),
NaO t-Bu (1.2 eq)

C<sub>7</sub>H<sub>8</sub>, 80°C
75%

Slow addition of the triflate may be required for good yields in some cases.

#### Homochiral Bisthiourea Ligand

The complex derived from  $(RuCl_2C_6H_6)_2$  (A) and chiral bis-thiourea ligand B, catalyses the asymmetric hydride transfer reduction of prochiral ketones.

A (5 mol%)
B (10 mol%)

t-BuOK (0.2 eq)
j-PrOH, 82°C, 17 h

96%, er = 96:4

1.1 ea

4 examples of reduction of simple phenyl ketones (yields 92-98%, %ee 85-94%). Extended reaction times (>12 h) are required for high conversions.

F. Touchard, P. Gamez, F. Fache, M. Lemaire Tetrahedron Lett., 1997, 38, 2275.

### 4-Hydroxyphenacyl Bromide

The title compound can be used to protect phosphates. The 4-hydroxyphenacyl protecting group is cleaved photochemically.

HO

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>3</sub>N

H<sub>4</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>2</sub>N

H<sub>3</sub>N

H<sub>4</sub>N

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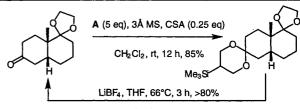
H<sub>5</sub>N

# 2-Trimethylsilylpropane-1,3-diol

1997, 119, 2453.

C.-H. Park, R. S. Givens J. Am. Chem. Soc.

The formation of cyclic acetals from carbonyl compounds and diol **A** provides 'cyclo-SEM' protection. The resulting 5-trimethylsilyl-1,3-dioxanes are easily cleaved by treatment with LiBF<sub>4</sub> in THF.



B. H. Lipshutz, P. Mollard, C. Lindsley, V. Chang *Tetrahedron Lett.*, **1997**, *38*, 1873.

7 other simpler examples (yields protection 45, 65-97%; yields deprotection 79-93%).

#### (S)-1-(3-Triethoxy propyl)sulfonyl-2-(1-methoxy-1-methylethyl)pyrrolidine Reagent Asymmetric cyclopentannulation of cyclic enones is accomplished with high enantioselectivity after OTMS .OEt reaction with the anion of the title sulfonamide. OEt C(OEt)<sub>3</sub> n-BuLi ÒEt (1.05 eq) -78°C, 45 min HMPA (8 eq) (b) Et<sub>3</sub>N, TMSCI 3 steps (4 eq), 30 min -78°C → 20°C -78°C, 30 min 48 % overall OMe er = 98:2C. Huart, L. Ghosez *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 634. 3 other examples are reported, yields 33-48%, %ee 92-98%.

Allyltri isopropylsilane		Reagent	
[3+2] Cycloaddition of the title silane and 1-acetylcycloalkenes in the presence of TiCl <sub>4</sub> provides exclusively silylbicycloalkanes in good yields instead of the Hosomi-Sakurai reaction products.	Si(FPr) <sub>3</sub>	+ A $\frac{\text{TiCl}_4 (1.1 \text{ eq})}{\text{CH}_2\text{Cb}}$ -78° $\rightarrow$ -20°C	Si(IPr) <sub>3</sub> 86%, anti product only
HJ. Knölker, N. Foitzik, H. Goesmann, R. Graf, P. G. Jones, G. Wanzl <i>Chem. Eur. J.</i> 1997, <i>3</i> , 538.		Various examples reported with different substra yields (25 - 82%) and good to excellent <i>anti:syn</i> :	

Tartrate Ester Modified AllyIsilanes		Reagent
These allylsilanes were found to serve as useful reagents for regiospecific and stereoselective allylation of aldehydes without any catalyst  L. C. Zhang, H. Sakurai, M. Kira Chem. Lett., 1997, 129.	CL CO <sub>2</sub> Pr	A (1.1 eq), 4Å MS  PhMe, rt, 40 h  76%, er = 9:1  Yields 45-93%, %ee 20-80%.

Sodium on Solid Support		
5-20 wt% of sodium on NaCl, glass powder, poly(ethylene) or poly(propylene) gave good yields for the acylation reaction of carboxylic acids.  M. Makosza, K. Grela Synlett 1997, 267.	Na/support A	RCO <sub>2</sub> Et  A (20 wt%)  C <sub>6</sub> H <sub>6</sub> , 45°C, 2 h 78%  R = n-heptyl  8 examples with mostly NaCl as the solid support. Yields 60-70%. The reagent may be prepared <i>via</i> low temperature (–33°C) deposition of sodium from its solution in liquid ammonia.

Methylalumoxane		Reagent
This extremely strong Lewis acid is a useful reagent for organic reactions such as the Diels-Alder reaction and amidation of esters.	(ALO)	CHO + CHo CHo CHO CHO CHO P : 91  7 examples of the Diels-Alder reaction; yields generally >85%.
M. Akakura, H. Yamamoto Synlett 1997, 277.		, , , , , , , , , , , , , , , , , , , ,

Diisopropylzinc-Magnesium Bromide Complex		Reagent
<ul> <li>i-Pr<sub>2</sub>Zn, generated in situ from iPr<sub>2</sub>MgBr (2 eq) and ZnBr<sub>2</sub> (1 eq), leads to a smooth iodine–zinc exchange in secondary alkyl iodides.</li> <li>L. Micouin, P. Knochel Synlett 1997, 327.</li> </ul>	<i>i-</i> Pr₂Zn•MgBr₂ <b>A</b>	(a) A (1.5 eq), Et <sub>2</sub> O (0.3 M solution) rt, 1 h  (b) CuCN•LiCl (2 eq) (c) allyl bromide (3 eq), -78 → 0°C  8 examples, yields 60-80%. Racemisation occurs with chiral alkyl iodides.

Tetrachlorosilane	, , ,,		Reagent
Trichlorosilyl ethers prepared from trimethylsilyl ethers and the title compound undergo highly selective asymmetric aldol reactions.  S. E. Denmark, KT. Wong, R. A. Stavenger J. Am. Chem. Soc. 1997, 119, 2333.	SiCl <sub>4</sub> A	The anti aldol product is favored in the presence of the Lewis base promoter (B) (11 examples).  In the absence of B the syn product is favored (15 examples).  A (3 eq)  O°C, 78%  Me  Ph.  Me  (10 mol%)  PhCHO, -78°C, 2h	95%, er = 97:3 syn:anti = 1:61

Lithium Tri- tert-butylzincate		Reagent
The title compound metallates alkyl and aryl iodides to the corresponding mixed zincates which react with electrophiles without transfer of the tert-butyl group.  Y. Kondo, M. Fujinami, M. Uchiyama, T. Sakamoto J. Chem. Soc, Perkin Trans. 1, 1997, 799.	( <i>t</i> -Bu) <sub>3</sub> ZnLi <b>A</b>	(a) A (1 eq)  -78°C, 4 h  (b) benzoyl chloride  -78°C → rt, 12h  56%

85%

Reagent

Reagent

Reagent

#### N,N-Diethylaniline•Borane (DEANB) Complex

The commercially available complex A effectively reduces a variety of functional groups, including: aldehydes, ketones, carboxylic acids, amides and lactams

See following paper for use of DEANB (A) as borane source in CBS reduction reactions.

A. M. Salunkhe, E. R. Burkhardt Tetrahedron Lett., 1997, 38, 1519,

11 varied examples (yields 51, 85-94%). A is also an effective hydroboration reagent, showing good regioselectivity.

#### N-Chlorosuccinimide / Thiourea

Successive treatment of aldoximes with NCS (A) followed by thiourea (B) and triethylamine, produces the corresponding isothiocyanates in excellent yield.

J. N. Kim, K. S. Jung, H. J. Lee, J. S. Son *Tetrahedron Lett.*, **1997**, *38*, 1597.

#### 2,2'-Bipyridinium Chlorochromate / 3-Chloroperoxybenzoic Acid

Oxidative cleavage of benzylidene acetals to hydroxy esters is effected by the title reagent pair. Possible oxidation of the released hydroxyl function is negligible.

10 examples (yields 48, 69-79%).

F. A. Luzzio, R. A. Bobb Tetrahedron Lett., 1997, 38, 1733.

# Bromotriphenylphosphonium 2,4,6-Tribromophenoxide

Primary and secondary alcohols are smoothly converted to the corresponding bromides under mild conditions by treatment with A . THP ethers can also be directly transformed to bromides

A. Tanaka, T. Oritani Tetrahedron Lett , 1997, *38*, 1955.

#### Zinc Amalgam

A complex system of A, Lil and TMSOTf allows for the in situ regeneration of Sml2 from Sm(III) species. Thus Sml2 mediated reactions can be made catalytic in samarium

Zn•Hg

Ar = mesityl

Lil (5 eq), A TMSOTf (2 eq) THF, rt, 8 h

Reagent

5 examples of spiroannulation of ketones with mesityl acrylate (yields 70-84%). Also demonstrated: deoxygenation of styrene oxide (67% yield), and cyclisation of 6-iodo-1-phenylhex-1-yne (82% yield).

A

E. J. Corey, G. Z. Zheng Tetrahedron Lett., 1997 38, 2045