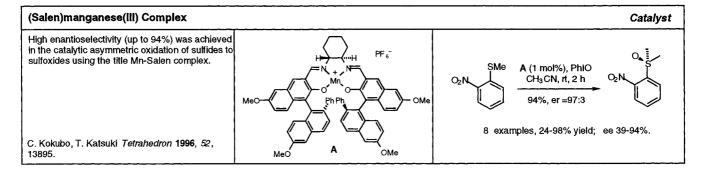
SYNTHESIS ALERTS

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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(Pyridine-2,6-dicarboxylate)(HMPA)Mo(O)	02	Cata				
The title molybdenum peroxo complex catalyses the regioselective allylic amination of alkenes by aryl amines with <i>tert</i> -butyl hydroperoxide as oxidant. R. S. Sricastava, K. M. Nicholas <i>Chem. Commun.</i> 1996, 2335.	(dipic)(HMPA)Mo(O)O₂ A	A (2 mol%) PhNH 2*BuOOH (1:3) dioxane-CH ₂ Cl ₂ , 70-80°C 64% NHPh 7 examples, yields from 51-91%.				

Homochiral Cobalt Catalyst The title catalyst together with sodium borohydride and a tetrahydrofurfuryl alcohol enantioselectively reduces aromatic ketones. A (1 mol%), NaBH 4 (1.5 eq) (1.5 eq) (2.5 eq), THFA (20 eq), THFA (20

Titanium(IV) Chloride Tris(trifluoromethanesulfonate)

Catalyst

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Catalytic Friedel-Crafts acylation of aromatic compounds with carboxylic anhydrides may be achieved with the title compound together with triflic acid.

TiCl(CF3SO3)3

14 examples: 5 aromatics, 4 anhydrides, yields 60-98%

J. Izumi, T. Mukaiyama Chem. Lett. 1996, 739.

Nickel(II) Acetylacetonate Catalyst Catalyses the hydrozincation of terminal olefins to afford functionalised organozinc reagents. The nickel reagent also catalyses halogen-zinc (a) Ni(acac)₂ (5 mol%), Et₂Zn (2 equiv),0°C exchange with primary alkyl halides. C₆H₁₃ (b) CuCN•2LiCI (10 mol%), THF, -60°C CO₂Et Ni(acac)₂ (c) H₂C=C(CH₂Br)CO₂Et (0.7 eq) 74% Over 20 examples documented. S. Vettel, A. Vaupel, P. Knochel J. Org. Chem. 1996, 61, 7473.

Trimethyltin Acetate Catalyst The title compound acts as a co-catalyst in intramolecular Pd-catalysed trimethylene Pd(OAc) 2 (0.0225 mmol) methane cycloadditions to electron deficient Me₃SnOAc (0.0450 mmol) alkenes. (i-PrO)₃P (0.135 mmol) Me₃SnOAc 3Å MS (144 mg) PhMe (7 mL), ∆, 3 h 42.5% (0.900 mmol scale) (+40% yield of B. M. Trost, Higuchi, R. I. J. Am. Chem. Soc. two isomers) 1996, 118, 10094.

η^5 -Pentamethylcyclopentadienyl- η^5 -2-[(triethylsilyloxy)methyl]pyrrolyliron

Catalyst

The title compound was one of 4 new chiral (r-heterocycle)FeCp* complexes evaluated as catalysts in the kinetic resolution of secondary alcohols and in cyanohydrin formation form aldehydes.

J. C. Ruble, G. C. Fu J. Org. Chem. 1996, 61, 7230.

(1*R,2 S*)-2-Amino-3,3-dimethylindan-1-ol

Chiral Auxiliary

Oxazolidinones prepared from the title compound are efficient chiral auxiliaries.

A
$$\frac{3 \text{ steps}}{92\%}$$
 $\frac{\text{(a) LDA, THF, -78°C}}{\text{(b) Etl, -78 \to 0°C}}$ $\frac{\text{(a) LDA, THF, -78°C}}{\text{(b) Etl, -78 \to 0°C}}$

A. Sudo, K. Saigo *Tetrahedron: Asymmetry* 1996, 7, 2939.

This chiral auxiliary also undergoes efficient asymmetric alkylation (4 examples), acylation (2 examples), hydroxylation (1 example) and bromination (1 example).

Chiral Auxiliary

Ligand

(1S,5 R,7 S)-3-Ethyl-2-oxo-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-exo-carboxylic Acid

Chiral Auxiliary

1-Acetylvinyl esters prepared from the title compound undergo regio- and diastereoselective Diels-Alder reactions promoted by BF 3 OEt2.

Preparation of the title compound from (R, R)-tartaric acid: L. H. Hurley, J. Med. Chem. 1989, 9, 2027.

Z. Dienes, P. Vogel J. Org. Chem. 1996, 61, 6958.

$$\begin{array}{c} \text{HeO} & \text{OMe} \\ \text{A} & \text{OMe} \\ \text{A} & \text{OMe} \\ \text{A} & \text{A} & \text{A} & \text{A} & \text{A} \\ \end{array}$$

1,1'-Binaphthalene-8,8'-diol

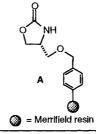
 α,β -Unsaturated monoesters of A undergo conjugate addition of simple lithium dialkyl cuprates with high diastereoselectivity.

Me 2CuLi -20 →rt, 3.5 h 85%, er = 99:1

Following 1,4-addition, a formal 1,2-addition of the nucleophile occurs to yield the corresponding ketone. 11 examples illustrating reaction of various $\alpha\beta$ -unsaturated monoesters of **A** with dimethyl or dibutyl cuprates (yields 54-91%, ee 96-100%). K. Fuji, X. Yang, K. Tanaka, N. Asakawa Tetrahedron Lett. 1996, 37, 7373.

Polymer Bound Oxazolidinone

An oxazolidinone bound to Merrifield resin provides a chiral auxiliary for solid phase asymmetric alkylation of carbonyl compounds.

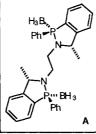


Chiral Auxiliary (a) LDA (2 eq),THF, 0°C (CH₃CH₂CO)₂O (b) PhCH₂Br (2 eq) **DMAP (10 mol%)** (c) NH₄Cl_(aq) Et₃N (1 eq) THF, ∆, 4 ďays 42% LIOH+H2O er = 98:2THF, H₂O

S. M. Allin, S. J. Shuttleworth Tetrahedron Lett. 1996.37.8023.

Azaphosphole Borane Complex

Synthesis and applications of a new class of C2 symmetric phosphorus donor ligand for asymmetric catalysis



Α

,CO₂Me MeO₂C A (0.025 eq), $[(C_3H_5)PdCI]_2$ (0.01 eq) MeO₂CCH₂CO₂Me (1.1 eq) 95% (er = 77:23)

> The title ligand can be in asymmetric hydrogenation (1 example) and hydrositylation (3 examples).

G. Brenchley, M. Fedouloff, E. Merifield, M. Wills Tetrahedron: Asymmetry 1996, 7, 2809.

N-Tosyl-($\alpha S, \beta R$)- β -methyltryptophan Ligand Arylboron complex A prepared from the title Ph-4-Cl compound and dichloro-(4-chlorophenyl)borane catalyse enantioselective cleavage of w^{Ts} OMe 2-aryl-1,3-dioxolanes with ketene acetals. A (10 mol %) CH2Cl2, -20°C 82% (3 eq) er = 96:4 ÓМе 8 examples, 62-89%v yield; er = 92:8 - 96:4

M. Kinugasa, T. Harada, A. Oku J. Org. Chem.

Ligand

Ligand

Ligand

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

The title compound is a ligand in the intramolecular Pd-catalysed ipso substitution of an aryl halide with an alcohol to generate benzo-fused oxacycles.

P(Tol)₂

HO Pd(OAc) 2 (5 mol%)
A (6 mol%)

K2O3 (1.2 eq)

A (6 mol%)

K₂©₃ (1.2 eq)
PhMe, 100°C
65%

7 examples using the conditions described above (60-90% yield).

M. Palucki, J. P. Wolfe, S. L. Buchwald J. Am.

Chem. Soc. 1996, 118, 10333.

A vamples using the conditions described above (60-90% yield).

A further 5 examples use 1,1'-bis(diphenylphosphino)ferrocene as ligand and sodium tert-butoxide as base (32-73% yield).

2,6-Dimethyl-9-phenyl-9-phosphabicyclo[3.3.1]nonane (9-PBN)

The preparation of the monodentate phosphine ligand A is descibed together with its application in a palladium catalysed asymmetric allylic substitution reaction.

TO

11 examples utilising predominantly the illustrated substrate with a range of malonate nucleophiles (yields 35-100%, ee 65-97%).

BSA = bis(trimethylsilyl)acetamide

Y. Hamada, N. Seto, H. Ohmori, K. Hatano Tetrahedron Lett. 1996, 37, 7565.

exo-2-Azabicyclo[2.2.1]heptane-3-carboxylic Acid

A chiral ligand for the copper catalysed asymmetric allylic oxidation of olefins by *tert*-butyl perbenzoate.

 $\bigcap_{\substack{N\\H}} \infty_2 H$

Cu(OAc)₂+H₂O (5 mol%) copper bronze (0.5 eq)

(+)-A (0.25 eq), PhCO $_2$ H (1 eq) BuOOC(O)Ph (1 eq), PhH, $_\Delta$, 4 h

O, O, Ph

Protecting Group

10 examples of oxidation of cyclopentene and cyclohexene under varying conditions. Proline and the analogous bicyclo[2.2.2]octane ligand were also tested (yields 25-67%, ee 11, 15, 44-65%).

M. J. Södergren, P. G. Andersson *Tetrahedron Lett.* **1996**, *37*, 7577.

Benzothiazole-2-sulfonyl Chloride

The title compound is prepared by reaction of the 2-mercaptobenzothiazole with chlorine in aqueous HOAc. It is stable at <0°C Indefinitely but gradually decomposes at rt. The sulfonamides prepared from **A** are useful amino protecting groups in peptide coupling reactions.

E. Vedejs, S. Lin, A. Klapars, J. Wang J. Am. Chem. Soc. **1996**, 118, 9796.

N so₂a

H Ph OH OH (pH 10-10.5) 10°C, 10 h 92-97%

Stable to TFA (Boc removal) and Et₂NH in DMF (Fmoc removal). Slow cleavage with 1 M NaOH and H₂-Pd/C-EtOAc (CDz removal).

HN OH

S <u>Deprotection conditions:</u>
(a) Zn/HOAc-EtOH, rt
(b) Al(Hg)/Et₂O-H₂O, rt
(c) H₃PO₂/DMF or THF, rt-reflux

5-Methyl-1,3,4-thiazole-2-sulfonyl Chloride

Protecting Group

The preparation and reactions of the title compound are very similar to benzothiazole-2-sulfonyl chloride (see accompanying abstract). The corresponding sulfonamides also have similar stability and are deprotected under the same conditions as the benzothiazole-2-sulfonyl (Bts) group.

E. Vedejs, S. Lin, A. Klapars, J. Wang *J. Am. Chem. Soc.* **1996**, *118*, 9796.

HPh HOBU 50% H₃PO₂ DMF, rt 95% H₂N DBn H

The 5-methyl-1,3,4-thiadiazole-2-sulfonyl group (Ths) group is more expensive than the related Bts group but it reacts faster with amino acids in aqueous suspension and it has improved solubility and crystallinity in some cases. The reductive deprotection conditions shown above do not affect *N*-tosylsulfonamides.

Cyanuric Fluoride		Reagent
The title compound induces 1,4-addition of alkenylboronic acids with α,β-unsaturated ketones to give γ,δ-unsaturated ketones. S. Hara, S. Ishimura, A. Suzuki <i>Synlett</i> 1996, 993.	, N F	Bu B(OH) ₂ Br A CH ₂ Cl ₂ 40°C, 4 d 81% Recognition A CH ₂ Cl ₂ Bu CO ₂ B 7 examples; yields 70-90%

Niobium Pentachloride		Reagent
α-[(TrialkyIstannyi)methyl]-β-oxo esters may be homologated to the corresponding γ-oxo esters with the title reagent. M. Yarnamoto, M. Nakazawa, K. Kishikawa, S. Kohmato <i>Chem. Commun.</i> 1996, 2353.	NbCl ₅	Ph

1,2-Dibromotetrafluoroethane Reag				
The title compound can be used as an entrainer to activate magnesium for the formation of Grignard reagents in substrates containing amine functionality.	Br-CF ₂ CF ₂ -Br	MeO MgBr MeO Mg, A THF, A MeO		
P. Chau, I. R. Czuba, M. A. Rizzacasa, G. Bringmann, KP. Gulden, M. Schäffer J. Org. Chem. 1996, 61, 7101.		See also A. I. Meyers, R. H. Hutchings J. Org. Chem. 1996, 61, 1004.		

Tetrabutylammonium Triphenyldifluoros	Reagent					
The title compound (abbreviated TBAT) is an easily handled source of anhydrous fluoride for silicon-carbon bond cleavage. It is non-hygroscopic, soluble in most organic solvents, and significantly less basic than TBAF.	F	O °	+	∕ SiMe ₃	A (1 eq) THF, 70°C, 24 h 96%	OSiMe ₃
	Ph I (bu 414)	<i>n</i> -C ₁₂ H ₂₃ Br	+	S SiMe ₃	A (2 eq) THF, 50°C, 22 h 52%	$\bigcup_{S}^{S} C_{12}H_{23}$
A. S. Pilcher, P. DeShong <i>J. Org. Chem</i> . 1996 , <i>61</i> , 6901.					silanes are also cleave I silanes do not react.	d

2-(Trimethylsilyl)ethanesulfonamide Reagent The title compound, together with iodonium d- sym-collidine perchlorate as electrophilic activator, effects sulfonamidoglycosylation of BnO SO2NH2 glycals. The *trans*-iodo sulfonamide adduct reacts with alcohols to give aminoglycosides in which the amine is protected as a 2-(trimethylsilyl)ethanesulfonamide. I(sym-coll) 2CIO. BnO⁻ HN BnO-SiMe: 4Å sieves **KHMDS** CH 2Cl 2, 0°C 78% Α D. A. Griffith, S. J. Danishefsky *J. Am. Chem. Soc.* **1996**, *118*, 9526. The 2-(trimethylsilyl)ethanesulfonyl protecting group is removed with CsF in

2,2-Dichloro-5-(2-phenylethyl)-4-(trimethylsilyl)furan-3-one (DPTF)		
A water-compatible dehydrating reagent for the synthesis of amide linkages. M. Murakami, M. Hayashi, N. Tamura, Y. Hoshino, Y. Ito <i>Tetrahedron Lett.</i> 1996 , <i>37</i> , 7541.	SiMe 3 CI Ph	HO Ph A, NEt Pr MeCN rt, 1 h 90% A examples of peptide elongation.