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.

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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

Chiral molybdenum metathesis catalyst

Complex A accomplishes an asymmetric synthesis of dihydrofurans *via* catalytic kinetic resolution or enantioselective desymmetrisation of diallyl ethers.

D. S. La, J. B. Alexander, D. R. Cefalo, D. D. Graf, A. H. Hoveyda, R. R. Schrock *J. Am. Chem. Soc.* **1998**, *120*, 9720.

Bu^t
Bu^t
Ph

4 examples of kinetic resolution in which *unreacted* diallyl ether is obtained in 75, 92-98% ee; 6 examples of desymmetrisation (yields 28, 83-91%; ee 10, 73-99%). Reactions are run neat.

Pt(OC₆H₄CO)[(R)-BINAP] Catalyst

The title compound catalyses the asymmetric aldol addition of methyl trimethylsilyl dimethylketene acetal to aldehydes.

O. Fujimura J. Am. Chem. Soc. 1998, 120,

10032

Ph₂P PPh₂

OMe OMe TfOH (5 mol%) OMe OMe OMe OMe (1.0 eq) (1.5 eq) CH₂Cl₂, -25°C, 170 h 96% (e.r. = 95:5)

7 aldehyde substrates tried. t-BuCHO does not work at all; c-C₆H₅CHO gives low yields. Unhindered aldehyde gives 66-99% yield and 10-91% ee

Tetrakis(triphenylphosphine)palladium(0)

Catalyst

Catalyst

Symmetrical dialkyl alkynes and phenyl alkyl alkynes react with pronucleophiles in the presence of Pd(0) and acetic acid to give allylation products.

Pd[PPh₃)₄

OMe MOMO-CH(CN)₂ MeO OMOM

A (5 mol%) CN

HOAc (50 mol%) CN

dioxane, 100°C

I. Kadota, A. Shibuya, Y. S. Gyoung, Y. Yamamoto *J. Am. Chem. Soc.* **1998**, *120*, 10262

10 examples involving 6 alkynes and 5 pronucleophiles gave 64-99% yield allylated products. 3 examples of intramolecular allylation (84-93%) are also reported.

SYNTHESIS ALERTS 199

Indium(III) Chloride		Catalyst
The title reagent catalyses the Michael reaction between primary or secondary amines and α, β -ethylenic compounds in water under mild conditions. A can be recovered and re-used without loss of activity.	InCl ₃	(<i>i</i> -Pr) ₂ NH
TP. Loh and LL. Wei <i>Synlett</i> 1998 , 975.		22 examples (yields 6-98%).

Microencapsulated Osmium Tetraoxide (MC OsO ₄)		Catalyst
Preparation and use of A for the dihydroxylation of olefins is reported. The catalyst can be recovered and re-used without loss of activity.	MC OsO ₄	MO (1.3 eq) H ₂ O-Me ₂ CO-MeCN (1:1:1), rt OH OH
S. Nagayama, M. Endo, S. Kobayashi <i>J. Org. Chem.</i> 1998 , <i>63</i> , 6094.		11 examples (yields 68-89%) are reported.

Bis(cyclopentadienyl)zirconium dichloride		Catalyst
The zirconium-catalysed reactions of alkynyl halides with EtMgBr are reported. The reaction proceeds <i>via</i> a zirconocene-ethylene complex and a zirconacycle to yield cyclobutene derivatives.	Cp ₂ ZrCl ₂	CI———C ₈ H ₁₇ EtMgBr (3 eq) A (10 mol%) THF, rt, 1 d 51%
K. Kasai, Y. Liu, R. Hara, T. Takahashi <i>Chem.</i> Commun. 1998 , 1989.		4 examples (yields 50-61%).

Tetrabutylammonium Bromide / Tetrabut	ylammonium lodide	Catalyst
Tetrabutylammonium halides promote carbonyl propargylation or allenylation. Selectivity between propargylation and allenylation depends on the halide. Y. Masuyama, A. Ito, M. Fukuzawa, K. Terada, Y. Kurusu <i>Chem. Commun.</i> 1998 , 2025.	Bu ₄ NBr A Bu ₄ NI B	X = Br SnCl ₂ (1 eq), A (30 mol%) H ₂ O, rt, 12 h 1, 63% (1:2 = 100:0) X = Cl; Nal (1.5 eq) Snl ₂ (1 eq), TBAI (10 mol%) H ₂ O,0°C, 4 d 2, 50% (1:2 = 7:93) 6 examples of propargylations (yields 48-77%, selectivity 100%) and 6 examples of allenylations (yields 50-80%, selectivity 80-98%) are reported.

m-Trifluoromethylstyrene		Ce	atalyst
A is a cocatalyst in the cross coupling of organozinc species and organic halides.	F ₃ C	$\begin{array}{c c} & & & & \\ \hline S & S & & & \\ \hline (CH_2)_2I & & & & \\ \hline & & & & \\ \hline (CH_2)_2I & & & \\ \hline & & & & \\ \hline & & & & \\ \hline & & & &$	₅ OPiv
R. Giovannini, T. Stüdemann, G. Dussin, P. Knochel <i>Angew. Chem. Int. Ed.</i> 1998 , <i>37</i> , 2387.		8 examples (yields 66-78%).	

(R)-Tol-BINAP-CuClO₄•(MeCN)₂

Catalyst

A catalyses the diastereo- and enantioselective alkylation of α -imino esters with enol silanes

TsHN A (5 mol%) **OTMS** ÖΕt (1.1 eq)Ph 86% CH_2CI_2 , $0^{\circ}C \rightarrow rt$, O/Ner = 99:1anti:syn = 25:1

D. Ferraris, B. Young, C. Cox, W. J. Drury III, T Dudding, T. Lectka J. Org. Chem 1998, 63, 6090.

7 examples (yields 71-86%, %ee 46-98%, $3:1 \le anti:syn \le 25:1$)

(BINOL-Me)-tin tetrachloride complex

Catalyst

The title Lewis acid-assisted Brønsted acid (LBA) catalyses highly regio- and stereoselective isomerisation of "kinetic" silyl enol ethers to "thermodynamic" silyl enol ethers. The catalytic system is applied to the enantiomer-selective isomerisation of a racemic enol ether.

OTBS (R)-A (5 mol%) PhMe, -78°C, 2 min 42 % 53% er = 99 :1

12 examples of isomerisation (yields 78-97%, thermodynamic : kinetic ratio ≥ 72:28) and the above example of enantiomer-selective isomerisation are reported.

K. Ishihara, H. Nakamura, S. Nakamura, H. Yamamoto J. Org. Chem. 1998, 63, 6444.

Bis(dibenzylideneacetone)palladium(0)

Catalyst

A catalyses inter- and intramolecular lpha-arylation of amides. Intramolecular amide arviation of 2-haloanilides represents a versatile methodology for preparing substituted oxindoles. The intramolecular reaction is significantly more tolerant of electronic and steric substrate modifications than the intermolecular reaction.

Pd(dba)₂ Α

A (10 mol%) BINAP (15 mol%) t-BuONa (1.5 eq) Dioxane, 100°C, 4 h Ме

K. H. Shaughnessy, B. C. Hamann, J. F. Hartwig J. Org. Chem. 1998, 63, 6546.

9 examples of intermolecular reactions (yields 16-72%), and 9 examples of intramolecular reactions (yields 52-83%) are described.

Rhodium N-(dodecylbenzenesulfonyl)prolinate [(Rh₂(S-DOSP)₄]

Catalyst

CO₂Me

A is utilised in the asymmetric synthesis of cyclopentenes by [3+2] annulations between vinylcarbenoids and vinyl ethers.

 $Ar = 4-C_{12}H_{25}Ph$

CO₂Me A (1 mol%) pentane, -78°C, 1 d (5 eq) 57% CO₂Me er = 94:6 Et₂AICI (2 eq) CH₂Cl₂ 7 examples of the synthesis of 80% cyclopentenes (yields 34-60%, %ee = 11, 74-86%) are described. –78°C → rt̄, 4 h er = 92:8

H. M. L. Davies, N. Kong, M. R. Churchill J. Org. Chem. 1998. 63, 6586.

Bis-(Triphenylphosphine)Ruthenium(II) Dichloride

Catalyst

The title catalyst mediates the intramolecular addition of a chiral gem-dichloroacyl moiety to a 2-oxazolone. The methodology is utilised in the synthesis of 2-amino alcohols containing three contiguous stereocentres.

RuCl₂(PPh₃)₃ Δ

A (10 mol%) PhH, ∆, 5 d

T. Morita, H. Matsunaga, E. Sugiyama, T. Ishizuka, T. Kunieda Tetrahedron Lett. 1998, 39,

7131.

Two examples (yields 75%, 83%) are described.

Chiral Auxiliary

Chiral Auxiliary

Ligand

Ligand

Palladium(0) Catalyst Catalyst

The title catalyst mediates the Wacker oxidation of alkenes in a perfluorooctane-benzene biphasic system.

$$C_7F_{15}$$
 C_7F_{15} C_7F_{15} C_7F_{15} C_7F_{15} C_7F_{15} C_7F_{15}

15 examples (yields 54-95%). A can be recovered from the fluorous phase and reused, though progressively longer reaction times are required.

N-(2,3,4,6-Tetra-O-pivaloyl-β-D-galactopyranosyl)pyrid-4-one

The title compound reacts with Grignard reagents to give 2-substituted 5,6-dehydropiperidin-4-ones with good to high stereoselectivity.

B. Betzemeier, F. Lhermitte, P. Knochel

Tetrahedron Lett. 1998, 39, 6667.

 $\mathbf{A} \qquad \frac{\text{(a) } \text{ } i\text{-Pr}_3\text{SiOTf}}{\text{(b) } \text{ } n\text{-PrMgCl},} \\ \text{THF, 1 h} \qquad \qquad \mathbf{X}_c \\ \mathbf{X}_$

M. Follmann and H. Kunz Synlett 1998, 989.

3 examples (yields 74–84%, dr [(S):(R)] = 90:10 - 0:100)

5,5-Ditolyl-(4S)-isopropyl oxazolidin-2-one

The title auxiliary directs the diastereoselective methylation, benzylation and azidation of its *N*-acylated derivatives. Furthermore, it is readily cleaved by LiOH.



 $\begin{array}{c|c} O & O \\ \hline O & N \\ \hline Ar & \\ \hline Ar & \\ \hline O^{\circ}C & \\ \hline & \\ \hline & &$

C. L. Gibson, K. Gillon, S. Cook *Tetrahedron Lett.* **1998**, *39*, 6733.

$$Ar = 4\text{-MeC}_6H_4$$

2 examples (yields 52, 66%, %de 94, 96%). Similar use of 2 other auxiliaries (R = 2-naphthyl, Ph) is described.

2-Dimethylamino-2'-(dicyclohexylphosphino)biphenyl

The title ligand together with Pd₂(dba)₃ is a very active catalyst which mediates a variety of coupling reactions such as the amination of aryl bromides and chlorides, Suzuki couplings, and arylation of ketone enolates—all at room temperature.

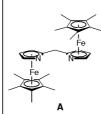
D. W. Old, J. P. Wolfe, S. L. Buchwald *J. Am. Chem. Soc.* **1998**, *120*, 9722.

$$\mathsf{Me}_2\mathsf{N} \qquad \qquad \mathsf{P}(\mathsf{Cy})_2$$

$$\qquad \qquad \mathsf{A}$$

C₂-Symmetric Bisazaferrocene

The title compound represents a new class of planar-chiral ligands which, together with CuOTf, catalyses the enantioselective cyclopropanation of alkenes.



Ph
$$=$$
 1% CuOTf 1.2% (R,R)-A $=$ CO₂Ar $=$ CH₂Cl₂, r.t. $=$ Ph $=$ Ph

6 examples or aryl-, alkyl- and silyl-substituted *terminal* alkenes: 64-90% yield; 87-96% ee; trans:cis = 93:7–96:4

M. M.-C. Lo, G. C. Fu *J. Am. Chem. Soc.* **1998**, *120*, 10270.

Ligand

NHAc

Ligand

51%

er > 99:1

(S,S)-1,2-Bis(2,5-dimethylphospholano)benzene (Me-DuPHOS)

A rhodium catalyst derived from the title ligand is utilised in a three-step procedure for the asymmetric catalytic reductive amination of ketones.

Me Me Me Me

 (a) NaOAc (1.1 eq), NH₂OH (1.1 eq) MeOH, rt, 8 h
 (b) Ac₂O (3 eq), HOAc (3 eq), Fe (2 eq) PhMe, 70°C, 4 h

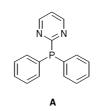
> (c) [**A**-Rh(COD)]BF₄ (0.2 mol%) H₂ (200 psi) MeOH, rt, 20 h

2 examples of reductive amidation using **A** and (R,R)-**A** are reported (yields 32, 51%, ee > 99:1).

M. J. Burk, G. Casy, N. B. Johnson *J. Org. Chem.* **1998**, *63*, 6084.

2-Pyrimidyldiphenylphosphine

The title ligand mediates the palladium(II)-catalysed carbonylation of terminal and internal alkynes.



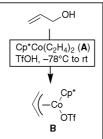
M. T. Reetz, R. Demuth, R. Goddard *Tetrahedron Lett.* **1998**, *39*, 7089.

6 examples (yields 25, 48->97%) are described. *Bis*- or *tris*- 2-pyridyl substituted phosphines resulted in significantly longer reaction times.

Cp*Co(C₂H₄)₂ Reagent

Complexes **B** derived from the title compound **A** undergo intermolecular allyl/alkyne [3+2+2] cycloaddition reactions to give cationic η^5 -cycloheptadienyl complexes which can alkylate soft nucleophiles.

N. Etkin, T. L. Dzwiniel, K. E. Schweibert, J. M. Stryker J. Am. Chem. Soc. 1998, 120, 9707.



2,2-Dimethoxypropane Reagent

The title compound, methanol and a catalytic amount of HCl selectively esterifies aliphatic carboxylic acids in the presence of aromatic carboxylic acids. The reaction gives high yields and takes place at room temperature.

OMe OMe A. Rodriguez, M. Nomen, B. W. Spur, J. J. Godfroid *Tetrahedron Lett.* **1998**, *39*, 8563.

6 examples of substrates with both aliphatic and aromatic carboxylic acids (>95% yield); 16 examples of aliphatic carboxylic acids (usually 100% yield). Even in the presence of 20 mol% TMSCI, aromatic carboxylic acids give very low yields of the ester (typically <3%).

N,N-Carbonyldiimidazole

A is utilised in a convenient conversion of α -aminoacids into NH-Boc protected α -aminoketones via imidazolides.

lm Im

(a) **A**, THF, rt, 30 min

(b) C₅H₁₁MgBr (2 eq)
Cul (6 mol%)

THF, 0°C, 3 h

Reagent

B. F. Bonini, M. Comes-Franchini, M. Fochi, G. Mazzanti, A. Ricci, G. Varchi *Synlett* **1998**, 1013.

9 examples (yields 30-68%).

1998, *54*, 10827.

Reagent Indium Treatment of a range of aromatic nitro compounds with **A** and aqueous ethanolic ammonium chloride results in selective reduction NH₂ of the nitro groups; ester, nitrile, amide and halide substituents are unaffected. In NH₄Cl, aq. EtOH Α Δ . 3 h 95% C. J. Moody and M. R. Pitts Synlett 1998,

11 examples (yields 60-99%).

Reagent Samarium(II) lodide / Nickel(II) lodide In the presence of the title reagent pair, β -lactones react with aldehydes, ketones and imines to afford tetrahydrofuranones and (a) A (2.2 eq), B (1 mol%) Sml₂ butanone (1 eq) pyrrolidinones in good to high yield. THF, rt, 1 h Α (b) 0.1 M HCl, rt, 30 min Nilo В 17 examples of coupling with aldehydes and ketones (yields 0, 74-98%) F. Machrouhi, J.-L. Namy Tetrahedron 1998, 54, and 7 examples of coupling with imines (yields 70-93%) are reported. 11111.

Metals on polyethylene solid support Reagent Convenient preparation of "high-surface alkali metals" deposited on solid-supports and Li-PE (2.2 eq) subsequent use in a variety of reactions is reported. The metals can be stored as stable $H_2C=CH(CH_2)_2Br$ (1.1 eq) suspensions in inert solvents if protected against M / Polyethylene (PE) THF, -78°C, 15 min oxygen. Preparation of Zn on solid-support is 76% also reported. M = Li, Na, K, Zn36 examples in total of the use of Na-PE in the acyloin reaction, formation of organolithium species using Li-PE and trapping with electrophiles, an intramolecular Dieckmann cyclisation utilising K-PE and Reformatsky and M. Makosza, P. Nieczypor, K. Grela Tetrahedron Barbier-type reactions using Zn-PE are reported. Yields are good to excellent.

Copper(I) Chloride		Reagent
The title reagent mediates the intermolecular homocoupling of alkenyltrimethylstannanes, to afford functionalised conjugated dienes and tetraenes in good to high yield.	CuCl A	A (2.5 eq) DMF, rt, 30 min 94%
E. Piers, P. L. Gladstone, J. G. K. Yee, E. J. McEachern <i>Tetrahedron</i> 1998 , <i>54</i> , 10609.		17 examples (yields 18-91%) are reported.

1-(Triisopropylsilyloxy)-1-(tert-butylthio)ethene Reagent Exceptional Cram-type selectivites in Mukaiyama aldol reactions of A are reported. The level of 1,2-asymmetric induction is promoted by the bulk BF₃•OEt₂ (1 eq) of the silyl group. t-BuS SBu CH₂Cl₂, -80°C, 30 min 0 i-Pr₃SiO ŌН 76% syn:anti = 130:1 A A. P. Davis, S. J. Plunkett, J. E. Muir Chem. 3 examples (yields 76-78%, $5:1 \le syn:ant\bar{n} \le 130:1$) are described. Commun. 1998, 1797.

(R)-2-Methoxy-6-(1-hydroxyethyl)phenylselenyl triflate

Reagent

Reagent

The asymmetric methoxyselenenylation of styrene derivatives using A is reported.

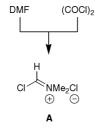
G. Fragale, M. Neuburger, T. Wirth Chem. Commun. 1998, 1867.

(Chloromethylene)dimethylammonium chloride

Reagent The title compound (generated in situ from DMF

and oxalyl chloride) reacts with secondary alcohols to form imidate esters. Reaction with potassium carboxylates or potassium phthalimide gives products with clean inversion of stereochemistry.

A. G. M. Barrett, D. C. Braddock, R. A. James, N. Koike, P. A. Procopiou J. Org. Chem. 1998, 63,



O₂CPh (a) A (1.2 eq), THF, 0°C, 5 min PhCO₂K (3 eq) THF. •. 18 h 91 % er = 99:1

17 examples of ester formation (yields 15-91%, %ee = 51->95%) and 9 examples of formation of phthalimido derivatives (yields 25-98%, %ee = 0,

2-(R)-1-[(Dimethylamino)propyl]thiophenol

In situ hydrozirconation of alkynes, transmetallation to zinc, and addition to aldehydes catalysed by A provides an efficient protocol for the asymmetric preparation of (E)-allylic alcohols.

$$C_{4}H_{9} = \begin{cases} \text{(a) } Cp_{2}ZrHCl \text{ (1.0 eq)} \\ CH_{2}Cl_{2}, \text{ rt, 5 min} \end{cases}$$

$$(b) \ \ Me_{2}Zn \text{ (1 eq), } \textbf{A} \text{ (10 mol%)} \\ PhMe, -65^{\circ}C \rightarrow -30^{\circ}C, 1 \text{ h} \\ \text{(c) } PhCHO \text{ (1 eq), } -30^{\circ}C, 12 \text{ h} \end{cases}$$

$$90\%$$

$$\text{er = 92:8}$$

$$10 \text{ examples (yields 63-90%, %ee 63-99)}$$

Lithium Hydroxide Reagent A promotes Horner-Wadsworth-Emmons dienylation of aldehydes and ketones EtO₂C EtO₂C A (1.1 eq) .CHO 4Å MS LiOH EtO₂C THF, Δ, 12 h EtO₂C 86% $(OEt)_2(O)P$ ∠CO₂Et J. M. Takacs, M. R. Jaber, F. Clement, C. Walters (1.1 eq)J. Org. Chem. 1998, 63, 6757. 9 examples (yields 64-99%).

N-Boc-4,4-dimethyl-1,3-oxazolidine

Reagent

Formation and reaction of the 2-metallated title reagent in the presence of (-)-sparteine is described representing a new chiral formyl anion equivalent. The two diastereoisomers are formed with high enantioselectivity although little diastereoselectivity is observed in the absence of MgBr₂.

N. Kise, T. Urai, J. Yoshida Tetrahedron: Asymmetry 1998, 9, 3125

A facilitates transmetallation from aluminium to tin in a preparation of tributylstannylprop-2-en-1-ols.

Bu₃SnOMe

A

Bu₃SnOMe

A

Bu₃SnOMe

A

Bu₃SnOMe (7.5 mol%)
LiAlH₄ (1.1 eq)
THF, 0°C, 1 h

(b) Bu₃SnOMe (1 eq)
4°C, 2 d
74%

OH

12 examples (yields 13-74%).

The title reagent, which is soluble in common organic solvents, mediates the practical acylation of amines.

CO₂Na

H
O
CICH₂COCI (1 eq)
NH₂

THF, rt
> 90%

J. Fitt, K. Prasad, O. Repic, T. J. Blacklock
Tetrahedron Lett. 1998, 39, 6991.

Manganese <i>tris</i> (acetylacetonate)		Reagent
The title catalyst mediates the diastereoselective oxidative coupling of seco-biaryl compounds to give symmetrical and unsymmetrical BINOL-derivatives.	Mn(acac) ₃ A	AcHN OH OH OH CH ₃ CN, 50°C 75%, dr = 95.5
B. H. Lipshutz, YJ. Shin <i>Tetrahedron Lett.</i> 1998 , <i>39</i> , 7017.		9 examples (yields 69-89%, %de 84-97%) are described.

The title reagent in aqueous THF mediates the reductive cleavage of *N*-acyloxazolidinones.

NaBH₄

A

NaBH₄

B

NaBH₄

A

NaBH₄

A

NaBH₄

CN

95%

er >99:1

13 examples (yields 75-95%, %ee >99%) are described. In contrast, use of LiBH₄ resulted in ~10% racemisation.