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:
Stephen Brand, John Christopher, Emma Guthrie, Philip Kocienski, Louise Lea, Russell McDonald, Graeme McAllister and Robert Narquizian of Glasgow University.

Georg Thieme Verlag does not accept responsibility for the accuracy, content, or selection of the data.

---

**Chiral molybdenum metathesis catalyst**

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

![Chiral molybdenum metathesis catalyst](image)

<table>
<thead>
<tr>
<th>Catalyst</th>
</tr>
</thead>
</table>

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.

**PI(OC₂H₅CO)[(R)-BINAP]**

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

![PI(OC₂H₅CO)[(R)-BINAP]](image)

<table>
<thead>
<tr>
<th>Catalyst</th>
</tr>
</thead>
</table>

7 aldehyde substrates tried. t-BuCHO does not work at all; o-C₆H₅CHO gives low yields. Unhindered aldehyde gives 68-99% yield and 90-91% ee.

**Tetrakis(triphenylphosphine)palladium(0)**

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

![Tetrakis(triphenylphosphine)palladium(0)](image)

<table>
<thead>
<tr>
<th>Catalyst</th>
</tr>
</thead>
</table>

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

The title reagent catalyses the Michael reaction between primary or secondary amines and \(\alpha,\beta\)-ethylenic compounds in water under mild conditions. \(\text{A}\) can be recovered and re-used without loss of activity.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{InCl}_3)</td>
<td>((\text{Pr}_2)\text{NH})CN (\text{A}) (20 mol%) (\text{H}_2\text{O}, \text{rt}, 16\ \text{h} )</td>
<td>82%</td>
</tr>
</tbody>
</table>


22 examples (yields 6-98%).

### Microencapsulated Osmium Tetraoxide (MC OsO₄)

Preparation and use of \(\text{A}\) for the dihydroxylation of olefins is reported. The catalyst can be recovered and re-used without loss of activity.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC OsO₄</td>
<td>(\text{A}) (5 mol%) NMO (1.3 eq) (\text{H}_2\text{O-Me}_2\text{CO-MeCN} (1:1:1), \text{rt} )</td>
<td>76%</td>
</tr>
</tbody>
</table>


11 examples (yields 68-89%) are reported.

### Bis(cyclopentadienyl)zirconium dichloride

The zirconium-catalysed reactions of alkynyl halides with EtMgBr are reported. The reaction proceeds via a zirconocene-ethylenic complex and a zirconacycle to yield cyclobutene derivatives.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{Cp}_2\text{ZrCl}_2)</td>
<td>(\text{Cl} = \text{C}=\text{C}_\text{H}_7) (\text{A}) (10 mol%) (\text{THF}, \text{rt}, 1 \text{ d} )</td>
<td>51%</td>
</tr>
</tbody>
</table>


4 examples (yields 50-61%).

### Tetrabutyllumonium Bromide / Tetrabutyllumonium Iodide

Tetrabutyllumonium halides promote carbonyl propargylation or allenylation. Selectivity between propargylation and allenylation depends on the halide.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{Bu}_4\text{NB}r)</td>
<td>(\text{X} = \text{Br}) (\text{SnCl}_2 (1 \text{ eq}), \text{A} (30 \text{ mol%) (\text{H}_2\text{O}, \text{rt}, 12 \text{ h} )</td>
<td>63% (12 = 100:0)</td>
</tr>
<tr>
<td>(\text{Bu}_4\text{NI})</td>
<td>(\text{X} = \text{Cl}) NaI (1.5 eq) (\text{SnCl}_2 (1 \text{ eq}), \text{TBAL} (10 \text{ mol%) (\text{H}_2\text{O}, 0^\circ\text{C}, 4 \text{ d} )</td>
<td>2 = 50% (12 = 7:93)</td>
</tr>
</tbody>
</table>


6 examples of propargylations (yields 48-77%), selectivity 100%) and 6 examples of allenylations (yields 50-80%, selectivity 80-98%) are reported.

### \(m\)-Trifluoromethylstyrene

\(\text{A}\) is a cocatalyst in the cross coupling of organozinc species and organic halides.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(\text{F}_3\text{C}) (\text{A}) (\text{[PivO(CH}_2)_2\text{Zn} (2 \text{ eq}), [Ni(acac)]_2 (10 \text{ mol%) (\text{THF-MP}, 2:1 ) (-78^\circ\text{C} \rightarrow -35^\circ\text{C}, 2.5 \text{ h} )</td>
<td>70 %</td>
</tr>
</tbody>
</table>
| | \(\text{CH}_2\text{O})\text{Piv} \) | 8 examples (yields 66-78%).

### (R)-Tol-BINAP-CuClO₄(MeCN)₂

A catalyst for the diastereo- and enantioselective alkylation of acylimino esters with enol silanes.

- **Catalyst**
- **R = 4-MeC₂H₄**
- 7 examples (yields 71-86%, %ee 46-98%, 3:1 ≤ anti/syn ≤ 25:1)

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>(R)-A (5 mol%)</th>
<th>TsHN-Ph</th>
<th>C/O/N</th>
</tr>
</thead>
<tbody>
<tr>
<td>OEt</td>
<td>Ph</td>
<td>86%</td>
<td>99:1</td>
</tr>
</tbody>
</table>


### (BINOL)-Me-tetrachloride complex

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

- **Catalyst**
- **R = 4-MeC₂H₄**
- 12 examples of isomerisation (yields 78-97%), thermodynamic : kinetic ratio ≥ 72:28, and the above example of enantiomer-selective isomerisation are reported.


### Bis(dibenzylideneacetone)palladium(0)

A catalyst for inter- and intramolecular α-arylation of amides. Intramolecular amide arylation 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.

- **Catalyst**
- **Pd(dbac)₂**
- 9 examples of intermolecular reactions (yields 16-72%), 9 examples of intramolecular reactions (yields 52-83%) are described.


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

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

- **Catalyst**
- **Ar = 4-C₃H₆Ph**
- 7 examples of the synthesis of cyclopentenes (yields 34-60%, %ee = 11, 74-86%) are described.


### Bis-(Triphenylphosphine)Ruthenium(II) Dichloride

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

- **Catalyst**
- **A (10 mol%)**
- Two examples (yields 75%, 83%) are described.

### Palladium(0) Catalyst

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

\[
\text{C}_2\text{F}_{15} - \text{O} - \text{O} - \text{C}_2\text{F}_{15} \quad \text{Pd} \quad \text{C}_2\text{F}_{15} - \text{O} - \text{O} - \text{C}_2\text{F}_{15}
\]

\[
\text{PivO} \quad \text{C}_2\text{F}_{15} - \text{O} - \text{O} - \text{C}_2\text{F}_{15} \quad \text{A} \quad \text{PivO} \quad \text{C}_2\text{F}_{15} - \text{O} - \text{O} - \text{C}_2\text{F}_{15}
\]

B. Betzemeier, F. Uhermitte, P. Knochel


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-dehydroderpinid-4-ones with good to high stereoselectivity.

\[
\text{R} = \text{Piv}
\]

M. Follmann and H. Kunz

*Synlett* 1998, 989.

3 examples (yields 74–84%, dr [([S]:[R]) = 90:10–1:100].

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

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

\[
\text{Ar} = 4-\text{MeC}_6\text{H}_4
\]

G. L. Gibson, K. Gillon, S. Cook


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 Pd(dba)_2 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.

\[
\text{Ph} \quad \text{P} \quad \text{Me}_2\text{N} \quad \text{Ph}
\]

D. W. Old, J. P. Wolfe, S. L. Buchwald


### C2-Symmetric Bisazaferrocene

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

\[
\text{Ph} \quad \text{CO}_2\text{Ar} \quad \text{Ph} \quad \text{Ar} = \text{BHT}
\]

M. M.-C. Lo, G. C. Fu


6 examples or aryl-, alkyl- and alky-substituted terminal alkenes: 64–90% yield, 87–96% ee; trans/cis = 93.7–96.4
(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.

\[
\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{P} & \quad \text{Me}^2 \\
\text{P} & \quad \text{Me}^2
\end{align*}
\]

\(\text{A}\)

- (a) \(\text{NaOAc} (1.1 \text{ eq}), \text{NH}_2\text{OH} (1.1 \text{ eq})\), MeOH, rt, 8 h
- (b) \(\text{Ac}_2\text{O} (3 \text{ eq}), \text{HAc} (3 \text{ eq}), \text{Fe} (2 \text{ eq})\), PhMe, 70°C, 4 h
- (c) \([\text{Rh}(\text{COD})\text{BF}_4] (0.2 \text{ mol})\), \(\text{H}_2 (200 \text{ psi})\), MeOH, rt, 20 h

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

2-Pyrimidyldiphenylphosphine

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

\[
\begin{align*}
\text{N} & \quad \text{P} \\
\text{N} & \quad \text{P}
\end{align*}
\]

\(\text{A}\)

- \(\text{n-Bu} \rightleftharpoons \text{A} (5 \text{ mol})\), \(\text{PdCl}_2 (0.06 \text{ mol})\), CO (60 bar), MeOH, NMP, 60°C, 2 h
- \(\text{n-Bu} \rightleftharpoons \text{MeO}_{2}\text{C}\)

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

\(\text{Cp}^+\text{Co(C}_2\text{H}_4\text{)}_2\)

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

\[
\begin{align*}
\text{OH} & \rightleftharpoons \text{A} (\text{Cp}^+\text{Co(C}_2\text{H}_4\text{)}_2 (\text{A})) \text{THF}, -78°C \rightleftharpoons \text{rt} \\
\text{Cp}^+ & \rightleftharpoons \text{Co} \quad \text{OTf} \\
\text{B} & \rightleftharpoons \text{CH}_2\text{Cl}_2 \quad -78°C \rightleftharpoons \text{rt}
\end{align*}
\]

- (a) \(\text{Na(CH}_2\text{CO}_2\text{Me}) (72\%)\)
- (b) \(\text{Cp}^+_\text{Fe}^+\text{PF}_6^- (50\%)\)

7 examples

2,2-Dimethoxypropane

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.

\[
\begin{align*}
\text{OMe} & \quad \text{OMe} \\
\text{A}
\end{align*}
\]

- \(\text{CO}_2\text{H} (48 \text{ ml}), \text{MeOH (12 ml)}\), TMSCI (3.0 mmol), rt, 16 h
- \(\text{CO}_2\text{H} \quad \text{CO}_2\text{Me}
\]

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%).

\(N,N\)-Carboxyimidazolide

A is utilised in a convenient conversion of \(\alpha\)-aminoacids into NH-Boc protected \(\alpha\)-aminoketones via imidazolides.

\[
\begin{align*}
\text{Im} & \quad \text{Im} \\
\text{A}
\end{align*}
\]

- (a) \(\text{A}, \text{THF, rt, 30 min}\)
- (b) \(\text{CH}_2\text{H}_5\text{MgBr (2 eq)}\), \(\text{Cul (6 mol%)}, \text{THF, 0°C, 3 h}\)
- \(\text{Ph} \quad \text{NHBOc}
\]

9 examples (yields 30–68%).
Indium

Treatment of a range of aromatic nitro compounds with A and aqueous ethanolic ammonium chloride results in selective reduction of the nitro groups; ester, nitrite, amide and halide substituents are unaffected.

\[
\begin{align*}
\text{In} & \quad A \\
\text{CH}_2\text{Cl}_2 & \quad \text{NH}_4\text{Cl}, \text{ eq. EIOH} \\
\Delta & \quad 3 \text{ h} \\
\text{NH}_2 & \quad 95% \\
\end{align*}
\]


11 examples (yields 60-90%).

Samarium(II) iodide / Nickel(II) iodide

In the presence of the title reagent pair, β-lactones react with aldehydes, ketones and imines to afford tetrahydrofuranones and pyrrolidinones in good to high yield.

\[
\begin{align*}
\text{SmI}_2 & \quad \text{A} \\
\text{NiI}_2 & \quad \text{B} \\
\end{align*}
\]


17 examples of coupling with aldehydes and ketones (yields 74-98%) and 7 examples of coupling with imines (yields 70-93%) are reported.

Metals on polyethylene solid support

Convenient preparation of "high-surface alkali metals" deposited on solid-supports and subsequent use in a variety of reactions is reported. The metals can be stored as stable suspensions in inert solvents if protected against oxygen. Preparation of Zn on solid-support is also reported.

\[
\begin{align*}
\text{M} & \quad / \text{Polyethylene (PE)} \\
\text{M} & \quad \text{Li, Na, K, Zn} \\
\end{align*}
\]


36 examples in total of the use of Na-PE in the acyloin reaction, formation of organolithium species using Li-PE and trapping with electrophilics, an intramolecular Diels-Alder cycle utilising K-PE and Reformatsky and Barbier-type reactions using Zn-PE are reported; Yields are good to excellent.

Copper(I) Chloride

The title reagent mediates the intermolecular homocoupling of alkenyltrimethylstannanes, to afford functionalised conjugated dienes and tetaenes in good to high yield.

\[
\begin{align*}
\text{CuCl} & \quad \text{A} \\
\text{DMF, rt, 30 min} & \quad 94% \\
\end{align*}
\]


17 examples (yields 18-91%) are reported.

1-(Trisopropylsilyloxy)-1-(tert-butythio)ethene

Exceptional Cram-type selectivities in Mukaiyama aldol reactions of A are reported. The level of 1,2-asymmetric induction is promoted by the bulk of the silyl group.

\[
\begin{align*}
\text{I-BuS} & \quad \text{A} \\
\text{BF}_3\text{OEt}_2 & \quad (1 \text{ eq}) \\
\text{CH}_2\text{Cl}_2, \text{ -80 °C, 30 min} & \quad 76\% \\
\text{syn,anti} & \quad 130:1 \\
\end{align*}
\]


3 examples (yields 76-78%, 5:1 ≤ syn,anti ≤ 130:1) are described.
(R)-2-Methoxy-6-(1-hydroxyethyl)phenylelenyl triflate

The asymmetric methoxyselelenylation of styrene derivatives using A is reported.

\[
\begin{align*}
\text{DMF} & \quad \text{(COCl)}_2 \\
\text{Me}_2\text{N} & \quad \text{CHO} \\
\text{A} & \quad \text{Me}_2\text{N} \\
\text{A} & \quad \text{CHO}
\end{align*}
\]

6 examples (yields 42-66%, %de = 20-96%).

Chloromethylene)dimethylammonium chloride

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.

\[
\begin{align*}
\text{A} & \quad \text{Me}_2\text{N} \\
\text{A} & \quad \text{CHO}
\end{align*}
\]

17 examples of ester formation (yields 15-91%, %ee = 51-95%) and 9 examples of formation of phthalimido derivatives (yields 25-98%, %ee = 0, 72-96%) are reported.

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

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

\[
\begin{align*}
\text{A} & \quad \text{Me}_2\text{N} \\
\text{A} & \quad \text{CHO}
\end{align*}
\]

10 examples (yields 63-90%, %ee 63-99).
### Tributyltin Methoxide

A facilitates transmetalation from aluminium to tin in a preparation of tributylstannyprop-2-en-1-ol.

<table>
<thead>
<tr>
<th><strong>Reagent</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Bu$_3$SnOMe</td>
</tr>
<tr>
<td><strong>Bu$_3$Sn</strong></td>
</tr>
</tbody>
</table>

- **(a)** NaOMe (7.5 mol%) LiAlH$_4$ (1.1 eq) THF, 0°C, 1 h
- **(b)** Bu$_3$SnOMe (1 eq) 4°C, 2 d; 74%


12 examples (yields 13-74%).

### Iodine / Bis(trifluoroacetoxy)iodobenzene

The title reagent pair effects the iodination of a variety of functionalised olefins.

<table>
<thead>
<tr>
<th><strong>Reagent</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>I$_2$</td>
</tr>
<tr>
<td>A (60 mol%), B (60 mol%)</td>
</tr>
<tr>
<td><strong>AcO</strong></td>
</tr>
<tr>
<td><strong>Ph</strong></td>
</tr>
</tbody>
</table>

- Pyridine (1.2 eq) CH$_2$Cl$_2$, rt, 36 h; 56%


10 examples (yields 23, 56-96%) are described.

### Sodium 2-Ethylhexanoate

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

<table>
<thead>
<tr>
<th><strong>Reagent</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>H$_2$N</td>
</tr>
<tr>
<td>A (1 eq) OCH$_3$COCl (1 eq)</td>
</tr>
<tr>
<td>NH$_2$</td>
</tr>
</tbody>
</table>

- THF, rt > 90%


4 examples (yields 80-90%) are described. The reaction does not proceed via a mixed anhydride and therefore gives single acylation products.

### Manganese tris(acetylacetonate)

The title catalyst mediates the diastereoselective oxidative coupling of sec-benzyl compounds to give symmetrical and unsymmetrical BINOL-derivatives.

<table>
<thead>
<tr>
<th><strong>Reagent</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>A (1.2 eq)</td>
</tr>
<tr>
<td>CH$_3$CN, 50°C</td>
</tr>
</tbody>
</table>

- 75%, $dr$ = 95:5


9 examples (yields 69-89%, $de$ 84-97%) are described.

### Sodium Borohydride

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

<table>
<thead>
<tr>
<th><strong>Reagent</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>NaBH$_4$</td>
</tr>
<tr>
<td>A (4 eq)</td>
</tr>
<tr>
<td>THF-H$_2$O (3:1), rt</td>
</tr>
</tbody>
</table>

- 95%, er > 99:1


13 examples (yields 75-95%, $%ee$ > 99%) are described. In contrast, use of LiBH$_4$ resulted in ~10% racemisation.