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.


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**Scandium(III) Trifluoromethanesulphonate**

A catalyses the Friedel-Crafts alkylation of a range of aromatic compounds with methanesulphonates derived from secondary alcohols.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sc(OTf)₃</td>
<td><img src="image" alt="Reaction Diagram" /></td>
</tr>
</tbody>
</table>

H. Kotsuki, T. Oshisi, M. Inoue *Synlett* 1998, 255.

11 examples (yields 36-98%). The catalyst can be reused without a significant loss of activity.

**Chiral (Salen) Mn(III) Complex / Ammonium Acetate**

The title reagent pair catalyse the asymmetric epoxidation of various unfunctionalised olefins by hydrogen peroxide.

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chiral (Salen) Mn(III) Complex / NH₄OAc</td>
<td><img src="image" alt="Reaction Diagram" /></td>
</tr>
</tbody>
</table>

R= t-Bu


3 examples given (yields 71-90%, %ee 84-96%).

**Microencapsulated Scandium(III) Trifluoromethanesulphonate**

Polystyrene microcapsules (MC) of scandium(III) triflate were found to catalyse a wide variety of reactions (eg imino aldo, aldo, Mannich, Michael, Friedel-Crafts acylation). The microencapsulated form of the Lewis acid was found to be more active than monomeric material and could be recovered via simple filtration.

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td>MC Sc(OTf)₃</td>
<td><img src="image" alt="Reaction Diagram" /></td>
</tr>
</tbody>
</table>


Various reactions are illustrated (yields >70%). In each case no decrease in activity was noted when the catalyst was re-used in subsequent transformations. The simple preparation of the catalyst is described.
### 1,10-Phenanthroline-Palladium(I) Complex

The title reagent catalyses the tandem cyclisation/hydrosilylation of functionalised 1,6-dienes to afford the corresponding trans cyclopentanes.


$$\text{Catalyst}$$

<table>
<thead>
<tr>
<th>A (5 mol%)</th>
<th>E怎么回事IH</th>
<th>CH₃Cl₂, 0°C</th>
<th>Me</th>
<th>Me</th>
<th>Me</th>
<th>Me</th>
<th>CH₃SiMe₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>MeOC</td>
<td>Ar = 3,5-bis(trifluoro-methyl)phenyl</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>64%, dr = 98:2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

16 examples (yields 43-99%, typically dr(trans) > 12:1).

### Tris( dibenzyldieneacetone) palladium(0)-Chloroform Adduct

The title reagent catalyses the regio- and stereoselective hydrocarboxylation of allylalenes.


$$\text{Catalyst}$$

<table>
<thead>
<tr>
<th>Pd(dba)₃·CHCl₃</th>
<th>A</th>
<th>cinnamic acid (1.1 eq)</th>
<th>PhCHO (1 eq)</th>
<th>THF, rt, 2 d</th>
</tr>
</thead>
<tbody>
<tr>
<td>dppf = 1,1′-bis(diphenylphosphino)ferrocene</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>80%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 examples (yields 70-96%).</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Nickel(II) Acetylacetonate

The title reagent catalyses the homolysisation of benzaldehyde with 1,3-dienes.


$$\text{Catalyst}$$

<table>
<thead>
<tr>
<th>Ni(acac)₂</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>(4 eq)</td>
<td></td>
</tr>
<tr>
<td>PhCHO</td>
<td></td>
</tr>
<tr>
<td>79%</td>
<td></td>
</tr>
<tr>
<td>10 examples (yields 55-66%). High 1,2, 1,3 and 1,2,3 diastereoisomers are typically obtained (1,3-anti/syn &gt; 15:1, 1,15 &lt; 1,2-anti/syn &lt; 5:2:1).</td>
<td></td>
</tr>
</tbody>
</table>

### Molybdenum Metathesis Catalyst

The title reagent catalyses the asymmetric ring-closing metathesis (ARCM) of racemic 1,6-dienes.


$$\text{Catalyst}$$

<table>
<thead>
<tr>
<th>MeBu</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhH, rt, 10 min</td>
<td></td>
</tr>
<tr>
<td>OTES</td>
<td></td>
</tr>
<tr>
<td>43%, er = 97:3</td>
<td></td>
</tr>
<tr>
<td>19%, er &gt; 99:1</td>
<td></td>
</tr>
<tr>
<td>(+38% dimer)</td>
<td></td>
</tr>
<tr>
<td>8 examples (product yields &lt;5, 40-65%, %ee &lt;5, 45-60%; recovered diene 17-50%, %ee &lt;5, 57, 91-99%).</td>
<td></td>
</tr>
</tbody>
</table>

### Sodium Lanthanum Tris(binanphthoxide)

The title reagent catalyses the enantioselective Michael addition of thiol to cycloalkenones. Analogous complex B catalyses enantioselective protonation in the Michael addition of thiol to acyclic thiocynoates.


$$\text{Catalyst}$$

<table>
<thead>
<tr>
<th>Ln = La</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td>PhMe-THF (60:4), -40°C, 4 h</td>
<td></td>
</tr>
<tr>
<td>94%, er = 78:22</td>
<td></td>
</tr>
<tr>
<td>6 examples of enantioselective conjugate addition employing A (yields 50-84%, %ee 59-93%); 5 examples of asymmetric protonation in Michael reactions employing B (yields 52-86%, %ee 79-92%).</td>
<td></td>
</tr>
</tbody>
</table>
### Butylisotannonic Acid

The title catalyst mediates the transesterification of esters under mild conditions.

![Chemical Structure](image)


### M(1,2,3,4,6,7,8,9-Octahydroanthracenesulfonyl)ephedrine

The title auxiliary mediates the stereoselective aldol reaction of propionate derivatives.

![Chemical Structure](image)


### 17-Diphenylphosphino-2,5,8,11,14-pentaoxybicycle[13.4.0]nonadeca-15,17,19-triene [PPh₂(bc-5)]

A Palladium(0) complex derived from the title ligand catalyses the cyanation of aryl halides with sodium cyanide.

![Chemical Structure](image)


### M[2-(Diphenylphosphino)benzylidene]2-phenylethylamine

A palladium(0) complex derived from the title ligand effects the syn selective carbostannylation of acetylenes by alkynyl stannanes.

![Chemical Structure](image)


### (R,R)-4,6-Dibenzo[1,2,3]dioxan-2-2'-bis(4-phenyloxazoline) (DBFOX/Ph)

Various cationic aqua complexes derived from the title ligand and transition metal(II) perchlorates catalyse highly enantioselective Diels-Alder reactions. The catalytic species are reasonably robust and can exhibit extreme chiral amplification.

![Chemical Structure](image)


### Catalyst

![Chemical Structure](image)

12 examples (yields 0, 46-100%) are described. The use of A in the acetylation / deacetylation of alcohols is also described.

### Chiral Auxiliary

![Chemical Structure](image)

9 examples (yields 60-98%, diastereofacial selectivity 92-8%, de = 55-94%).

### Ligand

![Chemical Structure](image)

6 examples (yields 85-93%).

10 examples (yields 52-82%). Addition is always exclusively syn although regioselectivity is highly substrate dependent.

The above reaction is extensively investigated in all regards (Mg, Mn, Fe, Cu, Zn, Co, Cr, Ga metal complexes are all studied). All yields and enantioselectivities are excellent in optimised cases (comparable to the illustrated example).
### Bis(dihydroquininy)anthraquinone

The title ligands mediate the regioselective aminohydroxylation of cinnamates to phenyl serines with high enantioselectivity.

B. Tao, G. Schlingloff, K. B. Sharpless

<table>
<thead>
<tr>
<th>Ligand</th>
<th>Reagent</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure" /></td>
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</table>

8 enantiocomplementary examples (yields 40-68%, %ee 87-96) are described.

**X** = A: 58% (2R,3S), er = 98:2
**X** = B: 62% (2S,3R), er = 96:4

### Phenyl(dimethylsilyl)lithium

Lithium enolates are prepared from silyl enol ethers using the title reagent.

I. Fleming, R. S. Roberts, S. C. Smith

<table>
<thead>
<tr>
<th>Reagent</th>
<th>A</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure" /></td>
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</table>

2 examples (yields 74, 77%).

### Phenyl(dimethylsilyl)lithium

Toluene-\(p\)-sulfonamides of secondary amines and indoles are cleaved by the title reagent in good yield.

I. Fleming, J. Frakenpohl, H. Ila

<table>
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7 examples (yields 72-91%). Azidine toluene-\(p\)-sulfonamides are opened by A to give \(p\)-silyl-ethylic sulfonamides.

Ts = \(p\)-toluenesulfonyl

### (Trifluoromethyl)trimethylsilane

A novel nucleophilic trifluoromethylation of esters with A is reported. The ester functionality is converted into the trifluoromethylcarbonyl group without formation of double addition products and the reaction is applicable to both enolisable and non-enolisable esters.

J. Wiedemann, T. Heiner, G. Moston, G. K. S. Prakash, G. A. Olah

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<tbody>
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8 examples (yields 0, 68-95%).

### Titanocene Dichloride

A 3-step synthesis of indoles is described. Pivotal aryl alkyl dibromide intermediates are realised via regioselective insertion of an olefin into a titanocene benzene complex.

K. Aoki, A. J. Peat, S. L. Buchwald

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure" /></td>
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Subsequent annulation with BrNH₂ under Pd(0) catalysis, followed by deprotection/oxidation affords indole products.

10 examples (yields (3-4 steps) 18-54%).
2,2'-Azobis(isobutyronitrile (AIBN) / Tributyltin Hydride

Tin(IV) radical enolates formed by the action of Bu₃SnH on α,β-unsaturated enones undergo facile [3,3]-sigmatropic rearrangement.

Reagent

\[
\text{Bu₃SnH} \quad \text{A} \quad \text{B} \quad (20 \text{ mol%}) \quad (1 \text{ eq}) \quad \text{PhH}, \text{ r.t}, 3 \text{ h} \quad 51\%
\]

6 examples (yields 51-74%).


Lithium Diisopropylamide (LDA)

Ortho metatllation of arenes with A utilising a neopentyl ester as a directing group is reported.

Reagent

\[
\text{(iPr)₂NLi} \quad \text{A} \quad \text{Br} \quad (a) \quad \text{A} \quad (1.1 \text{ eq}) \quad \text{B(OH)₂} \quad (2.6 \text{ eq}) \quad \text{THF}, \text{ } -78\text{°C}, 5 \text{ min}
\]

(b) diethanolamine (1.1 eq) PhMe, rt 84%

8 examples (yields 52-93%).


(+)-N-Fluoro-2,10-(3,3-dichlorocamphorsultam)

The title compound mediates the electrophilic asymmetric fluorination of enolates.

Reagent

\[
\text{F₃C} \quad \text{Cl} \quad \text{A} \quad (a) \quad \text{NaHMDS} \quad (1.1 \text{ eq}) \quad \text{THF}, \text{ } -78\text{°C} \rightarrow 0\text{°C}, 45 \text{ min}
\]

(b) A (1.5 eq) THF, -78°C

53%, er = 88:12

6 examples (yields <5-95%, %ee 0-76%).


Samarium(II) Iodide / Tetrakis(triphenylphosphine) Palladium

The title reagent pair mediates the ring contraction of methyl 5-arylpyrano-sides to 2-vinyl cyclopentanols with moderate trans selectivity.

Reagent

\[
\text{SmI₂} \quad \text{A} \quad \text{B} \quad \text{Pd}(PPh₃)₄ \quad \text{BrO₃} \quad (3 \text{ eq}) \quad \text{A} \quad (3 \text{ eq}) \quad \text{B} \quad (5 \text{ mol%})
\]

THF, 75°C, 2.5 h

54% dr = 96:4

24% dr = 68:32


Iodine

Iodine in methanol mediates the selective cleavage of alkyl silyl ethers in the presence of aryl silyl ethers.

Reagent

\[
\text{A} \quad \text{A} \quad \text{Bk} \quad \text{TBSO₃Me} \quad \text{MeOH, rt, 5.7 h}
\]

97%

12 examples of selective alkyl vs aryl TBS, TIPS and TBDPS cleavage (yields 56-100%) are described.

Manganese / Copper(II) Chloride

The title reagent pair mediates the homo- and cross-coupling of alkyl halides in aqueous media.

\[
\begin{array}{c|c}
\text{Mn} & \text{Ph-Br} \\
\text{A} & \text{A (3 eq), B (10 mol%), } \text{H}_{2}\text{O, rt, 16 h, 85%} \\
\text{CuCl}_2 & \text{Ph-Ph} \\
\text{B} & \\
\end{array}
\]

8 examples of homo-coupling (yields 60-100%) and 2 examples of cross-coupling with an allyl bromide (yields 62, 79%) are described.


Tributyltin Hydride

The title reagent mediates the reductive decomposition of acetylene biscobalt(hexacarbonyl) complexes to form the corresponding cis alkenes.

\[
\begin{array}{c}
\text{n-Bu}_3\text{SnH} \\
\text{A} \\
\end{array}
\]

8 examples (yields 35-85%) are described. A similar decomposition using triethylsilane gives cis-vinyllsilanes.


Carboxethoxypropionyl Cyanide

The title reagent reacts regioselectively with ketone enolates to form 1,3-dicarbonyl compounds.

\[
\begin{array}{c}
\text{NO}_2\text{COCH} \rightarrow \text{COMe} \\
\text{A} \\
\end{array}
\]

6 examples (yields 73-95%) of C-acylation under kinetic and thermodynamic conditions are described.


1,1,2,2-Tetraphenylsilane

The title reagent participates in the reduction of alkyl bromides, addition to alkenes and alkylation of heterocyclic bases.

\[
\begin{array}{c}
\text{Ph}_3\text{HSi-SiPh}_2 \\
\text{A} \\
\end{array}
\]

26 examples are described.


Dichlorodinindium Hydride

Dichlorodinindium hydride mediates the reduction of aldehydes, ketones and alkyl halides.

\[
\begin{array}{c}
\text{InCl}_3 & \text{n-Bu}_3\text{SnH} \\
\text{THF} \rightarrow \text{C}_2\text{InH} \\
\end{array}
\]

16 examples (yields 23-99%) are described. Nitro, cyano and ester groups are unreactive.