**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.


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<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Tris(6,6,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato)ytterbium</th>
<th>Ketene acetal derived from mannopyranose and glucopyranose serve as electron-rich dienophiles in facially selective, Lewis acid-catalysed inverse electron demand hetero-Diels-Alder reactions.</th>
<th>Yb(OD)₃</th>
<th>Ph, Δ</th>
<th>81%</th>
<th>dr = 84:16</th>
<th>4 examples (yields 50-97%, 1:1 ≤ endo:exo ≤ 32:1).</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>Scandium(III) Trifluoromethanesulfonate</th>
<th>A catalyses the Strecker-type reaction of aldehydes, amines and tributyltin cyanide to afford α-amino nitriles in high yields. The reactions proceed smoothly in both organic and aqueous solutions and complete recovery of both the catalyst and all tin compounds is achieved.</th>
<th>Sc(O Tf)₃</th>
<th>Bu₃SnCN (1.5 eq)</th>
<th>H₂O, rt, 20 h</th>
<th>89%</th>
<th>6 examples (yields 79-94%).</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>(S,S)-Ethylene-1,2-bis(5,4,5,6,7-tetrahydro-1-indenyl)titanium difluoride</th>
<th>A highly enantioselective titanium-catalysed hydrosilylation of imines to give secondary amines is described. The slow addition of primary amine additives greatly expands the scope of the reaction, isobutylamine giving the best results with high reaction rate and enantioselectivity.</th>
<th>A</th>
<th>PMHS = polymethylhydrosiloxane</th>
<th><strong>(a)</strong> A (1 mol%), PhSH₂ (3 mol%), piperidine-MeOH (1:1)</th>
<th>60°C, 20 min</th>
<th>96%, er = 96:4</th>
<th>9 examples (yields 73-97%, %ee 69, 91-99%). Enantioselectivity is not limited by the E:Z ratio of the imine.</th>
</tr>
</thead>
</table>
Poly-L-leucine

A new procedure for the Julia-Colonna asymmetric epoxidation is described in the synthesis of (+)-clausenamide. A is mixed with the oxidant and immobilised on cross-linked aminomethylpolystyrene to furnish a fixed bed reactor convenient for continuous flow synthesis of optically active epoxides.


Catalyst

\[
\text{A, DBU (6 eq) H}_2\text{O}_2 (4.8 eq) \xrightarrow{\text{THF, rt, 1.5 h}} \text{Ph} = \text{O} \overline{\text{O}} \text{Ph}
\]

78%, er = 92:8

3 examples of oxidation using poly-L-leucine catalysts (conversion 66-89%, %ee 83-89%).

Tungsten(0) Pentacarbonyl Tetrahydrofuran Complex

The title reagent promotes the cycloisomerisation of \(\gamma\)-hydroxyalkynes. The resultant glycals are a source of 2,3,6-trideoxyhexoses. Glycosylation with an acyclic alkynyl alcohol allows for repetitive application of the cycloisomerisation reaction and to oligosaccharide synthesis.


Catalyst

\[
\text{O} \overline{\text{O}} \text{Ph} \quad \text{BnO}
\]

6 examples of ring closure (yields 23-47%). A sensitive trisaccharide unit of the natural product PI-080 is synthesised via iteration of the methodology.

Chiral Copper(I) Lewis Acid

A catalyses the enantioselective alkylation of \(\alpha\)-imino esters by enol silanes.


Catalyst

\[
\text{Ar}_2\text{Cu(MeCN)}\text{ClO}_4
\]

Ar = p-toly

8 examples (yields 65-95%, %ee 89-98%). Products are often solids and can be recrystallised to near optical purity.

Hexahydro-6-oxo-1,1,4,4-tetramethyl-1H-1,4-diazepinium bis(trifluoromethanesulfonate)

The title compound is a general and efficient catalyst for the epoxidation of olefins.


Catalyst

\[
\text{N} \quad \text{Me} \quad \text{Me}
\]

11 examples (yields 33, 74-94%).

Planar-chiral DMAP derivative

The title compound catalyses the deracemisation/ring opening of azlactones affording protected \(\alpha\)-amino acids.


Catalyst

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

9 examples (yields 94-98%, %ee 44-78%).
Palladium(II) Acetate

The title compound catalyses the oxidation of primary and secondary allylic and benzylic alcohols.

\[
Pd(OAc)_2 \quad A
\]

\[
\text{O}_2 \quad (1 \text{ atm})
\]

\[
\text{DMSO, } 80^\circ\text{C, 2 d}
\]

90%

17 examples (yields 42-96%). The reaction is effective on a 100 mmol scale with no decrease in reactivity or yield.


Yttrium complex

Complex A catalyses the cyclisation/silylation of dienes containing 1,1-disubstituted olefins.

\[
[(\text{CpTMS})_2\text{YMe}]_2 \quad A
\]

\[
\text{PhSiH}_3 \quad (1.3 \text{ eq})
\]

\[
\text{C}_6\text{H}_{12}, \text{rt, 20 h}
\]

77%

12 examples (yields 49-98%).


Chromium(II) Chloride

The title compound catalyses a variant of the Takai-Utimoto reaction of acrolein acetals with aldehydes.

\[
\text{CrCl}_2 \quad A
\]

\[
\text{H}_2\text{C} = \text{CH-CH(OMe)}_2 \quad (2.3 \text{ eq})
\]

\[
\text{Mn (2.5 eq), TMSCl (3.2 eq)}
\]

\[
\text{THF, } -30^\circ\text{C, 12 h}
\]

88%, anti:syn = 11:1

12 examples (yields 46-94%, 1:1.5 ≤ anti:syn ≤ 20:1).


N-Benzylchinchoninium Bromide

The title catalyst mediates the enantioselective Horner-Wadsworth-Emmons olefination of a variety of symmetrical cyclohexanones, under phase transfer conditions.

\[
A
\]

\[
\text{RbOH (5 eq)}
\]

\[
\text{PhH, rt, 8 d}
\]

69%
er = 79:21

5 examples (yields 15-89%, %ee 7-57%) are described. A variety of phase-transfer catalysts are investigated.


Tris(dibenzylideneacetone)dipalladium(0)

The title catalyst mediates selective amination by a primary amine in the presence of a secondary amine.

\[
Pd_2(dba)_3 \quad A
\]

\[
\text{NaOH (3 eq)}
\]

\[
\text{PhMe, 85^\circ\text{C, 2 h}}
\]

84%

12 examples (yields 58-95%) are described. Selectivity for the primary amine ranges from 9:1 to >99:1.

### Bis(triphenylphosphine)palladium(II) Dichloride

The title catalyst mediates the coupling of thiol esters with organozinc reagents, to give ketones.

**Catalyst**

\[
\text{Pd(PPh}_3\text{)}_2\text{Cl}_2 \quad \text{A}
\]


28 examples (yields 50-99%) are described.

### N-Trimethylsilyl-bistrifluoromethanesulfonimide

The title catalyst (prepared in situ) mediates the conjugate allylation of enones and enoates.

**Catalyst**

\[
\text{Me}_3\text{Si N} \quad \text{HNTf}_2\text{SiMe}_3 \quad \text{A}
\]


8 examples (yields 55-97%) are described.

### Chloro- p-cymene-(N-p-toluenesulfonyl-1,3-diaminopropane)ruthenium(II)

The title catalyst mediates the efficient cyclopropanation of olefins with alkyl diazoacetates.

**Catalyst**

\[
\text{Ru} \quad \text{N} \quad \text{Ts} \quad \text{H}_2\text{NCl} \quad \text{CO}_2\text{Et} \quad \text{A}
\]


2 examples (yields 89 and 94%) are described. The use of 5 other monotosylated diamine ligands is also described.

### (Anthraquinone-1,8-dioxy)bis(triisopropoxy-titanium)

The title bidentate catalyst activates carbonyl groups and epoxides in nucleophilic reactions.

**Catalyst**

\[
\text{O} \quad \text{O} \quad \text{O} \quad \text{Ti(OiPr)}_3 \quad \text{Ti(OiPr)}_3 \quad \text{A}
\]


4 examples (yields 54-99%) are described. \( \text{A} \) is a stronger Lewis acid than \( \text{Ti(OiPr)}_4 \).

### Rh(acac)\[(S\text{-binap)}

Aryl- and alkenyl-boronic acids undergo enantioselective 1,4-addition to enones in the presence of a chiral phosphine-rhodium catalyst.

**Catalyst**

\[
\text{Rh(acac)}(\text{C}_2\text{H}_4)_2 \quad \text{A}(\text{3 mol}%) \quad \text{B(OH)}_2 \quad \text{Ph}
\]


Arylboronic acids substituted with electron donating or electron withdrawing groups worked equally well. 12 examples: yields typically 51-99%; \( \text{ee} \geq 91\% \).
2-[2-Methylamino-4-chloro-1-phenyl]-1,2,3,4-tetrahydroisoquinoline

The title compound catalyses the asymmetric protonation of amide enolates.


Catalyst

\[
\begin{array}{c}
\text{A} \\
\end{array}
\]

(a) s-BuLi (1.5 eq) THF, rt, 1 h
(b) A (0.1 eq) THF, –78°C, 15 min
(c) Me₂N (2 eq) THF, –78°C 1.5 h

er = 96:4

2 examples (yields >94%, %ee 92, 94%).

Planar-chiral DMAP derivative

The title compound catalyses the kinetic resolution of arylalkylcarbinols.


Catalyst

\[
\begin{array}{c}
\text{A} \\
\end{array}
\]

A (1 mol%) Ac₂O (1.5 eq)

\text{r-amyl alcohol, 0°C, 2 d}

43%, er = 99:1

39%, er > 99:1

(+ 16% monoacetate)

7 examples (%ee 95-99% at 51-56% conversion).

Bis(dicyclopentadienyl)vanadium Dichloride

The title compound catalyses the pinacol coupling of secondary aliphatic aldehydes with excellent diastereoselection. The chlorosilane additive plays an important role in the construction of catalytic systems and also assists the stereoselection.


Catalyst

\[
\begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{Ph} \\
\text{O} \\
\text{OH} \\
\text{OH} \\
\text{A} (3 mol%) Me₃SiCl (2 eq) THF, 20°C, 13 h
\end{array}
\]

96%, dl :meso = 94:6

8 examples (yields 67-100%, 50:50 ≤ dl :meso ≤ 94:6).

(1S,2S)-Pseudoephedrine

Aryllithium reagents react rapidly and efficiently with \( \beta \)-aryl-\( \beta \)-unsaturated tert-butyl esters bearing a chiral oxazolidine (derived from the title compound) to give 1,4-addition products in high yields and optical purity.


Chiral Auxiliary

\[
\begin{array}{c}
\text{MeO} \text{CHO} \\
\text{Ph} \\
\text{t-BuOK (2 eq)} \\
\text{THF, –78°C, 30 min} \\
\text{HCl} \\
\text{PhMe, , 3.5 h} \\
\text{A} (1.1 eq), HCl \\
\text{5 examples (yields 66-90%, %ee >98%).} \\
\end{array}
\]

87%, er > 99:1

2-Hydroxypinan-3-one

The diastereoselective protonation of potassium enolates of chiral Schiff bases derived from the title compound and racemic \( \alpha \)-amino esters is reported.


Chiral Auxiliary

\[
\begin{array}{c}
\text{Ph} \\
\text{OH} \\
\text{H} \\
\text{R = N=Xc} \\
\text{B(OH)₃} \\
\text{R = NH₂} \\
\text{5 examples (yields 66-90%, %ee >98%).} \\
\end{array}
\]

88%, er > 99:1
### (S,S)-1,2-Bis(2,5-diethylphospholano)benzene (Et-DuPHOS)

A cationic rhodium(I) complex derived from the title ligand catalyses the asymmetric hydrogenation of α-acyloxy acrylates. The resultant products are easily hydrolysed to α-hydroxyesters or reduced to yield 1,2-diols.


![Diagram](image)

\[ \text{Rh(I)}^* = [(\text{cod})\text{Rh}(S,S)-\text{Et-DuPHOS}]OTf \]

14 examples (all full conversions, %ee >93%). The E/Z ratio of the enol ester had little effect on the enantioselectivity of the reduction.

### N,N',N''-Trimethyl-1,4,7-triazacyclonone (Cn)

A ruthenium catalyst derived from the title ligand catalyses the oxidation of alcohols to aldehydes and ketones.


### (2S,2'S)-Bis(diphenylphosphinoxy)-(1R,1'S)-dicyclopentane (BICPO)

A cationic rhodium(I) complex derived from the title ligand catalyses the enantioselective hydrogenation of dehydroamino acids.


### (Z)-4-Iodo-1-(tributylstannyl)but-1-ene

The bifunctional title compound is employed as an alkylating agent in a novel cyclohexenone annulation procedure.

E. Piers, S. L. Boulet, Synlett 1998, 516

### Vanadium(V) Oxytrinitrate

Nitration of a range of substituted aromatic compounds with A under mild conditions is reported.

### Triphenylphosphine / Carbon Tetrabromide

In the presence of ethyl acetate, the title reagent pair selectively acetylates primary alcohols in high yield.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>A PPh₃</td>
<td><img src="image" alt="Triphenylphosphine" /></td>
</tr>
<tr>
<td>B CBr₄</td>
<td><img src="image" alt="Carbon Tetrabromide" /></td>
</tr>
</tbody>
</table>


25 examples including 12 examples of formylation using ethyl formate as the solvent (yields 5, 19-100%).

### Ruthenium(III) Chloride Hydrate

The title reagent is utilised in a convenient preparation of ruthenium carbene complexes.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>RuCl₃•3H₂O</td>
<td><img src="image" alt="Ruthenium(III) Chloride Hydrate" /></td>
</tr>
</tbody>
</table>


2 examples (yields 75% and 76%).

### Tetrabutylammonium Triphenyldifluorosilicate (TBAT)

The title compound is an effective phenylation reagent in palladium-catalysed coupling reactions.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ph Si Ph</td>
<td><img src="image" alt="Tetrabutylammonium Triphenyldifluorosilicate" /></td>
</tr>
</tbody>
</table>


5 examples with complete inversion of configuration (yields 60-75%).

### N,N'-Difluoro-2,2'-bipyridinium bis(tetrafluoroborate)

The title reagent is a highly reactive and easy-to-handle electrophilic fluorinating agent with high effective fluorine content.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="N,N'-Difluoro-2,2'-bipyridinium bis(tetrafluoroborate)" /></td>
<td></td>
</tr>
</tbody>
</table>


13 examples (yields 28-82%).

### Methyl Nitroacetate

Knoevenagel condensation of the title compound with aldehydes gives α-nitro enoate esters which undergo easy conjugate addition of zinc reagents. The sequence is a versatile synthesis of α-amino acid derivatives.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Methyl Nitroacetate" /></td>
<td></td>
</tr>
</tbody>
</table>


4 examples of Knoevenagel condensation (yields 46-88%).
(Aminomethyl)tri-n-butylstannane  
Condensation of an aldehyde with A followed by tin-lithium exchange, forms a 2-azaallyl anion which participates in an intramolecular cycloaddition.


Lithium (1R)-Menthloxyacetylide  
The title compound acts as an ester homoenolate equivalent in the highly enantioselective preparation of N-protected (S)-(S)-[1-aminoalkyl]-γ-lactones.


Methyl (E)-tert-butoxymethylenepyruvate  
A is used in a hetero Diels-Alder reaction to afford heterocycloadducts with high diastereomeric purity, giving access to enantiopure 2,4-dideoxysugar lactones.


Copper(II) Acetate  
The title reagent mediates the coupling of arylboronic acids with a variety of N- and O-containing compounds, in the presence of a base.


Copper(II) Acetate  
The title reagent mediates the arylation of phenols with arylboronic acids.

### Tris(pentafluorophenyl)borane

Stereoselective addition of weak nucleophiles to α- and β-alkoxy ketones is mediated by pentacoordinate complexes generated in situ using the commercially available title compound or Me₃Al.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>B(C₆F₅)₃/A</td>
<td>Ph₃O, OMe</td>
<td>Ph₃OH, OMe</td>
</tr>
</tbody>
</table>


### [β-(Trimethylsilyl)acryloyl]-tert-butyldimethylsilane

Reaction of the E and Z isomers of the title compound with lithium enolates of α,β-unsaturated methyl ketones afford cis-5,6- and trans-5,6-disubstituted 3-cycloheptenones respectively. The reaction involves a Brook rearrangement followed by a divinylcyclopropane rearrangement.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>OLi</td>
<td>BuMe₂SiO</td>
</tr>
</tbody>
</table>


### Diethylzinc

A new easy route to dialkylzinc reagents is based on the irradiation of iodoalkanes with diethylzinc in dichloromethane at rt at λ ≥ 280 nm. A simple GE sunlamp suffices.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Et₂Zn</td>
<td>CH₂Cl₂, hν</td>
<td>Et₂Zn (1 eq)</td>
</tr>
</tbody>
</table>


### Ethoxyoxovanadium(V) Dichloride

Alanes and alanates undergo oxidative coupling using the title reagent.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO(OEt)Cl₂/A</td>
<td>AlBu₂-Li</td>
<td>C₆H₅H₂</td>
</tr>
</tbody>
</table>


### Fluoroform

The title reagent is a trifluoromethylating agent when deprotonated in DMF with a base.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Reaction</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF₃/A</td>
<td>KH</td>
<td>OH</td>
</tr>
</tbody>
</table>

**Copper(II) Toluene sulfonate**

The title reagent mediates the α-sulfonyloxylation of unsymmetrical ketones.

\[ \text{CuO} \xrightarrow{\text{TsOH} \ (2 \text{ eq})} \text{Cu(OTS)}_2 \]


15 examples (yields 62-84%) using methanesulfonic, p-toluene sulfonic and p-nitrobenzenesulfonic acid are described.

**Benzotriazol-1-1-oxys(trimethylamino)phosphonium Hexafluorophosphate (BOP)**

Hydroxybenzotriazolyl esters, formed in situ from carboxylic acids and the above reagent undergo reduction, under relatively mild conditions, with sodium borohydride.

\[ \text{MeO} \xrightarrow{(a) \ (1.1 \text{ eq}), \text{DIPEA} \ (1.2 \text{ eq})} \text{OMe} \]


11 examples (yields 80-99%) are described.

**Bis(cyclopentadienyl)titanium-bis(triethylphosphite)**

The title reagent mediates the desulfurisation of thioacetals in the presence of trialkylsilanes to give the corresponding tetraalkylsilanes.

\[ \text{Cp}_2\text{TiCl}_2 \xrightarrow{(1.2 \text{ eq})} \text{Cp}_2\text{Ti[P(OEt)_3]_2} \]


11 examples of the synthesis of silanes (yields 58-90%) are described. A can also be used for the corresponding synthesis of stannanes and germanes, 9 examples (yields 20-90%) are reported.

**N-Chloro-N-sodium-2-trimethylsilylethyl Carbamate**

The title reagent is a new nitrogen source for the asymmetric aminohydroxylation of olefins.

\[ \text{Me}_3\text{Si} \xrightarrow{(3.1 \text{ eq})} \text{Me}_3\text{Si} \]


6 examples (yields 70-86%, %ee 91-99%) are described.