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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MeO-Polyethyleneglycol-Bound DHQ and DHQD Ligands

<table>
<thead>
<tr>
<th>Ligands</th>
<th>Catalyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymmetric dihydroxylation with the title polymer-modified ligand yields diols with comparable enantioselectivity to the original Sharpless system (up to 98.2% er).</td>
<td>A, OsO₄ (0.4 mol%) K[Fe(CN)₆] acetone / H₂O Me OH OH 89%, er = 98.2</td>
</tr>
</tbody>
</table>


Ruthenium Hydride and Dihydride Phosphine Complexes

<table>
<thead>
<tr>
<th>Complexes</th>
<th>Catalyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>The title complexes act as very active catalysts for transfer hydrogenation of ketones and imines by propan-2-ol.</td>
<td>A (0.1 mol%) KOH (20 mol%) propan-2-ol, 1 h, 85 °C 85% B (0.5 mol%) KOH (20 mol%) propan-2-ol, 18 h, 85 °C 89%</td>
</tr>
</tbody>
</table>


(1S,5R,8S)-8-Hydroxy-8-(/naphthylmethyl)-2-(4-pyridyl)-2-azabicyclo[3.3.0]octane

<table>
<thead>
<tr>
<th>Alcohol</th>
<th>Catalyst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonaenzymatic kinetic resolution of racemic alcohols through an induced fit process.</td>
<td>(l-BuCO₂)₂O (1.4 eq) A (5 mol%) 2,6-collidine (1 eq) PhMe, rt, 5 h OCOPr racemic OCOPr + OCOPr 69% 27%, er = 88:12</td>
</tr>
</tbody>
</table>

Tris[(E,E)-1,5-diphenylpenta-1,4-dien-3-one]bis[palladium(0)]


\[
Pd_2(dba)_3 \rightarrow \begin{array}{c} \text{Br} \\ \text{OH} \end{array} \quad \begin{array}{c} (1.2 \text{ eq}) \\ \text{PhMe, 50°C} \end{array} \rightarrow \begin{array}{c} \text{A (1.5 mol%)} \\ \text{ Tol-BINAP (3.6 mol%)} \\ \text{NaH (2.0 eq)} \end{array}
\]


A comparison between catalysed and uncatalysed etherification reactions was carried out (12 examples).

Methylrhenium Trioxide (MTO)

Aqueous catalysis: methyl rhenium trioxide as a homogeneous catalyst for the Diels-Alder reaction.

\[
\begin{array}{c} \text{Me} \\ \text{O} \end{array} \quad \begin{array}{c} \text{A} \\ \text{Me} \end{array} \quad \begin{array}{c} \text{A (1 mol%)} \\ \text{H}_2\text{O, rt, 16 h} \end{array} \rightarrow \begin{array}{c} \text{90%} \\ \text{isomer ratio > 99:1} \end{array}
\]


The β-substituted dienophiles are less reactive under these conditions (32 examples).

(5S,8R,9R)-8,9-(Isopropylidenedioxy)-2,2-dimethyl-1,3,6-trioxaspiro[4.5]decan-10-one

Treatment of ketone A with oxone generates a dioxirane intermediate capable of asymmetric epoxidation of olefins. Strict pH control was necessary for good results.

\[
\begin{array}{c} \text{Ph} \\ \text{OMe} \end{array} \quad \begin{array}{c} \text{Me} \\ \text{O} \end{array} \quad \begin{array}{c} \text{A (0.3 eq)} \\ \text{Oxone (1.4 eq)} \\ \text{K}_2\text{CO}_3 (6 \text{ eq}) \end{array} \quad \begin{array}{c} \text{Na}_2\text{B}_4\text{O}_7+10\text{H}_2\text{O} \\ \text{CH}_3\text{CN} \end{array} \rightarrow \begin{array}{c} \text{Ph} \\ \text{OMe} \end{array} \quad 76\%, \text{ er} = 95:5
\]


8 examples (yields 66-93%, %ee 90-97%).

Bis(triphenylphosphine)palladium Dichloride

Catalyses the cross-coupling reaction of unsaturated vinyl chlorides with Grignard reagents.

\[
\begin{array}{c} \text{Cs} \\ \text{BrMg} \end{array} \quad \begin{array}{c} \text{2 eq} \\ \text{A (5 mol%)} \\ \text{Et}_3\text{N (8 eq)} \end{array} \quad \begin{array}{c} \text{THF, rt, 20 min} \\ \text{55%} \end{array} \rightarrow \begin{array}{c} \text{C}_9\text{H}_1 \end{array}
\]


16 examples (yields 42-95%). All products were isomerically pure.

Magnesium Triflimide

A useful alternative to magnesium perchlorate for the catalysis of nucleophilic substitution reactions of allylic and benzylic acetates.

\[
\begin{array}{c} \text{MeO} \\ \text{Ac} \end{array} \quad \begin{array}{c} \text{A (2 eq)} \\ \text{OTBS} \end{array} \quad \begin{array}{c} \text{Mg(NTf)_2} \end{array}
\]


10 examples (yields 48, 78-99%). In the majority of cases catalyst A is superior to Mg(ClO_4)_2.
Tetra-n-propylammonium Perruthenate (TPAP)

Treatment of alkyl boranes with a catalytic quantity of TPAP (A) in the presence of N-methylmorpholine N-oxide (NMO) results in their oxidation to carbonyl compounds. A, a novel hydroboration / oxidation sequence allows for a one-pot synthesis of carbonyl compounds from olefins.


Chiral Diron Acyl Complex

Synthesis of and asymmetric cycloaddition with chiral diron acyl complexes.


(2S)-(N-Benzoylpyrrolidin-2-yl)diphenyloxcarbimol

The title compound is a ligand for the asymmetric Nozaki-Hiyama coupling of organochromium reagents with aldehydes.


2,2'-Bis[(4S)-4-isopropyl-1,3-oxazolin-2-yl]biphenyl

The title ligand forms one diastereoisomer when complexed with Cu(I). The resultant complex catalyses the asymmetric cyclopropanation of styrene.


(1,1')-Bi(dibenzofuranyl)-2,2'-dicol (BIFOL)

Resolution of the C2-symmetric title compound via recrystallisation of a 1:1 mixture of diastereomeric cyclic phosphorimidates gave both enantiomers in good yield and with >98% enantiopurity.

### N-Substituted-2,5-bis[(tri isopropyl]oxy)pyrrole (BISOP) Protecting Group

- Primary amines are diprotected as their BISOP derivatives A.

<table>
<thead>
<tr>
<th>Protecting Group</th>
<th>7 examples of protection (yields 68-87%).</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td></td>
</tr>
<tr>
<td>OTIPS OTIPS</td>
<td></td>
</tr>
<tr>
<td>Br</td>
<td></td>
</tr>
<tr>
<td>Br</td>
<td></td>
</tr>
<tr>
<td>PhH, δ, 2 h</td>
<td></td>
</tr>
<tr>
<td>(a) t-BuLi, Et₂O</td>
<td></td>
</tr>
<tr>
<td>(b) AcCl, 1 h</td>
<td></td>
</tr>
<tr>
<td>(c) TIPSOT (2.2 eq)</td>
<td></td>
</tr>
<tr>
<td>(d) Et₃N (3.2 eq)</td>
<td></td>
</tr>
<tr>
<td>CH₂Cl₂, rt, 2 h</td>
<td></td>
</tr>
<tr>
<td>(e) n-HexCHO</td>
<td></td>
</tr>
<tr>
<td>(f) R = BISOP</td>
<td></td>
</tr>
<tr>
<td>(g) R = H₂</td>
<td></td>
</tr>
</tbody>
</table>


### Ethyl-4-methyl-2,6,7-trioxabicyclo[2.2.2]octane Reagent

- The title reagent is a novel and easy to handle propiolate anion equivalent: a concise preparation is presented.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>7 examples of the addition of metallated A to various electrophiles (yields 61-95%). The bridged ortho ester is easily cleaved to yield the corresponding acid.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>(a) BuLi, THF -10°C, 1 h</td>
<td></td>
</tr>
<tr>
<td>(b) -10°C → rt, 2 h</td>
<td></td>
</tr>
<tr>
<td>86%</td>
<td></td>
</tr>
</tbody>
</table>


### Trisallylmanganylmagnesium Chloride Reagent

- The title reagent was used for the allylation and diallylation of acetylenic compounds in moderate to good yields.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>Examples with other substrates and electrophiles are also presented (yields 50-90%). A version of the reaction with catalytic amounts of Mn salts is also reported (yields 75-78%).</th>
</tr>
</thead>
<tbody>
<tr>
<td>(CH₂=CHCH₂)₂MnCl</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>a) A, THF-HMPA</td>
<td></td>
</tr>
<tr>
<td>b) H₂O⁺</td>
<td></td>
</tr>
<tr>
<td>90%, E:Z = 100:0</td>
<td></td>
</tr>
</tbody>
</table>


### Poly-(l)-Leucine Reagent

- Urea-hydrogen peroxide complex is an organic solvent in the presence of DBU and the title polymer causes rapid asymmetric epoxidation of enones.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>4 examples (yields 0, 67-87%, or &gt; 20:1). The product epoxides may be alkylated (at C=O) with RLi + C₂H₅.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poly-(l)-Leucine A</td>
<td></td>
</tr>
<tr>
<td>(a) (400 mg/mmol of substrate)</td>
<td></td>
</tr>
<tr>
<td>urea-H₂O₂ (1.2 eq)</td>
<td></td>
</tr>
<tr>
<td>DBU (1.2 eq), THF, rt, 3 h</td>
<td></td>
</tr>
<tr>
<td>85%, er &gt; 97:3</td>
<td></td>
</tr>
</tbody>
</table>


### Polyethylene glycol-triarylporphosphine Conjugate Reagent

- The title reagent may be employed in the Staudinger and Mitsunobu reactions as a liquid phase reagent support. The PEG reagent is in solution but, when spent, may be easily precipitated making product isolation a simple procedure.

<table>
<thead>
<tr>
<th>Reagent</th>
<th>4 examples (yields &gt;90%).</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td></td>
</tr>
<tr>
<td>(a) (1.1 eq), H₂O (1.1 eq)</td>
<td></td>
</tr>
<tr>
<td>CH₂Cl₂, rt, 2 h</td>
<td></td>
</tr>
<tr>
<td>95%</td>
<td></td>
</tr>
<tr>
<td>(b) allyl alcohol (1 eq) DEAD (1.1 eq), rt, 2 h</td>
<td></td>
</tr>
<tr>
<td>82%</td>
<td></td>
</tr>
</tbody>
</table>

Diethyl isopropylthioborane

With this borane, efficient catalytic asymmetric prop-2-ynylation of achiral aldehydes with allenyltributylstannane promoted by a BINOL-Ti(IV) complex is achieved with high ee.

C.-M. Yu, S.-K. Yoon, H.-S. Choi, K. Baek

\[
\text{ElBSPr A} \quad \text{A (1.2 eq)}
\]
\[
\text{CH}_2\text{C}_2\text{C}_2\text{CH}_2\text{SH} \quad \text{(S)-BINOL-Ti(OPr)}_{14} \quad \text{(10 mol%)}
\]
\[
\text{C}_2\text{H}_2\text{C}_2\text{Cl}_2, -20^\circ\text{C}, 9 \text{ h}
\]
75%, ee = 96:4

7 examples (yields 52-88%, ee: 88-95%). The reaction may also be performed with (S)-BINOL-Zn(OH)_{2}.

Nitrido[\(N,N'-(1,1,2,2\text{-tetramethyl})\text{ethylenbis(salicylideneaminato)\}]\text{manganese(IV)}

Novel stereoselective synthesis of 2-amino saccharides


\[
\text{OPMB} \quad \text{A} \quad \text{A (1 eq)} \quad \text{(CF}_3\text{CO)}_2\text{O}
\]
\[
\text{CH}_2\text{Cl}_2 \quad \text{CH}_2\text{Cl}_2
\]
\[
\text{(b) silica gel or H}_2\text{O}^+ \quad \text{PMBO} \quad \text{OPMB} \quad \text{OPMB} \quad \text{OPMB}
\]
\[
\text{NHCOCF}_3
\]
75%, \(\alpha/\beta = 1:7\)
The formation of labile aziridine intermediate occurred either on the \(\alpha\) or \(\beta\) face depending on the substitution pattern of glycals (9 examples).

Phthalimidesulfenyl Chloride

Sulfinimide derivatives generated by reaction of the title compound with phenols react with pyridine to generate \(\alpha\)-thioguaninone which undergo cycloaddition with electron-rich alkenes and alkynes to give 1,4-benzoxathins.


\[
\text{MeO} \quad \text{OH} \quad \text{(excess)} \quad \text{MeO} \quad \text{OH}
\]
\[
\text{CHCl}_3, \text{rt}
\]
\[
\text{SNPhet}
\]
\[
\text{O}
\]
\[
\text{C}_2\text{H}_2\text{C}_2\text{Cl}_2, 60^\circ\text{C}, 50 \text{ h}
\]
12 examples (yields 44-89%).

Quinolinium fluorochromate (QFC)

The title compound selectively desilylates 1° TBS ethers with concomitant oxidation of the liberated alcohol to aldehydes in the presence of secondary TBS ethers.


\[
\text{[FCrO]_4} \quad \text{A (3 eq)} \quad \text{OTBDMS}
\]
\[
\text{C}_4\text{H}_4\text{S}_8 \quad \text{DMF, rt, 12 h}
\]
\[
\text{OTBDMS}
\]
12 examples (yields 64-92%).

Aluminium Tris(2,6-diphenylphenoxide) (ATPH)

Enone complexation with A allows Michael addition of alkylolithiums and lithium enolates.


\[
\text{Ph}_3\text{O} \quad \text{O-Al}
\]
\[
\text{A (1 eq)} \quad \text{PhMe, -78^\circ C}
\]
\[
\text{OTBDMS}
\]
\[
\text{C}_4\text{H}_4\text{S}_8 \quad \text{1N HCl, 1 h}
\]
7 examples of sequential inter- and intramolecular 1,4-addition (yields 28, 58-76%).
**B-Chlorodi isopinocampherylborane (DIP-Chloride™)**

An *in situ* preparation of DIP-Chloride™ (A) is described.

![Chemical Structure](image)


**Dimethylaluminium Chloride/ N-Methoxy-N-methylamine Hydrochloride**

N-Methoxy-N-methyl amides (Weinreb amides) can be efficiently prepared from lactones and esters by treatment with the title reagent pair.

![Chemical Structures](image)


**Lithium i-Butyl-N-tosyloxycarbamate (LiBTOC)**

The title reagent provides a competent (+)-NHBOc synthon. Chiral cis-aminoindanol derived amide cyanocuprates are electrophobically aminated by A in a highly diastereoselective manner.

![Chemical Structures](image)


**(2R)-N-([(R)]-p-Tolysulfinyl)bornane-10,2-sultam**

The use of camphor sultam A as a chiral sulfinyl transfer reagent is described.

![Chemical Structures](image)


**η²-Propenyltitaniumdi isopropoxide**

Treatment of cyclic allylic bromides and carbonates with A yields the corresponding allylic titanium complexes. These undergo diastereoselective addition to aldehydes and imines.

![Chemical Structures](image)