

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:

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Article Identifier:

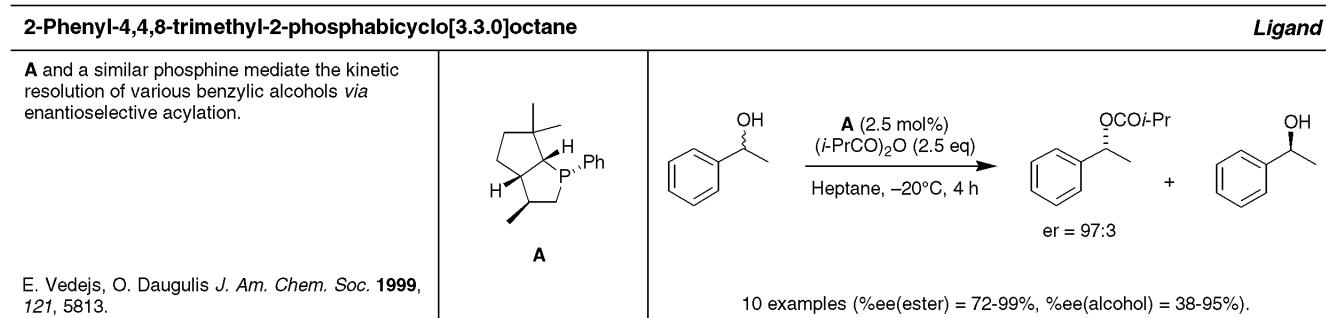
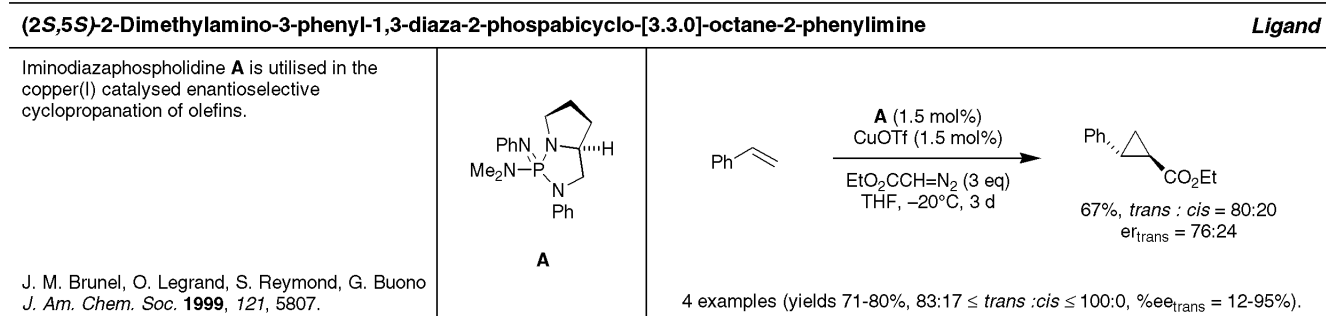
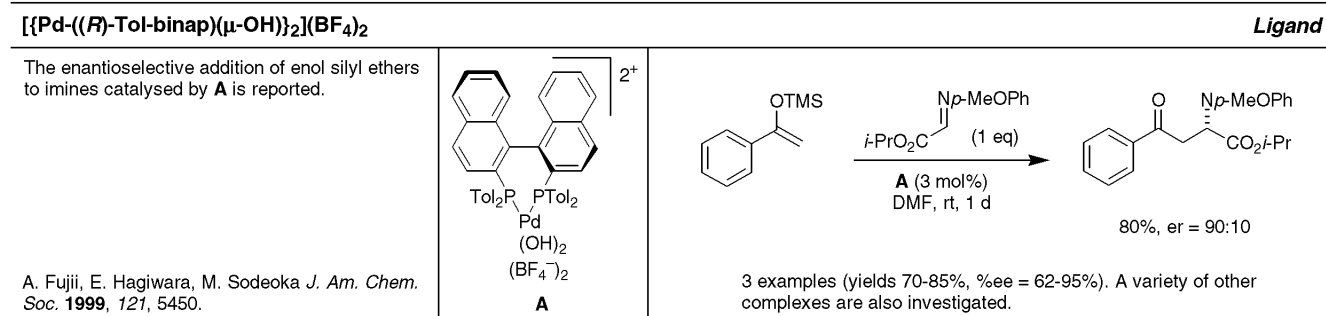
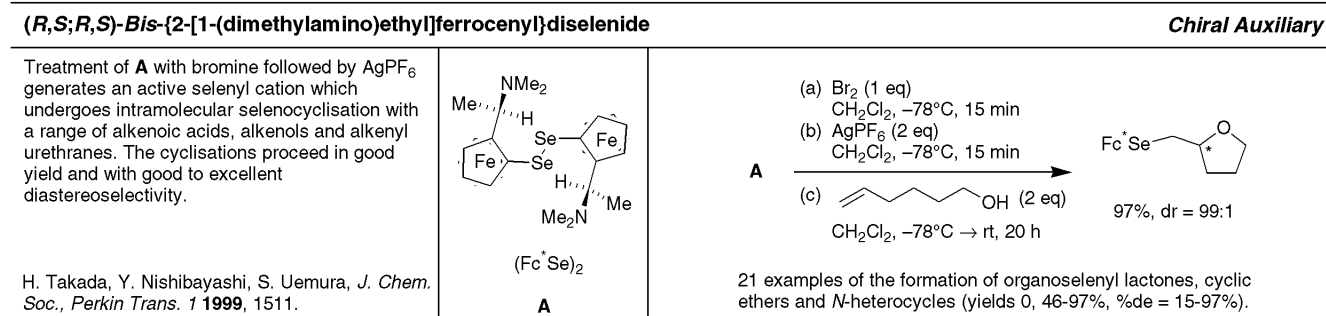
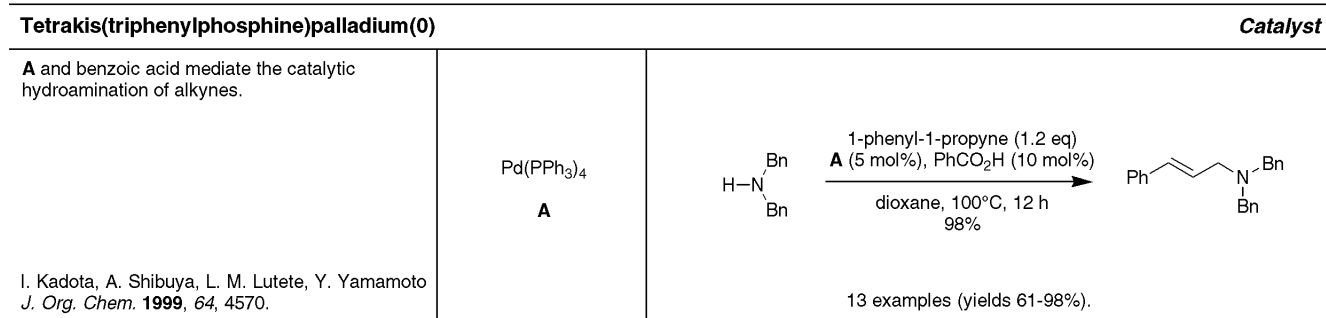
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The journals regularly covered by the abstractors are:

Angewandte Chemie International Edition
 Bulletin of the Chemical Society of Japan
 Chemical Communications
 Chemistry A European Journal
 Chemistry Letters
 Collection Czechoslovak Chemical Communications
 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

(S)-10,10'-Diphenyl-1,1'-biphenanthren-2,2'-dioxyborane		Catalyst
A catalyses asymmetric aziridination.		<p>9 examples (yields 51-77%, 3:1 ≤ <i>cis:trans</i> ≤ 50:1, %<i>ee</i> = 91-98%).</p>
J. C. Antilla, W. D. Wulff <i>J. Am. Chem. Soc.</i> 1999 , <i>121</i> , 5099.	A	
Chlorotriphenylphosphino ruthenium(I)		Catalyst
A catalyses the stereo- and regioselective <i>anti</i> -Markovnikov addition of thiophenols to terminal alkynes to afford the <i>trans</i> -addition products.		<p>12 examples (yields 62-97%) are described.</p>
A. Ogawa, T. Ikeda, K. Kimura, T. Hirao <i>J. Am. Chem. Soc.</i> 1999 , <i>121</i> , 5108.	A	
Chlorotriphenylphosphino ruthenium(I)		Catalyst
A mediates the [5+2]-cycloaddition of suitably functionalized vinylicyclopropanallenes.		<p>11 examples (yields 68-93%) are reported.</p>
P. A. Wender, F. Glorius, C. O. Husfeld, E. Langkopf, J. A. Love <i>J. Am. Chem. Soc.</i> 1999 , <i>121</i> , 5348.	A	

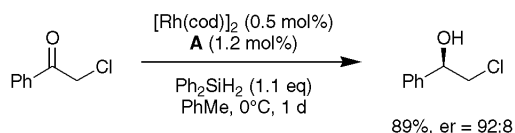
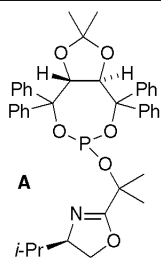
Ytterbium(III) Trifluoromethanesulfonate Hydrate		Catalyst
<p>A in combination with $\text{Mn}(\text{OAc})_3$ mediates the diastereoselective radical cyclisation of unsaturated β-keto esters.</p>		<p>D. Yang, X.-Y. Ye, S. Gu, M. Xu <i>J. Am. Chem. Soc.</i> 1999, <i>121</i>, 5579.</p> <p>3 examples (yields 27-77%, %de = 80-95%) are described.</p>
Nickel on Charcoal		Catalyst
<p>A mediates Negishi couplings between functionalised zinc reagents and substituted aryl chlorides.</p>		<p>B. H. Lipshutz, P. A. Blomgren <i>J. Am. Chem. Soc.</i> 1999, <i>121</i>, 5819.</p> <p>11 examples (yields 62-92%) are reported.</p>
Bis(dibenzylideneacetone)palladium(0)		Catalyst
<p>A mediates cross-coupling between alkenylsilacyclobutanes and aryl or vinyl halides.</p>		<p>S. E. Denmark, J. Y. Choi, <i>J. Am. Chem. Soc.</i> 1999, <i>121</i>, 5821.</p> <p>17 examples (yields 65-95%).</p>
Tetrakis(triphenylphosphine)palladium(0)		Catalyst
<p>Pd-catalyzed [2+2+2]-cycloaddition of benzynes with alkynes to give phenanthrenes is reported.</p>		<p>D. Peña, D. Pérez, E. Guitián, L. Castedo <i>J. Am. Chem. Soc.</i> 1999, <i>121</i>, 5827.</p> <p>6 examples (yields 28-84%) are reported.</p>
Ruthenium Carbene Complex		Catalyst
<p>A and other ruthenium carbene complexes containing imidazolin-2-ylidene ligands are used to catalyse the formation of tetrasubstituted cycloalkenes by ring closing metathesis.</p>		<p>L. Ackermann, A. Fürstner, T. Weskamp, F. J. Kohl, W. A. Herrmann <i>Tetrahedron Lett.</i> 1999, <i>40</i>, 4787.</p> <p>9 examples of ring closing metathesis using A (yields 64-96%) are reported.</p>



TADDOL-Derived Chiral Phosphite

Ligand

A catalyst prepared *in situ* from $[\text{Rh}(\text{cod})\text{Cl}]_2$ and ligand **A** directs silyl hydride addition to the *Re* faces of ketones with good to excellent selectivity.



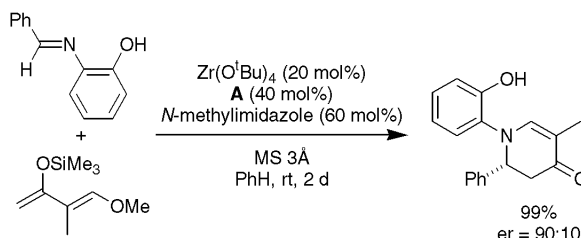
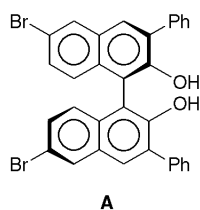
D. K. Heldmann, D. Seebach *Helv. Chim. Acta* **1999**, *82*, 1096.

17 examples (yields 71-91%, %ee = 3-95%) are described.

6,6'-Dibromo-3,3'-diphenyl-1,1'-bi-2-naphthol

Ligand

The title ligand mediates zirconium-catalysed asymmetric aza Diels-Alder reactions.



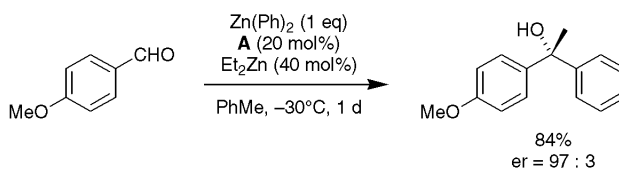
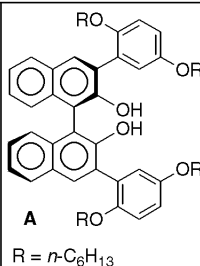
S. Kobayashi, K.-i. Kusakabe, S. Komiyama, H. Ishitani *J. Org. Chem.* **1999**, *64*, 4220.

12 examples (yields 64-100%, %ee = 80-91%).

2,2'-Bis(1,4-di-n-hexyloxyphen-2-yl)-1,1'-bi-2-naphthol

Ligand

The title ligand mediates the enantioselective addition of diphenylzinc to aldehydes.



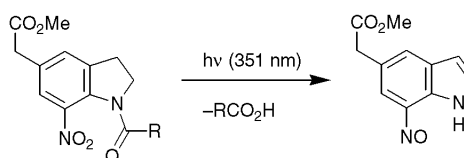
W.-S. Huang, L. Pu *J. Org. Chem.* **1999**, *64*, 4222.

5 examples (yields 66-94%, %ee = 83-94%).

Methyl 1-Acyl-7-nitroindoline-5-acetates

Protecting Group

The title derivatives undergo clean and efficient laser flash photolysis in neutral aqueous solution to release a carboxylic acid.



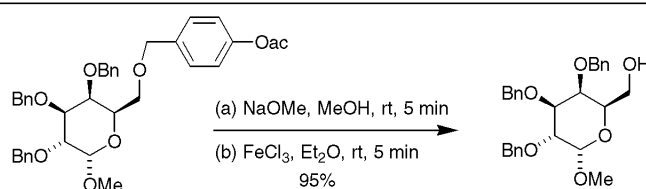
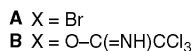
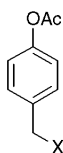
G. Papageorgiou, D. C. Ogden, A. Barth and J. E. T. Corrie, *J. Am. Chem. Soc.* **1999**, *121*, 6503.

The technique was developed for the photorelease of neuroactive amino acids. Only one example (L-glutamate).

p-Acetoxybenzyl Ether (PAB)

Protecting Group

The *p*-acetoxybenzyl (PAB) group is installed by reaction of a hydroxyl group with *p*-acetoxybenzyl bromide (**A**) using silver triflate or *p*-acetoxybenzyl trichloroacetimidate (**B**) using triflic acid. Cleavage involves basic methanolysis followed by mild oxidation with FeCl_3 in Et_2O . Other mild oxidants include DDQ, iodobenzene diacetate or silver carbonate.



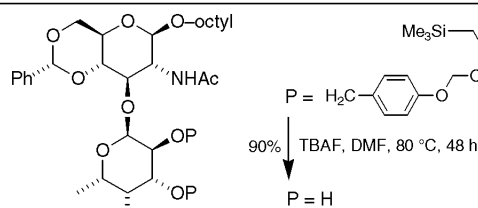
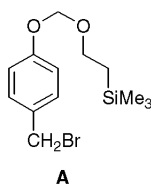
J. L. Jobron and O. Hindsgaul, *J. Am. Chem. Soc.*, **1999**, *121*, 5835.

2 substrates examined involving carbohydrate derivatives. The method was developed for benzyl ether cleavage on the solid phase with soluble reagents.

2-(Trimethylsilyl)ethoxymethoxybenzyl Ether (*p*-SEM-benzyl)

Protecting Group

Phenolate anions generated by treatment of 2-(trimethylsilyl)ethoxymethoxybenzyl ethers with TBAF in DMF at 80 °C undergo efficient elimination to give the deprotected alcohol. The protecting group is introduced with reagent **A** and silver triflate.



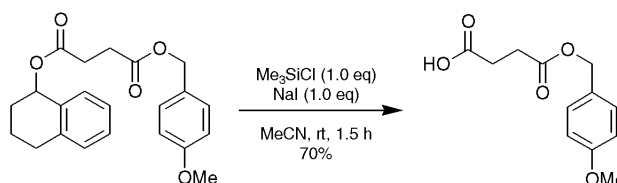
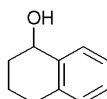
only one example

L. Jobron and O. Hindsgaul, *J. Am. Chem. Soc.*, **1999**, *121*, 5835.

1,2,3,4-Tetrahydro-1-naphthyl Esters

Protecting Group

The title compounds can be selectively cleaved in the presence of alkyl and aryl esters using sodium iodide in acetonitrile at rt—conditions which leave benzhydryl and *p*-methoxybenzyl esters intact.



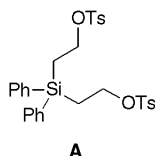
8 examples; yields 90–82%. 1,2,3,4-Tetrahydro-1-naphthyl esters also cleave with TFA (in CH₂Cl₂, rt, 1 h) and H₂-Pd/C but they are stable towards sodium borohydride in MeOH at 0°C, CAN and DDQ.

C. J. Slade, C. A. Pringle and I. G. Sumner, *Tetrahedron Lett.*, **1999**, *40*, 5601.

Diphenylsilyldiethylene Group

Protecting Group

The diphenylsilyldiethylene group is introduced by the reaction of a 1° amine with bis[2-(*p*-toluenesulfonyloxy)ethyl]diphenylsilane (**A**) which is itself prepared in 3 steps (83% overall) from diphenyldichlorosilane. More hindered 2° amines react very slowly and give, at best, monoalkylation products. Deprotection requires an equimolar mixture of TBAF and CsF in DMF or THF at rt.



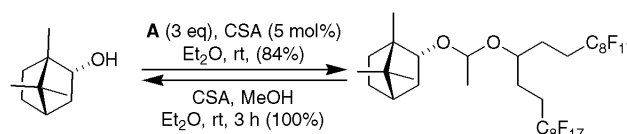
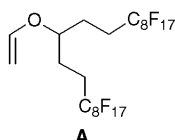
12 examples of protection (50–96%); 3 examples of deprotection 80–92%. Diphenylsilyldiethylene derivatives are resistant to acidic, basic or hydrogenolytic conditions required for the deprotection of Boc, phthalimide and Cbz groups.

B. M. Kim and J. H. Cho, *Tetrahedron Lett.*, **1999**, *40*, 5333.

1,5-Di(perfluorooctyl)pent-2-yl Vinyl Ether

Protecting Group

1,5-Di(perfluorooctyl)pent-2-yl vinyl ether (**A**) has been developed as a fluoros phase analogue of the popular ethyl vinyl ether protecting group for alcohols. Reaction of the alcohol (1.0 equiv.) with **A** (3 equiv.) in the presence of CSA (5 mol%) at room temperature affords the protected derivative after 3 h. The reaction works equally well for 1°, 2° and 3° alcohols. Deprotection is accomplished with CSA in MeOH.



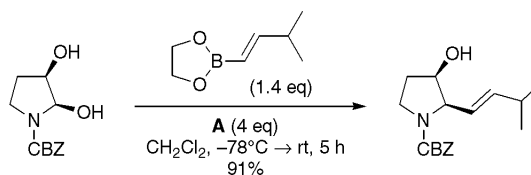
7 examples: protection 38, 61–93%; deprotection 78–100%. Examples include *tert*-butanol and *N*-protection of 2-fluoroaniline.

P. Wipf and J. T. Reeves, *Tetrahedron Lett.*, **1999**, *40*, 5139.

Boron Trifluoride Diethyl Etherate

Reagent

A mediates the crotonylation of *N*-acyliminium ions formed *in situ* from pyrrolidine derivatives.



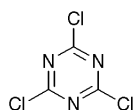
11 examples (yields 64–99%).

R. A. Batey, D. B. MacKay, V. Santhakumar *J. Am. Chem. Soc.* **1999**, *121*, 5075.

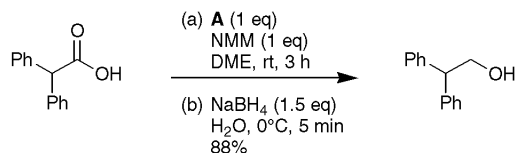
Cyanuric Chloride

Reagent

The title reagent is used along with aqueous sodium borohydride for the mild reduction of carboxylic acids to the corresponding alcohols.



A



12 examples (yields 73-98%) are reported.

NMM = *N*-methylmorpholine

M. Falorni, A. Porcheddu, M. Taddei
Tetrahedron Lett. **1999**, *40*, 4395.

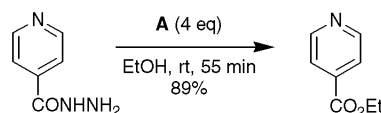
Ceric(IV) Ammonium Nitrate (CAN)

Reagent

Treatment of hydrazides with **A** and an alcohol yields the corresponding esters.



A



18 examples (yields 76-98%) are reported.

B. Stefane, M. Kocevar, S. Polanc
Tetrahedron Lett. **1999**, *40*, 4429.

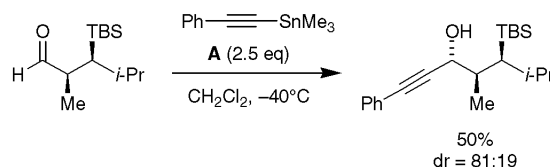
Dimethylaluminium Chloride

Reagent

The title reagent mediates the addition of stannylacetylenes to β -alkoxy and β -silyloxy-aldehydes with high levels of chelation control.



A



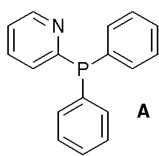
5 examples (yields 34, 50-80%, %de = 62-94%) are reported.

D. A. Evans, D. P. Halstead, B. D. Allison
Tetrahedron Lett. **1999**, *40*, 4461.

Diphenyl 2-Pyridylphosphine / Di-*tert*-butylazodicarboxylate

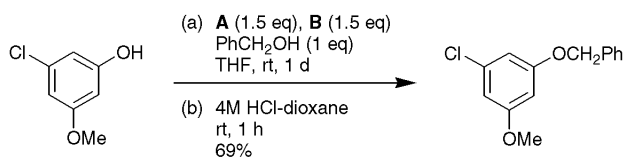
Reagent

The title reagent pair is utilised in an improved procedure for the Mitsunobu reaction. An acid workup removes byproducts from the reaction mixture leaving crude products of excellent purities.



$t\text{-BuO}_2\text{CN}=\text{NCO}_2t\text{-Bu}$

B



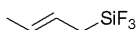
6 examples (yields 30, 52-69%) are reported.

M. Kiankarimi, R. Lowe, J. R. McCarthy, J. P. Whitten
Tetrahedron Lett. **1999**, *40*, 4497.

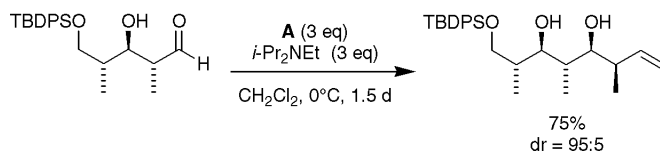
(E)-Crotyltrifluorosilane

Reagent

The title reagent is used in the allylation and crotylation of 2,3-*anti*- β -hydroxy- α -methyl aldehydes. The reaction proceeds with high selectivity and in contrast, analogous reactions of the 2,3-*syn*- β -hydroxy- α -methyl aldehydes are generally less selective.

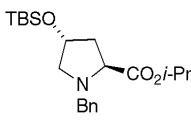
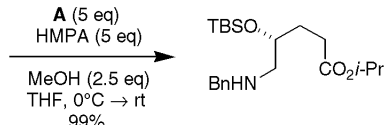
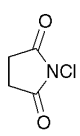
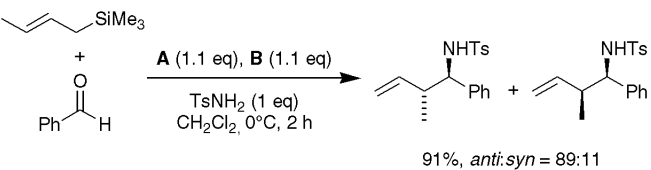
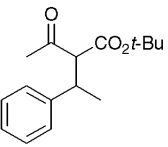
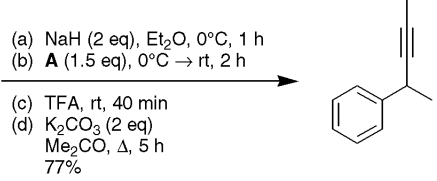
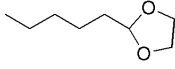
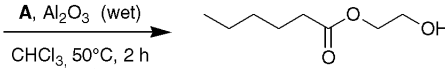
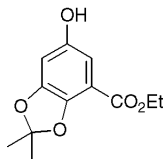
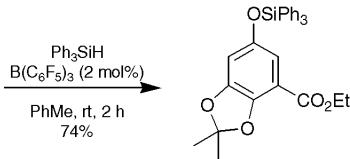


A



7 examples (yields 42, 75-80%, %de = 44-90%). Reactions with allyltrifluorosilane and *(Z)*-crotyltrifluorosilane are also described.

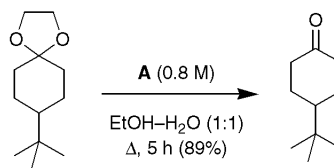
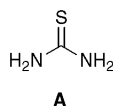
S. R. Chemler, W. R. Roush
Tetrahedron Lett. **1999**, *40*, 4643.

		<i>Reagent</i>
Samarium(II) Iodide		
<p>The title compound promotes reductive deamination of α-aminocarbonyl compounds under neutral reaction conditions, in the presence of a range of other functional groups.</p> <p>T. Honda, F. Ishikawa <i>Chem. Commun.</i> 1999, 1065.</p>	<p>SmI₂</p> <p>A</p> 	 <p>18 examples (yields 50-99%) are reported.</p>
Tin(II) Chloride / <i>N</i>-Chlorosuccinimide		
<p><i>N</i>-Tosyliminium species, prepared <i>in situ</i> from carbonyl compounds, TsNH₂ and the title reagent pair, undergo nucleophilic addition of allylic silanes to produce the corresponding homoallylic amines. Reaction with but-2-enyltrimethylsilane proceeds regio- and diastereoselectively.</p> <p>Y. Masuyama, J. Tosa, Y. Kuruu <i>Chem. Commun.</i> 1999, 1075.</p>	<p>SnCl₂</p> <p>A</p>  <p>B</p>	 <p>91%, <i>anti:syn</i> = 89:11</p> <p>5 examples (yields 48-91%, 89:11 ≤ <i>anti:syn</i> ≤ 92:8) using but-2-enyltrimethylsilane and 14 examples (yields 17-96%) using allyltrimethylsilane are described.</p>
Trifluoromethanesulfonic Anhydride		
<p>Enol triflates of β-keto esters undergo decarboxylative elimination to yield the corresponding acetylenes.</p> <p>I. Fleming, C. Ramarao <i>Chem. Commun.</i> 1999, 1113.</p>	<p>Tf₂O</p> <p>A</p> 	 <p>11 examples (yields 54-86%).</p>
Potassium peroxymonosulfate (Oxone)		
<p>The title reagent is used in the oxidation of symmetrical acetals to esters and for the cleavage of tetrahydropyranyl ethers.</p> <p>M. Curini, F. Epifano, M. C. Marcotullio, O. Rosati <i>Synlett</i> 1999, 777.</p>	<p>2KHSO₅·KHSO₄·K₂SO₄</p> <p>A</p> 	 <p>9 examples of acetal oxidation (yields 60-98%) and 11 examples of THP cleavage (yields 48-91%) are reported.</p>
Tris(pentafluorophenyl)borane		
<p>Dehydrogenative silylation of alcohols can be accomplished with as little as 2 mol % of the title compound and a silane such as Ph₃SiH or Et₃SiH, <i>t</i>-BuMe₂SiH, or PhMe₂SiH (but not <i>i</i>-Pr₃SiH). The reaction works with 1°, 2° and 3° alcohols as well as phenols. 1,2- and 1,3-diols give the corresponding silylene derivatives using Ph₂SiH₂.</p> <p>J. M. Blackwell, K. L. Foster, V. H. Beck and W. E. Piers, <i>J. Org. Chem.</i>, 1999, 64, 4887.</p>	<p>(C₆F₅)₃B</p> <p>A</p> 	 <p>74%</p> <p>40 examples, yields generally >85%. Alkenes, alkynes, alkyl halides, nitro compounds, methyl and benzyl ethers, esters and lactones are inert under the conditions but epoxides cleave.</p>

Thiourea

Reagent

A 0.8 M solution of thiourea in refluxing EtOH-H₂O cleaves 1,3-dioxolanes, dimethyl acetals and THP ethers in good yield.



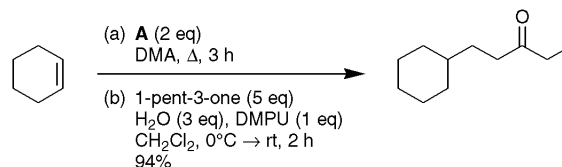
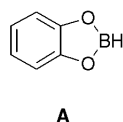
S. Majumdar and A. Bhattacharya, *J. Org. Chem.*, **1999**, *64*, 5682.

17 examples; yields typically 75–93%. MOM ethers and 2° TBS ethers do not react.

Catecholborane

Reagent

Reaction of the title reagent with olefins yields 2-alkylbenzo[d][1.3.2]dioxaboroles which are excellent radical precursors. Subsequent addition to α,β-unsaturated ketones and aldehydes proceeds in good yield.



C. Ollivier, P. Renaud *Chem. Eur. J.* **1999**, *5*, 1468.

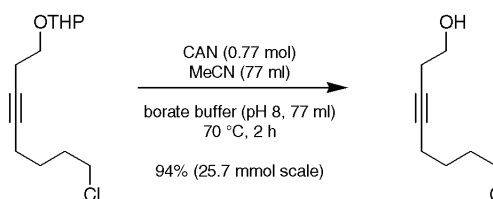
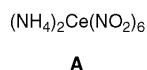
13 examples (yields 43, 60-94%) are reported.

DMA = *N,N*-dimethylacetamide

Ceric Ammonium Nitrate

Reagent

A very mild method for deprotecting THP and THF ethers employs **A** (3 mol%) in MeCN and borate buffer (pH 8.0). Esters, nitriles, ketones, enones, halides, sulfides, alkenes, and alkynes are all compatible. Trityl ethers survive the reaction conditions but ketone acetals are cleaved selectively.



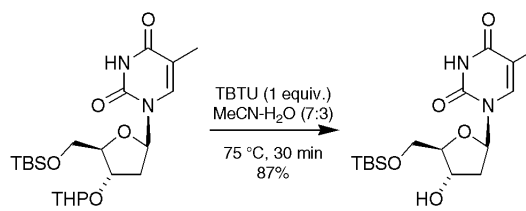
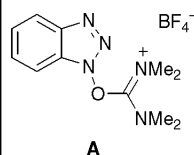
I. E. Markó, A. Ates, B. Augustyns, A. Gautier, Y. Quesnel, L. Turet and M. Wiaux, *Tetrahedron Lett.*, **1999**, *40*, 5613.

11 examples; yields 82-99%

O-(Benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium Tetrafluoroborate

Reagent

The title reagent **A** in MeCN-H₂O (7:3) at 75 °C selectively cleaves THP and DMTP ethers in the presence of TBS ethers, isopropylidene groups, benzyl ethers, Boc groups and Cbz groups. The hydrolysis is probably mediated by the production of HF and boric acid arising from decomposition of the tetrafluoroborate anion.



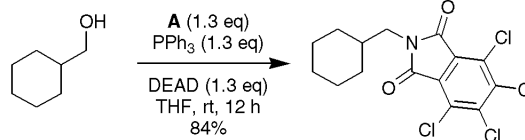
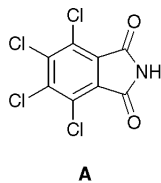
K. S. Ramasamy and D. Averett, *Synlett*, **1999**, 709.

14 examples; yields typically >90%

Tetrachlorophthalimide (TCP-NH)

Reagent

A is an excellent agent for the Mitsunobu displacement of 1° and 2° hydroxyl groups.



Z. J. Jia, S. Kelberlau, L. Olsson, G. Anilkumar, B. Fraser-Reid *Synlett* **1999**, 565.

10 examples (yields 55-90%).