

**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:

John Cooksey, Victoria Coombes, Axel Jansen, Stephen McAteer, Bernard Otto, Joanne Peach and Josephine Yuen, Department of Chemistry, Leeds University, Leeds, LS2 9JT, UK.

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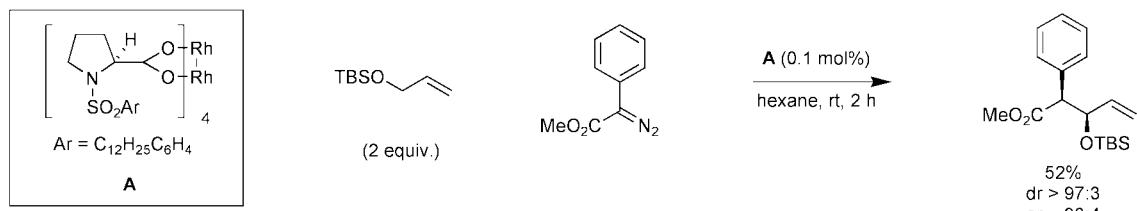
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The journals regularly covered by the abstractors are:

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  
Organic and Biomolecular Chemistry  
Organic Letters  
Organometallics  
Synlett  
Synthesis  
Tetrahedron  
Tetrahedron Asymmetry and Tetrahedron Letters

Synthesis of silyl-protected  $\beta$ -hydroxy esters via a catalytic, asymmetric C-H insertion.  
Davies, H. M. L.; Beckwith, R. E. J.; Antoulinakis, E. G.; Jin, Q. *J. Org. Chem.* 2003, 68, 6126.

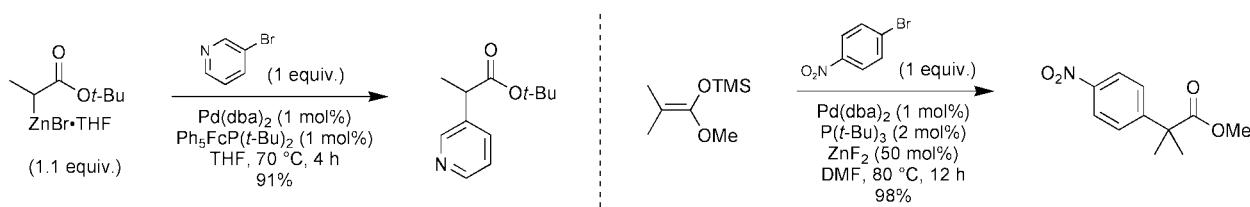
### C-H Insertion



39 examples (yields 23–98%, %de 40–98%, %ee 62–96%). The use of allyl and alkyl silyl ethers is reported.

Pd-catalyzed  $\alpha$ -arylation of esters and amides under neutral conditions.  
Hama, T.; Liu, X.; Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* 2003, 125, 11176.

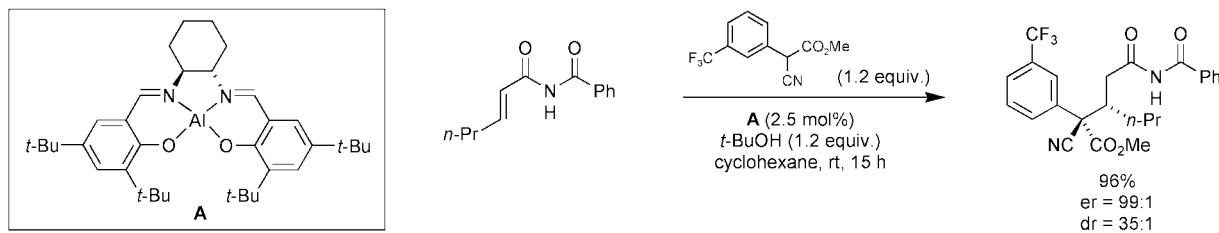
### sp<sup>3</sup>-sp<sup>2</sup> Coupling



Reformatsky reagents: 29 examples (yields 66–97%). Silyl ketene acetals: 12 examples (yields 67–99%). Fc = ferrocenyl.

Enantioselective Michael additions to  $\alpha,\beta$ -unsaturated imides.  
Taylor, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* 2003, 125, 11204.

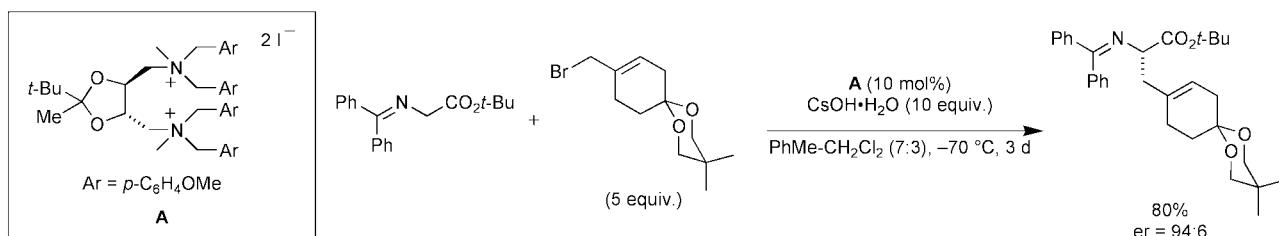
### 1,4-Addition



22 examples (yields 68–99%, %ee 86–98%).

Synthesis of Aeruginosin 298-A utilising a catalytic asymmetric phase-transfer alkylation.  
Ohshima, T.; Gnanadesikan, V.; Shibuguchi, T.; Fukuta, Y.; Nemoto, T.; Shibasaki, M. *J. Am. Chem. Soc.* **2003**, *125*, 11206.

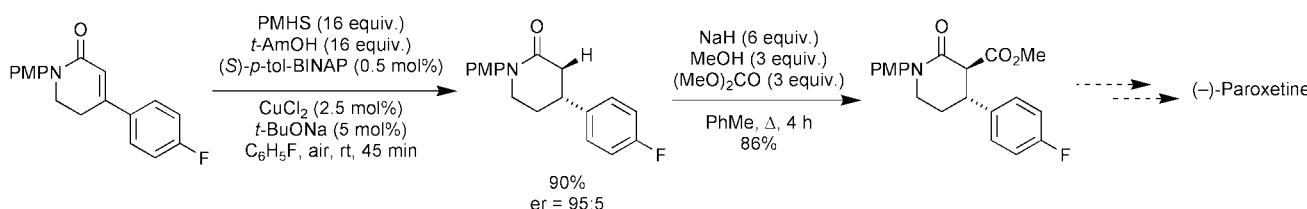
### Asymmetric Alkylation



A total synthesis of Aeruginosin 298-A is reported.

Catalytic enantioselective conjugate reduction of lactones and lactams.  
Hughes, G.; Kimura, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 11253.

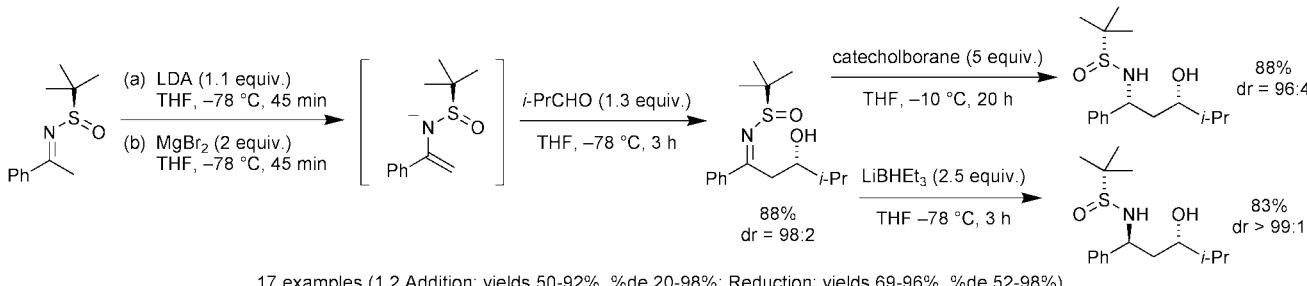
### Conjugate Reduction



PMHS = polymethylhydrosiloxane. 16 examples (yields 34-94%, %ee 71-94%).

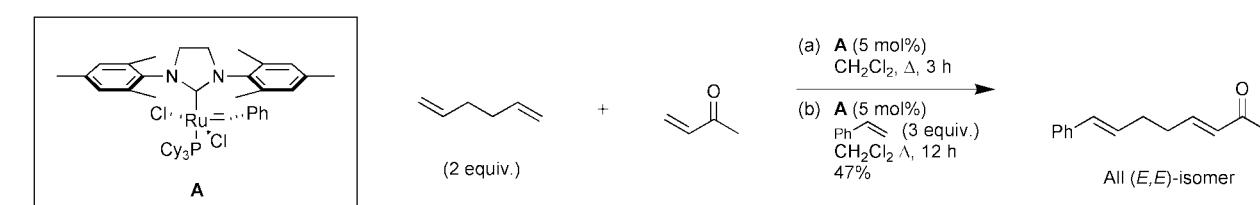
Asymmetric synthesis of *syn* and *anti*-1,3-amino alcohols.  
Kochi, T.; Tang, T. P.; Ellman, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 11276.

### Diastereoselective 1, 2-Addition/Reduction



A general model for selectivity in olefin cross-metathesis.  
Chatterjee, A. K.; Choi, T.-L.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003**, *125*, 11360.

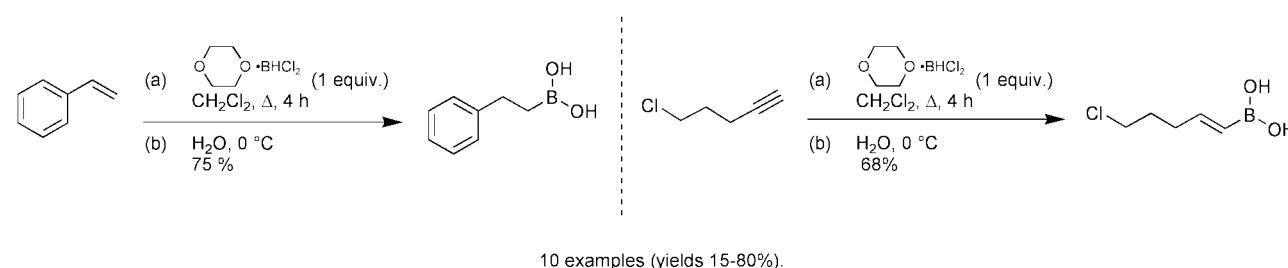
### Cross-Metathesis



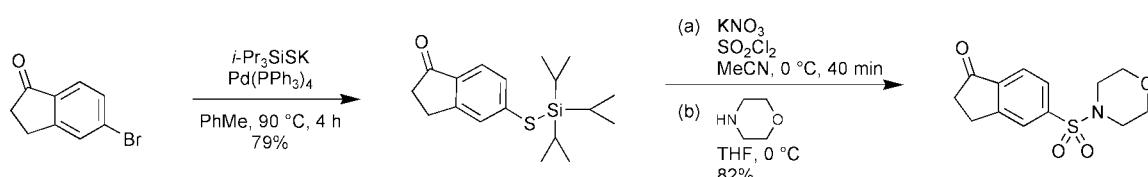
Model applied to unprecedented three-component intermolecular olefin cross-metathesis reactions. 6 examples (yields 34-89%).

Preparation of alkenyl- and alkylboronic acids using a dichloroborane-dioxane reagent.  
Josyula, K. V. B.; Gao, P.; Hewitt, C. *Tetrahedron Lett.* **2003**, *44*, 7789.

### Hydroboration

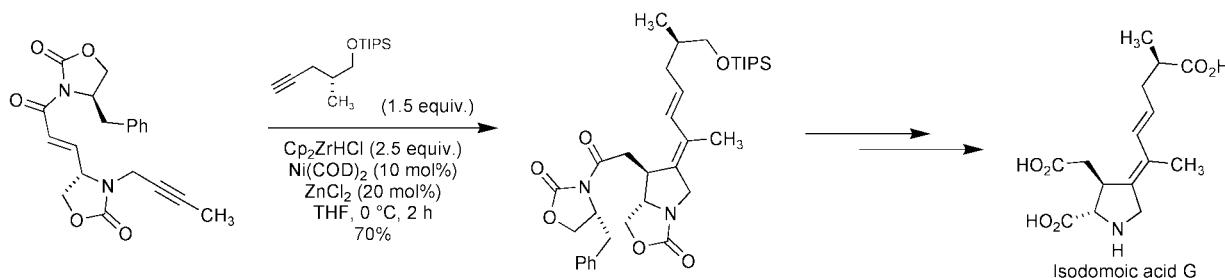


Synthesis of sulfonamides from triisopropylsilyl sulfanyls.  
Gareau, Y.; Pellicelli, J.; Laliberte, S.; Gauvreau, D. *Tetrahedron Lett.* **2003**, *44*, 7821.

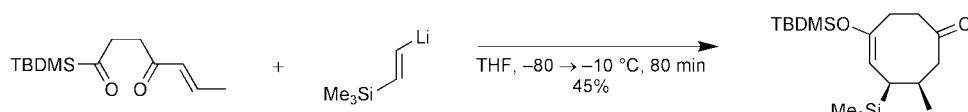
**sp<sup>3</sup>-sp<sup>2</sup> Coupling**

18 examples (yields 9-71%).

First total synthesis and stereochemical definition of Isodomoic acid G.  
Ni, Y.; Amarasinghe, K. K. D.; Ksebat, B.; Montgomery, J. *Org. Lett.* **2003**, *5*, 3771.

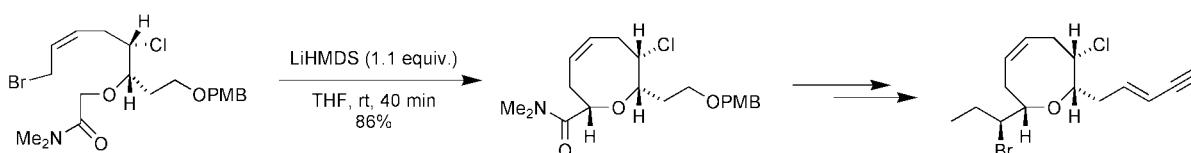
**sp-sp<sup>2</sup> Coupling/1,4-Addition**

Synthesis of eight-membered carbocycles by Brook rearrangement mediated annulation.  
Takeda, K.; Haraguchi, H.; Okamoto, Y. *Org. Lett.* **2003**, *5*, 3705.

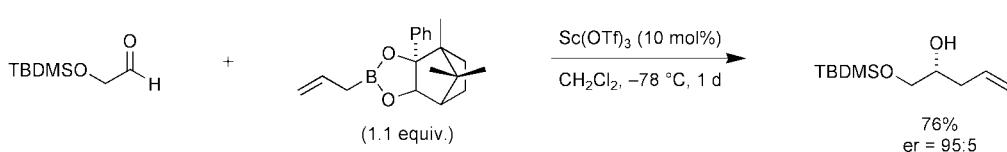
**Annulation**

4 examples (yields 42-45%).

Olefin-geometry dependent internal alkylation: asymmetric total synthesis of (+)-3-(E)- and (+)-3-(Z)-Pinnatifidenyne.  
Kim, H.; Choi, W. J.; Jung, J.; Kim, S.; Kim, D. *J. Am. Chem. Soc.* **2003**, *125*, 10238.

**Alkylation**The *trans* allylic halide gave exclusively S<sub>N</sub>2' product, whilst the *cis* allylic halide gave predominantly the S<sub>N</sub>2 product.

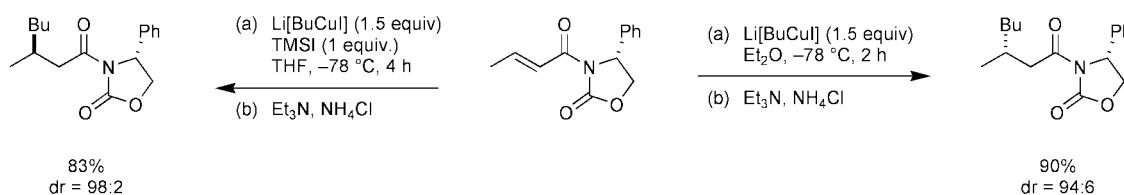
Sc(OTf)<sub>3</sub> catalyzed enantioselective allylboration.  
Lachance, H.; Lu, X.; Gravel, M.; Hall, D. G. *J. Am. Chem. Soc.* **2003**, *125*, 10160.

**Asymmetric Allylation**

12 examples of allylations (yields 62-90%, %ee 77-98%). 8 examples of crotylations (yields 52-74%, %ee 94-97%, %de &gt;98%).

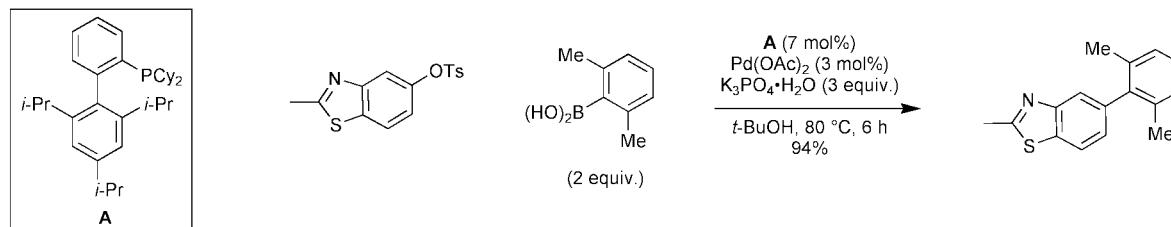
Reversal of the stereoselectivity in the conjugate addition of Li[BuCu] to a chiral *N*-crotyl-2-oxazolidinone.  
Dambacher, J.; Bergdahl, M. *Org. Lett.* **2003**, 5, 3539.

1,4-Addition



Optimization studies investigated.

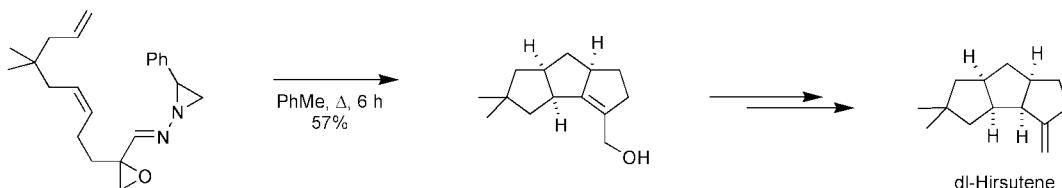
Pd-catalyzed Suzuki-Miyaura and carbonyl enolate coupling of aryl sulfonates.  
Nguyen, H. N.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, 125, 11818.

sp<sup>2</sup>-sp<sup>2</sup> Coupling

10 examples of Suzuki–Miyaura couplings and 6 examples of carbonyl enolate couplings with aryl sulfonates (yields 75–95%).

Triquinanes from alkylidene carbenes via trimethylene diyls.  
Lee, H-Y.; Kim, Y. *J. Am. Chem. Soc.* **2003**, 125, 10156.

Carbene Insertion/Radical Cyclization

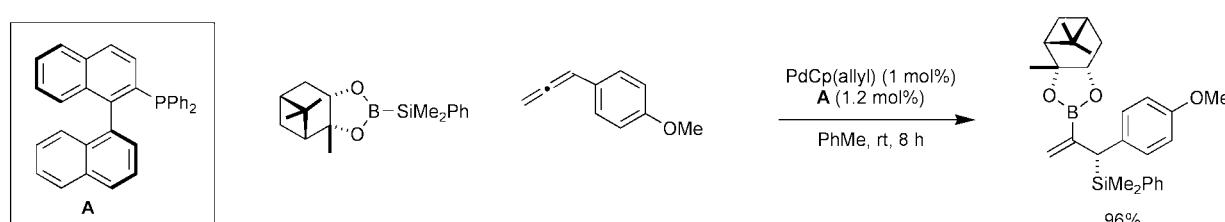


7 examples of cyclization step (yields 35–68%).

Enantioselective palladium-catalyzed silaboration of allenes.

Sugino, M.; Ohmura, T.; Miyake, Y.; Mitani, S.; Ito, Y.; Murakami, M. *J. Am. Chem. Soc.* **2003**, 125, 11174.

Silaboration

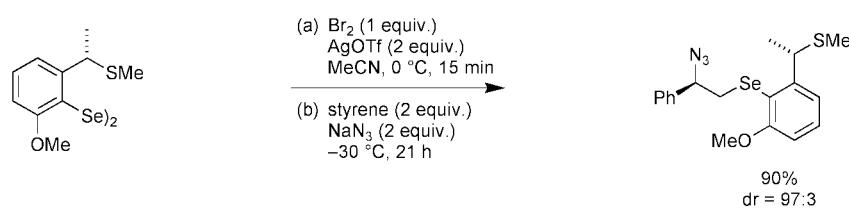


The chiral pinanediol group on the boron atom is necessary for enantioface discrimination.  
16 examples (yields 88–96%, %de 1–96%).

Asymmetric azidoselenenylation of alkenes.

Tiecco, M.; Testaferrri, L.; Santi, C.; Tomassini, C.; Marini, F.; Bagnoli, L. *Temperini, A. Angew. Chem. Int. Ed.* **2003**, 42, 3131.

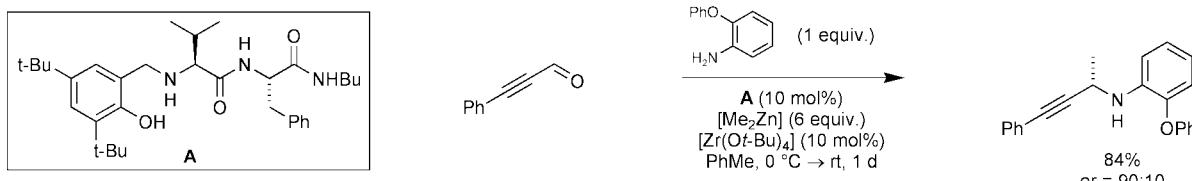
Asymmetric Addition



6 examples (yields 70–90%, %de 90–98%).  
Conversion of azidoselenides into optically active oxazolines, aziridines and triazoles is described.

Enantioselective Zr-catalyzed addition of alkylzinc reagents to alkynylimines.  
Akullian, L. C.; Snapper, M. L.; Hoveyda, A. M. *Angew. Chem. Int. Ed.* **2003**, *42*, 4244.

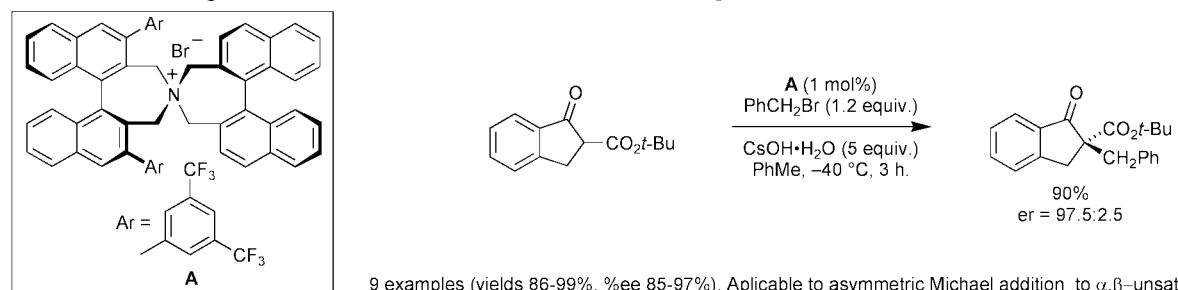
## Asymmetric Addition



17 examples (yields 60-94%, %ee 5-98%).

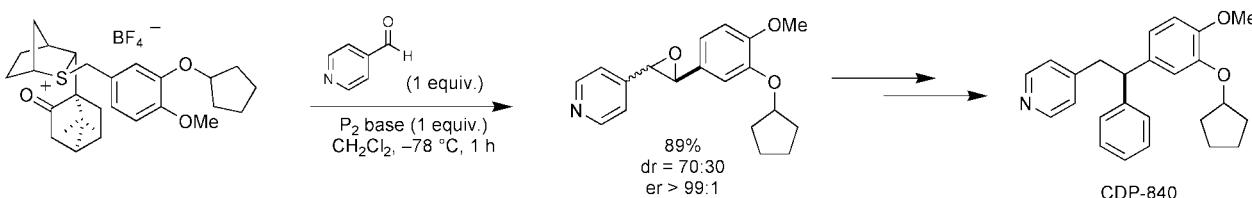
Phase-transfer catalytic asymmetric alkylation and Michael reaction on  $\beta$ -keto esters.  
Ooi, T.; Miki, T.; Taniguchi, M.; Shiraishi, M.; Takeuchi, M.; Maruoka, K. *Angew. Chem. Int. Ed.* **2003**, *42*, 3796.

## Alkylation/1,4-Addition

9 examples (yields 86-99%, %ee 85-97%). Applicable to asymmetric Michael addition to  $\alpha,\beta$ -unsaturated carbonyls.

Sulfur-ylide mediated synthesis of epoxides.  
Aggarwal, V. K.; Bae, I.; Lee, H. Y.; Richardson, J.; Williams, D. T. *Angew. Chem. Int. Ed.* **2003**, *42*, 3274.

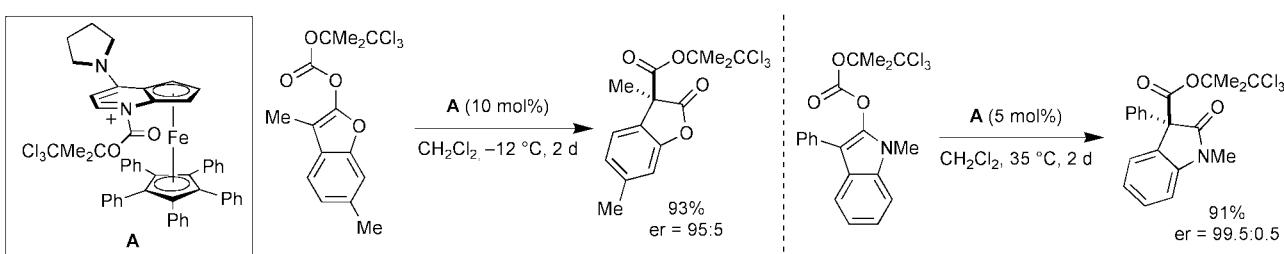
## Asymmetric Epoxidation



18 examples (yields 19-96%, %de 20-98%, %ee 71->99%).  
P<sub>2</sub> base = *N,N,N',N'*-tetramethyl-*N*-(tris(dimethylamino)phosphoranylidene)phosphoric triamide diethylimine.

Enantioselective synthesis of oxindoles and benzofuranones.  
Hills, I. D.; Fu, G. C. *Angew. Chem. Int. Ed.* **2003**, *42*, 3921.

## O-C Rearrangement

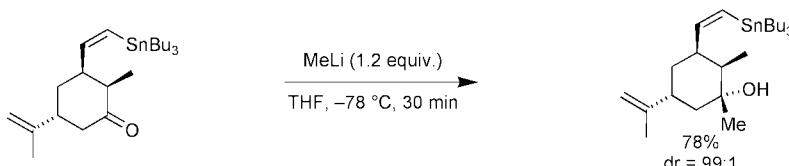


3 examples (yields 81-95%, %ee 88-97%).

9 examples (yields 72-98%, %ee 58-99%).

Diastereoselective addition of organometallic compounds to tin containing cyclic ketones.  
Barbero, A.; Pulido, F. J.; Rincon, J. A. *J. Am. Chem. Soc.* **2003**, *125*, 12049.

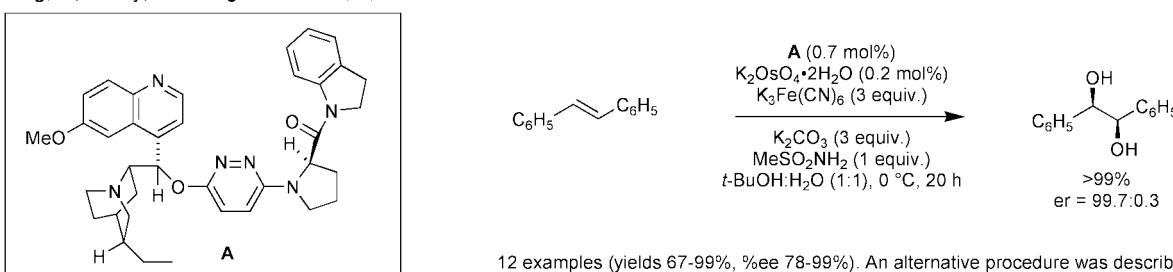
## Diastereoselective Nucleophilic Addition



Proposed mechanism is via a chelation controlled intramolecular nucleophile transfer, with an optimum Sn/CO distance of 5 bonds.  
27 examples (yields 71-96%, %de 50-98%).

A new reagent for the highly enantioselective, catalytic dihydroxylation of olefins.  
Huang, J.; Corey, E. J. Org. Lett. 2003, 5, 3455.

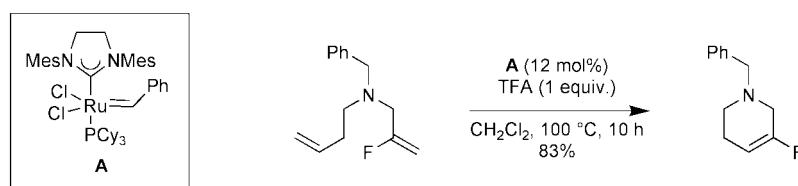
### Asymmetric Dihydroxylation



12 examples (yields 67–99%, %ee 78–99%). An alternative procedure was described requiring only 10 mol%  $\text{K}_3\text{Fe}(\text{CN})_6$  with the addition of 50 mol%  $\text{NaClO}_2$  as oxidant.

Synthesis of heterocyclic and carbocyclic fluoro-olefins by ring-closing metathesis.  
Salim, S. S.; Bellingham, R. K.; Satcharoen, V. Brown, R. C. D. Org. Lett. 2003, 5, 3403.

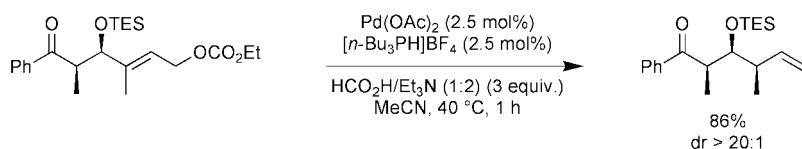
### Ring-Closing Metathesis



9 examples (yields 40–90%).

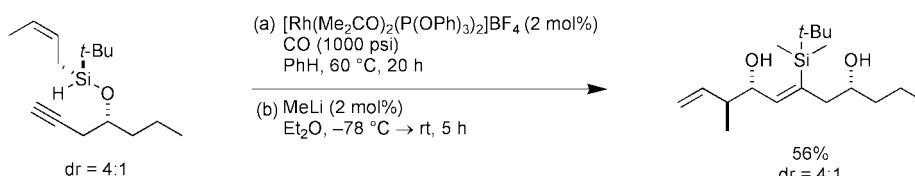
Diastereoselective Pd-catalyzed formate reduction of allylic carbonates.  
Lautens, M.; Paquin, J. F. Org. Lett. 2003, 5, 3391.

### Reduction



9 examples (yields 60–87%, %de 16–90%).

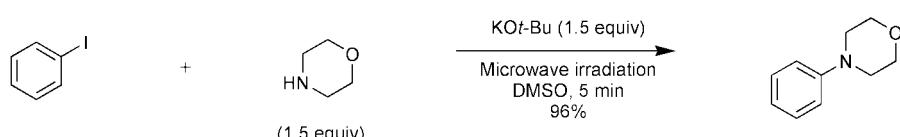
Tandem silylformylation-crotylsilylation and application to the synthesis of Dolabelides A and B. **Tandem Silylformylation-Crotylsilylation**  
Schmidt, D. R.; Park, P. K.; Leighton, J. L. Org. Lett. 2003, 5, 3535.



A synthesis of the C(15)-C(30) fragment of dolabelides A and B is described.

Rapid and efficient microwave-assisted amination of electron-rich aryl halides without a transition metal catalyst.  
Shi, L.; Wang, M.; Fan, C-A.; Zhang, F-M.; Tu, Y-Q. Org. Lett. 2003, 5, 3515.

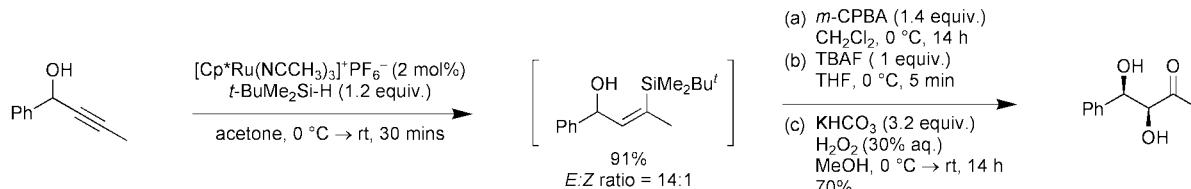
### $\text{SN}_{\text{Ar}}$ Reaction



A variety of aryl halides, secondary aliphatic and aromatic amines were investigated. 19 examples (yields 61–97%) including optimization of reaction conditions.

Regioselective hydrosilylation of propargylic alcohols as an aldol surrogate.  
Trost, B. M.; Ball, Z. T.; Jöge, T. *Angew. Chem. Int. Ed.* **2003**, *42*, 3145.

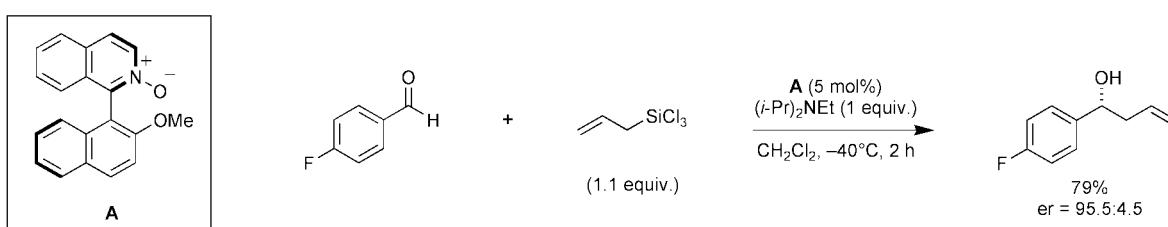
## Hydrosilylation



13 hydrosilylation examples (yields 8-99%, E:Z ratio 5:1->20:1).

Asymmetric allylation of aromatic aldehydes catalyzed by a isoquinoline N-oxide derivative.  
Malkov, A. V.; Dufková, L.; Farrugia, L.; Kocovsky, P. *Angew. Chem. Int. Ed.* **2003**, *42*, 3674.

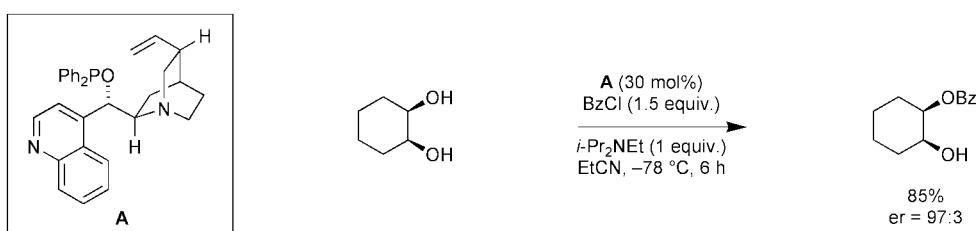
## Asymmetric Allylation



16 examples (yields 25-86%, %ee 5-96%).

Asymmetric desymmetrization of meso-1,2-diols by phosphinites derivatives of Cinchona alkaloids.  
Mizuta, S.; Sadamori, M.; Fujimoto, T.; Yamamoto, I. *Angew. Chem. Int. Ed.* **2003**, *42*, 3383.

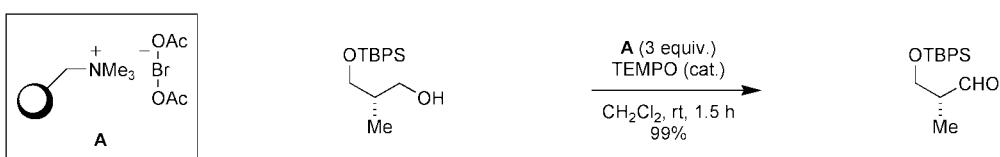
## Desymmetrization



5 examples (yields 80-99%, %ee 76-94%).

TEMPO-mediated oxidations of primary and secondary alcohols assisted by a polymer-bound bromate complex.  
Brünjes, M.; Sourkouni-Argirusi, G.; Kirschning, A. *Adv. Synth. Catal.* **2003**, *635*.

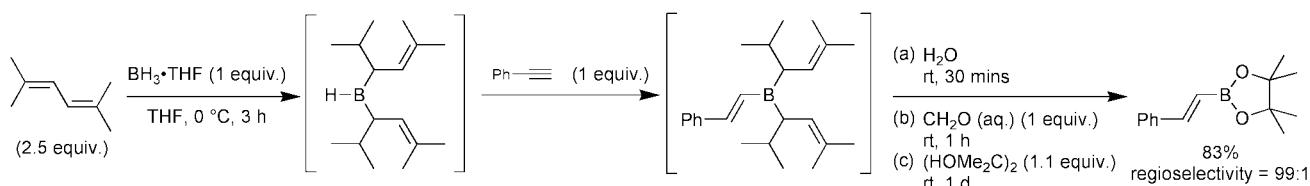
## Oxidation



20 examples (yields 56-99 %).

A new hydroboration reagent for the synthesis of alkyl and alkenyl boronic acids.  
Kalinin, A. V.; Scherer, S.; Snieckus, V. *Angew. Chem. Int. Ed.* **2003**, *42*, 3399.

## Hydroboration

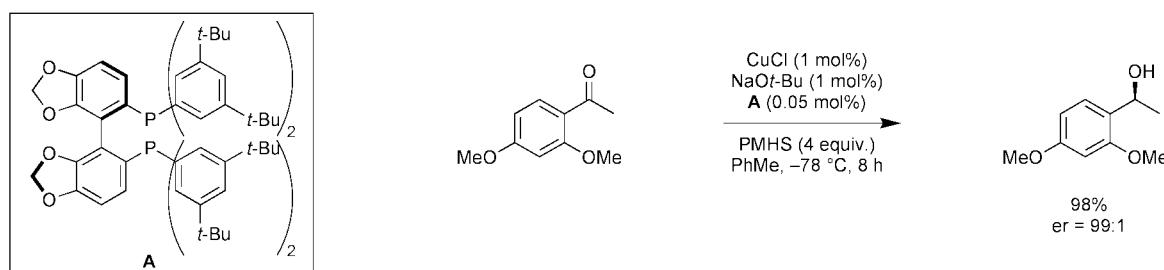


38 examples (yields 41-86%, regioselectivities 83:17-100%).

A sequential one-pot hydroboration/Suzuki-Miyaura cross coupling is also reported.

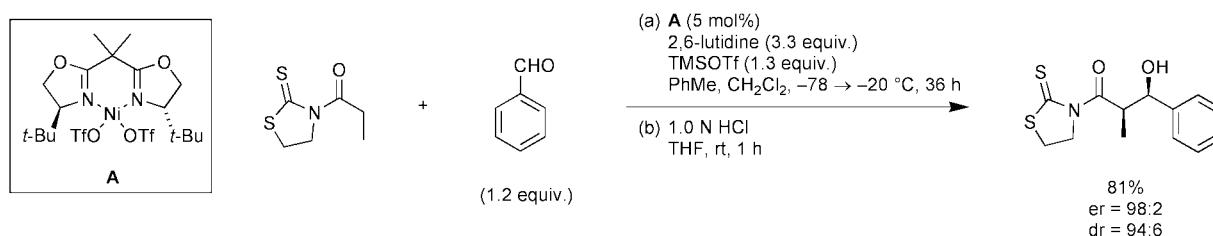
Asymmetric hydrosilylation of aryl ketones catalyzed by copper hydride.  
Lipshutz, B. H.; Noson, K.; Chrisman, W., Lower, A. *J. Am. Chem. Soc.* **2003**, 125, 8779.

### Asymmetric Hydrosilylation



Enantioselective *syn*-Aldol reaction in the presence of silyl triflates.  
Evans, D. A.; Downey, C. W.; Hubbs, J. L. *J. Am. Chem. Soc.* **2003**, 125, 8706.

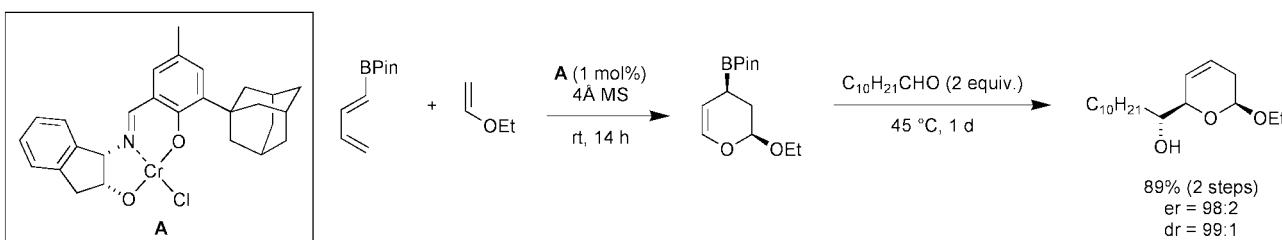
### Catalytic Asymmetric Aldol



11 examples (yields 46-86%, %de 76-94%, %ee 90-97%).

Enantio- and diastereoselective Cr(III)-catalyzed three-component [4+2]/allylboration.  
Gao, X.; Hall, D. G. *A. J. Am. Chem. Soc.* **2003**, 125, 9308.

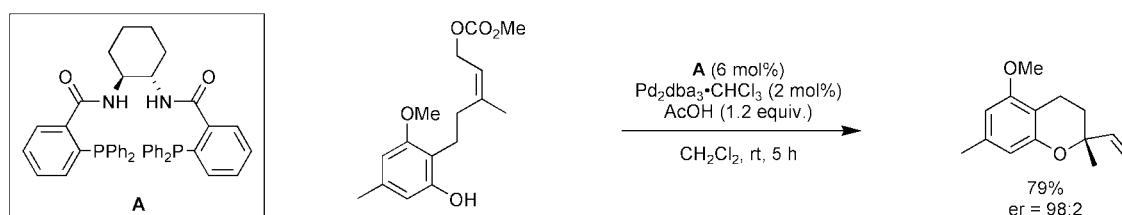
### Hetero[4+2]/Allylboration



8 examples of the one-pot, 3 component reaction (yields 61-92%, %dr >98%, %ee 96%). Pin = pinocarboate.

Synthesis of chiral chromans.  
Trost, B. M.; Shen, H. C.; Dong, L.; Surivet, J.-P., A. *J. Am. Chem. Soc.* **2003**, 125, 9276.

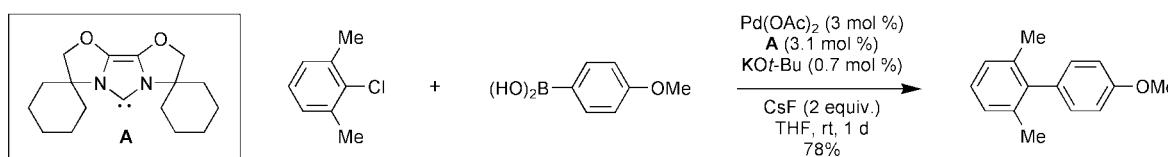
### Asymmetric Allylic Alkylation



28 examples (yields 24-99%, %ee 22-97%). Applied to the total synthesis of (+)-Clusifoliol.

Suzuki cross-coupling of sterically hindered aryl chlorides with a new *N*-heterocyclic carbene ligand.  
Altenhoff, G.; Goddard, R.; Lehmann, C. W.; Glorius, F. *Angew. Chem. Int. Ed.* **2003**, 42, 3690.

### sp<sup>2</sup>-sp<sup>2</sup> Coupling



14 examples (yields 69-95%).