Perkin 1 Abstracts: Solid Phase Organic Synthesis

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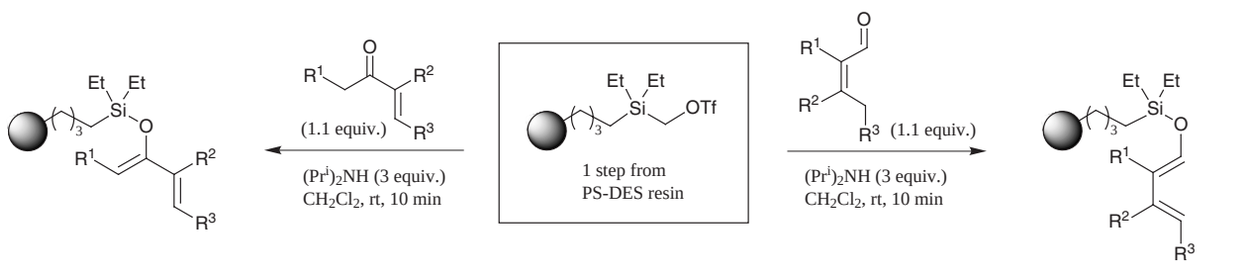
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances in new linker design are also covered.

Polymer supported silyl triflate: synthesis and solid-phase Diels-Alder reactions of silyloxydienes

Linker

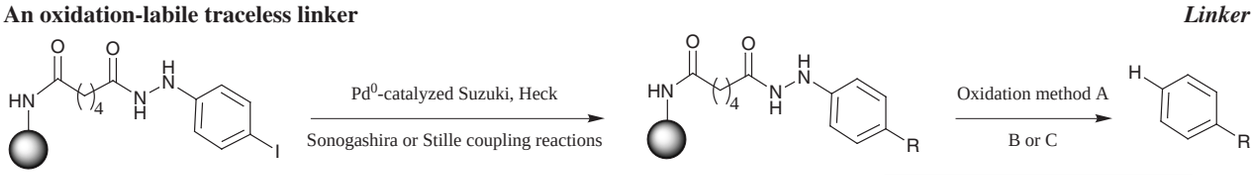


E. M. Smith, *Tetrahedron Lett.*, 1999, **40**, 3285.

13 examples of Diels-Alder reactions (yields 18-100%, purities 69-98%).

An oxidation-labile traceless linker

Linker



3 steps from
polystyrene, TentaGel
or ArgoPore resin

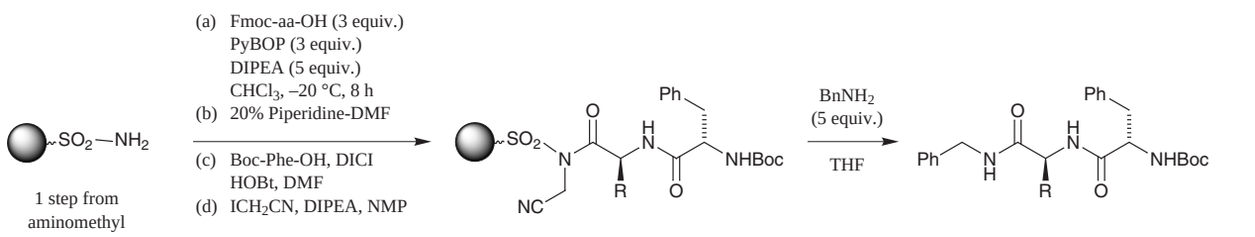
Method A = $Cu(OAc)_2$, Py, MeOH
B = $Cu(OAc)_2$, *n*-propylamine
C = *N*-bromosuccinimide, py
MeOH, CH_2Cl_2

F. Stieber, U. Grether and H. Waldmann, *Angew. Chem. Int. Ed.*, 1999, **38**, 1073.

8 examples using oxidation method A and/or B and/or C (yields 37-96%, HPLC, GC-MS and NMR purity > 90%).

Alkanesulfonamide "Safety-Catch" linker

Linker



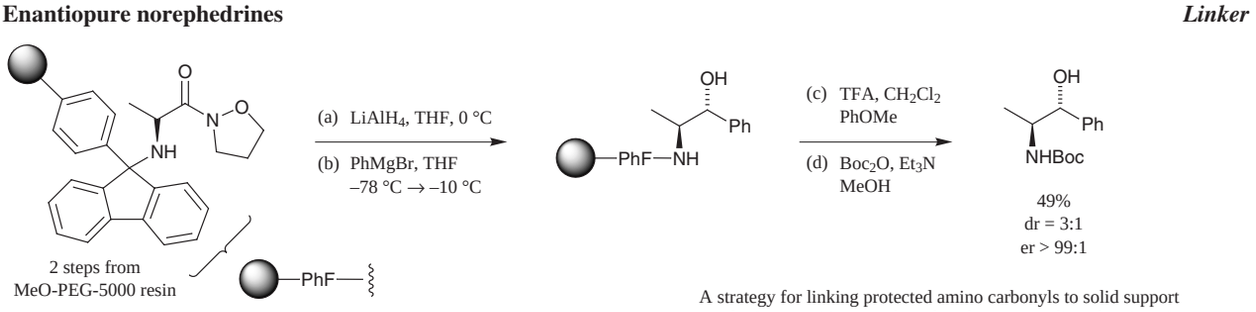
1 step from
aminomethyl
polystyrene resin

A novel linker is described. Treatment with ICH_2CN provides an activated *N*-cyanomethyl derivative that can be cleaved by a variety of nucleophiles. 21 examples (yields 54-96%, HPLC purity 75-97%).

B. J. Backes and J. A. Ellman, *J. Org. Chem.*, 1999, **64**, 2322.

Enantiopure norephedrines

Linker

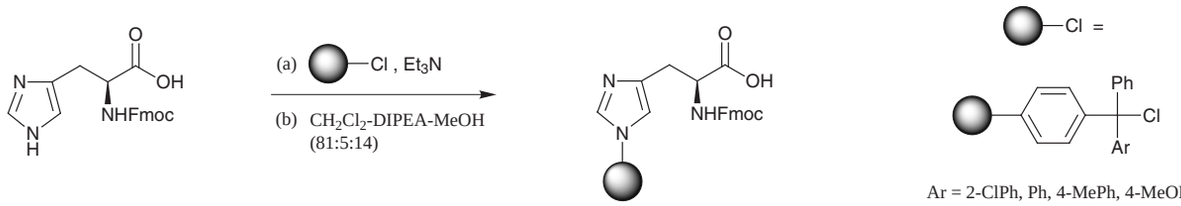


2 steps from
MeO-PEG-5000 resin

A strategy for linking protected amino carbonyls to solid support employing transition metal catalysed cross-coupling chemistry is reported. The strategy is illustrated by the synthesis of enantiopure norephedrines.

F. Gosselin, J. V. Betsbrugge, M. Hatam and W. D. Lubell, *J. Org. Chem.*, 1999, **64**, 2486.

Attachment of histidine, histamine and urocanic acid to trityl-type resins



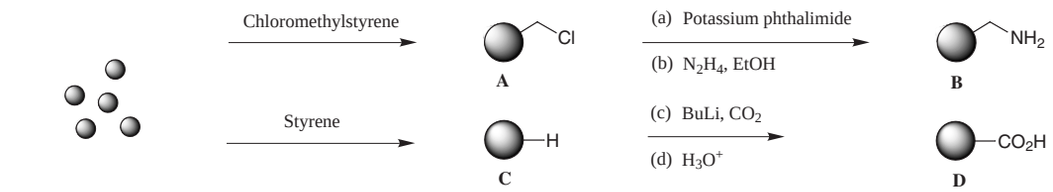
Ar = 2-ClPh, Ph, 4-MePh, 4-MeOPh

S. Eleftheriou, D. Gatos, A. Panagopoulos, S. Stathopoulos and K. Barlos, *Tetrahedron Lett*., 1999, **40**, 2825.

Attachment of histidine, histamine and urocanic acid to trityl-type resins through the N^{Im} function is reported. Cleavage from the resin is achieved using TFA.

A new high loading paramagnetic support

Support



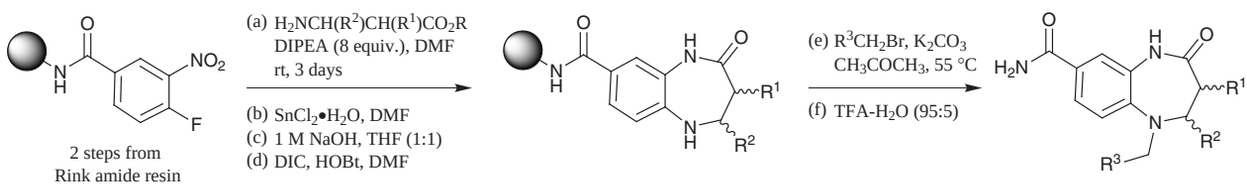
Primary paramagnetic beads
(Magnetite crystals encased in high cross-linked polystyrene)

Composite paramagnetic beads

I. Sucholeiki and J. M. Perez, *Tetrahedron Lett*., 1999, **40**, 3531.

Synthesis of high-loading paramagnetic supports **A**-**D** is described. The supports are stable in organic solvents and can be separated from reaction mixtures magnetically. The utility of the new supports is illustrated by their use as scavenging resins and in the synthesis of a tetrapeptide.

3,4,5-Substituted 1,5-benzodiazepin-2-ones

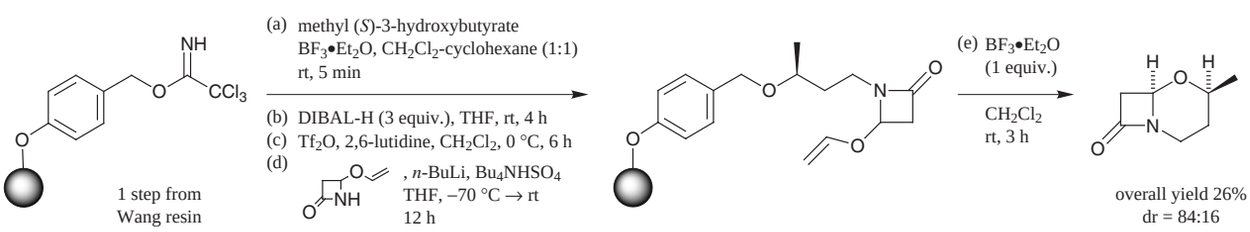


2 steps from Rink amide resin

J. Lee, D. Gauthier and R. A. Rivero, *J. Org. Chem*., 1999, **64**, 3060.

35 examples (yields 46-98%).

Stereoselective synthesis of β-lactams - a novel cyclisation/cleavage step towards 1-oxacephams



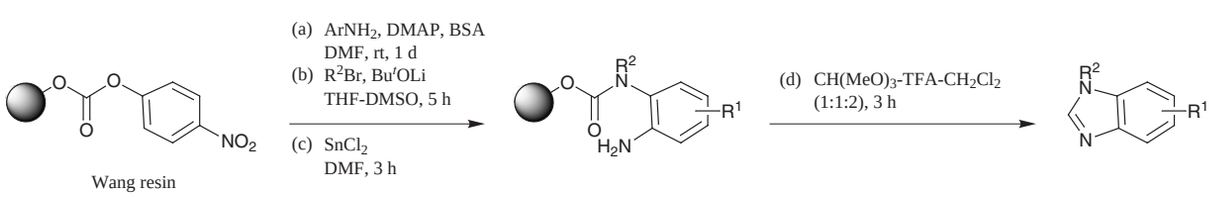
1 step from Wang resin

overall yield 26%
dr = 84:16

B. Furman, R. Thürmer, Z. Kaluza, R. Lysek, W. Voelter and M. Chmielewski, *Angew. Chem. Int. Ed.*, 1999, **38**, 1121.

1 other example (yield 30%, > 97% de).

Benzimidazoles



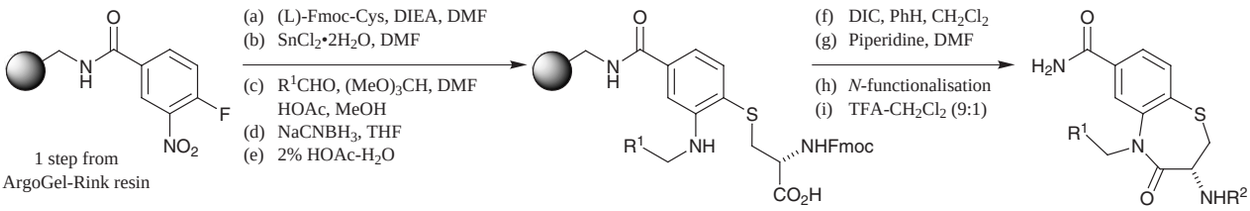
Wang resin

BSA = Bis(trimethylsilyl)acetamide

W. Huang and R. M. Scarborough, *Tetrahedron Lett*., 1999, **40**, 2665.

9 examples (yields and HPLC purity >80%).

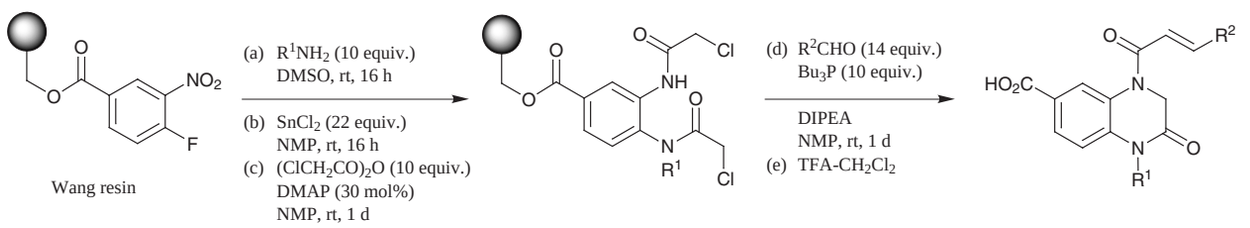
3,5-Disubstituted 2,3-dihydro-1,5-benzothiazepin-4(5*H*)-ones



M. K. Schwarz, D. Tumelty and M. A. Gallop, *J. Org. Chem*., 1999, **64**, 2219.

55 examples (yields 37-83%, HPLC purity 80-98%).

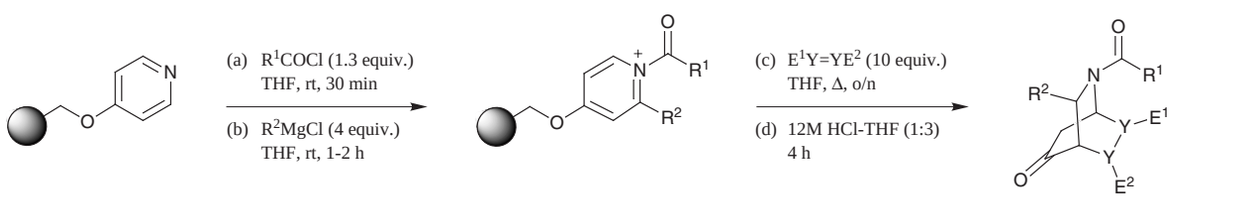
Substituted 4-acyl-1,2,3,4-tetrahydroquinoxalin-2-ones



F. Zaragoza and H. Stephensen, *J. Org. Chem*., 1999, **64**, 2555.

4 examples (yields 26-43%).

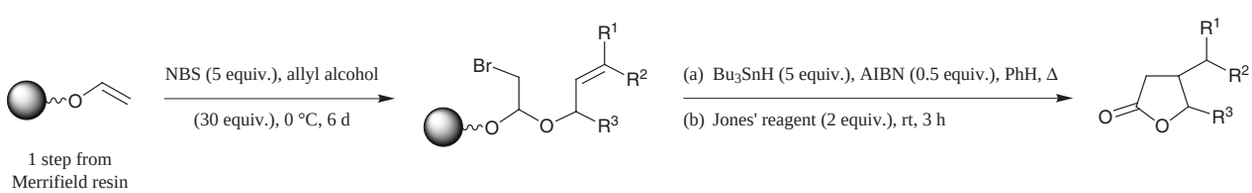
2-Acyl-3,7,8-substituted-5-oxo-2-azabicyclo[2.2.2]octane and triaza analogs



C. Chen and B. Munoz, *Tetrahedron Lett*., 1999, **40**, 3491.

13 examples (yields 0, 15-83%, HPLC purities 60->90%).

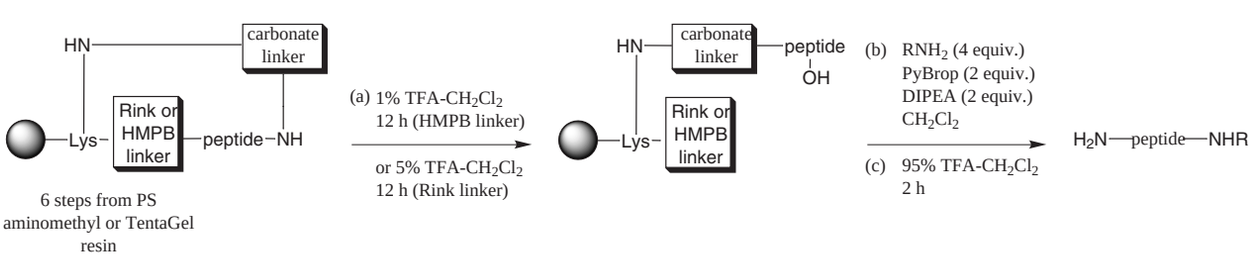
γ-Butyrolactones



Y. Watanabe, S. Ishikawa, G. Takao and T. Toru, *Tetrahedron Lett.*, 1999, **40**, 3411.

6 examples (yields 47-93%).

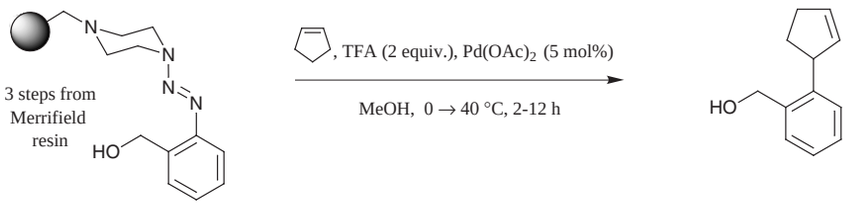
Internal resin capture: a self purification method for the synthesis of C-terminally modified peptides



M. Davies and M. Bradley, *Tetrahedron*, 1999, **55**, 4733.

6 examples (yields 45-75%). 1 other example is also described.

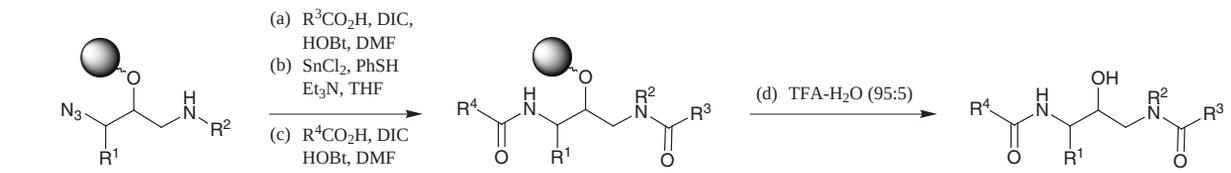
An efficient cleavage-cross-coupling strategy: a modular building system for combinatorial chemistry



S. Bräse and M. Schroen, *Angew. Chem. Int. Ed.*, 1999, **38**, 1071.

15 further examples of the synthesis of cycloalkenyl-, alkynyl-, cycloalkyl and aryl-substituted heteroarene derivatives (yields 45-97%).

1,3-Diaminopropan-2-ol derivatives as potential aspartic acid inhibitors

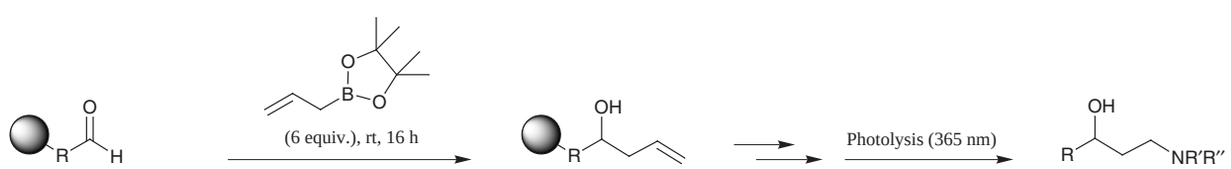


2 steps from dihydropyran functionalized polystyrene resin

J. Zhou, A. Termin, M. Wayland and C. M. Tarby, *Tetrahedron Lett.*, 1999, **40**, 2729.

92 examples (yields 39-77%, purity 85-99%).

Allylation of resin-bound aromatic and aliphatic aldehydes

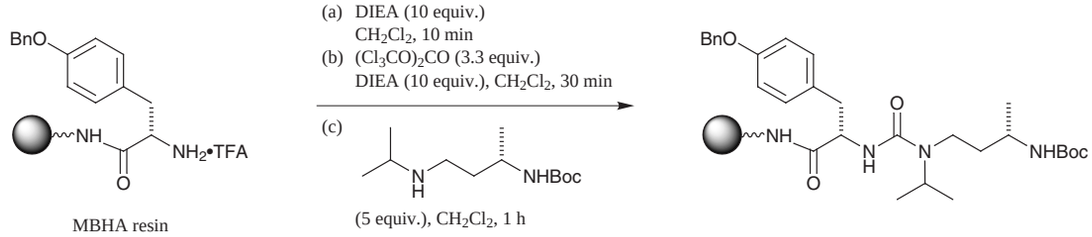


TentaGel S-NH_2 or polystyrene resin

C. L. Cavallaro, T. Herpin, B. F. McGuinness, Y. C. Shimshock and R. E. Dolle, *Tetrahedron Lett.*, 1999, **40**, 2711.

10 examples of allylation (yields 70-100%) and 2 examples of crotylation (yields 65, 93%) are reported. The methodology is applied to the synthesis of hydroxypropylamines.

N,N′-Unsymmetrically substituted ureas

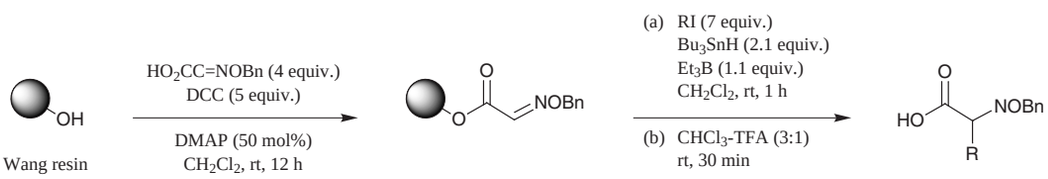


MBHA resin

D. Limal, V. Semetey, P. Dalbon, M. Jolivet and J.-P. Briand, *Tetrahedron Lett.*, 1999, **40**, 2749.

Synthesis of the above urea as an intermediate in the preparation of a *N*-monoprotected propylene diamine is reported.

α-Amino acid derivatives

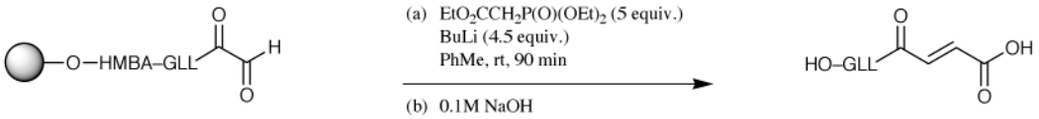


Wang resin

H. Miyabe, Y. Fujishima and T. Naito, *J. Org. Chem.*, 1999, **64**, 2174.

7 examples (yields 24-78%) are reported.

Synthesis of peptide isosteres on a novel polyethylene glycol based resin

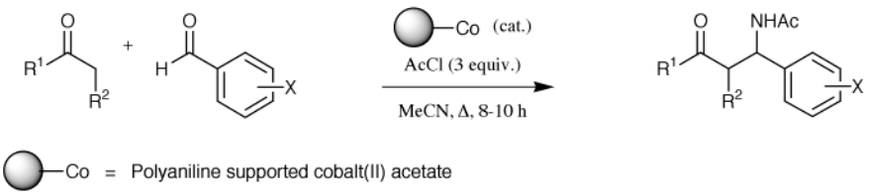


6 steps from polyoxyethylene / polyoxypropylene copolymer resin

Preparation of the novel POEPOP-400 resin is reported. The resin is demonstrated to be compatible with a wide range of nucleophilic reaction conditions in the synthesis of peptide isosteres.

J. Rademann, M. Meldal and K. Bock, *Chem. Eur. J.*, 1999, **5**, 1218.

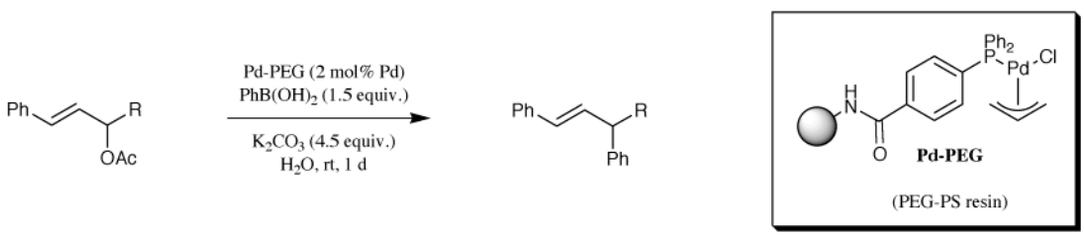
β-Amino acid derivatives



E. N. Prabhakaran and J. Iqbal, *J. Org. Chem.*, 1999, **64**, 3339.

10 examples (yields 46-68%, HPLC purity 95-100%) are reported.

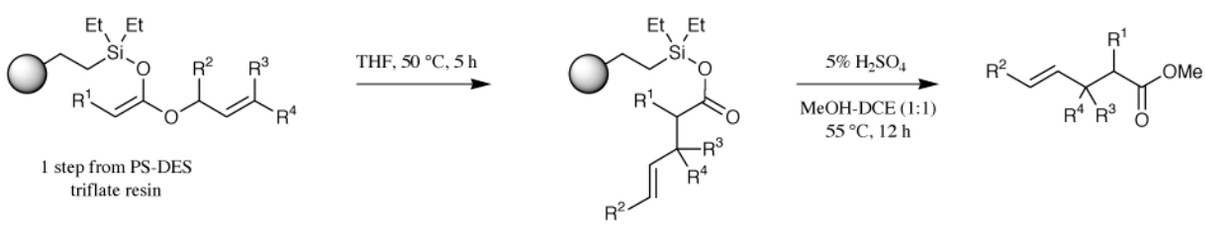
Cross-coupling of aryl halides and allyl acetates with arylboron reagents in water



Y. Uozumi, H. Danjo and T. Hayashi, *J. Org. Chem.*, 1999, **64**, 3384.

20 examples (yields 14-99%).

Ester enolate Claisen rearrangement using a polymer-supported silyl triflate

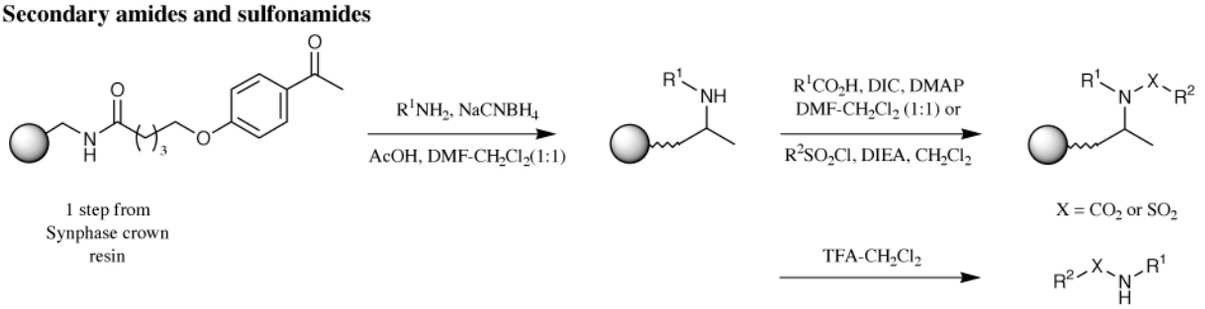


1 step from PS-DES triflate resin

Y. Hu and J. A. Porco, *Tetrahedron Lett.*, 1999, **40**, 3289.

5 examples (52-60%, GC purities 86-100%).

Secondary amides and sulfonamides



1 step from Synphase crown resin

C. T. Bui, A. M. Bray, F. Ercole, Y. Pham, F. A. Rasoul and N. J. Maeji, *Tetrahedron Lett.*, 1999, **40**, 3471.

11 examples (yields not specified).