Perkin 1 Abstracts: Solid Phase Organic Synthesis

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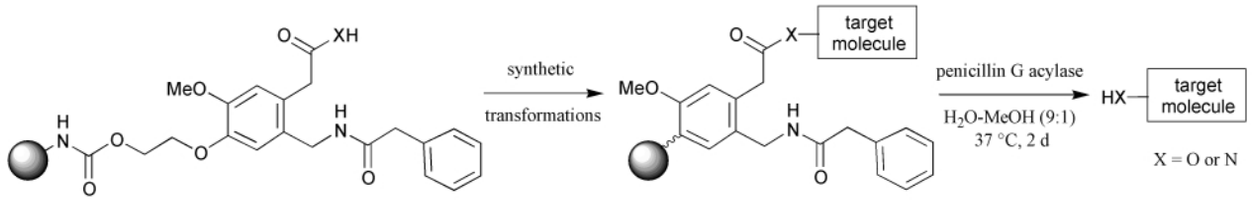
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

Enzyme-labile safety-catch linker. ***Linker***

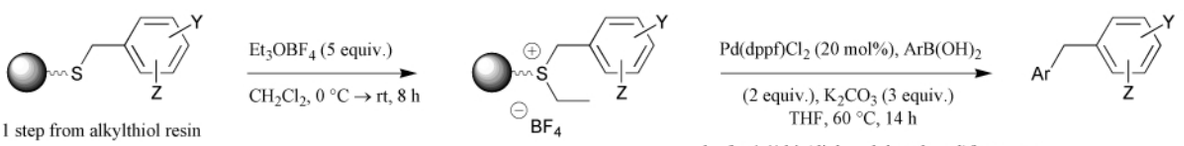


1 step from polyethyleneglycol$_{6000}$

7 examples, which demonstrate the suitability of the illustrated linker in various reaction types, including Heck, Suzuki, Sonogashira, Mitsunobu and Diels–Alder reactions, are reported (yields 60-94%, purity >95%).

U. Grether and H. Waldmann, *Angew. Chem., Int. Ed.*, 2000, **39**, 1629.

Traceless synthesis of biarylmethane derivatives *via* Pd-catalysed release of polymer-bound benzylsulfonium salts. ***Linker***



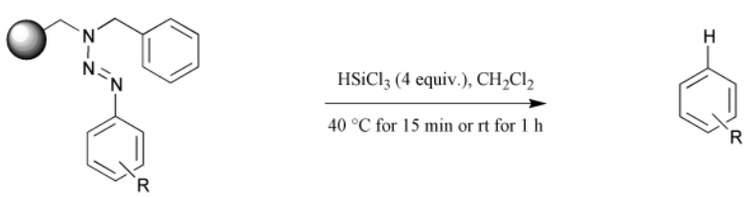
1 step from alkylthiol resin

dppf = 1,1'-bis(diphenylphosphanyl)ferrocene

15 examples (yields 24-99%). 1 example of two successive Pd catalysed reactions using the illustrated benzylthiol linker is also reported (yield 57%).

C. Vanier, F. Lorgé, A. Wagner and C. Mioskowski, *Angew. Chem., Int. Ed.*, 2000, **39**, 1679.

Traceless cleavage of a triazene linker. ***Linker***

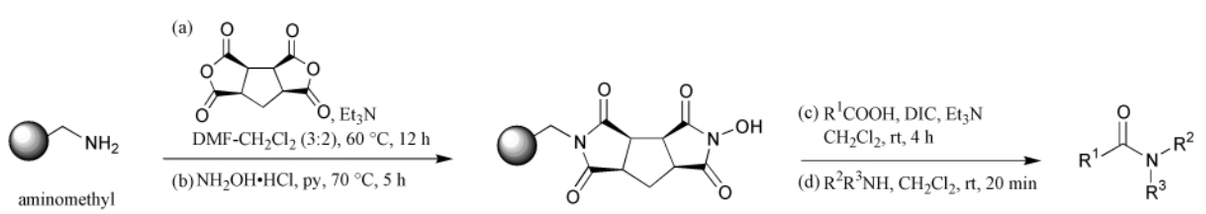


1 step from benzylaminomethyl polystyrene resin

9 examples (yields 70-95%, GC purity 91-96%).

M. Lormann, S. Dahmen and S. Bräse, *Tetrahedron Lett.*, 2000, **41**, 3813.

N*-Hydroxysuccinimidyl active ester linker.** ***Linker

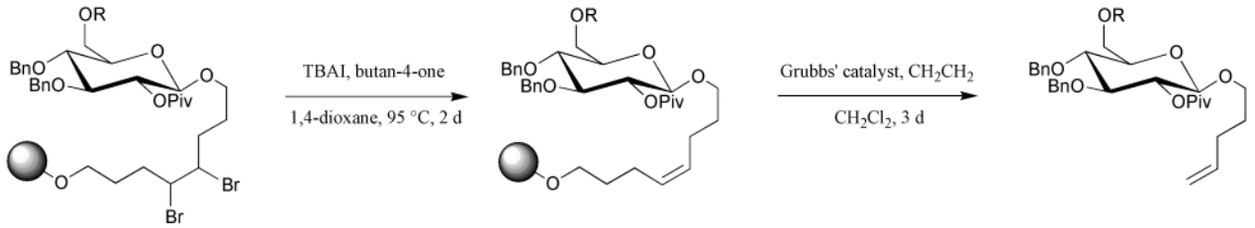


aminomethyl polystyrene resin

16 examples (yields 68-93%, LCMS purity 86-100%).

H. Shao, Q. Zhang, R. Goodnow, L. Chen and S. Tam, *Tetrahedron Lett.*, 2000, **41**, 4257.

4,5-Dibromooctane-1,8-diol linker for oligosaccharide synthesis. ***Linker***

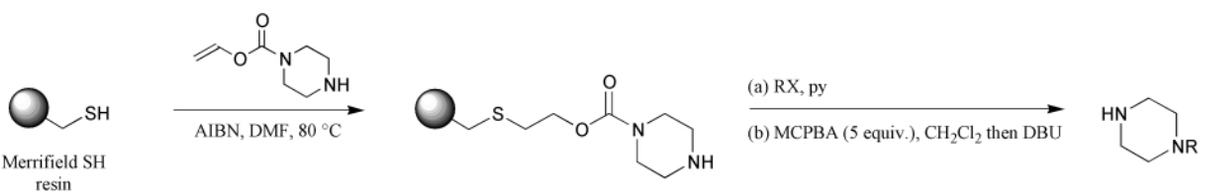


9 steps from Merrifield resin TBAI = tetrabutylammonium iodide

L. G. Melean, W.-C. Haase and P. H. Seeberger, *Tetrahedron Lett.*, 2000, **41**, 4329.

Preparation of 1 trisaccharide is reported (yield 9%).

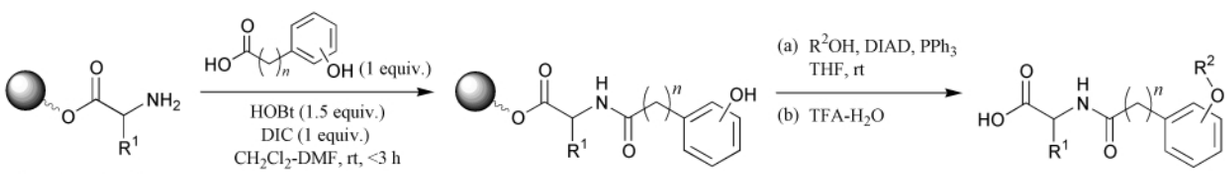
Traceless 2-(thiobenzyl)ethyl carbamate linker. ***Linker***



Z. Timár and T. Gallagher, *Tetrahedron Lett.*, 2000, **41**, 3173.

2 examples (yields 47-50%, HPLC purity >90%).

Synthesis of aryl ethers using high loading dendrimer resin. ***Support***

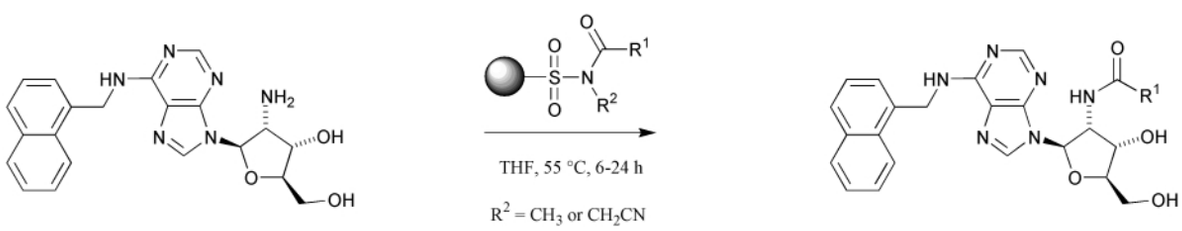


3 steps from dendrimer resin

A. Basso, B. Evans, N. Pegg and M. Bradley, *Tetrahedron Lett.*, 2000, **41**, 3763.

20 examples (yields 62-88%, HPLC purity 67-100%). Synthesis of dendrimer resin from TentaGel resin is also reported.

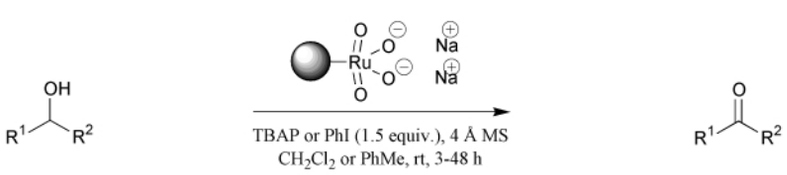
Amidation of 2′-amino-2′-deoxy-N^6-(1-naphthylmethyl)adenosine: inhibitors of glycosomal GAPDH. ***Reagent***



A. Golisade, S. Van Calenbergh and A. Link, *Tetrahedron*, 2000, **56**, 3167.

8 examples (yields 70-97%, HPLC purity 85-98%). Solution-phase synthesis of the illustrated adenosine, prior to solid-phase amidation, is also reported (yield 97%).

Oxidation of alcohols by polymer-bound sodium ruthenate. ***Catalyst***

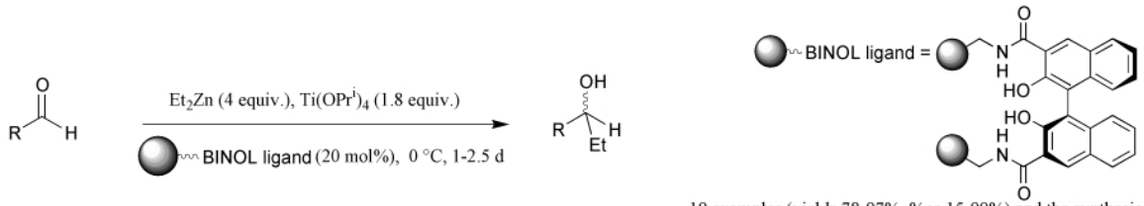


TBAP = tetrabutylammonium periodate

H. B. Friedrich and N. Singh, *Tetrahedron Lett.*, 2000, **41**, 3971.

9 examples (yields 0, 55-100%). The illustrated, recyclable, poly(4-vinylpyridine)-supported sodium ruthenate catalyst selectively oxidizes benzylic and allylic alcohols to their corresponding oxidation products.

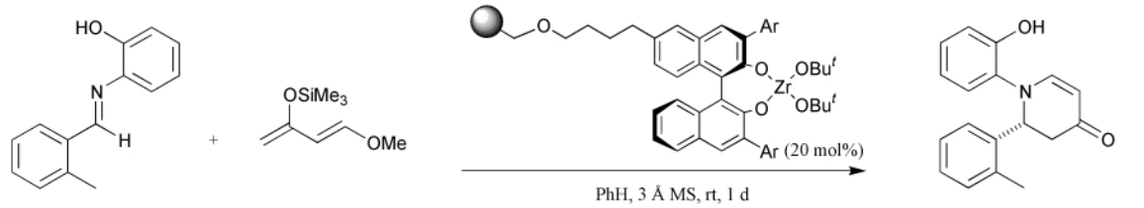
Titanium-BINOL complexes as chiral catalysts in the enantioselective addition of diethylzinc to aldehydes. ***Catalyst***



19 examples (yields 78-97%, %ee 15-99%) and the synthesis of the illustrated BINOL ligand, in 2 steps from aminomethyl polystyrene resin, is reported. 19 similar examples, using a BINOL ligand with a single polymer attachment and a solution-phase BINOL analogue, are reported (yields 82-95%, %ee 3-82%).

X. Yang, W. Su, D. Liu, H. Wang, J. Shen, C. Da, R. Wang and A. S. C. Chan, *Tetrahedron*, 2000, **56**, 3511.

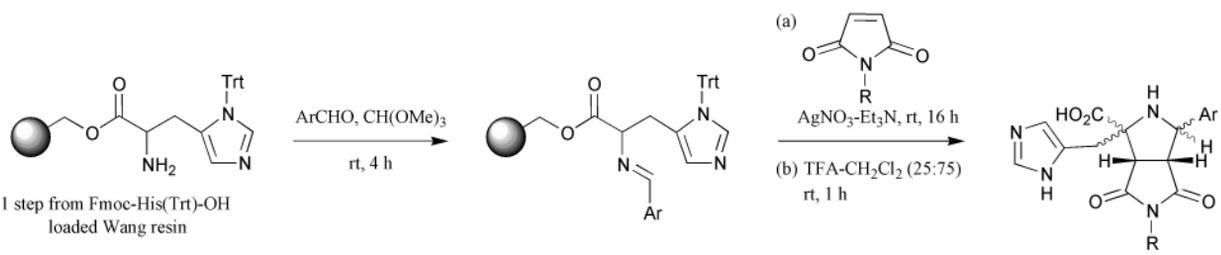
Piperidine derivatives *via* asymmetric aza Diels–Alder reactions. ***Catalyst***



17 examples of the illustrated asymmetric aza Diels–Alder reaction, with various Ar groups on the chiral catalyst, are reported (yields 58-92%, %ee 44-83%). 13 aza Diels–Alder reactions using a solution-phase catalyst are also reported (yields 61-93%, %ee 83-94%).

S. Kobayashi, K.-I. Kusakabe and H. Ishitani, *Org. Lett.*, 2000, **2**, 1225.

Proline analogues by azomethine cycloaddition.

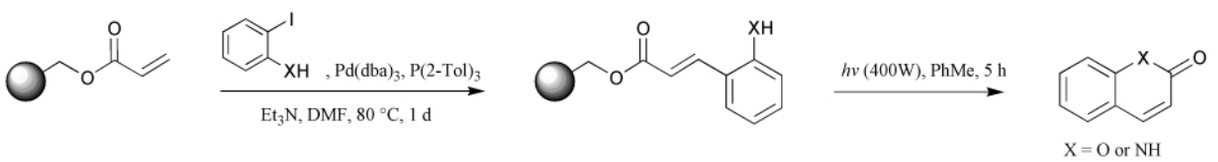


1 step from Fmoc-His(Trt)-OH loaded Wang resin

26 examples (yields 26-82%).

B. Henkel, W. Stenzel and T. Schotten, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 975.

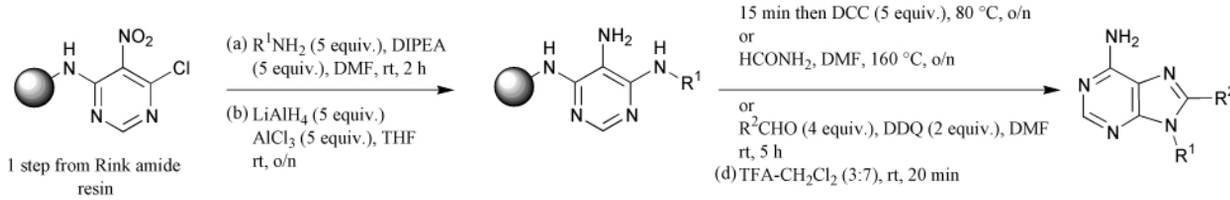
Photoinduced cyclorelease for condensed heteroaromatic synthesis.



2 examples (yields 62-66%). 1 example of a noncyclorelease type photoinduced cyclisation is also reported (yield 77%).

Y. Kondo, K. Inamoto and T. Sakamoto, *J. Comb. Chem.*, 2000, **2**, 232.

Purines from pyrimidines.

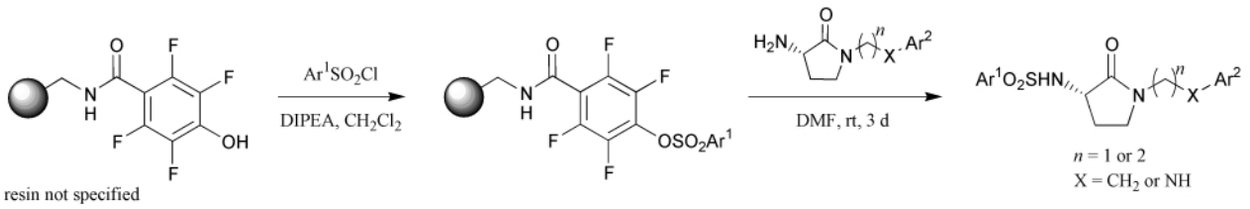


1 step from Rink amide resin

10 examples (yields 7-45%).

R. Di Lucrezia, I. H. Gilbert and C. D. Floyd, *J. Comb. Chem.*, 2000, **2**, 249.

Azarene pyrrolidinones: factor Xa inhibitors.

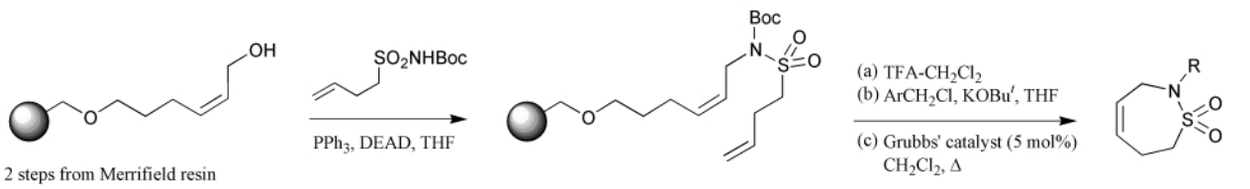


resin not specified

Y. Gong, M. Becker, Y. M. Choi-Sledeski, R. S. Davis, J. M. Salvino, V. Chu, K. D. Brown and H. W. Pauls, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1033.

Synthesis and biological activity of 56 pyrrolidinones are reported (yields 23-99%, ELSD purity 27-99%).

Cyclic sulfonamides *via* a ring-closing metathesis-cleavage strategy.

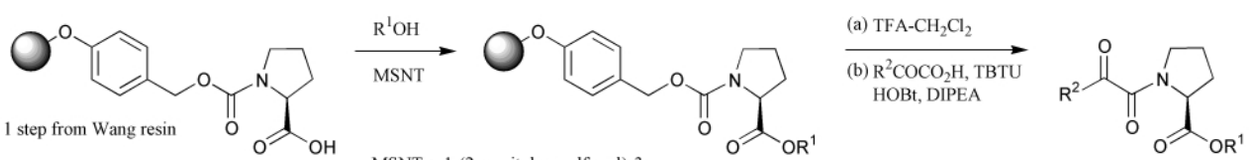


2 steps from Merrifield resin

R. C. D. Brown, J. L. Castro and J.-D. Moriggi, *Tetrahedron Lett.*, 2000, **41**, 3681.

3 examples (yields 49-59%).

Neuroimmunophilin ligands.



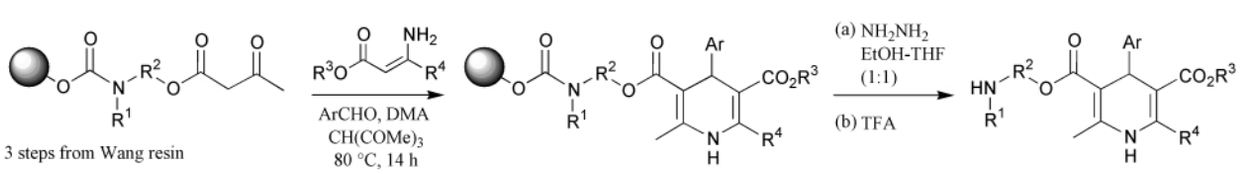
1 step from Wang resin

MSNT = 1-(2-mesitylenesulfonyl)-3-nitro-1,2,4-triazole

M. Rabinowitz, P. Seneci, T. Rossi, M. Dal Cin, M. Deal and G. Terstappen, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1007.

18 examples from an 880-member library are reported (yields 12-70%, HPLC purity 35-92%).

4-Aryl-1,4-dihydropyridines *via* the Hantzsch three component condensation.

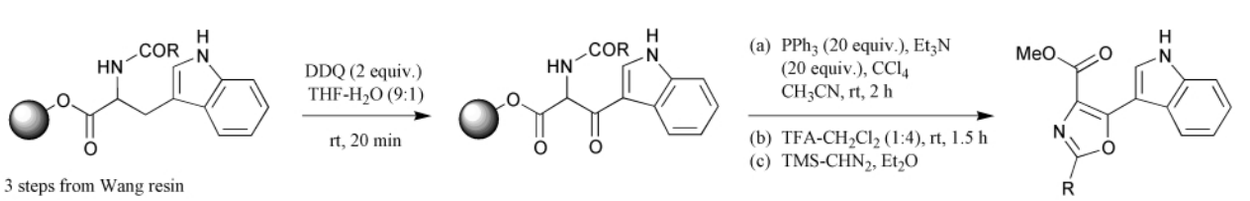


3 steps from Wang resin

Preparation of a 192-member library is reported (44-88%, HPLC purity 57-90%). Elaboration of the illustrated polymer-bound dihydropyridines generates an additional 80-member library (yields 41-60%, HPLC purity 51-59%).

J. G. Breitenbucher and G. Figliozzi, *Tetrahedron Lett.*, 2000, **41**, 4311.

5-(Indol-3-yl)oxazoles.

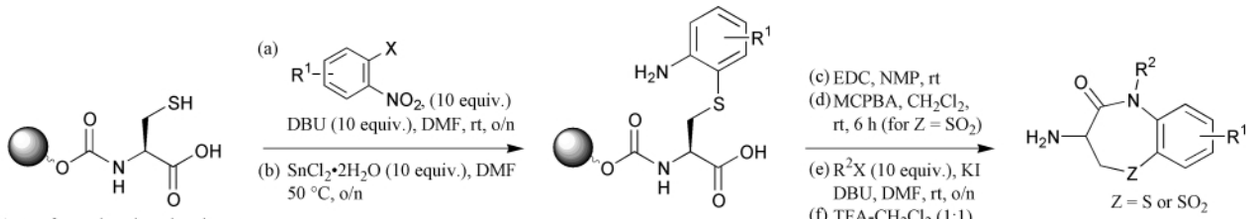


3 steps from Wang resin

A. Nishida, M. Fuwa, S. Naruto, Y. Sugano, H. Saito and M. Nakagawa, *Tetrahedron Lett.*, 2000, **41**, 4791.

8 examples (yields 9-42%).

1,5-Benzothiazepin-4-one derivatives.

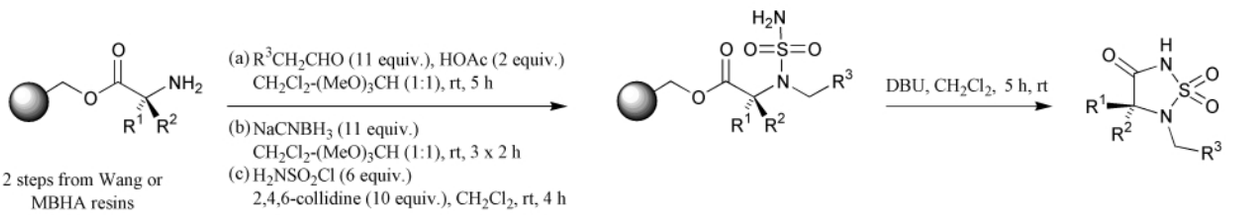


1 step from nitrophenyl carbonate Wang resin

G. C. Morton, J. M. Salvino, R. F. Labaudinière and T. F. Herpin, *Tetrahedron Lett.*, 2000, **41**, 3029.

18 examples (yields 49-78%, HPLC purity 67-100%).

Sulfahydantoins.

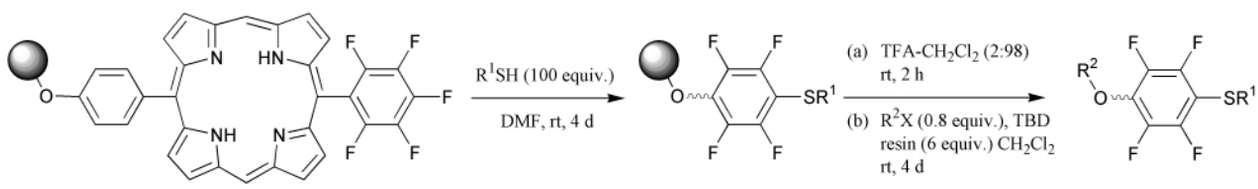


2 steps from Wang or MBHA resins

F. Albericio, J. Garcia, E. L. Michelotti, E. Nicolás and C. M. Tice, *Tetrahedron Lett.*, 2000, **41**, 3161.

11 examples (yields 7-31%, HPLC purity 60-100%).

Unsymmetrically substituted 5,15-diphenylporphyrins.



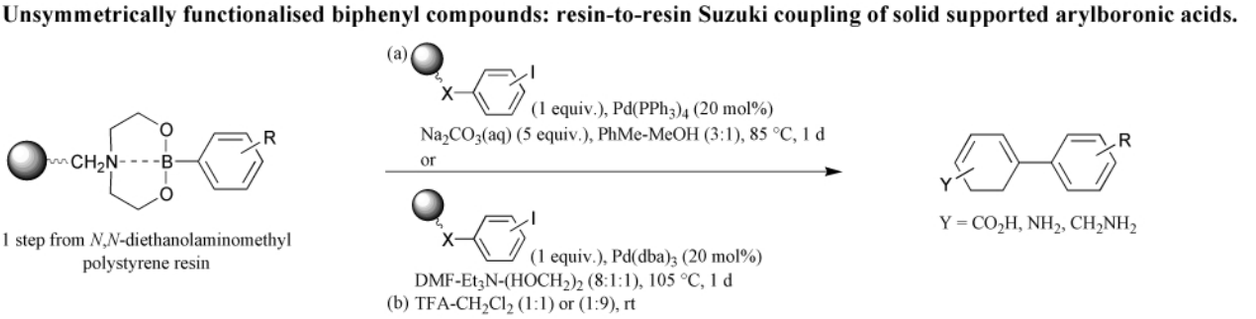
1 step from 2-chlorotrityl chloride resin

TBD = 1,5,7-triazabicyclo[4.4.0]dec-5-ene

28 examples (HPLC purity 43-96%). Solution-phase diversification of the illustrated porphyrin, after cleavage from the resin, is also reported (3 examples 47-87%).

K. J. Elgie, M. Scobie and R. W. Boyle, *Tetrahedron Lett.*, 2000, **41**, 2753.

Unsymmetrically functionalised biphenyl compounds: resin-to-resin Suzuki coupling of solid supported arylboronic acids.

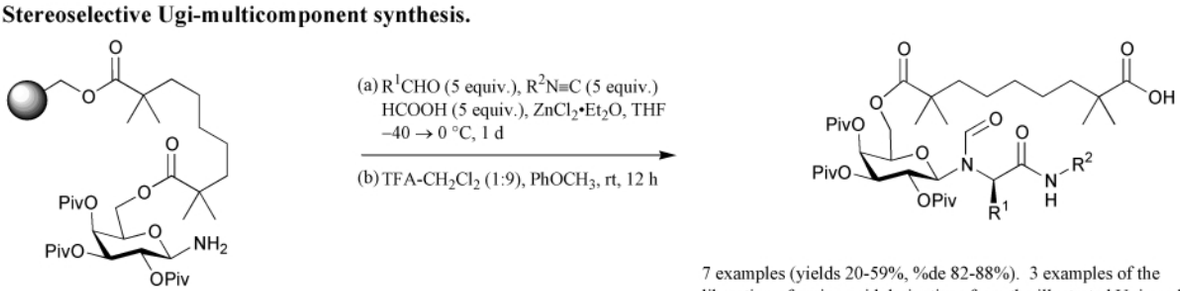


1 step from *N*,*N*-diethanolaminomethyl polystyrene resin

M. Gravel, C. D. Bérubé and D. G. Hall, *J. Comb. Chem.*, 2000, **2**, 228.

10 examples (yields 55-100%, NMR purity >90%).

Stereoselective Ugi-multicomponent synthesis.

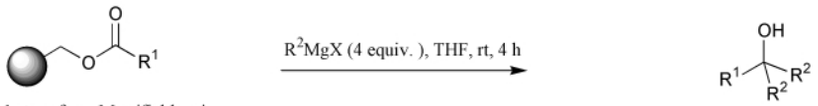


2 steps from Wang resin

K. Oertel, G. Zech and H. Kunz, *Angew. Chem., Int. Ed.*, 2000, **39**, 1431.

7 examples (yields 20-59%, %de 82-88%). 3 examples of the liberation of amino acid derivatives from the illustrated Ugi product, by removal of the formyl group and cleavage of the *N*-glycosidic bond both in solution and from Merrifield resin, are also reported.

Tertiary alcohols from the addition of Grignard reagents to polymer-bound esters.

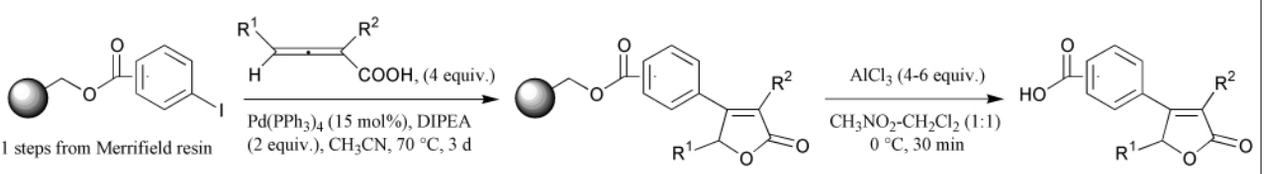


1 steps from Merrifield resin

S. Chandrasekhar, M. B. Padmaja and A. Raza, *J. Comb. Chem.*, 2000, **2**, 246.

20 examples (yields 65-90%).

Butenolides.

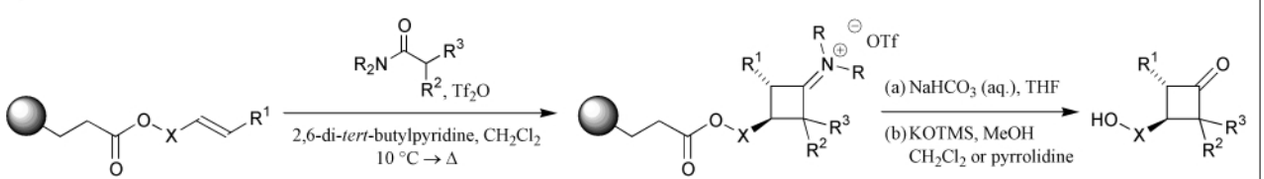


1 steps from Merrifield resin

S. Ma, D. Duan and Z. Shi, *Org. Lett.*, 2000, **2**, 1419.

6 examples (yields 84-100%, HPLC purity 85-96%). Butenolide synthesis *via* a similar route, using phenolic and benzylic ether linkers and a different cleavage method, are also reported (5 examples, yields 75-89%, HPLC purity 76-94%).

Cyclobutanone derivatives.

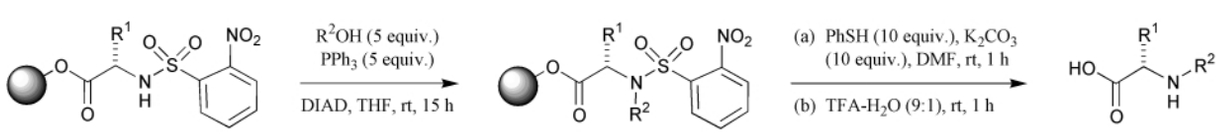


3 steps from Merrifield resin

R. C. D. Brown, J. Keily and R. Karim, *Tetrahedron Lett.*, 2000, **41**, 3247.

2 examples (yields 38-96%). Synthesis of cyclobutylamines, cyclobutanols γ-lactams and a γ-lactone from the illustrated polymer-bound cyclobutanone iminium species is also reported (13 examples, yields 57-97%).

***N*-substituted α-amino acid derivatives using Fukuyama's sulfonamide protecting group.**

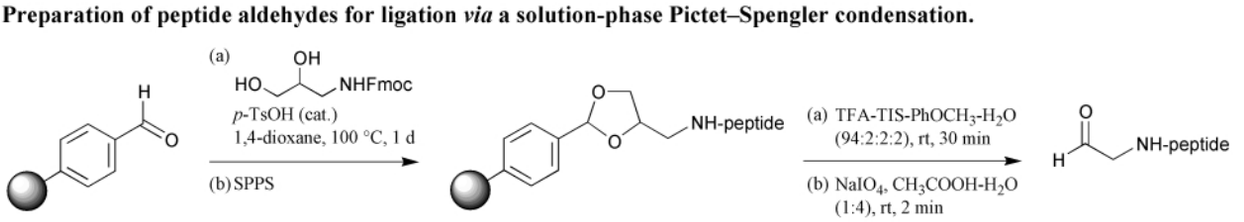


3 steps from Wang resin

X. Lin, H. Dorr and J. M. Nuss, *Tetrahedron Lett.*, 2000, **41**, 3309.

7 examples (yields 85-96%, HPLC purity 88-99%). 10 examples of cleavage before desulfonylation (yields 89-99%, HPLC purity 90-99%) and 2 examples of trisubstituted dihydropiperazine synthesis *via* a similar route are also reported (yields 70-92%, HPLC purity 91-95%).

Preparation of peptide aldehydes for ligation *via* a solution-phase Pictet–Spengler condensation.



benzaldehyde polystyrene resin

X. Li, L. Zhang, S. E. Hall and J. P. Tam, *Tetrahedron Lett.*, 2000, **41**, 4069.

Ligation of 2 peptide aldehyde fragments, prepared on the solid support (yields 95%), using the solution-phase Pictet–Spengler reaction is reported.