Perkin 1 Abstracts: Solid Phase Organic Synthesis

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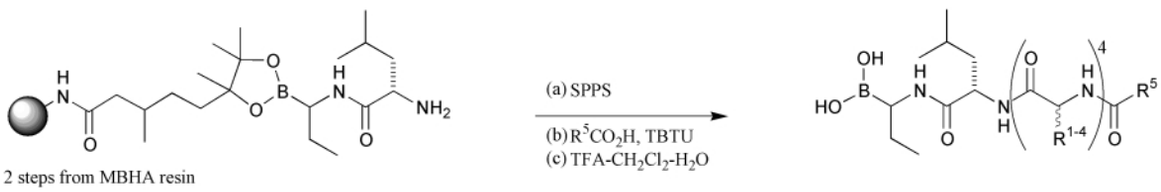
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

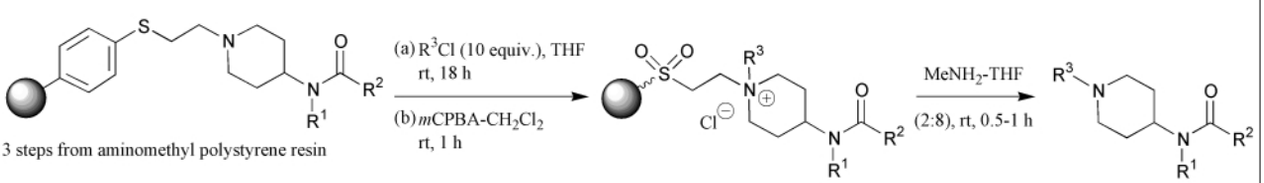
Aminoboronic acids: potent inhibitors of the Hepatitis C virus NS3 proteinase. ***Linker***



R. M. Dunsdon, J. R. Greening, P. S. Jones, S. Jordan and F. X. Wilson, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1577.

Use of a polymer-bound diol as a boronic acid protecting group has been developed to allow parallel synthesis of the illustrated library (number of examples and yields not given, LC-MS purity >80%).

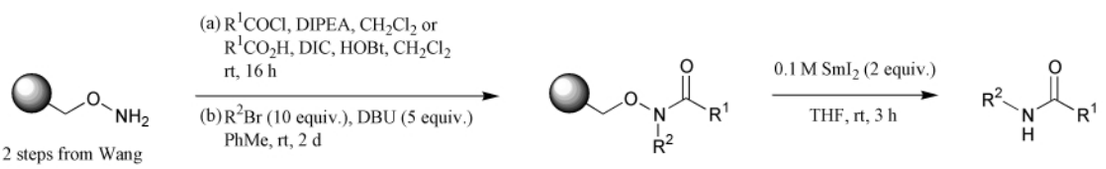
A base-cleavable sulfide safety catch linker. ***Linker***



W. S. Wade, F. Yang and T. J. Sowin, *J. Comb. Chem.*, 2000, **2**, 266.

13 examples (yields 8-41%).

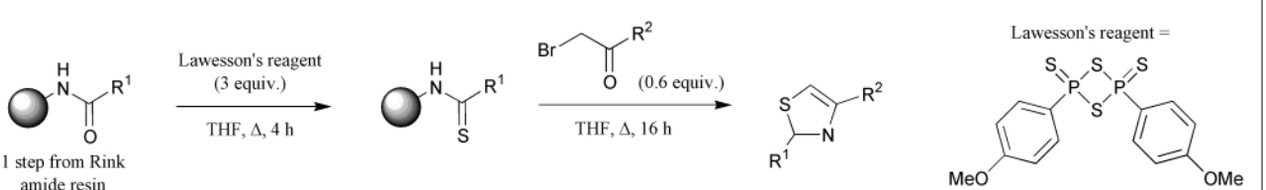
Reductive cleavage of N–O bonds using samarium(II) iodide in a traceless release strategy. ***Linker***



R. M. Myers, S. P. Langston, S. P. Conway and C. Abell, *Org. Lett.*, 2000, **2**, 1349.

8 examples (yields 30-54%, HPLC purity 46-99%)

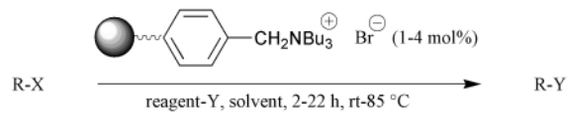
Thiazole formation *via* traceless cleavage from Rink resin. ***Linker***



J.-F. Pons, Q. Mishir, A. Nouvet and F. Brookfield, *Tetrahedron Lett.*, 2000, **41**, 4965.

15 examples (HPLC purity 63-99%). Use of α-chloroketones in the same route is also described (2 examples, HPLC purity 20-100%).

A polymer-supported quaternary ammonium salt: a recyclable phase-transfer catalyst. ***Catalyst***

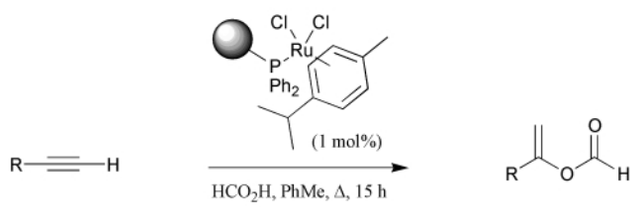


X = Br, OH or NH
Y= I, CN, OBn, or *N*-Bn

R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi and G. Tocco, *Org. Lett.*, 2000, **2**, 1737.

15 examples (yields 18-97%).
Synthesis of the illustrated catalyst in 3 steps from MeOPEG resin is also reported.

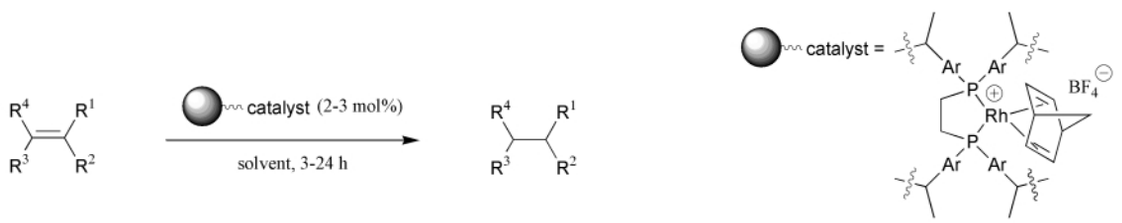
Polymer-supported arene-ruthenium complex: enol formate synthesis and olefin cyclopropanation. ***Catalyst***



N. E. Leadbeater, K. A. Scott and L. J. Scott, *J. Org. Chem.*, 2000, **65**, 3231.

2 examples (yields 76-95%) and 3 examples of enol formate synthesis using terminal diynes are reported (yields 76-83%). Synthesis of the illustrated, reusable catalyst and its use in 3 cyclopropanation reactions is also reported (yields 68-80%).

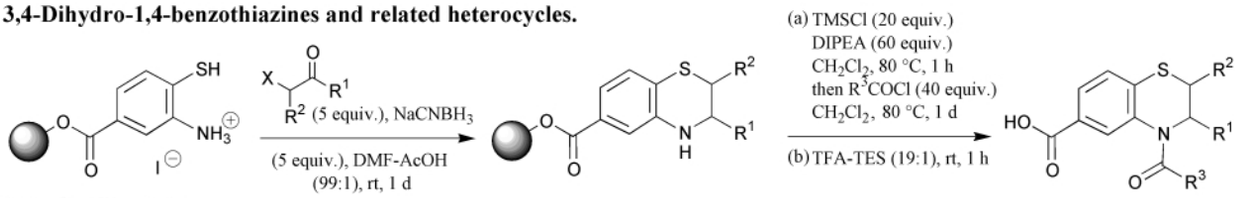
Alkene hydrogenation and hydroboration using a polymer-supported rhodium catalyst. ***Catalyst***



R. A. Taylor, B. P. Santora and M. R. Gagné, *Org. Lett.*, 2000, **2**, 1781.

7 examples (yields 88-99%). 1 example of the hydroboration of styrene using the illustrated catalyst (yield 85%) and synthesis of the catalyst from ethylene glycol dimethacrylate is also reported.

3,4-Dihydro-1,4-benzothiazines and related heterocycles.

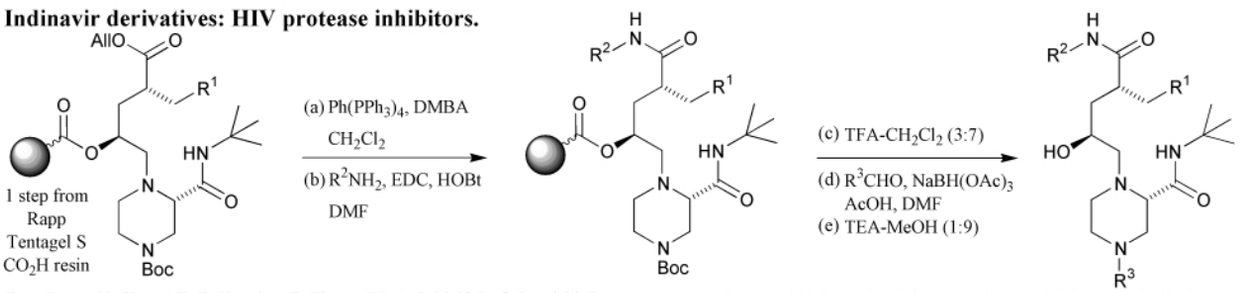


4 steps from Wang resin

T. S. Yokum, J. Alsina and G. Barany, *J. Comb. Chem.*, 2000, **2**, 282.

15 examples (yields 40-70%, HPLC purity 65-96%). Benzothiazoles, 3,4-dihydro-1,4-benzothiazine 1,1-dioxides, 3,4-dihydro-3-oxo-1,4-benzothiazines, 3,4-dihydro-3-oxo-1,4-benzothiazine 1,1-dioxides were also synthesised *via* similar routes (24 examples, yields 48-72%, HPLC purity 83-95%).

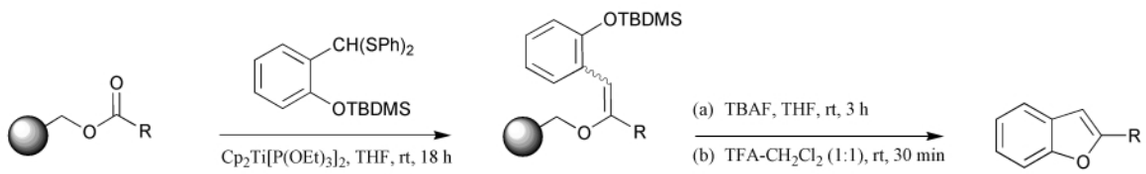
Indinavir derivatives: HIV protease inhibitors.



T. A. Rano, Y. Cheng, T. T. Huening, F. Zhang, W. A. Schleif, L. Gabryelski, D. B. Olsen, L. C. Kuo, J. H. Lin, X. Xu, T. V. Olah, D. A. Mcloughlin, R. King, K. T. Chapman and J. R. Tata, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1527.

Synthesis and biological activity of the illustrated library and 2 further "indinavir-based" libraries using similar chemistry is reported (number of examples, yields and purities not given).

Traceless synthesis of 2-substituted benzofurans *via* alkylidenation of esters.

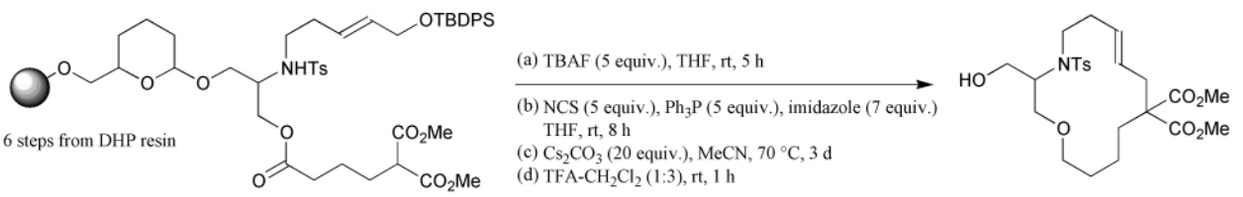


1 step from Wang resin

E. J. Guthrie, J. Macritchie and R. C. Hartley, *Tetrahedron Lett.*, 2000, **41**, 4987.

4 examples (yields 38-83%). Cleavage of the illustrated polymer-bound enol ethers yielding ketones is also reported (4 examples, yields 65-79%).

14-Member macro-heterocycles

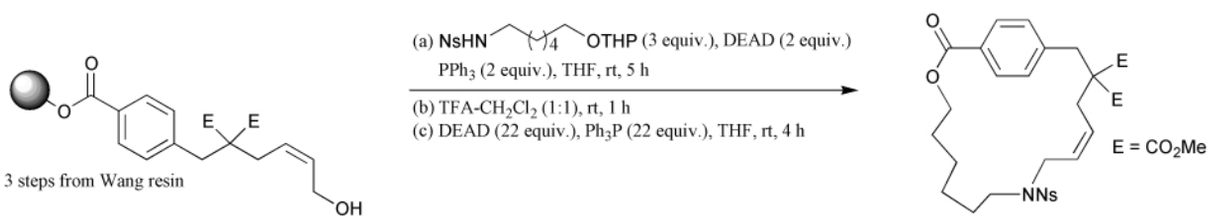


6 steps from DHP resin

M. Ramaseshan, J. W. Ellingboe, Y. L. Dory and P. Deslongchamps, *Tetrahedron Lett.*, 2000, **41**, 4743.

1 example (yield 8%). Synthesis of a 14-member cyclic ester is also reported (yield 45%).

Macrolactones

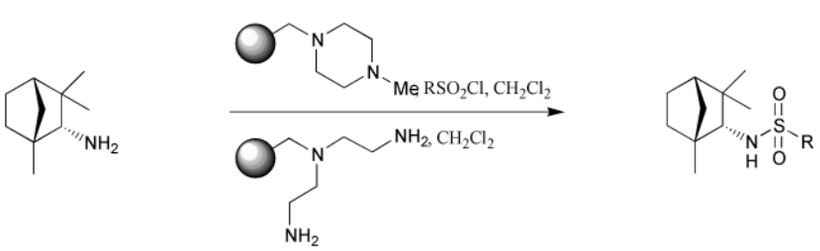


3 steps from Wang resin

R. Gagnon, Y. L. Dory and P. Deslongchamps, *Tetrahedron Lett.*, 2000, **41**, 4751.

1 example (yield 28%) and 1 other similar example (yield 45%) is reported.

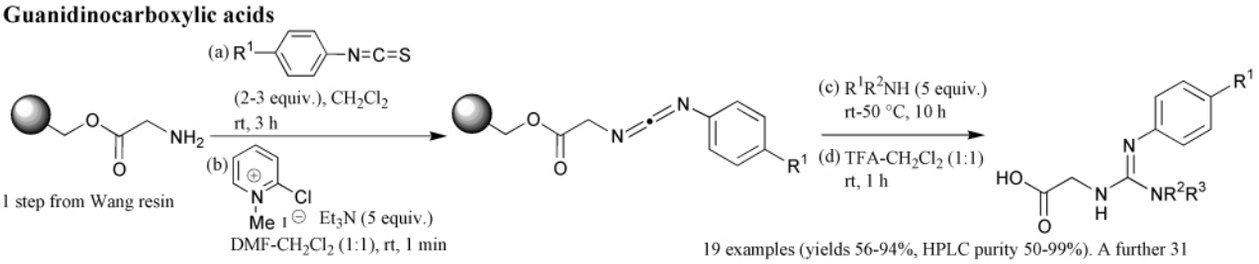
Synthesis of fenchylamine sulfonamide (inhibitors of amyloid β-peptide production) using polymer-supported reagents.



G. M. Rishton, D. M. Retz, P. A. Tempest, J. Novotny, S. Kahn, J. J. S. Treanor, J. D. Lile and M. Citron, *J. Med. Chem.*, 2000, **43**, 2297.

Synthesis and biological activity of >100-member library is reported (no yields or purities given).

Guanidinocarboxylic acids

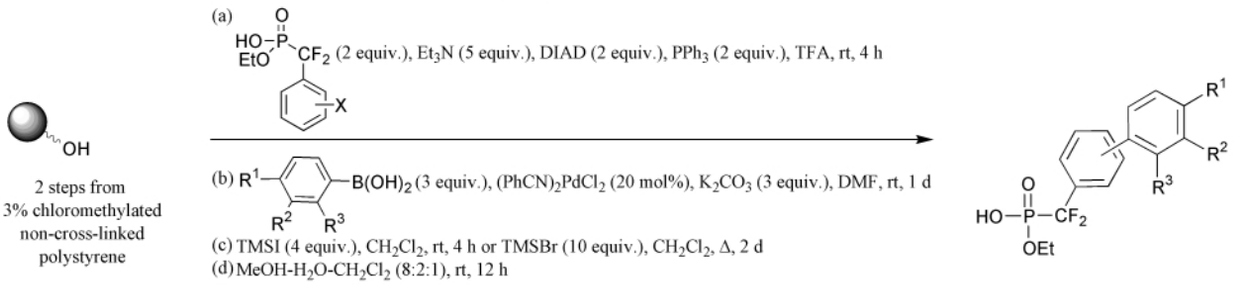


1 step from Wang resin

J. Chen, M. Pattarawarapan, A. J. Zhang and K. Burgess, *J. Comb. Chem.*, 2000, **2**, 276.

19 examples (yields 56-94%, HPLC purity 50-99%). A further 31 guanidinocarboxylic acids are prepared *via* a similar route (yields 53-96%, HPLC purity 53-99%) and solution-phase synthesis of 6 dimeric and 2 trimeric guanidinoacetic acid derivatives is also reported (yields 16-92%, HPLC purity 60-95%).

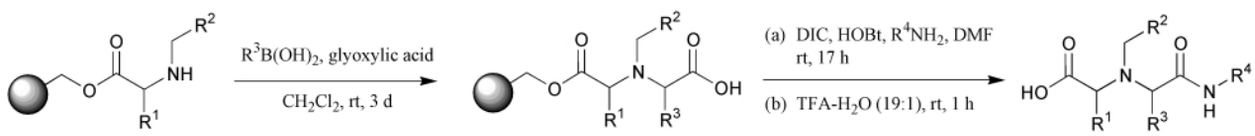
Liquid-phase synthesis of α,α-difluoromethylenephosphonic acids.



G. Hum, J. Grzyb and S. D. Taylor, *J. Comb. Chem.*, 2000, **2**, 234.

28 examples (yields 43-90%, HPLC purity 91-99%).

Peptide mimetics *via* a Petasis reaction.

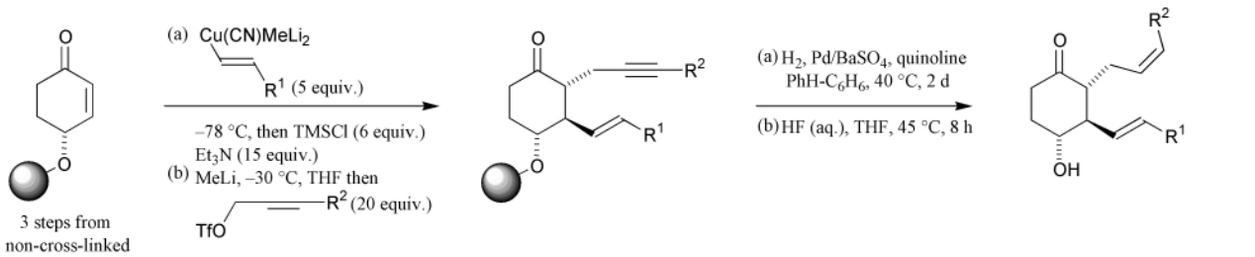


2 steps from Fmoc-Gly loaded Wang resin

S. R. Klopfenstein, J. J. Chen, A. Golebiowski, M. Li, S. X. Peng and X. Shao, *Tetrahedron Lett.*, **41**, 4835.

Preparation of a 96-member library is reported (yields 35-91%, LC-MS purity 57-88%).

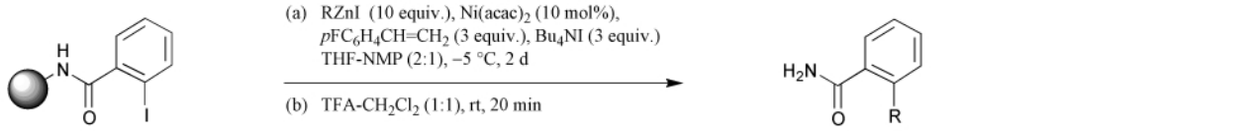
Liquid-phase synthesis of six-member ring prostanoids.



J. A. López-Pelegrin and K. D. Janda, *Chem. Eur. J.*, 2000, **6**, 1917.

5 examples (yields 76-88%).

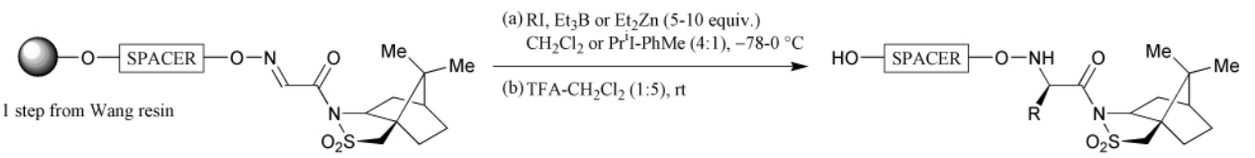
Nickel-catalysed cross-coupling reactions between substituted aryl iodides and alkylzinc iodides.



A. E. Jensen, W. Dohle and P. Knochel, *Tetrahedron*, 2000, **56**, 4197.

4 examples (HPLC purity 89–94%). 6 similar solution-phase examples are also reported (yields 70-84%).

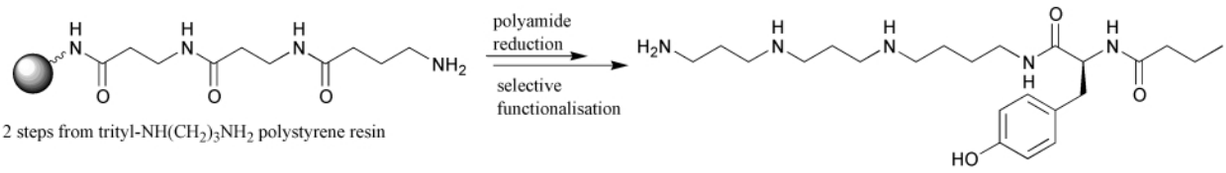
Stereoselective radical addition to oxime ethers.



H. Miyabe, C. Konishi and T. Naito, *Org. Lett.*, 2000, **2**, 1443.

5 examples (yields 41-74%, %de 90-95%).

Polyamine toxins HO-416b and PhTX-433: a reduction strategy that facilitates access to branched analogues.

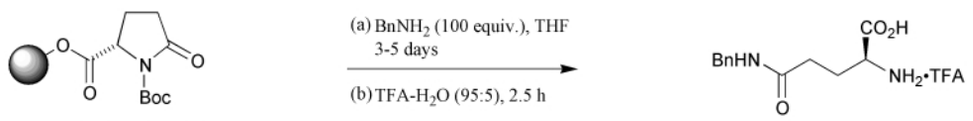


2 steps from trityl-NH(CH$_2$)$_3$NH$_2$ polystyrene resin

Synthesis of the illustrated PhTX-433 toxin is reported (yield 55%, HPLC purity >90%). Preparation of HO-416b toxin and a structural isomer of the illustrated polyamine, *via* similar methods, is also reported (yields 37-75%, HPLC purity 88-90%).

F. Wang, S. Manku and D. G. Hall, *Org. Lett.*, 2000, **2**, 1581.

Glutamic acid derivatives.

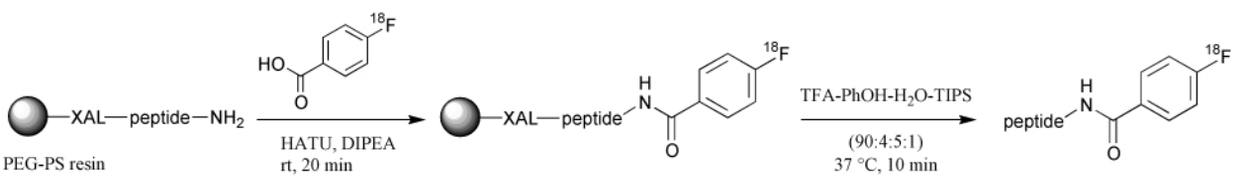


2 steps from Wang resin

Preparation of a 42-member library is reported (yields 30-98%, ^{1}H NMR purity >95%). 14 similar examples of nucleophilic ring opening using benzyl alcohol derivatives, amino alcohols and a benzyl thiol are also reported (yields 12-100%).

J. de Blas, E. Domínguez and J. Ezquerra, *Tetrahedron Lett.*, 2000, **41**, 4567.

^{18}F Labelled peptides for positron emission tomography.



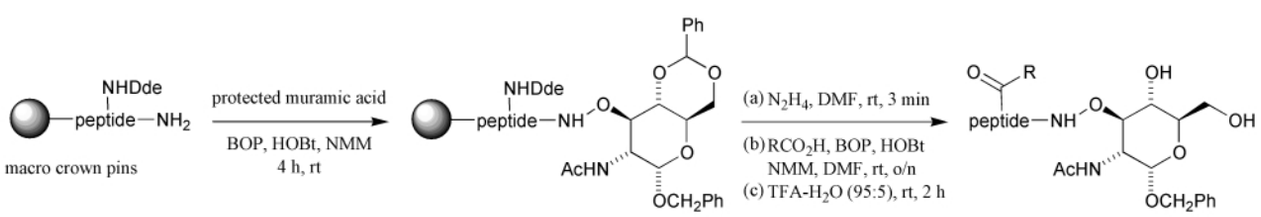
PEG-PS resin

XAL = xanthen-2-oxovalerate linker

J. L. Sutcliffe-Goulden, M. J. O'Doherty and S. S. Bansal, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1501.

1 example (yield 80%, HPLC purity >95%).

Synthesis of muramyl dipeptide derivatives using multipin method.

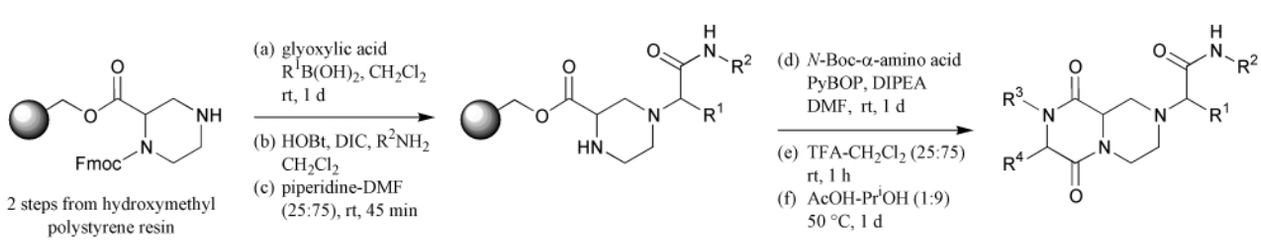


macro crown pins

G. Liu, S.-D. Zhang, S.-Q. Xia and Z.-K. Ding, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1361.

Preparation of a 60-member library is reported (purity >75%).

β-Turn mimetics *via* a Petasis reaction/diketopiperazine formation.



2 steps from hydroxymethyl polystyrene resin

A. Golebiowski, S. R. Klopfenstein, J. J. Chen and X. Shao, *Tetrahedron Lett.*, 2000, **41**, 4841.

Preparation of the illustrated library is reported (representative yields 56-96%, LCMS purity 70-88%).