Perkin 1 Abstracts: Solid Phase Organic Synthesis

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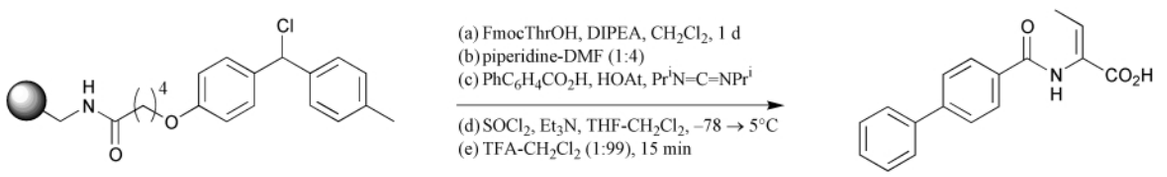
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

4-[4-Methylphenyl(chloro)methyl]phenoxy linker: synthesis of pseudopeptides. ***Linker***

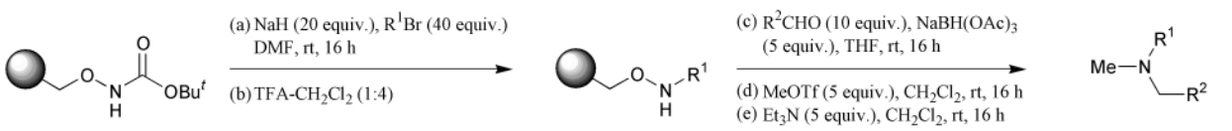


1 step from aminomethyl polystyrene resin

1 example (yield 96%, HPLC purity 75%). The utility of the linker was also demonstrated in the synthesis of 1 *N*,*O*-protected nonapeptide, 2 *N*-acyl amino acid derivatives, 2 protected pseudopeptides, 4 sulfonamide amino acid derivatives, 2 hydroxamic acid derivatives and 1 biaryl amino acid derivative.

G. E. Atkinson, P. M. Fischer and W. C. Chan, *J. Org. Chem.*, 2000, **65**, 5048.

Tertiary methylamines *via* reductive alkylation-fragmentation using a hydroxylamine linker. ***Linker***

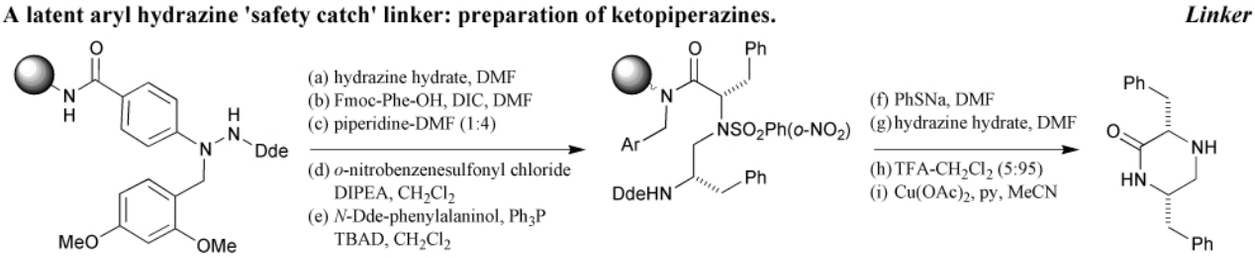


3 steps form hydroxymethyl polystyrene resin

15 examples (yields 34-80%, LCMS purity >99%). Details of the robustness of the linker, when subjected to strong organometallic reagents and strong acidic conditions, are also reported.

P. Blaney, R. Grigg, Z. Rankovic and M. Thoroughgood, *Tetrahedron Lett.*, 2000, **41**, 6635.

A latent aryl hydrazine 'safety catch' linker: preparation of ketopiperazines. ***Linker***



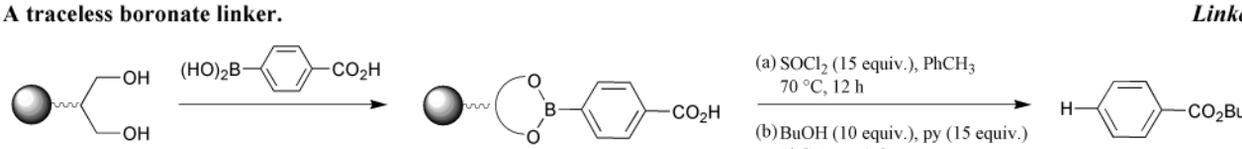
1 step from AgroGel resin

TBAD = di-*tert*-butyl azodicarboxylate

1 example and 3 other examples of ketopiperazine formation *via* similar routes (yields 34-76%, NMR purity 75->95%).

F. Berst, A. B. Holmes, M. Ladlow and P. J. Murray, *Tetrahedron Lett.*, 2000, **41**, 6649.

A traceless boronate linker. ***Linker***

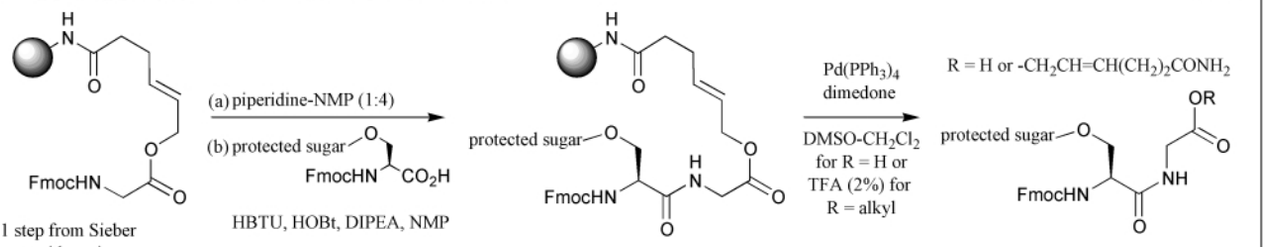


resin not specified

The utility of the boronate linker was demonstrated in the synthesis of the illustrated aryl ester and an aryl sulfonamide (yields 45-56%, purity 80->90%). The illustrated resin is also used to capture organoboron products from reaction mixtures (3 examples, yields 57-75%, purity >90%->95%).

C. Pourbaix, F. Carreaux, B. Carboni and H. Deleuze, *Chem. Commun.*, 2000, 1275.

Serglycin glycopeptides on a new allyl ester linker. ***Linker***

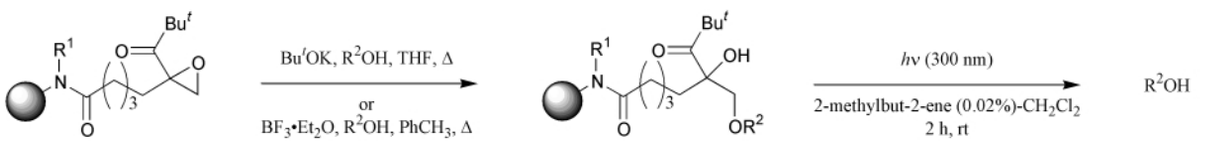


1 step from Sieber amide resin

1 example (yield 100%). Preparation of 6 serglycin glycopeptides, up to a hexadecapeptide, using similar chemistry is also reported (yields 66-100%).

Y. Nakahara, S. Ando, M. Itakura, N. Kumabe, H. Hojo, Y. Ito and Y. Nakahara, *Tetrahedron Lett.*, 2000, **41**, 6489.

A new photocleavable linker for ether cleavage. ***Linker***

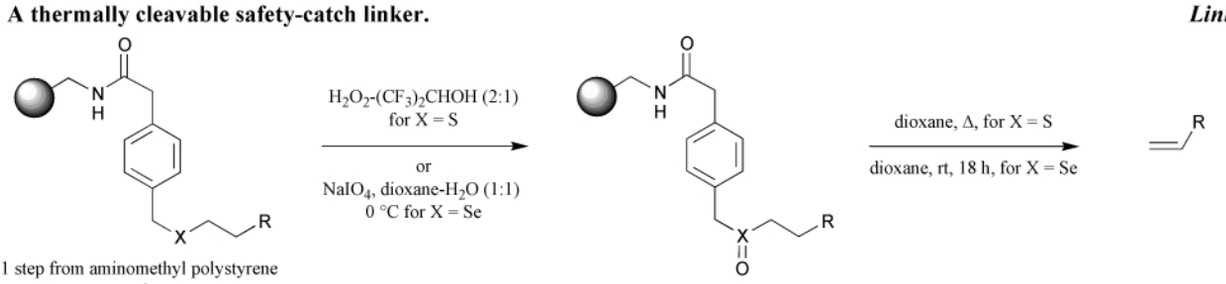


1 step from Tenta Gel S-NH_2 or PS-NHMe resin

3 examples (yields 61-78%). Synthesis of the linker, optimisation of the photolytic cleavage step and stability of the linker towards different reagents is also reported.

R. Glatthar and B. Giese, *Org. Lett.*, 2000, **15**, 2315.

A thermally cleavable safety-catch linker. ***Linker***

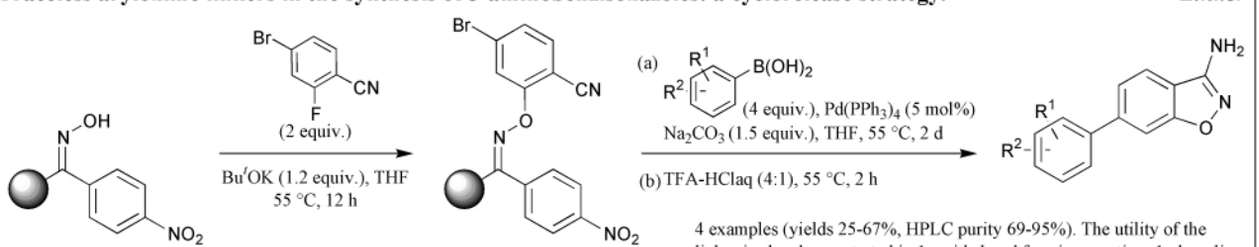


1 step from aminomethyl polystyrene resin

3 examples (yields 31-45%, HPLC purity >95-96%). Synthesis of the linker is also reported.

H. E. Russel, R. W. A. Luke and M. Bradley, *Tetrahedron Lett.*, 2000, **41**, 5287.

Traceless aryloxime linkers in the synthesis of 3-aminobenzisoxazoles: a cyclorelease strategy. ***Linker***

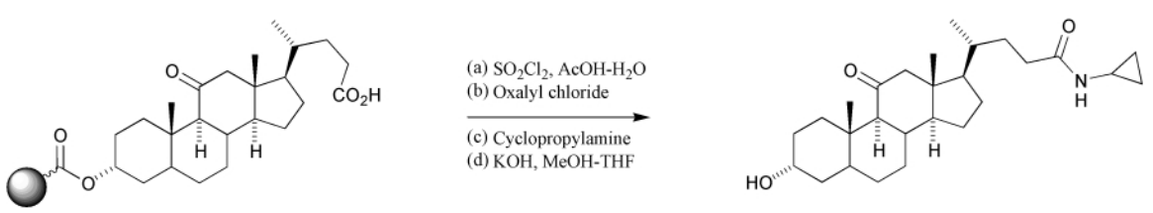


Kaiser-oxime resin

4 examples (yields 25-67%, HPLC purity 69-95%). The utility of the linker is also demonstrated in 1 amide bond forming reaction, 1 phenolic Mitsunobu reaction, 3 nucleophilic aromatic substitution reactions, 1 Sonogashira and 1 Horner–Emmons olefination reaction (yields 25-81%, HPLC purity 83->96%).

S. D. Lepore and M. R. Wiley, *J. Org. Chem.*, 2000, **65**, 2924.

Xanthate transfer technology for the formation of a soluble support: steroid transformations. ***Support***

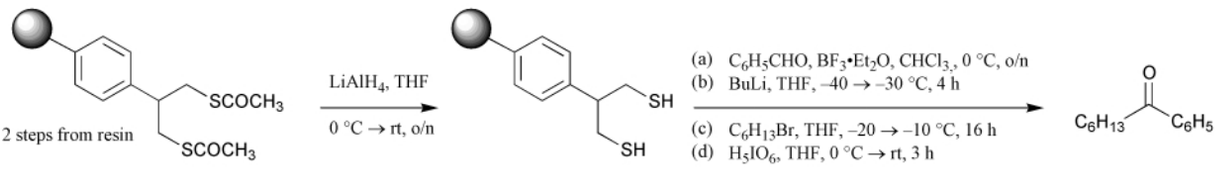


A xanthate resin

1 example (yields 62%). Synthesis of the illustrated resin and attachment of 5 complex structures to the resin are also reported.

B. Quiclet-Sire, A. Wilczewaka and S. Z. Zard, *Tetrahedron Lett.*, 2000, **41**, 5673.

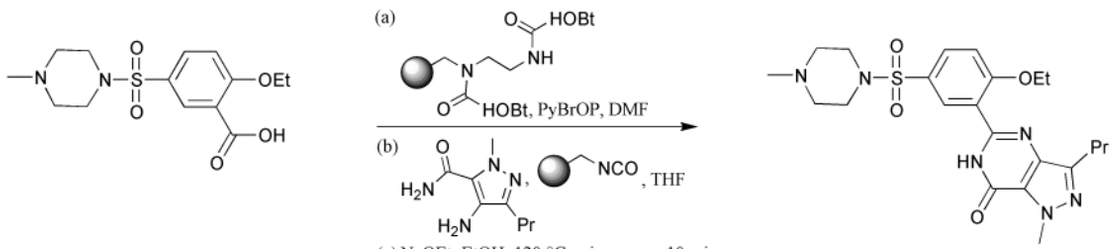
Soluble and odorless polymer-supported propane-1,3-dithiol reagents. ***Reagent***



V. Bertini, F. Lucchesini, M. Pocci and A. De Munno, *J. Org. Chem*., 2000, **65**, 4839.

6 examples of the illustrated transformation using 6 different dithiol resins, made by the copolymerisation of styrene and a sulfone monomer, are reported (yields 74-79%).

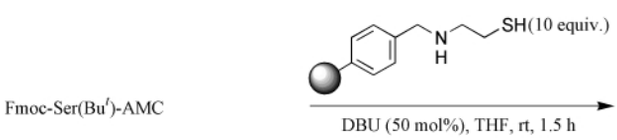
Polymer-supported reagents for the synthesis of Sildenafil (Viagra). ***Reagent***



I. R. Baxendale and S. V. Ley, *Bioorg. Med. Chem. Lett*., 2000, **10**, 1983.

Yield (100%).

A dibenzofulvene scavenger for use in Fmoc deprotections. ***Scavenger***

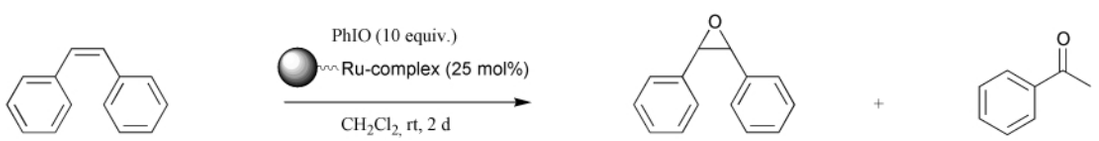


AMC = 7-amino-4-methylcoumarin

J. E. Sheppeck II, H. Kar and H. Hong, *Tetrahedron Lett.*, 2000, **41**, 5329.

1 example (yield 90%, purity 100%). Regeneration of the scavenger resin using piperidine and solution-phase Fmoc deprotection using DBU/octanethiol is also reported.

Optimisation of variables for screening polymer-supported metal complexes as oxidation catalysts. ***Catalyst***



A. Natarajan and J. Madalengoitia, *Tetrahedron Lett*., 2000, **41**, 5783.

Optimised conditions for the oxidation of stilbene are reported.

4-Substituted imidazoles.

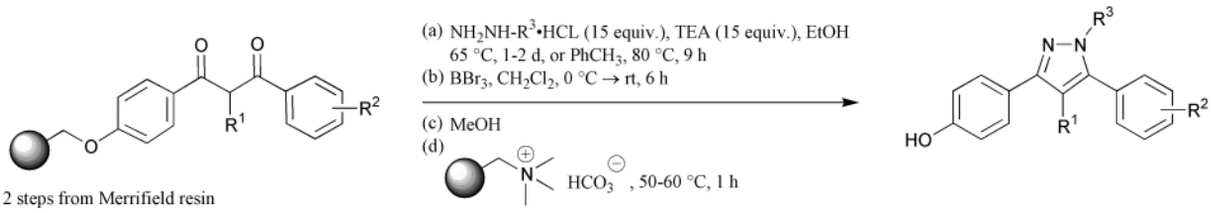
1 step from 2-chlorotrityl chloride resin

X = H, OH, O or S

E. Gelens, W. J. Koot, W. M. P. B. Menge, H. C. J. Ottenheijm and H. Timmerman, *Bioorg. Med. Chem. Lett*., 2000, **10**, 1935.

31 examples (yields 21-100%, ^{1}H NMR purity 10-86%).

Tetrasubstituted pyrazoles: novel ligands for the estrogen receptor.

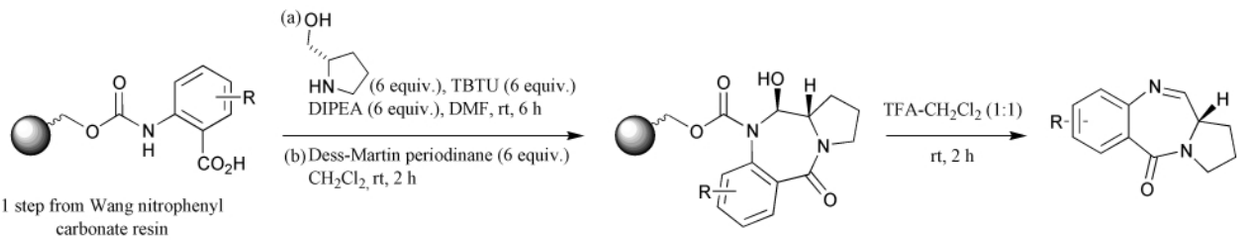


2 steps from Merrifield resin

S. R. Stauffer and J. A. Katzenellenbogen, *J. Comb. Chem.*, 2000, **2**, 318.

12 examples from a 96-member library are reported (HPLC purity 23-99%).

Pyrrolo[2,1-*c*][1,4]benzodiazepines: DNA-interactive, antibiotic antitumour agents.

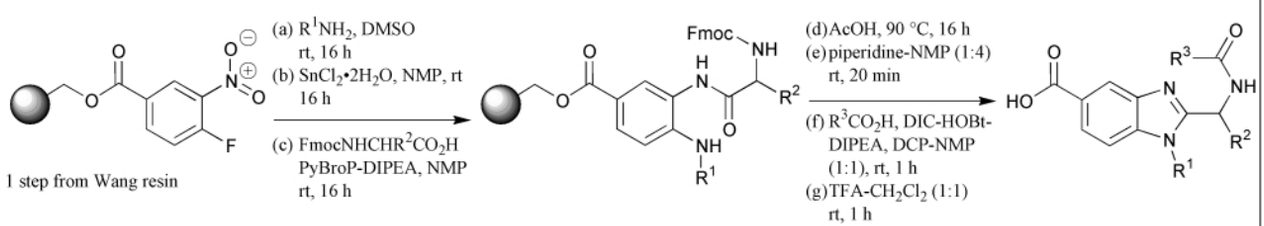


1 step from Wang nitrophenyl carbonate resin

J. M. Berry, P. W. Howard and D. E. Thurston, *Tetrahedron Lett.*, 2000, **41**, 6171.

5 examples (yields 37-68%).

Substituted 2-aminomethylbenzimidazoles.



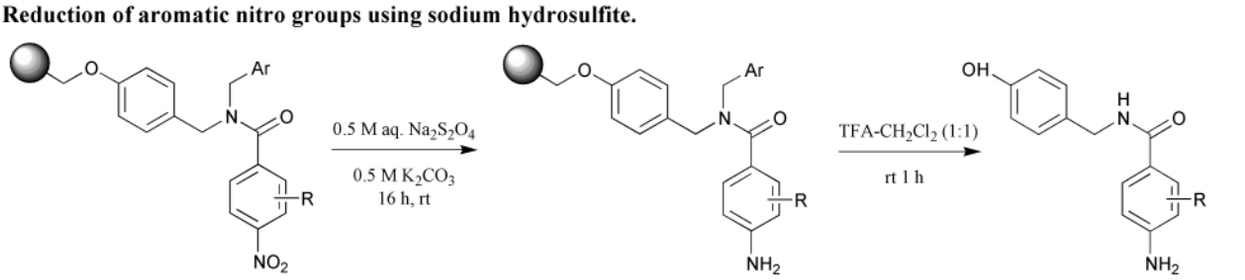
1 step from Wang resin

DCP = 1,2-dichloropropane

J. P. Kilburn, J. Lau and R. C. F. Jones, *Tetrahedron Lett.*, 2000, **41**, 5419.

6 examples (yield 36-86%, ELS purity 70-99%).

Reduction of aromatic nitro groups using sodium hydrosulfite.

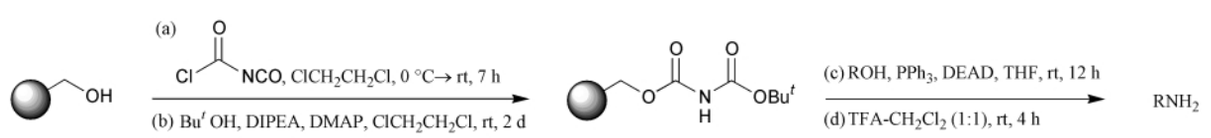


3 steps from tentagel MB PHB resin

R. A. Scheuerman and D. Tumelty, *Tetrahedron Lett.*, 2000, **41**, 6531.

74 examples (HPLC purity 100%). 1 example of nitro reduction on a Rink polystyrene resin is also reported.

Synthesis of primary amines from polymer-bound iminodicarbonate.

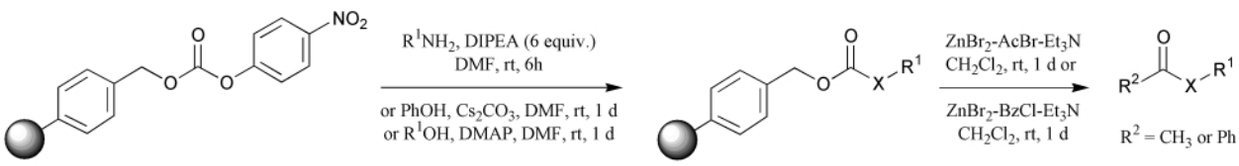


Wang resin

C. Subramanyam, *Tetrahedron Lett.*, 2000, **41**, 6537.

9 examples (yields 0, 33-85%).

Lewis acid-catalysed cleavage of carbamate and carbonate resins: preparation of amides and esters.

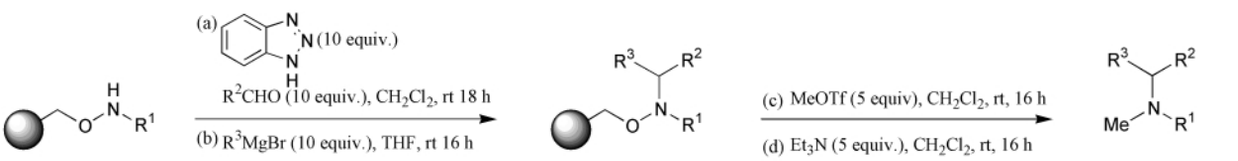


3 steps from Merrifield resin

W.-R. Li, Y.-S. Lin and Y.-C. Yo, *Tetrahedron Lett.*, 2000, **41,** 6619.

9 examples (yields 10-97%).

Application of Grignard reagents to the synthesis of tertiary methylamines *via* resin-bound oxyiminium ions.

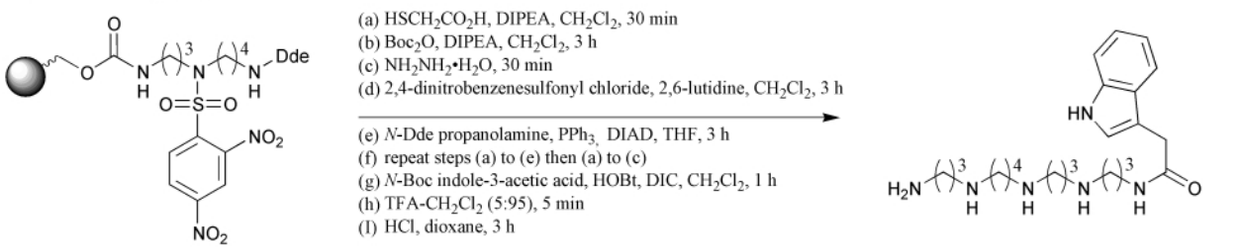


resin not specified

P. Blaney, R. Grigg, Z. Rankovic and M. Thoroughgood, *Tetrahedron Lett.*, 2000, **41**, 6639.

22 examples (yields 18-72%, HPLC/LC-MS purity >99%). Synthesis of the racemic MAO inhibitor α-methylpargyline and the analgesic tramadol by similar routes is also reported (yields 57-75%, HPLC purity 99%).

Agel 416: an acylpolyamine.

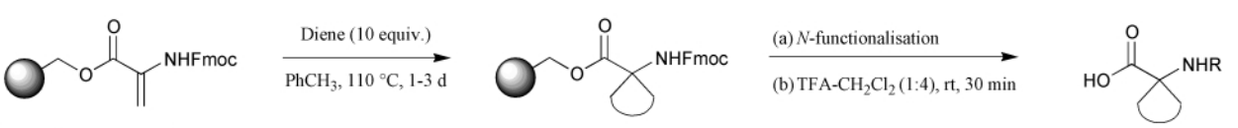


3 steps from Wang carbamate resin

N. D. Hone and L. Payne, *Tetrahedron Lett.*, 2000, **41**, 6149.

1 example (yield 88%, LCMS purity >70%).

Cycloaliphatic amino acids.

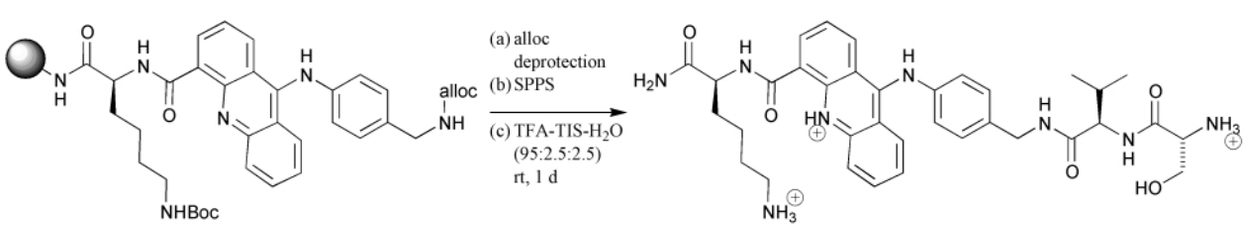


3 steps from Wang resin

B. A. Burkett and C. L. L. Chai, *Tetrahedron Lett.*, 2000, **41**, 6661.

7 examples (yields 48-68%).

An acridine-based amino acid.

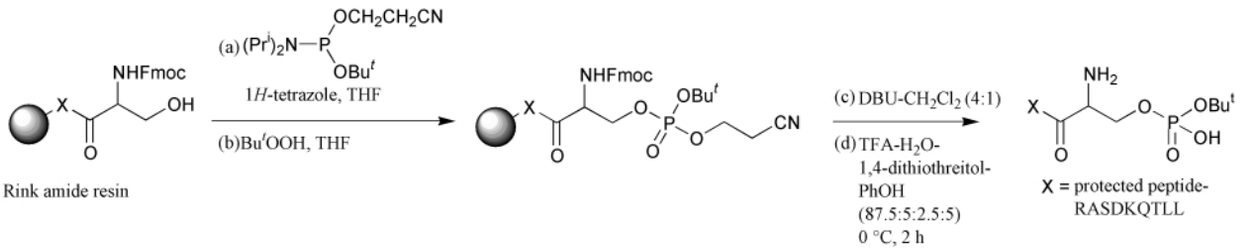


1 step from *N*-ε-Boc lysine loaded Rink amide AM resin

C. B. Carlson and P. A. Beal, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1979.

No yield or purity given. Biological activity of the illustrated acridine-based amino acid is also evaluated.

Phosphopeptides



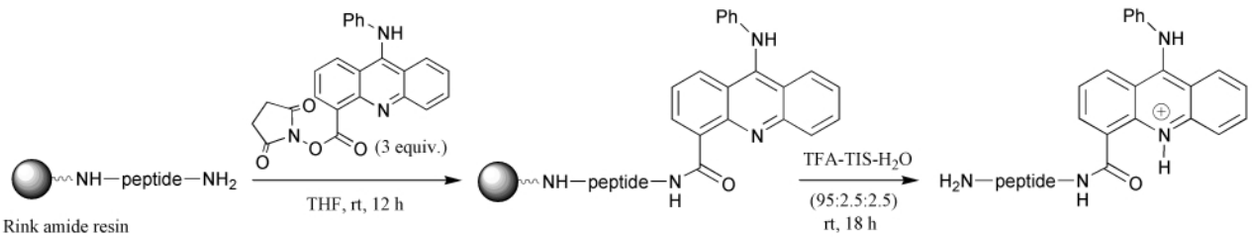
Rink amide resin

X = protected peptide-RASDKQTLL

Z. Kupihár, G. Váradi, E. Monostori and G. K. Tóth, *Tetrahedron Lett.*, 2000, **41**, 4457.

1 example (no yield or purity given).

Acridine-peptide conjugates.

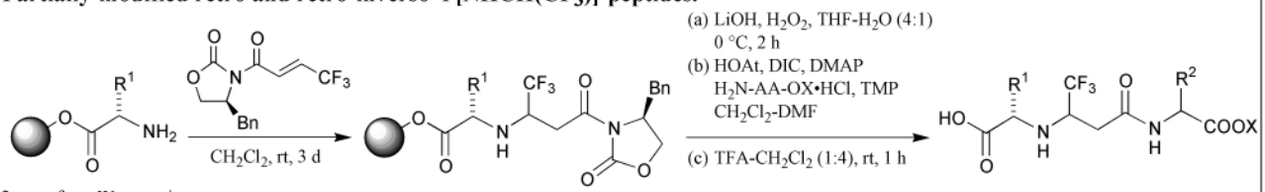


Rink amide resin

C. B. Carlson and P. A. Beal, *Org. Lett.*, 2000, **2**, 1465.

Preparation of a 16-member library is reported (no yields or purities given).

Partially-modified retro and retro-inverso Ψ[NHCH(CF_3)]-peptides.



2 steps from Wang resin

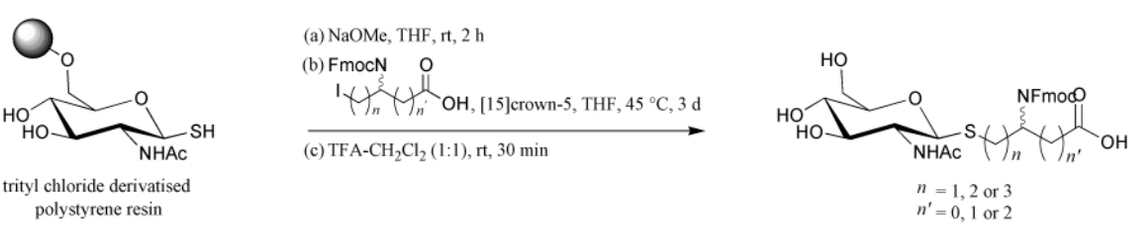
TMP = *syn*-collidine

R^1 = H or Pr^i
R^2 = L-Phe, L-Ala, D-Ala, L-Leu L-Pro, L-Val, Gly or L-Ile
X = Bn or Me

A. Volonterio, P. Bravo, N. Moussier and M. Zanda, *Tetrahedron Lett.*, 2000, **41**, 6517.

9 examples (yields 49-79%, ^{19}F and ^1H NMR purity 75-> 95%).

S-Glycoamino acids.

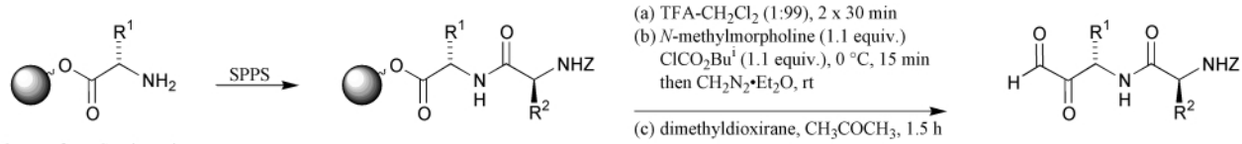


trityl chloride derivatised polystyrene resin

5 examples (yields 75-82%). Solution-phase synthesis of the illustrated iodo amino acids and solid-phase synthesis of a *S*-glycoamino acid using threonine (yield 50%) *via* a similar route is also reported.

L. Jobron and G. Hummel, *Org. Lett.*, 2000, **2**, 2265.

Peptidyl α-keto-β-aldehydes: inhibitors of cathepsin L.



3 steps from Sasrin resin

J. F. Lynas, S. J. Hawthorne and B. Walker, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1771.

4 examples (yields and purity not given). Biological evaluation of the illustrated α-keto-β-aldehydes is also reported.