Perkin 1 Abstracts: Solid Phase Organic Synthesis

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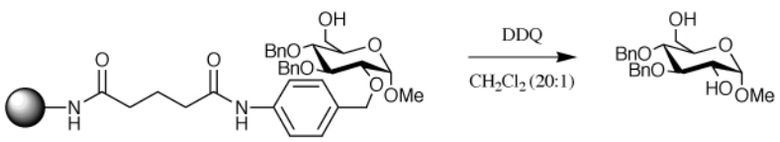
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

A novel oxidatively removable traceless linker: application to α-selective oligosaccharide synthesis on a macroporous polystyrene support. ***Linker***

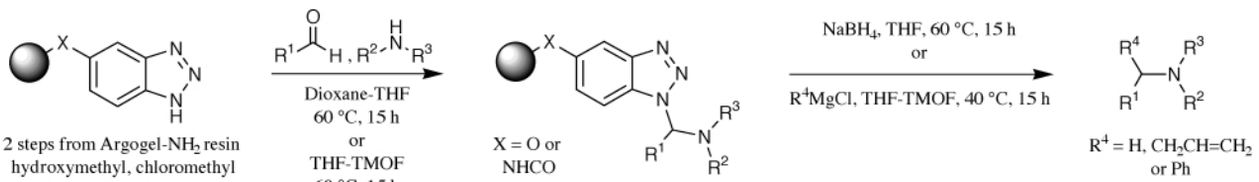


1 step from ArgoPore™ amine resin

The *p*-acylaminobenzyl ether linker is smoothly cleaved: demonstrated by monosaccharide cleavage (1 example, yield 91%). Glycosylation was investigated by reacting 3 different glycosyl donors with the illustrated resin-bound benzylated monosaccharide, 10 examples (yields 41-82%, α:β = 2:1 → 9:1). 2 examples of trisaccharide synthesis are also reported (yields 42-50%)

K. Fukase, Y. Nakai, K. Egusa, J. A. Porco, Jr. and S. Kusumoto, *Synlett*, 1999, **55**, 1074.

Amines using solid-supported benzotriazoles as traceless linkers. ***Linker***



2 steps from Argogel-NH_2 resin hydroxymethyl, chloromethyl or aminomethyl polystyrene resin

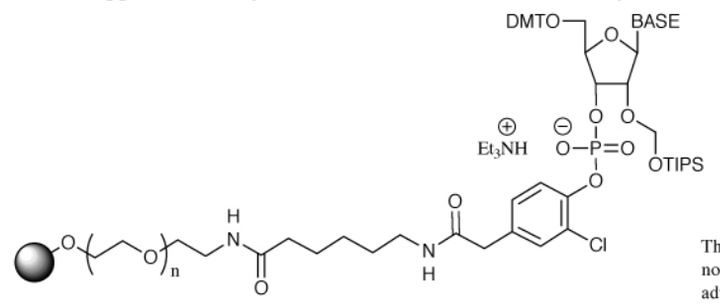
X = O or NHCO

R^4 = H, $CH_2CH{=}CH_2$ or Ph

A. Paio, A. Zaramella, R. Ferritto, N. Conti, C. Marchioro and P. Seneci, *J. Comb. Chem.*, 1999, **1**, 317.

27 examples (yields 11-65%, HPLC purity 13-100%)

A novel support for the synthesis of small- to medium-sized cyclic RNA oligonucleotides. ***Support***

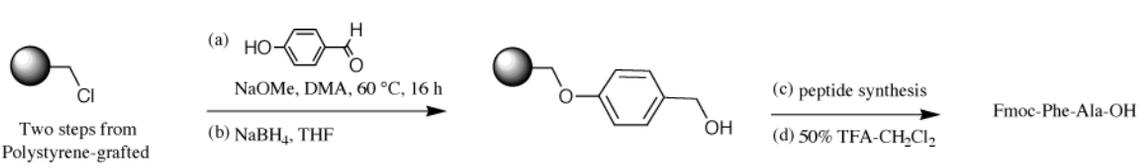


BASE : A^{Ac}, C^{Ac}, G^{Ac}, U

The above support (prepared from TentaGel S NH_2 resin) is utilised in a novel synthesis of 24 cyclic RNA oligonucleotides (yields 1-25%). An advantage of the reported approach is the lack of restrictions on sequence variety with respect to the four standard bases.

R. Micura, *Chem. Eur. J.*, 1999, **5**, 2077.

Chloromethyl polystyrene-grafted multipin™ solid support. ***Support***



Two steps from Polystyrene-grafted synphase crowns

To evaluate the quality of the chloromethyl support, generated *via* diazotisation of aminomethyl polystyrene-grafted crowns, a model dipeptide was synthesised (yield 63%, HPLC purity 90%).

C. T. Bui, N. Joe Maeji, F. Rasoul and A. M. Bray, *Tetrahedron Lett.*, 1999, **40**, 5383.

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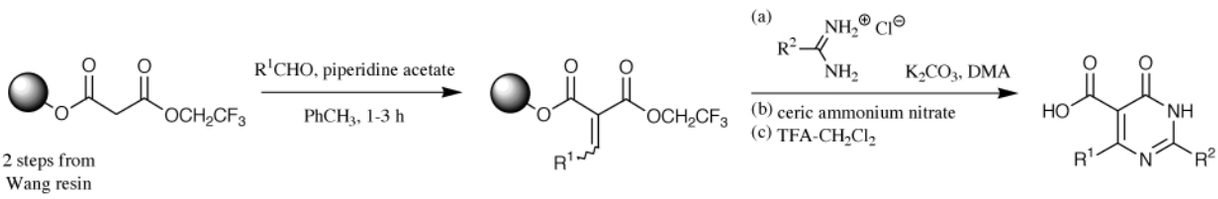
Malonic acid resin: synthesis of dihydropyrimidinones and pyrimidinone carboxylic acids. ***Support***

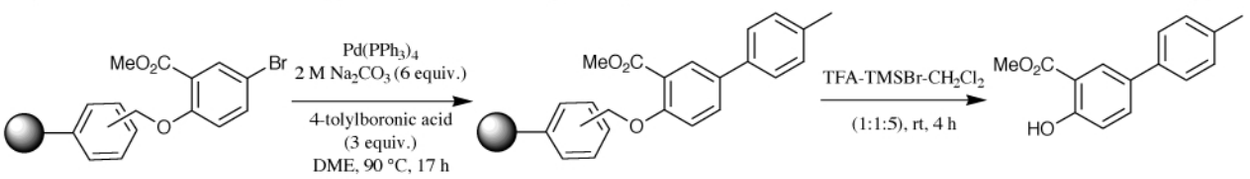


2 steps from Wang resin

10 examples (yields 49->99%, NMR and LCMS purity >85%). The use of malonic acid resins in the preparation of pyrimidinone carboxylic acids are also reported (10 examples, yields 0-66%).

B. C. Hamper, K. Z. Gan and T. J. Owen, *Tetrahedron Lett.*, 1999, **40**, 4973.

Polymer discs: an alternative support format for solid phase synthesis. ***Support***

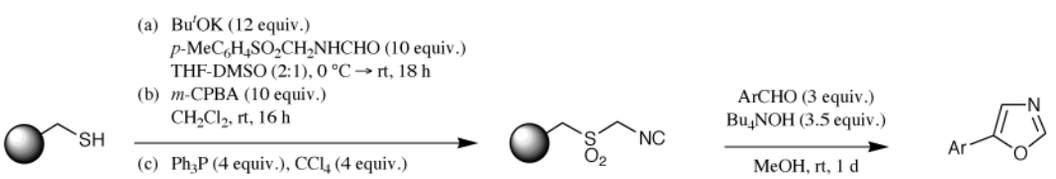


1 step from vinylbenzyl chlorine based polymer discs

3 examples using 3 different vinylbenzyl chloride based discs (yields 4-11 %). The preparation of polystyrene and vinylbenzyl chloride-based discs are also reported, 2 of which were chosen for a probe reaction: quaternisation with NMe_3 (yields 59-100%).

N. Hird, I. Hughes, D. Hunter, M. G. J. T. Morrison, D. C. Sherrington and L. Stevenson, *Tetrahedron*, 1999, **55**, 9575.

Polymer-supported *p*-tolylsulfonylmethyl isocyanide (TosMIC): synthesis of oxazoles. ***Reagent***

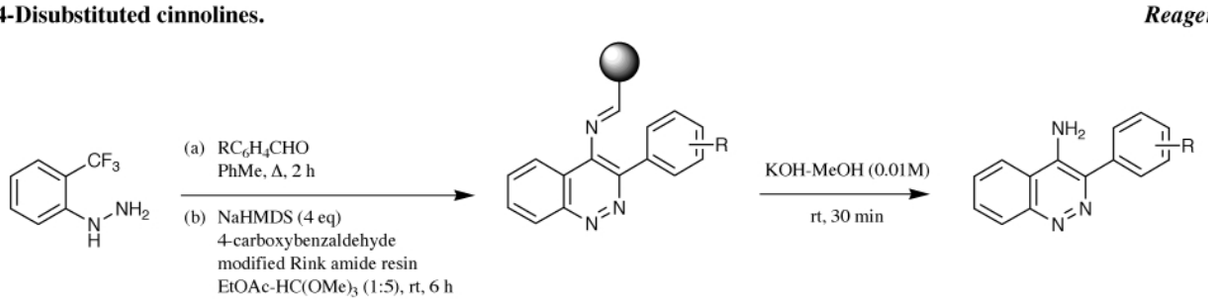


2 steps from Merrifield resin

10 examples (yields 25-50%).

B. A. Kulkarni and A. Ganesan, *Tetrahedron Lett.*, 1999, **40**, 5633.

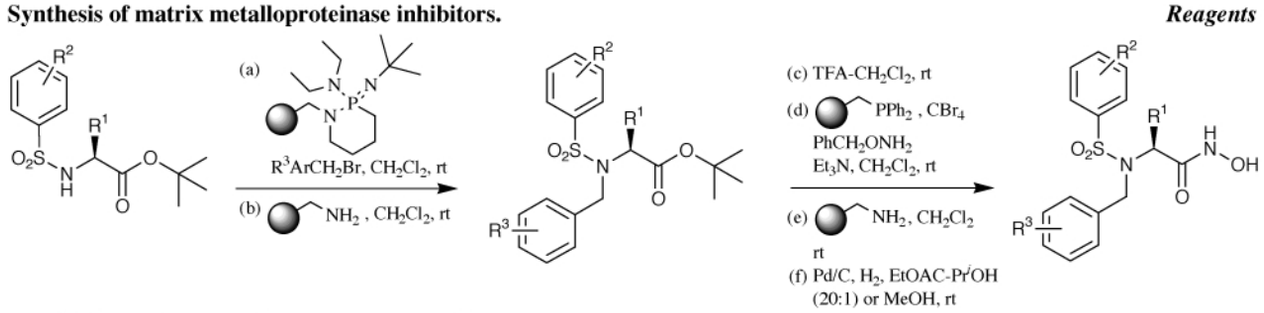
3,4-Disubstituted cinnolines. ***Reagent***



8 examples (yields 63-73%).

A. S. Kiselyov and C. Dominguez, *Tetrahedron Lett.*, 1999, **40**, 5111.

Synthesis of matrix metalloproteinase inhibitors. ***Reagents***



27 examples (yields 59-100%, LC-MS purity 90->98%).

M. Caldarelli, J. Habermann and S. V. Ley, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 2049.

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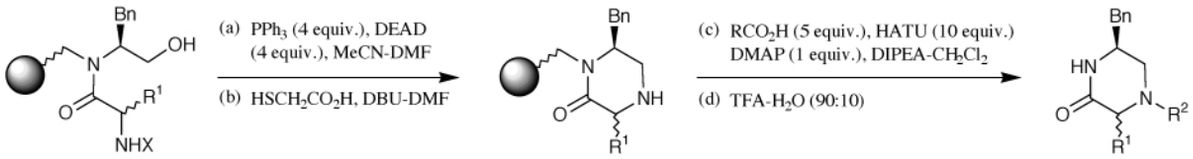
Tetrahydropyrazine-2-ones.

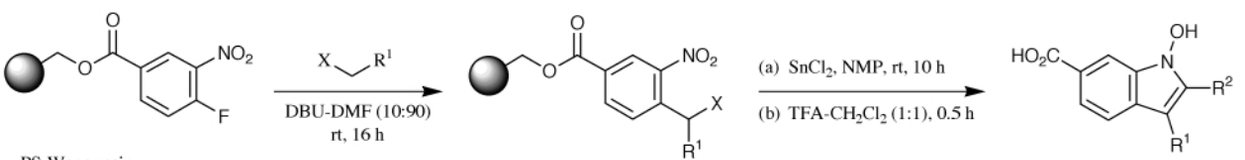


7 steps from ArgoGel-MB-CHO resin

2 examples reported (yields 75-96%, HPLC purity 89-94%) also 2 examples of *N*-derivatisation with phenyl isocyanate (yields 61-80%, HPLC purity 89-91%).

P-P. Kung and E. Swayze, *Tetrahedron Lett.*, 1999, **40**, 5651.

_N_-Hydroxyindoles and benzo[*c*]isoxazoles.



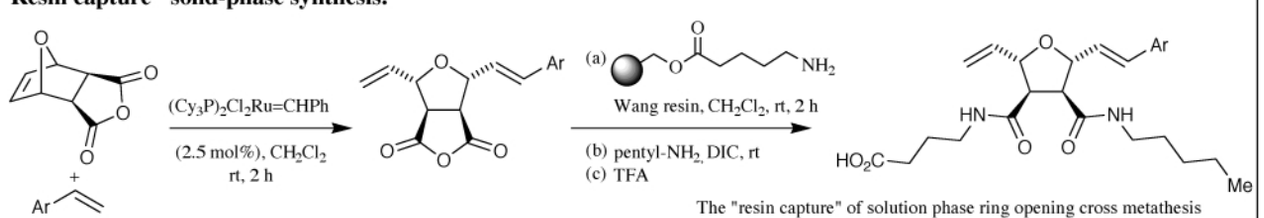
PS-Wang resin

X = COR^2 or CN
R^1 = $COCH_3$, CONHPh or SO_2CH_3

3 examples (yields 39-74%) and 1 example of a benzoisoxazole (yield 66%).

H. Stephensen and F. Zaragoza, *Tetrahedron Lett.*, 1999, **40**, 5799.

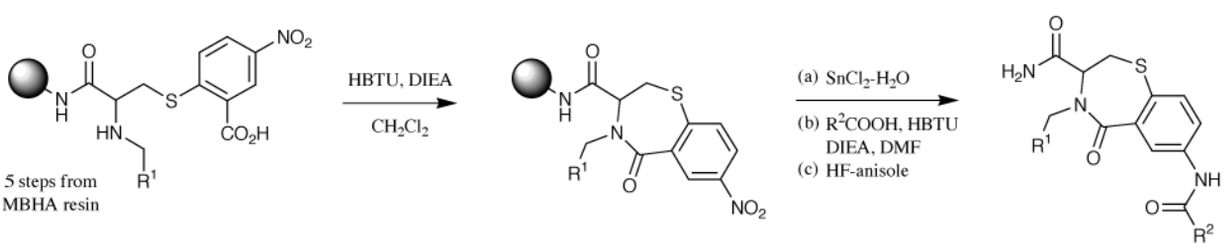
"Resin capture" solid-phase synthesis.



The "resin capture" of solution phase ring opening cross metathesis (ROM) products by resin bound amines is reported (2 examples, yields 25-95%). 1 example of solution phase ROM of an unsymmetrical alkene with a styrene derivative (yield, 50%) and solution phase ROM of a variety of symmetrical bicyclic alkenes with styrene derivatives (4 examples, yields 59-82%) are also reported.

G. D. Cuny, J. Cao, A. Sidhu and J. R. Hauske, *Tetrahedron*, 1999, **55**, 8169.

1,4-Benzothiazepin-5-one derivatives.

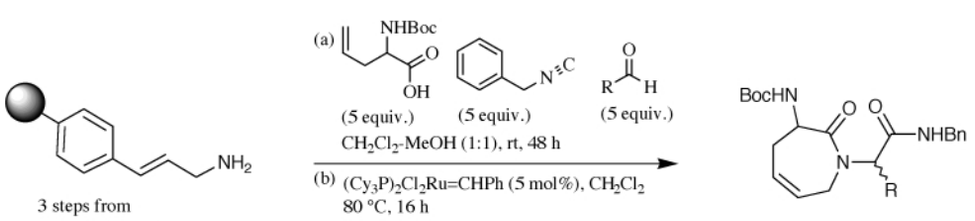


5 steps from MBHA resin

The parallel synthesis of 12 derivatives are reported (yields >90%, HPLC purity 87->95%).

A. Nefzi, N. A. Ong, M. A. Giulianotti, J. M. Ostresh and R. A. Houghten, *Tetrahedron Lett.*, 1999, **40**, 4939.

Ring closing metathesis: preparation of Freidinger lactam β-turn mimetics.



3 steps from cinnamyl alcohol resin

3 examples (yields 21-62%). The synthesis of a four amino acid β-turn mimetic (yield 61%, HPLC purity >95%) and Freidinger lactams *via* an alternate ring closing metathesis route are also described, 10 examples (yields 15-36%).

A. D. Piscopio, J. F. Miller and K. Koch, *Tetrahedron*, 1999, **55**, 8189.

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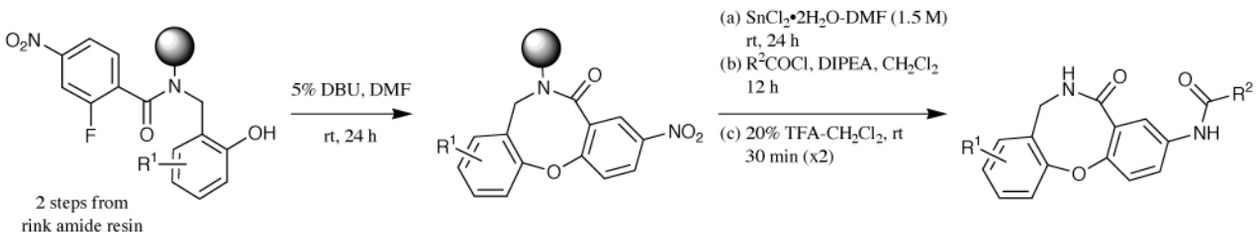
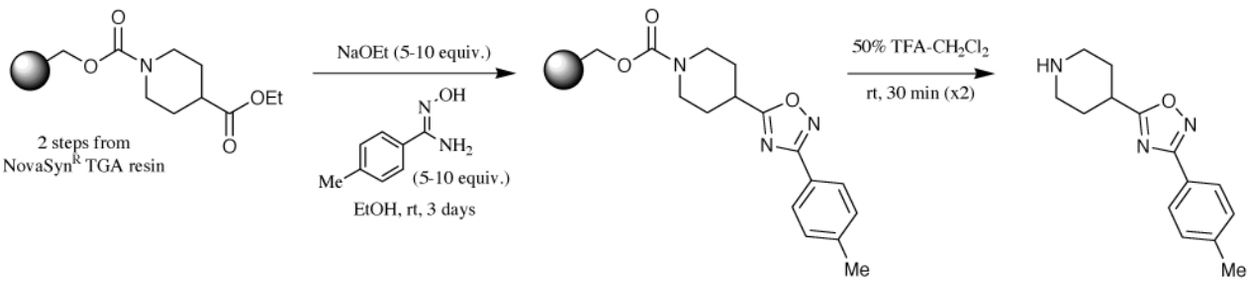
Substituted dibenzo[*b*,*f*]oxazocines.



X. Ouyang and A. S. Kiselyov, *Tetrahedron*, 1999, **55**, 8295.

Generation of a 15-membered library is reported (yields 55-87%, HPLC purity 92-95%).

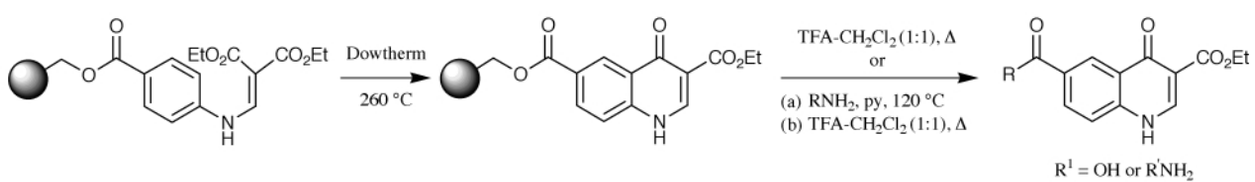
Oxadiazoles.



G-B. Liang and X. Qian, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 2101.

7 examples (yields 75-99%, HPLC purity 81-99%). A method to access *N*-methylpiperidine derivatives is also reported.

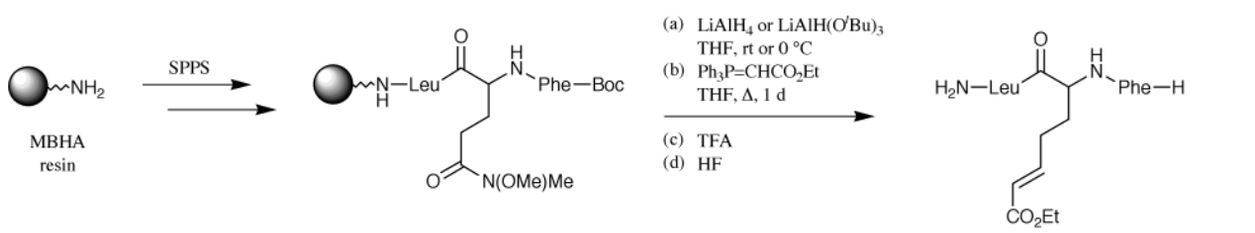
Quinolones.



S. K. Srivastava, W. Haq, P. K. Murthy and P. M. S. Chauhan, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1885.

5 examples (yields 68-98%, ^{1}H-NMR and preparative TLC purity >90%).

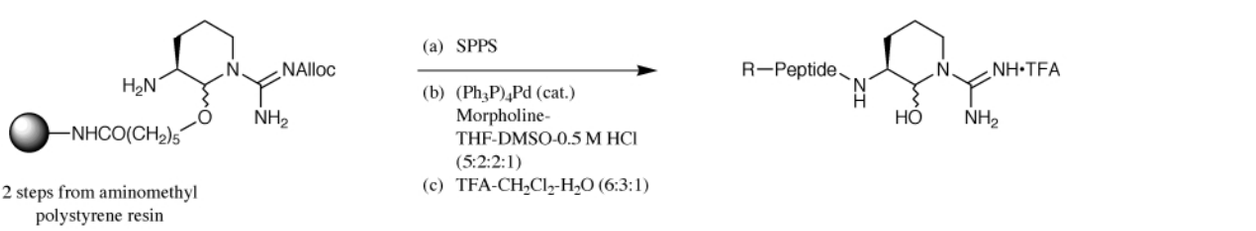
Modification of aspartyl or glutamyl residue side-chains on solid-support.



M. Paris, C. Douat, A. Heitz, W. Gibbons, J. Martinez and J-A. Fehrentz, *Tetrahedron Lett.*, 1999, **40**, 5179.

1 example (HPLC purity 82%). 5 further examples of the synthesis of oligopeptides containing modified aspartyl or glutamyl derivatives (yields 57-90%).

Peptidyl and peptidomimetic argininal derivatives.



D. V. Siev, J. A. Gaudette and J. E. Semple, *Tetrahedron Lett.*, 1999, **40**, 5123.

20 examples (yields 17-83%, HPLC purity 90-98%).

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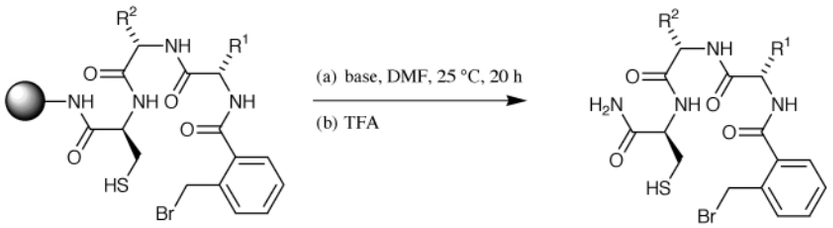
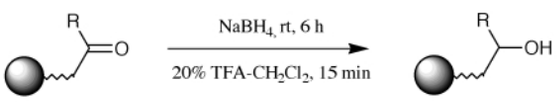
S_N2 macrocyclisation reactions to form β-turn mimics.



13 examples (yields 15-44%, HPLC purity 60-88%). Conformational analysis of the macrocyclisation products showed both type I and type II β-turn conformations in solution.

Y. Feng, M. Pattarawarapan, Z. Wang and K. Burgess, *Org. Lett.*, 1999, **1,** 121.

Novel solid state reduction of organic functional groups.

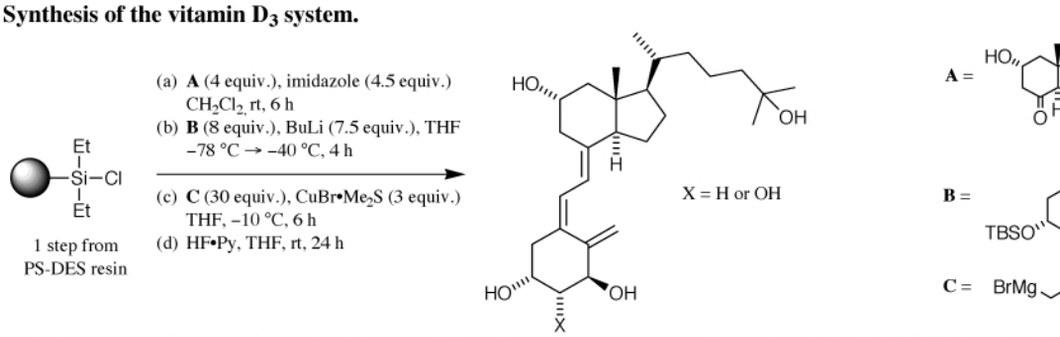


1 step from Merrifield resin

3 examples (yields 58-81%). 2 examples of solid state reduction of epoxy functionalised resins with $LiAlH_4$ are also reported (yields 60-64%).

S. Chandrasekhar, A. Raza, M. B. Padmaja, *Synlett*, 1999, **7**, 1061.

Synthesis of the vitamin D_3 system.

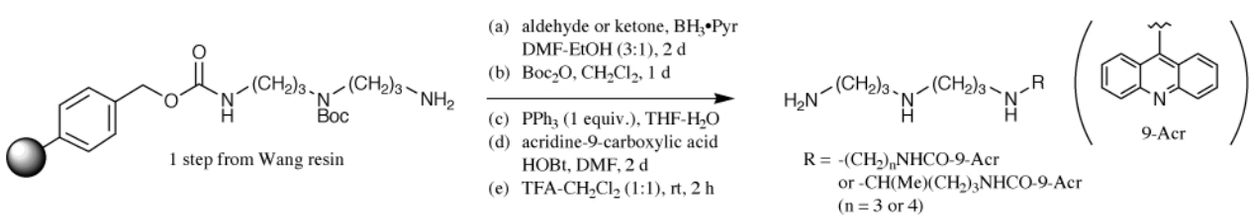


1 step from PS-DES resin

2 examples (yields 61-62%, HPLC purity >95%).

T. Doi, I. Hijikuro and T. Takahashi, *J. Am. Chem. Soc.*, **121**, 6749.

Unsymmetrical polyamines *via* reductive alkylation.



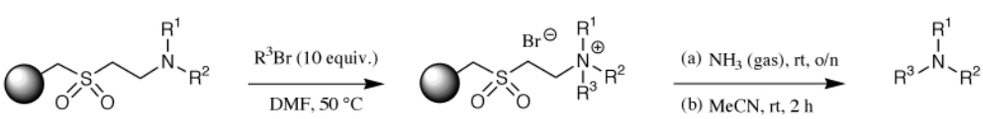
1 step from Wang resin

R = -$(CH_2)_n$NHCO-9-Acr or -$CH(Me)(CH_2)_3$NHCO-9-Acr (n = 3 or 4)

3 examples (no yields reported). 2 further examples of the formation of unsymmetrical polyamines *via* reductive alkylation are reported, one of which yielded 35% over 6 steps.

S. Carrington, J. Renault, S. Tomasi, J-C. Corbel, P. Uriac and I. S. Blagbrough, *Chem. Commun.*, 1999, **14**, 1341.

Tertiary amines *via* vapour-phase Hoffmann elimination.



1 step from vinylsulfonylmethyl polystyrene resin

8 examples (yields 10-64%, HPLC purity 64->95 %).

A. R. Brown, *J. Comb. Chem.*, 1999, **1**, 283.

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