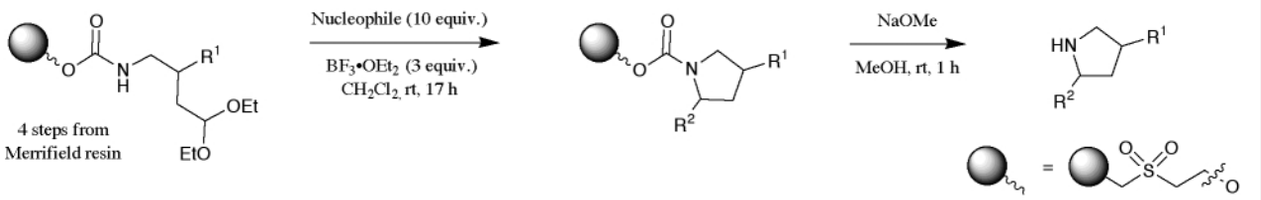
Perkin 1 Abstracts: Solid Phase Organic Synthesis

Compilers: John Christopher, Catherine McCusker, Susan Booth and Jason Tierney

Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ

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.

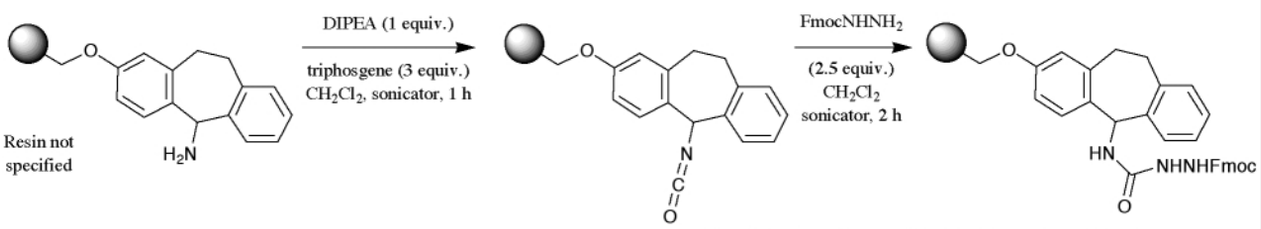
Carbamate linker for *N*-acyliminium ion reactions: synthesis of substituted pyrrolidines. *Linker*



J. J. N. Veerman, F. P. J. T. Rutjes, J. H. van Maarseveen and H. Hiemstra, *Tetrahedron Lett.*, 1999, **40**, 6079.

6 examples (yields 36-98%). Synthesis of the carbamate linker is also reported.

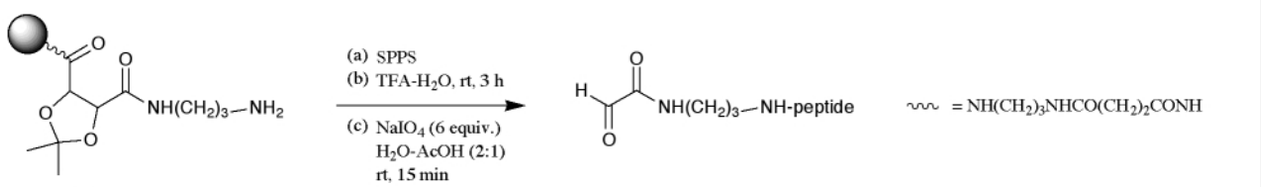
Semicarbazide linker for the synthesis of peptide C-terminal semicarbazones and aldehydes. *Linker*



J. A. Patterson and R. Ramage, *Tetrahedron Lett.*, 1999, **40**, 6121.

The utility of the linker, synthesised *via* the illustrated route, was demonstrated in the synthesis of 5 peptide aldehydes (yields 38-62%).

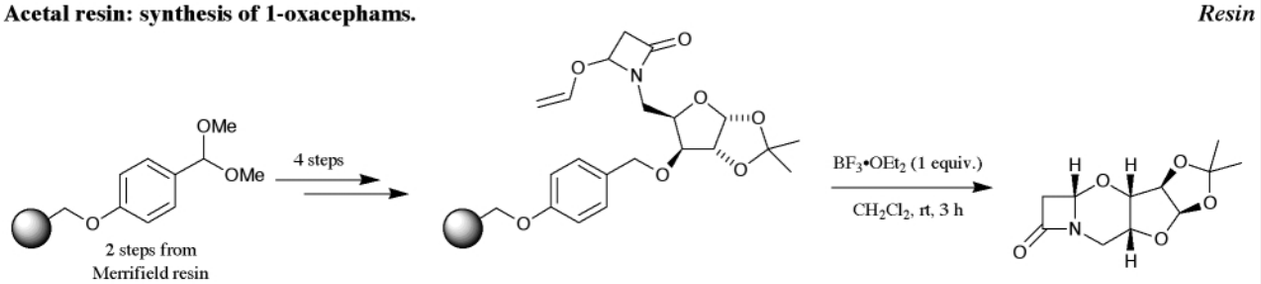
Tartaric acid-based linker for the synthesis of C-terminal peptide α-oxoaldehydes. *Linker*



J-S. Fruchart, H. Gras-Masse and O. Melnyk, *Tetrahedron Lett.*, 1999, **40**, 6225.

3 examples (yields 26-38%). Synthesis of the tartaric acid linker is also reported.

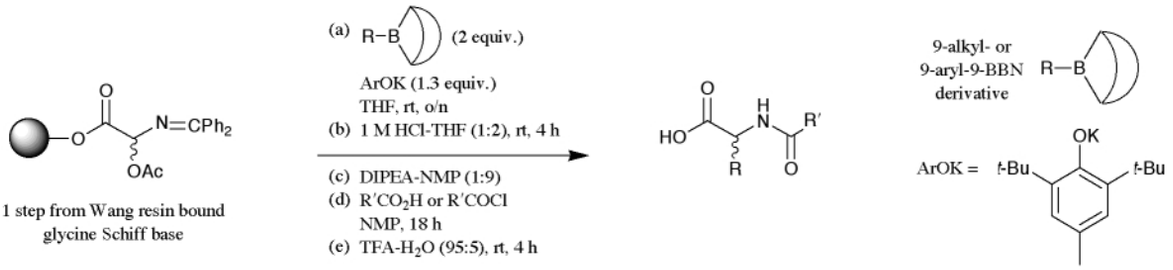
Acetal resin: synthesis of 1-oxacephams. *Resin*



B. Furman, R. Thürmer, Z. Kaluza, W. Voelter and M. Chmielewski, *Tetrahedron Lett.*, 1999, **40**, 5909.

2 examples (yields 20%).

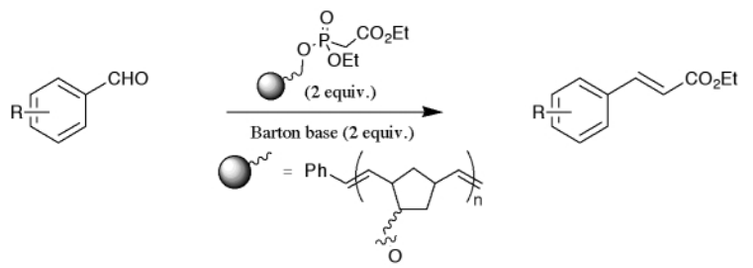
Resin bound glycine cation equivalent: synthesis of unnatural α-amino acid derivatives. *Resin*



M. J. O'Donnell, F. Delgado, M. D. Drew, R. S. Pottorf, C. Zhou and W. L. Scott, *Tetrahedron Lett*., 1999, **40**, 5831.

14 examples (yields 51-99%, purity 75-100%).

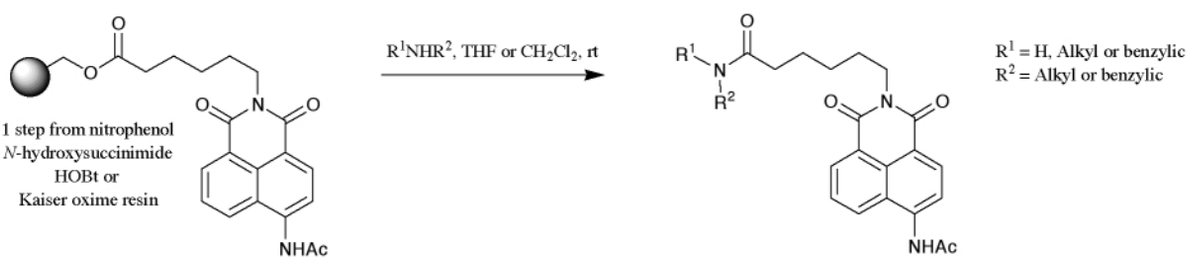
Rompgels as reagents in Horner–Emmons synthesis. *Reagent*



9 examples (yields 82-96%, GCMS purity >95%, *E*:*Z* = 99:1). 9 examples of α,β-unsaturated nitrile synthesis (yields 85-98%, GCMS purity >95%, *E*:*Z* = 70:30-100:0) using a different functionalised rompgel, and the synthesis of rompgels *via* ring-opening metathesis of the corresponding monomers are also reported.

A. G. M. Barrett, S. M. Cramp, R. S. Roberts and F. J. Zecri, *Org. Lett*., 1999, **1**, 579.

Fluorescent labelling of amines *via* solid phase activated esters. *Reagent*

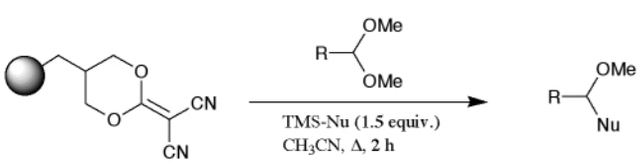


R^1 = H, Alkyl or benzylic
R^2 = Alkyl or benzylic

Y-T. Chang and P. G. Schultz, *Bioorg. Med. Chem. Lett*., 1999, **9**, 2479.

A labelled mixture of 10 amines, detected by HPLC, was reported.

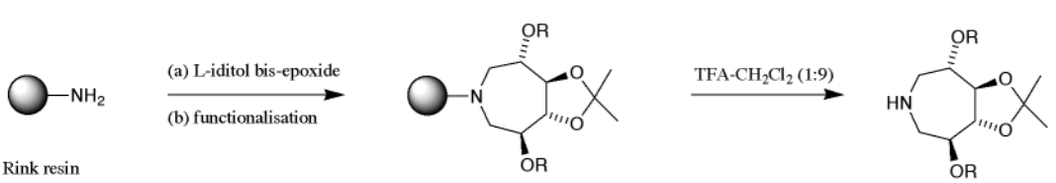
Polymer-supported acid catalyst in the carbon-carbon bond formation of acetals with silylated nucleophiles. *Catalyst*



22 examples (yields 0, 15-99%). The illustrated polymeric dicyanoketene acetal was synthesised by co-polymerisation of a styrene monomer bearing a dicyanoketene acetal moiety and ethylene glycol dimethacrylate.

N. Tanaka and Y. Masaki, *Synlett*, 1999, 1277.

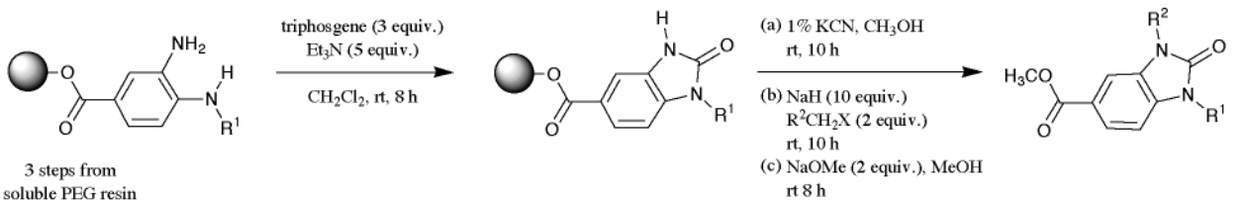
Azepane scaffolds.



L.Gauzy, Y. Le Merrer and J-C. Depezay, *Tetrahedron Lett*.,1999, **40**, 6005.

6 examples (yields 53-93%, NMR purity ≥ 90%).

Liquid phase synthesis of substituted benzimidazolones.

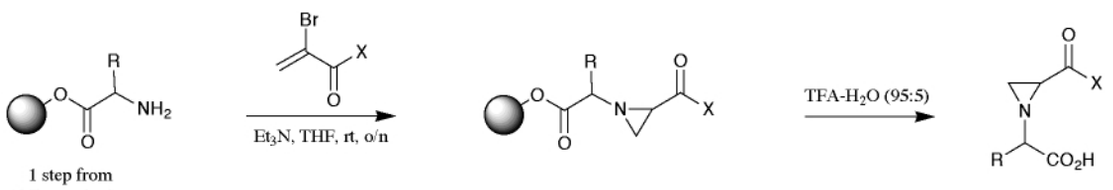


3 steps from soluble PEG resin

P-C. Pan and C-M. Sun, *Tetrahedron Lett*., 1999, **40**, 6443.

17 examples (yields 75-98%, HPLC purity 77-96%).

Aziridine 2-carboxylates

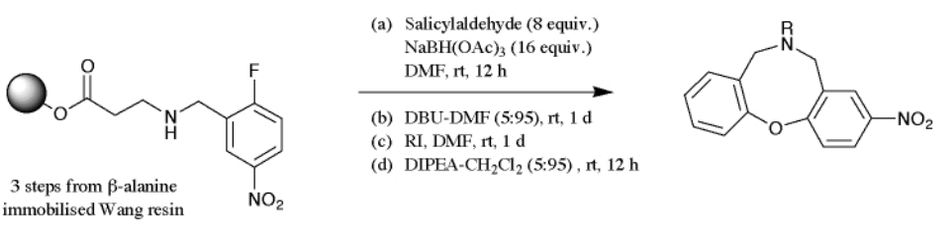


1 step from *N*-Fmoc glycine loaded Wang resin

S. N. Filigheddu, S. Masala and M. Taddei, *Tetrahedron Lett*., 1999, **40**, 6503.

9 examples (no yields given). 12 further examples (no yields given) of the synthesis of aziridine carboxylic acids, *via* an analogous route, are also described.

Dibenzo[*b*,*g*][1,5]-oxazocines

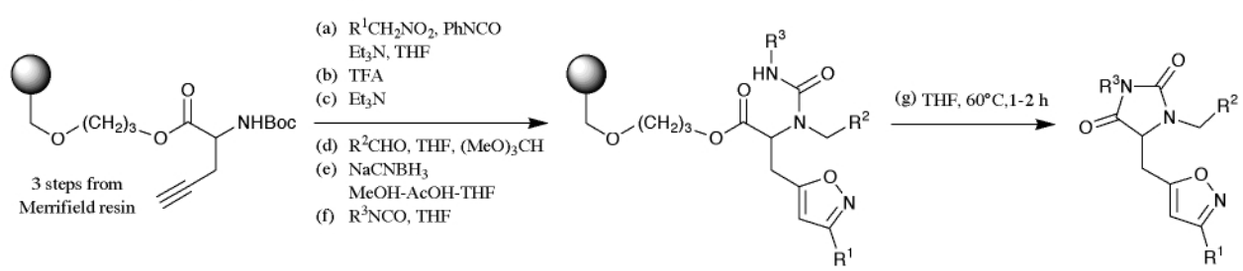


3 steps from β-alanine immobilised Wang resin

X. Ouyang and A. S. Kiselyov, *Tetrahedron Lett*., 1999, **40**, 5827.

5 examples (yields 38-53%, HPLC purity 96->99%).

An uncatalysed cyclo-elimination process: synthesis of isoxazoloimidazolidinediones.

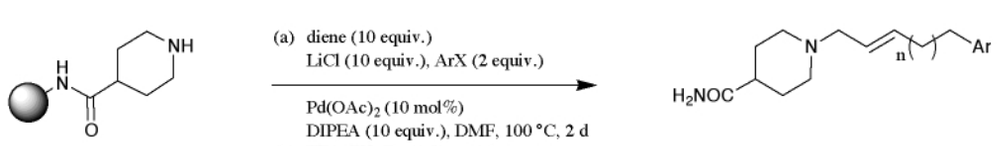


3 steps from Merrifield resin

K-H. Park and M. J. Kurth, *Tetrahedron Lett*., 1999, **40**, 5841.

18 examples (yields 20-35%, NMR purity >95%).

Palladium-catalysed three component coupling: synthesis of aryl-substituted allylic amines.

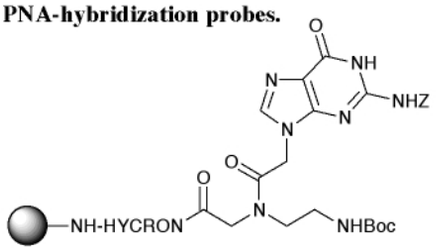


1 step from Rink resin

Y. Wang and T-N. Huang, *Tetrahedron Lett*., 1999, **40**, 5837.

17 examples (yields 70-95%, LCMS purity 53-92%). 4 further examples of Pd-catalysed three component coupling using 4 different amine supported nucleophiles (yields 75-87%, LCMS purity 52-69%) are also reported.

PNA-hybridization probes.

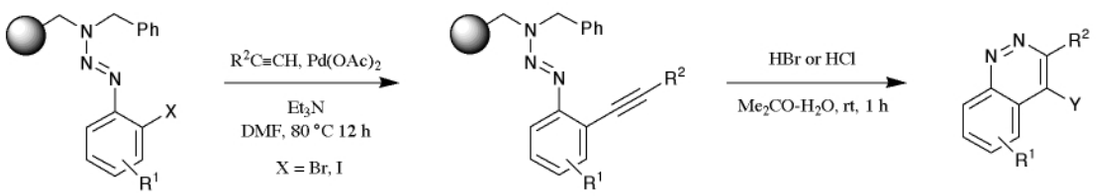


5 steps from aminomethylpolystyrene resin

The allylic HYCRON linker provides orthogonal stability with commonly used protecting-group strategies for the synthesis of the illustrated peptide nucleic acid (PNA). Peptide nucleic acids can act as DNA analogues in which the entire sugar-phosphate backbone is replaced by a pseudopeptide backbone. The synthesis of PNA conjugates, which serve as hybridisation oligomers, and the synthesis of PNA-fluorophore conjugates, which might serve as a new tool for real-time sequence analysis of DNA, are also reported.

O. Seitz, F. Bergmann and D. Heindl, *Angew. Chem., Int. Ed.*, 1999, **38**, 2203.

Substituted cinnolines.

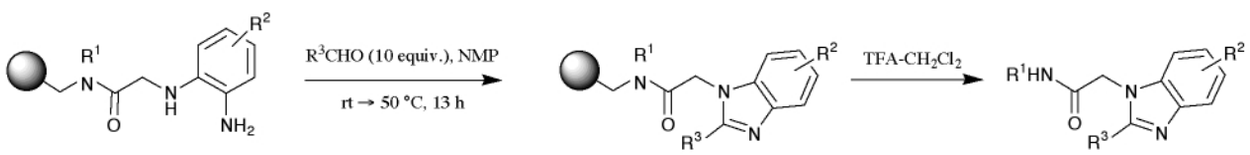


1 step from benzylaminomethyl polystyrene resin

S. Bräse, S. Dahmen and J. Heuts, *Tetrahedron Lett.*, 1999, **40**, 6201.

5 examples (yields 47-95%, GCMS purity 60-95%).

Substituted benzimidazoles.

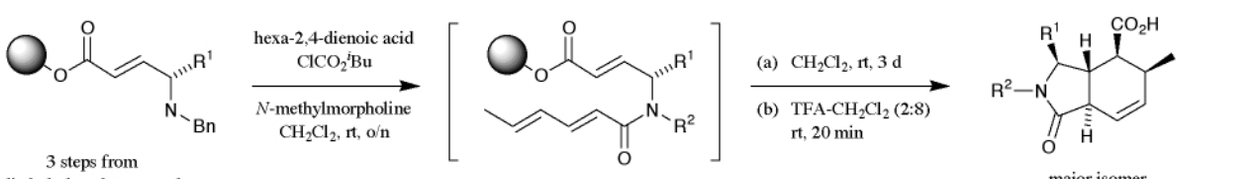


5 steps from ArgoGel-MB-CHO resin

D. Tumelty, M. K. Schwarz, K. Cao and M. C. Needels, *Tetrahedron Lett.*, 1999, **40**, 6185.

12 examples (yields 43-80%, HPLC purity 55-85%).

Solid-phase Diels–Alder reactions of amino acid derived trienes.



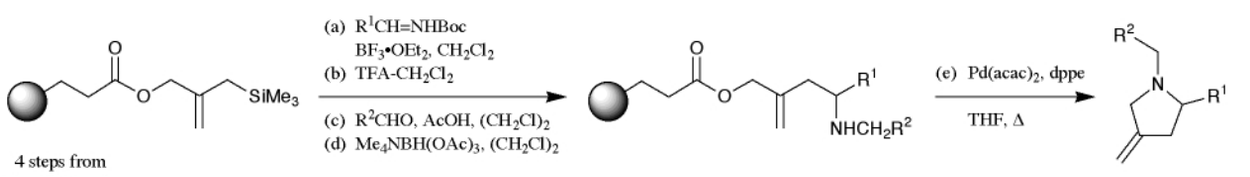
3 steps from diethyl phosphonoacetyl Wang resin

major isomer

2 examples (yields 38–48%). 2 further examples of hydroisoindole synthesis by a method similar to the illustrated route (yields 32-55%) and 6 examples of Diels–Alder reactions using furan derived trienes are also reported (yields 37-65%).

S. Sun and W. V. Murray, *J. Org. Chem.*, 1999, **64**, 5941.

Pyrrolidines.

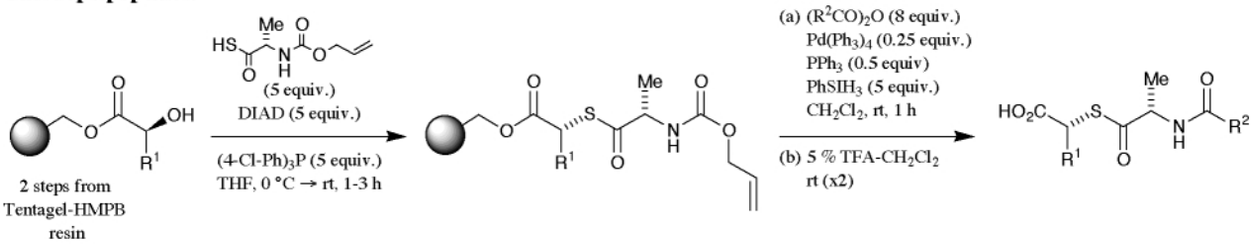


4 steps from Merrifield resin

R. C. D. Brown and M. Fisher, *Chem. Commun.*, 1999, 1547.

6 examples (yields 16-95%).

Thiodepsipeptides.

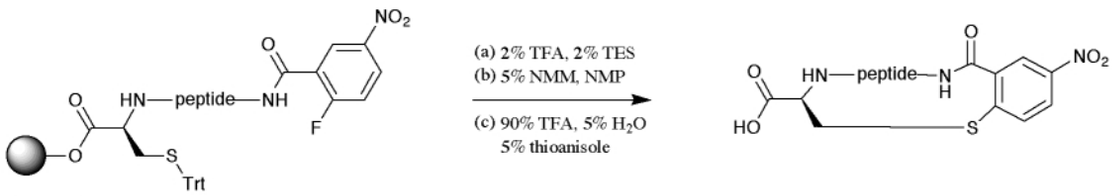


2 steps from Tentagel-HMPB resin

M. L. Greenlee, J. B. Laub, J. M. Balkovec, M. L. Hammond, G. G. Hammond, D. L. Pompliano and J. H. Epstein-Toney, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 2549.

38 examples (yields 80-95%, HPLC purity >90%). 18 other thioesters and thiols were also prepared using similar Mitsunobu chemistry.

Macrocyclisation of peptides *via* intramolecular S_NAr reactions.

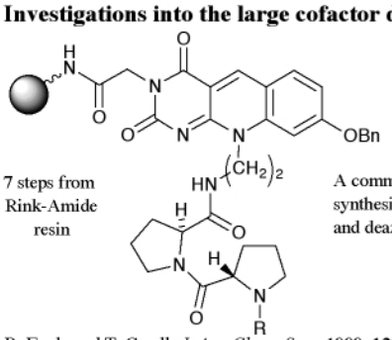


Wang resin

C. Fotsch, G. Kumaravel, S. K. Sharmn, A. D. Wu, J. S. Gounarides, N. R. Nirmala and R. C. Petter, *Bioorg. Med. Chem. Lett*, 1999, **9** , 2125.

(average yields 40%, RP-HPLC purity >90%).

Investigations into the large cofactor distance in the repair efficiency of DNA photolyases.



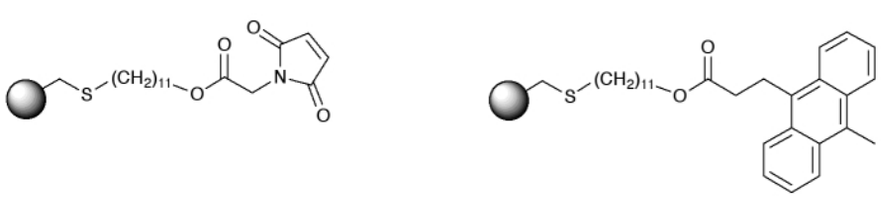
7 steps from Rink-Amide resin

A common intermediate in the synthesis of of flavin-deazaflavin and deazaflavin-proline peptides.

DNA photolyases are repair enzymes which correct UV-induced cyclobutane DNA lesions. Solution phase synthesis of a series of compounds, which contain a model DNA lesion covalently connected to a flavin and a deazaflavin , were synthesised to determine the effect of the large cofactor distance in the repair efficiency of DNA photolyases. Solid-phase synthesis of flavin-deazaflavin and deazaflavin-proline peptides were required for the preparation of the model compounds.

R. Epple and T. Carell, *J. Am. Chem. Soc.*, 1999, **121**, 7318.

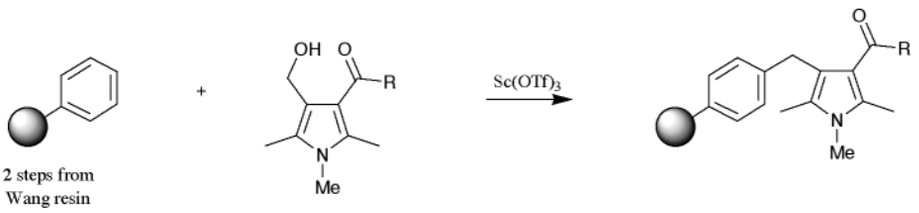
Organic reactivity at a solid–solid interface through an inter-bead Diels–Alder reaction.



I. P. Thomas, J. A. Ramsden, T. Z. Kovacs and J. M. Brown, *Chem. Commun.*, 1999, 1507.

The illustrated polystyrene resins carrying respectively maleimide and anthracene groups attached to extended side-chains adhere to one another in a manner consistent with an inter-bead cycloaddition reaction.

A chemical encoding strategy for combinatorial synthesis using Friedel–Crafts alkylation.



2 steps from Wang resin

R. H. Scott, C. Barnes, U. Gerhard and S. Balasubramanian, *Chem. Commun.*, 1999, 1331.

Ytterbium(III) triflate catalysed Friedel–Crafts alkylation is used to insert a set of hydroxymethyl pyrrole amide tags on to polystyrene resins under mild conditions. The technique is used to encode a split and mix peptide library.