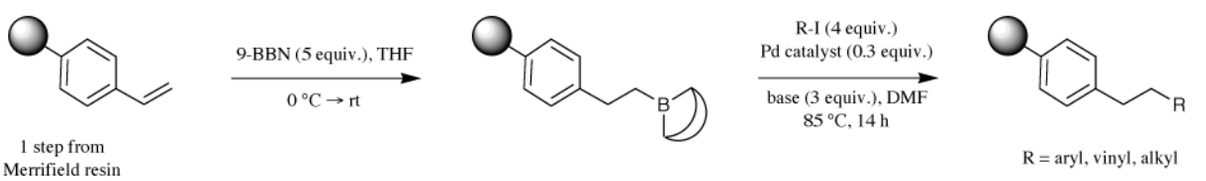
Perkin 1 Abstracts: Solid Phase Organic Synthesis

Compilers: John Christopher,[a] Catherine McCusker,[a] Susan Booth[b] and Jason Tierney[b]

[a] *Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ*
[b] *Organon Laboratories Ltd, Newhouse, Lanarkshire, UK ML1 5SH*

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.

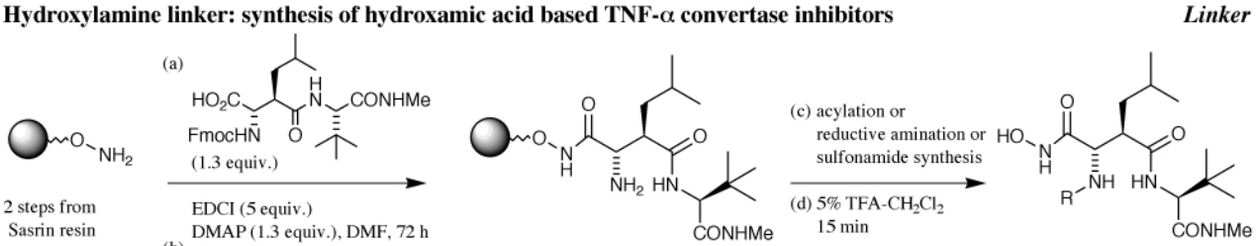
Preparation of new functionalised hydrocarbon linkers *via* Suzuki cross coupling reaction ***Linker***



1 step from Merrifield resin

C. Vanier, A. Wagner and C. Mioskowski, *Tetrahedron Lett.*, 1999, **40**, 4335. 5 examples (yields 55-85%).

Hydroxylamine linker: synthesis of hydroxamic acid based TNF-α convertase inhibitors ***Linker***

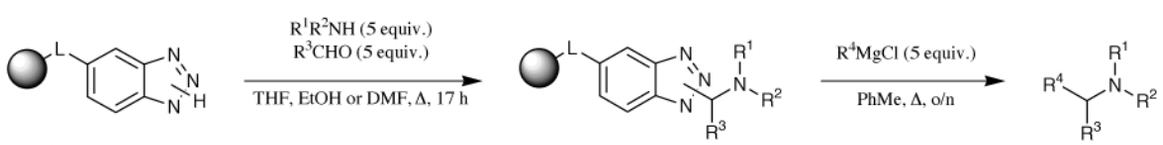


2 steps from Sasrin resin

The versatility of the linker was demonstrated by the functionalisation of TNF-α inhibitors (multiple parallel synthesis): 7 examples of acylation (yields 54-100%), 13 examples of reductive amination (yields 48-100%) and 10 examples of sulfonamide synthesis (yields 43-97%).

B. Barlaam, P. Koza and J. Berriot, *Tetrahedron*, 1999, **55**, 7221.

2° and 3° amines *via* a polymer-supported benzotriazole as a novel traceless linker ***Linker***

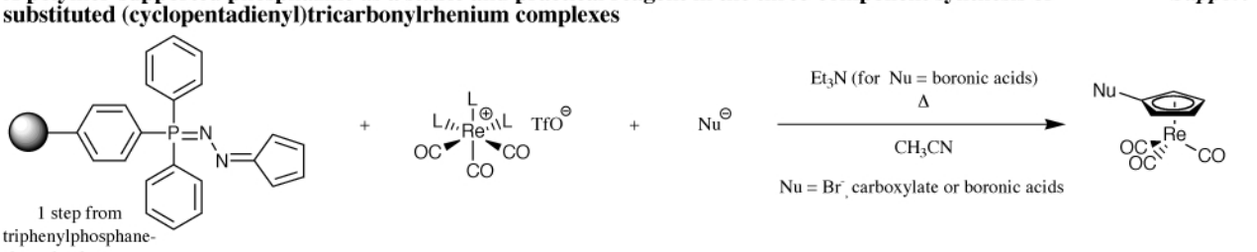


Polystyrene resin

L = -CH_2-, -CH_2OCH_2- or -$CH_2O(CH_2)_6OCH_2$-

K. Schiemann and H. D. H. Showalter, *J. Org. Chem.*, 1999, **64**, 4972. 15 examples (yields 0, 20-77%).

A polymer-supported phosphazine as a stable and practical reagent in the three-component synthesis of substituted (cyclopentadienyl)tricarbonylrhenium complexes ***Support***



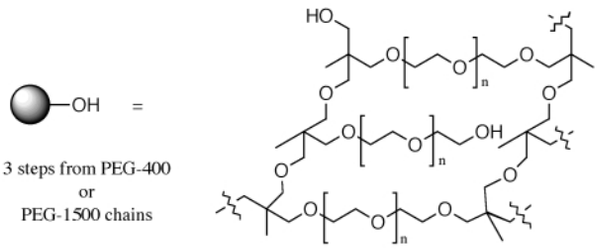
1 step from triphenylphosphane-bound polystyrene resin

The reactivity of polymer-supported phosphazine was demonstrated by the synthesis of (cyclopentadienyl)tricarbonylrhenium complexes (10 examples, yields 41-71%).

F. Minutolo and J. A. Katzenellenbogen, *Angew. Chem., Int. Ed.*, 1999, **38**, 1617.

SPOCC: a resin for solid-phase organic chemistry and enzymatic reactions on solid phase

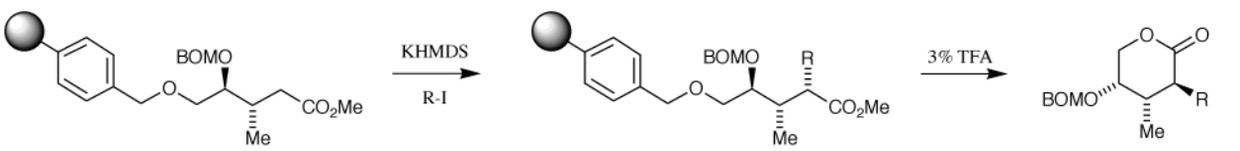
Support



Synthesis of a novel support, *via* bulk polymerisation or suspension polymerisation in silicone oil, is reported. Further functionalisation of the hydroxy-polymer provided amine and thiol resins. The versatility of the amine-polymer was demonstrated in the synthesis of *N*-terminal peptide aldehydes, *via* on-resin tetrapeptide construction and periodate cleavage, followed by Wittig and Horner-Wadsworth-Emmons-type reactions yielding peptide isosteres (2 examples, yields 40-64%). Synthesis of a glalactopyranosyl-peptide is also reported (yield 55%). Furthermore, enzymatic proteolytic cleavage of a resin-bound decapeptide on treatment with 27 kDa protease subtilisin BNP' is reported.

J. Rademann, M. Grøtli, M. Meldal and K. Bock, *J. Am. Chem. Soc.*, 1999, **121**, 5459.

Stereocontrolled solution and solid phase enolate alkylations and hydroxylations: generation of three and four contiguous stereogenic carbon atoms in acyclic systems

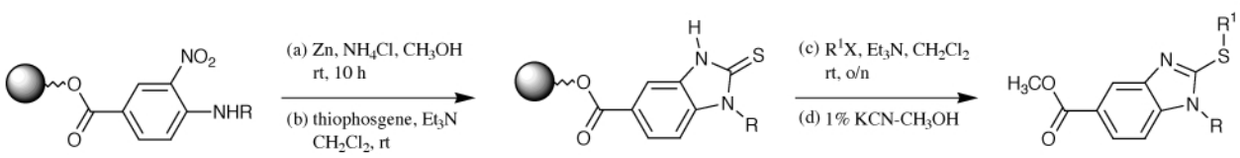


3 steps from Wang resin

4 examples (average yield 75% for 2 steps). Further examples of enolate hydroxylation (yield 70%) and polypropionate synthesis (yield 92%), on solid support, are described. 3 examples of enolate alkylations (yields 82-86%) and 1 example of an aldol-type condensation (yield 64%), in solution, are also described.

S. Hanessian, J. Ma and W. Wang, *Tetrahedron Lett.*, 1999, **40**, 4631.

Rapid parallel liquid-phase synthesis of benzimidazoles

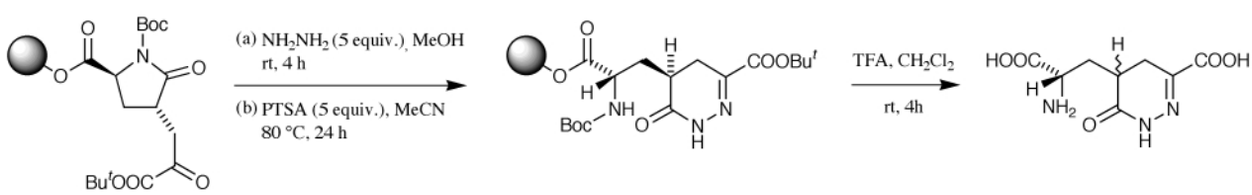


Soluble PEG resin

12 examples (yields 64-92%, HPLC purity 70-94%).

C-M. Yeh and C-M. Sun, *Synlett*, 1999, 810.

Synthesis of inhibitors of late enzymes in the bacterial pathway to lysine

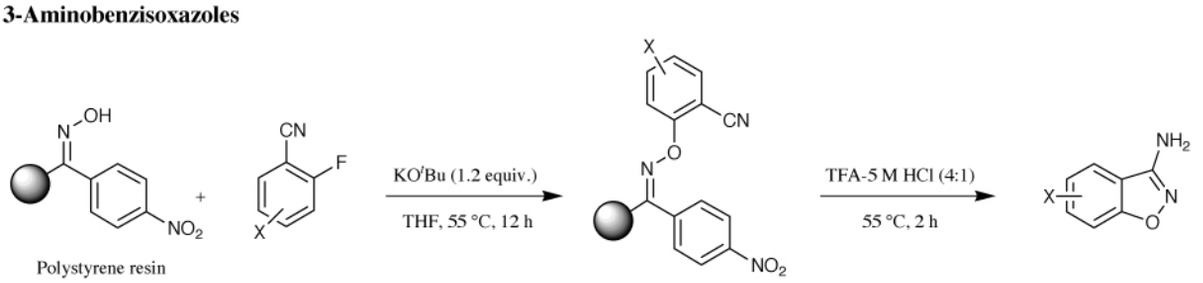


1 step from wang resin

1 example is reported. Various solution-phase synthesis of late enzyme inhibitors of lysine are also reported (8 examples, yields 42-100%).

M. Steger and D. W. Young, *Tetrahedron*, 1999, **55**, 7935.

3-Aminobenzisoxazoles

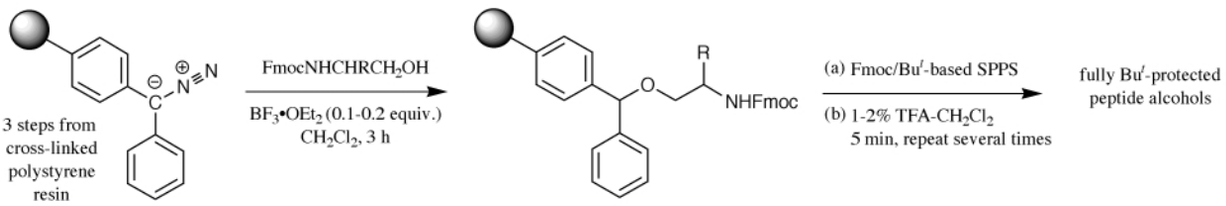


Polystyrene resin

12 examples (yields 55-86%, HPLC purity 79->96%).

S. D. Lepore and M. R. Wiley, *J. Org. Chem.*, 1999, **64**, 4547.

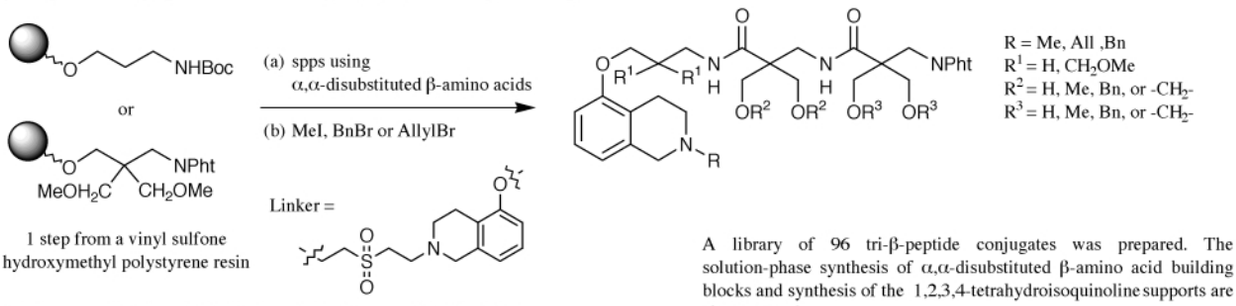
Synthesis of fully protected peptide alcohols



M. Mergler, F. Dick, J. Gosteli and R. Nyfeler, *Tetrahedron Lett.*, 1999, **40**, 4663.

11 examples (yields 42-90%).

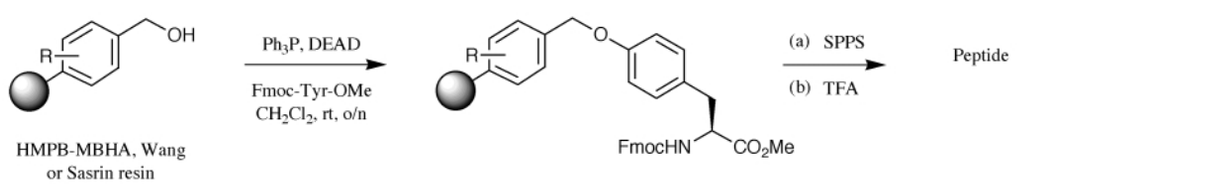
β-Peptide conjugates of *N*-2-alkyl-1,2,3,4-tetrahydroisoquinolines



P. Heinonen, P. Virta and H. Lönnberg, *Tetrahedron*, 1999, **55**, 7613.

A library of 96 tri-β-peptide conjugates was prepared. The solution-phase synthesis of α,α-disubstituted β-amino acid building blocks and synthesis of the 1,2,3,4-tetrahydroisoquinoline supports are also reported.

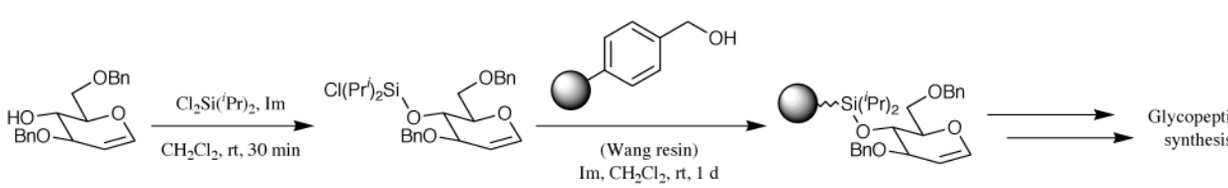
Tyrosine-containing cyclic peptides



C. Cabrele, M. Langer and A. G. Beck-Sickinger, *J. Org. Chem.*, 1999, **64**, 4353.

A new technique for the synthesis of peptides *via* attachment of the amino acid side chain to solid-phase is reported, and demonstrated by the synthesis of 9 linear and cyclic Tyrosine-containing peptides.

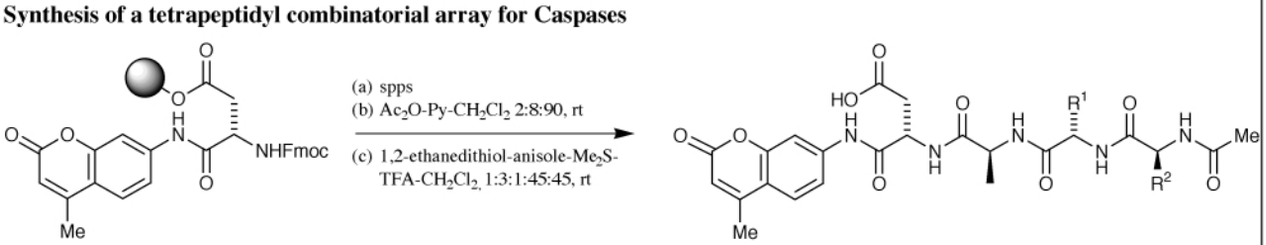
A new polymer supported silylene linking method for hindered hydroxy-bearing systems



K. A. Savin, J. C. G. Woo and S. J. Danishefsky, *J. Org. Chem.*, 1999, **64**, 4183.

A new strategy for the attachment of sterically hindered alcohols to solid support is reported, and illustrated by the synthesis of a glycopeptide.

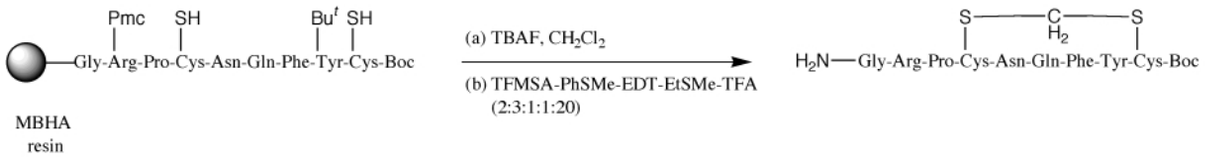
Synthesis of a tetrapeptidyl combinatorial array for Caspases



D. Lee, J. I. Adams, M. Brandt, W. E. DeWolf, Jr., P. M. Keller and M. A. Levy, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1667.

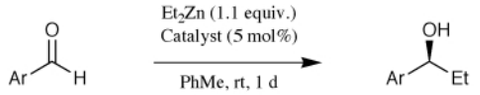
A 100-member array was synthesised.

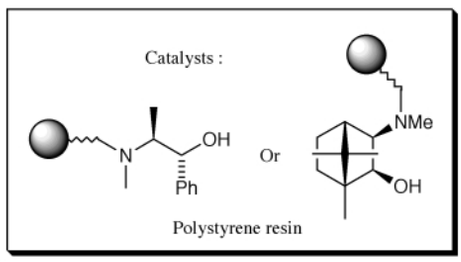
Synthesis and biological activities of [Arg^8]-Vasopressin methylenedithioether



M. Ueki, T. Ikeo, M. Iwadate, T. Asakura, M. P. Williamson and J. Slaninova, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1767.

Polymer supported catalysts for the enantioselective addition of diethylzinc to aldehydes

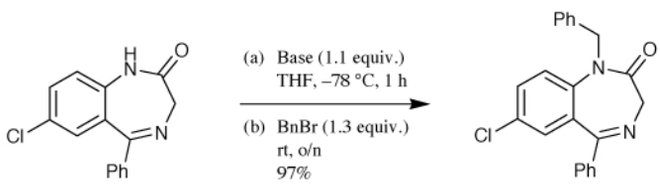


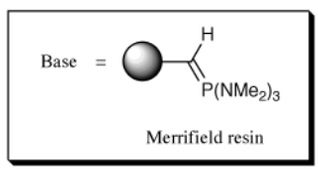


D. W. L. Sung, P. Hodge and P. W. Stratford, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1463.

3 examples of the addition of diethylzinc to aldehydes (yields 81-94%, ee = 81-98%) are described.

A supported phosphorus ylide as a strong neutral Brønsted base

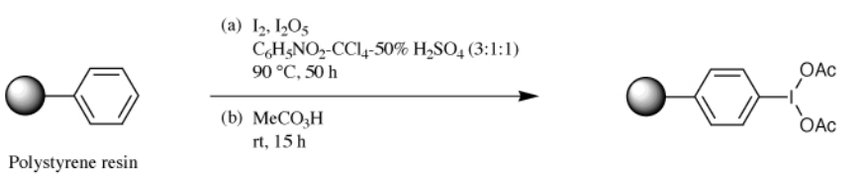




S. Goumri-Magnet, O. Guerret, H. Gornitzka, J. B. Cazaux, D. Bigg, F. Palacios and G. Bertrand, *J. Org. Chem.*, 1999, **64**, 3741.

Preparation of the supported ylide and one example of its use as a strong base are reported.

Polymer-supported phenyliodine(III) diacetate

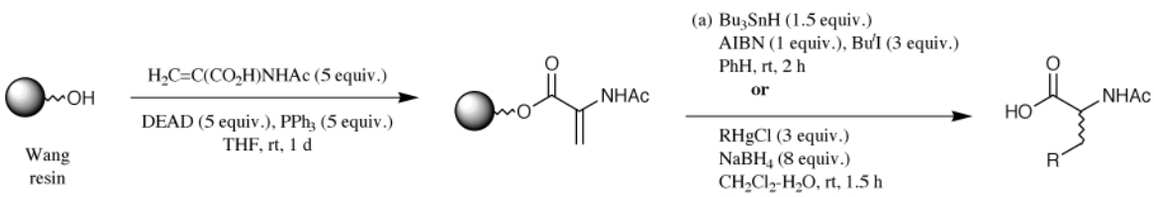


Polystyrene resin

Preparation of the title resin and the use in a variety of oxidation reactions are described, including 4 examples of the oxidation of thiophenols to disulfides (yields 89-93%) and 3 examples of the selective oxidation of sulfides to sulfoxides (yields 65-80%).

G.-P. Wang and Z.-C. Chen, *Synth. Commun.*, 1999, **29**, 2859.

α-Amino acids



A.-M. Yim, Y. Vidal, P. Viallefont and J. Martinez, *Tetrahedron Lett.*, 1999, **40**, 4535.

3 examples (yields 49-60%).