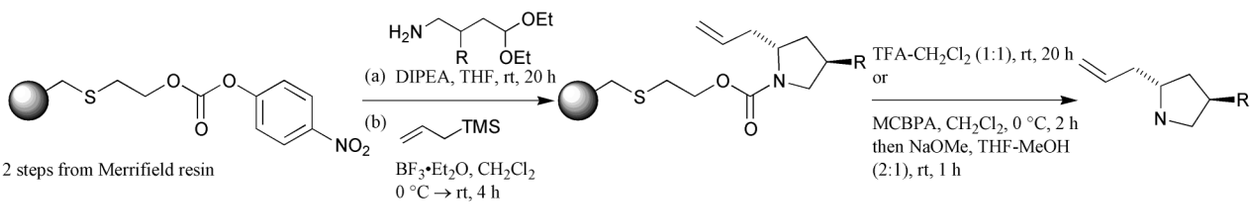
Perkin 1 Abstracts: Solid Phase Organic Synthesis

Fabrice Anizon,[a] Jennifer Delaney,[a] Andrew Gunn,[a] Hassan Mamdani,[a] Catherine McCusker,[a] Fiona McKerlie[b] and Tanya Wildman[a]

[a] *Department of Chemistry, Leeds University, Leeds, UK LS2 9JT*
[b] *Department of Chemistry, Glasgow University, 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.

Linkers for *N*-acyliminium ion chemistry. ***Linker***

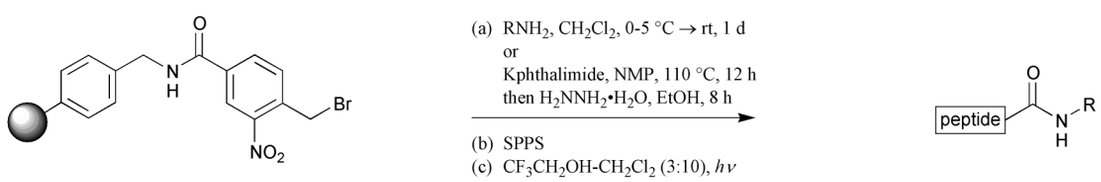


2 steps from Merrifield resin

J. H. van Maarseveen, W. J. N. Meester, J. J. N. Veerman, C. G. Kruse, P. H. H. Hermkens, F. P. J. T. Rutjes and H. Hiemstra, *J. Chem. Soc., Perkin Trans. 1*, 2001, 994.

4 examples (yields 33-73%). Preparation of the 2-thioethyl linker and its stability towards acid and base are reported. Allyl and 2-sulfonylethyl linkers are also prepared and evaluated.

A photolabile linker for peptide synthesis. ***Linker***

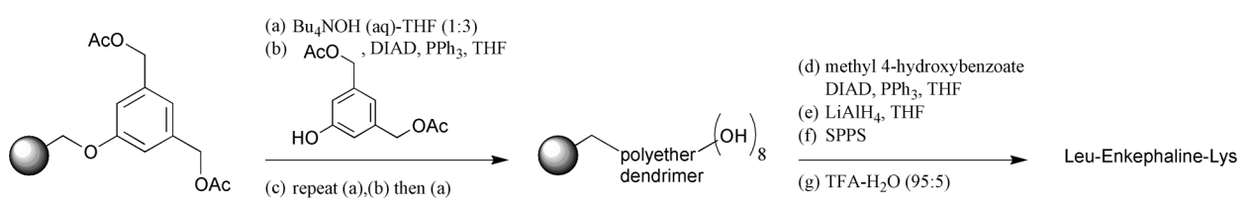


3 steps from PS resin

K. S. Kumar, M. Roice and V. N. Rajasekharan Pillai, *Tetrahedron*, 2001, **57**, 3151.

10 examples (yields 64-80%). Preparation of *C*-terminal peptide acids *via* a similar route (5 examples, yields 65-75%) is also reported.

An aryl ether dendrimer as a linker to increase resin loading. ***Linker***

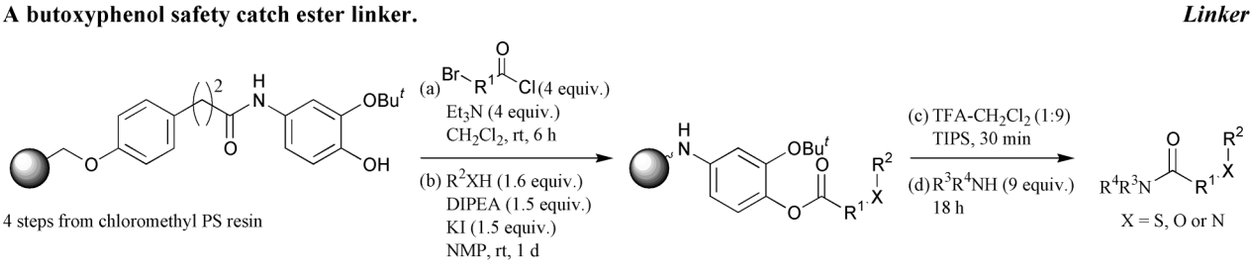


2 steps from Merrifield resin

A. Basso, B. Evans, N. Pegg and M. Bradley, *Chem. Commun.*, 2001, 697.

1 example (yield 66%). The illustrated polymer-supported polyether dendrimer has a loading three times greater than the starting hydroxymethyl resin.

A butoxyphenol safety catch ester linker. ***Linker***



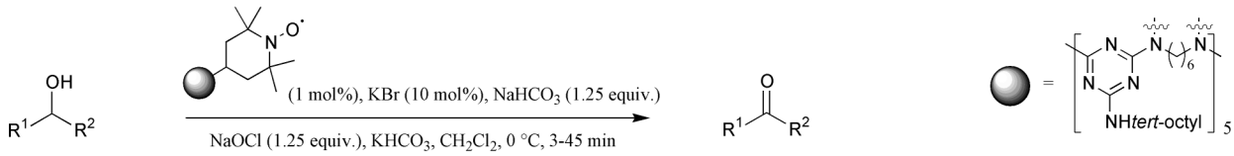
4 steps from chloromethyl PS resin

C. L. Beech, J. F. Coope, G. Fairley, P. S. Gilbert, B. G. Main and K. Plé, *J. Org. Chem.*, 2001, **66**, 2240.

10 examples (yields 0, 39-100%, HPLC purity 52-97%). The illustrated linker is compared, in kinetic studies, to other commercially available linkers and resins with superior results.

This journal is © The Royal Society of Chemistry 2001

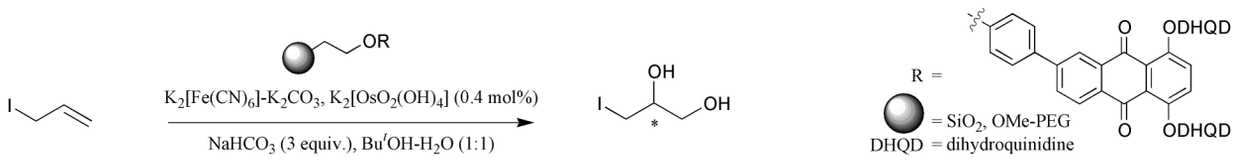
Polymer-supported TEMPO (PIPO) as a heterogeneous catalyst for oxidation of alcohols. ***Catalyst***



2 examples (yields 99%). Solvent-free conditions (yield 99%) and PIPO-CuCl catalysis of the aerobic oxidation of benzyl alcohol are also reported.

A. Dijksman, I. W. C. E. Arends and R. A. Sheldon, *Synlett*, 2001, **1**, 102.

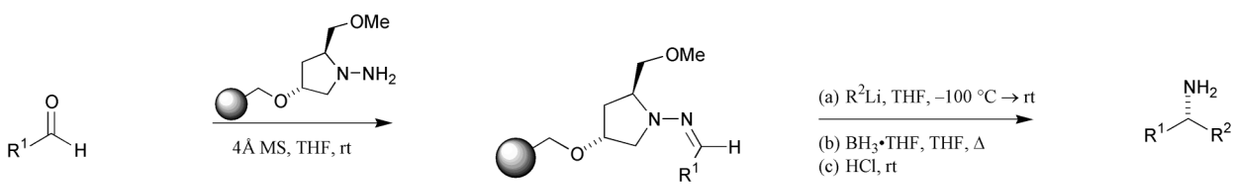
Asymmetric dihydroxylations using polymer-supported alkaloids with an anthraquinone core. ***Catalyst***



4 examples (yields 52-65%, %ee 73-80%). Asymmetric dihydroxylation of indene *via* a similar route (5 examples, yield 72-84%, %ee 47-57%) and preparation of the alkaloid ligand and a related dihydroquinine-based ligand are also reported.

C. Bolm and A. Maischak, *Synlett*, 2001, **1**, 93.

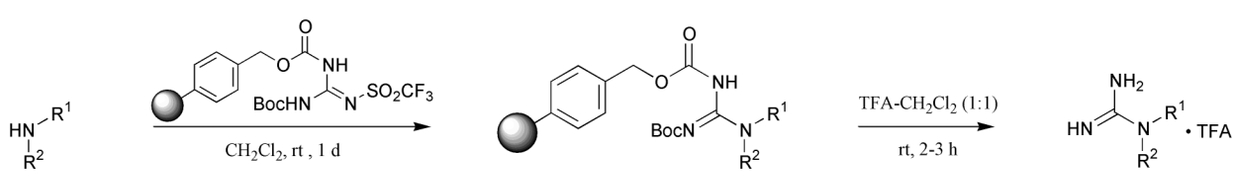
Polymer-supported hydrazine for asymmetric synthesis of α-branched primary amines. ***Reagent***



4 examples (yields 24-43%, %ee 66-83%). Preparation of the illustrated chiral polymer-supported hydrazine and a second, which provides the opposite amine stereochemistry (3 examples, yield 28-51%, %ee 50-86%) are also reported.

D. Enders, J. H. Kirchhoff, J. Köbberling and T. H. Peiffer, *Org. Lett.*, 2001, **3**, 1241.

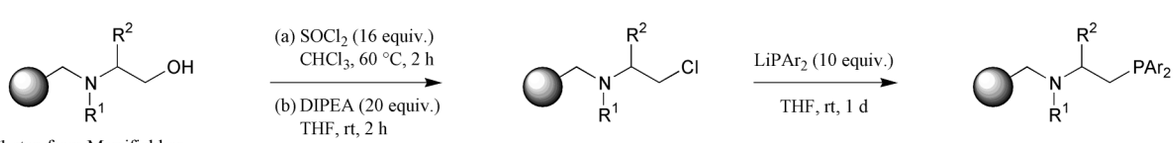
A reagent for *N,N*-disubstituted guanidine preparation. ***Reagent***



8 examples (yields 33-100%). Preparation of the polymer-supported guanidinylating reagent is also reported.

C. W. Zapf, C. J. Creighton, M. Tomioka and M. Goodman, *Org. Lett.*, 2001, **3**, 1133.

β-Aminophosphine ligands. ***Reagent***



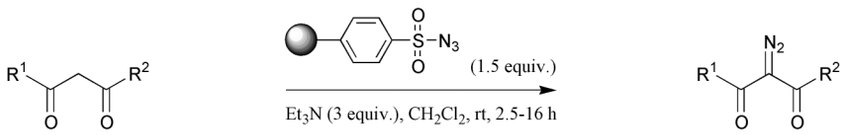
1 step from Merrifield or Wang bromo resin

5 examples (sample yields 91, 95%).

A. Mansour and M. Portnoy, *J. Chem. Soc., Perkin Trans. 1,* 2001, 952.

This journal is © The Royal Society of Chemistry 2001

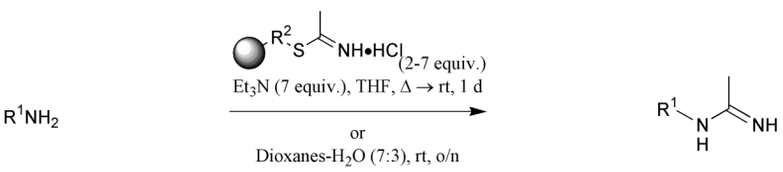
Benzenesulfonyl azide: a diazo transfer reagent. ***Reagent***



G. M. Green, N. P. Peet and W. A. Metz, *J. Org. Chem.*, 2001, **66**, 2509.

7 examples (yields 0, 63-98%). Preparation of the diazo transfer reagent (3 steps from PS resin) is also reported.

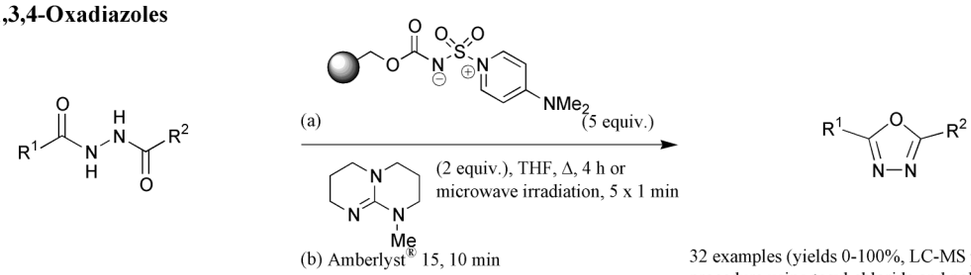
Thioimidates as reagents for the synthesis of amidines. ***Reagent***



A. Ursini, M. Delpogetto, G. Guercio, A. Perboni and T. Rossi, *Synlett*, 2001, **3**, 388.

3 examples (yields 60-84%). Preparation of the thioimidates (1 step from Argopore, chloromethyl PS and Wang bromo resin) is also reported.

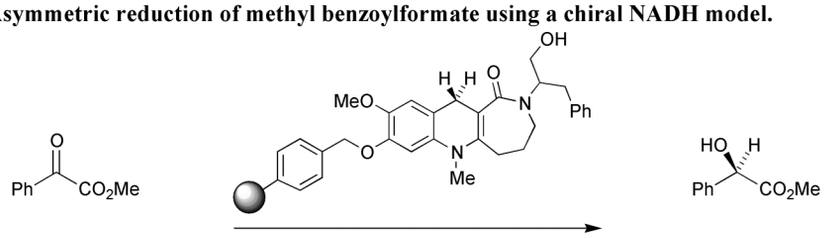
1,3,4-Oxadiazoles ***Reagent***



C. T. Brain and S. A. Brunton, *Synlett*, 2001, **3**, 382.

32 examples (yields 0-100%, LC-MS purity 17-100%). An alternative procedure using tosyl chloride and polymer-supported phosphazene base (P-BEMP) (32 examples, yields 38-100%, LC-MS purity 33-100%) and the preparation of the polymer-supported dehydrating reagent (2 steps from hydroxymethyl PS resin) are also reported.

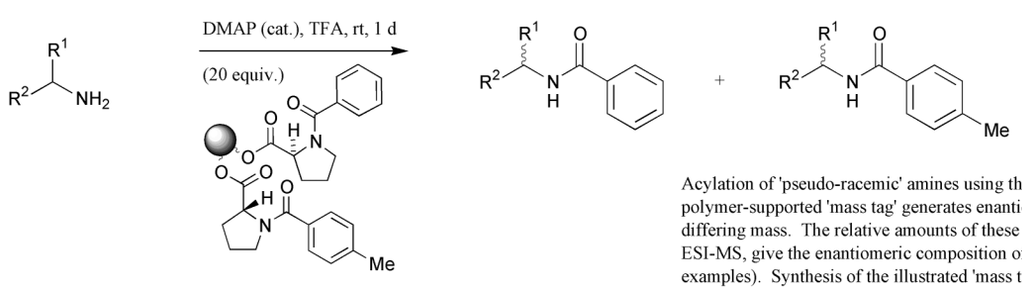
Asymmetric reduction of methyl benzoylformate using a chiral NADH model. ***Reagent***



C. Vitry, J.-L. Vasse, G. Dupas, V. Levacher, G. Quéguiner and J. Bourguignon, *Tetrahedron*, 2001, **57**, 3087.

1 example (yield 50%, %ee 72%) and 2 further asymmetric methyl benzoylformate reductions, using 2 similar solution-phase NADH models (yields 50, 100%, %ee 84, 95%). Preparation of the illustrated polymer-supported NADH model and 2 solution-phase NADH models, are also reported.

Measurement of %ee of amines by mass spectrometry following kinetic resolution with a chiral acylating agent. ***Reagent***

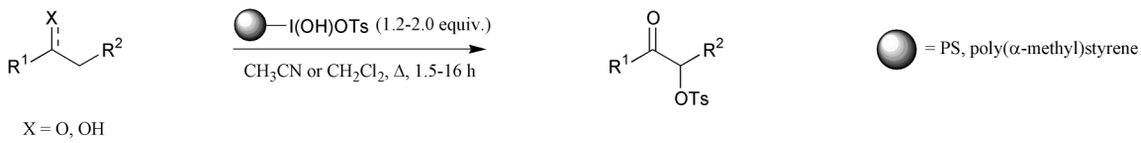


D. D. Díaz, S. Yao and M. G. Finn, *Tetrahedron Lett.*, 2001, **42**, 2617.

Acylation of 'pseudo-racemic' amines using the illustrated polymer-supported 'mass tag' generates enantiopure amide products of differing mass. The relative amounts of these products, measured by ESI-MS, give the enantiomeric composition of the starting substrate (8 examples). Synthesis of the illustrated 'mass tag' (4 steps from aminomethyl PS resin) is also reported.

This journal is © The Royal Society of Chemistry 2001

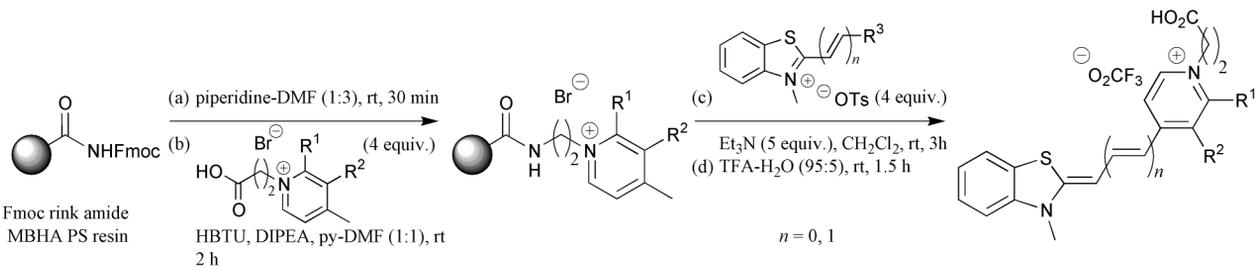
Poly[4-hydroxy(tosyloxy)iodo]styrenes as tosyloxylation reagents. ***Reagent***



S. Abe, K. Sakuratani and H. Togo, *Synlett*, 2001, **1**, 22.

14 examples (yields 33-94%). Recycling of the reagents is also reported.

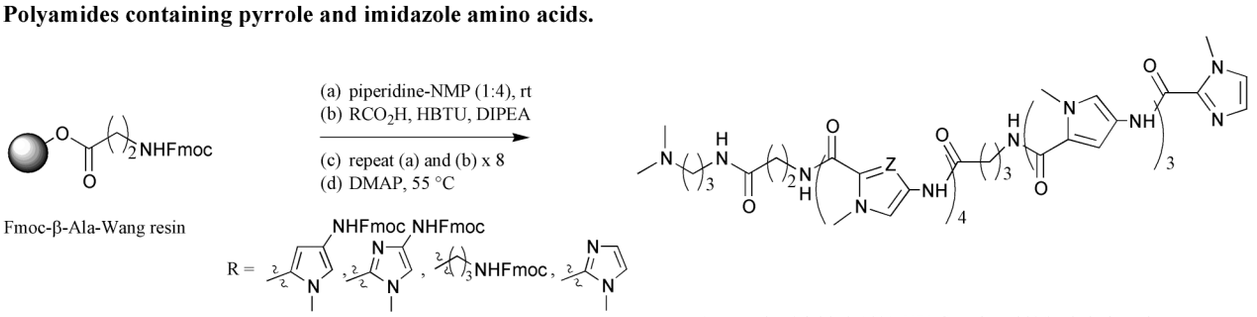
Asymmetric cyanine dyes.



J. Isacsson and G. Westman, *Tetrahedron Lett.*, 2001, **42**, 3207.

4 examples (no yields or purities given). Synthesis of a 'light up' probe *via* a similar route is also reported.

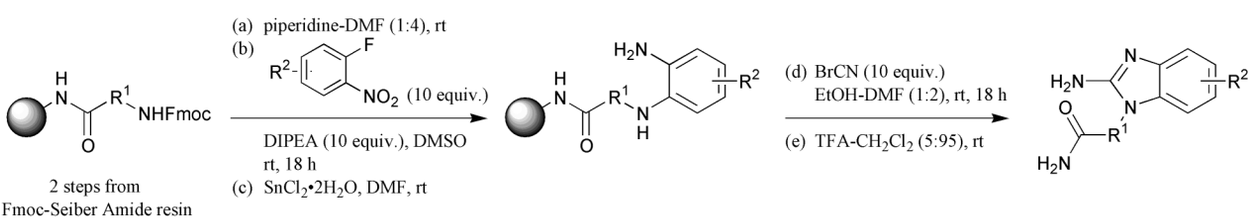
Polyamides containing pyrrole and imidazole amino acids.



N. R. Wurtz, J. M. Turner, E. E. Baird and P. B. Dervan, *Org. Lett.*, 2001, **3**, 1201.

2 examples (yields 9-38%, HPLC purity >98%). Solution-phase preparation of Fmoc-py and Fmoc-Im acid is also reported.

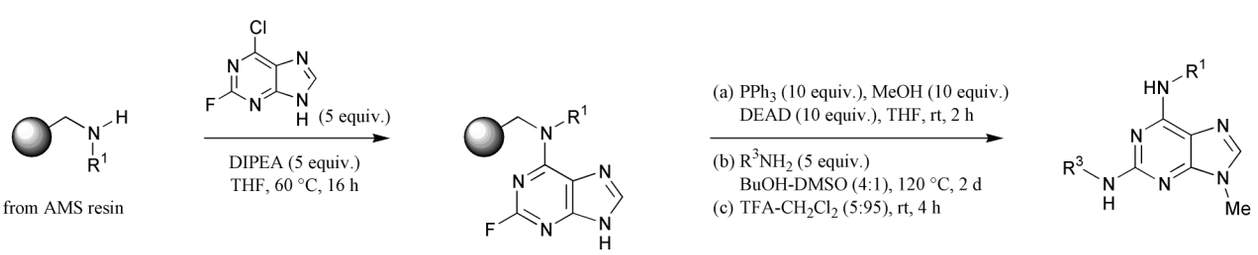
2-Aminobenzimidazoles



J. Lee, A. Doucette, N. S. Wilson and J. Lord, *Tetrahedron Lett.*, 2001, **42,** 2635.

9 examples (yields 84-99%, HPLC purity 69-98%, %ee 98%).

2,6,9-Trisubstituted purines.

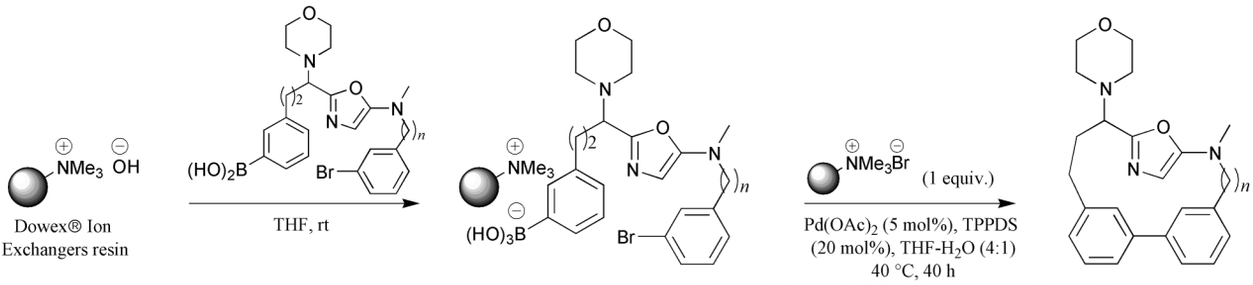


P. H. Dorff and R. S. Garigipati, *Tetrahedron Lett.*, 2001, **42,** 2771.

4 examples (yields 54-100%, ELSD purity 70-100%).

This journal is © The Royal Society of Chemistry 2001

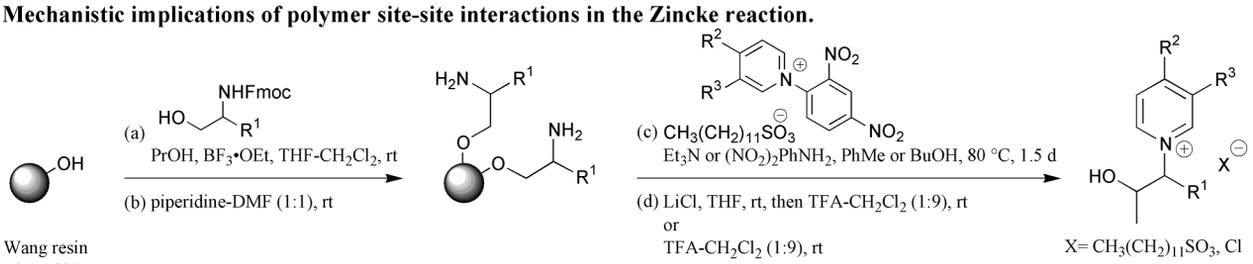
Macrocyclisation *via* Suzuki–Miyaura coupling using 'resin-capture-release' methodology.



V. Lobrégat, G. Alcaraz, H. Bienaymé and M. Vaultier, *Chem. Commun.*, 2001, 817.

3 examples (yields 16-22%). Intermolecular Suzuki–Miyaura reactions (6 examples, yields 22-86%) are also reported.

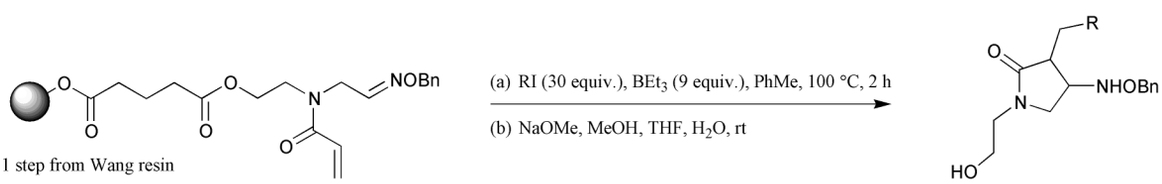
Mechanistic implications of polymer site-site interactions in the Zincke reaction.



M. Eda and M. J. Kurth, *Chem. Commun.*, 2001, 723.

2 examples (yields 1-91%). Based on results from various resin loadings and reaction conditions, it is concluded that the solid-phase Zincke reaction proceeds *via* a proton transfer mechanism, obviating the need for covalent bond site-site interactions.

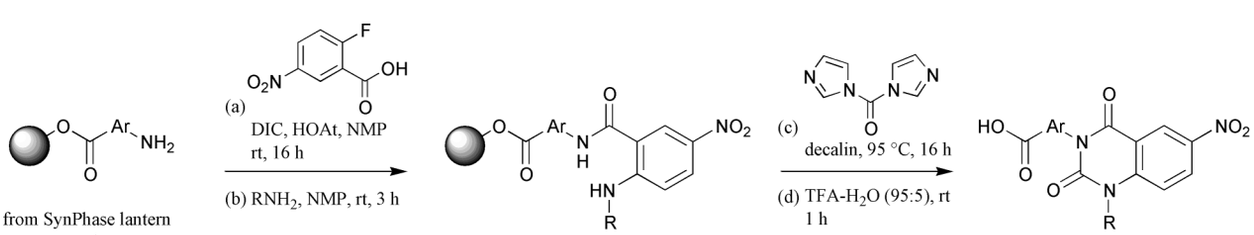
Tandem radical addition–cyclisation of oxime ethers.



H. Miyabe, K. Fujii, H. Tanaka and T. Naito, *Chem. Commun.*, 2001, 831.

4 examples (yields 54-69%). Stereoselective application of the reaction (3 examples, yields 50-92%, %de 78%) is also reported.

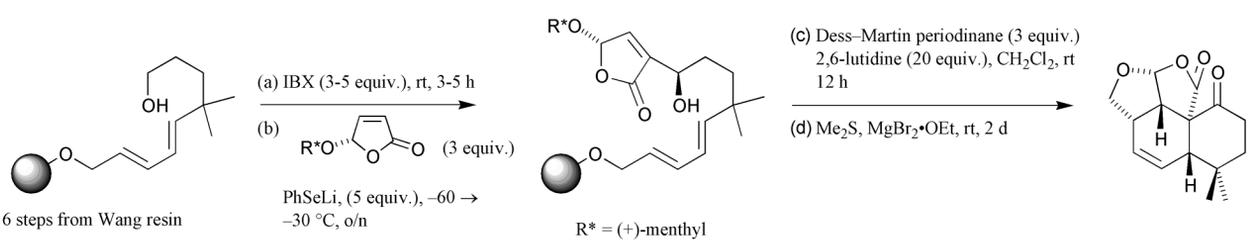
Quinazoline-2,4-diones



S. Makino, N. Suzuki, E. Nakanishi and T. Tsuji, *Synlett*, 2001, **3**, 333.

17 examples (yields 44-98%, HPLC purity 83-95%). Preparation of an oligomer with 4 quinazoline-2,4-dione units (yield 22%) is also reported.

Synthesis of a marasmane building block.

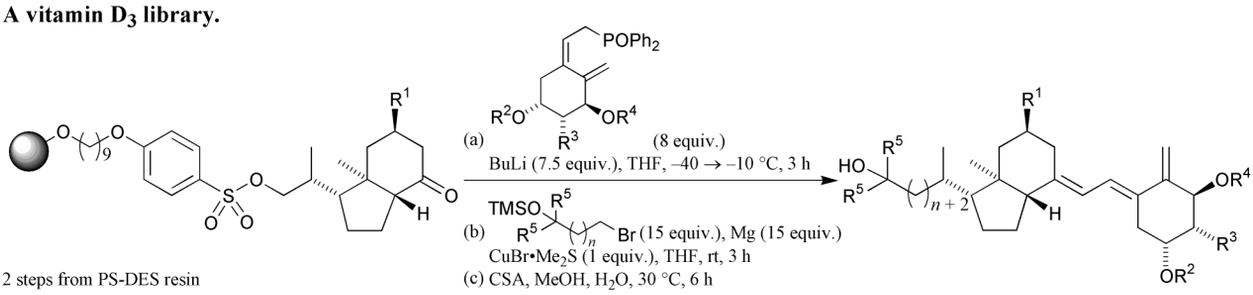


U. Reiser and J. Jauch, *Synlett*, 2001, **1**, 90.

1 example (no yield or purity reported).

This journal is © The Royal Society of Chemistry 2001

A vitamin D_3 library.

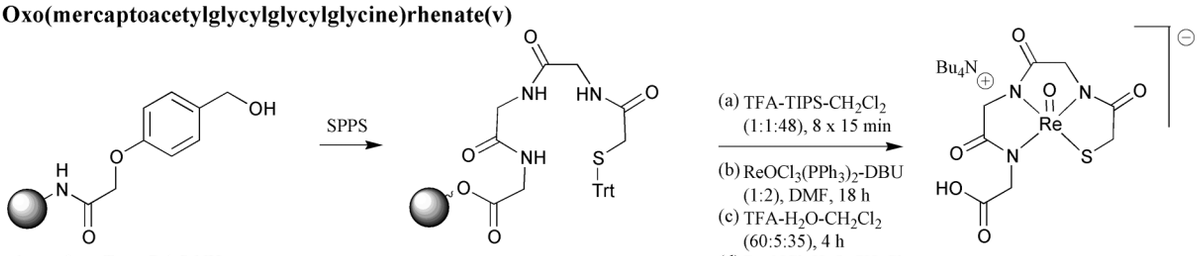


2 steps from PS-DES resin

Preparation of a 72-member library of vitamin D_3 analogues is described (sample yield 47%). Solution-phase synthesis of various A ring moieties (7 examples) is also reported .

I. Hijikuro, T. Doi and T. Takahashi, *J. Am. Chem. Soc.*, 2001, **123**, 3716.

Oxo(mercaptoacetylglycylglycylglycine)rhenate(v)

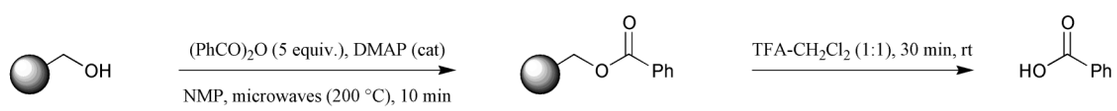


1 step from TentaGel-S-NH_2 or aminomethyl PS resin

HPLC purity 91%. Use of the illustrated polymer-supported bi-functional chelate in labelling experiments is also reported.

J. A. Bravo, A. Gibson, K. Loughran and M. Bradley, *Chem. Commun.*, 2001, 837.

Microwave irradiation of carbodiimide-mediated esterifications.

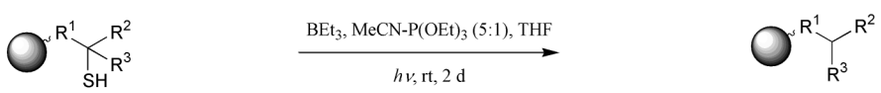


Wang resin

1 example of the illustrated symmetrical anhydride coupling protocol (yield 99%). Reaction times are reduced from days, using conventional coupling conditions at room temperature, to only minutes using microwave irradiation. Details of the unsuitability of the *O*-acylisourea coupling protocol in microwave rate enhancement experiments are also reported.

A. Stadler and C. O. Kappe, *Tetrahedron*, 2001, **57**, 3915.

Photochemical desulfurisation.

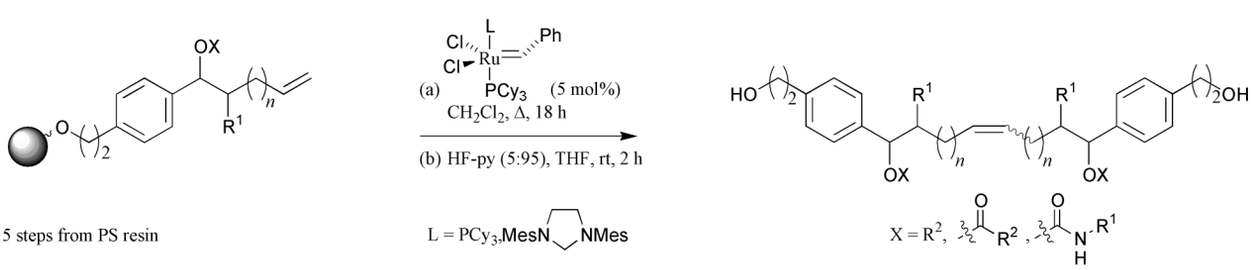


from Wang, Merrifield Rink or MBHA resins

9 examples (sample yields 65-89%).

G. Arsequell, A. González and G. Valencia, *Tetrahedron Lett.*, 2001, **42,** 2685.

Dimeric molecules *via* 'intra-site' olefin cross-metathesis.



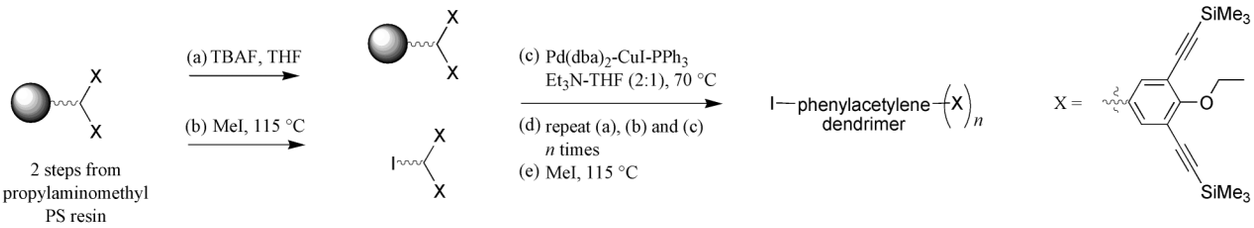
5 steps from PS resin

14 examples (yields 5-98%, *E*:*Z* ratios 1-9:1). Optimisation of the cross-metathesis reaction conditions is also reported.

H. E. Blackwell, P. A. Clemons and S. L. Schreiber, *Org. Lett.*, 2001, **3**, 1185.

This journal is © The Royal Society of Chemistry 2001

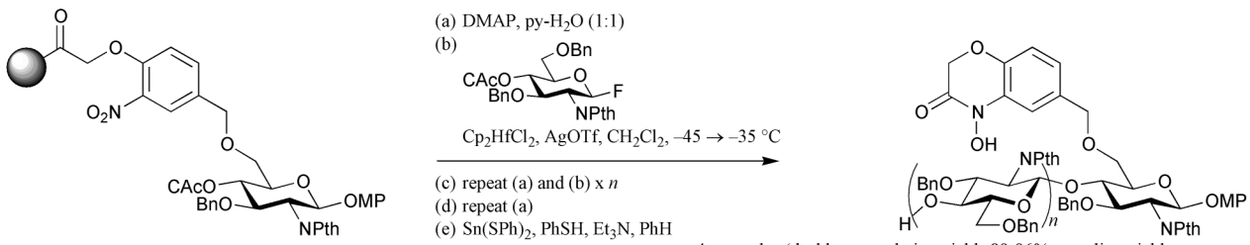
An iterative divergent/convergent strategy for the synthesis of phenylacetylene dendrimers.



C. Chi, J. Wu, X. Wang, X. Zhao, J. Li and F. Wang, *Tetrahedron Lett.*, 2001, **42**, 2181.

1 example (no yield or purity reported).

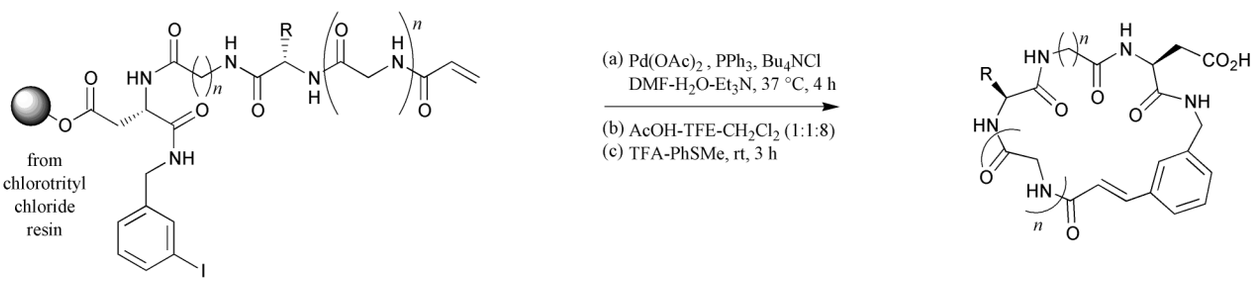
A tag-reporter strategy for oligosaccharide synthesis.



H. Ando, S. Manabe, Y. Nakahara and Y. Ito, *J. Am. Chem. Soc.*, 2001, **123**, 3848.

4 examples (dechloroacetylation yields 89-96%, coupling yields 96-98%). Monitoring of dechloroacetylation and coupling reaction is performed using colouring with *p*-nitrobenzylpyridine-piperidine and MALDI-TOF MS spectra respectively.

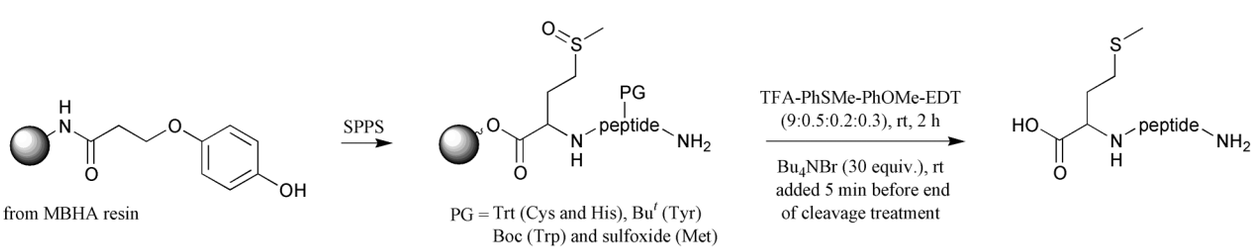
Macrocyclization using the Heck reaction.



K. Akaji, K. Teruya, M. Akaji and S. Aimoto, *Tetrahedron,* 2001, **57**, 2293.

Preparation of 2 split and mix 15-member libraries is reported (yields 9-20%)

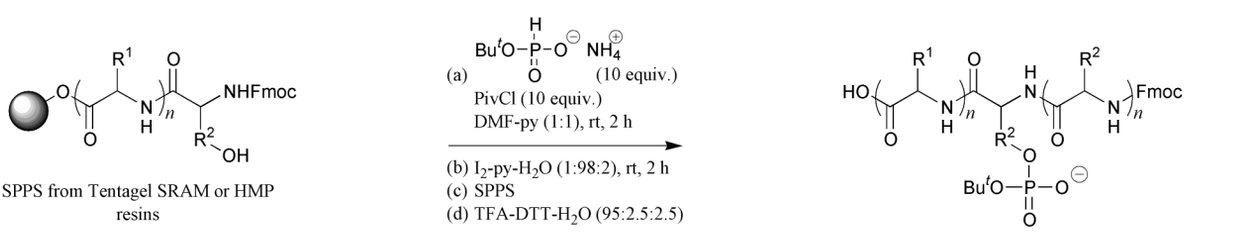
One-pot peptide deprotection and resin cleavage: methionine sulfoxide reduction with Bu_4NBr.



L. Taboada, E. Nicolás and E. Giralt, *Tetrahedron Lett.*, 2001, **42**, 1891.

6 examples (no yields or purity reported).

Phosphopeptides.

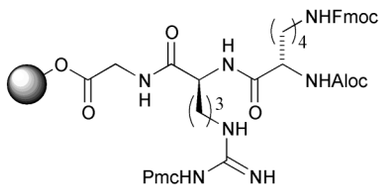


Z. Kupihár, Z. Kele and G. K. Tóth, *Org. Lett.*, 2001, **3**, 1033.

2 examples (no yields or purities reported). Preparation of free amine phosphopeptides *via* a similar route (2 examples) is also reported.

This journal is © The Royal Society of Chemistry 2001

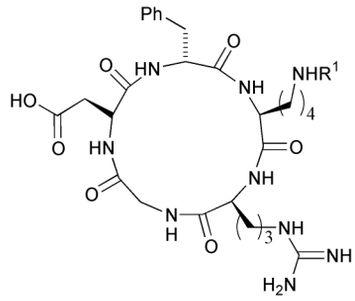
Lysine functionalisation of an RGD based peptide.



SPPS from *o*-chlorotrityl chloride® or Sasrin® resin

(a) piperidine-DMF (1:4)
(b) BocR^1OH (2 equiv.), PyBOP (2 equiv.), DIPEA (5 equiv.)
(c) $Pd(PPh_3)_4$ (10 mol%), $PhSiH_3$ (50 equiv.)

(d) SPPS
(e) TFA-CH_2Cl_2 (1:99)
(f) PyBOP (1.2 equiv.), DIPEA (3 equiv.), DMF
(g) TFA-TIS-H_2O (95:2.5:2.5), Et_2O

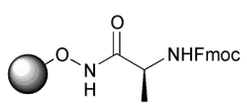


Pmc = 2,2,5,7,8-pentamethylchroman-6-ylsulfonyl

9 examples (yields 60-80%). Cyclisation is performed post-cleavage. A route *via* a solution-phase lysine side chain modification is also reported.

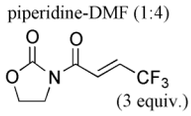
D. Boturyn and P. Dumy, *Tetrahedron Lett.*, 2001, **42,** 2787.

Partially modified retro-ψ[NHCH(CF_3)]-peptidyl hydroxamates.



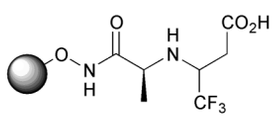
3 steps from Wang resin

(a) piperidine-DMF (1:4)
(b)



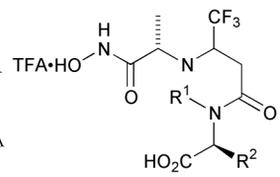
(3 equiv.)
CH_2Cl_2, rt, 3 d

(c) LiOH (1 equiv.), H_2O_2 (4 equiv.), THF-H_2O 0 °C, 2 h



(d) HCl• R^1HN CO_2R^3
HOAt, DIC, TMP-DMAP
DMF, rt

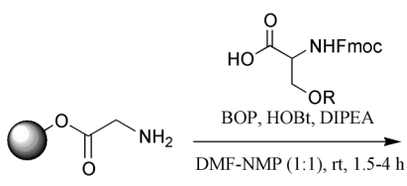
(e) TFA, CH_2Cl_2, rt, 1 h
or
LiOH (4 equiv.), then TFA
CH_2Cl_2, rt, 1 h



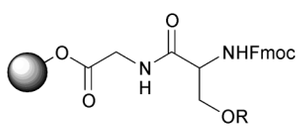
5 examples (sample yields 60-98%, purity 73-96%). Preparation of tetrapeptidyl and tripeptidyl hydroxamates *via* a similar route (3 examples, sample yields 68, 98%, purity, 73-98%) is also reported.

A. Volonterio, P. Bravo and M. Zanda, *Tetrahedron Lett.*, 2001, **42,** 3141.

***O*-Linked glycopeptide enkephalin analogues.**

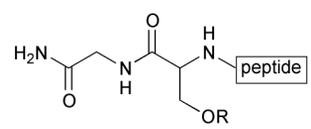


BOP, HOBt, DIPEA
DMF-NMP (1:1), rt, 1.5-4 h



(a) SPPS
(b) H_2NNH_2-MeOH (8:1) rt, 2 h

(c) TFA-CH_2Cl_2-Et_3SiH-H_2O-$PhNH_2$ (180:20:5:5:1), rt, 2 h



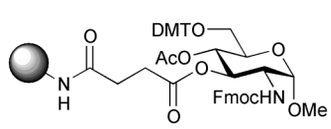
1 step from Fmoc-Gly Rink resin

R = mono-, di-glycoside

11 examples. Post-cleavage cyclisation of Cys -SH groups and solution-phase preparation of *N*-α-Fmoc amino acid glycosides (17 examples, yields 20-99%) are also reported.

S. A. Mitchell, M. R. Pratt, V. J. Hruby and R. Polt, *J. Org. Chem.*, 2001, **66**, 2327.

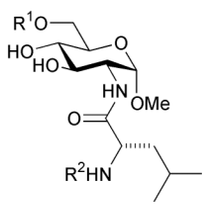
Glycoconjugate biomolecules.



2 steps from tentagel-NH_2 resin

(a) SPPS
(b) Ac_2O-py (1:1), rt, 30 min
or
$CHCl_2CO_2H$-CH_2Cl_2 (2:98)

(c) NH_4OH (conc. aq.), 50 °C, 6 h

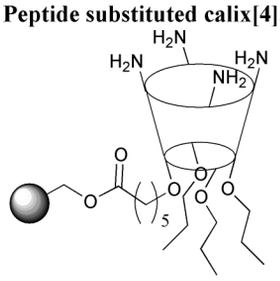


R^1 = $PhC(PhOMe)_2$, H
R^2 = Ac, peptide

2 examples (yields 85, 97%). Preparation of a glyconucleotide (1 example, yield 95%), and a nucleo-glyco-amino acid (1 example, yield 93%) *via* a similar route, and the polymer-supported 2-amino sugar is also reported.

G. Di Fabio, A. De Capua, L. De Napoli, D. Montesarchio, G. Piccialli, F. Rossi and E. Benedetti, *Synlett*, 2001, **3**, 341.

Peptide substituted calix[4]arene.

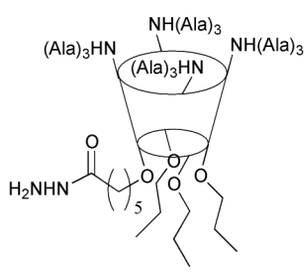


3 steps from amino-funtionalised ArgoPore beads

(a) Fmoc-Ala, HATU, DIPEA, DMF, rt
(b) Piperidine, DMF, rt

(c) repeat (a) and (b) x 2
(d) H_2NNH_2, DMF, rt

= calix[4]arene



1 example (no yield or purity reported). Solution-phase synthesis of the calixarene scaffold is also reported.

S. B. Shuker, J. Esterbrook and J. Gonzalez, *Synlett*, 2001, **2**, 210.

This journal is © The Royal Society of Chemistry 2001