Perkin 1 Abstracts: Solid Phase Organic Synthesis

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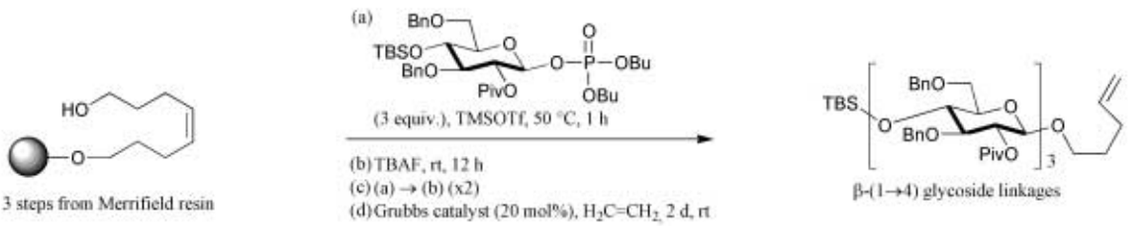
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

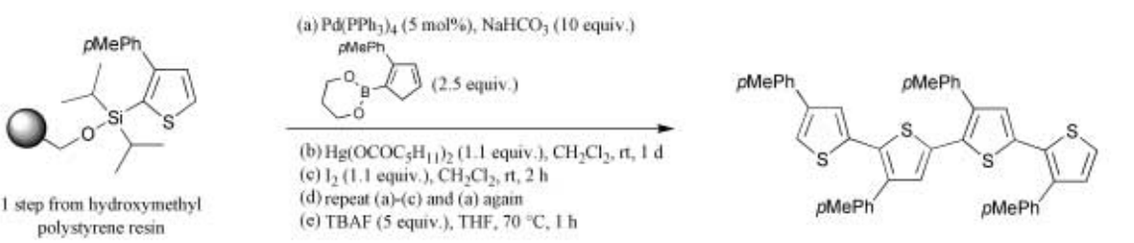
Octenediol linker: application to oligosaccharide synthesis ***Linker***



R. B. Andrade, O. J. Plante, L. G. Melean and P. H. Seeberger, *Org. Lett.*, 1999, **1**, 1811.

1 example (yield 53%). Preparation of a β-(1→6) & an α-(1→2)-linked trisaccharide, a pentasaccharide and a heptasaccharide *via* similar routes is also reported (yields 9-76%).

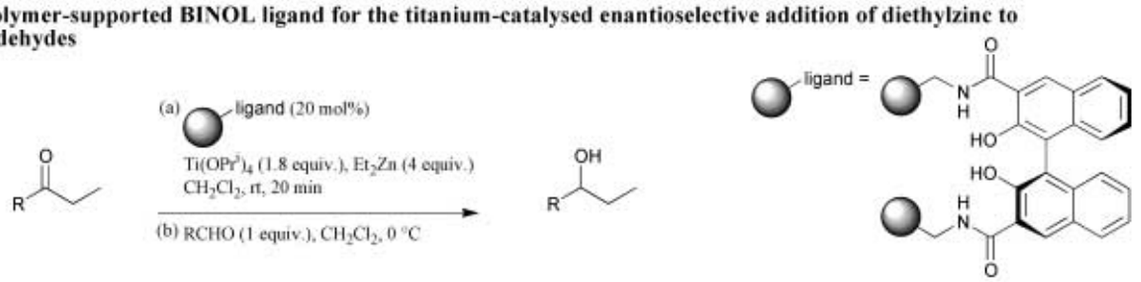
Synthesis of an oligo(3-arylthiophene) *via* a traceless silyl linker ***Linker***



C. A. Briehn, T. Kirschbaum and P. Bäuerle, *J. Org. Chem.*, 2000, **65**, 352.

1 example (yield 48%). Solution-phase oligomer synthesis (yield 91%) and synthesis of monomeric thiophene building blocks is also reported.

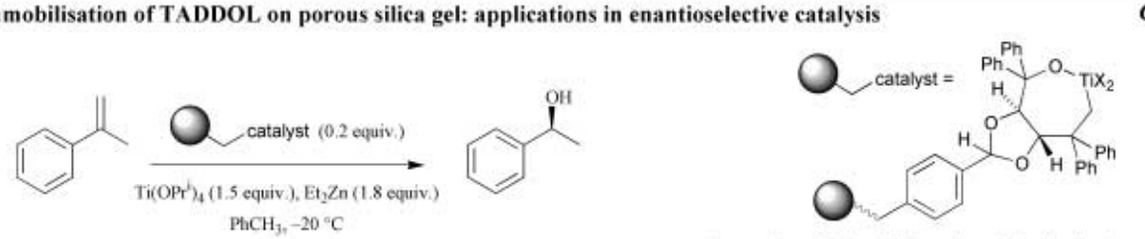
Polymer-supported BINOL ligand for the titanium-catalysed enantioselective addition of diethylzinc to aldehydes ***Ligand***



X.-W. Yang, J.-H. Sheng, C.-S. Da, H.-S. Wang, W. Su, R. Wang and A. S. C. Chan, *J. Org. Chem.*, 2000, **65**, 295.

19 examples (yields 52-97%, ee 57-99%). Preparation of the illustrated ligand from aminomethylated polystyrene resin is also reported.

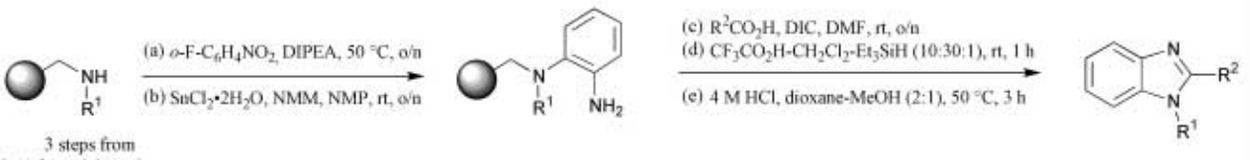
Immobilisation of TADDOL on porous silica gel: applications in enantioselective catalysis ***Catalyst***



A. Heckel and D. Seebach, *Angew. Chem., Int. Ed.*, 2000, **39**, 163

4 examples of Et_2Zn addition to benzaldehyde using 4 catalysts with the illustrated general structure (but with differing loading and pore sizes) are reported (yields >95%, ee 87-98%). Synthesis of the catalysts and their use in a [3+2] cycloaddition is also reported (yield 91%, de 83%, ee 85%).

Traceless synthesis of benzimidazoles

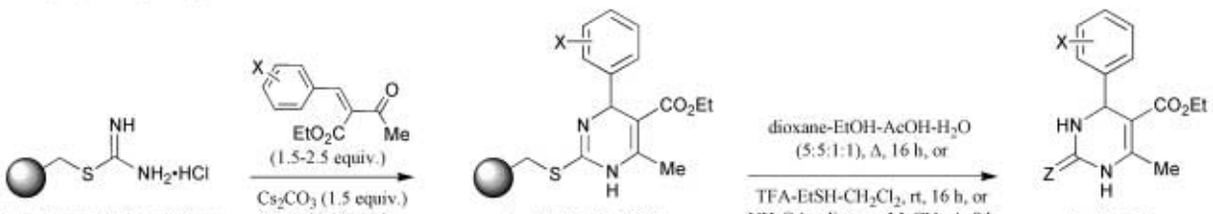


3 steps from 2-(4-formyl-3-methoxy-phenoxy)ethyl polystyrene resin

9 examples (yields 77-98%, HPLC purities 79-95%). Preparation of 4 5-(benzimidazol-2-yl)benzimidazoles *via* a similar route is also reported (yields 88-95%, HPLC purity 90-95%).

A. Mazurov, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 67.

4-Aryl-3,4-dihydropyrimidines



1 step from chlorinated Wang resin

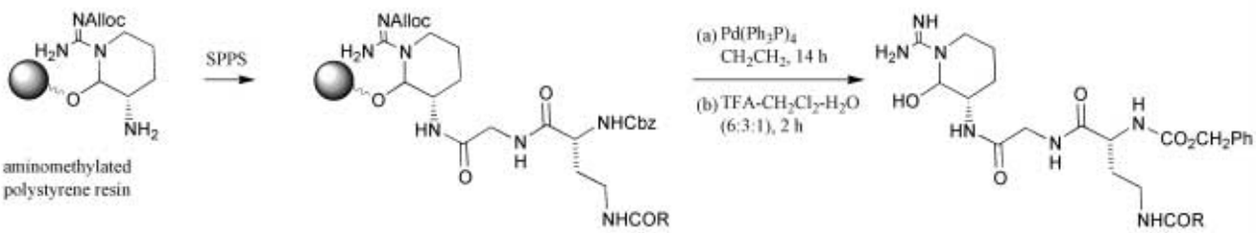
X = H, 3-NO_2, 2,3-Cl_2 2-CF_3 or H

Z = O or S

9 examples (yields 59-71%). Preparation of 3 other dihydropyrimidines *via* a similar route is also reported (yields 41-55%).

C. Oliver Kappe, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 49.

Factor Xa inhibitors.

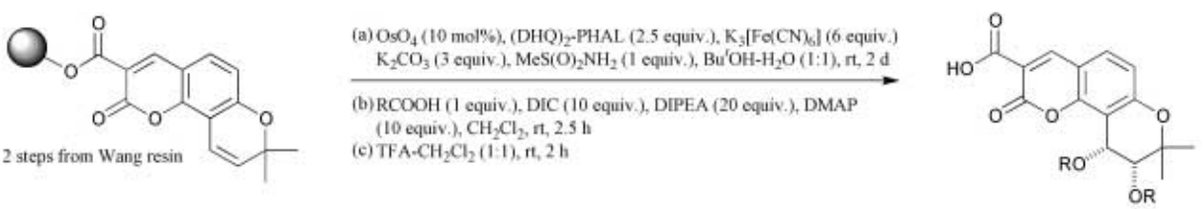


aminomethylated polystyrene resin

Preparation and biological evaluation of the illustrated 6-member library and of another similar 8-member library is reported (yields 41-89%, HPLC purity 90-99%).

J. Z. Ho, O. E. Levy, T. S. Gibson, K. Nguyen and J. E. Semple, *Bioorg. Med. Chem. Lett.*, 2000, **9**, 3459.

(3'*R*, 4'*R*)-Di-*O*-*cis*-acyl-3-carboxy khellactones

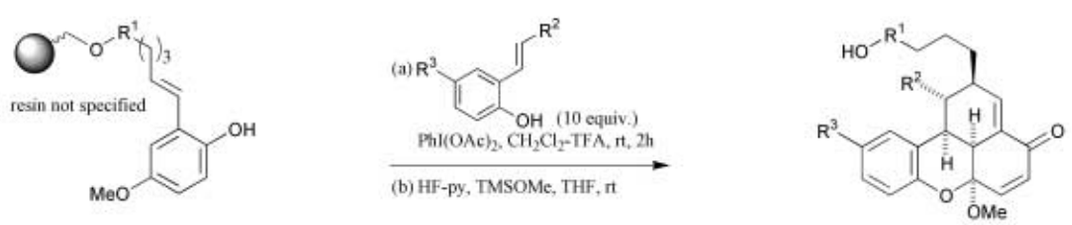


2 steps from Wang resin

6 examples (yields 23-43%, ee >91%).

Y. Xia, Z.-Y. Yang, A. Brossi and K.-H. Lee, *Org. Lett.*, **1**, 2113.

Biomimetic synthesis of carpanone-like molecules

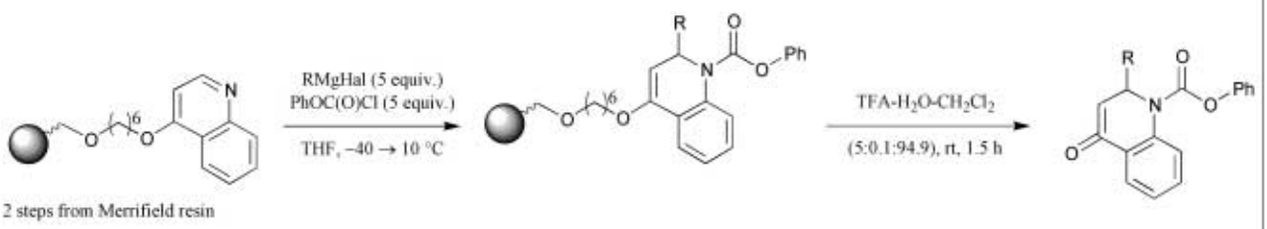


resin not specified

6 examples (yields 55-81%).

C. W. Lindsley, L. K. Chan, B. C. Goess, R. Joseph and M. D. Shair, *J. Am. Chem. Soc.*, 2000, **122**, 422.

2,3-Dihydroquinolin-4-ones

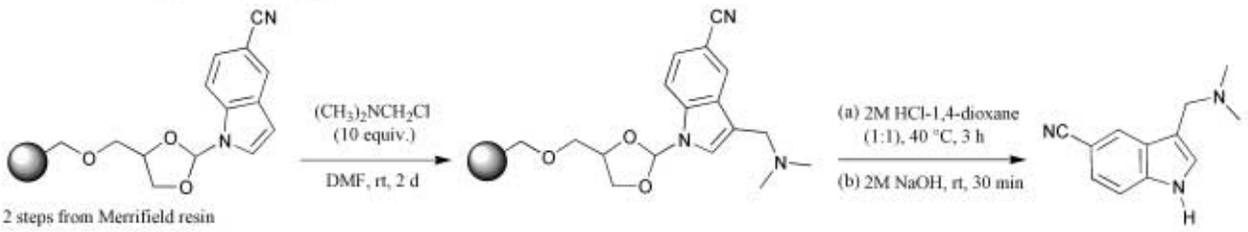


2 steps from Merrifield resin

13 examples (yields 57-100%, NMR purity >70->95%). Preparation of 12 dihydroquinolin-4-ones *via* 2 different routes is also reported (yields 35-80%, NMR purity 80-95%).

S. Wendeborn, *Synlett*, 2000, 45.

Traceless linking of indoles: application to Mannich and Stille reactions

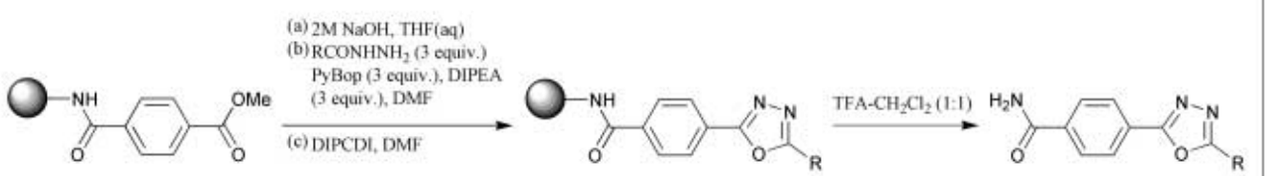


2 steps from Merrifield resin

1 example (yield 99%, NMR purity >98%) and 1 example of Stille coupling using a tin-derivatised polymer-bound indole (yield 66%). Immobilisation and cleavage of 5 indoles is also reported.

J. Kraxner, M. Arlt and P. Gmeiner, *Synlett*, 2000, 125.

Synthesis of 1,3,4-oxadiazoles using diisopropylcarbodiimide to induce cyclodehydration



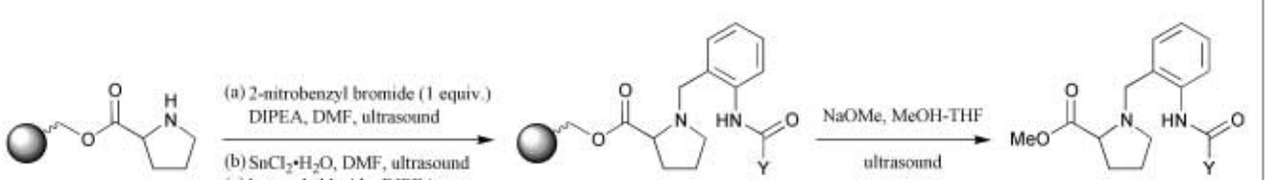
2 steps from ArgoPore-Rink resin

DIPCDI = diisopropylcarbodiimide

B. J. Brown, I. R. Clemens and J. K. Neesom, *Synlett*, 2000, 131.

10 examples (yields 60-78%, HPLC purity 71-96%).

Power ultrasound for the synthesis of compounds targeting κ-opioid receptors

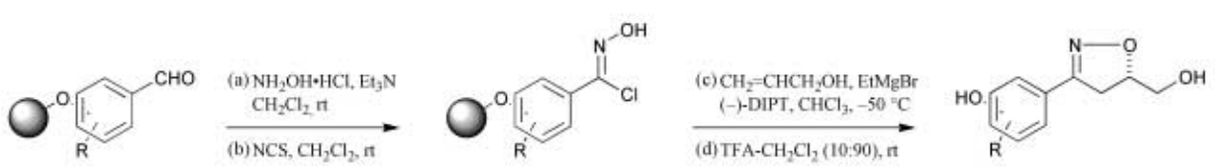


2 steps from hydroxymethyl derivatised paramagnetic resin

J. M. Perez, E. J. Wilhelm and I. Sucholeiki, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 171.

2 examples (yields 40-44%).

Isoxazolines



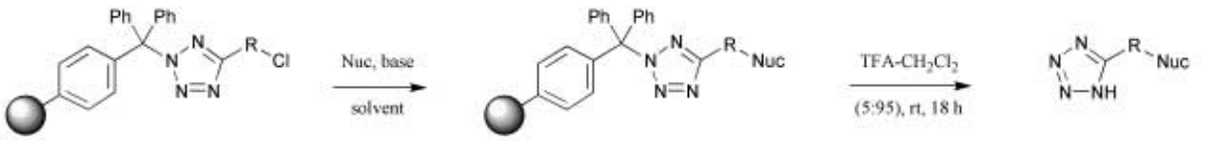
1 step from Wang resin

(−)-DIPT = diisopropyl tartrate

N. Zou and B. Jiang, *J. Comb. Chem.*, 2000, **2**, 6.

6 examples (yields 63-78%, HPLC purity 75-90%, ee 62-95%).

Alkyl tetrazole derivatives

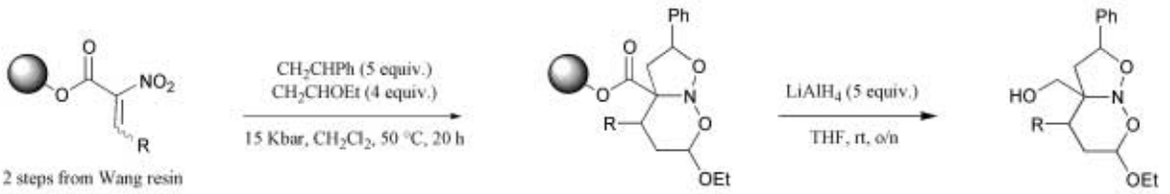


1 step from trityl chloride resin

D. P. Matthews, J. E. Green and A. J. Shuker, *J. Comb. Chem.*, 2000, **2**, 19.

30 examples (yields 24-100%, HPLC purity 73-100%).

High pressure promoted cycloadditions of polymer-supported nitroalkenes

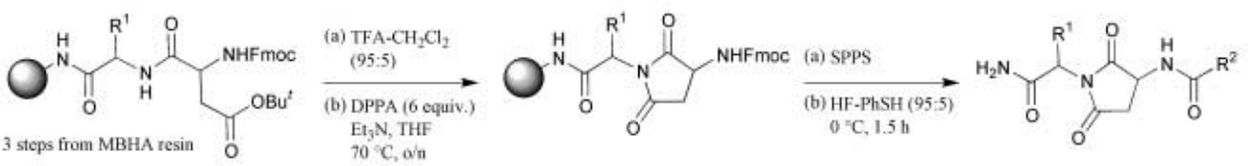


2 steps from Wang resin

5 examples of tandam cycloadditions (yields 29-56%). A high pressure promoted Diels–Alder reaction for the preparation of cyclic arylethylamines is also reported (no yields given).

G. J. Kuster and H. W. Scheeren, *Tetrahedron Lett.*, 2000, **41**, 515.

1,3-Disubstituted succinimides



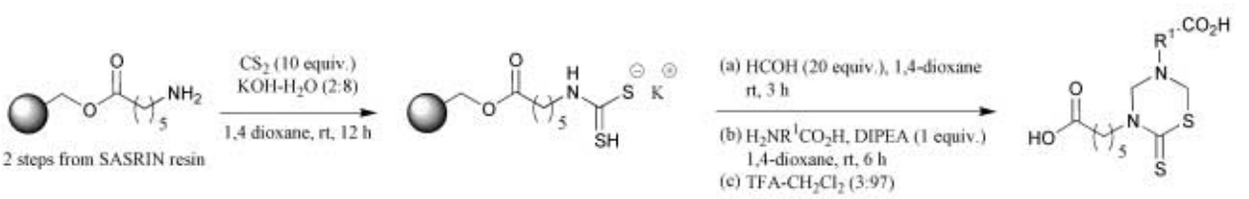
3 steps from MBHA resin

DPPA = diphenylphosphoryl azide

J. M. Alvarez-Gutierrez, A. Nefzi and R. A. Houghten, *Tetrahedron Lett.*, 2000, **41**, 609.

12 examples (yields 82->95%).

3-(5′-Carboxypentyl)-5-substituted tetrahydro-2*H*-1,3,5-thiadiazin-2-thione derivatives

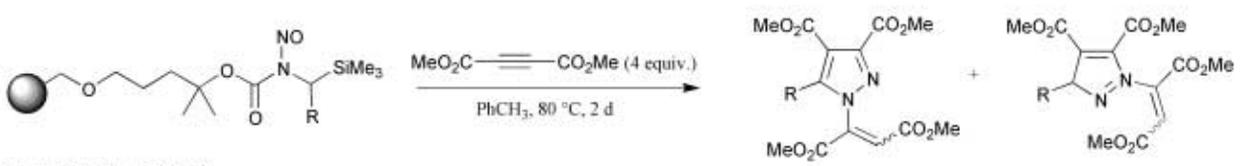


2 steps from SASRIN resin

R. Pérez, O. Reyes, M. Suarez, H. E. Garay, L. J. Cruz, H. Rodriguez, M. D. Molero-Vilchez and C. Ochoa, *Tetrahedron Lett.*, 2000, **41**, 613.

6 examples (yields 30-81%, HPLC purity 70-95%).

Traceless synthesis of pyrazoles from polymer-supported α-silylnitrosoamides

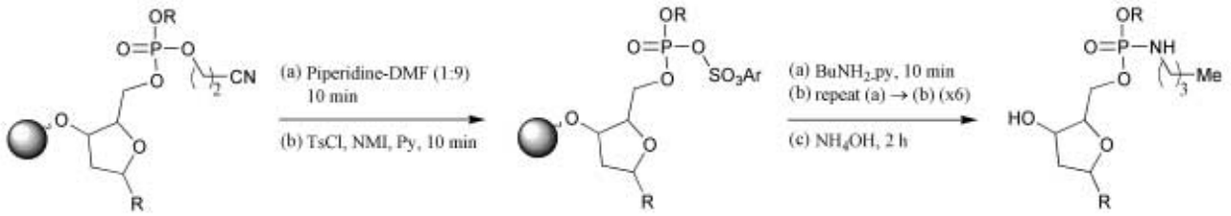


4 steps from Merrifield resin

K.-I. Washizuka, K. Nagai, S. Minakata, I. Ryu and M. Komatsu, *Tetrahedron Lett.*, 2000, **41**, 691.

4 examples (yields 23-70%). Cycloaddition using ethyl propiolate to give 3-substituted pyrazole products is also reported (yield 57%).

Amidate linkages in oligonucleotides



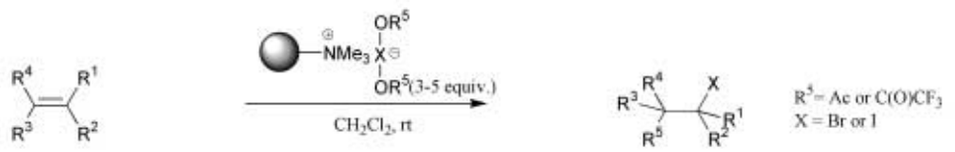
resin not specified

P. W. Davis and S. A. Osgood, *Bioorg. Med. Chem. Lett.*,1999, **9**, 2691.

1 example (yield 98%, HPLC purity 97%).

Polymer-supported acyl hypohalite equivalents for 1,2-haloacetoxylations of alkenes, alkynes and alkoxyallenes

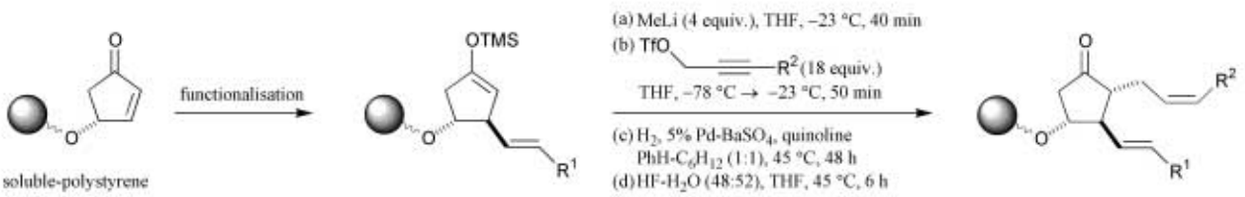
Reagent



H. Monenschein, G. Sourkouni-Argirusi, K. M. Schubothe, T. O'Hare and A. Kirshning, *Org. Lett.*, **1**, 2101.

13 examples (yields 12-93%) and 8 examples of 1,2-haloacetoxylations of alkynes & alkoxyallenes using the illustrated reagents (yields 57-83%). Preparation of the illustrated reagents from polystyrene-bound halides is also reported.

Prostanoids

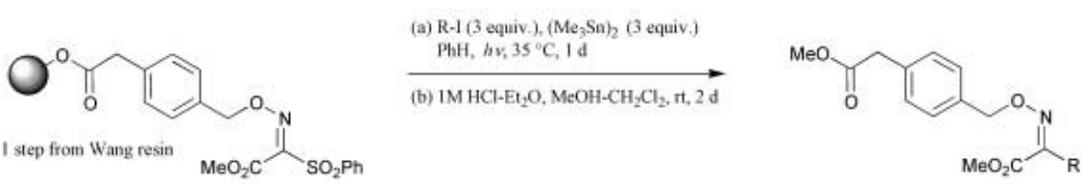


soluble-polystyrene

K. Joo Lee, A. Angulo, P. Ghazal and K. D. Janda, *Org. Lett.*, **1**, 1859.

Preparation and biological evaluation of a 16-member library is reported (yields 26-38%).

Radical reaction of phenylsulfonyl oxime ethers: synthesis of α–amino-esters

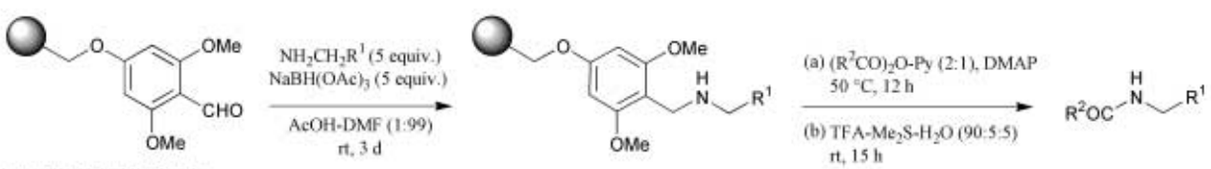


1 step from Wang resin

G.-H. Jeon, J.-Y. Yoon, S. Kim and S. Soo Kim, *Synlett*, 2000, 128.

6 examples (yields 22-50%). Solution-phase reduction of 3 of the illustrated oxime ethers to give the corresponding α–amino-esters is also reported (yields 65-73%).

Phenylalkylamide derivatives: melatoninergic ligands for human mt_1 and MT_2 receptors

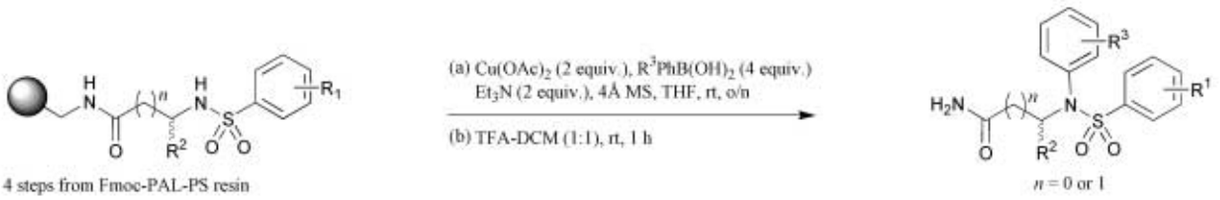


1 step from Merrifield resin

C. Pégurier, S. Curtet, J-P. Nicolas, J. A. Boutin, P. Delagrange, P. Renard and M. Langlois, *Bioorg. Med. Chem.*, 2000, **8**, 163.

Preparation and biological evaluation of a 108-member library is reported.

N-Arylation of sulfonamides

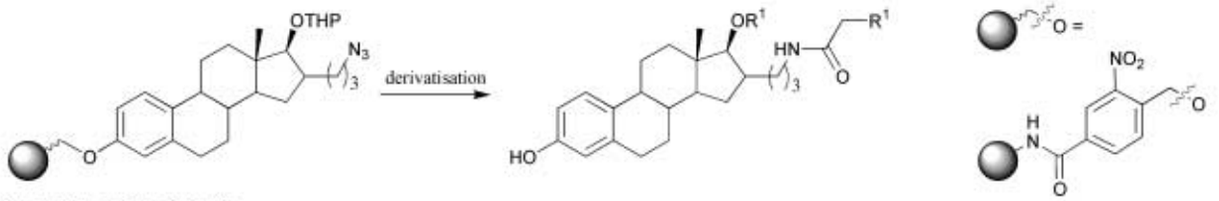


4 steps from Fmoc-PAL-PS resin

A. P. Combs and M. Rafalski, *J. Comb. Chem.*, 2000, **2**, 29.

13 examples (yields 0, 43-81%)

Estradiol derivatives

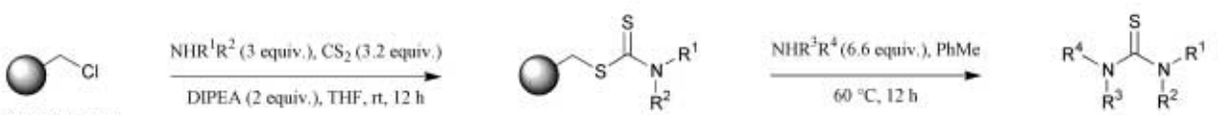


2 steps from aminomethyl resin

M. R. Tremblay and D. Poirier, *J. Comb. Chem.*, 2000, **2**, 48.

3 examples (yields 20-31%) and 1 other example of estradiol preparation (yield 31%). Preparation of Steroidal precursors and the use of 4 other less efficient linker strategies are also reported.

Traceless synthesis of *N,N'*-substituted thioureas

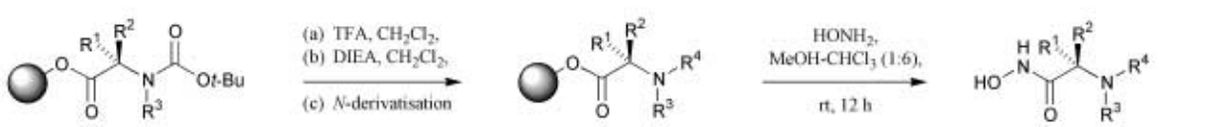


Merrifield resin

L. Gomez, F. Gellibert, A. Wagner and C. Mioskowski, *J. Comb. Chem.*, 2000, **2**, 75.

12 examples (yields 33-97%, HPLC purity >90%).

Nucleophilic displacement of resin-bound carboxylates with hydroxylamine

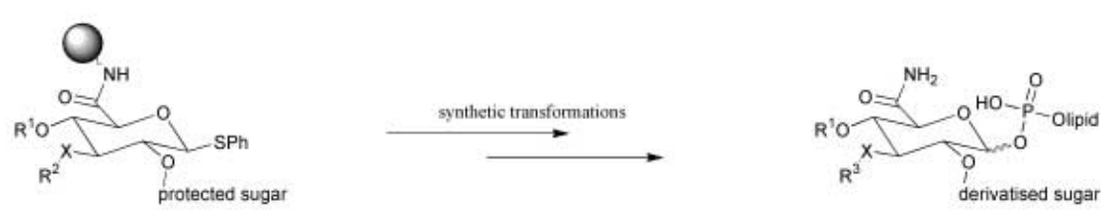


1 step from oxime resin

E. Thouin and W. D. Lubell, *Tetrahedron Lett.*, 2000, **41**, 457.

9 examples (yields 48->99%, NMR or HPLC purity 77-96%).

Disaccharide antibacterial agents

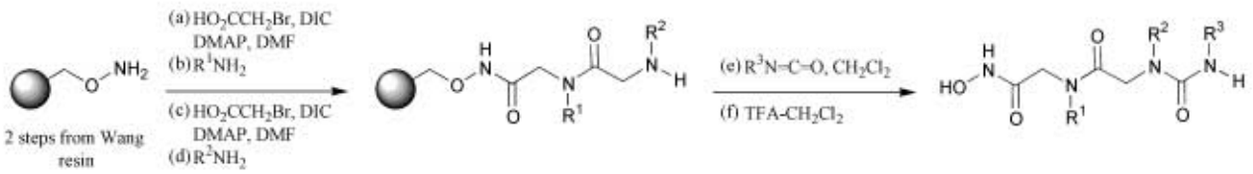


1 or 2 steps from Aminoethyl-photolinker AM resin

M. J. Sofia *et al*, *J. Med. Chem.*, 1999, **42**, 3193.

Preparation and biological evaluation of a 1300-member library are reported.

Hydroxamate/urea-based gelatinase inhibitors

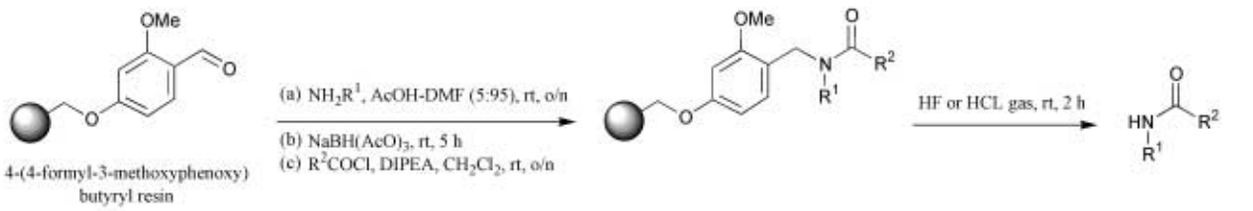


2 steps from Wang resin

Y. Zhang, D. Li, J. C. Houtman, D. T. Witiak, J. Seltzer, P. J. Bertics and C. T. Lauhon, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 2823.

Preparation and biological evaluation of >1000 compounds is reported.

Gaseous HF and HCL cleavage of amino acids

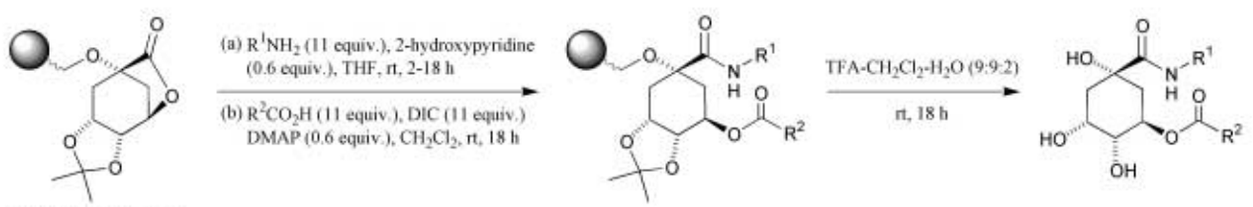


4-(4-formyl-3-methoxyphenoxy) butyryl resin

A. Kerschen, A. Kanizsai, I. Botros and V. Krchnák, 1999, *J. Comb. Chem.*, **1**, 480.

11 examples (yields 92->99%, HPLC purity 95-99%). 10 Wang resin-bound Fmoc amino acids are also cleaved using gaseous acid (yields 11-88%).

D-(−)-Quinic acid derivatives

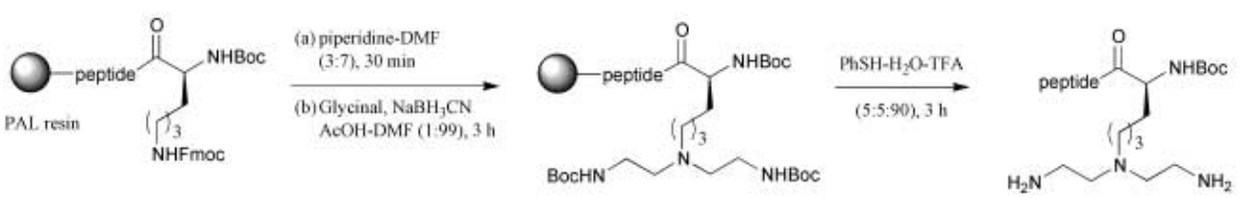


1 step from brominated Wang resin

C. W. Phoon and C. Abell, *J. Comb. Chem.*, 1999, **1**, 485.

10 examples (yields 62-92%, HPLC purity 84-99%). Preparation of 8 quinic acid derivatives *via* 2 similar routes is also reported (yields 63-84%, HPLC purity 91-97%).

Synthesis of an antimicrobial peptide using an unnatural amino acid as a building block

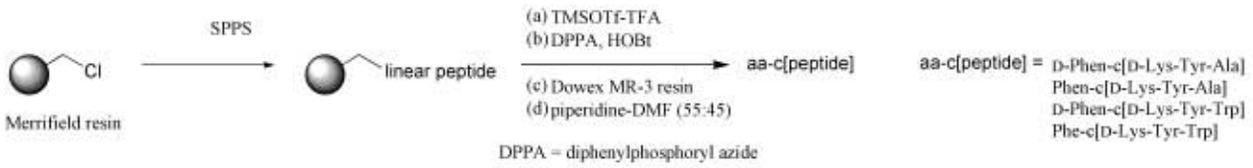


PAL resin

J. Eun Oh and K. Hyeung Lee, *Bioorg. Med. Chem.*, 1999, **7**, 2985.

Preparation and biological evaluation of a small library of peptides are reported.

Analogues of the opioid peptide YKFA



Merrifield resin

DPPA = diphenylphosphoryl azide

J. E. Burden, P. Davis, F. Porreca and A. F. Spatola, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 3441.

Synthesis and biological activities of 4 analogues of YKFA, in which the usual Tyr^1-Phe^3 combination found in the opioid peptides has been transposed, are reported.