

Compilers: John Christopher,^a Louise Lea,^a Catherine McCusker,^a Susan Booth^b and Jason Tierney^b

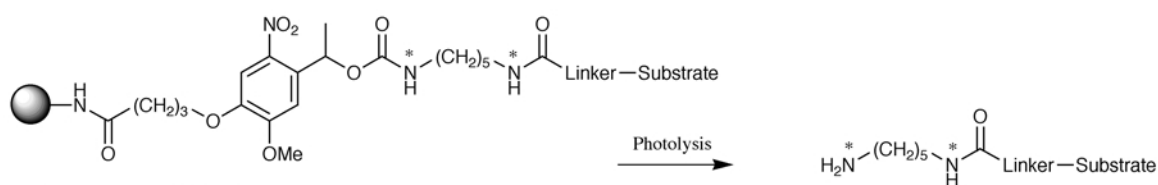
^a Department of Chemistry, University of Glasgow, Glasgow, UK G12 8QQ

^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.

A photolabile carbamate based dual linker analytical construction

Linker



Amino polystyrene-PEG resin

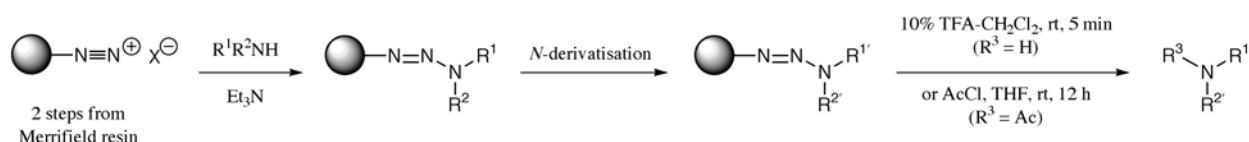
* 50% labelled with ¹⁵N

S. C. McKeown, S. P. Watson, R. A. E. Carr and P. Marshall, *Tetrahedron Lett.*, 1999, **40**, 2407.

A novel technique for the monitoring of solid phase chemistry is reported. Photochemical cleavage from the solid-support affords an analytical fragment containing the substrate which is sensitised to electrospray mass spectrometry.

Triazenes as robust and simple linkers for amines.

Linker

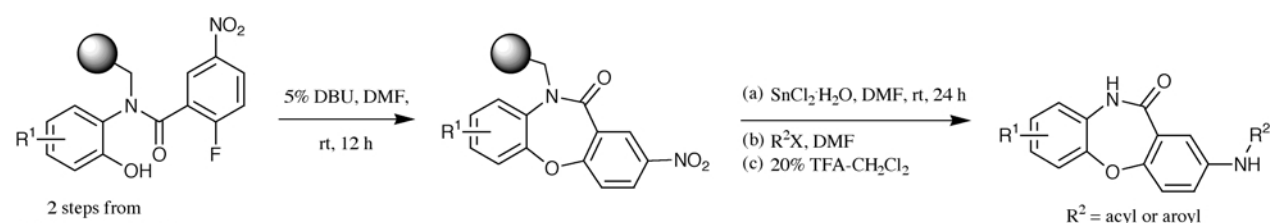


2 steps from Merrifield resin

S. Bräse, J. Köbberling, D. Enders, R. Lazny, M. Wang and S. Brandtner, *Tetrahedron Lett.*, 1999, **40**, 2105.

9 examples including various on-resin chemical transformations.

2-Substituted dibenz[b,f]oxazepin-11(10H)-ones via S_NAr methodology on AMEBA resin.

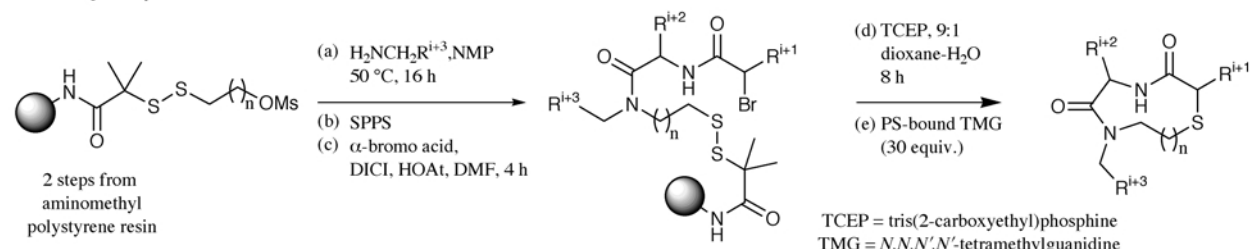


2 steps from methoxybenzaldehyde polystyrene resin

X. Ouyang, N. Tamayo and A. S. Kiselyov, *Tetrahedron*, 1999, **55**, 2827.

16 examples (yields 35-95%, HPLC purity 95-99%).

Heterocyclic β-turn mimetics

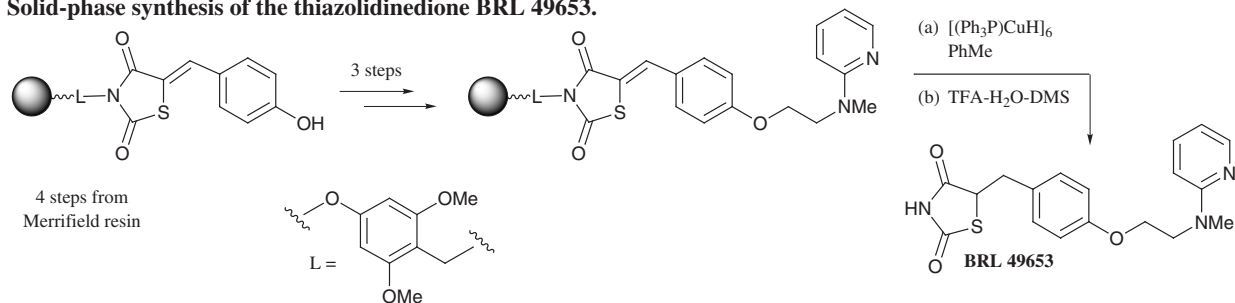


2 steps from aminomethyl polystyrene resin

A. J. Souers, A. A. Virgilio, Å. Rosenquist, W. Fenuik and J. A. Ellman, *J. Am. Chem. Soc.*, 1999, **121**, 1817.

7 examples (yields 51-64%, HPLC purity 86-94%). Also described is a 172 member library of Somatostatin mimetics.

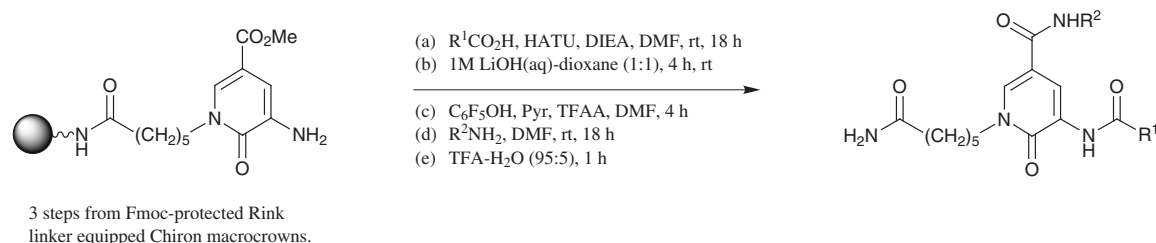
Solid-phase synthesis of the thiazolidinedione BRL 49653.



K. M. Brummond and J. Lu, *J. Org. Chem.*, 1999, **64**, 1723.

A key feature is the use of the 4-formyl-3,5-dimethoxyphenol linker for the attachment and cleavage of an imide nitrogen to / from the solid support.

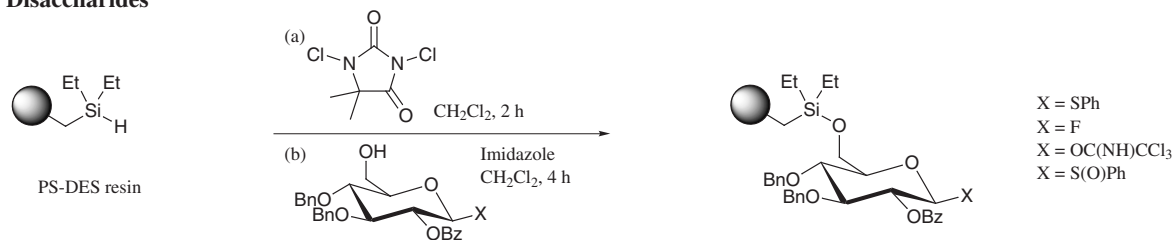
1,3,5-Trisubstituted pyridin-2-ones



J. A. Linn, S. W. Gerritz, A. L. Handlon, C. E. Hyman and D. Heyer, *Tetrahedron Lett.*, 1999, **40**, 2227.

The use of a pyridin-2-one scaffold to create a library of 1,3,5-trisubstituted pyridinones using macrocrowns as a solid support is described.

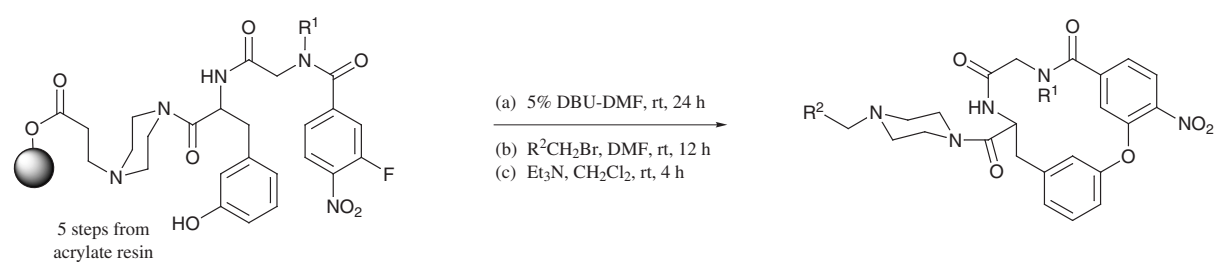
Disaccharides



T. Doi, M. Sugiki, H. Yamada, T. Takahashi and J. A. Porco, *Tetrahedron Lett.*, 1999, **40**, 2141.

Glycosidation of silicon-connected glycosyl donors on PS resin is described; 3 examples (yields 90-100%, HPLC purities 69-96%).

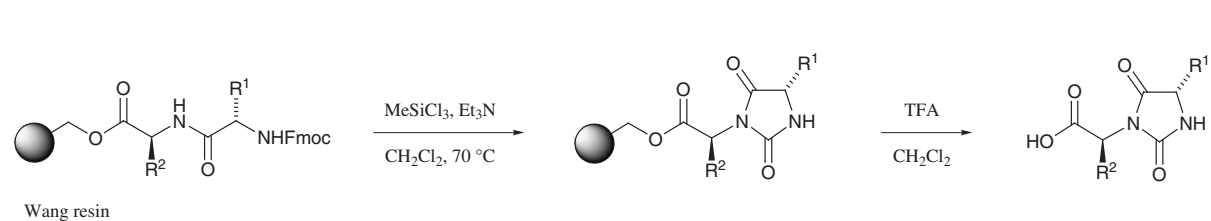
Biaryl 14-membered macrocycles



A. S. Kiselyov, S. Eisenberg and Y. Luo, *Tetrahedron Lett.*, 1999, **40**, 2465.

20 examples (yields 52-68%, purities 82-96%).

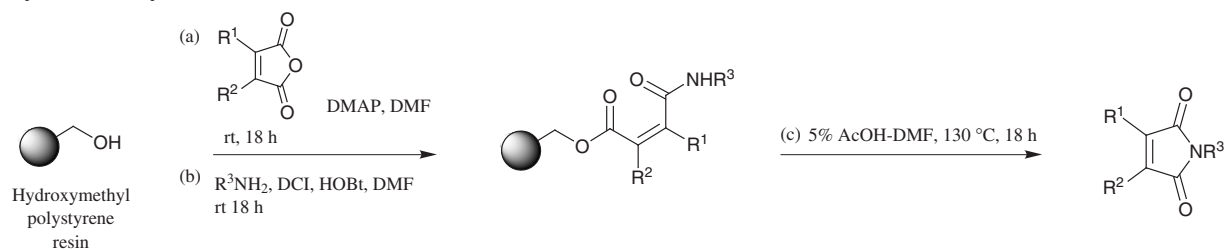
Hydantoins



P. Y. Chong and P. A. Petillo, *Tetrahedron Lett.*, 1999, **40**, 2493.

7 examples (HPLC purities 73, 91-98%).

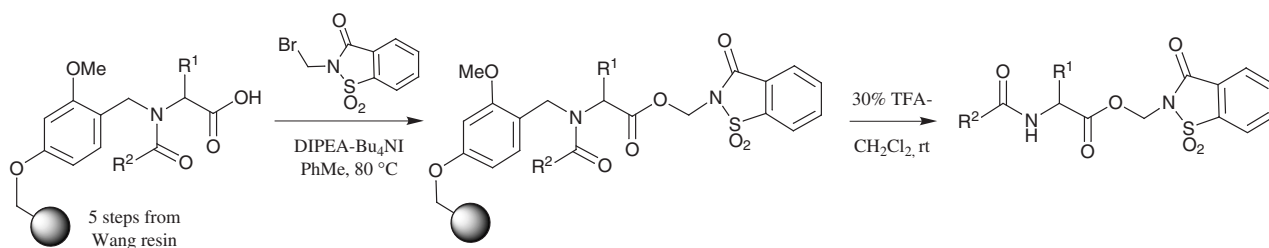
Synthesis of cyclic imides.



39 examples are reported (yields 4-72%, LCMS purity 72-99%). The methodology was applied to the synthesis of a new class of δ -opioid receptor ligands.

D. R. Barn and J. R. Morphy. *J. Comb. Chem.*, 1999, **1**, 151

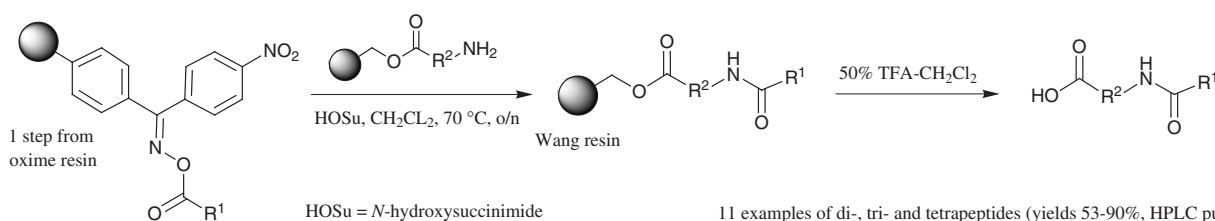
Benzoisothazolones as serine protease inhibitors.



K.-L. Yu, R. Civello, D. G. M. Roberts, S. M. Seiler and N. A. Meanwell. *Bioorg. Med. Chem. Lett.*, 1999, **9**, 663.

84 examples (HPLC purity > 70%).

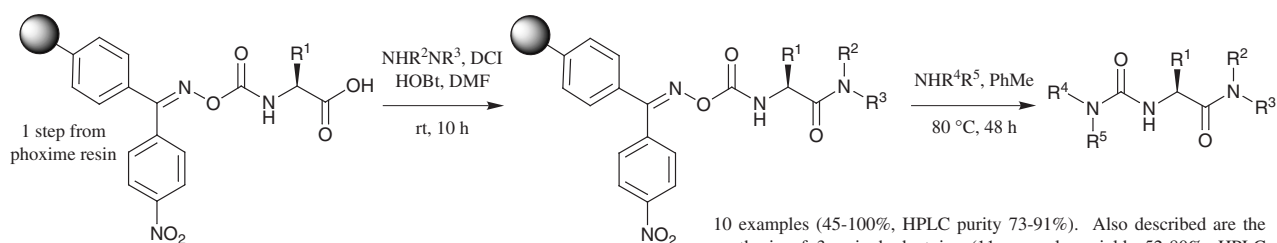
Resin-to-resin acyl- and aminoacyl-transfer reactions using oxime supports.



Y. Hamuro, M. A. Scialdone and W. F. DeGrado. *J. Am. Chem. Soc.*, 1999, **121**, 1636.

11 examples of di-, tri- and tetrapeptides (yields 53-90%, HPLC purity 68-97%). Also described is the use of phosgenated oxime resin, which reacts with amines to form oxime-derived carbamates. Thermolysis of these carbamates leads to the formation of ureas via isocyanate intermediates. Hydantoin formation is also described.

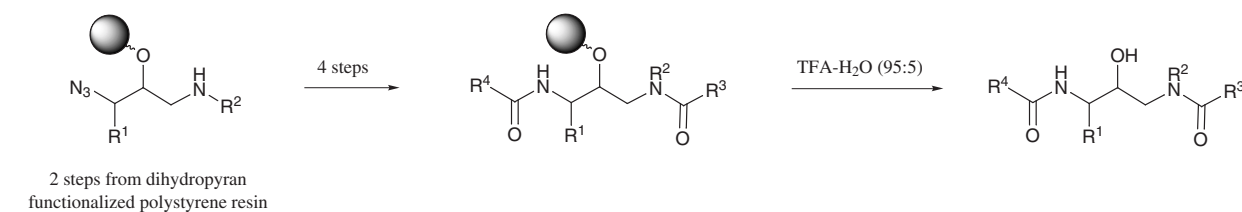
Synthesis of acyclic and heterocyclic amino acid derived urea peptidomimetics.



Y. Hamuro, W. J. Marshall and M. A. Scialdone. *J. Comb. Chem.*, 1999, **1**, 163.

10 examples (45-100%, HPLC purity 73-91%). Also described are the synthesis of 3-aminohydantoin (11 examples, yields 52-80%, HPLC purity 35-96%) and 1,2,4-triazine-3,6-diones (6 examples, yields 32-62%, HPLC purity 22-87%).

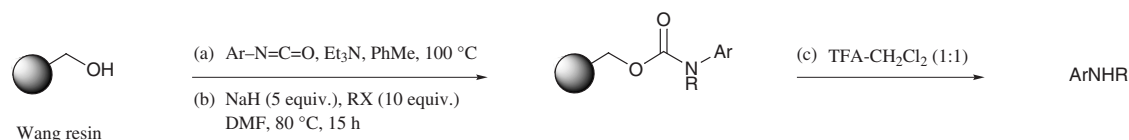
1,3-Diaminopropan-2-ol derivatives



J. Zhou, A. Termin, M. Wayland and C. M. Tarby. *Tetrahedron Lett.*, 1999, **40**, 2729.

92 examples (yields 39-77%, purity 85-99%). The methodology allows the incorporation of either an alkyl group or H at the R² site of hydroxyethylamine isostere.

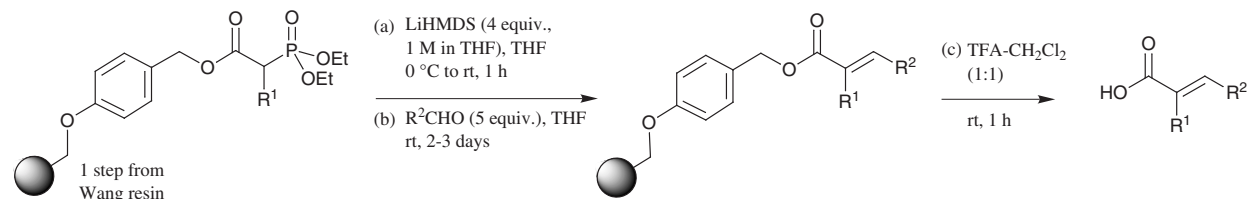
Aryl and heteroaryl amines



S. Sunami, T. Sagara, M. Ohkubo and H. Morishima, *Tetrahedron Lett.*, 1999, 1721.

14 examples (yields 77, 90->95%, HPLC purity 82-94%).

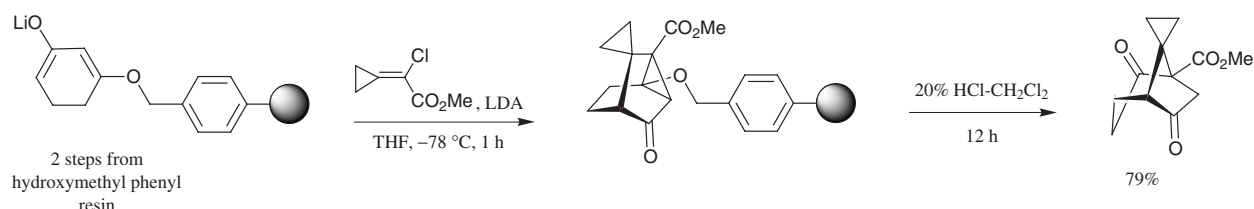
Horner-Emmons synthesis of olefins.



J. M. Salvino, T. J. Kieson, S. Darnbrough and R. Labaudiniere, *J. Comb. Chem.*, 1999, 1, 134.

48 examples (yields 69-95%, HPLC purity 48-97%).

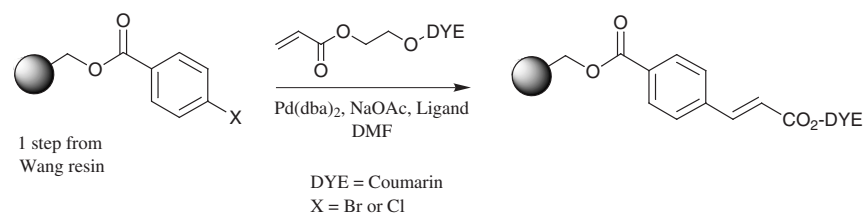
Anionically induced domino reactions; synthesis of functionalized carbocyclic compounds.



H-J. Gutke and D. Spitzner, *Tetrahedron*, 1999, 55, 3931.

2 other examples (yields 19-58%).

A fluorescence-based assay for high throughput screening of coupling reactions.



Rapid visual analysis of large numbers of parallel reactions has been described. 45 ligands were screened for their ability to form active catalysts with palladium for the Heck coupling. Two ligands chosen by the assay, P(Bu^t)₃ and (ferrocene)P(Bu^t)₂, were found to be the most active systems to date for the olefination of unactivated aryl bromides, and (ferrocene)P(Bu^t)₂ is the most efficient ligand for olefination of unactivated aryl chlorides

K. H. Shaughnessy, P. Kim and J. F. Hartwig, *J. Am. Chem. Soc.*, 1999, 121, 2123

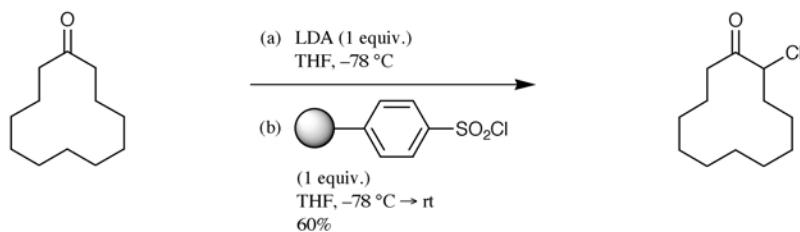
Polymer-supported (diacetoxyiodo)benzene (PSDIB)



S. V. Ley, A. W. Thomas and H. Finch, *J. Chem. Soc., Perkin Trans. 1*, 1999, 669.

Utilisation of the title reagent (prepared in 2 steps from polystyrene) in a variety of oxidative reactions (18 examples, yields 75-100%, LC or NMR purity 90-95%) is reported.

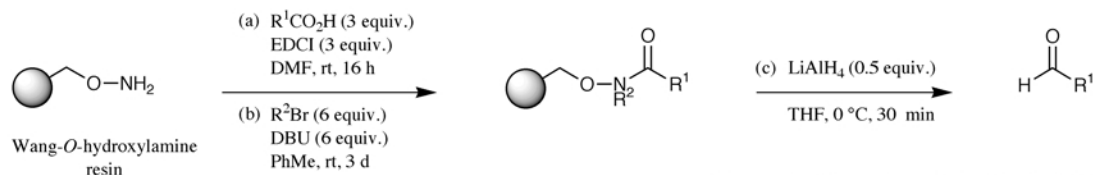
α -Chlorination of ketones.



K. M. Brummond and K. D. Gesenberg, *Tetrahedron Lett.*, 1999, **40**, 2231.

α -Chlorination of the above ketone using commercially available chloro-*p*-toluenesulfonyl resin is reported.

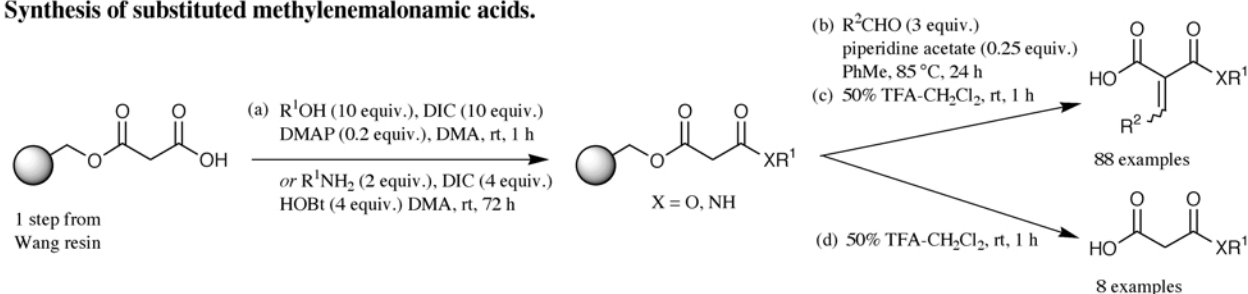
Synthesis of aldehydes and ketones using a novel supported Weinreb amide.



J. M. Salvino, M. Mervic, H. J. Mason, T. Kiesow, D. Teager, J. Airey and R. Labaudiniere, *J. Org. Chem.*, 1999, **64**, 1823.

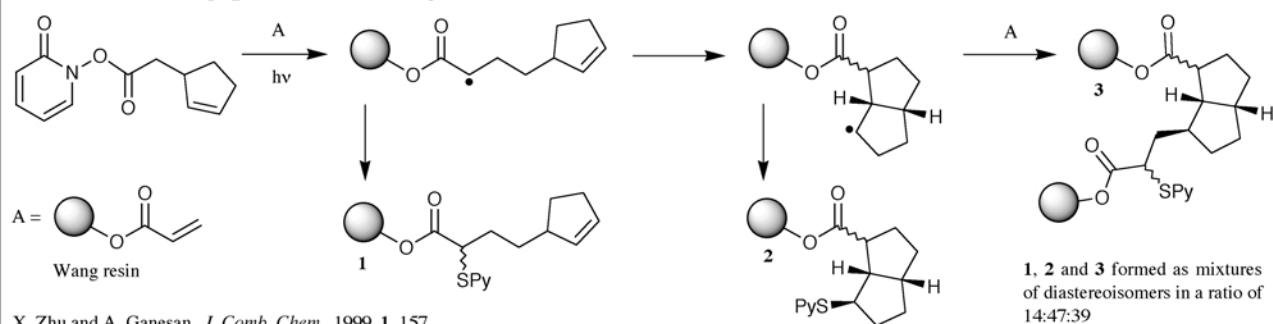
22 examples of aldehyde synthesis (yields 0, 11-54%, NMR purity 67-98%) and 2 examples of the preparation of ketones (yields 23, 68%, NMR purity 78, 97%) are reported. The purity of the aldehydes is sufficient for use directly in a sensitive solid-phase Horner-Emmons reaction.

Synthesis of substituted methylenemalonamic acids.



B. C. Hamper, D. M. Snyderman, T. J. Owen, A. M. Scates, D. C. Owsley, A. S. Kesselring and R. C. Chott, *J. Comb. Chem.*, 1999, **1**, 140.

Intermolecular conjugate addition of alkyl radicals.



X. Zhu and A. Ganesan, *J. Comb. Chem.*, 1999, **1**, 157.