Perkin 1 Abstracts: Solid Phase Organic Synthesis

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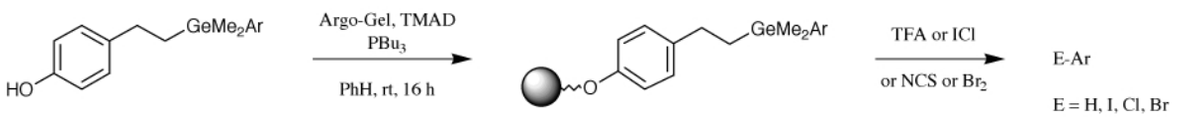
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

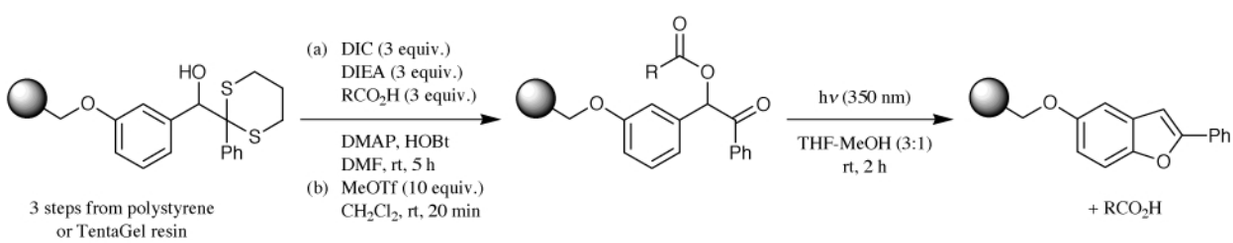
A new germanium based linker for the solid-phase synthesis of aromatic compounds. ***Linker***



TMAD = *N*,*N*,*N*′,*N*′-Tetramethyl azodicarboxylate

A. C. Spivey, C. M. Diaper and A. J. Rudge, *Chem. Commun.*, 1999, 835. 4 examples.

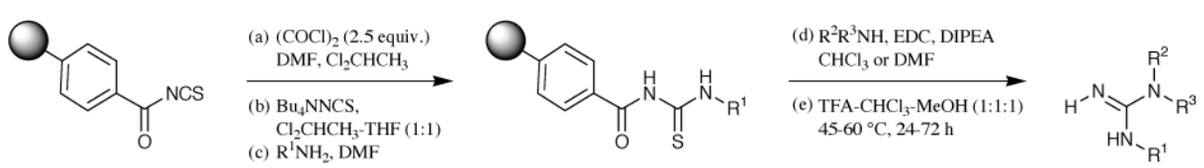
A dithiane-protected benzoin photolabile safety catch linker for solid-phase synthesis. ***Linker***



H. B. Lee and S. Balasubramanian, *J. Org. Chem.*, 1999, **64**, 3454.

Synthesis of a novel dithiane protected linker and the subsequent loading and photolytic release of carboxylic acids is reported.

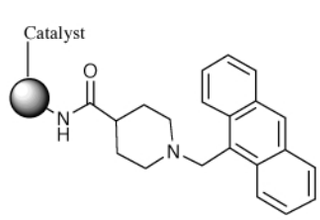
Acyl isothiocyanate resin: a traceless linker approach to substituted guanidines. ***Support***



EDC = 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride

L. J. Wilson, S. R. Klopfenstein and M. Li, *Tetrahedron Lett.*, 1999, **40**, 3999. 8 examples (yields 38-74%, HPLC purity > 97%).

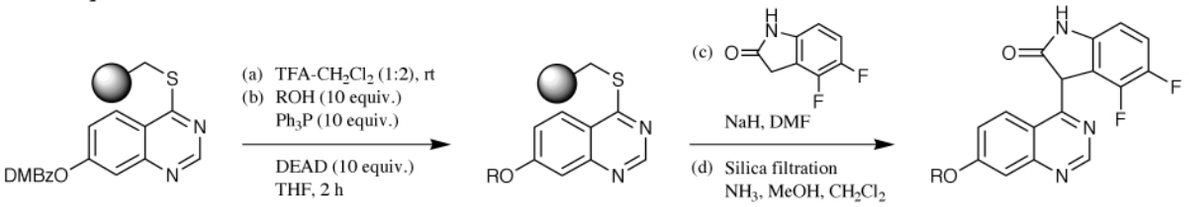
A chemosensor-based approach to catalyst discovery in solution and on solid support. ***Support***



Development of a fluorescence-based assay for the screening of catalysts for acyl transfer reactions is described. Aminomethylanthracene, which fluoresces when protonated, was attached to the resin with concomitant functionalisation with catalysts of known solution-phase reactivity. The relative intensities of the beads, after exposure to standard acyl transfer reaction conditions, paralleled the reactivity trends of the catalysts in solution. This approach could be used for the screening of single-bead-single-catalyst libraries using either fluorescence microscopy or fluorescence-activated bead sorting. A solution-phase fluorescence-based assay is also described.

G. T. Copeland and S. J. Miller, *J. Am. Chem. Soc.*, 1999, **121**, 4306.

Oxindole quinazolines.



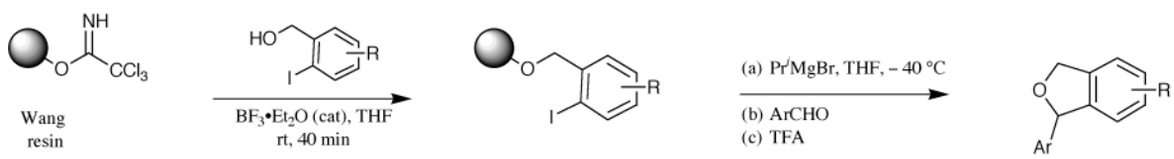
1 step from Merrifield resin

DMBz = dimethoxybenzyl

L. F. Hennequin and S. Piva-Le Blanc, *Tetrahedron Lett.*, 1999, **40**, 3881.

13 examples (yields 0, 35-72%).

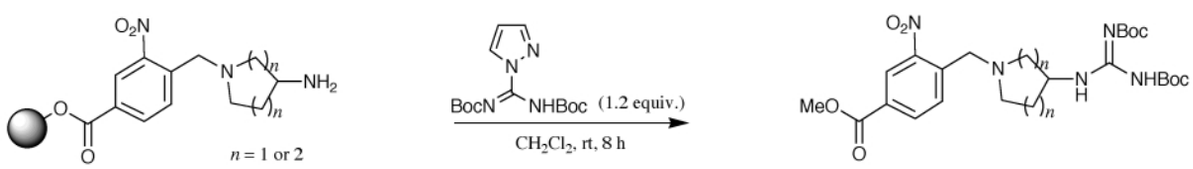
2,4-Disubstituted 2,5-dihydrofurans and 1-substituted 1,3-dihydroisobenzofurans.



M. Rottlander and P. Knochel, *J. Comb. Chem.*, 1999, **1**, 181.

A 30-compound array is reported.

Solution phase parallel synthesis of guanidines.

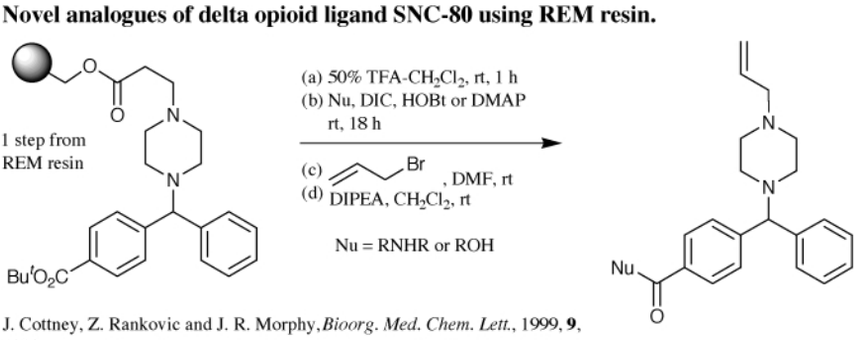


2 steps from soluble MeO-PEG resin

K.-C. Ho and C.-M. Sun, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1517.

12 examples in total are reported (yields 72-85%, HPLC purity 76-98%). 3 other guanylating agents were investigated.

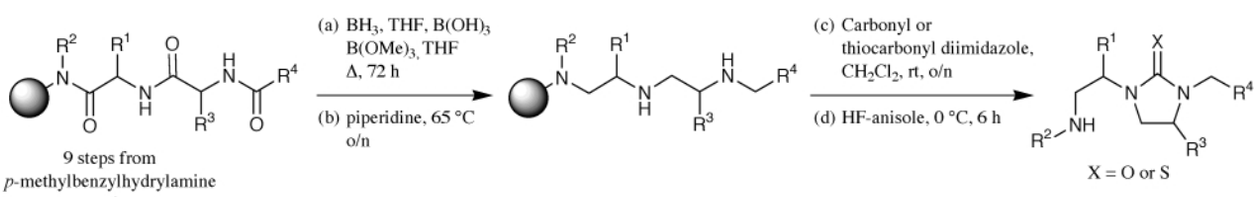
Novel analogues of delta opioid ligand SNC-80 using REM resin.



A complementary route, employing the Stille coupling, was used to generate opioid ligand analogues. Two focused libraries of >120 compounds are reported (24 examples are given).

J. Cottney, Z. Rankovic and J. R. Morphy, *Bioorg. Med. Chem. Lett.*, 1999, **9**, 1323.

Trisubstituted 2-imidazolidones and imidazolidinethiones.

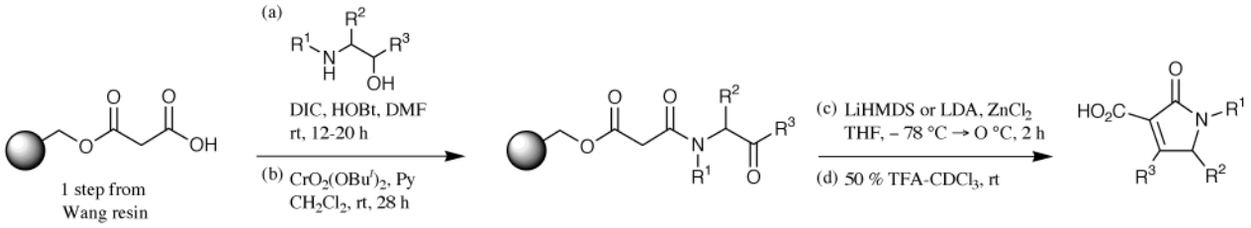


9 steps from *p*-methylbenzylhydrylamine resin

A. Nefzi, J. M. Ostresh, M. Giulianotti and R. A. Houghten, *J. Comb. Chem.*, 1999, **1**, 195.

60 examples (average HPLC purity 80%). Larger scope optimisation libraries and positional scanning combinatorial libraries were also synthesised.

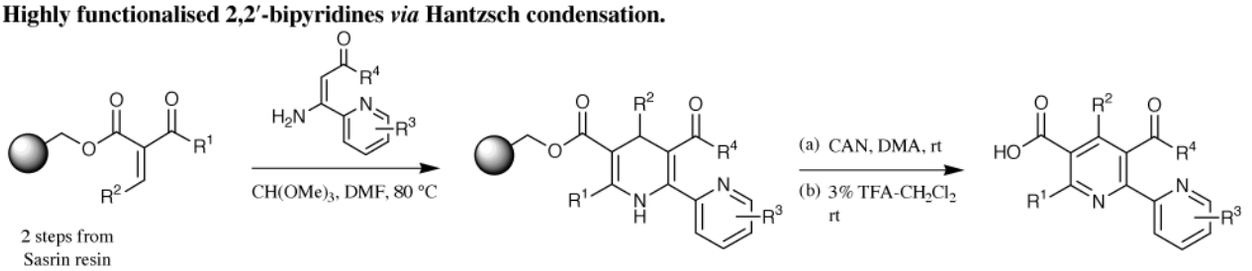
Carboxypyrrolinones



P. C. Miller, T. J. Owen, J. M. Molyneaux, J. M. Curtis and C. R. Jones, *J. Comb. Chem.*, 1999, **1**, 223.

11 examples (yields 43-80%, NMR purity > 95%).

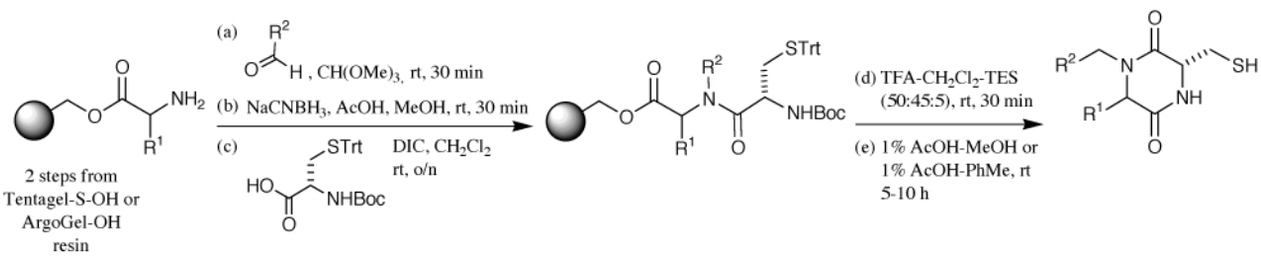
Highly functionalised 2,2′-bipyridines *via* Hantzsch condensation.



S. Tadesse, A. Bhandari and M. A. Gallop, *J. Comb. Chem.*, 1999, **1**, 184.

12 examples (yields 28-84%, HPLC purity 70-98%). A complementary route is reported to generate functionalised 2,2′-bipyridines. Generation of a 500 bipyridine library using split/pool synthesis is also reported.

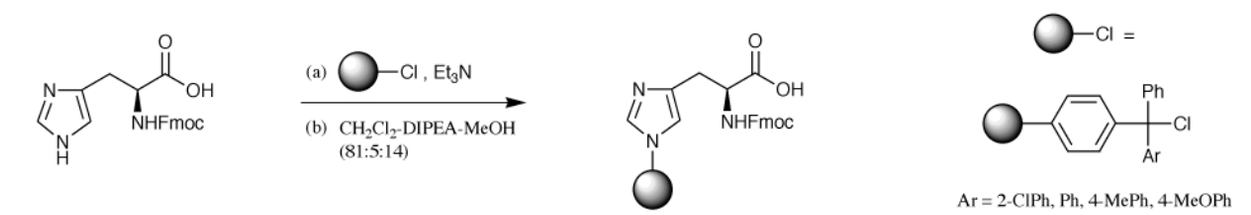
Diketopiperazines as highly selective inhibitors of collagenase-1.



A. K. Szardenings, V. Antonenko, D. A. Campbell, N. DeFrancisco, S. Ida, L. Shi, N. Sharkov, D. Tien, T. Wang and M. Navre, *J. Med. Chem.*, 1999, **42**, 1348.

A 1225 membered library is reported.

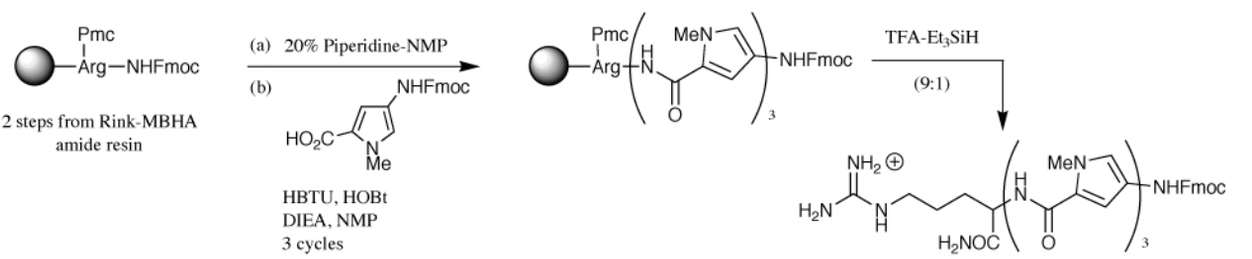
Attachment of histidine, histamine and urocanic acid to trityl-type resins.



S. Eleftheriou, D. Gatos, A. Panagopoulos, S. Stathopoulos and K. Barlos, *Tetrahedron Lett.*, 1999, **40**, 2825.

Attachment of histidine, histamine and urocanic acid to trityl-type resins through the N^{Im} function is reported. Cleavage from the resin is achieved using TFA.

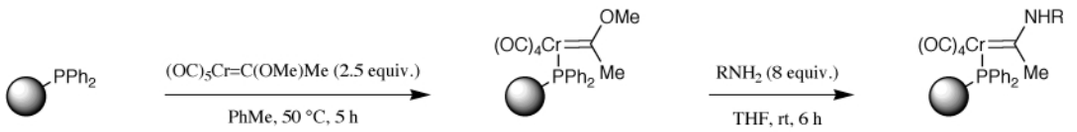
Linear polypyrrole-peptide conjugates



E. Vázquez, A. M. Caamaño, L. Castedo and J. L. Mascareñas, *Tetrahedron Lett.*, 1999, **40**, 3621.

A new method for the synthesis of oligopyrrole-peptide conjugates is reported, and illustrated by 2 examples.

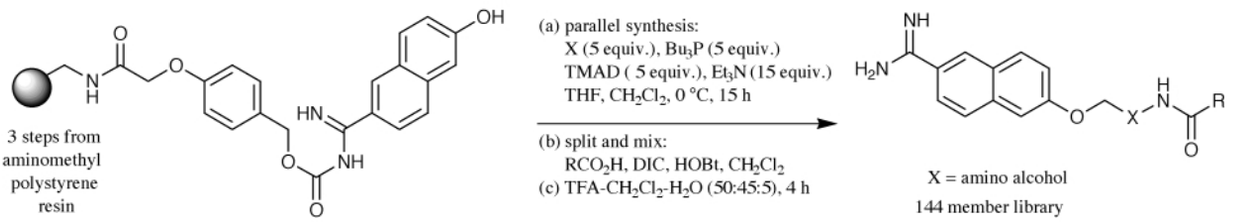
Polymer-bound Fischer chromium alkoxy- and aminocarbene complexes.



S. Maiorana, P. Seneci, T. Rossi, C. Baldoli, M. Ciraco, E. de Magistris, E. Licandro, A. Papagni and S. Provera, *Tetrahedron Lett.*, 1999, **40**, 3635.

4 examples (yields 82-100%). In addition, synthesis of immobilized aminocarbenes *via* carbene attachment to a resin-bound amine is reported.

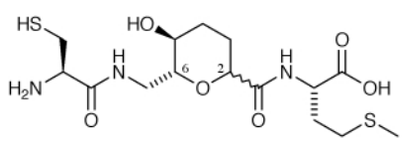
Inhibition of the tissue factor/factor VIIa complex: lead optimisation using combinatorial chemistry.



P. Roussel, M. Bradley, P. Kane, C. Bailey, R. Arnold and A. Cross, *Tetrahedron*, 1999, **55**, 6219.

43 other examples are described (average HPLC purity 60%).

Design and synthesis of a protein–farnesyltransferase inhibitor based on sugar amino acids.

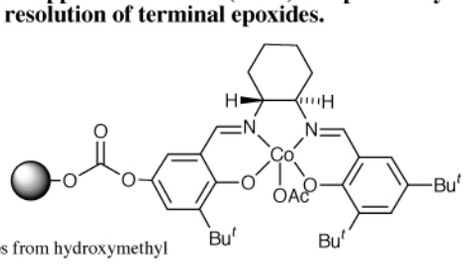


2 examples (yields 15-20%)

The solid phase synthesis of (2,6-*trans*) and (2,6-*cis*) peptidomimetics, inhibitors of farnesyltransferase, are described. Solution phase synthesis of 2,6-*trans* and 2,6-*cis*-pyranoid sugar amino acids, building blocks of the peptidomimetics, *via* Ferrier rearrangement from tri-acetylated D-glucal is reported. The synthesis represents a protocol for the design and synthesis of more powerful inhibitors *via* a combinatorial approach.

H. S. Overkleeft, S. H. L. Verhelst, E. Pieterman, N. J. Meeuwenoord, M. Overhand, L. H. Cohen, G. A. van der Marel and J. H. van Boom, *Tetrahedron Lett.*, 1999, **40**, 4103.

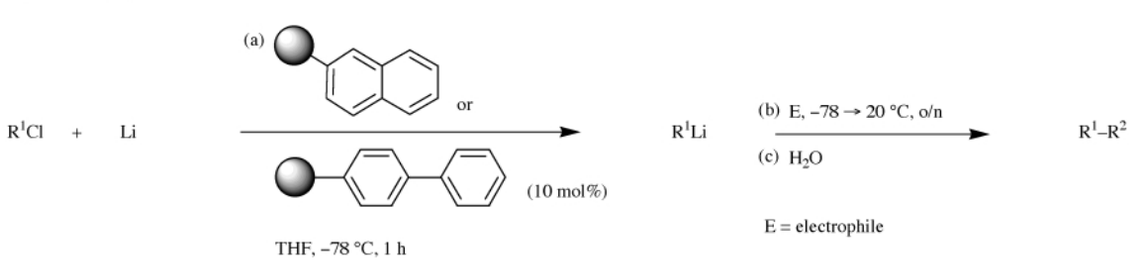
Polymer-supported chiral Co(salen) complexes: synthetic applications and mechanistic investigations in the hydrolytic kinetic resolution of terminal epoxides.



2 examples of hydrolytic kinetic resolution (HKR) of terminal epoxides (yields 36-41%, 94.4- >99% ee), 1 example of dynamic HKR of terminal epoxides (yield 94%, 96% ee) and 2 examples of kinetic resolution of terminal epoxides by the addition of phenols (yields 90-98%, 96- >99% ee) using an easily prepared, recyclable, polymer-bound chiral Co(salen) catalyst are reported. Preparation of silica-bound Co(salen) calalysts, their use in HKR (1 example, 96.3% ee), application to a continuous flow system, and mechanistic investigation of the HKR of terminal epoxides using silica-bound Co(salen) catalysts are also reported.

D. Allen Annis and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1999, **121**, 4147.

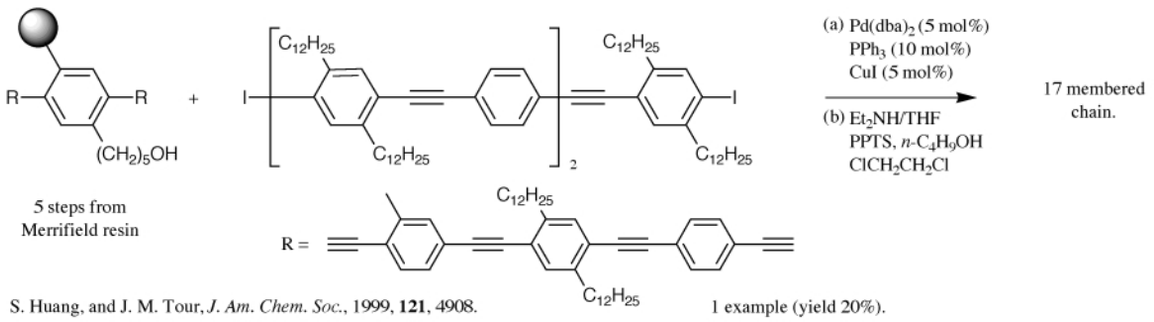
Polymer supported arene-catalysed lithiation reactions.



49 examples (yields 41-99%). 32 further examples of arene-catalysed lithiations using Barbier-type conditions (yields 47-99%).

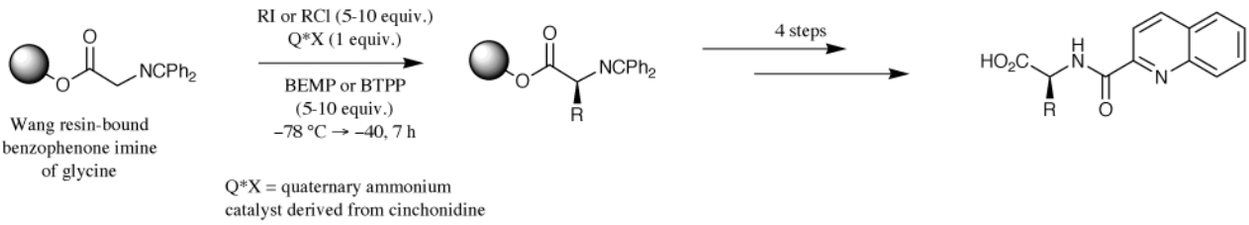
C. Gomez, S. Ruiz and M. Yus, *Tetrahedron*, 1999, **55**, 7017.

Rapid solid-phase synthesis of oligo(1,4-phenylene ethynylene)s by a divergent/convergent tripling strategy.



S. Huang, and J. M. Tour, *J. Am. Chem. Soc.*, 1999, **121**, 4908.

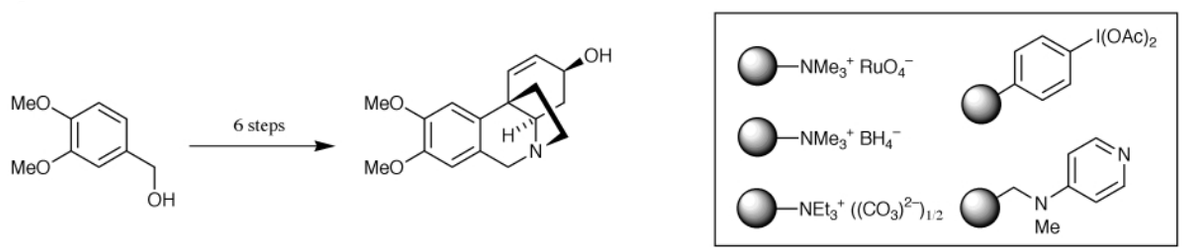
Enantioselective solid-phase synthesis of α-amino acid derivatives.



M. J. O'Donnell, F. Delgado and R. S. Pottorf, *Tetrahedron*, 1999, **55**, 6347.

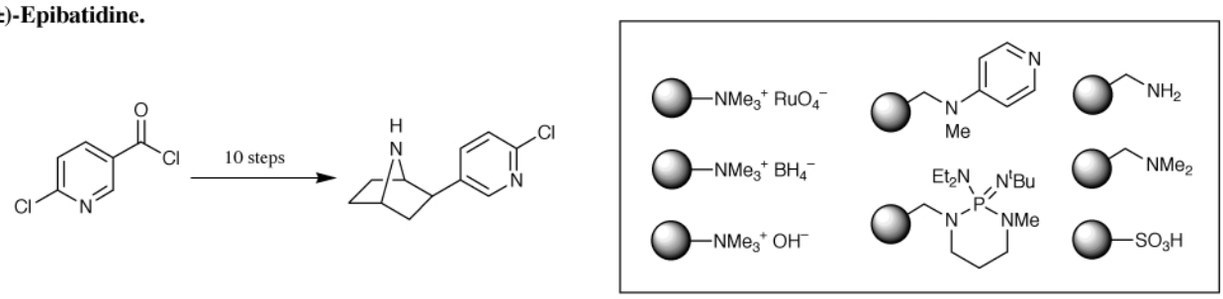
17 examples (yields 70-100%, 51-89% ee, HPLC purity 25-99%).

(±)-Epimaritidine.



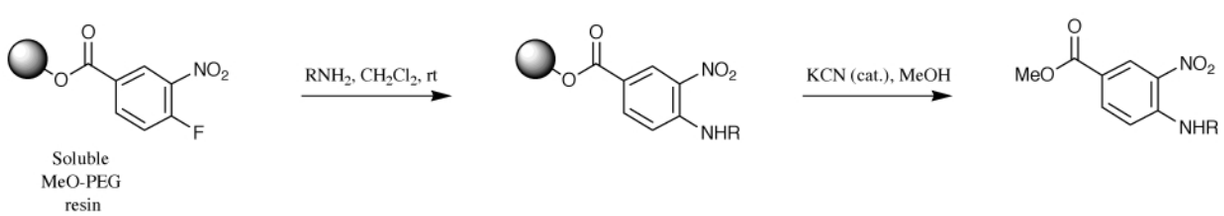
S. V. Ley, O. Schucht, A. W. Thomas and P. J. Murray, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1251.

(±)-Epibatidine.



J. Habermann, S. V. Ley and J. S. Scott, *J. Chem. Soc., Perkin Trans. 1*, 1999, 1253.

Solution phase synthesis of arylamines.



P.-C. Pan and C.-M. Sun, *Bioorg. Med. Chem. Lett.*, 1999, **9** 1537.