Perkin 1 Abstracts: Solid Phase Organic Synthesis

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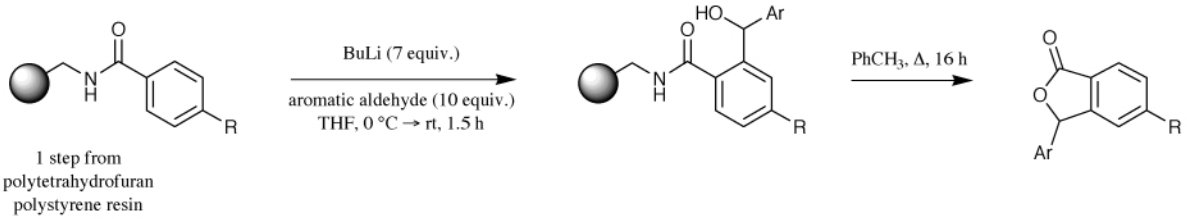
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

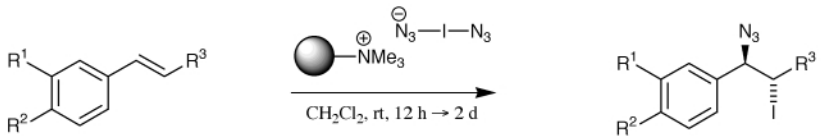
Polytetrahydrofuran cross-linked polystyrene resin: synthesis of a phthalide library. ***Support***



P. Garibay, P. H. Toy, T. Hoeg-Jensen and K. D. Janda, *Synlett*, 1999, 1438.

24-member library (yields 41-81%, NMR purity >95%). Synthesis of the resin is also reported.

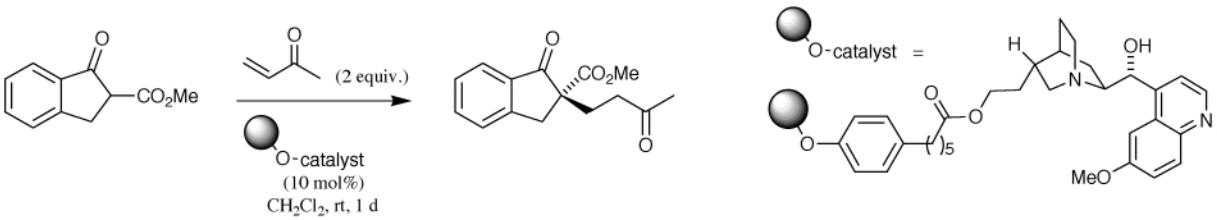
Polymer-bound iodine azide. ***Reagent***



A. Kirschning, H. Monenschein and C. Schmeck, *Angew. Chem., Int. Ed.*, 1999, **38**, 2594.

6 examples (yields 38-94%). 9 further examples of azido-iodination, *via* the illustrated route, using 9 different alkenes are also reported (yields 48-98%).

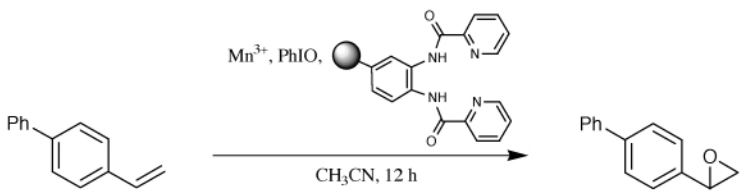
Catalysts derived from *Cinchona* alkaloids: their use in the asymmetric Michael reaction. ***Catalyst***



R. Alvarez, M-A. Hourdin, C. Cavé, J. d'Angelo and P. Chaminade, *Tetrahedron Lett.*, 1999, **40**, 7091.

1 example (yield 85%, 87% ee) and 11 further examples of asymmetric Michael reactions using 11 different, less superior, catalysts (yields 75-95%, 12-45% ee). Synthesis of the catalysts is also reported.

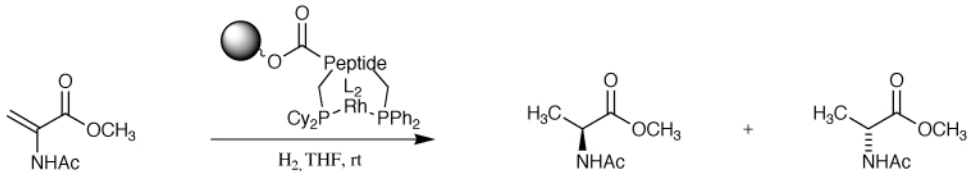
Polymer-supported metal catalysts: oxidation of alkanes and alkenes by diamide manganese complexes. ***Catalyst***



M. Havranek, A. Singh and D. Sames, *J. Am. Chem. Soc.*, 1999, **121**, 8965.

1 example (yield 96%) and 1 other example of alkane oxidation using the illustrated catalyst (yield 60%). The synthesis of a library of manganese catalysts, from which the illustrated catalyst and one other catalyst were identified as the most efficient, is also reported.

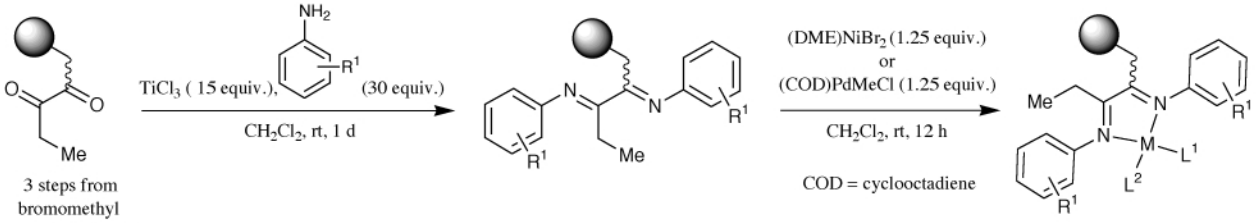
Parallel synthesis of peptide-based phosphine rhodium complexes: catalysts for the asymmetric hydrogenation of enamides. ***Catalyst***



2 libraries of phosphine containing peptides are synthesised, complexed with rhodium and screened for their ability to catalyse the illustrated asymmetric hydrogenation.

S. R. Gilbertson and X. Wang, *Tetrahedron*, 1999, **55**, 11609.

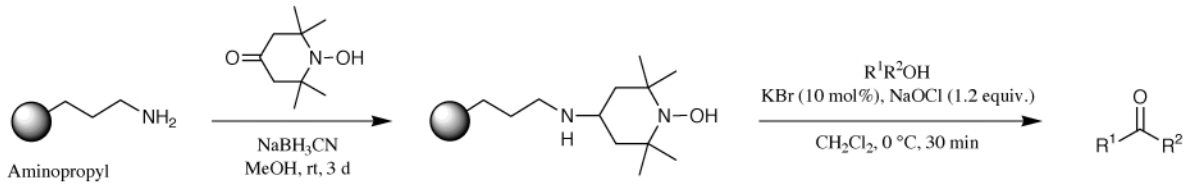
Parallel synthesis, screening, and encoding strategies for olefin-polymerisation catalysts. ***Catalyst***



96-member library of Ni(II) and Pd(II) catalysts. A chemical encoding strategy for the catalysts, employing sub-stoichiometric 2° amine tags is also reported.

T. R. Boussie, V. Murphy, K. A. Hall, C. Coutard, C. Dales, M. Petro, E. Carlson, H. W. Turner and T. S. Powers, *Tetrahedron*, 1999, **55**, 11699.

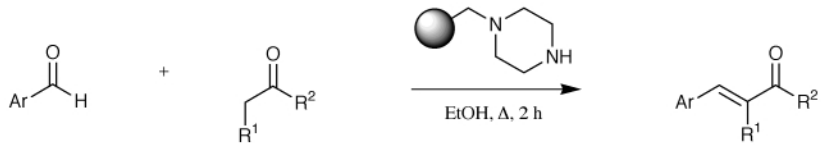
TEMPO oxidations with a silica-supported catalyst. ***Catalyst***



10 examples (yields 60-96%) of the formation of aldehydes and ketones.

C. Bolm and T. Fey, *Chem. Commun.*, 1999, 1795.

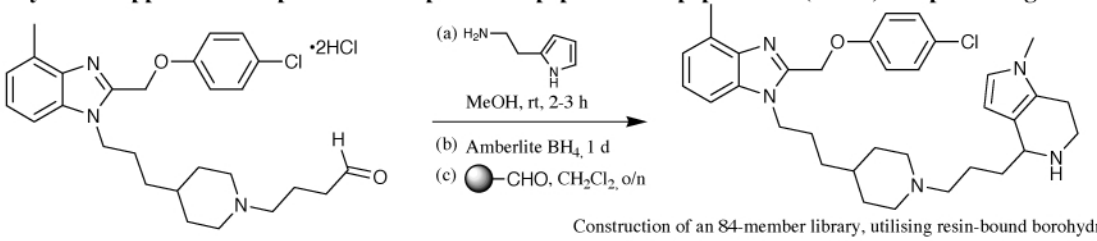
Knoevenagel catalyst. ***Catalyst***



20 examples (yields 65-100%).

J. Simpson, D. L. Rathbone and D. C. Billington, *Tetrahedron Lett.*, 1999, **40**, 7031.

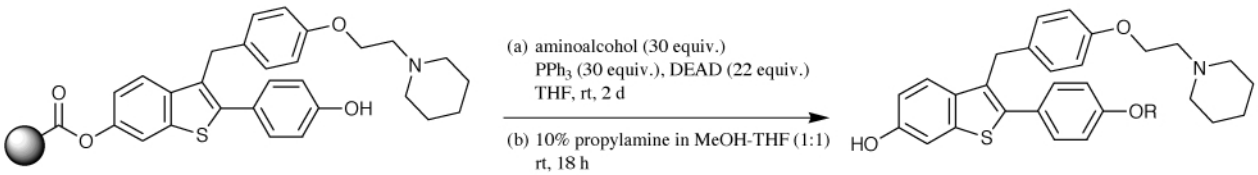
Rapid parallel synthesis applied to the optimisation of potent nonpeptide neuropeptide Y-1 (NPY1) receptor antagonists.



Construction of an 84-member library, utilising resin-bound borohydride as a reductant and resin-bound aldehyde as a scavenger for unreacted starting material, is reported. The illustrated compound, a side product of the parallel synthesis, revealed a 5-fold improvement in binding to the NPY1 receptor over the already potent lead.

M. G. Siegel, M. O. Chaney, R. F. Bruns, M. P. Clay, D. A. Schober, A. M. Van Abbema, D. W. Johnson, B. E. Cantrell, P. J. Hahn, D. C. Hunden, D. R. Gehlert, H. Zarrinmayeh, P. L. Ornstein, D. M. Zimmerman and G. A. Koppel, *Tetrahedron*, 1999, **55**, 11619.

SAR development of a novel class of thrombin inhibitors.

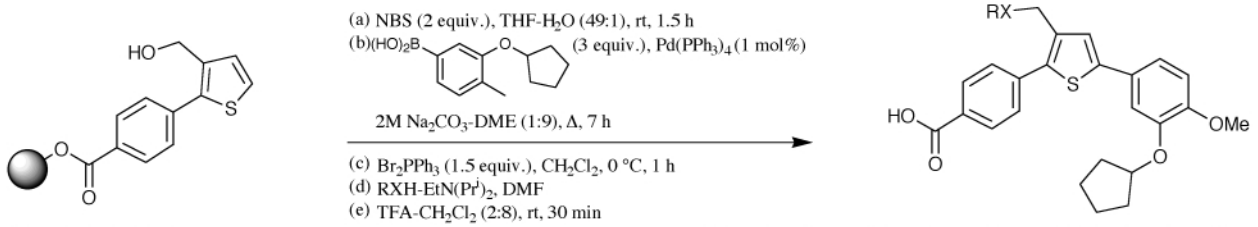


2 steps from polystyrene resin

M. G. Johnson, D. D. Bronson, J. E. Gillespie, D. S. Gifford-Moore, K. Kalter, M. P. Lynch, J. R. McCowan, C. C. Redick, D. J. Sall, G. F. Smith and R. J. Foglesong, *Tetrahedron*, 1999, **55**, 11641.

A 346-member library was prepared *via* the illustrated route and 3 other similar routes to rapidly advance the SAR of a novel series of thrombin inhibitors. Detailed descriptions of the evaluation methods are also reported.

Parallel synthesis of substituted thiophene derivatives and identification of novel phosphodiesterase-4 (PDE-4) inhibitors.

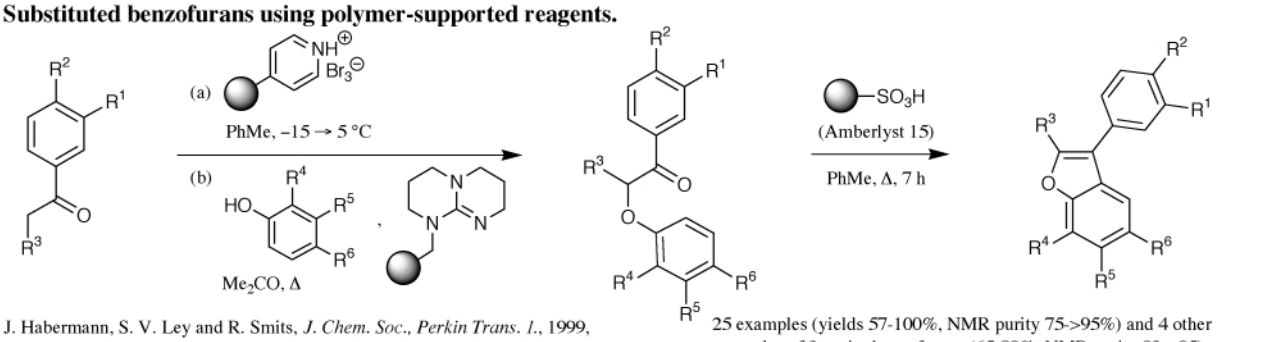


1 step from Wang resin

Y. Han, A. Giroux, C. Lépine, F. Laliberté, Z. Huang, H. Perrier, C. I. Bayly and R. N. Young, *Tetrahedron*, 1999, **55**, 11669.

19-member library (yields 45-84%, NMR or HPLC purity 50-92%) from which a series of PDE-4 inhibitors were developed. Exploration of cleavage conditions and the use of a variety of different boronic acids, linkers and nucleophiles are also reported.

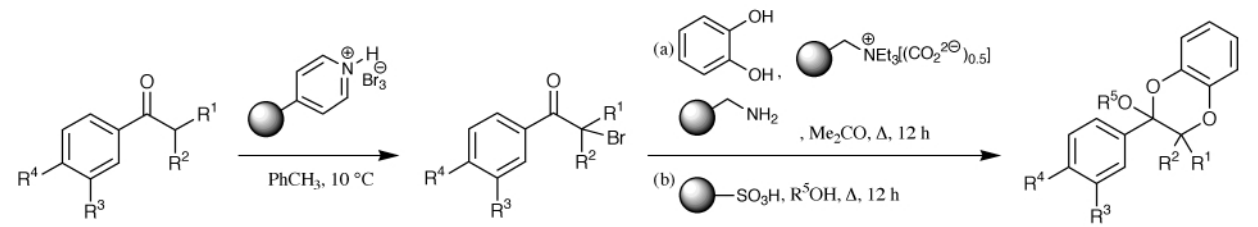
Substituted benzofurans using polymer-supported reagents.



J. Habermann, S. V. Ley and R. Smits, *J. Chem. Soc., Perkin Trans. 1.*, 1999, 2421.

25 examples (yields 57-100%, NMR purity 75->95%) and 4 other examples of 3-aminobenzofurans (65-89%, NMR purity 93->95).

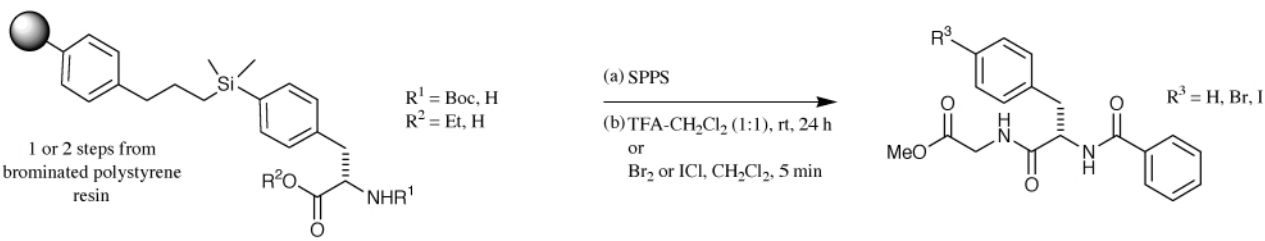
1,4-Benzodioxane and 1,3-thiazole derivatives using polymer supported reagents.



J. Habermann, S. V. Ley, J. J. Scicinski, J. S. Scott, R. Smits and A. W. Thomas, *J. Chem. Soc., Perkin Trans. 1*, 1999, 2425.

8 examples (yields 90-98%, LCMS purity 94->95%) and 9 other examples of 1,3-thiazole derivatives (yields 47->95%, LCMS purity >85->95%).

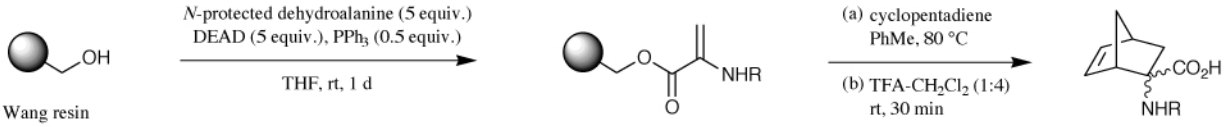
Synthesis of compounds containing phenylalanine and its derivatives *via* side-chain attachment to the polymer support.



Y. Lee and R. B. Silverman, *J. Am. Chem. Soc.*, 1999, **121**, 8407.

3 dipeptides (yields 91-97%, NMR purity ≥95%) are synthesised from 2 polymer-bound phenylalanine precursors. Synthesis of the phenylalanine precursors is also reported.

Diels–Alder reactions of polymer-bound dehydroalanine derivatives.

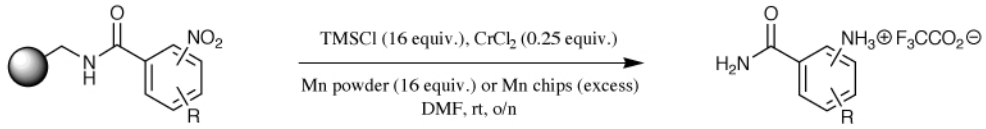


Wang resin

3 examples (yields 67-73%, *exo*:*endo* 2:1-4:1) and 2 further examples of carbocyclic amino acids *via* a similar route (yields 51-81%, *exo*:*endo* 2:1-4:1).

B. A. Burkett and C. L. L. Chai, *Tetrahedron Lett.*, 1999, **40**, 7035.

Transfer catalysis between two solids: application to the reduction of nitroarenes.

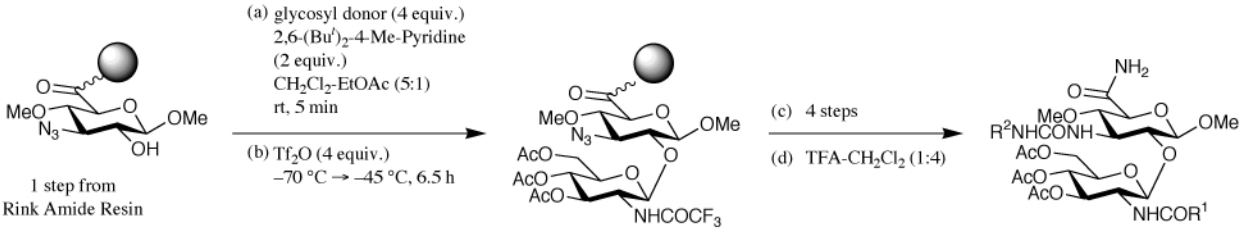


1 step from Rink amide or Wang resin

7 examples (yields 58-84%). 2 further examples of nitroarene reduction on solid support (yields 82-86%) and 7 examples of solution-phase reduction using similar conditions (yields 0, 55-85%) are also reported.

A. Hari and B. L. Miller, *Angew. Chem., Int. Ed.*, 1999, **38**, 2777.

β-Linked disaccharides.



1 step from Rink Amide Resin

D. J. Silva, H. Wang, N. M. Allanson, R. K. Jain and M. J. Sofia, *J. Org. Chem.*, 1999, **64**, 5926.

48-member library of disaccharides (no yields, LCM purity >85%).