Perkin 1 Abstracts: Solid Phase Organic Synthesis

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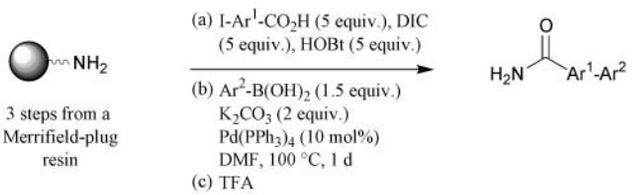
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

Discrete, easy to handle resin plugs as mini reactors. ***Support***

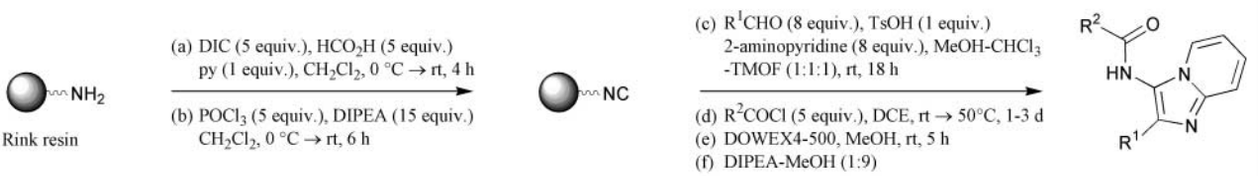


3 steps from a Merrifield-plug resin

B. Atrash, M. Bradley, R. Kobylecki, D. Cowell and J. Reader, *Angew. Chem., Int. Ed.*, 2001, **40**, 938.

Resin plugs, prepared by sintering a synthesis resin with an inert polymer matrix, are used to prepare the illustrated 10-member library (sample yield 58%, HPLC purity 65-98%), an encoded 100-member library of sulfonamides, tertiary amines, ureas and amides, and a 10-member library of 3,4-disubstituted 7-carbamoyl-1,2,3,4-tetrahydroquinoxalin-2-ones (yields 36-86%, HPLC purity 39-95%). Further reactions are performed on the plugs including oxidation, reduction, Mitsunobu reactions and peptide synthesis. Preparation of 9 different resin-plugs and their comparison with identical loose resin are also reported.

A Rink-isonitrile resin for traceless synthesis of 3-acylamino imidazo[1,2-*a*]pyridines. ***Support***

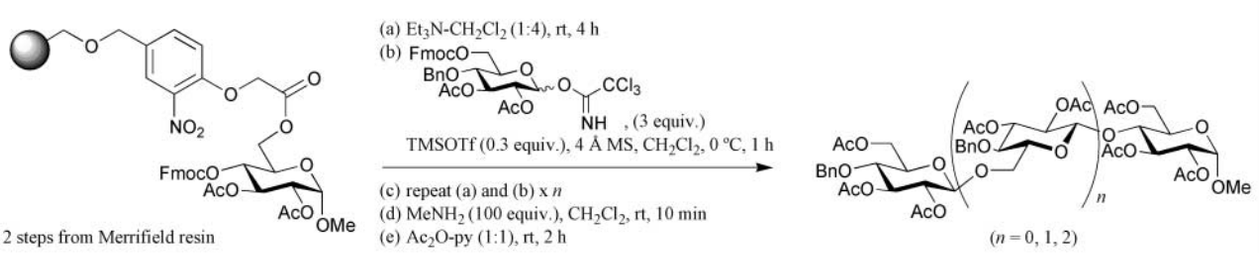


Rink resin

J. J. Chen, A. Golebiowski, J. McClenaghan, S. R. Klopfenstein and L.West, *Tetrahedron Lett.*, 2001, **42**, 2269.

7 examples (yields 31-64%, LCMS purity 86-100%).

A phenoxyacetate-based linker for oligosaccharide synthesis. ***Linker***



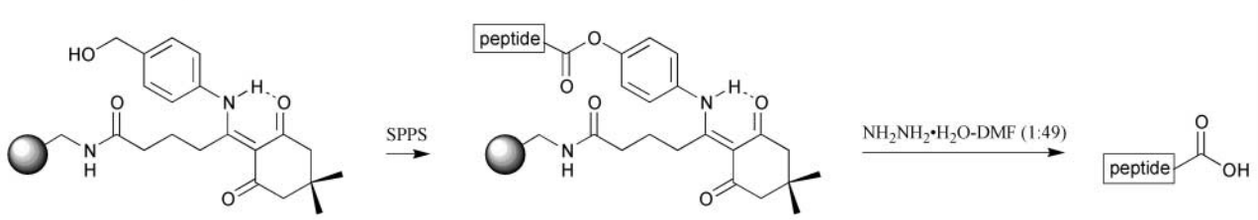
2 steps from Merrifield resin

(n = 0, 1, 2)

X. Wu, M. Grathwohl and R. R. Schmidt, *Org. Lett.*, 2001, **3**, 747.

3 examples (yields 34-85%).

Dde-based carboxy linker. ***Linker***



2 steps from aminomethyl polystyrene resin

S. R. Chhabra, H. Parekh, A. N. Khan, B. W. Bycroft and B. Kellam, *Tetrahedron Lett.*, 2001, **42**, 2189.

2 examples (Leucine-Enkephaline and Human Angiotensin II peptides). Synthesis of the linker is also reported.

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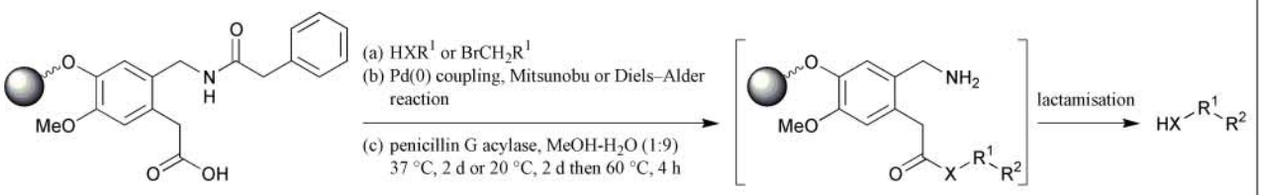
Enzyme-labile safety catch linker. ***Linker***

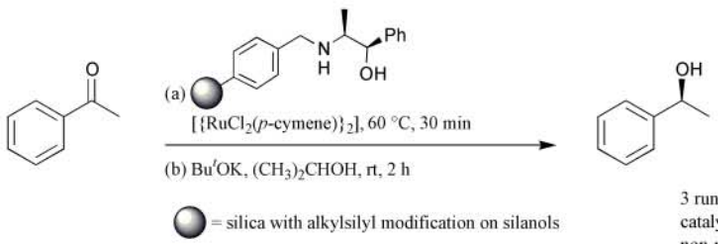


2 steps from diamino-functionalized POE 6000 X = O, NH

7 examples (yields 60-94%, sample purity >95%). Preparation of the linker is also described.

U. Grether and H. Waldmann, *Chem. Eur. J.*, 2001, **7**, 959.

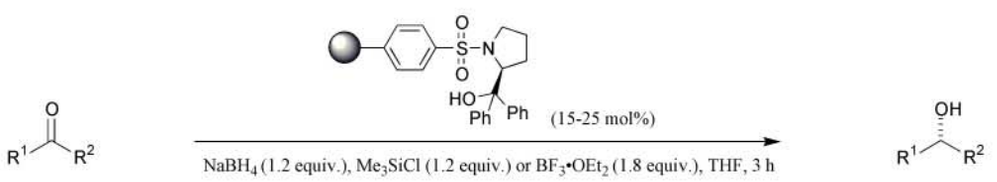
A ruthenium, silica-supported catalyst for asymmetric hydrogenation. ***Catalyst***



3 runs of catalyst (yields 34-51%, %ee 85-92%). Comparison of the catalyst with its corresponding solution-phase, homogeneous silica and non-modified silica analogue, along with its use in a continuous flow reactor is reported. Synthesis of the illustrated catalyst, and a further 5 silica-based chiral ruthenium complexes *via* a similar route, are also reported.

A. J. Sandee, D. G. I. Petra, J. N. H. Reek, P. C. J. Kamer and P. W. N. M. van Leeuwen, *Chem. Eur. J.*, 2001, **7**, 1202.

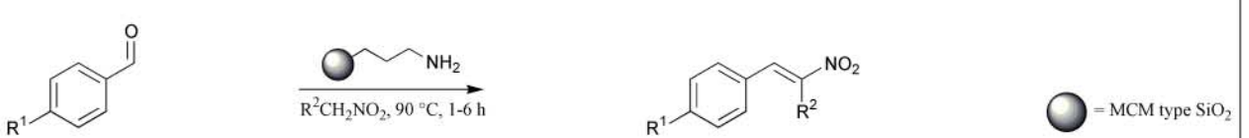
Sulfonamide catalyzed enantioselective reduction of ketones. ***Catalyst***



11 examples (yields 91-99%, ee% 48-97%). Preparation of the catalyst (2 steps from polystyrene resin), recycling experiments and optimisation of reaction conditions are also reported.

J. Hu, G. Zhao and Z. Ding, *Angew. Chem., Int. Ed.*, 2001, **40**, 1109.

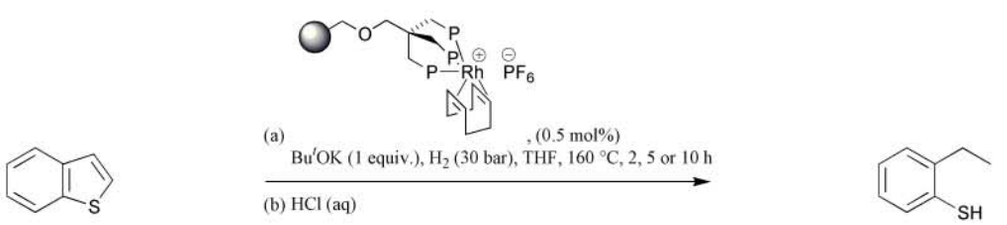
(*E*)-Nitrostyrenes *via* an amine catalysed nitroaldol reaction. ***Catalyst***



10 examples (yields 88-98%, GC purity 97-99%).

G. Demicheli, R. Maggi, A. Mazzacani, P. Righi, G. Sartori and F. Bigi, *Tetrahedron Lett.*, 2001, **42**, 2401.

Hydrogenolysis of benzo[*b*]thiophene by a tripodal triphosphine rhodium catalyst. ***Catalyst***



3 examples (yields 49-74%, TON 97-349). Catalyst recycling (2 examples, yields 48%, TON 95-96) and preparation of the catalyst are also reported.

C. Bianchini, M. Frediani and F. Vizza, *Chem. Commun.*, 2001, 479.

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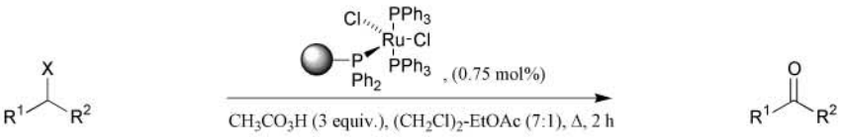
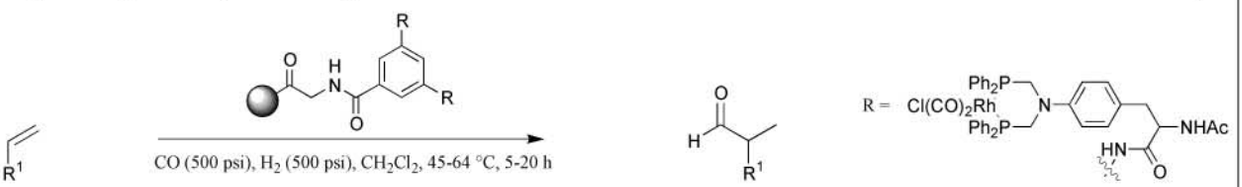
Ruthenium phosphine complex for hydrocarbon oxidation and transfer hydrogenation. ***Catalyst***



6 examples (yields 45-89%). Preparation of the catalyst and its use and reusability in transfer hydrogenation (4 examples, yields 40-83%) are also reported.

N. E. Leadbeater, *J. Org. Chem.*, 2001, **66**, 2168.

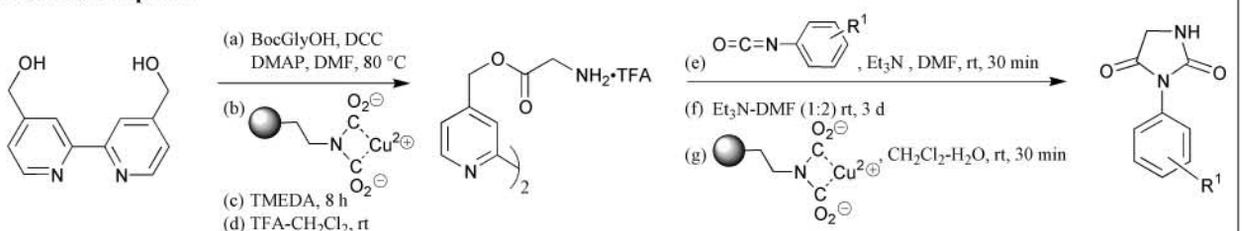
A recyclable hydroformylation catalyst. ***Catalyst***



4 examples (1st cycle yields 73-99%, 5th cycle yields 56-99%). The minor linear regioisomer is also produced (ratios vary). Preparation and application of a second, more highly branched catalyst with better recycling properties are also reported.

P. Arya, G. Panda, N. V. Rao, H. Alper, S. C. Bourque and L. E. Manzer, *J. Am. Chem. Soc.*, 2001, **123**, 2889.

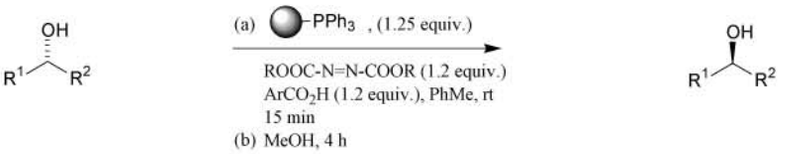
A phase-switch method employing immobilisation through metal-chelated tagging: synthesis of hydantoins and benzodiazepines. ***Scavenger***



6 examples (yields 91-99%, ^{1}H NMR purity > 92-> 93%). Synthesis of benzodiazepines *via* a similar route is also reported (2 examples, yields 49-51%, ^{1}H NMR purity > 90%).

S. V. Ley, A. Massi, F. Rodríguez, D. C. Horwell, R. A. Lewthwaite, M. C. Pritchard and A. M. Reid, *Angew., Chem., Int. Ed.*, 2001, **40**, 1053.

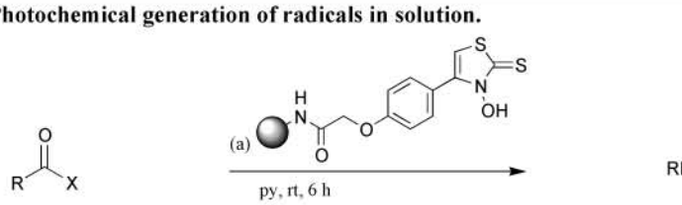
Mitsunobu reaction using triphenylphosphine linked to non-cross-linked polystyrene. ***Reagent***



3 examples (yields 71-83%). Mitsunobu reaction on a Baylis–Hillman adduct, using polymer-supported PPh_3, is also reported (1 example, yield 90%).

A. B. Charette, M. K. Janes and A. A. Boezio, *J. Org. Chem.*, 2001, **66**, 2178.

Photochemical generation of radicals in solution. ***Reagent***



4 examples (yields 62-92%). Preparation of the radical generator (2 steps from *N*-Fmoc-Gly-Wang resin) and its use in tetrahydrofuran synthesis *via* alkoxy radicals (2 examples) are also reported.

L. De Luca, G. Giacomelli, G. Porcu and M. Taddel, *Org. Lett.*, 2001, **3**, 855.

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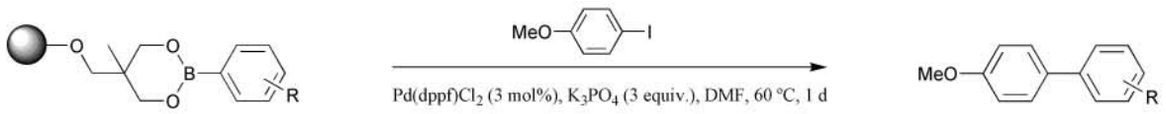
C–C bond formation *via* metal catalyzed release of supported boronic acids. ***Reagent***

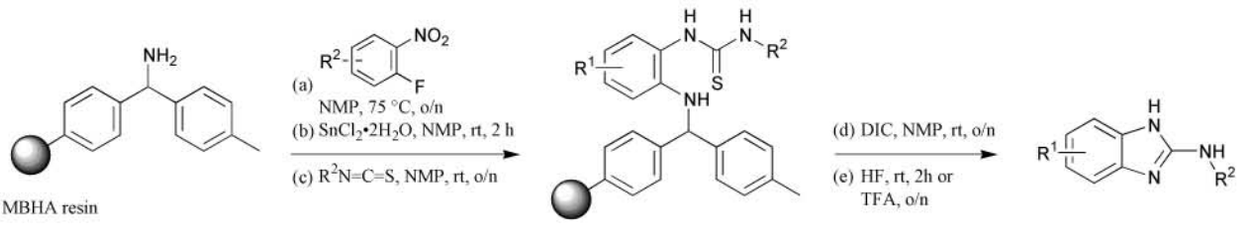


resin not specified

6 examples (yields 45-75%). Rhodium-catalysed nucleophilic addition to aldehydes and enones using supported boronic acids (9 examples, yields 43-81%, GC or ^{1}H NMR purity 98%) is also reported.

C. Pourbaix, F. Carreaux and B. Carboni, *Org. Lett.*, 2001, **3**, 803.

Traceless synthesis of 2-arylaminobenzimidazoles.

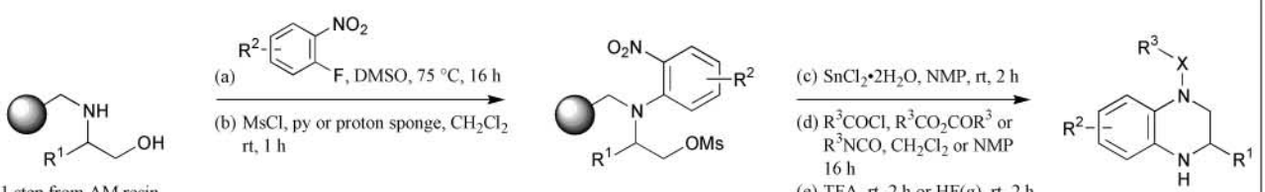


MBHA resin

6 examples (HPLC purity 79-98%). Further derivatisation of resin-bound aminobenzimidazoles by alkylation with electrophiles (2 examples) is also reported.

V. Krchnák, J. Smith and J. Vágner, *Tetrahedron Lett.*, 2001, **42**, 1627.

Traceless synthesis of tetrahydroquinoxalines.

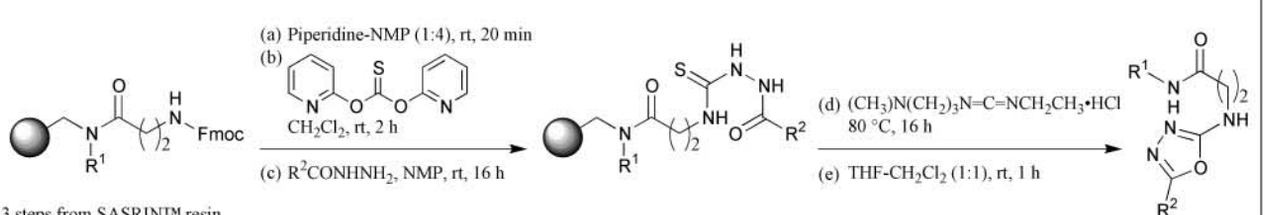


1 step from AM resin

5 examples (yields 79-96%, HPLC purity 85-95%). Preparation of tetrahydroquinoxalines without *N*-substitution (5 examples, yields 76-91%, HPLC purity 84-87%) is also reported.

V. Krchnák, J. Smith and J. Vágner, *Tetrahedron Lett.*, 2001, **42**, 2443.

1,3,4-Oxadiazoles.



3 steps from SASRIN™ resin

6 examples (yields 44-92%, ELS purity 90-100%).

J. P. Kilburn, J. Lau and R. C. F. Jones, *Tetrahedron Lett.*, 2001, **42**, 2583.

Pyridinium, tetrahydropyridine and piperidine derivatives.

2 steps from trityl resin

6 examples (yields 80-93%). Preparation of tetrahydropyridine and piperidine derivatives *via* a similar route is also reported (12 examples, yields 28-61%).

M. Eda and M. J. Kurth, *Tetrahedron Lett.*, 2001, **42**, 2063.

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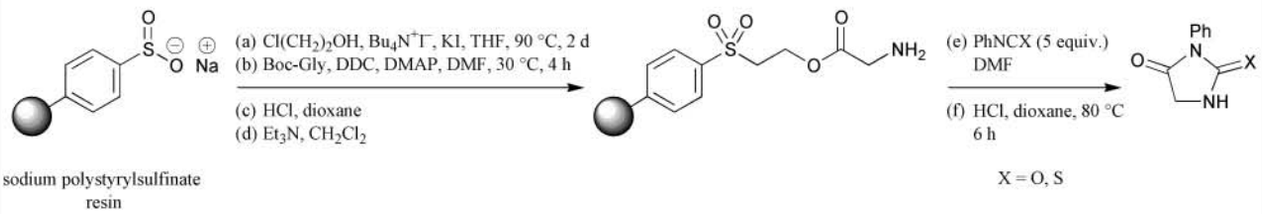
Hydantoins and ureas.

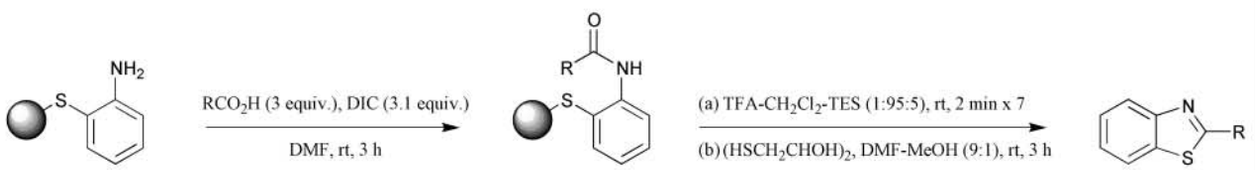


sodium polystyrylsulfinate resin

W. Huang, S. Cheng and W. Sun, *Tetrahedron Lett.*, 2001, **42**, 1973.

2 examples (yields 20-29%). Preparation of urea derivatives *via* a similar route (2 examples, yields 21-30%) is also reported.

Benzothiazolyls.

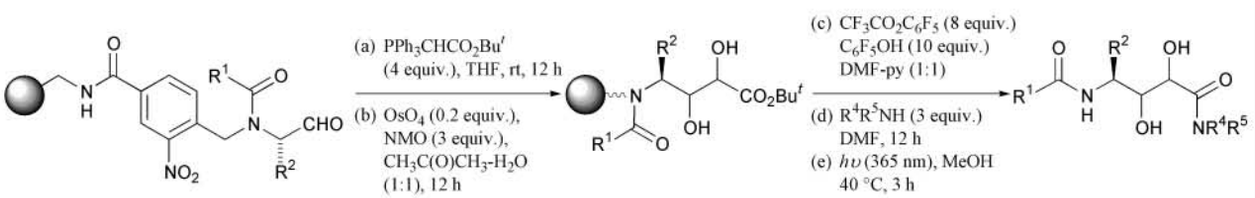


1 step from various trityl resins

S. Mourtas, D. Gatos and K. Barlos, *Tetrahedron Lett.*, 2001, **42**, 2201.

40 examples (yields 80-90%, HPLC purity 90-97%).

α-Hydroxy phosphonates and hydroxystatine amides.

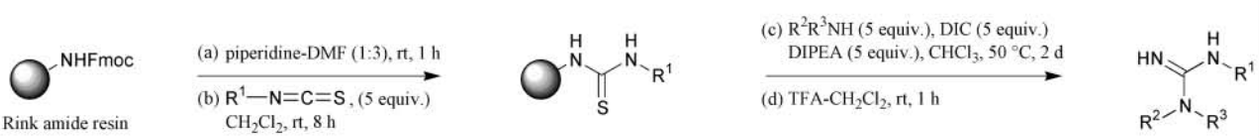


5 steps from Tentagel resin

R. E. Dolle, T. F. Herpin and Y. C. Shimshock, *Tetrahedron Lett.*, 2001, **42**, 1855.

6 examples (yields 65-72%). Preparation of α-hydroxy phosphonates using the same starting material (5 examples, yields 85-92%) is also described.

Disubstituted guanidines.

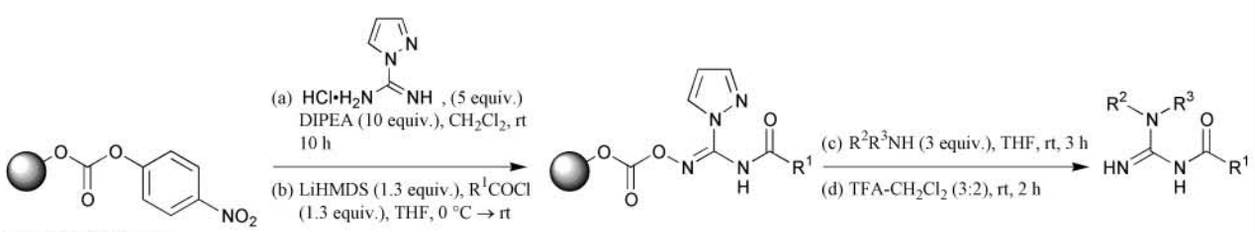


Rink amide resin

M. Li, L. J. Wilson and D. E. Portlock, *Tetrahedron Lett.*, 2001, **42**, 2273.

12 examples (yields 70-100%, HPLC purity 54-95%).

***N*-Acyl-*N'*-alkyl/aryl disubstituted guanidines.**



1 step from Wang resin

A. K. Ghosh, W. G. J. Hol and E. Fan, *J. Org. Chem.*, 2001, **66**, 2161.

14 examples (yields 61-88%).

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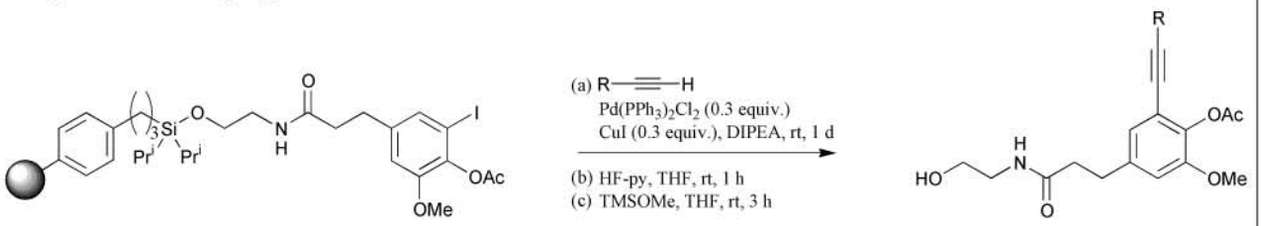
Sonogashira cross-coupling.

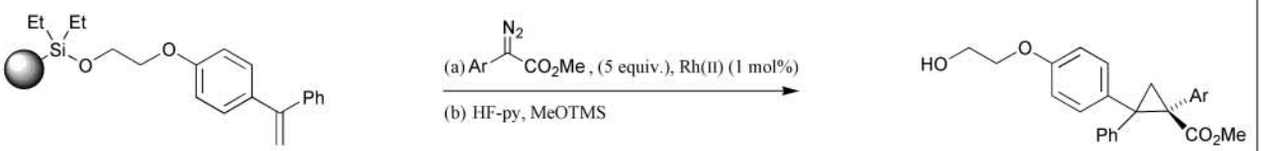


polystyrene macrobeads

Y. Liao, R. Fathi, M. Reitman, Y. Zhang and Z. Yang, *Tetrahedron Lett.*, 2001, **42**, 1815.

12 examples (^{1}H NMR purity >95%). Preparation of the substrates and Sonogashira cross-coupling of a supported terminal alkyne with aryl/vinyl halides/triflates (16 examples, ^{1}H NMR purity 85-100%) are also reported.

Catalytic asymmetric cyclopropanation.



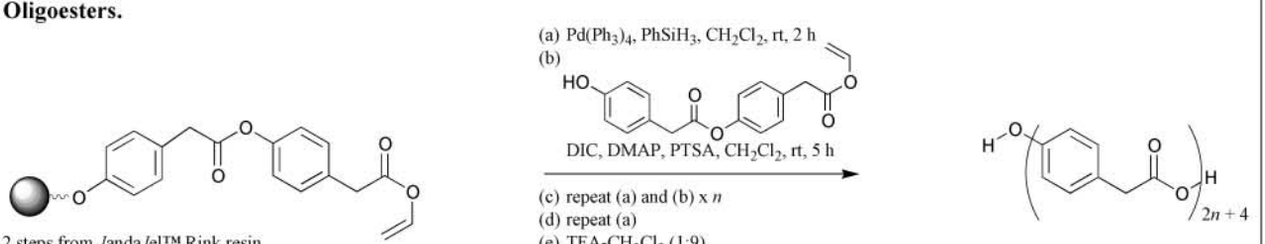
2 steps from PS-DES-SiH resin

source of Rh(II) = Rh_2(*S*-DOSP)$_4$ or Rh_2(TPA)$_4$

T. Nagashima and H. M. L. Davies, *J. Am. Chem. Soc.*, 2001, **123**, 2695.

7 examples (yields 16, 59-96%, *E*:*Z* 75:25-88:12, %ee of *E* isomer 86-93%).

Oligoesters.

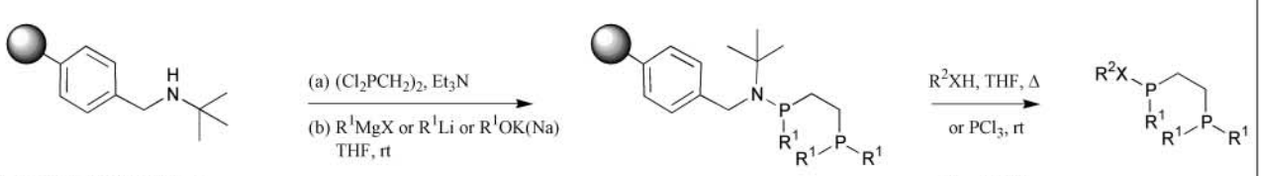


2 steps from Janda*el*™ Rink resin

O. Brümmer, B. Clapham and K. D. Janda, *Tetrahedron Lett.*, 2001, **42**, 2257.

4 examples (yields 47-79%, sample ^{1}H NMR purity 86-90%). Solution-phase synthesis of the dimeric ester building block is also reported.

Bidentate phosphorus-containing ligands.

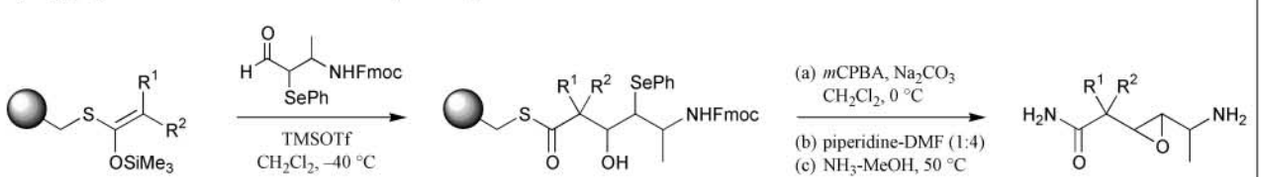


1 step from Merrifield resin

G. Y. Li, P. J. Fagan and P. L. Watson, *Angew. Chem., Int. Ed.*, 2001, **40**, 1106.

14 examples (yields 24-75%). Synthesis of a phosphinite-chlorophosphinite (yield 56%) *via* a similar route is also reported.

Epoxy peptidomimetics: inhibitors of cysteine proteases.



3 steps from Merrifield resin

M. Demarcus, M. L. Ganadu, G. M. Mura, A. Porcheddu, L. Quaranta, G. Reginato and M. Taddei, *J. Org. Chem.*, 2001, **66**, 697.

Preparation and biological evaluation of a 9-member library is reported (sample yield 67%, sample HPLC purity >80%). Solution-phase synthesis of the illustrated epoxy peptidomimetics and their incorporation into a solid-phase peptide sequence, as a mimic of a dipeptide frame, are also reported.

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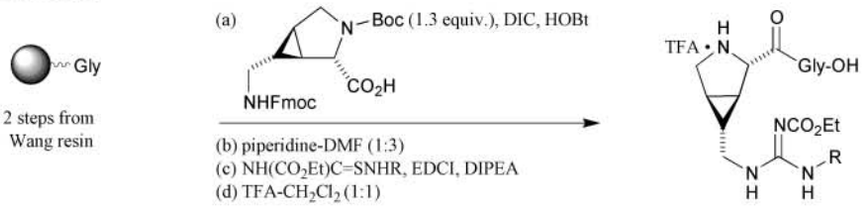
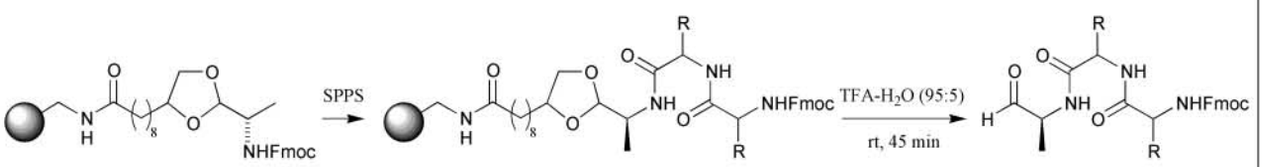
Guanidinylation of proline-templated amino acids: diversification strategy for poly-L-proline type II peptide mimic scaffolds.



13 examples (yields 63-83%, ^{1}H NMR purity >90%). Guanidinylation of a similar class of proline-templated ornithines *via* a similar route (yields 73-81%) and synthesis of 2 model pentapeptides on PAM resin is also reported.

A. Mami and J. S. Madalengoitia, *Org. Lett.*, 2001, **3**, 561.

Peptide aldehydes.

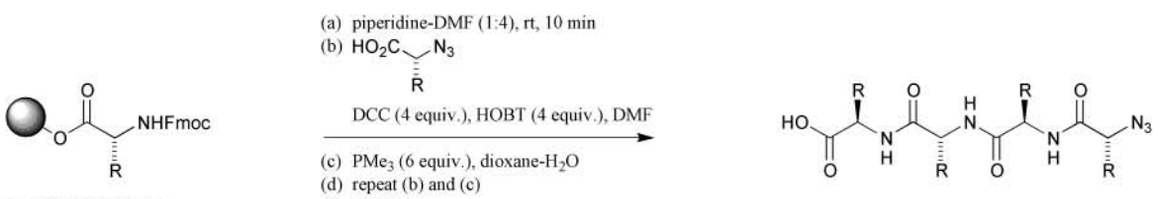


1 step from aminomethylated resin

4 examples (yields 91-95%, purity 75-89%). Solution-phase synthesis of the linker is also reported.

W. Yao and H. Y. Xu, *Tetrahedron Lett.*, 2001, **42**, 2549.

α-Azido acid building blocks to suppress diketopiperazine formation in peptide synthesis.

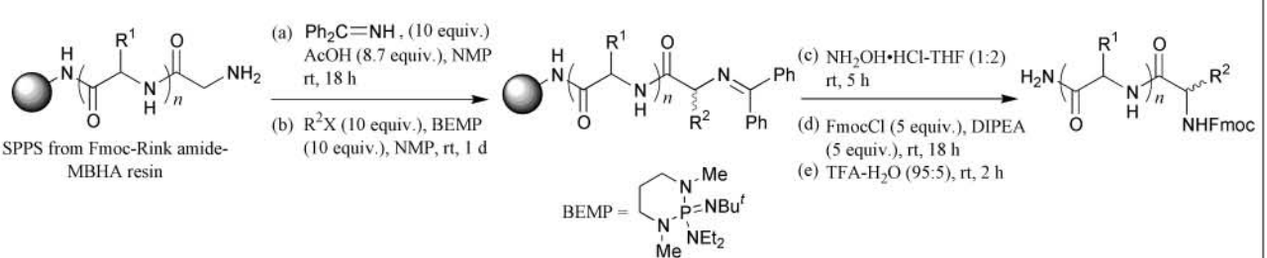


1 step from Wang resin

8 examples (yields 15-76%). Application of the procedure to tripeptide synthesis (4 examples, yields 46-81%) and solution-phase preparation of α-azido acid building blocks (28 examples, yields 41-89%) are also reported.

J. T. Lundquist and J. C. Pelletier, *Org. Lett.*, 2001, **3**, 781.

Amino amides and peptide amides bearing unnatural side-chains.

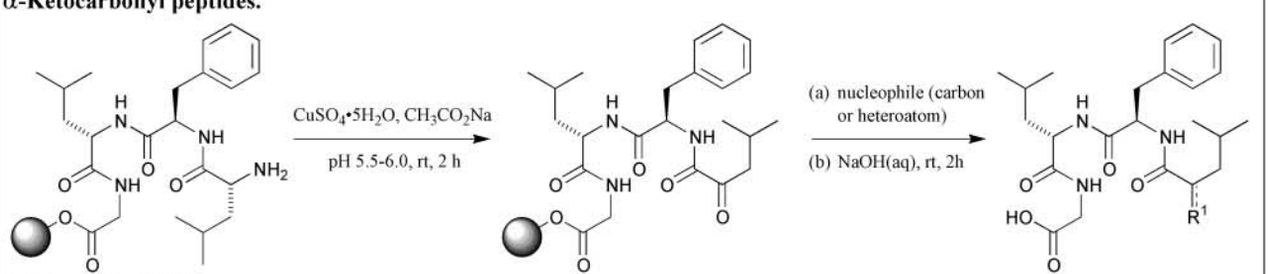


SPPS from Fmoc-Rink amide-MBHA resin

W. L. Scott, F. Delgado, K. Lobb, R. S. Pottorf and M. J. O'Donnell, *Tetrahedron Lett.*, 2001, **42**, 2073.

24 examples (yields 81-100%, HPLC purity 56-99%).

α-Ketocarbonyl peptides.



SPPS from POEPOP-400 resin

A. Papanikos, J. Rademann and M. Meldal, *J. Am. Chem. Soc.*, 2001, **123**, 2176.

5 examples (yields for diastereoisomers 52-63%). Transamination reactions on a variety of peptides are also reported (10 examples).

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