Perkin 1 Abstracts: Solid Phase Organic Synthesis

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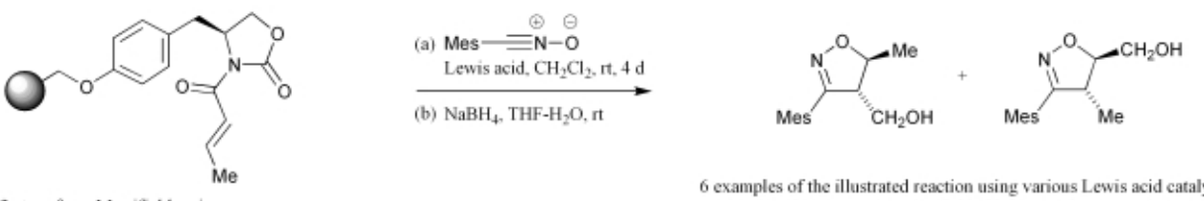
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

A reusable chiral linker based on an oxazolidinone chiral auxiliary: asymmetric 1,3-dipolar cycloadditions. ***Linker***

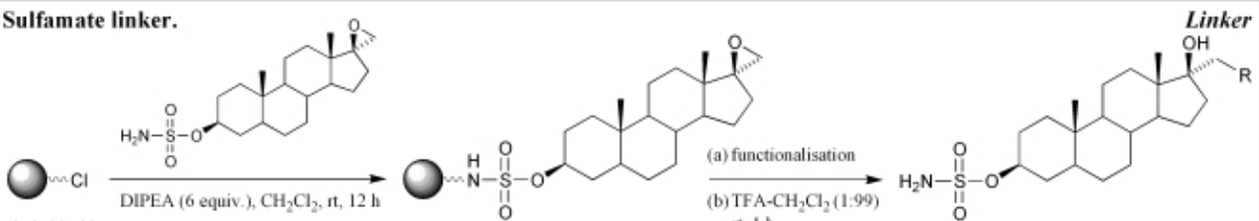


2 steps from Merrifield resin

6 examples of the illustrated reaction using various Lewis acid catalysts (yields 51–62%, isomeric ratio 67:33–72:28, ee of major regioisomer 26–60%). 6 examples of a similar reaction, using diphenylnitrone as the 1,3-dipole and various Lewis acid catalysts, are also reported (yields 20–43%, isomeric ratio 56:44–30:70, ee 6–89%).

G. Faita, A. Paio, P. Quadrelli, F. Rancati and P. Seneci, *Tetrahedron Lett.*, 2000, **41**, 1265.

Sulfamate linker. ***Linker***

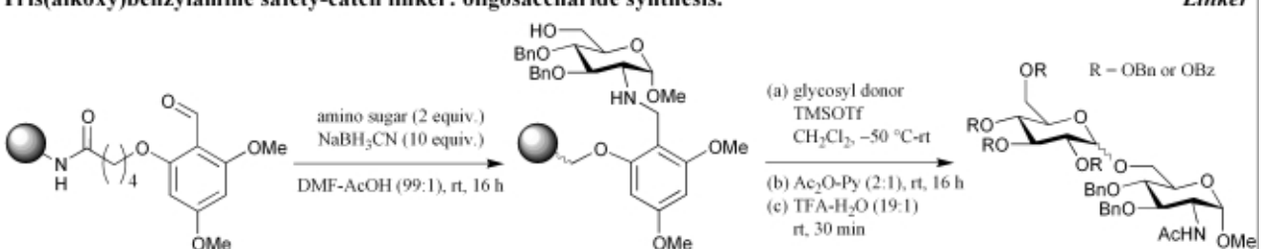


trityl chloride resin

The utility of the sulfamate linker is demonstrated in the preparation of 2 steroid derivatives (no yields given). Loading and cleavage studies of the sulfamate linker are also reported: acidic cleavage conditions regenerate sulfamates whereas nucleophilic cleavage of aryl sulfamates generates the corresponding phenols.

L. C. Ciobanu, R. Maltais and D. Poirier, *Org. Lett.*, 2000, **2**, 445.

Tris(alkoxy)benzylamine safety-catch linker: oligosaccharide synthesis. ***Linker***

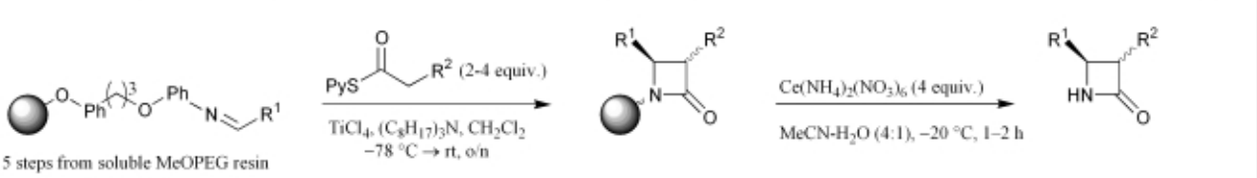


1 step from aminomethylated polystyrene resin

2 examples (yields 35–82%, R = OBn then α:β = mixed, R = OBz then α:β = <1:10). Anchoring and cleavage of 4 amino sugars from the illustrated linker are also reported (yields 41–96%).

J. F. Tolborg and K. J. Jensen, *Chem. Commun.*, 2000, 147.

Liquid-phase synthesis of β-lactams from modified poly(ethylene glycol). ***Support***

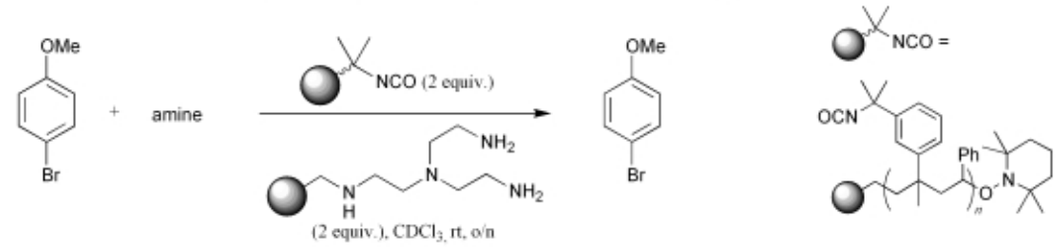


5 steps from soluble MeOPEG resin

4 examples of β-lactam synthesis *via* the illustrated route and 2 similar routes (yields 40–57%, varying *cis:trans* ratios). 3 examples of stereoselective β-lactam synthesis, using enantiomerically pure enolates and an enantiomerically pure polymer-supported imine, are also reported (yields 21–39%).

R. Annunziata, M. Benaglia, M. Cinquini and F. Cozzi, *Chem. Eur. J.*, 2000, **6**, 133.

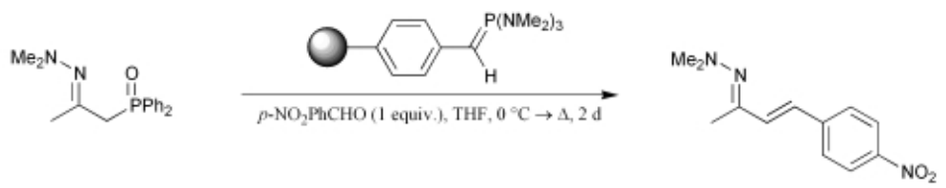
Preparation of "Rasta" isocyanate supports: application as amine scavengers. ***Reagent***



8 examples (no yields given). Preparation of the illustrated Rasta-NCO support and 4 different Rasta-NCO supports, *via* solvent-free, living free radical suspension polymerisation, from Merrifield resin is also reported.

J. C. Hodges, L. S. Harikrishnan and S. Ault-Justus, *J. Comb. Chem.*, 2000, **2**, 80.

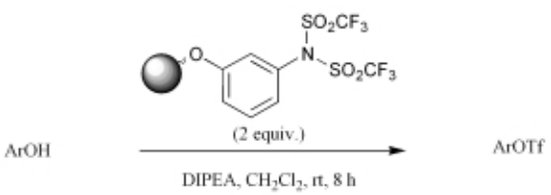
Polymer-supported phosphorus ylide: a reusable, neutral, non-nucleophilic Brønsted base. ***Reagent***



1 example (yield 65%). Synthesis of the illustrated polymer-bound ylide from Merrifield resin and its use in a Henry reaction and the C-alkylation of a benzophenone-imine derivative of glycine are also reported (yields 70–84%).

F. Palacios, D. Aparicio, J. M. de los Santos, A. Baceiredo and G. Bertrand, *Tetrahedron*, 2000, **56**, 663.

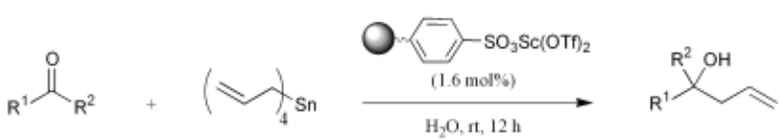
A soluble polymer-supported triflating reagent: preparation of aryl and enol triflates. ***Reagent***



8 examples (yields 88–97%, HPLC purity 92–97%). Preparation of the illustrated polymer-bound triflimide in 3 steps from PEG_{3400}-dimesylate and its use in triflating 5 lithium enolates are also reported (yields 72–92%).

A. D. Wentworth, P. Wentworth Jr., U. F. Mansoor and K. D. Janda, *Org. Lett.*, 2000, **2**, 477.

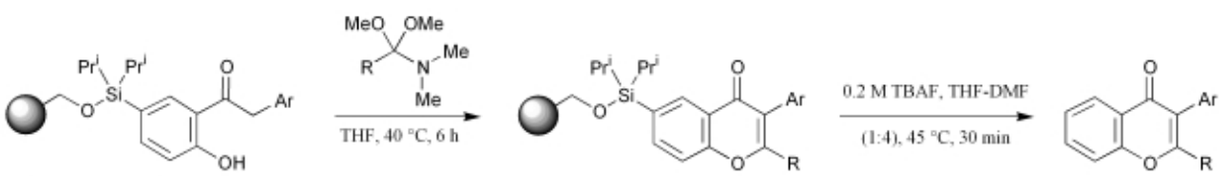
A reusable polymer-supported scandium catalyst which shows high activity in water. ***Catalyst***



The utility of the polymer-bound Lewis acid-surfactant combined catalyst, which promotes organic reactions in water, is demonstrated in the preparation of 10 homoallylic alcohols *via* the illustrated route (yields 72–100%). Preparation of the illustrated catalyst from a polystyrene support and its use in a Diels-Alder, a Strecker and an aldol-type reaction are as also reported (yields 77–98%).

S. Nagayama and S. Kobayashi, *Angew. Chem., Int. Ed.*, 2000, **39**, 567.

Traceless synthesis of 2,3-disubstituted benzopyran-4-ones.

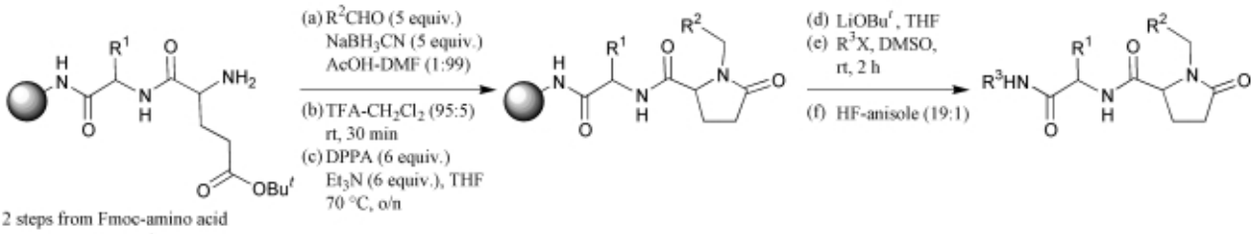


hydroxymethyl polystyrene resin

A previously established traceless diisopropylsilyloxy linker methodology was used to construct 10 of the illustrated benzopyranones and 1 silanol derivatised benzopyranone *via* a similar route (yields 20–74%, HPLC purity 51–100%).

L. S. Harikrishnan and H. D. Hollis Showalter, *Tetrahedron*, 2000, **56**, 515.

Disubstituted pyrrolidin-2-ones

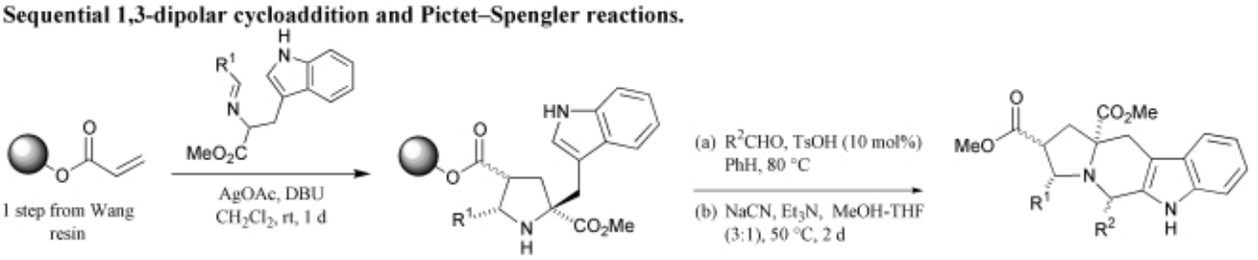


2 steps from Fmoc-amino acid MBHA resin

15 examples (yields 73–100%).

J. M. Alvarez-Gutierrez, A. Nefzi and R. A. Houghten, *Tetrahedron Lett.*, 2000, **41**, 851.

Sequential 1,3-dipolar cycloaddition and Pictet–Spengler reactions.

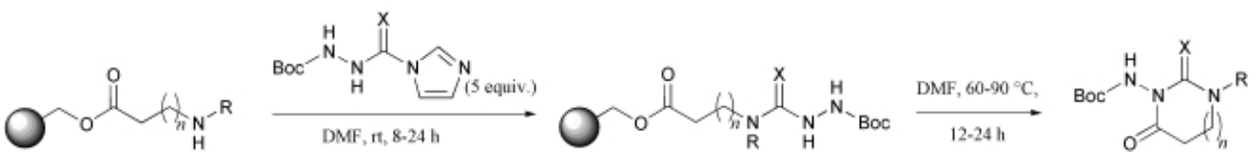


1 step from Wang resin

Preparation of a 100-member library is reported. Acid cleavage of 4 polymer-bound Pictet–Spengler products to give the corresponding acids (yields 33–46%) and 3 sequential 1,3-dipolar cycloaddition–Pictet–Spengler–palladium catalysed reactions is also reported (yields 36–42%).

H. A. Dondas, R. Grigg, W. S. Maclachlan, D. T. MacPherson, J. Markandu, V. Sridharan and S. Suganthan, *Tetrahedron Lett.*, 2000, **41**, 967.

3-Aminohydantoin, dihydrouracil, thiohydantoin and dihydrothiouracil derivatives.



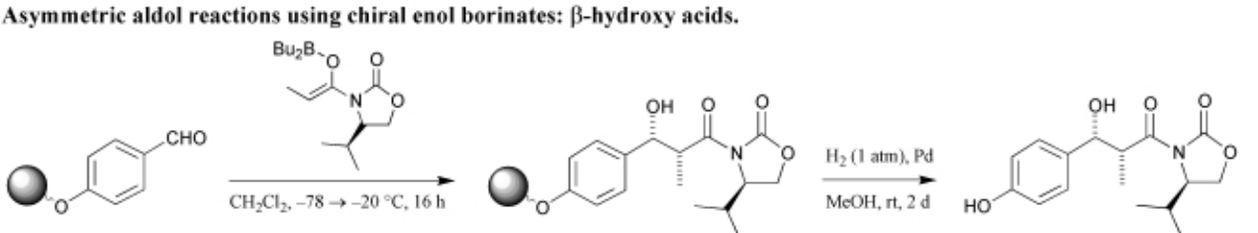
2 steps from Merrifield resin

n = 0 or 1
X = O or S

23 examples (yields 21–69%, HPLC purity 66–98%).

S. Wu and J. M. Janusz, *Tetrahedron Lett.*, 2000, **41**, 1165.

Asymmetric aldol reactions using chiral enol borinates: β-hydroxy acids.

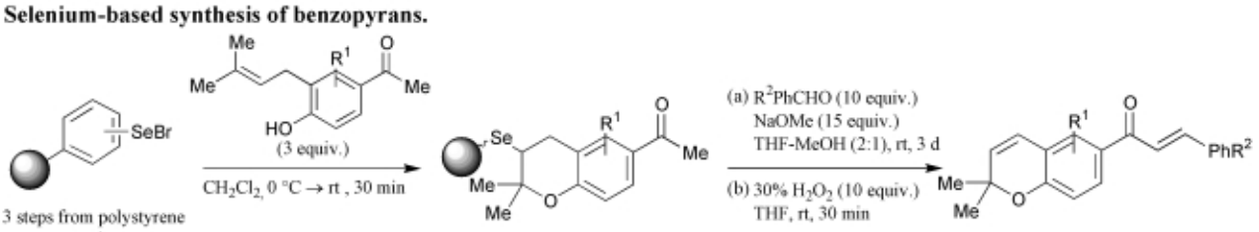


2 steps from soluble MeOPEG resin

1 example (yield 85%, NMR purity ≥ 97%). 5 other polymer-bound diketides, similar to the illustrated example, are prepared using various chiral enol borinates (yields 57–88%, NMR purity ≥ 97%).

M. Reggelin, V. Brenig and C. Zur, *Org. Lett.*, 2000, **2**, 531.

Selenium-based synthesis of benzopyrans.

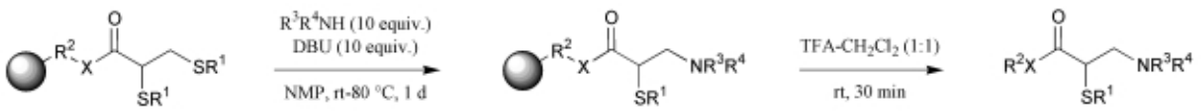


3 steps from polystyrene resin

9 examples (yields 54–91%). The illustrated selenium-based linking strategy for the formation of 2,2-dimethylbenzopyrans is also used for the synthesis of 8 pyranocoumarins, a stilbene, a macrophylloside heptaacetate, 14 functionalised benzopyrans and a small library of aldosterone biosynthesis inhibitors.

K. C. Nicolaou, G. Cao and J. A. Pfefferkorn, *Angew. Chem., Int. Ed.*, 2000, **39**, 734 and 739.

2-Thio-3-aminopropionic acid derivatives *via* sequential nucleophilic substitution.

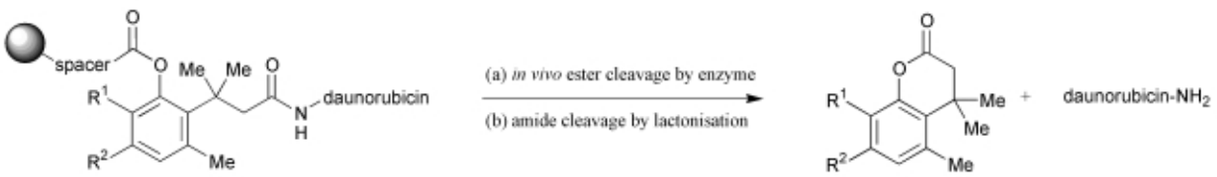


2 steps from Wang or an amine-bound resin

F. Zaragoza and H. Stephensen, *Angew. Chem., Int. Ed.*, 2000, **39**, 554.

10 examples (yields 31–95%).

Drug delivery systems based on trimethyl lock lactonisation: poly(ethylene glycol) double pro-drugs of amino-containing compounds.

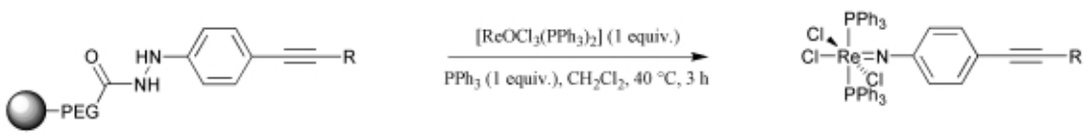


1 step from poly(ethylene glycol)

R. B. Greenwald, Y. H. Choe, C. D. Conover, K. Shum, D. Wu and M. Royzen, *J. Med. Chem.*, 2000, **43**, 475.

Preparation of 7 of the illustrated PEG-ester pro-drugs, 1 PEG-carbonate and 1 PEG-carbamate pro-drug is reported. All synthesised pro-drugs are evaluated *in vitro* and *in vivo* to examine their biological and hydrolytic activity.

Polymer-supported hydrazine substrate for labelling estradiol ligands with rhenium.



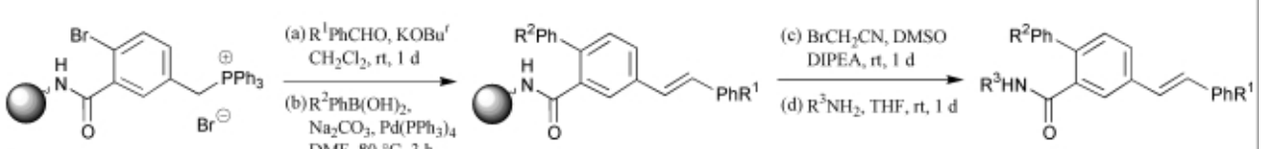
1 step from carboxy tentagel resin

R = estradiol derivative

J. B. Arterburn, K. Venkateswara Rao and M. C. Perry, *Angew. Chem., Int. Ed.*, 2000, **39**, 771.

1 example (yield 82%).

Blockers of human T cell KV1.3 potassium channels.

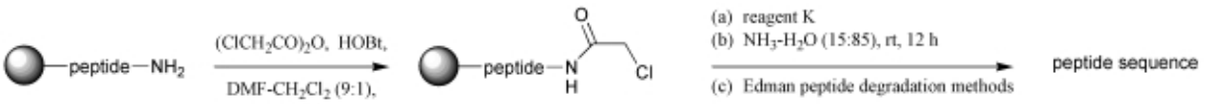


resin not specified

A. Lew and A. R. Chamberlin, *Bioorg. Med. Chem., Lett.*, 1999, 3267.

Using Biosym/MSI's ligand design program LUDI, the preparation and biological evaluation of a 400-member library is reported.

α-Chloroacetyl *N*-terminal capping of peptides for Edman sequencing.



PEGA resin

reagent K = TFA-PhOH-H_2O-PhSH-$HSCH_2CH_2SH$ (82.5:5:5:5:2.5)

M. A. Shogren-Knaak, K. A. McDonnell and B. Imperiali, *Tetrahedron Lett.*, 2000, **41**, 827.

>100 000 peptides (23 residues each) are capped with the α-chloroacetyl group: 3 of the capped peptides are converted to glycine by NH_3, as illustrated above, to perform *N*-terminal Edman peptide sequencing.