Perkin 1 Abstracts: Solid Phase Organic Synthesis

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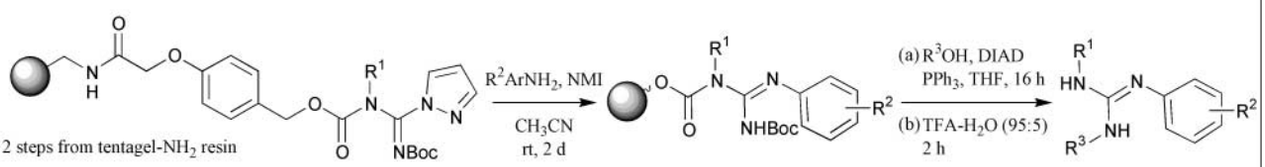
Perkin 1 Abstracts: Solid Phase Organic Synthesis are a selection of significant papers published in the recent literature covering the broad area of Solid Phase Organic Synthesis (SPOS). The abstracts cover preparation of single compounds on solid support as well as combinatorial libraries. Advances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

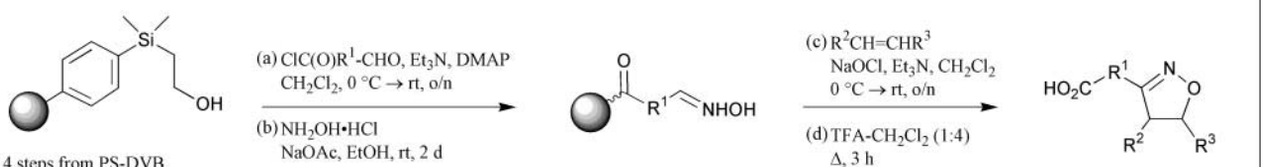
Synthesis of substituted guanidines using a novel acid labile linker. ***Linker***



M. Patek, M. Smrcina, E. Nakanishi and H. Izawa, *J. Comb. Chem.*, 2000, **2**, 370.

Preparation of an 880-member library is reported (yields 80-95%, HPLC purity 50-95%).

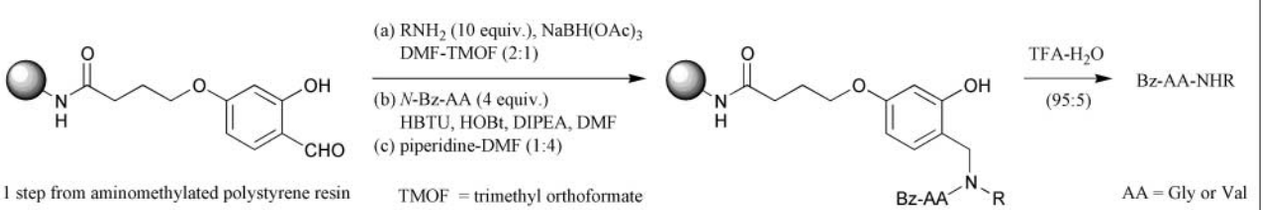
β-Dimethylphenylsilylethyl ester linker: isoxazoline synthesis. ***Linker***



C. Alonso, M. H. Nantz and M. J. Kurth, *Tetrahedron Lett.*, 2000, **41**, 5617.

9 examples and 3 similar examples of isoxazoline synthesis using the illustrated linker are reported (yields 50-75%).

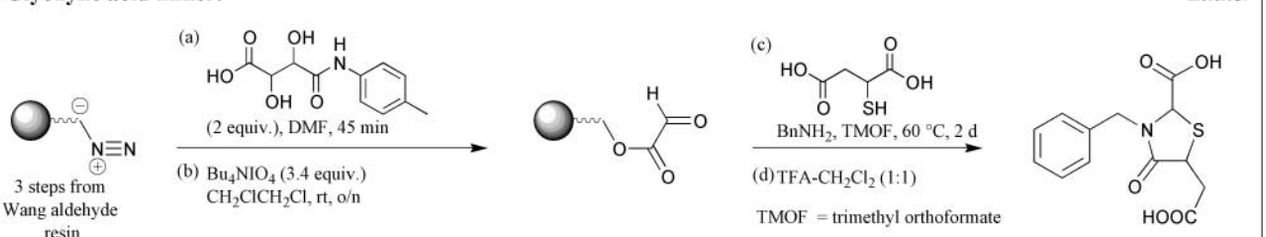
4-Alkoxy-2-hydroxybenzaldehyde linker for the synthesis of *C*-terminal modified peptides and peptidomimetics. ***Linker***



T. Okayama, A. Burritt and V. Hruby, *Org. Lett.*, 2000, **2**, 1787.

3 examples (yields 78-97%). Preparation of a Boc protected peptide and a Boc protected hydrazone, from an *O*-acyl derivative of the illustrated aldehyde linker, is also reported (yields 64-74%).

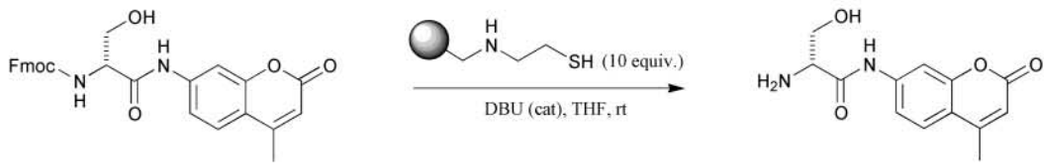
Glyoxylic acid linker. ***Linker***



N. Schlienger, M. R. Bryce and T. K. Hansen, *Tetrahedron Lett.*, 2000, **41**, 5147.

1 example (yield 33%). Preparation of a *p*-nitrophenylhydrazone derivative, from the illustrated ester-linked glyoxylic acid, and preparation of a polymer-bound amide-linked glyoxylic acid derivative are reported.

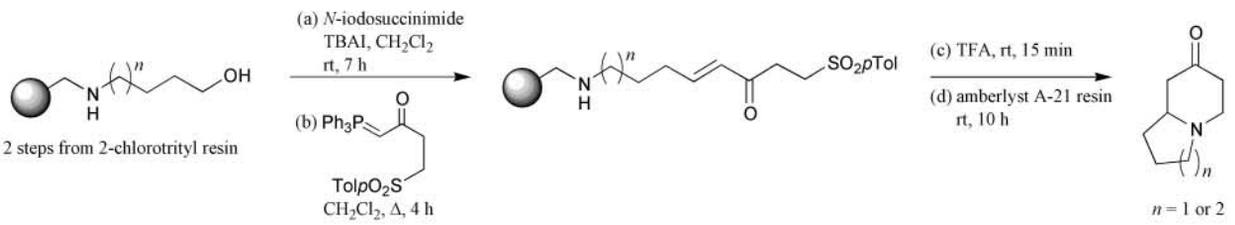
_N_-(2-Mercaptoethyl)aminomethyl polystyrene as a dibenzofulvene scavenger. ***Scavenger***



1 example (90%). Solution-phase Fmoc deprotection of different starting materials using a catalytic DBU–octanethiol reagent system is also reported (5 examples, yields 81-100%, HPLC purity >95%).

J. E. Sheppeck II, H. Kar and H. Hong, *Tetrahedron Lett.*, 2000, **41**, 5329.

Indolizidine and quinolizidine derivatives.

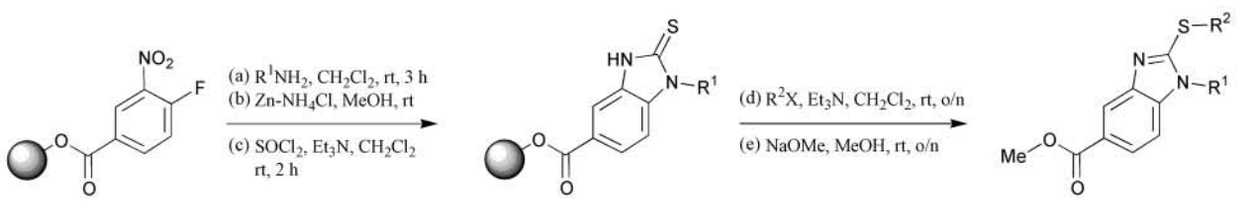


2 steps from 2-chlorotrityl resin

A. Barco, S. Benetti, C. De Risi, P. Marchetti, G. Piero Pollini and V. Zanirato, *J. Comb. Chem.*, 2000, **2**, 337.

2 examples (yields 40-46%).

Liquid-phase synthesis of benzimidazole derivatives.

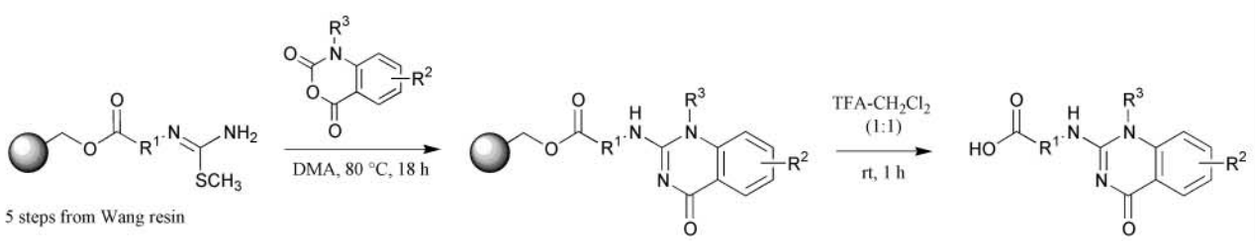


1 step from soluble MeO-PEG-OH resin

C.-M. Yeh, C.-L. Tung and C.-M. Sun, *J. Comb. Chem.*, 2000, **2**, 341.

26 examples (yields 64-99%, HPLC purity 41-94%).

2-Aminoquinazolin-4(1*H*)-one derivatives.

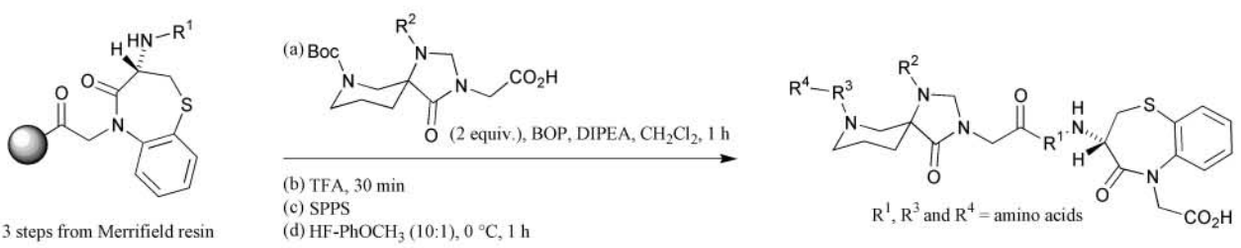


5 steps from Wang resin

A. Gopalsamy and H. Yang, *J. Comb. Chem.*, 2000, **2**, 378.

11 examples (yields 85-95%, HPLC purity 60-85%).

(3*S*)-Amino-5-carbonylmethyl-2,3-dihydro-1,5-benzothiazepin-4(5*H*)-one (D-BT) derivatives: bradykinin B_1 antagonists.

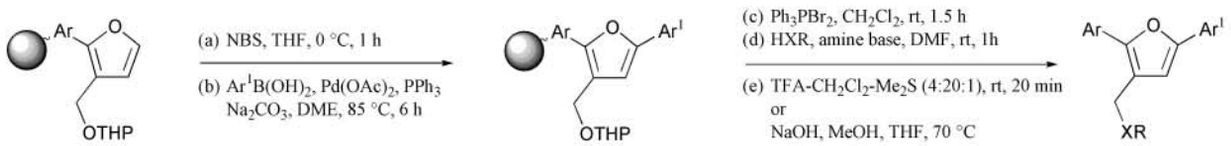


3 steps from Merrifield resin

P. Bedos, M. Amblard, G. Subra, P. Dodey, J.-M. Luccarini, J.-L. Paquet, D. Pruneau, A. Aumelas and J. Martinez, *J. Med. Chem.*, 2000, **43**, 2387.

11 examples (HPLC purity >98%).

Substituted bi-aryl furan derivatives.



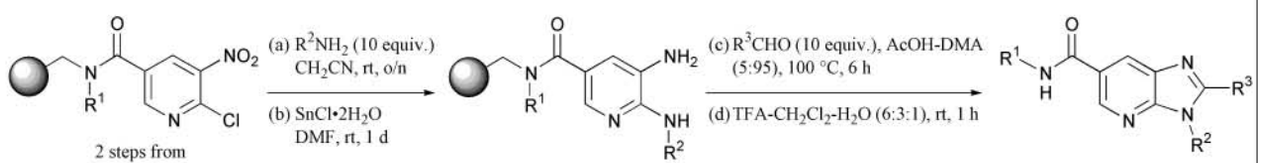
Wang resin

X = N or S

Y. Han, A. Roy and A. Giroux, *Tetrahedron Lett.*, 2000, **41**, 5447.

18 examples (yields 42-74%, LCMS purity 40-94%).

Substituted 7-azabenzimidazoles.

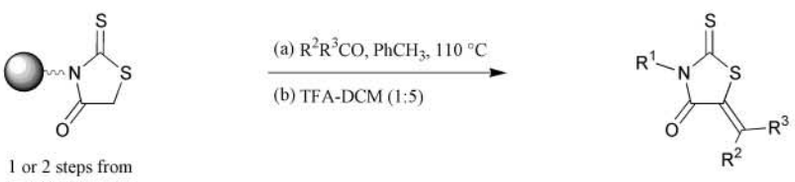


2 steps from
4-formyl-3-methoxyphenyloxymethyl
polystyrene resin

E. Farrant and S. S. Rahman, *Tetrahedron Lett.*, 2000, **41**, 5383.

8 examples (yields 50-94%, HPLC purity 81-98%).

5-Arylalkylidenerhodanine.

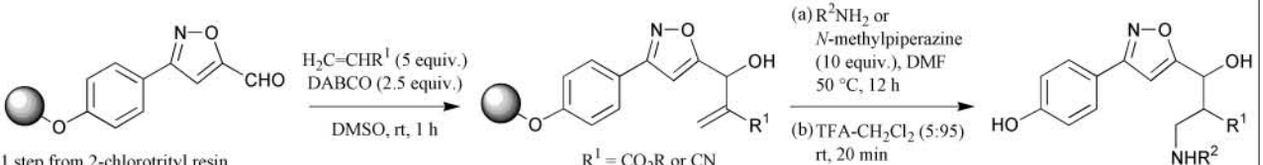


1 or 2 steps from
5 different resins

C. L. Lee and M. M. Sim, *Tetrahedron Lett.*, 2000, **41**, 5729.

12 examples (yields 60-88%, HPLC purity 54-91%).

Isoxazoles.



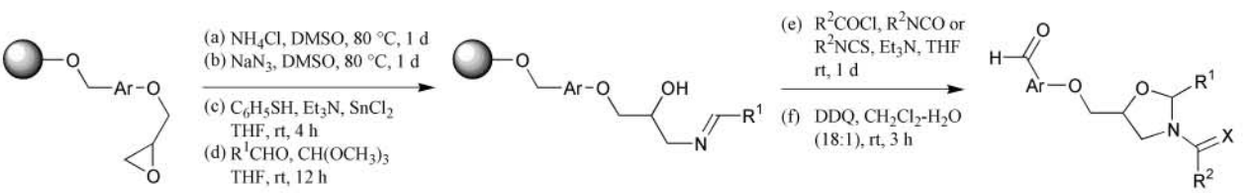
1 step from 2-chlorotrityl resin

$R^1 = CO_2R$ or CN

32 examples (representative yields 65-97%, HPLC purity 69-94%). 2 Wittig reactions, 2 nitroaldol condensation reactions and the preparation of 1 oxime and 3 enamines from the illustrated polymer-bound isoxazolecarboxaldehyde are also reported (yields 76-96%, HPLC purity 85-97%).

S. Batra, S. K. Rastogi, B. Kundu, A. Patra and A. P. Bhaduri, *Tetrahedron Lett.*, 2000, **41**, 5971.

1,3-Oxazolidine derivatives.



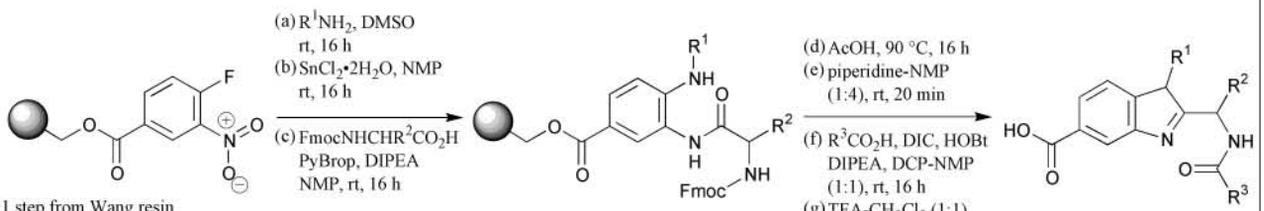
1 step from Wang resin

X = O or S

H. S. Oh, H. Hahn, S. H. Cheon and D.-C. Ha, *Tetrahedron Lett.*, 2000, **41**, 5069.

16 examples (yields 6-92%).

Substituted 2-aminomethylbenzimidazoles.

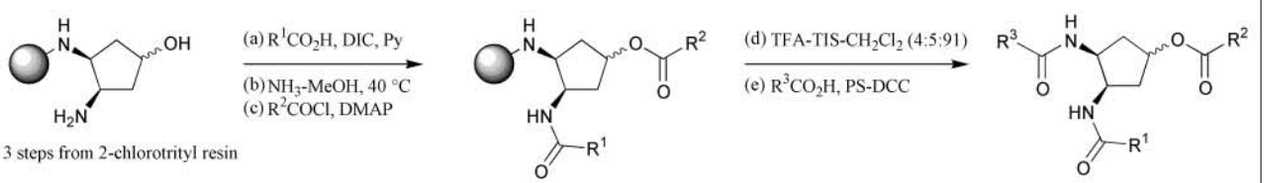


1 step from Wang resin

J. P. Kilburn, J. Lau and R. C. F. Jones, *Tetrahedron Lett.*, 2000, **41**, 5419.

6 examples (yields 36-86%, ELS purity 70-99%).

3,4-Diaminocyclopentanol scaffolds.

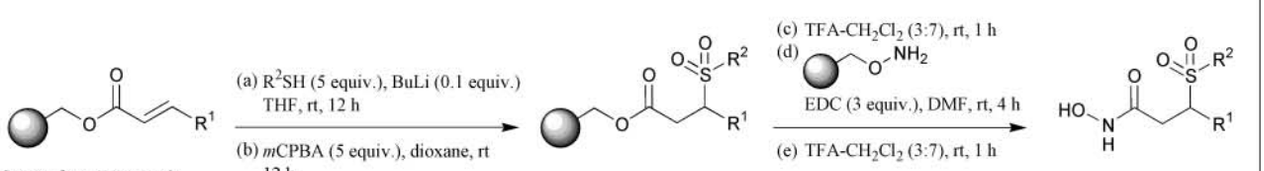


3 steps from 2-chlorotrityl resin

Y. Guan, M. A. Green and D. E. Bergstrom, *J. Comb. Chem.*, 2000, **2**, 297.

54 examples (yields 44-100%, HPLC purity 20-92%).

Arylsulfonehydroxamate derivatives.

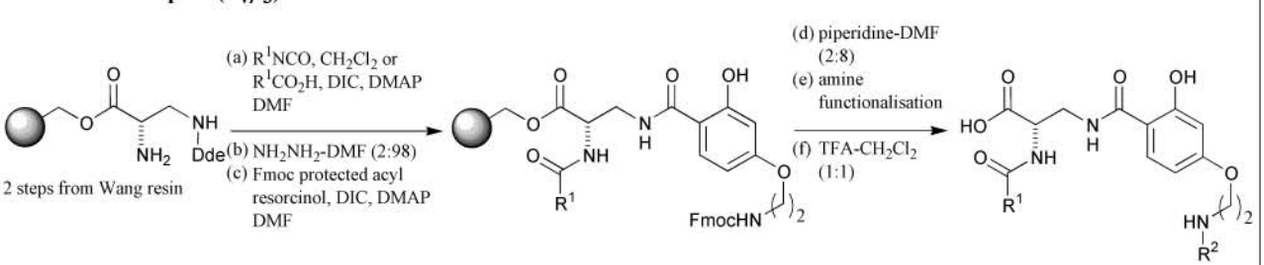


2 steps from Wang resin

J. M. Salvino, R. Mathew, T. Kiesow, R. Narensingh, H. J. Mason, A. Dodd, R. Groneberg, C. J. Burns, G. McGeehan, J. Kline, E. Orton, S.-Y. Tang, M. Morrisette and R. Labaudininiere, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1637.

Preparation and biological evaluation of a 50-member library is reported (HPLC purity >80%).

Vitronectin receptor ($\alpha_v\beta_3$) inhibitors.

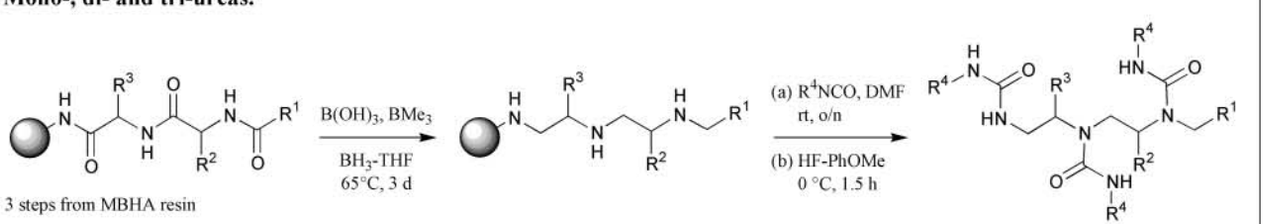


2 steps from Wang resin

A. Gopalsamy, H. Yang, J. W. Ellingboe, K. L. Kees, J. Yoon and R. Murrills, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1715.

Preparation and biological evaluation of a 112-member library is reported (yields 55-88%, HPLC purity >90%).

Mono-, di- and tri-ureas.

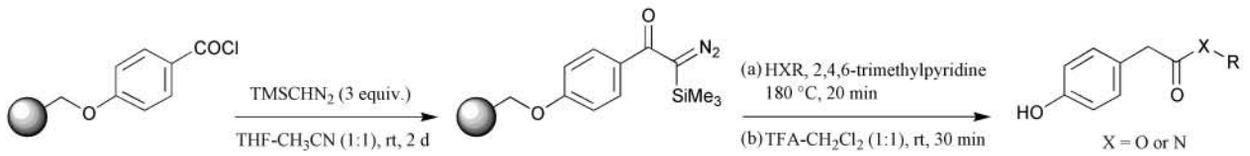


3 steps from MBHA resin

A. Nefzi, N. A. Ong and R. A. Houghten, *Tetrahedron Lett.*, 2000, **41**, 5441.

Preparation of a 135-member library is described (representative yields 85-98%, HPLC purity >95%). Preparation of 23 mono-ureas and 4 di-ureas, *via* a similar route, is also reported (HPLC purity >95%).

α-TMSdiazoketones

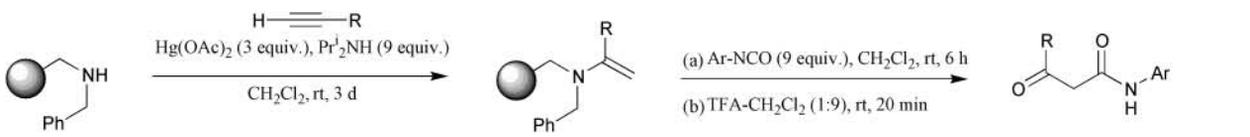


3 steps from Wang resin

4 examples (yields 46-63%). The use of the illustrated resin-bound TMSdiazoketone is also demonstrated in the preparation of 6 substituted oxazoles, 4 α-keto substitution reactions and 1 Buchner reaction (yields 41-66%).

Y. Iso, H. Shindo and H. Hamana, *Tetrahedron*, 2000, **56**, 5353.

Polymer-bound enamines: synthesis of β-ketoamides and γ-nitroketones.

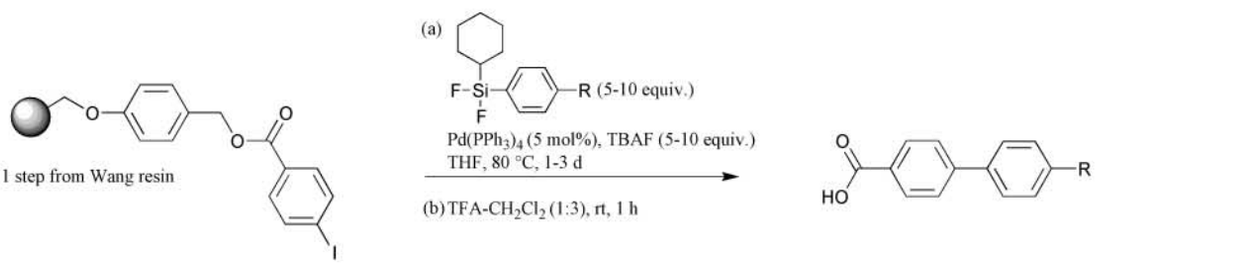


1 step from Wang bromo polystyrene resin

9 examples (yields 45-72%, HPLC purity 45-72%). Preparation of 10 γ-nitroketones from the illustrated polymer-bound enamine is also reported (yields 49-87%, HPLC purity 71-90%).

F. Aznar, C. Valdés and M.-P. Cabal, *Tetrahedron Lett.*, 2000, **41**, 5683.

Palladium catalysed cross-coupling reaction of aryl(fluoro)silanes with 4-iodobenzoic acid.

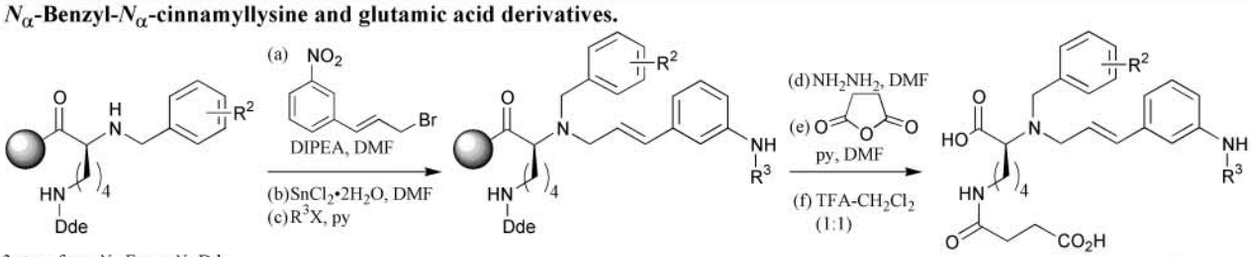


1 step from Wang resin

8 examples (yields 91-100%).

F. Homsi, K. Nozaki and T. Hiyama, *Tetrahedron Lett.*, 2000, **41**, 5869.

N_α-Benzyl-N_α-cinnamyllysine and glutamic acid derivatives.

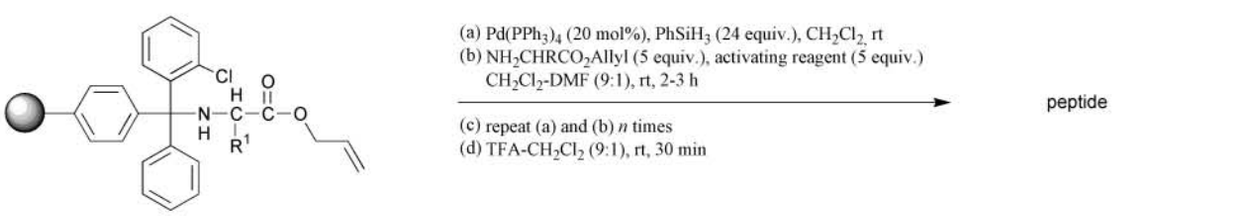


3 steps from N_α-Fmoc-N_ε-Dde lysine loaded Wang resin

Preparation of a 17-member library is reported (yields 35-85%, ^{1}H NMR purity >85%). Preparation of 7 N_ε-unsubstituted lysine derivatives and 14 *N*-benzyl-*N*-cinnamylglutamic acids, *via* a similar route, is also reported (yields 30-85%).

P. J. Connolly, K. N. Beers, S. K. Wetter and W. V. Murray, *Tetrahedron Lett.*, 2000, **41**, 5187.

Peptide synthesis in the reverse (*N* → *C*) direction.



1 step from 2-chlorotrityl resin

7 examples (HPLC purity 20-73%).

N. Thieriet, F. Guibé and F. Albericio, *Org. Lett.*, 2000, **2**, 1815.