Insoluble Polymer Supports as Monoblocking Agents of Symmetrical Diamines

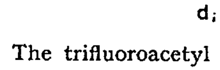
By Dilip M. Dixit and Clifford C. Leznoff*

(Department of Chemistry, York University, Downsview, Ontario, Canada M3J 1P3)

Summary Benzoylation of monoprotected polymer-bound symmetrical aliphatic diamines at the free amino end and cleavage with trifluoroacetic acid yields the unsymmetrical diamides, $CF_3CONH[CH_2]_nNHCOPh$, where n = 4, 6, 8, 10, or 12.

Although symmetrical diamines are inexpensive substrates for an organic synthesis, their use is often limited to the formation of symmetrical products derived from reaction at both ends of the molecule. The use of symmetrical diamines in the synthesis of spermidine[1,2] and spermidine-type analogues is marred by the fact that the symmetrical diamine must be monoprotected in the very first step. Acetylation of 1,4-diaminobutane with 1 equiv. of acetic anhydride gives *N*-acetyl-1,4-diaminobutane in only 22—23% yield.[2,3] Alternatively, debenzoylation of *NN'*-dibenzoyl-1,4-diaminobutane gives *N*-benzoyl-1,4-diaminobutane in low yield.[4]

We have previously shown that insoluble polymer supports can be used as monoblocking agents of symmetrical diols,[5,6] dialdehydes,[7] diacid chlorides,[8] and dihydroxy aromatic compounds.[9] We now report that insoluble polymer supports can be used as monoblocking agents of symmetrical diamines. Thus a 2% crosslinked divinylbenzene–styrene copolymer, containing 1·1 equiv. of benzyl chloride functional groups,[10] was converted into the polymer-bound benzyl alcohol[10] (**1**), which upon treatment with *p*-nitrophenyl chloroformate gave a polymer-bound benzyl *p*-nitrobenzyl carbonate (**2**). Treatment of (**2**) with a large excess of the symmetrical aliphatic diamines $H_2N[CH_2]_nNH_2$ (**3a**—**e**), where n = 4, 6, 8, 10, or 12, respectively, for 24—48 h at room temperature in benzene yielded the polymer-bound aminocarbamates (**4a**—**e**). Benzoylation of (**4a**—**e**) with a five-fold excess of benzoyl chloride and triethylamine in benzene for 24 h at room temperature gave the polymer-bound *N*-benzoyl carbamates (**5a**—**e**), which on treatment with a mixture of trifluoroacetic acid, trifluoroacetic anhydride, and chloroform (10 : 1 : 10) liberated 0·3—0·8 mmol g^{-1} of the *N*-benzoyl-*N'*-trifluoroacetyl-1,ω-diaminoalkanes (**6a**—**e**) in 50—80% yield with almost quantitative conversions. A small amount of unchanged (**3a**—**e**) was recovered in each case as the *NN'*-ditrifluoroacetyl-1,ω-diaminoalkanes (**7a**—**e**). The unsymmetrical diamides (**6a**—**e**) were readily separated from the symmetrical diamides (**7a**—**e**) by preparative t.l.c. on silica gel using methanol–chloroform (1 : 4) as eluant.



(1); R = H

(2); $R = -CO_2-p-NO_2C_6H_4$

(4a-e), $R = -CONH[CH_2]_nNH_2$

(5a-e), $R = -CONH[CH_2]_nNHCOPh$

$R^1HN[CH_2]_nNHR^2$

(6a-e); $R^1 = CF_3CO$, $R^2 = PhCO$

(7a-e), $R^1 = R^2 = CF_3CO$

a; $n = 4$ b; $n = 6$ c; $n = 8$
d; $n = 10$ e; $n = 12$

The trifluoroacetyl group of (**6a**—**e**) can be selectively removed by treatment with mild base[11] to afford mono-amine monoamides. All spectroscopic and analytical data of (**6a**—**e**) and (**7a**—**e**) confirmed the structures of these unknown compounds. The mass spectra of (**6a**—**e**) and (**7a**—**e**) exhibited weak parent ions and fragmentation patterns consistent with the assigned structures.[12] Polymer (**2**), recovered from the synthetic scheme, can be recycled. The recovery of (**7a**—**e**) indicates that some of the (**3a**—**e**) was attached to the polymer at both ends (doubly-bound),[6] although the possibility that the benzoylation was incomplete cannot be entirely ruled out.

The monoprotection of symmetrical diamines by insoluble polymer supports can find wide applications in the synthesis of alkaloids and in the preparation of monomers for polymerization to nylons.

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