Application of the Macrocyclic Polyether 18-Crown-6 to the Synthesis of *N*-Alkyl- or -Aryl-2-(*p*-nitrophenoxy)ethylamines

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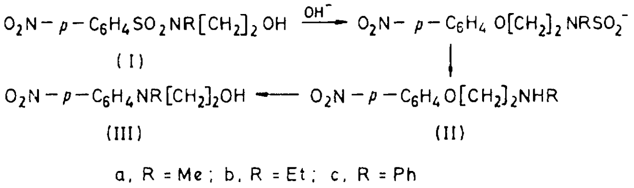
Summary *N*-Alkyl- or *N*-aryl-2-(*p*-nitrophenoxy)ethylamines (II) have been synthesized by desulphonative Smiles' rearrangement of *N*-alkyl- or *N*-aryl-*N*-(2-hydroxyethyl)-*p*-nitrobenzenesulphonamides (I) which is promoted by reaction with 18-crown-6-complexed potassium hydroxide in methylene chloride; the subsequent Smiles' rearrangement of (II) to the corresponding *N*-alkyl- or *N*-aryl-2-(*p*-nitroanilino)ethanols (III) is thus effectively prevented.

We recently reported[1] the kinetics of desulphonative double Smiles' rearrangement of *N*-(2-hydroxyethyl)-*p*-nitrobenzenesulphonamides (I) to the corresponding 2-(*p*-nitroanilino)ethanols (III) in aqueous alkali. We now report a method of synthesis of the proposed intermediates (II).



Previous attempts to isolate (II) by a variety of procedures have failed because of subsequent rearrangement to the corresponding amino alcohols (III).[2] Our recent kinetic observations[1] on the double Smiles' rearrangement of *N*-alkyl-*N*-(2-hydroxyethyl)-*p*-nitrobenzenesulphonamides (Ia,b) in aqueous solution also indicated that the relative rates of the rearrangement steps were sufficient to prevent appreciable accumulation of (IIa,b) during formation of (IIIa,b) from (Ia,b).

A change to a much less polar solvent increases the rate of the first Smiles' rearrangement relative to that of the second. Thus, we have been able to prepare (IIa—c) by reaction of the corresponding sulphonamides (Ia—c) with KOH in CH_2Cl_2 containing 18-crown-6.

A pellet of KOH was added to a solution of the sulphonamides (Ia—c) (0·1 g) and 18-crown-6 (0·1 g) in CH_2Cl_2 (2 cm^3): the mixture was shaken and formation of the product (λ_{max} *ca.* 310 nm) was monitored periodically. Once (II) had reached its maximum concentration, the mixture was worked up as follows. The pellet of KOH was removed, the solution was diluted with CH_2Cl_2, washed once with water, and extracted with 4N HCl (20 cm^3). The acidic solution was then shaken with ethyl acetate (50 cm^3), and basified (pH 11) with 8N NaOH with vigorous stirring. The organic layer was washed with water, dried ($MgSO_4$), and evaporated to give (IIa,b): (IIa), 70%, m.p. 33—34 °C; δ (60 MHz, $CDCl_3$) 8·20 (2H, d, *J* 9·3 Hz), 7·00 (2H, d, *J* 9·3 Hz), 4·20 (2H, t, *J* 5·3 Hz), 3·15 (2H, t, *J* 5·3 Hz), and 2·56 (3H, s); (IIb), 80%, m.p. 13—14 °C; δ ($CDCl_3$) 8·23 (2H, d, *J* 9·3 Hz), 7·00 (2H, d, *J* 9·3 Hz), 4·22 (2H, t, *J* 5·3 Hz), 3·28—2·58 (4H, m), and 1·18 (3H, t, *J* 6·6 Hz). Upon formation of (IIc) (which, in view of its weak basicity, could not be extracted effectively into 4N HCl), the reaction mixture was diluted with CH_2Cl_2, washed with water, dried ($MgSO_4$), and evaporated to yield (IIc) in admixture with 18-crown-6. The catalyst was subsequently removed by washing with light petroleum–CCl_4 (1 : 1) to give (IIc), 28%, m.p. 107 °C; δ ($CDCl_3$) 8·14 (2H, d, *J* 9·0 Hz), 6·93 (2H, d, *J* 9·0 Hz), 7·40—6·50 (5H, m), 4·22 (2H, t, *J* 6·0 Hz), and 3·58 (2H, t, *J* 6·0 Hz). 2-(*p*-Nitrophenoxy)ethylamine (II, R = H) could not be synthesised by this method owing to the limited solubility of the corresponding sulphonamide (I, R = H) or its potassium salt under the reaction conditions.

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