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DESULPHONATIVE DOUBLE SMILES' REARRANGEMENTS OF *N*-(2-HYDROXYALKYL)*p*-NITROBENZENE SULPHONAMIDES IN AQUEOUS ALKALI: ISOLATION OF INTERMEDIATE 2-(*p*-NITROPHENOXY)ALKYLAMINES

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We recently reported (1) that by repetitive-scan ultraviolet-visible absorption spectroscopy an intermediate (λ_{max} = 315 nm) could be detected during the desulphonative conversion of I_a to IV_a upon reaction in aqueous sodium hydroxide at 61°. The intermediate was believed to be 2-(*p*-nitrophenoxy) ethylamine (III_a), in keeping with a reaction sequence (below) previously proposed by Kleb (2) for desulphonation of a variety of *N*-(2-hydroxyalkyl)-*p*-nitrobenzene sulphonamides.

$$\begin{tikzcd} \underset{I}{p\text{-}NO_2C_6H_4SO_2NR^1CR^2R^3CHR^4OH} \arrow[r, "OH^-"] & \underset{II}{[ArOCHR^4CR^2R^3NR^1SO_2^-]} \arrow[d, "H^+"', "-SO_2, \text{ fast}"] \\ \underset{IV}{ArNR^1CR^2R^3CHR^4OH} & \underset{III}{[ArOCHR^4CR^2R^3NHR^1]} \arrow[l] \end{tikzcd}$$

a, R^n = H; b, R^4 = Me; c, $R^{2,3}$ = Me; d, R^1 = Me; e, R^1 = Et;
$R^1 = Y\cdot C_6H_4$ where Y = f, H; g, *p*-Me; h, *p*-MeO; i, *m*-MeO; j, *p*-Cl; k, *m*-Cl.

We now wish to report (for reactions of I_a, I_c, and I_{f-k}) the isolation and characterisation of the corresponding intermediates of their desulphonative double Smiles' rearrangement and to confirm that they are indeed 2-(*p*-nitrophenoxy) alkylamines (III), none of which have been reported previously.

Kinetic investigations (3) revealed that desulphonation of each *N*-aryl sulphonamide (5×10^{-5} M) occurred in two essentially separate steps, such that I_{f-k} was almost completely converted to III_{f-k} before an appreciable amount of IV could be detected. We were therefore able to estimate the optimum reaction time for synthesis of III_{f-k} alone. However, since the sulphonamides (I_{f-k}) are only slightly soluble in aqueous sodium hydroxide (0.3 M) at 61° we found it necessary to add acetone (30% v/v) in order to prepare a sufficiently concentrated (0.02 M) homogeneous solution from which III could be obtained on a reasonable scale (*ca*. 500 mg).

During each reaction the p-nitrophenyl ether (III) gradually appeared on the surface of the reaction mixture, as a yellow oil which crystallised on cooling. The following compounds (III, m.p., yield) were obtained: III_f, 107, 37%, III_g, 129, 62%; III_h, 104, 49%; III_i, 95, 73%; III_j, 100, 55%; III_k, 107, 80%. In each case the u.v., i.r. and n.m.r. spectra and the elemental analyses were consistent with the assigned structure.

The greater solubilities of intermediates III_a and III_c, combined with the comparable rates of their formation and subsequent decomposition, prevented their preparation (from I_a and I_c respectively) by the procedure adopted for their N-aryl analogues. Thus, a procedure was developed whereby the intermediate III is formed upon reaction of I ($pK_a < 10$) in aqueous alkali and protected against subsequent reaction by immediate extraction into benzene.

The following results were obtained upon reaction of a solution of $I_{a,c}$ (0.5 g) in aqueous sodium hydroxide (1.0 M; 200 ml) in admixture with benzene (200 ml) at 80° for a period of 6 min.: III_a, m.p. 29°, 35% yield; III_c, m.p.~15°; 40% yield. Once again elemental and spectral analyses were consistent with the structures assigned.

The syntheses here reported constitute the first successful preparations of 2-aminoalkyl nitroaryl ethers. Previous attempts to synthesise such compounds by reaction of corresponding 2-chloroalkyl ethers with ammonia (4), or by hydrolysis of phthalamide derivatives (5) have been confounded by their subsequent Smiles' rearrangement under the reaction conditions. The availability of intermediates (III) will now facilitate detailed kinetic study of the rearrangement III → IV. The base dependence of this step is of particular interest in view of the continuing interest in mechanisms of intermolecular aromatic displacement promoted by amine nucleophiles (6,7) and in the role of spiro-Meisenheimer intermediates in related intramolecular reactions (8,9).

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