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KINETICS OF DESULPHONATIVE DOUBLE SMILES' REARRANGEMENT OF N-(2-HYDROXYALKYL)p-NITROBENZENESULPHONAMIDES IN AQUEOUS ALKALI

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In 1968 Kleb reported (1) an interesting desulphonation reaction by which a series of N-(2-hydroxyalkyl)p-nitrobenzenesulphonamides were converted to the corresponding N-(2-hydroxyalkyl)p-nitroanilines in refluxing aqueous sodium hydroxide (6%). Kleb proposed the following mechanism which involves "double Smiles' (2) rearrangement" (I → III and III → IV)

$$\begin{tikzcd}
ArSO_2NR_1CR_2R_3CHR_4OH \arrow[r, "OH^-"] & {[ArOCHR_4CR_2R_3NR_1SO_2^-]} \\
I & II \arrow[d, "H^+"', "-SO_2"] \\
ArNR_1CR_2R_3CHR_4OH & {[ArOCHR_4CR_2R_3NHR_1]} \arrow[l] \\
IV & III
\end{tikzcd}$$

I_a,R_n = H; I_b, R_4 = CH_3; I_c,$R_{2,3}$ = CH_3;

I_d,R_1 = CH_3; I_e,R_1 = C_2H_5;

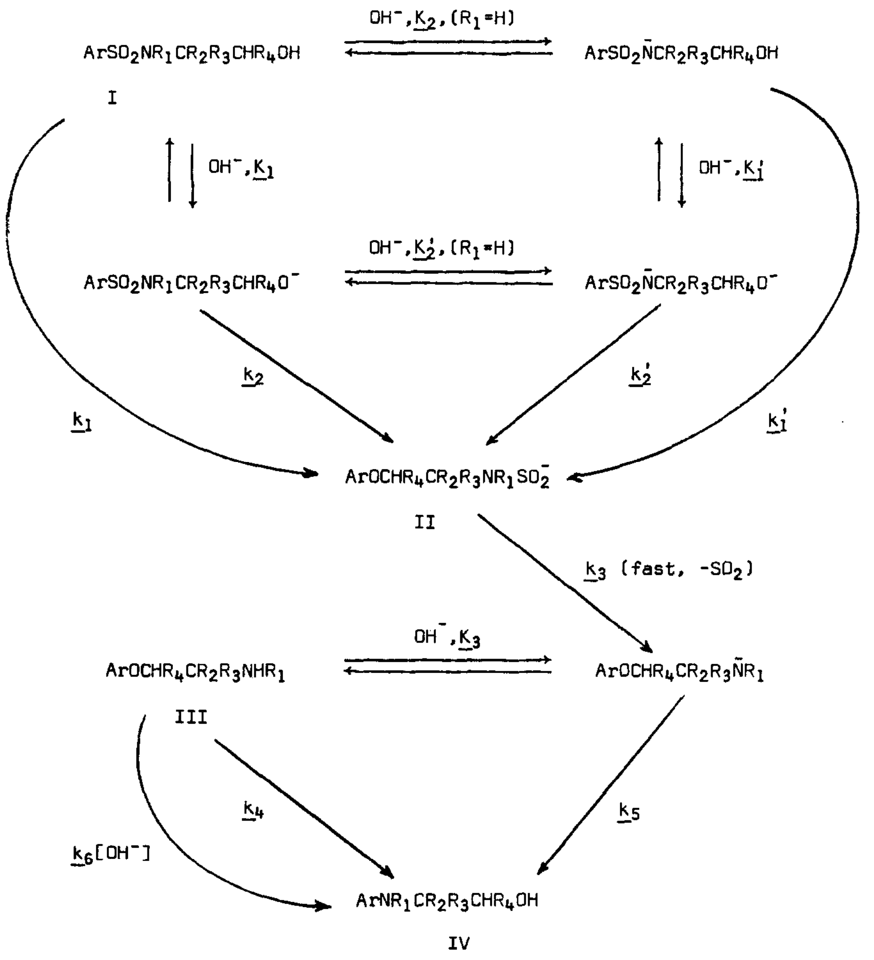
I_f,R_1 = C_6H_5; I_g,R_1 = p-Tolyl.

Remaining R groups = H; Ar = p-NO_2.C_6H_4-

In no case was there direct experimental evidence for intermediates II or III (which have never been reported) nor was the base dependence of reaction I → II or III → IV determined. Although it was suggested that formation of III from II would be rapid, no attempt was made to estimate or compare the relative rates of the sequence of reaction steps for a range of compounds I.

We now wish to report kinetic and spectroscopic evidence in support of the double Smiles' rearrangement of I_{a-g} via intermediates III_{a-g}.

The time dependence of the ultraviolet-visible spectrum during formation of amino alcohol IV (λ_{max} = ca. 410 nm) from the corresponding sulphonamide I (1×10^{-5}M, λ_{max} = ca. 265 nm) in aqueous sodium hydroxide (0.1 - 1.0M) at 60° was appropriately analysed in order to determine the rate and base dependence of the formation, and subsequent decomposition, of the intermediate aminoether III (λ_{max} = ca. 315 nm). Our kinetic results can be explained with reference to the following reaction scheme, where k_{1-5} are first order rate constants, k_6 is a second order rate constant for general base catalysis by hydroxide ion and K_{1-3} represent deprotonation equilibrium constants for reactions: $AH + OH^- \rightleftharpoons A^- + H_2O$.



In each case (I_{a-g}) a first order dependence on hydroxide concentration was found for the first Smiles' rearrangement I → II. This reaction must therefore proceed by S_Ni displacement of the aminosulphonyl anion upon reaction between the neighbouring alkoxy anion (rather than the unionised alcohol) and the p-nitro-activated aryl ring. Thus for reaction I → III, at constant base concentration, the pseudo first order rate constant k_A (corresponding to the rate determining step I → II) is given by $k_A = k_2K_1[OH^-]$ (or $k_2'K_1'[OH^-]$ where $R_1 = H$ and $K_2[OH^-] >$ *ca.* 10^2) and k_A is directly proportional to the base concentration.

For the second Smiles' rearrangement (III → IV), at constant hydroxide concentration, the pseudo first order rate constant k_B was also determined for several base concentrations where: $k_B = k_4 + k_5K_3[OH^-] + k_6[OH^-]$. The extent of dependence of k_B on hydroxide concentration is markedly affected by substituents R_{1-4}. The values k_4 and ($k_5K_3 + k_6$) were determined, respectively, from the intercept and slope of a plot of k_B versus $[OH^-]$ and are in the Table along with values for k_2K_1 (or $k_2'K_1'$).

Table

Kinetics of reaction of sulphonamides I in aqueous sodium hydroxide (0.1 - 1.0*M*) at 61°. The constants k_2K_1 (or $k_2'K_1'$), k_4 and ($k_5K_6 + k_6$) were determined by analysis of the base dependence of rate determining pseudo first order constants, k_A and k_B, corresponding to I → III and III → IV respectively.

Substrate	$(10^3k_2K_1)^*/dm^3\ mol^{-1}\ s^{-1}$	$10^5k_4/s^{-1}$	$10^5(k_5K_3 + k_6)/dm^3\ mol^{-1}\ s^{-1}$
I_a	0.71	113	<5
I_b	0.47	$(1\text{-}5 \times 10^2)^‡$	
I_c	18.6	ca. 130	
I_d	3.6	> 1800	-
I_e	8.2	> 3600	-
I_f	4.1	< 0.05	5.7
$I_g^†$	4.8	< 0.05	46.8

* For I_{a-c} the values correspond to ($k_2'K_1'$)

† The reaction mixture contained acetone (10% v/v)

‡ This value is approximate since k_4 was greater than k_A by an amount just sufficient to prevent its accurate estimation.

For formation of $IV_{a,b}$, $k_4 >> (k_5K_3 + k_6)$; $IV_{f,g}$, $k_4 << (k_5K_3 + k_6)$, while the second Smiles' rearrangement to form $IV_{d,e}$ is too fast, relative to the first, to permit determination of k_B. It is probable, however, that N-alkyl substituents (R_1) enhance the rate of reaction $III_{d,e} \rightarrow IV_{d,e}$ (relative to $III_a \rightarrow IV_a$) by increasing the nitrogen nucleophilicity (4) and hence increasing k_4. Thus it is to be expected that for reactions of $III_{d,e}$, $k_4 >> (k_5K_3 + k_6)$. We have not yet obtained reliable results for reactions of III_c but have established that k_B is, in this case, only slightly base dependent.

The second order component $(k_5K_3 + k_6)$ of k_B for formation of IV_f need not necessarily be dominated by k_6 since a value of k_5 close to the diffusion controlled rate limit of ca. 10^{11} s^{-1} would be sufficient (since $pK_3^{III_f} = (pK_a^{III_f} - pK_w) =$ *ca.* 14; *cf.* aniline, $pK_a = 27$) to ensure that k_5K_3 is comparable in magnitude to k_3.

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