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EFFECTS OF N-ALKYL SUBSTITUTION ON THE FORMATION AND RATE-LIMITING DEPROTONATION OF THE SPIRO-MEISENHEIMER INTERMEDIATE OF SMILES' REARRANGEMENT OF 2-(p-NITROPHENOXY)ETHYLAMINE.

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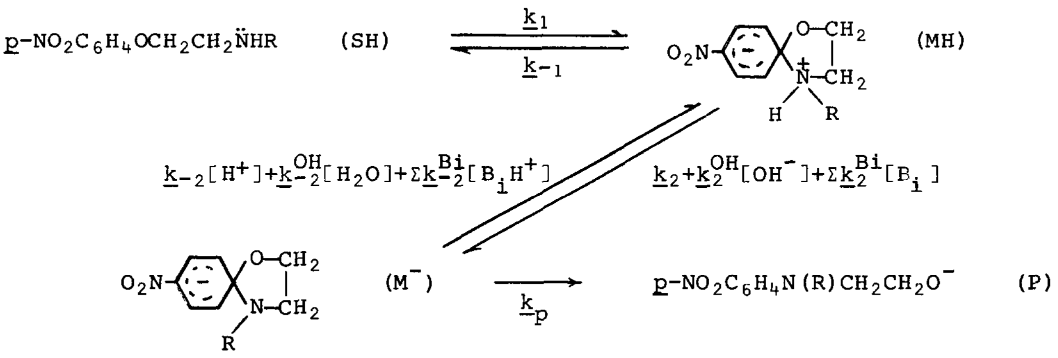
General base catalysis, and N-alkyl group dependence, of the title rearrangement (which approaches a rate limit at high base concentration) has been interpreted:

We recently reported (1) that kinetic studies of intramolecular nucleophilic aromatic displacement of alkoxide ion by the amino group in 2-(p-nitrophenoxy)ethylamine (SH) support a mechanism (SCHEME, R=H) whereby, at low base concentration, the rate of Smiles' rearrangement is dependent upon the rate of general base-catalysed deprotonation of a spiro-Meisenheimer intermediate (MH); at high base concentrations the base independent rate of formation of the Meisenheimer intermediate becomes rate limiting.



This suggestion complements recent proposals made by Bernasconi (2) for reactions of analogous di- and tri-nitro systems but is in contrast with the more generally accepted mechanism (3) for general base-catalysed intermolecular S_NAr reactions of primary and secondary amines with activated aromatic ring systems; a fast acid-base equilibrium between an initially formed zwitterionic Meisenheimer intermediate and its conjugate base, followed by general acid-catalysed expulsion of the leaving group, constitutes the latter "SB-GA" mechanism.

We have extended our kinetic investigations to include formation of

N-alkyl N-(2-hydroxyethyl) p-nitroanilines (P; λ_{max} ca. 410 nm) by Smiles' rearrangement of corresponding N-alkyl derivatives of 2-(p-nitrophenoxy)ethyl·amine (SH, R=Me, Et, Pr^i; λ_{max} ca. 315 nm) for which appropriate syntheses were recently developed (4); interpretation of the base dependence observed for such reactions in water at 60° (μ=1.0) is the topic of this communication.

For each substrate (SH; R=Me, Et, Pr^i) the rate of reaction, which was monitored spectrophotometrically, is linearly dependent upon hydroxide concentrations below 0.01M but approaches a limiting value (k_1) at concentrations above 0.1M; the same rate limit is apparently approached in the presence of high concentrations of general base catalysts (morpholine and ethanolamine). This behaviour is consistent with the SCHEME, although the possibility that P is formed from MH by a concerted base-catalysed process, without the intervention of M^-, cannot be ruled out.

It is reasonable to assume (1) that in each case $k_p > 10^5\ s^{-1} \geq k_{-2}^{OH}$ and that return of M^- to SH is consequently appreciably slower than is its conversion into P; thus, by steady state treatment of the reactive intermediates MH and M^- it can be established that

$$k_{obs} = k_1(k_2+k_2^{OH}[OH^-]+k_2^{B}[B])/\{k_{-1}+(k_2+k_2^{OH}[OH^-]+k_2^{B}[B])\}$$

For hydroxide concentrations in excess of 0.01M ($k_2 \ll k_2^{OH}[OH^-]$), the equation

$$1/k_{obs} = 1/k_1 + k_{-1}/k_1k_2^{OH}[OH^-]$$

applies for reaction in absence of other bases; thus, from a rectilinear plot of $1/k_{obs}$ versus $1/[OH^-]$ the limiting rate ratio k_2^{OH}/k_{-1} can be evaluated. For reactions conducted in aqueous sodium hydroxide (0.01M) containing varying amounts of a general base B the rate ratio k_2^{B}/k_{-1} can subsequently be obtained from the slope of a rectilinear plot of $1/\{(k_1/k_{obs})-1\}$ versus [B], since:-

$$1/\{(k_1/k_{obs})-1\} = k_2/k_{-1} + k_2^{OH}[OH^-]/k_{-1} + k_2^{B}[B]/k_{-1}$$

Values obtained for k_1, k_2^{OH}/k_{-1} and k_2^{B}/k_{-1} where R=H, Me, Et and Pr^i are tabulated below.

Rate constants for intramolecular rearrangement of
p-$NO_2 \cdot C_6H_4OCH_2CH_2NHR$ catalysed by general bases[§] in water
at 60°C, $\mu = 1.0$

R	$k_1/10^{-4}s^{-1}$	rate ratios*/ℓ mol^{-1}				β[†]
		k_2^{OH}/k_{-1}	k_2^{E}/k_{-1}	k_2^{M}/k_{-1}	$k_2^{H_2O}/k_{-1}$	
H	8.2	239	42.5	14.30	ca. 0.0002	0.22-0.35
Me	515	21.3	2.0	0.80	ca. 0.0008	0.18
Et	485	15.8	-	-	-	-
Pr^i	100	7.2	0.24	0.072	-	0.25

[§] For reactions conducted in the presence of a general base, sodium hydroxide (0.01M) was added to maintain pH ≥ $pK^{SH_2} + 1$.

[*] k_2^{OH}, k_2^{E}, k_2^{M} and $k_2^{H_2O}$ are catalytic rate constants k_2^{B} where B = hydroxide ion, ethanolamine, morpholine and water, respectively (*i.e.* $k_2^{H_2O} = k_2/[H_2O]$)

[†] Brönsted coefficient estimated from a plot of $\log(k_2^B/k_{-1})$ vs pK_a^{BH} where B = HO^-, ethanolamine and morpholine.

The sixty-fold increase of k_1 caused by alkylation (R=Me or Et) of the parent amino-ether can be attributed to enhanced nitrogen nucleophilicity; where R is a branched alkyl group this may, however, be partially offset by steric hindrance and thus the net rate enhancement is only twelve-fold where R = Pr^i. These competing factors find parallel in intermolecular S_NAr reactions of amine nucleophiles with p-chloronitrobenzene in ethanol (5) but detailed comparison reveals that our intramolecular reaction is less subject to steric retardation.

Variations in k_2^B/k_{-1} must necessarily reflect the relative influences of R on the free energies of the transition states for forward (k_2^B) and reverse (k_{-1}) reactions of MH. The low values of the Brönsted coefficients are consistent with a mechanism of rate limiting deprotonation at close to the diffusion controlled limit.

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