Deuterium Isotope Effect and Base Catalysis in σ-Complex Formation Between 1,3,5-Trinitrobenzene and Aniline

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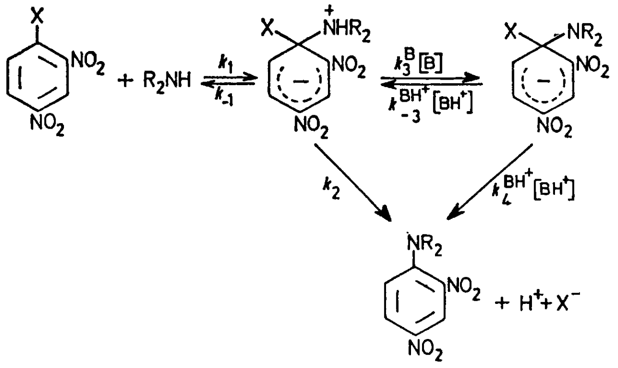
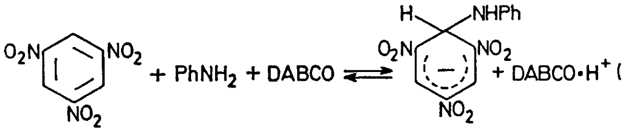
Summary The diazabicyclo-octane-catalysed σ-complex formation between 1,3,5-trinitrobenzene and aniline in dimethyl sulphoxide involves rate-limiting proton transfer from nitrogen and is subject to a small kinetic isotope effect.

The major difficulty associated with interpretation of kinetic isotope effect (K.I.E.) and base catalysis studies in aromatic nucleophilic substitution (S_NAr) processes can be ascribed to the number of elementary steps which appear to be involved (Scheme),[1] and the consequent difficulty of identifying which step is rate-determining. An alternative approach to the problem has hence involved the study of stable σ-complexes,[2] as models of the metastable intermediates postulated in S_NAr reactions. It is then possible[3] in favourable cases to study some of the constituent processes pertaining to the Scheme separately. We now report the results of a study of σ-complex formation which has yielded information uniquely relevant to the K.I.E. problem in S_NAr reactions and the related aspect of base catalysis.



Scheme

Though 1,3,5-trinitrobenzene (TNB) and aniline alone have not been observed to yield a σ-complex (in contrast to the TNB–aliphatic primary/secondary amine systems),[4] we reported that σ-complex formation occurs readily in the presence of tertiary amines {triethylamine or 1,4-diaza-[2.2.2]bicyclo-octane (DABCO)} in dimethyl sulphoxide (DMSO) media.[5] In continuation of this work, we have performed a kinetic study of the reaction in equation (1) and have evaluated the isotope effect with respect to $PhNH_2$–$PhND_2$ on the equilibrium, as well as the forward and reverse rate processes, in the DMSO medium.



(1)

The rate of formation of the TNB-anilide σ-complex (λ_{max} 446 nm, ε 30,400 l mol^{-1} cm^{-1}; λ_{max} 522 nm, ε 17,700 l mol^{-1} cm^{-1}) was measured spectrophotometrically under pseudo-first-order conditions, with $PhNH_2$ and DABCO in large excess over TNB. Under these conditions the system reduces to $TNB \underset{k_r^2}{\overset{k_f^1}{\rightleftharpoons}} TNB{\cdot}NHPh^- + DABCO{\cdot}H^+$, *i.e.* a mixed first-order (forward) and second-order (reverse) reaction. The pseudo-first-order rate constant for the forward reaction, k_f^1, can be evaluated using the appropriate rate expression.[6] The second- and third-order forward rate constants are then obtained as $k_f^2 = k_f^1/[PhNH_2]$ and $k_f^3 = k_f^2/[DABCO]$ respectively. The equilibrium constant K is given by the usual mass law relationship, while the second-order reverse rate constant is obtained as $k_r^2 = k_f^3/K$. Kinetic data obtained under the above conditions and using a constant concentration (0·1 M) of tetraethylammonium chloride as electrolyte are given in Table 1.

It is shown by these results that formation of the TNB–anilide σ-complex is subject to base catalysis. Moreover, since a plot of k_f^2 *vs.* [DABCO] is linear and passes through the origin, it follows that DABCO acts as the sole catalyst for this process. This finding can be accommodated on the basis of the mechanism in equation (2), with the first stage a rapidly established pre-equilibrium and the deprotonation stage rate limiting. This result differs from the TNB–aliphatic amine system where formation of the zwitterionic σ-complex was found to be rate limiting.[3a]

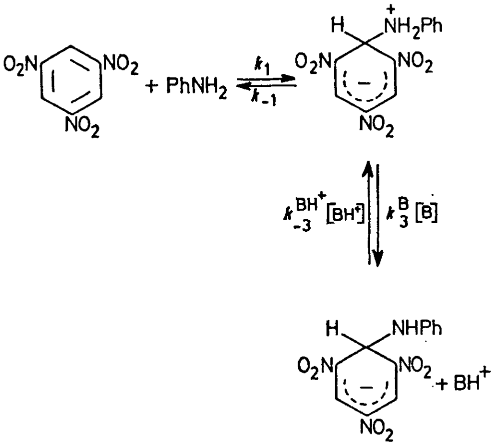
The isotope effect with respect to $PhNH_2$ and $PhND_2$ has been evaluated and the results are given in Table 2. These runs were performed analogously to the experiments in Table 1 but with the omission of tetraethylammonium chloride; traces of moisture could not be removed from the salt, leading to isotopic exchange and hence to ambiguous

Table 1

Dependence of rate and equilibrium data for reaction in equation (1) on DABCO concentration, in DMSO at 25 °C ([TNB] = 0·98 × 10^{-4} M, [$PhNH_2$] = 4·8 × 10^{-3} M, [Et_4NCl] = 0·1 M)

[DABCO]/M	% Conversion	K/l mol^{-1}	k_f^1 × 10^4/s^{-1}	k_f^2 × 10^2/l mol^{-1} s^{-1}	k_f^3/l^2 mol^{-2} s^{-1}	k_r^2/l mol^{-1} s^{-1}
0·002	32·2	1·80	2·80	5·71	29·1	16·3
0·010	56·1	1·52	12·6	25·7	26·0	17·1
0·020	70·1	1·71	25·1	51·3	26·1	15·2
0·040	79·3	1·65	52·4	107	26·9	16·3

K.I.E. results. This problem was, however, eliminated under the conditions of the measurements. Thus the K.I.E. values obtained for $PhNH_2$–$PhND_2$ are: for the forward reaction, $(k^2_f)_H/(k^2_f)_D = 1{\cdot}12$; for the reverse reaction, $(k^2_r)_H/(k^2_r)_D = 1{\cdot}25$; and for the equilibrium constant, $K_H/K_D = 0{\cdot}90$.



(2)

TABLE 2.

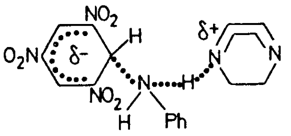
Deuterium isotope effect data for reaction in equation (1) ($[TNB]_0 = 8{\cdot}51 \times 10^{-5}$ M, $[DABCO]_0 = 1{\cdot}68 \times 10^{-3}$ M, in DMSO at 25° C).

	Reactant		
	$PhNH_2$[a]	$PhND_2$[b]	Isotope effect[c]
% Conversion	40·0	42·0	
	40·9	41·9	
	41·0	42·1	
K/l mol^{-1}	0·179	0·207	0·86
	0·189	0·205	0·93
	0·190	0·209	0·91
k^1_f/s^{-1}	5.32	4·66	1·14
	5·41	4·66	1·16
	5·28	4·75	1·11
k^2_f/l mol^{-1} s^{-1}	6·88	6·12	1·12
	7·00	6·12	1·14
	6·82	6·24	1·09
k^2_r/l mol^{-1} s^{-1}	229	176	1·31
	220	178	1·24
	213	178	1·20

[a] $[PhNH_2] = 7{\cdot}73 \times 10^{-2}$ M. [b] $[PhND_2] = 7{\cdot}61 \times 10^{-2}$ M.
[c] The isotope effect is evaluated for each pair of experiments, performed consecutively.

Since the base catalysis experiments (Table 1) have established that proton transfer from nitrogen is rate-determining, the K.I.E. results (Table 2) can only be interpreted as representing a primary isotope effect. It seems logical to extend this result to S_NAr systems (Scheme 1) since the process of equation (2) is analogous while simplified by the absence of a leaving group. It may thus be concluded that when deprotonation of the zwitterionic intermediate in an S_NAr reaction is rate-determining, the reaction will be subject to a small isotope effect. Conversely it follows also that when an S_NAr reaction does not exhibit an isotope effect then deprotonation of the zwitterionic intermediate is not rate-determining.

It has been pointed out[7] that it is possible in theory to have primary isotope effects which are very small in magnitude. A small isotope effect in the present case could result if σ-complex formation occurred in a *concerted* manner, *via* the transition state (**1**) since according to Swain's solvation rule[8] the proton being transferred would be expected to lie in a stable potential. The possibility of a concerted mechanism of σ-complex formation in S_NAr systems is an interesting one, but it is doubtful whether such a situation would obtain in general.[1b]



(1)

In the two-stage, σ-complex intermediate mechanism (equation 2), the k_3 step is expected to be largely diffusion controlled since the proton transfer occurs in the thermodynamically favoured direction.[3,9] With this condition, and an unsymmetrical transition state,[7] a small isotope effect will obtain. This explanation would account for the results in the present system as well as in S_NAr reactions, for which k_H/k_D values in the range 1·0–1·5 have been observed.[10]

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