Mechanism of the Reactions of Substituted Anilines with Phenyl 2,4,6-Trinitrophenyl Ether in Benzene: Evidence for a Cyclic Transition State involving an Eight-membered Ring

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Rates and activation parameters have been determined for the reactions of phenyl 2,4,6-trinitrophenyl ether with substituted anilines in benzene. For some of the nucleophiles, the rates decrease with increasing temperature in the range 5—35 °C resulting in negative activation enthalpies ($\Delta H^\ddagger$ −3.1 to −27.3 kJ mol^{-1}). This is strong evidence for a stepwise mechanism involving (at least) a pre-equilibrium. These base-catalysed nucleophilic substitution reactions are sensitive to the nature of the arylated amine as indicated by the Hammett's constant (ρ −7.7).

In previous publications,[1,2] we presented information on the base-catalysed reactions of phenyl 2,4,6-trinitrophenyl ether with some primary and secondary amines in benzene. The results obtained led us to propose that the reactions in each case proceeded through a cyclic transition state involving either a four-, six-, or eight-membered ring. The purpose of the present investigation is to provide evidence for this cyclic transition state mechanism. To do this, we have studied the reaction of phenyl 2,4,6-trinitrophenyl ether with various substituted anilines at different temperatures. The reactions were followed spectrophotometrically with the amines in sufficient excess to give pseudo-first-order kinetics and the absorbance readings at infinity agreed with the calculated ones. The observed second-order rate constants k_A are listed in Table 1.

As in the previously reported case of aniline,[1] the rate data fitted into equation (1), *i.e.* the reaction is first order

$$\text{Rate}/[\text{Substrate}]\,[\text{Amine}] = k_A = k' + k''[\text{RNH}_2]^2 \quad (1)$$

in substrate and third order in nucleophile and a plot of the second-order rate coefficient k_A against the square of the aniline concentration gave an intercept k' and slope k'' (Figure 1).

The rates were also measured over a range of temperatures (5—35 °C) at a constant ratio between concentration of substrate and amine (Figure 2). Surprisingly, the rates in this case fell into two categories depending on the nature of the aniline; for anilines with electron-releasing substituents, the rates were found to decrease (though slightly) with increasing temperature while for the anilines with electron-withdrawing substituents the rates increased (also slightly) with increasing temperature (Table 1). The change in the values of the rate constant is only *ca.* 6% (for the smallest) to *ca.* 28% (for the highest).

DISCUSSION

In discussing the mechanism of the reactions, the pieces of evidence to be accommodated are (1) the value of the second-order coefficient k' (Table 2), obtained by extrapolation to infinite dilution of amine, does not depend on the temperature of the reaction but on the base

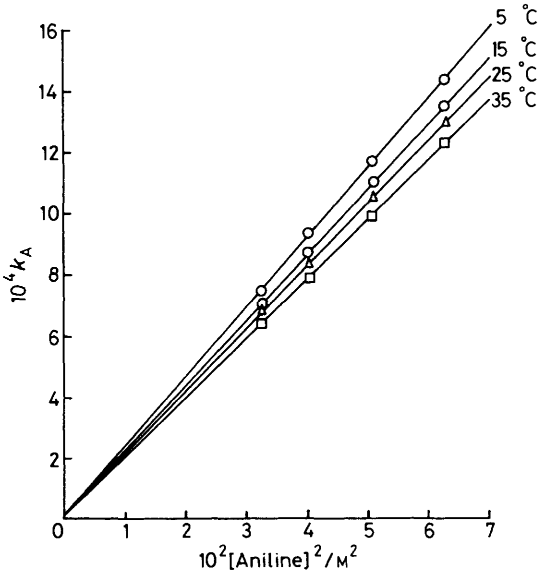


FIGURE 1 Plots of k_A against the square of aniline concentration for the reaction of phenyl 2,4,6-trinitrophenyl ether at different temperatures. The correlation coefficient (r), intercept (k'), and slope (k'') are in Table 2

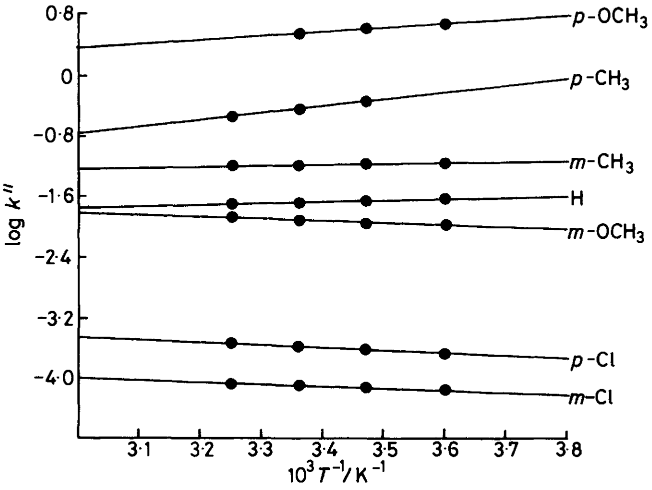


FIGURE 2 Arrhenius activation energy plots. The slopes, standard deviations, and correlation coefficients are in Table 3

TABLE 1

Influence of temperature on the reaction of phenyl 2,4,6-trinitrophenyl ether[a] with substituted anilines in benzene

X	10^2 $[XC_6H_4NH_2]$/M	10^4k_A/l mol^{-1} s^{-1} 5 °C	15 °C	25 °C	35 °C
H	18.0	7.49	7.10	6.80	6.47
	20.0	9.40	8.70	8.35	7.95
	22.5	11.70	11.00	10.50	9.96
	25.0	14.43	13.54	12.98	12.35
m-CH_3	18.0	21.9	21.5	21.2	20.4
	20.0	26.6	26.2	25.6	25.35
	22.5	33.6	32.9	32.1	31.4
	25.0	41.5	40.8	40.1	39.0
p-CH_3	7.0		22.7	18.0	14.9
	8.0		29.3	23.3	18.8
	9.0		36.8	29.0	23.6
	10.0		45.0	35.5	28.8
m-OCH_3	35.0	12.75	13.9	14.9	12.3
	40.0	16.6	18.0	19.2	16.0
	45.0	20.98	22.66	24.0	20.3
	50.0	25.8	28.1	30.1	25.0
p-OCH_3	4.0	87.3	77.5	69.5	
	5.0	129.0	113.0	102.0	
	6.0	180.0	158.0	140.0	
	7.0	240.0	209.0	186.0	
m-Cl	90.0	0.570	0.620	0.670	0.724
	100.0	0.695	0.755	0.818	0.883
	110.0	0.835	0.903	0.981	1.062
	120.0	0.982	1.071	1.160	1.255
p-Cl	45.0	0.698	0.776	0.855	0.928
	50.0	0.870	0.952	1.050	1.140
	55.0	1.038	1.154	1.275	1.381
	60.0	1.230	1.360	1.500	1.630

[a] [Substrate] = 5.0×10^{-4}M.

strength of the aniline used; (2) the third-order coefficient *k''* (Table 2) depends on the temperature of the reaction as well as the base strength of the aniline; and (3) the energy of activation is slightly negative for the reactions involving anilines with electron-releasing groups (see Arrhenius plots in Figure 2). Points (2) and (3) indicate that the reaction in each case occurs stepwise; the rate-determining step must be preceded by at least one fast equilibrium (the forward step of which will be exothermic) whereby the expected increase in rate for the slow step with increasing temperature would be neutralised by a shift of the preceding equilibrium (or equilibria) towards the reagents (the backward step which will be endothermic).

According to the general mechanism of nucleophilic aromatic substitution, base catalysis occurs after the formation of a zwitterionic adduct from the substrate and one molecule of protic amine.[3] Therefore, this adduct must be involved in both the uncatalysed and the catalysed steps. Point (1) above indicates that the uncatalysed step proceeds with apparent absence of energy of activation over the whole range of temperature (5—35 °C); this suggests that the rate-limiting step is not just the final transfer of a proton but that this is preceded by a process controlled by some geometric factors, presumably the formation of a hydrogen-bonded or a somewhat properly oriented complex.

The observation of a negative activation energy for some of these reactions is a striking piece of evidence for a multi-step mechanism.[4,5] A mechanism that accounts for all the experimental observations involves an intermediate formation of a weak complex within which the reactant molecules can rotate into a suitable orientation where hydrogen bonding (inter or intra) is possible or else separate again. Hence we arrive at the three-step Scheme for both the uncatalysed and the catalysed steps; the intermediate complex in the uncatalysed step being a four-membered ring formed through intra-hydrogen bonding while that in the catalysed step[6] is an eight-membered ring formed through a network of inter-hydrogen bonding between the zwitterionic intermediate and two aniline molecules (the latter two acting bifunctionally,[7] one as proton donor to the leaving group and the other as proton acceptor from the positively charged nitrogen of the zwitterion) and is expected to be more favoured than the former;[8,9] no wonder then the ratio of the catalytic rate coefficient *k''* to the non-catalytic one *k'* is of the seventh order of magnitude. The reaction is thus predominantly base-catalysed.[10] The overall rate for both uncatalysed and catalysed reactions thus accords with equation (1).

The observation that amines with electron-releasing groups proceed with decrease in rate with increasing

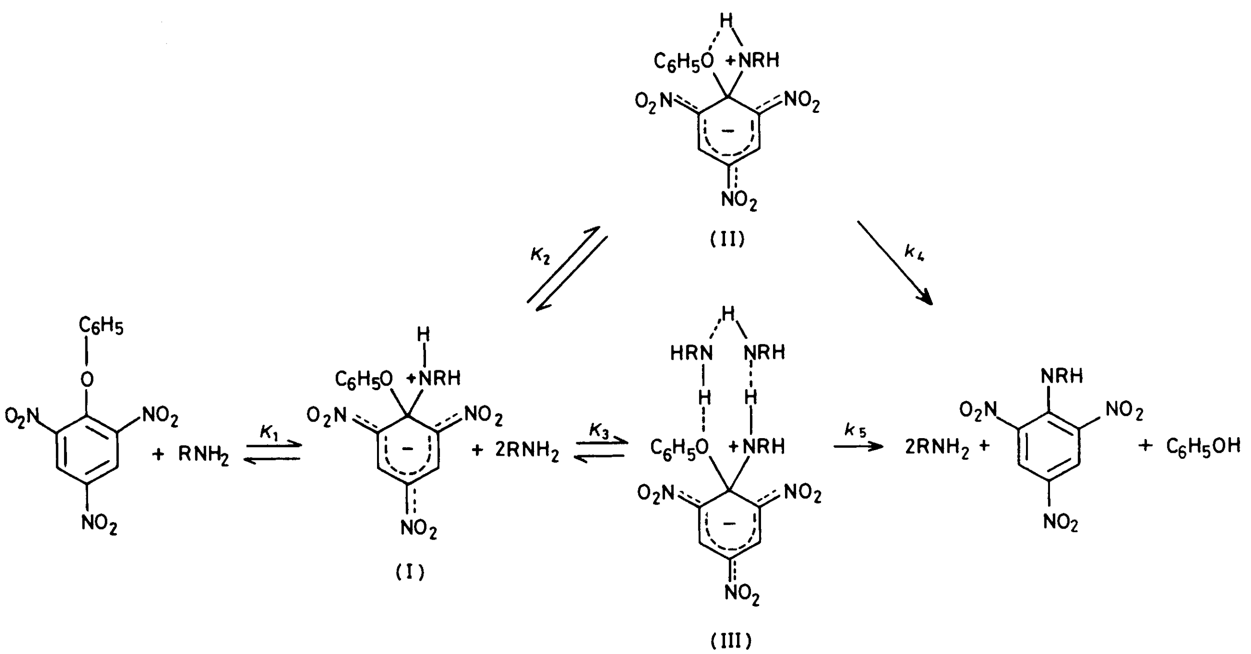
TABLE 2

Values of intercepts and slopes of the plot of k_A *versus* $[XC_6H_4NH_2]^2$ for the reaction of phenyl 2,4,6-trinitrophenyl ether in benzene at different temperatures

X	pK_a [a,b]	*r* [c]	$10^5k'$ [d]/l mol^{-1} s^{-1}	$10^4k''$/l^3 mol^{-3} s^{-1} 5 °C	15 °C	25 °C	35 °C
H	4.58	0.9999	1.45 [*]	229.0	214.0	205.0	195.0
m-CH_3	4.69	0.9999	6.18	653.0	641.0	629.0	613.0
p-CH_3	5.12	0.9999	13.20		4 380	3 420	2 750
m-OCH_3	4.20	0.9999	1.45	103.0	112.0	119.0	127.0
p-OCH_3	5.29	0.9999	134.0	46 300	39 900	35 200	
m-Cl	3.34	0.9999	0.401	0.655	0.715	0.778	0.844
p-Cl	3.98	0.9999	0.205	3.36	3.73	4.12	4.48

[a] In water at 25 °C. [b] See A. Albert and E. P. Serjeant, 'Ionization Constants of Acids and Bases,' Wiley, New York, 1962, p. 144. Linear correlation coefficient. [d] Same for all four temperatures.

[*] The value of the intercept *k'* reported here for aniline is somewhat different from the previously reported[1] value of 6.7×10^{-5} l mol^{-1} s^{-1} while that of the slope *k''* reported here for 25 °C agrees with the previously reported value of 2.0×10^{-2} l^3 mol^{-3} s^{-1}. As indicated in that publication, the value of *k'* as obtained by extrapolation to infinite dilution of aniline falls in the proximity of the origin and may be affected by serious errors, thus the present value of 1.45×10^{-5} l mol^{-1} s^{-1} calculated to be the same at four different temperatures can be regarded as a more accurate value.



SCHEME

temperature while those with electron-withdrawing groups behave in the reverse manner readily finds explanation in the Scheme; electron-releasing groups make the nitrogen atom of the bifunctional amine in complex (III) a relatively electron-rich centre thus making the hydrogen bond in which it is involved stronger, giving rise to a stronger or more stable intermediate complex and hence a higher value of the equilibrium constant K_3. Since the formation of this complex is exothermic, an increase in temperature will result in a shift of the equilibrium in favour of the rather endothermic backward reaction thus giving a lower rate of reaction. The nitrogen atom of the anilines with electron-withdrawing substituents on the other hand are by electron withdrawal rendered less basic resulting in a loosely hydrogen-bonded intermediate complex, the formation of which (as a result) is much less exothermic (if at all) and hence less stable with an attendant low value of the equilibrium constant K_3. Thus these reactions are very slow and proceed conventionally with increase in rate with increasing temperature. In comparison, the ratio of the catalytic rate coefficient k'' to the non-catalytic one k' for this category of amines is of the second order of magnitude.

$$K_1 = [(\mathrm{I})]/[\mathrm{Ether}][\mathrm{RNH_2}] \therefore [(\mathrm{I})] = K_1[\mathrm{Ether}][\mathrm{RNH_2}]$$
$$K_2 = [(\mathrm{II})]/[(\mathrm{I})] \qquad \therefore [(\mathrm{II})] = K_2[(\mathrm{I})]$$
$$K_3 = [(\mathrm{III})]/[(\mathrm{I})][\mathrm{RNH_2}]^2 \therefore [(\mathrm{III})] = K_3[(\mathrm{I})][\mathrm{RNH_2}]^2$$

For the uncatalysed reaction, Rate

$$\begin{aligned} &= k_4[(\mathrm{II})] = k_4K_1K_2[\mathrm{Ether}][\mathrm{RNH_2}] \\ &= k'[\mathrm{Ether}][\mathrm{RNH_2}] \text{ where } k' = k_4K_1K_2 \end{aligned}$$

For the catalysed reaction, Rate

$$\begin{aligned} &= k_5[(\mathrm{III})] = k_5K_3[(\mathrm{I})][\mathrm{RNH_2}]^2 \\ &= k_5K_1K_3[\mathrm{Ether}][\mathrm{RNH_2}]^3 \\ &= k''[\mathrm{Ether}][\mathrm{RNH_2}]^3 \text{ where } k''=k_5K_1K_3 \end{aligned}$$

As can be seen from the equations derived from the depicted Scheme the values of the rate coefficients k' and k'' depend on the relative values of the equilibrium constants K_1, K_2, and K_3 (apart from k_4 or k_5 as the case may be) and thus the observed small changes in the overall rate constant k_A therefore depend among other factors on the relative changes in the various equilibrium constants.

The effects of substituents on the uncatalysed and catalysed rates were investigated by means of the Hammett plots involving the non-catalytic rate coefficient k' and the catalytic rate coefficient k'', respectively, and the σ constants of the aniline substituents. Two different values of reaction constant ρ were obtained for the Hammett plots: -4.7 (r 0.9870) for the k' plot and -7.7 (r 0.9978) for the k'' plot. The plots show that the reaction rate depends on the electron density of the nitrogen atom of the aniline; electron-donating substituents, in fact, increase the rate (except in the case of *m*-methoxy which has been known to be deactivating [11]) while electron-withdrawing substituents decrease it. The electron-donating substituents stabilize the association complex in two ways: they make the zwitterion and the two amine molecules react faster and slow down the dissociation rates of the complexes. The unusually high value of -7.7 for ρ indicates a high sensitivity of the rates of the base-catalysed reaction to substituents in the aniline while the value of -4.7 shows a smaller sensitivity for the uncatalysed reaction.

As can be seen from Table 2, the values of the rate constants for these reactions show that the reaction rate depends on the electron density on the nitrogen atom.

TABLE 3

Activation parameters for the reaction of phenyl 2,4,6-trinitrophenyl ether with substituted anilines in benzene

Substituent	r [a]	E_A/kJ mol^{-1}	$\Delta H^{\ddagger}$ [c]/kJ mol^{-1}	$\Delta S^{\ddagger}$ [c]/J mol^{-1} K^{-1}
H	0.9980	-3.81 ± 0.03 [b]	-13.7 ± 0.03 [b]	-216 ± 0.57 [b]
m-CH_3	0.9991	-1.65 ± 0.01	-11.6 ± 0.01	-233 ± 0.19
p-CH_3	0.9999	-17.41 ± 0.10	-27.3 ± 0.10	-194 ± 1.9
m-OCH_3	0.9939	4.98 ± 0.04	-4.9 ± 0.04	-241 ± 0.76
p-OCH_3	0.9999	-9.50 ± 0.06	-19.4 ± 0.06	-283 ± 1.14
m-Cl	0.9985	5.94 ± 0.05	-4.0 ± 0.05	-203 ± 0.95
p-Cl	0.9958	6.76 ± 0.05	-3.1 ± 0.05	-219 ± 0.95

[a] Linear correlation coefficient. [b] Standard deviations. [c] At 25 °C.

Since the basicity also depends on the electron density, one should expect a correlation between the rates and the basicity of the anilines. The Brönsted plot (β -3.0) obtained by using the log k'' values at 25 °C and the pK_a of the anilines in water is linear; this verifies that the reaction rate depends on the basicity of the nucleophilic reagent. There is of course a limitation in discussing the value of the Brönsted coefficient since the reaction rates were measured in benzene and the pK_a values in water.

The activation parameters for the examined reactions are reported in Table 3 together with the linear correlation coefficients and standard deviations.

It is not surprising that the reactions are accompanied by negative activation entropies as the formation of an encounter complex and of a defined aggregate is usually accompanied by a loss in entropy; the formation of hydrogen bonds subsequent to the existence of the zwitterion makes the whole complex rigid due to ring closure resulting in loss of entropy. Also, the formation of a highly polar structure like the zwitterion leads to structural reordering in the surrounding solvent and may, as well, be the cause of highly negative activation entropies.

EXPERIMENTAL

Materials.—The preparation of phenyl 2,4,6-trinitrophenyl ether was described previously.[1] The anilines used were purified to constant m.p. or b.p. by recrystallization or distillation from zinc dust (after drying with KOH) as the case may be and the products of their reactions with the substrate prepared by standard methods. AnalaR benzene was further purified by first drying with calcium chloride, then over sodium wire and then distilled.

Kinetic Procedure.—The rates of formation of the products of the reactions were determined spectrophotometrically by the pipette procedure previously described.[1] With all the compounds, excellent pseudo-first-order plots were obtained up to at least 70% reaction and the absorption spectrum of each reaction mixture at infinite time corresponded within 2% to the 'mock' infinity prepared by using the respective 2,4,6-trinitrophenylaniline obtained as a product of the reaction. The second-order rate constants k_A were obtained by dividing the pseudo-first-order rate constants by the aniline concentration. All rates were run in duplicate and the rate constants are accurate to within ±2%. At temperatures other than 25 °C, rate constants were corrected for thermal expansion of the solvent. The activation parameters were calculated from a least-squares treatment of log k_A against $1/T$.

Grateful acknowledgement is made by O. B. for a grant-in-aid of research from the Senate Research Committee of the University of Lagos.

[2/224 *Received, 8th February,* 1982]

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