The Stabilities of Meisenheimer Complexes. Part 26.[1] The Reactions of Some Aromatic Nitro-compounds with Base in t-Butyl Alcohol–Water Mixtures

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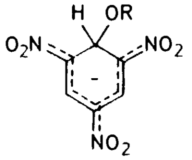
Kinetic and equilibrium data are reported for the reaction of three nitro-compounds with tetramethylammonium hydroxide in t-butyl alcohol containing water. In all solvent systems studied the reactive nucleophile is thought to be the hydroxide ion rather than the t-butoxide ion. The reaction of 1,3,5-trinitrobenzene with base gives a σ-adduct, while 1-chloro-2,4-dinitrobenzene gives 2,4-dinitrophenol. The rates of both these reactions fall rapidly with increasing water in the solvent. In contrast the rate of formation of picric acid from the third substrate, picryl chloride, increases with water content due to the initial formation of the 3-hydroxy-adduct.

In previous Parts we have examined the reactions of various aromatic nitro-compounds with methoxide,[2] ethoxide,[3] n-propoxide,[4] or isopropoxide[5] ions in the corresponding alcohol. The initial reaction of 1,3,5-trinitrobenzene is to give the σ-adducts (1; R = alkyl) while alkyl ethers of 2,4,6-trinitrophenol generally yield the 3-alkoxy-adducts (2) which isomerize to the thermodynamically more stable 1,1-dialkoxy-adducts (3). Our results have shown the importance in these reactions of ion-association with alkali-metal cations of the alkoxide ions and the negatively charged σ-adducts; the 1,1-dialkoxy-complexes associate particularly strongly with cations.



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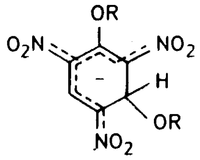

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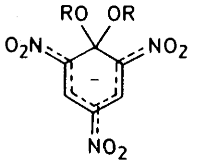


(3)

There have been relatively few reports of σ-complex formation involving t-butoxide ions. Gan and Norris[6] reported kinetic data for formation of an adduct from 1,3,5-trinitrobenzene and sodium t-butoxide in t-butyl alcohol. The linearity of plots of k_{obs} *versus* base concentration was taken to indicate the absence of ion-pairing effects. However a more recent study[7] from the same laboratory of the reaction of 2,4,6-trinitro-[$^2H_3$]toluene with sodium and potassium t-butoxides, in which σ-complex formation is thought to compete with deuteron transfer, recognises the importance of ion-association.

In order to minimise the effects of ion-pairing we have used tetra-alkylammonium as the counter-ion, since we have shown[8] that in dilute solutions it associates with alkoxide ions and σ-adducts much less strongly than do alkali-metal cations.

A further complication is the possibility that in the presence of traces of water t-butoxide ions will be converted to hydroxide ions [equation (1)]. Murto has defined[9] an equilibrium constant [equation (2)] in terms of mole fractions of water, X_{H_2O}, and alcohol X_{BuOH}, for which he quotes a value of $\leqslant 5 \times 10^{-4}$. Two methods which have been used previously to dry t-butyl alcohol are distillation from potassium, by which

$$Bu^tO^- + H_2O \rightleftharpoons Bu^tOH + OH^- \qquad (1)$$

$$K_{ha}' = \frac{X_{H_2O}}{X_{BuOH}} \cdot \frac{[BuO^-]}{[OH^-]} \qquad (2)$$

Bethell[10] obtained a product containing 0.05% w/w of water, or refluxing with molecular sieve followed by distillation.[7] We obtained similar results using AnalaR t-butyl alcohol treated by either of these methods. ^1H N.m.r. spectra of the dried product showed a small band due to residual water whose intensity indicated a water content of 0.07% v/v. Solutions of base were obtained by diluting with t-butyl alcohol a concentrated (*ca.* 2M) aqueous solution of tetramethylammonium hydroxide. This necessarily increases the water content of the solvent. However in dilute base solutions the water added in this way is small compared with the residual water in the solvent. Thus a base concentration of 2×10^{-4}M will increase the water content by 0.01% v/v.

1,3,5-Trinitrobenzene.—In the presence of dilute solutions of base, prepared as above, 1,3,5-trinitrobenzene (TNB) gives an orange species whose visible spectrum obtained by stopped-flow or conventional spectrophotometry shows maxima at 430 (ε 2.2×10^4 l mol^{-1} cm^{-1}) and 500 nm (1.5×10^4). This spectrum is typical of that of 1 : 1 σ-adducts formed by attack on TNB of oxygen bases[11] so that we formulate the reaction as shown in equation (3). With base in excess of the nitro-compound equation (4) will apply.

Kinetic measurements were made by stopped-flow spectrophotometry in dried t-butyl alcohol and in its mixtures with water. Only a single colour-forming reaction was observed on the stopped-flow time-scale

$$\mathrm{TNB} + \mathrm{OR}^- \underset{k_r}{\overset{k_f}{\rightleftharpoons}} (1) \qquad (3)$$

$$k_{obs} = k_f[\mathrm{OR}^-] + k_r \qquad (4)$$

under all conditions. Data are in Table 1. In media containing 10% water or less conversion of 1,3,5-trinitrobenzene into adduct is essentially complete at equilibrium in solutions containing very low base concentrations. This indicates very high values for K, the equilibrium constant for adduct formation, so that $k_f[\mathrm{OR}^-] \gg k_r$. Hence the values in column 4 of Table 1 give values of k_f, the rate coefficient for base attack on TNB.

TABLE 1

Kinetic data for the reaction of 1,3,5-trinitrobenzene [a] with base in t-butyl alcohol–water at 30°

10^4[Base]/ M	% Water by volume	k_{obs}/s^{-1}	$k_{obs}[\mathrm{Base}]^{-1}$/ l mol^{-1} s^{-1}	OD (480 nm) [b]
0.57	0.07	135 ± 10	2.4×10^6	0.030
0.85	0.07	240	2.8×10^6	0.030
1.15	0.07	320	2.8×10^6	0.030
1.0	0.32	150	1.5×10^6	0.030
1.0	0.57	95	9.5×10^5	0.030
1.0	1.07	55	5.5×10^5	0.028
2.0	1.08	110	5.5×10^5	0.032
2.0	2.08	48	2.4×10^5	0.028
2.0	4.08	17	8.5×10^4	0.028
1.0	7.07	2.4	2.4×10^4	0.030
1.0	10.1	1.9	1.9×10^4	0.030
100	50	6.5	6.5×10^2	0.020
100	65	5.0	5.0×10^2	0.015
100	80	6.5 ± 1		0.009
200	80	8		0.013
400	80	10.5		0.017
100	90	15 ± 1		0.0025
200	90	13		0.0046
400	90	14		0.0095
600	90	14		0.0125

[a] [TNB] is 1×10^{-5}M throughout. [b] Measured by stopped-flow spectrophotometry with 2-mm cell.

In media rich in water conversion to adduct is incomplete at equilibrium. If we assume that the extinction coefficient at 480 nm is unaffected by change in solvent we may use the equilibrium optical densities to calculate values of the equilibrium constant. Values so calculated are 35 ± 10 l mol^{-1} in 80% water and 10 ± 2 in 90% water. The rate measurements in 80% water yield values of k_f 140 l mol^{-1} s^{-1} and k_r 5 s^{-1}. In 90% water the rate expression [equation (4)] is dominated by the k_r term which has a value of 14 s^{-1}.

One interpretation of our data is that attack by the t-butoxide ion on 1,3,5-trinitrobenzene yields the adduct (1; R = $\mathrm{Bu^t}$). The decrease in the value of k_f with increase in water in the solvent could then be attributed to a depletion in the t-butoxide concentration *via* the equilibrium shown in equation (1) and also to a solvent effect which reduces the nucleophilicity of the t-butoxide ion.

A second interpretation, and one which we favour, is that the reactive species is the hydroxide ion and that the decrease in its nucleophilicity with increasing water content is due to a solvent effect. Using a value [9] for K_{ha}' of 5×10^{-4} we calculate [equation (2)] that even in our dried solvent the concentration of hydroxide will be about seven times higher than that of butoxide. It might be argued that the t-butoxide ion should have considerably higher reactivity than the hydroxide ion. However, the t-butoxide adduct of 1,3,5-trinitrobenzene would be subject to considerable steric strain which will lower its stability. Thus recent crystallographic evidence [12] indicates that even the methoxide adduct of TNB is subject to steric strain. Further, the value of rate and equilibrium constants which we calculate in water-rich media are similar to those reported by Bernasconi and Bergstrom [13] for reaction of TNB with hydroxide ions in 81 : 19 water–ethanol. (Their values are k_f 70 l mol^{-1} s^{-1}, k_r 7 s^{-1}, K 10 l mol^{-1}.)

The regular increase in reactivity of the hydroxide ion as the proportion of t-butyl alcohol in the solvent is increased can be attributed to its progressive desolvation. This in agreement with the observation by Bethell [10] that the addition of small quantities of water to t-butyl alcohol containing benzyltrimethylammonium hydroxide drastically reduces the ability of the medium to abstract a proton from the indicator 4-nitroaniline.

Further evidence that the reactive species is the hydroxide ion comes from a study of the reaction of 1-chloro-2,4-dinitrobenzene with base in t-butyl alcohol–water mixtures.

1-*Chloro*-2,4-*dinitrobenzene*.—In the presence of tetramethylammonium hydroxide in t-butyl alcohol, 1-chloro-2,4-dinitrobenzene is converted into a yellow species whose visible spectrum is identical with that of 2,4-dinitrophenol in the same medium, $\lambda_{max.}$ 367 (ε 17 500 l mol^{-1} cm^{-1}) and 410 nm (17 000). In media containing 1% or more of water conversion is essentially quantitative. In media containing less water 2,4-dinitrophenol is the major product as judged by u.v.–visible spectroscopy, but conversion is not complete. Here the visible spectra show more absorption in the 300—350 nm region than does 2,4-dinitrophenol indicating the formation of another product, possibly the t-butyl ether of 2,4-dinitrophenol. The increase with time of the absorption at all wavelengths above 300 nm proceeds at the same rate indicating that formation of 2,4-dinitrophenol and the side-product is concurrent rather than consecutive.

There are several possible mechanisms available for the formation of 2,4-dinitrophenol. The most straightforward is the direct S_NAr replacement of halide by hydroxide ion. However, the formation of radical anions upon interaction of halogenonitrobenzenes with alkoxides is well documented.[14] That these radicals may contribute to the overall substitution process has been shown by Scorrano and his co-workers in the reaction of 1-halogeno-2,4-dinitrobenzenes with potassium isopropoxide in isopropyl alcohol–benzene mixtures,[15] and in the reactions of 4-chloronitrobenzene with alkoxides.[16] Characteristic features of reactions involving radicals [15,16] are a less than first-order dependence on base concentration and a susceptibility to the presence of oxygen. Our data in Table 2 show neither of these characteristics. Thus the results in rows 13—15 indicate a strictly first-order dependence on base concentration while those in rows 9—11 indicate that the presence or absence of oxygen has little effect on reaction rate. While we cannot rule out the possibility that a small amount of reaction proceeds by radical intermediates, particularly in those media containing the least water, our data are in accord with the formation of 2,4-dinitrophenol by direct attack of hydroxide ions on 1-chloro-2,4-dinitrobenzene. The decrease in reaction rate with increasing proportion of water in the solvent is shown in Figure 1. The variation is similar to that of the TNB–hydroxide reaction, indicating that it is very likely that the same nucleophile, OH^-, is the reactive species in each case.

TABLE 2

Kinetic data for reaction of 1-chloro-2,4-dinitrobenzene [a] with base in t-butyl alcohol–water at 30°

10^3[Base]/ M	% Water by volume	10^3k_{obs}/ s^{-1}	k_{obs}[Base]$^{-1}$/ l mol^{-1} s^{-1}	OD (410 nm)
0.2	0.08	2.2	11	0.45
0.4	0.09	4.0	10	0.32
0.6	0.10	4.3	7	0.40
1.0	0.12	7.4	7	0.42
2.0	0.16	12.3	6	0.44
1.0	0.35	2.2	2.2	0.52
1.0	0.59	1.5	1.5	0.60
1.0	1.06	0.84	0.84	0.62
1.0	2.06	0.40	0.40	0.64
0.43 [b]	2.10	0.18	0.42	0.63
0.43 [c]	2.10	0.15	0.35	0.63
1.0	3.95	0.14	0.14	0.60
10	5.6	0.83	0.083	0.65
7.7	5.5	0.59	0.078	0.63
5.1	5.3	0.41	0.080	0.64
57	13	0.54	0.01	0.67
54	18	0.35	0.007	0.67
51	23	0.19	0.004	0.67
45	32	0.09	0.002	0.67

[a] 1-Chloro-2,4-dinitrobenzene is 4×10^{-5}M. [b] Solutions flushed with nitrogen. [c] Solutious flushed with oxygen.

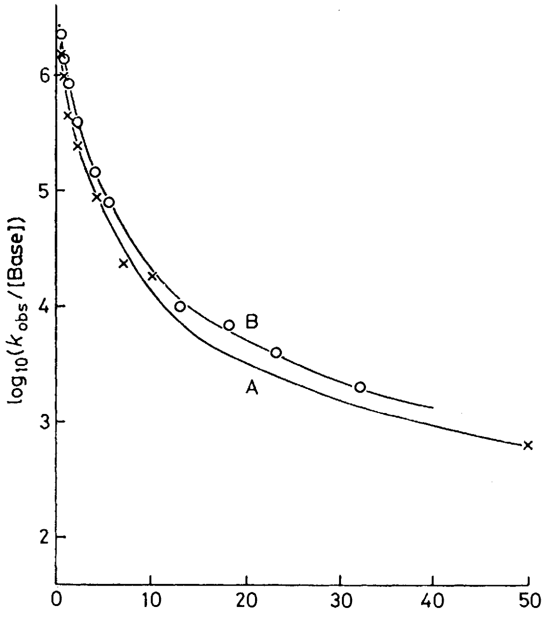


FIGURE 1 Variation with solvent composition of the rate coefficients for base attack on A, 1,3,5-trinitrobenzene; and B, 1-chloro-2,4-dinitrobenzene. For the latter compound the scale is 6 + $\log_{10}$ (k_{obs}/[Base])

1-*Chloro*-2,4,6-*trinitrobenzene*.—The reaction of picryl chloride with dilute solutions of tetramethylammonium hydroxide in t-butyl alcohol proceeds in two stages. There is a rapid reaction giving an orange species whose visible spectrum, with maxima at 425 and 480 nm, is typical of a σ-adduct. This is followed by a slower reaction giving a yellow species whose visible spectrum, $\lambda_{max.}$ 365 nm, is identical with that of picric acid in the same medium. Spectra are shown in Figure 2.

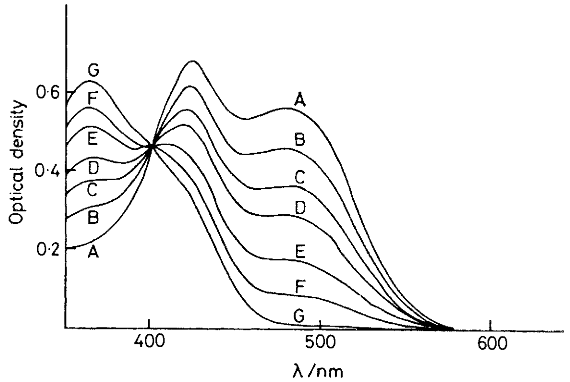


FIGURE 2 Visible spectra of picryl chloride (4×10^{-5}M) and tetramethylammonium hydroxide (5×10^{-4}M) in 99 : 1 v/v t-butyl alcohol–water. The change with time is A ⟶ G

We interpret our data according to the reactions shown in the Scheme. The initially formed adduct (4) might result from attack of either t-butoxide or hydroxide ions. Our data relating to this reaction (Table 3) are in accord with attack by hydroxide. Thus the decrease in the value of k_3 ($\equiv k_{obs}$/[Base]) with increasing water in the solvent parallels the decrease in rate coefficients for hydroxide attack on 1,3,5-trinitrobenzene and 1-chloro-2,4-dinitrobenzene. In media containing 5 or 10%

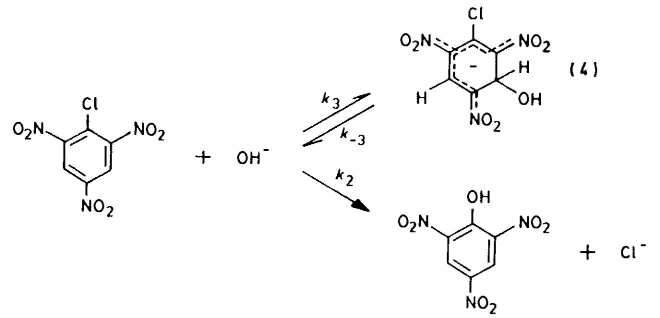
TABLE 3

Kinetic and equilibrium data for the rapid reaction of picryl chloride (10^{-5}M) with base in t-butyl alcohol–water at 30°

10^4[Base]/ M	% Water by volume	10^3k_{obs}/ s^{-1}	k_{obs}[Base]$^{-1}$/ l mol^{-1} s^{-1}	OD (480 nm)[a]	K_3[b]/ l mol^{-1}
0.5	0.07	60 ± 10	1.2×10^6	0.030	
1.0	0.07	130	1.3×10^6	0.030	
1.5	0.07	250	1.7×10^6	0.030	
1.1	0.30	50	4.5×10^5	0.030	
1.0	0.6	24	2.4×10^5	0.030	
1.0	1.1	14	1.4×10^5	0.028	
1.0	5.0	1.8		0.020	2×10^4
1.0	10.0	1.3		0.006	2×10^3

[a] At the completion of the rapid reaction. [b] Defined as OD (480)/[0.030 − OD (480)] [Base].

water only partial conversion to the σ-adduct is achieved with 1×10^{-4}M-base. The optical densities at completion of this reaction, but before appreciable conversion to picric acid has occurred, allow the calculation of values of K_3. These values, together with the values of k_{obs}, give values in 5% water of k_3 1.2×10^4 l mol^{-1} s^{-1} and k_{-3} 0.6 s^{-1}, and in 10% water of k_3 2.2×10^3 l mol^{-1} s^{-1} and k_{-3} 1.1 s^{-1}.



SCHEME

Comparison of Tables 1 and 3 show that at a given solvent composition values of rate constants and equilibrium constants for hydroxide attack at the 3-position of picryl chloride are lower than those for attack at an unsubstituted position of 1,3,5-trinitrobenzene. A similar reactivity order has been found previously in studies of methoxide [17] or ethoxide [18] attack on these substrates. The lower reactivity of picryl chloride may be due to steric interference between the chlorine atom and the nitro-groups, which disrupts the planarity of the molecule and reduces the electron-withdrawing ability of the nitro-groups.

In previous work [19] we have shown that in water containing sodium hydroxide the hydroxy-group in adducts such as (4) will ionise to give a dianionic species. However, little ionisation occurs in solutions containing $<10^{-2}$M-base. At the very low base concentrations used in the present work we would not expect appreciable ionisation of (4) to occur.

With time picryl chloride is converted to picric acid. In all media examined conversion is >80%. We have no evidence that reaction occurs other than by direct displacement of chloride by hydroxide ion. Thus visible spectra show an isosbestic point at 400 nm indicating the absence of any reaction intermediate such as the t-butyl ether of picric acid. The kinetic expression corresponding to the reaction sequence shown in the Scheme is given in equation (5). At the base concentrations used to measure the slow reaction $K_3[OH^-] > 1$, so that equation (5) reduces to (6). Measurements obtained at 480 nm

$$k_{obs}' = k_2[OH^-]/(1 + K_3[OH^-]) \qquad (5)$$

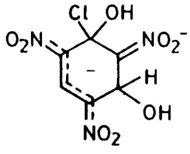
$$k_{obs}' = k_2/K_3 \qquad (6)$$

are in Table 4. They show that, as required by equation (6), values of k_{obs}' are independent of base concentration in media containing >2% water. In media containing less water there appears to be a component of the rate which increases with base concentration. Thus the first three results in Table 4, referring to solutions where the water content changes little, show a marked dependence on base concentration. It is possible that in these solutions where the hydroxide ions will be least solvated and thus most reactive, attack of hydroxide occurs on the σ-adduct (4) to give nucleophilic substitution *via* the di-adduct (5). Such an adduct would be unstable with respect to loss of chloride ion and would not be an observable intermediate. That such a pathway exists in water containing high concentrations of sodium hydroxide has been shown previously.[19]

TABLE 4

Rate data for the ' slow ' reaction of picryl chloride (4×10^{-5}M) with base in t-butyl alcohol–water at 30°

10^4[Base]/M	Volume % water	10^4 k_{obs}'/s^{-1}
2.0	0.08	3.6 ± 0.3
4.0	0.09	5.2
8.4	0.11	10
30	0.22	30
50	0.32	40
4.8	1.1	23
25	1.2	33
4.8	2.1	42
25	2.2	44
4.8	3.1	62
25	3.2	67
4.8	4.1	84
25	4.2	89
5	5.0	97
10	5.0	108
20	5.0	105
50	5.0	96
100	5.0	87
10	10.0	200
20	10.0	210
50	10.0	200
100	10.0	180



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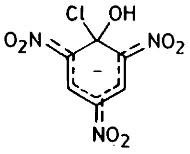

(6)

It is worth noting that our kinetic data allow us to discount the possibility that the σ-adduct we have observed is (6) rather than (4). The argument is as follows. If we were to assume that the observed adduct is (6) then the rate constants in Table 4 would refer to loss of chloride ion from this adduct and would give a value in 5% water of 1×10^{-2} s^{-1}. However the measurements of the more rapid reaction give a value in the same solvent system for expulsion of hydroxide ion of 0.6 s^{-1}. Since chloride is known [19] to be a considerably better leaving group than hydroxide this hypothesis is untenable.

From the known values of k_{obs}' and K_3 we calculate, using equation (6), a value for k_2 of 200 l mol^{-1} s^{-1} in a medium containing 5% water. Since base addition will be the rate-limiting step in the substitution reaction, this value refers to the rate of hydroxide attack at the 1-position of picryl chloride. The corresponding value for hydroxide attack at the 3-position is 1.2×10^4 l mol^{-1} s^{-1} in the same medium. That attack at the unsubstituted position is faster than at the chloro-substituted position is in agreement with results obtained in water.[19]

Our results (Table 4) indicate that the rate of conversion of picryl chloride to picric acid increases with water content of the solvent. This is in marked contrast with the large decrease in rate of conversion of 1-chloro-2,4-dinitrobenzene to 2,4-dinitrophenol with increasing water. The difference in behaviour is understandable when it is remembered that the equation relevant to picryl chloride is equation (6). As outlined below it is expected that the values of both k_2 and K_3 will decrease with increasing proportion of water in the solvent. However, if the decrease in K_3 is larger than the decrease in k_2 then the value of k_{obs}' will increase. The change in value of K_3 with solvent composition will depend on the change in energy of the adduct (4) relative to the reactants. A major factor contributing to the expected decrease in value is likely to be the better solvation and corresponding lowering in energy of the hydroxide ion as the proportion of water is increased. Similarly the value of k_2 will be expected to decrease as the water concentration is increased. However, here the relevant energy change is between the transition state for formation of (6) and the reactants. Since in the transition state desolvation of the hydroxide ion will be incomplete, the smaller decrease in value of k_2 can be understood.

EXPERIMENTAL

Nitro-compounds were recrystallised commercial specimens. A concentrated aqueous solution of tetramethylammonium hydroxide (2M) in water was diluted with t-butyl alcohol and titrated with standard acid. AnalaR grade t-butyl alcohol was dried by distillation from potassium[10] or by refluxing with molecular sieve followed by distillation,[7] and was subsequently protected from moisture.

Visible spectral measurements were made with Unicam SP500 and SP8000 and Beckman S25 instruments or with a Canterbury stopped-flow spectrophotometer. Kinetic measurements were made under first-order conditions with [Base] $\gg$ [Substrate] using the above instruments. All measurements were made at 30 ± 0.5°.

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