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Solvent Dependence of the Ionization of Nitrophenylmethanes

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The solvent dependence of proton abstraction from various nitrophenylmethanes has been examined for aqueous dimethyl sulphoxide and methanolic dimethyl sulphoxide solutions. Even though the compounds studied vary considerably in thermodynamic acidity (pK_a), their proton-abstraction rates all show the same solvent dependence. It is suggested that the transition states for these reactions all occur at similar positions on the reaction pathway, and that transition state imbalances exist for these proton transfers.

In recent years, numerous studies of the reactions of carbon acids with bases have been reported,[1] providing information regarding the competition between complex formation resulting from nucleophilic attack and proton abstraction,[2] substituent effects upon acidities,[1b] pK_a values *etc.*[3] Because of the normally extremely low solubility of carbon acids (*e.g.*, hydrocarbons, ketones, nitriles, and nitroaromatics) in water or highly aqueous media, most acidity measurements have been carried out in either alcoholic media, or solutions containing dimethyl sulphoxide (up to 100%). Both aqueous dimethyl sulphoxide (DMSO) and alcoholic dimethyl sulphoxide solutions have been used, but the widely differing acidities of carbon acids often requires measurements of kinetic data to be made in different solvent systems, thus rendering their direct comparison difficult.

To overcome this problem, some authors have carried out quantitative studies of the influence of solvent composition upon the forward (k_1) and reverse (k_{-1}) rate constants of equation (1).[1a,4–9] The data obtained may be interpreted in

$$R_1R_2R_3CH + B^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} R_1R_2R_3C^- + BH \qquad (1)$$

terms of the reaction mechanism, and used to infer the nature of the transition state for proton abstraction,[1a,1f] in addition to providing extrapolated data for comparison purposes. However, the detailed dependence of reaction rates upon solvent composition is normally dependent on the substrate's thermodynamic acidity, pK_a.[1a]

In our studies of the ionization of nitrophenylmethanes, having significantly different pK_a values, we have observed that they exhibit the *same* solvent dependence in aqueous or methanolic DMSO mixtures. We report here our observations, together with their possible implications for transition-state structures for these proton abstractions.

Results

Rates of proton abstraction from various nitrophenylmethanes by hydroxide ion, in aqueous-DMSO solutions at 25 °C, and the rates of protonation of the corresponding carbanions by the solvent have been measured, and the data obtained are shown in Table 1. Also included in this Table are literature data for proton abstraction from nitroethane,[13] phenylnitromethane,[12] and 4-nitrophenylacetonitrile[8] in aqueous DMSO mixtures. In Table 2 similar data are presented for proton abstraction by methoxide ion in methanolic DMSO solutions at 25 °C, together with carbanion protonation rates (by methanol) where data were obtainable.

To illustrate the behaviour of these nitroaromatics towards changing solvent composition, we have plotted the logarithms of the k_1 values of Table 1 as a function of the mole fraction of DMSO (X_{DMSO}) in the Figure. The log k_1 values for the nitrophenylmethanes, including 4-nitrophenylacetonitrile, have been normalised with respect to 2,2′,4,4′-tetranitrodiphenylmethane by means of an increment, Δ, which is constant for a given compound. It can be seen from the Figure that these normalised data, within the experimental errors, fall upon a single linear relationship which has a slope dlog $k_1^{H_2O}/dX_{DMSO} = 8.2$. The values of Δ are given in Table 1. The corresponding k_{-1} data are insufficient to allow us to draw reliable conclusions regarding their variation with solvent composition.

Also shown in the Figure are the literature data for nitroethane[13] and phenylnitromethane[8] ionization. These also exhibit linear relationships of the form dlog $k_1^{H_2O}/dX_{DMSO}$ with slopes of 6.7 and 5.7, respectively, for nitroethane and phenylnitromethane.

Analogous treatment of the data of Table 2 for reactions in methanolic DMSO also yields a single linear relationship, with a slope dlog k_1^{MeOH}/dX_{DMSO} of 4.6. The increments, Δ, used to normalise the data to 2,2′,4,4′-tetranitrodiphenylmethane are given in Table 2.

Discussion

An inspection of the data of Table 1 shows clearly the far greater *kinetic* acidifying effect of electron-withdrawing substituents upon the α-carbon atom than of an additional *ortho*-NO_2 group (*cf.* 2,4-dinitrotoluene, α-chloro-4-nitrotoluene, and 4-nitrophenylacetonitrile; 2,4,4′-trinitrodiphenylmethane and α-bromo-4,4′-dinitrodiphenylmethane). The effect of additional *ortho*-NO_2 groups seems to be additive however, which suggests that additional steric interactions are not introduced by a fourth NO_2 group (*cf.* 4,4′-dinitrodiphenylmethane,† 2,4,4′-trinitrodiphenylmethane, and 2,2′,4,4′-tetranitrodiphenylmethane). Further, the kinetic acidifying effect of an α-phenyl group is considerably less than that of an α-halogen atom in aqueous DMSO solutions.

Similar substituent effects are found for reactions in methanolic DMSO (Table 2). Thus an α-phenyl substituent has only a weak kinetic acidifying effect in these media also (*cf.* 4,4′-dinitrodiphenylmethane and 4,4′-dinitrotriphenylmethane), whereas an α-methyl substituent upon 2,2′,4,4′-

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† The values quoted in Table 1 for 4,4′-dinitrodiphenylmethane differ from those originally reported.[11] We have repeated these measurements several times, with different batches of product, to confirm their accuracy, and are unable to account for the values previously found.

Table 1. Proton-abstraction rates (k_1) and carbanion reprotonation (k_{-1}) for nitrophenylmethanes in aqueous DMSO solutions at 25 °C

	Compounds		DMSO (% v/v)										Reference
			0	10	20	30	40	50	60	70	80	90	
1	2,2′4,4′-Tetranitrodiphenylmethane $\Delta = 0$	$k_1{}^a$	1.06	1.05	2.77	4.26	8.65	70, 46.6^d	230	1 245	1.1×10^4		10
		$k_{-1}{}^b$	0.15	0.07	0.015	0.007	18×10^{-4}	–, $5.5 \times 10^{-4\,d}$					
		K^c	7.07	15	185	608	4 805	–, $8.5 \times 10^{4\,d}$					
2	2,4,4′-Trinitrodiphenylmethane $\Delta = 1.4$	k_1			0.34	0.34	0.64	2.16^d		62	504	8 200	10
		k_{-1}			0.11	0.01		$4.9 \times 10^{-4\,d}$					
		K			31	46		4 400^d					
3	4,4′-Dinitrodiphenylmethane $\Delta = 2.8$	k_1						*ca.* 9×10^{-2}	0.54	3.36	26.7	412	This work
		k_{-1}						*ca.* 1×10^{-2}	8×10^{-3}				
		K						9	67				
4	α-Bromo-4,4′-dinitrodiphenylmethane $\Delta = 0.9$	k_1						6	35.8	220	2 280	5.25×10^4	11
		k_{-1}						0.52	0.45	0.3	0.1		
		K						11.5	79.5	733	2.28×10^4		
5	α-Chloro-4,4′-dinitrodiphenylmethane $\Delta = 1$	k_1						4.05	27.2	188	2 500	6×10^4	11
		k_{-1}						0.1	0.18	0.17	0.1		
		K						40.5	151	1 106	2.5×10^4		
6	4,4′-Dinitrotriphenylmethane^{e,f} $\Delta = 2.4$	k_1								6.92	72		This work
		k_{-1}								0.023			
		K								301			
7	2,4-Dinitrotoluene $\Delta = 3$	k_1							0.48	1.4	9.9	180	This work
		k_{-1}							0.012	0.004			
		K							40	350			
8	α,α-Dichloro-4-nitrotoluene $\Delta = 0.2$	k_1							190	1 190	1.64×10^4		11
		k_{-1}							35	40	15		
		K							5.4	30	1 093		
9	α-Chloro-4-nitrotoluene $\Delta = 3.2$	k_1									19.2	331	11
		k_{-1}									0.27	0.24	
		K									71	1 380	
10	4-Nitrophenylacetonitrile $\Delta = -2.7$	k_1				2 080^g	4 910^h	33 800^i	$1.97 \times 10^{5\,j}$				8
		k_{-1}				2.78^g	2.26^h	1.54^i	0.334^j				
		K				748	2 173	21 950	5.9×10^5				
11	Phenylnitromethane $\Delta = 0$	k_1	151			448^k		1 730		13.280^l			12
12	Nitroethane $\Delta = 2$	k_1	5.2				18^m		275^n	1 542^o	6 310^p	19 800^q	13

[a] k_1 in l mol^{-1} s^{-1}. [b] k_{-1} in s^{-1}. [c] $K = k_1/k_{-1}$ in l mol^{-1}. [d] Values at constant ionic strength. 0.5M-NMe_3Cl. [e] 75% DMSO; $k_1 = 24$; $k_{-1} = 0.03$; $K = 800$. [f] $t = 20$ °C. [g] $X_{DMSO} = 0.10$. [h] $X_{DMSO} = 0.14$. [i] $X_{DMSO} = 0.20$. [j] $X_{DMSO} = 0.30$. [k] 33.33% DMSO. [l] 66.67% DMSO. [m] $X_{DMSO} = 0.13$. [n] $X_{DMSO} = 0.26$. [o] $X_{DMSO} = 0.37$. [p] $X_{DMSO} = 0.48$. [q] $X_{DMSO} = 0.58$.

Table 2. Proton-abstraction rates (k_1) and carbanion reprotonation (k_{-1}) for nitrophenylmethanes in methanol–DMSO solutions at 25 °C

Compound		DMSO (% v/v)									Reference
		0	20	40	50	60	70	80	90	95	
2,2,4,4′-Tetranitrodiphenylmethane $\Delta = 0$	k_1[a]	26.3	151	494		3 280		3.2×10^4			14
	k_{-1}[b]	0.73	0.05								
	K[c]	36	3 020								
4,4′-Dinitrodiphenylmethane $\Delta = 2.5$	k_1					8.55	33.1	136	843	3 800	15
	k_{-1}					0.49	0.13				
	K					17.5	255				
4,4′,4″-Trinitrotriphenylmethane[d] $\Delta = 0.75$	k_1	1.33	22.16	79.3		592		5 500			This work
	k_{-1}	4.32	4	1.2		0.2					
	K	0.3	5.5	66.1		2 960					
4,4′-Dinitrotriphenylmethane $\Delta = 2.2$	k_1		0.5	1.24		18.83		221			15
	k_{-1}		0.375	0.29		0.13		0.04			
	K		1.3	4.27		145		5 525			
4-Nitrotriphenylmethane[d] $\Delta = 3.9$	k_1							4.13	24.8		This work
	k_{-1}							0.04	0.08		
	K							103	310		
2,4-Dinitrotoluene $\Delta = 2.65$	k_1					5.16	24.7	87.7	566.5		This work
	k_{-1}					0.334	0.035				
	K					15.5	706				
2,4,6-Trinitrotoluene $\Delta = 0.3$	k_1	13.3		225	530	1 000					5, 16
	k_{-1}	1.07									
	K	12.4									
1,1-Bis-(2,4-dinitrophenyl)ethane $\Delta = 3.05$	k_1				0.9	2.67					This work
	k_{-1}				*ca.* 10^{-3}	*ca.* 10^{-3}					
	K				*ca.* 900	*ca.* 2 670					

[a] k_1 in l mol^{-1} s^{-1}. [b] k_{-1} in s^{-1}. [c] $K = k_1/k_{-1}$ in l mol^{-1}. [d] t = 20 °C.

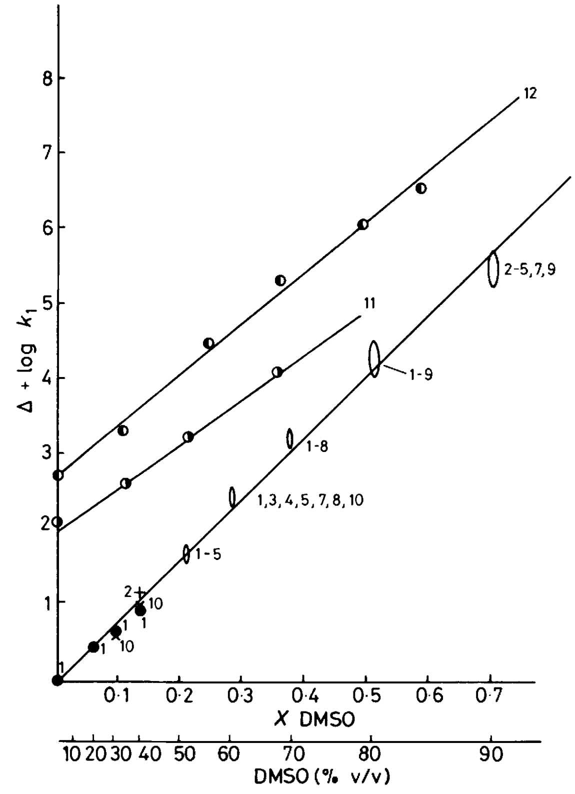

Figure. The variation of log k_1 for proton abstraction from nitroethane, phenylnitromethane, and nitrophenylmethanes by hydroxide ion in aqueous DMSO mixtures with mole fraction of DMSO. Data for the nitrophenylmethanes are normalised as discussed in the text; for clarity, the data for nitroethane have been plotted as log k_1 + 2. The numbering of the derivatives is indicated in Table 1.

tetranitrodiphenylmethane has an acid-weakening effect [*cf.* 1,1–bis-(2,4-dinitrophenyl)ethane]. An additional *ortho*-NO_2 group in monocyclic systems has a large kinetic acid-strengthening effect (*ca.* 200-fold) (*cf.* 2,4-dinitrotoluene and 2,4,6-trinitrotoluene), and comparable behaviour has been found in aqueous DMSO solutions for the introduction of an *ortho*-NO_2 group into 4-nitrotoluene (*ca.* 100-fold).*

In contrast to their influence upon the kinetic acidities of nitrophenylmethanes, electron-withdrawing α-substituents (*e.g.*, halogen) are less effective than ring NO_2 substituents in increasing the thermodynamic acidities, in aqueous or methanolic DMSO solutions. The effect of α-phenyl substitution on thermodynamic acidities is also much greater, because of its greater stabilizing influence upon the carbanions, as seen from the decreased k_{-1} values.

Whereas the data of Tables 1 and 2 show that the majority of the compounds studied are amenable to measurement in 80% DMSO solutions, and thus comparisons of data in those solutions may be made directly, it is not always possible to make such comparisons because of the wide variety of solvent systems used for kinetic–thermodynamic measurements. However, approximate linear relationships between $\log_{10} k_1$ and the mole fraction of one component of a series of solvent mixtures are expected from considerations of the well known acidity function dependence of the rates of acid- or base-catalysed reactions, the Zucker–Hammett hypothesis[17] or Bunnett's treatment.[18] By making use of such relationships, data comparisons are facilitated.

For aqueous or alcoholic DMSO mixtures the H_- functions increase approximately linearly with DMSO content, significant deviations from linearity being observed only for solutions containing more than 90% DMSO by volume.[1a,1f] In these regions of high DMSO content, the H_- *versus* X_{DMSO} relationships show sharp upward curvature. Thus in aqueous or methanolic DMSO solutions containing <90% DMSO, approximately linear relationships between log k_1 and X_{DMSO} should be found, allowing extrapolation of log k_1 values into solutions less rich in DMSO.

Several reports of linear variations of log k_1 with X_{DMSO} for carbon acids have appeared,[4–9] but little use has been made of such relationships. In previous studies of proton abstraction from 4-nitrotoluenes we noted such a relationship, and used it for the extrapolation of data.[11] The data presented in Tables 1 and 2 for various nitrophenylmethanes show that, within the average experimental error, they exhibit an *identical response to changes in the solvent medium*, corresponding to identical acidity function dependence for a given solvent pair (Figure).

The interpretation of the solvent variations of proton-abstraction rates from carbon acids generally derives from an expression of the form of equation (2), where x = numerical

$$\log_{10} k_1 = H_- + x \log_{10} a_w + \text{constant} \qquad (2)$$

factor, often taken as unity, and a_w = activity of the solvent (water or methanol) in the medium.[17,18] This expression assumes that the carbon acid behaves similarly to the acids used to set up the H_- scale, and it is known that acidity scales based upon nitrogen or carbon acids are comparable.[19,20] From equation (2), a slope of $d\log_{10}k_1/dH_-$ of unity is predicted if either the activity term is assumed to be constant or its value is very small in comparison with H_-. Deviations from a slope of unity have been considered to indicate the resemblance of the transition state to reactants or products.[1a,21]

Some authors have suggested that a linear dependence of log values of proton abstraction rates upon acidity function values is in itself characteristic of rate-determining proton abstraction, as opposed to some subsequent reaction of a carbanion generated in a fast reaction step.[4] Weak acids should have product-like transition states and values of $d\log_{10} k_1/dH_-$ near unity, whereas increasing acid strength should shift the transition state towards the reactant and $d\log_{10} k_1/dH_-$ should decrease.[1a] Increasing base strength should have the same effect as increasing acid strength.

From the experimental variations of H_- with X_{DMSO} values of $d\log_{10} k_1/dH_-$ may be obtained using the $d\log k_1/dX_{DMSO}$ values (see Results section), and these, together with a number of other values,[1a] are given in Table 3. In this Table, estimates for the pK_a values of the substrates are also given, from which it can be seen that a single linear solvent relationship for all the nitrophenylmethanes studied, spanning some 8 or more pK units, is somewhat unexpected. The values of Table 3 for nitroethane and phenylnitromethane suggest transition states for these molecules which are less carbanion-like than those for the nitrophenylmethanes. This is in accord with the significantly different solvent rearrangement-requirement for carbanion formation from α-nitro derivatives than from ring-nitro derivatives. Table 3 also shows that increased carbon acid strength generally leads to lower $d\log_{10} k_1/dH_-$ values, and thus more reactant-like transition states.

In detailed studies of proton abstraction from 2,4,4′-trinitrodiphenylmethane and 2,2′,4,4′-tetranitrodiphenylmethane we have shown that the transition states for reactions in both aqueous and methanolic DMSO are carbanion-like, but that transition-state imbalance is evident in these media.[10,14] Such

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* Accordingly, the greater thermodynamic acid-strengthening effect of a *para*-NO_2 group relative to an *ortho*-NO_2 group essentially reflects a greater decrease of k_{-1}.

Table 3. The variation of rate constants for carbon acid ionization in water or methanol. Values for the present work calculated from the data of Tables 1 and 2, assuming dH_-/dX_{DMSO} = 8.2 for H_2O and 6.7 for MeOH

Carbon Acid	pK_a	$d\log k_1/dH_-$	Reference
Phenylnitromethane	6.88	0.57 (H_2O)	12
Nitroethane	8.6	0.67 (H_2O)	13
Nitrophenylmethane	*ca.* 13—23	0.82 (H_2O) 0.69 (MeOH)	
Acetophenone	*ca.* 19.7	0.54 (H_2O, more basic) 0.42 (H_2O, less basic) 0.4 (MeOH) 0.31 (EtOH)	21
Phenylmethylacetophenone	*ca.* 20	0.49 (H_2O)	22
Menthone	*ca.* 21	0.48 (H_2O)	23
9-t-Butylfluorene	23.4	0.70 (H_2O)	1*a*
p-Chlorophenyl methyl sulphone	23—25	0.70 (H_2O)	1*a*
Chloroform	*ca.* 24	0.8 (MeOH)	24
DMSO	*ca.* 32	0.93 (H_2O)	19

imbalances are not uncommon in the ionization of carbon acids leading to highly delocalised carbanions, and these reactions are believed to proceed *via* transition states leading initially to sp^3-hybridized carbanions.[25–27] The nitrophenylmethanes of Tables 1 and 2 all yield highly delocalised carbanions, and their identical response to changing solvent composition, corresponding to transition states at similar points on the reaction pathway, suggests that transition-state imbalances exist in all of these ionizations. Transition-state imbalance may therefore be the norm, rather than the exception, in carbon acid ionizations.

Experimental

Materials.—All compounds were synthesized according to standard literature procedures and crystallized to constant literature melting points.

Measurements.—Solutions *etc.* were made up as previously described.[10] Kinetic measurements were made using a Durrum stopped-flow spectrophotometer, with a cell-housing, thermostatted to ±0.5 °C.

Acknowledgements

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