The Stabilities of Meisenheimer Complexes. Part 22.[1] The Ionisation of 2,4-Dinitroaniline, its *N*-Alkylated Derivatives, and 2,6-Dinitroaniline in Methanol–Dimethyl Sulphoxide containing Sodium Methoxide

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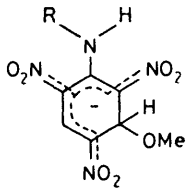
2,4-Dinitroaniline and its *N*-alkylated derivatives react with sodium methoxide in methanol–dimethyl sulphoxide to give the conjugate base. However, in the case of 2,6-dinitroaniline, base addition at the 3-position competes with proton loss. The effects of *N*-alkylation on the acidity of 2,4-dinitroaniline are considered and are compared with the effects of similar substitution in 2,4,6-trinitroaniline.

THE major modes of 1 : 1 reaction of 2,4,6-trinitroaniline (picramide) and its *N*-alkyl derivatives with sodium methoxide in methanol–dimethyl sulphoxide are base addition at the 3-position to give the σ-adducts (1; R = H or alkyl) or proton loss to give the conjugate bases (2; R = H or alkyl).[2–5] Kinetic and equilibrium data relating to these processes have recently been reported.[6] Spectroscopic studies of the parent molecules have shown that the presence of *N*-alkyl substituents causes steric crowding around the 1-position which is relieved by rotation from the ring-plane of the adjacent nitro-group.[7,8] The ability of such nitro-groups to delocalise negative charge in anionic species will be reduced. The decreases in acidity as the substituent R is varied in the series Me, Bu^n, Pr^i, Bu^t has been attributed [6] to this effect.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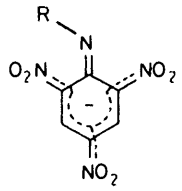
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N-Alkyl-2,4-dinitroanilines (3) and their conjugate bases (4) should be less subject to these unfavourable steric interactions since they can adopt a *trans*-configuration.[9] We report here on the ionisation equilibria of these compounds and also, for comparison, 2,6-dinitroaniline.

RESULTS AND DISCUSSION

Anilines containing one or two nitro-groups with or without halogeno ring-substituents have been widely used in determining acidity functions in alkaline media,[10] the assumption being made that reaction with base results in proton loss rather than base addition. In the case of 2,4-dinitroaniline there is ^{1}H n.m.r. evidence [3] for this mode of ionisation [equation (1)] in methanol–DMSO containing sodium methoxide. Thus increasing the concentration of base up to a molar ratio of 1 : 1 was found to cause a smooth shift to high field of the ring-proton resonances, consistent with rapid exchange between the parent and its conjugate base. Measurements with *N*-alkyl-2,4-dinitroanilines similarly indicate that proton loss is the major reaction with base. Data are in Table 1. In 80 : 20 v/v DMSO–methanol no new bands attributable to σ-adducts were detected and we estimate that >95% of the 1 : 1 interaction results in proton loss.

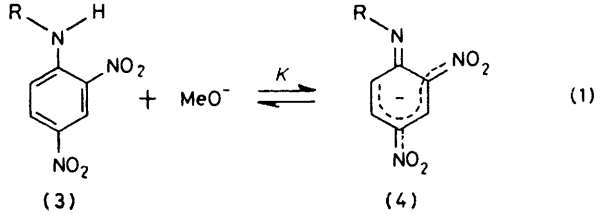
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TABLE 1

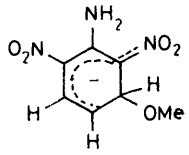
^{1}H N.m.r. chemical shifts (δ) for *N*-alkyl-2,4-dinitroanilines and their conjugate bases

Aniline	Ring protons 3-H [b]	5-H [c]	6-H [d]	*N*-Alkyl	N–H
(3; R = H) [a]	8.71	8.10	7.04		8.3
(4; R = H)	8.71	7.52	6.52		
(3; R = Me)	8.85	8.27	7.15	3.10	8.9
(4; R = Me)	8.40	7.55	6.45	3.05	
(3; R = Bu^n)	8.84	8.23	7.21	3.46, 1.5, 0.93	8.8
(4; R = Bu^n)	8.35	7.49	6.39	3.18, 1.45, 0.90	
(3; R = Pr^i)	8.82	8.24	7.26	4.1, 1.3	8.4
(4; R = Pr^i)	8.33	7.54	6.47	3.8, 1.1	
(3; R = Bu^t)	8.84	8.21	7.41	1.51	8.7
(4; R = Bu^t)	8.24	7.64	6.68	1.33	

[a] From ref. 3. [b] d, *J* 2.5 Hz. [c] dd, *J* 10, 2.5 Hz. [d] d, *J* 10 Hz.

In contrast the spectra of 2,6-dinitroaniline indicate that base addition competes with proton loss. The spectrum of the parent shows spin-coupled bands at δ 6.85 and 8.5 due to ring protons and a broad band at δ 8.4 due to amino protons (Figure 1). Increasing the mol ratio of sodium methoxide in 80 : 20 v/v DMSO–methanol (fully deuteriated solvents were used) caused a smooth shift to high field of the ring-proton bands, and in the presence of 1 mol. equiv. of base the shifts were δ 5.8 and 7.7, respectively. Also new bands were observed due to the ring-protons of the 3-methoxy adduct (5). Analysis as an ABX spectrum gave values of δ 5.25 (3-H), 5.40 (4-H), and 7.10 (5-H) with $J_{3,4}$ 6 Hz,

$J_{4.5}$ 10, and $J_{3.5}$ small. The chemical shifts are quite similar to those for similarly oriented protons in the adduct (6) from 1,3-dinitrobenzene.[11] When CD_3OD was replaced as solvent by CH_3OH a new band at δ 3.10



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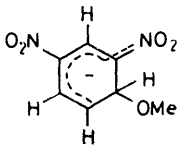


(6)

was observed and is attributed to the added methoxy-group in (5). In 80 : 20 v/v DMSO–methanol base addition accounts for *ca.* 30% of the 1 : 1 interaction. This proportion increases slightly with proportion of methanol in the solvent which is to be expected since the two modes of ionisation differ by a molecule of methanol.

Visible spectra of 2,4-dinitroaniline and its *N*-alkylated derivatives were recorded in methanol–DMSO containing 0.026M-sodium methoxide. As the proportion of DMSO in the solvent was increased new bands in the visible region were observed (Table 2). In view of the n.m.r. data these are attributed to the conjugate bases (4). Nevertheless the spectra of the *N*-alkyl derivatives showed a small bump at 500 nm (see Figure 2) which may indicate a small proportion (<5%) of base addition in these compounds. The spectral shapes were independent of the solvent composition in the range of solvents used. The spectra of the anions (4) derived from the *N*-alkyl derivatives showed a maximum at *ca.* 430 nm with a shoulder at longer wavelength. In the case of 2,4-dinitroaniline the greater energy separation of the bands probably reflects the contribution of structure (7) in which the energy of the transition involving the *o*-nitro group will be lowered and that involving the *p*-

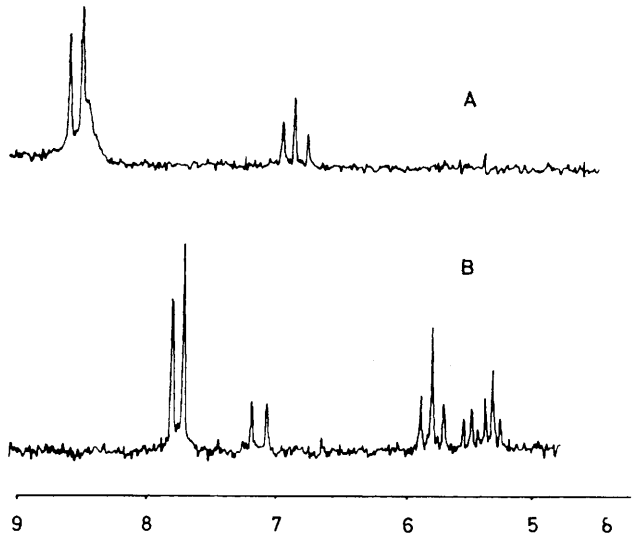


FIGURE 1 ^1H n.m.r. spectra of A 2,6-dinitroaniline in [$^2H_6$]-DMSO, and B after the addition of 1 mol. equiv. of $NaOCD_3$ in [$^2H_4$]methanol

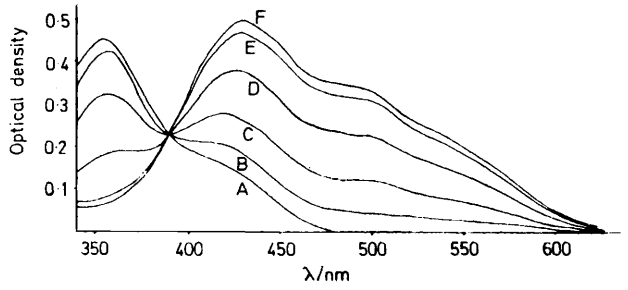
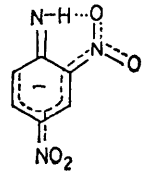


FIGURE 2 Visible spectra of *N*-isopropyl-2,4-dinitroaniline (2.5×10^{-5}M) and sodium methoxide (0.026M) in methanol–DMSO mixtures containing the following proportions (by volume) of DMSO: A, 60; B, 70; C, 75; D, 80; E, 85; F, 90%

nitro-group correspondingly raised.[7,9] The spectrum of 2,6-dinitroaniline itself shows a maximum at 420 nm. In the presence of base new absorptions are observed at 430 and 550 nm. The relative intensities of these



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bands varies with the solvent composition, the latter band being favoured in media rich in DMSO. We attribute this band primarily to the conjugate base and the band at 430 nm primarily to the σ-adduct (5).

TABLE 2

Visible spectra of conjugate bases in MeOH–DMSO

Base	$\lambda_{max.}$/nm	$10^{-4}\epsilon$/ l mol^{-1} cm^{-1}	$\lambda_{max.}$/nm	$10^{-4}\epsilon$/ l mol^{-1} cm^{-1}
(4; R = H)	380, 400sh	2.0 ±0.1	515	1.4 ±0.1
(4; R = Me)	420	1.8	500	1.2
(4; R = Bu^n)	430	2.0	500	1.4
(4; R = Pr^i)	430	2.0	500	1.4
(4; R = Bu^t)	440	2.0	500	1.4

Equilibrium Measurements.—Equilibrium constants K for formation of the conjugate bases [equation (1)] were determined using the H_M acidity function which refers to methanol as the standard state.[10] The acidity function is defined by equation (2) were K_a^M is the acid dissociation constant of the substrate in methanol. Equation (3) relates K and K_a^M *via* the autoprotolysis constant of methanol (pK_{MeOH} 16.92).

$$H_M = pK_a^M + \log_{10} (\text{indicator ratio}) \quad (2)$$

$$pK = pK_a^M - pK_{MeOH} \quad (3)$$

Indicator ratios and derived values of H_M are in Table 3. The value of H_M for 0.026M-sodium methoxide in methanol was taken to be 15.34 (pK_{MeOH} − log [NaOMe]). For the *N*-alkyl-2,4-dinitroanilines it is possible that a small proportion (<5%) of base addition occurs in competition with proton loss, but this proportion is not sufficiently large to influence these measurements.

TABLE 3

Values of $\log_{10}$ (indicator ratio) and H_M values for methanol–DMSO containing 0.026M-sodium methoxide at 25°

Indicator [a]	Vol % DMSO 0	5	10	15	20	25	30	35	40	45	50
2,4,4′-Trinitrodiphenylamine (490)	0.15	0.43	0.70	1.00							
6-Bromo-2,4-dinitroaniline (500)			−1.07	−0.73	−0.46	−0.21	0.10	0.39	0.67		
2,4-Dinitrodiphenylamine (500)			−1.58		−0.99		−0.39	−0.06	0.25	0.61	0.92
H_M	15.34	15.62	15.89	16.19	16.48	16.75	17.05	17.36	17.65	18.00	18.32

Indicator [a]	Vol % DMSO 40	45	50	55	60	65	70	75	80	85
2,4-Dinitroaniline (520)	−1.14	−0.80	−0.46	−0.11	0.26	0.56				
N-Methyl-2,4-dinitroaniline (500)						−1.42	−0.92	−0.35	0.31	
N-n-Butyl-2,4-dinitroaniline (500)							−0.85	−0.37	0.32	
N-Isopropyl-2,4-dinitroaniline (500)							−1.08	−0.48	0.23	
N-t-Butyl-2,4-dinitroaniline (500)								−1.38	−0.64	0.12
H_M	17.65	18.00	18.32	18.67	19.04	19.34	19.84	20.39	21.09	21.85

[a] Wavelength of measurement in parentheses. The precision of $\log_{10}$(indicator ratio) is greater when values are close to 0.0. Values are, at worst, precise to ±0.03.

Stewart and his co-workers [12] have reported a H_- acidity scale in methanol–DMSO containing 0.025M-sodium methoxide. However, they used pK_a values for the indicators determined in aqueous media, a procedure which has been criticised [10] since the term $pK_a - pK_a^M$ varies with the nature of the base. Our scale increases in basicity by 6.5 units on going to 85 vol % DMSO and is considerably steeper than the previous scale [12] which increases by 5.0 units for a similar solvent change. For comparison J_M scales in methanol–DMSO mixtures containing 0.10M-sodium methoxide increase, for a similar solvent change, by 6.0 units (methoxide addition to substituted nitroanisoles) [13] and 7.33 units (methoxide addition to 1-X-3,5-dinitrobenzenes).[14]

As an alternative method for comparison of the values of K for 2,4-dinitroaniline and its *N*-alkyl derivatives we made measurements in a medium of 75 : 25 v/v DMSO–methanol containing various sodium methoxide concentrations. A typical set of data relating to the *N*-methyl derivative is in Table 4. A value for K of 16 ± 2 l mol^{-1} was determined by extrapolation to zero base concentration.

The conjugate base of 2,6-dinitroaniline absorbs at 550 nm. However here base addition competes successfully with proton loss as the mode of ionisation. Since the ratio of these interactions varies somewhat with solvent composition we limited measurements to the single solvent system of 75 : 25 v/v DMSO–methanol. The data in Table 5 give a value for K_T, the sum of the equilibrium constant for the two processes of proton loss and base addition. Since the n.m.r. data indicate that *ca.* 30% of base addition occurs we calculate a value of 110 ± 30 l mol^{-1} for K relating to proton loss.

TABLE 4

Calculation of K for the ionisation of *N*-methyl-2,4-dinitroaniline (2.5×10^{-5}M) in 75 : 25 v/v DMSO–methanol at 25°

[NaOMe]/M	OD [a] (500 nm)	K/l mol^{-1}
0.013	0.055	16.3
	±0.005	±1.5
0.026	0.095	16.6
0.040	0.122	16.4
0.053	0.152	18.3
0.066	0.175	19.6
0.088	0.195	19.2
0.11	0.222	23.1
0.14	0.24	24.5

[a] Value for complete conversion is 0.31, determined in 90 : 10 v/v DMSO–methanol.

TABLE 5

Calculation of K_T for ionisation of 2,6-dinitroaniline in 75 : 25 v/v DMSO–methanol at 25°

[NaOMe]/M	OD [a] (550 nm)	K_T/l mol^{-1}
0.0094	0.15	170
	±0.005	±15
0.0141	0.17	160
0.0188	0.18	150
0.0235	0.20	190
0.0265	0.205	190
0.053	0.22	
0.105	0.23	
0.132	0.23	

[a] Value for complete conversion is 0.245, determined *via* a Benesi–Hildebrand plot.

The values of K for reaction of 2,4-dinitroaniline and its *N*-alkylated derivatives with sodium methoxide are larger by a factor of *ca.* 10^5 in 75 : 25 v/v DMSO–methanol than in methanol. The constancy of this factor adds confidence to these values. The data are compared in Table 6 with those for 2,4,6-trinitroaniline and its derivatives. Values are precise within 10%.

One interesting feature is that while the acidity of picramide is similar to that of its *N*-alkyl derivatives, 2,4-dinitroaniline is *ca.* 100 times more acidic than its derivatives. A possible explanation for this difference is that in contrast to the other compounds in Table 6 the ionisation of 2,4-dinitroaniline involves loss of a proton in which intramolecular hydrogen-bonding to an *o*-nitro group is not possible. Such hydrogen bonding [15,16] will stabilise the parent molecules and reduce their acidities.

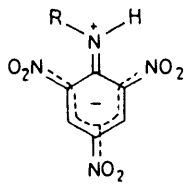
TABLE 6

Comparison of the acidities of 2,4-dinitroaniline and 2,4,6-trinitroaniline and their *N*-alkylated derivatives at 25°

1-Substituent	2,4,6-Trinitro [a] K/l mol^{-1}	2,4-Dinitro [b] K/l mol^{-1}	2,4-Dinitro [c] K/l mol^{-1}
NH_2	9	1.4×10^{-2}	1 500
NHMe	20	1.4×10^{-4}	16
NHBu^n	8.3	1.5×10^{-4}	13
NHPr^i	5.5	1.1×10^{-4}	12
NHBu^t	0.5	1.5×10^{-5}	1.5

[a] In methanol. [b] Determined *via* the H_M acidity function, referred to methanol as standard state. [c] In 75 : 25 v/v DMSO–methanol.

The inductive electron release of an alkyl substituent increases with increasing chain length and chain branching. Since such electron release is acid-weakening the decrease in acidity as the *N*-substituent is varied along the series Me, Bu^n, Pr^i, Bu^t might be attributed to this source. However steric factors are also likely to be important, especially in the *N*-alkyl-2,4,6-trinitroanilines. Thus spectroscopic studies [7,8] have shown that *N*-alkyl substitution in 2,4,6-trinitroaniline causes severe steric crowding around the 1-position which is partially relieved by rotation from the ring plane of the adjacent nitro-group. One consequence of this crowding will be the reduction in mesomeric interaction of type (8) (which



(8)

is maximised in a planar system) and hence destabilisation of the parent molecules. However in the conjugate base molecules (2) which carry a full negative charge the strain associated with obtaining planarity of the =NR group (necessary for delocalisation of the negative charge into the aromatic ring) will be even more serious. Hence overall the effect of increasing the size of the *N*-alkyl substituent will be acid-weakening. This form of steric strain will be very much reduced in *N*-alkyl-2,4-dinitroanilines since they can adopt a *trans*-configuration [9] and here there is little change in acidity as the substituent is charged in the series methyl, n-butyl, isopropyl. Molecular models indicate that in *N*-t-butyl-2,4-dinitroaniline an unfavourable steric interaction is present between the butyl group and the aromatic ring and this accounts for its decreased acidity.

σ-Complex Formation.—Proton loss is the major mode of reaction of 2,4-dinitroaniline and its *N*-alkyl derivatives with sodium methoxide in the DMSO–methanol mixtures we have examined. Although the fraction of σ-complex formation might be expected to increase somewhat as the proportion of DMSO is increased we would expect that in methanol proton loss would still be favoured. This behaviour contrasts with 2,4,6-trinitroaniline and its derivatives where proton loss and base addition are fairly evenly balanced. A major factor favouring proton loss in the case of 2,4-dinitroaniline is the presence of an amino-proton not internally hydrogen bonded to a nitro-group. This evidently has an acid strengthening effect. We deduce that proton loss will similarly be the major interaction in other compounds, such as 2,4-dinitro-6-halogenobenzenes, possessing a relatively 'free' amino-proton. Electron-withdrawing groups attached to the amino-nitrogen will also be acid strengthening so that diphenylamines ionise by proton loss.[3,6]

In contrast the ionisation of 2,6-dinitroaniline gives a considerable amount of the σ-adduct (5). Here both amino-protons will be intramolecularly hydrogen bonded to nitro-groups with a corresponding decrease in their acidity. Also there is evidence that nitro-groups *para* to the position of base addition are more effective in stabilising anions than those in an *ortho*-position.[17] In the case of 2,6-dinitroaniline base addition occurs *ortho* and *para* to nitro-groups while proton loss gives a negative charge *ortho* to two nitro-groups.

Our visible spectra indicate that a small proportion of base addition may occur with *N*-alkyl-2,4-dinitroanilines. However the fraction is much smaller than in the 2,4,6-trinitro-series. This may be a consequence of the destabilisation by steric interactions of the conjugate bases of type (2). This effect will be much smaller in the 2,4-dinitrianiline series. Previous measurements [6] indicate that σ-complex formation is not similarly disadvantaged by steric factors in the 2,4,6-trinitro-series, probably because coplanarity of the NHR group in adducts of type (1) is not essential.

EXPERIMENTAL

The following *N*-alkyl-2,4-dinitroanilines were prepared by reaction of 1-chloro-2,4-dinitrobenzene with the appropriate amine in methanol and were recrystallised from methanol: *N*-methyl, m.p. 179° (lit.,[18] 177°); *N*-n-butyl, m.p. 90° (lit.,[19] 90°); *N*-isopropyl, m.p. 95° (lit.,[20] 95°); *N*-t-butyl, m.p. 155° (lit.,[20] 153°). Other substrates were recrystallised commercial specimens. Solvents and base solutions were prepared as before.[13]

^{1}H N.m.r. measurements were made at 22° on 0.2M solutions with a Bruker HX 90 E instrument modified for Fourier transform operation and using a deuterium lock. Tetramethylsilane was used as internal reference. Visible spectral measurements were made with Unicam SP 8000 and SP 500 instruments with substrate concentrations of $2—5 \times 10^{-5}$M.

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