Kinetic and equilibrium studies of the ambident reactivity of aniline, and some derivatives, towards 4,6-dinitrobenzofuroxan† ‡

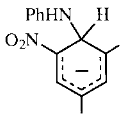
Michael R. Crampton* and Lynsey C. Rabbitt

Chemistry Department, Durham University, Durham, UK DH1 3LE

Received (in Cambridge) 19th April 1999, Accepted 2nd June 1999

The reactions of aniline and its derivatives at the 7-position of 4,6-dinitrobenzofuroxan (DNBF) may result in rapid reaction *via* the nitrogen centre to give anionic σ-adducts. Equilibrium constants for these reactions in DMSO are reported and correlate with pK_a values of the corresponding anilinium ions. Slower reactions are observed involving electrophilic substitution by DNBF at ring-carbon atoms of the aniline derivatives; rate constants are reported. These reactions produce zwitterionic carbon-bonded σ-adducts which, in the presence of excess aniline, are in rapid equilibrium with deprotonated forms. Equilibrium constants for this acid–base process have been measured and indicate that the negatively charged DNBF moiety is electron withdrawing relative to hydrogen.

Aniline usually acts as a nitrogen nucleophile and will, for example, form σ-adducts, such as **1**, with 1,3,5-trinitrobenzene.[1–3] Nevertheless its ambident reactivity has been shown in reactions with 4,6-dinitrobenzofuroxan (DNBF) which is noted for its "super-electrophilic" properties.[4–6] Here adducts have been detected involving bonding to the nitrogen or ring-carbon atoms of aniline.[7–12] In acidic solutions, where aniline is nearly completely protonated, reaction *via* nitrogen is inhibited. However a carbon–carbon bonded adduct is slowly formed by reaction at the 4-position. A kinetic study[13] in water–dimethyl sulfoxide solvent has shown that this adduct results from electrophilic substitution by DNBF on the unprotonated aniline; the results allow a comparison, with other arenes, of the reactivity of aniline towards electrophilic attack.



1

Here we report on the reactions in DMSO of DNBF with aniline, **2a**, and with some *N*- and ring-substituted anilines. Our results for aniline are in accord with the processes shown in Scheme 1. The N-bonded adduct **4** is kinetically preferred but the C-bonded adduct **5**, in equilibrium with its deprotonated form, **6**, is the thermodynamically favoured product. Our aims were to determine rate and equilibrium data for these reactions, to investigate the effects of substituents, and to compare the reactivity of DNBF with that of other electron-deficient aromatics.

Results and discussion

We have made measurements with aniline and with six substituted anilines, as detailed in Table 1. In general, the symbol An is used to represent the neutral form, and AnH^+ the protonated form of the aniline derivatives.

Table 1 pK_a Data for anilinium ions

Substance	pK_a (DMSO)	pK_a (water)[b]
2a, Aniline	3.82[a]	4.58
2b, *N*-Methylaniline	2.94	4.85
2c, *N*,*N*-Dimethylaniline	2.70	5.06
2d, 3-Methylaniline	3.86	4.69
2e, 3-Methoxyaniline	3.29	4.20
2f, 4-Methylaniline	4.34	5.12
2g, 4-Chloroaniline	2.79	3.98

[a] From ref. 16. [b] From ref. 14.

The kinetic and equilibrium results, to be described, show that equilibration between DNBF and the N-bonded adducts, **4**, is a considerably faster process than the formation of C-bonded adducts, **5**. K_N, the equilibrium constant for formation of **4** is defined by eqn. (1), and is related by eqn. (2) to the individual constants K_1 and K_2. The acid–base equilibrium between **5** and **6** involves an equilibrium constant defined in eqn. (3).

$$K_N = \frac{[\mathbf{4}][AnH^+]}{[DNBF][An]^2} \qquad (1)$$

$$K_N = K_1K_2 \qquad (2)$$

$$K_3 = \frac{[\mathbf{6}][AnH^+]}{[\mathbf{5}][An]} \qquad (3)$$

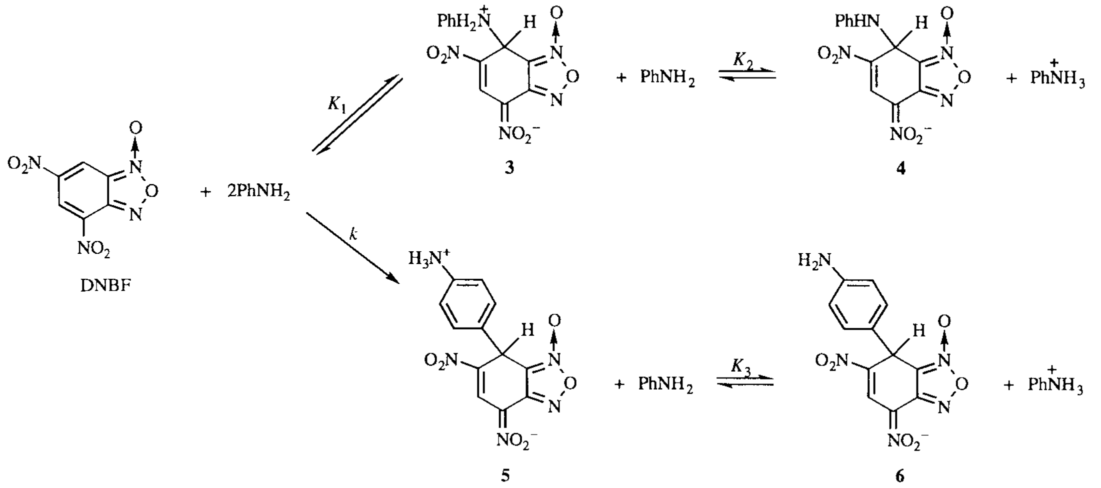
pK_a Values of anilines in DMSO

In order to compare reactivities of the substituted anilines in these systems, pK_a values of the protonated forms were required. Although values are available in water,[14] and in water–DMSO mixtures,[15] the only value available in DMSO is that for aniline[16] itself, pK_a = 3.82. Values for substituted anilines were calculated using a spectrophotometric method with the indicator 2,4-dinitrophenol. In a typical experiment spectra were recorded with a constant concentration (4×10^{-5} mol dm^{-3}) of indicator in solutions buffered with an aniline derivative and its hydrochloride salt. Measurements were usually made with salt concentrations of 0.01 mol dm^{-3}; or with the ionic strength, $I = 0.01$ mol dm^{-3}, maintained with tetra-*n*-butylammonium

---

† The IUPAC name for 4,6-dinitrobenzofuroxan is 4,6-dinitrobenzoxadiazole 1-oxide.

‡ Tables 9–21 are available as supplementary data. For direct electronic access see http://www.rsc.org/suppdata/p2/1999/1669, otherwise available from BLDSC (SUPPL. NO. 57572, pp. 13) or the RSC Library. See instructions for Authors available *via* the RSC web page (http://www.rsc.org/authors).



Scheme 1

Table 2 Absorbance data for 2,4-dinitrophenol (4×10^{-5} mol dm^{-3}) in DMSO containing 3-methylaniline and its hydrochloride salt at 25 °C

[An]/mol dm^{-3}	[AnH$^+$]/mol dm^{-3}	Abs. (430 nm)	K_4[b]
0.00	0.01	0.014	—
0.02	0.01	0.097	0.057
0.04	0.01	0.197	0.072
0.06	0.01	0.200	0.049
0.08	0.01	0.219	0.042
0.10	0.01	0.297	0.053
0.20	0.01	0.456	0.059
0.00[a]	0.00	0.831	—

[a] Made alkaline with sodium hydroxide. [b] Calculated as $\frac{(\text{Abs} - 0.014)}{(0.831 - \text{Abs})} \times \frac{[\text{AnH}^+]}{[\text{An}]}$.

chloride. Absorbance measurements at 430 nm, the maximum for In$^-$, yielded values for equilibrium constants, K_4, for eqn. (4). Typical data are given in Table 2, and results for other

$$\text{HIn} + \text{An} \overset{K_4}{\rightleftharpoons} \text{In}^- + \text{AnH}^+ \qquad (4)$$

derivatives are reported as supplementary information in Tables 9–13.‡ pK_a values for the anilinium ions were then calculated from eqn. (5) using a value[17] of 5.12 for the pK_a of the indicator, 2,4-dinitrophenol.

$$\log_{10} K_4 = \text{p}K_a(\text{AnH}^+) - \text{p}K_a(\text{HIn}) \qquad (5)$$

Values obtained in DMSO are compared, in Table 1, with values in water. For compounds not substituted on nitrogen acidities are *ca.* 0.7 units higher in DMSO than in water. However for *N*-methylaniline the difference is 1.9 units and for *N*,*N*-dimethylaniline 2.4 units. It is expected that solvation, involving hydrogen bonding of NH$^+$ protons, will be important in stabilising the acidic cations.[15,16,18–20] Since DMSO is known to be an extremely good hydrogen-bond acceptor[21] the stabilisation of cationic species in this solvent will be expected to decrease as the number of NH$^+$ protons available for hydrogen-bonding decreases. This may explain the comparative increases in acidity in DMSO on going from primary, to secondary and tertiary amines.

NMR Results

^{1}H NMR spectra of DNBF in [^{2}H$_6$]DMSO containing one equivalent or less of aniline indicate the formation of **5a** with bands due to H7 and H5 at δ 5.36 and 8.73 respectively. In the presence of higher mole ratios of aniline additional bands are observed at δ 6.04 and 8.64, attributed to H7 and H5 of **4a**, the nitrogen-bonded adduct. The latter bands gradually decrease in intensity with time as the bands due to the thermodynamically more stable carbon-bonded adduct increase in intensity. As the concentration of excess aniline is increased it is noticeable that the bands due to the carbon-bonded adduct move to lower frequency reaching limiting positions of δ 5.14 and 8.70. These changes reflect deprotonation of **5a** to give **6a**, the two forms being in rapid equilibrium. Acidification, with excess deuterium chloride, reversed this change with bands due to the C-bonded adduct shifting to the positions expected for **5a**; bands due to **4a**, the N-bonded adduct, were lost immediately. Our results and interpretation are largely in accord with previous work on this system.[8,9,11,12]

Table 3 ^{1}H NMR data for adducts from DNBF in [^{2}H$_6$]DMSO

Parent aniline[a]	^{1}H NMR Shifts			
	Carbon-bonded adducts **5**			
	H7	H5	Aromatic	Other
2a	5.36	8.73	7.19(d), 7.33(d), *J* 8 Hz	—
2b	5.37	8.72	7.30(d), 7.37(d), *J* 8.5 Hz	2.90 (NMe)
2c	5.39	8.74	7.40(m)	3.12 (NMe$_2$)
2d	5.60	8.72	7.08(m)	2.58 (Me)
2e	5.56	8.66	6.89(s), 6.87(d), 7.34(d), *J* 7.4 Hz	3.68 (OMe)
2f	5.83	8.73	6.92(s), 7.10(d), 7.16(d), *J* 8 Hz	2.20
	Deprotonated adducts **6**			
	H7	H5	Aromatic	Other
2a	5.14	8.70	6.53(d), 6.90(d)	—
2b	5.15	8.71	6.52(d), 6.97(d)	2.63 (NMe)
2c	5.16	8.70	6.60(d), 7.0(d), *J* 8 Hz	2.86 (NMe$_2$)
2d	5.40	8.68	6.64(d), 6.50(d), *J* 8 Hz	2.42 (Me)
2e	5.33	8.63	6.2(m), 6.87(d), *J* 8 Hz	3.54 (OMe)
2f	5.56	8.71	6.54(s), 6.60(d), 6.76(d)	2.04 (Me)
	Nitrogen-bonded adducts **4**			
	H7	H5	Aromatic[b]	Other[b]
2a	6.04	8.64		
2d	6.01	8.65		
2f	5.96	8.63		

[a] See Table 1 for identities of the anilines. [b] Shifts uncertain because of rapid chemical exchange with bulk amine.

^{1}H NMR data for adducts from amines **2a**–**f** are collected in Table 3. Values are given for **5**, the zwitterionic forms of the carbon-bonded adducts, **6**, the deprotonated forms produced in the presence of excess of the parent amine and, in some cases, **4**,

Table 4 NMR data for reaction of DNBF with *N*-methylaniline, **2b**, in [$^2H_6$]DMSO

$[\mathrm{DNBF}]_{\mathrm{stoich}}$/mol dm^{-3}	$[\mathbf{2b}]_{\mathrm{stoich}}$/mol dm^{-3}	$[\text{4-Chloroaniline}]_{\mathrm{stoich}}$/mol dm^{-3}	Chemical shifts				
			H7	H5	Aromatic[a]	[**6**][b]/[**5**]	K_3[c]
0.099	0.050	—	5.37	8.72	7.30, 7.37	—	
0.099	0.100	—	5.37	8.72	7.30, 7.37	—	
0.099	0.130	—	5.31	8.72	7.08, 7.26	0.39	3.4
0.098	0.170	—	5.25	8.71	6.88, 7.15	1.2	4.0
0.050	0.100	—	5.24	8.70	6.84, 7.12	1.5	2.3
0.050	0.200	—	5.17	8.70	6.59, 7.00	11	4.3
0.048	0.400	—	5.15	8.71	6.52, 6.97	—	
0.099	0.099	0.10	5.26	8.71	6.91, 7.16	1.0	1.0[d]
0.099	0.099	0.20	5.21	8.71	6.71, 7.07	2.8	1.6[d]

[a] Ring hydrogen resonances of complexed **2b**; doublets, *J* 8 Hz. [b] Calculated from eqn. (6). These are the average values from data for H5 and each of the aromatic shifts. [c] Calculated from eqn. (3). [d] These are values of $K_{3,\mathrm{Cl}}$ calculated from eqn. (7).

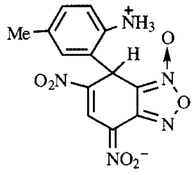
Table 5 NMR data for reaction of DNBF with 4-methylaniline to give **5f** and **6f** in [$^2H_6$]DMSO

$[\mathrm{DNBF}]_{\mathrm{stoich}}$/mol dm^{-3}	$[\text{4-Methylaniline}]_{\mathrm{stoich}}$/mol dm^{-3}	[4-Methylaniline $H^+Cl^-]_{\mathrm{stoich}}$/mol dm^{-3}	Chemical shifts			
			H7	H5	[**6**][a]/[**5**]	K_3[b]
0.10	0.05	—	5.83	8.73	—	—
0.05	0.20[c]	0.40[c]	5.64	8.72	2.4	9
0.05	0.20[d]	0.20[d]	5.60	8.71	5.7	13
0.05	0.40	—	5.56	8.71	—	

[a] Calculated from eqn. (6), with δ_o 5.83, δ_∞ 5.56. [b] Calculated from eqn. (3). [c] The equilibrium concentrations are calculated to be 0.115 and 0.435 mol dm^{-3} respectively. [d] Equilibrium concentrations are calculated to be 0.108 and 0.242 mol dm^{-3} respectively.

the nitrogen-bonded adducts. NMR spectra were not observed for adducts **4** derived from *N*,*N*-dimethylaniline, which lacks the NH hydrogen required for formation of an anionic adduct, or from *N*-methylaniline or 3-methoxyaniline. In the latter case kinetic evidence, from UV results, suggests that isomerisation to the carbon-bonded adduct will be rapid.

The spectra confirm, in agreement with previous work,[8,9,12] that the adduct from 4-methylaniline, where the ring position *para* to the amino group is blocked, is formed by reaction at the 2-position to give **5f**.



5f

Values of K_3

It was of interest to use NMR shifts to calculate values for K_3, the acid–base equilibrium defined in eqn. (3). Values were obtained for adducts formed from aniline, **2a**, *N*-methylaniline, **2b**, and 4-methylaniline, **2f**. Since **5** and **6** are in rapid equilibrium, on the NMR timescale, their relative proportions may be calculated using eqn. (6).

$$\frac{[\mathbf{6}]}{[\mathbf{5}]} = \frac{\delta_o - \delta}{\delta - \delta_\infty} \qquad (6)$$

Here δ_o is the shift of **5**, the fully protonated form, δ_∞ is the shift of **6**, the fully deprotonated form, and δ is the measured shift.

A measurement in a solution made up from DNBF (0.05 mol dm^{-3}), aniline (0.40 mol dm^{-3}) and aniline hydrochloride (0.40 mol dm^{-3}) gave a band due to H7 at δ 5.21. Knowledge of the values of δ_o, 5.36, and δ_∞, 5.14, gave a value for [**6**]/[**5**] of 2.14. Since in this solution, containing added aniline hydrochloride, no bands were observed at equilibrium due to the N-bonded adduct **4a**, the final concentrations of aniline, 0.316 mol dm^{-3}, and its salt, 0.434 mol dm^{-3}, are readily calculated. Use of eqn. (3) gave a value for K_3 of 3 ± 0.5. Since the pK_a value of aniline is 3.82, this leads to a value of 3.3 for the pK_a value of **5a**.

NMR spectra of DNBF in solutions containing *N*-methylaniline, **2b**, indicated formation of **5b** in equilibrium, in the presence of excess amine, with its deprotonated form, **6b**. No bands were observed due to the N-bonded adduct **4b**, probably due to steric hindrance. The chemical shifts in Table 4 show that as the excess of *N*-methylaniline is increased, bands due to H7 of complexed DNBF and to the ring hydrogens of complexed **2b** move to lower frequencies. The shift of the H5 band shows little change. Calculation of the ratio [**6**]/[**5**] using eqn. (6) allowed the determination of values of K_3 for the *N*-methylaniline system. There is some spread in values, but the value obtained of 3.5 ± 0.5 again indicates that the adduct **5b** is a stronger acid, by 0.5 pK_a units, than the parent amine **2b**.

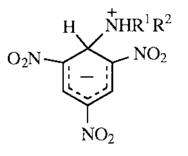
The last two items in Table 4 refer to experiments in which equimolar amounts of DNBF and **2b** were allowed to form **5b** quantitatively, before the addition of 4-chloroaniline. The latter amine, although unreactive towards DNBF on the timescale of the experiment, partially deprotonated **5b** to yield an equilibrium mixture with **6b**. The measured shifts allowed the calculation of a value for $K_{3,\mathrm{Cl}}$, defined by eqn. (7), of 1.3 ± 0.3. This

$$K_{3,\mathrm{Cl}} = \frac{[\mathbf{6}]}{[\mathbf{5}]} \times \frac{[\text{4-chloroaniline H}^+]}{[\text{4-chloroaniline}]} \qquad (7)$$

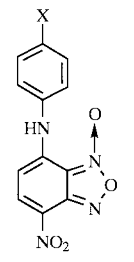
value is lower than the value of K_3, reflecting the weaker basicity of 4-chloroaniline than of *N*-methylaniline (Table 1).

Data for the formation of the C-bonded adduct from 4-methylaniline, **2f**, are given in Table 5. Measurements in solutions containing **2f** and its hydrochloride salt, yield a value for K_3 of 11 ± 2.

Interestingly the results show that values of K_3 are greater than unity, indicating that the DNBF moiety in **5**, although negatively charged, is electron withdrawing relative to hydrogen. When reaction occurs *para* to the amino function as in the aniline, **5a**, and *N*-methylaniline, **5b**, derivatives, the acid strengthening effect is *ca.* 0.5 pK_a units. The effect is expected to increase with proximity of the DNBF and the positive centre. Thus for reaction *ortho* to the amino function in the 4-methylaniline derivative, **5f**, the effect is worth *ca.* 1 pK_a unit. It is known[22,23] that the presence of a trinitrocyclohexadienate ring in the zwitterions **7** will acidify the attached ammonium proton by a factor of *ca.* 500. Likewise the zwitterionic adducts **3**, where the ammonium group is directly bonded to the ring, are expected to be considerably more acidic, by several orders of magnitude, than the parent anilinium ions. Hence there is no evidence in the present work for their accumulation. Further evidence for the powerful electron withdrawing ability of the negatively charged moiety of DNBF is that in water[24] the DNBF–hydroxide adduct dissociates to give a dianion with a pK_a value of 11.80. It is also worth noting[25] that the acidities of 7-(4-X′-anilino)-4-nitrobenzofuroxans, **8** are *ca.* three times greater than those of similarly X′-substituted 2,4,6-trinitrodiphenylamines.



7



8

Kinetic results

Kinetic measurements of the reactions of DNBF with anilines **2a–f** were made spectrophotometrically in DMSO containing 1% by volume of water. The ionic strength, $I \equiv \frac{1}{2}\Sigma c_i z_i^2$, was 0.1 mol dm^{-3} for all measurements. Rate constants were determined using two sets of conditions: a) in the presence of excess hydrochloric acid, and b) in solutions buffered with mixtures of the aniline and its hydrochloride salt. In all cases the stoichiometric concentration of aniline was in large excess of the concentration of DNBF, and first order kinetics were observed. The presence, in a), of excess hydrochloric acid had the effect of reducing concentrations of free amine to very low levels, and here there was no evidence for nucleophilic attack *via* the nitrogen centre of the aniline to give **4**. Under these conditions direct conversion of DNBF to the carbon-bonded adducts **5** was observed. It was, however, necessary to allow for the rapid equilibration of DNBF and its hydroxide adduct,[26] eqn. (8), for

$$\text{DNBF} + H_2O \rightleftharpoons \text{DNBF}{\cdot}OH^- + H^+ \qquad (8)$$

which the equilibrium constant is defined by eqn. (9). Here the

$$K_{H_2O} = \frac{[\text{DNBF}{\cdot}OH^-][H^+]}{[\text{DNBF}]} \qquad (9)$$

value of K_{H_2O} includes the activity of the water in the medium. Spectrophotometric measurements at 470 nm gave a value for K_{H_2O} of 0.050 mol dm^{-3} in the medium used, containing 1% water. We define by eqn. (10) the second order rate constant, *k*,

$$\frac{-d[\text{DNBF}]}{dt} = k[\text{DNBF}][\text{Aniline}] \qquad (10)$$

for reaction of DNBF and amine. It is readily shown that *k* is related to k_{obs}, the first order rate constant, by eqn. (11), where

Table 6 Kinetic data for reaction of DNBF[a] with aniline in acidic solutions to give **5a**

[Aniline H$^+$Cl$^-$]/ mol dm^{-3}	[HCl]/ mol dm^{-3}	k_{obs}[b]/ 10^{-4} s^{-1}	k[c]/dm^3 mol^{-1} s^{-1}
0.010	0.090	0.80	7.5
0.020	0.080	2.0	8.6
0.030	0.070	3.7	9.8
0.040	0.060	4.7	8.6
0.050	0.050	6.7	8.9
0.060	0.040	8.0	8.0

[a] DNBF concentration is 4×10^{-5} mol dm^{-3}; solvent is 99 : 1 (v/v) DMSO–water. [b] Colour forming reaction at 489 nm. [c] Calculated from eqn. (12) with K_a, 1.51×10^{-4} mol dm^{-3} and K_{H_2O}, 0.050 mol dm^{-3}.

Table 7 Summary of data for reaction of DNBF with aniline and its derivatives in DMSO

Aniline	pK_a	K_N/dm^3 mol^{-1}	k/dm^3 mol^{-1} s^{-1}	k[a]/dm^3 mol^{-1} s^{-1}
2a	3.82	19 000	8.6 ± 1	4.0
2b	2.94	—	10.0 ± 1	10.3
2c	2.70	—	2.8 ± 0.4	6.0
2d	3.86	30 000	62 ± 10	27
2e	3.29	3 500	3800 ± 700	1300
2f	4.34	36 000	5.7 ± 0.7	1.1

[a] Values in this column are in 70/30 (v/v) DMSO–water from ref. 13.

$$k_{obs} = k[\text{Aniline H}^+]\left[\frac{K_a}{K_a + [H^+]}\right]\left[\frac{[H^+]}{[H^+] + K_{H_2O}}\right] \qquad (11)$$

K_a is the dissociation constant of the anilinium ion. Since in these measurements the condition $[H^+] \gg K_a$ applies, eqn. (11) reduces to eqn. (12).

$$k = \frac{k_{obs}}{K_a}\frac{[K_{H_2O} + [H^+]]}{[\text{Aniline H}^+]} \qquad (12)$$

Data for reaction with aniline are given in Table 6 and lead to a value for *k* of 8.6 ± 1 dm^3 mol^{-1} s^{-1}. Corresponding data for substituted anilines **2b–f** are reported as supplementary information in Tables 14–18.‡ Data are summarised in Table 7. It should be noted that formation of adducts **5** involves an electrophilic aromatic substitution in the aniline derivative. Hence two steps will be involved: carbon–carbon bond formation followed by elimination of a proton. Data have been reported previously[13] for reaction in water–DMSO mixtures. Values of the kinetic isotope effect k_H/k_D, obtained by comparison of reactions of aniline and pentadeuterioaniline, were found to be 2.0, indicating that the initial reaction of DNBF and aniline is largely rate-determining.

Kinetic measurements in solutions containing mixtures of aniline and its hydrochloride, corresponding to condition b), showed two reactions. The first, which was too fast to measure on the stopped-flow timescale, gave a species with λ_{max} 480 nm. The NMR evidence indicates that this is the N-bonded adduct, **4a**.

With time the absorption maximum shifted to 489 nm corresponding to conversion to the thermodynamically more stable C-bonded adduct, **5a**. Kinetically this was found to be a first-order process, and it is readily shown that the rate constant k'_{obs} is related to individual rate and equilibrium constants by eqn. (13). Our results indicate that under the conditions used $K_N[\text{An}]^2 \gg [\text{AnH}^+]$ so that eqn. (13) reduces to eqn. (14). The

$$k'_{obs} = \frac{k[\text{An}][\text{AnH}^+]}{K_N[\text{An}]^2 + [\text{AnH}^+]} \qquad (13)$$

Table 8 Kinetic data for the conversion of **4a** to **5a**

[Aniline][a]/ mol dm^{-3}	k'_{obs}/ 10^{-4} s^{-1}	K_N[b]/ dm^3 mol^{-1}
0.04	11.6	18500
0.07	6.4	19200
0.10	4.4	19500
0.20	2.2	19500

[a] All solutions contain aniline hydrochloride, 0.1 mol dm^{-3}. [b] Calculated from eqn. (14) with k 8.6 dm^3 mol^{-1} s^{-1}.

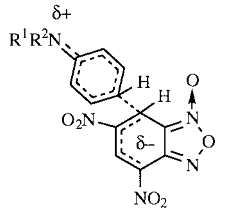
$$K_N = \frac{k[AnH^+]}{k'_{obs}[An]} \qquad (14)$$

data in Table 8 were used to obtain a value for K_N of 19000 dm^3 mol^{-1}. Similar data for reactions with anilines **2d**, **2e** and **2f** are reported as supplementary information in Tables 19–21.‡

Comparisons

The data summarised in Table 7 show that values of K_N, for reaction at the nitrogen centre of the anilines, correlate with the pK_a values. Thus the highest value of K_N is found for the reaction of 4-methylaniline, the most basic amine, and the lowest value for the reaction of 3-methoxyaniline, the least basic ring-substituted derivative. *N*,*N*-Dimethylaniline is not able to form an anionic adduct of type **4**. The failure to observe reaction at the nitrogen centre of *N*-methylaniline may be due to steric hindrance.

There is, as expected, no correlation with pK_a values of the values of k since the latter reflect reactivity at ring carbon atoms. The largest value here is found for reaction at the 4-position of 3-methoxyaniline where there is activation by *p*-NH_2 and *o*-OMe groups. The substituent effects in 70/30 (v/v) DMSO–water have been discussed previously,[13] but it is worth making a brief comparison of the solvent effect on the values of k. For ring-substituted anilines the value of k increases by a factor of 2–3 when the solvent is changed from DMSO–water to DMSO. However for the *N*-methyl derivative there is little variation in k, while with the *N*,*N*-dimethyl derivative the value of k decreases on transfer to DMSO. The initial electrophile–nucleophile combination will be largely rate-limiting[13] in the formation of **5**, so that the transition state will have structure **9**.

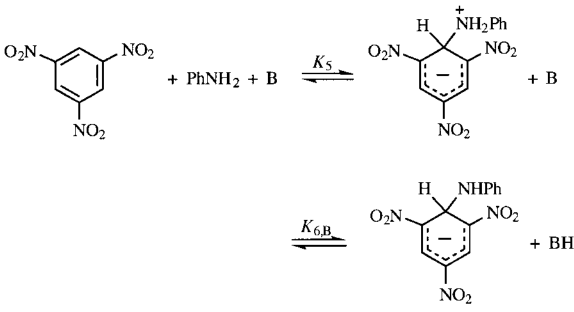


9

The excellent ability of DMSO to stabilise cationic nitrogen centres by hydrogen bonding interaction[21] was referred to earlier in this paper. Thus when $R^1 = R^2 = H$ increasing the proportion of DMSO in the solvent will be expected to stabilise **9**. However the stabilisation will diminish when $R^1 = H$, $R^2 = Me$, and disappear when $R^1 = R^2 = Me$.

It is of interest to compare the electrophilicity of DNBF with that of 1,3,5-trinitrobenzene (TNB) in these systems. Whilst DNBF readily reacts with the nitrogen centre of aniline to yield adduct **4**, reaction of TNB with aniline requires the presence of a strong base, such as DABCO. Buncel and co-workers[2,27] have shown that in DMSO in the presence of DABCO and with tetraethylammonium chloride (0.1 mol dm^{-3}) the equilibrium constant, $K_5K_{6,DABCO}$, for the overall process shown in eqn. (15) has a value of 1.8 dm^3 mol^{-1}.

However it is known[16] that the pK_a values of the protonated forms of aniline and DABCO are 3.82 and 9.06 respectively. Hence it is possible, using eqn. (16), to calculate a value of 1.0×10^{-5} dm^3 mol^{-1} for $K_5K_{6,An}$, which is the overall equilibrium constant for eqn. (15) with aniline acting as the base.



(15)

$$K_5K_{6,An} = K_5K_{6,DABCO}\frac{K_a(DABCOH^+)}{K_a(AnH^+)} \qquad (16)$$

This value is directly comparable with the value of 2×10^4 dm^3 mol^{-1} obtained for K_N for reaction of DNBF with aniline. The ratio of 2×10^9 testifies to the highly electrophilic nature of DNBF compared to TNB.

This ratio is similar in value to those observed[28] for the reactions of DNBF and TNB with methoxide ions in methanol (1×10^9), or with hydroxide ions in water (5×10^9). In these cases adduct formation involves reaction to give an anionic adduct directly. In contrast the reaction with aniline involves formation of a zwitterion, **3**, followed by proton transfer to give the anionic form, **4**. Hence for DNBF, K_N is the product of the equilibrium constants K_1 and K_2 (eqn. (3)), while in the case of TNB the overall equilibrium constant is the product of K_5 and K_6. The similarity in reactivity ratios for all three nucleophiles, aniline, methoxide and hydroxide probably indicates that the major difference between DNBF and TNB is in the $K_1 : K_5$ ratio rather than in the $K_2 : K_6$ ratio. Hence the acidifying effect, on the adjacent ammonium proton, of the anionic DNBF moiety in **3** is expected to be rather similar to that of the anionic TNB moiety in **7**, which is worth a factor of *ca.* 500. The acidifying effect will be attenuated with distance from the positive centre and our NMR results indicate that in **5** it is reduced to a factor of *ca.* 3.

Experimental

4,6-Dinitrobenzofuroxan was prepared by Drost's method;[7] mp 172 °C (lit.[7] 172–174 °C). All other reagents and solvents were the purest available commercial products.

^1H NMR spectra were recorded in [$^2H_6$]DMSO with a Varian Mercury 200 MHz spectrometer. UV-vis spectra and kinetic measurements were made at 25 °C with a Perkin-Elmer Lambda 2 spectrophotometer, a Shimadzu UV-2101 PC spectrometer or an Applied Photophysics SX-17 MV stopped-flow spectrophotometer. Reported rate constants are the means of several determinations and are precise to ±5%.

Acknowledgements

We thank Zeneca Fine Chemicals, Huddersfield for financial assistance.

References

1 E. Buncel and J. G. K. Webb, *Can. J. Chem.*, 1972, **50**, 129.
2 E. Buncel and W. Eggimann, *J. Am. Chem. Soc.*, 1977, **99**, 5958.
3 M. R. Crampton and I. A. Robotham, *Can. J. Chem.*, 1998, **76**, 627.
4 F. Terrier, *Nucleophilic Aromatic Displacement*, VCH, New York, 1991.

5 E. Buncel, R. A. Manderville and J. M. Dust, *J. Chem. Soc.*, *Perkin Trans. 2*, 1997, 1019.
6 J.-C. Hallé, D. Vichard, M.-J. Pouet and F. Terrier, *J. Org. Chem.*, 1997, **62**, 7178.
7 P. Drost, *Liebigs Ann. Chem.*, 1899, **307**, 49.
8 R. J. Spear, W. P. Norris and R. W. Read, *Tetrahedron Lett.*, 1983, **24**, 1555.
9 R. W. Read, R. J. Spear and W. P. Norris, *Aust. J. Chem.*, 1984, **37**, 985.
10 R. W. Read and W. P. Norris, *Aust. J. Chem.*, 1985, **38**, 435.
11 M. J. Strauss, R. A. Renfrow and E. Buncel, *J. Am. Chem. Soc.*, 1983, **105**, 2473.
12 E. Buncel, R. A. Renfrow and M. J. Strauss, *J. Org. Chem.*, 1987, **52**, 488.
13 M. R. Crampton, L. C. Rabbitt and F. Terrier, *Can. J. Chem.*, 1999, **77**, in the press.
14 D. D. Perrin, *Dissociation Constants of Organic Bases in Aqueous Solution*, Butterworths, London, 1972.
15 K. Yates and G. Welch, *Can. J. Chem.*, 1972, **50**, 474.
16 M. R. Crampton and I. A. Robotham, *J. Chem. Res.* (*S*), 1997, 22.
17 F. G. Bordwell, J. C. Branca, D. L. Hughes and W. N. Olmstead, *J. Org. Chem.*, 1980, **45**, 3305.
18 E. M. Arnett, *Proton Transfer Reactions*, ed. E. F. Caldin and V. Gold, Chapman and Hall, London, 1975.
19 A. Mucci, R. Domain and R. L. Benoit, *Can. J. Chem.*, 1980, **58**, 953.
20 M. R. Crampton and S. Lord, *J. Chem. Soc.*, *Perkin Trans. 2*, 1997, 369.
21 M. J. Kamlet and R. N. Taft, *J. Am. Chem. Soc.*, 1976, **98**, 377.
22 M. R. Crampton and B. Gibson, *J. Chem. Soc.*, *Perkin Trans. 2*, 1981, 533.
23 C. F. Bernasconi, M. C. Muller and P. Schmid, *J. Org. Chem.*, 1979, **44**, 3189.
24 F. Terrier, F. Millot and W. P. Norris, *J. Am. Chem. Soc.*, 1976, **98**, 5883.
25 J.-C. Halle, M. Mokhtari, P. Soulie and M.-J. Pouet, *Can J. Chem.*, 1997, **75**, 1240.
26 F. Terrier, H. A. Sorkhabi, F. Millot, J.-C. Halle and R. Schaal, *Can. J. Chem.*, 1980, **58**, 1155.
27 E. Buncel, W. Eggimann and H. W. Leung, *J. Chem. Soc.*, *Chem. Commun.*, 1997, 55.
28 F. Terrier, *Chem. Rev.*, 1982, **82**, 77.

Paper 9/03123E