Rate-limiting proton-transfer in the σ-adduct forming reactions of 1,3,5-trinitrobenzene and 4-nitrobenzofuroxan with substituted anilines in dimethyl sulfoxide

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Kinetic and equilibrium results are compared for the reactions in dimethyl sulfoxide of 1,3,5-trinitrobenzene, **1**, and 4-nitrobenzofuroxan, **4**, with a series of substituted anilines in the presence of Dabco or in, some cases, quinuclidine. pK_a values for the corresponding anilinium ions are reported. The reactions of **1** and **4** are likely to proceed through nucleophilic attack by the aniline to yield zwitterionic intermediates which may transfer an acidic proton to the bases present to yield the anionic adducts **9** or **12** respectively. In the formation of **9** from **1** the proton transfer step is rate-limiting; however, the slower interconversion of **4** and its zwitterion leads to only partial rate-limiting proton transfer in the formation of **12**. Results with substituted anilines including 2-substituted and *N*-methyl aniline indicate that steric effects are not a major factor in determining rates of proton-transfer in these systems. Contrary to previous reports no evidence was found for a strong interaction between **1** and Dabco in DMSO.

Introduction

The reaction of 1,3,5-trinitrobenzene, **1**, with aliphatic amines[1,2] in dimethyl sulfoxide, DMSO, results in the spontaneous formation of anionic σ-adducts, **3**. Kinetic studies are consistent with the two step process shown in Scheme 1, and have shown that the proton-transfer step may be rate-limiting.[3–5] Even though this step is thermodynamically favourable in the direction **2** → **3**, hydrogen bonding of acidic hydrogens to DMSO may lower the values of rate constants to below the diffusion limit.[6–8] Other factors which have been shown to reduce the value of k_p are increasing steric congestion at the reaction centre, greater with secondary than with primary amines,[3,4] and the presence of a group that is bulkier than hydrogen at the site of nucleophilic attack.[9,10]

The corresponding reaction with aniline does not occur since the initial formation of the zwitterion is thermodynamically unfavourable; the pK_a value for protonated aniline[11] is 3.82 in DMSO. However, Buncel and co-workers, importantly, showed that the presence of a strong base, such as the methoxide ion or Dabco, made the second step (proton-transfer) sufficiently thermodynamically favourable as to allow observation of the anilide adduct.[12–15] Kinetic studies in the presence of Dabco showed that proton-transfer was rate limiting.[16–20]

4-Nitrobenzofuroxan, **4**, is known to react with anionic nucleophiles, such as methoxide[21–23] or sulfite,[24] to yield adducts, **5** or **6** respectively, at the 5- or 7-ring positions. Its reaction with aliphatic amines in DMSO may also yield σ-adducts and kinetic studies have shown that here too proton-transfer may be rate-limiting.[25] Reactions of **4** with aromatic amines have not previously been investigated.

5   **6**
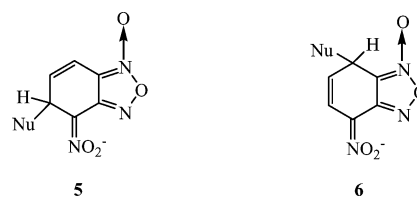
In this paper we report kinetic and equilibrium results for the reactions of **1** and **4** with a series of substituted anilines in the presence of Dabco, or in some cases of quinuclidine, in DMSO. Measurements were made in the presence of Dabco and its hydrochloride salt allowing a more complete evaluation of the competing processes than was achieved in earlier studies. The pK_a values for the substituted anilinium ions in DMSO were measured since they are relevant to the work. Our aims were to investigate the effects of both the structure of the nitro-compound and of substituents in the aniline on rate constants for proton transfer and on the nature of the rate-determining step. We also consider the recent claim[26,27] that the reaction of TNB with Dabco in DMSO yields a zwitterionic σ-adduct in spectroscopically observable amounts.

Results and discussion

pK_a Values for substituted anilinium ions in DMSO

The pK_a values for the dissociation of a number of protonated amines in DMSO are known;[11] values corresponding to aniline and Dabco are 3.82 and 9.06 respectively. However, values for the substituted anilines used in the present work have not been reported previously in DMSO.
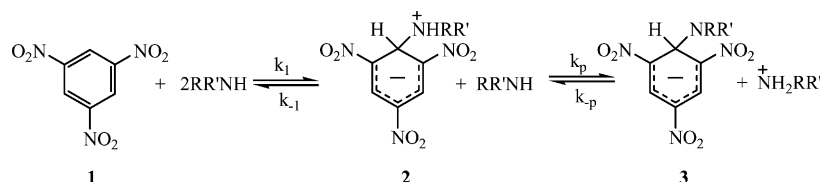
Scheme 1

Here, as previously,[11] a spectrophotometric method using 2,4-dinitrophenol (DNP) as an indicator was used to measure values of the equilibrium constant, K, for the process shown in eqn. (1). The pK_a value of DNP is known[28] to be 5.12 ± 0.04 in DMSO, so values of $pK_a(AnH^+)$ for the substituted anilines were calculated using eqn. (2). Absorbance
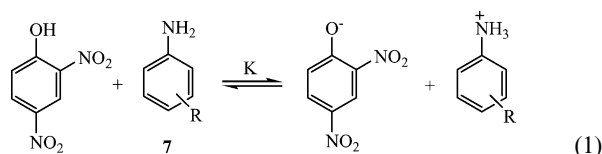
$$pK_a(AnH^+) = \log K + pK_a(DNP) \qquad (2)$$

measurements were made at 430 nm, the λmax value for the dinitrophenolate anion, in solutions containing excess concentrations of the aniline, **7**, and corresponding anilinium ions. In some cases it was necessary to make small corrections for the absorbance due to the substituted aniline. Wherever possible measurements were made with solutions containing a concentration of 0.01 mol dm⁻³ of the aniline hydrochloride. For less basic amines where concentrations of hydrochloride lower than 0.01 mol dm⁻³ were required, the ionic strength was maintained at 0.01 mol dm⁻³ with tetraethylammonium chloride. Representative data are shown in Table 1, and pK_a values are listed in Table 2.

The values for anilines **7a–f** carrying substituents remote from the reaction centre give an excellent correlation with Hammett σ-values[30] with a value for ρ of −4.46. The high acidity of the *N*-methylanilinium ion in DMSO deserves comment. It is known[11,31] that DMSO is an extremely good hydrogen-bond acceptor so that stabilisation of the cationic species will decrease as the number of NH⁺ hydrogens available for hydrogen-bonding decreases. The reduced number, relative to anilinium, of such acidic hydrogens in the *N*-methylanilinium ion is likely to be an important factor here. Some steric inhibition of solvation by DMSO of the 2-substituted anilinium ions may also be expected.
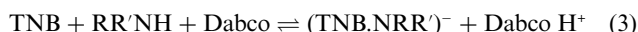
The pK_a value for the quinuclidinium ion in DMSO was calculated to be 10.05 ± 0.05 using measurements of absorbance at 450 nm in solutions containing the indicator 2,4,6-trinitrodiphenylamine.[11]

Reaction of 1,3,5-trinitrobenzene, 1, with substituted anilines and Dabco in DMSO

¹H NMR spectra of **1**, 0.025 mol dm⁻³, in [²H₆]-DMSO containing the substituted anilines **7a–f**, 0.23 mol dm⁻³ and Dabco, 0.08 mol dm⁻³, indicated the formation of the σ-adducts **9a–f**, as shown in Scheme 2. The results are shown in Table 3. It is interesting that spin-coupling, *ca.* 9 Hz, is observed between H$_b$ and the NH hydrogen indicating that the amine hydrogen exchanges relatively slowly with other labile hydrogens. After addition of a trace of deuterium oxide, the NH band was lost due to deuteration. The UV–visible spectra of solutions containing **1**, 5×10^{-5} mol dm⁻³, anilines **7**, 0.1 mol dm⁻³, and Dabco, 0.1 mol dm⁻³ showed bands at 445 nm, ε 3.0 × 10⁴ dm³ mol⁻¹ cm⁻¹, and 530 nm, ε 1.8 × 10⁴ dm³ mol⁻¹ cm⁻¹, attributed to the adducts **9**. These were stable for several hours. These spectroscopic results are in good accord with those previously reported[12–14] for related systems.

There was no evidence for a strong interaction in solutions containing **1** and anilines in the absence of Dabco. However, it is necessary to comment on recent claims that **1** and Dabco will react in DMSO to give the zwitterionic adduct **10** as shown in Scheme 3. ¹H NMR bands at δ 8.34 and 6.14 have been attributed[27] to **10**, and the UV–visible absorbance at 452 nm and 562 nm has been used[26] to measure rate and equilibrium constants for the interaction. A value for the equilibrium constant of *ca.* 70 dm³ mol⁻¹ was obtained. Our studies do not confirm these results. Although solutions containing **1**, 1×10^{-4} mol dm⁻³, and Dabco 0.1 mol dm⁻³ show some absorbance at 450 nm and 550 nm, this is reduced to very low values, Abs < 0.05, in the presence of Dabco hydrochloride, 0.01 mol dm⁻³. This reduction is not compatible with the formation of the zwitterion, **10**, which should be unaffected by Dabco hydrochloride. Also, we find that in a ¹H NMR spectrum of **1**, 0.025 mol dm⁻³, and Dabco, 0.067 mol dm⁻³, in [²H₆]-DMSO the bands at δ 8.3 and 6.2 are barely detectable. Calculation of the value, using the integrated intensities, of the equilibrium constant based on Scheme 3 yields *ca.* 0.1 dm³ mol⁻¹.

It seems likely, and in agreement with our observations, that **1** and Dabco do not interact strongly in DMSO and that the observed spectroscopic effects result from the reaction of **1** with very low concentrations of impurities present in the Dabco. These impurities, which are probably primary or secondary amines, interact with **1** and Dabco as indicated in eqn. (3).

$$TNB + RR'NH + Dabco \rightleftharpoons (TNB.NRR')^- + Dabco\ H^+ \qquad (3)$$

The reaction is effectively inhibited by Dabco hydrochloride.

Table 1 Absorbance data for 2,4-dinitrophenol, 4×10^{-5} mol dm⁻³, in DMSO containing 4-methylaniline, **7b**, and its hydrochloride salt at 25 °C

[**7b**]/mol dm⁻³	[**7b**·HCl]/mol dm⁻³	Abs(430 nm)	Abs*[a]	K[b]
0	0.01	0.0124	0.0124	—
0.025	0.01	0.213	0.212	0.22
0.050	0.01	0.322	0.320	0.24
0.075	0.01	0.373	0.370	0.23
0.10	0.01	0.410	0.405	0.22
0.15	0.01	0.453	0.446	0.22
0.20	0.01	0.488	0.479	0.23
0.30	0.01	0.523	0.509	0.23
0.40	0.01	0.542	0.523	0.23
0.40	0	0.595	0.580	—
0.60	0	0.606	0.580	—

[a] Abs* values have been corrected for absorption by **7b**. [b] Calculated as $\left(\frac{Abs^* - 0.0124}{0.58 - Abs^*}\right)\frac{[\mathbf{7b} \cdot HCl]}{[\mathbf{7b}]}$.

Table 2 pK_a Values for substituted anilinium ions in DMSO

Aniline	R	K[a]	pK_a (DMSO)	pK_a (water)[c]
7a	4-OMe	0.92 ± 0.05	5.08 ± 0.05	5.36
7b	4-Me	0.23 ± 0.01	4.48 ± 0.05	5.12
7c	H[b]	—	3.82 ± 0.04	4.58
7d	4-Cl	$(5.5 \pm 0.6) \times 10^{-3}$	2.86 ± 0.04	3.98
7e	3-Cl	$(1.66 \pm 0.14) \times 10^{-3}$	2.34 ± 0.04	3.46
7f	3-CN	$(1.74 \pm 0.18) \times 10^{-4}$	1.36 ± 0.04	2.75
7g	2-Me	0.048 ± 0.002	3.80 ± 0.05	4.39
7h	2-Et	0.043 ± 0.002	3.75 ± 0.05	4.37
7i	*N*-Me	$(6.2 \pm 0.3) \times 10^{-3}$	2.91 ± 0.05	4.85

[a] Defined in eqn. (1). [b] From ref. 11. [c] From ref. 29.

Table 3 ¹H NMR data for adducts **9a–f**, formed from **1** with anilines and Dabco in [²H₆]-DMSO

	¹H Shifts			
Adducts **9**	H$_a$	H$_b$	NH	$J_{b\text{-}NH}$/Hz
a R = 4-OMe	8.34	6.08	5.51	8.8
b R = 4-Me	8.34	6.14	5.70	8.8
c R = H	8.35	6.21	5.88	9.2
d R = 4-Cl	8.36	6.18	6.12	8.8
e R = 3-Cl	8.37	6.20	6.26	9.2
f R = 3-CN	8.36	6.25	6.46	9.2
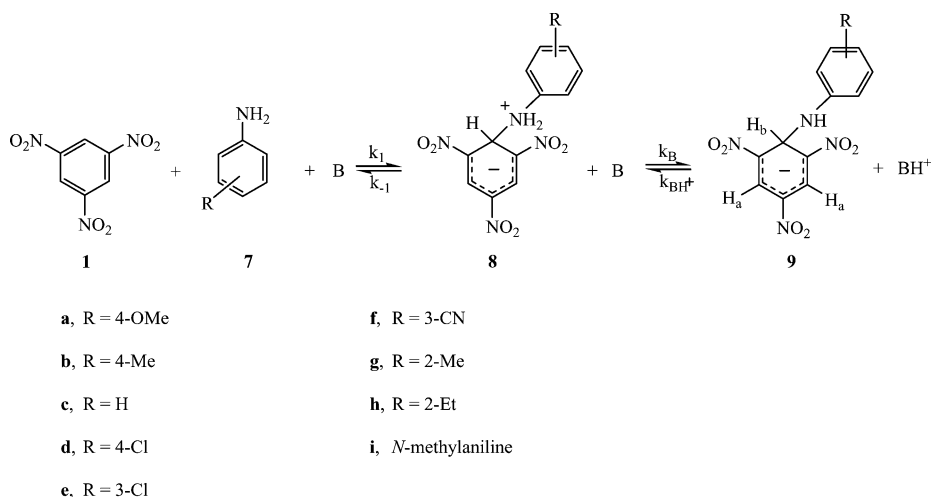
Scheme 2
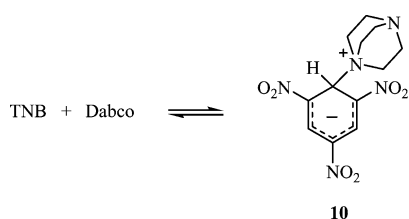
Scheme 3

Kinetic and equilibrium studies

Spectrophotometric measurements were made at the absorption maximum of the adducts formed, 445 and/or 530 nm, using the stopped-flow technique. The concentration of **1** was kept at 4×10^{-5} mol dm^{-3} and was very much lower than that of the other components, one of the substituted anilines **7a–i** and Dabco. All measurements were made in the presence of Dabco hydrochloride, 0.01 mol dm^{-3}. This kept the ionic strength of the solutions constant and inhibited any possible reaction between **1** and Dabco. Under these conditions, accurate first-order kinetics were observed and the variation in value of the rate constant with aniline and Dabco concentrations was examined. The specimen data are shown in Table 4.

The treatment of the zwitterions **8** in Scheme 2 as steady state intermediates leads to eqn. (4), where [An] represents the concentration of the subsitited aniline.

$$k_{obs} = \frac{k_1[An]k_B[B] + k_{-1}k_{BH^+}[BH^+]}{k_{-1} + k_B[B]} \qquad (4)$$

Our results are compatible only with the condition $k_{-1} \gg k_B[B]$, corresponding to rate limiting proton transfer. Eqn. (4) then simplifies to eqn. (5), where $K_1 = k_1/k_{-1}$.

$$k_{obs} = K_1 k_B[An][B] + k_{BH^+}[BH^+] \qquad (5)$$

Buncel and Eggimann[16] have previously examined the kinetics of the reaction of **1** with unsubstituted aniline, **7c**, in the presence of Dabco, but in the absence of added DabcoH$^+$. Under these conditions the reaction in Scheme 2 gives first order kinetics in the forward direction and second order kinetics in the reverse direction, making the evaluation of rate constants more difficult. They showed, importantly, that the proton-transfer step was rate limiting. It was also shown[18] that stabilisation of DabcoH$^+$ by association with chloride ions may result in increases in the overall equilibrium constant for adduct formation. Hence in our work we have worked at constant and low concentrations of chloride ions, 0.01 mol dm^{-3}.

Buncel and Eggimann[16] assumed that only Dabco would be effective as a base in the proton-transfer stage of the reaction. However, it has been shown[20] in a related system that aniline, even though it is a much weaker base, might also contribute to the proton transfer equilibrium. Thus it is known that the trinitrocyclohexadienate group in **8**, even though negatively charged, is electron-withdrawing relative to hydrogen.[3,4,14,32] Hence **8** will be more acidic than the corresponding anilinium ion, so the proton-transfer step $\mathbf{8} \rightleftharpoons \mathbf{9}$ will be thermodynamically favoured even when the reaction involves aniline as B and the corresponding anilinium ion as BH$^+$. Hence eqn. (5) takes the form of eqn. (6) where k_{Dabco} and k_{An} represent k_B when

Table 4 Kinetic results for the reaction of **1** with 4-methoxy- or 3-chloro-aniline and Dabco in DMSO at 25 °C

[Substituted aniline]/mol dm^{-3}	[Dabco]/mol dm^{-3}	Aniline **7a**		Aniline **7e**	
		k_{obs}/s^{-1}	k_{calc}[b]/s^{-1}	k_{obs}/s^{-1}	k_{calc}[c]/s^{-1}
0.05	0.10	11.3	10.9	0.047	0.043
0.10	0.10	13.0	13.1	0.053	0.052
0.15	0.10	15.8	15.4	0.060	0.061
0.20	0.10	17.9	17.7	0.071	0.071
0.30	0.10	23.1	22.6	0.088	0.092
0.10	0.05	11.0	11.6	0.048	0.049
0.10	0.08	12.2	12.4	—	—
0.10	0.15	14.8	14.9	0.058	0.057
0.10	0.20	17.1	16.7	0.063	0.062
0.10	0.30	20.3	20.5	0.072	0.073

[a] All solutions contain Dabco hydrochloride, 0.01 mol dm^{-3}. Measurements were made at 445 nm using the stopped-flow method. [b] Calculated from eqn. (7) with $K_1 k_{Dabco}$ 380 dm^6 mol^{-2} s^{-1}, k_{DabcoH^+} 880 dm^3 mol^{-1} s^{-1}, and k_{An}/k_{Dabco} 0.04. [c] Calculated from eqn. (7), with $K_1 k_{Dabco}$ 1.2 dm^6 mol^{-2} s^{-1}, k_{DabcoH^+} 3.5 dm^3 mol^{-1} s^{-1} and k_{An}/k_{Dabco} 0.10

Table 5 Summary of results for the reactions of **1** with anilines **7a–k** and Dabco in DMSO at 25 °C

Aniline		$K_1 k_{Dabco}/dm^6\ mol^{-2}\ s^{-1}$	$k_{DabcoH^+}/dm^3\ mol^{-1}\ s^{-1}$	$K_1 K_{Dabco}{}^a/dm^3\ mol^{-1}$	k_{An}/k_{Dabco}
7a	4-OMe	380 ± 20	880 ± 30	0.43 ± 0.04	0.04 ± 0.01
7b	4-Me	95 ± 10	280 ± 20	0.34 ± 0.06	0.04 ± 0.01
7c	H	28 ± 3	90 ± 20	0.31 ± 0.10	0.05 ± 0.01
7d	4-Cl	4.5 ± 1	13 ± 1	0.35 ± 0.10	0.05 ± 0.01
7e	3-Cl	1.2 ± 0.2	3.5 ± 0.1	0.34 ± 0.07	0.1 ± 0.02
7f	3-CN	0.25 ± 0.02	1 ± 0.2	0.25 ± 0.10	0.05 ± 0.01
7g	2-Me	8 ± 1	80 ± 20	0.10 ± 0.04	0
7h	2-Et	8 ± 2	60 ± 10	0.13 ± 0.05	0
7i	N-methyl	2.0 ± 0.3	14 ± 2	0.14 ± 0.05	0

^{a} Calculated as $K_1 k_{Dabco}/k_{DabcoH^+}$.

the reaction involves Dabco and aniline, respectively, while k_{DabcoH^+} and k_{AnH^+} represent k_{BH^+} for reactions with the appropriate conjugate acids. Since K_{Dabco} ($= k_{Dabco}/k_{DabcoH^+}$) and K_{An} ($= k_{An}/k_{AnH^+}$) are related by the relative acidities of the conjugate acids, the number of variables in eqn. (6) may be reduced to give eqn. (7).

$$k_{obs} = K_1[An]\,(k_{Dabco}[Dabco] + k_{An}[An]) \\ + k_{DabcoH^+}[DabcoH^+] + k_{AnH^+}[AnH^+] \qquad (6)$$

$$k_{obs} = K_1 k_{Dabco}[An]\left([Dabco] + \frac{k_{An}}{k_{Dabco}}[An]\right) \\ + k_{DabcoH^+}[DabcoH^+]\left(1 + \frac{k_{An}[An]}{k_{Dabco}[Dabco]}\right) \qquad (7)$$

Variations in the values of k_{obs} with the concentrations of aniline and of Dabco were used to calculate the values of the parameters $K_1 k_{Dabco}$, k_{DabcoH^+} and k_{An}/k_{Dabco}. The specimen results are listed in Table 4, and the data are summarised in Table 5. For anilines **7a–f**, carrying substituents remote from the reaction centre, Hammett plots of the values of $K_1 k_{Dabco}$ gave a ρ value of -3.8, while values of k_{DabcoH^+} gave $\rho = -3.6$. Compensation for these terms leads to values of the overall equilibrium constant $K_1 K_{Dabco}$ ($= K_1 k_{Dabco}/k_{DabcoH^+}$) which show little variation with the nature of the substituent. For these anilines **7a–f**, a positive value of k_{An}/k_{Dabco} was required to adequately fit the data. For anilines **7g–i**, with substituents close to the reaction centre, no improvement in fit was obtained using non-zero values of k_{An}/k_{Dabco}. Also shown, Fig. 1, are logarithmic plots of the values *versus* the pK_a values of the corresponding anilinium ions.
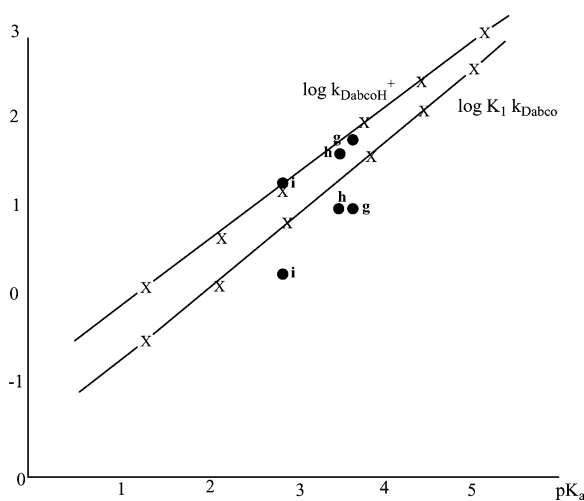

Fig. 1 Plots of $\log k_{DabcoH^+}$ and $\log K_1 k_{Dabco}$ for the reaction of **1** with anilines *versus* the pK_a values of the corresponding anilinium ions. The slopes are 0.80 and 0.87 respectively. Points g, h and i represent 2-methyl-, 2-ethyl- and N-methyl-anilines respectively.

We briefly investigated the effects of substituting quinuclidine for Dabco as the added base. The results are given in Table 6. They show that for these two bases values of $K_1 k_B$ are independent of the nature of the base, implying that values of k_B are determined by factors other than basicity. Values of k_{BH^+} show a direct dependence on the values of the acidity of the conjugate acids (pK_a values, DabcoH$^+$ 9.06; quinuclidine H$^+$, 10.05). This is also shown by the dependence of values of the equilibrium constant, $K_1 K_B$, on the basicity of the base used.

We will delay further discussion until results for 4-nitrobenzofuroxan have been given.

Reactions of 4-nitrobenzofuroxan, 4, with substituted anilines and Dabco in DMSO

The UV–visible spectrum of **4** in DMSO shows a band at 411 nm, $\varepsilon = 1.28 \times 10^4\ dm^3\ mol^{-1}\ cm^{-1}$. In the presence of aniline and Dabco, a new band at 350 nm, $\varepsilon = 2.8 \times 10^4\ dm^3\ mol^{-1}\ cm^{-1}$ is observed attributed to the σ-adduct **12** as shown in Scheme 4. The justification for showing this as the 7-adduct rather than the 5-adduct will be given later. This species was sufficiently stable for kinetic measurements on the stopped-flow timescale to be made; however, slower irreversible reactions occurred which precluded NMR measurements. In accord with previous work,[33] **4** and Dabco alone in DMSO did not react, and there was no reaction with aniline in the absence of Dabco.

The general kinetic expression corresponding to Scheme 4 is eqn. (4). However, in contrast to the behaviour of **1**, the results were not compatible with the condition $k_{-1} \gg k_B[B]$ which leads to eqn. (5). Hence the results were fitted to eqn. (8). No significant improvement was obtained by including terms representing proton transfer to aniline as the base, $k_{An}/k_B < 0.1$. Representative data are shown in Table 7.

$$k_{obs} = \frac{K_1 k_{Dabco}[An][Dabco] + k_{DabcoH^+}[DabcoH^+]}{1 + \dfrac{k_{Dabco}[Dabco]}{k_{-1}}} \qquad (8)$$

They allow calculation of values, of the parameters $K_1 k_{Dabco}$, k_{DabcoH^+} and k_{Dabco}/k_{-1}. It is worth noting that since eqn. (8) contains a term involving [Dabco] in both the numerator and denominator, both increases and decreases in the values of k_{obs} may be expected as [Dabco] is increased. Values for the anilines **7a–e** are collected in Table 8, which includes values for the equilibrium constant $K_1 K_{Dabco}$ ($= K_1 k_{Dabco}/k_{DabcoH^+}$) and k_1 ($= K_1 k_{Dabco}.k_{-1}/k_{Dabco}$).

Hammett plots, not shown, give the following values of ρ; $K_1 k_{Dabco} - 3.7$, $k_{DabcoH^+} - 2.8$, $k_1 - 3.1$ and $K_1 K_{Dabco} - 0.9$.

The values of $K_1 K_{Dabco}$ listed in Table 8 for the reaction with **4** are between three and ten times larger than those for the reaction of the corresponding anilines with **1**. If a statistical correction were applied to take account of the three equivalent ring positions in **1**, then the factors would be three times larger. For the reactions in DMSO of **4** with aliphatic amines,[25] which are considerably more reactive than aniline, isomeric attack at the five- and seven-positions is observed. For the reaction with

Table 6 Results for the reactions[a] of **1** with anilines **7a,c,d** and quinuclidine in DMSO at 25 °C

Aniline	$K_1 k_{quin}$/dm^6 mol^{-2} s^{-1}	k_{quinH^+}/dm^3 mol^{-1} s^{-1}	$K_1 K_{quin}$[b]/dm^3 mol^{-1}
7a 4-OMe	350 ± 20	70 ± 10	5 ± 1
7c H	33 ± 3	7 ± 1	4.7 ± 1
7d 4-Cl	4.5 ± 0.5	1.2 ± 0.1	3.8 ± 0.8

[a] Kinetic measurements were made in solutions containing quinuclidine hydrochloride, 0.01 mol dm^{-3} with various concentrations of aniline and quinuclidine. [b] Calculated as $K_1 k_{quin}/k_{quinH^+}$.

Scheme 4

Table 7 Kinetic results[a] for the reaction of **4** with aniline or 4-methylaniline and Dabco in DMSO at 25 °C

		Aniline **7b**		Aniline **7c**	
[Substituted Aniline]/mol dm^{-3}	[Dabco]/mol dm^{-3}	k_{obs}/s^{-1}	k_{calc}[b]/s^{-1}	k_{obs}/s^{-1}	k_{calc}[c]/s^{-1}
0.03	0.05	0.055	0.054		
0.06	0.05	0.077	0.075		
0.09	0.05	0.098	0.095		
0.12	0.05	0.12	0.12		
0.15	0.05	0.14	0.14		
0.05	0.03	0.074	0.071		
0.05	0.06	0.062	0.067		
0.05	0.09	0.060	0.065		
0.05	0.12	0.061	0.064		
0.05	0.15	0.059	0.063		
0.04	0.10			0.018	0.016
0.07	0.10			0.020	0.021
0.10	0.10			0.027	0.027
0.15	0.10			0.036	0.036
0.20	0.10			0.047	0.045
0.10	0.04			0.025	0.026
0.10	0.07			0.024	0.026
0.10	0.15			0.026	0.027
0.10	0.20			0.028	0.028

[a] All solutions contain Dabco hydrochloride 0.01 mol dm^{-3}, and **4** 2.5×10^{-5} mol dm^{-3}. Measurements were made in the range of 350–370 nm using stopped-flow spectrophotometry. [b] Calculated from eqn. (8) with $K_1 k_{Dabco}$ 32 dm^6 mol^{-2} s^{-1}, k_{DabcoH^+} 8 dm^3 mol^{-1} s^{-1} and k_{Dabco}/k_{-1} 27 dm^3 mol^{-1}. [c] Calculated from eqn. (8) with $K_1 k_{Dabco}$ 5.7 dm^6 mol^{-2} s^{-1}, k_{DabcoH^+} 2.5 dm^3 mol^{-1} s^{-1} and k_{Dabco}/k_{-1} 20 dm^3 mol^{-1}.

Table 8 Summary of results for the reaction of **4** with anilines **7a–e** and Dabco in DMSO at 25 °C

Aniline	$K_1 k_{Dabco}$/dm^6 mol^{-2} s^{-1}	k_{DabcoH^+}/dm^3 mol^{-1} s^{-1}	k_{Dabco}/k_{-1} dm^3 mol^{-1}	$K_1 K_{Dabco}$/dm^3 mol^{-1}	k_1/dm^3 mol^{-1} s^{-1}
7a 4-OMe	130 ± 10	38 ± 3	25 ± 5	3.4 ± 0.6	5.2 ± 1.8
7b 4-Me	32 ± 5	8 ± 1	27 ± 2	4.0 ± 1.0	1.2 ± 0.3
7c H	5.7 ± 0.3	2.5 ± 0.5	20 ± 1	2.3 ± 0.7	0.3 ± 0.03
7d 4-Cl	2.0 ± 1.0	1.4 ± 0.1	20 ± 1	1.4 ± 0.6	0.1 ± 0.05
7e 3-Cl	0.37 ± 0.03	0.36 ± 0.01	10 ± 2	1 ± 0.2	0.037 ± 0.013

n-butylamine, the values of the overall equilibrium constants $K_{c,5}$ and $K_{c,7}$ are 110 dm^3 mol^{-1} and 5.6×10^3 dm^3 mol^{-1} respectively. The corresponding value[4] for the reaction with **1** for the process given in Scheme 1 is 1×10^3 dm^3 mol^{-1}. Hence the ratio for **4** (seven-position): **1** is 5.6 which is similar to the ratio obtained with aniline. This similarity is strong evidence that the process we have observed with **4** corresponds to formation of the seven-adduct as shown in Scheme 4. The five-adduct is, then expected to have a much lower thermodynamic stability, so it is not observed under our conditions.

Rate constants for proton transfer

The experimental results show that proton transfer is rate limiting, $k_{-1} \gg k_{Dabco}$[Dabco], in the formation of **9** from **1**. However, in the corresponding reaction of **4** there is a balance between nucleophilic attack and proton transfer as the rate limiting step, $k_{-1} \sim k_{Dabco}$[Dabco]. Although it is not possible to obtain experimental values of k_{Dabco}, the results do give values of k_{DabcoH^+}, the rate constant for protonation of the anionic adducts by DabcoH$^+$. The results given in Tables 5 and 8 show that for the

Table 9 Derived values for the reaction of **1** in DMSO

Aniline	$K_a{}^a(AnH^+)/mol\ dm^{-3}$	K_{Dabco}	K_{An}	$k_{An}/dm^3\ mol^{-1}\ s^{-1}$	$k_{AnH^+}/dm^3\ mol^{-1}\ s^{-1}$	$K_1/dm^3\ mol^{-1}$
7a 4-OMe	8.3×10^{-6}	1.1×10^5	12	4×10^6	3.3×10^5	3.9×10^{-6}
7b 4-Me	3.3×10^{-5}	3.6×10^5	9.5	4×10^6	4.2×10^5	9.4×10^{-7}
7c H	1.5×10^{-4}	1.1×10^6	6.3	5×10^6	8.0×10^5	2.8×10^{-7}
7d 4-Cl	1.4×10^{-3}	7.7×10^6	4.9	5×10^6	1.0×10^6	4.5×10^{-8}
7e 3-Cl	4.6×10^{-3}	2.9×10^7	5.5	1×10^7	1.8×10^6	1.1×10^{-8}
7f 3-CN	4.4×10^{-2}	1.0×10^8	2.0	5×10^6	2.5×10^6	2.5×10^{-9}
7g 2-Me	1.6×10^{-4}	1.3×10^6	7.1	—	—	7.7×10^{-8}
7h 2-Et	1.8×10^{-4}	1.7×10^6	3.3	—	—	7.6×10^{-8}
7i N-Me	1.2×10^{-3}	7.1×10^6	5.0	—	—	2.0×10^{-8}

^{a} Values from Table 2.

Table 10 Derived values for the reaction of **4** in DMSO

Aniline	K_{Dabco}	K_{An}	$K_1/dm^3\ mol^{-1}$	$k_1/dm^3\ mol^{-1}\ s^{-1}$	k_{-1}/s^{-1}
7a 4-OMe	2.6×10^6	270	1.3×10^{-6}	5.2	4×10^6
7b 4-Me	1.3×10^7	330	3.2×10^{-7}	1.2	3.8×10^6
7c H	4.0×10^7	230	5.8×10^{-8}	0.3	5×10^6
7d 4-Cl	7.1×10^7	45	1.9×10^{-8}	0.1	5×10^6
7e 3-Cl	2.8×10^8	53	3.6×10^{-9}	0.04	1.0×10^7

correspondingly substituted anilines, values are around an order of magnitude higher in protonation of **4** than of **12**, implying a higher energy gap in the latter case.

It is interesting to speculate as to the likely values of k_{Dabco} in these systems. The process involved, Scheme 2 and Scheme 4, is a strongly thermodynamically favoured proton transfer between nitrogen atoms. In the TNB reaction, Buncel and Eggimann[16] proposed a value of $1 \times 10^9\ dm^3\ mol^{-1}\ s^{-1}$, which is close to the diffusion limit. However, it is now known[4,8] that in DMSO values for such proton transfers may be slowed by hydrogen-bonding to the solvent as shown in **13**. It is necessary to break the hydrogen-bond before the proton can be transferred. Steric congestion at the reaction centre may also reduce proton transfer rates.[3,4,9,10] However, for anilines **7a–f** carrying remote substituents, any possible steric effects are likely to be constant. Furthermore, since values of k_{DabcoH^+} will also be subject to steric effects, the plot in Fig. 1 *versus* pK_a values is informative. It shows that even for **7g–i** the values of k_{DabcoH^+} do not deviate from linearity. The implication is that for these primary amines, and even for N-methylaniline, there are no serious steric effects on proton transfer between the zwitterions, **8**, and anions, **9**. We note that here proton transfer involves Dabco, which should be relatively unhindered.
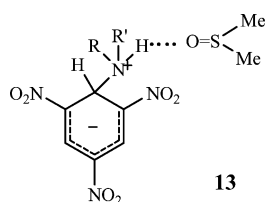
13

In previous cases where steric hindrance has been observed, the reaction has involved bulky secondary amines both as the nucleophile and proton-acceptors base (*e.g.* Scheme 1, R–R′ = piperidine), or the presence of a ring-substitutent bulkier than hydrogen at the reaction centre.[9,10]

Hence we will assume a value for k_{Dabco} of $1 \times 10^8\ dm^3\ mol^{-1}\ s^{-1}$, reduced below the diffusion limit only by hydrogen bonding to the solvent. The value will be independent of the aniline nucleophile. The correspondence in values of $K_1 k_{Dabco}$ and $K_1 k_{quin}$, for corresponding anilines, in Tables 5 and 6 indicates that values of k_{Dabco} and k_{quin} are equal. If steric effects on proton transfer are unimportant in reactions of **1**, they are also likely to be unimportant in reactions involving **4** and **7a–e**.

Hence it is reasonable to assume in this system, too, a value for k_{Dabco} of $1 \times 10^8\ dm^3\ mol^{-1}\ s^{-1}$.

On this basis it is possible to calculate, using eqn. (9) and eqn. (10) values for K_{Dabco} and K_{An}. The latter corresponds to the equilibrium constant for the proton-transfer stage of Scheme 2 or Scheme 4 when aniline acts as the base as well as the nucleophile.

$$K_{Dabco} = \frac{k_{Dabco}}{k_{DabcoH^+}} \quad (9)$$

$$K_{An} = K_{Dabco}\frac{K_a(DabcoH^+)}{K_a(AnH^+)} \equiv \frac{k_{An}}{k_{AnH^+}} \quad (10)$$

$$k_{An} = 1 \times 10^8\frac{K_{An}}{k_{Dabco}} \quad (11)$$

Values of k_{An} for reactions involving **1** were calculated with eqn. (11) using experimental values of the ratio k_{An}/k_{Dabco}. Then $k_{AnH^+} (= k_{An}/K_{An})$ and $K_1 (= K_1 K_{Dabco}/K_{Dabco})$ could be determined. For reactions involving **4**, values of k_{-1} were calculated as $k_{-1} = k_1/K_1$. Derived data are collected in Tables 9 and 10.

In the reactions of both **1** and **4**, values of K_{Dabco} increase strongly as the substituent R is made more electron withdrawing. These changes reflect increases in acidity of the zwitterionic intermediates **8** and **11** respectively. Values of K_{An} show little dependence on the nature of R showing that, here, changes in the acidity of the zwitterions are compensated by changes in acidity of the corresponding anilinium ions. For reactions of **1**, values of K_{An} are *ca.* 10 and are lower than the value, *ca.* 500, previously estimated for the corresponding reactions involving aliphatic amines. It should, however, be noted that the value for K_{An} depends directly on the value taken for k_{Dabco}. Nevertheless, there may be a real difference in the acidifying effect of the trinitrocyclohexadienate moiety when reaction involves aliphatic and aromatic amines. In the latter case acidities are already high so that potential electron withdrawing effect of the trinitrocyclohexadienate ring is reduced. The trend (reduction) in values of K_{An} seen in Table 9 as R is changed from 4-OMe to 3-CN may also illustrate this effect.

These results for reaction of **1** allow the schematic energy diagram shown in Fig. 2 to be drawn, illustrating the requirement for the presence of a strong base to allow adduct formation to be observed.

The values of K_1 decrease strongly as the substituent R is changed from 4-OMe to 3-CN. The ρ value is -3.8 for reaction
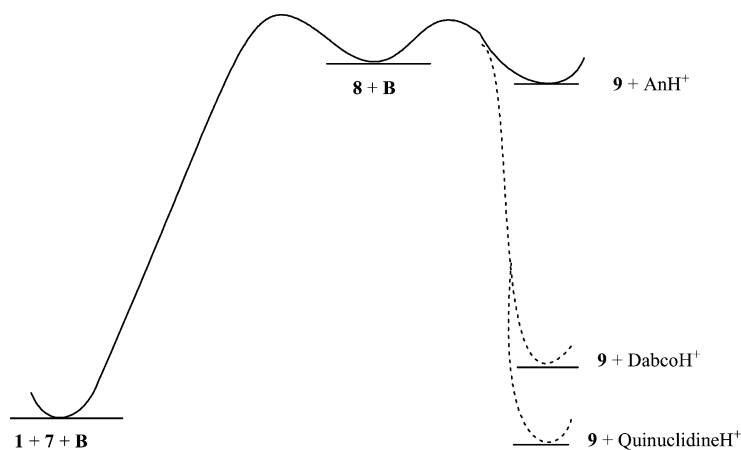
Fig. 2 Schematic energy diagram representing Scheme 2. The base **B** may be aniline, Dabco or quinuclidine.

of **1** and −3.7 for reaction of **4**. The plot, in Fig. 1, *versus* pK_a values has a slope of 0.87. It may be significant that the points for 2-methyl, 2-ethyl and *N*-methylanilines fall before the line defined by remote substitutents. This may indicate some steric hindrance to the formation of the zwitterions, **8**, in these derivatives leading to reductions in values of K_1.

It has already been noted that for the anilines **7g–i**, values of k_{DabcoH^+}, and by inference also values of k_{Dabco}, are not reduced by steric factors. However, for these anilines the proton transfer process k_{An}, relating to proton transfer from zwitterion **8** to substituted aniline, was not observed. This is likely to reflect the increased steric hindrance, referred to earlier, when *both* the nucleophile and the proton-accepting base have substituents close to the reaction centre.

Comparisons between 1 and 4

For reactions of **4**, values of k_1, listed in Table 10, show a strong dependence on the nature of the substituent R, with $\rho = -3.1$, while values of k_{-1} show a much smaller dependence. This indicates a product-like transition state for nucleophilic attack where bonding between the nucleophile and ring is well-developed. For aniline **7c**, values are k_1 0.3 dm^3 mol^{-1} s^{-1} and k_{-1} 5 × 10^6 s^{-1}. Values for the corresponding reaction of **1** are not observable since the conversion of **1** and its zwitterion **8** is a rapid equilibrium. However, it is possible to calculate minimum values for these parameters as follows. The results require that $k_{-1} \gg k_{Dabco}$[Dabco], so that we may estimate that, when [Dabco] = 0.3 mol dm^{-3}, then

$$\frac{k_{-1}}{k_{Dabco}[Dabco]} > 10$$

$$k_{-1} > 10 \times 1 \times 10^8 \times 0.3$$

$$k_{-1} > 3 \times 10^8 \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$$

For aniline, **7c**, the value of k_1 may be estimated to be k_1 (= $K_1 \cdot k_{-1}$) > 2.8 × 10^{-7} × 3 × 10^8, > 84 dm^3 mol^{-1} s^{-1}. These lower limits for k_1 and k_{-1} for **1** are larger than the corresponding values for **4** by factors of *ca.* 100. This may be attributed to the high intrinsic barrier associated with adduct formation at the seven-position of **4**, due to the extensive charge delocalisation which is possible.[25,34] In the corresponding reactions with aliphatic amines, values of k_1 were found[25] to be considerably larger for reactions of **1** than **4**. This analysis suggests that the reason for the change in nature of the rate determining step for reaction of **1** and **4** is the higher value of k_{-1} for **1**. This leads to rate determining proton transfer. The data in Tables 9 and 10 show that for a given aniline values of K_{Dabco}, and also of K_{An}, are larger by factors of *ca.* ten for reaction of **4** than of **1**. This indicates that the zwitterions **11** are more acidic than zwitterions **8**. Apparently

the negatively charged 4-nitrobenzofuroxan moiety in **11** is more electron-withdrawing than the trinitrocyclohexadienate moiety in **8**. Independent support for this idea comes from the observation[35] that 7-anilino 4-nitrobenzofurazan, pK_a 7.68, is more acidic than 2,4,6-trinitrodiphenylamine, pK_a 8.20. We note also that in the present work ρ values for Hammett plots of the overall equilibrium constant, $K_1 K_{Dabco}$, have slopes of −0.3 for reaction of **1** but −0.9 for reaction of **4**. This suggests greater polarisation to give positive charge on the aniline nitrogen in the adduct **12** than in the adduct **9**.

It should be noted that recently[36] Terrier *et al.* have reported rate measurements of substitution reactions of two nitrobenzofurazan derivatives, 4-chloro-7-nitro-benzofurazan and 3-methyl-1-(4-nitrobenzofurazanyl)-imidazolium ion, with a series of 4-substituted anilines. In these reactions, in water–DMSO mixtures, nucleophilic addition is rate limiting. Unexpectedly high values of β_{nuc}, ≥1, were found and were interpreted as possible evidence for a two-step SET mechanism. This would involve fast electron transfer from the nucleophile to the substituted ntirobenzofurazan followed by slow coupling of the resulting cation and anion radicals. In the present work a plot, not shown, of the values of log k_1 for the reaction of **4** with anilines **7a–e** *versus* the pK_a values of the anilines gave a value for β_{nuc} of 0.72. This value falls within the normal range[36,37] expected for S_NAr type reactions, so here zwitterion formation is unlikely to involve the intervention of free radical intermediates.

Experimental

1,3,5-Trinitrobenzene,[8] 4-nitrobenzofuroxan[25] and 2,4-dinitrophenol[7] were available from previous work. Anilines, Dabco, quinuclidine and DMSO were the purest available commercial samples. Amine salts were prepared in solution by the accurate neutralisation of amines with concentrated hydrochloric acid.

^{1}H NMR spectra [^{2}H$_6$]-DMSO were recorded using a Bruker Avance −400 MHz instrument. UV–visible spectra and kinetic measurements were made with an Applied Photophysics SX-17MV stopped-flow instrument, or with Shimadzu UV-2101 PC or Perkin Elmer Lambda 2 spectrophotometers. All measurements were made at 25 °C. First order rate constants, precise to ±3%, were evaluated using standard methods. Fits of experimental data to eqn. (7) for trinitrobenzene or eqn. (8) for 4-nitrobenzofuroxan were made by minimising the standard deviation between observed and calculated values.

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