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σ-Adduct formation and oxidative substitution in the reactions of 4-nitrobenzofurazan and some derivatives with hydroxide ions in water

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The reactions of hydroxide ions with 4-nitrobenzofurazan, **1a**, 4-nitrobenzofuroxan, **1b**, and with three 4-nitro-7-substituted benzofurazans have been examined using ^{1}H NMR and UV-visible spectroscopies. In each case initial reaction is at the 5-position to give an anionic σ-adduct. Kinetic and equilibrium results are reported. NMR spectra show that in the case of **1a** oxidation of the anionic adduct yields 4-nitro-5-hydroxybenzofurazan. In the case of **1b** rearrangement of the 5-hydroxy adduct to the thermodynamically more stable 7-hydroxy adduct, possibly by a Boulton–Katritzky mechanism, precedes oxidation. When the 7-substituent in the 4-nitrobenzofurazan is Cl, OMe or OPh the eventual product is 7-hydroxy-4-nitrobenzofurazan produced by nucleophilic displacement of the substituent.

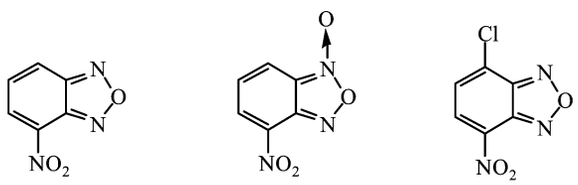
Introduction

4,6-Dinitrobenzofuroxan is known to be one of the strongest neutral organic electrophiles,[1–4] and readily forms anionic σ-adducts with neutral nucleophiles, such as water.[5] Reduction of the number of nitro-groups to one naturally reduces the electrophilicity; nevertheless it is found that σ-adducts from 4-nitrobenzofuroxan have considerably higher thermodynamic stabilities than corresponding adducts from 1,3,5-trinitrobenzene, the bench-mark electrophile.[1]

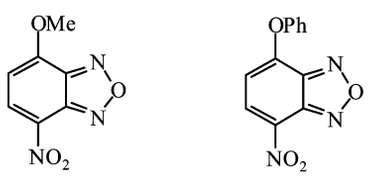
One source of interest in the reactions of 4-nitrobenzofurazan, **1a**, 4-nitrobenzofuroxan, **1b**, and their derivatives is their ability to act as *in vitro* inhibitors of nucleic acid and protein biosynthesis in animal cells.[6–9] These reactions occur in aqueous solutions, and it is surprising that, although detailed studies have been reported of the reactions of **1a** and **1b** with methoxide ions in methanol,[10–13] aryloxide ions,[14] sulfite ions,[15] and with amines[16,17] and carbanions[18–20] in dimethyl sulfoxide, quantitative information about their reactions with hydroxide, the lyate ion in water, is sparse. Values of equilibrium constants for hydroxide attack have been reported as 2200 dm^3 mol^{-1} for **1a**,[6] and 4800 dm^3 mol^{-1} for **1b**,[21] and some kinetic data is available for reactions with 7-chloro-4-nitrobenzofurazan,[9] **1c**, and with lysozyme-bound-4-nitrobenzofurazan.[22]

Here we report a detailed study of the reactions of **1a**–**c** and the 7-methoxy- and 7-phenoxy-4-nitrobenzofurazans, **1d** and **1e** respectively, with hydroxide ions. ^{1}H NMR spectroscopy has been used to investigate the initial σ-adduct forming reactions and to follow the progress of subsequent reactions. Kinetic and equilibrium data have been measured using both NMR and UV/visible methods.

There is current interest in the possibility of the oxidative substitution of ring hydrogen atoms with nucleophiles.[1,23] Such substitutions are known to occur in the reactions of 4-nitrobenzofuroxan, **1b**, with methoxide ions[12] and with amines.[17,24] Here substitution of hydrogen at the 7-position is observed but is accompanied by reduction of the *N*-oxide function. However there is a report that the reaction of **1b** with hydroxide ions in DMSO may yield 7-hydroxy-4-nitrobenzofuroxan.[17] Recently it has been shown that anionic adducts derived by reaction of the 2-nitropropenide ion at the 7-position of **1a** or **1b** may be readily oxidised either electrochemically or chemically to yield the neutral substitution products.[18,19] Interestingly the ease of oxidation was found to depend inversely on the electron deficiency of the parent molecule.



1a **1b** **1c**



1d **1e**

Our results presented here provide initial evidence that the hydroxide adducts formed from **1a** and **1b** may undergo oxidation to yield the hydroxydehydro-substitution products.

Results and discussion

^{1}H NMR studies

For solubility reasons it was necessary to make measurements in 80 : 20 (v/v) water–DMSO, using deuteriated solvents. For each parent, **1a**–**e**, at a concentration of 0.01 mol dm^{-3}, the presence of one equivalent of sodium deuteroxide resulted in the rapid and virtually quantitative formation of the 5-adduct. In the adducts H5 is at *ca.* δ 5.6 and is coupled, *J ca.* 5 Hz, to H6. Data are summarised in Table 1.

The subsequent behaviour depended markedly on the nature of the parent but can be discussed in terms of Scheme 1 for **1a**,**1c**–**e** and Scheme 2 for **1b**. In the case of **1a**, 4-nitrobenzofurazan, there was no evidence for isomerisation to the 7-hydroxy adduct. Instead the spectra, Fig. 1, showed the gradual conversion of **2a**[25] to a species with spin-coupled, *J* 10 Hz, bands at δ 7.15 and 7.84. This is identified as **3a** by comparison with the spectrum of 5-hydroxy-4-nitrobenzofurazan prepared by hydroxy-dechlorination of the 5-chloro derivative.

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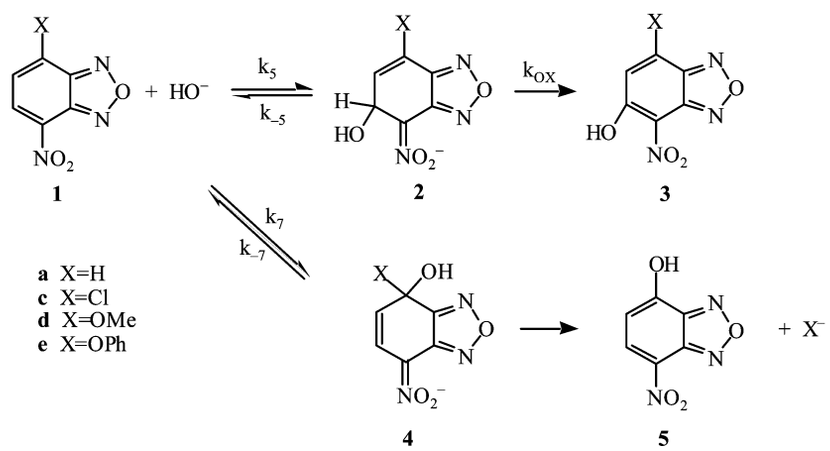
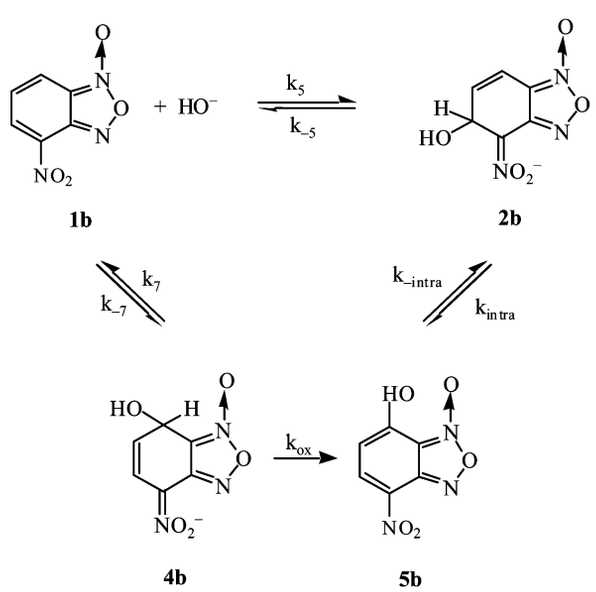
Table 1 Spectroscopic data for parent molecules, adducts and products

	^{1}H NMR data[a]							
	δ						UV absorbance[b]	
	H5	H6	H7	Other	J_{56}	J_{67}	λ_{max}/nm	ε/dm^3 mol^{-1} cm^{-1}
1a	8.72	7.84	8.48	—	7.2	8.8	327	6500
1b	8.65	7.57	8.04	—	7.2	9.2	401	7000
1c	8.67	8.01	—	—	7.8	—	339	10,000
1d	8.76	7.01	—	4.24 (OMe)	8.6	—	383	12,000
1e	8.70	6.72	—	7.45–7.70 (OPh)	8.4	—	380	9,500
2a	5.56	6.46	6.85	—	4.6	10.4	325	11,000
2b	5.54	6.34	6.49	—	4.7	10.1	327	10,500
2c	5.64	6.61	—	—	5.6	—	325	12,000
2d	5.59	5.70	—	3.75 (OMe)	5.5	—	326	10,000
2e	5.68	5.72	—	7.2–7.5 (OPh)	5.6	—	323	11,000
4b	6.91	5.63	5.37	—	10.8	4.8	323	12,000
3a	—	7.15[c]	7.84[c]	—	—	10.0	—	—
5	8.42[d]	6.08[d]	—	—	9.7	—	466[d]	27,000[d]
5b	8.11[d]	5.73[d]	—	—	10.0	—	470[d]	—

[a] In 80:20 (v/v) D_2O-[$^2H_6$]DMSO. [b] In water. [c] Position depends on ionisation state of the hydroxy group; δ 6.80, 7.70, in presence of excess base, δ 7.37, 8.16 in presence of excess acid. [d] Corresponds to ionised form (in presence of excess base).



Scheme 1



Scheme 2

Both the reaction product and the synthesized samples of **3a** showed the expected peak at *m*/*z* 180 $(M - H)^-$ in the negative electrospray mass spectrum. It is worth noting that the NMR shifts of **3a** depend on the acidity of the medium, consistent with the behaviour expected for an *ortho*-nitrophenol. In the presence of acid bands are at δ 7.37 and 8.16 and in the presence of base at 6.80 and 7.70 corresponding to the ionisation, **3a** to **6a**.

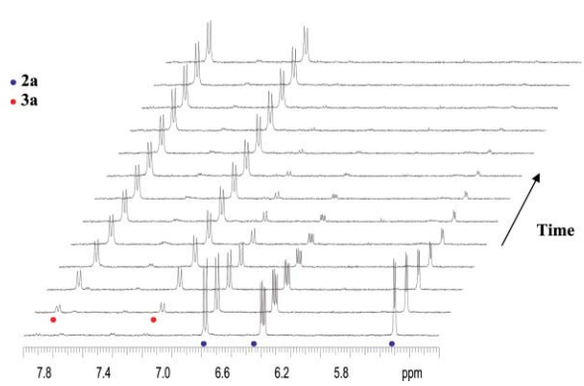
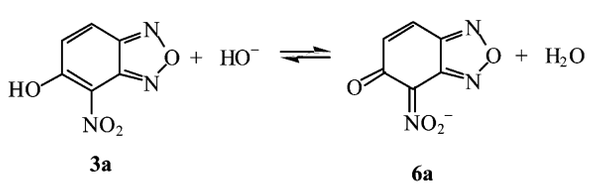
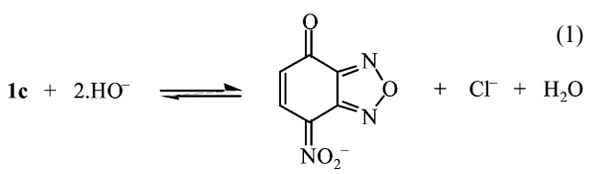


Fig. 1 ^{1}H NMR array showing the reaction of **1a** (0.01 mol dm^{-3}) with one equivalent of NaOD in 80 : 20 (v/v) D_2O–[$^2H_6$] DMSO. Spectra recorded at 10 minute intervals.



Integration of the bands shown in Fig. 1 allowed the calculation of a value for k_{ox} of (6 ± 0.3) × 10^{-4} s^{-1} under the conditions used.

The rapid formation of **2c** from 7-chloro-4-nitrobenzofurazan was followed by a slower reaction giving bands at δ 8.42 and 6.08 attributed to **5**, the product of hydroxydechlorination. Interestingly with a 1 : 1 ratio of **1c** : OH^- the spectrum after 24 hours contained bands due to **5** and the reformed parent in equal proportion. This indicates that **5** is sufficiently acidic to exist as its conjugate base **7** so that the stoichiometry is given by eqn. (1). In the presence of a five fold excess of hydroxide the eventual products are **7** and a species showing a singlet at δ 5.55 in the proton NMR spectrum. It is possible that this band may be due to H6 of **3c** formed by oxidation of the initially formed 5-hydroxy adduct, although we have no confirmation of this.



(1)

7

The spectra of **1d** and **1e** in the presence of excess base show the slow but quantitative conversion to the substitution product **5** together with bands due to the displaced methoxide or phenoxide respectively.

The reaction of **1b** differed from that of **1a** in that rapid formation of the 5-adduct was followed by slower conversion to the 7-adduct. The two isomers may be distinguished principally from the shift of H6 which is expected [11,12,15] to have a higher value in the 5-adduct than in the 7-adduct. In the presence of one equivalent of deuteroxide the rate constant for the isomerisation, obtained using the variation with time of NMR intensities was (2.2 ± 0.2) × 10^{-4} s^{-1}. After twenty four hours two new NMR bands, doublets J 9.6 Hz, were present in the spectrum and grew with time at the expense of those due to **4b**. In the presence of a five-fold excess of base this change occurred more rapidly so that after several hours the only observable species had a spectrum with doublets, J 9.6 Hz at δ 5.74 and 8.11. These bands are close, but not identical, in position to those of 7-hydroxy-4-nitrobenzofurazan **5** and are thus reasonably attributed to **5b** formed by oxidation of **4b**. A further very slow change was observed in which the bands due to **5b** were gradually replaced by bands at δ 6.08 and 8.42 indicating the eventual reduction of the *N*-oxide function of **5b** to give **5**.

UV-visible studies

Measurements were made in water without DMSO with parent concentrations 1 × 10^{-4} mol dm^{-3}. For each reactant **1** a rapid reaction with hydroxide was observed giving changes in the spectrum consistent with equilibration with the corresponding 5-hydroxy adduct. Absorption maxima and molar absorption coefficients are in Table 1. Kinetics were measured, using the stopped-flow method, with hydroxide concentrations in large excess of the parent or in buffered solutions. Under these conditions first order kinetics were observed and it was found that rate constants, k_{fast}, were related to hydroxide concentrations by eqn. (2)

$$k_{fast} = k_5[HO^-] + k_{-5} \quad (2)$$

Values of k_5 were obtained from the slopes of linear plots of k_{fast} *versus* hydroxide concentration in the range 0.001–0.1 mol dm^{-3}.

In some cases, notably with **1a**–**c**, the intercepts of such plots were too small to give precise values of k_{-5}. Here measurements were also made in buffer solutions, pH 9–10, where the reverse, k_{-5}, term in eqn. (2) was dominant. Representative data are given in Tables 2 and 3 and results are summarised in Table 4. Values of K_5 calculated as k_5/k_{-5} or using absorbance data at completion of the reaction are in good agreement.

For each reactant much slower reactions were observed following equilibration with the 5-adducts. In the case of **1b** the UV changes are consistent with the processes shown in Scheme 2 involving formation of the 7-adduct followed by its oxidation to **5b**. The spectra in Fig. 2, with [HO^-] 6.3 × 10^{-5} mol dm^{-3}, show the rapid but incomplete formation of the 5-adduct followed by the slower formation of the 7-adduct with λ_{max} 323 nm. A very much slower reaction resulted in increases in absorbance at 470 nm consistent with formation of the 7-hydroxy-4-nitro derivative, **5b**. The latter process was inconveniently slow for kinetic measurements, but rate constants for the isomerisation to the 7-adduct were measured. The rate expression for formation of **4b** by the intermolecular pathway is eqn. (3). The corresponding expression for intramolecular isomerisation is eqn. (4). The form of these two equations is similar so that it is

$$k_{slow} = \frac{k_7[HO^-]}{1 + K_5[HO^-]} + k_{-7} \quad (3)$$

$$k_{slow} = \frac{K_5 k_{intra}[HO^-]}{1 + K_5[HO^-]} + k_{-intra} \quad (4)$$

not possible to distinguish between the two mechanisms purely from the kinetics. Assuming the intermolecular route the data in Table 2 yield values of k_7 1.6 ± 0.1 dm^3 mol^{-1} s^{-1} and k_{-7} (2.0 ± 0.1) × 10^{-5} s^{-1}. These lead to a value for K_7 (= k_7/k_{-7}) of (8.0 ± 0.5) × 10^4 dm^3 mol^{-1}. This is *ca.* 15 times larger than the value of 5400 dm^3 mol^{-1} found for K_5, indicating the higher thermodynamic stability of the 7-adduct. The sum of K_5 + K_7 values calculated from absorbance data is (8.5 ± 0.5) × 10^4 dm^3 mol^{-1} in good agreement with the kinetic data.

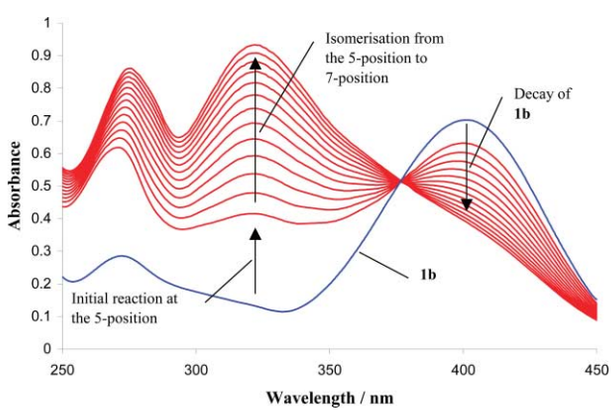


Fig. 2 UV-visible spectra of **1b**, 1 × 10^{-4} mol dm^{-3}, in water, and in a buffer solution with [HO^-] 6.3 × 10^{-5} mol dm^{-3} initially and at 15 minute intervals.

In the case of **1a** in the pH range 9.5–11 very slow increases in absorbance at 323 nm were observed consistent with formation of the 7-hydroxy isomer. However, the absorbance changes were small and in the more alkaline solutions, where reactions were faster, there was interference from a fading reaction presumed to be oxidation to give **3a**. Hence a quantitative treatment was not attempted, but results allowed an estimate for k_7 of 0.2 ± 0.1 dm^3 mol^{-1} s^{-1}. It is noteworthy that the behaviour here is different from that occurring under the NMR condition when relatively rapid oxidation precedes isomerisation.

For **1c**–**e** the slow reaction resulted in formation of a strong absorption at 465 nm consistent with the substitution product

Table 2 Kinetic and equilibrium results for the reaction of **1b** with hydroxide ions in water at 25 °C

$[HO^-]$/- 10^{-3} mol dm^{-3}	k_{fast} [a]/ s^{-1}	k^{calc}_{fast} [b]/s^{-1}	Abs- (323nm)$_{fast}$ [c]	K_5 [d]/ 10^3 dm^3 mol^{-1}	k_{slow} [e]/ 10^{-5} s^{-1}	k^{calc}_{slow} [f]/10^{-5} s^{-1}	Abs (323nm)$_{slow}$ [g]	$K_5 + K_7$ [h]/ 10^4 dm^3 mol^{-1}
0.019					5.0	4.8	0.67	8.5
0.023					4.8	5.2	0.71	7.9
0.037					5.9	6.9	0.84	8.9
0.047	0.013	0.013						
0.058					7.7	9.0	0.91	8.6
0.063	0.015	0.015	0.27	5.6				
0.087					11.4	11.5	0.97	9.0
0.110	0.019	0.018	0.35	4.7	13.3	13.0		
0.166	0.023	0.021	0.55	6.8	17	16		
0.65			0.82	5.8	24	25		
1.0	0.077	0.070						
2.5	0.14	0.16						
5.0	0.30	0.30						
10	0.56	0.60						
25	1.48	1.49						
50	2.94	2.96						

[a] Colour forming reaction at 327 nm. [b] Calculated from eqn. (2) with k_5 59dm^{-3} mol^{-1} s^{-1} and k_{-1} 0.011 s^{-1}. [c] At completion of formation of 5-adduct. [d] Calculated as Abs/(1.04 − Abs)$[OH^-]$. [e] Colour forming reaction at 323 nm. [f] Calculated from eqn. (3) with k_7 1.6 dm^3 mol^{-1} s^{-1}, k_{-7} 2.0×10^{-5} s^{-1} and K_5 5400 dm^3 mol^{-1}. [g] At completion of adduct forming reactions. [h] Calculated as Abs/(1.09 − Abs)$[OH^-]$.

Table 3 Kinetic data for reaction of **1e** with hydroxide ions in water at 25 °C

$[HO^-]/10^{-3}$ dm^3 mol^{-1} s^{-1}	k_{fast} [a]/s^{-1}	k^{calc}_{fast} [b]/s^{-1}	k_{slow} [c]/10^{-4} s^{-1}	k_{slow} [d]/10^{-4} s^{-1}
0.063			0.12	0.11
0.10			0.18	0.17
0.16			0.23	0.26
2.0	0.054	0.051	1.3	1.5
4.0	0.080	0.081	1.7	1.8
7.0	0.125	0.126	2.1	2.1
10.0	0.165	0.171	2.2	2.2
20	0.31	0.32	2.4	2.3
40	0.62	0.62		
60	0.90	0.92	2.5	2.4
80	1.24	1.22		
100	1.52	1.52	2.5	2.5

[a] Fading reaction at 380 nm. [b] Calculated from eqn (2) with k_5 15 dm^3 mol^{-1} s^{-1} and k_{-5} 0.021 s^{-1}. [c] Colour forming reaction at 465 nm. [d] Calculated from eqn (5) with k_7 0.18 dm^3 mol^{-1} s^{-1} and K_5 720 dm^3 mol^{-1}.

Table 4 Summary of rate and equilibrium data [a] in water at 25 °C

	k_5/dm^3 mol^{-1} s^{-1}	k_{-5}/s^{-1}	K_5/dm^3 mol^{-1}	k_7/dm^{3}mol^{-1} s^{-1}	$k_{-7}/10^{-5}$ s^{-1}	K_7/dm^3 mol^{-1}	$k_{ox}/10^{-4}$ s^{-1}
1a	30	0.011	2700	0.2 ± 0.1	—	—	6.0 [b]
1b	59	0.011	5400	1.6	2.0	80000	
1c	92	0.015	6100	0.08	—	—	—
1d	8.0	0.06	130	0.25	—	—	—
1e	15	0.021	720	0.18	—	—	—
TNB [c]	46	13.5	3.4	—	—	—	—

[a] Unless otherwise stated values are ±5%. [b] In 80 : 20 (v/v) D_2O–[$^2H_6$]DMSO. Oxidation of 5-adduct [c] Data from ref. 26 for reaction at unsubstituted ring positions of TNB. Data have not been statistically corrected.

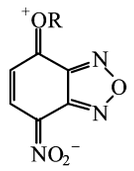
5. There was no evidence for accumulation of the intermediate on the substitution pathway so that nucleophilic attack will be rate limiting leading to eqn (5).

$$k_{slow} = \frac{k_7\left[HO^-\right]}{1 + K_5\left[HO^-\right]} \qquad (5)$$

Representative data, for **1e**, are in Table 3 and values are collected in Table 4. It is worth noting that for **1e** only, in solutions with pH > 11, the spectra indicate formation, in competition with **5**, of a species with λ_{max} 307 and 362 nm. Values of k_7 here were obtained in less alkaline solutions. It is possible that the process observed is oxidation of the 5-adduct to give **3c**. The ^{1}H NMR spectrum shows a singlet consistent with this interpretation.

Comparisons

For each parent **1** initial reaction occurs *ortho* to the nitro group to give the 5-hydroxy adduct. Results are summarised in Table 4. The introduction of the *N*-oxide function in **1b** results in a twofold increase in thermodynamic stability similar in magnitude to that observed in the corresponding methoxide adducts [10] and sulfite adducts.[15] The larger K_5 value for **1c** than for **1a** is consistent with the inductive effect expected for chlorine, σ_m 0.37, *meta* to the reaction site.[27] However, the considerably lower values of K_5 for **1d** and **1e** indicate that the inductive effects of the methoxy group, σ_m 0.08, and phenoxy group,[27] σ_m 0.25, are eclipsed by the effect of resonance stabilisation, **8**, present in the parent which will be largely lost in the negatively charged adducts. The changes in value of K_5 reflect changes in value of rate constants k_5 and k_{-5}.



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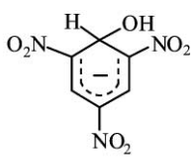
It is of interest to compare values of equilibrium constants with that for the reaction of hydroxide with 1,3,5-trinitrobenzene (TNB) to give **9**. The data in Table 4 indicate a ratio for **1a** : TNB of *ca*. 1000. This is similar to the ratio of 6000 observed[15] when sulfite is the nucleophile, again in water as solvent. Corresponding ratios are 6 for reaction with methoxide in methanol[10] and <1 for reaction with amines[16] in dimethyl sulfoxide (DMSO). These differences in the relative stabilities of the adducts are likely to be largely attributable to the effects of solvation. Water is known to solvate localised charges very effectively.[28,29] Hence the adducts **2** where negative charge is localised on the 4-nitro group will be well solvated in water, while **9**, where negative charge is more delocalised, will be less well solvated. This contrasts with the situation in methanol and particularly DMSO which will solvate large polarisable anions, such as those formed from TNB, more effectively than anions with localised negative charge.[1]



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Reaction at the 7-position

The usual behaviour observed with 4-nitrobenzofurazan and its derivatives is that while nucleophilic attack at the 5-position is kinetically preferred the 7-adducts are thermodynamically more stable. Methoxide ions[10] and nitrogen[16] and carbon[18] nucleophiles follow this pattern. With hydroxide ions too our NMR and UV results indicate that **1b** behaves similarly with a value of 15 for the ratio of K_7 : K_5. For **1a** there is evidence in dilute solutions in water for isomerisation from **2a** to **4a** although in more concentrated solutions in water–DMSO the oxidation of the 5-adduct precludes the possibility of isomerisation. The kinetic preference for 5-attack, but the thermodynamic preference for 7-attack has been explained[16,18] in terms of the extent of charge delocalisation present in the adducts. The greater delocalisation in the 7-adducts resulting in greater stability but a higher kinetic barrier for formation. The presence of a nitro group *para* to the reaction centre may also stabilise the 7-adducts.

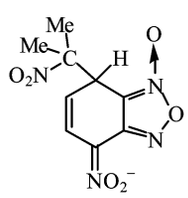
In the case of **1c**–**e** hydroxide attack at the 7-position is the rate-limiting step in the substitution pathway. The results in Table 4 show that values of k_7 decrease in the order **1b** > **1d** ~ **1a** ~ **1e** > **1c**. However the spread in values is relatively small so that the value for attack at the unsubstituted 7-position of **1a** is only three times higher than that for attack at the 7-chloro position of **1c**. It seems likely that there is a compromise between the increased polarisation of the C–Cl bond in **1c** which should encourage reaction, and the repulsive interaction between the electronegative entering and leaving groups which slows nucleophilic attack.[1,13] With **1d** and **1e** ground state stabilisation of the reactant will also be a factor. Steric effects are unlikely to be important in these nitrobenzofurazans. It is of interest to compare the data with those for substitution in the corresponding trinitrobenzene derivatives where steric effects will be important; here the relative rate of attack[26,30] at carbons carrying H, OMe, OPh and Cl is 1 : 0.11 : 0.10 : 0.027.

The considerably higher value of k_7 obtained for **1b** than for **1a** deserves comment. Only in the case of **1b** is there the possibility, as indicated in Scheme 2, for intramolecular rearrangement from the 5-adduct to the 7-adduct by a Boulton–Katritzky mechanism.[15,31] In the case of the corresponding sulfite adducts[15] isomerisation from 5- to 7-adduct occurs one hundred times more rapidly in the benzofuroxan than in the benofurazan derivative and there is definite evidence for the intramolecular pathway. In the present case the evidence is less clear cut. However, assuming an intramolecular pathway and using eqn. (4), leads to values for k_{intra} 3.0×10^{-4} s^{-1} and k_{-intra} 2.0×10^{-5} s^{-1}. Interestingly the value for k_{intra} is similar to that, 5.7×10^{-4} s^{-1}, reported for rearrangement of the sulfite adduct,[15] adding to the likelihood that in the case of the hydroxide adduct too rearrangement occurs intramolecularly.

Oxidation of hydroxide adducts

The NMR results suggest that in 80 : 20 D_2O–[$^2H_6$] DMSO the 5-hydroxy adduct of **1a** is oxidised to give 5-hydroxy-4-nitrobenzofurazan, **3a**. Confirmation was provided by the identity of NMR and mass spectra with an independently synthesized sample. In the case of **1b** rearrangement from the 5- to the 7-hydroxy adduct occurs before oxidation. The product 7-hydroxy-4-nitrobenzofuroxan, **5b**, eventually suffers reduction to the corresponding furazan, **5**, under the reaction condition. There is some, but less convincing, evidence for the oxidation of the 5-hydroxy adduct of **1c**.

Recently the oxidation has been reported[18] of the adducts, such as **10**, formed from a series of mono- and di-nitrobenzofurazans and the corresponding furoxans by reaction with 2-nitropropenide, a carbon nucleophile. It was found that the ease of oxidation of the adducts, as judged by $E°$ value, increased with decreasing electron deficiency in the six-membered ring. For example adducts from 4-nitrobenzofuroxan were more easily oxidised than those from 4,6-dinitrobenzofuroxan. In general there was an inverse relationship between the ease of oxidation and the thermodynamic stabilities of the adducts. However, 4-nitrobenzofurazan adducts were more easily oxidised than TNB adducts despite the higher equilibrium constants for their formation.



10

Our results show the relatively easy oxidation of the hydroxy adducts of **1a** and **1b**. They suggest that oxidation is faster in the more concentrated solutions, 0.01 mol dm^{-1}, used in NMR studies than in the dilute, 1×10^{-4} mol dm^{-3}, solutions used in UV work. The oxidative pathway is not clear, it may be that the DMSO used in the NMR studies plays an active role in the oxidation process, which appears to be quantitative. Also we have not investigated the effects of the exclusion/addition of oxygen. Clearly we do not have a good mechanistic understanding of the oxidation process, but believe that the results are worth reporting at this time.

Experimental

Parent compounds **1** were available from previous work.[15] Distilled water was boiled to expel carbon dioxide and was subsequently protected from the atmosphere. Solutions of known hydroxide concentration were prepared either by dilution of AnalaR sodium hydroxide solution or by using borax or

biocarbonate buffers. The pH values of buffer solutions were checked using a Jenway 3020 pH meter.

^{1}H NMR spectra were measured with Varian Mercury 200 MHz, Bruker AM-400 MHz, Varian VXR-400 MHz or Varian Inova 500 MHz spectrometers. UV-vis spectra and kinetic measurements were made at 25 °C with a Perkin Elmer Lambda 2 spectrophotometer, a Shimadzu UV-2101 PC spectrophotometer or an Applied Photophysics SX-17 MV stopped-flow instrument. Reported rate constants are the mean of several determinations and are precise to ±5%.

5-Hydroxy-4-nitrobenzofurazan was prepared in three steps starting from commercially available 6-chlorobenzofuroxan. Reaction at room temperature for 1 hour in 2 : 1 (v/v) ethanol–water with 1.2 equiv. of hydroxylamine and 2.4 equiv. of potassium hydroxide gave 5-chlorobenzofurazan.[6] The ethanol was removed at reduced pressure and the remaining solution was steam distilled to yield the product as a pale yellow solid, 40% yield; ^{1}H NMR δ[$^2H_6$ DMSO] 7.65 (dd, H6), 8.18 (d, H7), 8.37 (d, H4), (J_{67} 9.6 Hz, J_{46} 1.6 Hz). Nitration was achieved by reaction with 1.1 equiv. of fuming nitric acid in sulfuric acid at 0 °C. The mixture was poured into ice and the precipitated 5-chloro-4-nitrobenzofurazan was recrystallised from ethanol, 20% yield; ^{1}H NMR δ[$^2H_6$ DMSO] 7.95 (d, H6), 8.55 (d, H7) (J_{67} 9.6 Hz); MS (EI) *m*/*z* 199 $C_6H_2N_3O_3{}^{35}Cl$, 201 $C_6H_2N_3O_3{}^{37}Cl$. 5-Hydroxy-4-nitrobenzofurazan was produced in solution[13] by reaction of 5-chloro-4-nitrobenzofurazan with excess sodium deuteroxide in 80 : 20 v/v D_2O–[$^2H_6$] DMSO. In this medium the ^{1}H NMR spectrum showed bonds δ 6.80 (d) and 7.70 (d), *J* 10 Hz. Negative electrospray mass spectrometry showed the expected peak at *m*/*z* 180 $(M - H)^-$.

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