Formation and stability of zwitterionic complexes between nitrobenzofuroxans and amines †

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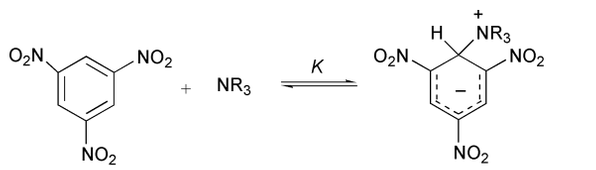
Received (in Cambridge, UK) 1st December 2000, Accepted 30th May 2001
First published as an Advance Article on the web 3rd July 2001

Spectroscopic and kinetic investigations on the reactions between 4,6-dinitrobenzofuroxan, 4-nitrobenzofuroxan and tertiary and secondary amines (*i.e.* 1,4-diazabicyclo[2.2.2]octane, quinuclidine, 1,8-diazabicyclo[5.4.0]undec-7-ene and piperidine) indicate the formation of zwitterionic or anionic complexes. The equilibrium between zwitterionic and anionic complexes is discussed (for reaction with piperidine) on the basis of ^{1}H NMR spectral data, which indicate the presence of anionic complexes arising from the zwitterionic complex by a fast proton departure. The stability and the rate of formation of title complexes are discussed and compared to similar reactions of 1,3,5-trinitrobenzene.

Introduction

In previous papers we reported[1–4] spectroscopic and kinetic investigations on the reactions between 1,3,5-trinitrobenzene (TNB) and tertiary amines (1,4-diazabicyclo[2.2.2]octane (DABCO), quinuclidine (QN), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), 1,5-diazabicyclo[4.3.0]non-5-ene (DBN), according to Scheme 1. This equilibrium is of interest because it is a simple

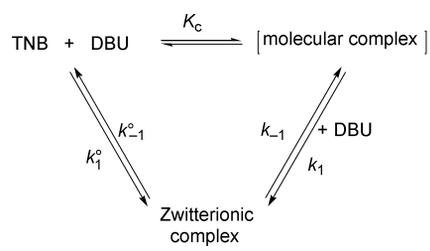


Scheme 1

model of nucleophilic neutral nitrogen attack on an activated sp^2 aromatic carbon atom, without complications arising from the presence of protons (on the entering nitrogen) and of the leaving group, as in usual amino-dehalogenation reactions *via* the S_NAr pathway. In S_NAr reactions in apolar aprotic solvents both the proton and leaving group are claimed to depart[5,6] in a rate determining equilibrium, which may be base catalyzed.

The reaction between TNB and DBU in toluene[4] provided an instance of self-catalytic kinetic behaviour without leaving group and proton departure. We explained[4,7] the common kinetic feature (k_{obs} increases on increasing $[amine]_0$, value of initial concentration of the amine) by the presence of a donor–acceptor equilibrium preceding the nucleophilic attack as reported in Scheme 2.

However, while primary and secondary amines were extensively investigated in S_NAr reactions, tertiary amines have been rarely studied because of their low reactivity. Tertiary amines are usually considered unreactive and they are used as catalysts in the reaction of primary or secondary amines to perform the "base catalysis". In fact, tertiary amines can compete with



Scheme 2

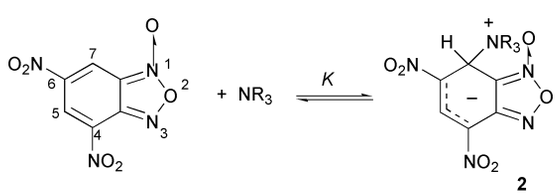
primary or secondary amines in complexing the electrophilic substrate and/or reacting with it.

With the aim of collecting more information on the equilibrium of formation of zwitterionic complexes with amines, we now report some data on the reactions between nitrobenzofuroxans and various tertiary amines and, for a comparison, with piperidine (PIP).

Results and discussion

Formation of complexes

When solutions of 4,6-dinitrobenzofuroxan (DNBF) and DABCO, QN or DBU are mixed in DMSO a red colour quickly develops, according to the formation of a σ complex, as reported in Scheme 3.



NR$_3$ = (a) DABCO, (b) QN, (c) DBU, (d) PIP

Scheme 3

In principle, alternative structures to complexes **2** (such as complexes in the 5 position) cannot be completely ruled out. However, all the NMR evidence reported in the literature[6,8] agree with nucleophilic addition to the 7 position of DNBF. There are reports[9] in the literature of the probable formation of the complex **2a** between DABCO and DNBF.

A careful investigation of the DNBF–amine reaction mixtures by ^{1}H NMR in DMSO-d_6 in comparison with the H_2O–

† The IUPAC name for benzofuroxan is [1,2,5]benzoxadiazole 1-oxide.

 DOI: 10.1039/b009650o

Table 1 Selected ^{1}H NMR spectral data[a] in DMSO-d_6 of derivatives of 2,7-dinitrobenzofuroxan (DNBF) and of 4-nitrobenzofuroxan (NBF)

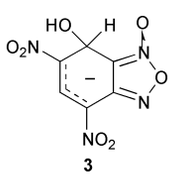
Compound	H-5	(Signal multiplicity, *J*/Hz)	H-6	(Signal multiplicity, *J*/Hz)	H-7	(Signal multiplicity, *J*/Hz)
DNBF	9.05				9.37	
2a (**4a**)	8.64; 8.69				6.84; 6.86	
2c (**4c**)	8.75; 8.64				5.35; 5.60	
2d	8.64				6.20–6.40	(m)
3	8.67	(d, *J* 0.7)			5.93	(m)
NBF	8.71	(d, *J* 7.2)	7.64	(dd, *J* 7.2 and 8.8)	8.23	(d *J* 8.8)
6c	8.40	(d, *J* 9.1)	6.94	(dd, *J* 9.9 and 9.1)	5.67	(d, *J* 9.9)
6d	7.12	(d, *J* 10.3)	5.10	(dd, *J* 10.3 and 4.3)	4.64	(d, *J* 4.3)
7[b]	6.98	(d, *J* 10.2)	5.37	(dd, *J* 10.2 and 4.2)	5.26–5.32	(m)
10	8.54	(d, *J* 9.3)	6.74	(d, *J* 9.3)		
11[c]	8.41	(d, *J* 9.7)	6.00	(d, *J* 9.7)		
12[c]	8.12	(d, *J* 9.6)	5.51	(d, *J* 9.6)		
13	8.60	(d, *J* 8.9)	6.50	(d, *J* 8.9)		

[a] Internal reference TMS. All signals are singlets unless otherwise indicated; all ratios [substrate] : [nucleophile] are 1 : 1, except in the case of the formation of **10** and **13** (see Experimental section). [b] See Experimental section. [c] Interchangeable.

OH^- mixtures reveals that the major signal at $\delta = 5.9$ ppm is related to complex **3**.[10,11] Complex **3** (in DMSO-d_6) is present in variable and large amounts (from 40 to 60%) in comparison with the signals related to the zwitterionic complexes **2**. Traces of water and the equilibrium of Scheme 4 are responsible for the

Scheme 4

formation of **3**. Attempts to eliminate water from DMSO-d_6 failed and consequently the complex **3** remains in the reaction mixtures.



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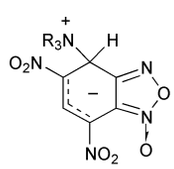
In the reaction mixtures of DNBF and amine, together with signals related to **3**, there are other signals which may be attributed to complexes **2**. Selected ^{1}H NMR data for DNBF and related complexes **2**, **3** are collected in Table 1.

In principle, two other isomers[12] **4** and **5** of **2** and **3** respec-



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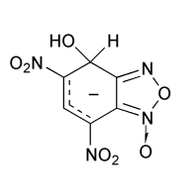
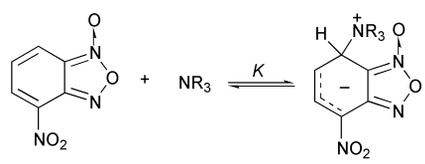


5

tively, may be present in the reaction mixtures. Compound **4** may arise from an interconversion[13] like that recently reported by Terrier[14] through a dinitroso derivative. For DABCO and DBU only, the ^{1}H NMR spectrum shows signals which may be related to the presence of both isomers **2a** and **4a** (and **2c**, **4c**), see Table 1.

In THF, the addition of an NR_3 solution to a DNBF solution produced dark red tars, with the exception of DABCO for which a red solid separated (mp 207–209 °C). This solid is soluble in DMSO. ^{1}H NMR inspection of this solution in DMSO-d_6 showed the presence of signals related to both **2a** and **4a** and to other unidentified compounds. In THF no evidence of the formation of complexes with water was obtained.

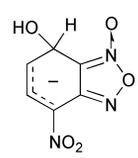
To provide a comparison with a secondary aliphatic amine, data describing the complex between DNBF and piperidine, together with data concerning the formation of complexes **6** of 4-nitrobenzofuroxan (NBF) with amines, (according to Scheme 5) are also shown in the same table.



NR_3 = (c) DBU, (d) PIP **6**

Scheme 5

In the case of the less reactive NBF, the complex with OH^- (**7** and related isomer) is observed only when NaOH is added to solutions (in DMSO-d_6) of NBF. The solutions of **6** obtained from NBF and DBU or PIP did not show the presence of complex **7** and its isomeric form **8** (see Experimental section).



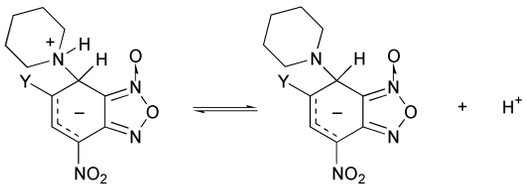
7, **8**

Under our experimental conditions, DABCO and QN are unreactive toward NBF in both the DMSO and THF solvents. ^{1}H NMR inspection of the reaction mixtures of NBF with amines, did not show the presence of isomeric forms of complexes **6**.

The data in Table 1 allow some interesting observations. All signals related to the proton bonded to the sp^3 carbon atom (H-7) of the reported complexes are shifted considerably downfield compared to the starting DNBF or NBF as required by the change of hybridization (from sp^2 to sp^3). These signals are sensitive to the nature of group bonded to the sp^3 carbon.[6,15,16]

For complexes with DNBF, when the positive charge of the zwitterionic complex is localized on the nitrogen of the amine moiety, there is a large deshielding of the proton bonded to the sp^3 carbon atom (for compounds **2a**, **4a**, $\delta = 6.8$) compared to the corresponding proton of **2c** in which the positive charge is supported by two nitrogen atoms ($\delta = 5.6$).

In the case of the piperidine there are two main possibilities as reported in Scheme 6. The H-7 signal of the complex between piperidine and DNBF (**2d**) falls at $\delta = 6.3$ (see Table 1) and it is intermediate between the corresponding proton signals of **2a** and **2c**. In the case of complexes **6d** between NBF and piperidine, the H-7 signal falls at $\delta = 4.6$ and is strongly shielded compared to the signal of **6c** ($\delta = 5.7$). The differences seen in H-7 chemical shift indicate that in **6d** (and probably in **2d**) the

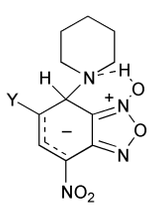


Scheme 6

presence of a positive charge on the nitrogen of the amine moiety is very improbable. Moreover, the H-7 chemical shifts of **6d** ($\delta = 4.6$) are at a lower field compared to the corresponding proton of complex **7** ($\delta = 5.3$). The inductive electronic effect[17] of OR group (R = H, Me) is higher (as measured by σ^I values = 0.25) than that of NR_2 (R = H, Me, $\sigma^I = 0.1$). Both σ^I values are much lower than that of the positively charged nitrogen (σ^I of $^+NMe_3$ group is 0.99).

The spectrum of the complex between TNB and butylamine in DMSO shows a ^1H NMR signal at $\delta = 5.7$ for the proton bonded to the sp^3 carbon atom: this proton is more shielded than the proton of the complex with OH^- ($\delta = 6.1$) and this feature is in accordance with the presence of a neutral nitrogen atom. Moreover, the signal at $\delta = 4.6$ is a sharp doublet and no coupling with N–H proton was observed.

Even if these observations involve some assumptions and simplifications, for complexes between DNBF, NBF and piperidine, the ^1H NMR data indicate the presence of anionic species arising from the zwitterionic complex through fast proton departure in an equilibrium like that in Scheme 6. Alternatively, we suggest structure **9**, because the same chemical shift is also recorded when less piperidine is present than DNBF and NBF. Thus the proton abstraction may arise from an intermolecular H bonding interaction rather than from the amine present in the reaction mixtures.



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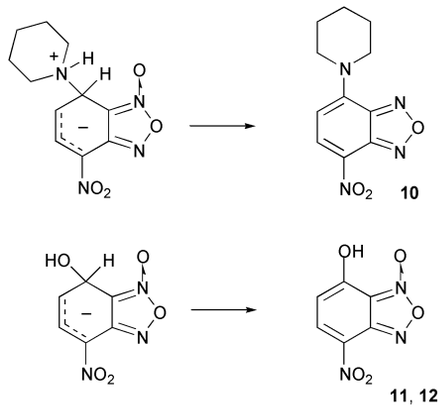
In conclusion, there is evidence that the proton is strongly separated from the nitrogen of the secondary amine moiety, in both complexes **2d** and **6d**. This confirms our statement[18] to explain "anomalous" kinetic features (the so-called base-catalysis[5]) by the formation of a complex substrate–nucleophile preceding the nucleophilic attack in a reaction pathway like that in Scheme 2. This is an alternative to the mechanism involving proton and leaving group departure after the formation of the zwitterionic complex.

Further reactions

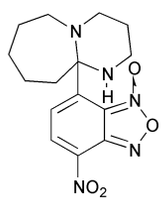
The reactions between NBF and PIP or ^-OH give products of apparent hydrogen substitution[19] and of deoxygenation, as reported in Scheme 7. The reactions shown in Scheme 7 occur in the presence of an excess of nucleophile (see Experimental section) and they are slower than the formation of the starting complexes.

DBU quickly affords the zwitterionic complex **6c** and slowly shows a neutral compound (yield = 40%) to which structure **13** may be tentatively assigned on the basis of NMR spectral data (see Experimental section).

If the formation of compounds **10**, **11**, **12** and **13** arises from the zwitterionic complexes, it seems that this transformation involves the departure of a hydride ion caused by an oxidation



Scheme 7



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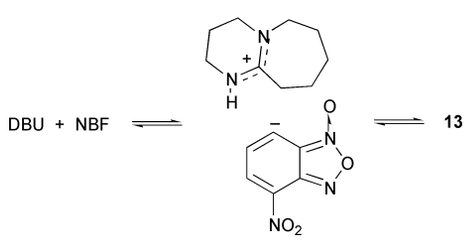
reaction. The nucleophilic substitution of nuclear hydrogen is not a common process since the hydride ion is a very poor leaving group. Formation of **10** may be a specific dismutation of the complex, involving the N–O group of the furoxan ring.[19] Formation of compound **11** (and **13**) is a less clear reaction but appears to be a "spontaneous" oxidation of the zwitterionic complex which contains oxidizing groups,[6] while the formation of **10** is an intramolecular oxidation–reduction reaction. Compound **13** may arise from a different reaction from that of the oxidation of the σ complex. Scheme 8 shows a possible pathway



Scheme 8

which involves starting compounds (DBU and NBF) in an acid–base-like equilibrium followed by C–C bond formation which may be contemporaneous with the proton donating equilibrium.

In conclusion, even though some of the reported structures cannot be unambiguously identified, our data and interpretation agree with the accumulated evidence of the literature.

UV/vis spectroscopic measurements

Inspection of the reaction mixtures in DMSO by the UV/vis spectrophotometric method (data are reported in Table 2) confirms the observation made by ^1H NMR spectroscopy: **3** is the main product of the reactions between DNBF and tertiary amines. UV/vis spectral data for DNBF–amine mixtures are very close to those obtained with DMSO–water which may be explained by the presence of only complex **3**.

On the other hand, UV/vis spectroscopic data obtained in THF for DNBF and amines may be related to the presence of the equilibrium of Scheme 3. Spectral data are unaffected by the addition of a few percent (2–5% by vol.) of water. UV/vis spectral data for NBF and amines are shown in Table 2 and they are related (in every case) to the presence of the equilibrium of Scheme 6.

Under the experimental conditions in which no complex with water (or with OH^-) is detectable in the reaction mixtures, we calculated the stability constant of the complexes using Benesi Hildebrand treatment[20] of the UV/vis spectrophotometric data. Table 3 shows the K values obtained together with some other statistical data.

For reactions between DNBF and DABCO or QN in THF it was possible to obtain kinetic data (k_{obs} in s^{-1}) which are shown in Table 4. From these data, the usual equation [eqn (1)][21]

$$k_{obs} = k_{-1} = k_1[R_3N]_0 \quad (1)$$

(obtained under the experimental conditions $[R_3N]_0 \gg [DNBF]_0$ where $[\ ]_0$ represents the initial concentration values of the reagents) allows calculation of k_1 and k_{-1} values which are shown in Table 5. DABCO data are corrected for the statistical factor.

Table 2 Selected UV/vis spectroscopic data of complexes between DNBF or NBF and amines. $[DNBF]_0$ and $[NBF]_0 = 1 \times 10^{-4} - 2 \times 10^{-4}$ (mol dm^3); $[Amine]_0 \geq 1 \times 10^2$

Substrate	Solvent	Amine	λ_{max}/nm	ε/dm^{-3} mol^{-1} cm^{-1}
DNBF	DMSO	—	447	1.97×10^4
DNBF	DMSO	DABCO	471	2.90×10^4
DNBF	DMSO	QN	472	2.87×10^4
DNBF	DMSO	DBU	475	2.87×10^4
DNBF	DMSO	PIP	474	2.87×10^4
DNBF	THF	—	419	6.40×10^3
DNBF	THF	DABCO	430	1.14×10^4
DNBF	THF	QN	430	1.51×10^4
DNBF	THF	PIP	459	2.26×10^4
NBF	DMSO	—	410	7.66×10^3
NBF	DMSO	DABCO[a]	409	7.71×10^3
NBF	DMSO	QN[a]	409	7.31×10^3
NBF	DMSO	DBU	346	1.46×10^4
NBF	DMSO	PIP	349	1.55×10^4
NBF	THF	—	407	7.65×10^3
NBF	THF	DABCO[a]	406	7.50×10^3
NBF	THF	DBU	349	8.83×10^3
NBF	THF	PIP	337	1.43×10^4

[a] No reaction was observed.

Stability of complexes: comparison of substrates

Clearly, the data in Table 3 confirm[6] that in THF the stability of complexes follows the order $K_{DNBF} > K_{NBF}$.

We saw no evidence of reactions between NBF and DABCO or QN. The only direct comparison between DNBF and NBF is for complexes with piperidine in THF. The ratio $K_{DNBF}/K_{NBF} = 350$ strongly favours the dinitro derivative compared to the mononitro derivative.

A comparison of these data with the same data for 1,3,5-trinitrobenzene (TNB) enables some interesting observations. In THF, the DNBF–DABCO complex is slightly more stable than the TNB–DABCO[1] complex ($K_{DNBF}/K_{TNB} = 4$). The stability order in DMSO, TNB < NBF was seen[22] for complexes with aliphatic primary or secondary amines. In DMSO, the stability order TNB > NBF is observed for complexes with DBU, but the inverse order TNB < NBF is observed with PIP. In DMSO the stabilisation of the negative charge by the nitro groups is less important than in THF, since the more polar solvent (DMSO) is more able to assist the charge separation than the less polar solvent (THF).

Comparison of amines

The data in Table 3, related to DNBF, indicate that the piperidine complex is more stable than the complex with DABCO or QN. The DABCO complex is slightly less stable than the QN complex. The basicity of DABCO is slightly lower[23] than that of QN. An explanation is that the second nitrogen atom of DABCO depresses by an electron-withdrawing inductive effect the lone pair availability of the first nitrogen atom.

The K value for the complex between piperidine and NBF moderately agrees with the K value calculated from kinetic data.[22] The complexes between NBF and piperidine or DBU are similar in stability. In DMSO the complex with piperidine is more stable than that of DBU $K_{PIP}/K_{DBU} = 3.5$. THF favours DBU compared to piperidine: $K_{PIP}/K_{DBU} = 0.25$. Clearly both complexes are more stable in DMSO than in THF: $K_{DMSO}/K_{THF} = 350$ and 25 for piperidine and DBU respectively. For the complex between TNB and DABCO the increase of solvent polarity produces a small increase in complex stability. $K_{DMSO}/K_{THF} = 1.7$. The tertiary amine shows a complex which is less affected by the variation of the polarity of the medium than the

Table 3 Stability of the zwitterionic complexes between DNBF (or NBF) and amines

$[DNBF]_0$[a]	Amine	Solvent	K[b]	λ[c]	ε[d]	n[e]	R[f]
1.00×10^{-4}	QN	THF	3.69×10^2	430	1.78×10^4	6	0.999
2.95×10^{-4}	QN	THF	4.62×10^2	505	8.50×10^2	11	0.990
2.78×10^{-4}	DABCO	THF	1.52×10^2[g]	436	1.37×10^4	7	0.991
1.57×10^{-4}	DABCO	THF	2.28×10^2[g]	430	1.58×10^4	6	0.989
1.00×10^{-4}	PIP	THF	7.08×10^3	457	3.50×10^4	7	0.995
$[NBF]_0$[a]							
1.20×10^{-4}	PIP	DMSO	6.86×10^3	348	1.82×10^4	10	0.982
8.90×10^{-5}	DBU	DMSO	1.94×10^3	346	1.94×10^4	11	0.995
1.28×10^{-4}	PIP	THF	1.70×10	336	2.07×10^4	8	0.982
1.50×10^{-4}	DBU	THF	7.89×10	349	1.01×10^4	6	0.985
TNB							
	DABCO	THF	4.1×10[h]				
	DABCO	DMSO	6.5×10[h]				
	QN	DMSO	1.2×10^2[h]				
	DBU	DMSO	1.8×10^4[h]				
	PIP	DMSO	2.1×10^3[i]				

[a] mol dm^{-3}. [b] mol dm^{-3}. [c] Used in the determinations. [d] dm^3 mol^{-1} cm^{-1}. [e] Number of points. [f] Correlation coefficient. [g] Corrected by statistical factor. [h] Ref. 1. [i] Ref. 22.

Table 4 k_{obs} values (s^{-1}) for reactions between DNBF and QN and DABCO in THF at 25 °C

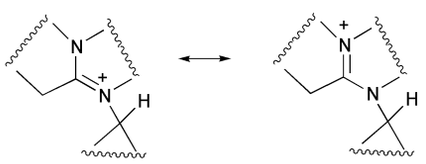
$10^3[QN]_0$/mol dm^{-3}	2.29	2.75	3.20	3.23	3.66	3.70	4.12	4.16	4.30
$10^3k/s^{-1}$	1.49	1.64	1.76	1.80	1.84	1.85	1.90	1.90	1.90
$10^3[QN]_0$/mol dm^{-3}	4.62	5.98	6.77	7.33	8.37	8.46	9.02	9.57	10.8
$10^3k/s^{-1}$	1.95	2.15	2.34	2.40	2.77	2.80	3.01	3.19	3.43
$10^3[DABCO]_0$/mol dm^{-3}	0.659	0.791	0.923	1.05	1.18	1.45			
$10^3k/s^{-1}$	2.90	2.95	3.20	3.59	3.60	4.07			

Table 5 k_1 and k_{-1} values [see eqn. (1)] for the formation of zwitterionic intermediates between amines and DNBF

Amine	Solvent	k_1[a]	k_{-1}[b]	K[c]	n[d]	R[e]
QN	THF	$(2.15 \pm 0.08) \times 10^{-1}$	$(1.01 \pm 0.01) \times 10^{-3}$	213	18	0.989
DABCO[f]	THF	$(7.8 \pm 1) \times 10^{-1}$	$(1.83 \pm 0.01) \times 10^{-3}$	426	6	0.981

[a] In s^{-1} mol^{-1} dm^3. [b] In s^{-1}. [c] In mol dm^{-3}. [d] Number of points. [e] Correlation coefficient. [f] Corrected by statistical factor.

complexes with protic amines. We explained this conclusion by considering that the charge separation of the zwitterionic complex may be "self-assisted". In accordance with this, DMSO is more able, with respect to THF, to stabilise the complex with piperidine than the complex with DBU. This difference may be explained by the self-stabilising ability of the DBU moiety in **2** by delocalising the positive charge on the second nitrogen atom (see Scheme 9): DBU showed a more stable complex with TNB[1]



Scheme 9

than with DABCO or QN. DBU is an enamine in which the availability of the lone pair of the sp^2 nitrogen atom is enhanced by the electron donating effect of the sp^3 nitrogen atom in the α position.

In **2c**, the carbon bearing the two nitrogen atoms is positive in character and may allow the formation of compound **13** from the zwitterionic complex **2c** (see Scheme 9), in an alternative pathway to that of Scheme 8.

Kinetic data

In contrast to that previously reported for complexes with RN_3 and TNB,[1] in THF, the k_1 value of DABCO is slightly higher (see Table 5) than the k_1 value of QN: $k_1^{DABCO}/k_1^{QN} = 3.6$. However, the differences between DABCO and QN are not very high for both substrates (TNB and DNBF). In THF, the stability of complex DNBF–DABCO, calculated as k_1/k_{-1}, is slightly higher than that of QN: $K_{DABCO}/K_{QN} = 2$. Probably the greater or lesser efficiency of DABCO with respect to QN also depends on the interactions with solvents. As expected (even if the difference in solvent does not allow a full comparison), piperidine is ≈10^5 times more reactive than DABCO or QN; the k_1 value of the nucleophilic attack of piperidine toward DNBF[20] is 1.8×10^4 s^{-1} mol^{-1} dm^3.

The data in Table 5 show that the nucleophilic attack of DABCO on DNBF is much faster than the same attack on TNB[1] ($k_1 = 1.5 \times 10^{-4}$ s^{-1} mol^{-1} dm^3, k_{-1} 3.7 for the complex TNB–DABCO in THF) $k_1^{DNBF}/k_1^{TNB} = 5 \times 10^3$. By considering the kind of tertiary amines used, this ratio may be free from steric requirements and it is an indication of the actual high electrophilicity of dinitrobenzofuroxan derivatives with respect to other strongly electron-deficient substrates, such as 1,3,5-trinitrobenzene.

We emphasize that the data for tertiary amines are related to the stability of the zwitterionic complexes, without conjectured equilibria involving the parent σ-anionic complex. Furthermore, the k_1 values are a measure of simple nucleophilic attack, without complications arising from the departure of protons bonded to the amine, or of the leaving group bonded to the substrate.

Experimental

CAUTION: the Meisenheimer complexes and all the compounds isolated in this work are explosives. Consequently, preparations were carried out only on a small scale (<1 g) behind suitable protective shielding. 4,6-Dinitrobenzofuroxan (DNBF) is a powerful high explosive with a sensitivity level comparable to that of dry picric acid.

General

The ^1H and ^{13}C NMR spectra were recorded with a Varian Gemini 300 spectrometer at 300 and 75.46 MHz, respectively. The ^1H NMR spectra were recorded in DMSO-d_6 because of the low solubility of the starting furoxans and of the complexes in other solvents. Chemical shifts were measured in δ (ppm) with reference to the solvent (7.27 and 77.0 ppm for $CDCl_3$ and 2.6 ppm and 39.5 ppm for DMSO-d_6 for ^1H NMR and ^{13}C NMR, respectively). J Values are given in Hz. Signal multiplicities were established by DEPT experiments. MS spectra were recorded at an ionisation voltage of 70 eV by a VG 7070 E spectrometer. Chromatographic purifications (FC) were carried out on columns of silica gel (Merck, 230–400 mesh) at medium pressure. Melting points were measured on a Büchi 535 apparatus and are uncorrected. UV/vis spectra were recorded on Perkin-Elmer Lambda 5 and Lambda 12 spectrophotometers. Kinetic runs were performed by following the appearance of the reaction product at 560 nm. The reproducibility of k_{obs} values was ±4%.

Materials. NBF was prepared from benzofuroxan (Sigma-Aldrich) according to Green's method,[24] mp 142–143 °C (lit.,[24] 143 °C). In the same way, DNBF (**1**) was prepared by nitration of benzofuroxan[25] and recrystallized from ethyl acetate, mp 172–173 °C (lit.,[25] 172 °C). DABCO (Fluka) was purified by crystallization from anhydrous toluene then by sublimation *in vacuo*. QN (Fluka) was purified by sublimation. THF (Carlo Erba) was dried over sodium and distilled then, immediately before use, redistilled from $LiAlH_4$, under a nitrogen atmosphere.[26] DMSO was purified using the usual procedures.[26] DMSO-d_6 was treated with molecular sieves (Carlo Erba 4 Å).

Study of complex formation by ^1H NMR spectroscopy

An accurately weighed amount of amine was poured into a ^1H NMR tube and was dissolved by adding $(CD_3)_2SO$. To this solution, an accurately weighed amount of NBF or DNBF was added. The ^1H NMR spectrum was recorded at various intervals but generally as rapidly as possible at the start of the reaction and then at progressively longer intervals as the reaction

proceeded. The system was monitored until no further change could be detected in the recorded spectrum. In addition to the signals shown in Table 1, the spectrum of **6c** showed other signals of unidentified compounds. Although radical incursion can hardly be excluded, there was no evidence of the presence of paramagnetic species in the reaction mixtures.

Reaction between NBF and NaOH: synthesis of 7-hydroxy-4-nitro[1,2,5]benzoxadiazol-1-ium-1-olate

This reaction was performed in an NMR tube and monitored by ^{1}H NMR spectroscopy: 0.1 mmol of H_2O was added to 1.0 mL of DMSO-d_6, then 0.1 mmol of NaH was added. After the evolution of hydrogen, due to the reaction between NaH and water, 0.09 mmol of NBF was added. The ^{1}H NMR obtained spectra showed the following sets of signals.

7: δ_H (300 MHz; DMSO-d_6) 5.26–5.32 (1H, m, 7-H), 5.37 (1H, dd, *J* 10.2 and 4.2, 6-H), 6.98 (1H, d, *J* 10.2, 5-H).

8: δ_H (300 MHz; DMSO-d_6) 5.54–5.64 (1H, m, 7-H), 6.40 (1H, dd, *J* 10.4 and 4.6, 6-H), 6.73 (1H, d, *J* 10.4, 5-H).

11: δ_H (300 MHz; DMSO-d_6) 6.00 (1H, d, *J* 9.7, 6-H), 8.41 (1H, d, *J* 9.7, 5-H).

12: δ_H (300 MHz; DMSO-d_6) 5.51 (1H, d, *J* 9.6, 6-H), 8.12 (1H, d, *J* 9.6, 5-H).

In Table 1 adduct **7** was reported as the more stable complex.

Signals of compounds that were assigned as structures **7** and **8** (interchangeable)[27] were present in the spectrum recorded after two minutes from the NBF addition. However these signals gradually decayed with time (10 min for **8** and about 20–25 min for **7**), as new signals of **11** and **12** appeared. These signals were stable for a long time (about 60 h), but at this time other minor signals became evident.

Reaction between NBF and piperidine: synthesis of 4-nitro-7-piperidino[1,2,5]benzoxadiazole (10)

A total of 0.434 g (5.09 mmol) of piperidine was added to a solution of 0.127 g (0.70 mmol) of NBF in 10 mL of dimethyl sulfoxide. After 30 min the reaction mixture was treated with water and extracted with dichloromethane. The organic layer was dried over anhydrous Na_2SO_4. After filtration and removal of the solvent *in vacuo*, the FC of the residue (eluent: CH_2Cl_2) gave a red–purple solid, identified as 4-nitro-7-piperidino-[1,2,5]benzoxadiazole (4-nitro-7-piperidinobenzofurazan)[28] (62%), mp 167–168 °C, lit.,[28] 169 °C. δ_H (300 MHz; DMSO-d_6) 1.80–1.90 (6H, m, NCH_2CH_2 and $NCH_2CH_2CH_2$), 4.18–4.30 (4H, m, NCH_2), 6.74 (1H, d, *J* 9.3, 6-H), 8.54 (1H, d, *J* 9.3, 5-H). δ_C (75.46 MHz; DMSO-d_6) 23.44, 25.85, 51.01, 103.13, 120.08, 136.38, 144.74, 145.01, 145.18; *m/z* 248 (M^+, 99%), 202 (7), 192 (9), 171 (100), 116 (17).

Reaction between NBF and DBU: synthesis of 4-nitro-7-{octahydropyrimido[1,2-*a*]azepin-10a(6*H*)-yl}[1,2,5]benzoxadiazol-1-ium-1-olate (13)

A total of 0.238 g (1.57 mmol) of DBU was added to 0.143 g (0.79 mmol) of NBF in 12 mL of DMSO. Immediately after mixing, a dark red colour developed. The reaction mixture was poured into an ice–water mixture and extracted with dichloromethane. After drying ($MgSO_4$) and elimination of the solvent, the crude reaction product was chromatographed (silica gel, eluent acetone–CH_2Cl_2 1 : 9). A dark red solid, identified as 4-nitro-7-{octahydropyrimido[1,2-*a*]azepin-10a(6*H*)-yl}[1,2,5]-benzoxadiazol-1-ium-1-olate (**13**) (0.105 g, 40%) was obtained. The main mass of this solid melted at 151–153 °C and the residue gradually darkened and melted at 207–230 °C with the evolution of a gas (Found: C, 54.00; H, 5.80; N, 20.95, $C_{15}H_{19}N_5O_4$ requires C, 54.05; H, 5.75; N, 21.01%). δ_H (300 MHz; DMSO-d_6) 1.58–1.82 (6H, m), 1.88–2.20 (2H, m), 2.48–2.56 (2H, m), 3.44–3.52 (6H, m), 6.50[a] (1H, d, *J* 8.9, 6-H), 8.60[a] (1H, d, *J* 8.9, 5-H), 9.55 (1H, br s, NH, disappears after addition of D_2O); δ_C (75.46 MHz; DMSO-d_6) 23.0 (t), 26.4 (t)[a], 28.4 (t), 29.2 (t), 36.5 (t), 41.1 (t)[a], 44.9 (t), 48.5 (t), 99.1 (d)[a], 120.7 (s)[a], 134.0 (s), 137.9 (d)[a], 144.4 (s), 145.1 (s), 174.8 (s). δ_H (300 MHz; $CDCl_3$) 1.60–1.85 (6H, m), 1.85–2.00 (2H, m), 2.55–2.70 (2H, m), 3.35–3.45 (2H, m), 3.45–3.70 (4H, m), 6.16 (1H, d, *J* 8.8, 6-H), 8.30 (1H, br s, NH, disappears after addition of D_2O), 8.44 (1H, d, *J* 8.8, 5–H); δ_C (75.46 MHz; $CDCl_3$) 23.4 (t), 26.9 (t), 28.6 (t), 29.9 (t), 37.1 (t), 40.4 (t)[a], 45.5 (t), 50.1 (t), 98.3 (d)[a], 123.5 (s)[a], 135.2 (s), 136.2 (d), 144.2 (s), 144.5 (s), 177.5 (s).

[a]These signals appeared broad in the spectra recorded at 25 °C, and became more sharp recording the spectra at 50 °C; this fact can be an indication that the molecule is subject to rotational constraints.

m/z 333 (M^+, 13%), 256 (6), 220 (100), 203 (24), 126 (50), 114 (54), 98 (48).

Acknowledgements

The authors thank the Ministero dell'Università e della Ricerca Scientifica e Tecnologica, the Consiglio Nazionale delle Ricerche (CNR, Roma) and the University of Bologna (funds for selected research topics 1999–2001).

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