PERKIN 2

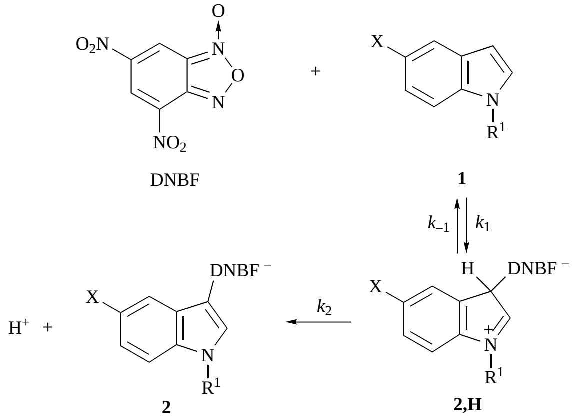
Electrophilic heteroaromatic substitutions: the coupling of 4,6-dinitrobenzofuroxan† with 3-methoxythiophene in H_2O–Me_2SO mixtures

Elyane Kizilian, François Terrier,* Alain-Pierre Chatrousse, Khalid Gzouli and Jean-Claude Hallé*

Laboratoire SIRCOB, EP CNRS 102, Department of Chemistry, University of Versailles,
45, Avenue des Etats-Unis, 78035 Versailles Cedex, France

Rate constants have been determined in three aqueous Me_2SO mixtures for the S_EAr substitution of 3-methoxythiophene (5) by super-electrophilic 4,6-dinitrobenzofuroxan (DNBF). The absence of a significant dependence of the rates of reactions on the hydrogen or deuterium labelling at C_α of the thiophene ring indicates that electrophilic addition (k_1^{DNBF}) of DNBF at this position is the rate-limiting step of the substitution process. A notable increase in the k_1^{DNBF} rate constant with increasing water content of the solvent mixtures is observed. This trend is consistent with the idea that the addition step proceeds through a highly dipolar transition state where the development of negative charge in the DNBF moiety is concomitant with that of a partial positive charge in the thiophene ring. Assuming that the behaviour of 5 fits the rate-equilibrium, Brønsted-type relationship previously established for the coupling of DNBF with nitrogen heterocycles, a $pK_a^{H_2O}$ value of −6.5 may be estimated for the protonation of 5 in aqueous solution. Interestingly, a similar estimate is obtained when the reactivity of 5 is compared with that of an homogeneous series of enol methyl ethers. Despite a low carbon basicity, comparable to that of a rather weakly basic enol ether, 5 appears to be one of the most reactive thiophene compounds toward electrophilic reagents.

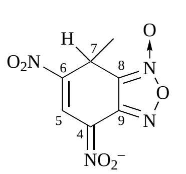
Despite its neutral character, 4,6-dinitrobenzofuroxan (DNBF) is a more powerful electrophile than the proton and also a much stronger electrophile than the *p*-nitrobenzenediazonium cation.[1,2] This makes DNBF an important probe to assess the reactivity of weakly nucleophilic carbon centres.[3–8] A number of aromatics (phenols and related aryl ethers) whose C-protonation is known to occur only in superacid media[9,10] have thus been found to react under mild experimental conditions with DNBF, affording quantitatively stable anionic carbon-bonded σ-adducts which are formally the products of S_EAr substitution of the aromatic donor.[3,4,8] Similar substitutions occur with anilines or π-excessive heteroaromatics like pyrrole, indole, thiophene or furan derivatives.[1,2,3–8,12–14] Coupling to weakly activated double bonds as well as with weak nitrogen or oxygen bases is a process that is also much more readily achieved with DNBF than with any other electrophilic aromatic.[3,4,15–19]



(1)

a R^1 = H, X = CN
b R^1 = H, X = Br
c R^1 = H, X = Cl
d R^1 = X = H
e R^1 = H, X = Me
f R^1 = H, X = OMe
g R^1 = Me, X = H

with DNBF$^-$ =



In our laboratory, we have recently carried out a kinetic study of the coupling of DNBF with a number of indole and pyrrole derivatives whose pK_a values for C-protonation in aqueous solution range from −6 (5-cyanoindole) to 3.75 (2,4-dimethyl-3-ethylpyrrole).[1,2] In all instances, the rates of formation of the expected C-adducts **2** and **4** according to reaction (1) or (2) were found to be essentially unaffected by the H- or D- labelling at the reactive C_β or C_α positions of the parent heterocycles. This showed that electrophilic attack by DNBF to give the Wheland-type intermediates **2,H** or **4,H** was the rate determining step of the reactions, allowing us to derive the second-order rate constants k_1^{DNBF} for this process directly from the experimental rate data. Interestingly, the k_1^{DNBF} values were found to increase regularly with increasing C-basicity and satisfactory linear Brønsted-type correlations were obtained when the log k_1^{DNBF} values measured in each of the solvents studied were plotted against the $pK_a^{H_2O}$ values measured for protonation of the parent indole or pyrrole compounds in aqueous solution.[2]

Assuming to a first approximation that the above correlations are appropriate to describe the nucleophilic behaviour of any structurally related π-excessive aromatic substrate, measurement of a k_1^{DNBF} rate constant may then serve to assess the carbon basicity of compounds whose pK_a^{CH} values cannot be measured through classical equilibrium studies. This approach has actually proved to be successful in estimating the C-basicity of 3,4-diaminothiophene, providing a better understanding of the strong enaminic character of this derivative.[13]

In this paper, we report a kinetic investigation of the coupling of DNBF with 3-methoxythiophene **5** and 3-methoxy[2-$^2H_1$]-thiophene (**5d**) to give the very stable anionic C-bonded adduct **6** according to reaction (3) in various H_2O–Me_2SO mixtures. As will be seen, our results allow us to quantify the C_α carbon basicity of **5**, and support the view that this heterocycle exhibits some vinyl ether behaviour.[20–22]

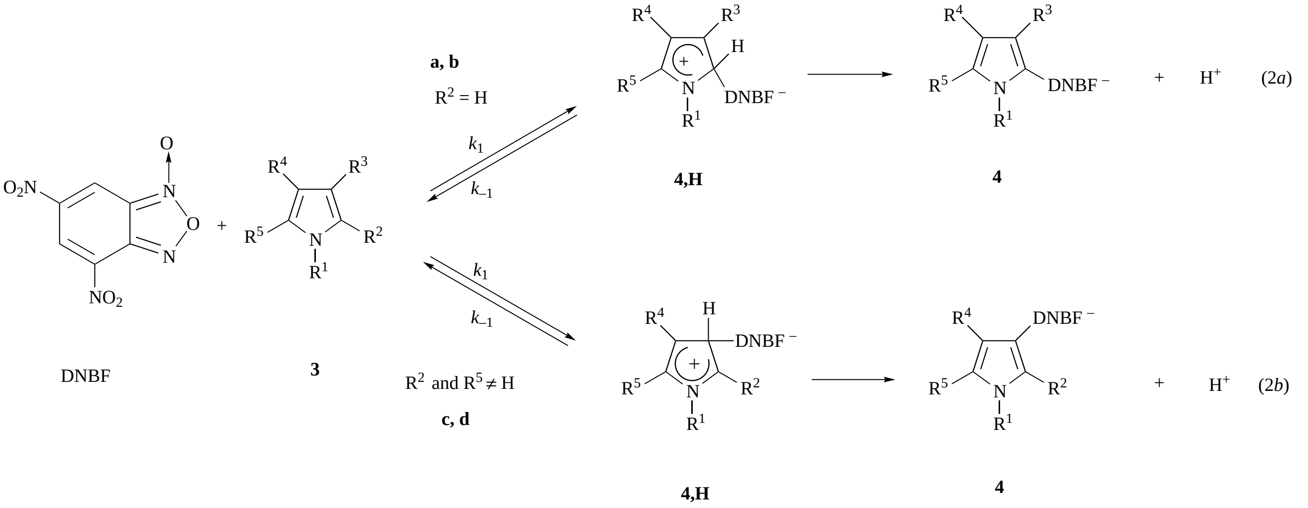
---

† 4,6-Dinitrobenzofurazan *N*-oxide.

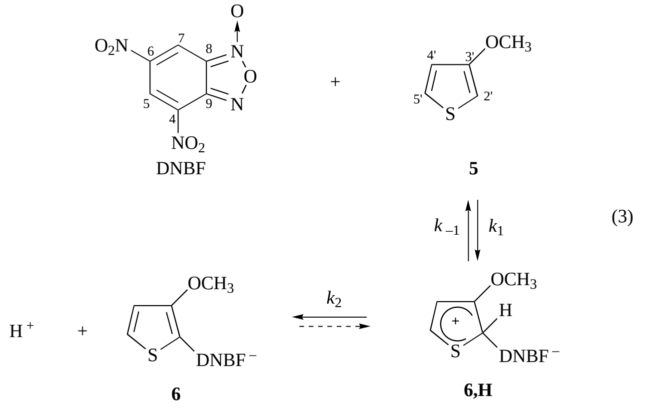
Table 1 ^{1}H NMR data for thiophenic σ-adducts and related parent substrates[a]

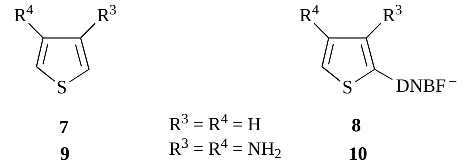
Compounds	$\delta H^{2'}$	$\delta H^{3'}$	$\delta H^{4'}$	$\delta H^{5'}$	δH^5	δH^7	δOCH_3	Coupling constants, J/Hz
DNBF	—	—	—	—	9.26	8.94	—	
3-MT **5**	6.55	—	6.76	7.40	—	—	3.73	$J_{H2'H4'}$ 1.47; $J_{H2'H5'}$ 3.31; $J_{H4'H5'}$ 5.15
σ-Adduct **6**	—	—	6.94	7.33	8.62	5.63	3.71	$J_{H4'H5'}$ 5.52
Thiophene **7**	7.47	7.11	7.11	7.47	—	—	—	
σ-Adduct **8**	—	6.98	6.93	7.36	8.66	5.70	—	$J_{H3'H4'}$ 3.52; $J_{H3'H5'}$ 1.34; $J_{H4'H5'}$ 5.11
3,4-DAT **9**	5.83	—	—	5.83	—	—	—	
σ-Adduct **10**	—	—	—	5.73	8.61	5.73	—	

[a] Relative to internal $SiMe_4$; solvent $(CD_3)_2SO$.



a $R^1 = R^2 = R^3 = R^4 = R^5 = H$
b $R^1 = Me; R^2 = R^3 = R^4 = R^5 = H$
c $R^1 = R^3 = R^4 = H; R^2 = R^5 = Me$
d $R^1 = R^2 = R^5 = Me; R^3 = R^4 = H$
[see reaction (1) for the meaning of $DNBF^-$]





Results

Structural studies

The reaction of DNBF with **5** was first studied in Me_2SO where a mixture of equimolar amounts of the two reagents was found to afford quantitatively the adduct **6** in its acid form. The most representative NMR data are summarized in Tables 1 and 2, together with those for the parent substrates. Also given for comparison is similar information previously reported for related σ-complexes, notably the adducts **8** and **10** derived from the interaction of DNBF with unsubstituted thiophene **7** and 3,4-diaminothiophene **9**.[13] Especially noteworthy in the ^{1}H NMR spectra of **6** is the H^7 resonance which appears at δ 5.63, being in the range commonly found for C-bonded DNBF σ-adducts, *e.g.* δ 5.73 for **10** and 5.70 for **8**.[3,8,13] Also in accord with previous observations showing that the chemical shift of the H^5 proton located between the two nitro groups of the negatively charged DNBF moiety depends very little on the nature of the C-bonded structure,[6] the H^5 resonance for **6** (δ 8.62) is essentially the same as those found for the related thiophene adducts **8** and **10** as well as the indole or pyrrole adducts **2** or **4**, *e.g.* δ 8.71 for **4**.[1,2,13] Regarding the ^{13}C NMR data, a noteworthy result is that the substitution of **5** by DNBF results in a significant low-field shift of the C-2′ carbon of the thiophene ring ($\Delta\delta \approx 18$ ppm). This result is fully consistent with the fact that a negatively charged DNBF structure still exerts a considerable $-I$ effect.[23]

As described in the Experimental section, the adduct **6** could also be isolated as a crystalline sodium salt, allowing conformation of its structure by mass spectrometry. Also, the visible spectrum of **6** was typical of a C-bonded σ-adduct of DNBF: $\lambda_{max} = 485$ nm, $\varepsilon = 33\,000$ dm^3 mol^{-1} cm^{-1} in a 50% H_2O–50% Me_2SO (v/v) mixture.

Kinetic studies

The kinetics of reaction (3) were investigated at 25 °C under pseudo-first-order conditions with respect to 3-methoxythiophene as the excess component in three aqueous dimethyl sulfoxide mixtures, namely 70–30, 50–50 and 30–70 (v/v) H_2O–Me_2SO, because of the poor solubility of **5** in aqueous solution. In each of these solvent mixtures, the ionic strength was kept

Table 2 ^{13}C NMR data for thiophenic σ-adducts and related parent substrates[a]

Compounds	$\delta C^{2'}$	$\delta C^{3'}$	$\delta C^{4'}$	$\delta C^{5'}$	δC^4	δC^5	δC^6	δC^7	δC^8	δC^9	δOCH_3
DNBF	—	—	—	—	136.72	126.52	144.83	120.80	116.64	145.02	—
3-MT **5**	97.19	158.42	119.13	125.34	—	—	—	—	—	—	57.11
σ-Adduct **6**	115.12	155.16	117.18	123.35	109.60	130.17	126.54	31.09	113.11	148.43	59.03
3,4-DAT **9**	95.85	139	139	95.85	—	—	—	—	—	—	—
σ-Adduct **10**	107.30	138.71	136.36	94.04	109.32	130.05	127.43	31.95	114.04	148.22	—

[a] Relative to internal $SiMe_4$; solvent $(CD_3)_2SO$.

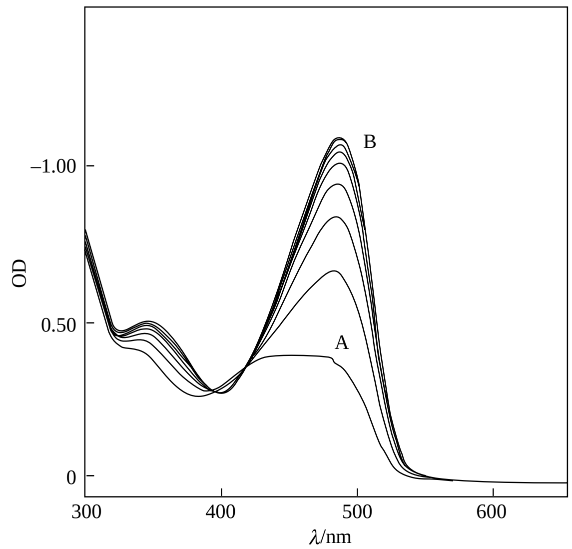
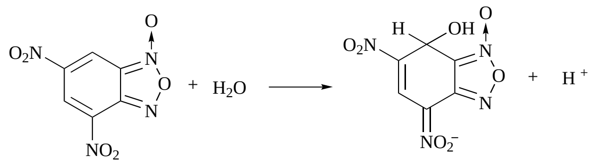


Fig. 1 Visible spectra showing the progressive formation of the σ-adduct **6** (curve B) from the reaction of DNBF (3.5×10^{-5} mol dm^{-3}) and 3-methoxythiophene (10^{-2} mol dm^{-3}) in 30% H_2O–70% Me_2SO ($T = 25$ °C; $[H^+] = 0.1$ mol dm^{-3}): first scan (A) at $t = 20$ s; other scans after 60 s intervals.

constant at 0.5 mol dm^{-3} (NMe_4Cl). Experiments were carried out by mixing 0.2 or 0.1 mol dm^{-3} HCl solutions of DNBF (*ca.* 3×10^{-5} mol dm^{-3}) with equal volumes of solutions of **5** (4×10^{-3}–6×10^{-2} mol dm^{-3}) in the cell of a conventional spectrophotometer. Under the final acid conditions (0.1 or 0.05 mol dm^{-3} HCl), no interference between reaction (3) and the formation of the hydroxide adduct **11** according to reaction (4)



(4)

DNBF 11

occurred[23] and only one process corresponding to the quantitative formation of the adduct **6** was observed in all cases. A typical experiment is illustrated in Fig. 1 which shows the set of UV–VIS absorption spectra describing the progressive conversion of the reagents to the adduct **6**. That the process was very clean is confirmed by the presence of two isosbestic points at $\lambda = 390$ and 415 nm. In particular, no appreciable hydrolysis of the methoxy group **5** appeared to take place under our experimental conditions.[21] In all experiments, pseudo-first-order rate constants k_{obs} for the formation of **6** were readily determined from the time dependence of the observed absorbance variations at $\lambda = 480$ nm.

Based on reaction (3), the general expression for k_{obs}, as derived under the assumption that the zwitterion **6,H** is a low concentration ('steady-state') intermediate,[1,2] is given by eqn. (5).

$$k_{obs} = \frac{k_1 k_2}{k_{-1} + k_2}[\mathbf{5}] = k[\mathbf{5}] \qquad (5)$$

Table 3 Second-order rate constants k ($= k_1^{DNBF}$) and kinetic deuterium isotope effects for DNBF addition to 3-methoxythiophene **5** in aqueous Me_2SO mixtures[a]

	30% Me_2SO	50% Me_2SO	70% Me_2SO
k_H/dm^3 mol^{-1} s^{-1}	0.72	0.49	0.162
k_D/dm^3 mol^{-1} s^{-1}	0.62	0.50	0.153
$\frac{k_H}{k_D}$	1.16	0.98	1.05

[a] $T = 25$ °C; %Me_2SO by volume.

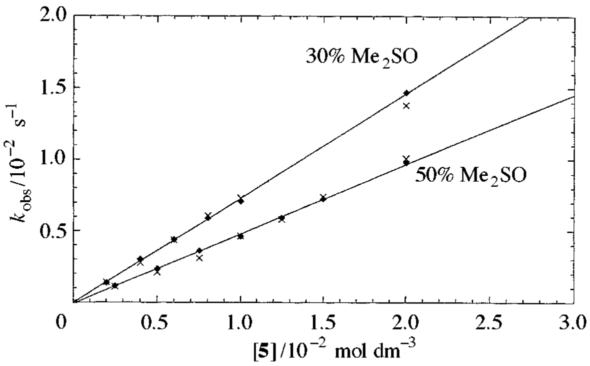


Fig. 2 Effect of pH and of the concentration of 3-methoxythiophene on the rate of σ-complexation of DNBF in 70–30 H_2O–Me_2SO (v/v) and 50–50 H_2O–Me_2SO (v/v) [× HCl 0.1 mol dm^{-3}; ◆ HCl 0.05 mol dm^{-3}].

In accordance with eqn. (5), excellent straight lines with zero intercepts were obtained in the three solvent mixtures studied when the k_{obs} values were plotted *vs.* the 3-methoxythiophene concentration, with no evidence for a pH dependence of the rates (Fig. 2). This confirmed the absence of reaction (4), as well as of any process like the hydrolysis of **5**, and made the determination of the second-order rate constants k from the slopes of the k_{obs} *vs.* [**5**] plots straightforward. The results are given in Table 3 which also includes the rate constants k deduced from experiments carried out with 2-deuteriated-3-methoxythiophene (**5d**) under similar experimental conditions.

Discussion

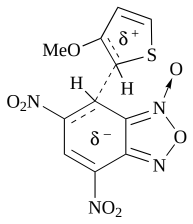
Table 3 shows that the second-order rate constant k for formation of the anionic adduct **6** according to reaction (3) is essentially unaffected by the hydrogen or deuterium labelling at C_α of **5** in the three H_2O–Me_2SO mixtures studied. The deuterium kinetic isotope effects are close to unity: the k_H/k_D ratio is equal to 1.16, 0.98 and 1.05 in 30%, 50 and 70% Me_2SO, respectively. This result indicates that elimination of the proton from the zwitterionic intermediate **6,H** is rapid and therefore, that electrophilic attack by DNBF is the rate-determining step in the formation of **6** ($k_2 \gg k_{-1}$). It follows that the rate constants k may in all cases be safely equated to the second-order rate constants k_1^{DNBF} for DNBF addition to **5**.

Interestingly, Table 3 also shows that the k_1^{DNBF} rate constants are notably sensitive to the solvent polarity, the observed reactivity sequence being 70–30 H_2O–Me_2SO > 50–50 H_2O–

Table 4 Carbon nucleophilicity of various π-excessive heterocycles towards DNBF in 50% H_2O–50% Me_2SO and 70% H_2O–30% Me_2SO[a]

Compound	$pK_a^{H_2O\,b}$	$k_1^{DNBF_{50/50}}$/dm^3 mol^{-1} s^{-1}	$k_1^{DNBF_{70/30}}$/dm^3 mol^{-1} s^{-1}
3-Methoxythiophene	−6.5[c]	0.49	0.72
5-Cyanoindole	−6.00	1.14	2.8
5-Bromoindole	−4.30, −4.57	46.2	125
5-Chloroindole	−4.53	52	125.5
Pyrrole	−3.79	520	650
Indole	−3.46	555	1110
5-Methylindole	−3.30	2100	5000
5-Methoxyindole	−2.90	2613	5260
N-Methylindole	−2.32	3510	6980
1,2,5-Trimethylpyrrole	−0.49	24 000	48 800
3,4-Diaminothiophene	1.5–2[d]	9×10^5	—

[a] $T = 25$ °C. [b] $pK_a^{H_2O}$ values of pyrroles and indoles taken from ref. 26–29. [c] This work. [d] Ref. 13.



12

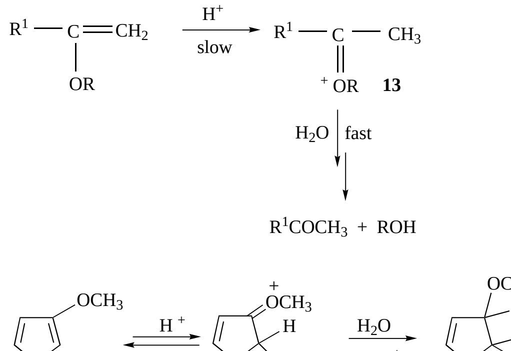
Me_2SO > 30–70 H_2O–Me_2SO. This trend is fairly consistent with the idea that the rate-limiting step of the reaction involves the strongly dipolar transition state **12**, where the development of negative charge in the DNBF moiety is concomitant with that of a partial positive charge in the thiophene ring. Based on classical theories of solvent effects,[24,25] such a transition state is expected to be especially stabilized in highly aqueous solvents.

Table 4 compares the k_1^{DNBF} value for **5** with similar rate constants previously measured for the coupling of DNBF at C_α of 3,4-diaminothiophene **9** as well as at C_α or C_β of some pyrrole and indole derivatives. As can be seen, 3-methoxythiophene is the least reactive heterocycle, being 10^6 times less prone to complexation than its 3,4-diaminothiophene analogue, and also 3–4 times less reactive than the least basic indole, *i.e.* 5-cyanoindole ($pK_a = -6.00$).

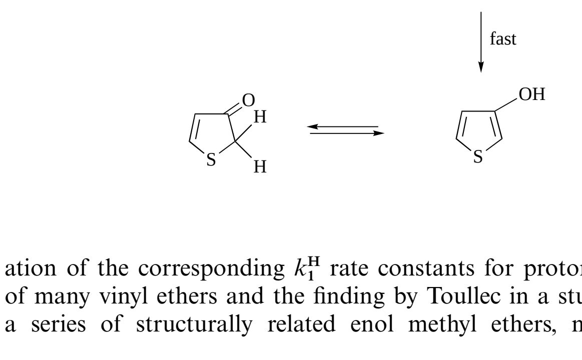
In the case of 5-X substituted indoles and some pyrrole compounds, linear Brønsted-type relationships were obtained on plotting the log k_1^{DNBF} values measured in each of the solvents studied *vs.* the pK_a values measured for C-protonation of these heterocycles in aqueous solution.[26–29] Assuming that these correlations will also fit the nucleophilic behaviour of related π-excessive aromatic and heteroaromatic substrates, we previously used the plots to derive the $pK_a^{H_2O}$ value for C_α protonation of the diaminothiophene **9** from the relevant k_1^{DNBF} rate constants.[13] It turns out that the estimated value of the pK_a (1.5–2) was fairly consistent with the acid–base and nucleophilic properties of **9** in 50% H_2O–50% Me_2SO. Thus, this pK_a value indicated a high susceptibility to protonation of the C_α position of this compound, supporting the experimental observation that **9** behaves as an efficient carbon nucleophile and exhibits a strong enaminic character,[30,32] but it also revealed that the basicity at C_α remains at least 2 p*K* units lower than that of nitrogen atoms of the amino groups ($pK_a = 3.96$) Acid–base titrations of **9** carried out by ^1H and ^{13}C NMR in Me_2SO or by potentiometric methods in H_2O–Me_2SO mixtures showed exclusively N-protonation, even though the coupling of this compound with electrophiles was in most cases predominantly at the C_α carbon,[30–32]

Applying the same reasoning to the DNBF–3-methoxythiophene system, a $pK_a^{H_2O}$ value of ≈−6.5 derived for the C_α protonation of **5** in aqueous solution. This appreciably negative pK_a value together with the corresponding low k_1^{DNBF} rate constant may at first appear in conflict with the reported experimental evidence that **5** is one of the most reactive thiophene derivatives in reactions with electrophiles.[33] Recalling, however, that among the five-membered ring heterocycles thiophene compounds are by far the least prone to electrophilic addition or substitution processes,[34,35] the above $pK_a^{H_2O}$ and k_1^{DNBF} values can be readily reconciled with the idea that the C_α position of **5** bears a significantly greater electron density than the potentially reactive carbons of most thiophene derivatives. Comparing the few available data for protonation of thiophenes with those reported for structurally related nitrogen heterocycles is illustrative in this respect. Thus, the pK_a value for C_α protonation of 2,5-di-*tert*-butylthiophene is equal to −10.16, as compared with a $pK_a^{H_2O}$ value of −1.01 for protonation of 2,5-di-*tert*-butylpyrrole.[36] A similarly large difference is found between the basicities of 2-methylbenzothiophene ($pK_a = -10.40$) and 2-methylindole ($pK_a = -0.28$). On the basis of these large differences in basicity between the pyrrole and thiophene series, it is obvious that the $pK_a^{H_2O}$ of **5** makes this thiophene compound occupy a remarkable place in the range of reactivity of thiophenes. In accord with these large differences in basicity, acid-catalyzed hydrogen exchanges at C_α or C_β positions of thiophenes were reported to occur at considerably lower rates than in related pyrroles.[35,37–39] In such reactions, however, as well as in some other electrophilic substitution processes, thiophenes are commonly found to be more reactive than similarly substituted benzenes. This reactivity trend holds in fact for S_EAr substitutions involving DNBF as the electrophile since no complexation of DNBF by anisole occurs under the experimental conditions where 3-methoxythiophene is quantitatively converted to the σ-adduct **6**. As noted earlier, even the unsubstituted thiophene ring slowly reacts with DNBF to give the σ-adduct **8** in pure Me_2SO.

Based on the observation that the introduction of the OMe group at C_β of the thiophene ring induces strong upfield shifts of the H_α and C_α resonances (Tables 1 and 2), Gronowitz *et al.* as well as Takahashi *et al.* have suggested that the nucleophilic behaviour of **5** may be appropriately related to that of vinyl ethers.[20,22] Interestingly, protonation of the double bond to form the oxocarbenium-ion intermediate **13** is commonly the rate-limiting step in the H^+-catalysed hydrolysis of these derivatives [reactions (6) and (7)].[40–42] This has allowed a facile determination of the corresponding k_1^H rate constants for protonation of many vinyl ethers and the finding by Toullec in a study of a series of structurally related enol methyl ethers, namely



(6)



(7)

α-methoxystyrenes, that the rates of protonation decrease regularly with decreasing C-basicity of the starting enol.[43] In the hydrolysis of **5**, it turns out that it is the hydration and not the formation of the intermediate cation [reaction (7)] which is the rate-limiting step so that the k_1^{H} rate constant could not be directly measured.[21] In this case, however, an estimate of k_1^{H} can be derived from the k_1^{DNBF} rate constant measured in the more aqueous solvent, *i.e.* 30% Me_2SO, since there is now accumulated evidence that the neutral DNBF molecule is a stronger electrophile than the proton by at least a factor of 30.[1,2] One thus obtains: $k_1^{\mathrm{H}} \approx 2 \times 10^{-2}$ dm^3 mol^{-1} s^{-1}. Then, assuming that the behaviour of **5** also fits the Brønsted correlation ($\beta = 0.58$) described by Toullec for the protonation of α-methoxystyrenes of $\mathrm{p}K_\mathrm{a}^{\mathrm{CH}}$ values ranging between −4.32 and −0.03,[43] a $\mathrm{p}K_\mathrm{a}^{\mathrm{CH}}$ value of the order of −7 may be estimated for 3-methoxythiophene. Given the approximations involved in this approach, this value agrees satisfactorily with that deduced above by comparing the rates of DNBF addition to **6** with similar data for nitrogen heterocycles. It thus appears that the carbon basicity of **5** is comparable to that of a rather weakly basic enol ether, accounting well for the peculiar reactivity of this compound within the thiophene series.

Experimental

Materials

4,6-Dinitrobenzofuroxan was prepared according to the procedure of Drost:[44] mp, 172 °C (lit., 172–174.5 °C).[8,11,23,44] 3-Methoxythiophene **5** was a commercial product (Aldrich) which was purified by distillation under vacuum (bp 54–56 °C at 30 mmHg).[21]

Deuteriation of **5** was effected by acid-catalysed exchange using the same procedure as that previously developed by various authors for H/D exchange at C_α or C_β of many five-membered ring heterocycles.[1,2,13,45–48] Deuterium incorporation at C_α of **5** was found to be ⩾98% on the basis of a 300 MHz ^{1}H NMR spectrum recorded in $(CD_3)_2SO$ on a Bruker spectrometer.

Reaction (3) afforded the adduct **6** in its acid form, which is not very stable in air. Exchanging the H^+ counterion, for a K^+ or Na^+ cation was therefore the best way to isolate **6** as a crystalline alkali salt.[1,2,4,12,18] A solution of 0.528 g of DNBF (2.33 mM) in 4.5 ml of dioxane and a solution of 0.265 g of **5** in 4.5 ml of dioxane were mixed with stirring at room temp. The resulting mixture rapidly turned dark red and was allowed to stand for about 15 min. Then, sodium hydrogencarbonate (0.196 g, 2.33 mM in 1 ml of water) was added and crystals began to form within a few minutes. After filtration, red crystals were obtained which were washed once with cooled methanol and then with copious amounts of diethyl ether. These were finally dried under vacuum to give 0.46 g (60%) of the sodium salt of **6**.

As with most alkali salts of DNBF σ-adducts, the crystals obtained for **6**, Na^+ were not found to melt without decomposition. Also, attempts to obtain satisfactory elemental analysis have failed. However, dissolution of the salt in $(CD_3)_2SO$ gave NMR spectra identical to those recorded in the *in situ* generation of the acid form of **6** in this solvent. Definitive evidence for the structure of this adduct comes from ESI mass spectra experiments which show the expected peak corresponding to the molecular ion of **6** (*m*/*z* 339). Also consistent with the C-bonded character of **6** was its stability in dilute HCl solutions.[4,12]

Measurements

Kinetic measurements were performed on a Kontron–Uvikon spectrophotometer, the cell compartment of which was maintained at 25 ± 0.2 °C. All kinetic runs were carried out in triplicate under pseudo-first-order conditions with a DNBF concentration of *ca.* 3×10^{-5} mol dm^{-3} and 3-methoxythiophene concentrations in the range 2×10^{-3}–3×10^{-2} mol dm^{-3}. In a given experiment, the rates were found to be reproducible to ±2–3% and the visible spectrum of the final solution was always strictly identical to the one recorded by dissolving a sample of the isolated sodium salt of the adduct **6** at the appropriate concentration in the H_2O–Me_2SO mixture at hand.

Acknowledgements

The authors are indebted to Professor Buncel for ESI mass spectra experiments which were carried out at the University of Kingston (Ontario, Canada) and to Marie-José Pouet for helpful assistance in NMR.

References

1 F. Terrier, E. Kizilian, J. C. Hallé and E. Buncel, *J. Am. Chem. Soc.*, 1992 **114**, 1740.
2 F. Terrier, M. J. Pouet, J. C. Hallé, S. Hunt, J. R. Jones and E. Buncel, *J. Chem. Soc.*, *Perkin Trans. 2*, 1993, 1665.
3 F. Terrier, *Nucleophilic Aromatic Displacement*, ed. H. Feuer, VCH, New York, 1991, pp. 142, 262.
4 E. Buncel, R. A. Renfrow and M. J. Strauss, *J. Org. Chem.*, 1987, **52**, 488.
5 R. J. Spear, W. P. Norris and R. W. Read, *Tetrahedron Lett.*, 1983, **24**, 1555.
6 W. P. Norris, R. J. Spear and R. W. Read, *Aust. J. Chem.*, 1983, **36**, 297.
7 R. W. Read, R. J. Spear and W. P. Norris, *Aust. J. Chem.*, 1984, **77**, 985.
8 (*a*) J. C. Hallé, M. P. Simonnin, M. J. Pouet and F. Terrier, *Tetrahedron Lett.*, 1985, **26**, 1307; (*b*) 1983, **24**, 2255.
9 A. J. Kresge, H. J. Chen, L. E. Hakka and J. E. Kouba, *J. Am. Chem. Soc.*, 1971, **93**, 6174.
10 A. J. Kresge, Y. Chiang and L. E. Hakka, *J. Am. Chem. Soc.*, 1971, **93**, 6167.
11 R. Taylor, *Electrophilic Aromatic Substitution*, Wiley, New York, 1990.
12 M. J. Strauss, R. A. Renfrow and E. Buncel, *J. Am. Chem. Soc.*, 1983, **105**, 2473.
13 F. Terrier, M. J. Pouet, E. Kizilian, J. C. Hallé, F. Outurquin and C. Paulmier, *J. Org. Chem.*, 1983, **58**, 4696.
14 F. Terrier, J. C. Hallé, M. P. Simonnin and M. J. Pouet, *J. Org. Chem.*, 1984, **49**, 4363.
15 J. Kind and H. J. Niclas, *Synth. Commun.*, 1993, **23**, 1569.
16 (*a*) H. J. Niclas, B. Göhrmann and E. Gründemann, *Synth. Commun.*, 1989, **19**, 2789; (*b*) H. J. Niclas and B. Göhrmann, *ibid.*, 1989, **19**, 2141.
17 B. Göhrmann and H. J. Niclas, *J. Prakt. Chem.*, 1989, **331**, 819.
18 F. Terrier, M. P. Simonnin, M. J. Pouet and M. J. Strauss, *J. Org. Chem.*, 1981, **46**, 3537.
19 E. Buncel, R. A. Manderville and J. M. Dust, *J. Chem. Soc.*, *Perkin Trans. 2*, 1997, 1019.
20 S. Gronowitz and R. A. Hoffmann, *Ark. Kemi.*, 1960, **16**, 539.
21 B. Capon and F. C. Kwok, *Tetrahedron*, 1987, **43**, 69.
22 K. Takahashi, T. Sone and K. Fujieda, *J. Phys. Chem.*, 1970, **74**, 2765.
23 F. Terrier, F. Millot and W. P. Norris, *J. Am. Chem. Soc.*, 1976, **98**, 5883.
24 C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, VCH, Weinheim, 2nd, edn, 1988, p. 147.
25 A. J. Parker, *Chem. Rev.*, 1969, **69**, 1.
26 R. L. Hinman and J. Lang, *J. Am. Chem. Soc.*, 1964, **86**, 3796.
27 E. B. Whipple, Y. Chiang and R. L. Hinman, *J. Am. Chem. Soc.*, 1963, **85**, 26.
28 R. A. Jones and G. P. Bean, *The Chemistry of Pyrroles*, Academic Press, 1977, ch. 11, p. 448.
29 Y. Chiang and E. B. Whipple, *J. Am. Chem. Soc.*, 1963, **85**, 2736.
30 F. Outurquin, P. Lerouge and C. Paulmier, *Bull. Soc. Chim. Fr.*, 1986, 259.
31 (*a*) F. Outurquin and C. Paulmier, *Bull. Soc. Chim. Fr.*, 1980, II, 151; (*b*) 1983, II, 153.
32 C. Paulmier and F. Outurquin, *Janssen Chem. Acta*, 1987, **5**, 9.
33 S. Rajappa, in *Comprehensive Heterocyclic Chemistry*, ed. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, vol. 4, ch. 14, p. 741.
34 R. M. Kellog, in *Comprehensive Heterocyclic Chemistry*, ed. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984, vol. 4, ch. 13, p. 713.

35 A. R. Katritzky and R. Taylor, *Adv. Heterocyclic Chem.*, 1990, **47**, 87.

36 M. P. Carmody, M. J. Cook, N. L. Dassariayake, A. R. Katritzky, P. Linda and R. D. Tack, *Tetrahedron*, 1976, **32**, 1767.

37 (*a*) R. Baker, C. Eaborn and R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1972, 97; (*b*) A. R. Butler and C. Eaborn, *J. Chem. Soc.*, (*B*), 1968, 370.

38 (*a*) A. R. Butler and J. B. Hendry, *J. Chem. Soc.*, (*B*), 1970, 852; (*b*) R. S. Alexander and A. R. Butler, *J. Chem. Soc., Perkin Trans. 2*, 1977, 1998.

39 (*a*) E. N. Zvyagintseva, V. E. Udre, M. G. Voronkov and A. I. Shatenshtein, *J. Gen. Chem.* (*USSR*), 1971, **41**, 2314; (*b*) E. N. Zvyagintseva, T. A. Yukushina and A. I. Shatenshtein, *J. Gen. Chem.* (*USSR*), 1968, **38**, 1933; (*c*) E. N. Zvyagintseva, L. I. Belenkii, T. A. Yukushina, Y. L. Goldfarb and A. I. Shatenshtein, *J. Gen. Chem.* (*USSR*), 1968, **38**, 1944.

40 (*a*) A. J. Kresge, *Chem. Soc. Rev.*, 1973, **2**, 475; (*b*) A. J. Kresge, *Acc. Chem. Res.*, 1975, **8**, 354.

41 A. J. Kresge, D. S. Sagatys and H. L. Chen, *J. Am. Chem. Soc.*, 1977, **99**, 7228.

42 Y. Chiang, W. K. Chwang, A. J. Kresge, L. H. Robinson, D. S. Sagatys and C. I. Young, *Can. J. Chem.*, 1978, **56**, 456.

43 J. Toullec, *J. Chem. Soc., Perkin Trans. 2*, 1989, 167.

44 P. Drost, *Justus Liebigs Ann. Chem.*, 1899, **307**, 49.

45 B. C. Challis and H. S. Rzepa, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1208.

46 A. H. Jackson and P. P. Lynch, *J. Chem. Soc., Perkin Trans. 2*, 1987, 1483.

47 F. Terrier, F. L. Debleds, J. F. Verchère and A. P. Chatrousse, *J. Am. Chem. Soc.*, 1985, **107**, 307.

48 B. C. Challis and E. M. Millar, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1116; 1618.

Paper 7/04426G
Received 23rd *June* 1997
Accepted 6th *August* 1997