Regioselectivity and Stereoelectronic Factors in the Reactions of Aryloxide Nucleophiles with 4-Nitrobenzofuroxan

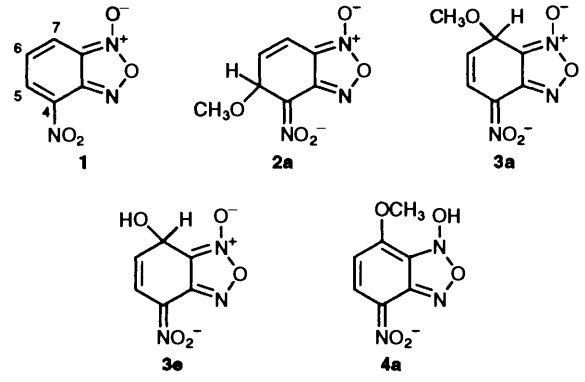
Richard A. Manderville and Erwin Buncel*
Department of Chemistry, Queen's University, Kingston, Ontario, Canada K7L 3N6

The reactivity of 4-nitrobenzofuroxan (NBF, **1**) with several aryloxide nucleophiles has been monitored by 400 MHz ^{1}H NMR spectroscopy in acetonitrile–glyme (CD_3CN–[$^2H_{10}$]glyme, 1:1, v/v) at reduced temperatures and in dimethyl sulfoxide ([$^2H_6$]DMSO) at ambient temperature. With the ambident (O- and C-) nucleophile phenoxide ion, formation of a C-7 O-adduct (**3b**) is observed in CD_3CN–[$^2H_{10}$]glyme at −40 °C. As the temperature is raised this adduct gives way to 7-hydroxy-4-nitrobenzofurazan (as the anion, **5**) and a 7-phenoxynitronate derivative (**4b**) that arises from transfer of the sp^3-bound proton (7-H) of the C-7 phenoxide O-adduct to the N-oxide function. These decomposition products are the sole species observed when the reaction is carried out in [$^2H_6$]DMSO. Thus in contrast to the reaction of **1** with methoxide ion, where the C-5 adduct (**2a**) is kinetically preferred while the C-7 adduct (**3a**) is thermodynamically more stable, no C-5 O-adduct of phenoxide is observed in the present system. In addition, C-adducts that could potentially arise from the ambident nature of phenoxide were not formed. A similar reaction sequence was found for the reaction of **1** with 3,5-di-*tert*-butylphenoxide ion and 2,4,6-trimethylphenoxide ion. However, C-attachment was observed in the reaction of **1** with 2,6-di-*tert*-butylphenoxide ion where O-attack is sterically blocked and, again, preference for C-7 attachment was found. Comparison is drawn between the present results concerning the reactivity of **1** with aryloxide nucleophiles and the reactivity displayed by methoxide ion. Stereoelectronic factors in the C-7 aryloxide O-adducts are also discussed.

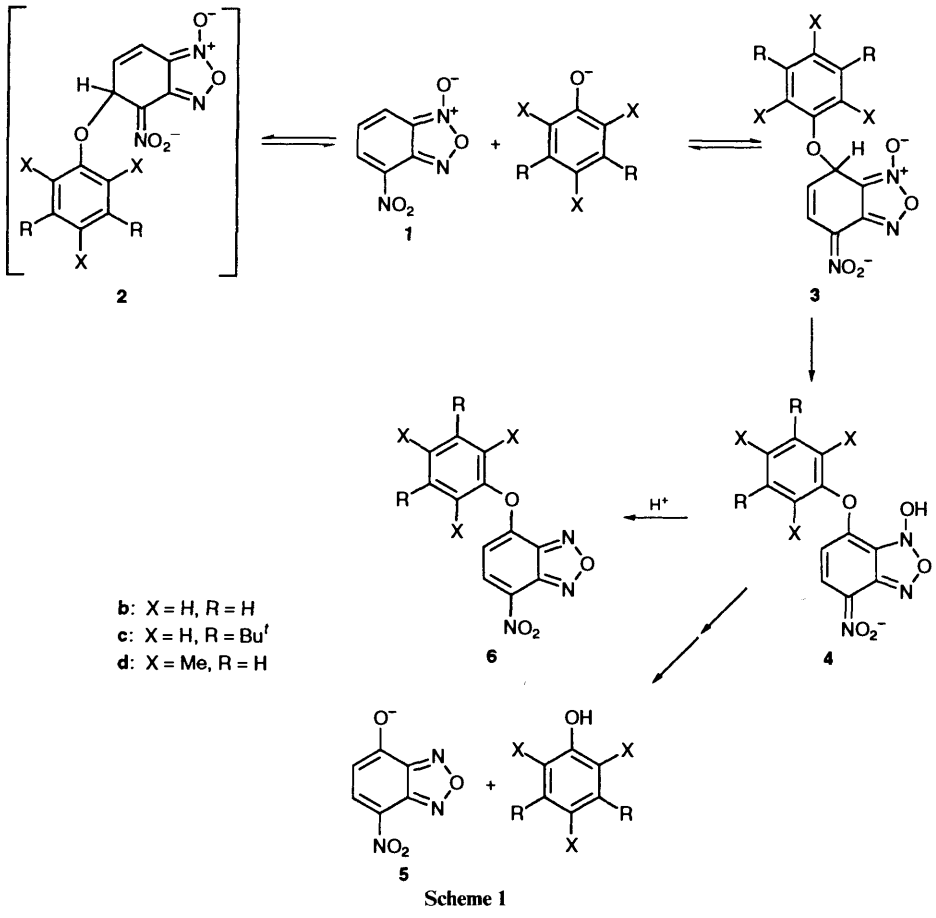
The earlier discovery [1] that 4-nitrobenzofuroxan (NBF, **1**) acts as an *in vitro* inhibitor of nucleic acid and protein biosynthesis in animal cells, possibly through formation of Meisenheimer-type anionic complexes (σ-adducts) with essential cellular thiol groups, has led to numerous studies of the reactivity of **1** and related benzofuroxan and benzofurazan derivatives with nucleophiles.[2] In this regard, formation of isomeric C-5 and C-7 alkoxide adducts of these NBF derivatives has been of particular interest.[3–5] In general, studies have shown a kinetic preference for C-5 attachment while σ-adduct formation at C-7 is thermodynamically the more stable. In the reaction of **1** with methoxide ion (MeO^-) in methanol, production of the C-5 σ-adduct **2a** occurs 70-fold faster, while the C-7 σ-adduct **3a** is more stable by a factor of 200.[3]

In addition to the kinetic and thermodynamic preferences, ^{1}H NMR spectral characteristics of **2a** and **3a** have also been determined.[4,5] Previously, we showed that in dimethyl sulfoxide–methanol ([$^2H_6$]DMSO–CH_3OD 70:30 v/v) the resonances of **2a** at δ 5.52 (5-H), dd, *J* 4.7, < 1), 6.43 (6-H, dd, *J* 4.7, 9.8) and 6.68 (7-H, d, *J* 9.8) can be observed at −20 °C free from signals due to the C-7 adduct, **3a**.[5] However, upon standing at −20 °C for 30 min signals due to **3a** appear at δ 7.19 (5-H, dd, *J* 10.3, < 1), 5.23 (6-H, dd, *J* 10.3, 4.4) and 5.32 (7-H, dd, *J* 4.4, < 1). The most striking feature of the observed peaks for **3a** is that 6-H occurs upfield of the sp^3-bound proton, 7-H (δ 5.23 *vs.* 5.32) and is significantly upfield of 6-H in the C-5 adduct, **2a** (δ 5.23 *vs.* 6.43). This upfield shift indicates that considerable charge localization occurs at C-6 upon C-7 adduct formation and these characteristic signals easily distinguish a C-7 adduct from a C-5 adduct by ^{1}H NMR spectroscopy.[4,5]

Upon subsequent monitoring of the NBF–MeO^- system in [$^2H_6$]DMSO–CH_3OD, we found that at ambient temperature signals due to **3a** were replaced by peaks which were ascribed to formation of the 7-methoxynitronate derivative (**4a**) and the oxyanion **5**.[5] These unexpected findings were attributed to breakdown of **3a**, which led, overall, to deoxygenation of the *N*-oxide function and substitution of an aromatic hydrogen by the methoxy or hydroxy function. For the nitronate derivative **4a** the resonances appear at δ 7.27 (5-H, d, *J* 8), 5.70 (6-H, d, *J* 8) and 10.5 (NOH, s), while peaks ascribed to the oxyanion, **5**, were found at δ 8.35 (5-H, d, *J* 10) and 5.90 (6-H, d, *J* 10).



More recently, we have been engaged in study of aryloxide nucleophiles, in particular ambident (O- and C-) phenoxide ion (PhO^-), with a variety of electron-deficient aromatic[6] and heteroaromatic[7] compounds. These studies have shown that in order to permit detection of the transient aryloxide O-adducts by NMR spectroscopy it is advantageous to monitor the systems in acetonitrile–glyme (CD_3CN–[$^2H_{10}$]glyme, 1:1, v/v), which solubilizes all of the reagents and products at temperatures as low as −50 °C[6a,b] and allows the observation of species not observable in DMSO. Prompted by the interesting and variable behaviour found with PhO^- as an O- nucleophile as compared to MeO^- in reactions with 1,3,5- trinitrobenzene (TNB)[6b] and 2,4,6-trinitroanisole,[6a] we have now extended our study of the reactivity of **1** to include its behaviour with the aryloxide nucleophiles, PhO^-, 3,5-di-*tert*-butylphenoxide ion (3,5-$DTBP^-$), 2,4,6-trimethylphenoxide ion



Scheme 1

(mesitoxide, $MesO^-$) and 2,6-di-*tert*-butylphenoxide ion (2,6-DTBP).

The salient feature of the reactions as determined by 400 MHz ^1H NMR spectroscopy in CD_3CN–[$^2H_{10}$]glyme at −40 °C, is that the C-7 O-adducts of PhO^-, 3,5-$DTBP^-$ and $MesO^-$ are kinetically favoured. No spectral evidence for C-5 attachment was found. The final products in these systems are the oxyanion **5** and the respective 7-aryloxynitronate derivatives, as a consequence of decomposition pathways previously described for the NBF–MeO^- system.[5] These products are the sole species observed when the reactions are carried out in DMSO. Attack at carbon by 2,6-$DTBP^-$, where O-attachment is sterically blocked, also occurs at C-7 and the resulting σ-adduct was stable in DMSO at ambient temperature. These results suggest that σ-adduct formation at C-7 is kinetically as well as thermodynamically preferred in these NBF–aryloxide systems. The present results are compared to the well studied NBF–MeO^- system.[3-5] Stereoelectronic factors in formation of the C-7 aryloxide O-adducts are also discussed.

Results

1. *Reaction of* **1** *with Equimolar* PhOK *in DMSO.*—Addition of 1.0 equiv. of PhOK in [$^2H_6$]DMSO to a [$^2H_6$]DMSO solution of **1** (final concentrations 0.06 mol dm^{-3}) produced a deep green solution. In the initially acquired ^1H NMR spectrum (*ca.* 3 min after mixing reagents) at ambient temperature a pair of sharp doublets at δ 5.56 (*J* 7.8) and 5.77 (*J* 9.8) were apparent along with a doublet at δ 8.25 (*J* 9.8) and a downfield singlet at δ 10.40. These peaks could not be attributed to σ-adduct formation, but instead represented species resulting from decomposition[5] of a putative C-7 O-bonded NBF·OPh^- adduct. The pair of doublets at δ 5.77 and 8.25 (*J* 9.8) were ascribed to 6-H and 5-H, respectively, of the oxyanion **5**,[5] while the signals at 5.56 (*J* 7.8) and 10.40 represented 6-H and N-OH of the 7-phenoxynitronate derivative, **4b** (Scheme 1, X = R = H). A doublet at δ 7.11 (*J* 7.8) corresponded to 5-H of **4b**, while the *m*- and *o*-phenoxy resonances could also be attributed to an apparent triplet centred at δ 7.40 and a doublet at 7.07 ppm, respectively.

Thus, as outlined in Scheme 1 (X = R = H), O-attack by PhO^- at C-7 of **1** to produce the putative σ-adduct, **3b**, might initially have occurred, but due to its relative instability was rapidly converted into **4b**. In turn, **4b** was converted into oxyanion **5** with concomitant formation of the phenol.[5]

Subsequent monitoring of the reaction showed that after 3 h the resonances due to **4b** were replaced by those of **5** and no further changes were seen over the next 9 h. Although other extraneous peaks were present in the acquired spectra, essentially the reaction produced signals attributable to the formation of **4b** and **5**. Interestingly, no peaks were found that could be assigned to the C-7 O-adduct, **3b**, or C-bonded adducts which would be formed as a consequence of the expected ambident nature of PhO^-.[6,7]

In a separate experiment, after the initial spectrum was recorded, 2 mm^3 of D_2O was added to the NMR tube. Under these conditions the singlet at δ 10.40 due to the NOH function of **4b** vanished. Injection of 5 mm^3 of trifluoroacetic acid (TFA) into the NMR tube caused peaks of **4b** to disappear and a new set of resonances was observed at δ 8.65 (5-H, d, *J* 8.4) and 6.68 (6-H, d, *J* 8.4). These peaks were attributable to formation of 7-phenoxy-4-nitrobenzofurazan, **6b**.[8] Full assignment of this species was obtained from a sample prepared on reaction of PhO^- with 7-chloro-4-nitrobenzofurazan (NBD-chloride; see Experimental section).[8]

2. *Reaction of* **1** *with Equimolar* PhOK *in* MeCN–*glyme.*—Since σ-adduct formation between **1** and PhO^- could not be

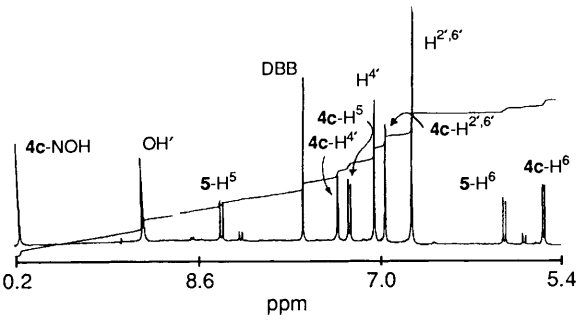


Fig. 1 ^{1}H NMR Spectrum of the 5.4–10.2 ppm region of NBF–3,5-DTBPK (1:1) taken after 3 min reaction time in [$^2H_6$]DMSO at ambient temperature. Highlighted are peaks due to the nitronate derivative, **4c**, the oxyanion, **5**, and 3,5-di-*tert*-butylphenol (OH', 4'-H, 2',6'-H). DBB represents 1,4-dibromobenzene.

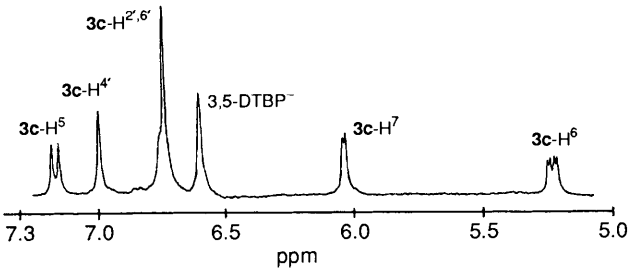


Fig. 2 ^{1}H NMR Spectrum of the 5.0–7.3 ppm region of NBF–3,5-DTBPK (1:1) taken after 3 min reaction time in CD_3CN–[$^2H_{10}$]glyme at −40 °C. Present are signals due to the C-7 NBF•3,5-DTBP$^-$ O-adduct, **3c**, and some unreacted 3,5-DTBPK.

observed under ambient reaction conditions in [$^2H_6$]DMSO, the reaction was repeated in CD_3CN–[$^2H_{10}$]glyme (1:1, v/v) at reduced temperatures. The decomposition products, **4b** and **5**, observed in the [$^2H_6$]DMSO study presumably were derived from the C-7 O-adduct, **3b**.[5] In addition, formation of the C-5 O-adduct **2b** could be possible if the reaction sequence between **1** and PhO^- mimics the reactivity of **1** with MeO^-

To a solution of **1** in CD_3CN–[$^2H_{10}$]glyme (1:1, v/v) cooled to −50 °C was added a similarly cooled solution of PhOK in CD_3CN–[$^2H_{10}$]glyme (final concentrations 0.08 mol dm^{-3}). In the initially acquired ^{1}H NMR spectrum taken at −40 °C, the resonances were broad and signals representing unreacted NBF and PhOK were present. Importantly, however, three unresolved equivalent peaks were observed at δ 7.14 (br d), 6.02 (br s) and 5.34 (br d). Upon subsequent monitoring of the system, by gradually allowing the temperature to rise, these three signals broadened further and eventually vanished within 1 h at −30 °C. Inspection of the NMR tube at ambient temperature revealed that a precipitate had formed and 100 mm^3 of [$^2H_6$]-DMSO was added to solubilize it. A spectrum of the resulting solution showed peaks at δ 5.77, 8.25 and 5.56, which could be attributed to the decomposition products, **5** and **4b**.

Since at −40 °C the acquired spectrum displayed resonances other than unreacted starting material (NBF and PhO^-), which could be attributed to formation of a single species, the signals at δ 7.14, 6.02 and 5.34 were tentatively assigned to 5-H, 7-H and 6-H, respectively, of the C-7 NBF•OPh^- O-adduct, **3b**. Comparison with the parameters of the C-7 NBF•OMe^- adduct, **3a**, obtained in [$^2H_6$]DMSO–CH_3OD (70:30 v/v),[5] where 5-H appears at δ 7.19, 6-H at 5.23 and 7-H at 5.32 ppm, showed that the chemical shift of 5-H and 6-H of **3a** and **3b** were comparable, while the sp^3-attached proton, 7-H, of **3b** was located *ca.* 0.7 ppm downfield of the comparable proton in **3a** (δ 6.02 *vs.* 5.32). This chemical shift difference in 7-H was consistent with expectations derived from previous studies on aryloxide systems,[6b] while the upfield shift in 6-H (δ 5.34) confirmed that the σ-adduct is due to O-attachment at C-7 and not C-5.[4,5] Further support for the present assignment of **3b** was obtained from study of the NBF–3,5-$DTBP^-$ and $MesO^-$ systems (*vide infra*).

3. *Reaction of* **1** *with Equimolar* 3,5-*DTBPK in DMSO.*—Introduction of 3,5-DTBPK in [$^2H_6$]DMSO into a [$^2H_6$]-DMSO solution of **1** (final concentrations 0.06 mol dm^{-3}) produced a dark green solution. Fig. 1 shows the ^{1}H NMR spectrum highlighting the downfield region of the reaction mixture, acquired *ca.* 3 min after mixing the reagents at ambient temperature. Similar to the NBF–PhO^- system, signals representing σ-adduct formation were not observed, but instead the spectrum shows resonances due to decomposition products, **5**, and the nitronate derivative **4c** (Scheme 1, X = Bu^t, R = H). For derivative **4c**, the peaks occurred at δ 10.17 (NOH, s), 7.22 (4'-H, t, *J* 1.6), 7.12 (5-H, d, *J* 7.8), 6.90 (2',6'-H, d, *J* 1.6), 5.43 (6-H, d, *J* 7.8) and 1.27 (Bu^t, s).

Subsequent monitoring of the reaction showed that the signals due to **4c** were slowly replaced by those due to **5**. Also, addition of 5 mm^3 of TFA converted resonances due to **4c** into peaks ascribable to 7-(3,5-di-*tert*-butylphenoxy)-4-nitrobenzofurazan, **6c** (Scheme 1). The full assignment of **6c** was obtained from a separately prepared sample (NBD-chloride and 3,5-DTBPK, see Experimental section).

4. *Reaction of* **1** *with Equimolar* 3,5-*DTBPK in* MeCN–*Glyme.*—Reaction of **1** with 1 equiv. of 3,5-DTBPK in CD_3CN–[$^2H_{10}$]glyme at −50 °C (final concentrations 0.06 mol dm^{-3}), produced a deep green mixture. Fig. 2 highlights the 5.0–7.3 ppm region of the ^{1}H NMR spectrum acquired at −40 °C, *ca.* 3 min after mixing. Other than peaks due to unreacted 3,5-DTBPK, the resonances can be attributed to a single species: the C-7 O-bonded NBF•3,5-$DTBP^-$ adduct, **3c**. For **3c**, the signals occurred at δ 7.16 (5-H, d, *J* 10.4), 7.00 (4'-H, br s), 6.75 (2',6'-H, br s), 6.07 (7-H, d, *J* 3.7), 5.29 (6-H, dd, *J* 10.4, 3.7) and 1.22 (Bu^t, s).

As the temperature of the system was gradually raised to −30 °C, the peaks due to **3c** broadened and declined in intensity. At −10 °C the acquired spectrum showed broad resonances representing NBF and 3,5-di-*tert*-butylphenol, while peaks ascribable to **3c** had vanished. At ambient temperature, inspection of the NMR tube showed that a precipitate had formed and after addition of 100 mm^3 of [$^2H_6$]DMSO the acquired spectrum displayed signals due to the presence of **4c** and **5**, indicating that **3c** had decomposed into these species (Scheme 1, X = Bu^t, R = H).

Study of the present system gave support to the assignments made in the NBF–PhO^- system. Because the acquired spectra (Figs. 1 and 2) were relatively well resolved, peak assignments were more definitive. Thus, in both the NBF–PhO^- and 3,5-$DTBP^-$ systems, O-attachment by the nucleophile to C-7 of **1** was observed, which rapidly gave way to products of decomposition (Scheme 1). Interestingly, in both systems evidence for C-5 attachment to produce **2b** and **2c**, respectively, was not obtained. To provide further support for structure of O-bonded NBF aryloxide σ-adducts, the reaction of **1** with mesitoxide ion was also examined in CD_3CN–[$^2H_{10}$]glyme at reduced temperatures.

5. *Reaction of* **1** *with Equimolar* MesOK *in* MeCN–*Glyme.*—Reaction of **1** with 1 equiv. of MesOK in CD_3CN–[$^2H_{10}$]glyme (final concentrations 0.1 mol dm^{-3}) at −40 °C produced an initially acquired ^{1}H NMR spectrum showing the presence of the C-7 NBF•$OMes^-$ O-adduct, **3d**. Although coupling of the protons was not fully resolved, the full chemical shift assignment of **3d** could be made: δ 7.08 (5-H, d, *J* 9.9), 6.73 (3',5'-H, s), 5.63 (7-H, br s), 5.07 (6-H, br d), 2.13 (*p*-CH_3, s) and 2.12 (*o*-CH_3, s).

Interestingly, the sp^3-attached proton, 7-H, at δ 5.63 and the

ring protons, 5-H and 6-H, at δ 7.08 and 5.06, respectively, of **3d** were found upfield of the corresponding protons in **3b** (6.02, 7.14 and 5.34) and **3c** (6.07, 7.16 and 5.29). The largest upfield shift occurred for the sp^3-bound proton, 7-H, which amounts to *ca.* 0.4 ppm, while for protons attached to the sp^2-hybridized carbons, 5-H and 6-H, the shift was only *ca.* 0.1 and 0.2 ppm respectively. This observation differs from the results obtained in our previous study of the 1,3,5-trinitrobenzene (TNB)–aryloxide systems,[6b] where there was no significant difference in the ^1H NMR chemical shift of the sp^3-bound proton, 1-H, of the corresponding phenoxide and mesitoxide TNB·OAr^- σ-adducts. Possible explanations for this chemical shift change in the NBF systems are outlined in the Discussion section.

As with the other two aryloxide systems, upon subsequent monitoring of the reaction, by slowly raising the temperature to −30 °C (*ca.* 30 min), the signals attributed to **3d** broadened and decreased in intensity and at −10 °C, only broad signals representing NBF and MesOH were observed. At ambient temperature, after addition of 100 mm^3 of [$^2H_6$]DMSO, the acquired spectrum displayed resonances due to the oxyanion **5** and MesOH (δ 6.68, 2.11 and 2.10). Peaks which could be attributed to the 7-mesitoxynitronate derivative, **4d** (Scheme 1, X = Me, R = H), were not observed in the present system.

6. *Reaction of* **1** *with Equimolar* Me_4NOH *in DMSO.*—To assess the potential for OH^- reactivity in the NBF–aryloxide systems, control experiments involving the reaction of **1** with tetramethylammonium hydroxide (Me_4NOH) were carried out, since equilibration between adventitious H_2O in the solvent systems used and the aryloxides may give rise to hydroxide σ-adducts.[6a,b]

Reaction of **1** in 70 mol% [$^2H_6$]DMSO–30 mol% H_2O–D_2O with equimolar Me_4NOH (stock solution 25 wt% in H_2O, 11 mm^3 for 1 equiv., 450 mm^3 [$^2H_6$]DMSO, 40 mm^3 D_2O) at ambient temperature led to the immediate formation of signals assignable to the C-7 NBF·OH^- adduct, **3e**, at δ 6.93 (5-H, d, *J* 10.3), 5.16 (7-H, d, *J* 4.4) and 5.04 (6-H, dd, *J* 10.3, 4.4). A resonance for the hydroxy proton of **3e** was not observed and hence its state of ionization is uncertain.

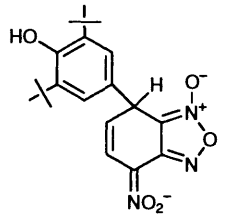
After 1 h, resonances due to **5** were also observed, although **3e** was still the dominant species. This experiment revealed that **3e** can be observed at ambient temperature in [$^2H_6$]DMSO, in contrast to the NBF aryloxide σ-adducts. Hence, if OH^- addition were a competitive process in the NBF–aryloxide systems, it is expected that **3e** would have been observed during the reaction sequence due to its inherent stability.

The C-5 adduct, **2e**, was not seen in the present system. This is consistent with previous work on the addition of methoxide to NBF[5] where a C-5 adduct could only be detected at lower temperatures (< 20 °C) and the C-7 adduct was the only observed adduct at room temp.

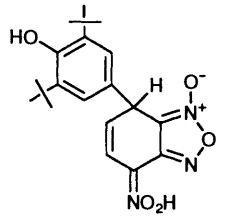
7. *Reaction of* **1** *with Equimolar* 2,6-*DTBPK in DMSO.*—Since the reaction of **1** with PhO^- did not give rise to C-adducts (*vide supra*), the reactivity of **1** with 2,6-di-*tert*-butylphenoxide (2,6-$DTBP^-$), where O-addition is sterically blocked, was examined in an attempt to study C-attack by an aryloxide nucleophile.

Reaction of **1** with 1 equiv. of 2,6-$DTBP^-$ in [$^2H_6$]DMSO (final concentrations 0.06 mol dm^{-3}) led to an initial ^1H NMR spectrum (acquired *ca.* 3 min after mixing reagents) displaying signals assignable to a single species, the C-7 C-adduct, **7**. Peaks attributed to **7** occurred at δ 6.92 (2′,6′-H, s), 6.91 (OH, s), 6.89 (5-H, dd, *J* 10.2, 1.7), 5.01 (6-H, dd, *J* 10.2, 4.3), 4.65 (7-H, dd, *J* 4.3, 1.7) and 1.33 (Bu^t, s). Further monitoring of the reaction by ^1H NMR showed no changes in the resonances due to **7** over a 5 h period.

Consistent with the present assignment was the upfield position of 6-H (δ 5.01), indicative of formation of C-7 adducts,[4,5] and the relative position of the sp^3-attached proton 7-H (δ 4.65), which was in accord with bonding to the less electronegative carbon atom.[2,6,7] In addition, acidifying the solution with TFA (5 mm^3) did not lead to destruction of the aforementioned resonances. A ^1H NMR spectrum of the acidified mixture shows that the 6-H resonance shifted downfield to 5.93 ppm, while the other signals remain unchanged. This observation was consistent with protonation of the C-4 NO_2^- function of **7** to produce the nitronic acid derivative, **8**.[6e,9] The downfield shift in the 6-H resonance occurred because in **8** transfer of electron-density from the NO_2H group to the C-6 position was no longer possible. Recent work by Terrier and co-workers[9] suggests that the pK_a of the nitronic acid derivative, **8**, should be of the order of 4.2–4.5.



7



8

Summary of Results.—The interaction of NBF (**1**) with aryloxide nucleophiles (PhO^-, 3,5,-$DTBP^-$, $MeSO^-$ and 2,6-$DTBP^-$) has revealed some interesting facets of the chemistry of the heteroaromatic system, NBF. In contrast to methoxide addition, where the C-5 adduct is formed under kinetic control, but the C-7 adduct is thermodynamically favoured, C-7 attachment in the NBF–aryloxide systems has been shown to be kinetically as well as thermodynamically favoured. The resulting C-7 O-bonded aryloxide σ-adducts, however, have transient life-times due to decomposition pathways and hence could not be observed by ^1H NMR spectroscopy in [$^2H_6$]DMSO at ambient temperature. To obtain their spectral features the systems were monitored in CD_3CN–[$^2H_6$]glyme (1:1, v/v) at low temperatures, which permitted the observation and characterization of the C-7 O-bonded σ-adducts.

In the NBF–PhO^- system C-adduct formation was not observed, which contrasts with previous results shown for other nitro-heteroaromatic–PhO^- systems.[7] Study of the NBF–2,6-$DTBP^-$ system, however, revealed that C-attachment to C-7 of NBF is a viable process. By blocking the pathway for O-attack, the alternative C-attack pathway is observed in accord with the ambident nature of phenoxide ion.[6,7]

^1H NMR parameters obtained for the NBF–aryloxide systems are summarized in Tables 1 and 2. In Table 1 are given the parameters of the C-7 NBF σ-adducts. The parameters for the aryl O-adducts (**3b**, **3c** and **3d**) were obtained in CD_3CN–[$^2H_{10}$]glyme at −40 °C, while parameters for the NBF·OH^- adduct, **3e**, and the C-bonded adduct, **7**, were acquired at ambient temperature in [$^2H_6$]DMSO. Table 2 contains the resonances for the decomposition products (**4b–d** and **5**) along with the benzofurazan ethers (**6b–d**) obtained from reaction of the aryloxide nucleophiles with NBD-chloride (see Experimental section).

Discussion

1. *Reaction Pathways: Kinetic* versus *Thermodynamic Control.*—(i) *O-Adduct formation in NBF–aryloxide systems.* Based upon the spectral observations in the present studies carried out in DMSO at ambient temperature and in MeCN–glyme (1:1) at reduced temperatures, it would appear that O-attack by phenoxide (PhO^-), 3,5-di-*tert*-butylphenoxide (3,5-$DTBP^-$)

Table 1 ^{1}H NMR Spectral characteristics[a] of the NBF σ-adducts in DMSO[b] and in MeCN–glyme (1 : 1)[c]

Adduct	5-H	6-H	7-H	Other
3b[c]	7.14 (br d)	5.34 (br d)	6.02 (br s)	obscured
3c[c]	7.16 (d, *J* 10.4)	5.29 (dd, *J* 10.4, 3.7)	6.07 (d, *J* 3.7)	7.00 (4′-H, br s), 6.75 (2′,6′-H, br s), 1.22 (Bu^t, s)
3d[c]	7.08 (d, *J* 9.9)	5.07 (br d)	5.63 (br s)	6.73 (3′,5′-H, s), 2.13 (*p*-CH_3, s), 2.12 (*o*-CH_3, s)
3e[b,d]	6.93 (d, *J* 10.3)	5.04 (dd, *J* 10.3, 4.4)	5.16 (d, *J* 4.4)	
7[b]	6.89 (dd, *J* 10.2, 1.7)	5.01 (dd, *J* 10.2, 4.3)	4.65 (dd, *J* 4.3, 1.7)	6.92 (2′,6′-H, s), 6.91 (OH, s, 1.33 (Bu^t, s)

[a] Chemical shifts are given in ppm measured at 400 MHz; coupling constants are in hertz; [b] $(CD_3)_2SO$ at ambient temperature; [c] CD_3CN–[$^2H_{10}$]glyme (1 : 1, v/v) at −40 °C; [d] The hydroxy peak was not observed.

Table 2 ^{1}H NMR Spectral characteristics[a] of decomposition products, **3b–d** and **5**, and benzofurazan ethers, **6b–d**, in DMSO[b]

Compound	5-H	6-H	Other
4b	7.11 (d, *J* 7.8)	5.56 (d, *J* 7.8)	10.40 (NOH, s), 7.40 (*m*-H, t), 7.07 (*o*-H, d)
4c	7.12 (d, *J* 7.8)	5.43 (d, *J* 7.8)	10.17 (NOH, s), 7.22 (4′-H, t, *J* 1.6), 6.90 (2′,6′-H, d, *J* 1.6), 1.27 (Bu^t s)
5	8.25 (d, *J* 9.8)	5.77 (d, *J* 9.8)	
6b	8.65 (d, *J* 8.4)	6.68 (d, *J* 8.4)	7.59 (*m*-H, t), 7.45 (*p*-H, t), 7.43 (*o*-H, d)
6c	8.66 (d, *J* 8.4)	6.64 (d, *J* 8.4)	7.45 (4′-H, t, *J* 1.5), 7.24 (2′,6′-H, d, *J* 1.5), 1.31 (Bu^t, s)
6d	8.60 (d, *J* 8.4)	6.30 (d, *J* 8.4)	7.09 (3′,5′-H, s), 2.31 (*p*-CH_3, s), 2.09 (*o*-CH_3, s)

[a,b] See Table 1.

and mesitoxide ($MesO^-$) ions occurs at C-7 of NBF, to produce the NBF·OAr^- adducts, **3b–d**, respectively, as the kinetically preferred interaction. These C-7 O-adducts are then rapidly transformed into products of decomposition, **4b–d** and **5** (Scheme 1).[5] In DMSO at ambient temperature, **4b–d** and **5** are the only detectable species. Formation of the NBF·OH^- adduct, **3e**, *via* competitive equilibria with adventitious water in the media is not observed, and neither is *p*-C-attack observed in the PhO^- system. These observations are in contrast with previous nitroaromatic–aryloxide systems, where C-attack by PhO^- and competitive formation of hydroxide adducts were generally favoured.[6a,b] It appears therefore that breakdown of the C-7 NBF aryloxide O-adducts occurs readily and these alternative pathways cannot compete effectively. The thermodynamically favoured products are hence the nitronate derivatives, **4b–d**, and the oxyanion, **5**.

This observed regioselectivity can be compared with the NBF–MeO^- system where attachment at C-5 to produce **2a** is kinetically preferred but the C-7 adduct **3a** is thermodynamically more stable.[3–5] For the aryloxide systems no evidence for C-5 attack was obtained under the present conditions (reagents mixed in MeCN–glyme at −50 °C, first spectrum acquired *ca.* 3 min after mixing). At −40 °C the acquired spectra displayed signals for the C-7 O-adducts, **3b–d**, and unreacted starting material. Therefore, a key question arises: do the putative C-5 aryloxide O-adducts, **2b–d**, form prior to the first NMR observations and decompose too rapidly to detect, or are the C-7 O-adducts both kinetically and thermodynamically favoured?

In this regard, kinetic studies of the NBF–MeO^- system in MeOH have shown[3] that the C-7 adduct **3a** is *ca.* 200 times more stable than the C-5 adduct, **2a**, but that **2a** is favoured kinetically by a factor of 70. As noted, the C-5 NBF·OMe^- adduct is detectable in DMSO–MeOH (80 : 20 v/v) at −20 °C.[5] The present study of NBF·ArO^- adducts was undertaken at a significantly lower temperature (−40 °C). If the kinetic preference for C-5 attack were assumed simply to be the same for ArO^- and MeO^- with no change in thermodynamic preference for C-7 adduct formation, one would have expected to observe both adducts at the lower temperature of the present work. In fact, ArO^- adducts of TNB are readily observable under these conditions.[6b] Comparable regioisomers in the reaction of 2,4,6-trinitroanisole (TNA) with 2,4,6-trimethylphenoxide (*i.e.* C-3 and C-1 O-adducts of TNA *vs.* the C-5 and C-7 O-adducts of NBF) have recently been fully characterized in our laboratories under these conditions[10] and the regioselectivity in the TNA–PhO^- system has been similarly elucidated using the low temperature MeCN–glyme solvent system.[6a] On these grounds, we strongly favour the straightforward interpretation that C-7 ArO^- adducts of NBF are the products of both thermodynamic and kinetic control, although we cannot categorically rule out the possibility that the C-5 aryloxide adducts of NBF are extraordinarily unstable and rearrange to their C-7 counterparts prior to first observation.

Reasons for this apparent change in regioselectivity in the aryloxide systems are not entirely clear but a possible model in favour of C-7 addition for the aryloxide nucleophiles could be that they react through later transition state (TS) structures. A later TS for C-7 adduct formation would be expected to benefit from through-conjugation to the 4-NO_2 group,[3] and the greater thermodynamic stability associated with the C-7 adduct compared to the C-5 adduct may be reflected in the kinetics of reactions proceeding through a later TS structure. For aryloxide nucleophiles, reactivity through a more product-like TS may arise from the fact that the resulting σ-adducts are probably less stable than those of methoxide. This is emphasized in the reaction of PhO^- and MeO^- with 2,4,6-trinitroanisole where the C-1 O-adduct of PhO^- decomposes faster than the C-1 MeO^- adduct by a factor of 4.5×10^6, while their rates of formation are comparable.[11] Thus according to the Hammond postulate[12] the TS for C-7 and C-5 aryloxide attachment would be expected to be more product-like than the corresponding TSs for methoxide attachment since the methoxide reaction is anticipated to be more exothermic.

The final products in the aryloxide systems are the 7-aryloxynitronate derivatives (**4b–d**) and the oxyanion **5** (Scheme 1). Formation of the former species is attributed to transfer of the sp^3-bound (7-H) proton of **3b–d** to the *N*-oxide function.[5] This process is similar to the Cope reaction[13] which leads to the production of olefins and hydroxylamines from amine oxides, though in the present system the products (olefin and hydroxylamine) remain intact forming **4b–d**. Subsequent transfer of the OH function to C-7 and loss of ArOH leads to formation of the oxyanion **5**.[5] In the NBF–mesitoxide system, the inability to observe **4d** presumably arises from rapid expulsion of MesOH which would be accompanied by relief of strain at C-7 due to the presence of the *o*-methyl groups of the mesitoxy moiety.

(ii) *C-Adduct formation in the NBF–2,6-DTBP$^-$ system.* In the

interaction of NBF (**1**) with 2,6-di-*tert*-butylphenoxide ion (2,6-DTBP$^-$), the observed process was C-attack at C-7 of **1** and the resulting σ-adduct, **7**, was characterized in [$^2H_6$]DMSO at ambient temperature. This system was remarkably clean and in the first spectrum acquired (*ca.* 3 min after mixing) signals representing **7** were the only peaks present and remained unchanged over a 5 h period.

C-Adduct formation plausibly involves two steps whereas O-attachment occurs *via* a single step. Thus in the former process a quinoidal complex is formed in the first step and then undergoes rearomatization in the second step to produce the observed σ-adduct. Under the basic conditions employed rearomatization is rapid and formation of the quinoidal complex is rate determining.[2,6,7] Therefore, if attack at C-5 occurred to give a quinoidal NBF·2,6-DTBP$^-$ intermediate then C-5 adduct formation would follow in the rapid rearomatization step. It follows therefore that, similar to O-attachment of aryloxide nucleophiles with NBF, the forward rate constant for C-7 C-attack is more favourable than for C-5 attack, which also contrasts with the NBF–MeO$^-$ system.[3,4,5]

Arguments based on TS structure may also apply here since 2,6-DTBP$^-$ may react through a later TS which for C-7 adduct formation would benefit from through-conjugation of the developing negative charge to the C-4 *p*-nitro group, as before. Relative to the methoxide adducts, **2a** and **3a**, quinoidal complexes of 2,6-DTBP$^-$ would be expected to be destabilized since aromaticity of the 2,6-DTBP moiety is disrupted and this would lead to a later TS.

2. *Stereoelectronic Factors in the C-7 NBF Aryloxide O-Adducts.*—It has been well documented that in the absence of steric hindrance, substituents with lone pairs attached to aromatic rings, such as methoxy, prefer planar conformations over gauche or perpendicular.[14] In the planar conformation, conjugation of the p-type lone pair orbital of the heteroatom with the aromatic π-electron system (p–π overlap) is maximized. When this type of resonance is operative the *o*- and *p*-positions of the aromatic ring are shielded relative to the *m*-position.

Previously we have found that ^{13}C NMR parameters of TNB·OAr$^-$ O-adducts[6b] could be used to assess conformational preferences in the σ-adducts.[15] It was deduced that the TNB·OAr$^-$ O-adducts prefer an approximately planar arrangement where p–π overlap is maximized. Since each of the TNB·OAr$^-$ O-adducts was shown to prefer a planar conformation, the similarity in the ^{1}H NMR shifts of the TNB$^-$ moiety for each adduct seemed reasonable.

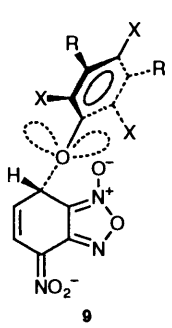
For the C-7 NBF aryloxide O-adducts, **3b–d**, ^{1}H NMR characteristics have been recorded in CD_3CN–[$^2H_{10}$]glyme at −40 °C (Table 1). The transient nature of the complexes, **3b–d**, did not allow for characterization by ^{13}C NMR spectroscopy in the present systems. In order to explore such conformational preferences in the NBF systems, trends in the ^{1}H NMR shift parameters of the NBF$^-$ moiety in **3b–d** (Table 1) are compared to those observed previously in the corresponding TNB systems.[6b]

Inspection of the ^{1}H NMR parameters (Table 1) reveals that for the NBF·OPh$^-$ adduct, **3b**, and the NBF·3,5-DTBP$^-$ adduct, **3c**, the chemical shifts of the NBF$^-$ moiety (5-H, 6-H, 7-H) are similar. The sp^3-bound protons, 7-H, are observed at δ 6.02 and 6.07 in **3b** and **3c**, while the 6-H protons are found at 5.34 and 5.29, and 5-H at 7.15 and 7.16, respectively. Hence, it is reasonable to assume that these two O-adducts occur in similar conformations.

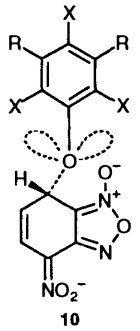
In contrast, the ^{1}H NMR shifts of the NBF$^-$ moiety in the mesitoxide adduct, **3d**, differ from those in **3b** and **3c**. For **3d**, 7-H is found at δ 5.63, 6-H at 5.07 and 5-H at 7.08. Relative to the corresponding shifts in **3b** and **3c**, 7-H resonates *ca.* 0.4 ppm upfield, while the sp^2-hybridized protons 6-H and 5-H are similarly located upfield, but not to the same extent (*ca.* 0.2 and 0.1 ppm, respectively). Hence it appears that the preferred conformer of **3d** differs from that of **3b** and **3c**. This rationale stems from the fact that in the corresponding TNB O-adducts the ^{1}H NMR shifts of the TNB$^-$ moiety and the conformational preferences were similar (*vide supra*).[6b]

To assess the nature of this apparent change in conformational preferences of the mesitoxide complex, **3d**, with respect to **3b** and **3c**, previous investigations of the methyl ethers, PhOMe and MesOMe, are informative. For anisole an approximately planar arrangement is preferred[13] which permits stabilization due to p–π overlap. For the mesityl ether, however, ^{13}C NMR results indicate that the methoxy group deviates from planarity.[16] For 2,6-dimethylanisole, Buchanan and co-workers predicted on the basis of ^{13}C NMR data that the angle of deviation is 44°.[14b] Hence the preferred conformer of MesOMe appears to be one with nearly perpendicular OMe, in which steric interactions between the OMe group and the aromatic *o*-Me groups are minimized and p–π overlap is correspondingly greatly diminished.

On the basis of the comparisons with the methyl ethers, PhOMe and MesOMe, and from inspection of the ^{1}H NMR parameters (Table 1) and molecular models (Darling), it appears that the preferred conformer of the NBF·OPh$^-$ adduct, **3b**, and the NBF·3,5-DTBP$^-$ adduct, **3c**, is one in which p–π overlap is operative. This points to an approximately planar geometry for the C-7–O–Ar grouping, with optimum overlap of the p-type orbital on the aryloxy oxygen with the π-electron system of the aryl ring. The conformer of **3b** which fits this description is shown by **9** (X = H, R = H). In this conformer, the sp^3-attached proton 7-H of the NBF$^-$ moiety is almost in the plane of the phenoxy ring while the furoxan ring is nearly perpendicular. For **3c**, an analogous conformer (**9**, X = H, R = Bu^t) is envisioned since the *m*-*tert*-butyl groups do not appear to exert a marked steric influence on the conformational preferences.



9



10

For the NBF·OMes$^-$ adduct, **3d**, a perpendicular geometry for the C-7–O–Ar grouping is expected with little or no p–π overlap between the lone pair on the mesitoxy oxygen and the aryl ring, analogous to the preferred conformer for MesOMe.[15] The conformation of **3d** which fits this characteristic is shown by **10** (X = Me, R = H). In this conformer the mesitoxy ring points upwards in the plane almost parallel to the NBF$^-$ ring. While steric interactions in this conformer are minimized, stabilization due to p–π overlap is greatly diminished.

The above predictions regarding the preferred conformations of the C-7 NBF·OAr$^-$ O-adducts, **3b–d**, appear consistent with the present ^{1}H NMR data (Table 1). For **3b** and **3c**, partial positive charge on the attached oxygen would be significant, since p–π overlap is expected in **9** (*vide supra*). The sp^3-attached proton, 7-H, is sensitive to the electronegativity of the attached group[2] and resonates downfield, *ca.* 6.0 ppm. In contrast, the

NBF·OMes$^-$ adduct, **3d**, has been shown to adopt a perpendicular conformation (**10**) which alleviates steric hindrance, but diminishes p–π overlap. Hence, the attached oxygen is more electron-rich and the sensitive 7-H proton resonates at δ 5.63, which is *ca.* 0.4 ppm upfield of the 7-H resonance in **3b** and **3c**.

Conclusions

The results of these studies on the course of the reactions of 4-nitrobenzofuroxan (NBF, **1**) with the aryloxide nucleophiles, phenoxide ion (PhO$^-$), 3,5-di-*tert*-butylphenoxide ion (3,5-DTBP$^-$), mesitoxide ion (MesO$^-$), and with 2,6-di-*tert*-butylphenoxide ion (2,6-DTBP$^-$), permit us to draw the following conclusions.

1. The C-7 NBF·OAr$^-$ O-adducts, **3b–d**, are kinetically favoured and are observed first in NMR studies at −40 °C in the MeCN–glyme solvent system. These O-adducts cannot be observed in [$^2H_6$]DMSO at ambient temperature due to a rapid decomposition pathway leading to formation of the 7-aryloxy nitronate derivatives, **4b–c**, which give way to the oxyanion **5**.

2. In the reaction of NBF with PhO$^-$, C-attachment by the potentially ambident (O- and C-attack) nucleophile was not observed. However, with 2,6-DTBP$^-$, where O-attachment is not sterically feasible, C-attack at C-7 of NBF occurs. The resulting σ-adduct **7** was stable in [$^2H_6$]DMSO over a 5 h period.

3. The regioselectivity displayed by the aryloxide nucleophiles was shown to differ from the behaviour displayed in the reaction of NBF with methoxide ion (MeO$^-$). In the NBF–MeO$^-$ system, the C-5 adduct, **2a**, is kinetically preferred, but the C-7 adduct, **3a**, is thermodynamically more stable. In the aryloxide systems, no evidence for C-5 attachment was found. This change in regioselectivity has been tentatively attributed to a decrease in adduct stability which may favour a more product-like transition state (TS) for reaction of aryloxide. A later TS would favour attachment at C-7 because it would benefit more from the stability gained in through-conjugation to the *p*-nitro group which operates in C-7 NBF adducts.

4. From the ^{1}H NMR chemical shifts of the NBF$^-$ moiety in the C-7 NBF·OAr$^-$ adducts, **3b–d**, it was concluded that an approximately planar configuration (**9**) is adopted by the phenoxide adduct, **3b**, and the 3,5-DTBP$^-$ adduct, **3c**. This geometry allows for conjugative overlap between the p-type orbital of the aryloxy oxygen with the π-electron system of the aromatic ring. In contrast, the mesitoxide adduct, **3d**, adopts a perpendicular geometry (**10**); this conformer does not possess optimal p–π overlap but is favoured on steric grounds.

Experimental

Materials and Methods.—4-Nitrobenzofuroxan (NBF, **1**) was prepared by the nitration of benzofuroxan [17] and recrystallized from ethyl acetate, m.p. 143 °C. CD_3CN, [$^2H_6$]DMSO and [$^2H_{10}$]glyme (Merck) were dried by treatment with 3 Å molecular sieves.[18] Trifluoroacetic acid (TFA) and tetramethylammonium hydroxide (Me_4NOH, 25 wt% solution in water) (Aldrich) were used without further purification. 1,4-Dibromobenzene (DBB, Eastman) was recrystallized from ethanol, m.p. 89 °C. Potassium ethoxide solutions were prepared from freshly cut potassium metal and dry EtOH (distilled from Mg turnings) under N_2 and standardized with potassium hydrogen phthalate. Phenol (BDH) and 2,6-di-*tert*-butylphenol (Aldrich) were distilled under vacuum and stored and handled in an argon-filled dry box. 2,4,6-Trimethylphenol (mesitol) and 3,5-di-*tert*-butylphenol (Aldrich) were purified by recrystallization from light petroleum. Melting points were measured on a Thomas–Hoover capillary apparatus and were not corrected.

Following the method described by Kornblum and Laurie for the preparation of phenoxide ion,[19] potassium 2,6-di-*tert*-butylphenoxide (2,6-DTBPK) was prepared from the phenol and EtOK–EtOH as a pale green powder. Its ^{1}H NMR spectrum in [$^2H_6$]DMSO showed the following resonances: δ 6.58 (2 H, d, *J* 7.3), 5.57 (1 H, t, *J* 7.3) and 1.32 (18 H, s). PhOK, MesOK and 3,5-DTBPK were prepared in a similar fashion and had spectra in agreement with those previously reported.[7a,6b]

NMR Experiments.—The NMR experiments were carried out on a Bruker AM-400 spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz) in CD_3CN–[$^2H_{10}$]glyme (1 : 1, v/v) and in [$^2H_6$]DMSO. In the mixed solvent system, CD_2HCN served as reference (^{1}H: δ 1.93) and lock signal, while spectra recorded in DMSO were referenced to the [$^2H_5$]DMSO-H peak (δ 2.50). Chemical shifts are given in parts per million (ppm), coupling constants in hertz (Hz). Wilmad pp-507 NMR tubes (5 mm) were used in all experiments. All stock solutions and NMR tubes were capped with rubber septa and swept out with N_2 prior to injection of the reactants by means of a syringe.

(a) *A representative room temperature experiment in DMSO.* The NBF stock solution (0.40 mol dm^{-3}) consisted of 36.4 mg of substrate dissolved in 500 mm^3 of [$^2H_6$]DMSO. Transfer of 75 mm^3 of stock NBF solution into an NMR tube containing solvent (340 mm^3) and DBB (5 mm^3 from a 1 mol dm^{-3} stock solution) afforded the initial sample. DBB functioned as the internal integration standard. Addition of 1 equiv. of 3,5-DTBPK (80 mm^3 from a 0.383 mol dm^{-3} solution) initiated the reaction. ^{1}H NMR spectra were recorded at various intervals, generally as rapidly as possible (within 3 min) at the start of the reaction and then at progressively longer intervals as the reaction proceeded.

In a separate experiment, 1 equiv. of 3,5-DTBPK was added to the NMR tube containing the NBF solution. After acquisition of an initial spectrum (*ca.* 3 min after mixing), D_2O (2 mm^3), followed by TFA (5 mm^3), were added and spectra were recorded after each addition.

(b) *Low temperature NMR experiments in* MeCN–*Glyme* (1 : 1). Typically, 1 equiv. of the aryloxide was dissolved in a 1 : 1 (v/v) mixture of CD_3CN–[$^2H_{10}$]glyme. This solution (300 mm^3) was injected into an NMR tube and the solution frozen by immersion in liquid N_2. To the frozen solution was added 1 equiv. of NBF (200 mm^3; final concentrations 0.06–0.1 mol dm^{-3}). The resulting mixture was placed in a dry ice–acetone bath, which had been maintained at −50 °C. The contents of the tube were allowed to mix and then the tube was again immersed in liquid N_2. The sample was transferred to the spectrometer probe (−40 °C) and spectra were recorded at various intervals, a standard sequence being 3, 5, 7, 9 min and then as warranted by the observed changes. At the same time the temperature of the probe would gradually be raised.

7-Aryloxy-4-nitrobenzofurazan Ethers, **6b–d**.—These compounds were prepared from the respective potassium aryloxide salt and 7-chloro-4-nitrobenzofurazan (NBD-chloride; Aldrich, 98%) *via* S_NAr displacement of chloride. The general procedure outlined by Ahnoff and coworkers [8] for the preparation of the 7-phenoxy derivative, **6b**, was followed.

7-Phenoxy-4-nitrobenzofurazan, **6b**. Phenol (0.82 g; 8.72 mmol) was dissolved in 20 cm^3 of dry ethanol and to this stirred solution was added 6 cm^3 of a 1.41 mol dm^{-3} stock EtOK solution (8.46 mmol). The mixture was stirred for 30 min and then an ethanolic solution (30 cm^3) of NBD-chloride (1.74 g, 8.72 mmol) was added. After 30 min, 100 cm^3 of distilled water was added and the resulting orange precipitate was collected. Recrystallization from ethanol produced a yellow powder (0.87 g, 40%), m.p. 116–120 °C (lit.[8] 114–119 °C).

*7-(3,5-Di-*tert*-butylphenoxy)-4-nitrobenzofurazan*, **6c**. NBD-

Chloride (0.763 g; 3.82 mmol) was dissolved in 80 cm^3 of ethanol and to this stirred solution was added 1 equiv. of 3,5-DTBPK (0.941 g; 3.85 mmol) in 20 cm^3 of ethanol. The mixture was stirred for *ca.* 30 min and 100 cm^3 of distilled water was added. The resulting pale yellow precipitate was collected and dried (1.4 g; 100%), m.p. 185–186 °C; $\delta_H([^2H_6]DMSO)$ 8.66 (1 H, d, *J* 8.4), 6.64 (1 H, d, *J* 8.4), 7.45 (1 H, t, *J* 1.5), 7.24 (2 H, d, *J* 1.5) and 1.31 (18 H, s); $\delta_C([^2H_6]DMSO)$ 153.8, 153.5, 145.4, 144.4, 135.8, 120.3, 114.8, 108.9, 34.9 and 31.0.

7-Mesitoxy-4-nitrobenzofurazan, **6d**. NBD-Chloride (0.72 g; 3.6 mmol) was dissolved in 50 cm^3 of ethanol and an ethanolic solution (20 cm^3) of potassium mesitoxide (0.629 g, 3.6 mmol) was added. The mixture was stirred at room temp. for 30 min and then distilled water (100 cm^3) was added. The yellow precipitate was collected (0.903 g; 84%) and dried, m.p. 159–160 °C. $\delta_H([^2H_6]DMSO)$ 8.60 (1 H, d, *J* 8.4), 6.30 (1 H, d, *J* 8.4), 7.09 (2 H, s), 2.31 (3 H, s) and 2.09 (6 H, s). $\delta_C([^2H_6]DMSO)$ 152.2, 146.9, 144.9, 144.5, 136.2, 135.7, 130.0, 129.4, 107.5, 20.3 and 15.3.

Acknowledgements

Financial support from the Natural Sciences and Engineering Research Council of Canada (NSERCC) in the form of an operating grant to E. B. is appreciated. The support of the Ontario Government in the form of a graduate scholarship to R. A. M. is also acknowledged.

References

1 (*a*) P. B. Ghosh and M. W. Whitehouse, *J. Med. Chem.*, 1968, **11**, 305; (*b*) M. W. Whitehouse and P. B. Ghosh, *Biochem. Pharmacol.*, 1968, **17**, 158; (*c*) P. B. Ghosh, B. Ternai and M. W. Whitehouse, *J. Med. Chem.*, 1972, **15**, 255.

2 (*a*) E. Buncel, M. R. Crampton, M. J. Strauss and F. Terrier, *Electron Deficient Aromatic- and Heteroaromatic-Base Interactions. The Chemistry of Anionic Sigma Complexes*, Elsevier, Amsterdam, 1984; (*b*) F. Terrier, *Nucleophilic Aromatic Displacement: The Influence of the Nitro Group*, VCH, New York, 1991; (*c*) E. Buncel, J. M. Dust, K. T. Park, R. A. Renfrow and M. J. Strauss, in *Nucleophilicity*, eds. J. M. Harris and S. P. McManus, ACS Advances in Chemistry Series 215; American Chemical Society, Washington, DC, 1987; pp. 369–383.

3 F. Terrier, A. P. Chatrousse and F. Millot, *J. Org. Chem.*, 1980, **45**, 2666.

4 F. Terrier, F. Millot, A. P. Chatrousse, M. J. Pouet and M. P. Simonnin, *Org. Magn. Reson.*, 1976, **8**, 56.

5 E. Buncel, N. Chuaqui-Offermanns, B. K. Hunter and A. R. Norris, *Can. J. Chem.*, 1977, **55**, 2852.

6 (*a*) E. Buncel, J. M. Dust, A. Jonczyk, R. A. Manderville and I. Onyido, *J. Am. Chem. Soc.*, 1992, **114**, 5610; (*b*) E. Buncel and R. A. Manderville, *J. Phys. Org. Chem.*, 1993, **6**, 71; (*c*) E. Buncel, J. M. Dust, R. A. Manderville, K. T. Park and I. Onyido, *Bull. Soc. Chim. Fr.*, 1988, **66**, 1712; (*d*) E. Buncel, S. K. Murarka and A. R. Norris, *Can. J. Chem.*, 1984, **62**, 534; (*e*) E. Buncel, and W. Eggimann, *Can. J. Chem.*, 1974, **54**, 2436.

7 (*a*) E. Buncel and J. M. Dust, *Can. J. Chem.*, 1988, **66**, 1712; (*b*) E. Buncel, R. A. Renfrow and M. J. Strauss, *J. Org. Chem.*, 1987, **52**, 488; (*c*) R. A. Renfrow, M. J. Strauss, S. Cohen and E. Buncel, *Aust. J. Chem.*, 1983, **36**, 1843.

8 L. Johnson, S. Lagerkvist, P. Lindroth, M. Ahnoff and K. Martinsson, *Anal. Chem.*, 1982, **54**, 939.

9 F. Terrier, G. Ah-Kow and A. P. Chatrousse, *J. Org. Chem.*, 1985, **50**, 4583.

10 R. A. Manderville and E. Buncel, *J. Am. Chem. Soc.*, in the press.

11 (*a*) C. F. Bernasconi and M. C. Muller, *J. Am. Chem. Soc.*, 1978, **100**, 5530; (*b*) C. F. Bernasconi, *Acc. Chem. Res.*, 1978, **11**, 147.

12 G. S. Hammond, *J. Am. Chem. Soc.*, 1955, **77**, 334.

13 J. March, *Advanced Organic Chemistry*, third edn., Wiley, New York, 1985, p. 909 and references cited therein.

14 (*a*) G. M. Anderson III, P. A. Kollman, L. N. Domelsmith and K. N. Houk, *J. Am. Chem. Soc.*, 1979, **101**, 2344, and references cited therein; (*b*) T. Schaefer, R. Laatikainen, T. A. Wildman, J. Peeling, G. H. Penner, J. Baleja and K. Marat, *Can. J. Chem.*, 1984, **62**, 1592 and references cited therein.

15 (*a*) K. S. Dhami and J. B. Stothers, *Can. J. Chem.*, 1966, **44**, 2855; (*b*) G. W. Buchanan, G. Montaudo and P. Finocchiaro, *Can. J. Chem.*, 1974, **52**, 767.

16 M. Fujita, M. Yamada, S. Nakajima, K. I. Kawai and M. Nagai, *Chem. Pharm. Bull.*, 1984, 2622.

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

18 D. R. Burfield and R. H. Smithers, *J. Org. Chem.*, 1978, **43**, 3966.

19 N. Kornblum and A. P. Laurie, *J. Am. Chem. Soc.*, 1959, **81**, 2705.

Paper 3/02065G
Received 13*th April* 1993
Accepted 7*th June* 1993