JOURNAL OF PHYSICAL ORGANIC CHEMISTRY, VOL. 9, 515–528 (1996)

REACTION PATHWAYS FOR AMBIDENT ARYLOXIDE O- AND C-NUCLEOPHILES IN S_NAr DISPLACEMENT VERSUS MEISENHEIMER COMPLEX FORMATION WITH PICRYL HALIDES. STEREOELECTRONIC EFFECTS ON REGIOSELECTIVITY

RICHARD A. MANDERVILLE†
Department of Chemistry, Wake Forest University, Winston-Salem, North Carolina 27109, USA
JULIAN M. DUST†
Department of Chemistry, Sir Wilfred Grenfell College, Corner Brook, Newfoundland, A2H 6P9, Canada
AND
ERWIN BUNCEL†
Department of Chemistry, Queen's University, Kingston, Ontario, K7L 3N6, Canada

To probe regioselectivity in Meisenheimer complexation, the reaction of two picryl halides (PiX where X = F, Cl) with a series of aryloxide nucleophiles (phenoxide, 2,4,6-trimethylphenoxide and 2,6-di-*t*-butylphenoxide) were monitored by ^{1}H NMR spectroscopy in dimethyl sulphoxide at ambient temperature and in acetonitrile–dimethoxyethane (MeCN–DME) at low temperature (−40 °C). The reactions of both picryl halides with the ambident (oxygen versus carbon) nucleophile, phenoxide ion (PhO^-), and 2,4,6-trimethylphenoxide (mesitoxide, $MesO^-$) leads to clean S_NAr displacement of X via the oxygen site of the nucleophile to form the respective aryl picryl ethers, i.e. phenyl picryl ether (3a) and mesityl picryl ether (3b). Meisenheimer complex formation at C-1 or C-3 was not detected in these systems. With 2,6-di-*t*-butylphenoxide (2,6-DTBPhO$^-$), where oxygen attachment of the aryloxide is precluded by the bulky *ortho t*-butyl groups, *para*-carbon attachment was found to occur at C-1 to give picryl 2,6-di-*t*-butylphenol (3d) in competition with C-attack at C-3 to give the respective carbon-bonded Meisenheimer complexes [X = Cl (4) and X = F (5)]. For both picryl halides, the ratio of 3d, the product of C-1 attack, to the product of C-3 attack, 4 or 5, was roughly 7:1. These findings are considered with regard to the nucleofugality of the halide, X, steric hindrance (F-strain) to attack by the aryloxides at the various positions and stereoelectronic stabilization of C-1 adducts afforded by n → σ^* donation.

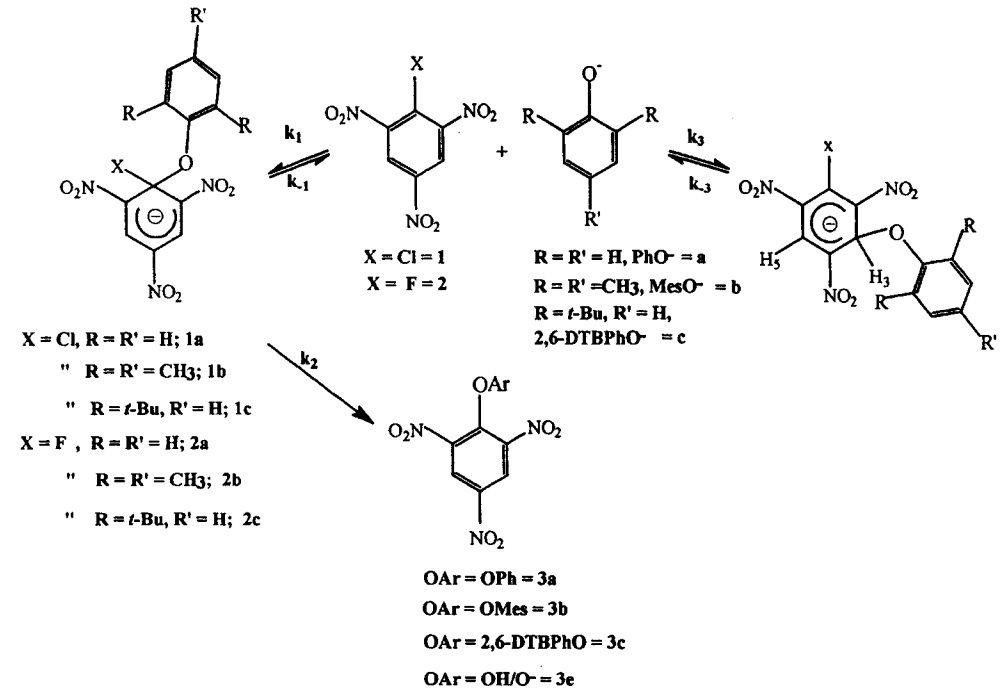
INTRODUCTION

Recent efforts in our laboratories have focused on the thermodynamics and kinetics of regioselectivity in Meisenheimer complexation.[1] In brief, a nucleophile, Nu:$^-$, may attack either C-1 or C-3 of a 1-X-2,4,6-trinitrobenzene (PiX).[2–4] As shown in Scheme 1 for the O-centred nucleophiles (i.e. Nu:$^-$ = ArO^-), attack at C-1 (rate constant k_1) leads to the formation of an anionic C-1 σ-bonded adduct, C-1 PiX·Nu$^-$ (**1a-3** and **2a-f**), in which the negative charge is delocalized over the ring and the *ortho* and *para* electron-withdrawing nitro groups; this adduct is termed a Meisenheimer[5] or Jackson–Meisenheimer[6] σ-complex. If X is a much better leaving group than the erstwhile nucleophile, Nu:$^-$, X:$^-$ may be rapidly ejected (k_2) to give rise to the S_NAr substitution product.[7] In this case, the rate constant for the second step is large relative to that for the first step ($k_2 > k_1$) and if the rate constant for the second step is also much larger than the constant for

* Part 53 in a series of anionic σ-complexes; for Part 52, see Ref. 1. This paper is also Part 6 in a series on regioselectivity of aryloxide ions in Meisenheimer complexation; for Parts 4 and 5 see Refs. 12a and 12b. Part 1 is Ref. 9b.
† Authors for correspondence.

CCC 0894–3230/96/080515–14

Received 21 December 1995
Revised 11 March 1996



Scheme 1

decomposition of the C-1 adduct back to PiX and Nu:$^-$ (i.e. $k_2 \gg k_{-1}$), k_1 becomes the rate-determining coefficient in the mechanism. In the inverse situation, where $k_{-1} \gg k_2$, k_2 becomes the rate determining constant.) Alternatively, Nu:$^-$ may attack at the unhindered C-3 position to give an unproductive C-3 PiX·Nu$^-$ adduct. If the departing X and the incoming Nu:$^-$ are of similar nucleofugality (or if X:$^-$ is a poorer nucleophile than Nu:$^-$), then both C-3 and C-1 Meisenheimer complexes may be detectable, depending on solvent and temperature.

^{1}H NMR is particularly valuable in identifying and characterizing these C-3 and C-1 regioisomeric adducts and in following their fates. Thus, in the classic study of Servis,[8] reaction of 2,4,6-trinitroanisole (TNA) with methoxide ion (MeO$^-$) was found to yield a ^{1}H NMR spectrum that contained signals assignable to both C-1 and C-3 adducts. Initially, the C-3 adduct resonances were dominant, but with time these peaks gave way in favour of those ascribed to the C-1 TNA·OMe$^-$ adduct. Finally, only signals of the C-1 complex were found in the NMR spectrum. Since then this pattern of kinetically preferred C-3 attack that eventually leads to formation of the C-1 adduct as the product of thermodynamic control has been documented in numerous picryl ether–alkoxide reaction systems.[9] We have classified this behaviour as K3T1 (kinetic preference for C-3 attack with thermodynamic preference for C-1 adduct formation).[10a]

More recently, our low temperature (−40 °C) ^{1}H NMR studies of the interactions of phenoxide ion (PhO$^-$), as an oxygen-centred nucleophile,[10a] and 2,4,6-trimethylphenoxide (mesitoxide, MesO$^-$)[11] with TNA have clearly demonstrated a wide range of reactivity in Meisenheimer complexation. In this regard, PhO$^-$ yields the C-1 TNA·OPh$^-$ O-adduct as the product of both kinetic and thermodynamic preference,[10] an example of K1T1 regioselectivity. Note that a C-3 TNA·OPh$^-$ Meisenheimer complex is not seen in this system at any time. With extended periods of observation, a carbon-centred C-3 adduct of phenoxide, the C-3 TNA·PhO(H)$^-$ complex, is found as the ultimate product of thermodynamic control. Assuming this C-3 C-adduct is thermodynamically more stable than its unseen C-1 counterpart (as is the case in Meisenheimer complexation of TNA with methide ion according to recent AM1 semi-empirical calculations),[12a] the behaviour of phenoxide as a C-nucleophile follows the K3T3 pattern of regioselectivity. Significantly, the reaction of mesitoxide, a bulky nucleophile that is restricted to attack via oxygen, manifests the final form of regioselectivity: K1T3. Here, C-1 attack is favoured kinetically and the C-1 TNA·OMes$^-$ adduct is the first Meisenheimer complex observed in the system at low

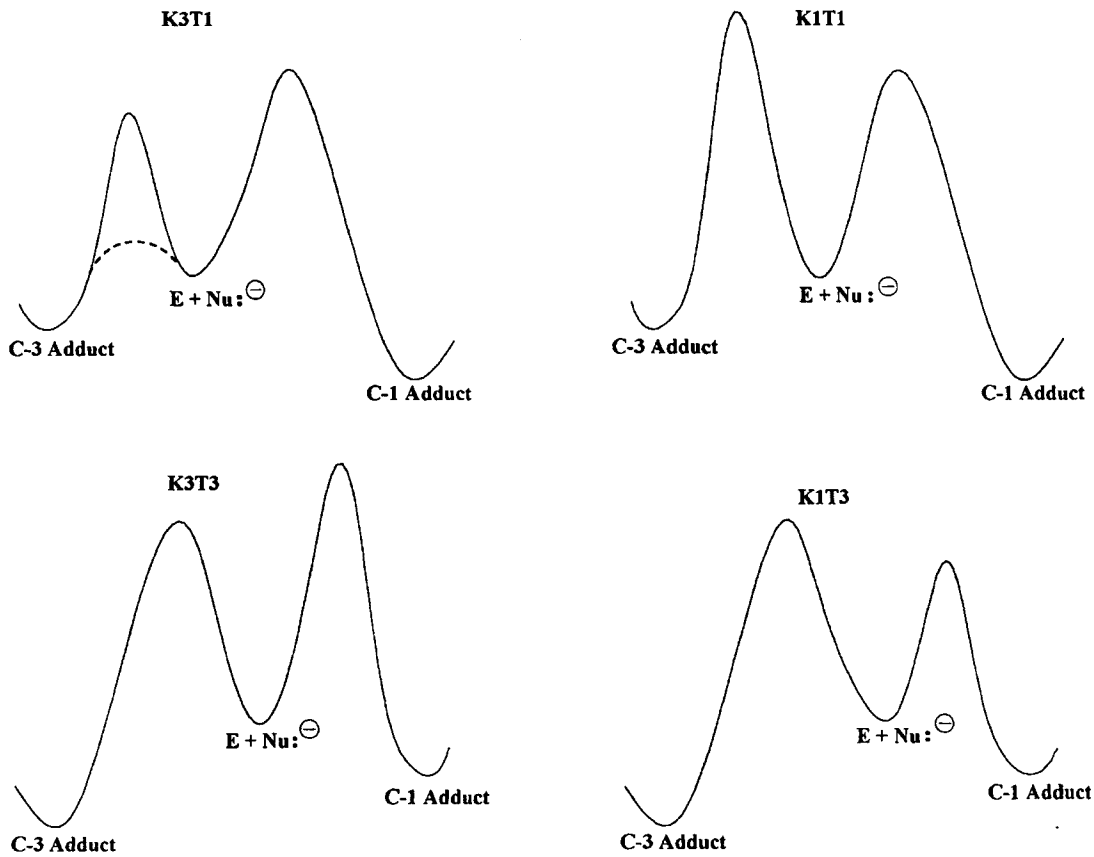


Figure 1. Regioselectivity in Meisenheimer complex formation is described by the four possible qualitative energy–reaction coordinate profiles shown. K3T1 represents the case where attack of a nucleophile at C-3 is kinetically favoured, but the C-1 adduct is the product of kinetic control. If attack at C-1 is favoured by both kinetics and thermodynamics the K1T1 profile obtains, whereas if attack at C-3 is similarly doubly favoured, the K3T3 profile applies. The regioselectivity that is opposite to K3T1 is labelled K1T3; the profile clearly shows that attack at C-1 is now favoured by kinetics whereas the thermodynamic product arises from C-3 adduct attack. The dashed line profile incorporated in the K3T1 diagram represents a 'pseudo-K1T1' regioselectivity, where a C-3 adduct may not be observed owing to the time-scale of the observational technique.

temperature (−40 °C). Over time the C-1 adduct is replaced by C-3 $MesO^-$ and C-1,3 di($MesO^-$) adducts. Therefore, C-1 ⟶ C-3 adduct isomerization is found in the TNA–$MesO^-$ reaction system.

Most recently, we have reviewed[12b] the literature concerning regioselectivity in Meisenheimer complexation and shown that the situations cited above are not isolated, but enrich the number of examples that support a broad range of regioselectivity. Figure 1 shows a qualitative energy–reaction coordinate profile for this and the other classes of regioselectivity found in Meisenheimer complexation: K3T1, K1T1, K3T3 and K1T3. It should also be pointed out that this classification scheme has now achieved general acceptance; Chamberlin and Crampton[13] have added to the examples with the finding that phenyl and ethyl picryl ethers react with *n*-butylamine, pyrrolidine and piperidine according to the K3T1 pattern, and while phenyl picryl thioether apparently follows the same K3T1 regioselectivity with *n*-butylamine, with pyrrolidine and piperidine the K3T3 pattern prevails.

The present study involves the reactions of two picryl halides, namely picryl chloride (**1**) and picryl fluoride (**2**) (i.e. PiX where X = Cl, PiX = PiCl and where X = F, PiX = PiF, respectively), with a series of aryloxides: phenoxide (PhO^-), 2,4,6-trimethylphenoxide (mesitoxide; $MesO^-$) and 2,6-di-*t*-butylphenoxide (2,6-$DTPhO^-$). These aryloxides vary in terms of steric bulk about the reactive oxygen nucleophilic centre. Thus, 2,6-$DTPhO^-$ is highly hindered about the O-centre and this hindrance declines in going to $MesO^-$ and to PhO^-, in turn. Further, $MesO^-$ is limited to O-attack, whereas

PhO^- and 2,6-DTPhO$^-$ may, in principle, act as ambident O- and C-nucleophiles. There is further differentiation between these aryloxides in the sense that PhO^- may potentially react via either *ortho* or *para* carbon centres, while 2,6-DTPhO$^-$, as a C-nucleophile, is clearly limited to reaction via the *para* ring carbon.

Therefore, in this paper we report the results of monitoring these PiX–ArO$^-$ systems both in dimethyl-d_6 sulphoxide (DMSO-d_6) at ambient temperature and in the acetonitrile-d_3–dimethoxyethane-d_{10} [MeCN-d_3–DME-d_{10} (1:1, v/v)] solvent medium at low temperature (−40 °C) using ^{1}H NMR spectroscopy. Previously, we have shown the utility of the latter medium, which is fluid to −50 °C, for NMR spectroscopic studies of Meisenheimer complexes and the reactions that involve them.[10a,11,14] These results will be discussed in terms of the relative leaving group abilities of the two halides, the regioselectivity of the nucleophiles (as elucidated in the picryl ether systems)[12] and the steric hindrance to attack expected for the nucleophiles and substrates (F-strain).[15,16] We have previously found stereoelectronic factors, notably $n \rightarrow \sigma^*$ stabilization of C-1 adducts that are geminally substituted with electronegative groups, to be significant in determining the regioselectivity in these systems. Consequently, in discussing regioselectivity in the current picryl halide–aryloxide reactions, the role of stereoelectronic stabilization of C-1 adducts will be highlighted.

RESULTS

Reaction of picryl chloride (PiCl) with phenoxide, mesitoxide and 2,6-di-*t*-butylphenoxide nucleophiles

Injection of 1 equiv. of potassium phenoxide (KOPh) solution (in DMSO-d_6 or MeCN-d_3–DME-d_{10}, as required) into an NMR tube that contained picryl chloride, **1**, (final concentrations 0.06 M) resulted in an initial spectrum (acquired within 4 min of mixing) either at ambient temperature, in the case of DMSO-d_6, or at −40 °C, in the case of the MeCN–DME medium, that no longer contains a signal for **1**. Chemical shifts of peaks are slightly different in the MeCN–DME medium (within 0.2 ppm; see Tables 1 and 2). However, the course of the reaction sequence is the same in both solvents and, for the sake of clarity, chemical shifts and other spectroscopic characteristics will be reported as found in the more commonly used DMSO solvent (Table 1), unless specified otherwise. Thus, in DMSO-d_6 the singlet of **1** at δ 9·24 (s, H-3,5) is no longer present in the first spectrum, although the trace does exhibit very small peaks that represent phenol at δ 9·28 (s, OH), 7·15 (apparent t,* H-*para*)

Table 1. Summary of ^{1}H NMR spectroscopic parameters[a] in DMSO-d_6 (at ambient temperature)

Species	H-5	H-3	Other signals
1	9·24 (s)	9·24 (s)	
2	9·18 (d, J = 5·6)	9·18 (d, J = 5·6)	
2f	8·65 (d, J = 3·9)	8·65 (d, J = 3·9)	
3a	9·23 (s)	9·23 (s)	7·39 (t[b], 2H, H-*meta*), 7·19 (t, 1H, H-*para*), 7·06 (d, H-*ortho*)
3b	9·11 (s)	9·11 (s)	6·90 (s, 2H, H-3,5 mesityl), 2·22 (s, 3H, CH_3-*para*), 2·03 (s, 6H, CH_3-*ortho*)
3d	9·12 (s)	9·12 (s)	7·63[c] (s, br, 1H, OH), 7·04[d] (s, 2H, H-3,5 phenolic moiety), 1·35 (s, 18H, 2,6-di-*t*-Bu), OH (ionized)
3e	8·58 (s)	8·58 (s)	
4	8·46 (d, J = 1·5)	5·79 (d, J = 1·5)	6·94 (s, 2H, H-3,5 phenolic moiety), 1·32 (s, 18H, 2,6-di-*t*-Bu), OH (ionized)
5	8·32 (d, J = 4·6)	5·64 (d, J = 5·8)	7·04 (s, 2H, H-3,5 phenolic moiety), 1·30 (s, 18H, 2,6-di-*t*-Bu), OH (ionized)

[a] Recorded at 400·1 MHz. Chemical shifts are given in parts per million (ppm), relative to residual CD_3SOCD_2H in the solvent. Coupling constants (J) are reported in Hz.

[b] The signal for the *para* proton is an *apparent* triplet, with unresolved coupling. This is typical of the signals for attached phenyl and phenoxyl moieties and, therefore, throughout this paper aryl-H (i.e. attached phenoxyl H) peaks reported as triplets or doublets should be taken as apparent triplets and apparent doublets.

[c] In the reaction medium the OH is ionized; assigned from authentic sample separately prepared.

[d] Overlapped with H-3,5 (phenolic moiety) singlet of **5** in the PiF-2,6-DTBPhO$^-$ reaction system.

* The signal for the *para* proton is an *apparent* triplet, with unresolved coupling. This is typical of the signals for attached phenyl and phenoxyl moieties and, therefore, throughout this paper aryl-H (i.e. attached phenoxyl H) peaks reported as triplets or doublets should be taken as apparent triplets and apparent doublets.

Table 2. Summary of ^1H NMR spectroscopic parameters[a] in MeCN-d_3–DME-d_{10} (1:1, v/v; −40 °C)

Species	H-5	H-3	Other signals
1	9·11 (s)	9·11 (s)	
2	9·16 (d, J = 5·6)	9·16 (d, J = 5·6)	
2f	8·64 (d, J = 3·9)	8·64 (d, J = 3·9)	
3a	9·09 (s)	9·09 (s)	7·34 (t[b], 2H, H-*meta*), 7·16 (t, 1H, H-*para*), 6·96 (d, 2R H-*ortho*)
3b	8·90 (s)	8·90 (s)	6·83 (s, 2H, H-3,5 mesityl), 2·18 (s, 3H, CH_3-*para*), 2·01 (s, 6H, CH_3-*ortho*)
3d	9·10 (s)	9·10 (s)	7·03 (s, 2H, H-3,5 phenolic moiety), 1·34 (s, 18H, 2,6-di-*t*-Bu), OH (ionized)
3e	8·60 (s)	8·60 (s)	

[a] Recorded at 400·1 MHz. Chemical shifts are given in parts per million (ppm), relative to residual CD_2HCN in the solvent. Coupling constants (J) are reported in Hz.
[b] See Table 1, footnote b.

and 6·74 (m, H-*meta* and -*ortho*). More importantly, a new singlet is observed at δ 9·23 (2H), which cannot be misidentified as belonging to **1** because it is in appropriate integral ratio to the peaks at 7·39 (t,* 2H), 7·19 (t, 1H) and 7·06 (d, 2H); these signals are attributed to H-3,5, H-*meta*, H-*para* and H-*ortho*, respectively, of 1-phenoxy–2,4,6-trinitrobenzene (**3a**), the product of S_NAr displacement of chloride from the picryl chloride. The signals for separately prepared **3a** match those recorded in the reaction system. In some experiments, a small singlet assignable to the equivalent ring protons (H-3,5) of picrate anion ($PicO^-$) (**3e**) could also be seen at δ 8·58 ppm from the very first spectrum.

At no time could Meisenheimer adducts be observed, including the necessary C-1 PiCl·OPh^- complex that leads to the displacement product, **3a** (Scheme 1). Furthermore, no adducts were observed that could be assigned to non-productive C-3 adducts such as C-3 PiCl·OPh^- or C-3 PiCl·OH^-. In related systems[10a–12] the corresponding C-3 hydroxide adducts have been readily observed; their presence is the result of equilibration between the aryloxide and residual small amounts of water in the reaction media and these hydroxide adducts ultimately lead to formation of picrate ion (**3e**), presumably via a transient C-1 OH^- adduct (**1e**, Scheme 1).[10a] The traces of $PicO^-$ found in some of the experimental runs probably arise from this pathway even though none of the hydroxide adducts were observed in the system.

Monitoring of the PiCl–$MesO^-$ reaction system yielded comparable results. Upon mixing equimolar potassium mesitoxide solution with the PiCl sample, the initial spectrum did not include the singlet for **1** and in its place resonances were recorded for the 2,4,6-trimethyl-2′,4′,6′-trinitrophenyl ether (mesityl picryl ether, PiOMes, **3b**). The peaks assigned to **3b** are located (in DMSO-d_6) at δ 9·11 (s, 2H, H-3′,5′ picryl), 6·90 (s, 2H, H-3,5 mesityl), 2·22 (s, 3H, CH_3-*para*) and 2·03 (s, 6H, CH_3-*ortho*). Again, regardless of whether the experiment was conducted at room temperature or at −40 °C, no signals were detected that could be assigned to any intermediate (i.e. the C-1 PiCl·$OMes^-$ complex, **1b**) or non-productive Meisenheimer complexes.

Addition of 1 equiv. of 2,6-DTBPhO$^-$ in DMSO-d_6 to a DMSO-d_6 solution of **1** (final concentrations 0·06 M) results in a deep blue solution. The first spectrum of the reaction mixture (acquired within 3 min of mixing) displays signals assignable to the biphenyl derivative (**3d**), a small amount of picrate anion, $PicO^-$ (δ 8·58, s, 2H, H-3,5), 2,6-di-*t*-butylphenol (δ 7·06, d, J = 7·8 Hz, 2H, H-3,5; 6·96, s br, 1H, OH; 6·75, t, J = 7·8 Hz, 1H, H-4; and 1·37, s, 18H, 2,6-di-*t*-Bu-2,6) and unmodified PiCl (δ 9·24). The signals ascribed to **3d** were confirmed by comparison to authentic 2,6-di-*t*-butyl-4-(2′,4′,6′-trinitrophenyl)phenol (picryl di-*t*-butylphenol); these resonances are located (in DMSO-d_6) at δ 9·12 (s, 2H, H-3′,5′), 7·63 (s br, 1H, OH), 7·04 (s, 2H, H-3,5 phenolic moiety) and 1·35 (s, 18H, 2,6-di-*t*-Bu). Significantly, peaks are also present that represent the C-3 carbon-bonded PiCl·[2,6-DTPhO(H)]$^-$ σ-complex (**4**) (Table 1), that arises from attack of the *para* carbon of the 2,6-DTBPhO$^-$ nucleophile on the C-3 position of PiCl. The signals for **4** appear at δ 8·46 (d, J = 1·5 Hz, 1H, H-5), 6·95 (s, 2H, H-3,5 phenolic moiety), 5·79 (d, J = 1·5 Hz, 1H, H-3) and 1·32 (s, 18H, 2,6-di-*t*-Bu). No signal was present for the OH of the attached aryl moiety and from the NMR evidence the state of ionization of this OH group would be uncertain. However, the dark blue colour of the solution is comparable to that found by Stahly[17] and attributed to the 670 nm absorbance of 2,6-di-*t*-butyl-4-(2′,4′-dinitrophenyl)phenoxide; the comparison suggests that the attached phenolic OH is ionized and that the solution is still alkaline at this stage in the reaction. Finally, note that the ratio of the product of C-1 attack (**3d**) to the product of C-3 attack (**4**) is 88%:12% = 7·3:1.

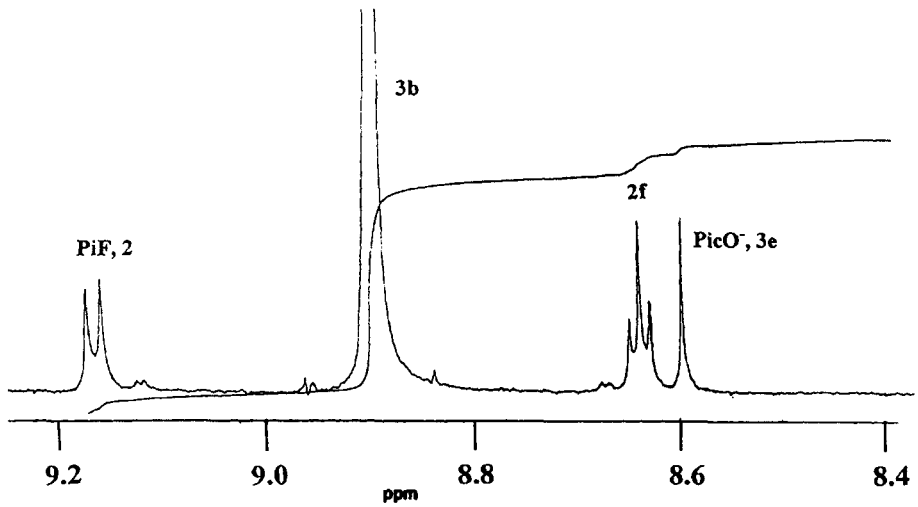
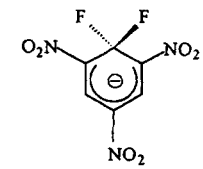


Figure 2. Initial ^{1}H NMR spectrum (400 MHz) of the PiF–MesO$^-$ reaction system (8·4–9·2 ppm region), recorded within 3 min of mixing of the reactants. The spectrum, acquired at −40 °C in MeCN-d_3–DME-d_{10} (1:1, v/v), displays peaks ascribed to the displacement product, mesityl picryl ether (**3b**), picrate anion (PicO$^-$, **3e**), unmodified PiF (**2**) and the geminal C-1 PiF·F adduct (**2f**)

Reaction of picryl fluoride (PiF) with phenoxide, mesitoxide and 2,6-di-*t*-butylphenoxide nucleophiles

The reaction of equimolar picryl fluoride (**2**) with PhO$^-$ mirrors the behaviour found in the PiCl–PhO$^-$ reaction system. The initial ^{1}H NMR spectrum contains signals for residual PiF (δ 9·18, d, J = 5·6, 2H, H-3,5) and for phenol. Again, no C-1 (such as the C-1 PiF·OPh$^-$ complex, **2a**) or C-3 adducts were observed in the reaction regardless of the experimental conditions and again the only observable product was the phenyl picryl ether **3a** (Scheme 1).

The reaction of **2** with MesO$^-$ in DMSO-d_6 was as clean as that described for the PiF–PhO$^-$ system; the corresponding mesityl picryl ether (**3b**) was formed without the apparent intervention of any Meisenheimer complexes, notably the C-1 PiF·OMes$^-$ adduct (**2b**). Interestingly, in the reaction of MesO$^-$ with **2** conducted in MeCN-d_3–DME-d_{10} at reduced temperatures, formation of **3b** was not the only process seen. Thus, while the initial spectrum, acquired within 3 min of mixing at −40 °C, is dominated by the intense signal for **3b** (Figure 2; δ 8·90, H-3,5 of **3b**, shifted slightly upfield relative to chemical shifts in DMSO-d_6) and contains resonances attributable to unreacted **2** and to **3e**, a triplet is also noted that is centred at δ 8·64 (J = 3·9 Hz). This resonance is assigned to the ring protons (H-3,5) of the geminal C-1 PiF·F$^-$ adduct (**2f**, Scheme 1). The spectroscopic parameters (Table 2) are in reasonable agreement with those reported by Terrier *et al.*[18] for the same Meisenheimer complex (δ 8·70, d, J = 3·9, 2H, H-3,5 as observed in MeCN solvent). Similar results were noted when the reaction at low temperature was repeated using an excess of MesO$^-$ (2 equiv.); **2f** was again seen along with a smaller amount of picrate ion and of unmodified **2** (in the initial spectrum recorded at −40 °C).



2f

Addition of 1 equiv. of 2,6-DTBPhO$^-$ in DMSO-d_6 to a DMSO-d_6 solution of **2** (final concentrations 0.06 M) produces a deep blue solution whose initial spectrum includes peaks of residual PiF, 2,6-di-*t*-butylphenol and PicO$^-$ (**3e**). However, the spectrum also contains prominent signals for picryl di-*t*-butylphenol (**3d**), the C-1 PiF·F$^-$ adduct (**2f**) (Table 1) and small resonances indicative of the presence of the C-3 C-adduct of *para*-attack of 2,6-DTBPhO$^-$ (**5**). The signals of **5** (in DMSO-d_6) are located at δ 8·32 (d, $J_{F,H}$ = 4·6 Hz, 1H, H-5), 7·04 (s, 2H, H-3,5 phenolic moiety), 5·64 (d, $J_{F,H}$ = 5·8 Hz, 1H, H-3) and 1·30 (s, 18H, 2,6-di-*t*-Bu). Again, the expected singlet for the OH of the attached aryl moiety is not seen but presumed to be ionized. The solution is basic at this point in the reaction.

Over time, the resonances assigned to the C-1 PiF·F$^-$ adduct (**2f**) gave way to those of the displacement product (**3d**), and the C-3 PiF·[2,6-DTBPhO(H)]$^-$ adduct (**5**). After a reaction time of 1 h, adduct formation (i.e. the sum of concentrations of **3d** and **5** as

products of adduct formation or as adducts) accounted for 52% of the overall products; 85% of this was due to **3d**, the product of C-1 attack (and putative C-1 PiF·OPhDTB$^-$ (**2c**) adduct formation).

DISCUSSION

The reactions described exhibit the following salient features. First, regardless of the picryl halide examined, and regardless of the aryloxide employed, C-1 attack was favoured over C-3 attack in every case. However, no observable Meisenheimer aryloxide oxygen adducts could be detected by the NMR method employed. Second, although phenoxide can potentially act as either a C- or O-nucleophile and even though ambident behaviour has been observed in the TNA–PhO$^-$ system,[10a] among others, in the present systems phenoxide behaved only as an O-nucleophile, mimicking the behaviour of mesitoxide ion, which is obliged to react as an O-nucleophile. Third, even in the case of 2,6-di-*t*-butylphenoxide ion (2,6-DTBPhO$^-$), where steric hindrance to reaction as an O-nucleophile converts the aryloxide into a strict C-nucleophile, C-1 attack to give displacement products is favoured over C-3 attack to yield a Meisenheimer complex in a ratio of about 7:1, again, regardless of the substrate. Finally, in the picryl fluoride systems, with MesO$^-$ or 2,6-DTBPhO$^-$ ions as nucleophiles, a C-1 PiF fluoride adduct is observed. No comparable chloride adduct is seen in the reactions of **1** with any of the aryloxides.

These general features will now be considered in detail and compared and contrasted with previous work.

Reaction pathways

In this study, the reactions of picryl chloride (**1**) and picryl fluoride (**2**) with a series of aryloxide nucleophiles, in which the steric hindrance about the oxygen nucleophilic centre was systematically increased, were monitored by ^{1}H NMR spectroscopy (400 MHz) in dimethyl sulphoxide (DMSO) (ambient temperature; Table 1) and acetonitrile–DME (−40 °C; Table 2). The results show that the reactions of the picryl halides with the unhindered C- and O-nucleophile phenoxide (PhO$^-$) ion and with the moderately hindered O-nucleophile 2,4,6-trimethylphenoxide (MesO$^-$) ion proceed overall according to the S_NAr mechanism[7] as outlined in Scheme 1. Moreover, although PhO$^-$ is potentially ambident it acts in the same way as mesitoxide, which is precluded from acting as a C-nucleophile, and, therefore, the ultimate products of reaction of either aryloxide with **1** and **2**, in either DMSO or acetonitrile–dimethoxyethane media, are the respective aryl picryl ethers, i.e. phenyl picryl ether (**3a**) and mesityl picryl ether (**3b**). On the other hand, when either substrate was allowed to react with 2,6-di-*t*-butylphenoxide (2,6-DTBPhO$^-$) the product was not the aryl picryl ether (**3c**) (Scheme 1) but the biphenyl derivative (**3d**).

These results are fully consistent with the previous work of Wright and Jorgensen,[19] who found that 2,6-dialkylphenyl-4′-nitrophenyl ethers could be prepared in good yields from 2,6-dialkylphenols and chloro-4-nitrobenzene, in the presence of added NaOH, where the 2,6-dialkyl groups comprised methyl, *iso*propyl or *sec*-butyl groups. However, with 2,6-di-*t*-butylphenol no ether was obtained; instead, 2,6-di-*t*-butyl-(4′-nitrophenyl)phenol was the product isolated in good yield. Interestingly, biaryl ether yields that were typically 60–82% were reduced to 20% when 2-(*t*-butyl)-6-methylphenol was used to generate the nucleophilic aryloxide.[19] These results were confirmed by Stahly,[17] who showed that 2,6-di-*t*-butylphenoxide reacts via the *para*-C to form 2,6-di-*t*-butyl[2′(or 4′)nitrophenyl-phenols with *ortho*- and *para*-X-substituted nitrobenzenes. Significantly, yields of 2,6-di-*t*-butyl(2′-nitrophenyl)phenol correlated with the known leaving group order in S_NAr displacement[7] where the rate-determining step is believed to be formation of the Meisenheimer complex;[7,20] the highest product yield was obtained from use of 1-fluoro-2-nitrobenzene as the substrate, with yields declining as the 1-halo group was varied from chloro or bromo to iodo.[17] The current work, therefore, extends the conclusions of Wright and Jorgensen[19] and Stahly[17] to the even more sterically demanding PiX–2,6-DTBPhO$^-$ systems.

Kinetic versus thermodynamic preferences on regioselectivity

Classification of regioselectivity

The results found for the picryl halide reactions with PhO$^-$ and MesO$^-$ are also consistent with the regioselectivity observed with these O-nucleophiles in the related picryl ether systems.[10,12] These nucleophiles both exhibit a kinetic preference for attack at the C-1 position of 2,4,6-trinitroanisole. However, while the C-1 TNA·OPh$^-$ adduct is both the kinetic[10b] and thermodynamic product of phenoxide O-attack (K1T1 behaviour),[10a] its kinetically preferred C-1 TNA·OMes$^-$ counterpart decomposes in favour of the more stable C-3 TNA·OMes$^-$ [and C-1,3 TNA·$(OMes)_2^{2-}$] adduct(s) (K1T3 pattern, Figure 1).[11] In the picryl halide systems, the rearrangement of the comparable C-1 PiX·OMes$^-$ adduct to the C-3 PiX·OMes$^-$ regioisomer is not observed. In fact, unlike the situation found in the TNA systems, no C-1 aryloxide O-adducts can be seen in the systems under investigation here, even at low temperatures.

A distinction should be made, then, between the PiX–PhO$^-$ and the PiX–MesO$^-$ systems. In the former case, there is no reason to expect any regioselectivity other than K1T1 and that is observed. In the latter

situation, rearrangement of a C-1 PiX·OMes$^-$ is prevented by the effectively irreversible formation of this adduct; expulsion of the halide ion, X^-, is rapid and precludes dissociation back to PiX and MesO$^-$ and subsequent attack of MesO$^-$ at C-3 to yield the regioisomeric adduct.

Even though no aryloxide O-adducts can be directly observed it is reasonable to postulate C-1 PiX·OAr$^-$ adducts as either metastable intermediates or as models for the transition state leading to the biaryl ether products. As such, formation of the C-1 phenoxide O-adducts may occur under K1T1 regioselectivity, where the C-1 adducts are both kinetically and thermodynamically preferred over their C-3 counterparts or, alternatively, the regioselectivity may be designated as 'pseudo-K1T1.' The latter case would apply if it is assumed that C-3 adduct formation and decomposition both occur more rapidly than can be detected by the method of observation.[12b] (Pseudo-K1T1 behaviour is illustrated by the addition of the dotted line portion of the K3T1 profile shown in Figure 1).

In summary, although the regioselectivity shown by PhO$^-$ (as an O-nucleophile) towards PiF and PiCl is consistent with that found in the TNA–PhO$^-$ reaction system,[10a] that shown by MesO$^-$ is clearly different. Now, MesO$^-$ appears to act according to the K1T1 pattern of behaviour, whereas with TNA[11] (or related picryl ethers),[21] the regioselectivity exhibited by MesO$^-$ was classified at K1T3.[12] However, it is the rapid displacement of halide from the putative C-1 PiX·OMes$^-$ adduct(s) that intervenes to prevent possible rearrangement to the C-3 regioisomeric adduct and which, consequently, prevents a clear designation of the mesitoxide systems as K1T1. Hence these systems must be considered apparent K1T1 cases. Interestingly, 2,6-DTBPhO$^-$ also reacts to yield a product of C-1 attack and displacement, the biphenyl derivative (**3d**), albeit via *para* C-attack rather than via the oxygen centre. However, in this case formation of the C-1 product occurs competitively with attack at C-3 to form the *para* C-bonded adduct, **4** (or **5**). This partitioning of products is also unexpected on the basis of comparison with the TNA–PhO$^-$ system where C-attack occurs only at C-3 of TNA to give a C-adduct that is preferred both by kinetics and thermodynamics (i.e. K3T3 regioselectivity).

As stated, these results are linked to the nature of the leaving groups involved: halides in the current system and alkoxides in the case of TNA and other picryl ethers. The effect of this change in leaving group ability will be considered next.

Effect of halide nucleofugality

The apparent difference in the thermodynamics observed in the two reaction systems, i.e. PiX versus PiOR (picryl ether), rests partly with the different relative leaving group abilities of the halides as compared with alkoxides or aryloxides. The order of reactivity for picryl halides with PhO$^-$ as an attacking O-nucleophile has been found to be $F \geq Cl \approx Br > I$.[20,22] This order derives from rate measurements. Thus, the rate of displacement of fluoride from PiF (in DMSO, 25 °C) by PhO$^-$ is *ca* 260-fold faster than the displacement of chloride from PiCl by the same nucleophile.[22]

The inability to observe O-centred adducts, either at C-1 or C-3 of **1** or **2** in the current study, is also in accord with the findings of the reaction of PhO$^-$ with the 2-(nitroaryl)–4,6-dinitrobenzotriazole 1-oxide series of compounds. Thus, with 2-picryl-4,6-dinitrobenzotriazole 1-oxide, PhO$^-$ reacts as an O-nucleophile to attack at the C-1′ site and to displace the delocalized 4,6-dinitrobenzotriazole 1-oxide anion leaving group, without competitive formation of a C-7 O-adduct,[23a] even though the C-7 site is generally considered to be the super-electrophilic site.[23] Picryl phenyl ether (**3a**) is the product of this S_NAr displacement. (When the electrophilicity of the C-1 position is reduced by the stepwise removal of NO_2 groups from the 2-nitroaryl ring, *para* and *ortho* C-adduct formation at the C-7 position becomes competitive with O-attack at the C-1′ position of the picryl moiety.)[23b] Again, in the 2-picryl-4,6-dinitrobenzotriazole 1-oxide case reaction with MesO$^-$ yields only picryl mesityl ether (**3b**) via preferential attack at C-1′ and without competitive formation of a C-7 adduct.[23c]

However, rates of displacement as a function of varying the leaving group arise from a number of factors other than the intrinsic nucleofugality of the leaving group. In this regard, overall reactivity (in S_NAr displacements where the first nucleophilic attack step is rate determining) resolves itself into effects on initial electrophilicity of the substrate, steric hindrance to attack at the *ipso* position and effects on the stability of the resultant Meisenheimer complex, as well as the inherent leaving group mobility. The C-1 site of PiF would be expected to be a more electrophilic site than the corresponding C-1 position of PiCl, as a result of the greater electronegativity of F compared to Cl. Another way of expressing this is in terms of the greater polarization of the C—X bond in PiF then PiCl.[7c,24] At the same time, F, as a substituent that is smaller than Cl,[25a] provides less F-strain[15,16] to C-1 attack than Cl does.

In fact, in assessing the propensity for attack of a nucleophile at C-1 as compared with C-3 sites, the size of F (and Cl) relative to H is a measure of relative F-strain to attack and, so, becomes significant. Both measurements[25a] and estimates[25b–d] of the van der Waals radius for F and H vary greatly. Thus, Bondi[25a] argued in favour of an upwards revision of the van der Waals radius for F from the Pauling value of 1·35 to 1·47 Å, which would make F significantly larger than H, to which a radius of 1·20 Å was assigned. However, in setting parameters for their molecular mechanics calculations, Allinger *et al.*[25b] found it necessary to assign to

H van der Waals radii ranging from 1·40 to 1·60 Å. Similar requirements in other force field calculations[25c] or in *ab initio* methods[25d] have consistently ascribed a van der Waals radius to H that is greater than Bondi's 1·20 (e.g. 1·38[25c] to 1·44 Å[25d]). Therefore, it seems reasonable to conclude that F is much the same size as H if not smaller than H. Chlorine, on the other hand, is clearly much larger than H; Bondi assigned it a van der Waals radius of 1·75 Å.[25a] Consequently, it may be concluded that F-strain to attack at C-1 and C-3 of PiF would be approximately equivalent, whereas F-strain to attack at C-1 of PiCl should be significantly greater than the same steric hindrance to attack at C-3 of this substrate.

Clearly, attack at C-1 of PiF is favoured by the relatively small size of F (compared with Cl) and product formation from either PiF or PiCl will be favoured by the inherent high nucleofugality of the halide leaving groups. Hence the kinetic factor in the regioselectivity found in these systems may be largely understood. The kinetics of attack at C-1 are favoured by the polarization of the C—X bond[7c,24] and, in the case of PiF, by diminished F-strain to attack at C-1 (see above). Therefore, the kinetic portion of the regioselectivity maybe described as 'K1' systems. In the following section we examine the thermodynamics of the regioselectivity observed in these reactions.

Stereoelectronic factors in σ-complex formation

The stability of the resultant C-1 Meisenheimer adducts is of particular interest to us.[10a-12] It is clear that F as the C-1 substituent as compared with Cl may provide greater inductive stabilization to the intermediate C-1 adduct.[26] Inasmuch as factors that stabilize the intermediate C-1 adducts may also stabilize a late rate-determining transition state for attack at C-1, this could account for the higher rates of displacement for PiF relative to PiCl.

A number of picryl ether–aryloxide systems[12b,21] have highlighted the significance of $n \rightarrow \sigma^*$ stabilizing interactions in the respective geminally disubstituted C-1 adducts. For an ideal C-1 adduct that approximates an acetal n-electron donation from the oxygen of one geminal R—O group into the σ^* orbital of the antiperiplanar C—O(R) bond (and *vice versa*) would lead to optimum stereoelectronic stabilization.[12,27] AM1 calculations on the C-1 TNA·OCH_3^- adduct yielded two energy minima. The global minimum, in the absence of a point positive charge (designed to simulate a counter cation), has a conformation that does not correspond to the optimum doubly antiperiplanar arrangement about the CH_3O—C(1)—OCH_3 axis but does permit partial stereoelectronic stabilization approximately equivalent to one full antiperiplanar $n \rightarrow \sigma^*$ interaction.[12a] In the C-1 TNA·OPh^- adduct a further diminishment in stereoelectronic stabilization probably occurs both as a result of steric congestion (that limits the degree of population possible for stabilizing rotameric forms) and as a result of the unsymmetrical nature of the adduct.[10a,12a] In the C-1 TNA·$OMes^-$ adduct, the inability of the acetal-like groups to attain any rotameric forms that would allow such stabilization combines with classical steric acceleration of decomposition to account for the rapid rearrangement of this C-1 adduct into its C-3 counterpart.[11]

Attack of PhO^- or $MesO^-$ on PiCl or PiF should result in formation of C-1 adducts, **1a/1b** or **2a/2b**, that would be expected to show a similar trend in the degree of stereoelectronic stabilization available to the adducts. Thus, attack of PhO^-, the least bulky of the aryloxides, on PiF (**2**), the least hindered of the picryl halides, should result in a C-1 adduct that would have the greatest probability of taking up rotameric forms that would result in stabilizing $n \rightarrow \sigma^*$ interactions. On the other hand, the efficacy of the $n \rightarrow \sigma^*$ stabilization depends on the relative energies of the two σ^* moieties, so such 'unsymmetrical' adducts are generally expected to achieve less stabilization from these stereoelectronic interactions.[27]

To summarize the preceding arguments, attack at C-1 of PiF should lead to C-1 adducts that would be somewhat more stabilized by stereoelectronic effects than their PiCl analogues (particularly with phenoxide as the attacking O-nucleophile) and to the extent that such stabilization would also apply to the transition state leading to their formation S_NAr displacement should be more facile from PiF than from PiCl. Notwithstanding the differences in stabilization afforded C-1 adducts of PiF as compared with those formed by PiCl, C-1 phenoxide O-adducts of both substrates should derive a degree of stereoelectronic stabilization, so the regioselectivity found for these examples involving phenoxide O-attack could be described as K1T1. With $MesO^-$, on the other hand, the C-1 adduct would not be expected to partake of significant stereoelectronic stabilization. If rapid reversion to the picryl halide and mesitoxide occurred, then rearrangement to the C-3 PiX·$OMes^-$ adduct could be expected (i.e. K1T3 regioselectivity). Instead, rapid expulsion of the halides from the mesitoxide C-1 O-adducts confers irreversibility upon formation of these adducts and yields *apparent K1T1 regioselectivity* for the PiX–$MesO^-$ systems.

It is useful to compare the results in the current systems with those reported by Crampton *et al.*[28] in the reaction of a series of picryl halides (X = F, Cl, Br and I) with hydroxide ion. These workers found that the ratios of the equilibrium constant for attack by OH^- at C-3 of the picryl halides as compared with attack at C-1 decreased in the order F > H > Cl > Br > I. The order was attributed to a combination of factors. First, steric disruption of the coplanarity of *ortho* (2,6) nitro groups in the picryl halides for X = Cl, Br and I would be

expected to destabilize the C-3 adducts, which would be unable to delocalize negative charge into these NO_2 groups effectively.[28] (Conversely, attack at C-1 of these picryl halides would result in conversion of the crowded sp^2 hybridized C-1 into an sp^3 hybridized carbon; the relief of strain accompanying the conversion provides relative stability to the C-1 adduct, notably the C-1 PiCl adduct in the present study.) Second, while the relatively small size of fluorine would permit the *ortho* NO_2 groups of PiF to achieve coplanarity, the high electronegativity of F could withdraw electron density from the C-3 site inductively and, consequently, lead to more rapid attack at C-3 of PiF than at a ring position of 1,3,5-trinitrobenzene (TNB).[28] In the same work, they found that attack of OH^- at C-1 of PiF (**2**) was more rapid than attack at C-3 of the same substrate and attributed this to the small size of F and the high electrophilicity of C-1 (arising from the polarization of the C—F bond).[28] Another view would hold that C-1 attack is preferred by OH^- because of the stereoelectronic $n-\sigma^*$ stabilization afforded the C-1 PiF·OH^- adduct. Note that Crampton *et al.*[28] suggested that the transition states for hydroxide attack could be late and so resemble the hydroxide adducts. Finally, AM1 calculation results indicate that the C-1 adduct formed by 1-fluoro-4-nitrobenzene with OH^- is thermodynamically more stable than its C-3 counterpart; we have attributed this stabilization to effective $n-\sigma^*$ interaction(s).[12a]

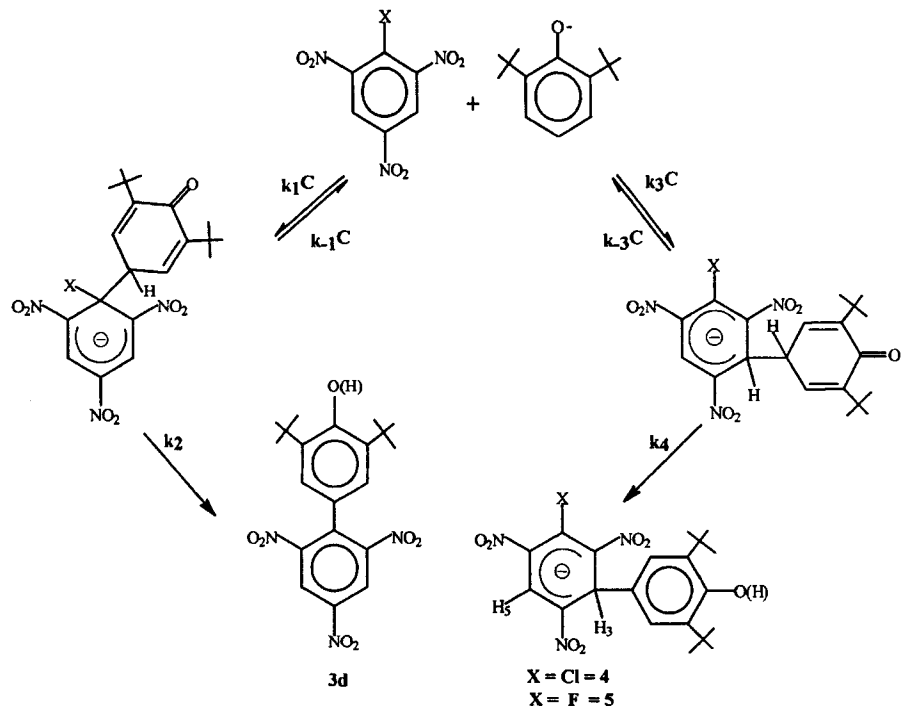
It is noteworthy that the ready attack of fluoride ion, displaced from PiF by $MesO^-$, leads to observation of the PiF·F^- adduct **2f**. This adduct has been directly observed previously by Terrier *et al.*[18] Its facile formation is likely not only a reflection of the full $n \longrightarrow \sigma^*$ stabilization afforded **2f**, but also the high degree of reactivity that F^-('naked fluoride') exhibits in dipolar aprotic solvents (such as DMSO and MeCN)[29] and the low F-strain involved in attack at C-1 of PiF. The lower degree of reactivity for 'naked' Cl^-; as well as greater F-strain to attack at C-1 of PiCl, would contribute to the inability to observe the corresponding PiCl·Cl^- adduct in the systems studied. In this context, it is noteworthy that Egorov *et al.*[30] observed the fluoride adduct of 1,3,5-trinitrobenzene (TNB·F^-) formed from TNB and tetramethylammonium fluoride, but failed to find the analogous TNB·Cl^- adduct. These results suggest that chloride adducts are generally less stable than their fluoride analogues and that this lesser stability coupled with the higher nucleophilicity of fluoride ion as compared with chloride ion, as well as the greater C-1 electrophilicity expected for PiF (**2**) relative to PiCl (**1**), account for the observation of **2f** in the PiF–F^- system and the inability to observe the C-1 PiCl·Cl^- adduct in the PiCl–Cl^- case.

Aryloxide carbon nucleophilicity

In considering the reactions of 2,6-DTBPhO^- with the substrates, steric hindrance is again a dominant issue. Clearly, the steric hindrance about the O-nucleophilic centre results in such F-strain to attack that oxygen attack simply does not occur in this or related systems.[17,19] F-strain probably also accounts for the preference of 2,6-DTBPhO^- to attack at C-1 of PiF. Recall that for **2** the C-1 site is comparable in steric hindrance to the C-3 site based on the comparative atomic radii of F and H.[25] However, the relative ease of loss of the halides again plays a role. Once attack has occurred at C-1 of either PiCl or PiF, rapid expulsion of the halide presumably occurs to yield the stable biphenyl derivatives. Rearrangement of the C-1 adducts to their C-3 counterparts is thus pre-empted. Evidence, both from calculations[12a] and product distributions in the vicarious nucleophilic substitution (VNS) reaction, which involves attack of carbanions on electron-deficient aromatics,[31] suggests that carbon nucleophiles form their most stable Meisenheimer adducts from attack at an unsubstituted position, e.g. C-3 of **1** or **2**. Our previous results gleaned from the TNA–PhO^- reaction system also show that, as a C-nucleophile, phenoxide favours attack at C-3 of 1-X-2,4,6-trinitrobenzenes.[10a]

As Scheme 2 highlights, attack of 2,6-DTBPhO^-, as a carbon nucleophile, at either the C-1 or C-3 position results initially in C-1 or C-3 zwitterionic Meisenheimer complexes. These complexes arise from attack via the *para* carbon of 2,6-DTBPhO^- because the O-centre is highly hindered and the *ortho* ring carbons are effectively blocked. Note, however, that in related systems where PhO^- was found to act as both an O- and a C-nucleophile, attack via the *para* carbon generally exceeded attack via an *ortho* position, regardless of the statistical factor that favours *ortho* C-reaction.[32,33] ^{13}C NMR spectra indicate that the *para* carbon bears a higher partial negative charge than does either *ortho* carbon.[14a] This higher intrinsic nucleophilicity, and also the lowered steric hindrance to attack associated with the *para* position,[32–34] result in preference for *para* attack over *ortho* reaction.

While attack of 2,6-DTBPhO^- as a C-nucleophile entails loss of aromaticity for the aryloxide, the second step (k_2 and k_4, Scheme 2) restores aromaticity. Thus, attack of aryloxides as C-nucleophiles has been taken to be slow since aromaticity is lost in the process, whereas subsequent tautomerization has been presumed to be fast because aromaticity is regained in the process. In this context, it is noteworthy that decomposition of the respective zwitterionic adducts back to starting PiX and 2,6-DTBPhO^- (k_{-1}^C and k_{-3}^C, Scheme 2) would also result in a restoration of aromaticity. However, whereas these decomposition steps are unimolecular, the forward tautomerization steps are bimolecular (in zwitterionic adduct and base) and would be favoured so long as the medium contained appreciable amounts of base. Recall that throughout monitoring of the PiX–2,6-DTBPhO^-



Scheme 2

reaction systems the solution remained blue as a result of the presence of the aryloxide product, 2,6-di-*t*-butyl-4-(2′,4′,6′-trinitrophenyl)phenoxide, indicative of the alkalinity of the medium throughout the course of the reaction. The bimolecular rearomatization steps (k_2 and k_4) would, therefore, be expected to be faster than the decomposition steps (k_{-1}^C and k_{-3}^C, respectively).

Furthermore, it is necessary to distinguish between the two different rearomatization steps; k_2 clearly involves loss of the leaving halide as well as rearomatization, whereas k_4 is a more straightforward tautomerization. The k_2 pathway could proceed in several ways.* However, k_2 could be taken to represent two separate steps, involving (1) expulsion of halide followed by tautomerization or (2) loss of H—X in an elimination step[34] followed by rearomatization. Current evidence does not permit us to discriminate between these processes.

CONCLUSIONS

The results of this study have highlighted the roles of several factors in C-1 versus C-3 attack in picryl halide displacement reactions: the importance of F-strain in attack at C-1, the importance of the intrinsic nucleofugality of the halides and the varying degree of stereoelectronic stabilization afforded the C-1 adducts.

Although C-1 O-adducts from attack of PhO^- or $MesO^-$ at C-1 of the PiX substrates were not observed by NMR, either at room or low temperature, the picryl ether products plausibly arise from such transient adducts. At the same time, C-3 adducts were also unobserved. The regioselectivity found in the PiX–PhO^- and PiX–$MesO^-$ systems has been designated K1T1 in the case of the former systems, partly on analogy with the related picryl ether systems.[10a,12b] In the latter systems the rapid displacement of halide from the putative C-1 PiX·$OMes^-$ adduct confers effective irreversibility on this pathway and precludes dissociation and rearrangement to the C-3 adduct. Therefore, the PiX–$MesO^-$ systems must be viewed as displaying apparent K1T1 regioselectivity. With 2,6-DTBPhO^-, steric hindrance about the O-nucleophilic centre precludes the formation of the

* A referee has suggested that the rearomatization could be effectively concerted with elimination of H—X. Such a concerted process would appear to require extensive electronic and structural reorganization. We thank the referee for contributing to the completeness of the discussion.

corresponding aryl picryl ether and instead good yields of the biphenyl derivative are obtained. Now, C-3 regioisomeric adducts resulting from *para* C-attack are observed; their formation is competitive with C-1 attack and consistent with the tendency to C-3 attack found in the picryl ether systems.[12]

The lack of C-nucleophilic reactivity shown by PhO^- arises from the ease of O-attack at C-1, which occurs in a single step, as compared with C-attack that reasonably occurs in two steps and involves loss of aromaticity for the attacking phenoxide nucleophile. Once a C-1 adduct is formed it is stabilized by $n-\sigma^*$ interactions; this stereoelectronic stabilization may also extend to the transition state for formation of the C-1 PhO^- (and to a lesser extent the C-1 $MesO^-$) adduct and, so, provide a rationale for kinetic preference for attack at C-1 together with a thermodynamic reason for attack at C-1. The small size of F also contributes to ease of attack at C-1 of PiF. However, the high nucleofugality of fluoride and chloride ions accounts for the rapid displacement and contingent inability to observe the C-1 adducts.

Kinetic preference by 2,6-$DTBPhO^-$ for attack at C-1 of PiCl and PiF and formation of the displacement product, as compared with formation of the C-3 C-centred adducts, **4** and **5**, is also rationalized partly by the decreased F-strain to attack at C-1 of PiF. Finally, the higher electrophilicity of the C-1 site in both PiF and PiCl that arises from the electronegativity of F and Cl and attendant polarization of the respective C-1—X bonds also favours C-1 attack.

EXPERIMENTAL

All common solvents and reagents were purchased from commercial sources and used without further purification. Melting points were determined using a Thomas–Hoover melting point apparatus and are reported without correction. The NMR spectra of the starting reagents were recorded in DMSO-d_6; chemical shifts are given in parts per million (ppm) relative to either tetramethylsilane (TMS) or residual DMSO-d_5H found in the solvent and coupling constants (J) are reported in hertz (Hz).

Picryl chloride (**1**). 1-Chloro-2,4,6-trinitrobenzene (picryl chloride, **1**) was prepared either by nitration of 1-chloro-2,4-dinitrobenzene as described by Frankland and Garner[35] or by reaction of pyridinium picrate with $POCl_3$;[36] either method gave **1** in yields of 60–91%; m.p. (after recyrstallization from CCl_4) 80–81 °C (lit.[35] 81 °C). ^{1}H NMR: 9·24 (s, 2H, H-3,5). ^{13}C NMR: 148·9, 146·4, 123·5 and 125·0 (C-1, C-2,6, C-3,5, C-4, respectively).

Picryl fluoride (**2**). 1-Fluoro-2,4,6-trinitrobenzene (picryl fluoride, **2**) was prepared by reaction of pyridinium picrate with diethylaminosulphur trifluoride (DAST), as reported previously.[37] Yield (after recrystallization from CCl_4), 23%; m.p. 127–129 °C (lit. 127–128 °C;[38] 122–123, 131–132 °C dimorphic[39]). ^{1}H NMR: 9.18 (d, $J_{F-H} = 5·6$ Hz, 2H, H-3,5). ^{13}C NMR: 154·9, 149·3, 126·1 and 121·6 (C-1, C-2,6, C-3,5, C-4, respectively).

2,6-Di-t-butyl-4-(2′,4′,6′-trinitrophenyl)phenol (**3d**). An authentic sample of **3d** was prepared from **1** and equimolar potassium 2,6-di-*t*-butylphenoxide in DMSO. The DMSO solution was stirred at room temperature for 3 h, then the dark blue solution was poured into an excess of 0·1 M HCl and the aqueous acid was extracted with $CHCl_3$ (5 × 100 ml). The chloroform extracts were combined, dried with Na_2SO_4 and concentrated under reduced pressure. Flash chromatography (Kieselgel 60, 230–400 mesh), according to the procedure of Still *et al.*,[40] with CH_2Cl_2–light petroleum [(b.p. 30–60°C (2:3)] afforded a yellow solution ($R_f = 0·6$). The dark yellow oil obtained from concentration of the solution yielded a canary yellow powder when treated with hexane. Yield, 41%; m.p. 148–150 °C. ^{1}H NMR: 9·12 (s, 2H, H-3′,5′), 7·63 (s, 1H, OH), 7·04 (s, 2H, H-3,5) and 1·3S (s, 18H, 2,6-di-*t*-Bu). ^{13}C NMR: 155·8, 150·3, 139·8, 133·9, 124·3, 121·6, 120·0, 34·7 and 30·1. Calc. for $C_{20}H_{23}N_3O_7$, C 57·55, H 5·55, N 10·07; found: C 56·76, H 5·38, N 9·85%.

Potassium aryloxides. The potassium aryloxide salts were prepared according to the method of Kornblum and Laurie.[41] Potassium phenoxide (PhOK) was obtained as a colourless solid. ^{1}H NMR: 6·67 (t, 2H, H-*meta*), 6·03 (d, 2H, H-*ortho*) and 5·82 (t, 1H, H-*para*). Potassium 2,4,6-trimethylphenoxide (mesitoxide, MesOK) was a pale brown powder (after thorough washing with light petroleum (b.p. 30–60 °C) with ^{1}H NMR characteristics (DMSO-d_6) in good agreement with the literature.[42] Potassium 2,6-di-*t*-butylphenoxide (2,6-DTBPhOK) was a lime green solid. ^{1}H NMR: 6·58 (d, $J = 7·3$, 2H, H-*meta*), 5·57 (t, $J = 7·3$, 1H, H-*para*) and 1·32 (s, 18H, 2,6-di-t-Bu).

NMR: general. NMR solvents were purchased from Merck or CDN. DMSO-d_6 was treated three times sequentially with 4A molecular sieves prior to use; according to Burfield and Smithers,[43] such treatment would reduce the residual water content to 10 ppm or less. NMR measurements were made with a Bruker AM-400 spectrometer operating at 400·1 MHz (^{1}H) and 100·0 MHz(^{13}C). The spectrometer was typically adjusted as reported previously.[10a] ^{13}C NMR spectra of the substrates (PiF, PiCl, etc.) were acquired using the J-modulated (JMOD) pulse sequence.[44] Potassium aryloxide solutions were prepared in volumetric flasks (1 ml) from weighed quantities of the salts and the appropriate NMR solvent in a nitrogen dry-box.

A representative NMR experiment: reaction of PiF with 2,6-di-t-butylphenoxide. Typical room-temperature and low-temperature experiments, in both solvents, have been published previously[10a,11,14] and the experiments undertaken in support of this work followed the same general outline. The reaction of PiF (**2**) with 2,6-DTBPhO$^-$ is representative of the investigations pursued in DMSO-d_6 solvent at ambient temperature and it is described in detail below.

A PiF stock solution (0·180 M) was prepared by dissolution of 20·8 mg of **2** in 500 µl of dry DMSO-d_6. The initial sample was prepared by injection of 165 µl of this substrate solution into a septum capped NMR tube that contained dry solvent (125 µl) and 1,4-dibromobenzene solution (10 µl of a 0·5 M solution of this integral standard in DMSO-d_6). Addition of the relevant quantity of 2,6-DTBPhOK (200 µl of a 0·149 M solution to give 1 equiv . of nucleophile) initiated the reaction. The initial ^{1}H NMR spectrum was recorded within 3 min of mixing (16 transients per FID). After the initial spectrum the reaction was monitored at various intervals. An FID of 32–64 transients sufficed to yield the data reported here. After *ca* 1 h, when the reaction was deemed complete, 5 µl of trifluoroacetic acid (TFA) were injected into the NMR tube and a final spectrum was acquired.

ACKNOWLEDGEMENTS

The authors acknowledge the continuing financial support of the Natural Sciences and Engineering Research Council of Canada (NSERCC to E.B.), the Principal's Research Fund of Sir Wilfred Grenfell College (to J.M.D.) and the American Cancer Society (to R.A.M.)

REFERENCES

1. E. Buncel, R. A. Manderville and J. M. Dust, *Zh. Org. Khim.* Submitted.
2. 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).
3. E. Buncel, in *The Chemistry of Functional Groups. Supplement F. The Chemistry of Amino Nitro and Nitroso Compounds*, pp. 1225–1260, edited by S. Patai, Wiley, Chichester (1982);
4. (a) G. A. Artamkina, M. P. Egorov and I.P. Beletskaya, *Chem. Rev.* **82,** 427 (1982). (b) F. Terrier, *Chem. Rev.* **82,** 77 (1982).
5. J. Meisenheimer, *Justus Liebigs Ann. Chem.* **323**, 205 (1902).
6. (a) C. J. Jackson and W. F. Boos. *Am. Chem. J.* **20**, 444 (1898); (b) C. J. Jackson and P. H. Gazzolo, *J. Am. Chem. Soc.* **23**, 376 (1900)
7. (a) J. F. Bunnett and R. E. Zahler, *Chem. Rev.* **49**, 272 (1951); (b) J. F. Bunnett. *Q. Rev. Chem. Soc.* **12**, 15 (1958); (c) J. Miller, *Nucleophilic Aromatic Substitution.* Elsevier, Amsterdam (1968); (d) F. Terrier, *Nucleophilic Aromatic Displacement. The Influence of the Nitro Group.* VCH, New York (1991).
8. (a) K. L. Servis, *J. Am. Chem. Soc.* **87**, 5495 (1965); **89**, 1508 (1967).
9. (a) M. P. Simonnin, J. C. Halle, F. Terrier and M. J. Pouet, *Can. J. Chem.* **63**, 866 (1985); (b) E. Buncel, S. K. Murarka and A. R. Norris, *Can. J. Chem.* **62**, 534 (1984); (c) F. Terrier, F. Debleds, J. C. Halle and M. P. Simonnin, *Tetrahedron Lett.* **23**, 4079 (1982); (d) A. D. A. Alaruri and M. R. Crampton, *J. Chem. Res. (S)* 140 (1980); *(M)* 2157 (1980); (e) M. P. Simonnin, M. J. Pouet and F. Terrier, *J. Org. Chem.* **43**, 855 (1978); (f) G. Baldini, G. Doddi, G. Illuminati and F. Stegel, *J. Org. Chem.* **41**, 2135 (1976); (g) C. F. Bernasconi, *J. Am. Chem. Soc.* **93**, 6975 (1971); (h) C. F. Bernasconi, *J. Am. Chem. Soc.* **92**, 4685 (1970); (i) R. A. Foster, C. A. Fyfe, P. H. Emslie and M. I. Foreman, *Tetrahedron* **23**, 227 (1967).
10. (a) E. Buncel, J. M. Dust, A. Jonczyk, R. A. Manderville and I. Onyido, *J. Am. Chem. Soc.* **114**, 5610 (1992); (b) C. F. Bernasconi and M. C. Muller, *J. Am. Chem. Soc.* **100**, 5530 (1978); (c) S. M. Shein and O. B. Byval-'kevich, *Zh. Org. Khim.* **8**, 323 (1972).
11. R. A. Manderville and E. Buncel, *J. Am. Chem. Soc.* **115**, 8985 (1993).
12. (a) E. Buncel, R. M. Tarkka and J. M. Dust, *Can. J. Chem.* **69**, 1709 (1994); (b) E. Buncel, J. M. Dust and F. Terrier, *Chem. Rev.* **95**, 2261 (1995).
13. R. A. Chamberlin and M. R. Crampton, *J. Chem. Soc., Perkin Trans. 2* 1831 (1995).
14. (a) E. Buncel and R. A. Manderville, *J. Phys. Org. Chem.* **6**, 71 (1993); (b) R. A. Manderville and E. Buncel, *J. Chem. Soc., Perkin Trans. 2* 1887 (1993).
15. (a) M. R. Crampton and V. Gold, *J. Chem. Soc.* 4293 (1964); (b) M. R Crampton and V. Gold, *J. Chem. Soc. B* 893 (1966).
16. M. R. Crampton and M. J. Willison, *J. Chem. Soc., Perkin Trans. 2* 901 (1976).
17. G. P. Stahly, *J. Org. Chem.* **50**, 3091 (1985).
18. F. Terrier, G. Aw-Kow, M. J. Pouet and M. P. Simonnin, *Tetrahedron Lett.* 227 (1976).
19. J. Wright and E. C. Jorgensen, *J. Org. Chem.* **33**, 1245 (1968).
20. (a) G. Illuminati, *Adv. Heterocycl. Chem.* **3**, 285 (1964); (b) G. Illuminati and F. Stegel, *Adv. Heterocycl. Chem.* **34**, 305 (1983).
21. R. A. Manderville, J. M. Dust, R. M. Tarkka and E. Buncel, unpublished results.
22. G. Bartoli and P. E. Todesco, *Tetrahedron* 24, 4867 (1968).
23. (a) E. Buncel, R. A. Renfrow and M. J. Strauss, *J. Org. Chem.* **52**, 488 (1987); (b) E. Buncel and J. M. Dust, *Can. J. Chem.* **66**, 1712 (1988); (c) J. M. Dust, PhD Thesis, Queens University (1987), p. 192; (d) R. A. Renfrow, M. J. Strauss, S. Cohen and E. Buncel, *Aust. J. Chem.* **36**, 1843 (1983).
24. G. Bartoli and P. E. Todesco, *Acc. Chem. Res.* **10**, 125 (1977).
25. (a) A. Bondi, *J. Phys. Chem.* **68**, 441 (1964); (b) N. L. Allinger, J. A. Hirsch, M. A. Miller, I. J. Tyminski and F. A. Van-Catledge, *J. Am. Chem. Soc.* **90**, 1199 (1968); (c) G. Rauhut, T. Clark and T. Steinke, *J. Am. Chem. Soc.*

115, 9174 (1993); (d) S. Miertus, E. Scrocco and J. Tomasi, *J. Chem. Phys.* **55**, 117 (1981).
26. A. J. Birch, A. L. Hinde and L. Radom, *J. Am. Chem. Soc.* **102**, 6430 (1980).
27. A. J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*. pp. 9–11, 82, 90. Springer, Berlin (1983).
28. M. R Crampton, A. B. Davis, C. Greenhalgh and J. A. Stevens, *J. Chem. Soc., Perkin Trans. 2* 675 (1989).
29. V. M. Vlasov, *J. Fluorine Chem.* **61**, 193 (1993).
30. M. P. Egorov, G. A. Artamkina, I. P. Beletskaya and O. A. Reutov, *Izv. Akad. Nauk SSSR, Ser. Khim.* 2431 (1978).
31. (a) M. Makosza, *Russ. Chem. Rev.* **58**, 747 (1989); (b) M. Makosza, W. Danieliewicz and E. Wojciechowski, *Phosphorus Sulfur Silicon* **53**, 457 (1990); (c) M. Makosza. *Pol. J. Chem.* **66**, 3 (1992).
32. (a) E. Buncel and W. Eggimann, *J. Am. Chem. Soc.* **99**, 5958 (1977); (b) E. Buncel, J. G. K. Webb and J. F. Wiltshire, *J. Am. Chem. Soc.* **99**, 4429 (1977); (c) E. Buncel and W. Eggimann, *Can. J. Chem.* **54**, 2436 (1976); (d) E. Buncel, A. Jonczyk and J. G. K. Webb, *Can. J. Chem.* **53**, 3761 (1975).
33. E. Buncel and J. G. K. Webb, *J. Am. Chem. Soc.* **95**, 8470 (1973).
34. G. Doddi, G. Illuminati and F. Stegel, *J. Org. Chem.* **36**, 1918 (1971).
35. P. F. Frankland and F. H. Garner, *J. Soc. Chem. Ind.* **39**, 257 (1921).
36. R. Boyer, E. Y. Spencer and G. F. Wright, *Can. J. Res.* **24B**, 200 (1946).
37. J. M. Dust and R. A. Manderville. *Org. Prep. Proced. Int. Briefs (OPPI Briefs)* **24**, 55 (1992).
38. K. B. Lam, J. Miller and P. J. S. Moran, *J. Chem. Soc., Perkin Trans. 2* 456 (1977).
39. M. L Sinnott and M. C. Whiting, *J. Chem. Soc. B* 965 (1971).
40. W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.* **43**, 2923 (1978).
41. N. Kornblum and A. P. Laurie, *J. Am. Chem. Soc.* **81**, 2705 (1959).
42. E. Buncel, R. Y. Moir, A. R. Norris and A. P. Chatrousse, *Can. J. Chem.* **59**, 2470 (1981).
43. D. R Burfield and R. H. Smithers, *J. Org. Chem.* **43**, 3966 (1978).
44. J. K. M. Sanders and B. K. Hunter, *Modern NMR Spectroscopy*, pp. 93–207, Oxford University Press, Oxford (1987).