ARTICLE

OBC
www.rsc.org/obc

High Brønsted β_{nuc} values in S_NAr displacement. An indicator of the SET pathway? †

François Terrier,*[a] Malika Mokhtari,[a,b] Régis Goumont,[a] Jean-Claude Hallé[a] and Erwin Buncel*[c]

[a] *Laboratoire SIRCOB, Institut Lavoisier-Franklin, ESA CNRS 8086, Université de Versailles, 45 Avenue des Etats-Unis, 78035-Versailles cédex, France. E-mail: terrier@chimie.uvsq.fr; Fax: 00139254452; Tel: 00139254450*

[b] *Laboratoire COSNA, Département de Chimie, Université Abou Bekr Belkaid, BP 119, 13000-Tlemcen, Algérie*

[c] *Department of Chemistry, Queen's University, Kingston, ON K7L 3N6, Canada*

Received 27th January 2003, Accepted 27th March 2003
First published as an Advance Article on the web 10th April 2003

Nucleophilic substitutions of 4-chloro-7-nitrobenzofurazan (NBD-Cl) and 3-methyl-1-(4-nitrobenzofurazanyl)-imidazolium ions (NBD-Im^+) with a series of 4-X-substituted anilines have been kinetically investigated in 70–30 (v/v) and 20–80 (v/v) H_2O–Me_2SO mixtures. The rate-limiting step in these reactions is nucleophilic addition with formation of Meisenheimer-type σ-adducts followed by fast expulsion of the leaving group (Cl^- or Im). The reactions are characterized by a notable sensitivity to basicity of the aniline nucleophiles, with Hammett ρ values of −2.68 and −3.82 in 30% and 80% Me_2SO, respectively, for NBD-Cl and even more negative values, −3.43 and −5.27, respectively, for NBD-Im^+. This is consistent with significant development of positive charge at the nitrogen atom of the zwitterionic σ-adduct. Unexpectedly, the Brønsted-type plots reveal abnormally high β_{nuc} values, *ca.* 1.0 and 1.3–1.4, respectively. Satisfactory correlations between the rates of the reactions and the oxidation potentials of the respective anilines support a SET mechanism for this process, *i.e.* initial (fast) electron-transfer from the aniline donor to the nitrobenzofurazan acceptor moiety and subsequent (slow) coupling of the resulting cation and anion radicals within the solvent cage with formation of the σ-adduct. An alternative possible explanation of the high β_{nuc} values being related to the strong $-I$ effect exerted by the negatively charged 4-nitrobenzofurazanyl structure, which would induce a greater positive charge at the developing anilinium nitrogen atom in the σ-adduct-like transition state as compared with the situation in the reference protonation equilibria of anilines, is considered less probable. It is thus proposed that obtention of abnormal β_{nuc} values may be an indicator of electron-transfer in nucleophilic aromatic substitution and highlights the transition from the polar (S_NAr) to the single electron-transfer (SET) mechanism.

Introduction

The significance of structure–reactivity correlations such as Hammett (ρ) and Brønsted (α,β) coefficients, as probes of reaction mechanisms in nucleophilic substitution or addition reactions, as well as in proton transfer processes, has been elegantly discussed by Jencks.[1] Thus, α/β values are commonly accepted as measures of the degree of charge transfer, from the base (nucleophile) to the acid (electrophile) partner, at the transition state (TS).[1,2] In that sense, it could be anticipated that the normal range of α/β values would be between 0 and 1. However, it was discovered through the work of Bordwell, Jencks, Bernasconi and others,[3–5] that certain processes were characterized by α/β values out of this normal range. Importantly, such unexpected α/β values have actually provided new insights into the understanding of transition state structures. Among other factors, the lack of synchronization in the progress of various events contributing to an elementary reaction has been recognized as a major source of anomalous α/β values, a situation now referred to as a transition-state imbalance.[5–9] In this regard, the ionisation of many carbon acids by oxygen or nitrogen bases, is typical of this behaviour, with the conclusion that the proton transfer itself occurs ahead of the resonance/solvation changes attendant on the formation of the resulting carbon bases.[5–8]

Imbalanced transition states have also been recognized in nucleophilic reactions.[6,9] Thus, a negative β_{nuc} value has been reported by Jencks for acyl group transfers between *p*-nitrophenyl phosphates and various quinuclidine bases, which has been interpreted as reflecting a need for desolvation of the amine functionality prior to attack at the electrophilic carbon center.[4] Other solvational imbalances have recently been reported in the reactions of *p*-nitrophenyl acetate with oximate α-nucleophiles.[9,10] At the other extreme, an abnormally high β_{nuc} value of 1.6 has been found for the aminolysis of acetylimidazole.[11] In this instance, however, the most reasonable explanation appears to be in terms of a greater sensitivity to polar substituents of the incoming amino nitrogen in the transition-state as compared to the reference equilibrium protonation.[11] On the other hand, while most S_N2 reactions are characterized by β_{nuc} values in the 0.2–0.5 range,[12] values close to or greater than 1 have been observed by Bordwell in some S_N2-type reactions of carbanions and nitranions with sulfonyl- and nitro-activated halides. These results were interpreted as indicative of the occurrence of complete electron transfer.[13]

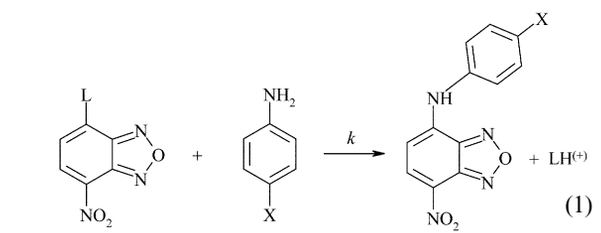
Regarding S_NAr reactions, it has been emphasized by Bordwell based on the numerous available results of β_{nuc} values falling in the range 0.5–0.7, that these entail a relatively large transfer of electronic charge in the TS.[13,14] In contrast, two examples of β_{nuc} values close to 1 have been recently found by Williams *et al.* in reactions of amines or phenoxide ions with 4-aryloxy-1,3,5-triazines.[15] Other evidence, however, indicated that these

† Electronic supplementary information (ESI) available: first-order rate constants for the reactions of NBD-Cl (Table S1) and NBD-Im^+ (Table S2) with *p*-X-substituted anilines and figures showing the influence of the oxidation potential on the rates of reaction of NBD-Im^+ with **1b**–**e** and **1f** in 70–30 (Fig. S1) and 20–80 (Fig. S2) (v/v) H_2O–Me_2SO. See http://www.rsc.org/suppdata/ob/b3/b301031g/

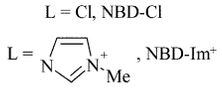
DOI: 10.1039/b301031g

reactions proceed through a concerted mechanism rather than the stepwise S_NAr pathway. ‡

As part of continuing investigations of S_NAr reactions in the nitrobenzofurazan and nitrobenzofuroxan series,[17–20] we report here a kinetic study of the reactions of *para*-X-substituted anilines, **1a**–**f**, on the one hand with 4-chloro-7-nitrobenzofurazan, commonly known as NBD-Cl, and on the other hand with 3-methyl-1-(4-nitrobenzofurazan-7-yl)imidazolium cations (NBD-Im^+) to give the 4-anilino-7-nitrobenzofurazans, **4a**–**f**, at 25 °C in aqueous Me_2SO solution (eqn. (1)).[21] Interestingly, analysis of the results in terms of Brønsted-type structure–reactivity relationships reveals that these nucleophilic aromatic substitutions are associated with some unprecedentedly high β_{nuc} values. As will be discussed, these results may be regarded as indicative of the incursion of a single electron transfer-type SET mechanism in the overall S_NAr displacements under study. §



L = Cl, NBD-Cl **1a-f** **4a-f**

L =  , NBD-Im^+

1a : X = Cl
1b : X = H
1c : X = Me
1d : X = OMe
1e : X = OH
1f : X = NH_2

Results

The reactions of NBD-Cl and NBD-Im^+ with the series of 4-X-substituted anilines **1a**–**f** have been kinetically studied at 25 °C in 70–30 and 20–80 (v/v) H_2O–Me_2SO mixtures with the ionic strength being maintained constant by addition of 0.2 M Me_4NCl (eqn. (1)). The reactions were conducted in buffers made up from **1a**–**f**, varying the concentrations of the anilinium and aniline components at constant pH while maintaining pseudo-first-order conditions with the buffer being in large excess throughout, *i.e.* [NBD-Cl] or [NBD-Im^+] = 3×10^{-5} mol dm^{-3}, $[\mathbf{1a}–\mathbf{f}]_{total}$ in the range 2×10^{-3}–0.14 mol dm^{-3}. All the reactions were monitored spectrophotometrically by following the increase of absorbance at the wavelength corresponding to the absorption maximum of the resulting 4-anilino-7-nitrobenzofurazans **4a**–**f** which are all formed quantitatively at completion of the disappearance of the electrophilic reagents.[21] Plots of the first-order rate constants, k_{obsd}, *versus* the aniline concentration were linear with negligible intercepts for all reaction systems studied. Examples of these plots are given in Figs 1 and 2 which also show that the points determined at different pH fall on the same line for a given buffer. This indicates that k_{obsd} is simply given by eqn. (2), allowing a facile determination

$$k_{obsd} = k[\mathbf{1a}–\mathbf{f}] \quad (2)$$

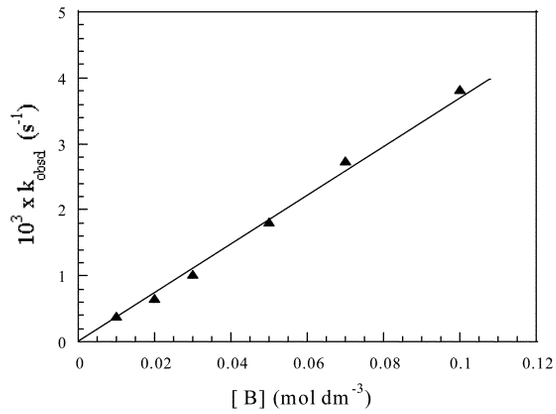


Fig. 1 Plot of k_{obsd} *vs.* [aniline; B] for the reaction of NBD-Cl in 70–30 (v/v) H_2O–Me_2SO; I = 0.2 mol dm^{-3} (Me_4NCl); pH = 4.15, ([B]/[BH^+] = 1); T = 25 °C.

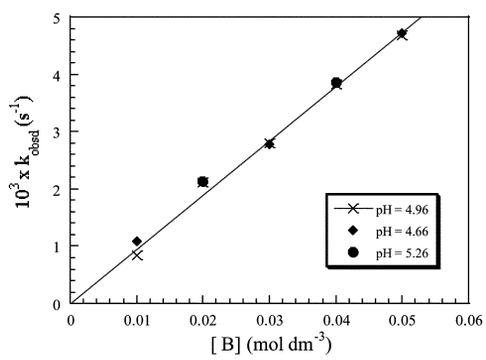


Fig. 2 Plot of k_{obsd} *vs.* [*p*-methoxyaniline; B] for the reaction of NBD-Im^+ in 70–30 (v/v) H_2O–Me_2SO; I = 0.2 mol dm^{-3} (Me_4NCl); pH = 4.66 (◆), 4.96 (×) and 5.26 (●), ([B]/[BH^+] = 1/2, 1 and 2, respectively); T = 25 °C.

of the second-order rate constants k. These rate constants, together with the pK_a values measured for the aniline reagents in the two solvent mixtures studied (see Experimental section) are summarized in Table 1. The complete set of k_{obsd} data obtained in 1 : 1 buffers are available as supplementary data. †

Discussion

Rate-limiting nucleophilic addition

A major feature of our results is the absence of general base catalysis in the overall substitution reactions of NBD-Cl and NBD-Im^+ with the aniline nucleophiles.[17,23,24,27] This indicates that the proton transfer step involved in the reactions is subsequent to the rate-limiting step. Keeping with the traditional interpretation of nucleophilic aromatic substitution by amines in general, this behaviour is in accord with the S_NAr mechanism shown in Scheme 1 where rate-limiting formation of the intermediate σ-complexes **2a**–**f** is followed by fast expulsion of the chloride or imidazole leaving groups.[17,24,27] This implies that deprotonation of the adducts **2a**–**f** to give the conjugate bases **3a**–**f** as well as the subsequent re-aromatisation of these species are fast processes relative to the nucleophilic addition step. This situation calls for some discussion, especially because in the NBD-Im^+ reactions the basicity of the leaving *N*-methylimidazole group (pK_a = 6.65 and 5.52, in 30 and 80% Me_2SO, respectively)[28] is in most cases greater than that of the incoming anilines (pK_a in the ranges 3.39–5.80 and 2.37–5.91 in 30 and 80% Me_2SO, respectively; see Table 1).

Regarding the proton transfer step corresponding to the conversion of the anilinium "acids" **2a**–**f** into the conjugate bases

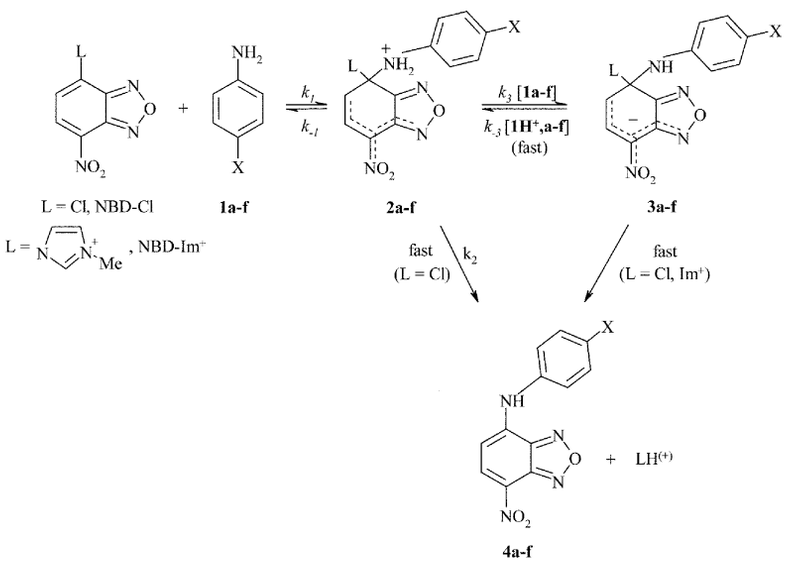
‡ While a β_{nuc} value of 0.91 has been reported for the reaction of 1-chloro-2,4-dinitrobenzene with phenoxides in methanol,[16] this value is not very meaningful, since the pK_a^{MeOH} values used in constructing the correlation were estimated from the $pK_a^{H_2O}$ values instead of being directly measured in methanol.

§ It may be noted that nucleophilic substitution in the nitrobenzofurazan structures should strictly be termed as heteroaromatic substitution, contrasting with purely aromatic displacements in the nitrobenzene series. However, ample evidence has been amassed in the literature, including numerous reviews,[17,22–25] that the two types of systems are subject to very similar principles in terms of reactivity and mechanism. Therefore, we deem it justified to discuss both our systems in terms of the S_NAr mechanism.

Table 1 Second-order rate constants (k) for the reactions of NBD-Cl and NBD-Im$^+$ with *p*-X-substituted anilines **1a**–**f** in H_2O–Me_2SO–0.2 mol dm^{-3} Me_4NCl mixtures (eqn. (1))[a]

p-X-substituted anilines (X)	σ_p^{X}[b]	H_2O–Me_2SO (% v/v)	pK_a[c]	$10^2 \times k$ /dm^3 mol^{-1} s^{-1}	
				L = Cl	L = Im$^+$
1a (Cl)	0.23	70–30	3.39	1.35	
		20–80	2.37	0.82	
1b (H)	0	70–30	4.15	3.80	1.03
		20–80	3.31	2.93	1.75
1c (Me)	−0.17	70–30	4.63	14.3	3.87
		20–80	4.08	11.6	8.62
1d (OMe)	−0.27	70–30	4.96	30.5	9.5
		20–80	4.56	42.7	35.4
1e (OH)	−0.37	70–30	5.24	52.7	
		20–80	4.87	161	
1f (NH_2)	−0.57	70–30	5.80	306	182
		20–80	5.91	1314	3192

[a] T = 25 °C. [b] Ref. 26 .[c] Apparent pK_a values of the *p*-X-substituted anilines referenced to the ternary mixture (see Experimental section); T = 25 °C.



Scheme 1

3a–**f**, it is noteworthy that Crampton and Rabbitt have recently reported that the deprotonation of the intermediate σ-adducts of type **5** involved in the addition of various amines to 4-nitrobenzofuroxan is both a thermodynamically and kinetically favorable process.[29] Based on the finding that the acidifiying effect exerted by a negatively charged 4-nitrobenzofuroxanyl structure on the ammonium site directly bonded to the sp^3 carbon amounts to 2.5–3 pK_a units,[29]¶ the pK_a values for deprotonation of the adducts **2a**–**f** should be in the range 0–3, as compared with pK_a values in the range 2.37–5.91 for the parent anilinium cations **1H**$^+$,**a**–**f**. This is consistent with essentially complete and fast formation of the adducts **3a**–**f** from the initially formed anilinium complexes **2a**–**f**, notably in the case of the NBD-Im$^+$ reactions where the repulsive interaction between the imidazolium and anilinium moieties in **2a**–**f** (L = Im$^+$) will further contribute to the ease of conversion of the species into the conjugate bases **3a**–**f**.

That the conversion of the adducts **3a**–**f** into the substitution products **4a**–**f** is also a fast process compared to the addition step can then be understood simply in terms of the extremely poor leaving group ability of an aniline moiety (pK_a = 30.6 in Me_2SO)[30] as compared with a chloride anion (pK_a ~ −7) or a *N*-methylimidazole molecule (pK_a = 6.65 and 5.52 in 30% and 80% Me_2SO, respectively).[28] The situation is especially relevant to the NBD-Im$^+$ reactions since the formation of **4a**–**f** through spontaneous rearomatisation of the initially formed adducts **2a**–**f** would clearly be more difficult as a result of the greater basicity of the *N*-methylimidazole structure relative to most of the parent anilines **1a**–**f**. However, some contribution of a rapid and direct decomposition of **2a**–**f** to **4a**–**f** cannot be excluded in the case of NBD-Cl reactions.

¶ There is evidence that the negatively charged 4-nitrobenzofurazanyl and 4-nitrobenzofuroxanyl structures exert similar acidifying (−*I*) effects.[17,18b]

Structure–reactivity correlations

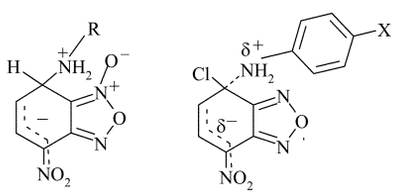
As is apparent from Table 1, increasing the basicity of the aniline nucleophile causes a marked increase in the ease of substitution of NBD-Cl and NBD-Im$^+$. This increase is roughly two orders of magnitude for NBD-Cl and three orders of magnitude for NBD-Im$^+$. Analysis of these variations in terms of Hammett plots gives very good correlations ($R \geq 0.99$) using σ_p substituent constants noting that due to a rather low reactivity of the related anilines no substituent with an appreciable $-M$ effect is included in this series. In the case of the chloro derivative, the ρ values, which are equal to −2.68 and −3.82 in 30% and 80% Me_2SO, respectively (Table 2), are comparable with the value of −3.70 reported by Ryan and Humffray for substitutions of picryl chloride by a similar set of anilines in 75–25 (v/v) EtOH–H_2O mixture.[31]

Rather similar ρ values have also been obtained for these reactions in methanol (ρ = −3.50) and in acetonitrile (ρ = −3.46).[32] The ρ values obtained in the present work are clearly consistent with significant development of positive charge at

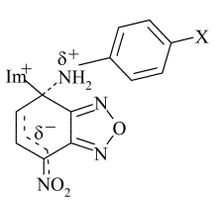
Table 2 Hammett (ρ) and Brønsted (β_{nuc}) values for the reaction of NBD-Cl and NBD-Im$^+$ with *p*–substituted anilines in H_2O–Me_2SO–0.2 mol dm^{-3} Me_4NCl mixtures (eqn. (1))

Moiety	H_2O–Me_2SO (% v/v)	ρ	β_{nuc}
NBD-Cl	70–30	−2.68	0.96
	20–80	−3.82	0.93
NBD-Im$^+$	70–30	−3.43	1.43
	20–80	−5.27	1.30

the nitrogen atom of the aniline moiety in the TS for formation of the zwitterionic intermediate σ-complex **6**. Interestingly, the values determined for the NBD-Im$^+$ system in a given solvent mixture are more negative than those for the NBD-Cl system: $\rho = -3.43$ and -5.27 in 30% and 80% Me_2SO, respectively. This greater sensitivity to substituent changes of the rates of nucleophilic addition may be related to the significant repulsive interaction between the positively charged imidazolium moiety and the developing positive charge in the TS for formation of the corresponding intermediate σ-complexes. Clearly, this repulsive interaction, represented in structure **7**, will be subject to a greater modulation by the nature of the X substituent in the aniline moiety. A clear manifestation of this effect is seen in the data in Table 1 which show that the NBD-Im$^+$ reactions proceed faster than the NBD-Cl reactions with the most basic amines but become slower with the less basic ones.



5 **6**



7

Further information as to the intimate mechanisms of reactions (1) becomes available through analysis of the results in terms of Brønsted-type plots, Figs. 3 and 4, because in the present systems we have determined the pK_a values of the various anilines **1a**–**f** in the two H_2O–Me_2SO solvent mixtures studied (Table 1). In this respect, Figs. 3 and 4 show that the reactivity of our systems is described by nicely linear correlations which lead, however, to unexpectedly high β_{nuc} values: for NBD-Cl, $\beta_{nuc} = 0.96$ and 0.93 in 30% and 80% Me_2SO, respectively, while for NBD-Im$^+$, $\beta_{nuc} = 1.43$ and 1.30 in 30% and 80% Me_2SO, respectively. Reports of β_{nuc} values close to or greater than unity have so far been very sparse for nucleophilic aromatic substitutions.[14,15,17] Our findings pertaining to the NBD-Cl and NBD-Im$^+$–aniline systems are therefore worthy of comment.

Why high β_{nuc} values?

As recalled in the introduction, β_{nuc} values close to or greater than 1 have been commonly interpreted either in terms of a similar or greater sensitivity to substituent changes on the reaction at hand relative to the reference ionisation equilibrium,[2a,11] or in the case of S_N2 reactions in terms of the advent of a SET pathway where full electronic transfer occurs prior to the coupling of the electrophilic and nucleophilic partners.[12–14] Focusing first on the argument dealing with the sensitivity to substituent

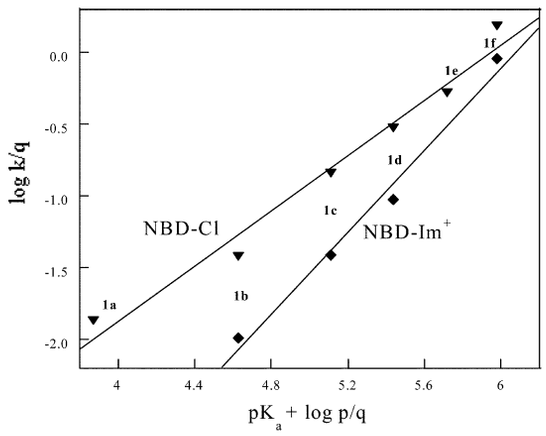


Fig. 3 Brønsted plots for the reactions of NBD-Cl and NBD-Im$^+$ with *p*-X-substituted anilines **1a**–**f** in 70–30 (v/v) H_2O–Me_2SO; $I = 0.2$ mol dm^{-3} (Me_4NCl); $T = 25$ °C. Numbering from Table 1.

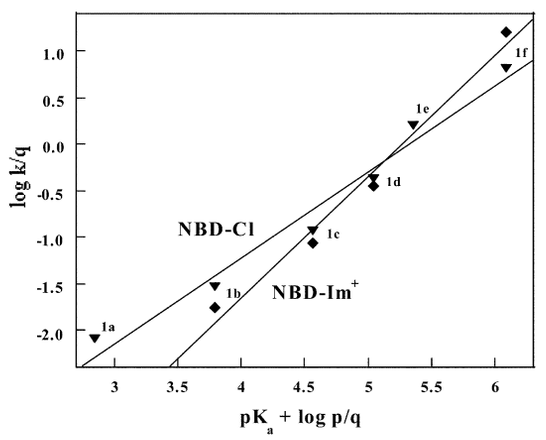
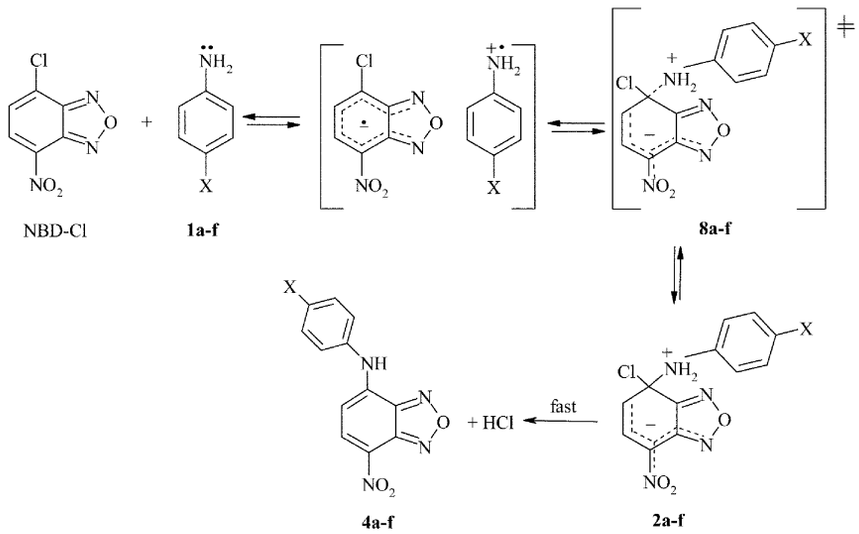


Fig. 4 Brønsted plots for the reactions of NBD-Cl and NBD-Im$^+$ with *p*-X-substituted anilines **1a**–**f** in 20–80 (v/v) H_2O–Me_2SO; $I = 0.2$ mol dm^{-3} (Me_4NCl); $T = 25$ °C. Numbering from Table 1.

changes of the anilinium reaction site, it is a major feature of the present system that the negatively charged structure of 4-nitrobenzofuroxan σ-adducts nevertheless exerts an especially strong $-I$ effect, comparable to that of a negatively charged 2,4,6-trinitrocyclohexadienylide structure. As discussed above, this effect enhances any acidic functionality attached at the sp^3 carbon of the σ-adduct by 2.5–3 pK_a units.[29] Due to this effect, it is therefore possible that the σ-complexation of NBD-Cl and NBD-Im$^+$ by anilines **1a**–**f** is accompanied by the generation of a greater positive charge at the nitrogen atom of the adducts **2a**–**f** than does the protonation of **1a**–**f**. Should this be true, one can anticipate that the degree of positive charge development on the nitrogen atom at the σ-adduct-like TS will also be much greater in reactions (1) than in S_NAr reactions of amines with less electrophilic nitroaromatic substrates.[14] This would explain the observed high β_{nuc} values, notably in the NBD-Im$^+$ reactions where the development of the positive charge will be accentuated by the additional $-I$ effect exerted by the *N*-methylimidazolium moiety.

Although it accounts reasonably well for the β_{nuc} values associated with reactions (1), it is more difficult to reconcile the above reasoning with other experimental findings. As further confirmed by the similarity of the rate constants for reaction of picryl chloride and NBD-Cl with MeO^- in methanol—the second-order rate constants k are equal to 17.7 and 7.7 dm^3 mol^{-1} s^{-1}, respectively[33,34]—the electrophilic character of 4-nitrobenzofurazan and 2,4,6-trinitrobenzene moieties is comparable. On this ground, substitutions involving these two types of structures should exhibit a similar sensitivity to substituent changes and therefore similar β_{nuc} values. In addition,



Scheme 2

Dixon and Bruice have previously reported that the β_{nuc} value associated with the reaction of picryl chloride with various amines is equal to 0.64 in aqueous solution,[35] *i.e.* it falls in the normal range recognized for substitutions adhering to a normal polar S_NAr mechanism.[14,17]

In fact, it is only in two nucleophilic aromatic substitutions proceeding through a concerted mechanism that meaningful β_{nuc} values out of the range 0.5–0.7 have been previously reported and explained in terms of an increased sensitivity of the transition state to substituent changes.[16] These reactions deal, respectively, with the displacement of 4-nitrophenoxide ion from 2-(4-nitrophenoxy)-4,6-dimethoxy-1,3,5-triazine (β_{nuc} = 0.95) and of 3,4-dinitrophenoxide ion from 4-(3′,4′-dinitrophenoxy)-2,6-dimethoxy-1,3,5-triazine by a series of substituted pyridines (β_{nuc} = 1.08). Interestingly, most other 1,3,5-triazinyl transfers studied have been found to obey a normal S_NAr mechanism with β_{nuc} values in the range of 0.5–0.7, including those occurring between two pyridine nucleophiles with the intermediacy of σ-adducts having two positively charged moieties bonded at the sp^3 carbon.[36] According to Williams and coworkers,[15] a concerted nucleophilic aromatic substitution can only take place in systems where the putative intermediate σ-adduct is of particularly high energy, a situation which can be rejected in reactions involving such powerful stabilizing σ-adduct structures as a 4-nitrobenzofurazanyl or a picryl moiety. As a result, the explanation of β_{nuc} values close to or greater than 1 in reactions (1) on the basis of a very high sensitivity of the transition states to the nature of the X-substituent of the incoming anilines, is not so convincing if these reactions really proceed *via* a normal polar S_NAr mechanism.

Can single electron transfer (SET) be a reasonable pathway?

The above inconsistencies lead us to envision that the high β_{nuc} values associated with our reactions may be the reflection of a SET pathway, as described in Scheme 2 for the NBD-Cl system as an example. This scheme depicts the formation of the σ-complex intermediates **2a**–**f** through initial (fast) electron transfer from the aniline donor to the nitrobenzofurazan acceptor moiety and subsequent (slow) coupling of the resulting cation and anion radicals within the solvent cage *via* the transition state **8**. The latter will have a full positive charge on the anilino nitrogen atom thus accounting for the observed corresponding equivalence of rate and equilibrium protonation, *i.e.* $\beta_{nuc} \sim 1$.[2b,14] In accord with the lack of observation of base catalysis in the present system, conversion of the σ-adducts to the final substitution products will then occur rapidly, as discussed earlier in this paper.

While schemes of this type have previously been proposed for substitution of nitro-substituted benzene derivatives with various nucleophiles,[17,37–42] including much weaker electron donors than anilines, the studies did not include determination of β_{nuc} values, relying chiefly on spectroscopic identification of radical anions with frequent attendant formation of side products. Thus, these studies did not permit the obtention of direct information concerning the progress of the reactions and the structure of the rate-determining transition-state.

We would like to emphasize two notable features that are consistent with the formulation of Scheme 2. A first salient feature which contrasts the present NBD-Cl–aniline systems with the previously investigated ones is the more facile $1e^-$-reduction of the nitrobenzofurazan structures relative to similarly electrophilic benzenoid systems.[43–47]‖ $E°$ values pertaining to the reduction of a number of nitrobenzofurazans and related 1-oxides (nitrobenzofuroxans) have been recently measured by us and found to fall in the range +0.10 to −0.44 V (relative to SCE).[43] For example, we have $E° = -0.44$ V for the reduction of 4-nitrobenzofurazan in Me_2SO solution.[43] Such $E°$ values are less negative than the corresponding $E°$ values of −0.58 to −1 V (relative to SCE) which have been reported for radical anion formation from a large set of dinitro- and trinitrobenzene derivatives, *e.g.* $E° = -0.68$ V for the reduction of trinitrotoluene.[45] While attempts to characterize the postulated radical anion of NBD-Cl through EPR have failed due to the low lifetime of this type of species in the benzofurazan and benzofuroxan series,[43]** it can reasonably be concluded from the available $E°$ values that the NBD-Cl–aniline system is characterized by a greater affinity to take part in an electron transfer process compared to picryl chloride–aniline systems. It is this difference in the affinity for electron capture which can be one of the driving forces for the proposed mechanistic change and favor the SET mechanism in our NBD-Cl system. Of interest also is the recent proposal that the formation of radical anions from nitroarenes and related substrates would be greatly facilitated in systems where the electron transfer between the electrophilic and nucleophilic partners could take place within an initially formed π-complex.[37,39–42,47,48] Then, the high propensity of nitrobenzofuroxans to form such π-complexes with a

‖ $E°$ values of the same order of magnitude have been measured for 1,3,5-trinitrobenzene and 2,4,6-trinitroanisole. We thank Dr Illuminada Gallardo (Universitat Autonoma de Barcelona) for this personal communication.

** Cyclic voltammetry experiments have shown that the reduction of nitrobenzofuroxans is an irreversible process in CH_3CN or Me_2SO, thus preventing a determination of the related E° values. These are therefore approximated from the observed reduction peaks.

number of electron-rich arenes, is an additional argument which can favor Scheme 2 for the reactions of NBD-Cl with the electron-rich anilines **1a**–**f**.[49]

A second and perhaps most important feature in favor of Scheme 2 is that the rate constants for substitution of NBD-Cl by the anilines **1a**–**f** are found to correlate satisfactorily with the oxidation potentials $E°$ of these species, as measured by Jonsson *et al.* in aqueous solution.[50] This is illustrated by the linear log k *vs.* $E°$ plots of Fig. 5 ($R = 0.970$) and 6 ($R = 0.983$) which describe the variations in reactivity in 30% Me_2SO and 80% Me_2SO, respectively. In this regard, it is worth noting that the quality of these correlations is largely related to the surprising behaviour of 4-chloroaniline which has the same $E°$ value as aniline while being less basic and therefore less reactive than the unsubstituted amine. As a matter of fact, if the points for 4-chloroaniline are omitted the correlation coefficients of Figs. 5 and 6 become equal to 0.993 and 0.991, respectively.

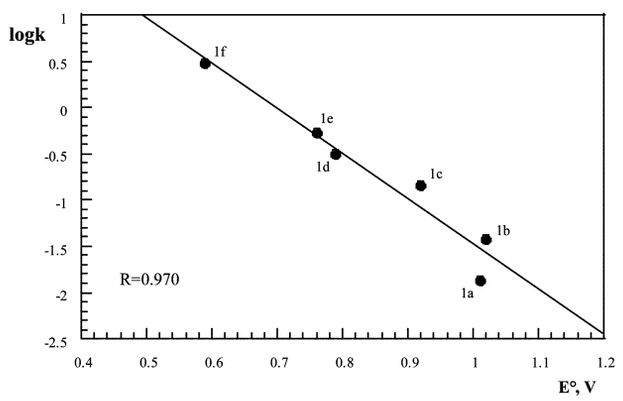


Fig. 5 The influence of the oxidation potential $E°$ of anilines on the rates of reaction of NBD-Cl with **1a**–**f** in 70–30 (v/v) H_2O–Me_2SO; $I = 0.2$ mol dm^{-3} (Me_4NCl); $T = 25$ °C. Numbering from Table 1.

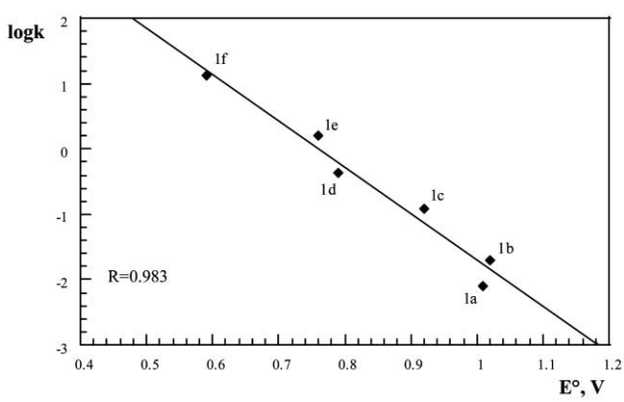


Fig. 6 The influence of the oxidation potential $E°$ of anilines on the rates of reaction of NBD-Cl with **1a**–**f** in 20–80 (v/v) H_2O–Me_2SO; $I = 0.2$ mol dm^{-3} (Me_4NCl); T = 25 °C. Numbering from Table 1.

Returning to the imidazolium substrate, NBD-Im$^+$, satisfactorily linear log k–$E°$ correlations can also be drawn from the data of Table 1 (Figs. S1 and S2), making it reasonable to postulate that Scheme 2 can also operate for substitutions by the anilines **1a**–**f** in this derivative. However, the coupling step would then involve the approach of a positively charged aniline radical towards a ring position bearing a positively charged leaving group moiety. Again, such an approach would involve a significant repulsive interaction which would be modulated by the nature of the X substituent in the aniline moiety, as discussed above for a normal polar S_NAr mechanism. The greater electronic effect which this calls for will result in a steeper dependence on the electron-donating/electron-withdrawing capability of X, *i.e.* a larger slope in the Brønsted plot or $E°$ correlations, as observed.

Even though the above features are clearly consistent with Scheme 2, we will not claim that they provide sufficient evidence for the implication of SET in our reactions. Based on the reasonable assumption that in this mechanistic route the aniline moiety in the transition state should closely resemble the radical cation, one would expect a better description of the reactivity of our systems in terms of σ_p^+ rather than σ_p Hammett substituent constants, which is not really borne out by experiments. It remains that the finding of satisfactory log k–$E°$ correlations is unprecedented for S_NAr substitutions and hence justifies to a possible transition from the polar to the SET mechanism in this field. Other investigations are currently being carried out in our laboratory to shed further light on this important facet of nucleophilic aromatic substitutions.

Conclusions

In conclusion, the present study of the reactions of substituted anilines with NBD-chloride and -imidazolium substrates, which are characterized by β_{nuc} values in the region of 1.0 and 1.3–1.4, respectively, highlights the possible role of the Brønsted β_{nuc} parameter as an indicator of the SET process. A salient feature of the present system which can induce the transition from the normal S_NAr pathway to the SET pathway, is the much more facile 1e$^-$ reduction of the nitrobenzofurazan structure relative to similarly electrophilic benzenoid systems such as picryl chloride. A significant result which is consistent with the SET mechanism is the finding that the rate constants for the substitutions of NBD-Cl and NBD-Im$^+$ correlate well with the oxidation potentials of the aniline nucleophiles. In addition, it has been shown that the marked sensitivity of rates to substituent changes in the present system is related to significant repulsive interactions in the S_NAr transition-states, which would be conducive to a transition to the SET mechanism as an energetically more favorable pathway.[51]

Experimental

Materials

Solvents were purified and solutions made up as previously described.[21,52,53] 4-Chloro-7-nitrobenzofurazan (NBD-Cl; Fluka BioChemika) was used as received. The preparation of the various substitution products **4a**–**f** was previously reported.[21] 3-Methyl-1-(4-nitrobenzofurazanyl)imidazolium chloride (NBD-Im$^+$Cl$^-$) was prepared as follows: 2 g (10 mmol) of NBD-Cl and 0.8 mL (10 mmol) of *N*-methylimidazole were dissolved in 50 mL butyl acetate and the mixture was heated to 40 °C. After ~10 minutes, a yellow precipitate began to form. The crystals deposited after 30 minutes were filtered, washed thoroughly with pentane and dried under vacuum. NBD-Im$^+$Cl$^-$ was thus obtained in 70% yield; mp 190 °C (with decomposition).

NMR data for NBD-Im$^+$Cl$^-$: ^{1}H NMR (δ in ppm, Me_2SO-d_6, Me_4Si): 10.32 (s, 1H, $H_{2'}$), 8.99 (d, 1H, $^3J_{H5H6} = 8.19$ Hz, H_5), 8.66 (d, 1H, $^3J_{H5'H4'} = 1.65$ Hz, $H_{5'}$), 8.39 (d, 1H, $^3J_{H5H6} = 1.65$ Hz, H_6), 8.17 (d, 1H, $^3J_{H5'H4'} = 1.65$ Hz, $H_{4'}$), 4.08 (s, 1H, CH_3). ^{13}C NMR (δ in ppm, Me_2SO-d_6, Me_4Si): 145.55 (C_8, $J_{C8H6} = 9.0$ Hz), 143.78 (C_9, $J_{C9H5} = 8.5$ Hz), 138.38 ($C_{2'}$, $J_{C2'H2'} = 227.2$ Hz, $J_{C2'H5'} = J_{C2'H4'} = 4.5$ Hz), 136.05 (C_4, $J_{C4H6} = 8.5$ Hz, $J_{C4H5} = 5.1$ Hz), 132.66 (C_5, $J_{C5H5} = 174.0$ Hz), 128.58 (C_7, $J_{C7H5} = 9.6$ Hz, $J_{C7H6} = 1.7$ Hz), 125.23 ($C_{4'}$, $J_{C4'H4'} = 206.6$ Hz, $J_{C4'H2'} = 11.2$ Hz, $J_{C4'H5'} = 3.4$ Hz), 123.62 (C_6, $J_{C6H6} = 174.0$ Hz), 121.83 ($C_{5'}$, $J_{C5'H5'} = 208.0$ Hz, $J_{C5'H2'} = 13.0$ Hz, $J_{C5'H4'} = 5.1$ Hz), 36.64 (CH_3, $J_{CH3} = 144.7$ Hz). HRMS calcd for $C_{10}H_8N_5O_3$: 246.0627 [M − Cl$^-$]$^+$, found *m*/*z* 246.0631.

Measurements

Kinetic measurements were carried out with either a conventional UV-visible Cary 1E spectrophotometer or an Applied

Photophysics SX. 18 MV stopped-flow spectrometer being both equipped with a thermostated cell compartment (25 °C ± 0.2). All rates were reproducible to within ± 3%. The acidity constants of the *p*-X-substituted anilines **1a**–**f** in the 70–30 and 20–80 (v/v) H_2O–Me_2SO mixtures containing 0.2 mol dm^{-3} Me_4NCl have been measured by potentiometry at 25 °C, using an electronic pH meter (Tacussel ISIS 20000) equipped with an hydrogen electrode and a Tacussel C8 reference calomel electrode. The cell and the procedures, previously described in detail,[52] allow the determination of apparent pK_a referenced to an infinitely diluted buffer solution in the H_2O–Me_2SO–Me_4NCl (0.2 mol dm^{-3}) ternary mixtures.

Acknowledgements

Authors are very indebted to CNRS for financial support (CNRS/DEF n° 12109). We also thank Professor J. Pinson (University Denis Diderot) for helpful comments.

References

1 (*a*) W. P. Jencks, *Bull. Soc. Chim. Fr.*, 1988, 218; (*b*) W. P. Jencks, in *Nucleophilicity*, ed. J. M. Harris and S. P. Mc Manus, Advances in Chemistry Series 215, American Chemical Society, Washington, DC, 1987, p. 155.
2 (*a*) A. Williams, *Chem. Soc, Rev.*, 1994, 93; (*b*) M. Page and A. Williams, in *Organic and Bio-organic Mechanisms*, Longman, Harlow, Chapter 3; (*c*) M. Eigen, *Angew. Chem., Int. Ed. Engl.*, 1964, **3**, 1; (*d*) A. J. Kresge, *Chem. Soc. Rev.*, 1973, **2**, 475.
3 (*a*) F. G. Bordwell and W. J. Boyle, *J. Am. Chem. Soc.*, 1972, **94**, 3907; (*b*) F. G. Bordwell and J. A. Hautala, *J. Org. Chem.*, 1978, **43**, 3116 and references therein.
4 W. P. Jencks, M. T. Haber, D. Herschlag and K. L. Nazaretian, *J. Am. Chem. Soc.*, 1986, **108**, 479.
5 C. F. Bernasconi, *Adv. Phys. Org. Chem.*, 1992, **27**, 119 and references therein.
6 (*a*) W. P. Jencks, S. R. Brant, J. R. Gandler, G. Friedrich and C. Nakamura, *J. Am. Chem. Soc.*, 1982, **104**, 7045; (*b*) D. J. Hupe and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 451.
7 D. J. Hupe and D. Wu, *J. Am. Chem. Soc.*, 1977, **99**, 7653.
8 C. F. Bernasconi, *Acc. Chem. Res*, 1987, **20**, 301.
9 (*a*) F. Terrier, G. Moutiers, L. Xiao, E. Le Guével and F. Guir, *J. Org. Chem.*, 1995, **60**, 1748; (*b*) E. Buncel, C. Cannes, A.-P. Chatrousse and F. Terrier, *J. Am. Chem. Soc.*, 2002, **124**, 8766 and references therein.
10 F. Terrier, P. Mc Cormack, E. Kizilian, J.-C. Hallé, P. Demerseman, F. Guir and C. Lion, *J. Chem. Soc., Perkin Trans. 2*, 1991, 153.
11 (*a*) M. I. Page and W. P. Jencks, *J. Am. Chem. Soc.*, 1972, **94**, 3263; (*b*) M. I. Page and W. P. Jencks, *J. Am. Chem. Soc.*, 1972, **94**, 8818.
12 F. G. Bordwell, J. C. Branca and T. A. Cripe, *Isr. J. Chem.*, 1985, **26**, 357.
13 F. G. Bordwell and A. H. Clemens, *J. Org. Chem.*, 1981, **46**, 1037.
14 F. G. Bordwell and D. L. Hugues, *J. Am. Chem. Soc.*, 1986, **108**, 5991.
15 (*a*) A. Hunter, M. Renfrew, D. Rettura, J. A. Taylor, J. M. Whitmore and A. Williams, *J. Am. Chem. Soc.*, 1995, **117**, 5484; (*b*) J. Shakes, C. Raymond, D. Rettura and A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1996, 1553.
16 G. D. Leahy, M. Liverio, J. Miller and A. J. Parker, *Aust. J. Chem.*, 1956, **9**, 382.
17 F. Terrier, in *Nucleophilic Aromatic Displacement*, ed. H. Feuer, VCH, New-York, 1991, Chapters 1 and 2.
18 (*a*) F. Terrier, E. Kizilian, J.-C. Hallé and E. Buncel, *J. Am. Chem. Soc.*, 1992, **114**, 1740; (*b*) F. Terrier, *Chem. Rev.*, 1982, **82**, 77; (*c*) E. Buncel, R. A. Renfrow and M. J. Strauss, *J. Org. Chem.*, 1987, **52**, 488; (*d*) E. Buncel, R. A. Renfrow and M. J. Strauss, *Can. J. Chem.*, 1983, **61**, 1690; (*e*) R. A. Renfrow, M. J. Strauss, S. Cohen and E. Buncel, *Aust. J. Chem.*, 1983, **36**, 1843; (*f*) E. Buncel, J. M. Dust, K. T. Park, R. A. Renfrow and M. J. Strauss, in *Nucleophilicity*, ed. J. M. Harris and S. P. Mc Manus, Advances in Chemistry Series 215, American Chemical Society, Washington, DC, 1987, p. 369.
19 F. Terrier, M.-J. Pouet, J.-C. Hallé, E. Kizilian and E. Buncel, *J. Phys. Org. Chem.*, 1998, **11**, 707 and references cited therein.
20 R. Goumont, M. Sebban, P. Sepulcri, J. Marrot and F. Terrier, *Tetrahedron*, 2002, **58**, 3249.
21 J.-C. Hallé, M. Mokhtari, P. Soulié and M.-J. Pouet, *Can. J. Chem.*, 1997, **75**, 1240.
22 G. Illuminati and F. Stegel, *Adv. Heterocycl. Chem.*, 1983, **34**, 305.
23 J. F. Bunnett, *Q. Rev. Chem. Soc.*, 1958, **12**, 1.
24 J. Miller, in *Aromatic Nucleophilic Substitution*, Elsevier; Amsterdam, 1968.
25 G. Consiglio, V. Frenna and D. Spinelli, *Topics in Heterocyclic Systems – Synthesis, Reactions and Properties. Base Catalysis in Aromatic Nucleophilic Substitutions: Current Views.* Research Signpost, Trivandrum (India), 1996, Vol. 1, p. 169.
26 O. Exner, in *Correlation Analysis in Chemistry: Recent Advances.* ed. N. B. Chapman and J. Shorter, Plenum Press, New York, 1978. Chapter 10: *"A Critical Compilation of Substituent Constants."*
27 C. F. Bernasconi, *MTP Int. Rev. Sci.: Org. Chem., Ser. 1*, 1973, **3**, 33.
28 J.-C. Hallé, C. Pichon and F. Terrier, *J. Biol. Chem.*, 1984, **259**, 4142.
29 M. R. Crampton, J. Delaney and L. C. Rabbitt, *J. Chem. Soc., Perkin Trans. 2*, 1999, 2473.
30 F. G. Bordwell, *Acc. Chem. Res.*, 1988, **22**, 456.
31 J. J. Ryan and A. A. Humffray, *J. Chem. Soc. B*, 1967, 1300.
32 J. Hirst and K. U. Rahman, *J. Chem. Soc., Perkin Trans. 2*, 1973, 2119.
33 J. Kavalek, M. Pastrnek and V. Sterba, *Collect. Czech. Chem. Commun.*, 1978, **43**, 1401.
34 L. Di Nunno, S. Florio and P. E. Todesco, *J. Chem. Soc., Perkin Trans. 2*, 1975, 1469.
35 J. E. Dixon and T. C. Bruice, *J. Am. Chem. Soc.*, 1972, **94**, 2052.
36 (*a*) N. R. Cullum, A. H. M. Renfrew, D. Rettura, J. A. Taylor, M. J. Whitemore and A. Williams, *J. Am. Chem. Soc.*, 1995, **117**, 9200; (*b*) A. H. M. Renfrew, J. A. Taylor, M. J. Whitemore and A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1994, 2383.
37 L. Grossi and S. Strazzari, *J. Chem. Soc., Perkin Trans. 2*, 1999, 2141.
38 C. Paradisi and G. Scorrano, *Acc. Chem. Res.*, 1999, **32**, 958.
39 T. Abe and Y. Ikegami, *Bull. Chem. Soc. Jpn*, 1977, **99**, 6677.
40 L. A. Blyumenfeld, L. V. Bryukhovetskayar, G. V. Fomin and S. M. Shein, *Russ. J. Phys. Chem.*, 1970, **44**, 518 and references therein.
41 (*a*) R. Bacaloglu, C. A. Bunton and G. Cerichelli, *J. Am. Chem. Soc.*, 1987, **109**, 621; (*b*) R. Bacaloglu, C. A. Bunton and F. Ortega, *J. Am. Chem. Soc.*, 1988, **110**, 3503; (*c*) R. Bacaloglu, C. A. Bunton and F. Ortega, *J. Am. Chem. Soc.*, 1988, **110**, 3512.
42 (*a*) R. Bacaloglu, C. A. Bunton and F. Ortega, *J. Am. Chem. Soc.*, 1989, **111**, 1041; (*b*) R. Bacaloglu, A. Blasko, C. A. Bunton, E. Dorwin, F. Ortega and C. Zucco, *J. Am. Chem. Soc.*, 1991, **113**, 238.
43 G. Moutiers, J. Pinson, F. Terrier and R. Goumont, *Chem. Eur. J.*, 2001, **7**, 1712.
44 (*a*) I. M. Sosonkin and G. L. Kalb, *Zh. Org. Khim.*, 1974, **10**, 1341; (*b*) I. M. Sosonkin, G. N. Strogov, A. Ya. Kaminskii, G. E. Troshin and F. F. Lakomov, *Zh. Org. Khim.*, 1980, **16**, 1711.
45 I. Gallardo, G. Guirado and J. Marquet, *Chem. Eur. J.*, 2001, **7**, 1759.
46 (*a*) I. Gallardo, G. Guirado and J. Marquet, *J. Org. Chem.*, 2002, **67**, 2548; (*b*) I. Gallardo, G. Guirado and J. Marquet, *Eur. J. Org. Chem.*, 2002, 251; (*c*) I. Gallardo, G. Guirado and J. Marquet, *Eur. J. Org. Chem.*, 2002, 261; (*d*) I. Gallardo, G. Guirado and J. Marquet, *J. Electroanal. Chem.*, 2000, **488**, 64.
47 L. Grossi, *Tetrahedron Lett.*, 1992, **33**, 5645.
48 V. Arca, C. Paradisi and G. Scorrano, *J. Org. Chem.*, 1990, **55**, 3617.
49 (*a*) A. S. Bailey and J. R. Case, *Tetrahedron*, 1958, **3**, 113; (*b*) C. Boga and L. Forlani, *J. Chem. Soc., Perkin Trans. 2*, 2001, 1408; (*c*) L. Forlani, *J. Phys. Org. Chem.*, 1999, **12**, 417.
50 (*a*) M. Jonsson, J. Lind, T. E. Ericksen and G. Merényi, *J. Am. Chem. Soc.*, 1994, **116**, 1423; (*b*) J. Bacon and R. N. Adams, *J. Am. Chem. Soc.*, 1968, **90**, 6596.
51 (*a*) A. Pross, *Acc. Chem. Res.*, 1985, **18**, 212; (*b*) A. Pross and S. S. Shaik, *Acc. Chem. Res.*, 1983, **16**, 363; (*c*) L. Eberson and F. Radner, *Acc. Chem. Res.*, 1987, **20**, 53.
52 (*a*) H. A. Achassi Sorkhabi, J.-C. Hallé and F. Terrier, *J. Chem. Res.*, 1978, **196 (S)**, 2545 (M); (*b*) H. A. Achassi Sorkhabi, J.-C. Hallé and F. Terrier, *J. Chem. Res.*, 1978, 1371 (M).
53 J.-C. Hallé, R. Gaboriaud and R. Schaal, *Bull. Soc. Chim. Fr.*, 1969, 1851.