Electrochemical Oxidation of σ-Complex-Type Intermediates in Aromatic Nucleophilic Substitutions

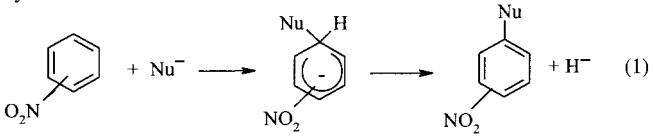
Gilles Moutiers,[a] Jean Pinson,[b] François Terrier,*[a] and Régis Goumont[a]

Abstract: A series of σ-adducts ($\mathbf{1H}^-$…$\mathbf{7H}^-$) derived from the addition of 2-nitropropenide ion to various nitrobenzofuroxans and nitrobenzofurazans have been oxidized electrochemically. The results show that the rearomatization of the carbocyclic ring of these adducts as well as that of a few additional 4,6-dinitrobenzofuroxan adducts ($\mathbf{8H}^-\mathbf{a}-\mathbf{c}$) is associated with much higher oxidation potentials than found for the same process in the dinitro- and trinitrobenzene series. Especially high E° values are measured for the oxidation of the 2-nitropropenide 4,6-dinitro- and 4-nitro-6-trifluoromethylsulfonylbenzofuroxan adducts $\mathbf{1H}^-$ and $\mathbf{4H}^-$ in acetonitrile: $E^\circ(\mathbf{1H}^-) = 1.15$ V versus SCE; $E^\circ(\mathbf{4H}^-) = 1.33$ V versus SCE. These values fit well with the available evidence that the chemical oxidation of these adducts requires the use of very strong oxidizing agents to proceed efficiently. The mechanism for the oxidation process has been established. It is shown to involve transfer of two electrons and liberation of one proton per σ-complex precursor with no evidence whatsoever for the intermediacy of radical anionic species.

Keywords: aromatic substitution · cyclic voltammetry · electrochemistry · Meisenheimer complexes · σ-adducts

Introduction

Nucleophilic substitution of a nuclear hydrogen atom of an electron-deficient aromatic group by an addition–elimination S_NAr mechanism is not a common process, since the hydride anion is a very poor leaving group.[1–3] However, reactions in which an aromatic hydrogen atom is replaced by a nucleophile are known. Like the common S_NAr reactions, they generally occur by initial addition of the nucleophile to the ring, with formation of σ-complex-type intermediates.[1] These subsequently decompose through various pathways, which formally leads to nucleophilic aromatic substitution of hydrogen in the aromatic ring, as exemplified in Equation (1) for a nitroarene system.[1–4]



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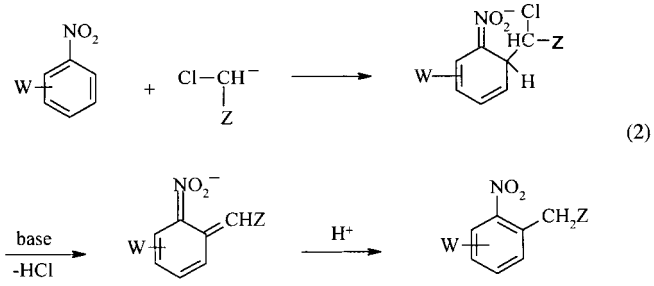
In this respect, two major strategies have been developed. A first efficient and elegant approach is the so-called vicarious nucleophilic aromatic pathway, which was developed by Makosza and extensively investigated in the case of carbanionic nucleophiles [Eq. (2)].[5–9] Several examples of this reaction with nitrogen and oxygen nucleophiles have also been reported.[3, 10–12] In these instances, however, the rearomatization of the σ-complex intermediate occurs by a base-induced β-elimination of a nucleofugal group which must be present at the reactive center in the incoming nucleophile [Eq. (2)]. A second and more general strategy involves a chemical oxidation of the intermediate σ complex through formal displacement of H^-.[1–4] This oxidative approach has proved to be useful for the functionalization of some nitroarenes as well as some nitroactivated heterocycles like nitropyridines, nitropyrimidines, or nitronaphthyridines.[1–4, 13–17]



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Nitro-substituted 2,1,3-benzoxadiazoles and related 1-oxides—commonly referred to as nitrobenzofurazans and nitro-

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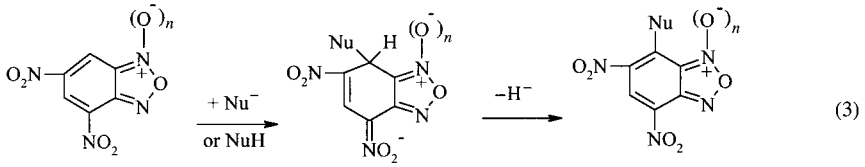
benzofuroxans, respectively—are 10π-electron heteroaromatic substrates which exhibit a considerably higher electrophilic character than electron-deficient aromatic compounds or heteroaromatic compounds like 1,3,5-trinitrobenzene or 3,5-dinitropyridine.[1] The 4,6-dinitro derivatives DNBF and DNBZ [Eq. (3)] have been thoroughly investigated because they undergo a facile coupling with many nucleophiles, including very weak neutral carbon nucleophiles such as enols, anilines, indoles, and thiophenes to afford very stable σ complexes.[18–21]

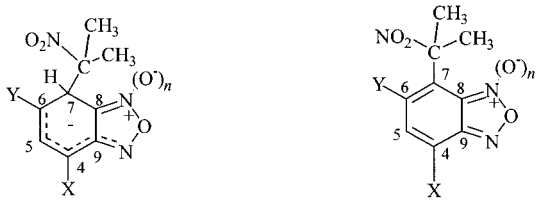


$n = 1$: DNBF
$n = 0$: DNBZ

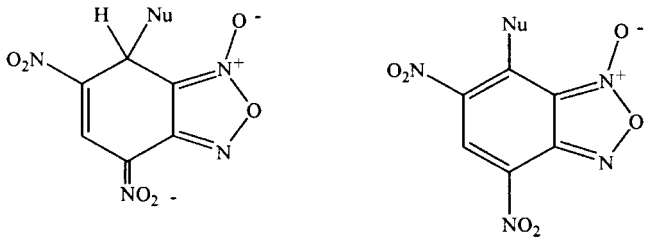
(3)

While the ease of formation and the high thermodynamic stability of σ-adducts of DNBF and DNBZ have led to numerous biological and analytical applications,[20–24] they have so far been of much less interest for synthetic purposes owing to the failure in converting efficiently most of these complexes into the corresponding substituted products [Eq. (3)].[9, 25, 26] A possible explanation for this failure was that the rearomatization of the σ adducts is associated with particularly high oxidative potentials as compared with those known to govern the oxidation of σ adducts in the benzene series, for example $E^\circ \approx 0.80$ V for the TNB adducts.[27, 28]

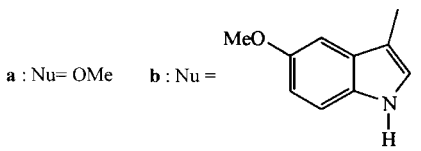
This idea led us to investigate the electrochemical oxidation of σ-adducts $\mathbf{1H}^-$ to $\mathbf{8H}^-$ (Scheme 1). We have measured the oxidation potentials of these adducts, and in some instances their standard potential. These actually appear as the highest so far reported for the oxidation of σ adducts, accounting very well for the difficulty to achieve the process with mild or moderately strong chemical oxidants.[29] The mechanism leading to the rearomatized products has been established.



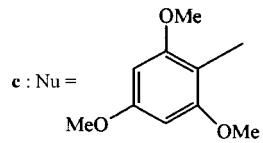
$\mathbf{1H}^-$	X=Y= NO_2 , $n = 1$	**1**
$\mathbf{2H}^-$	X = NO_2 , Y = H , $n = 1$	**2**
$\mathbf{3H}^-$	X = NO_2 , Y = H , $n = 0$	**3**
$\mathbf{4H}^-$	X = NO_2 , Y = SO_2CF_3 , $n = 1$	**4**
$\mathbf{5H}^-$	X = NO_2 , Y = CF_3 , $n = 1$	**5**
$\mathbf{6H}^-$	X = NO_2 , Y = CN , $n = 1$	**6**
$\mathbf{7H}^-$	X = CF_3 , Y = NO_2 , $n = 1$	**7**



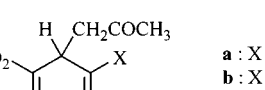
$\mathbf{8H}^-$ **8**



a : Nu= OMe **b** : Nu =



c : Nu =



a : X = OCH_3
b : X = CH_3
c : X = H
d : X = COOEt
e : X = CF_3
f : X = NO_2

$\mathbf{9H}^-$

Scheme 1. The series of 2-nitropropenide adducts discussed in this study. They were chosen because they can be readily isolated as pure crystalline alkali metal salts.[29]

Results

The cyclic voltammograms of compounds $\mathbf{1H}^-$ to $\mathbf{8H}^-$**a**–**c** were examined by cyclic voltammetry. In dimethyl sulfoxide (DMSO + 0.1M NBu_4BF_4) and acetonitrile (CH_3CN + 0.1M NBu_4BF_4) at low scan rates (0.2 $V s^{-1}$), all compounds are characterized by a well-defined irreversible oxidation wave (Ia) (Figure 1). The peak potentials of these waves are given in Table 1. As expected, the two adducts $\mathbf{2H}^-$ and $\mathbf{3H}^-$ derived from the parent 4-nitrobenzofuroxan and 4-nitrobenzofurazan are more readily oxidized than the adduct $\mathbf{1H}^-$ derived from 4,6-dinitrobenzofuroxan, the increasing number of electron-withdrawing nitro groups making the removal of an electron more and more difficult. A noteworthy result is that the 4-nitro-6-trifluoromethylsulfonyl adduct is about 300 mV more reluctant to oxidation than $\mathbf{1H}^-$, pointing out that in this instance the SO_2CF_3 group is a more powerful electron-withdrawing group than a nitro group. We have checked that the use of superdry conditions, as well as the addition of a base (addition of a 900-fold excess of 2,4,6-collidine to $\mathbf{5H}^-$) or of an acid (addition of a 0.17 molar ratio of trifluoroacetic acid to $\mathbf{1H}^-$) do not change the oxidation wave. On the reverse scan a reduction peak (IIc) can be observed provided that the oxidation peak has been scanned beforehand. As will be demonstrated later, this peak corresponds to the reduction of the oxidized product.

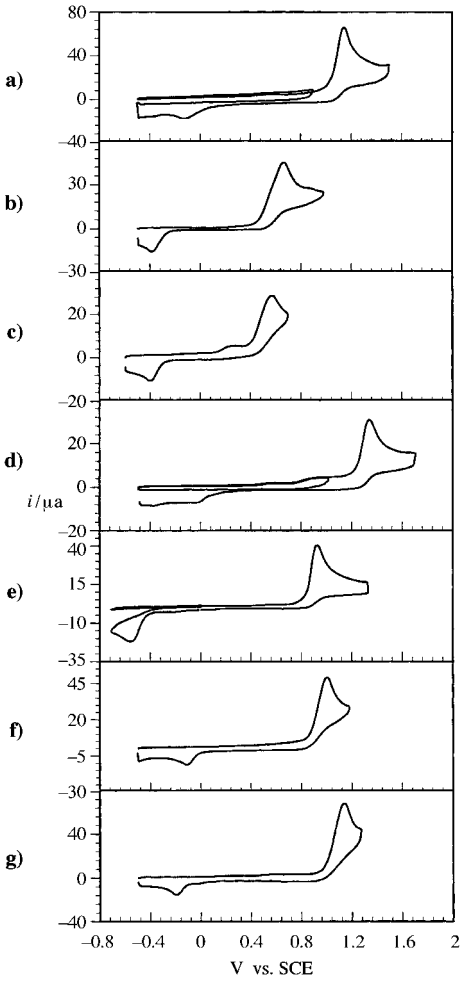


Figure 1. Cyclic voltammetry on a glassy carbon electrode at $v = 0.2\ V\,s^{-1}$, reference SCE of a) $\mathbf{1H}^-$, b) $\mathbf{2H}^-$, c) $\mathbf{3H}^-$, d) $\mathbf{4H}^-$, e) $\mathbf{5H}^-$, f) $\mathbf{6H}^-$, g) $\mathbf{8aH}^-$. Solvents: a), d), e) CH_3CN + 0.1 M NBu_4BF_4; b), c), f), g) DMSO + 0.1 M NBu_4BF_4.

Table 1. Cyclic voltammetry[a] of compounds $\mathbf{1H}^-$ to $\mathbf{8H}^-$.

Compound	DMSO + 0.1 M NBu_4BF_4		CH_3CN + 0.1 M NBu_4BF_4	
	E_{pIa}[b]	E_{pIIc}[b]	E_{pIa}[b]	E_{pIIc}[b]
$\mathbf{1H}^-$[c]	+1.04	−0.16	+1.16	−0.14
$\mathbf{2H}^-$	+0.63	−0.43	+0.59	−0.46
$\mathbf{3H}^-$	+0.55	−0.44	+0.48	−0.49
$\mathbf{4H}^-$	+1.31	+0.10	+1.33	−0.0 2
$\mathbf{5H}^-$	+0.95	−0.22	+0.94	−0.55
$\mathbf{6H}^-$	+0.96	−0.16	+0.96	−0.20
$\mathbf{7H}^-$	+0.84	−0.36	+0.91	−0.30
$\mathbf{8H}^-\mathbf{a}$[d]	+1.10	−0.25	+1.16	−0.20
$\mathbf{8H}^-\mathbf{b}$[d]	–	–	+1.06	−0.1
$\mathbf{8H}^-\mathbf{c}$[d]	–	–	+0.82	−0.16

[a] On a glassy carbon electrode. [b] E_p in V versus SCE. [c] $E^\circ = 1.17$ V for $\mathbf{1H}^-$ in acetone. [d] On a Pt electrode.

Increasing the scan rate (v) shifts the anodic peak Ia to positive potentials by 30 mV per log v in DMSO ($\mathbf{1H}^-$, $\mathbf{2H}^-$, $\mathbf{5H}^-$, $\mathbf{6H}^-$, $\mathbf{8H}^-$) as well as in CH_3CN ($\mathbf{1H}^-$, $\mathbf{2H}^-$) indicating that a first-order reaction occurs following the electron transfer.[30] For $\mathbf{1H}^-$, $\mathbf{6H}^-$, $\mathbf{8H}^-\mathbf{a}$ in DMSO the oxidation wave remains irreversible up to high scan rates, but for $\mathbf{1H}^-$ in CH_3CN and $\mathbf{5H}^-$ in DMSO the reversibility can be observed (Figure 2). Then, the standard potential can be obtained as the

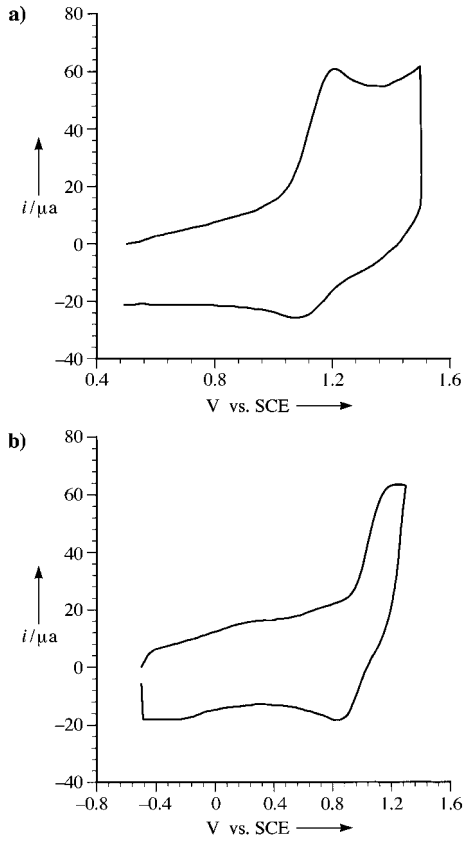


Figure 2. Cyclic voltammetry on a glassy carbon electrode (reference SCE) of a) $\mathbf{1H}^-$ in CH_3CN + 0.1 M NBu_4BF_4 at $v = 1000\ V\,s^{-1}$ and b) $\mathbf{5H}^-$ in DMSO + 0.1 M NBu_4BF_4 at $v = 100\ V\,s^{-1}$

midpoint of the cathodic Ic and anodic Ia peaks: $E^\circ = +1.15$ V for $\mathbf{1H}^-$ in CH_3CN and $E^\circ = +0.99$ V for $\mathbf{5H}^-$ in DMSO (these and all other potentials given herein were recorded against that of the saturated calomel electrode (SCE)). For these last two compounds, it is also possible[28] to derive the rate constant of the first-order process following the electron transfer from the E_p/log v plot: $130\ s^{-1}$ for $\mathbf{1H}^-$ and $\approx 40\ s^{-1}$ for $\mathbf{5H}^-$.

The oxidation of $\mathbf{1H}^-$ and $\mathbf{5H}^-$ was also examined by spectroelectrochemistry,[31] a technique which permits to record UV/Vis spectra of the solution close to the electrode while the potential is scanned. This method has been recently improved by the use of gold–LIGA structures (honeycombed microstructures with well-defined hexagonal holes in the range of a few micrometers). These electrodes decrease the time scale of the measurement and permit the detection of intermediates with lifetimes down to a few milliseconds.[31b]

Figure 3 shows the spectrum recorded starting from $\mathbf{1H}^-$ (in ACN + 0.1 M NBu_4BF_4) and scanning the potential of the electrode from 0.8 to 1.5 V at $0.2\ V\,s^{-1}$. At the beginning of the experiment, one observes the spectrum of $\mathbf{1H}^-$ ($\lambda_{max} = 478$ nm). Upon scanning the potential, this spectrum disappears at the expense of a new spectrum ($\lambda_{max} = 403$ nm) which

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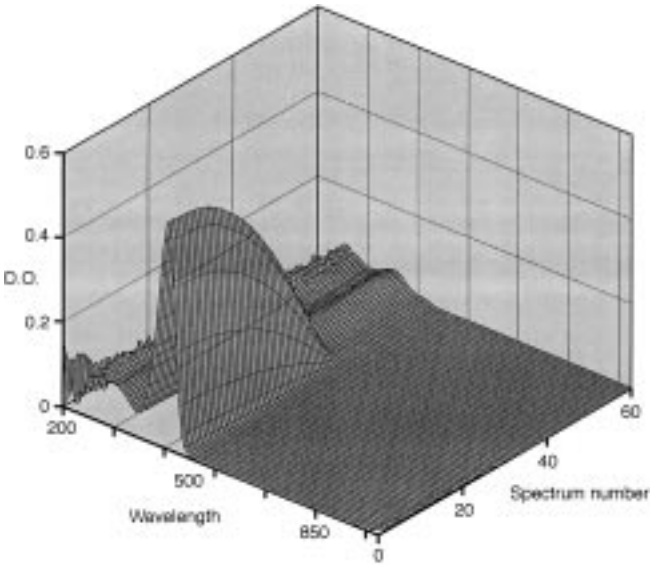
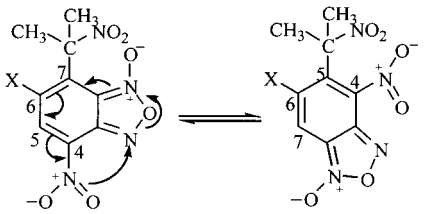


Figure 3. Spectrocyclovoltamogram of $\mathbf{1H}^-$ in CH_3CN + 0.1M NBu_4BF_4. Potential scanned from 0.8 to 1.5 V versus SCE at 0.2 V s^{-1}; 60 spectra were recorded during the scan.

corresponds to the final product **1**. No intermediate compound can be detected. A similar observation can be made starting from $\mathbf{5H}^-$, (λ_{max} = 374 nm) but in this case, the final product cannot be detected, its absorbance being beyond the limit of the xenon lamp of the spectrometer. To decrease the time scale of the experiment, in the hope of observing an intermediate, the electrode was subjected to a potential step from 0.8 to 1.5 V and a spectrum was recorded every 8.5 ms after the step; again no intermediate could be detected.

The number of electrons involved in the oxidation of the above compounds was measured by coulometry in DMSO + 0.1M $LiClO_4$ while following the consumption of the starting material by NMR spectroscopy. In this way we obtained values of 2.05, 2.50, and 2.28 F mol^{-1} for $\mathbf{1H}^-$, $\mathbf{5H}^-$, and $\mathbf{6H}^-$, respectively, indicating a bielectronic transfer.[57] The nature of the final compounds was ascertained by analysis of the ^1H and ^{13}C NMR spectra recorded at different stages of the reactions during a coulometric experiment in DMSO + 0.1M $LiClO_4^-$. In the case of the 4,6-dinitro, 4-CF_3-6-nitro, and 4-CN-6-nitro systems, the final substitution products **1**, **5**, and **6** (see Scheme 1) were identified as a mixture of two isomers, owing to the occurrence of a Boulton–Katritzky rearrangement.[23, 33–35] This rearrangement which is exemplified in Equation (4) is known to be typical of nitrobenzofuroxans. In



(4)

1a	X = NO_2	**1b**
4a	X = CF_3	**5b**
6a	X = CN	**6b**
2a	X = H	**2b**

these instances, no other product could be identified in significant amount and the overall yield of the two isomers of **1**, **5**, and **6** was 100, 96, and 83 %, respectively. A preparative electrolysis of $\mathbf{1H}^-$ was performed in CH_3CN + 0.1M NBu_4BF_4, and the resulting products were purified by chromatography. In this instance, the overall yield of the two isomers **1a** and **1b** was 60 % for a **1a**/**1b** ratio of 1.2.

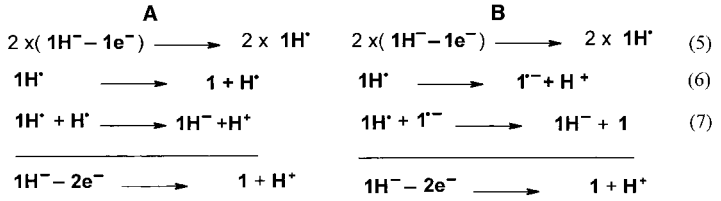
A voltammogram recorded in the cell at the end of the electrolysis in CH_3CN + 0.1M NBu_4BF_4 (but also in DMSO + 0.1M $LiCLO_4$) showed the disappearance of the oxidation peak Ia of $\mathbf{1H}^-$ and the concomitant appearance of a new and large peak at $E_{pIIc} = -0.14$ V. Evidently, this peak corresponds to the mixture of the two isomers **1a** and **1b** observed by NMR spectroscopy. In the same way, the reduction peak IIc of **6** and **3** could be observed at −0.20 and −0.48 V, respectively, at the end of the electrolysis of $\mathbf{6H}^-$ and $\mathbf{3H}^-$ in DMSO. As a comparison, the parent benzofuroxans of the adducts $\mathbf{1H}^-$ and $\mathbf{2H}^-$ are reduced irreversibly in CH_3CN at −0.09 and −0.50 V versus SCE, respectively. In CH_3CN, for $\mathbf{1H}^-$ as well as $\mathbf{6H}^-$, an oxidation peak ($E_{pa} = +0.55$ V) located at the same potential as that of nitrite ions is observed in the electrolysis solution. Since, we have checked (by UV spectroscopy) that $\mathbf{1H}^-$ is stable in this solvent, nitrite ions must be produced by decomposition of the final compound. If nitrite ions were produced during the electrolysis, due to their oxidation potential lower than that of $\mathbf{1H}^-$, they would be oxidized to nitrates which do not present any voltammetric signal in this potential range. We have also investigated the possible formation of the 2-nitropropenide anion (E° = 0.08 V) during the electrolysis, but we could not find any.

Since the oxidation of $\mathbf{1H}^-$ to **1** involves loss of hydrogen we have looked at the possible formation of protons or dihydrogen in the medium. First, a gas chromatographic analysis in the space over the catholyte in a gas-tight cell was carried out but no evidence of dihydrogen formation could be obtained. After completion of the electrolysis of $\mathbf{1H}^-$, and dilution of the catholyte with water, a titration of the generated acid with sodium hydroxide was performed; in this case, the number of protons was found to be equal to that for the starting material indicating that one mole of proton was released during the oxidation of each molecule.

Discussion

The results of the above experiments suggest that the oxidation of the σ adducts occurs through a three-step mechanism which can be formulated as the sequence given in Scheme 2A or that in Scheme 2B. As shown, Scheme 2A is by far the most likely one.

In the two sequences, the first step [Eq. (5)] involves loss of one electron by the adduct with formation of the corresponding radical. Then, this radical undergoes a rather slow (i.e. 130 s^{-1} for $\mathbf{1H}^-$) first-order C–H bond cleavage [Eq. (6)], as demonstrated by cyclic voltammetry, to give either the final rearomatized compound **1** and an hydrogen atom [Eq. (6A)] or the radical anion of the rearomatized compound $\mathbf{1}^{\bullet-}$ and a proton as earlier proposed by Sosonkin [Eq. (6B)].[27] The final oxidation of the hydrogen atom [Eq. (7A)] or of the



Scheme 2. Postulated three-step mechanisms A and B for the oxidation of the σ adducts. $E^{\circ}(\mathbf{1H}^{-}/\mathbf{1H}^{\bullet}) = +1.15$ V versus SCE, $k_{(6)} = 130\ s^{-1}$ in CH_3CN, $k_{(7)} = k_{diff}$.

radical anion [Eq. (7B)] is performed by the most powerful oxidant present in the medium, that is the radical $\mathbf{1H}^{\bullet}$. The final reoxidation involves more likely $\mathbf{1H}^{\bullet}$ than a reoxidation at the electrode, since the slow cleavage of $\mathbf{1H}^{\bullet}$ implies that this compound has time to diffuse to the bulk of the solution before being cleaved. It follows that $\mathbf{H}^{\bullet}$ or $\mathbf{1}^{\bullet-}$ must be formed in the solution and will be reoxidized there through a disproportionation reaction (DISP situation).[30] Another candidate for the reoxidation of $\mathbf{H}^{\bullet}$ might be the parent molecule itself, for example **1** is reduced at -0.14 V in DMSO, while $E^{\circ}(H^{+}/H_2) = -0.24$ V in water. However, this reaction should be much slower than the reoxidation by $\mathbf{1H}^{\bullet}$ since we have measured $E^{\circ} = +1.15$ V for the $\mathbf{1H}^{-}/\mathbf{1H}^{\bullet}$ couple. In view of the large difference between the redox potential of this couple and that of $\mathbf{1}/\mathbf{1}^{\bullet-}$ (it should be close to the reduction of **1**) or $\mathbf{H}^{+}/\mathbf{H}_2$, the reoxidation of both $\mathbf{H}^{\bullet}$ or $\mathbf{1}^{\bullet-}$ should be diffusion-controlled ($2 \times 10^{10}\ M^{-1}s^{-1}$ in CH_3CN).[36] In conclusion, the mechanisms A and B in Scheme 2 are kinetically equivalent; but reaction (6B) is unlikely. Indeed, radical anions are readily protonated so that the reverse reaction should be favored. For example, we have checked that the voltammogram of DNBF is irreversible up to a scan rate of $4000\ V s^{-1}$ indicating a first-order rate constant for the cleavage of at least $10^6\ s^{-1}$. The voltammogram of NBF is irreversible at low scan rates but reversibility can be observed at $2000\ V s^{-1}$. An addition of a fivefold excess of acetic acid restores the irreversibility of the wave. On the contrary, we did not observe any change upon addition of trifluoroacetic acid in our experiments. The fact that no intermediate can be observed by spectroelectrochemistry also agrees with the fact that **1** is formed directly from $\mathbf{1H}^{\bullet}$.

Table 1 reveals that the oxidation potentials E°, as measured or approximated by the E_{pla} values, are very much the same for the methoxide, 5-methoxyindole, and 2-nitropropenide adducts of 4,6-dinitrobenzofuroxan that is $\mathbf{8H}^{-}\mathbf{a}$, $\mathbf{8H}^{-}\mathbf{b}$, and $\mathbf{1H}^{-}$, with no major influence of the solvent ($E^{\circ} \approx 1.10 \pm 0.06$ V). Even though the E° value for the 1,3,5-trimethoxybenzene analogue $\mathbf{8H}^{-}\mathbf{c}$ is somewhat lower ($E^{\circ} \approx 0.87$ V), the overall evidence is that the feasibility of the oxidation process is for the most part related to the extent of charge delocalization in the cyclohexadienyl-type moiety of the adduct, a factor which is known to also play the predominant role in determining the thermodynamic stability of these species.[1, 4] Using reported equilibrium constant values for formation of methoxide or hydroxide σ adducts as a measure of the influence of the electron deficiency of the carbocyclic ring on the stability of the various structures,[1, 37–42] we were able to derive more information regarding the relationship between E° and complex stability (Table 2). The E° values quoted in Table 2 for the oxidation of the di- and trinitroacetonate adducts $\mathbf{9H}^{-}\mathbf{a}-\mathbf{f}$ are those previously measured by Sosonkin in acetone.[27]

Table 2. The effect of complex stability on the oxidation potential of σ adducts.

σ adducts	E° [V vs. SCE][a]	K_{MeOH}[b]	K_{H_2O}[c]
$\mathbf{9H}^{-}\mathbf{a}$	0.14[d]	–	–
$\mathbf{9H}^{-}\mathbf{b}$	0.22[d]	–	–
$\mathbf{9H}^{-}\mathbf{c}$	0.24[d]	10^{-6}[e]	–
$\mathbf{9H}^{-}\mathbf{d}$	0.50[d]	–	–
$\mathbf{9H}^{-}\mathbf{e}$	0.53[d]	≈ 0.01[f]	–
$\mathbf{9H}^{-}\mathbf{f}$	0.82[d]	23.1[g]	3.73[g]
$\mathbf{1H}^{-}$	1.15	2.1×10^{10}[j]	1.34×10^{10}
$\mathbf{2H}^{-}$	0.59	8500[h]	–
$\mathbf{3H}^{-}$	0.48	2940[h]	2200[i]
$\mathbf{4H}^{-}$	1.33	–	8.51×10^{10}[j]
$\mathbf{5H}^{-}$	0.94	–	1.7×10^{5}[j]
$\mathbf{6H}^{-}$	0.96	–	–

[a] True E° values or approximated from E_p values. [b] K_{MeOH} (in $L mol^{-1}$) refers to the equilibrium formation of the similarly substituted methoxide adduct. [c] K_{H_2O} (in $L mol^{-1}$) refers to the equilibrium formation of the similarly substituted hydroxide adduct. [d] Ref. [27]. [e] Ref. [37]. [f] Calculated from the value measured in H_2O/Me_2SO (50:50)[38] by taking into account the known effect of Me_2SO concentration on complex stability.[1] [g] Ref. [39]. [h] Ref. [40]. [i] Ref. [42]. [j] Ref. [43].

Inspection of the data in Table 2 reveals that the oxidation of the adducts of the moderately activated benzene derivatives $\mathbf{9H}^{-}\mathbf{a}-\mathbf{e}$ is associated with relatively low E° values ($E^{\circ} \leq 0.53$ V). This fits well the experimental finding that oxidative nucleophilic aromatic substitution of such substrates proceeds well with mild oxidizing agents.[1–4, 13–17] Activation of the benzene ring with a third nitro group causes a 10^7 increase in stability of the σ adduct $\mathbf{9H}^{-}\mathbf{f}$ as compared with that of the 1,3-dinitrobenzene analogue $\mathbf{9H}^{-}\mathbf{c}$.[1] This complex becomes therefore more reluctant to oxidation ($E^{\circ} = 0.82$ V), requiring the use of much stronger oxidants to undergo conversion into the substituted products.[27, 28] In accord with the experimental evidence that 4-nitrobenzofuroxan and 4-nitrobenzofurazan give rise to σ adducts of the same stability as that of TNB σ adducts,[40] the E° values for oxidation of the two nitropropenide complexes $\mathbf{2H}^{-}$ and $\mathbf{3H}^{-}$ compare well with those for oxidation of $\mathbf{9H}^{-}\mathbf{f}$. In contrast, there is an additional 10^6 increase in the equilibrium constant for adduct formation on going from TNB, the common reference aromatic electrophile, to the superelectrophile 4,6-dinitrobenzofuroxan.[41] As can be seen in Table 2, this strong gain in adduct stability brings the oxidation potential to such a level that only very strong oxidizing agents will be able to induce rearomatization of the carbocyclic ring, allowing the overall nucleophilic aromatic displacement to proceed efficiently. In fact, chemical conversion of DNBF adducts can be achieved only with couples like MnO_4^{-}/Mn^{2+} or Ce^{4+}/Ce^{3+}.[26]

As expected, substituting a NO_2 group for a less activating CN or CF_3 group decreases both the stability of the adducts and their oxidation potential.[42, 43] This is true in the benzene series, for example E° decreases by 0.3 V on going from TNB to 3,5-dinitrobenzotrifluoride,[27] as well as in the furoxan series, for example E° decreases from 1.15 to 0.99 V on going

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from DNBF to 6-trifluoromethyl-4-nitrobenzofuroxan. A most interesting feature relates, however, to the behavior of the σ adduct $\mathbf{4H}^-$ of 6-trifluoromethylsulfonyl-4-nitrobenzofuroxan. Consistent with previous findings in the benzene series that the SO_2CF_3 group exerts in many instances a greater electron-withdrawing effect than a NO_2 group,[44–46] this compound affords σ adducts which are more stable than the related DNBF adducts.[47–49] On this ground, the measurement of a highest E° value for $\mathbf{4H}^-$ than for $\mathbf{1H}^-$ fits well the trend discussed above. However, it is a significant result that the E° value then becomes so high that oxidation of the adduct $\mathbf{4H}^-$ is difficult to envision with commonly available chemical oxidants.

Conclusion

We have shown that the oxidation of nitrobenzofuroxan and nitrobenzofurazan σ adducts is associated with especially high oxidation potentials. This makes it considerably more difficult to achieve oxidative nucleophilic aromatic substitution of hydrogen with these heterocyclic substrates than with common reference aromatic electrophiles such as di- or trinitrobenzenes or nitropyridines and pyrimidines. The mechanism of the oxidation has been elucidated and shown to proceed in three steps: 1) loss of one electron from the adduct ($\mathbf{1H}^-$); 2) direct C–H bond cleavage in the resulting neutral radical ($\mathbf{1H}^\bullet$) to give the final substitution products (**1**) and a hydrogen atom ($H^\bullet$); 3) oxidation of $H^\bullet$ by the radical $\mathbf{1H}^\bullet$ which is the most powerful oxidant present in the medium. This mechanism contrasts with previously suggested pathways which all assumed the intermediacy of radical anionic species.[27, 50, 51]

Experimental Section

Materials: The methoxide adduct $\mathbf{8aH}^-$ as well as the 5-methoxyindole and 1,3,5-trimethoxybenzene adducts ($\mathbf{8bH}^-$, $\mathbf{8cH}^-$) were synthesized and characterized as previously described.[26, 52]

Adducts $\mathbf{1H}^- - \mathbf{7H}^-$ as crystalline potassium salts: Potassium 2-nitropropenide (1 equiv) suspended in 2-nitropropane (5 mL). was added to the parent nitrobenzofuroxan (0.226 g, 1 mmol)[10, 54] dissolved in 2-nitropropane (2 mL). After 5 min the resulting orange-red precipitates were filtered, washed with diethyl ether and dried under reduced pressure to give the salts K[**1H**–**7H**] in essentially quantitative yields. These salts were relatively stable in air but decompose violently upon heating (ca. 155–200 °C). As is the case for most σ adducts of nitrobenzofuroxans previously isolated as crystalline alkali metal salts,[18–21] attempts to obtain satisfactory elemental analysis for K[**1H**–**7H**] have failed. In contrast, an X-ray structure of K[**1H**] could be made.[55] In all cases, satisfactory mass spectra were obtained (ESI), base peaks corresponding to the loss of K^+ were observed, for example m/z 314 for K[**1H**], with no detection of the pseudomolecular ions.

In addition, a detailed ^1H and ^{13}C NMR study has been made by dissolving the isolated salts in $[D_6]Me_2SO$. The most significant data are summarized and compared with those for the parent nitrobenzofuroxans in Table 3. They agree very well with the structures of the adducts.[1, 18–21] Major diagnostic features are the following: 1) the H_7 and C_7 resonances suffer strong upfield shifts upon σ complexation, for example $\Delta\delta H_7 = 4$ ppm and $\Delta\delta C_7 = 79.06$ ppm for $\mathbf{1H}^-$. This is typical of the $sp^2 \rightarrow sp^3$ rehybridization resulting from the addition of the 2-nitropropane moiety at C_7 of the parent molecules.[1] 2) Owing to the chirality of this tetrahedral ring carbon, the two geminal methyl groups in $\mathbf{1H}^- - \mathbf{7H}^-$ are seen as being slightly nonequivalent in the ^1H as well as the ^{13}C NMR spectra. 3) Regarding the exocyclic nitropropane moiety, it is noteworthy that its bonding to the adjacent nitrobenzofuroxan or benzofurazan structures causes a notable shift of the C_α resonance to low field, for example $\delta C_\alpha \approx 90-92$ in $\mathbf{1H}^- - \mathbf{7H}^-$ and $\delta C_\alpha = 79.10$ in 2-nitropropane.[56] This result is in agreement with previous evidence that a negatively charged nitrobenzofuroxan or nitrobenzofurazan structure still exerts a considerable –I effect.[18–20]

Table 3. Diagnostic ^1H and ^{13}C NMR data for the adducts $\mathbf{1H}^- - \mathbf{7H}^-$ and the parent 4-X-6-Y-benzofuroxan or -benzofurazan molecules (denoted as 1M–7M) in $[D_6]Me_2SO$.[a,b]

Adduct or molecule	δ_{H_7}	δ_{CH_3}	δ_{C7}	δ_{C_α}	δ_{CH_3}
$\mathbf{1H}^-$	5.27	1.51/1.49	42.49	92.32	23.41/23.31
1M	9.27	–	120.80	–	–
$\mathbf{2H}^-$	4.37	1.55/1.51	42.22	92.00	23.43/23.30
2M	8.11	–	122.20	–	–
$\mathbf{3H}^-$	4.57	1.50/1.44	42.52	91.48	23.38/21.99
3M	8.34	–	124.50	–	–
$\mathbf{4H}^-$	4.56	1.54/1.52	41.29	92.41	23.04/22.75
4M	9.40	–	132.69	–	–
$\mathbf{5H}^-$	4.73	1.54/1.44	40.20	92.51	24.87/21.30
5M	8.87	–	122.55	–	–
$\mathbf{6H}^-$	4.58	1.61/1.56	42.49	92.64	23.53/22.92
6M	9.10	–	130.78	–	–
$\mathbf{7H}^-$	4.73	1.54/1.44	40.20	92.51	24.87/21.30
7M	9.07	–	118.52	–	–

[a] See the significance of the numbering of the hydrogen and carbon atoms in structures $\mathbf{1H}^- - \mathbf{7H}^-$ in the text. [b] δ in ppm, internal reference Me_4Si.

As mentioned in the Results section, the products of the electrochemical oxidation of $\mathbf{1H}^- - \mathbf{7H}^-$ as well as of **8a**, **b**, $\mathbf{cH}^-$ have been firmly identified as the rearomatized benzofuroxans and benzofurazans **1**–**7** and **8a**–**c** on the basis of ^1H and ^{13}C NMR spectra recorded at different stages of the reactions during coulometric experiments carried out in DMSO-d_6 solution. NMR parameters for structures **8a**, **8b**, and **8c** were available from previous work.[26, 52] In contrast, no data were available for **1**–**7**, making a thorough structural NMR investigation of these compounds of interest. Full details of this work, where the recognized diagnostic character of the C_8 and C_9 resonances in the benzofuroxan series ($\delta(C_8) = 112 \pm 5$, $\delta(C_9) = 150 \pm 5$) was useful to discriminate between the two Boulton–Katrizky isomers in the 4,6-dinitro-, 4-nitro-6-cyano-, and 4-nitro-6-trifluoromethyl systems, will be reported elsewhere.[29, 53] As an example, selected data for the 7- or 5-[1′-(1′-methyl-1-nitroethyl)]-4.6-dinitrobenzofuroxan molecules **1a** and **1b** are given. **Compound 1a**: ^1H NMR (300 MHz, $[D_6]Me_2SO$): $\delta = 8.67$ (s, 1H; H_5), 2.15 (s, 1H; CH_3); ^{13}C NMR (75.5 MHz, Me_2SO-d_6) $\delta = 122.28$ (C_5), 26.57 (CH_3), 89.07 (C_α), 107.51 (C_8), 151.84 (C_9). **Compound 1b**: ^1H NMR (300 MHz, $[D_6]Me_2SO_6$): $\delta = 9.12$ (s, 1H; H_7), 1.99 (s, 1H; CH_3); ^{13}C NMR (75.5 MHz, $[D_6]Me_2SO$): $\delta = 128.54$ (C_7), 25.77 (CH_3), 88.50 (C_α), 116.09 (C_8), 146.95 (C_9). The solvents were reagent grade and the supporting electrolytes were obtained from Fluka .

Electrochemical measurements: The electrochemical equipment included a Tacussel signal generator GSTP4, a home-made potentiostat, an Ifelec (LY 16100) recorder at low scan rates and a Nicolet (3091) oscilloscope at high scan rates. Coulometric measurements were performed with home-made equipment including potentiostat, ammeter, voltameter, and coulometer. Carbon electrodes, which were made of a 3 mm glassy carbon rod imbedded in epoxy resin, were always used in these experiments. Before every experiment the carbon disk was polished with 1 μm diamond paste and ultrasonically rinsed in acetone. The coulometric and preparative electrolysis were performed with carbon-felt cathodes in a two-compartment cell separated by a glass frit (G4).

Coulometric measurements of the number of electrons per molecule were performed by electrolyzing an approximately 10 mM solution of $\mathbf{1H}^-$ in $[D_6]$DMSO + 0.1M $LiClO_4$ at the peak potential of the compound and withdrawing small samples at regular intervals for NMR analysis. The yields of the initial and final products were calculated using the non deuterated DMSO as an internal reference. Protons in the final electrolysis

solution were titrated with an automatic titrator (Orion Research 960 Autochemistry system) using 0.01M sodium hydroxide as a titrant. Dihydrogen was tentatively measured in the empty space over the catholyte solution in a gas tight cell by withdrawing 200 μL of gas and injecting in a Shimadzu GC-14B gas chromatograph on a silica gel column. A calibration curve was established.

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DMSO, CH_3CN, CH_3NO_2, or $ClCH_2CH_2Cl$. As these numbers do not change much upon adding an acid or a base, the experimental data do not support a mechanism in which protons make a large contribution to the catalysis. The diffusion coefficient of $\mathbf{1H}^-$ has been measured in ACN by comparison of the height of the reversible wave at high scan rate with that of the monoelectronic wave of ferrocene.[32] Thus, we obtained $D = 1.65\ 10^{-5}\ cm^2 s^{-1}$, a value which is clearly unable to account for the smallness of the wave. Therefore the low numbers measured by cyclic voltammetry probably stem from some adsorption phenomena that block the electrode.

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