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Thermodynamic Study of σ^H Complexes in Nucleophilic Aromatic Substitution Reactions: Relative Stabilities of Electrochemically Generated Radicals

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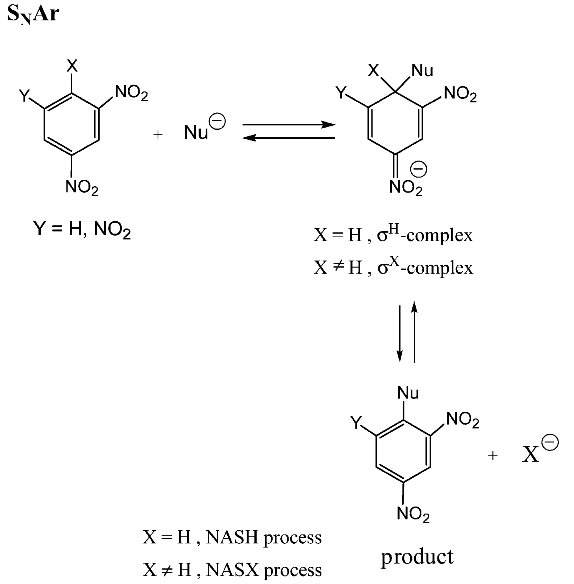
Keywords: σ^H Complexes / Nucleophilic substitution / Aromatic substitution / Electrochemistry / Oxidation / Reaction mechanisms

The mechanism for the electrochemical oxidation of σ^H complexes, such as 1-hydro-1-alkoxy/sulfoxy or -fluoro-2,4-dinitro/2,4,6-trinitrocyclohexadienyl anions, has been widely studied by means of cyclic voltammetry and controlled-potential electrolysis. Previous studies have shown that the electrochemical oxidation of σ^H complexes, formed by the addition of carbon or nitrogen nucleophiles followed by a two electron mechanism, corresponding to the formal elimination of the hydride anion (nucleophilic aromatic substitution of hydrogen mechanism, the NASH mechanism). For these σ^H complexes (Nu^- = OH^-, ^-OR, ^-SR, ^-F), the electrochemical reaction takes place by a one-electron mechanism and is followed by the radical elimination of the leaving group with the consequent recovery of the starting material. This mechanism is similar to that proposed for the electrochemical oxidation of σ^X complexes (nucleophilic aromatic substitution of a heteroatom, the NASX mechanism). The operating mechanism in each case, the NASH or NASX, can be rationalized in terms of thermodynamics. The standard potentials of the σ complex and/or the leaving group as well as the bond dissociation energies (BDEs) are determinant factors. This study has not led to a significant improvement in the electrochemical preparation of aromatic-substituted compounds, but does help to understand and predict the usefulness or uselessness of using the nucleophilic aromatic substitution route to obtain a desired product. Finally, the current approach extends the electrochemical methodology to different chemical fields, for example, to general nondestructive methods for the detection, identification, and quantification of either organic pollutants or explosives in different solvents.

Introduction

The nucleophilic aromatic substitution (S_NAr) of hydrogen, NASH, or of a heteroatom, NASX, constitutes an important step in numerous and important synthetic procedures, including the synthesis of herbicides, fungicides, pesticides, pharmaceutical products, medicines, and numerous antidepressants and antitumoral reagents,[1–5] so many mechanistic studies have been performed.[1] The most accepted mechanism for S_NAr is the addition/elimination mechanism, a polar mechanism in which the first step is the addition of an electron-rich compound (nucleophile) to an electron-deficient aromatic one, leading to an anionic intermediate commonly named a σ or Meisenheimer complex. The reaction is completed in a second step, the departure of a leaving group (Scheme 1).[1–4] The efficiency of the reaction is strongly related to the nature of the leaving group, so in the case of NASH processes, in which the hydride acts as the leaving group, it will rarely be effective. However, it is possible to electrochemically activate the NASH reaction. The mechanism for the electrochemical oxidation of the σ^H complex (**1**) involves the loss of two electrons and a proton, which corresponds to the formal elimination of a hydride anion (Scheme 2, A).[6] Moreover, from an electrochemical



Scheme 1. Nucleophilic aromatic substitution (S_NAr) of hydrogen (NASH) or of a heteroatom (NASX) following the addition/elimination mechanism.

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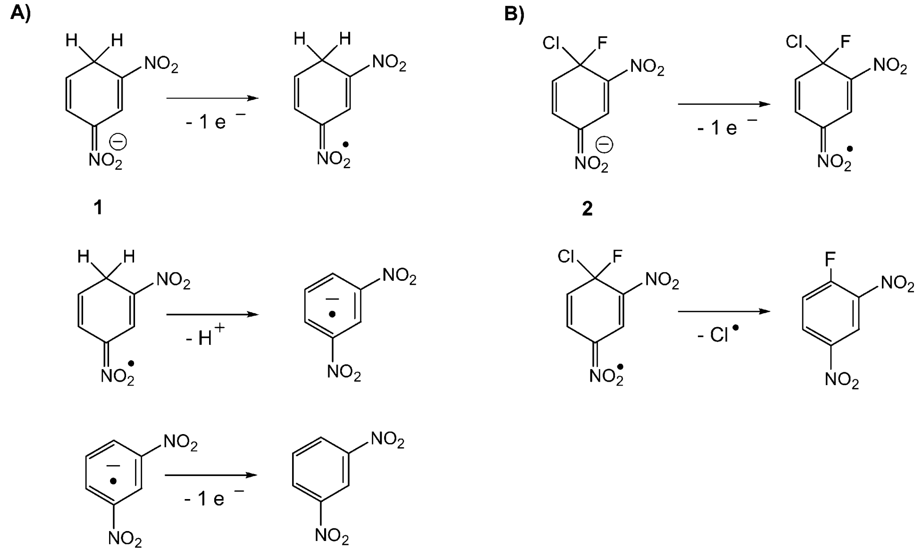
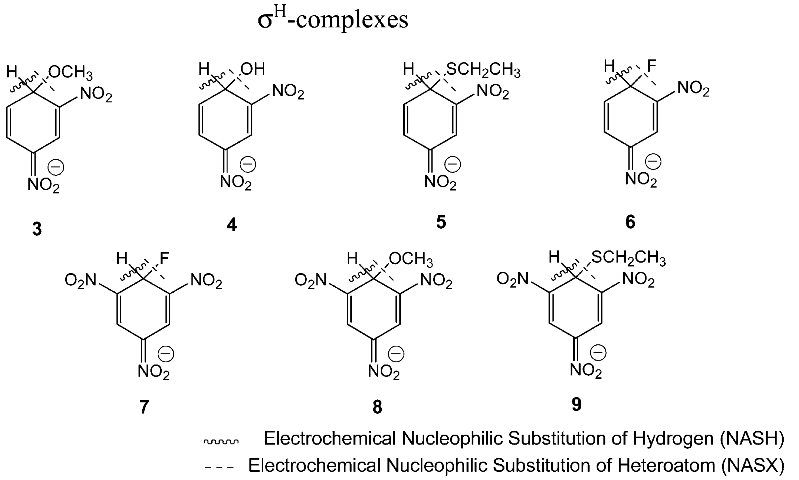


Scheme 2. Mechanism for the electrochemical oxidation of A) 1,3-dinitrobenzene + $(CH_3)_4NBH_4$ (σ^H complexes, the NASH process) and B) 1-chloro-2,4-dinitrobenzene + $(CH_3)_4NF$ (σ^X complexes, the NASX process).

point of view, the nucleophilic aromatic substitution of a heteroatom (the NASX process) can also be electrochemically promoted.[7] The NASX electrochemical mechanism also involves the elimination of a leaving group, although its departure is as a radical rather than as an anion (Scheme 2, B) as the rearomatization of the σ^X or *ipso* complex (**2**) involves the loss of an electron. This information is analogous to that obtained by combining other more traditional techniques, such as UV/Vis and NMR spectroscopy.[1-4, 8,9] Interestingly, the electrochemical oxidation of these σ^X complexes makes it possible to "jump" from the "polar" S_NAr addition/elimination mechanism (Scheme 1, σ^X complexes) to the "radical" heteroatom substitution in aromatic compounds (Scheme 2, B).

The methodology employed satisfies the most important requirements of "Green Chemistry" processes, providing a new general environmentally friendly synthetic procedure.[10] The promising results that have been published have used carbon-centered nucleophiles (such as CN^-, R^-, and $RCORCH_2^-$, where R is mainly an alkyl group) as well as nitrogenous ones, allowing a general method to be considered for an electrochemically promoted NASH process.[6] This methodology, in principle, would be equally valid when oxygen, sulfur, or fluoride anions are used as nucleophiles as these are also capable of reacting with electron-deficient compounds, such as nitroaromatic ones, and, therefore, are able to form the corresponding anionic intermediates (Scheme 3). Some of these σ^H complexes have been previously identified by UV/Vis (**3**–**8**)[11] or ^1H NMR spectroscopy (**5**, **7**, and **8**)[12] in the course of kinetic studies, although their chemical evolution after the chemical oxidation process has never been studied. Hence, the aim of this work was not only to analyze the scope of electrochemically promoted nucleophilic aromatic substitution, but also to disclose the mechanism for the electrochemical oxidation of the intermediates. Note that in the case of these σ^H com-



Scheme 3. σ^H Complex structures.

plexes derived from the attack of oxygen, sulfur, or fluorine anions, two mechanisms can potentially take place. The first, the NASH process, would involve the breaking of the C–H bond in what would be an attractive process from a synthetic point of view, whereas the second would involve the rupture of the C–X bond, similar to the NASX process, that is, a radical mechanism similar to that described above for σ^X complexes. Thus, the initial reactant would be recovered following an interesting mechanistic process.

Results and Discussion

The electrochemical analysis performed by using cyclic voltammetry of a DNB/MeOK mixture [1,3-dinitrobenzene (DNB)/potassium methoxide (MeOK), see the Exp. Sect.] showed the appearance of two new peaks at 0.72 and 1.33 V (vs. SCE) in the oxidation scan after the addition of potassium methoxide (Figure 1). A pure solution of potassium methoxide was analyzed by cyclic voltammetry and showed a one-electron oxidation peak at 1.33 V vs. SCE under the same experimental conditions. Thus, these two oxidation waves can be assigned to a σ complex and to the electrochemical response of the "free" methoxide anion present in the mixture, respectively.

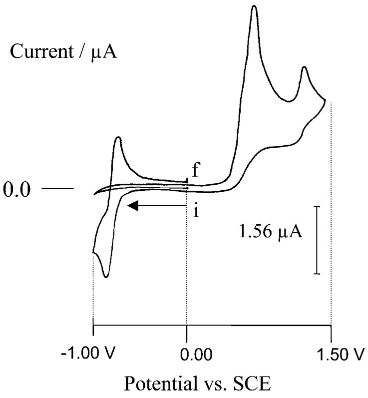


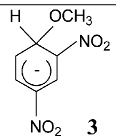
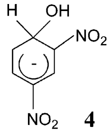
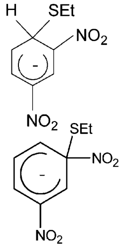
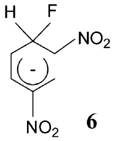
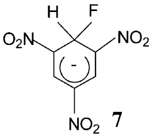
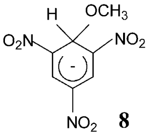
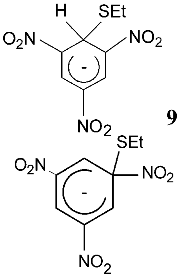
Figure 1. Cyclic voltammogram of 10 mM 1,3-DNB in anhydrous DMF under argon containing 0.1 M $TBABF_4$ as a supporting electrolyte after the addition of 10 equiv. of potassium methoxide (T = 13 °C). The scan range: 0.00/–1.00/+1.50/–1.00/0.00 V (two cycles); scan rate: 1 $V s^{-1}$; working electrode: glassy carbon disk with a diameter of 0.5 mm.

Note that after the addition of 10 equiv. of methoxide the reduction peak corresponding to the starting material, 1,3-DNB, in a first cathodic scan totally disappeared (Figure 1). Thus, as no "free" reactant was detected, it is possible to conclude that the nucleophilic attack corresponds to 100%, so the σ complex is formed quantitatively. Under these experimental conditions the electrochemical oxidation corresponds exclusively to the formation of the σ complex owing to the detection of a one-electron oxidation peak at 0.72 V in the anodic scan. As can be deduced from either a cathodic counter or after two cycles, the electrochemical response of the product obtained from the oxidation of the σ complex is 1,3-DNB, which indicates that the σ complex present in the mixture is the σ^H complex **3**. In this case the CH_3O group is lost rather than the hydrogen, which would have been lost under the NASH mechanism (Scheme 2).[13] These results were confirmed by oxidative controlled-potential electrolysis of the reaction mixture when 100% σ complexes were produced. The initial reagent was mainly recovered, 1,3-DNB (95%), and only 5% of the substituted product, 3-nitroanisole, was obtained after the passage of 1 F at 1.00 V. In none of the analyses of the oxidized mixtures was 2,4-dinitroanisole, which is the expected product for the NASH mechanism, even detected (Table 1).

Cyclic voltammetry experiments show that after each addition of a hydroxide nucleophile solution it is possible to observe in an anodic scan from 0.00 to 1.50 V the presence of two new peaks at 0.59 and 1.21 V (vs. SCE), respectively (see the Exp. Sect.). The current anodic peak values increase with the concentration of the added nucleophile. When a pure solution of TBAOH (tetrabutylammonium hydroxide) was analyzed by cyclic voltammetry, the presence of an oxidation peak was revealed at 1.21 V (vs. SCE). Thus, analogously to the experiments described above, it is possible to assign the anodic peak at 0.59 V to the oxidation of the formed σ^H complex (1-hydroxy-2,4-dinitrocyclohexadienyl anion, **4**). After the addition of 22.5 µL of the TBAOH solution (1.4 equiv.), it was possible to observe: 1) The complete disappearance, in a cathodic scan, of the first reduction peak of the initial nitroaromatic compound, 1,3-DNB, 2) that the oxidation wave assigned to the σ^H complex **4** at 0.59 V is a one-electron irreversible wave, and 3) that if a second cathodic scan was recorded after the oxidation counter part of the first scan, from 0.00/–1.00/1.50 to –1.00 V, the appearance of a reduction peak was observed, which corresponds to the product formed after the oxidation of the σ^H complex. In this case, the oxidation peak value is exactly the same as that previously determined for 1,3-DNB (starting material), as shown in Figure 1 for the methoxy adduct. Thus, for oxygenated adducts, it seems that the "oxidation" product obtained is the initial reagent rather than the substitution product (2,4-dinitrophenol), in contrast to the previously described examples of oxidation of σ^H complexes in which a NASH process takes place. These observations imply that the departure of the hydroxide group, which had been previously introduced, is electrochemically promoted. In order to confirm these voltammetric results, electrolysis of the mixture was performed. After the passage of 1 F at 1.00 V, the analysis of the noncolored solution by GC–MS confirmed the recovery of 1,3-DNB in a quantitative yield.

When an excess of sodium thiosulfate was added to the 1,3-DNB solution (molar ratio 10:1), the presence a new wide oxidation wave was observed at 0.47 V (vs. SCE) (see the Exp. Sect.). This should mainly be attributed to the presence of the corresponding σ complex and to excess of the thiosulfate anion [E_{pa} = 0.44 V (vs. SCE) at 1.0 $V s^{-1}$]. After exhaustive controlled-potential electrolysis, the DNB was not the only product recovered. The electrochemical oxidation also yielded two more products in moderate and

Table 1. Oxidative electrolysis of σ^H complexes.

Nitroarenes (**1**)	Nu^- (excess)	% Nu^- Attack	σ^H-complex	*E*pa [V] σ^H-complex	Percentage of NASX Products
1,3-Dinitro-benzene (= 1,3-DNB)	$^-OCH_3$	100	 **3**	0.72	1,3-DNB (95%) 3-nitroanisole (5%)
1,3-DNB	^-OH	100	 **4**	0.59	1,3-DNB (100%)
1,3-DNB	^-SEt	100	 **5**	0.47	1,3-DNB (20%) 3-nitrothiophenol (66%) ethyl 3-nitrophenyl thioether (14%)
1,3-DNB	F^-	100	 **6**	0.70	1,3-DNB (100%)
1,3,5-Trinitrobenzene (= TNB)	F^-	100	 **7**	1.09	TNB (97%) 1-fluoro-3,5-dinitrobenzene (2%)
TNB	$^-OCH_3$	100	 **8**	1.18	TNB (100%)
TNB	^-SEt	100	 **9**	1.06 0.44	TNB (68%) ethyl 3,5-nitrophenyl thioether (31%)

good yields: Ethyl 3-nitrophenyl thioether (14%) and thiophenol (64%). These two new products were obtained by NASX processes. Controlled-potential electrolysis and analysis of the product mixture allowed the type of σ complexes and also their concentrations to be determined. The recovery of the starting material indicates the σ^H complex **5**, whereas the nitrophenylthio derivatives suggest the existence of a σ^X complex derived from the attack of the nucleophile on a substituted position leading to the substitution of the nitro group NO_2. The fact that only one oxidation wave was obtained in the cyclic voltammogram can be explained by the oxidation potential values of the σ complexes present in the mixture. The anodic peak potential value of the σ^{H} complex **5** is expected to be between 0.5–0.7 as the molecule has two nitro groups. Similarly, the oxidation peak value of the σ^{X} complex is expected to be of the same potential range owing to the oxidation potential of the leaving group (NO_2^-). As a consequence, only one oxidation peak was detected by cyclic voltammetry. The higher yield of the 3-nitrothiophenol derivative can also be justified by the experimental conditions applied. The first product obtained during the electrolysis is the corresponding ethyl thioether. However, as the electrolysis was exhaustive this product can be oxidized leading to its radical cation. This radical cation is not a stable intermediate, and rupture of the S–C bond, corresponding to the alkyl chain, takes place. As a result, the final product is the corresponding thiophenyl derivative (Table 1). Finally, note that no products from aromatic hydrogen substitution were detected.

The last type of nucleophile tested in these studies was the fluoride anion. Fluoride solution was added until 1,3-DNB was no longer detected by cyclic voltammetry. Thus, all the nitroaromatics present in the mixture were derived from the σ^{H} complex. After an exhaustive oxidation of the reaction mixture (1 F), the only product obtained was the initial nitroaromatic reagent as a consequence of the oxidation of the σ^{H} complex **6**. Thus, the only oxidation product detected was a consequence of the loss of fluorine rather than hydrogen (Table 1).

Figure 2 shows the cyclic voltammogram of 1,3,5-trinitrobenzene (TNB) in anhydrous DMF containing 0.1 M of $TBABF_4$ after the addition of 1 equiv. of tetramethylammonium fluoride. In the initial cathodic scan, it is possible to observe the remaining TNB that has not been attacked by the fluorine ($E_{pa} = -0.53$ V vs. SCE),[14] so it was possible to calculate the percentage of the nucleophilic attack. In the corresponding anodic counter part two oxidation peaks at 0.26 and 1.09 V are observed. The first peak is associated with the reactivity of the TNB anion radical, as recently demonstrated, whereas the second one at 1.09 V corresponds to the oxidation of the σ^{H} complex **7** formed by the attack of the fluoride nucleophile on TNB.[14] These results were easily confirmed by analysis of a reaction mixture after controlled-potential electrolysis at 1.20 V (1 F) when 100% of **7** was formed; the main product obtained was the starting nitroaromatic compound (Table 1).

When either oxygen or sulfur nucleophiles were added to a solution of TNB until the quantitative formation of their corresponding σ^{H} complexes **8** and **9**, respectively, a one-electron wave was observed at around 1.00 V. The results obtained after controlled-potential electrolysis were very similar to those described above for the DNB derivatives.

The results obtained in these studies with different types of nucleophiles and nitroaromatic compounds are summarized in Table 1. In the case of σ^{H} complexes derived from oxygen-, sulfur-, or fluorine-centered nucleophiles, a one-electron oxidation wave was observed and no hydrogen substitution products were detected; in contrast, in our previously published studies of σ^{H} complexes derived from carbon- or nitrogen-centered nucleophiles, a two-electron oxidation process was observed (NASH mechanism). However, in some cases the results shown in Table 1 reveal the synthetic utility of this reaction. An oxidative nitro group substitution in 1,3-DNB and TNB by SEt^- occurs with preparative yields that range from modest to good when a huge excess of the nucleophile is used. The nucleophilic displacement of a nitro group activated by *ortho* or *para* functions other than nitro groups has been demonstrated in the chemical literature,[15] but only a few synthetically useful S_NAr reactions involving the displacement of the NO_2 group in 1,3-DNB have been reported.[15]

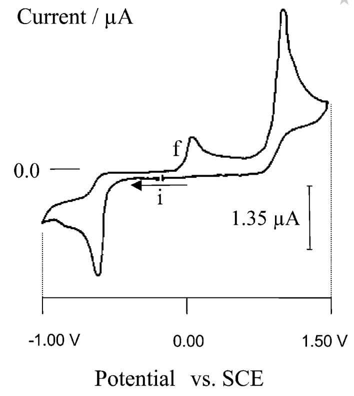
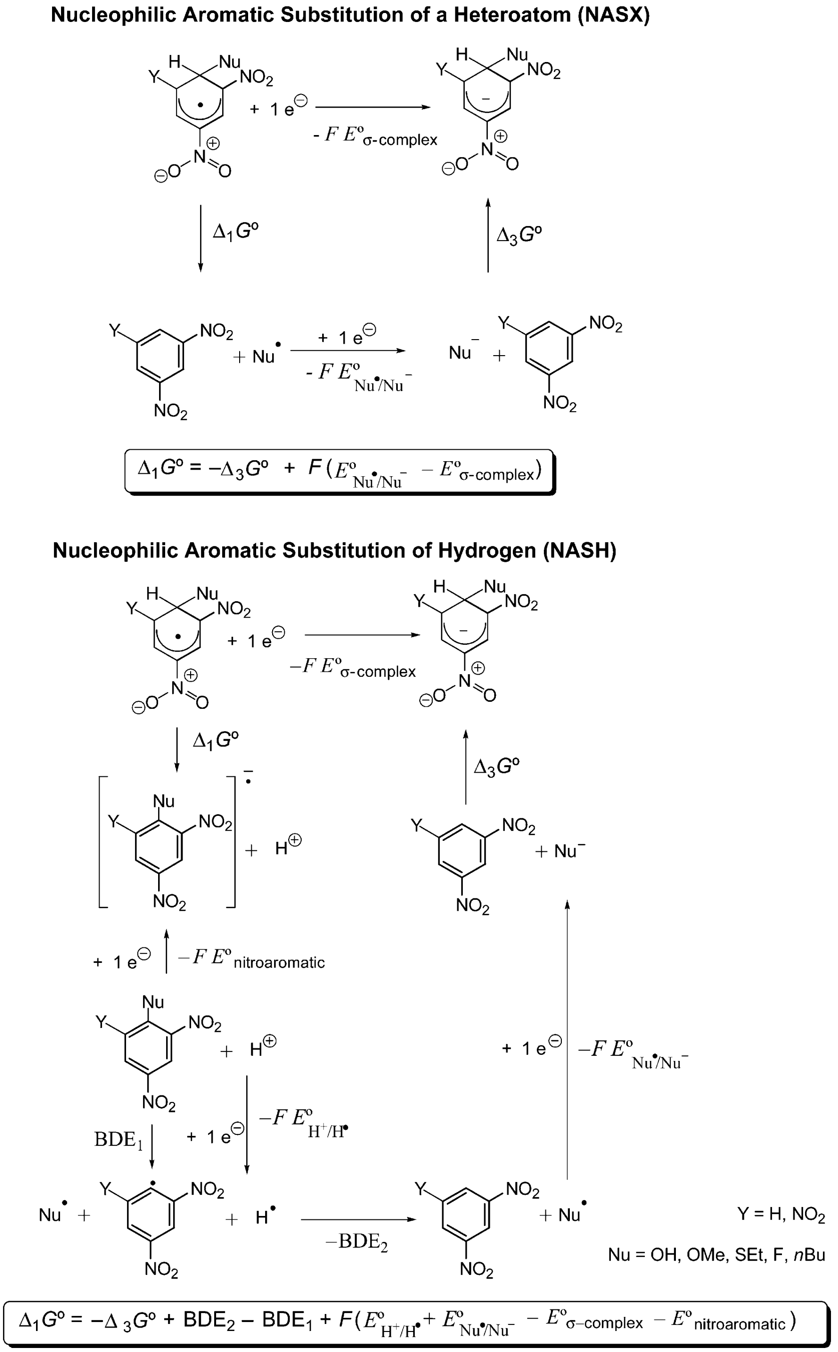


Figure 2. Cyclic voltammetry of 10 mM 1,3,5-trinitrobenzene (TNB) in anhydrous DMF under argon containing 0.1 M $TBABF_4$ as a supporting electrolyte after the addition of 5 equiv. of anhydrous tetramethylammonium fluoride (T = 13 °C). The scan range: 0.00/–1.00/+1.50/–1.00/0.00 V; scan rate: 1 $V s^{-1}$; working electrode: glassy carbon disk with a diameter of 0.5 mm.

These results led us to ask why the same type of σ^{H} complexes yield different substitution products, and consequently the different electrochemical oxidation pathways. This should be strongly connected to the ability of the substituent as a leaving group and to the bond dissociation energies (BDEs) of the corresponding C–Nu or C–H bond. The relationship between the thermodynamic properties of σ^{H} complexes and their radicals are conveniently schematized in the thermochemical mnemonic shown in Scheme 4 for the NASX and NASH processes. As the key step in both processes is the evolution of the σ complex radical ($\Delta_1 G°$), comparison of the Gibbs energy values of this step would indicate which process is operating in each case. It is remarkable that, as expected, the value of $\Delta_1 G°$ for the NASX process is related to the standard potential of the leaving group and the corresponding σ^{H} complex formed. However, the $\Delta_1 G°$ value for the NASH process also involves the standard potential values of $H^{\cdot}/H^{+}$ and the corresponding nitroaromatic compound. Moreover, the difference in BDEs between a C–H and a C–Nu bond should also be taken into account before analyzing the viability of the NASH process. The overall results obtained for different σ^{H} complexes and a σ^{X} complex are summarized in Table 2. For both processes, the values corresponding to the oxidation of the leaving group, $E^\circ_{Nu^\cdot/Nu^-}$, have previously been reported.[16] However, no E° values have been measured for the σ^H complexes; oxidation peak potential values are used as E° values. Fortunately, this will correspond to a systematic and unaffected error as these values would not be meaningfully different in these cases.[6,7,17] Moreover, for the NASH process, the $E^\circ_{H^+/H^\cdot}$ and E°(nitroaromatic/nitroaromatic anion radical) values are, respectively, –1.53 and –0.83 V, which are the most accepted potentials for both substances in organic nonprotic solvents, as has previously been published.[6a,12a,18] Finally, the BDE values used for the C–H and C–Nu bonds in relation to a benzene ring have also been published.[19–21] Note that the enthalpies (BDEs) are considered rather than the standard free energy of cleavage (ΔG°, the driving force for bond cleavage) because the ΔS° value (the entropy for C–H or C–Nu cleavage) corresponding to the formation of two molecules from one is small and does not vary significantly in the series and may be approximately equal to 1 meV K^{-1} (0.02 kcal mol^{-1}).[22] Moreover, the entropic terms corresponding to products and reactants can be simplified from the equation shown in Scheme 4 as the difference between

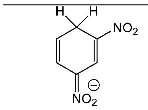
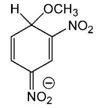
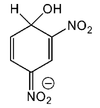
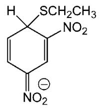
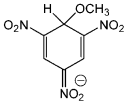
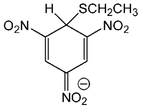
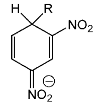
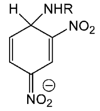
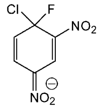


Scheme 4. Thermochemical mnemonic describing the NASX and NASH processes.

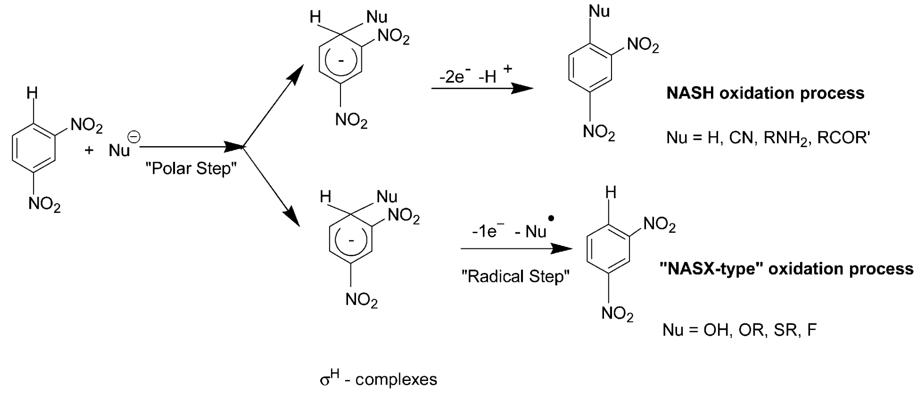
two standard free energies can be expressed in enthalpy and entropy terms, the entropic terms having the same values with the opposite sign. For reasons of comparison, the anionic intermediates **1**, **9**, and **10**, which undergo NASH processes,[6] are included in Table 2. For the same purpose, the σ^X complex **2** is also included as its electrochemical behavior[7] is well known and it can be used as a reference for the NASX process.

Note that the $\Delta_1G°$ values shown in Table 2 do not include $\Delta_3G°$, which corresponds to $\Delta G°$ for the formation of the σ^H complexes with the nucleophile. Most of these values are unknown with the exception of the thioethoxide, for which $\Delta_3G°$ is –6.33 kcal mol^{-1}.[23] However, as can be seen from the NASX and NASH thermodynamic equations, $\Delta_3G°$ is equally involved in both processes, so the calculated values of $\Delta_1G°$ will not be meaningfully different in terms

Table 2. Thermodynamic data.

Compound	$E°_{Nu^\cdot/Nu^-}$[a]	$E_{\sigma\text{-complex}}$[b]	BDE$_1$[c]	ΔBDE[c] (BDE$_{2,Ar–H}$) – (BDE$_1$)	$\Delta_1G° + \Delta_3G°$ (NASX)[c]	$\Delta_1G° + \Delta_3G°$ (NASH)[c]
 **1**	0.60 V (H$^-$)[d]	0.39[e]	111.3 (C–H)[f]	0.0	–22.8	**–39.0**[g]
 **3**	0.06 V ($^-$OCH$_3$)[h]	0.72	76.0 (C–O)[i]	35.3	**–15.2**	3.64
 **4**	0.06 ($^-$OH)[h]	0.59	82.0 (C–O)[j]	29.3	**–12.2**	4.8
 **5**	0.06 ($^-$SEt)[h]	0.44	61.7 (C–S)[j]	49.6	**–8.76**	24.4[d]
 **8**	0.06 ($^-$OCH$_3$)[h]	1.18	76.0 (C–O)[i]	35.3	**–25.8**	–7.37
 **9**	0.06 ($^-$SEt)[h]	1.06	61.7 (C–S)[j]	49.6	**–16.4**[k]	10.1[k]
 **10**	–1.0 ($^-$R)[l]	0.50	101.8 (C–C)[f]	9.5	–34.6	**–41.7**
 **11**	–1.0 ($^-$NR$_2$)[h]	0.50	103.2 (C–N)[m]	8.1	–37.4	**–45.0**
 **2**	2.59 (F$^-$)[n] 1.79 (Cl$^-$)[h]	1.39	–	–	27.7 (F$^\cdot$) **9.24 (Cl$^\cdot$)**	–

[a] E [V] vs. SCE. [b] E_{pa} [V] vs. SCE at 1 V s^{-1}. [c] In kcal mol^{-1}. [d] Data from ref.[18]. [e] Data from ref.[6a]. [f] Data from ref.[19]. [g] Energetically favored process is indicated in bold. [h] Data from ref.[17]. [i] Data from ref.[21]. [j] Data from ref.[20]. [k] $\Delta_1G°$ is a an absolute value as it includes the $\Delta_3G°$ value from ref.[23]. [l] Data from ref.[25]. [m] Data from ref.[26]. [n] Data from ref.[24].



Scheme 5. Mechanisms for the electrochemical oxidation of σ^H complexes.

of the relative energies of both processes. In all cases, $\Delta_1 G°$ (NASX) is more favorable than $\Delta_1 G°$ (NASH). Although the average differences are around 25 kcal mol^{-1}, they are well outside the experimental errors of the standard potential (10 mV, ca. 0.2 kcal mol^{-1}) and the BDEs (2 kcal mol^{-1}).

Note that when the S_NAr reaction involves either nitrogen- or carbon-centered nucleophiles, the experimentally observed mechanism corresponds to the NASH process. In this sense, the $\Delta_1 G°$ values for the NASX and NASH mechanisms confirm that the second mechanism is the thermodynamically favored one (σ^H complexes **10** and **11**, Table 2). Remarkably, in the case of σ^X complexes such as **2**, we previously reported that the electrochemically promoted S_NAr reaction involves the departure of a chlorine radical rather than a fluorine radical.[7a] This result can be easily explained in terms of the standard potential of the leaving group. As reported, the oxidation of F^- is at least 0.2 V more difficult than that of Cl^-, $E°_{F^{\cdot}/F^-,DMF}$=2.59 and 1.79 V at 298 K, respectively. Thus, $\Delta_1 G°$ in the NASX process is higher for the loss of fluorine, which effectively confirms that the departure of the leaving group from σ^X complexes is also thermodynamically controlled.

Finally, fluorinated compounds have not been considered because the literature BDEs for the aromatic fluorinated compounds vary from 87 to 127 kcal mol^{-1}. The peculiar nature of F^- led to larger discrepancies in the derived potential as no direct experimental electrochemical data is available. Hence, the standard potential for the oxidation of F^-, $E°_{F^{\cdot}/F^-,DMF}$ at 298 K, is estimated to be between 2.59 and 2.62 V from the available values of the free energy of transfer from water to DMF.[15,24] Clearly, this major uncertainty affects the use of the aforementioned thermodynamic cycles in estimating which process will operate in these cases.

Conclusions

The electrochemical oxidation of σ^H complexes, such as 1-hydro-1-alkoxy/sulfoxy or fluoro-2,4-dinitro/2,4,6-trinitrocyclohexadienyl anions, occurs by a one-electron mechanism followed by the radical elimination of the leaving group with the consequent recovery of the starting material. This mechanism is similar to that proposed for the electrochemical oxidation of σ^X complexes (the NASX mechanism). The "NASX-type" mechanism for these σ^H complexes (Nu^- = ^-OH, ^-OR, ^-SR, ^-F) contrasts with the NASH mechanism, a two-electron mechanism that corresponds to the formal elimination of a hydride anion when H^-, CN^-, RCOR′, and RNH_2 are used as nucleophiles. The two electrochemical oxidation pathways are compared in Scheme 5.

Thus, the quantitative formation of σ^H complexes **3**–**9** does not yield the substitution product after an electrochemical oxidation process. The nature of the nucleophile is a determinant factor. A thermodynamic study explains the operating mechanism (NASH or NASX) in terms of standard potentials as well as BDE values by comparison of the relative stabilities of the σ^H complex radicals generated by electrochemical oxidation. Although this study has not led to any significant improvement in the electrochemical preparation of aromatic-substituted compounds, with the exception of the use of sulfur nucleophiles to displace a nitro group, it does enable a better understanding of the experimental results. Finally, the current approach extends the electrochemical methodology to different chemical fields, for example, to general nondestructive methods for the detection, identification, and quantification of either organic pollutants[27] or explosives[28] in different solvents.

Experimental Section

Chemicals: Anhydrous acetonitrile (ACN) and *N*,*N*-dimethylformamide (DMF) stored in an inert atmosphere and molecular sieves were purchased from Across and SDS. Nitro aromatic compounds and nucleophiles of the highest available purity were purchased.

Synthesis of σ^H Complexes with Oxygen-, Sulfur-, and Fluorine-Centered Nucleophiles

Potassium Methoxide (MeOK): Different controlled amounts of potassium methoxide, which was used as a nucleophile, were added to a DMF solution (5 mL) of 1,3-DNB (10 mM) containing 0.1 M $TBABF_4$ (tetrabutylammonium tetrafluoroborate) as the supporting electrolyte. The reaction mixtures were simultaneously analyzed by UV/Vis spectrophotometry and cyclic voltammetry after each addition. The solution immediately became colored (λ_{max} = 578 nm), the blue color becoming darker as the concentration of the methoxide increased in the solution mixture. These general spectroscopic features are characteristic of the formation of the σ complex.[1] After the addition of 10 equiv. of potassium methoxide, intermediate **3** was obtained quantitatively.

Tetrabutylammonium Hydroxide (TBAOH): A solution of 5 mM of 1,3-DNB in DMF (5 mL, 0.1 M $TBABF_4$) was prepared under argon. Later, controlled aliquots of a 1.5 M TBAOH solution were carefully added. The voltammetric responses were registered after every addition of the nucleophile solution. Before the electrochemical measurements were performed, and after the addition of the TBAOH aliquots, the solution turned red-colored, which is indicative of the formation of σ complexes in solution. Thus, the presence of these complexes was first confirmed by UV/Vis spectroscopy; two characteristic absorption peaks for the σ complexes at 504 and 540 nm were clearly seen. After the addition of 1.4 equiv. of TBAOH, intermediate **4** was obtained quantitatively.

Sodium Thiosulfate: A similar approach to those described above were also applied to the sulfur nucleophile, sodium thiosulfate, and the same general trends were observed. After the addition of 10 equiv. of sodium thiosulfate to a solution of 10 mM 1,3-DNB in DMF (5 mL), intermediate **5** was obtained quantitatively.

Tetramethylammonium Fluoride: An anhydrous tetramethylammonium fluoride solution in DMF under argon was added to 1,3-DNB and 1,3,5-TNB solutions prepared under the same conditions. New oxidation waves at 0.70 and 1.09 V, corresponding to the formation of the σ^H complexes, were observed. The fluoride solution was added until the 1,3-DNB was no longer detected by cyclic voltammetry at which point all the nitroaromatic present in the mixture had been converted to the σ^H complex.

General Procedure for the NASX of σ^H Complexes in Nitroarenes: A solution of nitroarene (10–20 mM) in DMF (5 mL) containing NBu_4BF_4 (0.1646 g, 0.1 M) as the supporting electrolyte was prepared under nitrogen. The corresponding σ^H complex was prepared by careful addition of the nucleophile to the solution of the nitroarene under nitrogen. The oxidation peak potentials of the σ^H complexes were measured by cyclic voltammetry. Then electrolysis was carried out at values of potentials around 100 mV, which were more positive than the values measured for each σ^H complex, using a carbon graphite electrode as a working electrode. The electrolysis was stopped when the starting material had totally reacted. Then the mixture was extracted with water/toluene. The organic layer was dried with Na_2SO_4 and evaporated to afford a residue that was analyzed by gas chromatography. The analysis showed the presence of nitro compounds. The final products were analyzed by GC, GC–MS, ^{1}H NMR, and cyclic voltammetry and identified by comparing their spectroscopic behavior with either that reported in the literature or with pure samples in each case. The product yields were not optimized and were calculated by GC after verifying by ^{1}H NMR of the crude and cyclic voltammetry that only the substitution products and the starting material were present.

Cyclic Voltammetry: An electrochemical conical cell equipped with a methanol jacket, which made it possible to fix the temperature at 13 °C by means of a thermostat, was used for the set-up of the three-electrode system. For cyclic voltammetry experiments, the working electrode was in all cases a glassy carbon disk with a diameter of 0.5 mm. It was polished using a 1 µm diamond paste. The counter electrode was a Pt disk with a diameter of 1 mm. All the potentials were reported versus an aqueous saturated calomel electrode (SCE) isolated from the working electrode compartment by a salt bridge. The cyclic voltammetry apparatus was composed of a home-made solid-state amplifier potentiostat with positive feedback *iR* drop compensation and a Tacussel GSTP 4 generator. The voltammograms were displayed on a Tektronix (2212) instrument.[6]

Solutions were prepared using *N*,*N*-dimethylformamide (DMF) as solvent and were purged with argon before the measurements. Argon was allowed to flush the solutions during the measurements. The concentrations of the nitroaromatic compounds were around 10^{-3} M; 0.1 M tetrabutylammonium tetrafluoroborate was used as the supporting electrolyte.

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