FULL PAPER

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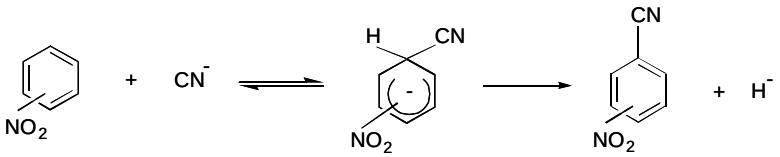
Chem Eur. J., **2001**, 7/8, 1759-1765



σ^H - Complex

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FULL PAPER

Nucleophilic Aromatic Substitution of Hydrogen: A Novel Electrochemical Approach to the Cyanation of Nitroarenes

Iluminada Gallardo,* Gonzalo Guirado, and Jordi Marquet[a]

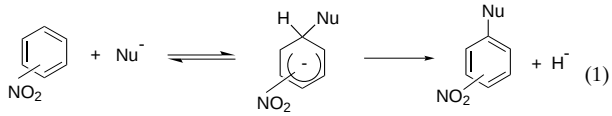
Abstract: The nucleophilic aromatic substitution of hydrogen through electrochemical oxidation of the intermediate σ complexes (Meisenheimer complexes) in simple nitroaromatic compounds is reported for the first time. The studies have been carried out with hydride and cyanide anions as the nucleophiles using cyclic voltammetry (CV) and preparative electrolysis. The cyclic voltammetry experiments allow for the detection and characterization of the σ complexes and led us to a proposal for the mechanism of the oxidation step. Furthermore, the power of the CV technique in the analysis of the reaction mixture throughout the whole chemical and electrochemical process is described.

Keywords: cyclic voltammetry · electrochemistry · Meisenheimer complexes · nucleophilic substitution · σ complexes

Introduction

The development of new environmentally favourable routes for the production of commercially relevant chemical intermediates and products is an area of considerable interest. These synthetic routes require, in most cases, the discovery of new atomically efficient chemical reactions. According to these requirements, we have focused our attention on the nucleophilic aromatic substitution in hydrogen reactions (NASH)[1, 2] as a means to generate functionalized aromatics without the need for halogenated materials or intermediates.[3] NASH reactions formally require the replacement of a hydride ion, and occur "spontaneously" consuming part of the starting material in the oxidation step, or they are promoted by the addition of external oxidants. Low yields (with few exceptions)[4] and lack of generality are the main drawbacks of these synthetic procedures.[1, 2] In addition, some of the chemical substances used as oxidants, are hazardous in their own right. In this respect, use of electrochemical techniques seem to be very attractive, but curiously enough, this approach has been almost completely neglected in the chemical literature.

Nucleophilic reagents react for example with nitroarenes. The initial step of these reaction is usually reversible addition to the unsubstituted 1- and 4-positions to produce the σ^H complexes[1, 2, 5, 6]



(1)

σ^H - complex

These σ^H complexes may be converted into products of hydrogen-atom replacement in two ways: *vicarious* nucleophilic substitution[7–11] extensively investigated in the case of carbanionic nucleophiles and with several examples of nitrogen and oxygen nucleophiles.[12] A second strategy involves a *chemical* oxidation of a intermediate σ^H complex through formal displacement of H^-.[1, 2, 5, 6] The rearomatization of σ^H adducts is difficult with mild or moderately strong chemical oxidants.[13, 14]

One variety of chemical oxidation is the electrochemical oxidation of σ^H adducts. In a very recent paper Terrier et al. have established,[15] by electrochemical methods, the mechanism leading to the rearomatized products for the 2-nitropropenide adducts of nitrosubstituted 1,2,3-benzoxadiazoles and related 1-oxides.

^{1}H NMR spectroscopy is the most widely used and reliable technique for investigating the structure and the reactivity of anionic σ complexes,[16] as well as ^{13}C and ^{15}N NMR spectroscopy, which have only recently been applied to this type of compound.[17] Stopped-flow (SF) and temperature-jump (TJ) are additional techniques that have been frequently employed.[18] Calorimetric studies,[19] radioactive exchange[20] and high-pressure stopped-flow experiments[21]have also been used to study complexation.

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Our work will show that electrochemical methods can provide additional information to the previously mentioned opening interesting possibilities in S_NAr reactions:

a) Such as determining precisely the position which has been attacked by the nucleophile, the number of σ^H complexes formed as a result of this attack, and the amount of σ^H complex formed, and
b) prove that the electrochemical oxidation of σ^H adducts leads to the rearomatized product and formal H^- substitution (from the starting nitroarene) in excellent yields.

In order to establish the mechanistic details and synthetic scope of the electrochemical method, this study has been carried out for a wide series of 1,3-dinitrobenzene derivatives and related compounds **1** to **15** (Scheme 1): 1-amino-2,4-dinitrobenzene (**1**), 1,3-dinitrobenzene (**2**), 1-methyl-2,4-dinitrobenzene (**3**), 1-methoxy-2,4-dinitrobenzene (**4**), 1-fluoro-2,4-dinitrobenzene (**5**), 1-chloro-2,4-dinitrobenzene (**6**), 1-bromo-2,4-dinitrobenzene (**7**), 3,5-dinitro-benzonitrile (**8**), 3-nitrobenzonitrile (**9**), 1,3,5-trinitrobenzene (**10**), 1-methyl-2,4,6-trinitrobenzene (**11**), 3-nitrobenzofluoride (**12**), 3,5-dinitrobenzofluoride (**13**), 2,4-dinitronaphthalene (**14**), and 2-nitrothiophene (**15**), with two nucleophiles: H^- and CN^-. The first one, H^-, has allowed us to establish the mechanism of electrochemical oxidation and subsequently the precise determination of the position which has been attacked by the nucleophile, the number of σ^H complexes formed as a result of this attack, and the amount of σ^H complex formed. The second one, CN^-, has been used to complement the study of the electrochemical oxidation of σ^H adducts and to establish a new environmentally friendly synthetic route for the cyanation of nitroarene systems.

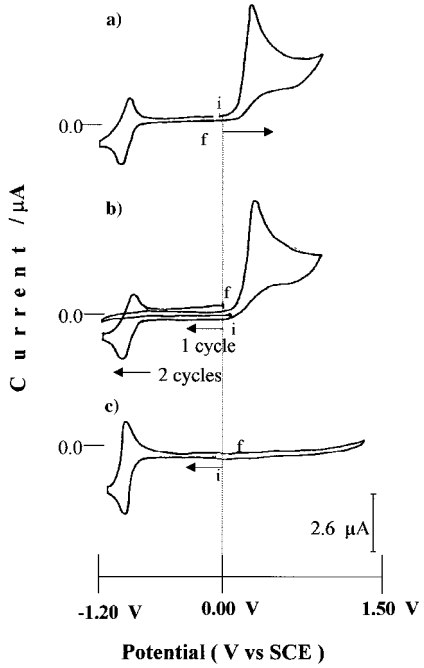


Figure 1. a) Cyclic voltammetry of $\mathbf{1a}^-$ (6.0 mM) in DMF+0.1 M nBu_4NBF_4 at 10 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/1.00/ − 1.20/0.00 V. b) Cyclic voltammetry of $\mathbf{1a}^-$ (6.0 mM) in DMF+0.1 M nBu_4NBF_4 at 10 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/ − 1.15/1.00/ − 1.15/0.00 V (two cycles). c) Cyclic voltammetry of **1a** (6.0 mM) in DMF+0.1 M nBu_4NBF_4 at 13 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/ − 1.10/1.35/0.00 V.

Results and Discussion

Hydride ion as a nucleophile (H^-)

The synthesis,[22] purification, characterisation and kinetics of σ^H complexes $\mathbf{1a}^-$ to $\mathbf{11a}^-$ (Scheme 1) has been previously reported.[23]

Electrochemical behaviour of compound $\mathbf{1a}^-$: The characteristic voltammogram (1.00 V s^{-1}) of **1a** in DMF is shown in Figure 1a. An irreversible two-electron oxidation wave (ca. 0.30 V) on the first anodic scan, and a reversible one-electron reduction wave (ca. − 1.03 V) are observed. The Figure 1b shows that, on the first cathodic scan, the reversible one-electron reduction wave does not exist, while the irreversible two-electron oxidation wave appears unchanged; on the second cathodic scan the reduction wave appears(ca. − 1.03 V). This reduction wave, at − 1.03 V, correspond to the product formed in the first anodic process.

The Figure 1c shows the cyclic voltammogram of **1**. A reduction wave is observed ($E_p = -1.03$ V) and no further oxidation wave is seen in the potential range of − 1.2 V to + 1.5 V.

Addition of authentic **1** to the solution of $\mathbf{1a}^-$ cause the increase of the reduction wave. Furthermore, after exhaustive controlled potential electrolysis (2F) of a solution of $\mathbf{1a}^-$ at + 0.50 V, cyclic voltammetric analysis of this solution indicated that **1** was the only final product, formed in quantitative yield. Therefore, the species arising from the oxidation of anionic σ^H complex $\mathbf{1a}^-$ can be identified as **1**.

The voltammogram of $\mathbf{1a}^-$ at 380 V s^{-1} (Figure 2) presents a reversible one-electron oxidation wave with $E^\circ = 0.325$ V. That is, if there are no chemical reactions linked to electron transfer, one-electron wave is observed.

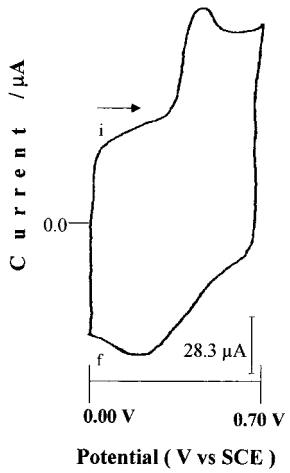
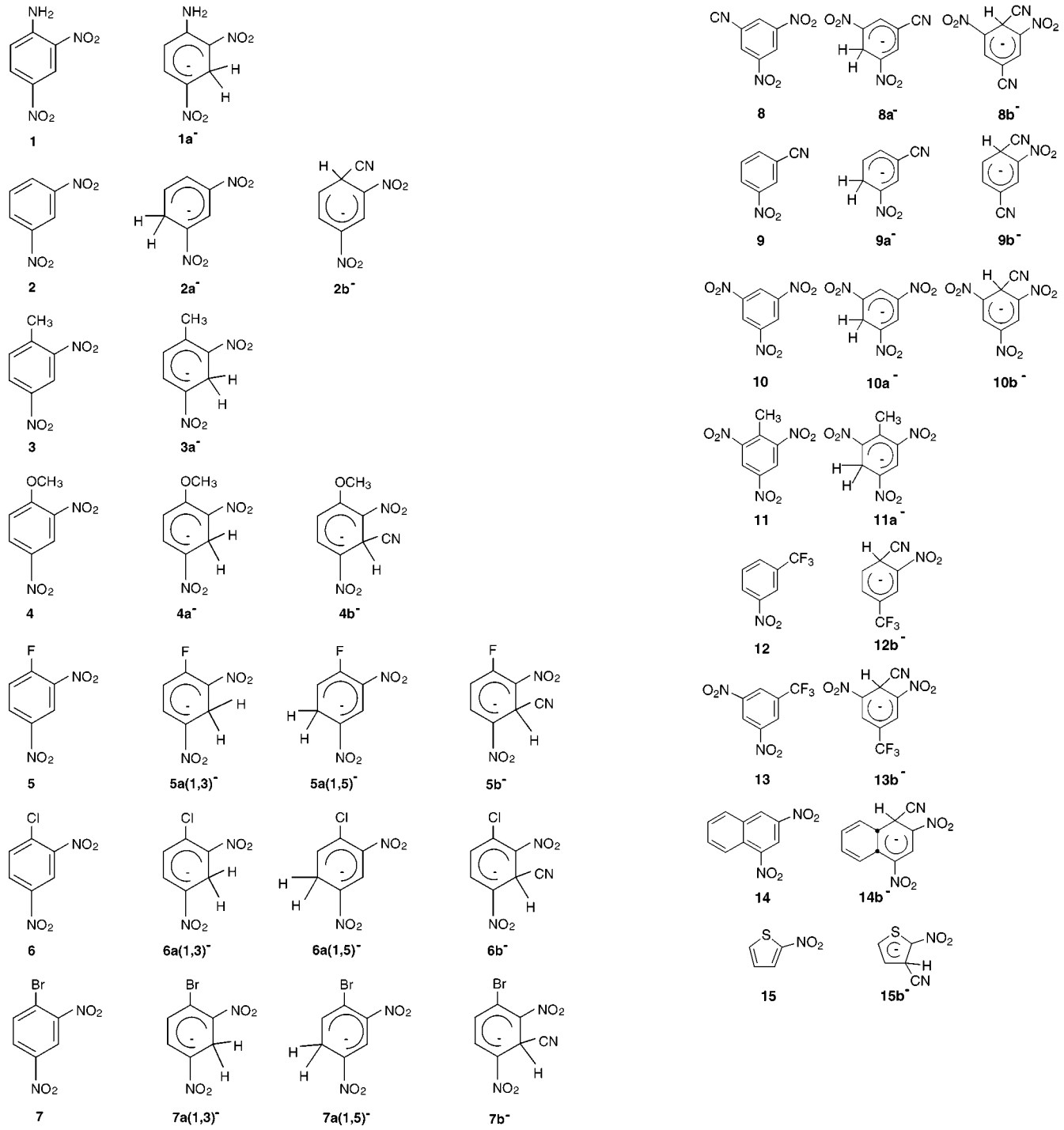


Figure 2. Cyclic voltammetry of $\mathbf{1a}^-$ (6.0 mM) in DMF+0.1 M nBu_4NBF_4 at 10 °C. Scan rate 380 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/0.70/0.00 V.

0947-6539/01/0708-1760 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 8



Scheme 1. Different intermediates and complexes **1**–**15**.

Mechanistic discussion: Our experimental results show that after exhaustive oxidation of σ^H complex $\mathbf{1a}^-$, the rearomatized substituted compound **1** is obtained as a result of formal loss of two electron and a proton. Furthermore, the voltammograms show that the oxidation of σ^H complex $\mathbf{1a}^-$ occurs through a three-step mechanism: a first electron transfer on the electrode, one chemical reaction and a second electron transfer in solution (DISP mechanism) or on the electrode (ECE mechanism).[24] In following Equations (2)–(5) three mechanistic hypothesis are formulated [Eqs. (2), (3a), (4a)/(2), (3b), (4b)/(2), (3b), (4c)].

$$\mathbf{1a}^- - 1\,e^- \rightarrow \mathbf{1a}^\bullet \quad (2)$$

$$\mathbf{1a}^\bullet \rightarrow \mathbf{1} + H^\bullet \quad (3a)$$

$$\mathbf{1a}^\bullet \rightarrow \mathbf{1}^{\bullet-} + H^+ \quad (3b)$$

$$\mathbf{1a}^\bullet \rightarrow \mathbf{1}^{\bullet-} + H^+ \quad (3c)$$

$$\mathbf{1a}^\bullet + H^\bullet \rightarrow \mathbf{1a}^- + H^+ \quad (4a)$$

$$\mathbf{1a}^\bullet + \mathbf{1}^{\bullet-} \rightarrow \mathbf{1a}^- + \mathbf{1} \quad (4b)$$

$$\mathbf{1}^{\bullet-} - 1\,e^- \rightarrow \mathbf{1} \quad (4c)$$

$$\mathbf{1a}^- - 2e^- \rightarrow \mathbf{1} + H^+ \quad (5)$$

In all cases, the first step [Eq. (2)] involves loss of one electron by the σ^H complex $\mathbf{1a}^-$ with formation of the corresponding radical, $\mathbf{1a}^\bullet$. This radical undergoes first-order C–H bond

cleavage [Eqs. (3)] to give either the final rearomatized compound **1**, and hydrogen atom (as proposed by Terrier in related systems)[15] or the radical anion of the rearomatized compound $\mathbf{1}^{\bullet-}$, and a proton as earlier proposed by Sosonkin.[25] The final oxidation of the hydrogen atom or of the radical anion, $\mathbf{1}^{\bullet-}$, can be performed by the radical, $\mathbf{1a}^{\bullet}$ or by the electrode. In conclusion, the three mechanism are kinetically equivalent. However, in our case, for compound $\mathbf{1a}^-$, the more likely mechanism would be the mechanism described in Equations (3b)/(4b) or Equations (3b)/(4c). The C–H acidity of cyclohexadienyl radicals of $\mathbf{1a}^{\bullet}$ type, where the corresponding aromatic radical anion is stabilized by electron attracting groups is very significant[26] and the voltammogram of a mixture of $\mathbf{1a}^-$ with 2,6-lutidine (1:0.5) shows irreversibility up to 20000 Vs^{-1}. Furthermore, the basicity of the radical anion of dinitroaromatic compounds is very weak.[27] The reduction wave of **1** remains reversible in the presence of small amounts of added water (a one-thousand-fold excess of water is necessary for the wave to become irreversible). In spite of the relative fast cleavage of $\mathbf{1a}^{\bullet}$, the present work does not give any evidence to the solve the uncertainly: ECE/DISP in the last step of the mechanism.[28]

Electrochemical behaviour of compounds $\mathbf{2a}^-$ to $\mathbf{11a}^-$: σ^H Complexes $\mathbf{2a}^-$ to $\mathbf{11a}^-$ were prepared by stoichiometric addition of tetramethylammonium borohydride to solutions of compounds **2** to **11** in DMF under inert atmosphere.

The same cyclic voltammetry experiments described for compound $\mathbf{1a}^-$ were also performed with compounds $\mathbf{2a}^-$ to $\mathbf{11a}^-$. The results are summarized in Table 1. From the Table 1, we see that, in these systems, the cyclic voltammetry allows for the:

1) determination of the efficiency of the hydride attack to nitroaromatic compound, **2** to **11**, in order to form the corresponding σ^H complexes. A 100% efficiency in σ^H complex formation implies that no reduction wave of nitroaromatic compound is observed, in the first cathodic scan. If a reduction wave in the first cathodic scan appears, it would correspond to the nitroaromatic compound which has not been attacked by the hydride ion. Thus, it is possible to determine the yield of formation σ^H complex. This resulted in a 100% yield for the series of σ^H complexes.
2) determination of how many σ^H complexes are present in the mixture and their relative amounts by regarding the number and potential values of the two-electron irreversible oxidation waves. For compounds **5**, **6** and **7**, two kinds of σ^H complexes are identified, probably adducts 1,3 and 1,5.
3) conclusion that oxidation of the cyclohexadienyl anions lead to the rearomatized nitroaromatic compound, **2** to **11**, by observing only their one-electron reversible reduction wave after one anodic scan of the solution. This is confirmed by exhaustive electrolysis at potential sufficient positive of solutions of σ^H complexes $\mathbf{2a}^-$ to $\mathbf{11a}^-$, were the only products obtained are rearomatized nitroaromatic compound, **2** to **11**, respectively.

As a summary of this part, once the mechanism of electrochemical oxidation of an authentical sample of $\mathbf{1a}^-$ has been established, we have demonstrated that cyclic voltammetry is a powerful tool for studying the σ^H complexes formed in situ. On the other hand, the evaluation of the nucleophilic attack will probably be related with the efficiency of the nucleophilic aromatic substitution. To obtain substituted products using nucleophiles different from hydride ion is the evident extension of this work.

Cyanide ion (CN^-) as a nucleophile

Electrochemical behaviour of σ^H complex $\mathbf{2b}^-$ (see Scheme 1): This adduct was prepared by careful stoichiometric addition of tetraethylammonium cyanide to a solution of **2** in DMF under inert atmosphere.

Altogether, cyclic voltammetry (Figure 3) and controlled-potential electrolysis (Table 2) experiments similar to the

Table 1. Electrolysis (2F) of $\mathbf{1a}^- - \mathbf{11a}^-$ (10 mM) at oxidation peak potential (column 4) plus about 100 mV.

Nitroarene	σ^H Complex	% σ^H Complex	E_{pa} [V][a] σ^H Complex	UV Spectra [nm] of the mixture	Oxidation product	Yield [%]	E° [V] Oxidation product[30]
1	$\mathbf{1a}^-$	100	0.30	268, 348, 578	**1**	100	– 0.95
2	$\mathbf{2a}^-$	100	0.39	288, 354, 532, 560 594, 672, 686	**2**	100	– 0.82
3	$\mathbf{3a}^-$	100	0.25	286, 314, 352 536, 600, 698	**3**	100	– 0.96
4	$\mathbf{4a}^-$	100	0.30	264, 326, 614, 658	**4**	100	– 1.00
5	$\mathbf{5a(1,3)}^-$ $\mathbf{5a(1,5)}^-$	100	0.33(80%) 0.44(20%)	268, 366, 430, 550 580, 670, 684	**5**	100	– 0.79
6	$\mathbf{6a(1,3)}^-$ $\mathbf{6a(1,5)}^-$	100	0.32(78%) 0.44(22%)	268, 320, 360, 370 530, 576, 654, 668	**6**	100	– 0.78
7	$\mathbf{7a(1,3)}^-$ $\mathbf{7a\ (1,5)}^-$	100	0.32(70%) 0.44(30%)	268, 320, 360, 370 530, 572, 654, 668	**7**	100	– 0.78
8	$\mathbf{8a}^-$	100	0.60	268, 312, 404, 532 574, 656, 670	**8**	100	– 0.62
9	$\mathbf{9a}^-$	100	0.19	268, 350, 478, 536	**9**	100	– 0.90
10	$\mathbf{10a}^-$	100	0.77	270, 348, 478 566, 606	**10**	100	– 0.58
11	$\mathbf{11a}^-$	100	0.62	260, 486, 516, 576	**11**	100	– 0.68

[a] In the case of products which form two isomeric adducts their E_p were assigned by comparison with the other products and by reported NMR data.[28, 30]

0947-6539/01/0708-1762 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 8

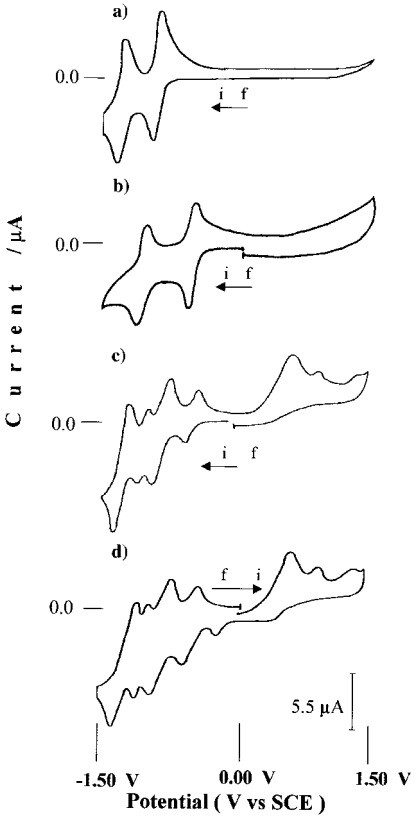
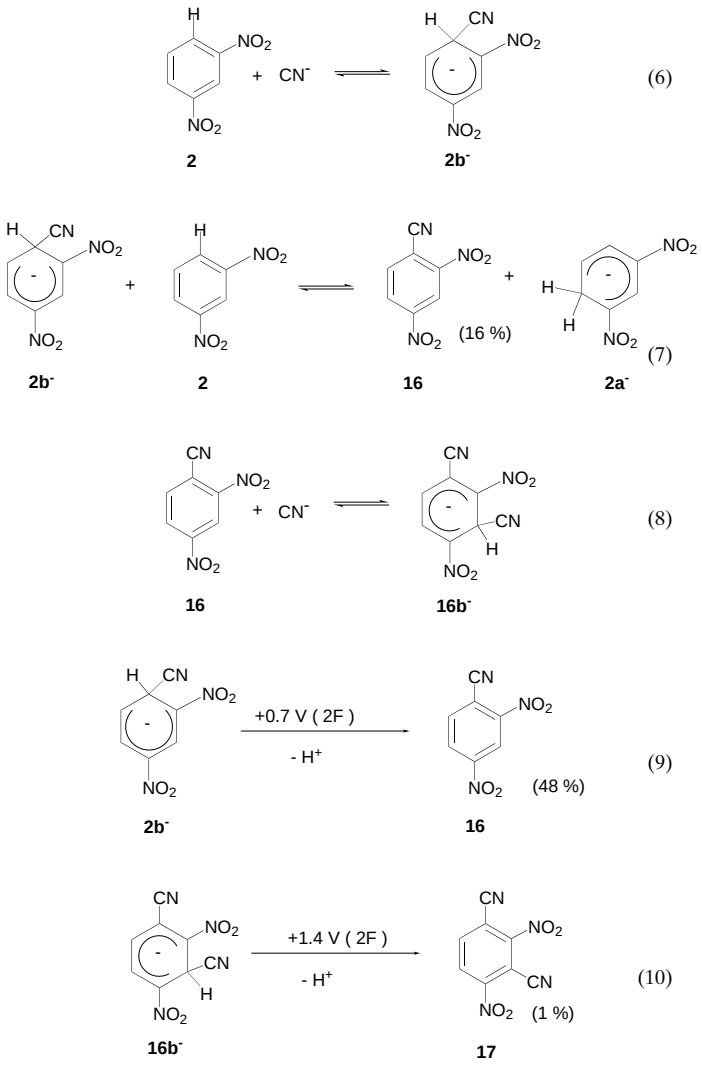


Figure 3. a) Cyclic voltammetry of **2** (6.0 mM) in DMF+0.1 M nBu_4NBF_4 at 13 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/ – 1.50/1.50/0.00 V. b) Cyclic voltammetry of **16** (6.0 mM) in DMF+0.1 M nBu_4NBF_4 at 13 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/ – 1.50/1.50/0.00 V. c) Cyclic voltammetry of the mixture between **2** (6.0 mM) and tetraethylamonium cyanide (6.0 mM) in DMF 1:1 under inert atmosphere +0.1 M nBu_4NBF_4 at 10 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/ – 1.50/1.50/0.00 V. d) Cyclic voltammetry of the mixture between **2** (6.0 mM) and tetraethylamonium cyanide (6.0 mM) in DMF 1:1 under inert atmosphere +0.1 M nBu_4NBF_4 at 10 °C. Scan rate 1.0 V s^{-1}, glassy carbon disk electrode (0.05 mm diameter). The scan is in the potential range: 0.00/1.50/ – 1.50/0.00 V.



ones described in the first part of the paper allow us to describe the formation of σ^H complex **2b**$^-$and further chemical and electrochemical reactions [Eqs. (6)–(10)].

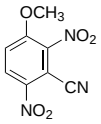
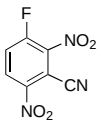
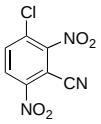
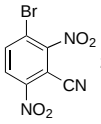
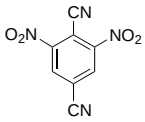
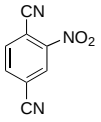
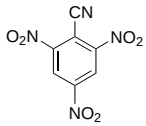
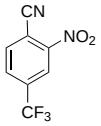
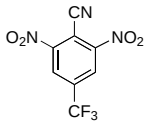
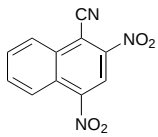
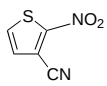
The first step [Eq. (6)] is a reversible addition of CN^- to **2** resulting in the σ^H complex **2b**$^-$ (yield 50 %). This σ^H complex undergoes a *thermal* process (yield 16 %). Upon reaction with **2** (in slow equilibrium process, fast enough to be established prior to cyclic voltammetry measurements but slow enough to be not displaced at slow scan rates) the rearomatized compound, 2,4-dinitrobenzonitrile (**16**)[29] is obtained [Eq. (7)]. Compound **16** gives a new σ^H complex, **16b**$^-$ with excess of CN^- [Eq. (8)]. σ^H Complexes **2b**$^-$and **16b**$^-$ undergo electrochemical oxidation at +0.70 V [Eq. (9)] and +1.40 V [Eq. (10)]. This oxidation involves formal loss of two electron and a proton and the final products are **16** (48 %) and 2,4-dinitroisophtalonitrile,**17** (5 %), respectively. Compounds **16** and **17** were identified by GC-MS, ^{1}H RMN and cyclic voltammetry.

The voltammograms show the electrochemical behaviour of compound **2** (Figure 3a), compound **16** (Figure 3b) and the mixture of **2**+CN^-(Figure 3c and Figure 3d). The Figure 3c shows, starting with a reduction scan, the reduction of compound **16** (formed according to [Eq. (7)] and the reduction of unreacted compound **2**. In an oxidation scan, σ^H complexes **2b**$^-$and **16b**$^-$ (E_p = +0.59 V and E_p = +0.98 V) and the unreacted CN^-(E_p = +1.24 V) are identified. A similar behaviour is obtained when the first scan is an oxidation scan (Figure 3d), the difference is the new peak reduction corresponding to compound **17** (E_p = –0.24 V). Complex **17** is formed according to Equation (10).

Our results indicate that the exhaustive controlled-potential oxidation of σ^H complex formed in S_NAr constitute a new route for the cyanation of nitroarenes. This study was extended to different nitroarenes (**4**–**10** and **12**–**15**) in order to establish the scope of the reaction.

Cyanation results: σ^H Complexes **4b**$^-$, **5b**$^-$, **6b**$^-$, **7b**$^-$, **8b**$^-$, **9b**$^-$, **10b**$^-$, **12b**$^-$, **13b**$^-$, **14b**$^-$ and **15b**$^-$ (see Scheme 1) were prepared by careful stoichiometric addition of tetraethylammonium cyanide to solutions of the nitroarenes in DMF under inert atmosphere. Its characterisation was carried out by cyclic

Table 2. Electrolysis (2F) of **2b**$^-$, **4b**$^-$ – **10b**$^-$, **12b**$^-$ – **15b**$^-$ (25 mM) at oxidation peak potential (column 4) plus about 100 mV.

Nitro-arene	% σ Complexes	σ^H Complex	E_{pa} [V] σ^H Complex	Product of NASH	Yield [%]	$r \times 100$ (r = Ar–CN/ σ complexes)
2	50	**2b**$^-$	0.59	**16**	48	96
4	40	**4b**$^-$	0.61	 **18**	15	38
5	48	**5b**$^-$	0.56	 **19**	8	17
6	57	**6b**$^-$	0.59	 **20**	7	13
7	86	**7b**$^-$	0.59	 **21**	6	7
8	46	**8b**$^-$	0.92	 **22**	40	87
9	45	**9b**$^-$	0.65	 **23**	45	88
10	65	**10b**$^-$	1.04	 **24**	60	92
12	38	**12b**$^-$	0.58	 **25**	35	92
13	48	**13b**$^-$	1.03	 **26**	43	90
14	35	**14b**$^-$	0.64	 **27**	35	100
15	35	**15b**$^-$	0.62	 **28**	35	100

voltammetry (oxidation peak potential and intensity of the remaining nitroarene reduction wave) (columns 2, 3 and 4, Table 2). The yield of formation of σ^H complexes is superior to 35 % in all the cases.

After exhaustive controlled potential electrolysis at oxidation peak potential plus about 100 mV, the rearomatized substituted compound is obtained as a result of formal loss of two electron and a proton (NASH product, column 5, Table 2). The yield in σ complex formation (column 2, Table 2) goes from 35 % to 86 %. Electrochemical efficiency goes from 35 % to 60 % (column 6, Table 2) or from 87 % to 100 % (column 7, Table 2). The reaction is very clean, recovering only starting material (column 1, Table 2) apart from the reaction products (column 5, Table 2). For the compounds **4**, **5**, **6** and **7**, where a low yield in NASH is observed, the compound **16** is obtained in 30 % yield.[30]

In summary, the electrochemical oxidation of σ^H complexes formed by addition by CN^- to nitroarenes is obtained with good yield giving rise to rearomatized compound in what formally constitutes a loss of H^-. Some advantages of this new cyanation method[31, 32] are: a) low-cost and high-availability of the reagents, b) atom economy, c) environmentally friendly (clean chemistry), d) high yields, close to 100 %, over non-recovered starting material. Almost no secondary products are produced.

We are currently working in the extension of this methodology to other nucleophiles and substrates.

Experimental Section

Chemicals: Compounds **1** – **9** and **12** – **15** were from Aldrich Chemical Co. Compound **10** was purchased from Supelco. Compound **11** was from Union Española de Explosivos. Tetramethylammonium borohydride was also from Aldrich Tetrabutylammonium tetrafluoroborate (puriss pa) and tetraethylamonium cyanide were from Fluka. Commercial products were of the highest purity available and used as received. Compound **1a**$^-$ was prepared as tetramethylamonium salt as in reference.[12] Compounds **2a**$^-$ – **11a**$^-$ were prepared in situ under nitrogen atmosphere by careful addition of one equivalent of tetramethylammonium borohydride to the corresponding nitroaromatic compound. Compounds **2b**$^-$, **4b**$^-$ – **10b**$^-$, **12b**$^-$ – **15b**$^-$ were prepared in situ under nitrogen

0947-6539/01/0708-1764 $ 17.50+.50/0 *Chem. Eur. J.* **2001**, *7*, No. 8

atmosphere by careful addition of one equivalent of tetraethylammonium cyanide to the corresponding nitroaromatic compound in DMF.

General procedure for NASH in nitroarenes: The corresponding anion ($2b^-$, $4b^- - 10b^-$, $12b^- - 15b^-$), prepared in situ in DMF with 0.1M nBu_4NBF_4, was oxidised electrochemically (2F) using a carbon graphite electrode. After the reaction was complete, the mixture was extracted with water/toluene. The organic layer was dried with Na_2SO_4 and evaporated affording a residue that was analized by gas cromatography. The analysis showed the presence of the nitrocompounds: **16**, **18**–**28**. The products were analysed by GC/MS, ^{1}H NMR and cyclic voltammetry and identified by comparison of their spectroscopic behaviour with the reported in the literature in each case (**16**,[33] **18**,[34] **23**,[35] **24**,[36] **25**,[37] **26**,[38] **28**,[39] **20**[40]). Compounds **19** and **21** gave the same voltammetric behaviour as **20**.

Compound **22**: ^{1}H NMR (250 MHz, CD_3CN, 25 °C, TMS): $\delta = 8.86$ (s, 1H); MS (70 eV): m/z (%): 218 (13) $[M]^+$, 188 (66), 172 (2), 168 (1), 158 (100), 128 (20), 126 (22), 102 (14), 100 (36), 99 (19), 87 (16), 75 (99), 46 (58); $E^o = -0.35$ V.

Compound **27**:[41] ^{1}H NMR (250 MHz, CD_3CN, 25 °C, TMS): $\delta = 8.86$ (s, 1H), 8.43 (d, $J = 7.89$ Hz, 1H), 8.10 (dd, $J = 5.26$, 1.33 Hz, 1H), 8.01 (dd, $J =$ 7.41, 5.26 Hz, 1H), 7.90 (dq, $J = 7.89$, 7.41, 1.33 Hz, 1H); MS (70 eV): m/z (%): 243 (74) $[M]^+$, 213 (10), 167 (13), 151 (100), 150 (20), 141 (29), 140 (14), 139 (45), 138 (13), 124 (32), 102 (11), 100 (13), 99 (15), 76 (19), 74 (22), 50 (17); $E^o = -0.33$ V.

Instrumentation and procedures: The electrochemical cell and measurement procedures for CV and electrolysis have been described previously.[42] All potentials are reported versus an saturated calomel electrode.

Acknowledgement

Financial support from the DGES through project No.PB96–1145 and from "Generalitat de Catalunya" through the project 1997GR00414 are gratefully acknowledged.

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Received: July 26, 2000 [F2628]

FULL PAPER

Electrochemical Synthesis of Nitroanilines

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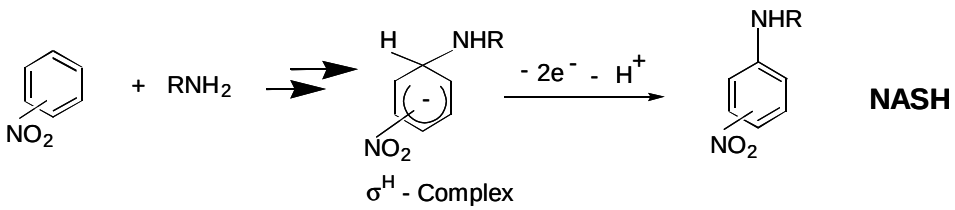


σ^H - Complex

Keywords: Nucleophilic substitution/ Amino derivates/ Electrochemistry / σ^H-complexes

Eur. J. Org. Chem., **2001**, in press

FULL PAPER

Electrochemical Synthesis of Nitroanilines[‡]

Iluminada Gallardo,*[a] Gonzalo Guirado,[a] and Jordi Marquet[a]

Keywords: Nucleophilic substitution / Amino derivatives / Electrochemistry / σ^H complexes

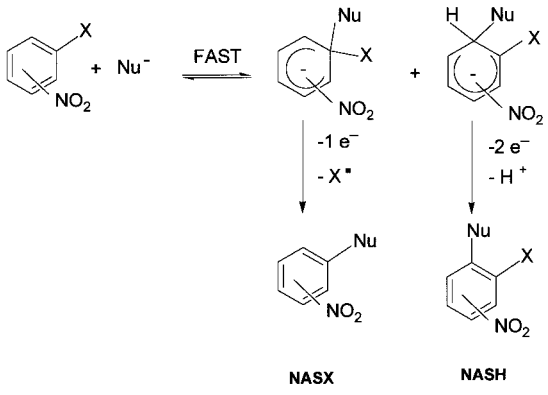
Alkylamines and amides are readily prepared by nucleophilic aromatic substitution of hydrogen in nitroarenes by electrochemical oxidation. Useful yields (15–85%) are achieved in a simple direct and regioselective amination process. The synthetic method has been examined in the absence and presence of external bases, used to promote the first step of the nucleophilic aromatic substitution reaction, i.e. the nucleophilic attack. In both cases, good results were obtained. The unreacted starting material can easily be recovered at the end of the electrochemical oxidation process. This new method represents an environmentally favourable route to amino- and amido-substituted nitroaromatic compounds.

Introduction

Nucleophilic aromatic substitution of halogen or other nucleofugal groups in nitroarenes, according to the S_NAr addition-elimination mechanism,[1] is a classical reaction of great practical value. Studies of the mechanisms of aromatic substitution of electron-deficient aromatic and heteroaromatic compounds,[2] establishing the factors that affect the choice of mechanistic path and the regioselectivity within a given mechanism, can have a major impact in such important areas as drug synthesis, polymer research, and environmental chemistry.[3] A thorough understanding of these mechanisms will be of high value in the practical choice of conditions, solvents, and nucleophiles for the preparation of new drugs and polymers, analytical standards for environmental investigations, and in the choice of procedures used in environmental amelioration.[4] We have recently contributed to this field by introducing a novel oxidative electrochemical approach to the S_NAr reaction for heteroatoms (NASX).[5a]

The development of new environmentally friendly routes for the production of commercially relevant chemical intermediates and products is an area of considerable interest. In most cases, such synthetic routes require the discovery of new atomically efficient chemical reactions. According to these requirements, we have focused our attention on nucleophilic aromatic substitution of hydrogen reactions (NASH)[1,2,6] as a means of generating functionalized aromatics without the need for halogenated starting materials or intermediates.[7,8] NASH reactions formally require the replacement of a hydride ion, and they either proceed "spontaneously" with consumption of part of the starting material in the oxidation step, or are promoted by the addition of external oxidants. Low yields (with few exceptions)[7,8] and a lack of generality are the main drawbacks of these synthetic procedures.[1,2,6] Moreover, some of the chemical substances used as oxidants are inherently hazardous.

In this respect, the use of electrochemical techniques would seem to be very attractive. Curiously, however, this approach had been completely neglected in the chemical literature until our previous work,[5b] in which we described for the first time the electrochemical cyanation of nitroarenes based on electrochemically promoted nucleophilic aromatic substitution of hydrogen. Scheme 1 depicts the electrochemical approaches to NASH and NASX.



Scheme 1

Several different methods for the direct amination of nitrobenzenes that do not require chloroaromatic compounds have been reported. Perhaps the best established of these is the vicarious nucleophilic substitution of hydrogen (VNS).[9–11] Although this method furnishes reasonable yields of aminated nitrobenzenes,[12] it still requires an auxiliary group. Very recently, we have described the amination of *m*-dinitrobenzene promoted by fluoride ions through photochemical activation.[7a] The substitution can be promoted by the addition of external oxidants. It has been known for many years that $KMnO_4$ in liquid ammonia is

[‡] Electrochemically Promoted Nucleophilic Aromatic Substitution of Hydrogen, I

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an excellent oxidant for σ^H complexes formed by the addition of ammonia or amide anions to electrophilic nitroarenes, particularly heteroarenes.[1] This oxidative variant of the Chichibabin reaction, introduced into organic synthesis by van der Plas, is a general process of great practical value,[6] but is restricted to ammonia as the nucleophile.[7b] Herein, we propose an even simpler way of achieving the direct amination of nitroaromatic compounds (see Scheme 3), i.e. by NASH using electrochemical techniques. Some advantages of this new amination method are: (a) low cost and ready availability of the reagents, (b) atom economy, (c) high yields, approaching 100% based on unrecovered starting material. Virtually no secondary products are produced.

Results and Discussion

Table 1 summarizes the results obtained in the oxidative electrochemical S_NAr of hydrogen for various nitroaromatic compounds (Scheme 2) with nBuNH$_2$: 1,3-dinitrobenzene (**1**), 3,5-dinitrobenzonitrile (**2**), α,α,α-trifluoro-3,5-dinitrotoluene (**3**), 1-chloro-2,4-dinitrobenzene (**4**), 1,3,5-trinitrobenzene (**5**), and 1,3-dinitronaphthalene (**6**). The σ^H complexes (column 5) were prepared by carefully adding the amine to solutions of the nitroarene in DMF under an inert gas at 13 °C. The percentage of attack or the extent of σ-complex formation under the initial conditions (fast equilibrium) (column 4) was determined, and the σ^H complexes (column 6) were characterized using cyclic voltammetry.[5] The yields ranged from fair to good (35−89%), except in the case of **13** (15%), and only the starting material (apart from the substitution product) was recovered at the end of the electrochemical oxidation process. The reaction (via A in Scheme 3) proved to be highly regioselective in all cases.

The excess of amine used varied from case to case. A large excess of amine was added in the reaction with **1** in order to promote the very inefficient nucleophilic attack (1% attack with a 200-fold excess of nBuNH$_2$). In the case of compounds **2**−**6**, a lower excess of amine was used in order to optimize the formation of σ^H complexes and to minimize further amination of the NASH product (column 7).

Note that in Entry 2 two isomers are obtained. The first one, **11a**, is the C-4 isomer, derived from electrochemical oxidation of the Meisenheimer adduct (E_{pa} = 1.21 V, 10%). The second one is the C-2 isomer **11b**. Electrochemical oxidation of the butylamine Meisenheimer adduct (C-2) leads to the corresponding amino derivative (E_{pa} = 1.03 V; 39%).

In the particular case of **5**, use of a large excess of amine (1:295, until no starting material remained in the solution) led, after exhaustive electrolysis at 1.6 V, to 2,4,6-trinitro-1,3-benzenediamine as the final oxidation product in almost quantitative yield (95%). Furthermore, no new oxidation waves appeared during cyclic voltammetry experiments on **5** and butylamine, even when a large excess was added.

In the case of **6** (Entry 6), a yield of 84% was obtained. Here, *n*-butylamine was added in a controlled way until the σ^H adduct was the only product present in the mixture. Cyclic voltammetry was used as an analytical tool in such a way that it was possible to know the concentrations of the different species present in the reaction mixture (reactant, zwitterionic complex, and σ^H complex), hence the amine could be added until neither the nitroaromatic initial reactant nor the zwitterionic first intermediate could be detected in the solution.

The reaction of 1-chloro-2,4-dinitrobenzene **4** (Entry 4, Table 1) is illustrative of the power of the electrochemical approach. In this case, a good leaving group (chloride) is present at an activated position of the aromatic ring and therefore the σ^X complex is produced as the major one. We have recently shown that oxidation at 1.35 V gives rise to the NASX product along with minor amounts of the NASH product.[5a] However, as shown in Table 1, selective NASH reaction can be achieved by applying a lower oxidation potential such that only the σ^H complex is oxidized (15% preparative yield; 15% based on unreacted starting material).

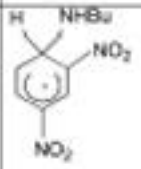
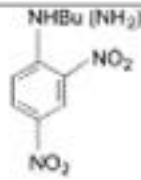
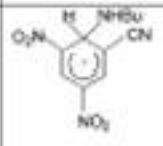
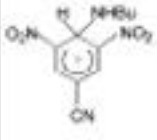
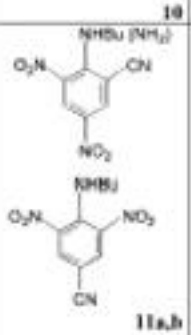
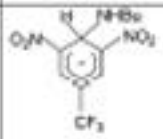
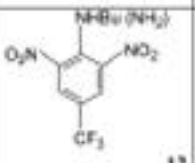
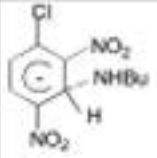
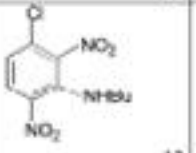
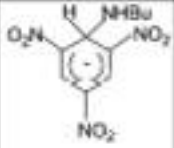
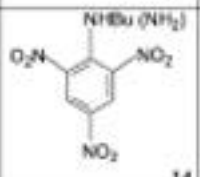
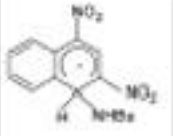
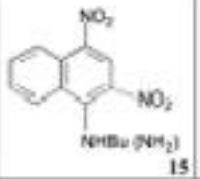
Furthermore, in some cases (Table 1, Entries 1−3 and 5), the yields of the substitution product are greater than the extent of nucleophilic attack. This can be attributed to a shift of the equilibrium of the first step to the right during the electrolysis.

From Table 1, it emerges that a limitation of the method would seem to be the low efficiency of the first step. Therefore, in an effort to improve efficiency, the reactions were carried out in the presence of several bases (nBu$_4$NF·3H$_2$O, Me$_4$NF, tBuOK). These bases are among the best suited for carrying out electrochemical experiments (their oxidations occur at very positive potentials). Use of the neutral base 1,4-diaza[2,2,2]bicyclooctane is not possible due to its lower oxidation potential (0.57 V vs. SCE).[13a] Indeed, its potential is very close to the oxidation potentials of the σ^H complexes. The results are summarized in Figure 1 and Table 2 (via B in Scheme 3).

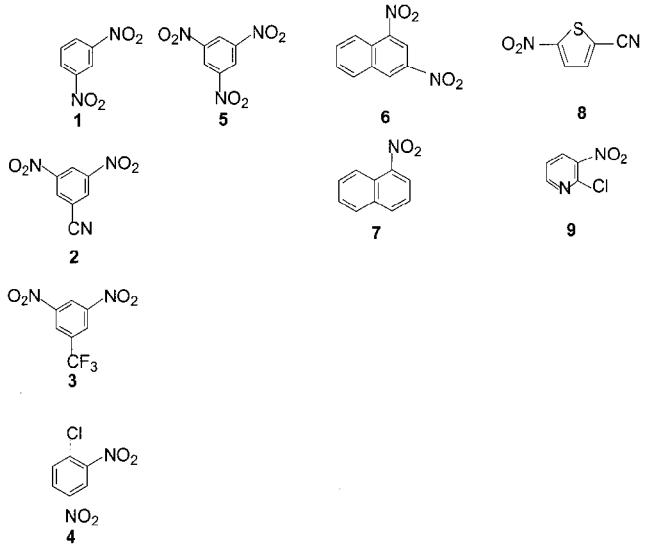
Figure 1 shows the electrochemical behaviour of nBuNH$_2$ alone (Figure 1a), a mixture of **1** and nBuNH$_2$ in the presence of tBuOK (Figure 1b), a mixture of **1** and nBuNH$_2$ in the presence of FTBA·3H$_2$O (Figure 1c), and pure 1,3-dinitrobenzene (**1**) (Figure 1d).

Figure 1a shows an irreversible one-electron wave at ca. 1.33 V vs. SCE in DMF. Figure 1b shows, starting with a reduction scan, no reduction waves, which implies that no starting material (Figure 1d) is present in the reaction mixture. An efficiency of 100% in the formation of the σ complex is observed. When the first scan is an oxidation scan, two oxidation waves are observed at 0.61 V and 1.33 V, the latter corresponding to the excess amine present in the mixture. The oxidation peak at 0.61 V must be assigned to the corresponding σ^H complex (Table 2, Entry 1) because during a second reduction scan a reduction wave appears at ca. 0.93 V, which corresponds to the rearomatized amino compound, **10**. Figure 1c shows on the first cathodic scan a reversible wave at −0.88 V, which corresponds to the unreacted starting material **1** (Figure 1d). The percentage of nucleophilic attack can be calculated by a comparison of

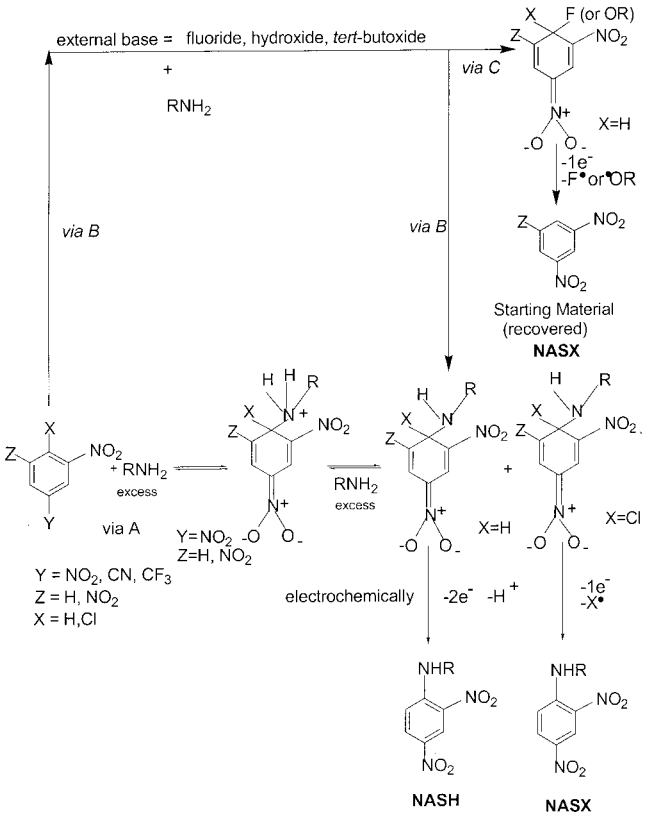
Table 1. Exhaustive electrolysis of σ complexes (at oxidation peak plus ca. 100 mV) obtained by reactions of nitroaromatic compounds with nBuNH$_2$

Entry	Nitro-arene	NuH (nitro arene:NuH)	% [a] σ-complexes [b]	σ^H-Complex	E_{pa} [c] (V) σ^H-Complex	NASH Products	% [d] Yield NASH products [% yield] [f]	r = [NASH-product]/[σ-compl.]
1	**1**	BuNH$_2$ ($1:10^4$)	30		0.62	 **10**	30 (5) [e] [86]	1.0 (0.2)
2	**2**	BuNH$_2$ (1:6)	45	 C-2  C-4	1.03 1.21	 **11a,b**	39 (**11b**) (3) [e] 10% (**11a**) [77]	1.1 (0.3)
3	**3**	BuNH$_2$ (1:6)	36		1.18	 **12**	34 (6) [e] [85]	0.9 (0.2)
4	**4**	BuNH$_2$ (1:2)	43		1.12	 **13**	15 [15]	0.2
5	**5**	BuNH$_2$ (1:3)	30		1.12	 **14**	30 (6) [e] [83]	1.0 (0.2)
6	**6**	BuNH$_2$ (1:16)	100		0.80	 **15**	84 (5) [94]	0.8 (0.05)

[a] Under the initial conditions (fast equilibrium). [b] The σ complexes were carefully prepared by addition of the nucleophile to solutions of the nitroarene (25 mM) in DMF + 0.1 M nBu$_4$NBF$_4$ under an inert gas at 13 °C. [c] Working electrode: graphite. [d] The oxidation products were analysed by cyclic voltammetry vs. SCE (1 Vs^{-1}), gas chromatography/mass spectrometry, and ^{1}H NMR. The preparative yields are 5−10% lower. [e] During the electrolysis, the equilibrium of the first step (Scheme 1) will be shifted to the right. [f] Yields based on unrecovered starting material.



Scheme 2



Scheme 3

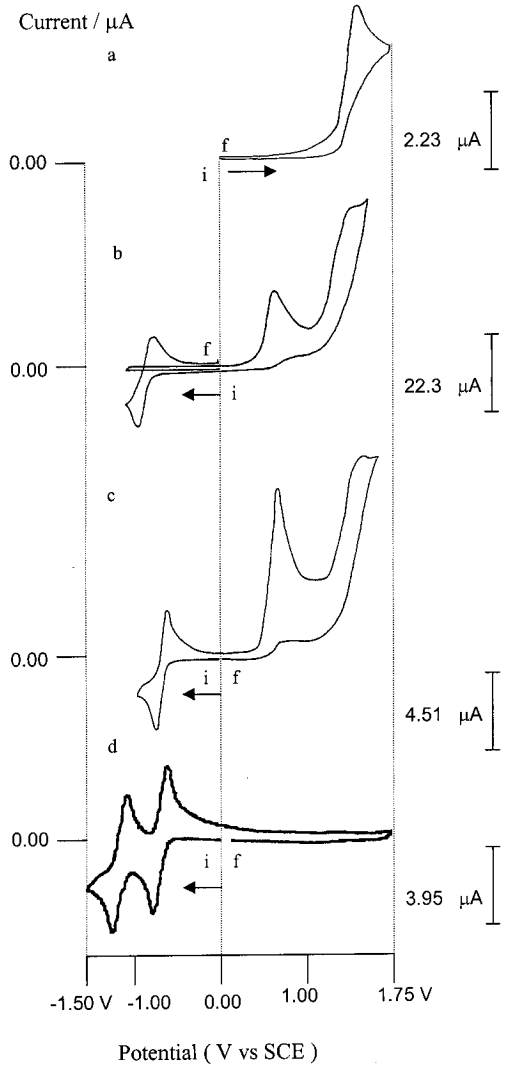


Figure 1. (a) Cyclic voltammetry of nBuNH$_2$ (10.0 mM) in DMF + 0.1 M nBu$_4$NBF$_4$ at 10 °C; scan rate 0.5 Vs^{-1}, glassy carbon disc electrode (0.05 mm diameter); the scan is in the potential range: 0.00/1.75/0.00 V; (b) cyclic voltammetry of a mixture of **1** (20.0 mM) and nBuNH$_2$ in the presence of tBuOK (1:5:2) in DMF + 0.1 M nBu$_4$NBF$_4$ under an inert gas at 10 °C; scan rate 1.0 Vs^{-1}, glassy carbon disc electrode (0.05 mm diameter); the scan is in the potential range: 0.00/−1.00/1.70/0.00 V (2 cycles); (c) cyclic voltammetry of a mixture of **1** (20.0 mM) and nBuNH$_2$ in the presence of nBu$_4$NF·3H$_2$O (1:5:5) in DMF + 0.1 M nBu$_4$NBF$_4$ under an inert gas at 10 °C; scan rate 1.0 Vs^{-1}, glassy carbon disc electrode (0.05 mm diameter); the scan is in the potential range: 0.00/−1.00/1.70/0.00 V; (d) cyclic voltammetry of **1** (6.0 mM) in DMF + 0.1 M nBu$_4$NBF$_4$ at 13 °C; scan rate 1.0 Vs^{-1}, glassy carbon disc electrode (0.05 mm diameter); the scan is in the potential range: 0.00/−1.50/1.75/0.00 V

the peak intensities at −0.88 V (Figure 1c and d). On the cathodic scan, two waves appear at 0.71 V and 1.33 V (nBuNH$_2$). Note that the first one corresponds to a mixture of adducts, where the minor σ complex is the butylamine Meisenheimer adduct (25% of the amino compound was found; Table 2, Entry 2).

In this case, a definitive quantification had to be performed after the electrolysis of the sample. The analysis and yield determination of the NASH product and the recovered starting material (from O-adducts/F-adducts and the starting material that had not reacted) allow us to calculate in a simple and quantitative way the concentration and nature of each σ complex.

To assess the influence of the presence of base, fivefold excesses of nBuNH$_2$, nHexNH$_2$, and AcNH$_2$ were tested as nucleophiles. The reaction was extended to one nitronaphthalene **7**, one nitrothiophene **8**, and one nitropyridine **9**. In

Table 2. Exhaustive electrolysis of σ complexes (at oxidation peak plus ca. 100 mV) obtained by reactions of nitroaromatic compounds with various amines and amides in the presence of difference bases

[a] Under the initial conditions (fast equilibrium). [b] The σ complexes were carefully prepared by addition of the nucleophile to solutions of the nitroarene (25 mM) in DMF + 0.1 M nBu_4NBF_4 under an inert gas at 13 °C. [c] Working electrode: graphite. [d] The oxidation products were analysed by cyclic voltammetry vs. SCE (1 $V \cdot s^{-1}$), gas chromatography/mass spectrometry, and ^1H NMR. The preparative yields are 5−10% lower. [e] During the electrolysis, the equilibrium of the first step (Scheme 1) will be shifted to the right. [f] Oxidative nitro group substitution involving a σ^X complex is observed (S_NAr reaction involving replacement of a nitro group by an amide anion nucleophile). [g] *N*-Butyl-3-nitro-2-pyridinamine was also obtained as a major product (42%) (after exhaustive electrolysis, replacement of the chloro substituent by amine occurred in a NASX process). [h] Yields based on unrecovered starting material.

all cases, the extent of nucleophilic attack by the amine (σ complex formed under the initial conditions) was found to increase considerably (Table 2, column 4). In this sense, the best results were achieved when the strongest base (*tert*-butoxide) was used. Using primary amines or amides, the yields were better in the presence of base than in its absence (e.g. 49% vs. 30% for **10**; Table 1, Entry 1 and Table 2, Entry 1, respectively). These yields are rather good considering that unchanged starting material is recovered and that the experimental procedure is very simple. The reactivity depends on the electrophilic character of the starting material, **5** being more reactive than **1** (Table 2, Entries 9 and 5) and **1** being more reactive than **7** (Table 2, Entries 1 and 6). The reactivity also depends on the size of amine (*n*HexNH$_2$ is less reactive than *n*BuNH$_2$; Table 2, Entries 1 and 4).

In the presence of base, the percentage of nucleophilic attack increases considerably. However, this is not only due to attack by the nucleophile, but also due to attack by the excess base (Table 2, Entries 1−4). This fact is of no significance from the point of view of the preparative reaction, since, as we have seen, the electrochemical oxidation of the oxygen or fluoride σ adducts leads to the initial nitroaromatic compound[13b] (via C in Scheme 3).

It is remarkable that in both the absence and presence of external base (*tert*-butoxide or fluoride), the reaction is totally regioselective. An exception is found in the case of amides in the presence of an external base, where the reaction is less regioselective and substitution of a nitro group by an amide group occurs (Table 2, Entries 5 and 9). When 2-chloro-3-nitropyridine (**9**) is used (Table 2, Entry 8), we observe 42% of the NASX product *N*-butyl-3-nitro-2-pyridinamine, arising from replacement of the chloro substituent by the amine. Moreover, in some cases (Table 2, Entries 7 and 10), the yields of the substitution products are greater than those of the product of nucleophilic attack. This can be attributed to a shift of the equilibrium of the first step to the right during electrolysis.

In most cases (Tables 1 and 2), small amounts of the NH$_2$ compounds are obtained as by-products (1−15%). This is due to the exhaustive oxidation of the mixture, which can result in oxidation of the first amino product formed by σ^H complex oxidation, leading to oxidative cleavage of the C−N bond.[14] When exhaustive electrolysis was carried out at 1.6 V, only NH$_2$ derivatives were obtained.

Finally, a comparison between chemical[7b] and electrochemical oxidation is presented (Table 3). When the oxidation potential of σ^H complexes is lower than 0.60 V, chemical oxidation is a useful process in spite of the fact that no starting material can be recovered (Table 3, Entry 1). Electrochemical oxidation (Table 3, Entry 2) allow us to recover the starting material, and no secondary products are found, hence it seems to be a more suitable oxidation process. However, the power of the electrochemical oxidation is shown in Entry 4, where a 90% yield of the NASH product was obtained, as compared to just 34% in Entry 3 (chemical process). The electrooxidation is more convenient when the oxidation peak potentials of the σ^H complexes are more positive than 0.6 V vs. SCE.

Conclusion

Our electrochemical approach offers a new and very selective methodology in the field of the synthesis of aromatic amino derivatives. Through selective electrochemical oxidation, we can obtain the NASH product (lower oxidation potential of the intermediate) or the NASX product. The σ^H complex can be oxidized in a selective way. The excess amine present in the mixture in not oxidized because the oxidation potential for primary amines is about 1.50 V vs. SCE. In all cases, the oxidation potential peak of the σ complex is lower than this. Furthermore, the use of electrochemical oxidation is the only way to achieve oxidation potentials higher than 0.70 V and, as can be seen in the tables, many polynitro-substituted σ complexes have oxidation potentials higher than this.

The success of this synthetic method can be attributed to two factors, firstly the control of the quantity of the amine used, and second, the careful control over the oxidation process. In this way, alkyl aniline products are obtained in fair to good yields. Exhaustive oxidative electrolysis leads to the dealkylated anilines in what constitutes a new, formally "chlorine-free" route.

Table 3. Chemical[7b] vs. electrochemical oxidation

Entry	Nitroarene	NuH + base (nitroarene/NuH/base)	Time	Type of oxidation chemical ($KMnO_4$)	Type of oxidation electro-chem.	E_{pa} [V] σ^H complex	NASH product (yield)	Recovered starting material
1	**1**	BuNH$_2$ + FTBA·3H$_2$O (1:5:5)	1.5h	yes		0.62	**10** (63%)	−
2	**1**	BuNH$_2$ + *t*BuOK (1:5:2)	1.5h		yes	0.62	**10** (49%)	46%
3	**6**	BuNH$_2$ + FTBA·3H$_2$O (1:5:5)	4.5h	yes		0.80	**15** (34%)	53%
4	**6**	BuNH$_2$ (1:16)	1.5h		yes	0.80	**15** (84%)	11%

Experimental Section

General Remarks

Electrochemical Measurements: The electrochemical cell and measurement procedures for cyclic voltammetry have been described previously.[15] All the potentials are reported vs. an aqueous saturated calomel electrode. A glassy carbon disc was used as the working electrode (0.05 mm diameter). Electrolyses were carried out using a PAR 273A potentiostat. A graphite rod was used as the working electrode.

Materials: DMF (SDS, "pour syntheses peptidiques") and nBu$_4$NBF$_4$ (Fluka, puriss.) were used without purification. 1,3-Dinitrobenzene (**1**), 3,5-dinitrobenzonitrile (**2**), α,α,α-trifluoro-3,5-dinitrotoluene (**3**), 1-chloro-2,4-dinitrobenzene (**4**), 1,3-dinitronaphthalene (**6**), and 1-nitronaphthalene (**7**) were purchased from Aldrich; 1,3,5-trinitrobenzene (**5**) was from Supelco; 5-nitrothiophene-2-carbonitrile (**8**) was from Lancaster; 2-chloro-3-nitropyridine (**9**) was from Acros Organics. Butylamine (nBuNH$_2$) and hexylamine (HexNH$_2$) (Aldrich); acetamide (AcNH$_2$) (Fluka); potassium *tert*-butoxide (Aldrich); tetramethylammonium fluoride (Me$_4$NF) and tetrabutylammonium fluoride trihydrate (nBu$_4$NF·3H$_2$O) (Aldrich) were obtained commercially as indicated.

General Procedure for NASH in Nitroarenes: A solution of the nitroarene (20 mM) in DMF (5 mL), which contained 0.1 M NBu$_4$BF$_4$ (0.1646 g) as a supporting electrolyte, was prepared under nitrogen. The corresponding σ^H complex was prepared by careful addition of the nucleophile (butylamine, acetamide, or butylamine/base, hexylamine/base, or acetamide/*tert*-butoxide mixtures) to the solution of the nitroarene under nitrogen. The oxidation peak potentials of the σ^H complexes were measured by cyclic voltammetry. Electrolysis was then carried out at potentials ca. 100 mV more positive than the value measured for each σ^H complex, using a graphite rod as the working electrode. The electrolysis was stopped when the starting material had been completely consumed and the mixture was subsequently partitioned between water and toluene. The organic layer was dried with Na_2SO_4 and the solvents were evaporated to leave a residue that was analysed by gas chromatography. The analysis showed the presence of nitro compounds. The final products were analysed by gas chromatography/mass spectrometry, ^{1}H NMR, and cyclic voltammetry, and were identified by comparison of their spectroscopic properties with those reported in the literature. The product yields were not optimized and were calculated by gas chromatography and by cyclic voltammetry, after verifying from the ^{1}H NMR spectrum of the crude product that only the substitution products and starting material were present.

Generation of 15 by Preparative Electrolysis: A solution of 1,3-dinitronaphthalene (70 mg) in DMF (7 mL), which contained 0.1 M Et$_4$NBF$_4$ (0.1519 g) as a supporting electrolyte, was prepared under nitrogen. The corresponding σ^H complex was prepared by careful addition of the nucleophile (butylamine, 510 mg) to the solution of the nitroarene under nitrogen. The crude product [or mixture of product(s) and reactants] was purified or separated by silica gel chromatography using chloroform as the eluent. *N*-Butyl-2,4-dinitro-1-naphthalenamine (**15**) was obtained as the main product (65 mg, 70%). As a minor product, 2,4-dinitro-1-naphthalenamine (**28**, 5 mg, 7%) was also obtained. Moreover, (10 mg, 14%) of the unreacted starting material, 2,4-dinitronaphthalene (**6**), was recovered.

Reaction Products

***N*-Butyl-2,4-dinitroaniline (10):**[16] Table 1, Entry 1 and Table 2, Entries 1−3. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 8.96 (d, J = 2.9 Hz, 1 H), 8.39 (s, 1 H), 8.20 (dd, J = 9.50, J = 2.20 Hz, 1 H), 7.05 (d, J = 9.50 Hz, 1 H), 3.13 (t, J = 6.25 Hz, 2 H), 1.58 (m, J = 6.25 Hz, J = 7.50 Hz, 2 H), 1.39 (m, J = 7.50 Hz, J = 6.90 Hz, 2 H), 1.13 (t, J = 6.90 Hz, 3 H). MS (70 eV): m/z (%) = 239 (17) [M]$^+$, 197 (10), 196 (100), 180 (6), 178 (5), 166 (7), 150 (10), 150 (10), 104 (9), 92 (6), 77 (9), 65 (5), 51 (5), 43 (5).

4-Butylamine-3,5-dinitrobenzonitrile (11a):[17] Table 1, Entry 2. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 9.15 (s, 1 H), 8.75 (s, 1 H), 3.13 (t, J = 6.25 Hz, 2 H), 1.58 (m, J = 6.25 Hz, J = 7.50 Hz, 2 H), 1.38 (m, J = 7.50 Hz, J = 6.90 Hz, 2 H), 1.13 (t, J = 6.90 Hz, 3 H). MS (70 eV): m/z (%) = 264 (16) [M]$^+$, 265 (12), 221 (75), 205 (32), 163 (16), 130 (15), 88 (17), 76 (13), 71 (35), 55 (15), 43 (100), 41 (58).

2-Butylamine-3,5-dinitrobenzonitrile (11b): Table 1, Entry 2. MS (70 eV): m/z (%) = 264 (13) [M]$^+$, 265 (3), 222 (11), 221 (100), 205 (13), 191 (10), 163 (9), 129 (24), 117 (15), 102 (18), 75 (10), 71 (18), 56 (14), 43 (27), 41 (30).

***N*-Butyl-2,6-dinitro-4-(trifluoromethyl)aniline (12):**[18] Table 1, Entry 3. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 9.09 (s, 1 H), 8.50 (s, 1 H), 3.00 (t, J = 6.25 Hz, 2 H), 1.68 (m, J = 6.25 Hz, J = 7.50 Hz, 2 H), 1.44 (m, J = 7.50 Hz, J = 6.90 Hz, 2 H), 0.96 (t, J = 6.90 Hz, 3 H). MS (70 eV): m/z (%) = 307 (13) [M]$^+$, 308 (2), 272 (16), 265 (8), 264 (81), 249 (4), 248 (37), 235 (9), 231 (10), 206 (21), 189 (12), 188 (12), 187 (12), 174 (13), 171 (15), 160 (17), 159 (23), 146 (10), 144 (22), 142 (11), 127 (7), 126 (10), 125 (7), 105 (13), 95 (6), 75 (11), 71 (57), 57 (10), 56 (10), 44 (13), 43 (100), 41 (66).

***N*-Butyl-3-chloro-2,6-dinitroaniline (13):** Table 1, Entry 4. This product could not be isolated and was tentatively assigned by GC/MS. MS (70 eV): m/z (%) = 273 (17) [M]$^+$, 275 (5), 274 (4), 230 (100), 214 (15), 213 (13), 184 (10), 171 (8), 156 (9), 137 (16), 126 (14), 102 (10), 90 (8), 75 (18), 71 (17), 51 (5), 43 (24).

***N*-Butyl-2,4,6-trinitroaniline (14):**[19] Table 1, Entry 5. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 9.19 (s, 1 H), 8.67 (s, 1 H), 3.13 (t, J = 6.25 Hz, 2 H), 1.58 (m, J = 6.25 Hz, J = 7.50 Hz, 2 H), 1.39 (m, J = 7.50 Hz, J = 6.90 Hz, 2 H), 1.13 (t, J = 6.90 Hz, 3 H). MS (70 eV): m/z (%) = 284 (17) [M]$^+$, 249 (23), 241 (100), 225 (47), 212 (13), 149 (17), 137 (19), 91 (16), 71 (34), 43 (54).

***N*-Butyl-2,4-dinitro-1-naphthalenamine (15):**[20] Table 1, Entry 6. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 9.73 (s, 1 H), 9.16 (s, 1 H), 8.75 (dd, J = 8.60 Hz, J = 0.70 Hz, 1 H), 8.32 (dd, J = 8.60 Hz, J = 0.70 Hz, 1 H), 7.80 (td, 1 H), 7.56 (td, 1 H), 3.89 (t, J = 6.80 Hz, 2 H), 1.68 (m, J = 6.80 Hz, J = 7.50 Hz, 2 H), 1.44 (m, J = 7.50 Hz, J = 6.90 Hz, 2 H), 0.96 (t, J = 6.90 Hz, 3 H). MS (70 eV): m/z (%) = 289 (58) [M]$^+$, 290 (10), 246 (38), 230 (24), 229 (100), 212 (22), 199 (14), 184 (10), 169 (19), 155 (24), 154 (20), 142 (12), 141 (30), 140 (22), 130 (13), 129 (16), 128 (34), 126 (25), 116 (14), 115 (19), 114 (27), 113 (16), 102 (13), 101 (14), 77 (12), 75 (13), 63 (13), 55 (10), 43 (22), 41 (36).

***N*-Hexyl-2,4-dinitroaniline (16):**[7] Table 2, Entry 4. ^{1}H NMR (250 MHz, CD$_3$CN): δ = 8.96 (d, J = 2.68 Hz, 1 H), 8.22 (dd, J = 9.55 Hz, 2.68 Hz, 1 H), 7.10 (d, J = 9.55 Hz, 1 H), 3.45 (q, J = 6.25 Hz, 2 H), 1.75 (m, 2 H), 1.38 (m, 6 H), 1.13 (t, J = 7.25 Hz, 3 H). MS (70 eV): m/z (%) = 267 (14) [M]$^+$, 232 (4), 204 (3), 196 (100), 190 (9), 180 (19), 177 (12), 166 (11), 150 (10), 104 (11), 92 (7), 77 (10), 43 (12).

***N*-(2,4-Dinitrophenyl)acetamide (17):**[21] Table 2, Entry 5. ^{1}H NMR (250 MHz, CD_3CN): δ = 10.10 (s, 1 H), 8.91 (s, 1 H), 8.72 (d, *J* = 8.80 Hz, 1 H), 8.21 (d, *J* = 8.80 Hz, 1 H), 3.01 (s, 3 H). MS (70 eV): *m*/*z* (%) = 224 (12) $[M]^+$, 226 (2), 183 (27), 167 (3), 153 (11), 137 (1), 107 (7), 91 (8), 63 (11), 53 (8), 43 (100). Quality identification 91%.[22]

***N*-Butyl-1-nitro-2-naphthalenamine (18):**[23] Table 2, Entry 6. MS (70 eV): *m*/*z* (%) = 244 (75) $[M]^+$, 245 (13), 211 (5), 209 (6), 202 (10), 201 (75), 184 (15), 182 (10), 173 (16), 171 (15), 168 (14), 156 (30), 155 (100), 153 (31), 143 (11), 129 (20), 128 (58), 127 (34), 116 (12), 115 (37), 114 (12), 101 (15), 77 (16), 41 (17).

4-Butylamine-5-nitro-2-thiophenecarbonitrile (19):[23] Table 2, Entry 7. ^{1}H NMR (250 MHz, CD_3CN): δ = 7.61 (s, 1 H), 7.21 (s, 1 H), 3.14 (t, *J* = 6.25 Hz, 2 H), 1.59 (m, *J* = 6.25 Hz, *J* = 7.50 Hz, 2 H), 1.39 (m, *J* = 7.50 Hz, *J* = 6.90 Hz, 2 H), 0.97 (t, *J* = 6.90 Hz, 3 H). MS (70 eV): *m*/*z* (%) = 225 (46) $[M]^+$, 226 (6), 227 (3), 180 (8), 182 (100), 187 (7), 156 (16), 164 (10), 154 (10), 152 (31), 137 (14), 136 (24), 125 (18), 152 (31), 137 (14), 136 (24), 125 (18), 124 (13), 110 (13), 109 (42), 96 (12), 83 (19), 77 (26), 71 (23), 70 (37), 51 (13), 45 (16), 43 (45), 41 (45).

***N*-Butyl-2-chloro-3-nitro-4-pyridinamine (20):**[23] Table 2, Entry 8. ^{1}H NMR (250 MHz, CD_3CN): δ = 8.37 (d, *J* = 9.00 Hz, 1 H), 6.45 (d, *J* = 9.00 Hz, 1 H), 6.06 (s, 1 H), 3.30 (t, *J* = 6.25 Hz, 2 H), 1.58 (m, *J* = 6.25 Hz, *J* = 7.50 Hz, 2 H), 1.40 (m, *J* = 7.50 Hz, *J* = 6.90 Hz, 2 H), 0.94 (t, *J* = 6.90 Hz, 3 H). MS (70 eV): *m*/*z* (%) = 230 (2) $[M]^+$, 231 (6), 229 (16), 200 (13), 194 (16), 188 (32), 187 (19), 186 (100), 173 (22), 154 (6), 140 (20), 140 (60), 112 (11), 76 (11), 41 (19).

***N*-(2,4,6-Trinitrophenyl)acetamide (21):**[24] Table 2, Entry 9. ^{1}H NMR (250 MHz, CD_3CN): δ = 10.28 (s, 1 H), 9.22 (s, 1 H), 2.28 (s, 3 H). MS (70 eV): *m*/*z* (%) = 240 (1), 238 (1), 237 (5), 236 (37), 198 (14), 195 (3), 194 (32), 122 (2), 148 (5), 77 (2), 67 (2), 52 (3), 43 (100). MS (chemical ionization, CH_4, NH_3): *m*/*z* (%) = 270 (100) $[M]^+$, 284 (15), 253 (47), 235 (78), 223 (31), 205 (47), 187 (15), 141 (84).

2-Hexylamine-3,5-dinitrobenzonitrile (22): Table 2, Entry 10. This product could not be isolated and was tentatively assigned. ^{1}H NMR (250 MHz, CD_3CN): δ = 9.06 (d, *J* = 2.85 Hz, 1 H), 8.96 (s, 1 H), 8.63 (d, *J* = 2.85 Hz, 1 H), 3.45 (q, *J* = 6.25 Hz, 2 H), 1.75 (m, 2 H), 1.38 (m, 6 H), 1.13 (t, *J* = 7.25 Hz, 3 H). MS (70 eV): *m*/*z* (%) = 292 (6) $[M]^+$, 257 (3), 245 (3), 221 (100), 217 (10), 208 (11), 205 (39), 191 (15), 175 (14), 163 (10), 129 (19), 117 (11), 102 (12), 99 (12), 81 (14), 56 (12), 43 (25).

Minor Products Obtained (1−15%)

2,4-Dinitroaniline (23): Table 1, Entry 1 and Table 2, Entries 1−3. MS (70 eV): *m*/*z* (%) = 183 (100) $[M]^+$, 153 (44), 107 (22), 91 (64), 65 (14), 66 (11), 65 (14), 64 (51), 63 (38), 52 (73), 41 (24). Quality identification 99%.[22]

2,4,6-Trinitroaniline (24): Table 1, Entry 5. MS (70 eV): *m*/*z* (%) = 228 (100) $[M]^+$, 212 (2), 199 (2), 198 (27), 166 (5), 152 (4), 135 (12), 90 (58), 89 (12), 63 (34), 52 (17), 51 (11). Quality identification 95%.[22]

2,6-Dinitro-4-(trifluoromethyl)aniline (25): Table 1, Entry 3. MS (70 eV): *m*/*z* (%) = 251 (100) $[M]^+$, 221 (13), 189 (19), 175 (11), 159 (36), 140 (10), 127 (10), 89 (10), 81 (10), 52 (31), 44 (17). Quality identification 95%.[22]

2-Amino-3,5-dinitrobenzonitrile (26): Table 1, Entry 2. MS (70 eV): *m*/*z* (%) = 208 (100) $[M]^+$, 178 (31), 162 (14), 132 (23), 116 (61), 104 (15), 89 (49), 88 (19), 77 (32), 62 (17), 61 (13), 53 (11), 52 (32).

1-Nitro-2-naphthalenamine (27): Table 2, Entry 6. MS (70 eV): *m*/*z* (%) = 188 (54) $[M]^+$, 171 (3), 158 (9), 142 (16), 131 (23), 115 (100), 103 (15), 89 (10), 77 (8), 63 (10). Quality identification 95%.[22]

2,4-Dinitro-1-naphthalenamine (28): Table 1, Entry 6. MS (70 eV): *m*/*z* (%) = 233 (100) $[M]^+$, 234 (12), 203 (24), 157 (19), 141 (42), 140 (42), 129 (33), 128 (10), 114 (57), 113 (22), 88 (12), 63 (15).

Acknowledgments

Financial support from the DGI (MCyT of Spain) through project BQU2000-0336 and from the "Generalitat de Catalunya" through project 1999-SGR00090 is gratefully acknowledged.

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Received May 25, 2001
[O01253]