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Article

Electrochemical Behavior of a Nitrobenzenesulfonyl Derivative of Aniline in Aqueous Solution

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O mecanismo de redução do composto N-fenil-4-nitrobenzenosulfonamida foi investigado em meio aquoso por polarografia de corrente direta e pulso diferencial, voltametria cíclica e coulometria a potencial controlado. Em $pH < 10$, o composto é reduzido em uma única etapa de 4 elétrons. Entretanto duas etapas de redução são verificadas em elevados valores de pH ($pH > 11$). A redução do grupo nitro à hidroxilamina na molécula é sempre o processo preponderante no mecanismo eletródico.

The electrochemical behavior of aniline protected by a nitrobenzene sulphonyl group in aqueous solution at a mercury electrode is reported. At $pH < 10$ the compound was reduced in a single well-defined step. Reduction of the nitro group involving a preceding protonation step was postulated. Two reduction steps are present at higher pH ($pH > 11$). Controlled potential electrolysis confirms that the reduction of the nitro group in a four-electron step to N-phenyl-4-hydroxylamine sulphonamide is always the preponderant process.

Keywords: *nitrobenzenesulphonamide, cathodic cleavage, amine unprotection*

Introduction

Electrochemical cleavage method using controlled potential electrolysis at a cathode under milder conditions as a selective way of removing reducible protecting groups has been investigated as a possible alternative to the drastic methods often used, such as alkali metal solutions, high temperature, and very acidic solutions, which can lead to degradation or racemisation in the molecule[1,2].

The cathodic cleavage of amines and amino-acids protected by a nitrobenzenesulphonyl group has been electrochemically investigated in recent years with the aim of studying a simple method of unprotection of the amino functional group[3-5]. In these studies, the reduction of N-butyl-2-, 3- or 4-nitro- benzenesulphonamide[3]; N,N-di-n-butyl-4-nitrobenzenesulphonamide; and N-phenyl -2-, 3-, or 4-nitrobenzenesulphonamide[5], and 4-nitrobenzenesulphonyl-alanine and 4-nitrobenzenesulphonyl-phenylalanine in N,N-dimethyl-formamide[4] has been investigated. In previous papers it is possible to ascertain that the electrochemical removal of the nitrobenzenesulphonyl group in an aprotic system occurs by S-N bond cleavage (essential for unprotection of amine or aminoacid), but it is greatly affected by the proton availability and features of the R group of the resulting amidic group. In general, a reduction mechanism of nitrobenzenesulphonyl derivatives of aliphatic amines and amino acids in N,N-dimethylformamide (DMF) leading to cleavage of the S-N bond after a two-electron transfer is always preponderant. However, the competitive N-H bond cleavage makes the electrochemical unprotection method unsuitable for aromatic amines, as cleavage of the S-N bond is not the major process.

The protection of an amine function is usually carried out by a reaction under slightly alkaline conditions. Although the control of pH is very important because it can facilitate the isolation of the electrochemical cleavage products easily, there are very few studies involving aqueous medium in the literature. Thus, it is the aim of the present work to describe the electrochemical behavior of an aromatic amine protected by the 4-nitrobenzenesulphonyl group in aqueous solution, as a simplest model to understand complex organic molecules.

Experimental

The N-phenyl-4-nitrobenzenesulphonamide was prepared from the corresponding nitrobenzenesulphonyl chloride and aniline in 5% KOH following a procedure developed by Schreiber *et al.*[6]. The product was recrystallized from 95% ethanol and dried under vacuum. It was checked for melting point, IR, nuclear magnetic resonance spectroscopy, and elemental analysis.

The supporting eletrolyte used was Britton-Robinson (B-R) buffer, prepared by mixing a solution containing 0.04 M orthophosphoric acid, 0.04 M acetic acid, and 0.04 M boric acid with the appropriate volume of 0.2 M sodium hydroxide solution.

The electrochemical measurements were made using an EG & PAR model 264 A polarographic analyzer and an EG & PAR model RE 0031 x-y recorder. An EG & PAR - 303 A stand was used in the DME mode for polarography and HMDE for cyclic voltammetry. The three-electrode system was completed using a glassy carbon auxiliary electrode and an Ag/AgCl (3 M KCl) reference electrode. The controlled-potential electrolysis was carried out in a three-compartment cell with a mercury pool cathode. The UV spectra were recorded on a Perkin Elmer Coleman 575 spectrophotometer.

All pH measurements were made with a Metrohm E 500 pH meter with a Metrohm EA 121 glass electrode, previously calibrated.

The differential-pulse mode was used with a pulse amplitude of 50 mV, a drop time (t_d) of 1 s and a scan rate of 3 mV s^{-1}, unless stated otherwise.

Results and Discussion

Polarography

The electrochemical reduction of aniline protected by a 4-nitrobenzenesulphonyl group was investigated using an aqueous solution in the pH range 2-12. Direct current (dc) and differential pulse (dp) polarograms of 1 x 10^{-4}M of N-phenyl-4-nitrobenzenesulphonamide (NBA) exhibit a single wave in the pH range 2-10, attributed to the reduction of the nitro group, as shown in Fig. 1, Curve I. This peak becomes broader as the pH increases and becomes a double peak in a solution of pH 12 (Fig. 1, Curve II). The height of the wave (i1) remains slightly pH-dependent at pH < 9 and gradually decreases to one-fifth of its original height at pH 12 (Fig. 2, Curve b). Concomitantly the half-wave ($E_{1/2}$) or peak potential (E_p) shift linearly to more negative values (Fig. 2, Curve a), indicating that protonation of the nitro group was not restricted to acidic media. Slopes of the linear segments of the $E_{1/2}$ = f(pH) or E_p = f(pH) were 53 mV and 54 mV respectively.

The logarithmic analysis of the waves at pH 2, 4, 6 and 9 resulted in straight lines and the αn values of 1.48 (where n = number of electrons involved and α = transfer coeffi-

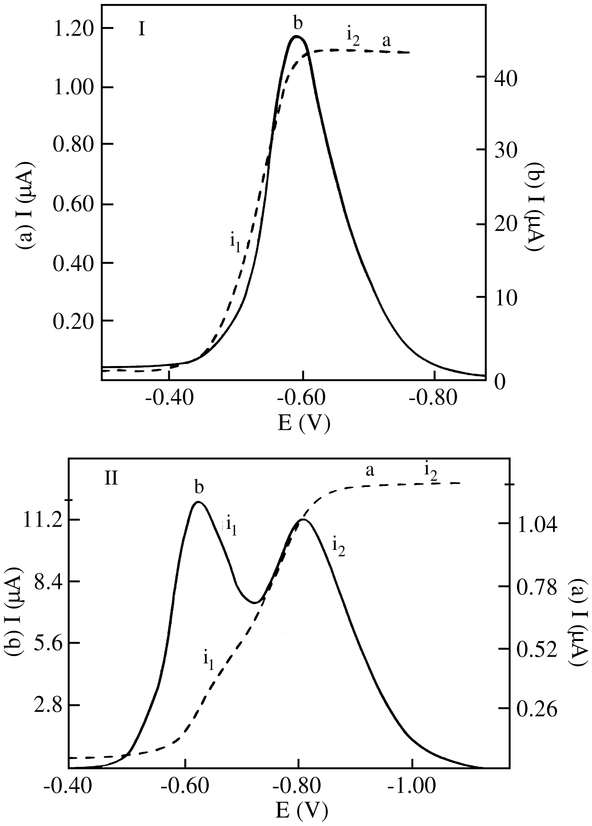

Figure 1. Response of N-phenyl-4-nitrobenzenesulphonamide (1.0 x 10^{-4} mol L^{-1}) in Britton-Robinson buffer pH 9.0 (Curve I) and pH 12.0 (Curve II): (a) direct current polarography and (b) differential pulse polarography.

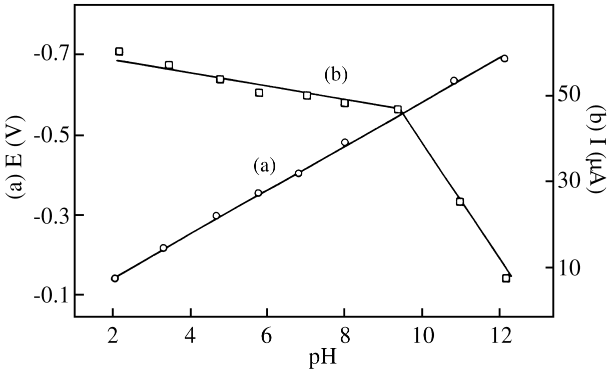

Figure 2. Dependence of the first peak potential (a) and peak current (b) obtained with a 1.0 x 10^{-4} mol L^{-1} N-phenyl-4-nitrobenzenesulphonamide solution on the pH.

cient) point to an irreversible behavior of the overall electrode process. The irreversibility of the system was confirmed by dp polarography. Values of $W_{1/2}$ (peak half-width) of approximately 102 mV were found for the range $2 < pH < 9$.

The process was found to be diffusion controlled, as shown by the linear plots of limiting current (i_l, by dc polarography) vs square root of height of the mercury reservoir and linear plots of peak current (i_p, by dp polarography) *vs.* $t^{2/3}$. Also plots of i_l and i_p vs NBA concentration exhibit good linearity over the range 2×10^{-5} to 1×10^{-3} M.

Cyclic voltammetry

The pH influence on the cyclic voltammetric behavior of NBA at a scan rate of 0.05 V s^{-1} is illustrated in Fig. 3. On the first cathodic scan (Fig. 3, Curve x and y) only one cathodic peak is seen at $2 < pH < 10$. Peak potentials of ip_{c1} are shifted by increasing the pH by about 54 mV/pH. The height of this wave diminishes by increasing the pH above 9, as verified previously.

On the reverse scan with the HMDE, an anodic peak (ip_{a1}) at -0.16 V is observed at $4.5 < pH < 10$ (Fig. 3y), but at lower pH values this peak is overlapped by the current of mercury dissolution (Fig. 3x). Linear plots of peak currents of ip_{c1} and ip_{a1} as a function of $\nu 1/2$ were obtained at pH 6.8 and 9.3 suggesting that the current is diffusion controlled. However the peak height (ip_{a1}) is only 30% or less of the peak current ip_{c1}.

On the second triangular voltage scan (Fig. 4), the peak potential of the cathodic reduction of the ip_{c1} is shifted by about 80 mV. The peak current ip_c* in the second cycle is about 30% lower than in the first. On subsequent scans, neither the height or potential peaks varies. However, at $pH > 4.5$ small additional cathodic peaks (ip_{c4} and ip_{c3}) are observed during the second cycle at potentials more positive than ip_{c1} (Fig. 4, Curve n). The peak ip_{c4} may be responsible for the corresponding reduction of the oxidation product readily apparent on the anodic sweep (ip_{a1}). The height of this peak increases gradually with increasing pH and concomitantly its potential is shifted to more negative potential. Whereas the Ep_{a1}-Ep_{c4} is always 29 mV indicating a reversible process involving 2 electrons. The ratio of peak currents ip_{c4}/ip_{a1} increases by increasing rate of voltage scanning reaching limits of 0.6 at 200 mV/s. The cathodic peak ip_{c3} is seen only on the subsequent scans (Fig. 4, Curve n). The anodic peak (ip_{a3}) on scan reverse is the mirror image of the cathodic peak reflected across the potential axis, clearly indicating the shape of the adsorption peaks[7]. This behavior suggests strong adsorption of the product generated in the successive scans.

Voltammograms recorded at a higher pH range (pH | 11) exhibited two cathodic peaks at potentials corre-

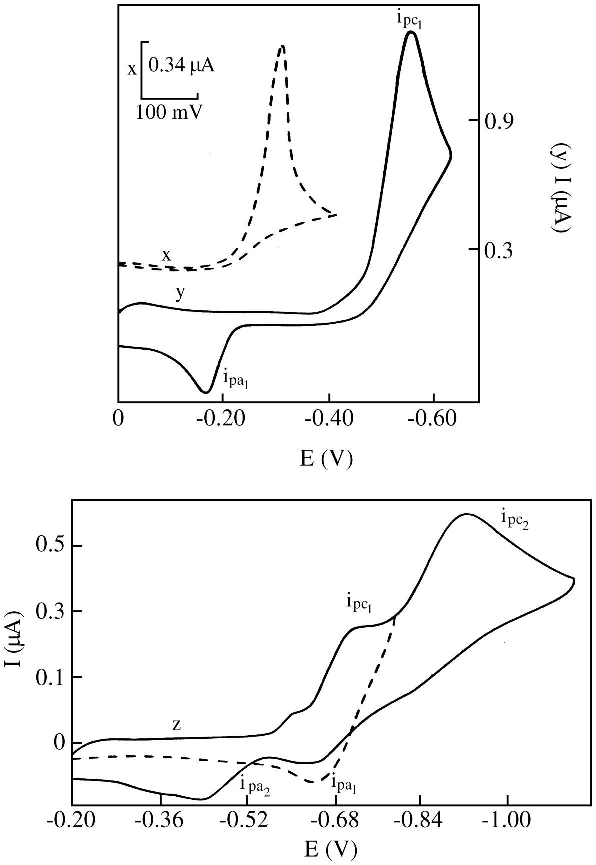

Figure 3. Typical cyclic voltammograms of N-phenyl-4-nitrobenzenesulphonamide 1.0×10^{-4} mol L^{-1} in B-R buffer: (x) pH 4.5; (y) pH 9.3 and (z) pH 12.0. Scan rate 50 mV/s.

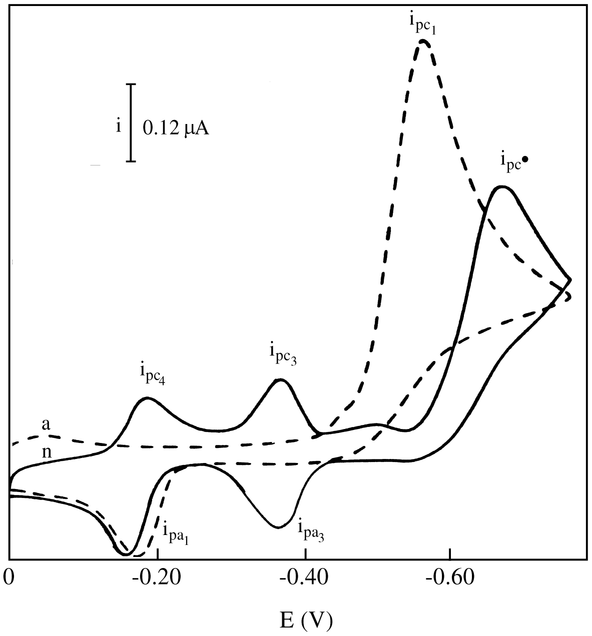

Figure 4. (a) Cyclic voltammogram of 1.0×10^{-4} mol L^{-1} solution of N-phenyl-4-nitrobenzenesulphonamide in B-R buffer pH 9.3 (n) and successive scans from 0-0.72 V. Scan rate 50 mV/s.

sponding to the two polarographic steps (Fig. 3z). A small oxidation peak (ip_{a1}) corresponding to the reoxidation of the first reduction product is readily apparent on the reverse scan. The ratio of the anodic - to - cathodic peak heights for this couple increased with the scan rate, indicating that the product of the first electron transfer reaction is consumed by a slow chemical reaction.

No significant anodic peak resulting from reoxidation of the second reduction step (ip_{c2}) was observed at any scan rate. Also the ratio between the magnitude of the second peak (ip_{c2}) and first peak (ip_{c1}) is almost constant. If switching of the negative sweep is held at the potential between the second (ip_{c2}) and first peak (ip_{c1}) before the complete sweep the behavior is practically the same, indicating the independent nature of both peaks. No anomalous behavior was verified on the successive scan, except a decrease in the peak current for both peaks due to diffusion problems.

Controlled potential electrolysis

Controlled potential electrolyses were carried out in a 1 mM solution of NBA using a mercury pool electrode. Taking into account the importance of understanding the reduction mechanism in sligthly alkaline solution, the electrolyses were performed in B-R buffer pH 9.3 at -1.0 V. The variation of current over a period of time was followed and the number of electrons consumed in the total reduction was determined. Values of n= 3.90 were obtained after three repetitions. A linear plot of log i vs time was obtained and the results show that four electrons are transferred in the reduction of NBA.

Aliquots of the electrolyzed solution were removed and nitrobenzensulphinate ion and aniline that could be formed by S-N bond cleavage and nitrobenzene produced as a result of the C-S bond cleavage were sought specifically. Nitrobenzenesulphinate was examined by the Smiles test[8]. Aniline and nitrobenzene were investigated by optical spectra. These products were not detected. However, taking into consideration the possible reduction of nitro group to hydroxylamine in aqueous solution, as predicted in the literature[9,10], the spectrophotometric spectra of the 1 x 10^{-4} M of NBA solution and the electrolyzed product were compared (see Fig. 5). At time intervals greater than 60 min the absorbance at 268 nm assigned to the nitro species was completely disappeared and the increase in absorbance at 236 nm attributed to the hydroxylamino compound occurred[9].

The product reduced by electrolysis at -1.0 V was titrated potentiometrically using potassium permanganate 0.0588 N. The end point occurs when about 1 equiv of permanganate is added to the electrolyzed solution resulting in an 80% yield . This finding supports the conclusion that the reduction of NBA in aqueous solution proceeds by preferential reduction of the nitro group to hydroxylamine.

Reduction mechanism

The foregoing experiments show that in N-phenyl-4-nitrobenzene sulphonamide, in contrast to the results obtained in an aprotic medium[3-5], the cleavage of S-N; N-H or C-S bonds are not predominating in the process in aqueous solution. On the other hand, as with other nitroaromatic compounds[9-14], the overall course of the reduction of the N-phenyl-4-nitrobenzenesulphonamide in aqueous solution probably involves the reduction of the nitro group to the hydroxylamine in a four electron process. The results can be explained by a scheme of the general mechanism for related nitro compounds[9-14]:

$$\text{R-NO}_2 + \text{H}^+ \rightleftharpoons \text{R-}\overset{+}{\text{N}}\text{O}_2\text{H} \qquad (1)$$

$$\text{R-}\overset{+}{\text{N}}\text{O}_2\text{H} + 3\text{H}^+ + 2\,\text{e-} \rightleftharpoons \text{R-NO} + \text{H}_2\text{O} \qquad (2)$$

$$\text{R-NO} + 2\text{H}^+ + 2\text{e-} \rightleftharpoons \text{R-NHOH} \qquad (3)$$

At 2 < pH < 10, the nitro group of NBA is reduced first to a hydroxylamine group in a single four-electron wave (Eqs. 1-3). This is consistent with n = 4 found by controlled potential eletrolysis. The pH dependence of half-wave potentials indicates that reduction of NBA involves preprotonation of the nitro group. The protons involved in the reaction have been determined and values of 1.3 were obtained[15]. It is possible to suggest a process involving one proton (Eq. 1), in which a corresponding equilibrium reaction is responsible for the decrease of the wave in alkaline solution and the appearance of another reduction step at more negative potential at pH 12. This indicates that the

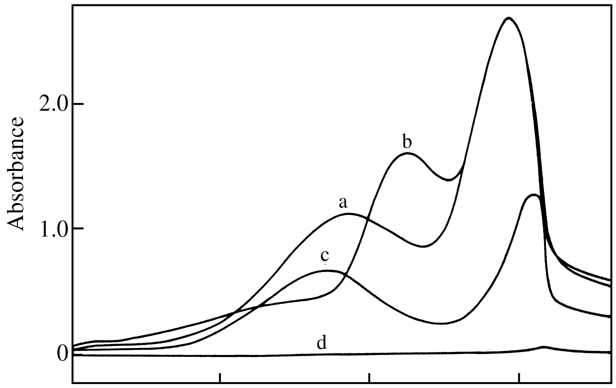

Figure 5. (a) UV spectrum of 1 x 10^{-3} mol L^{-1} N-phenyl-4-nitrobenzenesuphonamide in B-R buffer pH 9.3. (b) UV spectrum recorded at the end of electrolysis of 1 x 10^{-3} mol L^{-1} N-phenyl-4-nitrobenzenesulphonamide at E= -1.0 *vs.* SCE. (c) UV spectrum of 1 x 10^{-3} mol L^{-1} of nitrobenzene. (d) UV spectrum of B-R buffer pH 9.3.

surface preprotonation of the nitro group in this pH range is not fast enough, and the unprotonated nitro group is reduced at a more negative potential.

In agreement with the literature[13,14], our experimental evidence under conditions of cyclic voltammetry with HMDE indicates the presence of the hydroxylamine derivative as main product generated at the first cathodic peak, which can be electrooxidized to a nitrosobenzene derivative at -0.17 V (ip_{a1} peak). The subsequent cathodic peak (ip_{c4}) corresponding to the reduction of the electrogenerated nitroso group is seen on the second forward triangular voltage sweep[13,14]. The adsorption/desorption process of these products is seen in the sucessive scans when the experiments are carried out with a HMDE electrode on which the surface is not renewed (ip_{c3}, ip_{a3} peaks).

Although cathodic deprotection in aprotic media forms the basis of a useful preparative procedure for the removal of the nitrobenzenesulphonyl group from amines[3-5], our findings indicates that the cleavage of the S-N bond in the N-phenyl-4-nitrobenzenesulphonamide in aqueous solution is not significative under reductive conditions.The ease with which the nitro group is reduced to a hydroxylamine group in aqueous solution makes the electrochemical unprotection method unsuitable for amines protected by the nitrobenzenesulphonyl group.

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References

1. Mairanovsky, V.G. *Angew. Chem.* **1976**, *15*, 281.
2. Montenegro, I. *Electrochim. Acta* **1986**, *31*, 607.
3. Zanoni, M.V.B.; Stradiotto, N.R. *J. Electroanal. Chem.* **1991**, *312*, 141.
4. Zanoni, M.V.B.; Sartorello, C.H.; Stradiotto, N.R. *J. Electroanal. Chem.* **1993**, *361,* 103.
5. Zanoni, M.V.B.; Stradiotto, N.R. *Electroanalysis* **1995**, *7*, 365.
6. Schreiber, R.S.; Shriner, L.R. *J. Am. Chem. Soc.* **1952**, *74*, 2006.
7. Laviron, E. *J. Electroanal. Chem.* **1974**, *52*, 355.
8. Vogel, A.I. In *Elementary Practical Organic Chemistry;* Wiley & Sons, Inc., New York, **1961**, p 528.
9. Fijalek, Z.; Pugia, M.; Zuman, P. *Electroanalysis* **1993**, *5*, 65.
10. Lund, H. In *Organic Electrochemistry, an Introduction and Guide*; Baizer, M.M.; Lund, H., Eds.; Marcel Dekker Inc., New York, 1983, p 285.
11. Arcos, J.; Jammal, A. El.; Viré, J.C.; Patriarche, G.J.; Christian, G.D. *Electroanalysis* **1990**, *2*, 279.
12. Dumanovic', D.; Jovanovic', J.; Marjanovic', B.; Zuman, P. *Electroanalysis* **1993**, *5*, 47.
13. Reday, C.S.; Reddy, S.J. *Electroanalysis* **1992**, *5*, 595.
14. Morales, A.; Richter, P.; Toral, M.I. *Analyst* **1987**, *112*, 965.
15. Bond, A.M. In *Modern Polarographic Methods in Analytical Chemistry*; Marcel Dekker Inc., New York, 1980.

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