

# CYCLIC VOLTAMMETRY AND SPECTRAL STUDY OF SOME PHENYL-AMINO-3,6-DINITROCOUMARIN DERIVATIVES

Gabriela Dima, Elena Constantinescu and Elena Volanschi \*

Four derivatives of phenylamino-3,6-dinitrocoumarin were investigated in the present work using coupled electrochemical and *in-situ* absorption and EPR spectral techniques. The cyclic voltammograms recorded in dimethyl sulphoxide (DMSO) – 0.1 M tetra butylammonium perchlorate (TBAP), with both stationary and rotating (RDE) platinum electrodes, evidence an ECE sequence for the reduction mechanism. EPR spectra attest the presence of two paramagnetic species, assigned respectively to the anion- and dianion-radicals. UV-VIS spectra recorded during the electrolysis at the potential corresponding to the second electron transfer sustain this assignment. The experimental data are well accounted for by semiempirical calculations (AM1 Hamiltonian, MOPAC-program package) of the redox properties.

## Introduction

The study of the phenylamino-3,6-dinitrocoumarin derivatives presents both practical and theoretical interest. The practical interest is connected to their use in human therapy, having well known neurotropic and analgaesic activity [1,2]. The theoretical interest is determined by the presence on the coumarin ring of strong electron acceptor nitro groups and electron donors like the secondary amino group, in *ortho* with respect to the nitro substituent. The halogen substituents on the phenyl amino ring may also influence the reducibility of these systems. Therefore, four derivatives of phenylamino-3,6-dinitrocoumarin (Fig. 1) were synthesised and their behavior in electrochemical reduction processes in aprotic media was investigated using coupled electrochemical and *in-situ* spectral techniques, including UV-VIS absorption and EPR spectroscopies. The relevant redox properties and the energetics of the possible reaction sequences were calculated in the frame of the semiempirical AM1 method and the results are in good agreement with the experimental data.

A. 4-[N-(2,4-dichlorophenyl)-amino]-3,6-dinitrocoumarin

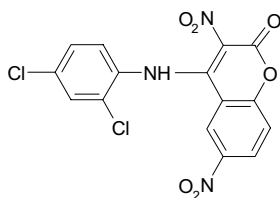
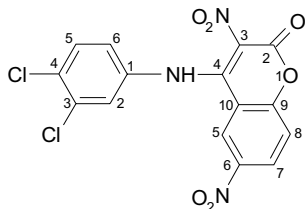


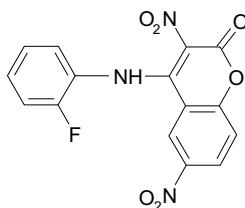
Fig.1: A, B, C, D investigated compounds.

\* Department of Physical Chemistry, Faculty of Chemistry, University of Bucharest, 4-12 Blvd. Elisabeta, Bucharest, Romania

## B. 4-[N-(3,4-dichlorophenyl)-amino]-3,6-dinitrocoumarin



## C. 4-[N-(2-fluorophenyl)-amino]-3,6-dinitrocoumarin



## D. 4-[N-(2-bromophenyl)-amino]-3,6-dinitrocoumarin

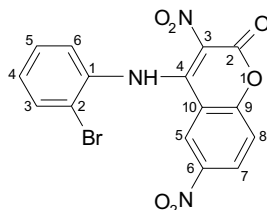


Fig. 1. (continued).

Their structure was attested by IR spectra and organic functional analysis.

## Experimental part

The electrochemical measurements were performed using a Princeton Applied Research model 173 potentiostat-galvanostat, a model 175 universal programmer and a model RE0074 X-Y recorder. The single-compartment electrochemical cell was equipped with a platinum disc working electrode ( $S = 0,0019 \text{ cm}^2$ ) used in both the stationary and rotating modes and a platinum plate counter-electrode; the reference electrode was an Ag wire [3] located close to the working electrode. All measurements were carried out in dimethylsulphoxide (DMSO) with 0.1 M tetrabutylammonium perchlorate (TBAP) as the supporting electrolyte. The concentration of the substrate was in the range  $(1\div3)\times 10^{-3} \text{ M}$ . The solutions were carefully degassed with dry argon. The bubbling was stopped during the measurements (with stationary electrode), to ensure semiinfinite linear diffusion conditions.

The EPR spectra were recorded on a JEOL-JES-3B spectrometer in the X-band frequency, using peroxyamine disulphonate ( $a_N = 13 \text{ G}$ ;  $g = 2.0055$ ) as standard, using *in-situ* techniques previously described [4]. The optical spectra were recorded on a Specord-uv-vis Carl Zeiss-Jena spectrometer during the electrolysis, using the same solutions as for the electrochemical and EPR studies.

## Results and discussion

### Electrochemical results

The cyclic voltammograms for these compounds recorded in the potential range 0 to  $(-1,5) \text{ V}$  at stationary electrode are similar and exhibit two reduction waves in the first scan. In the subsequent scans the first reduction wave located at potentials less negative ( $\approx -0,5 \text{ V}$ ) decreases strongly and disappears. The second reduction wave shows an important decrease of peak current, but it remains practically constant after seven cycles.

The cyclic voltammograms of compound A ( $\nu = 200 \text{ mVs}^{-1}$ ,  $c = 3 \cdot 10^{-3} \text{ M}$ ) are presented in Fig. 2.

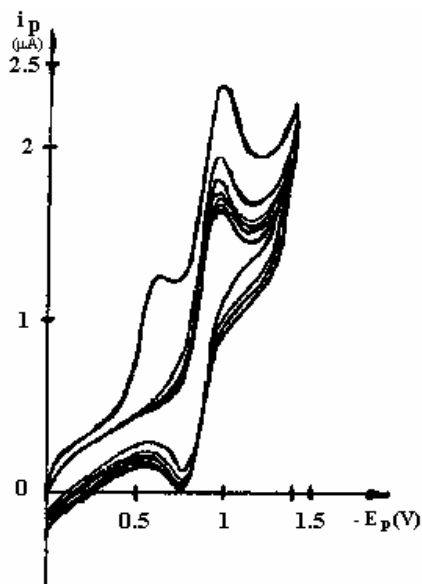


Fig. 2: Cyclic voltammograms of compound A at a scan rate of  $200 \text{ mVs}^{-1}$ ,  $c = 3 \cdot 10^{-3} \text{ M}$ .

The aspect of the voltammograms is the same for all scan rates ( $0,05$ ;  $0,1$ ;  $0,2$  and  $0,5 \text{ Vs}^{-1}$ ) and concentrations. The voltammograms were recorded in a restricted potential range  $(-0,6) \div (-1,25) \text{ V}$  with a ten times better resolution for potential value readings at different scan rates. Analysis of the wave located at  $\sim (-1) \text{ V}$  according to the usual electrochemical tests, shows that it corresponds to a quasi-reversible monoelectronic charge transfer.

The relevant electrochemical data are listed in Tables 1 and 2.

**Table 1. The voltammetric data for compounds A and B ( $c = 3 \times 10^{-3}$  M)**

$\nu$ (mVs <sup>-1</sup> )	A		B	
	$-E_p^C$ (V)	$-E_p^A$ (V)	$-E_p^C$ (V)	$-E_p^A$ (V)
50	0.934	0.790	0.987	0.879
100	0.958	0.779	1.001	0.873
200	1.020	0.769	1.015	0.864
500	1.054	0.758	1.036	0.854

**Table 2. The voltammetric data for compounds C and D ( $c = 3 \times 10^{-3}$  M)**

$\nu$ (mVs <sup>-1</sup> )	C		D	
	$-E_p^C$ (V)	$-E_p^A$ (V)	$-E_p^C$ (V)	$-E_p^A$ (V)
50	0.995	0.883	1.002	0.885
100	1.004	0.873	1.010	0.878
200	1.014	0.865	1.021	0.870
500	1.034	0.852	1.044	0.853

The standard rate constant  $k_s$  of the charge transfer process was calculated using the correlation established by Nicholson [5] between the anodic and cathodic peak potentials separation  $\Delta E_p$  and the function  $\psi$ :

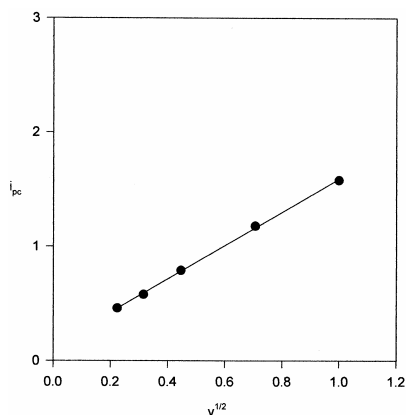
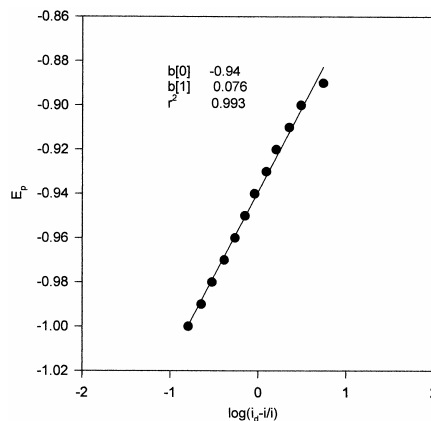
$$\psi = 28,8 k_s \nu^{-1/2} \quad (1)$$

One obtains  $k_s \cong 3 \times 10^{-3}$  cm s<sup>-1</sup> indicating an intermediate charge transfer process.

The peak current density, for all compounds increases with square roots of the sweep rate  $\nu^{1/2}$ . A plot of  $i_p$  as a function of  $\nu^{1/2}$  is linear, characteristic for a diffusion controlled process (Fig. 3).

Independent measurements using the rotating disk electrode (RDE) allowed the estimation of the limiting diffusion current  $i_d$ . Plotting  $E_p$  versus  $\log(i_d - i)/i$ , the obtained slope (60  $\div$  76 mV/decade) is consistent with a monoelectronic charge transfer process (Fig. 4.)

The assignment of this wave to a monoelectronic reduction of the substrate leading to the formation of a rather stable anion-radical is not straightforward. In the first place, it is strange that a system having a strong electronacceptor character like dinitrocoumarine should be reduced at such a negative potential, about -1V. Secondly, the presence of a first reduction wave on the first scan, which decreases and disappears on the subsequent ones, suggests a rather complex mechanism of the ECE type, where the first redox couple is situated at more positive potentials as against the second, and the chemical reaction is fairly rapid. Comparison with calculated voltammograms in literature [6] for a difference between the two reduction potentials of cca 0.4V and a rate parameter  $\lambda = RTk/nF\nu$  of about 3, sustains this assignment.

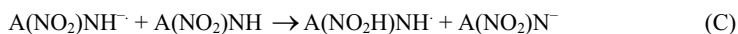
Fig. 3: Plot of  $i_{pc}$  versus  $v^{1/2}$  for compound A.Fig. 4: Plot of  $E_p$  versus  $\log(i_p - i)/i$  for compound A.

On another side, a similar behavior is reported for the electrochemical reduction of 4-nitroimidazole in dimethylformamide [7] and is assigned to the following ECE sequence:

- monoelectronic reduction to the anion-radical ( $E_1$ );
- deprotonation of the substrate by the anion-radical to form the anion (C);
- reduction of the anion to a dianion-radical ( $E_2$ ).

Other systems with a similar behaviour in reduction processes are the secondary amine substituted dinitrobenzenes [8]. In that case the dissolution of the substrate in highly polar aprotic solvents like DMSO is accompanied by the dissociation of the substrate, followed by the reduction to a dianion-radical, characterised by absorption and EPR spectra.

Taking into account all these aspects, we suggest the following mechanism for the electrochemical reduction of the investigated compounds:



where A stands for the coumarine moiety. The chemical step consists in the diffusion of the anion-radical into the bulk solution and the deprotonation of the substrate by the electro-generated base. The anion formed is further reduced at the potential of the second wave to a dianion-radical.

Alternative route would be the previous acid dissociation of the substrate:



followed by the reduction of the anion to the dianion-radical:



*i.e.* a CE sequence, in contradiction to the observed electrochemical behaviour.

### **EPR spectra**

In order to get a deeper insight into the reaction mechanism, EPR spectra were recorded during the electrolysis at the potential of the second wave ( $-1V$ ), using *in-situ* techniques.

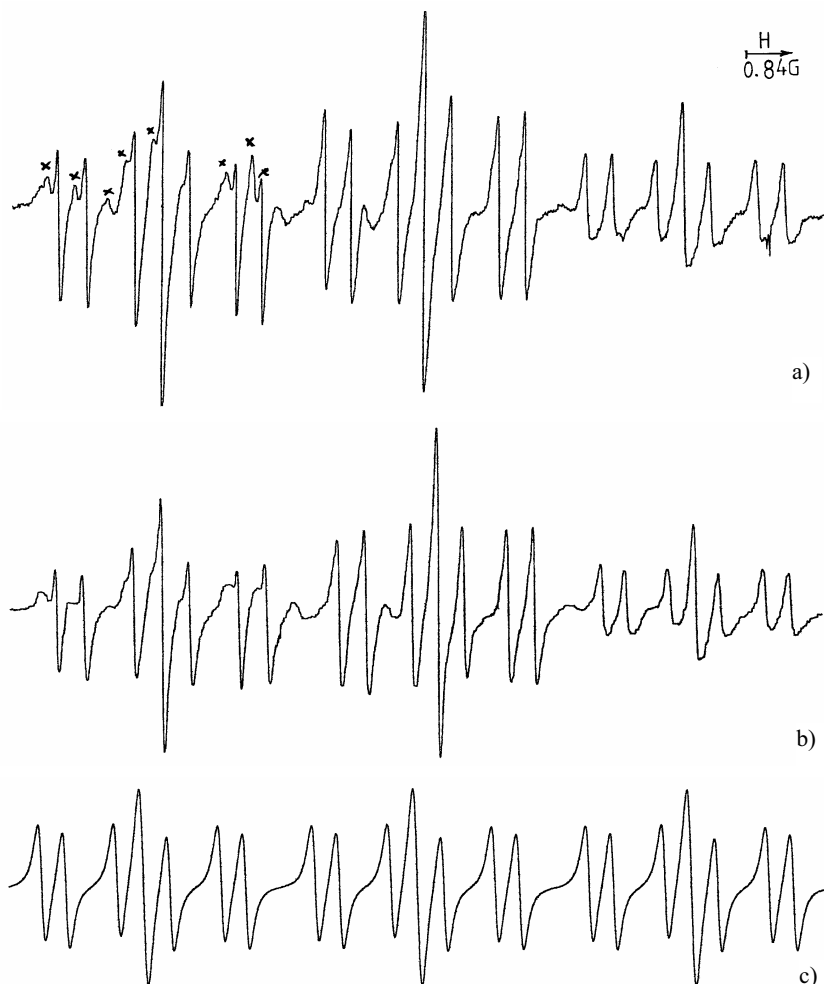


Fig. 5: EPR spectra in DMSO (electrochemical reduction at  $-1V$ ) a) Spectrum registered in the first moment (x-lines belonging to the anion-radical), b) Spectrum in presence of KOH in DMSO, c) Computer simulation of the spectrum assigned to the dianion-radical with the hfs. in text.

The spectrum obtained in the first moment from compound C is presented in Fig. 5a and was rationalised as a mixture of two radical species: one majoritary, assigned to the dianion-radical and some extra lines (marked x), presumably belonging to the

anion-radical. In order to verify this assumption, the electrolysis was also performed in the presence of strong alkali (added potassium hydroxide) and it was stated that the extra-lines decrease markedly in intensity (Fig. 5b). The spectrum of the dianion radical was simulated (Fig. 5c) with the following hyperfine splittings:  $a_N = 11.53\text{G}$   $a_H = 4.31\text{G}$   $a_H = 3.15\text{G}$  and  $a_H = 1.16\text{G}$ , *i.e.* a hf coupling distribution characteristic for a nitrosubstituted aromatic ring. Therefore they were assigned respectively to the nitro group nitrogen in site 6, the *ortho* protons (sites 5,7) and the *meta* proton (site 8). We may therefore infer that the odd electron in the dianion-radical is mainly delocalised on the benzenic ring of coumarin.

It is to be stressed that, if route CE would be operative, no other paramagnetic species besides the dianion-radical should be observed. Therefore, EPR spectra offer further experimental support for the ECE reduction mechanism.

### Optical spectra

The visible spectra were recorded during the electrolysis at the potential of the second wave (-1V), using *in-situ* techniques and are presented in Fig. 6.

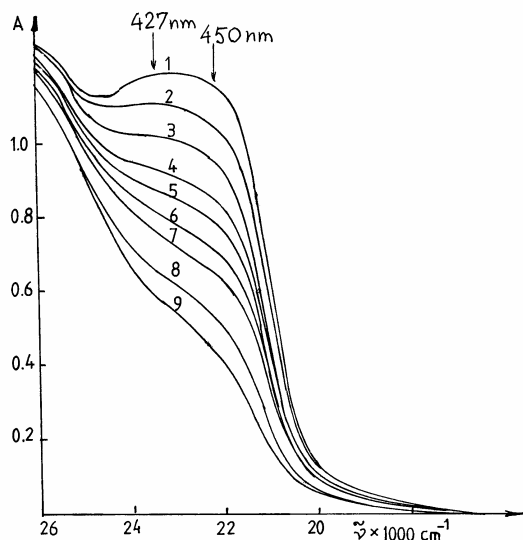


Fig. 6: Absorption spectra registered on electrochemical reduction of compound B, "in situ" techniques.

The parent molecule does not absorb in the visible range of the spectrum. On electrolysis, the appearance of a broad asymmetric band with maxima at 427 and 450 nm is observed. When the electrolysis is stopped and the solution is opened to air, these bands decrease. The time variation of their intensity ratio  $A_{450\text{nm}}/A_{427\text{nm}}$  points out that the two bands do not belong to the same species. As the ratio decreases in time, it means that the species absorbing at 450 nm is less stable, and therefore it was assigned to the anion-radical,

whereas the band at 427 nm was assigned to the dianion–radical, in agreement with electrochemical and EPR results.

### MO Modelling

In order to rationalize the experimental data and to furnish theoretical support to the proposed reduction mechanism, semiempirical MO calculations were performed, in the frame of the AM1 method in the MOPAC–7-program package. Restricted Hartree-Fock (RHF) formalism was employed for closed–shell and ROHF for open–shell structures. All optimisations were performed using the eigenvector following (EF) technique.

The relevant electronic structural features implied in redox processes of organic molecules [9] are:

- The ionisation potential, according to Koopman’s theorem:  $IP = -\epsilon_{\text{homo}}$
- The absolute electronegativity:  $X_v = \frac{1}{2} (\epsilon_{\text{homo}} + \epsilon_{\text{lmo}})$
- The adiabatic ionisation potential,  $IP_{\text{ad}}$ , defined as the enthalpy variation  $\Delta H$  for the reaction:  $A \rightarrow A^+ + e^-$
- The adiabatic electron affinity,  $EA_{\text{ad}}$ :  $-\Delta H$  for the reaction:  $A + e^- \rightarrow A^-$
- The adiabatic electronegativity:  $X_{\text{ad}} = \frac{1}{2} (IP_{\text{ad}} + EA_{\text{ad}})$

The results are presented in Table 3.

**Table 3. Relevant AM1 calculated electronic parameters implied in redox processes**

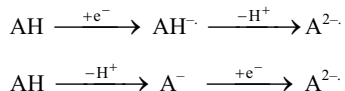
Compound (Model)	$\Delta H$	$\epsilon_{\text{homo}}$	$\epsilon_{\text{lmo}}$	$X_v$ (eV)	$IP_{\text{ad}}$ (kcal/mol) (eV)	$EA_{\text{ad}}$ (kcal/mol)	$X_{\text{ad}}$ (eV)
3,6 dinitro–phenylamino coumarin	22.33	–9.76	–1.98	5.87	199.48 (8.67)	72.97	5.92
A	10.55	–9.79	–2.13	5.96	201.22 (8.75)	77.51	6.06
B	11.72	–9.76	–2.17	5.97	201.53 (8.76)	77.73	6.07
C	–21.93	–9.80	–2.05	5.93	–	71.01	–
D	28.83	–9.83	–2.05	5.94	203.46 (8.85)	74.27	6.04

Analysis of the data in Table 3 evidences a low–lying l.e.m.o, attesting the strong electron-acceptor character of these compounds. A good agreement between the absolute and adiabatic electro-negativities, both having high values, is also observed. These values are in agreement with the cyclic voltammetry results, if the first reduction step is assigned to the first wave, *i.e.* around –0.5V.



As the experimental data have pointed out two possible reduction mechanisms, accounting for two different radical-species observed in the EPR spectra, we found interesting to analyse the energetics of these pathways using the AM1 calculated enthalpy values.

The following reduction pathways were considered:



and the enthalpy variations were calculated for each step and for the whole process leading from the starting compound to the corresponding dianion-radical. The results are presented in Table 4.

The first two columns correspond to the route implying dissociation of the substrate as a first step, i.e. the CE mechanism, whereas the next two ones correspond to the EC sequence.

**Table 4. Energetics of the possible reduction pathways of the phenylamino-3,6-dinitrocoumarins**

Compound	-H <sup>+</sup>		+e <sup>-</sup>		$\Delta H_{\text{tot}}$	$EA_{\text{ad}}$
	1	2	1	2		
Coumarin	-67.11	18.35	-72.97	24.21	-48.76	72.97
A	-70.90	14.32	-76.51	20.30	-56.21	77.51
B	-72.32	13.49	-77.73	18.90	-58.83	77.73
C	-68.24	16.71	-71.01	19.48	-51.53	71.01
D	-68.70	16.57	-74.27	22.13	-52.14	74.27

Examination of the data in Table 4 allows for the following comments:

- The electron transfer is more favourable than deprotonation, but the differences are small, both are energetically favourable, in agreement with experimental EPR data were both paramagnetic species were identified.
- The whole process, leading to the formation of the dianion-radical A<sup>2-</sup> is energetically favourable for all compounds.
- The values of  $\Delta H_{\text{total}}$  present the same trend as the electron affinities, being the greatest for the dichloro derivatives A and B, as expected. However the differences are very small, accounting for the similitude of the electrochemical behaviour of all investigated compounds.

In conclusion, corroboration of the electrochemical data with EPR and absorption spectral results, attest as more probable the ECE sequence for the reduction mechanism of the investigated phenylamino-3,6-dinitrocoumarin derivatives. The semi-empirical MO-calculations outline the strong electron-acceptor character of the investigated systems and support the suggested reaction mechanism.

## REFERENCES

1. Savalev, V. L. and al. (1975) *Khim. Farm. Zhurnal* 6, 10.
2. Prianisnikova, N. T. and al. (1978) *Khim. Farm. Zhurnal* 12, 58.
3. Constantinescu, E., Hillebrand, M., Volanschi, E., Andrei, M., Ivănescu, G. and Maior, O. (1995) *J. Electroanal. Chem.* 395, 211.
4. Ciureanu, M., Hillebrand, M. and Volanschi, E. (1990) *J. Electroanal. Chem.* 291, 201–232.
5. Nicholson, R. S. (1965) *Anal. Chem.* 37, 1351.
6. P.H.Rieger, P. H. (1985) *Electrochemistry*, John Wiley & Sons, New York, 303.
7. Tallec, A. (1985) *Electrochimie - Syntheses et mecanismes*, Masson, Paris, 6.
8. Ionescu, E., Hillebrand, M. and Volanschi, E. (1997) *Rev. Roum. de Chim.* 42(9), 897–905.
9. Sawyer, A., Sullivan, E. and Mariam, Y. (1996) *J. Comput. Chem.* 17, 204–225.