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ELECTROCHEMICAL STUDIES ON SOME INDOLIZINE CARBOXYLATES WITH POTENTIAL APPLICATION

Maria-Laura SOARE[1], Magdalena Rodica BUJDUVEANU[2], Eleonora-Mihaela UNGUREANU[3], Emilian GEORGESCU[4]

Lucrarea de faţă are ca obiect studiul electrochimic al compuşilor 1-etilcarboxilat de 3-(4-metilbenzoil) indolizina şi 1-etilcarboxilat de 3-[(2-etilfenil)carbamoil] indolizina prin voltametrie ciclică (CV) şi voltametrie în puls diferenţial (DPV). S-au stabilit caracterisiticile proceselor redox implicate. Compararea parametrilor electrochimici s-a corelat cu diferenţa dintre efectele grupărilor funcţionale grefate pe inelul indolizinic.

This work is devoted to the electrochemical study of ethyl 3-(4-methylbenzoyl) indolizine-1-carboxylate and ethyl 3-[(2-ethylphenyl)carbamoyl] indolizine-1-carboxylate by cyclic voltammetry (CV) and differential pulse voltammetry (DPV). There are established the number and characteristics of the redox processes for each compound. Comparison of the electrochemical parameters was connected to the difference between the effects of the functional groups grafted on the indolizinic ring.

Keywords: ethyl 3-(4-methylbenzoyl) indolizine-1-carboxylate, ethyl 3-[(2-ethylphenyl)carbamoyl] indolizine-1-carboxylate, cyclic voltammetry, differential pulse voltammetry

1. Introduction

In recent years, the synthesis of macrocyclic compounds, which can reversibly respond to external actions (thermal, photochemical, electrochemical, pH, etc.) by changing important properties and characteristics (the cavity size, the surface shape, the electronic structure, the complexing ability, etc.) due to the specially introduced functional groups or fragments, has taken a special place in supramolecular chemistry [1]. Such "sensitive" heterocyclophanes containing redox-active biindolizine systems can serve as molecular switches [2] and membrane carriers [3] and are of great interest in the design of new sensors for

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[1] PhD student, Faculty of Applied Chemistry and Material Sciences, University POLITEHNICA of Bucharest, Romania

[2] PhD student, Faculty of Applied Chemistry and Material Sciences, University POLITEHNICA of Bucharest, Romania

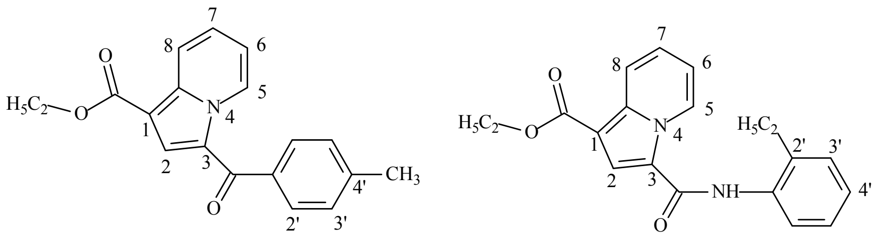
[3] Prof., Faculty of Applied Chemistry and Material Sciences, University POLITEHNICA of Bucharest, Romania

[4] Eng., S.C. Oltchim S.A., Uzinei Street, 1, 240050, Ramnicu Valcea, Romania

modern technologies based on molecular processes. Unlike redox-active compounds (ferrocenes, [4-5] tetrathiafulvalenes, [6-7] and quaternized 4,4′-bipyridines [8-9]), biindolizines have found little use as active regions, which make cyclophanes able to respond to external actions, in spite of the fact that biindolizines are quite stable two step redox systems, whose electrochemical behaviour has been studied in sufficient detail [10-15]. Indolizines are π-rich compounds, which are readily oxidized (~0.2-0.3 V relative to Fc/Fc^+) to form radical cations [10-14]. The stability and subsequent transformations of radical cations are determined primarily by the presence of hydrogen atoms in the pyrrole ring of the indolizine system. The radical cations and dications of 3,3′-biindolizines, in which all hydrogen atoms in the five-membered ring are replaced by alkyl or aryl groups, are quite stable and can be isolated and characterized as perchlorates [12]. The electrochemical behaviour of two diastereomers of macrocyclic biindolizines, in which both heterofragments are linked at positions 3,3′ and, through a bridge, at positions 1,1′, is different [13]. Thus, the diastereomer having the anti configuration is oxidized to form stable radical cations and dications, whereas the oxidation of the diastereomer having the syn configuration is followed by the intramolecular cyclization with the involvement of the C(5) and C(5′) atoms of the pyridine rings of the indolizine system having a favourable spatial arrangement [16].

Indolizine derivatives possess valuable biological activity and have been studied for their psychotropic, anti-inflammatory, analgesic, antimicrobial, antiexudative and hypoglycemial effects [17-20]. Certain 1-indolizinols are easily oxidized to stable free radicals [21]. Therefore, Oxygen-protected indolizinols may act as stable precursors for highly potent antioxidants, and it was found high inhibitory activity against lipid peroxidation in vitro for esters, ethers, carbonates, carbamates and sulfonates of indolizines as well as azaindolizines [22]. In order to establish the mechanism through which these antioxidant properties act, the electrochemical behaviour of several indolizine derivatives, esters, ethers, tolysilates, sulfonates and azaindolizines has been investigated by cyclic voltammetry and preparative electrolysis. The cyclic voltammetry data obtained were sensitive to the identities of the substituents and were used to characterise the principal oxidation process that took place in each case [20]. There are also some patents that stress the therapeutical effect of certain indolizine derivatives (1-glyoxylamide indolizines) in treating lung and ovarian cancer [23].

The present paper is focused on the electrochemical behaviour of two indolizine derivatives with similar structure which have a benzoyl or an imidoyl moiety, respectively connected to the position 3 of the indolizine fragment. The studied compounds were ethyl 3-(4-methylbenzoyl) indolizine-1-carboxylate (**I1**) and ethyl 3-[(2-ethylphenyl)carbamoyl] indolizine-1-carboxylate (**I2**), Fig. 1.



I1 **I2**

Fig. 1. Structural formula of the investigated indolizines

2. Experimental

Acetonitrile (CH_3CN) and tetrabutylammonium tetraborofluorate ($TBABF_4$) from Fluka were used as received as solvent and supporting electrolyte. The investigated compounds have been obtained by general procedure for synthesis of indolizines based on 1,3-dipolar cycloaddition reactions of heterocyclic-N-ylides with electron-deficient alkynes or alkenes, according to literature data [24-25].

The experiments were carried out by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) using a PGSTAT12 AUTOLAB potentiostat in a three-compartment cell. The working electrode was of glassy carbon disk (diameter of 3 mm). The active surface was polished before each determination with diamond paste (200 μm). The Ag/10 mM $AgNO_3$ in CH_3CN and 0.1 M $TBABF_4$ was used as reference electrode. The potential was referred to the potential of the ferrocene/ferricinium ion couple (Fc/Fc^+) which in our experimental conditions was +0.07 V. A platinum wire was used as auxiliary electrode. The determinations were performed at 25 ^oC under argon atmosphere.

Anodic and cathodic curves were recorded individually, starting from the stationary potential. The CV curves were generally recorded at 0.1V/s or at various rates (0.05 - 1V/s) when studying the influence of the scan rate. DPV curves were recorded at 0.01V/s with a pulse height of 0.025V and a step time of 0.2 s.

3. Results and Discussion

CV and DPV curves were recorded for different concentrations of indolizines **I1** and **I2** at different scan rates and on various scan domains.

Study of ***I1***

The CV and DPV curves for increasing concentrations of the indolizine **I1** are presented in Fig. 2. There are observed two anodic (1a and 2a) and three cathodic (1c - 3c) processes, which are seen both in CV and DPV. They were denoted in the order in which they appear in the voltammograms.

The influence of the concentration on the DPV and CV curves is shown in Fig. 2. Inset are given the peak currents (i_p) dependence on concentration.

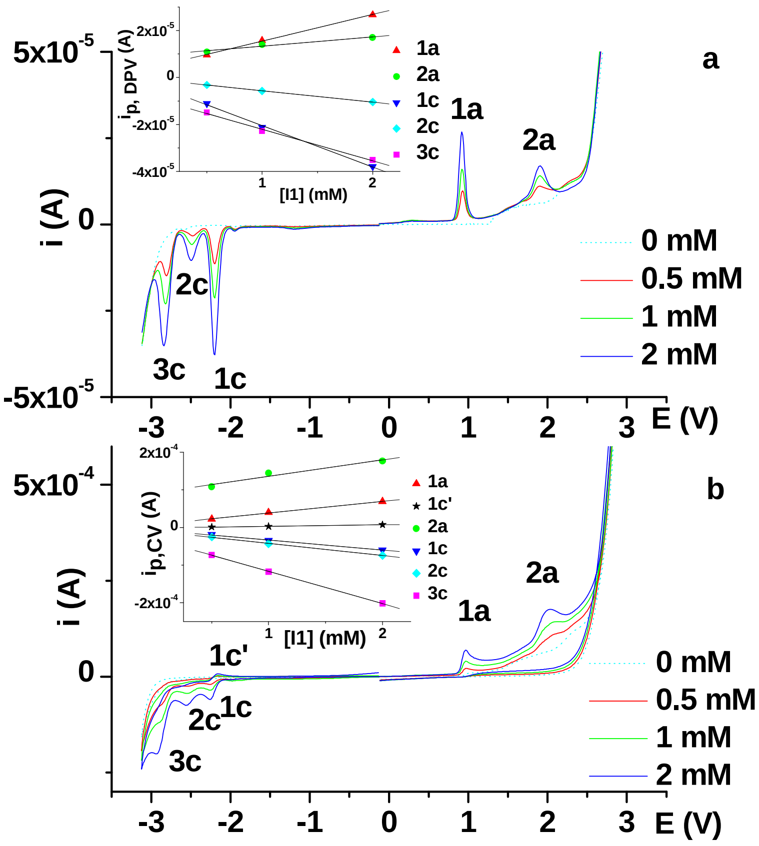


Fig. 2. (a) DPV and (b) CV curves for various concentrations of **I1**

For the DPV peak currents, linear dependences were obtained, with positive slopes for anodic processes and negative slopes for the cathodic processes. These slopes could be used for analytical purposes, in order to build the calibration curves for this compound. The peak potentials (E_p) are almost independent on concentration. Table 1 shows the equations of the peak currents versus concentration. They are useful to prove the faradaic nature of the implied processes, and not their association with adsorption phenomena. It is observed that the slope for the peak 1c is 1.5 times higher than the slope for the peak 1a. This aspect could be correlated to the nature of the processes resulted from the study of the scan rate influence. The slopes were calculated in order to compare the number of electrons implied in these successive processes. The different values obtained for 1a and 2a (with a slope of about half of that for 1a) show that the process 2a can represent a successive stage of electron transfer suffered by the intermediate generated in the process 1a. A similar conclusion can be drawn from the comparison between the vales of the slopes for 1c and 2c. The value obtained for 3c should be interpreted with reserve, since the current read is a total current, in the potential range in which the background has a more pronounced contribution. These aspects will be further correlated to the proposed mechanism.

The influence of concentration on the CV peak currents and potentials is similar to that reported for DPV, Fig. 2, Table 2.

Table 1

Linear DPV peak currents and potentials dependence on concentration for I1

Peak	i_p, DPV	E_p, DPV
	Y (i_p, A); X ([I1], mM)	E_p,V
1a	Y = 4.16E-6 + 1.13E-5 X $R^2 = 0.999$	0.921
2a	Y = 9.42E-6 + 3.93E-6 X $R^2 = 0.960$	1.903
1c	Y = -2.83E-6 - 1.76E-5 X $R^2 = 0.998$	-2.201
2c	Y = -8.15E-7 - 4.83E-6 X $R^2 = 0.999$	-2.482
3c	Y = -8.66E-6 - 1.34E-5 X $R^2 = 0.996$	-2.823

Table 2

Linear CV peak currents and potentials dependence on concentration for I1

Peak	i_p, CV	E_p, CV
	Y (i_p, A); X ([I1], mM)	E_p,V
1a	Y = 7.65E-6 + 3.08E-5 X $R^2 = 0.998$	0.971
2a	Y = 9.21E-5 + 4.37E-5 X $R^2 = 0.950$	2.060
1c	Y = -6.85E-6 - 2.66E-5 X $R^2 = 0.997$	-2.256
1c’	Y = -1.11E-6 + 4.11E-6 X $R^2 =0.992$	-2.157
2c	Y = -9.97E-6 - 3.23E-5 X $R^2 = 0.999$	-2.542
3c	Y = -3.12E-5 - 8.56E-5 X $R^2 = 0.999$	-2.889

The influences of the scan rate and scan domain on the CV curves are presented in Fig. 3. When the potential reaches 1c peak, in the reverse scan, it can be seen a counterpeak 1c’. 2c and 3c do not show clear counterpeaks in the reverse scans. The investigations were performed at a slow scan rate (0.1V/s) and at a higher scan rate (1V/s) in order to see if there are marked differences in the electrochemical reversibility of each process.

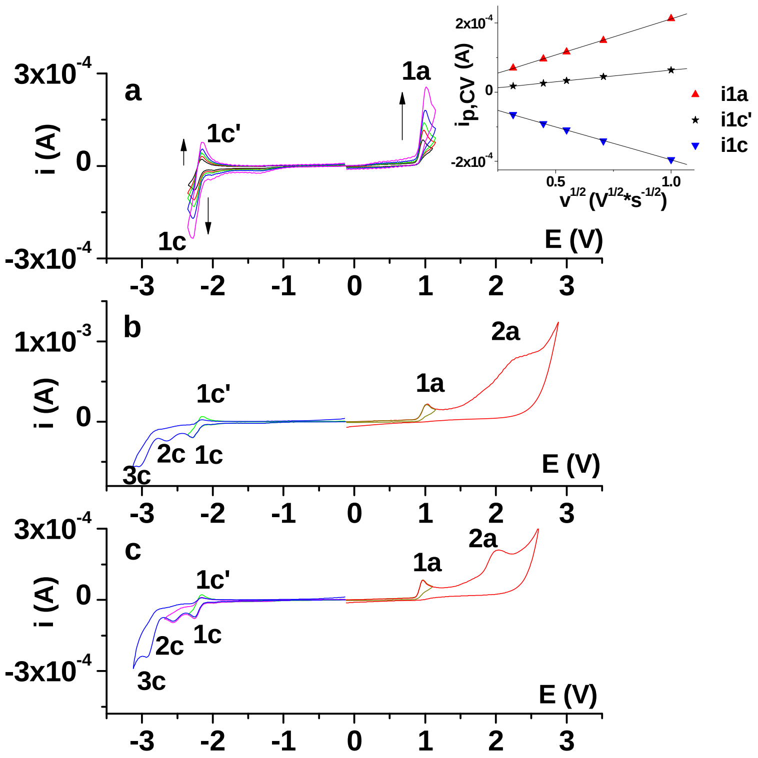


Fig. 3. CV curves for various scan rates: 0.1; 0.2; 0.3; 0.5; 1V/s (a) and scan domains at 1V/s (b) and 0.1V/s (c) for **I1** (2mM) in 0.1M $TBABF_4$, CH_3CN

The linear dependence of the peak currents and potentials for 1a, 1c’ and 1c on the scan rate is given in Table 3. For 1a and 1c’ positive slopes are obtained, while for 1c the slopes are negative. The peaks 1a and 1c, corresponding to the first electron transfers are further examined in detail in order to establish their characteristics. The subsequent peaks 2c and 3c appear to be electrochemically irreversible processes, as part of more complex mechanisms.

Table 3

Linear CV peak currents and potentials dependences on scan rate for I1

Peak	i_p, CV	E_p, CV
	Y (i, A); X ($v^{1/2}$, $(V/s)^{1/2}$)	Y (E, V); X (log (v, V/s))
1a	Y = 3.19E-6 + 2.09E-4 X $R^2 = 0.999$	Y = 1.01 + 0.04 X $R^2 = 0.969$
1c	Y = -5.10E-6 - 1.91E-4 X $R^2 = 0.999$	Y = -2.29 - 0.03 X $R^2 = 0.979$
1c’	Y = -3.86E-6 + 6.80E-5 X $R^2 = 0.999$	Y = -2.15 + 0.01 X $R^2 =0.968$

Study of ***I2***

Figure 4 shows the CV and DPV curves obtained for **I2**. There are observed three anodic (1a, 2a, 3a) and 2 cathodic processes (1c, 2c), which are correlated using the corresponding CV and DPV curves. The influence of the concentration on the DPV curves is shown in Fig. 4 and Table 4. For the peak currents, linear dependences were found, with positive/negative slopes for anodic/cathodic processes. The peak potentials of 1a and 1c are independent on concentration, while those for 2a, 3a and 2c show higher slopes than the theoretical value (0.059V for a monoelectronic transfer). Such values indicate that for 2a, 3a and 2c, multielectron processes are implied.

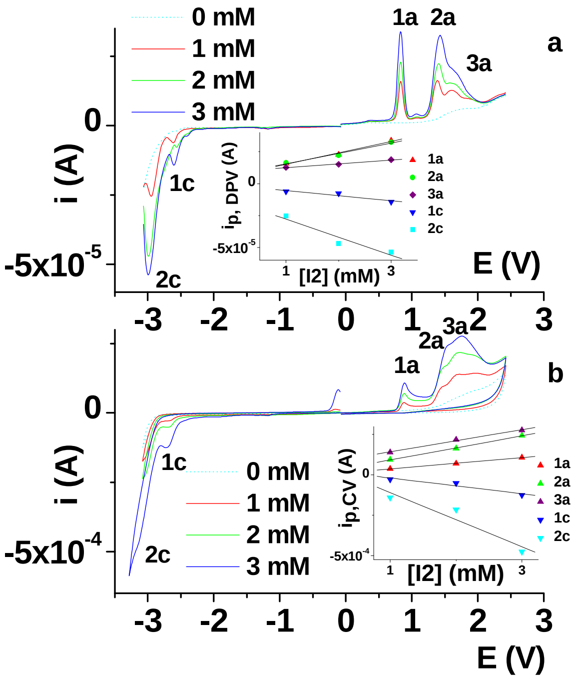


Fig. 4. (a) DPV and (b) CV curves for various concentrations of **I2**

Table 4

Linear DPV peak currents and potentials dependence on concentration for I2

Peak	DPV currents	DPV potentials
	Y (i, A); X ([I2], mM)	Y (E_p,V); X (log [I2], mM)
1a	Y = 6.15E-6 + 8.99E-6 X R^2 = 0.984	0.831
2a	Y = 7.37E-6 + 8.13E-6 X R^2 = 0.976	Y =1.386+0.083 X R^2 = 0.940
3a	Y = 9.47E-6 + 3.02E-6 X R^2 = 0.989	Y =1.599+0.158 X R^2 = 0.903
1c	Y = -1.41E-6 - 4.00E-6 X R^2 = 0.886	-2.606
2c	Y = -1.38E-5 - 1.41E-5 X R^2 = 0.915	Y =-2.951-0.103 X R^2 = 0.915

Table 5

Linear CV peak currents and potentials dependence on concentration for I2

Peak	CV currents	CV potentials
	Y (i, A); X ([I2], mM)	Y (E_p,V); X (log [I2], mM)
1a	Y = 1.15E-6 + 3.52E-5 X R^2 = 0.998	0.884
2a	Y = 1.77E-5 + 7.47E-5 X R^2 = 0.999	i
3a	Y = 7.42E-5 + 6.86E-5 X R^2 = 0.992	i
1c	Y = 2.94E-5 - 4.86E-5 X R^2 = 0.916	-2.725
2c	Y = 5.82E-5 - 1.68E-4 X R^2 = 0.905	i

*i = imprecise, difficult to be estimated

The influences of the scan rate and scan domain on the CV curves are given in Fig. 5 and Table 6. For the peaks 1a and 1c, the peak currents/potentials are linearly dependent on the square root/logarithm of the scan rate, respectively.

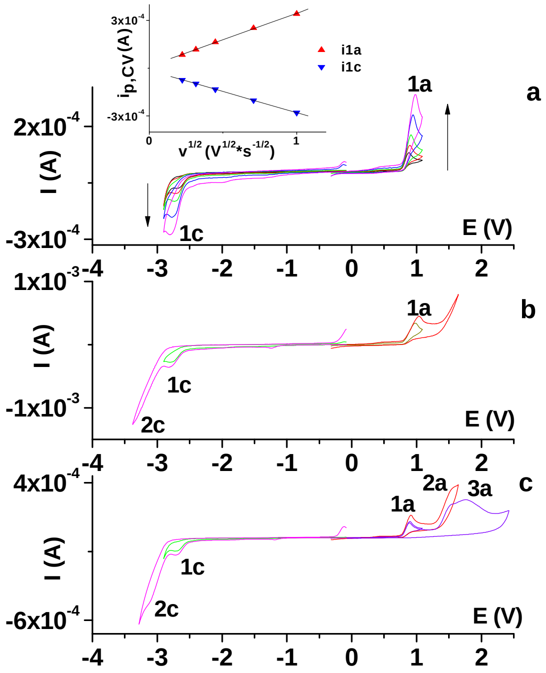


Fig. 5. CV curves for various scan rates: 0.05; 0.1; 0.2; 0.5; 1V/s (a) and scan domains at 1V/s (b) and 0.1V/s (c) for **I2** (3mM) in 0.1M $TBABF_4$, CH_3CN

Table 6

Linear CV peak currents and potentials dependence on scan rate for I2

Peak	CV currents	CV potentials
	Y (i, A); X ($v^{1/2}$, $(V/s)^{1/2}$)	Y (E, V); X (log (v, V/s))
1a	Y = 1.28E-5 + 3.32E-4 X R^2 = 0.999	Y = 0.97 + 0.08 X R^2 = 0.980
1c	Y = -1.34E-5 - 2.66E-4 X R^2 = 0.999	Y = -2.80 - 0.09 X R^2 = 0.988

The peaks 1a and 1c, corresponding to the first electron transfers of **I2** are further examined in detail. The subsequent peaks 2a, 3a and 2c appear to be electrochemically irreversible processes, as part of more complex mechanisms and they will be assigned also further.

Investigation of the first electron transfers nature

Among the electrochemical processes that are observed when scanning, the processes 1a and 1c are the most important, from the reaction mechanism point of view. They correspond to the first steps of electrochemical oxidation and reduction that occur for the investigated compound. As in the case of any organic substrate, these steps lead to the formation of the radical cation and radical anion. The electrochemical nature of these processes was analyzed separately, for each compound, against several specific criteria, described bellow. These criteria are expressed for the general case of a reduction process. For oxidation processes, the corresponding approach was used.

For the diagnosis of a **reversible** process in CV, the following criteria [26] were tested:

1. $\Delta E_p = E_{pa} - E_{pc} = 59/n$ mV,
2. $|E_p - E_{p/2}| = 59/n$ mV
3. $|i_{pa}/i_{pc}| \approx 1$
4. $i_p \sim v^{1/2}$ or $i_p/v^{1/2} = \text{const}$
5. E_p is independent on v
6. For $E > E_p$, $i^{-2} \sim t$.

where: E_{pa}, E_{pc}/i_{pa}, i_{pc} = anodic and cathodic peak potentials/currents, respectively; n = number of transferred electrons; $E_{p/2}$ = half-peak potential; v, E = scan rate and potential at a certain time, t.

The dependence of i_{pc} on concentration and scan rate for a reversible process can lead to the calculation of the diffusion coefficient of the oxidized species D_0 (in cm^2/s), according to (1).

$$i_{pc} = (2.69*10^5)\, n^{3/2} A c_0^* D_0^{1/2} v^{1/2}, \qquad (1)$$

where A = electrode surface (cm^2); c_0^* - concentration of the oxidized species in solution (mol/cm^3).

For the diagnosis of a **quasi-reversible** process in CV, the following criteria [26] were tested:

1. i_p increases with $v^{1/2}$, but not directly proportional,
2. $|i_{pa}/i_{pc}| \approx 1$ if $\alpha_c \approx \alpha_a \approx 0.5$
3. $\Delta E_p > 59/n$ mV and increases with v
4. E_{pc} shifts towards negative values when v increases

where α_c/α_a = cathodic/anodic charge transfer coefficients, and $\Delta E_p = E_{pa} - E_{pc}$

The standard rate constant of the electron transfer, k_s, can be obtained from the dependence of ΔE_p on $\log\Psi$ [27], $\Psi = \gamma^{\alpha/2} (RT)^{1/2} k_s/(nFD_0\pi v)^{1/2}$; γ =

D_0/D_R; D_R = diffusion coefficient of the reduced species; R = gas constant; T = absolute temperature; F = Faraday's constant. It results:

$$\Psi \approx 28.8\ k_s/v^{1/2} \qquad (2)$$

For both reversible and quasi-reversible processes, the ratio i_{pa}/i_{pc} was calculated with the following equation [27]:

$$i_{pa}/i_{pc} = (i_{pa})_0/\ i_{pc} + 0.485\ (i_{sp})_0/i_{pc} + 0.086, \qquad (3)$$

where $(i_{pa})_0$ = anodic peak current measured with respect to the potential axis; $(i_{sp})_0$ = current at the switching potential.

For the diagnosis of an **irreversible** process in CV, the following criteria [26] were tested:

1. Absence of the anodic peak
2. $i_{pc} \sim v^{1/2}$,
3. E_{pc} shifts with $30/\alpha_c n_\alpha$ mV per v decade (at 25°C)
4. $E_p - E_{p/2} = 47.7/\alpha_c n_\alpha$ mV,

where n_α - number of electrons transferred in the rate determining step.

For an irreversible process, D_0 can be calculated using (4):

$$i_p = -(2.99*10^5)n(\alpha_c\, n_\alpha)^{1/2}Ac_0^{\ *}D_0^{\ 1/2}\ v^{1/2}, \qquad (4)$$

For the diagnosis of an **EC type voltammogram**, the following criteria [26] were tested:

1) $i_{pa}/i_{pc} < 1$, but tends to 1 with v;
2) $i_{pc}/\ v^{1/2}$ slowly decreases with increasing v;
3) E_{pc} is situated towards positive values with respect to the potential corresponding to the reversible electron transfer;
4) E_{pc} shifts towards negative values with increasing v.

For the determination of the rate constant, k_c, of an irreversible chemical reaction following a charge transfer, the calibration curve

$$(i_{pa}/i_{pc}) = f(k_c\tau) \qquad (5)$$

has been used, in which

$$\tau = (E_\lambda - E_{1/2})/v \qquad (6)$$

τ being the scanning time between $E_{1/2}$ (potential corresponding to a current of 85.17% of i_p) and E_λ (switching potential).

The cyclic voltammograms of **I1** have been analyzed against the above criteria. When examining the nature of the peak 1c, it was concluded that it is associated to an EC type mechanism. The corresponding parameters of the process are: k_s = 0.029 cm/s; $k_c = 0.167 s^{-1}$. The diffusion coefficient, evaluated from the hypothesis that the charge transfer step is reversible (fast) is $2.8*10^{-5}$ cm^2/s.

For the peak 1a of **I1**, the possible irreversible nature has been analyzed. It was observed that the 1st and 2nd criteria are accomplished, since the counterpeak is absent and i1a is directly proportional to the square root of the scan rate. However, for the 3rd criterion, it has been seen that E1a shifts only with 40mV per v decade, that is less than 60mV, which is the theoretical value (for $\alpha_a = 0.5$). For the 4th criterion, the calculated potential difference (E_p - $E_{p/2}$ = 62mV) is also smaller than the theoretical one (95.4mV, also calculated with $\alpha_a = 0.5$). When considering the quasi-reversible behavior of process 1a, most criteria are not accomplished. It was concluded that the peak 1a corresponds to an irreversible process. The charge transfer step corresponding to 1a can also be an EC type process, since the 2nd and the 4th criteria are accomplished. The 1st criterion cannot be evaluated, since no counterpeak is observed in the scan rate domain provided by the electrochemical device. The radical cation is probably entirely consumed in a fast irreversible subsequent chemical step. The 3rd criterion cannot be evaluated, since the value of the potential corresponding to the reversible electron transfer is unknown. The diffusion coefficient calculated from 1a data is $5.2*10^{-5}$ cm^2/s (for an irreversible charge transfer). This value is twice larger than that obtained from the data of the peak 1c. This difference could be explained by the difference of the chemical steps that follow the first oxidation and reduction electron transfers.

For **I2**, a similar analysis has been performed. When examining the possible irreversible nature of the peak 1a, it was observed that the 1st and 2nd criteria are accomplished, since the counterpeak is absent and i1a is directly proportional to the square root of the scan rate. But, for the 3rd criterion, it has been seen that E1a shifts with 80mV per v decade, that is higher than 60mV, which is the theoretical value (for $\alpha_a = 0.5$). For the 4th criterion, the calculated potential difference (E_p - $E_{p/2}$ = 82mV) is smaller than the theoretical one (95.4mV, also calculated with $\alpha_a = 0.5$). When considering the quasi-reversible behavior of process 1a, most criteria are not accomplished. It was concluded that the peak 1a corresponds to an irreversible process. The charge transfer step corresponding to 1a can also be an EC type process, since the 2nd and the 4th criteria are accomplished. The 1st criterion cannot be evaluated, since no counterpeak is observed in the scan rate domain provided by the electrochemical device. The radical cation is probably entirely consumed in a fast irreversible subsequent chemical step. The 3rd criterion cannot be evaluated, since the value of the potential corresponding to the reversible electron transfer is unknown. The diffusion coefficient calculated from 1a data is $6.5*10^{-5}$ cm^2/s (for an irreversible charge transfer).

By analyzing the possible irreversible nature of the peak 1c from **I2**, it was observed that the 1st and 2nd criteria are accomplished, since the counterpeak is absent and i1a is directly proportional to the square root of the scan rate. But for the 3rd criterion, E1a shifts with 90mV per v decade, more than the theoretical shift of 60mV (for α_c = 0.5). As for the 4th criterion, the calculated potential difference (E_p - $E_{p/2}$ = 146mV) is much higher than the theoretical value (95.4mV, also calculated with α_c = 0.5).

When considering the quasi-reversible behavior of process 1a, most criteria are not accomplished. It was concluded that the peak 1a corresponds to an irreversible process. The charge transfer step corresponding to 1a can also be an EC type process, since the 2nd and the 4th criteria are accomplished. The 1st criterion cannot be evaluated, since no counterpeak is observed in the scan rate domain provided by the electrochemical device. The radical cation is probably entirely consumed in a fast irreversible subsequent chemical step. The 3rd criterion cannot be evaluated, since the value of the potential corresponding to the reversible electron transfer is unknown. The diffusion coefficient calculated from 1a data is $4.4*10^{-5}$ cm^2/s (for an irreversible charge transfer).

Comparison between ***I1*** *and* ***I2***

By analyzing the results obtained for the two compounds in CV (Fig. 6), it was observed that **I1** presents two anodic electrochemically irreversible processes (denoted 1a and 2a in Fig. 6), while **I2** presents three anodic electrochemically irreversible processes (denoted *1a*, *2a* and *3a*, with italic letters in Fig. 6). They occur easier for **I2** than for **I1**. **I1** is harder to oxidize and easier to reduce than **I2** (Table 7). These differences in behaviour could be due to a stronger electron attractive electromeric effect of carbonyl group (CO) with respect to amide (CO-NH).

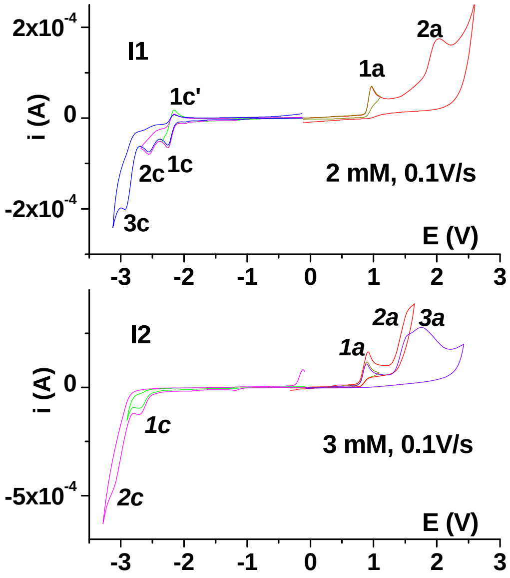


Fig. 6. Comparison between the CV curves of the indolizines **I1** and **I2** on all scan domains

The degree of reversibility of the first cathodic process of **I1** can be evidenced also by comparing its peak potential difference with that of the reversible couple Fc/Fc^+, their values being quite similar in the given experimental conditions (Table 7).

By comparing the potentials of the first reduction and oxidation peaks for the two compounds, Table 7, one can estimate their oxidant and reducing strength. An approximate electrochemical stability could be estimated from the value of the difference between the peak potentials from the formation of the radical cation and radical anion (ΔE1ac), even though the peaks have different features. It is observed that **I2** is more stable than **I1**, Table 7. The CV and DPV data are in good agreement.

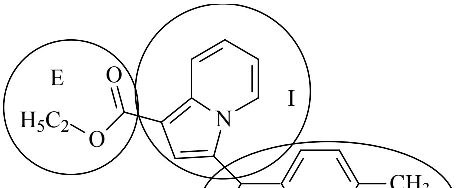
Table 7

Electrochemical DPV and CV data for the first anodic (1a) peak, first cathodic (1c) peak and its counterpeak (1c')

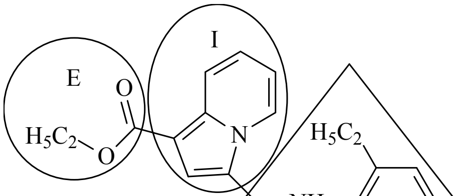
Compound	**I1**		**I2**	
Technique	*DPV*	CV	*DPV*	CV
E1a (V)	*0.918*	0.968	*0.831*	0.893
E1c (V)	*-2.201*	-2.259	*-2.600*	-2.728
E1c' (V)	-	-2.157	-	-
ΔE1c* (V)	-	0.102	-	-
ΔEpFc** (V)	-	0.086	-	0.128
ΔE1ac*** (V)	*3.119*	3.227	*3.431*	3.621

*ΔE1c = E1c' - E1c; **ΔEpFc = Epa - Epc; *** ΔE1ac = E1a - E1c

The reduction and oxidation processes of the compounds **I1** and **I2** can be assigned based on the examination of the chemical structures, taking into account the specific potential of activity for each functional group [28].



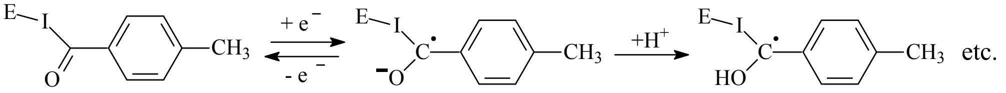
I1

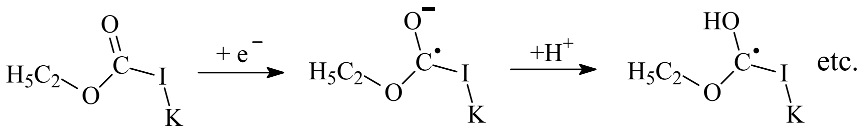


I2

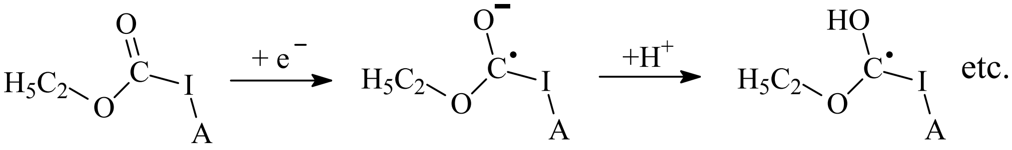
Fig. 7. Key fragments for the compounds **I1** and **I2**: E - ester fragment; I - indole fragment; K - ketone fragment; A - amide fragment

When analyzing the structure of the compound **I1**, it is observed that three reduction processes are most likely to occur at three particular functional groups, in the following order: the carbonyl group from the ketone fragment (K), the carbonyl group from the ester fragment (E) and the nitrogen atom from the indole fragment (I) [28]. Consequently, the process corresponding to the peak 1c from **I1** has been assigned to the reduction that takes place at the carbonyl group, since this is group is the most prone to be reduced. This reduction is a reversible process, which is also in agreement with the nature of the process 1c (Fig. 6). The second process that can occur for **I1** when increasing potential is the irreversible reduction of the carbonyl group from the ester fragment. This could correspond to the peak 2c (Fig. 6) which appears to be electrochemically irreversible. Finally, the reduction that occurs at the most negative potential in the case of **I1** could be attributed to the reduction at the nitrogen atom from the indole fragment. Since such a process is a destructive one, and could involve several electrons, it was assessed to the peak 3c (Fig. 6), which shows the same features.

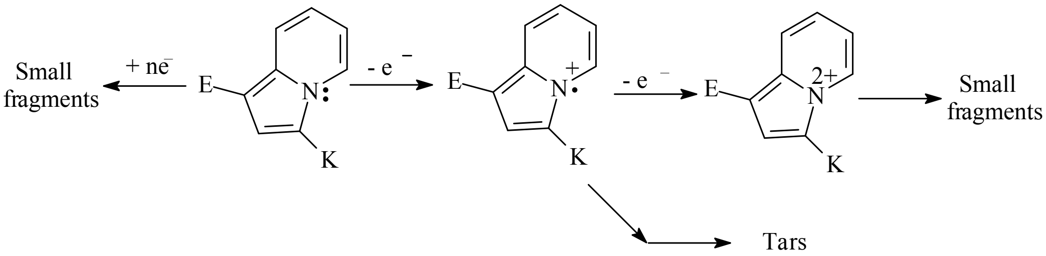




In the case of the compound **I2**, three reduction processes are possible, in the following order of potentials: at the carbonyl group from the ester fragment, at the nitrogen atom from the indole fragment, and at the amide fragment which is very hard to be reduced [28]. Consequently, the process corresponding to the electrochemically irreversible peak *1c* (Fig. 6) was assigned to the irreversible reduction of the carbonyl group from the ester fragment. A reduction that could take place at the nitrogen atom from the indole fragment is a destructive process, involving several electrons. The peak *2c* (Fig. 6) in the voltammogram could correspond to this reduction, as it appears to be a multielectron transfer. These assignments are verified since: (i) the potential of 2c from the compound **I1** is very close to the potential of *1c* from the compound **I2**, as both peaks correspond to the ester reduction, and (ii) the potential of 3c from the compound **I1** is very close to the peak potential of *2c* from the compound **I2**, since both peaks correspond to the indole reduction (Fig. 6).



As for the oxidation processes of the compounds **I1** and **I2**, it is observed that the nitrogen atoms from the indole fragments are the most oxidizable [28]. Consequently, in both cases, the processes corresponding to the peaks 1a (Fig. 6) have been assigned to the formation of the radical cations at the nitrogen atoms. These radical cations can further polymerize with tars formation (i) or can be further oxidized to dications (ii), followed by fragmentation. The processes denoted 2a from **I1**/ *3a* from **I2** (Fig. 6) could correspond to such subsequent unselective, destructive oxidations, as the current decreases after the last peak potential. The process corresponding to the peak *2a* from **I2** could be the oxidation of the amide (A) fragment, which occurs harder than the first indole oxidation.



4. Conclusions

The recorded data are important for the analytical detection of the investigated compounds by electrochemical methods. The investigated indolizines present similar electrochemical characteristics. The differences in behaviour are attributed to the structure differences. However, the common functional groups present electron transfers around the same potentials.

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