

Influence of the Solvent on the Electrochemical Behavior of 1H-3-Methyl-4-Ethoxycarbonyl-Benzylidene-Hydrazino-Pyrazole

L.V. Costea and V.N. Bercean

University "Politehnica" Timișoara, Faculty of Industrial Chemistry and Environmental Engineering, Piata Victoriei 2, 300006 Timisoara, Romania, Phone: +40-(0)256-404176, E-Mail: livius.costea@gmail.com

Abstract: The electrochemical properties of 1H-3-methyl-4-ethoxycarbonyl-5-benzylidenehydrazino-pyrazole have been investigated in two different aprotic nonaqueous solvents, at a platinum electrode. The voltammetric investigation of the above compound in anhydrous acetonitrile (AN) and dimethylsulfoxide (DMSO) respectively shows a somehow similar behavior but significant differences are also noticeable. The different peak separation and peak height can offer supplemental information in order to get a clearer view of the mechanism governing the anodic oxidation of the latter compound and to find the proper parameters to synthesize pyrazolo-triazoles by electro-synthesis.

Keywords: Cyclic voltammetry, Electrochemistry, Heterocycles, Nonaqueous solvents

1. Introduction

The main interest towards 1H-3-aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[5,1-c][1,2,4] triazoles (**I**) relies heavily on their biological activity [1], their use as intermediates in obtaining color photosensitive materials [2-4] as well as toners, inks and other photographic materials [5]. The latter compounds are used as precursors of color photographic light sensitive materials [2], toners, and ink jet printer dyes [5] as well as intermediates in producing solid-state dye-sensitized solar cells (DSSCs) [6].

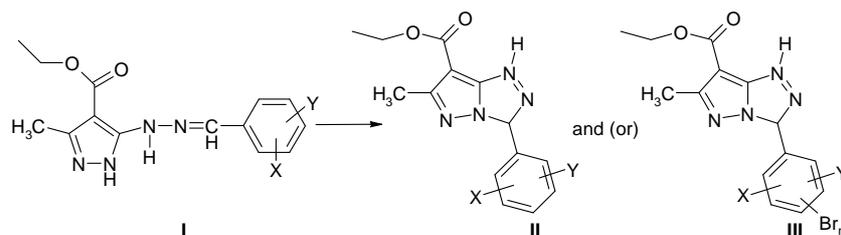
1H-3-Methyl-4-ethoxycarbonyl-5-arylidenehydrazino-pyrazoles are key intermediates in obtaining 1H-3-aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[5,1-c][1,2,4]triazoles. The intramolecular cyclization reaction of 1H-3-methyl-4-ethoxycarbonyl-5-arylidenehydrazono-pyrazoles (**I**) induced by either bromine in acetic acid [2] or using lead tetraacetate in acetic acid [7, 8] are the main ways of obtaining the 1H-3-aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[5,1-c][1,2,4] triazoles (Scheme 1).

In the presence of bromine and sodium acetate in glacial acetic acid, the hydrazones substituted with -Cl, -CH₃, -NO₂ [2] or -F, -CF₃, -4-pyridil [9] yield the corresponding pyrazolo-triazoles (**II**). If the substrate contains substituents like -OH, -OCH₃, the non-desired

brominated pyrazolo-triazoles (**III**) are formed (Scheme 1) [10]. In order to avoid this formation, we intended to obtain the desired compounds by electro synthesis [11-15]. Because, to our knowledge, no electrochemical investigation of this compound has been published so far, we present the results of an electrochemical investigation of 1H-3-methyl-4-ethoxycarbonyl-benzylidene-hydrazino-pyrazole (**Ia** X=Y=H) in various nonaqueous media in order to elucidate the mechanism of anodic oxidation. A better understanding of the electrochemical processes that take place at the electrode could help finding a more convenient way to obtain the desired pyrazolo triazoles by electro synthesis.

Therefore the study of the electrochemical behavior in various nonaqueous media of the unsubstituted hydrazone (**Ia**) using two different solvents is extremely important in order to get a better perspective on the electrochemical behavior of the latter.

With the aim of getting more relevant information regarding the mechanism of anodic oxidation of the hydrazone **I**, we've undertaken a comparative study of the electrochemical behavior of the latter compound in two nonaqueous solvents, namely *acetonitrile* (AN) and *dimethylsulfoxide* (DMSO) respectively by keeping all other experimental parameters constant.



Scheme 1. Synthetic pathways in the preparation of the 1H-3-aryl-6-methyl-7-ethoxycarbonyl-pyrazolo[5,1-c][1,2,4] triazoles (II) (III), (**Ia** X=Y=H)

2. Experimental

1H-3-methyl-4-ethoxycarbonyl-5-benzylidenehydrazinopyrazole, (**1a**, X =Y =H) was obtained according to the literature [2, 8, 9]. Dimethylsulfoxide (DMSO) and acetonitrile (AN) for synthesis (Fluka) as well as tetra-n-butylammonium tetrafluoroborate (TBATFB) (Merck) were used as purchased.

The purity of the compounds was >99%, as determined by HPLC. HPLC analyses were conducted with a Merck Chromolith Performance 2 column (fig.1), using acetonitrile/H₂O as eluant. Melting points were recorded with a Boetius PHMK (Veb-Analytik Dresden) apparatus; thin layer chromatography was performed using 60F₂₅₄ silica gel plates (Merck) and a mixture of benzene : ethyl acetate = 1:1 as eluant. IR spectra were recorded with a JascoFT/IR-410 Infrared Spectrophotometer using KBr disks and Bruker Avance 300 spectrometers were used for ¹H-NMR and ¹³C-NMR spectroscopy the characterization of the obtained compounds was reported elsewhere [16].

Cyclic voltammetry experiments were performed using a Jaisle 1200PCT potentiostat / galvanostat, coupled to an Agilent 33120A signal generator and an Agilent 34970A data acquisition system using Pt working electrodes and Pt auxiliary electrodes and were carried out in a single compartment cell with 7 cm³ of electrolyte solution containing $c=2\cdot 10^{-3}$ mol·L⁻¹ of substrate at room temperature. No correction was applied to compensate for the solution resistance. The solvent-supporting electrolyte system consisted of dry DMSO or AN and tetra-n-butylammonium tetrafluoroborate. Solutions for all voltammetric analyses were deoxygenated by bubbling with dry nitrogen and an atmosphere of dry nitrogen was maintained throughout the experiments All potentials were quoted with respect to the Ag/AgCl electrode at room temperature, which corresponds to a potential difference from that of Fc/Fc⁺ (Fc = ferrocene) standard redox couple

[17] of +0.45 V in DMSO / tetra-n-butylammonium tetrafluoroborate.

3. Results and Discussion

There are significant differences regarding physical constants between the two solvents, but the major common property that makes them useful for the studied processes is their high relative permittivity [18]. This allows them to influence the interactions between electric charges. The relative permittivity of the solvent has a paramount influence on the dissociation of electrolytes and on the solute-solvent interactions, both media being classified as polar solvents [19].

In order to determine the useful potential window that can be accomplished in both media, baring in mind that AN as well as DMSO are aprotic solvents, both the reduction and oxidation processes of the solvents are complicated and definite estimation of thermodynamic potential windows is almost impossible [19]. For these reasons, we determined the practical potential windows voltammetrically, using bright platinum working electrodes. A voltammogram was measured in the solvents under study, in the presence of TBATFB as supporting electrolyte.

The potential window of anhydrous AN / TBATFB 0,1M differs significantly of that of DMSO / TBATFB 0,1 M. As shown in fig. 2, the anodic potential limit of AN in the given conditions can reach values of up to 2,20 V, much broader than the values reached in DMSO. The negative limit is, on the other hand narrower in AN, reaching only -1,60 V. These data are in close accordance with the literature results [19, 20, 21] and to the general tendency that the negative potential limit expands to more negative values with the decrease in solvent acidity, while the positive potential limit expands to more positive values with the decrease in solvent basicity.

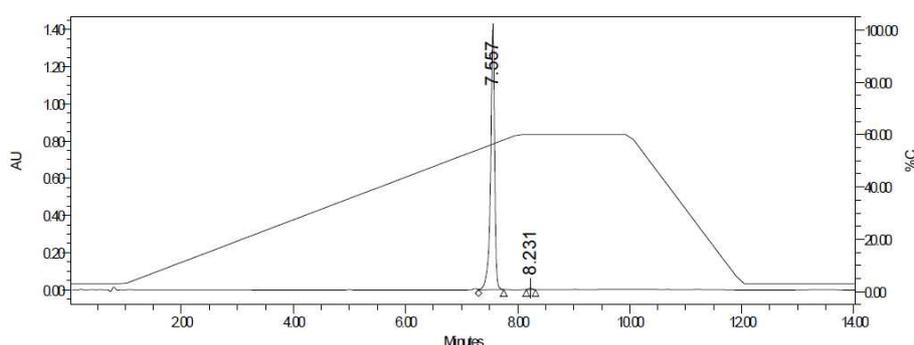


Figure 1. HPLC analysis of compound **1a**

Although both are aprotic solvents, meaning that they do not have a hydrogen atom joined to an electronegative atom, acetonitrile has a weaker basic character than DMSO, based on the value of their donor number. This has as a consequence the fact that in anhydrous AN cation radicals (**R⁺**) show a greater stability that in DMSO and

anion radicals (**R⁻**) have a much shorter lifetime [22, 23, 24]. In other words, one can assume that acetonitrile has a greater ability to transfer a hydrogen ion towards a radical anion thus making it more stable in its radical form than DMSO does.

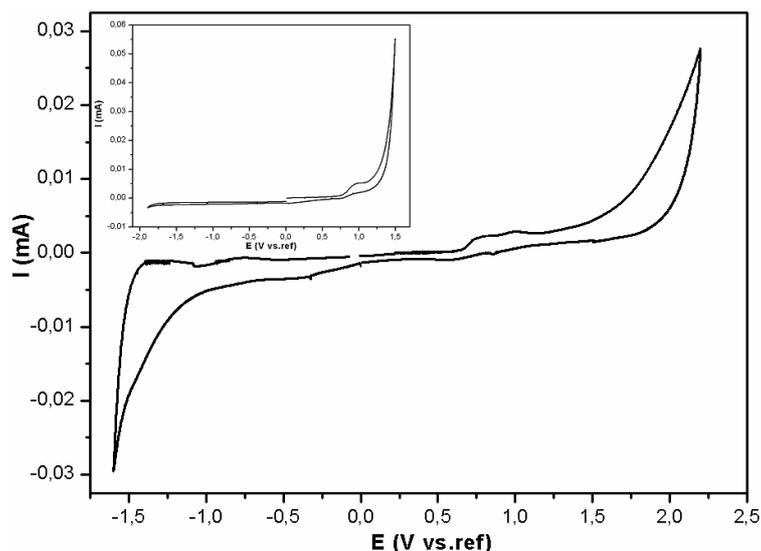


Figure 2. Cyclic voltammogram of the SSE in anhydrous AN. Conditions: supporting electrolyte: tetra-n-butyl ammonium tetrafluoroborate; working electrode: Pt; auxiliary electrode: Pt; reference electrode: Ag/AgCl; scan rate $50 \cdot 10^{-3} \text{ V} \cdot \text{s}^{-1}$. **Inset:** Cyclic voltammogram of the SES in anhydrous DMSO under the same experimental conditions.

Figure 3 shows the cyclic voltammetry curves at $50 \cdot 10^{-3} \text{ V} \cdot \text{s}^{-1}$ of a 10^{-3} M solution of compound **Ia** in AN/TBATFB 0,1M and DMSO/TBATFB 0,1M respectively onto a platinum electrode. During the oxidative scan a relatively small anodic current with a maximum at $E_{\text{pa}1} = +0,740 \text{ V/Ag:AgCl}$ can be observed (peak 1 fig. 3. inset). This peak current may be attributed to the formation of a cation radical. The irreversibility of the peak is likely due to the instability of the radical cation initially formed via electron transfer undergoing a fast

chemical reaction, probably a deprotonation process (scheme 2). [25, 26]. The similar shaped peak (1') can be observed during the voltammetric analysis carried out in DMSO. The main difference consists in the fact that under these conditions the signal appears at more positive potentials, i.e., $E_{\text{pa}1'} = +0,860 \text{ V}$. These findings lead to the conclusion that the first oxidation step of compound **I** occurs more slowly in DMSO in the first place due to its higher basicity compared to AN, leading to a less stable radical cation [22, 23].

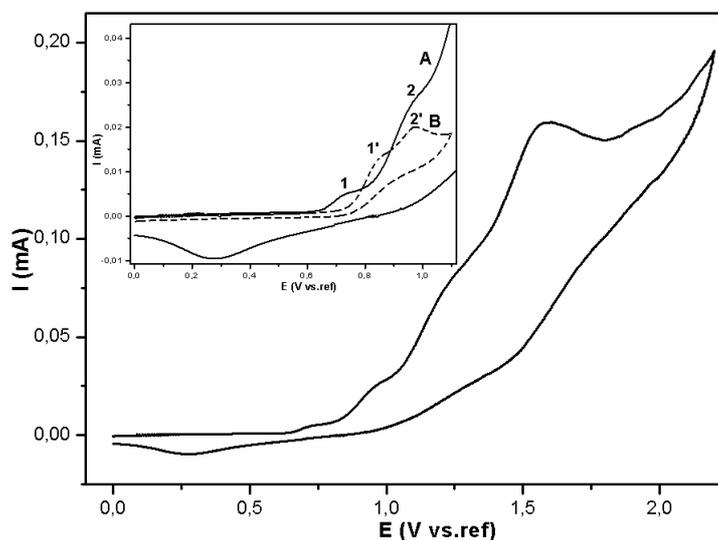


Figure 3. Cyclic voltammogram of **Ia** in anhydrous AN. Conditions: substrate concentration, $c=1 \cdot 10^{-3} \text{ mol} \cdot \text{L}^{-1}$; supporting electrolyte: tetra-n-butyl ammonium tetrafluoroborate; working electrode: Pt; auxiliary electrode: Pt; reference electrode: Ag/AgCl; scan rate $50 \cdot 10^{-3} \text{ V} \cdot \text{s}^{-1}$. **Inset:** Detailed view of the anodic scan of **Ia** in AN (curve A) and DMSO (B dotted line) under the same experimental conditions.

Variation of the electrode potential towards more positive values in AN reveals another anodic peak (2) situated at $E_{\text{pa}2} = +0,970 \text{ V}$. This signal may correspond to a second oxidation step of the intermediate formed after

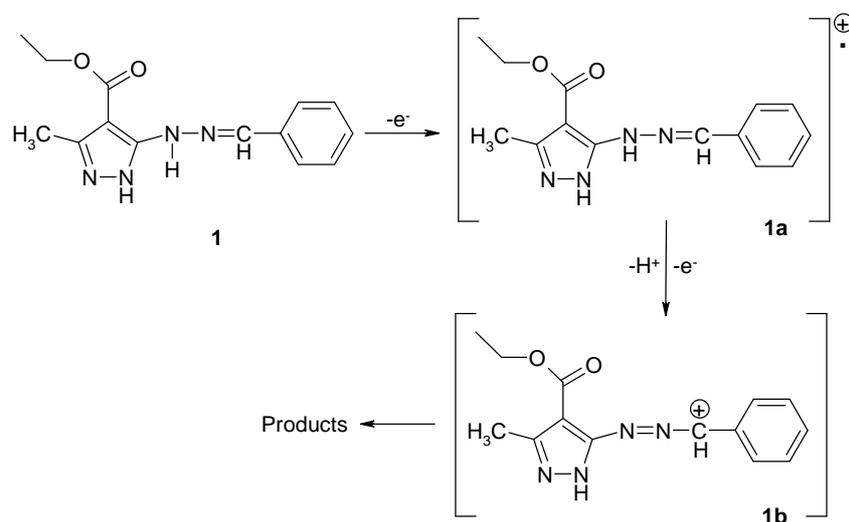
deprotonation occurred with the formation of a positively charged intermediate (scheme 2). It seems likely that this step is less influenced by the nature of the solvent. In DMSO the corresponding anodic signal (2', fig. 3 inset)

appears at a slightly more positive potential. A third well defined peak occurs in AN at a potential of about 1,6V, beyond the outermost boundary of the electrochemical potential window recorded in DMSO and corresponds most likely to the oxidative cyclization of the product resulting from the further transformation of carbocation **1b**. A more detailed report of the latter has been published elsewhere [16].

TABLE 1. Separation of the peak potentials of peaks 1 and 2 as a function of the utilized solvent

Solvent	ΔE_{p1-2} /mV
DMSO	113,5
AN	240,8

Reversing the scan direction and variation towards less positive potentials does not reveal any peaks related to the two oxidation signals 1' and 2' respectively (fig. 3



Scheme 2. Proposed anodic oxidation mechanism of compound **1a** on a Pt working electrode in anhydrous aprotic solvents

The peak separation of the first two anodic waves ΔE_{p1-2} is more than twice as wide in AN than in DMSO (Tab.1). Keeping in mind that the current-intensity curves have been recorded at the same voltage sweep rate, it follows that the radical intermediate **1a** that may result after the first oxidation step is significantly more stable in AN. Knowing that cation radicals are generally more stable in AN than in DMSO [22] we can assume that it is most likely that a radical cation intermediate (**1a** scheme 2) is formed after the first oxidation step.

One can observe a shift of the peak potentials towards less positive values in DMSO compared to AN. This fact may be due to the different stability of the cation radical formed after the first oxidation step in the two media [11, 22, 31], or due to the different reaction kinetics of the homogenous process of deprotonation with the formation of a positively charged intermediate [22, 32].

The stability of a radical ion depends firstly on the nature of the solvent [23, 24]. Radical cations are more stable in less nucleophilic solvents [22]. It has been shown

inset), recorded in DMSO during the forward scan. The broad shoulder observed in AN at about 0,276 V may be due to the irreversible reduction of the cyclization product previously formed [24, 27, 28].

The oxidation mechanism of hydrazone **1a** could thus follow an ECEC pattern [24], implying two electrochemical steps (scheme 2). The first electrochemical step, corresponding to peak 1 may have as a result the formation of a cation radical [29, 30]. After a homogenous step consisting of the deprotonation of the latter, the substrate loses one more electron forming the positively charged intermediate **1b** [30].

A comparative view of the voltammogram recorded in AN (curve A fig. 3 inset) and of that recorded in DMSO (curve B) under the same experimental conditions shows, aside of the aspects discussed above, a much greater peak separation in AN (table 1), thus in the solvent with the less basic character.

above that AN is not such a strong base as dimethylsulfoxide (DMSO), this leads to the fact that in anhydrous AN radical cations are more stable than in DMSO, i.e. the deprotonation occurs more slowly [22, 24]. Being more stable, hence having a greater lifetime, the two waves regarding the respective electron transfer steps show a greater peak separation in AN [24].

The charge delocalization within systems showing an extended π conjugation comes to further stabilize of the cation radical intermediate [33]. The solvent polarity, i.e. its permittivity is the third factor that affects the stability of the cation radical by influencing the coulombic force of attraction between the two oppositely charged ions (the cation radical and the counter ion originating from the electrolyte). That force is inversely proportional to the relative permittivity of the solvent, according to Eq. (1) [24, 34]. Therefore, the higher the relative permittivity and the larger the counter-ion (i.e. bigger a), the more ionic the intermediate would be [35].

$$E_{Per} = \frac{e_0^2}{\epsilon \cdot \epsilon_0 \cdot a} \quad (1)$$

where:

e_0 - electric charge of the electron, [C]

ϵ - permittivity of the solvent, [F m⁻¹]

ϵ_0 - permittivity of the vacuum, [F m⁻¹]

a - distance between the two electrical charges, [m]

Since both solvents have relative large permittivities, the electrostatic interaction between charges is weakened. The differences observed between the current-potential curves recorded in AN vs. DMSO could thus be generated by the increased polarity of the latter solvent [23, 24], leading to an intermediate having a predominant ionic character in DMSO [24, 34]. The latter intermediate is more likely to lose yet another electron during the second oxidation step leading to a significantly smaller peak separation.

4. Conclusion

A comparative view of the electrochemical response of the parent compound I in DMSO vs. AN shows a similar behavior of the substrate in both media. In anhydrous DMSO two very close but well defined oxidation peaks emerge, suggesting a two step irreversible anodic oxidation. The same pattern appears to be followed in anhydrous AN, but the peak separation is in this case more than twice as large. We can thus assume that the oxidation mechanism occurs in both solvents following an ECEC pattern meaning that the cation radical formed after the first oxidation step is significantly more stable in AN than in DMSO where it undergoes a rapid further transformation.

The second parameter that comes in favor of the assumption that the cation radical **1a** has a greater reactivity in DMSO is the potential at which the first oxidation step occurs. The process takes place at a less positive potential in AN, maybe because the formation of the cation radical intermediate is favored in this medium.

The second oxidation step with the loss of another electron and probable yielding of a carbocation occurs at roughly the same potentials in both solvents, leading to the assumption that the nature of the solvent has a lower influence over this electrode process.

The presented data reveal a decisive influence of the solvent over the mechanism of the investigated electrode processes. Due to its high polarity, DMSO facilitates the heterogeneous charge transfer steps disfavoring the deprotonation of the intermediate. Knowing that cation radicals are generally more stable in AN than in DMSO [22] we can assume that it is most likely that a radical cation intermediate is formed after the first oxidation step, further investigations being necessary in order to fully understand the studied reactions.

REFERENCES

1. Katsunori K., Takayuki S., Hiromi I., *JP 2002167305* (Konica Co., Japan) **2002**. "Industrial antibacterial and antifungal agent with reduced human toxicity".
2. Bailey J., *J.Chem.Soc.Perkin Trans.I*, **18**, **1977**, 2047-2052.
3. Bailey J., Bowes E., Marr P.A., *Brit. 1247493* **1967**, "Photographic colour processes".
4. Diehl D.R., Mbiya K., Wray C.S., *EP 20000628* (Eastman Kodak Co.USA) **2001**, "Photographic element containing pyrazolazole coupler".
5. Tawara K., Akira O., *EP 0763569A1* (Konica Co.Japan) **1997**, "Metal complex methin dye".
6. Aich R., Tran-Van F., Goubard F., Beouch L., Michaleviciute A., Grazulevicius J.V., Ratier B., Chevrot C., *Thin Solid Films*, **516**, **2008**, 7260.
7. Pizey J.S., "Synthetic Reagents", vol.3, John Wiley & Sons Inc., New York **1977**.
8. Bercean V., Ph. D. Thesis, University "Politehnica" Timișoara, **1998**.
9. Bercean V., V. Badea, M. Ilici, I. Neda, C. Csunderlik, *Rev. Chim.*, **56(3)**, **2005**, 297.
10. Csunderlik C., Bercean V., Peter F., Badea V., *ARKIVOC* (2002) (ii), **2002**, 133-141.
11. Fry Albert J, Britton W. E., Topics in Organic Electrochemistry, Plenum Press, New York, **1986**.
12. Gösser David K, Cyclic Voltammetry: Simulation and Analysis of Reaction Mechanisms, VCH, New York, **1993**.
13. Lazarescu Valentina, Vass M, *Roum Chem Quart Rev*, **6**, **1998**, 223.
14. Hammerich O, Methods for Studies of Electrochemical Reactions in: Lund H.; Hammerich O., Organic Electrochemistry (4th Edition) Marcel Dekker, Inc, New York, **2001**, 95-182.
15. Costea L, Bercean V, Badea V, Țăranu I; 11th Physical Chemistry Conference, Timișoara Romania, 2-5 Sept **2003**.
16. Costea L., Bercean, V., Badea, V., Gerdes, K., Jordis, U., *Monatshefte fuer Chemie/Chem. Monthly*, **137(6)**, **2006**, 737.
17. Gritzner G., Kuta J., *Pure and Appl. Chem.*, **56(4)**, **1984**, 461.
18. Riddick J. A., Bunger W. B., Organic Solvents, Physical Properties and Methods of Purification, 4th edn., Wiley & Sons, New York, **1986**.
19. Izutsu K., Electrochemistry in Nonaqueous Solutions, Wiley VCH Weinheim, **2002**.
20. Gritzner, G. *Pure Appl. Chem.*, **62**, **1990**, 1839.
21. Sabatino, A., LaManna, G., Paolini, I. *J. Phys. Chem.*, **1980**, **84**, 2641.
22. Volke J., Liska F., Electrochemistry in Organic Synthesis, Springer, **1994**.
23. Gösser David K, Cyclic Voltammetry: Simulation and Analysis of Reaction Mechanisms, VCH, New York, **1993**.
24. Bard A. J., Faulkner L. R., Electrochemical Methods: Fundamentals and Applications, 2-nd ed. John Wiley & Sons, New York, **2001**.
25. Gunic E., Tabakovic I., *J. Org. Chem.*, **53**, **1988**, 5081.
26. Simoin P., Farsang G., Amatore C., *J. Electroanal. Chem.*, **435**, **1997**, 165.
27. Fry Albert J., Synthetic Organic Electrochemistry, John Wiley & Sons, New York, **1989**.
28. Liang M., Xia X., Tingting C. Jie L., *Sensors*, **8**, **2008**, 1890.
29. Haiying W., Gang C., Xiaoping X., Hua C., Shunjun J., *Dyes and Pigments*, **86**, **2010**, 238-248.
30. Gunic E., Tabakovic I., *J. Org. Chem.*, **53**, **1988**, 5081.
31. Todres, Zory V., Ion-radical Organic Chemistry: Principles and Applications, (2nd Edition), CRC Press Taylor & Francis Group, **2009**.
32. Michalkiewicz S., Skorupa A., *Bioelectrochemistry*, **79**, **2010**, 57-65.
33. Lai R. Y., Kong Xiangxing, Jenekhe Samson A., Bard Allen J., *J. Am. Chem. Soc.*, **125(41)**, **2003**, 12631-12639.
34. Oldham K. B., Fundamentals of Electrochemical Science, Academic Press, San Diego, **1994**.
35. Reichardt Christian, Solvents and Solvent Effects in Organic Chemistry, Third Edition, Wiley VCH, Weinheim, **2003**.

Received: 14 April 2010

Accepted: 10 June 2010