Electrochemical Oxidation of Catechols in the Presence of Phenyl-Meldrum's Acid. Synthesis and Kinetic Evaluation

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Electrochemical oxidation of catechols in the presence of phenyl-Meldrum's acid as a nucleophile in aqueous solution has been studied in detail by means of cyclic voltammetry and controlled potential coulometry. The results indicate that the *o*-benzoquinone derived from catechols participates in Michael addition reaction with phenyl-Meldrum's acid to form corresponding products. We derived some new "highly oxygenated compounds with catechol ring" with good yields based on electrochemical oxidation in the controlled potential condition in aqueous solutions, without toxic reagents and solvents at carbon electrode in an undivided cell, using an environmentally friendly method. Furthermore, the observed homogeneous rate constants (k_{obs}) of the chemical reaction between *o*-benzoquinone and phenyl-Meldrum's acid were estimated by comparing the experimental cyclic voltammetric curves with the digitally simulated ones.

Key words catechol; phenyl-Meldrum's acid; highly oxygenated compound; cyclic voltammetry; homogeneous rate constant; digital simulation

Catechol, by itself, and mono-substituted catechols are active in part against *Pseudomonas*, *Bacillus*, but not *Penicillium* species. Many flavonoids and catechol derivatives turned out to be as antimicrobial agents.[1] In this connection, in order to synthesis catechol derivatives, we studied the electrochemical oxidation of benzenediols in the presence of CH acid nucleophiles,[2—4] SH acid nucleophiles,[5—9] nitrite ion[10] and triphenylphosphine.[11] Also, it is demonstrated that, in comparison with simple catechols, the "highly oxygenated compounds with catechol ring" exhibit interesting biological activities.[12,13] Therefore, the development of a simple synthetic route for the synthesis of "highly oxygenated compounds with catechol ring" from readily available reagents is one of the major tasks. In this direction, we recently reported the synthesis of some "highly oxygenated compounds with catechol ring."[14] This idea prompted us to investigate the electrochemical oxidation of catechols in the presence of phenyl-Meldrum's acid as a nucleophile and represents a facile and one-pot electrochemical method for the synthesis of some new "highly oxygenated compounds with catechol ring." Also, an additional purpose of this work is the kinetic and mechanistic study of the electrochemical oxidation of catechols in the presence of phenyl-Meldrum's acid and the estimation of the observed homogeneous rate constants (k_{obs}) of reaction of electrochemically generated *o*-benzoquinones with this nucleophile by digital simulation of cyclic voltammograms.

Results and Discussion

Electrochemical Investigations The cyclic voltammogram of 1.0 mM catechol (**1a**) in aqueous solution containing 0.2 M acetate buffer (pH=5.0) shows one anodic peak (A_1) and the corresponding cathodic peak which correspond to the transformation of catechol (**1a**) to *o*-benzoquinone (**2a**) and *vice-versa*, within a quasi-reversible two electron process (Fig. 1, curve a).[2—11] The electrooxidation of catechol (**1a**) in the presence of phenyl-Meldrum's acid (**3**) was studied in some detail. Fig. 1, curve b, shows the first cyclic voltammogram obtained for a 1.0 mM solution of **1a** in the presence of 0.1 mM phenyl-Meldrum's acid (**3**). The voltammogram exhibits one anodic peak (A_1) and one cathodic peak (C_1) that shows decreasing in comparison to the cathodic peak of catechol (**1a**) in the absence of **3**. In this figure, curve c is the voltammogram of **3** in the absence of **1a**.

The effect of potential sweep rate on shape of cyclic voltammograms of catechol (**1a**) in the presence of phenyl-Meldrum's acid (**3**) was studied, too. It is seen that, proportional to the augmentation of the potential sweep rate, the height of peak C_1 increases. A similar situation is observed when the **3** to **1a** concentration ratio is decreased. A plot of the peak current ratio (I_{pC1}/I_{pA1}) *versus* the scan rate for a mixture of catechol (**1a**) and phenyl-Meldrum's acid (**3**) confirms the reactivity of *o*-benzoquinone (**2a**) toward phenyl-Meldrum's acid (**3**), appearing as an increase in the peak cur-

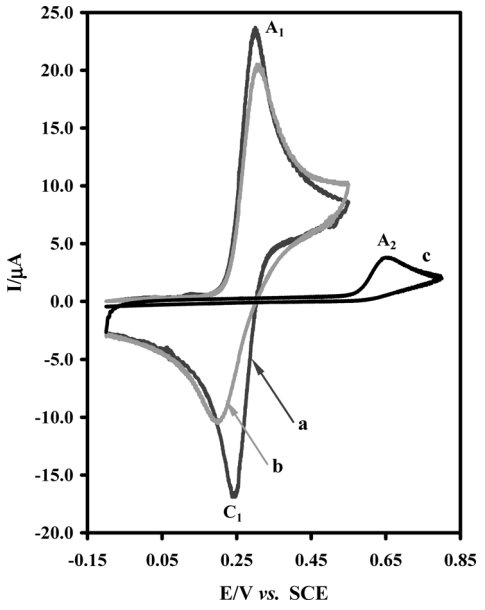

Fig. 1. Cyclic Voltammograms of (a) 1.0 mM Catechol (**1a**), (b) 1.0 mM Catechol (**1a**) in the Presence of 0.1 mM Phenyl-Meldrum's Acid (**3**) and (c) 0.1 mM Phenyl-Meldrum's Acid in the Absence of **1a** at a Glassy Carbon Electrode in Solution Containing 0.2 M Acetate Buffer (pH=5.0)

Scan rate: 100 mV s^{-1}; t=25±1 °C.

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rent ratio (I_{pC1}/I_{pA1}) at higher scan rates (Fig. 2). Furthermore, under these conditions, the current function for peak A_1, ($I_{pA1}/v^{1/2}$), changes only slightly with increasing the scan rate.

Controlled-potential coulometry was performed in an aqueous solution, containing 0.20 mmol of **1a** and 0.20 mmol of **3** at 0.35 V *vs.* SCE. The monitoring of electrolysis progress was carried out by linear sweep voltammetry (Fig. 3). It shows that, proportional to the advancement of coulometry, the anodic peaks A_1 and A_2 decreases and disappears when the charge consumption becomes about $2e^-$ per molecule of **1a** (Fig. 3, inset). Comparison of these voltammograms with curve c in Fig. 1 reveals that the peak A_2 in Fig. 3 corresponds to the oxidation of phenyl-Meldrum's acid (**3**).

Diagnostic criteria of cyclic voltammetry, the consumption of two electrons per molecule of **1a**, and the spectroscopic data (IR, ^{1}H-NMR, ^{13}C-NMR and MS) of the isolated product, indicated that the reaction mechanism of electrooxidation of **1a** in the presence of phenyl-Meldrum's acid (**3**) is *EC* (electrochemical and chemical reactions) mechanism[15] (Chart 1).

The 1,4-addition (Michael) reaction of phenyl-Meldrum's acid (**3**) to the *ortho*-benzoquinone intermediate **2b** and **2c** can conceivably occur at C-4 and C-5 resulting in products **4b** or **5b** and **4c** or **5c**, respectively (Fig. 4). The ^{1}H-NMR spectra of the isolated products display two doublet peaks (with *J* about 2 Hz) in each case with "no vicinal" coupling constants (see Experimental, Characteristic of Products section) in support of structures **4b** and **4c**.

Accordingly, the electrochemical oxidation catechols with electron-withdrawing groups, such as 2,3-dihydroxybenzoic

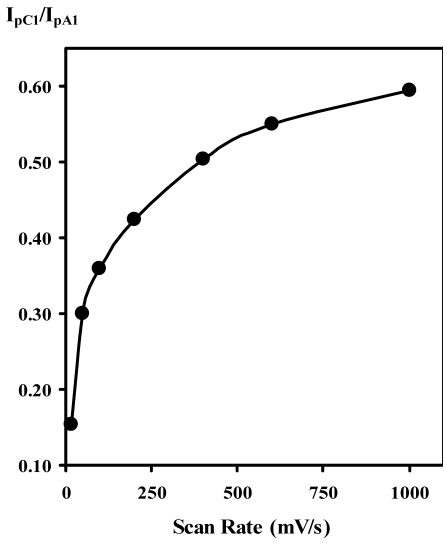


Fig. 2. Variation of Peak Current Ratio (I_{pC1}/I_{pA1}) *versus* Scan Rate in Electrochemical Oxidation of 1.0 mM Catechol (**1a**) in the Presence of 1.0 mM Phenyl-Meldrum's Acid (**3**) at a Glassy Carbon Electrode in Aqueous Solution Containing 0.2 M Acetate Buffer (pH=5.0)

t=25±1 °C.

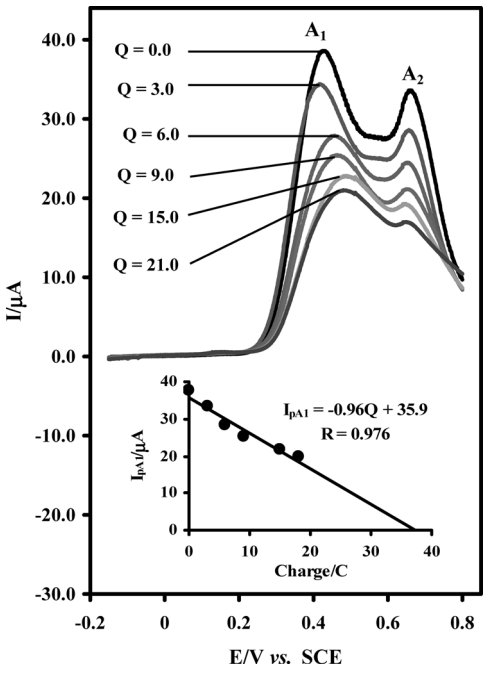
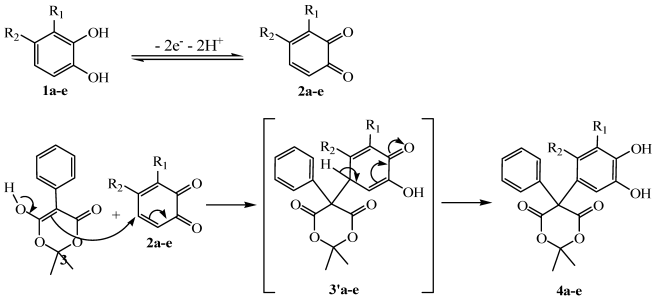


Fig. 3. Linear Sweep Voltammograms of 0.20 mmol Catechol (**1a**) in the Presence of 0.20 mmol Phenyl-Meldrum's Acid (**3**) in Solution Containing 0.2 M Actate Buffer (pH 5.0) at a Glassy Carbon Electrode during Controlled Potential Coulometry at 0.30 V *vs.* SCE

Inset: variation of peak current (I_{pA1}) *vs.* charge consumed. Scan rate 100 mV s^{-1}; t=25±1 °C.



	R_1	R_2	Isolated Yield (%)
4a	H	H	95
4b	CH_3	H	91
4c	OCH_3	H	92
4d	H	CH_3	96
4e	H	*tert*-Butyl	--

Chart 1

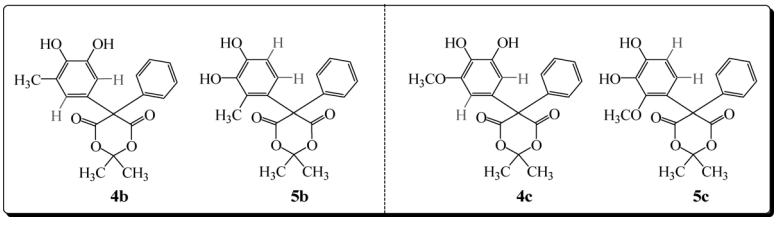


Fig. 4. The Possible Structures of Final Product of Electrochemical Oxidation of 3-Methylcatechol (**1b**) and 3-Methoxycatechol (**1c**) in the Presence of Phenyl-Meldrum's Acid (**3**)

acid, 3,4-dihydroxybenzoic acid, 2,5-dihydroxy-benzoic acid and 3,4-dihydroxybenzonitrile in the presence of phenyl-Meldrum's acid has been studied in detail by means of cyclic voltammetry and controlled potential coulometry. Contrary to the catechols with electron-donating groups (**1a**—**e**), our results indicate that the final products from oxidation of catechols with electron-withdrawing groups are "highly oxygenated compounds with benzoquinone ring."

Kinetic Studies A chart for the electrochemical oxidation of catechols in the presence of phenyl-Meldrum's acid (**3**) is proposed and tested by digital simulation. On the basis of an *EC* mechanism, the observed homogeneous rate constants (k_{obs}) of reaction of *o*-benzoquinones with phenyl-Meldrum's acid (**3**) have been estimated by comparison of the simulation results, (Fig. 5, curve b), with experimental cyclic voltammograms (Fig. 5, curve a). The transfer coefficient (α) was assumed to be 0.5, and the formal potentials were obtained experimentally as the average of the two peak potentials observed in cyclic voltammetry. The heterogeneous rate constants are estimated by use of an experimental working curve.[16] The procedure is performed for achieving the best fit between simulated and experimental cyclic voltammograms (Table 1). The method is developed for a variety of scan rates and nucleophile concentrations.

As shown in Table 1, the magnitude of the observed homogeneous rate constant (k_{obs}) is dependent on the nature and position of the substituted group on the catechol ring. The presence of electron-donating groups such as methyl (**1b**, **d**), methoxy (**1c**), or *tert*-butyl (**1e**) on the catechol ring causes a decrease in k_{obs}. In addition, the presence of substituted groups in the C-4 position of the catechol ring that is a reactive site of *o*-benzoquinones (**2**) causes a decrease in the observed homogeneous rate constant (k_{obs}) (Table 1, comparison of **1b** and **1d**). In this study, because of the electron-donating and steric characters of the *tert*-butyl group in the C-4 position of the catechol ring, the least observed homogeneous rate constant (k_{obs}) belongs to 4-*tert*-butylcatechol (**1e**).

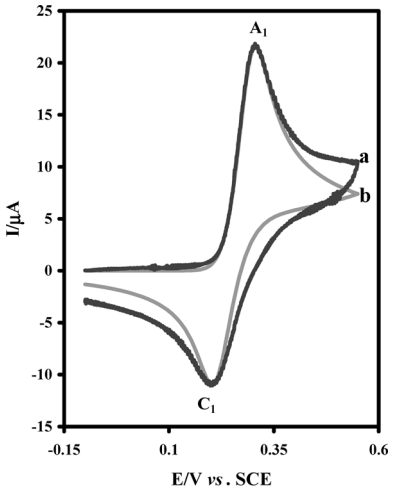


Fig. 5. Cyclic Voltammograms of 1.0 mM Catechol (**1a**) in the Presence of 1.0 mM Phenyl-Meldrum's acid (**3**) in Acetate Buffer Solution (pH 5.0) 0.2 M: (a) Experimental and (b) Simulated

Scan rate: 100 mV s^{-1}. Working electrode: glassy carbon electrode. t=25±1 °C.

Conclusion

In this study, we have investigated the use of the electrochemistry for the synthesis of some new "highly oxygenated compounds with catechol ring" (**4a**—**d**) *via* oxidation of catechols **1a**—**d** in the presence of phenyl-Meldrum's acid (**3**) in aqueous solutions. Final products are obtained *via* an *EC* mechanism, after consumption of 2e^- per molecule of catechols (**1a**—**d**). The present results complete the previous report on the anodic oxidation of catechols in the presence of Meldrum's and methyl-Meldrum's acid.[14] In this work, we derived products **4a**—**d** with good yields based on electrochemical oxidation under controlled potential conditions in aqueous solutions, without toxic reagents and solvents using an environmentally friendly method at a carbon electrode in an undivided cell. Also, the observed homogeneous rate constants (k_{obs}) were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results. The calculated observed homogeneous rate constants (k_{obs}) was found to vary in the order catechol (**1a**)>3-methylcatechol (**1b**)>3-methoxycatechol (**1c**)>4-methylcatechol (**1d**)>4-*tert*-butylcatechol (**1e**).

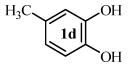
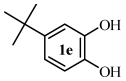
Experimental

Apparatus Controlled-potential coulometry, cyclic voltammetry, and preparative electrolysis were performed using an Autolab model PGSTAT 20 potentiostat/galvanostat. The working electrode used in the cyclic voltammetry experiments was a glassy carbon disc (1.8 mm^2 area) and a platinum wire was used as the counter electrode. The working electrode used in controlled-potential coulometry and macroscale electrolysis was an assembly of four carbon rods (31 cm^2) and a large platinum gauze constituted the counter electrode. The working electrode potentials were measured *versus* SCE (all electrodes from AZAR Electrodes). The homogeneous rate constants were estimated by analyzing the cyclic voltammetric responses, using the DigiElch simulation software.[17] C, H, N analyses were performed on a Vario EL III elemental analyzer.

Reagents All chemicals (catechols and phenyl-Meldrum's acid) were reagent-grade materials. Sodium acetate, solvents and reagents were of pro-analysis. These chemicals were used without further purification.

Electroorganic Synthesis of 4a—d In a typical procedure, 80 ml of acetate buffer (pH=5.0, c=0.2 M) was pre-electrolyzed at potential of peak A_1 in an undivided cell, and then 1 mmol of catechol (**1a**—**d**) and 1 mmol of phenyl-Meldrum's acid (**3**) were added to the cell. The electrolysis was terminated when the decay of the current became more than 95%. The process was interrupted during the electrolysis, and the graphite anode was washed in acetone to reactivate it. At the end of electrolysis, a few drops of acetic

Table 1. Calculated Observed Homogeneous Rate Constant (k_{obs}) for Michael Addition Reaction of Electrochemically Generated *o*-Benzoquinones with Phenyl-Meldrum's Acid (**3**) in Aqueous Acetate Buffer (pH 5.0, c=0.2 M)

Catechol	 **1a**	 **1b**	 **1c**	 **1d**	 **1e**
k_{obs} (M^{-1} s^{-1})[a]	197±1.55	122±1.23	104±0.945	38±0.55	3±0.02

a) Standard deviation of five independent simulations at various scan rates.

acid added were added to the solution and the cell was placed in a refrigerator overnight. The precipitated solid was collected by filtration and washed several times with water. After washing, products were characterized by IR, ^{1}H-NMR, ^{13}C-NMR, and MS. The isolated yields after washing are reported.

Characteristic of Products 5-(3,4-Dihydroxyphenyl)-2,2-dimethyl-5-phenyl-1,3-dioxane-4,6-dione (**4a**): mp 202—204 °C (dec.). IR (KBr) cm^{-1}: 3377, 2923, 1756, 1715, 1612, 1531, 1436, 1395, 1383, 1316, 1269, 1201, 1129, 1097, 1049, 1024, 977, 932, 902, 871, 830, 793, 762, 715, 678, 647, 625. ^{1}H-NMR (300 MHz, acetone-d_6) δ: 1.55 (s, 3H, methyl), 1.70 (s, 3H, methyl), 6.69 (dd, J=8.3, 2.1 Hz, 1H, aromatic in catechol ring), 6.85 (d, J=2.1 Hz, 1H, aromatic in catechol ring), 6.96 (d, J=8.4 Hz, 1H, aromatic in catechol ring), 7.22 (m, 5H, aromatic), 8.42, 8.48 (s, s, 2H, –OH). ^{13}C-NMR (75.4 MHz, acetone-d_6) δ: 27.0, 64.8, 105.7, 115.7, 115.8, 120.2, 126.3, 128.0, 128.3, 128.9, 139.4, 145.7, 146.0, 166.7. MS (EI): *m*/*z* (relative intensity): 328 $[M]^{+\cdot}$ (3), 226 (23), 197 (44), 152 (60), 115 (18), 43 (100). *Anal.* Calcd for $C_{18}H_{16}O_6$: C, 65.85; H, 4.91. Found: C, 65.22; H, 4.80.

5-(3,4-Dihydroxy-5-methylphenyl)-2,2-dimethyl-5-phenyl-1,3-dioxane-4,6-dione (**4b**): mp 207—209 °C (dec.). IR (KBr) cm^{-1}: 3476, 2926, 1768, 1728, 1615, 1541, 1452, 1337, 1295, 1204, 1082, 1030, 932, 839, 711. ^{1}H-NMR (300 MHz, acetone-d_6) δ: 1.48 (s, 3H, methyl), 1.80 (s, 3H, methyl), 2.23 (s, 3H, methyl), 6.63 (d, J=2.0 Hz, 1H, aromatic in catechol ring), 6.70 (d, J=2.0 Hz, 1H, aromatic in catechol ring), 7.20 (m, 5H, aromatic), 7.78 (s, 1H, –OH), 8.76 (s, 1H, –OH). ^{13}C-NMR (75.4 MHz, acetone-d_6) δ: 15.4, 26.8, 64.8, 105.6, 113.1, 121.8, 125.0, 125.3, 127.9, 128.1, 129.0, 139.7, 144.3, 145.0, 166.7. MS (EI): *m*/*z* (relative intensity): 342 $[M]^{+\cdot}$ (1), 211 (14), 165(18), 43 (100). *Anal.* Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 67.00; H, 5.17.

5-(3,4-Dihydroxy-5-methoxyphenyl)-2,2-dimethyl-5-phenyl-1,3-dioxane-4,6-dione (**4c**): mp 163—165 °C (dec.). IR (KBr) cm^{-1}: 3448, 2921, 1767, 1728, 1611, 1543, 1451, 1337, 1295, 1203, 1081, 1031, 931 839, 710. ^{1}H-NMR (300 MHz, acetone-d_6) δ: 1.50 (s, 3H, methyl), 1.72 (s, 3H, methyl), 3.76 (s, 3H, methoxy), 6.49 (d, J=2.1 Hz, 1H, aromatic in catechol ring), 6.56 (d, J=2.2 Hz, 1H, aromatic in catechol ring), 7.22 (m, 5H, aromatic), 8.11 (br s, 1H, –OH), 8.27 (br s, 1H, –OH). ^{13}C-NMR (75.4 MHz, acetone-d_6) δ: 26.9, 55.8, 65.0, 103.9, 105.8, 109.7, 125.0, 128.0, 128.2, 128.9, 134.9, 139.5, 146.0, 148.7, 166.7. MS (EI): *m*/*z* (relative intensity): 358 $[M]^{+\cdot}$ (5), 256 (27), 227 (16), 181 (18), 139 (27), 59 (20), 43 (100). *Anal.* Calcd for $C_{19}H_{18}O_7$: C, 63.68; H, 5.06. Found: C, 63.23; H, 4.91.

5-(4,5-Dihydroxy-2-methylphenyl)-2,2-dimethyl-5-phenyl-1,3-dioxane-4,6-dione ($C_{19}H_{18}O_6$) (**4d**): mp 213—215 °C (dec.). ^{1}H-NMR (300 MHz, acetone-d_6) δ: 1.21 (s, 3H, methyl), 1.79, (s, 3H, methyl), 1.95, (s, 3H, methyl), 5.85 (s, 1H, aromatic), 6.72 (s, 1H, aromatic), 7.50 (m, 5H, aromatic), 7.8 (br, 1H, –OH), 7.9 (br, 1H, –OH). ^{13}C-NMR (75.4 MHz, acetone-d_6) δ: 19.0, 26.3, 64.0, 105.9, 118.1, 118.3, 127.1, 128.7, 129.5, 130.0, 130.9, 133.3, 142.1, 144.4, 166.0. MS (EI): *m*/*z* (relative intensity): 342 $[M]^{+\cdot}$ (3), 240 (14), 211 (20), 195(16), 165 (23), 43 (100). *Anal.* Calcd for $C_{19}H_{18}O_6$: C, 66.66; H, 5.30. Found: C, 66.87; H, 5.19.

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References and Notes

1) Pauli A., "Third World Congress on Allelopathy," Tsukuba, August 26—30, 2002.
2) Nematollahi D., Alimoradi M., Husain S. W., *Electroanalysis*, **16**, 1359—1365 (2004).
3) Nematollahi D., Alimoradi M., Rafiee M., *J. Phys. Org. Chem.*, **20**, 49—54 (2007).
4) Nematollahi D., Dehdashtian S., Niazi A., *J. Electroanal. Chem.*, **616**, 79—86 (2008).
5) Nematollahi D., Tammari E., *J. Org. Chem.*, **70**, 7769—7772 (2005).
6) Namatollahi D., Azizian J., Sargordan-Arani M., Hesari M., Jameh-Bozorghi S., Alizadeh A., Fotouhi L., Mirza B., *Chem. Pharm. Bull.*, **56**, 1562—1566 (2008).
7) Nematollahi D., Rahchamani R. A., *Tetrahedron Lett.*, **43**, 147—150 (2002).
8) Nematollahi D., Rahchamani R. A., *J. Electroanal. Chem.*, **520**, 145—149 (2002).
9) Nematollahi D., Varmaghani F., *Electrochim. Acta*, **53**, 3350—3355 (2008).
10) Nematollahi D., Ariapad A., Rafiee M., *J. Electroanal. Chem.*, **602**, 37—42 (2007).
11) Nematollahi D., Tammari E., Esmaili R., *J. Electroanal. Chem.*, **621**, 113—116 (2008).
12) Sawayama Y., Tsujimoto T., Sugino K., Nishikawa T., Isobe M., Kawagishi H., *Biosci. Biotechnol. Biochem*., **70**, 2998—3003 (2006).
13) Bui V. P., Hansen T. V., Stenstrøm Y., Hudlicky T., *J. Green Chem.*, **2**, 263—265 (2000).
14) Nematollahi D., Shayani-Jam H., *J. Org. Chem.*, **73**, 3428—3434 (2008).
15) Bard A. J., Faulkner L. R., "Electrochemical Methods," 2nd ed., Wiley, New York, 2001, p. 497.
16) Greef R., Peat R., Peter L. M., Pletcher D., Robinson J., "Instrumental Methods in Electrochemistry," Ellis Horwood, New York, 1990, p. 189.
17) Rudolph M., *J. Electroanal. Chem.*, **529**, 97—108 (2002) see also: http://www.digielch.de.