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ORIGINAL PAPER

Electrochemical production of novel products from 2,3-dimethylhydroquinone in the presence of some *β*-diketones

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Abstract Electrochemical oxidation of 2,3-dimethylhydroquinone has been studied in the presence of *β*-diketones as nucleophiles in aqueous solution using cyclic voltammetry and controlled-potential coulometry. The results indicate that the derivatives of 2,3-dimethylhydroquinone participate in a Michael addition reaction to form the corresponding benzofuran derivatives. The electrochemical synthesis has been successfully performed at pH 7.0 and $E = 0.1$ V versus an Ag|AgCl|KCl (3 M) in an undivided cell in good yield and purity.

Keywords Cyclic voltammetry · Electrochemical synthesis · ECEC mechanism · ECECE mechanism · 2,3-Dimethylhydroquinone

Introduction

The importance of heterocyclic compounds can not be overstated; approximately one half of all known organic compounds contain a heterocyclic ring. These compounds, either natural products or designed molecules, are responsible for an amazing variety of biological processes and they feature in most pharmaceuticals [1]. Benzofuran derivatives are an important class of heterocyclic compounds that are known to possess important biological properties. Applications of substituted benzofurans include use as fluorescence sensors [2], oxidants [3], antioxidants [4], and brightening agents [5], and they are the basic skeleton of numerous compounds possessing cardiovascular activity [6] and of compounds used in other fields of chemistry and in agriculture [5].

As we know, one of the prime principles of green chemistry is to develop an alternative reaction medium, and synthesis in water by an electrochemical method is the basis for the development of many cleaner chemical technologies. With regard to electrochemical oxidation of hydroquinones in the presence of different nucleophiles, the main purpose of previous studies was to investigate mechanistic aspects [7–16]. It has been clearly shown that the electrooxidation of hydroquinones with electron–withdrawing groups in aqueous solution leads to corresponding benzoquinones with consumption of approximately two electrons per molecule in each step of the oxidation [17–20]. For this reason, we report the electrochemical oxidation of 2,3-dimethylhydroquinone in the presence of *β*-diketones as nucleophiles.

Results and discussion

The cyclic voltammogram of 2 mM 2,3-dimethylhydroquinone (1) in a mixture of water–acetonitrile (80:20) containing 0.20 M phosphate (KH_2PO_4/K_2HPO_4) solution at pH 7.0 shows one anodic peak (A_1) and a corresponding cathodic peak (C_1), which correspond to the transformation of 1 to *p*-benzoquinone (2) and vice versa, within a quasi-reversible two-electron process (Fig. 1, curve a). A peak current ratio (I_P^{C1}/I_P^{A1}) of nearly unity, particularly during repetitive recycling of the potential, can be considered as a criterion for the stability of *p*-benzoquinone produced at the surface of electrode under these experimental conditions. In other words, any possible hydroxylation [21–24] or dimerization [25] reactions are too slow to be observed on the time scale of the cyclic voltammetry. The oxidation

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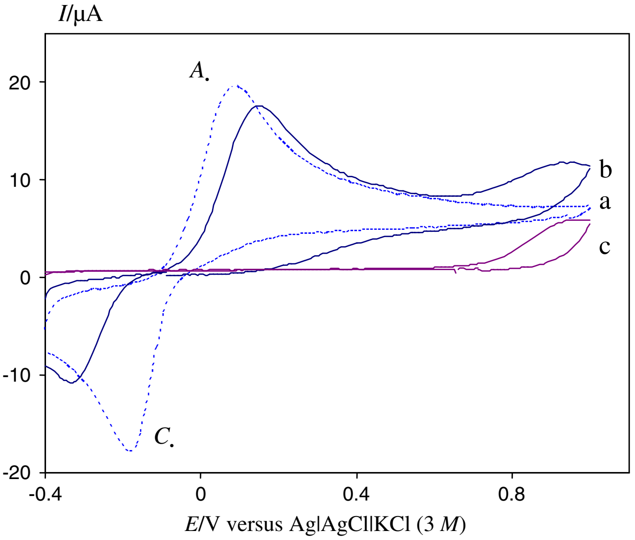


Fig. 1 Cyclic voltammograms of 2 mM 2,3-dimethylhydroquinone (1) in the absence *a* and presence *b* of 2 mM 4-hydroxy-1-methyl-2(*1H*)-quinolone (3a); (*c*) cyclic voltammogram of 2 mM 3a at a glassy carbon electrode (1.8 mm diameter) in a mixture of water–acetonitrile (80:20) containing 0.20 M phosphate (KH_2PO_4/K_2HPO_4) solution of pH 7.0. Scan rate: 100 mV s^{-1}; $t = 25 \pm 1$ °C

of 1 in the presence of 4-hydroxy-1-methyl-2(*1H*)-quinolone (3a) as a nucleophile was studied in some detail. Figure 1, curve b shows the cyclic voltammogram obtained for a 2 mM solution of 1 in the presence of 2 mM 3a. The voltammogram exhibits one anodic peak at 0.08 V versus an Ag|AgCl|KCl (3 M) electrode and the cathodic counterpart of the anodic peak (C_1) decreases. The anodic and cathodic peaks shift in the presence of 3a (Fig. 1, curve b), because of formation of a thin film of product at the surface of the electrode, inhibiting to some extent the performance of the electrode process. In this figure, curve c is the voltammogram of 2 mM 3a alone in the buffer solution.

It is seen that, in proportion to the augmentation of the potential sweep rate, the height of the C_1 peak increases (Fig. 2, curves a–d). A similar situation was observed when the concentration ratio of 3a to 1 was decreased. The current function for the A_1 peak, $I_P^{A1}/v^{1/2}$, changes with an increase in scan rate (Fig. 2, curve i). On the other hand, a plot of the peak current ratio (I_P^{C1}/I_P^{A1}) against the scan rate for a mixture of 1 and 3a, revealed an increase in the height of the cathodic peak (C_1) at higher scan rates (Fig. 2, curve j) and such behavior is adopted as indicative of an ECEC mechanism [23–25].

Controlled-potential coulometry was performed in an aqueous solution containing 0.25 mmol 1 and 0.25 mmol *β*-diketones 3a–3c at 0.10 V versus an Ag|AgCl|KCl (3 M) electrode. The electrolysis progress was monitored by the use of cyclic voltammetry (Fig. 3).

It is shown that, in proportion to the advancement of coulometry, the anodic peak (A_1) decreases and disappears when the charge consumption becomes approximately $4e^-$ per molecule of 1 in the presence of 3a and 3b and $6e^-$ in the presence of 3c. These observations allowed us to propose the pathway shown in Scheme 1 for electrochemical oxidation of 1 in the presence of 3a–3c. According to our results, it appears that the 1,4-Michael addition reaction of the anion enolate of 3a–3c with 2 (Eq. 2 in Scheme 1) is much faster than other secondary reactions, presumably leading to the intermediates 4a–4c. The oxidation of 4a–4c is easier than the oxidation of the parent starting molecule 1 by virtue of the presence of an electron-donating group [26] and it can be oxidized at the electrode surface (Eq. 3 in Scheme 1) or by chemical reaction (Eq. 4 in Scheme 1).

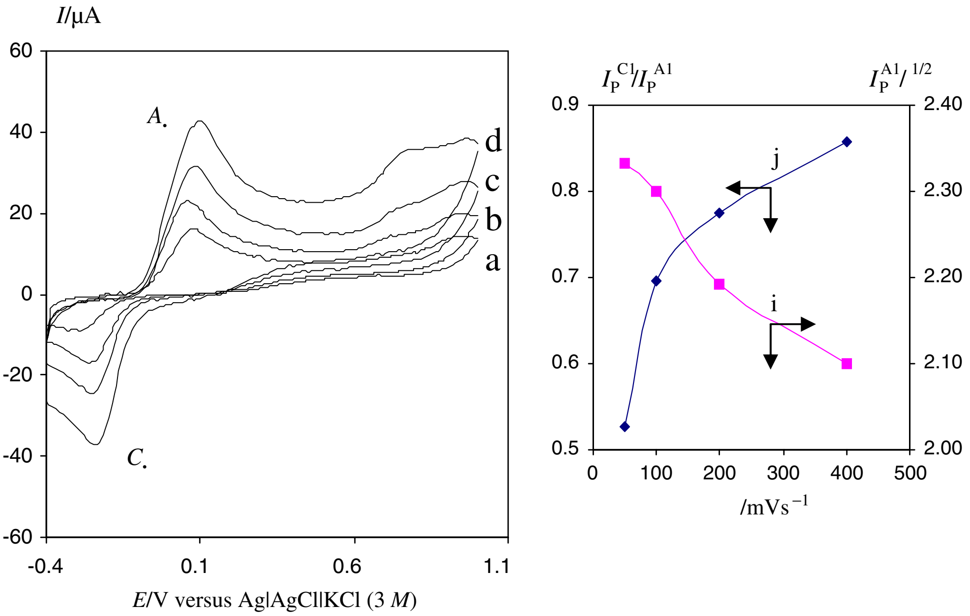


Fig. 2 Typical voltammograms of 2 mM 2,3-dimethylhydroquinone in the presence of 2 mM 4-hydroxy-1-methyl-2(*1H*)-quinolone at a glassy carbon electrode (1.8 mm diameter) and at various scan rates in a mixture of water–acetonitrile (80:20) containing 0.20 M phosphate (KH_2PO_4/K_2HPO_4) solution at pH 7.0. Scan rates from *a* to *d* are: 50, 100, 200, and 400 mV s^{-1}. (*i*) Variation of the peak current function ($I_P^{A1}/v^{1/2}$) versus scan rate. (*j*) Variation of the peak current ratio (I_P^{C1}/I_P^{A1}) versus scan rate; $t = 25 \pm 1$ °C

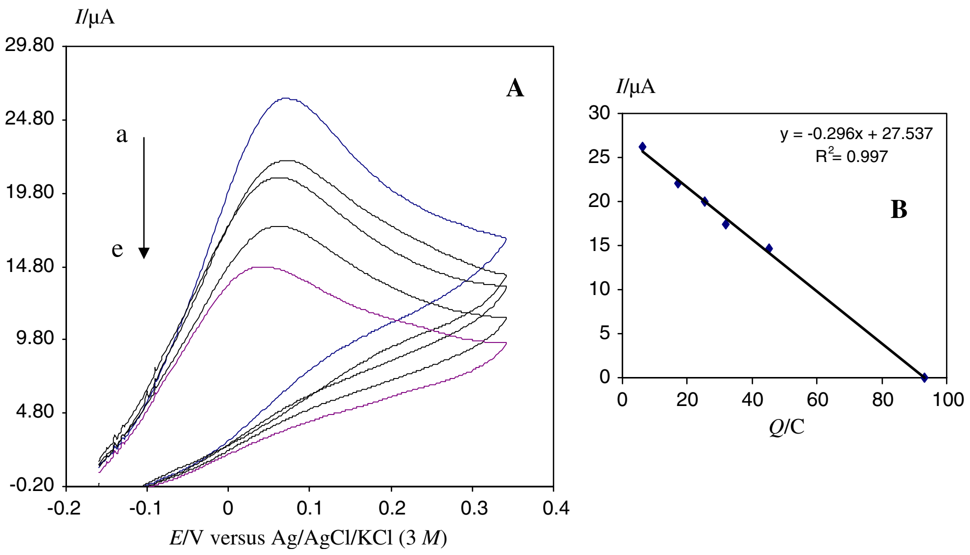


Fig. 3 (**a**) Cyclic voltammograms of 0.25 mmol 2,3-dimethylhydroquinone (1) in the presence of 0.25 mmol 4-hydroxy-1-methyl-2(*1H*)-quinolone (3a) in a mixture of water–acetonitrile (80:20) containing 0.20 M phosphate (KH_2PO_4/K_2HPO_4) solution at pH 7.0 at a glassy carbon electrode (1.8 mm diameter) during controlled-potential coulometry at 0.10 V versus an Ag|AgCl|KCl (3 M) electrode, after consumption of: (*a*) 6.33, (*b*) 17, (*c*) 25, (*d*) 32, and (*e*) 45 C electricity. (**b**) Variation of peak current (I_P^{A1}) versus charge consumed. Scan rate 100 mV s^{-1}; $t = 25 \pm 1$ °C

Thus, the apparent number of electrons transferred increases from the limits of $n = 2$ for 6a and 6b to $n = 4$ electrons per molecule for 6c. Whereas 6a and 6b are insoluble in the mixture of water–acetonitrile, 6c is soluble and can then be further oxidized to form 7c. The best results where achieved by working at a potential of 0.1 V versus (Ag|AgCl|KCl (3 *M*)) and purifying the products by washing with distilled water. The yields obtained were then 89 (6a), 90 (6b), and 95% (7c).

In conclusion, the results of this work show that 2,3-dimethylhydroquinone is oxidized in water to its respective benzoquinone. The benzoquinone is then attacked by the enolate anion of *β*-diketones to form benzofuran derivatives 6a, 6b, and 7c. The overall reaction mechanism for the anodic oxidation of 2,3-dimethylhydroquinone in the presence of nucleophiles is presented in Scheme 1. According to our results, it seems that the 1,4-Michael addition of these nucleophiles to *p*-benzoquinone leads to the formation of new benzofuran derivatives as final product, in good yield and purity.

Experimental

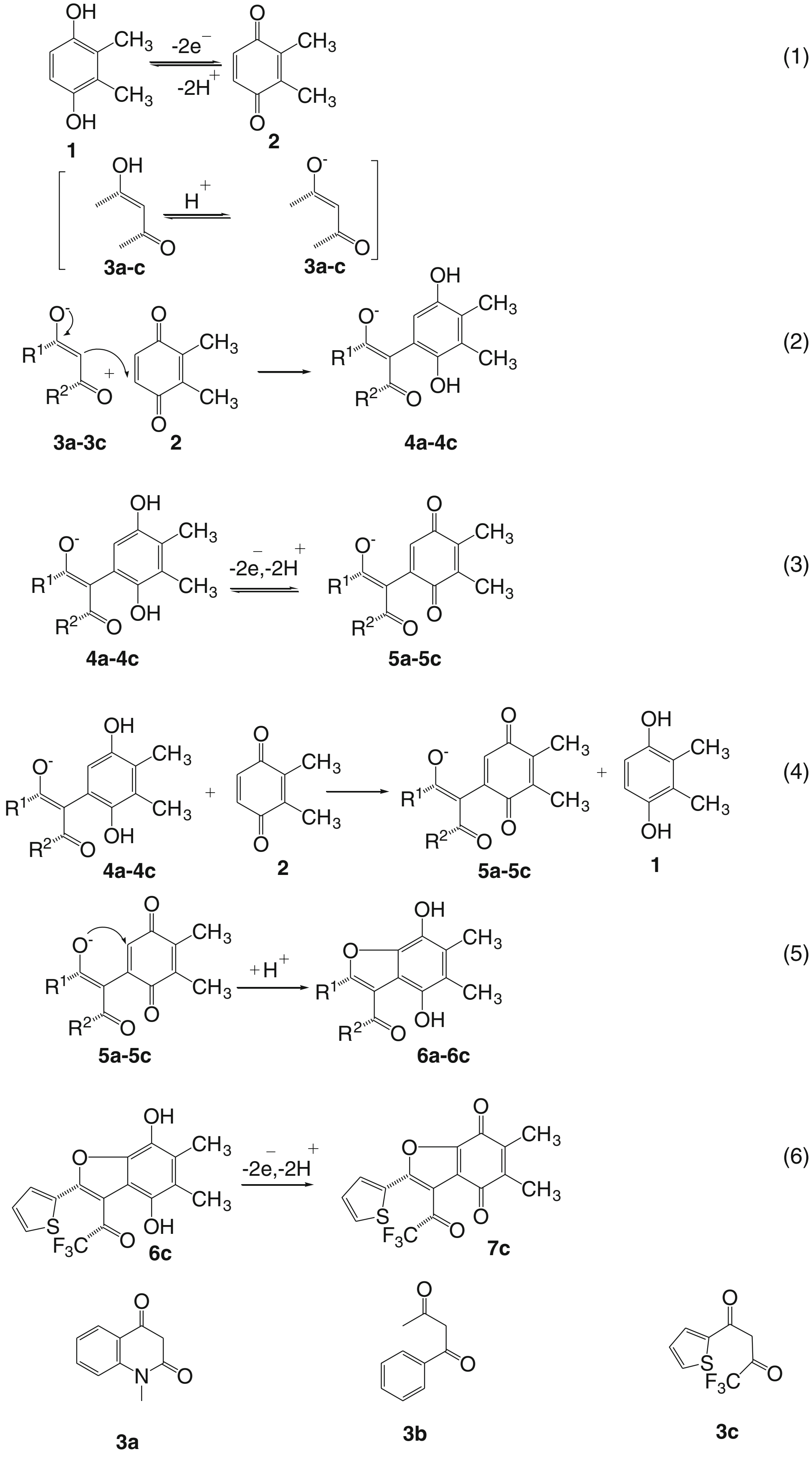
Cyclic voltammetry (CV) experiments were performed using a Metrohm computerized voltammetric analyzer model 747 VA stand. Controlled-potential coulometry and preparative electrolysis were performed using an SAMA potentiostat/galvanostat (Isfahan, Iran). The working electrode (WE) used in the voltammetry experiments was a glassy carbon disc (1.8 mm diameter) and a platinum wire (2 mm diameter and 2 cm length) was the counter electrode (CE). The WE used in controlled-potential coulometry and macroscale electrolysis was an assembly of three carbon rods (8 mm diameter and 6 cm length), and a large platinum gauze (2 × 2 cm^2) constituted the CE. The WE potentials were measured versus Ag|AgCl|KCl (3 M) as reference electrode (all electrodes were obtained from Azar Electrod, Urmia, Iran). NMR spectra were recorded on a Bruker DRX-300 Avance instrument. IR spectra were recorded on a Bruker IFS-66 FT-IR spectrophotometer. MS spectra were obtained using a QP-1100EX Shimadzu GC-MS (EI at 70 eV). Melting points of the product were obtained using an electrothermal melting point model 9200.

Electrochemical synthesis of ***6a****,* ***6b****, and* ***7c***

In a typical procedure, 100 cm^3 mixture of water–acetonitrile (80:20) containing 0.20 M phosphate (KH_2PO_4/K_2HPO_4) as a buffer (pH 7.0) and supporting electrolyte was pre-electrolyzed at the chosen potential (Table 1), in an undivided cell; subsequently, 2 mmol 2,3-dimethylhydroquinone (1) and 2 mmol *β*-diketone were added to the cell. The electrolysis was terminated when the decay of the current became more than 95%. The process was interrupted several times during the electrolysis and the carbon anode was washed in acetone in order to reactivate it. At the end of electrolysis, the precipitated solid was collected by filtration and washed with distilled water. The products were then characterized by using IR, ^{1}H NMR, ^{13}C NMR, and MS.

7,10-Dihydroxy-5,8,9-trimethylbenzofuro[3,2-c] quinolin-6(5H)-one (**6a**, $C_{18}H_{15}NO_4$)
Mp > 250 °C; IR (KBr): $\bar{\nu}$ = 3531(OH), 3077, 2900, 1650 (C=O), 1565, 1503 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ = 2.06 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 3.37 (s, 3H, CH_3), 7.19–7.90 (m, 4H, ArH), 8.97 (s, 1H, OH), 10.61 (s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6): δ = 12.8, 29.5, 40.8, 105.4, 115.1, 116.4, 122.2, 124.1, 131.9, 139.3, 140.9, 142.0,

Scheme 1


-2e⁻
-2H⁺
(1)
1
2
H⁺
3a-c
3a-c
(2)
3a-3c
2
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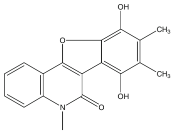
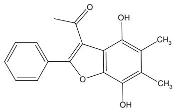
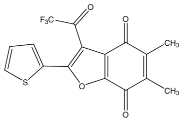
(3)
-2e,-2H
4a-4c
5a-5c
(4)
4a-4c
2
5a-5c
1
(5)
+H⁺
5a-5c
6a-6c
(6)
-2e,-2H
6c
7c
3a
3b
3c

Table 1 Electroanalytical and preparative data

Product	Applied potential (V) vs (Ag|AgCl|KCl (3 M))	Purification	Yield (%)
	0.1	Washing with distilled water	89
	0.1	Washing with distilled water	90
	0.1	Washing with distilled water	95

149.8, 151.1, 158.3, 159.8, 161.8 and 185.1 ppm; MS: *m/z* (%) = 309 (M^+, 25), 293 (15), 228 (15), 175 (25), 134 (100), 104 (65), 77 (80), 55 (40).

1-(4,7-Dihydroxy-5,6-dimethyl-2-phenylbenzofuran-3-yl)ethanone (**6b**, $C_{18}H_{16}O_4$)
Mp > 250 °C; IR (KBr): $\overline{\nu} = 3451$(OH), 3079, 2922, 1633 (C=O), 1596, 1476 cm^{-1}; ^{1}H NMR (DMSO-d_6): $\delta = 1.90$ (s, 3H, CH_3), 1.98 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 6,58 (s, 1H, OH), 7.48–7.97 (m, 5H, ArH), 9.25 (s, 1H, OH) ppm; ^{13}C NMR (DMSO-d_6): $\delta = 12.3$, 13.5, 20.6, 114.6, 122.6, 125.4, 128.7, 129.1, 130.0, 130.1, 133.6, 136.8, 140.4, 152.8, 169.4 and 197.6 ppm; MS: *m/z* (%) = 296 (M^+, 20), 256 (75), 238 (10), 176 (100), 151 (62.5), 105 (100), 77 (75), 43 (75).

5,6-dimethyl-2-(thiophen-2-yl)-3-(2,2,2-trifluoroacetyl)benzofuran-4,7-dione (**7c**, $C_{16}H_{11}F_3O_3S$)
Mp > 250 °C; IR (KBr): $\overline{\nu} = 3381$(OH), 2922, 1759(C=O), 1677(C=O), 1589, 1449 cm^{-1}; ^{1}H NMR (DMSO-d_6): $\delta = 1.790$ (s, 3H, CH_3); 1.92 (s, 3H, CH_3); 7.03–7.82 (m, 3H, ArH) ppm; ^{13}C NMR (DMSO-d_6): $\delta = 12.4$, 13.4, 122.8, 125.8, 128.3, 129.1, 132.6, 133.2, 139.3, 143.4, 146.1, 180.8, 182.4 and 189.1 ppm; ^{19}F NMR (DMSO-d_6): $\delta = -73.44$ ppm; MS: *m/z* (%) = 354 (M^+, 10), 285 (25), 269 (15), 203 (100), 176 (20), 111 (45), 33 (10).

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References

1. Pozharskii F, Soldatenkov AT, Katritzky AR (1997) Heterocyclic in life and society. Wiley, Chichester
2. Oter O, Ertekin K, Kirilmis C, Koca M, Ahmedzade M (2007) Sens Actuators B 122:450
3. Karatas F, Koca M, Kara H, Servi S (2006) Eur J Med Chem 41:664
4. Masataka F, Nobuo M, Tsutomu H, Tomihiro N (2002) Nippon Kagakkai Koen Yokoshu 81:1381
5. Bourgery G, Dostert P, Lacour A, Langlois M, Pourrias B, Tisneversailles J (1981) J Med Chem 24:159
6. Habermann J, Ley SV, Smits R (1999) J Chem Soc Perkin Trans 1:2421
7. Golabi SM, Nematollahi D (1992) J Pharm Biomed Anal 10:1035
8. Golabi SM, Pournaghi-Azar MH (1987) Electrochim Acta 32:425
9. Pournaghi-Azar MH, Golabi SM (1989) Iranian J Sci Technol 3:37
10. Petrova SA, Koiodyazhny MV, Ksenzhek OS (1990) J Electroanal Chem 227:189
11. Desbene-Monvernay A, Lacaze PC, Cheriguri A (1989) J Electroanal Chem 260:75
12. Katz EY, Brovkov VV, Evstigneeva RP (1992) J Electroanal Chem 320:197
13. Slavcheva E, Sokoiova E, Raicheva S (1993) J Electroanal Chem 360:271
14. Deakin MR, Wightman RM (1986) J Electroanal Chem 206:167
15. Bailey SI, Ritchie IM (1985) Electrochim Acta 30:3
16. Kano K, Uno B (1993) Anal Chem 65:1088
17. Golabi SM, Nematollahi D (1997) J Electroanal Chem 420:127
18. Nematollahi D, Goodarzi H (2001) J Electroanal Chem 510:108
19. Nematollahi D, Goodarzi H (2002) J Org Chem 67:5036
20. Fakhari AR, Nematollahi D, Shamsipur M, Makarem S, Davarani SSH, Alizadeh AA, Khavasi HR (2007) Tetrahedron 63:3894
21. Papouuchado L, Petrie G, Adams RN (1972) J Electroanal Chem 38:389
22. Papouuchado L, Petrie G, Shrp JH, Adams RN (1968) J Am Chem Soc 90:5620
23. Young TE, Griswold JR, Hulbert MH (1974) J Org Chem 39:1980
24. Brun A, Rosset R (1974) J Electroanal Chem 49:287
25. Rayan MD, Ueh AY, Wen-Yu C (1980) J Electrochem Soc 127:1489
26. Moghaddama AB, Kobarfard F, Fakhari AR, Nematollahi D, Davarani SSH (2005) Electrochim Acta 51:739