Mechanism of electrochemical oxidation of catechol and 3-substituted catechols in the presence of barbituric acid derivatives. Synthesis of new dispiropyrimidine derivatives

Davood Nematollahi,* Hassan Goodarzi and Esmail Tammari

Department of Chemistry, Faculty of Science, University of Bu-Ali-Sina, Hamadan, Iran.
E-mail: nemat@basu.ac.ir; Fax: 0098-81-8272404; Tel: 0098-81-8271541

Received (in Cambridge, UK) 26th July 2001, Accepted 30th January 2002
First published as an Advance Article on the web 14th February 2002

The electrochemical oxidation mechanism of catechol (**1a**), 3-methylcatechol (**1b**) and 3-methoxycatechol (**1c**) in the presence of barbituric acid (**3a**) and 1,3-dimethylbarbituric acid (**3b**) as nucleophile in aqueous solution has been studied in detail by cyclic voltammetry and controlled-potential coulometry. The results indicate that **1a**–**1c** *via* an ECEC (E, electrochemical; C, chemical) pathway, participating in a 1,4 (Michael) addition reaction, are converted to dispiropyrimidine derivatives **6a**–**6f**. The homogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results. The electrochemical synthesis of **6a**–**6f** has been successfully performed in an undivided cell in good yields and high purity.

Introduction

Many researchers have shown that *o*- and *p*-hydroxyphenols can be oxidized electrochemically to *o*- and *p*-quinones respectively.[1] The quinones formed are quite reactive and can be attacked by a variety of nucleophiles.[2,3] In this direction, we have reported the electrochemical oxidation of catechol and 4-methylcatechol,[4] 4-*tert*-butylcatechol and 3,4-dihydroxybenzaldehyde,[5] 3-methylcatechol and 2,3-dihydroxybenzaldehyde,[6] in methanol and have shown that these compounds undergo methoxylation reactions according to ECECE or ECE mechanisms, with consumption of 6 or 4 electrons per molecule, to give related methoxy-*o*-benzoquinone. In addition, we have investigated the electrochemical oxidation of catechol in ethanol, and have shown that the catechol undergoes ethoxylation according to an ECECE mechanism to afford 4,5-diethoxy-*o*-benzoquinone.[7] Moreover, we have studied the electrochemical oxidation of catechol and some catechol derivatives in aqueous solutions and in the presence of a variety of nucleophiles such as 4-hydroxycoumarin[8–10] and β-diketones.[11] The importance of pyrimidines with interesting pharmacological and biological activities,[12–14] caused many researchers to synthesize a number of pyrimidine derivatives.[15–25] Therefore, we have investigated the electro-oxidation of catechol and 3-substituted catechols such as 3-methylcatechol and 3-methoxycatechol in the presence of barbituric acid and 1,3-dimethylbarbituric acid as nucleophiles. The purpose of the investigation was to carry out a quantitative detailed study of the electrochemical oxidation of catechols in the presence of barbituric acid and 1,3-dimethylbarbituric acid in aqueous solution. Some electrochemical techniques such as: cyclic voltammetry using diagnostic criteria derived by Nicholson and Shain for various electrode mechanisms[26–29] and controlled-potential coulometry were used. These methods provide a powerful independent route for quantitative characterization of complex electrode processes. In addition, in this work, we have described a facile electrochemical method for synthesis of some new dispiropyrimidine derivatives.

Results and discussion

Electro-oxidation of catechol (1a) in the presence of barbituric acid derivatives

Cyclic voltammetry of 1 mM of catechol (**1a**) in aqueous solution containing 0.15 M sodium acetate as supporting electrolyte, shows one anodic (A_1) and the corresponding cathodic peak (C_1) which corresponds to the transformation of catechol (**1a**) to *o*-benzoquinone (**2a**) and *vice-versa* within a quasi-reversible two-electron process (Fig. 1, curve a). A peak

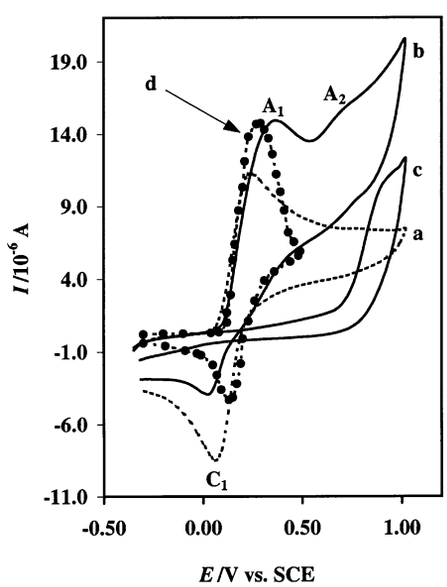


Fig. 1 Cyclic voltammograms of 1 mM catechol: (a) in the absence, (b) in the presence of 1 mM barbituric acid and, (c) 1 mM barbituric acid in the absence of catechol, at the glassy carbon electrode (1.8 mm diameter) in aqueous solution. Supporting electrolyte 0.15 M sodium acetate; scan rate: 100 mV s^{-1}; T = 25 ± 1 °C. (d) Simulated cyclic voltammogram based on EC mechanism.

current ratio (I_{pc1}/I_{pa1}) of nearly unity, particularly during the repetitive recycling of potentia,l can be considered as a criterion for the stability of *o*-quinone produced at the surface of electrode under the experimental conditions. In other words, any hydroxylation[30–33] or dimerization[34,35] reactions are too slow to be observed in the time scale of cyclic voltammetry. The oxidation of catechol (**1a**) in the presence of barbituric acid (**3a**) as nucleophile was studied in some detail. Fig. 1 (curve b), shows the cyclic voltammogram obtained for a 1 mM solution of **1a** in the presence of 1 mM barbituric acid (**3a**). The voltammogram exhibits two anodic peaks at 0.38 and 0.74 V *versus* SCE, and

DOI: 10.1039/b106794j

the cathodic counterpart of the anodic peak A_1 nearly disappears. The positive shift of peak A_1 in the presence of barbituric acid (Fig. 1, curve b), is probably due to the formation of a thin film of product at the surface of the electrode, inhibiting to a certain extent the performance of the electrode process.[8–11] In this figure, curve c is the voltammogram of barbituric acid. Furthermore, it is seen that the height of peak C_1 increases proportionally to the augmentation of potential sweep rate (Fig. 2 curves a–f). A similar situation is observed

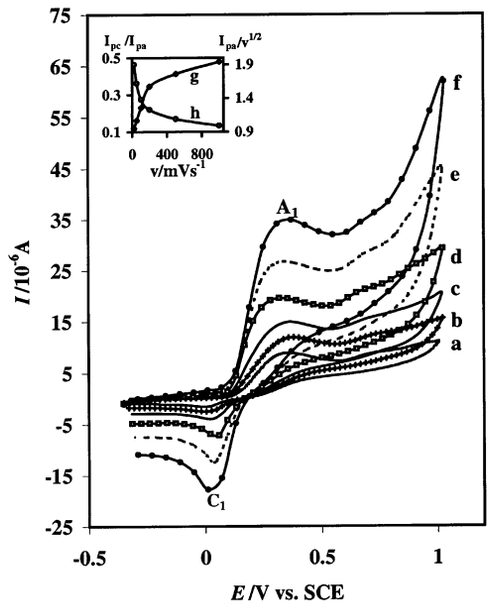


Fig. 2 Typical voltammograms of 1 mM catechol in water in the presence of 1 mM barbituric acid at the glassy carbon electrode (1.8 mm diameter) and at various scan rates. Scan rates from (a) to (f) are: 20, 50, 100, 200, 500, and 1000 mV s^{-1}, respectively. Supporting electrolyte: 0.15 M sodium acetate. (g and h): variation of peak current ratio (I_{pc1}/I_{pa1}) and peak current function ($I_{pa}/v^{½}$)/(μA $s^{½}$ $mV^{-½}$) respectively, *versus* scan rate. $T = 25 \pm 1$ °C.

when the barbituric acid (**3a**) to **1a** concentration ratio is decreased. A plot of peak current ratio (I_{pc1}/I_{pa1}) *versus* scan rate for a mixture of catechol and barbituric acid confirms the reactivity of **2a** towards barbituric acid (**3a**), appearing as an increase in the height of the cathodic peak C_1 at higher scan rates (Fig. 2, curve g). On the other hand, the peak current function for peak A_1, $I_{pa1}/v^{½}$, changes only slightly with increasing the scan rate (Fig. 2, curve h) and such a behavior is adopted as indicative of an ECEC mechanism.[8–11] Controlled-potential coulometry was performed in aqueous solution containing 5 mM of **1a** and 5 mM of barbituric acid (**3a**) at 0.45 V *versus* SCE. The monitoring of electrolysis progress was carried out by cyclic voltammetry (Fig. 3). It is shown that anodic peak A_1 (as well as A_2) decreases proportionally to the advancement of coulometry. All anodic and cathodic peaks disappear when the charge consumption becomes about $4e^-$ per molecule of **1a**. These observations allow us to propose the pathway in Scheme 1 for the electro-oxidation of **1a** in the presence of barbituric acid.

According to our results, it seems that the 1,4 (Michael) addition reaction of enolate anion **AE3a** to *o*-quinone (**2a**) [eqn. (2)] is faster than other secondary reactions, leading presumably to the intermediate (**4a**). The oxidation of this compound (**4a**) is easier than the oxidation of parent starting molecule (**1a**) by virtue of the presence of an electron-donating group. It can be seen from the mechanism written above that, as the chemical reaction [eqn. (2)] occurs, **1a** is regenerated through homogeneous oxidation [eqn. (5)] and hence, can be reoxidized at the electrode surface. Thus, as the chemical reaction takes place, the apparent number of electrons transferred increases from the limits of $n = 2$ to 4 electrons per molecule.

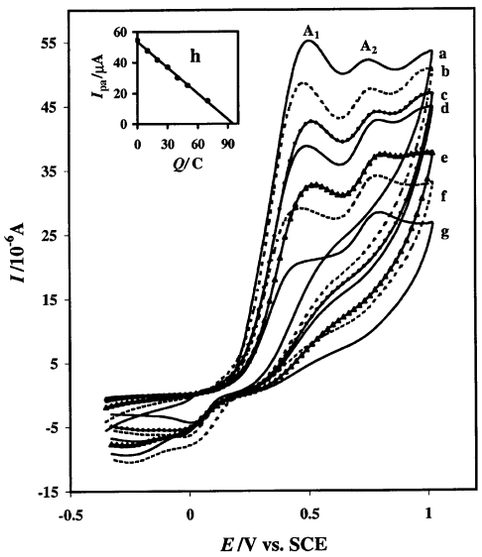


Fig. 3 Cyclic voltammograms of 5 mM catechol in the presence of 5 mM barbituric acid in 50 mL water, at the glassy carbon electrode (1.8 mm diameter) during controlled potential coulometry at 0.45 V *versus* SCE. After consumption of: (a) 0, (b) 10, (c) 20, (d), 30, (e) 40, (f) 50 and (g) 70 C. (h): Variation of peak current (I_{pa1}) *versus* charge consumed. Scan rate 50 mVs^{-1}; $T = 25 \pm 1$ °C.

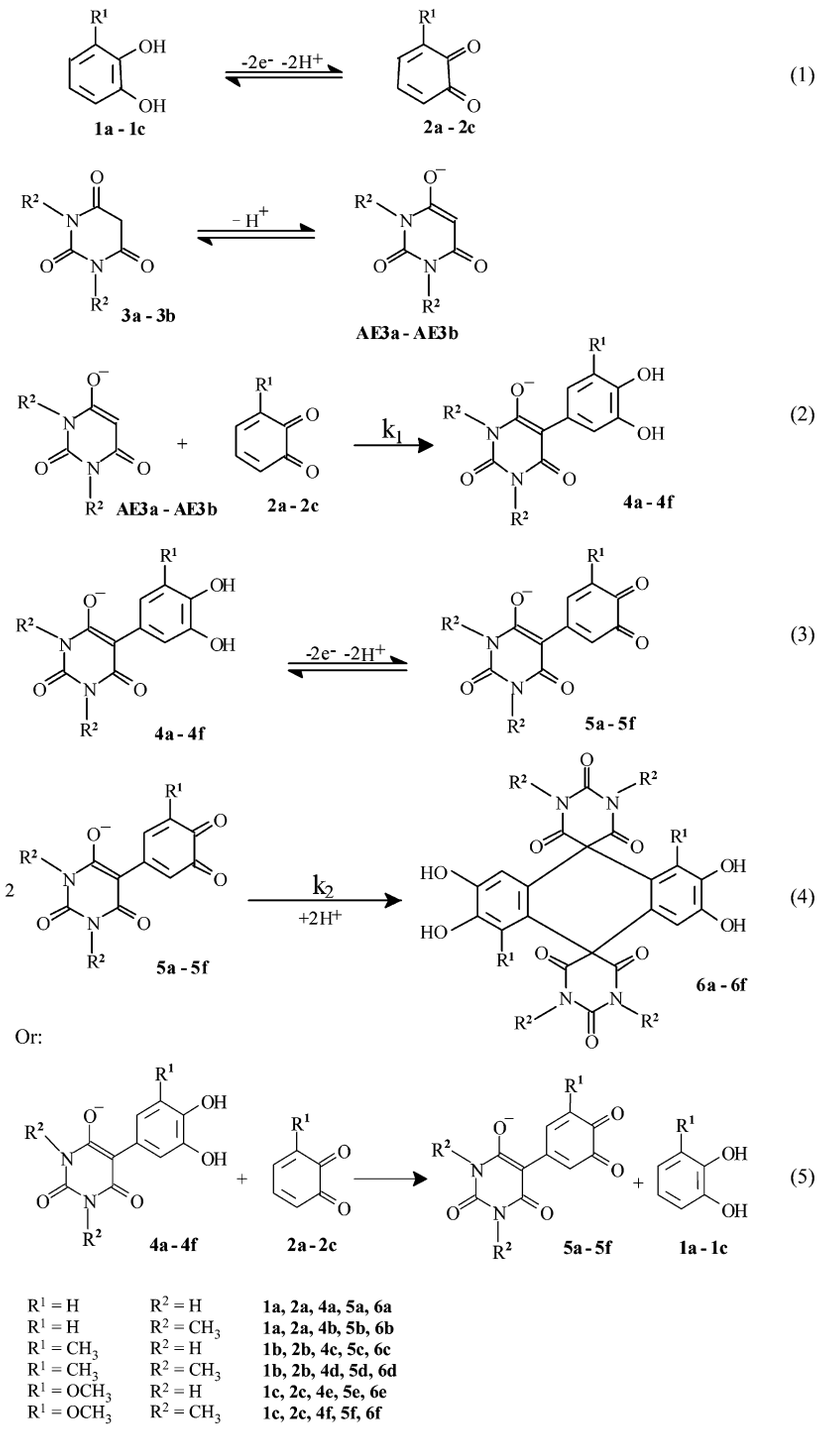
The reaction product (**6a**) can also be oxidized at a lower potential than the starting **1a** compound. However, overoxidation of **6a** was circumvented during the preparative reaction because of the insolubility of the product in water–sodium acetate media.

The oxidation of catechol (**1a**) in the presence of 1,3-dimethylbarbituric acid (**3b**) as a nucleophile was studied. Similar to the previous cases, in the presence of 1,3-dimethylbarbituric acid (**3b**), the peak current ratio, I_{pc1}/I_{pa1}, decreases proportionally to the augmentation in 1,3-dimethylbarbituric acid (**3b**) concentration, as well as to the decrease in potential sweep rate. The comparison of the voltammogram obtained in the presence of 1,3-dimethylbarbituric acid (**3b**) with curve b in Fig. 1, shows that because of the higher nucleophilicity of 1,3-dimethylbarbituric acid, the peak current ratio, I_{pc1}/I_{pa1}, is smaller than peak current ratio in the presence of barbituric acid (**3a**). This can be related to the presence of the methyl groups with electron-donating character on 1,3-dimethylbarbituric acid (**3b**). Other obtained results are similar to that of previous case.

Electro-oxidation of 3-methylcatechol (1b) in the presence of barbituric acid derivatives

Cyclic voltammetry of a 1 mM 3-methylcatechol (**1b**) in aqueous solution containing 0.15 M sodium acetate as supporting electrolyte exhibits anodic and cathodic peaks corresponding to the quasi-reversible two-electron transformation of 3-methylcatechol (**1b**) to 3-methyl-*o*-benzoquinone (**2b**) and *vice-versa*. The electro-oxidation of 1 mM of 3-methylcatechol (**1b**) in the presence of 1 mM of barbituric acid (**3a**) proceeds in a way similar to that of **1a**. The plot of peak current ratio *versus* scan rate confirms the reaction between the oxidation product of **1b** and barbituric acid (**3a**), appearing as an increase in peak current ratio, I_{pc1}/I_{pa1}, with increasing the scan rates. The reaction mechanism is similar to that of previous cases and, according to these results, it seems that the chemical reaction between barbituric acid (**3a**) and 3-methyl-*o*-benzoquinone (**2b**) is fast enough and leads presumably to the formation of product (**6c**).

The existence of the methyl group with electron-donating character at the C-3 position of the 3-methylcatechol (**1b**) probably causes the Michael acceptor (**2b**) to be attacked by the enolate anion (**AE3a**) from C-4 and C-5 positions to yield two types of products. However, the NMR results indicate that 3-methyl-*o*-quinone (**2b**) is attacked in all probability only in the



Scheme 1

C-5 (or C-4) position by enolate anion (**3a**) leading to the formation of the product **6c**. In this manner, electrochemical oxidation of 3-methylcatechol (**1b**) in the presence of 1,3-dimethylbarbituric acid (**3b**) as a nucleophile under the same conditions was studied. Similar to the previous cases, in the presence of 1,3-dimethylbarbituric acid (**3b**), the cathodic counterpart of anodic peak (C_1) decreases proportionally to the augmentation in 1,3-dimethylbarbituric acid (**3b**) concentration, as well as to the decrease of the potential sweep rate. Other obtained results in this study are similar to those of previous cases.

Electro-oxidation of 3-methoxycatechol (1c) in the presence of barbituric acid derivatives

The oxidation of 3-methoxycatechol (**1c**) in the presence of barbituric acid (**3a**) as a nucleophile was studied. Similar to the previous cases, in the presence of barbituric acid, the peak current ratio, I_{pc1}/I_{pa1}, decreases proportionally to the augmentation in barbituric acid concentration, as well as to the decrease in the potential sweep rate. Moreover, controlled-potential coulometry was performed at 0.40 V *versus* SCE, and cyclic voltammetric analysis carried out during the electrolysis shows the formation of a new anodic peak A_0 at 0.16 V *versus* SCE (Fig. 4). This peak can be attributed to the oxidation of intermediate **4e** to **5e** at the surface of electrode. The reaction mechanism is similar to that of previous cases. Contrary to other catechol cases, the observation of anodic peak A_0 during the controlled-potential coulometry, mainly because of the relative stability of intermediate **5e** than other same intermediates such as: **5a**, **5b**, **5c** and **5d**, arises from the presence of the methoxy group with electron-donating character at the C-3

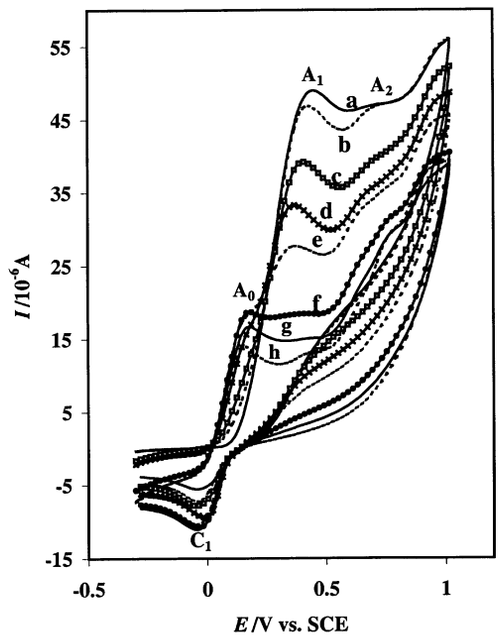


Fig. 4 Cyclic voltammograms of 5 mM 3-methoxycatechol in the presence of 5 mM barbituric acid in 50 mL water, at the glassy carbon electrode (1.8 mm diameter) during controlled potential coulometry at 0.40 V *versus* SCE. (a) At the beginning; (b–h) in the course of coulometry. Scan rate 50 mV s^{-1}; $T = 25 \pm 1$ °C.

position of *o*-quinone ring (**5e**). In this case, the NMR results indicate that 3-methoxy-*o*-quinone (**2c**) is attacked in all probability only at the C-5 (or C-4) position by enolate anion (**AE3a**) leading to the product **6e**. Also electrochemical oxidation of 3-methoxycatechol (**1c**) in the presence of 1,3-dimethylbarbituric acid (**3b**) in the same conditions was studied. Since obtained results in this study are similar to those of previous cases, the repetition is avoided and because of the interesting behavior of electro-oxidation of 3-methoxycatechol (**1c**) in the presence of 1,3-dimethylbarbituric acid (**3b**), the cyclic voltammograms obtained during the controlled-potential coulometry, are presented in Fig. 5.

A crucial test for dimerization step (4) is that the product must have individual pyrimidine rings in identical environments. The formation of isomers of **6** with R^1 groups pseudo-*trans* is precluded. ^{1}H NMR spectra for compounds **6a**–**6f** indicate that the –N–Me and –C–Me groups are indeed in identical respective environments. Crude reaction products showed no indication of the presence of a second isomer. The dimerization step (4) and structures assigned to these products are well supported.

Estimation of homogeneous rate constants

The scheme for the electrochemical oxidation of catechols in the presence of barbituric acids is proposed and tested by digital simulation. Based on an EC mechanism, the homogeneous rate constants (k_{obs}) of reaction of catechols with barbituric acids have been estimated by digital simulation of cyclic voltamograms and by establishing the theoretical working curves on the basis of peak current ratio. The results obtained for homogeneous rate constants of catechols (**1a**–**1c**) with barbituric acids (**3a**,**3b**) are listed in Table 1.

Table 1 Homogeneous rate constants (k_{obs}) of reaction of catechols (**1a**–**1c**) with barbituric acids (**3a** and **3b**) in aqueous sodium acetate solution (0.15 M) at 25 °C[a]

Catechol	Nucleophile	k_{obs}/s^{-1}
Catechol (**1a**)	Barbituric acid (**3a**)	0.17
Catechol (**1a**)	1,3-Dimethylbarbituric acid (**3b**)	0.38
3-Methylcatechol (**1b**)	Barbituric acid (**3a**)	0.16
3-Methylcatechol (**1b**)	1,3-Dimethylbarbituric acid (**3b**)	0.23
3-Methoxycatechol (**1c**)	Barbituric acid (**3a**)	0.15
3-Methoxycatechol (**1c**)	1,3-Dimethylbarbituric acid (**3b**)	0.17

[a] The probable solution electron transfer (SET) process [Scheme 1, eqn. (5)] has not been considered.

Experimental

Cyclic voltammetry, controlled-potential coulometry and preparative electrolysis were performed using an Autolab model PGSTAT 20 potentiostat/galvanostat. The working electrode used in the voltammetry experiment was a glassy carbon disc (1.8 mm diameter) and platinum wire was used as counter electrode. The working electrode used in controlled-potential coulometry and macroscale electrolysis was an assembly of four carbon rods (6 mm diameter and 4 cm length) and a large platinum gauze constituted the counter electrode. The working electrode potentials were measured *versus* SCE (all electrodes from AZAR electrode). The homogeneous rate constants were estimated by analysing the cyclyc voltammetric responses using the simulation *Cyclic Volt Sim* software.[36]

All chemicals (catechols, barbituric acid and 1,3-dimethylbarbituric acid) were reagent-grade materials from Aldrich and $NaCH_3COO$ was of pro-analysis grade from E. Merck. These chemicals were used without further purification.

Electro-organic synthesis of dispiropyrimidine derivatives (6a–6f)

In a typical procedure, 80 ml of sodium acetate solution in water (0.15 M) was pre-electrolyzed at the chosen potential (see Table 2), in an undivided cell, then 2 mmol of catechol (**1a**–**1c**) and barbituric acid (**3a**,**3b**) (2 mmol) were added to the cell. The electrolysis was terminated when the decay of the current become more than 95%. The process was interrupted several times during the electrolysis and the graphite anode was washed in acetone in order to activate it. At the end of electrolysis, a few drops of acetic acid were added to the solution and the cell was placed in a refrigerator overnight. The precipitated

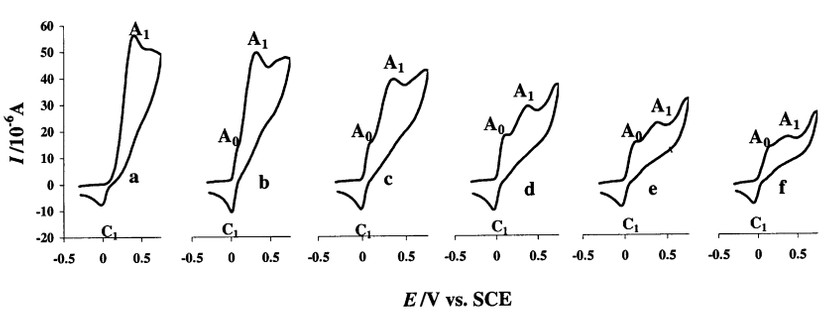


Fig. 5 Cyclic voltammograms of 5 mM 3-methoxycatechol in the presence of 5 mM 1,3-dimethylbarbituric acid in 50 mL water, at the glassy carbon electrode (1.8 mm diameter) during controlled potential coulometry at 0.40 V *versus* SCE. (a) At the beginning; (b–f) in the course of coulometry. Scan rate 50 mV s^{-1}; $T = 25 \pm 1$ °C.

Table 2 Electroanalytical and preparative data

Conversion	Applied potential/V *vs.* SCE	Crystallization solvent	Product yield (%)
1a ⟶ 6a	0.45	Methanol–water (70 : 30)	85
1a ⟶ 6b	0.45	Methanol–water (80 : 20)	83
1b ⟶ 6c	0.40	Chloroform–acetone (70 : 30)	78
1b ⟶ 6d	0.40	Acetone–methanol (60 : 40)	74
1c ⟶ 6e	0.40	Chloroform–DMSO[a]	70
1c ⟶ 6f	0.40	Chloroform–DMSO[a]	76

[a] Suitable crystals were obtained by diffusion of chloroform vapour into a DMSO solution

solid was collected by filtration and recrystallized from an appropriate solvent (see Table 2). After recrystallization, products were characterized by: UV, IR, ^{1}H NMR, ^{13}C NMR and MS.

Characteristics of the products

2′,3′,6′,7′-Tetrahydroxydispiro[pyrimidine-5,9′-anthracene-10′,5″-pyrimidine]-2,2″,4,4″,6,6″(1*H*,1′*H*,3*H*,3′*H*,5*H*,5′*H*)-hexone (6a). Mp > 310 °C (decomp.); λ_{max}(DMF)/nm 297; ν_{max}/cm^{-1} 3450, 3060, 1750, 1700, 1600, 1500, 1400, 1330, 1250, 1200 and 1090; δ_H (90 MHz; DMSO-d$_6$) 6.55 (4 H, s, Ph), 9.44 (4 H, s, OH) and 11.8 (4 H, s, NH).

2′,3′,6′,7′-Tetrahydroxy-1,1″,3,3″-tetramethyldispiro-[pyrimidine-5,9′-anthracene-10′,5″-pyrimidine]-2,2″,4,4″,6,6″(1*H*,1′*H*,3*H*,3′*H*,5*H*,5′*H*)-hexone (6b). Mp > 310 °C (decomp.); λ_{max}(DMF)/nm 297; ν_{max}/cm^{-1} 3300, 1700, 1650, 1545, 1450, 1380, 1250, 1110 and 1050; δ_H (90 MHz; DMSO-d$_6$) 3.28 (12 H, s, Me), 6.57 (4 H, s, Ph) and 9.21 (4 H, s, OH); δ_C (500 MHz; DMSO-d$_6$) 168.4, 150.3, 145.4, 122.5, 112.19, 56.38 and 27.83; *m*/*z* 524 (M$^+$, 12%), 454 (20), 416 (57), 370 (20), 302 (72), 228 (22), 83 (19) and 44 (100).

1′,5′-Dimethyl-2′,3′,6′,7′-tetrahydroxydispiro[pyrimidine-5,9′-anthracene-10′,5″-pyrimidine]-2,2″,4,4″,6,6″(1*H*,1′*H*,3*H*,3′*H*,5*H*,5′*H*)-hexone (6c). Mp > 310 °C (decomp.); λ_{max}(DMF)/nm 293; ν_{max}/cm^{-1} 3335, 3230, 2840, 1730, 1700, 1600, 1520, 1450, 1350, 1210, 1080 and 1040; δ_H (90 MHz; DMSO-d$_6$) 1.92 (6 H, s, Me), 6.84 (2 H, s, Ph), 8.79 (2 H, s, OH), 10.04 (2 H, s, OH) and 11.87 (4 H, s, NH); δ_C (500 MHz; DMSO-d$_6$) 171.4, 150.6, 145.7, 144.6, 123.5, 122.8, 122.4, 108.2, 57.7 and 12.5.

1′,5′-Dimethyl-2′,3′,6′,7′-tetrahydroxy-1,1″,3,3″-tetramethyl-dispiro[pyrimidine-5,9′-anthracene-10′,5″-pyrimidine]-2,2″,4,4″,6,6″(1*H*,1′*H*,3*H*,3′*H*,5*H*,5′*H*)-hexone (6d). Mp > 310 °C (decomp.); λ_{max}(DMF)/nm 294; ν_{max}/cm^{-1} 3370, 1750, 1700, 1645, 1610, 1520, 1440, 1380, 1350, 1280, 1210, 1120 and 1050; δ_H (500 MHz; DMSO-d$_6$) 1.78 (6 H, s, Me), 3.31 (12 H, s, Me), 6.68 (2 H, s, Ph), 8.82 (2 H, s, OH) and 9.92 (2 H, s, OH); *m*/*z* 552(M$^+$ 29%), 410 (17), 276 (27), and 44 (100).

1′,5′-Dimethoxy-2′,3′,6′,7′-tetrahydroxydispiro[pyrimidine-5,9′-anthracene-10′,5″-pyrimidine]-2,2″,4,4″,6,6″(1*H*,1′*H*,3*H*,3′*H*,5*H*,5′*H*)-hexone (6e). Mp > 310 °C (decomp.); λ_{max}(DMF)/nm 280; ν_{max}/cm^{-1} 3400, 3200, 2850, 1750, 1700, 1620, 1520, 1415, 1340, 1310, 1220, 1170, 1120 and 1085; δ_H (90 MHz; DMSO-d$_6$) 3.67 (6 H, s, OMe), 6.64 (2 H, s, Ph), 8.85 (2 H, s, OH), 9.91 (2 H, s, OH) and 11.52 (4 H, s, NH).

1′,5′-Dimethoxy-2′3′,6′,7′-tetrahydroxy-1,1″,3,3″-tetra-methyldispiro[pyrimidine-5,9′-anthracene-10′,5″-pyrimidine]-2,2″,4,4″,6,6″(1*H*,1′*H*,3*H*,3′*H*,5*H*,5′*H*)-hexone (6f). Mp > 310 °C (decomp.); λ_{max}(DMF)/nm 279; ν_{max}/cm^{-1} 3330, 2960, 1745, 1700, 1650, 1615, 1530, 1460, 1410, 1355, 1310, 1257, 1200, 1100, 1055 and 940; δ_H (500 MHz; DMSO-d$_6$) 3.32 (12 H, s, Me), 3.58 (6 H, s, OMe), 6.51 (2 H, s, Ph), 9.02 (2 H, s, OH), and 9.89 (2 H, s, OH); *m*/*z* 584 (M$^+$ 35%), 498 (27), 446 (63), 386 (60), 301 (47), 143 (12) and 44 (100).

Acknowledgements

This research project has been supported by a grant from National Research Projects and with the support of the National Research Council of Islamic Republic of Iran.

References

1 L. Homer and E. Geyer, *Chem. Ber.*, 1965, **98**, 2016.
2 Z. Gruioc, I. Tabakovic and M. Trkovnik, *Tetrahedron Lett.*, 1976, 4823.
3 I. Tabakovic, Z. Gruioc and Z. Bejtovic, *J. Heterocycl. Chem.*, 1983, **20**, 635.
4 D. Nematollahi and S. M. Golabi, *J. Electroanal. Chem.*, 1996, **405**, 133.
5 D. Nematollahi and S. M. Golabi, *J. Electroanal. Chem.*, 2000, **481**, 208.
6 D. Nematollahi and S. M. Golabi, *Electroanalysis*, 2001, **13**, 1008.
7 S. M. Golabi and D. Nematollahi, *Bull. Electrochem.*, 1997, **13**, 156.
8 S. M. Golabi and D. Nematollahi, *J. Electroanal. Chem.*, 1997, **420**, 127.
9 S. M. Golabi and D. Nematollahi, *J. Electroanal. Chem.*, 1997, **430**, 141.
10 D. Nematollahi and S. M. Golabi, *Bull. Electrochem.*, 1998, **14**, 97.
11 D. Nematollahi and S. M. Golabi, *Iran. J. Sci. Technol.*, 1997, **21**, 121.
12 A. Pani, P. Obino, P. Guarracino and P. LaColla, *Experientia*, 1994, **50**, 29.
13 R. I. Lindstad and J. S. Mckinley-Mckee, *FEBS Lett.*, 1997, **408**, 157.
14 S. Evangelista, R. Pirisino, F. Perretti, R. Fantozzi, S. Brunelleschi, P. Malmberg-Aiello and A. Bartolini, *Drugs Exp. Clin. Res.*, 1987, **13**, 501.
15 K. Ramasamy, N. Imamura, N. B. Hanna, R. A. Finch, T. L. Avery, R. K. Robins and G. R. Revankar, *J. Med. Chem.*, 1990, **33**, 1220.
16 P. K. Gupta, M. R. Nassiri, L. A. Coleman, L. L. Wotring, J. C. Drach and L. B. Townsend, *J. Med. Chem.*, 1989, **32**, 1420.
17 B. K. Bhattachary, J. O. Ojwang, R. F. Rando, J. H. Huffman and G. R. Rewankar, *J. Med. Chem.*, 1995, **38**, 3957.
18 H. B. Cottam, C. R. Petrie, P. A. Mckernan, R. J. Goebel, N. K. Dalley, R. B. Davidson, R. K. Robins and G. R. Revankar, *J. Med. Chem.*, 1984, **27**, 1119.
19 A. Gangjee, J. Shi, S. F. Queener, L. R. Barrows and R. L. Kisliuk, *J. Med. Chem.*, 1993, **36**, 3437.
20 P. K. Gupta, S. Daunert, M. R. Nassiri, L. L. Wotring, J. C. Drach and L. B. Townsend, *J. Med. Chem.*, 1989, **32**, 402.
21 K. G. Upadhya, Y. S. Sanghvi, R. K. Robins, G. R. Revankar and B. G. Ugarkar, *Nncleic Acids Res.*, 1986, **14**, 1747.
22 N. K. Saxena, B. M. Hagenow, G. Turk and L. B. Townsend, *J. Med. Chem.*, 1988, **31**, 1501.
23 F. M. El-Taweel, *J. Prakt. Chem.*, 1990, **332**, 762.
24 B. G. Ugarkar, H. B. Cottam, P. A. Mckernan, R. K. Robins and G. R. Revankar, *J. Med. Chem.*, 1984, **27**, 1026.
25 H. B. Cottam, Z. Kazimierczuk, S. Geary, P. A. Mckernan, G. R. Revankar and R. K. Robins, *J. Med. Chem.*, 1985, **28**, 1461.

26 R. S. Nicholson and I. Shain, *Anal. Chem.*, 1964, **36**, 706.
27 R. S. Nicholson and I. Shain, *Anal. Chem.*, 1965, **37**, 178.
28 R. S. Nicholson, *Anal. Chem.*, 1965, **37**, 1351.
29 R. S. Nicholson, *Anal. Chem.*, 1966, **38**, 406.
30 L. Papouchado, G. Petrie and R. N. Adams, *J. Electroanal. Chem.*, 1972, **38**, 389.
31 L. Papouchado, G. Petrie, J. H. Sharp and R. N. Adams, *J. Am. Chem. Soc.*, 1986, **90**, 5620.
32 T. E. Young, J. R. Griswold and M. H. Hulbert, *J. Org. Chem.*, 1974, **39**, 1980.
33 A. Brun and R. Rosset, *J. Electroanal. Chem.*, 1974, **49**, 287.
34 D. I. Stum and S. N. Suslov, *Biofizika*, 1979, **21**, 40.
35 M. D. Rayn, A. Yueh and C. Wen-Yu, *J. Electrochem. Soc.*, 1980, **127**, 1489.
36 This program can be download at: http://soulcatcher.chem.umass.edu/ cgi-bin/pickPage.cgi?downloads.html.