JOURNAL OF PHYSICAL ORGANIC CHEMISTRY
J. Phys. Org. Chem. 2007; **20:** 49–54

(www.interscience.wiley.com) DOI: 10.1002/poc.1125

Kinetic study of electrochemically induced Michael reactions of *o*-benzoquinones with 2-acetylcyclohexanone and 2-acetylcyclopentanone

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Received 31 July 2006; revised 14 September 2006; accepted 4 October 2006

ABSTRACT: The reaction of electrochemically generated *o*-benzoquinones (**2a-f**) as Michael acceptors with 2-acetylcyclohexanone (ACH) and 2-acetylcyclopentanone (ACP), as nucleophiles has been studied in various pHs using cyclic voltammetry. The results indicate that the participation of *o*-benzoquinones (**2a-f**) in the Michael reaction with acetylcyclohexanone (ACH) to form the corresponding catechol derivatives (**4a-f**). Based on an EC mechanism, the homogeneous rate constants were estimated by comparing the experimental cyclic voltammetric responses with the digital simulated results. Copyright © 2007 John Wiley & Sons, Ltd.

KEYWORDS: *o*-benzoquinones; cyclic voltammetry; 2-acetylcyclohexanone; digital simulation; EC mechanism; Michael reaction; homogeneous rate constants

INTRODUCTION

Some electrochemical techniques such as cyclic voltammetry, using diagnostic criteria derived by Nicholson and Shain for various electrode mechanisms and controlled-potential coulometry, have been used as a powerful independent route for quantitative characterization of complex electrode processes.[1–4] In addition; general treatment of the reaction mechanism is probably best carried out through digital simulations.[5]

In view of the fact that catechols are a promising group of compounds worthwhile for further investigation, which may lead to the discovery of selective acting, biodegradable agrochemicals having high human, animal, and plant compatibility,[6,7] we synthesized a number of new derivatives of them recently.[8] In this direction, for increasing of available data in electrochemical synthesis of new catechol derivatives, we have investigated the electrochemical oxidation of catechols, in the presence of 2-acetylcyclohexanone (ACH) and 2-acetylcyclopentanone (ACP) as CH-acidic nucleophiles. The purpose of this work is a kinetic and mechanistic study of the electrochemical oxidation of catechols, in the presence of ACH and ACP, and the estimation of the observed homogeneous rate constants (k_{obs}) of reaction of electrochemically generated *o*-benzoquinones, with these nucleophiles by digital simulation of cyclic voltammograms.

EXPERIMENTAL

Apparatus

Cyclic voltammetry, controlled-potential coulometry, and preparative electrolysis were performed using a Behpajoh model BHP-2062 potentiostat/galvanostat. The working electrode used in the voltammetry experiments was a glassy carbon disc (1.8 mm diameter), and platinum wire was used as the counter electrode. The working electrode, used in controlled-potential coulometry and macroscale electrolysis was an assembly of eight carbon rods (68 cm^2) and 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.[9]

Reagents

Catechols, ACP, and ACH were reagent-grade materials, sodium dihydrogen phosphate, disodium hydrogen phosphate, sodium acetate, and acetic acid were of

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pro-analysis grade from E. Merck. These chemicals were used without further purification.

RESULTS AND DISCUSSION

Reaction mechanism

The oxidation of catechol (**1a**), in the presence of ACH as a nucleophile was studied in some detail. Figure 1 shows cyclic voltammogram obtained for 1 mM solution of catechol (**1a**) in aqueous solution containing 0.2 M phosphate buffer (pH = 6.8). The voltammogram exhibits one anodic (A_1) (at 0.22 V vs. SCE) and the corresponding cathodic peak (C_1) (at 0.15 V vs. SCE) which corresponds to the transformation of catechol (**1a**) to *o*-benzoquinone (**2a**) and vice versa, within a quasi-reversible two-electron process.[10–15] In the presence of 1 mM ACH, the height of cathodic peak decreases (Fig. 1, curve b). In other words, in this condition, the peak current ratio ($I_p^{C_1}/I_p^{A_1}$) is less than unity and decreases with decreasing the potential sweep rate and increasing nucleophile concentration. Also, the current function for the A_1 peak ($I_p^{A_1}/v^{1/2}$), decreases (slightly) on increasing the scan rate. These confirm reactivity of *o*-benzoquinone (**2a**) towards ACH. In this Figure, curve c is the voltammogram of ACH. Controlled-potential coulometry was performed in aqueous solution containing 0.25 mmol of **1a** and 0.25 mmol of ACH at 0.35 V *versus* SCE. The monitoring of the progress of the electrolysis was carried out by cyclic voltammetry. It was shown that, proportional to the advancement of coulometry, anodic peak A_1 decreases and disappears when the charge consumption becomes about $2e^-$ per molecule of **1a**. Our experiences on electrochemical oxidation of catechols in the presence of ACP,[8] diagnostic criteria of cyclic voltammetry, consumption of two electrons per molecule of catechol, and the mass spectra of isolated products (Fig. 2), indicate that the reaction mechanism of electrooxidation of catechols in the presence of ACH is EC (Scheme 1).

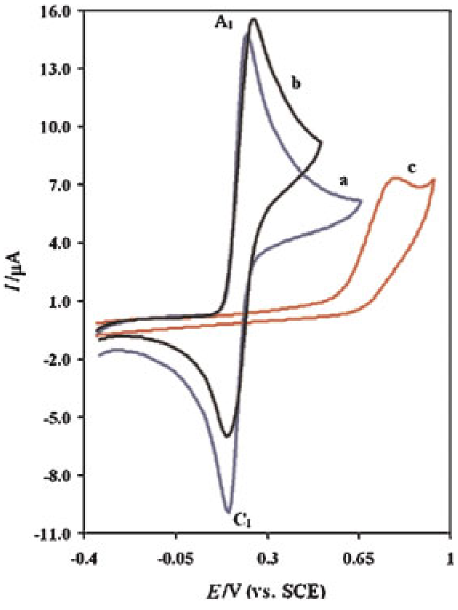

Figure 1. Cyclic voltammograms of 1 mM catechol (**1a**): (a) in the absence, (b) in the presence of 1 mM 2-acetylcyclohexanone (ACH), and (c) 1 mM ACH in the absence of catechol (**1a**), at a glassy carbon electrode, in aqueous solution containing 0.2 M phosphate buffer (pH = 6.8). Scan rate: 100 mV s^{-1}; $t = 25 \pm 1\,^{\circ}C$

According to our results, it seems that the Michael addition reaction of the anion anolate ACH or ACP to *o*-benzoquinone **2a** (Eqn 2) is faster than other side reactions,[10–15] leading to the product **4a**. The over-oxidation of **4a** was circumvented during the preparative reaction because of the presence of the β-diketone group with electron-withdrawing character on the catechol ring, as well as the insolubility of the product in the sodium acetate solution medium.

Kinetic evaluations

Based on an EC mechanism, the observed homogeneous rate constants (k_{obs}) of Michael reactions have been estimated by comparison of the simulation results with experimental cyclic voltammograms (Fig. 3). The transfer coefficients (α) were assumed to be 0.5, and the formal potentials were obtained experimentally as the midpoint potential between the anodic and cathodic peaks (E_{mid}). The heterogeneous rate constants are estimated by use of an experimental working curve.[16] The estimated values are about 0.002 cm s^{-1} and are used for simulation of cyclic voltammograms. The calculated homogeneous rate constants are given in Table 1. As shown in Table 1, the magnitude of 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**) or methoxy (**1c**) on catechol ring causes a decrease in k_{obs}. In contrast, the presence of carboxylic group (**1f**) with

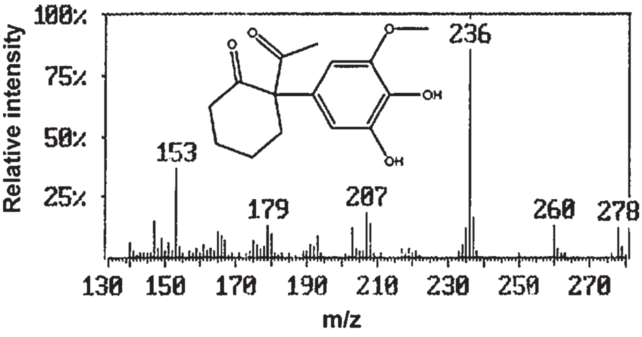

Figure 2. Mass spectrum of separated product (**4c**) from electrochemical oxidation of 3-methoxycatechol (**1c**), in the presence of ACH

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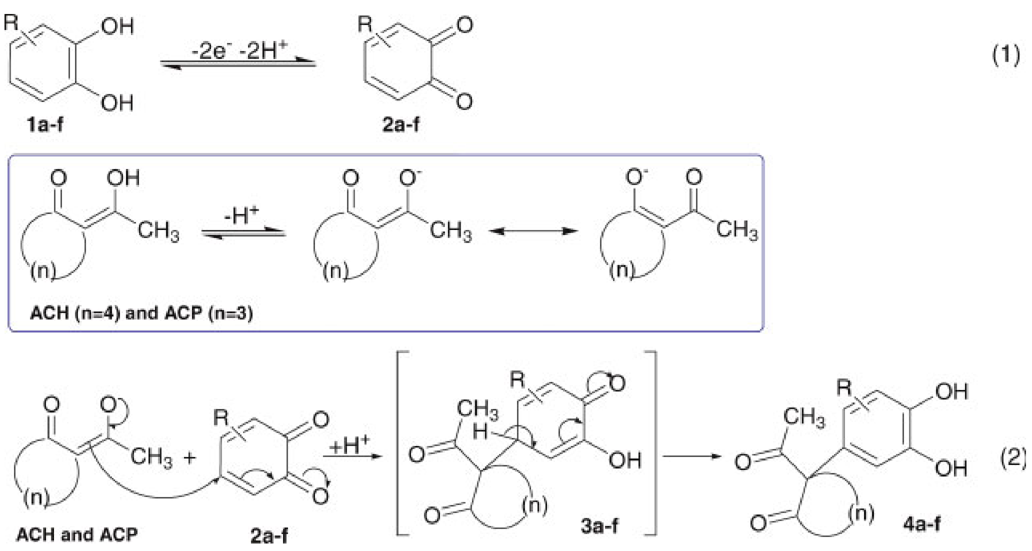

Scheme 1

electron-withdrawing character causes an increase in k_{obs}. In addition, the presence of substituted groups in C-4 position of catechol ring that is a reactive site of *o*-benzoquinones **2**, causes a decrease in k_{obs}. The observed homogeneous rate constants can be related with the Hammett ρ–σ parameters, where the Hammett equation is:

$$\log k_i = \log k_0 + \rho\sigma \tag{3}$$

where k_i is the rate constant for substituted catechol, k_0 is the rate constant for catechol, σ is a constant characteristic of a given substituent group,[17] and ρ is the slope of the log k_i-σ graph. The Hammett plot is shown in Fig. 4. The ρ values are 780.0 ($R = 0.992$) and 637.7 ($R = 0.996$) for electrochemical oxidation of catechols, in the presence of ACP and ACH, respectively. These positive ρ values mean that the transition states have substantial negative charge, because the reaction rates are increased significantly for electron-withdrawing substituents. This result is consistent with the attack of anion enolate ACP or ACH to the *o*-benzoquinone (**2**). As discussed before, the 3-methoxycatechol deviates significantly from the log k_i-σ line.[18] The deviation of 3,4-dihydroxybenzoic acid from the log k_i-σ line, is due to the presence of carboxylic

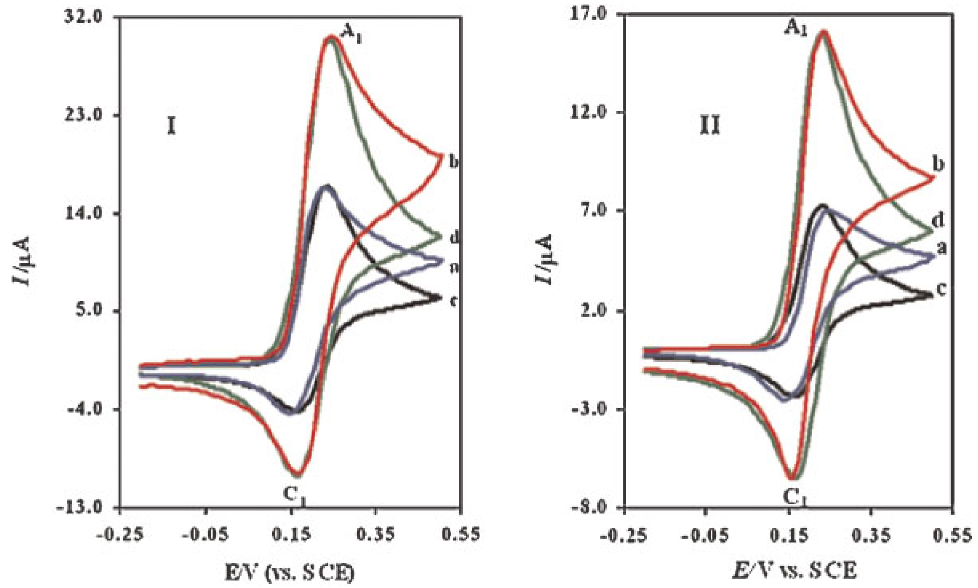

Figure 3. Experimental (curves a and b) and simulated (curves c and d) cyclic voltammograms of 1.0 mM catechol (**1a**) in the presence of: (I) 1.0 mM ACP, scan rates are: 100 and 400 mV s^{-1} and (II) 1.0 mM ACH scan rates are: 25 and 100 mV s^{-1}, respectively. At glassy carbon electrode, in phosphate buffer solution (pH = 6.8, $c = 0.20$ M). $t = 25 \pm 1$ °C

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group in C-4 position (reactive site) of *o*-benzoquinone ring.

Table 1. Observed homogeneous rate constant for various catechols in phosphate buffer (pH = 6.8)

	Observed homogenous rate constant k_{obs} ($M^{-1}\,s^{-1}$)	
Catechol derivative	ACH[a]	ACP[b]
Catechol	350 ± 25	870 ± 42
3-Methylcatechol	280 ± 23	670 ± 28
3-Methoxycatechol	200 ± 22	461 ± 26
4-Methylcatechol	—	219 ± 22
2,3-Dihydroxybenzoic acid	570 ± 27	1080 ± 36
3,4-Dihydroxybenzoic acid	310 ± 25	764 ± 27

[a] Standard deviation of three independent simulations at 25, 50 and 100 mV s^{-1}.

[b] Standard deviation of three independent simulations at 100, 250 and 500 mV s^{-1}.

pH dependence of cyclic voltammograms

Because of the dependence of catechol oxidation and the diketone dissociation on pH, the electrochemical oxidation of catechols in the presence of ACH and ACP has been studied at various pHs (Fig. 5). Cyclic voltammograms of catechol in aqueous solutions, with pH lower than 8, show one anodic (A_1) and a corresponding cathodic peak (C_1), with peak current ratio ($I_p^{C_1}/I_p^{A_1}$) of nearly unity which can be considered as a criterion for the stability of *o*-benzoquinone, produced at the surface of the electrode under the experimental conditions.[10–15] In basic solutions, the peak current ratio ($I_p^{C_1}/I_p^{A_1}$) is less than unity and decreases with increasing pH, as well as by decreasing the potential sweep rate. These can be related to the coupling of anionic or dianionic forms of catechols with *o*-benzoquinones (dimerization reaction).[19] The oxidation of catechol (**1a**), in the presence of ACH and ACP as nucleophiles was studied at various pHs (Fig. 5). As is shown, the height of the cathodic peak that is relevant to reduction of **2a** increases with decreasing pH. This is related to protonation of ACH or ACP's anion enolates and inactivation of them towards Michael addition reaction with *o*-benzoquinone (**2a**). Therefore, the rate of coupling reaction is pH dependent and enhanced by increasing pH. Comparison of voltammograms in second row with third row, show that at the same pH the height of cathodic peak (C_1) in the presence of ACH is more than the height of cathodic peak (C_1) in the presence of ACP. In other words, the observed homogeneous rate constants (k_{obs}) of Michael reaction of ACP's anion enolate with *o*-benzoquinone **2a** (Scheme 1, Eqn 2) is more than ACH ($k_{obs}^{ACP} > k_{obs}^{ACH}$). The rate of this type of reaction is pH dependent and the value of k_{obs} is given by[20]:

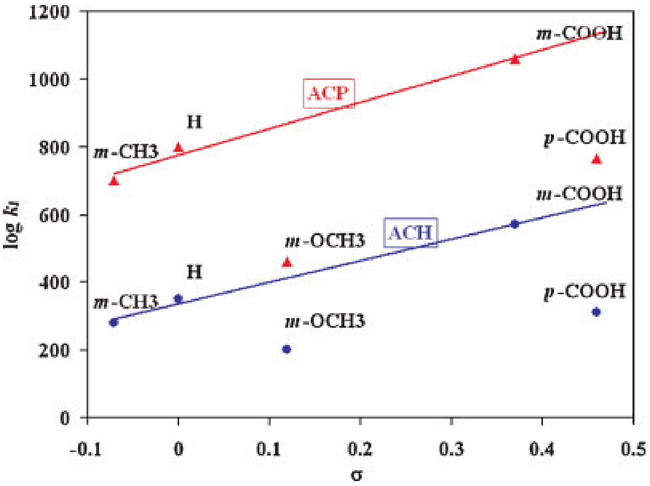

Figure 4. Hammett plot for electrochemical oxidation of catechols in the presence of: ACH (●) and ACP (▲)

$$k_{obs} = \alpha k \tag{4}$$

where α is the fraction of ACH or ACP in the ionized form, as defined by Eqn (5); k is the reaction rate constant of anion enolate ACP or ACH with *o*-benzoquinone **2a**.

$$\alpha = \frac{K}{[H_3O^+] + K} \tag{5}$$

where K is the dissociation constants of ACH or ACP.

Since, $pK_a^{ACP} = 8.25$ and $pK_a^{ACH} = 9.85$,[21,22] at the same pH: $k_{obs}^{ACP} > k_{obs}^{ACH}$.

Substitution of Eqn (5) into Eqn (4) and rearranging gives:

$$\frac{1}{k_{obs}} = \frac{1}{k} + \frac{[H_3O^+]}{k.K} \tag{6}$$

Figure 6 shows plot of $1/k_{obs}$ *versus* hydrogen ion concentration. We obtain the reaction rate constant (k) of the anion enolate ACP or ACH, with *o*-benzoquinone **2a** from the intercept of the plotted lines. The values of k for ACP and ACH are 1838 and 1105 $M^{-1}\,s^{-1}$, respectively. These values show that the homogeneous rate constants (k) of Michael reaction of ACP's anion enolate with *o*-benzoquinone **2a** is greater than ACH ($k^{ACP} > k^{ACH}$). In comparison with ACH, the anion enolate ring of ACP (five-membered ring) has more angular strain and the reaction of anion enolates ACP and ACH, with *o*-benzoquinone (**2**) moderates the angular strain via change of sp^2 carbon to sp^3. On the other hand, the steric interaction between axial substituents, bound to carbon atoms in a six-membered ring results in a steric destabilization. Therefore, we think that increasing of the chemical rate constant of anion enolate of ACP with *o*-benzoquinone (**2**) (Scheme 1, Eqn 2) can be related to a larger lowering of angular strain of the anion enolate ring of ACP, and/or 1,3-diaxial interaction between the axial

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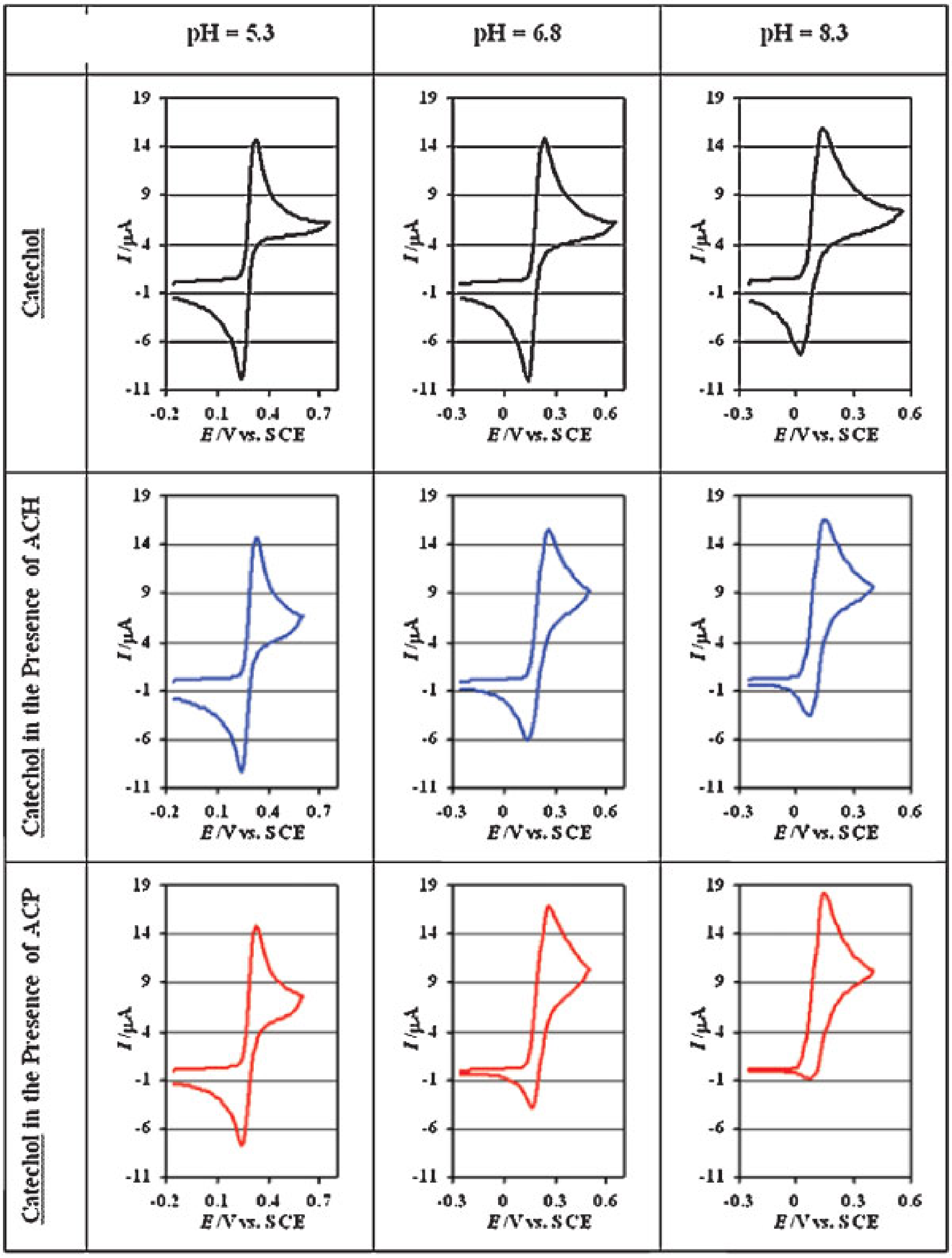

Figure 5. Cyclic voltammograms of 1 mM catechol in the absence, in the presence of 1 mM ACH, and in the presence of 1 mM 2-acetylcyclopentanone (ACP) in buffered solutions with various pHs and same ionic strength. Scan rate: 100 mV s^{-1}; $t = 25$ °C

hydrogens on the anion enolate ring of ACH and *o*-benzoquinone (**2**).

CONCLUSIONS

The results of this work show that catechols are oxidized in water to their respective *o*-benzoquinones. The quinones are then attacked by the anion enolate of ACH and ACP to form new catechol derivatives. The overall reaction mechanism for anodic oxidation of catechols, in the presence of *β*-diketones ACH and ACP is presented in Scheme 1. The kinetics of the reactions of electrochemically generated *o*-benzoquinones, with the ACH and ACP are studied by the cyclic voltammetric technique and the simulation of obtained voltammograms performed under EC mechanism. There is a good agreement between the simulated voltammograms with those obtained experimentally. The effects of pH on the oxidation pathway and the observed homogeneous rate constants (k_{obs}) have been discussed. Also, the rate constants (k) were calculated and significant differences in k, obtained in the cases of ACH and ACP have been discussed. In addition, the effects of the substituted groups on the catechol ring in k_{obs} (Hammett plot) have been studied.

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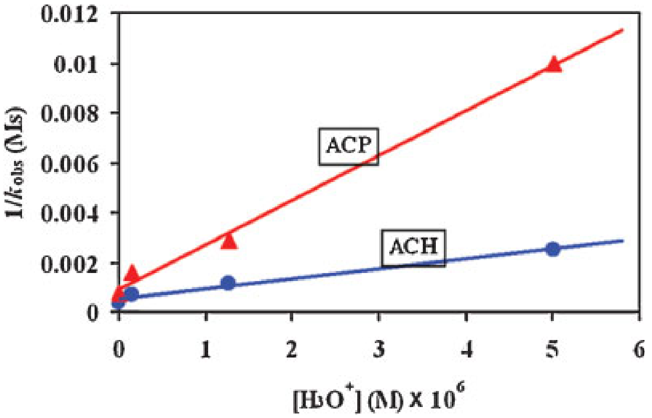

Figure 6. Plot of 1/k_{obs} *versus* hydrogen ion concentration for electrochemical oxidation of catechol (**1a**), in the presence of ACH (●) and ACP (▲)

Acknowledgements

We thank Professor M. A. Zolfigol and Dr R. Ghorbani for helpful discussions.

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DOI: 10.1002/poc