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Electrochemical behavior of some ethylenedioxycoumarins: Cathodic dimerization

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ABSTRACT

Electrochemical behavior of recently synthesized 7,8-ethylenedioxy-4-methyl-2(H)-1-benzopyran-2-one, (**1**), 7,8-ethylenedioxy-2(H)-1-benzopyran-2-one, (**2**), and 6,7-ethylenedioxy-4-methyl-2(H)-1-benzopyran-2-one, (**3**) was studied using cyclic voltammetry at a hanging mercury drop electrode and controlled-potential coulometric techniques. The results indicated that an irreversible one-electron cathodic peak was observed for each compound in the potential range from 0.0 to −2.0 V. The coulometric experiments were performed in a low yield and the products were identified by FT-IR spectrometry, ^{1}H NMR and mass spectrometry. The coulometric results indicated a dimeric product for each compound. A mechanism for the electrodimerization pathway was proposed.

1. Introduction

Many natural and synthetic coumarin derivatives having a lactone structure are used in a wide range of industrial [1], chemical [2,3] and biological [4] applications due to their spectral [5], and redox properties [4]. The redox status of a given biological environment is also crucial due to numerous essential and harmful processes in living cells that are governed and stimulated by redox reactions [6].

A large number of medicinal plants have been investigated for natural chemical components possessing antihepatotoxic activities [7]. Among the viable substances, Silybin has been found to be the most potent antihepatotoxic agent containing a 1,4-dioxane ring system (i.e. ethylenedioxy moiety) [8]. It is therefore thought that 1,4-dioxane ring plays an important role in inducing antihepatotoxic activity. Consequently some heterocyclic coumarin derivatives possessing the 1,4-dioxane ring system have been synthesized [9–12].

Considering the importance of the coumarin derivatives possessing 1,4-dioxane moiety, recently synthesized 7,8-ethylenedioxy-4-methyl coumarin, (**1**) and 7,8-ethylenedioxy coumarin, (**2**) and 6,7-ethylenedioxy-4-methyl coumarin (**3**) may exhibit novel biological and medicinal features as many others. The structures of the compounds studied are given in Fig. 1.

As shown in Fig. 1, the compounds **1** (IUPAC name: 7-methyl-2H-[1,4] dioxino [2,3-h] chromen-9(3H)-one), **2** (IUPAC name: 2H-[1,4] dioxino [2,3-h] chromen-9(3H)-one) and **3** (IUPAC name: 6-methyl-2H-[1,4] dioxino [2,3-h] chromen-9(3H)-one) are analogs of each other. Compared to 4-methylcoumarins which have been recently studied as novel antioxidants [13] the compounds **1**–**3** given in Fig. 1 may possess various biological activities. Therefore, the understanding of the redox mechanisms of these coumarins is important since their roles and applications in many aspects of biology and chemistry are based on their redox or electron transfer processes [14]. The compounds **1**–**3** establish one of the most popular model systems for studying redox activity properties, but up to date, no literature data are available about the electrochemical behavior of ethylenedioxy moiety substituted coumarin derivatives. Acid–base properties of **1** and **2** in Fig. 1 were studied using UV–vis spectrophotometry for the first time by Kılıç [15] in which chemical behavior in the pH range from 1.0 to 12.5 and the pK_a values were reported. Thus, it is critical to examine the electrochemical behavior of **1**–**3** accurately. Such knowledge is important for designing new tools or methods in industrial, chemical, biological, and medicinal applications.

In a previous study, electrochemical behavior of some new pyrimidine derivatives was examined by using cyclic voltammetry technique at a hanging mercury drop electrode (HMDE) and controlled-potential coulometry [16]. The same approach was also used in this work in order to (i) gain some insight about the effect of the pH on the voltammetric peak characteristics, (ii) determine voltammetric acidity constants of each compound and the effects of the ethylenedioxy and methyl groups and (iii) elucidate the coulometric products to find the most probable mechanistic pathway at the HMDE for each compound.

Electrochemical methods are the most widely applied techniques which offer high sensitivity and simplicity [17,18]. Among the electrochemical methods, cyclic voltammetry is widely used for the study of redox behavior of the drug compounds so that it can give insights

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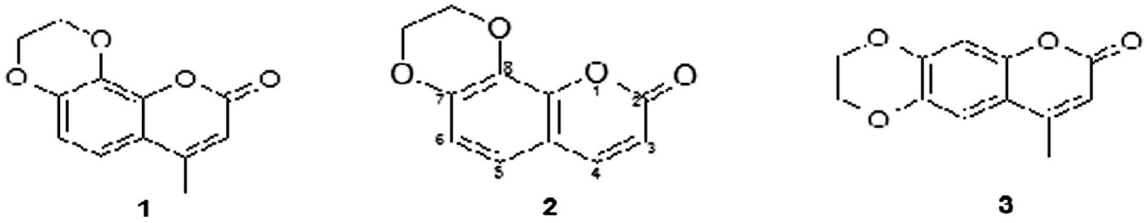

Fig. 1. Coumarins of this investigation.

about its fate. The pK_a values are generally important physico-chemical parameters in selecting pH of the buffers to be used and in evaluating bioavailability of drugs in the body.

2. Experimental

2.1. Chemicals and reagents

The synthesis of 7,8-ethylenedioxy coumarin, (**1**, $C_{11}H_8O_4$), 7,8-ethylenedioxy-4-methyl coumarin, (**2**, $C_{12}H_{10}O_4$) and 6,7-ethylenedioxy-4-methyl coumarin (**3**, $C_{11}H_8O_4$) was previously described in the literature [9,11]. Purity was tested by thin-layer chromatography using benzene–methanol (8:2 v/v) solvent mixture and verified by IR data. All chemicals were obtained from Fluka as reagent grade materials.

Compounds **1**–**3** are insoluble in water; therefore, the stock solutions (1.0 mM) were prepared in an appropriate volume of absolute methanol produced via distillation. Working solutions were prepared daily from the stock solutions in the concentration range between 0.0183 and 0.0550 mM for **1** and **3** and 0.0196 and 0.0588 mM for **2** to give the final methanol content of 90% by volume. The stock solutions of the compounds were kept in dark to avoid any decomposition. Triple-distilled water was used for the preparation of the aqueous solutions. Ionic strength was kept constant at 0.10 M using LiCl as a supporting electrolyte.

2.2. Instruments

Cyclic voltammetric and coulometric measurements were carried out by using a DT 2101 Model Potentiostat and a PP RI Model Wave Generator. A three-electrode cell system was used. Cyclic voltammograms were recorded on a YEW 3022 Model (Yogokawa Hokushin Electric) A4 x–y recorder and the controlled potential electrolysis recordings were obtained using a YEW 3021 Model (Yogokawa Hokushin Electric) y–t recorder. Mercury was purified electrochemically using the procedure described by Hanke [19]. Electrochemical data were processed using Microsoft Excel Program.

IR spectra were recorded as KBr disks in the range from 4000 to 400 cm^{-1} on a Shimadzu 8300 FT-IR Spectrometer. Melting points of the compounds, **1**–**3** and the isolated coulometry products, **1***–**3*** were measured on a Buchi 530 model instrument and correct values of the melting points were reported here. Combustion analysis for **2** was made with a LECO-932 CHN analyzer. The structural elucidations of **1***–**3*** were carried out with electron impact mass spectra (EIMS), ^1H NMR and IR. High resolution mass spectra were obtained with FISONS Instrument, model VG-ZABSPEC. ^1H NMR spectra were recorded in $CDCl_3$ at room temperature on a Bruker AVANCE 400CPX, tetramethylsilane (TMS) was used as the internal standard. The pH of the solutions prepared in a mixture of methanol–water (90% v/v methanol) was measured by a digital pH meter (Schott CG 841; ±0.001 pH unit) and a combined pH electrode that was standardized using standard aqueous buffers (pH 4.00 and 10.00) [20]. The pH values measured were not corrected and the symbol pH (defined as $-\log[H^+]$) was used in all cases. pH calibration was carried out before each experiment. An Eppendorf micro-pipette was used for the addition of solutions. A Sartorius A120 S analytical balance (sensitivity of ±0.0001 g) was used for weighing chemicals and compounds.

2.3. Measurements

Working solutions were stirred and purged with purified argon for 15 min during cyclic voltammetric studies. In the controlled potential coulometric studies, the working solutions were continuously stirred and purged with purified argon. A continuous flow of the argon maintained over the solution and cyclic voltammograms was recorded for each compound at three different concentrations in the pH range between 2.80 and 11.80 in increments of 1.0 pH unit, at room temperature. Voltammograms were recorded at four different scan-rates, 0.030, 0.080, 0.150 and 0.300 V/s. A cathodic scan was made first by varying the potential from 0 to −2000 mV, and then reversed to anodic direction.

2.3.1. Cyclic voltammetry

The three-electrode cell system is made up of a KCl aqueous saturated calomel electrode (SCE) as the reference electrode and a coil of platinum wire as the counter electrode were used. The working electrode was a stationary HMDE with a surface area of $S = 0.0393\ cm^2$. Britton–Robinson (BR) buffer system [20] was used for buffering the working medium.

2.3.1.1. Electrode preparation in cyclic voltammetry. A working electrode was prepared for each run. To form a sessile drop, a micrometer-type syringe was used [21]. For each run, a new mercury drop was hung up to the surface of the mercury-film coated electrode to achieve reproducibility. The hang-up operation was done just before each run by dropping mercury into a petri dish containing triply distilled water. The remaining mercury in the dish was discarded.

2.3.2. Controlled-potential coulometry

A silver wire was used as a counter electrode instead of a coil of platinum wire. The quiescent cathode area of the mercury pool was 12 cm^2. The electrolysis experiments were carried in 90% v/v methanol medium. The pH of the solutions was 5.60 for the three compounds, **1**–**3**. Citrate buffer system was used for buffering the working solution [22]. The electrolysis potentials were −1.670, −1.600 and −1.670 V (vs. SCE) corresponding to the crests of **1**, **2** and **3**, respectively.

The course of the electrolysis was followed by recording voltammetric curves before and after the electrolysis. Identification of the stable products was performed by thin-layer chromatography and IR spectroscopy. The completeness of the electrolysis experiments was monitored voltammetrically by the disappearance of the peak from the voltammogram. The number of electrons involved in the reduction of each compound was found by using the procedure outlined by Lingane [21,23].

2.4. Procedure

After the preparation of the working solution, the pH was checked and then an appropriate volume (50 ml) of it was placed into the cell. After removing the dissolved oxygen, a freshly prepared HMDE was

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