

Electrochemical study of two tris-*O*-substituted calix[4]arenes: 25,27-Dipropoxy-26-hydroxy-28-benzoyloxy-calix[4]arene-(*partial cone*) and 25,27-dibenzyl-26-hydroxy-28-benzoyloxy-calix[4]arene (*partial cone*). Electrosynthesis of the corresponding calix[4]arene-monoquinones

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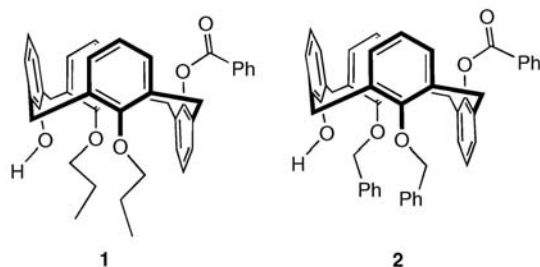
Abstract

The anodic oxidation of 25,27-dipropoxy-26-hydroxy-28-benzoyloxy-calix[4]arene **1** and 25,27-dibenzyl-26-hydroxy-28-benzoyloxy-calix[4]arene **2** in dichloromethane was investigated by electrochemical and spectroelectrochemical techniques. For both, the overall reaction is a two-electron oxidation of the phenolic group according to an ECE mechanism resulting in the ultimate formation of an observable phenoxylium cation. After reaction of the latter with traces of water and subsequent internal electron transfer, the corresponding calix[4]-monoquinones are formed.

Keywords: Calixarenes; Anodic oxidation; Electrosynthesis; Calix[4]monoquinone

1. Introduction

Calixarenes are macrocyclic phenol derivatives which provide unique platforms for the preparation of sophisticated, polytopic ligands [1]. As part of an ongoing programme aimed at the preparation of functionalised calixarenes, we report herein the results of the electrochemical oxidation of the partial-cone calix[4]arenes **1** and **2**. The present study complements our previous investigations on the electrochemical synthesis of calixquinones, starting from partially, lower rim-functionalised calix[4]arenes [2-4]. It was undertaken in order to investigate whether substituents lying in the vicinity of the hydroxyl group may sterically influence the oxidation process, for example by stabilising intermediates. The present electrochemical study is the first one dealing with calixarenes in the partial cone conformation, all previous studies concerning conical conformers. Electrochemical methodology is particularly valuable for the clean transformation of phenols. In particular, it offers the advantage of avoiding the use of poisonous thallium(III) salts, which are usually employed for the conventional synthesis of quinones [5-7].



2. Experimental

Cyclic voltammetric measurements were performed with a conventional three-electrode system using an EG&G 263 A potentiostat modulated by EG&G PAR M270 software. The working electrode was a platinum disk (EDI type, Radiometer), and a platinum wire was used as the counter electrode. During the whole electrochemical

study, no electrode fouling was observed. This was also verified when a glassy carbon working electrode was used. A saturated calomel electrode (SCE), which is placed in a separate compartment filled with the same solvent-supporting electrolyte solution as used in the cell, was used as the reference electrode for all electrochemical and UV-vis spectroelectrochemical experiments. Spectroelectrochemical measurements were carried out in a quartz cell constructed according the method described in the literature [8], and fitted with a fine platinum gauze as a working electrode. A Hewlett-Packard 8453A diode array spectrometer was used to obtain UV-vis spectra. Full scan MS and MS measurements were performed on a Finnigan LCQ (San Jose, CA) electrospray ion trap instrument. The ^1H and ^{13}C NMR spectra were recorded either on a Bruker AVANCE-400 or AVP-300 spectrometer. Macroelectrolysis and coulometry were carried out in the same cell, namely a three-compartment cell equipped with a platinum gauze (cylinder of height 50 mm and diameter 39 mm, BASi electrochemistry) as the working electrode and a platinum as the counter electrode. The working potential was controlled by a PJT 120-1 potentiostat (Radiometer).

Spectroscopic grade dichloromethane (CH_2Cl_2 , Merck) was used as received. Tetrabutylammonium hexafluorophosphate (Bu_4NPF_6 , electrochemical grade, Fluka) was used as supporting electrolyte throughout this study. 25,27-Dibenzyl-26-hydroxy-28-benzoyloxycalix[4]arene (2) was prepared and purified as described in the literature [9].

2.1. Synthesis of 25,27-dipropoxy-26-hydroxy-28-benzoyloxycalix[4]arene (1)

To a solution of 25,27-dipropoxycalix[4]arene (3.000 g, 5.90 mmol) in pyridine (25 mL) was added benzoylchloride (8.28 g, 59 mmol). The mixture was stirred at room temperature for 24 h and 1 N HCl (300 mL) was added. The insoluble material was filtered and recrystallised from CH_2Cl_2 -MeOH. Yield: 2.93 g, 81%; mp $>250^\circ\text{C}$; IR (KBr, cm^{-1}): $\nu(\text{C}=\text{O}) = 1732$. ^1H NMR (300 MHz, CDCl_3): δ 7.84 (s, 1H, OH), 7.31-7.28 (m, 2H, ArH), 7.22-7.15 (m, 4H, ArH), 6.83-6.75 (m, 3H, ArH), 6.60 (t, 2H, *p*-ArH, $^3J=7.4\text{Hz}$), 6.51-6.43 (m, 4H, ArH), 6.08 (t, 2H, *p*-ArH, $^3J=7.4\text{Hz}$), 4.21 and 3.32 (AB spin system, 4H, ArCH_2Ar , $^2J=13.0\text{Hz}$), 4.02 and 3.75 (AB spin system, 4H, ArCH_2Ar , $^2J=16.0\text{Hz}$), 3.94 and 3.65 (ABX₂ spin system, 4H, OCH_2 , $^3J(\text{AX}) = 6.5\text{Hz}$, $^2J(\text{AB}) = 8.9\text{Hz}$), 1.77-1.69 (m, 4H, OCH_2CH_2), 0.98 (t, 6H, CH_2CH_3 , $^3J=7.5\text{Hz}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (75 MHz, CDCl_3): δ 163.62 (s, C(O)), 154.40-119.00 (aryl C), 78.16 (s, OCH_2), 38.15 and 31.39 (2s, ArCH_2Ar), 23.35 (s, OCH_2CH_2), 10.70 (s, CH_2CH_3). Found: C, 80.31; H, 6.63. Calc. for $\text{C}_{41}\text{H}_{40}\text{O}_5$ ($M_r = 612.75$): C, 80.36; H, 6.58%.

2.2. Monoquinone 3

This compound was prepared electrochemically in CH_2Cl_2 (for details, see text), starting from 1 (0.050 g, $8.17 \cdot 10^{-5}$ mol). About 3-4 h after the electrolysis was completed, the solvent was removed in vacuo. The residue was dissolved in diethylether. The ether solution was filtered upon which it was evaporated to dryness. The reaction products were then purified by column chromatography on silica gel (60, Merck) using a dichloromethane-acetone mixture (99:1, v/v) as eluent. Yield: 0.021 g, 40%. ^1H NMR (400 MHz, CDCl_3): δ 7.50-7.45 (m, 1H, ArH), 7.30-7.24 (m, 4H, ArH), 7.20 (d, 2H, *m*-ArH, $^3J=7.5\text{Hz}$), 7.05 (t, 1H, *p*-ArH of $\text{ArOC}(\text{O})$, $^3J=7.6\text{Hz}$), 6.82 (d, 2H, *m*-ArH of $\text{ArOC}(\text{O})$, $^3J=7.8\text{Hz}$), 6.49 (s, 2H, $\text{H}_{\text{quinone}}$), 6.45 (d, 2H, *m*-ArH, $^3J=7.3\text{Hz}$), 6.31 (pseudo t, 2H, *p*-ArH, $^3J=7.5\text{Hz}$), 3.78 and 3.52 (AB spin system, 4H, ArCH_2Ar or ArCH_2 -quinone, $^2J=15.1\text{Hz}$), 3.64 and 3.34 (AB spin system, 4H, ArCH_2 -quinone or ArCH_2Ar , $^2J=14.4\text{Hz}$), 3.63-3.59 (m, 2H, OCH^{d}), 3.49-3.44 (m, 2H, OCH^{b}), 1.56-1.46 (m, 4H, CH_2CH_3), 0.80 (t, 6H, CH_2CH_3 , $^3J=7.3\text{Hz}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 188.61 and 186.27 (2s, C(O) of quinone), 168.05 (s, $\text{PhC}(\text{O})$), 156.35-122.92 (aryl-C), 73.22 (s, OCH_2), 37.31 (s, ArCH_2Ar), 34.24 (s, ArCH_2 -quinone), 23.14 (s, CH_2CH_3), 10.26 (s, CH_2CH_3). MS (ESI): m/z 683.27 [$\text{M} + \text{Me}_2\text{CO}]^+$. Found: C, 77.83; H, 6.42. Calc. for $\text{C}_{41}\text{H}_{38}\text{O}_6 \cdot \text{C}_3\text{H}_6\text{O}$ ($M_r = 626.30 + 58.08$): C, 77.17; H, 6.48%.

2.3. Monoquinone 4

This compound was prepared from 2, according to a method similar to that described above for 3. The product was purified by column chromatography (Silica gel 60) using dichloromethane-hexane (98:2, v/v) as eluent. Yield: 0.029 g, 46%. ^1H NMR (400 MHz, CDCl_3): δ 7.54-7.25 (10H, aromatic H), 7.07-7.05 (m, 5H, aromatic H), 6.98 (d, 2H, *m*-ArH of $\text{ArOC}(\text{O})$, $^3J=7.6\text{Hz}$), 6.88 (d, 2H, *m*-ArH, $^3J=7.2\text{Hz}$), 6.80 (t, 1H, *p*-ArH of $\text{ArOC}(\text{O})$, $^3J=7.6\text{Hz}$), 6.47 (d, 2H, ArH, $^3J \sim 7\text{Hz}$), 6.37 (pseudo t, 2H, *p*-ArH, $^3J \sim 7\text{Hz}$), 6.04 (s, 2H, $\text{H}_{\text{quinone}}$), 4.88 and 4.64 (AB spin system, 4H, PhCH_2O , $J = 12.0\text{Hz}$), 3.70 and 3.51 (AB spin system, 4H, ArCH_2Ar , $J = 15.2\text{Hz}$), 3.41 and 3.24 (AB spin system, 4H, Ar-CH_2 -quinone, $J = 14.4\text{Hz}$). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 187.72 and 186.25 (2s, C(O) of quinone), 164.12 (s, $\text{PhC}(\text{O})$), 155.84-123.45 (aryl-C), 73.22 (s, PhCH_2O), 37.33 (s, ArCH_2Ar), 34.68 (s, ArCH_2 -quinone). MS (ESI): m/z 745.13 [$\text{M} + \text{Na}]^+$. Found: C, 80.91; H, 5.40. Calc. for $\text{C}_{49}\text{H}_{38}\text{O}_6$ ($M_r = 722.822$): C, 81.42; H, 5.30%.

3. Results and discussion

3.1. Redox behaviour of 1 and 2

The cyclic voltammograms of 1 and 2 in CH_2Cl_2 with $0.1 \text{ mol dm}^{-3} \text{ Bu}_4\text{NPF}_6$ at different scan rates are depicted in Figs. 1 and 2, respectively. As expected, each cyclic voltammogram shows a single, well-defined oxidation peak at ca. 1.7 V. This peak, which corresponds to the oxidation of the hydroxyl group, is irreversible as there is no coupled reduction peak. The reverse scan showed a small cathodic peak (C_1) at ca. 0.8 V, that is at a potential which is more negative than the oxidation peak. This cathodic peak, which predominates at low scan rates, could arise from the reduction of a protonated calixquinone, probably straightforwardly formed after a deprotonation-protonation sequence of the oxidation product. This interpretation is in good agreement with the fact that a yellow colour, typical for calixquinones, developed on the time scale of the voltammetric measurements. On the other hand, when the scan rate was increased (from $v = 0.1 \text{ V/s}$ for 2), another cathodic peak (C_2) emerged at ca. 0.17 V, the height of which increased with increasing scan rate (Fig. 2 curves c-f). This cathodic peak is almost identical for both compounds and does not appear as long as the anodic scan has not swept beyond the oxidation peak, clearly indicating that the reacting species is generated as a stable product after oxidation. In each case, the variation of peak current function with changes in scan rate for the oxidation peak (Figs. 3 and 4) is in agreement with that of an ECE process with $\Delta E_0 > 0$ [10]. Moreover, a plot of peak current ratio $I_{p,c2}/I_{p,a}$ as a function of scan rate (Figs. 3 and 4) also confirmed the involvement of an ECE mechanism [11]. Such a mechanism is commonly accepted for the oxidation of phenolic compounds [12,13].

Fig. 1. Cyclic voltammograms of 2mM 1 in CH_2Cl_2 ($0.1 \text{ mol dm}^{-3} \text{ Bu}_4\text{NPF}_6$) at various scan rates. Scan rates from (a) to (e) were 25, 50, 100, 200 and 500 mV s^{-1} . (*) denotes the initial and final potential.

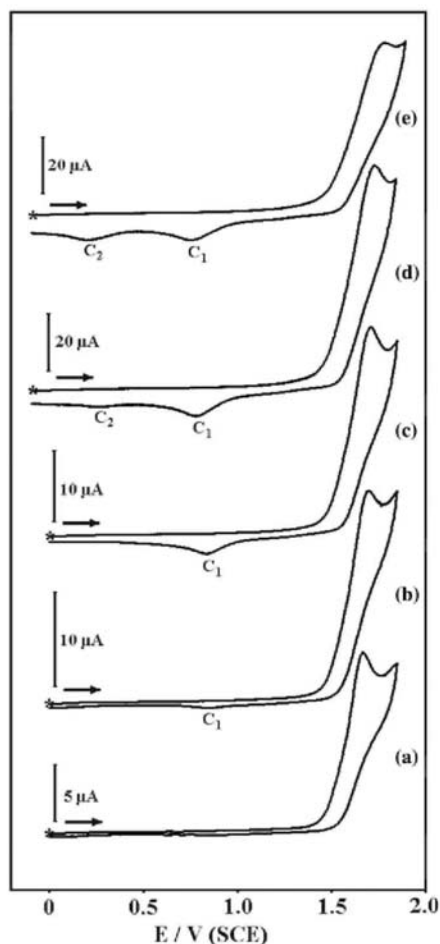


Fig. 2. Cyclic voltammograms of 1.6 mM **2** in CH_2Cl_2 ($0.1 \text{ mol dm}^{-3} \text{Bu}_4\text{NPF}_6$) at various scan rates. Scan rates from (a) to (e) were 25, 50, 100, 200 and 500 mV s^{-1} . (*) denotes the initial and final potential.

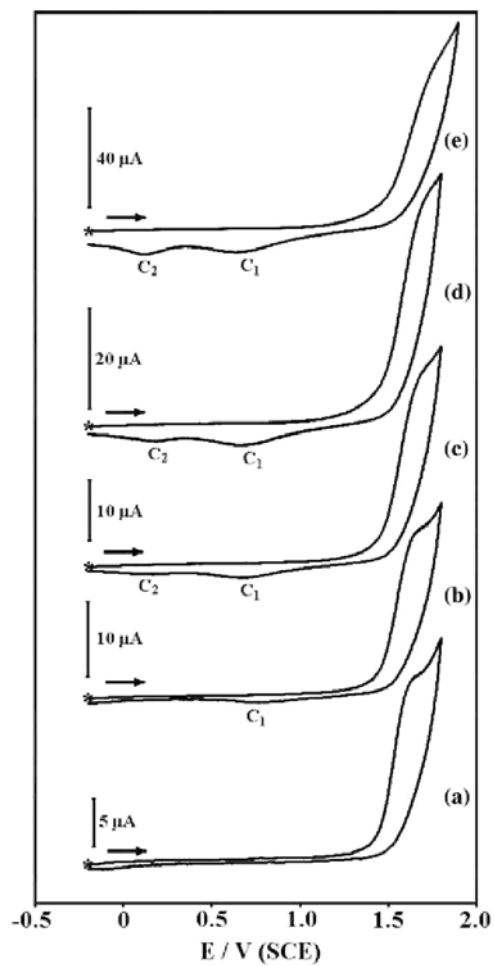


Fig. 3. Variation of current function ($I_{p,a}/v^{1/2}$) left and current ratio ($I_{p,C2}/I_{p,a}$) right as a function of scan rate for **1**.

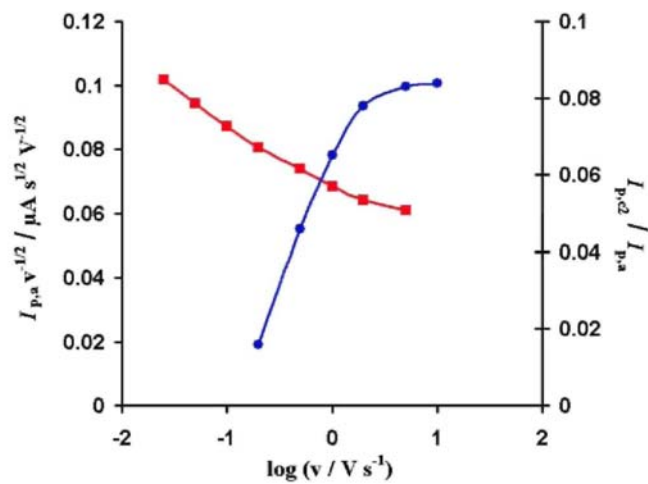
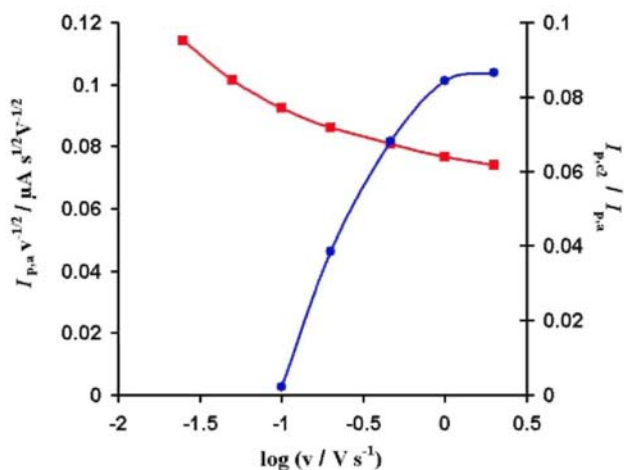


Fig. 4. Variation of current function ($I_{p,a}/v^{1/2}$) left and current ratio ($I_{p,c2}/I_{p,a}$) right as a function of scan rate for 2.

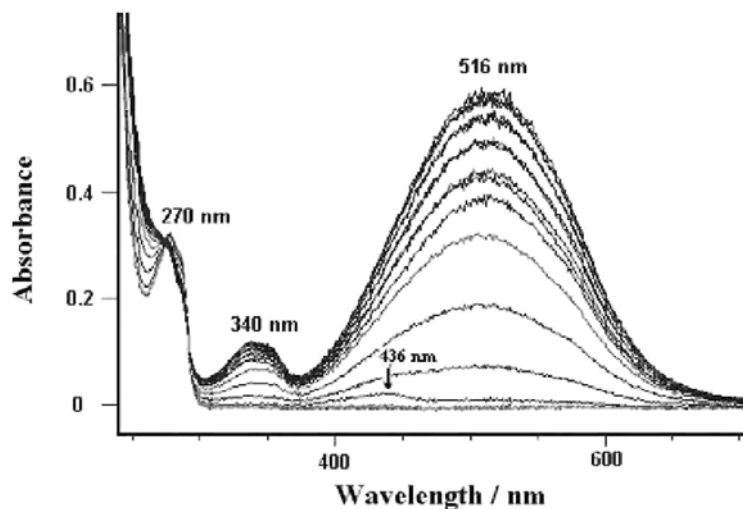


The ECE mechanism is further supported by the results obtained at rotating platinum-disk electrode. These showed that, for 1, $i_L/\omega^{1/2}C$ decreased when ω increased, while for 2 this ratio was independent of ω at low rotation rates and slightly increased with increasing ω , thus indicating the presence of fast chemical reactions taking place between the two electron transfers [14,15].

For each calix[4]arene, controlled-potential electrolysis was carried out at a potential of ca. 1.75 V. It was found that two electrons were exchanged in the oxidation step (see below).

Consistent with a number of studies on phenolic compounds, these findings strongly suggest that, on the time scale of the voltammetric measurements, the ultimate oxidation products of 1 and 2 are the phenoxylium cations $[1\text{-H}]^+$ and $[2\text{-H}]^+$, respectively.

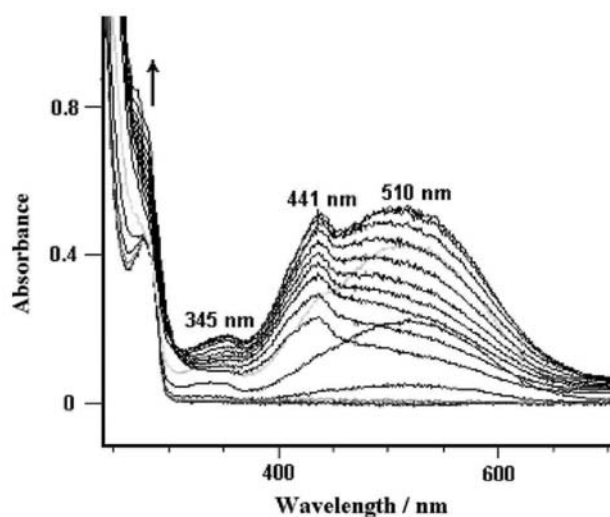
Fig. 5. Potential resolved thin-layer spectral changes of 1 in CH_2Cl_2 , $0.1 \text{ mol dm}^{-3} \text{ Bu}_4\text{NPF}_6$. Potential range = 0.80-1.80 V. Scan rate 10 mV/s.



Spectroelectrochemical experiments were performed with 1 and 2 in a thin-layer cell using a platinum grid as the anode. This technique permits observation of the absorption spectra of the compounds formed upon oxidation but over a longer time than cyclic voltammetry (a typical experiment had a duration of 200-300 s). The spectra recorded as the potential was stepped incrementally from 0.6 to 2.0 V. UV-vis spectral changes during oxidation of 1 in CH_2Cl_2 containing $0.2 \text{ mol dm}^{-3} \text{ Bu}_4\text{NPF}_6$ are shown in Fig. 5. Isosbestic points (ill-defined) located at

275 and 295 nm indicate a mixture of at least two absorbing species. The initial absorbance of 1, which is found in the range of 275-285 nm, gradually decreases in intensity, while new absorption peaks appear at ca. 270 (strong), 340 (strong), 436 (sh) and ca. 510 (strong) nm. Similar spectral changes occur during oxidation of 2 under identical experimental conditions (Fig. 6). For both, the band at 270 nm is typically due to the presence of aromatic rings, while that at ca. 340 nm lies in the range expected for carbonyl groups of phenoxylium cations [16]. The intense band centred at ca. 510 nm is characteristic of such species [17,18], while the shoulders observed around 440 nm are due to a minor species that could be considered as a phenoxy radical whose transformation into a phenoxylium cation is known to be much faster. These observations are in agreement with those reported by Pokhodenko et al. [19], who found that the one-electron oxidation of the phenoxy radical ($\lambda_{\text{max}} = 428$ nm) results in the formation of the corresponding phenoxylium cation ($\lambda_{\text{max}} = 520$ nm). Accordingly, it is reasonable to assume that a similar radical is also present in our case, but at a very low concentration. Again the observed spectral changes are totally irreversible, the spectra of the starting materials being not regenerated by a reverse potential scanning. These findings corroborate the CV data and hence establish that the electrochemical oxidation of 1 and 2 is chemically irreversible.

Fig. 6. Potential resolved thin-layer spectral changes of 2 in CH_2Cl_2 , $0.1 \text{ mol dm}^{-3} \text{ Bu}_4\text{NPF}_6$. Potential range = 0.80-1.80 V. Scan rate 10 mV/s.

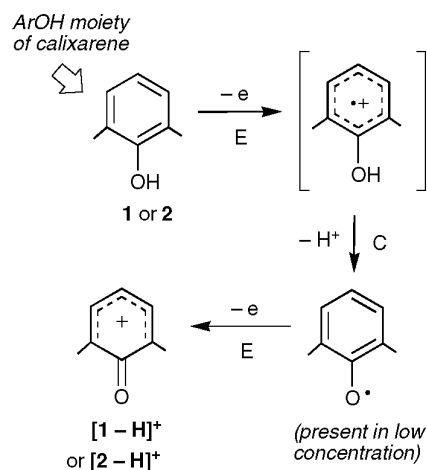


For both 1 and 2, coulometry was carried out at $E = 1.75$ V/SCE. As the electrolysis proceeded, the colour of the solution turned from yellow-green to deep pink; the number of electrons exchanged (n) was found to be 1.90. A typical electronic spectrum of the solution obtained immediately after the coulometry was completed (1-2 h) is depicted in Fig. 7. As seen in Fig. 5a, the band at 515 nm is still present, indicating that the phenoxylium cation is stable after extended electrolysis. The occurrence of chemical reactions coupled with the electron transfer process was confirmed by the final UV-vis spectrum measured ca. 2 h later, which showed only a weak, broad peak in the 300-350 nm range (Fig. 7b).

The combined electrochemical and spectroscopic data lead to the overall oxidation mechanism shown in Scheme 1.

The proposed ECE mechanism (on the voltammetric time scale), comprising two successive one-electron oxidation steps, is similar to that commonly accepted for non-macrocyclic phenolic compounds. The products formed are the phenoxylium cation $[1\text{-H}]^+$ or $[2\text{-H}]^+$.

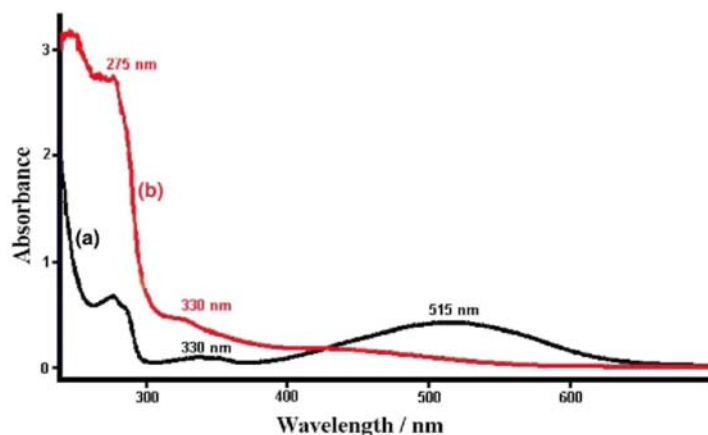
Scheme 1.



3.2. Electro synthesis of the calix[4]monoquinones 3 and 4

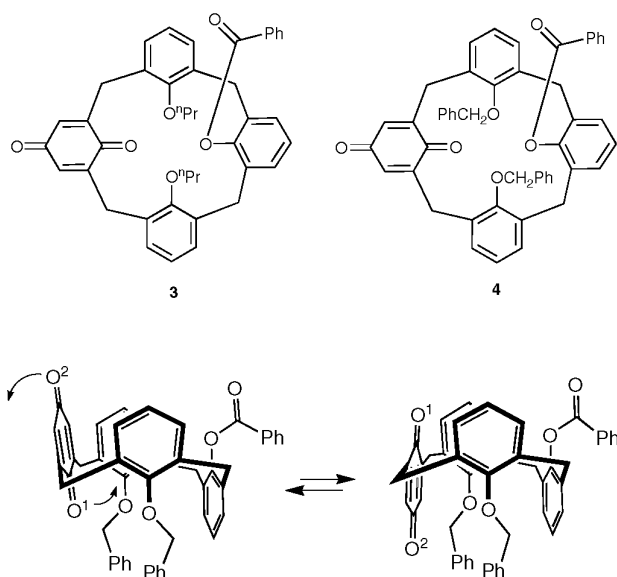
In view of our recent studies on lower-rim disubstituted calix[4]arenes, we anticipated that the electrogeneration of the phenoxylum cations $[1-H]^+$ and $[2-H]^+$ would provide a route to the preparation of the corresponding calix[4]monoquinones via an ECEC mechanism. Indeed, it is well known that a phenoxylum cation may, in the presence of traces of water, slowly convert into the corresponding quinone. Note, this transformation involves an internal transfer of two electrons, which are different from the two electrons measured during coulometry [13]. Aiming at the electrochemical synthesis of such compounds, macro-scale electrolysis was performed on 1 (0.050 g, electrolysis duration 2-3 h) and 2 (0.060 g, 2-3 h) at 1.75 V in CH_2Cl_2/Bu_4NPF_6 . About 3-4 h after the electrolysis was stopped, the solvent was removed in vacuo. The residue was dissolved in diethylether. The ether solution was filtered upon which the solvent was evaporated in vacuo.

Fig. 7. Typical electronic absorption spectra of the starting calix[4]arene in CH_2Cl_2 , $0.1 \text{ mol dm}^{-3} Bu_4NPF_6$: (a) immediately after controlled-potential oxidation at 1.75 V vs. SCE; (b) 1-2 h after the end of the coulometry.



In each case, the residue was then chromatographed on a silica gel column (see experimental part for details). The two products, 3 and 4, were characterized by 1H and ^{13}C NMR, mass spectrometry and elemental analysis. As expected for Cs-symmetrical compounds, the 1H and ^{13}C NMR spectra of both compounds reveal the presence of two distinct Ar CH_2 Ar groups (ratio 1:1). It is noteworthy that the Ar CH_2 Ar protons all appear as AB systems in which the AB separations are smaller than 0.5 ppm, hence indicating that the calixquinones adopt either a rigid 1,3-alternate conformation or a fluxional, partial cone conformation in which the quinone ring swings through the calix annulus. As revealed by 2D ROESY experiments, the quinonic H atoms of 4 correlate with both the axial and equatorial protons of the adjacent Ar CH_2 groups. We therefore assign to 4 a dynamic structure as shown in Scheme 2.

Scheme 2.



Overall, this study has led to the first electrochemical synthesis of calix-monoquinones. Both syntheses involve intermediate phenoxylium cations which are easily converted into the monoquinones by reaction with residual water. Further studies are aimed at exploiting the flexibility of the calix-monoquinones 3 and 4 which should be able to complex a wide variety of metal cations.

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