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ELECTROCHEMICAL STUDY OF TWO CURCUMIN-LIKE COMPOUNDS ON ACTIVATED GLASSY CARBON ELECTRODE

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The compounds having a similar backbone with the curcumin were investigated by using cyclic voltammetry (CV) and differential pulse voltammetry (DPV) techniques at an activated GCE in non-aqueous media. They exhibit a different redox behaviour in comparison with curcumin due to the absence of the hydroxyl groups in position 4 and 4' and of the methoxy groups in position 3 and 3'. The anodically activated GCE leads to a better electrochemical behaviour of the two compounds in comparison with their behaviour at the bare GCE, the charge transfer step being enhanced.

INTRODUCTION

Curcumin is the main pigment present in the rhizomes of the *Curcumina longa* possessing biological properties as anti-inflammatory, anti-angiogenic, antioxidant,etc. It inhibes free radical formation in blood and body tissues. It also prevents some cardio-vascular deseases.[1,2] The powerful curcumin antioxidant activity,[3-5] working especially when diverse free radical are produced as a result of physiological process is essentially an electrochemical property, so it has to be investigated from an electrochemical viewpoint in order to characterize its redox behaviour and its electrocatalytic role. In addition, the curcumins can act like very good ligands due to their 1,3-diketonic moiety which allow the isomerization to keto-enolic compounds; both structures (1,3-diketonic and keto-enolic) are able to experience the deprotonation either to the metylene group or to the enolic hydroxyl group. The keto-enolate ion could play a very good role as ligand too.

The two studied compounds, (1,7-bis[4-nitro]-1,6-heptadiene-3,5-dione), denoted as compound III, and (1,7-bis[4-N,N dimethylamino]-1,6-heptadiene-3,5-dione), denoted as compound IV, (see Fig. 1) exhibit different redox properties due to the different groups bonded in the position 4 of each aromatic moiety. Also they could be efficient chelating agent for different metallic cations as Fe^{3+}, Fe^{2+}, and Ni^{2+} leading to formation of complexes,[6-12] besides it can inhibit the oxidation of certain metal ions.[7,10] Their chelating effect is given by the 1,3 dione-type structure, analogue to the acethylacetone case (based on the equilibrium between the keto and enol forms of acetylacetone-type which coexist in solution as tautomers).

Both studied compounds have the same moiety (i.e., bis-α,β-unsaturated β-diketo(heptadiene-dione)) and undergo keto-enol tautomerism. But the biological activity of them is associated with the phenolic hydroxyl group and the diketonic structure [13] especially under pH 8, where the ketonic form of the heptadieno-dione chain predominates. Above pH 8, the enolate form of the heptadieno-dione chain predominates and curcumin exhibites kelatic properties towards the cations as Fe^{3+}, Fe^{2+},

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Cu^{2+}, Cd^{2+} and Ni^{2+}, the enolate form of curcumin acting as electron donor and good coordination sites. Curcumin can also protects against lead- and cadmium-induced lipid peroxidation and lead-induced tissue damage in rat brain, [13] or can participate in chelating the irons ions which, in turn, take part in oxygen transfer. [7] The study applied to other two curcumin-like compounds was accomplished at anodically activated GCE in different conditions of activation (the same activation electrode potential but different activation times) and different conditions for accumulation of the electroactive species (the same accumulation potential but six different times of accumulation) in order to increase the charge transfer rate.

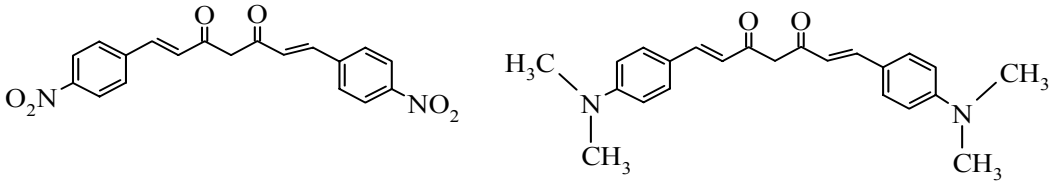

Fig. 1 – (1,7-bis[4-nitro]-1,6-heptadiene-3,5-dione), denoted as compound III, and (1,7-bis[4-N,N dimethylamino]-1,6-heptadiene-3,5-dione), denoted as compound IV.

EXPERIMENTAL

Apparatus: Electrochemical experiments were carried out using the potentiostat-galvanostat system AutoLab PGStat 12, controlled by General Purpose Electrochemical System (GPES) electrochemical interface for Windows (version 4.9.007). Three electrodes in one-compartment cell (10 ml) were used in all experiments. Glassy carbon electrode served as a working substrate electrode. All potentials were measured and given referred to SCE used as reference electrode. The counter electrode was a glassy carbon electrode rod-shaped.

Measurements: All measurements were carried out at room temperature. Oxygen was expelled from all the working solutions by bubbling dry argon stream for 5 min before every experiment and an argon atmosphere was maintained above the solution during the experiment.

Chemicals: All chemicals were reagent grade, DMSO (Carlo Erba) and $TBABF_4$ (Fluka) and the two curcumin-like compound were synthesised and purified in Organic Technology and Macromolecular Compounds Laboratory (Faculty of Applied Chemistry and Material Sciences, University Politehnica of Bucharest) were used without further purification. Before modification, the glassy carbon electrode surface was polished with alumina slurry on a polishing pad, washed with distilled water and sonicated for 3 minutes in doubly distilled water.

Activation of GCE

The anodically activated GCE was obtained as described but after the bare electrode was polished using 0.05 μm alumina slurry until a mirror-like finish was obtained; then rinsed with twice distilled water, cleaned by ultrasonication in twice distilled water for 3 min and finally dried in air. The interval times used for activating the GCE at +1.8 V were 60 s and 120 s. The improvement of the electrochemical response versus biological compounds, refer to the increase both of the activity and of reproducibility of the modified GCE. In addition, at the pretreated GCE some biological compounds can be adsorbed and, as a consequence, accumulated at the electrode surface prior to CV and/or DPV experiments. Anodic activation of the surface of GCE at high anodic electrode potential results in an oxidized film containing functional group, especially of carbon-oxygen type (maybe of quinone type). As a result the number of active sites at the GCE surface increases and the electron transfer reaction can be improved. [14-16]

RESULTS AND DISCUSSION

Two others curcumin-like compounds were studied by CV and DPV after the curcumin itself and *bis*demethoxycurcumin were also studied. [17]

Cyclic voltammetry behaviour of a solution containing 10^{-4} M curcumin III in DMSO containing 0.1 M $TBABF_4$, at inactivated GCE and at an anodically activated GCE at 1.8 V for 60 s in the potential range from -0.20 V to 0.75 V at 100 mV/s and an accumulation electrode potential at -0.5 V for 60 s puts in evidence the electrocatalytic effect of the film formed at the GCE surface (see Fig. 2). By this electrochemical treatment the peak currents increase and the peak potentials shift in the negative direction for the anodic peak.

This effect appears at each scan rate utilized as can be seen from Fig. 3. A single anodic peak at E_{pa} and I_{pa} from 0.292 V and 0.56 μA for 25 mV/s till 0.375 V and 7.00 μA for 250 mV/s and a single cathodic peak at E_{pc} and I_{pc} from 0.122 V and -0.55 μA for 25 mV/s till 0.216 V and -6.71 μA for 250 mV/s (ΔE_p increasing from 83 mV to 94 mV) appear at the inactivated GCE.

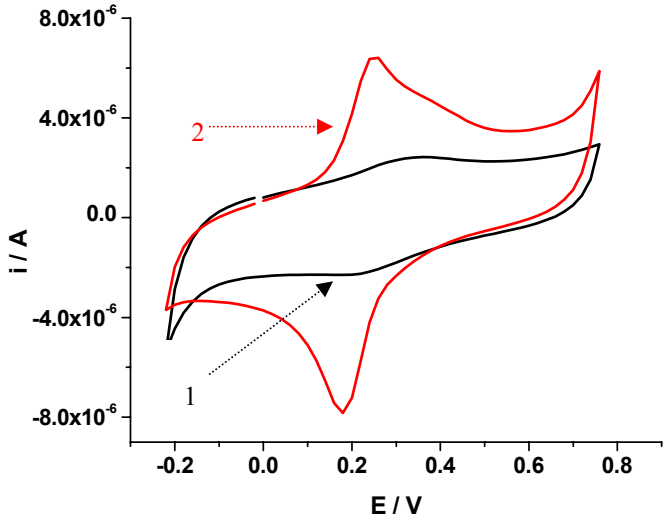

Fig. 2 – The behaviour of 10^{-4} M curcumin III in DMSO containing 0.1 M $TBABF_4$ at GCE bare electrode in the range from -0.20 V to 0.75 V at 100 mV/s (1) without activation, and (2) with activation at 1.8 V for 60 s and accumulation electrode potential at -0.5 V for 60 s.

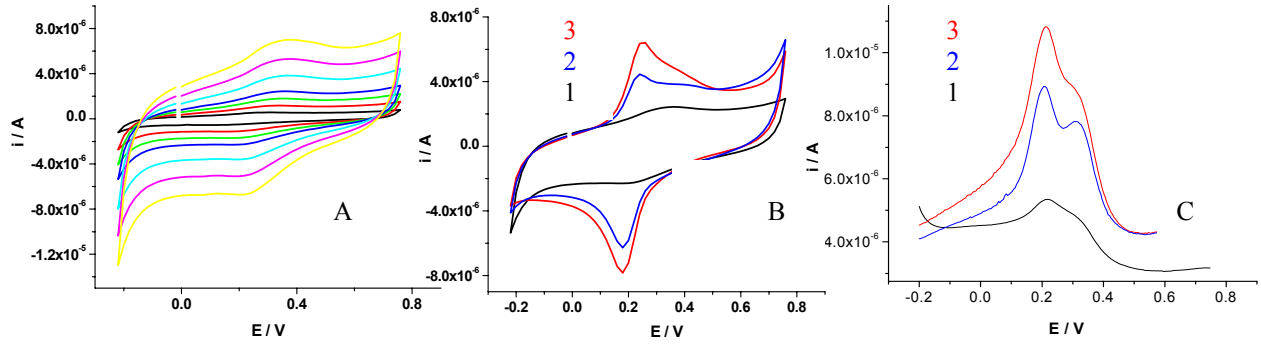

Fig. 3 – The cyclic voltammetry behaviour of 10^{-4} M curcumin III in DMSO containing 0.1 M $TBABF_4$ in the range from -0.20 V to 0.75 V at different sweep rates: 25, 50, 75, 100, 150, 200, 250 mV/s at inactivated GCE (A, 1 in B and C) and a comparison of CV-traces (B) 100 mV/s and DPV-traces (C) for SP (step potential) 5 mV and MA (modulation amplitude) 25 mV, at activated GCE at 1.8 V for 60 s (2) and at 1.8 V for 120 s (3) and accumulation electrode potential (at -0.5 V for 60 s).

In the case of an anodically activated GCE, the curcumin III cyclic voltammogram exhibits a single anodic peak at E_{pa} and I_{pa} from 0.220 V and 1.03 μA for 25 mV/s till 0.263 V and 11.00 μA for 250 mV/s and a single cathodic peak at E_{pc} and I_{pc} from 0.158 V and -1.19 μA for 25 mV/s till 0.180 V and -18.1 μA for 250 mV/s (ΔE_p decreasing from 43 mV to 22 mV).

The plot $\ln I_p$ versus $\ln v$ has a slope of 1 and a regression coefficient of 0.9914, being consistent with the linear dependence of I_p against v (regression coefficient of 0.9982) and also with the results of the plot I_p against $v^{1/2}$, which is not linear. So for the anodic peak occurrence is responsible Curcumin III as an adsorbed electroactive species (the diffusional contribution of the Curcumin III to the total faradaic current being negligible).

The effect of anodical activation of a bare GCE, at 1.8 V (vs. SCE) either for 60 s (curve 2 in Figs. 3 B and 3 C) or for 120 s (curve 2 in Figs. 3 B and 3 C) and of a preconcentration electrode potential of – 0.5 V applied for 60 s, can be seen in comparison with the inactivated GCE case (curve 1 in Figs. 3 B and 3 C) at the same scan rate of 100 mV/s. The electroactive species gives rise to a much

better defined cyclic voltammogram having both peak currents increased and peak potentials anticipated in comparison with the response recorded for an inactivated GCE. It can be noticed that simultaneously the hysteresis of the cyclic voltammogram at GCE modified by anodic activation increases as it is usually expected for chemically modified electrodes, but more for the anodic region. The activation of GCE for 60 s comparing with activation at 120 s, and both versus 0 s (inactivation case), seems to lead to a better electrochemical response (as regarding definition of the peak, as regarding the peak potential position, but not as regarding the peak current height). If we define the anodic peak separation as $\Delta E_{pa} = E_{pa,act} - E_{pa,inact}$, where $E_{pa,act}$ is the anodic peak potential in the case of the activated GCE and $E_{pa,inact}$ is the anodic peak potential in the case of the inactivated GCE, then the ΔE_{pa} = -72 mV (25 mV/s) and -112 mV (250 mV/s) for 60 s activation time is larger than ΔE_{pa} = -36 mV (25 mV/s and 250 mV/s) for 120 s activation time, i.e., the anticipation of the anodic peak is more efficient for the former case than for the latter. Also the anodic peak ratio, defined as $r_{pa} = \frac{I_{pa,act}}{I_{pa,inact}}$, gives a more efficient catalytic effect for 60 s activation time, r_{pa} =1.84 (25 mV/s) and 2.29 mV (250 mV/s) in comparison with the activation time of 120 s, where r_{pa} =1.45 (25 mV/s) and 1.30 (250 mV/s).

For an activation time of 60 s (see Fig. 4 A for a scan rate of 50 mV/s), the same procedure being applied for 120 s activation time too, at the activation potential of +1.8 V (vs. SCE), an accumulation electrode potential was imposed to the anodically activated GCE for different preconcentration time which has been changed in the range 10-60 s, with a step of 10 s. The cyclic voltammograms were recorded at different scan rate but Fig. 4 A presents only the CV–traces for 100 mV/s, while Fig. 4 B presents the DPV-traces (with SP=5 mV and MA=25 mV) at different accumulation time used.

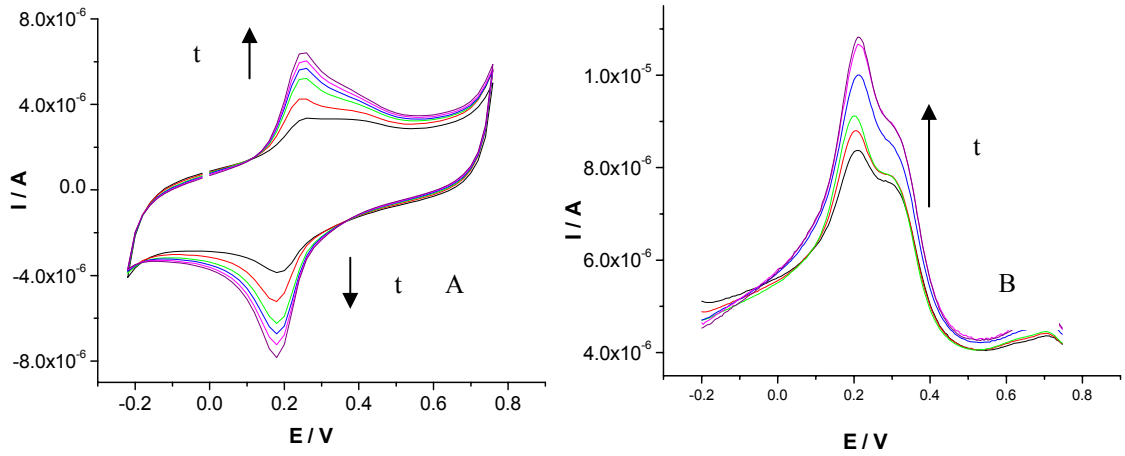

Fig. 4 – (A) The CV (100 mV/s) and (B) the DPV (SP=5 mV, MA=25 mV) behaviour of 10^{-4} M curcumin III in DMSO containing 0.1 M $TBABF_4$ at activated GCE bare electrode (at 1.8 V for 60 s) and at -0.5 V accumulation electrode potential in the range from -0.2 V to 0.75 V but for different accumulation times: 10, 20, 30, 40, 50 and 60 s.

The effect of increasing accumulation/ preconcentration time is the enhancement of peak currents in a curved manner, at the beginning a linear behaviour and then with a decreasing slope (a saturation effect could perhaps occurs at longer accumulation time, due to the attainment of an equilibrium between the two concentration of electroactive species from the electrodic interface and from the bulk of the solution). As concerns the peak potentials evolution, the anodic one moves very slightly, less than 10 mV variation, while the cathodic one is constant with increasing accumulation time.

Cyclic voltammetry behaviour of a solution containing 10^{-4} M curcumin IV in DMSO containing 0.1 M $TBABF_4$, at inactivated GCE and at an anodically activated GCE at 1.8 V for 60 s and an accumulation electrode potential at -0.5 V

for 60 s in the potential range from -0.25 V to 0.90 V at 100 mV/s puts in evidence a much smaller electrocatalytic effect of the film formed at the GCE surface compared with either the inactivated bare GCE (see Fig. 5 A, upper curve or 2 or Fig. 5 B, lower curve or curve 1) or the Curcumin III at an activated, in the same conditions, GCE (see Fig. 5 B, upper curve or curve 1).

This effect appears at each scan rate utilized as can be seen from Fig. 6. A single anodic peak at E_{pa} and I_{pa} from 0.317 V and 0.5 μA for 25 mV/s till 0.233 V and 5.4 μA for 250 mV/s and a single cathodic peak at E_{pc} and I_{pc} from 0.218 V and -0.9 μA for 25 mV/s till -0.089 V and -8.4 μA for 250 mV/s (ΔE_p decreasing from 43 mV to 22 mV) appear at the inactivated GCE. In the case of an anodically activated GCE, the curcumin IV cyclic voltammogram exhibits (see Fig. 6 B) a single anodic peak at E_{pa} and I_{pa} from 0.296 V and 0.50 μA for 25 mV/s till 0.357 V and 9.00 μA for 250 mV/s and a single cathodic peak at E_{pc} and I_{pc} from 0.200 V and -0.65 μA for 25 mV/s till 0.215 V and -10.70 μA for 250 mV/s (ΔE_p increasing from 99 mV to 322 mV). The plot $\ln I_p$ versus $\ln v$ has a slope of 1 and a regression coefficient of 0.9981, being consistent with the linear dependence of I_p against v (regression coefficient of 0.9952) and also with the results of the plot I_p against $v^{1/2}$, which is not linear. So for the anodic peak occurrence is responsible Curcumin III as an adsorbed electroactive species.

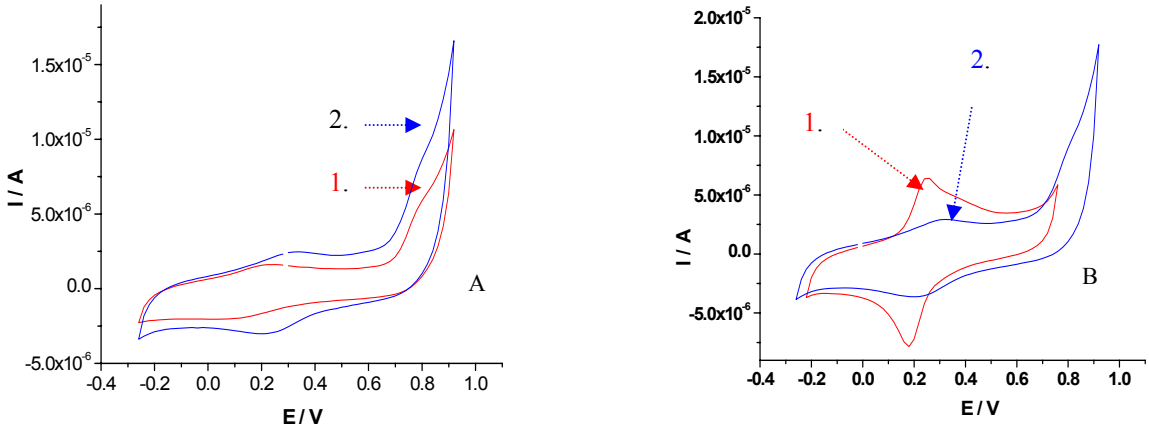

Fig. 5 – (A) The behaviour of 10^{-4} M curcumin IV in DMSO containing 0.1 M $TBABF_4$ at GCE in the range from -0.25 V to 0.90 V at 100 mV/s without activation (curve 1), and with activation at 1.8 V for 60 s and accumulation electrode potential at -0.5 V for 60 s (curve 2); (B) Comparison between the cyclic voltammograms of curcumin III (1) and curcumin IV (2) at an anodically activated GCE, (electrode potential 1.8 V for 60 s, accumulation electrode potential -0.5 V, kept for 60 s), 100 mV/s scan rate, different ranges of potential -0.20 V – 0.75 V (1) and -0.25 V – 0.90 V (2).

The effect of anodic activation of a bare GCE, at 1.8 V (vs. SCE) either for 60 s or for 120 s and of a preconcentration electrode potential of – 0.5 V applied for any accumulation time in the range from 0 s to 60 s, with a step of 10 s consists in a much better defined cyclic voltammogram having both peak currents increased and peak potentials anticipated in comparison with the response recorded for an inactivated GCE. It can be noticed that simultaneously the hysteresis of the cyclic voltammogram at GCE modified by anodic activation increases as it is usually expected for chemically modified electrodes, but more for the anodic region. The activation of GCE for 60 s and for 120 s are, more or less, comparable in efficiency, both of them seems to lead to a better electrochemical response (as regarding definition of the peak, as regarding the peak potential position, as regarding the peak current height) in comparison to the response at the inactivated GCE. If we consider again the anodic peak separation introduced above, then the ΔE_{pa} = -21 mV for 60 s activation time and, respectively, ΔE_{pa} = -26 mV for 120 s activation time show, both of them, a very weak activation for the electrode reaction

Also the anodic peak ratio, defined above gives a small catalytic effect for 60 s activation time, r_{pa} =1.42 (25 mV/s) and 1.67 mV (250 mV/s) and almost the same catalytic effect for the activation time of 120 s, where r_{pa} =1.45 (25 mV/s) and 1.70 (250 mV/s).

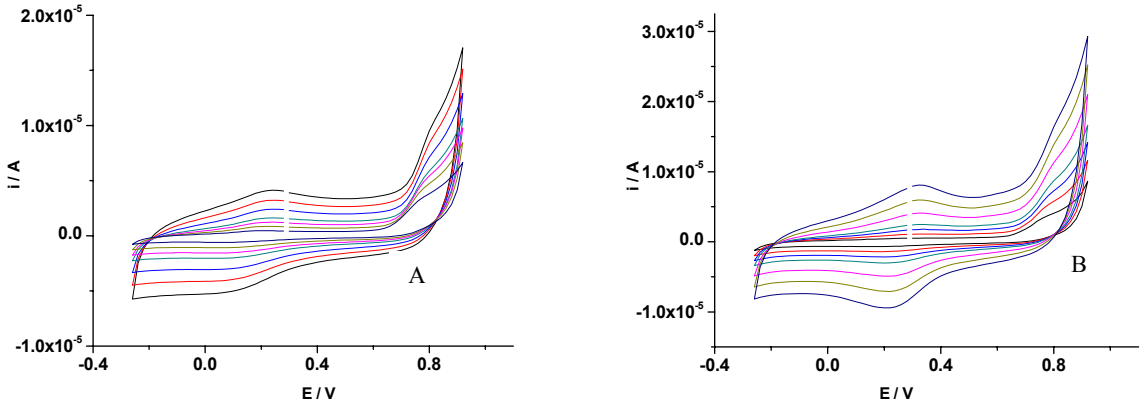

Fig. 6 – The CV (at different sweep rates: 25, 50, 75, 100, 150, 200, 250 mV/s) behaviour of 10^{-4} M curcumin IV in DMSO containing 0.1 M $TBABF_4$ in the range from -0.25 V to 0.90 V at inactivated GCE (A) and activated GCE bare electrode at 1.8 V for 60 s (B and at accumulation electrode potential (at -0.5 V for 30 s).

An accumulation electrode potential of -0.5 V was imposed to the anodically activated GCE for different preconcentration time which has been changed in the range 10-60 s, with a step of 10 s. Irrespective of the accumulation time used for an anodic activation potential of 1.8 V, both for an activation time of 60 s or for an activation time of 120 s, the peak current does not increase with the increase of the accumulation time but, on the contrary, it decreases slowly and the peak potential shifts toward anodic direction. The different behaviours of the two Curcumin-like compounds at an anodically activated GCE could be assigned to the different electronic effects exerted by nitro groups (negative inductive effect, -I, and negative mesomeric effect, -M) and dimethylamino groups (negative inductive effect, –I, and positive mesomeric effect, +M) from the 4- and 4'-positions of the two aromatic rings.

CONCLUSIONS

Two compounds (1,7-bis[4-nitro]-1,6-heptadiene-3,5-dione), and (1,7-bis[4-N,N dimethylamino]-1,6-heptadiene-3,5-dione) were studied in DMSO with 0.1 M $TBABF_4$ at anodically activated GCE. The GCE, modified by anodic activation, allows a better definition of the peaks in comparison with the bare GCE. In addition, the peak currents are increased and the peak potentials are anticipated in respect with the inactivated GCE behaviour, especially for Curcumin III. For Curcumin IV the effect of the anodic activation of the GCE has no efficiency, as well as the application of an accumulation potential for different accumulation time. The two Curcumin-like compounds seem to participate at the electron transfer only like an adsorbed species. They exhibit different redox behaviour in comparison with curcumin and *bis*demethoxycurcumin due to the absence of the hydroxyl groups in position 4 and 4' and of the methoxy groups in position 3 and 3'

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