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***In memoriam prof. dr. Ioan A. Silberg***

# ELECTRONIC PROPERTIES OF CHALCONES CONTAINING PHENOTHIAZINE UNITS

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**ABSTRACT.** Phenothiazinyl substituted enones were synthesized by the condensation of N-methyl-3-oxo-phenothiazine derivatives with several acetyl-ferrocene and benzaldehyde derivatives respectively, in alkaline conditions. The structures of new chalcones and *bis*chalcones thus obtained were assigned by high resolution NMR. Comparative electrochemical behaviour and UV-Vis spectra of chalcones containing phenothiazine and ferrocene or phenyl units are described.

## INTRODUCTION

This paper is a continuation of previous contributions showing a constant interest on the synthesis and structural investigation of phenothiazine derivatives containing conjugated unsaturated chains, in our research group [1-4]. Due to the low oxidation potential and the pronounced propensity to form stable radical cations, properly substituted phenothiazine derivatives may find applications in material science investigations and sensors studies. The target of this work was to synthesize some chalcones with cross conjugated structure, containing phenothiazine and ferrocene or other aromatic units as well as to characterize their electronic properties by UV-Vis spectroscopy and cyclic voltammetry. These structures might develop interesting unconventional physical properties due to the combination of the electron donor effects of phenothiazine [5], ferrocene or phenyl units, with those of an extended $\pi$ conjugated system.

The UV-Vis spectra of phenothiazine derivatives were recorded long time ago for analytical purposes (characterization, identification and dosage) due to the large extent of derivatives with practical applications (drugs, dyes, antioxidants). The correlation between UV spectra and the structure of phenothiazine derivatives was thoroughly investigated and important

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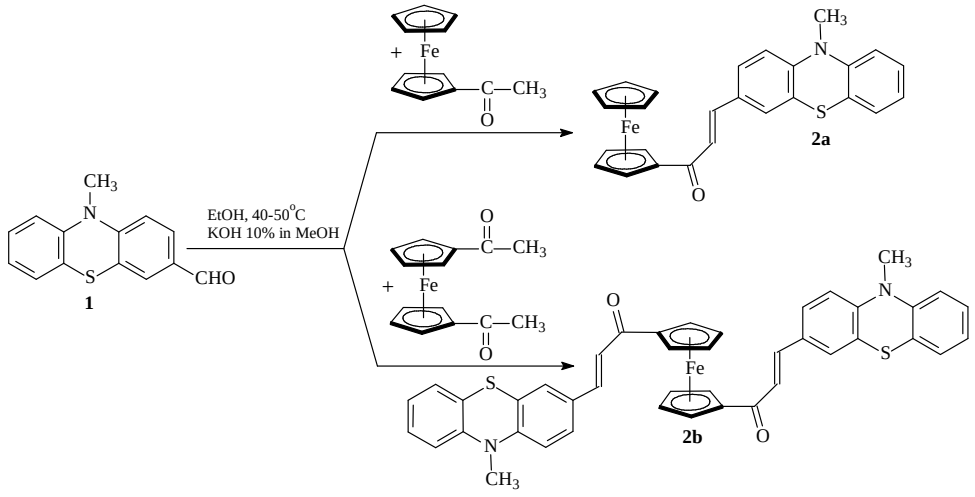
differences between 2- and 3-substituted derivatives were noticed, while the presence of a alkyl substituent in position 10 affects very little the spectrum. Greater influence was observed to be exerted by electron withdrawing groups such as $–NO_2$, $-SO_2$, -S-CO-R [6-8].

The electron donor properties of the phenothiazine nucleus were also clearly demonstrated by different methods including chemical [9] and electrochemical generation of the oxidized forms. The first systematic investigation of the anodic oxidation of phenothiazine at a platinum electrode [10] indicated a first step at + 270 mV *vs* $Ag/Ag^+$ $10^{-2}$M electrode and a second step situated at about +750 mV. Further, different electrochemical methods were also employed: polarography [11-13], cyclic voltammetry [14-19], chronoamperometry [8,20], especially in the range of positive potentials. However, much remains to be done in order to establish the influence exerted by functional groups on the redox behaviour of phenothiazine nucleus. We decided to use the cyclic voltammetric measurements for the investigation of the redox processes implied by the presence of different redox active groups and their reciprocal influences in the structure of phenothiazine containing chalcones.

## RESULTS AND DISCUSSIONS

### Synthesis

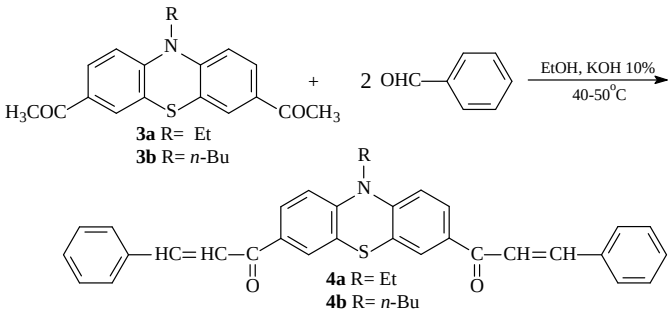
Chalcones containing phenothiazine and ferrocene units, **2a** and **2b** were previously synthesized by the condensation of N-methyl-formyl-phenothiazine with acetylferrocene and 1,1'-diacetylferrocene respectively (Scheme1). The reactions were performed in the presence of catalytic amounts of KOH, and afforded high yields of chalcones (>70%).




**Scheme 1**

An explanation of structure-reactivity relationship related to the nucleophilicity of the enolate anion generated by the acetylferrocene in the aldol condensation reaction was formulated based on density functional (DFT) calculations [21].

*Bis*-chalcones containing a 3,7-disubstituted phenothiazine unit were obtained in high yields by the condensation of 3,7-diacetyl-10-alkylphenothiazines with benzaldehyde in alkaline media (compounds **4a** and **4b** in Scheme 2).




**Scheme 2**

High resolution NMR (500 MHz $^{1}$H-NMR) and FT-IR spectra were used in order to completely assign the structures of the synthesized compounds **4a,b**. FT-IR spectroscopy indicates the stretching vibration of the carbonyl bond by the absorption band situated at 1654 cm$^{-1}$ for **4a** and 1659 cm$^{-1}$ for **4b** respectively; these low values are consistent with the vibration of an α,β unsaturated ketone and are accompanied by the absorption band situated at 1594 cm$^{-1}$ due to the vibration of the C=C bond. The formation of *E* diastereoisomers of **4a** and **4b** can be clearly identified by $^{1}$H-NMR spectra: two *doublet* signals situated at 7.4 and 7.8 ppm in the spectrum of **4a** were assigned to the vinyl protons and the coupling constant of 15.5 Hz is consistent with a *trans* geometry around the double bond. Similar chemical shifts and coupling pattern were observed in the spectrum of **4b.**

## UV-Vis spectra

For the unsubstituted phenothiazine, literature indicates two characteristic UV absorption maxima situated at 253 and 320 nm. Shifts and intensity variations of these maxima were observed and are due to substitution pattern of phenothiazine derivatives [5]. The UV spectrum for ferrocene shows maxima situated at 330 nm and 440 nm [22].

The UV-Vis spectra of compounds **2a, 2b** and **4a,** were recorded in DMF solution and are presented in figure 1. Compounds **2a** and **2b** contain the same chromophor unit: 1-ferrocenyl-3-phenothiazinyl-propenone; a very small bathocromic shift can be observed in the position of the absorption maxima of **2b** accompanied by an important increase in absorbance value due to additive effect of the identical two chromophor units in the molecular structure.

Compounds **4a** and **4b** contain as a chromophor the 3-phenyl-1-phenothiazinyl-propenone unit which produces in the UV-Vis spectrum an absorption band showing an important bathochromic shift as compared to compounds **2** (Figure 1)**,** a fact that suggests a longer π conjugated system which implies smaller energy amounts required for the n→ $\pi^*$ transition between the molecular orbitals.

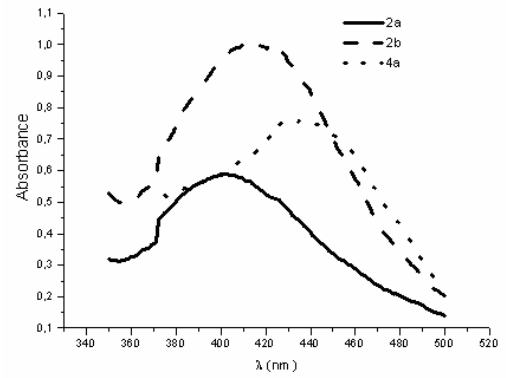
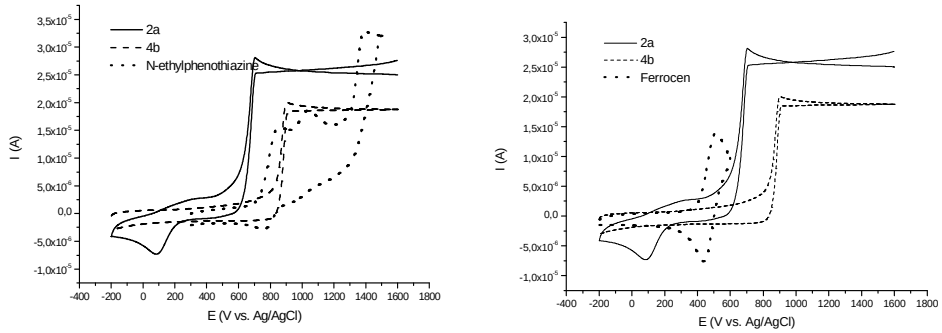



**Figure 1.** UV-Vis spectra of chalcones **2a, 2b** and **4a** solution $10^{-5}$ M in DMF.

## Electrochemical measurements

Cyclic voltammetric (CV) measurements were carried out in order to compare the electrochemical behaviours of chalcone derivatives **2, 4** with those of parent aromatic units: N-alkyl-phenothiazine and ferrocene respectively**.** The oxidation potentials determined by the presence of different redox active groups and their reciprocal influences can be observed in Figure 2.




A B

**Figure 2**. Cyclic Voltammograms of: A) **2a, 4b**, N-ethylphenothiazine; B) **2a, 4b**, ferrocen. Experimental conditions: solvent DMF, supporting electrolyte 0.1M $LiClO_4$, GC electrode, scan rate v=100 $mVsec^{-1}$

A shape of strong oxidation can be observed for **2a** and **4b** adsorbed on GC electrode; this process is continuing slowly, along a large potential range (800-1600 mV). This oxidation peak appears shifted towards lower positive values for **2a** as compared to **4b** ($\Delta E_{4b-2a}$= 200 mv).

The presence of extended π conjugated system in chalcones **2, 4** strongly affects the redox behaviour of phenothiazine nucleus as it can be observed in Figure 2A where CVs of N-ethylphenothiazine, **2a** and **4b** are ploted together. The characteristic redox behaviour of the phenothiazine unit (which can be clearly seen in the CV pattern of N-ethyl-phenothiazine), is suppressed in the CVs of chalcone derivatives **2a, 4b**.

Figure 2B shows the CVs of ferrocene, **2a** and **4b** ploted together. In the CV of chalcone **2a,** the intense oxidation peak is accompanied by the answer of ferrocene/ferrocynium system which appears strongly affected. This peak couple became almost irreversible and shifted towards lower positive potential values, as compared to that of the normal reversible answer of ferrocene/ferrocynium redox couple.

## EXPERIMENTAL PART

Melting points (uncorrected) were obtained with an Electrothermal IA 9200 digital melting point apparatus. IR spectra were recorded in KBr pellets with a BRUKER IFS 55FT-pectrometer. $^{1}$H- and $^{13}$C-NMR were recorded in $CDCl_3$ solution in 5mm tubes at RT, on a Bruker DRX 500 at 500MHz, using TMS as internal reference with deuterium signal of the solvent as the lock. UV-VIS spectra were recorded on a Spectrometer UV-VIS UNICAM Helios β in DMF solution $10^{-5}$ M.

The electrochemical measurements were performed using a potentiostatic set-up in a classical cell having three electrodes. All the samples were deaerated 20-30 minutes before each test. Because of low solubility of the complex in the protic medium, the non aqueous medium of DMF was chosen.

Cyclic voltammograms were recorded in a cell purged with argon. DMF used as solvent was purified according to standard procedures [9]. $LiClO_4$ dried in an oil pump vacuum at 100$^{o}$C was added as supporting electrolyte at a concentration of 0.1 M. Compounds under investigation were added at 10 mM concentration. The working electrode (GC) and platinum wire counter-electrode were used. An Ag/AgCl electrode, in a separate compartment served as reference electrode. CVs were recorded in positive-going direction at the starting potentials, at different scan rate using a BAS potentiostat equipped with BAS100W soft. All experiments were run at room temperature (22$^{o}$C).

Phenothiazine oxo-derivatives, 1,1'-diacetyl-ferrocen and ferrocenyl-enones **2a** and **2b** were prepared according to described procedures [23,24,7]. Spectral data and melting points of compounds **2a** and **2b** are according to the literature [21].

**General procedure for the preparation of phenothiazinyl chalcones 4a,b**

To a stirred solution of the appropriate 3,7-diacetyl-10-alkyl-phenothiazine (0.01 mol) and benzaldehyde (2.12g, 0.02 mol) in ethanol (20 $cm^3$), 10% methanol solution of KOH (1 $cm^3$) was added drop wise over 3 min at 25℃. The mixture was stirred for 8h at 50℃. The product precipitated on cooling was filtered and washed with cold ethanol (5 $cm^3$) then purified by column chromatography on silica using dichloromethane as eluent.

**3,7-*bis*[(E)-3-phenylprop-2-en-1-on]-10-ethyl-10*H*-phenothiazine (4a)**

Orange-red powder; yield 4.29g (88%); m.p. 153-154°C

IR (KBr) ν [$cm^{-1}$]: 1654, 1596, 1574, 1474, 1367, 1331, 1284, 1244, 1208, 763

500MHz, $^1$H-NMR ($CHCl_3$-$d_1$): $\delta_H$: 1.49ppm (t, 3H, $^3$J= 7Hz, $H_b$), 4.02ppm (q, 2H, $^3$J= 7Hz, $H_a$), 6.94ppm (d, 2H, $^3$J= 8.5Hz, $H_{1,9}$), 7.86ppm (dd, 2H, $^4$J= 2Hz, $^3$J= 8.5Hz $H_{2,8}$), 7.78ppm (d, 2H, $^4$J=2Hz, $H_{4,6}$), 7.65ppm (m, 4H, $H_{2',6'}$), 7.42ppm (m, 4H, $H_{3',5'}$), 7.42ppm (m, 2H, $H_{4'}$), 7.49ppm (d, 2H, $^3J_{trans}$= 15.5Hz, $H_\alpha$), 7.80ppm (d, 2H, $^3J_{trans}$= 15.5Hz, $H_\beta$). 100MHz $^{13}$C-NMR ($CHCl_3$-$d_1$): $\delta_c$: 13.1ppm ($CH_3$, $C_b$), 43.2ppm ($CH_2$, $C_a$); 115.0ppm (CH, $C_{1,9}$), 121.8ppm (CH, $C_\alpha$), 123.6ppm (Cq, $C_{4a,5a}$), 128.1ppm (CH, $C_{4,6}$), 128.9ppm (CH, $C_{2',6'}$), 129.2ppm (CH, $C_{2,8}$), 129.4ppm (CH, $C_{4'}$), 130.9ppm (CH, $C_{3',5'}$), 133.5 (Cq, $C_3$), 135.4 (Cq, $C_{1'}$), 144.8ppm (CH, $C_\beta$), 147.7ppm (Cq, $C_{9a,10a}$), 188.1ppm (CO)

**3,7-*bis*[(E)-3-phenylprop-2-en-1-on]-10-butyl-10*H*-phenothiazine (4b)**

Red powder; yield 3.66g (71%); m.p. 166℃

IR (KBr) ν [$cm^{-1}$]: 1657, 1595, 1575, 1476, 1367, 1328, 1281, 1252, 1204, 760

500MHz, $^1$H-NMR ($CHCl_3$-$d_1$): $\delta_H$: 0.95ppm (t, 3H, $^3$J= 7.5Hz, $H_d$), 1.50ppm (m, 2H, $H_c$), 1.83ppm (m, 2H, $H_b$), 3.95ppm (t, 2H, $^3$J= 7.5Hz, $H_a$), 6.92ppm (d, 2H, $^3$J= 8.5Hz, $H_{1,9}$), 7.87ppm (dd, 2H, $^4$J= 2Hz, $^3$J= 8.5Hz $H_{2,8}$), 7.79ppm (s, 2H, $H_{4,6}$), 7.65ppm (m, 4H, $H_{2',6'}$), 7.43ppm (m, 4H, $H_{3',5'}$), 7.41ppm (m, 2H, $H_{4'}$), 7.49ppm (d, 2H, $^3J_{trans}$= 20Hz, $H_\alpha$), 7.80ppm (d, 2H, $^3J_{trans}$= 20Hz, $H_\beta$). 100MHz $^{13}$C-NMR ($CHCl_3$-$d_1$) $\delta_c$: 14.1ppm ($CH_3$, $C_d$), 20.4ppm ($CH_2$, $C_c$), 29.1ppm ($CH_2$, $C_b$), 48.3ppm ($CH_2$, $C_a$), 115.5ppm (CH, $C_{1,9}$), 121.9ppm (CH, $C_\alpha$), 124.3ppm (Cq, $C_{4a,5a}$), 128.2ppm (CH, $C_{4,6}$), 128.9ppm (CH, $C_{2',6'}$), 129.2ppm (CH, $C_{2,8}$), 129.4ppm (CH, $C_{4'}$), 130.9ppm (CH, $C_{3',5'}$), 133.6 (Cq, $C_3$), 135.4 (Cq, $C_{1'}$), 144.8ppm (CH, $C_\beta$), 148.2ppm (Cq, $C_{9a}$), 188.2ppm (CO)

## CONCLUSIONS

Chalcones containing phenothiazine and ferrocen units were synthesized and their electronic properties were analyzed by UV-Vis spectroscopy and cyclic voltammetry. Their conjugated structure determined a bathocromic shift of the UV absorption maxima when compared to parent aromatic units. The electrochemical measurements of chalcones adsorbed on GC electrode show strong irreversible oxidation processes. It will be of interest to study their electrosorption process depending on the electrode nature.

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