



## Substituent effects of 1,2-dithiole groups on the electrochemical oxidation of some ferrocenyl-1,2-dithiole compounds

Marie-Laurence Abasq<sup>a,\*</sup>, Mokhtar Saidi<sup>b</sup>, Jean-Louis Burgot<sup>a</sup>, André Darchen<sup>c</sup>

<sup>a</sup> Laboratoire de Chimie Analytique, URU 337, U.F.R. des Sciences Pharmaceutiques et Biologiques, Université de Rennes-1, Avenue du Professeur Léon Bernard, 35043 Rennes cedex, France

<sup>b</sup> LVPRS, Université de Ouargla, 30000 Ouargla, Algeria

<sup>c</sup> UMR CNRS 6226 Sciences Chimiques de Rennes, ENSCR, Avenue du Général Leclerc, 35700 Rennes, France

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### ABSTRACT

New ferrocenyl compounds substituted by sulfur containing groups were synthesized leading to ferrocenyl-3H-1,2-dithiole-3-thiones and related compounds. The substituent of the ferrocene was a [3-thioxo-3H-1,2-dithiol]-4 or 5-yl, a [3-oxo-3H-1,2-dithiol]-4 or 5-yl or a [3-methylsulfanyl-3H-1,2-dithiolium]-4 or 5-yl cation group. Their anodic behavior was studied by cyclic voltammetry at a Pt electrode in aprotic solvent. All synthesized ferrocenes exhibited a one-electron reversible oxidation leading to the corresponding ferricenium cation. At low potential scan, the irreversible oxidation of 5-ferrocenyl-3H-1,2-dithiole-3-thione was observed and attributed to a dimerization involving the dithiolethione group. Redox potential of the reversible oxidation allowed the determination of the electronic effect of the 1,2-dithiole groups. The Hammett  $\sigma_p$  constants of the dithiole substituents were obtained from linear correlation between oxidation potentials and electronic effects. The results showed that the [3-thioxo-3H-1,2-dithiol]-5-yl and the [3-methylsulfanyl-3H-1,2-dithiolium]-5-yl cation groups were strong inductive electron withdrawing substituents characterized by  $\sigma_p$  values of 0.55 and 0.97, respectively.

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### 1. Introduction

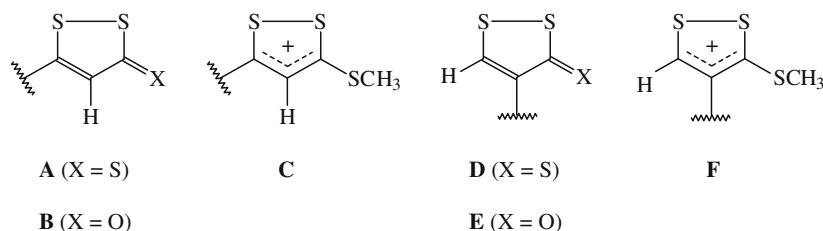
Physicochemical properties may exert an impact on the biological activity of a molecule. Quantitative structure–activity relationships (QSAR) studies attempt to correlate one or two parameters of a molecule to a pharmacological or biological activity including physicochemical properties and structural features of the molecule [1,2]. For example, the use of Hammett electronic parameters  $\sigma$  in the QSAR equations shows that electronic effect of the substituent may play an important role in DNA-binding of ligands [3].

A large number of drugs and biological relevant molecules contain heterocyclic system. Amongst the heterocyclic derivatives, 1,2-dithiole-3-thiones (DTT), a well-known activator series of the Nrf2-ARE pathway, are extensively studied concerning their chemopreventive properties [4–11]. For example, a phase IIb trial was performed on anethole dithiolethione (or 5-(4-methoxyphenyl)-3H-1,2-dithiole-3-thione) to determine the effect of this molecule in smokers with bronchial dysplasia [10,11]. Concerning the 1,2-dithiole series, some physicochemical data are known like lipophilicity [12], redox properties [13–21] and electronic param-

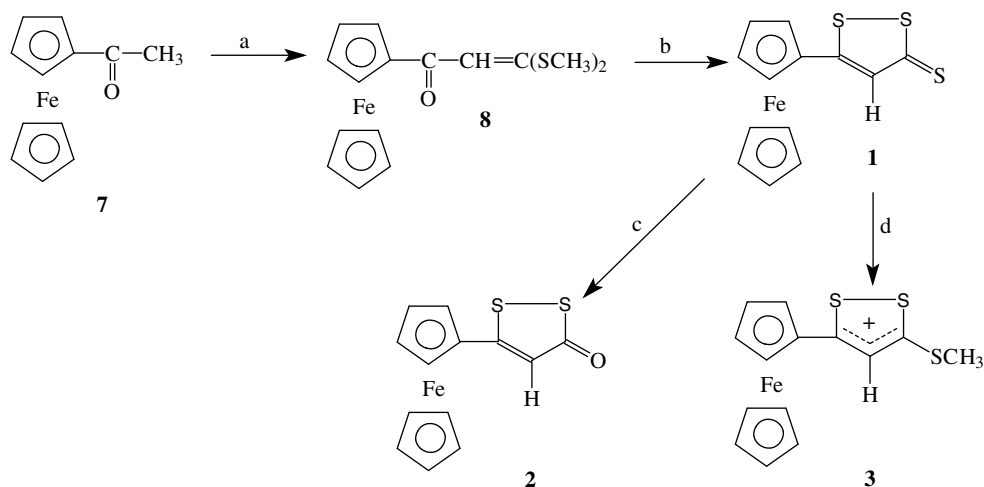
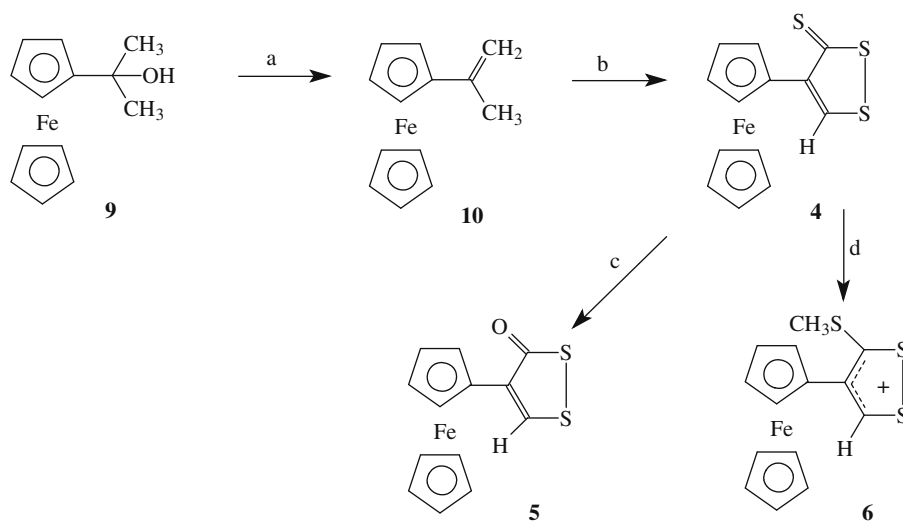
eters [22,23]. Substituent electronic effects are generally expressed by various kinds of  $\sigma$  parameter values, which are statistical data arising from several measurements and Hammett or Hammett-like correlations [24–26]. These electronic parameters are depending upon the structure and nature of equilibrium or reaction mechanism involved. Indeed we obtained  $\sigma_p^-$  parameters from the  $pK_a$  values of 1,2-dithiole compounds where the dithiole substituent exhibited resonance effect in phenol and anilinium derivatives and from the reduction potential values of nitrophenyl derivatives [22,23]. In order to get a full characterization of electronic effect of these 1,2-dithiole substituents, it is necessary to use new correlations involving another reactive group. To our knowledge, scarce investigations on QSAR have been carried out on analogous 1,2-dithiole compounds [12,27–30].

In this work, we focus on the determination of  $\sigma_p$  values of the following 1,2-dithiole substituent groups: [3-thioxo-3H-1,2-dithiol]-5-yl **A** or [3-thioxo-3H-1,2-dithiol]-4-yl **D**, [3-oxo-3H-1,2-dithiol]-5-yl **B** or [3-oxo-3H-1,2-dithiol]-4-yl **E**, [3-methylsulfanyl-1,2-dithiolium]-5-yl cation **C** or [3-methylsulfanyl-1,2-dithiolium]-4-yl cation **F** (Scheme 1). No data were available so far about the electronic effect of substituent **C** or **F**. This aim in view, ferrocenyl compounds **1–6** with 1,2-dithiole ring in their structure were synthesized in order to measure their oxidation potentials

\* Corresponding author. Tel.: +33 223 234 895; fax: +33 223 234 912.  
E-mail address: [marie-laurence.abasq@univ-rennes1.fr](mailto:marie-laurence.abasq@univ-rennes1.fr) (M.-L. Abasq).



Scheme 1. The 1,2-dithiole substituents.

Scheme 2. Reagents and conditions: (a) 2 equiv. sodium 2-methyl-2-butanoxide, 1 equiv. CS<sub>2</sub>, 2 equiv. CH<sub>3</sub>I, toluene, 20 °C; (b) P<sub>4</sub>S<sub>10</sub>, refluxing xylene; (c) C<sub>6</sub>H<sub>5</sub>C(Cl)NOH, N(Et)<sub>3</sub>, diethyl ether, 20 °C and (d) 3 equiv. (CH<sub>3</sub>)<sub>2</sub>SO<sub>4</sub> or 10 equiv. CH<sub>3</sub>I, refluxing acetone.Scheme 3. Reagents and conditions: (a) refluxing xylene; (b) 6 equiv. S<sub>8</sub>, refluxing xylene; (c) C<sub>6</sub>H<sub>5</sub>C(Cl)NOH, N(Et)<sub>3</sub>, diethyl ether, 20 °C and (d) 10 equiv. CH<sub>3</sub>I, refluxing acetone.

(Schemes 2 and 3). Indeed, oxidation potential values of ferrocenyl derivatives are often used as a probe in the study of the electronic properties of substituent [31]. Many correlations of the ferrocene/ferricenium redox potential with Hammett  $\sigma_m$  or  $\sigma_p$  parameters have already been described in the literature [32–36], despite the absence of substitution position in mono-substituted ferrocenyl compounds. Substituted ferrocenyl compounds with heterocyclic groups have been already used in the determination of electronic effect [37,38].

## 2. Experimental

### 2.1. General methods

All reagents and solvents were commercially available. Ferrocene and all substituted ferrocenyl compounds used in the linear correlation measurements were purchased from Strem Chemicals or Aldrich and used as received. Analyses were performed with the following instruments: IR spectra with a Perkin-Elmer FTIR

16PC, mass spectrometry with a Varian MAT 311 or a Finigan Mat-Incos 500 spectrometer,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra with a Bruker AM360 or a Varian EN360 spectrometer. Shifts are given relative to TMS as internal reference. Chemical analyses were performed by the Centre de Microanalyses du CNRS (Vernaison, France).

### 2.2. 5-Ferrocenyl-3H-1,2-dithiole-3-thione **1**

This compound has been already described by Curphey [39–41]. We followed another literature procedure [42] starting from acetylferrocene **7** by condensation of carbon disulfide in the presence of sodium 2-methyl-2-butanoxide (Scheme 2). After methylation with iodomethane (yield = 90%)  $\alpha$ -[bis-methylsulfanyl]methylene] propenone **8** was isolated and then reacted with  $\text{P}_4\text{S}_{10}$  in refluxing xylene for 30 min to give compound **1** after chromatographic separation on a silica column. Yield 40%. Red crystals, m.p. 162 °C (ethanol).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 4.23 (s, 5H,  $\text{C}_5\text{H}_5$ ); 4.61 (t, 1.8 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 4.72 (t, 1.8 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 7.20 (s, 1H, C(4)–H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 68.84 (CH,  $\text{C}_5\text{H}_4$ ); 71.28 (CH,  $\text{C}_5\text{H}_5$ ); 72.37 (CH,  $\text{C}_5\text{H}_4$ ); 74.93 (C,  $\text{C}_5\text{H}_4$ ); 113.60 (CH, C(4)); 176.90 (C(5)), 213.81 (C(3)).

### 2.3. 5-Ferrocenyl-3H-1,2-dithiole-3-one **2**

This compound was obtained by action of benzonitrile oxide prepared *in situ* from  $\alpha$ -chlorobenzaldehyde oxime [43] on corresponding dithiolethione **1** Yield: 70%. Red crystals, m.p. 126 °C (petroleum ether). Anal. Calc. for  $\text{C}_{13}\text{H}_{10}\text{OS}_2\text{Fe}$ : C, 51.65; H 3.31; Fe, 18.54. Found: C, 51.75; H, 3.35; Fe, 18.56%. EI-MS  $m/z$ : 301.9535 (Calc. for  $\text{C}_{13}\text{H}_{10}\text{OS}_2^{56}\text{Fe}$ : 301.9522).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 4.20 (s, 5H,  $\text{C}_5\text{H}_5$ ); 4.52 (s, 2H,  $\text{C}_5\text{H}_4$ ); 4.69 (s, 2H,  $\text{C}_5\text{H}_4$ ); 6.57 (s, 1H, C(4)–H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 68.04 (CH,  $\text{C}_5\text{H}_4$ ); 70.97 (CH,  $\text{C}_5\text{H}_5$ ); 71.49 (CH,  $\text{C}_5\text{H}_4$ ); 76.11 (C,  $\text{C}_5\text{H}_4$ ); 114.76 (CH, C(4)); 172.70 (C(5)), 194.04 (C(3)). IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 1662 (C=O).

### 2.4. 5-Ferrocenyl-3-methylsulfanyl-1,2-dithiolium cation **3** methylsulfate or iodide

This compound was prepared from 5-ferrocenyl-3H-1,2-dithiole-3-thione **1** by action of dimethyl sulfate (3 equiv.) or  $\text{CH}_3\text{I}$  (10 equiv.) in refluxing acetone within 24 h. Yield: 72%. Dark crystals. ESI-MS,  $[\text{M}]^+$  ion,  $m/z$ : 332.9524 (Calc. for  $\text{C}_{14}\text{H}_{13}\text{S}_3^{56}\text{Fe}$ : 332.9529).  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ ,  $\delta$  ppm): 2.78 (s, 3H,  $\text{SCH}_3$ ); 4.20 (s, 5H,  $\text{C}_5\text{H}_5$ ); 4.99 (s, 2H,  $\text{C}_5\text{H}_4$ ); 5.01 (s, 2H,  $\text{C}_5\text{H}_4$ ); 7.73 (s, 1H, C(4)–H),  $^{13}\text{C}$  NMR ( $\text{D}_2\text{O}$ ,  $\delta$  ppm): 18.53 ( $\text{SCH}_3$ ), 70.89 (CH,  $\text{C}_5\text{H}_4$ ); 72.83 (CH,  $\text{C}_5\text{H}_5$ ); 73.35 (C,  $\text{C}_5\text{H}_4$ ); 76.88 (CH,  $\text{C}_5\text{H}_4$ ); 127.67 (CH, C(4)); 188.19 (C(5)), 189.96 (C(3)).

### 2.5. 4-Ferrocenyl-3H-1,2-dithiole-3-thione **4**

Starting 2-ferrocenylpropan-2-ol **9** was synthesized by the reaction of ferrocene with acetone in the presence of concentrated sulfuric acid [44]. 2-ferrocenylpropene **10** was obtained by dehydration of **9** in refluxing xylene within 2 hours (yield = 70%). 4-ferrocenyl-3H-1,2-dithiole-3-thione **4** was then prepared by reaction of olefin **9** with an excess of sulfur (6 equiv.) in refluxing xylene during 20 h. Yield: 3% after chromatographic separation on a silica column. Brown crystals, m.p. 107 °C (petroleum ether). Anal. Calc. for  $\text{C}_{13}\text{H}_{10}\text{S}_3\text{Fe}$ : C, 49.05; H 3.14; Fe, 17.61; S, 30.18. Found: C, 49.05; H, 2.96; Fe, 17.53; S, 30.15%. EI-MS  $m/z$ : 317.9283 (Calc. for  $\text{C}_{13}\text{H}_{10}\text{S}_3^{56}\text{Fe}$ : 317.9294).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 4.17 (s, 5H,  $\text{C}_5\text{H}_5$ ); 4.34 (t, 1.8 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 4.94 (t, 1.8 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 8.39 (s, 1H, C(5)–H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm):

67.93 (CH,  $\text{C}_5\text{H}_4$ ); 69.04 (CH,  $\text{C}_5\text{H}_4$ ); 69.75 (CH,  $\text{C}_5\text{H}_5$ ); 78.79 (C,  $\text{C}_5\text{H}_4$ ); 146.80 (C(4)); 151.38 (CH,C(5)), 212.61 (C(3)).

### 2.6. 4-Ferrocenyl-3H-1,2-dithiole-3-one **5**

This compound was synthesized by action of benzonitrile oxide prepared *in situ* from  $\alpha$ -chlorobenzaldehyde oxime [43] on corresponding dithiolethione **4**. Yield: 55%. Orange crystals, m.p. 129 °C (petroleum ether). Anal. Calc. for  $\text{C}_{13}\text{H}_{10}\text{OS}_2\text{Fe}$ : C, 51.65; H 3.31; Fe, 18.54. Found: C, 51.40; H, 3.35; Fe, 18.39%. EI-MS  $m/z$ : 301.9535 (Calc. for  $\text{C}_{13}\text{H}_{10}\text{OS}_2^{56}\text{Fe}$ : 301.9522).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 4.12 (s, 5H,  $\text{C}_5\text{H}_5$ ); 4.32 (t, 1.9 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 4.74 (t, 1.9 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 8.10 (s, 1H, C(5)–H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 61.71 (CH,  $\text{C}_5\text{H}_4$ ); 69.11 (CH,  $\text{C}_5\text{H}_4$ ); 69.64 (CH,  $\text{C}_5\text{H}_5$ ); 78.79 (C,  $\text{C}_5\text{H}_4$ ); 132.48 (C(4)); 144.08 (CH,C(5)), 192.39 (C(3)). IR (KBr,  $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 1632 (C=O).

### 2.7. 4-Ferrocenyl-3-methylsulfanyl-1,2-dithiolium cation **6** iodide

This compound was prepared from corresponding dithiolethione **4** by action of iodomethane (3 equiv.) in refluxing acetone within 24 h. Yield: 76%. Claret crystals, m.p. 178 °C. ESI-MS,  $[\text{M}]^+$  ion,  $m/z$ : 332.9533 (Calc. for  $\text{C}_{14}\text{H}_{13}\text{S}_3^{56}\text{Fe}$ : 332.9529).  $^1\text{H}$  NMR ( $\text{D}_2\text{O}$ ,  $\delta$  ppm): 2.98 (s, 3H,  $\text{SCH}_3$ ); 4.27 (s, 5H,  $\text{C}_5\text{H}_5$ ); 4.47 (t, 1.8 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 4.71 (t, 1.8 Hz, 2H,  $\text{C}_5\text{H}_4$ ); 7.26 (s, 1H, C(5)–H),  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ,  $\delta$  ppm): 67.93 (CH,  $\text{C}_5\text{H}_4$ ); 69.04 (CH,  $\text{C}_5\text{H}_4$ ); 70.27 (CH,  $\text{C}_5\text{H}_5$ ); 78.79 (C,  $\text{C}_5\text{H}_4$ ); 146.80 (C(4)); 151.38 (CH,C(5)), 212.61 (C(3)).

### 2.8. Electroanalytical procedures

Cyclic voltammetric measurements were performed using a potentiostat/galvanostat PGSTAT 100 (Autolab instrument, Eco Chemie B.V., Utrecht, Netherlands). A three-electrode cell was used. The working electrode was a 1 mm diameter platinum disk. The reference electrode was a saturated calomel electrode (SCE). The counter electrode was a carbon graphite rod. All electroanalytical studies were carried out, under a nitrogen atmosphere, in acetonitrile or *N,N*-dimethylformamide (DMF) solutions containing 0.1 M  $\text{Bu}_4\text{NBF}_4$ .

### 2.9. Linear correlations

The linear correlations between oxidation potentials of a series of substituted ferrocenyl compounds ( $\text{C}_5\text{H}_4\text{R})\text{Fe}(\text{C}_5\text{H}_4\text{R}')$  and substituent electronic effect were established from home made measurements in acetonitrile solutions. The Hammett constants  $\sigma_m$  and  $\sigma_p$  of R and R' substituents and the oxidation potentials are gathered in Table 1.

## 3. Results and discussion

### 3.1. Synthesis

Ferrocenyl substrates **1–6** were synthesized accordingly to two synthetic approaches (Schemes 2 and 3). Except compound **1** which has already been described in the literature [39], the other ferrocenyl 1,2-dithiole compounds were prepared for the first time. The 5-yl derivatives were prepared starting from acetyl ferrocene **7** using the well-known procedure of Thuillier and Vialle (Scheme 2) [42]. Following this method, 1,2-dithiole-3-thione **1** was obtained from thionation of intermediate  $\alpha$ -[bis-methylsulfanyl]-methylene] propenone **8** which was prepared by reacting carbon disulfide in the presence of sodium 2-methyl-2-butanoxide, followed by methylation. Curphey uses reaction of  $\text{P}_4\text{S}_{10}$  on a ferrocenyl

**Table 1**

Structures and oxidation potentials of ferrocene derivatives (C<sub>5</sub>H<sub>4</sub>R)Fe(C<sub>5</sub>H<sub>4</sub>R') used in the linear correlations.

Substituents R, R'	$E_{1/2}$ (V vs. SCE) <sup>a</sup>	$\sigma_p^b$	$\sigma_m^b$
(CH <sub>3</sub> ) <sub>5</sub> , (CH <sub>3</sub> ) <sub>5</sub> <sup>c</sup>	-0.05	-1.4	-0.60
CH <sub>3</sub> , CH <sub>3</sub>	0.34	-0.28	-0.12
H, H	0.46	0	0
CH <sub>2</sub> =CH, H	0.47	-0.04	0.06
(CH <sub>3</sub> ) <sub>2</sub> NCH <sub>2</sub> , H	0.44	0.01	0
C <sub>6</sub> H <sub>5</sub> CO, H	0.69	0.46	0.36
CO <sub>2</sub> H, H	0.69	0.44	0.35
CO <sub>2</sub> CH <sub>3</sub> , H	0.70	0.44	0.35
CH <sub>3</sub> CO, H	0.67	0.44	0.35
CHO, H	0.73	0.47	0.41
Cl, Cl	0.76	0.48	0.74
CO <sub>2</sub> CH <sub>3</sub> , CO <sub>2</sub> CH <sub>3</sub>	0.89	0.88	0.70
COCH <sub>3</sub> , COCH <sub>3</sub>	0.92	0.94	0.72

<sup>a</sup> Oxidation potentials  $E_{1/2}$  were calculated as 0.5 ( $E_{pa} + E_{pc}$ ) from peak potentials measured at a Pt electrode in acetonitrile solutions containing 0.1 M Bu<sub>4</sub>NBF<sub>4</sub>.

<sup>b</sup> Data taken in Ref. [26].

<sup>c</sup> Decamethylferrocene.

3-oxo-ester in hexamethyldisiloxane solution for the preparation of dithiolethione **1** with a 36% yield [41]. In our hands, the preparation we have followed gave 40% yield.

The procedure to access to 1,2-dithiole-3-thione **4** began with a dehydration step leading to olefin **10** from alcohol ferrocene **9** in refluxing xylene (Scheme 3). Then, olefin **10** led to a low yield of **4** by thionation with S<sub>8</sub>.

The conversion of dithiolethiones **1** and **4** to dithiolones **2** and **5** were realized by action of benzonitrile oxide prepared *in situ* from  $\alpha$ -chlorobenzaldehyde oxime [43]. Dithiolium cations **3** and **6** were obtained from corresponding 1,2-dithiole-3-thiones **1** and **4** by action of either methyl sulfate or iodomethane in excess in toluene at 35 °C within 4 h.

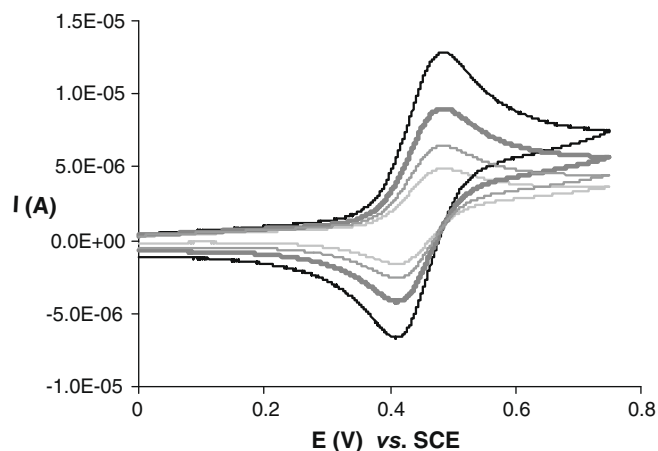
It is well-known that the synthesis ways to dithiolethione compounds are non ambiguous [19,45,46]. The spectroscopic data were in agreement with the expected structure of synthesized ferrocenyl derivatives.

### 3.2. Reversible electrochemical oxidation

The anodic behavior of 1,2-dithiole substituted ferrocenyl compounds **1–6** was examined using cyclic voltammetry at a platinum working electrode in acetonitrile or DMF 0.1 M Bu<sub>4</sub>NBF<sub>4</sub> solution. In acetonitrile solutions, the voltammograms appeared as expected for a reversible oxidation of the ferrocenyl group leading to the corresponding ferricinium cation. The reversible oxidation of **1** needed a fast potential scan rate (5 V s<sup>-1</sup>).

As representative, the cyclic voltammogram (CV) of **2** is shown in Fig. 1. Data in Table 2 show that potentials are in agreement with a reversible one-electron transfer reaction for compounds **2–5**:  $\Delta E_{1/2}$  is nearly constant to 0.07 V, they are little variations of the peak potential with scan rate and the ratio  $i_{pc}/i_{pa}$  is almost unity. The peak currents  $i_{pa}$  varied linearly with square root of scanning rate, indicating a diffusion-controlled process.

Iodide salt of dithiolium **6** was not enough soluble in acetonitrile for electrochemical measurement and the use of DMF as solvent was necessary. For compound **6** in DMF, the ratio  $i_{pc}/i_{pa}$  was significantly lower than one at slow potential scanning rates. This observation revealed instability of the electrogenerated ferricinium in DMF. The ratio  $i_{pc}/i_{pa}$  decreased with scan rate and new voltammetric peaks which appeared in the CV at +0.40 V vs. SCE were attributed to the redox couple Fe<sup>3+</sup>/Fe<sup>2+</sup>. This featured behavior is already described when ferrocene is substituted by an electron-withdrawing substituent which favors the decomposition of the ferricinium cation [47,48].



**Fig. 1.** Cyclic voltammogram of  $2.05 \times 10^{-3}$  M 4-ferrocenyl-3H-1,2-dithiol-3-one **5** in acetonitrile/0.1 M Bu<sub>4</sub>NBF<sub>4</sub> at a platinum electrode at different scan rates (0.05–0.1–0.2–0.5 V s<sup>-1</sup>).

**Table 2**

CV data of  $2.0 \times 10^{-3}$  M ferrocene compounds in 0.1 M Bu<sub>4</sub>NBF<sub>4</sub> acetonitrile. Sweep rate: 0.5 V s<sup>-1</sup>.

Compound	$E_{pa}^a$	$E_{pc}^a$	$\Delta E_p$	$E_{1/2}^a$	$\Delta E_{1/2}^b$
Ferrocene	–	–	–	+0.124	0
1	+0.77	+0.70	0.07	+0.735	+0.611
2	+0.76	+0.69	0.07	+0.725	+0.601
3	+0.95	+0.88	0.07	+0.915	+0.791
4	+0.57	+0.49	0.08	+0.53	+0.406
5	+0.55	+0.48	0.07	+0.515	+0.394
6 <sup>c</sup>	+0.66	+0.59	0.07	+0.625	+0.501

$E_{1/2} = \frac{1}{2}(E_{pa} + E_{pc})$  where  $E_{pa}$  and  $E_{pc}$  are anodic and cathodic peak potentials, respectively. The ( $E_{pa} - E_{pc}$ ) difference varied in the range 70–80 mV.

$\Delta E_{1/2}^b = E_{1/2}^a - 0.124$ .

<sup>a</sup> Potentials in V vs. SCE.

<sup>b</sup> Potentials in V vs. the  $F_c^+/F_c$  couple.

<sup>c</sup> Potentials were measured in DMF vs. the ferricinium/ferrocene couple and then calculated for acetonitrile.

### 3.3. Electrochemical reduction

All ferrocenyl compounds **1–6** exhibited a cathodic behavior relevant to the dithiole ring. This behavior probably followed a mechanism involving an intermediate radical and competitive pathways, as it was already discussed for other 1,2-dithiole-3-thione or 1,2-dithiolium derivatives [20,21]. It is out of the scope of this paper and it will be published elsewhere.

### 3.4. Oxidation of 5-ferrocenyl-3H-1,2-dithiole-3-thione **1**

Ferrocenyl compound **1** exhibited particular oxidation behavior with two irreversible oxidation peaks A1 and A2 as seen in Fig. 2 at 0.02 V s<sup>-1</sup> scanning rate. The chemical reversibility of the oxidation A1 was observed when the scan rate increased. The ratio  $i_{pc1}/i_{pa1}$  reached one at 5 V s<sup>-1</sup>, as seen in Fig. 3. Consequently, the ratio  $i_{pA2}/i_{pA1}$  decreased with the scan rate and peak A2 was not observed at a scan rate of 5 V s<sup>-1</sup> or when the CV was recorded at -24 °C with a scan rate of 0.1 V s<sup>-1</sup>.

All these observations were in agreement with an EC mechanism involving a chemical step C following the electron transfer E. At high scanning rate, compound **1** followed the expected oxidation process of the ferrocenyl group. Only one oxidation peak was seen as a reversible process (Fig. 3.). When the scanning rate decreased the oxidation product of compound **1** was involved in a chemical reaction leading to a new compound which was oxidized

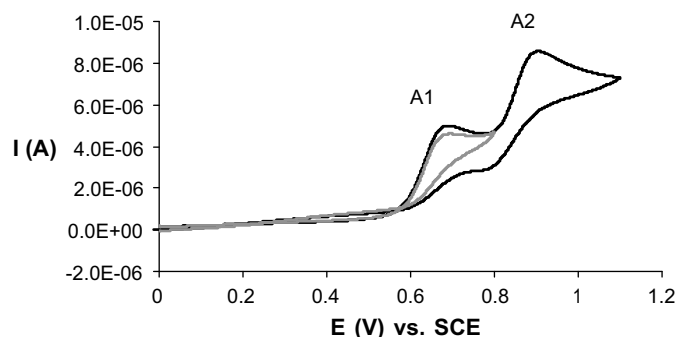


Fig. 2. Cyclic voltammogram of  $2.13 \times 10^{-3}$  M of 5-ferrocenyl-3H-1,2-dithiole-3-thione **1** in acetonitrile/0.1 M  $\text{Bu}_4\text{NBF}_4$  at a platinum electrode at a scan rate of  $0.02 \text{ V s}^{-1}$ .

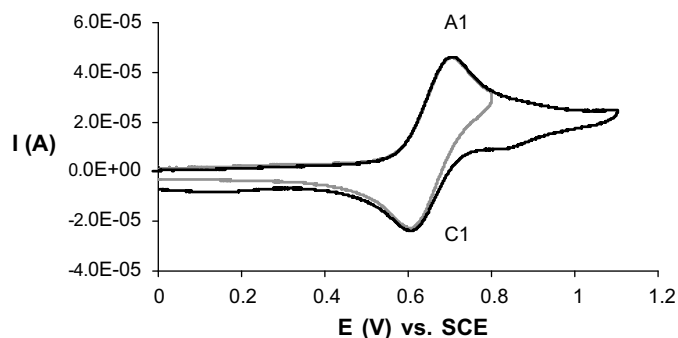


Fig. 3. Cyclic voltammogram of  $2.13 \times 10^{-3}$  M of 5-ferrocenyl-3H-1,2-dithiole-3-thione **1** in acetonitrile/0.1 M  $\text{Bu}_4\text{NBF}_4$  at a platinum electrode a scan rate of  $5 \text{ V s}^{-1}$ .

at higher potentials. The rate of the chemical reaction decreased with the temperature so the CV appeared as a reversible oxidation and the second oxidation peak was not observed.

In order to take into account all the observations we propose the mechanism of Scheme 4. The first step is the oxidation of the ferrocenyl group of **1** leading to the corresponding ferricinium  $1^+$ . An intramolecular electron transfer from ferricinium to the 1,2-dithiole-3-thio group, followed by a dimerization affords the ferrocenyl compound **11** substituted by a dithiolium cation. Parker and Pedersen show that oxidation of dithiolethiones leads to dimerized dithiolium cations [49]. Under preparative conditions,

dimeric dications bonded through S–S are isolated [49]. Scheme 4 involves a similar pathway in the oxidation of **1**. This hypothesis is confirmed by the fact that oxidation peak A2 ( $+0.90 \text{ V}$  at  $+0.02 \text{ V s}^{-1}$ ) which is attributed to the ferrocenyl oxidation of **11** appeared at the potential of the ferrocenyl oxidation in dithiolium cation **3**. The overall reaction may be seen as an indirect oxidation of the 1,2-dithiole-3-thione thanks to the electron donor effect of the ferrocenyl group. Analogous indirect oxidation of a ferrocenyl substituent has already been described [50].

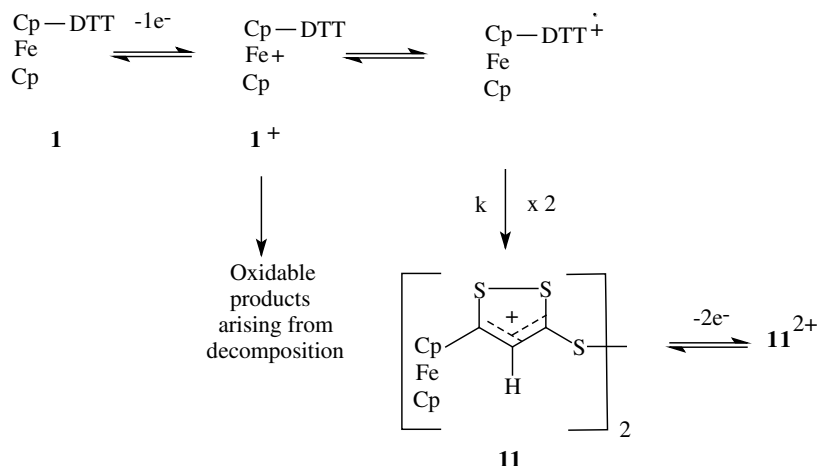
In Scheme 4, ferricinium  $1^+$ , which is substituted by an electron withdrawing substituent, is not very stable, as expected for analogous ferricinium [31,51]. This compound  $1^+$  undergoes a partial decomposition within the diffusion layer and affords by-products which are oxidized during the backward potential scan (Fig. 2). The oxidation of these by-products was not observed at high scanning rate, when the oxidation of **1** was a reversible reaction (Fig. 3).

### 3.5. Electronic effect of dithiole substituents

From the original work of Hammett [24], many studies were developed concerning the determination of electronic parameters  $\sigma$  of substituent from thermodynamic or kinetic data in benzene derivatives [25]. It was reported that  $\sigma$  values were also accessible from oxidation potential of ferrocenyl derivatives [31]. In this particular case, it was observed that linear correlations are better using  $\sigma_p$  values rather than  $\sigma_m$  values [31,48]. The best results were actually obtained with the statistical  $\sigma^* = 1/3(\sigma_m + 2\sigma_p)$  value since  $\sigma_p$  values used alone enhanced the resonance effect contribution [37,38].

The knowledge of the electronic effect of 1,2-dithiole groups A–F was not exhaustive. Some values of  $\sigma_p^-$  were determined for A, B, D, E and  $\sigma_m$  value for A from independent methods [22,23]. In this work, the oxidation potentials of a ferrocene series allowed us to determine new values of the electronic effect of the substituents A–F.

Two linear correlations were established from potential values measured in acetonitrile of a series of  $(\text{C}_5\text{H}_4\text{R})\text{Fe}(\text{C}_5\text{H}_4\text{R}')$  and the Hammett constants  $\sigma_p$  or  $\sigma^*$  of the different substituents R and R' (Table 1). Electronic parameters  $\sigma^*$  are mean values calculated by the equation  $\sigma^* = 1/3\sigma_m + 2/3\sigma_p$  which allows access to  $\sigma_m$  values. Calculated values  $\sigma_m$  are obtained with the equation  $\sigma_p = 1.19\sigma_m - 0.08$ . This relationship takes into account a high degree of collinearity between  $\sigma_m$  and  $\sigma_p$  for substituents which show very little resonance interaction [26].



Scheme 4.

$$E_{1/2} = 0.43\sigma_p + 0.50 \quad (R^2 = 0.982)$$

$$E_{1/2} = 0.50\sigma^* + 0.48 \quad (R^2 = 0.993)$$

From these correlations and the oxidation potentials of the 1,2-dithiole derivatives measured in the same conditions (Table 2) new electronic parameters  $\sigma_p$  and  $\sigma_m$  of the 1,2-dithiole substituents **A–F** were deduced and are gathered in Table 3. It is known that the correlation of ferrocene oxidation potentials with various Hammett-type  $\sigma$  constants results from the interaction occurring through inductive effects rather than resonance or conjugation ones [52]. Indeed, there are few differences between the electronic effects of dithiolethione and dithiolone groups.

The presence of (1,2-dithiole-3-thioxo)-5-yl group **A** directly linked to the ferrocene renders the oxidation of the ferrocene unit slightly more difficult than for (1,2-dithiole-3-oxo)-5-yl group **B**. In a first approximation, this is consistent with the electron withdrawing effect of the thioxo group. In this case, the  $\sigma_p$  and  $\sigma_m$  values of substituents **A** and **B** are in the range of that of a formyl substituent CHO ( $\sigma_p = 0.42$  [26]).

The electronic effect of **A** and **D** may be explained by the poor overlapping of  $\Pi$  orbitals of the double bond C=S allowing the electronic structures **G** and **H** (Scheme 5). The effect is particularly enhanced when the 1,2-dithiole ring **G** is linked by its 5 position to the cyclopentadienyl ring (Table 3). In structure **G** the positive charge is closer to the ferrocenyl group than in structure **H**.

The oxidation potentials of compounds **3** and **6** are under the electronic influence of charged groups. The ferrocenyl group in **3** is oxidized at high potential in agreement with a strong electron withdrawing effect as shown by structure **I**. In this case the substituent constant  $\sigma_p$  is analogous to that of a  $\text{Me}_3\text{N}^+$  substituent with  $\sigma_p$  values of 0.97 and 0.82 [26], respectively. When the charged dithiole group is linked by its 4-position, the electron withdrawing effect decreased the  $\sigma_p$  value at 0.29 which may be compared to  $\sigma_p = 0.44$  for  $\text{Me}_3\text{N}^+\text{CH}_2$  substituent [26].

The substituent constants  $\sigma_p$  determined for dithiole substituents **A–F** are in agreement with what was already known [22,23]. Linear free-enthalpy relationships based on  $\text{p}K_a$  values of phenols and anilinium cations involving dithiole substituted compounds show a strong electron withdrawing effect for the thioxo substituted dithiole **A** by both an inductive and a resonance effect ( $\sigma_p^- = 0.76$ ,  $\sigma_m = 0.44$  from the anilinium cation relationship;  $\sigma_p^- = 0.97$ ,  $\sigma_m = 0.45$  from the phenol relationship). The corresponding 3-oxo substituted dithiole **B** is notably less attractive than the 3-thioxo one ( $\sigma_p^- = 0.64$  from the anilinium cation rela-

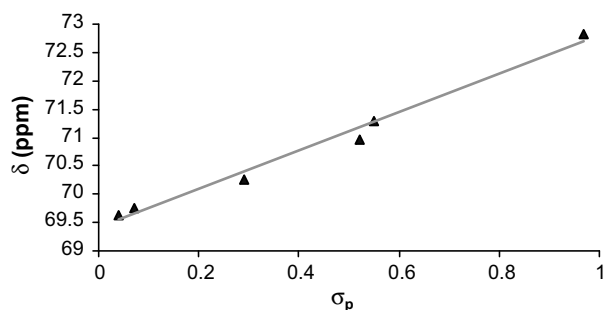


Fig. 4. NMR  $^{13}\text{C}$  shifts of cyclopentadienyl group of ferrocenyl compounds **1–6** vs.  $\sigma_p$  values of Table 3.

tionship;  $\sigma_p^- = 0.78$  from the phenol relationship). This result has been recognized in the literature and explained on the basis of a greater resonance effect in 1,2-dithiole-3-thiones than in 1,2-dithiole-3-ones [19]. The substituents **D** and **E** have only a weak electron withdrawing inductive effect ( $\sigma_p \approx \sigma_p^- \approx 0.2$ ) indicating a lack of conjugation between oxo or thioxo and phenyl dithiole nuclei in compounds **4** or **5** [22]. The  $\sigma_p^-$  values of **A** and **B** were also determined by an independent method based on a linear correlation involving standard potentials of substituted nitrobenzene and known  $\sigma_p^-$  ( $\sigma_p^- = 1.14$  and  $\sigma_p^- = 0.86$  for substituents 3-thioxo **A** and 3-oxo **B**, respectively) [23]. The constant  $\sigma_m$  could not be determined in this work because the corresponding nitro compounds did not follow the electrochemical reduction the nitro group. For the same reasons the substituent effects of **D** and **E** could not be evaluated using this method.

In order to check the substituent constants of Table 3, we used them in a linear correlation involving  $^{13}\text{C}$  chemical shifts. Indeed  $\sigma$  values are sometimes obtained from  $^{13}\text{C}$  NMR and it was observed that the chemical shifts of aromatic carbons were particularly sensitive to electronic effect of polar substituents [53]. This study shows a good linear correlation between the oxidation potentials and the  $^{13}\text{C}$  chemical shifts of the unsubstituted cyclopentadienyl group. Using the  $\sigma_p$  values of Table 3 we obtained the linear correlation presented in Fig. 4. ( $\delta = 3.39\sigma_p + 69.41$  ( $R^2 = 0.987$ )). The good linear correlation proves that the  $\sigma_p$  which characterizes dithiole groups may be of interest in other correlations.

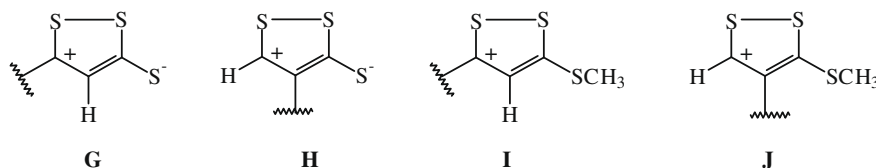
#### 4. Conclusions

New ferrocenyl compounds substituted by 1,2-dithiole groups have been prepared and their electrochemical oxidation has been investigated at a platinum electrode. In all cases, a reversible oxidation of the ferrocenyl group was observed leading to the corresponding ferricinium cation. A peculiar behavior was observed for compound **1** at low scan rate. This behavior was attributed to a chemical step involved during the electrochemical oxidation. From the reversible oxidation potentials and thanks to linear correlations, we obtained a set of the electronic substituent constant  $\sigma$  of six 1,2-dithiole groups. The [3-thioxo-3H-1,2-dithiol]-5-yl and [3-oxo-3H-1,2-dithiol]-5-yl groups (**A** and **B**) exhibited an induc-

Table 3  
Substituent constants of dithiole groups.

Substituent	$\sigma_p$	$\sigma^*$	$\sigma_m$
A	0.55	0.52	0.51
B	0.52	0.50	0.49
C	0.97	0.88	0.83
D	0.07	0.10	0.14
E	0.04	0.08	0.11
F	0.29	0.29	0.31

$$\sigma^* = 1/3\sigma_m + 2/3\sigma_p$$



Scheme 5.

tive electron withdrawing effect which may be compared to those of a formyl group. The [3-methylsulfanyl-3H-1,2-dithiolium]-5-yl cation group (C) had the most electron withdrawing effect which may be compared to those of an ammonium substituent.

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