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Controlling the acidity of the carboxylic group by a ferrocene based redox switch

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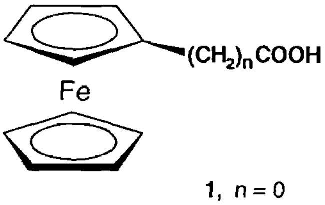
Abstract

The pH dependent oxidation behaviour of the ferrocene subunit in ferrocenylcarboxylic acids of formula $Fc(CH_2)_nCOOH$ ($n=0, 1, 2$) has been investigated through differential pulse voltammetry experiments in 4:1 acetonitrile/water solutions. Different voltammetric responses have been obtained depending whether the pH has been varied through a buffer (a single peak, whose $E_{1/2}$ value decreases with the increasing pH) or through an acid–base titration (two distinct peaks, the less anodic corresponding to the oxidation of the $FcCOO^-$ species, the more anodic corresponding to the oxidation of the FcCOOH species, whose relative intensities vary with the pH). The electrochemically determined pK_a values for the $Fc(CH_2)_nCOOH$ and $[Fc^+](CH_2)_nCOOH$ forms indicate that the Fc-to-Fc^+ oxidation process makes the acidity of the proximate carboxylic group increase. Such a switching effect, electrostatic in nature, decreases as n increases.

Keywords: Electrochemistry; Acidity; Ferrocene complexes; Ferrocenylcarboxylic acid complexes

1. Introduction

Ferrocene (Fc) undergoes a reversible one-electron oxidation to give the stable ferrocenium ion (Fc^+) [1]. The process, which involves a drastic colour change (orange to blue), takes place at a moderate potential (0.40 V versus NHE). For these reasons, ferrocene is frequently incorporated into systems of supramolecular nature, in which a chemically stable subunit providing a fast and reversible redox activity is required. In particular, ferrocene has been used to influence and modify a given property of an adjacent subunit, through the Fc/Fc^+ redox change [2]. For instance, the oxidation of an appended ferrocene subunit can reduce the coordinating tendencies of a multidentate ligand towards a metal ion M^+, due to the electrostatic repulsions between Fc^+ and M^+. Thus, binding of a given metal ion by a ligand can be controlled by varying the oxidation state of the proximate ferrocene fragment, which acts as a control unit or a switch. Redox switches based on ferrocene have been incorporated into the framework of crown ethers and cryptands, in order to control the complexation of s block metal ions [3–14]. In any case, oxidation to Fc^+ disfavours to some extent or in extreme cases prevents the incorporation of the metal centre into the ligand's cavity. In a special case, in which the ferrocene fragment had been appended to a diamine-diamide quadridentate ligand, oxidation to Fc^+ made the binding of Ni^{II} and Cu^{II} metal ions easier, rather than more difficult [15]. The apparent paradox has been explained by considering that coordination to the metal centre involves the simultaneous extrusion of two protons from the two amido groups of the ligand: it is this crucial process that profits from the electrostatic repulsion exerted by the proximate ferrocenium fragment.



1, n = 0

2, n = 1

3, n = 2

Quite curiously, the use of ferrocene-based redox switches, well documented in the case of the complexation of s block metal ions, has not been explored

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for the binding of the most simple cation, the hydrogen ion. We here report a study on the dissociation of ferrocenylcarboxylic acids ($Fc(CH_2)_nCOOH$, $n=0$, 1, 2) and of their oxidized counterparts ($[Fc^+](CH_2)_nCOOH$), carried out through electrochemical experiments. In particular, the acidity constant of the $Fc(CH_2)_nCOOH$ derivatives, $K_a(Fc)$, has been determined through potentiometric titrations. Moreover, the progressive decrease of the $E_{1/2}(Fc^+/Fc)$ quantity in buffered solutions of increasing pH, studied through voltammetry experiments at a platinum electrode, allowed the simultaneous determination of $K_a(Fc)$ and $K_a(Fc^+)$ quantities. Quite interestingly, further voltammetry studies carried out on unbuffered solutions showed that the acid $Fc(CH_2)_nCOOH$ and its conjugate base $Fc(CH_2)_nCOO^-$ undergo independent oxidation processes at a platinum electrode over a substantial pH range, giving rise to two distinct peaks, whose intensity is proportional to the concentration of the redox active species. Such a special situation allowed a further independent determination of the $pK_a(Fc)$ value. This study has indicated that the appended organometallic fragment behaves as a very efficient switch, making the strength of the carboxylic acid drastically increase through the Fc/Fc^+ change. Efficiency decreases as the switch is progressively moved away from the acidic site, due to the decrease of the electrostatic repulsive effects.

2. Experimental

2.1. Materials

Ferrocenecarboxylic acid (Aldrich, 97%) was used without further purification. Ferrocenylacetic acid [16] and β-ferrocenylpropionic acid [17] were prepared according to the literature methods.

2.2. Electrochemistry

Potentiometric and voltammetric experiments were carried out on aqueous acetonitrile solutions (MeCN 80%, H_2O 20%, in volume). Acetonitrile was refluxed over CaH_2, then distilled in a dinitrogen atmosphere, prior to use. The supporting electrolyte was $[Bu_4N]ClO_4$ (Fluka, polarographic grade), which was used without further purification. Potentiometric experiments were carried out using a glass electrode (Orion Research) and a saturated calomel electrode as a reference. The pH scale was calibrated prior to each titration experiment by the Gran method [18]. pH versus equivalents curves for the determination of the pK_a values were carried out by titrating with a 0.1 M standard solution of NaOH a 0.8/0.2 $MeCN/H_2O$ solution containing the ferrocenylcarboxylic acid and excess strong acid. The addition of the aqueous standard base (900 μl, at the end of the titration) was not considered to alter substantially the composition of the titrated solution (~30 ml). Voltammetric studies were performed in a conventional three-electrode cell, using a PAR 273 potentiostat/galvanostat controlled by a personal computer and driven by dedicated software. The working electrode was a platinum microsphere, the counter electrode was a platinum foil and the reference electrode was SCE. The pH of the investigated solutions was measured by means of a glass electrode, which was calibrated as described before. When required, the solutions were buffered with a chosen organic base and pH was adjusted to the desired value with standard $HClO_4$ (pyridine, pH 3.4–5.4; 2,6-dimethylpyridine, pH 5.3–7.3; ethylenediamine, pH 7.3–9.5). Fitting of non-linear equations to electrochemical data was performed using the software package SigmaPlot® for Windows (Jandel Scientific).

3. Results and discussion

3.1. FcCOOH

The acidity of ferrocenecarboxylic acid, FcCOOH (**1**), formal oxidation state of the metal centre +2, has been studied in an $MeCN/H_2O$ mixture (0.8/0.2 in volume). Such a composition was chosen as (i) the organic component allows a satisfactory solubility of the organometallic derivatives investigated in this work, and (ii) the aqueous component ensures a nernstian response of a glass electrode and a reliable determination of the pH. 0.1 M Bu_4NClO_4 was used as a background electrolyte. Titration with standard base of a solution of FcCOOH, containing excess strong acid, disclosed the pH versus equivalents profile of a weak acid, whose pK_a value is 7.76 ± 0.06. It should be noticed that this value is substantially different from that determined in an aqueous solution ($pK_a = 4.20$) [19]. Such a difference has to be ascribed to the medium. In particular, the $FcCOOH = FcCOO^- + H^+$ equilibrium is expected to be more displaced to the right in pure water, where the proton and the carboxylate ion can profit from solute–solvent interactions to a larger extent than in aqueous acetonitrile. Then, differential pulse voltammetry experiments were carried out on solutions whose pH was adjusted by appropriate buffers (pyridine, 2,6-dimethylpyridine, ethylenediamine). In all cases, a symmetric profile was observed, to be ascribed to the reversible one-electron oxidation of the organometallic subunit. The half-height width, $\delta_{1/2}$, was about 100 mV (canonical value for a fully reversible process, at 25 °C: 90 mV). Peak potential values, corresponding to $E_{1/2}$, are reported in Fig. 1.

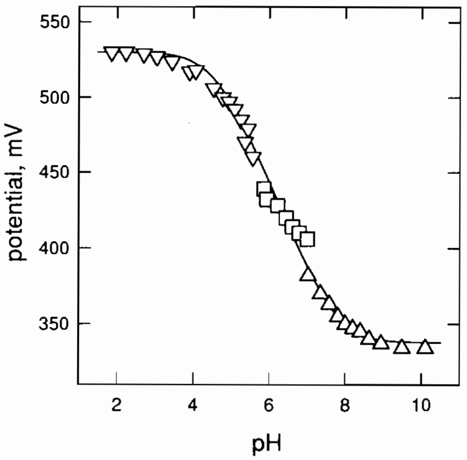

Fig. 1. $E_{1/2}$ values associated with the oxidation of the ferrocene subunit of the FcCOOH/FcCOO$^-$ system in MeCN/H_2O solutions (0.8/0.20 vol./vol.), made 0.1 M in Bu_4NClO_4, at 25 °C. The pH was adjusted by using the following buffers: ▽, pyridine + $HClO_4$; □, 2,6-dimethylpyridine + $HClO_4$; △, ethylenediamine + $HClO_4$.

$$\begin{tikzcd}
\text{FcCOOH} \arrow[r, "K_a(\text{Fc})"] \arrow[d, "E_{(-\text{COOH})}"] & \text{FcCOO}^- + \text{H}^+ \arrow[d, "E_{(-\text{COO}^-)}"] \\
[\text{Fc}^+]\text{COOH} \arrow[r, "K_a(\text{Fc+})"] & [\text{Fc}^+]\text{COO}^- + \text{H}^+
\end{tikzcd}$$

Scheme 1.

Fig. 1 shows that $E_{1/2}$ values exhibit a constant value in more acidic solutions (pH ⩽ 3), then decrease according to a reverse sigmoidal profile, and finally reach a constant value in distinctly basic solutions (pH ⩾ 9). Such a behaviour can be accounted for on the basis of Scheme 1.

Following Scheme 1, the $E_{1/2}$ value of each DPV profile should depend upon the acidity according to Eq. (1).

$$E_{1/2}=E°(\text{-COOH})-59.16\log\frac{K_a(\text{Fc}^+)+[\text{H}^+]}{K_a(\text{Fc})+[\text{H}^+]} \qquad (1)$$

Non-linear fitting of Eq. (1) to the dependent variable $E_{1/2}$ and to the independent variable $[\text{H}^+]$ gave the following values for the investigated parameters: $E°(\text{-COOH})=528\pm1$ mV; $\text{p}K_a(\text{Fc})=7.79\pm0.08$; $\text{p}K_a(\text{Fc}^+)=4.54\pm0.04$. Eq. (1) fits the data well, as indicated by the calculated solid line in Fig. 1. It should be noted also that for $[\text{H}^+] \ll K_a(\text{Fc}) < K_a(\text{Fc}^+)$ (i.e. at pH ⩾ 9) Eq. (1) becomes

$$E_{1/2}=E°(\text{-COOH})-59.16\log\frac{K_a(\text{Fc}^+)}{K_a(\text{Fc})}$$

$$=E°(\text{-COO}^-) \qquad (2)$$

In particular, for the FcCOOH acid, Eq. (2) gives $E°(\text{-COO}^-)=337$ mV. Such a value corresponds to the $E_{1/2}$ values measured at pH ⩾ 9. Finally, Eq. (2) can be rearranged to Eq. (3).

$$\Delta E=E°(\text{-COOH})-E°(\text{-COO}^-)$$

$$=59.16\log\frac{K_a(\text{Fc}^+)}{K_a(\text{Fc})} \qquad (3)$$

According to Eq. (3), the larger the separation of the limiting peaks the greater the difference of the acidic strength of the ferrocenium and ferrocene derivatives. It should be also noticed that the $\text{p}K_a(\text{Fc})$ value obtained through the voltammetric method agrees well with that obtained through the potentiometric titration.

Moreover, DPV studies were carried out following the same approach used in the potentiometric titration, i.e. by adding standard base (NaOH) to an acidic solution of FcCOOH. In distinctly acidic solutions (pH ⩽ 4) a peak centred at $E=530$ mV, corresponding to the reversible oxidation of the FcCOOH derivative, was observed. On further addition of base, the intensity of the peak centred at $E=530$ mV was observed to decrease, whereas a new symmetric peak developed at $E=335$ mV (see Fig. 2). At pH ⩾ 9, the more anodic peak had completely disappeared and the peak at 335 mV had reached a constant and limiting value. Such a peak should correspond to the oxidation of the FcCOO$^-$ species.

It should be noted that this type of voltammetric response is completely different from that observed in these experiments in which the pH had been adjusted by a 0.1 M buffer. In a *buffered* solution, the oxidation process alters the composition of the equilibrium mixture and the FcCOOH, FcCOO$^-$ and H^+ species present in the thin layer of solution at the electrode surface react to restore the pristine equilibrium conditions, according to Scheme 1. As the proton transfer is much

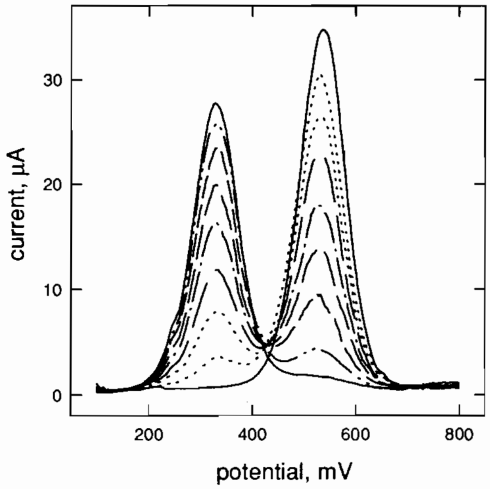

Fig. 2. DPV profiles for *unbuffered* solutions of FcCOOH of varying pH. Increasing the pH makes the peak at 530 mV (corresponding to the oxidation of the FcCOOH form) decrease and the peak at 335 mV (oxidation of the FcCOO$^-$ form) increase. The pH was varied through the addition of standard base to an acidic solution of FcCOOH.

faster than the electron transfer at the electrode, only a single peak is observed in the DPV profile, whose potential is determined by Eq. (1). On the contrary, in an *unbuffered* solution, H^+ ions have to move from the bulk solution to reach the surface layer. Such a migration process is slower than the electron transfer at the electrode. In these non-equilibrium conditions, on scanning the potential of the working electrode, first the oxidation of $FcCOO^-$ takes place, giving rise to its individual peak (at 335 mV). Then, at a more positive potential (530 mV), well before equilibrium (1) is restored, the intact FcCOOH species undergoes oxidation. Under these circumstances, the intensity of each peak is proportional to the concentration of the corresponding redox active species. In particular, the ratio of the current intensity of the peak centred at 530 mV, at a given pH value, over the intensity of the peak measured in strongly acidic solutions ($pH \leqslant 4$), should give the molar fraction of the FcCOOH form, χ_{FcCOOH}. On the other hand, the ratio of the intensity of the peak at 335 mV over the intensity of the peak measured in a definitively basic solution should give the molar fraction of the $FcCOO^-$ species χ_{FcCOO^-}. Thus, the $pK_a(Fc)$ value can be determined according to

$$pK_a(Fc) = pH - \log(\chi_{FcCOO^-}/\chi_{FcCOOH}) \quad (4)$$

A value of 7.5 ± 0.2 was obtained by averaging the data obtained over the 6.5–8.5 pH range. The rather large standard deviation would suggest that this approach is not especially suitable for the determination of $K_a(Fc)$.

3.2. $FcCH_2COOH$

The pH titration experiment disclosed a weak acid behaviour and a $pK_a(Fc)$ value of 8.14 ± 0.08. Then, DPV studies were carried out on *unbuffered* solutions and again a series of profiles displaying two distinct peaks was observed over the pH range 5–9 (see Fig. 3).

At $pH \leqslant 5$ a single peak centred at 336 mV was observed, which corresponds to the oxidation of the $FcCH_2COOH$ form. On the other hand, for solutions of $pH \geqslant 9$, a single peak was observed at 220 mV, corresponding to the oxidation of the $FcCH_2COO^-$ form. It should be noticed that the separation of the two peaks ΔE (116 mV) is considerably smaller than that observed with the FcCOOH derivative. Combination of $pK_a(Fc)$ and ΔE gives the $pK_a(Fc^+)$ value

$$pK_a(Fc^+) = pK_a(Fc) - \Delta E/59.16 = 6.2 \pm 0.1 \quad (5)$$

The partially overlapping peaks of the DPV profiles obtained under non-equilibrium conditions were deconvoluted through a non-linear fitting procedure which used gaussian equations to describe the voltammetric responses. Thus, current intensities of each peak were measured and the $pK_a(Fc)$ value was obtained from Eq. (4): 7.9 ± 0.2.

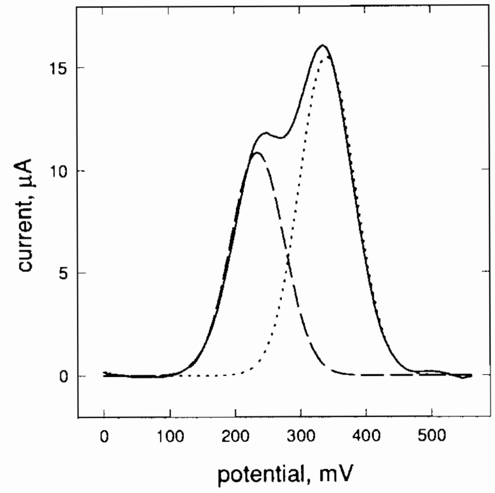

Fig. 3. DPV profile for an *unbuffered* solution of $FcCH_2COOH$ at $pH = 8.0$ (solid line). The DPV profile has been deconvoluted to give a peak centred at 335 mV (corresponding to the oxidation of the $FcCH_2COOH$ form) and a peak centred at 220 mV (corresponding to the oxidation of the $FcCH_2COO^-$ form).

3.3. $Fc(CH_2)_2COOH$

The $pK_a(Fc)$ value determined from the potentiometric titration is 8.17 ± 0.03. DPV profiles of acidic solutions ($pH \leqslant 5$) showed a single peak centred at 305 mV, ascribed to the oxidation of $Fc(CH_2)_2COOH$. In basic solutions ($pH \geqslant 9$), a peak at 225 mV was observed, corresponding to the oxidation of the $Fc(CH_2)_2COO^-$ form. On combination of the ΔE quantity (80 mV) and of the $pK_a(Fc)$, according to an equation of type (5), the $pK_a(Fc^+)$ value was obtained: 6.75 ± 0.06. Increasing the pH of an acidic solution by adding standard base under *unbuffered* conditions included an apparent shift of the peak towards more negative values (see Fig. 4).

However, the half-height width $\delta_{1/2}$, which is 100 mV in acidic solutions, becomes larger and larger on increasing the pH, to reach a maximum value of 155 mV at $pH \cong 8$. Then, $\delta_{1/2}$ decreases again to the constant minimum value of 100 mV in definitively basic solutions. Such a behaviour could correspond to the simultaneous formation of two distinct peaks, one centred at 305 mV, the other one centred at 225 mV, as expected for a voltammetric investigation carried out on an unbuffered solution. However, due to the very moderate separation ($\Delta E = 80$ mV), the two peaks overlap and a single broad signal is observed. Thus, any signal in the pH range 6–9 was deconvoluted into two peaks, through a non-linear least-squares procedure, which assumed a gaussian shape for the DPV peaks (see Fig. 4, as an example). Under these circumstances, at each pH value, in the range 6–9, the concentration of the $Fc(CH_2)_2COOH$ and $Fc(CH_2)_2COO^-$ forms could be

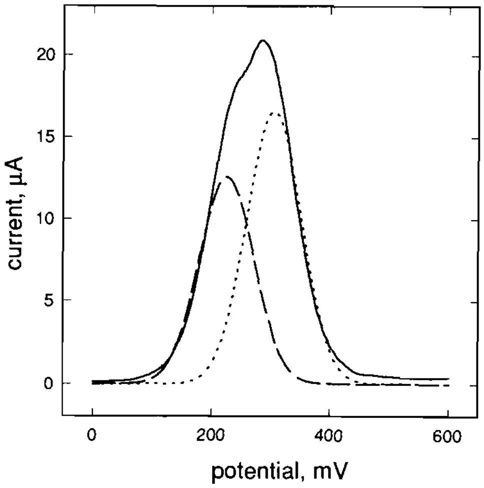

Fig. 4. DPV profile for an *unbuffered* solution of $Fc(CH_2)_2COOH$, of pH≈7.7. Deconvoluted profiles corresponds to the reversible oxidation of $Fc(CH_2)_2COOH$ (more anodic peak, centred 305 mV) and of $Fc(CH_2)_2COO^-$ (less anodic peak, centred at 225 mV).

calculated from the intensity of the deconvoluted peaks and the $pK_a(Fc)$ value (7.9 ± 0.2) could be determined by using Eq. (4).

3.4. Ferrocene as a redox switch

The acidic tendencies of ferrocenylcarboxylic acids, either in their reduced or oxidized forms, are directly expressed by the separation between the more anodic peak, measured in an acidic solution, and the less anodic peak, measured in a basic solution. In particular, the larger the separation, the greater the enhancement of the acidic behaviour. Such an effect is especially evident with the FcCOOH acid, in which the oxidation of the organometallic subunit makes the acidity increase 1700 times. In this case, the dissociation of the carboxylic group can be drastically modified through an external stimulus, by changing the oxidation state of an appended controlling subunit: ferrocene. This can be done by adding an appropriate oxidizing or reducing agent or by varying the potential of a working electrode.

Fig. 5 reports the pK_a values of the reduced and oxidized forms of the investigated ferrocenylcarboxylic acids. It is seen that the $\{pK_a(Fc^+) - pK_a(Fc)\}$ difference decreases with the increasing number of bridging $-(CH_2)-$ groups, i.e. with the distance of the acidic site from the metal centre. This indicates that the control exerted by the switch is essentially electrostatic in nature.

It should be noted also that the behaviour of the FcCOOH derivative is reminiscent of that of classical oxy acids, whose ionization constants increase by several log units on increasing the oxidation state of the central non-metal atom. Moreover, the effect on the acidity of moving the positive charge away from the acidic site is in some way similar to that observed with dications of the type $^{\oplus}H_3N(CH_2)_nNH_3^{\oplus}$, for which the $pK_{a2} - pK_{a1}$ difference decreases with the increase of n and approaches the statistical value ($0.6 = \log 4$) for $n = 6$ [20].

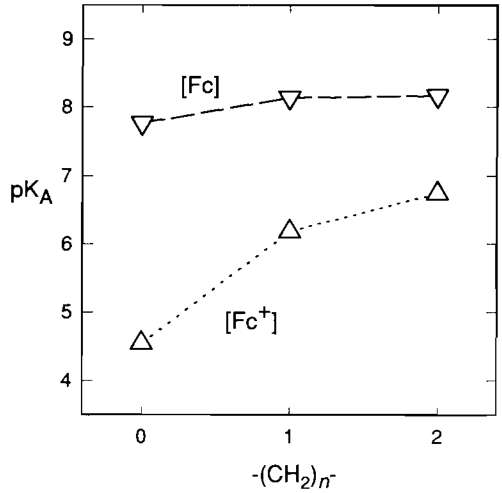

Fig. 5. pK_a values for the dissociation of $Fc(CH_2)_nCOOH$ (▽) and $[Fc^+](CH_2)_nCOOH$ (△) acids.

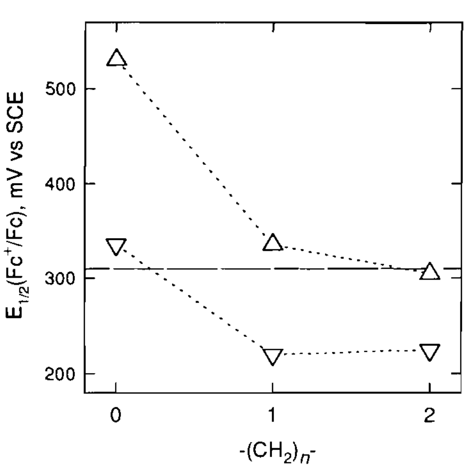

Fig. 6. $E_{1/2}$ values (mV vs. SCE) associated with the reversible oxidation of the ferrocene subunit in the $Fc(CH_2)_nCOOH$ acids (△) and in their conjugate bases $Fc(CH_2)_nCOO^-$ (▽). The long-dashed straight line indicates the $E_{1/2}$ value for the oxidation of plain ferrocene (0.310 V vs. SCE).

3.5. Substituent effects in the oxidation of the ferrocene subunit

Fig. 6 reports the $E_{1/2}$ values associated with the oxidation of the ferrocene moiety of the investigated carboxylic acids and the corresponding carboxylate anions. As far as $Fc(CH_2)_nCOOH$ systems are concerned, a remarkable substituent effect exists in the case of the FcCOOH acid. In particular, the directly bound –COOH group exerts a quite strong electron-withdrawing effect and makes the oxidation of the organometallic fragment take place at a potential 225 mV more positive than for plain ferrocene ($E_{1/2}$ in the same conditions: 310 mV versus SCE). Such an effect almost disappears when the –COOH group is interfaced by one or two –CH_2– segments. Noticeably, when directly linked to a cyclopentadienide ring, the negatively charged –COO^- group still disfavours the oxidation of the ferrocene fragment, even if to a much smaller extent. Again, in presence of an interfacing methylene group, any electron-withdrawing effect is excluded and the oxidation can profit completely from the presence of the proximate negative charge of the –COO^-. Thus, the Fc/Fc^+ process takes place at a potential distinctly more negative than in the case of plain ferrocene.

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