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Structural influences on the electrochemistry of 1,1′-di(hydroxyalkyl) ferrocenes. Structure of [Fe{η^5-C_5H_4—CH(OH)—$(CH_2)_3OH$}$_2$]

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ABSTRACT

A series of 1,1′-di(hydroxyalkyl)ferrocenes, [Fc′{$(CH_2)_n$OH}$_2$], with n = 1 (**1**), 2 (**2**), 3 (**3**) and 4 (**4**) and Fc′ = Fe(η^5-C_5H_4)$_2$, was synthesized. The electrochemistry of the di(hydroxyalkyl)ferrocenes was studied by cyclic voltammetry in CH_2Cl_2/0.1 M [N^nBu_4][PF_6] utilizing a glassy carbon working electrode. The ferrocenyl group showed reversible electrochemistry with the formal reduction potential, $E^{o'}$, inversely proportional to alkyl chain length and approximately 59 mV smaller than those of the corresponding mono(hydroxyalkyl)ferrocenes derivatives [Fc$(CH_2)_m$OH] with m = 1 (**1m**), 2 (**2m**), 3 (**3m**), and 4 (**4m**) and Fc = Fe(η^5-C_5H_5)(η^5-$C_5H_4^-$). The tetraalcohol [Fc′{CH(OH)$(CH_2)_3$OH}$_2$], **5**, possessing four OH functionalities, two in the terminal positions and two more, one on each of the two α-C relative to the ferrocenyl (Fc′ for dialcohols or Fc for monosubstituted derivatives) group, was isolated as a side product during the synthesis of **4**. The formal reduction potential of **5** was $E^{o'}$ = −24 mV *vs.* FcH/FcH$^+$ and closely approached $E^{o'}$ of [FcCH(OH)CH_3] ($E^{o'}$ = −11 mV), [Fc′{CH(OH)CH_3}$_2$] (−21 mV) and **1** (0.00 mV *vs.* FcH/FcH$^+$). The single crystal X-ray structure of the tetraalcohol **5** (Z = 8, orthorhombic, space group *Pbca*) was also solved.

1. Introduction

Ferrocene (FcH) and its derivatives are susceptible to a large number of organic reactions [1] such as alkylation [2], lithiation [3,4], Friedel—Crafts acylation [5] or metal promoted C—C cross-coupling reactions [6]. The ferrocenyl group (Fc) has strong electron donating properties [7] and exhibits reversible one electron transfer electrochemical behaviour [8]. These characteristics allow ferrocene and its derivatives to be useful in a wide range of different applications. Based on its electrochemical signature, ferrocene derivatives are extensively used as molecular sensors [9]. Additionally, the electron-donating characteristics of the ferrocenyl group, the electron-withdrawing properties of the oxidized ferrocenium species (Fc^+ possessing a Fe^{III} cation) [10] and the stability of both the oxidized and reduced states allow ferrocene derivatives to be used in electron transfer [11] and energy transfer studies [12]. They are also used as high burning rate catalysts in rocket propellants [13] and as catalyst in various chemical reactions [14,15]. As a part of a ligand system it will enhance oxidative addition reactions [16] but retard substitution processes [17]. These applications are mostly driven by manipulating the oxidation potential of the ferrocenyl moiety by introducing electron-donating or electron-withdrawing substituents onto the cyclopentadienyl ($C_5H_5^-$) rings. A particularly interesting application of ferrocene derivatives, which are strongly dependent on fine tuning of the ferrocenyl oxidation potential with suitable substituents, lies in the field of cancer therapy. It has been shown that the cytotoxicity of a series of mono(hydroxyalkyl)ferrocenes Fc$(CH_2)_m$OH (m = 1–4) [18] are directly proportional to $E^{o'}$ of the ferrocenyl group. Other ferrocene derivatives show similar trends [18b–18d]. However, many potentially good cytotoxic agents are clinically not usable due to their poor compatibility with an aqueous biological system [19]. To overcome this, a water-insoluble cytotoxic agent may be bound to a water-soluble polymeric drug carrier [20].

To incorporate ferrocene derivatives with different oxidation potentials into macromolecules or polymers, it is necessary to synthesize ferrocene species with side chains having reactive functional groups [21–23]. One of these functional groups which are often used to covalently bind the ferrocenyl moiety to larger target molecules is the alcohol functionality [24]. There are two main ways to include the ferrocenyl group into polymeric species. For the first approach, one may use a monofunctionalized ferrocenyl derivative to covalently bind the metallocenyl moiety *via* a short side chain to the polymer main chain [22]. Secondly, one may use difunctionalized cyclopentadienyl derivatives and condense

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them with other difunctionalized monomers into polymers bearing the ferrocenyl group as part of the main chain [23].

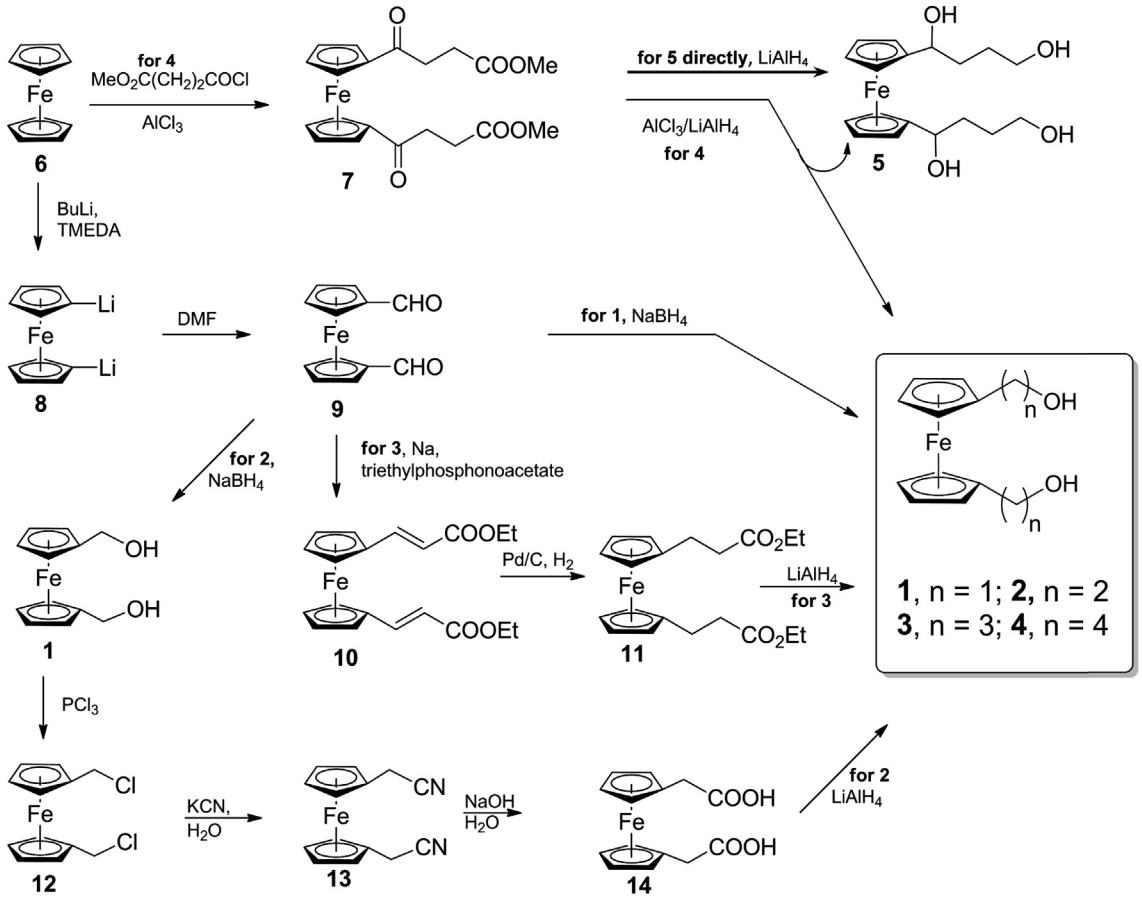
In this publication we describe efficient methods to synthesize and characterize a series of 1,1′-di(hydroxyalkyl)ferrocenes with general formula [Fc′{$(CH_2)_nOH$}$_2$] (compounds **1**–**4** with $n = 1, 2, 3$ and 4, Scheme 1) and we show how the formal oxidation potential of the ferrocenyl group changes with increase in alkyl chain length (*i.e.* larger values of *n*). Electrochemical results are compared with the ferrocenyl oxidation potentials of the related series of mono(hydroxyalkyl)ferrocenes [Fc$(CH_2)_m$OH] where $m = 1$–4, compounds **1m**–**4m**. In addition, we could isolate and characterise by single crystal X-ray analysis the tetraalcohol [Fc′-{$CH(OH)(CH_2)_3OH$}$_2$], **5**, which was obtained as a side product during the synthesis of **4**.

2. Results and discussion

2.1. Synthesis

The diol 1,1′-di(hydroxymethyl)ferrocene, **1**, was synthesized [25] by reduction of dialdehyde, **9**, with 1.5 equiv of $NaBH_4$ per aldehyde functionality (Scheme 1). The dialdehyde **9** was obtained in high yield utilizing Mueller and Westerhoff's general method [4,26] *via* dilithiation of ferrocene (**6**) in the presence of TMEDA (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine) and subsequent reaction with DMF (dimethylformamide). With this two-step protocol, **1** could be obtained in overall yield of 84%. Yields of the reduction of **9** to liberate **1** are highly dependent on the work-up method. For the synthesis of **1m**, [FcCH(OH)CH_3] and [Fc′{$CH(OH)CH_3$}$_2$] [13c,22b,27], we and other researchers used $LiAlH_4$- or $NaBH_4$-induced reduction of **9**, $FcCOCH_3$ and Fc$(COCH_3)_2$ and the reaction mixture was worked-up by quenching the reaction with water. For **1**, in our hands, this approach led to substantial decomposition and, hence, low yields of **1**. The observed decomposition if **1** is related to the elimination of H_2O from Fc-$(CH_2OH)_2$, a reaction which is driven by the stability of Fc-CH_2^+ cations [13c,22b,28]. We found it best not to quench the reaction with acid or H_2O initially, but to first filter the reaction medium through Celite. The remaining residue on the Celite was then extracted with THF and quenched with water. In this way we could increase yields of **1** to well above 80%.

1,1′-Di(2-hydroxyethyl)ferrocene, **2**, was obtained by a six-step synthesis [29] in an overall yield of 32% based on ferrocene (Scheme 1). A key precursor to obtain **2** is the dinitrile **13**. All attempts to obtain **13** from 1,1′-di(*N*,*N*,*N*-trimethylamoniummethyl) ferrocene diiodide, Fc′{$CH_2N(CH_3)_3$}$_2$2I [30], as is possible for the corresponding mononitrile, $FcCH_2CN$ [31], failed. Consequently, we synthesized **13** starting from **1** *via* the dichloride **12**. 1,1′-Di(chloromethyl)ferrocene, **12**, was obtained by treating **1** with PCl_3. Complex **12** is only moderately stable due to the relatively good leaving properties of chloride as an anion and especially the stabilisation effect the electron-donating ferrocenyl group has on Fc-$(CH_2^+)_2$ cations [28]. Hence **12** was not isolated but reacted *in situ* by addition of the crude reaction mixture containing **12** to an aqueous KCN solution. Chloride substitution from **12** by the cyanide anion resulted in the formation of the dinitrile **13** in 50% yield after column chromatography. Basic hydrolysis of the dinitrile afforded



Scheme 1. Synthesis of 1,1′-di(hydroxyalkyl)ferrocenes **1**–**4**. The tetrahydroxy derivative **5** can be made purposefully, but it was also isolated as a side product during the synthesis of **4**. Compound numbers **1m**–**4m** in the text refer to the analogous monosubstituted ferrocenyl alcohols [Fc$(CH_2)_m$OH] where $m = 1$–4.

ferrocenyl-1,1′-diacetic acid, **14**. $LiAlH_4$ reduction of **14** gave diol **2** as a yellow oil in near quantitative yield.

For the synthesis of 1,1′-di(3-hydroxypropyl)ferrocene, **3** [32], dicarboxaldehyde **9** was converted quantitatively to the unsaturated ester **10** with the Wittig–Horner reaction by treating **9** with the phosphonate anion obtained *in situ* from triethyl phosphonoacetate and sodium metal (Scheme 1). Quantitative hydrogenation of the double bonds of **10** with hydrogen in presence of 10% palladium-on-charcoal followed by the reduction of the ester groups with $LiAlH_4$ gave the target dialcohol **3** in 75% overall yield. An alternative route towards **3** that was also explored involves the reaction of **9** with malonic acid in the presence of piperidine to obtain ferrocene-1,1′-diacrylic acid followed by the hydrogenation of the double bonds with hydrogen in presence of 10% palladium-on-charcoal and reduction of the carboxylic acid groups. This route resulted in the formation of **3** in poor yields (5%) in our hands. The weakest step is low conversion of **9** to ferrocene-1,1′-diacrylic acid.

1,1′-Di(4-hydroxybutyl)ferrocene, **4**, was obtained in two steps (Scheme 1) first by performing a Friedel–Crafts diacylation on ferrocene with 3-(carbomethoxy)propionyl chloride [33] to obtain **7** in 35% yield. The subsequent one-pot reduction of all four carbonyl groups with one equivalent of $LiAlH_4$ and two equivalents of fresh $AlCl_3$ per each carbonyl group resulted in almost quantitative formation of **4**. Alternatively, **4** can be obtained in two steps *via* Clemmensen reduction of the keto groups of **7** followed by reduction of ester functionalities to give **4** in 25% overall yield [24b,23a]. To our surprise, we frequently also isolated the previously unknown tetraalcohol **5**, [Fc′-{CH(OH)–$(CH_2)_3$OH}$_2$], as a yellow oil that solidifies within three days from the reaction mixture during the synthesis of **4**. The use of fresh $AlCl_3$ in the indicated quantities proved to be essential to prevent formation of this previously unknown tetraalcohol.

Upon further investigating methods to obtain the tetraalcohol **5** during a purposeful synthesis (Scheme 1), we found **5** could be obtained in near quantitative yields by treating **7** with 4 equiv of $LiAlH_4$ in the absence of $AlCl_3$. Crystallographic quality crystals may be obtained by crystallization from ethyl acetate and the crystal structure of **5** was solved, see next section.

2.2. ^{1}H NMR and IR spectroscopy

^{1}H NMR analysis of the aliphatic disubstituted compounds [Fc′{$(CH_2)_n$X}$_2$] with n = 0–4 and X = OH, CN, COOEt, CHO or CO–CH_2CH_2COOMe showed only those complexes without any or with just one CH_2 spacer between the ferrocenyl group and an electron-withdrawing functional group, X, exhibited the characteristic two pseudo-triplets of the ferrocenyl moiety as two separate resonances in an ^{1}H NMR spectrum. These two pseudo-triplets were overlapping (*i.e.* they were unresolved) in complexes with two or more CH_2 spacers (n = 2, 3, 4). Fig. 1 summarises the influence of alkyl chain length on the coalescence of these two pseudo-triplets for compounds of this study. Additionally, the downfield shift of the pseudo-triplets with increasing value of n reached an asymptotic minimum at n = 4. This result was echoed in the electrochemical study described below. The ^{1}H NMR of **5**, [Fc′-{CH(OH)-$(CH_2)_3$OH}$_2$], bearing two chiral centers in the α position next to the ferrocenyl group was more complex. In particular, the signals of the two CH_2–OH molecular fragments were found at δ = 3.96–3.88 and 3.84–3.77 ppm, while those of the two CH(OH)–CH_2–CH_2 fragments were observed in an integral ratio of 1:3 rather than the expected ratio of 2:2 at δ = 2.26–2.17 and 2.02–1.89 ppm. This unexpected resonance pattern is at least in part attributed to hydrogen bonding patterns which may enforce inequivalence of the respective CH_2 species as discussed in the crystallographic section below. Especially the observed intramolecular bonds (see Table 2 crystallographic section) may contribute to this effect, but the use of different deuterated solvents did not induce a different integration pattern [34]. However, these CH_2 protons are enantiotopic, and enantiotopic protons have the same chemical shift in the vast majority of situations. However, if they are placed in a chiral environment, which is the case here, they will have slightly different and more complex chemical shifts, making them non-equivalent. This could also contribute to the observed integral ratio of 1:3 rather than the expected ratio of 2:2.

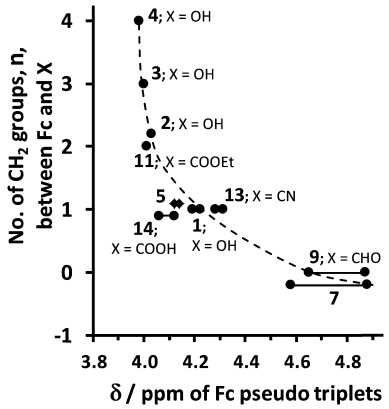


Fig. 1. The relationship between the number of CH_2 spacers, n, separating the ferrocenyl group and an electron-withdrawing substituent functionality X in disubstituted ferrocene derivatives [Fc′{$(CH_2)_n$X}$_2$] (*Y*-axis) and the ^{1}H NMR position (δ values/ppm) of each of the two C_5H_4 pseudo-triplets for the indicated compounds of this study highlights the pseudo-triplets are only resolved into two separate signal sets for n = 0 and 1. For $n \geq 2$ the pseudo-triplets moved so close to each other that they overlapped. For **7**, the substituent is $COCH_2CH_2COOMe$, *i.e.* no CH_2 spacer between Fc′ and CO while for **5** the substituent is CH(OH)–$(CH_2)_3$–OH implying n = 1.

The coupling constants for the two observed pseudo-triplets of the aromatic C_5H_4 group were ^3J = 1.73–1.95 Hz, depending on the compound. Coupling constants for the olefinic CH=CH group (^3J = 15.7 Hz for **10**) and aliphatic CH_2–CH_2 (^3J = 6.6 Hz for **2** or **7**) or CH_2CH_3 groups (^3J = 7.1 Hz for **10**, **11**) are much larger. The 15.7 Hz coupling constant of **10** is consistent with the *E*-isomer. Also, from **4**, it is evident that R^1–CH_2–CH_2–R^2 coupling is influenced by the substituent R^1 and R^2. For **4**, [Fc′(CH_2–CH_2–CH_2–CH_2–OH)$_2$], the coupling constant of the triplet of the CH_2 group next to the electron-donating ferrocenyl group is 6.6 Hz, while ^3J for the triplet of the CH_2 group next to the inductive electron-withdrawing OH functionality is 5.20 Hz. For **3**, [Fc′(CH_2–CH_2–CH_2–OH)$_2$], the same tendency was observed: the coupling constant of the triplet of the CH_2 group next to the electron-donating ferrocenyl group was ^3J = 8.20 Hz. This is 1.84 Hz larger than the coupling constant for the CH_2 group adjacent to the electron-withdrawing OH functionality.

Being disubstituted ferrocenyl derivatives, the IR of **1**–**5** did not show the unsubstituted C_5H_5 bands at 1000 and 1100 cm^{-1}, but the OH functionalities showed the typical broad, strong alcohol bands at 3200–3500 cm^{-1} (O–H stretching) and 1050–1211 cm^{-1} (C–O stretching). The strong C=O stretching bands of **7** (1650, 1730 cm^{-1}), **9** (1664 and 1684 cm^{-1}), **10** (1706 cm^{-1}) **11** (1737 cm^{-1}) and **14** (1675 cm^{-1}) were also observed. The nitrile groups of **13** exhibited an IR stretching frequency of 2260 cm^{-1}. C–H stretching frequencies were between 2900 and 3150 cm^{-1} with the aromatic ferrocenyl C–H stretching bands at slightly longer wavenumbers than the aliphatic C–H bands. Complex **10**, [Fc′(CH=CHCOOEt)$_2$], showed a C=C stretching vibrational band at 1626 cm^{-1}.

2.3. Single crystal X-ray structure of **5**

Crystallographic quality crystals were obtained by recrystallization of chromatographed **5**, after the oil that was obtained from the column solidified, from ethyl acetate. The molecular structure of **5** with atom numbering is shown in Fig. 2; selected bond distances (Å) and angles (°) are summarized in the caption. Refinement parameters and crystal data are summarised in Table 1. Compound **5** crystallizes in the orthorhombic space group *Pbca*. The cyclopentadienyl rings deviate 8.27° from an eclipsed conformation while the dihedral angle between the two alkyl chains is 63.87°. The distance between cyclopentadienyl rings from the centroid of C(1)–C(5) to the centroid of C(6)–C(10) is 3.300 Å and the dihedral angle between the two cyclopentadienyl planes is 1.97°.

The C–C bonds in the cyclopentadienyl rings show an average bond length of 1.421 Å for the two substituted rings. This is about 0.02 Å shorter than bond lengths in unsubstituted cyclopentadienyl rings [35]. The largest deviation (+0.015 Å) from this average was for C(6)–C(7). sp^3–sp^3 C–C single-bond distances and sp^3 C–O bond distances for the aliphatic portions of the alkyl chains averaged 1.510 and 1.432 Å respectively, and are in good agreement with published values [36]. Bond angles for the cyclopentadienyl rings approached 108° with the largest deviation of 1.9° for C(1)–C(5)–C(4), while C–C–C angles around atoms C(11)–C(18) were between C(12)–C(13)–C(14) = 110.1° and C(16)–C(17)–C(18) = 117.7°. The six O–C–C angles averaged 108.1°.

An extensive hydrogen bonding network was observed in **5**. The dihedral angle C(1)–C(11)–C(6)–C(15) = 63.9°, Fig. 2, is attributed to the intramolecular hydrogen bond O(1)–H···O(3) with an O(1)–O(3) distance of 2.738(5) Å, Table 2. The intermolecular hydrogen bonds *via* O–H···O interaction connects a central molecule of **5** with six adjacent molecules. Hydrogen bond lengths and angles are summarized in Table 2. Fig. S1 in Supplementary Information shows a second view of this hydrogen bonding network.

2.4. Electrochemical studies

The redox properties of the di(hydroxyalkyl)ferrocene compound series **1**–**5** were studied by cyclic voltammetry (CV). CV experiments were performed on 0.25 mM solutions of **1**–**5** in dry CH_2Cl_2/0.1 M $[N^nBu_4][PF_6]$, utilising a standard three-electrode cell. Electrochemical data are summarized in Table 3 and presented in Figs. 3 and 4. Quasi reversible electrochemical behaviour was observed for the ferrocenyl moiety in **1**–**5** with $\Delta E_p = E_{pa} - E_{pc} \leq 80$ mV at a scan rate of 100 mV s^{-1} (Table 3, Fig. 4). Electrochemical reversibility is ideally characterized by a theoretical ΔE_p value of 59 mV for a one-electron transfer process [37]. Peak cathodic/peak anodic current ratios for **1**–**5** were in the range $0.98 < ipc/ipa < 1$. Formal reduction potentials, $E^{o'} = 1/2(E_{pa} + E_{pc})$ were scan rate independent between 100 and 500 mV s^{-1} (Fig. 3).

A peculiarity is the $E^{o'}$ of **1** being exactly 0.00 V, *i.e.* at the same potential as the free FcH/FcH^+ couple. This is interpreted to imply that the combined electronic effect of two CH_2OH groups on the Fe^{II} centre of **1** *via* through-bond and through-space pathways, and promoted by a hydrogen bonding network similar to that described for **5** above and for Fc′{CH(OH)CH_3}$_2$ [38], accidently led to the observed oxidation potential. The observed negative shift of the $E^{o'}$ value with increasing alkyl chain length (Table 3) is a consequence of the larger alkyl spacer size between Fc and OH groups. It isolates the electron-withdrawing OH moiety from the ferrocenyl group more effectively with increasing alkyl chain length and ultimately the ferrocenyl group only experiences the electron-donating effect of the alkyl spacer.

The relationship between the alkyl chain length and $E^{o'}$ of dialcohols **1**–**5** and monoalcohols **1m**–**4m** [39] is shown in Fig. 5. The increase of the alkyl chain length from $n = 1$ to $n = 4$ causes $E^{o'}$ of compound series **1**–**4** to approach an asymptotic minimum at $n = 4$. An asymptotic minimum was also approached at $m = 4$ in the monofunctionalized ferrocene complexes (Fig. 5). The difference between the $E^{o'}$ of mono- and difunctionalized hydroxyalkylferrocenes **1**–**4** was for each $n = m$ value almost the same (Fig. 5, Table 3) and averaged 59 mV.

In addition, $E^{o'}$ values of **1** (0 mV), **5**, (−24 mV) and [Fc′{CH(OH)CH_3}$_2$] (−21 mV) [39] are very close to each other (Table 3, Fig. 5), which indicates that $E^{o'}$ for these compounds are mainly influenced by the alcohol functionality in the α-position. That $E^{o'}$ of the monoalcohol [FcCH(OH)CH_3] (−11 mV) [39] is so close to that of the other three α-hydroxylated compounds is consistent with an

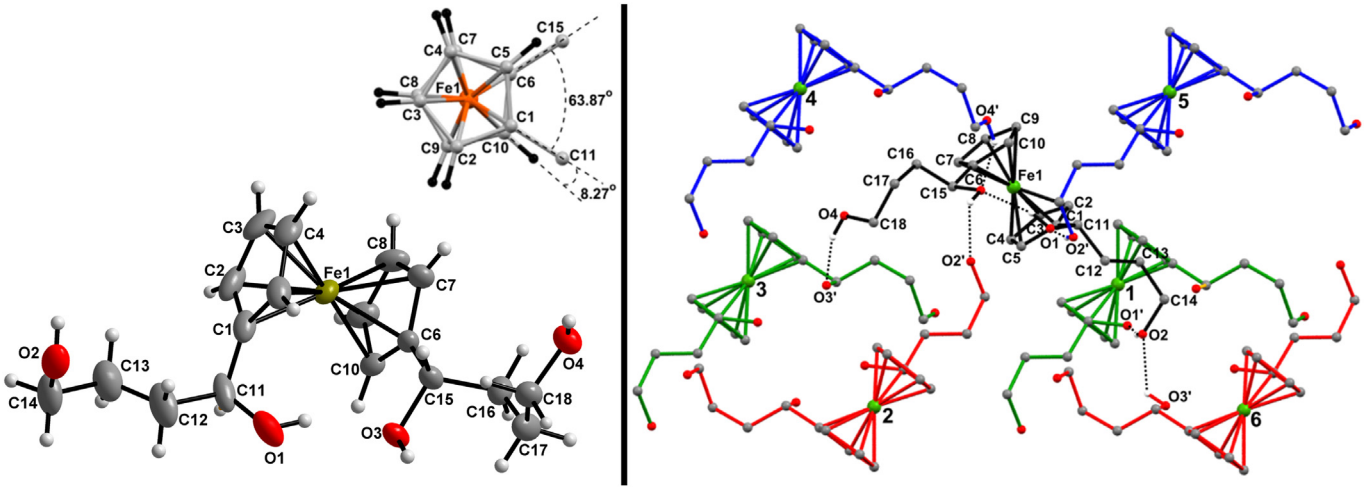


Fig. 2. Left: Molecular structure of [Fe{η^5-C_5H_4–CH(OH)–$(CH_2)_3$–OH}$_2$], **5**; thermal ellipsoids are drawn at 50% probability level. Selected bond length (Å) and angles (°) are: Fe(1)–C(1) 2.056(5), Fe(1)–C(2) 2.045(5), Fe(1)–C(3) 2.037(5), Fe(1)–C(6) 2.051(4), Fe(1)–C(7) 2.049(5), Fe(1)–C(9) 2.039(5), C(1)–C(2) 1.421(8), C(2)–C(3) 1.424(8), C(3)–C(4) 1.409(8), C(6)–C(7) 1.436(6), C(7)–C(8) 1.422(7), C(8)–C(9) 1.417(7), C(1)–C(11) 1.479(8), C(11)–C(12) 1.558(7), C(12)–C(13) 1.443(10), C(13)–C(14) 1.559(8), C(6)–C(15) 1.507(6), C(15)–C(16) 1.508(7), O(1)–C(11) 1.424(7), O(2)–C(14) 1.427(8), O(3)–C(15) 1.445(5), O(4)–C(18) 1.431(6), C(1)–C(11)–C(12) 115.7(5), C(6)–C(15)–C(16) 111.3(4), C(11)–C(12)–C(13) 114.0(6), C(15)–C(16)–C(17) 114.4(4), O(1)–C(11)–C(1) 110.4(4), O(2)–C(14)–C(13) 110.3(5), O(3)–C(15)–C(6) 107.0(4), O(4)–C(18)–C(17) 109.0(4). Right: Hydrogen bonding in **5**. Each molecule is hydrogen-bonded to six neighbouring molecules; these are labelled next to the Fe atom as 1 through 6. Symmetry transformations used to generate equivalent atoms may be found in Table 2, footnote "a".

Table 1
Crystal data and structure refinement for **5**.

Empirical formula	$C_{18}H_{26}FeO_4$	Absorption coefficient/mm^{-1}	0.922 mm^{-1}
Molecular weight	362.24	θ range for data collection/°	2.18–28.00°
Crystal size/mm^3	0.42 × 0.09 × 0.08	Index ranges	$-17 \le h \le 17$, $-12 \le k \le 8$, $-35 \le l \le 33$
Temperature/K	100(2)	Reflections collected	44,013
Wavelength/Å	0.71073	Independent reflections	4025 [R(int) = 0.0481]
Crystal system	Orthorhombic	Completeness to θ = 28.42°	99.9%
Space group	*Pbca*	Max. and min. transmission	0.9299 and 0.6981
Unit cell dimensions/Å	a = 12.9558(9)	Refinement method	Full-matrix least-squares on F^2
	b = 9.5202(6)	Data/restraints/parameters	3330/0/172
	c = 27.0387(19)	Goodness-of-fit on F^2	1.046
Volume/Å	3335.0(4) Å^3	Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.0789, $wR2$ = 0.1886
Z	8	R indices (all data)	$R1$ = 0.0981, $wR2$ = 0.2024
Density (calc.)/Mg m^{-3}	1.443	Largest diff. peak and hole/e Å^{-3}	1.605 and −1.044 e Å^{-3}
F(000)	1536		

intermolecular hydrogen bond network in [FcCH(OH)CH$_3$] imposing almost the same electron density on the Fe^{II} center of this compound as in the combined inter- and intramolecular networks of **5** and [Fc′{CH(OH)CH$_3$}$_2$].

3. Conclusions

The di(hydroxyalkyl)ferrocenes compound series [Fc′{(CH$_2$)$_n$OH}$_2$] with n = 1 (**1**), 2 (**2**), 3 (**3**), 4 (**4**) and [Fc′{CH(OH)(CH$_2$)$_3$OH}$_2$] (**5**) was synthesized. Compound **5** was separated as the main side product during the reduction of [Fc′{CO(CH$_2$)$_2$COOMe}$_2$], **7** to **4** with LiAlH$_4$/AlCl$_3$ and crystallizes in the orthorhombic space group *Pbca*. An extensive hydrogen bonding network exists in the crystal structure of **5**. The ferrocenyl groups of **1**–**5** all showed electrochemical reversible behaviour. Hydroxyalkyl chain length and oxidation potential potentials of **1**–**4** were inversely proportional to each other. Oxidation potentials of the dihydroxyalkyl ferrocenes were consistently approximately 59 mV smaller for each hydroxyalkyl substituent compared to the corresponding monohydroxyalkyl ferrocenes **1m**–**4m**. Hydroxylation in the α position relative to the ferrocenyl group in mono and dihydroxyalkyl derivatives **1**, **5**, [Fc(CHOH)CH$_3$] and [Fc′{(CHOH)CH$_3$}$_2$] resulted in oxidation potentials being grouped fairly close together in the range $0 < E^{o'} < 24$ mV *vs*. FcH/FcH$^+$ and is interpreted to be at least in part a consequence of the crystallographically observed hydrogen bonding networks.

4. Experimental

4.1. General procedures and instruments

All reactions were carried out under an argon atmosphere using standard Schlenk techniques. Tetrahydrofuran, diethyl ether and *n*-hexane were purified by distillation from sodium/benzophenone ketyl. Dichloromethane was dried over molecular sieves (4 Å). All reactants (Sigma–Aldrich or Merck) were used as received unless otherwise stated. Chromatography was performed on silica gel 60 (220–240 mesh, Fluka). Melting points were determined with an Olympus BX 51 microscope with a Linkham THMS 600 heating apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker Advance DPX 300 NMR spectrometer at 300.13 MHz and 20 °C with chemical shifts presented as δ values referenced to SiMe$_4$ as internal standard at 0.00 ppm utilizing CDCl$_3$ or DMSO-d_6 as solvents. The following abbreviations are used to describe peak patterns: s = singlet, br s = broad singlet, d = doublet, pt = pseudo-triplet, t = triplet, q = quartet, m = multiplet. IR spectra (cm^{-1}) were recorded on a Bruker Tensor 27 spectrometer with a PIKE MIRacle ATR-attachment. Elemental analysis was conducted by the Analytical Chemistry of Chemistry Department of the UFS on a Leco TruSpec Micro instrument.

4.2. Synthesis

4.2.1. 1,1′-Di(hydroxymethy1)ferrocene (**1**) via 1,1′-ferrocenedicarboxaldehyde (**9**)

*4.2.1.1. 1,1′-Ferrocenedicarboxaldehyde (**9**).* The literature procedure [26b] for the preparation of **9** was modified as follows: To a room temperature solution of ferrocene (10 g, 0.054 mol) in dry hexane (200 mL) was added *n*-butyl lithium solution (67 mL, 1.6 M in hexanes, 0.10 mol) dropwise followed by addition of tetramethylene ethylenediamine (TMEDA) (14.7 g, 0.25 mol). No difference in yields was detected if the additions were made at −50 °C. After stirring the reaction mixture for 18 h at room temperature, dilithiated ferrocene has precipitated as an orange solid. The suspension was cooled to 0 °C, DMF (7.85 g, 0.11 mol, 8.3 mL) was

Table 2
Hydrogen bonds (Å) and angles (°) in **5**.[a]

O–H···O′ interaction	d(H···O′)	d(O···O′)	<(OHO′)
O(1)–H(1A)···O(3)[b]	1.98	2.738(5)	149.2(3)
O(2)–H(2A)···O(1)$_{\#1}$[c]	1.85	2.678(6)	170.5(3)
O(3)–H(3A)···O(2)$_{\#2}$[c]	2.06	2.674(5)	129.3(2)
O(4)–H(4A)···O(3)$_{\#3}$[c]	2.11	2.850(5)	147.1(3)
C(12)–H(12B)···O(2)[b]	2.54	2.919(7)[d]	102.6(3)[d]

[a] Symmetry transformations used to generate equivalent atoms: #1: $-x + 1/2$, $y + 1/2$, z; #2: $x - 1/2$, $-y + 1/2$, $-z$; #3: $-x - 1/2$, $y + 1/2$, z; d(O–H) = 0.84 Å; D(C–H) = 0.99 Å.
[b] Intramolecular bond.
[c] Intermolecular bond from the parent molecule to adjacent molecule number 1, 2 or 3.
[d] d(C···O) and angle(CHO).

Table 3
Cyclic voltammetric data at 100 mV s^{-1} scan rate (potentials *vs*. FcH/FcH$^+$) of 0.25 mM solutions of **1**–**5** as well as the monoalkylalcohol complexes **1m**–**4m** in dry dichloromethane containing 0.1 M of [N^{n}Bu$_4$][PF$_6$] as a supporting electrolyte at 25 °C.[a]

Comp.	E_{pa} (mV)	$E^{o'}$ (mV)	ΔE_p (mV)	i_{pa} (μA)	i_{pc}/i_{pa}	Comp.	$E^{o'}$ [a] (mV)	$\Delta E^{o'}$ [c] (mV)
1	40	0	80	2.35	0.98	**1m**	60	60
2	−68	−106	76	2.36	1.00	**2m**	−46	62
3	−68	−107	78	2.36	0.98	**3m**	−52	50
4	−77	−114	74	2.39	1.00	**4m**	−54	60
5[b]	12	−24	72	2.39	1.00	**5m**[b]	−11	13

[a] Data for the monoalcohols **1m**–**4m** and complex **5m** are from Ref. [39].
[b] Complex **5** = [Fc′{CH(OH)–(CH$_2$)$_3$–OH}$_2$], complex **5m** = [FcCH(OH)CH$_3$]; $E^{o'}$ of [Fc′{CH(OH)CH$_3$}$_2$] is −24 mV [39].
[c] $\Delta E^{o'} = E^{o'}_{\text{Fc monofunctionalized}} - E^{o'}_{\text{Fc difunctionalized}}$.

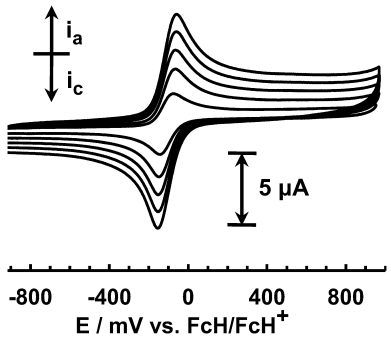


Fig. 3. CV's of **4** ($n = 4$) in CH_2Cl_2/0.100 M $[N^nBu_4][PF_6]$ at 25 °C and scan rates of 100 (the smallest current), 200, 300, 400, 500 (the largest current) mV s^{-1} at a glassy carbon working electrode.

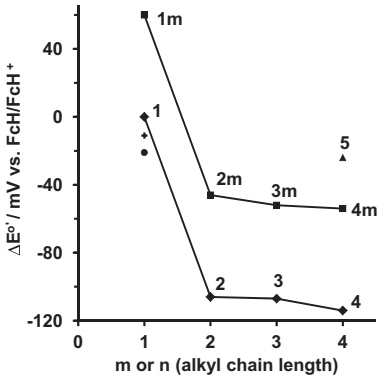


Fig. 5. Relation between $E^{o'}$ and the number of carbon atoms (m or n) in the alkyl chain of the mono-functionalized alcohols **1m**–**4m** (■), [$Fc(CH_2)_mOH$], and [FcCH(OH)CH_3] (+) [38], as well as difunctionalized alcohols **1**–**4** [Fc′{$(CH_2)_nOH$}$_2$] (◆), **5** [Fc′{$CH(OH)(CH_2)_3OH$}$_2$], (▲) and [Fc′{$CH(OH)CH_3$}$_2$] (●) [38].

added, and the stirring continued for further 2 h at room temperature. After quenching the reaction mixture with 200 mL ice-cooled 5 M aqueous HCl, it was extracted with diethyl ether (3 × 100 mL). The combined organic fractions were dried over $MgSO_4$ and the solvent was removed to give crude **9** as a dark red solid. The crude product was purified by column chromatography (hexane:dichloromethane v/v 1:1, $R_f = 0.65$) to afford pure **9** as red crystals (11.06 g, 85%), m.p. 181 °C. ^{1}H NMR ($CDCl_3$) δ/ppm: 4.65 (pt, $J = 1.9$ Hz, 4H, 2× C_5H_4), 4.87 (pt, $J = 1.9$ Hz, 4H, 2× C_5H_4), 9.93 (s, 2H, C*H*O). ^{13}C{^{1}H} NMR ($CDCl_3$) δ/ppm: 192.8 (*C*HO), 80.43 (C_{ipso}), 74.18 (Cp), 70.83 (Cp). IR, neat, ν_{max}/cm^{-1}: 1684, 1664, 1456, 1372, 1246, 1040, 745.

*4.2.1.2. 1,1′-Di(hydroxymethy1)ferrocene (**1**).* To a stirred mixture of $NaBH_4$ (350 mg, 8.8 mmol) in dry THF (15 mL), 1 g (4.12 mmol) of solid 1,1′-ferrocenedicarboxaldehyde, **9**, was added in small portions. The mixture was stirred at room temperature for 15 min and two more portions of $NaBH_4$ (each 200 mg, 5.3 mmol) was added within 10 min of each other. Thereafter the reaction is filtered through a pad of Celite and the Celite-residue washed with THF (3 × 20 mL). Caution: Quenching with water or dilute acid *before* filtering severely lowers yields. The Celite with remainder of the reaction residue still on it was suspended in THF (100 mL) and water (10 mL) was added. This suspension was stirred for 5 min, filtered, and the organic layer was separated and dried over $MgSO_4$. The combined THF fractions were evaporated to dryness to obtain the product, **1**, as yellow crystals. Yield 1.0 g (99%), m.p. 105–107 °C, R_f (DCM) = 0.5. ^{1}H NMR ($CDCl_3$) δ/ppm: 3.79 (s, 2H, O*H*) 4.19 (pt, $J = 1.9$ Hz, 4H, 2× C_5H_4), 4.22 (pt, $J = 1.9$ Hz, 4H, 2× C_5H_4), 4.39 (s, 4H, 2× CH_2). ^{13}C{^{1}H} NMR ($CDCl_3$) δ/ppm: 89.3 (C_{ipso}), 67.9 (Cp), 66.9 (Cp), 60.2 (CH_2). IR, neat, ν_{max}/cm^{-1}: 3276, 3081, 2935, 2858, 1197, 982.

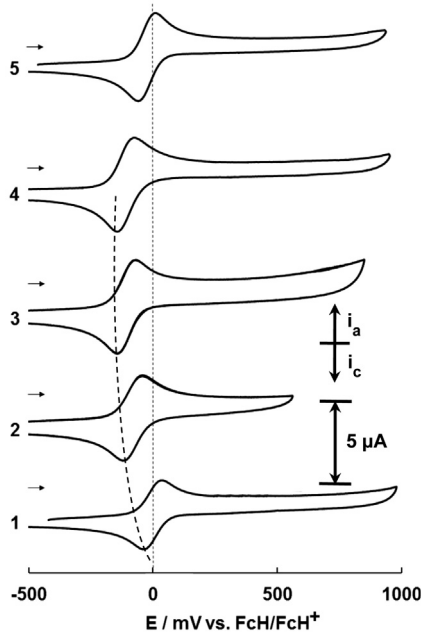


Fig. 4. CV's of complexes **1**–**5** at a scan rate of 100 mV s^{-1} utilising a glassy carbon working electrode in dichloromethane solutions (0.25 mmol L^{-1}) at 25 °C and a supporting electrolyte of 0.1 mol L^{-1} $[N^nBu_4][PF_6]$.

*4.2.2. 1,1′-Di(2-hydroxyethy1)ferrocene (**2**) via 1,1′-di(hydroxymethy1)ferrocene (**1**)*

Conversion of **1** to **2** takes place in four steps *via* the synthesis of 1,1′-di(chloromethyl)ferrocene, **12**, 1,1′-di(cyanomethyl)ferrocene, **13**, and ferrocenyl-1,1′-diacetic acid, **14**. Although the method was used before [29], neither full experimental details nor compound characterisation was provided. We adopted this procedure as follows:

*4.2.2.1. 1,1′-Di(chloromethyl)ferrocene (**12**).* A solution of **1** (5 g, 19.00 mmol) in dry (100 mL) THF containing pyridine (1 mL) was added to a solution of PCl_3 (2.5 g, 18 mmol) in THF (10 mL). After stirring for 3 h at room temperature the reaction mixture contained sufficient amounts of 1,1′-di(chloromethyl)ferrocene, **12**, to proceed with the synthesis of **13**, but **12** was not isolated due to its moderate stability. The reaction mixture containing **12** was thus transferred to a dropping funnel under an argon counter stream for use in the synthesis of 1,1′-di(cyanomethyl)ferrocene, **13**.

*4.2.2.2. 1,1′-Di(cyanomethyl)ferrocene (**13**).* In a 500 mL three-neck flask, KCN (15 g, 230 mmol) dissolved in water (30 mL; caution, HCN, b.p. 25.6 °C, may be evolved) was flushed with argon. Under rapid stirring the THF reaction mixture containing **12** was added dropwise at room temperature. The addition results in exothermic processes (e.g. water interacting with PCl_3) and may require occasional cooling in an ice bath to prevent thermal runaway that destroys **12**. The resulting mixture was stirred for a further hour before the THF layer was separated, washed with brine (3 × 50 mL), dried over $MgSO_4$ and after solvent removal, crude **13** is obtained as brownish crystals. Further purification by column chromatography utilizing hexane:dichloromethane = 1:1 v/v as eluent gives **13** ($R_f = 0.65$) as yellow crystals in 49% yield (2.6 g, 9.8 mmol), m.p.

68 °C. ^{1}H NMR ($CDCl_3$) δ/ppm: 4.31 (pt, J = 1.8 Hz, 4H, 2× C_5H_4), 4.28 (pt, J = 1.8 Hz, 4H, 2× C_5H_4), 3.47 (s, 4H, CH_2). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 118.1 (*C*N), 78.7 (C_{ipso}), 69.6 (Cp), 69.3 (Cp), 18.6 (CH_2). IR, neat, ν_{max}/cm^{-1}: 3140, 2260, 1408, 1300, 1237, 1041, 1029, 910.

*4.2.2.3. Ferrocene-1,1′-diacetic acid (**14**)* 1,1′-Di(cyanomethyl)ferrocene (2 g, 7.6 mmol) was dissolved in ethanol (10 mL) and NaOH (2 g, 50 mmol) dissolved in water (20 mL) was added in one portion. The reaction mixture was refluxed until the evolution of NH_3 had ceased (4 h). The mixture was allowed to cool to room temperature and then acidified with 20 mL ice cold 30% H_2SO_4. The fine yellow precipitate was collected by filtration, washed with water and dried under reduced pressure overnight to give **14** as a yellow crystalline solid in 97% (2.22 g, 7.35 mmol) yield, m.p. 169 (d) °C. Further recrystallization was not required. ^{1}H NMR (DMSO-d_6) δ/ppm: 12.19 (br s, 2H, COO*H*), 4.12 (s, 4H, 2× C_5H_4), 4.06 (s, 4H, 2× C_5H_4), 3.25 (s, 4H, CH_2). $^{13}C\{^1H\}$ NMR (DMSO-d_6) δ/ppm: 172.8 (*C*=O), 81.8 (C_{ipso}), 70.0 (Cp), 68.6 (Cp), 35.3 (CH_2). IR, neat, ν_{max}/cm^{-1}: 2906, 2256, 1705, 1685, 1401, 1327, 1294, 1239, 1211, 1158, 1401, 1022.

*4.2.2.4. 1,1′-Di(2-hydroxyethyl)ferrocene (**2**).* To a solution of **14** (1.75 g, 6.1 mmol) in THF (50 mL), $LiAlH_4$ (2.8 g, 7.3 mmol) was added in one portion and the mixture was refluxed overnight, allowed to cool to room temperature and quenched with water (10 mL). The water phase was extracted three times with dichloromethane, dried over $MgSO_4$ and after solvent removal the crude product was obtained as deep orange oil. Analytically pure **2** could be obtained in 99% yield (1.6 g; 5.84 mmol) by purification with column chromatography using dichloromethane/methanol in a ratio 98:2 as eluent (R_f = 0.35). ^{1}H NMR ($CDCl_3$) δ/ppm: 4.03 (br s, 8H, 2× C_5H_4), 3.67 (t, J = 6.6 Hz, 4H, C*H*$_2$–OH), 2.54 (t, J = 6.6 Hz, 4H, Cp–C*H*$_2$), 2.21 (br s, 2H, 2× O*H*). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 85.0 (C_{ipso}), 69.2 (Cp), 68.4 (Cp), 63.5 (*C*H$_2$OH), 32.7 (Cp-*C*H$_2$). IR, neat, ν_{max}/cm^{-1}: 3273, 3089, 2928, 2880, 1469, 1225, 1036, 805.

*4.2.3. 1,1′-Di(3-hydroxypropyl)ferrocene (**3**)*

1,1′-Di(3-hydroxypropyl)ferrocene, **3**, may be obtained from **9** in three steps *via* 1,1′-di[2-(ethyloxycarbonyl)ethenyl]ferrocene, **10**, and 1,1′-di[2-(ethyloxycarbonyl)ethyl]ferrocene, **11**.

*4.2.3.1. 1,1′-Di[2-(ethyloxycarbonyl)ethenyl]ferrocene (**10**).* After dissolving sodium (0.18 g, 8.16 mmol) in absolute ethanol (50 mL; caution, hydrogen is evolved), one equivalent of triethyl phosphonoacetate (1.62 mL, 8.16 mmol) followed by a solution of **9** (0.94 g, 3.88 mmol) in absolute ethanol (25 mL) was added dropwise at 0 °C. The mixture was allowed to warm up to room temperature and stirred for 1 h. Removal of the solvent followed by column chromatography (hexane:ether v/v 1:1) gave analytically pure **10** (R_f = 0.35) as a dark red crystalline solid in 80% (1.27 g, 3.1 mmol) yield w.r.t. **9**, m.p. 92–93 °C. ^{1}H NMR ($CDCl_3$) δ/ppm: 7.39 (d, J = 15.8 Hz, 2H, Cp–C*H*=CH), 5.96 (d, J = 15.8 Hz, 2H, Cp–CH=C*H*), 4.44 (pt, J = 1.8 Hz, 4H, 2× C_5H_4), 4.36 (pt, J = 1.8 Hz, 4H, 2× C_5H_4), 4.21 (q, J = 7.1 Hz, 4H, –C*H*$_2$–CH$_3$), 1.32 (t, J = 7.1 Hz, 6H, CH$_2$–C*H*$_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 166.9 (C=O), 143.7 (Cp–*C*H=CH), 116.2 (Cp–CH=*C*H) 79.9 (C_{ipso}),72.2 (Cp), 69.7 (Cp), 60.1 (CH_2), 14.2 (CH_3). IR, neat, ν_{max}/cm^{-1}: 3180, 2978, 2902, 1706, 1626, 1120, 1066.

*4.2.3.2. 1,1′ Di[2-(ethyloxycarbonyl)ethyl]ferrocene (**11**).* It was prepared according to a literature procedure [32] as follows: A solution of **10** (1.3 g, 3.15 mmol) and 10% palladium-on-charcoal (0.3 g, 2.82 mmol) in ethyl acetate (100 mL) was degassed under argon for 30 min. The mixture was then saturated with hydrogen, stirred vigorously for 72 h, filtered and the solvent removed under reduced pressure to give 1.2 g (99%) of **11** as a yellow oil. ^{1}H NMR ($CDCl_3$) δ/ppm: 4.06 (q, J = 7.16 Hz, 4H, 2O–C*H*$_2$–CH$_3$), 4.01 (br s, 8H, 2× C_5H_4), 2.59–2.72 (m, 4H, Cp–C*H*$_2$), 2.44–2.57 (m, 4H, C*H*$_2$–CO), 1.26 (t, J = 7.11 Hz, 6H, CH$_2$–C*H*$_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 172.7 (C=O), 87.4 (C_{ipso}), 68.4 (Cp), 68.1 (Cp), 60.1 (*C*H$_2$–CH$_3$), 35.7 (Cp-*C*H$_2$), 24.6 (*C*H$_2$–CO), 14.2(CH$_2$–*C*H$_3$). IR, neat, ν_{max}/cm^{-1}: 3160, 2978, 2902, 1684, 1178, 1086.

*4.2.3.3. 1,1′-Di(3-hydroxypropyl)ferrocene (**3**).* A solution of **11** (1.2 g, 3.12 mmol) in dry diethyl ether (10 mL) was added dropwise to a solution of $LiAlH_4$ (0.14 g, 3.70 mmol) in dry diethyl ether (10 mL). After 1 h of reflux, the mixture was allowed to cool to room temperature and hydrolysed by adding water (20 mL) drop by drop. The reaction mixture was acidified with concentrated HCl (3 mL) and extracted with diethyl ether (2 × 30 mL). The combined organic phases were washed with water and dried over $MgSO_4$. Removal of all volatiles at reduced pressure afforded **11** as a yellow oil in 78% yield (0.74 g). ^{1}H NMR ($CDCl_3$) δ/ppm: 4.00 (m, 8H, 2× C_5H_4), 3.66 (t, J = 6.36 Hz, 4H, 2× C*H*$_2$–OH), 2.41 (t, J = 8.20 Hz, 4H, 2× Fc–CH$_2$), 1.76 (m, 4H, 2× CH$_2$–C*H*$_2$–CH$_2$), 1.59 (bs, 2H, 2OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 89.0 (C_{ipso}), 69.1 (Cp), 68.3 (Cp), 62.9 (*C*H$_2$–OH), 34.5 (Cp–*C*H$_2$), 26.0 (CH$_2$–*C*H$_2$). IR, neat, ν_{max}/cm^{-1}: 3311, 3084, 2936–2866, 1444, 1033, 1018, 930, 909, 823, 804.

*4.2.4. 1,1′-Di(4-hydroxybutyl)ferrocene (**4**)*

Compound **4** was obtained in two steps from ferrocene and 1,1′-di(methyl-4-oxybutyrate)ferrocene, **7**, utilizing an adaptation of Navarro's procedure [32]:

*4.2.4.1. 1,1′-Di(methyl-4-oxybutyrate)ferrocene (**7**).* A solution of ferrocene (9.3 g, 50 mmol) in dry dichloromethane (75 mL) was added dropwise to an ice-cooled mixture of 3-(carbomethoxy) propionyl chloride (15 g, 100 mmol) [33] and $AlCl_3$ (26 g, 200 mmol) in dry dichloromethane (100 mL). The reaction mixture was heated for 2 h under reflux before being allowed to cool to room temperature. Stirring continued for an additional hour. The reaction mixture was poured onto ice (200 g), acidified with concentrated HCl (5 mL) and extracted with dichloromethane (3 × 100 mL). The combined organic phases were washed with water (3 × 50 mL), dried over anhydrous $MgSO_4$, filtered, and the solvent removed under reduced pressure. Crude **7** was purified by column chromatography utilizing hexane:diethyl ether = 1:3 v/v as eluent to afford pure **7** (R_f = 0.5) as a red crystalline solid, m.p. 103–104 °C, in 43% yield (8.9 g, 21.5 mmol) relative to ferrocene. ^{1}H NMR ($CDCl_3$) δ/ppm: 4.88 (pt, J = 1.95 Hz, 4H, 2× C_5H_4) 4.58 (pt, J = 1.95 Hz, 4H, 2× C_5H_4) 3.72 (s, 6H, –C*H*$_3$), 3.02 (t, J = 6.05 Hz, 4H, CO–CH$_2$–C*H*$_2$), 2.7 (t, J = 6.05 Hz, 4H, CO–C*H*$_2$–CH$_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 201 (C=O), 173 (COO), 79.5 (C_{ipso}), 73.4 (Cp), 70.4 (Cp), 51.4 (*C*H$_2$–COO), 34.1 (CO–*C*H$_2$), 27.9 (*C*H$_3$). IR, neat, ν_{max}/cm^{-1}: 3080, 3020, 2850, 1730, 1650, 1437, 1246, 1203, 905.

*4.2.4.2. 1,1′-Di(4-hydroxybutyl)ferrocene (**4**).* To an ice cold suspension of $LiAlH_4$ (623.2 mg, 16.4 mmol) in dry diethyl ether (10 mL), a suspension of $AlCl_3$ (2.39 g, 18 mmol) in dry diethyl ether (100 mL) was added slowly under an argon atmosphere. Compound **7** (1.7 g, 4.1 mmol) and $AlCl_3$ (2.04 g, 15.3 mmol) dissolved in dry diethyl ether (20 mL) was added and the mixture was stirred for 30 min at room temperature before being refluxed for 3 h. To the cooled solution, water (75 mL) followed by concentrated H_2SO_4 (3 mL) was added. The mixture was extracted with ether (3 × 200 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure to afford **4** as a yellow oil in 96% (1.30 g, 3.94 mmol) yield. ^{1}H NMR δ ($CDCl_3$) δ 3.98 (bs, 8H, 2× C_5H_4), 3.57 (t, J = 5.2 Hz, 4H, $\underline{CH_2}$–OH), 2.35 (t, J = 6.6 Hz, 4H, Fc–$\underline{CH_2}$), 1.58 (m, 8H, Fc–CH$_2$–*C*H$_2$–CH$_2$–OH), 1.37 (bs, 2H, OH). $^{13}C\{^1H\}$ NMR ($CDCl_3$) δ/ppm: 91.4 (C_{ipso}), 70.1 (Cp), 69.1 (Cp), 62.3 (*C*H$_2$–OH), 32.3 (Cp–*C*H$_2$), 28.6 and 27.1 (*C*H$_2$–*C*H$_2$). IR, neat, ν_{max}/cm^{-1}: 3334,

3084, 2931, 2858. If the $AlCl_3$ was not fresh (*i.e.* not optimally reactive) a chromatographic separation of **4** and **5** utilising first hexane:ether = 1:3 afforded **4** ($R_f = 0.15$), followed by elution with ethyl acetate allowed the isolation of **5** ($R_f = 0.66$; **5** does not elute in hexane:ether 1:3). Further characterisation of **5** is as per paragraph 4.2.5.

4.2.5. 1,1′-Bis(1,4-dihydroxybutyl)ferrocene (**5**)

$LiAlH_4$ (1.22 g, 32.1 mmol) in dry THF (40 mL) was stirred for 10 min and a solution of **7** (2.2 g, 5.3 mmol) in dry THF (15 mL) was added dropwise at such a rate as to maintain gentle THF reflux. The reaction mixture was stirred for 3–4 h at room temperature followed by cooling to 0 °C, quenching by slow addition of ice (5 g), and stirring for an additional 1 h. The reaction mixture was filtered and extracted with ether. After solvent removal, the residue was purified by column chromatography utilizing ethyl acetate as eluent to give the product as yellow oil in 95% yield. After three days the oil solidified. The crystals can be recrystallized from ethyl acetate, m.p. 158–159 °C. Elemental analysis (%): calc. for $C_{18}H_{26}O_4Fe$ (362.1): C, 59.7; H 7.2; found: C, 59.4; H 7.0. ^{1}H NMR ($CDCl_3$) δ/ppm: 4.72 (m, 2H, Fc–C*H*(OH)), 4.19–4.12 (m, 8H, 2× C_5H_4), 3.96–3.88 (m, 2H, CH_2–OH), 3.84–3.77 (m, 2H, CH_2–OH), 2.26–2.17 (m, 2H, –CH_2–), 2.02–1.89 (m, 6H, –CH_2–). ^{13}C{^{1}H} NMR ($CDCl_3$) δ/ppm: 93.9 (C_{ipso}), 93.6 (C_{ipso}), 69.9 (Cp), 69.2 (Cp), 67.6 (Cp), 67.5 (Cp), 67.4 (Cp), 66.7 (Cp), 66.1 (Cp), 65.7 (Cp), 62.5 (*C*H_2–OH), 37.3 (Cp–*C*H), 36.7 (Cp–*C*H), 29.1 and 28.9 (–*C*H_2–*C*H_2–). IR, neat, ν_{max}/cm^{-1}: 3284, 2941, 2859.

4.3. Single crystal X-ray crystallography

The reflection datasets were collected on a Bruker X8 Apex II 4K Kappa CCD diffractometer using the Apex2 software package [40]. The optimum measurement method to collect more than a hemisphere of reciprocal space was predicted by COSMO [41]. Frame integration and data reduction were performed using the SAINT-Plus and XPREP [42] software packages, and a multi-scan absorption correction was performed on the data using SADABS [43]. The structures were solved by the direct methods package SIR97 [44], and refinement using the WinGX [45] software package incorporating SHELXL [46]. All non H-atoms were refined anisotropically. All H-atoms were positioned geometrically and refined using the riding model with fixed C–H distances for aromatic C–H of 0.93 Å (CH) [U_{iso} (H) = 1.2 U_{eq}], for methylene 0.97 Å (CH) [U_{iso} (H) = 1.5 U_{eq}], for methine C–H of 0.98 Å (CH) [U_{iso} (H) = 1.5 U_{eq}] and for methyl C–H of 0.96 Å (CH) [U_{iso} (H) = 1.5 U_{eq}]. Molecular diagrams were drawn using the DIAMOND [47] package with a 50% thermal ellipsoid probability for non-hydrogen atoms. Table 1 summarises crystallographic data, the data collection parameters and the refinement parameters.

4.4. Electrochemistry

Cyclic voltammetric experiments were performed on ca. 0.25 mM solutions of **1**–**5** in dry dichloromethane/0.1 M [N^nBu_4][PF_6], utilizing a standard three-electrode cell, with a glassy carbon electrode of surface area 3.1 mm^2, a Pt-wire counter electrode and an Ag-wire reference electrode under argon at 25 °C connected to a Princeton Applied Research Parrstat 2273 advanced electrochemical system interfaced with a personal computer. The glassy carbon working electrode was pre-treated by polishing on a Buehler microcloth first with 1 micron and then with 1/4 micron diamond paste. All potentials presented in this study are referenced against FcH/FcH^+ as recommended by IUPAC [48]. However, because the ferrocene couple interferes with the ferrocenyl signals of **1**–**5**, each experiment was first performed in absence of any internal standard and then repeated in the presence of <0.5 mmol dm^{-3} decamethylferrocene (Fc^*) [49]. In a separate experiment only ferrocene and decamethylferrocene were measured under the identical conditions. Potentials were then manipulated in a spread sheet to allow potential reporting. Under the conditions of this study the Fc^*/Fc^{*+} couple was observed at −550 mV *vs.* FcH/FcH^+ or $E^{o'}$ = 670 mV *vs.* Ag wire, ipc/ipa = 0.99, ΔE_p = 73 mV.

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Appendix A. Supplementary material

CCDC 927232 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Appendix B. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2013.05.006.

References

[1] (a) A.J. Deeming, in: G. Wilkinson, F.G.A. Stone, E.W. Abel (Eds.), Comprehensive Organometallic Chemistry, vol. 8, Pergamon Press, Oxford, 1982, pp. 475–491;
(b) J.M. Osgerby, P.L. Pauson, J. Chem. Soc. (1961) 4604.
[2] W.G. Jary, A.-K. Mahler, T. Purkathofer, J. Baumgartner, J. Organomet. Chem. 629 (2001) 208.
[3] D. van Leusen, B. Hessen, Organometallics 20 (2001) 224.
[4] R. Sanders, U.T. Mueller-Westerhoff, J. Organomet. Chem. 512 (1996) 219.
[5] (a) D.E. Bublitz, K.L. Rinehart, Org. React. 17 (1975) 1;
(b) S.E. Creager, G.K. Rowe, J. Electroanal. Chem. 370 (1994) 203.
[6] V. Mamane, Mini Rev. Org. Chem. 5 (2008) 303.
[7] (a) W.C. Du Plessis, W.L. Davis, S.J. Cronje, J.C. Swarts, Inorg. Chim. Acta 314 (2001) 97;
(b) S. Otto, A. Roodt, J.J.C. Erasmus, J.C. Swarts, Polyhedron 17 (1998) 2447.
[8] (a) N.G. Connelly, W.E. Geiger, Chem. Rev. 96 (1996) 877;
(b) A. Auger, A.J. Muller, J.C. Swarts, Dalton Trans. (2007) 3623.
[9] A.R. Pike, L.C. Ryder, B.R. Horrocks, W. Clegg, B.A. Connolly, A. Houlton, Chem. Eur. J. 11 (2005) 344.
[10] (a) A. Hildebrandt, T. Rüffer, E. Erasmus, J.C. Swarts, H. Lang, Organometallics 29 (2010) 4900;
(b) K.C. Kemp, E. Fourie, J. Conradie, J.C. Swarts, Organometallics 27 (2008) 353.
[11] J.M. Speck, R. Claus, A. Hildebrandt, T. Rueffer, E. Erasmus, L. van As, J.C. Swarts, H. Lang, Organometallics 31 (2012) 6373.
[12] F. Spanig, C. Kolvacs, F. Hauke, K. Ohlubo, F. Fukuzumi, D.M. Guldi, A. Hirsch, J. Am. Chem. Soc. 131 (2009) 8180.
[13] (a) D. Saravanakumar, N. Sengottuvelan, V. Narayanan, M. Kandaswamy, T.L. Varghese, J. Appl. Polym. Sci. 119 (2011) 2517;
(b) H. Jungbluth, G. Lohmann, Nachr. Chem. Tech. Lab. 47 (1999) 534;
(c) P.J. Swarts, M. Immelman, G.J. Lamprecht, S.E. Greyling, J.C. Swarts, S. Afr. J. Chem. 50 (1997) 208.
[14] Q. Shen, S. Shekhar, J.P. Stambuli, J.F. Hartwig, Angew. Chem. Int. Ed. 44 (2005) 1371.
[15] V. Percec, L.-Y. Bae, D.H. Hill, J. Org. Chem. 60 (1995) 1060.
[16] J. Conradie, J.C. Swarts, Organometallics 28 (2009) 1018.
[17] T.G. Vosloo, W.C. du Plessis, J.C. Swarts, Inorg. Chim. Acta 331 (2002) 188.
[18] (a) R.F. Shago, J.C. Swarts, E. Kreft, C.E.J. Van Rensburg, Anticancer Res. 27 (2007) 3431;
(b) J.C. Swarts, T.G. Vosloo, S.J. Cronje, W.C. Du Plessis, C.E.J. Van Rensburg, E. Kreft, J.E. Van Lier, Anticancer Res. 28 (2008) 2781;
(c) I. Ott, K. Kowalski, R. Gust, J. Maurer, P. Mücke, R.F. Winter, Bioorg. Med. Chem. Lett. 20 (2010) 866;
(d) A. Gross, N. Hüsken, J. Schur, L. Raszeja, I. Ott, N. Metzler-Nolte, Bioconjug. Chem. 23 (2012) 1764.
[19] C.E.J. Van Rensburg, E. Kreft, J.C. Swarts, S.R. Dalrymple, D.M. Macdonald, M.W. Cooke, M.A.S. Aquino, Anticancer Res. 22 (2002) 889.
[20] (a) J.C. Swarts, D.M. Swarts, D.M. Maree, E.W. Neuse, C. La Madeleine, J.E. Van Lier, Anticancer Res. 21 (2001) 2033;
(b) J.T. Chantson, M.V.V. Falzacappa, S. Crovella, N. Metzler-Nolte,

J. Organomet. Chem. 690 (2005) 4564;
(c) M. Maschke, M. Lieb, N. Metzler-Nolte, Eur. J. Inorg. Chem. (2012) 5953.
[21] (a) R.D.A. Hudson, J. Organomet. Chem. 47 (2001) 637;
(b) A.S. Abd-El-Aziz, E.K. Todd, Coord. Chem. Rev. 246 (2003) 3.
[22] (a) H.R. Allcock, C. Kim, Macromolecules 24 (1991) 2846;
(b) E.W. Neuse, D.S. Trifan, J. Am. Chem. Soc. 85 (1963) 1952.
[23] (a) G. Wilbert, A. Wiesemann, R. Zentel, Macromol. Chem. Phys. 196 (1995) 3771;
(b) M. Vollmann, H. Butenschön, C. R. Chim. 8 (2005) 1282;
(c) T.E.O. Screen, J.R.G. Thorne, R.G. Denning, D.G. Bucknal, H.L. Anderson, J. Am. Chem. Soc. 124 (2002) 9712;
(d) S.C. Tenhaeff, D.R. Tyler, Organometallics 10 (1991) 473;
(e) E.H.L. Bunze, V. Enkelmann, F. Beer, Organometallics 14 (1995) 2490;
(f) I. Yamaguchi, K. Osakada, T. Yamamoto, M. Katada, Bull. Chem. Soc. Jpn. 72 (1991) 473;
(g) K. Gonsalves, L. Zhan-ru, M.D. Rausch, J. Am. Chem. Soc. 106 (1984) 3862.
[24] (a) B. Long, S. Liang, D. Xin, Y. Yang, J. Xiang, Eur. J. Med. Chem. 44 (2009) 2572;
(b) A.N. Patwa, S. Gupta, R.G. Gonnade, V.A. Kumar, M.M. Bhadbhade, K.N. Ganesh, J. Org. Chem. 73 (2008) 1508;
(c) J.M. Gibbs, S.-J. Park, D.R. Anderson, K.J. Watson, C.A. Mirkin, S.B.T. Nguyen, J. Am. Chem. Soc. 127 (2005) 1170.
[25] K. Yamakawa, M. Hisatome, J. Organomet. Chem. 52 (1973) 407.
[26] (a) U.T. Mueller-Westerhoff, Z. Yang, G. Ingram, J. Organomet. Chem. 463 (1993) 163;
(b) G.G.A. Balavoine, G. Doisneau, T. Fillebeen-Khan, J. Organomet. Chem. 412 (1991) 381.
[27] (a) P.J. Graham, R.V. Lindsey, G.W. Parshall, M.L. Peterson, G.M. Whitman, J. Am. Chem. Soc. 79 (1957) 3416;
(c) M. Rausch, M. Vogel, H. Rosenberg, J. Org. Chem. 22 (1957) 903;
(b) F.S. Arimoto, A.C. Haven, J. Am. Chem. Soc. 77 (1955) 6295.
[28] (a) D.W. Trifan, R. Bacskai, Tertrahedron Lett. 13 (1960) 1;
(b) P.L. Pauson, W.E. Watts, J. Chem. Soc. (1962) 3880;
(c) E.A. Hill, J.H. Richards, J. Am. Chem. Soc. 83 (1961) 3840;
(d) E.A. Hill, J.H. Richards, J. Am. Chem. Soc. 81 (1959) 3484.
[29] (a) T.B. Christensen, D. Riber, K. Daasbjerg, T. Skrydstrup, Chem. Commun. (1999) 2051;
(b) A. Ratajczak, B. Czech, L. Drobek, Synth. React. Inorg. Met. Org. Chem. 12 (1982) 557.
[30] C. Glidewell, B.J.L. Royles, D.M. Smith, J. Organomet. Chem. 527 (1997) 259.
[31] D. Lednicer, J.K. Lindsay, C.R. Hauser, J. Org. Chem. 23 (1958) 653.
[32] A.-E. Navarro, N. Spinelli, C. Moustrou, C. Chaix, B. Mandrand, H. Brisset, Nucleic Acids Res. 32 (2004) 5310.
[33] J. Cason, Org. Synth. 3 (1955) 169.
[34] The ^{1}H NMR spectrum of **5** was also collected in methanol-d_4 and pyridine-d_5 to establish if it was possible to separate the C$\underline{H}_2$–C$\underline{H}_2$ fragment signals in the expected ratio of 2:2, but these solvents did not disrupt the expected hydrogen bonds of 5 in such a way that a 2:2 integral ratio could be obtained. In addition to the chemical shifts reported in the experimental section for the solvent $CDCl_3$, the shifts in CD_3OD were: ^{1}H NMR (CD_3OD) δ/ppm: 4.79–4.72 (m, 2H, Fc–C*H*(OH)), 4.22–4.16 (m, 8H, 2× C_5H_4), 3.95–3.86 (m, 2H, CH_2–OH), 3.85–3.77 (m, 2H, CH_2–OH), 2.33–2.25 (m, 2H, –CH_2–), 2.07–1.96 (m, 6H, –CH_2–). In pyridine-d_5 the shifts were: ^{1}H NMR (pyridine-d_5) δ/ppm: 4.81–4.78 (m, 2H, Fc–C*H*(OH)), 4.36 (s, 2H, C_5H_4), 4.30 (s, 2H, C_5H_4), 4.23 (s, 4H, C_5H_4), 3.93–3.91 (m, 2H, CH_2–OH), 3.79–3.77 (m, 2H, CH_2–OH), 2.16–2.11 (m, 2H, –CH_2–), 1.91–1.79 (m, 6H, –CH_2–).
[35] (a) J.J.C. Erasmus, G.J. Lamprecht, J.C. Swarts, A. Roodt, A. Oskarsson, Acta Cryst. C52 (1996) 3000;
(b) G.J. Lamprecht, J.C. Swarts, J. Conradie, J.G. Leipoldt, Acta Cryst. C49 (1993) 82.
[36] M.B. Smith, J. March, March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, fifth ed., John Wiley and Sons, New York, 2001, pp. 20–36.
[37] (a) D.H. Evans, K.M. O'Connell, R.A. Peterson, M.J. Kelly, J. Chem. Educ. 60 (1983) 291;
(b) P.T. Kissinger, W.R. Heineman, J. Chem. Educ. 60 (1983) 702;
(c) H.J. Gericke, N.I. Barnard, E. Erasmus, J.C. Swarts, M.J. Cook, M.A.S. Aquino, Inorg. Chim. Acta 363 (2010) 2222;
(d) E. Fourie, J.C. Swarts, I. Chambrier, M.J. Cook, Dalton Trans. (2009) 1145;
(e) J.J. Van Benshoten, J.Y. Lewis, W.R. Heineman, J. Chem. Educ. 60 (1983) 772.
[38] D. Braga, L. Maini, F. Paganelli, E. Tagliavini, S. Casolari, F. Grepioni, J. Organomet. Chem. 637-639 (2001) 609.
[39] W.L. Davis, R.F. Shago, E.H.G. Langner, J.C. Swarts, Polyhedron 24 (2005) 1611.
[40] Bruker, Apex2 (Version 2011. 4-1), Bruker AXS Inc., Madison, Wisconsin, USA, 2011.
[41] Bruker, COSMO (Version 1.58), Bruker AXS Inc., Madison, Wisconsin, USA, 2007.
[42] Bruker, SAINT-plus (Version 7.68) (Including XPREP), Bruker AXS Inc., Madison, Wisconsin, USA, 2008.
[43] Bruker, SADABS (Version 2008/1), Bruker AXS Inc., Madison, Wisconsin, USA, 2008.
[44] A. Altomare, M.C. Burla, M. Camalli, G.L. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, G. Polidori, R. Spagna, J. Appl. Cryst. 32 (1999) 115.
[45] L.J. Farrugia. WinGX, J. Appl. Cryst. 32 (1999) 837.
[46] G.M. Sheldrick, SHELXL97. Program for Crystal Structure Refinement, University of Göttigen, Germany, 1997.
[47] K. Brandenberg, H. Putz, DIAMOND, Release 3.0c, Crystal Impact GbR, Bonn, Germany, 2005.
[48] G. Gritzner, J. Kuta, Pure Appl. Chem. 56 (1984) 461.
[49] Leading references describing the electrochemical activity and behaviour of ferrocene and decamethylferrocene in a multitude of organic solvents are: (a) I. Noviandri, K.N. Brown, D.S. Fleming, P.T. Gulyas, P.A. Lay, A.F. Masters, L. Phillips, J. Phys. Chem. B 103 (1999) 6713;
(b) M.J. Cook, I. Chambrier, G.F. White, E. Fourie, J.C. Swarts, Dalton Trans. (2009) 1136;
(c) J. Ruiz, D. Astruc, C.R. Acad. Sci. Ser. IIc Chim. 1 (1998) 21;
(d) R.J. Aranzaes, M.C. Daniel, D. Astruc, Can. J. Chem. 84 (2006) 288.