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A new synthesis and electrochemistry of 1,1'-bis(β-hydroxyethyl)ferrocene

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ABSTRACT

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1. Introduction

Ferrocene and its derivatives have been extensively studied since ferrocene was first discovered [1,2]. One of the properties of ferrocene derivatives that has been widely examined is the redox potential of the iron center in ferrocene derivatives [3]. Of particular interest are the heteroannularly disubstituted derivatives of ferrocene, for example, 1,1'-bis(diphenylphosphino)ferrocene (dppf) [4]. The redox potentials of these compounds are sensitive to the electronic nature of the groups bound to the ferrocene backbone [5]. The synthesis and subsequent reactions of 1,1'-dilithio-ferrocene are among the primary reasons that a wide array of groups can be bound to a ferrocene backbone [6].

While the 1,1'-bis(β -dihydroxyethyl) derivative of ferrocene (1) had been reported previously, it was somewhat surprising to discover that there were no synthetic routes that employed 1,1'-dilithioferrocene. The first reported synthesis of 1 required the initial synthesis of C₅H₅CH₂CH₂OH from lithium cyclopentadienide and ethylene oxide [7]. The C₅H₅CH₂CH₂OH was then purified by fractional distillation, reacted with butyl lithium and iron(II) chloride to give 1 in 19% yield. The second reported preparation, albeit with limited detail, involves the reduction of 1,1'-ferrocenediacetic acid [8]. A third synthetic method uses 1,1'-bis(hydroxymethyl)ferrocene as the starting material, and after reaction with phosphorus trichloride, potassium cyanide and lithium aluminum hydride, yields 1 in 56% [9]. An additional report in which 1 is obtained from an unpublished synthesis has also been made [10]. The final reported synthesis requires seven steps from ferrocene, one of which

requires the use of potassium cyanide, and gives **1** in a 22% yield from the initial ferrocene [11].

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In this report, the synthesis of **1** is carried out in three steps from ferrocene. The potential at which oxidation of **1** was determined and used to estimate the Hammett parameter for the – CH_2CH_2OH group. In addition, the synthesis, ¹H NMR and electrochemistry of (C_5H_4CHO)Fe(C_5H_4CH =CH₂) are presented.

2. Experimental

2.1. General procedures

The preparation of 1,1'-bis(β -hydroxyethyl)ferrocene (1) by oxidation of 1,1'-divinylferrocene is

described. Compound 1 has been characterized by ¹H and ¹³C{¹H} NMR, and cyclic voltammetry. The elec-

trochemical data are compared to ferrocene and the closely related 2-ferrocenylethanol, 2.

Preparative reactions and purifications were carried out using standard Schlenk techniques under an atmosphere of argon. Tetrahydrofuran (THF), hexanes, diethyl ether (Et₂O), and methylene chloride (CH₂Cl₂) were purified using a Solv-Tek solvent purification system similar to one previously described [12]. Ph₃PMeBr, Ph₃PMeI, dibenzo-18-crown-6, 1-formylpiperidene and BH₃ · THF (1.0 M in THF) were purchased from Aldrich. Tetramethylethylenediamine (TMEDA) was purchased from Aldrich and distilled prior to use. Ferrocene and decamethylferrocene were purchased from Strem. Electrochemical experiments were performed using HPLC grade CH₂Cl₂ distilled from CaH₂ under an argon atmosphere prior to use. Tetrabutylammonium hexafluorophosphate $([NBu_4]^+[PF_6]^-])$ was purchased from Aldrich and dried under vacuum prior to use. The ¹H and ¹³C{¹H} NMR spectra were obtained in CDCl₃ and recorded using a JOEL Eclipse 400 FT-NMR. The internal standard for ¹H and ¹³C{¹H} NMR data acquisition was TMS (δ 0.00 ppm). Microanalysis was performed by QTI.

2.2. Synthesis of ferrocene-1,1'-dicarbaldehyde (2)

Ferrocene (10.0038 g, 53.8 mmol) was suspended in 120 mL of hexanes and 67.2 mL of 1.6 M *n*-butyllithium in hexane



Note



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(107.5 mmol) were added. TMEDA (8.4 mL, 55.7 mmol) was added dropwise to the mixture; the reaction was stirred at room temperature for 14 h. A solution of 1-formylpiperidine (12 mL, 104.1 mmol) in 20 mL of diethyl ether was added dropwise and the reaction was allowed to stir for 30 min producing a deep red solution. The solution was extracted with deionized water (3×100 mL). The aqueous layer was then extracted with CH₂Cl₂ (4×100 mL). The CH₂Cl₂ layer was subsequently washed with 0.1 M aqueous HCl (2×100 mL) to remove unreacted 1-formylpiperidine, dried over MgSO₄, and filtered. The volume of the solution was then reduced to approximately 10 mL. The product was purified by column chromatography on silica gel using a mixture of CH₂Cl₂ and hexanes (v:v, 1:1) as the eluent. The solvent was removed *in vacuo* giving **2** as a dark red solid in an 80% yield. Spectral data agreed with the literature values [13].

2.3. Synthesis of divinylferrocene (3)

A mixture of Ph₃PMeBr (12.1559 g, 34.0 mmol), KO^rBu (3.8178 g, 34.0 mmol), and a catalytic amount of dibenzo-18crown-6 (0.0315 g, 0.09 mmol) was dissolved in 45 mL of THF and stirred for 30 min at room temperature. To this mixture, a solution of **2** (4.1183 g, 17.0 mmol) in 80 mL of THF was added over 10 min. The resulting dark red-brown solution was stirred for 14 h. Deionized water (80 mL) was added to the reaction mixture, and the solution was stirred for 10 min. The reaction was extracted with Et₂O (2 × 100 mL), and the organic layer was dried over Na₂SO₄. The solution was filtered, and the volume was reduced to approximately 5 mL. The resulting oil was purified by column chromatography on silica gel, and the product was eluted with hexanes. The solution was dried *in vacuo*, yielding **3** as a bright orange solid in a 63% yield. The ¹H NMR spectra were identical to literature values [13].

2.4. Synthesis of 1,1'-bis(β -hydroxyethyl)ferrocene (**1**)

Compound **3** (0.1763 g, 0.74 mmol) was dissolved in 10 mL of THF. BH₃ · THF (2.25 mL, 2.25 mmol) was added dropwise, and the solution stirred for 1 h. The reaction mixture was dried *in vacuo*, and 5 mL of THF were added. H₂O₂, 30% by wt. (0.2200 mL, 2.15 mmol) in 0.78 mL of 3 M NaOH was added and the reaction mixture was stirred for 30 min. The reaction was extracted with CH₂Cl₂ (2 × 50 mL) and dried over Na₂SO₄. The product was purified by column chromatography on silica gel, and **1** eluted with acetone. Compound **1** was isolated as an orange oil after removing solvent *in vacuo* and was obtained in a yield of 44%. Numerous attempts at growing crystals suitable for single crystal X-ray analysis were unsuccessful. ¹H NMR (CDCl₃): δ 4.03 (s, 8H, C₅H₄-), 3.67 (t, *J* = 6.6 Hz, 4H, -CH₂OH), 2.54 (t, *J* = 6.6 Hz, 4H, C₅H₄-CH₂-), 2.21 (br s, 2H, -OH). ¹³C{¹H} NMR (CDCl₃): δ 85.0 (s, *ipso*), 69.2 (s, C₅H₄), 68.4 (s, C₅H₄), 63.5 (s, -CH₂OH), 32.7 (s, C₅H₄-CH₂-).

2.5. Synthesis of 1-vinyl-1'-carboxaldehydeferrocene (4)

Compound **2** (0.8114 g, 3.35 mmol) was dissolved in 5 mL of benzene with Ph₃PMeI (2.0215 g, 4.98 mmol). To this mixture, 25% NaOH (9 mL, 75.0 mmol) was added and the reaction was stirred vigorously for 2 h. The reaction was extracted with Et₂O (50 mL) and the organic layer was washed with 20% K₂CO₃ (2 × 40 mL) and deionized water (3 × 100 mL). The organic layer was then dried over Na₂SO₄ and the product was purified by column chromatography on silica gel. The product was eluted with a mixture of CH₂Cl₂ and hexanes (v:v, 4:1). The solvent was removed *in vacuo* leaving a deep-red oil. ¹H NMR (CDCl₃): δ 9.87 (s, 1H, –CHO), 6.33 (dd, *J* = 17.2 and 10.6 Hz, 1H, –CH=CH₂), 5.38 (d, J = 17.2 Hz, 1H, –CH=CH₂), 5.13 (d, J = 10.6 Hz, 1H, –CH=CH₂),

4.71 (s, 2H, C_5H_4 -), 4.53 (s, 2H, C_5H_4 -), 4.44 (s, 2H, C_5H_4 -), 4.31 (s, 2H, C_5H_4 -). *Anal.* Calc. for $C_{13}H_{12}$ FeO: C, 65.04; H, 5.04. Found: C, 64.80; H, 4.64%.

2.6. Electrochemistry

All cyclic voltammetric measurements were conducted using a Princeton Applied Research 263-A potentiostat. Solutions used in analysis were kept under an atmosphere of argon throughout the experiments. A three-electrode configuration was used consisting of a 1.5 mm glassy-carbon working electrode, a platinum wire counter electrode, and a non-aqueous Ag/AgCl electrode, separated from the solution by a glass frit, as the reference electrode. Prior to use, the working electrode was polished with 1 µm diamond paste followed by 0.25 µm diamond paste. The electrode was rinsed with acetone after each polishing and rinsed with CH₂Cl₂ before experiments.

The oxidative electrochemistry of **1** and **4** was investigated in CH_2Cl_2 using 0.10 M ([NBu₄]⁺[PF₆]⁻]) as the supporting electrolyte. The analyte concentration was 1.0 mM, and experiments were conducted at scan rates at 50 mV/s and from 100 to 1000 mV/s at 100 mV/s increments. The electrochemical potentials were collected using Power Suite from Princeton Applied Research, and all data were collected at ambient temperature ($22 \pm 1 \,^{\circ}$ C). Decamethylferrocene was added toward the end of the experiment as an internal standard, and the analyte potential was referenced to ferrocene by subtracting 0.548 V [14].

3. Results and discussion

3.1. Synthesis

A new synthesis of **1** was carried out by hydroboration–oxidation of **3** with $BH_3 \cdot THF$ and H_2O_2 (Scheme 1). Compounds **2** and **3** were prepared using modifications of literature procedures [13]. Previous syntheses of **1** have characteristically involved many steps and low overall yields [7–11]. The new route presented herein gives **1** in three steps and an overall 22% yield from ferrocene.

While optimizing the conditions for the formation of **3**, alternate routes to generate **3** from **2** were examined. Based on the literature reaction of ferrocenecarbaldehyde with Ph₃PMeI and 25% NaOH in benzene to give vinylferrocene [15], a similar reaction was attempted using **2** and appropriately scaled amounts of Ph₃PMeI and 25% NaOH. However, these reactions would only yield the asymmetric compound **4**. The reaction of **4** with excess Ph₃PMeI in refluxing benzene did not produce **3**.

3.2. Electrochemistry

Cyclic voltammetry was used to determine the potential at which oxidation of 1 and 4 occur in CH₂Cl₂. The potentials at which oxidation occurred were measured for each compound and are listed in Table 1. A single reversible, one-electron wave was observed in the oxidative electrochemistry of both 1 and 4 (Fig. 1). The electrochemistry of 1 has been investigated previously in aqueous solution [16] and in a polymer electrolyte [17].

In comparing the potential at which oxidation of **1** occurs to that of the closely related 2-ferrocenylethanol [18], there is an excellent correlation between the potential and the number of – CH₂CH₂OH groups. For 1,1'-disubstituted ferrocenes, the Hammett parameter (σ_p) for the substituent is correlated with the potential at which oxidation occurs (E_L where $E_L = 1/2E^\circ$ versus NHE) [5]. Based on Eq. (1) and the potential at

$$E_{\rm L} = 0.45\sigma_{\rm p} + 0.36\tag{1}$$

which oxidation of **1** occurs, the σ_p for the $-CH_2CH_2OH$ substituent was calculated to be -0.17. The calculated σ_p value for $-CH_2CH_2OH$



Scheme 1. Synthesis of 1 from ferrocene.

Table 1

Electrochemical data for compounds 1-5 (in DCM)

Compound	E^{0} (V) vs. FcH ^{0/+}
$Fe(C_5H_4CH_2CH_2OH)_2 (1)$	-0.09
CpFeC ₅ H ₄ CH ₂ CH ₂ OH	-0.05 ^a
$Fe(C_5H_4CHO)_2$	0.56 ^b
$Fe(C_5H_4CH=CH_2)_2$	0.04 ^b
$Fe(C_5H_4CHO)(C_5H_4CH=CH_2) (4)$	0.30

^a Ref. [18].

^b Ref. [5].



Potential (V vs.FcH^{0/+})

Fig. 1. Cyclic voltammogram of 1 measured at 50 mV/s in a 1.0 mM solution of the analyte in CH_2Cl_2 with $[NBu_4]^*[PF_6]^-$ (0.1 M) as the supporting electrolyte.

was identical to that reported for the group $-CH_2CH(OH)Me$ [19].

The potential at which oxidation of **4** occurs was also determined and compared to the literature values of 1,1'-divinylferrocene and 1,1'-ferrocenedialdehyde. The E^0 value for asymmetric 1,1'-disubstituted ferrocenes can be estimated using the E_L values

for the individual substituents [5]. Based on the $E_{\rm L}$ values for – CHO and –CH=CH₂, the calculated potential for the oxidation of **4** is 0.30 V versus FcH^{0/+}, which is in good agreement with the experimental value. However, using Eq. (1) and the average of the $\sigma_{\rm p}$ values for –CHO (0.42) and –CH=CH₂ (–0.04) [19], the estimated E^0 for **4** is 0.23 V versus FcH^{0/+}, which suggest that Eq. (1) is not a valid means of estimating the potential at which oxidation of asymmetric 1,1'-disubstituted ferrocenes occurs.

4. Conclusions

A new synthesis of **1** has been developed in three steps from ferrocene. All three steps proceed in reasonable yield. The potentials at which oxidation of **1** and **4** occur in CH_2Cl_2 were determined by cyclic voltammetry. The effect on the potentials of the substituents on ferrocene is as expected.

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