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ORIGINAL PAPER

Synthesis and Characterization of Monomeric and Dimeric Structures of Calix[4]arenes Containing Amidoferrocene

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Abstract The reaction of 1,1′-bis(chlorocarbonyl) ferrocene with bis-aminobenzylcalix[4]arene gave amidoferrocene calix[4]arene monomer **1**. Compound **1** crystallized in the monoclinic system P21/c with $a = 11.196(6)$ Å, $b = 14.971(11)$ Å, $c = 32.007(2)$ Å, $\beta = 96.413(4)^\circ$ and $V = 5330.9(6)$ Å^3. X-ray diffraction analyses of **1** showed that the calix[4]arene scaffold was in cone conformation in which the intramolecular hydrogen bonding were formed through OH groups at the lower rim to stabilize the structure. Moreover, the intramolecular hydrogen bond between the amide groups of the amidoferrocene unit also presented in the crystal structure. On the other hand, the condensation of 1,1′-bis(chlorocarbonyl)ferrocene with *p-tert*-bis-aminobenzylcalix[4]arene resulted in the monomeric **2** and [2 + 2] dimeric compounds **3**. ^{1}H-NMR studies signified that the calix[4]arene building block in compounds **2** and **3** adopted the cone conformation.

Keywords Metallocene · Amidoferrocene · Calix[4]arene

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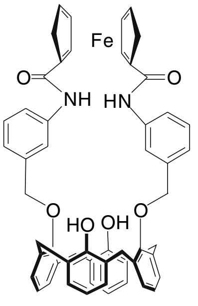
Introduction

Calixarenes are synthetic macrocycles used as building blocks in nanotechnology and supramolecular chemistry [1]. They were also used as molecular scaffolds for the preparation of novel selective receptors for ions and neutral molecules [2]. Moreover, calix[4]arene bearing a sensory unit have been attracted much chemist's attention in recent years owing to possible applications as chemical sensors [3–5]. For example, calixarenes functionalized with the amidoferrocene group have been shown to be very effective electrochemical sensors for cations [6–8] anions [9–12] and neutral molecules [13–14]. Herein, we report the synthesis and characterization of calix[4]arenes containing amidoferrocene units **1–3** including the crystal structure of **1** determined by X-ray diffraction analysis.



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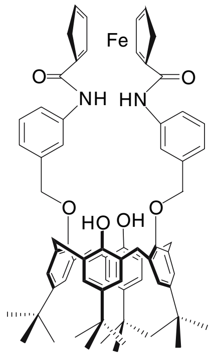

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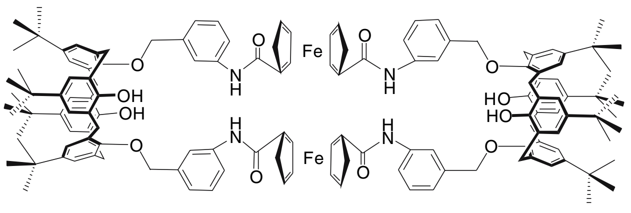

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Experimental

All reagents were of reagent grade and were used without further purification unless stated otherwise. ^{1}H-NMR, ^{13}C-NMR and 2D-NMR spectra were record in DMSO-d_6 on a BRUKER AVANCE 400 NMR spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 CHN elemental analyzer.

Synthesis of compound **1**

bis-*Nitrobenzylcalix[4]arene (**a**)*

Calix[4]arene (0.50 g, 1.20 mmol), K_2CO_3 (0.162 g, 1.20 mmol) and a catalytic amount of KI in 50 mL of dry acetonitrile were stirred at room temperature for 30 min under N_2. The solution of 3-nitrobenzylchloride (0.50 g, 2.90 mmol) in 30 mL of dried acetonitrile was then added dropwise and the solution mixture was refluxed for 24 h. After cooling to room temperature, the solvent was evaporated in vacuo and the residue was dissolved in CH_2Cl_2 (100 mL). The organic layer was washed with 3 M HCl (2 × 100 mL) and water (2 × 100 mL). The organic layer was dried with anhydrous $MgSO_4$ and filtered. The solvent was removed under a reduced pressure to obtain a residue. Purification by SiO_2 column chromatography using a mixture of CH_2Cl_2/hexane (1:1) as eluent gave *bis*-nitrobenzylcalix[4]arene (**a**) as a white powder (0.52 g, 63%).

bis-*Aminobenzylcalix[4]arene (**b**)*

Reduction of the *bis*-nitrobenzylcalix[4]arene (**a**) to *bis*-aminobenzylcalix[4]arene was carried out using Raney Nickel and hydrazine. Hydrazine (2.28 mL, 46 mmol) was added to the solution mixture of *bis*-nitrobenzylcalix[4]arene (0.50 g, 0.72 mmol) and Raney Nickel (0.376 g, 6.5 mmol) in the mixture of ethyl acetate:methanol (15:11 mL) under N_2 atmosphere. The solution was heated at 60 °C for 1 h. After cooling to room temperature, the solution was filtered and the solvent was evaporated. The residue was dissolved in 50 mL of CH_2Cl_2 and washed with water (2 × 50 mL). The organic layer was then dried with anhydrous $MgSO_4$, filtered and the solvent was evaporated to give *bis*-aminobenzylcalix[4]arene (**b**) in a quantitative yield.

*Compound (**1**)*

Compound **b** (0.40 g, 0.60 mmol) was reacted with 1,1′-*bis*(chlorocarbonyl)ferrocene (0.19 g, 0.60 mmol) in the presence of triethylamine (0.26 mL, 1.50 mol) in dried CH_2Cl_2 and the solution was stirred at room temperature for 4 h under N_2. The organic layer was washed with water (3 × 100 mL), dried with anhydrous $MgSO_4$ and filtered. The solvent was removed under reduced pressure. The residue was purified by SiO_2 column chromatography using CH_2Cl_2:EtOAc (2:1) as eluant to obtain compound **1** as an orange powder in 0.135 g (25% yield). Orange crystals of **1** suitable for X-ray structural investigations were obtained by slow evaporation of the solution of **1** in $CHCl_3$. ^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.49 (s, 2H, NH), 8.19 (s, 2H, O*H*), 8.10 (s, 2H, Ar*H*), 7.75 (d, 2H, Ar*H*), 7.32 (t, 2H, Ar*H*), 7.18 (d, 2H, Ar*H*), 7.08 (d, 4H, Ar*H*), 6.95 (d, 4H, Ar*H*), 6.82 (t, 2H, Ar*H*), 6.65 (t, 2H, Ar*H*), 5.01 (s, 4H, –OCH_2–), 4.86 (s, 4H, Cp*H*), 4.55 (s, 4H, Cp*H*), 4.32 (d, $J = 12$ Hz, AB system, Ar–CH_2–Ar), 3.95 (d, $J = 12$ Hz, AB system, Ar–CH_2–Ar). ESI-MS (positive mode) *m*/*z*: 873.34 $[M + H]^+$. Analysis calculated for $C_{54}H_{44}FeN_2O_6$: C 74.31, H 5.08, N 3.21%; found: C 74.35, H 5.10, N 3.25%.

Synthesis of Compounds **2** and **3**

p-tert-*Butyl*-bis-*nitrobenzylcalix[4]arene (**c**)*

A mixture of *p-tert*-butyl-calix[4]arene (2.00 g, 3.13 mmol), K_2CO_3 (0.435 g, 3.13 mmol) and a catalytic amount of KI in 50 mL of dried acetonitrile was stirred at room temperature under N_2 for 30 min. The solution of 3-nitrobenzylchloride (1.31 g, 7.63 mmol) in 30 mL of dried acetonitrile was added dropwise and the solution mixture was refluxed for 24 h. The solvent was evaporated in vacuo and CH_2Cl_2 (100 mL) was added. The organic phase was washed with 3 M HCl (2 × 100 mL) and water (2 × 100 mL). The organic layer was dried with anhydrous $MgSO_4$ and filtered. The solvent was removed to give crude **c**. The crude product was placed on a silica gel column using 30% Hexane:CH_2Cl_2 as eluant to obtain compound **c** as a white powder (1.982 g, 69%).

p-tert-*Butyl*-bis-*aminobenzylcalix[4]arene (**d**)*

Compound **c** (0.67 g, 0.73 mmol) and Raney Ni (0.42 g, 7.30 mmol) were suspended in a mixture of ethylacetate 15 mL and MeOH 11 mL under N_2. Subsequently, hydrazine (2.3 mL, 47 mmol) was added and the mixture was heated at reflux for 2 h. The unreacted Raney Ni was removed while the solution was still warm and the filtrate was removed under reduce pressure. The crude product was then dissolved in CH_2Cl_2 50 mL and washed with water (3 × 50 mL). The organic layer was separated and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo to obtain compound **d** as a white solid in a quantitative yield.

*Compounds (**2**) and (**3**)*

To a stirred solution of compound **d** (0.67 g, 0.73 mmol) and triethylamine (0.26 mL, 1.83 mmol) in 150 mL of CH_2Cl_2 was added a solution of 1,1′-*bis*(chlorocarbonyl)ferrocene (0.23 g, 0.73 mmol) in dichloromethane (20 mL). The solution was stirred at room temperature for 4 h. The solution was subsequently washed with water (2 × 100 mL) and the organic layer was dried over anhydrous Na_2SO_4. The solvent was removed by a rotary evaporator to give a red oily residue which was purified by column chromatography (SiO_2) using 20% EtOAc:CH_2Cl_2 as eluent. The orange solid of monomeric compound **2** ($R_f = 0.65$) (0.16 g, 22%) and dimeric compound **3** ($R_f = 0.78$) (0.24 g, 5%) were obtained.

*Compound (**2**)*

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.60 (s, 2H, NH), 8.08 (s, 2H, O*H*), 7.76 (s, 2H, Ar*H*), 7.67 (d, 2H, *J* = 6.4 Hz, Ar*H*), 7.28 (t, 2H, *J* = 7.2 Hz, Ar*H*), 7.17 (d, 2H, *J* = 7.6 Hz, Ar*H*), 7.03 (s, 4H, Ar*H*), 6.90 (s, 4H, Ar*H*), 4.95 (s, 4H, –OC*H*$_2$–), 4.87 (s, 4H, Cp*H*), 4.50 (s, 4H, Cp*H*), 4.27 (d, *J* = 13.2 Hz, AB system, Ar–C*H*$_2$–Ar), 3.31 (d, *J* = 12.8 Hz, AB system, Ar–C*H*$_2$–Ar), 1.26 (s, 18H, Ar–C*H*$_3$), 1.05 (s, 18H, Ar–CC*H*$_3$). ESI-MS (positive mode) *m*/*z*: 1154.24 $[M + H_2O + K]^+$. Analysis calculated for $C_{70}H_{76}FeN_2O_6$: C 76.63, H 6.98, N 2.55%; found: C 76.65, H 7.01, N 2.53%.

*Compound (**3**)*

^{1}H-NMR (400 MHz, $CDCl_3$, ppm): δ 8.85 (br, s, 2H, NH), 8.16 (br, s, 2H, Ar*H*), 8.03 (br, s, 2H, Ar*H*), 7.70 (br, s, 2H, O*H*), 7.43 (br, s, 2H, Ar*H*), 7.28 (br, s, 2H, Ar*H*), 7.13 (s, 4H, Ar*H*), 6.88 (s, 4H, Ar*H*), 5.05 (s, 4H, –OC*H*$_2$–), 4.56 (s, 4H, Cp*H*), 4.40 (s, 4H, Cp*H*), 4.39 (d, *J* = 12.0 Hz, AB system, Ar–C*H*$_2$–Ar), 3.39 (d, *J* = 11.6 Hz, AB system, Ar–C*H*$_2$–Ar). ^{13}C-NMR (400 MHz, $CDCl_3$, ppm): δ 168.98, 150.64, 149.52, 147.33, 141.87, 139.08, 137.89, 132.62, 129.89, 127.83, 125.66, 125.19, 121.71, 118.98, 117.34, 71.39, 71.03, 31.73, 31.01. ESI-MS (positive mode) *m*/*z*: 2212.03 $[M + H_2O + H]^+$. Analysis calculated for $C_{140}H_{152}Fe_2N_4O_{12}$: C 76.63, H 6.98, N 2.55%; found: C 76.66, H 6.96, N 2.57%.

X-ray Crystal Structure Determination

X-ray diffraction measurement for **1** was performed on a Bruker–Nonius Kappa CCD diffractometer with graphite-monochromated Mo-Kα radiation ($\lambda = 0.7107$ Å). The data collection was performed on COLLECT program [15]. Crystal cell refinement and data reduction were carried out using HKL DENZO and SCALEPACK [16]. The structures were solved by direct method and were refined on F^2 by full-matrix least-squares technique using the SHELXL-97 [17] program on WinGX package [18]. Crystal data, data collection parameters and structure refinement details are given in Table 1. During the last stage of the refinement, disorder on chlorine atoms of chloroform in the structure of **1** was found. The disorder was modeled with two equally weighted sets of chlorine atoms. The non-H atoms were refined with anisotropic displacement thermal

Table 1 Crystallographic data and final refinement parameters for (**1**)

	(**1**)
Chemical formula	$C_{56}H_{46}Cl_6N_2FeO_6$
Molecular weight	1111.49
Color	Orange
Size (mm^3)	0.284 × 0.203 × 0.113
Temperature (K)	293(2) K
Crystal system	Monoclinic
Space group	$P2_1/c$
a (Å)	11.1960 (6)
b (Å)	14.9700 (11)
c (Å)	32.007 (2)
α (°)	90
β (°)	96.413 (4)
γ (°)	90
V (Å)^3	5330.9 (6)
Z	4
F(000)	2284
D_{calc} (g cm^{-3})	1.384
μ (mm^{-1})	0.635
θ range for data collection	2.11–21.92^0
Index ranges	$-10 \le h \le 11$ $-15 \le k \le 14$ $-33 \le l \le 31$
Reflections collected/observed	15388/5976 [*R*(int) = 0.0783]
Data/restraints/parameters	5976/0/704
Goodness-of-fit on F^2	1.006
Final *R* indices [$I > 2\sigma(I)$]	*R*1 = 0.0740, *wR*2 = 0.1711
R indices (all data)	*R*1 = 0.1326, *wR*2 = 0.2084
Largest diff. peak and hole (e − Å^{-3})	0.358, −0.234

parameters at the latter stages of refinement. All hydrogen atoms (except H22, H27 and H45) are placed in geometrically idealized positions and refined using general isotropic temperature factors. The H atom bonded to C56 of the $CHCl_3$ solvent molecule in (**1**) is not found in the Fourier maps, but is accounted for in the formula sum and formula weight calculations.

Results and Discussion

Synthesis and Characterization

The synthetic methods of calix[4]arenes containing amidoferrocene **1**, **2** and **3** are summarized in Scheme 1. The structures of all compounds were characterized by ESI-MS, NMR and elemental analyses.

The cone conformation of the synthesized compounds was confirmed by ^{1}H-NMR spectrum. A typical AB pattern of the methylene bridge (Ar*CH*$_2$Ar) protons was observed at 4.37 and 3.13 ppm (J = 12.0 Hz), 4.37 and 3.13 ppm (J = 12.0 Hz), 4.37 and 3.13 ppm (J = 12.0 Hz) for compounds **1**, **2** and **3**, respectively. The NH amide protons were found at downfield positions around 8.50–8.85 ppm due to the formation of an intramolecular hydrogen bonding of the amidoferrocene unit, in agreement with the crystal structure, *vide infra*. The positive ion electrospray mass spectrometry of **1** and **2** show the peak corresponding to the monomer species at m/z = 1321.63 $[M + Na]^+$ and 1154.24 $[M + H_2O + K]^+$, respectively.

Interestingly, the ^{1}H-NMR spectra of compounds **2** and **3** (Fig. 1) show that the integration of all peaks in the spectrum of **3** is equal to that of **2**. However, the feature of the peaks of compounds **2** and **3** are totally different. The dimeric molecule **3** shows broader peaks in the ^{1}H-NMR spectrum. Moreover, the two singlet protons of the Cp ring of **3** are closer to each other than that of compound **2**. The dimeric structure of compound **3** was substantiated by ESI-MS revealing the $[M + H_2O + H]^+$ at m/z = 2212.03. The transannular 1,3-hydroxyl groups distance of *p-tert*-butylcalix[4]arene is probably small to allow only 1 + 1 or 2 + 2 bridged ferrocene-calixarene species to occur whereas the 3 + 3 oligomers can be produced from the wider transannular of unsubstituent *para*-calix[4]arene [19]. However, in our system the 2 + 2 and 3 + 3 bridge ferrocene-calix[4]arenes of compound **1** were not observed.

Molecular Structure of Compound **1**

Molecular structure of compound **1** is shown in Fig. 2. The conformation of **1** exists as a cone conformation. The two strong intramolecular O–H···O hydrogen bonding between the phenolic oxygens and the proximal ethereal oxygens,

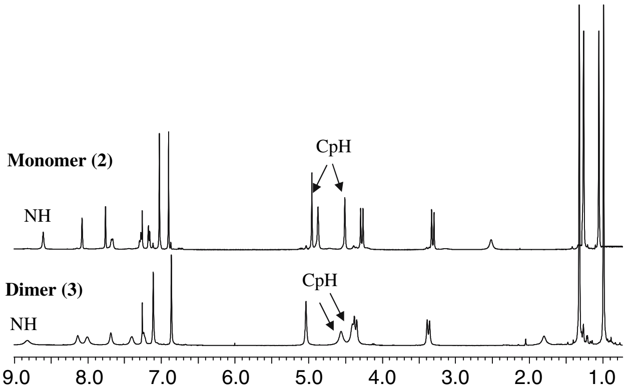
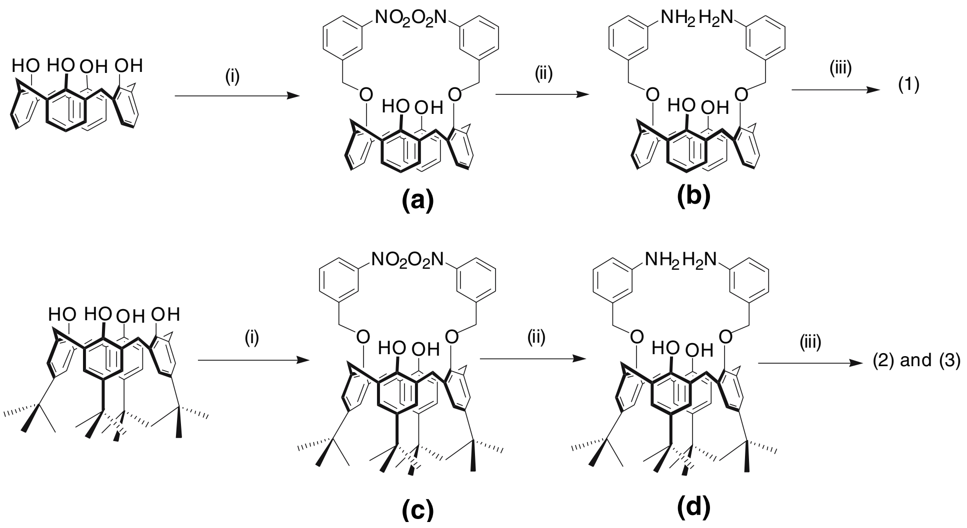


Fig. 1 ^{1}H-NMR spectra of monomer **2** and dimer **3** in $CDCl_3$

Scheme 1 Strategy for the synthesis of calix[4]arene amidoferrocene derivatives (**1**)–(**3**); (i) CH_3CN, KI, reflux 24 h, (ii) Raney/Ni, hydrazine, EtOAc:MeOH 15:11, reflux 60 °C 1 h and (iii) 1,1′-bis(chlorocarbonyl)ferrocene, CH_2Cl_2, rt, 3 h



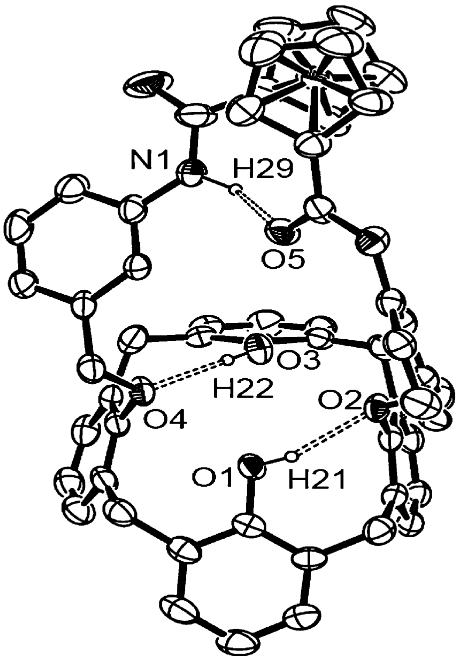


Fig. 2 A view of the asymmetric unit of **1**, displacement ellipsoids are drawn at 30% probability level and intramolecular hydrogen bonds are shown as dashed lines. H atoms have been omitted for clarity, except for those involved in hydrogen bonding

Table 2 (a) Selected bond lengths (Å) and angles (°) of compound **1**. (b) Hydrogen-bonding geometry (Å, °) for compound **1**

(a)

Bond lengths

C(20)–O(3)	1.370(7)	C(54)–O(4)	1.457(7)
C(26)–O(2)	1.409(7)	C(36)–O(5)	1.231(7)
C(29)–O(2)	1.452(6)	C(47)–N(1)	1.344(10)
C(47)–O(6)	1.212(10)	C(48)–N(1)	1.434(8)
C(4)–O(1)	1.368(8)	C(35)–N(2)	1.423(9)
C(13)–O(4)	1.403(7)	C(36)–N(2)	1.352(9)

Bond angles

O(1)–C(4)–C(5)	116.9(7)	N(2)–C(36)–C(37)	115.8(6)
O(1)–C(4)–C(3)	121.4(6)	N(1)–C(47)–C(46)	116.0(8)
C(8)–C(13)–O(4)	118.8(6)	C(53)–C(48)–N(1)	118.7(6)
C(12)–C(13)–O(4)	117.6(7)	C(49)–C(48)–N(1)	121.9(8)
O(3)–C(20)–C(15)	121.8(6)	O(4)–C(54)–C(52)	109.6(6)
O(3)–C(20)–C(19)	116.0(6)	C(26)–O(2)–C(29)	111.6(4)
O(2)–C(29)–C(30)	110.1(5)	C(13)–O(4)–C(54)	117.0(4)
C(33)–C(35)–N(2)	119.2(6)	O(6)–C(47)–N(1)	124.4(8)
C(34)–C(35)–N(2)	121.7(6)	O(6)–C(47)–C(46)	119.7(9)
O(5)–C(36)–N(2)	121.7(7)	C(47)–N(1)–C(48)	129.0(7)
O(5)–C(36)–C(37)	122.6(7)	C(36)–N(2)–C(35)	125.5(6)

(b)

D–H···*A*	*D*–H	H···*A*	*D*···*A*	*D*–H···*A*
O1–H21···O2	0.82	2.05	2.815(5)	155.9
O3–H22···O4	0.81(7)	1.95(8)	2.754(6)	173(8)
N1–H29···O5	0.96	2.16	2.925(7)	135.6

O(1)–O(2) 2.815 Å and O(3)–O(4) 2.754(6) Å, are jointly responsible for such a cone conformation. This result is in agreement with the reports by Brunink [20] and Böhmer [21] which presented that the presence of two vicinal or two opposite phenolic groups is sufficient to stabilize the cone conformation, with a preference for OH-depleted or substituted calix[4]arenes to adopt the 1,3-alternate formation. It should be mentioned that the distance of separation of the transannular 1,3-hydroxyl groups 3.169 Å which is larger than the distance of the original calix[4]-arene (ca. 2 Å) [22]. However, this distance is less than the cyclopentadienyl–cyclopentadienyl distance of 3.25 Å [23]. The average Fe–Cp(centroid) distance is 1.620 Å which is identical to other ferrocenyl derivatives [24–25], and the angle of Cp–Fe–Cp is 178.81°.

The more intriguing feature of this molecule is the intramolecular hydrogen bonding between amide groups of amidoferrocene, N(1)–O(5) 2.925(7) Å, was also observed and affected to the cyclopentadiene rings within the ferrocene unit are not perfectly eclipsed (Table 2).

Supplementary Material

CCDC-650164 contains the supplementary crystallographic data for this paper. Copies of available can be obtained free of charge on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1233-336033; e-mail: deposit@ccdc.cam.ac.uk).

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