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Synthesis and X-ray Structure of a Novel N′-Ferrocenylmethyl-N′-phenylbenzohydrazide

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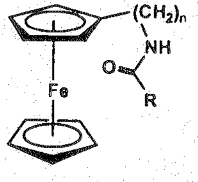
Reaction of ferrocenylmethyltrimethylammonium iodide with N′-phenylbenzohydrazide afforded a novel stable N′-ferrocenylmethyl-N′-phenylbenzohydrazide which was characterized by ^{1}H and ^{13}C NMR, mass spectroscopy and X-ray crystallography. The product crystallizes in the orthorhombic space group Pbca. The structure analysis confirms the optimized geometry obtained by molecular modelling calculations. The electrochemical behaviour of the N′-ferrocenylmethyl-N′-phenylbenzohydrazide derivative has been studied by cyclic voltammetry.

Key Words: Ferrocene, N′-ferrocenylmethyl-N′-phenylbenzohydrazide, X-ray crystal structure, Molecular modelling, Cyclic voltammetry.

INTRODUCTION

Our interest in amidoferrocenic compounds was prompted by the observation that similar derivatives **1** underwent a cyclization reaction to produce dihydropyridoferrocene[1] (**2**). These cyclic imines are key intermediaries for the synthesis of iron-free heterocyclic compounds[2, 3] (**3**).



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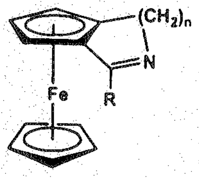

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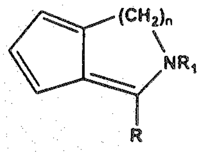

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n = 2, 3

R = H, Me or Ph; R_1 = H or Me

With a view to extending our work to the formation of binitrogen ferroceno-heterocyclic system, a substituent containing two nitrogen atoms to the ferrocenyl group is introduced. This was achieved by the reaction of the quaternary ammonium salt of ferrocenylmethyltrimethylamine iodide and N′-phenylbenzohydrazide to produce N′-ferrocenylmethyl-N′-phenylbenzohydrazide (**4**).

In this paper, the X-ray crystal structure of N′-ferrocenylmethyl-N′-phenylbenzohydrazide (**4**) is presented. The results of conformational studies and the electrochemical behaviour of the hydrazide derivative (**4**) is also presented.

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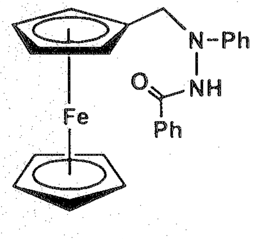

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EXPERIMENTAL

All chemicals were of reagent grade and were used without further purification. Solvents were purified according to standard methods[4]. All reactions were conducted under nitrogen. Solutions were dried over anhydrous magnesium sulphate and evaporated under reduced pressure using a rotary evaporator.

^{1}H NMR spectra were recorded on a Bruker AC 250 MHz spectrometer and the shifts are reported downfield from tetramethylsilane. ^{13}C NMR spectra were recorded on a Bruker 350 MHz spectrometer. The spectra reported are proton decoupled and the shifts are reported downfield from tetramethylsilane. Mass spectra were recorded on a triple quadripole Sciex API III Plus mass spectrometer. IR spectra were recorded on Perkin-Elmer 1000 FTIR spectrometer using KBr pellets. Melting points were obtained on a Gallenkamp melting point apparatus, and are uncorrected.

Synthesis

(Ferrocenylmethy)trimethylammonium iodide: The salt was synthesized according to literature procedures[5].

N′-Ferrocenylmethyl-N′-phenylbenzohydrazide (4): N′-Phenylbenzohydrazide (4.67 g, 22 mmol) was added to a well stirred solution of (ferrocenylmethy)trimethylammonium iodide (7.70 g, 20 mmol) in sodium-dried toluene (55 cm^3). The resulting suspension was heated under reflux for 6 h. It was then allowed to cool to room temperature and filtered. The filtrate was washed with water to remove any trace of unchanged quaternary ammonium salt. It was then dried and evaporated. The residue was recrystallized from ethanol to give N′-ferrocenylmethyl-N′-phenylbenzohydrazide (6.7 g, 82%) as yellow-orange needles, m.p. 169°C (decomp.). The designations Ha and Hb are used for the monosubstituted cyclopentadienyl ring.

ν_{max} (KBr, cm^{-1}): 3369.4, 3055.0, 2358.8, 1647.1, 802.3. ^{1}H NMR: δ 4.12 (t, 2H, Hb); 4.15 (s, 5H, C_5H_5); 4.19 (t, 2H, Ha); 4.60 (s, 2H, CH_2); 6.86 (t, 1H); 6.95 (d, 2H); 7.26 (t, 2H); 7.42 (m, 2H); 7.53 (t, 1H); 7.62 (s, 1H) and 7.72 ppm (m, 2H, C_6H_5 and NH). ^{13}C NMR: δ 51.20 (CH_2); 68.60 (C_5H_5); 69.80, 77.60 and 80.10 (C_5H_4); 113.40, 119.75, 127.20, 128.30, 129.20, 132.00, 132.80 and 148.80 (C_6H_5); 167.30 (CO). MS m/z M$^+$: $C_{24}H_{22}FeN_2O$ 410.010; calcd. 410.290 and major fragment ions at m/z 121 (16), 199 (100).

RESULTS AND DISCUSSION

X-ray diffraction studies

Single crystals of N′-ferrocenylmethyl-N′-phenylbenzohydrazide (4) suitable for X-ray analysis were grown by slow cooling of a solution of 4 in ethanol. An orange-yellow crystal of 4 was then mounted on a glass fibre and transferred to a Bruker-AXS CCD 1000 diffractometer.

The molecular structure of the hydrazide derivative **4** was then established (Fig. 1). All data for **4** were collected at low temperatures using an oil-coated shock-cooled crystal on a Bruker-AXS CCD 1000 diffractometer with MoK_α radiation ($\lambda = 0.71073$). The structure was solved by direct methods (SHELXS-97)[6] and all non-hydrogen atoms were refined anisotropically using the least-squares method on F^2.[7] Crystallographic data are given in Table-1.

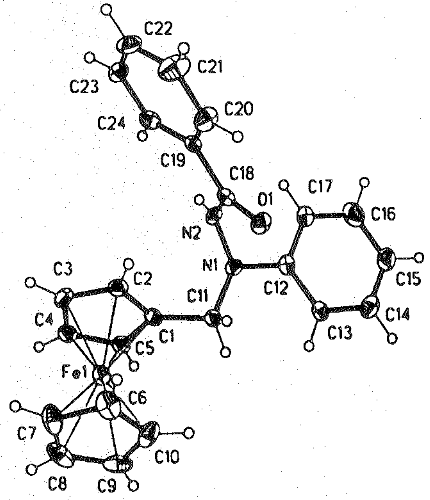

Fig. 1 Thermal ellipsoid drawing of compound 4 showing the atom numbering scheme (50% thermal ellipsoid)

TABLE-1
SUMMARY OF CRYSTAL DATA FOR COMPOUND 4

Empirical formula	$C_{24}H_{22}FeN_2O$
Formula weight	410.29
Crystal system	Orthorhombic
Space group	Pbca
Z	8
Crystal size, (mm)	0.02 × 0.05 × 0.6
Unit cell dimensions	a = 37.967(4) Å
	b = 10.352(1) Å
	c = 9.587(1) Å
F(000)	1712
Adsorption collection	Semi-empirical
Independent reflections	2678[R(int) = 0.1060]
Reflections collected	15544
Density (calculated) (mg/m^3)	1.447
θ range for data collection	5.16 to 23.25°
Final R indices [$I > 2$ sigma(I)]	$R_1 = 0.0525$, $wR_2 = 0.1009$
R indices (all data)	$R_1 = 0.0835$, $wR_2 = 0.1093$
Largest diff. peak and hole	0.348 and –0.377 eÅ

Computational calculations

Calculations were carried out using molecular modelling (molecular mechanics and molecular dynamics), with the P.C.M 6.1 program package[8], running on a PC IV. The molecular mechanics is a method for structure determination, which uses a quantum mechanical (VESCF) Π-system calculation in the iterative sequence and Allinger's MM2 force field[9]. These calculations use the "Monte Carlo" simulations and the Metropolis algorithm[10]. The conformational searching method included systematic and random conformational searches in both internal (torsion angle) and external (Cartesian) coordinate frames. The conformational study is based on molecular mechanics. The calculation of energy has been calculated by the PCM program, with the following options: dipole-dipole (dp-dp), self-consistent field (SCF) and restricted Hartree Fock (RHF).

The molecular dynamics are used for the conformational research with the following options: 1000 K, *in vacuo*, step size: 0.001 ps, relaxation time: 0.1 ps. Then, based on these calculations and the Boltzmann distribution[11]. Our aim is to find all these low-energy conformers. Boltzmann populations of the conformers were based on steric energies. For the N′-ferrocenylmethyl-N′-phenylbenzohydrazide (**4**), the two conformers in equilibrium are found. While the first conformer's carbonyl is "exo" with regard to the ferrocene, the second conformer's carbonyl is "endo". The calculations using the MM2 force field reveal a 1.14 kcal/mol difference between minor (endo) and major (exo) conformers, which corresponds to an equilibrium ratio of 43 : 57. The major conformer obtained by calculation is similar to that obtained by X-ray diffraction (Fig. 1). A good agreement between the calculated and experimental values is found; the maximum gap for the distances is 0.05 and 2.6° for the angles (Tables 2 and 3). This molecule has a weak conformational mobility, with regard to other macrocycles of macrolide type. In a window of 2 kcal/mol, only two privileged conformations is found[12–14].

Electrochemical studies

Electrochemical experiments were carried out using a potentiostat type voltalab 32. All experiments were carried out in acetontrile, which was dried over CaH_2 and distilled prior to use. Lithium perchlorate ($LiClO_4$) was used as supporting electrolyte 10^{-1} M. A three electrode configuration was used. The working electrode was a platinum disc (diameter 2 mm) sealed in glass. The reference electrode was a saturated calomel electrode (SCE). The counter electrode was a platinum wire. Potentials were calibrated against ferrocene. The experiments were carried out under a moisture free nitrogen atmosphere. Cyclic voltammetry was measured for an acetontrile solution of ferrocene and compound **4** (10^{-3} M) at scan rates equal to 100, 50, 25 and 10 mv s^{-1} (Fig. 2.).

These studies showed that oxidation of compound **4** appeared to be Nerstian and diffusion controlled. Plots of $(i_p)_{anod}$ *vs.* the square root of the scan rate ($v^{1/2}$) were linear. The peak-to peak separations are, however, significantly greater

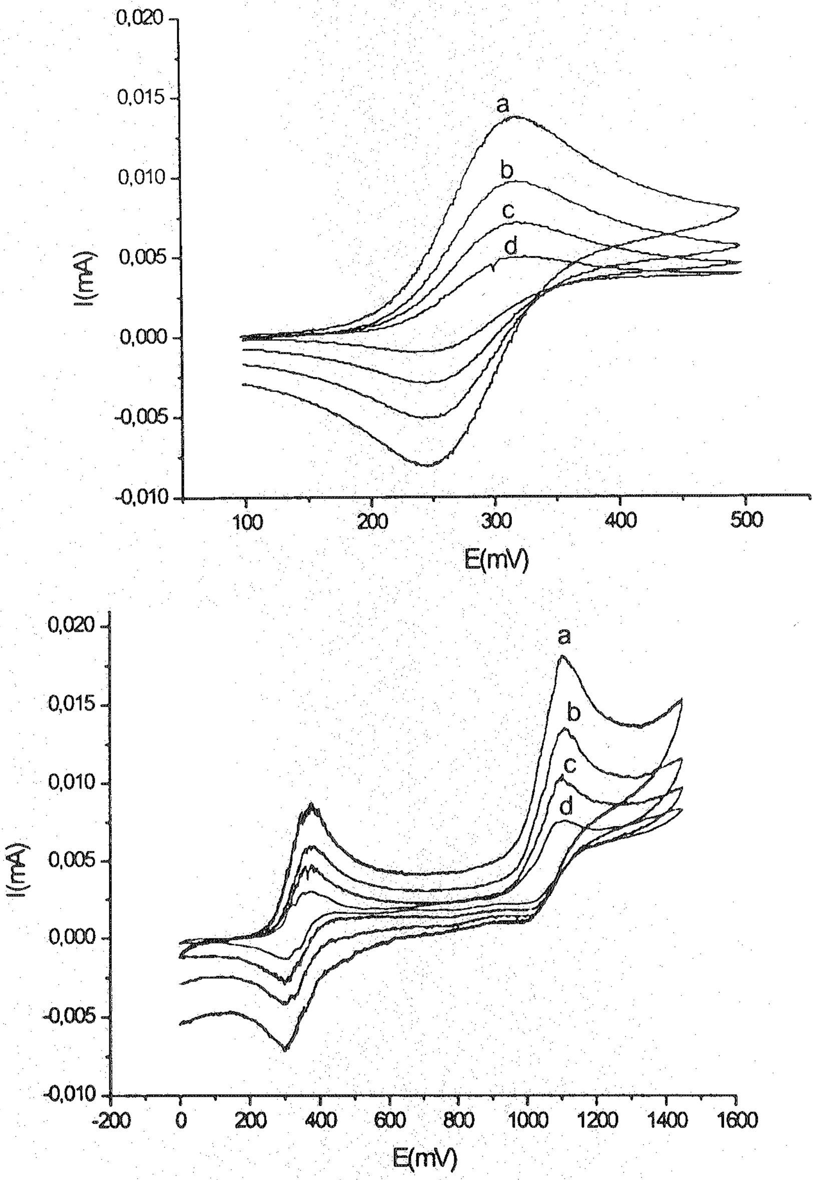

Fig. 2. Cyclic voltammogrammes on a glassy platinum electrode of a 10^{-3} M solution ferrocene (1) and compound 4 (2) in 10^{-1} M $KClO_4/CH_3CN$ at (a) 100; (b) 50; (c) 25 and (D) 10 mv s^{-1}

than the ideal value of 60 mvs^{-1} for a fully reversible one-electron processes. This may be due to a combination of uncompensated solution resistance and slightly slow electron-transfer kinetics. The $E_{1/2}$ of the studied compound, 333 mv, is higher compared to that of ferrocene, 314 mv. This difference may be explained by the influence of the electron withdrawing N′-phenylbenzohydrazide group in the N′-ferrocenylmethyl-N′-phenylbenzohydrazide (**4**). Relevant electrochemical data obtained from these experiments are summarized in Table-4.

TABLE-2

SELECTED BOND LENGTHS (Å)

Atoms a-b	Length (RX)	Length (MM)	Gap
C1-C2	1.42	1.41	0.01
C1-C5	1.43	1.41	0.02
C1-C11	1.50	1.50	0.00
C1-Fe1	2.04	2.03	0.01
C2-C3	1.42	1.40	0.02
C2-Fe1	2.02	2.03	0.01
C3-C4	1.42	1.40	0.02
C3-Fe1	2.04	2.04	0.00
C4-C5	1.41	1.40	0.01
Fe1-C6	2.04	2.04	0.00
Fe1-C7	2.04	2.03	0.01
C11-N1	1.47	1.46	0.01
C12-C17	1.40	1.41	0.01
C12-C13	1.39	1.41	0.02
C12-N1	1.42	1.42	0.00
C13-C14	1.39	1.40	0.01
C14-C15	1.37	1.40	0.03
N1-N2	1.41	1.47	0.06
N2-C18	1.35	1.37	0.02
C18-O1	1.23	1.23	0.00
C18-C19	1.50	1.49	0.01
C19-C24	1.39	1.41	0.02
C19-C20	1.39	1.41	0.02

MM: Molecular mechanics

TABLE-3

SELECTED ANGLES (°)

Atoms a-b-c	Angle (RX)	Angle (MM)	Gap
C2-C1-C5	106.7	107.9	1.2
C2-C1-C11	126.6	125.6	1.0
C5-C1-C11	126.6	126.5	0.1
C2-C1-Fe1	068.8	069.9	1.1
C11-C1-Fe1	126.4	124.6	1.8
C3-C2-C1	108.7	108.1	0.6
C3-C2-Fe1	070.2	070.4	0.2
C1-C2-Fe1	070.2	069.6	0.6
C2-C3-C4	108.0	107.9	0.1
C2-C3-Fe1	069.0	069.6	0.6
C5-C4-C3	107.5	108.1	0.6
C2-Fe1-C3	040.8	040.3	0.5
C5-Fe1-C3	068.3	067.7	0.6
C9-C8-C7	107.6	108.0	0.4
C8-C9-C10	108.8	108.0	0.8
N1-C11-C1	110.4	112.2	1.8
C17-C12-C13	118.4	117.4	1.0
C17-C12-N1	118.6	120.6	2.0
C13-C12-N1	122.8	122.0	0.8
C14-C13-C12	119.6	121.3	1.7
O1-C18-N2	121.9	119.3	2.6
O1-C18-C19	121.9	119.8	2.1
C24-C19-C20	118.8	118.7	0.1

TABLE-4

ELECTROCHEMICAL DATA FOR THE OXIDATION OF FERROCENE AND COMPOUND 4 MEASURED AT 25°C in 10^{-1} M $LiClO_4/CH_3CN$

Compound	Scan rate (mv s^{-1})	Epa_1	Epa_2	Epa_3	Epa_4	Epc_1	Epc_2	Epc_3	$Epa_1 - Epc_1$	$E_{1/2}$	E_{pc}/I_{pa}
Ferrocene	100	354	—	—	—	274	—	—	80	314	1.07
	50	348	—	—	—	284	—	—	64	316	1.07
	25	338	—	—	—	272	—	—	64	306	1.09
	10	336	—	—	—	272	—	—	68	302	1.03
Compound 4	100	366	850	1150	2120	300	1025	1690	66	333	0.98
	50	372	—	1110	—	294	—	—	78	333	1.04
	25	370	—	1100	—	298	—	—	72	334	1.00
	10	370	—	1100	—	302	—	—	68	336	1.01

Conclusion

The synthesis and NMR characterization of N′-ferrocenylmethyl-N′-phenylbenzohydrazide have been described and its X-ray crystal structure has been determined. Conformational studies have been carried out showing a number of interesting features, including the existence of two conformers in equilibrium of the N′-ferrocenylmethyl-N′-phenylbenzohydrazide compound. Electrochemical studies show that the electron withdrawing N′-phenylbenzohydrazide group introduced to the ferrocene influences the redox potential of the iron centre. This is may be due to the non-insulating effect of methylene between the N′-phenylbenzohydrazide group and the cyclopentadienyl ring of ferrocene.

Supplementary Material

CCDC-263224 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.

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