Journal of Organometallic Chemistry, 476 (1994) 63–72

Redox-active lithium-selective ionophores based on new 2,9-bis(ferrocenyl) substituted phenanthroline derivatives

Paul D. Beer * and Jonathan P. Danks

Inorganic Chemistry Laboratory, University of Oxford, South Parks Road, Oxford OX1 3QR (UK)

Michael G.B. Drew

Department of Chemistry, University of Reading, Reading RG2 6AD (UK)

Jerome F. McAleer

MediSense (UK), 38 Nuffield Way, Abingdon, Oxon OX14 1RL (UK)

(Received October 22, 1993)

Abstract

A variety of new redox-active 2,9-bis(ferrocenyl)-substituted phenanthroline derivatives have been prepared, and the structure of one of them, 2,9-bis(ferrocenyl)ethenyl-1,10-phenanthroline, has been determined by an X-ray diffraction study. Solution ^{1}H NMR complexation studies suggest the 2,9-bis(ferrocenyl)vinylic- and amine-linked phenanthroline ligands form complexes with the ligand and Li^+ in 2:1 stoichiometric ratio, whereas Schiff-base-containing ionophores produced an equilibrium mixture of 2:1 and 1:1 complexes. The 2,9-bis(ferrocenyl)amide-linked phenanthroline ligands formed solution lithium complexes of 1:1 stoichiometry. Electrochemical investigations reveal that the respective ferrocene-ferricenium redox couples of most of the ligands are shifted to more positive potentials on co-ordination of Li^+, but are electrochemically insensitive to Na^+ or K^+ guest cations. The above lithium redox-responsive ionophores recognise Li^+ electrochemically in the presence of equimolar concentrations of Na^+ and K^+.

Key words: Ferrocene; Iron; Electrochemistry; Host–guest species; Phenanthroline; Lithium

1. Introduction

The design of lithium-selective receptors for medical and analytical applications, such as in the treatment of manic depressive illness [1], has been the focus of intensive research in recent years [2–6]. Most of the types of ligands reported to date have been modified 14-crown-4 compounds [6–9]. Polyvinyl chloride (PVC) membrane electrodes containing simple 2,9-dialkyl-1,10-phenanthrolines have been shown to exhibit excellent selectivity for lithium cations rather than sodium and potassium cations [10]. In view of that work, and with the ultimate aim of producing a novel prototype amperometric-sensing device for lithium, we decided to attach ferrocene redox centres to the 2,9-positions of the phenanthroline moiety. We report below the syntheses, coordination chemistry and electrochemical properties of a variety of new 2,9-polyferrocenyl-substituted phenanthroline ligands, and the crystal structure of one of the ionophores. In addition, cyclic voltammetry has shown for the first time that some of these redox-active ligands can *selectively* electrochemically recognise the lithium guest cation in the presence of equimolar amounts of sodium and potassium ions.

2. Experimental details

2.1. Solvent and reagent pre-treatment

Where necessary, solvents were purified prior to use, and stored under nitrogen. Acetonitrile was pre-dried over 4 Å molecular sieves (4–8 mesh) and then distilled from CaH_2. Diethyl ether was pre-dried over

* Correspondence to: Dr. P.D. Beer.

0022-328X/94/$7.00
SSDI 0022-328X(93)24332-7

sodium wire, and distilled from sodium immediately prior to use. Dimethyl formamide (DMF) was dried overnight over activated 3 Å molecular sieves. Ethanol was distilled under nitrogen from sodium ethoxide. Methanol was distilled from $CaSO_4$, and stored over 4 Å molecular sieves. Tetrahydrofuran (THF) and toluene were distilled from sodium using benzophenone as an indicator. Triethylamine and dichloromethane were distilled from CaH_2.

Unless otherwise stated commercial grade chemicals were used without further purification. The following compounds were prepared by published procedures: 2,9-diformyl-1,10-phenanthroline [11], 4-aminophenylferrocene [12], and chlorocarbonylferrocene [13].

All elemental analyses were carried out by the Inorganic Chemistry Laboratory Microanalysis Service. The NMR spectra were recorded on a Brüker AM 300 instrument, operating at 300 MHz for ^1H NMR and 75.42 MHz for ^{13}C NMR spectra. Infrared spectra were recorded on a Mattson 10410E "polaris" Fourier Transform Spectrometer. Electrochemical measurements were conducted on a Princeton Applied Research Potentiostat/Galvanostat Model 273. Fast atom bombardment (FAB) mass spectra were carried out by the SERC mass spectrometry service at University College, Swansea. Melting points were recorded on a Gallenkamp melting point apparatus and are uncorrected.

2.2. Syntheses

2.2.1. 2,9-Bis(ferrocenyl)hydroxyethyl-1,10-phenanthroline (4)

A solution of 2,9-dimethyl-1,10-phenanthroline (4.16 g, 20 mmol) in anhydrous tetrahydrofuran (150 ml) was added to a stirred solution of lithium diisopropylamide (43 mmol) prepared from diisopropylamine (6 ml, 43 mmol) and butylithium (1.6 M solution in hexane, 27 ml, 43 mmol) at −78°C. The resulting dark-orange solution was allowed to warm to 0°C and was then stirred for 1.5 h. A solution of ferrocene carboxaldehyde (8.8 g, 41 mmol) in anhydrous tetrahydrofuran (30 ml) was added dropwise during 10 min, and stirring was continued at −78°C for 1 h and then at room temperature for 16 h. The mixture was then added to ice-water (300 g) and organic compounds extracted into dichloromethane (3 × 300 ml). The extracts were dried over magnesium sulphate and the solvent evaporated to leave an orange solid. This was chromatographed on silica gel with dichloromethane-methanol-ammonium hydroxide (100:5:1) as eluent to afford the diol as a yellow solid, 4.5 g, 35%.

Melting point: 170–171°C. Mass spectrum (FAB) m/z at $637 = (M + H)^+$. IR (KBr disc): 3381 cm^{-1}, OH stretch. Analysis: calc. for $C_{36}H_{32}N_2O_2Fe_2 + 0.5\ CH_2Cl_2$: C, 64.61; H, 4.86; N, 4.13%. Found: C, 64.30; H, 5.23; N, 3.99%. ^1H NMR ($CDCl_3$) δ: 3.53 (4H, m, CH_2), 4.14 (4H, m, cp), 4.30 (10H, s, cp), 4.41 (4H, m, cp) 5.30 (3H, m, –CH– aliphatic + CH_2Cl_2), 7.53 (2H, d, $J = 8.3$ Hz, phenanthroline CH), 7.78 (2H, s, phenanthroline CH), 8.18 (2H, d, $J = 8.3$ Hz, phenanthroline CH).

2.2.2. 2,9-Bis(ferrocenyl)ethenyl-1,10-phenanthroline L^1

A solution of (**4**) (1 g, 1.6 mmol) and pyridinium toluene-*p*-sulphonate (0.3 g) in dry toluene (160 ml) was refluxed for 16 h in a Dean and Stark apparatus to remove liberated water azeotrophically. The solution was cooled, shaken and washed with water, and dried over magnesium sulphate. The solvent was removed *in vacuo*, and the resulting red oil was eluted through a silica gel column with a dichloromethane-methanol gradient, and on removal of solvent this yielded the product as a deep red solid, 0.68 g, 72%.

Melting point: 266–268°C. Mass spectrum (FAB): m/z at $601 = (M + H)^+$. Analysis: calc. for $C_{36}H_{28}N_2Fe_2$, C, 72.05; H, 4.67; N, 4.67%. Found: C, 71.95; H, 4.26; N, 3.89%. ^1H NMR ($CDCl_3$) δ: 4.17 (10H, s, cp), 4.26 (4H, t, $J = 1.8$ Hz, cp–CH), 4.39 (4H, t, $J = 1.8$ Hz, cp–CH), 5.30 (CH_2Cl_2), 7.37 (2H, d, $J = 16.4$ Hz, olefinic CH), 7.49 (2H, d, $J = 16.4$ Hz, olefinic CH), 7.69 (2H, s, phenanthroline–CH), 7.88 (2H, d, $J = 8.4$ Hz, phenanthroline–CH), 8.14 (2H, d, $J = 8.4$ Hz, phenanthroline–CH. ^{13}C NMR ($CDCl_3$) δ: 67.78 (substituted cp ring), 69.46 (unsubstituted cp ring), 69.75 (substituted cp ring), 84.20 (*ipso* C on cp ring), 119.49, 125.46, 127.53, 127.98, 133.28, 136.22, 156.61, (olefinic and phenanthroline carbons).

2.2.3. 2,9-Bis(4-ferrocenylphenyl)iminomethyl-1,10-phenanthroline L^2

A solution of 2,9-diformyl-1,10-phenanthroline (**5**) (0.5 g, 2.13 mmol) in dry tetrahydrofuran (100 ml) was refluxed for 30 min. A solution of 4-aminophenylferrocene (**6**) (1.2 g, 4.3 mmol) in tetrahydrofuran (50 ml) was added dropwise during 1 h, and the resulting solution was refluxed for 3 h in a Dean and Stark apparatus to remove azeotropically the water produced in the reaction. The solvent was removed to yield a red solid which was eluted through a column with dichloromethane. A red band was collected, which after evaporation of the solvent gave a red solid, 1.0 g, 64%.

Melting point: 191–193°C. IR (KBr disc): 1620 cm^{-1} = –N=CH–stretch. Mass spectrum (FAB) m/z at 755 $= (M + H)^+$. Analysis: calc. for $C_{46}H_{34}N_4Fe_2 + 0.5\ CH_2Cl_2$: C, 69.58; H, 4.36; N, 6.98%. Found: C, 69.43; H, 4.16; N, 6.90%. ^1H NMR ($CDCl_3$) δ: 4.17 (10H, s,

cp), 4.26 (4H, t, $J = 1.7$ Hz, cp–CH), 4.39 (4H, t, $J = 1.7$ Hz, cp–CH), 5.30 (CH_2Cl_2), 7.37 (2H, d, $J = 16.4$ Hz, Ar–H), 7.49 (2H, d, $J = 16.4$ Hz, Ar–H), 7.69 (2H, s, phenanthroline–CH), 7.88 (2H, d, $J = 8.4$ Hz, phenanthroline–CH), 8.14 (2H, d, $J = 8.4$ Hz, phenanthroline–CH), 9.23 (2H, s, N=CH). ^{13}C NMR ($CDCl_3$) δ: 66.33, 69.03 (substituted cp ring) 69.52 (unsubstituted cp ring), 84.48 (*ipso* C on cp ring), 120.76, 121.67, 126.65, 127.33, (Ar–C), 129.61, 136.76, 138.78, 145.54, 147.82, 155.07, (phenanthroline–C), 159.29 (imine–C).

2.2.4. 2,9-Bis(3,4-dimethoxyphenyl)iminomethyl-1,10-phenanthroline, L^3

This was prepared in an analogous way to (L^2) except that aminoveratrole (**7**) was used instead of 4-aminophenylferrocene (**5**). The product was obtained as a yellow crystalline solid, 1.7 g, 79%.

Melting point: 229–231°C. IR: 1623 cm^{-1} = –N=CH– stretch. Mass spectrum (EI) m/z at 506 = M^+. Analysis: calc. for $C_{30}H_{26}O_4 + 0.5H_2O$: C, 69.92; H, 5.24; N, 10.87%. Found: C, 69.22; H, 5.25; N, 10.88%. ^{1}H NMR ($CDCl_3$) δ: 1.89 (H_2O), 3.96 (6H, s, OCH_3), 4.00 (6H, s, OCH_3, 6.97 (2H, d, $J = 9.2$ Hz, Ar–H), 7.13 (2H, d, $J = 9.2$ Hz, Ar–H), 7.15 (2H, s, Ar–H), 7.95 (2H, s, phenanthroline–CH), 8.42 (2H, d, $J = 8.3$ Hz, phenanthroline–CH), 8.67 (2H, d, $J = 8.3$ Hz, phenanthroline–CH), 9.21 (2H, s, N=CH). ^{13}C NMR ($CDCl_3$) δ: 56.00, 56.10 (OCH_3), 104.78, 111.42, 114.97, 120.76, 127.46, (Ar–C), 129.76, 136.94, 143.54, 148.87, 149.50, 155.32, (phenanthroline–C), 158.68 (imine–C).

2.2.5. 2,9-Bis(3,4-dimethoxyphenyl)aminomethyl-1,10-phenanthroline, L^4

A solution of L^3 (1 g, 1.9 mmol) in dichloromethane (20 ml) was added to a solution of sodium borohydride (3 g, 80 mmol) in methanol (100 ml) during 1 h. The resulting solution was stirred for 3 h and then refluxed for 1 h. Water (100 ml) was then added and the solvent was subsequently removed *in vacuo*. The resulting dark-yellow oil was eluted through a basic alumina column with a dichloromethane/methanol gradient (9:1). A yellow band was collected, and was evaporated to give an oil, which solidified on standing. The solid was recrystallised from dichloromethane and hexane to give yellow crystals (0.68 g, 68%).

Melting point: 105–106°C. IR: 3370 cm^{-1}, NH stretch. Mass spectrum (EI): m/z at 510 = M^+. Analysis: calc. for $C_{30}H_{30}O_4 + 0.5\ CH_2Cl_2$: C, 67.64; H, 5.69; N, 10.39%. Found: C, 67.54; H, 5.62; N, 10.46%. ^{1}H NMR ($CDCl_3$) δ: 1.95 (2H, bs, NH), 3.81 (6H, s, OCH_3), 3.82 (6H, s, OCH_3), 4.85 (4H, s, CH_2), 5.30 (CH_2Cl_2), 6.29 (2H, dd, $J = 8.6$ and 2.5 Hz, Ar–H), 6.47 (2H, d, $J = 2.5$ Hz, Ar–H), 6.74 (2H, d, $J = 8.6$ Hz, Ar–H), 7.76 (2H, d, $J = 8.2$ Hz, phenanthroline–CH), 7.79 (2H, s, phenanthroline–CH), 8.23 (2H, d, $J = 8.2$ Hz, phenanthroline–CH). ^{13}C NMR ($CDCl_3$) δ: 46.27 (–CH_2NH–), 51.43 (OCH_3), 95.05, 99.65, 109.12, 117.19, 121.72, 124.00 (Ar–C), 132.53, 137.45, 138.67, 140.64, 145.86, 155.33 (phenanthroline–C).

2.2.6. 2,9-Bis[(3,4-dimethoxyphenyl)-N,N,-ferrocenyl-oxo]aminomethyl-1,10-phenanthroline, L^5

Compound L^4 (245 mg, 0.48 mmols), triethylamine (480 mg, 48 mmol) and dimethylaminopyridine (1 microspatula) were dissolved in dichloromethane (50 ml). A solution of the chlorocarbonyl ferrocene (1.2 g, 4.8 mmol) in dichloromethane (30 ml) was added during 1 h under nitrogen. The mixture was stirred for 16 h and then refluxed for 4 h. The solvent was evaporated from the cooled solution and the residue was chromatographed on an alumina column (dichloromethane : methanol gradient) to yield a brown solid, which was rechromatographed on silica (dichloromethane/methanol, 98.2%).

The yellow band collected was evaporated to yield a yellow solid, 110 mg, 26%.

Melting point: 135–136°C. IR (KBr disc): 1618 cm^{-1}, carbonyl stretch. Mass spectrum (FAB) m/z at 935 = $(M + H)^+$. Analysis: calc. for $C_{52}H_{46}N_4O_6Fe_2 + 1.0\ CH_2Cl_2$: C, 62.46; H, 4.96; N, 5.49%. Found: C, 62.26; H, 5.22; N, 5.24%. ^{1}H NMR ($CDCl_3$) δ: 3.77 (6H, s, OCH_3), 3.86 (6H, s, OCH_3), 4.10 (10H, s, cp), 4.15 (8H, t, $J = 1.4$ Hz, cp), 5.30 (CH_2Cl_2), 5.49 (4H, s, CH_2), 6.78 (2H, d, $J = 8.5$ Hz, Ar–H), 7.75 (2H, s, phenanthroline–CH); 7.86 (2H, d, $J = 8.25$ Hz, phenanthroline–CH), 8.23 (2H, d, $J = 8.25$ Hz, phenanthroline–CH). ^{13}C NMR ($CDCl_3$) δ: 56.16 (OCH_3), 57.52 (CH_2), 69.75 (unsubstituted cp ring), 70.17, 72.00 (substituted cp ring), 75.65 (*ipso* C on cp ring), 111.25, 112.12, 121.00, 122.12, 126.10, 127.85 (Ar–C), 136.55, 136.94, 145.61, 148.65, 149.40, 158.71, (Phenanthroline–C), 170.88, (C=O).

2.2.7. 2,9-Bis(4-ferrocenylphenyl)aminomethyl-1,10-phenanthroline, L^6

This was prepared from L^2 by the method used for L^3. The product was isolated as a yellow solid, 0.35 g, 68%.

Melting point: decomposed > 148°C. IR (KBr disc): 3347 cm^{-1} N–H stretch. Mass spectrum (FAB): m/z at 758 = M^+. Analysis: Calc. for $C_{46}H_{38}N_4Fe_2 + 0.5\ CH_2Cl_2$: C, 69.75; H, 4.99; N, 7.00%. Found: C, 68.38; H, 4.47; N, 7.05%. ^{1}H NMR (CDCl) δ: 4.05 (10H, 5, cp–CH), 4.23 (4H, t, $J = 1.7$ Hz, cp–CH), 4.53 (4H, t, $J = 1.7$ Hz, cp–CH), 4.90 (4H, s, aliphatic CH_2), 5.30 (CH_2Cl_2), 6.78 (2H, d, $J = 16.4$ Hz, Ar–H), 7.39 (2H,

d, $J = 16.4$ Hz, Ar–H), 7.78 (2H, s, phenanthroline–CH), 7.80 (2H, d, $J = 8.4$ Hz, phenanthroline–CH), 8.26 (2H, d, $J = 8.4$ Hz, phenanthroline–CH).

2.2.8. 2,9-Bis[(4-ferrocenylphenyl)-N,N-ferrocenyloxo]aminomethyl-1,10-phenanthroline, L^7

This was prepared by the method used for L^4. The product was isolated as a yellow solid, 100 mg, 21%.

Melting point: 204–206°C. IR (KBr disc): 1638 cm^{-1}, carbonyl stretch. Mass spectrum (FAB): m/z at 1183 $= (M + H)^+$. Analysis: calc. for $C_{68}H_{54}N_4O_2Fe_4 + 2CH_2Cl_2$: C, 62.19; H, 4.29; N, 4.14%. Found: C, 62.25; H, 5.13; N, 3.92%. ^1H NMR ($CDCl_3$) δ: 4.00 (10H, s, cp), 4.11 (10H, s, cp–CH), 4.14 (8H, m, cp–CH), 4.33 (4H, t, $J = 1.4$ Hz, cp–CH), 4.64 (4H, t, $J = 1.4$ Hz, cp–CH), 5.30 (CH_2Cl_2), 5.56 (4H, s, CH_2), 7.40 (4H, d, $J = 8.4$ Hz, Ar–H), 7.42 (4H, d, $J = 8.4$ Hz, Ar–H), 7.77 (2H, s, phenanthroline–CH), 7.88, (2H, d, $J = 8.3$ Hz, phenanthroline–CH), 7.88 (2H, d, $J = 8.3$ Hz, phenanthroline–CH), 8.26 (2H, d, $J = 8.3$ Hz, phenanthroline–CH). ^{13}C NMR ($CDCl_3$) δ: 57.30 (aliphatic CH_2), 66.52, 69.33 (substituted cp ring), 69.61 (unsubstituted cp ring), 70.21, 71.62 (substituted cp ring), 75.77, 84.00 (*ipso* C on cp ring), 122.16, 126.10, 126.62, 128.62 (Ar–C), 136.66, 139.24, 141.60, 145.50, 158.69 (phenanthroline–C), 170.78 (C=O).

2.3. Structure determination-crystal data L^1

$Fe_2N_2Cl_6C_{38}H_{30}$, $M = 907.5$, monoclinic $a = 33.924(25)$ Å, $b = 7.753(8)$ Å, $c = 28.588(23)$ Å, $\beta = 109.8(1)°$, $U = 7072.2$ A^3, $F(000) = 7328$, $D_c = 1.70$ g cm^{-3}, $Z = 8$, Mo-Kα radiation ($\lambda = 0.7107$ Å), μ(Mo Kα) = 8.65 cm^{-1}, Spacegroup $I2/a$ (non-standard C2(c)).

A crystal of approximate size $0.3 \times 0.3 \times 0.3$ mm was mounted on a STOE-2 diffractometer to rotate around the a axis. Data were measured *via* ω scan with a 2Θ maximum of 50°. Background counts were for 20 s and a scan rate of 0.0333° s^{-1} was applied to a width of $(1.5 + \sin \mu/\tan \Theta)$. No decay in intensity was observed for the standard reflections. 4542 independent reflections were measured of which 1513 with $I > 2\sigma(I)$ were used in subsequent calculations. The structure was solved by heavy atom methods. Hydrogen atoms were placed in calculated positions. The iron and chlorine atoms were refined anisotropically, but all other atoms were refined isotropically. The structure was refined by full-matrix least squares with a weighting scheme $w = 1/[\sigma^2(F) + 0.003F^2]$. In the final cycle of refinement the maximum shift/error ratio was 0.1. In the final difference Fourier map, maximum and minimum peaks were at 0.62 eA^{-3} and -0.41 eA^{-3} respectively. Calculations were performed using SHELX76 [14] and some in-house programs on the Amdahl 5870 Computer at the University of Reading. The final R value was 0.093 ($R_w = 0.102$). Positional coordinates and selected molecular dimensions are listed in Tables 1 and 2 respectively.

TABLE 1. Atomic co-ordinates ($\times 10^6$) with estimated standard deviations in parentheses for L^1

Atom	x	y	z
FE(1)	1222(1)	7339(5)	5422(1)
C(11)	1670(7)	8100(33)	6076(8)
C(12)	1805(7)	8597(30)	5644(7)
C(13)	1470(7)	9612(33)	5353(9)
C(14)	1197(6)	9807(30)	5518(6)
C(15)	1288(6)	8919(28)	5980(7)
C(21)	1185(5)	4882(27)	5419(6)
C(22)	799(8)	5528(38)	5384(9)
C(23)	683(8)	6574(33)	4911(8)
C(24)	1005(8)	6244(36)	4724(9)
C(25)	1287(8)	5224(35)	5044(9)
FE(2)	4965(1)	7206(5)	6164(1)
C(41)	4971(9)	8319(38)	6822(10)
C(42)	5375(7)	7725(34)	6839(8)
C(43)	5472(8)	8682(33)	6469(9)
C(44)	5104(6)	9669(28)	6215(6)
C(45)	4836(9)	9450(38)	6414(9)
C(51)	5031(7)	5816(29)	5612(7)
C(52)	5024(7)	4751(30)	6044(7)
C(53)	4678(7)	4921(33)	6088(8)
C(54)	4427(8)	6217(31)	5718(8)
C(55)	4659(6)	6701(29)	5443(7)
C(71)	4057(7)	3699(30)	6899(8)
C(72)	4316(8)	2815(34)	7300(8)
C(73)	4233(7)	2282(33)	7695(8)
C(74)	3858(7)	2738(33)	7736(7)
C(75)	3737(7)	2363(31)	8156(7)
C(76)	3375(6)	2900(29)	8169(7)
C(77)	3078(7)	3818(31)	7788(8)
C(78)	2710(7)	4372(31)	7782(8)
C(79)	2443(7)	5182(31)	7404(7)
C(80)	2565(6)	5552(30)	6981(7)
N(81)	2924(6)	5054(28)	6954(7)
C(82)	3197(7)	4149(30)	7357(7)
C(83)	3581(7)	3722(30)	7326(8)
N(84)	3673(5)	4079(24)	6936(6)
C(85)	4157(6)	4234(28)	6507(7)
C(86)	4497(7)	4196(30)	6431(7)
C(87)	2278(6)	6475(26)	6546(6)
C(88)	1910(6)	6963(29)	6488(7)
C(1)	2811(10)	3720(44)	5820(11)
CL(1)	2365(3)	2752(15)	5778(3)
CL(2)	2748(5)	5785(18)	5535(5)
CL(3)	3135(3)	2521(14)	5609(3)
C(2)	1576(13)	3225(50)	3281(13)
CL(4)	1950(3)	4675(13)	3404(4)
CL(5)	1172(5)	3690(16)	3464(8)
CL(6)	1358(5)	3362(18)	2603(6)

TABLE 2. Molecular dimensions, distances, Å, angles, degrees, for L^1

FE(1)–C(11)	2.056(21)
FE(1)–C(12)	2.101(22)
FE(1)–C(13)	1.990(25)
FE(1)–C(14)	1.939(23)
FE(1)–C(15)	1.964(21)
FE(1)–C(21)	1.909(21)
FE(1)–C(22)	1.985(29)
FE(1)–C(23)	2.004(23)
FE(1)–C(24)	2.059(24)
FE(1)–C(25)	2.016(27)
C(11)–C(88)	1.474(28)
C(77)–C(82)	1.445(27)
C(78)–C(79)	1.309(26)
C(79)–C(80)	1.432(25)
C(80)–N(81)	1.305(25)
C(80)–C(87)	1.477(24)
N(81)–C(82)	1.397(25)
C(82)–C(83)	1.377(26)
C(83)–N(84)	1.284(23)
C(85)–C(86)	1.244(24)
C(75)–C(76)	1.307(26)
C(76)–C(77)	1.401(26)
C(77)–C(78)	1.315(27)
C(77)–C(82)	1.445(27)
C(78)–C(79)	1.309(26)
C(79)–C(80)	1.432(25)
C(80)–N(81)	1.305(25)
C(80)–C(87)	1.477(24)
C(87)–C(88)	1.263(24)
C(12)–C(11)–C(88)	124.7(19)
C(15)–C(11)–C(88)	131.1(19)
C(52)–C(53)–C(86)	132.1(24)
C(54)–C(53)–C(86)	118.2(20)
C(72)–C(71)–N(84)	113.4(20)
C(72)–C(71)–C(85)	125.6(21)
N(84)–C(71)–C(85)	120.9(20)
C(71)–C(72)–C(73)	127.8(24)
C(72)–C(73)–C(74)	117.9(23)
C(73)–C(74)–C(75)	124.3(20)
C(73)–C(74)–C(83)	115.8(20)
C(75)–C(74)–C(83)	119.9(19)
C(74)–C(75)–C(76)	119.9(21)
C(75)–C(76)–C(77)	125.1(20)
C(76)–C(77)–C(78)	127.4(22)
C(76)–C(77)–C(82)	114.7(19)
C(78)–C(77)–C(82)	118.0(21)
C(77)–C(78)–C(79)	123.7(24)
C(78)–C(79)–C(80)	118.5(22)
C(79)–C(80)–N(81)	122.1(20)
C(79)–C(80)–C(87)	120.9(19)
N(81)–C(80)–C(87)	117.0(19)
C(80)–N(81)–C(82)	118.2(19)
C(77)–C(82)–N(81)	119.5(19)
C(77)–C(82)–C(83)	123.8(20)
N(81)–C(82)–C(83)	116.5(19)
C(74)–C(83)–C(82)	116.3(19)
C(74)–C(83)–N(84)	122.4(20)
C(82)–C(83)–N(84)	121.1(21)
C(71)–N(84)–C(83)	122.4(19)
C(71)–C(85)–C(86)	130.7(22)
C(53)–C(86)–C(85)	138.3(23)
C(80)–C(87)–C(88)	126.5(19)
C(11)–C(88)–C(87)	122.5(20)

3. Results and discussion

3.1. Syntheses

2,9-Dimethyl-1,10-phenanthroline (**1**) in dry tetrahydrofuran (THF) was treated with two equivalents of lithium diisopropylamide (LDA), prepared from diisopropylamine and butyllithium, in an inert atmosphere to give the dilithium salt (**2**). A THF solution of two equivalents of ferrocenecarboxaldehyde (**3**) was added to the reaction mixture and the resulting product (**4**) isolated after silica column chromatographic purification, as a yellow solid in 35% yield (Scheme 1). Refluxing a dry toluene solution of (**4**) and pyridinium toluene-*p*-sulphonate (PTPS) gave the new bisferrocenyl vinyl-linked phenanthroline ligand L^1 as a deep red solid in 72% yield (Scheme 1).

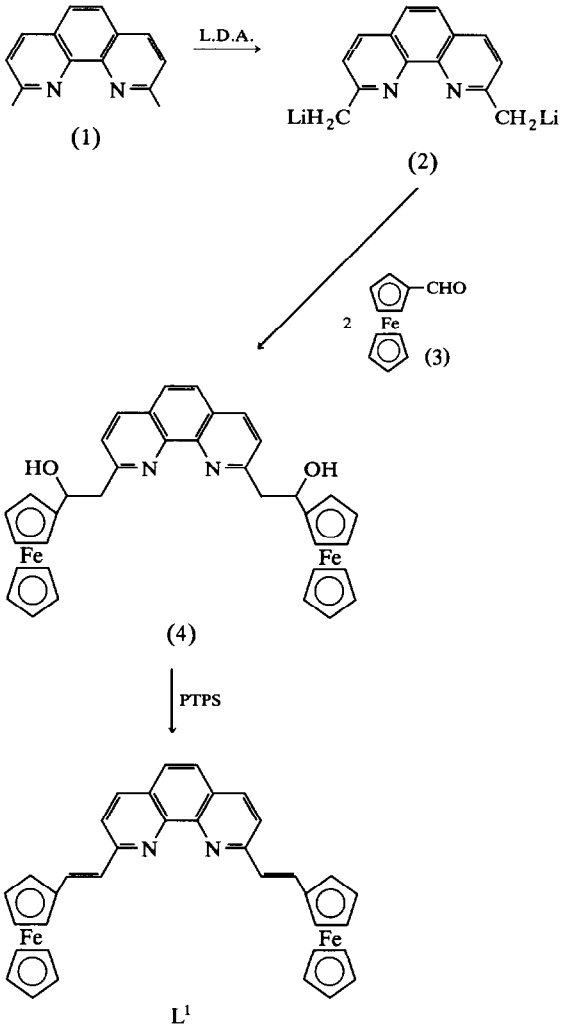
2,9-Diformyl-1,10-phenanthroline (**5**) [11] was dissolved in refluxing dry THF, and a THF solution of two equivalents of 4-aminophenylferrocene (**6**) [12] added dropwise. The resulting solution was refluxed for an additional 3 h using a Dean and Stark apparatus to remove azeotropically the water produced in the condensation reaction. Removal of solvent and purification on a Sephadex column gave the new Schiff-base ligand L^2 in 64% yield (Scheme 2). Ligand L^3 was prepared as a yellow solid in an analogous fashion to L^2, using two equivalents of 4-aminoveratrole (**7**) and (**5**) (Scheme 3). Sodium borohydride reduction of L^3 gave the amine ligand L^4, which was condensed with an excess amount of chlorocarbonylferrocene (**8**) [13] in the presence of triethylamine and dimethylaminopyridine DMAP, to give L^5 as a yellow powder in 26% yield (Scheme 4).

An analogous synthetic pathway starting with Schiff-base ligand L^2 gave, upon reduction, L^6 and on reaction with excess (**8**) the polyferrocene 2,9-substituted phenanthroline ligand L^7 as a yellow solid (Scheme 5). The structures of all these new ligands were characterised on the basis of spectroscopic and analytical evidence (see Section 2).

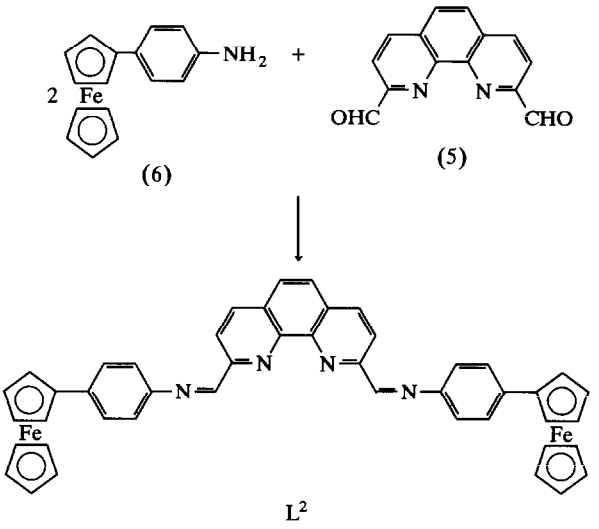
3.2. X-ray structural investigation of L^1

Deep red crystals of L^1 suitable for X-ray structural investigation were obtained from slow evaporation of a deuterated chloroform NMR solution.

The structure consists of discrete molecules of $Fe_2N_2C_{36}H_{28}$ (Fig. 1), together with two solvent molecules of deuterochloroform (not shown). The structure confirms that the isomer with a *trans–trans* arrangement about the vinylic bonds was isolated. Of particular interest is the planarity of the molecule (Fig. 2). The angle between the substituted cyclopentadiene ring and the adjacent pyridine ring is only 5.9° or 13.3°. All the atoms, except for the two iron atoms and the



Scheme 1.



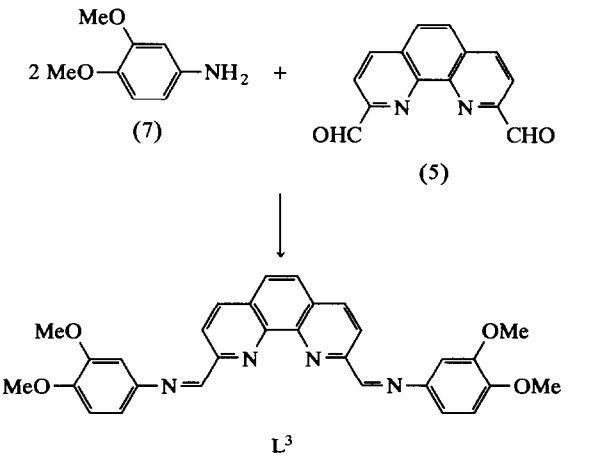
Scheme 2.

two unsubstituted cyclopentadiene rings, are approximately planar, with a maximum atomic deviation of 0.35 Å. Also noteworthy is the fact that the two unsubstituted cyclopentadiene rings lie respectively above and below the plane of the molecule (Fig. 2).

3.3. Co-ordination studies

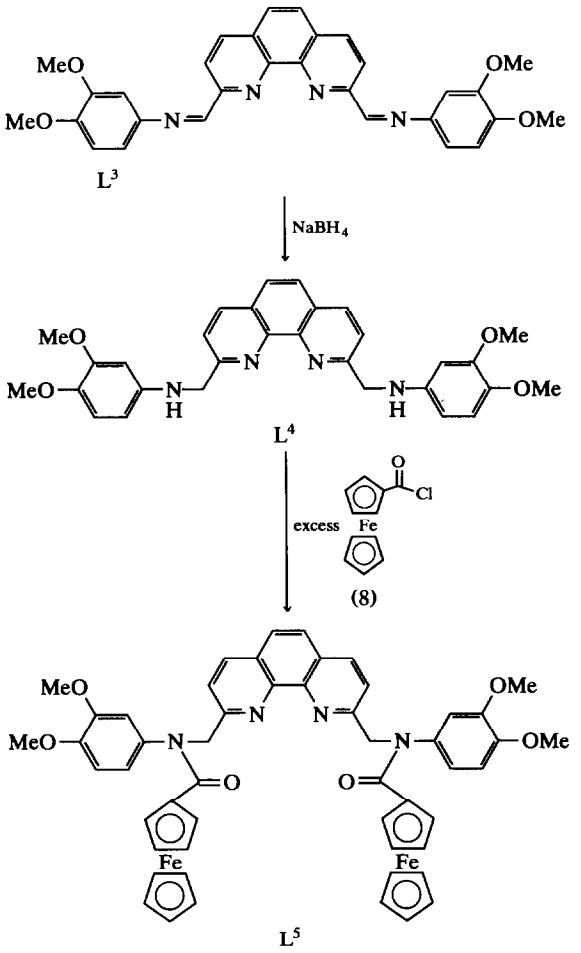
Solution complexation studies with the lithium cation were investigated by ^{1}H NMR spectroscopy. In a typical titration experiment, the stepwise addition of a concentrated solution of lithium tetrafluoroborate in deuterated acetonitrile to a deuterated acetonitrile solution of L^1 resulted in appreciable upfield shifts of the signals from the cyclopentadienyl (Cp) ring protons, in particular those of the unsubstituted Cp ring protons of up to 0.5 ppm. No further significant shifts were seen after addition of 0.5 equivalent of lithium salt, suggesting a solution stoichiometry of $2L^1$: Li^+ in which the lithium cation is possibly tetrahedrally co-ordinated, as depicted in Fig. 3. This proposed structure of the complex may account for the observed upfield shifts of the ferrocenyl Cp protons, resulting from the π-electronic shielding effects of the respective nearby phenanthroline moieties. Similar ^{1}H NMR spectral features have been seen for the 1,10-phenanthroline catenands and metallocatenates reported by Dietrich-Buchecker *et al.* [15].

Interestingly, analogous experiments with the Schiff-base ligands L^2 and L^3 (see Fig. 4) suggested the co-existence of complexes of both 2:1 and 1:1 ligand to lithium ratio in solution. Figure 4 shows the imine and methoxy proton titration curves of L^3 on addition of Li^+, and clearly illustrates that on addition of up to

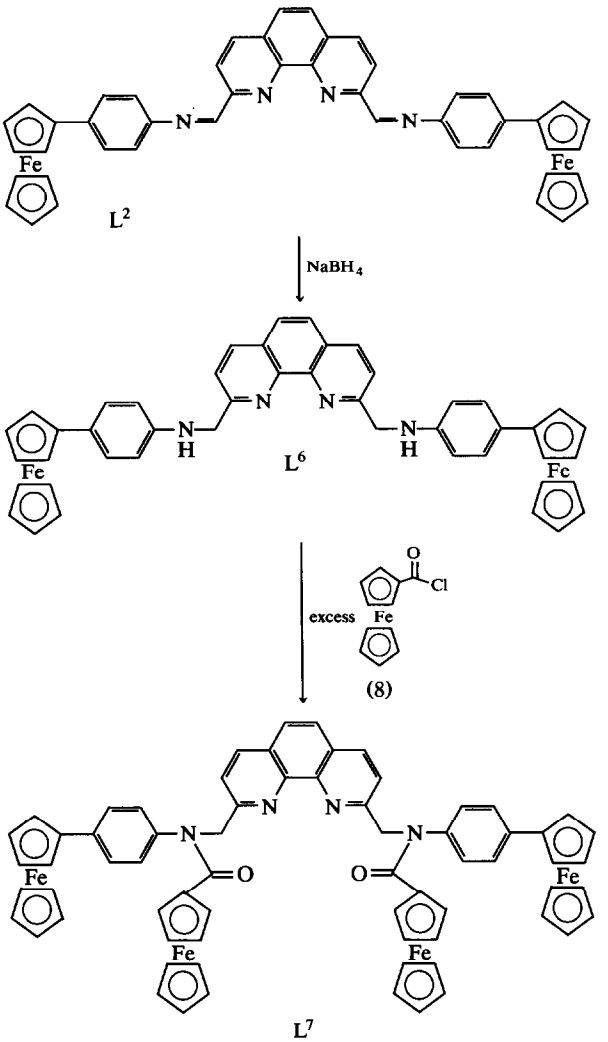


Scheme 3.

0.5 equivalents of lithium, significant upfield shifts of these ligand's protons are observed. However, with an addition of more Li^+ the signals of the relevant protons of L^3 move back downfield. A possible explanation for this behaviour is that at 0.5 equivalents of lithium the equilibrium between the 2:1 and 1:1 ligand to metal complexes lies to the left (Scheme 6). Increasing the concentration of lithium cations drives the equilibrium to the right, and consequently the 1:1 ligand-to-metal complex predominates in solution. The ^1H NMR titration curves obtained for the amine-linked phenanthroline ligands, L^4 and L^6, suggested the presence of only 2:1 ligand to lithium cation solution complexes. In contrast, for the ferrocenyl-amide-linked phenanthroline derivatives, L^5 and L^7, only 1:1 solution stoichiometries were observed. For example, the titration curves for some of the signals from various protons of L^5 on addition of Li^+ are shown in Fig. 5, and reveal perturbations of both ferrocenyl and phenanthroline protons. The lithium cation is known to form stable complexes with tertiary amide carbonyl groups [6,16,17] and so a possible mode of complexation for L^5 and L^7 may involve a four co-ordinate complex composed of the phenanthroline moiety and the two amide carbonyl oxygen donor atoms (Fig. 6).



Scheme 4.



Scheme 5.

Attempts were made to isolate lithium complexes of L^1–L^7 by refluxing acetonitrile solutions of the relevant ligand with an excess of lithium tetrafluoroborate. Upon cooling, oily products were always obtained, and despite repeated attempts at purification by Sephadex column chromatography these could not be crystallised. Consequently, although fast atom bombardment mass spectrometry detected both complexes with 2:1 and 1:1 ligand: Li^+ cation stoichiometries, satisfactory elemental analyses for these complexes were not obtained.

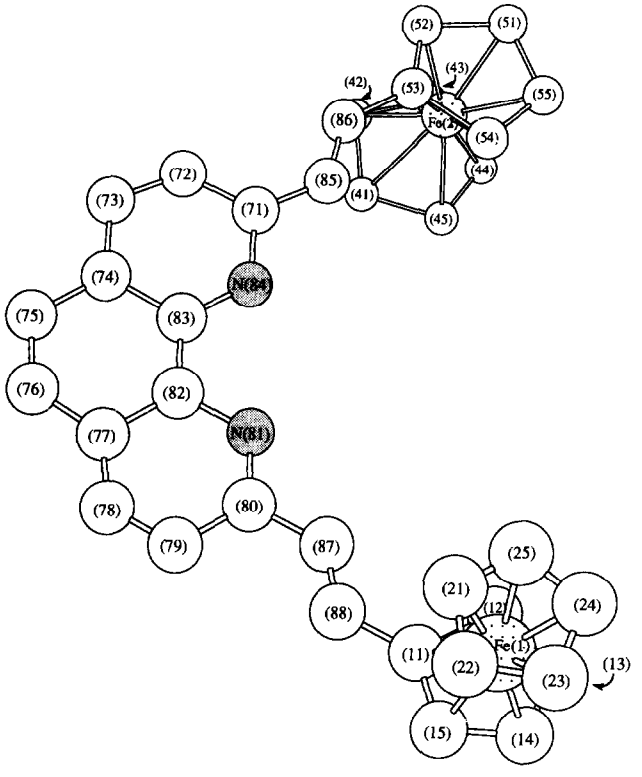


Fig. 1. The structure of L^1.

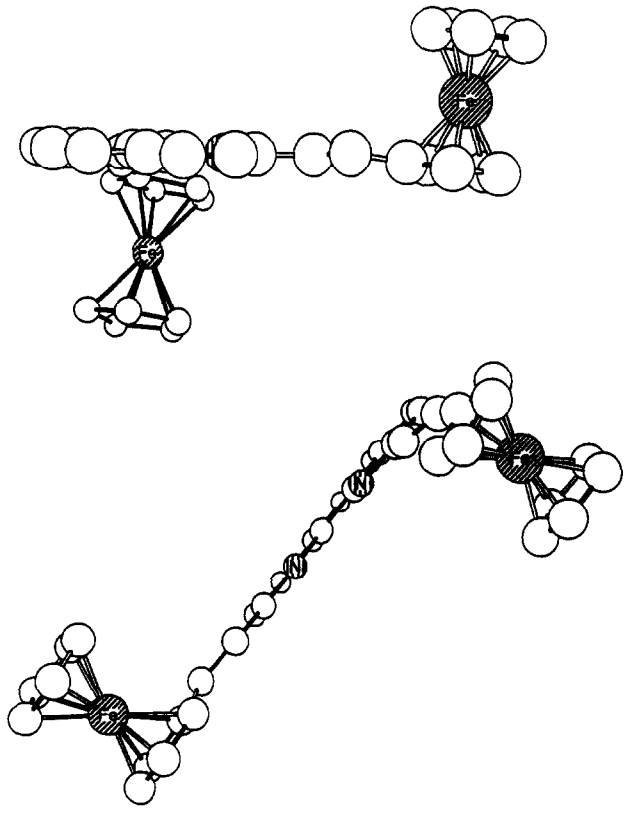


Fig. 2. The structure of L^1 illustrating the positions of the attached ferrocene moieties.

3.4. Electrochemical studies

The electrochemical properties of L^1, L^2, and L^5–L^7 were investigated in acetonitrile by cyclic voltammetry with $NBu^n_4BF_4$ as the supporting electrolyte. Ligands L^1, L^2, L^5 and L^6 each exhibited a one-wave reversible oxidation in the 0.3–0.7 V region (*vs.* SCE) typical of a substituted ferrocene derivative (Table 3). These electrochemical findings suggest that the two ferrocene moieties present in the ligands act independently of one another, and become oxidised in one step. Coulometric studies confirmed the respective oxidation waves to be two-electron processes. Ligand L^7, which contains two pairs of chemically distinct ferrocene moieties, exhibited two, two-electron reversible oxidation processes corresponding to the two aryl ferrocenes (+0.56) and two amide-substituted ferrocene moieties (+0.70) (Table 3).

Cyclic voltammograms were also recorded after progressively adding stoichiometric equivalents of Li^+, Na^+, K^+, and equimolar mixtures of $Li^+/Na^+/K^+$ to the respective electrochemical ligand containing solutions, and the results are summarised in Table 3. The lithium cation induced significant one wave anodic shifts in the ferrocene redox couples of ligands L^1, L^2, L^5 and L^7. Ligand L^6, which contains a saturated CH_2 linkage between the two ferrocene centres and the phenanthroline unit, did not sense the lithium cation, suggesting that the primary mode of electrochemical recognition of lithium cations with L^2 is electrochemi-

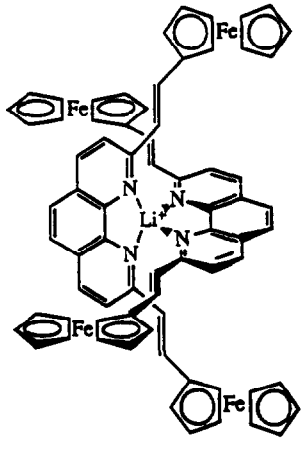


Fig. 3. Possible structure of the $2L^1$: Li^+ complex in solution.

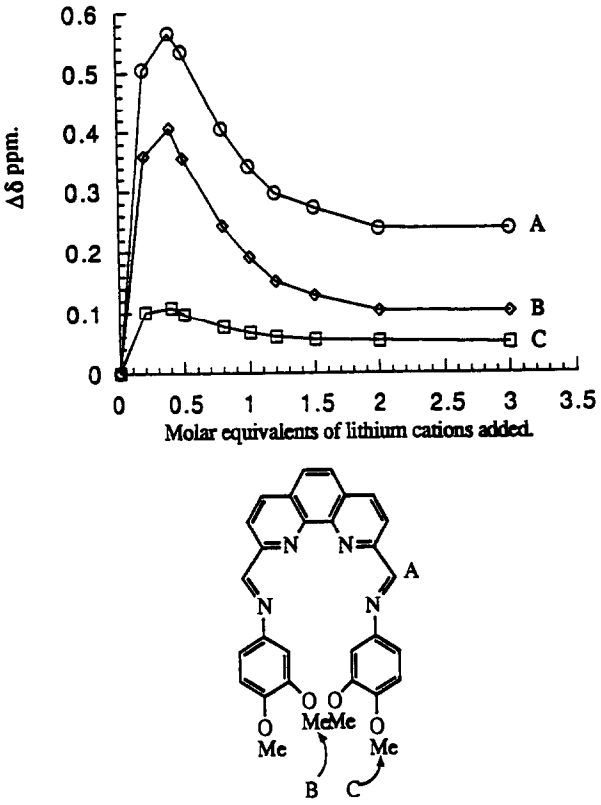


Fig. 4. Proton NMR titration of L^3 and Li^+ in CD_3CN.

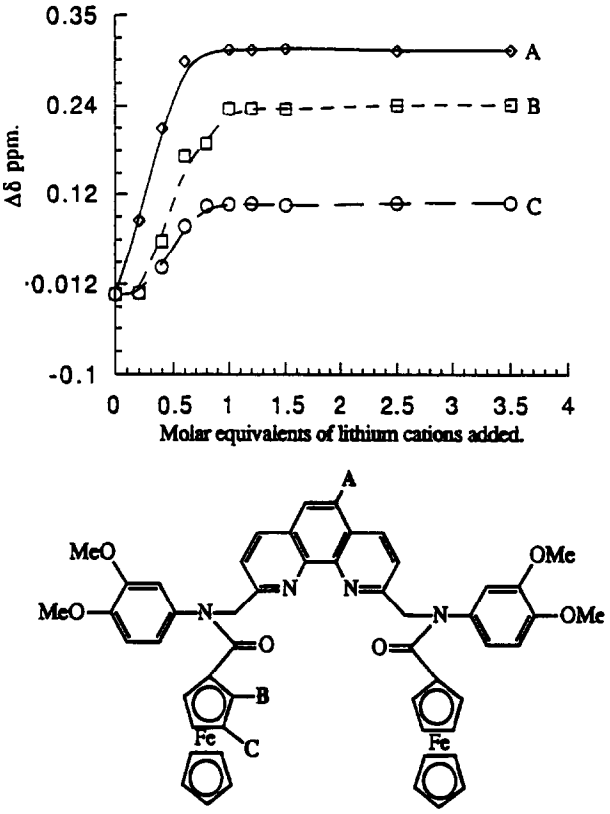
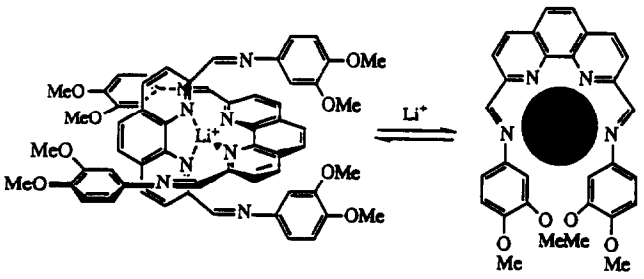


Fig. 5. Proton NMR titration of L^5 and Li^+ in CD_3CN.

cally communicated *via* the through-bond-conjugated Schiff-base linkage and not through space electrostatic interactions [18]. It is noteworthy that the first redox couple of L^7 displayed virtually no shift upon addition of lithium cations which, as for L^6, is probably because of the saturated CH_2 linkages insulating the aryl-substituted ferrocene redox centres from the phenanthroline recognition site of the metal cation.

The addition of an excess of sodium or potassium cations to the redox-active ligands did not lead to any detectable anodic shifts of the ferrocene redox couples, in agreement with ^1H NMR titration studies, which indicated only very small ligand proton perturbations ($\Delta\delta < 0.05$ ppm) with these cations.

The results of the electrochemical competition experiments are of particular relevance to chemical sensor technology. When an equimolar mixture of $Li^+/Na^+/K^+$ cations was added to electrochemical solutions of L^1, L^2, L^5 and L^7 the respective ferrocene redox couples were shifted anodically by the same



Scheme 6.

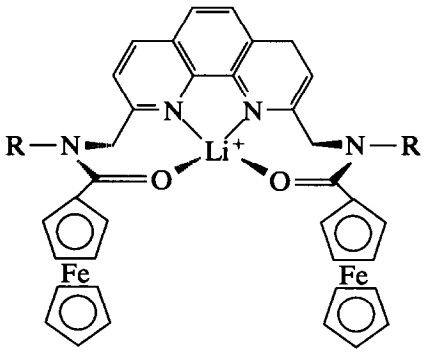


Fig. 6. Possible structure of the L^5 or L^7 1:1 lithium complex in solution.

TABLE 3. Electrochemical data for ferrocene-containing ligands

	L^1	L^2	L^5	L^6	L^7
E [a] (V)	+0.48 [b]	+0.46 [b]	+0.64 [b]	+0.37 [b]	+0.56 [b], +0.70 [b]
ΔE_p [c] (mV)	80	60	80	60	100, 100
$\Delta E(Li^+)$ [d] (mV)	30	30	40	< 10	< 10, 40
$\Delta E(Na^+)$ [d] (mV)	< 10	< 10	< 10	< 10	< 10, < 10
$\Delta E(K^+)$ [d] (mV)	< 10	< 10	< 10	< 10	< 10, < 10
$\Delta E(Li^+/Na^+/K^+)$ [e] (mV)	30	30	40	–	< 10, 40

[a] Solutions were *ca.* 2×10^{-3} mol dm^{-3} in compound, and potentials were determined with reference to the saturated calomel electrode. [b] Two-electron reversible oxidation process. [c] Separation between anodic and cathodic peak potentials; values for ferrocene under identical conditions ranged from 80 mV to 90 mV. [d] One wave shift in respective ferrocenyl oxidation potential produced by presence of guest metal cations (four equivalents) added as their tetrafluoroborate salt for lithium and hexafluorophosphate salts for sodium and potassium. [e] One wave shift in respective ferrocenyl oxidation potential produced by an equimolar mixture of metal cations (four equivalents).

amount as that induced by the Li^+ cation alone. This indicates these ligands exhibit a degree of selectivity for lithium cations in the presence of sodium and potassium cations.

4. Conclusions

The synthesis of a variety of new redox-active 2,9-polyferrocenyl-substituted phenanthroline derivatives designed to bind lithium cations has been achieved. The structure of one of the ionophores has been determined. Co-ordination chemical studies revealed that the 2,9-bis vinylic- and amine-ferrocene-linked phenanthroline ligands L^1, L^4, L^6 form two ligand: Li^+ complexes in solution, whereas the Schiff-base ligands L^2 and L^3 give an equilibrium mixture of 2:1 and 1:1 complexes. The 2,9 bis-amide ferrocene-linked phenanthroline ionophores L^5 and L^7 form 1:1 solution complexes with the lithium cation. Except for L^6, all the ferrocene-containing ligands electrochemically recognised the Li^+ cation but were not redox-responsive to either Na^+ or K^+ cations. Electrochemical recognition competition experiments with Li^+, Na^+ and K^+ showed L^1, L^2, L^5 and L^7 to be first-generation prototype amperometric-sensing reagents for Li^+.

Acknowledgments

We thank MediSense (UK) for a studentship (J.P.D.), and the SERC for use of the Mass Spectrometry Service at University College Swansea.

References

1 J.W. Jefferson, J.H. Geist, D.L. Ackerman and J.A. Carroll, *Lithium Encyclopaedia for Clinical Practice*, (2nd edn.), American Psychiatric Press, Washington, DC, 1987.
2 K. Hiratani, K. Taguchi, H. Sugihara and T. Okada, *Chem. Letts.*, (1986) 197.
3 M.J. Pugia, B.E. Knudsen and R.A. Bartsch, *J. Org. Chem., 52* (1987) 2617.
4 M. Inouye, M. Veno and T. Kitao, *J. Am. Chem. Soc., 112* (1990) 8977.
5 A.F. Scholl and I.O. Sutherland, *J. Chem. Soc., Chem. Commun.*, (1992) 1716.
6 U. Olsher, R.M. Izatt, J.S. Bradshaw and N.K. Dalley, *Chem. Rev., 91* (1991) 137, and references therein.
7 R. Kataky, P.E. Nicholson and D. Parker, *Tetrahedron Letters, 30* (1989), 4559.
8 K. Kimura, T. Yamashita, M. Kaneshige and M. Yokoyama, *J. Chem. Soc., Chem. Commun.*, (1992) 969.
9 Y. Habata, M. Ikeda and S. Akabori. *J. Chem. Soc. Perkins Trans., 1* (1992) 2651.
10 H. Sugihara, T. Okada and K. Hiratani, *Chem. Letts.*, (1987) 2391.
11 C.J. Chandler, L.W. Deady and J.A. Reiss, *J. Heterocyclic Chem., 18* (1981) 599.
12 A.N. Nesmeyanov, E.G. Perevalova, R.V. Grolovnya and L.S. Shilavtseva, *Doklady Akad. Nauk. S.S.S.R. 102* (1955) 535.
13 H.H. Lau and H. Hart, *J. Org. Chem. 24* (1959) 280.
14 G.M. Sheldrich, SHELX 76, *Package for Crystal Structure Determination*, University of Cambridge, 1976.
15 C.O. Dietrich-Buchecker, J.P. Sauvage and J.M. Kern, *J. Am. Chem. Soc., 106* (1984) 3043.
16 E. Metzger, R. Aeschimann, M. Egli, G. Suter, R. Dohner, D. Amman, M. Dobler and W. Simon. *Helvetica Chimica Acta, 69* (1986) 1821.
17 P.D. Beer, A.D. Keefe, H. Sikanyika, C. Blackburn, J.F. McAleer and M.G.B. Drew. *J. Chem. Soc., Dalton Trans.*, (1990) 3295.
18 P.D. Beer, *Chem. Soc. Rev., 18* (1989) 409; *Adv. Inorganic Chem., 39* (1992) 79.