Anion Recognition Properties of New Upper-Rim Cobaltocenium Calix[4]arene Receptors

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Received May 27, 1999

New isomeric upper-rim bis(cobaltocenium)calix[4]arene receptors L^1, L^2 and a novel upper-rim cobaltocenium-bridged calix[4]arene derivative L^3 have been synthesized and shown to selectively complex and electrochemically sense a variety of anionic guest species. Single-crystal X-ray structures of the chloride complexes of L^1 and L^3 emphasize the importance of hydrogen bonding and the topological nature of the upper-rim anion recognition site to the anion recognition process in the solid state. Proton NMR titration studies in deuterated DMSO solutions reveal these receptors form strong and remarkably selective complexes with $MeCO_2^-$ and $H_2PO_4^-$ anions dependent upon the positioning of lower-rim tosyl substituents. Cyclic voltammetric investigations have demonstrated these receptors to electrochemically recognize carboxylate, $H_2PO_4^-$, and Cl^- anions.

Introduction

The molecular recognition of anionic guest species of biochemical and environmental importance by positively charged or neutral electron-deficient abiotic receptor molecules is an area of ever increasing research activity.[1] Anions play numerous fundamental roles in biological and chemical processes,[2] as exemplified by the majority of enzymes binding anions as either substrates or cofactors, and many anions act as ubiquitous nucleophiles, bases, redox agents, and phase-transfer catalysts. Also their effects as environmental pollutants[3] have only recently been realized. Intensive arable farming has led to excess amounts of nitrate and phosphate contributing to the eutrophication of lakes and rivers. In addition the discharge of radioactive pertechnetate from the nuclear fuel cycle[4] and from radiopharmaceutical usage is of particular environmental concern. The main strategies in the design of synthetic anion complexing reagents have focused on cationic polyammonium,[5] polyguanidinium,[6] quaternary ammonium,[7] expanded porphyrin[8] host systems, and a variety of Lewis acidic containing receptors such as tin,[9] silicon,[10] boron,[11] mercury,[12] and uranyl.[13] Neutral organic receptors which bind anions solely via favorable hydrogen-bonding interactions have also been recently exploited.[14]

The unique topological calix[4]arene host structural framework[15] has been recently modified for the recognition of anions.[16] In particular, Atwood and co-workers have capped calixarene aromatic faces with positively charged transition metal organometallic arene centers

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to produce a range of π-metalated calixarene anion receptors.[17] We have initiated a research program aimed at the construction of innovative spectral and electrochemical sensory reagents for anions based on novel transition metal organometallic and coordination receptor systems.[18] We have recently shown that incorporating these inorganic signaling probes into the lower-rim calix[4]arene ligand framework leads to new receptor systems capable of selectively detecting dihydrogen phosphate anions.[19] To investigate anion recognition at the calix[4]arene upper-rim, we report here the syntheses and anion coordination properties of new upper-rim bis(cobaltocenium) calix[4]arene receptors and a novel cobaltocenium-bridged calix[4]arene derivative. These systems exhibit remarkable and contrasting anion thermodynamic stability and selectivity trends that are dependent upon the degree of preorganization of the upper-rim anion recognition site, which is dictated by the relative positioning of lower-rim tosyl substituents.[20]

Experimental Section

Instrumentation. Nuclear magnetic resonance spectra were obtained on a Varian 500 Unity instrument using the solvent deuterium signal as internal reference. Chemical shifts are given in ppm, and coupling constants (J) are given in hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, dd = double doublet, brs = broad singlet. Fast atom bombardment mass spectrometry was performed by the EPSRC mass spectrometry service at the University of Wales, Swansea, U.K. Electrochemical measurements were carried out using an E. G. and G. Princeton Applied Research 362 scanning potentiostat. Elemental analyses were performed at the Inorganic Chemistry Laboratory, University of Oxford, and were within ±0.4% of the theoretical values for the elements indicated unless otherwise noted. Melting points were determined on a simple melting point apparatus and are reported without correction. Thin-layer chromatography was used on either silica gel plates (Merck) with 254 nm fluorescent indicator or alumina plates (Fluka).

Solvent and Reagent Pretreatment. Solvents were purchased in their anhydrous form and used directly or dried by distillation from sodium benzophenone (THF), calcium hydride (CH_2Cl_2 and acetonitrile), or P_2O_5 (DMF). Unless otherwise indicated, commercial grade chemicals were used without further purification.

Syntheses. 25,26,27,28-Tetrahydroxycalix[4]arene (**1**),[21] chlorocarbonylcobaltocenium chloride,[22] 1,1'-bis(chlorocarbonyl)cobaltocenium chloride,[22] and **11**[20] were prepared according to literature procedures.

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25,27-Bis(benzyloxycarbonyloxy)-26,28-dihydroxycalix[4]arene (2). A mixture of 25,26,27,28-tetrahydroxycalix[4]arene (**1**) (4.2 g, 10 mmol) and NaH (80% in oil, 0.7 g, 23 mmol) in anhydrous THF (100 mL) was allowed to stir at room temperature for 1 h. Chlorobenzyl carbonate (3.2 mL) was then added, and the mixture was stirred for 6 h. The progress of the reaction was followed by monitoring the disappearance of **1** on TLC (SiO_2, toluene/hexane/acetonitrile, 80:18.2). When complete conversion was observed, the solvents were removed under reduced pressure, and the remaining residue was partitioned between water and CH_2Cl_2. Separation of the organic layer and evaporation of the solvent in vacuo yielded 6.6 g (96%) of crude product, which was purified by recrystallization from toluene/hexane to give white crystals. A sample for analysis was then purified by column chromatography on silica gel, by eluting the product with toluene/hexane/acetonitrile, 7:2:1 v/v. Mp: 185–187 °C. ^{1}H NMR (CD_2Cl_2): δ 7.72 (dd, J = 8.1 Hz, J = 1.3 Hz, 4H, ArH), 7.28 (m, 6H, ArH), 6.95 (d, J = 7.6 Hz, 4H, Ar 4,6,16,18-H), 6.74 (d, J = 7.4 Hz, 4H, 4H, Ar 10,12,22,24-H), 6.68 (s, 2H, OH), 6.67 (dd, J = 7.6 Hz, 2H, Ar 11,23-H), 6.64 (t, J = 74 Hz, 2H, Ar 5, 17-H), 5.20 (s, 4H, OCH$_2$Ar), 3.82 and 3.35 (Abq, J = 14.0 Hz, 8H, ArCH$_2$-Ar). ^{13}C NMR (CD_2Cl_2): δ 188.3 (s, C=O), 153.33 and 152.95 (2 × s, Ar 25,26,27,28-C), 146.02 (s, Ar–C), 135.41 (s, Ar–C), 132.82 (s, Ar–C), 129.47 (d, Ar 5,17-C), 129.34 (d, Ar 11,23-C), 129.15 and 129.04 (2 × s, Ar–C), 128.87 (d, Ar–C), 127.02 (d, Ar 10,12,22,24-C), 120.31 (d, Ar 4,6,16,18-C), 71.24 (t, OCH$_2$Ar), 32.21 (t, ArCH$_2$Ar). MS: m/z 692 (M$^+$, 100). Anal. Calcd for $C_{44}H_{36}O_8$ (692.77): C, 76.29; H, 5.24. Found: C, 76.20; H, 5.18.

5,17-Dinitro-25,27-bis(benzyloxycarbonyloxy)-26,28-dihydroxycalix[4]arene (3). To a solution of 25,27-bis(benzyloxycarbonyloxy)-26,28-dihydroxycalix[4]arene (**2**, 0.69 g, 1 mmol) in CH_2Cl_2 (30 mL) and glacial acetic acid (5 mL) was added 0.7 mL of HNO_3 (90%) at 0 °C. The reaction mixture was vigorously stirred at this temperature for 10 min and quenched with cold water (50 mL). Extraction with CH_2Cl_2 (4 × 50 mL) and removal of solvent in vacuo gave upon treatment with methanol (40 mL) 0.65 g (84%) of a crude product, which was purified by column chromatography (SiO_2, CH_2Cl_2/hexane/acetonitrile, 70:25.5 v/v). ^{1}H NMR (DMSO-d_6): δ 8.48 (brs, 2 H, OH), 8.13 (s, 4 H, ArH ortho to NO$_2$), 7.58 (d, J = 6.5 Hz, 4H, ArH), 7.46 (m, 6 H, ArH), 7.02 (d, J = 7.5 Hz, 4H, ArH), 6.68 (dd, 2H, ArH), 5.32 (s, 4H, OCH$_2$Ar), 3.74 and 3.39 (ABq, 8H, ArCH$_2$Ar). ^{13}C NMR (DMSO-d_6): δ 188.0 (s, C=O), 159.8 and 152.6 (s, 25,26,27,28-C), 147.0 (s, Ar–C), 139.0 (s, Ar–C), 135.1 (s, Ar–C), 131.1 (s, Ar–C), 129.7 (d, Ar–C0, 129.4 (d, Ar–C), 128.4 (d, Ar–C), 128.3 (d, Ar–C), 124.9 (d, Ar–C), 124.7 (d, Ar–C), 69.9 (t, OCH$_2$Ar), 32.4 (t,ArCH$_2$Ar). Anal. Calcd for $C_{44}H_{34}N_2O_{12}$ (782.7): C, 67.52; H, 4.38; N, 3.58. Found: C, 67.48; H, 4.35; N, 3.33.

5,17-Dinitro-25,27-bis(benzyloxycarbonyloxy)-26,28-bis(tolysulfonyloxy)calix[4]arene (4). After stirring the mixture of 5,17-dinitro-25,27-bis(benzyloxycarbonyloxy)-26,28-dihydroxycalix[4]arene (**3**) 0.78 g, 1 mmol) and NaH (80% in oil, 0.12 g, 4 mmol) in THF (20 mL) at room temperature for 10 min, toluene-4-sulfonyl chloride (0.5 g, 2.6 mmol) was added, and the reaction mixture was allowed to stir for 12 h. The progress of the reaction was followed by monitoring the disappearance of **3** on thin-layer chromatography (benzene/CH_2Cl_2, 75:25 v/v). The reaction was quenched with water (20 mL), and the organic layer was reduced to dryness. The residue was heated with *n*-hexane (2 × 50 mL), and yellow solid produced was purified by recrystallization from toluene/hexane to give 0.75 g (68%) yield. An analytical sample was purified by column chromatography on silica gel, eluting with benzene/CH_2Cl_2, 7:3 v/v. Mp: 215–218 °C. ^{1}H NMR (CDCl$_3$): δ 7.82 (d, J = 7.3 Hz, 4H, ArH), 7.54 (d, 4H, ArH), 7.56 (s, 4H, ArH, ortho to NO$_2$), 7.50 (m, 10H, ArH), 7.32 (d, J = 7.6 Hz, 4H, ArH), 7.16 (dd, 2H, ArH), 5.62 (s, 4H, OCH$_2$Ar), 4.02 and 3.00 (ABq, J = 13.9 Hz, 8H, ArCH$_2$Ar), 2.43 (s, 6H, CH$_3$). ^{13}C NMR

(CDCl$_3$): δ 188.0 (s, C=O), 154.4 (s, Ar−C), 148.1 (s, Ar−C), 136.7 (s, Ar−C), 134.1 (s, Ar−C), 131.7 (s, Ar−C), 130.0 (d, Ar−C), 129.2 (d, Ar−C), 128.8 (d, Ar−C), 128.7 (d, Ar−C), 128.6 (d, Ar−C), 128.3 (d, Ar−C), 127.2 (d, Ar−C), 124.0 (d, Ar−C), 71.1 (t, OCH$_2$Ar), 31.1 (t, ArCH$_2$Ar), 21.7 (q, CH$_3$). MS: *m/z* 1091 (M$^+$, 100). Anal. Calcd for C$_{58}$H$_{46}$N$_2$O$_{16}$S$_2$ (1091.1): C, 63.84; H, 4.25; N, 2.57. Found: C, 63.72; H, 4.20; N, 2.55.

5,17-Dinitro-25,27-dihydroxy-26,28-bis(tolylsulfonyloxy)-calix[4]arene (5). 5,17-Dinitro-25,27-bis(benzyloxycarbonyl-oxy)-26,28-bis(tolylsulfonyloxy)calix[4]arene (**4**, 1.09 g, 1 mmol) was suspended in 30 mL of dry CH$_2$Cl$_2$ under an argon atmosphere and was treated dropwise with trimethylsilyl iodide (0.5 mL) at room temperature over a period of 10 min. The mixture was then heated to reflux for 10 h, and 0.1 mol sodium thiosulfate solution (5 mL) was added. The reaction mixture was refluxed for 10 min and cooled to room temperature, distilled water (5 mL) was added, and the solution was stirred vigorously for 1 h. The phases were separated, and the aqueous phase was extracted with CH$_2$Cl$_2$ (30 mL). The organic layer was dried (Na$_2$SO$_4$), and solvent was removed in vacuo to furnish a yellow solid. This crude product was then treated with hot hexane. Crystallization (THF/*n*-hexane) and drying under high vacuum furnished 0.69 g (85%) of **5** as colorless crystals. An analytical sample was purified by column chromatography (CH$_2$Cl$_2$/hexane, 5:1). ^{1}H NMR (DMSO-d_6): δ 7.78 (dd, *J* = 8.2 Hz, *J* = 1.7 Hz, 4H, TosH), 7.55 (d, 4H, TosH), 7.41 (brs, 4H, ArH ortho to NO$_2$), 7.20 (brs, 2H, OH), 7.08 (d, *J* = 7.5 Hz, 4H, ArH), 6.73 (dd, 2H, ArH), 3.72 and 3.21 (ABq, *J* = 13.4 Hz, 8H, ArCH$_2$Ar), 2.43 (s, 6H, CH$_3$). ^{13}C NMR (DMSO-d_6): δ 152.7 (s, Ar−C), 149.5 (s, Ar−C), 146.3 (s, Ar−C), 143.7 (s, Ar−C), 136.2 (s, Ar−C), 131.6 (s, Ar−C), 130.3 (d, Ar−C), 129.6 (s, Ar−C), 129.1 (d, Ar−C), 128.4 (d, Ar−C), 123.3 (d, Ar−C), 119.6 (d, Ar−C), 32.0 (t, ArCH$_2$Ar), 21.1 (q, CH$_3$). MS: *m/z* 822 (M$^+$, 100). Anal. Calcd for C$_{42}$H$_{34}$N$_2$O$_{12}$S$_2$ (822.8): C, 61.31; H, 4.16; N, 3.40. Found: C, 61.40; H, 4.15; N, 3.44.

5,17-Diamino-25,27-dihydroxy-26,28-bis(tolylsulfonyloxy)-calix[4]arene Dihydrochloride (6)·2HCl. 5,17-Dinitro-25,27-dihydroxy-26,28-bis(tolylsulfonyloxy)calix[4]arene (**5**, 0.82 g, 1 mmol) was suspended in 30 mL of THF, and a catalytic amount of 10% Pd/C was cautiously added. The mixture was then hydrogenated at 50 psi at 45−50 °C for 1 h. An additional catalytic amount of 10% Pd/C was then added, and the mixture was hydrogenated a further 1 h at 50 psi. The reaction mixture was cooled to room temperature and filtered through Celite. The filtrate was then reduced in vacuo to dryness to give 0.73 g (98%) of free amine of **6**. This free base was then dissolved in a minimum amount of CH$_2$Cl$_2$, acidified with EtOH/HCl, and added to 30 mL of dry diethyl ether to furnish the dihydrochloride salt as a white solid. Crystallization (MeOH/Et$_2$O) and drying under high vacuum provided 0.59 g (71%) of **6·2HCl**. ^{1}H NMR free base (CD$_2$Cl$_2$): δ 7.80 (dd, *J* = 8.34 Hz, *J* = 1.70 Hz, TosH), 7.42 (d, 4H, TosH), 7.01 (d, *J* = 7.4 Hz, 4H, ArH), 6.73 (dd, 2H, ArH), 6.04 (s, 4H, ArH ortho to NH$_2$), 5.15 (s, 2H, OH), 3.89 and 3.02 (ABq, *J* = 14.1 Hz, 8H, ArCH$_2$Ar), 3.40 (m, 4H, NH$_2$), 2.50 (s, 6H, CH$_3$). ^{13}C NMR free base (CD$_2$Cl$_2$): δ 152.6 (s, Ar−C), 146.0 (s, Ar−C), 145.7 (s, Ar−C), 135.0 (s, Ar−C), 132.9 (s, Ar−C), 130.4 (s, Ar−C), 130.2 (d, Ar−C), 128.9 (d, Ar−C), 128.6 (d, Ar−C), 128.5 (d, Ar−C), 119.9 (d, Ar−C), 115.4 (d, Ar−C), 31.8 (t, ArCH$_2$Ar), 21.6 (q, CH$_3$). MS: *m/z* 762 (M$^+$, 66) Anal. Calcd for C$_{42}$H$_{38}$N$_2$O$_8$S$_2$ (762.8): C, 66.12; H, 5.02; N, 3.67. Found: C, 66.55; H, 5.21; N, 3.54.

^{1}H NMR **6·2HCl** (CD$_3$OD): δ 7.71 ((dd, *J* = 8.3 Hz, *J* = 1.70 Hz, 4H, TosH), 7.52 (d, 4H, TosH), 7.16 (d, *J* = 7.4 Hz, 4H, ArH), 6.84 (dd, 2H, ArH), 6.72 (s, 4H, ArH, ortho to NH$_2$), 4.08 and 3.11 (ABq, *J* = 14.0 Hz, 8H, ArCH$_2$Ar), 2.52 (s, 6H, CH$_3$). ^{13}C NMR (CD$_3$OD): δ 153.5 (s, Ar−C), 147.5 (s, Ar−C), 145.3 (s, Ar−C), 138.0 (s, Ar−C), 133.3 (s, Ar−C), 131.7 (s, Ar−C), 131.1 (d, Ar−C), 130.1 (s, Ar−C), 130.0 (d, Ar−C), 129.5 (d,

Ar−C), 123.7 (d, Ar−C), 122.0 (d, Ar−C), 32.6 (t, ArCH$_2$Ar), 21.5 (q, CH$_3$). Anal. Calcd for C$_{42}$H$_{40}$Cl$_2$N$_2$O$_8$S$_2$ (835.8): C, 63.84; H, 4.25; N, 2.57. Found: C, 63.72; H, 4.20; N, 2.55.

5,17-Bis(1-cobaltoceniumyl)carboxamido-25,27-dihy-droxy-26,28-bis(tolylsulfonyloxy)calix[4]arene, L^1. A THF solution (30 mL) containing 5,17-diamino-25,27-dihydroxy-26,28-bis(tolylsulfonyloxy)calix[4]arene dihydrochloride (**6**) (0.83 g, 1 mmol) and pyridine (0.8 mL, 10 mmol) was heated at 60 °C for 15 min under a nitrogen atmosphere. To this solution was added 1-(chlorocarbonyl)cobaltocenium chloride (0.65 g, 2.2 mmol) in dry acetonitrile (60 mL). After the mixture was stirred at room temperature for 5 h, the solvents were removed in vacuo to dryness. The residue was washed with water, treated with aqueous ammonium hexafluorophosphate, and partitioned between water and CH$_2$Cl$_2$. The organic layer was dried (Na$_2$SO$_4$) and evaporated. The resultant solid product was chromatographed on a short silica gel column, using CH$_3$-CN as eluent containing a small amount of ammonium hexafluorophosphate to give the crude product, which was then dissolved in a minimum amount of hot CH$_3$CN, and the product slowly crystallized as yellow crystals (0.82 g, 55% yield). ^{1}H NMR (CD$_3$CN): δ 8.57 (s, 2H, NHCO), 7.85 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 4H, TosH), 7.53 (d, 4H, TosH), 7.31 (s, 4H, ArH ortho to NHCO), 7.16 (d, *J* = 7.5 Hz, 4H, ArH), 6.81 (t, 2H, ArH), 6.01 (t, *J* = 2.1 Hz, 4H, CpH), 5.68 (t, 4H, CpH), 5.63 (s, 10H, CpH), 3.97 and 3.26 (ABq, *J* = 14.1 Hz, 8H, ArCH$_2$Ar), 2.51 (s, 6H, CH$_3$). ^{13}C NMR (CD$_3$CN): δ 160.6 (s, C=O), 153.0 (s, Ar−C), 142.9 (s, Ar−C), 141.2 (s, Ar−C), 137.7 (s, Ar−C), 136.2 (s, Ar−C), 132.9 (s, Ar−C), 131.3 (d, Ar−C), 130.0 (d, Ar−C), 129.3 (d, Ar−C), 129.1 (d, Ar−C), 121.7 (d, Ar−C), 94.5 (s, Cp-C), 87.1 (d, Cp-C), 86.8 (d, Cp-C), 32.2 (t, ArCH$_2$Ar), 21.8 (q, CH$_3$). FAB MS: *m/z* 1338 (M$^+$ − PF$_6$) Anal. Calcd for C$_{64}$H$_{54}$Co$_2$F$_{12}$N$_2$O$_{10}$P$_2$S$_2$ (1483.0): C, 51.82; H, 3.67; N, 1.89. Found: C, 51.80; H, 3.56; N, 1.82.

Cobaltocenium-Bridged Calix[4]arene L^3. 1,1'-Bis(chlo-rocarbonyl)cobaltocenium chloride (0.5 g, 1 mmol) in dry acetonitrile (30 mL) and 5,17-diamino-25,27-dihydroxy-26,28-bis(tolylsulfonyloxy)calix[4]arene (**6**) (0.78 g, 1 mmol) in aceto-nitrile (50 mL) containing 0.5 mL of triethylamine were added simultaneously to a vigorously stirring mixture of DMF (1 mL)−acetonitrile (50 mL) at room temperature over 30 min. The resulting reaction mixture was refluxed for an additional 1 h. After cooling the solvent the mixture was removed in vacuo to dryness. To the residue 50 mL of water was added, and a precipitate that formed was filtered and dried over P$_2$O$_5$. The resultant solid was chromatographed on a short silica gel column, using THF−CH$_3$CN−MeOH (2:3:1 v/v) as an eluent containing a small amount of ammonium hexafluorophosphate to give crude product (0.96 g) in 85.6% yield. The crude product was then recrystallized from a minimum amount of hot acetone to yield 0.43 g (38%) of pure compound. ^{1}H NMR (CD$_3$CN): δ 8.14 (s, 2H, NHCO), 7.76 and 7.47 (one pair of d, *J* = 6.6 Hz, 8H, TosH), 7.15 (d, *J* = 7.6 Hz, 4H, ArH), 6.91 (t, 2H, ArH), 6.74 (s, 4H, ArH ortho to NHCO), 6.14 and 5.81 (two t, *J* = 2.2 Hz, 8H, CpH), 4.00 and 3.02 (one pair of d, *J* = 15 Hz, 8H, ArCH$_2$Ar), 3.97 (s, 2H, OH), 2.48 (s, 6H, CH$_3$). ^{13}C NMR (CD$_3$-CN): δ 157.57 (C=O), 152.58, 147.00, 142.33, 136.50, 136.14, 132.55, 132.00, 130.62, 129.48, 128.92, 121.16 and 119.80 (Ar), 96.28 and 86.90, 85.13 (Cp), 30.28 (ArCH$_2$Ar), 21.21 (CH$_3$). FAB MS: *m/z* 1004 (M$^+$ − PF$_6$). Anal. Calcd for C$_{54}$H$_{44}$-Co$_1$F$_6$N$_2$O$_{10}$P$_1$S$_2$ (1148.9): C, 56.45; H, 3.86; N, 2.44. Found: C, 56.50; H, 3.88; N, 2.17.

25,27-Bis(tolylsulfonyloxy)-26,28-dihydroxycalix[4]-arene (7). To a solution of calix[4]arene **1** (4.2 g, 10 mmol) and triethylamine (2.8 mL, 20 mmol) in 80 mL of dry dichloromethane was added *p*-toluenesulfonyl chloride (4 g, 22 mmol) dissolved in 30 mL of CH$_2$Cl$_2$. The reaction mixture was stirred at 40 °C for 2 h and quenched with cold water (100 mL). The organic layer was separated and evaporated to dryness. The crude product was purified by recrystallization from ethyl acetate to give 6.4 g (88%) yield. ^{1}H NMR (CD$_2$-

Cl_2): δ 7.82 (d, $J = 6.9$ Hz, 4H, ArH), 7.41 (d, 4H, ArH), 7.06 (d, $J = 7.5$ Hz, 4H, ArH), 6.78 (m, 10H, OH, ArH), 4.00 and 3.15 (ABq, $J = 14.4$ Hz, 8H, CH_2), 2.50 (s, 6H, CH_3). ^{13}C NMR (CD_2Cl_2): δ 152.6 (s), 146.3 (s), 144.4 (s), 134.3 (s), 132.9 (s), 130.3 (s), 129.3 (d), 129.0 (d), 128.7 (d), 128.6 (d), 127.2 (d), 120.0 (d), 31.7 (t), 21.6 (q). FAB MS: m/z 731 (M^+ 100). Anal.Calcd for $C_{42}H_{36}O_8S_2$ (732.8): C, 68.83; H, 4.95; S, 8.75. Found: C, 68.77; H, 4.99; S, 8.70.

5,17-Dinitro-25,27-bis(tolsylsulfonyloxy)-26,28-dihydroxycalix[4]arene (8). To a solution of 25,27-bis(tolylsulfonyloxy)-26,28-dihydroxycalix[4]arene (7) (7.3 g, 10 mmol) in dichloromethane (150 mL) and glacial acetic acid (10 mL) was added 4 mL of HNO_3 (90%). The temperature was maintained below 0 °C during addition, then the mixture was vigorously stirred at room temperature for 30 min and quenched with cold water (50 mL). The organic layer was separated, washed with water, and evaporated to dryness. To the residue was added methanol to precipitate a mixture of dinitro and mononitro calixarenes. This crude mixture of products was then chromatographed on silica gel, eluting with CH_2Cl_2/CH_3-CN/cyclohexane (5:1.5:3.5 v/v) to give **8**, 5.7 g, 70% yield. ^1H NMR (CD_2Cl_2): δ 8.01 (s, 4H, ArH), 7.81 (d, $J = 8.4$ Hz, 4H, ArH), 7.45 (d, 4H, ArH), 6.84 (s, 6H, ArH), 5.94 (brs, 2H, OH), 4.01 and 3.34 (ABq, $J = 14.4$ Hz, CH_2), 2.52 (s, 6H, CH_3). ^{13}C NMR (CD_2Cl_2): δ 158.2 (s), 146.9 (s), 144.5 (s), 140.6 (s), 133.0 (s), 132.2 (s), 130.5 (d), 130.0 (d), 128.7 (d), 128.7 (d), 127.7 (d), 124.6 (d), 31.5 (t), 21.7 (q). Anal. Calcd for $C_{42}H_{34}N_2O_{12}S_2$ (822.8): C, 61.31; H, 4.16; N, 3.40; S, 7.79. Found: C, 61.30; H, 4.18; N, 3.55; S, 7.66.

5,17-Diamino-25,27-bis(tolylsulfonyloxy)-26,28-dihydroxycalix[4]arene (9)·2HCl. 5,17-Dinitro-25,27-bis(tolylsulfonyloxy)-26,28-dihydroxycalix[4]arene (8) (0.82 g, 1 mmol) was dissolved in 30 mL of dry dichloromethane and added to a 100 mL hydrogenation bottle. A catalytic amount of Pd/C (10%, catalytic) was added, and the resulting mixture was hydrogenated at 50 psi of hydrogen pressure at 35 °C for 5 h. After the hydrogenation was completed the white solid material that had formed and the catalyst were isolated using Celite powder on a glass frit. The solid was then suspended in dichloromethane (50 mL) and acidified in saturated HCl/methanol, and the resulting heterogeneous mixture was filtered. The filtrate was evaporated in vacuo to dryness, giving dihydrochloride **9**·2HCl as a white powder in 95% yield. ^1H NMR (DMSO-d_6): δ 10.14 (brs, NH_3^+), 7.70 (d, $J = 8.2$ Hz, 4H, TosH), 7.50 (d, 4H, TosH), 7.12 (s, 4H, ArH), 6.70 (dd, $J = 7.6$ Hz, 2H, ArH), 6.52 (d, 4H, ArH), 6.20 (s, 2H, OH), 3.84 and 2.92 (ABq, $J = 13.6$ Hz, CH_2), 2.45 (s, 6H, CH_3). ^{13}C NMR (DMSO-d_6): δ 152.01 (s), 145.88 (s), 144.30 (s), 133.36 (s), 132.94 (s), 131.68 (s), 130.19 (d, Tos−C), 128.51 (d, Tos−C), 128.49 (d, Ar−C), 126.07 (d, Ar−C), 123.88 (s), 123.06 (d, Ar−C ortho to NHCO), 30.89 (t, CH_2), 21.20 (q, CH_3). Anal. Calcd for $C_{42}H_{40}Cl_2N_2O_8S_2$ (835.8): C, 60.36; H, 4.82; N, 3.35. Found: C, 60.31; H, 4.66; N, 3.30. ^1H NMR free base (DMSO-d_6): δ 7.65 (d, $J = 7.9$ Hz, 4H, ArH), 7.46 (d, 4H, ArH), 6.64 (dd, $J = 7.3$ Hz, 2H, ArH), 6.48 (d, 4H, ArH), 6.30 (s, 4H, ArH), 5.00 (brs, 4H, NH_2), 3.86 and 2.62 (ABq, $J = 13.6$ Hz, 8H, CH_2), 2.45 (s, 6H, CH_3).

5,17-Bis(1-cobaltoceniumyl)carboxamido-26,28-dihydroxy-25,27-bis(tolylsulfonyloxy)calix[4]arene, L². To a DMF solution (25 mL) containing 5,17-diamino-26,28-dihydroxy-25,27-bis(tolylsulfonyloxy)calix[4]arene dihydrochloride (9) (0.83 g, 1 mmol) and triethylamine (1 mL), under a nitrogen atmosphere, was added (chlorocarbonyl)cobaltocenium chloride (0.65 g, 2.2 mmol) in dry acetonitrile (80 mL). After the mixture was stirred at room temperature for 3 h, the organic solvents were removed in vacuo to dryness. To the residue was added water (50 mL), and a solid material formed, which was filtered and dried. The crude product was chromatographed on a silica gel column, using CH_3CN/CH_2Cl_2, 1:1, as an eluent. The main fraction was separated and evaporated to dryness, and the residue was dissolved in a minimum amount of CH_3-

CN. To this solution was added an excess of NH_4PF_6 followed by water. The precipitate formed was filtered, washed with water, and dried to afford L². Yield: 0.73 g (49%). ^1H NMR (CD_3CN): δ 8.65 (s, 2H, NHCO), 7.77 (dd, $J = 8.4$ Hz, $J = 1.2$ Hz, 4H, TosH), 7.48 (d, 4H, TosH), 7.43 (s, 4H, ArH ortho to NHCO), 6.86 (d, $J = 7.3$ Hz, 4H, ArH), 6.80 (t, 2H, ArH), 6.18 (t, $J = 2.0$ Hz, 4H, CpH), 5.78 (t, 4H, CpH), 5.75 (s, 10H, CpH), 4.95 (s, 2H, OH), 3.14 (ABq, $J = 14.5$ Hz, 8H, ArCH$_2$Ar), 2.48 (s, 6H, CH_3). ^{13}C NMR (75 MHz, CD_3CN): δ 159.93 (s, C=O), 149.89 (s), 147.23 (s), 144.48 (s), 134.60 (s), 132.43 (s), 130.86 (s), 130.75 (d, Tos−C), 130.20 (s), 129.69 (d, Ar−C), 128.95 (d, Tos−C), 127.39 (d, Ar−C), 122.29 (d, Ar−C ortho to NHCO), 95.62 (s), 86.67 (d), 86.32 (d), 84.46 (d), 31.63 (t), 21.28 (q). FAB MS: m/z 1337 ($M^+ - PF_6$). Anal. Calcd for $C_{64}H_{54}$-$Co_2F_{12}N_2O_{10}P_2S_2$ (1483.0): C, 51.82; H, 3.67; N, 1.89. Found: C, 51.49; H, 3.63; N, 1.95.

Crystallography. Crystal data for **6**, **10**, and the chloride complexes of L² and L³ are given in Table 1 together with refinement details. Data for all four crystals were collected with Mo Kα radiation using the MARresearch Image Plate System. The crystals were positioned at 70 mm from the image plate. A total of 95 frames were measured at 2° intervals with a counting time of 2 min. Data analysis was carried out with the XDS program.[23] Default refinement details are described here, while differences for specific structures are included below. Structures were solved using direct methods with the SHELXS 86 program.[24] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms on the carbon atoms and nitrogen atoms were included in calculated positions and given thermal parameters equivalent to 1.2 times those of the atom to which they were attached. Hydrogen atoms on water molecules were not included. All structures were refined on F^2 till convergence using SHELXL.[25] All calculations were carried out on a Silicon Graphics R4000 workstation at the University of Reading. **6** contained a dichloromethane molecule which was refined with 50% occupancy with the carbon atom given an isotropic thermal parameter. **10** contains several solvent molecules that were refined isotropically including two acetonitrile molecules, one with full occupancy and one with 50% occupancy, and two ethanol molecules both with 50% occupancy. In L¹·2Cl⁻ one of the tosyl groups is rotationally disordered around the O−S bond and two different sets of positions were located for the $O_2C_7H_7$ moiety, which were refined with isotropic thermal parameters with 50% occupancy. A solvent acetonitrile molecule was also located and four water molecules, three of which were refined with 50% occupancy. These solvent molecules were also refined with isotropic thermal parameters.

L³·Cl⁻ contains an acetonitrile solvent molecule that was refined anisotropically with full occupancy.

¹H NMR Titrations. A solution of the receptor (500 μL) was prepared at a concentration typically on the order of 0.01 mol dm⁻³ in deuterated DMSO. The initial ^1H NMR spectrum was recorded, and aliquots of anion were added by a gastight syringe from a solution made such that 1 molar equiv was added in 20 μL. After each addition and mixing, the spectrum was recorded again and changes in the chemical shift of certain protons were noted. The result of the experiment was a plot of displacement in chemical shift as a function of the amount of added anion, which was subjected to analysis by curve-fitting since the shape is indicative of the stability constant for the complex. The computer program EQNMR[26] was used, which requires the concentration of each component and the observed chemical shift (or its displacement) for each data

(23) Kabsch, W. *J. Appl. Crystallogr.* **1998**, *21*, 1916.
(24) SHELXS 86: Sheldrick, G. M. *Acta Crystallogr. Sect. A* **1990**, *46*, 467.
(25) Sheldrick, G. M. *SHELXL*, program for crystal structure refinement; University of Göttingen, 1993.
(26) Hynes, M. J. *J. Chem. Soc., Dalton Trans.* **1993**, 311.

Table 1. Crystal Data and Structure Refinement for the Four Structures

	6	**10**	L[1]·2Cl[−]	L[3]·Cl^{−}
empirical formula	$C_{43}H_{35}Cl_2N_2O_{12}S_2$	$C_{69}H_{64.5}Fe_2N_{3.5}O_{11}S_2$	$C_{66}H_{62}Cl_2Co_2N_3O_{12.5}S_2$	$C_{56}H_{51}ClCoN_3O_{10}S_2$
fw	906.75	1294.56	1350.06	1084.50
temp/K	293(2)	293(2)	293(2)	293(2)
wavelength/Å	0.71073	0.71073	0.71073	0.71073
crystal system, space group	monoclinic, $P2_1/n$	monoclinic, $P2_1/n$	triclinic	orthorhombic, *Pbca*
unit cell dimensions (Å, deg)	a 12.196(7)	18.58(2)	11.846(12)	15.401(12)
	b 14.449(9)	19.44(2)	13.948(14)	17.418(14)
	c 23.99(2)	20.63(2)	21.56(2)	39.433(35)
	α		97.40(1)	(90)
	β 104.57(1)	105.23(1)	99.70(1)	(90)
	γ (90)	(90)	106.76(1)	(90)
volume/Å³	4091(4)	7189(14)	3302(6)	10578(15)
Z, calculated density/Mg m⁻³	4, 1.472	4, 1.196	2, 1.358	8, 1.362
abs coeff/mm⁻¹	0.329	0.518	0.709	0.515
F(000)	1876	2708	1398	4512
crystal size/mm	0.35 × 0.25 × 0.20	0.20 × 0.20 × 0.15	0.25 × 0.25 × 0.15	0.25 × 0.25 × 0.12
θ range for data collection/deg	2.55−24.95	2.27−22.53	2.26−24.97	2.65−24.64
index ranges	$0 \leq h \leq 13$,	$0 \leq h \leq 19$	$0 \leq h \leq 13$	$0 \leq h \leq 14$
	$-17 \leq k \leq 17$,	$-20 \leq k \leq 20$	$-16 \leq k \leq 15$,	$-18 \leq k \leq 16$
	$-28 \leq l \leq 27$	$-22 \leq l \leq 21$	$-25 \leq k \leq 24$	$-46 \leq l \leq 46$
no. of reflns collected/unique	10635/6612	15900/9054	9263	15659/6660
R(int)	0.0823	0.0735	−	0.0647
no. of data/restraints/ params	6612/0/553	9054/0/781	9263/0/795	6660/0/663
final *R* indices [$I > 2\sigma(I)$], R1	0.1003	0.0898	0.0811	0.0871
wR2	0.2762	0.2296	0.2429	0.2269
R indices (all data), R1	0.2277	0.1948	0.1088	0.1756
wR2	0.3345	0.3030	0.2740	0.2854
largest diff peak, hole/e Å⁻³	0.465, −0.327	0.415, −0.313	1.087, −0.623	1.419, −0.500

point. Typically these titration experiments were repeated three times with at least 15 data points in each experiment.

Results and Discussion

Syntheses of Upper-Rim Cobaltocenium Calix-[4]arene Receptors. The new amine-substituted calix-[4]arene derivatives containing tosyl groups para to the upper-rim amine substituent **6** and the corresponding 1,3-distal isomer **9** were prepared according to Schemes 1 and 2. The reaction of calix[4]arene (**1**)[21] with chlorobenzyl carbonate in the presence of sodium hydride in THF gave the 1,3-distal product **2** in 85−95% yield. Nitration of **2** using glacial acetic acid and 90% nitric acid afforded **3** as a yellow solid in 84% yield. A sodium hydride−THF solution of **3** was reacted with tosyl chloride to produce **4** in 68% isolated yield. The reaction of **4** with trimethylsilyl iodide and subsequently with sodium thiosulfate in dichloromethane produced **5** in 85% yield. Hydrogenation of **5** using 10% Pd/C in THF at 45−50 °C and 50 psi gave an unstable product in near quantitative yield, which was isolated as the hydrochloride salt **6**·2HCl in 71% yield (Scheme 1).

The reaction of tosyl chloride and **1** in the presence of triethylamine gave the 1,3-distal product **7** in 88% yield. Nitration of **7** afforded **8** in 70% isolated yield, and subsequent hydrogenation produced the isomeric amine **9**, which was again isolated as the hydrochloride salt **9**·2HCl (Scheme 2).

Condensation reactions of **6** and **9** with 2 equiv of chlorocarbonyl cobaltocenium chloride[22] and addition of excess NH_4PF_6 produced L[1], L[2] in 55% and 49% respec-

tive yields (Scheme 3). The bis(ferrocene) derivative analogue **10** of L[2] was prepared in a similar manner with chlorocarbonyl ferrocene and **9**.[20]

(10)
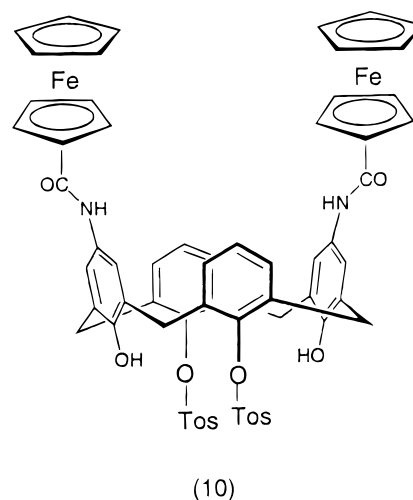
The condensation of 1,1'-bis(chlorocarbonyl) cobaltocenium chloride **11** with **6** in dry acetonitrile in the presence of triethylamine initially gave a crude product, which after silica column chromatography and addition of excess NH_4PF_6 afforded L[3] as a yellow powder in 38% yield (Scheme 4). All of the new receptors were characterized by ^{1}H, ^{13}C NMR, fast atom bombardment mass spectrometry, and elemental analyses (see Experimental Section). Comparing the ^{1}H NMR spectra of L[1]−L[3], it is noteworthy that the amide protons of the bridged
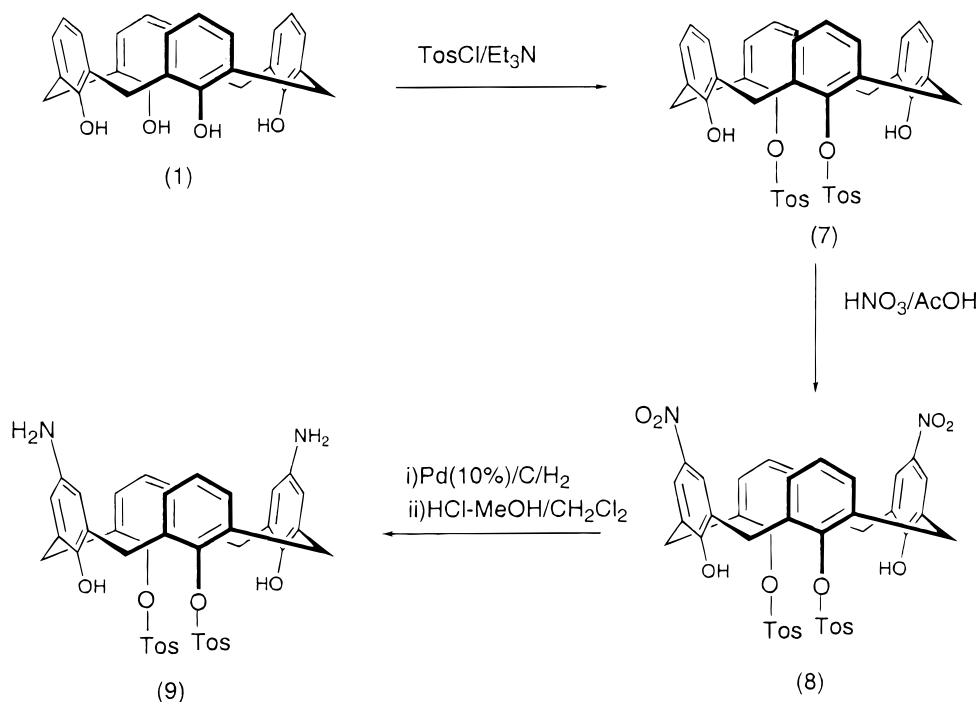
Scheme 1
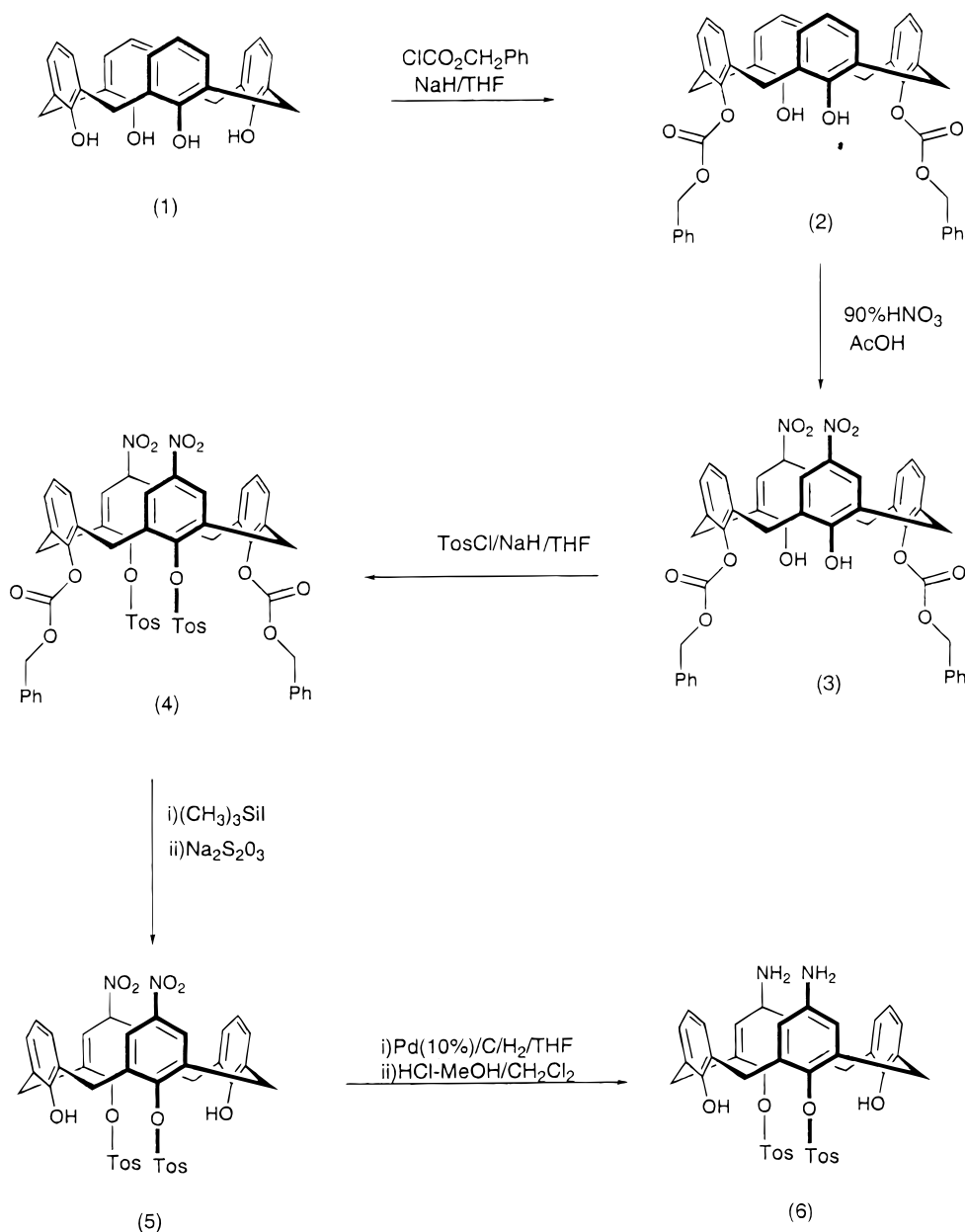
derivative L^3 at 8.14 ppm are significantly shielded relative to isomeric receptors L^1, L^2 at 8.57 and 8.65 ppm, respectively.

X-ray Structural Investigations of 6, 10, and the Chloride Anion Complexes of L^1 and L^3. Crystals of all four compounds and complexes suitable for structural determination were grown from acetonitrile–ethanol solvent mixtures. The four structures are shown in Figures 1–4 inclusive together with the common atomic numbering scheme. Dimensions in the molecules are unremarkable. All structures contain two tosylate groups at the bottom rim of the calix[4]arene in the 1,3 positions. Consequently all four structures show the C_2 distortion of the cone as demonstrated by the least-squares planes calculations reported in Table 2. This table shows the angles of intersection of the phenyl rings with the plane of the four methylene groups in the calix[4]arene. In all four cases, rings 1 and 3 (with the substituent tosylate groups at the bottom rim) intersect at angles far greater (range 72–107°) than for the

unsubstituted rings 2 and 4 (range 28–49°). Clearly this is due to the bulkiness of the tosylate groups, which are kept apart by large intersection angles. This conformation also allows for strong intramolecular hydrogen bonds around the lower rim with the two hydrogen atoms on atoms O(250) and O(450) forming hydrogen bonds to the substituted oxygen atoms O(150) and O(350). While there are several solvent molecules in the majority of the structures, these are positioned between molecules in the unit cell rather than in the top of the cone of the calix[4]arene, as is so often found in these types of structure. It seems likely that this is due to the fact that the space in the cone is restricted because of the C_2 distortion. The structure of **6** contains nitro groups at the top of the cone in the 1,3 positions, which make angles of 4.3, 16.1° with the phenyl rings to which they are attached, and tosylate groups at the bottom rim of the cone also in the 1,3 positions. As is shown in Figure 1, one tosylate group on O(150) is twisted toward and the other on O(350) away from the cone axis. Details

Scheme 2

Scheme 3
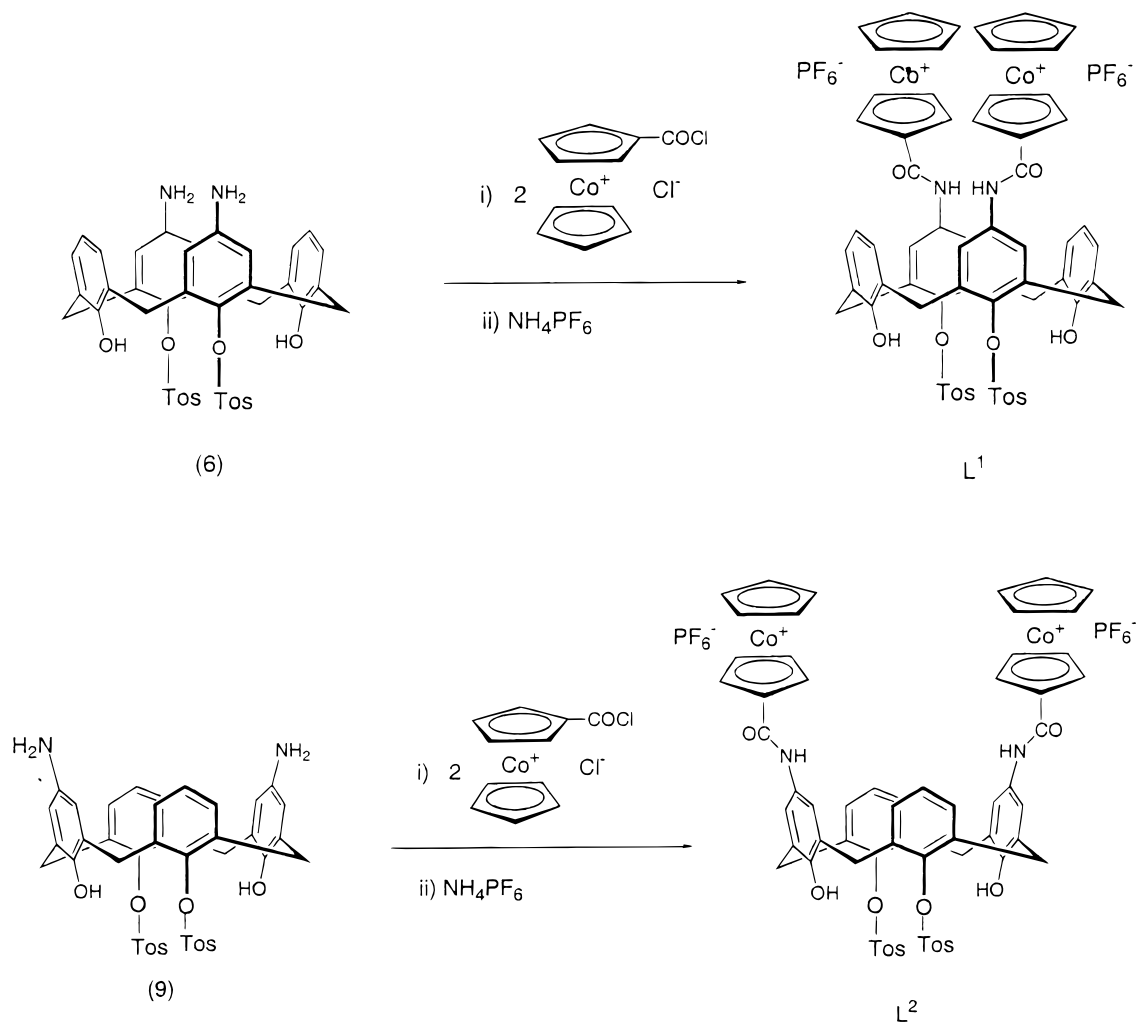
of this conformation are illustrated by the torsion angles in Table 3. There is only one intermolecular hydrogen

bond in this structure between a nitrate oxygen atom and an unsubstituted oxygen atom at the bottom rim
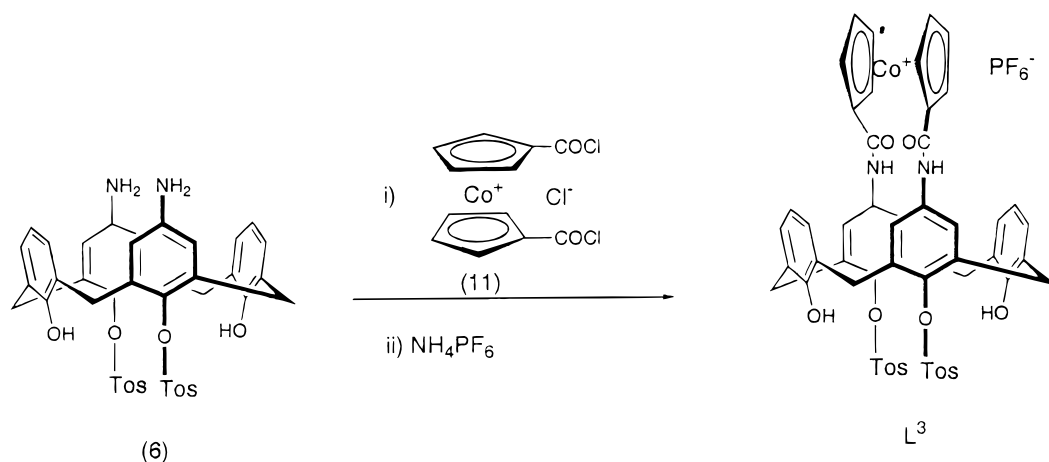
Scheme 4

(6)

Table 2. Least-Squares Planes Calculations

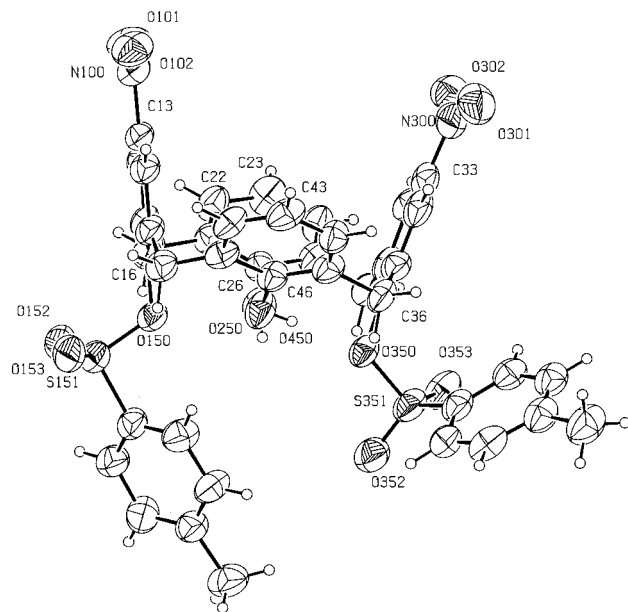| angle between planes	**6**	**10**	$L^1 \cdot 2Cl^-$	$L^3 \cdot Cl^-$
1 and 5	76.8	73.5	72.7	106.8
2 and 5	33.2	37.0	44.3	28.4
3 and 5	78.5	89.1	72.1	98.9
4 and 5	34.2	42.6	48.5	29.8

Figure 1. Structure of **6**. Ellipsoids shown at 30% probability.

of the cone. Details of intermolecular hydrogen bonds in the four structures are given in Table 4.

The structure of **10** is shown in Figure 2 and contains amide groups of the type NH–CO–ferrocene in the 2,4 positions at the upper rim of the cone. The conformation of the calix[4]arene shows the C_2 distortion, but in this case because the two upper-rim amide substituents are on rings 2 and 4, they are spread out away from the cone axis and the unsubstituted rings 1 and 3 are approximately perpendicular to the 4-methylene plane (Table 2).

As in **6** the two tosylate groups in the 1,3 positions at the bottom of the rim show different conformations, with one tosylate twisted toward the cone axis while the other is twisted away. As is apparent from Figure 2, the two ferrocene moieties have different orientations. For Fe-(1), the second cp ring (the one not attached to the top

Table 3. Hydrogen Bonds in the Four Structures (Distances, Å)

In 6	
O(101)···O(250)S1	3.21
Symmetry Element	
S1 $-x+1/2$, $y+1/2$, $-z+1/2$	
In 10	
N(400)···O(202)S1	3.03
N(200)···O(402)S2	2.83
Symmetry Elements	
S1 $x-1/2$, $1/2-y$, $z-1/2$	
S2 $1-x$, $1-y$, $1-z$	
In $L^2 \cdot 2Cl^-$	
Cl(1)···O(92)	3.19
Cl(1)···N(100)	3.21
CL(2)···O(91)S1	3.11
Cl(2)···O(91)S2	3.17
Cl(2)···O(92)S1	3.20
Cl(2)···N(300)	3.23
O(102)···O(94)S3	3.27
O(302)···O(93)S3	2.74
O(93)···O(352)S4	2.94
Symmetry Elements	
S1 x, $1+y$, z	
S2 $2-x$, $1-y$, $1-z$	
S3 $1-x$, $1-y$, $-z$	
S4 $2-x$, $1-y$, $-z$	
In $L^3 \cdot Cl^-$	
N(100)···Cl(1)	3.28
N(300)···Cl(1)	3.30

Table 4. Tosylate Conformations (Torsion Angles, deg)

	6	**10**	$L^1 \cdot 2Cl^-$ [a]	$L^3 \cdot Cl^-$
C(16)–O(150)–S(151)–C(154)	179.0	−163.9	76.6, 152.3	87.2
O(150)–S(151)–C(154)–C(155)	−131.0	−104.3	−102.5, −87.3	−89.7
C(36)–O(350)–S(351)–C(354)	70.0	88.5	−82.4	131.7
O(350)–S(351)–C(354)–C(355)	−93.7	87.7	89.5	88.4

[a] Tosylate group 1 is disordered such that there are two possible positions for C(154) and C(155).

of the calixarene) is orientated away from the cone axis, while for Fe(2) the second ring is orientated toward the cone axis. This asymmetry is reflected in the difference in angles of intersection of the phenyl rings with the 4-methylene plane (see Table 2). The two N–H groups form intramolecular hydrogen bonds to carbonyl groups in adjacent molecules (see Table 4). The two amide groups N(200), C(201), O(202) and N(400), C(401),
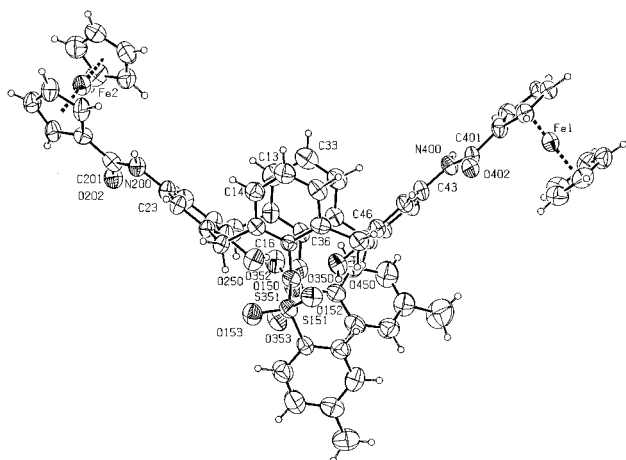
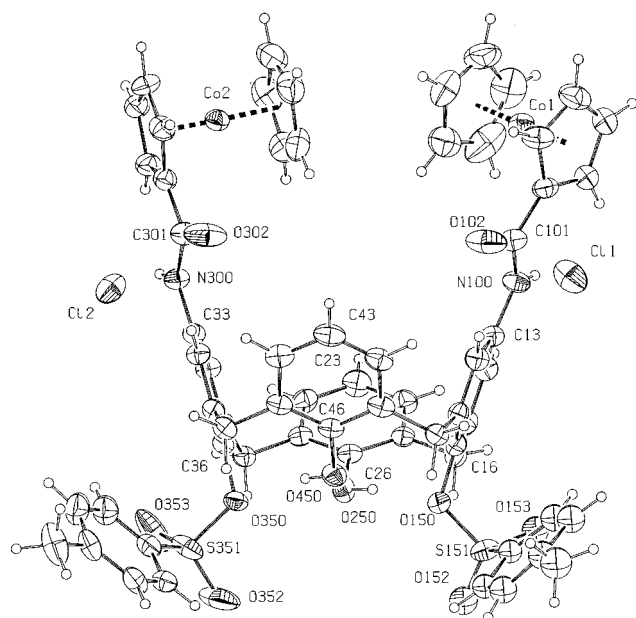**Figure 2.** Structure of **10**. Ellipsoids shown at 30% probability.

Figure 3. Structure of L¹·2Cl⁻. Ellipsoids shown at 30% probability. The tosylate at O(150) is disordered over two sites. Only one position is shown.

Figure 4. (a) Structure of L³·Cl⁻. (b) Amide groups hydrogen bonding to Cl⁻. Ellipsoids shown at 30% probability.

O(402) are twisted considerably from the phenyl ring to which they are attached, making angles of 30.2° and 19.5°, respectively.

The Fe−C distances fall within the expected range from 1.99(1) to 2.08(1) Å.

The structure of L¹·2Cl⁻ is shown in Figure 3 and contains amide groups of the type NH−CO−cobaltocenium in the 1,3 positions at the upper rim of the cone. Because the lower-rim tosylate substituents are also in the 1,3 positions, these 1,3 rings are approximately perpendicular to the 4-methylene plane. Unlike the ferrocene rings in **10**, the cobaltocenium rings in **3** are both twisted inward toward the cone axis. This gives rise to a closest C···C contact of 3.52 Å between the adjacent rings across the cone axis. The tosylate group in position 3 is twisted away from the cone axis, while the tosylate group in position 1 is disordered over two positions, one directed inward and the other directed outward from the cone axis. The two amide N−H groups form strong hydrogen bonds to the two chloride anions. In addition the chloride anions form hydrogen bonds to
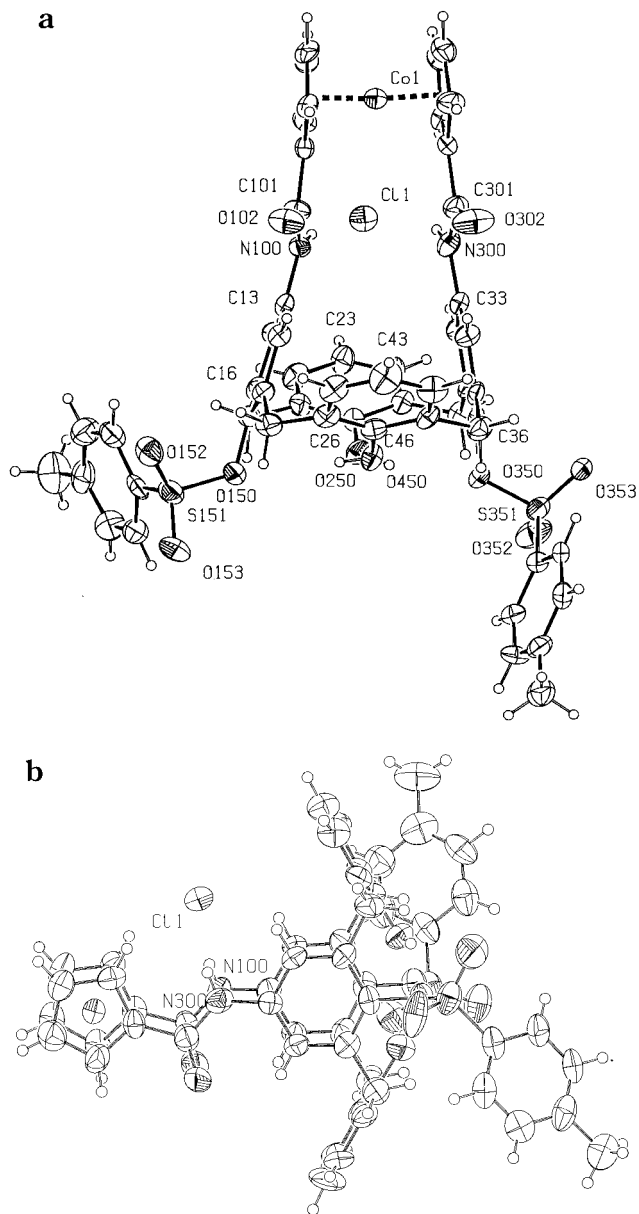
water molecules, as do the amide carbonyl oxygen atoms. Details are given in Table 4. The two amide groups N(100), C(101), O(102) and N(200), C(201), O(202) are twisted considerably from the phenyl ring to which they are attached, making angles of 22.7° and 27.9°, respectively. The Co−C distances are in the range 1.979(9)−2.040(7) Å.

The structure of L³·Cl⁻ is shown in Figure 4. The upper rim contains NH−CO−C₅H₅ moieties in the 1 and 3 positions which encapsulate a cobalt ion to form a cobaltocenium moiety. The two amide groups N(100), C(101), O(102) and N(300), O(302) are closely planar with the phenyl ring to which they are attached (16.6°, 12.7°). The calix[4]arene has a very flattened cone conformation with C_2 distortion. The angles made by the four phenyl rings and the plane of the four methylene carbon atoms are 106.8°, 28.4°, 98.9°, and 29.8°. The fact that two angles are greater than 90° illustrates that in the upper rim the tops of the two phenyl rings

Table 5. Anion Stability Constant Data (K^a/dm^3 mol^{-1}) for L^1, L^2, and L^3 in (CD$_3$)$_2$SO

anion	L^1	L^2	L^3	11
MeCO$_2^-$	21000	820	41520	1560
PhCO$_2^-$	4025	620	38400	
PhCH$_2$CO$_2^-$	8100	830	22270	
β-NfCO$_2^-$	2800	610	19750	
H$_2$PO$_4^-$	3100	2500	6380	320
Cl$^-$	weak^b	400	70	35
Br$^-$	weak^b		weak^b	
NO$_3^-$	weak^b		125	
HSO$_4^-$	weak^b		40	

^{a} Determined at 298 K; errors estimated to be ≤10%. ^{b} Very weak binding, a stability constant value could not be calculated in this solvent.

of the calixarenes are pulled together so that the cobaltocenium bridge can be formed. However despite being attached to the upper rim of the calixarene, the two cyclopentadiene rings are almost coplanar, intersecting at an angle of 7.6°. The Co–C distances (2.04-(1)–2.10(1) Å) are in the expected range. In addition to the cobaltocenium linkage, the two N–H groups form hydrogen bonds to the chloride anion Cl(1)···N(100) 3.28, N(300) 3.30 Å. The two tosylate groups in the 1,3 positions at the bottom of the rim are both twisted away from the cone axis.

Solution Anion Coordination Investigations. ^{1}H NMR Titrations. The anion coordination properties of L^1–L^3 were investigated by ^{1}H NMR anion titration experiments in (CD$_3$)$_2$SO solution with various tetrabutylammonium halide, nitrate, dihydrogen phosphate, hydrogen sulfate, and carboxylate salts. In the majority of cases substantial downfield perturbations of the respective receptor's amide, cyclopentadienyl, and aryl calix[4]arene protons were observed, especially with carboxylate anionic guests, suggesting anion binding is taking place at the upper-rim vicinity of the receptor. It is noteworthy that with benzoate and β-naphthylcarboxylate anions large upfield perturbations of receptor's L^3 aryl calix[4]arene protons of 0.6 ppm were also seen. Stoichiometric 1:1 stability constants were calculated from the resulting titration curves using EQNMR,[26] and these values are presented in Table 5, which includes stability constant data for acyclic receptor 1,1′-bis(phenylaminocarbonyl)cobaltocenium hexafluorophosphate, **11**. A comparison of the stability constant values for the isomeric receptors L^1, L^2 clearly suggests that exchanging the positions of the tosyl substituents on the calix[4]arene lower rim has a dramatic influence on the anion coordination properties of the upper rim. Receptor L^1 displays much larger magnitudes of thermodynamic stability for all anions except Cl$^-$ and exhibits the selectivity preferences for CH$_3$CO$_2^-$ ≫ PhCH$_2$CO$_2^-$ > PhCO$_2^-$ > β-NfCO$_2^-$ > H$_2$PO$_4^-$ ≫ Cl$^-$, Br$^-$, NO$_3^-$, HSO$_4^-$. In contrast the selectivity trend H$_2$PO$_4^-$ > PhCH$_2$CO$_2^-$, CH$_3$CO$_2^-$ > PhCO$_2^-$, β-NfCO$_2^-$ > Cl$^-$ is exhibited by isomeric L^2. Molecular modeling calculations (MM2) and CPK models suggest with L^1 the lower-rim bulky tosyl groups para to the upper-rim amide cobaltocenium substituents favor a receptor conformation in which the upper-rim Lewis acidic cobaltocenium moieties are rigidly held in close proximity to each other. The X-ray crystal structures of the bis(nitro) derivative **6** and the chloride complex of L^1 corroborate this postulation (see previous section) (Figures 1 and 3); the

Table 6. Electrochemical Data

receptor	E_f/V^a
L^1	−0.90^b
L^2	−0.88^b
L^3	−0.85

^{a} Obtained in acetonitrile solution containing 0.2 mol dm^{-3} Bu$_4$NBF$_4$ as supporting electrolyte. Solutions were ca. 1 × 10^{-3} mol dm^{-3} in receptor, and potentials were obtained with reference to a Ag–Ag$^+$ electrode at 293 K, scan rate = 100 mV s^{-1}. ^{b} E_f value represents a two-electron reduction process.

Table 7. Electrochemical Anion Recognition Data

	ΔE_f/mV^a		
anion	L^1	L^2	L^3
MeCO$_2^-$	120	100	155
PhCO$_2^-$	105		140
PhCH$_2$CO$_2^-$	130		150
β-NfCO$_2^-$	90		135
H$_2$PO$_4^-$	105	90	130
Cl$^-$	15	40	60
NO$_3^-$	10		20
HSO$_4^-$	5		10

^{a} Cathodic shift of respective cobaltocenium/cobaltocene redox couple produced by the presence of anions (up to 5 equiv) added as their tetrabutylammonium salts in acetonitrile at 293 K.

N(100)–N(300) distance between the nitro groups is 3.805 Å. With the relatively more flexible 1,3-distal isomer L^2, conformations in which the upper-rim cobaltocenium amide substituents are further apart are predicted by molecular modeling calculations. This is illustrated by the X-ray crystal structure of the bis-(ferrocene) derivative analogue of L^2 showing the N(200)–N(400) distance of the amide groups to be 11.635 Å (Figure 2). Accordingly, with this class of calix[4]arene anion receptor subtle changes of size, nature, and position of lower-rim substituents substantially alter the topology of the upper-rim anion recognition site and consequently the receptor's selective anion coordination properties; that is, L^1 is CH$_3$CO$_2^-$ selective, whereas isomeric L^2 selectively binds H$_2$PO$_4^-$.

The cobaltocenium-bridged calix[4]arene L^3 exhibits remarkable thermodynamic stability of larger magnitudes than either L^1 or L^2 (Table 5) and selectivity preferences for carboxylate anions, in particular for acetate over H$_2$PO$_4^-$ ≫ NO$_3$ > Cl$^-$ > HSO$_4$ > Br$^-$. In comparison **11** forms a much weaker complex with the acetate anion (Table 3). These novel anion coordination properties may be attributable to the upper-rim rigidly held cobaltocenium bridging unit of L^3 creating a unique and ideal bidentate amide (CO–NH) hydrogen-bond donor environment of complementary topology for recognizing bidentate anions such as carboxylates. The X-ray crystal structure of the chloride complex of L^3 discussed in the previous section corroborates this postulation.

Electrochemical Anion Recognition Studies. The electrochemical properties of L^1–L^3 were investigated in acetonitrile using cyclic voltammetry with Bu$_4$NBF$_4$ as the supporting electrolyte. Each compound exhibited a reversible redox reduction wave in the −0.85 to −0.90 V region (Table 6). Cyclic voltammograms were also recorded after progressively adding stoichiometric equivalents of anion guests to the electrochemical solutions, and the results are summarized in Table 7. Substantial one-wave cathodic shifts of the respective cobaltoce-
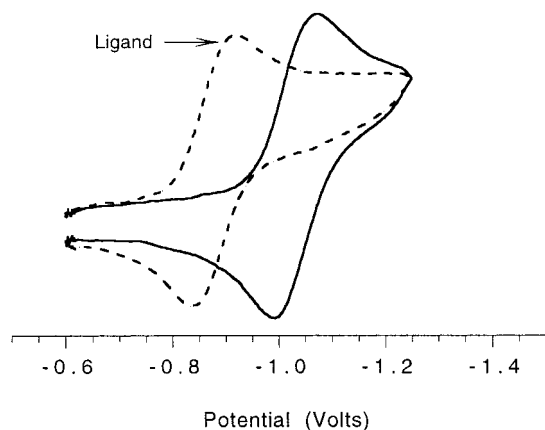
Figure 5. Cyclic voltammograms of L^3 in CH_3CN in the absence (- - -) and presence (—) of 3 equiv of Bu_4NCO_2Me.

nium/cobaltocene redox couple are generally observed with most anionic guest species (Figure 5). The complexed anion effectively stabilizes the positive charge of the cobaltocenium unit. It is noteworthy that the carboxylate and dihydrogen phosphate anions cause the largest magnitudes of cathodic perturbations of up to $\Delta E = 155$ mV for L^3 and acetate (Figure 5). This observation correlates with the NMR-determined stability constant data in which these anions form the most thermodynamically stable complexes with the cobaltocenium receptors (Table 3).

Conclusions

New isomeric upper-rim bis(cobaltocenium)calix[4]-arene receptors L^1, L^2 and a novel upper-rim cobaltocenium-bridged calix[4]arene derivative L^3 that have the capability to selectively complex and sense anionic guest species via electrochemical voltammetric techniques have been prepared.

The solid-state structures of synthon **6** and the chloride anion complexes of L^1, L^3 have been determined by X-ray analysis and highlight the importance of hydrogen bonding and the degree of preorganization of the upper-rim anion recognition site, as dictated by the positioning of lower-rim tosyl substituents, to the overall anion recognition process. Proton NMR anion titration studies in deuterated DMSO solutions have shown these receptors to exhibit remarkable and contrasting anion thermodynamic stability and selectivity trends. For example L^1 displays the selectivity trend $MeCO_2^- \gg H_2PO_4^-$, whereas with isomeric L^2 the selectivity preference is dramatically reversed. Clearly exchanging the positions of the tosyl substituents on the calix[4]arene lower rim significantly influences the anion coordination properties of the upper rim. The cobaltocenium-bridged calix[4]arene L^3 forms stronger anion complexes with carboxylate and dihydrogen phosphate anions than either L^1 or L^2 with notable selectivity for acetate. As evidenced from the L^3 chloride complex crystal structure, this selectivity preference may be rationalized by the upper-rim bidentate amide hydrogen bond donor cavity being of complementary topology for complexing bidentate anions such as carboxylates. Electrochemical investigations have demonstrated that L^1, L^2, L^3 electrochemically sense a variety of anions via substantial cathodic perturbations of the respective reversible cobaltocenium/cobaltocene redox couple by up to $\Delta E = 120$ for L^1 and 155 mV for L^3 with acetate. Consequently these redox-active calixarene-based receptors are first-generation prototype amperometric selective sensory reagents for carboxylate anionic guest species.

Supporting Information Available: Tables of positional parameters, bond lengths, bond angles, anisotropic thermal parameters, and hydrogen positions for **6**, **10**, $L^1 \cdot 2Cl^-$, and $L^3 \cdot Cl^-$. This material is available free of charge via the Internet at http://pubs.acs.org. Crystallographic files, in CIF format, are available on the Internet only.