New anion receptors based on cobalticinium–aza crown ether derivatives

Paul D. Beer and Andrew R. Graydon

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

(Received May 14, 1993)

Abstract

New mono- and bis-substituted amide-linked aza crown ether–cobalticinium compounds have been prepared and shown by ^1H nuclear magnetic resonance and electrochemical studies to accept chloride and bromide guest anions. Preliminary association constant determinations suggest that use of aza-crown-ether-complexed sodium cations in combination with an amide-linked positively charged cobalticinium redox centre leads to cooperative enhancement of the strength of anion complexation.

Key words: Cobalticinium; Aza crown ether; Anion receptors; Electrochemistry; Stability constants

1. Introduction

The molecular recognition of anions by abiotic receptors is an area of intense current interest [1,2]. This is because anions are known to play essential roles in chemical and biochemical processes and this field of coordination chemistry is still relatively new. Examples of anion receptors reported to date include Lewis acid–tin-containing ligands [3], cyclic ammonium quaternary salts [4], protonated polyammonium macrocycles [5] and guanidinium derivatives [6]. We have recently described new transition metal coordination and organometallic types of anion receptors [7–11], including the first redox responsive type of anion receptor containing the positively charged cobalticinium redox-active moiety. Crown ethers are well known to form complexes with alkali metal cations [12], and in combination with the cobalticinium unit the resulting potential anion receptor would contain an additional centre of positive charge. Consequently on electrostatic grounds, cooperation between the cobalticinium positive charge and the closely crown ether bound alkali metal cation would be expected to enhance anion complexation between the two regions of positive charge. This paper reports our initial efforts directed towards this objective and describes the syntheses, anion coordination and electrochemical properties of novel cobalticinium–aza crown ether derivatives.

2. Results and discussion

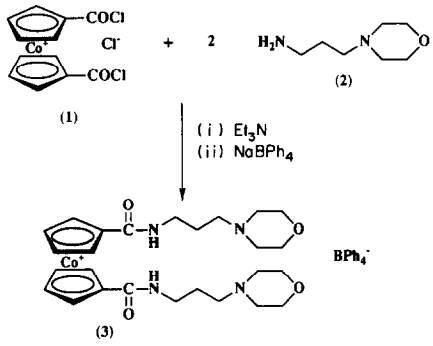
2.1. Syntheses

Initially "model" cobalticinium compounds containing morpholine moieties instead of aza crown ethers were prepared in order to check the feasibility of the proposed synthetic pathways. The condensation of 1,1'-bis(chlorocarbonyl)cobalticinium chloride (**1**) [13] with two equivalents of 4-(3-aminopropyl)morpholine (**2**) in the presence of triethylamine in dry acetonitrile gave a crude product that was purified by column chromatography on Sephadex® with acetonitrile as eluent. Addition of an excess of sodium tetraphenylborate gave the product **3** as a yellow powder with a 16% yield (Scheme 1). The monosubstituted analogue **5** was prepared with a 44% yield by the reaction of the activated ester **4** [11] and one equivalent of **2** (Scheme 2).

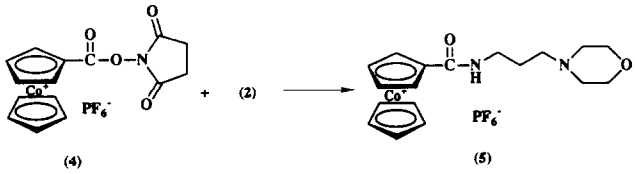
Michael addition of aza-15-crown-5 (**6**) to acrylonitrile afforded the intermediate nitrile, which was subsequently reduced to the amine **7** with diborane. The reaction of **4** and **7** in acetonitrile in the presence of triethylamine initially gave a mixture of products inseparable by Sephadex® chromatography, but the addition of an excess of $NaBPh_4$ to an aqueous solution of the

Correspondence to: Dr. P.D. Beer.

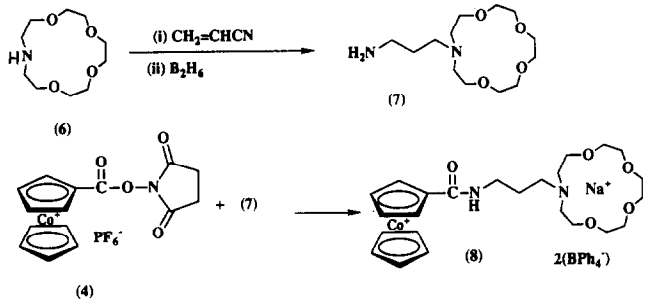
0022-328X/94/$7.00
SSDI 0022-328X(93)23987-9



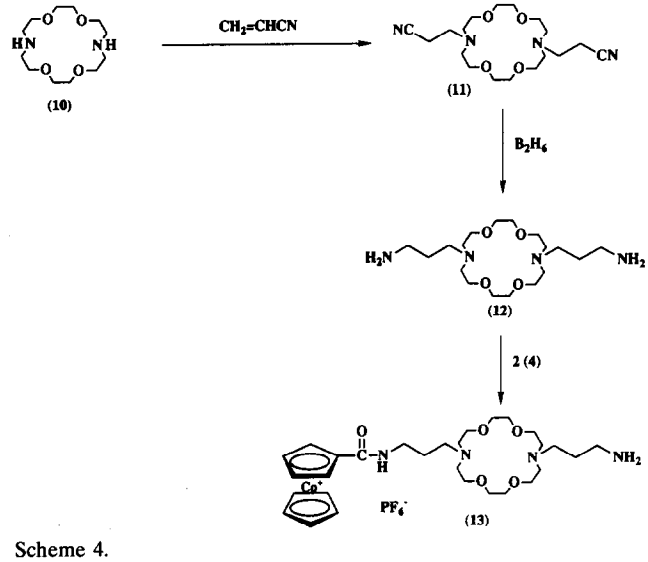
Scheme 1.



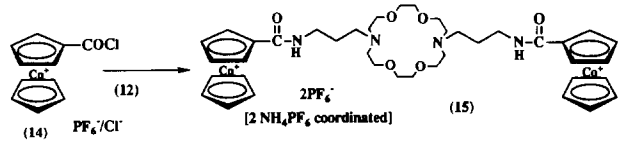
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

mixture led to precipitation of sodium complex **8** of the desired ligand with a low yield (Scheme 3).

Disappointingly, repeated attempts to prepare the corresponding bis-substituted analogue **9** from **1** and **7** failed. Various solvent combinations were used but with no success. Large amounts of cobalticinium bis acid and amine starting materials were always isolated, suggesting that moisture in the hygroscopic free amine may be responsible for this failure.

Diaza-18-crown-6 (**10**) was refluxed in acrylonitrile to give the *N,N'*-bis(propano-nitrile)-aza crown ether (**11**). Reduction with diborane gave the bis amine **12** with a 56% overall yield (Scheme 4). Reaction of **12** with two equivalents of the activated ester **4** in dry acetonitrile surprisingly gave only the monosubstituted product **13** in isolable quantities (yield, 18%) (Scheme 4).

In an attempt to prepare the desired bis-substituted compound the reaction of **12** with an excess of the more reactive chlorocarbonyl cobalticinium chloride (**14**) [13] was carried out in dry DMF. (Scheme 5). The crude reaction mixture contained, as indicated by ^{1}H NMR spectroscopy, a number of products that could not be separated by use of various column packings and eluents. Finally after the mixture had been dissolved in hot water and an excess of NH_4PF_6 added, a yellow powdery material was isolated. Although the ^{1}H NMR spectrum of this product suggested that it was the target compound, fast atom bombardment mass spectrometry (FABMS) indicated the presence of complexed ammonium cations. The binding of ammonium cations by crown ethers, in particular 18-crown-6, is well documented [14]. Elemental analysis suggested the inclusion of two equivalents of ammonium cation.

The aza-12-crown-4 cobalticinium derivatives **17** and **18** were prepared by the reaction of **1** and **4** with appropriate equivalent quantities of the aza crown ether **16** (Scheme 6). All these new compounds gave spectroscopic and analytical data in accordance with assigned structures (see Section 4).

2.2. *Anion coordination studies*

2.2.1. *Proton NMR titrations*

NMR spectroscopy has been widely used to investigate receptor–substrate interactions. In fact the first

TABLE 1. Association constants

Compound	Association constant (CD_3CN) K_a (mol^{-1} dm^3)	
	Cl^-	Br^-
5	400	270
8	3200	1600

reported evidence for anion binding by an abiotic host came from proton NMR studies [5a].

The addition of tetrabutylammonium chloride or bromide salts to deuterated acetonitrile ^1H NMR solutions of **3**, **5**, **8**, **13** and **15** resulted in remarkable downfield shifts of the signals from the protons of all five receptors. For example the addition of an excess of chloride ion to **5** caused a downfield shift of 2.5 ppm of the amide proton resonance. As observed previously with simple secondary amide-linked cobalticinium systems [8,9], these results suggest that CO–NH $\cdots$ X^- hydrogen bonding is a significant contributing factor to the overall anion complexation process. Subsequent ^1H NMR titration investigations with Cl^- and Br^- produced titration curves suggesting 1:1 receptor:anion stoichiometry with **3**, **5**, **8** and **13** (Fig. 1), and 1:2 receptor:anion stoichiometry with **15**.

Interestingly ^1H NMR titration studies of anion complexation with **17** and **18** revealed both compounds to be poor complexing agents for the halide anions, very small perturbations ($\Delta\delta \leq 0.04$ ppm) being observed. This result highlights the importance of favourable amide NH–anion hydrogen bonding interactions to the overall anion recognition process; compounds **17** and **18** contain only tertiary amide linkages.

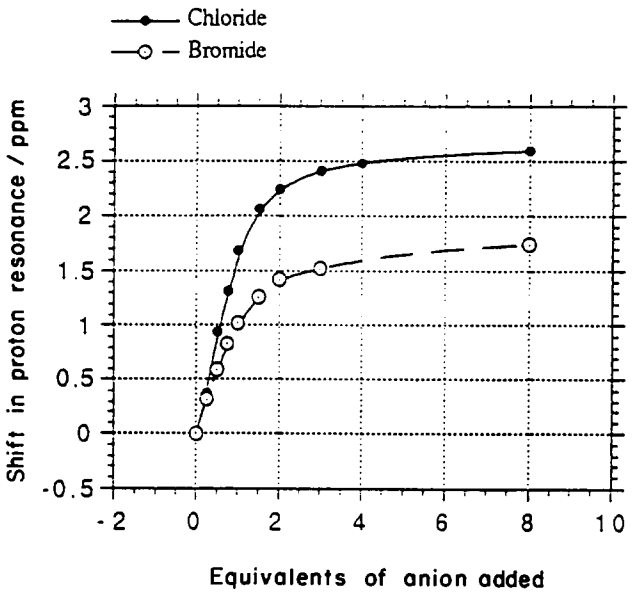
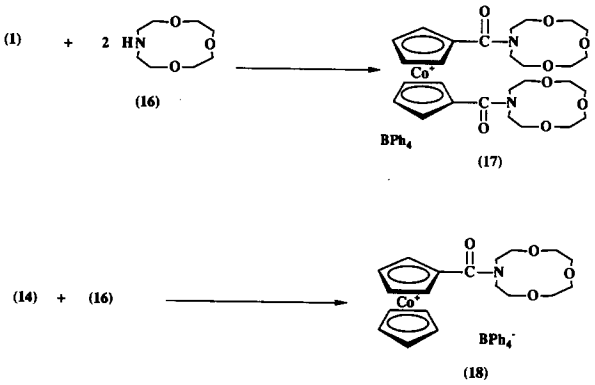


Fig. 1. Proton NMR titration curves of **5** and Cl^- (•) and Br^- (○) in CD_3CN. The shift is that of the amide proton.



Scheme 6.

A semiquantitative study was carried out in order to see whether the presence of an aza crown ether closely bound sodium cation, as in **8**, enhances anion complexation. In this study the association constants for complexation of halide ions with receptors **5** and **8** were determined from ^1H NMR titration data by use of a least-squares fit computer program [15], and the results are summarized in Table 1. Clearly, within experimental error, for both Cl^- and Br^- guest anions the presence of the complexed Na^+ in receptor **8** leads to stronger binding of anions. A tentative depiction of the Na^+ cooperative anion binding effect is shown in Fig. 2.

2.2.2. Electrochemical anion recognition studies

The electrochemical properties of these new cobalticinium derivatives were investigated in acetonitrily by cyclic voltammetry with $N^nBu_4BF_4$ as the supporting electrolyte. Each compound exhibited a reversible redox reduction wave in the region -0.55 to -0.75 V (*versus* a saturated calomel electrode (SCE)) (Table 2). Cyclic voltammograms were also recorded after progressively adding stoichiometric equivalents of anion guests to the electrochemical solutions, and the

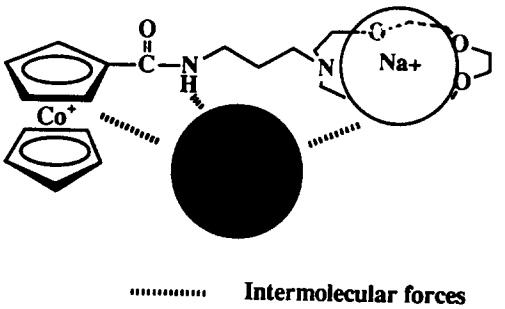


Fig. 2. Schematic representation of the aza-crown-ether-complexed sodium cation–anion cooperative binding effect.

TABLE 2. Electrochemical data

Compound	$E_{1/2}$ [a] (V)	$\Delta E(Cl^-)$ [b] (mV)	$\Delta E(Br^-)$ [b] (mV)
3	−0.55	55	45
5	−0.73	10	10
8	−0.72	10	10
13	−0.71	25	40
15	−0.74	65	25
17	−0.77	< 10	< 10
18	−0.78	< 10	< 10

[a] Obtained in acetonitrile solution containing $N^nBu_4BF_4$ (0.2 mol dm^{-3}) as supporting electrolyte. Solutions were about 2×10^{-3} mol dm^{-3} in the compound, and the potentials were obtained with reference to the SCE. [b] Cathodic shift in reduction potential produced by the presence of anions (up to four equivalents) added as their tetrabutylammonium salts.

results are also summarised in Table 2. Only when the cobalticinium receptor contains at least one amide N–H linkage are significant one-wave cathodic shifts produced with the halide anionic guest species, in agreement with the results obtained from ^1H NMR anion complexation experiments. It is noteworthy that compound **13** exhibits a relatively larger redox couple perturbation for Br^- than Cl^-, which is contrary to expectations based on these anions' respective charge to radius ratio polarizabilities. Surprisingly, relatively small halide-induced cathodic perturbations were observed with **5** and **8**, and consequently it is difficult to make an electrochemical assessment of the effect of the presence of the positive charge of the additional sodium cation on the anion complexation process.

3. Conclusions

A variety of new monosubstituted and bis-substituted amide-linked aza crown ether–cobalticinium compounds have been prepared. Halide anion coordination studies have shown that those cobalticinium compounds containing amide N–H groups can coordinate and electrochemically recognize chloride and bromide anionic guests through mutual electrostatic attraction and favourable amide N–H $\cdots$ anion hydrogen bonding interactions. Preliminary association constant determinations from ^1H NMR titration data suggest aza-crown-ether-complexed sodium cations in combination with an amide-linked positively charged cobalticinium redox centre can cooperatively enhance the strength of anion complexation. Further quantitative investigations concerning the effects of crown ether bound Group 1 and 2 metal cations on the overall anion recognition process by these and related cobalticinium aza crown ether derivatives are in progress.

4. Experimental details

4.1. Instrumentation

IR spectra were recorded on a Perkin–Elmer 1710 Fourier transform IR instrument (4000–400 cm^{-1}) as KBr discs. NMR spectra were obtained on a Bruker AM300 instrument with tetramethylsilane as an internal standard. Fast atom bombardment mass spectra were obtained from the SERC mass spectrometry service at University College, Swansea. Electrochemical measurements were carried out with an E.G. & G. Princeton Applied Research 362 scanning potentiostat. Elemental analyses were performed in the laboratory.

4.2. Solvent and reagent pre-treatment

Where necessary, solvents were purified prior to use and stored under nitrogen. Acetonitrile was pre-dried over 4A molecular sieves (4–8 mesh) and then distilled from calcium hydride. Thionyl chloride was distilled under nitrogen from triphenyl phosphite and triethylamine from potassium hydroxide pellets. Unless stated to the contrary, commercial-grade chemicals were used without further purification. The following compounds were prepared by published procedures: 1,1'-bis(chlorocarbonyl)cobalticinium chloride (**1**) [13], cobalticinium hexafluorophosphate-activated ester (**4**) [11] and chlorocarbonyl cobalticinium chloride (**14**) [13].

4.3. Syntheses

4.3.1. 1,1'-bis[3-morpholino-propyl-1-amino)carbonyl]cobalticinium tetraphenylborate (3)

1,1'-Bis(chlorocarbonyl)cobalticinium chloride (0.66 g, 1.44 mmol) was dissolved in acetonitrile (100 ml) to give a bright-green solution. To this a solution of 4-(3-aminopropyl)morpholine (0.41 g, 2.88 mmol) and triethylamine (0.34 g, 2.90 mmol) in acetonitrile (50 ml) was added dropwise under nitrogen. (Some fuming was observed owing to evolution of hydrogen chloride.) The mixture was stirred under nitrogen for 36 h to give an emerald-green solution. The solvent was removed under reduced pressure and the residue purified by column chromatography (Sephadex® LH-20-100, with acetonitrile as eluent). Fractions containing the product were identified by NMR spectroscopy, combined and the solvent removed. The residue was isolated by dropwise addition of sodium tetraphenyl borate to give an insoluble salt which was filtered off and washed with water. The final product was a yellow powder (yield, 0.20 g (16%)).

Elemental anal. Found: C, 71.91; H, 6.44; N, 6.49. $C_{50}H_{58}N_4O_4CoB$ calc.: C, 70.75; H, 6.88; N, 6.60%. IR: ν_{max} 3384br(NH), 1663 and 1540 (CO) cm^{-1}. ^1H NMR (CD_3CN): δ 2.00 (4H, m, NCH_2CH_2); 3.00–3.40 (16H,

m, NCH_2); 3.80–3.90 (8H, m, OCH_2); 5.70 (4H, m, Cp); 5.95 (4H, m, Cp); 6.80–7.40 (20H, m, ArH); 7.45 (2H, br m, CONH) ppm.

4.3.2. [(3-morpholino-propyl-1-amino)carbonyl]cobalticinium tetraphenylborate (5)

Cobalticinium-activated ester (**4**) was prepared *in situ* from mono(carboxy) cobalticinium hexafluorophosphate (0.38 g, 1.0 mmol) in acetonitrile (25 ml). The urea formed was removed by filtration, and the stirred filtrate treated dropwise under nitrogen with a solution of 4-(3-aminopropyl)morpholine (0.14 g, 1.0 mmol) and triethylamine (0.10 g, 1.0 mmol) in acetonitrile (25 ml). The mixture was stirred under nitrogen for 60 h, after which the solvent was removed to leave a yellow solid and a brown–orange oil. The crude product was purified by column chromatography (Sephadex® LH-20-100; acetonitrile as eluent) and fractions containing the product were identified by NMR spectroscopy. These were combined, the solvent removed and the residue taken up in water. Dropwise addition of sodium tetraphenylborate yielded the product as a yellow powder. However, analysis showed that it was contaminated with triethylamine hydrochloride, and so it was dissolved in a minimum amount of acetonitrile and precipitated once more by dropwise addition of water. The precipitate was filtered off and washed with water to give the final product (yield, 0.30 g (14%)).

Elemental anal. Found: C, 73.91; H, 6.44; N, 3.49. $C_{42}H_{44}N_2O_2CoB$ calc.: C, 74.3; H, 6.54; N, 4.13%. IR: ν_{max} 3401 (NH), 1676 and 1559 (CO) cm^{-1}. ^1H NMR (CD_3CN): δ 1.75–1.85 (2H, m, NCH_2CH_2); 2.50–2.60 (6H, m, NCH_2); 3.35–3.45 (2H, m, $CONCH_2$); 3.65–7.00 (4H, m, OCH_2); 5.65–5.70 (7H, m, CpH); 6.00 (2H, m, CpH); 6.65–7.30 (20H, m, ArH); 7.45 (2H, br m, CONH) ppm.

4.3.3. (3-aminopropyl)-1-aza-4,7,10,13-tetraoxacyclopentadecane (7)

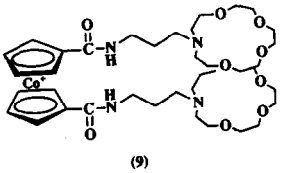
To a solution containing monoaza-15-crown-5 (0.50 g, 2.28 mmol) in (THF) (10 ml) was added acrylonitrile (50 ml). The mixture was refluxed for 48 h under nitrogen and then cooled to room temperature. The solvent and residual acrylonitrile were removed under reduced pressure to give the intermediate nitrile as a semisolid. ^1H NMR ($CDCl_3$): δ 2.50 (2H, t, CH_2CN); 2.80 (4H, t, NCH_2); 2.90 (2H, t, NCH_2CH_2CN); 3.60–3.70 (16H, m, OCH_2) ppm. This intermediate was dissolved in a minimum amount of dichloromethane and the cooled solution was treated under nitrogen with the borane–THF complex (50 ml, 1 M solution). The mixture was refluxed under nitrogen for 48 h and then cooled in an ice bath, and the reaction was quenched by careful dropwise addition of about 10 ml of ice–water. The solvent was removed to give the white solid aminoborate complex, which was subsequently refluxed for 24 h with 6 M hydrochloric acid. The solvent was then removed to leave the crystalline ammonium salt, which was dried *in vacuo* and taken up in the minimum volume of water. The solution was filtered and the amine regenerated with ion exchange resin (Dowex 1 × 8–100 (50–100 mesh)). The final product was isolated as a pale-yellow oil (yield, 0.49 g (78%)).

^1H NMR ($CDCl_3$): δ 1.60–1.70 (2H, m, $H_2NCH_2CH_2$); 2.55–2.70 (8H, m, NCH_2); 3.50–3.70 (16H, m, OCH_2) ppm.

4.3.4. {[3-(1-aza-4,7,10,13-tetraoxacyclopentadecane)propylamino]carbonyl}cobalticinium tetraphenylborate (8)

The amine **7** (0.28 g, 1.0 mmol) and triethylamine (0.1 g, 1.0 mmol) were dissolved in acetonitrile (15 ml). The solution was added dropwise under nitrogen to a stirred solution of mono-cobalticinium-activated ester (0.54 g, 1.0 mmol) in acetonitrile (15 ml). The mixture was stirred for 40 h and the solvent then removed to leave a yellow residue which was subjected to column chromatography (Sephadex® LH-20-100 eluted with 25:75 MeOH:MeCN v/v). This failed to yield pure fractions; so those containing the product in an impure form were combined and the chromatography repeated. Contamination with triethylamine was noted, and so the fractions containing the product were combined, the solvent was removed, and the residue was taken up in water. The product was precipitated by dropwise addition of sodium tetraphenylborate filtered off and washed with water. To ensure that the Na^+ bound in the ring was countered by tetraphenylborate (as opposed to hexafluorophosphate), the product was taken up in acetonitrile and an excess of sodium tetraphenylborate added. Dropwise addition of water precipitated the product one more, and it was filtered off, washed and dried to yield pure product as a yellow powder. The yield was poor, being about 10%.

Elemental anal. Found: C, 74.75; H, 6.56; N, 2.63. $C_{72}H_{76}N_2O_5CoB_2Na$ calc.: C, 75.01; H, 6.64; N, 2.43%. ^1H NMR (CD_3CN): δ 1.40–1.50 (2H, m, $CH_2CH_2CH_2$); 3.10–3.65 (24H, m, OCH_2, NCH_2); 5.55–5.60 (7H, m, CpH); 5.95 (2H, m, CpH); 6.64–7.30 (40H, m, ArH) ppm. IR: ν_{max} 3381 br (NH), 1653 and 1540 (CO) cm^{-1}.



(9)

4.3.5. N,N'-Bis(3-aminopropyl)-1,10-diaza-4,7,13,16-tetraoxacyclo-octadecane (12)

1,10-Diaza-4,7,13,16-tetraoxacyclo-octadecane (Kryptofix 22 (0.52 g, 2.0 mmol)) was dissolved in acrylonitrile (100 ml) and the resulting solution refluxed under nitrogen for 48 h. The excess of acrylonitrile was removed under reduced pressure to yield the intermediate nitrile.

^{1}H NMR ($CDCl_3$): δ 2.45 (4H, t, CH_2CN); 2.75 (8H, t, NCH_2); 2.90 (4H, t, NCH_2CH_2CN); 3.50–3.60 (16H, m, OCH_2) ppm. This nitrile was dried *in vacuo* and treated under nitrogen with the borane–THF complex (50 ml, 1M solution). The solution was refluxed under nitrogen for 48 h and then treated with about 6 ml of ice water. The solvent was removed under reduced pressure to give the aminoborate complex. As in the preceding experiment the complex was cleaved with 6 M hydrochloric acid and the amine regenerated by ion exchange as a pale-yellow oil (yield, 0.42 g (56%)).

^{1}H NMR ($CDCl_3$): δ 1.45 (4H, m, $H_2NCH_2CH_2$); 2.40–2.60 (16H, m, NCH_2); 3.35–3.50 (16H, m, OCH_2) ppm.

4.3.6. {[(3-(10-(3-aminopropyl))-1,10-diaza-4,7,13,16-tetraoxacyclooctadecane)-propylamino]carbonyl}-cobalticinium hexafluorophosphate (13)

The bis-amine **12** (0.42 g, 1.12 mmol) and triethylamine (0.19 g, 1.91 mmol) were dissolved in acetonitrile. Owing to the low solubility of the former, a large volume of solvent (about 100 ml) had to be used and warmed slightly. The solution was added dropwise under nitrogen to a stirred solution of mono-cobalticinium-hexafluorophosphate-activated ester **4** (1.03 g, 1.91 mmol) in acetonitrile. The solution changed from yellow to an orange colour, which deepened to brown. After stirring for 48 h, the solvent was removed to give a brown residue, and addition of solvent (25:75 MeOH:MeCN v/v) produced a yellow–orange solution and a brown insoluble residue. The solution was purified by column chromatography (Sephadex® LH-20-100) but did not yield pure fractions. The chromatography was repeated with acetonitrile alone as eluent and pure fractions were identified by NMR spectroscopy. The addition of water precipitated the product as a deep-orange powder which was filtered off and washed. At first it was thought that both amine functions and coupled with cobalticinium fragments but analytical and spectroscopic data revealed that only one had done so. The yield was 0.25 g (18%).

Elemental anal. Found: C, 50.82; H, 5.88; N, 6.09. $C_{29}H_{48}O_5N_4CoPF_6$ calc.: C, 47.3; H, 6.57; N, 7.61%. IR: ν_{max} 3630 and 3454 (NH), 1668 and 1541 (CO) cm^{-1}. ^{1}H NMR (CD_3CN): δ 1.70–1.80 (4H, m, $CH_2CH_2CH_2$); 2.60–2.70 (8H, m, NCH_2); 3.30–3.70 (24H, m, NCH_2, OCH_2); 5.65–5.75 (7H, m, CpH); 6.10 (2H, m, CpH); 7.60 (1H, br m, CONH) ppm. FAB MS: m/z 738 ($M^+PF_6^-$), 593 (M^+).

4.3.7. Bis-{[(N,N'-bis-(3-propylamino)-1,10-4,7,13,16-tetraoxacyclooctadecane)carbonyl]cobaliticinium}hexafluorophosphate (15)

Mono(carboxy)cobalticinium hexafluorophosphate (0.75 g, 2.0 mmol) was refluxed with $SOCl_2$ to give the corresponding acid chloride. After removal of the $SOCl_2$ under vacuum the solid was taken up in DMF (50 ml). The bis-amine **42** (0.24 g, 0.64 mmol) and triethylamine (0.15 g, 1.5 mmol) were dissolved in DMF (50 ml) and the solution was added dropwise under nitrogen with stirring to the acid chloride solution. The mixture was stirred for 48 h to give a yellow solution, from which the solvent was distilled off *in vacuo*. The residue was purified by column chromatography (Sephadex® LH-20-100 eluted with 25:75 MeOH:MeCN v/v). The fractions containing product were identified and combined, and the solvent was removed. The product separated as a dirty-yellow powder on addition of water, but a mixture of anions was found to be present. Thus the product was taken up in hot water, an excess of ammonium hexafluorophosphate was added, and the product was recrystallized. The final product contained bound ammonium which was not displaced by addition of five equivalents of potassium hexafluorophosphate in aqueous solution. The yield was 0.22 g (24%) on the assumption that two molar equivalents of bound ammonium were present.

Elemental anal. Found: C, 34.01; H, 4.39; N, 3.85. $C_{40}H_{56}N_4O_6Co_2P_2F_{12}2NH_4PF_6$ calc.: C, 33.8; H, 4.53; N, 5.90%. IR: ν_{max} 3618 and 3427 (NH), 1665 and 1546 (CO) cm^{-1}. ^{1}H NMR (CD_3CN): δ 2.00 (4H, m, $CH_2CH_2CH_2$); 3.25–3.30 (12H, m, NCH_2); 3.70–3.80 (16H, m, OCH_2); 5.70–5.80 (14H, m, CpH); 6.05 (4H, m, CpH); 7.35 (2H, br m, CONH) ppm. FAB MS: m/z 1097 ($M^+2PF_6^-$), 951 ($M^+PF_6^-$), 806 (M^+).

4.3.8. 1,1'-bis{[(1-aza-4,7,10-trioxacyclododecane)amino]carbonyl}cobalticinium tetraphenylborate (17)

A stirred solution of 1,1'-bis(chlorocarbonyl)cobalticinium chloride (**1**) (0.36 g, 0.78 mmol) in acetonitrile (100 ml) was treated dropwise with a solution of 1-aza-4,7,10-trioxacyclododecane (monoaza-12-crown-4) (16) (0.28 g, 1.60 mmol) and triethylamine (0.16 g, 1.60 mmol) under nitrogen. The mixture was stirred under nitrogen for 48 h and the solvent then removed under reduced pressure. The crude product was purified by column chromatography (Sephadex® LH-20-100; eluted with 50:50 MeOH:$CHCl_3$ v/v). The fractions containing the product were identified by NMR spec-

troscopy and combined, and the solvent was removed. The residue was taken up in water and the product precipitated as a yellow powder by dropwise addition of sodium tetraphenylborate. The precipitate was filtered off and washed with water to yield, after drying, the pure product (yield, 0.23 g (32%)).

Elemental anal. Found: C, 68.97; H, 6.98; N, 3.08. $C_{52}H_{60}N_2O_8CoB$ calc.: C, 68.6; H, 6.64; N, 3.07%. IR: ν_{max} 1636 (CO) cm^{-1}. ^1H NMR (CD_3CN): δ 3.55–3.80 (32H, m, OCH_2, NCH_2); 5.65 (4H, m, CpH); 6.25 (4H, m, CpH) ppm.

4.3.9. {[(1-aza-4,7,10-trioxacyclododecane)amino] carbonyl}cobalticinium tetraphenylborate (18)

Mono(carboxy)cobalticinium hexafluorophosphate (0.38 g, 1.0 mmol) was converted into the corresponding acid chloride salt, which was taken up in acetonitrile. To the stirred solution was added dropwise, under nitrogen, a solution of monoaza-12-crown-4 (**16**) (0.15 g, 0.86 mmol) and triethylamine (0.10 g, 1.0 mmol) in acetonitrile (30 ml). The mixture was stirred for 72 h under nitrogen, and the solvent then removed. The residue was purified by column chromatography (Sephadex® LH-20-100 eluted with acetonitrile). Fractions containing the pure product were identified and combined, and the solvent was removed. The residue was taken up in water and precipitated by addition of sodium tetraphenylborate as a yellow powder. This was filtered off, dissolved in acetonitrile and reprecipitated as a crystalline yellow solid by dropwise addition of water (yield, 0.28 g (46%)).

Elemental anal. Found: C, 72.72; H, 6.45; N, 2.06. $C_{43}H_{45}NO_4CoB$ calc: C, 72.8; H, 6.39; N, 1.97%. IR: ν_{max} 1630 (CO) cm^{-1}. ^1H NMR (CD_3CN): δ 3.45–3.80 (16H, m, OCH_2NCH_2); 5.60–5.70 (7H, m, CpH); 6.25 (2H, m, CpH); 6.85–7.35 (20H, m, ArH) ppm.

Acknowledgments

We thank the SERC for use of the Mass Spectrometry Service of University College, Swansea.

References

1 F.P. Schmidtchen, *Nachr. Chem. Tech. Lab., 36* (1988) 8.
2 H.E. Katz, J.L. Atwood, J.E.D. Davies and D.D. MacNicol (eds.), *Inclusion Compounds*, Vol. 4, Academic Press, New York, 1991, p. 391.
3 H.E. Katz, *Organometallics, 6* (1987) 1134; J.D. Wuest and B. Zacharie, *J. Am. Chem. Soc., 109* (1987) 4714; M.E. Jung and H. Xia, *Tetrahedron Lett., 29* (1988) 297.
4 F.P. Schmidtchen, *Angew. Chem., Int. Ed. Engl., 16* (1977) 720; F.P. Schmidtchen, A. Gleich and A. Schummer, *Pure Appl. Chem., 61* (1989) 1535 and references cited therein.
5 (a) C.H. Park and H.E. Simmons, *J. Am. Chem. Soc., 90* (1968) 2431; (b) B. Dietrich, M.W. Hosseini, R. Sessions and J.-M. Lehn, *J. Am. Chem. Soc., 103* (1981) 1982; (c) J.-M. Lehn, E. Sonveaux and A.K. Willard, *J. Am. Chem. Soc., 100* (1978) 4914; (d) D. Heyer and J.-M. Lehn, *Tetrahedron Lett., 27* (1986) 5869; (e) M.W. Hosseini and J.-M. Lehn, *Helv. Chim. Acta, 69* (1986) 587.
6 A. Echavarren, A. Cralán, J.-M. Lehn and J. de Mendoza, *J. Am. Chem. Soc., 111* (1989) 4994 and references cited therein.
7 P.D. Beer and A.D. Keefe, *J. Organomet. Chem., 375* (1989) C40.
8 P.D. Beer, D. Hesek, J. Hodacova and S.E. Stokes, *J. Chem. Soc., Chem. Commun.*, (1992) 270.
9 P.D. Beer, M.G.B. Drew, C. Hazelwood, D. Hesek, J. Hodacova and S.E. Stokes, *J. Chem. Soc., Chem. Commun.*, (1993) 229.
10 P.D. Beer, C.A.P. Dickson, N. Fletcher, A. Goulden, A. Grieve and T. Wear, *J. Chem. Soc., Chem. Commun.*, (1993) 1327.
11 P.D. Beer, C. Hazelwood, D. Hesek, J. Hodacova and S.E. Stokes, *J. Chem. Soc., Dalton Trans.*, in press.
12 C.J. Pedersen, *J. Am. Chem. Soc., 89* (1967) 7017.
13 J.E. Sheats and M.D. Rausch, *J. Org. Chem., 35* (1970) 3245.
14 H.M. Colquhoun and J.F. Stoddart, *J. Chem. Soc., Chem. Commun.*, (1981) 612.
15 E.S. Kucharski, modified by W. Richmond, Computer programs, University of Western Australia, 1991.