# Ferrocene – Cyclam: A Redox-Active Macrocycle for the Complexation of Transition Metal Ions and a Study on the Influence of the Relative Permittivity on the Coulombic Interaction between Metal Cations

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**Abstract:** The reaction of 1,1′-ferrocene-bis(methylenepyridinium) salt with 1,4,8,11-tetraazacyclotetradecane-5,12-dione, followed by $LiAlH_4$ reduction results in the formation of FcCyclam. Metal complexes of FcCyclam with $M^{2+} = Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, and $Zn^{2+}$ were synthesized from FcCyclam and the respective metal triflates. The complexation of $Cu^{2+}$ and FcCyclam in $CH_3CN$ is preceeded by a rapid electron transfer, followed by a slower complex formation reaction and a reverse electron transfer. The protonation constants of FcCyclam and the stability constants for the $Cu^{2+}$ complex of FcCyclam ($\log K = 9.26(4)$ for the formation of the $[Cu(FcCyclam)]^{2+}$ complex) were determined in 1,4-dioxane/water 70:30 v/v, 0.1 mol dm$^{-3}$, $KNO_3$, 25 °C. By using FcCyclam one can selectively sense the presence of $Cu^{2+}$ ions in the presence of $Ni^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Hg^{2+}$, and $Pb^{2+}$ with a very large $\Delta E \approx 200$ mV, depending on pH. The X-ray crystal structures of FcCyclam and of complexes with $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, and $Zn^{2+}$ were determined and Fe–$M^{2+}$ distances obtained: Fe–$Co^{2+}$ 395.9, Fe–$Ni^{2+}$ 385.4, Fe–$Cu^{2+}$ 377.7, and Fe–$Zn^{2+}$ 369.0 pm. The redox potential of FcCyclam is influenced in a characteristic manner by the complexation of $M^{2+}$. A linear correlation of $1/r \cong \Delta E$ [$r$ = distance Fe–$M^{2+}$ from crystal data, $\Delta E = E_{1/2}([M(FcCyclam)]^{2+}) - E_{1/2}(FcCyclam)$] was found; this is indicative of a mainly Coulomb type interaction between the two metal centers. The nature of the Fe$\cdots M^{2+}$ interaction was also investigated by determining $\Delta E$ in several solvents (mixtures) of different dielectric constants $\varepsilon$. The expected relation of $\Delta E \cong 1/\varepsilon$ was only found at very high values of $\varepsilon$. At $\varepsilon < 40$ increased ion-pairing appears to reduce the effective positive charge at $M^{2+}$ leading to progessively smaller values of $\Delta E$ with lowered $\varepsilon$. The dependence of $\Delta E$ and $\varepsilon$ can be calculated semiquantitatively by combining the Fuoss ion-pairing theory with the Coulomb model.

**Keywords:** coordination chemistry · electronic communication · ferrocene · macrocycles · redox chemistry

## Introduction

Macrocycles based on the 1,4,8,11-tetraazacyclotetradecane (cyclam) framework are among the most popular ligands for d- and f-block metal ions.[1] Consequently numerous derivatives of cyclam have been synthesized,[2] while many metal complexes have found applications in areas as diverse as catalysis,[3–7] magnetic or radio imaging,[8, 9] tumor targeting,[10–12] anion sensing,[13–16] biomimetic chemistry,[17–19] or redox-switching.[20] Numerous publications in recent years have dealt with the phenomenon of redox-switching.[21] Compounds possessing such properties comprise redox-active components such as ferrocene,[22–24] cobaltocene,[25] cymantrene,[26] tetrathiafulvene,[27] or others[28–32] and a macrocyclic ligand suited for the complexation of metal ions. In the oxidized state the binding of metal cations by a redox-active macrocyclic ligand is weak, due to repulsive charge interactions, whereas in the reduced state the binding is strong. In this manner the ability of the macrocyclic ligand to coordinate metal ions can be switched on or off, depending on the redox state of the redox-active component.[33] An efficient redox-switched ligand is characterized by a large difference of the redox potentials between the ligand and the respective ligand with a coordinated metal cation.

We are interested in accomplishing a better understanding of the factors governing the behavior of ferrocene-based

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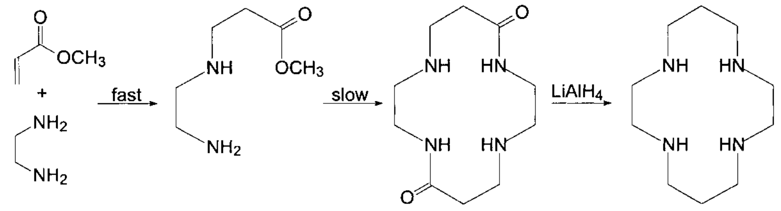
redox switches, which will be important for the optimization of their sensing properties on the way towards producing immobilized sensors or redox-switch devices. In this vein the nature of the interaction between the positively charged metal ion coordinated by a macrocyclic ring system and the redox-active ferrocene unit has to be elucidated. We have recently studied the influence of protonation of a ferrocenylamine on the redox potentials of the ferrocene unit.[34] A significant result of these studies was that the positively charged nitrogen and the iron of ferrocene communicate through electrostatics; despite several approximations and simplifications, Coulomb's law appeared adequate to describe such interactions. In another related study we correlated the reciprocal Fe–$Na^+$ distances obtained from X-ray data of the ferrocene/crown complexes with the shifts of the redox potentials observed upon complexation of $Na^+$.[36] It was already recognized then that this approach involves simplifications; first of all the assumption of identical structures of the ferrocene/crown/sodium complexes in the solid state and in solution. The coordination of alkali metal ions by crown ethers typically leads to highly dynamic complexes and bearing in mind the comparatively low-binding strength[37] in such species, reliable structural information in solution species is not easily obtained. The problem of how to predict the communication between the metal centers led Martínez-Máñez et al. to propose an empirical equation based on a Coulomb charge model, which accounts for the maximum oxidation shift as a function of the charge of the oxidized electroactive framework, the charge of the substrate, the number of electrons involved in the redox reaction, the distance between the redox-active groups, and the macroscopic relative permittivity of the medium.[38]



Scheme 1.

In contrast to crown ethers, cyclams typically form very stable and, depending on the steric bulk of the ligand, sometimes inert complexes with 3d metal(II) ions (= $M^{2+}$) in which the four nitrogen donors are arranged such that they form a square-planar environment for the metal cation. Depending on the donor strength of counterions or solvent molecules, weaker axial contacts between a metal ion and two additional ligands may arise, leading in the extreme to an octahedral coordination sphere.[39] The stable and spatially well-defined bonding of $M^{2+}$ by cyclam make it an ideal candidate for a detailed investigation of the Fe–$M^{2+}$ interactions in solution. Several cyclams with appended ferrocenes have been described,[40, 41] but these compounds are not suitable for our study as the distance Fe–$M^{2+}$ is rather large and ill-defined due to a flexible framework of the ligand.

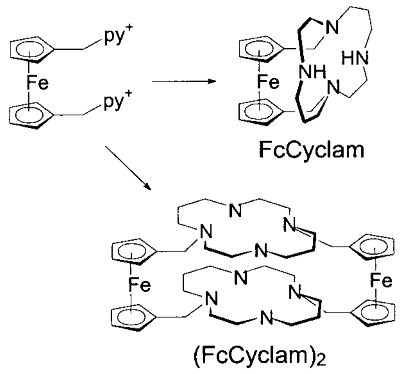
Consequently it was our target to first synthesize a molecule consisting of a ferrocene and a cyclam unit in close proximity, to prepare metal complexes of such a ligand in which a single $M^{2+}$ ion is held in close proximity to the ferrocene subunit, to structurally characterize such compounds, and to study their coordination chemistry. An extensive study of the electrochemistry of such complexes in solution hopefully will provide us with an improved understanding of the metal–metal interactions. Consequently, we wish to report here in detail about investigations of the $M^{2+}$ complexes of a new ligand, a redox-active cyclam we term FcCyclam.[42]

## Results and Discussion

### Synthesis

*Ligands*: 1,8-*N*,*N*-substituted cyclams are less easily available but nonetheless interesting starting materials for modified metal–cyclam complexes and consequently several groups are working towards the selective functionalization of cyclam.[43–49] Alternatively cyclams with NH groups of different reactivity can be synthesized from simple starting materials like 1,4,8,11-tetraazacyclotetradecane-5,12-dione, whose synthesis has been described in the patent literature. Consequently, we set out to repeat the synthesis by Tomalia and Wilson, which is not described in great detail in the patent.[50] The reaction of ethylenediamine and methylacrylate initially results in the quantitative formation *N*-(2-aminoethyl)-*β*-alanine as evidenced by the $^1H$ NMR spectrum of the crude reaction mixture (Scheme 1). The intermediate was dissolved in water to give an approximately 50% solution and left for 48 h. In contrast to the information given in the patent, we never observed product precipitation from aqueous solutions at this point. To isolate product from the mixture, the aqueous solution was continuously extracted with $CHCl_3$ for several hours. In this manner about 10% of the crude product were extracted into the organic solvent. The extract was composed of the desired product (cyclic dimer) together with cyclic monomer and trimer and contained between 10–15% of 1,4,8,11-tetraazacyclotetradecane-5,12-dione based on the $^1H$ NMR integral of the amide proton resonances at $\delta = 9.0$. After removal of $CHCl_3$ and redissolution of the oily residue in hot water, the desired product slowly precipitated upon cooling. From ten attempts, yields of 1,4,8,11-tetraazacyclotetradecane-5,12-dione varying between 1–1.5% were attained. This certainly is a very poor yield, nonetheless a single large batch generates between 14–19 g of product, since the weakly exothermic reaction itself requires no solvent and can be performed on a large scale owing to the low price of the starting materials.

1,4,8,11-tetraazacyclotetradecane-5,12-dione was treated with 1,1′-ferrocene-bis(methylenepyridinium) salt in refluxing acetonitrile (Scheme 2) to produce several macrocyclic com-



Scheme 2.

pounds. The main product of this reaction (ca. 50 % yield) is the 1+1 addition product ferrocene–cyclamdione. Apart from the expected macrocycle, higher oligomers are also produced in significant amounts. The 2+2 addition product can be isolated in yields of up to 25 % together with some 3+3 product (yield up to 5 %). In some reactions of 1,4,8,11-tetraazacyclotetradecane-5,12-dione with the 1,1′-ferrocenebis(methylenepyridinium) salt, the chromatographic separation of the products resulted in another mobile band after the 3+3 product, which may well be the 4+4 product. However, we did not attempt to isolate and characterize this material. The reduction of the initial 1+1 ferrocene–cyclamdione is effected by treatment with $LiAlH_4$ in $CH_2Cl_2$/THF mixtures to afford FcCyclam in 86 % yield, following a protocol used by Gokel et al. for the reduction of less reactive amides.[51]

*Metal complexes*: FcCyclam can be expected to produce stable complexes with transition metal ions. However, in contrast to cyclam itself, only the metal complexes of FcCyclam and $Cu^{2+}$ and $Zn^{2+}$ in $CH_3CN$ are readily formed at room temperature, whereas prolonged heating of the respective metal triflates and FcCyclam is required to effect the complexation of $Co^{2+}$ and $Ni^{2+}$. The relative inertness of FcCyclam towards metal complexation is attributed to the low degree of conformational flexibility of the tetraazamacrocycle bridged by a 1,1′-ferrocenedimethylene unit.[52]

*Mechanism of [Cu(FcCyclam)]$^{2+}$ formation*: Upon closer inspection, the synthesis of $[Cu(FcCyclam)]^{2+}$ in $CH_3CN$ turns out to be more complicated than anticipated. We observed that the initially orange solution of FcCyclam turns blue immediately following the addition of $Cu(CF_3SO_3)_2$ solution and that during the next couple of minutes the color changes from blue to the dark pink of the $[Cu(FcCyclam)]^{2+}$ complex.

Two facts are important here: Blue is a typical color for a ferrocenium ion, while it is also well known that $Cu^{2+}$ is a strong oxidant in $CH_3CN$.[53] Evidently upon mixing of the starting materials, instead of the complexation of copper there first appears to be a fast redox reaction between FcCyclam and $Cu^{2+}$ leading to the intermediate formation of $FcCyclam^+$ and $Cu^+$, which is later followed by a slower complex-formation/electron-transfer reaction that leads to the final product $[Cu(FcCyclam)]^{2+}$. There is clear evidence for this in the UV/Vis spectra (Figure 1).

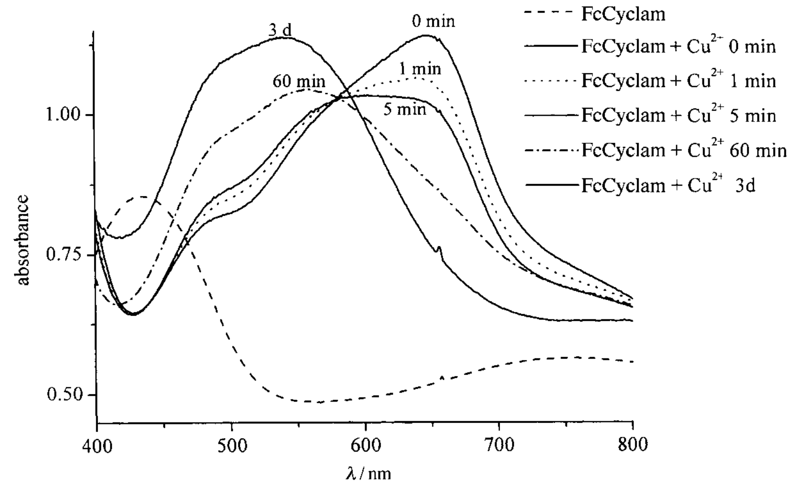


Figure 1. UV/Vis traces (ε vs λ) of the reaction of FcCyclam and $Cu^{2+}$ in $CH_3CN$.

We therefore propose the following to occur during complex formation: As stated before, the mixing of FcCyclam and $Cu^{2+}$ gives rise to the very fast formation of $FcCyclam^+$ and $Cu^+$.[54] $Cu^+$ certainly is not an ideal candidate for complexation by $FcCyclam^+$ as it is too large. We therefore believe, that $Cu^+$ is first coordinated peripherally by the two secondary nitrogen atoms of FcCyclam. This should lower the redox potential of $Cu^+$ sufficiently to allow the back transfer of an electron from $Cu^+$ to $FcCyclam^+$. Our proposal can be summarized as: $Cu^{2+} + FcCyclam \rightarrow Cu^+ + FcCyclam^+ \rightarrow Cu^+ \cdots FcCyclam^+ \rightarrow Cu^{2+} \cdots FcCyclam \rightarrow [Cu(FcCyclam)]^{2+}$.

To lend more support to this idea we have attempted to obtain information on the oxidation states of the two metal ions, that is, whether $[Cu(FcCyclam)]^{2+}$ consists of $Fe^{3+}/Cu^+$ or of $Fe^{2+}/Cu^+$. The X-ray crystal structure data, Mössbauer data,[55] and an ESR spectrum leave no doubt about a $Fe^{2+}/Cu^{2+}$ couple.

**X-ray crystal structures**: The crystal structures of a whole series of metal–FcCyclam complexes ($Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, $Zn^{2+}$) as well as that of FcCyclam itself were determined (Table 1, Table 2) in order to obtain the respective metal–metal distances in the solid state. In Figure 2 all complexes can be viewed normal to the plane formed by the four nitrogen atoms of the cyclam macrocycle. In Figure 3 the projection is such that the five carbon atoms belonging to one cyclopentadienyl ring are within the paper plane. The most important parameter obtained from the solid-state structures of metal–FcCyclam complexes are the distances between the iron of ferrocene and the respective metal ion coordinated within the macrocyclic unit; these are listed in Table 1. It can be seen that the $Fe-M^{2+}$ distances decrease in the series $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$,

Table 1. Bond lengths, angles, and nonbonded distances in FcCyclam, $[Co(FcCyclam)]^{2+}$, $[Ni(FcCyclam)]^{2+}$,[a] $[Cu(FcCyclam)]^{2+}$, and $[Zn(FcCyclam)]^{2+}$.

| | FcCyclam | FcCyclam–$Co^{2+}$ | FcCyclam–$Ni^{2+}$ | FcCyclam–$Cu^{2+}$ | FcCyclam–$Zn^{2+}$ |
|---|---|---|---|---|---|
| Fe–$M^{2+}$ [pm] | | 395.9(10) | 385.4(11) | 377.7(11) | 369.0(9) |
| Cp–Cp′ [°] | 4.6 | 7.3 | 6.4 | 9.8 | 4.9 |
| M–N [pm] | | 200.2(5), 197.7(5),<br>200.4(5), 197.6(5) | 195.9(5) 194.8(4) | 203.0(5), 202.3(5),<br>202.4(5), 201.6(5) | 208.0(4), 208.0(4)<br>203.5(4), 205.5(4) |
| N-M-N [°] | | | | | |
| N1-M-N2 | | 93.92(18) | 95.1(2) | 95.7(2) | 87.91(18) |
| N2-M-N3 | | 87.12(19) | 87.0(2) | 86.4(2) | 102.93(18) |
| N3-M-N4 | | 94.27(18) | | 96.4(2) | 87.99(17) |
| N4-M-N1 | | 87.16(19) | | 86.0(2) | 101.79(17) |
| N1-M-N3 | | 160.23(17) | 166.1(3) | 165.3(2) | 160.87(17) |
| N2-M-N4 | | 172.80(19) | 162.4(3) | 162.0(2) | 115.04(18) |
| *cis*-N–N [pm][b] | 295.4, 307.6,<br>295.3, 308.2 | 290.8, 274.3,<br>291.7, 274.2 | 269.0, 288.3 | 300.5, 277.1,<br>301.1, 276.0 | 285.7, 321.9,<br>287.2, 320.9 |
| M–X [pm][c] | | Co–N5 224.7 | Ni–O2 320.8 | Cu–O5 283.5 | |

[a] Data from ref. [42]. [b] Non-bonded inter-nitrogen distances, the longer distances are over $-(CH_2)_3-$ bridges and the shorter ones over $-(CH_2)_2-$ units. [c] Axial interactions of the metal ion with another donor atom, for $Co^{2+}$ this is $CH_3CN$, for $Ni^{2+}$ this is $(CH_3)_2CO$, and for $Cu^{2+}$ this is $CF_3SO_3^-$.

Table 2. Summary of X-ray crystal data of FcCyclam and the respective complexes with $Co^{2+}$, $Ni^{2+}$, $Cu^{2+}$, and $Zn^{2+}$.

| | FcCyclam | [Co(FcCyclam)] $(CF_3SO_3)_2 \cdot CH_3CN$ | [Ni(FcCyclam)] $(CF_3SO_3)_2 \cdot Me_2CO$[a] | [Cu(FcCyclam)] $(CF_3SO_3)_2 \cdot 2\,Me_2CO$ | [Zn(FcCyclam)] $(CF_3SO_3)_2$ |
|---|---|---|---|---|---|
| empirical formula | $C_{22}H_{34}FeN_4$ | $C_{26}H_{37}CoF_6FeN_5O_6S_2$ | $C_{27}H_{40}F_6FeN_4NiO_7S_2$ | $C_{30}H_{44}CuF_6FeN_4O_8S_2$ | $C_{24}H_{34}F_6FeN_4O_6S_2Zn$ |
| $M_r$ [$g\,mol^{-1}$] | 410.38 | 805.48 | 825.3 | 874.11 | 773.89 |
| $T$ [K] | 183 | 293 | 293 | 213 | 213 |
| crystal system | orthorhombic | orthorhombic | tetragonal | triclinic | monoclinic |
| space group | *Pbca* | $P2_12_12_1$ | $P4_32_12$ | $P\bar{1}$ | $P2_1/c$ |
| $a$ [pm] | 9.612(2) | 10.394(2) | 10.5735(15) | 10.328(8) | 18.741(4) |
| $b$ [pm] | 16.040(3) | 29.826(6) | 10.5735(15) | 12.974(7) | 10.679(2) |
| $c$ [pm] | 26.304(5) | 10.416(2) | 30.251(6) | 14.460(3) | 15.392(3) |
| $\alpha$ [°] | 90 | 90 | 90 | 102.311(15) | 90 |
| $\beta$ [°] | 90 | 90 | 90 | 105.458(19) | 102.48(3) |
| $\gamma$ [°] | 90 | 90 | 90 | 102.51(5) | 90 |
| $V$ [Å$^3$] | 4055.5(14) | 3229.1(11) | 3382.0(10) | 1745.8(16) | 3007.7(19) |
| $Z$ | 8 | 4 | 8 | 2 | 4 |
| $\rho_{calcd}$ [$g\,cm^{-3}$] | 1.344 | 1.657 | 1.621 | 1.663 | 1.709 |
| $\mu$ [$mm^{-1}$] | 0.758 | 1.175 | 1.192 | 1.231 | 1.502 |
| $F(000)$ | 1760 | 1648 | 1704 | 890 | 1584 |
| crystal size [mm] | 0.25 × 0.20 × 0.12 | 0.76 × 0.51 × 0.25 | 0.4 × 0.4 × 0.2 | 0.5 × 0.4 × 0.4 | 0.9 × 0.7 × 0.7 |
| $\theta$ range [°] | 1.6–28.3 | 1.4 – 23.5 | 2.7–26.0 | 3.6–25.0 | 2.9– 26.0 |
| index range (*hkl*) | – 12,12; – 20,17; – 31,33 | – 11,11; – 33,33; – 11,11 | 0,12; – 13,0; – 37,0 | – 12,12; – 15,15; – 13,17 | – 22,23; 0,13; – 18,0 |
| reflections collected/independent | 24559/4888 | 20297/4672 | 3524/3137 | 6107/5832 | 6124/5889 |
| data/parameters | 4888/252 | 4672/430 | 3137/219 | 5832/426 | 5889/397 |
| GooF | 0.796 | 1.066 | 1.057 | 1.060 | 1.095 |
| Final $R$ indices | | | | | |
| $R1/wR2$ [$I > 2\sigma(I)$] | 0.0438/0.0773 | 0.0438/0.1076 | 0.0452/0.1101 | 0.0811/0.2075 | 0.0679/0.1925 |
| $R1/wR2$ (all data) | 0.1125/0.089 | 0.0482/0.1090 | 0.1175/0.1323 | 0.1129/0.2300 | 0.0895/0.2040 |
| largest peak/hole [e Å$^{-3}$] | 0.46/ – 0.35 | 0.49/ – 0.63 | 0.42/ – 0.37 | 0.98/ – 0.88 | 3.12/ – 1.32 |

[a] Data from ref. [42].

$Zn^{2+}$ even though the respective radii of $M^{2+}$ increase.[56] Upon comparing the shifts of the redox potentials $\Delta E = E_{1/2}([M(FcCyclam)]^{2+}) - E_{1/2}(FcCyclam)$ and the Fe–$M^{2+}$ cation distances $r$(Fe–$M^{2+}$) an evident correlation between the two values can be observed, that is, a decreased $r$(Fe–$M^{2+}$) results in a larger $\Delta E$. This phenomenon will be discussed in more detail in the electrochemistry section.

The geometry of the ferrocene unit itself is unspectacular in all complexes. The two cyclopentadienyl rings are almost coplanar (tilt angle between 4.6–9.8°). In the $Co^{2+}$, $Ni^{2+}$, and $Cu^{2+}$ complexes of FcCyclam the coordination geometry around the metal ions can be best described as square-planar, when refering to the cyclam unit alone. The environment of the $Co^{2+}$ metal ion is better described as square-pyramidal owing to the weak coordination of an additional solvent molecule ($CH_3CN$). Apart from coordination by the four cyclam nitrogen atoms, several metal ions display additional (very) weak contacts to solvent molecules ($Co^{2+}$–$NCCH_3$, $Ni^{2+}$–$OC(CH_3)_2$) or counterions ($Cu^{2+}$–$O_3SCF_3$) (Table 1). No such contacts are seen in the case of $[Zn(FcCyclam)Zn]^{2+}$.

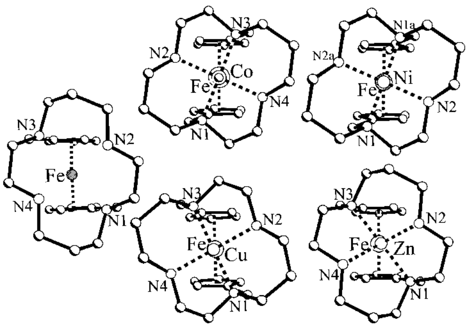


Figure 2. X-ray crystal structures of FcCyclam, $[Co(FcCyclam)]^{2+}$, $[Ni(FcCyclam)]^{2+}$, $[Cu(FcCyclam)]^{2+}$, and $[Zn(FcCyclam)]^{2+}$. All structures are viewed normal to the plane formed by the four nitrogen atoms of the cyclam ligand.

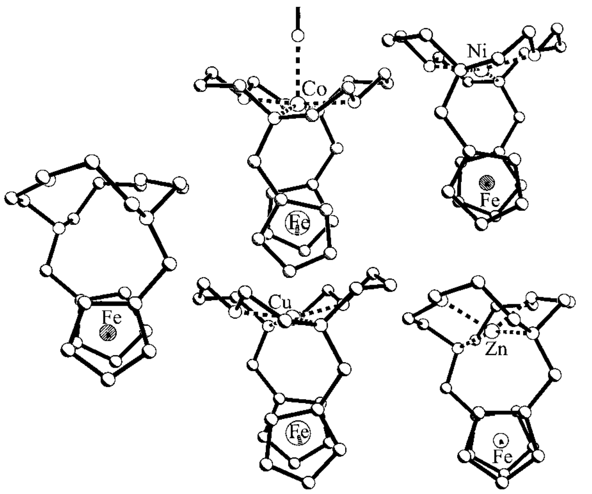


Figure 3. X-ray crystal structures of FcCyclam, $[Co(FcCyclam)]^{2+}$, $[Ni(FcCyclam)]^{2+}$, $[Cu(FcCyclam)]^{2+}$, and $[Zn(FcCyclam)]^{2+}$. All structures are viewed normal to the plane formed by five carbon atoms of a cyclopentadienyl ring. Only the nitrogen atom of the $CH_3CN$ molecule weakly coordinated to $Co^{2+}$ is shown.

Evidently this metal ion is well shielded within the cavity close to the ferrocene. The coordination sphere of $Zn^{2+}$ is somewhere between tetrahedral and square-planar, since the ferrocene unit linking the two tertiary nitrogen atoms enforces a near linear arrangement of the N-$Zn^{2+}$-N unit, whereas the two secondary amines are more flexible resulting in a much smaller N-$Zn^{2+}$-N angle (Table 2). Alternatively the geometrical environment around $Zn^{2+}$ may be viewed as trigonal pyramidal with one of the equatorial ligands missing. It is quite interesting to compare the conformations of the ligand in the different metal complexes; only the structure of the ligand in $[Zn(FcCyclam)]^{2+}$ is quite similar to that of FcCyclam itself, as can be seen in the residual-mean-square fit of the two structures in Figure 4.

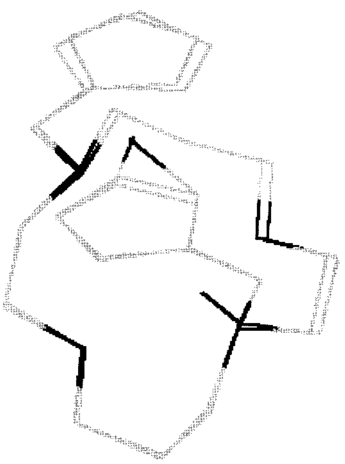


Figure 4. Root mean square fit of the X-ray crystal structures of FcCyclam and $[Zn(FcCcylam)]^{2+}$.

One interpretation is that the Fccylam ligand is perfectly suited for the complexation of $Zn^{2+}$. Another more convincing idea is that the $d^{10}$ ion $Zn^{2+}$, which is rather flexible with respect to coordination geometries, is most willing to accept the geometry provided by the ligand. Another similarity between FcCyclam complexes of $Co^{2+}$, $Ni^{2+}$, and $Cu^{2+}$ is the orientation of the NH units of the respective two secondary amines, which are pointing towards the ferrocene unit, with the macrocycle adopting the *trans* I configuration. Again the $Zn^{2+}$ complex is different in that the NH units are pointing away from the ferrocene towards the periphery of the complex, resulting in the *trans* V configuration. The metal–nitrogen distances observed are in the normal range for metal–cyclam complexes.[57]

**UV-visible spectroscopy**: The UV-visible spectra of the $Co^{2+}$, $Ni^{2+}$, and $Cu^{2+}$ complexes of FcCyclam are dominated by the d–d transitions of the respective $M^{2+}$ ions, whereas the spectra of $[Zn(FcCyclam)]^{2+}$ and FcCyclam itself display the much weaker ferrocene transitions (Figure 5). The $\lambda_{max}$ and the $\varepsilon$ values of FcCyclam and $[M(FcCyclam)]^{2+}$ (M = Co, Ni, Cu, Zn) are as follows: FcCyclam 434 (95), $[Co(FcCyclam)]^{2+}$ 460 (446), $[Ni(FcCyclam)]^{2+}$ 490 (305), $[Cu(FcCyclam)]^{2+}$ 520 (316), $[Zn(FcCyclam)]^{2+}$ 425 nm (125 $L\,M^{-1}cm^{-1}$).

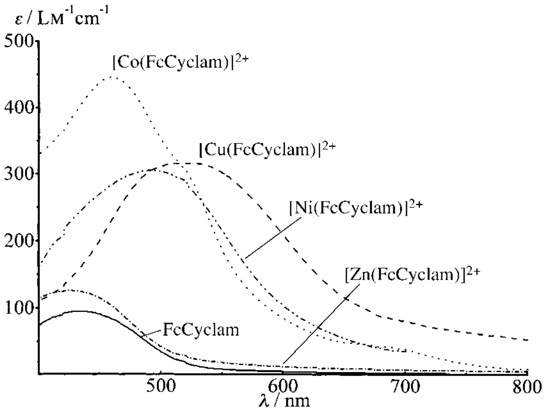


Figure 5. UV/Vis spectra ($\varepsilon$ vs $\lambda$) of FcCyclam and $[M(FcCyclam)]^{2+}$ complexes ($M^{2+}$ = Co, Ni, Cu, Zn) as a $10^{-3}$ mol dm$^{-3}$ solution in $CH_3CN$.

## Solution studies

*Protonation constants*: Solution studies directed toward the determination of protonation constants and stability constants for the formation of complexes of FcCyclam and $(FcCyclam)_2$

with $Cu^{2+}$ and phosphate in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ $KNO_3$) have been carried out. Other solvents such as water or DMSO/water mixtures were not used due to insolubility of the receptors. Protonation constants of FcCyclam and $(FcCyclam)_2$ are shown in Table 3, whereas Table 4 reports the stability constants found for the FcCyclam/$H^+$/$Cu^{2+}$ and $(FcCyclam)_2$/$H^+$/$Cu^{2+}$ systems. Figure 6 shows the distribution diagram of the FcCyclam/$H^+$/$Cu^{2+}$ system. Only three protonation processes have been found for FcCyclam in 1,4-dioxane/water (70:30 v/v). The logarithm of the first protonation process ($\log K = 9.21$) is close to that found in analogous functionalized polyazaalkanes in this medium.[58]

Table 3. Stability constants ($\log K$)[a] in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ potassium nitrate, 25 °C) for FcCyclam and $(FcCyclam)_2$.

| Reaction | L = FcCyclam | L = $(FcCyclam)_2$ |
|---|---|---|
| $L + H^+ \rightleftharpoons [HL]^+$ | 9.21(2) | 11.46(2) |
| $L + 2H^+ \rightleftharpoons [H_2L]^{2+}$ | 15.27(1) | 21.86(3) |
| $L + 3H^+ \rightleftharpoons [H_3L]^{3+}$ | 18.46(2) | 30.73(4) |
| $L + 4H^+ \rightleftharpoons [H_4L]^{4+}$ | – | 37.06(6) |
| $L + 5H^+ \rightleftharpoons [H_5L]^{5+}$ | – | 40.18(7) |
| $L + 6H^+ \rightleftharpoons [H_6L]^{6+}$ | – | 42.40(7) |
| $[HL]^+ + H^+ \rightleftharpoons [H_2L]^{2+}$ | 6.06 | 10.40 |
| $[H_2L]^{2+} + H^+ \rightleftharpoons [H_3L]^{3+}$ | 3.14 | 8.87 |
| $[H_3L]^{3+} + H^+ \rightleftharpoons [H_4L]^{4+}$ | – | 6.33 |
| $[H_4L]^{4+} + H^+ \rightleftharpoons [H_5L]^{5+}$ | – | 3.12 |
| $[H_5L]^{5+} + H^+ \rightleftharpoons [H_6L]^{6+}$ | – | 2.22 |

[a] Values in parentheses are standard deviations on the last significant digit.

Table 4. Stability constants ($\log K$)[a] for the formation of $Cu^{2+}$ complexes of FcCyclam and $(FcCyclam)_2$ in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ potassium nitrate, 25 °C).

| Reaction | L = FcCyclam | L = $(FcCyclam)_2$ |
|---|---|---|
| $Cu^{2+} + L + 3H^+ \rightleftharpoons [Cu(H_3L)]^{5+}$ | – | 37.78(7) |
| $Cu^{2+} + L + 2H^+ \rightleftharpoons [Cu(H_2L)]^{4+}$ | – | 33.65(6) |
| $Cu^{2+} + L + H^+ \rightleftharpoons [Cu(HL)]^{3+}$ | 13.85(5) | 27.51(7) |
| $Cu^{2+} + L \rightleftharpoons [Cu(L)]^{2+}$ | 9.26(4) | 19.62(7) |
| $Cu^{2+} + L + H_2O \rightleftharpoons [Cu(L)(OH)]^+ + H^+$ | – 3.31(6) | 8.83(8) |

[a] Values in parentheses are standard deviations on the last significant digit.

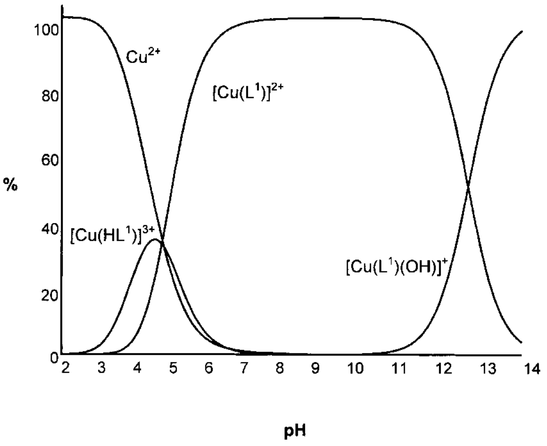


Figure 6. Distribution diagram of the FcCyclam-$H^+$-$Cu^{2+}$ system.

In a similar manner the difference between the logarithms of the first and second protonation processes ($\Delta\log K = 3.15$) compares well with those found in related compounds.[59] It is well known that the last protonation processes in small cyclic polyazacycloalkanes are much less basic due to large electrostatic repulsion between polyammonium groups.[60] This effect is also observed in FcCyclam with a logarithm of the stability constant for the third protonation of $\log K = 3.14$. In addition the last protonation process is too acidic to be observed under the working experimental conditions. The $(FcCyclam)_2$ ligand behaves as a hexaprotic base in 1,4-dioxane/water mixtures. The difference between the logarithm of the first and second protonation process is very small ($\Delta\log K = 0.76$), suggesting that the second protonation takes place in the cyclam ring that is still unprotonated. The third and fourth protons should attack cyclam units that are already monoprotonated with the resulting diminution of the protonation constant. The fifth and sixth protonations are much less basic; these two protonations should take place near two already protonated ammonium groups. The last two protonations for $(FcCyclam)_2$ were not observed.

*Metal and anion complexation*: The $Cu^{2+}$ complexes of FcCyclam and $(FcCyclam)_2$ in 1,4-dioxane-water are readily formed at room temperature, and we have not found any evidence in this aqueous–organic mixture of the mechanism of FcCyclam–$Cu^{2+}$ formation as described for $CH_3CN$. Potentiometric studies in the presence of $Cu^{2+}$ therefore allowed us to determine the complex stability constants with the FcCyclam and $(FcCyclam)_2$ receptors. The FcCyclam forms the mononuclear complexes $[Cu(HFcCyclam)]^{3+}$, $[Cu(FcCyclam)]^{2+}$, and $[Cu(FcCyclam)(OH)]^+$. The logarithm of the formation constant of the $[Cu(FcCyclam)]^{2+}$ complex ($Cu^{2+} + FcCyclam = [Cu(FcCyclam)]^{2+}$) is $\log K = 9.26$. This stability constant is almost $10^{18}$ times smaller than the stability constants of the $[Cu(cyclam)]^{2+}$ complex in water[61] (cyclam = 1,4,8,11-tetraazacyclotetradecane) and $10^{10}$ times smaller than the stability constant of the complex $[Cu(Fc_4cyclam)]^{2+}$ in THF/water (70:30 v/v). ($Fc_4cyclam$ = 1,4,8,11-tetrakis(ferrocenylmethyl)-1,4,8,11-tetraazacyclotetradecane).[3]

The stability constants of $Cu^{2+}$ with the receptor $(FcCyclam)_2$ (1:1 molar ratio) have also been determined by using potentiometric methods. The mononuclear complexes $[Cu(H_3(FcCyclam)_2)]^{5+}$, $[Cu(H_2(FcCyclam)_2)]^{4+}$, $[Cu(H(FcCyclam)_2)]^{3+}$, $[Cu((FcCyclam)_2)]^{2+}$, and $[Cu((FcCyclam)_2)(OH)]^+$ were found. Solution studies with $(FcCyclam)_2$ and $Cu^{2+}$ were carried out by using 1:1 metal-to-ligand rations and, therefore, only mononuclear complexes were found. Studies with metal-to-ligand 2:1 ratio will probably lead to found dinuclear complexes, but these experiments were not carried out.

The logarithm of the stability constants of the $[Cu\{(FcCyclam)_2\}]^{2+}$ complex ($Cu^{2+} + (FcCyclam)_2 = [Cu\{(FcCyclam)_2\}]^{2+}$) is $\log K = 19.62$. This value is $10^8$ times smaller than that found for cyclam in water ($Cu^{2+}$ + cyclam = $[Cu(cyclam)]^{2+}$, $\log K = 27.2$),[6] but is quite similar to that for $[Cu(Me_4cyclam)]^{2+}$ ($\log K = 18.3$, $Me_4cyclam$ = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) and that for

$[Cu(Fc_4cyclam)]^{2+}$.[3] The $(FcCyclam)_2$ receptor forms much more stable complexes with $Cu^{2+}$ than the related FcCyclam ligand.

We have also carried out potentiometric studies of the interaction of FcCyclam and $(FcCyclam)_2$ molecules with phosphate. The FcCyclam and $(FcCyclam)_2$ receptors are polybases; they form charged protonated species at neutral and acid pH and are good candidates for anion recognition through protonated ammonium–anion electrostatic and hydrogen-bonding interactions.[62] Tables 5 and 6 list the logarithms of the stability constants for the interaction of FcCyclam and $(FcCyclam)_2$ with this anion in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ potassium nitrate, 25 °C). Bearing in mind the values of the protonation constants of phosphate and the receptor FcCyclam, the different species $[LH_2PO_4]^-$, $[LH_3PO_4]$, $[LH_4PO_4]^+$, and $[LH_5PO_4]^{2+}$ existing in solution can tentatively be assigned to the interaction of $LH^+{-}HPO_4^{2-}$, $LH^+{-}H_2PO_4^-$, $LH_2^{2+}{-}H_2PO_4^-$, and $LH_3^{3+}{-}H_2PO_4^-$ species, respectively. Assuming these interactions, the logarithms of the stability constants for the interaction the $LH_j^{j+} + H_iPO_4^{(i-3)-}$ species to give the $[LH_{i+j}PO_4]^{(i+j-3)-}$ complexes are 4.38, 4.75, 4.83 and 5.11.

Table 5. Stability constants (log$K$)[a] for the interaction of FcCyclam with phosphate in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ potassium nitrate, 25 °C).

| Reaction[b] | L = FcCyclam |
|---|---|
| $L + 2H + PO_4 \rightleftharpoons LH_2PO_4$ | 25.33(2) |
| $L + 3H + PO_4 \rightleftharpoons LH_3PO_4$ | 34.00(2) |
| $L + 4H + PO_4 \rightleftharpoons LH_4PO_4$ | 40.14(2) |
| $L + 5H + PO_4 \rightleftharpoons LH_5PO_4$ | 43.56(1) |
| $HL + HPO_4 \rightleftharpoons LH_2PO_4$ | 4.38 |
| $HL + H_2PO_4 \rightleftharpoons LH_3PO_4$ | 4.75 |
| $H_2L + H_2PO_4 \rightleftharpoons LH_4PO_4$ | 4.83 |
| $H_3L + H_2PO_4 \rightleftharpoons LH_5PO_4$ | 5.11 |

[a] Values in parentheses are the standard deviations in the last significant digit. [b] Charges have been omitted for clarity.

Table 6. Stability constants (log$K$)[a] for the interaction of $(FcCyclam)_2$ with phosphate in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ potassium nitrate, 25 °C).

| Reaction[b] | $(FcCyclam)_2$ |
|---|---|
| $L + 3H + 2PO_4 \rightleftharpoons LH_3(PO_4)_2$ | 50.40(8) |
| $L + 4H + 2PO_4 \rightleftharpoons LH_4(PO_4)_2$ | 62.76(8) |
| $L + 5H + 2PO_4 \rightleftharpoons LH_5(PO_4)_2$ | 72.02(9) |
| $L + 6H + 2PO_4 \rightleftharpoons LH_6(PO_4)_2$ | 79.81(7) |
| $L + 7H + 2PO_4 \rightleftharpoons LH_7(PO_4)_2$ | 85.73(8) |
| $L + 8H + 2PO_4 \rightleftharpoons LH_8(PO_4)_2$ | 89.74(8) |
| $LH + 2HPO_4 \rightleftharpoons LH_3(PO_4)_2$ | 15.46 |
| $H_2L + 2HPO_4 \rightleftharpoons LH_4(PO_4)_2$ | 17.42 |
| $H_3L + 2HPO_4 \rightleftharpoons LH_5(PO_4)_2$ | 17.81 |
| $H_4L + 2HPO_4 \rightleftharpoons LH_6(PO_4)_2$ | 19.27 |
| $H_5L + 2HPO_4 \rightleftharpoons LH_7(PO_4)_2$ | 22.07 |
| $H_6L + 2HPO_4 \rightleftharpoons LH_8(PO_4)_2$ | 23.86 |

[a] Values in parentheses are the standard deviations in the last significant digit. [b] Charges have been omitted for clarity.

The formation of complexes between phosphate and the receptor $(FcCyclam)_2$ (molar ratio 2:1) has also been studied. Under these experimental conditions complexes of the type $[LH_j(PO_4)_2]^{j-6}$ have been found. Although the determination of the nature of the existing species in solution taking only into account potentiometric data is difficult, we have tentatively assigned the complexes $[LH_3(PO_4)_2]^{3-}$, $[LH_4(PO_4)_2]^{2-}$, $[LH_5(PO_4)_2]^-$, $[LH_6(PO_4)_2]$, $[LH_7(PO_4)_2]^+$, and $[LH_8(PO_4)_2]^{2+}$ to the interaction between the species $HL^+{-}HPO_4^{2-}{-}HPO_4^{2-}$, $H_2L^{2+}{-}HPO_4^{2-}{-}HPO_4^{2-}$, $H_3L^{3+}{-}HPO_4^{2-}{-}HPO_4^{2-}$, $H_3L^{3+}{-}HPO_4^{2-}{-}H_2PO_4^-$, $H_3L^{3+}{-}H_2PO_4^-{-}H_2PO_4^-$, and $H_4L^{4+}{-}H_2PO_4^-{-}H_2PO_4^-$. That gives logarithms of the stability constant for these interactions of 15.44, 17.42, 17.81, 17.30, 14.92, and 12.6, respectively.

**Electrochemical behavior**: One of the most promising applications of redox-functionalized molecules is their incorporation to amperometric sensing devices for target receptors.[63] To achieve this goal, the development of systems that show selectivity coupled to a large electrochemical shifts is of great interest. The FcCyclam molecule has a promising architecture with the metal-binding cavity very close to the iron atom of the ferrocenyl group. Consequently, the shift of the redox potential of the ferrocenyl groups in FcCyclam and $(FcCyclam)_2$ in the presence of several metal ions and anions has been studied.

First the electrochemical behavior of the FcCyclam and $(FcCyclam)_2$ receptors was studied in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ $KNO_3$) as a function of the pH and in the presence of the metal ions $Ni^{2+}$, $Cu^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Pb^{2+}$, and $Hg^{2+}$. Each metal ion was studied separately. The results are presented in Figures 7 and 8 for FcCyclam and $(FcCyclam)_2$, respectively. As already observed in related polyazaalkanes attached to ferrocenyl groups, there is a steady anodic shift of the redox potential of the ferrocenyl groups from basic to acidic pH due to the stepwise protonation of the amino groups.[64] In the presence of stoichiometric amounts of $Ni^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Pb^{2+}$, or $Hg^{2+}$ metal ions the $E_{1/2}$ versus pH curve for FcCyclam ligand ($E_{1/2}$ = half-wave potential from rotating disc electrode (RDE) techniques) is not modified significantly. In contrast, when the electrochemical studies were carried out in the presence of $Cu^{2+}$ there is a remarkable and selective anodic oxidation potential shift up to 210 mV at

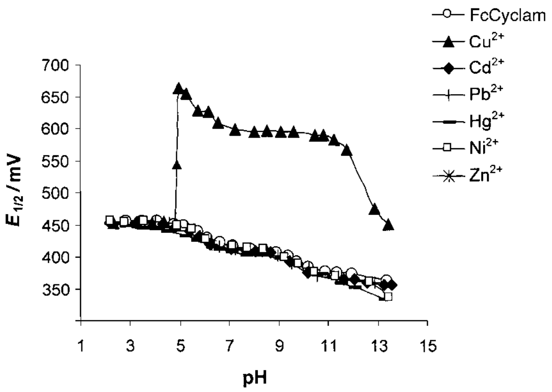


Figure 7. $E_{1/2}$ versus pH for the FcCyclam/$H^+$ and FcCyclam/$H^+$/$M^{2+}$ systems ($M^{2+} = Ni^{2+}$, $Cu^{2+}$, $Zn^{2+}$, $Cd^{2+}$, $Hg^{2+}$, and $Pb^{2+}$) in 1,4-dioxane/water (70:30 v/v).

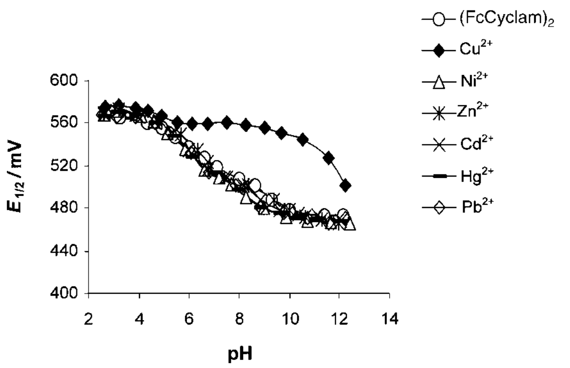


Figure 8. $E_{1/2}$ versus pH for the (FcCyclam)$_2$/H$^+$ and (FcCyclam)$_2$/H$^+$/M$^{2+}$ systems (M$^{2+}$ = Ni$^{2+}$, Cu$^{2+}$, Zn$^{2+}$, Cd$^{2+}$, Hg$^{2+}$, and Pb$^{2+}$) in 1,4-dioxane/water (70:30 v/v).

pH ≈ 5. This is, to the best of our knowledge, the largest electrochemical shift ever reported in electrochemical cation recognition in an aqueous medium with related receptors.

In general, there is good agreement between the potentiometric and electrochemical results. The [Cu(FcCyclam)]$^{2+}$ complex exists in a percentage higher than 90 % in the 6.5–12 pH range (see distribution diagram in Figure 6). The electrochemical behavior shows that in this pH range an almost constant oxidation potential of about 600 mV versus SCE is observed. When the complex [Cu(HFcCyclam)]$^{3+}$ is formed the oxidation potential is anodically shifted. At pH > 11 [Cu(FcCyclam)(OH)]$^+$ exists with a consequent decrease of the oxidation potential. In conclusion, the higher the positive charge of the complex the higher is the oxidation potential of the ferrocenyl groups.

The (FcCyclam)$_2$ ligand is also able to selectively sense the presence of Cu$^{2+}$ in 1,4-dioxane/water mixtures (see Figure 8) electrochemically. However, in this case the maximum electrochemical shift found in the presence of Cu$^{2+}$ is about 80 mV at pH 10. This displacement of the oxidation potential of the ferrocenyl groups is close to that found for the parent receptor Fc$_4$cyclam in the presence of Cu$^{2+}$, which displayed an anodic shift of 90 mV at pH ≈ 9 in THF/water (70:30 v/v) mixtures.[65] Despite the presence in both FcCyclam and (FcCyclam)$_2$ receptors of a ferrocenyl electro-signalling subunit and cyclam binding sites, the maximum electrochemical shift found in the presence of Cu$^{2+}$ is higher for the former receptor than for the latter; this points to the importance of the molecular architecture in the sensing event. This has to be related to the closer proximity between the Cu$^{2+}$ cation and the iron atom of the ferrocenyl group in FcCyclam upon metal coordination.

Studies on the interaction of FcCyclam and (FcCyclam)$_2$ with anions have also been carried out in 1,4-dioxane/water (70:30 v/v). The anions phosphate, sulfate, adenosine-5′-triphosphate (ATP), chloride, and bromide can hardly be expected to enter the cavity and therefore the shift of the oxidation potential of the ferrocenyl group should be small. In fact, although FcCyclam forms complexes with phosphate, the $E_{1/2}$ versus pH curve of the receptor in the presence of those anions does not differ from that of the free receptor. With respect to the (FcCyclam)$_2$ ligand, and despite the larger number of amino groups in this molecule and the formation of highly charged species in solution, no significant variation of the oxidation potential of the ferrocenyl groups has been observed in the presence of the studied anions. Therefore, both FcCyclam and (FcCyclam)$_2$ are anion-insensitive. This contrasts with the observed behavior of the related receptor Fc$_4$Cyclam that gives cathodic shifts up to 40 mV at low pH in the presence of ATP.[65]

*Influence of the solvent on the electrochemical shift*: The redox-active ligand FcCyclam offers a unique opportunity to study—through the ferrocene redox potential—in some detail the influence of more subtle effects, such as solvent variations on the through-space electronic interactions between the iron of ferrocene and a metal ion coordinated within the cyclam unit. This is possible as a reuslt of several favorable properties of the ligand. First of all large oxidation potential changes can be observed upon complexation of metal ions; this renders it possible to precisely probe the influence of minor effects on the redox potentials. Furthermore the tetraazamacrocyclic unit provides a thermodynamically stable and spatially well-defined bonding situation for a coordinated metal ion. This allows a reliable comparison of the Fe–M$^{2+}$ distances M$^{2+}$ = Co$^{2+}$, Ni$^{2+}$, Cu$^{2+}$, and Zn$^{2+}$ as determined by X-ray crystal structure analysis (see respective section) and the bonding situation in solution, which control the redox potentials.

In a previous paper the electrochemical shift $\Delta E$ found in acetonitrile for the complexes [M(FcCyclam)]$^{2+}$(CF$_3$SO$_3$)$_2$ (M$^{2+}$ = Co$^{2+}$, Ni$^{2+}$, Cu$^{2+}$, and Zn$^{2+}$) were measured ($\Delta E$ is defined as $E_{1/2}$ of [M(FcCyclam)]$^{2+}$(CF$_3$SO$_3$)$_2$ – $E_{1/2}$ of the free FcCyclam ligand).[42] Now, the precise distances between the iron atom and the metal ions coordinated in the cyclam cavity have been obtained from crystal structure determinations.

The first conclusion drawn from the X-ray data and electrochemical measurements is that there is a good correlation between the $\Delta E$ value of various metal–FcCyclam complexes and the reciprocal distance of the respective coordinated metal to the iron atom. In fact, the shorter the intermetallic distance, the larger is $\Delta E$. Figure 9 plots the linear dependence of $\Delta E$ versus $1/r$ for the [M(FcCyclam)](CF$_3$SO$_3$)$_2$ complexes in acetonitrile. This is clear evidence for a primarily Coulomb type interaction between the different metal centers Fe – M$^{2+}$.

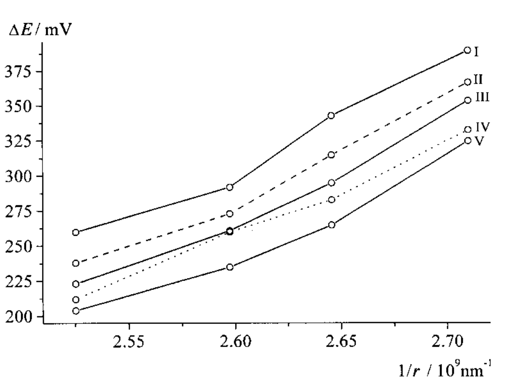


Figure 9. $\Delta E$ versus $1/r$ for the [M(FcCyclam)](CF$_3$SO$_3$)$_2$ complexes (M$^{2+}$ = Zn$^{2+}$, Cu$^{2+}$, Ni$^{2+}$, and Co$^{2+}$) in CH$_3$CN/THF mixtures (I 30:10; II 30:20; III 30:30; IV 20:30; V 10:30).

We wish to report here a detailed study on the influence of solvent, namely its dielectric constant, on the electrochemical shift of $[Zn(FcCyclam)](CF_3SO_3)_2$. Compared to the FcCyclam complexes of $Co^{2+}$, $Ni^{2+}$, and $Cu^{2+}$, the $Zn^{2+}$ complex appears best suited for such an investigation as the X-ray crystal structure shows that $Zn^{2+}$ is coordinatively saturated and localized inside the macrocyclic cavity. Consequently, there is a good chance that the geometry of $[Zn(FcCyclam)]^{2+}$ will be relatively invariant to solvent changes. For our study a number of suitable solvents have been chosen in order to cover a wide range of dielectric constant values (from 64.6 to 5.0). The dielectric constant for a mixture of solvents was calculated as $\varepsilon = \sum_i X_i \varepsilon_i$, where $X_i$ and $\varepsilon_i$ are the molar fraction and permittivity of solvent $i$. This certainly is no more than a reasonable approximation, but a more accurate calculation of the dielectric constant of binary mixtures is not straightforward.[66] Some simple formulas to obtain such data based on the permittivity of the respective pure solvents have been suggested, but appear to work satisfactorily only for solvents of similar $\varepsilon$ and with one solvent being the major component.[67, 68] However, there is a large number of measurements on binary mixtures—done mainly in the 1920s and 1930s—in which a good linear relationship between the molar fractions of the individual components and $\varepsilon$ has been observed.[69] This justifies our approach of calculating the permittivities of the binary mixtures. The results together with other electrochemical data are listed in Table 7, whereas Figure 10 shows the electrochemical shift as a function of the reciprocal permittivity. Assuming the law of Coulomb to apply, one would have expected a monotonous function of the type $\Delta E \cong 1/\varepsilon$, which is evidently not what is found in Figure 10.

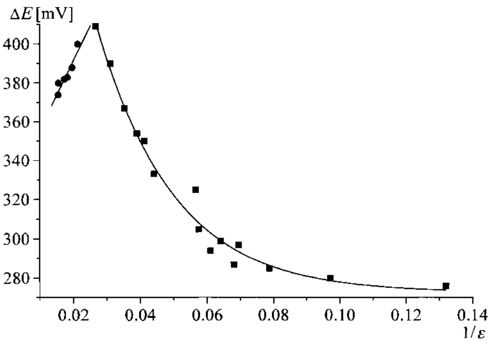


Figure 10. $\Delta E$ versus $1/\varepsilon$ for the $[Zn(FcCyclam)](CF_3SO_3)_2$ complex in various solvents as desrcibed in Table 7.

In order to come up with explanations one should be aware that in solvents with low dielectric constants there is an association process between anions and cations known as ion-pairing. The formation of ion pairs involves the creation of new species in solution that can be depicted as $FcCyclam{-}Zn^{2+}\cdots X^-$ and $FcCyclam{-}Zn^{2+}\cdots 2X^-$, in which $X^-$ is whatever anion present in the solution ($ClO_4^-$ from the supporting electrolyte or $CF_3SO_3^-$ from the $M^{2+}$ salt). The anions do not have to bind to $Zn^{2+}$ ($Zn^{2+}$ is coordinatively saturated as stated above), but may simply interact electrostatically with the positively charged side of the $[Zn(FcCyclam)]^{2+}$ complex. It is assumed here that the Fe–$Zn^{2+}$ distance ($r$) does not change upon ion-pair formation, even though this can not be excluded.[70] When the dielectric constant of the medium is high, ion-pairing will be negligible and the difference $\Delta E$ between the oxidation potential of the free-ligand FcCyclam and that of the respective $Zn^{2+}$ complex can be understood by using a coulombic model, with the electric work of removing an electron from the ferrocene in the presence of two positive charges of the metal cation $Zn^{2+}$ at a certain distance ($r$). Accordingly, for solvents with $37.5 < \varepsilon < 64.6$ the dependence of $\Delta E$ and $1/\varepsilon$ is as expected, since ion-pairing does not occur to a significant extent. However, at $\varepsilon \approx 40$ the trend of $\Delta E$ is reversed: upon decreasing $\varepsilon$, $\Delta E$ also decreases. We attribute this to the reduced polarity of the solvent; this increasingly favors ion-pairing and results in a decrease of the real positive charge of the $[Zn(FcCyclam)]^{2+}$ complexes due to its association with negatively charged counterions. Consequently the observed $\Delta E$ will also be smaller.[71] A third segment of the curve is found in the range of very low $\varepsilon$ solvents. Evidently at lowered $\varepsilon$ the initially linear relation tails off towards a limiting value of $\Delta E \approx 270$ mV. The curve obtained at $\varepsilon$ lower than 40 can be fitted by a first-order exponential decay. In order to understand this, one has

Table 7. Electrochemical data for the $[M(FcCyclam)](CF_3SO_3)_2$ complexes in certain solvents

| Solvent | $\varepsilon$ | $[Zn(FcCyclam)]^{2+}$ | $[Cu(FcCyclam)]^{2+}$ | $[Ni(FcCyclam)]^{2+}$ | $[Co(FcCyclam)]^{2+}$ |
|---|---|---|---|---|---|
| ethanol | 24.3 | 350 | – | – | – |
| $CH_3CN$ | 37.5 | 409 | 399 | 317 | 283 |
| propylene carbonate | 64.4 | 380 | – | – | – |
| THF | 7.58 | 276 | – | – | – |
| $CH_2Cl_2$/acetone 30:30 v/v | 14.4 | 297 | – | – | – |
| $CH_2Cl_2$/acetone 20:30 v/v | 15.6 | 299 | – | – | – |
| $CH_2Cl_2$/acetone 10:30 v/v | 17.4 | 305 | – | – | – |
| THF/$CH_3CN$ 30:2 v/v | 10.3 | 280 | – | – | – |
| THF/$CH_3CN$ 30:4 v/v | 12.7 | 285 | – | – | – |
| THF/$CH_3CN$ 30:6 v/v | 14.7 | 287 | – | – | – |
| THF/$CH_3CN$ 30:8 v/v | 16.4 | 294 | – | – | – |
| THF/$CH_3CN$ 30:10 v/v | 17.7 | 325 | 265 | 235 | 204 |
| THF/$CH_3CN$ 30:20 v/v | 22.7 | 333 | 283 | 260 | 212 |
| THF/$CH_3CN$ 30:30 v/v | 25.7 | 354 | 295 | 261 | 223 |
| THF/$CH_3CN$ 20:30 v/v | 28.4 | 367 | 315 | 273 | 238 |
| THF/$CH_3CN$ 10:30 v/v | 32.2 | 390 | 343 | 292 | 260 |
| $CH_3CN$/water 30:3 v/v | 46.8 | 400 | – | – | – |
| $CH_3CN$/water 30:5 v/v | 50.9 | 388 | – | – | – |
| $CH_3CN$/water 30:7.5 v/v | 54.8 | 383 | – | – | – |
| $CH_3CN$/water 30:10 v/v | 57.7 | 382 | – | – | – |
| $CH_3CN$/water 30:20 v/v | 64.6 | 374 | – | – | – |
| $r$ [pm][c] |  | 369.0(10) | 377.7(11) | 385.4(11) | 395.9(9) |

[a] $\Delta E$ [mV] $= E_{1/2}([M(FcCyclam)]^{2+}) - E_{1/2}(FcCyclam)$. [b] $\varepsilon$ for a mixture of solvents have been calculated as $\varepsilon = \sum_i X_i \varepsilon_i$, in which $X_i$ and $\varepsilon_i$ are the molar fraction and permittivity of solvent $i$, respectively. [c] $r$ = distances $M^{2+}$–iron from crystallographic data.

to realize that the dielectric constants given for the various solvents (mixtures) in Table 7 are based to the dielectric value of the respective pure solvents. However, it must be kept in mind that during the electrochemical measurements these solvents contain a significant amount of salt (0.1 mol dm$^{-3}$ $n$Bu$_4$NClO$_4$) as a supporting electrolyte. This polar admixture must have a significant influence on the real $\varepsilon$ of the solution in an otherwise low $\varepsilon$ solvent. Based on the data in Table 7 (see also Figure 10) it is reasonable to assume that in solvents with low dielectric constant the presence of supporting electrolyte prevents the real $\varepsilon$ from going below values of $\approx 10$.

An alternative explanation of the observed electrochemical behavior could be based on the binding of certain solvents to the Zn$^{2+}$ ion; this is possible only after a re-organization of the coordination environment of Zn$^{2+}$ in the FcCyclam complex. If that was the mechanism, one should be able to find a correlation between the Gutman donor number for a family of solvents and the electrochemical shift $\Delta E$. However, a plot of $\Delta E$ versus the donor number for pure solvents such as acetonitrile, DMF, ethanol, and propylene carbonate provides no evidence for such an idea.

In order to account for the actual behavior, at least in a semiquantitative manner, we have tried to combine both a Coulomb model (that accounts for the electrostatic interactions) with the Fuoss theory (that describes the formation of ion pairs).[72] The electrochemical shift $\Delta E$ is defined in Equation (1), in which $E_{\text{complex}}$ and $\mathrm{E}_{\text{ligand}}$ are the oxidation potentials of the corresponding FcCyclam–Zn$^{2+}$ complex and that of the free receptor, respectively. Additionally $E_{\text{complex}}$ can also be defined as in Equation (2), in which $W_{\mathrm{M}^{2+}}$ is the electric work of removing an electron from ferrocene in the presence of two positive charges of the metal ion at a certain $r$ distance. This in turn leads to Equations (3) and (4).

$$\Delta E = E_{\text{complex}} - E_{\text{ligand}} \tag{1}$$

$$-nFE_{\text{complex}} = -nFE_{\text{ligand}} + W_{\mathrm{M}^{2+}} \tag{2}$$

$$-nF\Delta E = \mathrm{W}_{\mathrm{M}^{2+}} - nFE_{\mathrm{M}^{2+}} \tag{3}$$

$$\Delta E = E_{\mathrm{M}^{2+}} \tag{4}$$

It has been recently reported that this oxidation potential difference between the ligand-substrate species and that of the free ligand can be calculated by using Equation (5).

$$\Delta E = \frac{1}{jn}\left[\frac{z_{\mathrm{a}} z_{\mathrm{b}} e^2 N_{\mathrm{A}}}{4\pi\varepsilon_0 \varepsilon F}\right] \sum_j \sum_i \frac{1}{r_{ji}} + B \sum_j \sum_i \frac{1}{r_{ji}} \tag{5}$$

In Equation (5) $z_{\mathrm{a}}$ is the charge of the oxidized electroactive group, $z_{\mathrm{b}}$ is the charge of the substrate, $j$ is the number of redox groups, and $i$ the number of substrates at a certain $r_{ji}$ distance from the redox centres. $B$ is an empirical parameter that takes into account the fact that the permittivity is not constant but a function of the distance. From previous data and those reported in this work we have observed that $B = 39000\frac{\ln\varepsilon}{\varepsilon}$.[73] Additionally bearing in mind that $e^2 N_{\mathrm{A}}/4\pi\varepsilon_0\varepsilon F = 14398/\varepsilon$, the above equation can be rewritten in our case ($z_{\mathrm{a}} = 1$, $z_{\mathrm{b}} = 2$, $j = 1$, $i = 1$) as Equation (6), in which $r$ is the Zn$^{2+}$–iron distance in Å, $\varepsilon$ is the relative macroscopic permittivity of the solvent, and $\Delta E$ is the electrochemical shift in mV.

$$\Delta E = E_{\mathrm{M}^{2+}} = \frac{14\,398}{\varepsilon}\left[\frac{2}{r}\right] + 39\,000\left(\frac{\log\varepsilon}{\varepsilon}\right)\frac{2}{r^2} \tag{6}$$

At low $\varepsilon$ values the formation of the species FcCyclam–Zn$^{2}\cdots$X$^-$ and FcCyclam–Zn$^{2+}\cdots$2X$^-$ have to be considered. These species would show oxidation potentials of $E_{\mathrm{M}^{2+}-\mathrm{X}^-}$ and $E_{\mathrm{M}^{2+}-2\mathrm{X}^-}$, respectively, that are generally different to that shown by the complex [Zn(FcCyclam)]$^{2+}$ ($E_{\mathrm{M}^{2+}}$). The oxidation potential of the ion pairs are related to the work of removing an electron from the ferrocene in the presence of a metal ion M$^{2+}$ at a distance $r$ and the presence of one or two anions X$^-$ at a distance $a$ from the [Zn(FcCyclam)]$^{2+}$ cation. In order to simplify the equations it is assumed that both anions X$^-$ are to the same distance ($a$) from the [Zn(FcCyclam)]$^{2+}$ cation and that the distance between both anions is 2$a$. Using Equation (5) we can calculate the oxidation potentials of $E_{\mathrm{M}^{2+}-\mathrm{X}^-}$ and $E_{\mathrm{M}^{2+}-2\mathrm{X}^-}$ [Eqs. (7) and (8)].

$$E_{\mathrm{M}^{2+}-2\mathrm{X}^-} = \frac{14\,398}{\varepsilon}\left[\frac{2}{r_{ji}} - \frac{1}{a}\right] + 39\,000\left[\frac{\ln\varepsilon}{\varepsilon}\right]\left[\frac{2}{r^{\,2}_{ji}} - \frac{1}{a^2}\right] \tag{7}$$

$$E_{\mathrm{M}^{2+}-2\mathrm{X}^-} = \frac{14\,398}{\varepsilon}\left[\frac{2}{r_{ji}} - \frac{2}{a}\right] + 39\,000\left[\frac{\ln\varepsilon}{\varepsilon}\right]\left[\frac{2}{r^2_{ji}} - \frac{2}{a^2}\right] \tag{8}$$

In the above equations $r$ describes the distance between the iron atom of the ferrocene and the Zn$^{2+}$ cation, whereas $a$ is related with the distance between the [Zn(FcCyclam)]$^{2+}$ cation and the anion.

For a certain solvent the actual observed oxidation potential shift $\Delta E$ would be given by Equation (9):

$$\Delta E = \Sigma X_{\mathrm{i}} E_{\mathrm{i}} = X_{\mathrm{M}^{2+}} E_{\mathrm{M}^{2+}} + X_{\mathrm{M}^{2+}-\mathrm{X}^-} E_{\mathrm{M}^{2+}-\mathrm{X}^-} + X_{\mathrm{M}^{2+}-2\mathrm{X}^-} E_{\mathrm{M}^{2+}-2\mathrm{X}^-} \tag{9}$$

in which $X_i$ are the molar fractions of the [Zn(FcCyclam)]$^{2+}$ complex and the ions pairs FcCyclam–Zn$^{2}\cdots$X$^-$ and FcCyclam–Zn$^{2+}\cdots$2X$^-$. $X_i$ can be obtained from the stability constants of the equilibria given in Equations (10)–(12):

$$\mathrm{TBA}^+ + \mathrm{X}^- \Leftrightarrow \mathrm{TBA}^+\cdots\mathrm{X}^- \qquad K_{A_0} \tag{10}$$

$$[\mathrm{Zn(FeCyclam)}]^{2+} + \mathrm{X}^- \Leftrightarrow [\mathrm{Zn(FeCyclam)}]^{2+}\cdots\mathrm{X}^- \qquad K_{A_1} \tag{11}$$

$$[\mathrm{Zn(FcCyclam)}]^{2+} + 2\,\mathrm{X}^- \Leftrightarrow [\mathrm{Zn(FcCyclam)}]^{2+}\cdots 2\,\mathrm{X}^- \qquad K_{A_2} \tag{12}$$

in which TBA$^+$ is the tetrabutylammonium cation from the supporting electrolyte. $K_{A_0}$ and $K_{A_1}$ can be evaluated from Fuoss' equation [Eq. (13)], which for a charge of the [Zn(FcCyclam)]$^{2+}$ ion of $+2$, a charge of $+1$ for the tetrabutylammonium and a charge of the anion of $-1$ at $T = 298$ K can be written as:

$$K_A = 0.002523a^3 \times 10^{243.16/\varepsilon a} \tag{13}$$

in which $a$ is the cation–anion distance in Å.

By taking only electrostatic considerations into account, $K_{A_2}$ can be calculated as from $K_{A_1}$ by using Equation (14):

$$RT\ln K_{A_2} = 2RT\ln K_{A_1} + W \tag{14}$$

in which $W$ is the electric work of bring the $X^-$ anion from the infinite to the distance $a$, bearing in mind the repulsive interactions of this anion with the anion $X^-$ that is already forming the ion-pair FcCyclam–$Zn^{2+}\cdots X^-$. As $W = -nFE$ and bearing in mind Equation (5) we get the following equation [Eq. (15)] for $K_{A_2}$:

$$\log K_{A_2} = \log K_{A_1} - \frac{F}{2.3\,RT\,1000}\left(\frac{14\,398}{\varepsilon}\left[\frac{1}{2a}\right] + 39\,000\left[\frac{\log\varepsilon}{\varepsilon}\right]\left[\frac{1}{(2a)^2}\right]\right) \quad (15)$$

in which it is assumed, as stated above, that the distance between the two anions is $2a$.

Equation (9) is only a function of the relative permittivity ($\varepsilon$) and the anion–cation distances ($a$) in ion pairs. In our system there are two $a$ distances corresponding to the distances between the $[Zn(FcCyclam)]^{2+}$ and $TBA^+$ ions and the corresponding anion (probably $ClO_4^-$ from the supporting electrolyte). A nonlinear regression fit of the experimental $\Delta E$ versus $\varepsilon$ allowed us to determine these two anion–cation distances ($a$). These values were 420 and 480 pm, respectively, which are reasonable anion–cation distances in ion pairs.[74] Figure 11 shows the good agreement between calculated and experimental $\Delta E$ values for the $[Zn(FcCyclam)](CF_3SO_3)_2$ complex. The fit is fairly good down to a dielectric constants of $\varepsilon \approx 10$.[73] As stated above, at lower values of $\varepsilon$ the supporting electrolyte seems to impose a residual value of the permittivity.

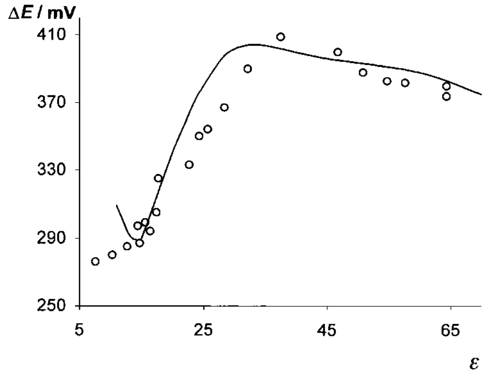


Figure 11. Fit of the $\Delta E$ versus $\varepsilon$ plot by applying the combined Fuoss and Coulomb theory.

The model also predicts that the oxidation potential $\Delta E$ increases as the dielectric constant decreases until $\varepsilon \approx 40$ from which $\Delta E$ decreases when the permittivity diminishes. Therefore, in solvents or solvent mixtures with dielectric constants of about 40, the maximum electrochemical shift will be observed. In this context, it is remarkable that many studies seeking the electrochemical recognition of substrates have been carried out in acetonitrile ($\varepsilon = 37.5$); the solvent for which the model described above predicts the electrochemical shift would be maximum. Solvents with lower dielectric constants will not increase the electrochemical shift, as it should be expected, but a decrease will be observed due to ion-pair formation. Despite the apparent success of merging Coulomb and Fuoss theory for the explanation of the data, one should be aware that our approach involves at least two simplifications. First of all it is debatable to use the bulk solvent permittivity for intramolecular interactions, furthermore the Coulomb model describes the interaction of point charges, which is certainly only a crude approximation for the interaction of iron with a transition metal $M^{2+}$.

The electrochemical behavior the $[M(FcCyclam)]^{2+}$ complexes ($M = Cu^{2+}$, $Ni^{2+}$ and $Co^{2+}$) have also been studied in certain solvents. The oxidation potential shifts observed are listed in Table 7. In general, a similar behavior to that shown by the $[Zn(FcCyclam)]^{2+}$ complex was found.

## Conclusion

The properties of FcCyclam have been studied in detail and the ligand shown to form complexes with $M^{2+} = Co^{2+}$, $Ni^{2+}$ $Cu^{2+}$, $Zn^{2+}$, which are less stable than complexes of cyclam and the respective $M^{2+}$. The most unusual property of this macrocycle is the redox activity of the ferrocene unit; this is influenced in a characteristic manner by the coordination of $M^{2+}$ by the macrocycle. The X-ray crystal structures of FcCyclam and of all four $[M(FcCyclam)]^{2+}$ complexes have been determined. The most important parameter obtained from these studies is the distance $r$ $Fe\cdots M^{2+}$, which decreases in the order $Co^{2+}$ (395.9 pm), $Ni^{2+}$ (385.4 pm), $Cu^{2+}$ (377.0 pm), $Zn^{2+}$ (369.0 pm), while $\Delta E \equiv \{E_{1/2}([M(FcCyclam)]^{2+}) - E_{1/2}(FcCyclam)\}$ increases in the same sequence of complexes: $\Delta E = +283$ mV, $+317$ mV, $+399$ mV, $+409$ mV, respectively. The relationship $\Delta E \cong 1/r$ is in accord with a Coulomb type interaction between $Fe\cdots M^{2+}$ even though this model involves several debatable simplifications for intramolecular interactions. The stable and spatially well-defined bonding of $M^{2+}$ within FcCyclam offers also the opportunity to study in some detail the influence of solvents, that is, a variable dielectric constant, on the propagation of the through space interaction between the charged metal centers. The simple relation of $\Delta E \cong 1/\varepsilon$ according to Coulomb only holds true for solvents with a very high $\varepsilon$ with a lower limtit of around 40. Upon further lowering the permittivity, ion-pairing as described by the Fuoss theory takes place and the effective positive charge of $[M(FcCyclam)]^{2+}$ is reduced and accordingly the values of $\Delta E$. The decrease is linear only initially and is best described by a first-order exponential decay to a limiting value of approximately 270 mV. The asymptotic behavior of the curve is attributed to the fact that the real permittivity of the solvents used for the experiments on the low polarity side can not be reduced further due to the presence of 0.1 mol dm$^{-3}$ $n$Bu$_4$NClO$_4$ of supporting electrolyte in the solvents needed for the cyclic voltammetry experiments. The dependence of $\Delta E$ and $\varepsilon$ can be described semiquantitatively by combining the Fuoss theory with the Coulomb model.

In conclusion, we have synthesized a new redox-active macrocyclic ligand, whose ligating properties can be influenced by the redox behavior of the ferrocene unit in a highly characteristic and controllable manner. In order to effect a maximum response of a redox-active receptor as well as a maximum redox-switching effect, the permittivity of the solvent should be chosen so as to bring about the best compromise between low $\varepsilon$ and a low degree of ion-pairing; $CH_3CN$ appears to be a very good choice.

## Experimental Section

**General**: Commercially available solvents and reagents were purified according to literature procedures.[75] All reactions were carried out under an atmosphere of argon and especially the Pd-catalyzed coupling reactions require strict exclusion of oxygen. Chromatography was performed over silica MN60 (63 – 200 μm). TLC was done with on Merck plates coated with silica gel 60F254. NMR spectra were recorded at 300 K with a Bruker Avance ($^1$H NMR 200 MHz, $^{13}$C NMR 50.3 Mhz) spectrometer. $^1$H NMR were referenced to residual $^1$H impurities in the solvent and $^{13}$C NMR to the solvent signals: $CDCl_3$ ($\delta = 7.26$ ($^1$H), 77.0 ($^{13}$C)), $C_6D_6$ ($\delta = 7.16$ ($^1$H), 128.0($^{13}$C)), $CD_3CN$ ($\delta = 1.93$ ($^1$H), 1.30 ($^{13}$C)). For the purpose of $^1$H NMR signal assignment CpH denotes a proton attached to the sp$^2$ carbon of cyclopentadiene or to the carbon of a ferrocene $\eta^5$-cyclopentadienyl ring. Mass spectra were recorded on a Finnigan MAT3800 instrument. IR spectra were recorded on a Bruker IFS-25 spectrometer in $CHCl_3$. UV/Vis spectra were measured on a JASCO-UV-570 spectrometer in $CH_2Cl_2$. Potentiometric titrations were carried out in 1,4-dioxane/water (70:30 v/v, 0.1 mol dm$^{-3}$ $KNO_3$) for FcCyclam and $(FcCyclam)_2$ using a reaction vessel water-thermostatted at $25.0 \pm 0.1\,^{\circ}C$ under nitrogen atmosphere. Experimental potentiometric details have been published previously.[76] The concentration of the $Cu^{2+}$ and the anion phosphate were determined by using standard methods. The computer program SUPERQUAD[77] was used to calculate the protonation and stability constants. The titration curves for each system (ca. 250 experimental points corresponding to at least three titration curves, $pH = -\log[H]$ range investigated ca. 2.5 – 10, concentration of the ligand being ca. $1.2 \times 10^{-3}$ mol dm$^{-3}$) were treated either as a single set or as separated entities without significant variations in the values of the stability constants. Finally the data sets were merged together and treated simultaneously to give the stability constants. Electrochemical data were carried out in several solvents, with a programmable function-generator Tacussel IMT-1, connected to a Tacussel PJT 120 – 1 potentiostat. The working electrode was platinum with a saturated calomel reference electrode separated from the test solution by a salt bridge containing the solvent/supporting electrolyte. The auxiliary electrode was platinum wire. The solvents used in the electrochemical experiments were rigorously purified prior use. The supporting electrolyte in all the electrochemical experiments was 0.1 mol dm$^{-3}$ tetrabutylammonium perchlorate. Elemental analyses were perfomrmed by the Mikroanalytisches Laboratorium der Chemischen Laboratorien, Universität Freiburg. Starting materials were available comercially or prepared according to literature procedures: 1,1′-ferrocene-bis(methylenepyridinium)tosyl chloride.[78]

**1,4,8,11-tetraazacyclotetradecane-5,12-dione**: This procedure was modified from that of Tomalia and Wilson.[50] Methyl acrylate (688 g, 8.0 mol) was added dropwise to neat ethylenediamine (680 g, 8.0 mol). The addition was conducted at such a rate that the reaction temperarure did not exceed 35 °C; addition time was approximately 8 h. The crude colorless intermediate formed in quantitative yield is *N*-(2-aminoethyl)-$\beta$-alanine [$^1$H NMR ($CDCl_3$): $\delta = 1.26$ (3H; NH), 2.51 (td, $J = 8.5$, 2.0 Hz, 2H; $CH_2$), 2.71 (cm, 4H; $CH_2$), 2.89 (td, $J = 8.5$, 2.0 Hz, 2H,; $CH_2$), 3.68 (s, 3H; $CH_3$)]. The intermediate was dissolved in water to give a 50 % solution and left standing for 48 h. The resulting solution was continuously extracted with $CHCl_3$ for 8 hours. After this time about 10 % of the total mass of the intermediate had been extracted by the organic solvent. The desired 14-membered macrocycle was then extracted quantitatively from the crude aqueous mixture with $CHCl_3$. The extract is composed of the 1+1 product (seven-membered ring), the 2+2 product (14-membered ring), and the 3+3 product (21-membered ring). The composition of this mixture was determined by $^1$H NMR spectroscopy, since the shift of the amide hydrogen is highly characteristic for the different products [$^1$H NMR ($CDCl_3$): $\delta = 6.75$ (CONH of 1+1 product), 8.35 (CONH of 3+3 product), 9.0 (CONH of 2+2 product)]. A typical extract contained about 72 % of the 1+1 product, 14 % of the 2+2 product, and 14 % of the 3+3 product. The extract was evaporated to dryness, and the remaining oil dissolved in hot water to give a concentration of ca. 25 % by weight. This solution was stored at 4 °C, whereupon the desired 2+2 product crystallized slowly (over several days) from the mixture. The product was filtered off, washed with cold water and dried at 100 °C (0.1 Torr) for several hours. Yield: 1 – 1.4 % (13.7 – 19.1 g). $^1$H NMR ($CDCl_3$): $\delta = 1.2$ (brs, 2H; NH), 2.39 (m, 4H; $CH_2$), 2.80 (t, $J = 5.3$ Hz, 4H; $CH_2$), 2.92 (t, $J = 5.5$ Hz, 4H; $CH_2$), 3.38 (m, 4H; $CH_2$), 8.97 (brs, 2H; CONH); $^{13}$C NMR ($CDCl_3$): $\delta = 35.42$, 38.44, 45.60, 48.37, 172.39.

**Ferrocene – cyclamdione**: 1,1′-ferrocene-bis(methylenepyridinium)tosyl chloride (5.12 g, 9.02 mmol), 1,4,8,11-tetraazacyclotetradecane-5,12-dione (2.06 g, 9.02 mmol), and $Na_2CO_3$ (7.0 g) were added to acetonitrile (400 mL) and heated under reflux for 60 h. The cold reaction mixture was filtered, and the filtrate evaporated to dryness. The residue was purified by chromatography ($CHCl_3/CH_3OH = 10{:}1$) to yield ferrocene – cyclamdione (2.0 g, 50 %), 2+2 product (0.94 g, 24 %), and 3+3 product (ca. 0.20 g, 5 %).

**(1+1) product**: $^1$H NMR ($CDCl_3$): $\delta = 2.11 - 2.29$ (m, 6H), 2.58 – 3.36 (m, 10H), 3.82 – 4.08 (m, 12H), 8.97 (s, NH), 9.02 (s, NH); $^{13}$C NMR ($CDCl_3$): $\delta = 36.11$, 53.46, 54.62, 67.54, 69.29, 71.03, 88.51, 127.60, 173.24; MS-EI: *m*/*z*: 438 $[M]^+$.

**(2+2) product**: $^1$H NMR ($CDCl_3$): $\delta = 2.13 - 4.17$ (m, 56H; Cyclam*H*/Fc*H*/FcC*H*$_2$), 8.40 – 8.50 (m, 4H; OCN*H*); $^{13}$C NMR ($CDCl_3$): $\delta = 29.22$, 30.34, 31.78, 35.10, 48.25, 49.08, 50.48, 51.11, 51.46, 68.69, 69.34, 69.94, 71.05, 81.21, 126.67, 171.84; MS-EI: *m*/*z*: 877 $[M]^+$.

**(3+3) product**: In the $^1$H NMR ($CDCl_3$) a complex collection of overlapping multiplets between $\delta = 1.0 - 5.1$ is observed MS-EI: *m*/*z*: 1316 $[M]^+$.

**FcCyclam**: Ferrocene – cyclamdione (4.4 g, 10 mmol) was dissolved in a mixture of THF (100 mL) and $CH_2Cl_2$ (200 mL). $LiAlH_4$ (7.6 g, 200 mmol) was added to the ice-cooled solution and stirring continued for 48 h. After careful hydrolysis of excess $LiAlH_4$ with water (70 mL), NaOH (200 mL; 15 % aq.) was added, and the product extracted with $CHCl_3$. The organic layer was separated, dried over $MgSO_4$ and filtered, and the filtrate evaporated to dryness. The residue was purified by chromatography ($CH_3OH/Et_2NH = 10{:}1$) to yield 3.5 g (86 %) of product. $^1$H NMR ($CDCl_3$): $\delta = 1.40$ (d, $J = 14$ Hz, 2H), 1.85 (d, $J = 12$ Hz, 2H), 2.14 (d, $J = 11$ Hz, 4H), 2.46 – 2.95 (m, 14H), 3.22 (td, $J = 7$, 3 Hz, 2H), 3.73 (s, 2H), 3.93 – 4.08 (m, 10H); $^{13}$C NMR ($CDCl_3$): $\delta = 25.64$, 47.02, 51.55, 53.40, 53.49, 58.20, 65.37, 65.76, 67.40, 70.26, 88.35; $^1$H NMR ($CD_3CN$): $\delta = 1.83 - 3.07$ (m, 20H, Cyclam*H*) 3.62 (s, 4H, FcC*H*$_2$), 3.95 – 3.97 (m, 8H, Fc*H*); $^{13}$C NMR ($CD_3CN$): $\delta = 26.77$, 30.88, 47.86, 52.45, 54.35, 54.69, 59.47, 66.45, 66.88, 68.38, 71.23, 89.54; MS-FD: *m*/*z*: 411 $[M]^+$.

**Metal complexes of FcCyclam**: Metal complexes of FcCyclam were synthesized by an equimolar mixture of ligand and metal triflate in $CH_3CN$ heating under reflux for 1 h. After evaporation of the solvent, the complex was recrystallized from $CH_3CN/Et_2O$.

**$[Co(FcCyclam)](CF_3SO_3)_2$**: elemental analysis calcd (%) for $C_{24}H_{32}CoF_6FeN_4O_6S_2$ (765.44): C 37.56, H 4.47, N 7.30; found C 37.66, H 4.21, N 7.29.

**$[Ni(FcCyclam)](CF_3SO_3)_2$**: $^1$H NMR ($CD_3CN$) : $\delta = 1.81 - 2.23$ (m, 10H; Cyclam*H*), 2.47 – 2.81 (m, 4H; Cyclam*H*), 3.08 – 3.34 (m, 6H; Cyclam*H*), 3.78 – 4.02 (m, 4H; FcC*H*$_2$), 4.53 – 4.70 (m, 8H; Fc*H*); $^{13}$C NMR ($CD_3CN$): $\delta = 23.58$, 51.00, 52.46, 58.26, 59.32, 59.81, 69.06, 70.70, 84.14; elemental analysis calcd (%) for $C_{24}H_{32}F_6FeN_4NiO_6S_2$ (765.20): C 37.57, H 4.47, N 7.30; found C 36.67, H 4.21, N 7.22.

**$[Cu(FcCyclam)](CF_3SO_3)_2$**: elemental analysis calcd (%) for $C_{24}H_{32}CuF_6FeN_4O_6S_2$ (770.0): C 37.43, H 4.19, N 7.28; found C 37.34, H 4.44, N 7.30.

**$[Zn(FcCyclam)](CF_3SO_3)_2$**: $^1$H NMR ($CD_3CN$): $\delta = 1.92 - 2.33$ (m, 4H; N*H*), 2.77 – 3.73 (m, 20H; Cyclam*H*, FcC*H*$_2$), 3.92 – 4.74 (m, 8H; Fc*H*); $^{13}$C NMR ($CD_3CN$): $\delta = 25.34$, 46.71, 50.72, 56.45, 57.30, 62.36, 64.70, 68.68, 69.28, 72.55, 85.98; elemental analysis calcd (%) for $C_{24}H_{32}F_6FeN_4O_6S_2Zn$ (771.90): C 37.25, H 4.43, N 7.24; found C 36.34, H 4.18, N 7.26.

**X-ray crystal structure determination**: Crystals suitable for X-ray crystal structure determinations were grown in the following manner: FcCyclam: recrystallization from $CH_3CN$; $[Co(FcCyclam)](CF_3SO_3)_2$ and $[Zn(FcCyclam)](CF_3SO_3)_2$: slow diffusion of $Et_2O$ into an $CH_3CN$ solution of the complex; $[Ni(FcCyclam)](CF_3SO_3)_2$ and $[Cu(FcCyclam)](CF_3SO_3)_2$: slow diffusion of $Et_2O$ into an $Me_2CO$ solution of the complex. Suitable crystals were mounted on top of a glass fiber. X-ray data were collected on an Enraf-Nonius CAD4 diffractometer or on a Siemens AED diffractometer with $Mo_{K\alpha}$ radiation (71.069 pm) and a graphite monochromator. All structure calculations were made by using SHELX-97,[79] the structures were refined against $F^2$ with anisotropic temperature coefficients for all non-hydrogen atoms. Hydrogen atoms were refined with fixed isotropic temperature coefficients and fixed site occupancy factors, but the coordinates were free to refine. An empirical absorption correction based on psi scans was applied.[35] Definition of *R* factors and goodness-of-fit

(GooF): $wR2=\{\Sigma 2\sigma(I)[w(F_o^2-F_c^2)^2]/\Sigma 2\sigma(I)[w(F_o^2)^2]\}^{1/2}$, $R1=\Sigma 2\sigma(I)\,||F_o|-|F_c||/\Sigma 2\sigma(I)\,|F_o|$; the goodness-of-fit is based on $F^2$: $\mathrm{GooF}=\{\Sigma 2\sigma(I)[w(F_o^2-F_c^2)^2]/(n-p)\}^{1/2}$, in which $n$ is the number of reflections and $p$ is the total number of parameters refined.

## Acknowledgements

This work was supported by the DFG and by the Fonds der Chemischen Industrie. We wish to thank Prof. Dr. Vahrenkamp for access to the CCD detector at the Institut für Anorganische und Analytische Chemie/University of Freiburg and Dipl.-Chem. A. Trösch and Dr. B. Kersting for the collection of the X-ray data sets. Experimental support concerning the stopped-flow kinetics was kindly provided by Dr. T. Poth and T. Schwalm. We wish to thank Prof. Dr. Dinse (TU Darmstadt) for recording an EPR spectrum of $[\mathrm{Cu(FcCyclam)}]^{2+}$. We wish to thank the DGICYT (proyecto PB98-1430-C02-02, 1FD97-0508-C03-01, and AMB99-0504-C02-01) for support.

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Received: December 4, 2000 [F2911]