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Julio C. Medina[a]; Bert C. Lynn[a]; Maria T. Rojas[a]; George W. Gokel[a]; Angel E. Kaifer[a]
[a] Department of Chemistry, University of Miami, Coral Gables, Florida, U.S.A.

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Redox-active macrocyles designed for direct attachment to electrode surfaces

JULIO C. MEDINA, BERT C. LYNN, MARIA T. ROJAS, GEORGE W. GOKEL* and ANGEL E. KAIFER*

Department of Chemistry, University of Miami, Coral Gables, Florida 33124, U.S.A.

A compound containing a redox-switchable ferrocene unit, a cation binding site (crown ether), a hydrophobic tail, and a functional group suitable for conversion into an electrode anchor has been synthesized. Its properties have been assessed by mass spectrometric and electrochemical methods and the effects of cations on the properties of this compound are presented. In addition, several hydrophobic ferrocene derivatives have been prepared and studied by the FAB/MS technique and results of those studies are also reported. These techniques demonstrate cation-mediated cooperativity between the redox center and cation binding site. Other effects resulting from the combination of subunits within a single molecule are also reported.

Compounds that complex cations have intrinsic rate and equilibrium properties such that binding (k_1 or k_{complex}) and cation release (k_{-1} *or* k_{release}) rate constants define the equilibrium $K_S(k_1/k_{-1})$. Although these constants are solvent and temperature dependent, their values vary in relation to each other and selectivities do not usually change appreciably.[1] One means to alter binding strengths and selectivities is to use a switching mechanism. The mechanism of interest to us involves a change in redox state that can make a system more electron rich (reduction) or poor (oxidation).[2] If the oxidatively switched subunit is incorporated in a cation binder, reduction will usually enhance cation binding strength whereas oxidation will diminish it. Because the cation binding strength changes with oxidation state, the electrochemistry of such systems is sensitive to the presence of cations. Thus different cations may alter the electrochemistry in differing ways making the ligand a sensor for the cations present in the system.

The remarkably versatile ferrocene system can be incorporated to form redox-sensitive ligands in a variety of ways and has a potential that makes it accessible in both aqueous and non-aqueous solvents.[3] We report here the design, synthesis, and characterization of a ligand that incorporates ferrocene and a cation binding site and that is the precursor to structures that, in principle at least, can be attached directly to an electrode surface for use as a sensor.

RESULTS AND DISCUSSION

Design of the ligand system

At a minimum, any directly attachable, electrode modifying sensor compound must have four elements. First, an anchoring element such as —CH_2SH should be incorporated that will provide chemical stability and have excellent affinity for the gold electrode surface.[4] Second, a redox switchable element must be present. In our case, ferrocene was chosen because of its synthetic versatility and convenient redox properties. The ferrocene molecule has ten equivalent positions that may be substituted by suitable synthetic modifications making it possible to keep the binding and redox sites in proximity to each other. This is a critical element for successful function of the compound. Third, a site suitable to bind cations present in the solution must be attached and close enough to affect the redox-active site. Based upon past experience, a crown ether element suggested itself for use in this subunit.[5] Finally, a hydrophobic tail (or element) is necessary to prevent access of undesired, hydrophilic species to the electrode surface. In addition, the hydrophobic tails, if close enough to each other, will interact by van der Waals forces to provide a stabilizing, organized assembly at the electrode surface. A schematic for the design of an electrode modifier is illustrated in Fig. 1.

Syntheses

The electrode modifier precursor, compound **7**, was prepared by the sequence of reactions shown in Fig. 2a. Commercially available 1,1′-dicarboxyferrocene, **1**, was converted to **2** by two different methods. One approach was to use a modification of the method reported by Arawaka.[6] In this procedure, **1** was mono-esterified by treatment with gaseous HCl in methanol at 0 °C, affording **2** in 44% yield. Alternatively, **1** was treated with methanol, water, and sodium hydroxide (Nesmeyanov procedure[7]) to give **2** in 41%

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*To whom correspondence should be addressed.

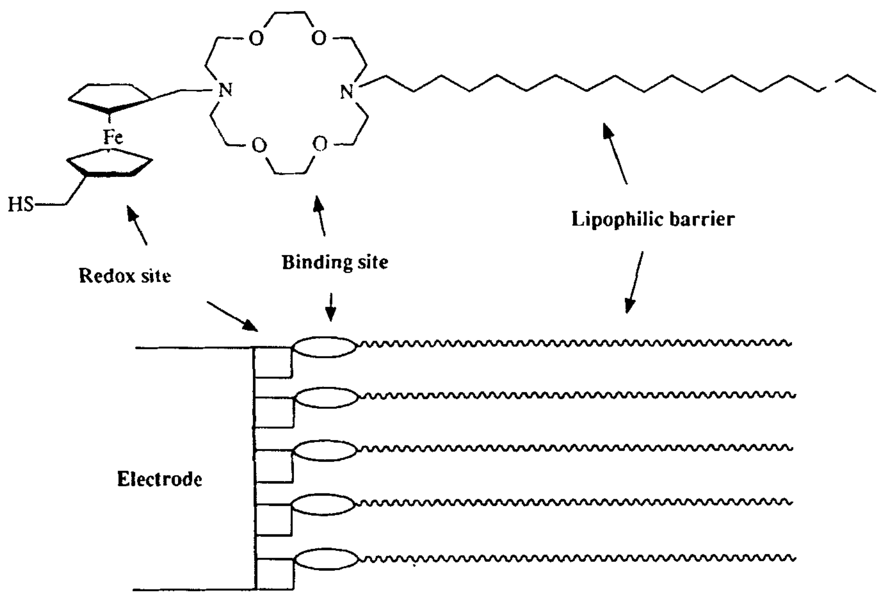


Figure 1 Schematic of electrode design.

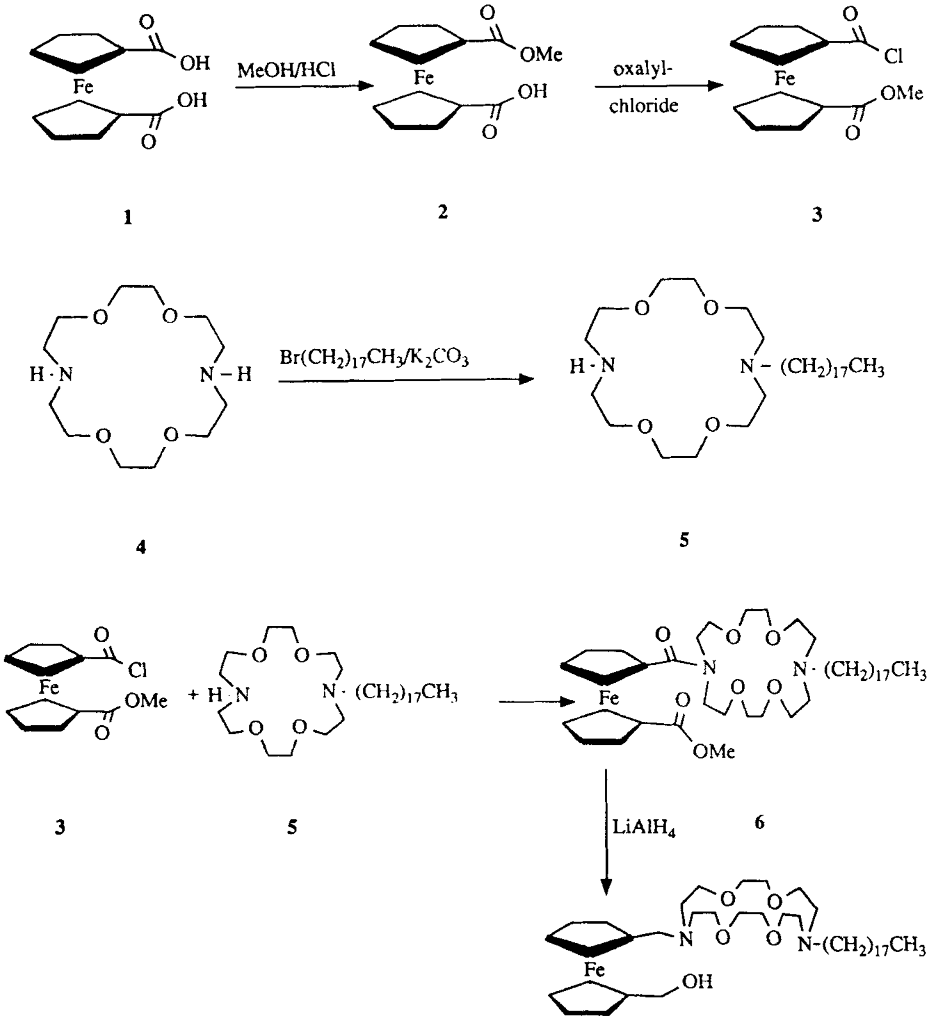


Figure 2a Synthesis of 7.

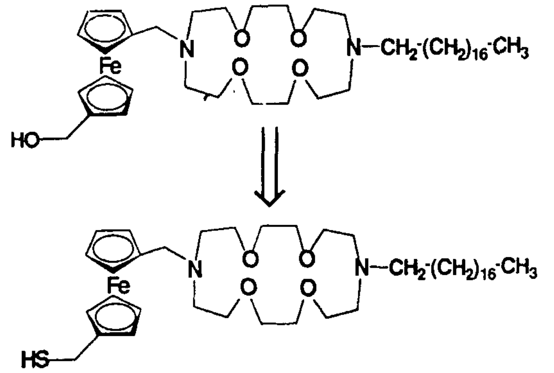


Figure 2b Anticipated conversion of **7** to the analog suitable for binding to an electrode surface.

yield. The half ester acid, **2**, was heated with oxalyl chloride and catalytic pyridine to afford ester acyl chloride, **3**, in 82% yield.

4,13-Diaza-18-crown-6 was converted into the mono-*N*-octadecyl derivative (**5**, 38%) by heating a butyronitrile solution of the crown with 1-bromooctadecane, K_2O_3C, and a small amount of KI. The reaction between **3** and **5** was conducted in CH_2Cl_2 to afford acid amide **6** in 42% yield. Finally, reduction with lithium aluminum hydride converted the tertiary amide into a tertiary amine and reduced the ester function to the hydroxymethyl group. Thus **7** was obtained as a yellowish wax, mp 39–42 °C, in 42% yield. Compound **7** can be converted to the desired electrode modifier such as **8** by conventional means (Fig. 2b).

Compounds **10–12** were prepared for purposes of comparison. These structures are expected to be redox-switchable and surface active (amphipathic) but not to have a well-developed binding site. Each was obtained by converting 1,1′-ferrocenedicarboxylic acid (**1**) into the diacyl chloride (**9**, 52%, mp 92–94 °C) by using oxalyl chloride and a catalytic amount of pyridine. Compounds **10**, **11**, and **12** were obtained by treatment of the dihalide with the appropriate alcohol or amine.

Mass spectral data

Fast atom bombardment mass spectrometry was used to study the novel structures presented in this report and to assess various aspects of their chemistry. In particular, we were interested to evaluate surface activity, cation binding ability with various cations, and to see if differences in cations affected surface activity, fragmentation, etc. Fast atom bombardment has been used in studies reported previously from our laboratories[8] and those of others.[9] The method has proved to be sensitive, convenient and to offer semi-quantitative information about cation complexation. The studies reported here were all conducted on a VG-TRIO 2 mass spectrometer in a *m*-nitrobenzyl alcohol matrix.

The FAB/MS spectrum of **6** showed $[P+H]^+$ (equivalent to the more traditional M + H, not used here because M represents a metal cation) as the base peak. The second primary fragment resulted from acyl-nitrogen fission of the amide bond (m/z 271). A doubly-charged ion that we attribute to $[P+2H]^{++}$ was observed at m/z 393. Four other low intensity ions (m/z 607, 569, 545, 513) were also observed that result, we believe, from fragmentation/rearrangement reactions. Compound **6** shows higher stability (P + H is the parent ion) than might have been expected. This seems likely because the amide is both tertiary and aromatic. Conjugation keeps the C—CO—N< fragment planar and hindered to attack of the large hydrocarbon chain that is transannular.

The constraints of the amide linkage are also reflected in the very poor cation binding behavior observed for **6** by using the FAB/MS technique. In particular, the amide has an important resonance form that places a formal positive charge on nitrogen, thus reducing its donicity. The formal C═N double bond also increases the macroring's overall rigidity. We assess binding by evaluating the ratio $[P+M]/[P+H]$ where M is a metal cation. In the case of **6** in the presence of Na^+ or K^+, this ratio is less than 0.1 which is only an order of magnitude above the detection limit in this experiment. No complexation of Ag^+ by **6** was detected.

Reduction of **6** to **7** removes the amide link, increasing the macroring's flexibility and nitrogen's donicity. The FAB mass spectrum of **7** exhibited a great deal of fragmentation and the base peak was observed at m/z 229 rather than corresponding to $[P+H]$ (*vide supra*). We assign the m/z 229 peak to ferrocene in which the 1-hydroxymethyl group is intact and the 1′-residue is $—CH_2^+$. This cation should be especially stable both because it is an α-ferrocenyl cation and because of possible anchimeric assistance by the hydroxymethyl group. Cleavage of the macroring to leave this fragment is no doubt facilitated by this cation's stability.

The next largest ion (m/z 515), resulting from the fragmentation of **7**, is assigned the structure of protonated mono-*N*-octadecyl-4,13-diaza-18-crown-6. In order to assess complexation, the molecular ion must be observable. Indeed, it is in this case ($[P+H]$ m/z 743), although its intensity (*ca.* 10% relative abundance) is relatively small.

Cation binding by **7** was assessed by the FAB/MS technique for Na^+, K^+, and Ag^+ as described above. Cation binding by both Na^+ and K^+ proved effective although relatively modest, exhibiting

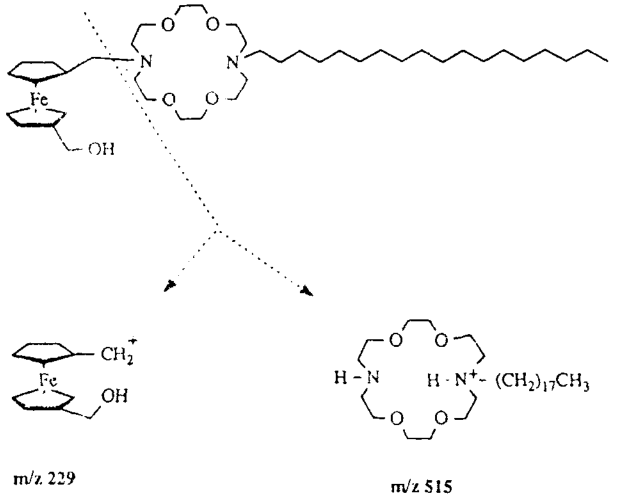


Figure 3 Proposed fragmentation observed for **7**.

[P + M]/[P + H] ratios of 3.3 and 6.2, respectively. The binding of Ag^+ by **7** proved to be much stronger ([P + M]/[P + H] ratio = 17) as shown in the spectrum (Fig. 4). This is expected because the two nitrogen atoms present in the macroring as well as the macroring size are both especially favorable for this cation. There may also be a direct interaction of the ferrocene as noted in the previous study.[10]

It is interesting to note that the fragmentation patterns observed for **7** in the presence of (M = Na^+), K^+, and Ag^+ varied in a surprising but regular way. In each case, a fragment corresponding to m/z 512 + M was observed. Thus, these fragments were observed at m/z 535, 551, and 619 respectively. No m/z 512 peak is observed in the absence of cations and this fragment is clearly unique. When a metallic cation is bound in the macroring of **7**, the CH_2 hydrogen atoms β to nitrogen are acidified. These may be deprotonated by the 1′-hydroxymethyl group acting as a base. Fragmentation to form a macrocyclic Schiff base with loss of 1-methyl-1′-hydroxymethylferrocene (or its alkoxide) could account for the m/z 512 fragment. The ferrocene derivatives, being neutral or anionic would not be detectable in this FAB/MS experiment. Macrocyclic Schiff bases are well known binders for a variety of metal ions.

One particularly unusual observation was the presence of an ion at m/z 843. Such a complex is higher in weight than could be ascribed to any single cation. An isotopic distribution of 3:1 was observed for this ion suggesting the presence of $^{35}Cl/^{37}Cl$. Indeed, the molecular weight corresponds to the formation of a complex $[P + H + H^+ClO_4^-]$. The source of ClO_4^- in this case was $Na^+ClO_4^-$ and perchloric acid might well have resulted from hydration of this anion. Obviously, **7** is well suited to double protonation and may even form an especially favorable structure in which the transannular >N—H groups are bridged by the perchlorate oxygen atoms.

Because compounds **6** and **7** contain a combination of redox center, cation binding site, and hydrophobic tail, we sought to evaluate a portion of the structure which contained only the redox center and hydrophobic tail. Compounds suitable for these "control" studies were available from a previous effort to design monomers for redox-switched vesicle formation.[3b] Thus compounds **10**, **11**, and **12** were studied using the FAB/MS technique.

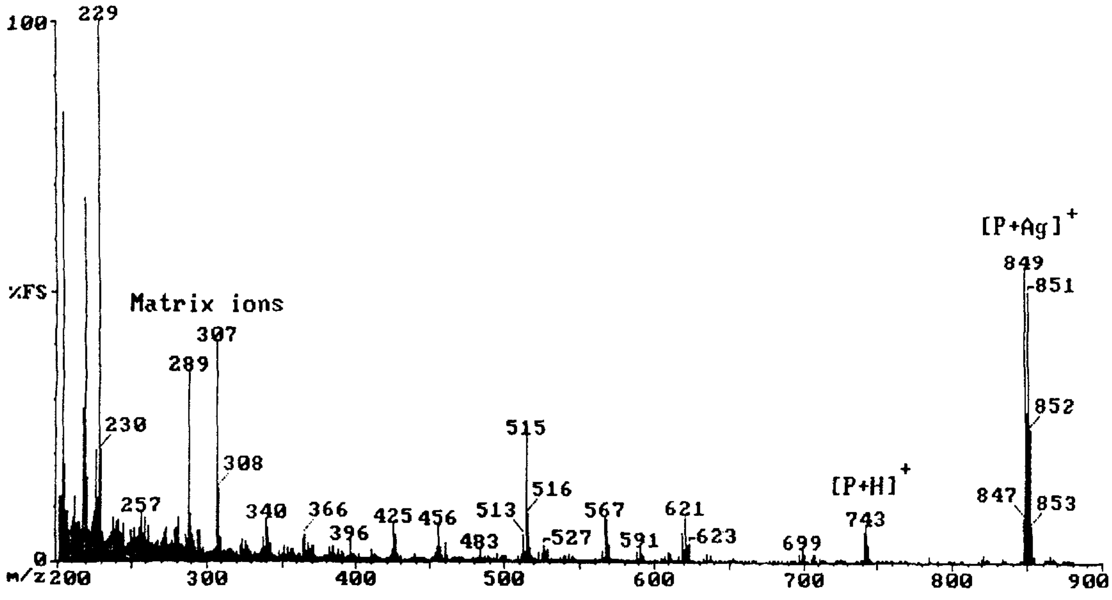
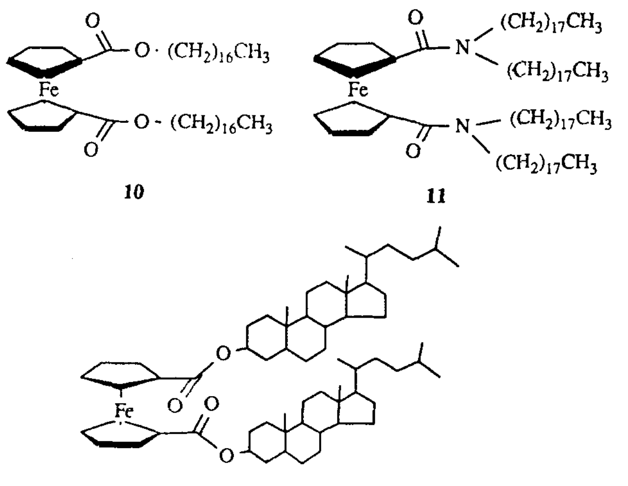


Figure 4 FAB mass spectrum of **7**·Ag^+.



10 11 12

Figure 5 Structures of compounds 10–12.

When surface active compounds are subjected to FAB/MS analysis, the intensity of matrix ions generally diminishes relative to the intensities of analyte ions with increasing surface activity.[11] Indeed, this expectation was realized with compound **9** in which the substituents in the ferrocene 1- and 1′-positions are —CO—O—(CH$_2$)$_{16}$CH$_3$. In the FAB mass spectrum of **10**, the majority of the signal results from the analyte rather than from matrix ions (m/z 289, 307) which are strongly suppressed. The base peak results from the analyte as expected but corresponds to $[P]^+$ rather than the expected $[P + H]^+$ ion (see Fig. 6). It is interesting to note that the second largest ion corresponds to cleavage of both sidearms and the formation of the protonated 1,1′-ferrocenedicarboxylic acid anhydride.

Quite different results from the above and from those anticipated were obtained with compounds **11** and **12**. These substances both have —CO—R sidearms in the 1,1′-positions but **11** is a diamide and **12** is a diester. The R group in **11** is N[(CH$_2$)$_{17}$CH$_3$]$_2$ and in **12** it is 3-oxycholestanyl. In both cases, molecular models suggest that the sidearms overlap or interdigitate if they are both on the same side of the ferrocene as expected for surface activity. This sort of interaction is expected for compounds having either multiple hydrocarbon or steroidal chains in proximity. The observation in the FAB mass spectra of these derivatives is that matrix ions are far greater than expected for an amphiphile, suggesting that the sidearms may be involving themselves intramolecularly rather than intermolecularly as required for surface activity. Thus these latter structures proved not to be effective models for **7** but proved to have an interesting chemistry of their own.

Electrochemical data

The electrochemistry of **7** was evaluated in CH$_3$CN solution containing 0.1 M tetrabutylammonium hexafluorophosphate (TBAP) as supporting electrolyte. The half wave potential for **7** in the solvent system described was found to be 395 mV (*vs.* SSCE) in the

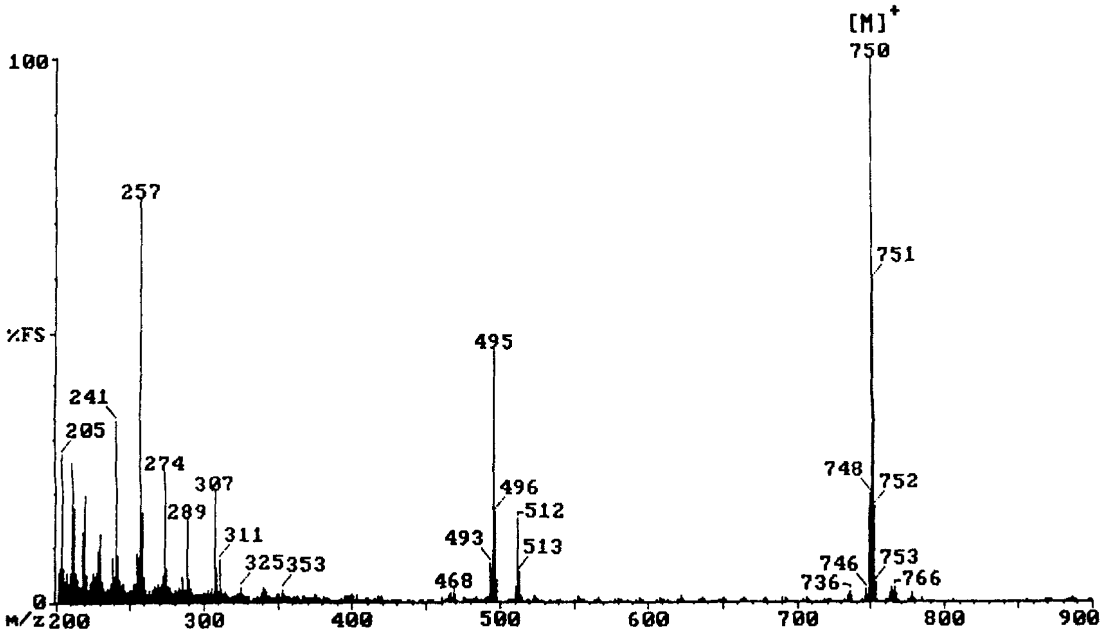


Figure 6 FAB mass spectrum of **9** demonstrating enhanced surface activity as determined by the ratio of analyte ions (m/z 750, 512, 495, and 257) to matrix ions (m/z 307 and 289).

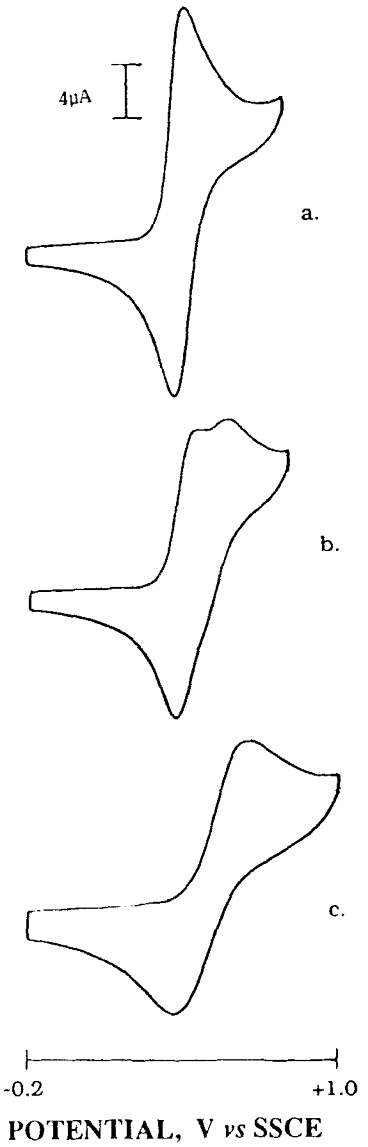


Figure 7 (A) Cyclic voltammetric response of 1.0 mM **7** in acetonitrile containing 0.1 M TBA $^+PF_6^-$ as supporting electrolyte. The working electrode was a glassy carbon disk (geometric area = 0.08 cm^2). (B) Same as in A after the addition of 0.5 mM $AgNO_3$. (C) Same as in A after the addition of 1.0 mM $AgNO_3$. All voltammograms were recorded at a scan rate of 100 mV/s.

absence of any metallic cation (see Fig. 7). This is, as expected, very close to the value known for ferrocene itself (398 mV) in this solvent. The electrochemical behavior was sensitive to the presence of sodium cations. In other studies of redox active ligands investigated in our laboratories, addition of sub-stoichiometric amounts of Na^+ or other metallic cations produced a second redox wave. This is distinguished from the more common behavior that we have dubbed "shifting" in which the observed half-wave potential changes with cation addition but a distinct, new wave does not appear. Compound **7** shows the latter behavior with Na^+. Thus, addition of sub-stoichiometric amounts of Na^+ gives a gradual change in potential. When one equivalent of Na^+ is present, the half-wave potential is observed to be 0.452 V. This increases further to 0.462 V upon addition of 5 equivalents of the cation.

The behavior of compound **7** is somewhat different in the presence of Ag^+. As is apparent from the cyclic voltammograms, a new oxidation wave is observed for $\mathbf{7}\cdot Ag^+$ but this complex is not obvious in the reverse scan. It appears that dissociation occurs after oxidation: $\mathbf{7}^+\cdot Ag^+ \rightarrow \mathbf{7}^+ + Ag^+$. This is consistent up to one equivalent of Ag^+. When a stoichiometric excess of Ag^+ is present, the excess silver is reduced at the initial potential of the experiment and precipitates, complicating the interpretation of the electrochemistry.

Two things distinguish **7** from the hoped-for sensor system. First, the hydroxymethyl group must be converted into a thiomethyl group so that attachment to the electrode surface will be facilitated. The second condition is that when the electrode surface is modified, the behavior of the ligand system may well be altered. Both the binding site and the redox switch (ferrocene) will presumably be embedded in an ordered array of hydrophobic residues and the system may be more or less effective than apparent with the monomer (**7**). The packing properties of the monolayer will be critically important to the success or failure of this approach so **7**, with its octadecyl chain, represents a first attempt to discover how this system will behave overall.

CONCLUSION

We have designed and prepared a novel structure containing a redox active site, a cation binding site, a hydrophobic tail, and an incipient anchor group that will ultimately be further modified. Electrochemical and mass spectral studies reveal that the redox active site and the cation binding site cooperate in the presence of appropriate cations and surface activity has also been confirmed for this structure and close relatives.

ACKNOWLEDGEMENTS

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EXPERIMENTAL SECTION

General information

Melting points were determined using a Thomas-Hoover 6406-k capillary melting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra were recorded in $CDCl_3$ and are reported in PPM (δ) on a Varian VXR 400 High Resolution NMR spectrometer unless otherwise specified. Infrared spectra were recorded on a Perkin-Elmer 599 spectrophotometer as KBr pellets and are reported in cm^{-1} unless otherwise noted. Elemental analyses were performed by Atlantic Microlab, Atlanta, Ga. All chemicals used were purchased from Sigma-Aldrich. Commercial chemicals and solvents were purified by standard methods. 1,1′-Ferrocenedicarboxylic acid, **1**, was purchased from Aldrich Chemical Co. and used without further purification. Reactions were performed under N_2 unless otherwise noted. Chromatography was performed using columns containing aluminum oxide (neutral, 150 mesh). The ratio of solvents used for chromatography are given in volumes. The desorption chemical ionization (DCI) mass spectra were determined by using methane as the reagent gas; results were obtained on a VG Trio-2 instrument.

Preparation of 1-(carboxy)-1′-(carbomethoxy)-ferrocene 2

Method A. Compound **2** was prepared by two different methods. The first was a modification of Arakawa's procedure.[6] A suspension of 1,1′-ferrocenedicarboxylic acid (10 g, 37 mmol) in anhydrous MeOH (4 L) at 0 °C was saturated with anhydrous HCl gas. The mixture was stirred for 8 h at 0 °C. Then, the pH was raised to pH 4 by addition of saturated $NaHCO_3$. The mixture was diluted with water and extracted 3 times with CH_2Cl_2. The organic phases were combined and dried with brine and $MgSO_4$. The solvent was evaporated under reduced pressure and the product chromatographed over silica using 1:20 $MeOH/CH_2Cl_2$ to afford **2** (4.6 g, 44%) as an orange powder, mp 142–143 °C ^1H NMR: 3.83 (s, 3H), 4.47 (s, 4H), 4.89 ppm (s, 4H). IR: 3650 – 2350 (m), 1730 (s), 1680 (m), 1590 (m), 1300 (m) cm^{-1}.

Method B. This method is a modification of Nesmeyanov's procedure.[7] To 1,1′-bis(carbomethoxy)-ferrocene (3.79 g, 12.5 mmol) was added a solution of MeOH (200 mL), H_2O (50 mL) and NaOH (5.0 g). The reaction was allowed to stir at ambient temperature for 6 h, and then acidified to pH 2 with 3*N* HCl. The reaction mixture was then diluted with H_2O and extracted with CH_2Cl_2, the organic phase dried with $MgSO_4$, the solvent evaporated under reduced pressure and the crude product chromatographed over silica using 1:20 $MeOH:CH_2Cl_2$ to afford **2** (1.5 g, 41%) as an orange powder mp 143–145 °C (lit.[2] mp 147–148 °C). Spectral data matched those reported in the literature.[7]

Preparation of 1-(chlorocarbonyl)-1′-(carbomethoxy)-ferrocene 3

To a mixture of 1-(carboxy)-1′-(carbomethoxy)-ferrocene **2** (1 g, 3.5 mmol), CH_2Cl_2 (10 mL) and a catalytic amount of pyridine (50 mg) was added 8 mL of oxalyl chloride. The reaction was allowed to stir at ambient temperature for 4 h. The solvent mixture was then evaporated to dryness under reduced pressure, the dark solid residue was dissolved in anhydrous Et_2O (50 mL), the mixture was filtered through a glass wool plug and the solvent evaporated to afford **3** as a dark red solid (878 mg, 82%) that was used without further purification. Mp 76–81 °C. ^1H-NMR: 4.92 (s, 4H), 4.58 (s, 4H), 3.85 (s, 3H) ppm.

Preparation of *N*(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane)octadecane 5

Preparation of *N*-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane)octadecane, **5**, was accomplished in one step from the starting material 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, **4**, as opposed to the four step synthesis previously reported.[12] 1,4,10,13-Tetraoxa-7,16,diazacyclooctadecane **4** (2.50 g, 9.5 mmol), 1-bromooctadecane (2.54 g, 7.6 mmol), K_2CO_3 (17.5 g, 127 mmol) and potassium iodide (50 mg, 0.3 mmol) were suspended in 75 mL of *n*-BuCN. The reaction was set to reflux for 12 h, then the reaction was filtered, diluted with H_2O and extracted 2x with CH_2Cl_2. The organic layer was dried with brine and $MgSO_4$, the solvent was evaporated under reduced pressure and the residue chromatographed over alumina with 0.5% $MeOH/CH_2Cl_2$, further purification by recrystallization from EtOH/hexane to afford 1.5 g of product (38%). Mp 54.5–55.0 °C. ^1H-NMR: 0.88 (t, J = 6.5 Hz, 3H), 1.25 (bs, 30H), 1.44 (bs, 2H), 2.49 (t, J = 7.6 Hz, 2H), 2.79 (m, 8H), 3.61 (bs, 16H) ppm. *Anal.* calcd. for $C_{30}H_{62}N_2O_4$: C, 69.99; H, 12.14%. Found: C, 69.74; H, 12.09%.

Preparation of 1-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7-octadecane-16-carbonyl)-1′-carbomethoxy-ferrocene 6

To *N*-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane)-octadecane, **5**, (1.4 g, 2.7 mmol) with Et_3N (3 mL, 22 mmol) in CH_2Cl_2 (60 mL) was added a solution of 1-(chlorocarbonyl)-1′-(carbomethoxy)ferrocene **3** (833 mg, 2.7 mmol) in CH_2Cl_2 (25 mL). The reaction was stirred for 3 h, then quenched with H_2O and extracted with CH_2Cl_2. The organic layer was dried with brine, the solvent evaporated and the residue chromatographed over alumina with 0.5% $MeOH/CH_2Cl_2$ to afford the product as a yellow-orange solid in 891 mg (42% yield). Mp 48–51 °C.

^{1}H-NMR: 0.88 (t, J = 6 Hz, 3H), 1.25 (bs, 30H), 1.74 (bs, 2H), 2.52 (bs, 2H), 2.82 (bs, 4H), 3.63 (bs, 16H), 3.71 (bs, 4H), 3.81 (s, 3H), 4.32 (s, 2H), 4.47 (s, 2H), 4.66 (s, 2H), 4.85 (s, 2H) ppm. IR (KBr) 2920 (s), 1710 (m), 1598 (m), 1385 (m), 1130 (s) cm^{-1}. *Anal.* calcd. for $C_{43}H_{72}N_2O_7Fe$: C, 65.80; H, 9.25%. Found: C, 65.77; H, 9.23%.

Preparation of 1-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7-octadecane-16-methyl)-1′-methylhydroxyferrocene 7

To 1-(1,4,10,13-tetraoxa-7,16-diazacyclooctadecane-7-octadecane-16-carbonyl)-1′-carbomethoxyferrocene (2.3 g, 2.9 mmol) in THF (25 mL) was added in portions $LiAlH_4$ (500 mg, 13 mmol). The reaction was stirred for 12 h, quenched by dropwise addition of H_2O, diluted with CH_2Cl_2 and washed with saturated potassium sodium tartate solution, H_2O, and the organic layer was dried with $MgSO_4$. The solvent was evaporated and the residue chromatographed over alumina using 2% 2-propanol/hexane (v/v) to afford 903 mg (42% yield) of the product as a yellowish wax. Mp 39–42 °C. ^{1}H NMR: 0.88 (t, J = 6.7 Hz, 3H), 1.25 (bs, 30H), 1.44 (bs, 2H), 2.50 (t, J = 7.2 Hz, 2H), 2.78 (m, 8H), 3.61 (m, 20H), 4.11 (s, 2H), 4.16 (m, 4H), 4.34 ppm (s, 2H). IR (KBr) 3360 (s), 2920 (s) 1460 (m), 1350 (m), 1105 (s) cm^{-1}. DCI (CH_4): m/z (relative intensity) 743 (<1, M + H$^+$), 742 (1, M$^+$), 516 (10), 229 (100). *Anal.* calcd. for $C_{42}H_{74}N_2O_5Fe$: C, 67.90; H, 10.04; N, 3.77%. Found: C, 67.70; H, 10.14; N, 3.71%.

Preparation of 1,1′-bis(chlorocarbonyl)ferrocene, 9

Was accomplished by a modification of the procedure by Petrovitch.[13] To 0.930 mg (4 mmol) of 1,1′-ferrocenedicarboxylic acid at ambient temperature were added 10 mL (0.114 mol) of oxalyl chloride followed by a catalytic amount of pyridine (0.1 mL). The reaction was then set to gently reflux in the dark for a period of 6 h (the reaction turned from a heterogeneous mixture to a dark red homogeneous solution). After 6 h of reflux the solution was allowed to cool to room temperature and the excess oxalyl chloride was evaporated under reduced pressure, the remaining residue was then washed with 500 mL of anhydrous Et_2O, the solvent was evaporated to afford 648 mg (52%) of a red solid mp 92–94 °C which was used without further purification. ^{1}H-NMR: 4.5 (4H, bs), 4.75 ppm. (4H, bs). The melting point, 92–94 °C, matched the literature value.[13]

Preparation of ferrocenyl 1,1′-carboxyheptadecanoate, 10

To 620 mg (2 mmol) of 1,1′-bis(chlorocarbonyl)-ferrocene in 15 mL of benzene, at ambient temperature was added a suspension of heptadecanol (1.024 g, 4 mmol) and Et_3N (404 mg, 4 mmol) in 10 mL of benzene followed by addition of 50 mg of 4-DMAP. The reaction was then set to reflux for a period of 5 h. The solvent was then evaporated and the remaining solid suspended in CH_2Cl_2 and chromatographed on silica 1:20 EtOAc/hexanes. The product was isolated and recrystallized from acetone to afford 1,031 mg for a 69% yield. Mp 65–67 °C. ^{13}C NMR: 170.509, 76.694, 73.099, 72.803, 72.803, 71.430, 71.430, 64.625, 31.930, 29.708, 29.708, 29.708, 29.708, 29.708, 29.677, 29.677, 29.639, 29.617, 29.374, 29.344, 28.858, 26.059, 22.698, 14.134 ppm. ^{1}H-NMR: 0.88 (t, J = 6.4 Hz, 6H), 1.15–1.60 (m, 56H), 1.72 (quintet, 4H), 4.21 (t, J = 6.7 Hz, 4H), 4.40 (s, 4H), 4.82 ppm (d, J = 1.6 Hz, 4H). IR (KBr) 2880 (m.), 1715 (bs.), 1280 (d.), 1160 (d) cm^{-1}. *Anal.* calcd. for $C_{46}H_{78}O_4Fe$: C, 73.57; H, 10.47%. Found: C, 73.52; H, 10.52%.

Preparation of ferrocenyl 1,1′-carboxydihydrocholesterate, 12

To 620 mg (2 mmol) of 1,1′-bis(chlorocarbonyl)-ferrocene in 20 mL of benzene at ambient temperature was added dropwise a solution of dihydrochlesterol (1.55 g, 4 mmol), 50 mg of 4-dimethylaminopyridine (DMAP) and (404 mg, 4 mmol) of Et_3N in 10 mL of benzene. The reaction was then allowed to reflux for 48 h. The solvent was then evaporated under reduced pressure, the residue dissolved in CH_2Cl_2 and chromatographed over silica using 1:20 EtOAc/hexanes. Further recrystallization from CH_2Cl_2/Et_2O afforded 668 mg of product for a 27% yield. Mp 287–291 °C, $[\alpha]_D = +24.4$ (C = 1, CH_2Cl_2). ^{13}C-NMR: 170.028, 127.525, 73.749, 73.377, 72.944, 72.944, 71.473, 71.367, 56.453, 56.309, 54.298, 44.793, 42.616, 40.022, 39.521, 36.843, 36.183, 35.812, 35.546, 35.523, 34.317, 32.034, 28.711, 28.249, 28.006, 27.786, 24.220, 23.856, 22.802, 22.552, 21.247, 18.675, 12.356, 12.098 ppm. ^{1}H-NMR ($CDCl_3$) 0.52–2.1 (steroidal, 92H), 4.36 (d, J = 1.6 Hz, 4H), 4.79 (d, J = 2 Hz, 4H), 4.85 (m, 2H) ppm. IR (KBr) 2960 (bs.), 2880 (d.), 1715 (s.), 1470 (bs.), 1290 (s.), 1160 (s.) cm^{-1}. *Anal.* calcd. for $C_{66}H_{102}O_4Fe$: C, 78.07; H, 10.12%. Found: C, 77.99; H, 10.13%.

Preparation of *N*,*N*-bis(octadecyl)ferrocene-1,1′-dicarboxamide, 11

To 620 mg (2 mmol) of 1,1′-bis(chlorocarbonyl)-ferrocene in 20 mL of benzene at ambient temperature was added a suspension of *N*,*N*-dioctadecylamine (1.93 g, 4 mmol) and Et_3N (404 mg, 4 mmol) in 10 mL of benzene. The reaction was then allowed to stir at ambient temperature for 3.5 h. After 3.5 h of stirring, the solvent was evaporated and the crude chromatograped over silica using 1:20 EtOAc/hexanes and recrystallized from a mixture of acetone and Et_2O to afford 1.972 g of product for a 77% yield. Mp 32–34 °C. ^{13}C-NMR: 169.226, 80.934, 71.687, 71.687, 71.459, 71.459, 31.945, 31.945, 31.945, 31.945, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.730, 29.684, 29.684, 29.684, 29.684, 29.648, 29.648, 29.684, 29.684, 29.388, 29.388, 29.388, 29.388, 22.780, 22.780, 14.141, 14.141 ppm. ^{1}H-NMR: 0.88 (t, J = 7 Hz, 12H), 1.05–1.43 (120H), 1.50–1.65 (bs, 8H), 3.35 (t, J = 7.8 Hz, 8H), 4.36 (s, 4H), 4.60 (s, 4H) ppm. IR: 2800 (m), 1660 (s), 1460 (m), 1370 (bs) cm^{-1}. *Anal.* calcd. for $C_{84}H_{156}N_2O_2Fe$: C, 78.70; H, 12.26%. Found: C, 78.60; H, 12.25%.

Electrochemistry

Acetonitrile was HPLC quality from EM Science. Tetrabutylammonium hexafluorophosphate was purchased from Fluka and used without further purification. All other salts were of the best quality commercially available.

Equipment. The electrochemical experiments were performed with a Princeton Applied Research Model 173/175/179 set-up and the current-potential traces were recorded in a Soltec VP-6423S X-Y recorder. The rotating disk electrode voltammograms were obtained using a Pine Model ASR Analytical Rotator Assembly.

Electrochemical experiments. Cyclic voltammetric data were recorded using a glassy carbon working electrode ($0.082\,cm^2$), a platinum counterelectrode, and a sodium saturated calomel half-cell as the reference electrode. Glassy carbon electrode surfaces were polished with 0.05 micrometer alumina, sonicated in water, and air-dried immediately before use. The acetonitrile solution (containing 0.1 M $TBA^+PF_6^-$, as supporting electrolyte, 1.0 mM of the ligand, and variable concentrations of metal salts) was placed in a single-compartment electrochemical cell and degassed by bubbling with $N_2(g)$ saturated with acetonitrile. A N_2 atmosphere was continuously maintained above the solution while the experiments were in progress.

Fast atom bombardment mass spectrometry

Fast atom bombardment spectra were acquired on a VG Trio 2 quadrupole mass spectrometer equipped with the Lab-Base data system. An 6.5 kV xenon atom beam was used to desorb samples from the 3-nitrobenzyl alcohol FAB matrix. In a typical experiment, one μL of matrix, one μL of a 6 mM macrocycle solution (CH_3CN), and one μL of a 10 mM cation (as the perchlorate) solution (CH_3CN) were carefully mixed on the FAB probe. Typically 10 scans were combined to produce the spectra used for intensity ratios. Binding trends were assessed from the ratio of [macrocycle•cation] complex to protonated macrocycle. The data for sodium binding resulted from single determinations, however the silver data are the average of a minimum of three separate assays.

NOTES AND REFERENCES

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