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Electrochemical and binding properties of a novel ferrocene-containing redox-active basket-shaped host molecule

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A novel basket-shaped host based on the rigid molecule diphenylglycoluril {3a,6a-diphenyltetrahydroimidazo-[4,5-*d*]imidazole-2,5(1*H*,3*H*)-dione} has been synthesized and characterised. It is able to bind cations in its crown ether rings and neutral organic substrates in its cavity. Differential pulse voltammetry experiments showed that the host is redox-responsive to cations. It forms 1 : 1 complexes with K^+ and NH_4^+ ions and 1 : 2 host–guest complexes with Na^+ ions. On addition of (di)ammonium salts, protonation of the host occurs. A complex was formed between the host and model substrate olivetol (5-pentylbenzene-1,3-diol). In the absence of additives, this complex is stabilised *via* hydrogen bonds and π–π stacking interactions. In the presence of Na^+ ions a complex consisting of the host, the diol, and 2 Na^+ ions was formed, in which hydrogen bonds are no longer present. In the presence of 2 Na^+ ions a four-fold increase in association constant has been found. Spectroscopic (NMR and IR) experiments have been used to elucidate the mode of co-operative co-ordination between the host, diol substrate and Na^+ ions.

Supramolecular chemistry has undergone a tremendous growth in the last three decades. After the early work of Pedersen,[1] Cram[2–4] and Lehn[5,6] and co-workers macrocyclic crown ether rings have been applied as building blocks to construct large molecular systems with specific properties.[7] Supramolecular chemistry has led to new applications, one of which is the development of ion-selective sensors.[8] Combinations of redox reactive centres and crown ethers have been used to design these chemical sensors. The first examples of redox-responsive molecules were (aza)crown ethers linked to a ferrocene or nitrobenzene unit.[9,10] These molecules showed different redox behaviour in the presence of positively charged molecules. Recently more elegant responsive compounds have been developed, containing a ferrocene or tetrathiafulvalene unit as the redox-active centre.[11–13] In general, these compounds exhibit a low response towards ammonium cations; only the triaza-crown-6 based sensors developed by Beer *et al.*[14] are very responsive to NH_4^+ ions. Sensors responsive to alkyl-substituted ammonium cations, however, have yet to be reported.

This paper describes the synthesis and properties of a new redox-active metallohost based on diphenylglycoluril {3a,6a-diphenyltetrahydroimidazo[4,5-*d*]imidazole-2,5-(1*H*,3*H*)-dione}, to which a ferrocene unit has been connected. Host molecules derived from diphenylglycoluril are capable of binding organic substrates like dihydroxybenzenes and hard cations like Na^+ or K^+. Other molecules that form complexes with these host molecules are substituted ammonium salts. Hydrogen bonds between the urea carbonyl groups of the host molecule and π–π stacking interactions between the aromatic walls of the host and the aromatic ring of the guest molecule contribute to the process of binding. The alkali metal ions are bound to the crown ether parts of the host molecule, whereas neutral molecules are clammed between the aromatic walls.

In this paper we present electrochemical studies and a study towards the binding of different guest molecules in the host. Cyclic voltammetry, differential pulse voltammetry, IR and NMR measurements were used to elucidate the nature of the host–guest binding processes taking place. A novel Na^+-promoted host–guest complex is presented as well.

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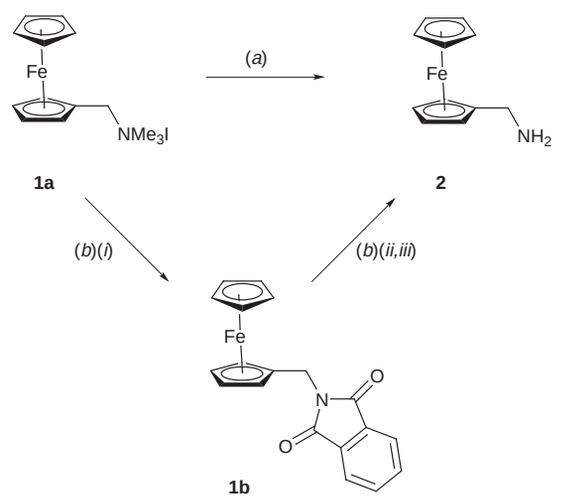
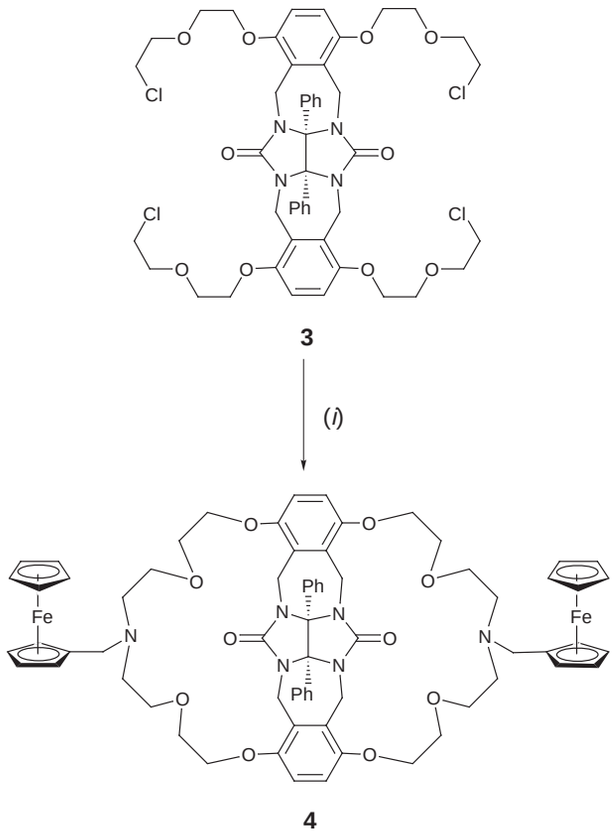


Scheme 1 Synthesis of compound **2**: (*a*) NH_3–MeOH, 80 °C, 24 h; (*b*) (*i*) potassium phthalimide, dmf, 90 °C; (*ii*) N_2H_4–EtOH; (*iii*) 10% HCl, 100 °C 1 h

Results and Discussion

Synthesis

The most frequently used method to produce tertiary amino-methylferrocene derivatives is the reaction of a primary amine with either chlorocarbonylferrocene,[11,13–15] ferrocenylmethyl-pyridinium toluene-*p*-sulfonate[16,17] or trimethylammonio-methylferrocene iodide **1a** (Scheme 1).[14,18] This method could not be applied to the synthesis of our target molecule because the preparation of the unprotected amine (**4b**) from the benzyl analogue (**4a**)[19] turned out to be rather troublesome and difficult to reproduce. Therefore a different reaction procedure for the synthesis of substituted aminomethylferrocenes was



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4

Scheme 2 Synthesis of compound **4**: (*i*) NaI–MeCN, 24 h reflux then **2**, 3 d reflux

developed. First aminomethylferrocene **2** was synthesized, which was then made to react with **3** to afford host **4** (Scheme 2).

Trimethylammoniomethylferrocene iodide[20] **1a** was used as the starting compound in the production of aminomethylferrocene. Two routes towards the desired product **2** were investigated: (*a*) direct conversion of **1a** into the amine by reaction with ammonia and (*b*) a classical Gabriel[21] synthesis using potassium phthalimide and subsequently hydrazine (see Scheme 1). To avoid the use of hazardous azidomethylferrocene, this method was not used.[22]

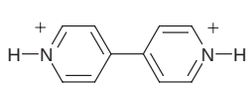
Route (*a*). Several conditions were investigated to convert trimethylammoniomethylferrocene iodide **1a** into aminomethylferrocene **2** in one step. Only the reaction of **1a** with NH_3 in MeOH at temperatures between 70 and 80 °C afforded **2** in acceptable yields (60% at 80 °C). This reaction was performed in an autoclave to prevent evaporation of NH_3. Reactions of **1a** performed at lower temperatures gave low conversions and in liquid NH_3 no reaction occurred. Lower yields were also obtained when the reaction was conducted at temperatures higher than 80 °C because undefined side products were formed. At the optimum temperature this route proved to be a very smooth one-step synthesis towards aminomethylferrocene and is preferred to the Gabriel synthesis or the method employing hazardous azides.

Route (*b*). Trimethylammoniomethylferrocene iodide was made to react under standard conditions with potassium phthalimide yielding 66% of 1-(phthalimidomethyl)ferrocene **1b** (lit.,[21] 99%). After isolation and reaction with hydrazine, aminomethylferrocene was obtained in 63% yield. The overall yield for the conversion of **1** into **2** was 42%. Routes (*a*) and (*b*) result in the formation of the desired product **2** according to ^1H, ^{13}C NMR and GC-MS measurements. Compound **2** is relatively stable, but it is recommended to use it in further reactions shortly after isolation. When stored over longer periods, decomposition occurs and the product liquefies with formation of volatile amines and cyclopentadiene.

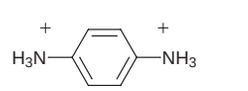
The final reaction in the synthesis of target molecule **4** consisted of a ring closure under high dilution conditions. This procedure was developed and optimised previously by Nolte and co-workers.[23,24] Compound **3** was converted *in situ* into its iodide analogue *via* a Finkelstein[25] reaction. When all the chlorine atoms had been replaced, amine **2** was slowly added allowing the ring closure reaction to take place. After standard work-up and column chromatography to remove side products, compound **4** was isolated in 45% yield. The product could be purified by column chromatography using silica gel and TLC plates impregnated with NaBr.[26]

Electrochemical experiments

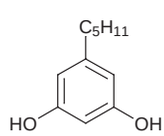
The electrochemical properties of compound **4** were studied using cyclic voltammetry (CV) and differential pulse voltammetry (DPV). Solvent mixtures of acetonitrile and dichloromethane were used in combination with $NBu^n_4PF_6$ as the electrolyte. Ferrocene could not be used as the internal reference in our experiments because of interference with the oxidation of compound **4**. The salt $[Co(\eta^5\text{-}C_5H_5)_2]PF_6$ was therefore used as the internal reference.[16] In separate experiments, the reference potential $E_{\frac{1}{2}}\{[Co(\eta^5\text{-}C_5H_5)_2]^{+/0}\}$ was determined to be −1.33 V *vs.* ferrocene–ferrocenium. Owing to the high molecular weight and thus small diffusion coefficient of compound **4**, only current responses of moderate intensity could be observed in the CV experiments. After additions of cations the anodic peaks became broad and new signals arose leading to a drop in current intensity, which made the exact determination of $E_{\frac{1}{2}}$ values from CV measurements difficult. Cyclic voltammetry was therefore only used to check the chemical reversibility of the processes and DPV was chosen to determine the exact values of $E_{\frac{1}{2}}$. The cationic guest molecules used in these experiments are only soluble in MeCN whereas compound **4** is hardly soluble in this solvent, therefore CH_2Cl_2 was added to obtain a homogeneous solution. In all experiments oxidation of a species adsorbed at the surface of the electrode was observed at 275 mV (*vs.* ferrocene–ferrocenium). At high cation concentrations this species disappeared, probably due to strong complexation to **4**.



5 • 2 BF_4^-



6 • 2 $CF_3SO_3^-$



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The DPV responses were recorded after progressively adding aliquots of stock solutions in MeCN containing substoichiometric equivalents of Na^+, K^+, NH_4^+, 4,4′-bipyridinium bis(tetrafluoroborate) **5** and 1,4-phenylenediammonium bis(trifluoromethanesulfonate) **6**. In the absence of additives a single anodic peak was observed for **4**. This implies that both ferrocene moieties are oxidised in one step. As compared to ferrocene itself, the oxidation of **4** is shifted to a slightly more negative value ($E_{\frac{1}{2}}$ = 30 mV *vs.* ferrocene–ferrocenium), which is in agreement with previous observations on multiple-ferrocene-containing crown ethers.[14] Significant anodic perturbations could be observed after addition of any of the cationic species mentioned above; the data obtained are summarised in Table 1. Ammonium cations possess the most pronounced influence

Table 1 Cation-dependent oxidation potentials of compound **4**[a]

	$\Delta E_{\frac{1}{2}}$/mV				
$E_{\frac{1}{2}}$[b]/mV	2 Na^+	1 K^+	1 NH_4^+	1 ($\mathbf{5}^{2+}$)	0.3 ($\mathbf{6}^{2+}$)
−30[c,d]	88[c]	64[c]	106,[c] 220[e]	232[d]	240[d]

[a] Obtained from DPV measurements using a 10^{-3} M solution of compound **4**; Na^+, K^+ and NH_4^+ were added as their trifluoromethanesulfonate salts. [b] *vs.* Ferrocene–ferrocenium. [c] Measured in CH_2Cl_2–MeCN (1:1, v/v). [d] Measured in CH_2Cl_2–MeCN (3:1, v/v). [e] After addition of 3.5 equivalents of NH_4^+.

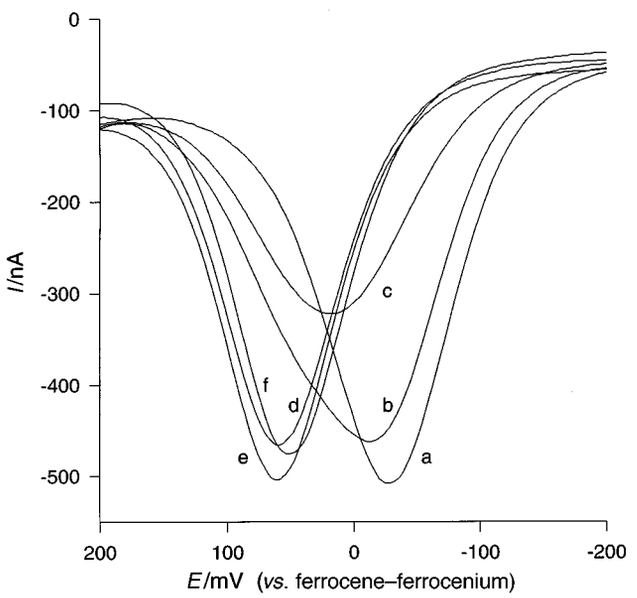


Fig. 1 The DPV responses of a titration of compound **4** with Na^+ ions, producing **4**·2Na^+; platinum disc (1 mm^2 apparent surface area) in CH_2Cl_2–MeCN (3:1, v/v), [**4**] = 10^{-3} M, [$NBu^n_4PF_6$] = 2×10^{-1} M, $\nu = 10$ mV s^{-1}, 293 K. Complex **4** plus a 0, b 0.5, c 1.0, d 1.5, e 2.0 and f 2.5 equivalents of Na^+ ions

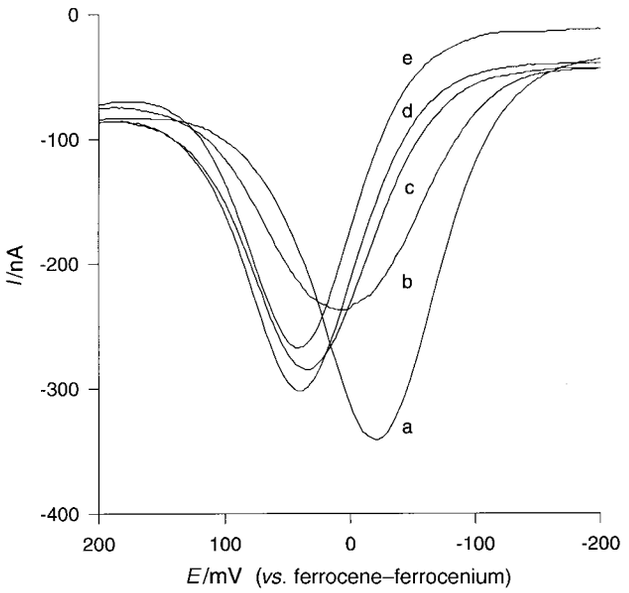
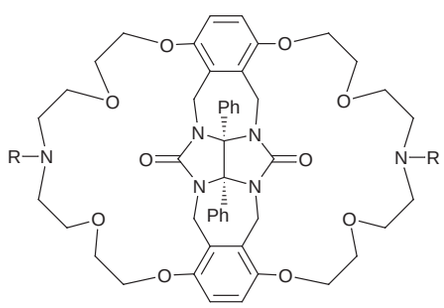


Fig. 2 The DPV responses of a titration of compound **4** with K^+ ions, producing **4**·K^+. Conditions as in Fig. 1. Complex **4** plus a 0, b 0.5, c 1.0, d 1.5 and e 2.5 equivalents of K^+ ions



4a, R = CH_2Ph
4b, R = H

on the oxidation potential of compound **4**, followed by sodium and potassium cations. The addition of ammonium ions resulted in separate DPV responses for **4** and **4**·NH_4^+, respectively. After the addition of 1 equivalent of NH_4^+ ions the response of the free host had disappeared. The addition of sodium and potassium ions resulted in a continuously shifting DPV response to the final $E_{\frac{1}{2}}$ value of the host–guest complexes, as can be seen from Figs. 1 and 2, respectively.

The difference between Na^+ ($\Delta E_{\frac{1}{2}} = 88$ mV) and K^+ ($\Delta E_{\frac{1}{2}} = 64$ mV) might be caused by the higher polarisability[13] of the latter cation, which causes a smaller anodic shift of the oxidation potential. Another explanation might be that K^+ forms a 1:1 complex with **4** whereas Na^+ affords a 1:2 host–guest complex, *i.e.* a species with a higher positive charge per ferrocenyl.[19,27,28] The larger positive shift caused by addition of NH_4^+ ions ($\Delta E_{\frac{1}{2}} = 106$ mV) is probably caused by a stronger interaction between the nitrogen atom of the aminomethylferrocene residue and NH_4^+ ions compared to Na^+ and K^+. The experiments were also performed using an excess of 5 equivalents of cation, resulting in unaffected oxidation potentials for the Na^+- and K^+-containing complexes. This confirms a very strong preference for the formation of a 1:1 complex of **4** with K^+ ions and the formation of a 1:2 host–guest complex with Na^+ ions. Addition of 4 equivalents or more of NH_4^+ ions, however, resulted in an additional anodic peak at a more positive oxidation potential ($\Delta E_{\frac{1}{2}} = 220$ mV). This is probably caused by protonation of part of the aminomethylferrocene nitrogen atoms (see below). The stoichiometries found for Na^+, K^+ and NH_4^+ are in good agreement with values obtained from picrate extraction experiments by Smeets *et al.*[19,27,28] These experiments were performed using **4a**, which has the same properties as those of **4** with regard to binding guest molecules.

Addition of ammonium salt **5** or **6** to host **4** resulted in the formation of an additional DPV response at a more anodic potential of $E_{\frac{1}{2}} \approx 200$ mV. Titration of **4** with the respective ammonium salts resulted in a gradual decrease of the parent signal whereas the signal of the host–guest complexes increased. The stoichiometry at which the original signal had disappeared differed for these two molecules. Beforehand it was expected that these dications (**5** and **6**) would give rise to a 1:1 adduct stoichiometry with **4**, and this indeed was found after titration of **4** with 1 equivalent of **5**. When **6** was used, however, a host–guest stoichiometry of 1:0.25 was observed. This difference in stoichiometry is not fully understood and is currently under investigation. The nearly identical oxidation potentials after addition of these two substrates indicate that the same product is formed after the addition of either **5** or **6**. This could be confirmed by NMR and IR experiments as is described below. The electrochemical experiments, as well as the NMR and IR data, suggest that after addition of either NH_4^+ ions, **5** or **6** protonation of the aminomethylferrocene nitrogen takes place. Plenio *et al.*[16] reported an anodic shift of $\Delta E_{\frac{1}{2}} = 250$ mV after protonation of one of the nitrogen atoms in a ferrocene-containing cryptand [based on 1,1′-bis(methylene)ferrocene and 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane, which is in good agreement with our findings.

A competition experiment between Na^+ ions and compound **5** was also performed (see Fig. 3). As can clearly be seen, after

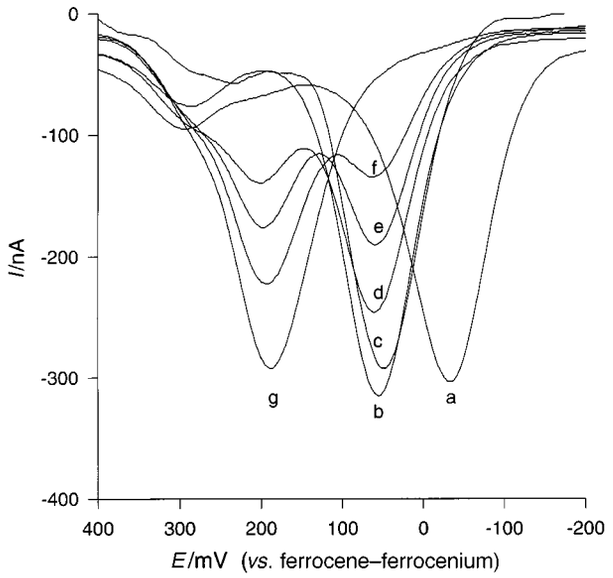


Fig. 3 The DPV responses of 10^{-3} M solutions of compound **4** and its complex with 2 equivalents of Na^+ and the response to subsequent additions of various amounts of **5**, producing **4·5**. Platinum disc (1 mm^2 apparent surface area) in CH_2Cl_2–MeCN (3:1, v/v), $[NBu^n_4PF_6] = 2 \times 10^{-1}$ M, $\nu = 10$ mV s^{-1}, 293 K. Complex **4** plus a 0 and b 2 equivalents of Na^+ ions; **4**·2Na^+ plus c 0.25, d 0.5, e 0.75, f 1.0 and g 1.25 equivalents of **5**

addition of 2 equivalents of Na^+ ions the oxidation potential of **4** shifts to a more positive value of $E_{\frac{1}{2}} = 54$ mV. After addition of 0.25 equivalent of **5** to this host–guest complex **4**·2Na^+ a new peak at $E_{\frac{1}{2}} = 200$ mV appears. This new signal grows on addition of more equivalents of **5** whereas a decrease in intensity of the original signal of **4**·2Na^+ is observed. After the addition of 1.25 equivalents of **5** the original signal has completely vanished. The $E_{\frac{1}{2}}$ value of the final product is in agreement with that found for the complex **4·5**, an indication that the Na^+ ions are not bound to **4** after protonation of the nitrogen atoms. When the order of addition was reversed, *i.e.* first substoichiometric amounts of **5** were added to **4** followed by the addition of Na^+ ions, the DPV response of the host–guest complex **4·5** was observed only.

Recently, Carr *et al.*[29] reported a sensor for neutral molecules. This ferrocene-containing molecule was responsive to the addition of carboxylic acids. We also investigated the influence of neutral guest molecules on the oxidation potential of host **4**. Substituted resorcinol derivatives were added to solutions containing **4**, but no effect could be detected. Resorcinol derivatives were also added to the preformed host–guest complex **4**·2Na^+, but the $E_{\frac{1}{2}}$ values remained unaffected. These experiments indicate that resorcinol derivatives do not influence the oxidation potential of host **4**.

Complexation of guest molecules in solution

Compounds **4a** and **4b** are able to bind hydroxy-substituted aromatic guest molecules and cations.[27,28] A particularly suitable guest molecule is olivetol (5-pentylbenzene-1,3-diol) **7**, because it is well soluble in organic solvents like CH_2Cl_2 and $CHCl_3$. It can easily be used in the determination of association constants (K) *via* NMR titration, which is the most often applied technique nowadays to determine such constants of host–guest complexes. The NMR titrations were carried out by monitoring the signals of both the host and the guest molecule. The method developed by Granot[30] was applied, and after curve fitting of the NMR data the association constants were obtained. Compound **4** was found to bind olivetol with an association constant of $K = 1724$ M^{-1} which is comparable with literature values of similar compounds.[31] The association constant was also determined in the presence of 10 equivalents of Na^+ ions (added as 4-dodecylbenzenesulfonate). As shown above, host **4** forms a complex in which 2 Na^+ ions are bound in its crown ether moieties. Interestingly, this experiment afforded an association constant which was approximately 4 times higher ($K = 7897$ M^{-1}) than that obtained from the experiment without Na^+ ions present. This is in contrast to the expectation that binding of organic molecules would be blocked when cations are bound in the host, as suggested by Coolen *et al.*[32]

Table 2 Association constants and IR shift data of host–guest complexes of compound **4**

Guest	K^a/M^{-1}	CIS/ppm	$\Delta\nu$(C=O)[b]/ cm^{-1}
7	1724 (35)	−0.51	−23
7 + 10 equivalents Na^+ [c]	7897 (1650)	−0.36	−2
7 + 5 equivalents **8** [d]	—	—	−27
5 equivalents **8**	—	—	−26
5-Cyanoresorcinol	n.d.[e]	n.d.[e]	n.d.[f]

[a] Obtained from NMR titrations using (0.5–0.75) × 10^{-3} M solutions of host and a (5–7.5) × 10^{-3} M solution of guest in $CDCl_3$. Association constants were calculated using the Granot[30] procedure; errors are given in parentheses. [b] Measured in CH_2Cl_2 solution; cell optical path 0.5 mm; $c = 1.5 \times 10^{-3}$ M, host : guest mole ratio 1 : 8. [c] Sodium dodecylbenzenesulfonate was used as the co-guest. [d] The NMR signals of compounds **4** and **7** remained unaffected on the addition of benzyldimethylammonium tetrafluoroborate **8**. [e] Not determined; K is estimated to be 1×10^5 M^{-1} based on a literature value of a similar compound.[31] [f] Not determined.

A comparison of the chemically induced shift (CIS) values obtained from the NMR titration experiments revealed that those (−0.36 ppm) of the protons of the aromatic sidewalls of compound **4** in the presence of Na^+ are much lower than those without Na^+ (−0.51 ppm) present, suggesting that the olivetol molecule is bound less deeply[33] in the cavity of **4**. Although the NMR data clearly showed that a different association process takes place between **4** and **7** in the presence of Na^+ ions, they did not reveal what type of interactions are involved between host and guest. Therefore IR experiments were performed in order to monitor the stretching vibration of the urea carbonyl groups of the host molecule. Several combinations of host, guest and Na^+ ions were studied and the values obtained are summarised in Table 2. When host **4** was measured without additives ν(C=O) was located at 1708 cm^{-1}. When 8 equivalents of olivetol were added to **4** a shift of ν(C=O) to 1685 cm^{-1} was observed. This shift of −23 cm^{-1} points to the formation of hydrogen bonds[33] between the carbonyl groups of **4** and the hydroxyl groups of the olivetol molecule. On the other hand a solution containing **4** and 10 equivalents of Na^+ afforded an IR spectrum in which ν(C=O) was similar to that of **4** without additives. The same unchanged carbonyl stretching frequency was found when the IR spectrum of a solution containing **4**, 8 equivalents of olivetol **7** and 10 equivalents of Na^+ was recorded. These results indicate that the hydroxyl groups of olivetol are not involved in hydrogen bonding with the carbonyl groups of the host when Na^+ ions are present, thus demonstrating a different type of binding between **4** and this guest in the presence of Na^+ ions.

Based on NMR and IR data we propose that the Na^+ ions partly block the entrance to the lower part of the cavity of compound **4**, making hydrogen bonding with the carbonyl groups impossible. However, the two-electron-poor alkali-metal cations are readily available for an interaction with the oxygen atoms of the incoming olivetol molecule, allowing them to be six-co-ordinated by these donor atoms, *viz*. four oxygen atoms and one nitrogen atom of **4** and one oxygen atom of olivetol. A computer-generated drawing (Cache molecular modelling program[34,35] using extended MM2 force field parameters) of the proposed binding modes is given in Fig. 4.

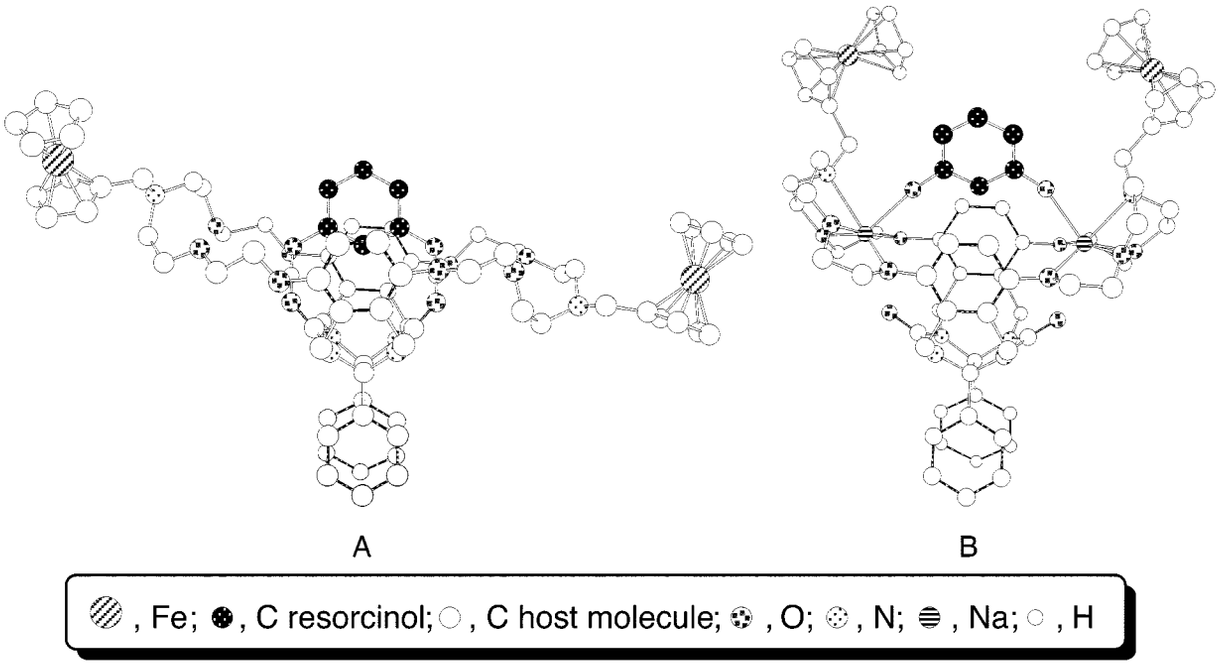


Fig. 4 Drawings of the host–guest complexes of compound **4**: **A** host **4** with resorcinol in the absence of Na^+; **B** host **4** with resorcinol in the presence of Na^+

Studies to investigate the effect of K^+ ions on the binding affinity between the host and olivetol were unsuccessful, probably because of the low solubility of the potassium salts tried. The salt having the highest solubility was potassium dodecylsulfate but even this resulted in turbid solutions unsuitable for NMR studies.

The NMR and IR experiments were also carried out to study the mode of binding of ammonium salts **5** and **6** in host **4**. Proton NMR experiments on **4**, performed in a mixture of $CDCl_3$ and CD_3CN, showed changes on the addition of substoichiometric amounts of these ammonium salts. The resonances of the CH_2N groups at δ 2.66 (in this solvent mixture) broadened and shifted to δ 3.23 on addition of either **5** or **6**. Additionally, a new relatively broad signal appeared at δ 4.4. Furthermore, shifting and some broadening of the large multiplet between δ 3.8 and 3.4 (CH_2O residues) occurred. Changes in the NMR signals of the wall protons and the guest protons were expected, due to mutual anisotropic ring effects, but significant changes could not be detected. The new signal at δ 4.4, the shift of the CH_2N protons and the lack of further changes in the NMR spectrum suggest that proton transfer takes place between **4** and the ammonium salts instead of the formation of a host–guest complex. The NMR experiments using organic acids and ammonium salts were performed to investigate the changes that take place in the NMR spectrum of **4**. Trifluoroacetic acid, 2,4,6-trichlorobenzoic acid and benzyldimethylammonium tetrafluoroborate **8** were used as the proton donors. When any of these three substrates was added to **4** the changes in the NMR spectra were identical to those observed for the ammonium salts **5** and **6**, thus implying that protonation of the nitrogen atoms of **4** takes place.

To investigate if resorcinol derivatives are still bound in a protonated host, these NMR experiments were also performed in the presence of 6 equivalents of 5-cyanoresorcinol. According to our findings this is the only resorcinol derivative that still binds to **4** in solvent mixtures with CD_3CN. The cyano group increases the strength of the hydrogen bonds with the carbonyl groups as well as the π-stacking interactions between host and guest, resulting in an overall high binding affinity. In the presence of solvents capable of formation of hydrogen bonds like CD_3CN the association constant will drop to lower values.[31] When 5-cyanoresorcinol is used, however, binding still occurs. The NMR signals of the aromatic walls of the host as well as signals of the guest can be monitored to determine whether a host–guest complex is formed in the presence of a proton source. All these experiments showed that after protonation of the nitrogen atom the diol is not bound in the host molecule. An additional IR experiment revealed a change in the ν(C=O) of **4** in the presence of 4 equivalents of benzyldimethylammonium tetrafluoroborate **8** (see Table 2), indicative of intramolecular hydrogen bonds between the carbonyl groups and the protonated nitrogen atoms of the host. Hence, it is concluded that these intramolecular hydrogen bonds prevent the formation of a host–guest complex with resorcinol derivatives. Attempts were made to investigate the association process with the two ammonium salts **5** and **6**. In order to obtain a homogeneous solution these experiments had to be performed in a solvent mixture of CH_2Cl_2 and MeCN. In this solvent mixture an intermolecular hydrogen bond between the proton donor and MeCN is favoured over the intramolecular hydrogen bond, therefore the carbonyl stretching frequency remains unaffected.

Conclusion

A novel redox-responsive host molecule based on diphenylglycoluril has been synthesized. This host molecule is able to bind both neutral organic guest molecules and positively charged ions. Cations like Na^+, K^+ and NH_4^+ have pronounced effects on the oxidation potential of compound **4**. Protonation of the aminomethylferrocenyl group of **4** also results in a shift of the oxidation potential of **4**. Binding studies in combination with electrochemical experiments show that **4** binds Na^+ in an 1:2 host–guest ratio, whereas K^+ and NH_4^+ are bound in a 1:1 ratio. Sodium ions have a pronounced effect on the association constant of the complexes between **4** and olivetol. An enhanced binding has been shown for this novel four-component (**4**, **7** and $2Na^+$) host–guest complex. A new co-ordination mode assisted by these Na^+ ions is presented, which can explain the relatively large association constant found for this multicomponent host–guest complex. Host **4** is responsive to the addition of primary ammonium salts, but instead of binding the ammonium salts protonation of the CH_2N groups of the host occurs.

Experimental

General

Proton (300.13 MHz) and ^{13}C-{^1H} NMR (75.48 MHz) spectra were measured on Bruker AMX 300 and DRX 300 machines, with $SiMe_4$ as the external reference, IR spectra on a Nicolet 510m FT-IR spectrophotometer. Melting points were determined on a Gallenkamp MFB-595 apparatus; the values are uncorrected. The GC-MS measurements were done on a Hewlett-Packard gas chromatograph, equipped with a DB-5MS column (length 12 m, inner diameter 0.2 mm, film thickness 0.33 μm). Column chromatography was performed with silica gel 60, 70–230 mesh ASTM (Merck). Analytical TLC was performed on TLC aluminium foil, silica gel 60 F_{254} (Merck). Silica gel and TLC plates were impregnated with NaBr according to a literature procedure.[26] Microanalyses were carried out in our own laboratory on an Elementar Vario EL apparatus (Foss Electric). Cyclic voltammetry and differential pulse voltammetry were performed using a EG&G PAR model 283 potentiostat. The electrochemical samples were 10^{-3} M in redox-active host and 2×10^{-1} M in $NBu^n_4PF_6$ as supporting electrolyte. The working electrode (1 mm disc) and the counter electrode (gauze) were made of Pt. The reference system consisted of a silver wire as the pseudo-reference electrode and $[Co(\eta^5\text{-}C_5H_5)_2]PF_6$ was used as standard internal reference.[16,36] The reported electrode potentials are given relative to the ferrocene–ferrocenium redox couple.

Chemicals

Acetonitrile and CH_2Cl_2 were distilled from CaH_2; $CDCl_3$ used in the association constant determinations was distilled from P_2O_5 before use. The salt $NBu^n_4PF_6$ was recrystallised twice from absolute ethanol and dried overnight at 80 °C *in vacuo* before use. Trimethylammoniomethylferrocene iodide[20] and compound **3**[37] were prepared according to literature procedures. Ammonium salts **5** and **6** were obtained after reaction of their amines with HCl and exchange with the respective NaX or AgX salts in MeOH or MeCN.

NMR experiments

Titration experiments were performed by monitoring the singlet at δ 6.73 in the ^1H NMR spectrum; on addition of olivetol the chemical shift of the protons shift to a lower value. From curve fitting assuming a 1 : 1 complex, *K* and CIS values were calculated according to literature procedures.[30,31,33] Protonation experiments using various proton sources were performed as follows: compound **4** (5 mg, 4 μmol), 5-cyanoresorcinol (0.5–0.6 mg, 40 μmol) and stoichiometric amounts of the various proton sources were measured separately and in combination. The solvent was $CDCl_3$–CD_3CN (1 : 1, v/v).

IR experiments

A number of 4×10^{-3} M solutions of host **4** in CH_2Cl_2 were prepared, followed by separate additions of 8 equivalents of **7**, 10 equivalents of dodecylbenzenesulfonic acid sodium salt and 5 equivalents of **8**, and the IR spectra were recorded. Combinations of the substrates **7**, **8**, and Na^+ were also added followed by recording of an IR spectrum. A mixture of CH_2Cl_2 and MeCN (1 : 1, v/v) had to be used in the experiments with **5** or **6**. These solutions had to be kept in an ultrasonic bath for prolonged periods in order to dissolve all components.

Electrochemical experiments

A three-electrode vacuum-tight voltammetric cell was loaded with host **4** (5 mg, 4 μmol), a small amount of $[Co(\eta^5\text{-}C_5H_5)_2]PF_6$ and electrolyte ($NBu^n_4PF_6$). The cell was evacuated and flushed with dry nitrogen twice, followed by addition of CH_2Cl_2 (2 cm^3) and MeCN (2 cm^3). Voltammetric (CV, DPV) responses were recorded and subsequently substoichiometric aliquots of guest molecules in MeCN (typically 100 μl) were added. In between all measurements the working electrode was polished using a 0.25 μm diamond paste.

Syntheses

Aminomethylferrocene 2. *Route* (*a*). A stainless-steel autoclave was loaded with methanol (30 cm^3), saturated with NH_3 and compound **1a** (0.5 g, 1.4 mmol) was added. The autoclave was closed and heated at 80 °C overnight. After cooling the autoclave was opened and the solution evaporated to dryness. The remaining solid was redissolved in CH_2Cl_2 (30 cm^3) and water (30 cm^3) was added. The organic layer was washed twice with 1 M NaOH (10 cm^3) and water (10 cm^3) and dried over $MgSO_4$. Finally the solvent was evaporated to afford **2** as an orange-red sticky solid, that turned into an oil on contact with air (0.14 g, 60% yield). NMR ($CDCl_3$): δ_H 4.14 (9 H, m, ferrocene H, NCH_2) and 3.5 (2 H, br, NH_2); δ_c 68.4, 68.1, 67.4, 66.9 and 37. EI mass spectrum: *m*/*z* 215 (M^+).

Route (*b*) (*i*) 1-(*Phthalimidomethyl*)*ferrocene* **1b**. This compound was prepared according to a literature procedure[21] from **1a** (0.5 g, 1.4 mmol) and potassium phthalimide (0.26 g, 1.4 mmol). An orange powder was obtained (0.3 g, 66% yield), m.p. 203 °C (decomp.) [lit.,[21] 201–202 °C (decomp.)]. IR ($CDCl_3$): $\tilde{\nu}_{max}/cm^{-1}$ 1716s (C=O), 1432m, 1393m and 1331m. NMR ($CDCl_3$): δ_H 7.80 (2 H, dd, $^3J = 5.4$, $^4J = 3.2$), 7.67 (2 H, dd, $^3J = 5.4$, $^4J = 3.2$ Hz), 4.61 (2 H, s, CH_2), 4.37 (2 H, s), 4.20 (5 H, s) and 4.10 (2 H, m); δ_C 167.7 (C=O), 133.7, 131.9, 123.0, 117.6, 69.3, 68.4, 68.1, 66.0 and 37.0.

(*ii*) *Aminomethylferrocene* **2**. This compound was prepared according to a literature procedure[21] from **1b** (0.3 g, 0.87 mmol) and hydrazine (50 μl). Compound **2** was obtained as an orange solid (95 mg, 63% yield). For identification see above.

Compound 4. A mixture of compound **3** (1.3 g, 1.31 mmol), NaI (1.76 g, 11.7 mmol) and Na_2CO_3 (2.1 g, 19.6 mmol) in MeCN (500 cm^3) was heated at reflux for 24 h. A solution of **2** (0.5 g, 2.5 mmol) in MeCN (300 cm^3) was then added to this refluxing mixture at a rate of 0.25 cm^3 min^{-1}. After 3 d the reaction mixture was cooled to room temperature, filtered and concentrated. After addition of CH_2Cl_2 (100 cm^3) and water (100 cm^3), the two layers were separated and the water layer was washed with CH_2Cl_2 (50 cm^3). The collected organic layers were washed three times with demineralised water (100 cm^3) and dried over $MgSO_4$. The solvent was evaporated and the product purified by column chromatography over silica gel impregnated with NaBr (gradient eluent 1% NEt_3–3–6% MeOH–CH_2Cl_2) to afford an orange-brown powder (0.7 g, 45%), m.p. 183 °C (decomp.). IR (KBr): $\tilde{\nu}_{max}/cm^{-1}$ 3447w, 2923–2870w, 1713s (C=O), 1459s, 1427m, 1258m, 1128m and 1105m. NMR ($CDCl_3$): δ_H 7.0 (10 H, m, aryl), 6.73 (4 H, s, aryl sidewall), 5.63 [4 H, d, $^2J = 16$, (CO)NCH*H*], 4.23–3.67 [50 H, m, OCH_2, ferrocenyl NCH_2, (CO)NC*H*H, ferrocenyl H] and 2.81 (8 H, br t, $^3J = 5.0$ Hz, CH_2N); δ_C 157.6, 151.2, 135.8, 134.4, 129.1, 128.7, 107.8, 85.3, 70.6, 70.4, 69.7, 68.8, 68.3, 55.2, 53.3 and 37.2. High-resolution mass spectrum (FAB): Found 1273.4386, $C_{70}H_{77}Fe_2N_6O_{10}$ requires 1273.4405 ($M + H$) (Found: C, 64.6; H, 5.9; N, 6.5. $C_{70}H_{76}Fe_2N_6O_{10}\cdot 1.5H_2O$ requires C, 64.7; H, 6.1; N, 6.5%).

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