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Articles

[(Ethylenediamine)Pt(uracilate)]$_4$, a Metal Analogue of Calix[4]arene. Coordination and Anion Host−Guest Chemistry Related to Its Conformational Dynamics

Jorge A. R. Navarro, Matthias B. L. Janik, Eva Freisinger, and Bernhard Lippert*

Department of Chemistry, Universität Dortmund, D-44227 Dortmund, Germany

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The open “molecular box” [(en)Pt(UH-N^1,N^3)]$_4$(NO$_3$)$_4$ (with en = 1,2-diaminoethane, UH = uracil monoanion) resembles calix[4]arenes in its structure and solution dynamics. It adopts a 1,3-alternate conformation in the solid-state (**1a**), but in solution and after deprotonation to [(en)Pt(U-N^1,N^3)]$_4$, a second major species (cone conformer (**1b**-4H$^+$)) occurs. **1b**-4H$^+$ acts as an efficient ligand for additional metal ions through the oxo-surface formed by the four O^2 exocyclic atoms of the uracil nucleobases. As shown here, **1b**-4H$^+$ can incorporate a single metal ion only, giving rise to the formation of species of type {[(en)PtU]$_4$M}(X)$_n$ with M = Zn^{II} (**2a**), Be^{II} (**3**) (not isolated in the solid state), and La^{III} (**4**); X = NO$_3$, SO$_4$/2; n = 2, 3. In addition, both the protonated species of the cone conformer (**1b**, pH 2−4) and compounds **2a** (at pH 3−8) and **3** (at pH 3−5) act as hosts for organic anions in water, as deduced from ^{1}H NMR studies. It is proposed that the cone conformers act as anion hosts due to a combination of positive charge as well as apolarity and size of the cavity. Host−guest complexes of type {[(en)PtU]$_4$Zn}(X)(NO$_3$,SO$_4$/2) with X = *p*-toluenesulfonate (**2b**) and 3-(trismethylsilyl)-1-propanesulfonate (**2c**) included in the cone cavity have been prepared and association constants have been determined by ^{1}H NMR spectroscopy. The fact that **4** does not act as a host may be due to a possible tetradentate coordination of La to **1b**-4H$^+$ which may result in a flatter cone cavity than in compounds **2** and **3**.

Introduction

The interest in the study of calixarenes and other similar macrocycles arises from the fact that, among others, they can behave as versatile hosts for inclusion of guest molecules due to their flexible cavities.[1] The inclusion of small neutral molecules in their cavities is a well-known phenomenon since the early crystallographic studies of this class of molecules.[2] In addition, calixarenes can act as O-donor ligands to metal ions, giving rise to versatile coordination compounds, with examples of mono-,[3] bi-,[4] and in some cases, polynuclear complexes formed.[5,6] Metal ions can also play an important role in the stabilization of different calixarene conformers.[1c] For example, capping of a calix[4]arene derivative with a tungsten-oxo group results in the formation of a rigid cone conformer which promotes, by means of a host−guest process, the formation of a columnar mesophase with liquid-crystal properties.[7]

The synthesis of inorganic macrocycles analogous to the organic calixarenes is also receiving great attention. Formation of such compounds frequently involves the spontaneous self-assembly of building blocks of appropriate geometry to produce cyclic complexes.[8] Different strategies have been employed to build diverse architectures. For example, the combination of a metal entity with right angles and a bifunctional organic ligand such as 4,4′-bipyridine gives rise to the formation of a “molecular box”.[9] It is also possible to produce “molecular squares” by placing the organic ligands at the corners and linear metal entities along the sides.[10,11]

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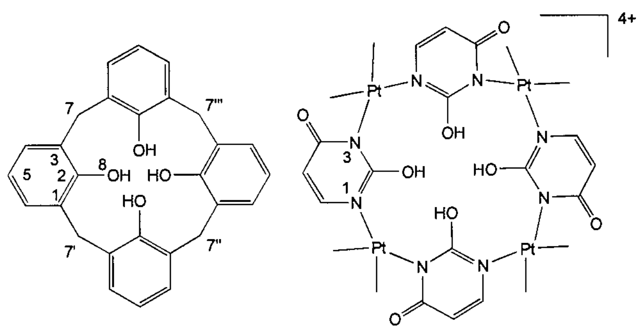
10.1021/ic9808394 CCC: $18.00

Chart 1



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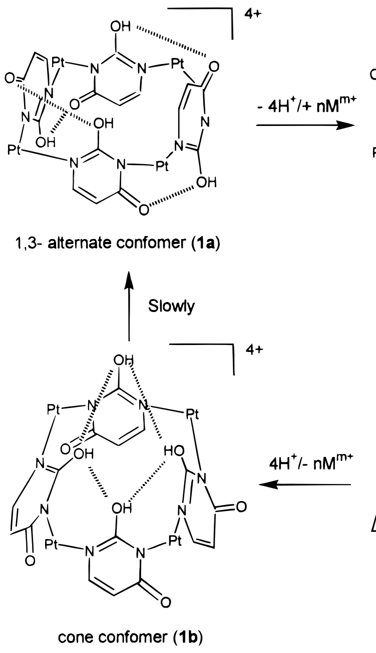
Scheme 1



Pt = enPt; M omitted for sake of clarity

We have previously reported[12] the formation, structure and solution dynamics of the "molecular box" $[(en)Pt(UH\text{-}N^1,N^3)]_4(NO_3)_4$ (with en = 1,2-diaminoethane, UH = uracil monoanion) which resembles calix[4]arenes in both its structure (Chart 1) and solution dynamics as well as in its propensity for metal complexation. Like calix[4]arenes, the cyclic uracil complex is conformationally flexible, adopting a 1,3-alternate conformation (**1a**) in the solid state, yet existing in a second major species (cone conformer, **1b**-$4H^+$) in solution following deprotonation to $[(en)Pt(U\text{-}N^1,N^3)]_4$. Subsequent reprotonation of the cone conformer (**1b**-$4H^+$) leads initially to **1b**, which over several hours converts back into **1a** (Scheme 1). In its 1,3-alternate conformation, **1a** was found to behave as an efficient ligand toward various transition metal ions, giving rise to the formation of octanuclear complexes after incorporation of four additional transition metal ions.[12c] At the same time, the early observation[13] that sodium trimethylsilyl-3-propanesulfonate (TSP) was unsuitable as a NMR standard in the pH range 2−4, when the protonated cone species (**1b**) was present, suggested to us that **1b** could act as a host for anions.

The fact that underivatized calixarenes do not behave as anion receptors[14] and the relatively few examples of anion host−guest chemistry of inorganic macrocycles[15,16] motivated us to develop a rationale for the stabilization of the cone conformer **1b** by metal complexation and to study the interaction of the resulting positively charged cone species with anions.

Results and Discussion

Cone Conformer. The flexible nature of **1** has previously been shown by us.[12b] It adopts a 1,3-alternate conformation (**1a**) in the solid-state and when dissolved in water. However, as observed by ^1H NMR spectroscopy, deprotonation of the uracil nucleobases (from UH to U) by means of NaOD is responsible for the slow appearance of a second major species, which corresponds to the cone conformer **1b**. Additional low intensity signals are probably due to the intermediates between 1,3-alternate and cone conformers. We now find that the efficiency of the 1,3-alternate → cone conversion of **1** is dependent on the nature of the base employed, following the trend $N(CH_3)_4OD < NaOD < Mg(OD)_2$. The formation of a Na^+ adduct of **1** is indirectly supported by the observation that the use of $N(CH_3)_4OD$ instead of NaOD causes the formation of sparingly soluble species of both conformers. On the other hand, the use of $Mg(OD)_2$ leads to formation of a soluble cone species and in this case the extent of 1,3-alternate → cone conversion is improved from about 66% in the case of NaOD to nearly 100% with $Mg(OD)_2$ used. The occurrence of the cone species in water at basic pH appears to be the result of several features, namely the loss of the intramolecular $O^4{-}H{\cdots}O^2$ hydrogen bonds, which contribute to the stabilization of the 1,3-alternate conformer[12b] and metal ion coordination by the cone species. Mg^{2+} is particularly efficient in this respect. In addition, the polar character of the solvent should also favor the formation of the cone species as has been also found in O-methylated calix[4]arenes, in which the percentage of the cone conformer is directly proportional to the polarity of the solvent.[1c]

Stabilization of the Cone Conformer by Metal Complexation. It has previously been shown by us that Ag^I is responsible for the spontaneous 1,3-alternate → cone conformer conversion at acidic pH, giving rise to the formation of $[(en)Pt(UH\text{-}N^1,N^3,O^2)Ag]_4(NO_3)_8{\cdot}4H_2O$.[12c] In this compound four Ag^I metal centers bind to the uracil O^2 donor atoms of the four uracil monoanions. Severe anion disorder has prevented us from publishing the structure of this compound. However, the structure of the cation is well defined, showing a pinched-cone arrangement of the uracil nucleobases.

The different H^+ affinities of the 1,3-alternate and cone conformers, as well as the slow kinetics of the 1,3-alternate → cone conformer conversion, has tentatively suggested to us that the two conformers may have different metal coordination properties and that it may eventually be possible to freeze the cone conformer by metal complexation.

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Table 1. ^{1}H NMR (200 MHz) Data in ppm for Compounds **2**−**4** in D_2O at 295 K^{a}

	H^6	H^5	en
Pt_4Zn **2** (pH* 6.5)	7.64	5.50	2.72
Pt_4Be **3** (pH* 4.5)	7.89, 7.72, 7.69, 7.42	5.77, 5.65, 5.46, 5.36	2.69
Pt_4La **4** (pH* 6.5)	7.64	5.54	2.69

^{a} Asterisks denote uncorrected pH meter reading.

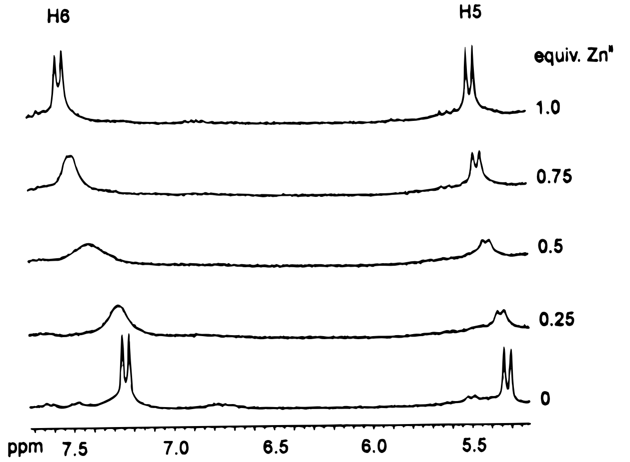
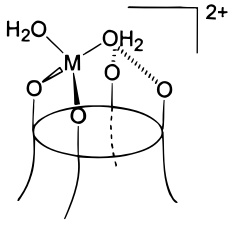


Figure 1. Effect of addition of Zn^{II} to a solution of the cone conformer of **1**. ^{1}H NMR (200 MHz) spectra in the aromatic region of uracil nucleobases (D_2O, 295 K, and pH* 7.2).

Chart 2



M = Zn^{II} (**2**), Be^{II} (**3**)

{[enPtU]$_4$ZnSO$_4$}, 2a. From ^{1}H NMR experiments it was clear that the 1,3-alternate and cone conformers give rise to different species upon addition of metal salts. For example, the addition of 4 equiv of Zn^{II} to a solution of **1a** (pH* 6.5) is responsible for a shift of the H^5 (+ 0.33 ppm) and H^6 (−0.10 ppm) resonances of uracil, whereas the addition of an equimolecular amount of Zn^{II} to a solution of the cone conformer **1b** (pH* 6.5) results in a significant downfield shift of the H^5 (+0.20 ppm) and H^6 (+0.35 ppm) resonances of uracil, suggesting the formation of thermodynamically stable species in both cases (Table 1). Titrating Zn^{II} to the cone conformer of **1** results in an initial ($r_{Zn:\mathbf{1}} < 1$) broadening of the uracil H,^{5}H^{6} resonances. With $r \gg 1$ the signals sharpen, and with $r > 1$ they undergo concentration dependent downfield shifts (Figure 1), indicative of formation of a labile complex of 1:1 stoichiometry. An ESI MS experiment reveals a peak of *m*/*z* 763.32, which corresponds to the species [M/2], {[enPtU]$_4$Zn}$^{2+}$. Zn^{II} binding to two uracil O^2 donor atoms of **1b** (Chart 2) should be in agreement with the solid-state structure of **2b** (see below). The presence of a single set of resonances for the four uracil H^5 and H^6 protons is consistent with labile binding of Zn^{II} to **1b** and rapid exchange of ligands at the oxo-surface.

{[enPtU]$_4$Be}$^{2+}$, 3. Addition of Be^{II} to an aqueous solution of each of the two conformers of **1** causes more complicated effects. Thus, addition of 4 equiv of Be^{II} to a solution of the 1,3-alternate conformer **1a** (pH* 4.5) has no effect on the uracil resonances, suggesting that this conformer is not able to bind Be^{II}, possibly as a consequence of the high tendency of this metal ion to hydrolyze at pH > 3.[17] However, addition of 1 equiv of Be^{II} to a solution of the cone conformer of **1b** (pH* 4.5) results in the appearance of four distinct sets of resonances for the H^5 and H^6 uracil protons (see Figure 2 and Table 1). Titration of a solution of **1b** with Be^{II} is in accord with the formation of a kinetically inert species, since signals of **1b** and **3** coexist when $r_{Be:\mathbf{1}} < 1$. The Pt_4Be species is only stable in acidic media (pH range 3−5). The efficiency of the cone conformer **1b** to bind Be^{II} is possibly related to the flexibility of its oxo-surface formed by the O^2 donor atoms of uracil. We propose the formation of a species of the type shown in Chart 2, which is analogous to **2a**. The fact that four sets of resonances for the H^5 and H^6 protons of uracil are observed can be explained considering the directions of the C^6−H^6 vectors in **1b** (see Scheme 1) and tetrahedral coordination of Be^{II} to the cone as shown in Chart 2. The proposed model leads to four different chemical environments of the uracil H^6 protons. Likewise, the four uracil H^5 protons in **3** would no longer be equivalent (see also NOESY and ROESY experiments below).

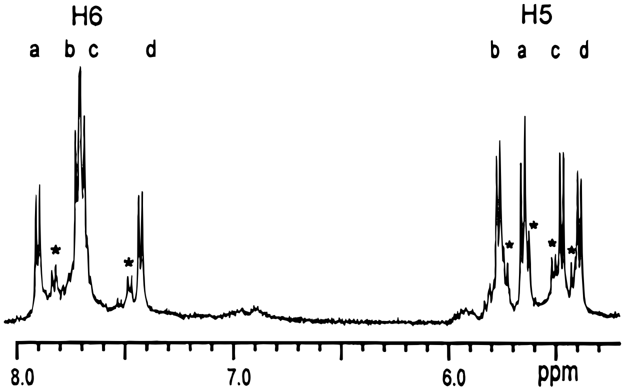


Figure 2. Uracil H^5/H^6 region in the ^{1}H NMR (400 MHz) spectrum of **3** (* denotes an unknown species that is always present; D_2O, 295 K, and pH* 4.5). Signal assignments were made with the help of a ^{1}H ^{1}H COSY experiment.

{[enPtU]$_4$La}(NO$_3$)$_3$, 4. Similarly, addition of 1 equiv of La^{III} to a solution of the cone conformer **1b** (pH* 6.5) accounts for a large downfield shift for the H^5 (+0.20 ppm) and H^6 (+0.37 ppm) resonances of uracil. As in the case of **3**, titration of the cone species with La^{III} leads to individual resonances for **1b** and **4** when $r_{La:\mathbf{1}} < 1$. An ESI MS experiment shows a peak with *m*/*z* 830.7, which corresponds to the species [M/2], {[enPtU]LaNO$_3$}$^{2+}$. Considering basic coordination chemistry of La[18] it is tempting to postulate a tetradentate binding to **1b** with the nitrate anion binding at the exo-side of La^{III} (Chart 3).

Anion Inclusion as a Probe of Cone Conformation. Addition of an equimolar amount of a Zn^{II} or Be^{II} salt to the cone conformer of **1** in the presence of an anion of type R−SO_3^- (R = aliphatic or aromatic substitutient, Chart 4) is responsible for large upfield shifts of the signals of the organic substitutients of the sulfonate anions (e.g. up to 0.6 ppm for the Si(Me)$_3$ resonances of TSP) as well as downfield shifts (up to 0.2 ppm) for the H^5 and H^6 resonances of uracil. In addition, cross-peaks between the H^5 and H^6 resonances of uracil and those of the

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Chart 3

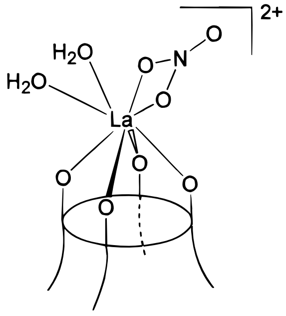

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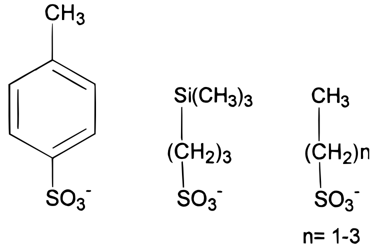
Chart 4



organic anions are also found in the NOESY and ROESY spectra (see below). These observations suggested to us that the metalated cone species act as hosts for organic anions and that this host−guest process could be used to probe the cone arrangement of the uracil nucleobases. In contrast, the 1,3-alternate species **1b** displays no apparent interaction with the anions whatsoever. The upfield shift of the guest resonances is in agreement with an apolar−apolar interaction between the cone cavity and the organic part of the anion. Multiple C−H$\cdots\pi$ type interactions inside the cavity, which possess typical binding energies in the 1−2 kcal mol^{-1} range,[19] may be invoked in the stabilization of the inclusion adducts. This type of interaction is well-known to occur in the cavity of classical calixarenes as a result of the electron-rich nature of the phenol rings.[20] The fact that the organic substitutient rather than the oxoanion is inside the cavity is not surprising considering the high hydration energy of oxoanions.[21] Only recently Atwood et al.[14] have shown an example of a metalated calixarene in which oxoanions such as HSO_4^- are included inside the calixarene cavity, as a consequence of a large acidification of the cavity due to the attachment of electron attracting metal entities at the external faces of the phenol rings. The incorporation of a metal entity in the π-system of an analogous system is responsible for the preferential inclusion of the oxoanion group of $CF_3SO_3^-$ rather than the apolar part.[22] In our system, the π-basic character of the cavity appears not to be modified after metal binding to the oxo surface since it does not show any special anion binding capacity when the apolar character of the anion decreases (see Chart 4 and Table 2). Thus, the metalated (M = Zn^{II}, Be^{II}) cone species show only in water an appreciable inclusion affinity for aliphatic sulfonate anions of type $CH_3(CH_2)_nSO_3^-$ when $n > 2$. The apolar−apolar interactions appear to play a very important role in the stabilization of the host−guest complex. It is maximized in the case of anions with the Si(Me)$_3$ and toluene motifs. It is important to note the high values for the K_{assn} of compounds **2** and **3** with the organic anions studied in water: they are in the same range of those found for complexation of K$^+$ by 18-crown-6 ether with K_{assn} being ca. 100 M^{-1}.[23] Normally, K_{assn} values for anions in a very competitive solvent such as water are much smaller.[14] In an attempt to evaluate the contribution of the apolar−apolar interactions to anion binding an experiment with *t*-butanol was carried out in order to mimic the effect of the Si(Me)$_3$ group. The fact that the K_{assn} value is about 6−9-fold lower (see Table 2) is indicative of a cooperative effect between hydrophobic and electrostatic interactions between the cone species and the anionic guest. Also, it is interesting to note the higher affinity of TSP for **3**, which may be related to the higher stability of this species as compared to **2a**.

Table 2. Association Constants of Compounds **2** and **3** (M^{-1}) with Different Anions in Water at 295 K; Values in Brackets Indicate Standard Deviations

anion	2	3
TSP$^-$	75(10)	159(9)
TS$^-$	50(10)	44(5)
PS$^-$	22(2)	25(2)
ES$^-$	0	0
MS$^-$	0	0
tert-butyl alcohol	13(2)	19(1)

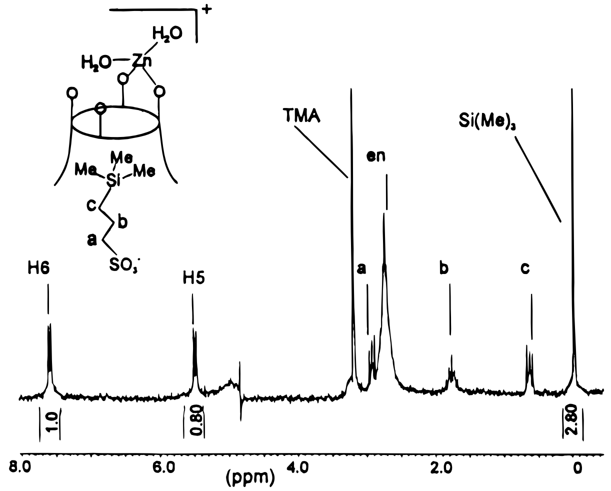


Figure 3. ^{1}H NMR (200 MHz) spectrum of **2c** (D_2O, 295 K, and pH* 6.5). The integral values are in agreement with the formation of a 1:1 aduct between **2a** and TSP. The schematic structure of the Zn^{II} complex taken into account the solid-state structure of **2b**. In solution, Zn^{II} rapidly exchanges between various O^2 sites (see also Figure 1).

In addition to the solution studies, it was also possible to isolate the adducts **2b** and **2c** containing, respectively, a TSP$^-$ (Figure 3) and a TS$^-$ entity included in the cone cavity.

As can be shown, the host−anion interaction is maximized when the stability of the metalated species is optimized. Thus, **2a** shows a maximum for the host−guest interaction at pH ∼ 7.4, as well as stability over the pH range 3−8. In the case of **3** there is only anion complexation at pH < 5, a range in which this species is stable (see above).

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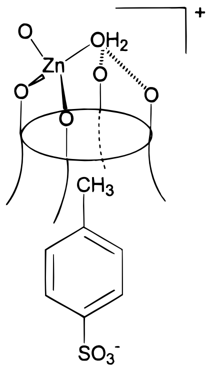
Chart 5



2b

4 does not behave as a host for the organic anions studied despite the cone arrangement of the uracil nucleobases. Model building suggests that tetradentate coordination of La^{III} to **1b** should be responsible for a much more open cone cavity than the one in complexes **2** and **3** which may not be capable of encapsulating the organic part of the anion.

Attempts were also made to crystallographically characterize a representative example of the host−guest complexes. Extremely small and sensitive crystal of **2b** were eventually isolated and examined by X-ray crystallography. The structure determination is not of high precision due to poor quality of the crystals and therefore is not reported here in detail. However, the composition of the compound was clearly confirmed. As anticipated from the solution studies, the compound displays a cone arrangement of the uracil nucleobases (see Chart 5), with zinc being coordinated to two O^2 donor atoms from two uracil moieties in a similar way as in a dinuclear PtZn compound containing two 1-methyluracilate bridges.[24] The cone arrangement of the uracil nucleobases appears to be additionally stabilized by the hydrogen bonding interaction between a water molecule coordinated to the metal center and two noncoordinated O^2 uracil atoms. The behavior of **2a** as a host for anions is also confirmed since the toluene fragment of the organic anion is inserted into the cavity.

NOESY and ROESY Experiments. Additional structural information of the host−guest complexes in solution was obtained by NOESY and ROESY[25] experiments. In the first stage, a 2D NOESY experiment was carried out for the system **2a** + TSP, at room temperature. Weak cross-peaks between the H5 and H6 resonances of uracil and the Si(Me)$_3$ resonances of TSP were observed and H5/H6 cross-peaks were not observed. We proceeded then to carry out a 2D ROESY experiment with the purpose of overcoming conditions of unfavorable molecular tumbling which give rise to weak NOE peaks ($\omega_0\tau_c \approx 1.12$).[25c] A new experiment carried out at 2 °C displayed intense cross-peaks between the H5 and H6 resonances of uracil and the Si(Me)$_3$ resonances of TSP (see Figure 4) which are clearly indicative of an inclusion adduct of **2a** with TSP in solution. It is also interesting to note that the H5 resonances of uracil give also rise to distinct cross-peaks with the propane chain of TSP. This result is in agreement with the orientation of the H5 protons of the uracil rings which make them easily accessible for the guest. In addition, the intensity of the cross-peaks between the H5 resonances of uracil and those of the propane chain decreases as a function of the separation between Si(Me)$_3$ group and the CH$_2$ groups. This finding indirectly proves the preferential complexation of the apolar Si(Me)$_3$ moiety rather than of the oxoanion (see above).

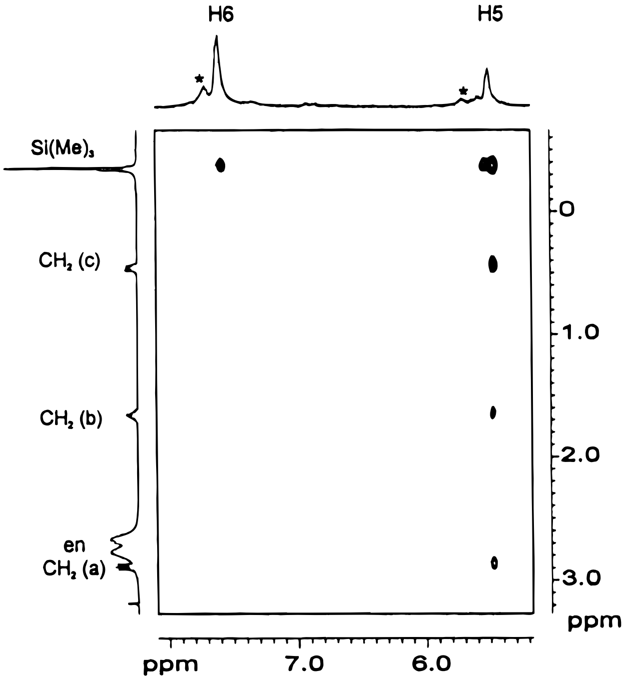


Figure 4. 2D ROESY (400 MHz) spectrum of **2a** and an equimolecular amount of TSP in the uracil H^5/H^6/TSP region (D$_2$O, 275 K, and pH* 7.1).

Analogously, in the case of **3** a 2D ROESY experiment carried out at 5 °C showed intense cross-peaks between the H5 and H6 resonances of uracil and the Si(Me)$_3$ resonances of TSP and also cross-peaks between the H5 resonances of uracil and the propane chain of TSP (see Figure 5). In addition to the cross-peaks between the H5 and H6 resonances of uracil and the TSP resonances, positive cross-peaks between the nonequivalent H6/H6 and H5/H5 resonances near the diagonal of the spectrum could be observed which may be due to chemical exchange[25c] as a result of internal rearrangements in **3** (see Figure 6). The effect of the temperature on the internal rearrangements in **3**, i.e., the presence of a higher number of chemical exchange cross-peaks between the nonequivalent H6/H6 and H5/H5 resonances of uracil at higher temperature, should be noted. It probably suggests that at higher temperatures (Figure 6b) the Be atom may start moving from one coordination site to the other at the oxo-surface of **1b**.

Comparison of the Metalated Cone Species and Classical Calix[4]arenes. The following analogies and differences are to be noted. First, the oxo-surface formed by the O^2 uracil atoms is considerably more extended as compared to classical calix[4]arenes. The separation between the 8 and 8″ sites (as given in Chart 1) is ca. 5.0 Å in **2b** versus ca. 3.7 Å in a classical calix[4]arene.[26] Second, the cavity of **2b** is well structured and comparable in size to classical calix[4]arenes (i.e. separation between the 5 and 5″ sites, as defined in Chart 1, is ca. 8.0 Å in **2b** and ca. 8.2 Å in a classical calix[4]arene).[26] In the case of the 1,3-alternate species and also in Pt$_4$Ag$_4$ (pinched cone)[12b]

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[24] Schöllhorn, H.; Thewalt, U.; Lippert, B. *Inorg. Chim. Acta* **1985**, *108*, 77.

[25] (a) Hwang, T.-L.; Shaka, A. J. *J. Am. Chem. Soc.* **1992**, *114*, 3157. (b) Hwang, T.-L.; Kadkhodaei, M.; Mohebbi, A.; Shaka, A. J. *Magn. Reson. Chem.* **1992**, *30*, S24. (c) Hull, W. E. In *Two-Dimensional NMR Spectroscopy. Applications for Chemists and Biochemists*; Croasmun, W. R., Carlson, R. M. K., Eds.; VCH: Weinheim, 1994; p 67.

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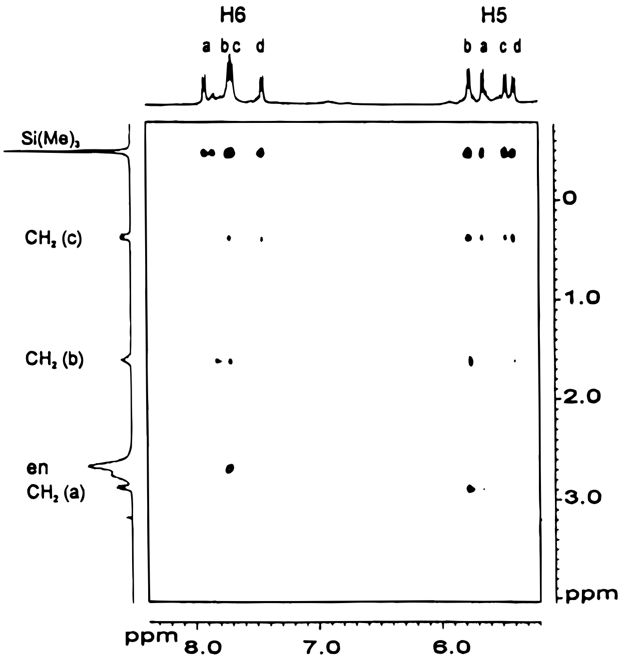

Figure 5. 2D ROESY (400 MHz) spectrum of **3** an equimolecular amount of TSP in the uracil H^5/H^6/TSP region (D$_2$O, 278 K, and pH* 4.5).

there is no well structured cavity suitable for guest inclusion. Third, the addition of charge by the metal entity bonded to the oxo-surface appears to be responsible for the fact that **2a** and **3** act as anion hosts, which is not common in nonsubstituted calix[4]arenes.[14] Moreover, it is the metal entity that is also responsible for an opening of the cone which creates a cavity of proper size for the entrance of a guest. Fourth, the π-basicity of the cavity of compounds **2a** and **3** appears to be similar to the classical calix[4]arenes and therefore both systems show a similar preference for guests of analogous nature such as the toluene motifs,[1] which were found in the first crystallographic reports on host−guest adducts of calixarenes.

Conclusions and Outlook

The 1,3-alternate and cone conformers of **1** possess different coordination chemistry properties. Thus, the 1,3-alternate conformer readily binds four additional metal entities. The cone conformer is capable of attracting between one and four metal entities, depending on the nature of the metal. However, only if a single metal ion such as Be^{II} and Zn^{II} is bound by the cone conformer, does it act as an anion host. A cooperativity between the positive charge introduced by the coordinated metal ion and the hydrophobic nature of the cone cavity appears to be responsible for anion complexation. The optimal anion binding ability is achieved when the stability of the complex is also maximized. In the case of Zn^{II}, anion binding is optimal at pH $\sim$ 7.4. This feature is of some interest considering that it is in the physiological pH range. La^{III} likewise stabilizes the cone conformer but the Pt$_4$La species is not able to incorporate an organic anion in the cone cavity, probably as a result of a higher opening of the cone cavity which do not permit efficient encapsulation of anion guests.

Experimental Section

Materials. enPtCl$_2$,[27] [enPtCl(UH-N^1)]Cl,[28] and [(en)Pt(UH-N^1,N^3)]$_4$(NO$_3$)$_4$ (**1**)[12b] were prepared from K$_2$PtCl$_4$, ethylenediamine, and uracil, respectively. Sodium *p*-toluenesulfonate (TS) was purchased from Merck, sodium 3-(trismethylsilyl)-1-propanesulfonate (TSP), sodium 1-propanesulfonate (PS), sodium ethylsulfonate (ES), and sodium methylsulfonate (MS) from Aldrich.

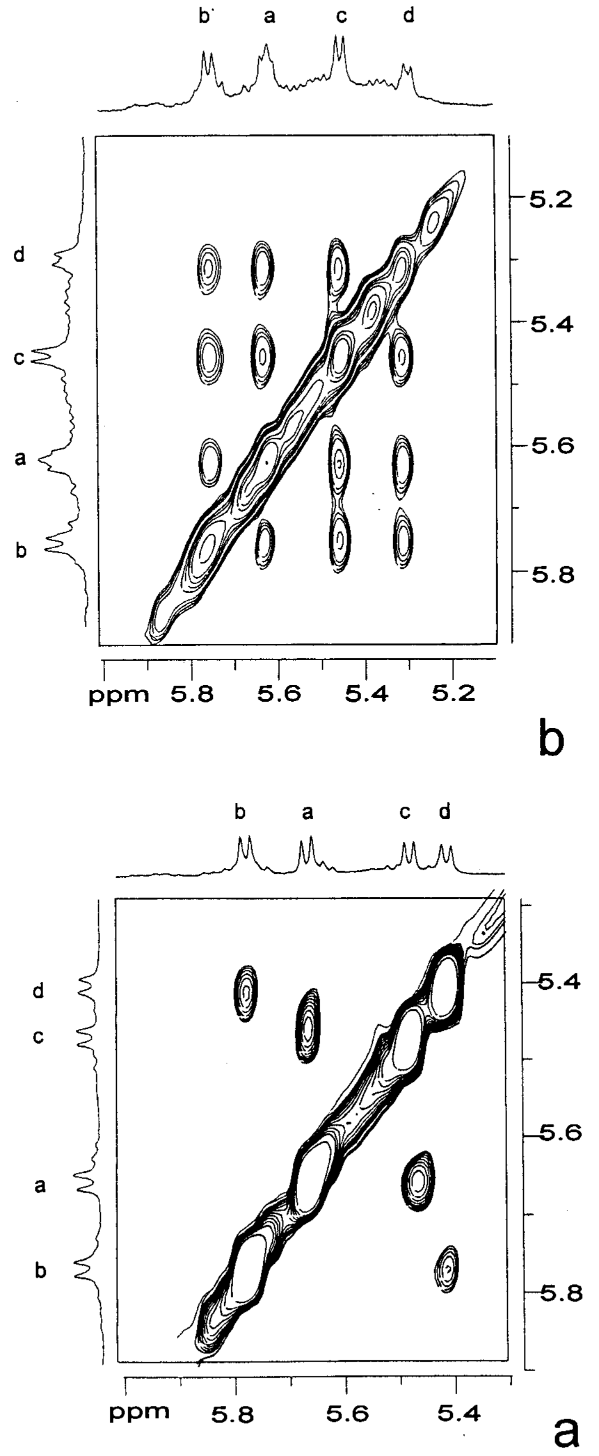

Figure 6. Effect of the temperature in the ROESY (400 MHz) spectra of **3** in the uracil H^5/H^5 region (positive cross-peaks are shown) at 278 K (a) and 293 K (b). D$_2$O and pH* 4.5.

Preparation of {[(en)Pt(U)]$_4$Zn}(SO$_4$) (2a). Mg(OH)$_2$ (3 mg) was added to a solution of **1** (30 mg in 1 mL H$_2$O) and the suspension was stirred at 40 °C for 12 h. The resulting solution (pH 8.5) was filtered from a small amount of precipitate. Subsequent addition of ZnSO$_4$·7H$_2$O (1 equiv, 5.0 mg in 0.1 mL of H$_2$O) gave rise to the formation of a pale yellow solution (pH 6.5), from which after several days a microcrystalline material precipitated. It was washed with a minimum amount of water and air-dried, yield 20%. Probe X-ray microanalysis (EPXMA) for Pt, Zn, and S was in agreement with composition

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$[(C_2H_8N_2)_4Pt_4(C_4H_2N_2O_2)_4Zn]SO_4$. ^1H NMR (D_2O, pH* 6.5): δ 2.72 (s, 4H; CH_2), 5.50 (d, $J = 7.0$ Hz, 1H; H5), 7.64 (d, $J = 7.0$ Hz, 1H; H6). ESI MS(+) 763.3 ($m/2$, $\{[enPtU]_4Zn\}^{2+}$).

Preparation of $[(en)_4Pt_4U_4Zn](TS)NO_3\cdot nH_2O$ (2b). A procedure similar to the one described for the synthesis of **2a** was followed but with addition of an equimolar amount of sodium toluenesulfonate. A crystalline precipitate of **2b** was isolated, yield 26%. Anal. Calcd for $[(C_2H_8N_2)_4Pt_4(C_4H_2N_2O_2)_4Zn](C_7H_7SO_3)NO_3\cdot 12H_2O$: C, 18.83; H, 3.24; N, 12.05. Found: C, 18.5; H, 3.0; N, 12.4. ^1H NMR (D_2O, pH* 6.5): δ 2.37 (s, 3H; CH_3), 2.72 (m, 4H; CH_2), 5.48 (d, $J = 6.9$ Hz, 1H; H5), 7.36 (d, $J = 8.1$ Hz, 1H; H3), 7.59 (d, $J = 6.9$ Hz, 1H; H6), 7.68 (d, $J = 8.1$ Hz, 1H; H2). Preliminary crystal data: $a = 16.546(3)$ Å; $b = 21.239(4)$ Å; $c = 15.130(3)$ Å; $\beta = 91.83(3)°$; monoclinic; $P2_1/c$; $Z = 4$.

Preparation of $[(en)_4Pt_4U_4Zn](TSP)(SO_4)_{0.5}\cdot nH_2O$ (2c). Using the previous procedure but with sodium-3-(trismethylsilyl)-1-propanesulfonate (TSP) instead of sodium toluenesulfonate gave a microcrystalline precipitate of **2c**, yield 20%. Anal. Calcd for $[(C_2H_8N_2)_4Pt_4(C_4H_2N_2O_2)_4Zn](C_6H_{15}SiSO_3)(SO_4)_{0.5}\cdot 10H_2O$: C, 18.43; H, 3.84; N, 11.47. Found: C, 18.5; H, 3.9; N, 11.8. ^1H NMR (D_2O, pH* 6.5): $\delta = -0.03$ (s, 9H; $Si(CH_3)_3$), 0.61 (t, $J = 8.4$ Hz, 2H; CH_2), 1.75 (m, 2H; CH_2), 2.91 (t, $J = 8.1$ Hz, 2H; CH_2), 5.48 (d, $J = 6.9$ Hz, 1H; H5), 7.58 (d, $J = 6.9$ Hz, 1H; H6).

Preparation of $\{[(en)Pt(U)]_4Be\}^{2+}$ (3). A procedure similar to the one described for the synthesis of **2a** was followed, on an NMR scale, applying $BeSO_4\cdot 4H_2O$ instead of $ZnSO_4\cdot 7H_2O$ and adjusting the pH* to 4.5. The compound was not isolated.

Caution! *Beryllium compounds are very toxic and should be handled with caution*.

Preparation of $\{[(en)Pt(U)]_4La\}(NO_3)_3$ (4). A procedure similar to the one described for the synthesis of **2a** was followed with $La(NO_3)_3\cdot 6H_2O$ applied instead of $ZnSO_4\cdot 7H_2O$. The resulting pale yellow solution (pH 5.3) gave, after a week, a microcrystalline precipitate of **4**, yield 15%. Probe X-ray microanalysis (EPXMA) for La and Pt was in agreement with a composition $[(C_2H_8N_2)_4Pt_4(C_4H_2N_2O_2)_4La](NO_3)_3$ (1785.4). ^1H NMR (D_2O, pH* 6.5): δ 2.69 (s, 4H; CH_2), 5.54 (d, $J = 7.0$ Hz, 1H; H5), 7.64 (d, $J = 7.0$ Hz, 1H; H6). ESI MS(+): 830.7 ($m/2$, $\{[enPtU]LaNO_3\}^{2+}$).

Instruments. IR spectra (KBr pellets) were recorded on a Bruker IFs 113v FT spectrometer. Probe X-ray microanalysis (EPXMA) experiments were carried out with a Stereoscan 360 Cambridge Instruments apparatus. Electrospray mass spectrometry (ESI MS) was performed on a Finnigan MAT 90 spectrometer equipped with a ESI II interface (Finnigan MAT, Bremen, Germany). A fused silica capillary (inner diameter 75 μm) was used. The 2-propanol sheath flow was 5−10 μL min^{-1}, and the sample flow rate 0.5−1 μL min^{-1}. The temperature of the desolvation was set to 250 °C. Cations were registered.

^{1}H NMR Experiments. The ^1H NMR experiments were recorded in D_2O on Bruker DRX 400 and Bruker AC 200 instruments with tetramethylammonium tetrafluoroborate (TMA) as internal reference (3.18 ppm relative to TMS). 2D ROESY[25] spectra were recorded at 275, 278, and 296 K with a mixing time of 400 ms. 2D NOESY spectra were recorded at 296 K with mixing times in the range between 300 ms and 1500 ms. For the ROESY and NOESY spectra a total of 256 t_1 increments, each with 2048 t_2 complex points, were collected with each FID as the average of 32 or 24 transients.

NMR Titrations. Stock solutions (1×10^{-2} M, 2×10^{-2} M, D_2O) of the cone conformer of **1** were prepared in D_2O. To a 0.40 mL sample of this solution was added an equimolar amount of a solution of the corresponding metal salt (0.2 M) of MSO_4 (M = Be, Zn) and afterward increasing aliquots of (0.4 M, 4M) solutions of NaX (X = TSP, TS, PS, ES, MS) in a 5 mm NMR tube at pH* 7.1 and 4.5 for **2a** and **3**, respectively. pH* indicates uncorrected pH meter reading. ^1H NMR spectra were recorded for 10 different mixtures and the shifts of the H^5 and H^6 resonances of uracil were analyzed following the method of Sigel et al.[29] by a nonlinear least-squares calculation. At least three experiments were made in order to estimate the error in each association constant evaluation.

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