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Nicola Edwards [a], Roger Helgeson [a], Yi-Lei Zhao [a] & K. N. Houk [a]

[a] Department of Chemistry and Biochemistry, University of California, Los Angeles, California

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Pyridine-Based Cavitands for Acid and Carboxylate Recognition

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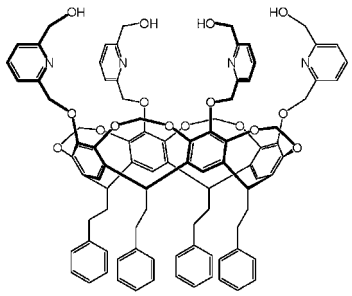

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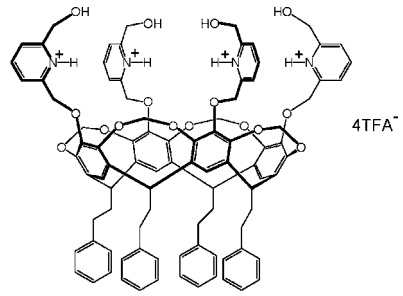

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The design, syntheses and binding capabilities of two novel cavitand-based receptors are described. Receptor **1***, contains a cyclic array of pyridine moieties in its appendages and was synthesized in a single step from the known tetrol: refluxing tetrol with 2-bromomethyl 6-hydroxymethylpyridine under basic conditions. Receptor* **2** *was obtained by stirring* **1** *in TFA. The binding capabilities of these receptors were explored using molecular mechanics calculations and NMR titration studies. Receptor* **1** *displayed recognition properties towards acids but only if proton transfer between receptor and substrate was facilitated. Aromatic carboxylate recognition was displayed by receptor* **2***.*

Keywords: carboxylate acid complexation; cavitand pyridine; recognition receptor

Address correspondence to K. N. Houk, Department of Chemistry and Biochemistry, University of California, 607 Charles E Young Dr. E, Los Angeles, CA 90095-1569, USA. E-mail: houk@chem.ucla.edu

INTRODUCTION

The development of supramolecular hosts with recognition properties is an area of research which has received considerable attention in recent years. A myriad of synthetic receptors for biologically and environmentally important small molecules and ions have been constructed on the basis of supramolecular hosts [1].

Cavitands, known better as synthetic modules for hemicarcerands and coordination cages, have been heavily utilized in this regard [2]. These supramolecular hosts are rigid bowl-shaped molecular cavities with one open surface derived from resorcinarene.

Previously reported examples of the attachment of pyridine to the resorcinarene scaffold have predominantly been for use in cavitand ligands for cage self-assembly via coordination to palladium or platinum precursors [3]. There are, however, very few pyridine-based cavitand receptors [4]: a cationic Pd pyridine complex (Fig. 1-A) reported by Hong and co-workers for carboxylate complexation, the family of water-soluble cavitands (Fig. 1-B) designed by Reinhoudt et al. for anion complexation, Paek and Lee cavitands (Fig. 1-C and D respectively) for cation recognition.

It is not surprising that a plethora of synthetic receptors have been designed for carboxylate recognition [5], given the prominence of the

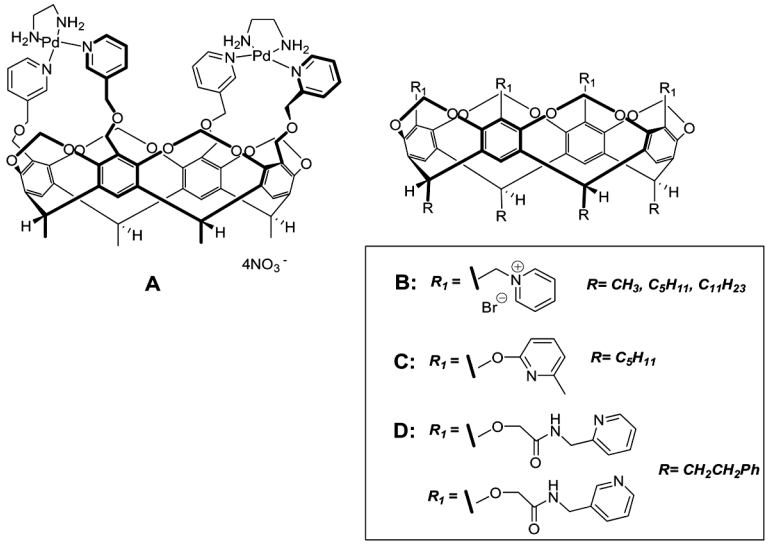


FIGURE 1 Examples of pyridine-based cavitand receptors for cation and anion recognition.

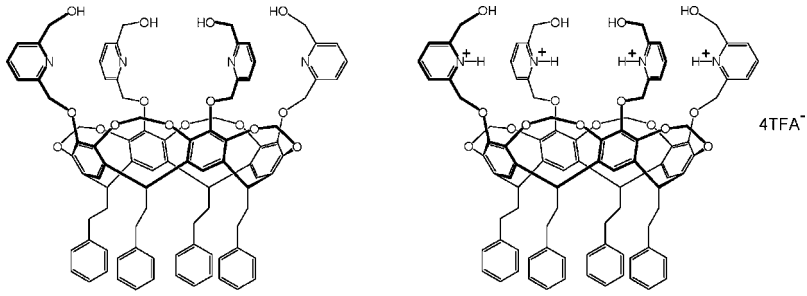


FIGURE 2 Receptors **1** and **2**.

carboxylate moiety in biological systems [6]. In contrast, there is a measurable number of reports [7] detailing receptors which display recognition properties towards acids. With the general aim of synthesizing receptors from cavitands, in this paper, the design and syntheses of two novel receptors (Fig. 2) are reported. Receptor **1** contains a cyclic array of pyridine moieties projected towards the inside of the cavity and displays recognition properties towards acids. Receptor **2** contains a cyclic array of pyridinium moieties and shows recognition properties towards aromatic carboxylates.

The synthesis of receptor **1** was accomplished in a single step from the known tetrol: refluxing tetrol with 2-bromomethyl 6-hydroxymethylpyridine under basic conditions overnight in acetonitrile. Receptor **2** was obtained by stirring **1** in TFA over a two-hour period. Molecular mechanics calculations and NMR titration studies were used to evaluate the binding capabilities of these novel receptors.

EXPERIMENTAL SECTION

Computational Methods

Force field calculations were carried out using the OPLS force field in the MACROMODEL program [8]. Conformations of receptors **1** and **2** were explored with a Monte Carlo (MC) search by varying the tortional angles of the rotatable bonds in the four appendages. The total MC steps are 4000, each MC step begins with the starting geometry of the least used structure of the previous MC steps. Starting geometries on the receptor-substrate complexes were obtained manually by docking the receptor inside the cavity of the substrate and the energy minimized with the OPLS force field and the GB/SA solvation model for water.

MATERIALS AND METHODS

All reactions were carried out under a blanket of argon. Tetrahydrofuran was dried via passage through an alumina-packed column. *N*-methylpyrrolidinone (NMP) and dimethylformamide (DMF) were degassed under high vacuum and *N*-bromosuccimide (NBS) was recrystallized from boiling water just prior to usage. All other solvents and reagents were of reagent grade and used as received. Deuterated solvents were purchased from Cambridge Isotopes and used without further purification. The syntheses of tetrol **3** and that of 2-bromomethyl-6-hydroxymethylpyridine followed those previously described in the literature [9]. The syntheses of the tetrabutyl ammonium salts of 1,4-phenylenediacetic acid and *p*-ethoxybenzoic acid were slightly modified from those described in the literature for other tetrabutyl ammonium salts [10]. ^{1}H NMR spectra were recorded on Bruker ARX 400, 500 and 600 spectrometers and mass spectra were obtained on IonSpec Ultima 7 T and Voyager-DE STR instruments. Elemental Analyses were done by Desert Analytics in Arizona. Chemical shifts for ^{1}H spectra were referenced relative to the solvent residual peaks.

General Procedures are as Follows

Receptor 1

150 mL of CH_3CN was added to **3** (110 mg, 0.11 mmol) and the suspension heated to effect complete dissolution. Cs_2CO_3(3.03 g, 9.3 mmol) was then added and the reaction mixture cooled to room temperature. This was followed by the addition of 2-bromomethyl-6-hydroxymethylpyridine (210 mg, 1.0 mmol) and the reaction mixture refluxed overnight. CH_3CN was removed in vacuo, the residue partitioned between 10% NaCl and $CHCl_3$ and stirred for approximately 1 h. The $CHCl_3$ extract was then dried with anhydrous Mg_2SO_4. The crude solid which was obtained following evaporation of the solvent, was washed with EtOH (3×15 ml) and dried to yield **1**(60 mg, 40 μmol, mol, 37.5%) as a cream-colored semi-crystalline solid. R_f 0.75 (7:3 ethylacetate/EtOH). ^{1}H NMR (DMSO-d_6, 400 MHz, 300 K): δ 2.49–2.65 (m, 16H, CH_2CH_2Ph), 4.39 (d, $J = 6.60$ Hz, 4H, inner OCH_2O), 4.65 (m, 4H, C*H* methine) 4.97 (s, 6H, pyCH_2OH), 5.00 (s, 2H, pyCH_2OH), 5.84–5.86 (m, 4H, outer OCH_2O), 7.16–7.22 (m, 24H, Ar*H* and C_6H_5), 7.36 (m, 4H, pyH_5), 7.52 (d, $J = 7.55$ Hz , 4H, pyH_3), 7.81 (m, 4H, pyH_4) O*H* protons are not observed. MS (MALDI-TOF) m/z 1501.7 $[M + H]^+$. Anal. Calcd. for $C_{92}H_{86}N_4O_{17}$ (**24**·H_2O): C, 72.71; H, 5.70; N, 3.63. Found: C, 72.55; H, 6.25; N, 3.98.

Receptor 2

20 mL of CF_3COOH was added to a RBF containing **1** (20 mg, 13 μmol). The reaction mixture was stirred for approximately 2 h. Removal of CF_3COOH under reduced pressure and an extended period of vacuum drying yielded **2** as a colorless oil. ^{1}H NMR (DMSO-d_6, 400 MHz, 300 K): δ 2.49–2.65 (m, 16H, CH_2CH_2Ph), 4.38 (d, $J = 7.52$ Hz, 4H, inner OCH_2O), 4.65 (m, 4H, C*H* methine), 5.04 (s, 8H, pyCH_2OH), 5.85–5.87 (m, 4H, outer OCH_2O), 7.16–7.22 (m, 20H, C_6H_5), 7.37 (s, 4H, Ar*H*), 7.48 (m, 4H, pyH_5), 7.54 (d, $J =$ 7.49 Hz, 4H, pyH_3), 7.95 (m, 4H, pyH_4) O*H* protons are not observed. ^{19}F NMR (DMSO-d_6, 400.1 MHz, 300 K): δ −75.3 (s, 12 H, $CF_3CO_2^-$).

RESULTS AND DISCUSSION

Design and Synthesis

Detailed structures of **1** and **2** were obtained via a Monte Carlo conformational search of highly symmetrical energy-minimized starting geometries using the OPLS force field and the GB/SA solvation model for water (closest in dielectric constant to DMSO, the solvent of choice for complexation studies) in Macromodel [8]. For computational simplicity, the pendant $C_6H_5CH_2CH_2$ groups in both **1** and **2** were replaced with methyl groups.

The global minimum of **1** is shown in Figure 3. To the resorcinarene base are attached four CH_2pyCH_2OH appendages leading to a structure of dimensions 12.5 Å × 8.6 Å. These appendages are quite flexible due to the fact that each contains three rotatable C-O-CH_2-py

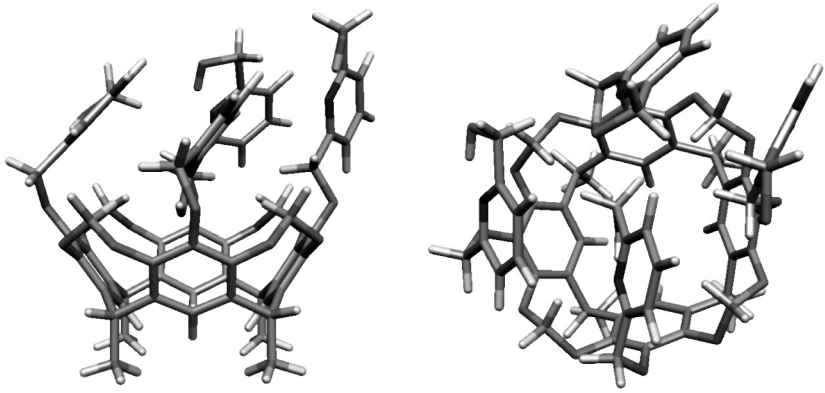


FIGURE 3 Side (left) and top (right) views of the global minimum of **1**.

bonds. Dihedral angles centered at the O-CH_2 bond (Ar-***O-CH$_2$***-py) range from 58.9° to 188.7°. All four benzene rings have electron pairs on the three adjacent oxygen atoms projected towards the outside of the cavity and the CH_2 groups projected inwards termed an 'in-in-in' conformation. The angle which the oxygen atom forms with the benzene ring and the CH_2 group in each appendage ranges from 117.3° to 151.6°. It is the flexible nature of these appendages which gives the cavity its irregular shape.

The pyridine moieties are tilted, and the nitrogen atoms point towards the inside of the cavity. Two of these moieties benefit from π—π stacking as the distance between carbons in position 4 of the phenyl ring is 4.1 Å. The pyridine moieties are also stabilized by multiple CH—π interactions from both the resorcinarene base and neighboring pyridine moieties. The lone pair on the N atom in each pyridine moiety participates in hydrogen bonding with the hydroxyl group forming five-membered rings. Hydrogen bond distances (N $\cdots$ H-O) range from 1.47 to 1.55 Å. Other higher energy conformers were found at values ranging between 1 and 28 kJ/mol from the global minimum in which rotation of the C-O-CH_2-py bonds (as demonstrated by the dihedral angles centered at the O-CH_2 bond and the Ar-O-CH_2 angles) varied.

The general picture of the global minimum of **1** appears to be one in which the appendages conglomerate in the hydrophobic cavity of the molecule so as not to be exposed to the solvent. This is in contrast to the global minimum of **2** (Fig. 4) in which the appendages turn outwards to the hydrophilic surroundings allowing for the $(N\text{-}H)^+$ centers to spread as far apart as possible. A complex of C_{4v} symmetry results if the minor tilting/rotating of the appendages is ignored.

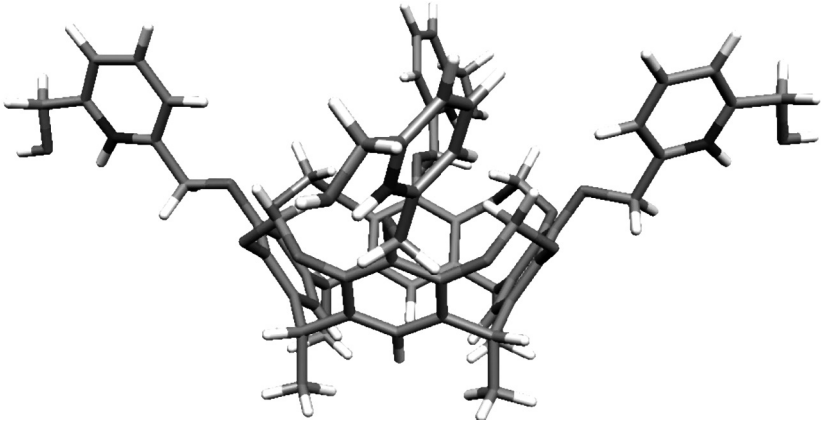


FIGURE 4 Side view of the global minimum of **2**.

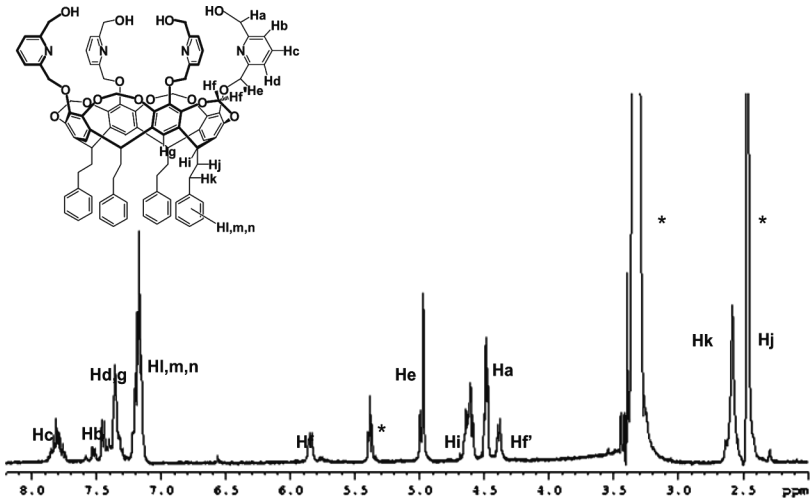
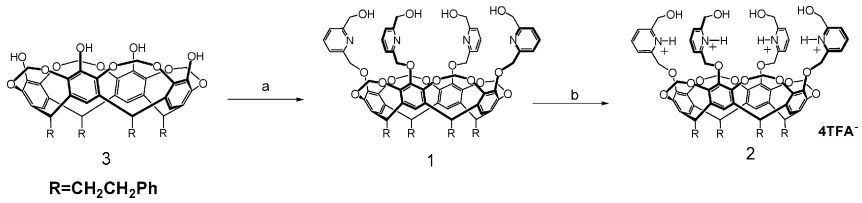


FIGURE 5 ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of **1**. The peak ascribed to the methine protons, Hi, is buried underneath the ethanol solvent peak at 4.65 ppm, and the peak ascribed to the Hj protons is buried underneath the solvent residual peak at 2.49 ppm. The peaks labeled with asterisks are those due to residual solvent.

Dihedral angles in the appendages centered at the O-CH_2 bond (Ar-***O-CH$_2$***-py) range from 161.0° to 178.0°. All four benzene rings have CH_2 groups on the bridge in an 'in-out-in' conformation where the CH_2 group in the appendage is projected outwards and the two adjacent CH_2 groups are projected towards the inside of the cavity. The angles which the oxygen atoms form with the benzene rings and the CH_2 groups in each appendage range from 115.4° to 116.1°. The $(N\text{-}H)^+$ centers participate in hydrogen bonding with the hydroxyl groups resulting in the formation of five-membered rings. Hydrogen bond distances (N-H $\cdots$ O-H) range from 1.71 to 1.77 Å.

Tetrol (**3**) and 2-bromomethyl-6-hydroxymethylpyridine were refluxed overnight in the presence of Cs_2CO_3 in acetonitrile (Scheme 1). Monitoring of the reaction by TLC analysis revealed the disappearance of spots corresponding to the presence of starting materials (R_f values = 0.42 and 0.75 in 4:1 EA: CH_2Cl_2) substituted by the presence of a highly polar compound ($R_f = 0.09$). Subsequent work-up, EtOH washing of the solid and an extended period of drying afforded **1** as a cream-colored semi-crystalline solid in approximately 40% yield. The ^{1}H NMR spectrum of the crude reaction product in $CDCl_3$ supported the formation of **1** (Fig. 5). The general spectroscopic signatures of the cavitand were preserved: the triplet due to the methine group and the doublets resulting



SCHEME 1 a: 2-bromomethyl 6-hydroxymethylpyridine, Cs_2CO_3, CH_3CN, reflux, 8 h b: TFA, 2 h.

from the inner and outer methylene (O***CH₂***O) protons Hf and Hf. This was also true of both the aromatic and aliphatic protons of the phenethyl feet in the spectrum, which exhibit similar coupling patterns in similar locations as those of the starting tetrol. The key feature of this spectrum was the appearance of a singlet at 5.12 ppm assigned to the py***CH₂***OAr protons He, which as expected is shifted downfield from the Ar***CH₂***OAr singlet appearing at 4.95 ppm in a tetrachloride derivative with benzene moieties in the appendages [11]. The pyridine moiety exhibited a similar pattern as observed in 2-bromomethyl-6-hydroxymethylpyridine with complicated spin-spin coupling presumably due to the formation of either intramolecular or intermolecular hydrogen bonds.

With **1** in hand, the synthesis of **2** proved to be uncomplicated. We sought a way to prepare a pyridinium salt which could be isolated and used for complexation studies. For this purpose, the methodology employed by Rajakumar and Dhanasekaran to protonate the pyridyl units within a pyridinoimidazolophane was utilized [12]. We were especially hopeful about applying this methodology as this cyclophane contained two imidazolium groups, sure to decrease the propensity of pyridinium formation. Stirring **1** in neat TFA over a two-hour period, followed by removal of the TFA in vacuo and an extended period of vacuum drying resulted in the formation of **2**. The presence of **2** was confirmed by its ^{1}H and ^{19}F NMR spectra in DMSO-d_6. As shown in Figure 6 (a comparison of the ^{1}H NMR spectra of **1** and **2**) whereas the spectroscopic signatures of the cavitand are unaffected by the protonation, the pyridyl protons are shifted downfield illustrating the deshielding effect caused by the protonation step [13].

Acid Complexation

Receptor **1** contains a cyclic array of pyridine moieties and is suitable for complexation with small molecules containing hydrogen-bond donors such as acids. The binding properties of various acids

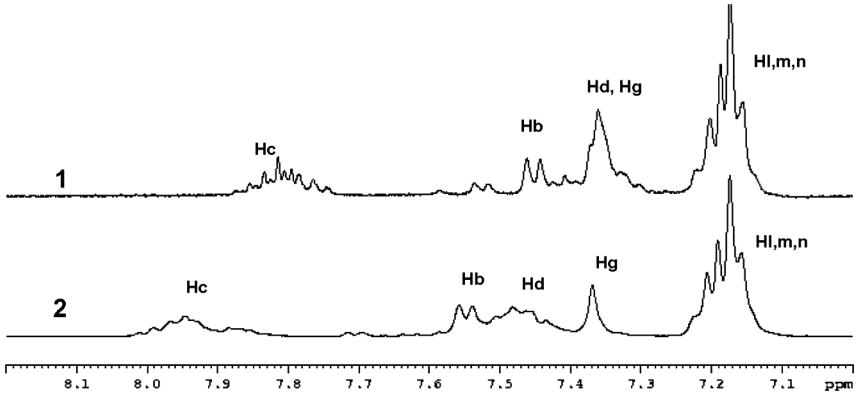


FIGURE 6 Partial ^{1}H NMR spectra (400 MHz, DMSO-d_6) of **1** and **2**.

were explored via molecular mechanics calculations and NMR titration studies. Potential substrates for NMR titration studies were screened on the basis of the complexes formed with receptor **1**

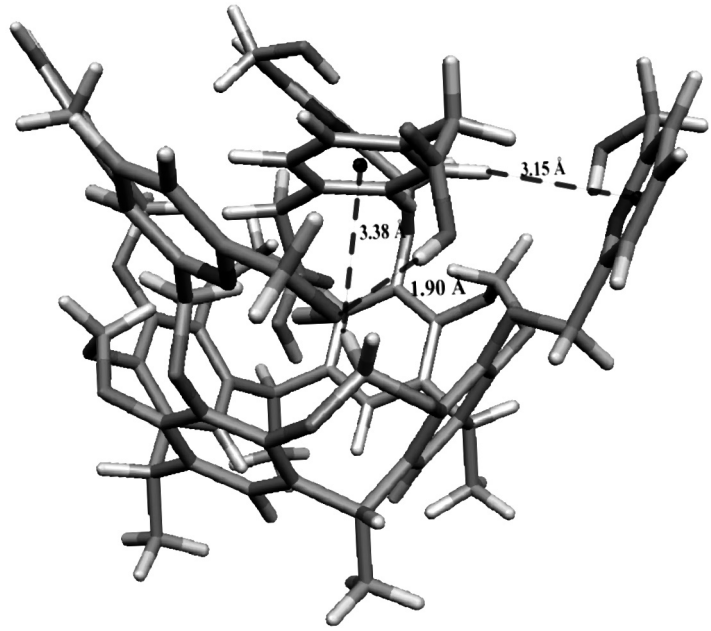


FIGURE 7 Calculated structure of the 1:1 complex between **1** and 1,4-phenylene diacetic acid.

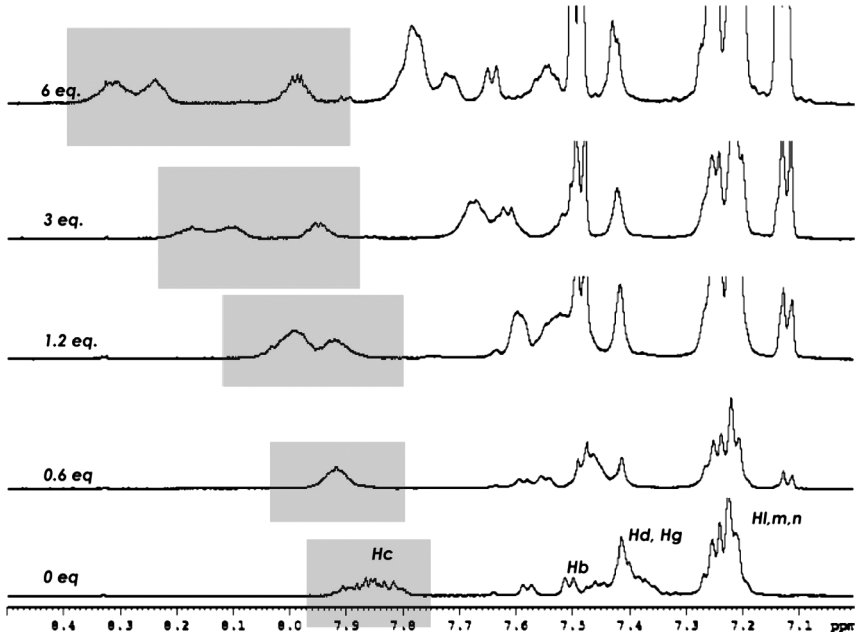


FIGURE 8 ^{1}H NMR titration (500 MHz, DMSO-d_6) of **1** with *p*-TsOH.

(obtained computationally) in terms of their size, shape and complexation energies.

- ***Molecular Mechanics Calculations***. A structure derived from the global minimum of **1** in which the appendages were removed from the cavity was used as the starting geometry for complexation studies. Its single point energy was calculated using the OPLS force field and the GB/SA solvation model for water (as its dielectric constant was closest to DMSO, the solvent of choice for NMR complexation studies) in MACROMODEL [8].

  The substrate was then placed inside the cavity, and the complexation energy was calculated according to the following equation:

$$\mathrm{E}_{\text{complexation}} = \mathrm{E}_{(\text{receptor-substrate complex})} - (\mathrm{E}_{(\text{receptor})} + \mathrm{E}_{(\text{substrate})})$$

- ***NMR Titration Studies***. To determine the binding properties of acids, NMR titration experiments were performed. A solution of **1** in DMSO-d_6(3.2 mM) was placed in an NMR tube and its spectrum recorded. The substrate (0.16 M) was then added to the NMR tube in 2 μL aliquots (0.2 equivalents), after each addition, its NMR spectrum recorded. Chemical shift changes that were dependent

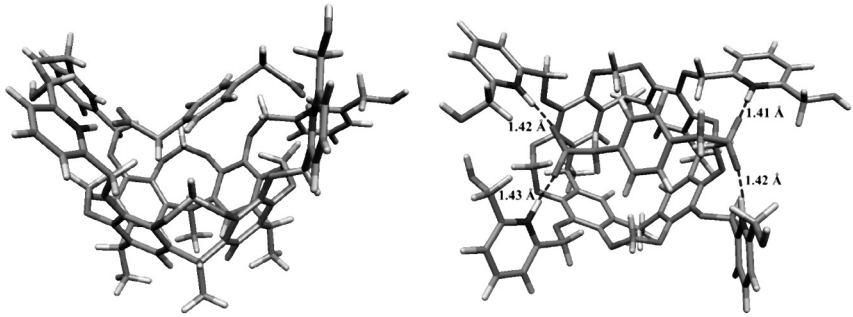


FIGURE 9 Top and side views of the calculated structure of the 1:1 complex between **2** and 1,4-phenylenediacetic acetate.

upon the substrate-receptor concentration were taken as evidence of complexation.

1,4-phenylene diacetic acid was explored as a prototype of this mode of complexation. Shown in Figure 7 is the calculated structure of **1** and 1,4-phenylene diacetic acid. Changes in the conformation of **1** upon complexation of the substrate are manifested in the dihedral angles centered at the O-CH_2 bond and the Ar-O-CH_2 angles. Ranges determined for these angles are 113.6–157.5° and 115.9–120.8° respectively. The five-membered rings resulting from hydrogen bonding between the lone pair of the N atom and the hydroxyl group are maintained in all pyridine moieties. Receptor-substrate stabilizing interactions come in the form of CH—π interactions between the benzene ring of the acid and the pyridine moiety as well as the resorcinarene base of **1**. The distance from a dummy atom placed at the center of the pyridine moiety to one of the aromatic hydrogen atoms of the acid was determined to be 3.15 Å. The distance from one of the hydrogen atoms of the resorcinarene base to a dummy atom placed at the center of the acid's benzene moiety was determined to be 3.38 Å. A distance of 1.90 Å between the H atom of one of the carboxylic groups and the O atom of the hydroxyl group was taken as evidence of hydrogen bonding between receptor **1** and the substrate.

The Proton Transfer Requirement

Molecular Mechanics calculations described above suggest that at least on the basis of size and shape 1,4-phenylene diacetic acid is an appropriate choice for complexation with **1**. That being the case,

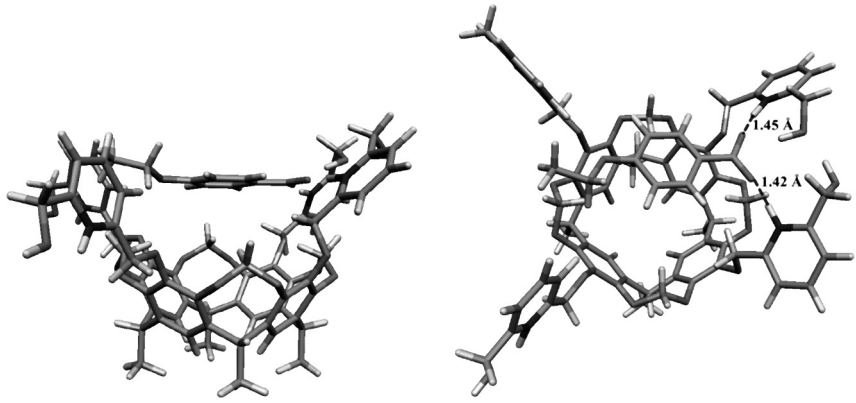


FIGURE 10 Top and side views of the calculated structure of the 1:1 complex between **2** and *p*-ethoxybenzoate.

then other factors which affect the binding of substrate to receptor must be considered. There are conflicting reviews as to whether proton transfer is a necessity for complexation between a receptor and substrate in which one has acidic sites and the other basic sites [7a,c,14]. To determine if proton transfer between receptor and substrate was a criterion for complexation in this system, NMR titration studies were performed with two substrates: 1,4-phenylenedioxy diacetic acid and *p*-TsOH. The first, 1,4-phenylene dioxydiacetic acid, an acid with similar structure but with lower pKa values than 1,4-phenylene diacetic acid and which on the basis of molecular mechanics calculations (complexation energy: $-37.5\,\mathrm{kJ/mol}$) was deemed to be an appropriate choice for complexation with **1**. The second, *p*-TsOH ($\mathrm{pKa} = 0.3$) although determined to be too small to form an optimized 1:1 complex with **1**, but which may form, for instance, a 2:1 complex and which contains benzene moieties which offer the advantage of possibly forming π—π stacking and CH—π interactions with **1**.

NMR titration studies indicated that complexation was observed between **1** and *p*-TsOH but not 1,4-phenylenedioxy diacetic acid. Shown in Figure 8, are the stacked NMR spectra depicting the changes which occur upon addition of incremental amounts of *p*-TsOH to **1**.

The only suitable spectroscopic probes for complexation were the protons at position 4 of the pyridine ring (labeled Hc) as all other protons on the pyridine ring were masked by the overlap of the aromatic

guest protons. General observations upon addition of incremental amounts of *p*-TsOH are as follows:

1. No changes in the substrate resonances are observed.
2. A downfield shift of the Hc protons is observed; other resonances of receptor **1** such as the inner and outer methylene and the methine protons are unaffected by the addition of *p*-TsOH.
3. Significant changes in the Hc protons are observed. Upon addition of 1.2 eq. of *p*-TsOH, the Hc protons formerly one singlet, now appear as two distinct singlets. Upon addition of 2.4 eq. the singlet appearing further downfield now appears as a doublet or as a set of overlapping singlets. All resonances shift further downfield upon addition of more *p*-TsOH. This downfield shift continues as more equivalents of *p*-TsOH are added, never reaching a maximum value even after the addition of 8 equivalents of *p*-TsOH.

No quantitative information could be extracted from this data set due to the difficulty in obtaining a tractable resonance to monitor complexation. Further attempts to assign these resonances will be made using 2D NMR experiments. Even after the addition of 4 equivalents of acid (the stoichiometic amount sure to ensure protonation of all pyridine units) three sets of resonances are seen for the Hc protons. The most plausible explanation would be the slow rates of complexation and decomplexation relative to the NMR timescale resulting in two distinct peaks for the Hc protons in the receptor-substrate complex and the receptor. This, however, does not account for the presence of a third set of protons. There is, most likely, a complex set of equilibria present owing in part to 2:1 substrate: receptor stoichiometry (higher order stoichiometries cannot be ruled out), the presence of protonated and unprotonated receptor molecules and protonated and deprotonated *p*-TsOH. This has been observed by Hamilton, Bowman-James and their co-workers in complexation studies with macrocycles containing both amine and amide sites and anions containing acidic protons, HSO_4^- and $H_2PO_4^-$ [15].

Anion Complexation

Receptor **2** contains a cyclic array of pyridinium moieties and is suitable for complexes small molecules containing hydrogen-bond acceptors such anions. The procedure used to evaluate complexation is analogous to that described for acid complexation except that molecular mechanics calculations involved the determination of binding energies and for NMR titration studies, substrates were

added in the form of concentrated DMSO solutions of their tetrabutylammonium salts.

- ***Binding Energy Determination***. The global minimum of **2** was used as the starting geometry for complexation studies. The substrate was docked inside the cavity and the structure reoptimized. The binding energy was determined to be the difference between the receptor-substrate complex and the average minimum energy resulting from the substrate being placed at distances which varied between 3.8 Å–9.0 Å from the starting geometry.

Shown in Figures 9 and 10 are the calculated structures of **2** and 1,4-phenylene diacetate and *p*-ethoxybenzoate. The global minimum of **2** (Fig. 4) contains appendages turned outwards, and upon binding substrate, the appendages turn inwards participating in $(N\text{-}H)^+ \cdots O$ (anion) hydrogen bonding interactions with the substrate. Four appendages turn inwards in the case of the dicarboxylate (Fig. 9) and two appendages turn inwards in the case of the monocarboxylate (Fig. 10). The average $(N\text{-}H)^+ \cdots O$ bond distance is 1.42 Å for the dicarboxylate and 1.44 Å for the monocarboxylate. Changes in the conformation of **2** upon complexation of the substrate are also manifested in the dihedral angles centered at the $O\text{-}CH_2$ bond and the $Ar\text{-}O\text{-}CH_2$ angles. Ranges determined for these angles are 155.2–169.4° and 116.1–120.1° for the monocarboxylate and 84.8–134.6° and 120.8–125.3° for the dicarboxylate. Additionally, multiple CH—π interactions exist between **2** and the substrates.

The stacked NMR spectra depicting the changes which occur upon addition of incremental amounts of the dicarboxylate are shown below (Fig. 11).

General observations upon addition of incremental amounts of 1,4-phenylene diacetate are as follows:

1. No changes in the substrate resonances are observed.
2. An upfield shift of the protons on the pyridyl unit (H_b, H_c, H_d) of the receptor is observed; other resonances of receptor **2** such as the inner and outer methylene and the methine protons are unaffected by the addition of the dicarboxylate.
3. The resonances of the Hb and Hd protons on the pyridyl unit become well-resolved upon binding. For example, upon addition of 0.4 eq. dicarboxylate the Hb protons appear as a well-resolved doublet of doublets.

The Hc protons on the pyridyl unit were used to obtain a quantitative assessment of carboxylate complexation (Table 1). Firstly, the 1:1

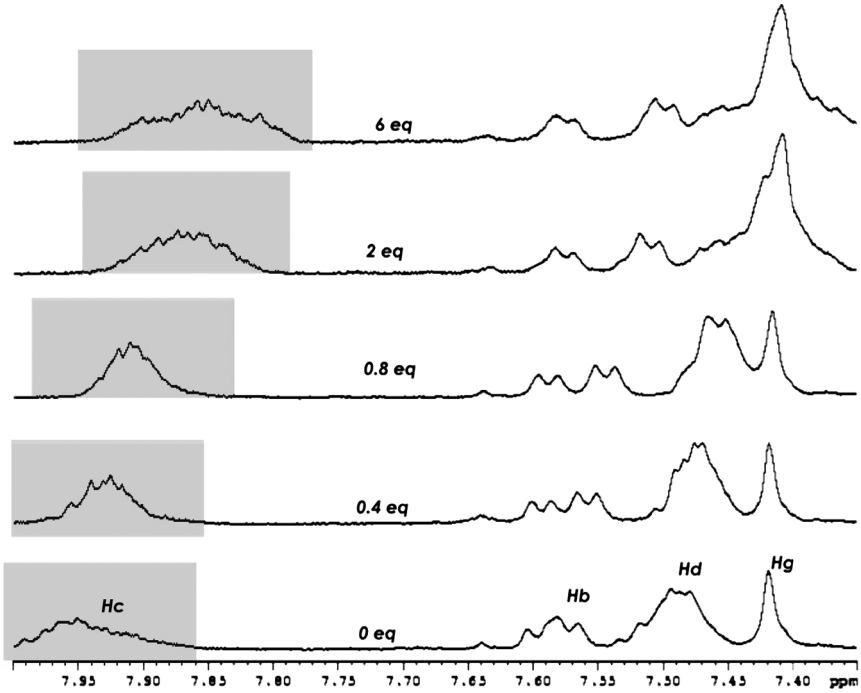
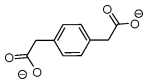
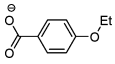


FIGURE 11 ^{1}H NMR titration (500 MHz, DMSO-d_6) of **2** with 1,4-phenylene-diacetate.

receptor: substrate stoichiometry shown in the calculated structures was confirmed experimentally by means of a Job Plot [16]: the maximum chemical shift of the Hc protons occurred when equimolar

TABLE 1 Quantitative Assessment of Carboxylate Complexation with **2**: Binding Energies and Constants in DMSO-d_6 at 25°C

Substrate[a]	$\Delta\delta_{max}$ (pyridyl proton)	Binding energy[b] kJ/mol	Binding constant[c] $(K_a)/M^{-1}$
	0.11	−237.7 (1.3)	150
	0.08	–198.4 (2.4)	80

[a]Carboxylates were added as concentrated DMSO-d_6 solutions of their tetrabutylammonium salts. [b]Maestro, OPLS force field, GB/SA H_2O, 4000 steps [c]obtained using the program NMRTit [17].

amounts of **2** and carboxylate were mixed. Favorable binding energies were obtained computationally for carboxylate complexation. Binding constants, albeit small, show very favorable thermodynamics for complexation in a highly competitive hydrogen-bonding solvent.

The general picture of complexation displayed in the calculated structures was confirmed experimentally. Anion recognition of receptor **2** takes place in its cyclic array of pyridinium moieties via $(N\text{-}H)^{+}\cdots O$ (anion) hydrogen bonding interactions with the substrates. Strong supporting evidence for these facts comes from the observed upfield shift of the protons of the pyridine moiety due to $(N\text{-}H)^{+}\cdots O$ (anion) hydrogen bonding and partial, if not complete proton transfer between receptor and substrate. The unchanged resonances of the substrate protons suggest that the substrate occupies the space encompassed by the cyclic array of pyridinium moieties and is not embedded in the resorcinarene cavity. If the substrate were embedded in the resorcinarene cavity, an upfield shift in the guest protons should have been observed.

CONCLUSION AND OUTLOOK

The design and syntheses of two novel receptor molecules has been described. These receptors are cavitand derivatives and contain pyridine moieties in their appendages. Receptor **1** was synthesized in a single step by means of the reaction of a tetrol cavitand derivative and excess of the precursor to the appendages at refluxing temperatures overnight. Receptor **2** was obtained by stirring receptor **1** in TFA for two hours.

Receptor **1**, contains a cyclic array of pyridine moieties and was found to display recognition properties towards acids but only if proton transfer between receptor and substrate was facilitated. Unfortunately, due to the complexity arising from several equilibria, further experimental work is necessary to abstract quantitative information from this data. Carboxylate recognition was displayed by receptor **2**, which contains a cyclic array of pyridinium moieties. The binding energies determined computationally for carboxylate complexation were very favorable. The binding constants obtained, albeit small, are quite respectable given that DMSO, a highly competitive hydrogen-bonding solvent used.

The screening of other small molecules, the attachment of chromophores and the synthesis of hemicarcerands will be the subject of future work.

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