

**A Glycoluril Dimer–Triptycene Hybrid Receptor: Synthesis  
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Journal:	<i>Organic &amp; Biomolecular Chemistry</i>
Manuscript ID	OB-ART-07-2018-001575.R1
Article Type:	Paper
Date Submitted by the Author:	17-Aug-2018
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Journal Name

FULL PAPER

## A Glycoluril Dimer–Triptycene Hybrid Receptor: Synthesis and Molecular Recognition Properties

Received 00th January 20xx,  
Accepted 00th January 20xx

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DOI: 10.1039/x0xx00000x

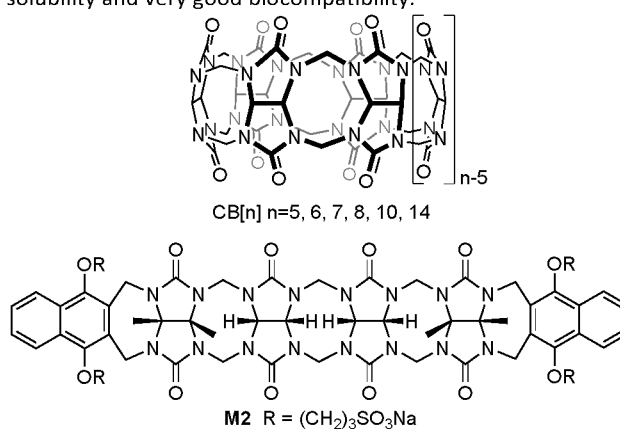
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The strategic combination of the methylene bridged glycoluril dimer and triptycene skeletons delivers acyclic water soluble hybrid receptor **1** which is analogous to cucurbit[6]uril. The molecular recognition properties of host **1** toward hydrophobic cationic guests are investigated in detail by a combination of <sup>1</sup>H NMR spectroscopy and isothermal titration calorimetry (ITC) studies. The fluorescence emission of **1** can be selectively and efficiently quenched upon the formation of **1•26** and **1•28** complexes.

### Introduction

One focal point in the field of supramolecular chemistry is the development of new macrocyclic compounds that function as receptors for complementary guest molecules in both organic and aqueous solution.<sup>1</sup> The goal of these studies is to deepen our understanding of the fundamental non-covalent interactions (e.g. H-bonds, hydrophobic effect, CH/π-π, electrostatic interactions) and utilize these new hosts to create complex and functional systems for advanced chemical or biological applications. Accordingly, a large body of work documents the preparation and application of numerous different macrocyclic host systems including cyclophanes, crown ethers, cyclodextrins, calixarenes, pillararenes, and self assembled systems.<sup>2</sup> We, and others, are particularly interested in the synthesis and supramolecular chemistry of cucurbit[n]urils (CB[n], n=5, 6, 7, 8, 10, 14, Figure 1)<sup>3</sup> largely due to their exceptionally high binding affinity ( $K_a$  up to  $10^{17}$  M<sup>-1</sup>).<sup>4</sup> CB[n] function as hosts for hydrophobic ammonium ions in water and display a confluence of intriguing properties including remarkably high binding affinity, high selectivity, and stimuli responsiveness.<sup>3a-d,4a,5</sup> Over the past decade, macrocyclic CB[n] and functionalized CB[n] derivatives have been employed to create a variety of functional systems

including molecular machines, chemical sensing ensembles, drug formulation and delivery systems, supramolecular polymers, frameworks, and materials.<sup>6</sup> Based on our synthetic and mechanistic knowledge of CB[n] formation, the Isaacs group designed and synthesized acyclic CB[n]-type receptors (e.g. **M2**, Figure 1) comprising a central glycoluril tetramer with aromatic sidewalls.<sup>3a,7</sup> Importantly, the polycyclic nature of acyclic CB[n]-type receptor **M2** preorganizes the system into a C-shape that retains the essential molecular recognition properties of macrocyclic CB[n] but with enhanced aqueous solubility and very good biocompatibility.



**Figure 1** Chemical structures of CB[n] and the prototypical acyclic CB[n]-type molecular container **M2**.

Accordingly, acyclic CB[n]-type receptors have been used as solubilizing excipients for insoluble drugs, pH triggered delivery agents, as *in vivo* reversal agents for neuromuscular blockers and a drug of abuse (methamphetamine), and as components of sensor arrays.<sup>7-8</sup> Taking inspiration from the pioneering work of Swager, Chen, and others,<sup>9</sup> we recently created an acyclic CB[n]-triptycene walled chimeric receptor that displayed intriguing self-association, self-folding, and molecular recognition properties toward very large compounds including Stoddart's (extended) blue box and Fujita's squares.<sup>10</sup> Related C-shaped receptors have also been

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<sup>†</sup> Electronic Supplementary Information (ESI) available: Details of synthesis, NMR, ITC, UV/Vis, and fluorescence experiments. See DOI: 10.1039/x0xx00000x

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studied by Klärner, Schrader, Yoshizawa, and Huang.<sup>2f,11</sup> In this paper, we continue along this line of inquiry by preparing an analogous host molecule (**1**) comprising a central methylene bridged glycoluril dimer unit along with two fluorescent triptycene sidewalls that we anticipated would strategically combine the recognition properties of CB[n]-type receptors with the intriguing properties of triptycene based hosts. Our expectation which was borne out experimentally was that **1** – based on the shorter glycoluril dimer – would be selective for narrower guests compared to **M2** which is selective for larger guests like cationic steroids.<sup>7f</sup>

## Results and Discussion

The synthesis of host **1** takes advantage of our well established building block method.<sup>12</sup> As the central glycoluril oligomer building block we choose the known bis(cyclic ether) **2** which can be prepared in three steps from butanedione, urea, and formaldehyde.<sup>13</sup> As the aromatic wall building block we selected **W1** which was prepared from anthracene, benzoquinone, and propanesultone as described in the literature.<sup>10,14</sup> The double electrophilic aromatic substitution reaction of **2** with **W1** was conducted in a 1:1 mixture of hot TFA and acetic anhydride. Host **1** was isolated in 44% yield after purification by gel permeation chromatography (Sephedex G25) and fully characterized spectroscopically. For example, the <sup>1</sup>H NMR spectrum of **1** (Figure 3a) displays a total of four Ar-H resonances for the two distinct *o*-xylylene blades of the triptycene sidewalls (H<sub>a</sub> – H<sub>d</sub>), a sharp singlet for the four symmetry equivalent triptycene methine (H<sub>e</sub>) protons, four resonances for the bridging methylene units (H<sub>i</sub>, H<sub>j</sub>, H<sub>m</sub>, H<sub>n</sub>) in the expected 4:4:2:2 ratio, three pairs of resonances for the diastereotopic methylenes of the (CH<sub>2</sub>)<sub>3</sub> linkers (H<sub>f</sub>/r', H<sub>g</sub>/g', H<sub>h</sub>/h'), and two CH<sub>3</sub> resonances (H<sub>k</sub> and H<sub>l</sub>). Host **1** is soluble up to at least 15 mM in water.

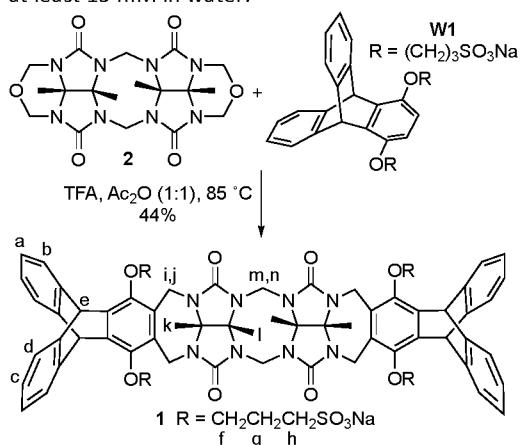


Figure 2 Synthesis of host **1**.

Before proceeding to investigate the molecular recognition properties of **1** we decided to perform <sup>1</sup>H NMR dilution experiments to check whether **1** undergoes self-association in water. At low concentrations (100 μM) a single set of resonances is seen (Figure 3a), however, as the concentration is raised to 12 mM H<sub>e</sub> is shifted upfield whereas new sets of

resonances are seen for H<sub>a</sub> – H<sub>d</sub> and H<sub>k</sub> – H<sub>l</sub> which indicates the presence of self-association. Figure 4 shows a plot of [1] versus the chemical shift of H<sub>n</sub> fitted to a 2-fold self-association model (Supporting Information) which allowed us to extract self-association constant K<sub>s</sub> = 507 ± 62 M<sup>-1</sup>.<sup>15</sup> Accordingly, we concluded that **1** remains monomeric in water at low concentrations and qualitatively and quantitatively investigated its molecular recognition properties.

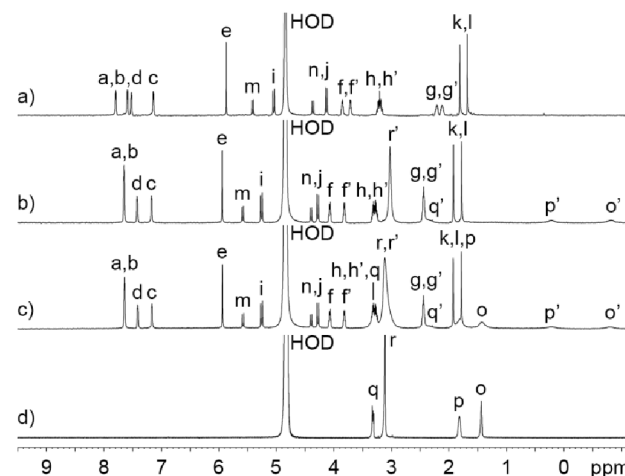


Figure 3 <sup>1</sup>H NMR spectra recorded (400 MHz, D<sub>2</sub>O) for: a) receptor **1**, b) **1** and **12** (1:1 mixture), c) **1** and **12** (1:2 mixture), d) guest **12**.

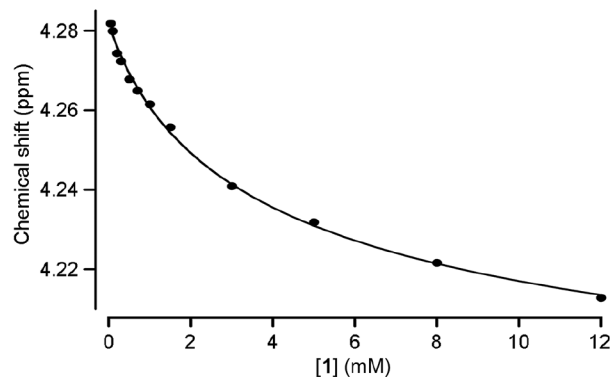
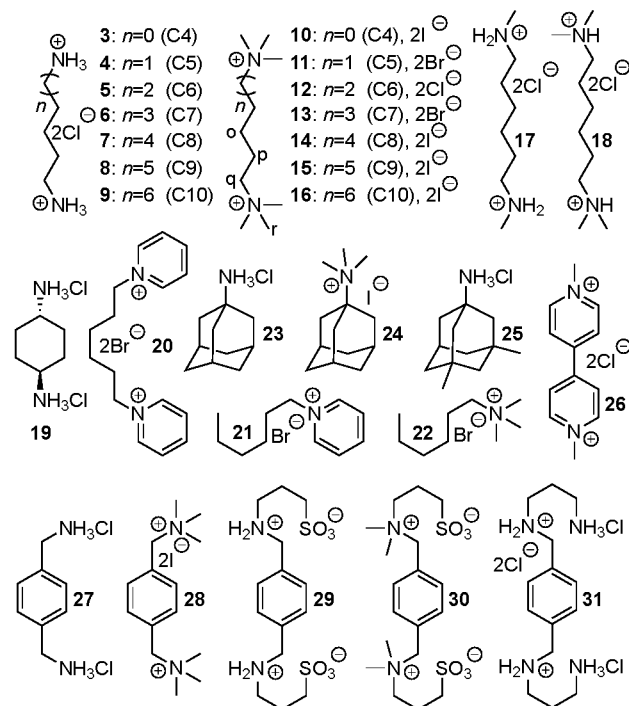


Figure 4 Plot of chemical shift of H<sub>n</sub> versus [1] used to determine the self-association constant K<sub>s</sub> = 507 ± 62 M<sup>-1</sup> for **1**.

First, we qualitatively investigated the recognition properties of **1** toward ammonium ion **12** (Figure 5) by <sup>1</sup>H NMR spectroscopy. Figure 3a-c shows the <sup>1</sup>H NMR spectra recorded for receptor **1** in the absence and presence (1 equiv. and 2 equiv.) of guest **12**. As can be readily seen, protons H<sub>a</sub> and H<sub>p</sub> of guest **12** are substantially upfield shifted upon the formation of **1**•**12** complex, indicating their locations inside the magnetic shielding cavity of **1**. Proton H<sub>q</sub> adjacent to the N-atoms undergoes less sizable upfield shifts suggesting that it is also located inside the cavity but closer to the C=O portals of receptor **1**.<sup>3c,16</sup> Proton H<sub>r</sub> undergoes negligible shifts because it is located outside the cavity of receptor **1**. Figure 3c shows separate resonances for **1**•**12** and excess free guest **12** which establishes slow exchange kinetics on the chemical shift time

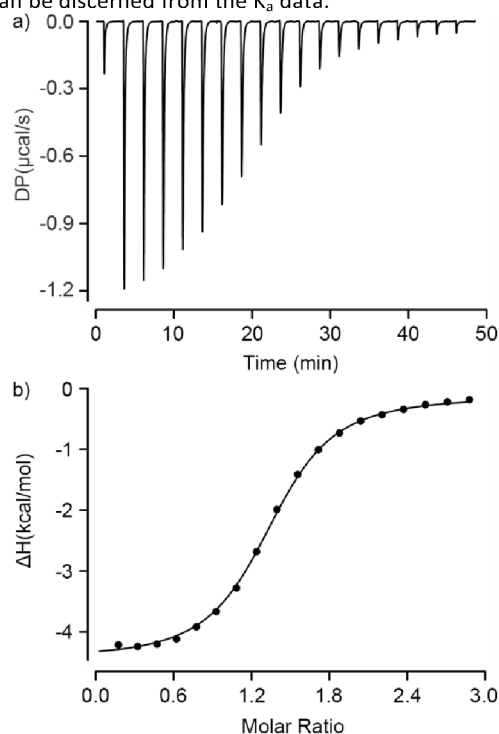
scale which is typically observed for higher affinity complexes.<sup>3c,17</sup> Analogous <sup>1</sup>H NMR titrations were performed between receptor **1** and a series of guests (**5**, **12**, **19**, **23**, **25**, **26**) to qualitatively probe the binding capacity of host **1** (Supporting Information). We find that receptor **1** is able to induce upfield <sup>1</sup>H NMR shifts indicative of cavity binding of guests derived from *n*-alkanes, *p*-substituted aromatics (e.g. methyl viologen **26**) and cyclohexane (e.g. **19**) but not adamantanes **23** or **25**.



**Figure 5** Chemical structures of guests used in this study.

With the basic binding properties of receptor **1** in mind, we then turned our attention to quantitative  $K_a$  measurements. Figure 5 shows the full range of guests (**3** - **31**) that were studied. Compounds **3** - **31** were specifically selected to probe the influence of guest size, guest charge, diammonium guest length, nature of head group ( $1^\circ$  -  $4^\circ$  ammonium, pyridinium), and secondary electrostatics. We elected to use ITC for these measurements because ITC is sensitive enough to allow the use of low concentrations of **1** (100  $\mu$ M) where dimerization will not impinge upon the planned  $K_a$  measurements. Figure 6 shows the ITC thermograms recorded during the titration of receptor **1** (100  $\mu$ M) with guest **11** (0 - 288  $\mu$ M). The  $K_a$  and  $\Delta H$  values for **1**•**11** complex are determined to be  $(2.28 \pm 0.3) \times 10^5 \text{ M}^{-1}$  and  $-4.34 \pm 0.04 \text{ kcal mol}^{-1}$  by fitting the data with the single set of sites model within the MicroCal PEAQ-ITC analysis software.  $K_a$  values for most of the guests were determined in an analogous manner by direct ITC titration (Supporting Information, Table 1).  $K_a$  values for the strongest binders (e.g. **18**) with  $K_a > 10^6 \text{ M}^{-1}$ , were measured by ITC competition assays using **27** as the competitor to obtain most accurate results.<sup>18</sup> A perusal of Table 1 shows that **1** is a tight binding

and somewhat selective host with  $K_a$  values ranging from too low to be determined (e.g. adamantane **25**) to weak ( $K_a = 3290 \text{ M}^{-1}$  for cyclohexane diammonium **19**) to quite strong ( $K_a = 1.03 \times 10^7 \text{ M}^{-1}$  for **18**). Below we discuss in more detail the trends that can be discerned from the  $K_a$  data.



**Figure 6** a) ITC thermogram recorded during the titration of receptor **1** (100  $\mu$ M) in the cell with guest **11** (1.5 mM) in the syringe, b) Fitting of the data to a 1:1 binding model with  $K_a = (2.28 \pm 0.3) \times 10^5 \text{ M}^{-1}$ .

**Table 1** Binding constants ( $K_a$ ,  $\text{M}^{-1}$ ) measured for the different host•guest (H•G) complexes (298 K, 20 mM  $\text{NaH}_2\text{PO}_4$  buffered water, pH 7.4).

H•G	$K_a$ ( $\text{M}^{-1}$ )
<b>1</b> • <b>3</b>	$(4.47 \pm 0.75) \times 10^{3[\text{a}]}$
<b>32</b> • <b>3</b>	$70 \pm 8^{[\text{d}]}$
<b>1</b> • <b>4</b>	$(1.23 \pm 0.05) \times 10^{5[\text{a}]}$
<b>1</b> • <b>5</b>	$(8.81 \pm 0.59) \times 10^{5[\text{a}]}$
<b>32</b> • <b>5</b>	$(6.98 \pm 0.1) \times 10^{2[\text{d}]}$
<b>1</b> • <b>6</b>	$(7.11 \pm 0.32) \times 10^{5[\text{a}]}$
<b>1</b> • <b>7</b>	$(6.27 \pm 0.41) \times 10^{5[\text{a}]}$
<b>32</b> • <b>7</b>	$(4.43 \pm 0.1) \times 10^{2[\text{d}]}$
<b>1</b> • <b>8</b>	$(5.23 \pm 0.34) \times 10^{5[\text{a}]}$
<b>1</b> • <b>9</b>	$(3.7 \pm 0.16) \times 10^{5[\text{a}]}$
<b>32</b> • <b>9</b>	$(3.50 \pm 0.1) \times 10^{2[\text{d}]}$
<b>1</b> • <b>10</b>	$(1.56 \pm 0.15) \times 10^{4[\text{a}]}$
<b>1</b> • <b>11</b>	$(2.28 \pm 0.13) \times 10^{5[\text{a}]}$
<b>1</b> • <b>12</b>	$(1.26 \pm 0.09) \times 10^{6[\text{a}]}$
<b>33</b> • <b>12</b>	$(2.6 \pm 0.4) \times 10^{7[\text{d}]}$
<b>1</b> • <b>13</b>	$(1.83 \pm 0.14) \times 10^{6[\text{b}]}$
<b>1</b> • <b>14</b>	$(2.27 \pm 0.13) \times 10^{6[\text{b}]}$
<b>1</b> • <b>15</b>	$(1.44 \pm 0.06) \times 10^{6[\text{b}]}$

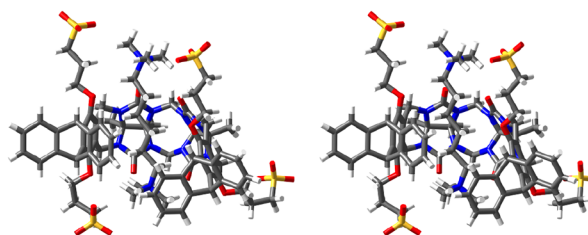
<b>1•16</b>	$(6.79 \pm 0.48) \times 10^{5[a]}$
<b>1•17</b>	$(5.86 \pm 0.27) \times 10^{6[b]}$
<b>1•18</b>	$(1.03 \pm 0.13) \times 10^{7[b]}$
<b>1•19</b>	$(3.29 \pm 0.71) \times 10^{3[a]}$
<b>32•19</b>	$57 \pm 5^{[d]}$
<b>1•20</b>	$(7.84 \pm 0.46) \times 10^{6[b]}$
<b>1•21</b>	$(6.18 \pm 0.2) \times 10^{4[a]}$
<b>1•22</b>	$(3.41 \pm 0.5) \times 10^{4[a]}$
<b>1•23</b>	–
<b>33•23</b>	$(1.4 \pm 0.1) \times 10^{6[d]}$
<b>1•24</b>	$(1.04 \pm 0.16) \times 10^{4[a]}$
<b>1•25</b>	n.b.
<b>1•26</b>	$(2.60 \pm 0.25) \times 10^{6[b]}$ $(1.41 \pm 0.18) \times 10^{6[c]}$
<b>32•26</b>	$(2.81 \pm 0.2) \times 10^{5[d]}$
<b>33•26</b>	$(2.8 \pm 0.4) \times 10^{7[d]}$
<b>1•27</b>	$(7.1 \pm 0.23) \times 10^{4[a]}$
<b>32•27</b>	$(1.89 \pm 0.1) \times 10^{4[d]}$ $(2.58 \pm 0.1) \times 10^{6[b]}$
<b>1•28</b>	$(1.09 \pm 0.18) \times 10^{6[c]}$
<b>1•29</b>	$(1.26 \pm 0.06) \times 10^{4[a]}$
<b>1•30</b>	$(4.93 \pm 0.13) \times 10^{4[a]}$
<b>1•31</b>	$(2.37 \pm 0.05) \times 10^{5[a]}$
<b>32•31</b>	$(4.48 \pm 1.2) \times 10^{4[d]}$

Measured by [a] direct ITC titration, [b] ITC competition assay using **27** as competitor, [c] Fluorescence titration. – = not determined, n.b. = no binding detected by  $^1\text{H}$  NMR. [d] Data from the literature.<sup>10,16</sup>  $K_a$  values for **33** measured in  $\text{H}_2\text{O}$ .

**Influence of Guest Size.** First, we decided to examine the influence of guest size / cross-section on their binding affinity toward host **1**. For example, within the ammonium ion series, we observe that narrow butanediammonium ion ( $K_o = 4.47 \times 10^3 \text{ M}^{-1}$ ) binds to **1** slightly stronger than the wider guest cyclohexylammonium ion **19** ( $K_o = 3.29 \times 10^3 \text{ M}^{-1}$ ); even wider adamantaneammonium ion **23** which is an excellent guest for acyclic CB[n]-type receptor **M2** and CB[7] is rejected by **1**. Within the quaternary ammonium ion series of guests, we observe that guests **12**, **26**, and **28** which feature alkane and *p*-phenylene derived binding epitopes complex with comparable affinity ( $K_a \approx 10^6 \text{ M}^{-1}$ ) whereas adamantane derived guest **24** binds significantly ( $\approx 100$ -fold) more weakly. We recognize that **24** is a monoammonium ion, whereas **12**, **26**, and **28** are diammonium ions. However, the adamantane skeleton is highly complementary to macrocyclic CB[n] and glycoluril tetramer based acyclic CB[n] where it binds as well as alkane and *p*-phenylene based dications.<sup>13,19</sup> Accordingly, the decrease in binding affinity seen for **24** likely reflects a combination of two factors. First, the cavity of **1** can only accommodate **24** after an energetically costly flexing of its three sets of methylene bridges; the  $\text{CH}_3$  groups on the convex face of **1** would be expected to increase this energetic cost relative to **M2**.<sup>8a,20</sup> Second, the cavity of **1** is shaped by four aromatic rings and only two glycolurils. Accordingly, the recognition behavior of **1** reflects a weighted blend of these

structural elements and therefore has a lower preference for the adamantane skeleton. Based on all this evidence we conclude that host **1** is most complementary to alkane derived dicationic guests but that guests with slightly wider *p*-phenylene and cyclohexane binding epitopes can be readily encapsulated by conformational flexing of **1** but that larger guests like adamantane derivatives are less able to pay the energetic costs to expand the cavity of **1**.

**Influence of Chain Length.** Macrocyclic CB[6] is well known to display a preference to bind to pentane and hexane derived diammoniums **4** and **5** over shorter and longer guests.<sup>4b</sup> Accordingly, we measured the  $K_a$  values for two chain length series of ammonium guests (1° ammonium: **3** – **9**, 4° ammonium **10** – **16**) as given in Table 1. Similar to CB[6], **1** displays a 197-fold preference for hexanediammonium **5** ( $K_o = 8.81 \times 10^5 \text{ M}^{-1}$ ) over butanediammonium **3** ( $K_o = 4.47 \times 10^3 \text{ M}^{-1}$ ) and a similar 81-fold preference for **12** ( $K_o = 1.26 \times 10^6 \text{ M}^{-1}$ ) over **10** ( $K_o = 1.56 \times 10^4 \text{ M}^{-1}$ ).<sup>21</sup> Unlike CB[6], receptor **1** binds the longer primary ammonium ion guests **6** – **9** (and **13** – **16**) with  $K_a$  values comparable to **5** (**12**) indicating that **1** is a tight binding host irrespective of guest length. A similar trend was observed previously for an acyclic CB[n]-type receptor based on glycoluril tetramer<sup>13</sup> which can be attributed to the flexibility of the acyclic CB[n] framework and the fact that the sulfonate solubilizing groups provide the possibility of compensating electrostatic interactions (e.g. ammonium-sulfonate) further away from the cavity. Figure 7 shows a stereoview on an MMFF minimized model of the **1•12** complex that shows that one quaternary ammonium sits at the C=O portal of **1** whereas the second extends toward the sulfonate solubilizing groups. Another noteworthy observation for methylated alkanediammonium guests **10–16** is that **1** shows higher affinity toward **14** ( $K_o = 2.27 \times 10^6 \text{ M}^{-1}$ ) with an octane chain instead of hexane derived guest hexamethonium (**12**,  $K_o = 1.26 \times 10^6 \text{ M}^{-1}$ ).  $^1\text{H}$  NMR spectra recorded for the **1•14** complex shows four upfield shifted resonances for the alkane chain of **14** (Supporting Information). This observation suggests either that the entire  $(\text{CH}_2)_8$  chain is wound up inside the cavity of **1** enabled by a flexing<sup>13,22</sup> at the pairs of bridging methylenes of **1** or that there is a fast shuttling between two equivalent conformations. Given the model shown in Figure 7 and the guest size trends (*vide infra*) we favor the latter explanation.



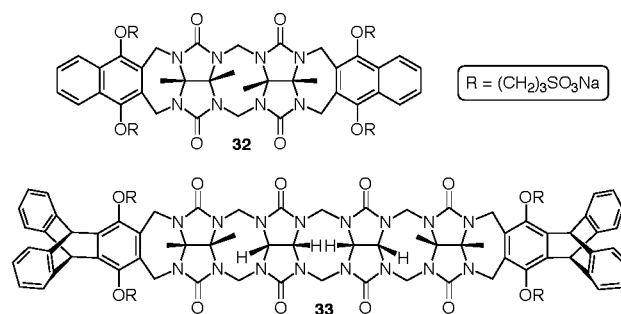
**Figure 7** Cross eyed stereoview of an MMFF minimized model of the **1•12** complex. Color code: C, grey; H, white; N, blue; O, red.

**Influence of the Cationic Head Group.** Binding affinities of host **1** toward primary alkanediammonium guests **3** – **9** are smaller than those of the corresponding quaternary ammonium guests **10**–**16**. For example, **1** binds to hexamethylbutanediammonium **10** ( $K_a = 1.56 \times 10^4 \text{ M}^{-1}$ ) about 3.5-fold stronger than to the primary ammonium **3** ( $K_a = 4.47 \times 10^3 \text{ M}^{-1}$ ). Similarly, **28** binds 36-fold more tightly than **27** toward **1** whereas **30** binds 3.9-fold more tightly than **29** toward **1**. Such preference for quaternary ammoniums has been seen previously for macrocyclic CB[n] hosts.<sup>4a,23</sup> To further investigate the influence of head group on binding affinity toward **1** we studied the corresponding secondary and tertiary ammonium ion guests **17** and **18**. We find that tertiary ammonium ion **18** ( $K_a = 1.03 \times 10^7 \text{ M}^{-1}$ ) is the tightest binder toward **1** among guest **5**, **12**, **17**, **18** with the same chain length with a difference of 12-fold between weakest and tightest. The detailed reasons for the selectivity among guests **5**, **12**, **17**, and **18** remain unclear, but are likely related to the changes in the number of N-H...O=C H-bonds and increased steric interactions as the guest is methylated. Interestingly, guest **20** with pyridinium head groups is one of the strongest binders with  $K_a = 7.84 \times 10^6 \text{ M}^{-1}$ .

**Influence of Guest Charge.** To gain insight into the relative importance of electrostatic interactions versus the hydrophobic effect as driving force for complexation inside host **1** we decided to compare analogous guests that differ in overall charge. For this purpose we selected monocationic guests **21** and **22** and compared their binding with dicationic guests **12** and **20**. We find that host **1** binds **12** 37-fold more tightly than **22** and that **20** 127-fold more tightly than **21**. We interpret this to mean that a substantial portion of the binding affinity of **1** toward diamines can be attributed to electrostatic (e.g. ion-dipole or ion-ion) interactions.

**Influence of Secondary Electrostatic Interactions.** To estimate the importance of secondary electrostatic interactions between the sulfonate ions of the host and the guest ions, we selected two guest series: **29** (neutral, zwitterion), **27** (dication), and **31** (tetracation) as well as **30** (neutral, zwitterion) and **28** (dication) and that contain a common *p*-xylylene diammonium binding epitope with arms containing sulfonates or ammonium ions. As expected, compared to dicationic guest **27** ( $K_a = 7.1 \times 10^4 \text{ M}^{-1}$ ), the tetracationic guest **31** ( $K_a = 2.37 \times 10^5 \text{ M}^{-1}$ ) binds 3.3-fold stronger, and the neutral zwitterionic guest **29** ( $K_a = 1.26 \times 10^4 \text{ M}^{-1}$ ) binds 5.6-fold weaker. Similarly, dicationic **28** binds 52-fold stronger than neutral zwitterion **30**. We attribute these differences to the presence of favorable ammonium–sulfonate secondary electrostatic interactions for **1**•**31** and destabilizing sulfonate–sulfonate interactions for **29**. The magnitude of these differences are smaller than those observed when comparing monocations versus dications (**20** versus **21** and **12** versus **22**, *vide supra*) which supports our contention that the interactions of the ammonium ions at the ureidyl C=O portals are the primary driving force for the interactions whereas the

ion-ion interactions remote from the cavity constitute secondary driving forces.

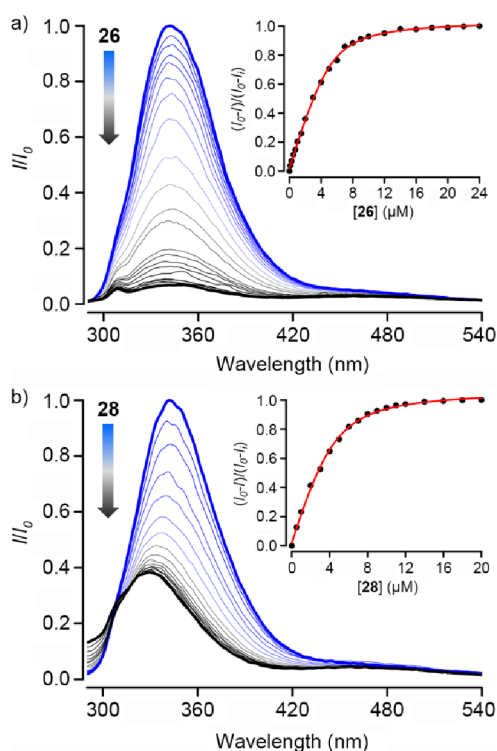


**Figure 8** Chemical structures of comparison hosts **32** and **33**.

**Comparison with Related Hosts.** Although we have studied acyclic CB[n]-type hosts extensively as solubilizing agents for insoluble drugs and as *in vivo* reversal agents, we have not routinely performed systematic binding studies.<sup>7,8c,8f</sup> Accordingly, only a limited set of comparative  $K_a$  values are available in the literature for hosts **32** and **33** (Table 1) that differ in the nature of the aromatic sidewall (e.g. **32** has a naphthalene rather than a triptycene sidewall) and the central glycoluril oligomer (e.g. **33** has a central tetramer rather than a glycoluril dimer). The data in Table 1 shows that host **1** is a much better host ( $\approx 10^2 - 10^3$ -fold) for alkanediammoniums **3**, **5**, **7**, **9**, and **19** than host **32** which is unsurprising given the coplanar nature of the naphthalene sidewalls of **32** which makes **32** selective for aromatics.<sup>16</sup> Host **1** also binds aromatic guests **26**, **27**, and **31** more strongly (4 – 10-fold) than **32** does, probably because the triptycene walls of **1** result in a more fully formed cavity rather than a cleft like receptor cavity. Comparison between the two triptycene walled hosts **1** and **33** shows that the **33** binds  $\approx 10$ -fold tighter toward alkanediammonium **12** and methyl viologen **26** and significantly stronger toward cationic adamantanes (e.g. **23** or **24**). This result is in accord with our previous results on drug solubilization which showed that solubilization efficiency and  $K_a$  values increased as the length of the glycoluril oligomer increases.

**Optical Properties of **1** and its Complexes.** Given that triptycene has been extensively studied as a fluorophore for the preparation of fluorescent materials and for fluorescence sensors and our experience with analogous systems based on glycoluril tetramer, we sought to study the optical properties of receptor **1**.<sup>9a-c,24</sup> Host **1** displays a UV/Vis absorbance maximum at 215 nm ( $\epsilon = 9.8 \times 10^4 \text{ M}^{-1} \text{ cm}^{-1}$ ) and a fluorescence emission maximum at 343 nm. Figure 9 shows the fluorescence spectra that were recorded when a solution of **1** ( $10 \mu\text{M}$ ) was treated with solutions of guests **26** and **28**. In both cases, we observe quenching of host fluorescence upon formation of the **1**•**26** and **1**•**28** complexes. The insets to figure 8 show the nonlinear least-squares best fits of the data to a standard 1:1 binding model within Scientist<sup>TM</sup> which deliver  $K_a = 1.41 \times 10^6 \text{ M}^{-1}$  and  $1.09 \times 10^6 \text{ M}^{-1}$  for **1**•**26** and

**1**•**28** complexes, respectively, which is in accord with our ITC measurements (Table 1). The quenching of the fluorescence of **1** by **26** is particularly efficient, presumably because of photoinduced electron transfer from the excited state of **1** to viologen guest **26**. Furthermore, the emission spectrum of **1**•**28** shows a maximum at 330 nm which represents a 13 nm hypsochromic shift relative to uncomplexed **1**. The fluorescence behavior of **1** (10  $\mu$ M) in the presence of 2 equiv. guests **5**, **12**, **23**, **24**, and **27** are shown in the Supporting Information. The fluorescence intensity of these **1**•guest complexes increases and is hypsochromically shifted. We attribute these spectral changes to guest induced changes in the spatial orientation of the two triptycene sidewalls upon guest binding. Swager and co-workers have pioneered the use of conjugated triptycene derived systems for the sensing of nitroaromatics.<sup>9a,9b</sup> Host **1** may offer similar opportunities to create fluorescence sensors for hydrophobic cations and especially viologens and related pyridinium species that are present in a variety of chemical and biological systems.



**Figure 9** Fluorescence spectra of receptor **1** (10  $\mu$ M) at 25  $^{\circ}$ C in water upon addition of incremental amounts of: a) **26** (0 - 24  $\mu$ M) and b) **28** (0 - 20  $\mu$ M),  $\lambda_{\text{ex}} = 278$  nm. Insets: Normalized titration isotherm corresponding to the guest-induced change of fluorescence intensity at maximum wavelength.

### Conclusions

In conclusion, we synthesized a new acyclic CB[n]-type receptor **1** bearing two triptycene derived aromatic sidewalls. Host **1** undergoes weak self-association ( $K_s = 507 \pm 62$   $\text{M}^{-1}$ ) as determined by  $^1\text{H}$  NMR dilution experiments. Detailed  $^1\text{H}$  NMR and ITC titrations reveal that **1** is able to encapsulate hydrophobic cationic guests that are typical CB[n] binders and displays similar host-guest properties to acyclic CB[n]-type

receptors based on glycoluril tetramer. Receptor **1** exhibits a strong UV/Vis absorbance at 215 nm ( $\epsilon = 9.8 \times 10^4$   $\text{M}^{-1}\cdot\text{cm}^{-1}$ ) and a fluorescence emission maximizing at 343 nm which can be selectively and efficiently quenched by guest **26** due to photo-induced electron transfer. We expect that receptor **1**, with its high fluorescence selectivity and very good affinity toward guests, has significant potential for the applications in sensor development.

### Experimental.

**General Experimental.** Starting materials were purchased from commercial suppliers and used without further purification or were prepared by literature procedures. Melting points were measured on a Meltemp apparatus in open capillary tubes and are uncorrected. IR spectra were recorded on a JASCO FT/IR 4100 spectrometer and are reported in  $\text{cm}^{-1}$ . NMR spectra were measured on Bruker DRX-400 instrument operating at 400 or 600 MHz for  $^1\text{H}$  and 100 or 125 MHz for  $^{13}\text{C}$  using  $\text{D}_2\text{O}$ ,  $\text{CDCl}_3$ , or  $\text{DMSO-}d_6$  as solvents. Chemical shifts ( $\delta$ ) are referenced relative to the residual resonances for HOD (4.80 ppm),  $\text{CHCl}_3$  (7.26 ppm for  $^1\text{H}$ , 77.16 ppm for  $^{13}\text{C}$ ), and  $\text{DMSO-}d_6$  (2.50 ppm for  $^1\text{H}$ , 39.51 ppm for  $^{13}\text{C}$ ). Mass spectrometry was performed using a JEOL AccuTOF electrospray instrument (ESI). ITC data were collected on a Malvern Microcal PEAQ-ITC instrument. UV-Vis absorbance was measured on Varian Cary 100UV spectrophotometer. Fluorescence was performed on Hitachi F-4500 fluorescence spectrophotometer.

**Host 1.** A mixture of dimethylglycoluril dimer bis(cyclic ether) **2**<sup>25</sup> (100 mg, 0.22 mmol) and **W1** (513 mg, 0.89 mmol) was dissolved in TFA/ $\text{Ac}_2\text{O}$  (1:1 (v:v), 10 mL). The mixture was stirred under  $\text{N}_2$  at 85  $^{\circ}$ C for 3.5 h and then was cooled to room temperature. EtOH (100 mL) was added to the reaction mixture and stirred for 30 min. The solvents were removed by rotary evaporation to obtain the crude product. Host **1** was purified by gel permeation chromatography (Sephadex G25, 30 mm  $\times$  200 mm) using water as eluent. The solvent was removed and the solid was dried at high vacuum to give the host **1** as a light yellow solid (150 mg, yield 44%). M.p. > 300  $^{\circ}$ C. IR (ATR,  $\text{cm}^{-1}$ ): 1710m, 1459m, 1811s, 1030s, 743m.  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  7.46 (m, 8H), 7.16 (m, 4H), 6.96 (m, 4H), 5.76 (s, 4H), 5.45 (d,  $J = 16$  Hz, 2H), 5.03 (d,  $J = 16$  Hz, 4H), 4.18 (d,  $J = 16$  Hz, 2H), 4.07 (d,  $J = 16$  Hz, 4H), 3.95 (m, 4H), 3.73 (m, 4H), 2.90 (m, 8H), 2.22 (m, 8H), 1.74 (s, 6H), 1.60 (s, 6H) ppm.  $^1\text{H}$  NMR (600 MHz,  $\text{D}_2\text{O}$ ),  $\delta$  7.74 (m, 4H), 7.54 (m, 4H), 7.47 (m, 4H), 7.08 (m, 4H), 5.82 (s, 4H), 5.36 (d,  $J = 16$  Hz, 2H), 4.99 (d,  $J = 16.7$  Hz, 4H), 4.31 (d,  $J = 16.2$  Hz, 2H), 4.08 (d,  $J = 16.7$  Hz, 4H), 3.80 (m, 4H), 3.67 (m, 4H), 3.14 (m, 8H), 2.16-2.06 (m, 8H), 1.76 (s, 6H), 1.63 (s, 6H) ppm.  $^{13}\text{C}$  NMR (125 MHz,  $\text{DMSO-}d_6$ ):  $\delta = 154.49, 147.45, 145.14, 144.47, 138.38, 129.09, 125.31, 125.01, 123.64, 77.38, 75.56, 74.07, 48.12, 47.40, 35.58, 26.23, 17.09, 16.19$  ppm. HR-MS (ESI, negative)  $m/z$  735.1784 [ $[\text{M} + 2\text{H} - 4\text{Na}]^{2-}$ , Cald. for  $\text{C}_{70}\text{H}_{70}\text{N}_8\text{O}_{20}\text{S}_4$  735.1795.

**Acknowledgements.** We thank the National Science Foundation (CHE-1404911 and CHE-1807486) and the International Graduate Exchange Program of Beijing Institute

of Technology for financial support.

## Conflicts of interest

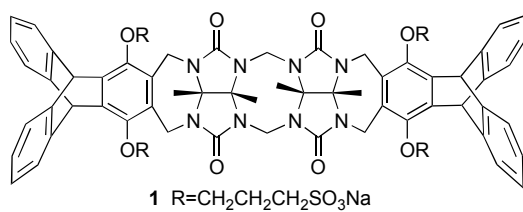
The authors have no conflicts of interest to declare.

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## Graphical Abstract



We report the preparation of methylene bridged glycoluril dimer **1** bearing two triptycene walls and its function as a host toward hydrophobic cations in water.