JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Molecular Snuggle and Stretch of a Tetraammonium Chain in the Construction of a Hetero-[4]pseudorotaxane with CyclopentanoQ[6] and Classical Q[7]

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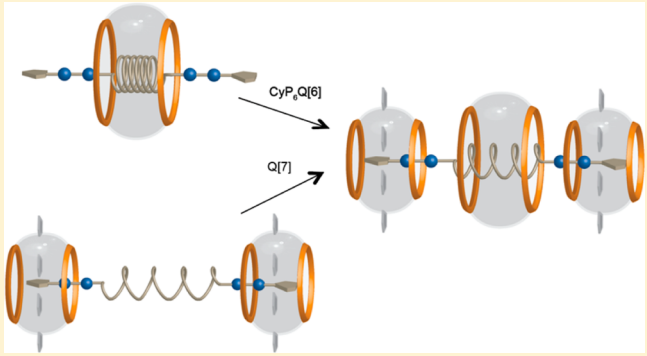
Supporting Information

ABSTRACT: A hetero-[4]pseudorotaxane was designed to perform a molecular machine function of contraction and expansion utilizing the binding features of $CyP_6Q[6]$ and classical Q[7]. First, the effect on guest binding of equatorial substitution on Q[6]'s was examined by comparing $Me_4Q[6]$ and $CyP_6Q[6]$ against classical Q[6] using eight guest molecules varying in shape, size, neutrality, or cations. Second, the binding data provided optimal structural features for the design of a tetraammonium ion chain to effect the synthesis of the hetero-[4]pseudorotaxane. Finally, the hetero-[4]-pseudorotaxane was constructed, and the order of component placement was examined for function and thermodynamic stability in relation to component order on the molecular axle.



INTRODUCTION

Recently we published the synthesis of the cyclopentanocucurbit[*n*]uril ($CyP_nQ[n]$) family, and we found that the binding constants for $CyP_6Q[6]$ and $CyP_7Q[7]$ were 1.8 and 1.9 times higher with the guest dioxane and the adamantyl ammonium ion, respectively, when compared to their unsubstituted cousins.[1] It has also been observed that metal ion coordination is preferential to the carbonyl O of a substituted glycoluril moiety of partially substituted Q[5] in the construction of rings, channels, and cantenanes in the solid state.[2] We proposed in these examples that the selective coordination of the carbonyl O of a substituted glycoluril moiety was as a consequence of an increase in electron density on this carbonyl O due to the alkyl substitution on that moiety. This was subsequently supported by theoretical calculations, which showed that the Mulliken atomic charge was higher when alkyl substitution was present.[3] A number of studies have been reported for the determination of cavity binding strengths of various molecular guests in the case of classical Q[*n*],[4−7] but there are limited examples for substituted Q[*n*].[1,8,9]

Here in, we report our exploration into evaluating the effect of substitution upon binding of a set of guests as ammonium salts and a set of neutral guests in three Q[6] hosts: classical Q[6] (no substitution), *α,α,δ,δ*-$Me_4Q[6]$, and $CyP_6Q[6]$ (Figure 1). In geometry, the cavity/portal regions of the hosts Q[6] and $CyP_6Q[6]$ occupy a spheroidal space, and each in dimension is indiscernible by single-crystal X-ray analysis.[1] However, *α,α,δ,δ*-$Me_4Q[6]$ is ellipsoidal.[10,11] In this context, guests were chosen in order to evaluate the effects of both shape and charge on the binding relationship.

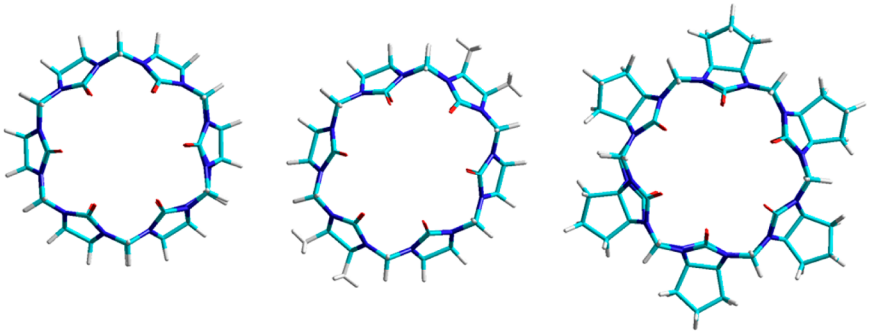
Classical Q[*n*] have symmetrically opposed portal openings with affinities for cations and their hydrophobic cavities, which are slightly larger in diameter than the portals, bind neutral or hydrophobic molecules. These structural features provide the opportunity for molecular threading and the synthesis of pseudorotaxanes and rotaxanes. The synthesis of supramolecular structures of this type are facilitated by the relatively high binding strengths to a number of cationic molecules and the space available within their cavities. With specific reference to organic cationic molecules, a number of relatively simple examples of pseudorotaxanes and rotaxanes have been reported.[12−16] There are only a small number where the Q[*n*] component is used multiple times in a single construction[17−20] or where different homologues are used in the same structure.[21,22]

In this study we examine the effect of equatorial substitution on guest binding and develop an understanding of the binding behavior effects as an aid to the rational design of supramolecular structures. We demonstrate this in the construction of a [4]pseudorotaxane using two different homologues and each with different substitution, as discussed in the latter part of this report. In addition, as part of this study, we report a molecular machine-like motion of contraction and expansion in the process of construction that is controlled by the order in which the molecular components are combined.

Synthetic examples of molecular movement, such as muscle-like function of contraction and expansion, has generally

Received: November 24, 2016
Published: May 10, 2017

DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515



Q[6] α,α,δ,δ–Me$_4$Q[6] CyP$_6$Q[6]

Figure 1. Molecular models of the three Q[6] used in this study: classical Q[6], a partially substituted Q[6] (*α,α,δ,δ*-Me$_4$Q[6]), and fully substituted CyP$_6$Q[6].

involved a variety of macrocyclic rotaxane-base systems with only limited explorations into the use of Q[*n*].[23] Machine-like function of combined molecular components has been a fascination for more than 6 decades and has been investigated with a variety of synthetic components.[24−26]

The use of classical Q[*n*] as a component in molecular machine-like motion was first reported in 1990 by Mock and Pierpont, through a pH-controlled switching mechanism.[27] In more recent years, a number of variations have also employed pH to trigger a molecular switch.[17,28−30] Switching motions have also been reported under the controls of redox chemistry,[31−33] temperature,[21,34] enzymes,[35,36] and metal ions.[37] The thermal motion of classical Q[*n*] as components has been shown for the molecular structure gyroscane, where the smallest Q[5] moves freely inside the cavity of the larger Q[10].[38]

The aforementioned machine-like actions all utilize the classical Q[*n*] with no examples reported for substituted Q[*n*]. In this report we discuss molecular motion as contraction and expansion, where the input is derived from the competitive differences in electrostatic attraction of substituted Q[6] and classical Q[7] for shared cations on an alkylammonium chain.

RESULTS AND DISCUSSION

Guest Binding and Q[6] Substitution. In this study, competitive binding was used to determine the binding constants for each guest and each Q type (with and without substitution and one example with an ellipsoidal cavity). The absolute K_a values for dioxane⊂Q[6] and dioxane⊂*α,α,δ,δ*-Me$_4$Q[6] were determined by titration using ^{1}H NMR to provide our initial reference point. These two association complexes form in a ratio of 1:1 with slow exchange kinetics relative to the ^{1}H NMR time scale (Supporting Information). Dioxane (**1**) as a symmetrical molecule has the advantage of having a clearly defined resonance as a singlet of 8 protons, which shifts upfield by Δ0.88−1.11 ppm depending upon the substitution carried by the Q[6] used. A comparative binding study of **1**, between Q[6] and Me$_4$Q[6] showed that the titrations were consistent (for simplicity in the remaining text, the *α,α,δ,δ*-position of Me$_4$Q[6] will not be denoted). All binding experiments were conducted in 10 mM buffer D$_2$O solution (K(C$_6$H$_4$CO$_2$DCO$_2$)/DCl, pD 4.0) with 4 repetitions. The use of this buffer avoided obscuring relevant resonances without compromising guest binding.

Suitable combinations of competitive guest binding (eqs 1−5) or competitive host binding (eqs 6−10) were selected to optimize integration values and provide clearly definable resonances with minimal interference. All spectra were recorded only after thermodynamic equilibrium had been established (verified by periodic NMR sampling for 24 h or more if necessary).

$$Q + G_1 \overset{K_{G_1}}{\rightleftharpoons} G_1 \subset Q \tag{1}$$

$$Q + G_2 \overset{K_{G_2}}{\rightleftharpoons} G_2 \subset Q \tag{2}$$

$$G_1 + G_2 \subset Q \overset{K_{rel}}{\rightleftharpoons} G_2 + G_1 \subset Q \tag{3}$$

$$K_{rel} = ([G_1 \subset Q][G_2])/([G_2 \subset Q][G_1]) \tag{4}$$

$$K_{G_1} = (K_{G_2})(K_{rel}) \tag{5}$$

$$Q_1 + G \overset{K_{Q_1}}{\rightleftharpoons} G \subset Q_1 \tag{6}$$

$$Q_2 + G \overset{K_{Q_2}}{\rightleftharpoons} G \subset Q_2 \tag{7}$$

$$Q_1 + G \subset Q_2 \overset{K_{rel}}{\rightleftharpoons} Q_2 + G \subset Q_1 \tag{8}$$

$$K_{rel} = ([G \subset Q_1][Q_2])/([G \subset Q_2][Q_1]) \tag{9}$$

$$K_{Q_1} = (K_{Q_2})(K_{rel}) \tag{10}$$

Using eq 5 for competitive guest binding or eq 10 to achieve competitive host binding, we were able to establish the binding constants for a selected series of guests **1**−**8** for each of the three Q[6] hosts (Figures 2 and 1, respectively). Each of these guests were intended to test a particular feature of each of the three Q[6]'s such as shape and portal polarity, as indicated in the introduction.

The binding constants of the neutral gases isobutene (**2**) and isobutane (**3**) have previously been reported in the classical Q[6] under two different conditions (water pH 3 and AcONa buffer 50 mM pH 5.5), and consequently a salt effect was observed in the latter.[7,40,41] In our study, the buffer concentration was 5-fold lower than that reported, and the K_a values for guests **2** and **3**, respectively, were 7.5 and 15.5 times lower than those determined in H$_2$O at pH 3 but were 5.9 and 23 times higher than the same report with an acetate buffer indicated previously. We have also observed a sensitive salting effect upon the binding of dioxane (**1**) (see Supporting Information). In contrast, the binding of the cyclopentyl

DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515

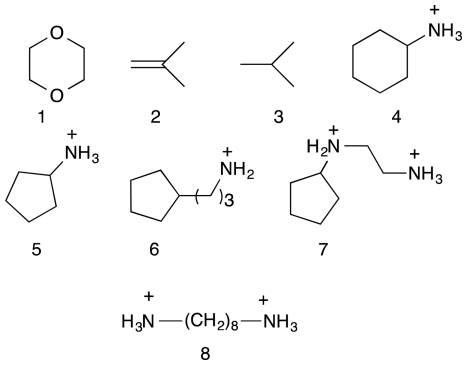


Figure 2. Selective guests for the comparative binding study between the three Q[6]'s carrying different substitution.

ammonium salt (**5**) to classical Q[6] was almost 2 orders of magnitude higher than its first reported K_a (6.25×10^3 M^{-1}, 50% formic acid 40 °C).[4]

The K_a for **1** and $CyP_6Q[6]$ was determined by comparative host binding with $Me_4Q[6]$, which then enabled the comparative guest binding for the three Q[6]'s between **1** and the two guests **2** and **4**. The K_a's of isobutane (**3**) were established by competitive guest binding of **1** and **3** in $CyP_6Q[6]$, then competitive host binding of the guest **3** between the $CyP_6Q[6]$ and the remaining two hosts. Competitive guest binding was then possible between the guest **3** and **5**, **6**, or **7**. An exception was in the determination of the K_a for **7** in $CyP_6Q[6]$, where a comparative host binding was first determined between $Me_4Q[6]$ and Q[7] for the guest **7**, and then with the same guest, a comparative binding between Q[7] and $CyP_6Q[6]$ was performed. Finally the binding of the diammonium ion **8** was determined by competitive guest binding between **3** and **8** for $Me_4Q[6]$, **5** and **8** for classical Q[6], and then a series of competitive host binding experiments using the combinations of $Me_4Q[6]$/Q[7] and $CyP_6Q[6]$/Q[7]. In Table 1, all examples presented have guest to host ratios that are not >1:1.

The results of Table 1 show that the binding of all the guests is higher in the cavity of $CyP_6Q[6]$ compared to the classical Q[6] with one exception, guest **6**, which had identical K_a. Generally the binding increase for each guest was of the order of 1.6−3.8 times higher. $Me_4Q[6]$, in contrast, showed decreased or equal K_a for most of the guests when compared to classical Q[6]. A 10-fold decrease was found for **7**, where as **1**, **2**, and **6** were decreased by between 2.2 and 3.3 times. However, the cyclohexyl ammonium salt **4** was an outstanding exception for both $Me_4Q[6]$ and $CyP_6Q[6]$, 30 and 119 times higher, respectively.

In the case of the neutral guests **1**−**3**, the binding is influenced by the packing coefficient (% of cavity occupancy), solvation, and the stability gain in the displacement of energetic water from the cavity.[39] Isobutane (**3**) binding as an example has a K_a 2.4 times higher in $CyP_6Q[6]$ compared to Q[6], yet in $Me_4Q[6]$, it is equal, which is contrary to the decrease in binding in this latter host for **1** and **2**. An increased binding for guests **1**−**3** in $CyP_6Q[6]$ could be as a consequence of a more rigid framework because of the substituents or an increase in the energy of the structured water due to increased portal electronegativity or a combination of both. The differences found in $Me_4Q[6]$ binding are likely to be as a consequence of molecular shape sensitivity. An increase in binding for the ammonium salts **4**, **5**, **7**, and **8** in $CyP_6Q[6]$ compared to Q[6] is insufficiently differentiated to attribute this entirely to an improved interaction between N^+ and an increase in the electronegativity of the portals, whereas the large differential for the guest **4** may speak to the increased rigidity of the Q framework with increasing substitution. The tightness of the guest was evident in the slowness to reach equilibrium at 25 °C (72 h) across all three Q.

In addition to features of shape (host or guest) and size, it is known for Q[6−8] that if two ammonium ion centers are included on a potential guest, then this has a significant effect on increasing binding affinity.[4−6] These cationic centers can be where one is at each portal or where both are at the same portal. The diammonium ion **7**, an example of the latter, has also been found to follow this same trend, at least for Q[6] and $CyP_6Q[6]$ compared to the parent monoammonium ion **5**, giving an ∼10-fold increase. In addition, the diammonium ion **8**, which traverses the cavity resulting in each cationic center being located at a portal, showed a significant binding increase in $CyP_6Q[6]$ (>8 times that of Q[6]). In contrast, binding in $Me_4Q[6]$ results in no improvement for either **7** or **8**.

The features that favor increased guest binding across the classical family of Q[*n*], such as cationic centers or H-bond donors that can sit at a portal, the size and shape of a guest facilitating an optimal occupation capacity, and the hydrophobic nature of a guest, have been established with reasonable predictability.[4−7,39−42] From the results reported here, it is also possible to add another parameter to the binding of guests by selecting a host with alkyl substitution, which can provide a mechanism to "fine-tune" binding, with either an increase or decrease in relative binding (Table 1). This statement is also supported by our recent study with substituted Q[5].[43]

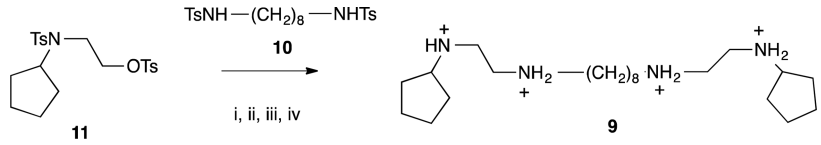
Table 1. Determined Values of K_a (M^{-1}) for Selected Guests and Comparative Effects of Substitution on Q[6] in 10 mM buffer D_2O Solution ($K(C_6H_4CO_2DCO_2)$/DCl, pD 4.0)[a]

	Q[6]	$Me_4Q[6]$	$Me_4Q[6]$/ Q[6]	$CyP_6Q[6]$	$CyP_6Q[6]$/Q[6]
1	$(2.78 \pm 0.01) \times 10^3$[b]	$(0.83 \pm 0.02) \times 10^3$[b]	0.3	$(4.44 \pm 0.22) \times 10^3$	1.6
2	$(1.12 \pm 0.04) \times 10^4$	$(5.03 \pm 1.64) \times 10^3$	0.5	$(1.74 \pm 0.13) \times 10^4$	1.6
3	$(5.47 \pm 0.12) \times 10^4$	$(5.53 \pm 0.09) \times 10^4$	1.0	$(1.29 \pm 0.12) \times 10^5$	2.4
4[c]	$(0.79 \pm 0.02) \times 10^3$	$(2.39 \pm 0.60) \times 10^4$	30.3	$(9.41 \pm 0.16) \times 10^4$	119.1
5	$(4.97 \pm 0.11) \times 10^5$	$(6.53 \pm 0.14) \times 10^5$	1.3	$(1.87 \pm 0.25) \times 10^6$	3.8
6	$(1.19 \pm 0.09) \times 10^5$	$(3.84 \pm 0.17) \times 10^4$	0.3	$(1.17 \pm 0.04) \times 10^5$	1.0
7	$(7.70 \pm 0.45) \times 10^6$	$(7.17 \pm 0.34) \times 10^5$	0.1	$(1.76 \pm 0.12) \times 10^7$	2.3
8	$(5.44 \pm 0.17) \times 10^6$	$(0.99 \pm 0.06) \times 10^6$	0.2	$(4.38 \pm 0.28) \times 10^7$	8.0

[a]The binding ratios relative to Q[6] for each substituted Q[6] are shown. [b]Determined by titration. [c]Slow to reach equilibrium (∼72 h).

DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515

Scheme 1[a]



[a]Reaction process: (i) NaOEt/EtOH; (ii) **11** added to the Na^+ salt of **10** in DMF; (iii) Li-naphthalide THF; (iv) conc HCl.

Substitution on Q not only provides a potential opportunity to "fine-tune" binding but also provides an advantage in binding interpretation. Encapsulated molecules in the cavity of substituted Q generally result in larger chemical shifts of proton resonances, which can add a higher degree of clarity to spectra.

Construction of a [4]Pseudorotaxane Using the Combination $CyP_6Q[6]/Q[7]$. As an extension to the idea of "fine-tuning" guest binding using a substituted Q[6], we set out to design a suitable guest that could demonstrate the advantage of the higher binding of $CyP_6Q[6]$. In addition, we wanted to also construct a molecular machine with features of contraction and expansion utilizing the capacity for an alkyl guest chain that could fold or extend within a larger Q cavity. In that context, we chose an 8-carbon methylene chain to build into our design.[44] This was anticipated to be achievable by combining the guest structural features of the 8-carbon chain **8** to be encapsulated in Q[7] and the highest binding guest **7** found for $CyP_6Q[6]$. The tetraammonium ion **9** then became our target where $CyP_6Q[6]$ was expected to bind on each cyclopentyl ammonium group and a Q[7] would bind the 8-carbon chain. Using stepwise additions, contraction, and expansion was anticipated.

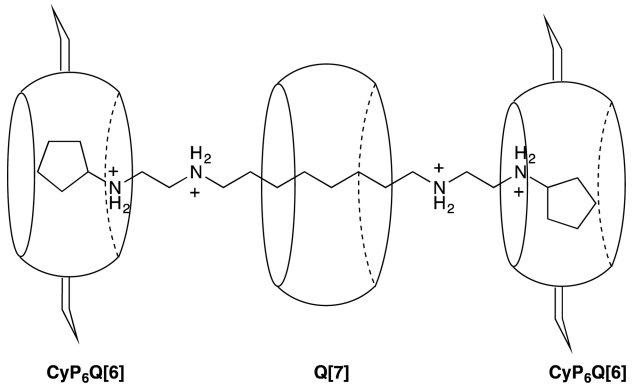
Prior to the synthesis of **9**, the K_a for the 8-carbon diammonium salt **8** and the diammonium salt **7** was determined for Q[7] by competitive host binding as combinations of $Me_4Q[6]/Q[7]$ and $CyP_6Q[6]/Q[7]$. The K_a for diammonium salt **8** and **7** in Q[7] were found to be $2.07 \pm 0.22 \times 10^8$ and $1.39 \pm 0.03 \times 10^7$ M^{-1}, respectively.

While the K_a for **8**⊂$CyP_6Q[6]$ was found to be only 3 times higher than that of **7**⊂Q[7], it was anticipated that the higher binding of **8**⊂Q[7] would favor the preferential binding of Q[7] over the 8-carbon alkyl chain of **9**. Given the multiple cation centers, binding at the center was expected to be even higher than the simple example of **8**. Prior evidence of the folding of the methylene chain of **8** in Q[7] was observed by ^{1}H NMR where all the methylene proton resonances shift upfield.[44]

The tetraammonium ion **9** was prepared by the alkylation of the tosylamide **10** with the tosylester **11**, followed by reductive detosylation and protonation of the free base with HCl to generate **9** as a salt (Scheme 1).

With the tetraammonium ion **9** in hand, the anticipated [4]pseudorotaxane **12**, as depicted in Figure 3, was then constructed in a two-step process in the order of adding 1 mol equiv of Q[7] and then 2 mol equiv of $CyP_6Q[6]$ under buffered conditions, as previously described. However, in line with our expectations, a number of significant changes were observed by ^{1}H NMR during the construction process.

At the first step, the addition of 1 equiv of Q[7] resulted in three sets of proton resonances shifting relative to their original positions (Figure 4a,b). These included all the methylene protons of the 8-carbon chain H_{h-k} shifting upfield (0.15−0.66 ppm), with the remaining two sets, the ethylene chain protons



12

Figure 3. Anticipated [4]pseudorotaxane **12**.

$H_{f,g}$ and the cyclopentyl methine protons H_e shifting downfield (0.19, 0.23, and 0.13 ppm, respectively). The change in the resonance for $H_{f,g}$ initially a singlet for the free cation **9** was further distinguished by these resonances occurring as a multiplet with H_f and H_g having slightly different chemical shift positions in the [2]pseudorotaxane **13** as a result of their different near-portal exterior locations (Figure 5). There was no evidence of Q[7] shuttling over the cyclopentyl groups, with no observable resonance changes for the cyclopentyl group that could indicate a meta stable state of Q[7] sitting at this position prior to its final location over the 8-carbon chain. This is in spite of the fact that Q[7] is capable of binding the cyclopentyl dication **7**, with slow exchange kinetics on the NMR time scale. Binding over the cyclopentyl group of the tetracation **9** was only observed when Q[7] was in a significantly large excess relative to **9**. The central location of Q[7], and the folding of the 8-carbon chain, was supported by all of its proton resonances shifting upfield with slow exchange on the NMR time scale (as indicated in Figure 4b). The magnitude of the chemical shift for the proton resonances H_i and $H_{j,k}$ (0.6 and 0.7 ppm respectively) indicates that these protons are located at the center of the Q[7] cavity, and the smaller shift of 0.15 ppm for H_h indicates that these protons are just inside the cavity. The rapid location to the central 8-carbon chain also occurs at very high ratios of tetracation **9** to Q[7] (15:1, respectively). Another indicator of a stable and central location of Q[7] is the sharpness of the Q[7] doublets at 4.21 and 5.70 ppm, which only occur as single sets of doublets demonstrating a symmetrical structure with both portals being magnetically equivalent (Figure 4b).

Support for the folding of the 8-carbon chain of **9** is found in the observation that when the simple 8-carbon diammonium salt **8** is encapsulated in Q[6][4] or $Cy_6Q[6]$ a downfield shift of the N−CH_2 α−protons of **8** occurs, while Q[7] encapsulation of **8** results in only upfield shifted proton resonances for all of its methylene protons, similar to those protons upfield shifted

DOI: 10.1021/acs.joc.6b02813
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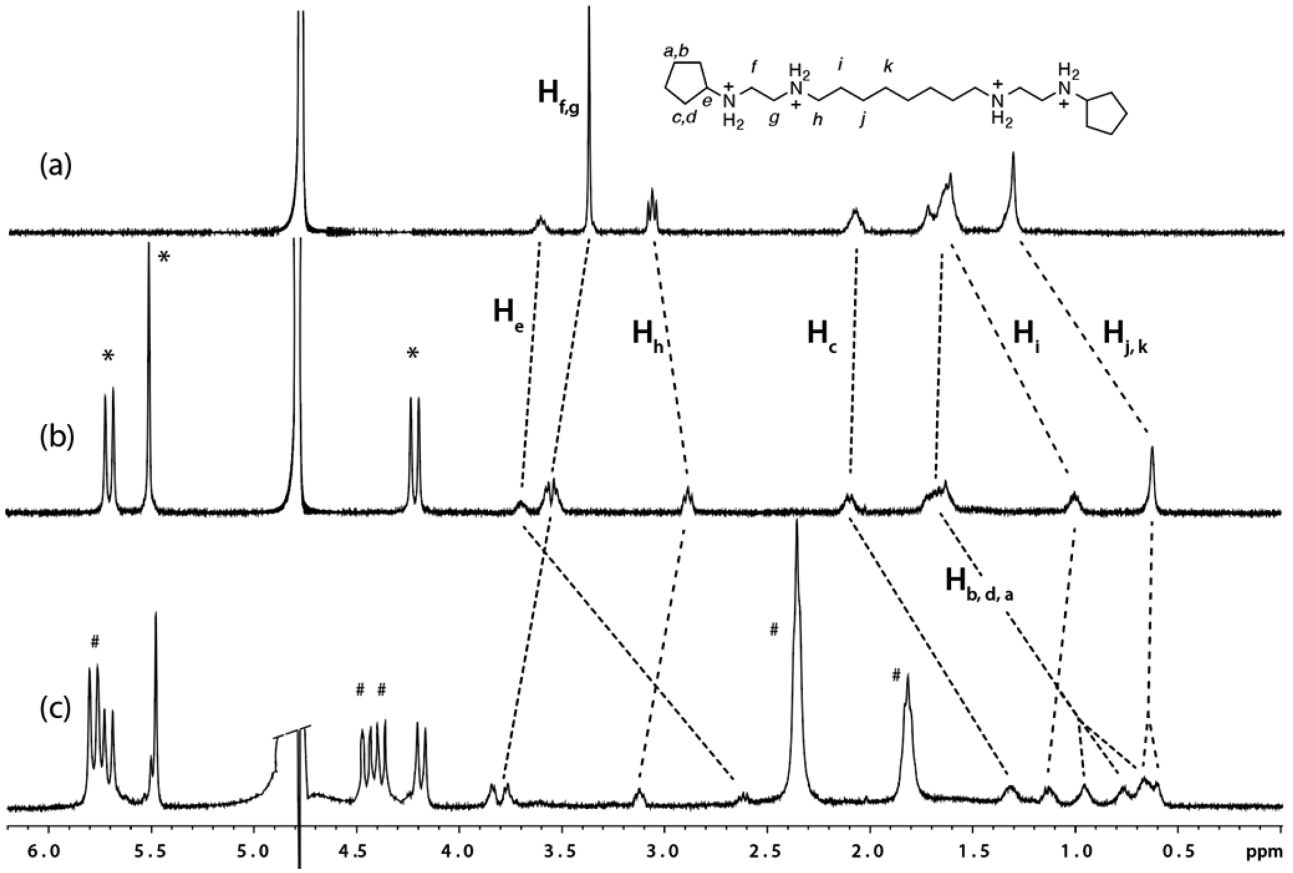
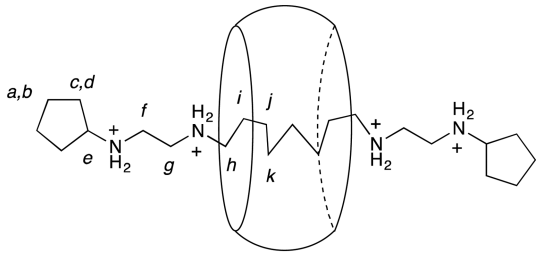


Figure 4. Stepwise preparation of [4]pseudorotaxane **12**. ^{1}H NMR spectra were recorded in buffered D_2O: (a) tetracation **9**, then (b) 1 equiv of Q[7] (marked as *) was added to give the [2]pseudorotaxane **13**, and then (c) 2 equiv of $CyP_6Q[6]$ (marked as #) was added forming **12**.



Q[7]

13

Figure 5. The first step forms exclusively the [2]pseudorotaxane **13**, derived from **9** and Q[7] (proton labels for tetracation **9** are shown).

for the tetracation **9** (especially relevant to H_h, see Supporting Information).

The second step, adding 2 equiv of $CyP_6Q[6]$, almost exclusively produced the [4]pseudorotaxane **12** (Figures 3 and 4c). Complete formation of **12** could be achieved with a slight excess of $CyP_6Q[6]$ (1:1:2.2 of **9**, Q[7] and $CyP_6Q[6]$, respectively). Clear encapsulation of the end cyclopentyl groups was evident in the large upfield shifts for the methylene ring protons H_{a-d} (Δ 0.78−1.03 ppm), and the methine proton resonances, both H_e, also shifted in the same direction, Δ 0.99 ppm relative to free **9** and 1.12 ppm relative to its chemical shift position in [2]pseudorotaxane **13**. The other notable resonance shifts were those on the ethylene groups H_f and H_g, which had moved further downfield (0.24 and 0.20 ppm) relative to their positions for **13**. The total shift, relative to the same proton resonances for the free **9**, was twice the shift that would be imposed by just a single portal (0.47 and 0.39 ppm), which is consistent with a deshielding effect of being sandwiched between two different exterior portal regions. A clear chemical shift separation between the resonances of the upfield methylene proton doublets of the two different Q (CyP_6Q-[6]/Q[7]) unambiguously allows the identification of Q[7] as the central Q, as **12** is symmetrical, and therefore because the Q[7] proton resonances occur as well-defined doublets, both of its portals experience the same environment. In contrast, the upfield doublet for the two $CyP_6Q[6]$'s appears as two doublets (4.3−4.5 ppm) of equal intensity, which is consistent with each of their two portals experiencing different magnetic environments, hence the $CyP_6Q[6]$'s are on the termini. Another important observation was that the 8-carbon chain in the [4]pseudorotaxane **12** has partially unfolded, as indicated by the two H_h proton resonances moving from their upfield chemical shift position of 2.90 to 3.11 ppm (**13** and **12** respectively, Δ0.21 downfield). Relative to the chemical shift position of H_h in free **9**, there was a small shift downfield of 0.06 ppm indicating that H_h had moved to just outside the portal for structure **12**. However, as the total shift difference of the H_h protons comparing **13** and **12** was Δ0.21 ppm downfield, this supports a significant unfolding event. In addition, the H_i protons also experienced small shifts downfield of 0.09 ppm toward the proton resonance position H_i of free **9**, with the remaining central protons virtually unaffected.

DOI: 10.1021/acs.joc.6b02813
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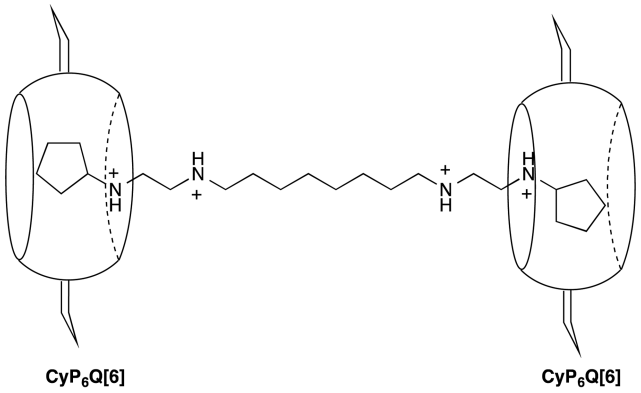
Intermediate stages of construction were also observed at ratios of 1:1:1 for each of the components, but even at this point, the major product was consistent with [4]-pseudorotaxane **12**, as indicated by an ∼50% proportion of **13** remaining as determined by the remaining proportion of the methine proton resonance of the Q[7] of **13** at 6.39 ppm.

We also investigated the construction of [4]pseudorotaxane **12** in the reverse order to establish the relative ease of formation of **12** through a process of disassembly and reassembly, allowing a self-sorting process to establishment the thermodynamically stable product **12**.

In this process, the $CyP_6Q[6]$ capped **14** was first prepared by the addition of $CyP_6Q[6]$ to the tetracation **9** in a ratio of 2:1 (Figure 6). Clearly definable changes in chemical shift



14

Figure 6. $CyP_6Q[6]$ capped **14** constructed by the addition of 2 mol equiv of $CyP_6Q[6]$ to the tetracation **9**.

occurred with the predominant effects being large upfield shifts (Δ0.82−1.05 ppm) for the cyclopentyl methylene protons H_{a-d} and a similar upfield shift for the methine H_e protons (Δ1.13 ppm, see Supporting Information). All of the other proton resonances were shifted downfield with diminishing differences ranging from Δ0.28−0.03 ppm for H_f to H_k, respectively. The upfield shifts of the cyclopentyl group and the downfield shifts of the entire methylene chain components, including the magnitudes of shifts, all support only termini encapsulation of **9** by each of the two $CyP_6Q[6]$'s added.

The progress of formation of **12** from **14** (17.58 mM) was followed by ^{1}H NMR after the addition of solid Q[7] (1 mol equiv). Equilibrium was obtained after ∼7 h at 25 °C (Figure 7). As mentioned previously, optimum formation of **12** was

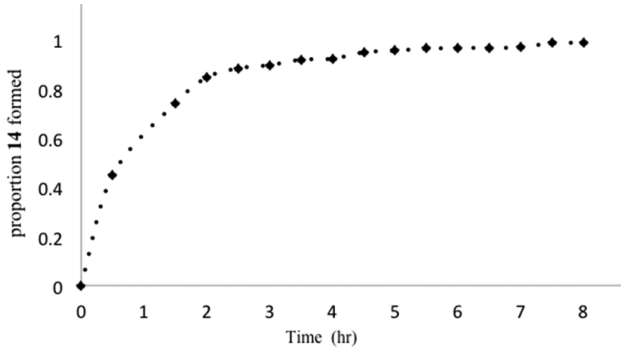


Figure 7. Reaction progress of $CyP_6Q[6]$ capped **14** (17.58 mM) to [4]pseudorotaxane **12** following the addition of 1 mol equiv of Q[7].

only possible with a slight excess of $CyP_6Q[6]$, but the starting point in this experiment was the performed **14** as a 2:1 complex ($CyP_6Q[6]$: **9**); the end point was therefore ∼98% as judged by the disappearance of the methylene protons resonances H_h from 3.24 ppm and the reappearance in their final position of 3.12 ppm for [4]pseudorotaxane **12**.

We have demonstrated the synthesis of the [4]-pseudorotaxane **12** utilizing the higher binding of $CyP_6Q[6]$ for the cyclopentyl group and have applied two approaches to its construction. The first relies upon utilizing determined K_a values and adding the individual components together in an order that favors locating the highest isotherm first and then the next in turn. The second method still relies upon utilizing determined K_a values but where no consideration of the order of addition is necessary. In this latter method, the most thermodynamically stable structure will be the final result under the circumstance of reversible reactions. This reaction process can also be described as "social self-sorting", a term coined by Isaacs.[45]

Expansion and Contraction. Apart from the self-sorting phenomena, the other interesting observation to be highlighted is that which occurs in the two-step construction process where the first-step forms the [2]pseudorotaxane **13** and the second-step forms [4]pseudorotaxane **12**. These steps have an affect upon the 8-carbon chain and the consequent distance between its two ammonium ions. The order of this process first following the addition of Q[7] results in contraction (folding) of the chain and then at the second-step expansion (unfolding) after the addition of 2 mol equiv of $CyP_6Q[6]$. The contracted and expanded states of the chain were most clearly evident in the change of chemical shift of the H_h proton resonances to the upfield position after the first step, then back to a downfield position after the second step (Figure 4). The reason for the expansion is not completely obvious, although Coulombic repulsion must play a role. Considering the extended distance between the two ammonium ions of the ethylene unit is 3.8 Å (N to N) and if the relevant portals of the $CyP_6Q[6]$'s resided at each cyclopentyl ammonium ion and the Q[7] portals reside nearest the octyldiammonium ions, then the distance between the portals would be >0.8 Å, including van der Waals radii. However, this assumption does not take into account a slightly stronger attraction to both ammonium ions of the ethylene unit by the $CyP_6Q[6]$'s. This could occur as a consequence of the smaller portal and hence a more confined electronegative ring as opposed to the larger Q[7] portal. Using a molecular model adjusted to fit the observed chemical shifts, this suggestion is supported with a resultant portal separation of ∼1.4−2.5 Å (van der Waals radii between O ← → O included, Supporting Information). The chemical shift of H_e for the $CyP_6Q[6]$ capped **14** compared to that of H_e of the free guest **9**, results in an upfield shift (Δ 1.13 ppm), which moves slightly downfield (Δ 0.14 ppm) with addition of Q[7] to form [4]-pseudorotaxane **12**. In the first instance, where the H_e proton shifted upfield, clearly indicates a central cavity location of H_e, and then a small adjustment occurs in the formation of **12** to give the new shift upfield (Δ 0.99 ppm) relative to free **9**, indicating only a small withdrawal of $CyP_6Q[6]$ away from each octylammonium ion. A stronger attraction of the $CyP_6Q[6]$ portal to the cationic centers and a necessary withdrawal by Q[7] aided by the relative ease of unfolding of the 8-carbon chain result in expansion.

DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515

CONCLUSION

There are only a small number of reported examples of hetero-Q[*n*] pseudorotaxanes reported, and these all involved the use of the classical Q[*n*].[21,22] In this report we combine the binding function of the classical Q[7] and $CyP_6Q[6]$, taking advantage of the differential binding between the two cavity sizes and the improved binding of the smaller cavity imparted through the cyclopentano substitution. While we have demonstrated the "fine-tuning" of binding with an increase as a consequence of equatorial substitution, we have also shown that this can be decreased especially when the substitution affects the shape of the cavity. Here, we present two examples of substituted Q[6] with affected binding constants, and previously we have reported some equatorially substituted Q[5] examples, which also showed binding differences.[43] This current report now adds a third cavity size example in the range Q[5−7] with different equatorial substitution that has been shown to have "finely tuned" binding constants for a number of guests.[1,8,43] Although the magnitude of difference in K_a relative to classical Q is generally not large (up to 8 times), there is at least one example guest (cyclohexyl ammonium ion **4**) that was bound 119 times higher in comparison. This guest's selective difference could be used as an advantage in a case specific environment and may be related to a tightness of fit, an area requiring further study. A greater K_a differential has been observed for the partially substituted $Me_4Q[6]$ and the fully substituted $CyP_6Q[6]$ of ∼25 and 44 times, respectively, for guests **7** and **8**. Differences like these, or better, may also provide exploitable opportunities in future supramolecular designs.

EXPERIMENTAL SECTION

Instrumentation. NMR spectra were recorded at 400 and 100 MHz, respectively, for the nuclei ^1H and ^{13}C. Chemical shifts for each nuclei were, respectively, reported with the solvent at the internal standard HDO 4.78 ppm and with external dioxane 67.19 ppm. APT was employed for the identification of each carbon. FTIR spectra were collected as KBr disc or as a film, at a resolution of 4 cm^{-1}.

^1H NMR Competitive Binding Experiments. Comparative binding as a measurement of relative binding affinities was carried out by ^1H NMR. The temperature was regulated at 25 °C/298 K, and the relaxation delay times for all hosts, guests, and their host−guest complexes were maintained at 10 s. Each experiment was performed in 10 mM potassium hydrogen phthalate ($K\text{-}C_6H_4CO_2DCO_2/DCl$) buffered D_2O (pD 4.0). The concentrations of all the host and guest samples were determined by standard solutions of *tert*-butanol. The concentration of *tert*-butanol was determined against benzoic acid prepared from a known weight and volume in D_2O/Na_2CO_3.

Error Analysis. All the measurements were performed with four repetitions independently prepared from stock solutions at similar ratios of the two competing guests or hosts. These were averaged, and the error determined as a standard deviation for each value of K_a.

General Procedure for Tosylation of Alcohols. To the alcohol product (0.01 mol) in DCM (20 mL), triethylamine (0.01 mol) and *p*-toluenesulfonyl chloride (0.01 mol) were added. Then the mixture was stirred at rt for 18 h. The product solution was extracted with saturated brine aqueous solution and DCM. The organic layer was washed with dilute HCl, dried over $MgSO_4$, filtered, and evaporated in vacuo. The excess of *p*-toluenesulfonyl chloride was removed by reaction with ethylenediamine, by stirring at rt for 30 min. Then the product solution was kept at 0 °C in a cool room overnight. Diethyl ether was added to dissolve the tosyl ester product, and the mixture was filtered. The crude product was obtained after evaporation of the solvent from the filtrate, and the residue purified by silica column chromatography to obtain the pure tosyl ester.

General Procedure for the Preparation of Azides. A mixture of tosyl ester (5.26 mmol) dissolved in 30 mL of dioxane was added to tetrabutylammonium chloride (0.53 mmol), sodium azide (13.2 mmol), and water (4 mL) and stirred at 80 °C for 40 h. Dilute NaOH aqueous solution was added, and the organic material extracted with DCM. The solvent DCM was then evaporated in vacuo. Phase transfer catalyst (PTC) was removed from the product mixture by silica column chromatography with an eluent of 5% EtOAc/petroleum ether.

General Procedure for the Preparation of Amines from Azides. The azide product (2.48 mmol) and palladium on carbon (10%) in 12 mL of ethanol were shaken in the Parr hydrogenator under ∼1 atm of hydrogen gas until no further hydrogen was consumed. The catalyst was removed by filtration through Celite, and the product was obtained after the removal of ethanol by evaporation in vacuo.

General Procedure for the Reduction of Tosyl Amides. Small freshly cut pieces of lithium (14.04 mmol) were added to naphthalene (14.04 mmol), which was dissolved in dry THF (8 mL), and stirred under nitrogen gas to provide a deep green solution of $Li\text{-}C_{10}H_8$. After about 3 h of stirring at rt, the dry amide (1.17 mmol) dissolved in dry THF (8 mL) was transferred by cannulation to the reaction mixture. The green color immediately changed into deep red. Eight mL of water was added cautiously to quench the reaction, and the THF was evaporated in vacuo. Ten mL of a solution of 32% HCl was added, and all volatiles evaporated. The hydrocarbons were removed with petroleum ether. The crude product was purified by Dowex cation resin column chromatography (45% HCO_2H/1 M HCl) and recrystallized to obtain a pure product.

General Procedure for the Preparation of Ammonium Salt Reactions. The amine compound (0.1 mol) and HCl (32%) (9.85 mL) were mixed together to give ammonium salts, after drying by vacuum.

*Cyclohexanamine Hydrochloride (**4**).* As described in the general procedure of the preparation of ammonium salts, **4** was prepared from cyclohexanamine (9.9 g, 0.1 mol). The pure product was obtained after drying under vacuum, yielding 12.8 g, 94%. The physical data of **4** were consistent with those previously reported.[20]

*Cyclopentanamine Hydrochloride (**5**).* As described in the general procedure of the preparation of ammonium salts, **5** was prepared from cyclopentanamine (8.5 g, 0.1 mol). The pure product was obtained after drying with vacuum, yielding 11.5 g, 95%. The physical data of **5** were consistent with those previously reported.[46]

*3-Cyclopentylpropan-1-ammonium Chloride (**6**).* **6** was prepared in a 4-step synthesis from 3-cyclopentylpropanol.[47] The four steps involved tosylation, azide formation, reduction, and salt formation as described below.

Following the general tosylation procedure, 3-cyclopentylpropanol (1.28 g, 0.01 mol) gave a crude product which was purified with eluent EtOAc and petroleum ether (15:85, v/v) 3-cyclopentylpropyl 4-methylbenzenesulfonate as light pink oil (1.48 g, 53%). ^1H NMR ($CDCl_3$): δ = 7.77 (d, J = 8.2 Hz, 2H), 7.32 (d, J = 7.8 Hz, 2H), 3.99 (t, J = 6.6 Hz, 2H), 2.43 (s, 3H), 1.73−1.57 (broad m, 5H), 1.57−1.52 (broad m, 2H), 1.52−1.40 (broad m, 2H), 1.32−1.24 (m, J = 7.2 Hz, 2H), 1.05−0.92 (broad m, 2H) ppm. ^{13}C NMR ($CDCl_3$): δ = 144.3 (CH_2), 132.8 (CH_2), 129.5 (CH), 127.5 (CH), 70.6 (CH_2), 39.1 (CH_3), 32.1 (CH_2), 31.3 (CH_2), 27.7 (CH_2), 24.7 (CH_2), 21.2 (CH) ppm. APT ($CDCl_3$): δ = 129.5 (CH), 127.5 (CH), 39.1 (CH_3), 21.2 (CH) ppm. IR (Film): ν = 3383, 2947, 1915, 1599, 1450, 1396, 1360, 1290, 1209, 1188, 1177, 1119, 1098, 1045, 995, 961, 937, 910, 831, 814, 791, 737, 665, 573, 554 cm^{-1}. MS (EI): m/z (%) 282.2 (0.3) [M^+], 67.1 (81.2), 82.1 (100), 91.1 (73.8), 110.1 (73.8), 173.1 (57.5). Anal. calcd (%) for $C_{15}H_{22}SO_3$: C, 63.80; H, 7.85; S, 11.35. Found: C, 63.85; H, 7.95; S, 11.12.

(3-Azidopropyl)cyclopentane. As described in the general procedure for the preparation of azides from 3-cyclopentylpropyl 4-methylbenzenesulfonate (1.48 g, 5.26 mmol), 3-azidopropyl)-cyclopentane was prepared. One fraction was collected to check by ^1H NMR with D_2O (0.55 g, 69%). ^1H NMR ($CDCl_3$): δ = 3.23 (t, J = 7.0 Hz, 2H), 1.82−1.67 (broad m, 3H), 1.67−1.53 (m, 2H), 1.53−

DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515

1.41 (m, 2H), 1.41−1.28 (m, 2H), 1.15−0.98 (broad m, 2H) ppm. IR (KBr): ν = 3383, 2947, 2866, 2359, 2095, 1593, 1452, 1350, 1285, 1258, 1188, 1179, 1159, 1117, 1098, 1045, 932, 905, 837, 814, 768, 745, 667, 619, 556, 355 cm^{-1}.

3-cyclopentylpropan-1-amine. As described in the general procedure for the (3-azidopropyl)cyclopentane (0.38 g, 2.48 mmol), 3-cyclopentylpropan-1-amine was prepared. The pure product was obtained eluting with $CDCl_3$ through alumina column, yielding (92%, 0.29 g). ^1H NMR ($CDCl_3$): δ = 2.63 (quin, J = 7.2 Hz, 2H), 1.74−1.62 (broad m, 3H), 1.62−1.50 (m, 2H), 1.50−1.37 (m, 4H), 1.37−1.31 (m, 2H), 1.08−0.96 (broad m, 2H) ppm.

The ammonium HCl salt **6** was recrystallized with dry ethanolic HCl and dry ether (v:v = 1:2) in −17 °C, yielding a colorless solid (14%, 52.2 mg). Decomp. 162 °C. ^1H NMR (D_2O): δ = 3.02−2.91 (m, 2H), 1.81−1.40 (broad m, 8H), 1.40−1.28 (broad m, 2H), 1.12−0.98 (broad m, 2H) ppm. ^{13}C NMR (D_2O): δ = 40.3 (CH_2), 39.6 (CH), 32.7 (CH_2), 26.7 (CH_2), 25.3 (CH_2) ppm. APT (D_2O): δ = 39.6 (CH) ppm. IR (KBr): ν = 2949, 2048, 1607, 1510, 1477, 1452, 1402, 1387, 1344, 1315, 1248, 1159, 1092, 1049, 1003, 986, 955, 935, 893, 839, 824, 752, 484 cm^{-1}. MS (ESI): m/z (%) 128.2 (70) $[M]^+$, 238.6 (100) $[M - NH_4]^+$. Anal. calcd for $C_8H_{18}NCl$: C, 58.70; H, 11.08; N, 8.56. Found: C, 58.95; H, 10.96; N, 8.54.

*N^1-Cyclopentylethane-1, 2-diammonium Dichloride (**7**)*. A five-step synthetic process starting from cyclopentanone was used to prepare the ammonium salt **7**.

To a stirred mixture of cyclopentanone (1.5 g, 17.8 mmol) and 2-aminoethanol (1.2 g, 19.7 mmol) in ethanol (3 mL) and formic acid (1 drop) at rt for 18 h, $NaBH_4$ (0.7 g, 18.5 mmol) was added with an ice bath. Then the reaction mixture was warmed to rt for 3 h and quenched by careful addition of concentrated HCl until pH = 1−2. The mixture was left overnight. The EtOH was then removed in vacuo. A small volume of water was added, followed by solid KOH, until an oily layer formed. Then the solution was extracted with DCM. The organic extract was dried over $MgSO_4$, and DCM solvent removed to give the crude product in vacuo, yield ∼78% of 2-(cyclopentylamino)ethanol was obtained by ^1H NMR.[48]

The crude 2-(cyclopentylamino)ethanol (1.8 g, 13.9 mmol) was reacted under tosylation condition described above with 2 mol equiv of TsCl. Pure 2-(*N*-cyclopentyl-4-methylphenylsulfonamido)-ethyl-4-methylbenzenesulfonate (**11**) was obtained as viscous oil (3.25 g, 53%) after the purification by flash silica column chromatography (DCM/petroleum ether, 2:1). ^1H NMR ($CDCl_3$): δ = 7.78 (d, J = 8.2 Hz, 2H), 7.63 (d, J = 8.0 Hz, 2H), 7.35(d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 4.20 (t, J = 7.1 Hz, 2H), 4.10 (quin, J = 8.6 Hz, 1H), 3.22 (t, J = 7.1 Hz, 2H), 2.44 (s, 3H), 2.40 (s, 3H), 1.67−1.53 (m, 2H), 1.53−1.47 (m, 2H), 1.47−1.34 (m, 2H), 1.25−1.09 (m, 2H) ppm. ^{13}C NMR ($CDCl_3$): δ = 145.2 (CH_2), 143.7 (CH_2), 136.3 (CH_2), 132.7 (CH_2), 130.1 (CH), 129.8 (CH), 128.1 (CH), 127.4 (CH), 69.4 (CH_2), 59.3 (CH), 42.2 (CH_2), 29.2 (CH_2), 23.5 (CH_2), 21.7 (CH), 21.6 (CH_3) ppm. APT ($CDCl_3$): δ = 130.1 (CH), 129.8 (CH), 128.1 (CH), 127.4 (CH), 59.3 (CH), 21.7 (CH_3), 21.6 (CH_3) ppm. IR (Film): ν = 3385, 2924, 2872, 1597, 1454, 1360, 1342, 1258, 1190, 1177, 1159, 1096, 1038, 974, 905, 816, 745, 664, 575,554, 519 cm^{-1}. MS (ESI): m/z (%) 438.5 (20) $[M + H]^+$, 460.4 (100) $[M + Na]^+$, 476.5 (15) $[M + K]^+$. Anal. calcd for $C_{21}H_{27}NS_2O_5$: C, 57.64; H, 6.22; N, 3.20; S, 14.65. Found: C, 57.86; H, 5.96; N, 3.47; S, 14.49.

The tosylated product above (1.55 g, 3.55 mmol) was reacted with sodium azide as described in the general procedure. Purification by silica column chromatography (EtOAc/petroleum ether, 0.15:0.85) gave *N*-(2-azidoethyl)-*N*-cyclopentyl-4-methylbenzenesulfonamide as a colorless oil (0.83 g, 76%). ^1H NMR ($CDCl_3$): δ = 7.69 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 4.14 (quin, J = 6.8 Hz, 1H), 3.57 (t, J = 7.2 Hz, 2H), 3.11 (t, J = 7.0 Hz, 2H), 2.41 (s, 3H), 1.74−1.62 (m, 2H), 1.62−1.50 (m, 2H), 1.50−1.36 (m, 2H), 1.31−1.17 (m, 2H) ppm. IR (Film): ν = 3030, 2953, 2926, 2872, 2737, 2683, 2583, 2496, 2367, 2104, 1908, 1599, 1492, 1463, 1444, 1392, 1345, 1337, 1309, 1287, 1238, 1200, 1184, 1157, 1092, 1045, 1027, 991, 918, 868, 816, 748, 717 cm^{-1}.

N-(2-azidoethyl)-*N*-cyclopentyl-4-methylbenzenesulfonamide (1.09 g, 3.54 mmol) was catalytically reduced, and the crude passed through an aluminum oxide column to give *N*-(2-aminoethyl)-*N*-cyclopentyl-4-methylbenzenesulfonamide as a viscous oil (0.83 g, 83%). ^1H NMR ($CDCl_3$): δ = 7.68 (d, J = 8.1 Hz, 2H), 7.25 (d, J = 8.4 Hz, 2H), 4.14 (quin, J = 8.4 Hz, 1H), 3.08−3.00 (m, 2H), 2.97−2.90 (m, 2H), 2.39 (s, 3H), 1.69−1.36 (broad m, 6H), 1.36−1.19 (m, 2H) ppm.

Finally the diammonium salt **7** was prepared as described in the general procedure for the reduction of a tosylamide, and then purification of the resultant amine was achieved by cation exchange resin chromatography. *N*-(2-aminoethyl)-*N*-cyclopentyl-4-methylbenzenesulfonamide (0.33 g, 1.17 mmol) was then treated with Li-$C_{10}H_8$ as previously described. The crude product was purified by Dowex column chromatography (45% HCO_2H/1 M HCl) and recrystalisation gave the pure **7** (35 mg, 18%). M.p 133−134 °C. ^1H NMR (D_2O): δ = 3.63 (quin, J = 6.6 Hz, 1H), 3.42−3.31 (m, 4H), 2.16−2.04 (m, 2H), 1.80−1.56 (m, 6H) ppm. ^{13}C NMR (D_2O): δ = 60.7 (CH), 43.5 (CH_2), 36.1 (CH_2), 29.8 (CH_2), 24.2 (CH_2) ppm. APT (D_2O): δ = 60.7 (CH) ppm. IR (KBr): ν = 3443, 2965, 2708, 2131, 1620, 1582, 1491, 1458, 1441, 1404, 1381, 1337, 1312, 1277, 1157, 1132, 1057, 1018, 993, 947, 822, 785, 567, 469, 426, 392, 361 cm^{-1}. MS (ESI): m/z (%) 112.1 (90) $[M - NH_4]^+$, 129.2 (100) $[M - H]^+$. Anal. calcd for $C_7H_{18}N_2Cl_2$: C, 41.78; H, 9.02; N, 13.93. Found: C, 41.59; H, 9.39; N, 13.65.

*N^1,$N^{1\prime}$-(Octane-1,8-diyl)bis(N^2-cyclopentylethane-1,2-diammonium) Tetrachloride (**9**)*. The tetraammonium ion **9** was obtained in a three-step synthesis from the tosyl ester **11**. Toluenesulfonyl chloride (19.06 g, 0.1 mol) was added to a mixture of 1,8-octanediamine (7.2 g, 0.05 mol), DMF (30 mL), and triethylamine (10.2 g, 8 mL) at 0 °C. The mixture was then allowed to equilibrate to rt and maintained at that temperature for 60 h. The mixture was then poured into water, and the solid collected by filtration. The product *N*,*N*′-(octane-1,8-diyl)bis(4-methylbenzenesulfonamide) (**10**) was recrystalised from EtOH and dried at 55 °C. Without further purification, this ditosyl amide **10** (4.13 g, 9.74 mmol) was added to a solution of EtONa/EtOH at 60 °C [NaOEt was freshly prepared in dry EtOH (50 mL) and clean Na (442 mg)]. A white solid appeared after 1.5 h. The reaction was maintained at 60 °C for an additional 12 h, and then the solvent was removed by distillation and completely dried under vacuum (0.1 mmHg). The tosyl ester **11** (8 g, 18.3 mmol) dissolved in double dried DMF (80 mL) was transferred via cannulation into a reaction flask containing the sodium salt of **10**, and the mixture was heated to 110 °C for 20 h. After cooling to rt, the reaction mixture was poured into water. After extraction with DCM (20 mL × 4), drying over $MgSO_4$ and removal of DCM in vacuo, the product *N*,*N*′-(octane-1,8-diyl)bis(*N*-(2-(*N*-cyclopentyl-4-methylphenylsulfonamido)ethyl)-4-methylbenzenesulfonamide) was purified by chromatography 20% EtOAc/petroleum ether, then recrystallized from (DCM/petroleum ether, 1:3) to obtain pure crystals (3.6 g, 37%). Mp 152−153 °C. ^1H NMR ($CDCl_3$): δ = 7.67−7.65 (d, J = 8.6 Hz, 8H), 7.30−7.28 (m, J = 8.6 Hz, 4H), 7.28−7.26 (d, J = 8.6 Hz, 4H), 4.22−4.11 (quin, J = 8.2 Hz, 2H), 3.30−3.22 (m, 4H), 3.22−3.13 (m, 4H), 3.13−3.03 (t, J = 7.1 Hz, 4H), 2.41 (s, 6H), 2.40 (s, 6H), 1.61 (broad s, 12H), 1.43 (broad s, 4H), 1.30 (broad s, 12H) ppm. ^{13}C NMR ($CDCl_3$): δ = 143.4 (CH_2), 136.7 (CH_2), 135.8 (CH_2), 129.9 (CH), 127.4 (CH), 127.3 (CH), 59.3 (CH), 50.5 (CH_2), 50.3 (CH_2), 44.1 (CH_2), 29.3 (CH_2), 28.9 (CH_2), 26.7 (CH_2), 23.7 (CH_2), 21.7 (CH_3) ppm. APT $CDCl_3$): δ = 129.9 (CH), 127.4(CH), 127.3(CH), 59.3(CH), 21.7(CH_3) ppm. IR (KBr,): ν = 2957, 1601, 1458, 1383, 1342, 1155, 1090, 1053, 999, 933, 872, 812, 725, 656, 548 cm^{-1}. MS (ESI): m/z (%) 1005.8 (100) $[M + Na]^+$. Anal. calcd for $C_{50}H_{70}N_4S_4O_8$: C, 61.07; H, 7.17; N, 5.70. Found: C, 61.20; H, 7.15; N, 5.50.

N,*N*′-(octane-1,8-diyl)bis(*N*-(2-(*N*-cyclopentyl-4-methylphenylsulfonamido)ethyl)-4-methylbenzenesulfonamide) (983.4 mg, 1.0 mmol) was then treated with Li-$C_{10}H_8$ as previously described. Portions of the crude product were purified by Dowex column chromatography (45% HCO_2H/3 M HCl) and crystallized in dry EtOH to obtain the pure ammonium salt **9** (42.6 mg, 3%). Decomp. 216.3 °C. ^1H NMR (D_2O): δ = 3.61 (quin, J = 6.85 Hz, 2H), 3.36 (s, 8H), 3.05 (t, J = 7.82 Hz, 4H), 2.13−2.02 (m, 4H), 1.77−1.54 (m, 16H), 1.30 (broad s, 8H) ppm. ^{13}C NMR (D_2O): δ = 60.0, 48.1, 42.9,

DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515

41.6, 29.0, 27.9, 25.4, 23.4 ppm. IR (KBr): ν = 2936, 2860, 2714, 2546, 2440, 2374, 1466, 1059, 798 cm^{-1}. MS (ESI): m/z (%) 367.5 (100) [free base + H]$^+$, 403.5 (23) [free base + 2H + Cl]$^+$. HRMS (ESI) m/z calculated for $C_{22}H_{47}N_4$ [free base + H]$^+$ 367.3801, found 367.3803. Anal. calcd for $C_{22}H_{50}N_4Cl_4(0.5H_2O)$: C, 50.67; H, 9.86; N, 10.74. Found: C, 50.83; H, 10.23; N, 10.56.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02813.

^{1}H spectra of classical Q[6], Me_4Q[6], CyP_6Q[6], and Q[7] used in the study plus new compounds **6**, **7**, **9**, **11** and some precursor compounds. In addition, the ^{1}H spectrum **14** and 2D NMR DQCOSY of the encapsulation of **9** (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the UNSW Canberra, Postgraduate Student Research Scholarship program.

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DOI: 10.1021/acs.joc.6b02813
J. Org. Chem. 2017, 82, 5507−5515