Molecular Meccano, Part 60[+]

The Influence of Macrocyclic Polyether Constitution upon Ammonium Ion/Crown Ether Recognition Processes

Stuart J. Cantrill,[a] David A. Fulton,[a] Aaron M. Heiss,[a] Anthony R. Pease,[a] J. Fraser Stoddart,*[a] Andrew J. P. White,[b] and David J. Williams*[b]

Abstract: Secondary dialkylammonium ($R_2NH_2^+$) ions are bound readily by dibenzo[24]crown-8 (DB24C8) to form *threaded* complexes, namely [2]pseudorotaxanes. The effect of replacing one or both of the catechol rings in DB24C8 with resorcinol rings upon the crown ether's ability to bind $R_2NH_2^+$ ions has now been investigated. When only one aromatic ring is changed from catechol to resorcinol, a crown ether with a [25]crown-8 constitution is created—namely benzometaphenylene[25]crown-8 (BMP25C8). A [2]pseudorotaxane is formed in the solid state when BMP25C8 is co-crystallized with dibenzylammonium hexafluorophosphate, as evidenced by its X-ray crystal structure. Furthermore, this crown ether has been shown to bind $R_2NH_2^+$ ions in solution, an observation which has been exploited in the synthesis of the first BMP25C8-containing [2]rotaxane. The methodology employed to generate this [2]rotaxane—the reaction of an amine with an isocyanate to form a urea—was tested initially on a system incorporating DB24C8 and was shown to work efficiently. Both [2]rotaxanes have been fully characterized by ^1H and ^{13}C NMR spectroscopies, FAB mass spectrometry and X-ray crystallography. Interestingly, the unsymmetrical nature of the dumbbell-shaped component in each of the two [2]rotaxanes renders each face of the encircling macrocyclic polyether diastereotopic, a feature that is apparent upon inspection of their ^1H NMR spectra. The resonances associated with the diastereotopic protons on each face of the macrorings are well enough resolved to enable the faces of the crown ethers to be readily identified with respect to their protons by ^1H NMR spectroscopy. Unambiguous assignments can be made as a result of the fact that the protons on each face of the macrocyclic polyether experience a unique set of through-space interactions, as evidenced by T-ROESY experiments. Additionally, the two-dimensional NMR analyses are in agreement with the X-ray crystallographic studies performed on these [2]rotaxanes, indicating that the crown ethers are located intimately around the NH_2^+ centers as expected. Replacement of both catechol rings in the DB24C8 constitution with resorcinol rings results in a crown ether with a [26]crown-8 constitution—namely bismetaphenylene[26]crown-8 (BMP26C8). All the evidence to date points to the fact that this further change in constitution results in a crown ether that does not bind $R_2NH_2^+$ ions in either the solution or solid states.

Keywords: crown ethers · hydrogen bonds · rotaxanes · secondary ammonium ions · self-assembly

Introduction

For many years, it has been recognized[1, 2] that crown ethers are exceptionally versatile hosts for a wide variety of cationic guests. Amongst the many guests that have been investigated are substituted ammonium ions, and although initially[3] the focus fell upon primary alkylammonium ions (RNH_3^+), more recently, secondary dialkylammonium ions ($R_2NH_2^+$) have received[4] considerable attention. The discovery[5] that $R_2NH_2^+$ ions are complexed by dibenzo[24]crown-8 (DB24C8) (**1**) in a *threaded* rather than a *face-to-face*[6] manner, heralded the arrival of a new paradigm for the construction of 1) discrete interlocked molecules[7] and 2) extended interwoven supramolecular arrays.[8] Indeed, the

---

[a] Prof. J. F. Stoddart, S. J. Cantrill, D. A. Fulton, Dr. A. M. Heiss, A. R. Pease
Department of Chemistry and Biochemistry
University of California, Los Angeles
405 Hilgard Avenue, Los Angeles, CA 90095-1569 (USA)
Fax: (+1) 310-206-1843
E-mail: stoddart@chem.ucla.edu

[b] Prof. D. J. Williams, Dr. A. J. P. White
Chemical Crystallography Laboratory
Department of Chemistry, Imperial College
South Kensington, GB-London, SW7 2AY (UK)
Fax: (+44) 20-7594-5835

[+] Part 59, see: B. Cabezon, J. Cao, F. M. Raymo, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **2000**, *6*, 2262–2273.

Supporting information for this article is available on the WWW under http://www.wiley-vch.de/home/angewandte/ or from the author.

0947-6539/00/0612-2274 $ 17.50+.50/0

$R_2NH_2^+$ ion/DB24C8 supramolecular synthon has proven to be extremely effective in the self-assembly[9] of many different kinds of architectures.[10] However, it is not without its problems. Our investigations[11] into the fabrication of higher order multicomponent aggregates[12]—rich in interlocked and/or intertwined motifs—necessitates the functionalization of either the crown ether or the dialkylammonium ion components in order to facilitate the formation of more elaborate threaded host–guest complexes. Formally, monosubstitution of one of the catechol rings of DB24C8 reduces the local symmetry of the macrocyclic polyether such that subsequent incorporation into interlocked molecules may result in the formation of isomeric compounds. This problem can be alleviated by the replacement (Figure 1) of either one or both[13] of the catechol with resorcinol rings. The fact of the matter is that substitution at the C-5 position on a resorcinol ring does not desymmetrize a macrocyclic polyether into which it has been incorporated. Herein we report our findings concerning the relative propensities with which DB24C8 (**1**), benzometaphenylene[25]crown-8 (BMP25C8) (**2**), and bismetaphenylene[26]crown-8 (BMP26C8) (**3**) bind $R_2NH_2^+$ ions to generate 1) [2]pseudorotaxanes (Figure 2) and subsequently 2) [2]rotaxanes, formed by the kinetic trapping of these supramolecular complexes.

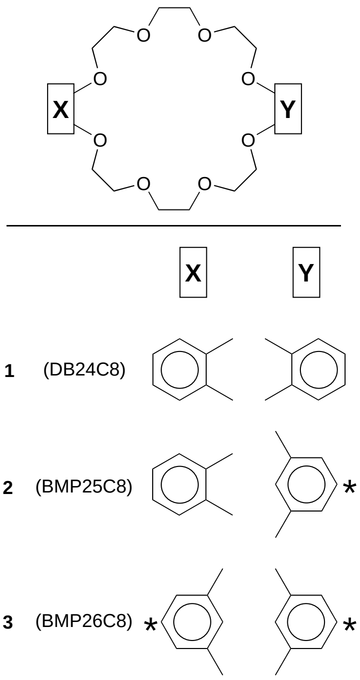


Figure 1. A generic crown ether framework—containing eight oxygen atoms—which incorporates two diametrically opposed aromatic rings which are derived from catechol or resorcinol. Therefore, the three possible permutations are 1) catechol/catechol that is, dibenzo[24]crown-8 (DB24C8) **1**, 2) catechol/resorcinol that is, benzometaphenylene[25]-crown-8 (BMP25C8) **2**, and 3) resorcinol/resorcinol that is, bismetaphenylene[26]crown-8 (BMP26C8) **3**. The constitutions of **2** and **3** allow substitution at the C-5 position (*) of either one or both of the aromatic units, respectively, without changing the local symmetry of the crown ether.

Results and Discussion

Dibenzo[24]crown-8 (DB24C8)

Background: Substantial evidence has been gathered[4, 5] which demonstrates that DB24C8 binds $R_2NH_2^+$ ions in the solution, solid, and gas phases by *threading* to generate [2]pseudorotaxanes. Unequivocal proof of such a binding motif has been established[4b] by a 'stoppering' approach in which the ends of a reactive threadlike component—positioned through the center of the crown ether's macroring–are allowed to react with a large capping group, affording (Figure 3) a [2]rotaxane. Recently, we communicated[7g] our preliminary findings of an investigation into the utility of bulky isocyanates as the reactive 'stoppering' reagents and now present our results, regarding this new protocol, in detail.

Synthesis: The template-directed synthesis of the [2]rotaxane **10**-H·O_2CCF_3 is illustrated in Scheme 1. 4-Aminobenzyl-3,5-

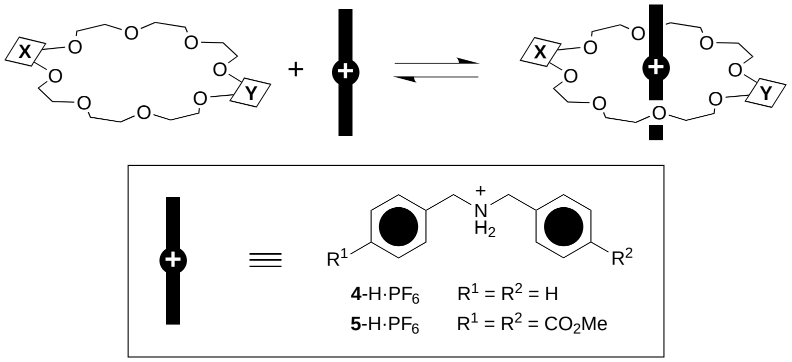


Figure 2. A schematic representation depicting how a generic crown ether can act as a host for substituted secondary dibenzylammonium ions. The cavity of the crown ether is pierced by the threadlike cation, resulting in the formation of a [2]pseudorotaxane which is stabilized predominantly by $N^+–H\cdots O$ and $C–H\cdots O$ hydrogen-bonding interactions.

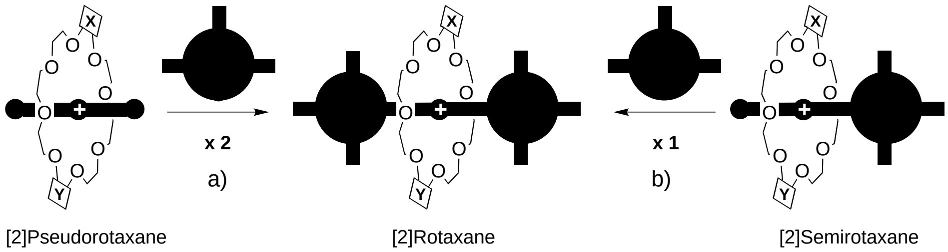
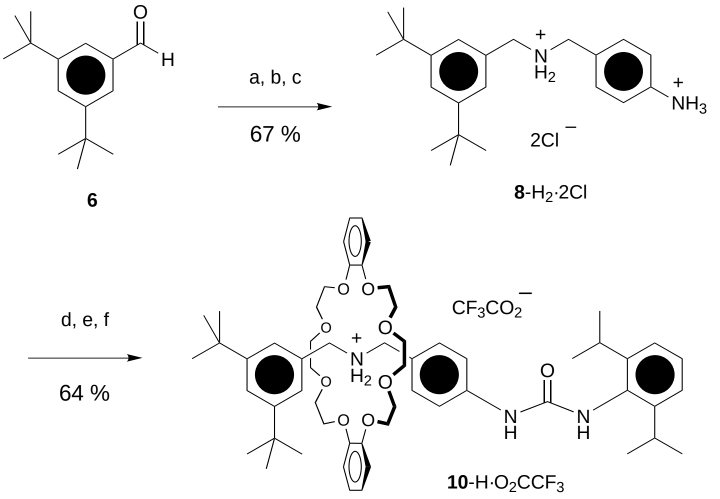


Figure 3. A schematic representation depicting two modifications of the *threading-followed-by-stoppering* approach for the synthesis of [2]rotaxanes. Either a) a [2]pseudorotaxane is formed, which is subsequently capped at both ends with large 'stopper' groups, or b) a semirotaxane—which contains a threadlike molecule with one bulky group already attached—is assembled, which is 'stoppered' at the terminus over which the crown ether had to pass to form the 1:1 complex.



Scheme 1. The synthesis of the [2]rotaxane **10**-H · O_2CCF_3: a) 4-azidobenzylamine, C_6H_6, reflux; b) $NaBH_4$/MeOH, room temperature; c) HCl, CH_2Cl_2/Et_2O, overall 67 %; d) NaOH, H_2O/CH_2Cl_2; e) DB24C8 (**1**), CF_3CO_2H, CH_2Cl_2; f) 2,6-diisopropylphenylisocyanate (**9**), room temperature, overall 64 %.

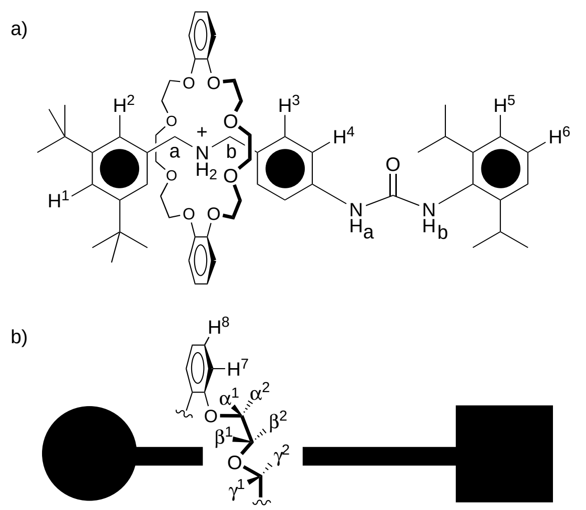


Figure 4. The structure of the [2]rotaxane **10**-H · O_2CCF_3, showing the labeling scheme for both a) the dumbbell and b) the crown ether components, used in describing its NMR spectroscopic properties. The schematic representation b) highlights the unsymmetrical nature of the dumbbell. The protons (α^1, β^1, γ^1) on one face of the DB24C8 macrocycle are oriented toward the 3,5-di-*tert*-butylphenyl stopper, whereas those protons (α^2, β^2, γ^2) on the opposite face of the macrocycle are directed toward the 2,6-diisopropylphenyl stopper, that is, the protons located on opposite faces of the crown ether are diastereotopic.

di-*tert*-butylbenzylamine (**8**) was prepared by $NaBH_4$ reduction of the imine generated from the condensation of 3,5-di-*tert*-butylbenzaldehyde (**6**)[14] and 4-azidobenzylamine (**7**).[15] It was isolated as its dihydrochloride salt **8**-H_2 · 2Cl in an overall yield of 67 %. Deprotonation of this salt was followed by the addition of one equivalent of CF_3CO_2H which presumably brought about the monoprotonation of the diamine **8** at the more basic secondary dibenzylamine site. As a consequence, an $R_2NH_2^+$ ion is generated which is capable of recognizing the DB24C8 molecules also present in the solution. Addition of 2,6-diisopropylphenylisocyanate, followed by work-up and subsequent chromatographic purification, afforded the [2]rotaxane **10**-H · O_2CCF_3 as the major product in a 64 % yield. This result supports the hypothesis that a reactive [2]pseudorotaxane must be formed under the reaction conditions since the interlocked molecule **10**-H · O_2CCF_3 can only be obtained via the intermediacy of a threaded 1:1 complex.

NMR spectroscopy: The full assignment of the ^1H NMR spectrum and in-depth analysis of the ^{13}C NMR spectrum (see Experimental Section) was made possible by two-dimensional ^1H-^1H correlation (COSY) and ^1H-^{13}C correlation (HMQC) experiments. The unsymmetrical nature of the dumbbell-shaped component of the [2]rotaxane **10**-H · O_2CCF_3 renders the protons on each face of the encircling macrocycle heterotopic (Figure 4). When a symmetrical thread/dumbbell is bound/encircled by a DB24C8 macroring, the resonances associated with the α- and β-OCH_2 protons of the crown ether appear as narrow multiplets, and the resonance of the γ-OCH_2 protons gives rise to a singlet. In the case of **10**-H · O_2CCF_3, there are now two distinct environments for each of these pairs of protons, respectively, that is, the protons (α^1, β^1, and γ^1) on the side of the macrocycle facing toward the 3,5-di-*tert*-butylphenyl stopper are different from those (α^2, β^2, and γ^2) facing the 2,6-diisopropylphenyl stopper on the other side of the macrocycle. The facial desymmetrization of the crown ether is evident and has a profound effect upon the ^1H NMR spectrum (Figure 5) of this compound. Although the resonances for the α-OCH_2 protons overlap, those associated with the β- and γ-OCH_2 protons are separated such that distinct multiplets are observed for β^1- and β^2-OCH_2 and γ^1- and γ^2-OCH_2 protons. The unambiguous assignment of the superscripts '1' and '2' (denoting the face of the macrocycle on which a particular proton resides) was made upon inspection of the T-ROESY spectrum. Two important probe protons on the dumbbell's backbone are H-2 and H-3. Should, as expected,[16] the DB24C8 macroring encircle the NH_2^+ center, in preference to the urea moiety, H-2 and H-3 will flank the macrocycle. Indeed, this hypothesis is confirmed upon inspection of the partial T-ROESY spectrum shown in Figure 6. Through-space interactions are observed[17] between H-2, on the dumbbell, and all of the OCH_2 protons (α^1, β^1 and γ^1) on only one side of the macrocycle. The corresponding pattern is observed for H-3, which only correlates to resonances arising from the α^2-, β^2- and γ^2-OCH_2 protons residing on the opposite face of the crown ether.

X-ray crystallography: Single crystals, suitable for X-ray crystallographic analysis, were obtained upon layering a CH_2Cl_2 solution of the [2]rotaxane **10**-H · O_2CCF_3 with hexanes. The X-ray crystal analysis of the [2]rotaxane shows the crystals to contain two independent molecules in the asymmetric unit. In both molecules, it is the NH_2^+ center that is encircled by the DB24C8 macrocycle with the urea component hydrogen bonded to the trifluoroacetate counterion. Stabilization in both independent molecules is by a combination of N^+–H ··· O and C–H ··· O hydrogen bonding interactions (Figure 7). The conformation of the cationic

0947-6539/00/0612-2276 $ 17.50+.50/0

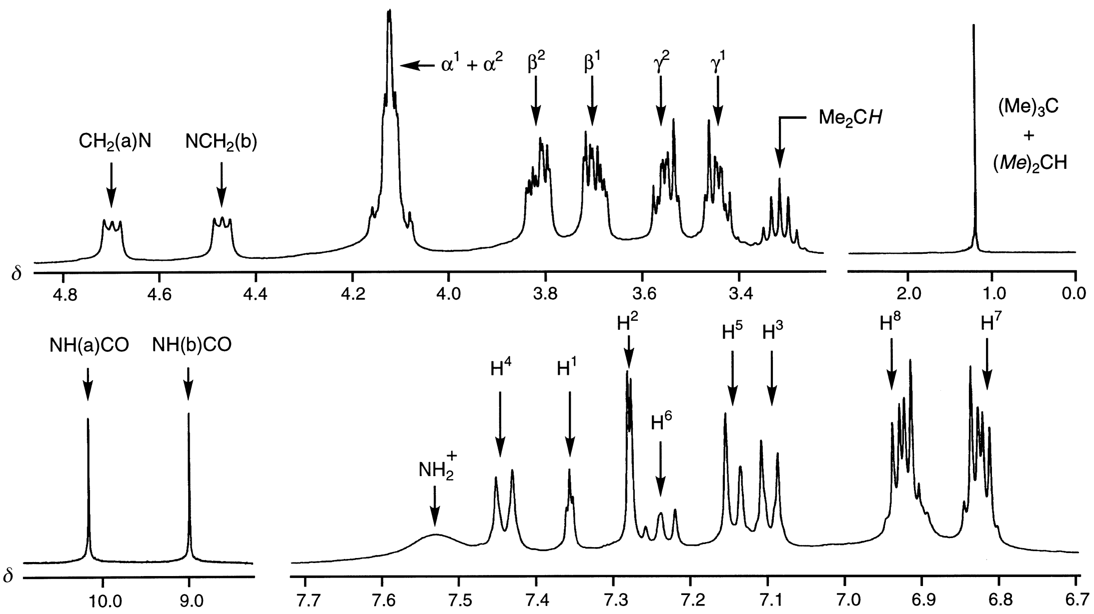


Figure 5. The partial ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of **10**-H · O_2CCF_3.

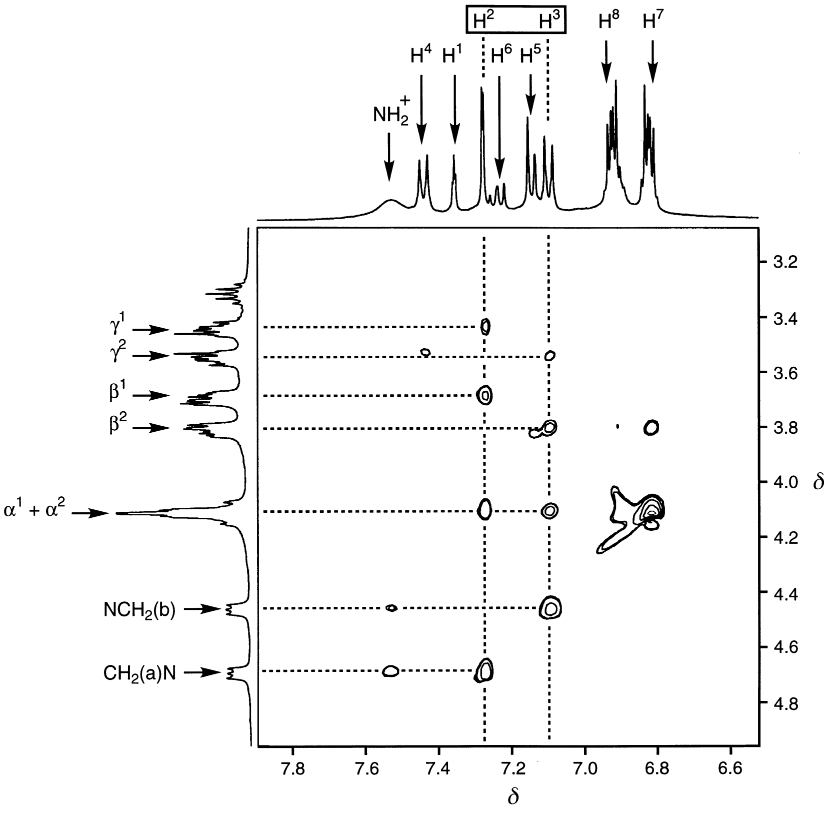


Figure 6. The partial T-ROESY spectrum (400 MHz, CD_2Cl_2) of **10**-H · O_2CCF_3. The most significant probe protons are H-2 and H-3, which each show a correlation to only *one* set of protons on only *one* face of the crown ether.

dumbbell in both molecules is essentially the same with the plane of the urea fragment steeply inclined to the plane of the terminal 2,6-diisopropylphenyl ring but lying close to the plane of the central *p*-toluidinyl ring (*w* and *x* in Table 1, respectively). The plane of the all-*anti* $CCH_2NH_2^+CH_2C$ backbone is steeply inclined to both the central *p*-toluidinyl and the 3,5-di-*tert*-butylphenyl ring systems (*y* and *z* in Table 1, respectively). However, the conformations of the two independent DB24C8 macrocycles differ, both crown ethers having an extended geometry, but with distinctly different geometries for one of the polyether linkages. In both independent molecules, there is an apparent overlaying of one of the catechol rings and the *p*-toluidinyl ring of the cationic dumbbell. The centroid–centroid distances (4.48 Å in **i** and 4.54 Å in **ii**) are, however, too great for any significant intramolecular π–π stacking interactions. There is also a marked absence of any inter-[2]rotaxane interactions, although there is evidence for a weak intermolecular C–H···π interaction (H···π 2.73 Å, C–H···π angle 148°) between one of the methylene hydrogen atoms in one of the polyether chains in molecule **ii** and one of the catechol rings of a symmetry-related [2]rotaxane.

Benzometaphenylene[25]crown-8 (BMP25C8)

Background: Replacement of one of the catechol rings of DB24C8 with resorcinol—affording a [25]crown-8 derivative—is desirable in the context of preserving local symmetry should subsequent functionalization of the crown ether be desired. However, this strategy is only sustainable if such a

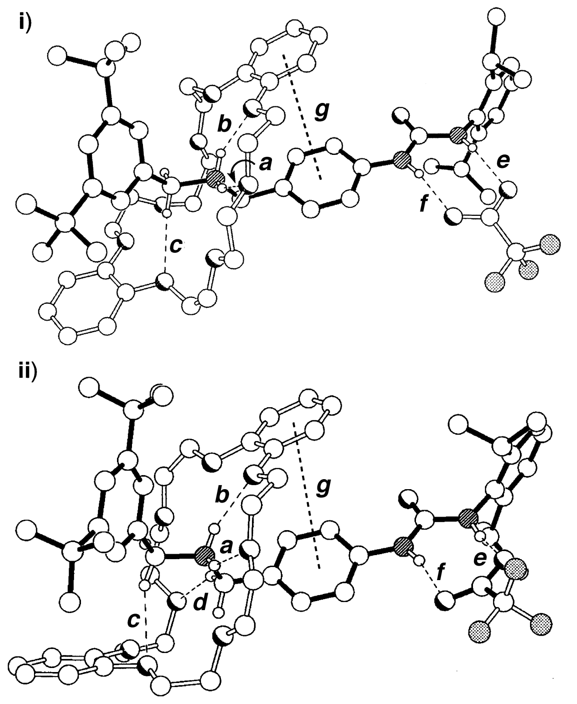
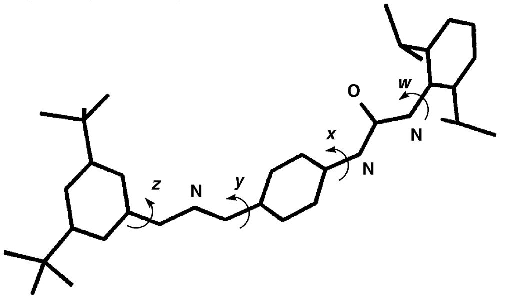


Figure 7. The molecular structures of the two crystallographically independent [2]rotaxanes present in the crystals of **10**-H $\cdot$ O_2CCF_3. Hydrogen bonding distances and angles [(X$\cdots$O), (H$\cdots$O) distances [Å], (X–H$\cdots$O) angles [°]]: for molecule **i**; *a*) 2.85, 2.01, 156; *b*) 2.89, 2.16, 137; *c*) 3.31, 2.36, 171; *e*) 2.89, 2.03, 159; *f*) 2.86, 1.98, 164; for molecule **ii**; *a*) 2.91, 2.11, 147; *b*) 3.01, 2.23, 145; *c*) 3.41, 2.51, 157; *d*) 3.25, 2.41, 147; *e*) 2.76, 1.92, 163; *f*) 2.91, 2.02, 168. The centroid–centroid distances *g*) for molecules **i** and **ii** are 4.48 and 4.54 Å, respectively.

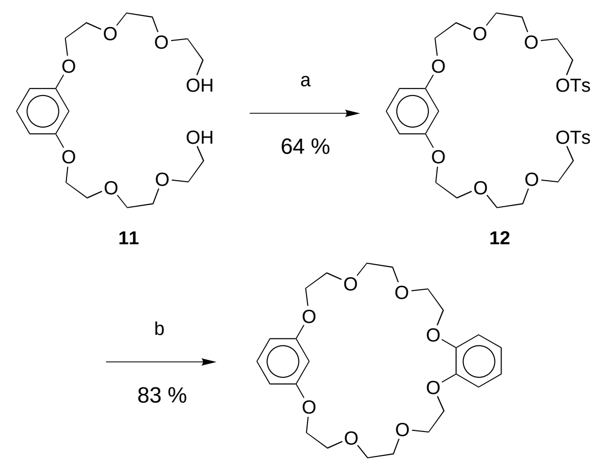
Table 1. The torsion angles (**w**, **x**, **y**, and **z**) observed for the DB24C8- and BMP25C8-containing rotaxanes, **10**-H $\cdot$ O_2CCF_3 and **14**-H $\cdot$ O_2CCF_3, respectively. In each structure, there are two crystallographically independent molecules (**i** and **ii**) in the asymmetric unit.



Torsion angles [°] Structure	*w*	*x*	*y*	*z*
{DB24C8}				
10-H $\cdot$ O_2CCF_3 (**i**)	84	10	86	64
10-H $\cdot$ O_2CCF_3 (**ii**)	70	16	85	63
{BMP25C8}				
14-H $\cdot$ O_2CCF_3 (**i**)	72	4	75	59
14-H $\cdot$ O_2CCF_3 (**ii**)	90	3	86	54

modification in the macrocyclic polyether's backbone does not hinder significantly its ability to bind $R_2NH_2^+$ ions.

Synthesis: The synthetic pathway leading to the formation of BMP25C8 (**2**) is depicted in Scheme 2. Tosylation of the diol[18] **11**, under standard conditions, afforded the ditosylate **12**. Subsequent macrocyclization of **12** with catechol **13**, in the presence of base, gave the crown ether in good yield. Single crystals suitable for X-ray crystallographic analysis were grown from an ethanolic solution upon slow evaporation.



11 **12** **2**

Scheme 2. The synthesis of BMP25C8 (**2**): a) TsCl, *N,N*-DMAP, Et_3N, CH_2Cl_2, 64%; b) catechol (**13**), Cs_2CO_3, MeCN, reflux, 83%.

X-ray crystallography: The X-ray analysis of BMP25C8 shows (Figure 8a) the macrocycle to have an extended geometry

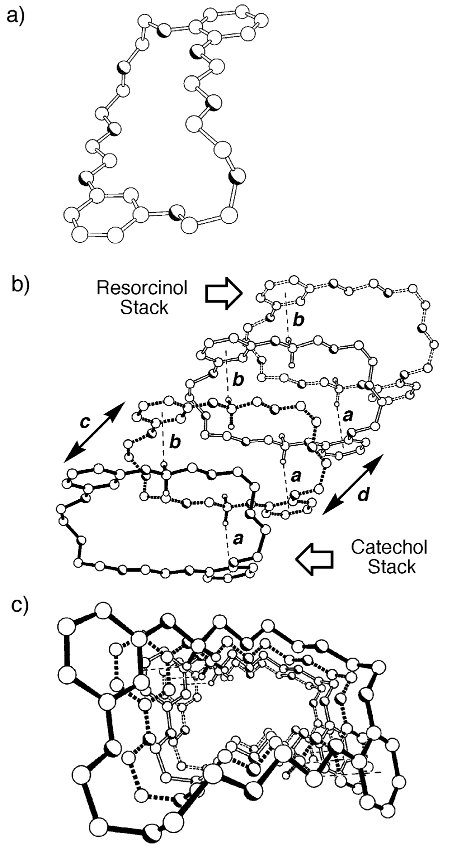


Figure 8. a) The crystal structure of BMP25C8 **2**. b) Adjacent molecules are stacked by virtue of pairs of C–H$\cdots\pi$ interactions, *a*) H$\cdots\pi$ distance 2.85 Å, C–H$\cdots\pi$ angle 140°; *b*) H$\cdots\pi$ distance 2.79 Å, C–H$\cdots\pi$ angle 137°, supplemented by π–π stacking interactions between the resorcinol and catechol moieties, interactions *c* and *d*, respectively. c) End-on view of the constricted nanotube formed by the stacking of BMP25C8 macrocycles.

with a fairly large central pathway through the center of the macroring. The molecules stack along the crystallographic *b* direction and are linked by pairs of C–H···π interactions (*a* and *b* in Figure 8b) involving one of the phenoxymethylene hydrogen atoms of both the catechol and resorcinol rings and their adjacent counterparts within the stack. These interactions are supplemented, to a lesser degree, by partial π–π overlap between the resorcinol rings and between the catechol rings (*c* and *d* in Figure 8b) of adjacent molecules (the centroid–centroid and interplanar separations are 5.14, 3.44 Å and 5.14, 3.52 Å, respectively). The combination of these intermolecular interactions produces (Figure 8c) constricted nanotubes that extend through the crystal. Adjacent nanotubes, in one direction in the crystal, are crosslinked by an additional C–H···π interaction between one of the resorcinol phenoxymethylene hydrogen atoms in one stack and a catechol ring in the next (the H···π distance is 2.91 Å and the C–H···π angle 148°).

Mass spectrometry: The FAB mass spectrum of a 1:1 mixture of BMP25C8 and **4**-H·PF_6 (Figure 2, $R^1=R^2=H$) reveals that, in the gas phase, a strong 1:1 complex is formed between these two components. Although the base peak corresponds to the uncomplexed dibenzylammonium cation **4**-H^+, a relatively intense signal (50%) arising from the 1:1 complex [**2**·**4**-H]$^+$ appears at *m/z* 646, suggesting[19] that the complex has a [2]pseudorotaxane, rather than a *face-to-face*, geometry.

NMR spectroscopy: The ^1H NMR spectrum of a 1:1 CD_2Cl_2 solution of BMP25C8 and **4**-H·PF_6 reveals the occurrence of complexation. However, the spectrum consists of both broad and sharp peaks—rather than a series of sharp well-defined peaks arising from the slow exchange of the free components and the [2]pseudorotaxane (as is the case with DB24C8)—indicating that, under the experimental conditions, neither a slow- nor fast-exchange regime is operating. This behavior precludes the determination of a stability constant by either the single-point method[20] or dilution/titration[21] techniques. By employing the bis(4-methoxycarbonylbenzyl)ammonium ion **5**-H^+—a threadlike molecule (Figure 2, $R^1=R^2=CO_2Me$) with slightly increased steric bulk at its termini—we have shown[22] that a K_a value can be obtained for the binding of an $R_2NH_2^+$ ion by BMP25C8. ^1H NMR spectra of a 1:1 mixture of BMP25C8 and **5**-H·PF_6 in CD_3CN solution were recorded at 243, 258, 273, and 288 K. At these temperatures, equilibration between the [2]pseudorotaxane and its free components is slow on the ^1H NMR time scale, allowing single-point determinations[20] of K_a values at each one of these temperatures. Extrapolation of the van't Hoff plot obtained using this data gives a value for K_a at 300 K of about $50\,M^{-1}$. Under comparable conditions, the K_a value for the equilibrium between DB24C8 and **5**-H·PF_6 was determined[22] to be $1100\,M^{-1}$. Therefore, BMP25C8 *does* bind[23] $R_2NH_2^+$ salts, though with a substantially lower K_a value (approximately one order of magnitude less) than that observed with the [24]crown-8 analogue.

X-ray crystallography: Single crystals of the [2]pseudorotaxane, suitable for X-ray crystallographic analysis, were obtained from a CD_2Cl_2 solution of an equimolar mixture of **2** and **4**-H·PF_6 upon layering with hexanes. The 1:1 complex formed between the dibenzylammonium cation and BMP25C8 shows (Figure 9) the ion to be threaded through the center of the polyether macrocycle which has an extended geometry similar to that in its uncomplexed state. The two phenyl rings in the cation are both fairly steeply inclined (by 41 and 68°, respectively) to the near planar all-*anti* $CCH_2NH_2^+CH_2C$ backbone. Stabilization of the [2]pseudorotaxane is via N^+–H···O hydrogen bonding, supplemented by a weak π–π stacking interaction (*d* in Figure 9) between the catechol ring in the crown ether macrocycle and one of the phenyl rings of the cation. These two ring systems are inclined by about 12° and have a centroid–centroid separation of 4.02 Å. The [2]pseudorotaxanes are linked by a combination of π–π and C–H···π interactions to form sheets (Figure 10). There are no obvious interactions involving the PF_6^- ions.

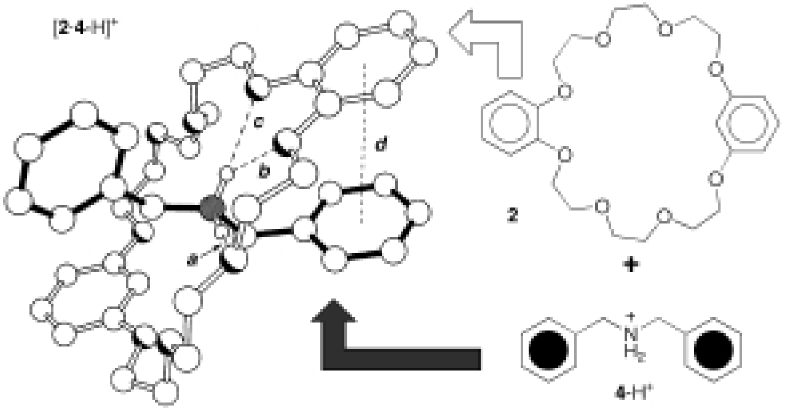


Figure 9. The X-ray crystal superstructure of the [2]pseudorotaxane [**2**·**4**-H]$^+$ formed between BMP25C8 (**2**) and the dibenzylammonium cation **4**-H^+. Hydrogen bonding distances and angles [(N···O), (H···O) distances [Å], (N–H···O) angles [°]]: *a*) 2.91, 2.06, 156; *b*) 2.94, 2.31, 127; *c*) 3.08, 2.21, 162.

The rotaxane 14-H·O_2CCF_3

Synthesis: Encouraged by the realization that BMP25C8 (**2**) can accommodate an $R_2NH_2^+$ ion within its macrocyclic cavity, the construction of a [2]rotaxane incorporating this crown ether was our next goal. By employing the same methodology as that shown to work for DB24C8 (**1**), the BMP25C8-containing [2]rotaxane **14**-H·O_2CCF_3 was obtained (Scheme 3) in 36% yield.

NMR spectroscopy: As in the case of the DB24C8-containing [2]rotaxane **10**-H·O_2CCF_3, the macrocyclic polyether component in **14**-H·O_2CCF_3 is also desymmetrized facially as a

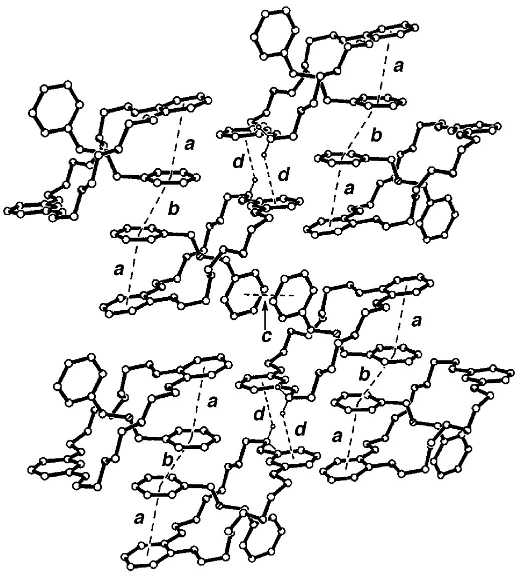
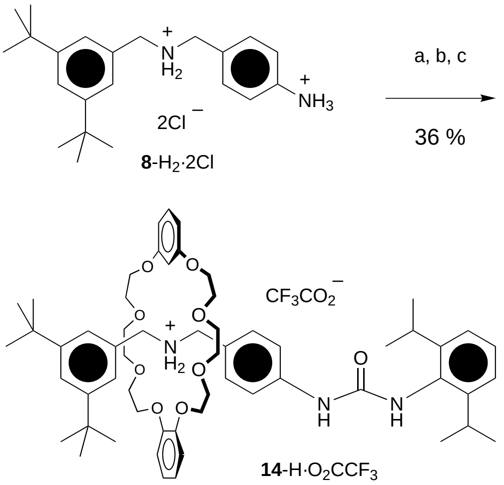


Figure 10. The sheet-like superstructure formed by the [2]pseudorotaxanes $[2\cdot4\text{-H}]^+$. The geometries of the π–π stacking interactions are *a*) centroid–centroid distance 4.02 Å, rings inclined by 12°; *b*) centroid–centroid distance 4.52 Å, mean interplanar separation 3.68 Å; *c*) centroid–centroid distance 3.99 Å, mean interplanar separation 3.71 Å. The C–H⋯π interaction (*d*) is characterized by an H⋯π distance of 2.84 Å and a C–H⋯π angle of 140°.



8-$H_2\cdot2Cl$

14-$H\cdot O_2CCF_3$

Scheme 3. The synthesis of the [2]rotaxane **14**-$H\cdot O_2CCF_3$: a) NaOH, H_2O/CH_2Cl_2; b) BMP25C8 (**2**), CF_3CO_2H, CH_2Cl_2; f) 2,6-diisopropylphenylisocyanate (**9**), room temperature, overall 36%.

consequence of the unsymmetrical nature of the dumbbell-shaped component. A sharp well-resolved ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) was obtained (Figure 11) for **14**-$H\cdot O_2CCF_3$. The separation of the resonances arising from the crown ether's polyether protons is evident. Additionally, the spectroscopic characteristics of the BMP25C8 component are considerably more complex than those of DB24C8 on account of there being six sets of chemically inequivalent OCH_2 groups ($\alpha, \beta, \gamma, \delta, \varepsilon$ and ϕ) in each polyether arc in BMP25C8, as opposed to only three (α, β and γ) in the case of DB24C8. Once again, a combination of two-dimensional NMR techniques—namely, COSY, T-ROESY and HMQC experiments—permitted a complete interpretation of the ^{1}H NMR spectrum. Each unique face of the macrocycle could be distinguished by inspection of the T-ROESY spectrum, wherein, as before, the resonances arising from the highly diagnostic H-2 and H-3 protons of the dumbbell only correlated (Figure 12) with the resonances associated with the OCH_2 protons located on the side of the macrocyclic polyether facing them. Several

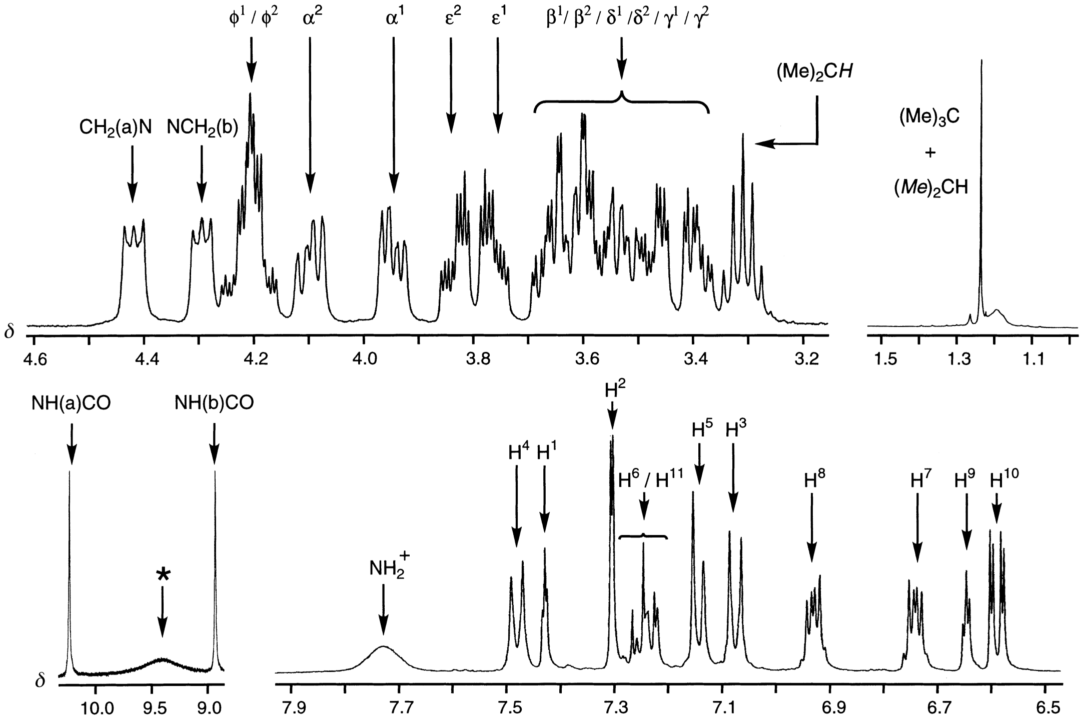


Figure 11. The partial ^{1}H NMR spectrum (400 MHz, CD_2Cl_2) of **14**-$H\cdot O_2CCF_3$. Note that the broad peak at $\delta = 9.4$ is a background signal arising from the NMR probe.

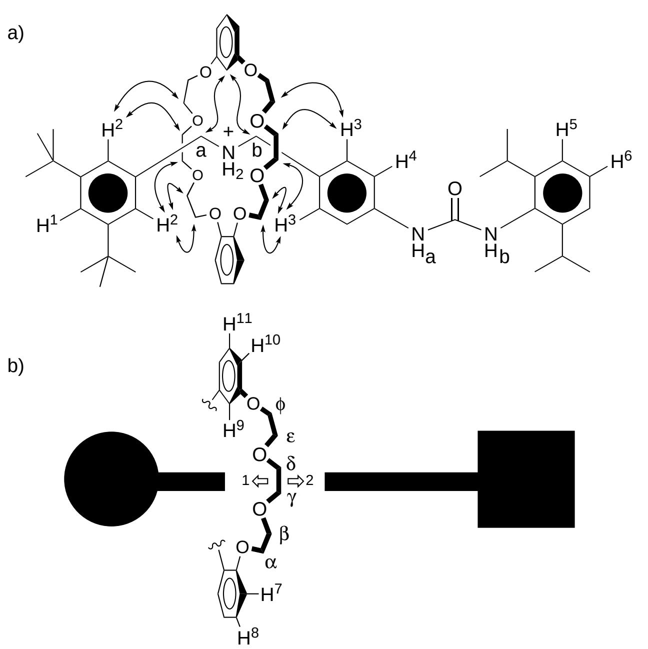


Figure 12. The structure of the [2]rotaxane **14**-H · O$_2$CCF$_3$, showing the labeling scheme for the protons on both a) the dumbbell and b) the crown ether components, used in describing its NMR-spectroscopic parameters. The through-space correlations determined by T-ROESY measurements are also highlighted in a) by double-headed arrows. The schematic representation (b) highlights the unsymmetrical nature of the dumbbell. The protons (α^1, β^1, γ^1, δ^1, ε^1, ϕ^1) on one face of the BMP25C8 macrocycle are oriented toward the 3,5-di-*tert*-butylphenyl stopper, whereas those protons (α^2, β^2, γ^2, δ^2, ε^2, ϕ^2) on the opposite face of the macrocycle are directed toward the 2,6-diisopropylphenyl stopper.

through-space correlations were detected in the T-ROESY experiment: some of the more important ones are indicated in Figure 12. Perhaps the most notable interaction is that observed between the H-9 resonance—the isolated aromatic proton attached to the resorcinol ring present in the BMP25C8 component—and the two benzylic methylene groups adjacent to the NH$_2^+$ center of the dumbbell. Such an interaction is not possible in a DB24C8 system since there are no protons oriented toward the center of the macrocyclic cavity. Another interesting feature—also observed in the case of **10**-H · O$_2$CCF$_3$—is the inequivalence of the methyl groups that constitute the isopropyl moieties on one of the stoppers. This heterotopicity is manifest in the ^{13}C NMR spectrum, wherein two resonances are observed for the carbon atoms of the isopropyl methyl groups. On warming up an NMR sample of **14**-H · O$_2$CCF$_3$ dissolved in CD$_3$CN/CD$_3$SOCD$_3$ (3:1), the two resonances are observed (Figure 13) to coalesce[24] between 312 and 317 K, indicating that the inequivalence arises as a consequence of a slow bond rotation with an energy barrier in the range of $\Delta G^{\ddagger} = 15.0-15.2$ kcal mol^{-1}. In order to determine the relative energetics of rotation about the groups attached to the 2,6-disubstituted stopper, a molecular mechanics investigation was undertaken. A Ramachandran-like plot (Figure 14) was constructed, whereby the torsion angles of the bonds from the phenyl group to the urea (defined by atoms C$_o$-C$_i$-N$_u$-H$_u$ and referred to as θ) and to the isopropyl group (defined by atoms C$_i$-C$_o$-C$_m$-H$_m$ and referred to as ϕ) were rotated by 360° in 10° increments from their initial angles of 90° and 0° respectively. All torsion angles were unconstrained except those being rotated. After construction of the model compound within the INPUT submode of MacroModel 5.5,[25] each set of torsion angles was varied sequentially, and the energy was minimized utilizing MM3*—the MacroModel implementation of the MM3 force field[26] by the PRCG algorithm[27] using a maximum of 10000 iterations or until the final energy gradient fell below 0.05 kJ Å^{-1}. Solvation was considered through use of the GB/SA model[28] for chloroform. Each energy value was scaled relative to the lowest energy point found on the potential surface. The average height of the energy barrier corresponding to rotation of an isopropyl group is roughly 6.5 kcal mol^{-1}, whereas rotation of the N–Ar bond is significantly more hindered, showing an average energy barrier of 14 kcal mol^{-1}, a value which is in good agreement with that determined experimentally (15.0 – 15.2 kcal mol^{-1}). The energy profile is dominated by two large 'mountains', corresponding to the direct clashing of the ureido oxygen atom with the methyl groups of the isopropyl unit, and two smaller 'mountains' corresponding to steric interactions between the

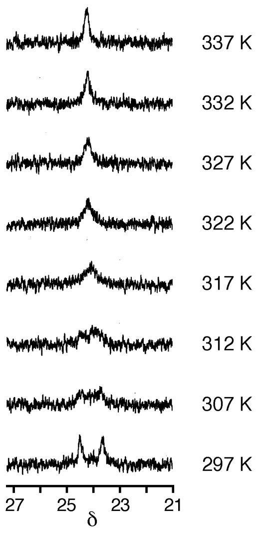


Figure 13. Partial ^{13}C NMR spectra (125 MHz, CD$_3$CN: CD$_3$SOCD$_3$ 3:1), recorded at various temperatures, showing the coalescence of the signal arising from the carbon atom of the methyl groups that constitute the isopropyl groups.

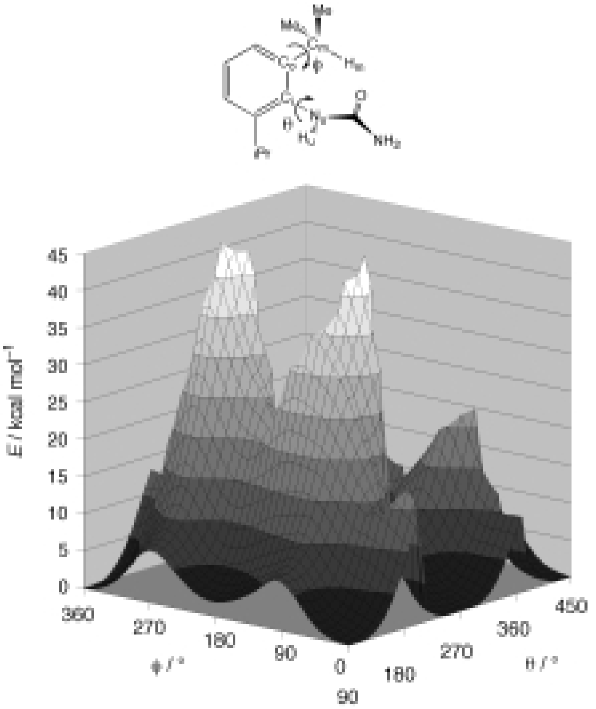


Figure 14. A Ramachandran-like plot depicting the energy profile of bond rotations associated with the 2,6-diisopropylphenyl stopper moiety.

methyl groups and the ureido hydrogen atom. The rest of the profile is divided into two broad valleys running parallel to the axis denoted ϕ, reflecting relatively facile rotation of the isopropyl group with respect to the phenyl ring. These valleys are lined with fairly high walls in the direction of θ, implying that rotation of the urea group is hindered more than rotation of the isopropyl units. The energy barrier to rotation about θ of 6.5 kcal mol^{-1} is easily surmountable at room temperature, whereas the 14 kcal mol^{-1} barrier will be significantly less readily overcome. It is reasonable to assume that the isopropyl groups are rotating rapidly about the ϕ bond, whereas rotation about the urea–phenyl bond is rapid on the NMR time scale only at elevated temperatures, as indicated by the coalescence between 312 and 317 K of the signal arising from the methyl carbon atom.

X-ray crystallography: Single crystals, suitable for X-ray crystallographic analysis, were obtained upon layering a CH_2Cl_2 solution of the [2]rotaxane **14**-H $\cdot$ O_2CCF_3 with hexanes. The structure (Figure 15) of the [2]rotaxane utilizing BMP25C8 (**2**) as the encircling macrocycle is very similar to that of the DB24C8 analog **10**-H $\cdot$ O_2CCF_3 in that the crystals contained two independent molecules in the asymmetric unit. In both of these molecules, the geometry of the cationic thread is very similar (Table 1) and differs only slightly from that observed in **10**-H $\cdot$ O_2CCF_3. The difference between the two crystallographically independent molecules of the [2]rotaxane **14**-H $\cdot$ O_2CCF_3 is in the relative orientations of the resorcinol ring systems with respect to the macrocycle as a whole. Stabilization of the [2]rotaxane is by a combination of N^+–H ··· O and C–H ··· O hydrogen bonds between the cation and the polyether macrocycle. As in **10**-H $\cdot$ O_2CCF_3, the urea component of the cation is hydrogen bonded to the trifluoroacetate anion. Also, in common with this [2]rotaxane, there is a similar apparent overlap between a catechol ring in the BMP25C8 macrocycle and the central *p*-toluidinyl ring of the cation. In both independent molecules, the two ring systems are inclined (by 19 and 24° in molecules **i** and **ii**, respectively) and the centroid–centroid separations are fairly long (4.22 and 4.29 Å in **i** and **ii**, respectively), thus minimizing any potential π–π interactions. It is interesting to note that the geometric relationship observed between these two ring systems in both independent molecules in **10**-H $\cdot$ O_2CCF_3 and **14**-H $\cdot$ O_2CCF_3 is probably a consequence of the adoption of a 'preferred' conformation for the cation and the ensuing sterically/hydrogen bonded enforced geometric relationship between the two components. The only inter-[2]rotaxane feature of note is a C–H ··· π interaction between H-11 (as defined in Figure 12) of the resorcinol ring of molecule **i** and the 2,6-diisopropylphenyl ring of the cation in molecule **ii** (the H ··· π distance is 2.77 Å and the associated C–H ··· π angle is 154°).

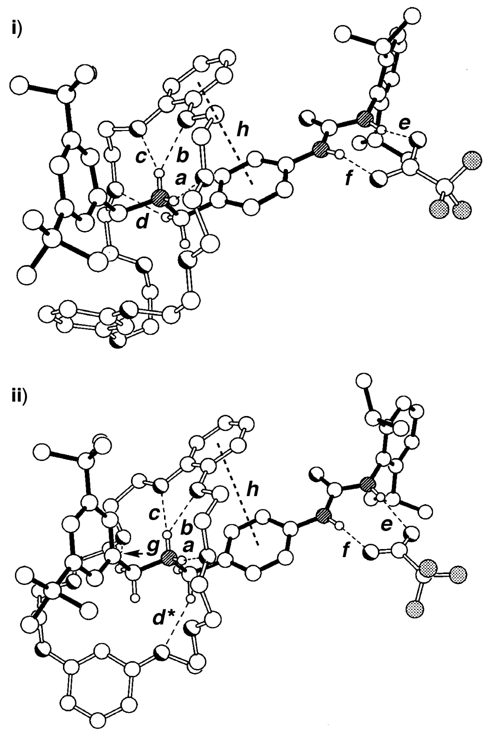


Figure 15. The molecular structures of the two crystallographically independent [2]rotaxanes present in the crystals of **14**-H $\cdot$ O_2CCF_3. Hydrogen bonding distances and angles [(X ··· O), (H ··· O) distances [Å], (X–H ··· O) angles [°]]: for molecule **i**; *a*) 2.90, 2.07, 152; *b*) 2.92, 2.17, 140; *c*) 3.06, 2.26, 149; *d*) 3.34, 2.48, 149; *e*) 2.83, 1.95, 163; *f*) 2.88, 2.00, 166; for molecule **ii**; *a*) 2.83, 1.94, 170; *b*) 2.95, 2.34, 125; *c*) 3.13, 2.26, 163; *d**) 3.30, 2.43, 150; *e*) 2.93, 2.04, 170; *f*) 2.89, 2.00, 172; *g*) 3.22, 2.42, 141. The centroid–centroid distances *h* for molecules **i** and **ii** are 4.22 and 4.29 Å, respectively.

Bismetaphenylene[26]crown-8 (BMP26C8)

Background: In BMP26C8 (**3**),[29] both of the catechol rings present in the parent DB24C8 (**1**) framework, have been replaced by resorcinol rings, allowing for symmetrical substitution of *both* aromatic moieties. However, as in the case of the [25]crown-8 analogue, this attribute is only useful—in the context of forming extended *threaded* arrays—if this particular crown ether constitution retains an appreciable affinity for $R_2NH_2^+$ ions.

Binding properties: This crown ether's ability to act as a host for $R_2NH_2^+$ ions has been studied by Gibson and co-workers.[13] In agreement with our own independent observations, association in solution of these two components could not be detected by ^{1}H NMR spectroscopy. However, in contrast to our observations,[30] mass spectrometric studies reported by Gibson et. al.,[13] revealed the presence of intense signals corresponding to 1:1 complexes.

Attempted rotaxanation: Our observations indicate that BMP26C8 (**3**) does not form threaded complexes with $R_2NH_2^+$ ions, either in the solution or the gas phase. As a consequence of these results, we predicted that subjecting BMP26C8 (**3**) to the rotaxanation protocol—employed successfully in the syntheses of DB24C8- and BMP25C8-containing [2]rotaxanes, **10**-H $\cdot$ O_2CCF_3 and **14**-H $\cdot$ O_2CCF_3, respectively—should afford *no* [2]rotaxane. Moreover, analysis of the crude reaction mixture by FAB mass spectrometry revealed *no* signal for the [2]rotaxane. Rather, the major products were dumbbell-shaped compounds in which either one or both of the amino functionalities of the diamine **8** had reacted with 2,6-diisopropylphenylisocyanate **9**. This result is consistent with our belief that BMP26C8 (**3**) does not bind $R_2NH_2^+$ ions in a *threaded* manner.

Conclusion

We have shown that, upon replacing one of the two catechol rings in the well-known DB24C8 receptor with a resorcinol moiety, the resulting crown ether—possessing a [25]crown-8 constitution—is still capable of recognizing and binding $R_2NH_2^+$ ions, not only in solution, but also in the gas phase and in the solid state. However, replacing both catechol with resorcinol rings perturbs the recognition elements so severely that $R_2NH_2^+$ ion binding is no longer observed in solution. By utilizing a kinetic stoppering methodology—employing the reaction of isocyanates with amines to generate ureas—we have demonstrated, initially with DB24C8, and then subsequently with BMP25C8, that [2]rotaxanes incorporating these crown ethers can be made and isolated. Moreover, the isolation of these compounds is a testament to the binding ability of the crown ethers employed during the synthesis, that is, the immediate precursor of the [2]rotaxane must be the corresponding [2]pseudorotaxane. The fact that no [2]rotaxane is generated when BMP26C8 is the macrocyclic component added to the reaction mixture suggests that this crown ether does not allow for the threading of $R_2NH_2^+$ ions through its macrocyclic cavity. In summary, the ability to add substituents at C-5 on the resorcinol ring, without reducing the symmetry of the BMP25C8 macrocycle—something that is not possible with DB24C8—in conjunction with its affinity for $R_2NH_2^+$ ions, suggests that BMP25C8 is a potentially useful building block for the construction of interlocked molecular architectures.

Experimental Section

General: Chemicals—including DB24C8 (**1**)—were purchased from Aldrich and used as received unless indicated otherwise.BMP26C8 (**3**),[29] **4-H** · PF_6,[4b] 3,5-di-*tert*-butylbenzaldehyde (**6**)[14] and 4-azidobenzylamine (**7**)[15] were prepared according to literature procedures. Anhydrous CH_2Cl_2 and MeCN were obtained by distillation from CaH_2 under an inert atmosphere (N_2 or Ar). Thin-layer chromatography was carried out using aluminium sheets precoated with silica gel 60F (Merck 5554). The plates were inspected by UV light and, if required, developed in I_2 vapor. Column chromatography was carried out using silica gel 60F (Merck 9385, 0.040–0.063 mm). Melting points were determined on an Electrothermal 9100 apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on either a Bruker AC300 (300 and 75 MHz, respectively), Bruker ARX400 (400 and 100 MHz, respectively), or Bruker ARX500 (500 and 125 MHz, respectively) spectrometer, using residual solvent as the internal standard. All chemical shifts are quoted on the δ scale, and all coupling constants are expressed in Hertz (Hz). All 2D NMR experiments were recorded with 1 K data points and 256 time increments in phase sensitive mode using TPPI, with the sample nonspinning. Double quantum filtered ^1H-^1H COSY experiments[31] were processed in a 1 K x 1 K matrix, and a forward linear prediction was performed in the F1 dimension. T-ROESY experiments[32] were performed with a spin lock mixing time of 300 ms, and processed in a 1 K × 1 K matrix with a forward linear prediction in the F1 dimension. All samples were degassed immediately before performing the T-ROESY experiments by sonicating the solution for approximately 30 min in an ultrasound bath. ^1H-^{13}C correlation by heteronuclear zero and double quantum coherence (HMQC) experiments[33] were performed using BIRD sequence for presaturation of protons not attached to ^{13}C nuclei, and processed in a 1 K x 1 K matrix. Fast atom bombardment (FAB) mass spectra were obtained using a ZAB-SE mass spectrometer, equipped with a krypton primary atom beam, utilizing a *m*-nitrobenzyl alcohol matrix. Cesium iodide or poly(ethylene glycol) were employed as reference compounds. Microanalyses were performed by either the University of North London Microanalytical Service (UK) or Quantitative Technologies, Inc (USA).

Bis(4-methoxycarbonylbenzyl)ammonium Hexafluorophosphate (5-H · PF_6): A solution of bis(4-methoxycarbonylbenzyl)amine (**5**)[7b] (1.0 g, 3.2 mmol) in MeOH (50 mL) was treated with 5 N HCl (10 mL) and the solvents were removed in vacuo. The resulting white solid was dissolved in H_2O (50 mL) and an excess of NH_4PF_6 was added until no further precipitation occurred. Filtration afforded the title compound as a white solid (1.35 g, 92 %); M.p. 240–242 °C; ^1H NMR (400 MHz, CD_3CN): δ = 3.88 (s, 6H; CH_3), 4.31 (s, 4H; CH_2-N-CH_2), 7.55–7.59 (m, 4H; ArH); 8.04-8.08 (m, 4H; ArH); ^{13}C NMR (100 MHz, CD_3CN): δ = 52.2 (CH_2-N-CH_2), 53.1 (CH_3), 130.9 and 131.5 (aromatic CH), 132.6 and 136.1 (quaternary aromatic), 167.2 (C=O); MS (FAB): *m/z*: 314 $[M - PF_6]^+$; $C_{18}H_{20}F_6NO_4P$ (459.3): calcd C 47.07, H 4.39, N 3.05; found C 47.12, H 4.28, N 2.84.

4-Aminobenzyl-3,5-di-*tert*-butylbenzylamine dihydrochloride (8-H_2 · 2 Cl): 4-Azidobenzylamine **7**[15] (1.70 g, 11.5 mmol) and 3,5-di-*tert*-butylbenzaldehyde (**6**)[14] (2.50 g, 11.5 mmol) were dissolved in C_6H_6 (100 mL), and the reaction mixture was heated to reflux over a 20 h period during which time the H_2O formed in the reaction was collected by means of a Dean–Stark trap. After the reaction mixture was allowed to cool down to ambient temperature, MeOH (50 mL) was added to it. The subsequent portionwise addition of $NaBH_4$ (4.35 g, 115 mmol) was completed in 30 min, and the reaction mixture was left to stir for 4 d under ambient conditions. Hydrochloric acid (5 N, 100 mL) was added and the solvents were removed in vacuo. The residue was partitioned between NaOH (2 N, 250 mL) and CH_2Cl_2 (250 mL) and, upon separation, the aqueous portion was washed further with CH_2Cl_2 before the organic extracts were combined, dried ($MgSO_4$), and evaporated to dryness to afford a thick yellow oil. The oil was dissolved in CH_2Cl_2 (100 mL) and HCl gas was bubbled through this solution for 25 min. After stirring for a further 30 min, Et_2O (100 mL) was added and the solution became cloudy. It was reduced in volume to about 100 mL, before adding more Et_2O (100 mL). Filtration afforded the title compound as a pale yellow solid (3.85 g, 67 %); m.p. > 200 °C (decomp); ^1H NMR (400 MHz, CD_3SOCD_3): δ = 1.29 (s, 18H; $C(CH_3)_3$), 4.07–4.18 (m, 4H; CH_2-N-CH_2), 7.35 (d of an AA′BB′, J = 8.4 Hz, 2H; ArH), 7.40 (m, 1H; ArH), 7.44 (m, 2H; ArH), 7.65 (d of an AA′BB′, J = 8.4 Hz, 2H; ArH), 9.84 (br s, 2H; NH_2^+); ^{13}C NMR (100 MHz, CD_3SOCD_3): δ = 31.2 (CH_3), 34.6 ($C(CH_3)_3$), 49.3 and 50.4 (CH_2-N-CH_2), 122.2, 122.7, 124.4, 130.8, 131.1, 131.6, 133.7 and 150.6 (aromatic C); MS (FAB): *m/z*: 326 $[M - 2Cl]^+$; $C_{22}H_{34}N_2Cl_2 \cdot 0.5H_2O$ (406.4): calcd C 65.01, H 8.68, N 6.89; found C 65.12, H 8.39, N 6.93.

1,3-Bis(2-{2-[2-(2-*p*-tolylsulfonyloxy)ethoxy]ethoxy}ethoxy)benzene (12): 1,3-Bis(2-{2-[2-(2-hydroxy)ethoxy]ethoxy}ethoxy)benzene (**11**)[18] (10.0 g, 26.7 mmol), Et_3N (27.0 g, 267 mmol), and a catalytic quantity of DMAP were dissolved in anhydrous CH_2Cl_2 (100 mL). This solution was cooled down to 0 °C in an ice bath and TsCl (25.5 g, 134 mmol) dissolved in dry CH_2Cl_2 (100 mL) was added dropwise over a 3 h period. The reaction mixture was allowed to warm up to ambient temperature before being stirred overnight. Hydrochloric acid (5 N, 200 mL) was added carefully to the reaction mixture before the organic phase was recovered and washed with 2 N HCl (200 mL) and saturated brine (200 mL). This solution was then dried ($MgSO_4$) and the solvents were removed in vacuo to afford a dark yellow oil, which was purified by chromatography (SiO_2: gradient elution with CH_2Cl_2 to 1:1 CH_2Cl_2/EtOAc) to yield the title compound as a pale yellow oil (11.8 g, 64 %); ^1H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 6H; CH_3), 3.56–3.87 (m, 16H; OCH_2), 4.04–4.19 (m, 8H; OCH_2), 6.45–6.54 (m, 3H; ArH), 7.14 (t, J = 8.3 Hz, 1H; ArH), 7.32 (d of an AA′BB′, J = 8.2 Hz, 4H; tosyl ArH), 7.79 (d of an AA′BB′, J = 8.2 Hz, 4H; tosyl ArH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (CH_3), 67.5, 68.8, 69.4, 69.9, 70.9 (OCH_2), 101.9, 107.2, 128.1, 130.0, 133.1, 145.0, 160.1 (aromatic C); MS (FAB): *m/z*: 683 $[M+H]^+$; $C_{32}H_{42}O_{12}S_2$ (682.8): calcd C 56.29, H 6.20; found C 56.12, H 6.24.

Benzometaphenylene[25]crown-8 (2): A solution of the ditosylate **12** (5.0 g, 7.3 mmol) and catechol **13** (0.81 g, 7.3 mmol) in dry MeCN (500 mL) was added dropwise over a 3 d period to a suspension of Cs_2CO_3 (11.9 g, 36.6 mmol) in refluxing MeCN (500 mL). After 4 d of heating under reflux, the reaction mixture was allowed to cool down. Subsequently, it was filtered to remove inorganic salts. The filtrate was evaporated to dryness and the residue partitioned between CH_2Cl_2 (250 mL) and K_2CO_3 solution (10% w/v, 250 mL). The organic phase was then washed with a further aliquot of aqueous K_2CO_3, before being dried ($MgSO_4$). The solvents were removed in vacuo and the crude product was subjected to chromatography (SiO_2: EtOAc/Hexane 9:1), yielding BMP25C8 (**2**) as a white solid (2.73 g, 83%); m.p. 66–68 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 3.71-3.75$ (m, 8H; OCH_2), 3.81–3.87 (m, 8H; OCH_2), 4.13-4.16 (m, 8H; OCH_2), 6.50 (dd, $J=$ 2.4 and 8.0 Hz, 2H; ArH), 6.70 (t, $J = 2.4$ Hz, 1H; ArH); 6.89-6.92 (m, 4H; catechol ArH), 7.12 (t, $J = 8.0$ Hz, 1H; ArH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 68.1$, 69.1, 70.0, 71.0 and 71.1 (OCH_2), 102.8, 107.9, 115.3, 121.8, 129.8, 149.1 and 160.1 (aromatic C); MS (FAB): m/z: 449 $[M+H]^+$; $C_{24}H_{32}O_8$ (448.5): calcd C 64.27, H 7.19; found C 64.33, H 7.12.

General procedure for rotaxanation: The dichloride salt **8**-$H_2 \cdot 2Cl$ (ca. 1.0 g) was partitioned between CH_2Cl_2 (100 mL) and NaOH (100 mL). After the mixture had been stirred for 10 min, the organic phase was collected, dried ($MgSO_4$), and evaporated to dryness. A portion of the residue (340 mg, 1.05 mmol) was dissolved in anhydrous CH_2Cl_2 and the crown ether (**1**, **2** or **3**) (1.41 g, 3.15 mmol) was added. Upon dissolution of the crown ether, trifluoroacetic acid (120 mg, 1.05 mmol) was added, and, after 5 min, 2,6-diisopropylphenyl isocyanate (1.07 g, 5.25 mmol) was introduced into the reaction mixture which was stirred under ambient conditions for a further 5 d. The solvents were removed in vacuo and the residue subjected to chromatography (SiO_2: gradient elution with CH_2Cl_2/MeOH, 99:1 to 9:1) affording pure rotaxanes when DB24C8 (**1**) and BMP25C8 (**2**) were employed as the crown ethers. Data for the DB24C8-containing [2]rotaxane **10**-$H \cdot O_2CCF_3$, isolated as an off-white powder (0.73 g, 64%); m.p. 117–119 °C; ^1H NMR (400 MHz, CD_2Cl_2): $\delta = 1.19$ (s, 30H; $C(CH_3)_3$ and $CH(CH_3)_2$), 3.32 (sept, $J = 7.0$ Hz, 2H; $CH(CH_3)_2$), 3.42–3.47 (m, 4H; H-γ^1), 3.52–3.58 (m, 4H; H-γ^2), 3.67–3.73 (m, 4H; H-β^1), 3.78–3.85 (m, 4H; H-β^2), 4.07–4.17 (m, 8H; H-α^1 and H-α^2), 4.45–4.49 (m, 2H; CH_2(b)), 4.68–4.71 (m, 2H; CH_2(a)), 6.79–6.85 (m, 4H; H-7), 6.88–6.95 (m, 4H; H-8), 7.10 (d of an AA'BB', $J = 8.5$ Hz, 2H; H-3), 7.14 (d, $J = 7.5$ Hz, 2H; H-5), 7.21–7.26 (m, 1H; H-6), 7.28 (d, $J = 1.5$ Hz, 2H; H-2), 7.35 (t, $J = 1.5$ Hz, 1H; H-1), 7.44 (d of an AA'BB', $J = 8.5$ Hz, 2H; H-4), 7.53 (br s, 2H; NH_2^+), 8.97 (s, 1H; NH(b)CO), 10.16 (s, 1H; NH(a)CO); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.5$ and 24.4 ($CH(CH_3)_2$), 28.6 ($CH(CH_3)_2$), 31.5 ($C(CH_3)_3$), 34.9 ($C(CH_3)_3$), 52.9 (CH_2(a)), 53.1 (CH_2(b)), 68.1 (C-α), 70.2 (C-β), 70.5 (C-γ), 112.8 (C-7), 118.4 (C-4), 122.0 (C-8), 122.4 (quaternary aromatic), 122.9 (C-5), 123.3 (C-1), 123.7 (C-2), 127.1 (C-6), 129.7 (C-3), 131.6, 133.2, 143.2, 147.4, 147.6 and 151.4 (quaternary aromatic), 155.7 (C=O); MS (FAB): m/z: 976 $[M - O_2CCF_3]^+$; $C_{61}H_{82}F_3N_3O_{11}$ (1090.3): calcd C 67.20, H 7.58, N 3.85; found C 66.68, H 7.55, N 3.58. Data for the BMP25C8-containing [2]rotaxane **14**-$H \cdot O_2CCF_3$, isolated as an off-white powder (0.41 g, 36%); m.p. 102-105 °C; ^1H NMR (400 MHz, CD_2Cl_2): $\delta = 1.19$ (br s, 12H; $CH(CH_3)_2$), 1.24 (s, 18H; $C(CH_3)_3$) 3.31 (sept, $J = 7.0$ Hz, 2H; $CH(CH_3)_2$), 3.35–3.70 (m, 12H; H-β, H-γ and H-δ), 3.73–3.79 (m, 2H; H-ε^1), 3.80–3.86 (m, 2H; H-ε^2), 3.91–3.98 (m, 2H; H-α^1), 4.06–4.13 (m, 2H; H-α^2), 4.15–4.26 (m, 4H; H-ϕ), 4.27–4.32 (m, 2H; CH_2(b)), 4.39–4.45 (m, 2H; CH_2(a)), 6.58 (dd, $J = 2.5$ and 8.5 Hz, 2H; H^{10}), 6.64 (t, $J = 2.5$ Hz, 1H; H-9), 6.72–6.76 (m, 2H; H-7), 6.90–6.95 (m, 2H; H-8), 7.07 (d of an AA'BB', $J = 8.5$ Hz, 2H; H-3), 7.14 (d, $J = 7.5$ Hz, 2H; H-5), 7.21–7.27 (m, 2H; H-6 and H-11), 7.30 (d, $J =$ 1.5 Hz, 2H; H-2), 7.43 (t, $J = 1.5$ Hz, 1H; H-1), 7.48 (d of an AA'BB', $J =$ 8.5 Hz, 2H; H-4), 7.73 (br s, 2H; NH_2^+), 8.94 (s, 1H; NH(b)CO), 10.23 (s, 1H; NH(a)CO); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 23.5$ and 24.4 ($CH(CH_3)_2$), 28.6 ($CH(CH_3)_2$), 31.5 ($C(CH_3)_3$), 35.0 ($C(CH_3)_3$), 52.7 (CH_2(a)), 53.2 (CH_2(b)), 67.9 (C-ϕ), 68.1 (C-α), 69.7 (C-β), 70.4 (C-ε), 70.7 (C-δ), 71.1 (C-γ), 103.9 (C-9), 107.6 (C-10), 112.5 (C-7), 118.5 (C-4), 121.3 (quaternary aromatic), 122.3 (C-8), 122.9 (C-5), 123.8 (C-1 and C-2), 127.2 (C-6), 129.8 (quaternary aromatic), 130.6 (C-3), 131.0 (C-11), 133.1, 143.5, 146.5, 147.5 and 151.8 (quaternary aromatic), 155.6 (C=O), 159.7 (quaternary aromatic); MS (FAB): m/z: 976 $[M - O_2CCF_3]^+$; $C_{61}H_{82}F_3N_3O_{11}$ (1090.3): calcd C 67.20, H 7.58, N 3.85; found C 67.66, H 7.70, N 3.78. When the crown ether component employed in an attempted rotaxanation was BMP26C8 (**3**), no evidence for the formation of the corresponding [2]rotaxane could be gathered. However, FAB mass spectrometric analysis of the crude reaction mixture revealed signals for 1) the dumbbell-shaped compound formed in the reaction between diamine **8** and 2,6-diisopropylphenyl isocyanate, and 2) the bis-urea derivative formed upon reaction of both amino groups present in **8** with the isocyanate.

X-ray crystallography: The X-ray crystal structure of **10**-$H \cdot O_2CCF_3$ has been discussed briefly in a preliminary communication.[7g]

Crystal data for **2**: $C_{24}H_{32}O_8$, $M_r = 448.5$, monoclinic, space group $P2_1/c$ (no. 14), $a = 17.974(2)$, $b = 5.140(1)$, $c = 24.851(3)$ Å, $\beta = 92.93(1)°$, $V =$ 2292.8(4) $Å^3$, $Z = 4$, $\rho_{calcd} = 1.299$ g cm^{-3}, $\mu(Mo_{K\alpha}) = 0.97$ cm^{-1}, $F(000) =$ 960, $T = 293$ K; clear prismatic needles, $0.83 \times 0.40 \times 0.27$ mm, Siemens P4/PC diffractometer, graphite-monochromated $Mo_{K\alpha}$ radiation, ω scans, 4028 independent reflections. The structure was solved by direct methods and the non-hydrogen atoms were refined anisotropically. The C–H hydrogen atoms were placed in calculated positions, assigned isotropic thermal parameters, $U(H) = 1.2U_{eq}(C)$, and allowed to ride on their parent atoms. Refinements were by full-matrix least-squares based on F^2 to give $R_1 = 0.062$, $wR_2 = 0.151$ for 2493 independent observed reflections $[|F_o| > 4\sigma(|F_o|), 2\theta \le 50°]$ and 289 parameters. All computations were carried out using the SHELXTL PC program system.[34].

Crystal data for [**2** · **4**-H][PF_6]: [$C_{38}H_{48}NO_8$][PF_6], $M_r = 791.7$, triclinic, space group $P\bar{1}$ (no. 2), $a = 11.265(1)$, $b = 12.853(3)$, $c = 14.495(2)$ Å, $\alpha =$ 104.12(2), $\beta = 102.72(1)$, $\gamma = 96.53(2)°$, $V = 1954.1(6)$ $Å^3$, $Z = 2$, $\rho_{calcd} =$ 1.346 g cm^{-3}, $\mu(Mo_{K\alpha}) = 1.50$ cm^{-1}, $F(000) = 832$, $T = 293$ K; clear prisms, $0.57 \times 0.33 \times 0.13$ mm, Siemens P4/PC diffractometer, graphite-monochromated $Mo_{K\alpha}$ radiation, ω scans, 5696 independent reflections. The structure was solved by direct methods. Disorder was found in one of the polyether arms and this was resolved into two partial occupancy orientations with the non-hydrogen atoms of the major occupancy orientation being refined anisotropically (those of the minor occupancy orientation were refined isotropically). The remaining non-hydrogen atoms were refined anisotropically. The N–H hydrogen atoms were located from a ΔF map and allowed to refine isotropically subject to an N–H distance constraint. The C–H hydrogen atoms were placed in calculated positions, assigned isotropic thermal parameters, $U(H) = 1.2U_{eq}(C)$, and allowed to ride on their parent atoms. Refinements were by full-matrix least-squares based on F^2 to give $R_1 = 0.083$, $wR_2 = 0.201$ for 2613 independent observed reflections $[|F_o| > 4\sigma(|F_o|), 2\theta \le 47°]$ and 480 parameters. All computations were carried out using the SHELXTL PC program system.[34]

Crystal data for **14**-$H \cdot O_2CCF_3$: [$C_{59}H_{82}N_3O_9$][CF_3CO_2] · 0.25 CH_2Cl_2 · 0.25 MeCN, $M_r = 1121.8$, triclinic, space group $P\bar{1}$ (no. 2), $a = 14.966(2)$, $b = 22.879(3)$, $c = 22.915(2)$ Å, $\alpha = 64.64(1)$, $\beta = 72.82(1)$, $\gamma = 76.20(1)°$, $V = 6717(2)$ $Å^3$, $Z = 4$ (there are two crystallographically independent molecules in the asymmetric unit), $\rho_{calcd} = 1.109$ g cm^{-3}, $\mu(Cu_{K\alpha}) =$ 8.41 cm^{-1}, $F(000) = 2400$, $T = 193$ K; clear rhombs, $1.00 \times 0.37 \times 0.13$ mm, Siemens P4/RA diffractometer, graphite-monochromated $Cu_{K\alpha}$ radiation, ω scans, 16840 independent reflections. The structure was solved by direct methods. In each of the independent molecules disorder was found in one of the polyether arms and in both of the *tert*-butyl groups; disorder was also present in one of the $CF_3CO_2^-$ ions. In each case this was resolved into two partial occupancy orientations with the non-hydrogen atoms of the major occupancy orientations being refined anisotropically (those of the minor occupancy orientations were refined isotropically). The remaining non-hydrogen atoms of the [2]rotaxanes and the anions were refined anisotropically, whilst those of the solvent molecules were refined isotropically. The N–H and C–H hydrogen atoms were placed in calculated positions, assigned isotropic thermal parameters, $U(H) = 1.2U_{eq}(C/N)$ $[U(H) = 1.5U_{eq}(C-Me)]$, and allowed to ride on their parent atoms. Refinements were by full-matrix least-squares based on F^2 to give $R_1 = 0.162$, $wR_2 =$ 0.420 for 7798 independent observed reflections $[|F_o| > 4\sigma(|F_o|), 2\theta \le 115°]$ and 1548 parameters. All computations were carried out using the SHELXTL PC program system.[34]

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-138348 (**10**-$H \cdot O_2CCF_3$), CCDC-138346 (**2**), CCDC-138347 ([**2** · **4**-H][PF_6]), and CCDC-138349 (**14**-$H \cdot O_2CCF_3$). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgement

This research was sponsored by the University of California, Los Angeles in the USA, and by the Engineering and Physical Sciences Research Council in the UK.

---

[1] For in-depth and historical analyses of cation/crown ether complexation, see:a) J. S. Bradshaw, R. M. Izatt, A. V. Bordunov, C. Y. Zhu, J. K. Hathaway in *Comprehensive Supramolecular Chemistry, Vol. 1* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, G. W. Gokel), Pergamon, Oxford, **1996**, pp. 35–95; b) R. M. Izatt, K. Pawluk, J. S. Bradshaw, R. L. Bruening, *Chem. Rev.* **1995**, *95*, 2529–2586; c) R. M. Izatt, K. Pawluk, J. S. Bradshaw, R. L. Bruening, *Chem. Rev.* **1991**, *91*, 1721–2085; d) G. W. Gokel, *Crown Ethers and Cryptands*, The Royal Society of Chemistry, Cambridge, **1991**, pp. 64–98; e) *Cation Binding by Macrocycles*, (Eds.: Y. Inoue, G. W. Gokel), Marcel Dekker, New York, **1990**; f) F. Vögtle, E. Weber in *Crown Ethers and Analogs* (Eds.: S. Patai, Z. Rappoport), Wiley, **1989**, pp. 207–304; g) I. Goldberg in *Inclusion Compounds, Vol. 2* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol), Academic Press, London, **1984**, pp. 261–335.

[2] For some recent examples, see: a) A. Drljaca, M. J. Hardie, C. L. Raston, L. Spiccia, *Chem. Eur. J.* **1999**, *5*, 2295–2299; b) A. P. Marchand, H.-S. Chong, S. Alihodzic, W. H. Watson, S. G. Bodige, *Tetrahedron* **1999**, *55*, 9687–9696; c) H. Liu, S. Liu, L. Echegoyen, *Chem. Commun.* **1999**, 1493–1494; d) S. Flink, F. C. J. M. van Veggel, D. N. Reinhoudt, *J. Phys. Chem. B* **1999**, *103*, 6515–6520; e) R. A. Bartsch, H.-S. Hwang, V. S. Talanov, G. G. Talanova, D. W. Purkiss, R. D. Rogers, *J. Org. Chem.* **1999**, *64*, 5341–5349.

[3] In Pedersen's seminal paper (C. J. Pedersen, *J. Am. Chem. Soc.* **1967**, *89*, 7017–7036), he noted that primary alkylammonium ions form 1:1 complexes with dibenzo[18]crown-6 (DB18C6). This ground-breaking discovery subsequently spawned much research in the areas of host–guest and supramolecular chemistry. For examples spanning from Pedersen's day until the present, see: a) E. B. Kyba, K. Koga, L. R. Sousa, M. G. Siegel, D. J. Cram, *J. Am. Chem. Soc.* **1973**, *95*, 2692–2693; b) D. J. Cram, J. M. Cram *Science* **1974**, *183*, 803–809; c) T. L. Tarnowski, D. J. Cram, *J. Chem. Soc., Chem. Commun.* **1976**, 661–663; d) J. M. Timko, S. S. Moore, D. M. Walba, P. C. Hiberty, D. J. Cram, *J. Am. Chem. Soc.* **1977**, *99*, 4207–4219; e) E. P. Kyba, J. M. Timko, L. J. Kaplan, F. de Jong, G. W. Gokel, D. J. Cram, *J. Am. Chem. Soc.* **1978**, *100*, 4558–4568; f) D. J. Cram, J. M. Cram *Acc. Chem. Res.* **1978**, *11*, 8–14; g) J. F. Stoddart, *Chem. Soc. Rev.* **1979**, *8*, 85–142; h) M. J. Bovill, D. J. Chadwick, M. R. Johnson, N. F. Jones, I. O. Sutherland, R. F. Newton, *J. Chem. Soc., Chem. Commun.* **1979**, 1065–1066; i) J.-M. Lehn in *IUPAC Frontiers of Chemistry*, (Ed. K. J. Laidler), Pergamon, Oxford, **1982**, pp. 265–272; j) I. Goldberg, *J. Am. Chem. Soc.* **1980**, *102*, 4106–4113; k) F. De Jong, D. N. Reinhoudt, *Adv. Phys. Org. Chem.* **1980**, *17*, 279–433. l) D. J. Cram, K. N. Trueblood, *Top. Curr. Chem.* **1981**, *98*, 43–106; m) J. S. Bradshaw, S. L. Baxter, J. D. Lamb, R. M. Izatt, J. J. Christensen, *J. Am. Chem. Soc.* **1981**, *103*, 1821–1827; n) K. N. Trueblood, C. B. Knobler, D. S. Lawrence, R. V. Stevens, *J. Am. Chem. Soc.* **1982**, *104*, 1355–1362; o) R. Aldag, G. Schröder, *Liebigs Ann. Chem.* **1984**, 1036–1045; p) I. O. Sutherland, *Chem. Soc. Rev.* **1986**, *15*, 63–91; q) J. F. Stoddart, *Top. Stereochem.* **1987**, *17*, 205–288; r) D. J. Cram, *Angew. Chem.* **1988**, *100*, 1041–1052; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 1009–1020; s) S. Misumi, *Pure Appl. Chem.* **1990**, *62*, 493–498; t) I. O. Sutherland, *Pure Appl. Chem.* 499–504; u) R. M. Izatt, T. Wang, J. K. Hathaway, X. X. Zhang, J. C. Curtis, J. S. Bradshaw, C. Y. Zhu, P. Huszthy, *J. Incl. Phenom.* **1994**, *17*, 157–175; v) M. T. Reetz, J. Huff, J. Rudolph, K. Töllner, A. Deege, R. Goddard, *J. Am. Chem. Soc.* **1994**, *116*, 11588–11589; w) B. L. Williamson, C. S. Creaser, *Int. J. Mass Spectrom.* **1998**, *188*, 53–61; x) A. P. Hansson, P.-O. Norrby, K. Wärnmark, *Tetrahedron Lett.* **1998**, *39*, 4565–4568; y) H. Tsukube, M. Wada, S. Shinoda, H. Tamiaki, *Chem. Commun.* **1999**, 1007–1008.

[4] a) P. R. Ashton, P. J. Campbell, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, J. F. Stoddart, P. A. Tasker, D. J. Williams, *Angew. Chem.* **1995**, *107*, 2001–2004; *Angew Chem. Int. Ed. Engl.* **1995**, *34*, 1869–1871; b) P. R. Ashton, E. J. T. Chrystal, P. T. Glink, S. Menzer, C. Schiavo, N. Spencer, J. F. Stoddart, P. A. Tasker, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1996**, *2*, 709–728; c) P. T. Glink, C. Schiavo, J. F. Stoddart, D. J. Williams, *Chem. Commun.* **1996**, 1483–1490; d) P. R. Ashton, M. C. T. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1997**, *119*, 12514–12524; e) P. R. Ashton, M. C. T. Fyfe, M.-V. Martínez-Díaz, S. Menzer, C. Schiavo, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1998**, *4*, 1523–1534; f) M. Montalti, L. Prodi, *Chem. Commun.* **1998**, 1461–1462; g) N. Yamaguchi, L. M. Hamilton, H. W. Gibson, *Angew. Chem.* **1998**, *110*, 3463–3466; *Angew. Chem. Int. Ed.* **1998**, *37*, 3275–3279; h) M. C. T. Fyfe, J. F. Stoddart, *Adv. Supramol. Chem.* **1999**, *5*, 1–53; i) E. Ishow, A. Credi, V. Balzani, F. Spadola, L. Mandolini, *Chem. Eur. J.* **1999**, *5*, 984–989; j) D. Fitzmaurice, S. N. Rao, J. A. Preece, J. F. Stoddart, S. Wenger, N. Zaccheroni, *Angew. Chem.* **1999**, *111*, 1220–1224; *Angew. Chem. Int. Ed.* **1999**, *38*, 1147–1150.

[5] P. R. Ashton, P. J. Campbell, E. J. T. Chrystal, P. T. Glink, S. Menzer, D. Philp, N. Spencer, J. F. Stoddart, P. A. Tasker, D. J. Williams, *Angew. Chem.* **1995**, *107*, 1997–2001; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1865–1869.

[6] Complexes formed between secondary dialkylammonium ions and crown ethers having less than 24 atoms in their macrorings have been observed to occur in a *face-to-face* manner. See: a) J. C. Metcalfe, J. F. Stoddart, G. Jones, *J. Am. Chem. Soc.* **1977**, *99*, 8317–8319; b) J. Krane, O. Aune, *Acta Chem. Scand. Sect. B* **1980**, *34*, 397–401; c) J. C. Metcalfe, J. F. Stoddart, G. Jones, A. Atkinson, I. S. Kerr, D. J. Williams, *J. Chem. Soc. Chem. Commun.* **1980**, 540–543; d) S. S. Abed-Ali, B. J. Brisdon, R. England, *J. Chem. Soc. Chem. Commun.* **1987**, 1565–1566.

[7] a) A. G. Kolchinski, D. H. Busch, N. W. Alcock, *J. Chem. Soc. Chem. Commun.* **1995**, 1289–1291; b) P. R. Ashton, P. T. Glink, J. F. Stoddart, P. A. Tasker, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1996**, *2*, 729–736; c) M.-V. Martínez-Díaz, N. Spencer, J. F. Stoddart, *Angew. Chem.* **1997**, *109*, 1991–1994; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1904–1907; d) P. R. Ashton, I. Baxter, M. C. T. Fyfe, F. M. Raymo, N. Spencer, J. F. Stoddart, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 2297–2307; e) P. R. Ashton, R. Ballardini, V. Balzani, I. Baxter, A. Credi, M. C. T. Fyfe, M. T. Gandolfi, M. Gómez-López, M.-V. Martínez-Díaz, A. Piersanti, N. Spencer, J. F. Stoddart, M. Venturi, A. J. P. White, D. J. Williams, *J. Am. Chem. Soc.* **1998**, *120*, 11932–11942; f) A. G. Kolchinski, N. W. Alcock, R. A. Roesner, D. H. Busch, *Chem. Commun.* **1998**, 1437–1438; g) S. J. Cantrill, D. A. Fulton, M. C. T. Fyfe, J. F. Stoddart, A. J. P. White, D. J. Williams, *Tetrahedron Lett.* **1999**, *40*, 3669–3672; h) S. J. Rowan, S. J. Cantrill, J. F. Stoddart, *Org. Lett.* **1999**, *1*, 129–132 i) S. J. Cantrill, M. C. T. Fyfe, A. M. Heiss, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Commun.* **1999**, 1251–1252; j) T. Takata, H. Kawasaki, S. Asai, Y. Furusho, N. Kihara, *Chem. Lett.* **1999**, 223–224; k) S. J. Cantrill, S. J. Rowan, J. F. Stoddart, *Org. Lett.* **1999**, *1*, 1363–1366.

[8] a) P. R. Ashton, P. T. Glink, M.-V. Martínez-Díaz, J. F. Stoddart, A. J. P. White, D. J. Williams, *Angew. Chem.* **1996**, *108*, 2058–2061; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1930–1933; b) P. R. Ashton, A. N. Collins, M. C. T. Fyfe, S. Menzer, J. F. Stoddart, D. J. Williams, *Angew. Chem.* **1997**, *109*, 760–763; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 735–739; c) P. R. Ashton, M. C. T. Fyfe, S. K. Hickingbottom, S. Menzer, J. F. Stoddart, A. J. P. White, D. J. Williams, *Chem. Eur. J.* **1998**, *4*, 577–589; d) M. C. T. Fyfe, J. F. Stoddart, *Coord. Chem. Rev.* **1999**, *183*, 139–155; e) N. Yamaguchi, H. W. Gibson, *Angew. Chem.* **1999**, *111*, 195–199; *Angew. Chem. Int. Ed.* **1999**, *38*, 143–147; f) N. Yamaguchi, H. W. Gibson, *Chem. Commun.* **1999**, 789–790.

[9] a) D. Philp, J. F. Stoddart, *Synlett* **1991**, 445–458; b) G. M. Whitesides, J. P. Mathias, C. T. Seto, *Science*, **1991**, *154*, 1312–1319; c) D. S. Lawrence, T. Jiang, M. Levett, *Chem. Rev.* **1995**, *95*, 2229–2260; d) D. Philp, J. F. Stoddart, *Angew. Chem.* **1996**, *108*, 1242–1286; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1154–1196; e) P. J. Stang, B. Olenyuk, *Acc. Chem. Res.* **1997**, *30*, 502–518; f) L. Cusack, S. N. Rao, J. Wenger, D. Fitzmaurice, *Chem. Mater.* **1997**, *9*, 624–631; g) M. M. Conn, J. Rebek, Jr., *Chem. Rev.* **1997**, *97*, 1647–1668; h) B. Linton, A. D. Hamilton, *Chem. Rev.* **1997**, *97*, 1669–1680; i) M. Fujita, *Chem. Soc. Rev.* **1998**, *27*, 417–425; j) T. L. Breen, J. Tien, S. R. J. Oliver, T. Hadzic, G. M. Whitesides, *Science* **1999**, *284*, 948–951; k) D. A. Tomalia, Z. G. Wang, M. Tirrel, *Curr. Opin. Colloid Interface Sci.*

1999, *4*, 3–5; l) T. Emrick, J. M. J. Fréchet, *Curr. Opin. Colloid Interface Sci.* **1999**, *4*, 15–23; m) R. P. Sijbesma, E. W. Meijer, *Curr. Opin. Colloid Interface Sci.* **1999**, *4*, 24–32.

[10] a) P. R. Ashton, A. N. Collins, M. C. T. Fyfe, P. T. Glink, S. Menzer, J. F. Stoddart, D. J. Williams, *Angew. Chem.* **1997**, *109*, 59–62; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 59–62; b) M. C. Feiters, M. C. T. Fyfe, M.-V. Martínez-Díaz, S. Menzer, R. J. M. Nolte, J. F. Stoddart, P. J. M. van Kan, D. J. Williams, *J. Am. Chem. Soc.* **1997**, *119*, 8119–8120; c) F. Diederich, L. Echegoyen, M. Gómez-López, R. Kessinger, J. F. Stoddart, *J. Chem. Soc. Perkin Trans. 2* **1999**, 1577–1586.

[11] Our investigations (P. R. Ashton, I. Baxter, S. J. Cantrill, M. C. T. Fyfe, P. T. Glink, J. F. Stoddart, A. J. P. White, D. J. Williams, *Angew. Chem.* **1998**, *110*, 1344–1347, *Angew. Chem. Int. Ed.* **1998**, *37*, 1294–1297) on a self-complementary ‘daisy-chain’ system—in which a secondary dialkylammonium ion-containing side chain is appended to one of the catechol residues of a DB24C8 framework—revealed that, upon oligo/polymerization, numerous stereoisomeric super-structures can be formed. It was immediately apparent that this complication could be circumvented by designing a compound in which the ammonium ion substituted catechol ring of the DB24C8 macrocycle is replaced by a resorcinol ring which carries the ammonium ion side-chain attached to its C-5 position. Such a ‘mutation’ of the monomer, although simplifying symmetry situation, has the implication of expanding the macroring from 24 to 25 atoms, thus raising the question - are crown ethers with a 25C8 constitution effective hosts for secondary dialkylammonium ions?

[12] For examples of interlocked macromolecules, see:a) F. M. Raymo, J. F. Stoddart, *Chem. Rev.* **1999**, *99*, 1643–1663; b) A. Harada, M. Okada, Y. Kawaguchi, M. Kamachi, *Polym. Advan. Technol.* **1999**, *10*, 3–12; c) J.-L. Weidmann, J.-M. Kern, J.-P. Sauvage, D. Muscat, S. Mullins, W. Kohler, C. Rosenauer, H. J. Räder, K. Martin, Y. Geerts, *Chem. Eur. J.* **1999**, *5*, 1841–1851; d) D. Muscat, W. Köhler, H. J. Räder, K. Martin, S. Mullins, B. Müller, K. Müllen, Y. Geerts, *Macromolecules* **1999**, *32*, 1737–1745; e) K. M. Park, J. Heo, S. G. Roh, Y. M. Jeon, D. Whang, K. Kim, *Mol. Cryst. Liq. Crys. A* **1999**, *327*, 65–70; f) T. Takata, H. Kawasaki, A. Asai, N. Kihara, Y. Furusho, *Chem. Lett.* **1999**, 111–112; g) C. Hamers, O. Kocian, F. M. Raymo, J. F. Stoddart, *Adv. Mater.* **1998**, *10*, 1366–1369; h) C. G. Gong, H. W. Gibson, *Angew. Chem.* **1998**, *110*, 323–327; *Angew. Chem. Int. Ed.* **1998**, *37*, 310–314; i) W. Herrmann, M. Schneider, G. Wenz, *Angew. Chem.* **1997**, *109*, 2618–2621; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2511–2514; j) H. W. Gibson, M. C. Bheda, P. T. Engen, *Prog. Polym. Sci.* **1994**, *19*, 843–945.

[13] Gibson and co-workers (W. S. Bryant, I. A. Guzei, A. L. Rheingold, J. S. Merola, H. W. Gibson, *J. Org. Chem.* **1998**, *63*, 7634–7639) comment on the symmetrical nature of bis-*meta*-phenylene-containing crown ethers when they are incorporated into polymeric interlocked systems.

[14] M. S. Newman, L. F. Lee, *J. Org. Chem.* **1972**, *37*, 4468–4469

[15] H. G. McFadden, J. N. Phillips, *Z. Naturforsch. C: Biosci.* **1990**, *45*, 196–206.

[16] The protons of the $R_2NH_2^+$ center are far more acidic than those of the urea moiety (pK_a values of about 10 and >20, respectively), thus bestowing upon them a much greater capacity for hydrogen bonding. Additionally, inspection of CPK space-filling molecular models reveals that insertion of the urea portion of the dumbbell into the cavity of the DB24C8 ring is not favored sterically as a consequence of the proximal 2,6-diisopropylphenyl group. Also, this geometry would result in an unfavorable electrostatic interaction between the carbonyl oxygen atom on the urea group and the ethereal oxygen atoms lining the perimeter of the macrocyclic cavity. Indeed, a brief Monte Carlo conformational search within MacroModel (1000 steps, all variable torsions considered, Amber* force field, GB/SA $CHCl_3$, extended nonbonded cutoffs of 4, 8, and 20 Å for van der Waals, hydrogen bonding and electrostatic interactions, respectively) of the complexes formed between 2,6-diisopropylcarbanilide and DB24C8 furnished a global minimum conformation in which the ureido proton closest to the diisopropylphenyl unit is sterically prevented from participating in hydrogen bonding interactions by virtue of its proximity to the two isopropyl moieties. The structure corresponding to the global minimum involves a lone hydrogen bond emanating from the sterically unhindered ureido proton to an ethereal oxygen atom of the crown ether, which is encircling the carbanilide derivative with a pseudorotaxane geometry. This phenomenon contrasts with the results of a similar experiment performed employing carbanilide (*N,N*-diphenylurea) as the thread compound, in which the global minimum structure involves the formation of hydrogen bonds from both ureido protons to one of the ethereal oxygen atoms. The carbonyl oxygen atom of the urea group constitutes an unfavorable electrostatic interaction, which repels the crown ether. Thus, in this case, the complete superstructure involves the crown ether interacting attractively with one side of the urea moiety, and repulsively with the other side. These results support the empirical hypothesis—deduced from some observations made on CPK space-filling molecular models and a consideration of the relative pK_a values—that the crown ether prefers to reside around the dialkylammonium center, rather than around the urea moiety.

[17] Unfortunately, the resonances arising from α^1 and α^2 are isochronous. Cross-peaks between this multiplet and the signals corresponding to both H-2 and H-3 are observed. As a consequence of this overlap, it is impossible to deduce that the H-2 resonance *only* gives a cross-peak with the α^1 resonance, and the H-3 resonance *only* gives a cross-peak with the α^2 resonance. However, based upon the patterns observed for the β and γ protons, it is not unreasonable to suppose, by analogy, that selective through-space interactions also occur for the α protons.

[18] I. J. A. Mertens, R. Wegh, L. W. Jenneskens, E. J. Vlietstra, A. van der Kerk-van Hoof, J. W. Zwikker, T. J. Cleij, W. J. J. Smeets, N. Veldman, A. L. Spek, *J. Chem. Soc. Perkin Trans. 2* **1998**, 725–735.

[19] Previously (see ref. [7d]), mass spectrometric analysis of an equimolar mixture of DB24C8 and bis(4-*tert*-butylbenzyl)ammonium hexafluorophosphate revealed the base peak in the spectrum to be that corresponding to the uncomplexed ammonium compound (*m/z* 310). However, a signal arising from the 1:1 complex formed between these two components was observed at *m/z* 758, with a relative intensity of 6%. The significance of this result lies in the fact that the bis(4-*tert*-butylbenzyl)ammonium cation is too large to thread through the cavity of DB24C8. This restriction means that any association of these two components must occur with a *face-to-face* geometry. In this case, the peak arising from the 1:1 complex $[\mathbf{2}\cdot\mathbf{4}\text{-H}]^+$ (*m/z* 646) has an intensity corresponding to 50% of that observed for **4**-H$^+$ (the base peak), implying that there is an interaction more enduring than a simple *face-to-face* association, that is, the threading of the cation through the macroring of DB24C8, resulting in the formation of a [2]pseudorotaxane in the gas phase.

[20] For leading references related to this method, see: J. C. Adrian, C. S. Wilcox, *J. Am. Chem. Soc.* **1991**, *113*, 678–680.

[21] For leading references, see: a) K. A. Connors, *Binding Constants*, Wiley, New York, **1987** ; b) H. Tsukube, H. Furuta, A. Odani, Y. Takeda, Y. Kudo, Y. Inoue, Y. Liu, H. Sakamoto, K. Kimura in *Comprehensive Supramolecular Chemistry, Vol. 8* (Eds.: J. L. Atwood, J. E. D. Davies, D. D. MacNicol, F. Vögtle, J. A. Ripmeester), Pergamon, Oxford, **1996**, pp. 425–482 and references therein.

[22] P. R. Ashton, R. A. Bartsch, S. J. Cantrill, R. E. Hanes, Jr., S. K. Hickingbottom, J. N. Lowe, J. A. Preece, J. F. Stoddart, V. S. Talanov, Z.-H. Wang, *Tetrahedron Lett.* **1999**, *40*, 3661–3664.

[23] However, a report has appeared in the literature (ref. [8e]) describing the inability of a derivative of **2** to form a [2]pseudorotaxane in $CD_3COCD_3/CDCl_3$ (1:1) solution with **4**-H · PF$_6$.

[24] The poor signal to noise ratio obtained when recording these ^{13}C NMR spectra preclude the calculation of *accurate* thermodynamic and kinetic parameters for this dynamic process. However, assuming that the coalescence of the two signals—corresponding to the *i*Pr groups—does occur in the range 312–317 K, estimates for the kinetic and thermodynamic parameters for this process can be obtained as described in I. O. Sutherland, *Annu. Rep. NMR Spectrosc.* **1971**, *4*, 71–235. The rate constant for this bond rotation (k_c) at the coalescence temperature (T_c) was calculated by employing the approximate expression $k_c = \pi(\Delta\nu)/(2)^{1/2}$, where $\Delta\nu$ is the limiting frequency difference (96 Hz) between the coalescing peaks. The relationship $\Delta G_c^{\ddagger} = -RT_c\ln(k_c h/k_B T_c)$—where R, h and k_B correspond, respectively, to the gas, Planck and Boltzmann constants—was used to determine the free activation barriers ($\Delta G_c^{\ddagger}$) of this bond rotation process at 312 and 317 K, respectively, thus giving the range 15.0–15.2 kcal mol^{-1}.

[25] F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caulfield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990**, *11*, 440–467.

[26] N. L. Allinger, Y. H. Yuh, J. H. Lii, *J. Am. Chem. Soc.* **1989**, *111*, 8551–8566.

[27] E. Polak, G. Ribière, *Rev. Fr. Informat. Rech. Oper.* **1969**, *16*, 35–43.

[28] W. C. Still, A. Tempczyk, R. C. Hawley, T. Hendrickson, *J. Am. Chem. Soc.* **1990**, *112*, 6127–6129.

[29] One of the earliest syntheses of bismetaphenyl-ene[26]crown-8 (sometimes referred to as dibenzo[26]-crown-8 (DB26C8)) was reported (G. Lindsten, O. Wennerström, R. Isaksson, *J. Org. Chem.* **1987**, *52*, 547–554) well over 10 years ago now. Subsequently, this compound was employed in the construction of an ion-selective electrode for the potentiometric sensing of guanidinium ions. See: F. N. Assubaie, G. J. Moody, J. D. R. Thomas, *Analyst* **1989**, *114*, 1545–1550. However, during the 1990s, three research groups have independently solved the X-ray crystal structure of this crown ether: the structural parameters reported by each group are, within experimental error, the same. See: i)E. Luboch, M. S. Fonar, Y. A. Siminov, V. K. Bel'sky, J. Biernat, *Izv. Akad. Nauk, Ser. Khim.* **1995**, 2458–2464, ii) G. W. Buchanan, M. Lefort, A. Moghimi, C. Bensimon, *J. Mol. Struct.* **1997**, *415*, 267–275, and iii) H. W. Gibson et. al. see ref. [13]. Interestingly, in neither of the latter papers is any mention made of the earlier X-ray crystallographic analyses. In only one paper, namely iii), is an earlier report of the synthesis of BMP26C8 acknowledged!

[30] The FAB mass spectrum of a 1:1 mixture of **3** and **4**-H $\cdot$ PF_6 contains only signals for the 'free' components, that is, the dibenzylammonium cation **4**-H^+ and BMP26C8. No peaks were observed for any complexes formed between these two components, suggesting that a [2]pseudorotaxane does not exist under the conditions employed during this particular analysis.

[31] A. Derome, M. Williamson, *J. Mag. Reson.* **1990**, *88*, 177–185.

[32] a) A. Bax, D. G. Davis, *J. Mag. Reson.* **1985**, *63*, 207–213; b) T. Hwang, A. J. Shaka, *J. Am. Chem. Soc.* **1992**, *114*, 3157–3159.

[33] A. Bax, S. Subramanian, *J. Mag. Reson.* **1986**, *67*, 565–569.

[34] SHELXTL PC version 5.03, Siemens Analytical X-Ray Instruments, Inc., Madison, WI, **1994**.

Received: January 10, 2000 [F2234]