ORGANIC
LETTERS

2000
Vol. 2, No. 1
61−64

Tribenzo[27]crown-9: A New Ring for Dibenzylammonium Rods

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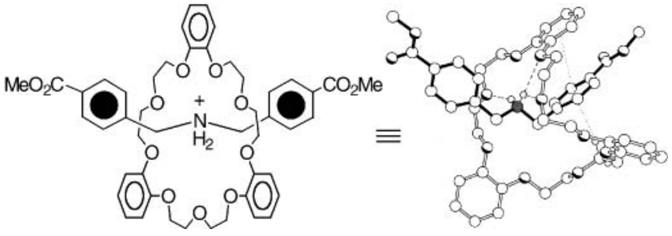
Received October 30, 1999

ABSTRACT



Dibenzylammonium (DBA$^+$) ions thread through the cavity of tribenzo[27]crown-9 (TB27C9) to generate [2]pseudorotaxanes that are stabilized principally by hydrogen-bonding interactions. The stabilities and complexation kinetics associated with these pseudorotaxanes depend markedly on the nature of the substituents situated on the phenyl rings of the DBA$^+$ ions. For example, the complex formed between TB27C9 and the DBA$^+$ ion bearing electron-withdrawing *p*-CO$_2$Me substituents is stronger than that obtained from TB27C9 and the "parent", unsubstituted DBA$^+$ ion itself. Furthermore, the "parent" complex equilibrates much more rapidly with its uncomplexed components than do the complexes generated from TB27C9 and substituted DBA$^+$ ions.

The so-called pseudorotaxanes[1] are supramolecular complexes in which one or more rings are pierced by one or more rodlike components as a result of noncovalent bonding interactions (Figure 1). They differ fundamentally from their mechanically interlocked congeners, the rotaxanes,[2] in that the termini of their rod component(s) do not possess bulky stopper groups that prevent dissociation of the ring(s). Pseudorotaxanes and rotaxanes have both been incorporated into simple molecular-sized machines[3] since, in some instances, the relative positions of their constituent parts can

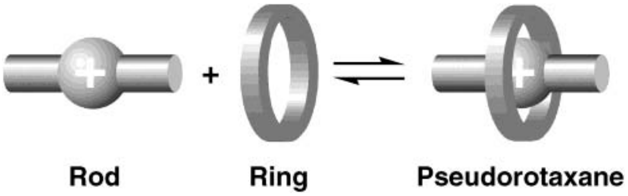


Figure 1. Schematic representation depicting the formation of a threaded 1:1 complex (a pseudorotaxane) between two complementary species wherein the cavity of a suitably sized ring is skewered by a linear rod.

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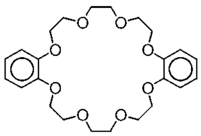
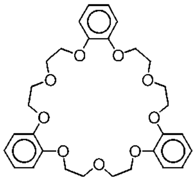
10.1021/ol991205j CCC: $19.00

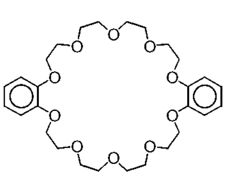
be altered by external stimuli. We have recently developed a route to the noncovalent synthesis[4] of multicomponent pseudorotaxanes that relies[5] on the interpenetration of crown ethers, such as dibenzo[24]crown-8 (**DB24C8**)[6] and dibenzo-[30]crown-10 (**DB30C10**),[7] by dialkylammonium ions, like



DB24C8



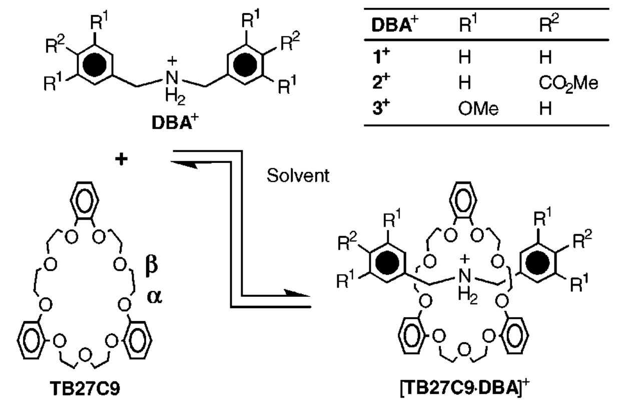
TB27C9



DB30C10

the dibenzylammonium (**DBA**$^+$) cation, principally as a consequence of [N$^+$−H···O] and [C−H···O] hydrogen bonds. Here, we report, for the first time, that the crown ether tribenzo[27]crown-9 (**TB27C9**),[8] which bears a macrocyclic cavity that is intermediate in size between those of **DB24C8** and **DB30C10**, is pierced (Scheme 1) by **DBA**$^+$ ions to produce [2]pseudorotaxanes as a result of hydrogen-bonding interactions. These pseudorotaxanes have been characterized (i) in solution by ^{1}H NMR spectroscopy, (ii) in the gas phase by FAB mass spectrometry, and (iii) in the solid state by X-ray crystallography.

Scheme 1



DBA$^+$	R^1	R^2
1$^+$	H	H
2$^+$	H	CO$_2$Me
3$^+$	OMe	H

The synthesis of **TB27C9** was first reported by Cram[9] in 1977, and the hexafluorophosphate salts of **1**$^+$ and **2**$^+$ have been reported[6,10] recently. Condensation of commercially available 3,5-dimethoxybenzaldehyde and 3,5-dimethoxybenzylamine, followed by sodium borohydride reduction, protonation, and counterion exchange, afforded the tetramethoxy-substituted dibenzylammonium salt **3**·PF$_6$ in a 75% overall yield.

The ability of **TB27C9** to act as a receptor for **DBA**$^+$ ions was first investigated by ^{1}H NMR spectroscopy. Each **DBA**·PF$_6$ salt was dissolved with an equimolar quantity of **TB27C9** in CDCl$_3$/CD$_3$CN (3:1). In the case of **1**$^+$, the rate of exchange of the 1:1 complex with its free components was *fast* relative to the ^{1}H NMR time scale, resulting in a spectrum consisting of time-averaged signals. The stability constant (K_a) for the [**TB27C9·1**][PF$_6$] complex was found to be 270 M^{-1} (at 300 K) from a ^{1}H NMR dilution[11] experiment which used the CH$_2$ protons in **1**$^+$ and the H$_\beta$ protons in **TB27C9** as probes. By contrast, the ^{1}H NMR spectrum obtained from a 1:1 mixture of **TB27C9** and **2**$^+$ contained three distinct sets of signals arising from (i) "free" **TB27C9**, (ii) "free" **2**$^+$, and (iii) the [2]pseudorotaxane [**TB27C9·2**]$^+$, indicating that the exchange between the 1:1 complex and its "free" components is *slow* on the ^{1}H NMR time scale. Accordingly, a K_a value of 710 M^{-1} could be calculated for this process (at 300 K) by employing the single-point method.[12] Initially, no signals which indicate the formation of a [2]pseudorotaxane are evident in the ^{1}H NMR spectrum (Figure 2) of a 1:1 mixture of **TB27C9** and **3**·PF$_6$.

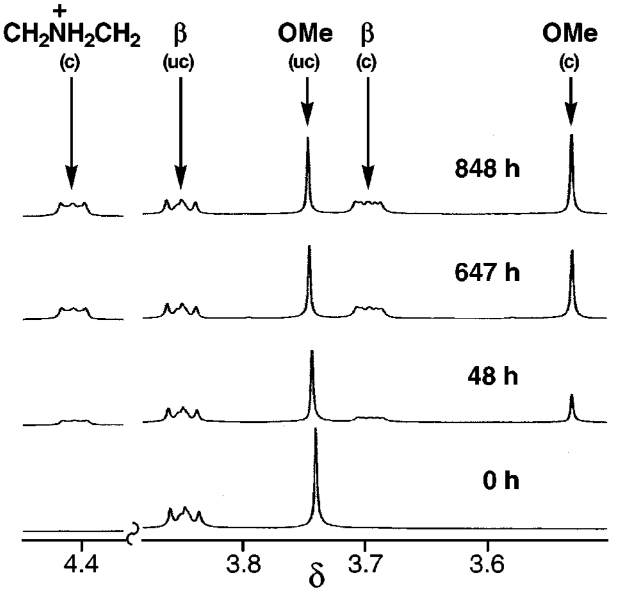


Figure 2. Partial ^{1}H NMR spectra (400 MHz, 300 K) of an equimolar mixture of **TB27C9** and **3**·PF$_6$ in CDCl$_3$/CD$_3$CN (3:1) recorded at various time intervals. Initially (t = 0 h), no signals corresponding to the 1:1 complex are observed. However, over a period of weeks, signals arising from the [2]pseudorotaxane [**TB27C9·3**]$^+$ are observed to "grow", until equilibrium is finally reached.

However, it soon became apparent that the kinetics associated with the complexation process are not only slow on the NMR

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(6) For an in depth study of how **DB24C8** interacts with **DBA**$^+$ cations, see: Ashton, P. R.; Chrystal, E. J. T.; Glink, P. T.; Menzer. S.; Schiavo, C.; Spencer, N.; Stoddart, J. F.; Tasker. P. A.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 709−728.

(7) For a study of the interaction between **DB30C10** and substituted secondary dibenzylammonium ions, see: Ashton, P. R.; Fyfe, M. C. T.; Schiavo, C.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Tetrahedron Lett.* **1998**, *39*, 5455−5458.

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time scale but also on the *laboratory* time scale! Numerous ^{1}H NMR spectra of an equimolar mixture of **TB27C9** and **3**·PF$_6$ were recorded at various intervals over a period of many weeks—selected spectra are shown in Figure 2—revealing that approximately *six weeks* are required for this system to reach equilibrium under the conditions of the experiment. The K_a value for this equilibrium at 300 K was determined, by the single-point method,[12] to be 270 M^{-1}. Additionally, by using well-known equations,[13] the kinetic and thermodynamic parameters—k_{on}, k_{off}, $\Delta G^{\ddagger}_{on}$, and $\Delta G^{\ddagger}_{off}$—for this process were calculated to be 6.17×10^{-5} M^{-1}s^{-1}, 2.29×10^{-7} s^{-1}, 23.1 kcal mol^{-1}, and 26.4 kcal mol^{-1}, respectively.

The "gas-phase" behavior of these systems was also investigated using fast atom bombardment mass spectrometry (FAB-MS). In the case of both **1**$^+$ and **2**$^+$, strong signals—corresponding to the 1:1 complexes formed with **TB27C9**—were observed in the mass spectra with *m*/*z* values of 739 and 855, respectively. However, mass spectrometric analysis of a freshly prepared 3:1 $CDCl_3/CD_3CN$ solution containing an equimolar mixture of **TB27C9** and **3**·PF$_6$ gave rise to a spectrum in which no signal could be observed for the 1:1 complex. However, after being allowed to equilibrate (1000 h), this sample was subjected to a repeat analysis, resulting in a spectrum that *did* contain a strong peak (*m*/*z* = 859) corresponding to the desired 1:1 complex, thus demonstrating the very slow kinetics of complexation. This point was reinforced by performing a "competition" experiment, in which a solution containing approximately equimolar amounts of **TB27C9**, **1**·PF$_6$, **2**·PF$_6$, and **3**·PF$_6$ was subjected to repeated FAB-MS analysis (Figure 3) over a period of 2 weeks. Initially (t = 0 d), peaks arising from [**TB27C9·1**]$^+$ and [**TB27C9·2**]$^+$ were observed, whereas no signal was present for [**TB27C9·3**]$^+$. However, after 6 days, a peak corresponding to the 1:1 complex formed between **TB27C9** and **3**$^+$ was noted, and its intensity was found to have increased when the analysis was repeated after a total of 14 days.

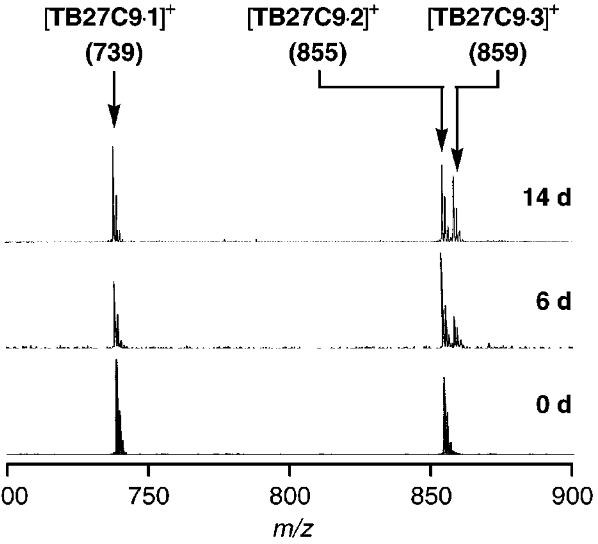

Figure 3. FAB mass spectra of an equimolar mixture of **TB27C9**, **1**·PF$_6$, **2**·PF$_6$, and **3**·PF$_6$, analyzed at various time intervals after the initial mixing. A peak with an *m*/*z* value of 859, corresponding to a 1:1 aggregate of **TB27C9** and **3**$^+$, is not present in the first spectrum (t = 0 d). However, as the solution equilibrates over time, mass spectrometric analysis reveals the emergence of an intense peak for this 1:1 complex.

X-ray quality single crystals[14] of the [2]pseudorotaxane [**TB27C9·2**][PF$_6$] were obtained upon layering a CH_2Cl_2/CH_3CN (6:1) solution—containing an equimolar mixture of **TB27C9** and **2**·PF$_6$—with hexane. The X-ray analysis shows the crown ether component to have a distinctly twisted conformation, with all three catechol units steeply inclined to each other and with all nine oxygen atoms directed inwards toward the macroring center. The 1:1 complex is stabilized by a combination of (i) [N$^+$−H···O] hydrogen bonds (a, b, and c in Figure 4), (ii) $\pi-\pi$ stacking (d) between one of the catechol rings of the crown ether and one of the phenyl rings of the cation, and (iii) a [C−H···π] interaction (e) between one of the OCH_2 protons of **TB27C9** and the phenyl ring of

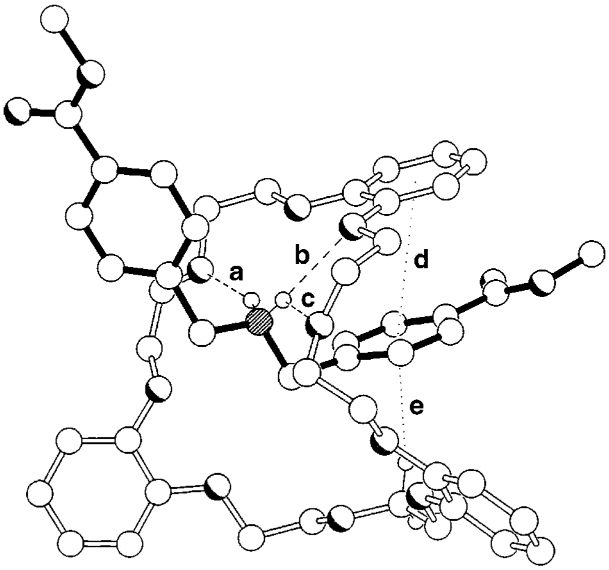

Figure 4. Solid-state superstructure of the 1:1 complex formed between **TB27C9** and **2**$^+$. The hydrogen-bonding geometries are as follows {[N$^+$···O], [H···O] Å, [N$^+$−H···O] (deg)}: (a) 2.88, 2.06, 155; (b) 3.17, 2.31, 158; (c) 2.99, 2.36, 127. The geometry of the $\pi-\pi$ stacking interaction (d): centroid−centroid separation 3.76 Å, mean interplanar separation 3.49 Å, the rings are inclined by 5°. The [H···π] distance and [C−H···π] angle for the [C−H···π] interaction (e) are 2.86 Å and 170°.

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(9) For Cram's original procedure, see ref 8. A slightly modified protocol was employed in our laboratories. For the details, see the Supporting Information.

(10) Ashton, P. R.; Bartsch, R. A.; Cantrill, S. J.; Hanes, R. E., Jr.; Hickingbottom, S. K.; Lowe, J. N.; Preece, J. A.; Stoddart, J. F.; Talanov, V. S.; Wang, Z.-H. *Tetrahedron Lett.* **1999**, *40*, 3661−3664.

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(12) For leading references on this method, see: Adrian, J. C.; Wilcox, C. S. *J. Am. Chem. Soc.* **1991**, *113*, 678−680.

the cation that also participates in the $\pi-\pi$ stacking. The 1:1 complexes pack to form sheets held together by an array of [C−H···π] interactions (f−h in Figure 5).

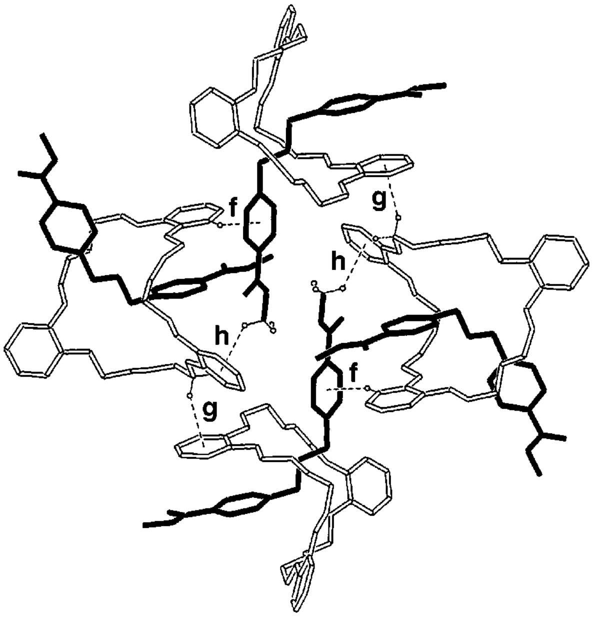

Figure 5. Part of one of the [C−H···π] linked sheets of the 1:1 complexes formed between **TB27C9** and $\mathbf{2}^+$. The [H···π] distances (Å) and [C−H···π] angles (deg) are (f) 2.91, 164; (g) 2.72, 143; and (h) 2.92, 124.

As part of our ongoing study[15] into the nature of the dialkylammonium ion/crown ether interaction, we have demonstrated here that the crown ether **TB27C9** is an effective receptor for $\mathbf{DBA}^+$ ions. The size of this macrocycle—intermediate between that of the well-studied [24]-crown-8 and [30]crown-10 systems—introduces yet another element of control into the self-assembly[16] processes associated with this recognition motif. As in previous examples,[17] the strength of the association between these complementary subunits can be controlled via judicious substitution of the phenyl rings of the $\mathbf{DBA}^+$ ion with either electron-withdrawing or electron-donating moieties. However, our preliminary investigations have revealed that the kinetics associated with the **TB27C9** macrocycle forming [2]pseudorotaxanes depend dramatically upon the size and disposition of substituents appended to the phenyl rings of the $\mathbf{DBA}^+$ ion. Indeed, the rates of complexation/decomplexation are reflected in the nature of the ^{1}H NMR spectroscopic experiments required to determine the stability constants for these systems, i.e., dilution or single point methodologies over a range of time scales. The rate of exchange between "free" and "bound" species is reduced significantly on going from the parent $\mathbf{DBA}^+$ ion ($\mathbf{1}^+$) to the *p*-CO_2Me-substituted system ($\mathbf{2}^+$), with the most dramatic slowing down being observed for the 3,5-di-OMe ion ($\mathbf{3}^+$).

Furthermore, the 3-fold symmetry of **TB27C9** and the potential to functionalize each aromatic ring of this crown ether offer an attractive route to the formation of interpenetrating/interlocked three-dimensional networks. The formation of hydrogen-bonded linear "one-dimensional" tapes[18] and two-dimensional sheets[19] has been achieved previously, in the solid state, with carboxyl-substituted $\mathbf{DBA}^+$ ions and **DB24C8**. The successful union of this paradigm with that of **TB27C9**/dialkylammonium ion binding will allow us to branch out into the next dimension using this reliable and versatile supramolecular synthon.[20]

Acknowledgment. We thank UCLA for generous financial support.

Supporting Information Available: Synthetic protocols for **TB27C9** and **3**·PF_6, crystal data for [**TB27C9·2**][PF_6]. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Crystal data for **[TB27C9·2][PF$_6$]**:[$C_{48}H_{56}NO_{13}$][PF_6]·MeCN, M = 1041.0, monoclinic, space group $P2_1/c$ (No. 14), a = 14.241(2), b = 16.425(2), and c = 22.169(2) Å, β = 93.94(1)°, V = 5173(1) Å^3, Z = 4, ρ_c = 1.337 g cm^{-3}, $\mu(\mathrm{Cu_{K\alpha}})$ = 12.1 cm^{-1}, $F(000)$ = 2184, T = 293 K; clear blocks, 0.23 × 0.20 × 0.13 mm, Siemens P4/PC diffractometer, graphite-monochromated Cu Kα radiation, ω-scans, 7680 independent reflections. The structure was solved by direct methods, and the full occupancy non-hydrogen atoms were refined anisotropically. Disorder was found in the included MeCN solvent molecule, and this was resolved into two partial occupancy orientations; the non-hydrogen atoms of the major occupancy orientation were refined anisotropically (those of the minor occupancy orientation were refined isotropically). The C−H hydrogen atoms were placed in calculated positions, assigned isotropic thermal parameters, $U(\mathrm{H}) = 1.2U_{\mathrm{eq}}(\mathrm{C})$ [$U(\mathrm{H}) = 1.5U_{\mathrm{eq}}(\mathrm{C{-}Me})$], and allowed to ride on their parent atoms. The N−H hydrogen atoms were located from a ΔF map and allowed to refine isotropically subject to an N−H distance constraint (0.90 Å). Refinements were by full matrix least-squares based on F^2 to give R_1 = 0.087, wR_2 = 0.215 for 3576 independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leq 120°$] and 670 parameters. All computations were carried out using the SHELXTL PC program system.

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