

## Secondary Dibenzylammonium Ion Binding by [24]Crown-8 and [25]Crown-8 Macrocycles

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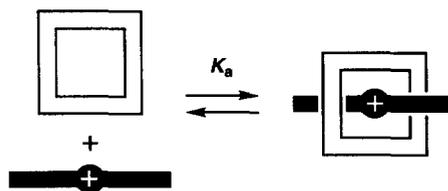
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**Abstract:** A range of crown ethers with either [24]crown-8 or [25]crown-8 constitutions have been demonstrated to form pseudorotaxanes with *para*-disubstituted dibenzylammonium ions, both in solution and in the “gas phase” by <sup>1</sup>H NMR spectroscopy and liquid secondary ion mass spectrometry, respectively. Substitution of the [24]crown-8 framework with increasing numbers of benzo rings is observed to lower the stability constants ( $K_a$ 's) from  $>10^3$  to  $\sim 0$  M<sup>-1</sup> in acetonitrile. A pronounced decrease in  $K_a$  values also occurs when the [24]crown-8 constitution is expanded to give a macroring containing 25 atoms — a modification that not only increases the size of the macrocyclic cavity but also disrupts the O-C-C-O repeating unit in the macrocycle's backbone. © 1999 Elsevier Science Ltd. All rights reserved.

**Keywords:** Crown Ethers; Pseudorotaxanes; Substituted Ammonium Ion Binding; Supramolecular Chemistry

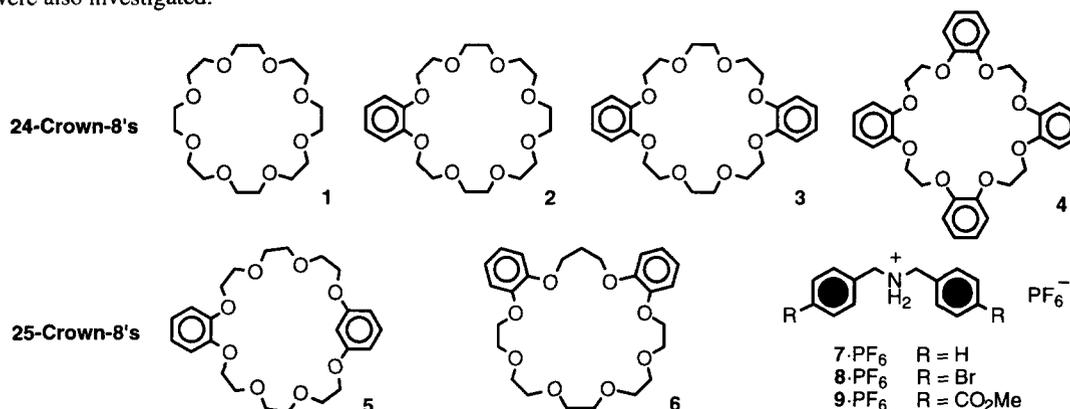
The serendipitous discovery of crown ethers by Pedersen<sup>[1]</sup> just over thirty years ago is arguably the origin of many aspects of supramolecular chemistry<sup>[2]</sup> as we know it today. Although not the first to synthesize macrocyclic polyethers, it was Pedersen who realized their importance in the context of host-guest chemistry, and went on<sup>[3]</sup> to investigate the binding properties of crown ether hosts with a wide variety of cationic guests. Among the many guests studied were the ammonium (NH<sub>4</sub><sup>+</sup>) and primary alkylammonium (RNH<sub>3</sub><sup>+</sup>) ions, which were shown<sup>[4]</sup> to bind dibenzo[18]crown-6 in a face-to-face manner. The binding of secondary dialkylammonium ions (R<sub>2</sub>NH<sub>2</sub><sup>+</sup>) was largely unexplored until recent times, whereupon it was discovered<sup>[5]</sup> that, if a [24]crown-8-containing macrocyclic polyether is employed, the R<sub>2</sub>NH<sub>2</sub><sup>+</sup> ion can interpenetrate fully (Scheme 1) the macrocyclic cavity, generating a so-called pseudorotaxane in which the cation is “threaded” through the center of the crown ether. For complexes exhibiting 1:1 stoichiometries, only dibenzo-[24]crown-8 (3) (DB24C8) has been studied in detail, revealing that the self-assembly<sup>[6]</sup> of the [2]pseudorotaxane proceeds with the formation of both [N<sup>+</sup>–H···O] and [C–H···O] hydrogen bonds, augmented by electrostatic and aromatic-aromatic interactions. More recently, it has been demonstrated<sup>[7]</sup> that the judicious substitution of the phenyl rings of the dibenzylammonium ions allows for the “fine-tuning” of this supramolecular system. Indeed, a linear free energy relationship exists between the stability constants ( $K_a$ 's) for the formation of the pseudorotaxanes and the Hammett substituent constants ( $\sigma$ ). In this



**Scheme 1.** A schematic representation depicting the binding of a dibenzylammonium ion by a crown ether to form a 1:1 complex known as a [2]pseudorotaxane.

communication, we report on how changing the crown ether host, as opposed to the thread-like guest, alters the  $K_a$ 's for pseudorotaxane formation.

The crown ethers (**Figure 1**) chosen for this investigation included [24]crown-8<sup>[8]</sup> (**1**) and three derivatives with one, two, and four fused benzo-rings — namely benzo[24]crown-8<sup>[9]</sup> (**2**), dibenzo[24]crown-8<sup>[10]</sup> (**3**) and tetrabenzo[24]crown-8<sup>[11]</sup> (**4**), respectively. Two macrocycles (**5**<sup>[12]</sup> and **6**<sup>[13]</sup>) with a [25]crown-8 constitution were also investigated.



**Figure 1.** The [24]crown-8 derivatives **1-4** and [25]crown-8 derivatives **5** and **6** whose binding properties were investigated with the *para*-disubstituted dibenzylammonium salts **7-9**·PF<sub>6</sub>.

It is evident (**Table 1**) that all of the crown ether hosts—*i.e.*, **1-6**—form 1:1 complexes with each of the secondary dibenzylammonium ion guests—*i.e.*, **7<sup>+</sup>-9<sup>+</sup>**—in the ‘gas phase’, as demonstrated by liquid secondary ion mass spectrometry (LSIMS). In each case, a peak was observed for (1) the crown ether adduct with Na<sup>+</sup>, (2) the uncomplexed dibenzylammonium cation and (3) the 1:1 complex formed between host and guest. Although a peak corresponding to a 1:1 complex does not necessarily infer pseudorotaxane formation, the relatively high intensities recorded in **Table 1** for all these species suggest very strongly—in our experience<sup>[14]</sup>—that they are indeed pseudorotaxanes and not just face-to-face complexes.

**Table 1.** Relative intensities of complexed and uncomplexed species in the “gas phase” as determined by LSIMS.<sup>(a)</sup>

Guest	Observed Species	Relative Intensities of Mass Peaks (%)					
		[24]Crown-8 ring				[25]Crown-8 ring	
		<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6</b>
<b>7</b> ·PF <sub>6</sub> (R = H)	Free Guest ( <b>7<sup>+</sup></b> )	47	48	46	175	200	141
	Free Crown ( <b>1-6</b> )	40	11	7	33	6	7
	1:1 Complex	100	100	100	100 <sup>(b)</sup>	100 <sup>(b)</sup>	100 <sup>(b)</sup>
<b>8</b> ·PF <sub>6</sub> (R = Br)	Free Guest ( <b>8<sup>+</sup></b> )	24	30	30	53	115	55
	Free Crown ( <b>1-6</b> )	10	18	22	96	12	17
	1:1 Complex	100	100	100	100	100 <sup>(b)</sup>	100
<b>9</b> ·PF <sub>6</sub> (R = CO <sub>2</sub> Me)	Free Guest ( <b>9<sup>+</sup></b> )	28	37	29	51	68	44
	Free Crown ( <b>1-6</b> )	13	20	10	37	4	8
	1:1 Complex	100	100	100	100	100	100

(a) The spectra were obtained on a VG Zabspec mass spectrometer, equipped with a cesium ion source and utilizing a *m*-nitrobenzyl alcohol matrix. (b) These values were scaled to 100 to aid comparisons between systems.

Each crown ether was mixed with an equimolar amount of the appropriate dibenzylammonium salt<sup>[15]</sup> and their <sup>1</sup>H NMR spectra (400 MHz, CD<sub>3</sub>CN, 300 K) were recorded. In most cases, three different sets of

resonances were observed, which could be assigned to (1) the free crown ether host, (2) the uncomplexed guest and (3) the 1:1 complex formed between the host and guest. This spectroscopic behavior indicates that the complexed and uncomplexed species are equilibrating slowly on the  $^1\text{H}$  NMR timescale, allowing  $K_a$  values (Table 2) to be calculated utilizing the so-called single-point<sup>[16]</sup> method.

Although investigations on the binding characteristics of TB24C8 (4) with dibenzylammonium salts were hampered by its low solubility in  $\text{CD}_3\text{CN}$ , it was sufficiently soluble in  $\text{CD}_3\text{COCD}_3$ <sup>[17]</sup> to permit binding measurements to be performed at 5 mM. Inspection of the resulting spectra of equimolar mixtures of this crown ether with the dibenzylammonium salts 7-9·PF<sub>6</sub> revealed that there are negligible chemical shift changes under these conditions and so the  $K_a$  values can therefore be assumed to be effectively zero. As expected,<sup>[7]</sup> for the crown ethers 1-3, the stability constants increase as the  $\pi$ -electron densities on the aromatic rings of the dibenzylammonium ion decrease, *i.e.*, on going from R = H to Br to CO<sub>2</sub>Me, the  $K_a$  values become larger.

**Table 2.** The stability constants ( $K_a$ 's) calculated for the formation of pseudorotaxanes incorporating crown ethers 1-3, 5 and 6 with guests 7-9·PF<sub>6</sub>.

Guest	R	$K_a$ (M <sup>-1</sup> ) (300 K, 10 mM, CD <sub>3</sub> CN)					
		[24]Crown-8 ring				[25]Crown-8 ring	
		1	2	3	4 <sup>(a)</sup>	5	6
7·PF <sub>6</sub>	H	1700	470	320	~0 <sup>(b)</sup>	— <sup>(c)</sup>	— <sup>(c)</sup>
8·PF <sub>6</sub>	Br	3500	720	800	~0	— <sup>(c)</sup>	— <sup>(c)</sup>
9·PF <sub>6</sub>	CO <sub>2</sub> Me	4500	880	1100	~0	<100 <sup>(d)</sup>	270

(a) Measurements made on TB24C8 (4) were conducted at 5 mM in  $\text{CD}_3\text{COCD}_3$ . (b) Although no binding can be detected in solution by this method, this host/guest system has been shown<sup>[18]</sup> to co-crystallize to give the [2]pseudorotaxane. (c) In these cases, the spectra consist of broadened peaks, indicating that the complexed and uncomplexed species are not equilibrating slowly enough on the  $^1\text{H}$  NMR timescale to use the single-point method to determine  $K_a$  values. (d) Since at 300 K, the complexed and uncomplexed species are not equilibrating slowly on the  $^1\text{H}$  NMR timescale, the stability constant was determined at lower temperatures (243-273 K) where the equilibration is slow and the values were used to extrapolate to an approximate room temperature value for  $K_a$ .

A comparison of how each crown ether host binds to any one particular guest, shows that, in the case of the [24]crown-8 constitution (1-4), the  $K_a$  values decrease<sup>[19]</sup> as more of the macroring oxygen atoms 'become' phenolic. This observation can be rationalized in terms of the reduced basicity of these atoms—with respect to dialkyl ether oxygen atoms—and, as such, their effectiveness as hydrogen bond acceptors is diminished. The crown ethers with [25]crown-8 constitutions (5 and 6) presumably have larger cavities than their [24]crown-8 counterparts, as evidenced by the increase in the rate of exchange between complexed and uncomplexed species when we consider the binding of either 7·PF<sub>6</sub> or 8·PF<sub>6</sub>. These [25]crown-8 macrocyclic polyethers also contain structural elements that deviate from the ideal<sup>[20]</sup> O-C-C-O repeating unit—there is a propyleneoxy moiety in 5 and a 1,3-phenylenedioxy moiety in 6—disrupting the array of donor atoms directed toward the center of the crown ether cavity. This distortion seemingly results in a less favorable geometry for interaction with the dibenzylammonium cation, hence giving rise to lower  $K_a$  values in comparison to the 24 atom-containing macrorings, *cf.* the binding of 9·PF<sub>6</sub> with crown ethers 1-3 as compared with 5 and 6.

Thus, it has been shown that crown ethers with either [24]crown-8 or [25]crown-8 constitutions bind<sup>[21]</sup> *para*-disubstituted dibenzylammonium ions both in solution and in the "gas phase" by  $^1\text{H}$  NMR spectroscopy and LSIMS, respectively. When considering the [24]crown-8 analogues, as more aromatic residues are appended to the macrocyclic framework, the affinity of the crown ethers toward the dibenzylammonium ions is diminished, and in the case of TB24C8 (4), no appreciable binding in solution could be detected. Moreover, increasing the size of the macrocyclic polyether ring from 24 to 25 atoms—necessarily disrupting the O-C-C-O repeating unit—reduces the  $K_a$  values for the formation of [2]pseudorotaxanes, demonstrating that not only substitution effects,

but relatively small changes in constitution, can also alter dramatically the crown ether's ability to encircle the secondary dibenzylammonium ion center.

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- [10] DB24C8 (**3**) was purchased from the Aldrich Chemical Company and used as received.
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- [12] Alkylation (K<sub>2</sub>CO<sub>3</sub> / MeCN) of resorcinol with 2-(2-(2-chloroethoxy)ethoxy)ethanol, followed by tosylation (TsCl / NaOH / THF / H<sub>2</sub>O) and its macrocyclization with catechol in the presence of Cs<sub>2</sub>CO<sub>3</sub> in refluxing MeCN, afforded the [25]crown-8 derivative **5** in an overall yield of 53 %.
- [13] Cyclization of 1,3-(*o*-hydroxyphenoxy)propane with pentaethyleneglycol dimesylate and Cs<sub>2</sub>CO<sub>3</sub> in refluxing MeCN afforded **6** in a 53 % yield.
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- [15] The amines from which the dibenzylammonium salts were derived are either commercially available (7-PF<sub>6</sub>) or easily prepared. For **8**-PF<sub>6</sub>, see ref. [7] and for **9**-PF<sub>6</sub>, see Ashton, P. R.; Glink, P. T.; Stoddart, J. F.; Tasker, P. A.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1996**, *2*, 729-736.
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- [17] K<sub>a</sub> Values for the 1:1 complex formed between DB24C8 (**3**) and 7-PF<sub>6</sub> have been determined previously (see ref. 5b) in both CD<sub>3</sub>CN and CD<sub>3</sub>COCD<sub>3</sub>. As the values obtained did not differ significantly, only approximate comparisons can be made between these solvents.
- [18] Diffusion of Et<sub>2</sub>O into an equimolar mixture of TB24C8 **4** and dibenzylammonium hexafluorophosphate 7-PF<sub>6</sub> dissolved in MeCN, afforded crystalline material suitable for X-ray crystallographic analysis, which revealed the formation of a threaded 1:1 complex.
- [19] The K<sub>a</sub> values calculated for hosts **2** and **3** are essentially the same within experimental error. An error of ca. 15 % is estimated for the calculated K<sub>a</sub> values in Table 2, the major source of the error originating from inaccuracies in the integrations of the appropriate <sup>1</sup>H NMR signals. Although there is little difference in complexation strengths between [24]crown-8 hosts incorporating one and two benzo units, as in **2** and **3** respectively, once all eight oxygen atoms 'become' phenolic in nature, *i.e.*, as in host **4**, the affinity of the [24]crown-8 framework for secondary dibenzylammonium ions becomes effectively zero.
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- [21] However, subsequent to the submission of our manuscript for publication, a report has appeared in the literature (Yamaguchi, N.; Gibson, H. W. *Angew. Chem. Int. Ed.* **1999**, *38*, 143-147) describing the inability of a derivative of **5** to form a pseudorotaxane in CD<sub>3</sub>COCD<sub>3</sub>/CDCl<sub>3</sub> (1:1) solution with 7-PF<sub>6</sub>.