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[2]Pseudorotaxane Formation with *N*-Benzylanilinium Axles and 24-Crown-8 Ether Wheels

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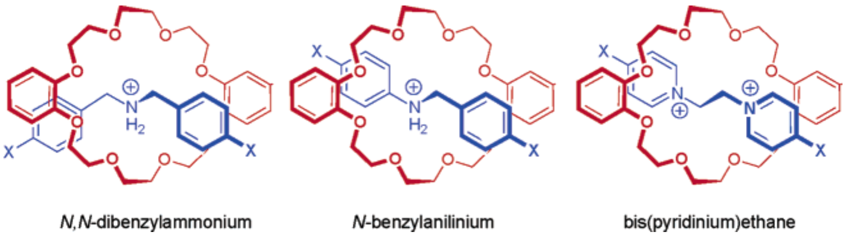
ABSTRACT



As a hybrid of the *N*,*N*-dibenzylammonium and 1,2-bis(pyridinium)ethane axles, various *N*-benzylanilinium cations were investigated as suitable axles for the formation of [2]pseudorotaxanes with the 24-membered crown ethers 24C8 and DB24C8. The effect of electron-donating OCH_3 and electron-withdrawing CF_3 groups on both the anilinium and benzyl aromatic rings was studied. Formation constants and structural details were compared to the [2]pseudorotaxanes formed by the two aforementioned dibenzylammonium and 1,2-bis(pyridinium)ethane axles.

A variety of [2]pseudorotaxanes have been reported that involve the interpenetration of dibenzo-24-crown-8 ether (**DB24C8**) by linear cationic molecules, thus acting as wheel and axle, respectively.[1] The first, extensively studied by Stoddart, uses secondary ammonium cations such as *N*,*N*-dibenzylammonium as the axle component.[2] A second, reported by us, utilizes 1,2-bis(pyridinium)ethane dications as the axles.[3] The dibenzylammonium cation binds to the crown ether by way of strong $NH\cdots O$ hydrogen bonds and $N^+\cdots O$ ion−dipole interactions whereas the bis(pyridinium)ethane axle relies on a series of much weaker $CH\cdots O$ hydrogen bonds, two sets of $N^+\cdots O$ interactions, and significant π-stacking between electron-poor pyridinium rings and electron-rich catechol rings on **DB24C8**. As these two pseudorotaxanes systems display approximately the same range of association constants[4] (MeCN at 25 °C), we were interested to know if a new *hybrid* axle could be created using what may be described as the “best” properties of each of the two axles.

To this end, we designed an axle that contains characteristics of both *N*,*N*-dibenzylammonium and bis(pyridinium)ethane axles. This new axle contains a two-atom bridge consisting of a $-CH_2NH_2^+-$ unit between two aromatic rings; an *N*-benzylanilinium. This recognition site should provide (i) a positively charged group suitable for electrostatic ion−dipole interactions with the crown ether oxygen atoms, (ii) two strongly acidic N−H protons for $NH\cdots O$ hydrogen bonding, (iii) two acidic benzyl CH protons for

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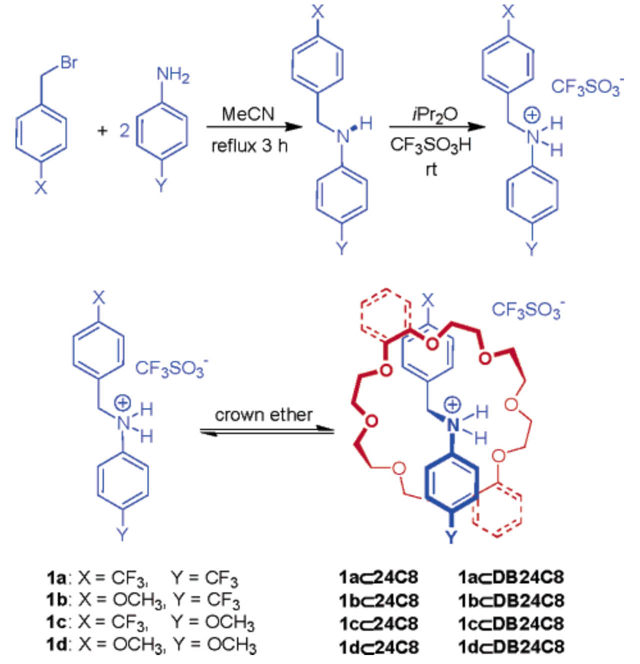
C*H*···O hydrogen bonding, and (iv) electron-poor aromatic rings for π-interactions with the catechol rings on the crown ether. Thus, potentially these new axles would be an excellent match, in size and shape, with the bis(pyridinium)ethane motif while providing the versatility of acid−base control reminiscent of the *N*,*N*-dibenzylammonium axles.

Herein, we present the synthesis of a series of new axles **1a**$^+$−**1d**$^+$ and their complexation by both **DB24C8** and **24C8** (24-crown-8) to yield pH-controllable [2]pseudorotaxanes (Scheme 1). Substituted *N*-benzylanilines were easily synthesized in high yields via a one step alkylation reaction from commercially available reagents. Two equivalents of the aniline and 1 equiv of the benzyl bromide are required as 1 equiv of the aniline acts as a base and helps to prevent the formation of tertiary amines.[5] The *N*-benzylanilinium axles **1a**$^+$−**1d**$^+$ are precipitated as the triflate salt from a solution of the corresponding *N*-benzylaniline in isopropyl ether upon addition of trifluoromethanesulfonic acid.

Scheme 1. Synthesis of Axles and [2]Pseudorotaxanes



The X-ray structure of **1c**$^+$ (Figure 1) shows that in the solid state the *N*-benzylanilinium cations display the anticipated *anti* conformation about the central C−N bond, which resembles the geometry observed for analogous 1,2-bis(pyridinium)ethane cations.[6]

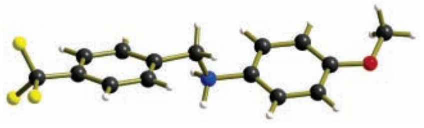


Figure 1. Ball-and-stick representation of the X-ray structure of **1c**$^+$ showing an *anti* conformation: dihedral angle = 171.8° (carbon = black, oxygen = red, nitrogen = blue, fluorine = yellow, hydrogen = white).

As a result of the enhanced acidity of these anilinium-based axles, the protonated (HA$^+$) and nonprotonated (A) axles are in equilibrium in solution. Both species are involved in fast exchange on the NMR time scale and only a single, averaged set of resonances is observed. The limiting chemical shifts and acidity constants (K_a) were obtained from titration experiments. In this method, each *N*-benzylaniline was titrated with increasing amounts of trifluoromethanesulfonic acid until saturation was indicated (see the Supporting Information). The chemical shift data were fitted using a nonlinear least-squares model.[7] Variation of the substituents in the 4-position on the aromatic rings of the axles allowed study of the effects of EWG or EDG on the acidity and ability to form [2]pseudorotaxanes. Results indicate a 100-fold increase in the acidity constants (K_a) between the axles with the change of a OCH_3 group for a CF_3 group on the aniline ring, regardless of the nature of the group on the benzyl ring.

When equimolar solutions of an axle and a 24-crown-8 ether macrocycle were mixed together at 25 °C in CD_3CN equilibrium was rapidly attained and a new set of peaks, in addition to those assigned to the free components, was observed in the ^1H NMR spectrum (see Figure 2).

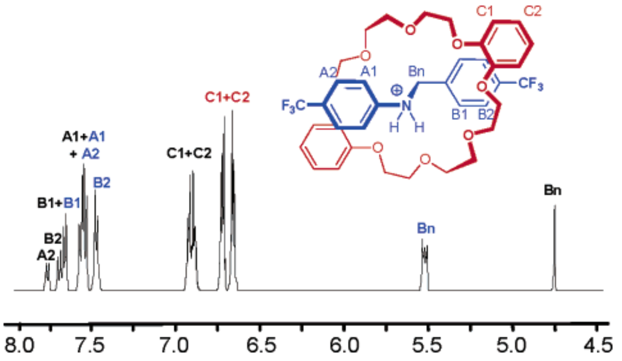


Figure 2. ^1H NMR spectrum in CD_3CN at 1.0×10^{-2} M of an equimolar solution of [**1a**][OTf] and **DB24C8** showing formation of [**1a⊂DB24C8**]$^+$ (red and blue labels = complexed components of the [2]pseudorotaxane, [**1a⊂DB24C8**]$^+$; black labels = uncomplexed axle, [**1a**]$^+$ and wheel **DB24C8**).

The chemical shifts of the new resonances are consistent with the formation of a [2]pseudorotaxane complex in solution with a rate of association−dissociation slow on the NMR time scale. Chemical exchange between the free components and the [2]pseudorotaxane was also confirmed by EXSY NMR experiments.[8]

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[5] For other examples, see (a) Onaka, M.; Umezomo, A.; Kawai, M.; Izumi, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 1202−1203. (b) Hayat, S.; Rahman, A.; Choudhary, M. I.; Khan, K. M.; Schumann, W.; Bayer, E. *Tetrahedron* **2001**, *57*, 9951−9957.

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In the case of the **24C8** complexes, the resonances due to $\mathrm{N}H_2$, $\mathrm{C}H_2$, and ortho aromatic C-H protons were shifted downfield relative to the free axle, which is indicative of hydrogen bonding. Thus in solution, a total of eight hydrogen bonds are responsible for maintaining the [2]pseudorotaxane structure (see Table 1).

Table 1. Summary of Changes in Chemical Shift ($\Delta\delta$ in ppm) of the [2]Pseudorotaxanes Relative to the Free Axles[a]

complex	B2	B1	Bn	A1	A2
[**1a**⊂**24C8**]$^+$	+0.07	+0.26	+0.58	+0.36	−0.03
[**1b**⊂**24C8**]$^+$	+0.12	+0.29	+0.55	+0.39	+0.02
[**1c**⊂**24C8**]$^+$	+0.09	+0.26	+0.58	+0.25	+0.11
[**1d**⊂**24C8**]$^+$	+0.14	+0.28	+0.55	+0.27	+0.09
[**1a**⊂**DB24C8**]$^+$	−0.24	+0.01	+0.76	+0.09	−0.29
[**1b**⊂**DB24C8**]$^+$	−0.13	+0.13	+0.73	+0.11	−0.37
[**1c**⊂**DB24C8**]$^+$	−0.34	−0.04	+0.77	+0.19	−0.16
[**1d**⊂**DB24C8**]$^+$	−0.18	+0.07	+0.72	+0.22	−0.21

[a] Positive: downfield shift; negative: upfield shift.

For the **DB24C8** adducts, the signals due to $\mathrm{N}H_2$ and $\mathrm{C}H_2$ protons were shifted downfield, but due to the lower basicity of the aromatic oxygen atoms on the crown ether, there are not significant aromatic $\mathrm{C}H\cdots\mathrm{O}$ interactions, regardless of the substituent group on the axle. However, the resonances due to the hydrogen atoms in meta positions on the CF_3−substituted rings are shifted upfield because of the shielding generated by the ring current of the catechol rings on the crown ether, indicating the presence of π-stacking interactions in a fashion similar to that observed in the bis(pyridinium)ethane [2]pseudorotaxanes (see Table 1).

Due to the presence of simultaneous equilibria between protonated/nonprotonated and complexed/uncomplexed species, an equation was derived (see the Supporting Information) to determine the association constants (K_{assoc}) from the measured experimental constant (K_{exp}), the acidity constant of the thread (K_a) and the solution concentration of thread at equilibrium that is nonprotonated, [A]. The concentration of (A) was calculated from integration and the observed chemical shift of the uncomplexed peak in the NMR spectrum. The results are summarized in Table 2.

Table 2. Summary of Equilibrium Constants[a]

		24C8		**DB24C8**	
	pK_a	K_{exp}	K_{assoc}	K_{exp}	K_{assoc}
1a	2.7	1163	2604	655	1100
1b	2.8	1274	2329	237	322
1c	4.3	1569	1605	310	314
1d	4.3	364	371	84	85

[a] The values for pK_a and K_{exp} were obtained using 0.01 M solutions in CD_3CN at 25 °C. K_{assoc} were calculated using the following equation (see the Supporting Information): $K_{\mathrm{assoc}} = K_{\mathrm{exp}}(1 + (K_a/[A]))$.

Four general observations can be made regarding the measured association constants. (1) Regardless of the crown ether used, the association constants are higher for the axles bearing electron withdrawing CF_3 groups (versus OCH_3) as would be expected on a purely electrostatic basis resulting in increased ion dipole interactions and stronger $\mathrm{N}H\cdots\mathrm{O}$ and $\mathrm{C}H\cdots\mathrm{O}$ hydrogen bonding. (2) Similar to the trend exhibited by dibenzylammonium axles[9] and contrary to that observed for bis(pyridinium)ethane cations,[3] higher K_{assoc} were observed with **24C8** than with **DB24C8**. This can be attributed to the better ability of aliphatic ether oxygen atoms to engage in ion−dipole interactions and hydrogen bonding relative to the aromatic catechol oxygen atoms. (3) For pseudorotaxanes formed with **24C8**, an EWG is more effective when placed on the anilinium ring than the benzyl ring consistent with $\mathrm{N}H\cdots\mathrm{O}$ hydrogen bonding being a major contribution to the overall K_{assoc}. (4) There appears to be significant π-stacking involved in binding when **DB24C8** is the wheel as indicated by upfield shifts for meta protons A2 and B2. The π-stacking is influenced equally by the inclusion of electron withdrawing groups on *either* the benzyl or anilinium ring and is magnified considerably when both rings contain the electron-withdrawing CF_3 (see Figure 3).[10] This is reminiscent of the trends observed for bis(pyridinium)ethane cations and **DB24C8** and is probably a direct result of the observed anti conformation of the two atom bridge between the aromatic rings.

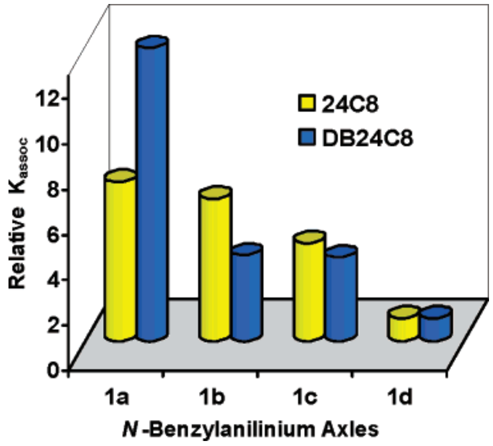

Figure 3. Bar graph comparing the relative association constants for the four different axles with **24C8** and **DB24C8**. For comparison purposes, the two sets of data have been normalized to **1d**$^+$.

In a fashion similar to that for the dibenzylammonium axles,[11] the addition of one equivalent of base (triethylamine) to solutions containing the [2]pseudorotaxanes caused

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dethreading of the macrocycle from the axle and shifted the equilibrium toward the nonprotonated species (A) which is incapable of complexation. This process can be reversed by the addition of one equivalent of acid (trifluoromethanesulfonic) which gives rise to the restoration of the [2]pseudorotaxane.

High-resolution ESI mass spectrometry measurements confirmed the presence of the 1:1 complex in the gas phase and allowed for exact mass determinations (see the Supporting Information). Solid-state structures of [**1a**⊂**DB24C8**][OTf] and [**1d**⊂**DB24C8**][OTf] also verified the [2]pseudorotaxane formation.

The structure of [**1a**⊂**DB24C8**]$^+$ (see Figure 4) has the crown ether arranged in a C-shaped conformation around the anilinium ring. Four hydrogen bonds are formed between the $-CH_2NH_2^+-$ unit of the axle **1a**$^+$ and **DB24C8**. The N···O distances vary from 2.78 Å (aliphatic oxygen) to 3.02 Å (aromatic oxygen) with N*H*···O angles of 170° and 147° respectively. The C···O distances vary from 3.30 Å (aliphatic oxygen) to 3.23 Å (aromatic oxygen) with C*H*···O angles of 172° and 159°, respectively. The other two aliphatic oxygen atoms are involved in an ion−dipole interaction with N$^+$ and C$^{\delta+}$ at 2.97 and 2.92 Å and a torsion angle O···N−C···O essentially linear at 179.8°. The distances between the centers of the aromatic rings on **DB24C8** to the center of the anilinium ring are 3.77 and 3.96 Å; these distances are in the upper range for π-stacking interactions.[10]

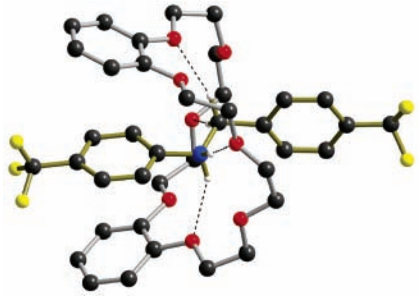

Figure 4. Ball-and-stick representation of the X-ray structure of [**1a**⊂**DB24C8**]$^+$ (carbon = black, oxygen = red, nitrogen = blue, fluorine = yellow, hydrogen = white).

In contrast to [**1a**⊂**DB24C8**]$^+$, in the structure of [**1d**⊂**DB24C8**]$^+$ (see Figure 5), **DB24C8** adopts the S-shaped conformation familiar in the structures of pseudorotaxanes formed with bis(pyridinium)ethane axles.[6] The difference is that there are no face-to-face π-stacking interactions between aromatic rings. This is attributed to the fact that both sets of aromatic rings are electron-rich which is known to be unfavorable for stabilizing π-stacking.[10] As a consequence, the crown ether adopts an orientation which optimizes hydrogen-bonding and ion−dipole interactions. Thus, in a fashion similar to [**1a**⊂**DB24C8**]$^+$, four hydrogen bonds between the unit $-CH_2NH_2^+-$ of the axle **1d**$^+$ and **DB24C8** are observed. The distances between N or C atoms and O-atoms varies from 2.96 Å (aliphatic oxygen) to 3.24 Å (aromatic oxygen) with N*H*···O and C*H*···O angles of 172° and 157° respectively. The other two aliphatic oxygen atoms are involved in ion−dipole interactions with N$^+$ and C$^{\delta+}$ at 3.05 Å. The torsion angle between O···N−C···O is linear; 180°.

Figure 5. Ball-and-stick representation of the X-ray structure of [**1d**⊂**DB24C8**]$^+$ (carbon = black, oxygen = red, nitrogen = blue, hydrogen = white).

In summary, we have shown that the hybrid *N*-benzylanilinium cations can function as suitable axles for the formation of [2]pseudorotaxanes with 24-membered crown ethers. These pseudorotaxanes are pH-sensitive and the threading-unthreading process is controllable by the alternate addition of acid and base. The binding behavior has characteristics of both dibenzylammonium and bis(pyridinium)ethane axles but probably is more similar to the ammonium ion axles. We are currently working toward the incorporation of this new recognition site into molecular shuttles and catenanes to complement our bis(pyridinium)ethane motif and generate acid−base controllable systems from these two structurally related axle components.

Acknowledgment. S.J.L. thanks NSERC of Canada for support of this research through a Discovery Grant.

Supporting Information Available: Synthesis, NMR, and MS data for all compounds. Derivation of equation for K_{assoc}. CIF files for [**1c**][OTf], [**1a**⊂**DB24C8**][OTf], and [**1d**⊂**DB24C8**][OTf]. This material is available free of charge via the Internet at http://pubs.acs.org.

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