Conjugated Schiff-Base Macrocycles

Ion-Induced Tubular Assembly of Conjugated Schiff-Base Macrocycles**

*Amanda J. Gallant and Mark J. MacLachlan**

The supramolecular assembly of molecular precursors into well-defined architectures is a promising way to develop new materials and devices.[1,2] Supramolecular polymers are linear chains of molecules held together by noncovalent interactions, and they may have unusual properties in solution and in the solid-state.[3] Rigid molecular precursors (e.g., cyclic peptides[4] and hydrogen bonded rosettes[5]) can be assembled into nanotubes through hydrogen bonding or coordination chemistry.[6] Conjugated macrocycles, such as porphyrins and phthalocyanines, can also be assembled into polymers.[7,8] However, the coordination of metals to flexible macrocycles, such as crown ethers, does not usually lead to polymeric structures, though dimer formation is common.[9,10]

The assembly of rigid, shape-persistent macrocycles can lead to porous supramolecular architectures.[11] For example, in polar solvent, phenyleneacetylene macrocycles (e.g., **1**) self-associate through face-to-face π-π interactions to form tubular structures.[12–14] These assemblies can be useful models for the rational design of columnar liquid crystals and organic nanotubes. We are investigating new conjugated, shape-persistent macrocycles that may be used to build supramolecular architectures. In particular, macrocycles that are capable of both binding transition-metal atoms and assembling into tubes may form the basis of catalytic nanomaterials or ion-conducting channels. Herein we report the ion-induced assembly of new well-defined conjugated macrocycles to form supramolecular assemblies.

We identified organic macrocycles such as **2** as ideal candidates for supramolecular assembly (Figure 1).[15,16] These macrocycles contain three tetradentate N_2O_2 binding sites organized in an equilateral triangle, as well as a pocket in the center that is surrounded by six phenolic oxygen atoms resembling [18]crown-6. The binding of ions to these types of macrocycles has not yet been explored.

Macrocycle **2** is insoluble in most solvents and takes about two weeks to synthesize.[16] We therefore developed a general and convenient route to macrocycles that have peripheral alkoxy chains. The reaction of 3,6-diformylcatechol with 1,2-dihexyloxy-4,5-phenylenediamine afforded a red, crystalline product **3** in 70% yield (Scheme 1). The structure of the macrocycle was verified by mass spectrometry and by NMR spectroscopy. The ^{1}H NMR spectrum of **3** shows the presence of single imine ($\delta = 8.54$ ppm) and OH resonances ($\delta = 13.23$ ppm), which are consistent with the D_{3h} symmetry of the macrocycle in solution. Unlike **2**, the macrocycles with peripheral alkoxy chains are soluble in a wide range of organic solvents such as chloroform and toluene.

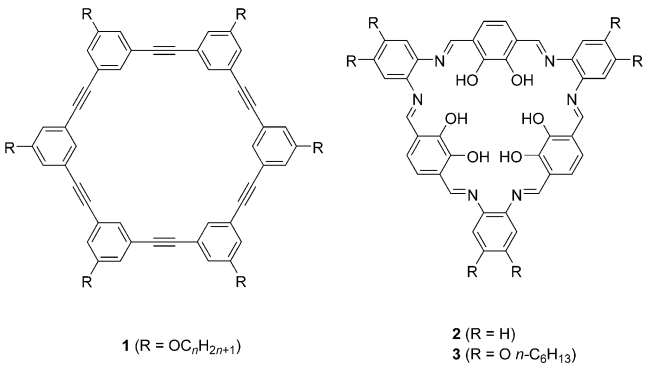
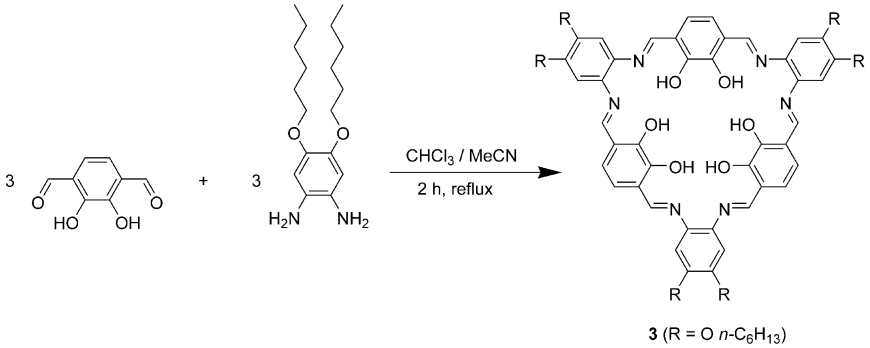


Figure 1. Conjugated macrocycles **1**–**3**.



Scheme 1. Synthesis of macrocycle **3**.

The electrospray mass spectrum (ESIMS) of macrocycle **3** shows the presence of not only the $[\mathbf{3}+H]^+$ ion, but also $[\mathbf{3}+Na]^+$ and $[\mathbf{3}_2+Na]^+$ species; the Na^+ ion is presumably a contaminant in the solvent or from the glass. When $NaBPh_4$ was added to a solution of **3**, the ESIMS (Figure 2) showed three sodium complexes—$[\mathbf{3}+Na]^+$, $[\mathbf{3}_2+Na]^+$, and $[\mathbf{3}_3+2Na]^{2+}$. As a mild ionization technique, ESIMS is known to give a meaningful picture of the species in solution.[17,18] Thus, it is most likely that these complex species are present in the solution before ionization. The observation of $[\mathbf{3}+H]^+$ but not any protonated aggregates also corroborates the formation of Na^+ bridged dimers and trimers.

The addition of alkali metal and ammonium salts ($MBPh_4$, $M^+ = Li^+$, Na^+, K^+, Rb^+, Cs^+, NH_4^+) to a solution of **3** in CH_2Cl_2 or $CHCl_3$ produced a change from orange to red-brown. Divalent metals (e.g., Mg^{2+}) caused precipitation of

[*] Prof. M. J. MacLachlan, A. J. Gallant
Department of Chemistry
University of British Columbia
2036 Main Mall, Vancouver, BC V6T 1Z1 (Canada)
Fax: (+1) 604-822-2847
E-mail: mmaclach@chem.ubc.ca

[**] We thank the University of British Columbia and the Natural Sciences and Engineering Research Council of Canada (NSERC) for funding this research. AJG thanks NSERC for a PGSA graduate fellowship award.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

 DOI: 10.1002/ange.200352395 © 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

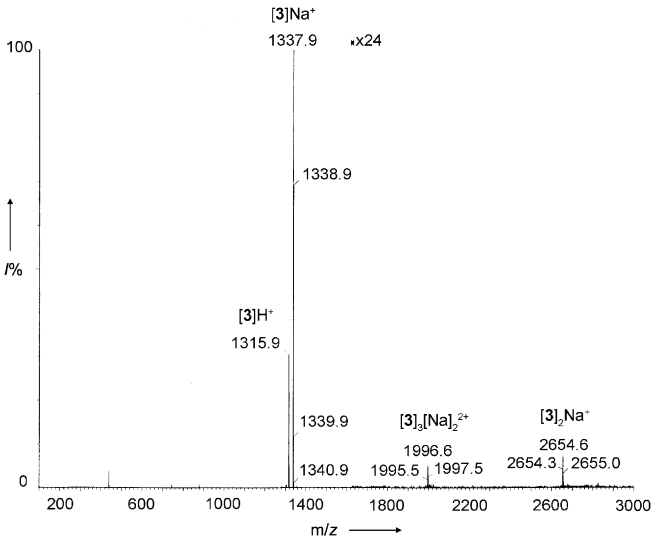


Figure 2. ESIMS of **3** with $NaBPh_4$ ($CHCl_3$/MeOH), I = relative intensity.

the macrocycle. The UV/Vis spectrum of **3** in $CHCl_3$ shows three large peaks centered near 310, 345, and 405 nm, as well as a weaker absorbance at 560 nm. To study the effect of small cations on the spectrum of **3**, a solution of **3** in about 95:5 $CHCl_3$:MeCN was prepared, and the salt in MeCN was added in aliquots.[19] All $MBPh_4$ ($M^+ = Na^+$, K^+, Rb^+, Cs^+, NH_4^+) produced similar changes to the visible spectrum of **3**. Figure 3 shows the effect of adding $NaBPh_4$ and $CsBPh_4$ to the macrocycle. Isosbestic points are seen at low salt concentrations (see insets in Figure 3), but are better defined in the case of $M^+ = Cs^+$. This can be rationalized as the conversion of the macrocycle to a cationic dimer, $[\mathbf{3}_2{+}Cs]^+$. In the case of $M = Na^+$, the macrocycle does not convert cleanly to a single product, even at low concentrations. As the ratio of salt to macrocycle is increased the isosbestic points disappear, which is consistent with the formation of trimers, tetramers, and higher aggregates.

The changes that occur in the electronic absorption spectrum of macrocycle **3** upon addition of small cations may arise from either electrostatic effects of coordinating the ions to the phenolic oxygen atoms or from an interaction between the π orbitals of the macrocycles as they are stacked. The lack of a single isosbestic point during the formation of the aggregates supports the latter conclusion, as the monomers, dimers, trimers, and larger aggregates appear to have different electronic spectra.

The interaction of macrocycle **3** with monovalent cations was also investigated by NMR spectroscopy. Figure 4a shows the ^{1}H NMR spectrum of **3** with varying concentrations of $NaBPh_4$.[20,21] As the [Na^+]:[**3**] increases, there is a gradual upfield shift in the position of the peaks. Notably, the imine and aromatic peaks shift by as much as 1.5 ppm at the [Na^+]:[**3**] of about 1:1. This dramatic upfield shift is characteristic of π–π stacking whereby proton resonances are affected by the ring currents of adjacent macrocycles.[22] As two rings approach in proximity, the electron density surrounding an attached proton is increased, thus resulting in an upfield

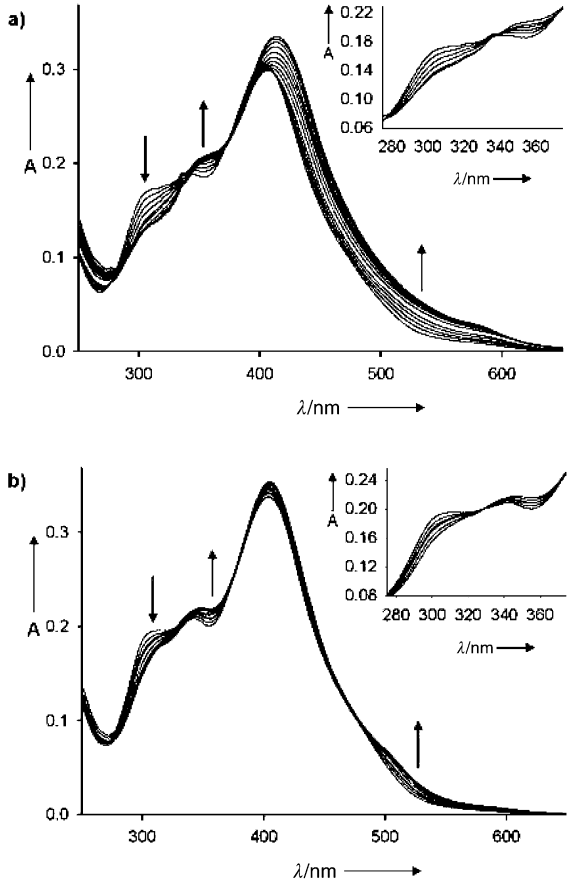


Figure 3. UV/Vis spectra of **3** upon adding: a) $NaBPh_4$, and b) $CsBPh_4$. Each line represents an increase of about. 0.1 equivalents of M^+ to **3**. The spectra show a ratio of [M^+]:[**3**] up to about 1.5. Insets: Low concentration experiments (0 to 0.5 equivalents of M^+).

chemical shift.[23] The presence of a single product by ^{1}H NMR spectroscopy, and the lack of any starting material after $NaBPh_4$ is added, indicates that the system is dynamic and that the macrocycles are freely interchanging between aggregates. Even at low concentrations of Na^+ ([Na^+]:[**3**] = 0.1:1), there is a single set of broad resonances that are consistent with this dynamic system.

The addition of $KBPh_4$ to **3** gives results similar to $NaBPh_4$, but NH_4BPh_4, $RbBPh_4$, and $CsBPh_4$ behave differently. Figure 4b shows the ^{1}H NMR spectral changes that occur for the addition of $CsBPh_4$ to **3**. Above [Cs^+]:[**3**] equal to about 0.3:1, there are only broad peaks that are significantly shifted upfield from the pristine macrocycle **3**, but broadened because of dynamic exchange and/or a distribution of aggregate sizes similar to the case for $NaBPh_4$. At lower concentrations, however, signals from other species are observed to grow. At a concentration of [Cs^+]:[**3**] = 0.05:1, the macrocycle and a small amount of another species, **4**, are present. The intermediate **4** has an OH resonance at δ = 13.55 ppm, an imine resonance at δ = 8.0 ppm, and two aromatic resonances at δ = 6.2 ppm and 6.5 ppm. From the integration of the ^{1}H NMR spectrum, the new species formed at low concentrations of Cs^+ has a formula of $[\mathbf{3}]_2Cs^+$, characteristic of a dimer. Moreover, the imine resonance at

 © 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

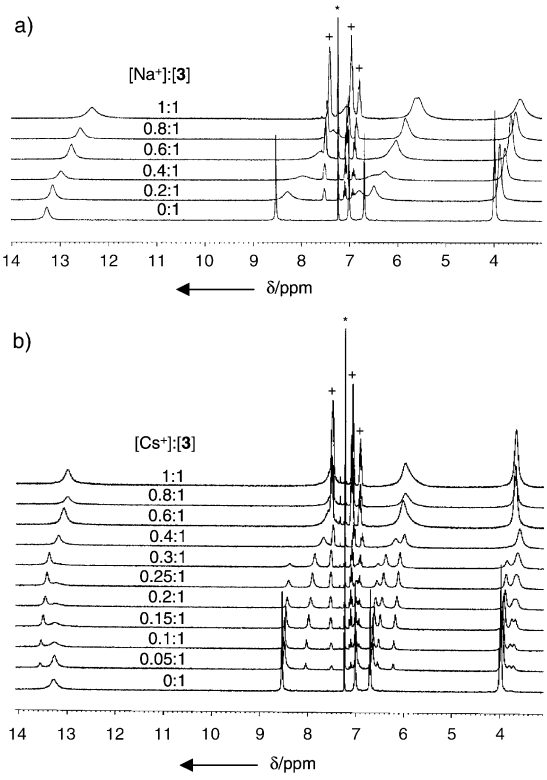


Figure 4. Stacked ^{1}H NMR spectra of macrocycle **3** with increasing amounts of a) $NaBPh_4$ and b) $CsBPh_4$. The ratio of $[M^+]$:[**3**] for each sample is shown. (∗ = $CHCl_3$; + = BPh_4^-).

$\delta = 8.0$ ppm is intermediate to that of the macrocycle ($\delta =$ 8.54 ppm) and the 1:1 $[Cs^+]$:[**3**] ($\delta = 7.5$ ppm) product. If the chemical shift of the 1:1 product corresponds to the macrocycle in a tubular assembly, the intermediate species **4** is most likely to be a dimeric sandwich complex. In this dimer, the aromatic protons would only experience the influence of the ring currents from a single neighbouring macrocycle, thus leading to half the change in chemical shift seen for a macrocycle in a tubular assembly.

In addition, the OCH_2 resonances of **4** are split into two multiplets. In a dimeric sandwich compound, these two protons are inequivalent (diastereotopic) as the mirror symmetry in the macrocycle is broken. Up to concentrations of $[Cs^+]$:[**3**] = 0.4:1, the free macrocycle is gradually replaced by species that result in broad peaks in the ^{1}H NMR spectrum, which is characteristic of aggregates. The two resonances of the OCH_2 groups merge into a single broad resonance when the symmetry of the macrocycle is restored in a tubular structure. It appears that the dimer does not readily undergo exchange, but macrocycle exchange does occur once the aggregates have grown.

The change in chemical shift in the protons of **3** upon addition of a salt appears to depend on the size of the cation, with the imine peak shifted most dramatically for the smallest cation, Na^+ ($\Delta\delta = 1.48$ ppm), and least for the larger Cs^+ cation ($\Delta\delta = 0.98$ ppm). The imine peaks of **3** with the intermediate sized cations (NH_4^+, K^+, and Rb^+) are found between those of Na^+ and Cs^+, but are obscured by peaks assigned to $CHCl_3$ and BPh_4^-. In a tubular structure in which macrocycles are bridged by cations, the size of the cation should affect the chemical shifts as it changes the proximity of the neighbouring macrocycles and their relative shielding.[21]

The data obtained from ESIMS, UV/Vis and ^{1}H NMR spectroscopies suggest that small cations induce the aggregation of macrocycles such as **3** to form tubular assemblies. At low $[M^+]$:[**3**] ratios, intermediate species (e.g., dimers) are observed while at higher concentrations dynamic stacked structures are formed. Postulated structures of the dimer **4** and the tubular assemblies are shown in Figure 5.

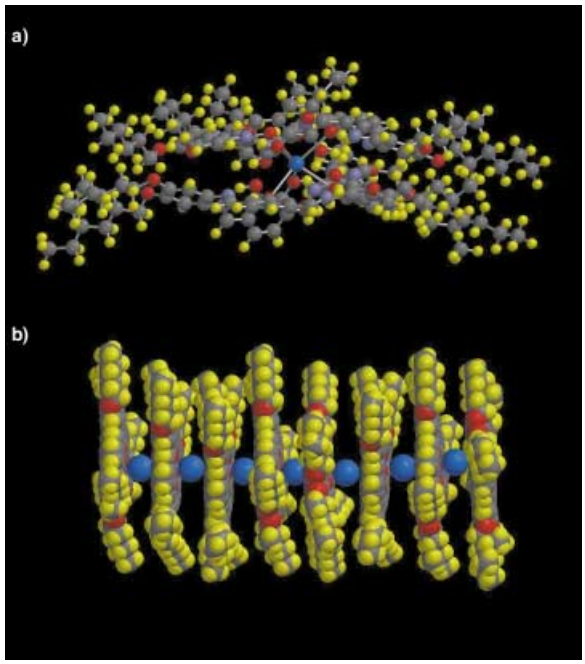
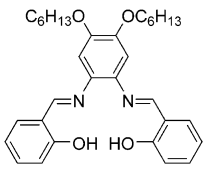


Figure 5. Postulated structures of a) the dimeric intermediate **4** (minimized with molecular mechanics force field) and b) the ion-induced tubular assembly of macrocycle **3**.

We believe that in the tubular structure, the small cations are coordinated to the central phenolic oxygen atoms of macrocycle **3** rather than to the tetradentate N_2O_2 ligands. A control experiment in which salphen **5** was mixed with an excess of $NaBPh_4$ in $CDCl_3$ showed no change in color nor in its ^{1}H NMR spectrum, thus indicating that **5** does not incorporate $NaBPh_4$ in $CDCl_3$. In addition, the final $[M^+]$:[**3**] ratio was nearly 1:1 for each cation; a larger ratio would be expected if the cations were coordinating to the N_2O_2 pockets of each macrocycle. Preliminary DFT calculations also indicate that a sodium ion has a strong affinity for binding to the phenolic oxygen atoms over the tetradentate N_2O_2 pockets offered by the macrocycle.



5

In summary, we report the first synthesis of soluble Schiff-base macrocycle, **3**, and show that upon addition of small cations, **3** changes color and aggregates to form ionic assemblies. Our results demonstrate that **3** can behave like a crown ether, in which the phenolic oxygen atoms inside the

 © 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

macrocycle coordinate to small cations seated at the center of the macrocycle. These results provide a new avenue for self-assembled materials and small-cation sensors.

Received: July 16, 2003 [Z52395]

Keywords: alkali metals · macrocycles · Schiff bases · self-assembly · supramolecular chemistry

[1] A. P. Alivisatos, P. F. Barbara, A. W. Castleman, J. Chang, D. A. Dixon, M. L. Klein, G. L. McLendon, J. S. Miller, M. A. Ratner, P. J. Rossky, S. I. Stupp, M. E. Thompson, *Adv. Mater.* **1998**, *10*, 1297 – 1336.

[2] For recent interesting examples of self-assembled architectures, see: a) F. Würthner, S. Yao, U. Beginn, *Angew. Chem.* **2003**, *115*, 3368 – 3371; *Angew. Chem. Int. Ed.* **2003**, *42*, 3247 – 3250; b) E. R. Zubarev, M. U. Pralle, E. D. Sone, S. I. Stupp, *Adv. Mater.* **2002**, *14*, 198 – 203; c) Y.-H. Luo, H.-W. Liu, F. Xi, L. Li, X.-G. Jin, C. C. Han, C.-M. Chan, *J. Am. Chem. Soc.* **2003**, *125*, 6447 – 6451.

[3] L. Brunsveld, B. J. B. Folmer, E. W. Meijer, R. P. Sijbesma, *Chem. Rev.* **2001**, *101*, 4071 – 4098.

[4] a) W. S. Horne, C. D. Stout, M. R. Ghadiri, *J. Am. Chem. Soc.* **2003**, *125*, 9372 – 9376; b) J. Sanchez-Quesada, M. P. Isler, M. R. Ghadiri, *J. Am. Chem. Soc.* **2002**, *124*, 10004 – 10005.

[5] H. Fenniri, P. Mathivanan, K. L. Vidale, D. M. Sherman, K. Hallenga, K. V. Wood, J. G. Stowell, *J. Am. Chem. Soc.* **2001**, *123*, 3854 – 3855.

[6] For other examples of tube formation induced by ions, see: a) D. T. Bong, T. D. Clark, J. R. Granja, M. R. Ghadiri, *Angew. Chem.* **2001**, *113*, 1016 – 1041; *Angew. Chem. Int. Ed.* **2001**, *40*, 988 – 1011; b) V. Sidorov, F. W. Kotch, M. El-Kouedi, J. T. Davis, *Chem. Commun.* **2000**, 2369 – 2370.

[7] K. M. Kadish, K. M. Smith, R. Guilard, *The Porphyrin Handbook, Vol. 6.* Academic Press, San Diego, **2000**.

[8] Y. Kim, M. F. Mayer, S. C. Zimmerman, *Angew. Chem.* **2003**, *115*, 1153 – 1158; *Angew. Chem. Int. Ed.* **2003**, *42*, 1121 – 1126.

[9] J. W. Steed, *Coord. Chem. Rev.* **2001**, *215*, 171 – 221.

[10] a) V. Percec, G. Johansson, G. Ungar, J. Zhou, *J. Am. Chem. Soc.* **1996**, *118*, 9855 – 9866; b) R. J. M. Klein Gebbink, A. J. Sandee, F. G. A. Peters, S. J. van der Gaast, M. C. Feiters, R. J. M. Nolte, *J. Chem. Soc. Dalton Trans.* **2001**, 3056 – 3064; c) H. Engelkamp, R. J. M. Nolte, *J. Porphyrins Phthalocyanines* **2000**, *4*, 454 – 459; d) W.-S. Xia, R. H. Schmehl, C.-J. Li, J. T. Mague, C.-P. Luo, D. M. Guldi, *J. Phys. Chem. B* **2002**, *106*, 833 – 843.

[11] D. Zhao, J. S. Moore, *Chem. Commun.* **2003**, 807 – 818.

[12] a) S. Lahiri, J. L. Thompson, J. S. Moore, *J. Am. Chem. Soc.* **2000**, *122*, 11315 – 11319; b) A. S. Shetty, J. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **1996**, *118*, 1019 – 1027; c) J. Zhang, J. S. Moore, *J. Am. Chem. Soc.* **1992**, *114*, 9701 – 9702.

[13] a) S. Höger, K. Bonrad, A. Mourran, U. Beginn, M. Möller, *J. Am. Chem. Soc.* **2001**, *123*, 5651 – 5659; b) S. Höger, J. Spickermann, D. L. Morrison, P. Dziezok, H. J. Rader, *Macromolecules* **1997**, *30*, 3110 – 3111.

[14] M. Pickholz, S. Stafström, *Chem. Phys.* **2001**, *270*, 245 – 251.

[15] W. T. S. Huck, F. C. J. M. van Veggel, D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas* **1995**, *114*, 273 – 276.

[16] S. Akine, T. Taniguchi, T. Nabeshima, *Tetrahedron Lett.* **2001**, *42*, 8861 – 8864.

[17] F. Inokuchi, S. Shinkai, *J. Chem. Soc. Perkin Trans. 2* **1996**, 601 – 605.

[18] The mass spectrum was not obtained under conditions from which reliable quantification of the species could be made. See: E. Leize, A. Jaffrezic, A. Van Dorsselaer, *J. Mass Spectrom.* **1996**, *31*, 537 – 544.

[19] We tested the effect of adding MeOH and MeCN to the macrocycle in $CHCl_3$. The addition of MeOH to **3** led to continuous changes in the spectrum. MeOH may induce stacking of the macrocycles as the solvent polarity increases. MeCN caused small changes to the spectrum only below concentrations of about 1–2%. We believe that the MeCN is acting as a guest in the macrocycles as we see the chemical shift of MeCN in **3** at $\delta =$ 1.99 ppm in $CDCl_3$ (compare with $\delta = 2.10$ ppm in neat $CDCl_3$). As well, the crystalline compound contains MeCN that is difficult to remove under vacuum.

[20] Samples for the NMR experiments were prepared as follows: A solution of **3** (about 7.6×10^{-3} M) in $CDCl_3$ was mixed for several minutes with a large excess of the tetraphenylborate salt of the cation (M^+). The resulting solution was filtered and aliquots were quantitatively transferred into NMR tubes. The salt solutions were then diluted with a standard solution of **3** in $CDCl_3$ so that the final volume and concentration of the macrocycle was approximately the same in each case. The original [M^+]:[**3**] ratio was determined by integration of the ^{1}H NMR spectrum of the most concentrated solution, and was near 1:1 in each case (M = Na, K, Rb, Cs, NH_4,). It was not possible to get a larger ratio of [M^+]:[**3**].

[21] When a solution containing macrocycle **3** and $NaBF_4$ (in a ratio of about 1:1) was analyzed, it showed the same shifts in the NMR spectrum, thus eliminating the BPh_4^- anion as the cause of the spectral shifts.

[22] D. Zhao, J. S. Moore, *J. Org. Chem.* **2002**, *67*, 3548 – 3554.

[23] C. Giessner-Prettre, B. Pullman, P. N. Borer, L.-S. Kan, P. O. P. Ts'o, *Biopolymers* **1976**, *15*, 2277 – 2286.

 © 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim