Bipyrrole-Based [2]Catenane: A New Type of Anion Receptor

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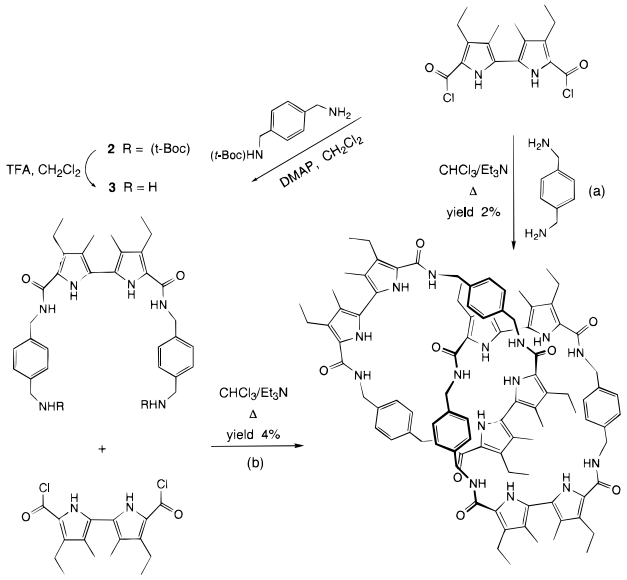
Interlocked molecules of complex architecture (e.g., catenanes, rotaxanes, and knots) have steadily moved from the realm of scientific curiosity into the more practical world of supramolecular chemistry.[1] This process has been accelerated by the development of template syntheses, which made certain catenanes and rotaxanes accessible in preparative yields,[1b−d] and by recent advances in engineering of interlocked "molecular devices" that are able to respond to changes in environmental conditions by altering their conformational behavior.[1b−d,2] Within that latter context, remarkable control over catenane conformation (gliding of one ring within the other)[3b] has been achieved electrochemically and photochemicaly, as well as by changing external conditions such as temperature, pH, and solvent composition.[3] In this communication we describe the synthesis of the bipyrrole-based amide catenane **1**, a novel system whose conformational properties, including relative ring orientations, are controlled by anion *chelation*.[4]

Catenane **1** was synthesized from appropriate bipyrrole diacyl chloride and *p*-xylenediamine building blocks in either a single step (route a, Scheme 1) or a stepwise fashion (route b), with the latter resulting in higher yields (4% vs 2%, *cf.* Supporting Information).[5,6]

The interlocked species **1** contains a wealth of hydrogen bonding donor groups (i.e., pyrrole and amide NH functionalities) and hydrogen bonding acceptor sites (amide carbonyl groups), whose mutual interactions provide, at least in part, the template

Scheme 1



effects considered necessary to facilitate catenane synthesis.[7,8] Some of these putative intermolecular hydrogen-bonding interactions are expected to be retained a priori in the catenane structure. On the other hand, we postulated, they might also be reoriented or disrupted should an anion with sufficiently high affinity for pyrrolic and/or amide H-bond donor groups be added in solution. To the extent such disruption occurs, the anion binding process, in turn, could provide a new means of effecting conformational and/or geometric control (i.e., modifications of relative ring-to-ring orientations) within a catenated system.

The conformational properties of catenane **1** were investigated in a dynamic sense with ^{1}H NMR spectroscopy. In a first set of experiments it was found that this species gives rise to spectra at ambient temperature that are characterized by broad peaks in a range of nonprotic solvents. Presumably, this peak broadening reflects both the effects of intramolecular hydrogen bonding as well as the dynamics of various circumrotation processes. In parallel studies it was found that the dynamic behavior of system **1** could be modulated by, e.g., changing the temperature of the solution. For instance, two different groups of signals corre-

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(1) For a classic, quarter of a century-old text, describing "directed" synthesis of catenanes and rotaxanes, and a prophetic mapping out of the future advances in the field of chemistry of interlocked molecules, see: (a) Schill, G. *Catenanes, Rotaxanes and Knots*; Academic Press: New York, 1971. For recent reviews from the leaders in the field, see: (b) Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725−2828. (c) Chambron, J.-C.; Dietrich-Buchecker, C. O.; Sauvage, J.-P. *Top. Curr. Chem.* **1993**, *165*, 131−162. (d) Jager, R.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 930−944.

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(3) (a) Asakawa, M.; Ashton, P. R.; Dehaen, W.; L'abbé, G.; Menzer, S.; Nouwen, J.; Raymo, F. M.; Stoddart, J. F.; Tolley, M. S.; Toppet, S.; White, A. J. P.; Williams, D. J. *Chem. Eur. J.* **1997**, *3*, 772−787. (b) Baumann, F.; Livoreil, A.; Kaim, W.; Sauvage, J.-P. *Chem. Commun.* **1997**, 35−36. (c) Bissell, R. A.; Córdova, E.; Kaifer, A. E.; Stoddart, J. F. *Nature* **1994**, *369*, 133−137. (d) Liu, Z. F.; Hashimoto, K.; Fujishima, A. *Nature* **1990**, *347*, 658−660. (e) Benniston, A. C.; Harriman, A.; Lynch, V. M. *J. Am. Chem. Soc.* **1995**, *117*, 5275−5291. (f) Marsella, M. J.; Carroll, P. J.; Swager, T. M. *J. Am. Chem. Soc.* **1995**, *117*, 9832−9841.

(4) (a) It has recently been reported that the PF_6^- anion assists in the formation of pseudorotaxanes by means of multiple C−H···F hydrogen bonds: Fyfe, M. C. T.; Glink, P. T.; Menzer, S.; Stoddart, J. F.; White, A. J. P.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2068−2070. (b) Counteranions were reported to influence the solid-state structures of cucurbituril-based polyrotaxane polymers: Whang, D.; Kim, K. *J. Am. Chem. Soc.* **1997**, *119*, 451−452. For general reviews of anion binding phenomena, see: (c) *Supramolecular Chemistry of Anions*; Bianchi, A., Bowman-James, K., García-España, E., Eds.; Wiley-VCH: New York, 1997.

(5) Catenane **1** was clearly identified and distinguished from its putative isomeric "single eight-pyrrolic macrocycle" by the characteristic mass spectrum. In particular, no fragmentation peaks were observed between those associated with the $[M/2 + H]^+$ and $[M + H]^+$ peaks corresponding to **1**. This was true when both soft (e.g., FAB) and hard (e.g., EI) mass spectrometric ionization techniques were used. Additional proof of the catenane structure was obtained from the series of multidimensional NMR experiments (Supporting Information).

(6) Surprisingly, no other macrocyclic (or catenated) products could be identified in the reaction mixture. This phenomenon has previously been observed within the class of amide-type catenanes, see: Johnson, A. G.; Leigh, D. A.; Murphy, A.; Smart, J. P.; Deegan M. D. *J. Am. Chem. Soc.* **1996**, *118*, 10662−10663 and references therein.

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(8) The single-crystal structure of the 4,4′-diethyl-3,3′-dimethyl-2,2′-bipyrrole-5,5′-di(benzylamide)—a benzylamide analogue of **2**—shows, for instance, the amide-functionalized bipyrrole units forming supramolecular dimers in the solid state, stabilized, among other things, by the bifurcated hydrogen bonds involving amide NH−CO and pyrrolic NH moieties (Supporting Information).

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sponding to xylyl protons are observed in DMSO-d_6 at 25 °C. As the temperature increased, however, both signals broaden, shift, and finally at ca. 70 °C coalesce (Supporting Information).

Against the above backdrop, it was found that the conformational and dynamic behavior of **1** could also be affected by *anion complexation*. For instance, when fluoride anion was titrated into a solution of **1** in 1,1,2,2-tetrachloroethane-d_2, the spectrum of **1** was observed to sharpen, with four distinct groups of signals, corresponding to four different (xylyl CH)$_2$−CH$_2$−NH−CO−C−NH(pyrryl) moieties, appearing. Likewise, four different singlets ascribable to methyl group protons were found to grow in when fluoride anion was added.[9] The addition of less than 2 equiv of fluoride anion (in the form of its tetrabutylammonium salt) to **1** resulted in full saturation and total shifts in the signals corresponding to amide and pyrrolic hydrogens on the order of 0.2−1 ppm. These results are taken as providing (1) prima facie evidence that the two macrocycles in this complex are equivalent under the conditions of the NMR experiments and (2) support for the conclusion that, unlike the free catenane, the fluoride anion complex of **1** has C_2 symmetry. In addition, the reduction in signal broadening observed upon addition of F^- is considered consistent with circumrotation processes involving the two constituent macrocycles becoming frozen out as a result of anion binding.

Further insight into the dynamics of fluoride anion complexation by catenane **1** was obtained from variable-temperature ^{19}F NMR spectroscopic studies. These studies revealed, among other things, that the spectrum of a 1:2 mixture of the catenane and tetrabutylammonium fluoride displays two lines (δ −75.5, −76.4 ppm) at −10 °C. The signal at higher field, which we assign to a catenane-bound fluoride anion complex on the basis of line-broadening ^{1}H−^{19}F couplings, grows broader and moves downfield with increasing temperature, until both signals overlap at 20 °C. These results lead us to infer that the magnetic environments of the catenane-bound and "free" (i.e., solvated) fluoride anion are distinct, and that at temperatures of 0 °C and below the rate of exchange between the two sites is slow on the ^{19}F NMR time scale.

Taken together, the above observations serve to prove that the catenane **1** (*i*) binds fluoride anion and (*ii*) changes its solution conformation to accommodate an anionic guest.[10] These same data also lead us to suggest that the fluoride anion is chelated in a "binding pocket" of approximate tetragonal symmetry in the vicinity of the pyrrole and amide NH functional groups, as shown schematically in Figure 1. Left undetermined by these data is whether **1** is a general anion binding receptor.

To test the versatility of compound **1** as an anion receptor, complexation experiments with a range of other anions were performed. Here, as in the case of F^-, the catenane concentration was held constant, while the guest anion concentration was steadily increased. The changes in the catenane spectrum, e.g., the complexation-induced shifts of the pyrrolic and amide proton signals, were then monitored and used to deduce both the stoichiometry of binding and the association constants.[11] The results (summarized in Table 1) confirmed that, at least in 1,1,2,2-tetrachloroethane-d_2, catenane **1** is a *strong and selective* anion receptor. Indeed, it was found that many anions are bound to **1** with affinities higher than that of F^-.[12] We view this as an important result that is consistent with subtle structural features (rather than just number and positioning of hydrogen bond donor sites) playing an important role in regulating the anion binding process.

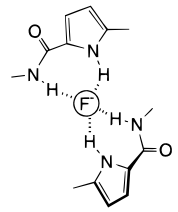

Figure 1.

Table 1. Binding Constants Measured for Catenane **1**, Its Precursor **3**, and Various Anions in 1,1,2,2-Tetrachloroethane-d_2

substrate[a]	K_a (M^{-1}) of **1**[b]	selectivity of **1**[e]	K_a (M^{-1}) of **3**[b]
F^-	1.48×10^5		2.18×10^3
Cl^-	3.55×10^6	24	8.00×10^2
Br^-	n.a.[c]	n.a.	3.40×10^2
$H_2PO_4^-$	$>1 \times 10^7$ [d]	>65	n.a.[f]
AcO^-	9.63×10^5	7	n.a.[f]

[a] Tetrabutylammonium salts were used. [b] Complexes of 1:1 stoichiometry were formed unless otherwise indicated. The stoichiometry of the complexes was deduced from curve fitting procedures (e.g., Whitlock algorithm) and from molar ratio plots.[11] [c] Small complexation-induced shifts precluded us from determining precisely the affinity constants associated with the presumed catenane−bromide interaction. [d] The shape of the titration curve indicated multiple equilibria occurring at low [$H_2PO_4^-$]/[**1**] ratios. [e] Compared to fluoride (i.e., the lowest binding constant recorded accurately). [f] Full titration curves could not be obtained as the result of an inability to detect the monitored NH signals throughout the course of the titration.

In a separate set of experiments, it was found that the anion binding affinities of catenane **1** are higher than those of the corresponding open-chain control **3** (Table 1). Presumably this reflects the fact that catenane **1** is either better preorganized for anion binding or/and is capable of adjusting readily its "receptor site" to accommodate negatively charged substrates. In either case, it is clear that catenane **1** serves to define a new type of anion binding agent whose generalized conformational properties (including circumrotation processes) may be readily modulated via substrate chelation.

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Supporting Information Available: Synthetic experimental, mass spectra, and NMR spectra of catenane **1** and X-ray structure of 4,4′-diethyl-3,3′-dimethyl-2,2′-bipyrrole-5,5′-di(benzylamide) (9 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(9) Unequivocal assignment of the resonances to the individual groups as well as connectivities between the different building blocks in the catenane−fluoride complex was carried out by a combination of ^{1}H,^{1}H-COSY and a series of NOESY NMR spectra recorded at different mixing times (Supporting Information).

(10) Although the exact conformation of two rings comprising the catenane in its fluoride complex and the location of fluoride anion could not be elucidated in full from the experimental data, some information about the relative orientation of the various moieties present in that complex could be obtained. For instance, the NOESY spectrum acquired in 1,1,2,2-tetrachloroethane-d_2 at 0 °C showed strong inter-ring NOE cross-peak between the most deshielded pyrrolic proton of one macrocycle (at ca. δ 10.67 ppm) and the benzylic protons of the other (at ca. δ 4.17 and 3.32 ppm).

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(12) Attempts to improve the yield by adding various putative anion templates, such as, e.g., F^- and $H_2PO_4^-$, have so far not met with success.