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A General Synthesis of Macrocyclic π-Electron-Acceptor Systems

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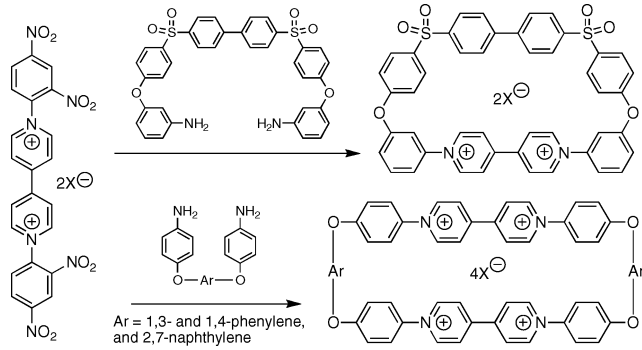
ABSTRACT



Cyclocondensations of aromatic diamines with 1,1′-bis(2,4-dinitrophenyl)-4,4′-bipyridinium salts afford doubly or quadruply charged, macrocyclic, *N,N*′-diarylbipyridinium cations. These are tolerant of a wide range of acids, bases, and nucleophiles, although they appear to undergo reversible, one-electron reduction by tertiary amines. Single-crystal X-ray analysis demonstrates the presence of a macrocycle conformation in which the 4,4′-bipyridinium and 4,4′-biphenylenedisulfonyl residues are suitably spaced and aligned for complexation with π-donor arenes, and NMR studies in solution indeed confirm binding to 1,5-bis[hydroxy(ethoxy)ethoxy]naphthalene.

Supramolecular, or host−guest, chemistry[1] has expanded tremendously as a research field over the past 30 years, advancing from an exploratory academic discipline to one which has yielded covalently and noncovalently bound species capable of controllable switching,[2] rotational motion,[3] and data storage.[4,5]

However, the individual components of these molecular machines (often based on mechanically interlocked macrocyclic structures such as catenanes and rotaxanes)[6] generally include rather delicate groups such as the *N*-benzylbipyridinium moiety, which is susceptible to cleavage under strongly nucleophilic or basic conditions.[7]

We have recently described more stable macrocyclic[8] and polymeric[9] hosts which can act as π-electron acceptors by virtue of their π-electron-poor aromatic diimide and biphenylenedisulfone subunits. These all-aromatic macrocyles (e.g, **1** and **2** in Figure 1) show high affinities for π-electron-rich aromatics such as pyrene and perylene,

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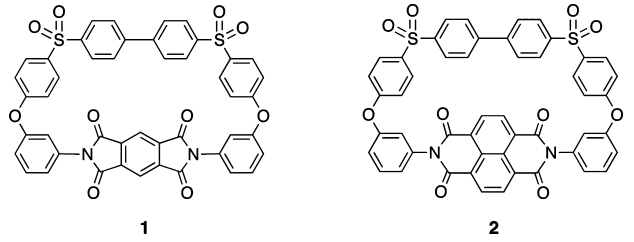

Figure 1. Macrocyclic aromatic ether-imide sulfones.[8]

but their rigid conformations and uncharged character mean that they have only very limited solubility in conventional organic solvents: binding studies, for example, required the use of strong proton-donor solvents such as chloroform/hexafluoropropan-2-ol. Here, we report the synthesis of a new and more tractable family of *cationic* aromatic macrocyclic host molecules. They contain either one or two 4,4′-bipyridinium residues and are readily accessible in single-step reactions from known materials. The all-aromatic character of these novel receptors leads to high stability and avoids the potential problem of N−C bond cleavage[7] when *N*-alkyl or -benzyl bipyridinium units are employed in the construction of molecular machinery.

The syntheses of the new macrocycles start from the known 1,1′-bis(2,4-dinitrophenyl)-4,4′-bipyridinium salt **3**, which can be produced readily on a 20 g scale in a single step.[10] This reagent is known to undergo nucleophilic ring opening by aromatic amines at the carbon adjacent to the pyridyl nitrogen.[10] Subsequent ring closure, with rearomatization by expulsion of 2,4-dinitroaniline, results in formation of *N*,*N*′-diarylbipyridinium ions.

In the present work we have found that the use of suitably designed aromatic *di*amines (**4**−**7** in Figure 2)[8,11] in such

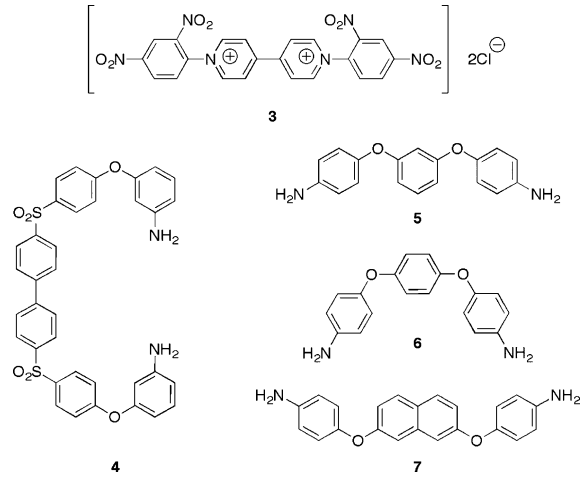

Figure 2. Components for macrocyclization: 1,1′-bis(2,4-dinitrophenyl)-4,4′-bipyridinium dichloride (**3**) and aromatic diamines **4**−**7**.

reactions enables the facile construction of all-aromatic, macrocyclic bipyridinium cations, isolable as their hexafluorophosphate salts (**8**−**11** in Figure 3). The binding properties

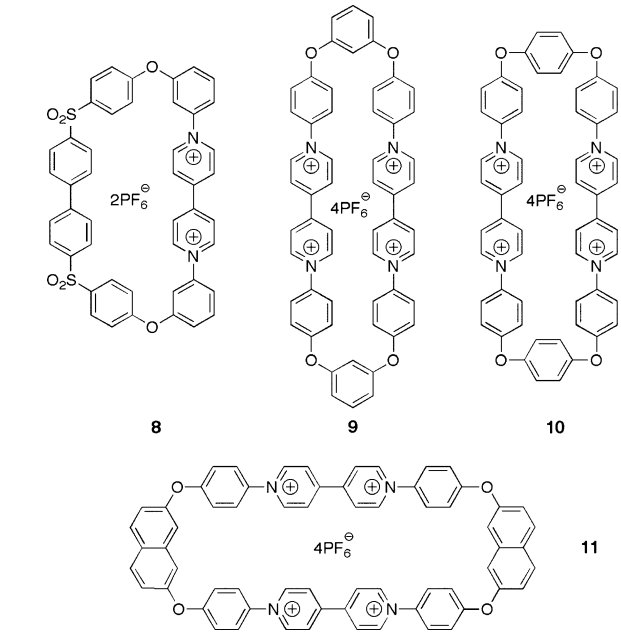

Figure 3. Macrocyclic diarylbipyridinium salts synthesized in this work.

of this class of receptors were investigated by ^{1}H NMR spectroscopic titration, in which increasing quantities of the π-electron-rich guest molecule bishydroxy(ethoxy)ethoxynaphthalene ("BHEEN", **12** in Figure 4)[12] were added to a 3.8 mM solution of macrocycle **8** in CD_3CN. The proton resonances of **8** showed significant complexation shifts, increasing with the proportion of **12** and clearly demonstrating the affinity of the macrocycle for the guest. Resonances corresponding to protons *A* and *J* show the greatest upfield shifts ($\Delta\delta$ = 0.22 and 0.20 ppm, respectively), indicating that these protons are exposed to the greatest aromatic ring current shielding effect from **12**. Conversely, resonances for protons *C* and *D* experience a downfield shift, indicating that they are located within the ring-current *de*shielding torus generated by the aromatic π-system of **12**. The 1:1 binding constant for [**8**⊃**12**], determined from ^{1}H NMR data, is 17 ± 1 M^{-1}. Computational modeling (molecular mechanics with charge equilibration) confirmed that the specific shielding and deshielding effects are fully consistent with a model in which the 1,5-dioxynaphthalene unit is encapsulated within the macrocycle, stacking face-to-face with the bipyridinium and biphenylenesdisulfonyl units.

We were unable to isolate crystals of the proposed inclusion complex [**8**⊃**12**], but computational modeling suggested that planar dianions such as [bis(dithiomaleonitrile)nickelate(2−)] might form stable, cavity-bound complexes with the cationic macrocycle of **8**. Indeed, simply mixing acetone solutions of **8** and tetra-*n*-butylammonium [bis(dithiomaleonitrile)nickelate(2−)][13] produced an im-

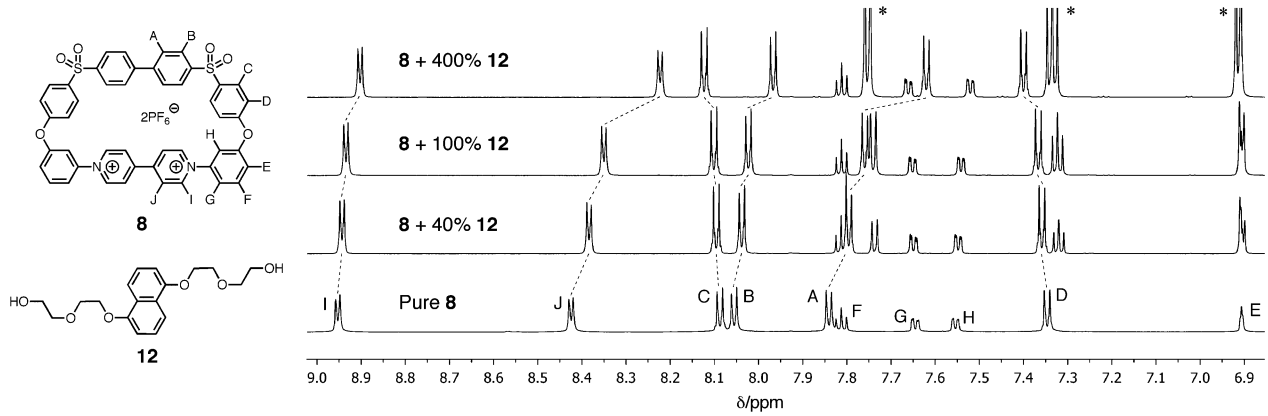

Figure 4. ^{1}H NMR (700 MHz) titration of guest species **12** ("BHEEN") against compound **8** (3.8 mM) in CD_3CN at 298 K. Molar ratios of host and guest are shown. Note especially the strong upfeld complexation shifts of resonances arising from macrocycle protons *A* and *J*, confirming that **12** binds within the macrocyclic cavity. Guest resonances (**12**) are marked with an asterisk.

mediate crystalline precipitate of the 1:1 (macrocycle + nickelate) salt, **13**, from which single crystals were obtained by vapor diffusion of methanol into a dimethylacetamide (DMAc) solution of **13**.

Single-crystal X-ray analysis revealed the crystals to be a DMAc solvate, in which one of the two independent [bis(dithiomaleonitrile)nickelate(2−)] dianions is encapsulated by two macrocyclic dications (Figure 5), with the other dianion being essentially uncomplexed elsewhere in the lattice. Formation of the anticipated 1:1 inclusion structure appears to be inhibited by a molecule of solvating DMAc (not shown in Figure 5) which partly occupies the cavity, in keeping with earlier studies showing that dipolar aprotic solvents such as dimethylformamide and dimethylsulfoxide are potent inhibitors of complementary aromatic $\pi-\pi$-stacking interactions.[14]

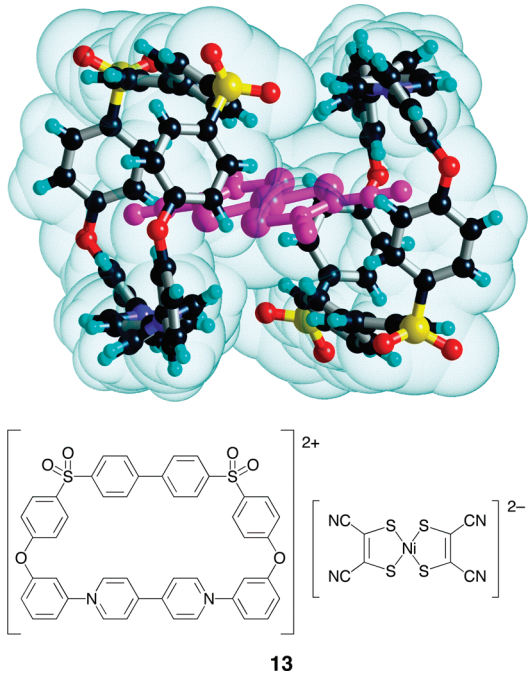

Figure 5. Solid-state structure of **13** showing the encapsulation of one dianion (magenta) by two macrocyclic dications. van der Waals surfaces are at 2.2 × covalent radii.

The stability of macrocycle **8** was investigated by exposure to a range of bases and nucleophiles, including those known to cleave cyclobis(paraquat-*p*-phenylene).[7] In a typical experiment, the ^{1}H NMR spectrum of the macrocyclic hexafluorophosphate salt **8**, 3.8 mM in CD_3CN, was acquired and the solution then treated with 10 mol equiv of the reagent under investigation and the ^{1}H NMR spectrum recorded once again. Over a 16 h time scale, the macrocycle was found to be stable to pyridine, sodium methoxide, triphenylphosphine, and tetra-*n*-butylammonium iodide, all of which will cleave cyclobis(paraquat-*p*-phenylene).[7]

Interestingly, treatment of all four new macrocyles (**8**−**11**) with aliphatic tertiary amines such as triethylamine produced an immediate color change from pale yellow to dark green. ^{1}H NMR spectra of the green solutions revealed that in all cases the resonances associated with protons *I* and *J* on the bipyridinium unit and *E*, *F*, *H*, and *G* on adjacent aromatic rings (Scheme 1) had vanished, though the resonances associated with the remainder of the macrocycle were still

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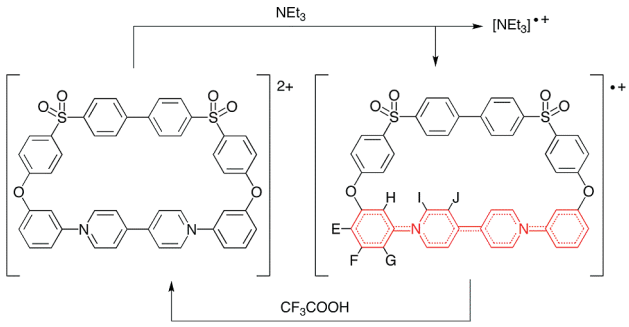
Scheme 1. Proposed Reversible One-Electron Reduction of Macrocycle **8**[a]



[a] Aromatic and heterocyclic rings shown in red indicate the region of delocalized, unpaired electron density.

evident, if broadened. However, neutralization of the system with trifluoroacetic acid (TFA) not only regenerated the original color of the solution but also restored all the missing signals in the ^{1}H NMR spectrum (Figure 6).

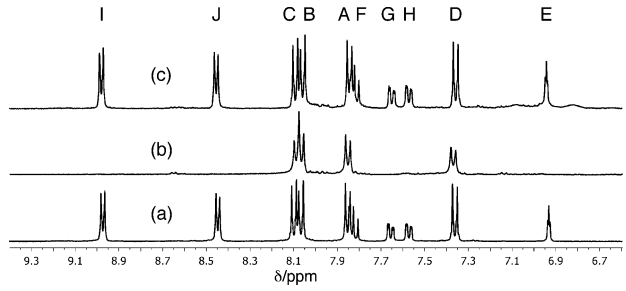


Figure 6. ^{1}H NMR spectra (298 K) of (a) compound **8** alone (3.8 mM in CD_3CN), (b) compound **8** after addition of triethylamine (10 equiv), and (c) solution (b) after adding excess trifluoroacetic acid.

These results suggest that the bipyridinium units of macrocycles **8**−**11** undergo reversible one-electron reduction[15] in the presence of the tertiary amine (Scheme 1), resulting in loss of NMR signals—due to extreme paramagnetic line-broadening—for protons immediately adjacent to the region of the molecule in which the unpaired but delocalized electron is located. Consistent with this interpretation, the same selective loss of ^{1}H NMR resonances is observed on reaction of macrocycle **8** with an equimolar amount of the one-electron reductant decamethylferrocene. Cyclic voltammetry supports the existence of two one-electron redox processes for **8**, with reduction waves at −0.06 and −0.36 V and corresponding oxidation waves at +0.01 and −0.29 V vs Ag/AgCl. In all cases, the amine-reduced macrocycles were stable for at least 10 min, as judged by the recovery of NMR resonances on acidification of the system. Work is now in progress to identify and quantify the redox pathways involved in these reactions.

In conclusion, a general route to macrocyclic *N*,*N*′-diarylbipyridinium ions has been developed. One of these macrocycles shows binding properties for an electron-rich aromatic molecule, and all show enhanced stability (relative to *N*,*N*′-dibenzyl analogs) toward degradation by nucleophilic and basic reagents, although chemically reversible one-electron reduction can occur. These attributes should enable the construction of redox-responsive supramolecular architectures with long-term stability in a wide range of chemical environments.

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Supporting Information Available: Full synthetic/analytical procedures and characterization data for all new compounds. Crystal data and full crystallographic information for **13** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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