

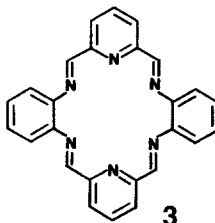
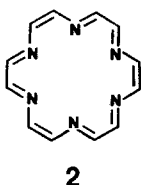
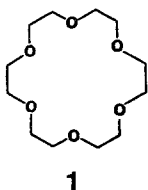
## TORANDS: PLANAR POLYAZAMACROCYCLIC LIGANDS FOR METAL IONS

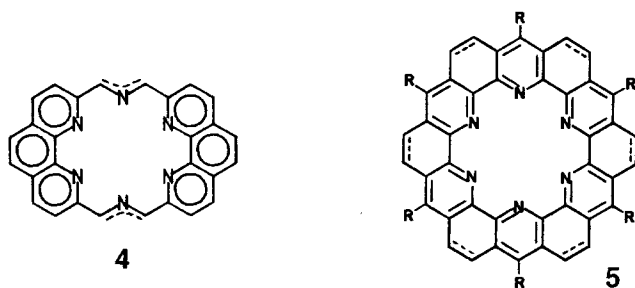
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**ABSTRACT.** A series of macrocyclic ligands related to hexaaza[18]-annulene form stable complexes with alkali metal and alkaline earth ions. A planar, substituent-solubilized "torand", consisting of multiply fused pyridine rings, has been synthesized and has been found to sequester calcium from a dilute source.

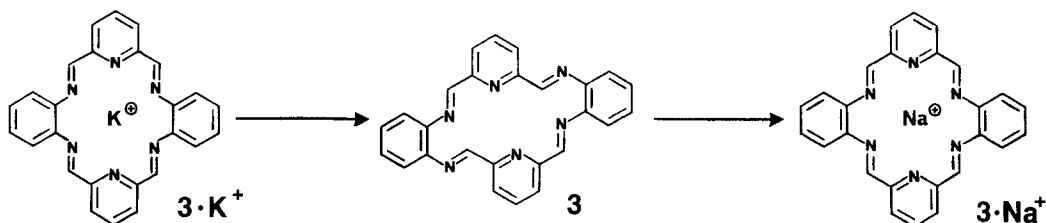
Since the discovery of crown ethers by Pedersen<sup>1</sup> there have been many attempts to design and synthesize hosts whose ion affinities and selectivities surpass those of the original cyclic polyethers. Particularly important examples are the cryptands<sup>2</sup> and spherands<sup>3</sup>. These polycyclic receptors form stronger complexes and are generally more selective than crown ethers, however their complexes equilibrate more slowly as a consequence of their more rigid, encapsulating structures. This report is focused on the development of a new class of macrocyclic hosts, the torands, whose rigid toroidal structures should permit rapid equilibration of complexes.

Replacement of the six oxygen atoms of 18-crown-6 (1) with six  $sp^2$  hybridized nitrogen atoms affords the hypothetical hexaaza[18]-annulene (2), an impractical host from the perspective of configurational and chemical stability. Fusion of six-membered rings to the periphery of 2 generates more feasible structures, such as 3, 4 and 5. Of these potential hosts, only 5 would have the shape of a rigid torus although we have also investigated 3 and 4 as more accessible model systems for 5. These model studies are important because saturated nitrogen analogues of crown ethers form considerably weaker alkali metal complexes.<sup>4</sup> This series of hosts also makes it possible to systematically examine the effects of rigidity on complexation properties.



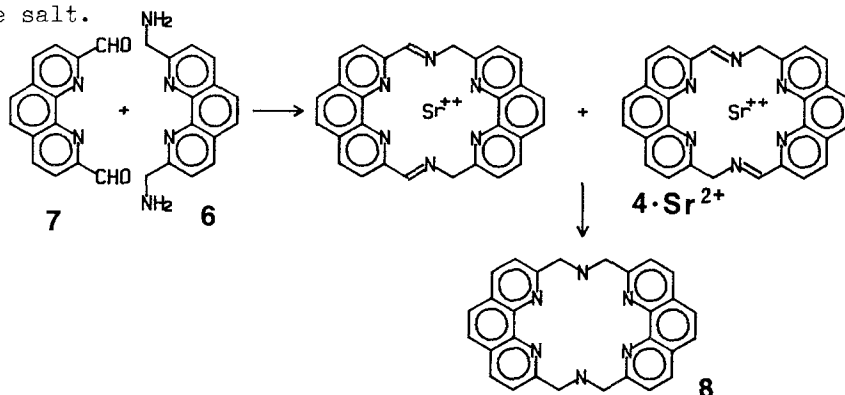


Torand model **3** was previously known only as alkaline earth, lead and cadmium perchlorate complexes, which were prepared by templated condensation of *o*-phenylenediamine with 2,6-pyridinedicarboxaldehyde.<sup>5</sup> We have successfully converted strontium perchlorate and trifluoromethanesulfonate (triflate) complexes of **3** to the corresponding potassium complexes ( $3 \cdot K^+$ ) using potassium fluoride.<sup>6</sup> Decomplexation of  $3 \cdot K^+$  with [2.2.2]-cryptand or excess 18-crown-6 then affords the free ligand (**3**), which in the solid state adopts the roughly elliptical conformation shown.<sup>7</sup> NMR data indicate that the solution conformation of **3** also deviates from the circular conformation observed in complexes<sup>5</sup>. Thus, macrocycle **3** does not exhibit the rigidity of a torand, nevertheless it may demonstrate how complex stabilities change when  $sp^2$  hybridized nitrogen replaces oxygen in a flexible system. We proceeded to synthesize  $3 \cdot Na^+$  from **3** and probed the stability constants of  $3 \cdot Na^+$  and  $3 \cdot K^+$  first by NMR<sup>6</sup> and more recently by means of ion selective electrodes. The latter, more accurate method affords stability constants in DMSO as follows:  $\log K_s(3 \cdot K^+) = 3.7$ ;  $\log K_s(3 \cdot Na^+) = 3.0$ . Torand model **3** is accordingly the first nitrogen analogue of 18-crown-6 to form stronger complexes with alkali metal ions (18-crown-6:  $\log K_s(K^+) = 3.2$ ;  $\log K_s(Na^+) = 1.5$ ).<sup>8</sup>



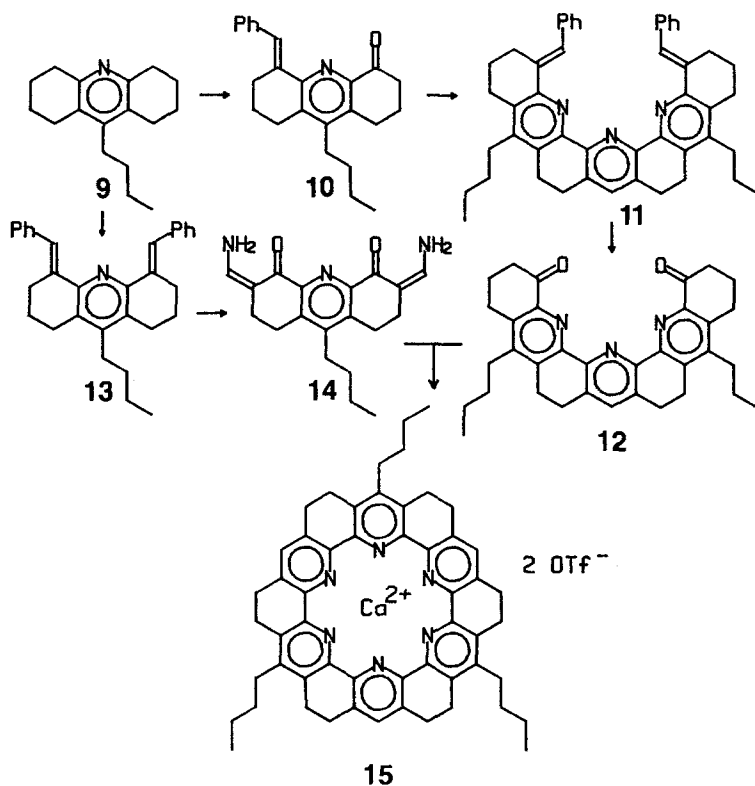
The flexibility observed in macrocycle **3** led us to search for more rigid, yet easily synthesized, torand models, such as diphenanthroline-diimines (**4**). Diamine **6** was prepared from the dihydrochloride<sup>9</sup> using alkaline Dowex 1-X8 50 anion exchange resin, then was condensed with dialdehyde **7**<sup>9</sup> in refluxing methanol in the presence of strontium triflate. Concentration of the reaction mixture, addition of benzene and filtration of the grey precipitate afforded  $4 \cdot Sr^{2+}$  in 39% yield. Micro-analytical data for Sr, H and N all agreed with the expected structure, whereas the carbon analysis was slightly high because of a trace impurity of benzene. The <sup>1</sup>HNMR spectrum of  $4 \cdot Sr^{2+}$  in DMSO-*d*<sub>6</sub> revealed a complex pattern that was temperature independent (20-80°C). Homonuclear decoupling experiments permitted the assignment of two structures, as shown. Symmetry arguments allowed identification of the minor isomer as the expected product, since it has two types of symmetrical phenanthroline

rings. The isomer ratio always remained 1:2, even when the mixture was reprecipitated, suggesting that interconversion may occur by a prototropic equilibrium. Our attempts to directly remove strontium from  $4 \cdot \text{Sr}^{2+}$  have not succeeded, so we reduced the unsaturated bridges using sodium borohydride in methanol, then isolated diphenanthrolinediamine **8** as its picrate salt.



These torand model studies demonstrate that effective complexing agents for alkali metal and alkaline earth ions may be constructed using  $\text{sp}^2$  hybridized nitrogen binding sites. In addition, the low solubilities of the model compounds led us to incorporate flexible, solubilizing substituents in our synthetic approaches to fully fused torands (**5**). We have already reported the synthesis of a soluble heptacyclic terpyridyl bearing *n*-butyl groups<sup>10</sup>. Summarized here is an extension of this methodology to the successful synthesis of a torand.<sup>11</sup> The *n*-butyloctahydroacridine **9** was converted to benzylidene ketone **10** (46%, three steps), which was dimerized by Newkome-Fischel pyrolysis of the trimethylhydrazonium salt<sup>10</sup>, yielding dibenzylideneheptacycle **11** (31%). Ozonolytic cleavage of the benzylidene groups afforded diketone **12** in 60% yield. The complementary segment, bis( $\beta$ -dimethylaminoenone) **14** was also prepared from **9** via dibenzylidene derivative **13**. Macrocyclization was effected by treating a 1:1 mixture of **12** and **14** with trifluoromethanesulfonic acid in hot acetic acid followed by ammonium acetate. Neutralization of the reaction mixture with lithium hydroxide and chromatography of the chloroform extract gave torand **15** as the calcium triflate complex in 12% yield. Calcium is introduced as a 0.3% impurity in the triflic acid used in this experiment. The spectroscopic properties of **15** are similar to those reported for the unsubstituted parent system.<sup>12</sup>

Efforts are now in progress to isolate the new torand as a free ligand and to survey the stabilities of alkali metal and alkaline earth complexes. At this point it is clear that this new host has unusual and potentially useful properties. Calcium is apparently sequestered from a dilute source yielding a lipophilic complex. Strong metal-ligand interaction is also implied by the FAB mass spectrum of **15**, which displays  $m/z$  975 ( $15\text{-CF}_3\text{SO}_3$ ) and  $m/z$  826 ( $15\text{-(CF}_3\text{SO}_3)_2$ ) as the two most abundant ions above  $m/z$  400. An investigation of the solution stability constant of **15** is now in progress. In conclusion, the model studies and the pilot synthesis of a torand complex described here indicate that the torands represent a promising new class of ionophores.



Acknowledgment is made to the National Institutes of Health and to the Petroleum Research Fund, administered by the American Chemical Society, for support of this research.

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