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Synthesis and Alkali Metal Picrate Extraction Capabilities of a 4-Oxahexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane-derived Cryptand. A New Ionophore for Selective Ion Complexation

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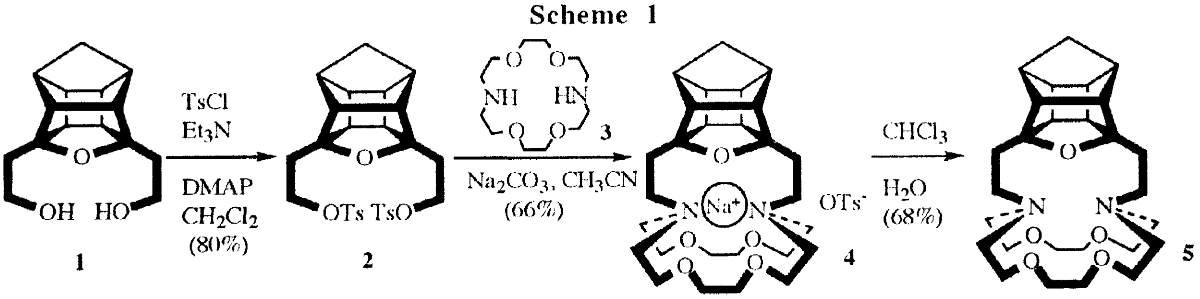
Abstract. The synthesis of a novel cage-functionalized cryptand, **5**, and the X-ray crystal structure of its 1:1 complex with Na^+, i.e. **4**, are reported. Host molecule **5** displays high avidity toward Na^+ and K^+ picrates and appears to extract these cations selectively. The X-ray crystal structure of **4** clearly indicates that Na^+ is bonded to all seven Lewis base centers (i.e., nitrogen and oxygen atoms) in the complex. In addition, the corresponding alkali metal picrate extraction profile was obtained for **10**, an adamantane-containing analog of **5**. With the possible exception of its ability to extract K^+ picrate, there appears to be relatively little difference between the alkali metal picrate extracting capabilities of host molecule **10** and a corresponding monocyclic model system, i.e., *N,N'*-diethyl-4,13-diaza-18-crown-6 (**6**). © 1998 Elsevier Science Ltd. All rights reserved.

Introduction. Pursuant to our ongoing interests in the synthesis and chemistry of novel polycarbocyclic cage compounds,[1] we recently reported the preparation of several examples of cage functionalized molecular clefts,[2-4] crown ethers,[5,6] and adamantane-containing macrocyclic thioethers.[7] Compounds of this type are of interest as members of a new class of "host" systems for the study of host-guest interactions (i.e., molecular recognition and inclusion phenomena). As an extension of these past studies, our attention has turned to the preparation of a new, cage-functionalized cryptand (i.e., **5**, Scheme 1). Compound **5** and related systems are of interest as complexing agents for selective metal ion separation and transport. The synthesis and characterization of **5** and the subsequent determination of its alkali metal picrate extraction profile are described herein.

Scheme 1



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Results and Discussion. Cryptand **5** was synthesized via the method shown in Scheme 1. Thus, diol **1**[5] was converted into the corresponding ditosylate, **2**. Subsequent Na^+ templated, base-promoted reaction of **2** with 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (i.e., "4,13-diaza-18-crown-6", **3**) in CH_3CN solvent produced the corresponding Na^+ complexed cryptand, **4** (66% yield). Unequivocal verification of the suggested structure for **4** was secured via application of X-ray crystallographic methods;[8] the resulting X-ray structure drawing of **4** appears in Figure 1.

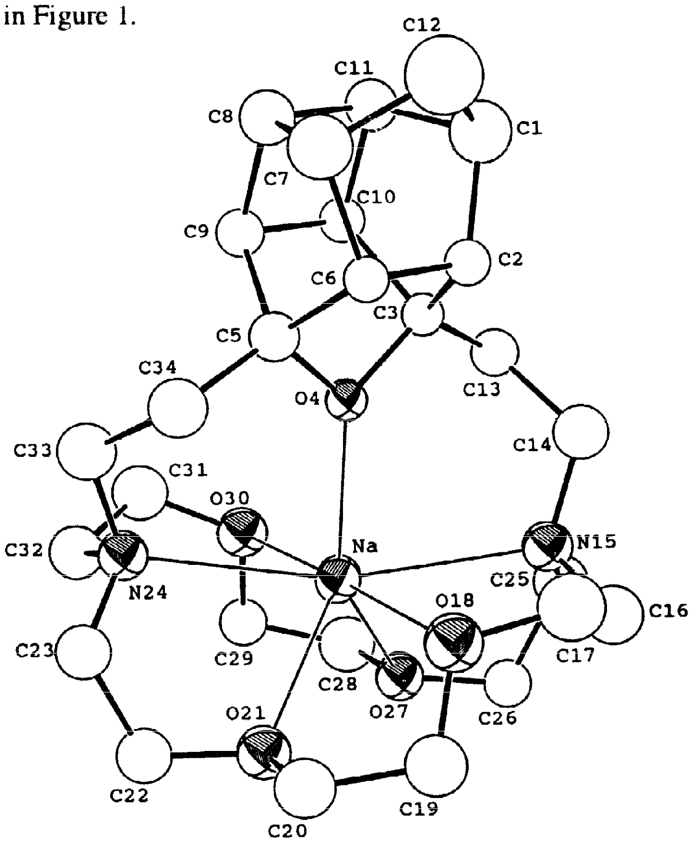
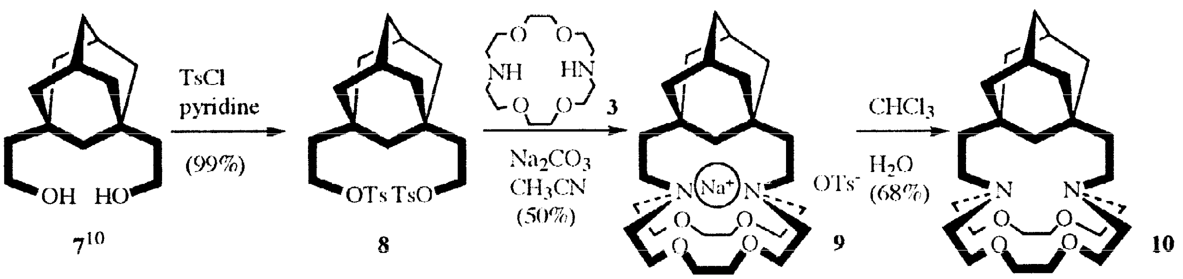


Figure 1. X-ray structure drawing of **4**.

In order to assess the role of the bridging ether oxygen atom located in the cage moiety in promoting complexation of cryptand **5** with alkali metal cations, a series of three model host compounds was obtained, i.e., 4,13-diaza-18-crown-6 (**3**), *N,N'*-diethyl-4,13-diaza-18-crown-6 (**6**)[9], and an *N,N'*-adamantane-bridged 4,13-diaza-18-crown-6 system, **10**. Compound **10** was prepared in three steps by starting with **7**[10] (see Scheme 2).

Scheme 2



With all four host systems in hand, it then became of interest to compare the alkali metal picrate extraction profile of **5** with the corresponding extraction data obtained for these three model systems. Relevant extraction data is shown in Table 1. Inspection of the data reveals three important features: (i) cryptand **5** is *by far* the most efficient alkali metal picrate extracting agent among the four host compounds studied; (ii) cryptand **5** displays pronounced selectivity in this regard, thereby showing a strong preference to form complexes with Na^+ and K^+ *vis-à-vis* the remaining alkali metal picrates; (iii) with the exception of its ability to extract K^+ picrate, there appears to be relatively little difference between the alkali metal picrate extracting capabilities of host molecule **10** and its corresponding monocyclic model system, **6**. All of these features clearly point to the pivotal role played by the bridging ether oxygen atom in promoting complexation of cryptand **5** with alkali metal cations. This conclusion is supported by the X-ray crystal structure of **4** (Figure 1), which clearly indicates that Na^+ is bonded to all seven Lewis base centers (i.e., nitrogen and oxygen atoms) in the complex.[11,12]

Table. 1. Alkali metal picrate extraction data.

	Percent of Picrate Extracted (%)				
Host Molecule	**Li^+**	**Na^+**	**K^+**	**Rb^+**	**Cs^+**
4,13-diaza-18-crown-6 (**3**)[a]	11.0 ± 0.7	10.4 ± 1.3	13.0 ± 2.0	9.1 ± 0.6	10.1 ± 0.3
N,N'-diethyl 4,13-diaza-18-crown-6 (**6**)[b]	3.3 ± 0.5	22.4 ± 0.6	34.8 ± 0.8	21.2 ± 0.7	16.0 ± 0.7
Host Molecule **10**[b]	11.2 ± 0.4	22.4 ± 0.6	46.7 ± 0.5	25.4 ± 0.7	22.1 ± 0.7
Cryptand **5**[a]	39.8 ± 0.8	95.1 ± 0.8	89.7 ± 1.2	56.1 ± 0.1	33.7 ± 0.7

[a] Averages and standard deviations calculated for data obtained from five independent extraction experiments. [b] Averages and standard deviations calculated for data obtained from four independent experiments.

Current efforts in our respective laboratories are directed toward the isolation and characterization of additional crystalline complexes of **5** with metal ions of the type M^+ and M^{+2}. In addition, we hope to be able to determine the relative stabilities of complexes of **5** with Na^+ *vis-à-vis* K^+, either via competitive extraction experiments or via direct determination of their respective dissociation constants.[13] The results of these efforts, when completed, will be described in the full paper.

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8. Selected X-ray crystallographic data for **4** ($C_{34}H_{49}N_2O_8NaS$): Space group: $P2_1/c$; a = 17.602 (8) Å; b =10.320 (4) Å; c = 18.111 (5) Å; β = 90.07 (3) °; V = 3290 (2) Å^3; Z = 4; μ = 1.57 cm^{-1}; D_{calc} = 1.350 g-cm^{-3}; R = 0.0642; R_w = 0.0676. A complete description will be given in the full paper.

9. Model crown ether **6** was prepared by starting with **3** via a modification of a literature procedure. See: Fages, F.; Desvergne, J.-P.; Bouas-Laurent, H.; Marsau, P.; Lehn, J.-M.; Kotzyba-Hibert, F.; Albrecht-Gary, A.-M.; Al-Joubbeh, M. *J. Am. Chem. Soc.* **1989**, *111*, 8672.

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11. Similarly, Na^+ is associated with all heteroatoms in, e. g., Na[2.2.2]NCS cryptate,[12a] Na[2.2.2]I cryptate,[12b,12c] and Na[2.2.2]Cl 3H_2O cryptate.[12d] We thank a Referee for having brought these examples to our attention.

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13. The importance of determining the relative stabilities of complexes of **5** with Na^+ *vis-à-vis* K^+ has been noted by a Referee.