Synthesis, Alkali Metal Picrate Extraction, and Alkali Metal Cation Binding Selectivities of Some New Cage-Annulated Polyoxamacrocyclic Crown Ethers†

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Five new cage-annulated crown ethers, *i.e.*, **4a**, **4b**, **6b**, **11a**, and **11b**, have been synthesized and their respective alkali metal picrate extraction profiles along with that of a previously synthesized host molecule, **6a**, have been obtained. These results are compared with the corresponding results obtained for electrospray ionization mass spectrometric (ESI-MS) measurements of relative binding selectivities displayed by the same hosts toward a series of alkali metal chlorides. Among the crown-5 hosts studied, **6a** displays enhanced avidity toward complexation with K^+ picrate in liquid-liquid extraction experiments. Among the three crown-6 hosts, **4b** proved to be the best alkali metal picrate extractant and displayed significant levels of avidity toward complexation with the larger alkali metal cations (*i.e.*, K^+, Rb^+, and Cs^+). The trends in the picrate extraction and the ESI-MS results obtained herein show several notable similarities and some differences. The similarities generally stem from size-selective binding properties that are intrinsic to the different cavity sizes of the cage-annulated macrocycles, whereas the differences reflect the important influence of solvation effects on the binding properties of the macrocycles.

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Introduction.

Macrocyclic crown ethers, first prepared by Pedersen in the 1960s [1], constitute an important class of host molecules that are used in studies of molecular recognition and inclusion phenomena (*i.e.*, "host-guest chemistry") [2]. Crown ethers have received considerable attention in recent years as useful agents for separation and selective transport of both ions and neutral molecules [3]. Recently, as an extension of our past interests in the synthesis and chemistry of novel polycarbocyclic "cage" compounds [4], our attention has turned to the preparation of macrocyclic polyethers that contain one or more cage moieties within the crown ether framework [5].

Typically, our cage-annulated crown ethers contain a 3,5-disubstituted-4-oxahexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]-dodecane ("oxahexacyclic") moiety and/or an oxaadamantane moiety as a rigidifying "spacer". In addition to conferring a measure of rigidity upon crown ethers, incorporation of one or more polycarbocyclic cage moieties serves also to increase the lipophilicity of the resulting crown ether. Also, each cage moiety contributes to overall preorganization and complexation properties of the host by helping to define the shape and size of the cavity within the crown ether.

It should be noted that simple, noncage-annulated monocyclic crown ethers lack facial differentiation, *i.e.*, there is no distinction between approach by a guest ion or molecule *via* the "topside" or "bottomside" of the approximate plane of the crown ether. However, the presence of a 3,5-disubstituted-4-oxahexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane cage moiety in a macrocyclic polyether negates this "top/bottom symmetry", thereby rendering the faces of the resulting crown ether diastereotopically nonequivalent.

We now report the syntheses of a variety of new cage-annulated polyoxamacrocyclic crown ethers; the alkali metal binding properties of these unusual host molecules have been evaluated *via* picrate extraction and electrospray ionization-mass spectrometric (ESI-MS) methods. ESI-MS has proven to be a versatile method for analysis of supramolecular complexes formed in solution and transported into the gas phase for detection [6-18]. Based upon the intensities of complexes in the resulting mass spectra, it is possible to estimate the relative binding selectivities of different hosts toward different guests. This general method has been used previously to assess the alkali metal binding properties of crown ethers [6,10,11,12], lariat ethers [13,14], and caged crown ethers [17,18], and it provides the basis for the results reported herein.

Results and Discussion.

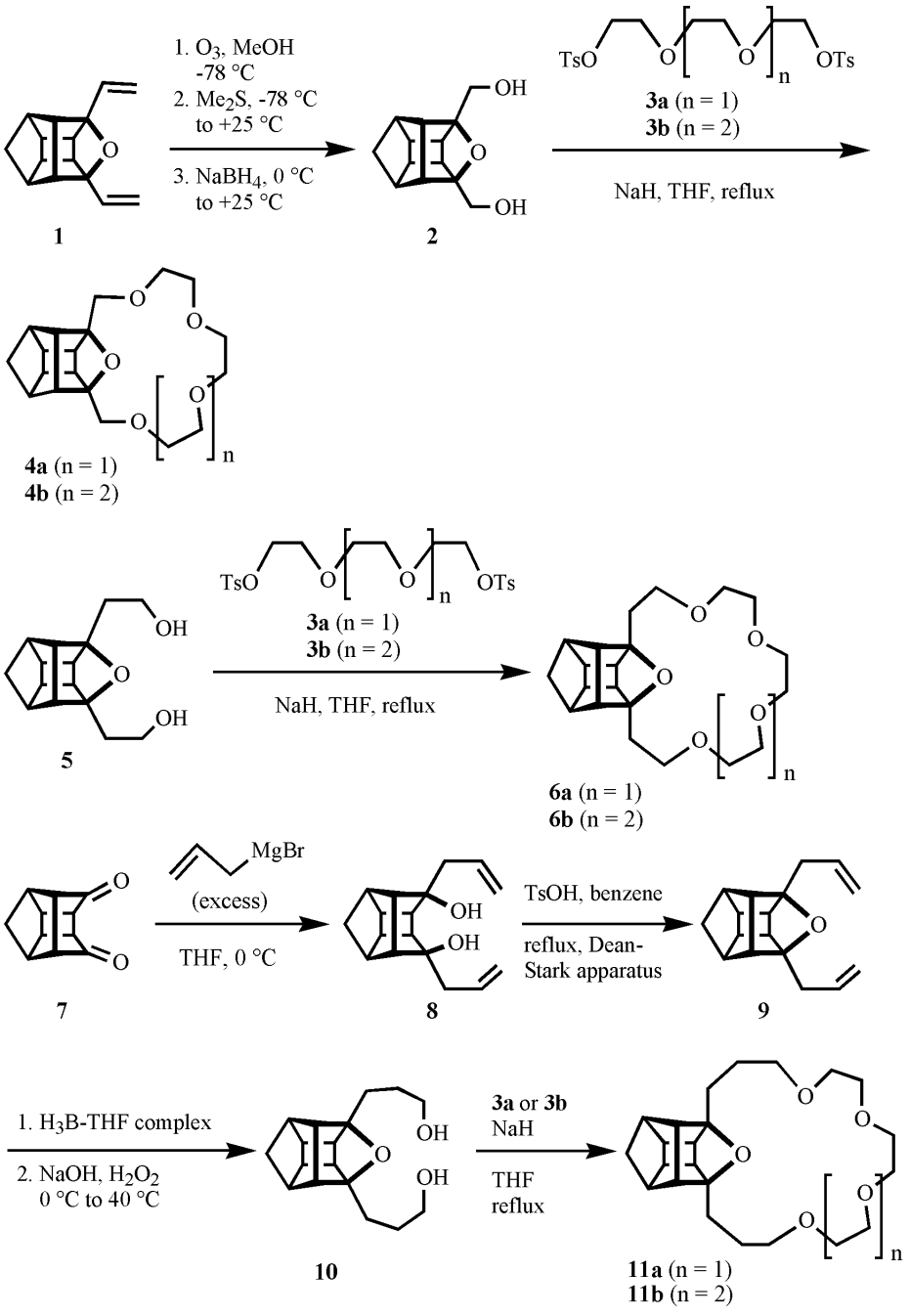
The method used to prepare five new cage-annulated polyoxamacrocyclic crown ethers, *i.e.*, **4a**, **4b**, **6b**, **11a**, and **11b**, is shown in Scheme 1. The starting material, 3,5-divinyl-4-oxahexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane (**1**) [5a], can be prepared readily *via* addition of vinylmagnesium bromide (2 equivalents) to pentacyclo-[5.4.0.0^{2,6}.$0^{3,10}$.$0^{5,9}$]undecane-8,11-dione (**7**, Scheme 1), a readily available pentacyclic cage diketone [19]. The three-step reaction sequence shown in Scheme 1 was employed to convert **1** into the corresponding diol, **2**.

Subsequent base promoted reaction of **2** with ditosylates **3a** and **3b** afforded the corresponding cage-annulated crown ethers, *i.e.*, **4a** and **4b**, respectively. Similarly, base promoted reaction of diol. **5** [5a] with ditosylates **3a** and **3b** produced cage-annulated crown ethers, *i.e.*, **6a** and **6b**. A closely analogous sequence of reactions was employed to prepare cage-annulated crown ethers **11a** and **11b**.

In Table 1, the results obtained *via* alkali metal picrate extraction experiments that employed cage-annulated crown ethers **4a**, **4b**, **6a**, **6b**, **11a**, and **11b** as hosts are compared with the corresponding results obtained for ESI-MS measurements of relative binding selectivities displayed by the same hosts toward a series of alkali metal chlorides. An example of the binding selectivity data obtained by using ESI-MS is shown in Figure 1 for **6b**. The peak areas in Figure 1 have been integrated and summed to give the percentages reported in Table 1.

Among the three crown-5 host molecules whose alkali metal picrate extraction profiles were determined in this study (*i.e.*, **4a**, **6a**, and **11a**), only **6a** displayed even modest

Scheme 1



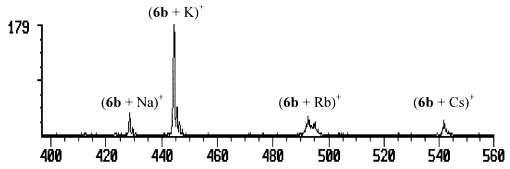
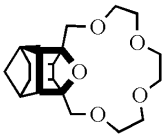
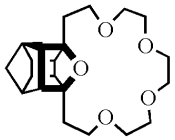
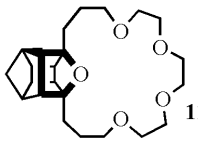
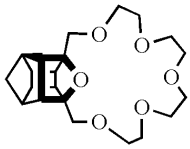
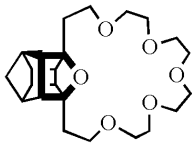
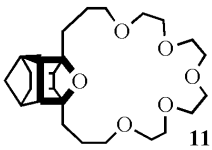


Figure 1. ESI-mass spectrum of a methanolic solution that contains **6b** and five alkali metal cations.

avidity toward complexation with any of the alkali metal picrates, particularly toward Na^+ and K^+. Here, it should be noted that these three crown-5 hosts contain cavities that are progressively larger than that of 15-crown-5, a readily available model compound. Thus, while 15-crown-5 is a selective Na^+ picrate extractant, **6a** displayed somewhat enhanced avidity and selectivity toward K^+.

Table 1

Alkali Metal Picrate Extraction and Corresponding ESI data for **4a**, **4b**, **6a**, **6b**, **11a**, **11b** and two Model Compounds *i.e.*, 15-Crown-5 and 18-crown-6

	Percent of Picrate Extracted (%)[a,b]				
Host Molecule	LI^+	Na^+	K^+	Rb^+	Cs^+
15-crown-5 (model system)	1.3 ± 0.5 (4)	15.3 ± 0.4 (35)	6.7 ± 0.2 (36)	3.7 ± 0.4 (17)	1.1 ± 0.3 (8)
 **4a**	BLD [c] (3)	2.1 ± 0.2 (28)	1.6 ± 0.8 (26)	1.3 ± 0.9 (29)	0.4 ± 0.4 (13)
 **6a**	2.8 ± 0.3 [d]	18.5 ± 1.0 [d]	29.0 ± 0.2 [d]	8.4 ± 1.3 [d]	BLD [c,d]
 **11a**	BLD [c] (2)	BLD [c] (11)	4.9 ± 0.5 (52)	0.9 ± 0.2 (28)	BLD [c] (6)
18-crown-6 (model system)	0.3 ± 0.3 (1)	5.3 ± 0.3 (6)	64.0 ± 0.4 (60)	57.8 ± 0.6 (24)	30.5 ± 0.4 (8)
 **4b**	BLD [b] (0)	11.3 ± 0.8 (6)	67.7 ± 0.2 (68)	60.0 ± 0.3 (22)	40.2 ± 0.8 (3)
 **6b**	BLD [b] (0)	0.07 ± 0.03 (13)	11.6 ± 0.1 (58)	7.8 ± 0.3 (20)	2.8 ± 0.1 (9)
 **11b**	BLD [b] (4)	BLD [b] (11)	0.6 ± 0.3 (24)	0.2 ± 0.3 (30)	1.9 ± 0.1 (31)

[a] Experimental conditions employed: 5 m*M* host in $CHCl_3$ solvent (0.5 mL). Aqueous phase (0.5 L) was 5.00 m*M* in alkali metal picrate; Averages and standard deviations are calculated for data obtained from three independent extraction experiments. [b] Data in parentheses taken from M. L. Reyzer, J. S. Brodbelt, A. P. Marchand, Z. Chen, Z. Huang, and I. N. N. Namboothiri, *Int. J. Mass Spectrom.* **244**, 133 (2001); see text. [c] BLD = below limit of detection. [d] Data taken from A. P. Marchand, K. A. Kumar, K. Mlinarić- Majerski, G. Kragol, *Tetrahedron*, **53**, 3467(1997).

Among the three crown-6 host molecules whose alkali metal picrate extraction profiles were determined in this study (*i.e.*, **4b**, **6b**, and **11b**), **4b** proved to be the best extractant and displayed significant levels of avidity toward complexation with the larger alkali metal cations (*i.e.*, K^+, Rb^+, and Cs^+). Indeed, **4b** showed enhanced avidity in these extraction experiments relative to that of a 18-crown-6, another readily available model compound.

For the ESI-MS measurements of binding selectivities, the intensities of the crown ether/alkali metal complexes in the mass spectra for the various 1:1:1:1:1:1 (host:Li^+:Na^+:Rb^+:K^+:Cs^+) solutions in methanol were measured and converted to percentages as shown in Table 1. These percentages reveal the trends in selectivity, but not absolute binding affinities, of the host molecules.

The trends in the picrate extraction and the ESI-MS results that are compared in Table 1 show several notable similarities and some differences. The similarities generally stem from size-selective binding properties that are intrinsic to the different cavity sizes of the cage-annulated macrocycles, whereas the differences reflect the important influence of solvation effects on the binding properties of the macrocycles.

In the ensuing discussion, it should be borne in mind that the picrate extraction results (Table 1) reflect both the alkali metal selectivities and avidities of each crown ether based on extraction of the metal ions from a highly polar aqueous environment into a much less polar ($CHCl_3$) environment. By way of contrast, the corresponding ESI-MS results reflect only selectivities and not avidities, since all data is normalized to *ca.* 100% total intensity for each macrocycle. In addition, the ESI-MS data as presented do not reveal which macrocycles possess the largest binding affinities; only their relative selectivities for the various alkali metals can be gleaned from this data. Thus, the picrate extraction results which suggest that host **4b** has the largest K^+ and Rb^+ affinities of all the caged crown ethers is an observation that is not directly comparable to any of the ESI-MS data. However, the statement that host **11a** shows a significant selectivity for K^+ relative to the other alkali metals is supported by both the picrate extraction and ESI-MS results.

The binding selectivity results obtained by the picrate extraction and ESI-MS methods for **11a**, **4b**, **6b**, and 18-crown-6 show the selectivity trend $K^+ > Rb^+ > Cs^+$, $Na^+ > Li^+$. Agreement between the selectivity trends for the ESI-MS and picrate extraction data suggest that cavity size plays a dominant role in influencing the binding properties of these three macrocycles. However, for 18-crown-6, **4b**, and **6b**, the enhanced selectivity shown toward K^+ *vis-à-vis* Rb^+, Cs^+, and Na^+ is significantly greater when measured by using the ESI-MS technique than was observed by using the alkali metal picrate extraction method. This enhancement in selectivity most likely stems from the difference in solvation energies of the metal cations in methanol *vs.* water. The very high solvation energies of alkali metal ions in water renders their encapsulation by the macrocyclic ligands more energetically demanding, thereby tempering the degree of differentiation among the alkali metal ions and reducing the selectivity observed in the picrate extraction experiments. In the less polar methanol environment, the metal cations are more easily desolvated; hence, a specific metal ion that best fits the cavity size can be complexed more selectively by each macrocycle, as reflected by the ESI-MS results.

It is interesting to note that among members of the series of cage-annulated crown-6 macrocycles (*i.e.*, **4b**, **6b**, and **11b**), the results obtained by using the ESI-MS technique indicate that K^+ selectivity is maximized for **4b** but diminishes for **6b** or **11b** as the cavity size is further expanded. In fact, **4b** exhibits slightly greater K^+ selectivity than 18-crown-6, thereby suggesting that the introduction of the cage moiety refines both the cavity size and the alignment of the oxygen dipoles with resulting optimal encapsulation of K^+. The addition of two more carbon atoms in the ring (*i.e.* by proceeding from **4b** to **6b**) expands the cavity sufficiently to relax this K^+ selectivity.

Host systems **4a**, **11a**, and **11b** display very low alkali metal binding affinities as judged by the picrate extraction data shown in Table 1. Thus, differences among trends in selectivity noted between the picrate extraction and ESI-MS data are not considered to be significant, nor do they merit detailed discussion. In fact, **4a** appears to be a nonselective ligand overall, a conclusion that is supported by both the picrate extraction and ESI-MS results shown in Table 1. As mentioned above, **11a** displays modest selectivity for K^+ over the other metals, but its low avidity renders it unsuitable as a candidate for further development as a host with targeted binding properties. Host molecule **11b** displays both low avidity and nondiscriminate selectivity toward alkali metal cations, results that render this compound a poor host for specific binding applications.

Summary and Conclusions.

In the course of this study, several new cage-annulated crown ethers (**4a**, **4b**, **6b**, **11a**, and **11b**) have been synthesized, and their respective alkali metal picrate extraction profiles along with that of a previously synthesized host molecule, **6a**, have been obtained. Host **6a** proved to be a moderately effective K^+ extractant, whereas **4b** proved to be an effective agent for extraction of K^+, Rb^+, and Cs^+. ESI-MS measurements of relative binding selectivities displayed by these hosts toward a series of alkali metal chlorides provide information regarding binding selectivities but not about binding avidities. The ESI-MS results obtained herein point to the importance of host cavity size in determining the binding characteristics of these cage-annulated crown ethers toward alkali metal cations in solution.

EXPERIMENTAL

Melting points are uncorrected. High-resolution mass spectral data reported herein were obtained by personnel at the Mass Spectrometry Facility at the Department of Chemistry and Biochemistry, University of Texas at Austin by using a ZAB-E double sector high-resolution mass spectrometer (Micromass, Manchester, England) that was operated in the chemical ionization mode. Elemental microanalytical data was obtained by personnel at M-H-W Laboratories, Phoenix, AZ.

8,11-Bis(hydroxymethyl)pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**2**).

A two necked round bottom flask equipped with a bubbler and a magnetic stirrer was charged with a solution of **1** [5a] (2.0 g, 9.4 mmol) in absolute methanol (50 ml), and the reaction vessel was cooled to -78 °C *via* immersion in an external dry ice-acetone cold bath. Ozone was bubbled through this cold solution until a blue color persisted (*ca.* 3 hours), at which time the ozone source was disconnected from the reaction flask, and the reaction mixture was allowed to stir at -78 °C during 0.5 hour. Argon was bubbled through the cold reaction mixture to purge excess ozone, and this was followed by dropwise addition of dimethyl sulfide (2.0 ml, 27 mmol) with stirring to the cold (-78 °C) reaction mixture. After all of the dimethyl sulfide had been added, the external cold bath was removed, and the resulting mixture was allowed to warm gradually to ambient temperature while stirring during 2 hours. The reaction mixture was cooled to 0 °C *via* application of an external ice-water bath, and sodium borohydride (500 mg, 13.2 mmol) then was added portionwise with stirring to the reaction mixture at such a rate that the temperature inside the reaction vessel did not exceed +5 °C. After all of the sodium borohydride had been added, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring overnight. Excess sodium borohydride was destroyed *via* careful, dropwise addition of 10% aqueous hydrochloric acid (10 ml, excess) to the reaction mixture. The resulting mixture was filtered, and the filtrate was concentrated *in vacuo*. The residue was decanted into water (10 ml), and the resulting aqueous suspension was extracted with ethyl acetate (3 × 20 ml). The combined organic layers were washed with brine (10 ml), dried (magnesium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% ethyl acetate-methylene chloride. Pure **2** was thereby obtained as a colorless microcrystalline solid, 1.62 g (78%), mp 82-83 °C; ir (potassium bromide): 3430 (s), 2967 (s), 2859 (m), 1653 (w), 1464 (w), 1345 (w), 1305 (w), 1260 (w), 1107 (w), 1024 (s), 882 (m), 870 (w), 840 cm^{-1} (w); ^{1}H nmr (deuteriochloroform): δ 1.50 (*A*B, J_{AB} = 10.8 Hz, 1 H), 1.88 (A*B*, J_{AB} = 10.3 Hz, 1 H), 2.33-2.44 (m, 2 H), 2.55-2.70 (m, 6 H), 3.43-3.54 (br s, 2 H), 3.71 (*A*B, J_{AB} = 12.0 Hz, 2 H), 3.80 (A*B*, J_{AB} = 12.0 Hz, 2 H); ^{13}C nmr (deuteriochloroform): δ 41.3 (d), 43.6 (t), 43.7 (d), 44.9 (d), 55.0 (d), 61.5 (t), 98.1(s).

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 71.02; H, 7.07.

Synthesis of **4a**.

A 100 ml single-necked round bottom flask was equipped with magnetic stirrer and argon flow protection, and the flask was charged with a solution of sodium hydride (320 mg, obtained as a 60% dispersion of sodium hydride in mineral oil, 8.0 mmol) in dry tetrahydrofuran (10 ml). The solution was cooled to 0 °C *via* application of an external ice-water bath. To the cooled solution under argon was added dropwise with stirring a solution of **2** (440 mg, 2.0 mmol) in dry tetrahydrofuran (10 ml). After the addition of **2** had been completed, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring during 2 hours. The external ice-water bath again was applied to the reaction mixture, and a solution of triethylene glycol ditosylate (**3a**, 1.28 g, 2.8 mmol) in dry tetrahydrofuran (10 ml) was added dropwise with stirring under argon to the cooled (0 °C) reaction mixture. After the addition of **3a** had been completed, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring during 15 hours. The reaction mixture was refluxed with stirring under argon during 3 days and then was quenched *via* dropwise addition of ice-water (300 mg, 17 mmol) to the stirred reaction mixture. The resulting aqueous suspension was extracted with ethyl acetate (3 × 30 ml). The organic layer was dried (magnesium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% ethyl acetate-methylene chloride. Pure **4a** was thereby obtained as a colorless oil, 123 mg (19%); ir (film): 2957 (s), 2864 (s), 1728 (m), 1447 (w), 1339 (w), 1292 (w), 1252 (w), 1132 (s), 930 (w), 899 (w), 860 cm^{-1} (w); ^{1}H nmr (deuteriochloroform): δ 1.50 (*A*B, J_{AB} = 10.3 Hz, 1 H), 1.88 (A*B*, J_{AB} = 10.3 Hz, 1 H), 2.32-2.40 (m, 2 H), 2.55-2.75 (m, 6 H), 3.55-3.85 (m, 16 H); ^{13}C nmr (deuteriochloroform): δ 41.3 (d), 43.67 (d), 43.74 (t), 45.3 (d), 55.1 (d), 69.5 (t), 70.1 (t), 70.5 (t), 71.8 (t), 97.2 (s).

Anal. Calcd. for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84. Found: C, 68.41; H, 7.79.

Synthesis of **4b**.

A 100 ml single-neck round bottom flask was equipped with magnetic stirrer and argon flow protection, and the flask was charged with a solution of sodium hydride (320 mg, obtained as a 60% dispersion of sodium hydride in mineral oil, 8.0 mmol) in dry tetrahydrofuran (10 ml). The solution was cooled to 0 °C *via* application of an external ice-water bath. To the cooled solution under argon was added dropwise with stirring a solution of **2** (440 mg, 2.0 mmol) in dry tetrahydrofuran (10 ml). After the addition of **2** had been completed, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring during 2 hours. The external ice-water bath again was applied to the reaction mixture, and a solution of tetraethylene glycol ditosylate (**3b**, 1.41 g, 2.8 mmol) in dry tetrahydrofuran (10 ml) was added dropwise with stirring under argon to the cooled (0 °C) reaction mixture. After the addition of **3b** had been completed, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring during 15 hours. The reaction mixture was refluxed with stirring under argon during 3 days and then was quenched *via* dropwise addition of ice-water (300 mg, 17 mmol) to the stirred reaction mixture. The resulting aqueous suspension was extracted with ethyl acetate (3 × 30 ml). The organic layer was dried (magnesium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% ethyl acetate-methylene chloride. Pure **4b** was thereby obtained as a colorless oil, 240 mg (32%); ir (film): 2945 (s),

2859 (s), 1435 (w), 1340 (w), 1292 (w), 1252 (w), 1121 (s), 988 (w), 928 (w), 893 cm^{-1} (w); ^1H nmr (deuteriochloroform): δ 1.45 (*A*B, J_{AB} = 9.5 Hz, 1 H), 1.83 (A*B*, J_{AB} = 9.5 Hz, 1 H), 2.28-2.38 (m, 2 H), 2.49-2.69 (m, 6 H), 3.52-3.77 (m, 20 H); ^{13}C nmr (deuteriochloroform): δ 41.3 (d), 43.5 (t), 43.6 (d), 45.0 (d), 55.0 (d), 69.3 (t), 70.3 (t), 70.49 (t), 71.54 (t), 70.8 (t), 97.1 (s).

Anal. Calcd. for $C_{21}H_{30}O_6$: $[M_r + H]^+$ 379.2121. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$ 379.2128.

Synthesis of **6b**.

Into a 250 ml two-neck round botom flask equipped with a magnetic stirrer and argon bubbling inlet was added a solution of sodium hydride (800 mg, obtained as a 60% dispersion of sodium hydride in mineral oil, 20 mmol) in dry tetrahydrofuran (50 ml). The solution was gently refluxed under argon *via* application of an external oil bath. To the refluxing solution under argon was added dropwise with stirring a solution of mixture of **5** (496 mg, 2.0 mmol) and tetraethylene glycol ditosylate (**3b**, 1.21 g, 2.4 mmol) in dry tetrahydrofuran (50 ml) during 5 hours. After the addition of **5** had been completed, the reaction mixture was refluxed for an additional 3 days. The reaction mixture then was cooled to 0 °C *via* application of an external ice-water bath, and the reaction was quenched *via* addition of ice-water (5 ml, excess). The reaction mixture was concentrated *in vacuo* to remove tetrahydrofuran. Water (50 ml) was added to the residue, and the resulting aqueous suspension was extracted with ethyl acetate (3 × 30 ml). The combined organic layers were dried (magnesium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 50% ethyl acetate-methylene chloride. Pure **6b** was thereby obtained as a colorless oil, 263 mg (32%); ir (film): 2957 (s), 2934 (s), 2863 (s), 1456 (w), 1354 (w), 1292 (w), 1252 (w), 1117 (s), 814 cm^{-1} (w); ^1H nmr (deuteriochloroform): δ 1.44 (*A*B, J_{AB} = 10.3 Hz, 1 H), 1.79 (A*B*, J_{AB} = 10.3 Hz, 1 H), 1.96 (t, *J* = 6.2 Hz, 2 H), 1.97 (t, J = 6.1 Hz, 2 H), 2.28-2.38 (m, 2 H), 2.48-2.58 (m, 4 H), 2.58-2.65 (m, 2 H), 3.48-3.68 (m, 20 H); ^{13}C nmr (deuteriochloroform): δ 32.3 (t), 41.4 (d), 43.4 (t), 44.0 (d), 47.9 (d), 58.9 (d), 68.0 (t), 70.2 (t), 70.6 (t), 70.96 (t), 71.00 (t), 94.3 (s).

Anal. Calcd. for $C_{23}H_{34}O_6$: $[M_r + H]^+$407.2437. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$407.2443.

exo-8-*exo*-11-Diallylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-*endo*-8-*endo*-11-diol (**8**).

A mechanically stirred suspension of freshly prepared allylmagnesium bromide [20] (2,250 ml of a 0.392 *M* solution in dry tetrahydrofuran, excess) was cooled to 0 °C *via* application of an external ice bath. To this suspension was added dropwise with vigorous stirring a solution of **7** (58.5 g, 336 mmol) in dry tetrahydrofuran (500 ml) at 0 °C during 2 hours. After the addition of **7** had been completed, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring under argon during 24 hours. The reaction was quenched *via* dropwise addition of saturated aqueous ammonium chloride solution until a pH of *ca.* 6-7 was reached. The layers were separated, and the aqueous layer was extracted with ethyl acetate (2 × 500 ml). The combined organic extracts were dried (magnesium sulftate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was recrystallized from hexane, thereby affording pure **8** as a colorless microcrystalline solid, 78.9 g (91%), mp 82-83 °C; ir (potassium bromide): 3169 (s), 2976 (s), 1639 cm^{-1} (m); ^1H nmr (deuteriochloroform): δ 1.05 (*A*B, J_{AB} = 10.8 Hz, 1 H), 1.49 (A*B*, J_{AB} = 10.8 Hz, 1 H), 1.97-2.24 (m, 6 H), 2.30-2.61 (m, 6 H), 5.01 (dd, J_1 = 8.0 Hz, J_2 = 2.6 Hz, 2 H), 5.04 (dd, J_1 = 16.9 Hz, J_q = 2.6 Hz, 2 H), 5.78-6.07 (m, 2 H), 6.52 (br s, 2 H); ^{13}C nmr (deuteriochloroform): δ 33.9 (t), 40.0 (d), 42.8 (d), 44.0 (d), 44.1 (t), 49.1 (d), 77.2 (s), 117.5 (t), 133.8 (d).

Anal. Calcd. for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.14; H, 8.42. Calcd. for $C_{17}H_{22}O_2$: $[M_r + H]^+$ 259.16981. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$ 259.16994.

3,5-Diallyl-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (**9**).

A solution of **8** (61 g, 0.236 mol) and *p*-toluenesulfonic acid (1.5 g, 0.79 mmol, catalytic amount) in benzene (1,200 ml) was refluxed in a Dean-Stark apparatus. Water which was removed from the reaction mixture by azeotropoic distillation was withdrawn periodically. Additional *p*-toluenesulfonic acid (500 mg) was added at 12 hour intervals. After 6 days, tlc analysis of the reaction mixture indicated the absence of unreacted **8**. The reaction mixture was allowed to cool gradually to ambient temperature and then was washed sequentially with 10% aqueous sodium bicarbonate (100 ml), water (100 ml) and brine (100 ml). The organic layer was dried (magnesium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified *via* column chromatography on silica gel by eluting with 5% ethyl acetate-hexane. Pure **9** was thereby obtained as a colorless oil, 46.5 g (82%); ir (film): 3075 (m), 2965 (s), 1640 (m), 997 (s), 910 cm^{-1} (s); ^{-1}H nmr (deuteriochloroform): δ 1.46 (*A*B, J_{AB} = 10.2 Hz, 1 H), 1.82 (A*B*, J_{AB} = 10.2 Hz, 1 H), 2.35 (br s, 2 H), 2.45-2.65 (m, 10 H), 4.96-5.15 (m, 4 H), 5.67-5.9 (m, 2 H); ^{13}C nmr (deuteriochloroform): δ 37.5 (t), 41.7 (d), 43.3 (t), 44.5 (d), 47.8 (d), 58.6 (d), 95.1 (s), 116.8 (t), 134.4 (d).

Anal. Calcd. for $C_{17}H_{20}O$: $[M_r + H]^+$ 241.1592. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$ 241.1601.

3,5-[Bis(3'-hydroxypropyl)]-4-oxahexacyclo-[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (**10**).

A solution of **9** (4.8 g, 20 mmol) in dry tetrahydrofuran (100 ml) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added dropwise with stirring a 1 *M* solution of borane-tetrahydrofuran complex (20 ml, 20 mmol). After the addition of the the hydroborating reagent had been completed, the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature while stirring under argon during 6 hours. The external ice-water bath was replaced, and then were added sequentially (i) a solution of sodium hydroxide (3.2 g, 80 mmol) in water (10 ml) followed by (ii) 30% aqueous hydrogen peroxide (10 ml, excess). The resulting mixture was stirred at 0 °C during 1 hour, at which time the reaction mixture was heated to 40 °C and was maintained at that temperature for 1 hour, during which time the reaction mixture became homogeneous. The reaction mixture was allowed to cool gradually to ambient temperature and then was extracted with ethyl acetate (3 × 100 ml). The combined organic extracts were washed with water (3 × 50 ml), dried (sodium sulfate) and filtered, and the filtrate was concentrated *in*

vacuo. The residue was purified by column chromatography on silica gel by eluting with 70% ethyl acetate-hexane. Pure **10** (3.3 g, 60%) was thereby obtained as a colorless, viscous oil; ir (film): 3333 (s), 2947 (s), 1059 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 1.52 (*A*B, J_{AB} = 10.4 Hz, 1 H), 1.58-1.91 (m, 9 H), 2.35-2.65 (m, 8 H), 2.90 (br s, 2 H), 3.60 (t, *J* = 5.7 Hz, 4 H); ^{13}C nmr (deuteriochloroform): δ 28.5 (t), 29.4 (t), 41.4 (d), 43.3 (t), 44.2 (d), 47.5 (d), 58.3 (d), 62.8 (t), 96.1 (s).

Anal. Calcd. for $C_{17}H_{24}O_3$: $[M_r + H]^+$ 277.1804. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$ 277.1809.

Synthesis of **11a**.

A solution of **10** (276 mg, 1.0 mmol) in dry tetrahydrofuan (30 ml) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added portionwise with stirring a mixture of sodium hydride (120 mg, obtained as a 60% dispersion of sodium hydride in mineral oil, 3.0 mmol) and solid potassium carbonate (138 mg, 1.0 mmol). The resulting mixture was stirred at 0 °C during 1 hour, at which time the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature during 3 hours. To the resulting mixture was added dropwise with stirring triethylene glycol ditosylate (**3a**, 458 mg, 1.0 mmol), and the resulting mixture was refluxed during 3 days. The reaction was quenched *via* dropwise addition of methanol (5 ml). The resulting mixture was extracted with ethyl acetate (3 × 30 ml), and the combined organic extracts were washed with water (3 × 30 ml). The organic layer was dried (sodium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel by eluting with 50% EtOAc-hexane. Pure **11a** was thereby obtained as a colorless oil, 256 mg (66%); ir (film): 2949 (s), 2863 (s), 1450 (w), 1123 cm^{-1} (s); ^1H nmr (deuteriochloroform): δ 1.46 (*A*B, J_{AB} = 10.5 Hz, 1 H), 1.60-1.86 (m, 9 H), 2.28-2.59 (m, 8 H), 3.46-3.69 (m, 16 H); ^{13}C nmr (deuteriochloroform): δ 25.7 (t), 27.7 (t), 41.3 (d), 43.5 (t), 43.9 (d), 47.5 (d), 58.4 (d), 69.9 (t), 70.5 (t), 70.8 (t), 71.2 (t), 95.8 (s).

Anal. Calcd. for $C_{23}H_{34}O_5$: $[M_r + H]^+$391.24845. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$391.24802.

Synthesis of **11b**.

A solution of **10** (276 mg, 1.0 mmol) in dry tetrahydrofuran (30 ml) under argon was cooled to 0 °C *via* application of an external ice-water bath. To this cooled solution was added portionwise with stirring a mixture of sodium hydride (120 mg, obtained as a 60% dispersion of sodium hydride in mineral oil, 3.0 mmol) and solid potassium carbonate (138 mg, 1.0 mmol). The resulting mixture was stirred at 0 °C during 1 hour, at which time the external ice-water bath was removed, and the reaction mixture was allowed to warm gradually to ambient temperature during 3 hours. To the resulting mixture was added dropwise with stirring tetraethylene glycol ditosylate (**3b**, 502 mg, 1.0 mmol), and the resulting mixture was refluxed during 5 days. The reaction was quenched *via* dropwise addition of methanol (5 ml). The resulting mixture was extracted with ethyl acetate (3 × 30 ml), and the combined organic extracts were washed with water (3 × 30 ml). The organic layer was dried (sodium sulfate) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel by eluting with 60% ethyl acetate-hexane. Pure **11b** was thereby obtained as a colorless oil, 121 mg (28%); ir (film): 2949 (s), 2858 (s), 1455 (m), 1116 cm^{-1} (s); ^{-1}H nmr (deuteriochloroform): δ 1.44 (*A*B, J_{AB} = 10.3 Hz, 1 H), 1.55-1.83 (m, 9 H), 2.30-2.58 (m, 8 H), 3.45-3.73 (m, 20 H); ^{13}C nmr (deuteriochloroform): δ 26.1 (t), 28.6 (t), 42.0 (d), 44.0 (t), 44.5 (d), 48.1 (d), 59.0 (d), 70.4 (t), 70.9 (t), 71.1 (t), 71.2 (t), 71.6 (t), 96.2 (s).

Anal. Calcd. for $C_{25}H_{38}O_6$: $[M_r + H]^+$ 435.2747. Found (high-resolution chemical ionization mass spectrometry): $[M_r + H]^+$ 435.2738.

Electrospray Ionization Mass Spectroscopy.

All ESI-MS results were obtained by using a Finnigan quadrupole ion trap mass spectrometer equipped with an electrospray interface modeled after the Oak Ridge National Laboratory design [21]· A Harvard syringe pump delivered the solutions at 3.0-5.0 $ml\text{-}min^{-1}$ to the stainless steel electrospray needle, which was maintained at 3.4-3.8 kV. The concentration ratios for the mixture of one host with five M^+X^- guests in methanol were 1:1:1:1:1:1; the concentration of each component was 1.5 x 10^{-4} *M*. The alkali metal guests (Li^+, Na^+, K^+, Rb^+, and Cs^+) were added to the solutions as their chloride salts.

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REFERENCES AND NOTES

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