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Synthesis and Alkali Metal Picrate Extraction Capabilities of Novel Cage-Functionalized 17-Crown-5 and 17-Crown-6 Ethers

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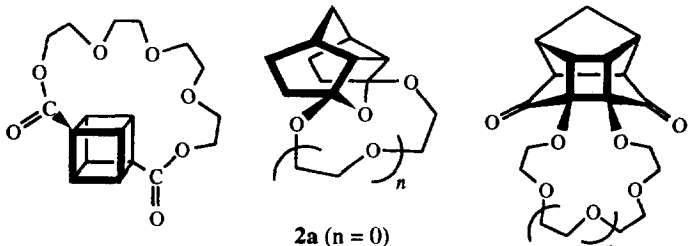
Abstract. The syntheses of three novel cage-functionalized 17-crown-5 and 17-crown-6 ethers, i. e., **10-12**, are reported and the results of alkali metal picrate extraction experiments performed by using each of these crown ethers in turn as the extractant are described. Their respective relative extraction efficiencies toward alkali metal picrates were compared with the corresponding efficiencies of 15-crown-5 and benzo-15-crown-5 solutions at the same concentration. The extraction profile of **10** (17-crown-5) toward alkali metal picrates is similar to that of 15-crown-5; however, **10** displays 33% greater avidity toward Na^+ picrate. The ability of **11** (benzo-17-crown-5) to extract Li^+, Rb^+, and Cs^+ picrates is similar to that of benzo-15-crown-5. Crown ether **10** is *ca.* 3 times more effective than **11** toward extraction of K^+ picrate. The alkali metal picrate extraction profile of **12** (17-crown-6) resembles that of **10**; however, **12** shows enhanced avidity *vis-à-vis* **10** toward Na^+, K^+, Rb^+, and Cs^+ picrates.

Introduction. Since crown ethers were first prepared in the 1960s,[1] a vast literature has accumulated which is concerned with their synthesis and with their applications (i) to the study of host-guest interactions (i. e., molecular recognition and inclusion phenomena) and (ii) to separation science.[2-4] Relatively few of the crown ethers which thus far have been synthesized contain a "cage" moiety which is part of the crown "backbone". Some representative structures of cage-functionalized crown ethers are shown in Scheme 1.[5-7] The cubane moiety in **1**[5] and the pentacyclic cage moiety in **3**[7] function in each case simply as a lipophilic "spacer". However, the oxygen atom which is contained in the oxatetracyclododecane moiety in **2** potentially can participate along with the other oxygen atoms in the crown ether moiety to form a 1:1 complex with a host ion or molecule.

Incorporation of the cage moiety into these crown ethers affects (i) their overall conformational mobility and (ii) their ability to serve as complexing ligands (relative to non cage-containing crown ethers) by introducing a measure of rigidity into the system. In addition, the cage moiety serves as a lipophilic component, thereby increasing the solubility of cage-containing crown ethers in nonpolar solvents.

It should be noted that some of the cage-functionalized crown ethers shown in Scheme 1 are not expected to be stable in aqueous acidic solution. Thus, **2**[6] contains two ketal moieties, and **3**[7] is a 1,7-dialkoxy substituted pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione (i. e., a substituted "PCU-8,11-dione"). "Push-pull" functionalized PCUs of the type **3** have been shown to undergo highly facile ring opening upon treatment with Lewis or protic acids).[8]

Scheme 1



1

2a (n = 0)
2b (n = 1)
2c (n = 2)
2d (n = 3)

3a (n = 1)
3b (n = 2)

As part of an extensive program which is involved with the synthesis and chemistry of novel polycarbocyclic cage compounds,[9] we have prepared three new crown ethers, **10-12**. Compounds **10** and **11** (Scheme 2) contain a 3,5-disubstituted-4-oxaheptacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane moiety as a rigidifying "spacer", whereas **12** (Scheme 3) contains an oxaadamantyl moiety which serves this same function. Crown ethers **10** and **11** do not contain a ketal moiety, nor are they "push-pull" functionalized in a manner that might render them particularly sensitive toward undergoing acid-promoted ring opening under mild conditions. As a result, they are expected to be stable in aqueous solution at low pH.

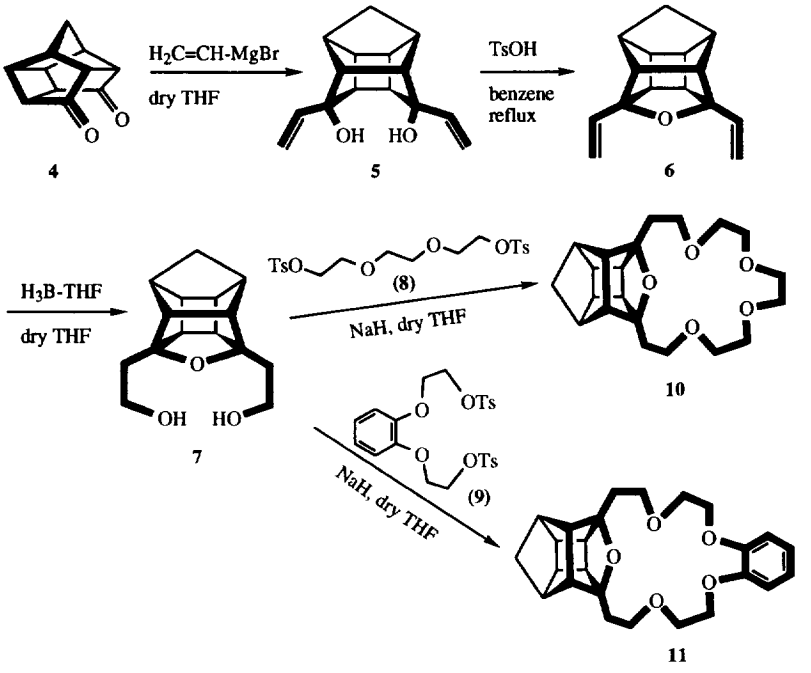
In addition, it should be noted that, due to symmetry considerations, simple monocyclic crown ethers lack facial differentiation, i. e., there is no distinction between approach by a guest ion or molecule toward the "topside" or "bottomside" of the approximate plane of the crown ether backbone. By way of contrast, the presence of the oxahexacyclic cage moiety in **10** and in **11** renders the crown ether "faces" inherently diastereotopically nonequivalent in each molecule.

Syntheses of 10 and 11. The method that was employed to prepare these novel cage-functionalized crown ethers is shown in Scheme 2. Thus, reaction of PCU-8,11-dione (**4**)[10] with excess vinylmagnesium bromide afforded the corresponding *endo*-8,*endo*-11 diol (**5**, 60%). Subsequent dehydration of diol **5** produced the corresponding hexacyclic ether, **6**. Hydroboration-oxidation[11] of **6** afforded the corresponding cage diol, **7**, in 85% yield.

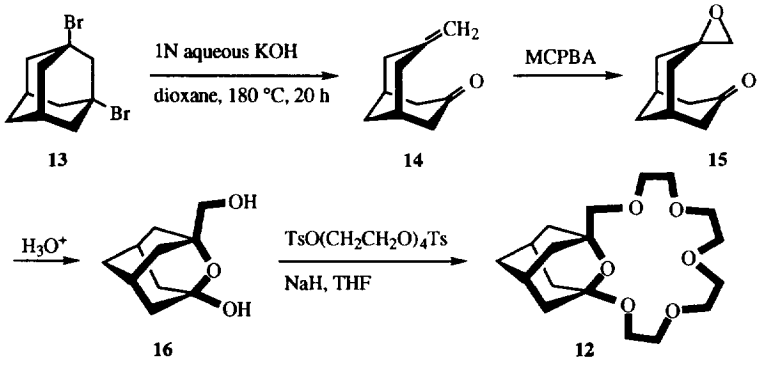
Cage-functionalized crown ethers **10** and **11** each were prepared from **7** by using Williamson syntheses. Thus, Na^+ templated reaction of the conjugate base of diol **7** with ditosylate **8** resulted in the formation of **10**, which possesses a 17-crown-5 skeleton, in 60% yield. Similarly, Na^+ templated reaction of the dianion derived from **7** with ditosylate **9** gave the corresponding benzo-17-crown-5 ether (**11**) in 62% yield.

Synthesis of 12. The method used to prepare [1,3-(2-oxaadamantano)]-17-crown-6 (**12**) is shown in Scheme 3. Thus, reaction of 1,3-dibromoadamantane[12] with aqueous KOH in dioxane solvent at 180 °C afforded 4-methylenebicyclo[3.3.1]nonan-7-one (**14**).[13] Subsequent oxidation of **14** with *m*-chloroperbenzoic acid (MCPBA) produced the corresponding oxirane (**15**, 95% yield).[14] Acid promoted cyclization of **15**[15] resulted in the formation of the corresponding oxaadamantanediol (**16**, 45% yield), which subsequently could be converted into crown ether **12** via a Na^+ templated, base promoted reaction with tetraethylene glycol ditosylate.

Scheme 2



Scheme 3



Alkali Metal Picrate Extraction Experiments. The extraction experiments were performed by using 5mM solutions of **10-12** in $CHCl_3$. Their relative extraction efficiencies toward alkali metal picrates were compared with the corresponding efficiencies of 15-crown-5, benzo-15-crown-5, and 18-crown-6 solutions, respectively, at the same concentration. The 15- and 18-crowns (rather than 17-crowns) were chosen for this purpose since they are commercially available and widely-used crown ethers whose extraction profiles can be

regarded profitably as being "industry standards". However, the same is not true for the corresponding 17-crowns, which are not readily available.

Alkali metal (Li^+, Na^+, K^+, Rb^+, and Cs^+) picrates were freshly prepared by reacting each of the respective alkali metal hydroxides, M^+OH^-, with picric acid.[16] Due to its high solubility in water and EtOH, Li^+ picrate was prepared *in situ* and subsequently used as thereby obtained. All other alkali metal picrates were isolated and then were dried prior to use. Subsequently, 5mM solutions of each alkali metal picrate were employed for the extraction experiments. Extraction profiles were examined by comparing absorption intensities of a blank (i. e., water-extraction of a $CHCl_3$ solution of the alkali metal picrate performed in the absence of added crown ether) and an experimental sample which consisted of a $CHCl_3$ solution of the crown ether host and alkali metal picrate. The extraction technique used in this study has been described elsewhere.[17,18] The extraction data obtained for the 15- and 18-crown standards in the present study agree closely with those reported in the literature.[17,18]

The results of the alkali metal picrate extraction experiments are shown in Table 1. Crown ether **10** displayed extraction characteristics toward Li^+, Rb^+, and Cs^+ picrates that are strikingly similar to those shown by 15-crown-5.[17] However, an important distinction is that **10** displayed 33% greater avidity toward Na^+ *vis-à-vis* 15-crown-5, and the corresponding extraction efficiency of **10** toward K^+ picrate is more than twice that of 15-crown-5 (see Table 1).

Table 1. Results of alkali metal extraction experiments.

	Percent of Picrate Extracted (%)[a]				
Host Molecule	**Li^+**	**Na^+**	**K^+**	**Rb^+**	**Cs^+**
15-crown-5	2.3 ± 0.2	13.9 ± 1.3	14.3 ± 0.3	9.6 ± 0.8	BLD[b]
10	2.8 ± 0.3	18.5 ± 1.0	29.0 ± 0.2	8.4 ± 1.3	BLD[b]
benzo-15-crown-5	BLD[b]	11.8 ± 1.8	19.3 ± 1.9	5.9 ± 1.2	4.1 ± 1.2
11	BLD[b]	10.6 ± 0.6	10.0 ± 1.8	5.7 ± 1.5	2.3 ± 1.2
18-crown-6	1.9 ± 0.8	4.5 ± 0.6	68.2 ± 0.6	56.6 ± 1.3	30.3 ± 0.9
12	2.4 ± 0.5	23.1 ± 0.7	39.7 ± 0.9	19.7 ± 1.2	7.5 ± 0.4

[a]Averages and standard deviations calculated for data obtained from three independent extraction experiments (15-crown-5, **10**, benzo-15-crown-5, and **11**) or from five independent extraction experiments (18-crown-6 and **12**). [b]BLD = Below limit of detection.

These results contrast markedly with the corresponding extraction characteristics of crown ether **11**. The alkali metal picrate extraction capabilities of **11** toward Li^+, Na^+, Rb^+, and Cs^+ closely parallel those for benzo-15-crown-5. However, **11** displayed decreased avidity toward K^+ picrate *vis-à-vis* that of benzo-15-crown-5 (see

data in Table 1). Comparison of the alkali metal picrate extraction ability of **10** with that of **11** indicates that they possess similar extraction capacities toward Li^+, Rb^+, and Cs^+ picrates. Crown ether **10** is noticeably superior to **11** in its ability to extract Na^+ and K^+ picrates; indeed, **10** is *ca.* three times more effective than **11** toward extraction of K^+.

Among the crown ethers included in the present study, the extraction characteristics of crown ether **12** most closely resemble those of **10** (Table 1). However, in comparison with the behavior of **10**, crown ether **12** displays enhanced avidity toward Na^+ (*ca.* 25%), K^+ (*ca.* 37%), Rb^+ (*ca.* 135%), and Cs^+. The results of a control experiment indicated that ketal **12** is stable to the conditions that were employed in the extraction studies (see the Experimental Section).

Summary and Conclusions. Efficient syntheses of three cage-functionalized crown ethers, **10-12**, have been developed. Crown ethers **10** and **11** have been prepared in four synthetic steps by starting with PCU-8,11-dione (**4**), a readily available starting material.[10] Crown ether **12** was synthesized via a four-step synthesis by starting with 1,3-dibromoadamantane.[12]

The alkali metal picrate extraction profiles of **10**, **11**, and **12** were examined. Crown ether **10** displays enhanced selectivity toward K^+ picrate extraction *vis-à-vis* that of 15-crown-5. The extraction profile of **12** most closely resembles that of **10** among the crown ethers studied; however, **12** displays enhanced avidity toward Na^+, K^+, Rb^+, and Cs^+ *vis-à-vis* **10**. Future studies will be directed toward structural modification of these unusual cage-functionalized crown ethers in an effort to produce more avid and more highly selective metal ion complexing agents.

Experimental Section

Melting points are uncorrected. Absorption intensities of alkali metal picrate solutions were measured at 374 nm by using a Hewlett-Packard Model 84524 Diode Array UV-visible spectrophotometer. An Orion Research Digital Ionalayzer/501 pH meter equipped with a glass electrode was used to obtain pH measurements of alkali metal picrate solutions at 25 °C. The pH meter was standardized at pH 4.0 and pH 7.0 against standard sodium phosphate buffer solutions. Elemental microanalyses were performed by personnel at M-H-W Laboratories, Phoenix, AZ.

***exo*-8-*exo*-11-Divinylpentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-*endo*-8-*endo*-11-diol (5).** To a solution of **4**[10] (1.00 g, 5.74 mmol) in dry THF (10 mL) under argon was added with stirring a 1 M solution vinylmagnesium bromide in dry THF (22.9 mL, 22.9 mmol). The resulting solution was stirred at ambient temperature for 3 h and then was heated to 50 °C and was stirred at that temperature for an additional 12 h. The reaction mixture was cooled to 0°C via application of an external ice-water bath, and the reaction was quenched via addition of cold saturated aqueous NH_4Cl (10 mL). The resulting aqueous suspension was extracted with EtOAc (3 x 30 mL), and the combined organic layers were washed with water (10 mL). The organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on silica gel by eluting with 20% EtOAc-CH_2Cl_2), thereby affording **5** (780 mg, 59%). Recrystallization of this material from CH_2Cl_2-hexane afforded analytically pure **5** as a colorless microcrystalline solid: mp 66-67 °C; IR (nujol) 3180 (m), 2980 (s), 1610 cm^{-1} (m); ^{1}H NMR ($CDCl_3$) δ 1.08 (d, J = 10.1 Hz, 1 H), 1.52 (d, J = 10.1 Hz, 1 H), 1.79-2.20 (m, 8 H), 4.90-5.22 (m, 4 H), 5.71-5.89 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 33.9 (t), 40.1 (d), 41.2 (d), 44.4 (d), 51.1 (d), 76.9 (s), 112.8 (t), 142.7 (d). Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.21; H, 8.00.

3,5-Divinyl-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (6). To a solution of **5** (1.00 g, 4.34 mmol) in dry benzene(30 mL) was added TsOH (81 mg, 0.43 mmol), and the resulting mixture was refluxed in a Dean-Stark apparatus until the distillate became clear (*ca.* 2 h). The layers in the distillate were separated, and the organic layer was washed sequentially with water (10 mL), 10% aqueous $NaHCO_3$ (10 mL), and water (10 mL). The organic layer was dried (MgSO4) and filtered, and the filtrate was concentrated *in vacuo*. The residue

thereby obtained was purified via column chromatography on neutral alumina by eluting with 1:1 CH_2Cl_2-hexane. Pure **6** (715 mg, 77%) was thereby obtained as an oil; bp 210-213 °C (1 mm Hg); IR (neat) 2985 (s), 1150 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.56 (d, J = 10.0 Hz, 1 H), 1.94 (d, J =10.0 Hz, 1 H), 2.50 (br s, 2 H), 2.72 (br s, 6 H), 5.08-5.32 (m, 4 H), 6.21-6.33 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 41.8 (d), 43.5 (t), 44.5 (d), 49.2 (d), 58.9 (d), 96.0 (s), 114.5 (t), 136.3 (d). Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.68; H, 7.50.

3,5-[2',2"-Bis(hydroxyethyl)]-4-oxahexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]dodecane (7). To a solution of **6** (610 mg, 2.87 mmol) in dry THF (20 mL) was added with stirring a 1 M solution of BH_3·THF in dry THF (2.84 mL, 2.84 mmol), and the resulting mixture was stirred at ambient temperature for 6 h. The reaction mixture was cooled to 0°C via application of an external ice-water bath. To this cooled mixture was added dropwise with stirring 30% aqueous NaOH (1 mL, 7.5 mmol) followed by 30% aqueous H_2O_2 (1.8 mL, excess). The resulting mixture then was heated to 40°C and was stirred at that temperature for 1 h. The reaction mixture was cooled and then was extracted with EtOAc (3 x 20 mL). The combined organic extracts were washed with water (10 mL), dried ($MgSO_4$), and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on silica gel by eluting with 30% EtOAc-hexane. Pure **7** (600 mg, 85%) was thereby obtained as a colorless microcrystalline solid: mp 153.0-153.5 °C; IR (nujol) 3320 (m), 2980 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.52 (d, J = 10.3 Hz, 1 H), 1.70-2.05 (m, 4 H), 2.28-2.69 (m, 9 H), 3.50-3.86 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 34.3 (t), 41.4 (d), 43.5 (t), 44.1 (d), 47.7 (d), 58.2 (d), 60.0 (t), 96.4 (s). Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.65; H, 8.06.

Crown Ether 10. To a suspension of NaH (21.5 mg, 0.85 mmol) in dry THF (5 mL) under argon was added dropwise a solution of **7** (86 mg, 0.43 mmol) in dry THF (15 mL), and the resulting solution was stirred at ambient temperature for 0.5 h. To the reaction mixture was added dropwise with stirring a solution of ditosylate **8** (195 mg, 0.43 mmol) in dry THF (25 mL) during 1 h. The resulting mixture was refluxed for 10 h, at which time the reaction mixture was concentrated *in vacuo*. Water (20 mL) was added to the residue, and the resulting aqueous suspension was extracted with CH_2Cl_2 (4 x 20 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on neutral alumina by eluting with 20% EtOAc-CH_2Cl_2. Pure crown ether **10** (90 mg, 60%) was thereby obtained as a colorless oil; IR (neat) 2980 (s), 1150 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.48 (d, J = 10.2 Hz, 1 H), 1.82 (d, J = 10.2 Hz, 1 H), 1.90-2.64 (m, 12 H), 3.56-3.80 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 32.3 (t), 41.4 (d), 43.5 (t), 43.8 (d), 48.1 (d), 58.8 (d), 68.3 (t), 70.2 (t), 70.8 (t), 71.5 (t), 94.5 (s). Anal. Calcd for $C_{21}H_{30}O_5$: C, 69.59; H, 8.34. Found: C, 69.70; H, 8.60.

Crown Ether 11. To a suspension of NaH (21 mg, 0.88 mmol) in dry THF (5 mL) under argon was added dropwise a solution of **7** (110 mg, 0.44 mmol) in dry THF (15 mL), and the resulting mixture was stirred at ambient temperature fo 0.5 h. To the reaction mixture was added dropwise with stirring a solution of ditosylate **9** (223 mg, 0.44 mmol) in dry THF (25 mL) during 1 h. The resulting mixture was refluxed for 14 h, at which time the reaction mixture was concentrated *in vacuo*. Water (15 mL) was added to the residue, and the resulting aqueous suspension was extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified via column chromatography on neutral alumina by eluting with 20% EtOAc-CH_2Cl_2. Pure crown ether **11** (112 mg, 62%) was thereby obtained as a colorless oil; IR (neat) 2985 (s), 1610 (w), 1130 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.40-2.78 (m, 14 H), 3.64-4.26 (m, 12 H), 6.80-7.00 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 34.3 (t), 41.4 (d), 43.5 (t), 43.9 (d), 48.3 (d), 59.1 (d), 69.0 (t), 69.25(t), 69.5 (t), 94.8 (s), 112.6 (d), 120.8 (d), 148.8 (s). Anal Calcd. for $C_{25}H_{30}O_5$: C, 73.15; H, 7.37. Found: C, 73.23; H, 7.15.

1-Hydroxy-3-hydroxymethyl-2-oxaadamantane (16). To a suspension of **15**[14] (1.01 g, 6.1 mmol) in water (25 mL) was added 70% $HClO_4$ (0.25 mL, catalytic amount), and the resulting mixture was stirred at ambient temperature for 3 h. The reaction mixture then was neutralized via careful, dropwise addition of saturated aqueous $NaHCO_3$, and the resulting aqueous suspension was extracted with $CHCl_3$ (3 x 20 mL). The combined organic extracts were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. Compound **16** (500 mg, 45%) was thereby obtained as a colorless microcrystalline solid: mp 114-116 °C (lit.[15] mp 116-117 °C); IR (KBr) 3350 (s), 3220 (s), 2930 (s), 2910 (s), 2870 (m), 1370 (m), 1340 (m), 1140 (s), 1075 (s), 1045 (s), 1015 (s), 990 (s), 910 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.38 (d, J = 12.3 Hz, 2 H), 1.72-1.81 (m, 8 H), 2.36 (br s, 2 H), 2.89 (br s, 1 H), 3.41 (s, 2 H), 3.89 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.8 (d), 34.1 (t), 35.0 (t), 40.8 (t), 69.2 (t), 77.1 (s), 94.8 (s). This material was used as obtained in the next synthetic step without additional purification or characterization.

Crown Ether 12. Sodium hydride (1.28 g, 26.7 mmol), obtained as a 50% suspension of NaH in mineral oil), was washed with pentane (3 x 40 mL) under nitrogen to remove the mineral oil. The pentane was decanted after the last washing, and dry THF (300 mL) was added under nitrogen to the residue. The resulting suspension was heated to reflux; to this refluxing mixture was added dropwise a solution of **16** (480 mg, 2.63 mmol) and tetrethylene glycol ditosylate (1.31 g, 2.63 mmol) in dry THF (200 mL) during 16 h. After dropwise addition of these reagents had been completed, the resulting mixture was refluxed for an additional four-day period. The reaction mixture was allowed to cool gradually to ambient temperature, and excess NaH was destroyed via careful, dropwise addition of water (*ca.* 2 mL). The resulting mixture was filtered, and the filtrate was concentrated *in vacuo*. Water (200 mL) was added to the residue, and the resulting aqueous suspension was extracted with CH_2Cl_2 (4 x 50 mL). The combined organic extracts were dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. The residue thereby obtained, a yellow oil, was purified via column chromatography on alumina (activated, grade I) by eluting with 2% MeOH-CH_2Cl_2. Pure **12** (530 mg, 60%) was thereby obtained as a colorless oil: bp 140 °C (10^{-3} mm Hg); IR (KBr) 2920 (s), 2860 (s), 1470 (m), 1450 (m), 1350 (m), 1295 (m), 1250 (m), 1180 (m), 1100 (br, s), 990 (m) 945 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.34 (d, J = 13.0 Hz, 2 H), 1.61 (d, J = 12.4 Hz, 2 H), 1.73 (br s, 2 H), 1.79 (d, J = 13.0 Hz, 2 H), 1.89 (d, J = 12.4 Hz, 2 H), 2.36 (br s, 2 H), 3.36 (s, 2 H), 3.60-3.86 (m, 16 H); ^{13}C NMR ($CDCl_3$) δ 28.7 (d, 2 C), 34.7 (t), 35.3 (t, 2 C), 38.3 (t, 2 C), 60.0 (t), 69.9 (t), 70.4 (t, 2 C), 70.6 (t, 2 C), 70.7 (t), 71.1 (t), 76.3 (s), 77.5 (t), 96.5 (s). Anal. Calcd for $C_{18}H_{30}O_6$: C, 63.14; H, 8.83. Found: C, 63.19; H, 8.91.

Alkali Metal Picrate Extraction Experiments. The procedure that was used for this purpose has been described elsewhere.[18] In view of the fact that **12** contains a ketal linkage, it was deemed necessary to perform a control experiment to establish whether or not this crown ether is stable to the conditions employed in the extraction experiments. To this end, a 4.96 mM solution of **12** in $CHCl_3$ was prepared by dissolving **12** (27 mg, 0.079 mmol) in $CHCl_3$ (15.9 mL; the $CHCl_3$ used in the control experiment had been washed previously with deionized water). A 5.0 mM solution of Li^+ picrate was prepared by dissolving $LiOH·H_2O$ (130 mg, 3.1 mmol) in deioinized water (25.00 mL). To an aliquot of this solution (1.00 mL, 0.04 mmol) was added picric acid (28.6 mg, 0.125 mmol), and the resulting solution was diluted with deionized water to a total volume of 25.00 mL, thereby affording a solution which contains $LiOH·H_2O$ (5.2 mg, 0.124 mmol) and picric acid (28.6 mg, 0.125 mmol). The pH of the resulting solution was measured and was found to be 7.2.

Equal volumes of the two solutions were placed in screw-top vials and then were shaken mechanically for 1 h. The sample vials were removed from the shaker apparatus and were allowed to stand at ambient temperature for an additional 1 h. The contents of each sample vial were placed in a separatory funnel, and the layers were separated. In each case, the organic layer was dried ($MgSO_4$) and filtered, and the filtrate was concentrated *in vacuo*. Each residue thereby obtained was dried *in vacuo* (*ca.* 0.01 mm Hg) for 12 h. The IR spectrum of each sample then was examined; in each case, no absorption band was found in the region 3200-3600 cm^{-1} (O-H stretching vibration). Analysis of their respective ^1H and ^{13}C NMR spectra (obtained in $CDCl_3$ solution) indicated that only starting material (i. e., unreacted **12**) had been recovered.

A second control experiment was performed by using a 5.0 mM solution of Na^+ picrate which had been prepared by dissolving previously synthesized,[16] isolated, and dried Na^+ picrate (31.4 mg, 0.125 mmol) in deionized water (25.00 mL). The pH of the resulting solution was measured and was found to be 7.2. Equal volumes of the Na+ picrate solution and a 4.96 mM solution of **12** in $CHCl_3$ (*vide supra*) were subjected to the procedure described above. Inspection of the IR, ^1H NMR, and ^{13}C NMR spectra obtained for each residue revealed that only recovered **12** had been isolated. On the basis of the foregoing observations, we conclude that **12** is stable to the conditions employed in both the Li^+ and Na^+ picrate extraction experiments, and we infer that it most likely is stable to the conditions employed in the remaining alkali metal picrate extraction experiments as well.

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