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Synthetic routes are established for the preparation of hydroxymethyl-substituted diazacrowns and cryptands with systematically varied cavity sizes.

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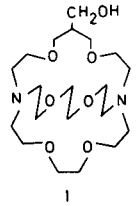
Crown ethers which bear synthetically-versatile hydroxymethyl groups are important synthetic intermediates for crown ether immobilization on polymers [1] and transformations into more complex crown compounds such as lariat crown ethers [2], ionizable crown ethers [3], biscrowns [4], and chromogenic crown ethers [5]. In contrast to the hydroxymethyl-substituted crown ethers, very little information is available concerning similarly-functionalized ligands which contain nitrogen heteroatoms in cyclic and bicyclic ring systems. Thus, no example of a diazacrown (Kryptofix®) molecule with a pendant hydroxymethyl group has been reported. Furthermore, known hydroxymethyl-functionalized cryptands are limited to compounds **1** and **2** which have been described by Tomoi [6] and Montanari [1b,7], respectively. Through their hydroxymethyl groups, **1** and **2** were bound to polymer matrices or lipophilized to provide novel phase-transfer catalysts [1b,6,7].

Due to the widespread interest in diazacrown and cryptand compounds for metal ion complexation in a variety of applications, establishment of general methods by which hydroxymethyl-substituted diazacrowns and cryptands could be prepared was undertaken. We now report viable synthetic routes to three novel hydroxymethyl-substituted diazacrowns and four hydroxymethyl-functionalized cryptands in which the cavity sizes are systematically varied.



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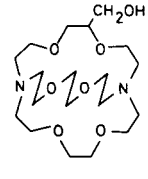

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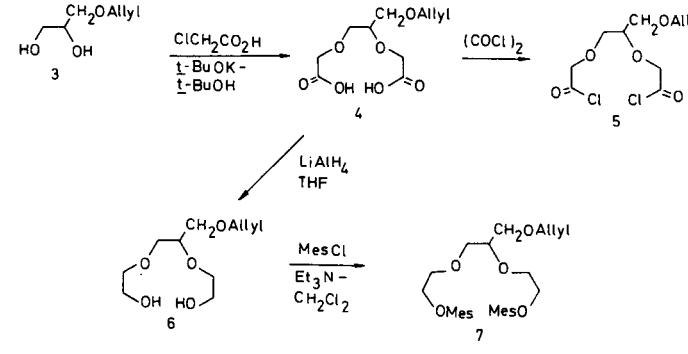
Results and Discussion.

Readily-available, allyl-protected glycerol **3** [2b,8] was the starting material for the preparation of diacid chloride **5** which was a key intermediate in the synthesis of the hydroxymethyl-substituted diazacrowns and cryptands [9]. The synthetic route to **5** is summarized in Scheme 1. Reaction of diol **3** with potassium *t*-butoxide and chloroacetic



Scheme 1

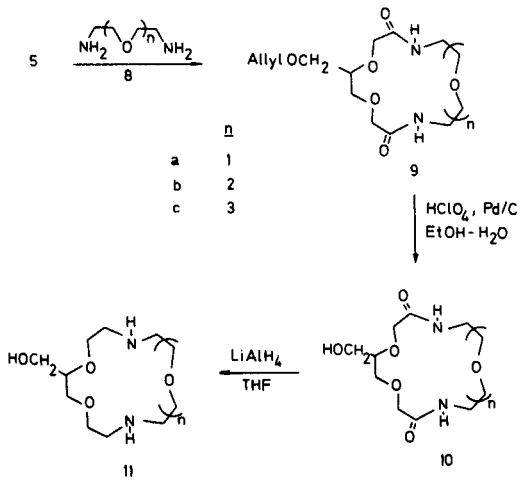
acid in *t*-butyl alcohol followed by careful workup and the use of high vacuum during distillation to prevent acid-catalyzed polymerization of the product provided a 55% yield of diacid **4**. Treatment of **4** with oxalyl chloride gave a quantitative yield of the desired diacid chloride **5**. In addition, reduction of **4** with lithium aluminum hydride in tetrahydrofuran afforded diol **6** in 80% yield. Mesylation of **6** proceeded in almost quantitative yield to produce dimesylate **7**.

Hydroxymethyl Diazacrowns.

The synthetic route to three novel hydroxymethyl diazacrowns is depicted in Scheme 2. Diacid chloride **5** was reacted with diamines **8a-c** [10,11] under high dilution conditions in the presence of triethylamine to form the (allyloxy)methyl-substituted cyclic diamides **9a-c** in yields of 43, 51, and 54%, respectively. Deprotection of **9a-c** by isomerization of the allyl groups with palladium on carbon followed by acid-catalyzed cleavage [12] gave the hydroxymethyl-substituted cyclic diamides **10a-c** in good yields (74-81%). The hydroxymethyl diazacrowns **11a-c** were obtained by reduction of **10a-c** with lithium aluminum hydride in tetrahydrofuran in good yields (73-78%). New compounds **9a-c**, **10a-c** and **11a-c** were fully characterized by ir and nmr spectra and by elemental analysis.

Due to the presence of rigidifying amide groups, the (allyloxy)methyl- and hydroxymethyl-substituted cyclic diamides **9** and **10** exhibit interesting ir and nmr spectral behavior. For the former, non-equivalence of the two amide protons is evident in the nmr spectra. For **9a** the N-H pro-

tons appear as two overlapping, broad absorptions with peaks at δ 7.13 and 7.20. As the ring size is increased in **9b**, the separation between the overlapping, broad absorptions becomes larger (peaks at δ 7.10 and 7.30). Then for **9c** the broad absorptions move downfield and become



Scheme 2

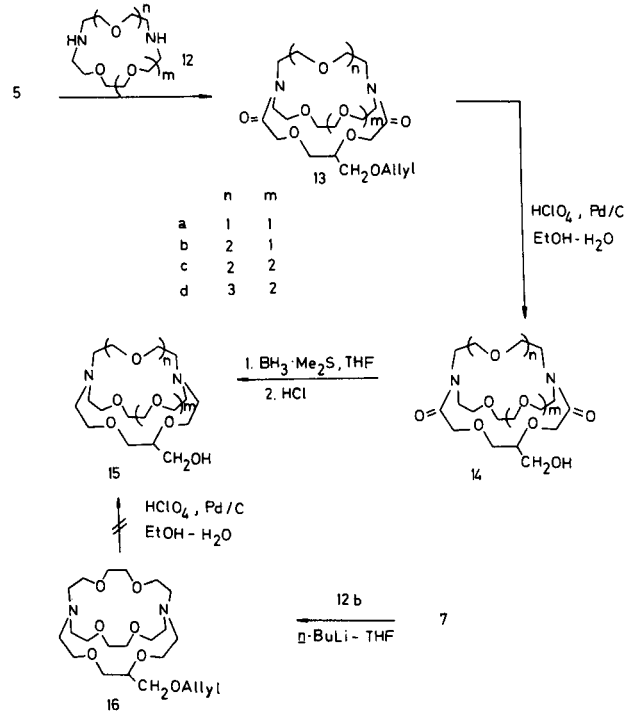
completely separated with peaks at δ 7.29 and 7.61. Differences in the N-H stretching absorptions for **9a-c** are also evident in their ir spectra. Thus, the N-H stretching absorptions for **9a** consist of a peak at 3418 cm^{-1} with a shoulder at ≈3370 cm^{-1} which changes to two clearly-defined absorptions at 3423 (stronger) and 3367 cm^{-1} (weaker) for **9b**. For **9c** the relative intensities of the two absorptions reverse with a weaker band at 3423 cm^{-1} and a stronger one at 3354 cm^{-1}. The carboxyl stretching absorptions for all three compounds appear at 1679 ±5 cm^{-1}.

For the hydroxymethyl-substituted cyclic diamides, the amide proton absorptions in the nmr spectra are broad single absorptions for **10a** (δ 6.95-7.5) and **10b** (δ 7.2-7.6); whereas for **10c** there are two broad, downfield absorptions with peaks at δ 7.61 and 8.14. Compared with **9a-c** the carbonyl stretching absorptions are lower by 10-15 cm^{-1} in the ir spectra of **10a-c**. This suggests the presence of intra- and/or intermolecular hydrogen-bonding interactions of the alcohol and amide carbonyl groups in the latter.

Hydroxymethyl Cryptands.

Under high dilution conditions, diacid chloride **5** was cyclized with diazacrowns **12a-d** in the presence of triethylamine to produce the (allyloxy)methyl cryptand diamides **13a-d** in yields of 61, 72, 52 and 58% respectively (Scheme 3). The allyl protecting groups of **13** were removed by the same isomerization-cleavage reaction sequence which was used to deprotect the (allyloxy)methyl diazacrowns **10**. The hydroxymethyl cryptand diamides **14a-d** were obtained in good to excellent yields (70-99%). Reduction of **14** with borane-dimethyl sulfide complex in tetrahydrofuran gave fair to good yields (42-72%) of hydroxymethyl cryptands **15a-d**.

In an attempted alternative approach to hydroxymethyl cryptand **15c**, diaza-18-crown-6 (**12c**, Kryptofix 2.2®) was reacted with *n*-butyl lithium and dimesylate **7** using a reported general method [13] to provide the (allyloxy)methyl cryptand **16** in 24% yield. Attempted removal of the allyl group from **16** under conditions which had affected deprotection of **9** and **13** was unsuccessful. Recovery of **16** unchanged indicates poisoning of the palladium on carbon catalyst by the basic cryptand nitrogen atoms which prevents isomerization of the allyl ether group to a 2-methylfinyl ether function. The lack of reactivity of **16** provides additional support for our recent observations concerning palladium catalyst poisoning by amines [14].



Scheme 3

New compounds **13a-d**, **14a-d**, **15a-d** and **16** were fully characterized by ir and nmr spectra, by elemental analysis, and, in most cases, by mass spectra.

A general characteristic of compounds **13**, **14** and **15** is their high propensity for strong coordination of neutral, polar molecules, such as water and chlorinated hydrocarbons. Thus all of these compounds were found to be very hygroscopic. Even after drying at elevated temperatures under vacuum following purification and again before combustion analysis, the viscous oils **13a** and **13d** analyzed as monohydrates and **15d** as a dihydrate. The hydroxymethyl cryptand diamides **14a-d** were difficult to free

from the chloroform which was a component of the chromatographic eluent. Although extended evacuation with heating after chromatography and then again before combustion analysis freed crystalline **14a** and the viscous oil **14c** of chloroform, the analysis results for viscous oils **14b** and **14d** were consistent with partial chloroform solvates. Hydroxymethyl cryptand **15a** formed a crystalline 1:1 solvate with chloroform. Others have noted the strong binding of chloroform by certain crown compounds [15].

EXPERIMENTAL

The ir spectra were obtained on neat samples (unless specified otherwise) with a Nicolet MX-S spectrometer. The nmr spectra were recorded with Varian EM360A or EM360 spectrometers and chemical shifts are reported in parts per million (δ) downfield from tetramethylsilane. Mass spectra were obtained on a Hewlett Packard 5995-B GC/MS instrument. Melting points were taken with either a Mel-Temp or Fisher-Johns melting point apparatus and are uncorrected. Elemental analysis was performed by Galbraith Laboratories, Inc. of Knoxville, Tennessee.

Unless specified otherwise reagent grade reactants and solvents were obtained from chemical suppliers and used as received. Tetrahydrofuran was purified by distillation from lithium aluminum hydride. The 3-(allyl)-oxy-1,2-propanediol (**3**) [2b,8], diamines **8a-c** [11] and diazacrowns **12c,d** [10] were prepared by known methods. Tetraglycolic acid, an intermediate in the synthesis of **12d**, was prepared by oxidation of tetramethylene glycol with nitric acid [10] and purified *via* its diethyl ester followed by acid-catalyzed hydrolysis [16].

3,6-Dioxa-4-(allyl)oxymethyl-1,8-octanedioic Acid (**4**).

To a solution of potassium *t*-butoxide (149.2 g, 1.33 moles) in *t*-butyl alcohol (1.1 *l*) was added 3-(allyl)oxy-1,2-propanediol (**3**, 43.8 g, 0.33 mole) under nitrogen. After stirring for 1 hour at room temperature, a solution of chloroacetic acid (62.6 g, 0.66 mole) in *t*-butyl alcohol (250 ml) was added dropwise over 2 hours at reflux. The mixture was stirred and refluxed for 18 hours and the solvent was removed *in vacuo*. The residue was dissolved in a small amount of water and the aqueous solution was extracted with diethyl ether (2 × 200 ml) and acidified with 6 *N* hydrochloric acid. The solution was extracted with ethyl acetate (5 × 200 ml) saturating the aqueous layer with sodium chloride between extractions. The combined extracts were washed with brine (100 ml) and dried over magnesim sulfate. Evaporation of the solvent *in vacuo* followed by vacuum distillation gave 44.9 g (55%) of **5** as a pale yellow viscous oil: bp 210-212°/0.007 Torr; ir (neat): 3700-2300 (COOH), 1651 (C=C), 1118 (C-O) cm^{-1}; nmr (dueteriochloroform): δ 3.3-4.7 (m, 11), 5.0-5.5 (m, 2), 5.6-6.3 (m, 1), 11.09 (s, 2).

Anal. Calcd. for $C_{10}H_{16}O_7 \cdot H_2O$: C, 45.10; H, 6.81. Found: C, 45.32; H, 6.76.

3,6-Dioxa-4-[(allyloxy)methyl]-1,8-octanedioic Acid Dichloride (**5**).

To a solution of diacid **4** (2.25 g, 9.06 mmoles) in 20 ml of benzene was added oxalyl chloride (10.7 g, 84.0 mmoles) and 3 drops of pyridine. The mixture was stirred for 72 hours at room temperature, then filtered and the solvent was removed *in vacuo*. The excess oxalyl chloride was removed by coevaporation with 4 portions of benzene to afford 3.0 g (100%) of **5** as a yellow oil; nmr (deuteriochloroform): δ 3.4-4.1 (m, 7), 4.48 (s, 2), 4.63 (s, 2), 5.0-5.45 (m, 2), 5.55-6.25 (m, 1).

3,6-Dioxa-4-[(allyloxy)methyl]-1,8-octanediol (**6**).

A solution of diacid **4** (6.26 g, 25.2 mmoles) in 20 ml of tetrahydrofuran was added dropwise to a suspension of lithium aluminum hydride (2.10 g, 53.3 mmoles) in tetrahydrofuran (40 ml). The reaction mixture was refluxed for 3 hours, cooled, and water (2 ml), 15% aqueous sodium hydroxide (2 ml) and water (6 ml) were added consecutively and the mixture was allowed to stand overnight at room temperature. The inorganic salts were filtered and washed with hot tetrahydrofuran several times. The combined filtrate and washings were evaporated *in vacuo* and the residue was vacuum distilled to produce 4.4 g (80%) of a colorless oil with bp 148-150°/0.2 Torr; ir (neat): 3406 (OH), 1647 (C=C), 1124 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.4-4.2 (m, 15), 5.0-6.3 (m, 3).

Anal. Calcd. for $C_{10}H_{20}O_5$: C, 54.53; H, 9.15. Found: C, 54.21; H, 9.16.

Dimesylate of 3,6-Dioxa-4-[(allyloxy)methyl]-1,8-octanediol (**7**).

A solution of diol **6** (4.00 g, 18.2 mmoles) and triethylamine (5.90 g, 58.3 mmoles) in dichloromethane (80 ml) was cooled to −10° and mesyl chloride (5.10 g, 44.2 mmoles) in 80 ml of dichloromethane was added dropwise. The mixture was stirred at 0° for 1 hour, diluted with cold dichloromethane (100 ml), and washed with 5% hydrochloric acid, then water, then 5% aqueous sodium carbonate, and then with water again. After drying over magnesium sulfate and evaporation of the solvent *in vacuo*, crude **7** was obtained. Final purification on a short silica gel column with dichloromethane-ethanol (100:1) as eluent afforded 6.7 g (98%) of a colorless oil; ir (neat): 1645 (C=C), 1350, 1173 (S=O), 1128, 1107 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.05 (s, 6), 3.3-4.5 (m, 15), 5.0-6.3 (m, 3).

Anal. Calcd. for $C_{12}H_{24}O_9S_2$: C, 38.29; H, 6.43. Found: C, 38.05; H, 6.32.

General Procedure for the Synthesis of (Allyloxy)methyl-substituted Cyclic Diamides **9a-c**.

The appropriate diamine (15.0 mmoles) and triethylamine (4.14 g, 40.9 mmoles) in 85 ml of toluene (Solution A) and the diacid chloride **5** (4.28 g, 15.0 mmoles) in 85 ml of toluene (Solution B) were added simultaneously to 250 ml of vigorously-stirred toluene at 0-5° during 8 hours under nitrogen. After the addition was completed, the mixture was stirred overnight at room temperature. Solid material was filtered and washed with toluene. The combined filtrate and washings were evaporated *in vacuo* and the residue was purified by column chromatography on alumina with chloroform as eluent to afford the analytically pure product **9**.

(Allyloxy)methyl diamide **9a** was prepared from 1.56 g of **8a** in 43% yield as a colorless hygroscopic oil; ir (neat): 3418 (NH), 1680 (C=O,C=C), 1128 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.0-4.5 (m, 19), 5.0-5.5 (m, 2), 5.6-6.25 (m, 1), 7.10 (br s, 2); ms: 316.4 (M^+).

Anal. Calcd. for $C_{14}H_{24}N_2O_6 \cdot 0.5\ H_2O$: C, 51.68; H, 7.74. Found: C, 51.57; H, 7.38.

(Allyloxy)methyl diamide **9b** was obtained from 1.78 g of **8b** in 51% yield as white crystals with mp 89-91°; ir (deposit): 3423, 3367 (NH), 1682 (C=O,C=C), 1114 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.1-4.2 (m, 23), 4.95-5.4 (m, 2), 5.5-6.1 (m, 1), 6.85-7.5 (m, 2); ms: 360.4 (M^+).

Anal. Calcd. for $C_{16}H_{28}N_2O_7$: C, 53.32; H, 7.83. Found: C, 53.08; H, 7.60.

(Allyloxy)methyl diamide **9c** was synthesized from 2.48 g of **8c** in 54% yield as a viscous colorless oil; ir (neat): 3423, 3354 (NH), 1674 (C=O,C=C), 1120 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.1-4.45 (m, 27), 5.0-5.5 (m, 2), 5.6-6.25 (m, 1), 7.29 (br s, 1), 7.61 (br s, 1); ms: 404.5 (M^+).

Anal. Calcd. for $C_{18}H_{32}N_2O_8$: C, 53.45; H, 7.98. Found: C, 53.12; H, 8.33.

General Procedure for the Synthesis of Hydroxymethyl-substituted Cyclic Diamides **10a-c**.

To a solution of the (allyloxy)methyl-substituted cyclic diamide **9** (5.4 mmoles) in a 1:1 (v/v) mixture of water and ethanol (12 ml) was added 5% palladium on carbon (0.15 g) and perchloric acid (0.12 ml). The mixture was stirred and heated at 80° for 24 hours.

The catalyst was removed by filtration and the filtrate was made basic with 25% aqueous ammonium hydroxide. The solvent was evaporated *in vacuo* and the residue was purified by column chromatography on alumina with chloroform-ethanol (50:1) as eluent to give pure **10**.

Hydroxymethyl diamide **10a** was obtained from 2.11 g of **9a** in 74% yield as white crystals with mp 110-112°; ir (film): 3410 (NH, OH), 1666 (C=O), 1128 (C=O) cm^{-1}; nmr (deuteriochloroform): δ 2.9-4.5 (m, 18), 7.20 (br s, 2).

Anal. Calcd. for $C_{11}H_{20}N_2O_6$: C, 47.82; H, 7.30. Found: C, 47.69; H, 7.39.

Hydroxymethyl diamide **10b** was prepared from 1.95 g of **9b** in 77% yield as white crystals with mp 91.5-92.5°; ir (deposit): 3445, 3360 (NH, OH), 1670, 1653 (C=O), 1126 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.3-3.9 (m, 18), 4.00 (s, 2), 4.10 (s, 2), 7.43 (br s, 2).

Anal. Calcd. for $C_{13}H_{24}N_2O_7$: C, 48.74; H, 7.55. Found: C, 48.45; H, 7.48.

Hydroxymethyl diamide **10c** was synthesized from 2.60 g of **9c** in 81% yield as white crystals with mp 76-77°; ir (deposit): 3348 (NH, OH), 1668 (C=O), 1116 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 3.1-4.5 (m, 26), 7.61 (br s, 1), 8.14 (br s, 1).

Anal. Calcd. for $C_{15}H_{18}N_2O_8$: C, 49.49; H, 7.74. Found: C, 49.24; H, 7.53.

General Procedure for the Synthesis of Hydroxymethyl Diazacrowns **11a-c**.

To a suspension of lithium aluminum hydride (0.87 g, 23.0 mmoles) in 25 ml of tetrahydrofuran was added in small portions the appropriate hydroxymethyl diamide **10** (3.0 mmoles) and the mixture was refluxed for 25 hours. After cooling, 2 ml of 5% aqueous sodium hydroxide was added dropwise and the mixture was stirred overnight at room temperature. Solid material was removed by filtration and the filtered material was washed several times with hot tetrahydrofuran. The combined filtrate and washings were evaporated *in vacuo* and the residue was purified by chromatography on alumina with chloroform-ethanol (25:1) as the eluent to afford **11**.

Hydroxymethyl diazacrown **11a** was prepared from 1.21 g of **10a** in 78% yield as a white waxy, extremely hygroscopic solid with mp 47-49°; ir (neat): 3315, 3180 (NH, OH), 1118 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.35-3.1 (m, 8), 3.15-4.1 (m, 16).

Anal. Calcd. for $C_{11}H_{24}N_2O_4 \cdot 0.75\ H_2O$: C, 50.46; H, 9.82. Found: C, 50.13; H, 9.74.

Hydroxymethyl diazacrown **11b** was synthesized from 0.97 g of **10b** in 75% yield as an extremely hygroscopic, colorless plates; ir (neat): 3313, 3213 (NH, OH), 1116 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.35-3.15 (m, 11), 3.4-3.95 (m, 17).

Anal. Calcd. for $C_{13}H_{28}N_2O_5 \cdot 1.25\ H_2O$: C, 49.59; H, 9.76. Found: C, 49.53; H, 9.70.

Hydroxymethyl diazacrown **11c** was obtained from 1.73 g of **10c** in 73% yield as a viscous colorless oil; ir (neat): 3312; 3200 (NH, OH), 1120 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.6-3.1 (m, 11), 3.3-4.0 (m, 21).

Anal. Calcd. for $C_{15}H_{32}N_2O_6$: C, 53.55; H, 9.59. Found: C, 53.36; H, 9.48.

General Procedure for the Synthesis of (Allyloxy)methyl Cryptand Diamides **13a-d**.

Under nitrogen, diacid chloride **5** (2.61 g, 9.2 mmoles) in 110 ml of toluene (Solution A) and the appropriate diazacrown **12** (9.2 mmoles) and triethylamine (2.50 g, 24.7 mmoles) in 110 ml of toluene (Solution B) were simultaneously added during 7 hours to 350 ml of vigorously stirred toluene at 0°. The mixture was stirred overnight at room temperature. The solid precipitate was filtered and washed with toluene. The combined filtrate and washings were evaporated *in vacuo* and the residue was purified by column chromatography on alumina with ethyl acetate-methanol (40:1) as eluent afforded **13**.

(Allyloxy)methyl cryptand diamide **13a** was obtained from 2.00 g of **2a** in 61% yield as a hygroscopic, colorless, viscous oil; ir (neat): 1645-1658 (C=O,C=C), 1120 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.3-5.45 (m, 33), 5.5-6.25 (m, 1); ms: 430.4 (M^+).

Anal. Calcd. for $C_{20}H_{34}N_2O_8 \cdot H_2O$: C, 53.56; H, 8.09. Found: C, 53.45; H, 8.13.

(Allyloxy)methyl cryptand diamide **13b** was prepared from 2.00 g of **12b** in 72% yield as a pale yellow oil; ir (neat): 1651 (C=O, C=C), 1120 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.4-5.45 (m, 37), 5.55-6.25 (m, 1).

Anal. Calcd. for $C_{22}H_{38}N_2O_9$: C, 55.68; H, 8.07. Found: C, 55.40; H, 8.03.

(Allyloxy)methyl cryptand diamide **13c** was synthesized from 3.00 g of **12c** in 52% yield as a colorless viscous oil; ir (neat): 1651 (C=O, C=C), 1120 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.3-4.95 (m, 39), 5.0-5.45 (m, 2), 5.6-6.3 (m, 1); ms: 518.5 (M^+).

Anal. Calcd. for $C_{24}H_{42}N_2O_{10}$: C, 55.58: H, 8.16. Found: C, 55.92; H, 8.29.

(Allyloxy)methyl cryptand diamide **13d** was obtained from 2.65 g of **12d** in 58% yield as a hygroscopic, colorless, viscous oil; ir (neat): 1651 (C=O, C=C), 1147-1054 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.4-4.95 (m, 43), 5.0-5.5 (m, 2), 5.6-6.3 (m, 1); ms: 562.7 (M^+).

Anal. Calcd. for $C_{26}H_{46}N_2O_{11} \cdot H_2O$: C, 53.77; H, 8.33. Found: C, 53.81; H, 8.26.

General Procedure for the Synthesis of Hydroxymethyl Cryptand Diamides **14a-d**.

To a solution of the (allyloxy)methyl cryptand diamide **13** (5.5 mmoles) in 11 ml of a 1:1 (v/v) mixture of ethanol and water was added 5% palladium on carbon (0.16 g) and 0.1 ml of perchloric acid. The mixture was stirred and heated at 80° for 24 hours. After filtration to remove the catalyst, the filtrate was neutralized with aqueous ammonium hydroxide, evaporated *in vacuo*, and the residue was chromatographed on alumina with chloroform-ethanol (20:1) as eluent to afford **14**.

Hydroxymethyl cryptand diamide **14a** was prepared from 2.35 of **13a** in 99% yield as white crystals with mp 178-179°; ir (deposit): 3418 (OH), 1651 (C=O), 1118 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.4-5.3 (m, 30); ms: 390.4 (M^+).

Anal. Calcd. for $C_{17}H_{30}N_2O_8$: C, 52.59; H, 7.75. Found: C, 52.61; H, 7.78.

Hydroxymethyl cryptand diamide **14b** was obtained from 2.00 g of **13c** in 70% yield as a viscous colorless oil; ir (neat): 3400 (OH), 1651-1633 (C=O), 1114 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.5-5.2 (m, 34); ms: 434.3 (M^+).

Anal. Calcd. for $C_{19}H_{34}N_2O_9 \cdot 0.4\ CHCl_3$: C, 48.31; H, 7.19. Found: C, 48.56; H, 7.32.

Hydroxymethyl cryptand diamide **14c** was synthesized from 2.30 g of **13c** in 90% yield as a colorless viscous oil; ir (neat): 3400 (OH), 1651 (C=O), 1109 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.5-5.0 (m, 38); ms: 478.5 (M^+).

Anal. Calcd. for $C_{21}H_{38}N_2O_{10}$: C, 52.70; H, 8.00. Found: C, 52.52; H, 6.95.

Hydroxymethyl cryptand diamide **14d** was prepared from 2.15 g of **13d** in 85% yield as a pale yellow oil; ir (neat): 3373 (OH), 1643 (C=O), 1116 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.6-4.9 (m, 42); ms: 522.6 (M^+).

Anal. Calcd. for $C_{23}H_{42}N_2O_{11} \cdot 0.3\ CHCl_3$: C, 50.11; H, 7.63. Found: C, 49.83; H, 7.84.

General Procedure for the Synthesis of Hydroxymethyl Cryptands **15a-d**.

To a solution of the hydroxymethyl cryptand diamide **14** (5.4 mmoles) in 10 ml of tetrahydrofuran was added dropwise 20 ml of 1 *M* borane-dimethyl sulfide complex and the mixture was refluxed for 9 hours.

Water (5 ml) was added slowly and the solvent was evaporated *in vacuo* to give a white solid which was treated with 6 *N* hydrochloric acid (15 ml) and water (10 ml). The resulted solution was refluxed for 12 hours, then aqueous ammonium hydroxide was added to adjust the *p*H to 10 and the solvent was removed *in vacuo*. The residue was dissolved in a small amount of methanol and the inorganic material was precipitated by addition of diethyl ether. After filtration of the precipitate, the filtrate was concentrated and purified by column chromatography on alumina with chloroform-methanol (25:1) as the eluent to afford pure **15**.

Hydroxymethyl cryptand **15a** was obtained from 2.10 g of **14a** in 46% yield as a pale-orange solid, mp 104-110°; ir (deposit): 3474, 3398, 3273 (OH), 1120-1091 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.2-3.2 (m, 12), 2.3-4.0 (m, 21), 5.35 (br s, 1); ms: 362.4 (M^+).

Anal. Calcd. for $C_{17}H_{34}N_2O_6 \cdot CHCl_3$: C, 44.87; H, 7.32. Found: C, 44.88; H, 7.66.

Hydroxymethyl cryptand **15b** was prepared from 1.35 g of **14b** and isolated as a sodium tetrafluoroborate complex in 72% yield. Spectral data for the complex were in agreement with those reported in the literature [1b].

Hydroxymethyl cryptand **15c** was synthesized from 1.60 g of **14c** in 69% yield as a colorless oil; ir (neat): 3300 (OH), 1105 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.5-3.0 (m, 12), 3.30 (br s, 1), 3.4-4.0 (m, 29); ms: 450.6 (M^+).

Anal. Calcd. for $C_{21}H_{42}N_2O_8$: C, 55.98; H, 9.40. Found: C, 55.74; H, 9.26.

Hydroxymethyl cryptand **15d** was obtained from 1.10 g of **14d** in 73% yield as a pale yellow hygroscopic oil; ir (neat): 3429 (OH), 1118 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.65-3.2 (m, 13), 3.35-4.1 (m, 33); ms: 494.6 (M^+).

Anal. Calcd. for $C_{23}H_{46}N_2O_9 \cdot 2H_2O$: C, 52.05; H, 9.50. Found: C, 51.71; H, 9.82.

Synthesis of (Allyloxy)methyl-substituted Cryptand **16**.

Under nitrogen, *n*-butyl lithium in hexane (0.49 g, 7.6 mmoles) was added dropwise to a stirred solution of **12b** (2.00 g, 7.6 mmoles) in tetrahydrofuran (40 ml). After stirring for 1 hour at room temperature, dimesylate **7** (2.87 g, 7.6 mmoles) in 30 ml of tetrahydrofuran was added and the mixture was stirred at room temperature overnight, and then refluxed for an additional 36 hours. The solvent was removed *in vacuo*, water (20 ml) was added and the mixture was extracted several times with dichloromethane. The combined extracts were dried over magnesium sulfate, evaporated *in vacuo*, and the residue was subjected to column chromatography on alumina with chloroform-acetonitrile (5:1) as eluent to give 0.82 g (24%) of **16** as a white solid, mp 83-85°; ir (neat): 1645 (C=C), 1134-1037 (C-O) cm^{-1}; nmr (deuteriochloroform): δ 2.65 (m, 12), 3.3-4.2 (m, 27), 5.0-6.2 (m, 3); ms: 446.5 (M^+).

Anal. Calcd. for $C_{22}H_{42}N_2O_7 \cdot CHCl_3 \cdot H_2O$: C, 47.31; H, 7.77. Found: C, 47.23; H, 7.58.

Attempted Deallylation of **16**.

Deprotection of **16** (0.76 g, 1.7 mmoles) was carried out under the conditions of the general procedure for deallylation of **9**, and **13**. Column chromatography (alumina, chloroform-methanol, 25:1) of the reaction product provided an almost quantitative recovery of unreacted (allyloxy)methyl cryptand **16**.

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