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SYNTHESIS OF MACROBICYCLIC POLYETHERS WITH NITROGEN ATOM BRIDGEHEADS

Jerald S. Bradshaw*, Haoyun An, Krzysztof E. Krakowiak, Geng Wu, and Reed M. Izatt

Department of Chemistry, Brigham Young University, Provo, UT 84602 U.S.A.

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Abstract. Macrobicyclic polyethers containing two 1,4-diaza-crown compounds condensed at the diaza nitrogen atoms (the di-ptychands) have been prepared using a simple and inexpensive procedure of treating the bis(2-hydroxyethyl)diaza-derivatives of 12-crown-4 (12C4), 15-crown-5 (15C5) and 18-crown-6 (18C6) macrocycles with the ditosylate derivatives of di-, tri-, tetra-, or pentaethylene glycol. Eleven di-ptychands were prepared as follows: 12C4-15C5, 12C4-18C6, 12C4-21-crown-7 (21C7), 12C4-24-crown-8 (24C8), 15C5-15C5, 15C5-18C6 (or 18C6-15C5), 15C5-21C7, 15C5-24C8, 18C6-18C6, 18C6-21C7 and 18C6-24C8. The starting bis(2-hydroxyethyl)diaza-crowns were prepared in good yields by reacting inexpensive N,N'-bis(2-hydroxyethyl)ethylenediamine with 1,2-bis(2-iodoethoxy)ethane (to give bis(2-hydroxyethyl)diaza-12-crown-4), diethylene glycol bis(2-chloroethyl)ether (to give bis(2-hydroxyethyl)diaza-15-crown-5) and the ditosylate derivative of pentaethylene glycol (to give bis(2-hydroxyethyl)diaza-18-crown-6). Log K values for di-ptychand 15C5-18C6 interactions with sodium and potassium ions were large with a selectivity factor of 6.17 [K (K^+)/K (Na^+)].

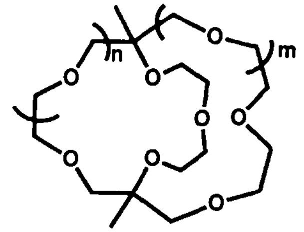
INTRODUCTION

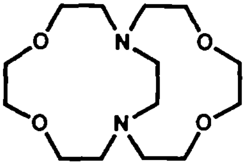
Selective alkali metal cation binding by macrocyclic ligands such as crown ethers, aza-crown ethers, and cryptands has been the subject of much research in recent years[1-5]. Due to the possibility of exchanging metal ions for protons in aza-crowns and cryptands by adjusting solution pH, these macrocycles could have industrial use for the separation of metal ions. However, the aza-crowns are not selective towards the alkali metal ions and the cryptands which do have high selectivity are very expensive. A complexing material must have high selectivity, large cation binding strength, low cost, and the metal ion must be releasable using a low cost stripping agent in order for that material to have practical use. The spherands selectively bind sodium ions and they are finding some industrial application[6]. It has also been found that one or two nitrogen atoms in the macrocycle ring can be helpful in certain instances for the selective complexation of alkali metals[7,8]. We have been exploring the possibility of adding another macroring to a diaza-crown with a view of having greater selectivity while maintaining their capability of releasing the complexed cation by adjusting the solution pH.

We have designed new methods[9-11] to prepare certain aza-crowns which have been shown to be superior cation complexing agents[4]. Our new methods are simple 1:1 cyclizations that do not need tosyl protecting groups on the nitrogen atoms. Many of these newly synthesized polyaza-crowns have reactive functional groups attached to the ring nitrogen atoms or unsubstituted ring nitrogen atoms which could be used to convert the polyaza-crowns into cage-like compounds[10-12]. Recently we have reported such syntheses in the simple one- or two-step preparation of cryptands[13]. In the present paper, we report the preparation of new macrobicyclic systems from some N,N'-bis(2-hydroxyethyl)diaza-crowns.

Some syntheses and complexation research of macrobicycles with carbon and nitrogen bridgehead atoms have been reported[14]. Okahara and his coworkers[15] reported the synthesis and complexing properties of macrobicyclic polyethers with carbon bridgehead atoms (Compounds 1-3). Macrobicyclic polyether 1 displayed a selectivity for potassium over sodium ion that was ten times greater than that of 18-crown-6 (18C6) which is a well known potassium ion complexing agent. Macrobicyclic polyether 3 displayed a forty times greater selectivity for sodium ion over potassium ion than that of 15-crown-5 (15C5) which is a well known sodium ion complexing agent. The results of Okahara and his co-workers show that the macrobicyclic polyethers can have higher selectivity for some metal cations than the corresponding mono crown ethers.

1, n = 2, m = 3
2, n = 1, m = 1
3, n = 1, m = 0





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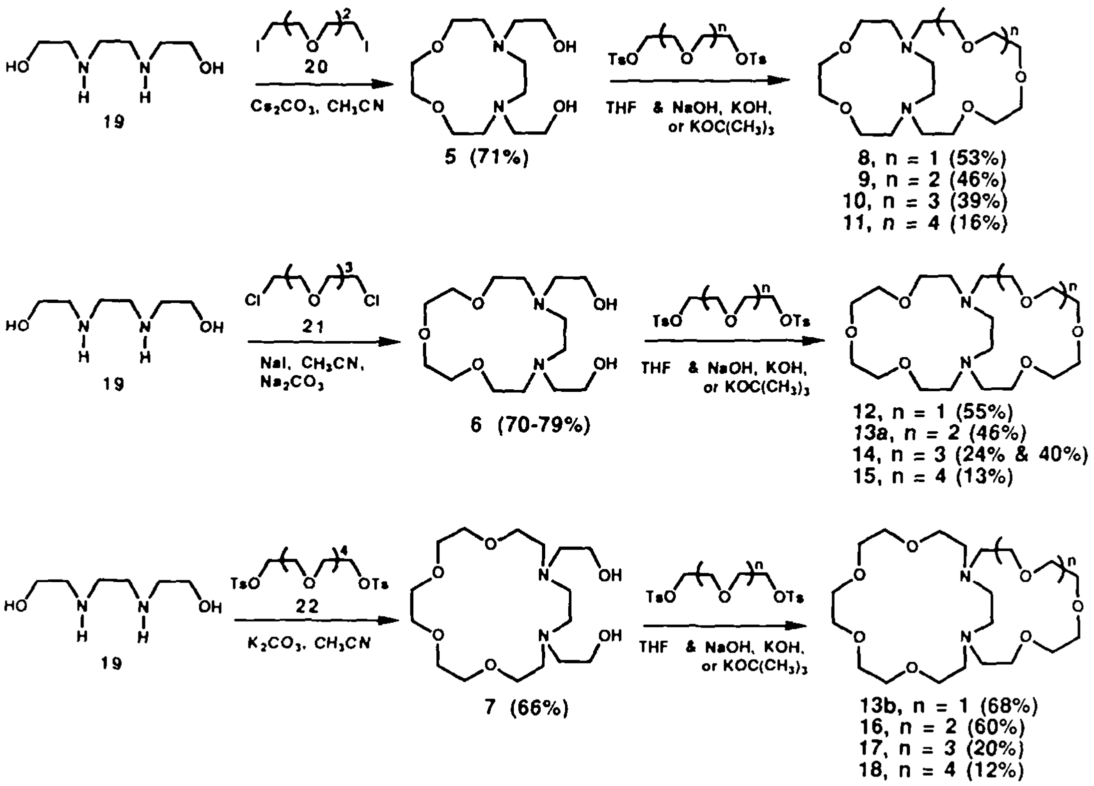
Macrobicyclic polyethers with nitrogen bridgehead atoms are rare. Dale and his coworkers[16] first reported the synthesis of a macrobicyclic polyether with nitrogen bridgehead atoms which consisted of two 12-membered rings (4). They also studied the complexing behavior of this new bis-crown ether which they called a "di-ptychand"[16,17]. Their di-ptychand demonstrated a very strong sodium ion selectivity in a sandwich-type complex. The free ligand could only be obtained by pyrolysis of its complex with sodium p-toluene sulfonate which was first isolated from the reaction mixture.

Macrocyclic polyethers with one[18] or two[19] side arms containing reactive functional groups have been prepared and some of them have been bonded to solid supports. These solid supported macrocycles exhibit excellent cation binding properties and can remove certain metal ions from water.[20,21] In order to obtain functionalized crown ethers which could be converted to the bis-crown ethers with high complexing abilities and high selectivities for certain metal cations, we have synthesized three difunctionalized macrocyclic polyethers (5-7, Scheme I) in high yields by one-step reactions. Our new difunctionalized crowns were reacted with available oligoethylene glycol ditosylates to give eleven macrobicyclic polyethers with nitrogen bridgehead atoms (8-18, Scheme I) and containing varying ring members. Di-ptychand **13a** formed strong complexes with sodium and potassium ions.

RESULTS AND DISCUSSION

N,N'-Bis(2-hydroxyethyl)ethylenediamine (19) was chosen as the starting material for the preparation of the new macrocycles and macrobicycles because it is inexpensive and has two types of reactive sites which have different reactivities for nucleophilic substitution.

Scheme 1. Preparation of Bis(2-hydroxyethyl)diaza-Crown Ethers (5-7) and Macrobicyclic Polyethers 8-18



We take advantage of these reactivity differences to cyclize two rings under different basic conditions. First, secondary amine groups act as nucleophiles with diiodide or ditosylate compounds to close one ring under weak carbonate basic conditions (see Scheme I). Then, alkoxide anions act as nucleophiles to close the second ring with different ditosylate moieties under strong hydroxide or t-butoxide basic conditions.

In our first attempt to prepare 7,10-bis(2-hydroxyethyl)diaza-12-crown-4 (5) using sodium carbonate as the base and reactants 19 and 20, the sodium iodide complex was isolated in a 79% yield. The sodium iodide complex of 5 could not be decomposed either by chromatography or by refluxing in various solvents. Pyrolytic distillation wasn't attempted because of the expected high boiling point of 5 under high vacuum conditions. Free ligand 5 was obtained easily using cesium carbonate as the base. Presumably, the cesium cation is too large to form a complex with ligand 5. A similar metal ion complex was reported for a bis(2-hydroxyethyl)diaza-18-crown-6 ligand[13]. For the preparation of crown 6, diethylene glycol bis(2-chloroethyl)ether 21, was first refluxed with sodium iodide in acetonitrile to form the corresponding diiodide. The resulting diiodide was reacted without purification with dihydroxy diamine 19 to form 6. Pentaethylene glycol ditosylate (prepared from pentaethylene glycol) was used to prepare 7. The reaction mixtures were refluxed in acetonitrile for 2 days to form 5 and 6, but at least 3 days to form 7. High yields of the cyclic products were obtained using cesium, sodium and potassium carbonates for the preparation of 5, 6 and 7, respectively. Purification of 5-7 was difficult due to the two hydroxy groups. Gradient elution chromatography on neutral alumina was used to purify these compounds. Carroy and his coworkers have synthesized similar difunctionalized macrocyclic polyethers starting from the diaza-crown ethers[22]. Their synthesis was longer and more expensive since some diaza-crowns are not available.

Dale and his co-workers reported only di-ptychand 4 with two 12-membered rings using a different procedure than that reported here, and suggested that it would be difficult to make di-ptychands with larger rings[17]. Nevertheless, we have obtained 11 new di-ptychands by a new method with the two ring sizes varying from 12 to 24 ring members. These materials were prepared by the reaction of difunctionalized crown ethers 5-7 with the di-, tri-, tetra- and pentaethylene glycol ditosylates. The 15C5 and 18C6 macrocycles are easily synthesized by the template effect of sodium and potassium cations, respectively. Di-ptychands 15C5-15C5 (**12**), 18C6-15C5 (**13b**), 15C5-18C6 (**13a**) and 18C6-18C6 (**16**) were easily obtained in relatively high yields by using sodium and potassium hydroxide as the base with sodium and potassium as the metal cation templates (Scheme I). Di-ptychands 12C4-15C5 (**8**) and 12C4-18C6 (**9**) were also obtained in the same manner except for the need to have longer reaction times. The template effect of potassium cation was still effective for the synthesis of di-ptychand 12C4-21C7 (**10**) and 15C5-21C7 (**14**), however, the yields were lower than for the synthesis of di-ptychands containing the 18C6 moiety. By using potassium t-butoxide, bicycle 14 was prepared in a 40% yield rather than 24% when using potassium hydroxide. Potassium hydroxide could not be used as basic catalyst for the syntheses of di-ptychands 12C4-24C8 (**11**), 15C5-24C8 (**15**), 18C6-21C7 (**17**) and 18C6-24C8 (**18**). The four large di-ptychands were obtained in low yields using THF as the solvent, potassium t-butoxide as the base and extending the reaction period to 3 or 4 days. Di-ptychands 15C5-18C6 (**13a**) and 18C6-15C5 (**13b**) are the same macrobicyclic polyethers obtained by different reaction routes (see Scheme I).

Most di-ptychands were easily purified on a neutral alumina column. Di-ptychands 11, 15 and 18 had to be purified a second time on a silica gel column in order to obtain satisfactory combustion analyses because the di-ptychands had some inorganic impurity. The dissolved alumina and perhaps other impurities were removed on the silica gel column.

The "butterfly-shaped" crown ethers 8-18 have the conformation and structure suitable to form sandwich-like complexes with some metal cations. According to metal ion complexation results using crown ethers 1-4[15,16], di-ptychand 12C4-15C5 (**8**) would be expected to have high selectivity for the sodium cation, di-ptychands 12C4-18C6 (**9**), 15C5-15C5 (**12**) and 18C6-

15C5 (13) could be expected to have high selectivity for potassium cation. The other di-ptychands with larger rings could possibly have selectivity for larger metal cations.

Compound **13a** formed strong complexes with sodium and potassium cations in 90% methanol as determined by a titration calorimetry technique[23]. The log K and (ΔH) values are 4.35 (-63.2 kJ/mole) for potassium ion and 3.56 (-35.4 kJ/mole) for sodium ion. These values correspond to a selectivity factor of 6.17 for potassium ion over sodium ion and are much higher than the log K values for diaza-18-crown-6. This good selectivity, coupled with a pH stripping capability and the effortless process of preparing these compounds, make **13a** a possible candidate for use in the separation of potassium cations. A comparison of cation complexation properties of various macrocyclic ligands is presented in Table I. As can be seen in Table I, **13a** has good overall properties to be effective in separation processes. Studies on the complexation properties of these new di-ptychands for various cations are continuing.

Table I. A Comparison of Complexation Properties (M + L = ML) of 13a and Various Related Macrocycles

macrocycle (L)	log K_{KL} (solvent)	log K_{NaL}	$K_{(K^+)}/K_{(Na^+)}$	Stripping	Dissociation Kinetics	Cost
15-crown-5	3.77[1] (MeOH)	3.48[1] (MeOH)	1.95	costly	fast	modest
18-crown-6	5.35[1] (9/1 MeOH)	3.66[1] (9/1 MeOH)	48.98	costly	fast	modest
A_2-18-crown-6	4.32[1] (MeCN)	4.30[1] (MeCN)	1.05	pH	fast	modest
cryptand 222	5.4[1] (H_2O)	3.9[1] (H_2O)	31.6	pH	slow	expensive
13a	4.35 (9/1 MeOH)	3.56 (9/1 MeOH)	6.17	pH	fast	modest

[1] Values taken from Ref 4.

EXPERIMENTAL

The proton nuclear magnetic resonance (^1H nmr) spectra were obtained on a Varian Gemini 200 spectrometer using deuterochloroform as the solvent with TMS as the internal standard. Infrared (ir) spectra were obtained on a Perkin-Elmer FT 1600 spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona. Molecular weights were determined by the electron impact method on a Finnegan 8430 High Resolution Mass Spectrometer. Starting materials were purchased from Aldrich, TCI and other chemical companies. Di-, tri-, tetra- and pentaethylene glycol ditosylates were prepared from corresponding oligoethylene glycols and p-toluenesulfonyl chloride according to the reported procedure[24]. Sodium and potassium nitrates were obtained in highest purity possible from Baker and methanol was obtained from Fisher.

7,10-Bis(2-hydroxyethyl)-1,4-dioxa-7,10-diazacyclododecane (5). A mixture of 5 g (0.034 mole) of N,N'-bis(2-hydroxyethyl)ethylenediamine (19), 13 g (0.035 mole) of 1,2-bis(2-iodoethoxyl)ethane (20), 750 ml of acetonitrile and 30 g of anhydrous cesium carbonate was stirred under reflux for 48 hours. The cooled mixture was filtered and the solid was washed with chloroform. The filtrate was evaporated under reduced pressure. Chloroform (200 ml) was added to the residue to dissolve the product. After shaking, the suspended solid was filtered and washed two times with chloroform. The combined organic solution was evaporated to give a yellow oil. The oil was purified by chromatography on neutral alumina using toluene/ethanol:30/1 and then 10/1 as the eluants. Evaporation of the solvent gave 6.28 g (71%) of 5 as a pale yellow oil; ^{1}H nmr: (δ) 2.51 (m, 12 H), 3.48-3.62 (m, 12 H), 4.15-5.00(b, 2 H, disappeared in D_2O); ms:m/e 261 (M-1), 244 (M-18), 231 (M-31), 162 (M-100, base peak).

Anal. Calcd. for $C_{12}H_{26}N_2O_4$: C, 54.94; H, 9.99. Found: C, 54.72; H, 9.80.

The Complex of 5 With Sodium Iodide. A mixture of 1 g (6.7 mmole) of 19, 2.78 g (7.5 mmole) of 20, 250 ml of acetonitrile and 25 g of anhydrous sodium carbonate was stirred under reflux for 3 days. The cooled mixture was filtered and the solid was washed with chloroform. Solid was still obtained after the solvent was removed from the filtrate under reduced pressure. Chloroform was added and the mixture was filtered. The solvent was evaporated from the filtrate to give the solid complex. Chromatography on neutral alumina also gave the solid complex. The solid complex was recrystallization from acetonitrile to give 2.2 g (79%) of 5-NaI complex as white crystals, m.p. 181.5-183°; ^{1}H nmr: (δ) 2.4-2.8 (m, 12 H), 3.5-4.0 (m, 14 H); ^{1}H nmr after mixing with D_2O: 2.55 (s, 12 H), 3.62 (s, 12 H); ms: m/e 261 (M-NaI-1), 244 (M-NaI-18), 231 (M-NaI-31), 162 (M-NaI-100, base peak).

Anal. Calcd. for $C_{12}H_{26}N_2O_4NaI$: C, 34.96; H, 6.36. Found: C, 35.12; H, 6.38.

10,13-Bis(2-hydroxyethyl)-1,4,7-trioxa-10,13-diazacyclopentadecane (6). A mixture of 8.6 g (0.037 mole) of diethylene glycol bis(2-chloroethyl)ether (21), 1000 ml of acetonitrile, 17 g (0.113 mole) of sodium iodide and 40 g of anhydrous sodium carbonate was stirred under reflux for 24 hours. Diamine 19 (5.5 g, 0.037 mole) was added to the cooled reaction mixture. The resulting mixture was stirred under reflux for 48 hours. The mixture was then treated as above for 5 using neutral alumina chromatography (toluene/ethanol:20/1 and then 2/1 as the eluants) to give 7.96-9.00 g (70-79%) of 6 as a pale yellow oil; ^{1}H nmr: (δ) 2.48-2.66 (m, 12 H), 3.45-3.65 (m, 16 H), 4.65 (b, 2 H, disappeared with D_2O); ms: m/e 305 (M-1), 288 (M-18), 275 (M-31), 206 (M-100, base peak).

Anal. Calcd. for $C_{14}H_{30}N_2O_5$: C, 54.88; H, 9.87. Found: C, 54.69; H, 9.66.

13,16-Bis(2-hydroxyethyl)-1,4,7,10-tetraoxa-13,16-diazacyclooctadecane (7). A mixture of 0.9 g (6.1 mmole) of 19, 200 ml of acetonitrile, 3.32 g (6.1 mmole) of pentaethylene glycol ditosylate and 20 g of anhydrous potassium carbonate was stirred under reflux for 3 days. The mixture was treated as above for 5 using neutral alumina chromatography (toluene/ethanol:30/1 and then 10/1) to give 1.38 g (65%) as a pale yellow oil. ^{1}H nmr: (δ) 2.42-2.70 (m, 12 H), 3.35-3.66 (m, 20 H), 4.50 (b, 2 H, disappeared with D_2O). ms: m/e 349 (M-1), 332 (M-18), 319 (M-31), 250 (M-100, base peak).

Anal. Calcd. for $C_{16}H_{34}N_2O_6$: C, 54.84; H, 9.78. Found, C, 54.97; H, 9.62.

4,7,10,16,19-Pentaoxa-1,13-diazabicyclo[11,8,2]tricosane (12C4-15C5) (8). Crown ether 5 (0.9 g, 3.4 mmole) in 50 ml of THF was added to 100 ml of THF containing 3 g (0.075 mole) of powdered sodium hydroxide. The resulting mixture was stirred at 60° for 1 hour. A solution of 1.42 g (3.4 mmole) of diethylene glycol ditosylate in 100 ml of THF was dropped to the above stirred solution at 60-66° for 1-2 hours and the resulting mixture was stirred under reflux for 48 hours. The cooled mixture was filtered and the solid was washed with THF. The filtrate was evaporated under reduced pressure and the residue was chromatographed on neutral alumina with toluene/ethanol:50/1 as the eluant to give 0.6 g (53%) of 8 as a pale yellow oil; ^{1}H nmr: (δ) 2.62-2.74 (m, 12 H), 3.52-3.70 (m, 20 H).

Anal. Calcd. for $C_{16}H_{32}N_2O_5$: C, 57.81; H, 9.70; mol. wt., 332.44. Found: C, 57.95; H, 9.65; mol. wt., 332.

4,7,10,13,19,22-Hexaoxa-1,16-diazabicyclo[14,8,2]hexacosane (12C4-18C6) (9). Polyether 9 was prepared as above for 8 from 0.98 g (3.7 mmole) of crown ether 5, 3 g (0.053 mole) of powdered potassium hydroxide and 1.71 g (3.7 mmole) of triethylene glycol ditosylate in THF. Purification by chromatography on neutral alumina using toluene/ethanol:60/1 as the eluant gave 0.64 g (46%) of 9 as a pale yellow oil; ^{1}H nmr: (δ) 2.60-2.84 (m, 12 H), 3.45-3.70 (m, 24 H).

Anal. Calcd. for $C_{18}H_{36}N_2O_6$: C, 57.42; H, 9.75; mol. wt., 376.49. Found: C, 57.58; H, 9.67; mol. wt., 376.

4,7,10,13,16,22,25-Heptaoxa-1,19-diazabicyclo[17,8,2]nonacosane (12C4-21C7) (10).

Macrobicyclic polyether 10 was prepared as above for 8 from 0.53 g (2.0 mmole) of crown ether 5, 2.5 g (4.5 mmole) of powdered potassium hydroxide and 1.02 g (2.0 mmole) of tetraethylene glycol ditosylate in acetonitrile. Purification by chromatography on neutral alumina using toluene/ethanol:45/1 as the eluant gave 0.33 g (39%) of 10 as a pale yellow oil; ^{1}H nmr: (δ) 2.64-3.05 (m, 12 H), 3.45-3.72 (m, 28 H).

Anal. Calcd. for $C_{20}H_{40}N_2O_7$: C, 57.12; H, 9.59; mol. wt., 420.547. Found: C, 56.88; H, 9.36; mol. wt., 420.

4,7,10,13,16,19,25,28-Octaoxa-1,22-diazabicyclo[20,8,2]dotriacotane (12C4-24C8) (11). Macrobicyclic polyether 11 was prepared as above for 8 from 0.7 g (2.7 mmole) of crown ether 5, 3 g (0.027 mole) of potassium tert-butoxide and 1.46 g (2.7 mmole) of pentaethylene glycol ditosylate in 500 ml of THF by stirring the reaction mixture under reflux for 4 days. Purification by chromatography on neutral alumina using toluene/ethanol:70/1 as the eluant and then on silica gel using methanol/ammonium hydroxide:10/1 as the eluant gave 0.2 g (16%) of **11** as a pale yellow oil; ^{1}H nmr: (δ) 2.58-2.85 (m, 12 H), 3.48-3.72 (m, 32 H).

Anal. Calcd. for $C_{22}H_{44}N_2O_8$: C, 56.88; H, 9.54; mol. wt., 464.60. Found: C, 56.88; H, 9.47; mol. wt., 464.

4,7,10,16,19,22-Hexaoxa-1,13-diazabicyclo[11,11,2]hexacosane (15C5-15C5) (12). A solution of 0.9 g (2.9 mmole) of crown ether **6** in 40 ml of THF was added to 50 ml of THF containing 1.5 g (0.038 mole) of powdered sodium hydroxide. The mixture was stirred at 60-65° for 1 hour. A solution of 1.22 (2.9 mmole) of diethylene glycol ditosylate in 30 ml of THF was dropped into the above stirred solution for 1 hour. The resulting mixture was stirred under reflux for 24 hours. The mixture was treated as above for **8** and purified by chromatography on neutral alumina using toluene/ethanol:30/1 as the eluant to give 0.6 g (55%) of **12** as a pale yellow oil; ^{1}H nmr; (δ) 2.62-2.78 (m, 12 H), 3.50-3.64 (m, 24 H).

Anal. Calcd. for $C_{18}H_{36}N_2O_6$: C, 57.42; H, 9.64; mol. wt., 376.494. Found: C, 57.51; H, 9.75; mol. wt., 376.

4,7,10,13,19,22,25-Heptaoxa-1,16-diazabicyclo[14,11,2]nonacosane (15C5-18C6) (13a). Macrobicyclic polyether **13a** was prepared as above for **12** from 1.07 g (3.5 mmole) of crown ether **6**, 2 g (0.036 mole) of powdered potassium hydroxide and 1.61 g (3.5 mmole) of triethylene glycol ditosylate in 150 ml of THF. Purification by chromatography on neutral alumina using toluene/ethanol:45/1 as the eluant gave 0.68 g (46%) of **13a** as a pale yellow oil; ^{1}H nmr: (δ) 2.60-2.80 (m, 12 H), 3.48-3.68 (m, 28 H).

Anal. Calcd. for $C_{20}H_{40}H_2O_7$: C, 57.12; H, 9.59; mol. wt., 420.547. Found: C, 56.93; H, 9.37; mol. wt., 420.

4,7,10,13,19,22,25-Heptaoxa-1,16-diazabicyclo[14,11,2]nonacosane (18C6-15C5) (13b). Macrobicyclic polyether **13b** was prepared as above for **12** from 1.3 g (3.7 mmole) of crown ether **7**, 2 g (0.05 mole) of powdered sodium hydroxide and 1.5 g (3.6 mmole) of diethylene glycol ditosylate in 250 ml of THF. Purification by chromatography on neutral alumina using toluene/ethanol:80/1 as the eluant gave 1.06 g (68%) of **13b** as a pale yellow oil; ^{1}H nmr; (δ) 2.60-2.78 (m, 12 H), 3.48-3.68 (m, 28 H).

Anal. Calcd. for $C_{20}H_{40}N_2O_7$: C, 57.12; H, 9.59; mol. wt., 420.547. Found: C, 57.29; H, 9.20; mol. wt., 420.

4,7,10,13,16,22,25,28-Octaoxa-1,19-diazabicyclo[17,11,2]-dotriacontane (15C5-21C7) (14). Macrobicyclic polyether **14** was prepared as above for **12** from 0.7 g (2.3 mmole) of crown ether **6**, 3 g (0.054 mole) of powdered potassium hydroxide and 1.14 g (2.3 mmole) of tetraethylene glycol ditosylate in THF. Purification by chromatography on neutral alumina using toluene/ethanol:40/1 as the eluant gave 0.25 g (24%; 40% when potassium t-butoxide was used) of **14** as a pale yellow oil; ^{1}H nmr: (δ) 2.62-2.85 (m, 12 H), 3.50-3.72 (m, 32 H).

Anal. Calcd. for $C_{22}H_{44}N_2O_8$: C, 56.88; H, 9.54; mol. wt., 464.60. Found: C, 56.88; H, 9.31; mol. wt., 464.

4,7,10,13,16,19,25,28,31-Nonaoxa-1,22-diazabicyclo[20,11,2]pentatriacontane (15C5-24C8) (15). Macrobicyclic polyether **15** was prepared as above for **11** from 0.92 g (3.0 mmole) of crown ether **6**, 3 g (0.027 mole) of potassium tert-butoxide and 1.64 g (3.0 mmole) of pentaethylene glycol ditosylate in 500 ml of THF by stirring the reaction mixture under reflux and in a nitrogen atmosphere for 4 days. Purification by chromatography on neutral alumina using toluene/ethanol:70/1 as the eluant and then on silica gel using methanol/ammonium hydroxide:18/1 as the eluant gave 0.2 g (13%) of **15** as a pale yellow oil; ^{1}H nmr: (δ) 2.60-2.80 (m, 12 H), 3.45-3.70 (m, 36 H).

Anal. Calcd. for $C_{24}H_{48}N_2O_9$: C, 56.67; H, 9.51; mol. wt., 508.65. Found: C, 56.63; H, 9.48; mol. wt., 508.

4,7,10,13,19,22,25,28-Octaoxa-1,16-diazabicyclo[14,14,2]-dotriacontane (18C6-18C6) (16). Macrobicyclic polyether **16** was prepared as above for **12** from 1.3 g (3.7 mmole) of crown ether **7**, 2 g (0.036 mole) of powdered potassium hydroxide and 1.66 g (3.6 mmole) of triethylene glycol ditosylate in THF. Purification by chromatography on neutral alumina using toluene/ethanol:100/1 as the eluant gave 1.08 g (60%) of **16** as a pale yellow oil; ^{1}H nmr: (δ) 2.62-2.78 (m, 12 H), 3.46-3.70 (m, 32 H).

Anal. Calcd. for $C_{22}H_{44}N_2O_8$: C, 56.87; H, 9.55; mol. wt., 464.60. Found: C, 56.61; H, 9.69; mol. wt., 464.

4,7,10,13,16,22,25,28,31-Nonaoxa-1,19-diazabicyclo[17,14,2]pentatriacontane (18C6-21C7) (17). Macrobicyclic polyether **17** was prepared as above for **11** from 1.06 g (3.0 mmole) of crown ether **7**, 2 g (0.016 mole) of potassium tert-butoxide and 1.52 g (3.0 mmole) of tetraethylene glycol ditosylate in 500 ml of THF by stirring the reaction mixture under reflux for 3 days. Purification by chromatography on neutral alumina using toluene/ethanol:100/1 and then 70:1 as the eluants gave 0.3 g (20%) of **17** as a pale yellow oil; ^{1}H nmr: (δ) 2.62-2.80 (m, 12 H), 3.48-3.68 (m, 36 H).

Anal. Calcd. for $C_{24}H_{48}N_2O_9$: C, 56.67; H, 9.51; mol. wt., 508.65. Found: C, 56.48; H, 9.29; mol. wt., 508.

4,7,10,13,16,19,25,28,31,34-Decaoxa-1,22-diazabicyclo[20,14,2]octatriacontane (18C6-24C8) (18). Macrobicyclic polyether **18** was prepared as above for **11** from 0.83 g (2.4 mmole) of crown ether **7**, 3 g (0.029 mole) of potassium tert-butoxide and 1.3 g (2.4 mmole) of pentaethylene glycol ditosylate in 500 ml of THF. Purification by chromatography on neutral alumina using toluene/ethanol:70/1 as the eluant and then on silica gel using methanol/ammonium hydroxide:10/1 as the eluant gave 0.16 g (12%) of **18** as a pale yellow oil; ^{1}H nmr: (δ) 2.60-2.78 (m, 12 H), 3.48-3.70 (m, 40 H).

Anal. Calcd. for $C_{26}H_{52}N_2O_{10}$: C, 56.50; H, 9.48; mol. wt, 552.70. Found: C, 56.43; H, 9.23; mol. wt., 552.

Calorimetry Experiments. Solutions were prepared using 9:1 (v/v) methanol/water as a solvent system. Metal solutions were prepared by dissolving an appropriate amount of the nitrate salts at less than 0.05 mole/liter in order to neglect ion pairing effects. Metal ion concentrations were checked against standard cryptand [2.2.2] solution. The solution containing **13a** was standardized by calorimetric titration with standardized potassium which gave a stoichiometric 1:1 endpoint in the 9:1 mixed methanol/water solvent. The uncertainties associated with the endpoints were less than ±3%. Procedures used to determine log K and ΔH values by direct calorimetric titration have been described[23].

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REFERENCES

[1] M. Takagi and K. Veno, Top. Curr. Chem., 121, 39 (1984).
[2] K. G. Heumann, Top. Curr. Chem., 127, 77 (1985).
[3] Y. Takeda, Top. Curr. Chem., 121, 1 (1984).
[4] R. M. Izatt, J. S. Bradshaw, S. A. Nielsen, J. D. Lamb and J. J. Christensen, Chem. Rev., 85, 271 (1985).
[5] M. Takagi and H. Nakamura, J. Coord. Chem., 56, 53 (1986).
[6] R. C. Helgeson, B. P. Czech, E. Chapoteau, C. R. Gebauer, A. Kumar and D.J. Cram, J. Am Chem. Soc., 111, 6339 (1989).
[7] H. Tsukube, K. Yamashita, T. Iwachido and M. Zenki, Tetrahedron Lett., 30, 3983 (1989).
[8] H. Tsukube, H. Adachi and S. Morosawa, J. Chem. Soc., Perkin Trans. I., 1537 (1989).
[9] K. E. Krakowiak, J. S. Bradshaw, R. M. Izatt and D. J. Zamecka-Krakowiak, J. Org. Chem., 54, 4061 (1989).
[10] K. E. Krakowiak, J. S. Bradshaw, N. K. Dalley, W. Jiang and R. M. Izatt, Tetrahedron Lett., 30, 2897 (1989).
[11] J. S. Bradshaw, K. E. Krakowiak and R. M. Izatt, J. Heterocyclic Chem., 26, 1431 (1989) and the references therein cited.
[12] J. S. Bradshaw, K. E. Krakowiak and R. M. Izatt, Tetrahedron Lett., 30, 803 (1989).
[13] K. E. Krakowiak, J. S. Bradshaw and R. M. Izatt, J. Heterocyclic Chem., in press.
[14] A. C. Coxon and J. F. Stoddard, J. Chem. Soc., Perkin I, 767 (1977); W. D. Curtis, J. F. Stoddart and G. H. Jones, J. Chem. Soc., Perkin I, 785 (1977); A. H. Haines and P. Karntiang, J. Chem. Soc., Perkin I, 2577 (1979).
[15] Y. Nakatsuji, T. Mori and M. Okahara, J. Chem. Soc., Chem. Commun., 1045 (1984).
[16] T. Alfheim, S. Buoen, J. Dale and K. D. Krautwurst, Acta Chem. Scand., B40, 40 (1986).
[17] T. Alfheim, J. Dale, P. Groth and K. D. Krautwurst, J. Chem. Soc., Chem. Commun., 1502 (1984).
[18] J. S. Bradshaw, K. E. Krakowiak, H. An and R. M. Izatt, Tetrahedron, in press.
[19] J. S. Bradshaw, K. E. Krakowiak, R. L. Bruening, B. J. Tarbet, P. B. Savage and R. M. Izatt, J. Org. Chem., 53, 3190 (1988);
[20] Y. Nakatsuji, T. Nakamura, M. Okahara, D. M. Dishong and G. W. Gokel, J. Org. Chem., 48, 1237 (1983).
[21] H. Tsukube, H. Adachi and S. Morosawa, J. Chem. Soc., Perkin Trans. I., 89 (1989).
[22] A. Carroy, C. R. Langick, J. M. Lehn, K. E. Matthes and D. Parker, Helv. Chim. Acta, 69, 580 (1986).
[23] R. M. Izatt, R. E. Terry, B. L. Haymore, L. D. Hansen, N. K. Dalley, A. G Avondet and J. J. Christensen, J. Am. Chem. Soc., 98, 7620 (1976).
[24] M. Ouchi, Y. Inoue, K. Kanzaki and T. Hakushi, J. Org. Chem., 49, 1408 (1984).