

# Synthesis of *N*-Unsubstituted Di- and Triaza Crown Ethers

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Facile syntheses of di- and triaza crown ethers by intramolecular cyclization of oligoethylene glycols containing two or three imino groups or by their intermolecular cyclization with oligoethylene glycol bis(*p*-toluenesulfonate)s are described.

*N*-Unsubstituted oligoaza crown ethers are important as intermediate in the synthesis of cryptands<sup>1)</sup> or macrotricyclic compounds.<sup>2–8)</sup> They can also be transformed into polymers having crown rings in the backbone.<sup>9–13)</sup> Diaza crown ethers as *N*-unsubstituted oligoaza crown ethers have been synthesized by the reaction between diamine and bis(acyl chloride),<sup>1,14)</sup> bis(tosylamide) or sodium tosylamine and ditosylate or dichloride,<sup>15–17)</sup> and bis(trifluoroacetamide) and ditosylate.<sup>18)</sup> However, in all these methods, the elimination of protecting groups is needed in the final step. The reaction of triethylene glycol dichloride with excess ammonia gives diaza-18-crown-6 in low yield with many by-products.<sup>18)</sup> Although the preparation by *N*-alkylation of diamine with dichloride<sup>19)</sup> or diiodide<sup>20)</sup> has been reported, the synthesis of *N*-unsubstituted diaza crown ethers by *O*-alkylation has not been published except some preparations of special diaza crown ethers.<sup>21,22)</sup>

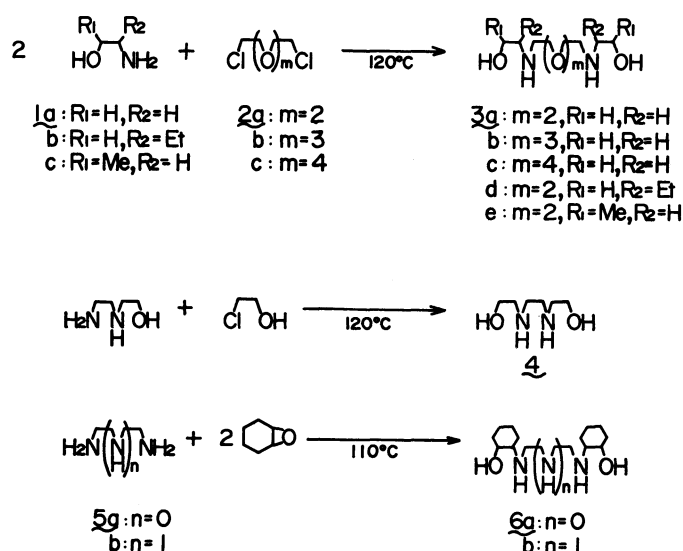
We have previously reported that *N*-unsubstituted monoaza crown ethers can be obtained by the reaction of readily available dialkanolamines with oligoethylene glycol bis(*p*-toluenesulfonate)s without protection of the amino group, based on the higher reactivity of alkoxide anion.<sup>23–25)</sup> We have also reported one-pot synthesis of substituted and unsubstituted crown ethers by treating various oligoethylene glycol derivatives with arenesulfonyl chlorides.<sup>26)</sup> In this paper, the results of the syntheses of *N*-unsubstituted di- and triaza crown

ethers by intramolecular cyclization of oligoethylene glycols including two or three imino groups or by intermolecular cyclization of them with oligoethylene glycol bis(*p*-toluenesulfonate)s are described.

## Results and Discussion

The starting materials, oligoethylene glycols (**3**) containing two imino groups, were obtained from 2-amino-1-hydroxy compounds (**1**) and oligoethylene glycol dichlorides (**2**) (Scheme 1). When **2** (*m*=1) was used in this reaction, a morpholine derivative was obtained from the intramolecular substitution by the attack of the amino group of the intermediate compound.<sup>18)</sup> On the other hand, as the use of 1,2-dichloroethane (**2**, *m*=0) may result in the formation of aziridine derivatives, it is necessary to use **2** having more than two oxyethylene units (*m*≥2) in order to get **3** in satisfactory yield. 2-[2-(2-Hydroxyethylamino)ethylamino]ethanol (**4**) and *N*,*N'*-bis(2-hydroxycyclohexyl)-oligoazaalkane- $\alpha,\omega$ -diamines (**6**) were obtained from the reaction of excess 2-(2-aminoethylamino)ethanol with 2-chloroethanol and the reaction of oligoazaalkane- $\alpha,\omega$ -diamine (**5**) with cyclohexene oxide, respectively.

The preparation of diaza crown ethers by the intramolecular cyclization of **3** was achieved (Scheme 2). After **3** was treated with an equimolar amount of *p*-toluenesulfonyl chloride in dioxane suspension of powdered alkali metal hydroxide at 60 °C, the product



Scheme 1.

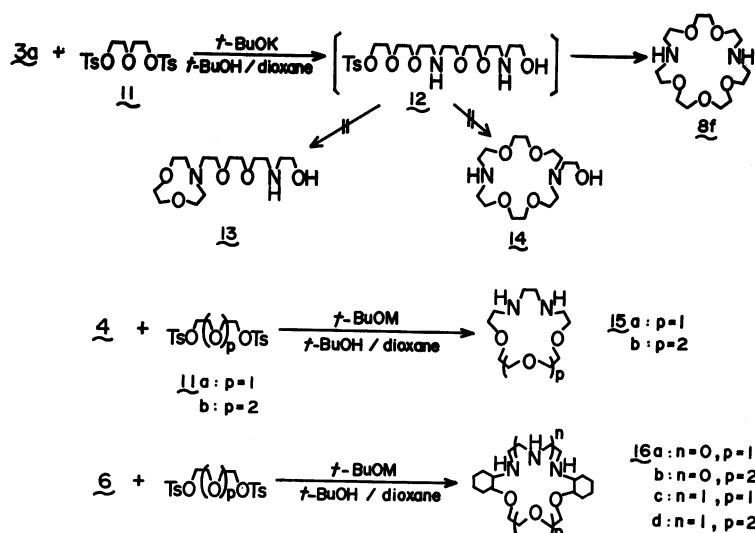
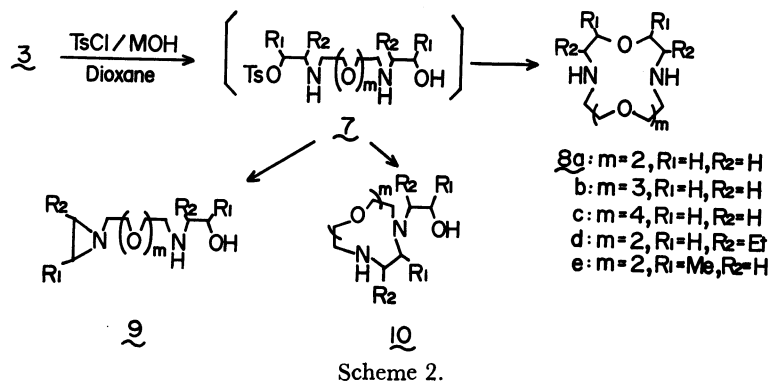


TABLE 1. SYNTHESIS OF DIAZA CROWN ETHERS BY THE REACTION OF **3** WITH *p*-TOLUENESULFONYL CHLORIDE

| Diaza crown ether                                | Starting material | Base | Yield %          | Mp $\theta_m/^\circ\text{C}$ or Bp $\theta_b/^\circ\text{C}$ (Torr) |
|--------------------------------------------------|-------------------|------|------------------|---------------------------------------------------------------------|
| 7,13-Diaza-15-crown-5( <b>8a</b> ) <sup>a)</sup> | <b>3a</b>         | NaOH | 26 <sup>b)</sup> | 91—93<br>80—85(0.015)                                               |
| 10,16-Diaza-18-crown-6( <b>8b</b> )              | <b>3b</b>         | NaOH | 11 <sup>b)</sup> | 101—103<br>100—105(0.002)                                           |
| 13,19-Diaza-21-crown-7( <b>8c</b> )              | <b>3c</b>         | KOH  | 11 <sup>b)</sup> | 120—125(0.005)                                                      |
| 8,12-Diethyl-7,13-diaza-15-crown-5( <b>8d</b> )  | <b>3d</b>         | NaOH | 12 <sup>c)</sup> | 100—105(0.04)                                                       |
| 9,11-Dimethyl-7,13-diaza-15-crown-5( <b>8e</b> ) | <b>3e</b>         | NaOH | 17 <sup>c)</sup> | 90—95(0.02)                                                         |

a) Total amine number(calcd): 505.6(514.0), tertiary amine number: 18.1. b) Purified by distillation. c) Purified by column chromatography.

was obtained by distillations in a Kugelrohr apparatus.

In this reaction, *p*-toluenesulfonyl chloride is first attacked by alkoxide anion to give mono(*p*-toluenesulfonate)s (**7**), and then an intramolecular attack by an alternative alkoxide anion can generate the diaza crown ethers (**8**). If *p*-toluenesulfonyl chloride reacts with imino groups, sulfonamide derivatives may be formed. But, the resonance of *p*-toluenesulfonamides is

hardly observed in the  $^1\text{H}$  NMR spectrum of the crude products of **8a—e** before distillation. While, intramolecular reactions of **7** with imino groups may result in *N*-substituted derivatives (**9** and **10**). In the  $^1\text{H}$  NMR spectrum of the crude product, in fact, resonances are observed at  $\delta$  1.16, 1.72, and 2.41, which are ascribed to the protons of aziridine derivatives. However, it is found that the products (**8a—c**) obtained by distillations are almost pure *N*-unsubstituted diaza crown ethers (**8**), probably because of the thermal instability of aziridine derivatives. As the distillation product for **8d, e** is a mixture of aziridine compound, **8d, e** is further purified by alumina column chromatography. Although the product obtained is a mixture of stereoisomers, further purification was not performed. These results are shown in Table 1.

**3a** and potassium metal were dissolved in *t*-butyl alcohol, then diethylene glycol bis(*p*-toluenesulfonate) (**11a**) in dioxane was added dropwise to the solution at  $40^\circ\text{C}$ . The crude product was distilled in a Kugelrohr apparatus to give diaza 21-crown-7 (**8f**) in 38% yield (Scheme 3).

This synthetic method is similar to that previously reported for the synthesis of monoaza crown ethers,<sup>22,23)</sup> and **8f** generated from selective *O*-alkylation under these conditions. Although it is confirmed by the measure-

TABLE 2. SYNTHESIS OF OLIGOAZA CROWN ETHERS BY THE REACTION OF DIHYDROXY AMINE AND OLIGOETHYLENE GLYCOL BIS(*p*-TOLUENESULFONATE)S (11)

| Crown ether                                    | Dihydroxy amine | Disulfonate (11) | Base            | Yield % | Mp $\theta_m$ /°C or Bp $\theta_b$ /°C (Torr) |
|------------------------------------------------|-----------------|------------------|-----------------|---------|-----------------------------------------------|
| 10,19-Diaza-21-crown-7(8f)                     | 3a              | 11a              | <i>t</i> -BuOK  | 38      | 120—125 (0.005)<br>39—41                      |
| 10,13-Diaza-15-crown-5(15a)                    | 4               | 11a              | <i>t</i> -BuONa | 32      | 85—90 (0.02)<br>46—48                         |
| 13,16-Diaza-18-crown-6(15b)                    | 4               | 11b              | <i>t</i> -BuONa | 39      | 105—110 (0.02)                                |
| "Dicyclohexyl-10,13-diaza-15-crown-5"(16a)     | 6a              | 11a              | <i>t</i> -BuONa | 42      | 137—141 (0.015)                               |
| "Dicyclohexyl-13,16-diaza-18-crown-6"(16b)     | 6a              | 11b              | <i>t</i> -BuONa | 42      | 155—160 (0.005)                               |
| "Dicyclohexyl-10,13,16-triaza-18-crown-6"(16c) | 6b              | 11a              | <i>t</i> -BuONa | 27      | 161—165 (0.02)                                |
| "Dicyclohexyl-13,16,19-triaza-21-crown-7"(16d) | 6b              | 11b              | <i>t</i> -BuOK  | 21      | 170—173 (0.03)                                |

ment of tertiary amine content of product **8f** that the isomeric hydroxy compounds (**13** and **14**) to be formed by *N*-alkylation of **12** are scarcely generated, diethylene glycol di-*t*-butyl ether is formed by the attack of *t*-butoxide anion on **11a** as a by-product.<sup>27)</sup>

In a similar manner to **8f**, di- and triaza crown ethers (**15** and **16**) have also been obtained (Table 2). The better yields of crown compounds (**16a**, **b**) with a cyclohexane ring than compounds (**15a**, **b**) without the ring may be explained by the higher solubility of their intermediate alkoxides in the solvent. In the case of crown ethers (**16c**, **d**) having three imino groups, the yields are lower and about half of the starting (**6b**) is recovered unreacted. This is due to the decrease of the template effect, because a softer *N*-donor than *O*-donor is not apt to complex with a hard alkali metal cation.<sup>28)</sup>

### Experimental

IR and <sup>1</sup>H NMR spectra were recorded on a Hitachi 260 spectrometer and a JEOL JNM-PS-100 spectrometer respectively. Mass spectral data were measured with a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV. GLC analyses were performed on a Shimadzu gas chromatograph GC-3BF using two 1 m × 3 mm columns packed with 10% Silicone SE-30 on Celite 545 and OV-1 on Unipore KS or on a Shimadzu gas chromatograph GC-3BT employing 0.7 m × 3 mm column packed with 10% Carbowax on Celite 545. Amine contents were determined by titration.<sup>29,30)</sup>

Most starting materials were obtained from commercial sources. Their purity was checked by GLC and when necessary they were purified by distillation.  $\alpha$ -(2-Chloroethyl)- $\omega$ -chlorooligo(oxyethylenes) (**2b**, **c**) were prepared from the corresponding glycols and thionyl chloride. 6,9-Dioxa-3,12-diazatetradecane-1,14-diol (**3a**)<sup>18)</sup> and oligoethylene glycol bis(*p*-toluenesulfonate)s (**11a**, **b**)<sup>31)</sup> were synthesized as described previously.

7,10-Dioxa-4,13-diazaheptadecane-2,15-diol (**3e**). 1,8-Dichloro-3,6-dioxaoctane (18.7 g, 0.1 mol) was added to a suspension of 1-amino-2-propanol (75.1 g, 1.0 mol) and powdered sodium carbonate (15.9 g, 0.15 mol), and the mixture was heated at 120 °C with stirring. After 30 h, methanol (100 ml) was added. The mixture was filtered, and the excess amine and methanol were removed from the filtrate.

The residue was distilled in a Kugelrohr apparatus at 175—180 °C (0.03 Torr) to give a crude product (15.5 g). It was purified by recrystallization from hexane-THF (50 : 50) to afford 11.9 g (45%) of **3e** as a white solid; mp 65—67.5 °C; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ =1.16 (d, 6H), 2.30—2.92 (m, 8H), 3.29 (s, 4H), 3.47—3.68 (m, 8H), 3.69—3.99 (m, 2H); MS, *m/e* (relative intensity) 249(3), 219(100), 164(59), 132(25), 102(76), 88(68), 44(49); IR (KBr) 3300, 2920, 2880, 1460, 1355, 1120 cm<sup>-1</sup>. Found: C, 54.25; H, 10.60; N, 10.33. Calcd for C<sub>12</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>: C, 54.52; H, 10.68; N, 10.60. Using a similar procedure, **3b**, **3c**, and **3d** were also obtained.

6,9,12-Trioxa-3,15-diazaheptadecane-1,17-diol (**3b**). Bp 180—185 °C (0.01 Torr, \*\* Kugelrohr distillation); yellowish viscous liquid; 20% yield; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ =2.56—2.93 (m, 8H), 3.39—3.95 (m, 16H), 3.64 (s, 4H); *m/e* (relative intensity) 249(11), 194(20), 176(28), 165(15), 88(42), 74(100), 44(30); IR (neat) 3300, 2930, 2880, 1460, 1360, 1110 cm<sup>-1</sup>. Found: C, 51.12; H, 9.89; N, 10.19. Calcd for C<sub>12</sub>H<sub>28</sub>N<sub>2</sub>O<sub>5</sub>: C, 51.41; H, 10.07; N, 9.99.

6,9,12,15-Tetraoxa-3,18-diazaeicosane-1,20-diol (**3c**). Bp 190—195 °C (0.005 Torr, Kugelrohr distillation); yellowish viscous liquid; 22% yield; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ =2.56—2.96 (m, 8H), 3.28 (s, 4H), 3.44—3.85 (m, 20H); MS, *m/e* (relative intensity) 293(18), 238(43), 220(37), 132(24), 100(24), 88(41), 74(100); IR (neat) 3290, 2930, 1460, 1355, 1100 cm<sup>-1</sup>. Found: C, 51.56; H, 10.02; N, 8.71. Calcd for C<sub>14</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>: C, 51.83; H, 9.94; N, 8.64.

2,13-Diethyl-6,9-dioxa-3,12-diazatetradecane-1,14-diol (**3d**). Bp 170—175 °C (0.01 Torr, Kugelrohr distillation); white waxy solid at 30 °C; 49% yield; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$ =0.92 (t, 6H), 1.24—1.64 (m, 4H), 2.37—2.96 (m, 6H), 3.02 (s, 4H), 3.24—3.76 (m, 12H); MS, *m/e* (relative intensity) 292 (M<sup>+</sup>, 1), 261(100), 243(6), 178(27), 116(61), 102(53), 44(71); IR (KBr) 3300, 2910, 2880, 1460, 1360, 1120 cm<sup>-1</sup>. Found: C, 57.88; H, 10.76; N, 9.71. Calcd for C<sub>14</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>: C, 57.50; H, 11.03; N, 9.58.

2-[2-(2-Hydroxyethylamino)ethylamino]ethanol (**4**). 2-Chloroethanol (8.5 g, 0.1 mol) was added to a suspension of 2-(2-aminoethylamino)ethanol (104 g, 1 mol) and powdered sodium carbonate (8.0 g, 0.08 mol); the reaction was continued with stirring at 120 °C for 29 h. After the reaction mixture cooled to room temperature, methanol (150 ml) was added, and the mixture was filtered. Evaporation of the filtrate gave a crude

\*\* 1 Torr  $\approx$  133.322 Pa.

product (15.5 g), which was recrystallized twice from THF to give 7.6 g (51%) of **4** as a white solid: mp 98–100 °C;  $^1\text{H}$  NMR ( $\text{CD}_3\text{OD}$ )  $\delta$ =2.40–2.92 (m, 8H), 3.63 (t, 4H); MS,  $m/e$  (relative intensity) 118(10), 74(100), 56(59), 44(62); IR (KBr) 3330, 2950, 2875, 1450, 1360, 1070  $\text{cm}^{-1}$ . Found: C, 48.34; H, 10.63; N, 19.14. Calcd for  $\text{C}_6\text{H}_{16}\text{N}_2\text{O}_2$ : C, 48.63; H, 10.88; N, 18.90.

*N,N'*-Bis(2-hydroxycyclohexyl)ethylenediamine (**6a**). Cyclohexene oxide (19.6 g, 0.2 mol) was added dropwise to ethylenediamine (6.02 g, 0.1 mol) at 85 °C. After the addition, the mixture was heated at 110 °C for 3 h and gradually became a solid. The crude product was recrystallized from methanol–water (99 : 1) to give 8.32 g (32%) of **6a** as a white solid:

mp 190–193 °C;  $^1\text{H}$  NMR ( $\text{CD}_3\text{COOD}$ )  $\delta$ =1.02–2.49 (m, 16H), 2.76–3.36 (m, 2H), 3.37–4.05 (m, 6H); MS,  $m/e$  (relative intensity) 220(8), 128(100), 100(27), 81(19), 44(17); IR (KBr) 3290, 2950, 2880, 1475, 1090  $\text{cm}^{-1}$ . Found: C, 65.55; H, 11.01; N, 10.90. Calcd for  $\text{C}_{14}\text{H}_{28}\text{N}_2\text{O}_2$ : C, 65.59; H, 11.01; N, 10.93.

*Bis*[2-(2-hydroxycyclohexylamino)ethyl]amine (**6b**). The above procedure was followed, using cyclohexene oxide (19.6 g, 0.2 mol) and bis(2-aminoethyl)amine (10.3 g, 0.1 mol). The crude product was recrystallized from THF to give 7.6 g (25%) of **6b** as a white solid: mp 132–135 °C;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ =0.69–2.13 (m, 16H), 2.14–3.03 (m, 10H), 2.86 (s, 5H), 3.04–3.47 (m, 2H); MS,  $m/e$  (relative intensity)

TABLE 3. CHARACTERIZATION OF DI- AND TRIAZA CROWN ETHERS

| Crown ether | IR(neat)<br>$\tilde{\nu}/\text{cm}^{-1}$ | $^1\text{H}$ NMR( $\text{CDCl}_3$ )<br>$\delta$                                              | MS(70 eV), $m/e$<br>(relative intensity)                                                       |
|-------------|------------------------------------------|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| <b>8a</b>   | 3330, 1110 <sup>a)</sup>                 | 2.47(s,2H), 2.75(t,8H), 3.48–3.76(m,12H)                                                     | 217( $\text{M}^+-1,1$ ), 187(4), 173(6), 150(36), 132(100), 118(10)                            |
| <b>8b</b>   | 3320, 1110 <sup>a)</sup>                 | 2.21(s,2H), 2.76(t,8H), 3.32–3.85(m,16H)                                                     | 261( $\text{M}^+-1,1$ ), 194(28), 176(100), 100(31), 88(54)                                    |
| <b>8c</b>   | 3320, 2930, 2880, 1460, 1350, 1120       | 2.45(s,2H), 2.78(t,8H), 3.49–3.92(m,20H)                                                     | 305( $\text{M}^+-1,2$ ), 288(5), 275(9), 238(37), 220(100), 206(19)                            |
| <b>8d</b>   | 3320, 2970, 2890, 1465, 1355, 1130       | 0.93(t,6H), 1.22–1.61(m,4H), 2.34–2.97(m,6H), 2.81(s,2H), 3.46–3.80(m,12H)                   | 274( $\text{M}^+$ ), 243(89), 160(76), 128(17), 103(45), 84(100)                               |
| <b>8e</b>   | 3320, 2980, 2880, 1460, 1355, 1125       | 0.99–1.35(m,6H), 2.19–3.11(m,8H), 2.41(s,2H), 3.43–3.39(m,10H)                               | 246( $\text{M}^+,3$ ), 201(11), 146(76), 118(22), 100(74), 74(100)                             |
| <b>8f</b>   | 3360, 2920, 2880, 1460, 1355, 1110       | 2.57(s,2H), 2.70(t,8H), 3.48–3.80(m,20H)                                                     | 305( $\text{M}^+-1,2$ ), 275(9), 238(25), 231(15), 187(13), 176(100)                           |
| <b>15a</b>  | 3310, 2910, 2875, 1460, 1355, 1130       | 2.33(s,2H), 2.62–2.91(m,8H), 3.41–3.90(m,12H)                                                | 218( $\text{M}^+,2$ ), 162(100), 118(21), 112(25), 100(36), 85(26)                             |
| <b>15b</b>  | 3310, 2920, 2880, 1460, 1360, 1120       | 2.57(s,2H), 2.68–2.95(m,8H), 3.44–3.84(m,16H)                                                | 262( $\text{M}^+,1$ ), 206(100), 162(9), 111(13), 100(23)                                      |
| <b>16a</b>  | 3320, 2940, 2890, 1460, 1360, 1120       | 0.80–2.23(m,16H), 2.24–2.69(m,2H), 2.47(s,2H), 2.75(s,4H), 2.86–3.28(m,2H), 3.32–4.04(m,8H)  | 325( $\text{M}^+-1,3$ ), 220(39), 216(100), 198(5), 155(11), 111(63)                           |
| <b>16b</b>  | 3320, 2950, 2880, 1455, 1365, 1115       | 0.80–2.22(m,16H), 2.22–2.56(m,2H), 2.71(s,4H), 2.73(s,2H), 2.90–3.31(m,2H), 3.32–3.99(m,12H) | 369( $\text{M}^+-1,5$ ), 260(100), 220(38), 123(20), 111(35)                                   |
| <b>16c</b>  | 3300, 2950, 2870, 1460, 1370, 1110       | 0.77–2.26(m,16H), 2.26–2.97(m,10H), 2.75(s,3H), 2.97–3.31(m,2H), 3.38–4.21(m,8H)             | 368( $\text{M}^+-1,4$ ), 325(100), 313(64), 247(86), 216(48), 110(58)                          |
| <b>16d</b>  | 3320, 2940, 2875, 1460, 1360, 1120       | 0.73–2.16(m,16H), 2.22–3.00(m,10H), 2.84(s,3H), 3.00–3.33(m,2H), 3.34–3.95(m,12H)            | 412( $\text{M}^+-1,4$ ), 369(88), 357(61), 260(67), 171(92), 128(91), 110(91), 81(80), 44(100) |

a) Nujol.

TABLE 4. ELEMENTAL ANALYSIS OF DI- AND TRIAZA CROWN ETHERS

| Crown ether | Molecular formula                                | Found (Calcd) (%) |              |              |
|-------------|--------------------------------------------------|-------------------|--------------|--------------|
|             |                                                  | H                 | C            | N            |
| <b>8a</b>   | $\text{C}_{10}\text{H}_{22}\text{N}_2\text{O}_3$ | 10.32(10.16)      | 54.65(55.02) | 12.89(12.83) |
| <b>8b</b>   | $\text{C}_{12}\text{H}_{26}\text{N}_2\text{O}_4$ | 10.26( 9.99)      | 54.78(54.94) | 10.76(10.68) |
| <b>8c</b>   | $\text{C}_{14}\text{H}_{30}\text{N}_2\text{O}_5$ | 9.92( 9.87)       | 54.78(54.88) | 8.80( 9.14)  |
| <b>8d</b>   | $\text{C}_{14}\text{H}_{30}\text{N}_2\text{O}_3$ | 11.13(11.02)      | 61.12(61.28) | 10.32(10.21) |
| <b>8e</b>   | $\text{C}_{12}\text{H}_{26}\text{N}_2\text{O}_3$ | 10.76(10.64)      | 58.70(58.51) | 11.18(11.37) |
| <b>8f</b>   | $\text{C}_{14}\text{H}_{30}\text{N}_2\text{O}_5$ | 9.65( 9.87)       | 55.01(54.88) | 8.97( 9.14)  |
| <b>15a</b>  | $\text{C}_{10}\text{H}_{22}\text{N}_2\text{O}_3$ | 10.35(10.16)      | 55.14(55.02) | 12.90(12.83) |
| <b>15b</b>  | $\text{C}_{12}\text{H}_{26}\text{N}_2\text{O}_4$ | 10.15( 9.99)      | 54.83(54.94) | 10.45(10.68) |
| <b>16a</b>  | $\text{C}_{18}\text{H}_{34}\text{N}_2\text{O}_3$ | 10.69(10.50)      | 65.84(66.22) | 8.65( 8.58)  |
| <b>16b</b>  | $\text{C}_{20}\text{H}_{38}\text{N}_2\text{O}_4$ | 10.53(10.34)      | 64.40(64.83) | 7.62( 7.56)  |
| <b>16c</b>  | $\text{C}_{20}\text{H}_{38}\text{N}_3\text{O}_3$ | 10.98(10.64)      | 64.65(65.00) | 11.48(11.37) |
| <b>16d</b>  | $\text{C}_{22}\text{H}_{43}\text{N}_3\text{O}_4$ | 10.78(10.48)      | 63.79(63.89) | 9.88(10.16)  |

171(100), 159(31), 128(83), 98(21); IR (KBr) 3270, 2950, 2870, 1460, 1140  $\text{cm}^{-1}$ . Found: C, 64.08; H, 11.08; N, 13.92. Calcd for  $\text{C}_{18}\text{H}_{33}\text{N}_3\text{O}_2$ : C, 64.18; H, 11.11; N, 14.03.

**1,4,10-Trioxa-7,13-diazacyclopentadecane (8a)** via *Intramolecular Cyclization*. *p*-Toluenesulfonyl chloride (3.81 g, 0.02 mol) dissolved in 20 ml of dioxane, was slowly added dropwise to a suspension of powdered sodium hydroxide (6.3 g, 0.15 mol) and 6,9-dioxa-3,12-diazatetradecane-1,14-diol (**3a**, 4.73 g, 0.02 mol) in 60 ml of dioxane over a period of 2 h at 60 °C. After the addition, the reaction was continued for 3 h and the reaction mixture filtered. The precipitate was washed with dichloromethane, and the solvent removed from the combined solution of filtrate and washings. Water (10 ml) was added to the residue and the solution extracted five times with dichloromethane. The solvent was removed from the dichloromethane extracts to give the crude product (3.51 g). In the  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) spectrum of it, resonances were observed at  $\delta$  1.16 and 1.72, which were ascribed to the aziridine ring protons. No resonances for *p*-toluenesulfonamides were observed. After the crude product was neutralized by hydrochloric acid, it was distilled in the presence of sodium carbonate (2.12 g, 0.02 mol) by Kugelrohr distillation at 75–90 °C (0.03 Torr) to give a white waxy solid (1.61 g, 37%). It was again distilled in a Kugelrohr apparatus at 80–85 °C (0.015 Torr) to afford 1.14 g (26%) of GLC-pure **8a** as a white solid: mp 91–93 °C (lit.<sup>1</sup> 89–90 °C). In the  $^1\text{H}$  NMR of the product, resonances of aziridine ring protons were no longer observed, because aziridine derivatives were lost by further reaction during distillation. This procedure was typical for the preparation of diaza crown ethers (**8b–e**) by intramolecular cyclization, and **8d**, **e** were separated from the first distillation product by alumina column chromatography (acetone–hexane 50 : 50), and further purified by distillation. Characterization of **8** was accomplished by a standard method (Tables 1 and 3) and elemental analysis of **8** is shown in Table 4.

**1,4,7,13,16-Pentaoxa-10,19-diazacycloheicosane (8f)** via *Intermolecular Cyclization*. 6,9-Dioxa-3,12-diazatetradecane-1,14-diol (**3a**, 4.73 g, 0.02 mol) and potassium metal (1.72 g, 0.044 mol) were dissolved in *t*-butyl alcohol (160 ml), and diethylene glycol bis(*p*-toluenesulfonate) (**11a**, 8.29 g, 0.02 mol) in dioxane (60 ml) was added dropwise to the solution at 40 °C during 2 h. After the addition, the reaction was continued for 2 h, when the reaction mixture was filtered. The precipitate was washed with dichloromethane, and the solvent removed from the combined solution of filtrate and washings. Water (10 ml) was added to the residue and the solution was extracted twice with hexane to remove by-products. It was then extracted several times with dichloromethane. The hexane was removed from the extracts, and the main by-product was isolated from the residue by preparative GLC and identified as diethylene glycol di-*t*-butyl ether:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  = 1.19 (s, 18H), 3.47–3.71 (m, 8H). The dichloromethane extracts were combined, the solvent evaporated. The crude product (5.48 g) was purified two distillations in a Kugelrohr apparatus at 120–124 °C (0.005 Torr) to give GLC-pure **8f** (2.33 g, 38%) as a clear liquid. The tertiary amine number of the product was found to be almost negligible (11.5), but the total amine number (363.6) agreed well with the calculated number (366.2). Using a similar procedure, oligoaza crown ethers (**15** and **16**) were also obtained (Tables 2 and 3).

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