2950, 1775, 1620, 1520, 1395, 1340, 1310, 1270, 1220, 1195, 1160, 1120, 1045, 750, 715, 630, 600, 570, 550 cm^{-1}. Anal. Calcd for $C_4H_8N_2O_4S$: C, 26.66; H, 4.44; N, 15.55; S, 17.77. Found: C, 26.62; H, 4.72; N, 15.47; S, 17.49.

(3*S*)-*cis*-3-Amino-4-methyl-2-oxoazetidine-1-sulfonic Acid (31). The crude product **28** (55.7 g, 106 mmol) from the above example was dissolved in 300 mL of 97% formic acid and stirred for 3 h. Filtration of the resulting slurry afforded 6.7 g of pure product. The mother liquor was then concentrated to ca. 150 mL and diluted with an equal volume of toluene. After the mixture was cooled at −20 °C for several hours an additional 1.7 g of product was obtained by filtration to afford a total of 8.4 g (44%) of the desired zwitterion **31**. Further attempts to recover additional material were unsuccessful: mp >200 °C dec; $[\alpha]_D$ −62° (*c* 3.15, H_2O); ^1H NMR (D_2O, 100 MHz) 4.8–4.1 (2 H, m obscured by HOD peak), 1.50 (3 H, d, J = 6.5 Hz); ^{13}C NMR (D_2O, dioxane standard) 160.5, 56.0, 53.8, 12.5; IR (KBr) 3420 (br), 3180 (br), 3010, 2950, 1765, 1525, 1315, 1280, 1230, 1050, 640 cm^{-1}. Anal. Calcd for $C_4H_8N_2O_4S$: C, 26.66; H, 4.44; N, 15.55; S, 17.77. Found: C, 26.63; H, 4.74; N, 15.30; S, 17.47.

Acknowledgment. We acknowledge the admirable efforts of our colleagues in the Chemical Process Development Department Manufacturing Division, E. R. Squibb & Sons) in scaling up these procedures to the multikilogram level. We want to especially note the efforts of Dr. Niel Anderson, who first observed the aminolysis of **17** in the reduction step, and Dr. Leroy High, who determined the feasibility and limitations of the portionwise addition of **14** during the cyclization reaction.

Registry No. **9**, 72229-74-4; **10**, 83511-25-5; **11**, 83511-26-6; **12**, 80543-39-1; **13**, 83511-27-7; **14**, 83511-28-8; **15**, 80575-79-7; **16**, 72229-73-3; **17**, 83542-13-6; **18**, 80543-40-4; **19**, 80582-03-2; **20**, 80582-06-5; **24**, 80082-81-1; **25**, 80082-47-9; **26**, 83511-30-2; **27**, 80082-60-6; **28**, 80582-08-7; **29**, 79720-18-6; **30**, 80082-65-1; **31**, 80582-09-8; L-serine, 56-45-1; methoxyamine hydrochloride, 593-56-6; L-threonine, 72-19-5; *allo*-threonine, 2676-21-3.

Sythesis of Aminomethyl Crown Ethers

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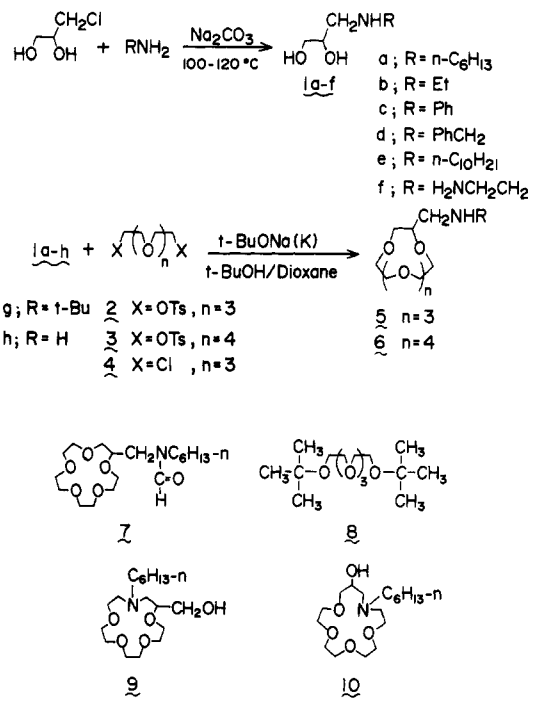
Various N-substituted or unsubstituted aminomethyl crown ethers, which possess a reactive amino group, were prepared in good yields by the reaction between 3-amino-1,2-propanediols or aminomethyl oligoethylene glycols and oligoethylene glycol ditosylates or dichlorides. The scope of the reaction was investigated and the complexing ability of these new crown ether derivatives with sodium and potassium ions in methanol was measured by potentiometric titration.

Recently, the syntheses and applications of many linear and network polymers including macrocyclic polyethers in the backbone or as a pendant group have been reported.[1,2] Although most of them are obtained from benzo crown compounds by utilizing the functional groups introduced in their benzene ring, some crown polymers are prepared from hydroxy crown ethers[3,4] or diaza crown ethers.[5-7]

We have previously reported some facile syntheses of crown ethers bearing functional groups such as chloromethyl,[8] hydroxymethyl,[9] and bromomethyl,[10] which are useful intermediates for the syntheses of immobilized crown compounds, lariat ethers,[11-13] bis crown ethers,[3,14] etc.

Scheme I



Crown compounds having amino groups can also be utilized for the above objectives. Montanari et al. have synthesized [(ethylamino)nonyl]-18-crown-6 and have reported that the immobilized crown ethers derived from it showed good activity as phase-transfer catalysts.[15-17]

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Table I. Synthesis of [(Hexylamino)methyl]-15-crown-5 (5a)[a]

run	solvent	X	base	reaction temp, °C	reaction time, h	isolated yield, %
1	*t*-BuOH/dioxane	OTs	*t*-BuONa	40	4	51
2	*t*-BuOH/dioxane	OTs	*t*-BuONa	40	4	33[b]
3	*t*-BuOH/dioxane	OTs	*t*-BuONa	40	4	63[c]
4	THF	OTs	*t*-BuOK	reflux	4.5	trace[d]
5	dioxane	OTs	NaOH	80	19	34
6	DMF	OTs	NaH	80	19	0[e]
7	dioxane	Cl	NaOH	reflux	19	6[d]
8	dioxane	Cl	NaOH	reflux	19	17[d,f]
9	*t*-BuOH	Cl	*t*-BuONa	reflux	19	17[d]

[a] 1a, 0.05 mol; 2 or 4, 0.05 mol; base, 0.1 mol; solvent, 400 mL. [b] Base (0.2 mol) was used. [c] 1a (0.075 mol) was employed. [d] Base (0.12 mol) was used. [e] 7 was obtained. [f] NaBr (0.1 mol) was added.

Table II. Syntheses of Aminomethyl Crown Ethers

compd	R	base	isolated yield, %	refractive index (20 °C)	amine value (calcd)
5a	n-C_6H_{13}	*t*-BuONa	51	1.4681	165.9 (168.2), 3.6[a]
5b	C_2H_5	*t*-BuONa	61	1.4701	200.0 (202.3)
5c	Ph	*t*-BuONa	43	1.5283	168.2 (172.4)
5d	$PhCH_2$	*t*-BuONa	56	1.5081	160.2 (165.3)
5e	n-$C_{10}H_{21}$	*t*-BuONa	48	1.4661	142.0 (144.0)
5f	$H_2NCH_2CH_2$	*t*-BuONa	35	1.4870	376.8 (383.8)
5g	$(CH_3)_3C$	*t*-BuONa	56	1.4663	181.7 (183.7)
5h	H	*t*-BuONa	trace	1.4848	218.4 (220.6), 4.3[b]
6a	n-C_6H_{13}	*t*-BuOK	50	1.4684	145.0 (148.6)
6b	C_2H_5	*t*-BuOK	51	1.4691	172.7 (174.5)
6c	Ph	*t*-BuOK	46	1.5251	151.1 (151.8)
6g	$(CH_3)_3C$	*t*-BuOK	51	1.4654	157.0 (160.5)
6h	H	*t*-BuOK	trace	1.4814	188.9 (191.2)

[a] Tertiary amine value. [b] Secondary and tertiary amine value.

In the present work, we describe a method for the facile synthesis of aminomethyl crown ethers having a reactive secondary or primary amino group in the side chain by treatment of 3-amino-1,2-propanediol or its homologues with oligoethylene glycol ditosylates or dichlorides. In addition, stability constants for these new substituted crown ethers with sodium and potassium cations have been determined and compared with those of unsubstituted crown ethers, monoaza crown ethers, and lariat ethers reported previously.[11-13,18,19]

Results and Discussion

The starting materials, 3-(N-substituted amino)-1,2-propanediols (1) were prepared from 3-chloro-1,2-propanediol and the appropriate primary amine. The diols and sodium or potassium metal were dissolved in *tert*-butyl alcohol, and then oligoethylene glycol ditosylates or dichlorides in appropriate solvents were added dropwise to the solution at 40–80 °C. The crude product complexes were thermolyzed in a Kugelrohr apparatus under reduced pressure to give aminomethyl crown ethers (Scheme I).

The results of the synthesis of [(hexylamino)methyl]-15-crown-5 (**5a**) by the reaction between 3-(hexylamino)-1,2-propanediol (**1a**) and tetraethylene glycol ditosylate (**2**) or dichloride (**4**) under various reaction conditions (changing solvents, bases, molar ratios of reactants, or temperature) are shown in Table I.

The solvent plays an important role in this reaction. In the reactions using ditosylates, the yields of the crown ethers are satisfactory in *tert*-butyl alcohol/dioxane, while the reactions in THF or dioxane give poorer yields, probably because of the limited solubility of the intermediate alkoxides. However, with NaH in DMF, where alkoxide solubility is increased, [(hexylformylamino)methyl]-15-crown-5 (**7**) is obtained in 38% yield instead of the desired crown ether, **5a**. Compound **7** is presumably produced from an amide exchange reaction of **5a** with DMF.[20]

With the less reactive dichlorides **4**, about half of the starting **4** is recovered unreacted, even after refluxing for 19 h in NaOH/dioxane. Although the reaction is somewhat accelerated by the addition of NaBr to this system, one-fourth of **4** is recovered. In *t*-BuONa/*t*-BuOH, yields in the reactions using ditosylates are better than those in reactions using dichlorides. In the reactions with ditosylates, tetraethylene glycol di-*tert*-butyl ether (**8**) is isolated as a byproduct. This is due to the competitive attack of *tert*-butoxide anion on tetraethylene glycol ditosylate.[21] There is an appreciable reduction in yield of **5a**, especially when excess base is used. On the other hand, excess **1a** increases the yield of **5a** (Table I, run 3).

One might have expected the isomeric hydroxy amines **9** and **10** to be formed by N- and O-alkylation of **1a**. However, the tertiary amine content of the reaction products is found to be almost negligible, but the total amine content agrees well with the calculated value for **5a**. Furthermore, no evidence for the presence of **9** and **10** is obtained by careful analysis of the reaction products by GLC and NMR. These results support the observations in the previously reported syntheses of monoaza crown ethers[22] and of aza crown ethers with oxetane[23] that O-alkylation predominates over N-alkylation under basic conditions which generate an alkoxide.

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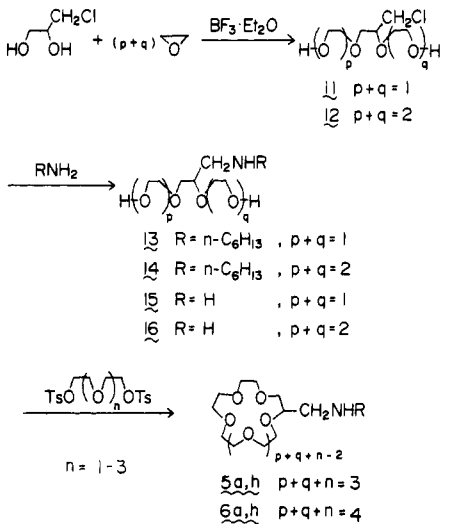
Scheme II



The syntheses of various aminomethyl crown ethers (Table II) have been achieved from oligoethylene glycol ditosylates by using the *t*-BuOM/*t*-BuOH system described above.

Both N-substituted (aminomethyl)-15-crown-5 and 18-crown-6 derivatives have been prepared in good yields, but the syntheses of N-unsubstituted aminomethyl crown ethers **5h** and **6h** have not been achieved. In these latter cases, a milky precipitate, which is assumed to be the alkoxide of 3-amino-1,2-propanediol (**1h**), separates before the addition of the ditosylate. The slight solubility of the alkoxide of **1h** may prevent the formation of the crown compounds. The somewhat lower yield of **5f** may also be explained on this basis.

Although **5h** can be obtained by the reductive debenzylation of [(benzylamino)methyl]-15-crown-5 (**5d**), direct preparation of the crown ethers with a primary amino group has been further investigated by changing strating materials. Since it is anticipated that the solubility of the alkoxides in *tert*-butyl alcohol could be improved by increasing the number of oxyethylene units of the diol, preparation of aminomethyl oligoethylene glycols **15** and **16** has been attempted.

(Chloromethyl)diethylene glycol (**11**) and (chloromethyl)triethylene glycol (**12**) are separated by fractional distillation from the chloromethyl oligoethylene glycol mixture obtained by the reaction of ethylene oxide with 3-chloro-1,2-propanediol in the presence of boron trifluoride etherate. They are allowed to react with ammonia or hexylamine to give aminomethyl (**15, 16**) and (hexylamino)methyl oligoethylene glycols (**13, 14**), respectively (Scheme II).

These aminomethyl oligoethylene glycols are probably isomeric mixtures. However, they are used without further separation, because the respective isomers should afford the same crown ethers by treatment with oligoethylene glycol ditosylates. Using the same procedures as before, [(hexylamino)methyl]-15-crown-5 (**5a**) and aminomethyl crown ethers **5h** and **6h** have been prepared (Table III). The yields of **5a** from **13** or **14** are slightly higher than from **1a**. this fact and the successful preparation of **5h** and **6h** suggest that solubility of the alkoxides is an important factor.

The stability constants for these aminomethyl crown ethers with sodium and potassium cations in methanol have been measured and are listed in Table IV.

The complexing ability of aminomethyl crown ethers is found to be somewhat lower than those of the parent crown ethers (15-crown-5 and 18-crown-6),[24] alkyl crown ethers,[9] and alkoxymethyl crown ethers[13] but better than those of unsubstituted monoaza crown ethers. The conclusion is that primary or secondary amino nitrogen atoms in the substituent do not effectively contribute to the complexation of hard cations, althouh the stability constants for **5f** which contains two amino groups are the highest for both sodium and potassium cations among the aminomethyl crown ethers investigated.

Table III. Syntheses of Aminomethyl Crown Ethers via the Reaction of Aminomethyl Oligoethylene Glycols with Oligoethylene Glycol Ditosylates

compd	R	$p+q$	n	base	isolated yield, %
5a	n-C_6H_{13}	1	2	*t*-BuONa	58
5a	n-C_6H_{13}	2	1	*t*-BuONa	61
5h	H	1	2	*t*-BuONa	53
5h	H	2	1	*t*-BuONa	41
6h	H	1	3	*t*-BuONa	43
6h	H	2	2	*t*-BuOK	40

Table IV. Stability Constants in Methanol at 25 °C

crown ether	log K_1' Na$^+$	log K_1' K$^+$
5a	2.82	2.95
5c	2.91	3.00
5f	2.92	3.06
5g	2.79	2.82
5h	2.82	3.01
15-crown-5	3.27	3.60
C_8H_{17}-15-crown-5	3.2[a]	3.1[a]
CH_3OCH_2-15-crown-5	3.03[b]	3.27[b]
monoaza-15-crown-5	2.06	[c]
6a	3.51	5.05
18-crown-6	4.30 (4.32)[d]	6.02 (6.10)[d]

[a] Reference 9. [b] Reference 13. [c] Reproducible data are not obtained for an undefined reason. [d] Reference 24.

Experimental Section

^{1}H NMR spectra were recorded at 100 MHz on a JEOL JNM-PS 100 spectrometer. Infrared spectra were obtained with a Hitachi 260-10 spectrometer. 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 with a 1 m × 3 mm column packed with 10% silicone SE-30 on Celite 545 or on a Shimadzu GC-3BT gas chromatograph employing a 0.7 m × 3 mm column packed with 10% Carbowax on Celite 545. Stability constants were measured with a Beckmann 4500 digital pH meter and calculated by the reported method.[24] Amine contents were determined by conventional titration procedures.[25-27]

Primary amines and 3-chloro-1,2-propanediol of analytical reagent grade were obtained from a commercial source. Their purity was checked by GLC, and they were purified by distillation when necessary. Tetraethylene glycol dichloride was prepared from tetraethylene glycol and thionyl chloride. Oligoethylene glycol ditosylates were synthesized as described previously.[28] 3-Amino-1,2-propanediol and 3-(*tert*-butylamino)-1,2-propanediol were commercial products.

3-(Hexylamino)-1,2-propanediol (1a). 3-Chloro-1,2-propanediol (55.5 g, 0.5 mol) was added to a suspension of hexylamine (404 g, 4.0 mol) and powdered sodium carbonate (40.3

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Table V. Preparation of 3-Amino-1,2-propanediols

compd	yield, %	bp, °C/torr (mp, °C)	^{1}H NMR (solvent), δ
1a	74	115–118/0.03 (45–48)	in $CDCl_3$: 0.88 (t, 3 H), 1.12–1.69 (m, 8 H), 2.28–2.89 (m, 4 H), 3.36–3.65 (m, 2 H), 3.65–3.89 (m, 1 H), 4.02 (s, 3 H)
1b	50	85–87/0.3	in $CDCl_3$: 1.11 (t, 3 H), 2.42–2.90 (m, 4 H), 3.40–4.16 (m, 3 H), 4.24 (s, 3 H)
1c	35	149–151/0.06 (41–45)	in $CDCl_3$: 2.72–3.19 (m, 2 H), 3.26–3.93 (m, 3 H), 4.21 (s, 3 H), 6.47–6.86 (m, 3 H), 7.00–7.30 (m, 2 H)
1d	51	125–130/0.015[a]	in $CDCl_3$: 2.48–2.82 (m, 2 H), 2.98 (s, 3 H), 3.35–3.65 (m, 3 H), 3.74 (s, 2 H), 7.27 (s, 5 H)
1e	57	152–155/0.07 (70–73)	in $CDCl_3$: 0.87 (t, 3 H), 1.11–1.70 (m, 16 H), 2.46–2.95 (m, 4 H), 3.52 (s, 3 H), 3.38–3.95 (m, 3 H)
1f	72	175–180/0.01 (54–57)	in D_2O: 2.44–2.85 (m, 6 H), 3.32–3.65 (m, 2 H), 3.66–3.94 (m, 1 H), 4.75 (s, 5 H)

[a] Kugelrohr distillation.

Table VI. Characterization of N-Substituted Aminomethyl Crown Ethers[a]

compd	bp, °C (torr)[b]	IR (neat), cm^{-1}	MS, *m/e* (rel intens)	^{1}H NMR ($CDCl_3$), δ
5a	115–120 (0.005)	3320, 1130	333 (M^+, 4.0), 262 (14.4), 133 (14.9), 114 (100)	0.88 (t, 3 H), 1.17–1.62 (m, 8 H), 2.21 (s, 1 H), 2.48–2.81 (m, 4 H), 3.42–3.96 (m, 19 H)
5b	90–93 (0.005)	3300, 1120	277 (M^+, 1.7), 247 (2.9), 133 (12.5), 58 (100)	1.12 (t, 3 H), 2.67 (s, 1 H), 2.42–2.90 (m, 4 H), 3.40–4.16 (m, 19 H)
5c	150–155 (0.01)	3370, 1100	352 (M^+, 17.3), 295 (4.3), 106 (100)	2.96–3.41 (m, 2 H), 3.20 (s, 1 H), 3.41–4.03 (m, 19 H), 6.57–6.82 (m, 3 H), 7.05–7.33 (m, 2 H)
5d	156–159 (0.01)	3320, 1110	339 (M^+, 1.8), 133 (7.7), 120 (63.1), 91 (100)	2.52 (s, 1 H), 2.60–2.80 (m, 2 H), 3.36–3.85 (m, 19 H), 3.78 (s, 2 H), 7.30 (s, 5 H)
5e	135–140 (0.005)	3300, 1120	389 (M^+, 1.0), 262 (3.6), 170 (100)	0.87 (t, 3 H), 1.11–1.66 (m, 16 H), 2.44–2.84 (m, 4 H), 2.98 (s, 1 H), 3.37–4.00 (m, 19 H)
5f	130–133 (0.002)	3320, 1130	292 (M^+, 1.0), 262 (100), 219 (3.6)	2.04 (s, 3 H), 2.27–2.98 (m, 6 H), 3.38–4.00 (m, 19 H)
5g	110–115 (0.005)	3300, 1130	305 (M^+, 1.9), 290 (47.6), 260 (4.2), 86 (100)	1.08 (s, 9 H), 2.30 (s, 1 H), 2.51–2.80 (m, 2 H), 3.42–3.93 (m, 19 H)
6a	130–135 (0.005)	3320, 1120	377 (M^+, 1.8), 306 (15.7), 133 (12.6), 114 (100)	0.88 (t, 3 H), 1.11–1.64 (m, 8 H), 2.08 (s, 1 H), 2.39–2.85 (m, 4 H), 3.45–4.02 (m, 23 H)
6b	110–115 (0.005)	3310, 1120	321 (M^+, 1.6), 133 (7.9), 89 (22.5), 58 (100)	1.09 (t, 3 H), 2.33 (s, 1 H), 2.49–2.85 (m, 4 H), 3.38–4.03 (m, 23 H)
6c	170–175 (0.007)	3380, 1110	369 (M^+, 4.9), 106 (100), 89 (74.1)	2.84–3.44 (m, 2 H), 3.40 (s, 1 H), 3.44–4.20 (m, 23 H), 6.46–6.84 (m, 3 H), 7.00–7.26 (m, 2 H)
6g	115–120 (0.001)	3300, 1120	349 (M^+, 1.5), 334 (37.0), 304 (4.5), 86 (100)	1.07 (s, 9 H), 1.68 (s, 1 H), 2.50–2.67 (m, 2 H), 3.42–3.90 (m, 23 H)

[a] Satisfactory combustion analyses were obtained (C, ±0.39; H, ±0.22; N, ±0.40). [b] Kugelrohr distillation.

g, 0.38 mol), and the mixture was heated at 110 °C with stirring. After 17 h, the mixture was cooled to room temperature and filtered, and the excess hexylamine was recovered from the filtrate. The residue was purified by distillation at 115–118 °C (0.03 torr) to give 64.8 g (74%) of **1a** as a white solid. By use of a similar procedure, 3-(N-substituted amino)-1,2-propanediols **1c–f** were also obtained (Table V).

3-(Ethylamino)-1,2-propanediol (1b). Into 387 g of 70% aqueous ethylamine solution (6.0 mol) containing 40.3 g (0.38 mol) of potassium carbonate was added with stirring 55.5 g (0.50 mol) of 3-chloro-1,2-propanediol. After the reaction mixture was refluxed for 32 h, water and excess ethylamine were evaporated off, and the residue was extracted with methanol. Evaporation of the extract gave the crude product, which was distilled under vacuum to give 29.7 g (50%) of **1b** as a pale yellow liquid.

[(Hexylamino)methyl]-15-crown-5 (5a). 3-(Hexylamino)-1,2-propanediol (**1a**; 8.8 g, 0.05 mol) and sodium metal (2.3 g, 0.1 mol) were dissolved in *tert*-butyl alcohol (340 mL), and tetraethylene glycol ditosylate (**2**; 25.1 g, 0.05 mol) in dioxane (60 mL) was added dropwise to the solution during 1.5 h at 40 °C. After the addition, the reaction was continued for 2.5 h, and then the reaction mixture was filtered. The precipitate was washed with dichloromethane, and the solvent was removed from the combined solution of filtrate and washings. The residue was distilled in a Kugelrohr apparatus to give a first fraction [0.2 g; 80–90 °C (0.005 torr)] and the main fraction [9.4 g; 110–160 °C (0.005 torr)]. The main product in the first fraction was isolated by using preparative GLC: ^{1}H NMR ($CDCl_3$) δ 1.19 (s, 18 H), 3.48–3.72 (m, 16 H); IR (neat) 2980, 2870, 1150, 1090 cm^{-1}. Anal. Calcd for $C_{16}H_{34}O_5$: C, 62.71; H, 11.18. Found: C, 62.34; H, 11.29. From these data, this product was identified as **8**. The main fraction was purified in a Kugelrohr apparatus at 115–120 °C (0.005 torr) to afford pure **5a** (8.5 g, 51%) as a pale yellow liquid.

This procedure was typical for the preparation of aminomethyl crown ethers. Characterization of N-substituted aminomethylcrown ethers **5** and **6** was accomplished by standard methods (Table VI).

The experiments for the investigation of the reaction conditions were carried out by using 3-(hexylamino)-1,2-propanediol (0.05 mol) and base (0.1 mol) in a solvent (340 mL) and tetraethylene glycol ditosylate or dichloride (0.05 mol) in a solvent (60 mL) in a manner similar to that described above.

[(Hexylformylamino)methyl]-15-crown-5 (7). To a suspension of 50% NaH (4.80 g, 0.1 mol) in 300 mL of DMF was added slowly a solution of 3-(hexylamino)-1,2-propanediol (**1a**; 8.75 g, 0.05 mol) in 40 mL of DMF. After cessation of hydrogen evolution, tetraethylene glycol ditosylate (25.1 g, 0.05 mol) in 60 mL of DMF was added dropwise to the solution during 1.5 h at 80 °C. After the addition, the reaction was continued for 17.5 h, the reaction mixture was filtered, and the solvent was removed. The residue was thermolyzed in a Kugelrohr apparatus under reduced pressure to give the crude product (7.51 g). It was further

distilled in a Kugelrohr apparatus at 140–145 °C (0.02 torr) to afford GLC-pure product (6.85 g) as a yellow liquid: 38% yield as **7**; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, CH_3, 3 H), 1.12–1.69 (m, CH_2, 8 H), 3.13–3.99 (m, NCH_2, $OCHCH_2O$, OCH_2CH_2O, 23 H), 8.08 (s, CHO, 1 H); mass spectrum, *m/e* (relative intensity) 361 (M^+, 9.7), 219 (19.5), 131 (18.6), 87 (100); IR (neat) 2930, 2860, 1680, 1470, 1360, 1130 cm^{-1}. Anal. Calcd for $C_{18}H_{35}NO_6$: C, 59.81; H, 9.76; N, 3.87. Found: C, 59.51; H, 9.74; N, 4.00.

Chloromethyl Oligoethylene Glycols. Ethylene oxide, which was purified by passage through a 40% NaOH aqueous solution and dried over NaOH pellets and soda lime, was introduced to 3-chloro-1,2-propanediol (111 g, 1.0 mol) in the presence of 1.5 g of boron trifluoride etherate at 80 °C. After a 66-g (1.5 mol) increase in weight was attained, the reaction was stopped, and the product was purged with nitrogen gas to remove unreacted ethylene oxide. (Chloromethyl)diethylene glycol (**11**, 27.4 g) and (chloromethyl)triethylene glycol (**12**, 19.4 g) were separated by fractional distillation under reduced pressure. **11**: bp 90–93 °C (0.015 torr); colorless liquid; ^{1}H NMR ($CDCl_3$) δ 3.56 (s, OH, 2 H), 3.50–3.85 (m, OCH_2, $ClCH_2$, 8 H), 3.85–4.12 (m, OCH, 1 H); IR (neat) 3340, 2960, 2870, 1300, 1120, 1060, 750 cm^{-1}. **12**: bp 121–123 °C (0.01 torr); pale yellow liquid; ^{1}H NMR ($CDCl_3$) δ 3.46 (s, OH, 2 H), 3.52–3.87 (m, OCH_2, $ClCH_2$, 12 H), 3.87–4.16 (m, OCH, 1 H).

[(Hexylamino)methyl]diethylene Glycol (13). The procedure for **1a** was followed by using **11** and hexylamine: bp 120–125 °C (0.005 torr; Kugelrohr distillation); pale yellow liquid; 58% yield; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, CH_3, 3 H), 1.12–1.68 (m, CH_2, 8 H), 2.45–2.84 (m, NCH_2, 4 H), 3.26 (s, OH, NH, 3 H), 3.40–4.02 (m, $OCHCH_2O$, OCH_2CH_2O, 7 H). Anal. Calcd for $C_{11}H_{25}NO_3$: C, 60.24; H, 11.49; N, 6.39. Found: C, 60.45; 11.67; N, 6.46.

[(Hexylamino)methyl]triethylene Glycol (14): bp 130–135 °C (0.005 torr, Kugelrohr distillation); pale yellow liquid; 58% yield; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H), 1.10–1.67 (m, 8 H), 2.45–2.83 (m, 4 H), 3.25 (s, 3 H), 3.44–4.02 (m, 11 H). Anal. Calcd for $C_{13}H_{29}NO_4$: C, 59.29; H, 11.10; N, 5.32. Found: C, 59.34; H, 11.31; N, 5.40.

(Aminomethyl)triethylene Glycol (16). Although this compound could be prepared from **12** by using the Gabriel method, the workup was difficult, because the intermediary phthalimide derivative could not be isolated by recrystallization in a pure state. The following procedure was employed. Into 26% aqueous ammonia solution (262 g, 4.0 mol) containing potassium carbonate (4.1 g, 0.03 mol) was added **12** (8.0 g, 0.04 mol) dropwise. After the mixture was stirred at room temperature for 55 h, water and ammonia were removed, and the residue was taken up in methanol, filtered, and distilled in a Kugelrohr apparatus to give **16** (3.1 g, 43% yield) as a pale yellow liquid: bp 145–148 °C (0.06 torr); ^{1}H NMR ($CDCl_3$) δ 2.50–2.99 (m, 2 H), 3.31 (s, 4 H), 3.43–3.92 (m, 11 H); IR (neat) 3350, 3280, 2940, 2870, 1460, 1360, 1120, 1070 cm^{-1}. Anal. Calcd for $C_7H_{17}NO_4$: C, 46.91; H, 9.56; N, 7.82. Found: C, 47.15; H, 9.61; N, 7.69.

(Aminomethyl)diethylene Glycol (15). The above procedure was adopted: bp 127–129 °C (0.15 torr); mp 47–52 °C; pale yellow solid; 53% yield; ^{1}H NMR ($CDCl_3$) δ 2.55–2.91 (m, 2 H), 3.52 (s, 4 H), 3.40–3.92 (m, 7 H); IR (neat) 3350, 3280, 2930, 2870, 1470, 1360, 1120, 1080 cm^{-1}. Anal. Calcd for $C_5H_{13}NO_3$: C, 44.43; H, 9.69; N, 10.36. Found: C, 44.03; H, 9.67; N, 10.14.

(Aminomethyl)-15-crown-5 (5h) from 15. By a procedure similar to that for **5a**, the reaction between **15** (6.8 g, 0.05 mol) and triethylene glycol ditosylate (22.8 g, 0.05 mol) was done in the presence of sodium metal (2.3 g, 0.1 mol) dissolved in *tert*-butyl alcohol: bp 113–117 °C (0.005 torr; Kugelrohr distillation); yellow liquid; 53% yield; ^{1}H NMR ($CDCl_3$) δ 2.58–2.91 (m, NCH_2, 2 H), 3.13 (s, NH_2, 2 H), 3.32–3.99 (m, $OCHCH_2O$, OCH_2CH_2O, 19 H); mass spectrum, *m/e* (relative intensity) 249 (M^+, 0.6), 219 (4.3), 177 (9.3), 133 (25.6), 89 (49.1), 46 (100); IR (neat) 3350, 3290, 2930, 2870, 1460, 1360, 1120 cm^{-1}. Anal. Calcd for $C_{11}H_{23}NO_5$: C, 53.00; H, 9.30; N, 5.62. Found: C, 53.22; H, 9.45; N, 5.48.

(Aminomethyl)-18-crown-6 (6h) from 15. The procedure for **5a** was followed by using sodium metal, **15**, and tetraethylene glycol ditosylate as reactants: bp 119–122 °C (0.005 torr; Kugelrohr distillation); yellow liquid; 43% yield; ^{1}H NMR ($CDCl_3$) δ 2.53–2.88 (s + m, NCH_2, NH_2, 4 H), 3.42–3.91 (m, $OCHCH_2O$, OCH_2CH_2O, 23 H); mass spectrum, *m/e* (relative intensity) 293 (M^+, 0.3), 263 (1.4), 177 (5.3), 133 (15.8), 89 (51.4), 45 (100); IR (neat) 3360, 3300, 2940, 2870, 1460, 1350, 1100 cm^{-1}. Anal. Calcd for $C_{13}H_{27}NO_6$: C, 53.23; H, 9.28; N, 4.77. Found: C, 52.73; H, 9.58; N, 4.65.

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Reactions of Lithio Trimethylsilyl Compounds with Nitrones

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The reactions of lithio compounds, generated in situ from 2-[(trimethylsilyl)methyl]pyridine (**1**), *N,N*-dimethyl(trimethylsilyl)acetamide (**2**), and ethyl (trimethylsilyl)acetate (**3**) and LDA in THF, with various nitrones have been investigated. The lithio compounds of **1**–**3** reacted with α,*N*-diarylnitrones to give the corresponding (*E*)-alkenes together with azoxybenzene and/or azobenzene. On the other hand, the reaction of lithio derivative of **1** with α-aryl-*N*-alkylnitrones, α,*N*-dialkylnitrones, and cyclic nitrones afforded the aziridine compounds as the major products, accompanied by hydroxylamine derivatives in some cases. The lithio derivative of **2** or **3** reacted with α,*N*-dialkylnitrones and cyclic nitrones to give the aziridine and/or isoxazolidinone derivatives. The pathways for the formation of the above products are also described.

Several kinds of reactions using metalated α-silyl derivatives have recently been developed. In particular, an important application of these derivatives is in the conversion of carbonyl compounds to the corresponding al-

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