335 °C[4b]) and an elemental analysis: C, 94.59; H, 5.39 (calcd: C, 94.70; H, 5.30).

Not surprisingly, the trans isomer is the only product observed. One indication is the melting point. This cis isomerizes to trans at 215 °C,[4c] and we saw no evidence for this in our product. The 270-MHZ ^{1}H NMR data matched that reported by Becker[4c] and Mislow[10] for the trans isomer. We also noted the appearance of an IR peak at 980 cm^{-1}, characteristic of trans alkenes.

We have ascertained that the remainder of the starting material was unchanged (by TLC and IR data). Although increasing the reaction time almost doubled the yield, the length of time is too long to consider trying for further improvement. We have also made a careful search (using IR and NMR) for any of the dimeric alcohol product reported in the literature,[6,7] with negative results.

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(10) Geiger, G. H.; Mislow, K. H. *J. Org. Chem.* **1986**, *51*, 5471.

Synthesis and Complexing Ability of *N*-Alkylmorpholino Crown Ethers and Their Derivatives

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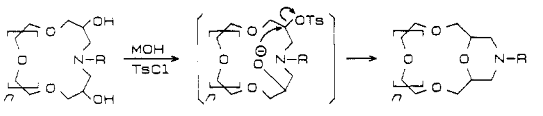
Crown ethers that bear a reactive group such as hydroxyl,[1-11] amino,[12,13] or haloalkyl[14] are important compounds for the formation of polymer-bound crown ethers, bis-crown ethers, lariat ethers, and other functionalized crown ethers. Easily prepared dihydroxy monoaza crown ethers 1[15] are also useful functionalized crown compounds, which can be transformed into cryptands[16] or polymers. In addition, their higher alkyl chain derivatives show interesting surface active behavior in aqueous solution.[17]

Scheme I



1 a, b, c

2 a, b, c

	n	MOH
a:	1	LiOH
b:	2	NaOH
c:	3	KOH

We report the synthesis and cation binding properties of novel morpholine ring-fused crown ethers 2, which can be easily prepared from 1 in good yield. These morpholino crown ethers 2 are anticipated to have selective and high complexing abilities toward alkali metal cations due to their highly symmetrical structures and rigid conformations. In contrast to aza crown ethers, chemical modifications on the nitrogen atom may be expected to produce only minor interference of the metal cation-binding property of the crown ring since the nitrogen atom is not located in the crown ring. Such modifications may give hydrophilic character to the lipophilic alkyl-substituted crown ethers and make them applicable as amphiphilic compounds or ionophores with controlled water solubility.

Results and Discussion

Dihydroxy monoaza crown ethers 1 were prepared by the reaction of equimolar amounts of oligoethylene glycol bis(glycidyl ether)[18] and primary amines in methanol, according to the method reported previously.[15]

N-Alkylmorpholino crown ethers 2 were prepared as pale yellow liquids by adding a dioxane solution of equimolar 1 and tosyl chloride to a suspension of excess pulverized alkali metal hydroxide in dioxane.

Lithium, sodium, and potassium hydroxides were found to produce the best cyclization yields of 12-crown, 15-crown, and 18-crown ethers, respectively, showing an apparent template effect of the alkali cations. A reaction pathway similar to that suggested for the cyclization of oligoethylene glycols to crown ethers[19,20] is proposed (Scheme I).

Product 2 should be composed of stereoisomers, which may have potentially different binding properties. This situation is reminiscent of the isomer problem of dicyclohexano-18-crown-6.[21] Distortionless enhancement by polarization transfer (DEPT) ^{13}C NMR spectra showed the presence of two kinds of methine carbons at 74.4 and 69.6 ppm for **2b** and 69.4 and 65.4 ppm for **2b**·HCl, respectively (77.0 ppm for $CDCl_3$). These two signals should represent the presence of cis and trans isomers, respectively. From single-pulse hetero decoupling without NOE (NNE), the ratios of these signal areas were 1.00:1.21 for **2b** and 1.00:0.91 for **2b**·HCl. In general, the signal at a lower field is generated in the trans isomer. But in this case, it cannot be concluded which signal corresponds to which isomer, since the area ratios are reversed for **2b** and **2b**·HCl. ^{1}H NMR spectra of **2b** also show the presence of two isomers.

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(1) Ashby, J.; Hull, R.; Cooper, M. J.; Ramage, E. M. *Synth. Commun.* **1974**, *4*, 113.

(2) Bradshaw, J. S.; Reeder, R. A.; Thompson, M. D.; Flanders, E. D.; Carruth, R. L.; Izatt, R. M.; Christensen, J. J. *J. Org. Chem.* **1976**, *41*, 134.

(3) Tomoi, M.; Abe, O.; Ikeda, M.; Kihara, K.; Kakiuchi, H. *Tetrahedron Lett.* **1978**, 3031.

(4) Montanari, F.; Tundo, P. *Tetrahedron Lett.* **1979**, 5055.

(5) Ikeda, I.; Yamamura, S.; Nakatsuji, N.; Okahara, M. *J. Org. Chem.* **1980**, *45*, 5355.

(6) Czech, B. *Tetrahedron Lett.* **1980**, *21*, 4197.

(7) Gokel, G. W.; Dishong, D. M.; Diamond, C. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1053.

(8) Heo, G. S.; Bartsch, R. A.; Schlobohm, L. L.; Lee, J. G. *J. Org. Chem.* **1981**, *46*, 3574.

(9) Ikeda, I.; Katayama, T.; Tsuchiya, K.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 2473.

(10) Jungk, S. J.; Moore, J. A.; Gandour, R. D. *J. Org. Chem.* **1983**, *48*, 1116.

(11) Ikeda, I.; Emura, H.; Okahara, M. *Synthesis* **1984**, 73.

(12) Maeda, H.; Kikui, T.; Okahara, M. *J. Org. Chem.* **1982**, *47*, 5167.

(13) Maeda, H.; Kikui, T.; Nakatsuji, Y.; Okahara, M. *Synthesis* **1983**, 185.

(14) Nakamura, T.; Nakatsuji, Y.; Okahara, M. *J. Chem. Soc., Chem. Commun.* **1981**, 219.

(15) Kikui, T.; Maeda, H.; Nakatsuji, Y.; Okahara, M. *Synthesis* **1984**, 74.

(16) Nakatsuji, Y.; Kikui, T.; Ikeda, I.; Okahara, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 315.

(17) Ikeda, I.; Ozawa, Y.; Nakatsuji, Y.; Okahara, M. *J. Am. Oil Chem. Soc.* **1987**, *64*, 1034.

(18) Gu, X.-P.; Ikeda, I.; Okahara, M. *Synthesis* **1985**, 649.

(19) Kuo, P.-L.; Miki, M.; Okahara, M. *J. Chem. Soc., Chem. Commun.* **1978**, 504.

(20) Kuo, P.-L.; Miki, M.; Ikeda, I.; Okahara, M. *Tetrahedron Lett.* **1978**, 4273.

(21) Frensdorff, H. K. *J. Am. Chem. Soc.* **1971**, *93*, 600.

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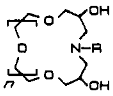
Signals from the six protons on the α-carbons to the nitrogen atom (in the case of **2b**) appear in six groups, which can be further divided into two groups based on the ratio of intensities, two triplets at 1.819 (J = 10.99 Hz) and 2.328 ppm (J = 7.90 Hz) and one doublet at 2.672 ppm (J = 9.89 Hz) (intensities = 1.00, respectively) and two doublet of doublets at 2.151 (J = 5.86, 10.99 Hz) and 2.465 ppm (J = 3.29, 10.99 Hz) and one doublet of triplet at 2.227 ppm (J = 7.33, 9.16 Hz) (intensities = 1.20, respectively). The triplet signal at 2.328 ppm that couples with a quintet at 1.486 (β to the nitrogen atom, confirmed by decoupling experiments) may be characterized as the α-protons in the octyl group of the cis isomer, since these two protons are magnetically equatorial because of C_s symmetry. Conversely, the signal for the same two protons in the trans isomer should be more complicated because of C_2 symmetry. And a doublet of triplet (intensities = 1.20) at 2.227, which couples with a quintet at 1.437, very likely arises from those two protons. From these results, the ratio of cis and trans isomers may be estimated to be 1.0:1.2. Furthermore, signals at 1.819 and 2.672 ppm should be assigned to the α-protons of the *cis*-morpholino moiety. The large chemical shift difference between these two signals should be attributable to the morpholino ring, in which the magnetic environment around the geminal two α-protons is quite different due to the unshared paired electrons on the nitrogen atom. Two triplets due to the terminal methyl groups appear at 0.897 ppm (area ratio, 1.19) and 0.891 ppm (area ratio, 1.00), representing a large structural effect between the stereoisomers.

Morpholinium hydrochlorides **2**·HCl, N-methylated quaternary morpholinium salts **3**, and N-oxidized morpholino crown ethers **4** were prepared by neutralization with gaseous hydrogen chloride in ether, quaternization with dimethyl sulfate in ether, or oxidization with hydrogen peroxide, respectively, to probe the effect of structural modification of the morpholino crown ethers **2**.

The stability constants for association of **2b**,**c**, **2b**·HCl, **2c**·HCl, **3b**,**c**, and **4b**,**c** with sodium and potassium cations in methanol were determined by potentiometry[21] (Table I). For comparison, stability constants were also determined for the starting *N*-octyl dihydroxy monoaza crown ethers **1**, *N*-octyl monoaza crown ethers **5**, and octyl crown ethers **6**.

Stability constants for association of *N*-octyl dihydroxy monoaza crown ethers **1** with both alkali cations was enhanced markedly by conversion to the bicyclic derivatives **2**. The complexing abilities of the alkylmorpholino crown ethers **2** surpass even those of typical alkyl crown ethers **6**, as well as the *N*-alkyl monoaza crown ethers **5**. This superiority of compounds **2** to compounds **6** may be reasonably explained in terms of lesser steric interaction of the alkyl chain substituent with the alkali cation[5] in the former in which the alkyl chain is held at a greater distance from the crown ring. The steric effect of the side chain is also shown, in reverse, by evaluation of the donation ability in the case of compound **2′b**. As has been seen in lariat ethers, oxyethylene moieties work to enhance the complexing ability of this compound (pK_1' (pK_2') is 3.35 (2.39) for Na$^+$ and 3.37 (3.04) for K$^+$, whereas the values are 3.31 (2.47) and 3.21 (3.04) for compound **2b** toward sodium and potassium cations, respectively). However, this contribution is very small compared with nitrogen pivot lariat ethers.[22,23]

Table I. Stability Constants of Morpholino Crown Ethers toward Sodium and Potassium Cations in Methanol at 25 °C[21]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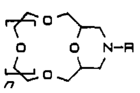
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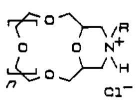
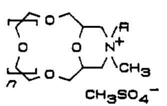

2·HCl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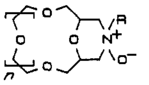
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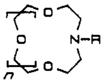
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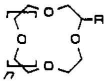
6

crown ether[a]	n	log K_1' (log K_2')[b] Na$^+$	log K_1' (log K_2')[b] K$^+$
1b	2	1.21	1.39
1c	3	2.67	2.93 (2.02)
2a	1	1.17 (2.66)	*c*
2b	2	3.31 (2.47)	3.21 (3.04)
2c	3	4.24 (2.61)	5.67 (3.06)
2′b[d]	2	3.35 (2.39)	3.37 (3.04)
2b·HCl	2	*e*	2.15 (0.24)
2c·HCl	3	*e*	2.71 (2.81)
3a	1	*c*	*c*
3b	2	1.95 (0.19)	1.88 (2.40)
3c	3	3.01 (2.34)	4.26 (3.24)
4a	1	*c*	*c*
4b	2	2.16 (2.91)	2.95 (3.05)
4c	3	3.93 (1.75)	4.84 (3.18)
5b	2	2.96 (2.33)	2.77 (2.49)
5c	3	3.34 (2.12)	4.44 (3.20)
6b	2	3.13 (1.90)	3.05 (2.32)
6c	3	3.87 (1.81)	5.36 (1.58)

[a] R = C_8H_{17}, unless otherwise stated. [b] Single figures shows log K. K_1' = stability constant for the formation of 1:1 complex, K_2' = value for 2 hosts:1 guest complex. [c] No rational value was obtained. [d] **2′b**; R = 3,6-dioxadecyl. [e] No stable reading was obtained with the glass electrode.

Morpholinium crown ether hydrochlorides (**2b**·HCl, **2c**·HCl) showed some affinity toward potassium cation in methanol, but the stability constant values are low even for the 18-crown-6 derivative (**2c**·HCl). Judging from the difference between the values for the hydrochloride (**2c**·HCl) and the quaternary salt (**3c**, see later), the proton in the hydrochloride salts may not be located only on the nitrogen atom but may be partially distributed on the ether oxygen atoms competing with the complexation of potassium cation.

Although both **2b**·HCl and **2c**·HCl did seem to have some affinity toward sodium cation, the calculated stability constant values were dependent on the concentration of the hydrochloride. Thus, they did not represent any stable electromotive force toward the sodium cation selective glass electrode in methanol and the values of stability constants could not be determined.

Quaternary morpholinium crown ether **3c** exhibits a somewhat lower stability constant toward potassium cation than does its parent morpholino crown ether **2c**, showing the influence of the cationic nitrogen atom, in the former. Nevertheless the stability constant value is still comparable to that for the corresponding monoaza crown ether **5c**. In the case of the corresponding 15-crown-5 compound **3b**, the effect of the cationic nitrogen atom is dramatic and only a slight affinity toward potassium cation is noted. This phenomenon is probably due to the shorter distance between the cationic nitrogen center and the cation upon the complexation for the crown ring which has the smaller cavity with the larger cation.

Oxidation of morpholino crown ethers **2** by aqueous hydrogen peroxide was rather slow and required a long

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(22) Schultz, R. A.; Dishong, D. M.; Gokel, G. W. *Tetrahedron Lett.* 1981, *22*, 2623.

(23) Masuyama, A.; Nakatsuji, Y.; Ikeda, I.; Okahara, M. *Tetrahedron Lett.* 1981, *22*, 4665.

reaction period and the gradual addition of hydrogen peroxide to the reaction system. Since the ^{1}H NMR spectrum of resultant compound was complicated (probably due to the presence of protons that are β to the oxidized nitrogen atom and, at the same time, α and β to the ether oxygen atom), the ^{15}N NMR spectrum was recorded. The observed signal was shifted 70.5 ppm downfield from that of starting morpholino crown ether **2b**, which is consistent with a report[24] that the ^{15}N NMR signal shifts 70–100 ppm upon oxidation and supports the formation of amine oxide **4b**. Inspection of CPK molecular models suggests that oxidation of the nitrogen atom of the morpholino crown ether may provide another strong donation site for cation complexation. However, the stability constants for **4** measured in methanol are lower than those of their parent compounds **2**. On the other hand they are still higher than those of morpholinium derivatives (**2**·HCl, **3**).

Experimental Section

^{1}H NMR and ^{13}C NMR spectra (including DEPT and NNE) were recorded on JEOL-PS-100, JEOL-GSX-400, or Bruker-AM-600 instruments in CDCl$_3$ with Me$_4$Si as internal standard. ^{15}N NMR spectra were recorded at 36.500 MHz on a Bruker WM 360 instrument in CDCl$_3$ with NO$_3^-$ or NH$_3$ as external standard. Mass spectra were measured on a Hitachi RMU-6E spectrometer. Infrared spectra were obtained on a Hitachi 260-10 spectrometer. All the reagents were of reagent grade and were used without further purification. *N*-Octyl dihydroxy monoaza crown ethers **1** were synthesized according to a reported procedure.[15] Evaporative distillation (Kugelrohr distillation) was performed from bulb to bulb with a glass tube oven Model GTO-250RS.

***N*-Octylmorpholino 18-Crown-6 Ether (2c); Typical Procedure.** A solution of compound **1c** (R = *n*-C$_8$H$_{17}$, *n* = 3) (4.36 g, 0.01 mol) and *p*-toluenesulfonyl chloride (1.91 g, 0.01 mol) in 150 mL of dioxane was added dropwise to a stirred suspension of pulverized potassium hydroxide (4.21 g, 0.075 mol) in 150 mL of dioxane at 60 °C, during a period of 5 h, and the reaction mixture was stirred overnight at 60 °C. After confirmation of the consumption of the starting compound **1c** by GLC, the solid material was filtered and the solvent was distilled from the filtrate. The residual oil was fractionated by distillation (Kugelrohr) to give **2c** as a pale yellow, viscous liquid: yield, 3.42 g (82%); bp 180 °C/0.05 Torr; ^{1}H NMR (CDCl$_3$) δ 0.86 (t, 3 H), 1.07–1.68 (m, 12 H), 1.68–2.70 (m, 6 H), 3.30–4.24 (m, 22 H); MS, *m/e* (rel intensity) 417 (M$^+$, 7), 318 (100); IR (neat) 2930, 2860, 1480, 1140 cm^{-1}. Anal. Calcd for C$_{22}$H$_{43}$NO$_6$: C, 63.28; H, 10.38; N, 3.35. Found: C, 63.32; H, 10.50; N, 3.44.

***N*-Octylmorpholino 12-crown-4 ether (2a)**: pale yellow, viscous liquid; yield, 2.34 g (0.01 mol scale) (71%); bp 140 °C/0.05 Torr; ^{1}H NMR (CDCl$_3$) δ 0.85 (t, 3 H), 1.12–1.56 (m, 12 H), 1.62–2.80 (m, 6 H), 3.22–4.20 (m, 14 H); MS, *m/e* (rel intensity) 329 (M$^+$, 10), 230 (100); IR (neat) 2930, 2850, 1465, 1130 cm^{-1}. Anal. Calcd for C$_{18}$H$_{35}$NO$_4$: C, 65.62; H, 10.71; N, 4.25. Found: C, 65.32; H, 10.92; N, 4.29.

***N*-Octylmorpholino 15-crown-5 ether (2b)**: pale yellow, viscous liquid; yield, 2.98 g (0.01 mol scale) (80%); bp 160 °C/0.05 Torr; ^{1}H NMR (CDCl$_3$) δ 0.891, 0.897 (two t, 3 H as a total), 1.29 (m, 10 H), 1.437 (quint, 1.09 H, coupled with a signal at 2.227), 1.486 (quint, 0.91 H, coupled with a signal at 2.328), 1.819 (t, 0.91 H), 2.151 (dd, 1.09 H), 2.227 (two dt, 1.09 H), 2.328 (t, 0.91 H), 2.465 (dd, 1.09 H), 2.672 (d, 0.91 H), 3.403 (dd, 1.1 H), 3.511 + 3.563 (dd, dd, 2.2 H as a total), 3.6–3.8 (m, 11.6 H), 3.819 (dt, 0.98 H, coupled with signals at 1.819, 2.672, 3.511, 3.563), 3.957 (dd, 1.03 H), 4.145 (two quint or m, 1.03 H, coupled with signals at 2.151, 2.465, 3.403, 3.957); ^{13}C NMR (NNE, CDCl$_3$) δ 13.555 + 13.570 (1.09 C as a total), 22.052 + 22.059 (0.93 C as a total), 25.863 (0.52 C), 25.925 (0.44 C), 26.726 (0.55 C), 26.887 (0.46 C), 28.539 (0.49 C), 28.694 (0.56 C), 28.881 (0.56 C), 28.925 (0.44 C), 31.236 + 31.251 (1.05 C), 53.591 (0.87 C), 54.268 (1.07 C), 58.332 (0.50 C), 58.445 (0.43 C), 69.557 (methine, 1.07 C), 69.751 (0.93 C), 70.054 (1.16 C) 70.215 (0.93 C), 70.270 (1.08 C), 70.314 (1.08 C), 70.639 (1.92 C), 71.967 (0.85 C), 74.443 (methine, 0.89 C); ^{15}N NMR (CHCl$_3$–CDCl$_3$) 371.1 ppm from NO$_3^-$ and 28.9 ppm from NH$_3$; MS, *m/e* (rel intensity) 373 (M$^+$, 7), 274 (100); IR (neat) 2925, 2855, 1470, 1135 cm^{-1}. Anal. Calcd for C$_{20}$H$_{39}$NO$_5$: C, 64.31; H, 10.52; N, 3.75. Found: C, 64.22; H, 10.77; N, 3.75.

***N*-(3,6-Dioxadecyl)morpholino 12-crown-4 ether (2′a)**: pale yellow liquid; yield, 1.19 g (0.01 mol scale) (33%); bp 130 °C/0.006 Torr; ^{1}H NMR (CDCl$_3$) δ 0.90 (t, 3 H), 1.05–1.65 (m, 4 H), 1.75–2.80 (m, 6 H), 3.34–4.30 (m, 22 H); MS, *m/e* (rel intensity) 361 (M$^+$, 2), 231 (14), 230 (100), 58 (10), 45 (6), 41 (7); IR (neat) 2950, 2880, 1480, 1140 cm^{-1}. Anal. Calcd for C$_{18}$H$_{35}$NO$_6$: C, 59.81; H, 9.76; N, 3.87. Found: C, 59.60; H, 10.04; N, 4.03.

***N*-(3,6-Dioxadecyl)morpholino 15-crown-5 ether (2′b)**: pale yellow liquid; yield, 1.66 g (0.01 mol scale) (41%); bp 150 °C/0.006 Torr; ^{1}H NMR (CDCl$_3$) δ 0.91 (t, 3 H), 1.05–1.75 (m, 4 H), 1.75–2.86 (m, 6 H), 3.34–4.30 (m, 26 H); MS, *m/e* (rel intensity) 405 (M$^+$, 2), 275 (15), 274 (100), 100 (3), 45 (4); IR (neat) 2950, 2880, 1480, 1140 cm^{-1}. Anal. Calcd for C$_{20}$H$_{39}$NO$_7$: C, 59.24; H, 9.69; N, 3.45. Found: C, 59.17; H, 9.78; N, 3.44.

***N*-Octylmorpholino 15-Crown-5 Ether Hydrochloride (2b·HCl); Typical Procedure.** To an ether solution of compound **2b** (R = *n*-C$_8$H$_{17}$, *n* = 2) (0.75 g, 2 mmol) was introduced hydrogen chloride gas by bubbling at room temperature. After the pH value of the solution was confirmed to be about 3 when tested with wet pH paper, the excess hydrogen chloride and the solvent were removed by evaporation to give 0.85 g of a waxy solid. The product was purified by recrystallization from ethanol/ether (80:20 v/v) to give **2b**·HCl as white scales: yield, 0.55 g (67%); mp 128.0–129.0 °C; ^{1}H NMR (CDCl$_3$) δ 0.88 (t, 3 H), 1.10–1.60 (m, 10 H), 1.60–2.04 (m, 2 H), 2.28–5.96 (m, 25 H); ^{13}C NMR (CDCl$_3$) δ 13.83 (methyl), 22.34, 22.96, 26.53, 28.78, 28.81, 31.45, 50.13, 53.09, 58.75, 65.39 (methine), 68.81, 69.43 (methine), 69.57, 69.86, 70.35, 70.41, 71.02, 71.63, 71.66; MS, *m/e* (rel intensity) 374 (2), 274 (100), 142 (12), 36 (12); IR (neat) 2945, 2870, 2500, 1460, 1135 cm^{-1}. Anal. Calcd for C$_{20}$H$_{40}$NO$_5$Cl: C, 58.59; H, 9.83; N, 3.42; Cl, 8.65. Found: C, 58.48; H, 9.74; N, 3.33; Cl, 8.55.

***N*-Octylmorpholino 18-crown-6 ether hydrochloride (2c·HCl)**: white scales; yield, 0.91 g (2 mmol scale) (44%[25]); mp 111.0–112.0 °C; ^{1}H NMR (CDCl$_3$) δ 0.90 (t, 3 H), 1.08–1.64 (m, 10 H), 1.68–2.12 (m, 2 H), 2.56–5.80 (m, 29 H); MS, *m/e* (rel intensity) 418 (2), 318 (100), 142 (14), 36 (15); IR (neat) 2920, 2860, 2450, 1465, 1115 cm^{-1}. Anal. Calcd for C$_{22}$H$_{44}$NO$_6$Cl: C, 58.20; H, 9.77; N, 3.08; Cl, 7.81. Found: C, 58.01; H, 9.83; N, 3.10; Cl, 7.82.

***N*-Methyl-*N*-octylmorpholinium 18-Crown-6 Ether Methyl Sulfate (3c); Typical Procedure.** *N*-Octylmorpholino 18-crown-6 ether (**2c**) (0.84 g, 2 mmol) and dimethyl sulfate (0.76 g, 6 mmol) were dissolved into 20 mL of ether and the solution was heated to reflux for 5 h. After removal of the solvent, the residual solid was purified by recrystallization from ethyl acetate/hexane (80/20 v/v) to give **3c** as a hygroscopic, white waxy solid: yield, 0.34 g (31%[25]); mp 73.0–74.0 °C; ^{1}H NMR (CDCl$_3$) δ 0.88 (t, 3 H), 1.08–1.56 (m, 10 H), 1.60–2.04 (br, 2 H), 3.30–3.96 (m, 32 H) 3.96–4.80 (m, 2 H); MS, *m/e* (rel intensity) 432 (1), 417 (2), 318 (100); IR (neat) 2940, 2875, 1475, 1360, 1120 cm^{-1}. Anal. Calcd for C$_{24}$H$_{49}$NO$_{10}$S: C, 53.02; H, 9.08; N, 2.58; S 5.90. Found: C, 52.91; H, 9.04; N, 2.57; S, 5.81.

***N*-Methyl-*N*-octylmorpholinium 12-Crown-4 Ether Methyl Sulfate (3a).** After the reaction of **2a** with dimethyl sulfate in ether, low-boiling materials were removed by evaporation at reduced pressure to give heavily viscous material containing a small amount of crystals. This material was purified by gel permeation chromatography (with a Japan Analytical Industry Co., Ltd. LC-07 chromatograph and elution with chloroform) to afford a deliquescent, white waxy solid: yield, 0.36 g (2 mmol scale) (38%); mp 98.1–101.9 °C; ^{1}H NMR (CDCl$_3$) δ 0.88 (t, 3 H), 1.08–1.60 (m, 10 H), 1.60–2.00 (br, 2 H), 3.00–4.00 (m, 24 H) 4.00–4.80 (m, 2 H); MS, *m/e* (rel intensity) 344 (1), 329 (5), 230 (100); IR (neat) 2940, 2870, 1470, 1375, 1120 cm^{-1}. Anal. Calcd for C$_{20}$H$_{41}$NO$_8$S: C, 52.73; H, 9.07; N, 3.07; S 7.04. Found: C,

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[24] Harris, R. K.; Mann, B. E. *NMR and the Periodic Table*; Academic Press: London, 1978; p 97.

[25] The yield is estimated to be almost quantitative from the weight and ^{1}NMR of crude product (in the case of **2c**·HCl) and HPLC (in the case of **2c**), although the yield after recrystallization was poor.

51.66; H, 9.11; N, 3.03; S, 6.92. In spite of careful handling, elemental analyses (three separate trials) did not give satisfactory results. This may be due to the strong deliquescence of the quaternary salt as verified by the IR and ^{1}H NMR spectra.

***N*-Methyl-*N*-octylmorpholinium 15-crown-5 ether methyl sulfate (3b)**: waxy, deliquescent solid: Yield, 0.44 g (2 mmol scale) (44%); mp 120.5–121.6 °C; ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3 H), 1.20–1.52 (m, 10 H), 1.68–2.04 (br, 2 H), 3.12–3.96 (m, 28 H) 3.96–4.80 (m, 2 H); MS, *m/e* (rel intensity) 389 (1), 373 (4), 274 (100); IR (neat) 2940, 2875, 1475, 1360, 1120 cm^{-1}. Anal. Calcd for $C_{22}H_{45}NO_9S$: C, 52.98; H, 9.08; N, 2.80; S, 6.42. Found: C, 52.85; H, 8.90; N, 2.84; S, 6.29.

***N*-Octylmorpholino 15-Crown-5 *N*-Oxide (4b); Typical Procedure.** To *N*-octylmorpholino 15-crown-5 ether (**2b**) (2.24 g, 6 mmol) heated to 60 °C was added 35% aqueous hydrogen peroxide (2.92 g, 30 mmol) dissolved in 7 mL of acetone dropwise during a period of 3 h. The solution was kept at the same temperature for 42 h. After the removal of the solvent, the reaction product was purified by column chromatography on alumina using benzene/2-propanol (98:2) as eluent to give **4b** as a white waxy solid: yield, 1.55 g (66%); mp 138.0–139.0 °C; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3 H), 1.20–1.56 (m, 10 H), 1.78–2.20 (br, 2 H), 2.80–4.00 (m, 22 H), 4.18–5.20 (m, 2 H); ^{15}N NMR ($CHCl_3$–$CDCl_3$) 300.6 ppm from NO_3^- and 99.4 ppm from NH_3; MS, *m/e* (rel intensity) 373 (5), 274 (100), 112 (34) 43 (84); IR (neat) 2920, 2850, 1465, 1350, 1115 cm^{-1}. Anal. Calcd for $C_{20}H_{39}NO_6$: C, 61.67; H, 10.09; N, 3.60. Found: C, 61.39; H, 9.81; N, 3.41.

***N*-Octylmorpholino 12-crown-4 *N*-oxide (4a)**: white waxy solid; yield, 1.57 g (6 mmol scale) (76%); mp 133.1–134.0 °C; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3 H), 1.14–1.64 (m, 10 H), 1.64–2.24 (br, 2 H), 2.66–4.16 (m, 18 H), 4.16–5.24 (m, 2 H); MS, *m/e* (rel intensity) 329 (11), 230 (100), 112 (34), 43 (55); IR (neat) 2940, 2870, 1460, 1370, 1125 cm^{-1}. Anal. Calcd for $C_{18}H_{35}NO_5$: C, 62.58; H, 10.21; N, 4.05. Found: C, 62.25; H, 9.84; N, 3.91.

***N*-Octylmorpholino 18-crown-6 *N*-oxide (4c)**: white waxy solid; yield, 2.10 g (6 mmol scale) (81%); mp 126.0–127.0 °C; ^{1}H NMR ($CDCl_3$) δ 0.89 (t, 3 H), 1.20–1.56 (m, 10 H), 1.76–2.20 (br, 2 H), 2.92–4.04 (m, 26 H), 4.20–5.04 (m, 2 H); MS, *m/e* (rel intensity) 417 (1), 318 (27), 112 (17), 43 (100); IR (neat) 2940, 2870, 1470, 1360, 1125 cm^{-1}. Anal. Calcd for $C_{22}H_{43}NO_7$: C, 60.94; H, 10.00; N, 3.23. Found: C, 60.79; H, 9.76; N, 3.10.

Registry No. **1a**, 117021-77-9; **1a′**, 106576-28-7; **1b**, 117021-75-7; **1b′**, 106576-29-8; **1c**, 117021-76-8; **2a**, 117039-38-0; **2a′**, 117039-39-1; **2b**, 117021-62-2; **2b**·HCl, 117021-64-4; **2b′**, 117021-63-3; **2c**, 117021-61-1; **2c**·HCl, 117021-65-5; **3a**, 117021-69-9; **3b**, 117021-71-3; **3c**, 117021-67-7; **4a**, 117021-73-5; **4b**, 117021-72-4; **4c**, 117021-74-6; **5b**, 75006-54-1; **5c**, 75006-58-5; **6a**, 74649-87-9; **6b**, 75507-22-1.

EPR Studies of Polycyclic Aromatic Cation Radicals Generated during Friedel–Crafts Reactions with Triphenylantimony

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Introduction

Radical cations have been detected by EPR measurements of Friedel–Crafts reactions[1-3] and resolved EPR spectra of the anthracene (I),[2] and 9,10-dimethylanthracene (II)[3] cation radical have been reported. It has recently been reported by ourselves[4] and others[5] that resolved EPR spectra can in general be observed from a Friedel–Crafts type reaction with benzene or substituted benzene carried out in originally air-saturated systems without degassing the samples on a vacuum line. HCl gas evolved during the Friedel–Crafts type reaction removes the dissolved oxygen in the solution, so that high-resolution EPR spectra are observed.

Previously[4,5] it was shown that a well resolved EPR spectrum of 9,10-diphenylanthracene (III) cation radical appeared whenever benzene was reacted with excess $AlCl_3$ in either $CHCl_3$, CBr_4, CCl_4, $CDCl_3$, and $PhCCl_3$ or upon reaction of Ph_3SiH[5] or Ph_3SiOH[5] in place of benzene. On the other hand, the reaction of benzene with $AlCl_3$ in CH_2Cl_2 solvent gave a resolved EPR spectra due only to the anthracene cation radical.[4] Presumably methylene chloride reacts with benzene in the presence of $AlCl_3$ to form benzyl chloride, which reacts further to give 9,10-dihydroanthracene in low yield. In the presence of excess $AlCl_3$, 9,10-dihydroanthracene reacts[6] to yield I. Reaction of I with excess $AlCl_3$ forms the anthracene radical cation[7-9] in millimolar concentrations, so that narrow line EPR spectra are observed from the HCl degassed solutions. However upon reaction with alkyl-substituted benzenes, the EPR pattern became extremely complex, presumably due to the appearance of several radicals, and is not as such interpretable. It seems likely that ENDOR methods may be extremely useful in analyzing the EPR spectra.

We have extended this work to the study of radical formation when triphenyl antimony ($SbPh_3$) reacts with an alkyl chloride as the solvent in the presence of excess aluminum chloride. It is known[10] that trialkyl- and triarylstibines (R_3M) react with alkyl halides ($R'X$) and upon heating in the presence of $AlCl_3$ from a halide salt ($R_3R'M^+X^-$). On the other hand triarylstibines[11] do not react with the alkyl halides above. Here we will show that the number and type of radicals identified by EPR methods depend on the concentration of the reactant. Highly resolved spectra, equal in quality to that produced by chemical oxidation of the parent material, have been observed. The added advantage with the Friedel–Crafts method is that various deuteriated radical cation radicals can be formed with relative ease.

Experimental Section

Materials. Triphenylantimony and 9,10-phenylanthracene were purchased from Aldrich Chemical and used without further purification. The various alkylating agents were purified by the usual methods prior to use.

Sample Preparation. Triphenylantimony was dissolved in an alkyl chloride solvent, and the solution was placed in a sample tube (4 mm o.d.) containing a 3-fold or more of solid anhydrous aluminum chloride. Gases evolved from the reaction mixture were found to be H_2 and HCl. EPR measurements indicated that

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(1) Adams, J. Q.; Nicksic, S. W. *J. Am. Chem. Soc.* **1962**, *84*, 4355.
(2) Banks, R. E.; Farnell, L. F.; Haszeldnie, R. N.; Preston, P. N.; Sutcliffe, L. H. *Proc. Chem. Soc. London* **1964**, 396.
(3) Saraev, V. V.; Tolmacheva, I. I.; Latysheva, L. E.; Laperdina, T. G.; Lipovich, V. G. *J. Gen. Chem. USSR (Engl. Transl.)* **1983**, *53*, 773.
(4) Wang, H. Q.; Sang, H.; Feng, L.-B.; Kispert, L. D. submitted for publication in *J. Phys. Org. Chem.*
(5) Lin, S-K.; Trapp, C. *J. Org. Chem.* **1988**, *53*, 698.
(6) Balaban, A. T.; Nenitzescu, C. D. In *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; Interscience: New York, 1964; Vol. II, Part II, pp 979–1047.
(7) Rooney, J. J.; Pink, R. C. *Proc. Chem. Soc.* **1961**, 142.
(8) Buck, H. M.; Bloemhoff, W.; Oosterhoff, I. J. *Tetrahedron Lett.* **1960**, 5.
(9) Courtneidge, L. L.; Davies, A. G. *Acc. Chem. Res.* **1987**, *20*, 90.
(10) Chatt, J.; Maun, F. G. *J. Chem. Soc.* **1940**, 1192.
(11) Wittig, G.; Torsell, K. *Acta. Chem. Scand.* **1953**, *7*, 1293.

0022-3263/88/1953-5967$01.50/0