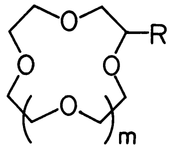
# Hydrophilicity and Complexing Ability of Alkyl Lariat Ethers

Isao IKEDA, Hiroshi EMURA, and Mitsuo OKAHARA*
*Department of Applied Chemistry, Faculty of Engineering, Osaka University, Yamadaoka 2-1, Suita, Osaka 565*
(Received October 17, 1983)

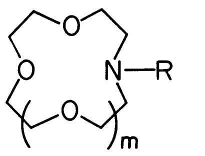
A series of long chain alkyl lariat ethers were synthesized and their aqueous properties in the absence and presence of alkali metal cations were investigated by measuring their cloud points and complex stability constants. In spite of the presence of ether oxygen(s) in the side chain, complexing abilities toward sodium and potassium cations did not significantly differ from those of the corresponding alkyl crown ethers. As the number of ether oxygens in the side chain of lariat ethers was increased, the water solubilities were much improved and showed high cloud points. However, the degree of salting-in effect decreased and the increment of cloud point caused by addition of salts decreased, probably due to the increase of acyclicity of the polyether molecule.

Since the crown ethers have strong interactions with metal cations and ammonium ions and show characteristic behaviors, many studies about their complexing ability, phase transfer catalysis, metal cation transport, and metal cation analysis have been reported. Various kinds of substituents have been introduced onto the crown ring to improve these functions.

As the crown ring acts as a hydrophile, some crown compounds having a suitable lipophilic substituent have been synthesized and declared to have interesting properties as nonionic surface active agents. LeMoigne,[1,2] Moroi,[3] and Kuwamura[4—7] reported the surface properties of some of these crown compounds. We also have synthesized long chain alkyl crown ethers (**1**)[8—11] and *N*-(long chain alkyl) monoaza crown ethers (**2**),[9,12] and investigated their surface properties[13,14] and clarified their behaviors toward metal cations in the aqueous solution.[8,15—17] Thus, alkyl crown ethers (**1**), unlike the usual acyclic poly(oxyethylene) type nonionic surfactants, show a salting-in effect in the presence of alkali metal cations based on the formation of metal-crown ring complex.[8,16]



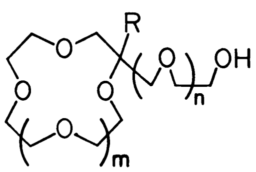
(1)



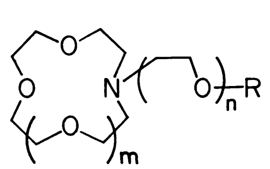
(2)

However, as the crown ring consists of a limited number of oxyethylene units and has no hydroxyl group, the hydrophilicity of this kind of surfactant is low compared with that of the usual nonionic surfactants.[15] Improvement of the hydrophilicity by enlarging the crown ring may affect the complexing ability with metal cations.

Recently, Gokel and his coworkers[18—23] and we[12,24] reported the synthesis and complexing ability of so-called "lariat ethers" (**3**, **4**) which have oxyethylene chain in the side arm. In the case of monoaza lariat ethers (**4**), not only the hydrophilicity but also the complexing ability of the molecule increased by the introduction of oligo-(oxyethylene) group.[12]



(3) R=H,CH3.

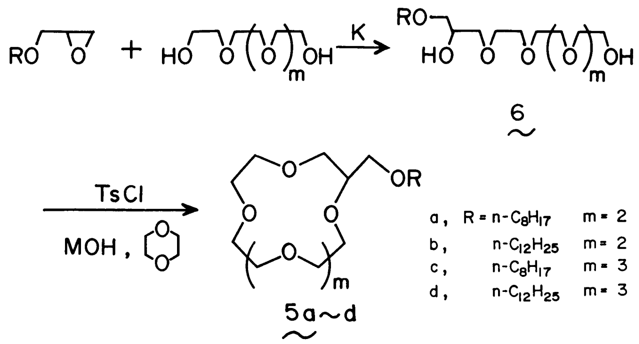


(4) R=H,alkyl.

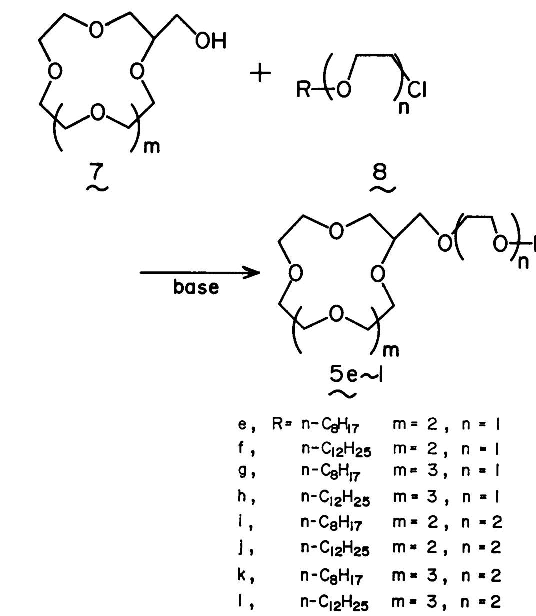
In this paper, we report the syntheses of long alkyl chain lariat ethers (**5**) having one to three ether oxygens in the side chain and their properties affected by the side oxyethylene chain, especially the increase of hydrophilicity and the variation of salt effect by measuring the cloud point of aqueous solution in the presence of sodium or potassium chloride. The contribution of ether oxygens in the side chain to the complexation toward sodium and potassium cations was directly examined from the measurement of complex stability constants.

## Experimental

*Materials.* The NaCl and KCl were commercial guaranteed-grade reagents, and were dried at 80 °C at reduced pressure [1 Torr(1 Torr=133.322 Pa), 6 h]. The water was deionized by passing through an ion-exchange resin column. Lariat ethers having one oxygen in the side chain (**5a—d**) were synthesized from alkyl glycidyl ethers and oligoethylene glycol according to the reported method (Scheme 1).[10] Lariat ethers having two or three oxygens in the side chain (**5e—l**) were synthesized by Williamson ether synthesis from hydroxymethyl crown ether (**7**)[10] and **8** which was prepared by chlorination of oligoethylene glycol monoalkyl ethers according to Scheme 2. As a typical procedure, preparation of 2-(dodecyloxy)ethoxymethyl-15-crown-5 (**5f**) is described. To 10 ml of *t*-butyl alcohol including 5 g (0.02 mol) of **7** ($m$=2), 0.35 g (0.015 mol) of sodium was dissolved and 7.5 g (0.03 mol) of 2-chloroethyl dodecyl ether (**8**, $n$=1) was added dropwise. After heating to reflux for 6 h, the *t*-butyl alcohol was evaporated off at reduced pressure. The residue was extracted with dichloromethane. After removal of the solvent, the oily




Scheme 1. Preparation of crown ethers having one oxygen atom in the side chain.




Scheme 2. Preparation of crown ethers having two to three oxygen atoms in the side chain.

material which remained was distilled by Kugelrohr apparatus to give a colorless oil (**5f**) 6.2 g (yield 67%). In Table 1 are listed the boiling points (Kugelrohr distillation) and the yields of **5**. All the ethers (**5**) showed the almost the same IR and NMR spectra. IR ($cm^{-1}$); 2940(s), 2860(s), 1470(m), 1350(m), 1290(w), 1250(w), 1120(s), and 940(w). NMR; $\delta$=0.89 (t, 3H), 1.28 (12 or 20H), 3.3—3.9 (m, $[4m+4n+15]$H). Elemental analyses showed the good agreement within 0.4% of deviation.

*Measurement of Cloud Point.* The cloud point ($T_{cp}$) of each aqueous solution of crown compound was determined by observation with naked eyes, using a solution of 10 mg of crown ether in 1 ml of water or the salt solution of specific concentration in a test tube of 10 mm of inner diameter under heating with a rate of *ca.* 0.5 °C/min.

*Measurement of Stability Constant of Complexes.* Stability constants were measured by Frensdroff's method.[25]

## Results and Discussion

Lariat ethers having a long alkyl group were synthesized by two procedures: those having one oxygen in the side chain (**5a—d**) were synthesized by the cyclization of alkoxymethyl oligoethylene glycol (**6**) (Scheme 1),[10,11] and those having two or three ether oxygens in the side chain (**5e—l**) were synthesized from hydroxymethyl crown ethers (**7**)[10] and $\alpha$-alkyl-$\omega$-chlorooligo (oxyethylene) (**8**) by Williamson ether synthesis (Scheme 2) since the oligoethylene glycols having an excessively long side chain were not desirable as a precursor for cyclization, from the point of difficulty in purification due to their high boiling points.

Cloud points of twelve kinds of long chain alkyl lariat ethers are listed in Table 2, together with those of alkyl crown ethers (**1**) for comparison.

When the size of crown ring and the length of alkyl chain were the same, cloud points of the crown compounds rose almost linearly with increasing the number of ether oxygen atoms in the side chain. The slopes of four straight lines were almost equal. The degree of rise in cloud point with increase of the number of ether oxygen atom in the side chain was

Table 1. Synthetic and spectral data of crown ethers

| Crown ether | | | MOH | Bp[a] | MS | Yield[b] |
|---|---|---|---|---|---|---|
| | $m$ | $n$ | | $\theta_b$/°C (Torr) | ($M^+$) | % |
| **5a** | 2 | 0 | NaOH | 130(0.03) | 362 | 59 |
| **5b** | 2 | 0 | NaOH | 150(0.05) | 418 | 56 |
| **5c** | 3 | 0 | KOH | 150(0.01) | 406 | 55 |
| **5d** | 3 | 0 | KOH | 180(0.01) | 462 | 51 |
| **5e** | 2 | 1 | NaOH | 150(0.01) | 406 | 65 |
| **5f** | 2 | 1 | NaOH | 180(0.05) | 406 | 67 |
| **5g** | 2 | 2 | NaOH | 180(0.01) | 462 | 71 |
| **5h** | 2 | 2 | NaOH | 200(0.01) | 506 | 66 |
| **5i** | 3 | 1 | KOH | 180(0.05) | 450 | 71 |
| **5j** | 3 | 1 | KOH | 200(0.03) | 494 | 66 |
| **5k** | 3 | 2 | KOH | 200(0.01) | 506 | 67 |
| **5l** | 3 | 2 | KOH | 220(0.01) | 550 | 64 |

a) Kugelrohr distillation. b) **5a—d**: Yields of cyclization, **5e—l**: yields of side chain introduction.

Table 2. Cloud points of aqueous solution of crown ethers

| Crown ether | | | Cloud point | Crown ether | | | Clound point |
|---|---|---|---|---|---|---|---|
| | $m$ | $n$ | °C | | $m$ | $n$ | °C |
| **1**[a] | 2 | — | 14.0 | **1**[a] | 3 | — | 31.0 |
| **5a** | 2 | 0 | 25.0 | **5c** | 3 | 0 | 43.0 |
| **5e** | 2 | 1 | 39.0 | **5g** | 3 | 1 | 52.5 |
| **5i** | 2 | 2 | 50.0 | **5k** | 3 | 2 | 60.0 |
| **1**[b] | 2 | — | <0 | **1**[b] | 3 | — | 18.5 |
| **5b** | 2 | 0 | 6.0 | **5d** | 3 | 0 | 28.5 |
| **5f** | 2 | 1 | 22.0 | **5h** | 3 | 1 | 41.0 |
| **5j** | 2 | 2 | 28.5 | **5l** | 3 | 2 | 51.0 |

a) R=$C_8H_{17}$. b) R=$C_{12}H_{25}$.

about 50 to 70% of that with increase of the oxygen number in the crown ring.

Many studies about the effect of added inorganic electrolytes on the cloud points of open chain poly(oxyethylene) type nonionics have been reported.[26–29] In the presence of metal salts except for the salts having a counter anion of water-destructuring type, such as $SCN^-$, $NO_3^-$, and so on, the cloud points of these open chain poly(oxyethylene) type nonionics usually fall down, due to the salting-out effect. In the case of crown ethers, however, a salting-in effect based on the complexation of crown ring with metal cations causes the rise of cloud point compared with the cases in the absence of metal salts.[8,16,17] Figures 1 and 2 show the

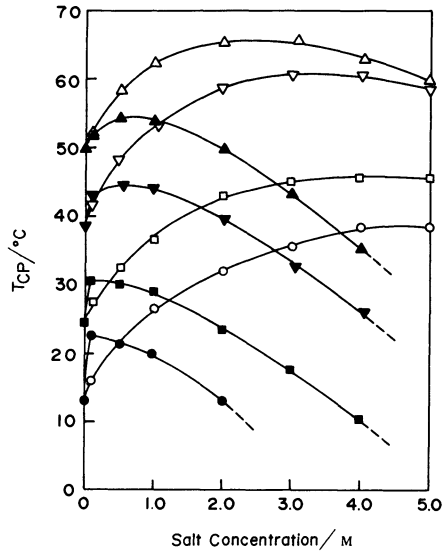



Fig. 1. Cloud points of aqueous solution of alkyl lariat ethers. —Octyl 15-crown-5 ethers—

| Crown Ether | m | n | NaCl | KCl |
|---|---|---|---|---|
| 1 | 2 | - | ○ | ● |
| 5a | 2 | 0 | □ | ■ |
| 5e | 2 | 1 | ▽ | ▼ |
| 5i | 2 | 2 | △ | ▲ |

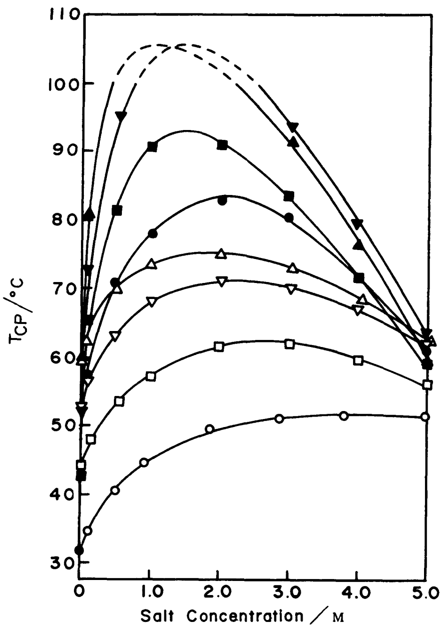



Fig. 2. Cloud points of aqueous solution of alkyl lariat ethers. —Octyl 18-Crown-6 ethers—

| Crown Ether | m | n | NaCl | KCl |
|---|---|---|---|---|
| 1 | 3 | - | ○ | ● |
| 5c | 3 | 0 | □ | ■ |
| 5g | 3 | 1 | ▽ | ▼ |
| 5k | 3 | 2 | △ | ▲ |

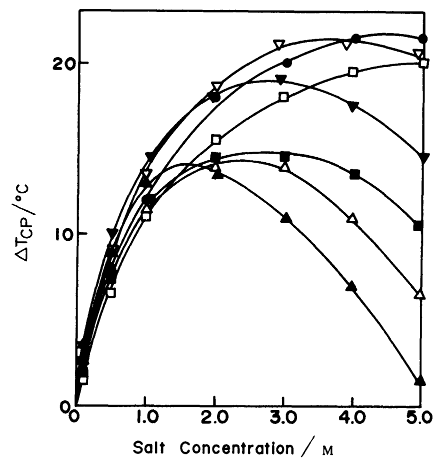



Fig. 3. Differences of cloud points ($\Delta T_{cp}$) in the absence and presence of sodium chloride. —Dodecyl derivatives—

| Crown Ether | m | n | | Crown Ether | m | n | |
|---|---|---|---|---|---|---|---|
| | | | | 1 | 3 | - | ● |
| 5b | 2 | 0 | □ | 5d | 3 | 0 | ■ |
| 5f | 2 | 1 | ▽ | 5h | 3 | 1 | ▼ |
| 5j | 2 | 2 | △ | 5l | 3 | 2 | ▲ |

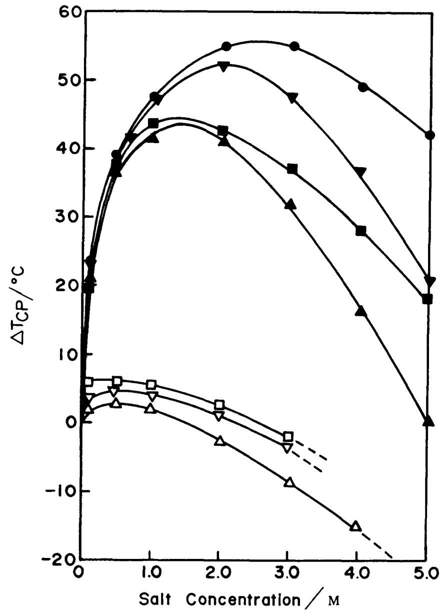



Fig. 4. Differences of cloud points ($\Delta T_{cp}$) in the absence and presence of potassium chloride. —Dodecyl derivatives—

| Crown Ether | m | n | | Crown Ether | m | n | |
|---|---|---|---|---|---|---|---|
| | | | | 1 | 3 | - | ● |
| 5b | 2 | 0 | □ | 5d | 3 | 0 | ■ |
| 5f | 2 | 1 | ▽ | 5h | 3 | 1 | ▼ |
| 5j | 2 | 2 | △ | 5l | 3 | 2 | ▲ |

correlations between the cloud points of aqueous solutions of octyl derivative series of lariat ethers and the concentrations of sodium and potassium chlorides as examples. In Figs. 3 and 4 are shown the correlations of the concentration of salt and the difference of cloud point ($\Delta T_{CP}$) between the values in the absence and presence of sodium or potassium chloride, using dodecyl derivatives as examples.

*15-Crown-5-NaCl System (Figs. 1 and 3).* When the salts were added to the aqueous solutions of these crown ethers, the cloud points rose, since the salting-in effect is superior to the salting-out effect. However, as the salting-out effect works concurrently, the cloud points began to fall above a certain salt concentration.[16] In the case of octyl-15-crown-5, the $\Delta T_{cp}$ was the maximum at around the concentration of 4.5 m of NaCl. And the higher the number of ether oxygen atoms in the side chain, the lower the concentration of salts at which the $\Delta T_{cp}$ was maximum, though the cloud points themselves were higher (Fig. 1). As the cloud point of dodecyl-15-crown-5 in the absence of salts was below 0 °C, the maximum values of $\Delta T_{cp}$ could not be calculated, but the homologues having one and more than one ether oxygens in the side chain, showed the same tendency as the octyl derivatives showed. This can be explained by the following reasons: as the number of oxygen atoms in the side chain increased, the water-solubility of the whole molecule was enhanced, but it became easier to salt out the molecule, probably because the acyclicity of the molecule increased. Acyclicity causes the salting-out effect, and lariat ethers are apt to be salted-out even at a lower salt concentration. The higher the number of ether oxygens in the side chain, the larger the degree of fall of cloud point by the salting-out effect.

*18-Crown-6-NaCl System (Figs. 2 and 3).* In this system the salting-in effect works strongly in general and the $T_{cp}$s rise markedly. Upon the increase of number of oxygen in the side chain, the salting-out effect became also larger and the salt concentration showing the maximum $\Delta T_{cp}$ shifted to the lower region.

*18-Crown-6-KCl System (Figs. 2 and 4).* It is well known that the complexes of this combination are the most stable of all the crown ether-alkali metal cation systems. They showed the largest $\Delta T_{cp}$ values, 40—50 °C, showing that they are affected by the strong salting-in effect due to the strong complexation.

*15-Crown-5-KCl System (Figs. 1 and 4).* In this system, different from others, the complexing ability is small and the salting-in effect is so weak that $\Delta T_{cp}$ did not exceed 10 °C. The salting-out effect begins to overcome the salting-in effect even at as low as 2 m of salt concentration.

In all the systems, the changes of $\Delta T_{cp}$ caused by the difference of alkyl chain length were almost the same in both the octyl and dodecyl series and it is obvious that the additional methylene units in the side chain bring about only the increase of lipophilicity of the molecule. Considering from the changes of cloud point of a series of the lariat ethers which have the same alkyl chain and the same crown ring, it can be concluded that ether groups in the side chain are related to hydration, namely aqueous solubility, rather than the complexation with metal cations. To confirm directly the participation of ether oxygens in the side chain to the complexation, the stability constants of complexes with sodium and potassium cations in methanol were measured and are shown in Table 3. $\Delta T_{cp}$ of lariat ethers, especially in the low salt-concentration region where the neat effect of salting-in phenomenon was revealed, showed a good correlation with their complex stability constants, as was reported in the case of alkyl crown ethers[8,15,16] and alkyl aza crown ethers.[17]

Little differences of the stability constant were found within a series of the lariat ethers which had the same crown ring.

We already reported that, for the lariat ethers **3** (R=$CH_3$) and **4**, the higher the number of ether oxygen atoms in the side chain, the larger the stability constants. This fact was explained as due to the participation of the ether oxygens in the side chain. In the case of **3**, the geminal methyl group forces sterically oligo(oxyethylene) chain to take an advantageous position to complexation.[24,30] And in the case of **4**, the oligo-

Table 3. Stability constants of crown ethers with sodium and potassium cations

| Crown ether | | | $Na^+$ log $K_1^s$ | | $K^+$ log $K_1^s$ (+log $K_2^s$) | |
|---|---|---|---|---|---|---|
| | $m$ | $n$ | MeOH[a, c] | MeOH-$H_2O$[b, c] | MeOH[a, c] | MeOH-$H_2O$[b, c] |
| 15-Crown-5 | | | 3.31[e] | — | 3.35(+2.62)[d] | — |
| **1**[f] | 2 | — | 3.18±0.03 | 2.73±0.03 | 3.05(+2.32)[d] | 2.52±0.06 |
| **5a** | 2 | 0 | 3.18±0.04 | 2.72±0.02 | 3.22(+2.41)[d] | 2.56±0.05 |
| **5e** | 2 | 1 | 3.22±0.04 | 2.72±0.03 | 3.14(+2.30)[d] | 2.57±0.05 |
| **5i** | 2 | 2 | 3.23±0.04 | 2.75±0.02 | 3.28(+2.20)[d] | 2.71±0.07 |
| 18-Crown-6 | | | 4.30[e] | — | 6.10[e] | — |
| **1**[f] | 3 | — | 3.91±0.03 | 3.17±0.05 | 5.39±0.01 | 4.7[g] |
| **5c** | 3 | 0 | 3.97±0.05 | 3.27±0.03 | 5.64±0.05 | 4.8[g] |
| **5g** | 3 | 1 | 4.00±0.06 | 3.24±0.06 | 5.49±0.00 | 4.8[g] |
| **5k** | 3 | 2 | 3.97±0.08 | 3.26±0.06 | 5.50±0.01 | 4.8[g] |

a) in methanol. b) In water/methanol=10/90 (v/v). c) At 25 °C, values in 95% of confidence interval. d) Calculated by Frensdorff's equation. e) Values reported in Ref. 24. f) R=$n$-$C_8H_{17}$. g) Since values are dependent on the ratio of ligand and cation in the range of measured conditions, values at specific conditions (KCl=2.5 mmol·$l^{-1}$, 50 ml; ligand=12 mmol·$l^{-1}$, 20 ml) are shown.

(oxyethylene) chain can easily participate in the complexation because the junction (the nitrogen atom) of the crown ring and the side chain is flexible.[17] In the case of **5**, to the contrary, contribution of the side oligo(oxyethylene) chain to the complexation is found to be quite small. It is natural to consider that the oxygens in the side chain are apt to be located too far from the crown plane to induce-fit effectively the metal cation which complexes with the crown ring.

To determine the complexation of lariat ethers in the aqueous solution, the stability constants in methanol containing 10% of water were measured. Gokel measured the stability constants of complexes of 15-crown-5 and 18-crown-6 with sodium cation in the mixture of methanol and water and reported that the stability constants enhanced proportionally to the ratio of methanol in the mixture, and that no confusion in the order of stability constants was found between any two crown ethers.[31]

The results are shown in Table 3. The values were smaller than those in methanol, but the tendency was quite the same with that in methanol, showing that the ether oxygens in the side chain did not contribute to complexation in water either.

As a result, it can be concluded that the lariat ethers having desirable HLB and with complexing ability and selectivity of the parent alkyl crown ethers toward alkali metal cations could be designed by combining an alkyl group and a crown ring with a suitable length of oxyethylene chain.

### References


1) J. LeMoigne, Ph. Gramain, and J. Simon, *J. Colloid Interface Sci.*, **60**, 565 (1977).

2) J. LeMoigne and J. Simon, *J. Phys. Chem.*, **84**, 170 (1980).

3) Y. Moroi, E. Pramauro, M. Grätzel, E. Pelizzetti, and P. Tundo, *J. Colloid Interface Sci.*, **69**, 341 (1979).

4) T. Kuwamura and T. Kawachi, *Yukagaku*, **28**, 195 (1979).

5) T. Kuwamura and S. Yoshida, *Nippon Kagaku Kaishi*, **1980**, 427.

6) S. Inokuma, N. Aoki, E. Kameyama, and T. Kuwamura, *Yukagaku*, **29**, 767 (1980).

7) S. Inokuma, T. Negishi, E. Kameyama, and T. Kuwamura, *Nippon Kagaku Kaishi*, **1982**, 479.

8) M. Okahara, P. -L. Kuo, S. Yamamura, and I. Ikeda, *J. Chem. Soc., Chem. Commun.*, **1980**, 586.

9) P. -L. Kuo, M. Miki, I. Ikeda, and M. Okahara, *J. Am. Oil Chemists'. Soc.*, **57**, 227 (1980).

10) I. Ikeda, S. Yamamura, Y. Nakatsuji, and M. Okahara, *J. Org. Chem.*, **45**, 5355 (1980).

11) I. Ikeda, H. Emura, S. Yamamura, and M. Okahara, *J. Org. Chem.*, **47**, 5150 (1982).

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

13) P. -L. Kuo, I. Ikeda, and M. Okahara, *Tenside Detergents* **19**, 4 (1982).

14) P. -L. Kuo, I. Ikeda, and M. Okahara, *Tenside Detergents*, **19**, 204 (1982).

15) P. -L. Kuo, I. Ikeda, and M. Okahara, *Bull. Chem. Soc. Jpn.*, **55**, 3356 (1982).

16) P. -L. Kuo. K. Tsuchiya, I. Ikeda, and M. Okahara, *J. Colloid Interface Sci.* **92**, 463 (1983).

17) A. Masuyama, P. -L. Kuo, I. Ikeda, and M. Okahara, *Nippon Kagaku Kaishi*, **1983**, 249.

18) G. W. Gokel, D. M. Dishong, and C. J. Diamond, *J. Chem. Soc., Chem. Commun.*, **1980**, 1053.

19) D. M. Dishong, C. J. Diamond, and G. W. Gokel, *Tetrahedron Lett.*, **22**, 1663 (1981).

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

21) R. A. Schultz, D. M. Dishong, and G. W. Gokel, *J. Am. Chem. Soc.*, **104**, 625 (1982).

22) R. A. Schultz, E. Schlegel, D. M. Dishong, and G. W. Gokel, *J. Chem. Soc., Chem. Commun.*, **1982**, 242.

23) D. M. Dishong, C. J. Diamond, M. I. Cinoman, and G. W. Gokel, *J. Am. Chem. Soc.*, **105**, 586 (1983).

24) Y. Nakatsuji, T. Nakamura, M. Okahara, D. M. Dishong, and G. W. Gokel, *Tetrahedron Lett.*, **23**, 1351 (1982).

25) H. F. Frensdorff, *J. Am. Chem. Soc.*, **93**, 600 (1971).

26) M. J. Schick, *J. Colloid Interface Sci.*, **17**, 801 (1962).

27) H. Schott, *J. Colloid Interface Sci.*, **43**, 150 (1973).

28) H. Schott and S. -K. Han, *J. Pharm. Sci.*, **64**, 658 (1975).

29) F. Tokiwa and T. Matsumoto, *Bull. Chem. Soc. Jpn.*, **48**, 1645 (1975).

30) Y. Nakatsuji, T. Nakamura, M. Okahara, D. M. Dishong, and G. W. Gokel, *J. Org. Chem.*, **48**, 1237 (1983).

31) D. M. Dishong and G. M. Gokel, *J. Org. Chem.*, **47**, 147 (1982).