  Bull. Chem. Soc. Jpn., 55, 2181—2185 (1982) 

# Synthesis and Cation-complexing Ability of Oxo Crown Ethers

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(Received October 9, 1981)

3-Substituted 2-oxo crown ethers and a novel dioxo crown ether with a point symmetry were synthesized by the cyclization of the corresponding substituted oligoethylene glycol monocarboxymethyl ethers using benzenesulfonyl chloride in the presence of alkali metal carbonates. The reaction mechanism was discussed. Their stability constants toward sodium and potassium cations were determined and the relation between their structures and complexing properties was discussed.

Since crown ethers were first synthesized by Pedersen, several thousand publications concerning these compounds and their derivatives have appeared.[1,2] Among them, attention has recently been denoted to the oxo crown compounds,[3,4] since some of these were shown to have a different complexing tendency towards cations than normal crown ethers. They may be considered as model compounds of natural macrocyclic antibiotics such as valinomycin and nonactin,[5,6] and those having the pyridine ring as mimics of enzymes such as NADH.[7,8]

A large number of oxo crown compounds have been synthesized and their properties investigated by Bradshaw,[9–17] Vögtle,[18–20] and Kellogg,[7,8,21,22] but most of these compounds were prepared through either the reaction between diacids and dihalides (ditosylates) of oligoethylene glycols, or the reaction between di(acid chloride)s and oligoethylene glycols; thus, the oxo crown compounds so far synthesized are mainly restricted to di- and tetraesters with limited kinds of substituents.

On the other hand, there are a few reports on the synthesis of monooxo crown ethers with rather special structure. Kellogg[23] prepared monooxo benzocrown ethers starting from salicylic acid, $Cs_2CO_3$ and oligoethylene glycol dibromides, while Newkome and coworkers[24,25] have synthesized pyridine macrocyclic lactones from 2-chloronicotinoyl chloride and oligoethylene glycol.

In the previous communications,[26,27] we have reported the synthesis of unsubstituted 2-oxo crown ethers *via* the intramolecular cyclization of monocarboxymethylated oligoethylene glycols. Here we describe the extension of this new method to the synthesis of monooxo crown ethers with substituents and a novel symmetrical dioxo crown ether. The characteristics of the complexing ability of monooxo crown ethers toward alkali metal cations were also examined in comparison with normal crown ethers and dioxo crown ethers.

## Experimental

The $^1$H NMR spectra were taken at 100 MHz on a JEOL-JNM-PS 100 spectrometer using tetramethylsilane as the internal standard. The infrared spectra were obtained on a Hitachi 260-10 spectrometer. The mass spectra were measured with a Hitachi RMU-6E mass spectrometer at an ionization potential of 70 eV. The GLC analyses were performed on a Shimadzu GC-3BF using a 2 m×3 mm column packed with 10% Silicone SE-30 on 60—80 mesh Celite 545. Stability constants were determined by potentiometry using an ion-selective electrode at 25 °C in methanol according to the literature.[28] Toko $Na^+$ 1100 and Toko $K^+$ 1200 were used as ion-selective electrodes for $Na^+$ and $K^+$ respectively. The emf was measured with a Beckmann 4500 digital pH meter.

*General Procedure for Preparation of 2-Oxo Crown Ethers (**4**).* In an appropriate oligoethylene glycol (**2**), one eighth molar amount of alkali metal was dissolved at 90—100 °C. To this solution, one eighth molar amount of alkali metal salt of a halo fatty acid (**1**) was added; the mixture was then stirred at 80—90 °C for 4—5 h. In some cases, where a halo acid was used in place of its salt, one quarter molar amount of alkali metal was used. The excess **2** was distilled off from the reaction mixture under reduced pressure, the residue was then dissolved in 2-propanol and the insoluble matter (alkali metal halide) was removed by filtration. The solvent was evaporated to give the intermediate **3**. One quarter molar amount of pulverized alkali metal carbonate was suspended together with **3** in dioxane. To this suspension, one eighth molar amount of benzenesulfonyl chloride in dioxane was added over a 2—3 h period at 65—70 °C, and the mixture was stirred for another 3 h. The insoluble salt was removed by filtration and the solvent was distilled off under reduced pressure. The residue was submitted to pyrolytic distillation using a Kugelrohr apparatus to give **4** as a distillate. Further purification of **4** was accomplished through redistillation or silicic acid column chromatography.

*2-Oxo-15-crown-5 (**4a**).* The sodium salt of tetraethylene glycol carboxymethyl ether (**3**, $n$=2, $R^1$, $R^2$=H), which was prepared according to the general procedure mentioned above from tetraethylene glycol (97.9 g, 0.504 mol), sodium metal (2.90 g, 0.126 mol), and bromoacetic acid (8.76 g, 0.063 mol), was treated with benzenesulfonyl chloride (11.1 g, 0.063 mol) and sodium carbonate (13.4 g, 0.126 mol) in dioxane (200 ml+50 ml) to give sodium cation complex of **4a**. The complex was destructively distilled and purified by redistillation to give a pale yellow oil. 2-Oxo-18-crown-6 (**4b**) was obtained according to a similar procedure. Spectral and analytical data have already been reported in the previous communication.[26]

*2-Oxo-21-crown-7 (**4c**).* A pale yellow oil; bp 134—137 °C/0.04 Torr (1 Torr=133.322 Pa) (Kugelrohr apparatus); $n_D^{20}$ 1.4665; IR (neat) 2880(s), 1760—1740(s), 1455(m), 1350(m), 1290(m), 1250(m), 1200(m), 1135(s), 1040(w), 1000(w), 945(m), 850(w) cm$^{-1}$; $^1$H NMR ($CCl_4$) $\delta$ 3.50—3.70 (m, 22H, $OCH_2CH_2O$), 4.12 (s, 2H, $OCH_2COO$), 4.16—4.28 (m, 2H, $COOCH_2CH_2O$); mass spectrum, *m/e* (relative intensity) 322 ($M^+$), 103(45), 102(23), 89(35),

87(34), 86(28), 73(28), 59(25), 58(27), 45(100), 44(29), 43(50), 42(21). Found: C, 51.82; H, 8.38%. Calcd for $C_{14}H_{26}O_8$: C, 52.16; H, 8.13%.

*3-Methyl-2-oxo-15-crown-5* (**4d**). A pale yellow oil; IR (neat) 1730—1750 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 1.30 (d, 3H), 3.52—3.72 (m, 14H), 3.88—4.40 (m, 3H); mass spectrum, *m/e* 248 ($M^+$). Found: C, 52.89; H, 8.31%. Calcd for $C_{11}H_{20}O_6$: C, 53.22; H, 8.12%.

*3,3-Dimethyl-2-oxo-15-crown-5* (**4e**). A pale yellow oil; IR (neat) 1720—1740 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 1.35 (s, 6H), 3.30—3.74 (m, 14H), 4.18 (t, 2H); mass spectrum, *m/e* 262 ($M^+$). Found: C, 54.66; H, 8.69%. Calcd for $C_{12}H_{22}O_6$; C, 54.95; H, 8.45%.

*3-Ethyl-2-oxo-15-crown-5* (**4f**). A pale yellow oil; IR (neat) 1720—1740 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 0.92 (t, 3H), 1.68 (m, 2H), 3.55—3.78 (m, 14H), 3.85 (t, 1H), 4.00—4.40 (m, 2H); mass spectrum, *m/e* 262 ($M^+$). Found: C, 54.69; H, 8.76%. Calcd for $C_{12}H_{22}O_6$: C, 54.95; H, 8.45%.

*3-Hexyl-2-oxo-15-crown-5* (**4g**). A pale yellow oil; IR (neat) 1720—1750 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 0.88 (t, 3H), 1.20—1.50 (m, 8H), 1.50—1.76 (m, 2H), 3.50—3.76 (m, 14H), 3.85 (t, 1H), 4.00—4.40 (m, 2H); mass spectrum, *m/e* 318 ($M^+$). Found: C, 60.20; H, 9.71%. Calcd for $C_{16}H_{30}O_6$: C, 60.35; H, 9.50%.

*3-Phenyl-2-oxo-15-crown-5* (**4h**). A pale yellow oil; IR (neat) 1730—1750 ($\nu_{C=O}$), 730, 700 cm$^{-1}$; $^1$H NMR ($CCl_4$) $\delta$ 3.50—3.78 (m, 14H), 3.92—4.40 (m, 2H), 4.98 (s, 1H), 7.15—7.45 (m, 5H); mass spectrum, *m/e* 310 ($M^+$). Found: C, 61.74; H, 7.29%. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15%.

*3-Methyl-2-oxo-18-crown-6* (**4i**). A pale yellow oil; IR (neat) 1730—1745 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 1.34 (d, 3H), 3.55—3.76 (m, 18H), 3.92—4.32 (m, 3H); mass spectrum, *m/e* 292 ($M^+$). Found: C, 53.20; H, 8.46%. Calcd for $C_{13}H_{24}O_7$: C, 53.41; H, 8.28%.

*3,3-Dimethyl-2-oxo-18-crown-6* (**4j**). A pale yellow oil; IR (neat) 1730—1745 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 1.36 (s, 6H), 3.36—3.80 (m, 18H), 4.20 (t, 2H); mass spectrum, *m/e* 306 ($M^+$). Found: C, 54.55; H, 8.80%. Calcd for $C_{14}H_{26}O_7$: C, 54.89; H, 8.55%.

*3-Ethyl-2-oxo-18-crown-6* (**4k**). A pale yellow oil; IR (neat) 1720—1740 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 0.92 (t, 3H), 1.68 (m, 2H), 3.55—3.80 (m, 18H), 3.90 (t, 1H), 4.15—4.35 (m, 2H); mass spectrum, *m/e* 306 ($M^+$). Found: C, 54.82; H, 8.81%. Calcd for $C_{14}H_{26}O_7$: C, 54.89; H, 8.55%.

*3-Hexyl-2-oxo-18-crown-6* (**4l**). A pale yellow oil; IR (neat) 1730—1750 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 0.88 (t, 3H), 1.20—1.48 (m, 8H), 1.50—1.76 (m, 2H), 3.50—3.76 (m, 18H), 3.88 (t, 1H), 4.10—4.28 (m, 2H); mass spectrum, *m/e* 362 ($M^+$). Found: C, 59.36; H, 9.71%. Calcd for $C_{18}H_{34}O_7$: C, 59.65; H, 9.45%.

*3-Phenyl-2-oxo-18-crown-6* (**4m**). A pale yellow oil; IR (neat) 1740—1760 ($\nu_{C=O}$), 740, 700 cm$^{-1}$; $^1$H NMR ($CCl_4$) $\delta$ 3.56—3.70 (m, 18H), 3.90—4.40 (m, 2H), 5.06 (s, 1H), 7.16—7.48 (m, 5H); mass spectrum, *m/e* 354 ($M^+$). Found: C, 60.70; H, 7.59%. Calcd for $C_{18}H_{26}O_7$: C, 61.00; H, 7.40%.

*3-Methyl-2-oxo-21-crown-7* (**4n**). A pale yellow oil; IR (neat) 1730—1750 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 1.32 (d, 3H), 3.55—3.75 (m, 22H), 4.05 (quartet, 1H), 4.24 (t, 2H); mass spectrum, *m/e* 336 ($M^+$). Found: C, 53.19; H, 8.50%. Calcd for $C_{15}H_{28}O_8$: C, 53.56; H, 8.39%.

*3,3-Dimethyl-2-oxo-21-crown-7* (**4o**). A pale yellow oil; IR (neat) 1720—1740 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 1.35 (s, 6H), 3.40—3.72 (m, 22H), 4.20 (t, 2H); mass spectrum, *m/e* 350 ($M^+$). Found: C, 54.77; H, 8.80%. Calcd for $C_{16}H_{30}O_8$: C, 54.84; H, 8.63%.

*3-Ethyl-2-oxo-21-crown-7* (**4p**). A pale yellow oil; IR (neat) 1730—1750 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 0.95 (t, 3H), 1.68 (m, 2H), 3.50—3.80 (m, 22H), 3.88 (t, 1H), 4.18—4.30 (m, 2H); mass spectrum, *m/e* 350 ($M^+$). Found: C, 55.00; H, 8.81%. Calcd for $C_{16}H_{30}O_8$: C, 54.84; H, 8.63%.

*3-Hexyl-2-oxo-21-crown-7* (**4q**). A pale yellow oil; IR (neat) 1730—1760 cm$^{-1}$ ($\nu_{C=O}$); $^1$H NMR ($CCl_4$) $\delta$ 0.88 (t, 3H), 1.20—1.40 (m, 8H), 1.50—1.70 (m, 2H), 3.50—3.85 (m, 22H), 3.90 (t, 1H), 4.15—4.28 (m, 2H); mass spectrum, *m/e* 406 ($M^+$). Found: C, 58.72; H, 9.53%. Calcd for $C_{20}H_{38}O_8$: C, 59.09; H, 9.42%.

*3-Phenyl-2-oxo-21-crown-7* (**4r**). A pale yellow oil; IR (neat) 1720—1760 ($\nu_{C=O}$), 730, 700 cm$^{-1}$; $^1$H NMR ($CCl_4$) $\delta$ 3.50—3.72 (m, 22H), 4.10—4.28 (m, 2H), 5.00 (s 1H), 7.15—7.30 (m, 3H), 7.32—7.45 (m, 2H); mass spectrum, *m/e* 398 ($M^+$). Found: C, 59.93; H, 7.68%. Calcd for $C_{20}H_{30}O_8$: C, 60.29; H, 7.59%.

*2,11-Dioxo-18-crown-6* (**5**). Metallic sodium (9.2 g, 0.4 mol) was dissolved in diethylene glycol (170 g, 1.60 mol) and bromoacetic acid (27.8 g, 0.2 mol) was added to the resultant solution at 90—100 °C; the mixture was then stirred at 95—100 °C for 5 h. The excess diethylene glycol was removed *in vacuo*. Methanol (200 ml) was added to the distillation residue and the sodium bromide was removed by filtration. On evaporation of the methanol from the filtrate, the sodium salt of diethylene glycol carboxymethyl ether (**3s**) was obtained. The intermediate was suspended in dioxane (250 ml) and sodium carbonate (31.8 g, 0.3 mol) and benzenesulfonyl chloride (35.3 g, 0.2 mol) in dioxane (60 ml) was added dropwise to the mixture at 65—70 °C for 4 h under stirring and the mixture was stirred for another 3 h. The resultant mixture was cooled to room temperature, and the insoluble matter was removed by filtration. The filtrate was evaporated under reduced pressure to give a brown solid. The crude product was pyrolized in a Kugelrohr apparatus under reduced pressure and recrystallized from acetone to give a white solid (10.5 g, 18%). Mp 115.0—116.0 °C; IR (KBr) 2930—2850(s), 1750 (s, $\nu_{C=O}$), 1450(m), 1405(m), 1350(m), 1215(s), 1125(s), 1030(m), 940(m), 860 cm$^{-1}$ (m); $^1$H NMR ($CDCl_3$) $\delta$ 3.65—3.88 (m, 12H), 4.28—4.45 (m, 8H); mass spectrum, *m/e* (relative intensity) 292 ($M^+$, 10), 249(7), 248(8), 147(29), 103(100), 102(65), 86(66), 73(25), 45(66). Found: C, 49.34; H, 6.90%. Calcd for $C_{12}H_{20}O_8$: C, 49.31; H, 6.93%.

*Reaction of Tetraethylene Glycol with the Mixture of Acetic Acid and Benzenesulfonyl Chloride in the Presence of Sodium Carbonate.* To a stirred suspension of 3.88 g (0.02 mol) of tetraethylene glycol and 8.48 g (0.08 mol) of sodium carbonate in 80 ml of dioxane, a mixture of 2.40 g (0.04 mol) of acetic acid and 10.71 g (0.06 mol) of benzenesulfonyl chloride in 20 ml of dioxane was added over a 1-h period at 60 °C. The reaction was followed by GLC and the peak corresponding to the desired ester was observed soon after the addition of the reagents. The mixture was then stirred at 60 °C for 30 h. The resultant mixture was cooled to room temperature and insoluble matter was removed by filtration. The solvent was evaporated under reduced pressure. Water (100 ml) was added to the residue and the mixture was extracted with dichloromethane (50 ml). The dichloromethane solution was concentrated to give 5.54 g of a slightly yellow liquid. The crude product was distilled under reduced pressure to give 3.42 g (61%) of tetraethylene glycol diacetate as a colorless liquid. Bp 163 °C/0.03 Torr (Kugelrohr apparatus); IR (neat) 2960(m), 2880(s), 1735(s), 1460(m), 1380(s), 1245(s), 1130(s), 1060(s), 960(m), 855(w)

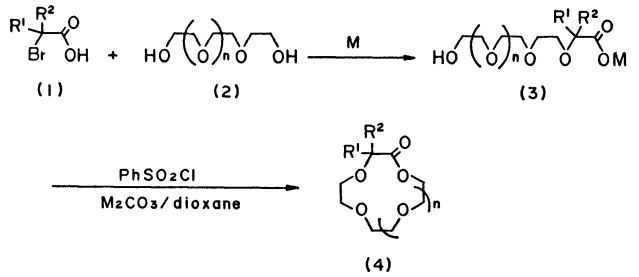
$cm^{-1}$; $^1H$ NMR ($CDCl_3$) $\delta$ 2.05 (s, 6H), 3.52—3.80 (s+m, 12H), 4.20 (t, 4H).

*Reaction of Tetraethylene Glycol Ditosylate with Acetic Acid in the Presence of Sodium Carbonate.* A suspended mixture of 2.60 g ($5.17\times10^{-3}$ mol) of tetraethylene glycol ditosylate, 0.95 g (0.0158 mol) of acetic acid, and 1.65 g (0.0156 mol) of sodium carbonate in 25 ml of dioxane was stirred at 60 °C for 30 h. The required ester was not detected by GLC anlysis.

## Results and Discussion

The alkali metal salts of oligoethylene glycol monocarboxymethyl ethers and their alkyl derivatives(**3**) were prepared from 2-halo carboxylic acids(**1**) and the appropriate oligoethylene glycols(**2**) through the Williamson ether synthesis, and successively cyclized to 2-oxo crown ethers (**4**) by the treatment with benzenesulfonyl chloride in dioxane in the presence of alkali metal carbonates (scheme 1). The results of synthesis of **4** are summarized in Tables 1 and 2.

The yields of unsubstituted 2-oxo crown ethers were not influenced significantly by the difference in the halogen atom (Table 1). However, the kind of alkali metal cation was observed to effect the yield considerably. Thus yields of both 2-oxo-15- and 2-oxo-18-crown ethers in the reactions with sodium carbonate were better than those with potassium carbonate, while for 2-oxo-21-crown-7 potassium carbonate gave good yields compared with sodium carbonate. A caesium base had been used to improve the yields in esterification and the related reactions instead of more common alkali metal bases,[29] and the effect of a change in the alkali metal cation on the yields in the synthesis of 2-oxo crown ethers was examined in this study. Although the general trend of the effect of the caesium cation was not clearly observed, the partial replacement of sodium carbonate by this cation gave somewhat improved yield in the case of **4a** as shown in Table 1.




Scheme 1.

Table 1. Examination of reaction conditions in the synthesis of unsubstituted 2-oxo crown ethers(**4**)

| Compd | $n$ | $R^1$ | $R^2$ | X | M | Yield/%[a] |
|---|---|---|---|---|---|---|
| **4a** | 2 | H | H | Cl | Na | 15 |
| | | | | Br | Na | 16 |
| | | | | Br | K | 11 |
| | | | | Br | Na:Cs (9:1) | 16 |
| | | | | Br | Na:Cs (8:2) | 24 |
| **4b** | 3 | H | H | Cl | Na | 42 (60)[b] |
| | | | | Cl | K | — (30)[b] |
| | | | | Br | Na | — (60)[b] |
| | | | | Br | K | 26 (30)[b] |
| | | | | Br | Cs | 37 |
| **4c** | 4 | H | H | Cl | Na | 10 |
| | | | | Cl | K | 20 |
| | | | | Br | K | 23 |

a) Isolated yield. b) Determined by GLC.

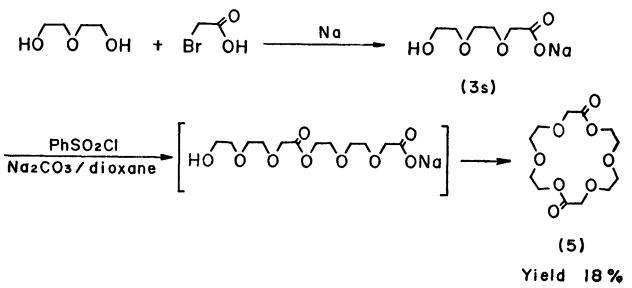
In spite of the difference in the substituent group, the yields of 3-monosubstituted-2-oxo-15-, 18-, and 21-crown ethers were approximately 20, 40, and 25% respectively. In addition, it is noteworthy that the temperature used for pyrolytic distillation of the reaction products under reduced pressure in a Kugelrohr apparatus were almost constant for the crown ethers with the same ring size; the distillation conditions were as follows: 160 °C/0.03 Torr for 15-crown, 175 °C/0.02 Torr for 18-crown, and 190 °C/0.02 Torr for 21-crown ethers. This finding suggests that above-cited conditions correspond to the decomposition temperature of the complex with the alkali metal cation.

On the other hand, the sodium salt of diethylene glycol monocarboxymethyl ether(**3s**) was submitted

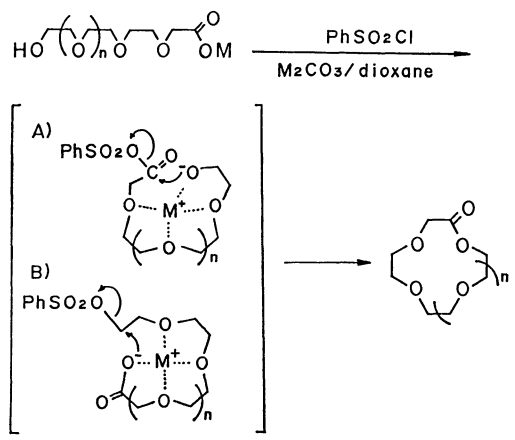
Table 2. Synthesis of 3-substituted 2-oxo crown ethers(**4**)

| Compd | $n$ | $R^1$ | $R^2$ | X | M | Yield/% |
|---|---|---|---|---|---|---|
| **4d** | 2 | $CH_3$ | H | Br | Na | 15 |
| **4e** | 2 | $CH_3$ | $CH_3$ | Br | Na | 10 |
| **4f** | 2 | $C_2H_5$ | H | Br | Na | 21 |
| **4g** | 2 | $C_6H_{13}$ | H | Br | Na | 17 |
| **4h** | 2 | Ph | H | Br | Na | 20 |
| **4i** | 3 | $CH_3$ | H | Br | Na | 39 |
| **4j** | 3 | $CH_3$ | $CH_3$ | Br | Na | 32 |
| **4k** | 3 | $C_2H_5$ | H | Br | Na | 41 |
| **4l** | 3 | $C_6H_{13}$ | H | Br | Na | 37 |
| **4m** | 3 | Ph | H | Br | Na | 41 |
| **4n** | 4 | $CH_3$ | H | Br | Na, K[a] | 18 |
| **4n** | 4 | $CH_3$ | H | Br | K | 28 |
| **4o** | 4 | $CH_3$ | $CH_3$ | Br | K | 17 |
| **4p** | 4 | $C_2H_5$ | H | Br | K | 24 |
| **4q** | 4 | $C_6H_{13}$ | H | Br | K | 23 |
| **4r** | 4 | Ph | H | Br | K | 21 |

a) Metallic sodium and potassium carbonate were used at the first and the second steps respectively.




Scheme 2.




Scheme 3.

to the bimolecular esterification with each other followed by intramolecular cyclization in the presence of an effective template ion to give 2,11-dioxo-18-crown-6(**5**); this is a novel type of dioxo crown ethers possessing a point symmetry.

The postulated reaction mechanism of the cyclization to monooxo crown ethers was offered in Scheme 3. Two possible routes of cyclization (route **A** and **B**) can be conceived: differing in the first reaction site with the benzenesulfonyl chloride. Brewster *et al.* reported that the lactone formation reaction of *trans*-2-hydroxycyclohexaneacetic acid using *p*-toluenesulfonyl chloride in the presence of pyridine proceeded without losing its geometrical configuration.[30] This can be explained by assuming the first formation of a mixed acid anhydride. In addition, two model reactions under conditions similar to the case of 2-oxo crown ethers were carried out to clarify the mechanism. One was the reaction of oligoethylene glycol with acetic acid using benzenesulfonyl chloride in the presence of sodium carbonate in dioxane; the other was the reaction of oligoethylene glycol ditosylate with acetic acid in the presence of sodium carbonate in dioxane. Only the former reaction could give the required product, and from all these results route **A** seems to be probable in this case.

Finally, the complexing ability of the synthesized oxo crown ethers toward sodium and potassium cations was examined according to the method using ion selective electrode in methanol at 25 °C,[28] and compared with that of dioxo and normal crown ethers (Table 3).

The increase of the number of ester group was observed drastically to decrease the complexing ability toward alkali metal cations as expected from the decrease of the electron-donating ability of coordination sites. In general, monooxo crown ethers were concluded to be intermediate in properties between normal crown ethers and dioxo crown ethers.

As for the effect of the substituent, the introduction of alkyl substituent(s) on an oxo crown ring slightly reduced their complexing ability; a phenyl substituent does not affect the complexing ability as indicated by the fact that 3-phenyl-2-oxo-18-crown-6(**4m**) showed almost the comparable stability constant to that of unsubstituted 2-oxo-18-crown-6(**4b**).

On the other hand, the difference in the position of the ester groups of dioxo crown ethers does not seem to influence the complexing ability.

Table 3. Stability constant of oxo crown ethers

| Compound | $Na^+$ | $K^+$ |
|---|---|---|
| 15-Crown-5 | (3.48)[a,b] | (3.77)[a,b] |
| 2-Oxo-15-crown-5(**4a**) | 1.98 | 2.12 |
| 3-Hexyl-2-oxo-15-crown-5(**4g**) | 1.48 | 1.90 |
| 2,6-Dioxo-15-crown-5 | ( — )[a,b,d] | ( — )[a,b,d] |
| 18-Crown-6 | 4.30<br>(4.36)[a,c] | 6.02<br>(6.06)[a,c] |
| 2-Oxo-18-crown-6(**4b**) | 3.27 | 4.18 |
| 3-Methyl-2-oxo-18-crown-6(**4i**) | 3.07 | 4.05 |
| 3,3-Dimethyl-2-oxo-18-crown-6(**4j**) | 2.93 | 3.99 |
| 3-Hexyl-2-oxo-18-crown-6(**4l**) | 2.90 | 3.84 |
| 3-Phenyl-2-oxo-18-crown-6(**4m**) | 3.23 | 4.23 |
| 2,6-Dioxo-18-crown-6 | (2.5 )[1,2] | (2.79)[a,b] |
| 2,11-Dioxo-18-crown-6(**5**) | 2.29 | 2.70 |
| 3-Hexyl-2-oxo-21-crown-7(**4q**) | 2.40 | 3.39 |

a) Determined by a colorimetric titration procedure. b) Ref. 6. c) Ref. 31. d) Very small (unmeasurable).

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