<특별 강연>

Several Aspects of Crown Ethers and Related Compounds

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In 1967, Charles J. Pedersen, who is a Du Pont chemist of Japanese and Norwegian extraction, first reported on the syntheses of novel cyclic ethers, such as shown as **1a~c**, and also described that they complex selectively with hard cations, such as those of alkali and alkaline earth metals.[1a, b] He named these cyclic compounds crown ethers because they are shaped like a crown(e. g. **2b**). The ether oxygens in these cyclic oligomers of ethylene oxide act together as a ligand, and the ring size of the molecule helps to decide which cation is selected.

1a   **1b**


1c
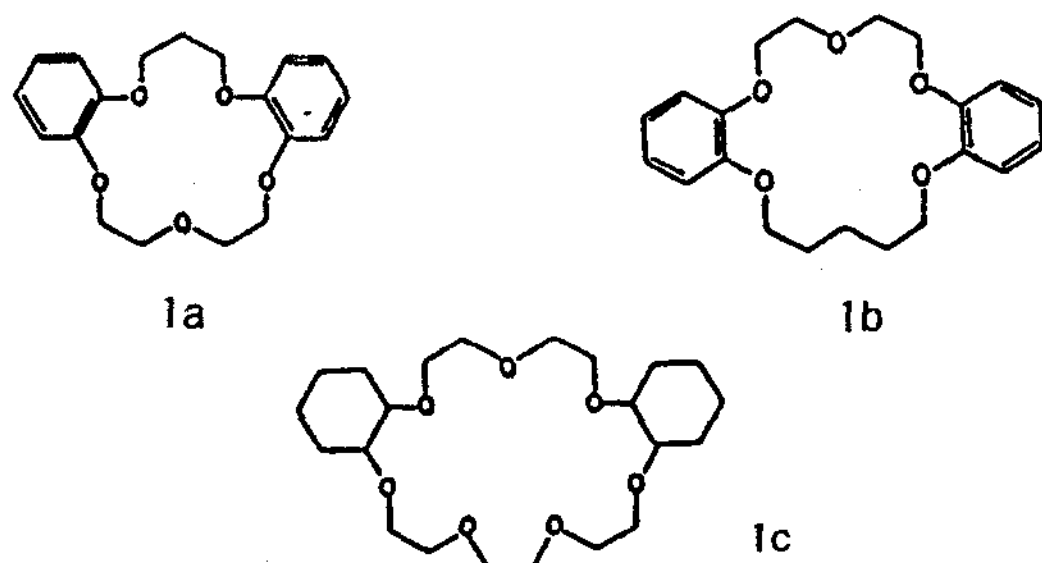
This was the first example of what might be called the recognition of a substance by a chemical compound that was not an enzyme.

Later, the resemblance of this selection to the first step of enzymatic reactions attracted the attention of chemists. In enzyme reactions, a "host substance" of high molecular weight complexes with a specific substrate as its "guest compound." The substrate held in the complex then very quickly undergoes a reaction under the influence of the host molecule.

This field of chemistry has developed greatly during the two decades since then. For example, Professor D. J. Cram synthesized chiral crown compounds(e. g. **3**) that recognize asymmetry,[2] and started the field known as "host-guest chemistry." Professor J. -M. Lehn has synthesized a series of ligands called cryptands,[3] (e. g. **4**) and opened up a new field that named "supramolecular chemistry." These three researchers won the Nobel Prize in 1987.
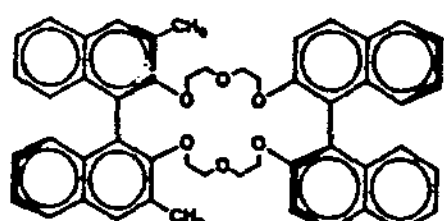

12-crown-4   **15-crown-5**

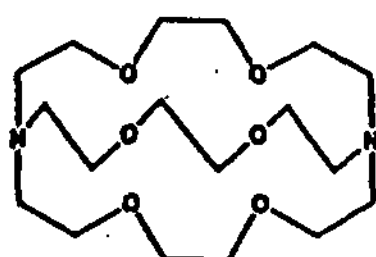**2a**   **2b**
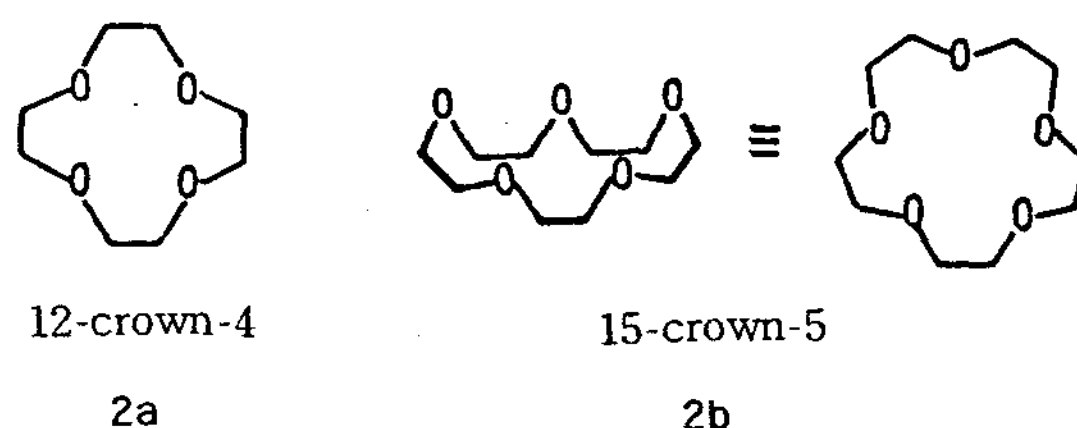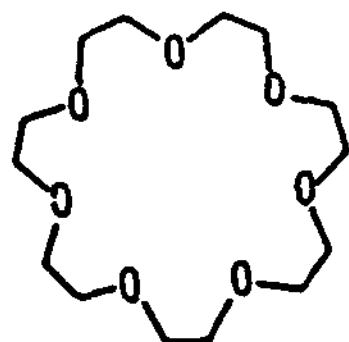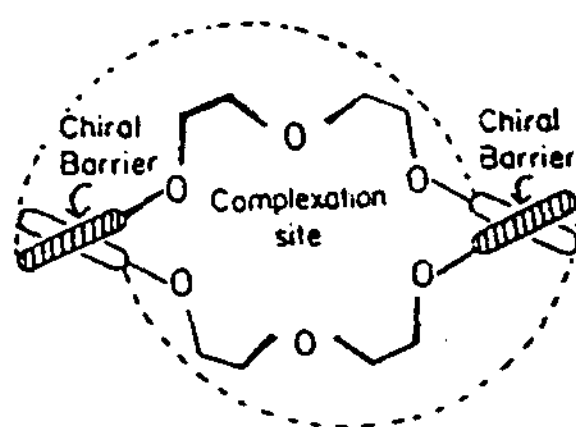
21-crown-7
2c
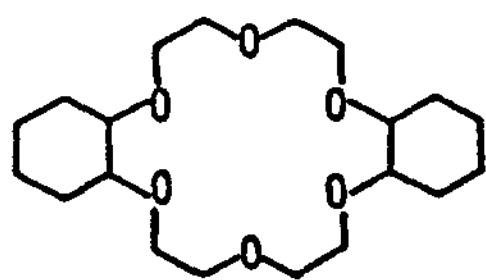
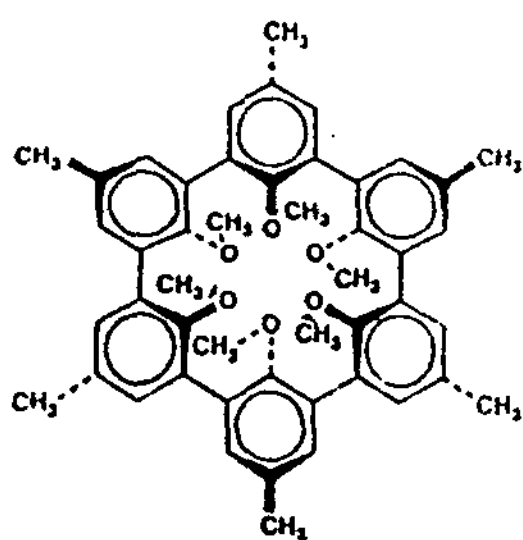dicylohexano-18-crown-6
2d

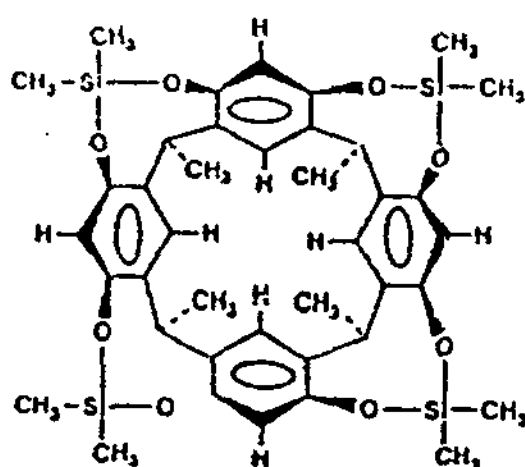chiral crown ether
3

cryptand
4

Later, various sophisticated kinds of ligands with complicated structure, such as those shown as 5, 6, and 7, were also synthesized.
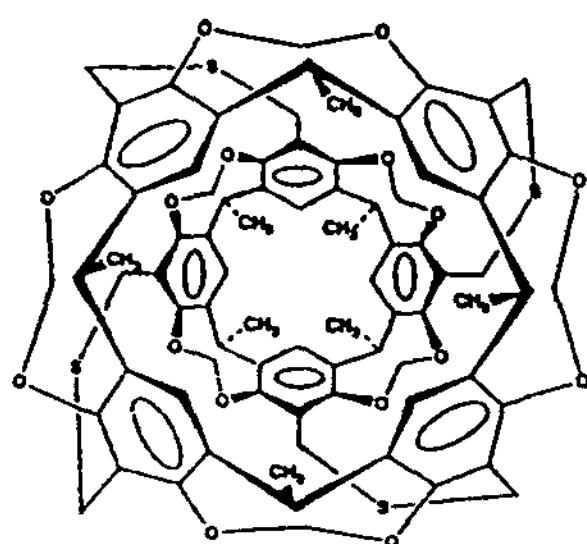

spherand
5

cavitand
6

carcerand
7

Based on the complexing properties of crown compounds, many applications have been developed, including their use in ion selective electrodes, selective transport membranes for ions, selective scavenging, concentrating agents for metal ions, and synthetic ionophores for cation transport. Some of these uses are summarized in Table 1.

The IUPAC name of these compounds are cumbersome, and a system of trivial names, originally proposed by Mr. Pedersen, is widely uesd. Thus compound 2d is designated in the IUPAC system as "2, 3, 11, 12-cyclohexano-1, 4, 7, 10, 13, 16-hexaoxacyclooctadecane", but in Pedersen's nomenclature, it is called "dicyclohexano-18-crown-6". This method for naming gives in this order, the number and kind of hydrocarbon rings attached to the cyclic ether, the total number of atoms in the polyether ring, the class name "crown", and the number of oxygens in the polyether ring.

Again, crown ethers are cyclic oligomers of ethylene oxide, which is a common raw material in the oil chemical industry. In addition, these ethers are hydrophilic, but the introduction of a hydrophobic group or groups into the molecule makes them amphiphilic, and they become surface-active. For these reasons, crown compounds may be said that they are very familiar substances in the field of oleochemistry.

Here, I would like to stress that among the contributors to the development of this field of chemistry, there are many Korean and Japanese researchers.

I have been studying synthetic methods for these compounds and also the properties of their products in the group led by the late Professor Okahara and Professor Ikeda of Osaka University. This group has made a number of contributions to this field of chemistry[4], but perhaps their development of new synthetic

Table 1. Applications of crown ethers

機　　能	用　途　分　野	應　用　例
Selective capture, separation, and transport of cations **Solubilization of inorganic salts** **Activation of anions** **Solubilization of alkali metals**	① 無機化學 …………	Study of the Solution Chemistry of Alkall metal
	② 無機合成 …………	Synthesis of complexes and metal carbonyls
	③ 無機化學工業 ……	Purification, concentration, separation and recovery of rare, noble or heavy metals
	④ 金屬工業 …………	Purification, concentration, separation, recovery and removal of inorganic salts
	⑤ 原子力工業 ………	Recovery, concentration and purification of U and Th. separation of isotopes
	⑥ 電氣化學 …………	Transport of ions, non-aqueous electrolysis
	⑦ 有機化學 …………	Study of reaction mechanism and reaction kinetics
	⑧ 有機合成 …………	Organic syntheses with use of phase −Transfer catalysts or inorganic salts
	⑨ 立體化學 …………	D, L 分割, 不齊合成
	⑩ 高分子合成 ………	Anionic polymerization with use of solubilized alkali metals
	⑪ 分析化學 …………	Ion selective electrode, polarography, anallysis of metal ione, non-aqueous titrations and esterification for HLC and GLC.
	⑫ 環境化學 …………	Scavenging and removal of hazardous metal ions
	⑬ 生化學, 生物化學 …	Mimics of the substances in living body such as synthetic ionophore
	⑭ 醫・農藥 …………	Removal of hazardous metal ions, supply of metal ions in need

methods are best known. Some of these methods provide simple routes to unsubstituted and substituted crown ethers and their aza- in sert thia-, or oxo-analogs, and others permit the synthesis of crown compound having side-chain(s) which have functional group(s) on it.

We also developed a new system for selective cation transport with N-substituted lipophilic aza crown ethers, using the large change in the coordination ability of the nitrogen that occurs when protonation and de-protonation take place.

The field of crown chemistry is very broad and its content is versatile, a few topics of interest that I have chosen arbitratily, will be given in this short review about the syntheses and applications of crown ethers and related substances. I will mainly cite the work done by the members of our group.
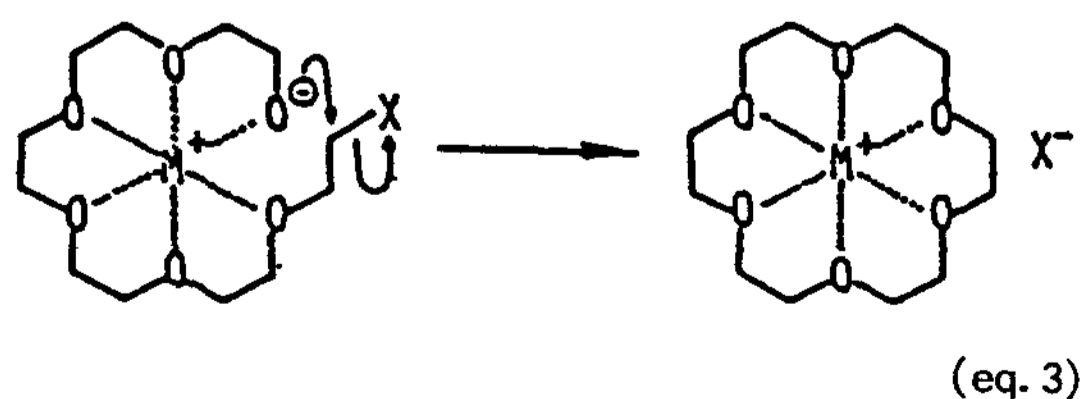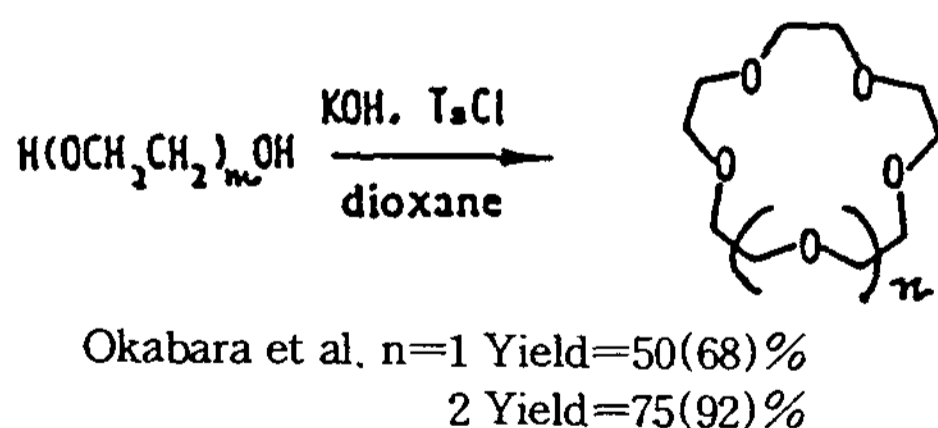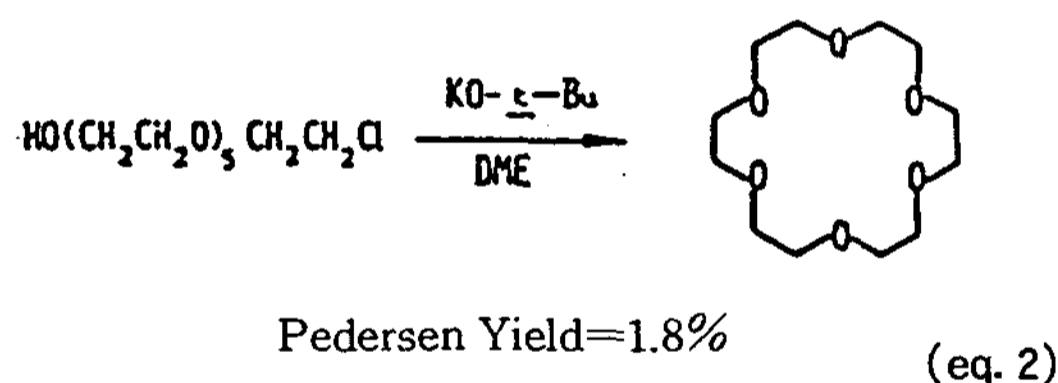
1. Synthetic Methods of Unsubstituted Crown Ethers and their Analogs

1) One-pot Process of Crown Ether Synthesis

Crown ethers have generally been synthesized through an intermolecular coupling reaction of diols with dihalides or ditosylates at highly diluted conditions(eq. 1). Intramolecular cyclization of chlorohydrin also been used(eq. 2), but the yield was very poor.[1]

In a newer process, however, easily accessible oligoethylene glycol is used as the starting material. An appropriate glycol is treated by

arenesulfonyl chloride in the presence of powdered alkali metal hydroxide(MOH) in an aprotic polar solvent, cyclization is carried out in a one-step operation via monotosylate formed *in situ* a according to the formula shown as eq. 3.[5] M^+ in the reaction system behaves as a template to assist the cyclization of the acyclic oligoethylene glycol.

$$\text{(eq. 1)}$$

Pedersen Yield=1.8%

$$\text{(eq. 2)}$$

Okabara et al. n=1 Yield=50(68)%
2 Yield=75(92)%

$$\text{(eq. 3)}$$
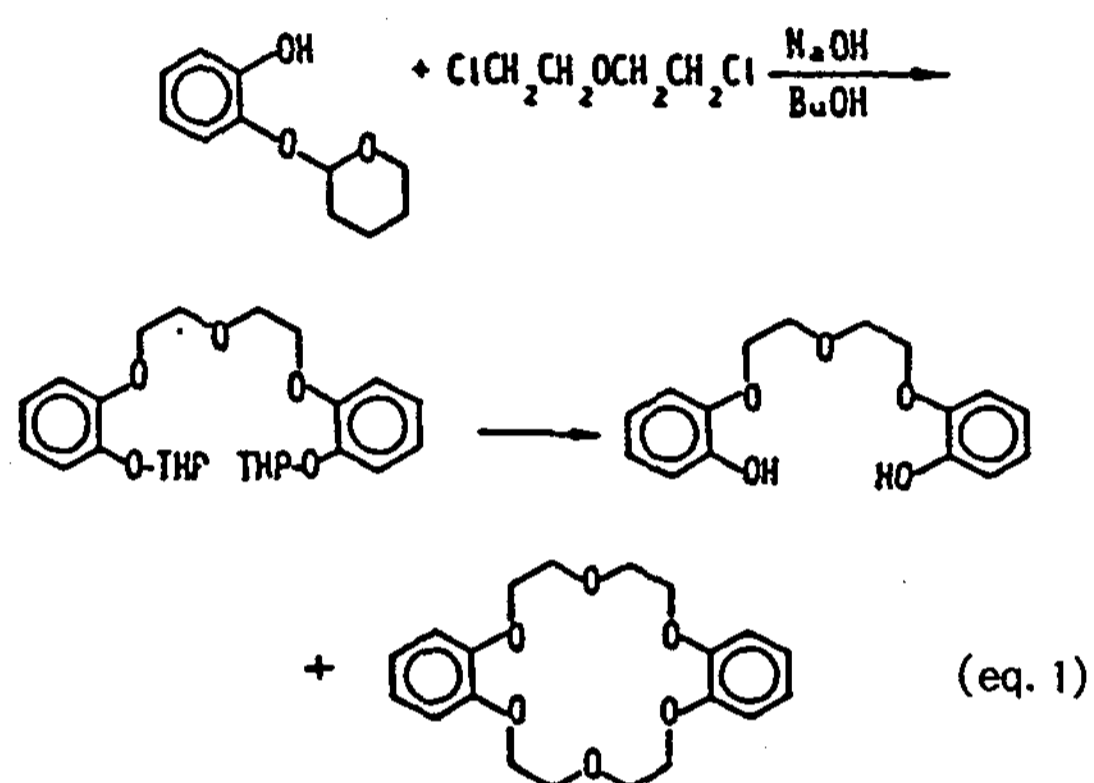
2) Synthesis of Ester Crowns

Bradshaw and other researchers[6] have pre-

pared many crown compounds containing ester linkages in their ring structure. They used the reaction between di-acid chloride and oligoethylene glycol, and consequently, their products were mostly di- (8) or tetra-ester compounds (9).

8   9
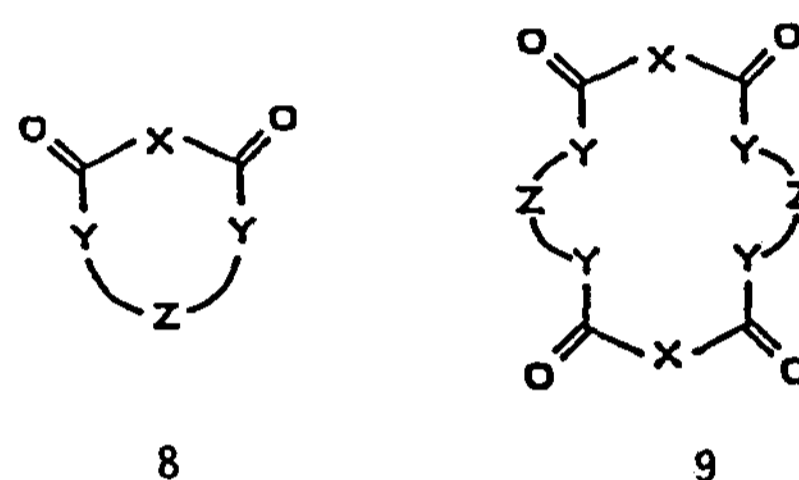
X : Various hydrocarbons and N-Containing groups *etc.*
Y : O or S
Z : Various hydrocarbons and oligoethylene glycols

I developed a process that involves the intramolecular cyclization of carboxymethylated oligoethylene glycols to obtain the oxo-analogs, ester-crown compounds. This method enables the preparation of many members of a new class of substances, mono-ester crowns. The method is also applicable to the preparation of their substituted derivatives and analogs.

① Unsubstituted Ester Crowns[7]

Appropriate oligoethylene glycols were carboxymethylated by treatment with chloro- or bromoacetic acid in a basic condition. The intermediates obtained were treated in dioxane with equimolar amounts of arenesulfonyl chlorides in the presence of alkali metal carbonates, to make use of the template effect of the metal cations, as shown in the eq. 4.
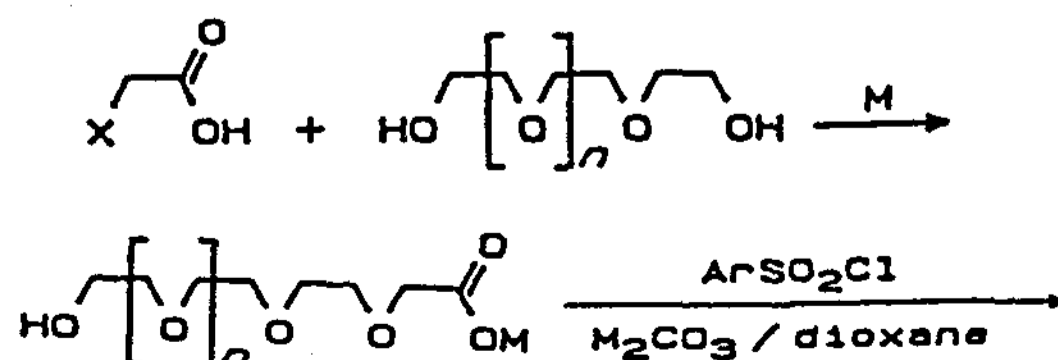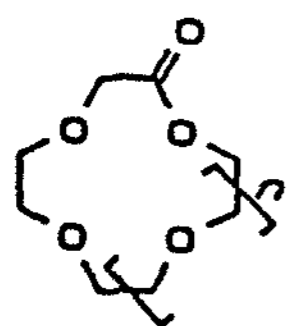
(eq. 4)

On the examination of the mechanism of the cyclization reaction, two possible pathways are assumed, one passes through mixed anhydride (A) and the other through sulfonate ester(B) (eq. 5). Of two reactions done as the model, a mixture consisted of oligoethylene glycol, acetic acid, and benzenesulfonyl chloride, treated with sodium carbonate, gave the corresponding diester, but a combination of oligoethylene glycol ditosylate and acetic acid, gave no product in similar treatment. On the basis of this result and another rationale[8] (eq. 6), the former pathway(A) seems more likely.
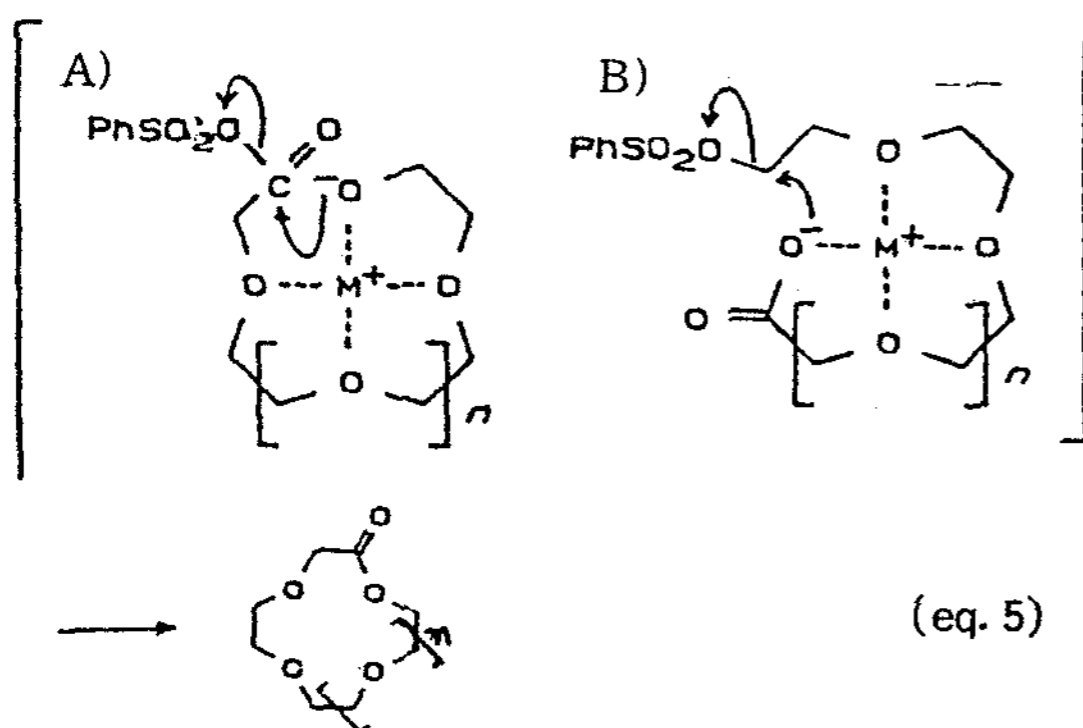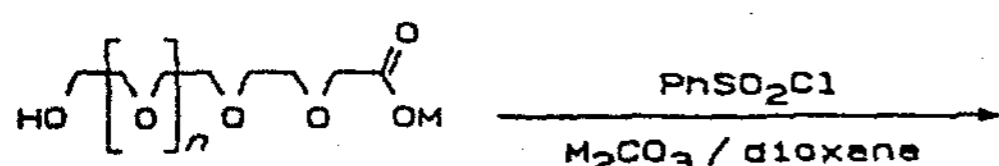
(eq. 5)
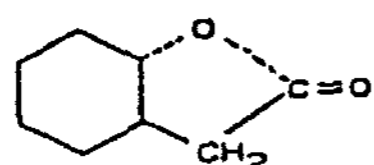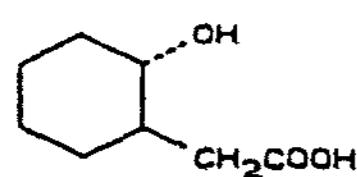
(eq. 6)

· J. H. Brewster(1955)

Alternative methods for the preparation of

these ester crown compounds were explored and two new methods that make use of ester exchange(method B) or dehydration(method C), were developed and compared with the original method(method A)(eq. 7). Compound 10, with n=1, was obtained by method C only.[9]
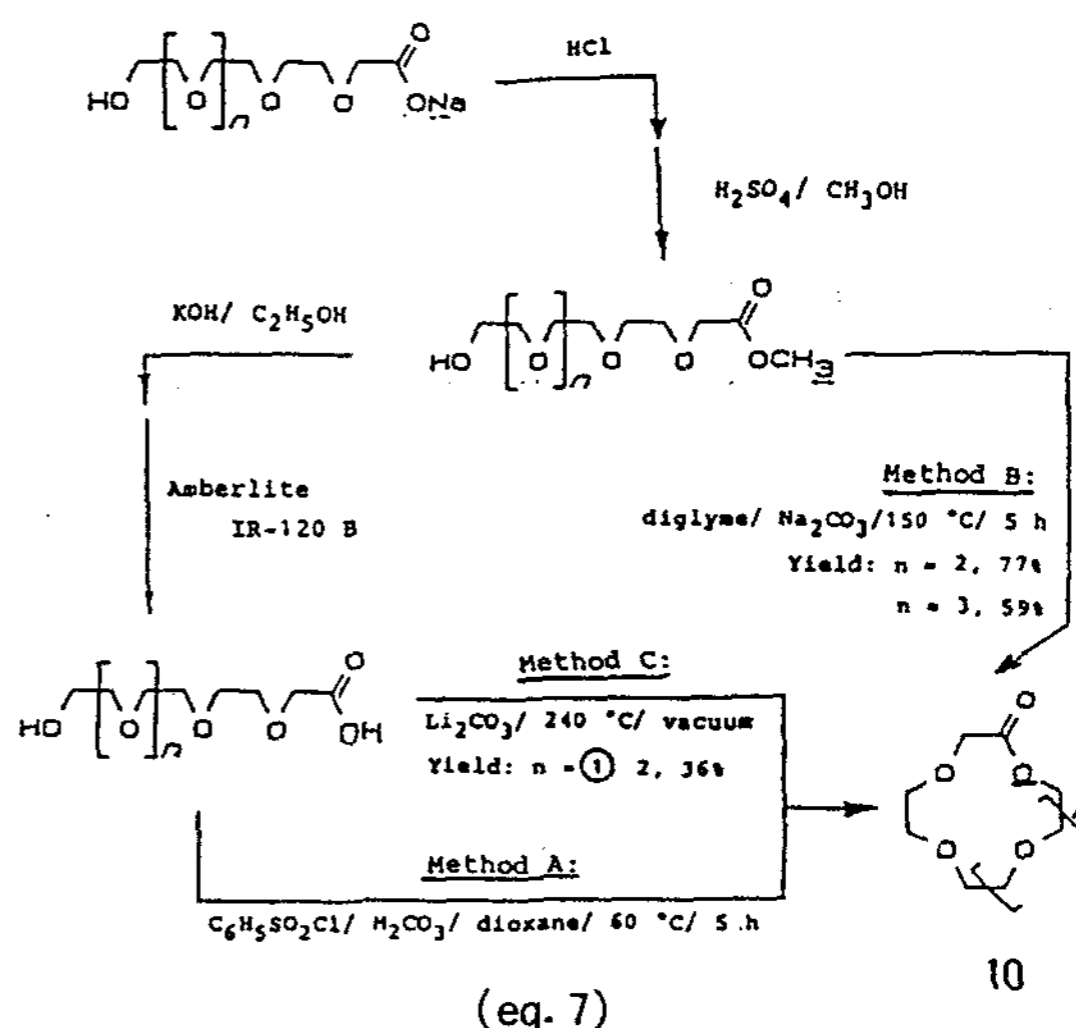
(eq. 7)

② Substituted Ester Crowns[10]

Oligoethylene glycols were reacted with α-bromo-fatty acids in place of bromoacetic acid, and the intermediates thus obtained were then cyclized as described in the preceding section to yield substituted macrocycles(eq. 8).
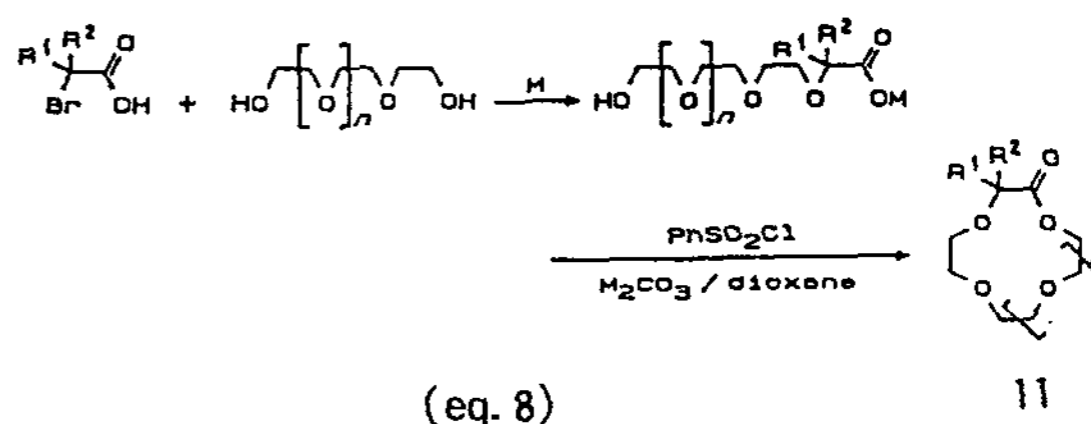
(eq. 8)

Compound(11)		Yield /%		
R^1	R^2	n=2	3	4
CH₃	H	15	39	28
CH₃	CH₃	10	32	17
C₂H₅	H	21	41	24
C₆H₁₃	H	17	37	23
pH	H	20	4	21

than those of normal crown ethers, and in turn, stronger than those of the corresponding diester crowns that have been reported. The introduction of side-chain or substitution of the coordinating atom also changes this ability.

3) Improved Methods for Aza Crown Synthesis

Nitrogen analogs of crown ethers, the so called aza crown ethers, in which one or more oxygens are replaced by >NH or >NR, have generally been prepared through the two methods shown in eq. 12[12] and eq. 13.[13] The first involves amide formation in the cycliz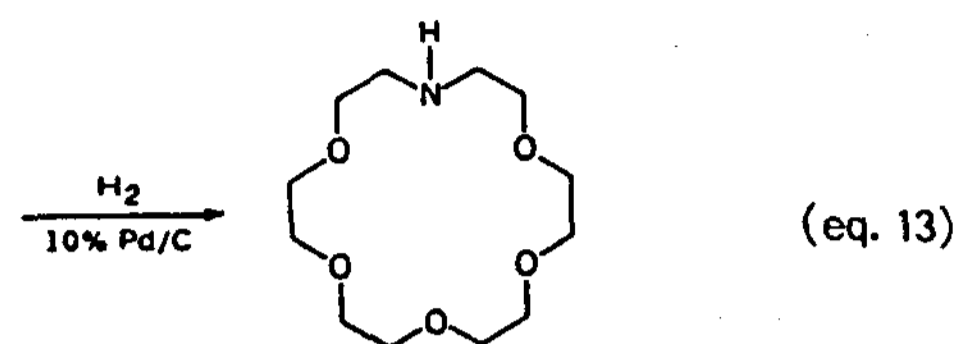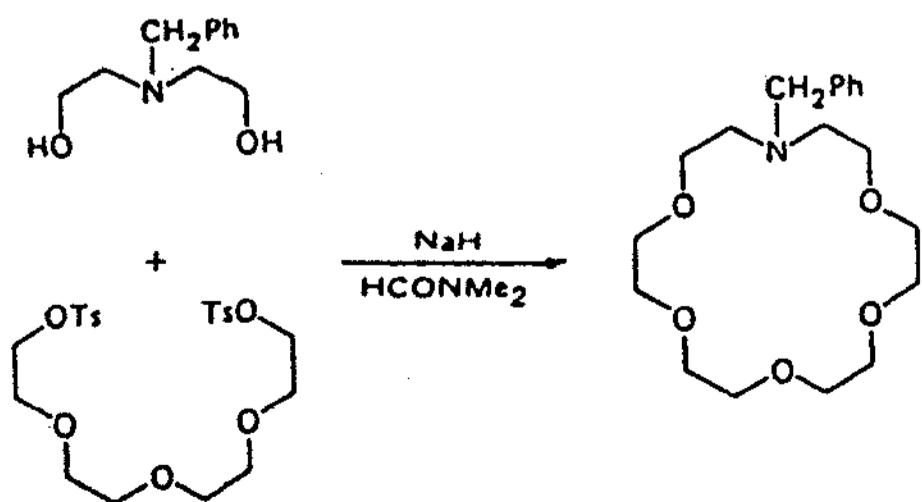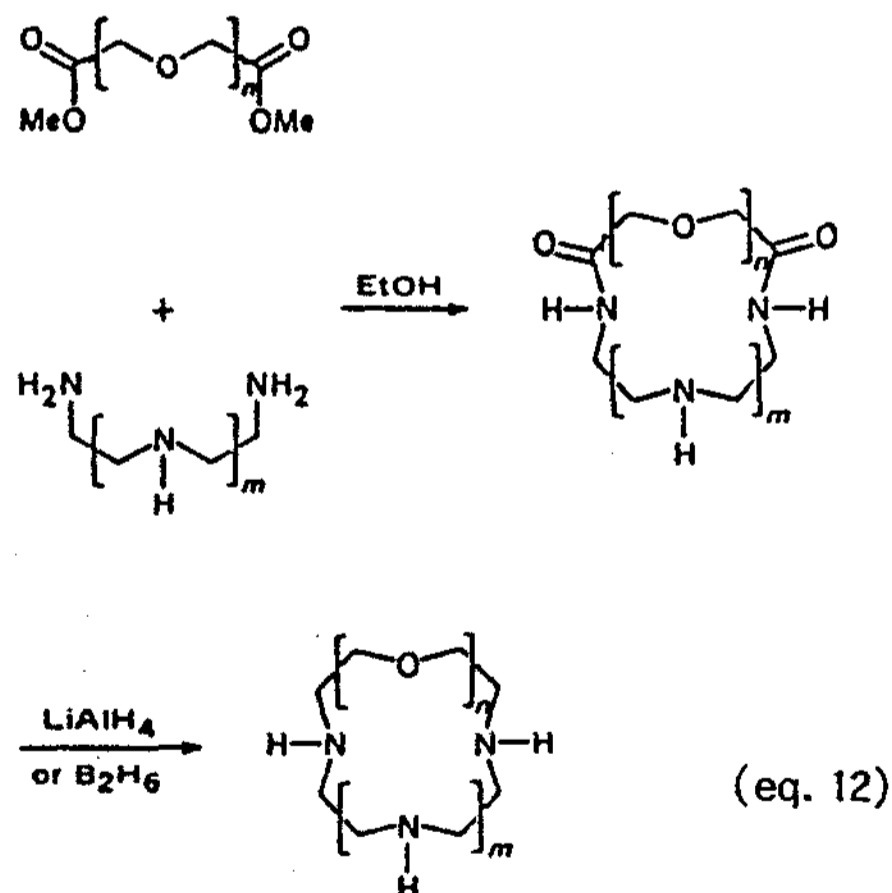ation step followed by reduction to the desired cyclic amine, and the other involves intermolecular Williamson-cyclization to obtain protected amino compound. In the latter case, deprotection of the intermediate is needed to yield N-unsubstituted aza crown ethers.

(eq. 12)

(eq. 13)

Maeda and others in our group developed simpler processes to obtain N-unsubstituted aza crown compounds directly without the use of any protecting group.

① Intermolecular Cyclization without Protection of the Amino Group[14,15]

One of the most common chemicals, diethanolamine was reacted with oligoethylene glycol di(p-toluenensulfonate) or the corresponding dichlorides in t-butyl alcohol-dioxane in the presence of Na or K t-butoxide(eq. 14). The target compound was extracted and purified by Kugelrohr distillation.

X : Cl, Tos

(eq. 14)
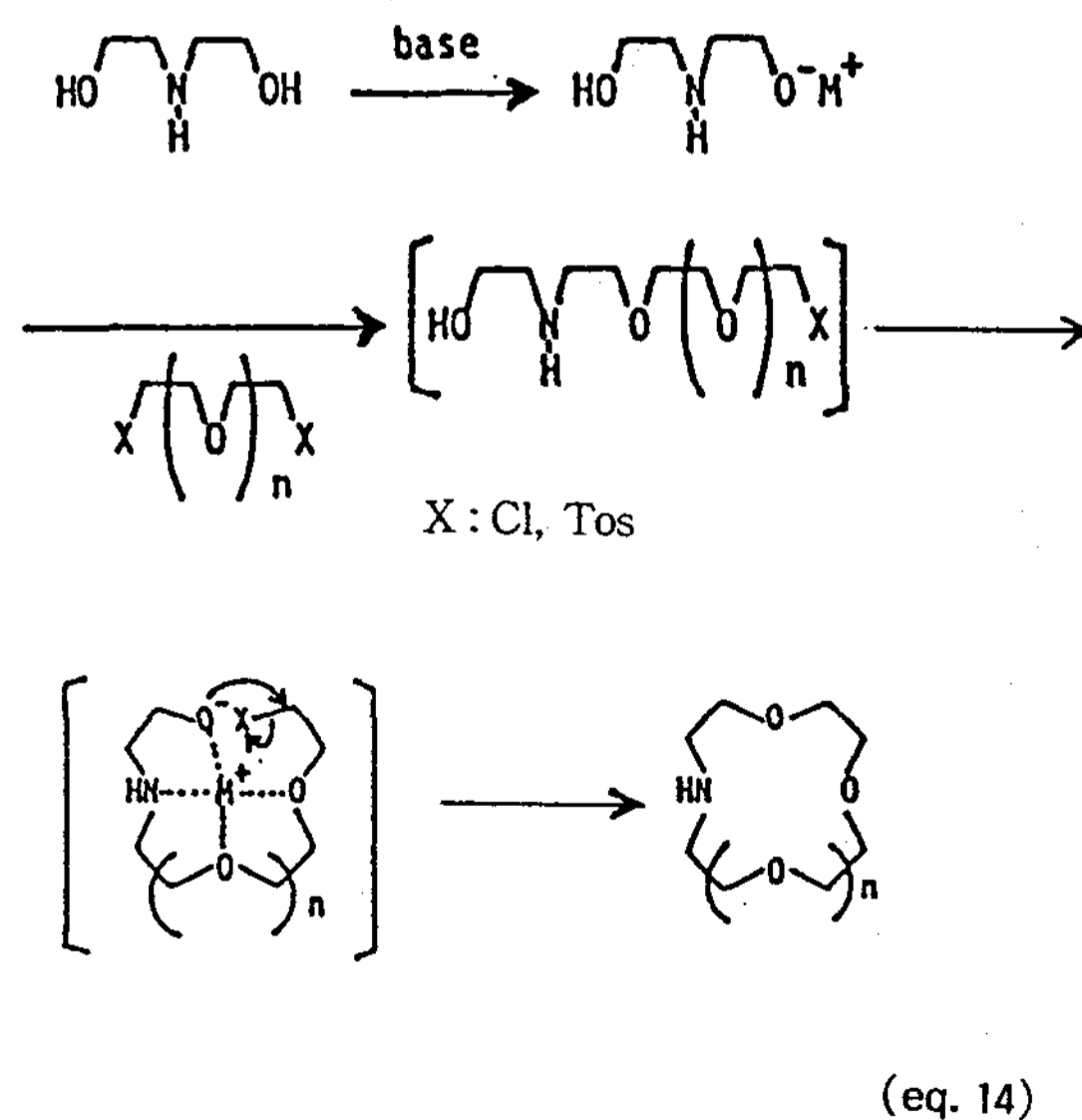
Substituted or unsubstituted ethanolamine was converted to the corresponding diethanolamine derivative(eq. 15), it was then cyclized by the reaction with ditosylate to yield 2, 3-substituted aza crown ethers(eq. 16).

(eq. 15)

(eq. 16)
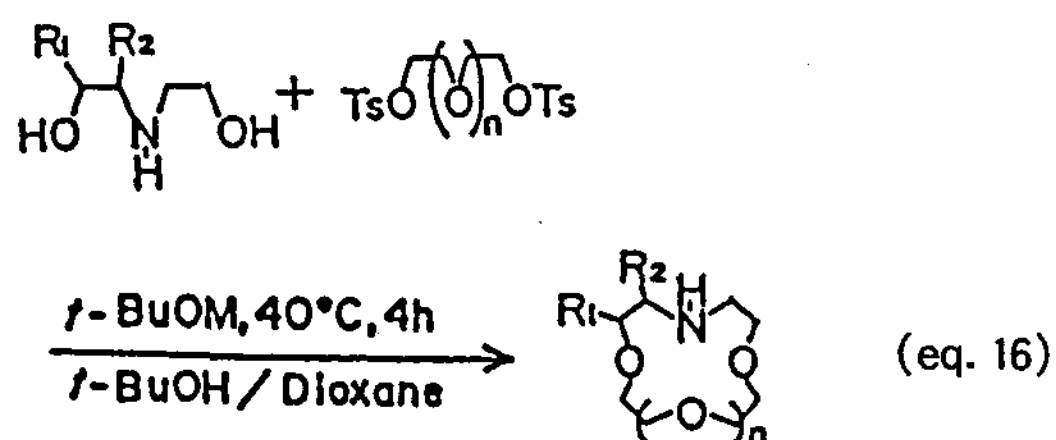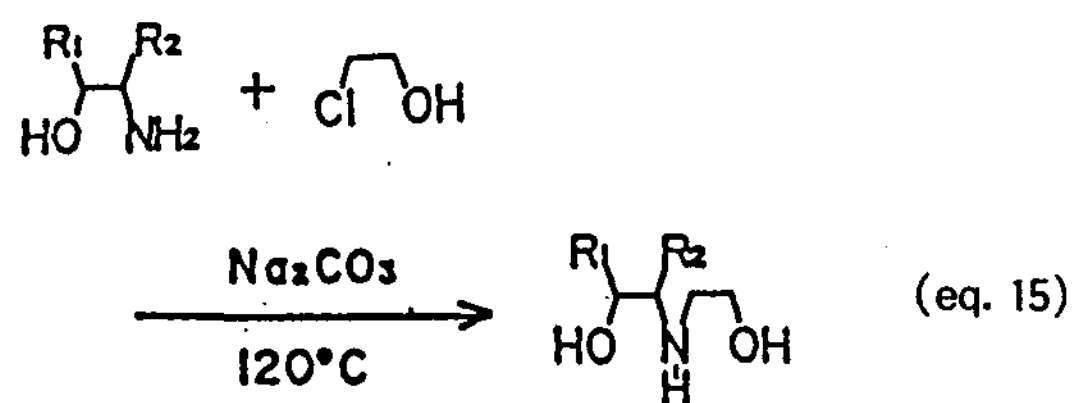
Similarly N-(ethylamino)-ethanolamine was hydroxyethylated yielding diaza analog of triethylene glycol(eq. 17), and then submitted to the cyclization reaction with appropriate ditosylate to yield 1, 4-diaza crown ether(eq. 18).

(eq. 17)

p=1
p=2

(eq. 18)
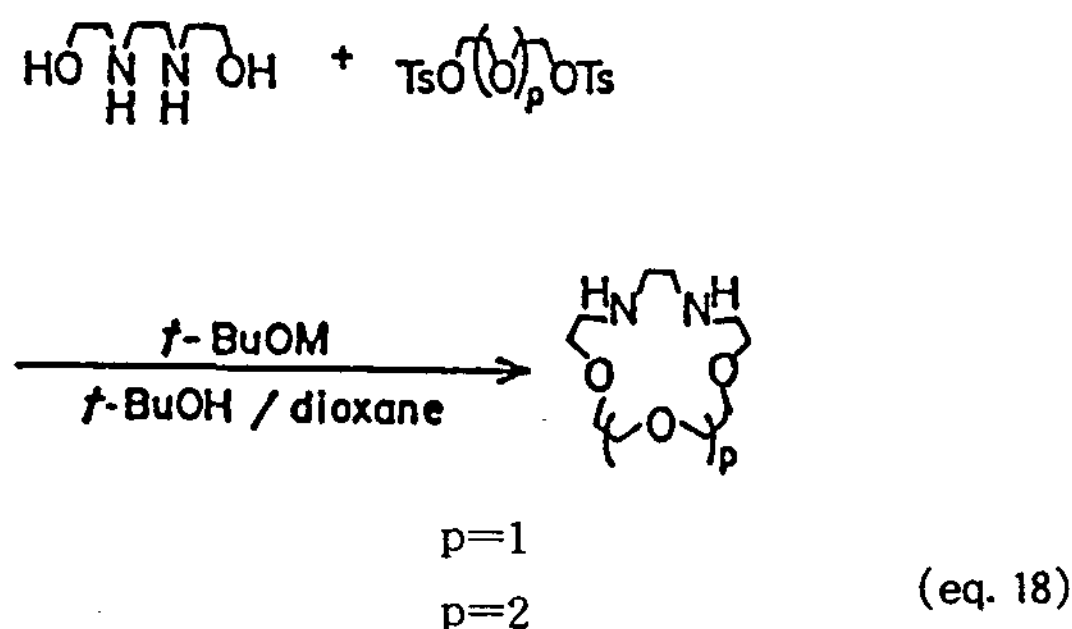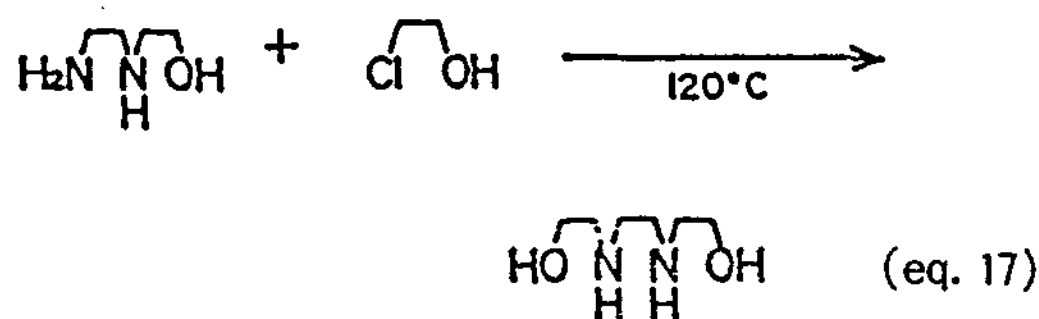
Two molar equivalent ethanolamine was reacted with dichloride of triethylene glycol(eq. 19) and the product was cyclized by the reaction with diethylene glycol di(p-toluenesulfonate) to yield 1, 10-diaza crown ether(eq. 20).

(eq. 19)

(eq. 20)
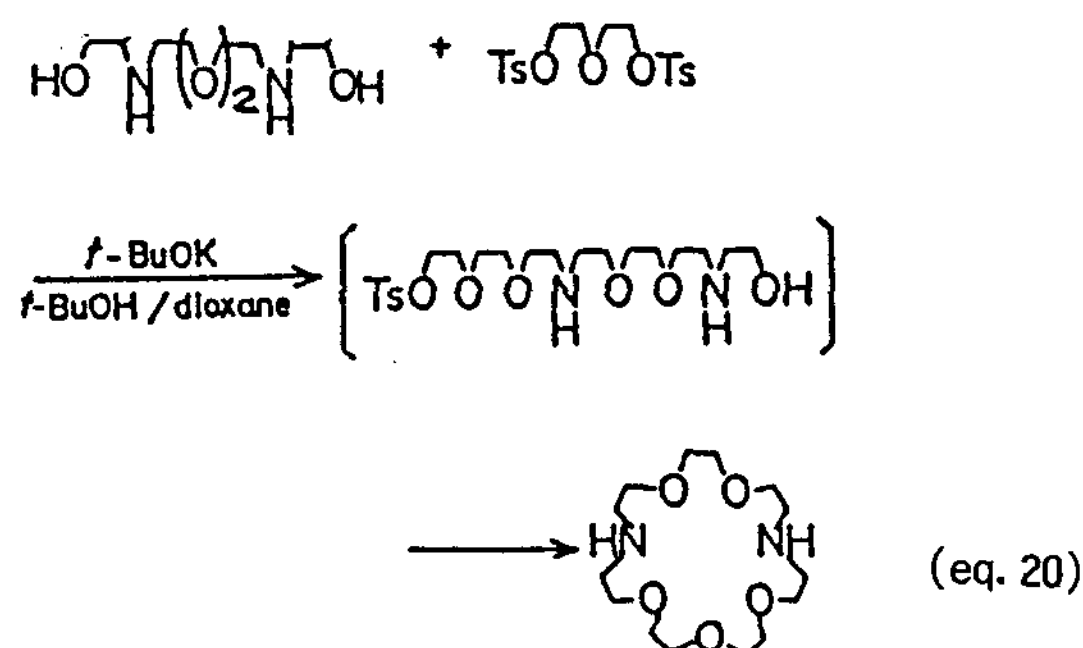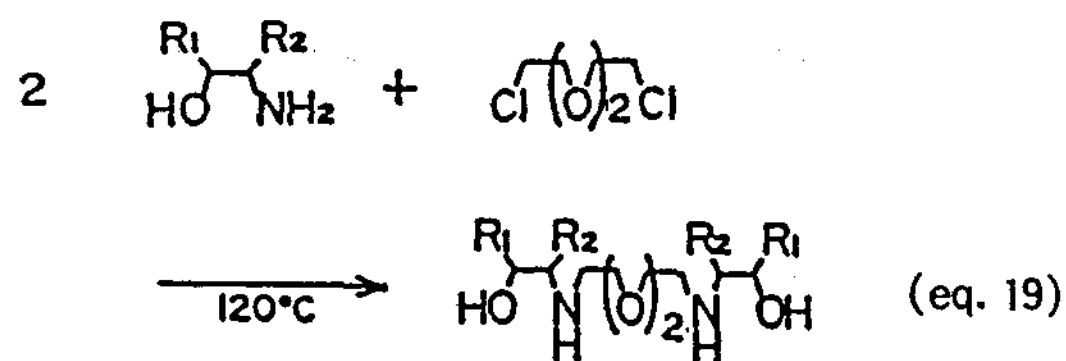
② Intramolecular Cyclization without Protection of Amino Group[14, 15]

Hydroxyethylation of ethanolamine just described above(eq. 15) was extended to their oligoethoxylated derivatives, it was cyclized in intramolecular fashion by means of one-pot process described in section 1, 1 to yield N-unsubstituted aza crown ethers(eq. 21).

(eq. 21)

Two molar equivalents of substituted- or unsubstituted ethanolamine were reacted with dichloride of oligoethylene glycol(cf. eq. 19) and cyclized by the action of arenesulfonyl chloride in the presence of caustic alkali, yielding 1, 7-diaza crown ether(eq. 22).

(eq. 22)

2. Synthesis of Crown Compounds with Side-Chain(s)

Introduction of various side-chain into crown ring affords not only the change of the properties of original compound but also further derivatization to a wide variety of their relating compounds, utilizing functional group(s) included in the chain. Although syntheses of a few oxo and aza crown compounds having side chain(s) using substituted starting material, were already described, newer methods to obtain crown compounds having side chain(s) will be shown in this section.

1) Facile Synthesis of Alkly-(Aryl-) substituted Crown Ethers

α-Olefin was treated with N-bromoacetamide in the presence of oligoethylene glycol, alkoxy-bromination reaction took place, and addition product of anti-Markovnikov type was obtained. The adduct was, then, cyclized by intramolecular reaction(eq. 23).[16a, b]

(eq. 23)

Aza[16c, d] and thia-[16e] crown ethers with side chain(s) were also obtained through similar processes.

2) Synthesis of Polymethyl Crown Ethers

Oligopropylene glycols, in place of oligoethylene glycols, were intramolecularly cyclized, to obtain more lipophilic macrocycles than ordinary crown ethers(eq. 24).

(eq. 24)

Presence of polymethyl groups somewhat inhibited the complexation ability of crown ring toward cations. The stability of complexes, however, remained still high; especially for the product(n=4) with K^+ and also for another one(n=3) with Na^+.

3) Synthesis of Crown Ethers having Hydroxyl Group

Crown compounds having -OH group on their ring structure have been synthesized via several steps of reactions. When oligoethylene glycols were reacted with epichlorohydrin in the presence of base, hydroxy-substituted crown ethers were given in one step process. Of the two products supposed to be obtained, no hydroxymethylated crown compounds were detected in the reaction mixtures.[18] On the other hand, the latter compounds were also successfully synthesized through the sequential reactions shown in eq. 26.[19]

(eq. 25)

(eq. 27)

$CH_2 = CH$ ... KOH, 80°C

$CH_2 - O - CH_2 - CH = CH_2$

When di-methallylated glycol was used as starting material, bi-functionalized crown ether was obtained (eq. 28).

$CH_2 - O - CH_2 - CH = CH_2$

TosCl / LiH (n=2)
NaOH (n=3), or KOH (n=4)

$CH_2 - O - CH_2 - CH = CH_2$

PhSO₂Cl

NaOH or KOH

5 % Pd–C /70% HClO₄

$CH_2 - OH$

(eq. 26)

(eq. 28)

4) Synthesis of Bromomethylated Crown Ether with Alkyl Side Chain at the Bridge-head Carbon

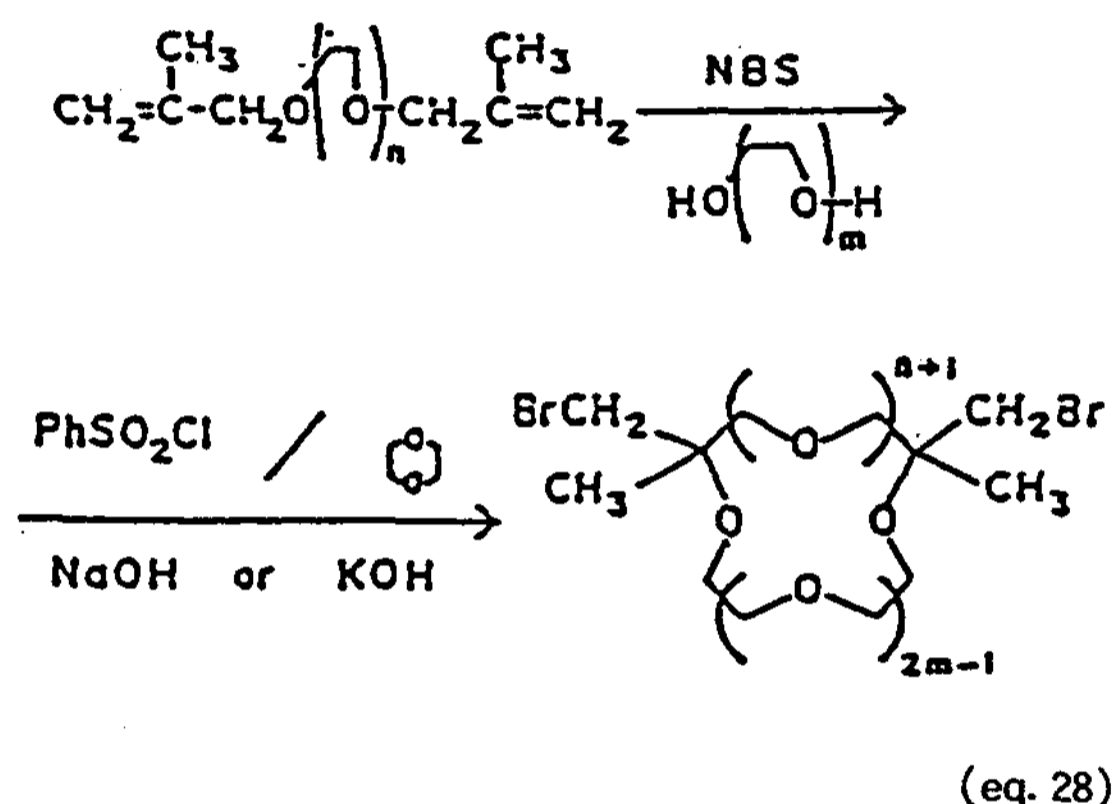Methallylated oligoethylene glycol, obtained by treatment of the apropriate glycol with methallyl chloride, was cyclized through intramolecular alkoxylation under the effect of bromonium cation (eq. 27).[20] In addition to the presence of reactive bromomethyl group, useful to further derivatization, the alkyl side chain at the bridge-head carbon was also found to have significant role in the selectivity of complex formation with cation, the reaction products have been utilized as one of the most important intermediates for the synthesis of ionophores.

5) Synthesis of Aminomethylated Crown Ether

3-(N-substituted amino)-1, 2-propane diol, which was prepared by the reaction of 3-(chloro-1, 2-propanediol with appropriate primary amine, was cyclized similarly as described in section 1. 3). ① with oligoethylene glycol di-(p-toluenesulfonate) in the presence of Na or K t-butoxide to yield aminomethylated derivative 12 (eq. 29).

CH_2NHR

$HO \quad OH \quad + \quad TsO$ ... OTs

CH_2NHR

12

(eq. 29)

$CH_2 = C - CH_2O$ ... OH NBS / MBF₄
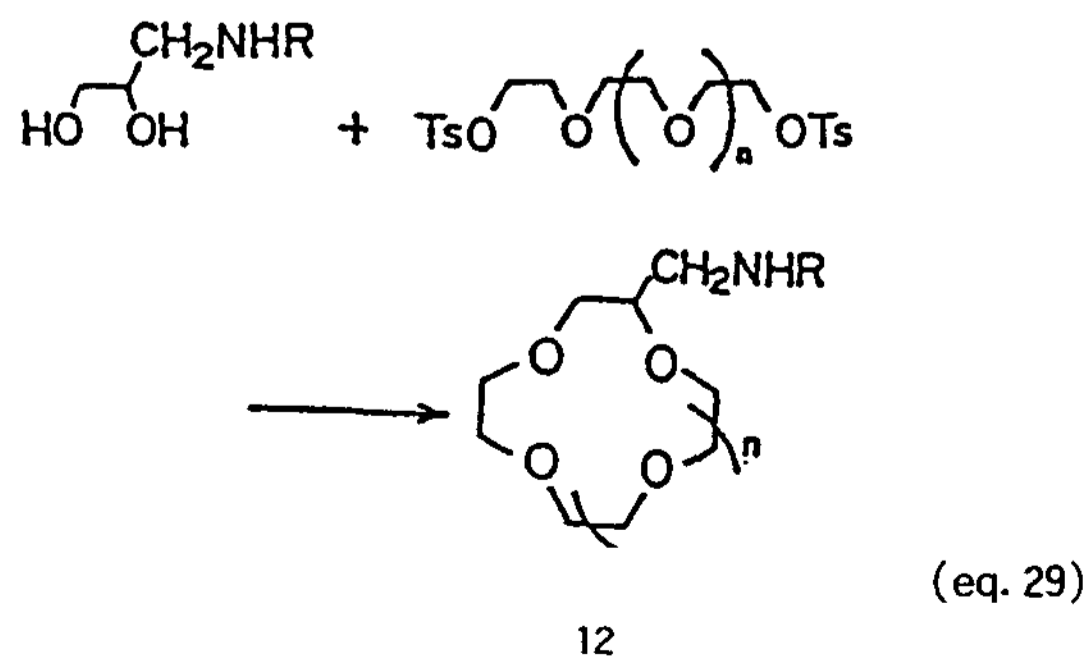
The products were very reactive, for example, by the reaction with methacryloyl chloride, easily polymerizable amide 13 was obtained. This is useful intermediate of the polymer having crown pendant 14.[21] When the cyclization was carried out in the mole ratio of 2 : 1, bifunctional product 15 was obtained.
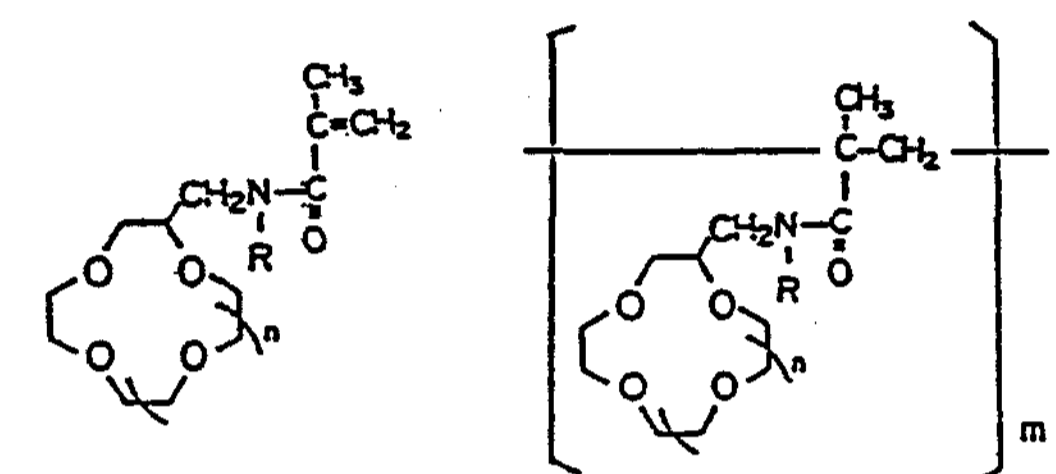
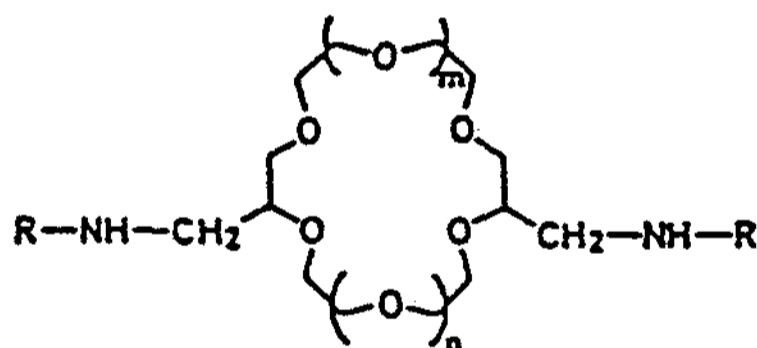Polymerizable monomer   Polymeric crown ether
having crown group

13   14

Bi-Functional crown ether

15

6) Synthesis of Several Crown Compounds Utilizing Reactive Diglycidyl Ethers of Oligoethylene Glycols

Because of the many by-products, Williamson type reaction between alcohol and epichlorohydrin to yield glycidyl ethers have relatively been less utilized for preparative purposes. Gu et al. of our group reported, however, that this reaction proceeds in the presence of a phase transfer catalyst to give the corresponding glycidyl ethers effectively.[22] Diglycidyl ethers, thus prepared(eq. 30) were utilized to yield a wide variety of crown compounds.
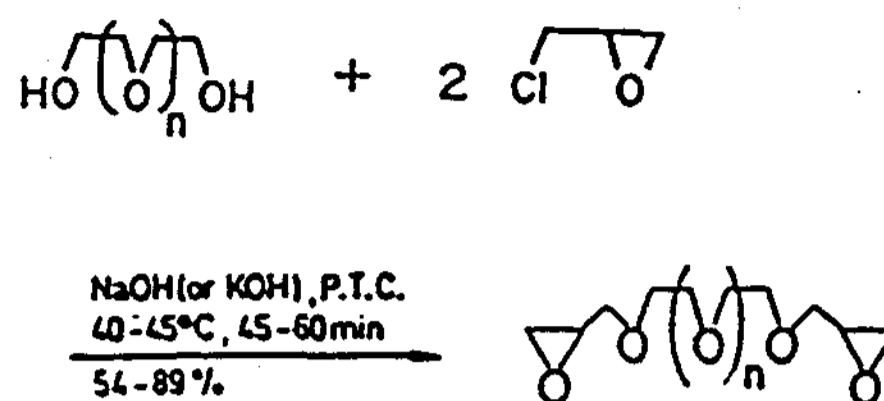
(eq. 30)

Diglycidyl ether was reacted with primary amine, the dihydroxy-dimethylamino derivative thus obtained was then cyclized by the reaction with the ditosylate to give the bis(alkylamino) crown compounds(eq. 31).[23]
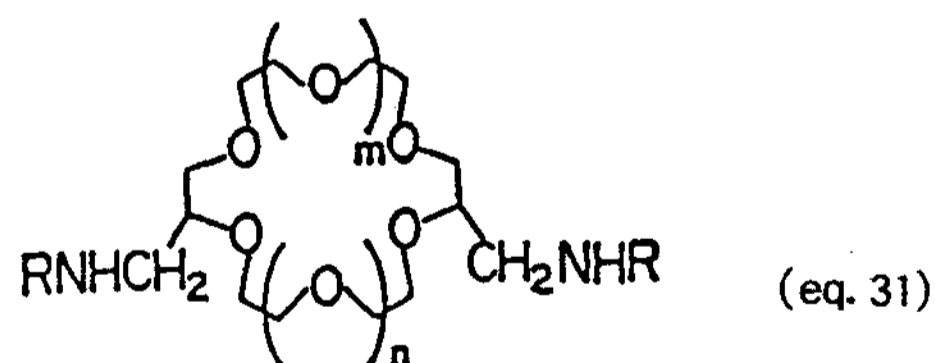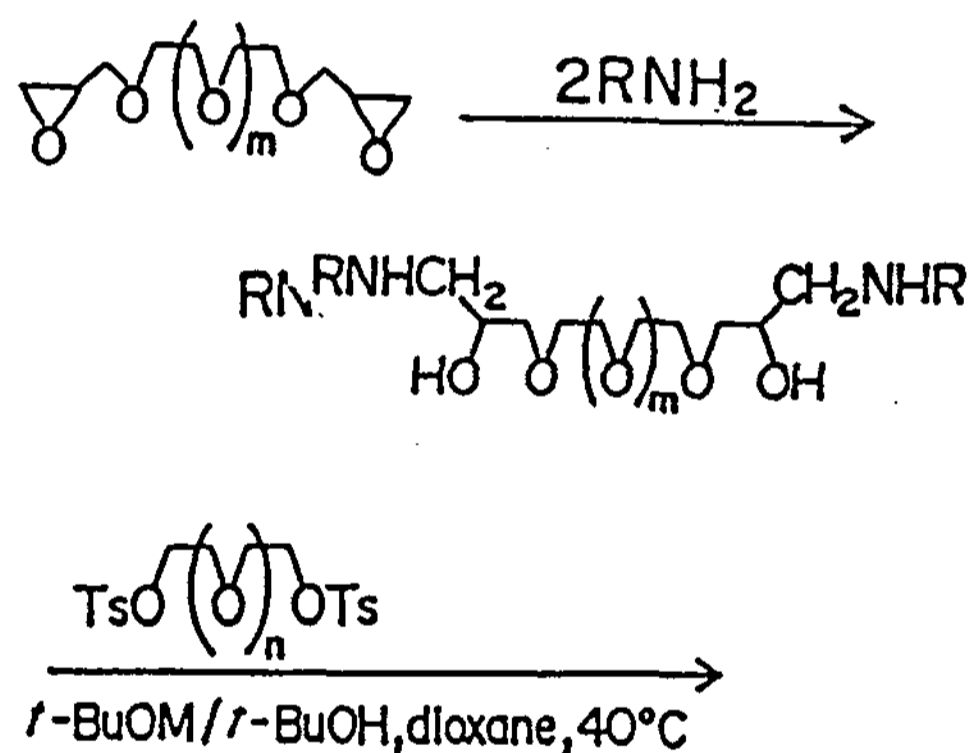
(eq. 31)

Furthermore, as summarized in eq. 32, the ethers were cyclized by the action of monovalent reagents (Y-), to give hydroxyl crown ethers having a side chain. If bivalent reagents (-X-) were used, dihydroxyl derivatives were obtained, in the latter cases, the products were further cyclized in succession yielding novel bicyclic crown compounds.

(eq. 32)
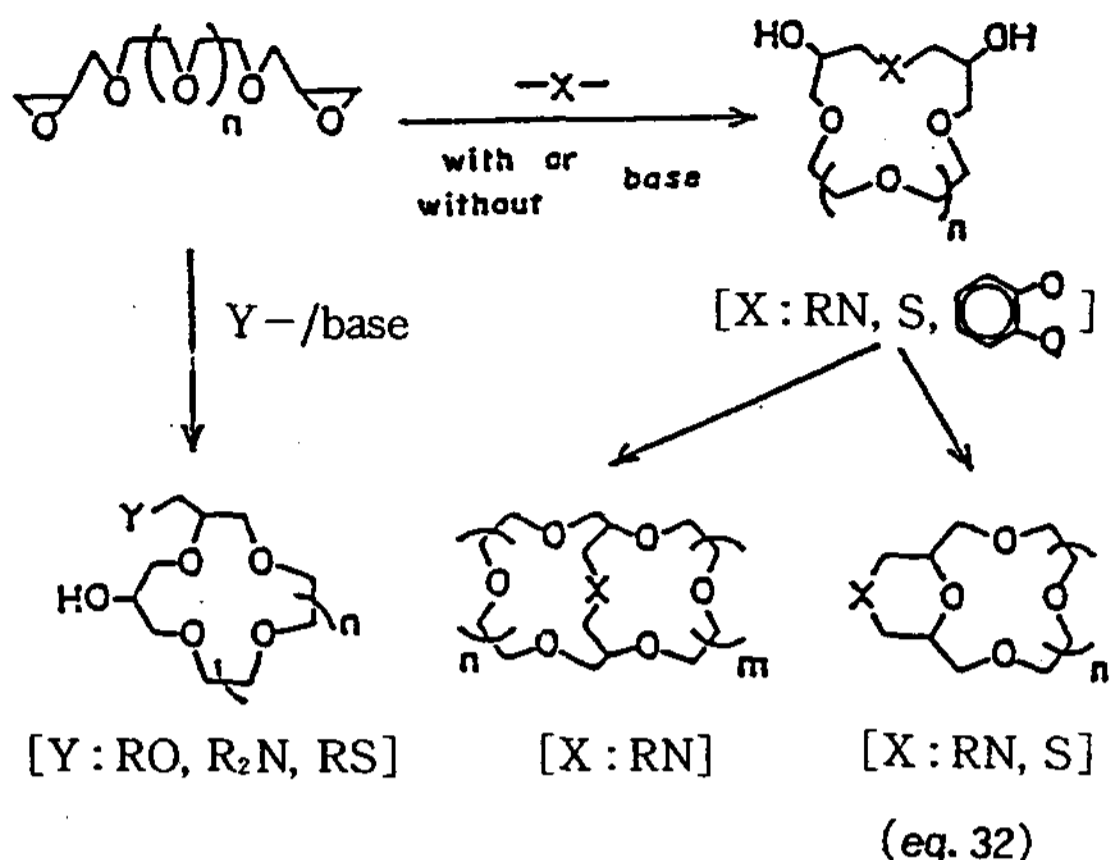
3. Selective Transport of Cations with Crown Compounds

Some kinds of natural antibiotics complex selectively with cations that are essential to the living body. The cations thus complexed, are transported through lipophilic membranes against the slope of their concentration. The structures of such natural ionophores[e. g. 16] are, in general, too complicated to modify easily so as to clarify their interaction with the cations.

Valinomycin,

16

In recent years, the molecular design of new classes of biomimetic host compounds have become a subject of increasing interest. We intended this work, with use of lipophilic aza
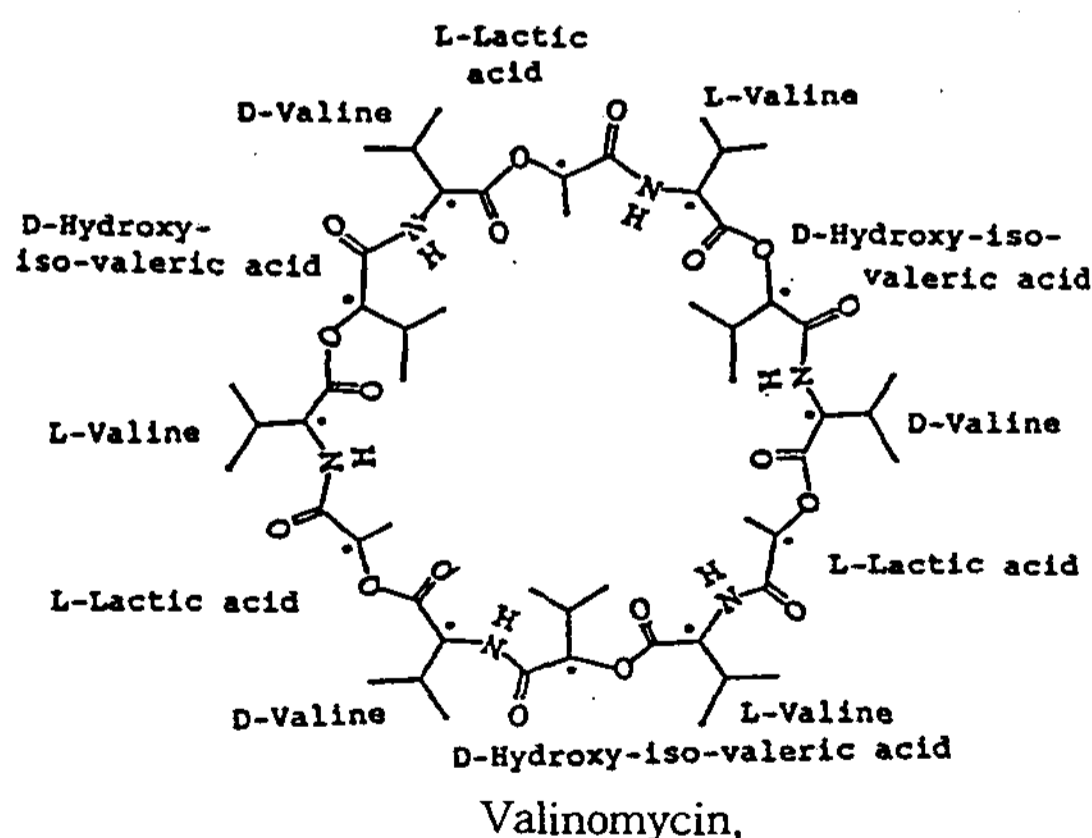
crown ethers as the ionophore, aiming both at the explication of the mechanism of molecular recognition based on host-guest interaction by virtue of the ion-dipole interaction which acts between the hard cations and the donating atoms of crown compounds and also at practical applications. The ionophores were estimated mainly on the basis of amount of cations transported by the two types of transport, on which the concepts are illustrated with another one in Fig. 1. Results of liquid-liquid extraction experiments were also taken into consideration.
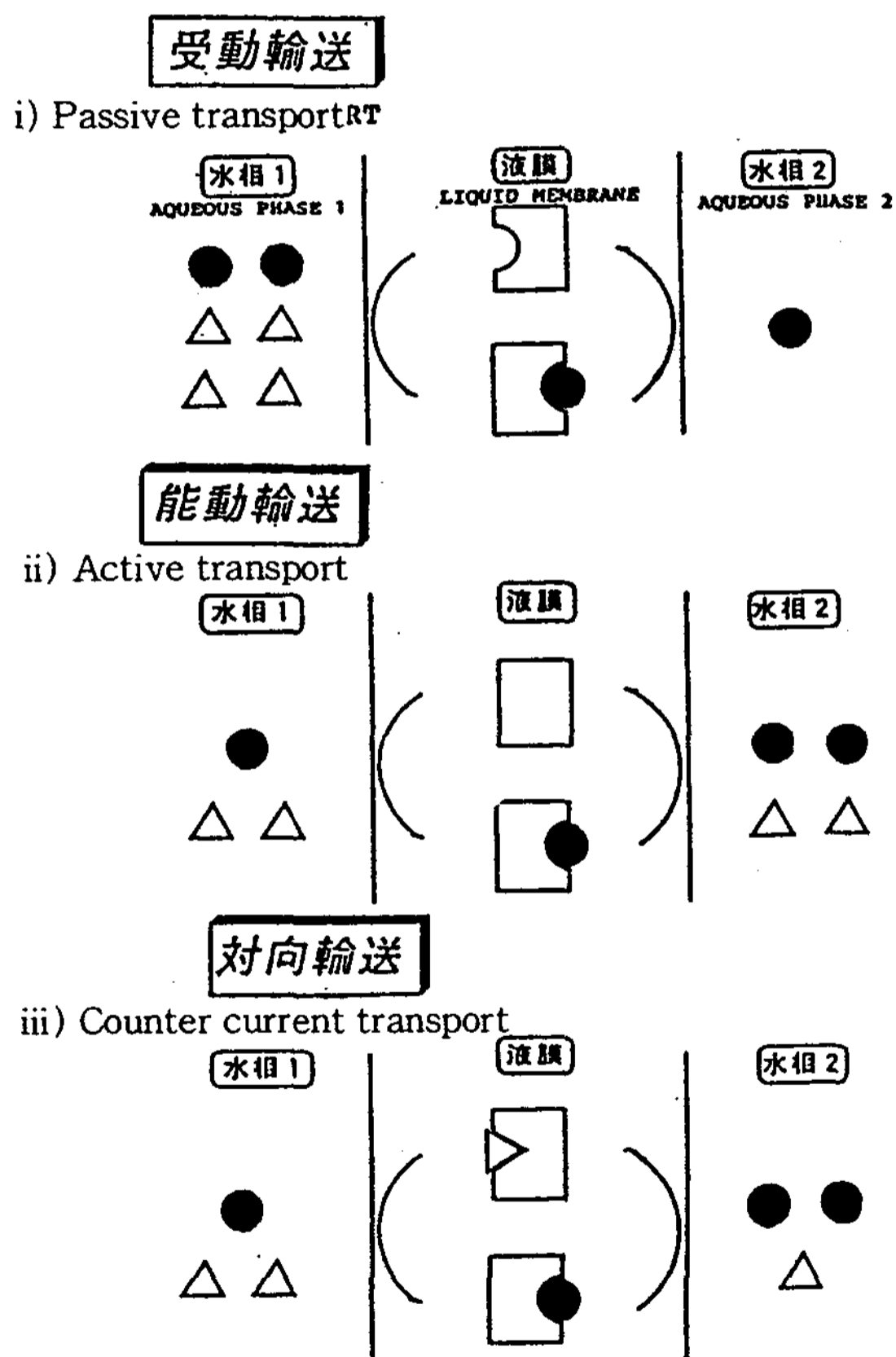

Fig. 1. Three types of selective transport by use fo Ionophore.
   i) Transport along the slope of concentration of a substance.
   ii) Transport agaist the slope of concentration of a substance.
   iii) Counter current transport along the each slopes of concentration of two substances.

1) Selective Transport of Cations with N-substituted Aza Crown Ethers[24]

Active transport experiments were done in U-type tube apparatus as shown in Fig. 2, cations in aqueous phase(phase 1; basic) were transported to another aqueous phase(phase 2; acidic) through organic liquid membrane, in which an N-substituted aza crown ether(C_8 EO1-N15 or C_8 EO2-N18) was contained as ionophore. Difference of proton concentration between Phase 1 and Phase 2 acted as driving force for the metal cations. To increase the amount to be transported, relatively lipophilic inorganic ion SCN^- was selected as counter anion in this system.

R	n = 1	n = 2
C_8H_{17}	C_8 N15	C_8 N18
$C_8H_{17}O$	C_8 EO1-N15	C_8 EO1-N18
$C_8H_{17}O O$	C_8 EO2-N15	C_8 EO2-N18
$C_8H_{17}O O O$	C_8 EO3-N15	C_8 EO3-N18

1~4 stirrer

Phase 1 (Basic) H_2O, 10 mL

KSCN   0.1 M Me_4NOH 0.1
NaSCN   0.1 M

Phase 2 (Acidic) H_2O, 10 mL

KSCN   0.1 M   HCL   0.1 M
NaSCN   0.1 M

Liquid Membrane CH_2CL_2, 20 mL
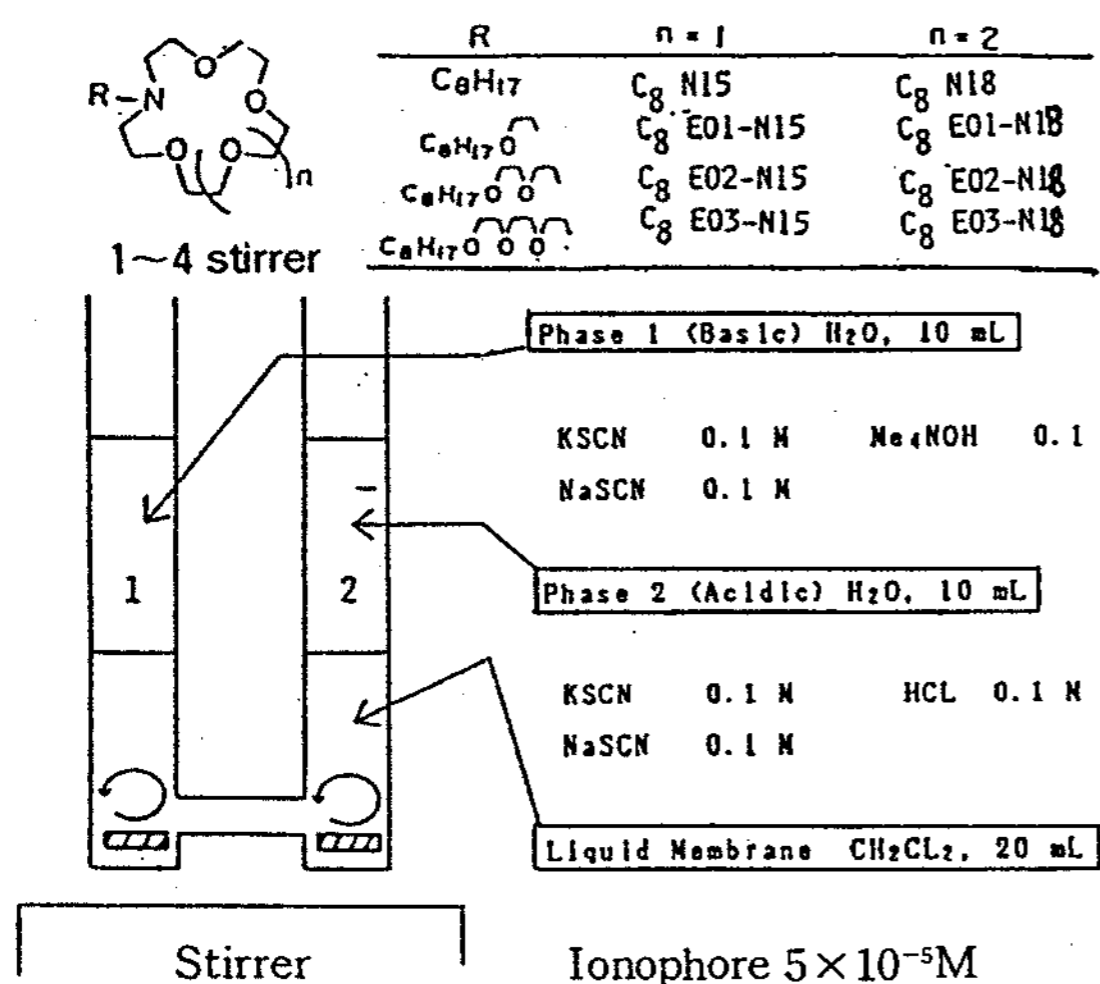
Stirrer   Ionophore 5×10^{-5}M

Fig. 2. Selective active transport of ctions with use of N-substituted aza crown ethers.

The transport process might be explained as shown in Fig. 3. Cations in phase 1(basic) were selectively complexed with the ionophore at the interface with liquid membrane(CH_2Cl_2), the complexes formed were transported by migration to another interface with phase 2 (acidic), thence the amino-nitrogens were protonated missing their coordination ability.

The released cations were transferred into phase 2(acidic), the protonated ionophore went back to opposite side trough the membrane. There, the ammonium type compounds were converted again to the original tertially amine derivatives and functioned there as ligand.

Basic (phase 1)

M^+ H-N$^+$R SCN^-

H^+ M-N^R SCN^-

Acidic (phase 2)

M^+

H^+

KSCN   0.1 M
NaSCN 0.1 M
Me_4NOH 0.1 M
(H_2O, 10 ml)

Ionophore: 5×10^{-5} mol
(CH_2Cl_2, 20 ml)

KSCN   0.1 M
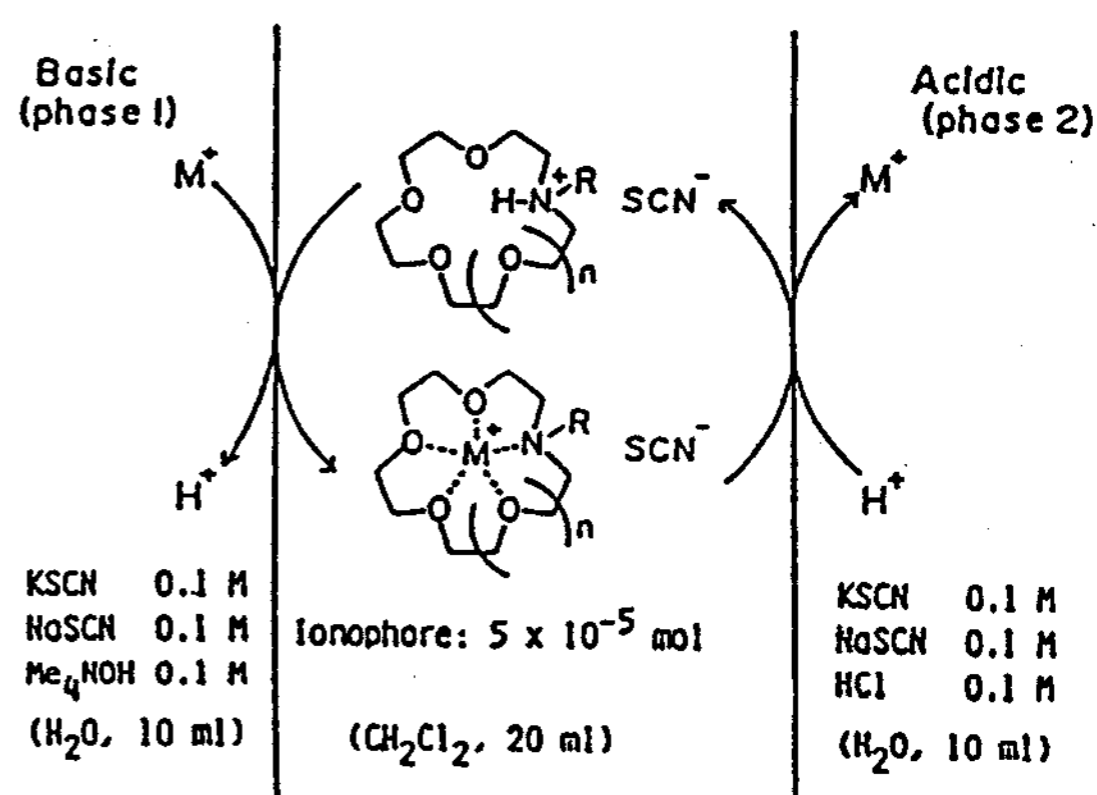NaSCN 0.1 M
HCl   0.1 M
(H_2O, 10 ml)

Fig. 3. Transport process with use of lipophilic monoaza crown ethers.

The series of C_8 EO2-N18 were more effective to transport cations than that of C_8 EO2-N 15. Although K^+/Na^+ selectivity of 4.4~5.5 was easily obtained by use of the former series, comparable Na^+/K^+ selectivity was not attained by any members of the latter series. While the amounts of cations transported were increased with the number of oxygen atoms present in side chain (N-lariat crown ethers), selectivity for these two cations was tend to decrease.

2) Selective Transport of Cations by Use of Cooperative Function of N-substituted Aza Crown Ethers and Picric Acid[25, 26]

The system for selective transport for cations, just described in the preceding section, was reinforced by the introduction of picric acid, an organic anion(Pic^-) generating compound, into the liquid membrane. All results of experiments such as extraction, active and

transporting ability. Ionophores tested were N-substituted derivatives of aza crown-15 and -18, having C_m- and $C_m EO1$- side arms. Typical data of competitive active transport with two anion, SCN^- and Pic^- are compared in Fig. 4.

Amount of Na^+ ion transported by $C_8 N15$ was increased from 4% in the system with SCN^- to 65% in that with Pic^-. Similarly K^+ transported was increased from 25% to 75%. At the same time selectivity of 12 for Na^+/K^+ and 24 for K^+/Na^+ were obtained respectively.
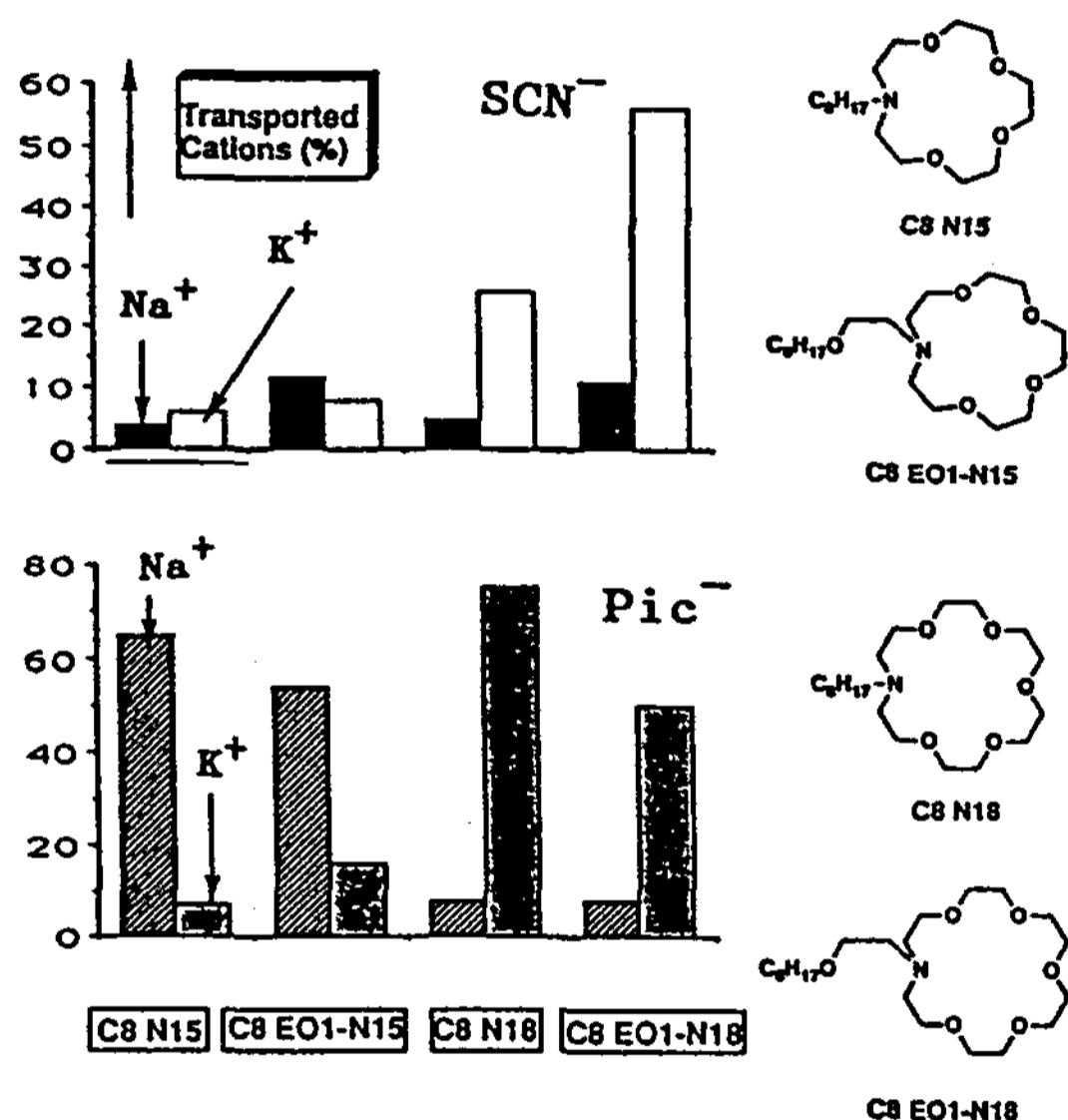
Stability constants in MeOH at 25℃

	Na^+	K^+
$C_8 N_{15}$	3.08	2.82
$C_8 EO1\text{-}N15$	3.83	3.58
$C_8 N_{18}$	3.59	4.87
$C_8 EO1\text{-}N_{18}$	4.21	5.73

**Fig. 4.** Competitive active transport data after 48 hour.

3) Structural Effects on the Complexibility of the Ligands[27]

Although ether and amide carbonyl oxygens contained in natural ionophores are known as ef-fective coordination elements, amide groups have rarely been introduced for this purpose in synthetic macrocyclic multidentates. We have synthesized four types of compounds and their complexing ability was evaluated by extraction (Table 3).

Amide carbonyl groups(17a, b) in side chain, seems to participate to the coordination little, and those contained in ring structures(18a, b, 19a, b) are apparently playing a role. As expected, acyclic ligands are poor in their complexibility. It is found that the compounds 19 having more freely rotatable carbonyl group in their ring structure, extract cations more effectively than those 18 do. This is explained by the importance of orientation of the group on the coordination toward cations.

Table 3. Effect of freedom of orientation of carbonyl group in the ring structure, exrtacting ability(%) of synthetic multidentate ligands(17~20)

17a~20a : n=2
17b~20b : n=1
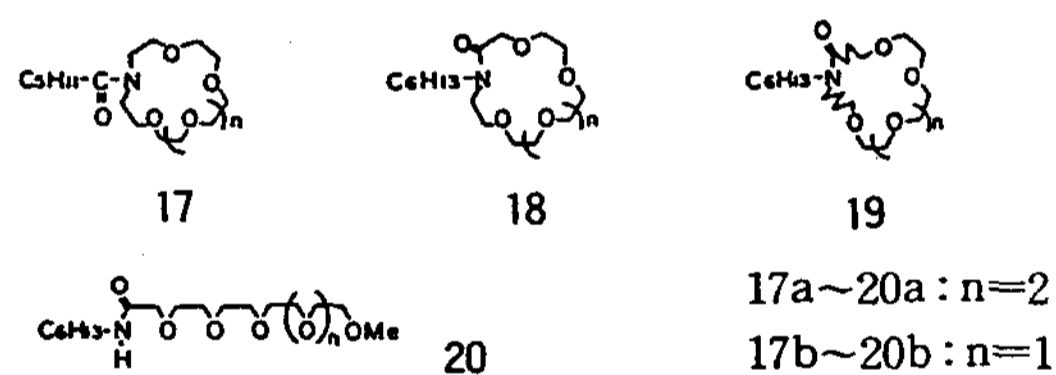
Cation	17a	18a	19a	20a	17b	18b	19b	20b
Na^+	5	20	15	9	3	12	12	9
K^+	6	19	16	12	4	14	17	9
Ca^{2+}	5	37	25	4	3	20	26	4
Ba^{2+}	5	43	70	24	5	18	22	14

a) Extraction conditions[9] : 25℃ : aqueous phase(10m l) : $(M^{n+}(NO_3)n)=1.0\times10^{-2}$ M : [Picric acid] $=7.0\times10^{-3}$M.
Organic phase $(CH_2Cl_2, 10ml)$: [Ligand]$= 1.4 \times 10^{-2}$M.

Side chains of crown ethers are also found to have important meaning in selectivity of complex-forming. Thus, compounds 22 have K^+

/Na$^+$ selectivity, while compounds 23(n=0~3) with C-pivot methyl group show inverted large selectivity of Na$^+$/K$^+$ as shown in Fig. 5.
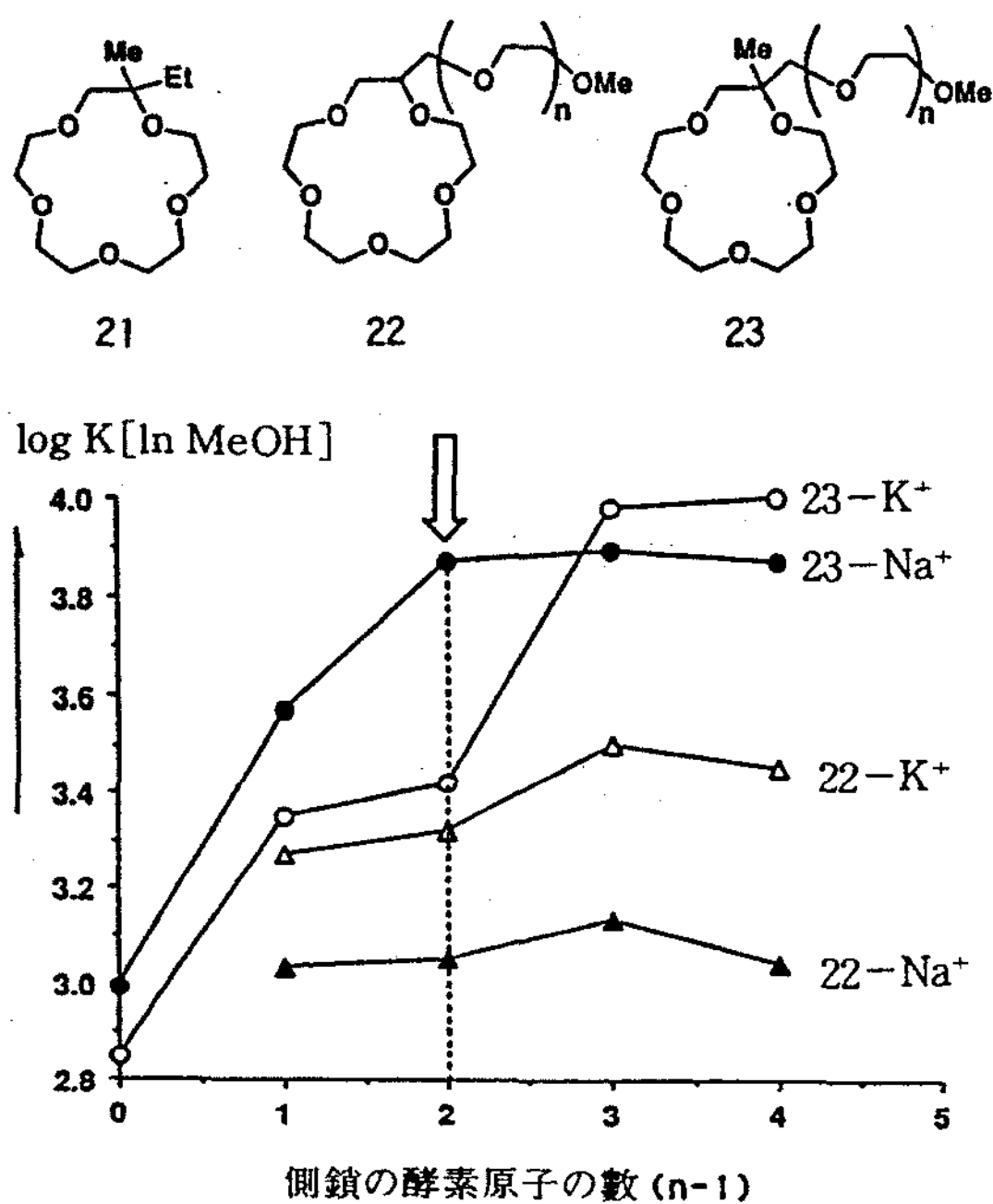

21　　　　　22　　　　　23

Fig. 5. Effect of C-Pivot methyl group on compl-exibility.

Of the many C-pivot lariat ethers synth-esized, a quinoline derivative Q18 C8 showed extraordinary large selectivity(Table 4).

Table 4. Comparison of complexing ability of crown ethers having quinoline in side chain

Q15C5　　　Q16C5-A　　　Q16C5-B　　　Q18C8

Stability Constants of C-Pivot Lariat Ethers in MeOH at 25°C

Compound	log K		Selectivity	
	Na$^+$	K$^+$		
Q15C5	4.87 (36.3)	3.56 (1.7)	20	
Q16C5-A	4.20 (4.9)	3.10 (3.0)	13	(Na$^+$)
Q16C5-B	3.78 (1.9)	2.66 (0.9)	13	
Q18C8	4.15 (0.7)	6.28 (1.8)	135	(K$^+$)
15-crown-5	3.31	3.34	0.9	(Na$^+$)
16-crown-5	3.51	2.63	7.6	
18-crown-6	4.30	6.02	52	(K$^+$)

4. Miscellaneous Ligands

At present, many ligands other than crown compounds are synthesized and their character-istic properties are being studied. Among them, cyclophanes(e. g. Fig. 6), calixarenes(Fig. 7~9) and cyclodextrins are perhaps well known.

Calixarenes are easily synthesized by the re-action(eq. 33). Their remarkable molecular ge-ometry that all coordinating sites(-OH) in the molecules are present in a plane, makes them advantageous to coordinate toward uranyl ion (Fig. 10), and thus, they are interested as ex-cellent concentrating agent for uranium resou-rces. Calix[4] arene is also interested because of its characteristic stereoisomerism(Fig. 9).
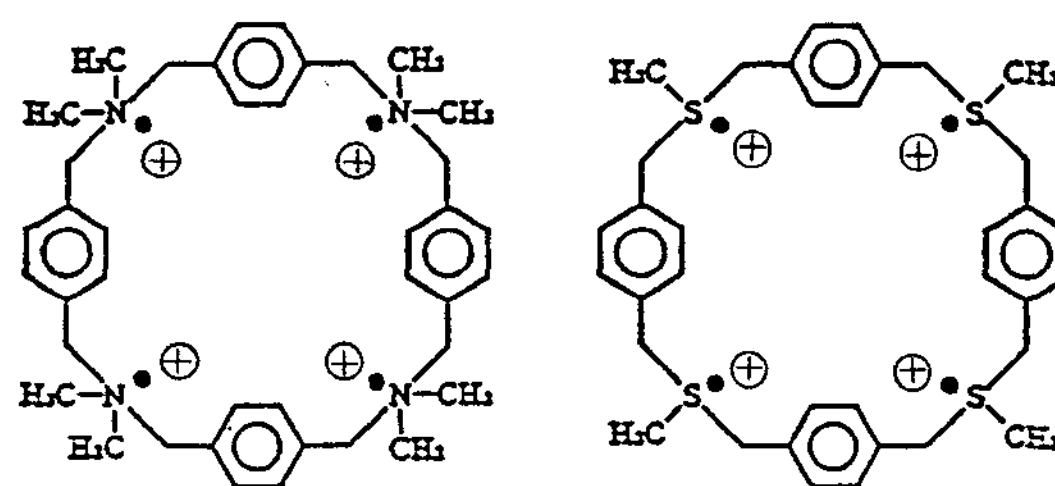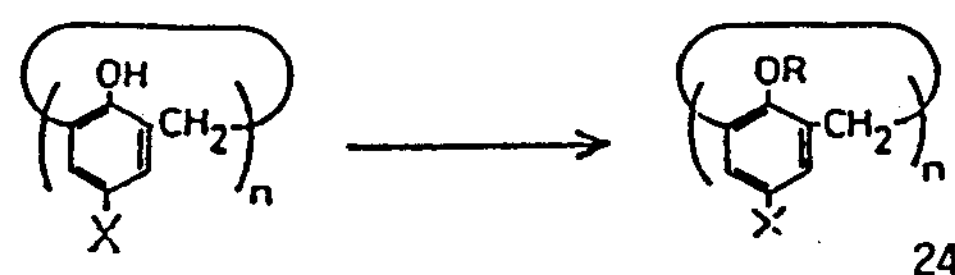

Fig. 6. Cyclophanes.

24

R=−CH$_2$CH$_3$, −CH$_2$−CH=CH$_2$, −CH$_2$Ar, −SiMa$_3$, −CH$_2$CO$_2$Et
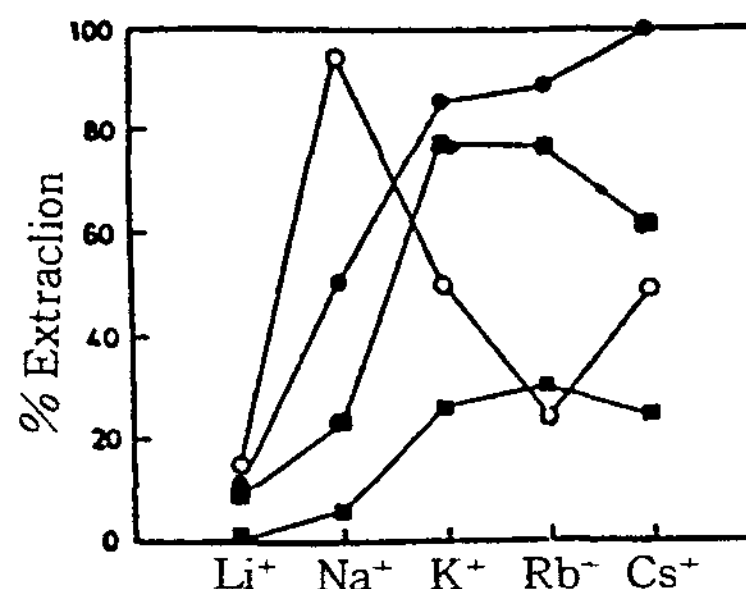
Fig. 7. Extraction of alkali metal picrate in CHCl$_3$ at 20°C. 24(R =CH$_2$CO$_2$ Et, X=t−Bu) : ○:n =4, ● : n =6, ■ : n =8, ■ : 18-crown -6.

Table 5. Cation transport from basic solution through a liquid membrane[a]

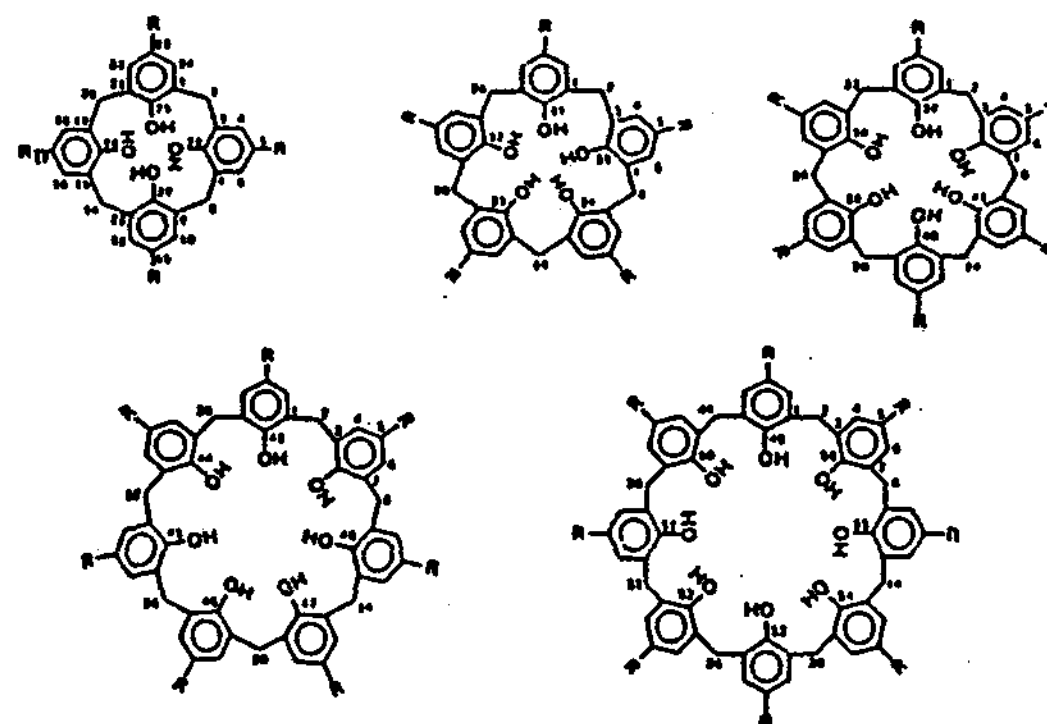| Source	p-tert-Butylicalix[x]arane		
	n=4	n=8	n=8
Na+	2	13	9
K+	<0.9	22	10
Rb+	6	71	340
Ca+	260	810	1,000

a) Data are given as $10^5 \cdot flux/mol \cdot s^{-1} \cdot m^{-2}$

Fig. 8. Strucbures and numbering of intraannul-aly-hydroxylated calix[n]arenes.

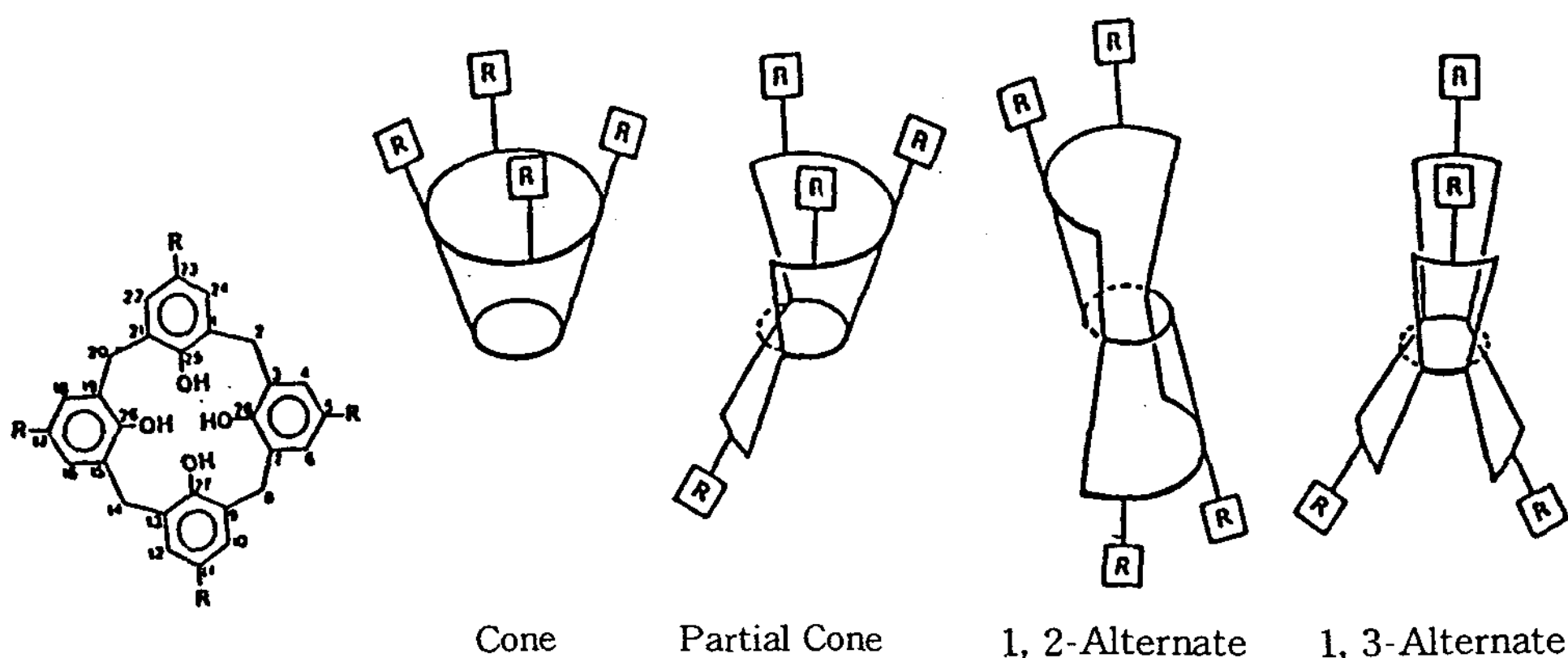Cone   Partial Cone   1, 2-Alternate   1, 3-Alternate

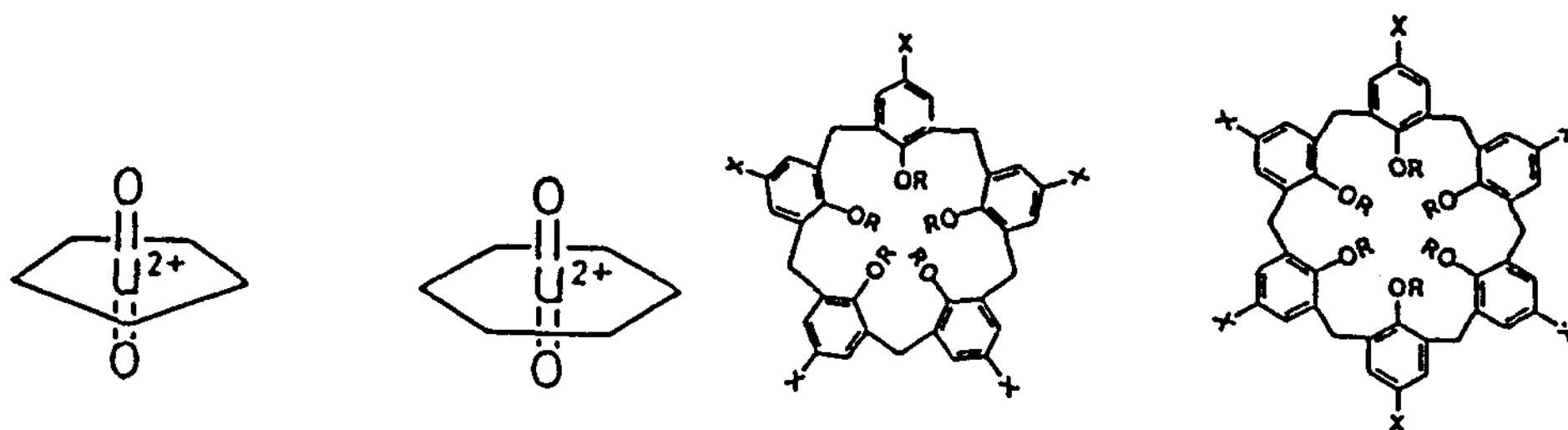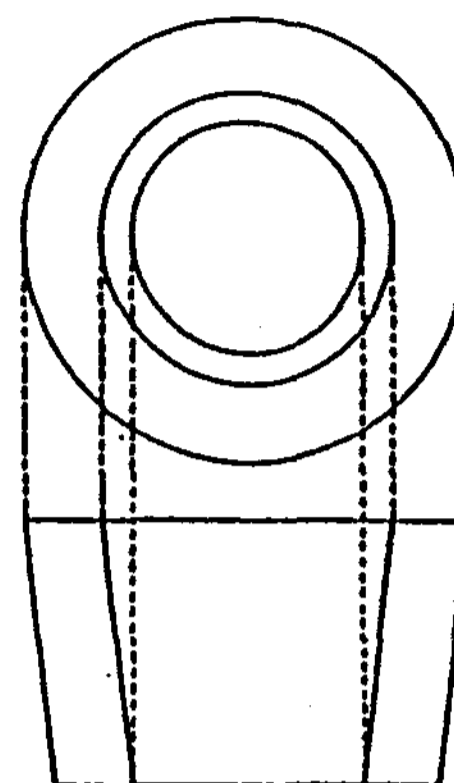Fig. 9. Conformations of the calix[4]arenes.

Fig. 10. "Super-uranophile".

Cyclodextrins are cyclic oligomers of glucose prepared through enzymatic reaction, accordingly they are applicable to food, cosmetic and medical field, The shape of their molecule resemble to buckets and their cavity, in which guest molecules are hold, are very large than those of the other synthetic ligands mentioned above.

Structure of α-cyclodextrins
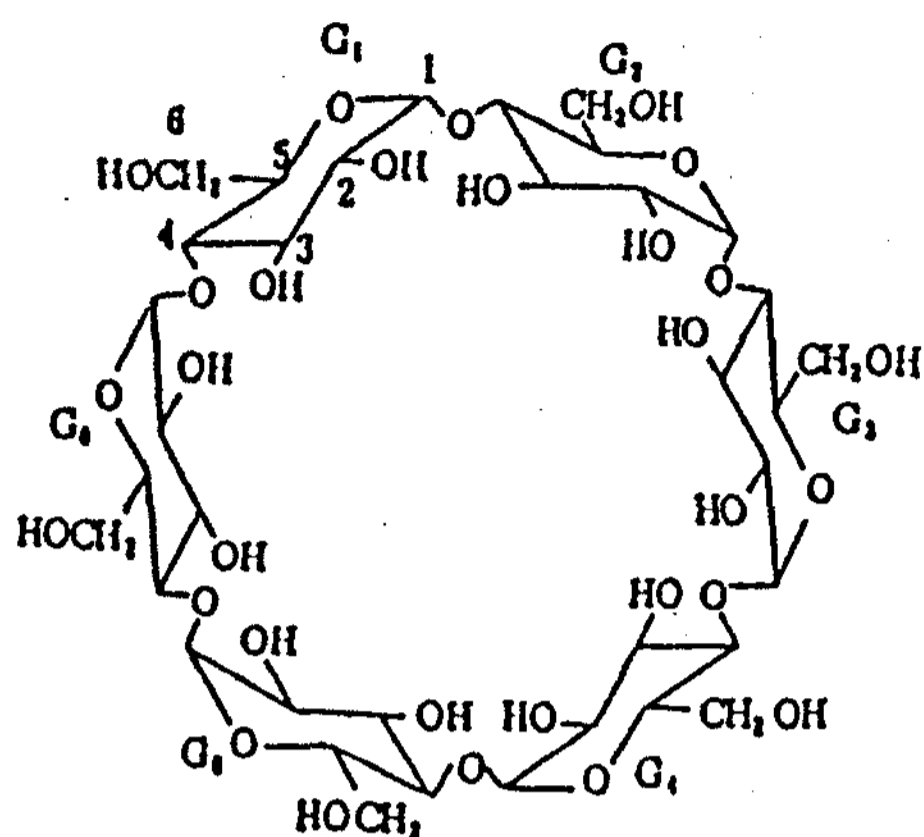
Steric structure of cyclodextrins

Properties of cyclodextrins

Cyclodextrin	Number of glucose resesidue	Nolecular weight	Solubility in $H_2O(g/100ml)$	(α)	Diameter of cavity$(nm \times 10)$	$pk_1{}^{a)}(25°C)$
α	6	97q	14.5	150.5 ± 0.5	4.7~5.2	12.332
β	7	1135	1.85	162.5 ± 0.5	6.0~6.4	12.201
γ	8	1297	23.2	177.4 ± 0.5	7.5~8.3	12.081

: D. Franch, M. L. Levine, J. H. Pazur, E. Norberg, *J. Am. Chem. Soc.*,71, 353 (1949)

Fig. 11. Cyclodextrines.

Cyclodextrins make stable inclusion compounds with easily vaporizable or liquid substances, and the compounds thus formed can be worked up into powdery products. In this sence, cyclodextrins are, one of the most interesting coordinating substance consumed in large commercial scale.

The field of "host-guest" chemistry is very rapidly growing, and the chemists of Korea as well as Japan will no doubt continue to play important roles in crown and related chemistry.

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