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# Crystal and Molecular Structure of Double Macrocyclic Inclusion Complexes, γ-Cyclodextrin·12-Crown-4·NaCl, a Model for the Transport of Ions through Membranes

Shigehiro KAMITORI, Ken HIROTSU,* and Taiichi HIGUCHI
Department of Chemistry, Faculty of Science, Osaka City University,
Sumiyoshi-ku, Osaka 558
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The crystal structure of a γ-cyclodextrin·12-crown-4·NaCl (3:3:1) inclusion complex was determined by an X-ray method to be space group $P42_12$, $a=b=23.816(3)$ Å, $c=23.072(3)$ Å. The inclusion complex has a $C_4$ symmetry, and the cation, $Na^+$, is coordinated by two 12-crown-4 molecules in a hydrophobic channel formed by tail-to-tail oriented two γ-cyclodextrin molecules.

γ-Cyclodextrin (CD) is a truncated cone-shaped cyclic oligosaccharide composed of eight D-glucoses. It has a hydrophobic cavity with a diameter of 8.5 Å, and eight hydroxyl groups (primary hydroxyl group) at the narrow side and sixteen hydroxyl groups (secondary hydroxyl group) at the wide side of the molecule. γ-CD has an ability to form inclusion complexes with various organic compounds, as well as α-CD and β-CD. It was therefore expected to mimic a biological function, such as enzyme catalysis.[1,2]

There have been many structural investigations of the inclusion compounds of α-CD and β-CD by X-ray crystal analyses, whose guest molecules are relatively rigid, e.g. benzene, adamantane, and their derivatives.[3,13] However X-ray structural studies of the CD's inclusion complexes which have flexible or functional molecules as guests have been very few. We expected that the structures of flexible guest molecules in the inclusion complexes are affected by the interior shape of the host molecules, and reported on an X-ray structural study of the γ-CD·12-crown-4 (1:1) inclusion complex.[14] The 12-crown-4 molecule is flexible and can have various conformations to form complexes with cations; also, its affinities to various cations are different, depending on cation diameters.[15] As expected, the 12-crown-4 molecule in a γ-CD cavity of approximate $C_8$ symmetry has a $C_4$ ring conformation, which was found in its complexes with cations, e.g. 12-crown-4·LiSCN,[16] $(12\text{-crown-4})_2NaClO_4$,[17] while free 12-crown-4 molecule has a $C_i$ symmetry.[18] This result suggested that the 12-crown-4 molecules included in γ-CD cavities have an ability to coordinate cations.

Next, we prepared the crystals of two inclusion complexes composed of γ-CD, 12-crown-4, and $Li^+$ or $K^+$ cation,[19] and determined their crystal structures in order to reveal the cations' positions in the inclusion complexes. According to our work, a cation coordinates eight oxygen atoms of two 12-crown-4 molecules; this sandwich-type complex of $(12\text{-crown-4})_2\cdot Li^+$ or $(12\text{-crown-4})_2\cdot K^+$ was completely encapsulated in the hydrophobic channel formed by two tail-to-tail oriented γ-CD molecules. These double macrocyclic inclusion complexes showed some interesting characteristics, as follows: 1) Cations exist in a hydrophobic environment by means of 12-crown-4 molecules. 2) Because the $(12\text{-crown-4})_2$·cation complexes suffer from particular constraints of γ-CD cavities, abnormal structural changes in 12-crown-4·cation complexes occur, e.g. the cation-oxygen distances and the chirality of the 12-crown-4 ring conformation. 3) These double macrocyclic inclusion complexes may be models of the transport of ions through membranes; γ-CDs act as lipid bilayer membranes forming hydrophobic region in their interior,[3] and 12-crown-4 molecules act as ionophores.

Here, we report on the crystal structure of an inclusion complex composed of γ-CD, 12-crown-4 and $Na^+$, with an intermediate cation diameter between $Li^+$ and $K^+$. $Na^+$ forms a double macrocyclic inclusion complex as well as $Li^+$, $K^+$. We then tried to make a double macrocyclic inclusion complex with $Rb^+$; it was in vain because of the large cation diameter of $Rb^+$.

For a clear discussion, the inclusion complexes were numbered as follows:

| | |
|---|---|
| γ-CD·12-crown-4 (1:1) | **(1)** |
| γ-CD·12-crown-4·LiSCN (3:3:1) | **(2)** |
| γ-CD·12-crown-4·NaCl (3:3:1) | **(3)** |
| γ-CD·12-crown-4·KCl (3:3:1) | **(4)** |

## Experimental

**Preparation of the Crystalline Complex of γ-CD·12-Crown-4·NaCl (3:3:1) (3).** Equimolar quantities of dry NaCl, 12-crown-4, and γ-CD were dissolved in a hot, aqueous solution, and left in an open test tube at 50 °C. Beautiful crystals of γ-CD·12-crown-4·NaCl appeared within 2 weeks.

**X-Ray Structure Determination.** A crystal for data collection, a rectangular block of 0.4×0.4×0.6 mm, was sealed in a glass capillary with a drop of mother liquor in order to avoid any crystal degradation. Diffraction intensities were measured on a Rigaku AFC-6A automatic diffractometer using Cu $K\alpha$ radiation ($\lambda=1.5418$ Å). Lattice constants were determined by least-squares methods with 20 reflections in $38°<2\theta<48°$. 3844 independent reflections (2833 with $I>3\sigma(I_0)$) were collected up to $2\theta=100°$, using a $\omega/2\theta$-scan mode at room temperature. No correction was

made for an absorption effect. Crystal data of **3** are as follows.

$C_{48}H_{80}O_{40}\cdot C_8H_{16}O_4\cdot 1/3(NaCl)\cdot 7.7H_2O$, tetragonal, space group $P4_12_12$, $a=b=23.816$ (4)Å, $c=23.0.72(3)$Å, $Z=6$

This complex is isomorphous with the γ-CD·12-crown-4 inclusion complex **1** which we reported previously.[14] The phase problem was solved by using atomic coordinates of γ-CDs of **1**; guest molecules and water molecules were located on a difference Fourier synthesis.[20] One of the primary oxygen atoms O(6)1 is disordered at two positions (O(6)A1 and O(6)B1). The structures were refined to $R=0.168$ by full-matrix least-squares methods,[21] using isotropic temperature factors for all atoms. The $R$ value is pretty high because of insufficient data at high angles in $2\theta$ and the highly disordered water molecules. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$ with $w=1.0$. Final atomic coordinates and temperature factors are given in Table 1. Tables of the complete bond distances and bond angles, and observed and calculated structure factor amplitudes, are deposited to the Chemical Society of Japan (Document No. 8831).

## Results and Discussion

**1. The Crystal Structure of γ-CD·12-Crown-4·NaCl Inclusion Complex (3).** Three γ-CD molecules are stacked along the c-axis, forming a channel-type structure, and 12-crown-4 molecules are included in 1:1 stoichiometry in γ-CDs at the secondary sides of γ-CDs. Also, $Na^+$ is located between two γ-CD·12-crown-4 inclusion complexes, as shown in Fig. 1.[22] Host and guest molecules are centered on the four-fold crystallographic rotation axis so that three quarters of the γ-CD molecules are in an asymmetric unit. γ-CD **A** (the γ-CD molecule in the complex **A**) and γ-CD **B**, **B** and **C** and **C** and **A′** are in tail-to-tail, head-to-head, and tail-to-head orientations, respectively. Intermolec-

Table 1. Fractional Coordinates and Temperature Factors with Estimated Standard Deviations

| Atom | X | Y | Z | B | Atom | X | Y | Z | B |
|---|---|---|---|---|---|---|---|---|---|
| Na(1) | 0.5 | 0.0 | 0.792(1) | 3.4(7) | O(3)4 | 0.721(1) | 0.188(1) | 0.734(1) | 2.6(5) |
| C(1)1 | 0.666(2) | 0.241(2) | 0.951(2) | 2.6(8) | O(4)4 | 0.646(1) | 0.198(1) | 0.644(1) | 2.2(5) |
| C(2)1 | 0.705(2) | 0.228(2) | 0.899(1) | 2.4(8) | O(5)4 | 0.755(1) | 0.109(1) | 0.578(1) | 3.1(6) |
| C(3)1 | 0.712(2) | 0.161(2) | 0.893(2) | 2.6(8) | O(6)4 | 0.717(1) | 0.195(1) | 0.508(1) | 6.2(8) |
| C(4)1 | 0.733(2) | 0.136(2) | 0.944(2) | 2.8(8) | C(1)5 | 0.740(2) | 0.161(2) | 0.281(2) | 2.9(9) |
| C(5)1 | 0.688(2) | 0.148(2) | 0.995(2) | 3.2(9) | C(2)5 | 0.774(2) | 0.136(2) | 0.234(2) | 3.7(9) |
| C(6)1 | 0.707(2) | 0.122(2) | 1.054(2) | 4.(1) | C(3)5 | 0.757(2) | 0.076(2) | 0.223(2) | 3.3(9) |
| O(2)1 | 0.681(1) | 0.252(1) | 0.851(1) | 3.3(6) | C(4)5 | 0.767(2) | 0.045(2) | 0.277(2) | 3.0(9) |
| O(3)1 | 0.752(1) | 0.154(1) | 0.845(1) | 2.5(5) | C(5)5 | 0.730(2) | 0.069(2) | 0.323(2) | 3.2(9) |
| O(4)1 | 0.734(1) | 0.078(1) | 0.937(1) | 2.4(5) | C(6)5 | 0.730(2) | 0.043(2) | 0.385(2) | 6.(1) |
| O(5)1 | 0.687(1) | 0.210(1) | 1.001(1) | 2.8(5) | O(2)5 | 0.765(1) | 0.168(1) | 0.180(1) | 3.8(6) |
| O(6)A1 | 0.662(3) | 0.134(3) | 1.093(2) | 5.(1) | O(3)5 | 0.794(1) | 0.053(1) | 0.178(2) | 5.6(8) |
| O(6)B1 | 0.769(2) | 0.142(2) | 1.061(2) | 3.(1) | O(4)5 | 0.748(1) | −0.015(1) | 0.2668(9) | 2.4(5) |
| C(1)2 | 0.450(2) | 0.286(2) | 0.948(2) | 3.5(9) | O(5)5 | 0.748(1) | 0.127(1) | 0.329(1) | 3.6(6) |
| C(2)2 | 0.484(2) | 0.304(2) | 0.899(2) | 3.5(9) | O(6)5 | 0.788(2) | 0.048(2) | 0.403(2) | 8.(1) |
| C(3)2 | 0.533(2) | 0.263(2) | 0.892(2) | 2.9(8) | C(1)6 | 0.559(1) | 0.286(1) | 0.282(2) | 1.9(7) |
| C(4)2 | 0.568(2) | 0.262(2) | 0.946(2) | 4.(1) | C(2)6 | 0.597(2) | 0.292(2) | 0.235(2) | 3.1(9) |
| C(5)2 | 0.529(2) | 0.240(2) | 0.996(2) | 3.4(9) | C(3)6 | 0.628(2) | 0.236(2) | 0.221(2) | 3.5(9) |
| C(6)2 | 0.558(2) | 0.234(2) | 1.055(2) | 4.(1) | C(4)6 | 0.657(2) | 0.218(2) | 0.277(2) | 2.3(8) |
| O(2)2 | 0.451(1) | 0.306(1) | 0.847(1) | 3.6(6) | C(5)6 | 0.611(2) | 0.212(2) | 0.325(2) | 3.8(9) |
| O(3)2 | 0.569(1) | 0.287(1) | 0.845(1) | 3.7(6) | C(6)6 | 0.636(2) | 0.193(2) | 0.384(2) | 4.(1) |
| O(4)2 | 0.612(1) | 0.221(1) | 0.938(1) | 1.9(5) | O(2)6 | 0.567(1) | 0.308(1) | 0.181(1) | 3.3(6) |
| O(5)2 | 0.483(1) | 0.280(1) | 1.000(1) | 3.5(6) | O(3)6 | 0.667(1) | 0.241(1) | 0.173(1) | 2.8(5) |
| O(6)2 | 0.588(2) | 0.285(2) | 1.063(2) | 9.(1) | O(4)6 | 0.684(1) | 0.164(1) | 0.266(1) | 2.5(5) |
| C(1)3 | 0.640(2) | 0.257(2) | 0.628(2) | 3.2(8) | O(5)6 | 0.585(1) | 0.265(1) | 0.331(1) | 3.8(6) |
| C(2)3 | 0.611(2) | 0.285(2) | 0.680(2) | 2.8(9) | O(6)6 | 0.679(1) | 0.236(1) | 0.403(1) | 4.4(7) |
| C(3)3 | 0.553(2) | 0.263(2) | 0.692(2) | 2.9(9) | O(1)A | 0.512(2) | 0.086(2) | 0.859(2) | 9.(1) |
| C(4)3 | 0.519(2) | 0.270(2) | 0.631(2) | 2.8(8) | C(1)A | 0.558(4) | 0.076(4) | 0.889(3) | 11.(2) |
| C(5)3 | 0.548(2) | 0.234(2) | 0.583(2) | 2.7(8) | C(2)A | 0.595(3) | 0.035(3) | 0.893(3) | 9.(2) |
| C(6)3 | 0.520(2) | 0.237(2) | 0.526(2) | 3.7(9) | O(1)B | 0.573(1) | 0.048(1) | 0.725(1) | 5.4(8) |
| O(2)3 | 0.645(1) | 0.281(1) | 0.730(1) | 3.5(6) | C(1)B | 0.549(3) | 0.082(3) | 0.685(2) | 7.(1) |
| O(3)3 | 0.523(1) | 0.295(1) | 0.731(1) | 3.6(6) | C(2)B | 0.487(3) | 0.095(3) | 0.700(3) | 8.(2) |
| O(4)3 | 0.4642(9) | 0.244(1) | 0.643(1) | 2.0(5) | O(1)C | 0.531(3) | 0.085(3) | 0.189(3) | 14.(2) |
| O(5)3 | 0.604(1) | 0.259(1) | 0.577(1) | 2.7(5) | C(1)C | 0.579(3) | 0.064(3) | 0.213(3) | 10.(2) |
| O(6)3 | 0.519(1) | 0.294(1) | 0.508(2) | 6.2(9) | C(2)C | 0.589(3) | 0.010(4) | 0.235(3) | 12.(2) |
| C(1)4 | 0.777(2) | 0.085(2) | 0.626(2) | 3.2(9) | Cl(1) | 0.121(2) | 0.175(2) | 0.543(2) | 4.(1) |
| C(2)4 | 0.778(2) | 0.123(2) | 0.679(2) | 3.3(9) | Ow1 | 0.811(3) | 0.150(3) | 0.468(3) | 18.(3) |
| C(3)4 | 0.720(2) | 0.146(2) | 0.691(2) | 2.4(8) | Ow2 | 0.417(2) | 0.426(2) | 0.166(2) | 11.(1) |
| C(4)4 | 0.700(2) | 0.174(2) | 0.632(2) | 3.1(9) | Ow3 | 0.084(2) | 0.088(2) | 0.153(2) | 13.(2) |
| C(5)4 | 0.699(2) | 0.131(2) | 0.586(2) | 3.0(9) | Ow4 | 0.561(2) | 0.416(2) | 0.386(2) | 12.(2) |
| C(6)4 | 0.683(2) | 0.153(2) | 0.525(2) | 4.(1) | Ow5 | 0.548(3) | 0.410(3) | 0.047(3) | 15.(2) |
| O(2)4 | 0.801(1) | 0.097(1) | 0.729(1) | 3.2(6) | Ow6 | 0.100(3) | 0.156(3) | 0.557(3) | 13.(3) |

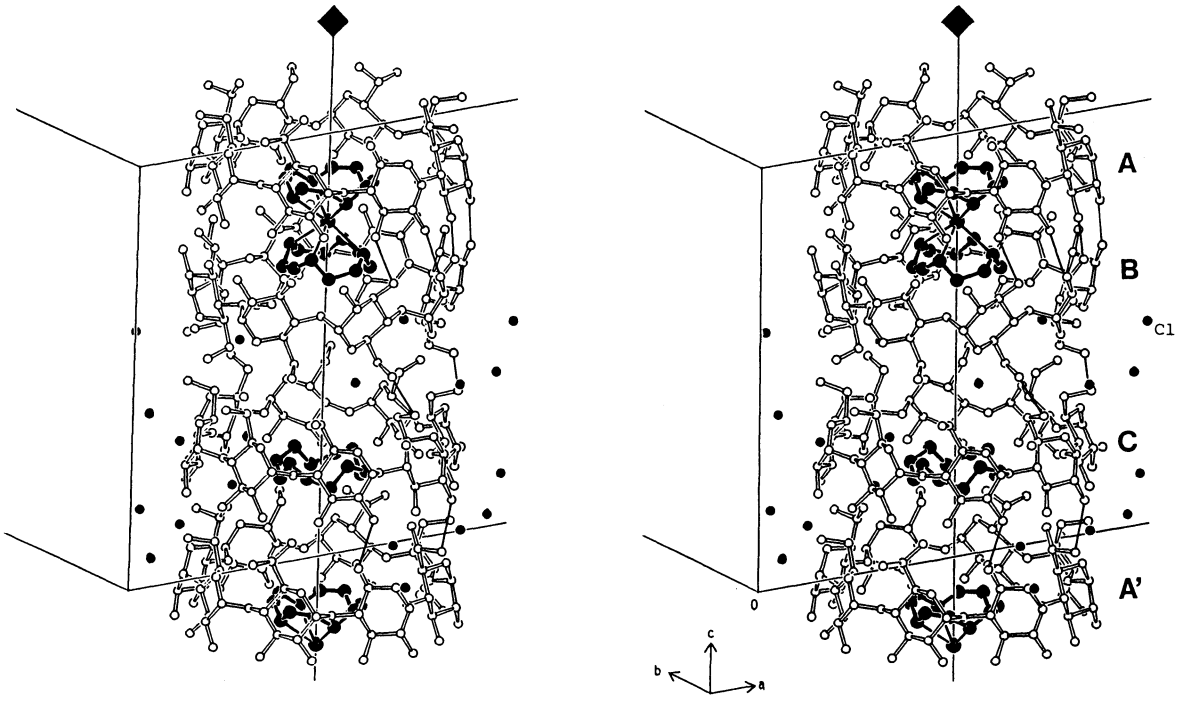



Fig. 1. The stereo view of the channel-type structure of γ-CD·12-crown-4·NaCl (3:3:1) inclusion complex. $Na^+$, 12-crown-4 molecules, $Cl^-$ labeled by "Cl" and water molecules are shown by full circles. Only symmetry independent intermolecular hydrogen bonds are indicated by straight lines.

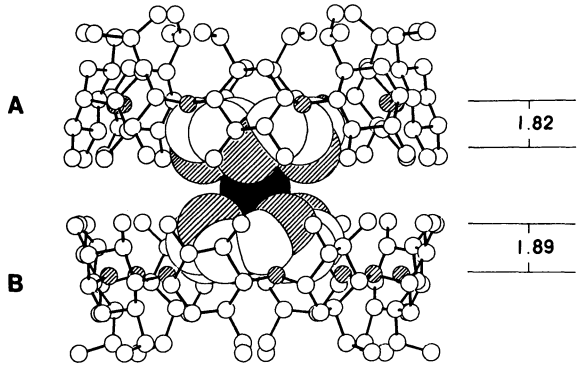
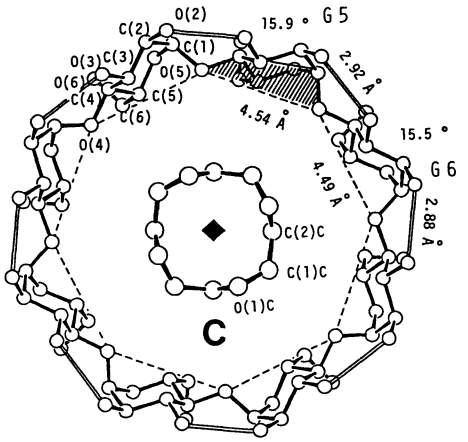



Fig. 2. The structures of γ-CD·12-crown-4·$Na^+$ inclusion complexes. Cations and 12-crown-4 molecules are plotted in space filling mode, indicated by full and hatched circles, respectively. O(4) atoms are also indicated by hatching. Interplanar distances(Å) between O(4) atoms plane and oxygen atoms of 12-crown-4 molecules are given.



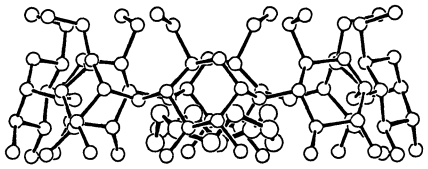



Fig. 3. The structure of the complex C with $C_4$ symmetry. One of O(4)'-C(1)-C(4)-O(4) atoms planes is indicated by hatching, and geometrical values are shown.

ular hydrogen bonds are formed between O(2,3) (secondary hydroxyl groups (see Fig. 3.)) of the γ-CD **A** and O(2,3) of the γ-CD **B**, O(6) (primary hydroxyl groups) of **B** and O(6) of **C**, O(2,3) of **C** and O(6) of **A'**; the hydrogen bond distance of O(2)1···O(2)3 is 3.00, O(3)1···O(3)4 2.79, O(2)2···O(2)4 2.95, O(3)2···O(3)3 2.85, O(6)3···O(6)5 2.90, O(6)4···O(6)6 2.80, O(2)5···O(6)B1 2.82, O(2)6···O(6)2 2.85 Å.

The $Na^+$ coordinates to eight oxygen atoms of two

Table 2. Geometrical Data

| Complex | | H-Bond distance (Å) | Distance (Å) | Tilt-angle (°) |
|---|---|---|---|---|
| **A** | G1 | 2.81 | 4.45 | 11.9 |
| | G2 | 2.80 | 4.55 | 11.3 |
| **B** | G3 | 2.89 | 4.48 | 15.9 |
| | G4 | 2.86 | 4.50 | 17.6 |
| **C** | G5 | 2.92 | 4.54 | 15.9 |
| | G6 | 2.89 | 4.49 | 15.5 |

a) The H-bond distance is defined as the O(3)$n$–O(2)$n$+1 distance. b) The distance is defined as the O(4)$n$–O(4)$n$+1 distance. c) The tilt-angle is defined as the angle made by (O)4 atoms plane and the plane formed by O(4)$n$+1, C(1)$n$, C(4)$n$, O(4)$n$ of each glucose residue.

12-crown-4 molecules to form a 1:2 sandwich-structure complex, which is included by two tail-to-tail oriented γ-CDs **A** and **B**. Therefore, as shown in Fig. 2,[23] 12-crown-4 and γ-CD molecules could form complexs with $Na^+$ in a 2:2:1 ratio, as well as $Li^+$ and $K^+$. The distance between a $Na^+$ and $Cl^-$ is 11.5 Å, showing a very weak electrostatic interaction between them.

The conformation of complex **B** is shown in Fig. 3, and the geometrical data of γ-CDs are given in Table 2, indicating very normal and more symmetrical structures compared with γ-CD hydrates.[24,25] As is well known, the secondary hydroxyl groups between neighboring glucose residues form intramolecular hydrogen bonds to maintain the round shape of the γ-CD ring; O(2)$n$···O(3)$n$+1 hydrogen bond distances are in the range 2.80—2.92 Å. The eight glycosidic O(4) oxygen atoms are coplanar within 0.01, 0.01, and 0.02 Å for γ-CDs **A**, **B**, and **C**, and the average distances of O(4)$n$···O(4)$n$+1 in each complex are 4.50, 4.49, and 4.51 Å. The glucose residues are inclined to the four-fold rotation axis so as to make the primary hydroxyl side narrow, and the secondary hydroxyl side wide. The tilt angles of glucose residues are defined as the angles made by the plane through O(4) atoms and the plane formed by O(4)$n$+1, C(1)$n$, C(4)$n$, O(4)$n$ of each glucose.[24] The average tilt angles are 11.6, 16.8, and 15.7° for **A**, **B**, and **C**, respectively.

As pointed out in previous X-ray studies, the differences of the tilt angles among three γ-CDs are derived from the intermolecular hydrogen bonds between γ-CDs; the intermolecular hydrogen bonds between γ-CD **A** and **C** make the ring of γ-CD **A** wide at the primary site, so γ-CD **A** has more cylindrical geometry than **B** and **C**. This difference of γ-CD's geometries directly affects the locatins of 12-crown-4 molecules in **1**; the 12-crown-4 molecule is included more deeply in γ-CD **A** than in **B** and **C**, which have inclined cone structures. However, in **2**, **3**, and **4**, the existence of cations make this situation more complicated.

The interplanar distance between the four O(1) atoms plane of a 12-crown-4 molecule and the eight O(4) atoms plane of γ-CD could be adopted as an indicator of the inclusion depth. These distances in complexes **A** and **B** are given in Table 3 for **1**, **2**, **3**, and **4**. The distances of complexes **A** and **B** in **1** are 1.25 and 1.64 Å, respectively, and each value is the smallest among the corresponding complexes in Table 3, showing that each 12-crown-4 molecule of complexes **A** and **B** in **1** are deeply included in the γ-CD cavity. In the cases of **2**, **3**, and **4**, the locations of 12-crown-4 molecules depend not only on the shape of γ-CDs but also on the cation diameters. In **2** where the small cation, $Li^+$, exists, 12-crown-4 molecules are shallowly included in γ-CDs; on the other hand, in **4** 12-crown-4 molecules enter the γ-CD's cavities deeply due to the large cation diameter of $K^+$. In **3**, the distance at complex **A** is an intermediate value between the values of **2** ($Li^+$) and **4** ($K^+$), but the distance at complex **B** is almost same as in **2**. This result is due to the difference in the geometries of γ-CDs **A** and **B** mentioned above. Since γ-CD **A** is in a cylindrical structure and γ-CD **B** is in a cone-like structure, a 12-crown-4 molecule could more easily enter the cavity of γ-CD **A** than that of γ-CD **B**, as in **1**.

Table 3. Interplanar Distances

| Complex | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| **A** | 1.25 | 2.09 | 1.82 | 1.50 |
| **B** | 1.64 | 1.86 | 1.89 | 1.69 |

The conformation of the (12-crown-4)$_2$·$Na^+$ complex and the main short contacts between the γ-CD molecules and the (12-crown-4)$_2$·$Na^+$ complex are shown in Fig. 4. The structure of the (12-crown-4)$_2$·$Na^+$ complex in the hydrophobic channel of γ-CD molecules is quite normal. This complex has an approximate $S_8$ symmetry and the $Na^+$–O bond distances at the sites of complexes **A** and **B** are 2.58(5) and 2.58(4) Å, respectively. These values are normal compared with the $Na^+$–O distances of 2.474(8)—2.543(8) Å of (12-crown-4)$_2$·$NaClO_4$.[17] However, the $Li^+$–O distances of **2** are unusually long; 2.45(8) and 2.54(8) Å at complexes **A** and **B**. The $Li^+$–O average distance of the 12-crown-4·LiSCN 1:1 complex[26] is 2.08 Å, and that of [Li(12-crown-4)$_2$][$AsPh_2$] and

$[Li(12\text{-crown-}4)_2][PPh_2]$,[27] where $Li^+$ has a coordination number of 8, as in **2** is 2.35 Å. The attractive forces by the van der Waals interaction between 12-crown-4 molecules and γ-CD molecules make the $Li^+$–O bond distances long. The $K^+$–O bond distances of **3** are 2.80(8) and 2.99(9) Å at complexes **A** and **B**, respectively. Although in terms of the large esd's, these values are almost normal compared with the $K^+$–O distances of 2.77—2.83 Å in the 18-crown-6·KSCN complex,[28] the 12-crown-4 molecule can not form a complex with $K^+$ by itself.

**2. Attempt to Form the Double Macrocyclic Inclusion Complex by 12-Crown-4, γ-CD and $Rb^+$.** Comparing the interplanar distances at complexes **A** and **B** in **1** with the values in **4**, it was expected that 12-crown-4 molecules and γ-CDs might form a double macrocyclic inclusion complex with a larger cation than $K^+$, i.e. $Rb^+$. The crystal was prepared by the same procedure as in **3**, using RbCl instead of NaCl.

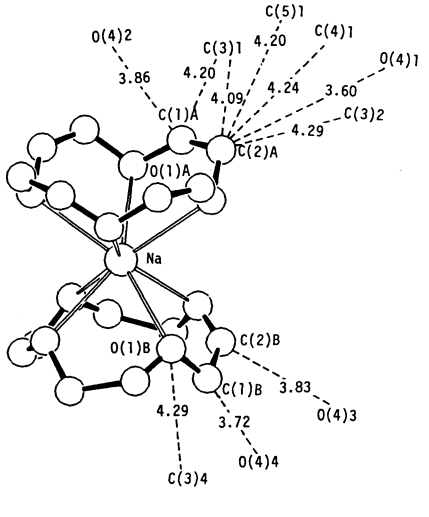



Fig. 4. The structures of $(12\text{-crown-}4)_2Na^+$ complexes. Intermolecular contacts with γ-CDs (less than 4.3 Å) are shown by dotted lines.

3845 independent reflections (2663 with $I > 3\sigma(I_0)$) were collected up to 100° in $2\theta$. A diffference Fourier synthesis was calculated using the atomic coordinates of the γ-CDs of **3**. Atoms of 12-crown-4 molecules were found, but the peak of cation did not appear, as is shown in Fig. 5. There was a very low peak (0.50, 0.0, 0.79) compared with the peak of $Na^+$. However, the peak of $Rb^+$ does not appear with a low ocupancy, but may be that of contaminated cation, probably $Na^+$ with a low occupancy, since, in **2**, a contaminated $Na^+$ of 1.9% was detected by atomic absorption analysis.[19] Therefore, this system composed of γ-CDs and 12-crown-4 molecules can not catch $Rb^+$ cations.

## Conclusion

The $Na^+$ cation can exist in a hydrophobic circumstance of γ-CD cavities by forming a sandwich structure complex with two 12-crown-4 molecules, as well as $Li^+$ and $K^+$. The $(12\text{-crown-}4)_2\cdot Na^+$ sandwich structure complex in the γ-CDs **A** and **B** has normal $Na^+$–O bond distances, while unusually long $Li^+$–O bond distances of 2.45 and 2.54 Å were found in **2**.[19] The cation–oxygen bond distances are mainly determined by two interactions, i.e., electrostatic interaction between the cation and oxygen atoms of 12-crown-4 molecules, and van der Waals interaction between 12-crown-4 molecules and γ-CDs. The latter strongly affects the $Li^+$–O bond distances in **2**. The $Na^+$ may be more fit to enter the space between complexes **A** and **B** than $Li^+$, since these two interactions are reasonably balanced in **3**.

These double macrocyclic inclusion complexes catching cations may be models of the transport of ions through lipid bilayer membranes by an ionophore, such as Valinomycin. Although CD molecules are not as flexible as lipid bilayer membranes, the channel of two tail-to-tail oriented CDs, γ-CDs **A** and **B** in this paper, is analogous to lipid bilayer membranes at several points, such as the existence in

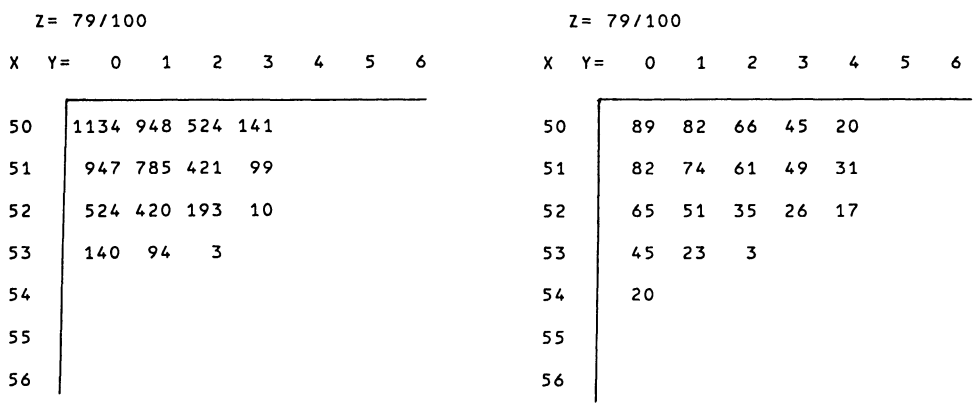



Fig. 5. Difference Fourier map of the $Na^+$ position (left) and corresponding map of the complex with $Rb^+$(right). These two difference Fourier syntheses were calculated by the same scale.

an aqueous solution and the exchange of their guest molecules, as described by Stezowski et al.[3] The presented system, that γ-CDs include cations through the intermediary of the hydrophobic methylene rings of 12-crown-4 molecules, is similar to the situation that lipid bilayer membranes permit cations caught by ionophores to diffuse in them by an interaction between the hydrophobic interior of membranes and the hydrophobic exterior of ionophore·cation complexes.

This system could also have ion selectivity by the above-mentioned interactions among γ-CDs, 12-crown-4 molecules and cations. From only the presented work about this system, it is difficult to elucidate the difference of affinities of the double macrocyclic inclusion complex to three cations ($Li^+$, $Na^+$, and $K^+$) in detail. However, at least, the affinity of this system to $Rb^+$ is very small.

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