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A High-resolution ^{13}C NMR Study of Some Ethylene Oxide Oligomers, Cryptands and Crown Ethers Complexed with a Variety of Metal Ions in the Solid State. Conformational Change of Ligand Molecules as Viewed from the Conformation-dependent Displacements of ^{13}C Chemical Shifts

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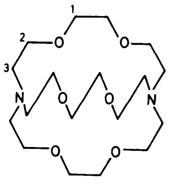
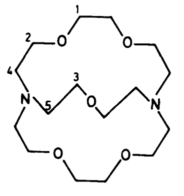
We recorded high-resolution solid-state ^{13}C NMR spectra of ethylene oxide oligomers, cryptands, and crown ethers complexed with metal ions, determined by cross polarization-magic angle spinning (CP-MAS) NMR method. It is found that peak-intensities of these complexes are significantly enhanced by the presence of metal ions which act toward conformational fixation of flexible ligand molecules. The ^{13}C chemical shifts of ethylene oxide oligomers complexed with $HgCl_2$ or $CdCl_2$ as open-chain analogues of crown ethers were successfully related with a pair of torsion angles of nearby single bonds. ^{13}C Chemical shifts of cyclic ionophores were displaced (up to 6 ppm) together with conformational changes of ligand molecules. In addition, the ^{13}C chemical shifts of the carbons neighbored with nitrogen atoms of cryptands [2.2.2] and [2.2.1] were well related with a pair of torsion angles of neaby bonds. Further, we found that several kinds of metal complexes with *cis-syn-cis* and *cis-anti-cis* isomers of dicyclohexano-18-crown-6 gave rise to substantially different spectral profiles, resulting in the occurrence of significant conformational changes of these ligand molecules as a result of complex formation.

It is well known that synthetic macrocyclic ionophores such as crown ethers and cryptands show a marked ability to form metal complexes with a variety of alkaline and alkaline earth metal ions[1-9] like naturally occurring ionophores such as valinomycin, nonactin, monensin, *etc.* These ionophores have gained much interest in relation to their models of naturally occurring antibiotics as carriers of cations through biological and model membranes, phase-transfer catalysis for salt solubility enhancement and anion activation in synthesis.[1-9] In many instances, these ligand molecules undergo marked conformational changes during ion-binding to achieve stability and ion-selectivity of complexes. Accordingly, it is very important to analyze these conformational changes of ligand molecules both in the solid

$CH_3O(CH_2CH_2O)_4CH_3$	Tetraethylene glycol dimethyl ether (1) (TEGM)
$CH_3CH_2O(CH_2CH_2O)_4CH_2CH_3$	Tetraethylene glycol diethyl ether (2) (TEGE)
$CH_3CH_2O(CH_2CH_2O)_6CH_2CH_3$	Hexaethylene glycol diethyl ether (3) (HEGE)



Cryptand [2.2.2] (4)



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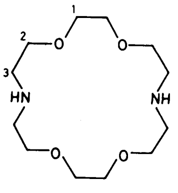
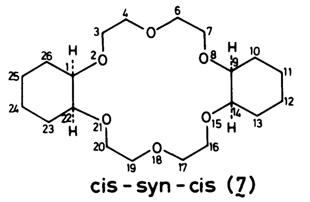
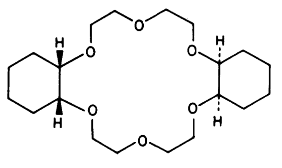


Cryptand [2.2] (6)



cis-syn-cis (7)



cis-anti-cis (8)

Dicyclohexano-18-crown-6

Fig. 1. Chemical structures of ethylene oxide oligomers, dicyclohexano-18-crown-6, and cryptands.

and solution, in order to gain insight of the manner of metal-ligand interaction in the complexes.

As a convenient complementary means to X-ray diffraction, we previously showed that the manner of such conformational changes in the ligand molecules in the solid state is conveniently examined when sizable amounts of displacements of the conformation-dependent ^{13}C chemical shifts, as determined by cross polarization-magic angle spinning (CP-MAS) technique, are seen for any carbons of backbones.[10–19] The major advantage of the present approach is to provide reference data to examine whether particular conformation observed in the solid state is retained in solution or not.

In order to gain insight how ^{13}C chemical shifts of these ligand molecules are varied with conformational changes associated with complexation, we recorded ^{13}C CP-MAS NMR spectra of ethylene oxide oligomers [tetraethylene glycol dimethyl ether (TEGM), tetraethylene glycol diethyl ether (TEGE), hexaethylene glycol diethyl ether (HEGE)], cryptands ([2.2.2], [2.2.1], and [2.2]), and *cis-syn-cis* and *cis-anti-cis* isomers of dicyclohexano-18-crown-6 (see Fig. 1 for chemical structure) complexed with a variety of metal ions. We studied ethylene oxide oligomers as open-chain analogues of cyclic ionophores, because conformations of the former resembles those of the latter and detailed X-ray diffraction data[20–23] are available for the former. We found that the ^{13}C chemical shifts were significantly varied among a variety of complexes, reflecting the conformational changes of ligand molecules. We also attempted to relate these displacements of shifts with a pair of torsion angles of the nearby single bonds. Finally, we compared ^{13}C chemical shifts between the solid and solution in order to evaluate whether or not the conformations achieved in the solid state are retained in solution.

Experimental

Materials. Tetraethylene glycol dimethyl ether (TEGM) and tetraethylene glycol diethyl ether (TEGE) were purchased from Tokyo Kasei Kogyo Co., Ltd., Tokyo and Aldrich Chemical Company, USA, respectively. Hexaethylene glycol diethyl ether (HEGE) was prepared by the reaction of hexaethylene glycol (Aldrich) and ethyl iodide over NaH dissolved in anhydrous dimethyl sulfoxide. $HgCl_2$ or $CdCl_2$ complexes were prepared by the procedure described by Iwamoto.[20–23]

Cryptands [2.2.2], [2.2.1], and [2.2] were purchased from Merck Chemical Company, West Germany. Colorless plate-shaped crystal of cryptand [2.2] with NaSCN was formed by dissolving these two chemicals in methanol-1-butanol solution. KSCN complex with cryptand [2.2] (colorless prism) was grown from benzene containing small amount of water.[24] $Pb(SCN)_2$ complex with cryptand [2.2](prism) was obtained by methanol-1-butanol solvent.[25] NaSCN and KSCN complexes with [2.2.1] were obtained from methanol-1-butanol solution.[26] $CaBr_2$,[27] TlHCOO,[28] NaSCN and KSCN complexes with cryptand [2.2.2] were obtained from methanol–ethyl acetate solvent, whereas $Ba(SCN)_2$ complex was obtained from methanol-1-butanol solvent.[29]

Cis-syn-cis and *cis-anti-cis* isomers of dicyclohexano-18-crown-6 (Aldrich Chemical Company, USA) were isolated by the procedure of Izatt *et al.*[30] utilizing OH_3ClO_4 and $Pb(ClO_4)_2$, respectively, as agents for complex formation. Plate-shaped. NaBr-complexes with both isomers were obtained from a solution of equimolecular quantity of individual *cis-syn-cis* or *cis-anti-cis* isomers and sodium bromide (5% excess) in ethanol–acetone which was allowed to evaporate in air.[31] In a similar manner, complexes with $La(NO_3)_3$,[32] KI_3,[33] CsSCN,[33] $Pb(ClO_4)_2$,[30] OH_3ClO_4,[30] KI,[34] NH_4SCN,[34] and $Ba(SCN)_2$[34] were prepared by the procedure published already.

^{13}C CP-MAS NMR Spectra. Single-contact ^{13}C CP-MAS NMR spectra were recorded on a Bruker CXP-300 spectrometer at 75.46 MHz, equipped with a CP-MAS NMR accessory. Samples were placed in an Andrew-Beams type rotor machined from perdeuterated poly(methylmethacrylate) and spun by compressed air. A contact time used was usually 800 μs, although several spectra were obtained by varying contact time from 500 μs to 5 ms. Repetition times were 2—4 s and spectral width and data points were 30 kHz and 8 K data points, respectively. Resolution-enhancement was made by a gaussian multiplication.[35] Spectra were accumulated more than 2000 times. Chemical shifts were calibrated through external benzene and converted to the values from tetramethylsilane (TMS).

High Resolution ^{13}C NMR. High resolution ^{13}C NMR spectra were recorded in deuterated chloroform and methanol on a Bruker CXP-300 spectrometer. Chemical shifts were calibrated with respect to external tetramethylsilane in a capillary.

Results

Figure 2 shows 75.46 MHz ^{13}C CP-MAS NMR spectra of ethylene oxide oligomers complexed with $HgCl_2$ or $CdCl_2$ in the solid state. The ^{13}C NMR signals of the terminal methoxyl or ethoxyl groups were readily assigned in view of the data of uncomplexed samples in chloroform solution (see Table 1). Several peaks were well resolved for the internal methylene carbons of polyether moiety and peak-positions and relative peak-intensities are summarized in Table 1. These ^{13}C NMR signals are also split into several peaks even in the uncomplexed molecules in solution state (Table 1). Such a splitting of peaks in the random-coil state is not necessarily caused by variations of local conformers among methylene groups but simply by substituent effects of the terminal methoxyl or ethoxyl groups. In particular, the peaks marked by **a** in the solid and solution states are assigned to the carbons which are neighbored with the terminal methoxyl or ethoxyl groups, in view of the relative peak-intensities and displacements of peaks (Table 1).

Table 1. ^{13}C Chemical shifts of oligomers of ethylene oxide complexed with $HgCl_2$ or $CdCl_2$ in the solid state$^{a)}$ (ppm from TMS)

	Internal CH_2		Terminal	
	I$^{b)}$	II	CH_3	CH_2
TEGM-$HgCl_2$	72.1$^{c)}$ (2), 71.2*(3), 69.2 (3)	—	58.9 (1) 58.2 (1)	
TEGM (soln)$^{d)}$	71.9$^{c)}$ (2), 70.5*(4), 70.4 (2)	—	58.9 (2)	
TEGM-$CdCl_2$	71.9$^{c)}$ (1), 70.5*(3), 69.5 (1), 68.2$^{c)}$ (1)	67.1 (1) 67.9 (1)	60.5 (2)	
HEGE-$HgCl_2$	72.0$^{c)}$ (2), 71.6 (2), 70.4*(6), 68.9 (2)	67.6 (1) 66.8 (1)	15.3 (2)	67$^{e)}$ (2)
HEGE (soln)$^{d)}$	70.5*(10), 69.7$^{c)}$ (2)		15.1 (2)	66.5 (2)
TEGE-$HgCl_2$	69.5*(8)		15.1 (2)	65.8 (2)
TEGE (soln)$^{d)}$	70.5*(6), 69.8$^{c)}$ (2)		15.1 (2)	66.5 (2)

a) Numbers in parenthesis denote relative peak-intensities normalized to the total number of carbons. b) Peaks asterisked stand for the most intense signals. c) CH_2O group neighbored with the terminal CH_3 or CH_2CH_3 groups. d) In chloroform solution (uncomplexed). e) Superimposed on the internal CH_2 signals (peak II).

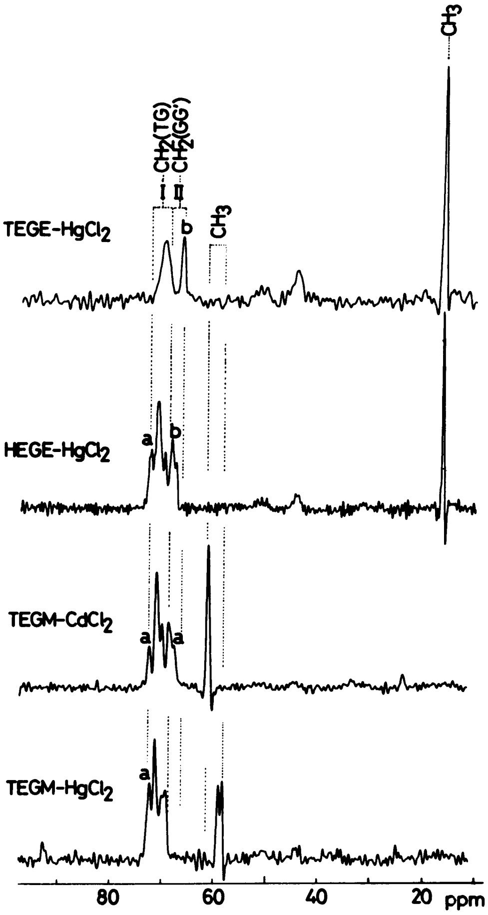


Fig. 2. 75.46 MHz ^{13}C CP-MAS NMR spectra of $HgCl_2$ or $CdCl_2$ complexes with ethylene oxide oligomers in the solid state. The peaks **a** and **b** stand for the peak of carbons neighbored with the terminal methoxyl (or ethoxyl) groups and methylene signal of the terminal ethoxyl groups, respectively.

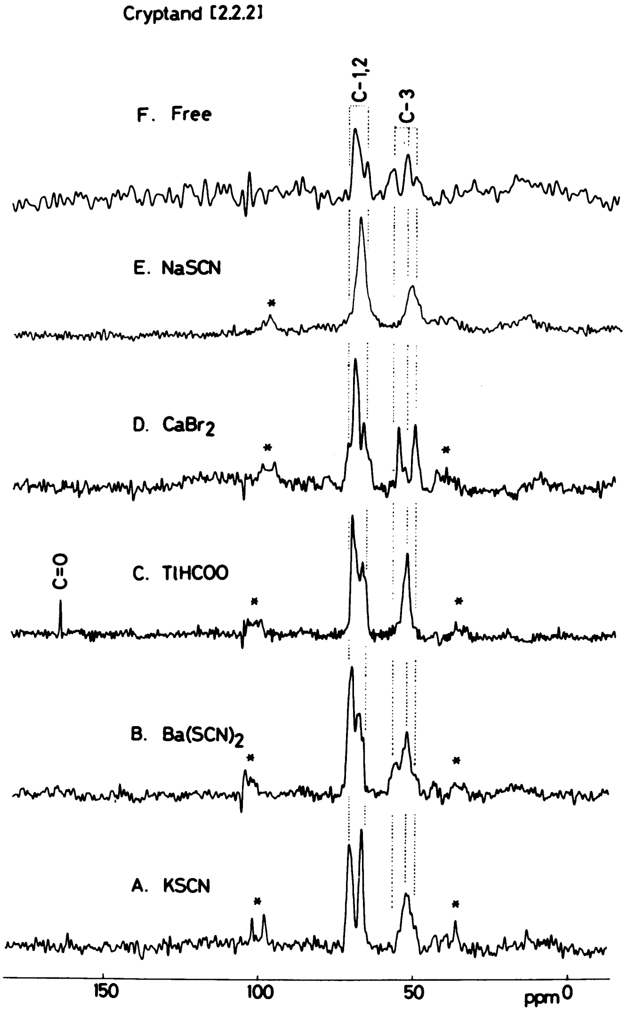


Fig. 3. 75.46 MHz ^{13}C CP-MAS NMR spectra of cryptand [2.2.2] complexed with a variety of metal ions in the solid state. The peaks asterisked are spinning side-bands of the central intense signals.

Figure 3 shows the ^{13}C CP-MAS NMR spectra of cryptand [2.2.2] complexed with a variety of metal ions. Interestingly, the peak-intensities of uncomplexed molecules are very weak as compared with those of the complexed molecules. The assignment of peaks was made on the basis of the solution NMR data. Spectral features are substantially different among complexes. Similarly, the splitting of the C-4,5 signals of cryptand [2.2.1] is quite different between the Na^+ and K^+ complexes, reflecting differences in the molecular conformations as revealed by X-ray diffraction[26] (Fig. 4). By contrast, very little change was observed among NaSCN, $Pb(SCN)_2$, and KSCN complexes with cryptand [2.2] (Table 2). The ^{13}C NMR spectra of uncomplexed [2.2] and [2.2.1] in the solid state turned out to be very difficult to observe, because molecular motion prevents from building up of ^{13}C NMR signals for the former and free molecule is in liquid state for the latter. These ^{13}C chemical shifts in the solid state are summarized in Table 2.

Figures 5 and 6 illustrate the ^{13}C CP-MAS NMR spectra of *cis-syn-cis* and *cis-anti-cis* isomers of dicyclohexano-18-crown-6, respectively, complexed with a variety of metal ions. Again, the peak-intensities of uncomplexed molecules are considerably suppressed as compared with those of the complexed molecules. It is expected that the ^{13}C NMR peaks of the C-1, C-9, C-14, and C-22 carbons of cyclohexane moiety in the solid state are split into a pair of doublet caused by the presence of the ether substituents at the axial (O_{ax}) and equatorial (O_{eq}) positions. The doublet peaks can be readily identified, because the center of the doublet should be very close to the ^{13}C NMR peaks observed in solution state (Table 3). The observation of the doublet peak was possible in solution state upon cooling (−75°)[36] and the magnitude of the separation of peaks (5—7 ppm) is similar to the data observed in the crystalline state (see Table 4). (Note that these doublet peaks are seen for the *cis-syn-cis* and *cis-anti-cis* isomers complexed with $La(NO_3)_3$ even at ambient

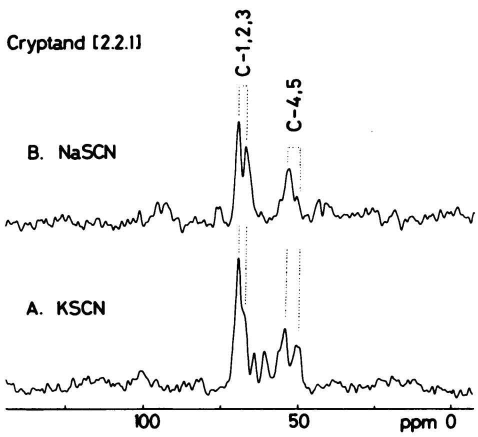


Fig. 4. 75.46 MHz ^{13}C CP-MAS NMR spectra of cryptand [2.2.1] complexed with KSCN (A) or NaSCN (B) in the solid state.

Table 2. ^{13}C Chemical shifts of some cryptands complexed with a variety of metal ions in the solid and solution (ppm from TMS, ±0.4 ppm for the solid)

[2.2.2]	Free		$CaBr_2$		TlHCOO		$Ba(SCN)_2$		KSCN		NaSCN	
	Solid	Soln	Solid	Soln	Solid	Soln	Solid	Soln	Solid	Soln	Solid	Soln
C-1 } a)	70.4	70.7	69.9(71.9)[b)]	69.4	69.1	70.0	70.5	70.5	71.4	70.3	68.5	68.8
C-2	66.5	69.8	67.3(65.1)	68.7	67.3	68.0	67.9	67.7	67.3	67.4		67.8
C-3	58.8 53.6 50.7	56.1	56.3 51.0	53.9	53.8	54.4	56.7 52.8	54.2	52.9	53.7	52.0	53.1

[2.2.1]	Free		KSCN		NaSCN	
	Solid	Soln	Solid	Soln	Solid	Soln
C-1 } a)	—[c)]	70.5	69.6	69.1	69.8	68.8
C-2	—	69.7	67.5	67.6	67.1	66.5
C-3	—	69.9		69.5		67.0
C-4	—	56.5	56.2	57.7	56.4	52.8
C-5	—	56.3	54.4	53.6	53.8	53.6

[2.2]	Free		KSCN		NaSCN		$Pb(SCN)_2$	
	Solid	Soln	Solid	Soln	Solid	Soln	Solid	Soln
C-1 } a)	—[d)]	70.4	70.2	70.6	68.5	69.2	70.6	70.3
C-2	—	70.2		69.9		68.9	69.2	69.5
C-3	—	49.3	50.3	49.4	48.5	48.2	49.9	49.3

a) These peak cannot be distinguished in the solid state, although assigned separately in solution($CDCl_3$ or $CDCl_3$ containing a few drops of methanol): see Ref. 39. b) Shoulder peaks. c) Liquid state. d) Not detected.

temperature, see Table 3.) For NaBr complex with *cis-anti-cis* isomer,[31] the C-1 and C-14 carbons are ascribed to the O_{eq}, while the C-9 and C-22 are ascribed to the O_{ax} peak. The remaining ^{13}C NMR peaks resonating between 71 and 61 ppm are undoubtedly ascribed to the eight polyether carbons, C-3, 4, 6, 7, 16, 17, 19, 20.

Discussion

Peak-intensities. We found that the peak-intensities of the ^{13}C NMR spectra of uncomplexed cryptands and crown ethers in the solid state are generally weak or suppressed as compared with those of the complexed samples (Figures 3F, 5H, and 6H). In addition, no ^{13}C CP-MAS NMR data are available for uncomplexed cryptands [2.2.1] and [2.2] and ethylene oxide oligomers, because these samples except for cryptand [2.2] complex are in liquid state. The reason why the peak-intensities in the solid state are in many instances suppressed is undoubtedly caused by the presence of plausible molecular motion even in the solid state which might prevent from building up of the ^{13}C NMR signals through cross polarization.[37] In this connection, we were unable to observe ^{13}C CP-MAS NMR spectra of NaI complex with cryptand [2.2.2]. Further, the recording of the ^{13}C CP-MAS NMR spectra of 18-crown-6 complexed with a variety of metal ions was unsuccessful at room temperature because of the reason mentioned above (unpublished finding), although observation of the solid-state high-resolution ^{23}Na NMR signals of sodium complex by a single pulse experiment was not difficult.[38] Therefore, it is probable that the

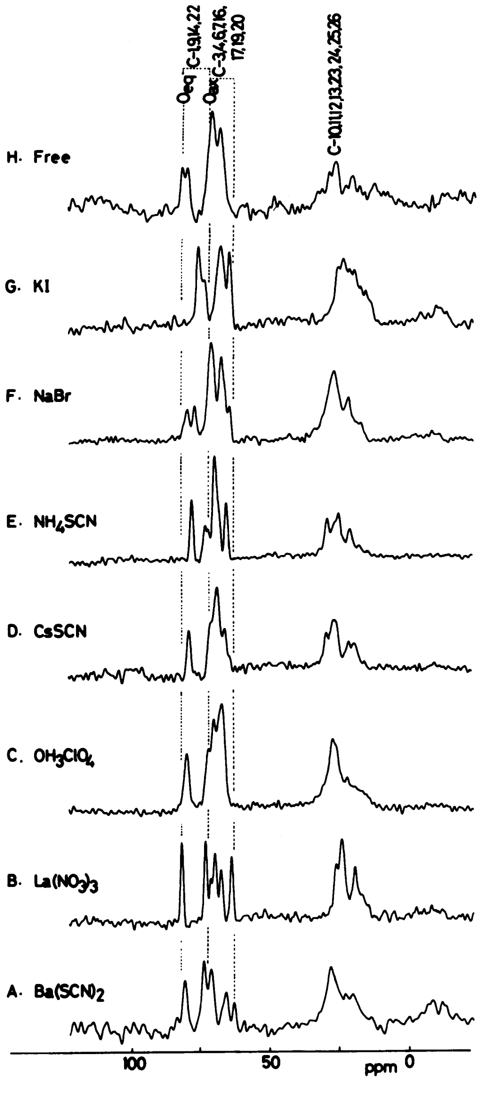


Fig. 5. 75.46 MHz ^{13}C CP-MAS NMR spectra of *cis-syn-cis* isomer of dicyclohexano-18-crown-6 complexed with a variety of metal ions in the solid state. Number of transients are 2000—5000.

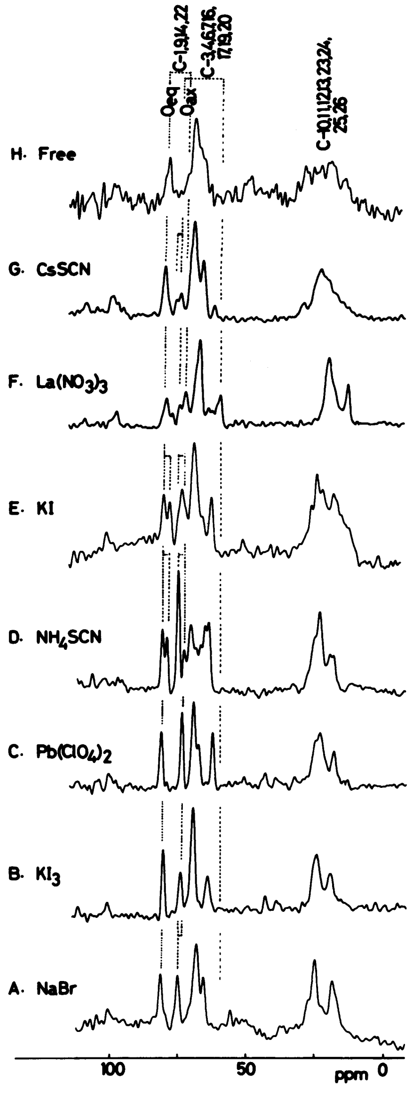


Fig. 6. 75.46 MHz ^{13}C CP-MAS NMR spectra of *cis-anti-cis* isomer of dicyclohexano-18-crown-6 complexed with a variety of metal ions in the solid state. Number of transients are 2000—5000.

Table 3. ^{13}C Chemical shifts of *cis-anti-cis* and *cis-syn-cis* isomers of dicyclohexano-18-crown-6 complexed with various metal ions in solution (ppm from TMS)[a]

Carbon No.	*cis-anti-cis*							
	Free	KI	CsSCN	NaBr	NH_4SCN	$La(NO_3)_3$	$Pb(ClO_4)_2$	KI_3
	$CDCl_3$	$CDCl_3$	$CDCl_3$	CD_3OD	CD_3OD	CD_3OD	DMSO-d_6	DMSO-d_6
1,9,14,22	77.4	78.3	77.8	78.6	79.0	81.7, 78.1	77.5	78.1
4,6,17,19	70.6	70.4	70.4	70.9	71.0	72.6, 71.3	70.7	70.8
3,7,16,20	67.9	66.3	66.9	67.0	67.0	68.5, 68.2	68.3	67.0
10,13,23,26	27.6	25.7	26.5	26.3	26.1	27.8, 25.9	28.2	26.4
11,12,24,25	22.0	21.4	21.7	21.9	21.8	22.3, 21.4	22.6	22.1
Carbon No.	*cis-syn-cis*							
	Free	KI	CsSCN	NaBr	NH_4SCN	$La(NO_3)_3$	OH_3ClO_4	$Ba(SCN)_2$
	$CDCl_3$	CD_3OD	$CDCl_3$	CD_3OD	CD_3OD	CD_3OD	CD_3OD	CD_3OD
1,9,14,22	77.5	78.2	77.5	78.2	78.1	81.3, 77.9	78.3	80.3
4,6,17,19	71.1	71.1	70.7	70.4	71.1	72.4, 70.9	71.2	70.8
3,7,16,20	68.0	67.3	67.4	66.9	67.5	68.5, 67.7	68.2	68.0
10,13,23,26	27.5	26.4	26.9	26.5	26.6	27.8, 25.6	27.3	26.3
11,12,24,25	22.0	22.0	21.7	21.9	22.0	22.3, 20.4	22.1	21.6

a) Assignment of peaks based on Ref. 36.

Table 4. ^{13}C Chemical shifts of *cis-anti-cis* and *cis-syn-cis* isomers of dicyclohexano-18-crown-6 complexed with various metal ions in the solid state ($\pm$0.4 ppm; ppm from TMS)

Carbon No.	*cis-anti-cis*							
	Free	KI	CsSCN	NaBr	NH_4SCN	$La(NO_3)_3$	$Pb(ClO_4)_2$	KI_3
1,9,14,22	81.0 a)	81.7, 79.5 75.0, a)	81.1 77.0, 75.2	81.7 75.6	81.1, 79.5 75.4,[a] 73.2	80.7, 78.7 76.1, 73.6	81.9 74.4	81.1 74.6
4,6,17,19 3,7,16,20	71.1 68.1	70.8 64.5	71.0 67.5	68.7 66.3	75.4 73.2 70.8 68.9 67.1 65.9 64.5	69.0 65.7 61.1	70.3 68.3 63.1	70.4 65.1
10,13,23,26 11,12,24,25	b)	25.5 19.6	24.5 —	25.3 19.0	23.5 19.0	21.9 14.8	24.1 19.2	25.9 20.4
Carbon No.	*cis-syn-cis*							
	Free	KI	CsSCN	NaBr	NH_4SCN	$La(NO_3)_3$	OH_3ClO_4	$Ba(SCN)_2$
1,9,14,22	82.1 80.3	76.8 74.8	80.5 72.4	80.5, 77.6 71.6[c]	78.9 73.8, 72.8	82.7 74.0, 72.2	81.0 73.2	81.9 74.6
4,6,17,19 3,7,16,20	70.8 68.1	68.0 64.7	70.0 67.1	67.9 64.7	70.4 69.1	70.6 68.3 64.5	71.3 68.0	71.8 66.5 63.5
10,13,23,26 11,12,24,25	24.9 18.6	21.9 —	26.3 20.0	25.5 20.6	24.3 (28.3) 19.8	25.5, 23.0 18.3	26.8 20.8	27.5 21.6

a) Overlapped with a signal of C-4,6,17,19,3,7,16,20. b) Obscured by line-broadening. c) Tentative assignment: another plausible assignment is one of C-4,6,17,19,3,7,16,20.

recording of the ^{13}C CP-MAS NMR spectra at lower temperature is very useful for the samples whose peak-intensities are suppressed at ambient temperature.

Ethylene Oxide Oligomers. Iwamoto[20–23] previously analyzed detailed molecular conformation of TEGM, HEGE, and TEGE complexed with $HgCl_2$ or $CdCl_2$ by X-ray diffraction method. The local conformations of these complexes are summarized in Fig. 7, as defined by sets of torsion angles. Our view is that the ^{13}C NMR signals of particular carbons are primarily influenced by the local conformations

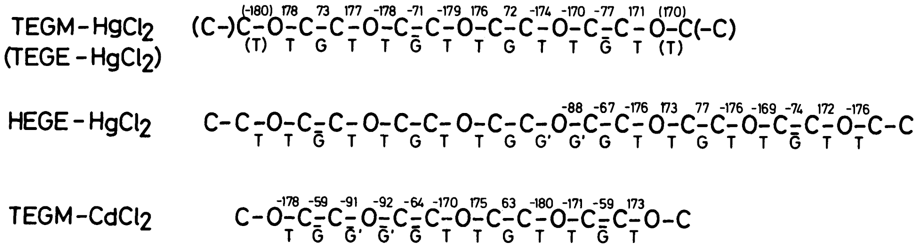
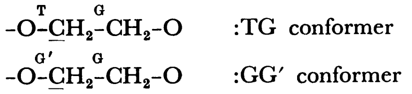


Fig. 7. Conformations of TEGM, TEGE, HEGE complexed with $HgCl_2$ or $CdCl_2$ in the solid state (Data taken from Refs. 20—23). The symbols T, G ($\overline{G}$), and G′ ($\overline{G}'$) stand for the *trans*, *gauche* (minus *gauche*), and torsion angle of about 90°, respectively.

defined by a pair of torsion angles of nearby single bonds. This view has been proven correct for a number of peptides, proteins, carbohydrates, and polysaccharides.[10–19] Accordingly, it is expected that the presence of the following two types of local TG and GG′ conformers in the complexes (Fig. 7) give rise to different types of signals:



$$-\overset{T}{O-}\underline{C}H_2\overset{G}{-}CH_2-O \quad \text{:TG conformer}$$

$$-\overset{G'}{O-}\underline{C}H_2\overset{G}{-}CH_2-O \quad \text{:GG' conformer}$$

where the symbols T and G stand for *trans* and *gauche* conformations, respectively, and G′ stands for the torsion angles of about 90°. It is expected from Figure 7 that the relative peak-intensity of the conformer TG with respect to that of the conformer GG′ is 8:0, 8:0, 10:2, and 6:2 for TEGM–$HgCl_2$, TEGE–$HgCl_2$, HEGE–$HgCl_2$ and TEGM–$CdCl_2$, respectively. Therefore, the peaks in regions I and II of the internal CH_2 group in Fig. 2 are ascribed to the TG and GG′ conformers, respectively, as substantiated from the relative peak-intensities of the individual peaks in Table 1 and the population of the TG and GG′ conformers in Fig. 7. Note that the peaks marked by **b** should be ascribed to the methylene carbons of the terminal ethoxyl groups in TEGE and HEGE, although they are within the region II of CH_2 (GG′). In particular, there exists no GG′ conformer in TEGE–$HgCl_2$ complex, as seen from Fig. 7. It is also mentioned that the TG and T$\overline{G}$ conformers gave the identical ^{13}C chemical shifts.

Torsion angles of the |T|, |G|, and |G′| rotamers are 174°±3°, 70°±3°, 90°±2°, respectively (Fig. 7) and the peaks of the TG and GG′ conformers should be observed as two separate single peaks. On the contrary, the TG signals are split into two or three signals as shown in Fig. 2, although the most intense with relative peak-intensity larger than 3 should be ascribed to the carbons at the central core of these oligomers which are not influenced by the presence of the terminal methoxyl or ethoxyl groups. Displacement of peaks from the most intense signals within the peaks of the TG conformers (region I) is less than 1.5 ppm and the positions of the TG conformers are well separated from those of the GG′ conformers which are resonated at higher field by 2 ppm. It is probable that direct effect of metal coordination over the carbon chemical shifts might have some contribution to the splittings of peaks. Such an effect, however, is not larger than 1.5 ppm, if it exists.

Cryptands. The individual assignment of peaks to the C-1 and C-2 in cryptands [2.2] and [2.2.2] and to the C-1, C-2, and C-3 in [2.2.1] in the solid state is difficult,[39] if one considers the maximum separation of the peaks is about 4 ppm which is in the range of the conformation-dependent ^{13}C chemical shifts of single carbon. However, we attempted to relate the ^{13}C chemical shifts of the C-4 plus C-5 and C-3 chemical shifts of cryptands [2.2.1] and [2.2.2], respectively, with the pairs of torsion angles, namely, rotation about N-C-4 and C-4-C-2, and N-C-5 and C-5-C-3 for cryptand [2.2.1] and rotation about N-C-3 and C-3-C-2 for cryptand [2.2.2]. It is now possible to plot the ^{13}C chemical shifts of the C-3 (for cryptand [2.2.2]), and C-4 plus C-5 (for cryptand [2.2,1]) against the torsion angles about N-C-4 and N-C-5 (cryptand [2.2.1]) and N-C-3 (cryptand [2.2.2]),[26–29,40] because the torsion angles C-4-C-2 and C-5-C-3

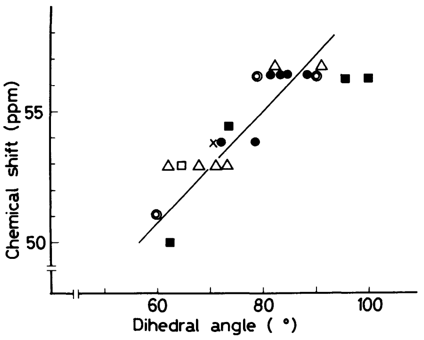


Fig. 8. A plot of C-3 (cryptand [2.2.2]), C-4 plus C-5 (cryptand [2.2.1]) ^{13}C chemical shifts of cryptands [2.2.2] and [2.2.1] against the N-C-3 ([2.2.2]) and N-C-4 and N-C-5 ([2.2.1]) torsion angles. □, K-[2.2.2]; △, Ba-[2.2.2]; ◎, Ca-[2.2.2]; ×, Tl-[2.2.2]; ●, Na-[2.2.1]; ■, K-[2.2.1].

(cryptand [2.2.1]) and C-3-C-2 (cryptand [2.2.2]) do not depart from the standard value (60°±10°) irrespective of the variety of complexes (Fig. 8).[41] Accordingly, it is found that the manner of peak-splittings in the C-3, C-4, and C-5 carbons of cryptands [2.2.2] and [2.2.1] can be well explained in terms of the variation of torsion angles characteristic of nearby local conformations.

Crown Ethers. Dalley *et al.*[42] showed by X-ray diffraction that in the both isomers the cavity surrounded by the six oxygen atoms is elliptical in shape with the two axial oxygen atoms O-21 and O-8 pointing out of the cavity. Consistent with this, the ^{13}C NMR spectra of free *cis-syn-cis* (Fig. 5H) and *cis-anti-cis* (Fig. 6H) are very similar (except for the doubling of the O_{eq} peak in the latter).[43] When NaBr or $Ba(SCN)_2$ salts[44] are complexed with *cis-anti-cis* or *cis-syn-cis* isomers, respectively, macrocyclic conformations are changed either to possess C_i symmetry[31] or to have C_2 symmetry.[44]

Interestingly, the ^{13}C chemical shifts of the O_{ax} and O_{eq} peaks of *cis-anti-cis* isomer are very similar among the eight kinds of complexes, suggesting the presence of similar conformation for cyclohexane moiety as observed for the NaBr complex. However, the conformations of the two cyclohexane moieties are not identical for the complexes with NH_4SCN, KI, $La(NO_3)_3$, and CsSCN, as manifested from the observation of the two pairs of doublets ascribable to the C-1, C-9, C-14, and C-22 carbons, probably reflecting the presence of some steric strain in the ligands. Conformation of two cyclohexane moieties becomes identical when KI_3 is coordinated to *cis-anti-cis* isomer in place of KI, although the ^{13}C NMR profile of polyether moiety remains unchanged. By contrast, the O_{eq} peaks are significantly displaced upfield for *cis-syn-cis* isomer complexed with KI, NaBr, and NH_4SCN (Fig. 5E-G). This finding is readily rationalized by the presence of strong ring strain in cyclohexane rings as a result of coordination at the polyether moiety.

The ^{13}C NMR peaks of the polyether carbons are in many instances split into two peaks, the intensity of which being 3:1 in spite of the presence of eight kinds of carbons. These doublet patterns are modified to yield three peaks (the intensity of which being 2:1:1) for *cis-syn-cis* isomer-$Ba(SCN)_2$ (Fig. 5A), four peaks for *cis-syn-cis* isomer-$La(NO_3)_3$ (Fig. 5B) or seven peaks for *cis-anti-cis* isomer-NH_4SCN complex (Fig, 6D). These observations are consistent with a possibility that local conformation of polyether moiety is C_2 or C_i symmetry, except for *cis-anti-cis* isomer-NH_4SCN complex whose arrangement of polyether moiety is highly distorted. It is interesting to note that the ^{13}C chemical shifts of the highest peak-intensity at 69-71 ppm in the solid state are not strongly varied among complexes with a variety of metal ions and are very close to those observed in solution state (70.8±0.4 ppm) (Table 3). Obviously, these peaks are straightforwardly ascribed to the carbons of the TG conformers in view of their chemical shifts as compared with those of ethylene oxide oligomers. This view is supported by X-ray diffraction study of *cis-anti-cis* isomer of NaBr complexes which is the only available detailed data of dicyclohexano-18-crown-6 complex: all of the torsion angles about the polyether moiety are within the typical TG conformer.[31]

Nevertheless, the upper peak of NaBr-*cis-anti-cis* isomer at 66.3 ppm should be ascribed to the TG conformer, although this position is rather high as compared with that of ethylene oxide oligomers. This may be caused by that the C-3, C-7, C-16, and C-20 peaks are not completely free from the substituent effect of cyclohexane rings. It is emphasized that the ^{13}C chemical shifts of peaks with lower peak-intensities vary with variety of metal ions, depending also on the conformation of the polyether moiety. In particular, the largest upfield displacement of peaks is 7.0 ppm for $La(NO_3)_3$-*cis-anti-cis* isomer. The observation of peaks at such a higher field region (>67 ppm) could be ascribed to the presence of the GG and TT conformers as seen for NaSCN-18-crown-6[45] or uncomplexed 18-crown-6.[46] Further study, however, is required to prove this view.

Conformation in Solution State. It is now possible to examine whether or not the conformations achieved in the solid state are also retained in solution by comparing the ^{13}C chemical shifts of solution with those of the solid state. This kind of information is closely related with stability of complexes in solution, because any conformational change of ligand molecules would lead to decomposition of complexes. It is worthwhile to note that metal complexes with cryptands are generally many orders of magnitude more stable than those with crown ethers.[8,9] In particular, the association constant of the potassium ion both in aqueous or methanol solutions decreases in the following order: [2.2.2]>[2.2.1]>*cis-syn-cis*>*cis-anti-cis*>[2.2]. In the case of the sodium ion, [2.2.1]>[2.2.2]. Consistent with this, [2.2.2] and [2.2.1] complexed with a variety of metal ions maintain their overall conformations achieved in the solid even in solution state, although conformational fluctuation about the N-C-3, N-C-4 or N-C-5 is evident as seen from the time-averaging process in the ^{13}C NMR signals, as judged from the similarity of the ^{13}C chemical shifts between the solid and solution. On the contrary, the presence of ring-puckering in two cyclohexane rings of the crown ethers as seen in solution state is responsible for reduction of stability and selectivity of complexes. Nevertheless, it appears that no drastic conformational change occurs between the solid and solution for [2.2] as inferred from Table 2, although association constant of this molecule is usually lower than crown ethers.[8,9] Obviously, consideration of steric requirement of ligand molecules in adapting to different metal ions is also very important to explain relative stability of complexes.

Concluding Remarks

We have showed that the ^{13}C NMR peaks of backbone carbons of ethylene oxide oligomers, crown ethers and cryptands exhibit substantial amounts of displacement of peaks (up to 6 ppm) upon complex formation with a variety of metal ions, as determined by cross polarization-magic angle spinning method. These changes of the ^{13}C chemical shifts are mainly ascribed to conformational changes induced by metal-binding as revealed by X-ray diffraction and can be utilized as intrinsic indicators of conformational changes. Analysis of ^{13}C NMR spectra in the solid state can be conveniently performed, when conformational features by X-ray diffraction studies are available. This approach is also suitable for comparative study of conformational changes of these ionophores induced by complexation with a variety of metal ions, even if detailed X-ray diffraction data are unavailable. Further, it is easily evaluated on the basis of the conformation-dependent ^{13}C chemical shifts whether or not the conformations of these ionophores achieved in the crystalline state is retained in solution state.

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