Preparation of Bicyclic Crown Ethers Containing Amide Groups: Coordination of the Oxygen Atoms of the Amide Groups

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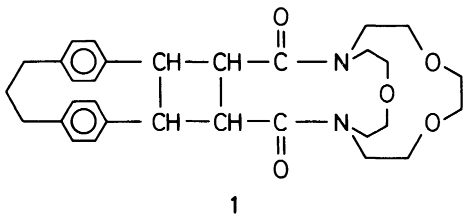
Synopsis. 9,12,23,26,31,36-Hexaoxa-1,6,15,20-tetraaza-3,4:17,18-dibenzotricyclo[18.8.5.5^{6,15}]octatriaconta-3,17-diene-2,5,16,19-tetraone (**7a**) was obtained by the reaction of phthaloyl dichloride with 1,4,10-trioxa-7,13-diazacyclopentadecane in 38% yield, and related compounds were prepared by a similar method. Compound **7a** showed high extraction abilities toward alkali, alkaline earth, and other metal cations (Ag$^+$, Tl$^+$, and Pb^{2+}), especially lithium and sodium cations.

Diazacrown ethers are well-known as complexing agents toward alkali and alkaline earth metal cations.[1] Especially, the complexing abilities of cryptand-type bicyclic crown ethers toward alkaline earth metal cations are considerably high.[2] We previously reported that cyclobutane-incorporated diazacrown ether **1**[3,4] had high complexing abilities toward alkali, alkaline earth, and other metal cations (Ag$^+$, Co^{2+}, Ni^{2+}, and Cu^{2+}) without remarkable selectivities. The structures of the complexes of cyclobutane-incorporated diazacrown ether **1** with lithium and/or mercury(II) were revealed by X-ray analyses.[3,4] The results suggested that the metal cation was not incorporated into the cavity of the crown ether moiety, but was coordinated by the oxygen atoms of the two amide groups. On the other hand, Vögtle et al.[5] isolated the 1:1 complexes of diazacrown ethers **2c**, **2d**, **3c**, and **3d** with Na$^+$ or K$^+$, and suggested that the metal cation was incorporated into the cavity of the crown ether moiety. However, they did not discuss the complexing ability of diamide **2a**, **2b**, **3a**, and **3b**. Noting these results, we were interested in the complexing abilities of the crown ethers containing amide groups. We therefore prepared the novel azacrown ethers **6b**, **6d**, **7a**, and **7c** in order to discuss their complexing abilities and the structures of their metal complexes.



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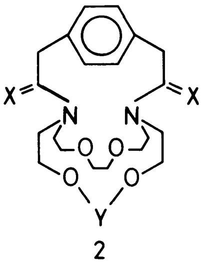
Results and Discussion

Compound **7a** was prepared by the reaction of 1,4,10-trioxa-7,13-diazacyclopentadecane (**4a**) with phthaloyl dichloride (**5**) in the presence of triethylamine in 38% yield. Also, the compounds **6b**, **6d**, and **7c** were prepared by the similar methods, as described above. However, in these reactions compounds **6a**, **6c**, **7b**, and **7d** were not obtained. The ^{1}H NMR spectrum of **6b** showed the signals of methylene protons in the δ=4.38 to 2.88 region as a considerably complicated splitting pattern. The 2D COSY ^{1}H NMR spectrum of **6d** showed an interesting spectral pattern. As shown in Fig. 1, four protons (Ha and Hb), which were expected to be equivalent, appeared as four independent peaks. The signals of two protons (Ha), which are methylene protons adjacent to the nitrogen atoms and also close to the oxygen atoms of the carbonyl group, appeared at δ=4.36 (t, J=4.3 Hz, 1H) and 4.32 (t, J=4.3 Hz, 1H), whereas the other protons (Hb), which are attached to the same carbon atoms, are shifted upfield to δ=2.95 (q, J=3.8 Hz, 1H) and 2.91 (q, J=3.8 Hz, 1H). From the Corey-Pauling-Koltom



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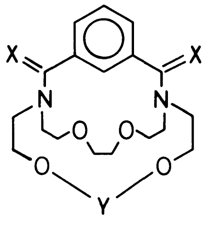

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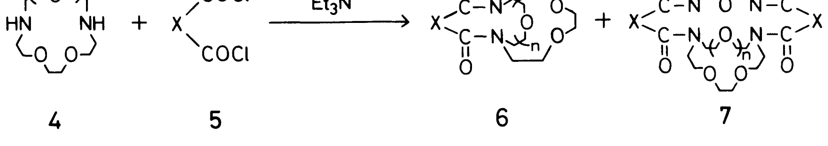
a : X = O , Y = $-CH_2CH_2-$
b : X = O , Y = o-phenylene
c : X = H_2 , Y = $-CH_2CH_2-$
d : X = H_2 , Y = o-phenylene



4 5 6 7

a : n = 1
b : n = 2

a : X = o-phenylene
b : X = $-CH_2CH_2-$

a : X = o-phenylene , n=1
b : X = o-phenylene , n=2
c : X = $-CH_2CH_2-$, n=1
d : X = $-CH_2CH_2-$, n=2

(CPK) molecular model, these unusual shifts of the methylene protons were attributed to a steric compression between the carbonyl group and the methylene protons adjacent to nitrogen atoms.[3] However, in the ^{1}H NMR spectra of **7a** and **7c**, the signals of the methylene protons did not give a well-separated pattern; therefore, those signals could not be assigned. The CPK molecular models suggest that the structures of **7a** and **7c** were sterically very crowded and that the mobility of the molecule was obstructed at ambient temperature.

The reaction of **6b** with mercury(II) thiocyanate gave 1:2 complex **8** in 22% yield, and its composition was defined by elemental analysis. In the ^{1}H and ^{13}C NMR spectra, however, only slight differences in the chemical shifts between **6b** and **8** were observed. In the ^{13}C NMR spectra, the chemical shift differences of all carbon atoms between compound **6b** and complex **8** were less than 1.0 ppm. The signals showed that the greatest chemical shift difference was due to the carbonyl carbon atoms, though only 0.98 ppm. These results suggested that if the crown ether moiety and the oxygen atoms of the amide groups are concerned with complexation, coordination becomes presumably very weak.

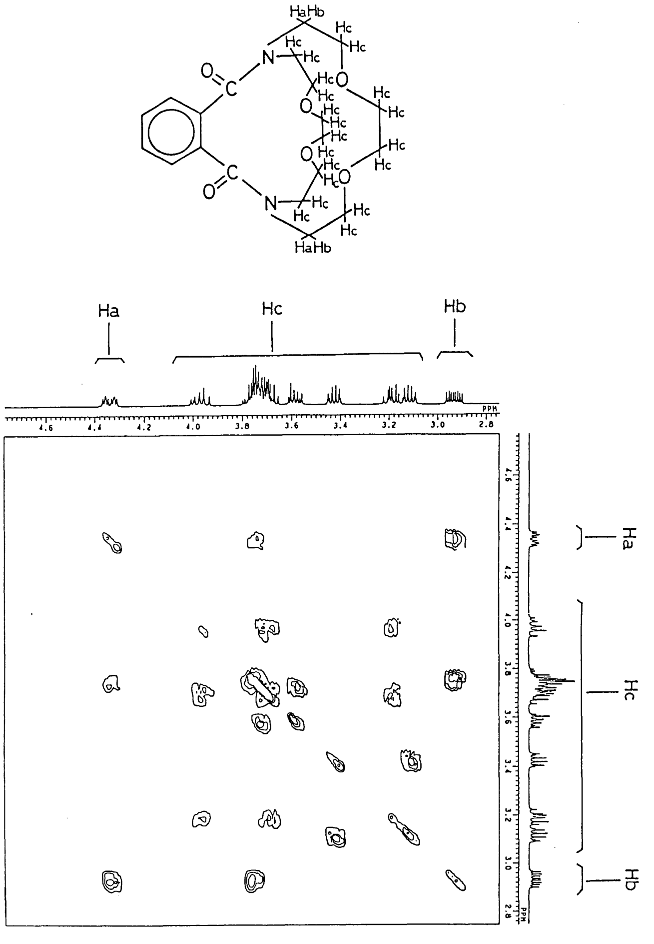


Fig. 1. 400 MHz 2D COSY ^{1}H NMR Spectrum of **6b**.

In the IR spectra, $\nu_{C=O}$ (1616 cm^{-1}) of **8** was shifted to a low wavenumber compared with that (1624 cm^{-1}) of **6b**, and $\nu_{C\equiv N}$ of **8** appeared at 2100 and 2075 cm^{-1}, whereas that of $Hg(SCN)_2$ showed only one absorption band at 2120 cm^{-1}. These results suggested a coordination of the oxygen atoms of the amide groups and the presence of the two kinds of thiocyanate anions. As shown in Fig. 2, the structure of complex **8** was thought to be such that the first of the two mercury atoms is coordinated by the two oxygen atoms of the amide groups, while the second is coordinated by the two nitrogen atoms of the thiocyanate anions of the first one, besides each of the counter anions.

The extraction abilities of the compounds **6b**, **6d**, **7a**, and **7c** toward alkali, alkaline earth, and other metal cations were determined by a method described by Pedersen.[6] However, this determination was carried out using a concentration of azacrown ethers of 7.0×10^{-3} mol dm^{-3}, instead of 7.0×10^{-4} mol dm^{-3}, in order to define the ion selectivities of these azacrown ethers. The results are summarized in Table 1. Compounds **6b** and **7a** showed significant extraction abilities toward alkali and alkaline earth metal cations. Especially, **7a** showed high selectivities toward Li$^+$(39%) and Na$^+$(65%). Also **7a** showed high extraction abilities toward Ag$^+$(49%), Tl$^+$(42%), and Pb^{2+}(24%). However, **6d** and **7c** showed low extraction

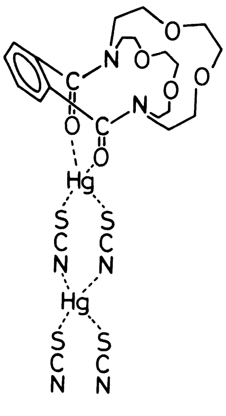


Fig. 2.

Table 1. Extraction of Metal Picrates from the Aqueous to the Organic Phase (%)[a]

Compd	Li$^+$	Na$^+$	K$^+$	Rb$^+$	Cs$^+$	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Ag$^+$	Tl$^+$	Pb^{2+}
6b	13	13	13	12	12	9	11	11	11	30	43	18
6d	4	5	5	4	3	1	5	7	21	19	61	35
7a	39	65	22	22	23	21	22	21	21	49	42	24
7c	3	2	1	2	3	1	2	2	2	28	19	4

a) Solvent: Water and dichloromethane (equal volumes). Azacrown ether=7.0×10^{-3} mol dm^{-3}. Picric acid=7.0×10^{-5} mol dm^{-3}. Metal nitrate=0.1 mol dm^{-3}.

abilities and selectivities toward alkali and alkaline earth metal cations, although they showed high extraction abilities toward Ag^+, Tl^+, and Pb^{2+} cations. Restricted to alkali and alkaline earth metal cations, the significant extraction abilities of **6b** and **7a** may be attributed to an increased basicity of the carbonyl oxygen atoms due to the presence of the *o*-phenylene group. Furthermore, the lower complexing abilities of **6b** toward alkali and alkaline earth metal cations compared with those found in **7a** were presumably caused by difference in the number of carbonyl oxygen atoms. Therefore, compound **7b**, which contains four carbonyl groups as the binding site, showed a stronger affinity toward alkali and alkaline earth metal cations than those of compound **6b**, which contains two carbonyl groups.

Experimental

The melting points were uncorrected. The IR spectra were measured on a JASCO IRA-2 Diffraction Grating Infrared Spectrometer. The ^1H and ^{13}C NMR spectra were obtained on a JEOL GX400 Spectrometer, with TMS as an internal standard. Solvent extraction was carried out according to the method reported previously.[7]

Materials. All reagents and solvents were either commercial or prepared by the usual methods.

The Reaction of 4 with 5. To a solution of triethylamine (1.50 g, 15 mmol) in benzene (400 cm^3), the solution of phthaloyl dichloride (**5a**) (1.02 g, 5.0 mmol) in benzene (100 cm^3) and 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane (**4b**) (1.00 g, 4.6 mmol) in benzene (100 cm^3) were added dropwise at the same rate over a period of 6 h and then stirred for 19 h at room temperature. The precipitated triethylamine hydrochloride was filtered off, and the filtrate was washed with aqueous 10% hydrochloric acid and then water. The mixture was dried by anhydrous magnesium sulfate and concentrated in vacuo. The residue was chromatographed on activated alumina using ethyl alcohol as an eluant. The first fraction was collected and the solvent was removed in vacuo. The residue was recrystallized from benzene to give **6b** as a colorless powder in 13% yield. Mp 216.0—217.0 °C. Found: C, 61.21; H, 7.27; N, 7.12%. Calcd for $C_{20}H_{28}N_2O_6$: C, 61.21; H, 7.19; N, 7.14%. MS (70 eV) m/z 392 (M^+). ^1H NMR (CD_3CN) δ=7.45—7.37 (m, 4H), 4.36 (t, J=4.3 Hz, 1H), 4.32 (t, J=4.3 Hz, 1H), 4.01—3.93 (m, 2H), 3.80—3.65 (m, 10H), 3.61—3.56 (m, 2H), 3.45—3.40 (m, 2H), 3.22—3.16 (m, 2H), 3.14—3.09 (m, 2H), 2.95 (q, J=3.8 Hz, 1H), 2.91 (q, J=3.8 Hz, 1H). ^{13}C NMR (CD_3CN) δ=169.76 ($\underline{C}$=O), 136.47 (bridgehead-C), 129.35 (aromatic-C_β), 128.98 (aromatic-C_α), 72.71, 70.74, 70.43, 70.16 (-$\underline{C}H_2O$-), 51.66, 47.28 (-$\underline{C}H_2N$-). IR (KBr disk) 1627, 1163, 1138, 1125, and 1115 cm^{-1}.

6d, Yield 12%. Mp 163.0—165.0 °C. Found: C, 55.89; H, 8.24; N, 8.12%. Calcd for $C_{16}H_{28}N_2O_6$: C, 55.80; H, 8.19; N, 8.13%. MS (70 eV) m/z 344 (M^+). ^1H NMR($CDCl_3$) δ=4.50 (t, J=5.2 Hz, 1H), 4.47 (t, J=5.2 Hz, 1H), 3.98 (t, J=6.0 Hz, 1H), 3.94 (t, J=6.0 Hz, 1H), 3.82—3.56 (m, 12H), 3.35—3.28 (m, 2H), 3.04 (t, J=5.8 Hz, 1H), 3.00 (t, J=5.2 Hz, 1H), 2.67 (t, J=4.9 Hz, 1H), 2.63 (t, J=4.9 Hz, 1H), 2.50—2.43 (m, 2H), 2.17 (s, 4H). IR (KBr disk) 1632, 1133, and 1118 cm^{-1}.

7a, Yield 38%. Mp 281.0—283.0 °C. Found: C, 60.76; H, 6.81; N, 7.63%. Calcd for $C_{36}H_{48}N_4O_{10}\cdot H_2O$: C, 60.49, H, 7.05; N, 7.84%. MS (70 eV) m/z 696 (M^+). ^1H NMR ($CDCl_3$) δ=7.52—7.31 (m, 8H), 4.75—2.58 (m, 38H), 1.68 (br, 2H). IR (KBr disk) 1618, 1191, and 1100 cm^{-1}.

7c, Yield 28%. Mp 239.0—240.0 °C. Found: C, 54.70; H, 8.35; N, 9.16%. Calcd for $C_{28}H_{48}N_4O_{10}\cdot 1/6C_6H_6$: C, 54.79; H, 8.05; N, 9.13%. MS (70 eV) m/z 600 (M^+). ^1H NMR ($CDCl_3$) δ=4.60—3.23 (m, 40H), 2.71 (br, 16H). IR (KBr disk) 1619, 1188, 1142, and 1122 cm^{-1}.

Isolation of Complex 8. Compound **6b** (20 mg, 5.1×10^{-5} mol) in acetonitrile (3 cm^3) was added to the solution of $Hg(SCN)_2$ (32 mg, 10.2×10^{-5} mol) in acetonitrile (3 cm^3) and the mixture was concentrated to 3 cm^3. The mixture was cooled in a refrigerator and precipitated colorless crystals were obtained in 22% yield. Mp 169.0—170.0 °C. Found: C, 28.09; H, 2.75; N, 8.19%. Calcd for $C_{24}H_{28}Hg_2N_6O_6S_4$: C, 28.09; H, 2.78; N, 8.23%. ^1H NMR (CD_3CN) δ=7.39—7.47 (m, 4H), 4.37 (q, J=2.9 Hz, 1H), 4.33 (q, J=2.9 Hz, 1H), 4.02—3.93 (m, 2H), 3.81—3.66 (m, 2H), 3.61—3.56 (m, 10H), 3.45—3.40 (m, 2H), 3.23—3.18 (m, 2H), 3.15—3.10 (m, 2H), 2.96 (q, J=3.7 Hz, 1H), 2.93 (q, J=3.7 Hz, 1H). ^{13}C NMR (CD_3CN) δ=170.74 ($\underline{C}$=O), 135.87 (bridgehead-C), 129.77 (aromatic-C_β), 129.07 (aromatic-C_α), 114.75 ($S\underline{C}N$), 72.67, 70.54, 70.10, 69.96 (-$\underline{C}H_2O$-), 51.83, 47.71 (-$\underline{C}H_2N$-). IR (KBr disk) 2100, 2075, 1616, 1124, and 1104 cm^{-1}.

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