Guest Entrapment via Type and Size of Dibenzo–Monoaza–Crowns-based *N*,*N*-Bis(alkyl-2-hydroxybenzyl)alkylamine Host

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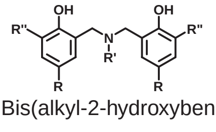
A simple but effective preparation of ring-enlarged dibenzo–monoaza–crowns, 12- to 14-membered macrocycles **3**–**6**, obtained from the reaction of *N*,*N*-bis(alkyl-2-hydroxybenzyl)-alkylamine with ditosylated compound is proposed. Studies on alkali ion extraction using Pedersen's technique clarify that the ion-extraction efficiency is achieved as a consequence of the structure and size of the cavity of the macrocycles. An extension study on dibenzo–monoaza–12-crown-3, **4**, confirms unique performance in terms of being a ligand to accept a perchlorate anion.

Crown ethers and their derivatives have been known for decades as a type of macrocyclic host to include various guest species.[1] Ágai et al. reported the synthesis of dibenzo–monoaza–crown ethers in 10–30% yield from the reaction of bisphenol and an alkylating agent under basic conditions.[2] In the past, our group reported *N*,*N*-bis(alkyl-2-hydroxybenzyl)alkylamine (HBA) (Scheme 1) as the compound inevitably obtained from the single ring opening of benzoxazine with monophenols.[3–5] The crystallographic data pointed out that HBA and its derivatives are in strong inter- and intramolecular hydrogen-bond networks.[3,4] On the basis of the hydrogen-bond network of HBA, we succeeded in simple, selective, and effective preparation of [1 + 1] and [2 + 2] dibenzo–monoaza–crowns.[6–8] Although we have reported the inclusion properties of those macrocycles, comparative studies on the structural factors related to the ion-acceptance abilities have not yet been carried out. The present work, therefore, focuses on dibenzo–monoaza–crowns and how their structures are involved with the metal-ion selectivity.

Compounds **1** and **2** were prepared as reported previously.[5] Dibenzo–monoaza–14-crown-4, **3**, was obtained from a solution of **1** (0.299 g, 1 mmol) in acetonitrile (150 mL) containing sodium hydroxide (0.084 g, 2.1 mmol). The reaction was carried out under reflux for 1 h, followed by adding a solution of ditosylated diethylene glycol (0.414 g, 1 mmol) in acetonitrile (50 mL) and allowing the reaction to proceed in reflux for 3 days, as reported elsewhere (Figure 1).[9] With the same procedures as **3**, 1,3-bis(tosyloxy)propane and 1,4-bis(tosyloxy)butane were used instead of ditosylated diethylene glycol to obtain the crude products of **4** and **5**, respectively. The crude products were recrystallized from a mixed solvent of isopropanol and chloroform (2:1, v/v). As the recrystallization of **3** is still under investigation, single crystal analyses were done only for **4**–**6**. In addition, **2** reacted with ditosylated diethylene glycol under the same conditions as **3**, to give macrocycle **6**.



1 : R = CH_3, R' = CH_3, R'' = CH_3
2 : R = CH_3, R' = C_3H_7, R'' = CH_3

N,*N*-Bis(alkyl-2-hydroxybenzyl)alkylamine (HBA)

Scheme 1.

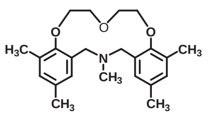


Figure 1. Chemical structure of **3**.

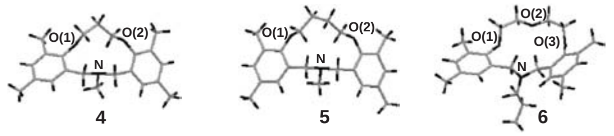


Figure 2. Crystal structures of **4**, **5**, and **6**.

Various characterization techniques were applied to confirm the structures of the macrocycles.[10] Crystal structure analysis reveals that **4** is a 12-membered-ring molecule packed in a triclinic unit cell, **5** is a 13-membered-ring molecule packed in a monoclinic unit cell, and **6** is a 14-membered-ring molecule packed in an orthorhombic unit cell.[11] Figure 2 shows the molecular structures of **4**–**6**, which are made of HBA linked with the ditosylated compound, resulting in [1 + 1] macrocyclic compounds.

The alkali ion (Na^+, K^+, and Cs^+)-extraction abilities of macrocycles were studied by using Pedersen's technique.[1] The solutions of macrocycles **3**–**6** in chloroform and alkali metal picrates (sodium picrate, potassium picrate, and cesium picrate) in water were prepared at equimolar concentrations (7×10^{-5} M). Absorbance at 356 nm was observed to determine the alkali ion extraction of macrocycles. Figure 3 shows the alkali ion-extraction abilities of **3**–**6**. Macrocycle **3** shows an alkali ion-extraction ability of about 40%, corresponding to the 5:2 host–guest stoichiometry obtained from the molar ratio method reported in our previous work.[9] In contrast, macrocycles **4** and **5** show an ion-extraction percentage at about 10%. In the case of **6**, the macrocycle shows an alkali ion-extraction efficiency of about 40%, which is similar to that of **3**. The results suggest that **3** and **6** show higher alkali ion-extraction abilities than **4** and **5**. This might be due to i) an increase of electron donor atoms (from two to three O atoms) or ii) an increase of the macrocyclic size (from 12-, 13-, to 14-membered ring). However, considering the differences in the structures of **3** and **6**, it is also important to note that the change of the alkyl chain at the aza position from methyl to propyl has no effect on alkali ion-extraction abilities. Presently, we are putting our effort into clarifying the host–guest complexes, based on the single crystal structure of these host–guest compounds, to confirm our speculation.

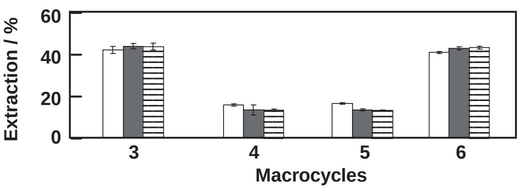


Figure 3. Extraction percentage of (□) sodium picrate, (■) potassium picrate, and (▤) cesium picrate by **3**–**6** in $CHCl_3$ at a concentration of 7×10^{-5} M, observed at 356 nm.

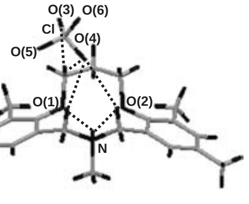


Figure 4. Crystal structure of **7**.

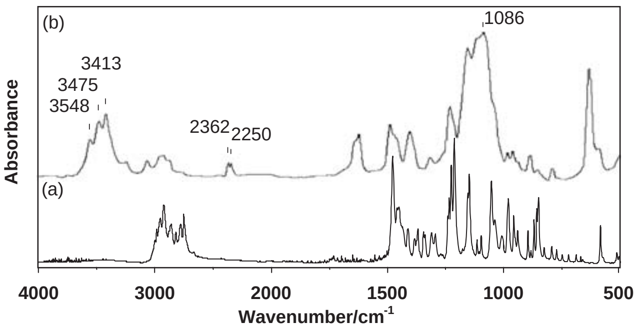


Figure 5. FTIR spectra of (a) **4** and (b) **7**.

Mason and Eick showed that 12-crown-4 formed a complex with sodium perchlorate.[12] The crystal structure indicated that two of the 12-crown-4 rings sandwiched a sodium ion. Considering this for our work, the 12- and 13-membered macrocycles **4** and **5** may form a similar sandwich structure. Compounds **4** and **5** were recrystallized in methanol containing $NaClO_4$, as we expected the incorporation of sodium ion in the host. To our surprise, **4** gave a crystal structure of an ion-pair between the protonated form of **4** at N atom and perchlorate anion to be **7**.

Figure 4 illustrates the molecular structure of **7**, which indicates that the ion-pair structure is stabilized under N^+–H···O and C–H···O hydrogen bonds. Indirect evidence, e.g. FTIR, was also obtained. Compared to the FTIR spectrum of **4** (Figure 5a), **7** shows peaks with significant differences at 3600–2000 cm^{-1} (Figure 5b). As the high-frequency peaks at 3600–3400 cm^{-1} are sharp, it is difficult to interpret them as the general cases of O–H···O involving water molecules. Because ClO_4^- is incorporated in **7**, as shown in Figure 4, we speculated that **7** is protonated at the aza group to give the ionic interaction in terms of N^+–H···$OClO_3^-$, resulting in the significant peaks at 3548, 3475, and 3413 cm^{-1}. This speculation is also supported by the peaks at 2362 and 2250 cm^{-1} (tertiary amine salt) and at 1086 cm^{-1} (ClO_4^-).[13,14] In the case of **5**, no inclusion was observed. In other words, 13-membered macrocycle did not show anionic-guest inclusion. Up to the present, we have found that the HBA-based macrocycles accept various types of metal ions;[6,7,9] however, here is the first time to see the guest species as anion.

Božić et al. reported that the host–guest system of a mixed dioxa–diaza macrocycle and sodium salts, NaX (X = ClO_4, BF_4, PF_6, and SCN), in methanol gave ion-pair compounds containing the cation of protonated macrocyclic ligand and the anion of sodium salt.[13] Crystallograpic and infrared spectroscopic data indicated that the proton-to-ligand ratio was 1:1. Based on this viewpoint,[13] we suspect that **4** may provide a similar host–guest system to accept the anionic species. At present, other host-anions of **4**, for example NaSCN, to confirm the protonation and anionic-guest acceptance are under investigation.

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10 Spectroscopic results of macrocycles **4**–**6** were shown as follows. **4**: 80% yield; mp 124.5 °C; FTIR (KBr, cm^{-1}): 1480 (vs, tri-substituted benzene), 1213 (vs, C–N stretching), 1053 (s, C–O–C); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.94 (3H, s, N–CH_3), 2.11 (2H, t, CH_2–CH_2–CH_2), 2.25 (12H, s, Ar–CH_3), 3.62 (4H, s, Ar–CH_2–N), 4.11 (4H, t, Ar–O–CH_2), 6.79 (2H, s, Ar–H), 6.91 (2H, s, Ar–H). MALDI-TOF MS: m/z 340.23 $[M+H]^+$.; Anal. Calcd for $C_{22}H_{29}NO_2$: C, 77.84; H, 8.61; N, 4.13%. Found: C, 77.63; H, 8.40; N, 4.12%. **5**: 76% yield; mp 172.8 °C; FTIR (KBr, cm^{-1}): 1481 (vs, tri-substituted benzene), 1213 (vs, C–N stretching), 1076 (s, C–O–C); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.96 (3H, s, N–CH_3), 2.00 (4H, t, O–CH_2–CH_2), 2.25 (15H, s, Ar–CH_3, N–CH_3), 3.55 (4H, s, Ar–CH_2–N), 4.01 (4H, t, O–CH_2–CH_2), 6.85 (2H, s, Ar–H), 6.92 (2H, s, Ar–H). MALDI-TOF MS: m/z 354.13 $[M+H]^+$.; Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.15; H, 8.84; N, 3.96%. Found: C, 77.35; H, 8.82; N, 3.88%. **6**: 90% yield; mp 100.8 °C; FTIR (KBr, cm^{-1}): 1482 (vs, tri-substituted benzene), 1214 (vs, C–N stretching), 1057 (s, C–O–C); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 0.73 (3H, t, N–C_3H_7), 1.41–1.48 (2H, m, N–C_3H_7), 2.26 (12H, s, Ar–CH_3), 2.34 (2H, t, N–C_3H_7), 3.87 (4H, t, CH_2–O–CH_2), 3.93 (4H, s, Ar–CH_2–N), 4.03 (4H, t, Ar–O–CH_2), 6.82 (2H, s, Ar–H), 6.88 (2H, s, Ar–H). MALDI-TOF MS: m/z 398.27 $[M+H]^+$.; Anal. Calcd for $C_{25}H_{35}NO_3$: C, 75.53; H, 8.87; N, 3.52%. Found: C, 75.24; H, 8.76; N, 3.49%.

11 Crystallographic data reported in this manuscript have been deposited with Cambridge Crystallographic Data Centre as supplementary publication number CCDC 671193 (**4**), 671194 (**5**), 692237 (**6**), and 692236 (**7**). Copies of the data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

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