Synthesis of Amidocrownophanes with 27- and 28-Membered Rings and Their Molecular Recognition toward Urea and its Derivatives

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Novel crownophanes with 27- and 28-membered rings having two hydroxyl groups, two amide groups, and aromatic moieties such as naphthalene, pyridine, and phenyl rings were successfully synthesized by a one-step reaction from the corresponding macrocyclic polyethers *via* "tandem Claisen rearrengement" in moderate yields. They can solubilize urea and its derivatives into chloroform solution, while the corresponding macrocyclic polyethers do not solubilize them. According to NMR studies, crownophanes **1** and **2** interact with urea and its derivatives forming 1:1 complexes.

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Introduction.

Macrocycles which have rigid aromatic moieties and flexible oligoethylene glycol parts within the macrocyclic rings are called "crownophanes" [1]. These structurally-hybridized macrocycles are expected to exhibit special functions or properties which are different from those of basic macrocycles such as crown ethers [2], cyclophanes [3], calixarenes [4], and spherands [5].

Several interesting properties of crownophanes having one or more phenol moieties have been reported so far [6-8]. Furthermore, they are extensively studied from the viewpoints of molecular recognition, artificial catalysts, supramolecular structures and so on [9]. In order to realize the molecular recognition, the design of host molecules for specific guests is one of the most important points. Although most of the complexation studies with crown ethers starting from the pioneering work by Pedersen [10] have concentrated on metal cations [11], organic cations [12] and anions [13] as the guest species, there is also a significant interest in the complexation of neutral molecules [14]. In the biological systems, weak interactions such as H-bonding, van der Waals forces and electrostatic interactions are mainly responsible for complexation of receptors with organic substrates. In particular, H-bonding plays a very important role in the molecular recognition toward organic molecules. Therefore, precise design of host molecules exhibiting H-bonding ability is very important in these kinds of studies.

In our work, we designed and succeeded in synthesizing crownophane type derivatives **1, 2** and **3** *via* "tandem Claisen rearrangement (TCR)"[15-20] which consist of 27- and 28-membered rings containing cyclophane and oligoethylene glycol units, two hydroxyl groups and two amide groups. Moreover, pyridine or phenyl group is introduced into the macrocycles as a part of the ring. They could be expected to exhibit high affinity and good selectivity not only for ionic guest species but also for neutral organic molecules, because both proton donating and accepting groups existing within the macrocycles can form H-bonding with guest molecules. In particular, introduction of amide groups is expected to result in strengthening of hydrogen bonding for the specific guests.

In one of the first papers on crown ether chemistry, Pedersen showed that urea interacts with simple crown ethers such as benzo-18-crown-6 [21]. After that, although there have been reported many macrocycles which can exhibit molecular recognition with neutral molecules, there is no report of macrocyclic receptor as shown in Figure 1. Using our designed and synthesized macrocyclic receptor having both proton donating and accepting groups, we investigated their molecular recognition properties with some neutral organic guest molecules such as urea and urea derivatives. As guest species of urea derivatives, we selected thiourea, ethylene urea, propylene urea and glutarimide for complexation.

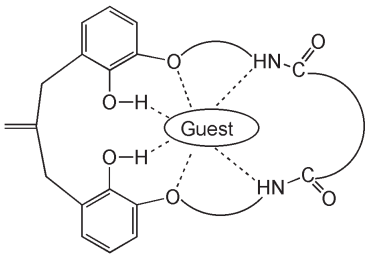


Figure 1. Molecular recognition using multi-H bonding interactions.

Results and Discussion.

Synthesis of Amidocrownophanes.

In this study, we prepared three amidocrownophanes **1**~**3** in order to compare either the hetero atom effect or ring size effect, where **1** and **2** have a 28-membered and **3** has a 27-membered ring.

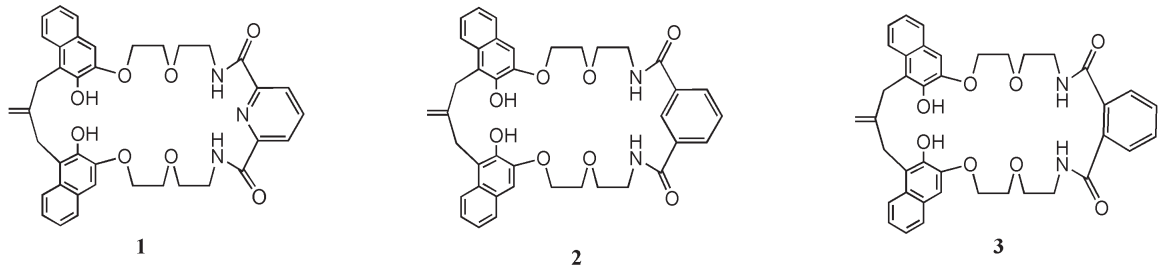
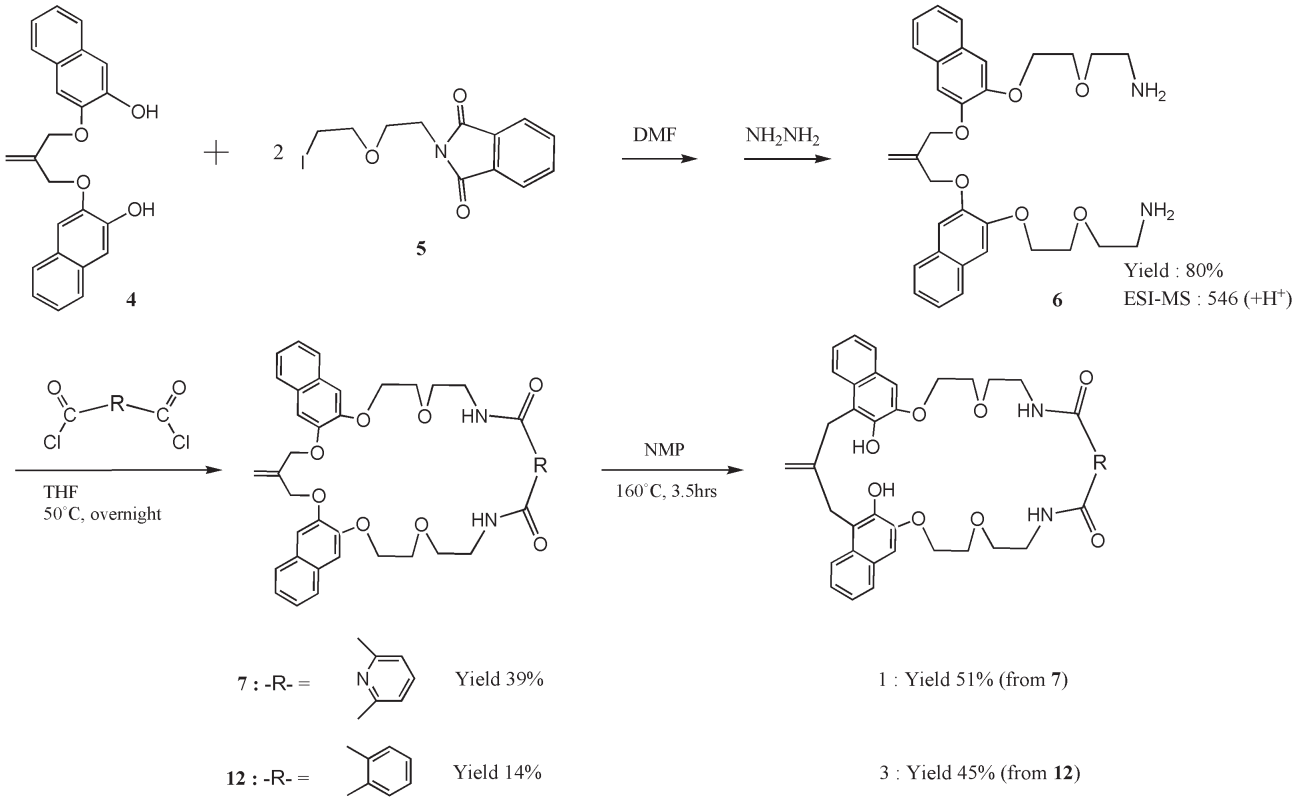


Figure 2. Structures of 28-membered and 27-membered ring crownophanes.

The 28-membered macrocyclic polyether **7** was prepared from diamine **6** and 2,6-pyridinedicarbobonyl dichloride under high dilution conditions as shown in Scheme 1. To find out the role of the nitrogen atom of the pyridyl group, a macrocycle having an *m*-phenylene group was introduced for comparison. Macrocyclic polyether **11** was obtained by the reaction between ditosylate **10** and 2-methylene-1,3 bis(3-hydroxynaphthyl-2-oxy)propane (**4**) using Cs_2CO_3 and KI in DMF under high dilution conditions as shown in Scheme 2. Furthermore, in order to find out the effect of the introduced benzene moiety, macrocycle **12** was prepared in a similar manner by the reaction of **6** with phthalic acid dichloride under high dilution conditions (see Scheme 1). By thermal reaction of the macrocyclic polyethers, **7**, **11** and **12** at 160 ºC, 3.5 hrs in *N*-methyl-2-pyrrolidinone (NMP), the corresponding crownophanes **1-3** were successfully obtained in moderate yields, respectively.

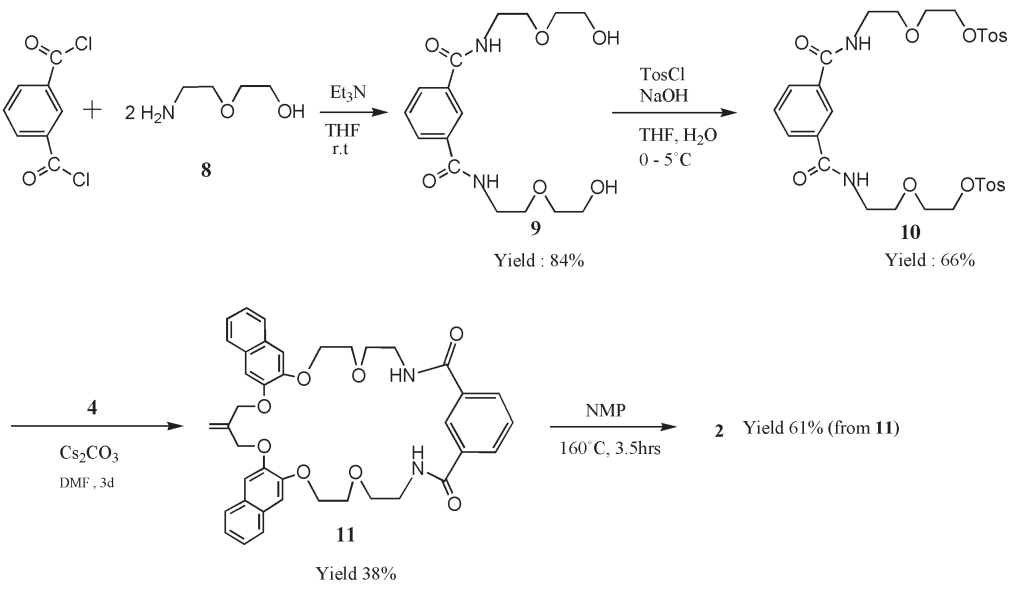
From the ^{1}H NMR spectra shown in Figures 2, 3 and 4, it is clear that macrocycles **7, 11** and **12** were successfully converted into crownophanes **1, 2** and **3** by thermal reaction, relatively. After tandem Claisen rearrangement (TCR), chemical shifts and line shapes of the proton signals changed drastically, and new peaks appeared due to the phenolic OH protons in the NMR spectra. The peaks based on the isobutenyl unit shifted upfield significantly, attributed to the formation of *C*-isobutenyl bonds from *O*-isobutenyl bonds. Products **1, 2** and **3** were con-

Scheme 1



Synthetic route of novel crownophanes *via* macrocyclic polyethers.

Scheme 2



Synthetic route of novel crownophanes **2** and **11**.

firmed by ESI mass, ^{1}H NMR spectral data, IR spectral data and elemental analysis. In the elemental analysis it was observed that products **1-3** contain H_2O molecules. This is probably because they preferably form H-bonding with H_2O for the existence of hydroxyl groups, amide groups and ether oxygen atoms into the crownophanes.

Complexation with Urea and its Derivatives.

We tested the interaction of macrocycles **1~3, 7, 11** and **12** with urea and urea derivatives such as thiourea, propylene urea, ethylene urea and glutarimide using the NMR technique. In each of the NMR sample tubes, we mixed up the macrocycles and the guest species in $CDCl_3$ respectively. After sonification, and keeping the sample tubes overnight, we measured their ^{1}H NMR and obtained the following results, which are shown in Tables 1 and 2. The chemical shifts of amidocrownophanes **1** and **2** clearly changed when adding guest molecules, while amidocrownphane **3** and crown ether derivatives before

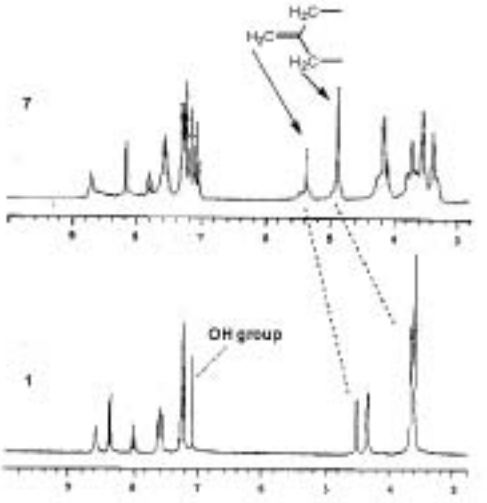


Figure 2**(Second Fig 2)**. ^{1}H NMR spectra of crownophanes **7** (before TCR) and **1**(after TCR).

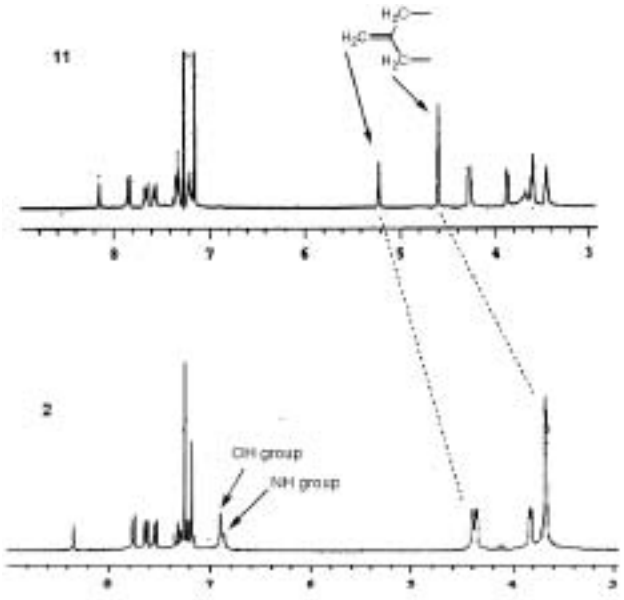


Figure 3. ^{1}H NMR spectra of crownophanes **11** (before TCR) and **2** (after TCR).

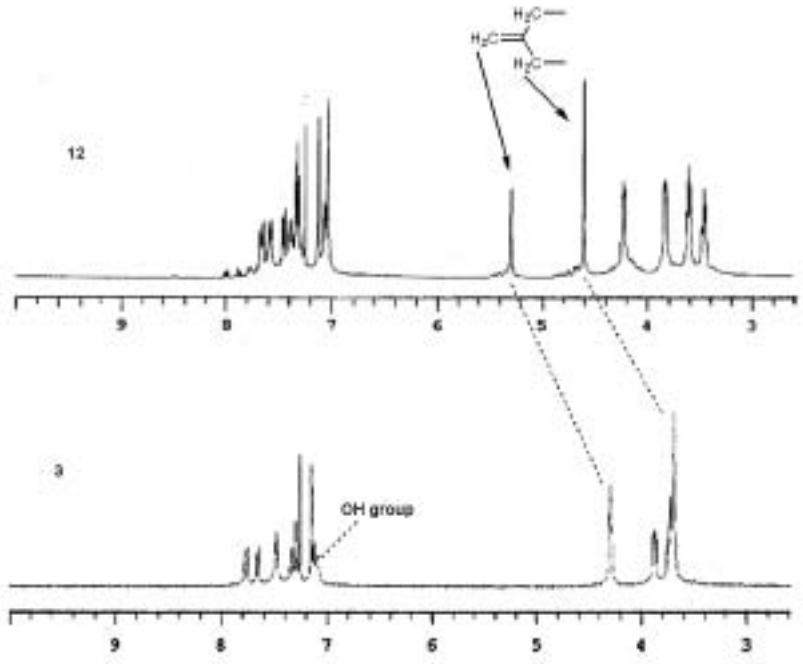
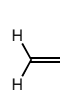
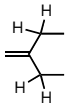
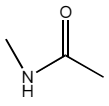
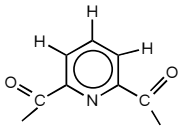
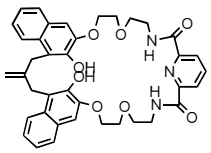
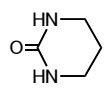
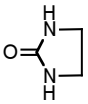
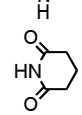


Figure 4. ^{1}H NMR spectra of crownophanes **12** (before TCR) and **3**(after TCR).

Table 1

^{1}H NMR Chemical Shift Values Between Free Ligand (**1**) and Ligand (**1**) with Guest Molecules

Ligand **1** / Ligand **1** with guest molecules.			—OH	Ethylene glycol chain Ar-O-C*H*$_2$-C*H*$_2$-O *2	-NH-C*H*$_2$-C*H*$_2$-O *2			Chemical shift of Guest Molecules
 **1**	4.55 (2H, s)	3.69 (4H, s)	7.06 (2H, s)	4.39 (4H, m)	3.64 (12H, m)	8.55 (2H, s)	8.00(1H, t) 8.37(2H, d)	
1 + 	4.48	3.77	*1	4.36 3.72	3.68	8.95	7.98 8.35	6.93 (N-H)
1 + 	4.34	3.81	*1	4.34 3.79	3.73	8.71	8.00 8.37	5.91 (N-H)
1 + 	4.48	3.76	7.18	4.35	3.70	9.02	7.97 8.32	4.85 (N-H) 3.30 (N-CH$_2$) 1.87 (C-CH$_2$-C)
1 + 	4.49	3.76	*1	4.35	3.70	8.86	7.95 8.32	Undetected (N-H)
1 + 	4.49	3.78	7.15	4.36	3.65	8.88	7.95 8.30	8.53 (N-H)

*1 After addition of guest molecules, peak of hydroxyl groups of the ligand **1** was disappeared. This is probably due to the severe broadening of hydroxyl groups after complexation; *2 Values of the chemical shifts are taken in the center of the peaks.

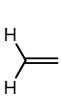
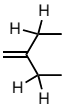
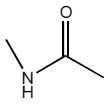
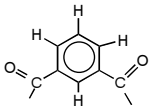
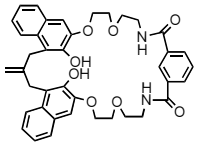
TCR **7**, **11**, and **12** did not show any change in the NMR spectrum by adding urea and urea derivatives. This phenomenon shows the lack of strong electron donating components such as hydroxyl groups, which are formed after the "tandem Claisen rearrangement (TCR)". Surprisingly, **3** was the only compound where no change in the NMR spectra was observed when adding urea and urea derivatives among crownophanes, **1~3**. Therefore, it is assumed that there is some structural effect among them.

cal shifts of –OH groups. NH protons of amide groups also showed downfield chemical shifts after the incorporation of guest species. In addition, new peaks were observed based on the amino protons and the methylene protons of the guest molecules.

^{1}H NMR titration experiment of crownophane **2** and ethylene urea as guest was carried out in $CDCl_3$. From the chemical shift data, it was shown that the complexation of ligand **2** with ethylene urea gives only one species of the

Table 2

^{1}H NMR Chemical Shift Values Between Free Ligand (**2**) and Ligand (**2**) with Guest Molecules

Ligand **2** / Ligand **2** with guest molecules.			—OH	Ethylene glycol chain Ar-O-C*H*$_2$-C*H*$_2$-O	-NH-C*H*$_2$-C*H*$_2$-O *2			Chemical shift of Guest Molecules
 **2**	4.41 (2H,s)	3.69 (4H, s)	6.90 (2H, s)	4.37 (m) 3.83 (m)	3.68 (m)	6.89 (2H, t)	8.35 (1H, s) 7.76(2H, d) 7.32 (1H, t)	
2 + 	4.40	3.72	6.93	4.35 3.84	3.68	7.11	8.34 7.77 7.31	4.83 (N-H)
2 + 	4.39	3.70	7.02	4.36 3.85	3.70	6.98	8.33 7.76 7.30	6.27 (N-H)
2 +	4.40	3.73	7.20	4.35 3.86	3.71 3.73	7.197	8.39 7.83 7.35	5.00 (N-H) 3.23~3.27(N-CH$_2$-) 1.87 (C-CH$_2$-C)
2 + 	4.39	3.70	*1	4.36 3.84	3.70	7.03	8.35 7.77 7.38	Undetected (N-H)
2 + 	4.40	3.71	7.07	3.89	3.71	7.16	8.38 7.81 7.34	8.48 (N-H)

*1 It was not possible to detect the chemical shift of hydroxyl group probably due to the severe broadening after addition of guest molecule; *2 Values of the chemical shifts are taken in the center of the peaks.

In fact, protons of these groups obviously shifted in the ^{1}H NMR spectra which are summarized in Tables 1 and 2. The large chemical shift values were observed by the complexation of the crownophane **1** with urea and propylene urea. Propylene urea is soluble in $CDCl_3$, however after complaxation, the chemical shift of amino groups and methylene groups change to downfield shift {NH : δ: 4.85 ppm (in the case of **1**), 5.00 ppm (in the case of **2**), -CH_2-; δ: 1.87 ppm}. The chemical shift of the amide protons of crownophane **1** drastically changes to downfield shift (δ: 9.02 ppm) compared to the amide protons of the free ligand (δ : 8.55 ppm). Similarly, the OH protons of ligand **1** change from δ: 7.06 to 7.18 ppm probably due to complexation between them. On the other hand, in the ^{1}H NMR spectrum of crownophane **2**, the OH protons after complexation with the guests, showed downfield chemi-

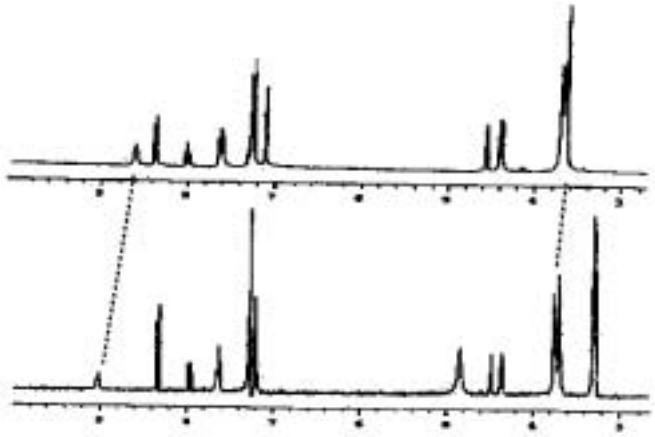


Figure 5. ^{1}H NMR spectra of complexation between ligand **1** and propylene urea

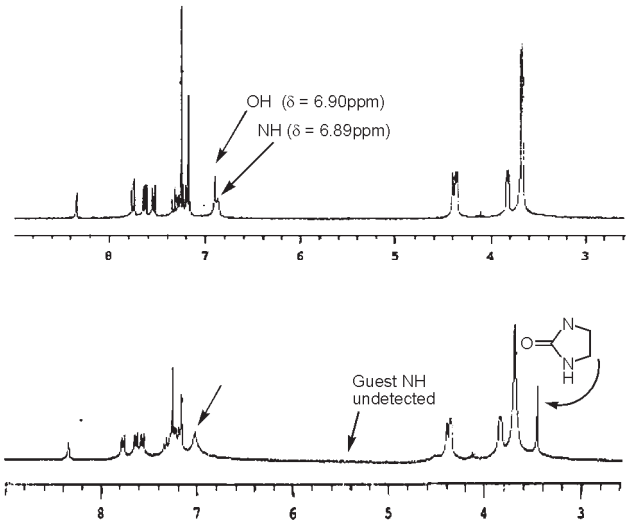


Figure 6. ^{1}H NMR spectra of complexation between ligand **2** and ethylene urea.

complex. Figure 7 shows that ligand **2** forms 1:1 complex with ethylene urea.

In conclusion, we have synthesized novel 28-membered ring size crownophanes **1** and **2** acting as the receptor for neutral guest molecules such as urea and urea derivatives based on the rigid disposition of hydrogen bonding groups

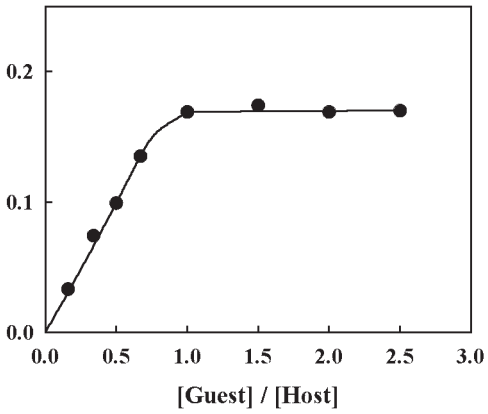


Figure 7. ^{1}H NMR titration experiment between ligand **2** as host and ethylene urea as guest.

in the interior of the macrocyclic scaffold. On the contrary, crownophanes **7**, **11** and **12** have no complexation ability due to the absence of hydroxyl groups indicating that these groups play an important role in the formation of strong complexes. We also have shown the ability of crownophanes **1** and **2** to dissolve urea and thiourea into the less polar solvent chloroform, whereas crownophane **3** does not have that ability at all. The host molecules **1** and **2** with incorporation of the ability for bio-molecules and their derivatives are expected to be used for molecular sensor and separating reagent.

EXPERIMENTAL

General Procedure.

Commercially available reagents were purchased from Wako, Aldrich, TCI, and Cica, and used without further purification. Melting points were taken on Micro melting point apparatus and are not corrected. ^{1}H NMR spectra were recorded with a Varian (300MHz) spectrometer in $CDCl_3$ using TMS as an internal standard. All chemical shifts are given in parts per million relative to tetramethylsilane (δ, 0.00 ppm). Electrospray ionization mass spectra (ESI-MS) were performed in the following conditions: a sample solution was sprayed at a flow rate of 2 μL min^{-1} at the tip of needle biased by a voltage of 4.5 KV higher than that of a counter electrode. IR spectra were obtained on a FT/IR-430 spectrometer. Elemental analyses were obtained on a Fisons EA1108 CHNS-O. The silica gel for the column chromatography was from Cica-silica gel 60 (63-210 μm). The progress of the reactions was followed by TLC using Merck silica gel 60 F_{254}.

Synthesis of Macrocyclic Polyether **7**.

Solutions (100 ml THF) of diamine **6** (1.83 mmol) and 2,6-pyridinedicarbobonyl dichloride (1.83 mmol) were simultaneously added dropwise to the solution of THF (350 ml) containing Et_3N (3.65 mmol) as a base at 50 ºC in 5-6 hours. After the addition was complete, the reaction mixture was stirred overnight. The solvent was removed under reduced pressure. The residue was dissolved in $CHCl_3$, washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation of $CHCl_3$, the residue was subjected to column chromatography on silica gel using AcOEt:$CHCl_3$ (1:3) as an eluent. Further purification was performed using GPC (Gel Permeation Column Chromatography) with $CHCl_3$ as an eluent. Macrocycle **7** was obtained as the main product. Colorless solid; yield 39%; R_f=0.28; m.p. 86-87 ºC; ^{1}H NMR: δ 3.39 (C*H*$_2$-NH, 4H, m), 3.55 (O-C*H*$_2$-CH$_2$-NH, 4H, m), 3.73 (O-C*H*$_2$-CH$_2$-, 4H, m), 4.19 (Ar-O-C*H*$_2$-CH$_2$, 4H, m), 4.90 (=C-CH$_2$-O, 4H, s), 5.39 (C=CH$_2$, 2H, s), 7.09 (Ar-H, 2H, s), 7.18 (Ar-H, 2H, s), 7.3(Ar-H, 4H, m), 7.6(Ar-H, 4H, m), 7.81(Py-H, 1H, t, 8Hz), 8.17 (Py-H, 2H, d, 8Hz), 8.73(NH, 2H, broad); IR (KBr, ν/cm^{-1}): 1663, 1509, 1485, 1258, 1115. ESI-Mass: Calcd. for $C_{39}H_{39}N_3O_8$, [M + Na$^+$]: 700.27. Found: [M + Na$^+$]: 700.4.

Anal. Calcd. for $C_{39}H_{39}N_3O_8$•H_2O: C,68.21; H, 5.87; N, 6.12. Found: C, 67.98; H, 6.05; N, 5.94.

Synthesis of Macrocyclic Polyether **11**.

Cesium carbonate (5.28 mmol), KI (catalytic amount) were placed into a round bottomed flask in dry DMF (300 ml). The flask was placed in the oil bath and was warmed at 70 ºC with stirring. 2-Methylene-1,3-bis (3-hydroxynapthyl-2-oxy)propane (**4)** (2.15 mmol), and compound **10** (2.33 mmol) were dissolved in dry DMF (100 ml) and were placed into an automatic magnetic dropping funnel. The solution was added dropwise over a period of 15 min. Reaction was continued for 3 days maintaining the temperature at 70 ºC. After removal of the solvent under vacuum, the residue was extracted with $CHCl_3$, washed with H_2O and dried over anhydrous Na_2SO_4. After evaporation of $CHCl_3$,

the macrocyclic polyether **11** was isolated by column chromatography eluted with AcOEt: $CHCl_3$ (1:3) followed by GPC eluted with $CHCl_3$. Pale yellow solid; yield 38%; R_f = 0.17; m.p. 85-86 ºC; ^{1}H NMR: δ 3.43~3.48 (N-CH_2-, 4H, m), 3.59~3.62 (-O-CH_2-, 4H, m), 3.87~3.89 (-O-CH_2-, 4H, m), 4.27~4.29 (Ar-O-CH_2-, 4H, m), 4.60 (=C-CH_2-O-, 4H, s), 5.22 (C=CH_2, 2H, s), 7.15 (Ar-H, 4H, s), 7.20 (Ar-H, 1H, t, 8Hz), 7.21 (NH, 2H, broad), 7.31~7.35 (Ar-H, 4H, m), 7.57 (Ar-H, 2H, d, 7Hz), 7.66 (Ar-H, 2H, d, 7Hz), 7.85 (Ar-H, 2H, d, 8Hz), 8.15 (Ar-H, 1H, s); IR (KBr, ν/cm^{-1}): 1648, 1509, 1484, 1256, 1115. ESI-Mass: Calcd. for $C_{40}H_{40}N_2O_8$, [M + Na$^+$]: 699.28. Found: [M + Na$^+$]: 699.4.

Anal. Calcd. for $C_{40}H_{40}N_2O_8$•H_2O: C, 68.28; H, 6.13; N, 3.98. Found: C, 68.38; H, 6.10; N, 3.96.

Synthesis of Macrocyclic Polyether **12**.

Procedure is the same as that described for macrocyclic polyether **7**. White solid; yield 14 %, R_f = 0.19. m.p. 183-184 ºC; ^{1}H NMR: δ 3.44~3.48 (NH-*C*H_2-, 4H, m), 3.57~3.62(O-CH_2-C*H*$_2$-N, 4H, m), 3.82~3.88 (-CH_2-O-CH_2-, 4H, m), 4.22~4.25 (Ar-O-C*H*$_2$-CH_2-O, 4H, m), 4.60 (=C-CH_2-O, 4H, s), 5.29 (C=CH_2, 2H, s), 7.00~7.14 (Ar-H & NH, 6H, m), 7.3~7.4 (Ar-H, 6H, m), 7.45~7.50 (Ar-H, 2H, m), 7.6~7.7 (Ar-H, 4H, m); IR (KBr, ν/cm^{-1}): 1651, 1508, 1485, 1257, 1114. ESI-Mass: Calcd. for $C_{40}H_{40}N_2O_8$, [M + H$^+$]:677.28. Found: [M + H$^+$]: 677.0

Anal. Calcd. for $C_{40}H_{40}N_2O_8$•H_2O: C, 70.06; H, 6.03; N, 4.08. Found: C, 69.98; H, 6.23; N, 3.92.

Synthesis of Crownophane **1**.

After tandem Claisen rearrangement, macrocycle **7** was converted to target crownophane **1** using NMP as solvent at 160 ºC for 3.5 hours under Argon atmosphere. The solvent (NMP) was removed under reduced pressure. The residue was subjected to column chromatography on silica gel using AcOEt:$CHCl_3$ (1:1) as an eluent. Compound **1** was obtained as the main product. Colorless crystal; yield 51%, R_f = 0.17; m.p. 221-222 ºC; ^{1}H NMR: δ 3.6~3.7 (CH_2-CH_2-O, 12H, m), 3.69 (=C-CH_2-Ar, 4H, s), 4.37~4.40 (Ar-O-C*H*$_2$-CH_2, 4H, m), 4.55 (C=CH_2, 2H, s), 7.06 (OH, 2H, s), 7.2~7.3 (Ar-H, 8H, m), 7.55~7.63 (Ar-H, 4H, m), 8.00 (Py-H, 1H, t, 8Hz), 8.37 (Py-H, 2H, d, 8Hz), 8.55 (NH, 2H, broad); ^{13}C NMR: δ 31.58, 68.40, 70.68, 71.42, 110.82, 112.28, 118.20, 123.58, 124.79, 125.08, 127.27, 128.77, 130.21, 138.66, 145.49, 145.63, 146.12, 148.98, 164.32; IR (KBr, ν/cm^{-1}): 1665, 1541, 1448, 1266, 1070. ESI-Mass: Calcd. for $C_{39}H_{39}N_3O_8$, [M + Na$^+$]: 700.27. Found: [M + Na$^+$]: 700.4.

Anal. Calcd. for $C_{39}H_{39}N_3O_8$•H_2O: C,67.34; H, 5.90; N, 6.04. Found: C, 67.26; H, 5.63; N, 6.07.

Synthesis of Crownophane **2**.

Procedure is the same as that described for the preparation of crownophane **1**. Pale yellow crystal; yield 61%; R_f = 0.08; m.p. 110-111 ºC; ^{1}H NMR: δ 3.6~3.7 (-O-C*H*$_2$C*H*$_2$-O, 8H, m), 3.69 (=C-CH_2-Ar, 4H, s), 3.81~3.84 (Ar-O-CH_2-C*H*$_2$, 4H, m), 4.36~4.40 (Ar-O-C*H*$_2$-CH_2, 4H, m), 4.41 (C=CH_2, 2H, s), 6.89 (NH, 2H, broad), 6.90 (OH, 2H, s), 7.16~7.30 (Ar-H, 4H, m), 7.19 (Ar-H, 2H, s), 7.32 (Ar-H, 1H, t, 6Hz), 7.54 (Ar-H, 2H, d, 8Hz), 7.69 (Ar-H, 2H, d, 8Hz), 7.76 (Ar-H, 2H, d, 6Hz), 8.35 (Ar-H, 1H, s); ^{13}C NMR δ 31.87, 68.74,69.83, 69.94, 109.43, 110.77, 117.93, 123.57, 124.50, 126.53, 127.15, 128.71, 128.91, 129.48, 129.78, 134.79, 144.70, 145.61, 145.96, 167.21; IR (KBr, ν/cm^{-1}): 1647, 1537, 1475, 1449, 1283, 1070. ESI-Mass: Calcd. for $C_{40}H_{40}N_2O_8$, [M + Na$^+$]: 699.28. Found: [M + Na$^+$]: 699.4.

Anal. Calcd. for $C_{40}H_{40}N_2O_8$•H_2O: C, 69.15; H, 6.09; N, 4.03. Found: C, 68.80; H, 5.86; N, 4.19.

Synthesis of Crownophane **3**.

Procedure is the same as that described for crownophane **1**. White solid; yield 45%; Rf = 0.1 ; m.p. 192-193 ºC; ^{1}H NMR: δ 3.66~3.76 (=C-CH_2-O, CH_2-NH & CH_2-O, 4H, m), 3.84~3.90 (O-CH_2, 4H, m), 4.26~4.32 (C=CH_2 & Ar-O-CH_2, 6H, m), 7.09 (OH, 2H, broad), 7.12~7.16 (Ar-H, 2H, m), 7.15 (Ar-H, 2H, s), 7.26~7.36 (Ar-H, 4H, m), 7.46~7.50 (Ar-H & NH, 4H, m), 7.65 (Ar-H, 2H, d, 8Hz), 7.76 (Ar-H, 2H, d, 8Hz); ^{13}C NMR: δ 32.03, 68.12, 68.62, 69.99, 70.16, 109.28, 110. 40, 118.65, 123.27, 124.43, 127.13, 127.83, 128.66, 128.76, 129.86, 129.90, 130.86, 132.40, 135.10, 144.92, 145.75, 146.70, 167.75; IR (KBr, ν/cm^{-1}): 2929, 1728, 1645, 1448, 1284, 1118. ESI-Mass: Calcd. for $C_{40}H_{40}N_2O_8$, [M + H$^+$]: 677.28. Found: [M + H$^+$]: 677.0

Anal. Calcd. for $C_{40}H_{40}N_2O_8$•H_2O: C, 69.15; H, 6.09; N, 4.03. Found: C, 68.87; H, 5.79; N, 4.14.

Synthesis of Diamine **6**.

Diamine was prepared from the reaction between 2-methylene-1,3-bis(3-hydroxynaphthyl-2-oxy)propane and 1-iodo-5-pthalyl-glycol using KOBu-*t* as base in DMF at 70 ºC for 12 hours. After evaporating the solvent and extracting/washing the reaction mixture by $CHCl_3$/H_2O, it was subjected to column chromatography to separate the intermediate product as diphthalimide which was then treated with hydrazine monohydrate and EtOH at room temperature overnight to obtain the expected diamine with high yield (80%). ^{1}H NMR: δ 1.71 (NH_2, 4H, s), 2.80~2.84 (O-CH_2-C*H*$_2$-NH_2, 4H, m), _3.54~3.59 (O-C*H*$_2$-CH_2-NH_2, 4H, m), 3.85~3.90 (O-CH_2-C*H*$_2$-O, 4H, m), 4.2~4.3 (Ar-O-C*H*$_2$-CH_2-O, 4H, m), 4.88(__=C-CH_2-O_ 4H, s),_ 5.51(=C-CH_2, 2H, s), 7.19 (Ar-H, 4H_, s), 7.30~7.35 (Ar-H, 4H, m), 7.57~7.70 (Ar-H, 4H, m).

Synthesis of Compound **10**.

Isophthaloyl dichloride and 2-(2-aminoethoxy)ethanol **8** were treated with Et_3N as base in THF at room temperature for 1-2 hours to obtain compound **9** and it was then converted to compound **10** after tosylation [22]. ^{1}H NMR: δ 2.42(Ar-CH_3, 6H, s), 3.60~3.61(CH_2, 8H, m), 3.68~3.70 (CH_2, 4H, m), 4.19~4.22 (CH_2, 4H, m), 6.91(NH, 2H, s), 7.32 (Ar-H, 4H, d, 8Hz), 7.54(Ar-H, 1H, t, 8Hz), 7.75 (Ar-H, 4H, d, 8Hz), 8.03 (Ar-H, 2H, d, 8Hz), 8.15(Ar-H, 1H, s).

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