A novel crownophane trapping CO_2 as carbonic acid at room temperature†

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A 25 membered crownophane with two hydroxy and two amide groups around the cavity has been reported for the first time to be able to include carbonic acid formed from both carbon dioxide and water molecules to give a stable 1 : 1 complex at room temperature.

The hydration of carbon dioxide is one of the most fundamental reactions in many biological and ecological systems.[1] At neutral pH, the dominant process in the reaction of carbon dioxide and water is the formation of carbonic acid which is in rapid equilibrium with the bicarbonate ion. Even now, very little is known about this important compound. In biological systems the carbon dioxide hydration and the reverse reaction are catalyzed by the enzyme carbonic anhydrase.[2] The mechanism of the enzymatic reaction is, however, still under debate. In the enzyme, carbon dioxide might be included as carbonic acid into the reactive site such as a cavity. To elucidate the mechanism of such biological behavior, it could be helpful and significant to construct a stable recognition site toward carbon dioxide, or carbonic acid composed of both carbon dioxide and water molecules.

In addition, much attention has been paid to carbon dioxide fixation from the viewpoints of environmental problems and biological behavior.[3] Although the development of novel methods for the chemical fixation of CO_2 to carboxylate anion, carbamates, urethanes, *etc.* is ongoing, there are few methods utilizing host–guest chemistry under neutral conditions.[4] Recently, the complexation of *p-tert*-butylcalix[4]arene with CO_2 (not H_2CO_3) has been reported at high pressure (30 MPa).[5] On the other hand, etherated carbonic acid was isolated for the first time as white, snow-like crystals at -78 °C in 1961.[6] In 1965, another research group reported that monodimethyletherate of carbon monoxide bishydroxide (O=C(OH)$_2$/OMe$_2$) is also isolated at -80 °C.[7] To elucidate its structure and properties, the equilibrium geometry and the stability of carbonic acid in the reaction of carbon dioxide with water have also been calculated.[8] However, even now not only has the formation of carbonic acid proved to be rather elusive even at low temperature, but also carbonic acid is still an elusive molecule in the sense that it has defied efforts for its detection in the gas phase by spectroscopic techniques.[9]

We report here on the stable complexation of three components composed of carbon dioxide, water, and a 25-membered ring-macrocycle, namely, crownophane **4** which has two hydroxy and two amide groups in the macrocyclic ring, where carbonic acid is included as a single molecule into the macrocyclic cavity. Crownophane **4** was prepared as shown in Scheme 1. Macrocyclic polyether **3** was prepared in 20% yield by the reaction of isobutenyl binaphthyl ether derivative **1**[10] with dichloride **2** in THF under high dilution conditions. Thermal reaction ("tandem Claisen rearrangement")[11] of **3** in 1-methyl-2-pyrrolidinone (NMP) at 160 °C, 3 h gave crownophane **4** in high yield (80%). The structure of this

compound was confirmed by NMR, IR, ESI-Mass, and elemental analysis.† A 25-membered crownophane **5** used in the CO_2 trapping experiment for comparison is also shown in Scheme 1.[10] Compound **4** has two hydroxy and two amide groups within a 25-membered ring. As previously reported, 22-membered ring crownophane having two hydroxy groups and five ether oxygen atoms can include a single water molecule inside the cavity by four hydrogen bonds.[12] In that case, two hydroxy groups work as the proton donating part for the oxygen atom of the water molecule and ethereal oxygen atoms of the 22-membered ring crownophane work as the proton accepting part for the two hydrogen atoms of the water molecule. In a similar manner, it is expected that 25-membered crownophane **4** might include an appropriate guest molecule which fits the size of the cavity and the position of functional groups for hydrogen bonding.

We tried to make a complex of **4** with carbon dioxide as a guest molecule because carbon dioxide might become carbonic acid in the presence of water. When bubbling carbon dioxide into a chloroform or acetonitrile solution of **4** containing a small amount of water (< 5 v/v%) and standing the sealed flask under a saturated CO_2 atmosphere for a few days, white solids separated out. The IR spectra of the solids before and after CO_2 bubbling change clearly. In particular, several fine peaks appear around 3440 cm^{-1} after CO_2 bubbling which might mean the formation of plural hydrogen bonding with carbonyl and hydroxy groups of carbonic acid. The original crystal showed a broad peak (3334 cm^{-1}) based on phenolic OH and amide NH groups, and the signal at 1656 cm^{-1} due to the original amide carbonyl group of **4** shifted to 1668 cm^{-1} in the solid produced after CO_2 bubbling and its signal strength became large compared to the other peaks.† This means that the additional peak due to the carbonyl group of trapped CO_2 as carbonic acid is accumulated together with the amide carbonyl peak of **4** by coincidence.
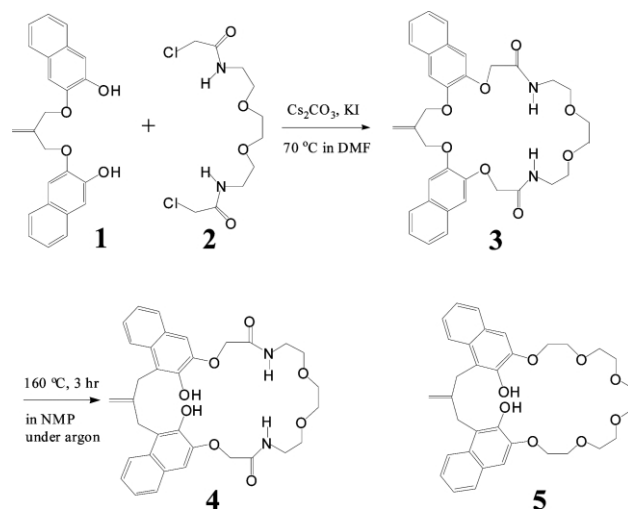
Scheme 1 Reaction process of 25-membered crownophane **4** and the structure of its analog **5**.

In order to confirm the complexation of **4** with CO_2 and H_2O, thermal analyses, DTA and TGA, were conducted in order to clarify the complexation and decomplexation of **4** with carbonic acid by weak interaction.[13] That is, the decrease in weight obtained by TGA analysis and the observation of whether the removal of the guest molecule occurs endothermically or exothermically by DTA analysis allow speculation about the identity of the guest molecule. An 8.6% weight loss by TGA and an endothermic peak by DTA in the temperature range 33 °C to 80 °C were observed.† This weight loss nearly equals the calculated loss (9.36%) of one equimolar carbonic acid in a 1 : 1 complex of **4** with carbonic acid.

Fig. 1 shows the ^{1}H NMR spectrum of **4** before and after bubbling CO_2 gas directly into the NMR tube containing a $CDCl_3$ solution of **4** at room temperature. After CO_2 bubbling for a few minutes, the chemical shifts of the spectrum changed distinctly. That is, the chemical shifts at 3.29 (singlet, O–CH_2CH_2–O), 3.50 (m, NH–CH_2–CH_2–O), and 7.33 (broad, NH) ppm shift to downfield, 3.53 (s, O–CH_2CH_2–O), 3.59 (broad singlet, NH–CH_2–CH_2–O), and 7.75 (broad, NH) ppm, respectively. The downfield shifts of these protons might imply the formation of hydrogen bonding. Additionally, the peak assigned to OH protons (6.78, singlet) completely disappears in the NMR spectrum after CO_2 bubbling. This may mean that a very rapid exchange of protons occurs in solution, that is, there is equilibrium between complexation and decomplexation in solution. Meanwhile, the solids separated out slowly from the solution as a complex of **4** with carbonic acid which could be supported by IR spectrum and thermal analyses. After heating at 50 °C for a few hours, the chemical shifts returned to their original values. Again, when CO_2 was bubbled into the tube, the spectrum accorded completely with the spectrum of the first sample after bubbling with CO_2. This phenomenon was observed repeatedly.

The complexation of **5**[10] with CO_2 and H_2O was also investigated. Compound **5** has the same 25-membered ring as **4**. Using the same conditions as for **4**, we tried to fix carbonic acid, but did not find any proof of interaction from the NMR spectrum and no solids separated out. It should be noticed that the amide groups play a crucial role in fixing carbonic acid at room temperature. We calculated the lowest energy conformer of the complex of **4** with carbonic acid by using Macro Model version 7.0,[14] because we have not yet succeeded in making a single crystal of the complex for X-ray analysis. Fig. 2 shows the optimized conformer obtained by energy minimization using Amber force field and chloroform salvation parameters, where carbonic acid fits the cavity bound with plural hydrogen bonding. Two protons of the hydroxy groups of **4** are located near the carbonyl oxygen atom of the carbonic acid forming hydrogen bonds, and two protons of OH groups of
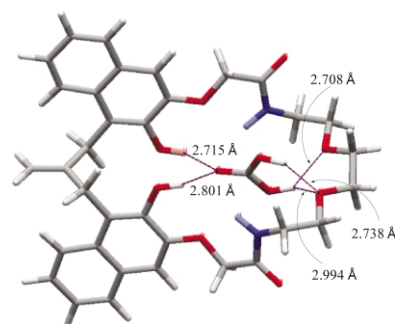

Fig. 2 The calculated structure of the 1 : 1 complex between **4** and carbonic acid. The heteroatom–heteroatom distances are shown in Ångstrom scale.

carbonic acid are located near the ethereal oxygen atoms of the oxyethylene chain. The amide protons might work by hydrogen bonding with the oxygen atoms of carbonic acid to stabilize the complex.

It can be concluded from these results that the solid produced in the way described should be the 1 : 1 complex of **4** with carbonic acid which is formed from CO_2 and H_2O. Two amide groups in the ring might play an important role to make a stable 1 : 1 complex at room temperature. Based on this finding, novel receptors, which can exhibit more stable complexation with carbonic acid, will be designed and synthesized in the near future, and will contribute not only to elucidate the functions of carbonic acid in biological systems, but also to the construction of artificial systems to fix or activate carbon dioxide.

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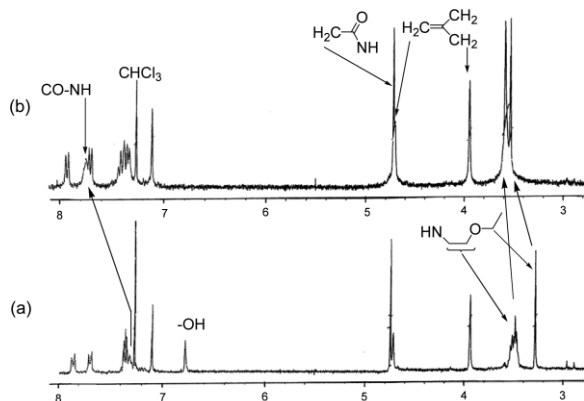
Fig. 1 ^{1}HNMR spectrum of **4** before (a) and after (b) bubbling CO_2 in $CDCl_3$.