Host–Guest Systems

Size-Selective and Reversible Encapsulation of Single Small Hydrocarbon Molecules by a Cavitand–Porphyrin Species**

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Small hydrocarbon molecules are subject to processes of biological isolation, sequestration, and selective reactions that are mediated by biomolecular recognition events.[1] One particularly noteworthy biological process of hydrocarbons is the enzymatic monooxygenation of methane and related small hydrocarbons.[2,3] The mechanisms through which these chemical transformations occur are of particular interest in light of their potential applicability for the development of catalysts for large-scale industrial chemical transformations.[4]

One of the major shortcomings of artificial hydrocarbon-recognition model systems is the absence of the requisite strong interactions between the host and the guest molecules. This feature of hydrocarbons makes the selective recognition processes less efficient. One of the most effective natural mechanisms for the recognition of hydrocarbons is an encapsulation process mediated by capsulelike molecules that have a hydrophobic cavity with a given shape and volume.[5] Various guest-encapsulating carcerands and related molecules have been reported.[6] These compounds typically have rigid enclosed structures and are not suitable for release or exchange of encapsulated guest molecules. For further reaction of the encapsulated guest molecules, the host requires an active site with a flexible portal for guest exchange.

Other researchers have reported host compounds with cup-shaped calix[4]arenes,[7] cavitands,[8] cyclodextrin, etc.[9] that have cavities suitable to accommodate small organic molecules in combination with a flat porphyrin, which acts both as a lid for the cavity and as a ligand for metal ions. These compounds have been demonstrated to encapsulate pyridines, imidazoles, adamantanes, etc.

In work described herein, we have designed a new cavitand–porphyrin **1** as a host compound for smaller hydrocarbons such as methane and ethane. To accommodate small guest molecules and to retain suitable flexibility of the portal, the cavitand and the porphyrin are connected by two ether linkages. With use of **1** as a host, we have successfully demonstrated size-selective and reversible encapsulation of small hydrocarbons within the host cavity.

Williamson-type coupling between A,B-type bis(chloromethyl)cavitand **3**[10] and *meso*-bis(2-hydroxyphenyl)diphenylporphyrin (**4**) (used as a mixture of four regio- and atropisomers: 5,10; 5,15; α,α; and α,β)[11] gave *syn* (**1**, 46% yield based on **3**) and *anti* (**2**, 14% yield) cavitand–porphyrin species (Supporting Information).

The structures of the two isomers were determined by ^{1}H NMR spectra as follows: The ^{1}H NMR signals of all bridged -OCH_2O- protons of the *syn* isomer **1** showed large upfield shifts relative to those of the starting cavitand **3** (H_{ao}, H_{ai}, H_{bo}, and H_{bi}: $\Delta\delta = -3.41$, -5.65, -0.52, and -2.42 ppm, respectively) owing to the large anisotropic effect of the porphyrin ring current (Supporting Information). This observation suggests that the cavitand and porphyrin moieties of **1** adopt a fully overlapping geometry and that the portal is very narrow.

We examined the encapsulation of various small hydrocarbon molecules in **1** (Figure 1). Upon exposure of CH_4 gas to a solution of **1** in $CDCl_3$, a new proton signal appeared at $\delta = -7.19$ ppm (Figure 1b), which disappeared when Ar was bubbled into the solution.[12] The large upfield shift ($\Delta\delta = -7.34$ ppm) from the signal of free methane ($\delta = 0.15$ ppm) is rationalized by anisotropic effects arising from both the cavitand and porphyrin aromatic ring systems which are

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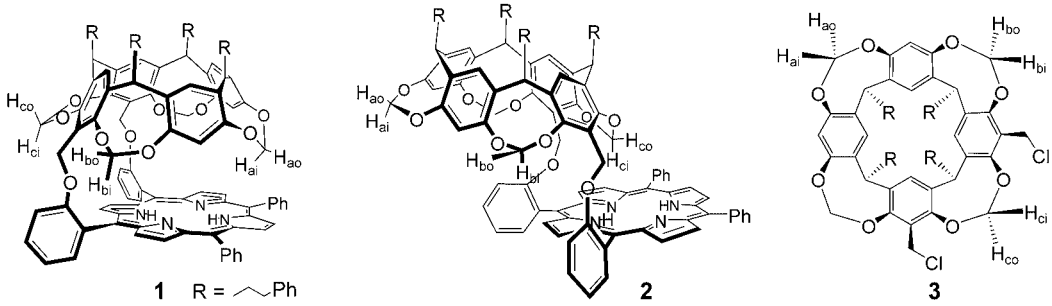

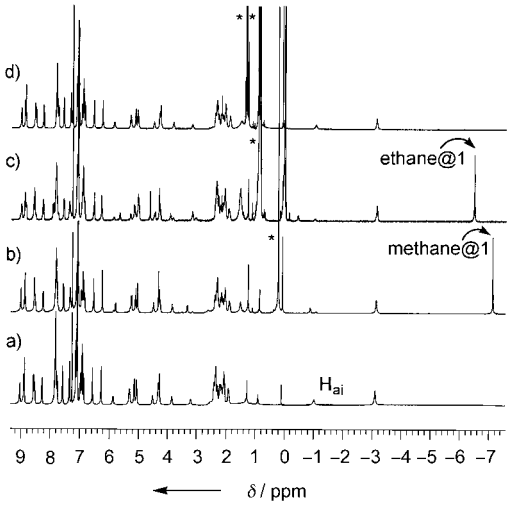

Figure 1. ^{1}H NMR spectra of **1** with hydrocarbons in $CDCl_3$ under atmospheric pressure at 25 °C. a) **1**, b) **1** with methane, c) **1** with ethane, d) **1** with propane. *Signals of the free hydrocarbons.

estimated to contribute to the upfield shift of the signal for the encapsulated molecule by $\delta = -3$–-4[5b,c,13] and $\delta = -4$–-5 ppm,[14] respectively. Thus, the signal at $\delta = -7.19$ ppm is assigned to the protons of the encapsulated methane molecule. Only one CH_4 molecule was trapped in the cavity, as confirmed by the integration ratio of the ^{1}H NMR signals. Furthermore, the solvent $CDCl_3$ is not trapped in the cavity, as confirmed by ^{13}C NMR spectroscopy.

The perfect separation of the signals corresponding to free and encapsulated methane protons indicates that the guest-exchange rate in **1** with the bulk solvent phase is slower than the ^{1}H NMR timescale. The fact that CH_4 is trapped in and purged from the cavity when CH_4 or Ar, respectively, are bubbled into the solution suggests that the portal of the cavity has enough flexibility to exchange the encapsulated guest.

Encapsulation of other small hydrocarbons in **1** was also observed, as indicated by the ^{1}H NMR chemical shifts of various encapsulated small hydrocarbons in **1** (Table 1). Ethane, ethylene, acetylene, and cyclopropane encapsulated by **1** give rise to signals upfield to those for the protons of the free hydrocarbons. However, addition of either propane or CH_2Cl_2 to the solution of **1** does not cause an upfield shift of the proton signals, indicating that **1** cannot encapsulate hydrocarbons larger than cyclopropane.

Each proton signal of the encapsulated hydrocarbon appears as a sharp singlet, thus indicating that the encapsulated hydrocarbons in the cavity of **1** are capable of free rotation.

Table 1: ^{1}H NMR chemical shifts[a] and binding constants K_{11}[b] of hydrocarbons in **1**.

Guest	δ_{free} [ppm]	$\delta_{@1}$ [ppm]	$\Delta\delta$ [ppm]	K_{11} [M^{-1}]
methane	0.15	−7.19	−7.34	81 ± 18
acetylene	1.91	−5.37	−7.28	130 ± 20
ethylene	5.39	−2.07	−7.46	49 ± 5
ethane	0.85	−6.49	−7.34	9.4 ± 1.4
cyclopropane	0.23	−6.95	−7.18	9.6 ± 2.3
propane	1.31, 0.88		–[c]	

[a] Chemical shifts relative to TMS in $CDCl_3$. [b] Conditions: [**1**] = 5 mM in $CDCl_3$ at 25 °C, 1 atm. [c] Not encapsulated.

Upon the encapsulation of hydrocarbons, the ^{1}H NMR signals of the peripheral protons of the cavitand moiety of **1** undergo a downfield shift. In particular, a remarkable downfield shift is observed for H_{ai} for the cavitand -OCH_2O- segment (Figure 1),[15] that is located closest to the porphyrin plane and which acts as a sensitive marker of the portal shape. The magnitude of this shift shows a positive correlation with guest volumes[16] (Figure 2). This is attributed to a process in which the cavitand is forced to move away from the porphyrin plane upon complexation with a guest molecule. A concomitant decrease in the porphyrin anisotropic effect accompanies this movement.

To evaluate the affinity and selectivity of guest binding of **1**, we determined the 1:1 binding constant K_{11} of the

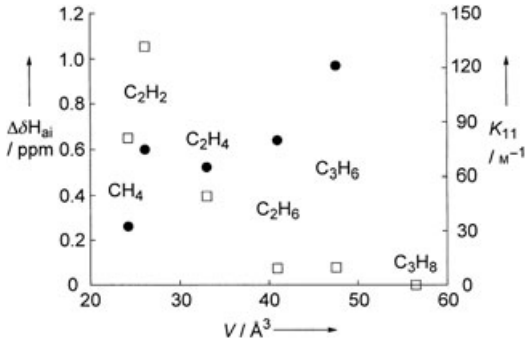

Figure 2. ^{1}H NMR chemical shift difference $\Delta\delta H_{ai}$ (●) and binding constant K_{11} (□) versus guest molecular volume *V*. $\Delta\delta H_{ai} = \delta(H_{ai}$ of hydrocarbon@**1**$) - \delta(H_{ai}$ of **1**$)$. Guest volumes (Connolly solvent-excluded volumes) were estimated according to the method described in reference [16].

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hydrocarbon encapsulation. The K_{11} values are shown in Table 1. Acetylene exhibits the greatest affinity of encapsulation in the cavity, and the binding constants decrease in the following order: acetylene ≫ methane > ethylene ≫ cyclopropane ≈ ethane. Among the saturated hydrocarbons examined in this work, large differences in K_{11} values were observed (methane/ethane/propane = 8.6:1.0:≈0). The selectivity of encapsulation appears to be related to the volume and shape of the guest molecules. Figure 2 shows the plot of K_{11} versus molecular volumes[16] for various hydrocarbons. An inverse correlation is observed between K_{11} and guest volumes for most of the small hydrocarbons examined. However, the remarkable large binding constant of acetylene cannot be explained only in terms of molecular volume. Since the acetylene protons favor stronger CH/π interactions with electron-rich aromatic π systems that act as electron donors,[17] the high affinity of acetylene may be due to this attractive effect induced by the aromatic walls of the host molecule.

Prior to this work, the cavitand compound with the smallest cavity observed was the benzene-capped cavitand reported by Paek et al.[5b] This compound encapsulates a wide range of guest sizes, from methanol to tetrahydrofuran to *n*-propanol (K_{11} = 238, 14, and 3 M^{-1}, respectively, measured at −40 °C). However, **1** has an even smaller cavity and narrower portal, and shows higher selectivity for small guest molecules.

In summary, we have synthesized a new capsule-shaped host **1**, which can selectively and reversibly bind a single hydrocarbon molecule of sizes ranging from methane to cyclopropane. The binding constants are inversely correlated with the molecular volumes of the guest hydrocarbons with the exception of acetylene. Compound **1** has the smallest cavity among known cavitand compounds and the high size selectivity for small hydrocarbons reported thus far. The syntheses of metal complexes of this cavitand–porphyrin and investigations of their guest-encapsulation properties and reactivity are in progress in our laboratory.

Experimental Section

Determination of binding constants: Hydrocarbon gas was bubbled directly into the solution of **1** in $CDCl_3$ (5 mM, 0.6 mL) in an NMR tube with a gas-tight screw cap. ^{1}H NMR spectra were measured at various hydrocarbon concentrations (5–50 mM) at 25 °C. The amount of free and encapsulated hydrocarbons were determined by the integration of their proton signals relative to the host signals at δ = 7.13–6.84 ppm (20 protons). The [$\mathbf{1}_{free}$] values were estimated from the amount of trapped hydrocarbon. The 1:1 binding constants were calculated by using Equation (1).

$$K_{11} = \frac{[\text{hydrocarbon}_{@\mathbf{1}}]}{[\mathbf{1}_{free}][\text{hydrocarbon}_{free}]} \quad (1)$$

The average value and standard deviation of K_{11} were determined by ten independent measurements.

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