MM2 Molecular Mechanics and ^{13}C NMR Studies on Conformations of *n*-Alkanes Enclathrated in Dianin's Compound

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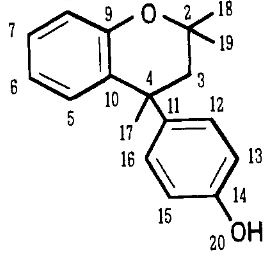
Abstract: MM2 molecular mechanics calculations for clathrates of Dianin's compound with *n*-pentane, *n*-hexane, *n*-heptane, *n*-octane, and *n*-nonane showed the existence of various conformers for enclathrated *n*-alkanes. The all-anti conformer of *n*-pentane as well as that of *n*-hexane comprises ca. 90% of all the probable conformers in the cavity, but that of *n*-heptane comprises less than 1%. The all-anti conformers of *n*-octane or *n*-nonane cannot exist in the clathrate. The possibility of formation of the clathrates is discussed on the basis of free energies evaluated for the inclusion process, which can reproduce the experimental guest selectivity of the Dianin's compound host for *n*-alkanes. On the assumption of the occurrence of dynamical conformational disorder for the enclathrated *n*-alkanes, observed ^{13}C chemical shift changes of the *n*-alkanes due to enclathration are well-correlated with those obtained by ab initio calculations using Ditchfield's gauge-invariant atomic orbitals.

Six molecules of Dianin's compound (I), 4-(*p*-hydroxyphenyl)-2,2,4-trimethylchroman, form an hourglass-shaped cavity in the crystalline state,[1] which can enclathrate a wide variety of organic and inorganic compounds.[2] Although thermal expansion of the trigonal cell has recently been reported to depend on the presence of guest molecules,[3] the dimensions of the cages determined so far by X-ray diffraction are very similar: [1,4,5] the cage is ~11 Å long and ~2.8, ~4.2, and ~6.3 Å wide at the terminal, the center, and the point of maximum extension, respectively, as illustrated in Figure 1. Both terminals of the cage are so narrow that longer *n*-alkane molecules are difficult to enclathrate in I, contrary to the case of urea inclusion compounds since the urea host can accommodate even polymers. Guest compounds are, therefore, considered to be located within the cavity.



Dianin's compound (I)

From the measured molar ratios of the host I to the guest *n*-alkanes, *n*-hexane (**6**), *n*-heptane (**7**), *n*-octane (**8**), *n*-nonane (**9**), and *n*-decane (**10**), in the clathrates, Goldup and Smith[6] concluded that each cavity should be occupied by a single molecule of **6**, **7**, or **8**, but that many cavities should remain unfilled for the clathrate with **9** or **10**. For *n*-butane (**4**), Barrer and Shanson[7] claimed that the cavity may enclathrate three molecules of **4** from their gas-absorption experiments. The all-anti conformer of **8** is 12.9 Å long, considering the van der Waals radius of the two terminal methyl groups, and is much longer than the length of the cage; therefore, the enclathrated conformer of **8** should have some gauche bonds in its carbon chain. Recently, Lee et al.[5] pointed out the existence of terminal gauche bonds for the enclathrated molecule of **8** to explain the observed notably upfield displacement of its ^{13}C NMR chemical shifts compared to the corresponding shifts in solution.

In the present work, probable conformers for five *n*-alkanes from *n*-pentane (**5**) to *n*-nonane (**9**) enclathrated in I were investigated by MM2 molecular mechanics calculations,[8] and thermodynamical parameters were evaluated in order to elucidate whether or not the clathrates with **5**–**9** can be prepared and, further, to confirm guest selectivity of I, the experimental parameters for which were reported by Goldup and Smith.[6]

^{13}C chemical shifts of the enclathrated molecules of **5**-**8** were measured by ^{13}C CPMAS NMR spectroscopy, and the observed chemical shift changes due to enclathration were examined on the basis of the chemical shifts obtained by ab initio calculations using Ditchfield's gauge-invariant atomic orbitals (the GIAO method).[9]

Experimental Section

Dianin's compound (I) was prepared according to the reported procedure.[10] "Guest-free" I was obtained by recrystallization from **9** or **10**. Recrystallization of I from **8** gave the clathrate of I with **8** as colorless needles. The other clathrates of I with **5**–**7** were obtained as colorless powders by the Soxhlet extraction of I with the corresponding *n*-alkanes. Molar ratios of the host I to the guest *n*-alkanes for all of the clathrates thus prepared were equal to 6 within the experimental error of the elemental analysis.

^{13}C CPMAS NMR spectra were measured at room temperature on a home-built spectrometer operating at 22.6 MHz with a spinning rate of ca. 3 kHz. Room-temperature ^{13}C solution-state NMR spectra were taken on a JEOL GX-400 spectrometer operating at 100 MHz. Chemical shifts were referenced to the methylene carbons of adamantane (38.7 ppm from TMS) in the solid state and to $CDCl_3$ (76.85 ppm from TMS) in the solution state as secondary standards.

A model cage of the clathrate for the present MM2 molecular mechanics calculations was constructed as follows: on the basis of the X-ray crystal structure of the clathrate with two ethanol molecules in the cavity,[1] the atomic coordinates of I except for the 12 aromatic carbon atoms and the hydroxyl oxygen and hydrogen atoms were optimized by MM2 calculations. Lone-pair groups of the hydroxyl and ethereal oxygen atoms in I were neglected throughout calculations in this work, but the van der Waals parameters for these oxygen atoms were replaced by those for the carbonyl oxygen atom to include the contribution of the lone-pair groups. By using the atomic coordinates of I thus obtained and the

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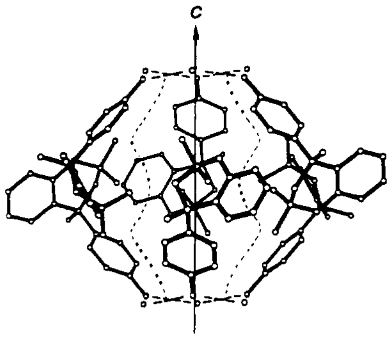

Figure 1. Structure of the model cage by Dianin's compound (**I**). The shape of the cavity is depicted in broken lines. Hydrogen atoms are not drawn for clarity.

Table I. ^{13}C Chemical Shifts (ppm) for *n*-Alkanes **5–8** Measured in the Clathrates of Dianin's Compound (**I**) and in $CDCl_3$ Solutions[a]

n-alkane		C1	C2	C3	C4
5	clth	13.6	22.9	35.2	
	soln	13.9	22.2	34.0	
	Δ_{exptl}	−0.3	0.7	1.2	
6	clth	15.5	23.1	32.6	
	soln	13.9	22.6	31.6	
	Δ_{exptl}	1.6	0.5	1.0	
7	clth	14.8	21.4	30.7	26.0
	soln	13.9	22.7	31.9	29.1
	Δ_{exptl}	0.9	−1.3	−1.2	−3.1
8	clth	14.0	20.2	28.9	24.5
	soln	14.0	22.7	31.9	29.4
	Δ_{exptl}	0.0	−2.5	−3.0	−4.8

[a] Δ_{exptl} denotes the chemical shift change due to enclathration.

experimental crystal lattice parameters the crystal of **I** was constructed, from which the hourglass-shaped model cage was taken out as shown in Figure 1: it consists of six molecules of **I** and six additional hydroxyl groups which are used to form the two hydrogen-bond networks at the top and bottom of the cage. The structure of the model cage was finally reoptimized by fixing the atomic coordinates of 120 aromatic carbon and hydrogen atoms and 24 hydroxyl oxygen and hydrogen atoms, yielding −18.51 kcal mol^{-1} as the steric energy[11] of the model cage (SE_l°).

The clathrates in the present calculations consist of the model cage and a single molecule of **5–9** or two molecules of **5** located in the cavity. Conformers of **5–9** were generated by MM2 calculations using the TREE option.[12] The long axis of each conformer was situated along the *c* axis of the cavity, and the conformer was translated along and/or rotated around the *c* axis to obtain optimum structures rapidly. Since the *c* axis coincides with the C_3 symmetry axis of the cavity, initial angles to rotate the conformers are restricted within 0° to 120°. The structures of the clathrates were determined under the same restriction used for the reoptimization of the cage structure. The iterative procedure of the structure optimization was stopped when the difference between two successive steric energies became smaller than 0.001 kcal mol^{-1}.

The ^{13}C NMR chemical shifts for three probable conformers of **8** enclathrated in **I** (vide infra) were calculated by the GIAO method on the basis of geometries optimized in the isolated state by ab initio molecular orbital calculations using the 4-31G basis set.

Results

^{13}C NMR Chemical Shifts. Table I lists ^{13}C chemical shifts for **5–8** measured in the clathrates and in the $CDCl_3$ solutions. The numbers of observed ^{13}C resonance lines for **5–8** enclathrated in **I** are in accord with those of the corresponding unique carbons in **5–8** as seen in the solution spectra; therefore, each enclathrated *n*-alkane species should be either a single, geometrically symmetrical conformer or a mixture of various conformers at equilibrium. These resonance lines do not disappear with dipolar dephasing[13] of 60 μs, suggesting that the enclathrated *n*-alkane molecules undergo at least rotation about the *c* axes of the cavities. No ^{13}C lines due to **9** were observed in the ^{13}C MAS spectra with and without CP for the compound obtained by recrystallization of **I** from **9**, supporting the assumption that the compound is "guest-free". Changes in the ^{13}C chemical shifts of all of the carbons of the cage with enclathration of **5–8** were within 1 ppm except those for the C18 methyl carbon,[14] whose shifts were invariably ca. 2 ppm downfield, suggesting that the structure of the cage is essentially unchanged during enclathration of the present guest compounds. The ^{13}C resonance lines of all of the methylene carbons of **8** move remarkably upfield compared to the corresponding shifts in solution, as previously reported by Lee et al.[5] A similar, notably upfield shift is also found for the C4 carbon of **7**, whereas the ^{13}C chemical shifts of the methylene carbons of **5** and **6** move significantly downfield with enclathration.

Table II. Stabilization of Steric Energy due to Enclathration, ΔSE, and Fractional Population, *p*, for Representative Clathrates of Dianin's Compound (**I**) with Conformers of *n*-Alkanes **5–9** at 298 K[a]

conformer	ΔSE	*p*/%	SE_a^{incl}	SE_a^{isol}	SE_l
5					
$a\cdot a$	−21.81 (1)	89.9	2.93	2.82	−18.30
$g^+\cdot a$	−19.70 (2)	5.2	3.93	3.72	−18.16
$g^-\cdot a$	−19.66 (2)	4.8	3.95	3.72	−18.15
5$_2$[b]					
$g^+\cdot g^-$, $g^-\cdot g^+$	−14.53 (1)	100.0	16.43	12.08	−14.06
6					
$a\cdot a\cdot a$	−25.76 (1)	90.6	3.56	3.46	−18.28
$g^-\cdot a\cdot a$	−23.37 (2)	3.2	4.67	4.35	−18.17
$g^+\cdot a\cdot a$	−23.27 (2)	2.7	4.66	4.35	−17.96
$a\cdot g^+\cdot a$	−22.97 (2)	1.6	4.61	4.40	−18.09
7					
$g^+\cdot a\cdot g^-\cdot a$	−24.34 (2)	23.7	6.72	6.04	−18.05
$g^+\cdot a\cdot a\cdot a$	−24.34 (2)	23.5	6.41	4.99	−18.17
$g^-\cdot a\cdot g^+\cdot a$	−24.04 (2)	14.2	6.51	6.04	−17.98
$g^+\cdot g^+\cdot a\cdot g^-$	−23.95 (2)	12.2	7.10	6.71	−17.87
$g^-\cdot a\cdot a\cdot a$	−23.92 (2)	11.6	5.98	4.99	−17.89
$g^+\cdot a\cdot a\cdot g^-$	−23.33 (1)	2.1	6.60	5.86	−17.69
$g^-\cdot a\cdot g^-\cdot a$	−23.31 (2)	4.1	6.59	5.83	−17.91
$g^+\cdot a\cdot g^+\cdot a$	−23.13 (2)	3.0	7.40	5.83	−18.07
$g^+\cdot g^+\cdot a\cdot g^+$	−22.77 (2)	1.7	7.39	6.45	−17.71
8					
$g^+\cdot a\cdot g^+\cdot a\cdot g^-$	−24.31 (2)	55.3	9.28	7.46	−18.08
$g^+\cdot a\cdot a\cdot a\cdot g^-$	−24.30 (1)	27.1	7.90	6.51	−18.10
$g^+\cdot g^+\cdot a\cdot g^-\cdot g^-$	−23.87 (1)	13.2	8.70	7.90	−17.49
$g^+\cdot a\cdot g^-\cdot a\cdot g^+$	−22.06 (2)	1.2	10.56	7.68	−17.98
$g^-\cdot g^+\cdot a\cdot g^-\cdot g^-$	−21.97 (2)	1.1	10.76	9.53	−17.61
9					
$g^+\cdot g^+\cdot a\cdot g\cdot g^-\cdot g^+$	−19.29 (2)	89.3	12.93	10.80	−16.11
$g^+\cdot g^+\cdot a\cdot g^+\cdot a\cdot g^-$	−17.78 (2)	7.0	13.00	8.73	−16.89

[a] Steric energies are given in units of kcal mol^{-1}. Multiplicity of conformers in the cavity is designated in parentheses. Clathrates with fractional populations of less than 1% are omitted. [b] The clathrate with two molecules of **5**.

Structures of Inclusion Compounds by MM2 Calculations. The number of conformers for *n*-alkanes, excluding those with a (+)-gauche–(−)-gauche or (−)-gauche–(+)-gauche (abbreviated as $g^+\cdot g^-$ or $g^-\cdot g^+$, respectively, and similar abbreviations are hereafter used) bond in the middle of the carbon chain except for **5** and **6**, is 9, 25, 63, 153, and 369 for **5–9**, respectively. Since the cavity is chiral and centrosymmetric (the upper half of the present cage consists of the three (*R*) enantiomers of **I**, whereas the lower half consists of the three (*S*) enantiomers), the number of unique conformers in the cavity amounts to 6, 14, 33, 81, and 190 for **5–9**, respectively. For example, when the C1 carbon of an *n*-alkane molecule is located in the upper half of the cavity, the $g^+\cdot a\cdot a\cdot a$ and $a\cdot a\cdot a\cdot g^-$ conformers are equivalent, but the former and the $g^-\cdot a\cdot a\cdot a$ conformer are not. In this article, one conformer

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[11] The steric energy of a molecule is defined as the thermally averaged energy relative to the hypothetical molecule with the same constitution, but with all bond lengths and bond and torsion angles at their strainless values and the atoms with van der Waals and electrostatic interactions corresponding to infinite separation of the atoms [Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, D.C., 1982; p 172].

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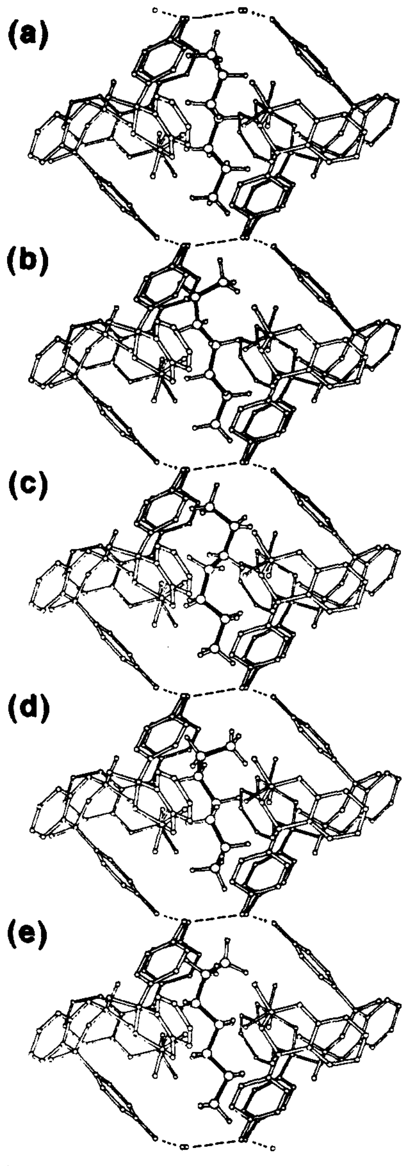

Figure 2. Calculated structures of the clathrates of Dianin's compound (**I**) with five representative conformers of *n*-heptane (**7**). The clathrates are fused and rotated by 30° around the *c* axis from Figure 1. (a) For the $g^{+}\cdot a\cdot g^{-}\cdot a$ conformer. (b) For the $g^{+}\cdot a\cdot a\cdot a$ conformer. (c) For the $g^{-}\cdot a\cdot g^{+}\cdot a$ conformer. (d) For the $g^{+}\cdot g^{+}\cdot a\cdot g^{-}$ conformer. (e) For the $g^{-}\cdot a\cdot a\cdot a$ conformer.

will represent a pair of conformers. After the structure optimization, stabilization of the steric energy due to enclathration, ΔSE, for the individual clathrates is obtained according to the following equation:

$$\Delta SE = SE_{i} - SE_{l}^{\circ} - SE_{a}^{\circ} \qquad (1)$$

where SE_i, SE_l°, and SE_a° stand for the steric energies of the individual clathrates, the "guest-free" cage (vide supra), and the corresponding all-anti conformers in the isolated state, respectively. Values for SE_a° are 2.82, 3.46, 4.10, 4.74, and 5.38 kcal mol^{-1} for **5**–**9**, respectively. The fractional Boltzmann populations of the individual clathrates or the individual enclathrated conformers are evaluated on the basis of ΔSE and the multiplicity of the conformers in the cavity. Table II summarizes the clathrates of I with **5**–**9** comprising more than 1% of all of the calculated probable clathrates for **5**–**9** at 298 K and also lists values for the steric energies of the corresponding conformers in the enclathrated and in the isolated states, SE_a^{incl} and SE_a^{isol}, respectively, together with that of the cage of the corresponding clathrates SE_l. Although some conformers are found to have different stable sites along the *c* axis with similar steric energies, the most stable clathrates are employed to evaluate various parameters. The prominent features of the individual clathrates are described below.

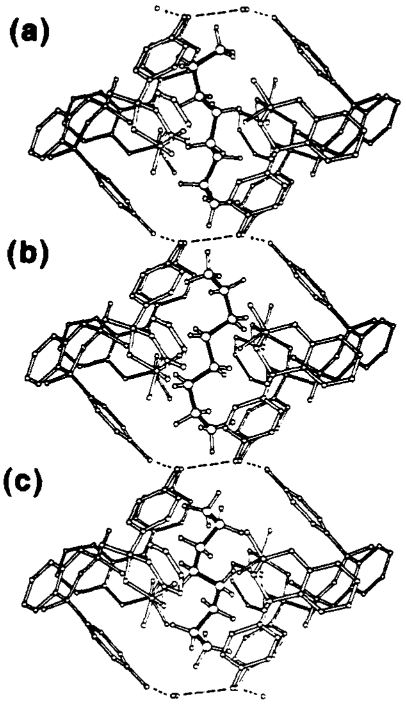

Figure 3. Calculated structures of the clathrates of Dianin's compound (**I**) with three representative conformers of *n*-octane (**8**). The clathrates are fused and rotated by 30° around the *c* axis from Figure 1. (a) For the $g^{+}\cdot a\cdot g^{+}\cdot a\cdot g^{-}$ conformer. (b) For the $g^{+}\cdot a\cdot a\cdot a\cdot g^{-}$ conformer. (c) For the $g^{+}\cdot g^{+}\cdot a\cdot g^{-}\cdot g^{-}$ conformer.

For both **5** and **6**, the all-anti conformer comprises ca. 90% of all the probable conformers in the cavity. The all-anti conformer of **6** is 10.4 Å long, being only slightly smaller than the length of the cavity. This inherently stable, all-anti conformer fits into the cavity so well that it should bring about the largest ΔSE value among all of the present clathrates. When two molecules of **5** are enclathrated in I, they are forced to be located separately with high-energy $g^{+}\cdot g^{-}$ and $g^{-}\cdot g^{+}$ conformations in the upper and lower halves of the present model cavity, respectively.

It is of much interest that the all-anti conformer of **7**, which is 11.6 Å long, comprises less than 1% of all the probable conformers in the cavity; the ΔSE value for the all-anti conformer is 1.52 kcal mol^{-1} higher than that for the most probable conformer, $g^{+}\cdot a\cdot g^{-}\cdot a$. Five conformers comprising more than 10% of all of the probable conformers involve at least one gauche bond in terminal positions, as shown in Figure 2. The first and the third conformers as well as the second and the fifth ones listed in Table II are enantiomers with each other, but the steric energies of their clathrates are different due to the optically active character of the cavity. It should be noted that the geometry of any of the five conformers is not symmetrical about the central C4 carbon, suggesting the existence of equilibration, at least between the pair conformers in the cavity, to explain the number of the observed ^{13}C resonance lines.

There are three probable conformers of **8** comprising more than 10% in the cavity. The conformation of both terminal positions of the carbon chain in the three conformers is gauche, as depicted in Figure 3. Present calculations show that the all-anti conformer of **8** cannot exist in the cavity, since it transforms to other conformers during the structure optimization. The most probable $g^{+}\cdot a\cdot g^{+}\cdot a\cdot g^{-}$ conformer is geometrically nonsymmetrical, so that the existence of equilibration between the pair conformers in the cavity should be recalled.

Although 190 initial conformers of **9** are considered in the present calculations, it is of much interest that the most probable $g^{+}\cdot g^{+}\cdot a\cdot g^{-}\cdot g^{-}\cdot g^{+}$ conformer, as illustrated in Figure 4, comprises 89.3% of all of the probable conformers in the cavity, but it, of course, contributes very little to the conformers of **9** in the isolated state.

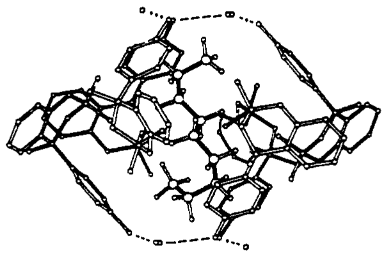

Figure 4. Calculated structure of the clathrate of Dianin's compound (I) with the $g^+ \cdot g^+ \cdot a \cdot g^- \cdot g^- \cdot g^+$ conformer of *n*-nonane (**9**). The clathrate is rotated by 30° around the *c* axis from Figure 1.

Discussion

Thermodynamics for Inclusion. The present MM2 calculations show that various conformers of *n*-alkanes from **5** to **9** can exist in the cavity. In order to explain the apparent geometrically symmetrical, single conformations for the enclathrated *n*-alkane molecules observed by the ^{13}C CPMAS NMR spectra, the probable conformers should be equilibrating in the cavity, bringing about the dynamical disorder of conformations for the guest *n*-alkanes.[15] However, the question of whether or not the clathrates can be formed should be discussed on the basis of free energies for the inclusion process. According to the consideration by Schlenk[16] and Tabushi et al.,[17] the total inclusion process can be divided into three subprocesses: The first is the vaporization of *n*-alkane molecules, the second is the crystal structure change of the host molecules due to clathration, and the third is the clathration of the vaporized *n*-alkane molecules into the empty host cavities.

The free energy of the vaporization process, ΔG_{vap}, is estimated from the literature.[18] That for the crystal structure change of I can be neglected, because the cage structure is considered to be invariant with enclathration on the basis of the observation of no significant displacement of the ^{13}C chemical shifts for I. That for the last process can be evaluated on the basis of the MM2 molecular mechanics method. The enthalpy change for this process, ΔH_{incl}, is given by

$$\Delta H_{\text{incl}} = \overline{\Delta \text{SE}} + \Delta \text{BE} + \Delta \text{PFC} \qquad (2)$$

with

$$\overline{\Delta \text{SE}} = \overline{\text{SE}}_{\text{a}}{}^{\text{incl}} - \overline{\text{SE}}_{\text{a}}{}^{\text{isol}} - \text{SE}_{\text{l}}{}^{\circ} \qquad (3)$$

where $\overline{\text{SE}}_{\text{a}}{}^{\text{incl}}$ and $\overline{\text{SE}}_{\text{a}}{}^{\text{isol}}$ are the average steric energies of *n*-alkane in the enclathrated state and that in the isolated state, respectively, considering the conformational distributions of *n*-alkane. Since BE, respesenting the sum of bond and structural energy increments, is independent of the conformational change of a molecule, ΔBE should vanish in this process. The partition function contribution (PFC) consists of the internal energies (the translational, rotational, and torsional energies) and the PV term which is due to the conversion of energy to enthalpy. For this process, the change of the torsional contribution can be neglected, and the internal energy of the isolated *n*-alkane amounts to $3RT$ as the translational and rotational contributions, but that of the enclathrated one is $^1/_2RT$ as the rotational contribution, because the enclathrated *n*-alkane is considered to be allowed only to rotate around the *c* axis of the cavity. Entropy terms necessary for this process are the translational, rotational, and mixing contributions, which can readily be evaluated.

Table III. Calculated Thermodynamical Parameters for the Inclusion Process of the Clathrates of Dianin's Compound (I) with *n*-Alkanes **5**–**9** at 298 K[a]

n-alkane	ΔH_{incl}	ΔS_{incl}	$-T\Delta S_{\text{incl}}$	ΔG_{incl}	ΔG_{vap}	ΔG_{total}
5	−23.58	−56.93	16.97	−6.61	0.22	−6.39
$\mathbf{5}_2$[b]	−18.51	−112.18	33.43	14.92	0.45	15.37
6	−27.74	−59.86	17.84	−9.90	0.89	−9.02
7	−26.46	−58.98	17.58	−8.88	1.50	−7.38
8	−26.85	−63.20	18.83	−8.01	2.12	−5.90
9	−22.01	−66.65	19.86	−2.15	2.68	0.53

[a] Enthalpies and free energies are given in units of kcal mol^{-1}, and entropies are given in units of eu. [b] For clathration of two molecules of **5** in one cavity.

Table IV. Calculated ^{13}C Chemical Shifts (ppm) for Three Probable Conformers of *n*-Octane (**8**)[a]

carbon	$g^+ \cdot a \cdot g^+ \cdot a \cdot g^-$	$g^+ \cdot a \cdot a \cdot a \cdot g^-$	$g^+ \cdot g^+ \cdot a \cdot g^- \cdot g^-$
C1	194.08	194.02	195.15
C2	186.37	186.78	190.81
C3	180.67	178.79	181.08
C4	181.81	180.38	187.48
C5	181.92	180.38	187.47
C6	181.17	178.79	181.08
C7	187.08	186.78	190.82
C8	194.18	194.02	195.15

[a] Calculated shifts are given in absolute values, and therefore large values stand for upfield shifts.

The free energies for the inclusion process at 298 K thus evaluated are listed in Table III. For the clathrate with a single *n*-alkane molecule in the cavity, all of the ΔG_{incl} values are negative, and the values for the total process, ΔG_{total}, are also negative for **5**–**8**, but the latter is slightly positive for **9**, indicating the clathrate with **9** cannot be formed. If only the most probable conformers of **5**–**9** in Table II were enclathrated in the individual cavities of I, the ΔG_{total} value at 298 K would amount to −6.36, −8.98, −6.50, −5.36, and 0.60 kcal mol^{-1} for **5**–**9**, respectively. Each value is larger than the corresponding value listed in Table III, indicating that the clathrates can be stablized by the dynamical disorder of conformations. The ΔG_{total} value for the clathrate with two molecules of **5** in the cavity is positive and very large, supporting another result indicating that the cavity is occupied with a single molecule of **5**.

The guest selectivity of I for various hydrocarbon molecules was investigated by Goldup and Smith[6] on the basis of their competitive inclusion experiments carried out in a sealed tube at 150 °C. They defined the relative accommodation factor, RAF, for the guest selectivity as

$$\text{RAF} = (W_{\text{I}}/W_{\text{R}})/(w_{\text{I}}/w_{\text{R}}) \qquad (4)$$

where W_{I} and W_{R} are the weights of components I (guest *n*-alkanes, **5**–**8**) and R (the reference, **7**) in the clathrate, and w_{I} and w_{R} are their respective weights in the mixture from which clathration occurred; the values are 4.5, 9.0, 1.0 (defined), and 0.06 for **5**–**8**, respectively. The RAF value can be estimated from free energies for the inclusion process by

$$\text{RAF} = \exp(-\overline{\Delta\Delta G}_{\text{total}}/RT) \qquad (5)$$

where $\overline{\Delta\Delta G}_{\text{total}}$ is the difference between $\overline{\Delta G}_{\text{total}}$ of arbitrary *n*-alkane and that of **7** at 150 °C in a sealed tube. Under these conditions, the values for $\overline{\Delta G}_{\text{total}}$ are calculated to be −3.28, −5.12, −3.28, −0.93, and 5.88 kcal mol^{-1} for **5**–**9**, respectively, yielding the RAF values of 1.0, 9.0, 1.0, and 0.061 for **5**–**8**, respectively, which are in excellent agreement with the corresponding experimental values except for **5**. The underestimation of the calculated RAF value for **5** might be attributed to a residual degree of freedom of motion for **5** in the cavity.

^{13}C Chemical Shift Changes due to Enclathration. Relevant ^{13}C NMR chemical shifts for *n*-alkane conformers can be obtained by the ab initio GIAO method using the 4-31G basis set. On the assumption that in the solution state various conformers of each *n*-alkane are at a thermal equilibrium according to the Boltzmann distribution, one can readily evaluate the solution-state ^{13}C chemical shifts from those calculated for *n*-alkane conformers and

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Table V. Calculated ^{13}C Chemical Shifts for *n*-Alkanes **5**–**8** in the Clathrates of Dianin's Compound (**I**) and in the Solution State[a]

n-alkane		C1	C2	C3	C4
5	clth	192.21	185.49	176.14	
	soln	192.69	186.46	177.01	
	Δ_{calcd}	0.48	0.97	0.87	
6	clth	192.15	185.35	177.07	
	soln	192.64	186.29	178.56	
	Δ_{calcd}	0.49	0.94	1.49	
7	clth	193.31	187.01	179.35	182.19
	soln	192.66	186.26	178.36	180.07
	Δ_{calcd}	−0.65	−0.75	−0.99	−2.12
8	clth	194.24	187.30	180.34	182.22
	soln	192.68	186.24	178.35	179.89
	Δ_{calcd}	−1.56	−1.06	−1.99	−2.33

[a] Values are given in units of ppm. Δ_{calcd} denotes the chemical shift change due to enclathration, and negative Δ values indicate upfield shifts.

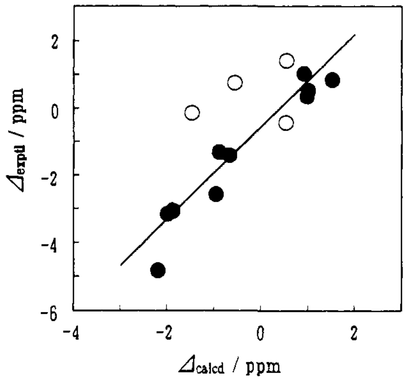

Figure 5. Plot of the experimental chemical shift changes, Δ_{expll}, against the calculated ones, Δ_{calcd}, for *n*-alkanes **5**–**8** due to enclathration in Dianin's compound (**I**). (●) The methylene carbons. (○) The methyl carbons. A solid line is the best-fit line for the methylene carbons.

their energies. The values for **5**–**7** should be reported elsewhere,[19] whereas those for **8** can be estimated from the additivity rule found for the calculated ^{13}C chemical shifts for *n*-alkanes.[19] It should be noted that the experimental chemical shift values are systematically larger than the corresponding calculated values by a factor of 1.25. The ^{13}C chemical shifts of **5**–**8** enclathrated in I are evaluated on the basis of the calculated values for all of the conformers of **5**–**7**, and those for the first three conformers of **8** (individual chemical shifts are shown in Table IV) are evaluated with the fractional populations listed in Table II. Since only positionally unique carbons of each *n*-alkane can be distinguished in the experimental spectrum, the ^{13}C chemical shifts are averaged over positionally equivalent carbons as listed in Table V.

Differences between the ^{13}C chemical shifts in the solution and those in the enclathrated states yield the calculated chemical shift changes due to enclathration, Δ_{calcd}, where negative Δ values stand for upfield shifts according to the definition used in usual NMR experiments. The experimental chemical shift changes Δ_{expll} (Table I) are plotted against Δ_{calcd} in Figure 5. For the methylene carbons the correlation is satisfactory, and the slope (1.38) of the best-fit line is close to the factor (1.25) for the experimental and calculated chemical shift ratio. If any one of the first three conformers of **8** in Table II is enclathrated in the cavity, one cannot obtain such a good correlation, supporting the existence of the conformational equilibration. The discrepancy between the observed and the calculated chemical shift changes for the methyl carbons might be attributed to intermolecular interactions between the *n*-alkane terminals and the host I.

Conclusion

The present MM2 calculations showed that *n*-alkanes **5**–**9** enclathrated in the cavity of I are in various conformations (Table II and Figures 2–4); the leading conformations are that with all-anti bonds for **5** and **6**, those with at least one terminal gauche bond for **7**, those with gauche bonds at both ends of the chain for **8**, and that involving a $g^{\pm}\cdot g^{\mp}$ bond for **9**. Thermodynamical parameters for the inclusion process estimated on the basis of the MM2 method determined that the free energy of the total process ΔG_{total} is negative for the clathrates with a single molecule of **5**–**8**, but is positive for that with two molecules of **5** and that with a single molecule of **9** (Table III), which is in accord with the present experimental results. The experimental guest selectivity for **5**–**8** was also explained by the calculated relative ΔG values. The observed ^{13}C chemical shift changes of the methylene carbons of *n*-alkanes due to the enclathration are well-correlated with those obtained by ab initio GIAO calculations on the assumption of the fractional populations of conformations in the cavity determined by the present MM2 calculations (Table V and Figure 5). All of the present results support the occurrence of the dynamical disorder of conformations for **5**–**8** enclathrated in the cavity of I.

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