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A Possible Model of Aromatic-Guest Recognition in Paracyclophane-Guest Inclusion Processes

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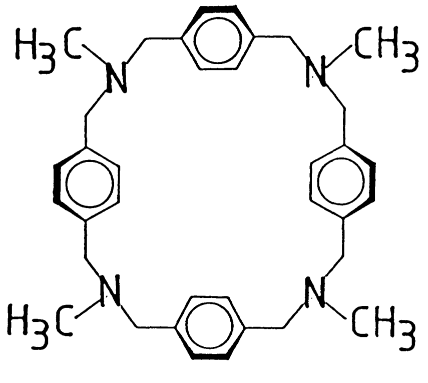
On the basis of the MMP2 molecular mechanics calculations, a possible mechanism is proposed for aromatic-guest selectivity found in the formation of paracyclophane-guest inclusion complexes.

Paracyclophanes (PCP's) are macrocyclic compounds containing benzene ring(s) linked at the para-position(s) in their macrocyclic skeletons. PCP's selectively admit guest molecules into their hydrophobic cavities in solution.[1-4] PCP's composed of diphenylmethane units (DPM-PCP's), for example, form stronger complexes with aromatic guests than with aliphatic ones.[5,6] It is of great interest to clarify the molecular origin of the guest-selectivity, which information may serve as a clue for the molecular design of PCP's with higher guest-selectivity. N,N',N'',N'''-Tetramethyl-2,11,20,29-tetraaza[3.3.3.3]PCP (**1**) may be the most suitable for this purpose, because its structure and properties have been extensively studied in both crystal and solution.[7-14] Here, on the basis of the MMP2 molecular mechanics calculations,[15] a possible mechanism for this guest-selectivity is proposed.

Guest molecules studied here are benzene (C_6H_6), dichloromethane (CH_2Cl_2), ethanenitrile (CH_3CN), and propane (C_3H_8). These guests except C_3H_8 have been shown to form complexes with host **1**.[7,12,13]



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It has been reported that Allinger's force field well reproduces the X-ray structure of **1** in the isolated state.[16] At the beginning, in order to ascertain the reliability of the MMP2 method for studying the complexation process in the host **1**-guest systems, the MMP2 method was used to optimize the geometry of **1**-CH_2Cl_2 complex starting from its X-ray geometry. We found that the optimized geometry was very close to the initially assumed one; the standard deviation of the host-guest interatomic distances between in the optimized geometry and in the initial one is not larger than 0.021 nm. This example indicates that the MMP2 calculation satisfactorily reproduces the host-guest orientation in the inclusion state. Considering the applicability of Allinger's force field to a wide variety of molecules, the host-guest orientation in the other cases studied here should be also predictable by means of the MMP2 method as long as the initial geometry is appropriately selected. There would be a variety of local minima on the potential surface for the host-guest interaction. In order to reach the global minimum efficiently, the initial geometry of inclusion complexes was determined with the aid of the CPK molecular model on the assumption that in the most stable complex the van der Waals contact between host **1** and each guest become maximum. The backbone of host **1** was assumed to retain C_4-symmetry[17)] irrespective of the type of guest molecules.

The host-guest interaction energy (E_{int}) in the complex state is given as follows: $E_{int} = E_{complex} - (E_{host} + E_{guest})$, where $E_{complex}$ is the total steric energy of a complex, and E_{host} and E_{guest} represent the contributions of host- and guest-parts to $E_{complex}$, respectively (Table 1). Table 1 indicates that benzene interacts more strongly with host **1** than the other guests studied here. On the other hand, the stabilization-energy (E_{stab}) of the complex relative to the isolated state can be defined as follows: $E_{stab} = E_{complex} - (E'_{host} + E'_{guest})$, where E'_{host} and E'_{guest} are the steric energies of the host and guest, respectively, in each optimized geometry. In the case of benzene, the value of E_{stab} is most greatly different from that of E_{int}. On complexation, appreciable conformational change should be induced in host **1** and/or benzene.

Table 1. Host-Guest Interaction Energy (E_{int}) in the Complex State and Stabilization Energy (E_{stab}) Relevant to the Inclusion of Guest Molecule by Host **1** Calculated by Means of MMP2 Method

	E_{int} / kJ mol^{-1}				E_{stab} / kJ mol^{-1}			
Guest	C_6H_6	CH_2Cl_2	CH_3CN	C_3H_8	C_6H_6	CH_2Cl_2	CH_3CN	C_3H_8
vdW[a)]	-48.48	-36.87	-25.71	-41.38	-42.86	-36.97	-24.19	-39.35
Dipole[b)]	0.00	-1.98	-3.27	0.00	-0.01	-1.34	-1.51	-0.03
Others[c)]	-0.01	-0.06	-0.03	-0.02	6.93	1.36	-0.88	-0.67
Total	-48.49	-38.91	-29.01	-41.40	-35.94	-36.95	-26.58	-40.05

a) Van der Waals interaction energy calculated between all pairs of atoms not bound to each other or to a common atom. b) Dipole interaction energy calculated between all pairs of bond moments. c) Sum of compression, bending, stretch-bend, and torsional energies.

When the benzene molecule was initially orientated parallel to a diagonal of the square cavity (Fig. 1A), two types of characteristic conformational change could be induced in the host molecule through a geometry-optimization process. One is the distortion of its skeleton from a regular square to a rhombus (Fig. 1C), and the other is the increase in the tilting angles of the aromatic residues to the mean molecular plane of the macroring, leading nearly to the "face to face" conformation.[18] Even if the guest benzene was initially oriented parallel to a pair of the host benzene rings (Fig. 1B), the final geometry was found to become similar to that shown in Fig. 1C. Therefore the geometry of host **1**-benzene complex always converges to the structure shown in Fig. 1C irrespective of the initial host-guest orientation. Thus, host **1** behaves as if it traps benzene (guest) into its cavity. This motion, so called "induced fitting," is mainly driven by the intermolecular van der Waals forces. It is evident from a geometrical consideration that the structure as shown in Fig. 1C is the most stable because it corresponds to the maximum van der Waals contact between a C_4-symmetric molecule and a planar one. Therefore, whether the above induced-fitting occurs or not should not depend on the parameters of the force-field used. Although the X-ray data for the host **1**-benzene system have not been published yet, we can find a good example of the Fig. 1C-like structure in the DPM-PCP-durene complex.[19]

In conclusion, PCP's of C_4-symmetry can recognize a planar guest molecule through the induced-fit mechanism proposed here. Detailed studies including effects of entropy and solvation will be published in future.

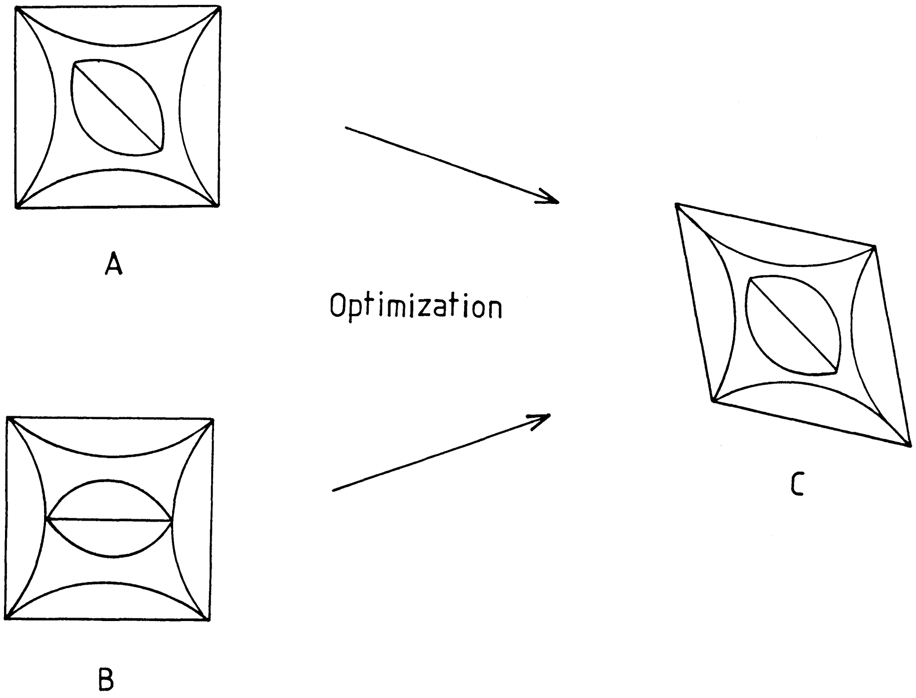

Fig. 1. Schematic representation of complexation between host **1** and benzene. Each illustration is drawn on the mean molecular plane of the macroring. A square represents the macrocyclic skeleton of host **1**, and four "bow" like curves do a force-field inside the cavity. Benzene molecule (guest) is represented by oppositely contacting "bow" like shape. In Fig. 1A, benzene is oriented in the direction of one of the diagonals (N-N distances: 1.02 nm). In Fig. 1B, benzene is oriented parallel to a pair of the benzene rings of host **1**. In Fig. 1C is shown the final geometry of **1**-benzene complex after optimization starting from the states

A and B. The lengths (N-N distances) of the two diagonals are 1.06 nm (long) and 0.98 nm (short) in the case of C.

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References

1) Y. Murakami, Top. Curr. Chem., 115, 107 (1983).
2) I. Tabushi and K. Yamamura, Top. Curr. Chem., 113, 145 (1983).
3) I. Tabushi, Y. Kimura, and K. Yamamura, J. Am. Chem. Soc., 103, 6486 (1981).
4) K. Saigo, R.-J. Lin, M. Kubo, A. Youda, and M. Hasegawa, J. Am. Chem. Soc., 108, 1996 (1986).
5) K. Odashima, T. Soga, and K. Koga, Tetrahedron Lett., 22, 5311 (1981).
6) F. Diederich and K. Dick, J. Am. Chem. Soc., 106, 8024 (1984).
7) Y. Urushigawa, T. Inazu, and T. Yoshino, Bull. Chem. Soc. Jpn., 44, 2546 (1971).
8) I. Tabushi, Y. Kuroda, and Y. Kimura, Tetrahedron Lett., 1976, 3327.
9) I. Tabushi, Y. Kimura, and K. Yamamura, J. Am. Chem. Soc., 100, 1304 (1978).
10) I. Tabushi, Y. Kimura, and K. Yamamura, J. Am. Chem. Soc., 103, 6486 (1981).
11) S. J. Abbott, A. G. M. Barrett, C. R. A. Godfrey, S. B. Kalindjian, G. W. Simpson, and D. J. Williams, J. Chem. Soc., Chem. Commun., 1982, 796.
12) I. Tabushi, K. Yamamura, H. Nonoguchi, K. Hirotsu, and T. Higuchi, J. Am. Chem. Soc., 106, 2621 (1984).
13) K. Hirotsu, S. Kamitori, T. Higuchi, I. Tabushi, K. Yamamura, and H. Nonoguchi, J. Incl. Phenom., 2, 215 (1984).
14) H. Takemura, M. Suenaga, K. Sakai, H. Kawachi, T. Shinmyozu, Y. Miyahara, and T. Inazu, J. Incl. Phenom., 2, 207 (1984).
15) For a recent review: U. Burkert and N. L. Allinger, "Molecular Mechanics," American Chemical Society, Washington, D.C. (1982), ACS Monograph 177; N. L. Allinger, Quantum Chemistry Program Exchange, Chemistry Department, Indiana University, U.S.A.
16) K. Hirotsu and T. Higuchi, Nippon Kessho Gakkaishi, 28, 261 (1986).
17) It was confirmed by means of the MMP2 calculations that the C_4-structure corresponds to a local minimum on the potential energy surface of host **1**, not including any guest molecules.
18) I. Tabushi, H. Yamada, and Y. Kuroda, J. Org. Chem., 40, 1946 (1975).
19) See Fig. 8 in Ref. 16.

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