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A novel clathrate host allowing structural adjustment during the inclusion of 1,2-diaminoethanes

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Abstract—Dimethyl 5-hydroxy-2-oxo-4,5-diphenylcyclopent-3-ene-1,3-dicarboxylate (1a) forms relatively stable inclusion complexes with compounds having 1,2-diaminoethane moiety.

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Recently, we reported that the Diels–Alder (DA) adducts (I) of phencyclone and *N*-arylmaleimides act as non-hydroxylic clathrate hosts (clathrands), which include aromatic guests. ^{1a} On the other hand, the DA adducts (II) of tetracyclone and some 2-alkenoic acids or 2-alkenamides serve as hydroxylic clathrate hosts ^{1b} showing inclusion ability toward alcohols, ethers, and ketones. ^{1c}

The X-ray analyses of the inclusion compounds showed that the complexes are stabilized by C–H··O hydrogen bond² and edge-to-face interaction (aromatic CH– π hydrogen bond)³ besides strong O (or N)–H··O hydrogen bond between the host and guest.

In this letter, we wish to show that a cyclopentadienone precursor (1a) acts as an efficient clathrate host for

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recognition of molecules bearing 1,2-diaminoethane moiety.

When 1,4-diazabicyclo[2.2.2]octane (2a) (0.046 g) was added to a suspension of dimethyl 5-hydroxy-2-oxo-4,5-diphenylcyclopent-3-ene-1,3-dicarboxylate (1a) (0.25 g) in benzene (1.5 mL), the solid immediately dissolved with change of color (colorless — yellow) to give pale yellow precipitates (3aa) (mp 131–132 °C, yield 26% in MeCN and 69% in benzene). The ¹H NMR spectrum showed that 3aa is a stable 2:1 host–guest complex. The structure of 3aa was established by the single crystal X-ray analysis (Fig. 1),⁴ showing that the guest molecule is included as two rotational isomers⁵ around the axis through the two nitrogen atoms of 2a.

As shown in Figure 1, both nitrogen atoms of 2a are hydrogen bonded to the hydroxy groups of the host molecules. Four ethano-bridge hydrogens (C7-C8) of 2a form tetradentate C-H·O hydrogen bonds with the enone-carbonyl oxygen of an adjacent host molecule. The $>C=O \cdot C_7$ and $>C=O \cdot C_8$ distances are 3.20 and 3.23 Å, respectively. On the other hand, four hydrogens of the hexahydropyrazine moiety (N₁-C₆) also make weak tetradentate C-H·O hydrogen bonds with the enone-carbonyl oxygen of another host molecule. The residual four hydrogens are also linked to the oxygen atoms of the methoxycarbonyl groups of the hosts by C-H··O hydrogen bonds. Thus, all of the hydrogen atoms of 2a make C-H-O hydrogen bonds with the oxygen atoms of the host molecules. Inspection of the packing diagram of **3aa** indicates that the host–host network is stabilized by the edge-to-face interactions between the phenyl rings of host molecules (see Fig. 2). The host

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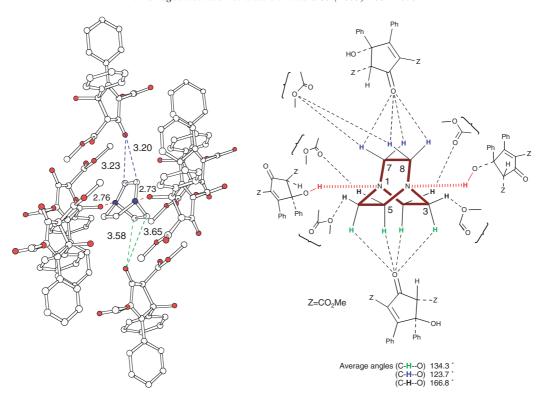


Figure 1. Packing illustration of the crystal structure of 3aa and schematic representation of the important interactions between 1a and 2a. Hydrogen bonds are indicated by dashed lines: red O–H··N hydrogen bonds; blue and green tetradentate C–H··O hydrogen bond; black C–H··O hydrogen bond.

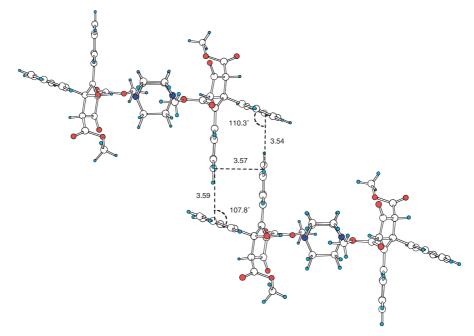


Figure 2. Host-host network between the phenyl rings through edge-to-face interactions in 3aa.

effectively recognizes the guest, indicating that the threedimensional structural feature of the host molecule is very suitable for the recognition of 2a.

The two O-H··N hydrogen bonds are probably retained in solution. The ¹H NMR spectrum of the complex in CDCl₃ exhibited an extremely wide broadening of the methyl signal of the methoxycarbonyl group on C₁

(see 1a), indicating the presence of restricted rotation of the methoxycarbonyl group due to the interference of the bulky guest molecule hydrogen bonded to the C₅–OH group. The visible absorption spectrum of the reaction mixture showed the appearance of a new absorption band near 400 nm (shoulder), suggesting the charge-transfer (CT) complex formation between the host and guest.

With piperazine (2b), 1a forms stable 2:1 host-guest complex 3ab (mp 136-137 °C, yield 90%). The X-ray analysis of the 2:1 host-guest complex (3ab)⁶ showed a different inclusion mode compared to the case of 3aa, in which there are strong hydrogen bonds of two types not only between the enolic O-H hydrogen of 1a (enol form)⁷ and the nitrogen lone pair of 2b, but also between the N-H hydrogen and the ester carbonyl of 1a (see Fig. 3).

As can be seen in Figure 3, the 2,5-dihydroxycyclopentadiene moieties of **2b** form a cyclic diol dimer in a face-toface manner, stabilizing the host-host network (see also Fig. 4).

1,2-Diaminoethane (2c) forms a 1:1 host-guest complex (3ac, mp 105–108 °C, 57%) with 1a.8 1-Aza-bicy-clo[2.2.2]octane (2d) forms an unstable 1:1 host-guest complex 3ad (mp 118–120 °C, 71%) with 1a in nonpolar solvents such as benzene, which gradually transformed to an equilibrium mixture during purification by recrystallization.9 Monoalkylamines such as triethylamine did

not form crystalline host–guest complexes with **1a** but showed yellow coloration due to the CT complex formation. Pyrazine (**2e**), dioxane (**2f**), and hexamethylenetetramine (**2g**) did not form the host–guest complexes with **1a**, indicating that 1,2-diaminoethane moieties are specifically recognized. A less electron-deficient host, 2,5-diethyl-4-hydroxy-3,4-diphenylcyclopent-2-enone (**1b**) did not act as a clathrate host. ¹⁰

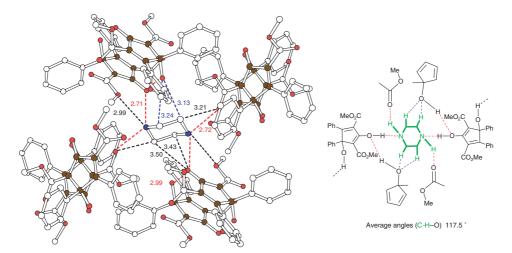


Figure 3. Packing illustration of the crystal structure of **3ab** and important interactions between **1a** and **2b**. Hydrogen bonds are indicated by dashed lines: red N–H·O, O–H·O, and O–H·N hydrogen bonds; blue lines: C–H·O hydrogen bond.

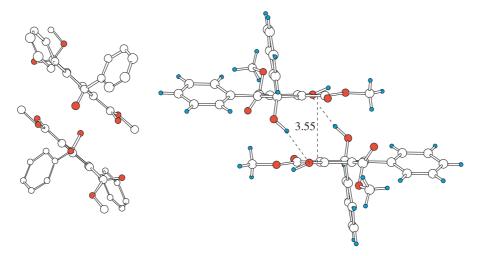


Figure 4. Host-host interaction between the 2,5-dihydroxycyclopentadiene moieties through cyclic O·H-O hydrogen bonds in 3ab.

The present host molecule is considered to have induced-fit-type binding ability toward 1,2-ethanediamines, regardless of the type of the diamines, in which two >O-H·N hydrogen bonds between the C₅-OH and diamines play a leading role in recognition of the 1,2-diaminoethane moiety. With primary and secondary 1,2-diaminoethane, the host molecule isomerizes to the enol form acting as hydrogen-bond donor towards the diamines. In both cases, the conformational flexibility of the methoxycarbonyl groups plays an important role for the effective accumulation of the weak C-H·O interactions between host and guest.

We are currently investigating the inclusion behavior of more electron-deficient host having 4,5-dipyridin-2-yl groups and the crystallographic analyses of the inclusion complexes.

Supplementary data

The procedure of single-crystal X-ray analyses, ORTEP drawings and NMR data for **3aa** and **3ab** are available. With this article and can be found, in the online version, at doi:10.1016/j.tetlet.2004.12.085.

X-ray crystallographic data: Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 255495 and 221324. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0) 1223 336033 or deposit@ccdc.cam.ac.uk].

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- 4. Crystal Data of **3aa**; $C_{24}H_{24}NO_6$, M = 422.46. triclinic, space group P1, a = 9.842 (3), b = 15.123 (4), c = 8.221 (3) Å, $\alpha = 100.54$ (3), $\beta = 113.02$ (2), $\gamma = 96.42$ (2) °, V = 1084.2 (7) ų, Dc = 1.294 gcm⁻³, Do = 1.290 gcm⁻³, Z = 2, R = 0.099, Rw = 0.100. CCDC reference number 255495.
- 5. The disorder of **3aa** is schematically shown below. The line drawing with numbering sequence is shown in the supplementary data.



- 6. Crystal Data of **3ab**; $C_{23}H_{23}NO_6$, M = 409.44. monoclinic, space group P21/c, a = 14.323 (6), b = 13.443 (8), c = 10.689 (4) Å, $\beta = 92.90$ (3)°, V = 2055 (1) ų, $Dc = 1.323 \text{ gcm}^{-3}$, $Do = 1.308 \text{ gcm}^{-3}$, Z = 4, R = 0.081, Rw = 0.131. CCDC reference number 221324.
- 7. The distances and angles of the enol moiety are shown in the supplementary data.
- 8. The IR spectra (nujol) of **3ab** and **3ac** suggest that the host transforms to the enol form. The NMR spectral patterns closely resemble to that of **3aa**, indicating that the structure in solution is different from the crystal structure.
- 9. The preliminary experiment shows that K_{assoc} is 44.8 M⁻¹.
- 10. A referee pointed out that the β-ketoester moiety is important for the inclusion ability.