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Carboxylic acid clathrate hosts of Diels–Alder adducts of phencyclone and 2-alkenoic acids. Role of bidentate C–H · · · O hydrogen bonds between the phenanthrene and carbonyl groups in host–host networks †

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Carboxylic acid host compounds (**3**) having a phenanthrene-condensed bicyclo[2.2.1]hept-2-en-7-one skeleton have been synthesized by the [4 + 2]π cycloaddition of phencyclone (**1a**) with 2-alkenoic acids (**2**) and their inclusion behavior was investigated. The *endo* [4 + 2]π cycloadducts (**3**) enclathrated alcohols and ethers besides aromatics and ketones. The X-ray crystallographic analysis of the inclusion compound (**3ac**·dioxane) of the *endo* [4 + 2]π cycloadduct (**3ac**) of phencyclone and *trans* 2-butenoic acid (**2c**) indicated that dioxanes are located at the opposite side of the bridged carbonyl of the bicyclo[2.2.1]hept-2-en-7-one moiety, in which the O–H · · · O and C–H · · · O hydrogen bonds play an important role in the inclusion complex formation. Similarly, a pair of 3-pentanone molecules were included in the *endo* [4 + 2]π cycloadduct (**3ae**) of **1a** and cinnamic acid (**2e**). In both cases, the hosts are linked by the edge-to-face interaction between the phenanthrene and phenyl rings and the "bidentate" C–H · · · O hydrogen bonds between the phenanthrene-ring hydrogens and the bridged carbonyl or the carboxylic carbonyl group. The *endo* [4 + 2]π cycloadduct (**3bl**) of tetracyclone (**1b**) and acrylamide (**2l**) also showed a wide-range inclusion behavior, in which alcohols are included by making a hydrogen-bond loop with the amide groups. The inclusion behavior of the carboxylic acid Diels–Alder hosts is discussed on the basis of the single crystal X-ray analysis, thermal analysis and semiempirical molecular orbital calculation data.

Introduction

Crystalline inclusion compounds (clathrates) have become an important subject of supermolecular chemistry owing to their great potential for a variety of fundamental and practical issues.[1a,b] During the last decade, detailed studies have been made on host molecules of typical shapes, in which particular steric requirements of the host molecule and role of functional group interactions between host and guest have been clarified, giving new strategies for crystalline inclusion formation leading to the design of novel host types.[1]

In the course of our studies on the pericyclic reaction behavior of cyclopentadienones, we observed that the *endo* [4 + 2]π cycloadducts [Diels–Alder (DA) adducts] of phencyclone (**1a**) and some dienophiles form crystalline inclusion complexes with recrystallization solvents.[2] In connection with this, we have reported that non-hydroxylic clathrate hosts of the DA adducts of phencyclone and *N*-aryl maleimides showed an efficient inclusion behavior.[3] Single crystal X-ray analyses indicated that the void space (region A or B) on the phenanthrene ring plane of the DA adducts plays an important role in complex formation (see Fig. 1). In the *endo* DA adduct hosts in which region B is occupied with the large endo-oriented substituent of the dienophiles, the inclusion of guests occurs in region A. However, these nonhydroxylic host compounds could not include alcoholic solvents, indicating that a hydroxy or carboxylic group is necessary for hydrogen-bond formation with alcoholic guests.

Previously-reported works[1c,f] describing the inclusion behavior of hosts having carboxylic group(s) indicate that the main host–host interactions in guest-free hosts are the hydrogen bonds which form the carboxylic acid dimer in which alcoholic guests are inserted into the 8-membered hydrogen-bonded ring, forming a 12-membered hydrogen-bonded loop with the carboxyl groups from the hosts. On the other hand, in our non-hydroxylic DA-adduct hosts, the host–host framework of a guest-free host is built by edge-to-face interactions[4] between the phenanthrene and phenyl rings attached to the α positions of the bridged carbonyl. In their inclusion complexes, the aromatic guests are engaged in the aryl–aryl interaction with the phenanthrene ring in place of the edge-to-face interaction between hosts.

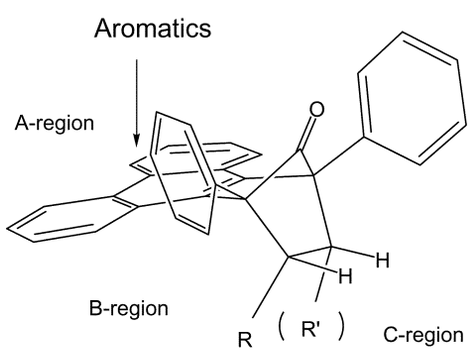

Fig. 1 Structures of the [4 + 2]π cycloadducts (**3**) of phencyclone and some dienophiles and schematic representation of the recognition sites.

On the basis of this background, we considered that a combination of these two host characteristics may give us a new carboxylic acid DA-adduct host. Along this concept, we can thus draw the inclusion scheme (Fig. 2) for a wide-range inclusion for various solvents. Here we report the inclusion behavior of the carboxylic acid DA-adduct hosts on the basis of the

† Electronic supplementary information (ESI) available: structures and packing diagrams. See http://www.rsc.org/suppdata/ob/b2/b212129h/

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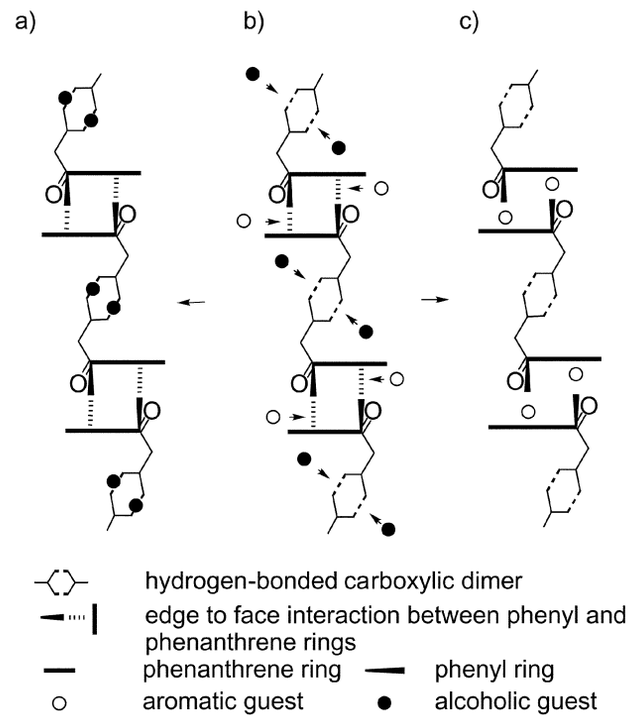


Fig. 2 Possible inclusion modes a) inclusion of alcoholic guests; b) host-host framework (guest free); c) inclusion of aromatic guests.

X-ray crystal and semiempirical molecular-orbital calculation structures of the inclusion compounds of the DA adducts of phencyclone and tetracyclone.

Results

Preparation of the hosts and their inclusion behavior

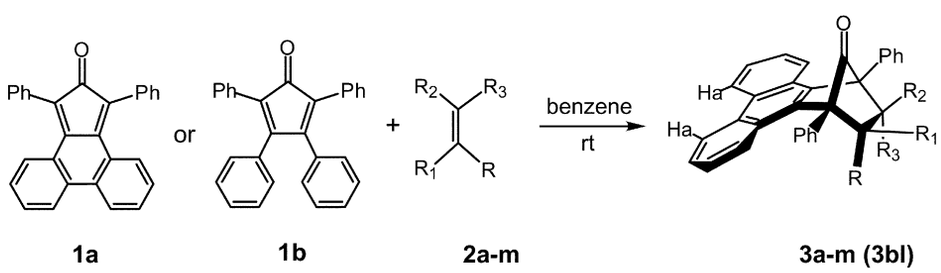
The *endo* DA-adducts (**3a**–**f**) having the 7-oxo-bicyclo[2.2.1]-hept-5-ene-2-carboxylic acid skeleton were prepared from the thermal reactions of phencyclone (**1a**) with acrylic acid (**2a**), *trans* 2-butenoic acid (**2b**), *trans* 2-pentenoic acid (**2c**), *trans* 2-hexenoic acid (**2d**), cinnamic acid (**2e**) and 1-methylacrylic acid (**2f**). The DA-adducts (**3ag**, **3ah**) of maleic acid (**2g**) and fumaric acid (**2h**), the esters (**3ai**, **3aj** and **3ak**) derived from **3aa**, **3ag** and **3ah** and the amide derivatives (**3al**, **3am**) of **3aa** and **3af** were also studied for comparison (Scheme 1 and ESI-1†). The *endo*/*exo* nature of the DA adduct hosts were established by inspection of the O=*C*–C–C–*H* correlation in the ^{1}H-NMR spectra.[5]

A variety of solvents (17 solvents of four types; alcohols, ketones, ethers and aromatics) was used to test the inclusion properties of the host compounds **3aa**–**ah** having free carboxyl group(s). The inclusion compounds were obtained by recrystallization of the host compounds from the respective guest solvents. The results are summarized in Table 1. The host : guest ratios were evaluated by ^{1}H-NMR spectral integration.

As shown in Table 1, the DA adduct **3aa** did not enclathrate straight-chain alcohols but included branched alcohols. With ketonic and aromatic solvents, the 1 : 1 and 2 : 1 inclusion complexes were formed. In the case of **3ab** having an *exo*-methyl group at the 3-position, wide range inclusions involving straight-chain alcohols are observed, in which aromatic solvents afford the 2 : 1 complexes. The DA adduct **3ac** bearing an *exo*-3-ethyl group is an efficient host, showing similar inclusion behavior to that observed in **3ab**. However, the DA adduct **3ad** bearing an *exo*-3-propyl group allows fewer inclusions. The effect of the *exo*-3-phenyl substituent of **3ae** is not significant, in which the phenyl substituent probably changes the character of the host–host network of the alkyl-substituted hosts to a different one (see below). The *exo*-2-methyl derivative **3af** formed 2 : 1 inclusion compounds with six-membered-ring guest compounds.

The esterified DA adducts (**3ai**,**3aj**) of **3aa** afforded no clathrates with the solvents used, indicating that the carboxylic acid group plays a crucial role in clathrate formation.

The dicarboxylic acid hosts showed poor inclusion ability in comparison with the monocarboxylic acid hosts. The inclusion compound formation of the host (**3ag**) derived from fumaric acid did not occur with aromatic solvents, whereas the host (**3ah**) derived from maleic acid only complexed with ketones. This is attributable to the insolubility of the host compounds in the solvents used. The DA adducts (**3al**, **3am**) bearing an amide group showed poor inclusion ability.



1a **1b** **2a-m** **3a-m (3bl)**

2a: R=COOH, R_1=R_2=R_3= H,

2b: R=COOH, R_1=H, R_2=Me, R_3=H

2c: R=COOH, R_1=H, R_2=Et, R_3=H

2d: R=COOH, R_1=H, R_2=n-Pr, R_3=H

2e: R=COOH, R_1=H, R_2=Ph, R_3=H

2f: R=COOH, R_1=Me, R_2=H, R_3=H

2g: R=COOH, R_1=H, R_2=COOH, R_3=H

2h: R=COOH, R_1=H, R_2=H, R_3=COOH

2i: R=COOMe, R_1=R_2=R_3=H

2j: R=COOMe, R_1=H, R_2=COOMe, R_3=H

2k: R=COOMe, R_1=H, R_2=H, R_3=COOMe

2l: R=$CONH_2$, R_1=R_2=R_3=H

2m: R=$CONH_2$, R_1=Me, R_2=H, R_3=H

Scheme 1

Table 1 Crystalline inclusion compounds (host : guest molar ratio)

Guest solvent	Host compound[a]												
	3aa	**3ab**	**3ac**	**3ad**	**3ae**	**3af**	**3ag**	**3ah**	**3ai,aj**	**3ak**	**3al**	**3am**	**3bl**
Acetone	1 : 1	1 : 1	1 : 1		1 : 1	1 : 1	[d]	2 : 1	—	—	—	—	1 : 1
2-Butanone	2 : 1	1 : 1	1 : 1		1 : 1	1 : 1	2 : 1	2 : 1	—	—	—	—	1 : 1
3-Pentanone	2 : 1	1 : 1	1 : 1		1 : 1	1 : 1	1 : 1	1 : 1	—	—	—	—	1 : 1
Methanol		1 : 1	1 : 1				2 : 1	[e]	—	—	—	—	1 : 1
Ethanol	1 : 1					1 : 1	[e]		—	—	—	—	1 : 1
n-Propanol		1 : 1	1 : 1		1 : 1	1 : 1	1 : 1	[e]	—	—	—	—	1 : 1
i-Propanol	1 : 1	1 : 1	1 : 1		1 : 1		1 : 1	[e]	—	—	—	—	1 : 1
n-Butanol		1 : 1	1 : 1		1 : 1	[b]	1 : 1	[e]	—	—	—	—	1 : 1
i-Butanol	1 : 1	1 : 1	1 : 1		1 : 1	1 : 1	1 : 1	[e]	—	—	—	—	1 : 1
t-Butanol	1 : 1	1 : 1	1 : 1		1 : 1	[c]			—	—	—	—	—
THF	1 : 1	1 : 1	1 : 1	1 : 2	1 : 1		1 : 1		—	—	—	—	1 : 1
1,4-Dioxane	1 : 1		1 : 1	1 : 1		2 : 1	1 : 1	1 : 1	—	1 : 1	—	—	[d]
Benzene	1 : 1		3 : 2		1 : 1	2 : 1	[b]		—	—	2 : 1	—	1 : 1
Toluene	2 : 1	2 : 1	2 : 1	2 : 1	2 : 1	2 : 1	[b]		—	—	—	—	1 : 1
o-Xylene	1 : 1	2 : 1	2 : 1		2 : 1	2 : 1	[b]		—	—	2 : 1	—	1 : 1
m-Xylene	2 : 1	2 : 1	2 : 1		2 : 1	2 : 1	[b]		—	—	—	—	1 : 1
p-Xylene	1 : 1	2 : 1	2 : 1	2 : 1	2 : 1	1 : 1	[b]		—	—	2 : 1	—	1 : 1

[a] Blank: no inclusion. [b] Easily soluble in solvent. [c] Slightly soluble in solvent. [d] Ratio dependent on recrystallization condition. [e] Decomposition.

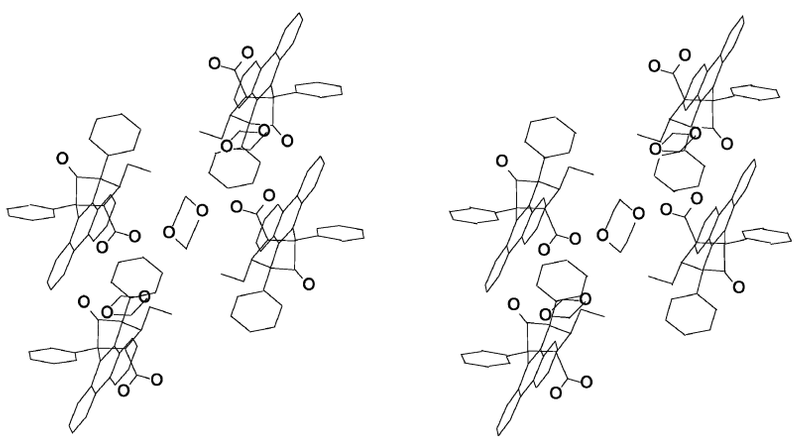


Fig. 3 Stereoview of the molecular packing of the inclusion compound of **3ac**·1,4-dioxane (1 : 1).

A mention should be made of the inclusion behavior of aromatic guests which do not have any strong hydrogen-bond acceptors. In general terms, aromatic solvents were included as 2 : 1 (host : guest) complexes although some exceptions are present.

As for the inclusion of xylenes, **3aa** and **3af** showed a somewhat different inclusion behavior depending upon the structure of the xylenes. The host **3aa** includes *o*-xylene and *p*-xylene as the 1 : 1 (host : guest) complex whereas it favors the 2 : 1 stoichiometric ratio for *m*-xylene. These results are supported by the thermogravimetry (TG) and differential thermal analysis (DTA) data. In the DTA spectrum of **3aa**·*p*-xylene (1 : 1), two endothermic peaks were observed at 120° and 170 °C, showing a two-step weight decrease.

The inclusion compound **3af**·*p*-xylene is a 1 : 1 complex, showing a two step TG pattern at 124 and 172 °C, whereas other aromatic solvents and dioxane formed 2 : 1 complexes showing a single peak.[6] The inclusion compounds **3af**·*o*-xylene (2 : 1) and **3af**·*m*-xylene (2 : 1) showed only low-temperature peaks corresponding to the weak host–guest interactions and **3af**·benzene (2 : 1) and **3af**·toluene (2 : 1) showed only high-temperature peaks.

It is worthy of note that the DA adduct (**3bl**) of tetracyclone (**1b**) and acrylamide (**2l**) showed very interesting inclusion behavior although good inclusions have not yet been observed in the DA adducts of tetracyclone and various dienophiles. The X-ray analysis of the inclusion compound of **3bl**·ethanol showed that the role of the $CONH_2$ group is similar to the COOH group of the phenanthrene analogs.

X-Ray structural studies §

Crystallographic data and details of the structure refinement calculations of the inclusion compounds **3ac**·dioxane (1 : 1), **3ae**·3-pentanone (1 : 1) and **3bl**·ethanol (1 : 1) are given in Table 2. The numbering sequences are given in ESI-2a, ESI-3a and ESI-4a †.

1) Crystal structure of 3ac·dioxane

The computer-generated drawing (stereoview) of the crystal structure of **3ac**·dioxane is shown in Fig. 3. The numbering sequence is given in ESI-2a †. The host compound **3ac** is the *endo* DA adduct with respect to the COOH group of the dienophile (*trans*-pent-2-enoic acid), in which the C3–C4 bond considerably elongates to 1.598(6) Å, the angle of the bridged carbonyl C1–C7–C4 is 99.1(3)° and the phenanthrene is planar judged from the dihedral angle (C12–C13–C19–C18 0.1(7)°).

At the final stage of the structure determination, the atom assignment of the dioxane was made on the basis of intermolecular atomic distances. The closest intermolecular atomic distance (2.734(6) Å) between the dioxane molecule and the host was assigned to the hydrogen bond between the hydroxy oxygen of the carboxylic acid moiety and an oxygen atom of the dioxane (–C(=O)–*O*–H ··· *O*<). This was confirmed by comparison of the X-ray distance with many reported values.[7]

§ CCDC reference numbers 199766–199768. See http://www.rsc.org/suppdata/ob/b2/b212129h/ for crystallographic data in .cif or other electronic format.

Table 2 Crystal data and intensity measurement

Compound	**3ac**·1,4-Dioxane (1 : 1)	**3ae**·3-Pentanone (1 : 1)	**3bl**·Ethanol (1 : 1)
Formula	$C_{38}H_{33}O_3 \cdot C_4H_8O_2$	$C_{38}H_{26}O_3 \cdot C_5H_{10}O$	$C_{32}H_{25}NO_2 \cdot C_2H_6O$
Mp/°C	269–270	252–253	189–192
Formula weight	569.68	616.76	501.62
Crystal system	Triclinic	Triclinic	Triclinic
Lattice type	Primitive	Primitive	Primitive
Lattice parameters			
a/Å	12.031(5)	11.899(1)	11.882(5)
b/Å	14.718(7)	13.792(1)	12.857(3)
c/Å	9.702(3)	11.684(1)	10.411(5)
α/°	107.60(3)	98.192(8)	98.94(3)
β/°	102.69(3)	111.951(7)	104.64(4)
γ/°	68.07(3)	67.864(7)	63.49(2)
V/Å^3	1507(1)	1647.3(3)	1375.4(9)
Space group	*P*(−1)(#2)	*P*(−1)(#2)	*P*(−1)(#2)
Z	2	2	2
*D*c/g cm^{-3}	1.257	1.243	1.211
*D*m/g cm^{-3}	1.251	1.238	1.225
Solvent	1,4-Dioxane	3-Pentanone	Ethanol
Radiation	MoKα (λ = 0.71069 Å)	MoKα	MoKα
Scan range/°	$2\theta < 55.0$	$2\theta < 55.0$	$2\theta < 55.0$
Unique data collected	6927	7557	7630
Unique data used (I>3.00 σ(I))	2750	5530	6902
R	0.067	0.042	0.067
*R*w	0.076	0.032	0.091

Each ether oxygen of dioxane was hydrogen-bonded with the COOH group of the host and geometrically correlated with a center of symmetry of dioxane. The carbonyl oxygen of the COOH moiety makes a *C*–H ··· *O*=C type hydrogen bond[8] (3.20(1) Å) with the α-methylene carbon of dioxane. The relative position of the host and guest are depicted in Fig. 4 (see also ESI-2b-e†).

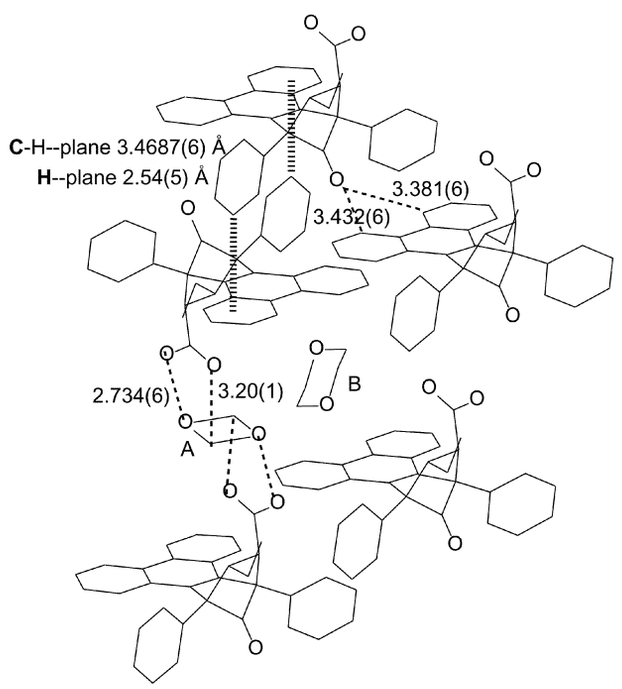


Fig. 4 Relative positioning of host and guest molecules and host–host (edge to face and bidentate C-H ··· O) and host–guest (O–H ··· O and C–H ··· O) interactions for **3ac**·1,4-dioxane (1 : 1).

The analysis also suggests the presence of the C–H ··· π interaction[4f,4g] between the α-methylene hydrogen of dioxane and the phenanthrene ring, in which the nearest C ··· C distance (3.571(8) Å) is found between the α-carbon of the dioxane and the carbon atom (3-position) of the phenanthrene moiety.

Another molecule (dioxane B) of dioxane located at the (0.5, 0.5, 0.5) position is free from strong O–H ··· O< type hydrogen bonds. The dioxane B is considered to be enclathrated by the interaction of an α-methylene hydrogen of dioxane with both the carbonyl oxygen of the carboxylic acid group (*C*–H ··· *O*=C 3.59 Å, C–*H* ··· *O*=C 2.59 Å) and the phenanthrene ring (distance between the α-methylene carbon-phenanthrene plane is *ca.* 3.5 Å).

Host–host network. The host framework is built by "bidentate" Ar–H ··· O= and "edge-to-face" interactions. Along the *c*-axis, the host molecules form a "head-to-tail" arrangement between the bridge carbonyl oxygen and the two hydrogens (C12–H and C18–H) of the phenanthrene moiety (see Fig. 4), in which the bridged carbonyl acts as a double proton acceptor and builds weak C–H ··· O interactions with the phenanthrene-ring hydrogens.

The "edge-to-face" interaction is found between the phenanthrene-ring plane and the diphenyl ring of the adjacent host molecule, in which the two phenanthrene-condensed 1,3-diphenylcyclopent-3-enone moieties are linked to each other through a (0.5, 0.0, 0.5) point of symmetry. As can be seen in Fig. 2, this structural feature is assumed to be an inclusion mode of aromatic guests into the region A, stabilizing the host–host network. Along the *a*-axis, the host molecules are linked by C–H ··· π interactions between the phenyl rings.

2) Crystal structure of 3ae·3-pentanone

The crystal packing diagram (stereoview) of **3ae**·3-pentanone is shown in Fig. 5. The numbering sequence is given in ESI-3a†. The host compound **3ae** is the *endo* DA adduct with respect to the carboxylic group of the dienophile (*trans*-cinnamic acid), in which the bond elongations are observed in C1–C2 (1.580(2) Å), C2–C3 (1.571(2) Å) and C3–C4 (1.570(2) Å) of the bicyclo[2,2,1]hept-2-en-7-one moiety reflected by the ring strain and steric repulsion due to the introduction of the exo-oriented phenyl group. The angle of the bridged carbonyl C1–C7–C4 is 99.8(1)° and the phenanthrene ring is almost planar (C12–C13–C19–C18 0.8(2)°).

The important host–host and host–guest interactions are shown in Fig. 6 (see also ESI-3b†). The distance (–CO*O*–

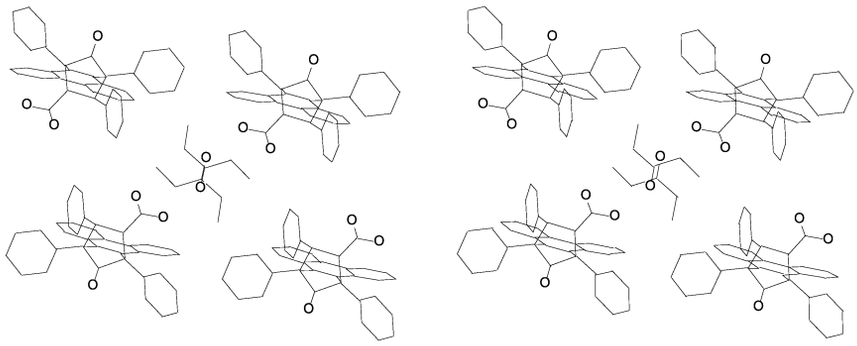


Fig. 5 Stereoview of the molecular packing of the inclusion compound of **3ae**·3-pentanone (1 : 1).

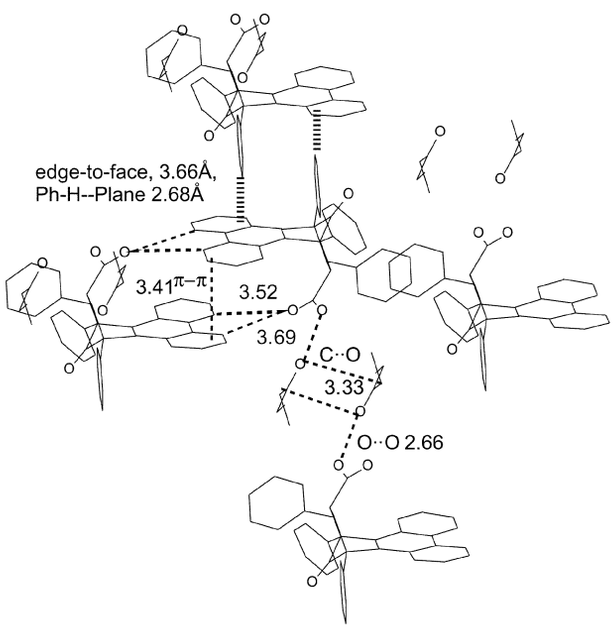


Fig. 6 Relative positioning of host and guest molecules: host–host (edge to face, face to face, and bidentate C–H ··· O) and host–guest (O–H ··· O and C–H ··· O) interactions for **3ae**·3-pentanone (1 : 1).

H ··· *O*=C<) between the hydroxylic oxygen of the COOH moiety and the carbonyl oxygen of 3-pentenone is 2.66 (2) Å, characteristic for the H bond. The hydrogen-bonded 1 : 1 units are related by the center of symmetry. The guest ketones are arranged in such a way as to cancel the dipole–dipole interaction of the carbonyl functions, in which the intermolecular C ··· O distance is 3.329 (2) Å.

The carbonyl oxygen of the COOH group makes C–H ··· O=C type hydrogen bond (C ··· O 3.743(3) Å) with an α-hydrogen of the guest ketone (see ESI-3b†). The host and guest molecules are arranged through the network of CH ··· O and O–H ··· O hydrogen bonds along the *c*-axis. Looking through the bc plane, the two guest molecules are included in the large cavity surrounded by the eight phenyl groups of the four host molecules (see ESI-3c,d†).

Host–host network. The "edge-to-face" interaction similar to that observed in **3ac**-dioxane is also found between the phenanthrene-ring plane and the diphenyl ring of the neighboring host molecule. The "face-to-face" interaction is observed between the phenanthrene rings, in which the nearest atom-plane distance (3.227(4) Å) is found between the best plane (C8–C13) and the C16 atom of the neighboring host, shorter than the VDW distance. This close contact between the phenanthrene rings is associated with the π–π interaction clamped by the two "bidentate" Ar–H ··· O=C< hydrogen bonds between the phenanthrene-ring hydrogens and the carbonyl oxygen of the COOH group (see Fig. 6).

3) Crystal structure of 3bl·ethanol

The packing diagram (stereoview) of **3bl**-ethanol and important host–host and host–guest interactions are shown in Figs 7 and 8, respectively (see also ESI-4†). The numbering sequence is given in ESI-4a. The two molecules of ethanol are included by hydrogen bond with the host amide moieties forming 12-membered ring (Fig. 8). The host-guest hydrogen-bond distances of H_2N–C=*O* ··· *H*O-Et and –N–*H* ··· *O*(H)-Et are 1.92(3) and 2.07(3) Å, respectively.

Host–host network. The host frame is stabilized by two interactions. The strong N–H ··· O interaction is found between the bridged carbonyl oxygen and the amide hydrogen of the neighboring host molecule (N*H* ··· *O* 2.28(3) Å), showing a face-to-face disposition of the 1,3-diphenyl-2-propanone moieties.

The "edge-to-face" interaction is also found between the phenyl rings of the stilbene moieties. The interatomic distances between the hydrogen at the 2-position of a phenyl ring of the stilbene moiety and the carbon atoms (1, 2, 3, 4 positions) of another phenyl ring of the neighboring host molecule are within a range of 3.0–3.2 Å. The distance between the hydrogen atom (C3–H) of the phenyl group and the phenyl ring plane of the neighboring host molecule is near to 2.8 Å.

Molecular modeling of the intermolecular interactions. On the basis of the structural information of the known inclusion compounds, we tried to anticipate the structures of new inclusion compounds by a computer-modelling technique using semiempirical molecular orbital methods.[9] The molecular modellings were performed using the interaction modes observed in the crystals. The hydrogen bond interaction between the carboxylic moieties of hosts and/or guests and edge-to-face and bidentate C–H ··· O host–host interactions are depicted in Fig. 9. The stabilization energies are summarized in Table 3.

The calculation indicates that a sizable stabilization energy will be gained by the 12-membered hydrogen-bonded loop formation (11.6 kcal/mol in PM5). The dual edge-to-face interaction energy is estimated to be 1.91 kcal/mol in PM5, within the commonly accepted value.[4f] The bidentate C–H ··· O interaction energy is 1.51 kcal/mol in PM5, which is comparable to the value at HF/6-31+G(d,p) level.[10]

The structures of the 2 : 1 inclusion compound of aromatic guests in the carboxylic acid hosts were calculated using **3ab**·toluene. The most probable structure is the one in which a toluene molecule is included at the cavity created by docking of two units of the carboxylic acid dimer with the bidentate CH ··· O interactions. The interaction energy due to the complex formation was calculated to be 17.5 kcal/mol.

Discussion

It is important to note that the regions A in **3ac**·dioxane and **3ae**·3-pentanone are occupied by the phenyl substituents of neighboring host molecules, stabilizing the host–host network

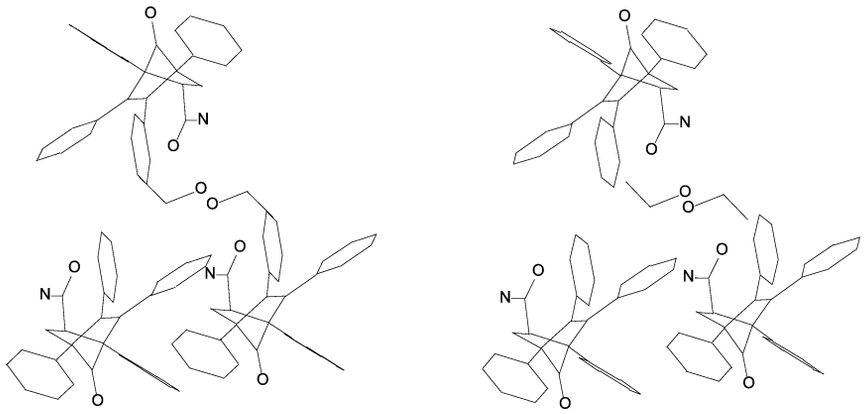


Fig. 7 Stereoview of the molecular packing of the inclusion compound of **3bl**·ethanol (1 : 1).

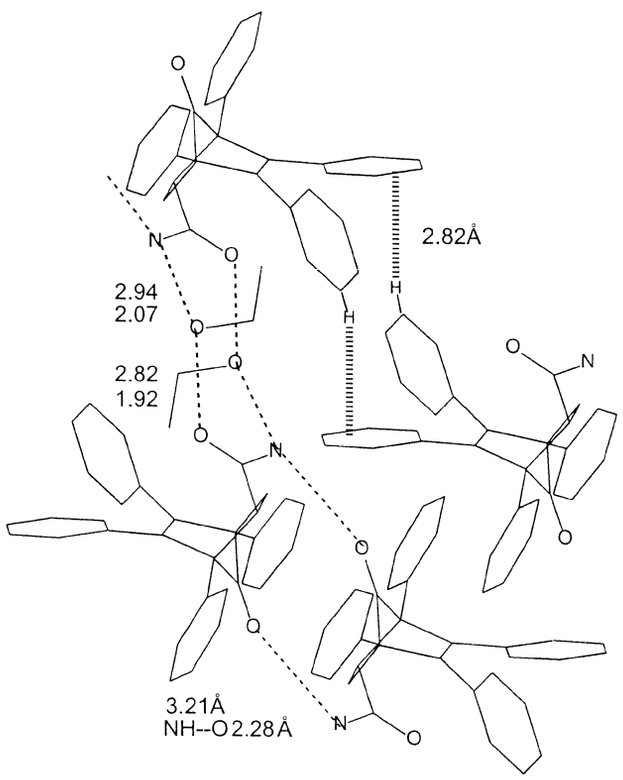


Fig. 8 Relative positioning of host and guest molecules and host–host (edge to face and N–H ··· O) and host–guest (N–H ··· O and O–H ··· O) interactions for **3bl**·ethanol (1 : 1).

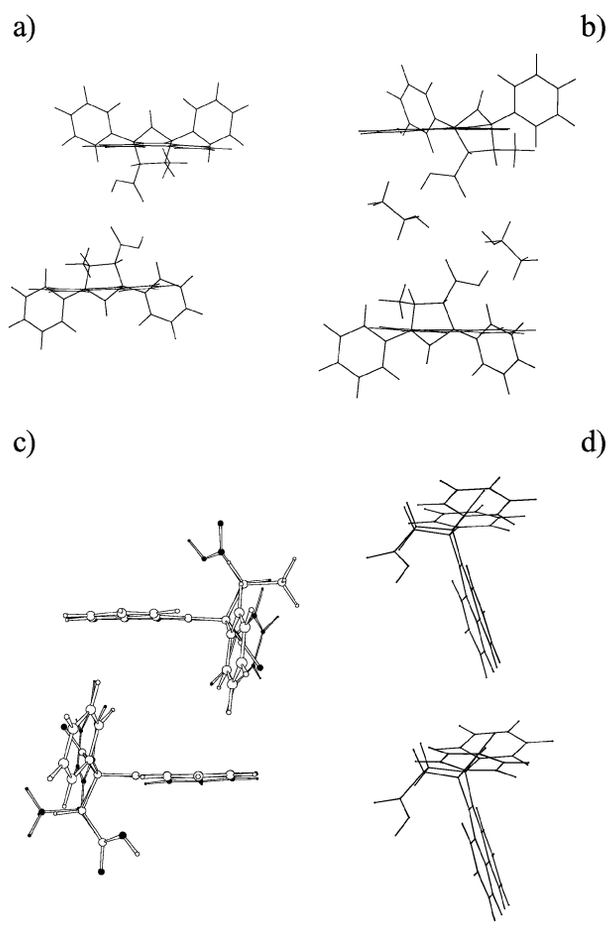


Fig. 9 PM5-calculated partial interaction structures extracted from the inclusion compounds of **3aa**: a) the carboxylic dimer, b) the 12-membered hydrogen-bond loop of the carboxylic acid and ethanol, c) the edge-to-face interaction of **3aa**, d) the bidentate C–H ··· O interaction between **3aa**.

by "edge-to-face" interactions (see Figs 4 and 6). A similar structural feature was also observed in the inclusion compound **3bl** of the tetracyclone-DA-adduct host (see Fig. 8).

As described above, the introduction of a COOH group into the phenanthrene-condensed bicyclo[2.2.1]hept-2-en-7-one skeleton at the endo 2-position exhibited a clear-cut effect on the inclusion of guest molecules having alcoholic, ethereal or ketonic oxygen by the O–H ··· O hydrogen bonding.

The inclusion mode of alcohols in the carboxylic acid hosts of the bicyclo[2.2.2]octane derivatives derived from the DA reaction of anthracene with 2-alkenoic acids was clarified by Weber *et al.* on the basis of the X-ray crystallographic data,[1e] illustrating that a 12-membered ring (H atoms included) is formed *via* hydrogen bonds with carboxyl groups of the hosts. This hydrogen bond loop was also found in the clathrates of the 1,1′-binaphthyl-2,-2′-dicarboxylic acid host with MeOH, EtOH or *n*–PrOH as guests.[1c,f]

On the basis of these findings, alcoholic guests are considered to be enclathrated by cyclic O–H ··· O hydrogen bond among the hosts and guests. This assumption is supported by the fact that alcohols were included as 1 : 1 complexes without exception and by the X-ray structure of **3bl**·ethanol.

The inclusion behavior of the carboxylic acid hosts toward alcohols depends upon the structural feature of the dienophilic moiety. The methyl or ethyl substituent attached to the *exo*-C3 position adjacent to the carboxylic group seems to make a suitable cavity for inclusion of alcohols (see Table 1).

Unfortunately, we could not obtain crystal structural evidence of the inclusion complex of phencyclone DA-adduct hosts and alcohols. Therefore we tried to calculate the 12-membered loop structures between the hosts and ethanol using the semiempirical MO method. Inspection of the calculated

Table 3 Heats of formation and stabilization energies (kcal mol^{-1}) for the formation of the 12-membered hydrogen-bond loop between **3ab** and ethanol and the typical intermolecular interactions

Substrates	PM3	PM5	AM1
Host (**3ab**)	14.2	−13.5	31.5
EtOH	−56.8	−53.6	−62.7
12-Membered hydrogen-bond ring formation (Host : guest = 2 : 2)	−100.0	−145.7	−78.3
Stabilization energy	14.6	11.6	15.9
Carboxylic host dimer by hydrogen-bond	19.7	−31.2	56.3
Stabilization energy	8.6	4.1	6.6
Host dimer by edge to face	26.0	28.9	62.4
Stabilization energy	2.37	1.91	0.48
Bidentate interaction (head-to-tail)	33.26	−21.89	61.3
Stabilization energy	4.95	1.51	1.59

structures of **3ab**–**d**·ethanol (2 : 2 complex) indicate that change of the C3-alkyl group of the host from methyl, ethyl to propyl causes an increase in the steric crowding between the alkyl chains of the guest and host. From this, the lack of the inclusion ability of **3ad** (R_1 = *n*-propyl) toward alcohols can be attributed to the steric interference between the alkyl group of the guest alcohols and the C3-propyl substituent of the host (see the PM3-optimized structures for **3ad**·ethanol (2 : 2 complex) depicted in ESI-5†).

The guests bearing ethereal or ketonic groups are recognized by the hydrogen bond between the carboxylic OH of the hosts and the ethereal or ketonic oxygen of guests, which are strengthened by the C–H ··· O type weak hydrogen bond between the α-methylene hydrogen of the guest and the carbonyl oxygen of the COOH group of the hosts.

The intermolecular bidentate C–H ··· O bond between the bridged carbonyl group and phenanthrene ring hydrogens acts as another stabilizing force of the host–host network. As observed in the crystal structure of **3ae**·3-pentanone, the presence of the *exo*-C2-phenyl hinders the bidentate C–H ··· O bond formation between the bridged carbonyl and phenanthrene ring hydrogens, resulting in an alternative bidentate C–H ··· O bond formation between the carbonyl group of the COOH moiety and the phenanthrene ring. This probably affords a larger cavity, affecting the inclusion behavior.

Aromatic solvents are included as 2 : 1 (host : guest) complexes with the exception of some cases. The 1 : 1 inclusion behavior of the carboxylic acid hosts can be explained by consideration of two inclusion modes. One molecule of aromatic guests is assumed to be included into region A, whereas another guest molecule is located between the hydrogen-bonded carboxylic acid dimer moieties (region C). In thermal analyses of the 1 : 1 inclusion compounds of aromatic solvents, a peak at the lower temperature than the boiling point (bp) was observed, ascribable to nonhydroxylic recognition by region A. This may be supported by the DSC data of the inclusion compound[3b] of *p*-xylene with the DA-adduct host of phencyclone and *N*-(3-methylphenyl)maleimide.[11] In addition to this inclusion mode, another stronger interaction force must be operative in the 1 : 1 inclusion compound. This is perhaps a result of inclusion into a cavity created by strong host–host linkage of carboxylic acid moieties and the effective bidentate C–H ··· O bond between the phenanthrene ring and the bridged carbonyl group.

During the course of the study, we always tested the inclusion ability of the DA adducts of tetracyclone and various dienophiles in comparison with the corresponding inclusion behaviors of the phencyclone DA adducts. In general, the tetracyclone DA adducts showed poor inclusion properties. However, the DA adduct of tetracyclone and acrylamide showed an unexpected inclusion behavior (see Table 1). The X-ray analysis of **3bl**·ethanol indicates that the amide groups make 12-membered cyclic hydrogen bond links with ethanols in a similar manner to the known hosts bearing carboxyl groups.[1c,f] The host **3bl** did not enclathrate *tert*-butyl alcohol, presumably due to the difficulty in the formation of the cyclic hydrogen bonds among the hosts and guests. In comparison with the carboxylic acid hosts, the role of the two amide hydrogens seems to be important, in which one is used for host–guest binding and the other for host–host binding. The strong interaction of the N–H ··· O hydrogen bonds reflected on the DTA spectrum that the desorption endotherm temperature of **3bl**·ethanol is 128 °C. As for the inclusion mode other than the hydrogen bond interaction, the flexibility of the four phenyl rings would play an important role in the recognition of the guest molecules of various types.

In summary, the inclusion-pattern diagrams clarified in this study are shown in Fig. 10. The newly-prepared carboxylic acid hosts of the *endo* DA adduct of phencyclone and 2-alkenoic acid showed the high inclusion ability for different types of guests.

The carboxylic groups play a leading role for uptake of polar guests by hydrogen-bond loop formation, in which the

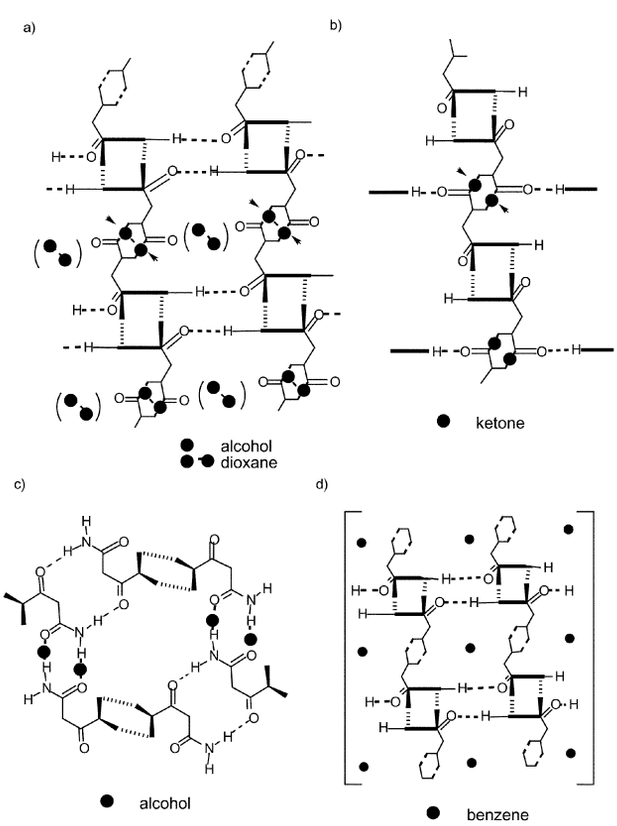


Fig. 10 Inclusion-pattern diagrams: a) alcoholic and ethereal (dioxane) guests in **3aa**; b) ketonic guests in **3af**; c) alcoholic guests in **3bl** and aromatic guests in **3aa** (by MO calculation).

"edge to face" and "bidentate" C–H ··· O hydrogen-bond interactions stabilizes the host framework. The cavity for the 2 : 1 inclusion complex of aromatic guests is considered to be formed by connecting the two carboxylic acid dimer units by the bidentate C–H ··· O hydrogen-bond interactions between the carbonyl group and the phenanthrene ring.

Experimental

Melting points were uncorrected. The IR spectra were taken with a Hitachi 270–30 spectrophotometer. ^{1}H-NMR and ^{13}C-NMR spectra were recorded using JEOL JNM-EX 270 (270 MHz) and JNM-A 500 (500 MHz) spectrometers with *ca*. 10% solution of TMS as an internal standard; chemical shifts are expressed as values (ppm) and the coupling constants (*J*) are expressed in Hz. Mass spectra were obtained using a JEOL JMS-DX 303 instrument. UV spectra were recorded on a Shimadzu UV-2500PC spectrophotometer. Thermal analyses were performed on a PERKIN ELMER 7 SERIES/UNIX DSC 7 (Differential Scanning Calorimeter DSC), a PERKIN ELMER 7 SERIES/UNIX TGA 7 (thermogravimetric analysis TG) and a Shimadzu DTG-50/50H Simultaneous TG/DTA instrument.

Material

Phencyclone (mp 245–255 °C) was prepared according to the previously reported method using triton B (trimethyl benzylammonium hydroxide). The product was washed with ethanol, yield 98%.[12]

[4 + 2]π Cycloadducts (3aa) of 1a and acrylic acid (2a) (general procedure)

A solution of **1a** (0.3 g, 0.79 mmol) and **2a** (0.057g, 0.79 mmol) in toluene (4.0 ml) was refluxed at 110 °C until the dark green color had faded out. After cooling, benzene was added to the reaction mixture. The precipitated crystals were collected and dried under vacuum to give a colorless powder (0.3 g, yield 84%, mp 277–278 °C).

3aa: Yield: 84%. Mp. 277–278 °C. IR (KBr): 1784 (bridge >C=O), 1736 (>C=O), 1718 (>C=O) cm^{-1}. ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 2.65 (dd, 1H, J = 12.2, 4.6, >CH–*H* (*endo*)), 3.11 (dd, 1H, J = 12.2, 10.2, >CH–*H* (*exo*)), 4.14 (dd, 1H, J = 10.2, 4.6, >CH- (*exo*)), 7.02–7.86 (m, 16H, aromatic H), 8.66 (d, 1H, J = 8.6, Ha), 8.71 (d, 1H, J = 8.6, Ha). MS (*m*/*z*) 454 (M^+), 426 ($M^+ - CO$). Anal. calcd $C_{32}H_{22}O_3$: C, 84.56; H, 4.88. Found: C, 84.33; H, 4.97.

[4 + 2]π Cycloadducts (3ab) of 1a and crotonic acid (2b)

3ab: Yield: 75%. Mp. 270–272 °C. IR (KBr): 1780 (bridge >C=O), 1694 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 1.35 (d, 3H, J = 6.7, methyl), 3.36 (m, 1H, >C–*H*(*endo*)), 3.74 (d, 1H, J = 3.1, >C–*H*(*exo*)), 7.02–7. 69 (m, 16H, aromatic H), 8.83 (dd, 2H, J = 8.5, 12.2, Ha). MS (*m*/*z*): 468 (M^+), 440 ($M^+ - CO$). Anal. calcd for $C_{33}H_{24}O_3$: C, 84.59; H, 5.16. Found: C, 84.56; H, 5.33.

[4 + 2]π Cycloadducts (3ac) of 1a and trans-2-pentenoic acid (2c)

3ac: Yield: 80%. Mp. 269–270 °C. IR (KBr) cm^{-1}: 1782 (bridge >C=O), 1704 (C=O). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.05 (m, 4H, $-CH_3$, $-CHHCH_3$), 2.34 (d, 1H, J = 6.1, $-CHHCH_3$), 3.17 (d, 1H, J = 7.9, >CH- (*endo*)), 3.82 (d, 1H, J = 3.1, >CH- (*exo*)), 7.03–8.80 (m, 16H, aromatic H), 8.83 (dd, 2H, J = 8.5, 19.5, Ha). MS (*m*/*z*): 482 (M^+), 454 ($M^+ - CO$). Anal. calcd $C_{34}H_{26}O_3$: C, 84.62; H, 5.43. Found: C, 84.81; H, 5.17.

[4 + 2]π Cycloadducts (3ad) of 1a and trans-2-hexenoic acid (2d)

3ad: Yield: 90%. Mp. 266 °C. IR (KBr): 1782 (bridge >C=O), 1702 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 0.92 (m, 3H, methyl), 1.00 (m, 1H, $-CHH-CH_2CH_3$), 1.47 (m, 1H, $-CH_2-CHH-CH_3$), 1.50 (m, 1H, $-CH_2-CHH-CH_3$), 2.24 (m, 1H, $-CHH-CH_2CH_3$), 3.25 (m, 1H, Hb), 3.84 (d, 1H, J = 3.1, Hc), 7.04–8.22 (m, 16H, aromatic H), 8.83 (dd, 2H, J = 8.5, 19.5, Ha). MS (*m*/*z*): 496 (M^+), 468 ($M^+ - CO$. Anal. calcd for $C_{35}H_{28}O_3$: C, 84.65; H, 5.68. Found: C, 84.78; H, 5.73.

[4 + 2]π Cycloadducts (3ae) of 1a and cinnamic acid (2e)

3ae: Yield: 71%. Mp. 252–253 °C. IR (KBr): 1776 (bridge >C=O), 1696 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.93 (d, 1H, J = 4.9, >C–*H*(*exo*)), 4.11 (d, 1H, J = 4.9, >C–*H*(*endo*)), 6.92–7. 65 (m, 21H, aromatic H), 8.82 (dd, 2H, J = 8.6, 12.8, Ha). MS (*m*/*z*): 531 (M^+), 503 ($M^+ - CO$). Anal. calcd for $C_{38}H_{26}O_3$: C, 86.02; H, 4.94. Found: C, 86.22; H, 4.94.

[4 + 2]π Cycloadducts (3af) of 1a and methacrylic acid (2f)

3af: Yield: 60%. Mp. 254–257 °C. IR (KBr): 1782 (bridge >C=O), 1690 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 1.72 (s, 3H, methyl), 2.72 (d, 1H, J = 12.2, >CH–*H*(*endo*)), 3.02 (d, 1H, J = 12.2, >CH–*H*(*exo*)), 6.98–7.76 (m, 16H, aromatic H), 8.82 (dd, 2H, J = 8.6, 12.8, Ha). MS (*m*/*z*): 469 (M^+), 440 ($M^+ - CO$). Anal. calcd for $C_{33}H_{24}O_3$: C, 84.59; H, 5.16. Found: C, 84.56; H, 5.17.

[4 + 2]π Cycloadducts (3ag) of 1a and fumalic acid (2g)

3ag: Yield: 86%. Mp. 280–281 °C. IR (KBr) cm^{-1}: 1796 (bridge >C=O), 1726 (C=O).^{1}H-NMR (270MHz, $CDCl_3$) δ: 3.82 (d, 1H, J = 4.0, >CH- (*exo*)), 4.27 (d, 1H, J = 4.0, >CH- (*endo*)), 6.89–7.85 (m, 16H, aromatic H), 8.61 (d, 1H, J = 8.6, Ha), 8.66 (d, 1H, J = 8.3, Ha). MS (*m*/*z*): 498 (M^+), 470 ($M^+ - CO$). Anal. calcd $C_{33}H_{22}O_5$: C, 79,51; H, 4.45. Found: C, 79.15; H, 4.10.

[4 + 2]π Cycloadducts (3ah) of 1a and maleic acid (2h)

3ah: Yield: 84%. Mp. 286–286 °C. IR (KBr): 1788 (bridge >C=O), 1704 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, DMSO-d_6) δ: 5.15 (s, 2H, methine), 6.96–8.18 (m, 16H, aromatic H), 8.91 (d, 2H, J = 8.4, Ha). MS (*m*/*z*): 498 (M^+). Anal. calcd for $C_{33}H_{22}O_5$: C, 79.51; H, 4.45. Found: C, 79.09; H, 3.99.

[4 + 2]π Cycloadducts (3ai) of 1a and methyl acrylate (2i)

3ai: Yield: 88%. Mp. 238–239 °C. IR (KBr): 1788 (bridge >C=O), 1736 (C=O) cm^{-1}.^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.76 (dd, 1H, J = 4.3, 12.2, >CH–*H*(*endo*)), 3.12 (dd, 1H, J = 9.8, 12.2, >CH–*H*(*exo*)), 3.18 (s, 3H, methyl), 4.22 (dd, 1H, J = 4.3, 9.8, methine), 7.05–7.96 (m, 16H, aromatic H), 8.70 (dd, 2H, J = 9.5, Ha). MS (*m*/*z*): 468 (M^+), 440 (M^+–CO). Anal. calcd for $C_{33}H_{24}O_3$: C, 84.59; H, 5.16. Found: C, 84.56; H, 5.33.

[4 + 2]π Cycloadducts (3aj) of 1a and dimethyl fumalate (2j)

3aj: Yield: 93%. Mp. 253–254 °C. IR (KBr): 1794 (bridge >C=O), 1736 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 3.20 (s, 3H, $>COOCH_3$ (*endo*)), 3.65 (s, 3H, $>COOCH_3$ (*exo*)), 3.99 (d, 1H, J = 4.3, >C–H (*endo*)), 4.35 (d, 1H, J = 4.3, >C–H (*exo*)), 6.97–7.95 (m, 16H, aromatic H), 8.68 (dd, 2H, J = 9.5, Ha). MS (*m*/*z*): 526 (M^+), 498 ($M^+ - CO$). Anal. calcd for $C_{33}H_{26}O_5$: C, 79.83; H, 4.98. Found: C, 80.11; H, 5.05.

[4 + 2]π Cycloadducts (3ak) of 1a and dimethyl maleate (2k)

3ak: Yield: 88%. Mp. 310 °C. IR (KBr): 1790 (bridge >C=O), 1728 (C=O) cm^{-1}. ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 3.30 (s, 6H, methyl), 4.50 (s, 2H, methine), 7.10–7.72 (m, 16H, aromatic H), 8.70 (d, 2H, J = 8.4, Ha). MS (*m*/*z*): 526 (M^+), 498 ($M^+ - CO$). Anal. calcd for $C_{33}H_{26}O_5$: C, 79.83; H, 4.98. Found: C, 79.63; H, 4.75.

[4 + 2]π Cycloadducts (3al) of 1a and acrylamide (2l)

3al: Yield: 80%. Mp. 264–266 °C. IR (KBr): 1784 (bridge >C=O), 1666 (C=O) cm^{-1}, 1448 (NH_2). ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 2.29 (dd, 1H, J = 5.5, 11.0, >C–*H*(*endo*)), 329 (dd, 1H, J = 11.0, 10.5, >C–*H*(*exo*)), 4.01 (dd, 1H, J = 5.5, 10.5, methine), 6.96–7.93 (m, 16H, aromatic H), 8.80 (d, 1H, J = 8.6, Ha), 8.86 (d, 1H, J = 8.5, Ha). MS (*m*/*z*): 454 (M^+), 426 ($M^+ - CO$). Anal. calcd for $C_{32}H_{23}NO_3$: C, 84.74; H, 5.11; N, 3.09. Found: C, 84.56; H, 5.15; H, 3.17.

[4 + 2]π Cycloadducts (3am) of 1a and methacrylamide (2m)

3am: Yield: 78%. Mp. 178–180 °C. IR (KBr): 1780 (bridge >C=O), 1682 (C=O) cm^{-1}. ^{1}H-NMR (500 MHz, DMSO-d_6) δ: 1.71 (s, 3H, methyl), 2.66 (d, 1H, J = 12.2, >C–*H*(*endo*)), 2.94 (d, 1H, J = 12.2, >C–*H*(*exo*)), 4.84, 5.25 (s, 1H, –$CONH_2$), 6.97–7.62 (m, 16H, aromatic H), 8.66 (d, 1H, J = 10.4, Ha), 8.68 (d, 1H, J = 9.2, Ha). MS (*m*/*z*): 467 (M^+). Anal. calcd for $C_{33}H_{25}O_2$: C, 84.77; H, 5.39; N, 3.00. Found: C, 85.46; H, 570; N, 2.84.

[4 + 2]π Cycloadducts (3bl) of 1b and acrylamide (2l)

3bl: Yield: 94%. Mp. 189–192 °C. IR (KBr): 1772 (bridge >C=O), 1688 (C=O) cm^{-1}, 1448 (NH_2). ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 2.69 (dd, 1H, J = 5.5, 11.0, >C–*H*(*endo*)), 2.74 (dd, 1H, J = 10.0, 11.0, >C–*H*(*exo*)), 3.75 (dd, 1H, J = 5.5, 10.0, >C–*H*(*exo*)), 5.93 (s, 1H, NH), 6.09 (s, 1H, NH), 6.83–7.36 (m, 20H, aromatic H). MS (*m*/*z*): 456 (M^+), 428 ($M^+ - CO$). Anal. calcd for $C_{40}H_{35}NO_2$ (as **3bl**·*p*-xylene (1 : 1)): C, 85.53; H, 6.28; N, 2.49. Found: C, 85.48; H, 6.31; N, 2.48.

Preparation of inclusion complexes

The host compound was dissolved under heating in a minimum amount of a guest solvent. The solution was allowed to cool in a water bath to ensure crystallization of the inclusion compounds. After standing for several days at 25 ± 3 °C, the crystals were collected by suction filtration and dried.

Single crystal X-ray analysis

The crystal structure of **3ac**·1,4-dioxane (1 : 1) was determined as follows: the reflection data were measured on a RIGAKU AFC7R four-circle autodiffractometer with a graphite monochromated Mo-Kα radiation (λ = 0.7107 Å) and a rotating anode generator. The structures were solved by direct method. The hydrogen atoms were placed in calculated positions. The non-hydrogen atoms were refined anisotropically and the hydrogen atoms were refined isotropically. The final cycle of full-matrix least-square refinement was based on 2750 observed reflections (Io>3.00σI) and converged with unweighted (R) and weighted agreement factors (R_w) of 0.067 and 0.076, respectively.

Similarly, the X-ray analyses of **3ae**·3-pentanone (1 : 1) and **3bl**·ethanol (1 : 1) were performed. The X-ray analysis data (crystal data, final atomic coordinates, distance and angles) are summarized as supporting information (deposited in CCDC). All calculations were performed on a Silicon Graphics O2 WS with *teXsan*[13] Crystal Structure Analysis Package.

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(*c*) The partial structures of the interactions extracted from the crystal structures of the complexes were roughly reproduced by PM5 calculations. The PM3 calculation seems to overestimate the interaction energies.
10 The HF/6-31G*, HF/6-31+G** and B3LYP/6-31+G* calculations on a model bidentate C–H ··· O interaction between acetone and phenanthrene (4,5-hydrogens) are 2.37, 2.10 and 1.89 kcal/mol, respectively (see ESI-7).
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