

Ritter Reactions. X. Structure of a New Multicyclic Amide–Benzene Inclusion Compound

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Abstract. *5H*-Dibenzo[*a, d*]cyclohepten-5-ol **1** can undergo Ritter reaction with acetonitrile and sulfuric acid to afford either the acetamide derivative **2** or the multicyclic amide **3** depending on the conditions used. The X-ray structure of the inclusion compound of **3** with benzene is reported here and analysed in structural terms. This material [(C₁₉H₁₈N₂O)·(C₆H₆), *Cc*, *a* = 10.694(5), *b* = 22.843(5), *c* = 9.901(4) Å, β = 124.02(2)°, *Z* = 4, *R* = 0.054] has molecules of **3** linked by —N—H···O=C intermolecular hydrogen bonds to form parallel chains along *c*. Additional inter-host stabilisation is achieved by face–face interactions involving one of the two benzo rings of **3**. A hydrogen atom of the other host benzo group participates in an edge–face interaction with the benzene guest molecule to produce the inclusion compound. Benzene···benzene inter-guest interactions provide a further, but minor, contribution to the net stability of the structure.

Key words: Amide hosts, benzene, hydrogen bonding, edge–face and face–face aromatic interactions, Ritter reaction.

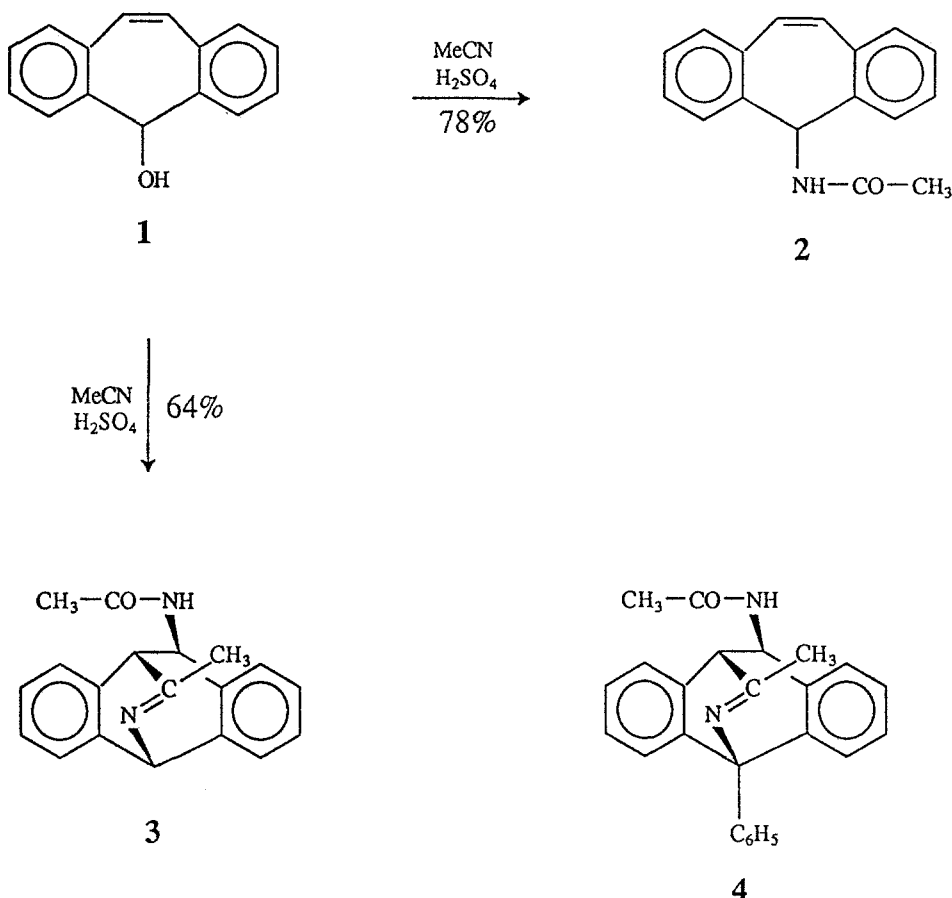
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1. Introduction

Many types of lattice inclusion compound depend on the presence of a strong hydrogen bonding network to position the host molecules in appropriate geometrical arrangements, thereby allowing guest inclusion to take place. Functionalities such as the hydroxy and carboxylic acid groups traditionally have been the most widely used [1]. In contrast, the amide group has been much less popular for the design and synthesis of new lattice inclusion compounds [2–4] despite its excellent hydrogen bonding characteristics.

Our recent work [5] on synthetic applications of the Ritter reaction [6, 7] has demonstrated that multicyclic systems bearing amide groups have a tendency to form hydrogen-bonded lattices which can trap guest molecules [8, 9]. For example, the cyclic alcohol *5H*-dibenzo[*a, d*]cyclohepten-5-ol **1** undergoes efficient Ritter reactions with acetonitrile in the presence of sulfuric acid. Under mild

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Scheme I.

reaction conditions the outcome is the conventional Ritter reaction amide product *N*-(5*H*-dibenzo[*a, d*]cyclohepten-5-yl) acetamide, **2**, which forms a 1 : 2 inclusion compound with dioxane [9].

More vigorous reaction conditions result in the alternative conversion of **1** into the bridged multicyclic amide **3**. In this process the nitrilium ion produced initially undergoes intramolecular capture by the alkene functionality present in the central seven-membered ring. Hence a formal 1,4-addition of acetonitrile takes place across the central ring of **1**, resulting in formation of a 1-azacyclohexene moiety and a carbenium ion. The latter then reacts with a second molecule of acetonitrile by a conventional (but stereoselective) Ritter reaction thus yielding the ultimate product **3** [5]. This bridged amide forms an unstable inclusion compound with benzene which is the subject of this paper.

2. Experimental

2.1. PREPARATIVE WORK

^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded using a Bruker AC300F instrument and are reported as chemical shifts (δ) relative to SiMe_4 . Substitution of carbon atoms was determined by the DEPT procedure. The melting point was determined with a Kofler instrument and is uncorrected; the IR spectrum was recorded on a Perkin Elmer 298 spectrophotometer; and the elemental analysis was carried out at The University of New South Wales by Dr. H.P. Pham.

2.1.1. (5 α ,10 α ,11 α)-N-{12-Methyl-10,11-dihydro-5,10-(nitrilometheno)-5H-dibenzo[a,d]cyclohepten-11-yl}acetamide **3**

Concentrated sulfuric acid (98%, 0.8 mL) was cooled to 0 °C in a round-bottomed flask fitted with a condenser and drying tube. Alcohol **1** [9] (0.42 g, 2 mmol) was dissolved in acetonitrile (5 mL) and then added dropwise to the flask via the condenser. The reaction mixture was stirred at 0 °C for 30 min and then for not less than 16 h at room temperature. Water (10 mL) was added and after stirring for 30 min the material was transferred to a separating funnel containing sodium hydroxide (1 M, 30 mL). Organic material was extracted several times with chloroform. The combined extracts were washed with water (4 \times 25 mL) and dried (Na_2SO_4). The filtrate was evaporated to dryness to give the *bridged amide* **3**, yield (0.33 g, 57%), m.p. 242–244 °C (from benzene); lit. [5] 64%, m.p. 223–224 °C (from diethyl ether). Crystallisation from benzene gave an unstable inclusion compound which rapidly lost solvent at room temperature. Deliberate grinding and warming gave material with microanalytical data for the pure host. (*Found*: C, 78.90; H, 6.40; N 9.64%. $\text{C}_{19}\text{H}_{18}\text{N}_2\text{O}$, *requires* C, 78.59; H, 6.25, N 9.65%). ν_{max} (paraffin mull) 3275s, 3180w, 3030m. 1650s, 1535s, 1275m, 1170m, 1080m, 975m, 935w, 785m, 765s, 745m, 735m, 695s, 685s, 620m cm^{-1} . ^1H δ (DMSO- d_6) 8.61, d, 1H, NH, J 8.2Hz; 7.44–7.01, m, 8H; 5.76, s, 1H; 4.88, dd, 1H, J 8.2 and 3.8Hz; 4.14, d, 1H, J 3.8Hz; 2.16, s, 3H; 1.95, s, 3H. ^{13}C δ (DMSO- d_6) 173.0 (C), 169.3 (C), 143.4 (C), 140.5 (C), 135.2 (C), 134.0 (C), 132.1 (CH), 128.1 (CH), 127.8 (CH), 127.5 (CH), 127.2 (CH), 126.94 (CH), 126.86 (CH), 124.0 (CH), 67.4 (CH), 50.3 (CH), 49.2 (CH), 27.9 (CH_3), 22.8 (CH_3); plus 128.6 (CH), C_6H_6 guest.

2.2. X-RAY DATA COLLECTION, PROCESSING, AND REFINEMENT FOR THE STRUCTURE (3)·(BENZENE)

Reflection data were measured with an Enraf-Nonius CAD-4 diffractometer in $\theta/2\theta$ scan mode using nickel filtered copper radiation ($\lambda = 1.5418 \text{ \AA}$). Data were not corrected for absorption as the crystal was coated with glue to prevent decomposition and assignment of crystal faces was therefore impossible. Reflections with $I > 3\sigma(I)$ were considered observed. The structure was determined by direct

phasing (MULTAN) [10] and Fourier methods. The atoms of the lattice benzene molecule were apparent, although their geometry was far from ideal. Refinement was therefore carried out with the benzene molecule being included as a rigid group of ideal geometry [11] and its position and orientation were allowed to vary. Hydrogen atoms of the molecule **3** were included in calculated positions and were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisotropic thermal parameters for the non-hydrogen atoms of **3** were refined using full matrix least squares. The thermal motion of the benzene molecule was described as a 15-parameter TLX group (where T is the translational tensor, L is the librational tensor and X is the origin of libration). Refinement converged with $R = 0.054$. In the final difference map the largest residual peak was $0.21 \text{ e } \text{\AA}^{-3}$.

Reflection weights used were $1/\sigma^2(F_0)$, with $\sigma(F_0)$ being derived from $\sigma(I_0) = [\sigma^2(I_0) + (0.04I_0)^2]^{1/2}$. The weighted residual is defined as $R_w = (\sum w\Delta^2 / \sum wF_0^2)^{1/2}$. Atomic scattering factors and anomalous dispersion parameters were from *International Tables for X-ray Crystallography* [12]. ORTEP-II [13] running on a Macintosh IICx was used for the structural diagrams, and a DEC Alpha AXP workstation was used for calculations. A summary of data collection parameters is given in Table I.

The supplementary data deposited comprises fractional coordinates for the hydrogen atoms, thermal parameters and structure factors.

3. Results and Discussion

3.1. DESCRIPTION OF THE STRUCTURE

First of all, the X-ray determination confirms that the molecular structure of the multicyclic amide **3** is indeed that assigned in previous work [5]. When the Ritter addition product of a nitrile across the 5*H*-dibenzo[*a, d*]cycloheptene skeleton was first observed, it was realised that two isomeric structures could result depending on which way round the addition took place. Addition in the 5,10-nitrilometheno sense was deduced through use of $^1\text{H-NMR}$ Overhauser measurements [14]. Subsequently we have prepared and characterised five further products of this type and addition in the 5,10-nitrilometheno sense was confirmed by the X-ray structure determination for one of these examples **4** [5]. The present structure, and the extreme similarity between the ^1H and ^{13}C NMR spectra of these various adducts, provides secure evidence that these compounds are all of the same type.

Figure 1 shows the crystallographic numbering system used to designate the two molecular components of (**3**)·(benzene). Positional parameters for the non-hydrogen atoms are listed in Table II. Bond lengths and bond angles for the structure are presented in Tables III and IV.

Molecules of **3** may be considered to have a butterfly shape, with one wing bearing the amide functional group. There is $\text{—N—H} \cdots \text{O=C}$ intermolecular hydrogen bonding linking these amide functionalities in **3** to give chains of *c*-glide related

TABLE I. Numerical details of the solution and refinement of the structure of (3)·(benzene).

Formula, formula mass	(C ₁₉ H ₁₈ N ₂ O)·(C ₆ H ₆), 368.5
Space group	Cc
a/Å	10.694(5)
b/Å	22.843(5)
c/Å	9.901(4)
β/°	124.02(2)
V/Å ³	2005(1)
Temp./°C	21(1)
Z	4
D _{calc.} /g cm ⁻³	1.22
Radiation, λ/Å	CuK _α , 1.5418
μ/cm ⁻¹	5.48
Crystal dimensions/mm	~0.4 × 0.1 × 0.1
Scan mode	θ/2θ
2θ _{max} /°	120
ω scan angle	(0.60 + 0.15 tan θ)
No. of intensity measurements	1621
Criterion for observed reflection	I/σ(I) > 3
No. of independent obsd. reflections	1111
No. of reflections (m) and variables (n) in final refinement	1111, 218
$R = \sum^m \Delta F / \sum^m F_0 $	0.054
$R_w = [\sum^{m_w} \Delta F ^2 / \sum^{m_w} F_0 ^2]^{1/2}$	0.066
$s = [\sum^{m_w} \Delta F ^2 / (m - n)]^{1/2}$	2.33
Crystal decay	1 to 0.82
Largest peak in final diff. map/e Å ⁻³	0.21

molecules running in the *c* direction (Figure 2), and dimensions associated with this inter-amide hydrogen bonding are given in Table V. The hydrogen bonding between amide molecules in this structure is analogous to that found in the structures of (2)·(dioxane)₂ [9] and 4 [5]. However, the spatial arrangement of the wings of the butterfly-shaped molecules relative to the nearly linear hydrogen bonded O—NH· · O—NH· · O—NH spine differs.

In both the latter structures adjacent hydrogen bonded amide molecules have their wings directed outward from the hydrogen bonded spine but in opposite directions. Hence their orientations *alternate* along the chain, as illustrated for (2)·(dioxane)₂ (see Fig. 4 in Ref. [9]). In (3)·(benzene), however, adjacent hydrogen bonded amide molecules are positioned above each other on *one* side of the hydrogen bonded spine. Consequently the wing of each molecule of 3 bearing the amide substituent group interleaves with others of the same type belonging to its enantiomeric neighbours. Thus a stack of benzo groups interacting in a face-face manner [15] is produced. This results in a secondary mode of inter-host stabilisation. The shortest distance between these rings is 3.05 Å.

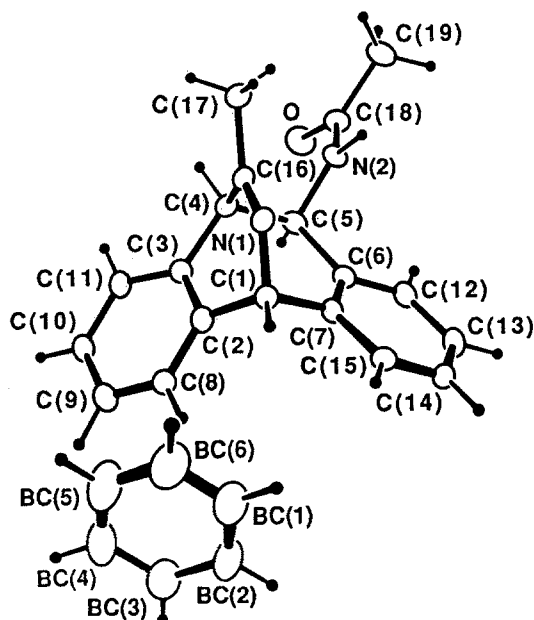


Fig. 1. Molecular structure of **3** and benzene in the crystal structure of (**3**)-(benzene) showing the crystallographic numbering system employed. The symbolism BC has been used to designate benzene carbon atoms. Aromatic hydrogen atom HC(8) is positioned almost equidistantly from the six benzene carbons in an edge-face relationship which provides the major host-guest interaction.

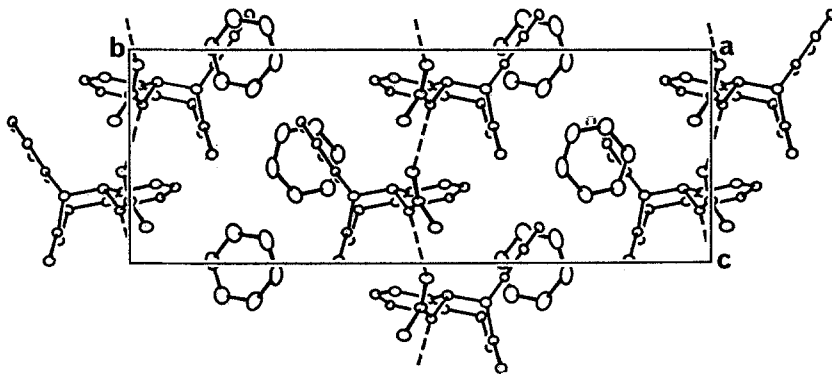


Fig. 2. The unit cell of (**3**)-(benzene) viewed down *a*. Molecules of **3** are arranged in parallel chains along *c* with intermolecular $\text{—N—H}\cdots\text{O=C}$ hydrogen bonding linking them. Each benzene guest is nearly orthogonal to the wing of **3** with which it forms six $\text{HC(8)}\cdots\text{BC}$ close contacts. The zig-zag arrangement of the benzene guest molecules, which lies in the direction of the short *ac* diagonal, is also apparent. Hydrogen atoms are omitted for clarity.

3.2. THE ROLE OF THE BENZENE COMPONENT

The wing of **3** which does not support the amide group is closely associated with the included benzene guest molecule. Although both face-face and edge-face packing

TABLE II. Atomic coordinates for the non-hydrogen atoms of (3)·(benzene).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> _{eq}
O	0.4589	0.0124(2)	0.5680	6.8(1)
N(1)	0.2161(8)	0.1225(2)	0.8877(8)	5.3(1)
N(2)	0.4027(8)	0.0190(2)	0.7533(8)	4.7(1)
C(1)	0.0618(9)	0.1066(3)	0.7478(9)	4.9(1)
C(2)	0.0179(9)	0.1422(3)	0.5988(9)	4.9(1)
C(3)	0.1269(9)	0.1464(3)	0.5659(9)	4.9(1)
C(4)	0.2726(9)	0.1143(3)	0.6814(9)	5.0(1)
C(5)	0.2564(9)	0.0479(3)	0.6481(9)	4.6(1)
C(6)	0.1407(8)	0.0163(3)	0.6653(8)	4.3(1)
C(7)	0.0532(9)	0.0425(3)	0.7114(8)	4.5(1)
C(8)	-0.1204(10)	0.1693(3)	0.4973(10)	5.6(1)
C(9)	-0.1476(11)	0.2005(3)	0.3624(11)	6.7(1)
C(10)	-0.0363(11)	0.2059(3)	0.3327(10)	5.9(1)
C(11)	0.1023(10)	0.1794(3)	0.4345(10)	5.4(1)
C(12)	0.1223(9)	-0.0439(3)	0.6290(9)	5.1(1)
C(13)	0.0229(10)	-0.0775(3)	0.6412(10)	5.8(1)
C(14)	-0.0629(9)	-0.0518(3)	0.6920(9)	5.6(1)
C(15)	-0.0470(9)	0.0077(3)	0.7274(9)	5.0(1)
C(16)	0.3116(10)	0.1262(3)	0.8536(9)	5.1(1)
C(17)	0.4763(10)	0.1404(3)	0.9853(10)	6.5(1)
C(18)	0.4899(8)	0.0018(3)	0.7056(8)	4.9(1)
C(19)	0.6336(9)	-0.0276(4)	0.8295(10)	6.6(1)
BC(1)	0.1014(13)	0.3415(5)	0.1452(14)	14.5(8)
BC(2)	-0.0024(13)	0.3590(3)	-0.0156(17)	13.2(7)
BC(3)	-0.0440(11)	0.3203(6)	-0.1435(12)	15.4(8)
BC(4)	0.0182(14)	0.2642(5)	-0.1107(16)	17.5(9)
BC(5)	0.1220(14)	0.2467(3)	0.0502(20)	18.1(9)
BC(6)	0.1636(11)	0.2853(6)	0.1780(13)	17.4(9)

motifs are commonly encountered in structures of aromatic molecules [15], on this occasion it is the latter arrangement which is the predominant interaction between the two different molecular components of the inclusion compound. Although the Ar—H bond is not directed at the centre of the benzene molecule, the angle of tilt is such that the aromatic hydrogen atom HC(8) is positioned almost equidistantly from each of the six carbon atoms of the ring (see Figure 1). The actual distances are 3.00, 3.10, 3.09, 2.98, 2.88 and 2.89 Å for HC(8)···BC(1) to HC(8)···BC(6), respectively.

This Ar—H···benzene interaction has an interesting parallel with the crystal structure of **4** [5]. The multicyclic amide **4** includes no guest molecules, but its 5-phenyl substituent participates in an analogous Ar—H···phenyl interaction with

TABLE III. Bond lengths and standard deviations (Å) for (3)·(benzene).

O—C(18)	1.233(7)	N(1)—C(1)	1.489(8)
N(1)—C(16)	1.245(8)	N(2)—C(5)	1.464(7)
N(2)—C(18)	1.320(7)	C(1)—C(2)	1.511(8)
C(1)—C(7)	1.498(9)	C(2)—C(3)	1.378(8)
C(2)—C(8)	1.384(9)	C(3)—C(4)	1.510(9)
C(3)—C(11)	1.395(8)	C(4)—C(5)	1.542(9)
C(4)—C(16)	1.536(8)	C(5)—C(6)	1.522(8)
C(6)—C(7)	1.386(8)	C(6)—C(12)	1.405(8)
C(7)—C(15)	1.412(8)	C(8)—C(9)	1.394(10)
C(9)—C(10)	1.382(10)	C(10)—C(11)	1.382(10)
C(12)—C(13)	1.370(9)	C(13)—C(14)	1.398(10)
C(14)—C(15)	1.388(9)	C(16)—C(17)	1.529(9)
C(18)—C(19)	1.485(9)	BC(1)—BC(2)	1.396

TABLE IV. Bond angles and standard deviations (°) for (3)·(benzene).

C(1)—N(1)—C(16)	114.5(5)	C(5)—N(2)—C(18)	124.6(5)
N(1)—C(1)—C(2)	110.8(5)	N(1)—C(1)—C(7)	110.5(5)
C(2)—C(1)—C(7)	110.4(5)	C(1)—C(2)—C(3)	115.2(6)
C(1)—C(2)—C(8)	124.9(6)	C(3)—C(2)—C(8)	119.9(6)
C(2)—C(3)—C(4)	116.0(5)	C(2)—C(3)—C(11)	121.0(6)
C(4)—C(3)—C(11)	123.0(6)	C(3)—C(4)—C(5)	111.8(5)
C(3)—C(4)—C(16)	106.2(5)	C(5)—C(4)—C(16)	109.9(5)
N(2)—C(5)—C(4)	110.1(5)	N(2)—C(5)—C(6)	108.6(5)
C(4)—C(5)—C(6)	116.3(5)	C(5)—C(6)—C(7)	124.9(5)
C(5)—C(6)—C(12)	116.2(5)	C(7)—C(6)—C(12)	118.9(6)
C(1)—C(7)—C(6)	122.6(5)	C(1)—C(7)—C(15)	118.2(5)
C(6)—C(7)—C(15)	119.2(6)	C(2)—C(8)—C(9)	119.4(7)
C(8)—C(9)—C(10)	120.4(6)	C(9)—C(10)—C(11)	120.3(6)
C(3)—C(11)—C(10)	118.9(7)	C(6)—C(12)—C(13)	122.0(6)
C(12)—C(13)—C(14)	119.6(6)	C(13)—C(14)—C(15)	119.3(6)
C(7)—C(15)—C(14)	121.1(6)	N(1)—C(16)—C(4)	122.3(6)
N(1)—C(16)—C(17)	120.7(6)	C(4)—C(16)—C(17)	116.9(6)
O—C(18)—N(2)	122.0(6)	O—C(18)—C(19)	121.1(6)
N(2)—C(18)—C(19)	116.8(5)	BC(1)—BC(2)—BC(3)	120.0

a neighbouring molecule. However, the six Ar—H···C distances vary more in this instance (from 2.71 to 3.54 Å).

The interaction of one benzene guest with each molecule of **3** leads to distinct regions within the crystal lattice. Chains of amide molecules lie in *ac* planes around $b = 0$ and $b = 0.5$, with the benzene molecules in between at $b = 0.25$ and $b = 0.75$ (see Figure 2). The benzene molecules pack in a zig-zag arrangement. Whereas

TABLE V. Dimensions associated with the hydrogen bonding in (3)·(benzene).

$O \cdots N(2)^a$	2.914(6)
$O \cdots HN(2)^a$	1.94(2)
$C(18) - O \cdots N(2)^a$	154.2(4)
$C(5)^a - N(2)^a \cdots O$	111.8(3)
$C(18)^a - N(2)^a \cdots O$	123.0(4)
$O \cdots HN(2)^a - N(2)^a$	165(3)

^aEquivalent position indicator: $x, -y, -\frac{1}{2} + z$.

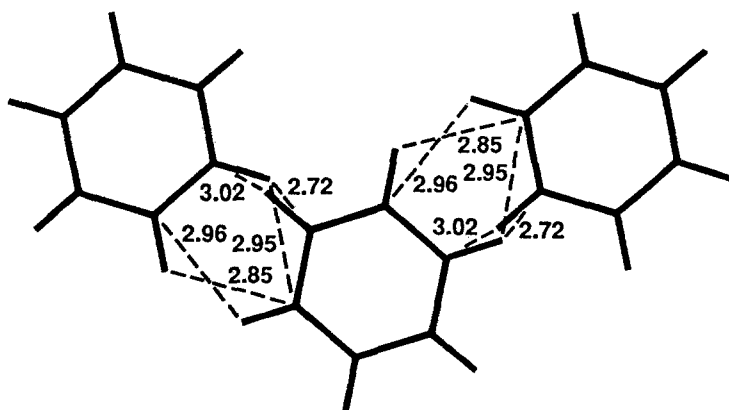


Fig. 3. The zig-zag association of benzene guest molecules present in (3)·(benzene) showing the short inter-guest Ar—H \cdots C distances (Å).

the classic edge-face packing has the angle between the normals to the planes of 90° , in this case the arrangement is much flatter with that angle reduced to 40.1° . Where the rings abut the shortest ArH \cdots C contacts range from 2.72 to 3.02 Å as shown in Figure 3. Hence it can be concluded that this guest-guest interaction is of least energetic significance amongst the various types of molecular interaction present in this new inclusion structure.

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