Journal of Inclusion Phenomena and Molecular Recognition in Chemistry **22:** 187–201, 1995.

Inclusion Compounds of (±) Gossypol. Structure of the Gossypol–*n*-Valeric Acid (1/2) Coordinato-clathrate

MARIA GDANIEC and HONORATA CZAJKA
Faculty of Chemistry, A. Mickiewicz University, Grunwaldzka 6, 60-780 Poznań, Poland

(Received: 21 December 1994; in final form: 8 June 1995)

Abstract. The crystal structure of the inclusion compound of gossypol with *n*-valeric acid as a guest molecule has been determined by X-ray structure analysis. The crystals of $C_{30}H_{30}O_8 \cdot (C_5H_{10}O_2)_2$, are triclinic, space group $P\bar{1}$, $a = 6.912(2)$, $b = 14.506(3)$, $c = 19.387(4)$ Å, $\alpha = 78.85(2)°$, $\beta = 83.92(3)°$, $\gamma = 86.78(3)°$ $V = 1895(1)$ Å^3, $Z = 2$, $D_x = 1.267$ g cm^{-3}, μ (Cu K_α) = 0.768 mm^{-1}, $T = 292$ K. The structure has been solved by direct methods on intensity data collected for a twinned crystal and refined to the final R value of 0.062 for 1606 observed reflections and 470 refined parameters.

Gossypol–*n*-valeric acid (1/2) coordinato-clathrate is not isostructural with any of the previously investigated gossypol inclusion compounds but shows some structural similarities to gossypol–acetic acid (1/1). The host and one of the carboxylic acid molecules are connected via hydrogen bonds into molecular assemblies of a column type which are further bonded to centrosymmetric dimers of the second *n*-valeric acid molecule. In effect, host and guest molecules are assembled into layer-type H-bonded aggregates. Structural features common to gossypol–*n*-valeric acid (1/2) and other earlier reported gossypol inclusion compounds are discussed.

Key words: Inclusion compounds, gossypol, crystal structure, hydrogen bonds.

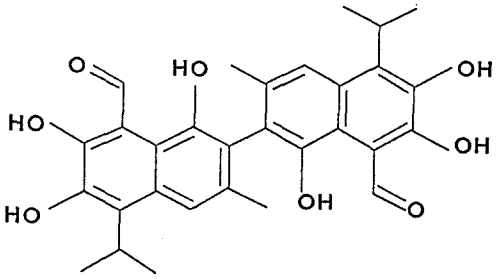
Supplementary Data relevant to this article have been deposited with the British Library under the number SUP 82194 (9 pages)

1. Introduction

Among numerous inclusion compounds formed with protic and aprotic organic solvents by the natural product gossypol (scheme), the one which is best known and predominantly used for biomedical studies is gossypol–acetic acid (1/1). This is the form in which gossypol was first isolated by Marchlewski [1] from the cotton plant. Adams and coworkers [2], who worked on the structure and chemistry of gossypol in the 'thirties, reported that similar adducts were formed by gossypol with formic, propionic and butyric acids. Ibragimov *et al.* [3, 4] who determined unit-cell parameters for a large group of gossypol inclusion compounds reported that the above solvates were isostructural with gossypol–acetic acid (1/1) whose structure had been published earlier by Changfu *et al.* [5]. Isostructuralism has not been observed for the next member in the carboxylic acid homologous series,

i.e. n-valeric acid [3]. The inclusion compound obtained from this solvent had triclinic symmetry and a 1 : 2 host : guest ratio [3]. Comparison of the unit-cell parameters of these crystals with the triclinic unit-cell parameters of gossypol–acetic acid (1/1) indicated that some common structural features can be expected for these two inclusion compounds. An axial parameter of length 6.9–7.2 Å is characteristic of a special arrangement of the host and a polar guest in gossypol crystals – in such a case column-type host–guest assemblies are formed in which the host centrosymmetric dimers are fastened together by H-bonds to the guest molecules (Figure 1). These host–guest assemblies are further connected into layer-type aggregates whose structure depends on the functionality and size of guest molecules [4, 6]. According to the nomenclature proposed by Weber and Josel [7] the above compounds can be classified as coordinato-clathrates because topological as well as hydrogen-bond interactions play a role in their formation.

Taking into account the elongation by about 4 Å of one of the unit cell parameters of gossypol–n-valeric acid (1/2), we expected to find the layer-type host-guest aggregate similar to that observed in gossypol–acetic acid (1/1), plus an additional guest molecule accommodated in the inter-layer in the form of a typical carboxylic acid dimer. This work, which reports the crystal structure of gossypol–n-valeric acid (1/2), has been undertaken to address the question of the role played by the second n-valeric acid molecule in the formation of this inclusion compound.



2. Experimental

Gossypol recrystallized from n-valeric acid forms stable, very small, twinned, yellow, needle-shaped crystals. For our studies a twinned specimen, with dimensions $0.35 \times 0.15 \times 0.01$ mm, was chosen from a crystalline sample obtained by vapor diffusion of chloroform/benzene 1 : 1 mixture into a gossypol solution in n-valeric acid. The gossypol solution was placed in a small, open container and that, in turn, was placed in a larger container with a small amount of the chloroform/benzene mixture. The larger container was then tightly closed. The crystals, which appeared, were removed from the mother liquor and dried in air. ^{1}H-NMR spectra of this crystalline sample indicated a 1 : 2 gossypol–n-valeric acid ratio and no trace of benzene or chloroform in the crystals. The specimen was used for all measurements on a KM-4 diffractometer. Fifty reflections were found in a peak search procedure. All these reflections could be divided into three groups: those belonging to the first crystal twinned component, those belonging to the second component and those

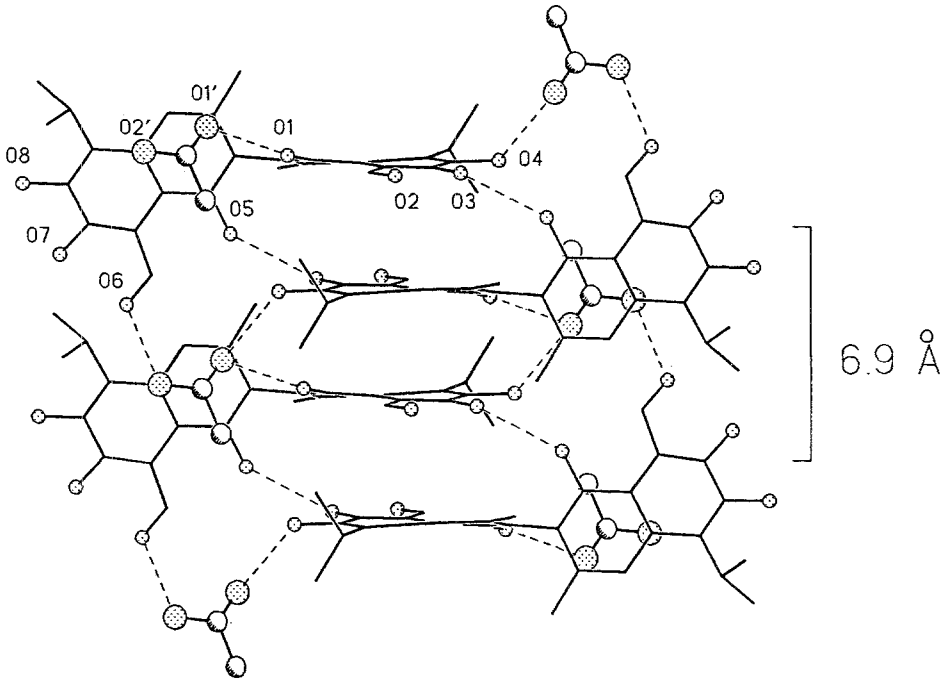


Fig. 1. Characteristic packing pattern of the gossypol O(5)—H···O(3) dimers and guest molecules observed in triclinic gossypol crystals with an axial parameter length of 6.9–7.2 Å (guest molecule-acetic acid).

common to both components. In the first step, the orientation matrix for one of the crystal twinned components was determined and unit-cell parameters were refined by a least-squares fit of the setting angles of 48 reflections with 2θ in the range 17–43°. The same procedure was repeated for the second component and differences in the corresponding unit-cell parameters were within three e.s.d.s. Reflections $0kl$ were superimposing with $0\bar{k}\bar{l}$ reflections of a second component indicating [100] as a twin axis. Intensity measurements of the reflections with the same hkl indices for the two twin components have shown that the domains had the same diffracting volume and therefore intensities of the $0kl$ reflections taken for calculations have had to be divided by 2.

The crystal data are as follows: $C_{30}H_{30}O_8 \cdot (C_5H_{10}O_2)_2$, triclinic, space group $P\bar{1}$, $a = 6.912(2)$, $b = 14.506(3)$, $c = 19.387(4)$ Å, $\alpha = 78.85(2)°$, $\beta = 83.92(3)°$, $\gamma = 86.78(3)°$, $V = 1895(1)$ Å^3, $Z = 2$, $D_x = 1.267$ g cm^{-3}, $\mu(\mathrm{Cu}K_\alpha) = 0.768$ mm^{-1}, $T = 292$ K.

Reflection intensities were measured with graphite-monochromatized CuK_α radiation up to $2\theta_{max} = 100°$. No significant intensity variation was observed for 2 standard reflections monitored after each group of 100 reflections. The data were corrected for Lorentz and polarization effects but not for absorption. Intensities of the $0kl$ reflections were divided by 2. Out of 3884 reflections measured only 1606

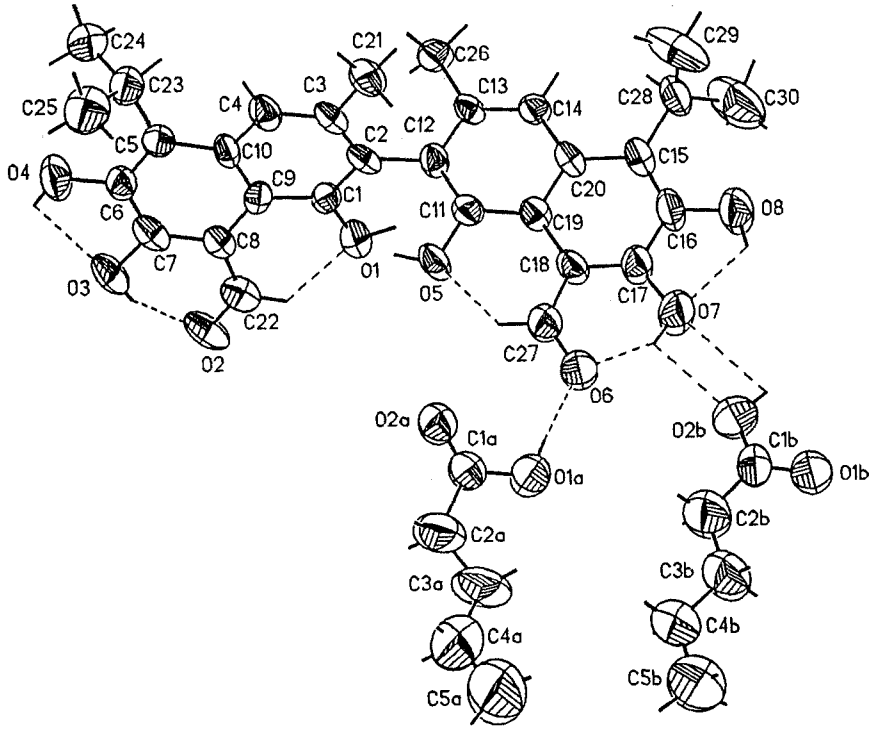


Fig. 2. Thermal ellipsoids (50% probability level) and atom labeling scheme for the gossypol–*n*-valeric acid (2/1) coordinato-clathrate.

had $I > 1.5\sigma(I)$ (result of the small crystal size). The structure was solved by direct methods using the program SHELXS-86 [9]. Atoms from the gossypol molecule and some atoms of the guest molecules were located from the first E-map. Subsequent difference Fourier syntheses showed the positions of the remaining non-H atoms. The structure has been refined anisotropically by the full-matrix least-squares method. All H atoms were placed in idealized positions, assuming C–H and O—H distances of 0.96 Å and 0.85 Å, respectively. The positions of H atoms in the hydroxyl groups were calculated assuming coplanarity with the naphthyl ring and intramolecular hydrogen bonds analogous to those observed in other inclusion compounds of gossypol. The refinement converged with final $R = 0.062$ and $wR = 0.063$. Structure-factor weights were assigned as $w = 1/[\sigma^2(F) + 0.0002F^2]$ and the quantity minimized was $\sum w(F_o - F_c)^2$. The maximum Δ/σ value in the final cycle of refinement was less than 0.1. The final difference Fourier map had electron density between -0.21 and 0.22 e Å^{-3}. Atomic scattering factors used were those incorporated in SHELX76 [8]. Final atomic coordinates are given in Table I. Lists of bond lengths and angles, anisotropic thermal parameters, H-atom coordinates and lists of structure factors have been deposited with the British Library Lending Division, and copies may be ordered quoting Sup. No. 82194 (9 pp.).

TABLE I. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement coefficients ($Å^2 \times 10^3$)

	x	y	z	U (eq)
C(1A)	−7128(17)	1632(8)	7771(8)	71(8)
C(2A)	−8802(22)	991(10)	7918(8)	127(7)
C(3A)	−10169(25)	950(13)	8559(9)	158(9)
C(4A)	−11844(33)	445(15)	8666(10)	188(12)
C(5A)	−13077(30)	436(16)	9258(12)	232(15)
O(1A)	−7003(11)	2056(6)	8306(4)	101(4)
O(2A)	−6101(11)	1765(5)	7234(4)	77(3)
C(1B)	−6810(23)	4040(9)	9942(7)	88(6)
C(2B)	−8118(22)	3317(11)	9863(8)	132(8)
C(3B)	−9774(21)	3083(10)	10355(8)	117(7)
C(4B)	−10986(25)	2333(11)	10251(8)	142(8)
C(5B)	−12701(26)	2139(13)	10740(9)	172(10)
O(1B)	−7214(11)	4554(6)	10375(5)	106(4)
O(2B)	−5220(14)	4094(6)	9544(5)	118(5)
C(1)	2387(13)	1601(7)	5410(6)	42(4)
C(2)	2026(13)	2580(6)	5285(6)	44(4)
C(3)	1616(13)	3016(6)	4599(6)	46(4)
C(4)	1728(13)	2500(7)	4070(5)	54(4)
C(5)	2308(14)	1027(8)	3616(6)	54(5)
C(6)	2483(14)	63(8)	3752(7)	51(5)
C(7)	2529(13)	−422(7)	4445(7)	52(5)
C(8)	2534(13)	17(8)	5038(7)	43(4)
C(9)	2334(12)	1049(7)	4886(6)	41(4)
C(10)	2124(13)	1510(7)	4197(6)	44(4)
C(21)	1109(15)	4053(5)	4430(5)	63(4)
C(22)	2634(14)	−585(9)	5699(7)	60(5)
C(23)	2319(17)	1554(8)	2859(6)	71(5)
C(24)	4116(19)	1335(9)	2391(6)	103(6)
C(25)	474(19)	1422(8)	2543(6)	94(6)
O(1)	2777(9)	1144(4)	6064(4)	57(3)
O(2)	2788(10)	−1448(4)	5805(4)	74(3)
O(3)	2601(9)	−1371(4)	4522(4)	65(2)
O(4)	2560(10)	−424(4)	3220(4)	78(3)
C(11)	607(15)	3143(6)	6358(5)	48(8)
C(12)	2120(14)	3132(6)	5839(5)	47(4)
C(13)	3746(13)	3679(5)	5845(5)	43(4)
C(14)	3713(14)	4238(6)	6332(5)	48(4)
C(15)	2187(16)	4893(6)	7369(5)	55(4)
C(16)	723(17)	4842(7)	7898(6)	72(5)
C(17)	−781(16)	4193(7)	7962(6)	65(5)
C(18)	−985(14)	3674(7)	7470(5)	54(4)
C(19)	528(14)	3685(6)	6895(5)	46(4)

TABLE I. Continued.

	x	y	z	U (eq)
C(20)	2185(15)	4273(6)	6863(5)	50(4)
C(26)	5483(13)	3667(6)	5309(5)	55(4)
C(27)	−2771(17)	3154(7)	7550(6)	72(5)
C(28)	3724(16)	5628(7)	7269(6)	71(5)
C(29)	3223(21)	6473(8)	6786(7)	128(7)
C(30)	4540(22)	5804(10)	7900(8)	140(8)
O(5)	−977(9)	2584(4)	6377(3)	63(3)
O(6)	−3943(11)	3109(5)	8089(4)	88(3)
O(7)	−2013(11)	4197(5)	8547(4)	97(4)
O(8)	644(11)	5406(5)	8395(4)	103(4)

3. Discussion

3.1. Molecular Structure

There are two solvent molecules and one host molecule in the asymmetric unit. Thermal ellipsoids of atoms drawn at the 50% probability level as well as the numbering scheme are shown in Figure 2. As a consequence of the limited number of observed reflections, the bond lengths and angles are accompanied by high standard errors (0.01–0.03 Å and 0.8–1.8°, respectively) and do not warrant detailed discussion of the molecular geometry. However, based on the structural data obtained, the following conclusions can be drawn:

- the host molecule is in the aldehyde tautomeric form,
- the dihedral angle between gossypol naphthalene units is 69° and is similar to that observed for gossypol–acetic acid (1/1) (68°),
- the naphthalene moieties are not planar, deviations of the ring atoms from their 'best plane' are as high as 0.10 Å,
- C(23) and C(28), the tertiary carbon atoms of the isopropyl group, are the substituent atoms most strongly deviating from the plane of the naphthyl rings (0.28 Å).

n-Valeric acid molecules, A and B, adopt a fully extended conformation. For molecule A, an evident difference in the bond lengths O(1A)—C(1A) and O(2A)—C(1A) [1.32(2) and 1.18(2) Å, respectively] clearly indicates carbonyl [O(2A)] and hydroxy [O(1A)] oxygen atoms in the molecule. This assignment is additionally supported by the H-bond pattern for this molecule. For the second solvate molecule, which forms centrosymmetric carboxylic acid dimers, the C(1B)—O(1B) and C(1B)—O(2B) bonds have similar lengths [1.24(2) and 1.27(2) Å, respectively]. Despite the fact that the acidic H atom is probably disordered within the acid dimer we have calculated its position as bonded to O(2B) because the C(1B)—O(2B) bond is 0.03 Å longer than the other C—O bond and additionally, this proton

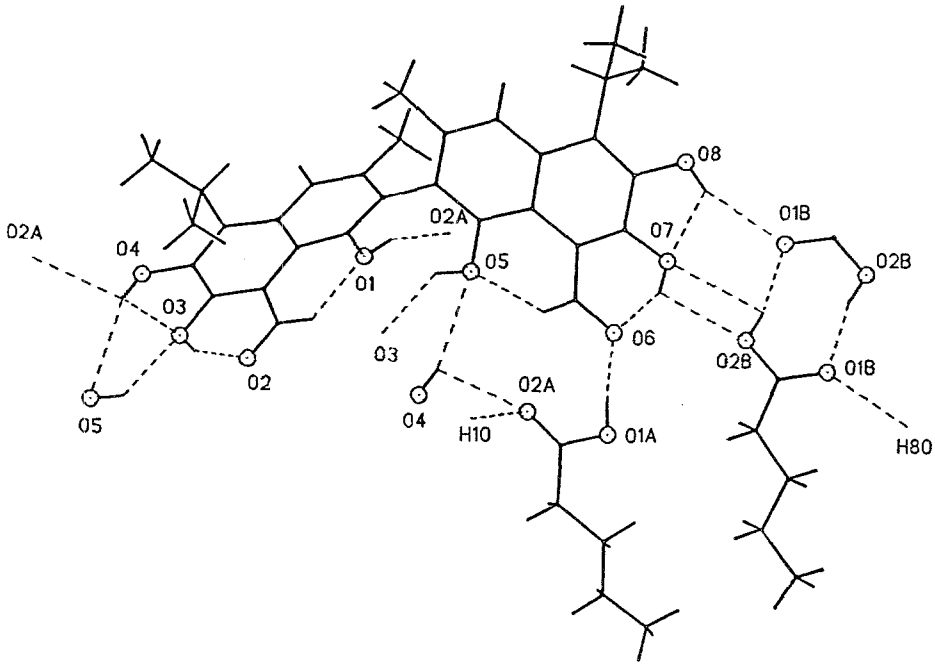


Fig. 3. H-bond pattern for the host and guest molecules.

location allows for interaction between the guest B O(2B)—H group and the host O(7)—H hydroxyl.

3.2. Crystal Packing

Gossypol OH groups are involved in an extended system of intramolecular hydrogen bonds [10–12] and therefore they are rather poorly accessible for intermolecular interactions. Hydrogen bonds formed by those groups are weak and often multicenter in nature. The most frequently observed associate of the host molecules in crystals is the so called 'centrosymmetric O(5)—H· · ·O(3) dimer' which is stabilized by four weak hydrogen bonds and stacking interactions between gossypol C(1)—C(10) naphthalene units. This type of host dimer is also observed in the gossypol–*n*-valeric acid (1/2) coordinato-clathrate. There are no other hydrogen bonds between gossypol molecules in this structure. The H-bond connectivity of the host and guest molecules is presented in Figure 3. Polar groups located on one side of the host C(11)–C(20) naphthalene moiety are extensively surrounded by polar groups of the three guest molecules which are nearly coplanar with this gossypol fragment. The geometries of intermolecular hydrogen bonds and some short contacts are collected in Table II.

TABLE II. Intermolecular hydrogen bonds and short contacts in gossypol–*n*-valeric acid (1/2).

D—H···A	D···A (Å)	D—H (Å)	H···A (Å)	D—H···A (°)
O(5)—H···O(3^{i})	3.04(2)	0.85	2.36	137
O(4)—H···O(5^{i})	3.30(1)	0.85	2.54	150
O(1)—H···O(2A^{ii})	2.79(2)	0.85	2.05	146
O(4)—H···O(2A^{i})	3.20(1)	0.85	2.77	113
O(8)—H···O(1B^{iii})	3.19(2)	0.85	2.39	157
O(7)—H···O(2B)	2.77(2)	0.85	2.45	103
O(1A)—H···O(6)	2.63(2)	0.85	1.78	175
O(2B)—H···O(1B^{iii})	2.69(2)	0.85	1.86	166
O(2B)—H···O(7)	2.77(2)	0.85	2.71	86

Symmetry codes: (i) $-x, -y, 1-z$
(ii) $1+x, y, z$,
(iii) $-2-x, 1-y, 2-z$.

The host 'O(5)—H···O(3)' dimers, which stack along the x axis, are connected *via* H-bonds to the guest molecules of type A. The host–guest A molecular assembly thus formed is similar to that presented in Figure 1 for gossypol–acetic acid (1/1).

Guest molecules of type B form typical carboxylic acid dimers. They join through O(8)—H···O(1B) bonds to the host–guest A assemblies and, as a result, a layer-type aggregate is formed, shown in Figure 4, composed of the host, guest A and guest B. A short contact of 2.77(2) Å which arises between the host O(7)—H and the guest O(2B)—H groups within this layer is probably a result of a significant dipole–dipole interaction between the two strongly polarized O—H bonds. This arrangement of the OH groups would give rise to a formation of the, so called, 'tandem hydrogen bond' [13] (Figure 3). However, the fact that H atom positions have been calculated and not determined experimentally, does not allow for a more detailed discussion of this interaction here.

The crystal packing in the gossypol–*n*-valeric acid (1/2) coordinato-clathrate is shown in Figure 5. Host–guest layers pack parallel to (0 $\bar{1}$ 1) and there are only van der Waals contacts between molecules in the nearest layers. This type of packing is probably a reason for the twinning observed for those crystals. Twinning occurs when, instead of two adjacent layers related by translation, two layers related by 180° rotation around the x axis pack together.

3.3. Other Gossypol Coordinato-Clathrates with Similar Packing Motifs

Among gossypol inclusion compounds for which crystal data have been published there is a group of triclinic crystals having one of the lattice parameters in the range

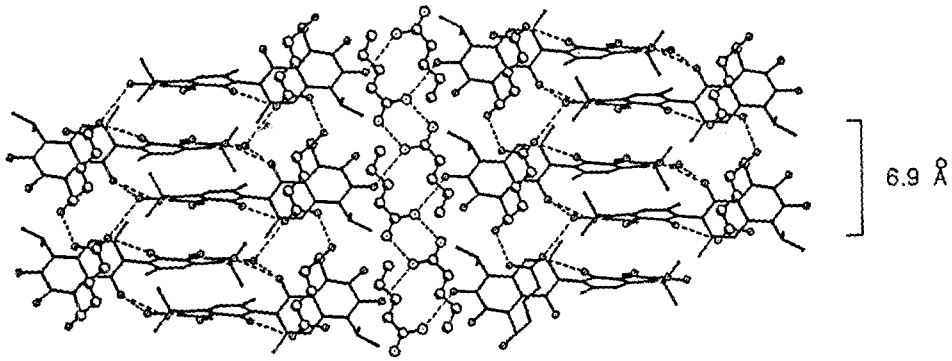


Fig. 4. Structure of the layer-type host–guest aggregate in the gossypol–*n*-valeric acid (2/1) coordinato-clathrate. H-bonds are shown as dashed lines. H atoms have been omitted for clarity. No intramolecular H-bonds are indicated.

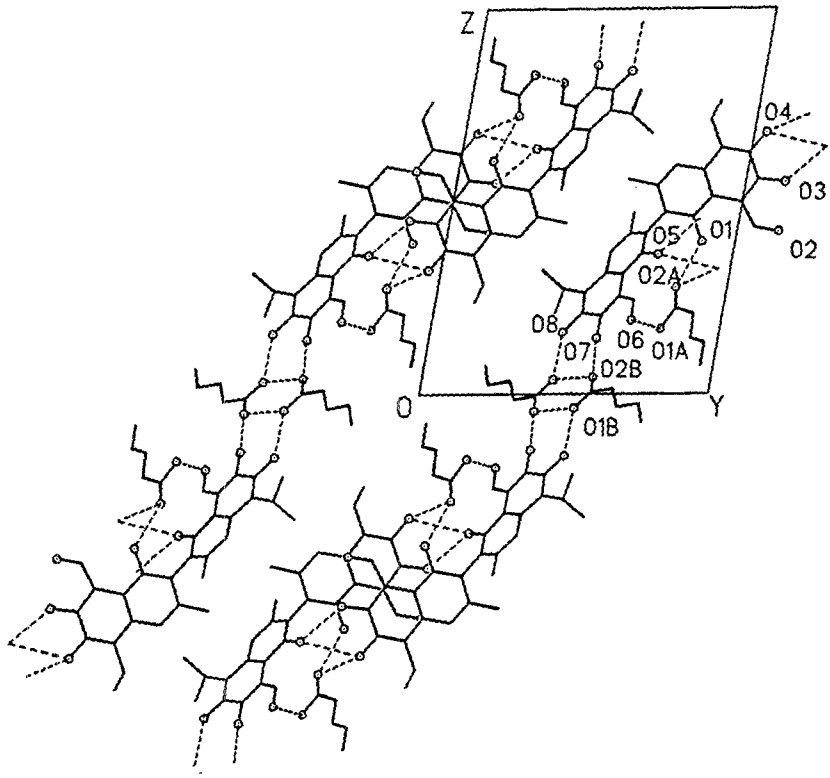


Fig. 5. Projection of the crystal packing for the gossypol–*n*-valeric acid (2/1) coordinato-clathrate. H-bonds are shown as dashed lines. O atoms are represented as small circles and H atoms have been omitted for clarity.

TABLE III. Unit-cell parameters of some triclinic gossypol inclusion compounds with packing motifs similar to gossypol–*n*-valeric acid (1/2).

Guest molecule	*h* : *g* ratio	*a* (Å)	*b* (Å)	*c* (Å)	α (°)	β (°)	γ (°)
Acetic acid [5]	1 : 1	14.278(7)	6.924(5)	14.706(6)	91.90(5)	92.34(3)	98.71(5)
Propionic acid [4]	1 : 1	14.669(5)	6.929(2)	14.774(6)	91.33(3)	91.96(3)	99.73(3)
Butyric acid [4]	1 : 1	15.104(2)	6.917(5)	14.823(9)	92.44(4)	92.03(5)	100.12(5)
Acrylic acid [4]	1 : 1	14.39(1)	6.966(7)	14.79(2)	91.19(1)	90.74(9)	99.47(7)
Methyl formate [6]	1 : 1	14.174(2)	7.080(1)	14.651(2)	93.08(1)	85.91(1)	97.70(1)
Methanol [4]	1 : 1	13.420(3)	7.156(2)	14.508(3)	93.51(1)	98.17(1)	94.95(1)
Ethanol [4]	1 : 1	15.002(9)	7.113(3)	14.695(6)	91.25(3)	67.05(4)	93.90(4)
DMSO [6]	1 : 1	15.132(2)	7.207(1)	14.726(2)	90.90(1)	66.94(1)	96.15(1)
n-valeric acid	1 : 2	19.387(2)	6.912(1)	14.506(2)	93.22(2)	78.85(2)	96.08(2)

6.9–7.2 Å [4–6] (Table III). This value of the unit-cell parameter imposes a special packing pattern on the host O(5)—H···O(3) centrosymetric dimers. The dimers stack along the crystal short axis and the overlap of the C(1)—C(10) naphthalene units is observed not only within the host dimers but also between the dimers along the stack (Figure 1). Two shallow grooves lined with the hydroxyl and aldehyde groups are formed along this stack. The arrangement of the host polar groups in the groove leads to an extensive H-bond interaction of protic as well as aprotic polar guest molecules with the host.

The crystal structures of three gossypol inclusion compounds with functionally different guest molecules showing the above described host packing pattern have been reported: gossypol-acetic acid (1/1) [5], gossypol–methanol (1/1) [4] and gossypol–DMSO (1/1) [6] coordinato-clathrates. Several important structural features of those compounds, which have gone unnoticed in the original papers reporting their crystal structures, have become more evident when the crystal structure of gossypol–*n*-valeric acid (1/2) was solved.

Projections of the crystal packing along the x axis for the above inclusion compounds as well as the structure of the host–guest H-bonded aggregates are shown in Figures 6 and 7, respectively. It is worth mentioning here that for highly polar solvents such as DMSO and methanol an equilibrium between gossypol aldehyde and hemiacetal tautomers has been observed in solution [14, 15]. However, in its crystalline solvates gossypol was found exclusively in the aldehyde form.

In the gossypol-acetic acid (1/1) coordinato-clathrate the carboxylic acid molecule interacts with the host molecules as an H-bond donor to the aldehyde O(6) and then as an acceptor of H-bonds from the hydroxyl groups O(1)–H and O(4)–H. These host polar groups are located along the groove. An additional hydrogen bond between the host O(8)–H group and the guest O(2′) atom connects the above described host-guest assemblies into layer-type aggregates (Figure 7a). The guest

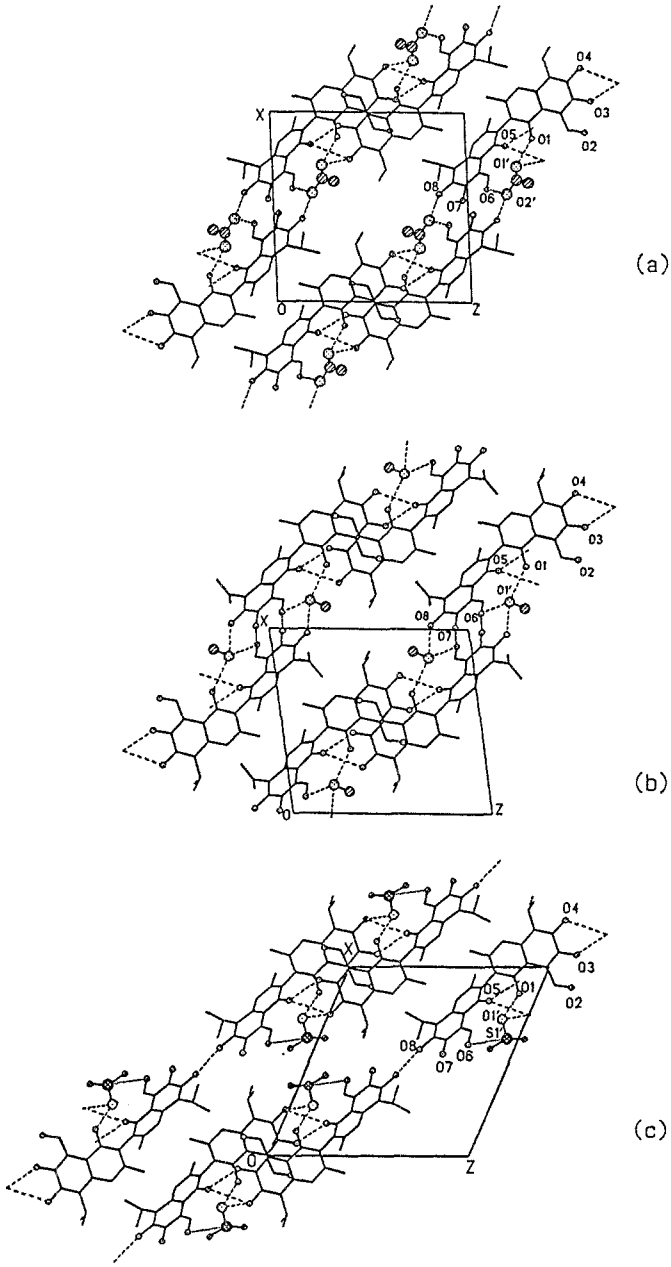


Fig. 6. Projection of the crystal structures of gossypol–acetic acid (1/1) (a), gossypol–methanol (1/1) (b) and gossypol–DMSO (1/1) (c) along the crystal short axis.

molecules are accommodated in narrow channels parallel to the crystal short axis (Figure 6a).

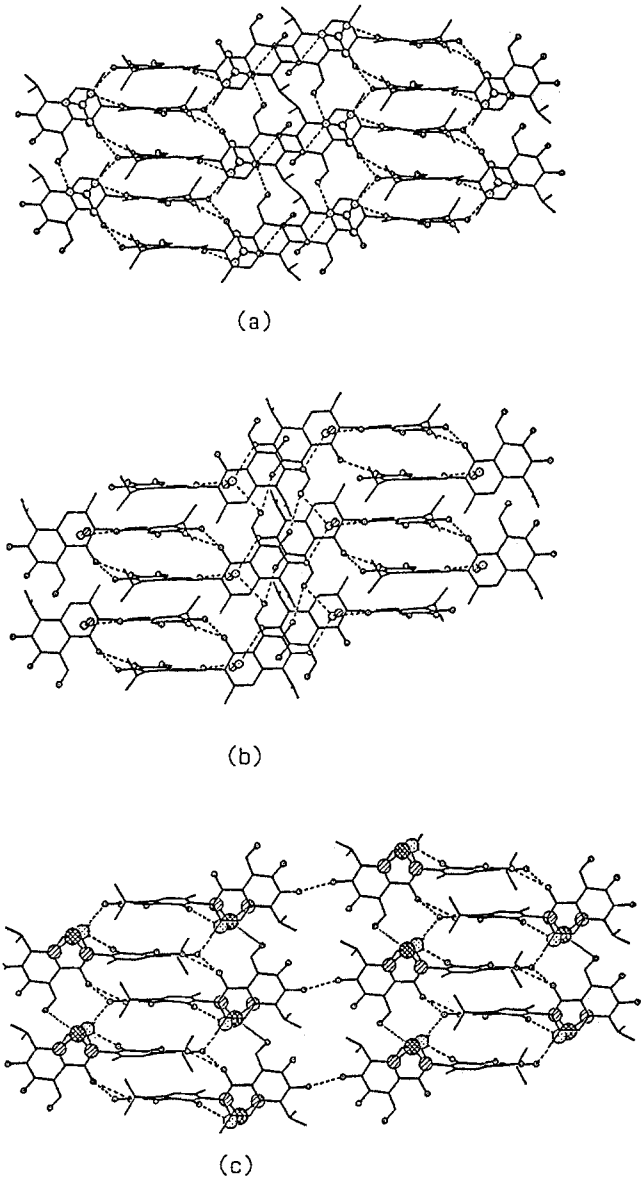


Fig. 7. Structure of the host–guest aggregates observed in: (a) gossypol–acetic acid (1/1); (b) gossypol–methanol (1/1); (c) gossypol–DMSO (1/1).

In contrast to the carboxylic group, the OH group has its proton-donor and proton-acceptor abilities concentrated at one oxygen atom. This group is much less voluminous and therefore substitution of an extensively interacting carboxylic acid molecule to an alcohol molecule, without introducing large structural changes in the host matrix, is seldom observed. However gossypol, with its numerous H-bond donors and acceptors grouped on one side of the naphthalene ring, is able

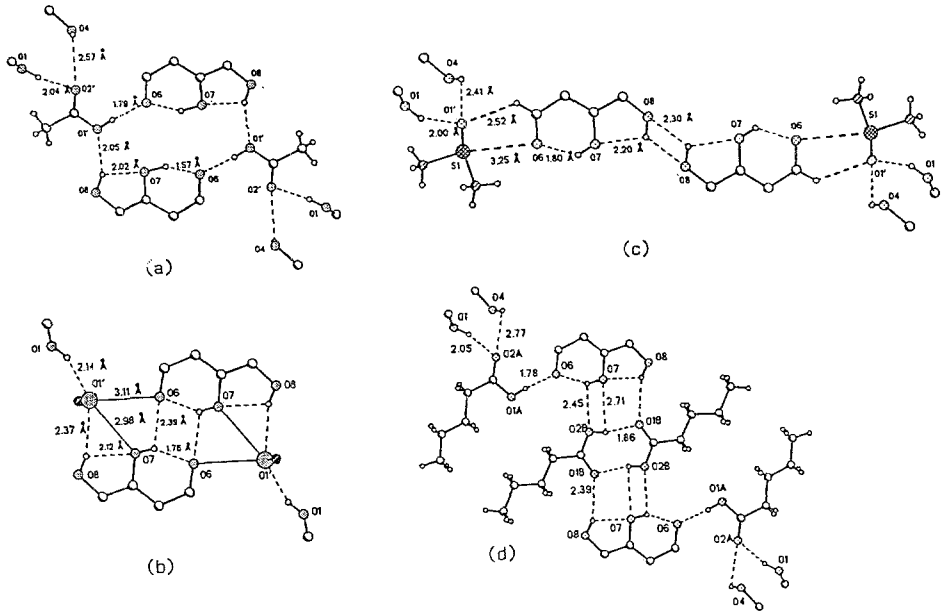


Fig. 8. Fragment of the H-bond network showing host–guest interaction: (a) gossypol–acetic acid (1/1); (b) gossypol–methanol (1/1); (c) gossypol–DMSO (1/1); (d) gossypol–n-valeric acid. The positions of hydrogen atoms of the O–H groups have been calculated.

to adjust its structure to the chemical nature, size and shape of a new substrate by only slightly modifying its H-bond network. Isostructuralism of the inclusion compounds is, to a large extent, preserved as demonstrated by the structures of the gossypol–acetic acid (1/1) and gossypol–methanol (1/1) coordinato-clathrates (Figures 6b, 7b). In the latter case a weak interaction O(4)—H· · ·O(1′) is not observed but the methanol O—H group has now two H-bond donors, O(1)—H and O(8)—H, and two H-bond acceptors, O(6) and O(7), in close proximity. A three-center hydrogen bond is probably formed by the methanol O—H group. This interaction, in turn, leads to a short contact between O(7)—H and O(6) of the inversion center related host molecules [O(7)· · ·O(6) 2.83(2) Å] (Figure 8b). This is the second case observed to date where gossypol hydroxyl groups O(7)—H or O(3)—H, involved in a strong intramolecular hydrogen bond, can also act as a hydrogen bond donor in the intermolecular H-bond [16].

The above examples present cases of a protic solvent inclusion. However, there are also aprotic guest molecules such as DMSO or methyl formate (Table III) which can also interact with the host polar groups located in the groove. The O atom of the DMSO molecule accepts hydrogen bonds from O(1)—H and O(4)—H of two different host molecules. A close nonbonding contact of 3.25 Å between the DMSO S atom, which has a partial positive charge, and the host aldehyde O(6) atom, with partial negative charge, substitutes for a hydrogen bond between a

protic guest and the aldehyde group. The host O(8)—H group does not interact with the guest molecule as in the previous structures. Instead, the O(8)—H groups of the host molecules related by an inversion center form a 'tandem' hydrogen bond [13]. Such configuration of H-bonds is seldom observed due to repulsive H···H interactions. In this case, however, when the two C(16)—O(8) bonds are coplanar, the hydroxyl H atom is nearly colinear with the C—O bond of the acceptor group and the O···O distance is 2.66 Å. Some stabilization of this atomic configuration *via* a hydrogen bond is probably achieved. With an assumed O—H length of 0.85 Å and a C—O—H angle of 109.5° a H···H separation of 2.23 Å is calculated. In this arrangement, disorder of the hydroxyl-group H-atoms, as postulated by Jeffrey and Saenger [13], while not influencing the H···H separation, could only weaken the hydrogen bond interaction in the system.

As is evident from Figures 6–8 in the gossypol–DMSO (1/1) coordinato-clathrate, despite the similarity of some structural fragments, the layer-type host–guest aggregate differs significantly from that observed in the gossypol–acetic acid (1/1) coordinato-clathrate and therefore those compounds are no longer considered as isostructural.

However, unit-cell parameters given in Table III indicate that gossypol–ethanol (1/1) [4] is isostructural with gossypol–DMSO and not the gossypol–methanol solvate as suggested by Ibragimov *et al.* [4].

The main purpose of this section was to show that despite differences in the unit-cell parameters and the host:guest stoichiometry the above inclusion compounds and gossypol–*n*-valeric acid (1/2) have a common feature: the host dimers stacking along the crystal short axis which are fastened together by hydrogen bonds with guest molecules (Figures 4 and 7). These host–guest assemblies can further be joined into a layer-type aggregate in one of three ways: (a) *via* hydrogen bonds between the host O(8)—H groups and the guest acceptor groups; (b) the tandem hydrogen bonds between the host O(8)—H groups; or (c) by including an additional guest molecule as a bridge molecule which accepts hydrogen bonds from the host O(8)–H hydroxyls.

The guest functionality and size governs which of the above interactions takes place.

Acknowledgements

The authors wish to thank the Institute of Bioorganic Chemistry in Tashkent, Uzbekistan, for the gossypol sample. This work was supported by the State Committee of Scientific Research, grant 2 0725 91 01.

References

1. L. Marchlewski: *J. Pract. Chem.* **60**, 84 (1889).
2. K.N. Campbell, R.C. Morris, and R. Adams: *J. Am. Chem. Soc.* **59**, 1723 (1937).

3. B.T. Ibragimov, S.A. Talipov, B.N. Dadabaev, G.B. Nazarov, and T.F. Aripov: *Khim. Prir. Soed.* 675 (1988) [*Chem. Abstr.* (1989), **111**, 58080].
4. B.T. Ibragimov, S.A. Talipov, B.N. Dadabaev and A.A. Abduvakhabov: *Khim. Prir. Soed.*, 191 (1992).
5. X. Changfu, H. Cunheng, B. Guanghong, and M. Shantian: *Scientia Sinica* **B25**, 1194 (1982).
6. B.T. Ibragimov, S.A. Talipov, B.N. Dadabaev, and A.A. Abduvakhabov: *Khim. Prir. Soed.*, 330 (1992).
7. E. Weber and H.-P. Josel: *J. Incl. Phenom.* **1**, 79 (1983).
8. G.M. Sheldrick: SHELX76. *Program for crystal structure determination.* University of Cambridge, England (1976).
9. G.M. Sheldrick: SHELXS-86. *Program for the solution of crystal structures,* University of Göttingen, Germany (1986).
10. M. Gdaniec, B.T. Ibragimov, and S.A. Talipov: *Acta Crystallogr.* **C46**, 810 (1990).
11. M. Gdaniec, B.T. Ibragimov, and S.A. Talipov: *Acta Crystallogr.* **C47**, 573 (1991).
12. B. Brzeziński, S. Paszyc, and G. Zundel: *Chem. Phys. Lett.* **167**, 7 (1990).
13. G.A. Jeffrey and W. Saenger: *Hydrogen Bonding in Biological Structures,* Springer-Verlag, Berlin, Heidelberg, New York (1991).
14. F.G. Kamaev, N.I. Baram, A.I. Ismailov, V.B. Leontev, and A.S. Sadykov: *Izv. Akad. Nauk SSSR, Ser. Khim.* 1003 (1979) [*Chem. Abstr.* (1979), **91**, 55761].
15. B. Brzeziński, J. Olejnik, and S. Paszyc: *J. Mol. Struct.* **220**, 261 (1990).
16. B.T. Ibragimov, M. Gdaniec, and B.N. Dadabaev: *J. Incl. Phenom.* **8**, 333 (1990).