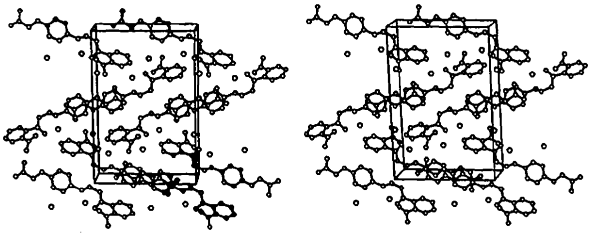

Fig. 3. Molecular packing of AM49 (*ORTEP*; Johnson, 1965). *a* is into the plane of the paper, *b* is horizontal and *c* is vertical.

crystal forms. Fig. 2 compares the conformation of AM49 (Fig. 2*a*) with the two independent molecules of BZF (Figs. 2*b* and 2*c*), and the deoxyhemoglobin-BZF bound conformation (Fig. 2*d*). The decrease in oxygen affinity for hemoglobin (a measure of allosteric effector activity) was equivalent for BZF and AM49, with ΔP_{50} = 10 mm of Hg at 10 m*M* drug concentration and 2·7 m*M* hemoglobin. Thus it appears that the addition of an *o*-COOH group did not change the allosteric effector activity as envisioned.

Fig. 3 shows the molecular packing of AM49, drawn using *ORTEP* (Johnson, 1965).

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Lattice Inclusion Compounds of Gossypol. Structure of 2/1 Gossypol/Di-*n*-propyl Ether Coordinatoclathrate

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Abstract. $C_{30}H_{30}O_8.1/2C_6H_{14}O$, M_r = 569·65, monoclinic, $C2/c$, a = 11·544 (3), b = 30·602 (7), c = 16·472 (4) Å, β = 90·84 (2)°, V = 5818 (3) Å^3, Z = 8, D_x = 1·30 g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, μ = 7·28 cm^{-1}, $F(000)$ = 2424, T = 293 K, R = 0·078 for 1998 observed reflections. Despite its potential C_2 symmetry, the di-*n*-propyl ether molecule is statistically disordered in the cage with C_2 symmetry; it is non-symmetrical, with C—C torsion angles (+)antiperiplanar and one C—O torsion angle (−)anticlinal, the other (+)synclinal. The guest molecule is hydrogen bonded to one of the two O(5)—H hydroxyls located on the wall of the cage. Crystal data for some other inclusion compounds, isostructural with gossypol/di-*n*-propyl ether crystals, are also given.

Introduction. Gossypol [1,1′,6,6′,7,7′-hexahydroxy-5,5′-diisopropyl-3,3′-dimethyl-(2,2′-binaphthalene)-8,8′-dicarboxaldehyde] shows remarkable inclusion ability towards a number of chemically different guest substrates (Ibragimov, Talipov, Dadabaev, Nazarov & Aripov, 1988). The host structure is easily rearranged to accommodate guests of proper size, shape and chemical nature and therefore numerous structural types of gossypol inclusion compounds are observed. Some carboxylic acid esters and ketones with carbon–oxygen or carbon chains, five, six or seven atoms long form isostructural inclusion compounds of a cage type (Ibragimov, Talipov & Gdaniec, 1990; Ibragimov, Talipov & Dadabaev, 1988). The presence of a carbonyl group in the guest molecule was believed to be a necessary condition for formation of inclusion compounds of this structural type. Recently, inclusion compounds of gossypol with di-*n*-propyl ether, butyl ethyl ether, propyl butyrate, acetonylacetone and methyl (*S*)-(−)-2-chloroacetate were crystallized. Space group and unit-cell parameters indicate that these crystals belong to the same structural type and that the conclusions concerning size, shape and chemical constitution of the guest molecule which can be enclosed in the cage were premature.

This paper presents the crystal structure of the 2/1 gossypol/di-*n*-propyl ether coordinatoclathrate.

Experimental. Gossypol was obtained from the Institute of Bioorganic Chemistry, Tashkent, USSR. Crystals of gossypol inclusion compounds with ethyl acrylate, acetonylacetone, propyl butyrate, di-*n*-propyl ether, butyl ethyl ether and methyl (*S*)-(−)-2-chloropropionate were obtained by recrystallization of gossypol from the respective solvent. Unit-cell parameters were determined with a Syntex $P2_1$ diffractometer by least-squares fit of the setting angles of 15 reflections with 2θ in the range 15–30° (see Table 3). X-ray structure analysis was performed for the 2/1 gossypol/di-*n*-propyl ether complex. Diffraction data were collected from a crystal of dimensions $0{\cdot}25 \times 0{\cdot}17 \times 0{\cdot}03$ mm in the θ–2θ mode to a maximum 2θ value of 115° using graphite-monochromatized Cu $K\alpha$ radiation, in the indices range: h $0 \rightarrow 12$, k $0 \rightarrow 32$ and l $-17 \rightarrow 17$. Two standard reflections were monitored every 100 intensity measurements. The maximum variation of their intensity was 2·5%. Out of 4179 reflections measured 1998 had $I > 1{\cdot}5\sigma(I)$ and were considered observed. No corrections for extinction or absorption were used. The structure was solved with *MULTAN*80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). All atoms of the host molecule with the exception of the isopropyl methyl groups were located from the 'best' E map. These methyl groups and the guest molecule were found in subsequent difference Fourier maps. The di-*n*-propyl ether molecule is disordered around a twofold axis. Positional and anisotropic thermal parameters of non-H atoms of the host and positional and isotropic thermal parameters of non-H atoms of the guest were refined by full-matrix least-squares method (on F) with the program *SHELX*76 (Sheldrick, 1976). The H atoms attached to O(1), O(3) and O(4) and those of the methyl groups C(21) and C(26) were located from difference Fourier maps. The positions of the H atoms at O(5), O(7) and O(8) were calculated assuming coplanarity with the naphthyl ring and hydrogen bonds analogous to those observed in isostructural inclusion compounds (Ibragimov, Talipov & Gdaniec, 1990). The remaining H atoms were placed in idealized positions, assuming a C—H distance of 1·08 Å. The positional parameters of the H atoms located from the difference Fourier maps were included in the refinement. Unit weights were used throughout the refinement and the quantity minimized was $\sum w(F_o - F_o)^2$. The refinement converged at $R = 0{\cdot}078$ and $wR = 0{\cdot}068$. The high value of R is due to disorder of the di-*n*-propyl molecule and a rather small number of observations. The maximum Δ/σ value in the final cycle of refinement was less than 0·1 for the host molecule and less than 0·2 for the guest molecule, final $\Delta\rho$ max. and min. were 0·21 and $-0{\cdot}20$ e Å^{-3}, respectively. Atomic scattering factors were those incorporated in *SHELX*76 (Sheldrick, 1976). The atomic parameters are given in Table 1.* An XT IBM PC computer was used to carry out all crystallographic calculations.

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters with e.s.d.'s in parentheses*

$$U_{eq} = (1/3)\sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq} (Å^2)
C(1)	0·8044 (5)	0·0255 (2)	0·7119 (4)	0·050 (2)
C(2)	0·7725 (6)	0·0042 (2)	0·6411 (4)	0·056 (2)
C(3)	0·7608 (6)	0·0285 (2)	0·5683 (4)	0·058 (2)
C(4)	0·7726 (6)	0·0730 (2)	0·5707 (4)	0·059 (2)
C(5)	0·8031 (6)	0·1429 (2)	0·6456 (5)	0·065 (2)
C(6)	0·8395 (7)	0·1631 (2)	0·7159 (5)	0·074 (2)
C(7)	0·8634 (6)	0·1389 (2)	0·7876 (5)	0·067 (2)
C(8)	0·8590 (6)	0·0939 (2)	0·7892 (4)	0·055 (2)
C(9)	0·8241 (6)	0·0710 (2)	0·7161 (4)	0·051 (2)
C(10)	0·7997 (6)	0·0952 (2)	0·6441 (4)	0·055 (2)
C(11)	0·6357 (7)	−0·0584 (2)	0·6459 (5)	0·073 (2)
C(12)	0·7509 (6)	−0·0437 (2)	0·6416 (4)	0·060 (2)
C(13)	0·8420 (6)	−0·0748 (2)	0·6362 (4)	0·065 (2)
C(14)	0·8151 (7)	−0·1183 (2)	0·6365 (5)	0·074 (2)
C(15)	0·6775 (9)	−0·1803 (2)	0·6395 (5)	0·089 (3)
C(16)	0·5659 (9)	−0·1943 (3)	0·6453 (6)	0·108 (3)
C(17)	0·4726 (9)	−0·1647 (3)	0·6474 (6)	0·107 (3)
C(18)	0·4883 (7)	−0·1195 (3)	0·6471 (5)	0·090 (3)
C(19)	0·6071 (7)	−0·1035 (2)	0·6447 (5)	0·080 (3)
C(20)	0·6993 (8)	−0·1338 (2)	0·6396 (5)	0·080 (3)
C(21)	0·7350 (10)	0·0061 (3)	0·4886 (6)	0·092 (4)
C(22)	0·8982 (6)	0·0732 (2)	0·8640 (5)	0·071 (2)
C(23)	0·7664 (8)	0·1685 (2)	0·5689 (5)	0·085 (3)
C(24)	0·8687 (9)	0·1782 (3)	0·5163 (6)	0·107 (3)
C(25)	0·6935 (9)	0·2091 (3)	0·5844 (7)	0·127 (4)
C(26)	0·9661 (7)	−0·0597 (2)	0·6277 (6)	0·074 (3)
C(27)	0·3857 (9)	−0·0919 (3)	0·6501 (6)	0·120 (4)
C(28)	0·7729 (9)	−0·2152 (3)	0·6309 (6)	0·103 (3)
C(29)	0·8518 (8)	−0·2181 (3)	0·7077 (6)	0·114 (4)
C(30)	0·8410 (10)	−0·2116 (3)	0·5509 (7)	0·132 (4)
O(1)	0·8144 (5)	0·0020 (1)	0·7824 (3)	0·071 (1)
O(2)	0·9186 (5)	0·0942 (2)	0·9274 (3)	0·092 (2)
O(3)	0·8919 (5)	0·1639 (2)	0·8517 (3)	0·089 (2)
O(4)	0·8527 (5)	0·2079 (2)	0·7191 (4)	0·100 (2)
O(5)	0·5486 (4)	−0·0278 (2)	0·6514 (4)	0·096 (2)
O(6)	0·2849 (6)	−0·1077 (2)	0·6503 (5)	0·150 (3)
O(7)	0·3636 (5)	−0·1821 (2)	0·6498 (4)	0·135 (2)
O(8)	0·5390 (6)	−0·2384 (2)	0·6490 (4)	0·132 (2)
C(1′)	0·109 (3)	0·384 (1)	0·436 (2)	0·16 (1)*
C(2′)	0·039 (2)	0·401 (1)	0·410 (2)	0·15 (1)*
C(3′)	0·067 (3)	0·427 (1)	0·344 (2)	0·15 (1)*
O(4′)	−0·027 (1)	0·439 (0)	0·284 (1)	0·12 (1)*
C(5′)	−0·047 (3)	0·422 (1)	0·198 (2)	0·15 (1)*
C(6′)	−0·042 (2)	0·385 (1)	0·177 (2)	0·14 (1)*
C(7′)	−0·080 (3)	0·361 (1)	0·080 (2)	0·18 (1)*

* Isotropic temperature factor.

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* Lists of structure factors, anisotropic thermal parameters, bond lengths, bond angles, least-squares planes and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53824 (20 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Discussion. An *ORTEP* (Johnson, 1976) representation of the complex with atom labelling is shown in Fig. 1. The geometrical features of the gossypol molecule are in good agreement with the values observed in other inclusion compounds of this host (Ibragimov, Talipov & Gdaniec, 1990; Ibragimov, Talipov & Dadabaev, 1988). E.s.d.'s for bond lengths are in the range 0·008–0·015 Å and for bond angles 0·05–0·09°. The two naphthyl moieties form a dihedral angle of 100·7 (2)° and the hydroxyl O(1)—H and O(5)—H O atoms are 3·836 (9) Å apart. The isopropyl substituents in the two equivalent halves of the molecule have different orientations. The isopropyl group at C(5) has its methine H atom directed towards C(4) and that at C(15) towards O(8). Table 2 gives the geometry of intramolecular hydrogen bonds. O(7) and O(8) have rather high temperature factors and therefore H(70) and H(80) could not be located on difference Fourier maps. Their positions have been calculated assuming that they are involved in intramolecular hydrogen bonds.

As a detailed description of the host lattice in gossypol inclusion compounds of this structural type has been given elsewhere (Ibragimov, Talipov & Gdaniec, 1990; Ibragimov, Talipov & Dadabaev, 1988), only the main features of this structure are discussed here. Two O(4)—H and two O(8)—H groups [O(4)—H and O(8)—H correspond to each other in the equivalent parts of the gossypol molecule] form a C_2-symmetric tetrahedron of homodromic hydrogen bonds. Hydrogen-bonded host molecules pack into a layer parallel to (001) (Fig. 2). The layer is composed of molecules of the same chirality. Holes within the layers are closed on both sides by naphthyl rings of neighbouring layers. The cages have C_2 symmetry and an approximate size of 5·5 × 6·5 × 10·5 Å. One of the cage walls is hydrophilic, with two O(5)—H groups on its surface, while the other walls are hydrophobic (Fig. 2).

Table 2. *Geometry of hydrogen bonds*

D—H···*A*	*D*···*A* (Å)	*D*—H (Å)	H···*A* (Å)	*D*—H···*A* (°)
(a) Intramolecular hydrogen bonds				
O(3)—H(30)···O(2)	2·488 (8)	0·90 (8)	1·71 (6)	143 (7)
O(7)—H(70)···O(6)	2·451 (9)	1·00	1·64	135
O(4)—H(40)···O(3)	2·600 (8)	0·97 (6)	2·00 (6)	118 (4)
O(8)—H(80)···O(7)	2·658 (9)	1·00	2·31	99
(*b*) Intermolecular hydrogen bonds				
O(5)—H(50)···O(4^{i})	2·930 (9)	1·00	2·10	139
O(4)—H(40)···O(8^{i})	2·985 (9)	0·97 (6)	2·14 (6)	145 (5)
O(8)—H(80)···O(4^{ii})	2·954 (9)	1·00	2·10	142

Symmetry codes: (i) 1·5 − *x*, 0·5 − *y*, 1·5 − *z*; (ii) −1 + *x*, −1 + *y*, *z*.

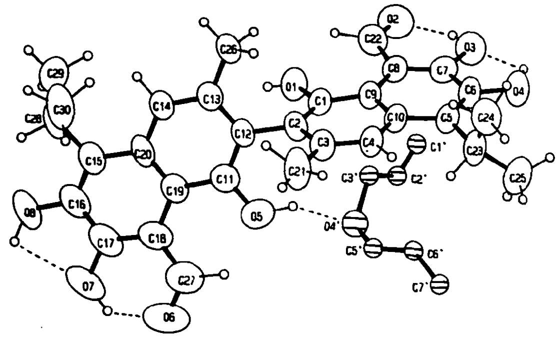

Fig. 1. Atom-numbering scheme (*ORTEP*II; Johnson, 1976).

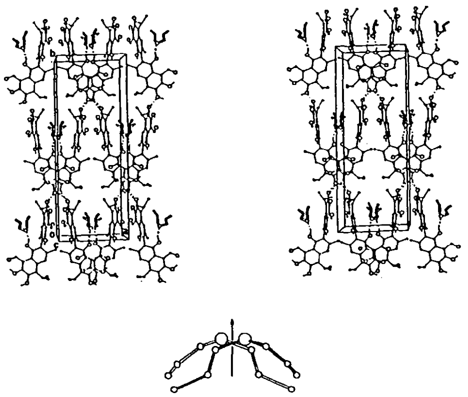

Fig. 2. Structure of the gossypol (001) layer with the included guest molecules and the pattern of disorder of the di-*n*-propyl ether molecule. Hydrogen bonds are marked with dashed lines. H atoms bonded to C atoms are omitted for clarity (*PLUTO*; Motherwell & Clegg, 1978).

There are only van der Waals interactions between the neighbouring (001) layers and therefore the host structure should be most easily expanded in the **c** direction. The long axis of the guest molecule enclosed in the cage is nearly parallel to the crystal *c* axis and, therefore, assuming an extended all-*trans* conformation of the guest molecule, the length of the guest should correlate with the unit-cell *c* parameter. Table 3 shows that *c* is about 16·5 Å when the guest molecule has a carbon–oxygen or carbon chain five atoms long, and 17·0 Å (with the exception of di-*n*-propyl ether) when the chain is seven or eight atoms long. However, the *a* parameter also varies significantly [11·011 (3)–11·544 (3) Å] in this type of inclusion compound.

Di-*n*-propyl ether and butyl ethyl ether form isostructural inclusion compounds with gossypol. As these guests have the same molecular length when adopting the extended all-*trans* conformation the *c* parameter for their inclusion compounds should not differ significantly. However, *c* is 0·438 (5) Å shorter for gossypol/di-*n*-propyl ether, indicating that butyl ethyl ether is accommodated in the cage in the extended conformation while di-*n*-propyl ether is not. That the di-*n*-propyl ether molecule is not in the

Table 3. *Crystal data for inclusion compounds isostructural with gossypol/dipropyl ether*

Guest molecule	Space group	*a* (Å)	*b* (Å)	*c* (Å)	*β* (°)	*V* (Å^3)	D_x (g cm^{-3})
1. Methyl acrylate*	*C2/c*	11·011 (3)	30·747 (8)	16·545 (5)	90·26 (2)	5601	1·33
2. Methyl propionate*	*C2/c*	11·079 (2)	30·724 (11)	16·515 (5)	90·46 (2)	5621	1·33
3. Ethyl acetate*	*C2/c*	11·143 (2)	30·769 (5)	16·507 (3)	90·25 (2)	5659	1·32
4. Acetylacetone*	*C2/c*	11·011 (5)	30·74 (2)	16·638 (6)	91·91 (2)	5628	1·34
5. Ethyl acrylate†	*C2/c*	11·079 (2)	30·737 (5)	16·569 (3)	90·12 (1)	5642	1·34
6. Ethyl bromoacetate*	*C2/c*	11·158 (3)	30·67 (3)	16·645 (3)	90·50 (3)	5696	1·40
7. Acetonyl acetone†	*C2/c*	11·186 (4)	30·701 (6)	16·685 (3)	91·31 (2)	5728	1·34
8. Butyl acetate*	*C2/c*	11·221 (2)	30·538 (9)	17·023 (2)	90·48 (4)	5833	1·31
9. Ethyl acetoacetate*	*C2/c*	11·095 (2)	30·604 (9)	16·955 (5)	88·27 (2)	5755	1·35
10. Propyl butyrate†	*C2/c*	11·352 (5)	30·590 (20)	17·086 (8)	92·43 (3)	5928	1·31
11. Dipropyl ether†	*C2/c*	11·544 (3)	30·602 (7)	16·472 (4)	90·84 (2)	5818	1·30
12. Butyl ethyl ether†	*C2/c*	11·201 (5)	30·642 (7)	16·910 (3)	90·82 (3)	5803	1·30
13. Methyl (*S*)-(−)-2-chloropropionate†	*C2*	11·332 (3)	30·705 (9)	16·534 (4)	92·18 (2)	5749	1·34

Host/guest ratio 2/1.

* Ibragimov, Talipov & Gdaniec (1990).
† This work.

fully extended conformation is further demonstrated by the unit-cell *a* parameter which is 0·343 (6) Å longer than in the gossypol/butyl ethyl ether coordinatoclathrate. The cage has C_2 symmetry but it accommodates non-symmetrical molecules which have to be statistically disordered. The di-*n*-propyl ether molecule has C_2 symmetry in the all-*trans* conformation and could be placed in the cage without statistical disorder. However, the conformation [torsion angles along the chain C(1′)—C(2′)—C(3′)—O(4′) −157 (3), C(2′)—C(3′)—O(4′)—C(5′) +107 (3), C(3′)—O(4′)—C(5′)—C(6′) −45 (5), O(4′)—C(5′)—C(6′)—C(7′) −172 (2)°], which the molecule adopts in the gossypol clathrate, renders it non-symmetrical. As a consequence, di-*n*-propyl ether is like the other guests, statistically disordered (Fig. 2). That a guest molecule in a conformation other than all-*trans* can be accommodated in the cage explains why some guests, with carbon–oxygen chains longer than seven atoms, form this type of structure. For example, the *c* parameter of the inclusion compound with propyl butyrate (eight-membered chain) does not differ much from that with butyl acetate (seven-membered chain). However, their *a* parameters are significantly different (Table 1) indicating that propyl butyrate adopts a folded conformation in the cage. Amyl acetate has, like propyl butyrate, an eight-membered chain but its ester carbonyl group is further displaced from the molecular centre. Thus, it forms an inclusion compound of another structural type (Gdaniec, Ibragimov & Talipov, 1990).

Only molecules which have hydrogen-bond accepting group(s) can be enclosed in the cage. The host–guest hydrogen bond stabilizes this type of inclusion compound structure. Guest molecules are hydrogen bonded to one or two O(5)—H groups located on one of the cage walls. If the hydrogen-bond acceptor lies on the twofold axis, it can interact with both O(5)—H groups. When it is displaced from the twofold axis by a translation along the cage long axis, one of the hydrogen bonds is weakened or even broken. The di-*n*-propyl ether guest molecule has its O atom displaced from the twofold axis and is hydrogen bonded to one of the two O(5)—H groups only. This means that the two O(5)—H groups have different surroundings – one is involved in hydrogen bonding while the other is in close contact with lipophilic groups. The two different surroundings of this hydroxyl in the crystal structure may give rise to a disorder of the O(5)—H proton, which could not be localized from difference Fourier maps.

The hydroxyl O(1)—H is not involved in any hydrogen bonding in this structural type of inclusion compound. The O(1)—H vector points in the direction of the nearest acceptor group, the aldehyde O(6) atom of the dyad-related host molecule. However, the O(1)···O(6) and H···O(6) distances are long [3·721 (9) and 3·08 (7) Å, respectively] and indicative of very weak or no hydrogen-bond formation.

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