

Inclusion Complexes of the Natural Product Gossypol. Strong Influence of the Guest on the Host Structure in Channel-Type Isostructural Inclusion Complexes of Gossypol

B. T. IBRAGIMOV,^a M. GDANIEC,^b and B. N. DADABAEV^a

^aInstitute of Bioorganic Chemistry of Uz.S.S.R. Academy of Sciences, 700143 Tashkent, M. Gorky Pr. 83, U.S.S.R.

^bFaculty of Chemistry, A. Mickiewicz University, 60780 Poznan, Poland

(Received: 6 December, 1988; in final form: 11 April 1989)

Abstract. The crystal structures of 1:1 inclusion complexes of gossypol with tetrahydrofuran (GPTHF), cyclohexanone (GPCHN) and butanal (GPBTA) have been determined by X-ray structure analysis. The crystals of GPTHF are triclinic, space group $P\bar{1}$, $a = 10.788(2)$, $b = 10.979(3)$, $c = 13.880(2)$ Å, $\alpha = 80.11(2)$, $\beta = 103.87(1)$, $\gamma = 77.96(2)^\circ$, $V = 1517.8(6)$ Å³, $Z = 2$, $R = 0.052$ for 2701 observed reflections. The crystals of GPCHN are triclinic, space groups $P\bar{1}$, $a = 10.803(4)$, $b = 11.157(5)$, $c = 15.428(6)$ Å, $\alpha = 108.75(3)$, $\beta = 106.93(3)$, $\gamma = 103.34(3)^\circ$, $V = 1573(1)$ Å³, $Z = 2$, $R = 0.071$ for 1879 observed reflections. The crystals of GPBTA are triclinic, space group $P\bar{1}$, $a = 10.190(2)$, $b = 11.335(1)$, $c = 14.665(2)$ Å, $\alpha = 73.04(1)$, $\beta = 103.74(1)$, $\gamma = 81.07(1)^\circ$, $V = 1529.9(5)$ Å³, $Z = 2$, $R = 0.068$ for 2964 observed reflections. Crystal data for another 13 isostructural inclusion complexes are given.

In this isostructural group of complexes guest molecules are accommodated in channels and are hydrogen bonded to the host molecules *via* an O(1)—H \cdots O(1') hydrogen bond. The molecular association changes significantly with the shape and size of the guest component. In GPTHF centrosymmetric dimers of gossypol formed *via* O(5)—H \cdots O(3) hydrogen bonds are associated in columns *via* a weak O(4)—H \cdots O(8) hydrogen bond. In GPCHN the latter bond disappears as the distance O(4)—O(8) is increased to 3.73 Å. In GPBTA the O(5)—H \cdots O(3) bond is replaced by three centre hydrogen bonds O(5)—H \cdots O(2) and O(3)—H \cdots O(5), and a centrosymmetric dimer of a new type is formed. These dimers are further connected by two weak hydrogen bonds to form columns. The butanal molecule interacts with the host structure *via* two hydrogen bonds. This indicates that a guest component can activate or deactivate different functional groups of the host in channel inclusion complexes of gossypol for hydrogen bond formation.

Key words. crystal structure, X-ray crystallography, gossypol inclusion complexes.

Supplementary Data relating to this material deposited with the British Library under reference number 82082 (54 pages).

1. Introduction

We have previously reported that gossypol forms inclusion compounds with many organic molecules [1–3]. Gossypol inclusion compounds exhibit channel, layer and clathrate type structures, however, within each type of structure many classes can be distinguished. Up to now we have been able to characterize five different isostructural channel-type classes and one of them will be presented in this paper. We shall call it an acetone-type class as the crystal structure of a member of that

class, the inclusion complex of gossypol with acetone, has already been published [4]. Our recent studies have shown that many other molecules of a polar nature form acetone-type inclusion complexes with gossypol and that they can be divided into three groups: those containing functional groups which can be hydrogen bond donors, those which act as hydrogen bond acceptors, and those which can be both hydrogen bond donors and acceptors. This paper deals with inclusion complexes of gossypol where guest molecules belong to the first group and presents the crystal structure of complexes with tetrahydrofuran, cyclohexanone and butanal. The following abbreviations are used throughout the text: GPACK for gossypol:acetone; GPTHF for gossypol:tetrahydrofuran; GPCHN for gossypol:cyclohexanone; and GPBTA for gossypol:butanal.

2. Experimental

Single crystals of inclusion complexes with tetrahydrofuran, cyclohexanone and butanal were grown by slow evaporation of the solvent from a gossypol solution at room temperature. Unit-cell parameters were determined on a Syntex P2₁ diffractometer by a least-squares fitting of the setting angles of 15 reflections. Crystal data, some details concerning data collection and structure refinement are given in Table I. Although these complexes belong to the same isostructural class of inclusion compounds of gossypol their structures have not been solved in isostructural unit cells. The parameters of the isostructural cells with axes chosen as in the case of

Table I. Crystal data for GPTHF, GPCHN and GPBTA

	GPTHF	GPCHN	GPBTA
Formula	C ₃₄ H ₃₈ O ₉	C ₃₆ H ₄₀ O ₉	C ₃₄ H ₃₈ O ₉
Crystal system	triclinic	triclinic	triclinic
Space group	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
<i>a</i> (Å)	10.788(2)	10.803(4)	10.190(2)
<i>b</i> (Å)	10.979(3)	11.157(5)	11.355(1)
<i>c</i> (Å)	13.880(2)	15.428(6)	14.665(2)
α (deg)	80.11(2)	108.75(3)	73.04(1)
β (deg)	103.87(1)	106.93(3)	103.71(1)
γ (deg)	77.96(2)	103.34(3)	81.07(1)
<i>V</i> (Å ³)	1518	1573	1530
ρ (g cm ⁻³)	1.29	1.30	1.28
<i>Z</i>	2	2	2
Radiation	Cu <i>K</i> _α	Mo <i>K</i> _α	Cu <i>K</i> _α
μ (λ)(cm ⁻¹)	7.28	0.87	7.22
2 θ _{max}	120	47	120
Unique data	4490	4689	4530
observed data	2701	1879	2964
σ criterion for			
observed data	3 σ	4 σ	4 σ
Weighting scheme	1/ σ^2	1/[$\sigma^2 + 0.0002^2$]	1/[$\sigma^2 + 0.0004F^2$]
<i>R</i>	0.052	0.071	0.068
<i>R</i> _w	0.066	0.079	0.092

GP THF are given in Table V. To facilitate further discussion we shall refer to this setting of axes by a subscript τ .

The structures were determined by direct methods using the program MULTAN-80 [5] and refined by full-matrix least-squares method with the program SHELX-76 [6]. In GP THF the hydrogen atoms of the isopropyl methyl groups and those of tetrahydrofuran were calculated from geometrical conditions and their positional parameters were not refined. The remaining hydrogen atoms were located on a ΔF map and their parameters included in the subsequent refinement cycles. In GP CHN the hydrogen atoms of the gossypol hydroxyl groups were localized on a ΔF map and coordinates of the remaining H atoms were calculated for the expected positions. They were given a common temperature factor $U = 0.07$ and their parameters were not included in the refinement. In GP BTA only H atoms from the hydroxyl groups were located on a ΔF map and refined. The positions of the remaining hydrogen atoms of the host molecule were calculated from geometrical conditions. Hydrogen atoms of the guest molecule were not determined. The aliphatic chain of the butanal molecule shows disorder. The sum of occupancy factors of the two orientations of this chain has been fixed to 1.0 and the occupancy factor has refined to 0.78(2). In GP CHN and GP BTA an empirical extinction parameter χ was applied to correct F_c according to $F'_c = F_c(1 - \chi F_c^2/\sin \theta)$. Atomic scattering factors used were those included in SHELX-76 [6].

3. Results and Discussion

The atomic parameters are given in Table II. Tables of hydrogen atom coordinates, anisotropic thermal parameters, distances, angles, selected torsion angles and structure factors are in the Supplementary Material. The numbering scheme of gossypol and the guest molecules is shown in Figure 1.

3.1. MOLECULAR STRUCTURE

The gossypol molecule can have one of the following tautomeric forms [7–9]: aldehyde, lactol and quinoid. In the crystal structures solved up to now gossypol has had an aldehyde form [3–4, 10–15] and this form is also observed in acetone-type channel inclusion complexes. The highest symmetry which the isolated gossypol molecule can possess is C_2 with the 2-fold axis perpendicular to the C(2)—C(12) bond. This symmetry is slightly disturbed in crystals due to a different environment of the two symmetrical parts of the gossypol molecule. The isopropyl groups have an identical orientation and the hydrogen atoms at C(23) and C(28) are oriented towards C(4) and C(14), respectively. The naphthyl moieties C(1)—C(10) and C(11)—C(20) are nearly planar and form dihedral angles of 82.9, 83.9, 83.0 and 86.7° in GP ACT, GP THF, GP CHN and GP BTA, respectively.

There are four intramolecular hydrogen bonds in the gossypol molecule. The H atoms of the hydroxyl groups O(3)—H and O(7)—H are involved in strong intramolecular hydrogen bonds which are part of a six-membered conjugated ring system. Hydrogen bonds O(4)—H...O(3) and O(8)—H...O(7) close five membered rings, are much weaker and are minor components of three-centre bonds. The geometry of these hydrogen bonds is given in Table III.

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

$$U_{\text{eq}} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j.$$

Atom	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>	<i>U_{eq}</i>
a. <i>gossypol</i> : tetrahydrofuran (GP THF)				
C(1)	0.2894(3)	0.8553(3)	1.0138(2)	0.042(1)
C(2)	0.2862(3)	0.7300(3)	1.0130(2)	0.042(1)
C(3)	0.3240(3)	0.6762(3)	0.9362(2)	0.044(1)
C(4)	0.3633(3)	0.7483(3)	0.8640(3)	0.047(2)
C(5)	0.4088(3)	0.9491(3)	0.7845(2)	0.052(2)
C(6)	0.4041(4)	1.0742(3)	0.7848(3)	0.056(2)
C(7)	0.3695(3)	1.1305(3)	0.8620(3)	0.050(2)
C(8)	0.3348(3)	1.0629(3)	0.9408(2)	0.044(1)
C(9)	0.3310(3)	0.9318(3)	0.9409(2)	0.041(1)
C(10)	0.3681(3)	0.8764(3)	0.8630(2)	0.042(1)
C(11)	0.3351(3)	0.5906(3)	1.1853(3)	0.046(1)
C(12)	0.2437(3)	0.6534(3)	1.0926(2)	0.044(1)
C(13)	0.1142(4)	0.6382(3)	1.0750(3)	0.051(2)
C(14)	0.0835(4)	0.5622(4)	1.1495(3)	0.057(2)
C(15)	0.1373(4)	0.4210(4)	1.3231(3)	0.063(2)
C(16)	0.2291(5)	0.3675(4)	1.4154(3)	0.066(2)
C(17)	0.3615(4)	0.3780(3)	1.4337(3)	0.065(2)
C(18)	0.4037(4)	0.4434(3)	1.3591(3)	0.054(2)
C(19)	0.3066(4)	0.5097(3)	1.2626(2)	0.048(1)
C(20)	0.1754(4)	0.4969(3)	1.2446(3)	0.053(2)
C(21)	0.3217(5)	0.5398(4)	0.9335(4)	0.061(2)
C(22)	0.3066(4)	1.1302(4)	1.0159(3)	0.062(2)
C(23)	0.4514(5)	0.8901(4)	0.7023(3)	0.073(2)
C(24)	0.5881(6)	0.8996(9)	0.6974(6)	0.139(4)
C(25)	0.3480(7)	0.9428(7)	0.5990(4)	0.138(4)
C(26)	0.0109(5)	0.7080(5)	0.9744(4)	0.070(2)
C(27)	0.5454(4)	0.4319(4)	1.3821(3)	0.073(2)
C(28)	0.0009(5)	0.3971(5)	1.3044(4)	0.087(2)
C(29)	-0.0816(6)	0.4680(8)	1.3604(6)	0.141(5)
C(30)	0.0030(7)	0.2562(6)	1.3229(5)	0.129(4)
O(1)	0.2529(3)	0.9111(2)	1.0861(2)	0.072(1)
O(2)	0.3075(3)	1.2456(2)	1.0099(2)	0.077(1)
O(3)	0.3736(3)	1.2525(2)	0.8544(2)	0.066(1)
O(4)	0.4328(3)	1.1501(3)	0.7082(2)	0.083(2)
O(5)	0.4611(2)	0.6084(3)	1.2061(2)	0.062(1)
O(6)	0.6239(3)	0.3750(3)	1.4680(2)	0.092(2)
O(7)	0.4421(4)	0.3158(3)	1.5271(2)	0.086(2)
O(8)	0.1994(4)	0.2986(3)	1.4941(2)	0.091(2)
O(1')	0.1312(3)	0.8615(3)	1.2266(2)	0.100(2)
C(2')	0.1934(6)	0.8262(7)	1.3304(4)	0.115(3)
C(3')	0.0892(7)	0.8365(10)	1.3803(5)	0.177(5)
C(4')	-0.0329(7)	0.8800(11)	1.3041(6)	0.175(5)
C(5')	-0.0032(6)	0.9051(9)	1.2062(5)	0.147(4)

Table II. (Continued)

Atom	x/a	y/b	z/c	U_{eq}
b. <i>gossypol</i> :cyclohexanone (GPCHN)				
C(1)	0.7207(7)	0.3518(7)	0.4986(5)	0.051(4)
C(2)	0.7314(6)	0.2330(7)	0.5062(4)	0.049(4)
C(3)	0.6225(7)	0.1112(7)	0.4414(5)	0.051(4)
C(4)	0.5057(6)	0.1077(7)	0.3721(5)	0.052(4)
C(5)	0.3672(6)	0.2234(7)	0.2934(5)	0.056(4)
C(6)	0.3629(8)	0.3451(8)	0.2904(6)	0.065(5)
C(7)	0.4726(8)	0.4704(8)	0.3543(5)	0.061(5)
C(8)	0.5927(7)	0.4802(7)	0.4225(5)	0.052(4)
C(9)	0.6033(6)	0.3544(7)	0.4290(5)	0.050(4)
C(10)	0.4932(6)	0.2284(7)	0.3650(4)	0.044(4)
C(11)	0.8570(7)	0.2724(7)	0.6794(6)	0.061(5)
C(12)	0.8562(7)	0.2398(7)	0.5864(5)	0.051(5)
C(13)	0.9659(7)	0.2074(7)	0.5659(5)	0.057(5)
C(14)	1.0761(7)	0.2168(7)	0.6429(5)	0.055(5)
C(15)	1.1997(7)	0.2565(7)	0.8194(6)	0.065(5)
C(16)	1.1981(9)	0.2895(8)	0.9121(6)	0.073(6)
C(17)	1.0850(9)	0.3147(8)	0.9316(6)	0.073(6)
C(18)	0.9693(8)	0.3080(8)	0.8595(6)	0.066(5)
C(19)	0.9687(7)	0.2772(7)	0.7607(5)	0.055(4)
C(20)	1.0829(7)	0.2511(7)	0.7407(6)	0.055(4)
C(21)	0.6290(7)	-0.0199(7)	0.4469(5)	0.066(5)
C(22)	0.6951(8)	0.6122(8)	0.4791(6)	0.074(5)
C(23)	0.2461(8)	0.0927(8)	0.2256(6)	0.072(5)
C(24)	0.1264(9)	0.0836(9)	0.2585(6)	0.108(6)
C(25)	0.2053(11)	0.0530(11)	0.1168(6)	0.140(8)
C(26)	0.9657(8)	0.1740(8)	0.4625(6)	0.073(5)
C(27)	0.8609(10)	0.3310(9)	0.8886(7)	0.096(7)
C(28)	1.3234(9)	0.2301(9)	0.8006(6)	0.083(6)
C(29)	1.4612(8)	0.3520(10)	0.8648(7)	0.114(8)
C(30)	1.3363(9)	0.1020(8)	0.8123(7)	0.110(7)
O(1)	0.8258(4)	0.4739(4)	0.5626(3)	0.074(4)
O(2)	0.6810(5)	0.7143(5)	0.4694(4)	0.091(4)
O(3)	0.4489(5)	0.5783(5)	0.3410(4)	0.081(3)
O(4)	0.2466(5)	0.3450(5)	0.2236(4)	0.095(4)
O(5)	0.7508(5)	0.3048(5)	0.7017(3)	0.080(3)
O(6)	0.8636(6)	0.3532(7)	0.9750(5)	0.116(5)
O(7)	1.0967(6)	0.3410(6)	1.0267(4)	0.104(4)
O(8)	1.3044(5)	0.2942(5)	0.9884(3)	0.098(4)
O(1')	0.8933(6)	0.4764(7)	0.3491(5)	0.122(5)
C(1')	0.829(1)	0.401(1)	0.2579(7)	0.104(6)
C(2')	0.918(1)	0.359(1)	0.2052(6)	0.111(8)
C(3')	0.8288(9)	0.2082(9)	0.1384(7)	0.111(6)
C(4')	0.680(1)	0.178(1)	0.0751(7)	0.111(6)
C(5')	0.612(1)	0.239(1)	0.1399(8)	0.138(9)
C(6')	0.6866(9)	0.381(1)	0.2046(7)	0.109(7)

Table II. (Continued)

Atom	x/a	y/b	z/c	U_{eq}
c. <i>gossypol</i> :butanal (GPBTA)				
C(1)	0.8237(3)	0.3246(3)	0.5286(2)	0.049(1)
C(2)	0.7856(3)	0.2214(3)	0.5075(2)	0.049(2)
C(3)	0.8705(3)	0.0984(3)	0.5652(2)	0.052(1)
C(4)	0.9894(3)	0.0842(3)	0.6384(2)	0.052(2)
C(5)	1.1625(3)	0.1696(3)	0.7338(2)	0.052(2)
C(6)	1.1956(3)	0.2736(3)	0.7524(2)	0.057(2)
C(7)	1.1084(4)	0.3962(3)	0.7038(2)	0.058(2)
C(8)	0.9848(3)	0.4208(3)	0.6289(2)	0.053(2)
C(9)	0.9441(3)	0.3135(3)	0.6049(2)	0.048(2)
C(10)	1.0318(3)	0.1886(3)	0.6594(2)	0.049(2)
C(11)	0.6763(3)	0.2599(3)	0.3288(2)	0.046(1)
C(12)	0.6604(3)	0.2411(3)	0.4221(2)	0.049(2)
C(13)	0.5268(3)	0.2391(3)	0.4343(2)	0.058(1)
C(14)	0.4194(3)	0.2514(3)	0.3534(2)	0.059(2)
C(15)	0.3184(3)	0.2803(4)	0.1734(2)	0.065(2)
C(16)	0.3372(3)	0.3025(4)	0.0822(2)	0.066(2)
C(17)	0.4642(3)	0.3233(3)	0.0651(2)	0.057(2)
C(18)	0.5781(3)	0.3151(3)	0.1426(2)	0.050(2)
C(19)	0.5645(3)	0.2837(3)	0.2421(2)	0.046(1)
C(20)	0.4335(3)	0.2719(3)	0.2566(2)	0.053(1)
C(21)	0.8280(4)	-0.0169(3)	0.5447(3)	0.068(2)
C(22)	0.9058(4)	0.5519(3)	0.5844(3)	0.071(2)
C(23)	1.2627(4)	0.0404(3)	0.7892(3)	0.061(2)
C(24)	1.4015(5)	0.0343(5)	0.7689(4)	0.096(2)
C(25)	1.2791(6)	-0.0062(5)	0.8994(3)	0.107(2)
C(26)	0.5052(4)	0.2214(5)	0.5363(3)	0.085(2)
C(27)	0.6966(4)	0.3518(4)	0.1141(3)	0.068(2)
C(28)	0.1799(4)	0.2594(6)	0.1878(3)	0.102(3)
C(29)	0.0612(5)	0.3722(8)	0.1262(5)	0.164(5)
C(30)	0.1531(7)	0.1405(7)	0.1723(4)	0.149(5)
O(1)	0.7436(3)	0.4446(2)	0.4745(2)	0.071(1)
O(2)	0.9422(3)	0.6398(2)	0.6088(2)	0.081(2)
O(3)	1.1555(3)	0.4864(3)	0.7348(2)	0.078(1)
O(4)	1.3163(3)	0.2623(3)	0.8244(2)	0.078(2)
O(5)	0.8077(2)	0.2522(2)	0.3173(2)	0.056(1)
O(6)	0.7065(3)	0.3746(3)	0.0289(2)	0.083(2)
O(7)	0.4660(3)	0.3523(3)	-0.0300(2)	0.076(1)
O(8)	0.2340(3)	0.3057(4)	0.0016(2)	0.101(2)
O(1')	0.4691(5)	0.4416(4)	0.7059(3)	0.125(2)
C(2')	0.5806(8)	0.4276(7)	0.7055(7)	0.157(5)
C(31')	0.718(1)	0.380(1)	0.788(1)	*0.129(5)
C(32')	0.680(3)	0.284(3)	0.818(2)	*0.13(1)
C(41')	0.760(1)	0.237(1)	0.809(1)	*0.157(5)
C(42')	0.827(3)	0.300(2)	0.836(2)	*0.11(1)
C(5')	0.9031(8)	0.1844(9)	0.8970(5)	0.189(5)

* isotropic temperature factors.

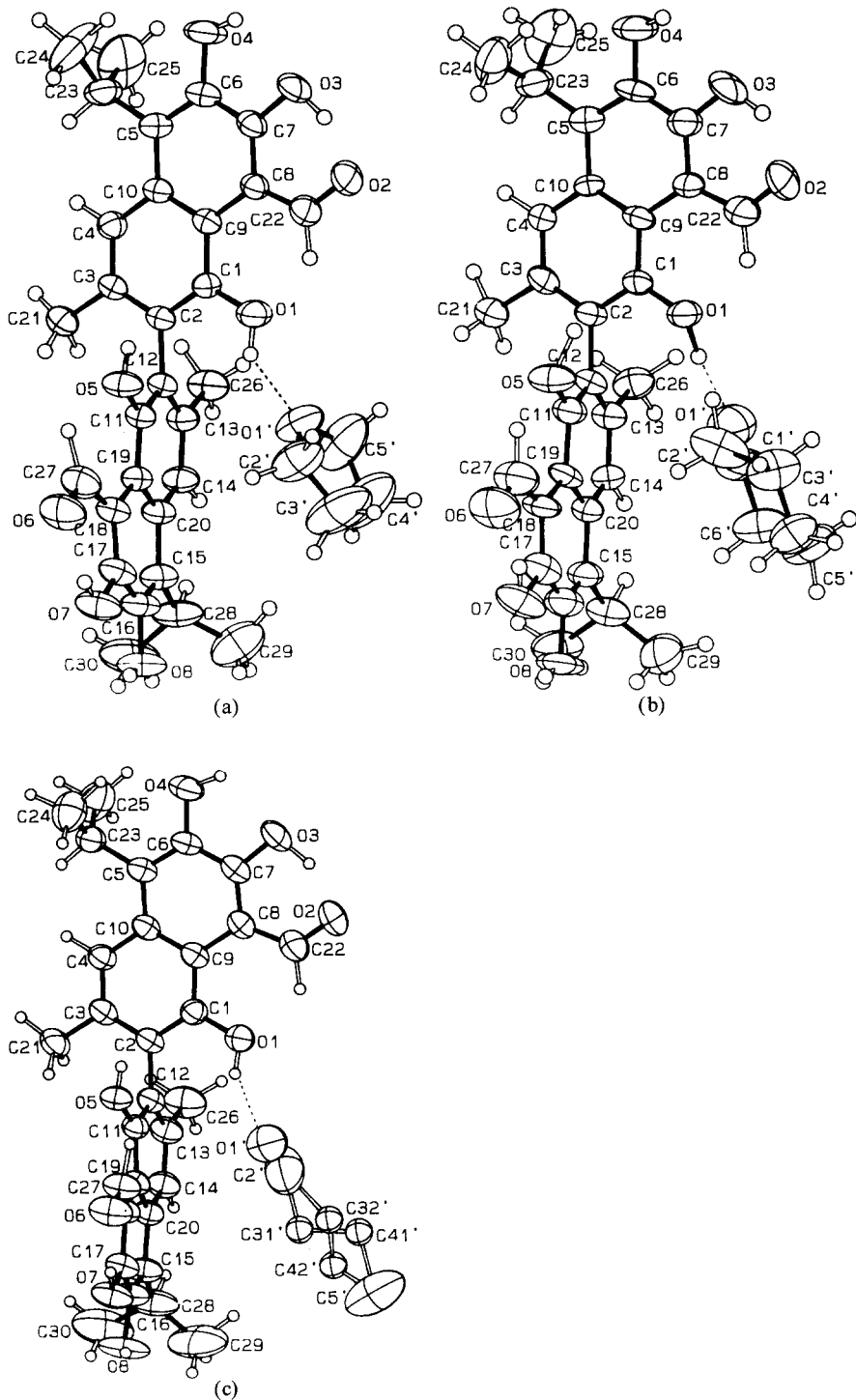


Fig. 1. Thermal ellipsoid representation (ORTEP [17]) and labelling scheme of gossypol and guest molecules: (a) GPTHF, (b) GPCHN, (c) GPBTA.

Table III. Intramolecular hydrogen bonds in acetone-type channel inclusion complexes of gossypol

	O(3)—H···O(2)	O(4)—H···O(3) three-centre type	O(7)—H···O(6)	O(8)—H···O(7) three-centre type	
GPTHF	O···O(Å)	2.445(5)	2.626(4)	2.462(5)	2.600(4)
	O—H(Å)	0.97(5)	0.85(5)	0.91(6)	0.87(4)
	O···H(Å)	1.51(5)	2.14(5)	1.67(6)	2.11(4)
	<O—H···O(°)	156(5)	116(4)	143(5)	116(4)
GPCHN	O···O(Å)	2.436(7)	2.621(7)	2.460(9)	2.595(8)
	O—H(Å)	1.01	0.98	1.00	1.01
	O···H(Å)	1.57	2.11	1.52	2.05
	<O—H···O(°)	142	111	154	111
GPBTA	O···O(Å)	2.492(4)	2.573(4)	2.475(4)	2.617(4)
	O—H(Å)	1.07(5)	1.07(7)	1.01(5)	0.90(7)
	O···H(Å)	1.48(5)	2.05(7)	1.61(5)	2.01(7)
	<O—H···O(°)	154(3)	105(4)	141(3)	124(5)

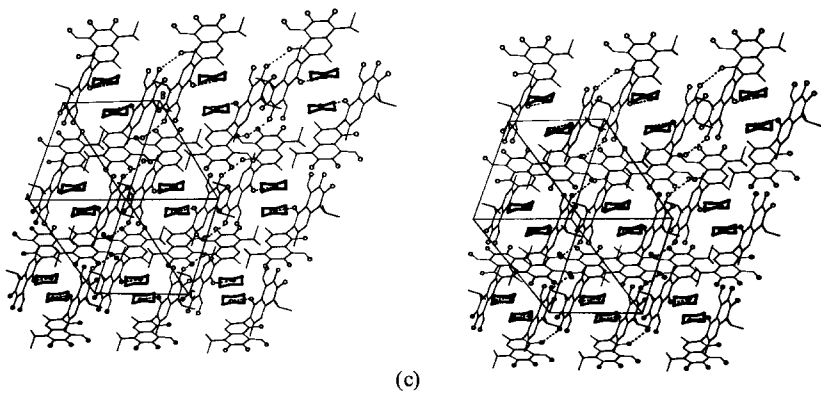
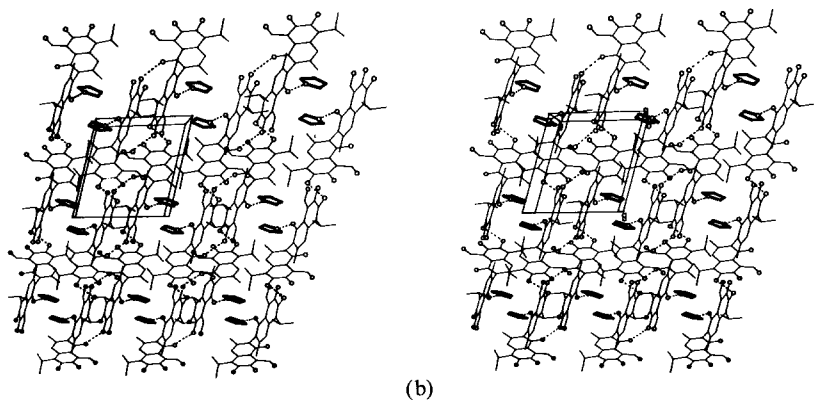
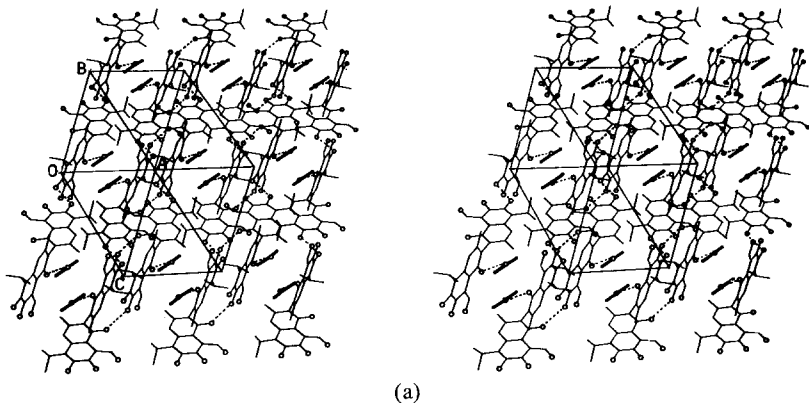
3.2. CRYSTAL STRUCTURE

The gossypol used for crystallographic studies was racemic. In the crystals of GPACT, GPTHF and GPCHN enantiomeric molecules of gossypol form centrosymmetric dimers *via* hydrogen bonds O(5)—H···O(3). These dimers are arranged in columns and joined together *via* the hydrogen bond O(8)—H···O(4) whose length is very different from that of the O(5)—H···O(3) bond and is determined by the geometry of the guest molecule. The geometry of these hydrogen bonds is given in Table IV. In the GPTHF setting of axes (see the Experimental Section above), the columns run parallel to the $[0 - 1 1]_T$ direction. The hydrophobic part of the naphthyl moiety C(11)—C(20) projects from the surface of a column and is in contact with the same fragment of the molecule at $-x, 1 - y, 2 - z$ of the neighbouring column. When the columns pack in crystals centrosymmetric channels running parallel to the c_T axis are formed (Figures 2 and 3). There are only van der Waals interactions between neighbouring columns. Those contacts differ, however, from the van der Waals contacts in the other inclusion complexes of gossypol because they are no longer purely hydrophobic or hydrophilic in nature. Along the channels polar groups of the C(1)—C(10) moiety are in contact with the hydrophobic part of the C(1)—C(10) moiety of the nearest column. For example, the hydroxyl group O(1) which is a donor of the hydrogen bond to a guest molecule is close to the methyl group C(24) and C(26), and O(2) is close to the methyl group C(21).

The channels formed by the host structure can be filled with guest molecules which have one functional group able to form hydrogen bonds. The guest molecules are always hydrogen bonded to the hydroxyl O(1)—H and occupy the space 'above' the naphthyl ring C(11)—C(20). The hydroxyl groups O(1)—H, surrounded by nonpolar groups, lie opposite each other, about 5.2 Å apart, on a surface of the

Table IV. Intermolecular hydrogen bonds and short oxygen-oxygen contacts(*) in acetone-type channel inclusion complexes of gossypol

H-bond	O(1)-H...O(1')	O(4)-H...O(1')	O(5)-H...O(3)	O(5)-H...O(2)	O(3)-H...O(5)	O(8)-H...O(4)	O(4)-H...O(7)
GPTHF { O...O(Å) O-H(Å) O...H(Å) <O-H...O(°)	2.643(5)		2.762(4)			3.296(4)	*2.785(4)
	0.91(6)		0.84(4)			0.87(4)	0.85(5)
	1.90(6)		2.19(4)			2.45(4)	2.77(5)
	138(5)		125(4)			164(4)	
symm. code	x, y, z		1 - x, 2 - y, 2 - z			x, 1 + y, z - 1	x, 1 + y, z - 1
GPCHN { O...O(Å) O-H(Å) O...H(Å) <O-H...O(°)	2.775(8)		2.795(7)			*3.747(7)	*2.978(8)
	1.15		1.18			1.01	0.98
	1.70		1.96			2.75	3.00
	153		124			165	
symm. code	2 - x, 1 - y, 1 - z		1 - x, 1 - y, 1 - z			x - 1, y, z - 1	x - 1, y, z - 1
GPBTA { O...O(Å) O-H(Å) O...H(Å) <O-H...O(°)	2.789(5)	3.129(5)	*2.948(5)	3.100(4)	2.948(4)	3.059(5)	2.853(5)
	0.88(4)	1.07(5)		0.81(4)	1.07(5)	0.90(7)	1.07(4)
	2.02(4)	2.39(7)	2.91(6)	2.53(4)	2.50(5)	2.44(7)	2.34(7)
	144(3)	124(4)		129(3)	104(3)	126(5)	108(4)
symm. code	1 - x, 1 - y, 1 - z	x - 1, y, z	2 - x, 1 - y, 1 - z	2 - x, 1 - y, 1 - z	2 - x, 1 - y, 1 - z	1 + x, y, 1 + z	x - 1, y, z - 1



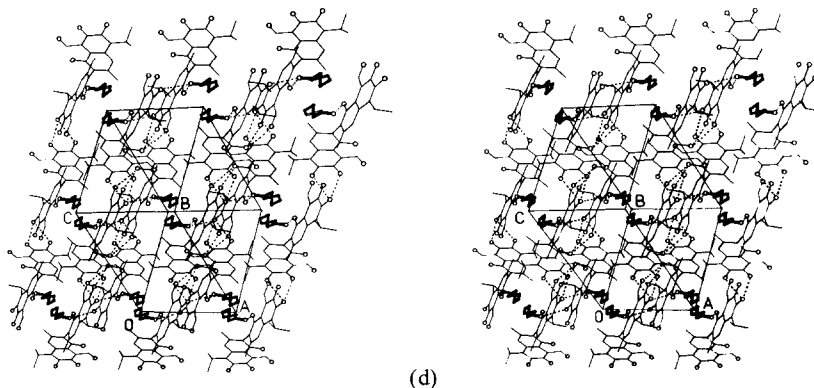


Fig. 2. Projections of the crystal structures of GPACT, GPTHF, GPCHN and GPBTA along $[0\ 0\ 1]_T$ (PLUTO [16]).

channel and cause the channel to narrow at this part. The shape and size of the guest molecule influence the degree of overlap of the naphthyl units $C(11)–C(20)$ $[x, y, z]$ and $C(11)–C(20)[x, 1 + y, z - 1]$ along the column (Figure 4b) and also, as a result, the shape of the channel.

In the case of GPACT, with the smallest guest molecule, the two nearest centrosymmetric dimers along the column show a significant overlap of their $C(11)–C(20)$ naphthyl units. The polar groups attached to those rings are able to closely approach the $O(6)–O(8)$ region of the dimer and a hydrogen bond $O(8)–H\cdots O(4)$ with a donor–acceptor distance of $2.949(6)$ Å is formed. When the size of the guest molecule is increased the space ‘above’ the naphthyl moiety is in large part occupied by the guest and therefore a contact between the $O(6)–O(8)$ and $O(3)–O(4)$ regions is hindered (Figure 4a). In GPTHF the hydrogen bond $O(8)–H\cdots O(4)$ is elongated to $3.296(4)$ Å and in GPCHN it disappears as the $O(8)\cdots O(4)$ distance is increased to $3.747(7)$ Å.

Butanal represents a special case as a guest component. It has a linear shape, the same molecular formula C_4H_8O as tetrahydrofuran and it is not as symmetrical as the remaining guests described here. The host structure has to undergo a significant rearrangement to accommodate the butanal molecule in a channel, otherwise the aliphatic chains of the guest molecules would be too close. It can be noticed from Table V that for complexes with guest molecules having an aliphatic chain joined to a polar group longer than three carbon atoms the cell parameters a_T are decreased and c_T are substantially increased. This means that, while the unit cell parameter along the channel becomes elongated, the channel becomes narrowed in the direction of the a_T axis. The rearrangement of the structure is mostly achieved by a shift of the two molecules forming a centrosymmetric dimer in the direction nearly parallel to the c_T axis. Naphthyl moieties $C(1)–C(10)$ do not overlap any longer, the hydrogen bonds $O(5)–H\cdots O(3)$ are broken and centrosymmetric dimers are formed *via* two new hydrogen bonds $O(5)–H\cdots O(2)$ and $O(3)–H\cdots O(5)$ (Figure 4). As a result the $O(4)–H$ hydroxyl group is deshielded and can be better approached by the gossypol molecule related translationally along the $[0\ -1\ 1]_T$ direction. This hydroxyl group is able to accept hydrogen bonds from hydroxyl

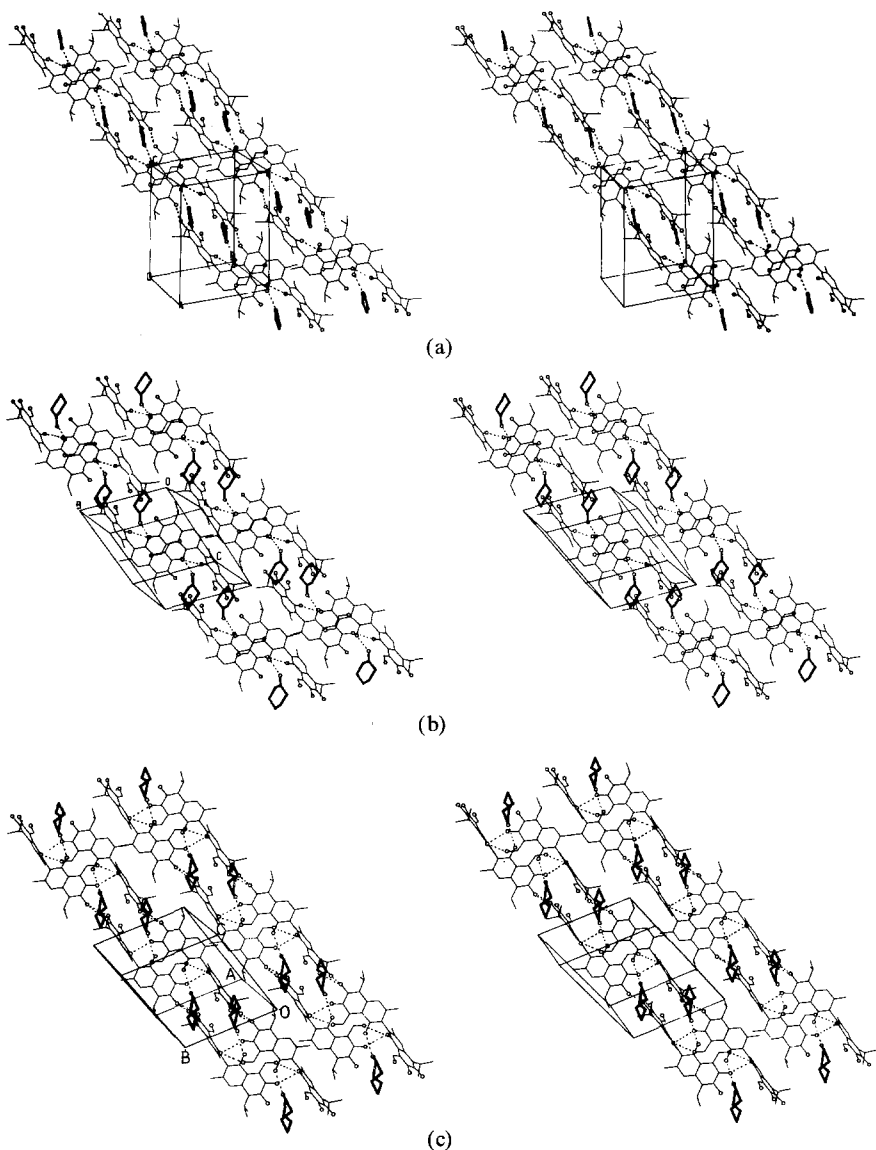


Fig. 3. Crystal packing of GPTHF, GPCHN and GPBTA projected onto the $(0\ 1\ 1)_T$ plane (PLUTO [16]).

groups O(7)—H and O(8)—H and a column of gossypol molecules parallel to the $[0\ -1\ 1]_T$ direction is formed. The hydroxyl O(4)—H also becomes a donor of a hydrogen bond to the aldehyde group of the guest molecule.

The aliphatic chain of butanal molecules accommodated in a channel of the host structure is disordered. It can adopt two different conformations in which the aldehyde carbonyl group and C(5') carbon atom occupy the same positions but differ in the positions of two methylene groups. The occupancy factors of these two positions are not equal and amount to 0.22(2) and 0.78(2), respectively.

Table V. Crystal data for acetone-type channel inclusion complexes of gossypol. Space group $P\bar{1}$, host: guest ratio is 1:1

No.	guest compound	a (Å)	b (Å)	c (Å)	$\alpha(^{\circ})$	$\beta(^{\circ})$	$\gamma(^{\circ})$	V	$d(\text{g/cm}^{-3})$
1.	acetone	10.665(2)	11.135(2)	14.379(3)	76.47(2)	108.67(1)	77.72(1)	1493	1.28
2.	butanone	10.775(2)	11.114(3)	14.421(2)	77.05(2)	108.74(1)	78.77(2)	1526	1.29
3.	cyclohexanone	10.803(4)	11.157(5)	14.692(6)	75.39(3)	104.73(3)	76.66(3)	1573	1.30
4.	1-propanol	10.841(4)	11.073(2)	14.205(4)	77.68(2)	109.87(3)	78.87(2)	1500	1.28
5.	1-butanol	11.09(2)	11.09(2)	14.51(2)	77.4(1)	110.9(1)	78.9(1)	1554	1.27
6.	2-propen-1-ol	10.861(5)	11.035(3)	14.142(7)	78.40(3)	110.49(3)	79.55(3)	1496	1.28
7.	1-methylethanol	10.585(1)	11.152(1)	14.017(2)	78.47(1)	108.80(1)	82.36(1)	1500	1.28
8.	2-methyl-1-propanol	10.780(3)	11.204(5)	14.399(3)	76.81(3)	107.53(2)	78.39(3)	1545	1.27
9.	3-methyl-1-butanol	10.048(4)	11.677(5)	15.426(9)	69.92(4)	107.64(4)	85.31(3)	1585	1.27
10.	butanal	10.190(2)	11.355(1)	15.613(2)	73.04(1)	108.46(1)	81.07(1)	1530	1.28
11.	3-buten-1-al	10.258(3)	11.271(3)	15.781(5)	69.32(2)	109.99(3)	81.03(2)	1523	1.28
12.	pentanal	10.343(5)	11.643(3)	14.928(2)	71.17(3)	106.47(3)	84.60(3)	1597	1.26
13.	metacrylic acid	10.996(2)	11.065(3)	13.452(2)	81.76(2)	107.09(2)	85.70(2)	1536	1.31
14.	trichloroacetic acid	11.425(2)	11.178(2)	13.139(2)	82.93(2)	107.39(2)	84.94(2)	1575	1.44
15.	acetonitrile	10.938(1)	10.982(2)	14.162(2)	77.99(1)	112.24(1)	77.25(1)	1453	1.28
16.	tetrahydrofuran	10.788(2)	10.979(3)	13.880(2)	80.11(2)	103.87(1)	77.96(2)	1518	1.29

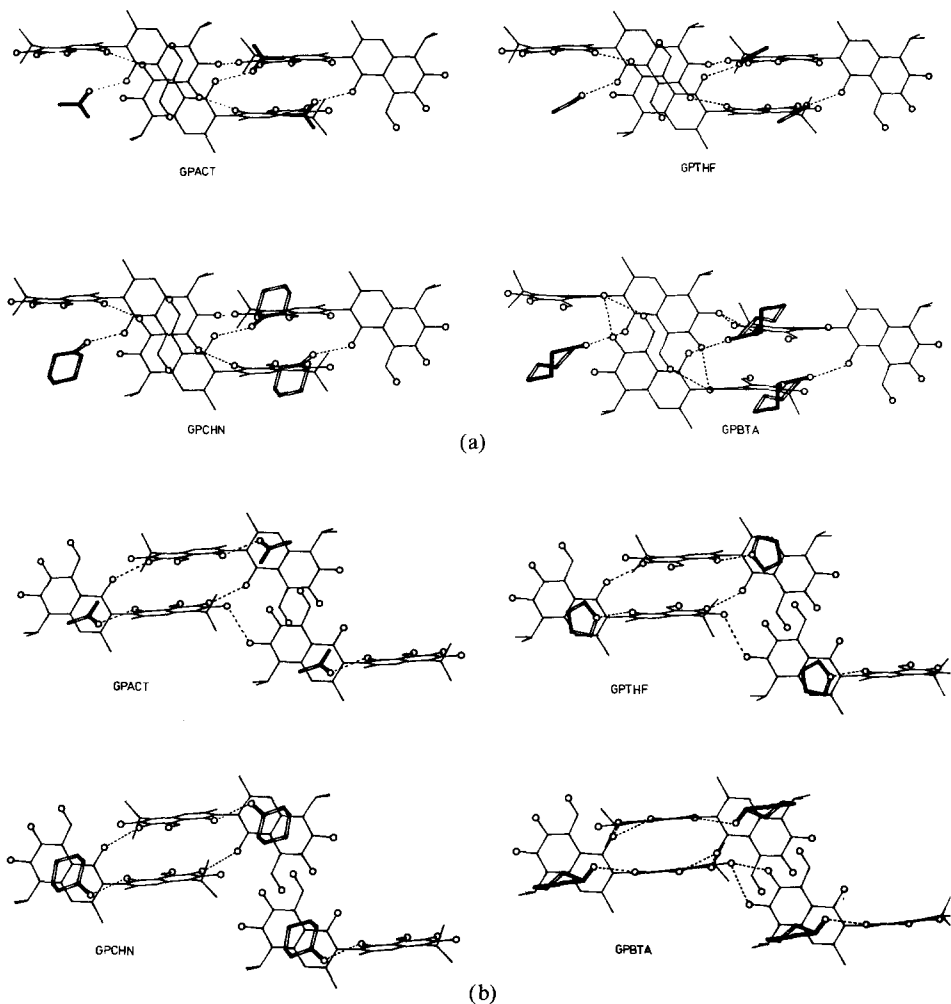


Fig. 4. Centrosymmetric gossypol dimers and the nearest molecule along the column together with the associated guest molecules: (a) view perpendicular to the C(1)—C(10) naphthyl ring; (b) view perpendicular to the C(11)—C(20) naphthyl ring.

3.3. OTHER ACETONE-TYPE CHANNEL INCLUSION COMPOUNDS

Among complexes of gossypol with organic guests for which single crystals have been obtained a large group belongs to the acetone-type inclusion compounds. The unit cell parameters of these complexes are given in Table V. This type of complex is formed by branched and non-branched alcohols, branched carboxylic acids and their haloderivatives, acyclic aldehydes and acetonitrile. Each group of guests has an upper limit in size. When the guest molecule exceeds this limit an inclusion compound of the other type is formed. An X-ray structure analysis of some of these complexes is now in progress.

4. Final Remarks

In acetone-type inclusion compounds of gossypol the host structure can change significantly in order to include a guest of a proper size, shape and chemical nature. When one guest molecule is replaced by another the hydrogen bonds in the associates may become weaker, disappear or a new hydrogen bond can be formed. These effects occur both for host–host as well as for host–guest interactions. There are eight functional groups in gossypol that are capable of participating in intermolecular hydrogen bonds. Depending on the guest molecule, different functional groups are involved in hydrogen bonding. The highest number of hydrogen bonds is formed in GPBTA where only the carbonyl oxygen O(6) is not involved in intermolecular hydrogen bond interactions. However, these bonds are weak when compared to those in the structures where a lower number of hydrogen bonds is observed. In acetone-type inclusion complexes guest molecules may hinder some polar groups from participating in hydrogen bonding but they can also activate the other groups for hydrogen bond formation.

Acknowledgements

The authors wish to thank Professor Z. Kosturkiewicz and Dr. T. F. Aripov for helpful discussions and for interest in their work. M. G. thanks MEN project RP.II.13.2.13 for financial support.

References

1. B. T. Ibragimov, S. A. Talipov, G. B. Nazarov, T. F. Aripov and A. I. Ismailov: *Khimiya prir. soed.*, **663** (1984); *Chem. Abstr.* **102**, 42891w (1985).
2. B. T. Ibragimov, S. A. Talipov, B. N. Dadabaev, G. B. Nazarov and T. F. Aripov: *Khimiya prir. soed.*, 675 (1988).
3. B. T. Ibragimov, S. A. Talipov, T. F. Aripov and A. S. Sadykov: *J. Incl. Phenom.* **8**, 323 (1990).
4. S. A. Talipov, B. T. Ibragimov, G. N. Tishchenko and T. F. Aripov: *Kristallografiya* **34**, 327 (1989).
5. P. Main, S. J. Fiske, S. E. Hull, L. Lessinger, G. Germain, J.-P. Declercq and M. M. Woofson: *MULTAN-80*. A system for the Automatic Solution of Crystal Structures from X-ray Diffraction Data. Universities of York, England, and Louvain, Belgium (1980).
6. G. M. Sheldrick: *SHELX-76*. Program for crystal structure determination. University of Cambridge, England (1976).
7. R. Adams, R. C. Morris, T. A. Geissman, D. J. Butterbaugh and E. C. Kirkpatrick: *J. Am. Chem. Soc.* **60**, 2193 (1938).
8. F. G. Kamaev, N. I. Baram, A. I. Ismailov, V. B. Leontyev and A. S. Sadykov: *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1003 (1979); *Chem. Abstr.* **91**, 55761h, (1979).
9. J. Reyes, S. D. Wyrick, L. Borriero and D. J. Benas: *Biochem. Biophys Acta* **863**, 101 (1986).
10. X. Changfu, H. Cunheng, B. Guanghong and M. Shantian: *Scientia Sinica* **B25**, 1194 (1982).
11. S. A. Talipov, B. T. Ibragimov, G. B. Nazarov, T. F. Aripov and A. S. Sadykov: *Khimiya prir. soed.*, 835 (1985); *Chem. Abstr.* 104, 139743d (1986).
12. B. T. Ibragimov, S. A. Talipov, G. B. Nazarov, B. N. Dadabaev and A. S. Sadykov: *Khimiya prir. soed.*, 837 (1985); *Chem. Abstr.* **104**, 159926u (1986).
13. S. A. Talipov, B. T. Ibragimov, B. N. Dadabaev, T. F. Aripov and A. S. Sadykov: *Khimiya prir. soed.*, 112 (1986); *Chem. Abstr.* **105**, 226156d (1986).

14. B. T. Ibragimov, S. A. Talipov, G. B. Nazarov, R. G. Mardanov, T. F. Aripov, A. I. Ismailov and A. S. Sadykov: *Khimiya prir. soed.*, 113 (1986); *Chem. Abstr.* **105**, 227069q (1986).
15. S. A. Talipov, B. T. Ibragimov, G. N. Tishchenko, T. F. Aripov, G. B. Nazarov, B. V. Strokopytov and K. M. Polyakov: *Kristallografiya* **33**, 384 (1988).
16. W. D. S. Motherwell and W. Clegg: *PLUTO*. Program for drawing crystal and molecular structures. University of Cambridge, England.
17. C. K. Johnson: *ORTEP*. Report ORNL-5138. Oak-Ridge National Laboratory, Tennessee (1976).