Polymorphism of Inclusion Complexes and Unsolvated Hosts. I. Trimorphism of the Host–Guest Complex of Gossypol with Dichloromethane. The Structure of the β-Phase

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Abstract. The formation of host–guest complexes of gossypol at different temperatures has been investigated for the same pressure and concentration. Gossypol forms three different clathrates with dichloromethane within the temperature interval of 22–36 °C. Single crystals of these three modifications (phases) were obtained and their crystallographic parameters measured. The structure of the α-phase has been determined previously and the γ-phase is isostructural to the inclusion complex of gossypol with benzene, while the structure of the β-phase has been solved during the present research. Crystals of $C_{30}H_{30}O_8 \cdot CH_2Cl_2$ are triclinic, space group $P\bar{1}$, $a = 8.604(1)$, $b = 11.858(2)$, $c = 14.405(2)$ (Å), $\alpha = 84.60(1)$, $\beta = 89.14(1)$, $\gamma = 89.73(1)°$, $V = 1463(1)$ Å^3, $Z = 2$, $R = 0.089$ for 2419 observed reflections.

Under ambient conditions gossypol forms unstable tubulates of the α-phase; the γ-phase is a stable cage-type clathrate (cryptate) and the host–guest complex of the β-phase is a clathrate of intermediate tubulato-cryptate type.

Key words. Crystal structure, X-ray crystallography, H-bond, gossypol, α- and β-phase of the host-guest complexes.

Supplementary data relevant to this article have been deposited with the British Library Publication No. SUP 82210 (16 pages).

1. Introduction

Our investigations of clathrate formation by some well known host compounds have revealed that a given host may form different inclusion complexes with the same guest depending on the crystallization conditions, i.e. by varying temperature, concentration and pressure it is possible to obtain different clathrates. This dependence is well known from the theoretical point of view, but has not been investigated extensively experimentally – hitherto there has been little or no systematic structural consideration. For this reason we started a systematic X-ray crystallographic research of the inclusion compounds formed by versatile hosts such as gossypol [1], its derivatives [2], 1,1-dinaphthyl-2,2-dicarboxylic acid [3] etc. under different thermodynamic conditions in order to establish what structural correlations exist

between the clathrates formed. For simplicity we have investigated the dependence of the clathrate formation on one parameter while the two others are kept constant. Namely, we have considered the dependence of the host–guest formation on the temperature when the pressure and concentration assumed fixed values.

Polymorphic modifications of a certain host–guest pair should have different crystal structures but the same host–guest ratio. We will consider as polymorphs even complexes which are characterized by different host–guest ratios, although we of course well understand that this is not strictly correct. In order to identify the polymorphs we use Greek letters: α is used for the lowest temperature phase (commonly this is the modification obtained under ambient conditions) and subsequent letters designate phases obtained at gradually increasing temperatures. The present article is devoted to the investigation of the polymorphism of the clathrates formed between gossypol (**1**) and dichloromethane and the structure of the β-phase.
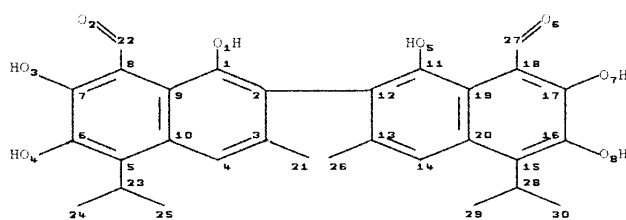
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2. Experimental

In order to obtain single crystals of the α-, β- and γ-phases by evaporation of the solvent from gossypol solutions in dichloromethane (15 mg/mL), samples were placed into thermostats at 22–24°, 28–30° and 34–36°C, respectively.

All measurements were carried out with a Syntex P2$_1$ diffractometer. Lattice parameters were determined by a least-squares fitting of the setting angles of 15 reflections within the 2θ range 25–30°. Data were collected by the $\theta/2\theta$ scan method on CuK_α radiation. Two standard reflections monitored every 100 intensity measurements during the data collection varied up to 3%. Data were corrected for Lorentz and polarization effects but not for absorption. Out of 4632 measured reflections 2419 had $I > 2\sigma(I)$ and were used for further calculations.

The structure was solved by direct methods using the program SHELXS-86 [4]. All atoms of the structure were located from the 'best' E map. The structure was refined first with isotropic and then with anisotropic temperature factors by least-squares methods using the program SHELXL93 [5].

The hydrogen atoms were placed in calculated positions. Final values of R and wR were 0.089, 0.085 respectively. In the final δF map, calculated after the last cycle of refinement, the maximum and minimum peaks were 0.33 and -0.45 e Å^{-3} respectively.

Figure 1. Morphotropic and thermotropic transitions for gossypol clathrates with chloroderivatives of methane.

Final atomic coordinates are listed in Table I. Hydrogen atom parameters, anisotropic thermal parameters and structure factors are in the Supplementary Data.

3. Discussion

Prism-shaped crystals of the α-phase belonging to the space group $C2/c$ and having a $1:1$ host : guest ratio were obtained from concentrated solutions of gossypol in dichloromethane under ambient conditions. The crystals are unstable and desolvate quickly when removed from the mother liquor. After loss of the guest molecules from this tubulate the channels do not collapse and single crystals with fairly wide and empty channels are conserved without destruction. The structure of this organic zeolite has been described earlier [6]. Crystal data of the three modifications of gossypol clathrate with dichloromethane are given in Table II.

When the temperature of crystallization is 28–30° a stable host–guest complex of the β-phase is formed. A stable γ-phase of the gossypol–dichloromethane inclusion complex is formed at 34–36 °C. In other words, after each increase of temperature of 6 °C a specific thermotropic phase transition occurs and a new modification of the host–guest complex is formed (Figure 1).

Clathrates formed at temperatures different from ambient are not new – they are isostructural with known clathrates. The morphotropic transitions in a range of gossypol complexes with the chloroderivatives of methane have been discussed [6]. A host–guest complex isostructural with the β-phase is obtained with CCl_4 [7]. During morphotropic transitions an intercalate type inclusion complex that is not observed among the clathrate modifications obtained by thermotropic tran-

Table I. Atomic coordinates ($\times 10^{-4}$) and isotropic temperature factors ($\text{Å}^2 \times 10^{-3}$) of the β-phase.

Atom	x/a	y/b	z/c	$U_{\text{eq}*}^{\text{iso}}$
C(1)	−2194(9)	−1670(7)	3347(5)	41(3)
C(2)	−1870(9)	−2285(7)	2590(6)	42(3)
C(3)	−570(11)	−2988(8)	2588(6)	49(3)
C(4)	396(9)	−3049(7)	3344(5)	45(3)
C(5)	1121(10)	−2587(8)	4921(6)	54(4)
C(6)	772(11)	−1998(9)	5663(6)	60(4)
C(7)	−577(12)	−1321(8)	5687(6)	55(4)
C(8)	−1603(10)	−1156(7)	4955(6)	49(3)
C(9)	−1234(9)	−1766(7)	4144(5)	39(3)
C(10)	74(10)	−2460(7)	4136(5)	44(3)
C(11)	−2690(9)	−1506(7)	1006(5)	42(3)
C(12)	−3005(10)	−2233(8)	1796(5)	47(3)
C(13)	−4319(10)	−2914(8)	1824(6)	49(3)
C(14)	−5289(10)	−2820(8)	1081(6)	51(3)
C(15)	−6051(10)	−2071(8)	−527(6)	49(3)
C(16)	−5713(11)	−1350(8)	−1289(6)	54(4)
C(17)	−4411(10)	−649(8)	−1340(5)	48(3)
C(18)	−3349(9)	−660(7)	−626(5)	40(3)
C(19)	−3653(9)	−1402(7)	213(5)	37(3)
C(20)	−5016(10)	−2099(7)	261(5)	44(3)
C(21)	−214(12)	−3690(10)	1803(7)	77(4)
C(22)	−2905(12)	−462(9)	5099(7)	72(4)
C(23)	2502(12)	−3358(10)	4962(7)	75(4)
C(24)	2320(18)	−4418(13)	5624(10)	133(7)
C(25)	4022(14)	−2827(13)	5152(10)	118(7)
C(26)	−4688(12)	−3717(9)	2667(6)	75(4)
C(27)	−2010(10)	31(9)	−817(6)	61(4)
C(28)	−7462(11)	−2858(10)	−500(7)	71(4)
C(29)	−7182(18)	−3795(13)	−1057(14)	174(9)
C(30)	−8972(13)	−2284(13)	−767(9)	117(6)
O(1)	−3449(6)	−978(5)	3330(4)	58(2)
O(2)	−3187(9)	−6(7)	5824(5)	94(3)
O(3)	−759(8)	−829(6)	6485(4)	77(3)
O(4)	1640(8)	−2057(7)	6449(4)	98(4)
O(5)	−1392(6)	−837(5)	964(4)	56(2)
O(6)	−1754(7)	652(6)	−1544(4)	71(3)
O(7)	−4232(7)	27(6)	−2140(4)	64(2)
O(8)	−6637(8)	−1335(6)	−2063(4)	74(3)
C(31)	−2860(30)	6868(13)	−2469(17)	302(15)
C1(1)	−2727(5)	6117(4)	−1330(4)	164(3)
C1(2)	−2317(7)	6163(4)	−3343(4)	186(3)

$^*\ U = \frac{1}{3} \sum \sum U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j.$

Table II. Crystal data for the α-, β- and γ-phases.

Parameters/Phases	α	β	γ
a (Å)	21.320(1)	8.604(1)	11.241(3)
b (Å)	19.129(2)	11.858(2)	14.986(4)
c (Å)	15.7135(2)	14.405(2)	17.380(4)
α (°)	90	84.60(1)	98.84(2)
β (°)	113.05(2)	89.14(1)	99.86(2)
γ (°)	90	89.73(1)	98.91(2)
V (Å^3)	5916	1463	2800
Sp. gr.	C2/c	$P\bar{1}$	$P\bar{1}$
Host : guest	1 : 1	1 : 1	2 : 1
Z	8	4	4
D_x (g/cm^3)	1.35	1.29	1.32

Table III. Intermolecular hydrogen bonds in the β-phase complex.

Bond	Distance (Å)			Angle
	O$\cdots$O	O—H	H$\cdots$O	O—H$\cdots$O (grad.)
O(5)—H$\cdots$O(3)[i]	2.811(8)	0.72(7)	2.16(7)	151(7)
O(1)—H$\cdots$O(2)[ii]	2.860(8)	0.84(7)	2.33(7)	122(6)
O(4)—H$\cdots$O(5)[i]	3.150(8)	0.66(6)	2.50(7)	168(8)
O(8)—H$\cdots$O(4)[iii]	2.837(9)	0.97(7)	2.34(7)	111(5)

Symm. code (i) $-x - 1, -y, -z$; (ii) $-x, -y, -z$; (iii) $x + 1; y; z + 1$.

sitions (at least within the tested temperature interval) is formed [8] (Figure 1). The clathrate of the γ-phase is isostructural with the gossypol–benzene inclusion complex [9] in which guest molecules are placed in closed cages (cryptate-type inclusion compound). These cages are formed inside the crystal when columns formed from hydrogen bonded gossypol molecules are packed.

Clathrates of the β-phase are isostructural to the complexes of gossypol with CCl$_4$ and m-xylene [7]. Since the structures of these complexes have been discussed
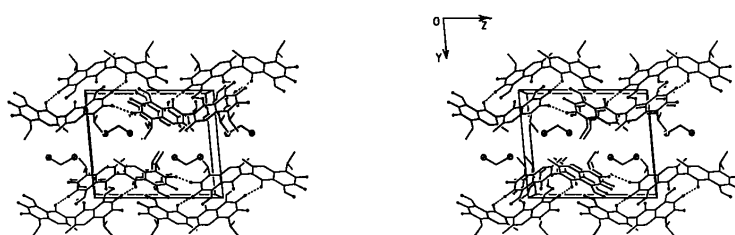

Figure 2. Stereoview of the β-phase complex of gossypol with dichloromethane.

earlier in detail, we confine ourselves to a brief consideration here. Host molecules are linked by intermolecular hydrogen bonds to bimolecular layers (Table III). All polar groups of the gossypol molecules are packed in the interior of the bilayer while non-polar groups are directed outwards. The surface of the bilayers is not smooth – it contains values and peaks (Figure 2). In the crystal structure hydrophobic cages in which guest molecules are enclathrated are formed between valleys of the two neighboring bilayers. These cages are joined through narrow channels. Though guest molecules are held in the channels under ambient conditions, near to the melting point of the complex, for example, in the gossypol-CCl_4 clathrate, the enclosed guest component escapes through these channels. Therefore the β-phase of the gossypol–CH_2Cl_2 complex is related to the tubulato-cryptate intermediate type.

Thus clathrates of gossypol with dichloromethane are characterized by trimorphism. On raising of the temperature the initially formed tubulate gives a tubulate-cryptate and finally a cryptate type clathrate.

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