

Polymorphism of Inclusion Complexes and Unsolvated Hosts. II. Structure of the β -Dimorph of the Host–Guest Complex of Dianilinegossypol with Ethylacetate

K. M. BEKETOV, B. T. IBRAGIMOV, S. A. TALIPOV, K. MAKHKAMOV and T. F. ARIPOV

Institute of Bioorganic Chemistry, Kh. Abdullaev Str. 83, Tashkent 700143, Uzbekistan.

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Abstract. Depending on crystallization conditions, dianilinegossypol and ethylacetate form low (ambient temperature, α -phase) and high temperature ($t = 35^\circ\text{C}$, β -phase) clathrate modifications. The structure of the α -phase has been discussed earlier [1]. Crystals of the 1:1 β -phase complex, $\text{C}_{42}\text{H}_{40}\text{O}_6\text{N}_2 \cdot \text{C}_4\text{H}_8\text{O}_2$, are monoclinic, space group $P2_1/c$, $a = 11.362(6)$, $b = 19.479(9)$, $c = 19.085(9)\text{\AA}$, $\beta = 103.21(4)^\circ$, $V = 4112(3)\text{\AA}^3$, $Z = 4$, $R = 0.084$ for 3210 observed reflections.

In these complexes centrosymmetric dimers of dianilinegossypol molecules formed via $\text{O}(5)\text{---H} \cdots \text{O}(3)$ hydrogen bonds are associated into columns by a weak $\text{O}(8)\text{---H} \cdots \text{O}(7)$ H-bond. A difference in the structure of these two phases is in the packing mode of the columns. The angle formed by intersecting host columns is about 126° for the α -phase and 104° for the β -modification. Guest molecules are hydrogen bonded to the host molecules via an $\text{O}(1)\text{---H} \cdots \text{O}(10)$ bond and are accommodated in channels in α -phase complex and in cavities in β -phase complex.

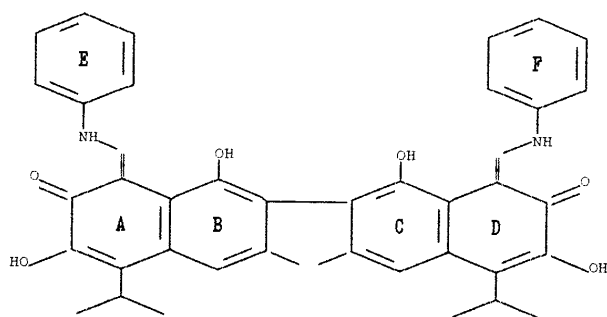
Key words: β -Dimorph, crystal structure, dianilinegossypol ethylacetate 1:1 clathrate, packing motifs.

Supplementary data relevant to this article have been deposited with the British Library Publication No. SUP 82211 (14 pages).

1. Introduction

Gossypol, a biologically active compound of cotton seed kernels [2–5], is a versatile host [6]. Schiff's base-type gossypol derivatives, prepared by simple condensation of gossypol with amines, also easily form inclusion compounds. For example, dianilinegossypol (Scheme) gives clathrates with all types of organic substances, except alcohols and carboxylic acids. Single crystals of 30 dianilinegossypol host–guest complexes have been prepared and their crystallographic parameters have been determined [7].

Most of the dianilinegossypol clathrates are unstable under ambient conditions. Dianilinegossypol host–guest complexation is dependent on crystallization parameters such as temperature, concentration and pressure. For instance, at room



Scheme

temperature a channel-type clathrate is formed from the solution of dianilinegossypol in ethylacetate (α -phase or dimorph) while a cage-type inclusion compound (β -phase or dimorph) is obtained by increasing the temperature up to 35° under constant concentration and pressure. This paper is devoted to the β -phase structure determination and comparative discussion of the structures of the α - and β -phase complexes.

2. Experimental

Single crystals of the β -phase complex of dianilinegossypol with ethylacetate were obtained by adding 0.05 mL aniline to a solution of 100 mg gossypol in 4 mL ethylacetate at 35°C . A prism shaped brown crystal of dimensions $0.3 \times 0.4 \times 0.9$ mm was used for measurements on a Syntex P2₁ diffractometer. The unit cell parameters were determined by a least-squares fitting of the setting angles of 15 reflections (2θ in the range $25\text{--}30^\circ$). Crystal data for the β -dimorph as well as details concerning data collection and structure solution are given in Table I.

Intensities of the reflections were measured with graphite monochromatized $\text{CuK}\alpha$ radiation up to $2\theta_{\text{max}} = 116^\circ$. No significant intensity variation was observed for two standard reflections monitored after each group of 100 reflections. Data were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods with the program SHELX-86 [8]. Dianilinegossypol and guest molecules were located on the 'best' E map. The structure was refined first with isotropic and then with anisotropic thermal parameters by a least-squares methods using the program SHELXL93 [9]. Hydrogen atom positions were determined from the ΔF maps and their positional and isotropic thermal parameters were included in the refinement. In the final ΔF map, calculated after the last cycle of refinement, the maximum and minimum peaks were 0.86 and $-0.53 \text{ e } \text{\AA}^{-3}$.

Table I Crystal data for the β -phase complex of dianilinegossypol with ethylacetate

Formula	C ₄₂ H ₄₀ O ₆ N ₂ ·C ₄ H ₈ O ₂
Crystal system	Monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>
<i>a</i> (Å)	11.362(6)
<i>b</i> (Å)	19.479(9)
<i>c</i> (Å)	19.085(9)
β (°)	103.21(4)
<i>V</i> (Å ³)	4112
<i>Z</i>	4
<i>D_x</i> (g/cm ³)	1.22
Radiation	CuK α
Absorption coefficient (mm ⁻¹)	0.68
Unique data collection	5012
No. of reflections with $I > 2\sigma(I)$	3210
Weighting scheme	1/[$\sigma^2 + 0.0005F^2$]
Final <i>R</i> indices [$I > 2\sigma(I)$]	<i>R</i> = 0.085, <i>R_w</i> = 0.085
<i>R</i> (all data)	<i>R</i> = 0.128
Goodness-of-fit	1.02

3. Results and Discussion

Atom coordinates and equivalent thermal parameters are given in Table II. Hydrogen atom parameters, anisotropic thermal parameters and structure factors are in the Supplementary Material.

3.1. MOLECULAR STRUCTURE

In contrast to gossypol, which only exists in the aldehyde tautomeric form of the molecule in the crystalline state [10–12], its dianiline derivative is in the quinoid form [1, 13], as in the present clathrate modification. The isopropyl groups have identical orientations: the hydrogen atoms at C(23) and C(28) are oriented towards C(4) and C(14), respectively (Figure 1). The naphthyl moieties of the dianilinegossypol molecule are planar and the dihedral angle between their least-squares planes is $\hat{A}\hat{B}\hat{C}\hat{D} = 103^\circ$. Because of the rotational freedom of the molecule around the N(1)—C(31) and N(2)—C(37) bonds the dihedral angles between the aniline rings and the corresponding naphthyl moieties are easily varied from one structure to another. In β -phase complexes the *E* and *F* rings are nearly parallel to their naphthyl groups – the corresponding dihedral angles are equal to $\hat{A}\hat{B}\hat{E} = 8.4^\circ$ and $\hat{C}\hat{D}\hat{F} = 8.7^\circ$.

There are four intramolecular hydrogen bonds in the dianilinegossypol molecule (Table III). The H-atoms of the N(1)—H and N(2)—H groups are involved in strong intramolecular hydrogen bonds which are part of a six-membered conjugated

Table II Atom coordinates ($\times 10^4$) and temperature factors ($\text{\AA}^2 \times 10^3$)

Atom	x/a	y/b	Z/c	$U_{\text{eq}}^{\text{iso} *}$
C(1)	8045(5)	4520(3)	565(3)	45(2)
C(2)	8007(5)	4091(3)	1133(3)	47(2)
C(3)	8761(6)	4222(3)	1818(3)	55(2)
C(4)	9438(6)	4814(3)	1902(3)	51(2)
C(5)	10147(6)	5921(3)	1486(3)	50(2)
C(6)	10156(6)	6336(3)	921(4)	55(2)
C(7)	9563(6)	6173(3)	194(4)	55(2)
C(8)	8830(5)	5584(3)	36(3)	44(2)
C(9)	8776(5)	5117(3)	638(3)	42(2)
C(10)	9452(5)	5279(3)	1336(3)	45(2)
O(1)	7346(5)	4374(2)	-102(2)	71(2)
O(3)	9690(4)	6617(2)	-291(3)	78(2)
O(4)	10734(5)	6958(3)	1009(3)	90(2)
N(1)	8235(5)	5903(3)	-1208(3)	59(2)
C(31)	7611(6)	5845(4)	-1937(4)	62(3)
C(32)	6989(8)	5263(4)	-2212(4)	82(3)
C(33)	6387(8)	5247(7)	-2923(5)	105(4)
C(34)	6399(10)	5803(8)	-3365(5)	112(5)
C(35)	7025(11)	6369(7)	-3093(5)	112(5)
C(36)	7653(8)	6398(5)	-2374(4)	85(4)
C(11)	7375(5)	2870(3)	823(3)	41(2)
C(12)	7100(6)	3514(3)	1049(3)	48(2)
C(13)	6012(6)	3613(3)	1248(4)	63(3)
C(14)	5270(6)	3050(3)	1253(4)	63(3)
C(15)	4692(6)	1825(3)	1029(3)	52(2)
C(16)	4864(6)	1238(3)	693(3)	52(2)
C(17)	5874(5)	1130(3)	364(3)	51(2)
C(18)	6778(5)	1645(3)	430(3)	42(2)
C(19)	6579(5)	2300(3)	759(3)	42(2)
C(20)	5527(5)	2395(3)	1024(3)	47(2)
C(21)	8796(9)	3749(4)	2439(4)	89(3)
C(22)	8203(5)	5471(3)	-675(3)	52(2)
C(23)	10708(7)	6150(3)	2259(4)	69(3)
C(24)	11971(8)	6483(4)	2367(4)	91(3)
C(25)	9862(10)	6607(5)	2521(5)	106(4)
C(26)	5647(8)	4310(4)	1470(6)	106(4)
C(27)	7771(5)	1504(3)	134(3)	45(2)
C(28)	3698(7)	1882(4)	1455(4)	72(3)
C(29)	3766(9)	1320(5)	2014(5)	102(4)
C(30)	2457(8)	1919(5)	956(6)	106(4)
O(5)	8461(4)	2757(2)	648(2)	59(2)
O(7)	5912(4)	556(2)	49(3)	69(2)
O(8)	4078(4)	696(2)	637(3)	69(2)

Table II Continued

Atom	x/a	y/b	Z/c	$U_{\text{eq}}^{\text{iso} *}$
N(5)	7908(4)	934(2)	-211(3)	49(2)
C(37)	8884(5)	758(3)	-509(3)	47(2)
C(38)	8837(6)	121(3)	-843(3)	57(3)
C(39)	9797(8)	-107(4)	-1103(4)	73(3)
C(40)	10803(7)	293(5)	-1056(4)	72(3)
C(41)	10853(7)	928(4)	-734(4)	72(3)
C(42)	9895(6)	1161(3)	-461(4)	60(3)
C(43)	3256(13)	3283(9)	-733(9)	183(9)
C(44)	4447(11)	3296(6)	-783(7)	117(5)
C(45)	6039(10)	2803(6)	-1159(7)	141(6)
C(46)	6182(9)	2166(6)	-1611(6)	409(4)
C(9)	4778(5)	2765(3)	-1142(3)	96(2)
C(10)	5132(11)	3755(6)	-601(7)	200(6)

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

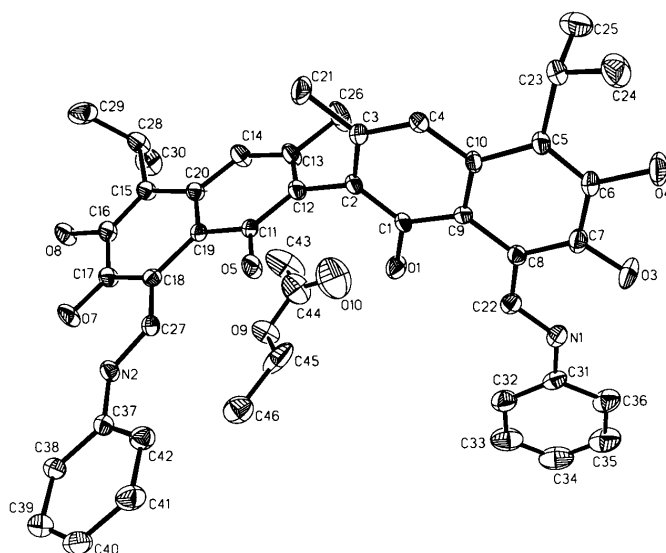


Figure 1. ORTEP drawing and atom labelling scheme for the host and guest molecules in the β -phase complex of dianilinegossypol with ethylacetate.

ring system. Much weaker hydrogen bonds O(4)—H \cdots O(3) and O(8)—H \cdots O(7) close five membered rings. Bond lengths and bond angles of the host are in good agreement with those observed in [1, 13].

Table III. Intra- and intermolecular H-bonds in the β -phase complex

Bond	O...O (Å)	O—H (Å)	H...O (Å)	O—H...O (°)
(a) Intramolecular H-bonds				
N(1)—H...O(3)	2.53	0.90	1.80	136
O(4)—H...O(3)	2.58	0.76	1.93	142
N(2)—H...O(7)	2.54	0.77	1.86	147
O(8)—H...O(7)	2.60	0.89	2.05	118
(b) Intermolecular H-bonds				
O(5)—H...O(3) ⁱ	2.65	0.81	2.10	125
O(8)—H...O(7) ⁱⁱ	2.76	1.00	1.93	138
O(1)—H...O(10)	2.76	0.85	2.02	144

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

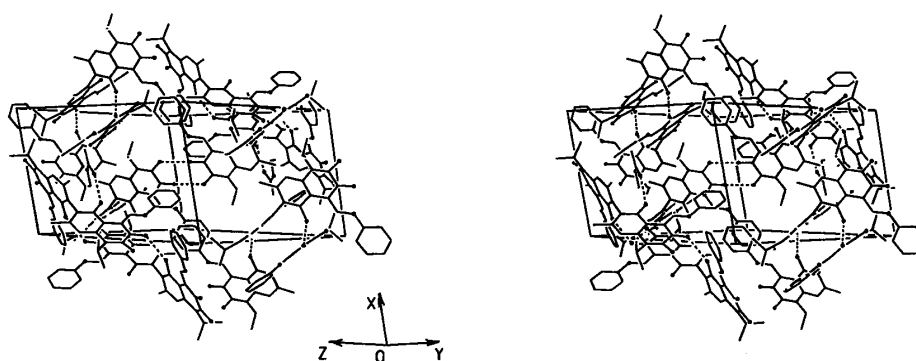


Figure 2. Packing of the crystal structure of the β -phase complex of dianilinegossypol with ethylacetate (stereoscopic view).

3.2. CRYSTAL STRUCTURE

Dianilinegossypol molecules are incorporated in centrosymmetric dimers typical of many gossypol crystal structures by means of the two symmetrically related H-bonds O(5)—H...O(3). Further, these dimers are associated into columns by O(8)—H...O(7) H-bonds which are also centrosymmetric (Table III). There are two series of such columns in the crystal structure. The columns of the first series are parallel to the $[110]$ direction while the columns of the other series lie along $[\bar{1}10]$. The angle between the columns of different series is about 104° . As a consequence of the packing of such columns closed cages are formed in the crystal structure. The ethylacetate molecules located inside these cages are hydrogen bonded to the O(1)—H groups of host molecules (Figure 2).

The cages are formed by five host molecules relating to four columns. The **CD**-half of the dianilinegossypol molecule $\mathbf{I}(\mathbf{x}, \mathbf{y}, \mathbf{z})$ serves as the 'floor' of the cage. The 'ceiling' or the cage consists of the same fragment of the second column

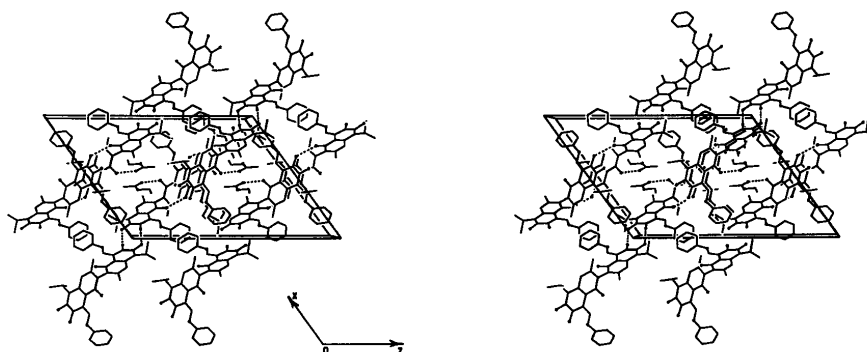


Figure 3. Packing of the crystal structure of the α -phase complex of dianilinegossypol with ethylacetate (stereoscopic view).

molecule $\text{II}(x, 0.5 - y, -0.5 + z)$. Two opposite walls of the cages are formed from the O(1)—H group of molecule $\text{I}(x, y, z)$; the O(4), C(24) and C(25) atom groups of molecule $\text{III}(2-x, 0.5-y, -z)$, which is a centrosymmetric pair of molecules $\text{I}(x, y, z)$ and the F ring of molecule $\text{IV}(-1-x, y, z)$ relating to the third column. Later columns are parallel to the first columns. Two other opposite walls of the cage are built from the AB-half of the molecule $\text{V}(1-x, 1-y, -z)$ of the fourth host column and the C(21), C(26) atom groups of molecule II .

3.3. CONCLUDING REMARKS

The conformation of the dianilinegossypol molecules in α -phase complexes is different from those in the β -phase: dihedral angles are $\hat{A}BCD = 88^\circ$, $\hat{A}BE = 38.3^\circ$, $\hat{C}DF = 26.6^\circ$ instead of the given values in the β -phase. In α -phase complexes the same type of H-associates (columns) exists. One series of columns is parallel to the $[111]$ direction and another series is parallel to $[1\bar{1}1]$. The angle between the columns of these series is about 126° . As a result of the packing of such columns a channel type host structure is formed. Ethylacetate molecules H-bonded to the O(1)—H group of the host are located in the channels of the 1 : 1 tubulate inclusion compound (Figure 3).

As a result of raising the temperature from ambient up to 35°C , a cage type inclusion compound with the same stoichiometry is formed instead of a channel type structure. This is achieved by the definite alteration of the molecular conformation and changing of the packing mode of the columns which are the same in both phases.

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