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The Crystal Structure of the 2 : 1 Cholic Acid – Benzophenone Clathrate

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Abstract. The 2 : 1 cholic acid – benzophenone clathrate crystallizes in the space group $P2_1$ with the unit-cell parameters a = 25.498(6), b = 7.942(1), c = 28.309(6) Å, β = 101.85(2)°. There are four symmetrically independent host molecules in the unit cell: two of them with the steroidal side chain assuming *gauche* and the remaining two with the side chain in the *trans* conformation. Pairs of the host molecules adopting similar conformations alternate along the [$\bar{2}$01] direction of the bilayer. The guest molecules are accommodated in two crystallographically independent but topologically similar channels running parallel to [010]. Benzophenone molecules are disordered and included in each channel in two different conformations.

Key words: inclusion compounds, cholic acid, benzophenone, chiral conformations.

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1. Introduction

The inclusion phenomenon of steroidal bile acids has received considerable attention in recent years [1]. In particular, many cholic acid (CA) inclusion compounds have been obtained and their crystal structures determined [1–4]. This bile acid is known to aggregate in crystals *via* hydrogen bonds to form bilayer-type host assemblies. A large variety of organic guest molecules can be accommodated in the lipophilic space between the adjacent host bilayers. Since the CA molecules are able to adjust their association mode and conformation to fit different types of guests, these host assemblies show guest-dependent polymorphism [1, 3]. In the majority of CA inclusion compounds guest molecules are accommodated in chiral channels formed between the corrugated host bilayers, whereas the host molecules arrange in a head-to-head-tail-to-tail (*hh-tt*) fashion (Figure 1) [1]. The shape of the channel can be modified by a conformational change of the steroidal side chain, which can assume either a fully extended (*trans)* or folded (*gauche*)

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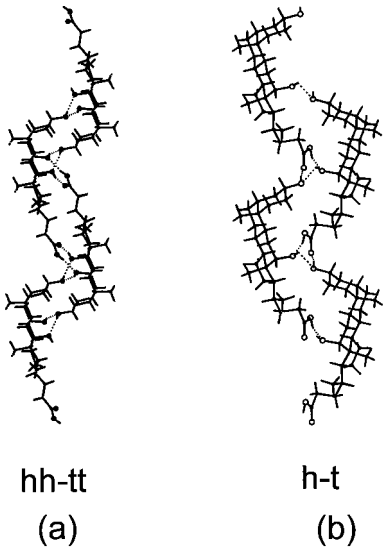
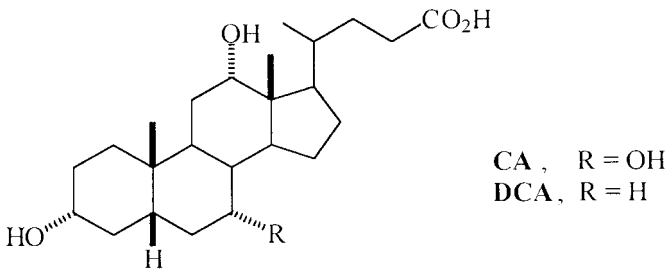


Figure 1. Bilayer structure with (a) head-to-head- tail-to-tail (*hh-tt*) arrangement of cholic acid molecules and (b) with head-to-tail (*h-t*) arrangement of deoxycholic acid molecules.



Scheme 1.

conformation. The channel geometry may also be influenced by mutual shifts of the host bilayers. Usually, these inclusion compounds exhibit a 1 : 1 host : guest ratio (or smaller). Nakano *et al.* [4] have recently reported some CA inclusion compounds with aromatic hydrocarbons of 2 : 1 stoichiometry; however, in this case the host molecules adopted a head-to-tail (*h-t*) arrangement within the bilayer. A similar bilayer structure is also characteristic of the deoxycholic acid (DCA) inclusion compounds crystallizing in the orthorhombic system, which generally have a host : guest ratio greater than 1 [5].

Recently, we have prepared several bile acid clathrates with aromatic ketones, including benzophenone, in order to study their induced optical activity [6]. Previously, Miyata *et al.* [7] have assigned a 1 : 1 host : guest ratio to the CA-benzophenone clathrate. However, the benzophenone molecule is too large to be accommodated within the typical CA channel preserving the 1 : 1 stoichiometry and therefore some modifications in the structure of the host matrix could be

expected. The NMR and elemental analysis revealed a 2 : 1 stoichiometry of this complex as well as some other CA complexes with various biaryl guests of similar size. Our preliminary X-ray data for the CA-benzophenone inclusion compound have indicated that it is not isostructural with any of the reported CA complexes and therefore we decided to undertake its full structural characterization by X-ray analysis.

2. Experimental

Recrystallization of CA from melted benzophenone with a small amount of ethyl ether resulted in needle-like crystals of the inclusion compound with the 2 : 1 stoichiometry (Found: C 73.46%; H 8.99%. Calcd for $2C_{24}H_{40}O_5.C_{13}H_{10}O$: C 73.31%; H 9.08%). A ^{1}H NMR spectrum recorded using a Varian Unity-Plus (500 MHz) in DMSO-d_6 confirmed the 2 : 1 host–guest molar ratio. All X-ray measurements were carried out at room temperature on a KUMA Diffraction KM-4 diffractometer [8] equipped with a graphite monochromator for a crystal with dimensions 0.6 × 0.25 × 0.05 mm. The unit-cell parameters and the orientation matrix were obtained from a least-squares fit of 32 reflections with θ in the range 11–27°.

Crystal data for $2CA.C_{13}H_{10}O$: m.p. 172 °C, monoclinic, $P2_1$, a = 25.498(6), b = 7.942(1), c = 28.309(6) Å, β = 101.85(2)°, V = 5610(2) Å^3, Z = 4, D_x = 1.183 g cm^{-3}, D_m = 1.180 g cm^{-3}.

Intensity data were collected by the ω-2θ scan technique using Cu Kα (λ = 1.54178 Å) radiation up to $2\theta_{max}$ = 115°. The reciprocal sphere was collected in the range h: $-27 \rightarrow 27$, k: $0 \rightarrow 8$, l: $0 \rightarrow 30$. A total of 8315 reflections were measured, of which 8154 were unique and 4414 had $F > 4\sigma(F)$. All intensities were converted to $|F|^2$ in a conventional manner. No corrections for absorption or secondary extinction effects were applied.

The structure could not be solved straightforwardly with the program SHELXS-86 [9]. The E-map calculated for the combination of phases with best figures of merit showed three entire and a fragment of the fourth host molecule; however, the refinement of the model was unstable and the ΔF maps did not reveal missing host atoms. Therefore we decided to use PATSEE [10] to find rotational and translational parameters for our model consisting of four CA molecules with side chains in the *gauche* conformation and forming the host bilayer in the *hh-tt* fashion. The coordinates of the model obtained from the best rotational and translational search refined well showing however that the conformation of the steroidal side chain of two host molecules had to be changed to *trans*. The difference electron density map calculated at this stage showed the highest maxima located in the region of the two crystallographically independent channels. The electron density maxima did not form the benzophenone skeleton clearly and therefore it became apparent that the guest molecules were disordered and that the pattern of disorder in the two channels differed. Atoms of the host molecules were refined with anisotropic displacement parameters for all O atoms and for the C atoms of the methyl groups and the

steroidal side chain. The positions of the H atoms bonded to the C atoms and those from carboxylic groups were calculated from geometrical conditions. The positions of the H atoms of the OH groups were calculated assuming a cyclic hydrogen bond scheme typical of the CA *hh-tt* bilayers. The H atom positions were refined using a riding model and isotropic displacement parameters 1.2 times higher than U_{eq} of the atoms to which they were bonded. The program SHELXL-93 [11] has been used for full-matrix least-squares refinement on 6692 reflections with positive F^2. At that stage approximate models of two benzophenone molecules could be built from the highest electron density maxima. These guest molecules were refined with occupancy factors of 0.5 for all atoms and with all 1–2 and 1–3 distances restrained to the expected value. Restraints were also imposed on the planarity of the phenyl rings and C_{ar}—CO—C_{ar} groups. Because benzophenone has two rotational degrees of freedom the torsions about C_{ar}—C_{sp2} were not restrained during the refinement process. Atoms of the guest molecules were refined with individual isotropic displacement parameters. The ΔF map calculated at this stage showed maxima which gave the second orientation of the guest in each channel. The geometry of these molecules was similarly restrained as indicated above. The sum of occupancy factors of the guest molecules in one channel was fixed to 1 but individual occupancies were allowed to refine. The ratio of the benzophenone orientations refined to 0.74(1) : 0.26(1) in one channel and to 0.59(1) : 0.41(1) in the second. Because the isotropic displacement parameters of some atoms in the guest molecules were quite high we have checked if the refinement with displacement parameter equal for all atoms in one guest molecule would influence the ratio of benzophenone conformers. This refinement gave no significant change in the occupancy factors and conformation of the guest molecules.

A total of 932 parameters with 173 restraints imposed were refined in the last cycle giving $R = 0.068$ and $wR_2 = 0.19$ for 4414 reflections with $F > 4\sigma(F)$ ($R = 0.17$ and $wR_2 = 0.25$ for all reflections). The final difference map showed minima and maxima ranging from $-0.27(5)$ to 0.42(5) e Å^{-3}.

Final atomic parameters are given in Table I.

3. Results and Discussion

The six-membered rings of the steroidal skeleton are conformationally rigid, whereas the five-membered ring is relatively flexible. Giglio [5] has indicated that there is a correlation between the conformation of the side chain and the five-membered ring geometry, i.e., when the side chain assumes the *gauche* conformation [the C(17)–C(20)–C(22)–C(23) torsion angle is ca. 60°] the ring approaches a half-chair conformation, whereas for the *trans* conformation of the side chain (the above torsion angle is ca. 180°) it adopts an envelope conformation.

The asymmetric part of the unit cell of the 2 : 1 CA-benzophenone inclusion compound consists of four host and two guest molecules. It is apparent from Table II that the side chains in two CA molecules, assigned as A and B, are in

Table I. Fractional atomic coordinates, isotropic (or equivalent isotropic *) displacement coefficients, occupancies (if fractional) for non-hydrogen atoms and fractional atomic coordinate of H atoms from the O–H groups

	x	*y*	*Z*	*U*	*f*
O(1F)	0.2697(14)	0.5374(29)	0.3278(7)	0.252(30)	0.262(8)
C(7F)	0.2610(7)	0.4161(23)	0.3502(5)	0.130(20)	0.262(8)
C(1F)	0.2439(5)	0.2578(24)	0.3249(5)	0.091(13)	0.262(8)
C(2F)	0.2604(9)	0.1053(25)	0.3472(7)	0.131(20)	0.262(8)
C(3F)	0.2445(11)	−0.0455(25)	0.3237(10)	0.085(15)	0.262(8)
C(4F)	0.2120(10)	−0.0437(31)	0.2777(9)	0.120(18)	0.262(8)
C(5F)	0.1955(12)	0.1087(36)	0.2554(7)	0.091(15)	0.262(8)
C(6F)	0.2114(10)	0.2596(31)	0.2790(6)	0.207(36)	0.262(8)
C(11F)	0.2677(5)	0.4290(17)	0.4028(5)	0.029(6)	0.262(8)
C(21F)	0.2370(8)	0.3296(24)	0.4271(7)	0.067(10)	0.262(8)
C(31F)	0.2435(11)	0.3425(31)	0.4769(7)	0.127(20)	0.262(8)
C(41F)	0.2807(11)	0.4551(32)	0.5023(6)	0.106(16)	0.262(8)
C(51F)	0.3115(10)	0.5545(33)	0.4779(6)	0.075(12)	0.262(8)
C(61F)	0.3049(8)	0.5416(26)	0.4281(6)	0.070(10)	0.262(8)
O(22F)	0.6918(9)	0.1792(28)	0.1696(7)	0.402(25)	0.587(10)
C(72F)	0.7205(6)	0.2332(16)	0.1444(4)	0.215(16)	0.587(10)
C(12F)	0.7171(5)	0.1627(13)	0.0961(4)	0.111(8)	0.587(10)
C(22F)	0.6757(5)	0.2080(18)	0.0584(5)	0.101(7)	0.587(10)
C(32F)	0.6722(7)	0.1414(24)	0.0125(5)	0.142(10)	0.587(10)
C(42F)	0.7109(8)	0.0278(24)	0.0043(6)	0.139(10)	0.587(10)
C(52F)	0.7525(8)	−0.0179(28)	0.0420(7)	0.211(17)	0.587(10)
C(62F)	0.7558(6)	0.0490(25)	0.0879(6)	0.268(22)	0.587(10)
C(13F)	0.7580(4)	0.3688(13)	0.1635(4)	0.108(7)	0.587(10)
C(23F)	0.7725(7)	0.3891(20)	0.2133(4)	0.144(10)	0.587(10)
C(33F)	0.8080(8)	0.5165(24)	0.2324(5)	0.199(18)	0.587(10)
C(43F)	0.8287(7)	0.6226(21)	0.2017(7)	0.137(10)	0.587(10)
C(53F)	0.8142(8)	0.6023(20)	0.1519(7)	0.116(9)	0.587(10)
C(63F)	0.7786(7)	0.4746(19)	0.1329(5)	0.113(9)	0.587(10)
O(1G)	0.7759(7)	0.0603(20)	0.1686(5)	0.155(10)	0.413(10)
C(7G)	0.7668(4)	0.1758(18)	0.1410(4)	0.084(8)	0.413(10)
C(1G)	0.7862(4)	0.3451(17)	0.1571(4)	0.072(7)	0.413(10)
C(2G)	0.8008(7)	0.3814(22)	0.2061(5)	0.126(12)	0.413(10)
C(3G)	0.8192(8)	0.5419(24)	0.2210(6)	0.088(9)	0.413(10)
C(4G)	0.8227(8)	0.6646(21)	0.1867(8)	0.130(14)	0.413(10)
C(5G)	0.8080(10)	0.6283(21)	0.1378(8)	0.125(15)	0.413(10)
C(6G)	0.7897(8)	0.4681(21)	0.1230(5)	0.093(10)	0.413(10)
C(11G)	0.7366(4)	0.1475(17)	0.0917(4)	0.075(7)	0.413(10)
C(21G)	0.7450(7)	0.0017(20)	0.0670(5)	0.103(10)	0.413(10)

Table I. Continued

	x	*y*	*Z*	*U*	*f*
C(31G)	0.7164(8)	−0.0251(24)	0.0203(6)	0.112(11)	0.413(10)
C(41G)	0.6792(6)	0.0932(26)	−0.0022(5)	0.084(8)	0.413(10)
C(51G)	0.6709(7)	0.2388(24)	0.0226(5)	0.111(10)	0.413(10)
C(61G)	0.6996(6)	0.2654(19)	0.0693(5)	0.076(7)	0.413(10)
O(22G)	0.2111(7)	0.1045(20)	0.4211(5)	0.325(14)	0.738(8)
C(72G)	0.2320(4)	0.1868(13)	0.3944(4)	0.166(9)	0.738(8)
C(12G)	0.2611(3)	0.3401(12)	0.4129(3)	0.100(5)	0.738(8)
C(22G)	0.2675(5)	0.3786(16)	0.4617(3)	0.162(9)	0.738(8)
C(32G)	0.2950(6)	0.5233(18)	0.4802(4)	0.149(9)	0.738(8)
C(42G)	0.3162(5)	0.6293(16)	0.4497(5)	0.145(8)	0.738(8)
C(52G)	0.3097(5)	0.5908(15)	0.4010(5)	0.126(7)	0.738(8)
C(62G)	0.2822(4)	0.4459(15)	0.3826(4)	0.099(5)	0.738(8)
C(13G)	0.2269(3)	0.1278(13)	0.3446(3)	0.091(5)	0.738(8)
C(23G)	0.2519(6)	−0.0201(15)	0.3350(5)	0.226(17)	0.738(8)
C(33G)	0.2465(6)	−0.0741(18)	0.2874(5)	0.165(9)	0.738(8)
C(43G)	0.2165(5)	0.0185(21)	0.2499(4)	0.134(7)	0.738(8)
C(53G)	0.1914(7)	0.1664(23)	0.2595(4)	0.191(14)	0.738(8)
C(63G)	0.1969(6)	0.2205(18)	0.3070(4)	0.157(8)	0.738(8)
C(1A)	0.4168(3)	1.0050(13)	0.4098(3)	0.054(2)	
C(2A)	0.4392(3)	1.0254(13)	0.4640(3)	0.053(2)	
C(3A)	0.4251(3)	1.2036(13)	0.4793(3)	0.053(2)	
C(4A)	0.4467(3)	1.3321(13)	0.4507(3)	0.047(2)	
C(5A)	0.4275(3)	1.3135(12)	0.3964(3)	0.046(2)	
C(6A)	0.4498(3)	1.4557(13)	0.3694(3)	0.051(2)	
C(7A)	0.5088(3)	1.4329(13)	0.3672(3)	0.047(2)	
C(8A)	0.5184(3)	1.2550(11)	0.3481(2)	0.035(2)	
C(9A)	0.4977(3)	1.1146(12)	0.3766(3)	0.042(2)	
C(10A)	0.4369(3)	1.1341(12)	0.3767(3)	0.041(2)	
C(11A)	0.5118(3)	0.9413(12)	0.3576(3)	0.047(2)	
C(12A)	0.5708(3)	0.9180(13)	0.3557(3)	0.045(2)	
C(13A)	0.5918(3)	1.0610(12)	0.3270(2)	0.038(2)	
C(14A)	0.5777(3)	1.2280(12)	0.3481(3)	0.039(2)	
C(15A)	0.6061(3)	1.3604(13)	0.3238(3)	0.053(2)	
C(16A)	0.6586(3)	1.2715(13)	0.3196(3)	0.055(2)	
C(17A)	0.6533(3)	1.0830(12)	0.3327(3)	0.039(2)	
C(18A)	0.5651(3)	1.0402(13)	0.2738(3)	0.050(2)*	
C(19A)	0.4025(3)	1.1104(15)	0.3259(3)	0.063(3)*	
C(20A)	0.6858(3)	0.9688(13)	0.3043(3)	0.047(2)*	
C(21A)	0.6769(4)	0.7806(13)	0.3113(3)	0.067(3)*	
C(22A)	0.7444(3)	1.0175(14)	0.3193(3)	0.057(2)*	

Table I. Continued

	x	*y*	*Z*	*U*	*f*
C(23A)	0.7819(3)	0.9444(15)	0.2904(3)	0.070(3)*	
C(24A)	0.8379(3)	1.0132(18)	0.3055(3)	0.063(3)*	
O(25A)	0.4486(2)	1.2240(10)	0.5298(2)	0.061(2)*	
H(25A)	0.4284(2)	1.2805(10)	0.5444(2)	0.074	
O(26A)	0.6007(2)	0.9149(10)	0.4051(2)	0.0540(15)*	
H(26A)	0.6273(2)	0.8482(10)	0.4115(2)	0.065	
O(27A)	0.8731(2)	0.8970(11)	0.3003(2)	0.067(2)*	
H(27A)	0.9040(2)	0.9401(11)	0.3094(2)	0.080	
O(28A)	0.8486(3)	1.1539(12)	0.3201(3)	0.086(2)*	
O(29A)	0.5441(2)	1.4535(10)	0.4128(2)	0.0509(14)*	
H(29A)	0.5293(2)	1.5173(10)	0.4304(2)	0.061	
C(1B)	1.1057(3)	0.5312(14)	0.3420(3)	0.062(2)	
C(2B)	1.0837(3)	0.5478(14)	0.2877(3)	0.061(2)	
C(3B)	1.0959(4)	0.7232(15)	0.2718(3)	0.069(3)	
C(4B)	1.0738(3)	0.8541(14)	0.3006(3)	0.060(2)	
C(5B)	1.0940(3)	0.8378(13)	0.3553(3)	0.053(2)	
C(6B)	1.0704(3)	0.9753(13)	0.3820(3)	0.052(2)	
C(7B)	1.0123(3)	0.9500(13)	0.3853(3)	0.046(2)	
C(8B)	1.0031(3)	0.7723(12)	0.4043(3)	0.040(2)	
C(9B)	1.0261(3)	0.6336(12)	0.3768(3)	0.041(2)	
C(10B)	1.0860(3)	0.6603(13)	0.3759(3)	0.051(2)	
C(11B)	1.0129(3)	0.4614(12)	0.3959(3)	0.048(2)	
C(12B)	0.9539(3)	0.4297(12)	0.3971(3)	0.044(2)	
C(13B)	0.9316(3)	0.5712(12)	0.4254(3)	0.040(2)	
C(14B)	0.9444(3)	0.7395(12)	0.4037(2)	0.037(2)	
C(15B)	0.9136(3)	0.8728(12)	0.4270(3)	0.044(2)	
C(16B)	0.8625(3)	0.7774(13)	0.4309(3)	0.056(2)	
C(17B)	0.8700(3)	0.5895(12)	0.4195(3)	0.036(2)	
C(18B)	0.9580(3)	0.5578(12)	0.4794(2)	0.048(2)*	
C(19B)	1.1213(3)	0.6422(15)	0.4261(3)	0.068(3)*	
C(20B)	0.8374(3)	0.4734(12)	0.4462(3)	0.048(2)*	
C(21B)	0.8463(3)	0.2827(13)	0.4391(3)	0.060(2)*	
C(22B)	0.7778(3)	0.5187(14)	0.4293(3)	0.058(2)*	
C(23B)	0.7404(3)	0.4362(14)	0.4589(3)	0.066(3)*	
C(24B)	0.6841(4)	0.5061(16)	0.4443(3)	0.062(3)*	
O(25B)	1.0725(3)	0.7435(11)	0.2210(2)	0.085(2)*	
H(25B)	1.0923(3)	0.8022(11)	0.2077(2)	0.102	
O(26B)	0.9246(2)	0.4233(10)	0.3478(2)	0.0554(15)*	
H(26B)	0.8974(2)	0.3592(10)	0.3409(2)	0.066	
O(27B)	0.6486(2)	0.3902(10)	0.4519(2)	0.068(2)*	

Table I. Continued

	x	*y*	*Z*	*U*	*f*
H(27B)	0.6179(2)	0.4353(10)	0.4435(2)	0.082	
O(28B)	0.6737(3)	0.6422(12)	0.4270(3)	0.089(2)*	
O(29B)	0.9760(2)	0.9691(10)	0.3392(2)	0.0520(14)*	
H(29B)	0.9865(2)	1.0545(10)	0.3256(2)	0.062	
C(1C)	−0.0725(3)	1.0374(13)	0.1656(3)	0.052(2)	
C(2C)	−0.0439(3)	1.0508(13)	0.2174(3)	0.054(2)	
C(3C)	−0.0533(3)	1.2258(13)	0.2369(3)	0.049(2)	
C(4C)	−0.0373(3)	1.3580(13)	0.2051(3)	0.051(2)	
C(5C)	−0.0626(3)	1.3434(12)	0.1520(3)	0.048(2)	
C(6C)	−0.0441(3)	1.4829(14)	0.1223(3)	0.059(2)	
C(7C)	0.0128(3)	1.4589(13)	0.1132(3)	0.052(2)	
C(8C)	0.0195(3)	1.2823(12)	0.0937(3)	0.043(2)	
C(9C)	0.0030(3)	1.1404(12)	0.1251(3)	0.042(2)	
C(10C)	−0.0563(3)	1.1633(12)	0.1312(3)	0.045(2)	
C(11C)	0.0156(3)	0.9640(12)	0.1080(3)	0.048(2)	
C(12C)	0.0723(3)	0.9422(13)	0.0992(3)	0.049(2)	
C(13C)	0.0868(3)	1.0776(12)	0.0658(3)	0.040(2)	
C(14C)	0.0777(3)	1.2518(12)	0.0878(3)	0.041(2)	
C(15C)	0.1017(3)	1.3769(14)	0.0576(3)	0.059(2)	
C(16C)	0.1508(3)	1.2810(13)	0.0475(3)	0.058(2)	
C(17C)	0.1472(3)	1.0971(13)	0.0639(3)	0.044(2)	
C(18C)	0.0524(3)	1.0544(14)	0.0152(3)	0.056(2)*	
C(19C)	−0.0957(3)	1.1425(15)	0.0820(3)	0.069(3)*	
C(20C)	0.1727(3)	0.9781(13)	0.0305(3)	0.051(2)*	
C(21C)	0.1670(4)	0.7903(14)	0.0423(4)	0.075(3)*	
C(22C)	0.2300(3)	1.0240(14)	0.0298(3)	0.059(2)*	
C(23C)	0.2676(4)	1.0117(17)	0.0791(3)	0.080(3)*	
C(24C)	0.3227(4)	1.0769(18)	0.0796(3)	0.067(3)*	
O(25C)	−0.0247(2)	1.2422(10)	0.2854(2)	0.058(2)*	
H(25C)	−0.0231(2)	1.3408(10)	0.2974(2)	0.070	
O(26C)	0.1076(2)	0.9450(10)	0.1462(2)	0.059(2)*	
H(26C)	0.1319(2)	0.8884(10)	0.1368(2)	0.071	
O(27C)	0.3575(3)	0.9604(16)	0.0754(3)	0.119(3)*	
H(27C)	0.3879(3)	1.0062(16)	0.0764(3)	0.143	
O(28C)	0.3325(3)	1.2253(15)	0.0823(3)	0.117(3)*	
O(29C)	0.0527(2)	1.4863(10)	0.1559(2)	0.064(2)*	
H(29C)	0.0527(2)	1.5723(10)	0.1738(2)	0.077	
C(1D)	0.5958(3)	0.5712(14)	0.0851(3)	0.057(2)	
C(2D)	0.5680(3)	0.5856(14)	0.0330(3)	0.063(2)	
C(3D)	0.5735(3)	0.7620(14)	0.0139(3)	0.060(2)	

Table I. Continued

	x	*y*	*Z*	*U*	*f*
C(4D)	0.5556(3)	0.8937(13)	0.0448(3)	0.054(2)	
C(5D)	0.5827(3)	0.8765(13)	0.0987(3)	0.054(2)	
C(6D)	0.5628(3)	1.0136(14)	0.1277(3)	0.061(2)	
C(7D)	0.5064(3)	0.9818(14)	0.1370(3)	0.059(2)	
C(8D)	0.5011(3)	0.8063(12)	0.1567(3)	0.040(2)	
C(9D)	0.5205(3)	0.6683(12)	0.1255(3)	0.043(2)	
C(10D)	0.5792(3)	0.6960(13)	0.1201(3)	0.049(2)	
C(11D)	0.5095(3)	0.4915(13)	0.1448(3)	0.050(2)	
C(12D)	0.4532(3)	0.4599(14)	0.1518(3)	0.052(2)	
C(13D)	0.4356(3)	0.5941(12)	0.1845(3)	0.042(2)	
C(14D)	0.4443(3)	0.7688(12)	0.1623(3)	0.038(2)	
C(15D)	0.4173(3)	0.8930(13)	0.1912(3)	0.052(2)	
C(16D)	0.3685(3)	0.7923(13)	0.2015(3)	0.054(2)	
C(17D)	0.3749(3)	0.6092(13)	0.1865(3)	0.047(2)	
C(18D)	0.4698(3)	0.5736(13)	0.2360(3)	0.051(2)*	
C(19D)	0.6192(3)	0.6857(15)	0.1686(3)	0.071(3)*	
C(20D)	0.3504(3)	0.4859(13)	0.2177(3)	0.056(2)*	
C(21D)	0.3572(3)	0.3005(13)	0.2053(3)	0.060(2)*	
C(22D)	0.2916(3)	0.5272(15)	0.2186(3)	0.069(3)*	
C(23D)	0.2547(3)	0.5018(17)	0.1698(3)	0.084(3)*	
C(24D)	0.1991(4)	0.5636(20)	0.1700(4)	0.083(4)*	
O(25D)	0.5435(3)	0.7733(10)	−0.0350(2)	0.073(2)*	
H(25D)	0.5451(3)	0.8725(10)	−0.0459(2)	0.087	
O(26D)	0.4182(2)	0.4578(10)	0.1052(2)	0.058(2)*	
H(26D)	0.3918(2)	0.4041(10)	0.1120(2)	0.070	
O(27D)	0.1642(3)	0.4608(18)	0.1717(4)	0.163(5)*	
H(27D)	0.1341(3)	0.5107(18)	0.1649(4)	0.196	
O(28D)	0.1911(4)	0.7167(17)	0.1636(4)	0.156(5)*	
O(29D)	0.4660(2)	1.0071(10)	0.0946(2)	0.065(2)*	
H(29D)	0.4659(2)	1.0943(10)	0.0772(2)	0.078	

the *trans* conformation (Figure 2a) whereas in the remaining two, C and D, are in the *gauche* conformation (Figure 2b). In all of these four molecules the five-membered ring assumes a slightly deformed half-chair conformation (Table III) and therefore, in our case, the ring geometry seems not to be influenced by the side chain conformation.

In contrast to the orthorhombic DCA inclusion compounds, where the *h*-*t* bilayers are usually constructed from the steroidal molecules with the side chain in a

Table II. Torsion angles [°] characterizing the side chain conformation of the host molecules

	Host A	Host B	Host C	Host D
C(16)–C(17)–C(20)–C(22) (ψ_1)	62.2(8)	60.8(9)	56.8(9)	53.6(10)
C(17)–C(20)–C(22)–C(23) (ψ_2)	−169.9(8)	−169.7(8)	61.3(11)	66.8(11)
C(20)–C(22)–C(23)–C(24) (ψ_3)	174.8(8)	172.2(8)	−173.0(9)	−172.7(10)
C(22)–C(23)–C(24)–O(27) (ψ_4)	146.9(8)	151.8(8)	−97.6(11)	−104.2(13)

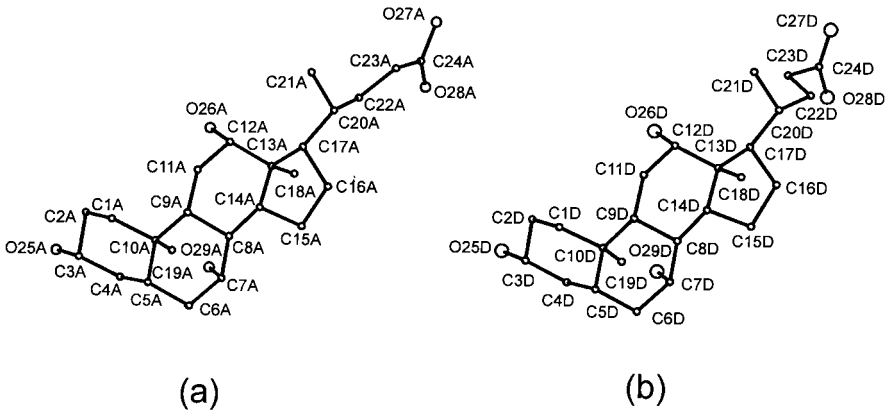


Figure 2. Labeling of atoms and conformation of the host molecules: (a) molecule A with the side chain in the trans conformation; (b) molecule D with the side chain in the gauche conformation.

gauche conformation, the *hh-tt* bilayers in the CA inclusion compounds can be formed from the molecules in any of two possible side-chain conformations, due to the antiparallel arrangement of the host molecules in two sheets forming the bilayer.

The host molecules in the CA-benzophenone clathrate are associated by a cyclic system of hydrogen bonds between the hydroxyl and carboxyl groups O—H···O—

Table III. Endocyclic torsion angles [°] in the five-membered rings of the host molecules A-D

Torsion angle	Host A	Host B	Host C	Host D
C(13)–C(14)–C(15)–C(16)	−36	−36	−36	−35
C(14)–C(15)–C(16)–C(17)	10	10	10	10
C(15)–C(16)–C(17)–C(13)	18	18	19	19
C(16)–C(17)–C(13)–C(14)	−39	−38	−40	−39
C(17)–C(13)–C(14)–C(15)	48	47	48	46

Table IV. Geometry of the hydrogen bonds

D–H···A	D···A (A)	D–H(A)	H···A (A)	D–H···A (°)
O(25A)–H(25A)···O(26A_$1)	2.866 (7)	0.85	2.04	163
O(26A)–H(26A)···O(28B)	2.840 (9)	0.85	2.02	164
O(27A)–H(27A)···O(29B)	2.692 (7)	0.85	1.87	162
O(29A)–H(29A)···O(25A_$1)	2.676 (8)	0.85	2.01	135
O(25B)–H(25B)···O(26C_$2)	2.937 (8)	0.85	2.17	150
O(26B)–H(26B)···O(28A_$3)	2.885 (9)	0.85	2.06	163
O(27B)–H(27B)···O(29A_$3)	2.715 (8)	0.85	1.91	158
O(29B)–H(29B)···O(25C_$2)	2.647 (8)	0.85	1.86	153
O(25C)–H(25C)···O(26B_$4)	2.790 (7)	0.85	2.24	122
O(26C)–H(26C)···O(28D)	2.763 (10)	0.85	2.06	139
O(27C)–H(27C)···O(29D)	2.731 (9)	0.85	1.95	152
O(29C)–H(29C)···O(25B_$4)	2.727 (8)	0.85	1.90	164
O(25D)–H(25D)···O(26D_$5)	2.802 (7)	0.85	2.19	127
O(26D)–H(26D)···O(28C_$3)	2.831 (10)	0.85	2.12	141
O(27D)–H(27D)···O(29C_$3)	2.792 (10)	0.85	2.05	146
O(29D)–H(29D)···O(25D_$5)	2.684 (8)	0.85	1.84	172

Symmetry codes: $1 = $-X + 1, Y + 0.5, -Z + 1$; $2 = $X + 1, Y, Z$; $3 = $X, Y - 1, Z$; $4 = $X - 1, Y + 1, Z$; $5 = $-X + 1, Y + 0.5, -Z$.

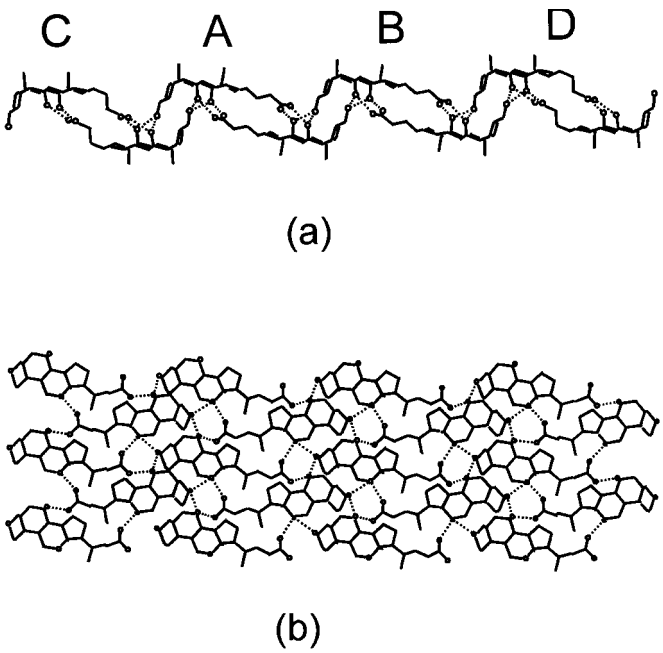


Figure 3. Structure of the host bilayer in the 2 : 1 cholic acid – benzophenone clathrate: (a) view along [010]; (b) view perpendicular to the bilayer.

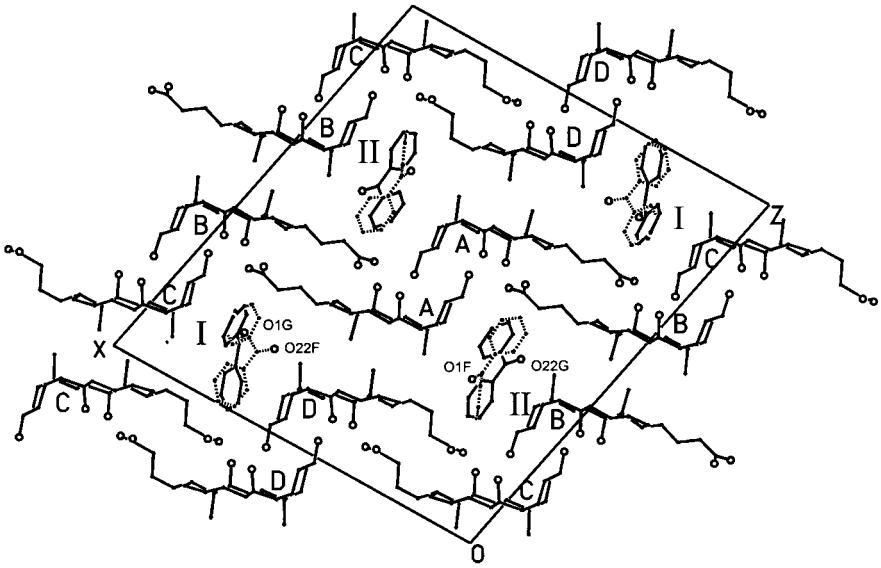


Figure 4. Crystal packing in the 2 : 1 cholic acid – benzophenone clathrate. Hydrogen atoms have been omitted for clarity.

H···O—H···O—H···O=C—OH (Table IV) and form the *hh-tt* bilayer parallel to (201). This bilayer is characterized by typical features of the CA bilayers, i.e. it is corrugated, it has a hydrophobic outside surface and a hydrophilic interior (Figure 3). The host molecules pack along [$\bar{2}$01] in the A, B, D, C, A, B, D, C ... sequence and form a single sheet, together with molecules related by a translation along [010]. The arrangement of the sheets into the *hh-tt* bilayer allows only for contacts between the CA side chains assuming the same conformation, i.e. contacts between the side chains of the A and B or C and D molecules. In consequence two types of grooves are formed on the bilayer hydrophobic surface; those that are located in the region of the C and D host molecules with the side chain in the *gauche* conformation are deeper and those in the region of the host A and B with the side chains in the *trans* conformation are more shallow.

The neighboring bilayers, forming the CA host matrix, arrange in such a manner that the shallow grooves are packed vis-à-vis the deeper grooves, forming asymmetric wavy channels running parallel to [010] (Figure 4). There are two crystallographically independent channels, I and II, which are topologically similar and arrange in a sequence I–I–II–II–I–I–II–II... along the [$\bar{2}$01] direction. The unit-cell parameter along the channel [b = 7.942(1) A] is large enough to allow accommodation of the translation related benzophenone molecules in the channel without disorder. Obviously, it would not be possible if the 2_1 axis was directed along the channel (a feature typical of most channel-type inclusion compounds of CA). Nevertheless, the benzophenone molecules are disordered and two different conformers are included in each channel.

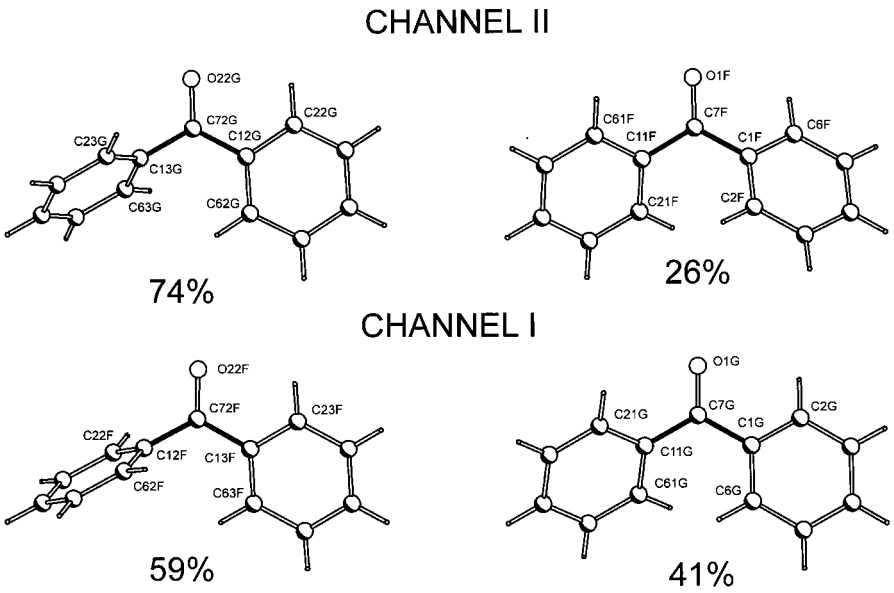


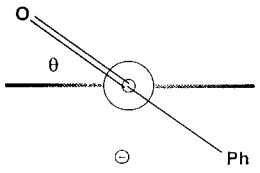
Figure 5. The four benzophenone conformers found in the 2 : 1 cholic acid – benzophenone clathrate.

For steric reasons the benzophenone molecule cannot assume planar geometry. It possesses two rotational degrees of freedom and a wide variety of experimental and theoretical methods [12, 13] have indicated that the benzophenone molecules prefer a helicoidal conformation, with both C_{ar}-C_{sp^2} torsion angles φ_1 and φ_2 equal, different methods however, give different values of these angles. According to molecular modeling, the minimum energy form corresponds to a propeller conformation with $\varphi_1 = \varphi_2 = 30°$ (or $-30°$ for the enantiomer) [12, 13] and a very similar geometry has been observed in the crystal structure [14]. There are three possible rotational routes for enantiomerization of the benzophenone molecule: a zero-, one- and two-ring flip. The molecular mechanics calculations and the structure correlation method have indicated that the minimum energy path for the correlated rotation of the phenyl rings in benzophenone is a one ring flip and the conformer with $\varphi_1 = 0$, $\varphi_2 = 90°$ (or $\varphi_1 = 90°$, $\varphi_2 = 0°$) is a transition state point on the isomerization pathway. The calculated energy barrier height for this process is 5.9 kJ mol^{-1} [13].

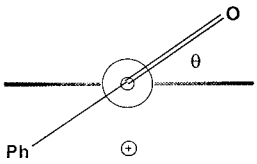
The guest molecules trapped in the host matrix of the 2 : 1 CA-benzophenone inclusion compound exist in four different chiral conformations, despite the close topological similarity of the two crystallographically independent channels. The occupancies of different conformers in each channel are not equal. The guest molecules are shown in Figure 5 and the corresponding torsion angles φ_1 and φ_2 are given in Table V. The benzophenone molecules enclosed in channel I show opposite helicity, with the *P P* conformer prevailing. The torsion angles of the less populated *M M* conformer included in channel II are close to those observed in the

Table V. Torsion angles [°] for the benzophenone molecules accommodated in the CA channels

				Guest helicity
Guest molecules in channel I				
C(61G)C(11G)C(7G)C(1G)	−38.3(9)	C(11G)C(7G)C(1G)C(6G)	−18.3(9)	MM
C(62F)C(12F)C(72F)C(13F)	77.6(11)	C(12F)C(72F)C(13F)C(63F)	22.1(10)	PP
Guest molecules in channel II				
C(21F)C(11F)C(7F)C(1F)	−29.3(13)	C(11F)C(7F)C(1F)C(2F)	−34.4(14)	MM
C(62G)C(12G)C(72G)C(13G)	5.1(7)	C(12G)C(72G)C(13G)C(63G)	−67.6(8)	PM



M



P

energy minimum form. The carbonyl group in the second conformer of the *PM* helicity is approximately coplanar with one of the phenyl rings and the second ring is oriented nearly perpendicularly to them. All four conformers can be located on the interconversion path of the benzophenone enantiomers.

The initial objective of this study was a determination of the absolute configuration of the benzophenone molecules enclosed in the CA host matrix in order to correlate the molecular chirality with the circular dichroism (CD) sign measured in the solid state spectra of the CA inclusion compound. However, a contribution from four different conformers of the guest molecules included in the host matrices complicates interpretation of the spectra. We hope that CA complexes with some substituted benzophenones which have been recently prepared in our laboratory, showing much stronger CD in the solid state, may be better models for studying mechanisms governing the optical activity of the benzophenone chromophore.

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