

## Références

- AHMED, F. R., HALL, S. R., PIPPY, M. E. & HUBER, C. P. (1966). NRC Crystallographic Programs for the IBM/360 System. National Research Council, Ottawa, Canada.
- BUCOURT, R. & HAINAUT, D. (1966). *Bull. Soc. Chim. Fr.* (2), pp. 501–505.
- CRUICKSHANK, D. W. J. (1965). *Computing Methods in Crystallography*, édité par J. S. ROLLETT, pp. 113, 114. Oxford: Pergamon Press.
- GUY, E. & WINTERNITZ, F. (1969). *Ann. Chim. (Paris)*, **4**, 57–65.
- International Tables for X-ray Crystallography* (1968). Tome III. Birmingham: Kynoch Press.
- MAIN, P., LESSINGER, L., WOOLFSON, M. M., GERMAIN, G. & DECLERCQ, J. P. (1976). *MULTAN 76. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univ. de York, Angleterre, et Louvain-la-Neuve, Belgique.
- ROQUES, R., CHEZEAU, N., GUY, E. & LAPASSET, J. (1976). *Acta Cryst.* B **32**, 1885–1888.

*Acta Cryst.* (1979). B **35**, 2941–2944

## The Tetragonal Phase of the 2:1:1 Canal Complex between Deoxycholic Acid, Ethanol and Water

By V. M. COIRO

*Laboratorio di Strutturistica Chimica 'Giordano Giacomello' CNR, Area della Ricerca, CP10, 00016 Monterotondo Stazione, Roma, Italy*

AND A. D'ANDREA AND E. GIGLIO

*Istituto di Chimica Fisica, Università di Roma, 00185 Roma, Italy*

(Received 1 June 1979; accepted 3 July 1979)

### Abstract

$2C_{24}H_{40}O_4 \cdot C_2H_6O \cdot H_2O$ , tetragonal,  $P4_12_12$ ,  $a = 14.068$  (2),  $c = 49.334$  (8) Å,  $Z = 8$ ,  $D_m = 1.16$ ,  $D_c = 1.16$  Mg m<sup>-3</sup>, Cu  $K\alpha$  radiation,  $\mu(Cu K\alpha) = 63.1$  mm<sup>-1</sup>.  $R = 0.08_3$  and  $R_w = 0.12_5$  for 2448 observed data with  $I > 3\sigma(I)$ . The side-chain and ring  $D$  conformations of deoxycholic acid are similar to those of the orthorhombic phases. The deoxycholic acid molecules are held together mainly by hydrogen bonds and form bilayers perpendicular to  $c$ . The ethanol and water molecules contribute to the hydrogen-bonding scheme of the double layers which are different from those of the choleic acid orthorhombic phases. These molecules are accommodated in canals, running inside the bilayers, with interior surfaces which are essentially hydrophilic. Only weak van der Waals interactions occur between two adjacent bilayers.

### Introduction

$3\alpha,12\alpha$ -Dihydroxy- $5\beta$ -cholan-24-oic acid (deoxycholic acid, DCA) forms canal complexes crystallizing in orthorhombic (Craven & DeTitta, 1972; Candeloro De Sanctis, Giglio, Pavel & Quagliata, 1972; Friedman, Lahav, Leiserowitz, Popovitz-Biro, Tang & Zaretskii,

1975; Lahav, Popovitz-Biro, Tang & Leiserowitz, 1977; Lahav, Leiserowitz, Popovitz-Biro & Tang, 1978) and hexagonal (Candeloro De Sanctis, Coiro, Giglio, Pagliuca, Pavel & Quagliata, 1978; Candeloro De Sanctis, Giglio, Petri & Quagliata, 1979) phases. This paper deals with the crystal structure determination of a tetragonal phase described by Bonamico & Giacomello (1962).

The title compound (hereafter DCAETW) was crystallized at about 278 K from an acetone/ethanol dilute solution by slow evaporation. Colourless tetragonal-bipyramidal crystals were obtained. Differential scanning calorimetry showed that the crystals lose some occluded molecules within a range of temperature centred at about 403 K by an endothermic process and subsequently melt at 447 K after reorganization at about 429 K.

A specimen with a maximum dimension of 0.8 mm was chosen to determine the cell constants by least-squares refinement from 15 reflections and to collect intensities up to  $2\theta = 104^\circ$  only, since beyond this value no reliable intensities were recorded, on a Syntex  $P2_1$  automated diffractometer with graphite-monochromatized Cu  $K\alpha$  radiation ( $\lambda = 1.5418$  Å). The data were measured by the  $\omega$ -scan mode at a scan rate within the range  $1.5\text{--}29^\circ \text{ min}^{-1}$ , depending on the peak intensity, with a scan width of  $0.8^\circ$ . Three reflections,

selected for orientation control and measured every 100 reflections, remained essentially constant. Backgrounds were estimated by stationary counting for half the scan time. Lorentz and polarization corrections were applied taking into account the monochromator crystal (Azaroff, 1955) but no absorption corrections were made.

While the DCAETW structure determination was in progress we became aware of the crystal structure solution of a DCA tetragonal phase, containing DCA and water molecules in the ratio 2:3 and crystallizing from methanol in the same space group as DCAETW with  $a = 13.999$  and  $c = 48.902$  Å (Lahav, Leiserowitz & Tang, 1977). Thus the  $E$  map that we had computed from the best set of phases obtained with *MULTAN* (Main, Woolfson, Lessinger, Germain & Declercq, 1974) was easily interpreted with the aid of a drawing, sent to us by Dr Leiserowitz, representing the projection on the  $bc$  plane of the DCA molecular packing. The space group  $P4_32_12$  was discarded on the basis of structure factor and least-squares calculations.

A difference synthesis showed the heavy atoms of ethanol and water. The structure was refined by isotropic and anisotropic block-diagonal least squares with programs of Domenicano, Spagna & Vaciago (1969). Scattering factors for C and O were from Cromer & Mann (1968) and for H from Hanson, Herman, Lea & Skillman (1964). The function mini-

mized was  $\sum w(|F_o| - |F_c|)^2$ , with  $w = (a + |F_o| + b|F_o|^2)^{-1}$ .

The H atoms were generated at the expected positions, except for those of the hydroxyl and carboxyl

Table 1. Fractional coordinates ( $\times 10^4$ ) with e.s.d.'s in parentheses

	$x$	$y$	$z$
C(1)	-2277 (8)	1411 (8)	603 (2)
C(2)	-2341 (8)	1706 (9)	904 (2)
C(3)	-1543 (8)	2436 (7)	964 (2)
C(4)	-586 (8)	1996 (8)	894 (2)
C(5)	-512 (7)	1692 (7)	602 (2)
C(6)	490 (8)	1259 (8)	547 (2)
C(7)	622 (8)	306 (8)	674 (3)
C(8)	-142 (8)	-425 (7)	605 (2)
C(9)	-1134 (7)	-2 (7)	671 (2)
C(10)	-1319 (7)	954 (7)	526 (2)
C(11)	-1909 (7)	-747 (7)	631 (2)
C(12)	-1736 (7)	-1679 (7)	765 (2)
C(13)	-775 (8)	-2107 (7)	689 (2)
C(14)	-14 (7)	-1358 (7)	744 (2)
C(15)	906 (8)	-1894 (8)	711 (3)
C(16)	691 (9)	-2909 (8)	807 (3)
C(17)	-404 (8)	-2980 (8)	850 (2)
C(18)	-825 (10)	-2394 (9)	382 (2)
C(19)	-1325 (10)	814 (8)	212 (2)
C(20)	-777 (8)	-3962 (8)	797 (2)
C(21)	-1865 (9)	-4057 (8)	820 (2)
C(22)	-270 (9)	-4727 (8)	968 (2)
C(23)	-459 (10)	-4628 (10)	1276 (2)
C(24)	33 (10)	-5418 (8)	1425 (2)
O(25)	-1612 (6)	2680 (6)	1240 (1)
O(26)	-1781 (5)	-1562 (5)	1060 (1)
O(27)	-109 (7)	-6237 (6)	1394 (2)
O(28)	680 (7)	-5127 (6)	1602 (1)
C(29)	1890 (9)	6383 (9)	2346 (3)
C(30)	1828 (9)	6695 (9)	2059 (3)
C(31)	947 (12)	7330 (10)	2006 (3)
C(32)	76 (7)	6864 (7)	2100 (2)
C(33)	118 (8)	6539 (8)	2400 (2)
C(34)	-794 (8)	6053 (8)	2488 (2)
C(35)	-923 (7)	5066 (7)	2354 (2)
C(36)	-72 (8)	4413 (7)	2403 (2)
C(37)	857 (7)	4916 (7)	2306 (2)
C(38)	989 (8)	5870 (8)	2454 (2)
C(39)	1726 (8)	4242 (8)	2324 (2)
C(40)	1550 (7)	3282 (7)	2178 (2)
C(41)	626 (7)	2802 (7)	2279 (2)
C(42)	-171 (7)	3482 (7)	2246 (2)
C(43)	-1074 (8)	2874 (8)	2312 (3)
C(44)	-810 (9)	1937 (9)	2184 (2)
C(45)	280 (7)	1932 (7)	2107 (2)
C(46)	796 (11)	2474 (9)	2576 (2)
C(47)	1145 (10)	5760 (11)	2766 (2)
C(48)	712 (11)	955 (8)	2141 (2)
C(49)	1755 (9)	944 (9)	2037 (3)
C(50)	142 (10)	172 (8)	1988 (2)
C(51)	-79 (10)	369 (8)	1705 (2)
C(52)	-601 (8)	-430 (8)	1558 (2)
O(53)	918 (10)	7557 (7)	1728 (3)
O(54)	1492 (5)	3505 (5)	1887 (1)
O(55)	-646 (9)	-1240 (7)	1650 (2)
O(56)	-1039 (6)	-213 (5)	1348 (1)
O(57)	1492 (7)	2316 (7)	1443 (2)
O(58)	2638 (15)	2965 (18)	1103 (4)
C(59)	2314 (23)	3805 (28)	995 (6)
C(60)	2719 (26)	4628 (28)	1187 (7)

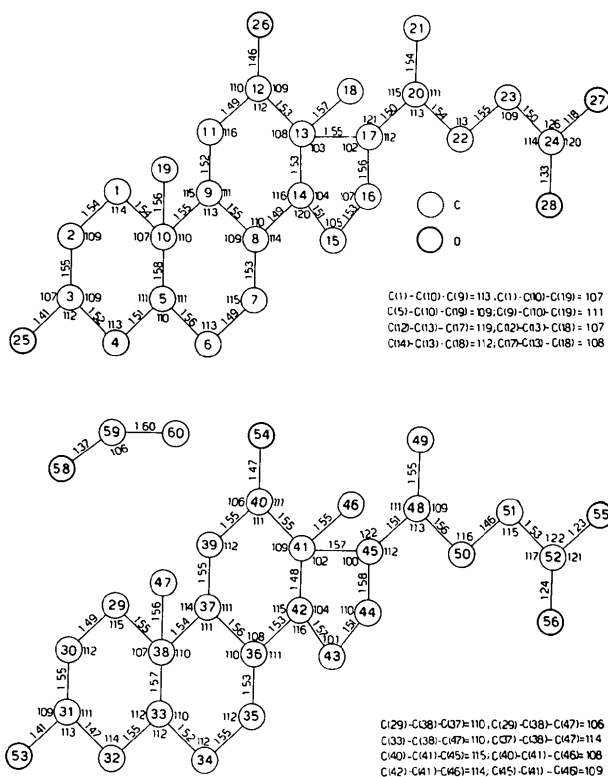


Fig. 1. Bond distances (Å) and angles ( $^{\circ}$ ) of DCAETW.

Table 2. Torsion angles ( $^{\circ}$ ) for the side chain and ring *D* of the two independent DCA molecules together with  $\Delta$  and  $\varphi_m$ The e.s.d.'s lie within the range 0.9–1.7 $^{\circ}$ .

	Molecule 1	Molecule 2		Molecule 1	Molecule 2
C(13)–C(17)–C(20)–C(22)	177	170	C(13)–C(14)	44	50
C(17)–C(20)–C(22)–C(23)	66	50	C(14)–C(15)	–33	–38
C(20)–C(22)–C(23)–C(24)	178	178	C(15)–C(16)	9	12
C(13)–C(17)–C(20)–C(21)	–55	–69	C(16)–C(17)	18	16
C(16)–C(17)–C(20)–C(21)	–176	174	C(13)–C(17)	–37	–39
C(21)–C(20)–C(22)–C(23)	–64	–73	$\Delta$	11	4
C(22)–C(23)–C(24)–O(27)	–60	–15	$\varphi_m$	44	50
C(22)–C(23)–C(24)–O(28)	119	160			

groups and of ethanol and water. Their *B*'s (5 Å<sup>2</sup>) and positional parameters were kept fixed. The C and O atoms of ethanol and water were refined isotropically. *R* and *R<sub>w</sub>* were 0.08<sub>3</sub> and 0.12<sub>5</sub> respectively. The final atomic coordinates are reported in Table 1.\*

The bond lengths and angles are given in Fig. 1. Their average e.s.d.'s are 0.016 Å and 0.9 $^{\circ}$  with maximum values of 0.022 Å and 1.3 $^{\circ}$  for DCA and of 0.051 Å and 2.5 $^{\circ}$  for ethanol.

### Discussion

Since the intensities were recorded only up to  $2\theta = 104^{\circ}$  the e.s.d.'s in the atomic coordinates and in the bond lengths and angles are rather large. However, the main interest of this crystal structure lies in the new packing mode of the DCA molecules compared with that of the orthorhombic phases, the DCA geometry being known from other crystal structures.

The side-chain and ring *D* torsion angles, together with  $\Delta$ , the phase angle of pseudorotation, and  $\varphi_m$ , the maximum angle of torsion (Altona, Geise & Romers, 1968), are reported in Table 2 according to the convention of Klyne & Prelog (1960). The side-chain dihedral angles are similar to those of the orthorhombic phases and, in particular, C(17)–C(20)–C(22)–C(23) differs from those of the hexagonal phases. In this case also the carboxyl groups do not give rise to the best van der Waals energy (Giglio & Quagliata, 1975) and their orientations are mainly controlled by the ability to form hydrogen bonds.

The *D* rings approach the half-chair form coupled with the *gauche* side-chain conformation of the orthorhombic phases.

The molecular packing, shown in Fig. 2, is characterized by an assembly of wavy bilayers, extended into

the *ab* plane. A bilayer is generated from the adjacent ones by the  $4_1$  axis. The packing mode of the bilayers does not give rise to empty canals as in the orthorhombic phases and accounts for the relationships occurring between tetragonal and orthorhombic cell constants:  $a_{\text{tetr}} \sim 2c_{\text{orth}}$ ;  $b_{\text{tetr}} \sim b_{\text{orth}}$ ;  $c_{\text{tetr}} \sim 2a_{\text{orth}}$ . The structure of a bilayer (Fig. 3) is supported by an efficient scheme of hydrogen bonds which are the driving force in the double-layer formation (Table 3). The surfaces of both sides of the bilayer are hydrophobic with the methyl groups protruding outward. A monolayer is composed of rows of DCA molecules, linked in each row by head-to-tail hydrogen bonds involving O(27) or O(55) and O(25) or O(53) of two consecutive molecules. In a monolayer each row is intermediate between two rows, about 7 Å from it, to which it is connected by hydrogen bonds in a different way by means of DCA's, belonging to the other monolayer, ethanol and water molecules (Fig. 3). The guest molecules are placed in canals, running inside the bilayers, with sections approximately rectangular in shape and with interior surfaces covered mainly by hydrophilic groups.

The rows of two monolayers face each other and are at about the same *a* height in the case of the bilayer of Fig. 3, at variance with the situation in the orthorhombic phases where the two monolayers are shifted by  $\sim 3.6$  Å.

Table 3. O...O distances (Å) concerning the hydrogen bonds in a bilayer

The e.s.d.'s lie within the range 0.015–0.024 Å.

O(25)...O(26 <sup>I</sup> )	2.69	O(53)...O(55 <sup>II</sup> )	2.80
O(25)...O(27 <sup>II</sup> )	2.72	O(53)...O(58 <sup>IV</sup> )	2.67
O(26)...O(56)	2.59	O(54)...O(57)	2.76
O(28)...O(54 <sup>III</sup> )	2.64	O(57)...O(58)	2.50

Symmetry code

- |      |                                                      |       |                                                     |
|------|------------------------------------------------------|-------|-----------------------------------------------------|
| (i)  | $-\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{2} - z$ | (iii) | $x, -1 + y, z$                                      |
| (ii) | $x, 1 + y, z$                                        | (iv)  | $\frac{1}{2} - x, \frac{1}{2} + y, \frac{1}{4} - z$ |

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34629 (14 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

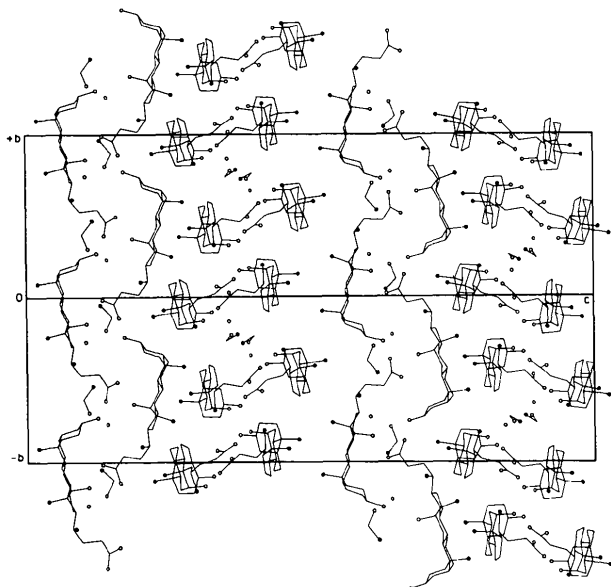


Fig. 2. A partial view of the crystal packing of DCAETW along *a*. Filled and open circles represent methyl groups and O atoms respectively. No hydrogen bonds are shown.

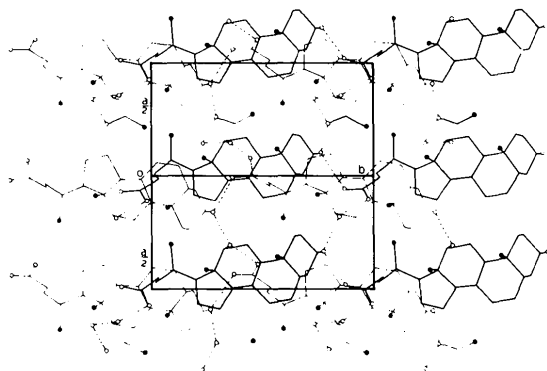


Fig. 3. A view of a bilayer along *c*. The symbols have the same meaning as in Fig. 2. Broken lines indicate hydrogen bonding.

Weak van der Waals interactions are present among bilayers since the interatomic distances are greater than the sum of the van der Waals radii of the atoms concerned.

AD and EG thank the Consiglio Nazionale delle Ricerche for financial support.

#### References

- ALTONA, C., GEISE, H. J. & ROMERS, C. (1968). *Tetrahedron*, **24**, 13–32.
- AZAROFF, L. V. (1955). *Acta Cryst.* **8**, 701–704.
- BONAMICO, M. & GIACOMELLO, G. (1962). *Gazz. Chim. Ital.* **92**, 647–650.
- CANDELORO DE SANCTIS, S., COIRO, V. M., GIGLIO, E., PAGLIUCA, S., PAVEL, N. V. & QUAGLIATA, C. (1978). *Acta Cryst.* **B34**, 1928–1933.
- CANDELORO DE SANCTIS, S., GIGLIO, E., PAVEL, N. V. & QUAGLIATA, C. (1972). *Acta Cryst.* **B28**, 3656–3661.
- CANDELORO DE SANCTIS, S., GIGLIO, E., PETRI, F. & QUAGLIATA, C. (1979). *Acta Cryst.* **B35**, 226–228.
- CRAVEN, B. M. & DETITTA, G. T. (1972). *Chem. Commun.* pp. 530–531.
- CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* **A24**, 321–324.
- DOMENICANO, A., SPAGNA, R. & VACIAGO, A. (1969). *Atti Accad. Naz. Lincei Cl. Sci. Fis. Mat. Nat. Rend.* **47**, 331–336.
- FRIEDMAN, N., LAHAV, M., LEISEROWITZ, L., POPOVITZ-BIRO, R., TANG, C. P. & ZARETZKII, Z. (1975). *Chem. Commun.* pp. 864–865.
- GIGLIO, E. & QUAGLIATA, C. (1975). *Acta Cryst.* **B31**, 743–746.
- HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040–1044.
- KLYNE, W. & PRELOG, V. (1960). *Experientia*, **16**, 521–523.
- LAHAV, M., LEISEROWITZ, L., POPOVITZ-BIRO, R. & TANG, C. P. (1978). *J. Am. Chem. Soc.* **100**, 2542–2544.
- LAHAV, M., LEISEROWITZ, L. & TANG, C. P. (1977). Private communication.
- LAHAV, M., POPOVITZ-BIRO, R., TANG, C. P. & LEISEROWITZ, L. (1977). Fourth European Crystallographic Meeting, Abstract PII 136, p. 688.
- MAIN, P., WOOLFSON, M. M., LESSINGER, L., GERMAIN, G. & DECLERCQ, J. P. (1974). *MULTAN 74. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.