Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

(+)-3,12-Dioxo-5β-cholanic acid: hydrogen bonding in a diketo bile-acid derivative

Elizabeth M. Kikolski, Mark Davison, Roger A. Lalancette* and Hugh W. Thompson

Carl A. Olson Memorial Laboratories, Department of Chemistry, Rutgers University, Newark, NJ 07102, USA

Correspondence e-mail: rogerlal@andromeda.rutgers.edu

Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.002 Å
R factor = 0.028
wR factor = 0.072
Data-to-parameter ratio = 11.3

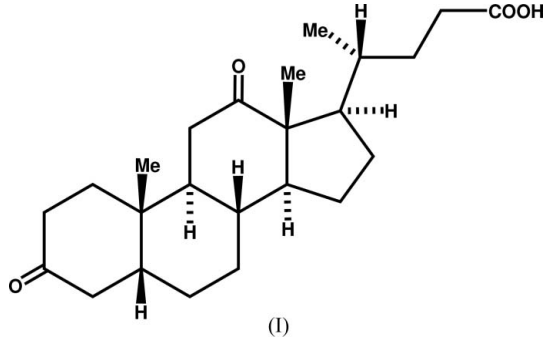
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 24 May 2006
Accepted 25 May 2006

The asymmetric unit of the title crystal structure, $C_{24}H_{36}O_4$, contains two independent molecules, differing only in their side-chain conformations and linked though O—H···O hydrogen bonds by carboxyl pairing [O···O = 2.6715 (17) and 2.6544 (17) Å; O—H···O = 170 and 179°]. Six intermolecular C—H···O=C close contacts were found.

Comment

The title compound, (I), supplements our previous reports on solid-state hydrogen bonding in diketo acids related to the bile acids (Thompson *et al.*, 2001; Kikolski, Lalancette *et al.*, 2006) and similar steroidal compounds (Newman *et al.*, 2002; Lalancette & Thompson, 2003; Kikolski, Thompson *et al.*, 2006) The natural bile acids are distinguished by an acid in the C17 side-chain, a *cis AB* ring junction and oxygenation at the 3-position; many are also oxygenated at the 6-, 7- and/or 12-positions. This ring oxygenation typically involves hydroxyl groups, but a few natural bile acids contain ketone functions as well (Fieser & Fieser, 1959). Major amounts of these acids appear in various combinations in vertebrate bile, where they function as surfactants, and are isolable directly from gall bladders. Compound (I), which is not known to occur naturally, was synthesized (*Experimental*) by oxidation of deoxycholic acid, present in human bile.



(I)

Fig. 1 shows the asymmetric unit of (I), consisting of two independent molecules, designated (I*A*) and (I*B*), which have significant conformational differences only toward the end of the five-C-atom acid chain attached at C17. Both molecules have staggered/*anti* conformational arrangements about the C20—C22 bond, but only (I*A*) also has an *anti* conformation about C22—C23, whose torsion angle (C20—C22—C23—C24) is 177.34 (14)°. In (I*B*), this torsion angle is 62.2 (2)°, corresponding to a *gauche* conformation. This is possible principally because the planar hybridization at C24 allows the carboxyl group to adopt a rotational conformation that

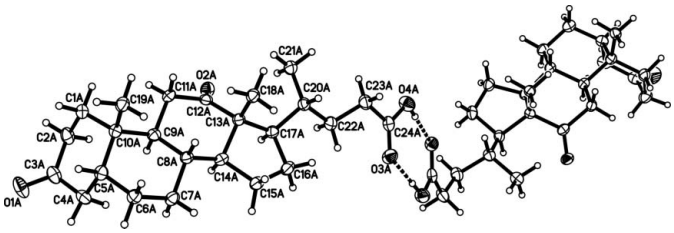


Figure 1
The dimerically linked asymmetric unit for (I), whose two identically numbered molecules differ significantly only in their side-chain conformations. Displacement ellipsoids are drawn at the 50% probability level. Dashed lines indicate hydrogen bonds.

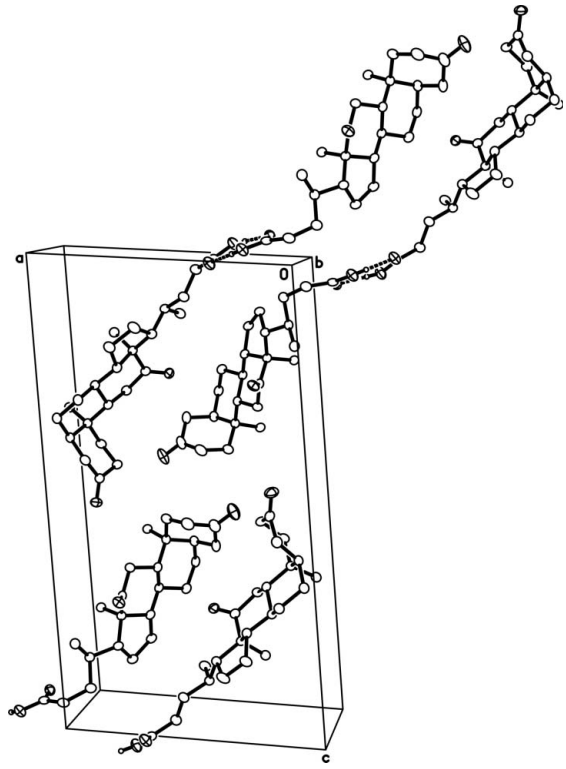


Figure 2
A partial packing diagram. For clarity, all carbon-bound H atoms have been omitted. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen bonds are shown as dashed lines.

minimizes interactions with C20 and its substituents. Thus, (I*A*) and (I*B*) also differ in the conformations of their carboxyl groups; the O3—C24—C23—C22 torsion angle is −30.8 (2)° for (I*A*) and 6.8 (2)° for (I*B*). Superimposition of truncated molecules of (I*A*) and (I*B*) lacking the carboxyl group (C24) and with all H atoms removed shows negligible differences, with an r.m.s. deviation of less than 0.118 Å.

Although not observed in other hydrogen-bonding modes, full or partial averaging of carboxyl C—O bond lengths and C—C—O angles by disorder is often seen in dimeric acids. However, both carboxyl groups in (I) show negligible disordering (Table 1). The absence of any element of symmetry in the dimer is a phenomenon much more commonly encountered in chiral non-racemic cases, such as (I), than where centrosymmetry is possible (Gavezzotti & Filippini, 1994; Allen *et al.*, 1999; Sørensen & Larsen, 2003).

Fig. 2 illustrates the packing in the unit cell. Six intermolecular C—H···O═C close contacts exist (Table 2) within the 2.7 Å range we employ as standard for such non-bonded C—H···O packing interactions (Steiner, 1997).

Experimental

Deoxycholic (3α,12α-dihydroxy-5β-cholanic) acid, obtainable from the bile of numerous mammalian species, including man, was purchased from Acros Organics/Fisher Scientific, Springfield, NJ, USA. It was dissolved in acetone and subjected to Jones oxidation, yielding (I) . The crystal used was obtained by slow evaporation of an acetone solution (m.p. 464 K). The sign of rotation for (I) is that assigned by Gauthier & Quy (1947), and its absolute stereochemistry, confirmed by its Flack (1983) parameter, conforms to that of other steroids (Fieser & Fieser, 1959; Klyne & Buckingham, 1978). The solid-state (KBr) IR spectrum of (I) has a single broad combined C═O absorption centered at 1706 cm^{-1}, which appears at 1705 cm^{-1} in $CHCl_3$.

Crystal data

$C_{24}H_{36}O_4$
M_r = 388.53
Monoclinic, $P2_1$
a = 12.9462 (3) Å
b = 7.0036 (1) Å
c = 23.5856 (5) Å
β = 96.163 (1)°
V = 2126.15 (7) Å^3
Z = 4
D_x = 1.214 Mg m^{-3}
Cu $K\alpha$ radiation
μ = 0.64 mm^{-1}
T = 100 (2) K
Plate, colorless
0.32 × 0.24 × 0.05 mm

Data collection

Bruker SMART CCD APEX-II area-detector diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Blessing, 1995)
T_{min} = 0.823, T_{max} = 0.969
12746 measured reflections
5723 independent reflections
5594 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 62.6°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.028
$wR(F^2)$ = 0.072
S = 1.03
5723 reflections
508 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.039P)^2 + 0.4209P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.15 e Å^{-3}
$\Delta\rho_{min}$ = −0.14 e Å^{-3}
Extinction correction: *SHELXL97*
Extinction coefficient: 0.00065 (13)
Absolute structure: Flack (1983), 2023 Friedel pairs
Flack parameter: 0.01 (12)

Table 1
Selected geometric parameters (Å, °).

O3*A*—C24*A*	1.220 (2)	O4*A*—C24*A*	1.313 (2)
O3*B*—C24*B*	1.216 (2)	O4*B*—C24*B*	1.320 (2)
O3*A*—C24*A*—C23*A*	123.23 (15)	O3*B*—C24*B*—C23*B*	124.51 (16)
O4*A*—C24*A*—C23*A*	113.76 (16)	O4*B*—C24*B*—C23*B*	112.53 (16)

Table 2
Hydrogen-bond and close-contact geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O4A—H4AC···O3B	0.84	1.84	2.6715 (17)	170
O4B—H4BC···O3A	0.84	1.81	2.6544 (17)	179
C1A—H1AA···O1A^{i}	0.99	2.65	3.562 (2)	154
C19A—H19A···O1A^{i}	0.98	2.53	3.419 (2)	151
C19B—H19E···O2B^{ii}	0.98	2.65	3.632 (2)	178
C8B—H8BA···O2B^{ii}	1.00	2.60	3.400 (2)	136
C6B—H6BA···O2B^{ii}	0.99	2.49	3.311 (2)	140
C23B—H23C···O3B^{iii}	0.99	2.38	3.327 (2)	159

Symmetry codes: (i) $-x+2, y+\frac{1}{2}, -z+1$; (ii) $x, y+1, z$; (iii) $-x, y-\frac{1}{2}, -z$.

All H atoms for (I) were found in electron density difference maps. The hydroxyl H atoms were constrained to idealized positions with distances fixed at 0.84 Å and U_{iso}(H) = 1.5U_{eq}(O). The methyl H atoms were placed in ideally staggered positions with C—H distances of 0.98 Å and U_{iso}(H) = 1.5U_{eq}(C). The methylene and methine H atoms were placed in geometrically idealized positions and constrained to ride on their parent C atoms with C—H distances of 0.99 and 1.00 Å, respectively, and U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT-Plus* (Bruker, 2000); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2000); software used to prepare material for publication: *SHELXTL*.

MD and HWT are grateful to the Rutgers Undergraduate Research Support program for financial support. HWT is grateful to Professor Gree Loober Spoog for helpful consultations.

References

Allen, F. H., Motherwell, W. D. S., Raithby, P. R., Shields, G. P. & Taylor, R. (1999). *New J. Chem.* **23**, 25–34.
Blessing, R. H. (1995). *Acta Cryst.* A**51**, 33–38.
Bruker (2000). *SHELXTL* (Version 6.10), *SMART WNT/2000* (Version 5.622) and *SAINT-Plus* (Version 6.02). Bruker AXS Inc., Madison, Wisconsin, USA.
Fieser, L. F. & Fieser, M. (1959). *Steroids*, ch. 3, 10, 14. New York: Reinhold.
Flack, H. D. (1983). *Acta Cryst.* A**39**, 876–881.
Gauthier, B. & Quy, N. H. (1947). *Ann. Pharm. Fr.* **5**, 556–569.
Gavezzotti, A. & Filippini, G. (1994). *J. Phys. Chem.* **98**, 4831–4837.
Kikolski, E. M., Lalancette, R. A. & Thompson, H. W. (2006). *Acta Cryst.* C**62**. In the press.
Kikolski, E. M., Thompson, H. W. & Lalancette, R. A. (2006). *Acta Cryst.* C**62**. In the press.
Klyne, W. & Buckingham, J. (1978). *Atlas of Stereochemistry: Absolute Configurations of Organic Molecules*, 2nd ed., Vol. 1, pp. 121–126. New York: Oxford University Press.
Lalancette, R. A. & Thompson, H. W. (2003). *Acta Cryst.* C**59**, o274–o276.
Newman, J. M., Lalancette, R. A. & Thompson, H. W. (2002). *Acta Cryst.* C**58**, o402–o404.
Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. Release, 97-2. University of Göttingen, Germany.
Sørensen, H. O. & Larsen, S. (2003). *Acta Cryst.* B**59**, 132–140.
Steiner, T. (1997). *Chem. Commun.* pp. 727–734.
Thompson, H. W., Lalancette, R. A. & Brunskill, A. P. J. (2001). *Acta Cryst.* C**57**, 632–633.