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3β,7α,12α-Triformyloxy-24-nor-5β-chol-22-ene

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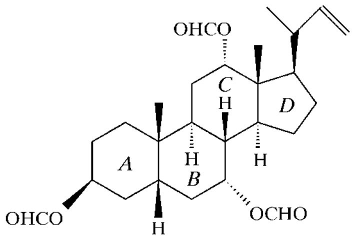
The title compound, alternatively called 24-nor-5β-chol-22-ene-3β,7α,12α-triyl triformate, $C_{26}H_{38}O_6$, has a *cis* junction between two of the six-membered rings. All three of the six-membered rings have chair conformations that are slightly flattened and the five-membered ring has a 13β,14α-half-chair conformation. The 3β, 7α and 12α ring substituents are axial and the 17β group is equatorial. The 3β-formyloxy group is involved in one weak intermolecular C—H···O bond, which links the molecules into dimers in a head-to-head fashion.

Comment

The bile acids, such as cholic acid, have proved particularly useful as 'engineering components' for supramolecular chemistry (Davis, 1993). The size, chirality and rigid polycyclic framework of a steroid-based synthetic receptor confers on it a high degree of preorganization. An examination of the structures of synthetic receptors and their synthetic intermediates, on a crystallographic basis, could help to improve our understanding of molecular-recognition principles. In an attempt to construct a steroid-based synthetic receptor, the title compound, (I), has been synthesized as an intermediate according to the method reported by Davis & Walsh (1996), although different reactions have been used, as described in the *Experimental* section. This cholic acid derivative, without the C(24)OOH group in the 17β side chain, contains three formyloxy groups with a 3β,7α,12α configuration. Cholic and deoxycholic acids provide tunnel-like spaces, reported as a channel-like inclusion ability (Jones & Nassimbeni, 1990; Miki *et al.*, 1990), in which guest molecules can be accommodated. Examination of the crystal structure of (I) shows no guest molecules and a small solvent-accessible volume (*i.e.* 4 × 15 Å^3).

An *ORTEP*II (Johnson, 1976) plot of (I) is shown in Fig. 1. Bond lengths and angles are within the expected ranges (Allen *et al.*, 1987), the mean O—Csp^3, O—Csp^2 and O═Csp^2 distances being 1.467 (3), 1.331 (3) and 1.189 (2) Å in the three formyloxy groups, and the mean Csp^3—Csp^2 and Csp^2═Csp^2 distances being 1.503 (3) and 1.304 (4) Å in the 17β group. The distance between the terminal atoms O31 and C23 is 13.275 (4) Å and the C19—C10···C13—C18 pseudo-torsion angle is 3.0 (2)°. The *A*/*B* ring junction is 5β,10β-*cis* [C1—C10—C5—C4 = 51.3 (3)° and C9—C10—C5—C6 = 55.1 (2)°]. The angle between ring *A* and the least-squares plane that includes the atoms of rings *B*, *C* and *D* is 63.16 (5)°. Rings *A*, *B* and *C* have slightly flattened chair conformations, with average torsion angles of 52.6 (7), 52.0 (14) and 55.0 (16)°, respectively, as shown by the values of the θ puckering parameter [Cremer & Pople, 1975; Boeyens, 1978; 177.0 (3), 8.0 (2) and 6.6 (2)° for *A*, *B* and *C*]. The five-membered ring *D* assumes a 13β,14α-half-chair conformation [puckering parameters, calculated using the atom sequence C13–C17: q_2 = 0.461 (2) Å and φ_2 = 195.4 (3)°; pseudo-rotation (Altona *et al.*, 1968) and asymmetry parameters: Δ = −3.8 (2)°, φ_m = 46.8 (1)°, $\Delta C_s(13)$ = 16.0 (2)°, $\Delta C_s(14)$ = 19.4 (2)° and $\Delta C_2(13,14)$ = 2.7 (2)°]. This unusual ring conformation is different from that observed in cholic acid (Jones & Nassimbeni, 1990). The three 3β,7α,12α-ring substituents are axial (Luger & Bulow, 1983), with angles of 6.3 (2), 9.9 (1) and 4.6 (1)°, respectively. The angle between the planes defined by the 3β group and ring *A* is 80.5 (2)°, and the angles between the planes of the 7α and 12α groups and the mean plane of rings *B*, *C* and *D* are 85.6 (3) and 89.6 (2)°. The 17β chain is equatorial. The orientation of the C5–C17 reference plane relative to the C17/C20/C21 and C20/C22/C23 least-squares planes is 19.54 (19) and 77.30 (19)°, respectively, with the angle between these two planes being 85.0 (2)°. By comparison with the structure of cholic acid (Jones & Nassimbeni, 1990; Miki *et al.*, 1990), the absence of the COOH group in the side chain attached to atom C17 may be responsible for the unusual values of the C17—C20—C22—C23 and C21—C20—C22—C23 torsion angles [−109.7 (3) and 126.7 (3)°], corresponding to −*ac* and +*ac* descriptors, respectively, instead of −*ap* and +*sc*.



(I)

The crystal structure contains no classical hydrogen bonds and thus cohesion of the structure is mainly achieved by van der Waals interactions and weak C—H···O interactions. Four intramolecular C—H···O short contacts are present; the C4—H4*A*···O7 interaction is probably a destabilizing interaction, while the other three may be qualified as weak hydrogen

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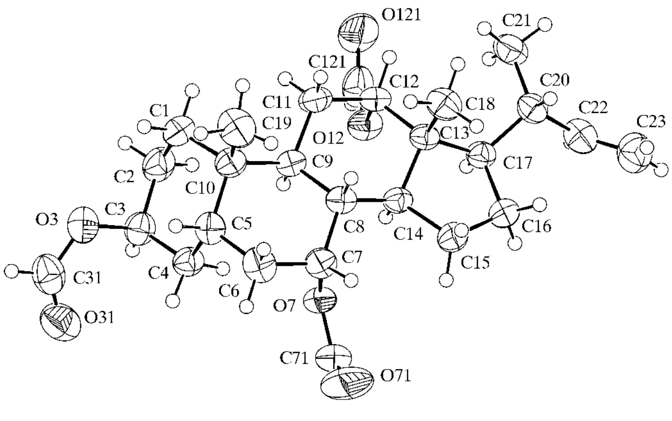

Figure 1
The molecular structure of (I), showing the atomic numbering scheme.

bonds, with distances and angles in the ranges 2.750 (3)–2.929 (2) Å and 102–108°, respectively (Table 1). An intermolecular C31—H31···O31^{i} interaction [symmetry code: (i) $x - \frac{1}{2}, \frac{1}{2} - y, 1 - z$] is also present, linking the molecules head-to-head into dimers in a head-to-head fashion.

Experimental

The title compound was prepared according to previously described procedures, starting from formylation of cholic acid (Tserng & Klein, 1977) with formic and perchloric acids, followed by oxidative decarboxylation (Concépcion *et al.*, 1986) with iodosobenzene diacetate, selective 3α-deformylation with sodium acetate in methanol, and finally a C-3 Mitsunobu inversion (Bose *et al.*, 1973) with formate, diethyl azodicarboxylate and triphenylphosphine. Crystals suitable for X-ray analysis were obtained from an ethyl acetate solution by slow evaporation. ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (1H, *s*), 8.09 (1H, *s*), 8.05 (1H, *s*), 5.67–5.55 (1H, *m*), 5.27 (1H, *br t*), 5.16 (1H, *br s*), 5.07 (1H, *d*, *J* = 2.4 Hz), 4.91 (1H, *dd*, *J* = 17.1, 1.8 Hz), 4.83 (1H, *dd*, *J* = 10.2, 1.8 Hz), 0.98 (3H, *s*), 0.95 (3H, *d*, *J* = 6.6 Hz), 0.78 (3H, *s*); ^{13}C NMR (75.25 MHz, $CDCl_3$): δ 160.7, 160.5, 144.2, 112.3, 75.2, 71.0, 70.1, 46.8, 45.0, 43.0, 40.5, 37.7, 36.3, 34.5, 32.7, 30.9, 30.1, 28.1, 27.3, 25.8, 24.7, 22.7, 19.5, 12.3.

Crystal data

$C_{26}H_{38}O_6$
$M_r = 446.56$
Orthorhombic, $P2_12_12_1$
$a = 7.365$ (3) Å
$b = 15.5549$ (12) Å
$c = 21.199$ (4) Å
$V = 2428.6$ (10) Å^3
$Z = 4$
$D_x = 1.221$ Mg m^{-3}

Cu *Kα* radiation
Cell parameters from 25 reflections
$\theta = 22.7$–28.7°
$\mu = 0.69$ mm^{-1}
$T = 293$ (2) K
Prism, colourless
0.37 × 0.24 × 0.24 mm

Data collection

Nonius MACH3 diffractometer
ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
$T_{min} = 0.744$, $T_{max} = 0.847$
4523 measured reflections
2731 independent reflections
2293 reflections with $I > 2\sigma(I)$

$R_{int} = 0.031$
$\theta_{max} = 71.9°$
$h = 0 \rightarrow 9$
$k = 0 \rightarrow 19$
$l = -26 \rightarrow 26$
3 standard reflections every 200 reflections intensity decay: 9.9%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.035$
$wR(F^2) = 0.101$
$S = 1.03$
2731 reflections
292 parameters
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0653P)^2 + 0.1429P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.15$ e Å^{-3}
$\Delta\rho_{min} = -0.13$ e Å^{-3}

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C4—H4*A*···O7	0.97	2.35	3.029 (3)	126
C12—H12···O121	0.98	2.37	2.750 (3)	102
C14—H14···O12	0.98	2.53	2.929 (2)	104
C17—H17···O12	0.98	2.43	2.890 (3)	108
C31—H31···O31^{i}	0.93	2.49	3.396 (4)	166

Symmetry code: (i) $x - \frac{1}{2}, \frac{1}{2} - y, 1 - z$.

Friedel pairs were merged because the anomalous dispersion of the light atoms at the Cu *Kα* wavelength was negligible, and thus the absolute configuration was not determined from the X-ray data. However, the configuration was known from the synthesis route.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *PLATON* (Spek, 2003); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1674). Services for accessing these data are described at the back of the journal.

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