Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

(+)-3-Oxo-4-pregnene-20*β*-carboxylic acid: catemeric hydrogen bonding in a steroidal keto acid

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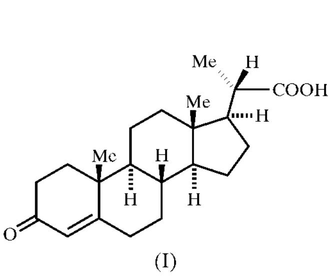
Received 28 September 2001
Accepted 2 November 2001
Online 14 December 2001

The title keto acid, (+)-23,24-dinor-3-oxochol-4-en-22-oic acid, $C_{22}H_{32}O_3$, forms carboxyl-to-ketone hydrogen-bonding catemers [O···O = 2.699 (4) Å and O—H···O = 173°], linking molecules screw-related in *b*. The four molecules in the cell form two parallel counter-directional chains, screw-related in *a*. Intermolecular C—H···O═C close contacts to different neighboring molecules were found for the ketone and the acid.

Comment

Our interest in the crystal structures of keto-carboxylic acids concerns the molecular characteristics that control their five known hydrogen-bonding patterns. The acid dimers that characterize functionally unelaborated acids also predominate generally in keto acids. However, in non-racemates with significant conformational restrictions, the prevalence of acid-to-ketone catemers rises dramatically (Brunskill *et al.*, 1999). Consequently, we have sought subject materials with terpenoid origins, and now report the crystal structure and hydrogen-bonding behavior of (I), the seventh in our series of steroidal keto acids.



(I)

Fig. 1 shows the asymmetric unit of (I) with its steroid numbering. Among the few conformational options present, the substituents at C20, which has the *S* configuration, are staggered with respect to those at C17, so that the C16—C17—C20—C21 torsion angle is 176.8 (3)°. The carboxyl plane coincides approximately with the C20—H20 bond, but the carboxyl group is turned with its carbonyl group toward the bottom (*α*) face of the molecule [torsion angle C17—C20—C22—O2 = 73.8 (6)°]. In both of the steroids we have previously examined having this 23,24-dinor-22-oic acid side chain, the hydrogen-bonding patterns are very different from that in (I), and in both, the carboxyl carbonyl group is oriented *β* (Lalancette *et al.*, 1998; Thompson *et al.*, 1999).

Complete or partial averaging of carboxyl C—O bond lengths and C—C—O angles by disorder is frequent in hydrogen-bonding dimers (Leiserowitz, 1976). However, catemers, hydrates and other hydrogen-bonding structures whose geometry precludes the usual carboxyl-disordering processes are highly ordered, as is found here. Our own survey of 56 keto acid structures which are not acid dimers gives average values of 1.20 (1) and 1.32 (2) Å, and 124.5 (14) and 112.7 (17)° for these lengths and angles, respectively, in accord with typical values of 1.21/1.31 Å and 123/112°, respectively, cited for highly ordered dimeric carboxyls (Borthwick, 1980). In (I), these lengths and angles are 1.185 (5)/1.311 (5) Å and 124.3 (4)/113.1 (4)°, respectively. No disorder was detected in the three methyl groups (C18, C19 and C21), which all adopt staggered arrangements.

Fig. 2 shows the packing of the cell and illustrates the two parallel hydrogen-bonding catemers created by the acid-to-ketone hydrogen bonding among molecules screw-related in *b* [O···O = 2.699 (4) Å and O—H···O = 173°]. The two chains are screw-related in *a*, and lie with their long axes parallel, but with opposite end-to-end orientations. In spite of a relatively slight change in molecular shape, this is dramatically different from the case of the 5-*α*-dihydro analog, whose hydrogen bonding is of the acid-to-acid type (Lalancette *et al.*, 1998).

Within each molecule of (I), the dihedral angle between the carboxyl (C20/C22/O2/O3) and ketone (C2/C3/C4/O1) planes is 79.3 (2)°. However, for each hydrogen bond, the intermolecular dihedral angle between these two planes is 64.4 (3)°. We characterize the geometry of hydrogen bonding to carbonyls using a combination of the H···O═C angle and the H···O═C—C torsion angle. These describe the approach of the H atom to the O atom in terms of its deviation from, respectively, C═O axiality (ideal = 120°) and planarity with the carbonyl (ideal = 0°). In (I), these angles are 128 and −3°, respectively.

Intermolecular C—H···O═C close contacts to different neighboring molecules were found, involving O1 (2.69 Å to H21*A*) and O2 (2.64 Å to H6*B*). These distances lie within the 2.7 Å range we often employ for non-bonded C—H···O packing interactions (Steiner, 1997). Using compiled data for a

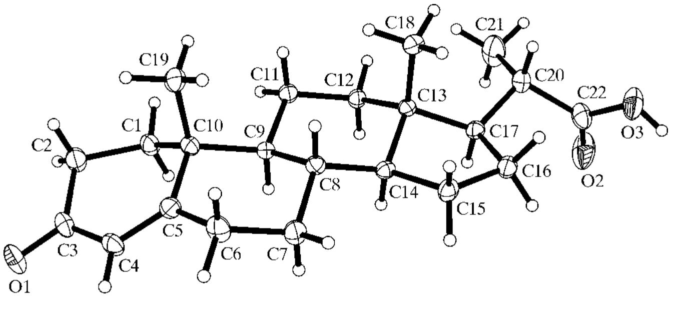


Figure 1
A view of compound (I) with its steroid numbering. Displacement ellipsoids are set at the 20% probability level.

DOI: 10.1107/S0108270101018601

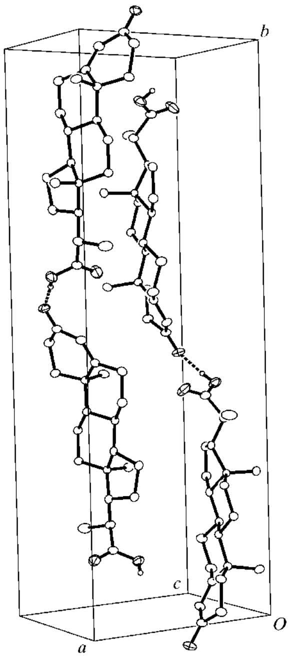


Figure 2
A packing diagram illustrating the screw-related parallel counter-directional pair of catemers passing through the cell in the *b* direction. All carbon-bound H atoms have been omitted for clarity. Displacement ellipsoids are set at the 20% probability level.

large number of such contacts, Steiner & Desiraju (1998) find significant statistical directionality even as far out as 3.0 Å, and conclude that these are legitimately viewed as 'weak hydrogen bonds', with a greater contribution to packing forces than simple van der Waals attractions.

We categorize subtypes of catemers by describing the relationship of adjacent molecules in the chains as homochiral (screw and translation) and heterochiral (glide). Among hydrogen-bonding catemers overall, the observed prevalence within the former grouping, appropriate to (I), is screw > translation; however, this is our first observation of a screw-related steroidal catemer. Among the six previous steroidal keto acids whose X-ray structures we have reported, all three of the cases displaying catemeric hydrogen bonding were translational.

The KBr IR spectrum of (I) displays C═O absorptions at 1723 (COOH) and 1649 cm^{-1} (ketone), consistent with known shifts produced when hydrogen bonding is removed from carboxyl C═O and added to a ketone, plus an alkene absorption at 1614 cm^{-1}. In $CHCl_3$ solution, where dimers predominate, these peaks appear, normally, at 1707 and 1660 cm^{-1}, with the C═C peak at 1614 cm^{-1} and a large carboxyl-dilution shoulder at *ca* 1732 cm^{-1}.

Experimental

Compound (I), of known absolute stereochemistry and rotation, was purchased from Steraloids Inc., Newport, RI, USA, and recrystallized from 95% ethanol (m.p. 532 K).

Crystal data

$C_{22}H_{32}O_3$
$M_r = 344.48$
Orthorhombic, $P2_12_12$
$a = 9.684$ (3) Å
$b = 27.325$ (7) Å
$c = 7.281$ (4) Å
$V = 1926.7$ (13) Å^3
$Z = 4$
$D_x = 1.188$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 2.4$–9.7°
$\mu = 0.08$ mm^{-1}
$T = 296$ (2) K
Hexagonal rod, colorless
0.31 × 0.15 × 0.10 mm

Data collection

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
Absorption correction: numerical (Sheldrick, 1997)
$T_{\min} = 0.98$, $T_{\max} = 0.99$
7753 measured reflections
1990 independent reflections
1453 reflections with $I > 2\sigma(I)$
$R_{\text{int}} = 0.072$
$\theta_{\max} = 25.0°$
$h = -11 \rightarrow 11$
$k = -32 \rightarrow 32$
$l = -8 \rightarrow 8$
3 standard reflections every 97 reflections intensity variation: <3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.114$
$S = 1.06$
1990 reflections
227 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0512P)^2 + 0.1332P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.04$
$\Delta\rho_{\max} = 0.15$ e Å^{-3}
$\Delta\rho_{\min} = -0.13$ e Å^{-3}
Extinction correction: *SHELXTL*
Extinction coefficient: 0.0048 (13)

Table 1
Selected geometric parameters (Å, °).

O2—C22	1.185 (5)	O3—C22	1.310 (5)
O2—C22—C20	124.3 (4)	O3—C22—C20	113.0 (4)
C16—C17—C20—C21	176.8 (3)	C17—C20—C22—O2	73.8 (6)

All H atoms were found in electron-density difference maps but were placed in calculated positions and allowed to refine as riding models. C—H distances were 0.93–0.98 Å, and the O—H group was constrained to be 0.82 Å. A torsional parameter was refined for each methyl group.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1353). Services for accessing these data are described at the back of the journal.

References

Borthwick, P. W. (1980). *Acta Cryst.* B**36**, 628–632.
Brunskill, A. P. J., Thompson, H. W. & Lalancette, R. A. (1999). *Acta Cryst.* C**55**, 566–568.
Lalancette, R. A., Thompson, H. W. & Brunskill, A. P. J. (1998). *Acta Cryst.* C**54**, 421–424.
Leiserowitz, L. (1976). *Acta Cryst.* B**32**, 775–802.
Sheldrick, G. M. (1997). *SHELXTL*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.
Siemens (1996). *XSCANS*. Version 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Steiner, T. (1997). *Chem. Commun.* pp. 727–734.
Steiner, T. & Desiraju, G. R. (1998). *Chem. Commun.* pp. 891–892.
Thompson, H. W., Brunskill, A. P. J. & Lalancette, R. A. (1999). *Acta Cryst.* C**55**, 1677–1680.