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(+)-3,11-Dioxoandrost-4-ene-17β-carboxylic acid: catemeric hydrogen bonding in a steroidal keto acid

Jacob M. Newman, 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

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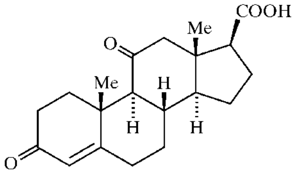
The title keto acid, $C_{20}H_{26}O_4$, forms carboxyl-to-ketone hydrogen-bonding catemers [O$\cdots$O = 2.653 (5) Å and O—H$\cdots$O = 172 (5)°], linking translationally related molecules *via* the *A*-ring ketone. The two molecules in the cell form two parallel counter-directional chains, screw-related in *b*. A total of four intermolecular C—H$\cdots$O═C close contacts was found, involving both ketone functions.

Comment

The single hydrogen-bonding donor and single acceptor of a carboxylic acid generate a high predominance of dimers in the absence of other functional groups. Our interest in the crystal structures of keto acids concerns the molecular characteristics that control their five known hydrogen-bonding patterns. While acid dimers also predominate generally in keto acids, in non-racemates with significant conformational restrictions, the prevalence of acid-to-ketone catemers rises dramatically (Brunskill *et al.*, 1999). In studying this, we have sought subject materials with terpenoid origins, and now report the crystal structure and hydrogen-bonding behavior of (+)-3,11-dioxo-androst-4-ene-17β-carboxylic acid, (I), the eighth in our series of steroidal keto acids.



(I)

Fig. 1 shows the asymmetric unit of (I) with the steroid numbering. Among the few conformational options, both methyl groups adopt the expected staggered arrangements and the carboxyl carbonyl group is turned toward atom C16 so that C16 lies near the carboxyl plane [torsion angle C16—C17—C20—O3 = −6.8 (5)°]. In both of the 17β-carboxy keto steroids we have previously examined, the carboxyl group is similarly oriented (Brunskill *et al.*, 1997; Thompson *et al.*, 1999).

Complete or partial averaging of carboxyl C—O bond lengths and C—C—O angles (Table 1) by disorder is common 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 survey of 56 keto acid structures which are not acid dimers gives average values of 1.20 (1)/1.32 (2) Å and 124.5 (14)/112.7 (17)° for these lengths and angles, respectively, in accord with typical values of 1.21/1.31 Å and 123/112° cited for highly ordered dimeric carboxyls (Borthwick, 1980). In (I), these lengths and angles are 1.192 (4)/1.311 (5) Å and 124.8 (4)/112.0 (3)°, respectively. No significant disorder was detected in either methyl group.

Fig. 2 shows the packing in the cell and illustrates the two parallel catemers created by the acid-to-ketone hydrogen bonding among translationally related molecules. This hydrogen bonding involves only the remote *A*-ring ketone. The conjugated ketone would be both the more basic and more sterically accessible of the two. However, the choice here may be dictated more by the forces directing the packing of the non-polar portions of these generally planar molecules than by any such competition. The two chains are screw-related in *b*, and lie with their long axes parallel, but with opposite end-to-end orientation. This arrangement is identical to that seen in 3-oxoandrosta-1,4-diene-17β-carboxylic acid (Thompson *et al.*, 1999), but differs markedly from that in 3-oxoandrost-4-ene-17β-carboxylic acid, whose chains diverge (Brunskill *et al.*, 1997).

We categorize subtypes of catemers by describing the relationship of adjacent molecules in the chains as homochiral (screw and translation) and heterochiral (glide). For hydrogen-bonding catemers overall, the observed prevalence within the former grouping, appropriate to (I), is screw > translation. Among the seven steroid keto acids whose X-ray structures we have previously reported, four cases displayed catemeric hydrogen bonding. Of these four, three were translational, including both 17β-carboxy keto steroids (Brunskill *et al.*, 1997; Thompson *et al.*, 1999), and one involved a screw relationship. Translational catemers are not

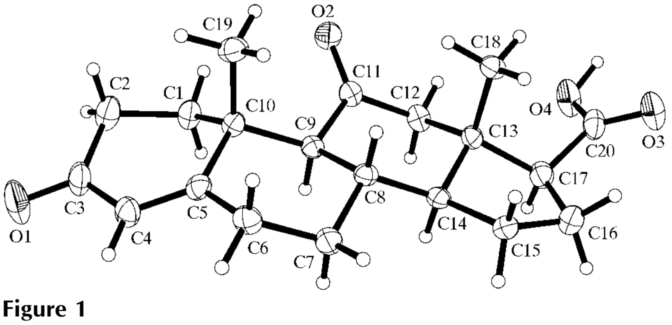


Figure 1
View of compound (I) with the steroid numbering. Displacement ellipsoids are set at the 20% probability level.

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constrained to follow any crystallographic axis. Although molecules of (I) are aligned generally lengthwise along the *c* axis, this does not correspond to the hydrogen-bonding axis, which follows the [101] direction.

For each hydrogen bond [O···O = 2.653 (5) Å and O—H···O angle = 172 (5)°], the dihedral angle between the carboxyl (C17/C20/O2/O3) and ketone (C2′/C3′/C4′/O1′) planes is 36.9 (2)°, which is identical to the intramolecular dihedral angle, since the chains are translational. In addition, 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 both C═O axiality (ideal = 120°) and planarity with the carbonyl (ideal = 0°). In (I), these angles are 136 (2) and −6 (3)°, respectively.

A total of four intermolecular C—H···O═C close contacts to neighboring molecules was found for both ketones (see Table 2), all lying within the 2.7 Å range we normally employ for non-bonded C—H···O packing interactions (Steiner, 1997). Using compiled data for a 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.

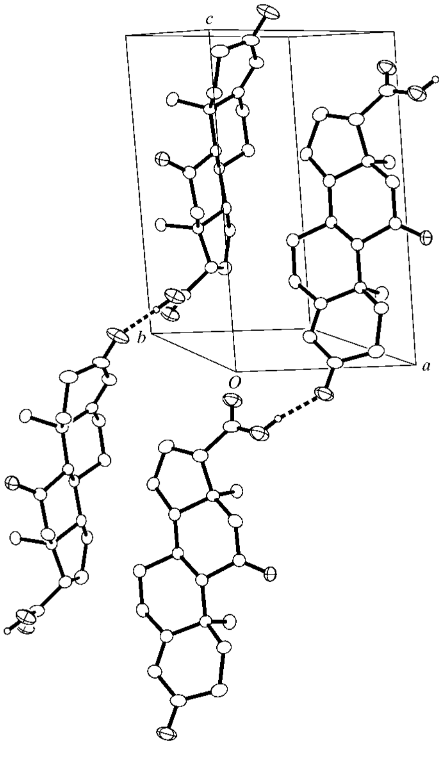

Figure 2
Packing diagram with extracellular molecules, included to illustrate the parallel screw-related pair of catemers passing counter-directionally through the cell. All C-bound H atoms have been removed for clarity. Displacement ellipsoids are set at the 20% probability level.

The KBr IR spectrum of (I) displays C═O absorptions at 1726 (COOH) and 1645 cm^{-1} (enone), consistent with known shifts produced when hydrogen bonding is, respectively, removed from carboxyl C═O and added to a ketone, plus a peak at 1704 cm^{-1} for the 11-oxo group. In $CHCl_3$ solution, where dimers predominate, the acid and 11-oxo absorptions merge into a single broad peak at 1705 cm^{-1}, with a carboxyl-dilution shoulder at *ca* 1745 cm^{-1}. The enone peak appears, normally, at 1664 cm^{-1}, revealing a C═C peak at 1616 cm^{-1}, seen in the KBr spectrum only as a slight shoulder.

Experimental

11β,21-Dihydroxy-4-pregnene-3,20-dione, of known absolute stereochemistry, was purchased from Steraloids Inc. (Newport, Rhode Island, USA) and was oxidatively cleaved by $NaIO_4$ in aqueous dioxane. Jones oxidation of the crude product provided compound (I), of known rotation (Mason *et al.*, 1937). Crystals suitable for X-ray analysis were obtained by recrystallization from acetone (m.p. 543 K).

Crystal data

$C_{20}H_{26}O_4$
$M_r = 330.41$
Monoclinic, $P2_1$
$a = 6.699$ (2) Å
$b = 11.409$ (3) Å
$c = 11.764$ (3) Å
$\beta = 94.98$ (2)°
$V = 895.7$ (4) Å^3
$Z = 2$
$D_x = 1.225$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 36 reflections
$\theta = 3.5$–11.3°
$\mu = 0.08$ mm^{-1}
$T = 296$ (2) K
Parallelepiped, colorless
0.38 × 0.27 × 0.14 mm

Data collection

Siemens *P*4 diffractometer
2θ/θ scans
Absorption correction: numerical (*SHELXTL*; Sheldrick, 1997)
$T_{\min} = 0.97$, $T_{\max} = 0.99$
3582 measured reflections
1657 independent reflections
1245 reflections with $I > 2\sigma(I)$
$R_{\mathrm{int}} = 0.057$
$\theta_{\max} = 25.0°$
$h = -7 \rightarrow 7$
$k = -13 \rightarrow 13$
$l = -13 \rightarrow 13$
3 standard reflections every 97 reflections intensity variation: <3.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.085$
$S = 1.07$
1658 reflections
222 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0103P)^2 + 0.0570P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.11$ e Å^{-3}
$\Delta\rho_{\min} = -0.11$ e Å^{-3}
Extinction correction: *SHELXTL*
Extinction coefficient: 0.0187 (17)

Table 1
Selected geometric parameters (Å, °).

O3—C20	1.192 (4)	O4—C20	1.311 (5)
O3—C20—C17	124.8 (4)	O4—C20—C17	112.0 (3)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O4—H4$\cdots$O1^{i}	1.01 (6)	1.65 (6)	2.653 (5)	172 (5)
C15—H15$B\cdots$O2^{ii}	0.97	2.57	3.514 (4)	165
C18—H18$C\cdots$O2^{ii}	0.96	2.65	3.546 (4)	156
C7—H7$B\cdots$O2^{iii}	0.97	2.69	3.656 (5)	172
C6—H6$B\cdots$O1^{iv}	0.97	2.64	3.373 (5)	133

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

All H atoms were found in electron-density difference maps but were placed in calculated positions and allowed to refine as riding models, except for the hydroxyl H atom, whose positional and displacement parameters were allowed to refine. The vinyl H atom was fixed at a distance of 0.93 Å, the methine H atoms at 0.98 Å, the methylene H atoms at 0.97 Å, and the methyl H atoms at 0.96 Å from their respective C atoms. The $U_{\rm iso}$ value for each methylene H atom was fixed at 120% of the anisotropic displacement parameter of its C atom and for each methyl H atom, at 150% of that of its C atom. The absolute configuration of (I) was not determined (see *Experimental*); Friedel pairs were averaged.

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*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1378). Services for accessing these data are described at the back of the journal.

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