

(+)-3,11-Dioxo-5 α -androstanecarboxylic acid: catemeric hydrogen bonding in a steroidal diketo acid

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The title compound, C₂₀H₂₈O₄, aggregates catemericly, with hydrogen-bonding links from each carboxylic acid group to the 3-oxo group in the *A* ring of a molecule translationally related in both the *a* and the *b* directions [$O\cdots O = 2.7537(18)$ Å and $O-H\cdots O = 162^\circ$]. The 11-oxo group in the *C* ring is not involved in the hydrogen bonding. A single intermolecular $C-H\cdots O$ close contact connects the carboxyl $C=O$ group to a methyl group on an adjacent molecule.

Comment

For our study of hydrogen-bonding modes in crystalline keto acids, steroid examples are of special value as molecularly rigid single enantiomers with the potential to bear multiple ketone receptors. The title compound, (I), supplements our previous reports on steroidal diketo acids (Thompson *et al.*, 2001; Lalancette & Thompson, 2003; Kikolski *et al.*, 2006). Compound (I) is distantly related to the surfactant steroidal acids isolatable from vertebrate bile, but is directly derived from (+)-3,11-dioxoandrost-4-ene-17 β -carboxylic acid, whose structure we have also published (Newman *et al.*, 2002) and which served as its synthetic source (see *Experimental*).

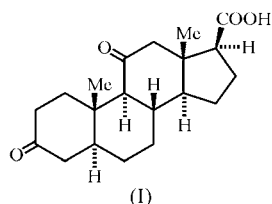


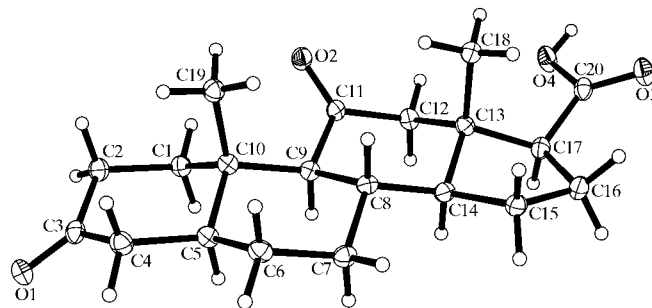
Fig. 1 shows the asymmetric unit for (I), which is conformationally rigid, with significant rotational options only at the carboxyl group attached at atom C17. The $O3-C20-C17-C16$ torsion angle is $5.3(3)^\circ$.

Full or partial averaging of $C-O$ bond lengths and $C-C-O$ angles by disorder is often seen in dimeric carboxylic acids, but not in other hydrogen-bonding modes, whose geometry cannot support the averaging mechanisms. Because (I) is

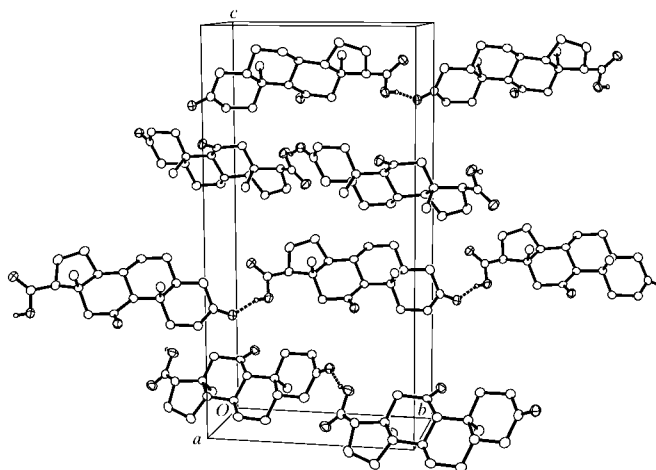
found to aggregate catemericly (see below), the values in (I) are comparable to those typical of highly ordered dimeric carboxyls (Borthwick, 1980) (see Table 1).

Fig. 2 shows the packing of the cell and includes extra molecules to illustrate the translational acid-to-ketone hydrogen-bonding scheme. Each carboxylic acid group is linked to the 3-oxo group in the *A* ring of a molecule translationally related in both the *a* and the *b* directions, with the *C*-ring oxo group not involved in the hydrogen bonding. Four hydrogen-bonding chains pass through the cell, the order of their directional alignments along *c* being $-a-b$, $+a-b$, $+a+b$, $-a+b$. Within the 2.7 Å range that we standardly survey for non-bonded $C-H\cdots O$ packing interactions (Steiner, 1997), a single 2.58 Å intermolecular close contact was found, connecting atom O3 with a C19 methyl H atom in a translationally related molecule (Table 2).

We characterize the geometry of hydrogen bonding to carbonyls using a combination of $H\cdots O=C$ angle and $H\cdots O=C-C$ torsion angle. These describe the approach of the acid H atom to the receptor O atom in terms of its deviation from, respectively, $C=O$ axially (ideal = 120°) and planarity with the carbonyl (ideal = 0°). In (I), these two angles are 136 and -2.3° .

**Figure 1**

The asymmetric unit for (I). Displacement ellipsoids are drawn at the 30% probability level.

**Figure 2**

A partial packing diagram, with extra molecules included to illustrate the translational acid-to-ketone hydrogen-bonding chains. For clarity, all C-bound H atoms have been omitted. Displacement ellipsoids are drawn at the 50% probability level.

There is a very strong similarity in both molecular shape and carboxyl conformation between (I) and the Δ^4 -enone from which it was derived (Newman *et al.*, 2002). The only significant difference appears to be the flattening that occurs in the enone around atoms C4 and C5 as a result of their sp^2 -hybridization. It is therefore not surprising that the two molecules aggregate similarly, *viz.* as translational catemers. Despite these similarities, the packing arrangements for the two compounds are quite different, with the enone crystallizing in a monoclinic cell ($P2_1$, $Z = 2$) and (I) crystallizing in an orthorhombic system ($P2_12_12_1$, $Z = 4$).

The solid-state (KBr) IR spectrum of (I) has $C=O$ absorptions at 1731 and 1704 cm^{-1} , with a peak separation typical of the shifts seen in catemers, due, respectively, to removal of hydrogen bonding from the acid $C=O$ group and addition of hydrogen bonding to the ketone. In $CHCl_3$ solution, where dimers predominate, these coalesce to a single peak at 1705 cm^{-1} .

Experimental

For the preparation of (I), (+)-3,11-dioxoandrost-4-ene-17 β -carboxylic acid, prepared as described by Newman *et al.* (2002), was hydrogenated in ethanol solution over a 5% Pd/C catalyst. Crystals suitable for X-ray analysis were obtained from ethyl acetate (m.p. 559 K, with decomposition, requiring that the apparatus be preheated to near the melting point before sample introduction).

Crystal data

$C_{20}H_{28}O_4$	$Z = 4$
$M_r = 332.42$	$D_x = 1.313 \text{ Mg m}^{-3}$
Orthorhombic, $P2_12_12_1$	Cu $K\alpha$ radiation
$a = 6.3684$ (1) \AA	$\mu = 0.72 \text{ mm}^{-1}$
$b = 11.6102$ (1) \AA	$T = 100$ (2) K
$c = 22.7430$ (2) \AA	Block, colorless
$V = 1681.58$ (3) \AA^3	$0.26 \times 0.18 \times 0.08 \text{ mm}$

Data collection

Bruker SMART CCD APEX-II area-detector diffractometer	8793 measured reflections
φ and ω scans	2741 independent reflections
Absorption correction: multi-scan (SADABS; Blessing, 1995)	2503 reflections with $I > 2\sigma(I)$
$T_{\min} = 0.833$, $T_{\max} = 0.947$	$R_{\text{int}} = 0.021$
	$\theta_{\text{max}} = 65.0^\circ$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0422P)^2 + 0.4552P]$
$R[F^2 > 2\sigma(F^2)] = 0.035$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.085$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.04$	$\Delta\rho_{\text{max}} = 0.22 \text{ e \AA}^{-3}$
2741 reflections	$\Delta\rho_{\text{min}} = -0.17 \text{ e \AA}^{-3}$
220 parameters	Absolute structure: Flack (1983)
H-atom parameters constrained	Flack parameter: 0.1 (2)

All H atoms were found in electron-density difference maps, but were placed in calculated positions and allowed to refine as riding on their respective C or O atoms. The O—H distance was fixed at 0.84 \AA ,

Table 1
Selected geometric parameters (\AA , $^\circ$).

O3—C20	1.201 (2)	O4—C20	1.338 (2)
O3—C20—C17	125.50 (19)	O4—C20—C17	111.61 (16)

Table 2
Hydrogen-bond geometry (\AA , $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O4—H4 \cdots O1 ⁱ	0.84	1.94	2.7537 (18)	162
C19—H19A \cdots O3 ⁱⁱ	0.98	2.58	3.518 (2)	159

Symmetry codes: (i) $x - 1, y - 1, z$; (ii) $x, y + 1, z$.

while methyl, methylene and methine C—H distances were fixed at 0.98, 0.99 and 1.00 \AA , respectively. The sign of rotation for (I) is that assigned by Mason *et al.* (1937) and its absolute stereochemistry, confirmed by its Flack parameter (based on 1081 Friedel pairs, 91.4% coverage), conforms to that of other steroids (Fieser & Fieser, 1959; Klyne & Buckingham, 1978).

Data collection: *SMART WNT/2000* (Bruker, 2000); cell refinement: *SMART WNT/2000*; data reduction: *SAINT-Plus* (Bruker, 2000); 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*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3023). Services for accessing these data are described at the back of the journal.

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