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(–)-2-(1,2,3,4,4a,5,6,7,8,8a*α*-Decahydro-4a*β*,8*α*-dimethyl-7-oxo-2*β*-naphthyl)propionic acid: catemeric hydrogen bonding in a bicyclic sesquiterpenoid *ζ*-keto acid

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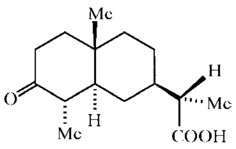
In the title compound, $C_{15}H_{24}O_3$, derived from a naturally occurring sesquiterpenoid, the asymmetric unit consists of two molecules differing by 167.4 (8)° in the rotational conformation of the carboxyl group. Each molecule aggregates separately with its own type as carboxyl-to-ketone hydrogen-bonding catemers [O···O = 2.715 (6) and 2.772 (6) Å, and O—H···O = 169 and 168°]. This generates two crystallographically independent single-strand hydrogen-bonding helices passing through the cell in the *b* direction, with opposite end-to-end orientations. One intermolecular C—H···O=C close contact exists for the carboxyl group of one of the molecules. The structure is isostructural with that of a closely related unsaturated keto acid reported previously.

Comment

Our crystallographic study of keto acids explores the molecular characteristics that control their hydrogen-bonding modes. As we have illustrated previously, carboxyl dimerization is the most common hydrogen-bonding pattern for achiral molecules and racemates, but is suppressed whenever centrosymmetry is precluded (Lalancette *et al.*, 1998). In chiral non-racemates then, formation of acid-to-ketone chains becomes the dominant hydrogen-bonding mode (Brunskill *et al.*, 1997). The title compound, (I), derived from an anthelmintic sesquiterpenoid isolated from *Artemisia*, is a bicyclic *ζ*-keto acid present as a single enantiomer. We have previously described the structures and hydrogen-bonding behaviors of two unsaturated keto acids related to (I), both of which were found to display catemeric acid-to-ketone hydrogen bonding (Brunskill *et al.*, 2001, 2002). We now report that the same hydrogen-bonding mode is adopted in the solid state by (I), and that (I) is isostructural with one of the above cited compounds [Cambridge Structural Database (Allen, 2002), reference code AFUVEC (Brunskill *et al.*, 2002)].

Fig. 1 shows the asymmetric unit of (I), which, as in the case of AFUVEC, consists of two molecules, (I*A*) and (I*B*), the difference between which lies principally in the rotation of the carboxyl group about the C9—C10 bond. In both (I*A*) and (I*B*), the substituents at C9, which have the *S* configuration, are staggered with respect to those at C2, so that the methyl group is *anti* to C1; the C11—C9—C2—C1 torsion angle is 179.9 (5)° in (I*A*) and 175.0 (5)° in (I*B*), a difference of only 4.9 (7)°. However, in (I*A*), the carboxyl group is rotated so that its C=O group is turned toward the molecular face bearing the angular methyl group (C13), a *cisoid* arrangement, in which the O3—C10—C9—C2 torsion angle is 72.4 (6)°, while in (I*B*), this relationship is *transoid* and the corresponding angle is −120.2 (5)°, a difference of 167.4 (8)°. An alternative measure of the conformation of the carboxyl group is provided by the dihedral angle for the O2/O3/C10/C9 carboxyl plane relative to the C10/C9/C2 plane, which is 72.9 (4)° for (I*A*) and 58.7 (4)° for (I*B*), a difference of 14.2 (6)°. Despite this, the intramolecular ketone *versus* carboxyl dihedral angles for (I*A*) and (I*B*) differ by 26.1 (5)°. The apparent discrepancies among these various measures of carboxyl conformation arise in part because of the above-mentioned differential staggering around C9—C2, and in part because of significant flattening in the ketone ring in the case of (I*A*). This flattening is revealed in the dihedral angles for the plane of the ketone *versus* that for the adjacent portion of the ketone ring (O1/C7/C6/C8 *versus* C5/C6/C8/C8a). This angle is 28.4 (3)° for (I*A*) and 36.0 (3)° for (I*B*), a difference of 7.6 (4)°.



(I)

The averaging of the C—O bond lengths and C—C—O angles by disorder, often seen in dimeric acids, is not observed in catemers. Hence, no significant averaging is observed for (I*A*), the C—O bond lengths of which are 1.192 (6) and 1.330 (7) Å, with C—C—O angles of 125.9 (6) and 112.2 (5)°; for (I*B*), the corresponding bond lengths are 1.201 (7) and 1.317 (7) Å, and the corresponding angles are 123.3 (7) and 112.0 (6)°. Our own survey of 56 non-dimeric keto acid structures gives average values of 1.200 (10) and 1.32 (2) Å, and 124.5 (14) and 112.7 (17)° for these lengths and angles, in accord with typical values of 1.21 and 1.31 Å, and 123 and 112° cited for highly ordered dimeric carboxyls (Borthwick, 1980). The three methyl groups present are fully ordered in both (I*A*) and (I*B*), and are staggered relative to the substituents at their points of attachment.

Fig. 2 illustrates the packing of (I*A*) and (I*B*) in the cell and the formation of acid-to-ketone catemers, in which the intermolecular O···O distance and O—H···O angle are 2.715 (6) Å and 169°, respectively, within the type (I*A*) chains, and 2.772 (6) Å and 168°, respectively, within the type (I*B*) chains. The hydrogen-bonding arrangements of (I*A*) and (I*B*)

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and their differences adhere so closely to the isostructural case of AFUVEC that readers are referred for a fuller discussion to that presented by Brunskill *et al.* (2002).

Consistent with the difference of 167.4 (8)° in carboxyl rotation between the two molecules of (I) and the observed flattening of the ketone ring in molecule (I*A*), but unlike the case of AFUVEC, the geometry of the hydrogen bonding itself displays significant differences between molecules (I*A*) and (I*B*). 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*A*), these angles are 119.8 and −27.1°, respectively, while in (I*B*), the same angles are 123.6 and 4.3°, respectively, the former approach being quite significantly out of the ketone plane.

However, molecules (I*A*) and (I*B*) lie so nearly parallel that, despite these differences, the overall shapes of the helices produced by their chain formation are remarkably similar. Thus, the intermolecular ketone *versus* carboxyl dihedral angles for screw-related neighbors involved in hydrogen bonding are quite similar, at 113.9 (4)° for the type (I*A*) chains and 123.6 (3)° for the type (I*B*) chains. This is in marked contrast to the case of AFUVEC (Brunskill *et al.*, 2002), where the intermolecular dihedral angles within its two types of helices differ much more dramatically. Compound (I) and AFUVEC are isostructural not only because they are isoskeletal, but also because of their strong similarity in shape. A major contributor to the latter is the *trans* ring junction in (I), which, much more than would a *cis* arrangement, confers both a generally planar shape and a conformational rigidity closely resembling AFUVEC. In addition, the 8-methyl group in (I) has the (thermodynamically favored) equatorial configuration, again resembling its placement in AFUVEC far more than the axial alternative would.

Within the 2.7 Å range we usually employ for non-bonded C—H···O packing interactions (Steiner, 1997), one intermolecular C—H···O=C close contact exists for the type (I*A*) carboxyl group, with a distance of 2.63 Å to atom H5′*B* in a type (I*B*) molecule of a translationally related asymmetric unit. Using compiled data for a large number of C—H···O contacts, Steiner & Desiraju (1998) have found 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.

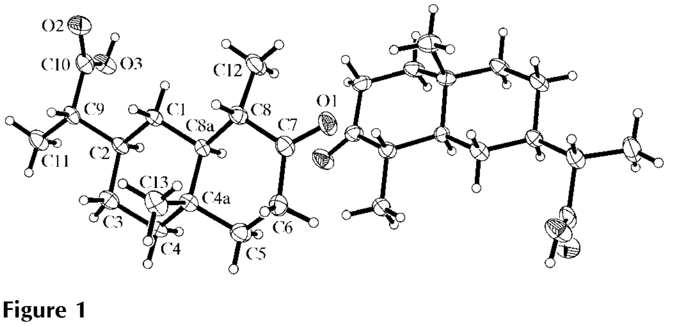

Figure 1
The asymmetric unit of (I), with the atom numbering shown only for molecules (I*A*); the unlabeled molecule is (I*B*). Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii.

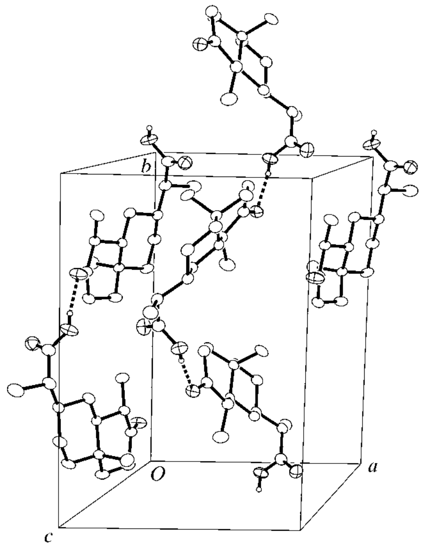

Figure 2
A partial packing diagram for (I), with extracellular molecules included to illustrate the two counterdirectional single-strand helical catemers proceeding in the *b* direction. Those with their axis nearest the *bc* face are of type (I*B*). For clarity, all H atoms bound to C atoms have been omitted.

The solid-state (KBr) IR spectrum of (I) displays C=O absorptions at 1723 and 1678 cm^{-1}, consistent with known hydrogen-bonding shifts, due to hydrogen-bond removal from acid C=O and its addition to a saturated ketone, respectively. In $CHCl_3$ solution, dimers predominate, and these absorptions merge into a single peak at 1704 cm^{-1}.

Experimental

Commercial (−)-α-santonin of known relative and absolute stereochemistry (Barton *et al.*, 1962; Nakazaki & Arakawa, 1962; Asher & Sim, 1965; Coggin & Sim, 1969) was obtained from the Aldrich Chemical Co., Milwaukee, Wisconsin, USA, and subjected to Li–NH_3 reduction (Bruderer *et al.*, 1956; Howe *et al.*, 1959). The resulting α,β-unsaturated ketone was then hydrogenated over Pd/C catalyst and chromatographed on alumina, providing (I). Crystals of (I) (m.p. 384 K) suitable for X-ray diffraction analysis were obtained from ether–hexane. The stereochemistry found agrees with that previously assigned to the isomer (of negative optical rotation) having this melting point (Miki, 1955; Abe *et al.*, 1956; Djerassi *et al.*, 1958; Ando *et al.*, 1980).

Crystal data

$C_{15}H_{24}O_3$
$M_r = 252.34$
Monoclinic, $P2_1$
$a = 10.136$ (3) Å
$b = 14.867$ (4) Å
$c = 10.238$ (3) Å
$\beta = 111.36$ (2)°
$V = 1436.8$ (7) Å^3
$Z = 4$
$D_x = 1.167$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 28 reflections
$\theta = 2.1$–10.5°
$\mu = 0.08$ mm^{-1}
$T = 296$ (2) K
Parallelepiped, colorless
0.25 × 0.22 × 0.07 mm

Data collection

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
Absorption correction: numerical (*SHELXTL*; Sheldrick, 1997)
$T_{\min} = 0.96$, $T_{\max} = 0.99$
5322 measured reflections
2590 independent reflections
1462 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.060$
$\theta_{\max} = 25°$
$h = -11 \rightarrow 11$
$k = -17 \rightarrow 17$
$l = -12 \rightarrow 12$
3 standard reflections every 97 reflections intensity variation: <4.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.055$
$wR(F^2) = 0.120$
$S = 1.05$
2590 reflections
328 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0354P)^2 + 0.1319P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.14$ e Å^{-3}
$\Delta\rho_{\min} = -0.13$ e Å^{-3}
Extinction correction: *SHELXL*97 in *SHELXTL* (Sheldrick, 1997)
Extinction coefficient: 0.0114 (17)

Table 1
Selected geometric parameters (Å, °).

Unprimed atom labels indicate molecule (I*A*) and primed labels indicate molecule (I*B*).

O2—C10	1.192 (6)	O2′—C10′	1.201 (7)
O3—C10	1.330 (7)	O3′—C10′	1.318 (7)
O2—C10—C9	125.9 (7)	O2′—C10′—C9′	123.3 (7)
O3—C10—C9	112.2 (5)	O3′—C10′—C9′	112.0 (6)

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

Unprimed atom labels indicate molecule (I*A*) and primed labels indicate molecule (I*B*).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O3—H3$\cdots$O1$^{\rm i}$	0.82	1.96	2.772 (6)	169
O3′—H3′$\cdots$O1′$^{\rm ii}$	0.82	1.91	2.715 (6)	168

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

Friedel-related data were averaged. All H atoms were found in electron-density difference maps. C-bound H atoms were placed in calculated positions (C—H = 0.97 Å for methylene H, 0.98 Å for methane H and 0.96 Å for methyl H atoms) and allowed to refine as riding models on their respective C atoms; their displacement parameters were fixed at 120% of those of their respective C atoms, except for the methyl H atoms, which were fixed at 150% of their respective C atoms. Hydroxyl H atoms were fixed at O—H = 0.82 Å and their displacement parameters were fixed at 120% of those of their respective O atoms.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXS*97 in *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 in *SHELXTL*; molecular graphics: *SHELXP*97 in *SHELXTL*; software used to prepare material for publication: *SHELXL*97 in *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1424). Services for accessing these data are described at the back of the journal.

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