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(−)-Metasantonic acid: alteration of the hydrogen-bonding mode in a diastereomer of santonic acid

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The title compound, (−)-(1*R*,3a*S*,4*R*,5*S*,7a*S*,9*R*)-octahydro-α,3a,5-trimethyl-6,8-dioxo-1,4-methano-1*H*-indene-1-acetic acid, $C_{15}H_{20}O_4$, aggregates in the solid state as a catemer, with the hydrogen-bonding following a 2_1 screw axis from each carboxyl to the ketone of a neighboring molecule [O···O = 2.6595 (14) Å and O—H···O = 166 (2)°]. Two parallel counter-directional screw-related single-strand chains pass through the cell in the *a* direction. Compared with the case of its C-9 diastereomer, santonic acid, also a catemer, the hydrogen-bonding receptor in the title compound is not the ε- but the γ-ketone. Three intermolecular C—H···O═C close contacts exist.

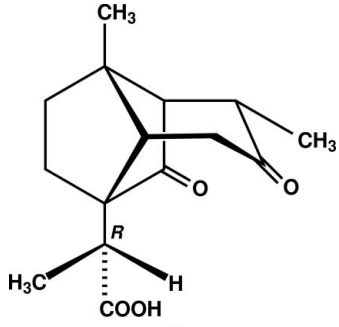
Key indicators

Single-crystal X-ray study
T = 100 K
Mean σ(C–C) = 0.002 Å
R factor = 0.027
wR factor = 0.070
Data-to-parameter ratio = 11.7

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Comment

We have previously reported structures for several keto-acid derivatives of (−)-α-santonin, a sesquiterpenoid isolate of *Artemisia* (Brunskill *et al.*, 2001, 2002; Thompson & Lalancette, 2003; Zinczuk *et al.*, 2004, 2006). The title compound, (I), is a tricyclic γ,ε-diketo acid, epimeric with santonic acid, (II) (Brunskill *et al.*, 1999), at C9, whose configuration is independent of the remainder of the molecule. In the trivial nomenclature for (I) '*meta*' appears to have no specific meaning, merely indicating an isomer of (II).



(I)

Fig. 1 shows the molecular structure of (I), numbered identically with (II); C9 has the *R* configuration, as shown. Conformationally significant rotations are possible only about C1—C9 and C9—C10. Compounds (I) and (II) both have staggered conformations at C9, in which the substituents are essentially transposed in accord with the opposite C9 configurations. The net result of this, plus the carboxyl conformation, is that the hydrogen-bond donor (O4—H4) projects from the molecule at a markedly different angle in (I) *vis-a-vis* (II).

Disordering of C—O bond lengths and C—C—O angles is not observed in (I) (Table 1), since the geometry of catemers (see below) cannot support the usual averaging processes.

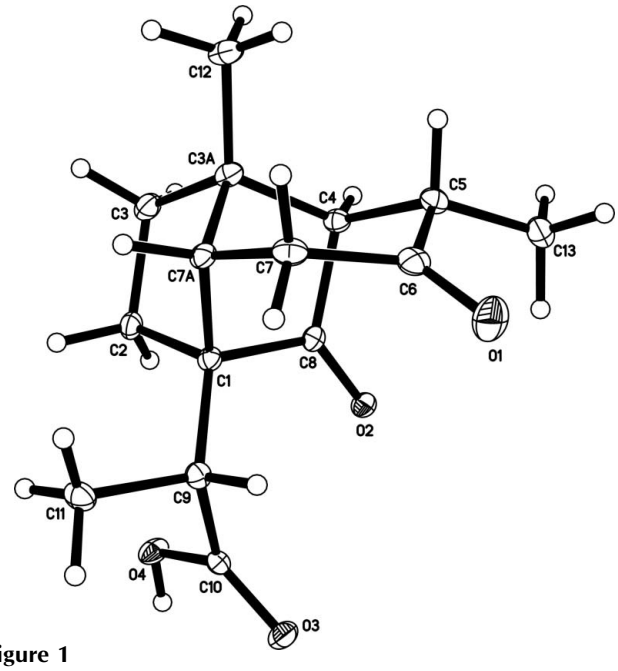


Figure 1
The molecular structure of (I), with its numbering. Displacement ellipsoids are drawn at the 30% probability level.

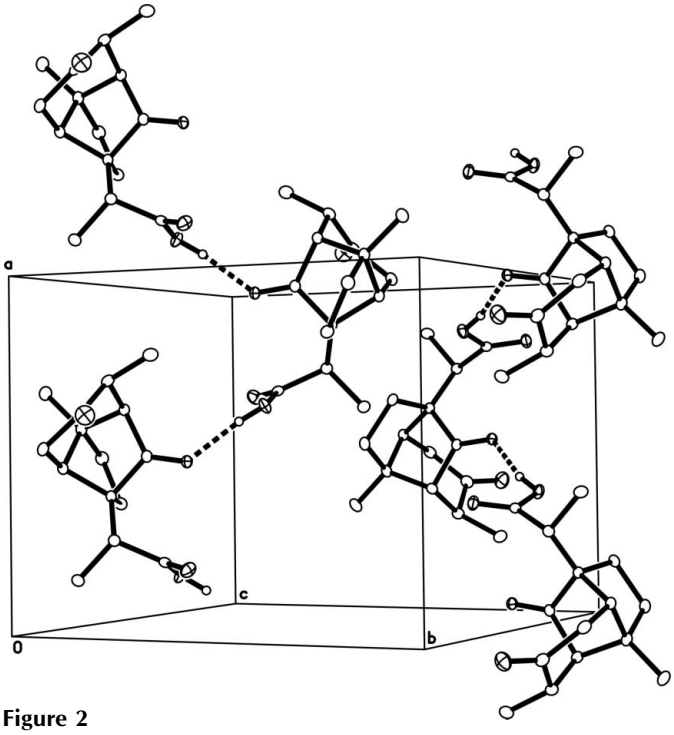


Figure 2
A partial packing diagram for (I), illustrating the two parallel, counter-directional, screw-related, single-strand hydrogen-bonding chains (dashed lines) passing through the unit cell in the *a* direction. Displacement ellipsoids are drawn at the 30% probability level. All C-bound H atoms have been omitted for clarity.

Fig. 2 illustrates the packing, with catemers whose hydrogen bonding follows a 2_1 screw axis along *a*, from each carboxyl to the γ-ketone (O2) in a neighbor (Table 2). This represents a major alteration in hydrogen bonding relative to (II), whose receptor is the ε-ketone (O1).

We characterize the geometry of hydrogen bonding to carbonyls using a combination of H···O=C angle and H···O=C—C torsion angle. These describe the approach of the acid H atom to the receptor O in terms of its deviation from, respectively, C=O axiality (ideal = 120°) and coplanarity with the carbonyl (ideal = 0°). In (I) the values for these two angles are 128.3 (6) and −20.0 (8)°; for (II) the corresponding values (involving O1) are 135 and 6.6°.

Within the 2.6 Å range we routinely survey for non-bonded H···O packing interactions (Steiner, 1997), three C—H···O=C close contacts are found (Table 2).

Acid-to-ketone catemerization, known to supplant acid dimerization as the dominant hydrogen bonding mode in chiral non-racemates, is present in both (I) and (II). The most obvious difference in the packing arrangement involves the change to O2, the γ-ketone, as the hydrogen-bonding receptor, rather than O1. Since the two ketones are expected to have very similar basicities, this evidently arises because of the change in the overall donor–receptor alignments of the molecule, resulting from the altered carboxyl orientation.

Experimental

(−)-Santonic acid, derived from (−)-α-santonin of known relative and absolute stereochemistry (Barton *et al.*, 1962; Nakazaki & Arakawa, 1962; Asher & Sim, 1965; Coggin & Sim, 1969), was converted to γ-metasantonin by heating with H_2SO_4, as described by Woodward & Yates (1963). Basic hydrolysis similar to that described for parasantonide by Woodward & Kovach (1950) yielded (I). Crystallization from ethyl acetate gave crystals melting at 442 K. The solid-state (KBr) infrared spectrum of (I) has C=O absorptions at 1740 (carboxyl) and 1706 cm^{-1} (ε-ketone, plus strained but hydrogen-bonded γ-ketone). The shifts involved conform to those typically seen in catemers, due to removal of hydrogen bonding from carboxyl C=O and its addition to a ketone. In $CHCl_3$ solution, where dimers predominate, the strained γ-ketone is seen at 1745 cm^{-1}, while the remaining absorptions appear as a single peak at 1706 cm^{-1}.

Crystal data

$C_{15}H_{20}O_4$
M_r = 264.31
Orthorhombic, $P2_12_12_1$
a = 9.4191 (2) Å
b = 11.7706 (2) Å
c = 12.2382 (2) Å
V = 1356.83 (4) Å^3
Z = 4
Cu $K\alpha$ radiation
μ = 0.76 mm^{-1}
T = 100 (2) K
0.48 × 0.34 × 0.20 mm

Data collection

Bruker SMART CCD APEXII area-detector diffractometer
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2001)
T_{min} = 0.801, T_{max} = 0.871
5501 measured reflections
2087 independent reflections
2083 reflections with $I > 2\sigma(I)$
R_{int} = 0.019

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.027
$wR(F^2)$ = 0.070
S = 1.07
2087 reflections
179 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.22 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}
Absolute structure: Flack (1983), 760 Friedel pairs
Flack parameter: 0.03 (17)

Table 1
Selected geometric parameters (Å, °).

O3—C10	1.2047 (18)	O4—C10	1.3304 (18)
O3—C10—C9	124.92 (13)	O4—C10—C9	111.67 (12)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H4*B*···O2^{i}	0.85 (2)	1.83 (2)	2.6595 (14)	166 (2)
C12—H12*B*···O1^{ii}	0.98	2.58	3.519 (2)	160
C7—H7*A*···O2^{iii}	0.99	2.58	3.3780 (18)	137
C12—H12*C*···O3^{iii}	0.98	2.58	3.497 (2)	155

Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{1}{2}, -z+1$; (ii) $-x+\frac{5}{2}, -y+1, z-\frac{1}{2}$; (iii) $-x+2, y+\frac{1}{2}, -z+\frac{3}{2}$.

All H atoms for (I) were found in electron density difference maps. The methyl H atoms were placed in ideally staggered positions with C—H distances of 0.98 Å and U_{iso}(H) = 1.5U_{eq}(C). The methylene and methine Hs were placed in geometrically idealized positions and constrained to ride on their parent C atoms with C—H distances of 0.99 and 1.00 Å, respectively, and U_{iso}(H) = 1.2U_{eq}(C). The carboxyl H was allowed to refine freely in position; U_{iso}(H) = 1.5U_{eq}(O).

Data collection: *APEX2* (Bruker, 2006); cell refinement: *APEX2*; data reduction: *SAINT* (Bruker, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Sheldrick, 2004); software used to prepare material for publication: *SHELXTL*.

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