(–)-Isosantonic acid: alteration of the hydrogen-bonding mode by configurational inversion at a single centre in a γ,ε-diketocarboxylic acid

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organic papers

(−)-Isosantonic acid: alteration of the hydrogen-bonding mode by configurational inversion at a single centre in a γ,ε-diketocarboxylic acid

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Key indicators

Single-crystal X-ray study
$T = 100$ K
Mean σ(C–C) = 0.002 Å
R factor = 0.025
wR factor = 0.066
Data-to-parameter ratio = 9.2

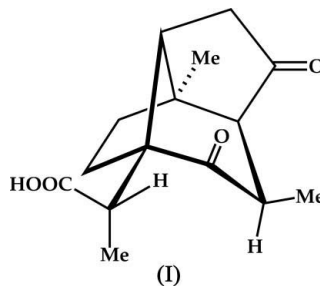For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The title diketo acid, (1R,3aS,6aS,7R,9S)-(−)-α,3a,7-trimethyl-5,8-dioxo-1,4-ethanoperhydropentalene-1-acetic acid (C$_{15}$H$_{20}$O$_4$), is shown to aggregate in the crystal structure as acid-to-ketone hydrogen-bonding catemers, whose chains follow 2_1 screw axes from each carboxyl to a ketone in a neighbouring molecule [O···O = 2.7472 (13) Å and O···H—O = 172.7 (17)°]. Two parallel counterdirectional screw-related single-strand hydrogen-bonding chains pass through the cell in the a direction. Six intermolecular C—H···O=C close contacts are found. Comparisons are drawn with a diastereomer having the opposite configuration at the methylated chiral centre adjacent to the carboxyl group.

Comment

Transformations of (−)-α-santonin, a sesquiterpenoid *Artemisia* isolate, offer a rich vein of chiral non-racemic keto acids (Brunskill *et al.*, 1999, 2001, 2002; Thompson & Lalancette, 2003). Several such compounds provide opportunities to examine hydrogen-bonding changes due to inversion at a single chiral centre.

The title compound, (I), is a tricyclic diketo acid having the absolute S configuration at C9, whose chirality is independent of the tricyclic framework. Compound (I) is thus the C9-diastereomer of (−)-parasantonic acid, (II) (Zinczuk *et al.*, 2004).

Fig. 1 shows the asymmetric unit of (I) and its numbering. The rigidity of the system leaves significant rotations around only C1—C9 and C9—C10. The arrangement about C1—C9 is staggered, with the carboxyl and γ-ketone (O1) anti to one another [torsion angle C8—C1—C9—C10 = 166.09 (10)°]. The carboxyl is rotated to give a C1—C9—C10—O3 torsion angle of 79.95 (15)°. This arrangement of the carboxyl relative to the tricyclic framework differs markedly from that in the C9-diastereomer, (−)-parasantonic acid, (II), where these angles are −50.7 (5) and 146.0 (4)°, respectively (Fig. 2). In (II), the carboxyl and γ-ketone carbonyls are roughly parallel [torsion angle O1—C8···C10—O3 = 28.1 (5)°], but in (I) they point
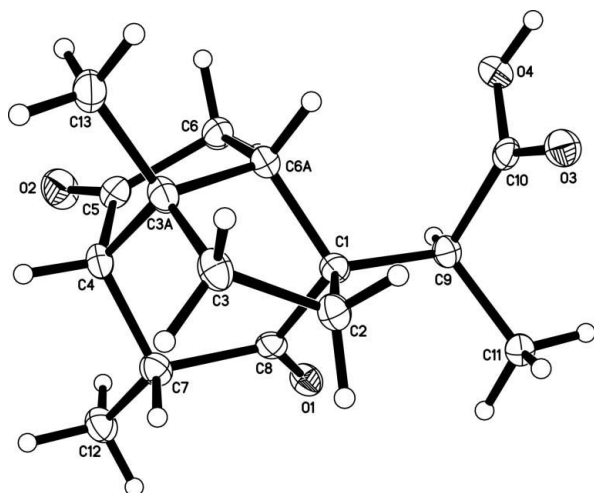
Figure 1
The molecular structure of (I), showing displacement ellipsoids drawn at the 50% probability level.
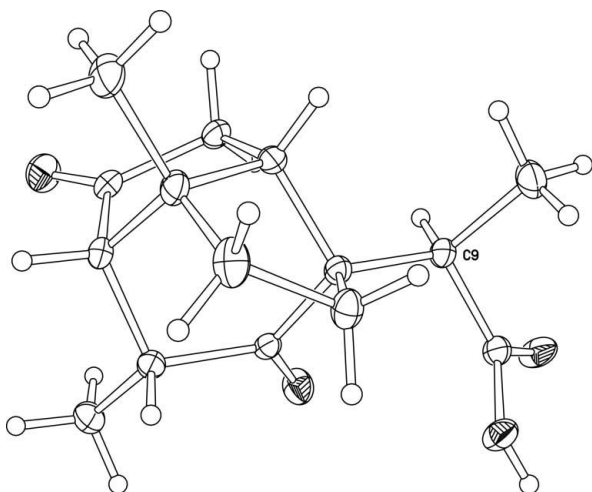

Figure 2
The molecular structure of (−)-parasantonic acid, (II), which differs from (I) only in the configuration around C9.

Figure 3
A partial packing diagram for (I), illustrating the two parallel counter-directional screw-related single-strand hydrogen-bonded (dashed lines) chains passing through the cell in the *a*-axis direction. Displacement ellipsoids are drawn at the 40% probability level. H atoms not involved in hydrogen bonding have been omitted.

away from one another [torsion angle O1—C8···C10—O3 = −126.05 (12)°], a difference of more than 150°. The observed C1—C9 conformations for (I) and (II) both position atom H9*A* where it is bracketed by atoms C6a and C8, and presumably minimize torsional crowding. The resulting change in the angular arrangement of the carboxyl has dramatic consequences for the packing of (I) *versus* (II) (see below). As (I) is not dimeric, disorder-averaging of carboxyl bond lengths and angles is absent, and these values (Table 1) resemble those in highly ordered dimeric carboxyls.

Fig. 3 illustrates the packing of (I), involving acid-to-ketone catemers, whose hydrogen-bonding follows a 2_1 screw from each carboxyl to the γ-ketone (O1) in a neighbour [O···O = 2.7472 (13) Å and O—H···O = 172.7 (17)°]. Two parallel counterdirectional chains pass through the cell along the *a* axis. This mode predominates among chiral non-racemic keto acids, but differs from the rare acid-to-acid hydrogen bonding found in (II). This change results specifically from the inversion at C9 and the extension of O4—H4 at a markedly altered
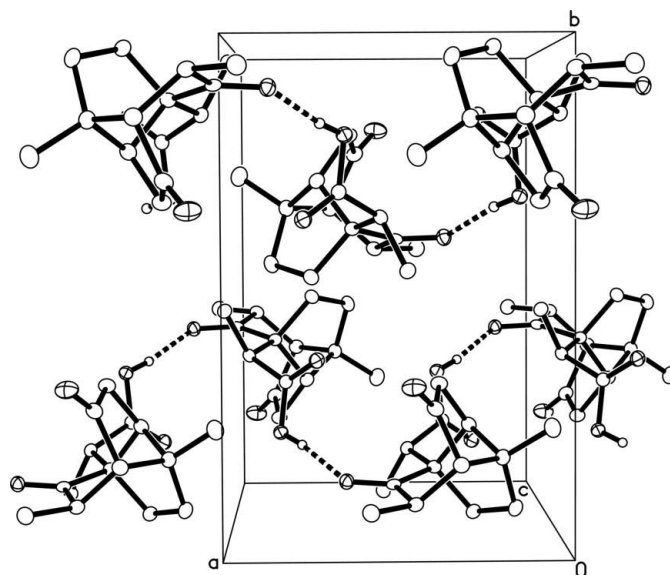
angle relative to the remainder of the molecule in (I) compared with (II).

We characterize the geometry of hydrogen bonding to carbonyls using a combination of H···O=C angle and H···O=C—C torsion angle. In (I), these two angles are 137.7 (5) and −20.1 (8)°, respectively.

Compound (I) has six intermolecular C=O···H—C close contacts (Table 2).

Experimental

Crystal data

$C_{15}H_{20}O_4$	$Z = 4$
$M_r = 264.31$	$D_x = 1.317$ Mg m^{-3}
Orthorhombic, $P2_12_12_1$	Cu $K\alpha$ radiation
$a = 8.3801$ (2) Å	$\mu = 0.77$ mm^{-1}
$b = 12.5398$ (2) Å	$T = 100$ (2) K
$c = 12.6852$ (2) Å	Parallelepiped, colourless
$V = 1333.02$ (4) Å^3	$0.50 \times 0.34 \times 0.26$ mm

Data collection

Bruker SMART CCD area-detector diffractometer	15403 measured reflections
φ and ω scans	2321 independent reflections
Absorption correction: multi-scan ($SADABS$; Blessing, 1995)	2320 reflections with $I > 2\sigma(I)$
$T_{min} = 0.750$, $T_{max} = 0.820$	$R_{int} = 0.017$
	$\theta_{max} = 69.2°$

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} < 0.001$
$R[F^2 > 2\sigma(F^2)] = 0.025$	$\Delta\rho_{max} = 0.21$ e Å^{-3}
$wR(F^2) = 0.066$	$\Delta\rho_{min} = -0.16$ e Å^{-3}
$S = 0.98$	Extinction correction: $SHELXL97$ (Sheldrick, 1997)
2321 reflections	Extinction coefficient: 0.0065 (5)
253 parameters	Absolute structure: Flack (1983), with 950 Friedel pairs
H-atom parameters constrained	Flack parameter: 0.02 (15)
$w = 1/[\sigma^2(F_o^2) + (0.0435P)^2 + 0.3883P]$ where $P = (F_o^2 + 2F_c^2)/3$	

Table 1
Selected bond lengths (Å).

O3—C10	1.2098 (15)	O3—C10	1.2098 (15)
O3—C10—C9	124.96 (11)	O4—C10—C9	112.21 (11)

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O4—H4$\cdots$O1^i	0.847 (19)	1.90 (2)	2.7472 (13)	172,7 (17)
C11—H11$B\cdots$O2^{ii}	0.991 (17)	2.650 (16)	3.1916 (17)	114.5 (11)
C3—H3$A\cdots$O3^{iii}	1.001 (15)	2.666 (15)	3.6268 (16)	161.1 (12)
C6—H6$A\cdots$O3^{iv}	0.945 (18)	2.652 (18)	3.5891 (17)	171.4 (14)
C7—H7$A\cdots$O3^{iii}	0.979 (18)	2.519 (18)	3.4278 (16)	154.3 (13)
C9—H9$A\cdots$O3^{iv}	0.960 (15)	2.542 (15)	3.4964 (15)	172.6 (11)
C9—H9$A\cdots$O4^{iv}	0.960 (15)	2.669 (15)	3.3816 (16)	131.3 (11)

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

All H atoms were found in electron-density difference maps, placed in calculated positions and allowed to refine freely, both positionally and isotropically.

Data collection: $SMART$ (Bruker, 2000); cell refinement: $SAINT$-$Plus$ (Bruker, 2000); data reduction: $SAINT$-$Plus$; 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: $SHELXTL$.

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