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(±)-2-Oxocyclohexanepropionic acid: dual conformational selection and hydrogen bonding in a δ-keto acid, and a two-phase technique for crystallizing acids by contact with aqueous solutions of their salts

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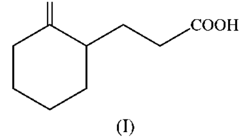
The asymmetric unit of the title compound, $C_9H_{14}O_3$, consists of two molecules having conformations that differ by 121.7 (4)° in their rotation about the equatorial substituent bond, so that the side chain extends away from the ring in different directions in the two species. The hydrogen-bonding mode is acid-to-acid dimerization. However, despite the centrosymmetric space group ($P\overline{1}$), the dimers are asymmetric, formed by pairing molecules of identical chirality but differing conformational type [$O\cdots O$ = 2.681 (2) and 2.654 (2) Å, and $O-H\cdots O$ = 175 (3) and 176 (3)°]. Two intermolecular $C-H\cdots O{=}C$ close contacts exist, involving the ketone group of one of the molecules. A two-phase technique is described for slow reforming of crystals of a water-insoluble acid by contact with an aqueous solution of its water-soluble salt.

Comment

When a ketone and a carboxylic acid co-exist within a single molecule, the excess of hydrogen-bond receptors over donors provides hydrogen-bonding opportunities beyond those available to simple acids. Our long-term study of the crystallography of keto acids has offered numerous examples encompassing all five of the known hydrogen-bonding modes, along with discussions of the factors that contribute to the choice of mode (Lalancette *et al.*, 1998, 1999; Brunskill *et al.*, 1999). As part of a continuing study of simple cyclohexane and cyclopentane keto acids, we report here the crystal structure of the title compound, (I), and we discuss the crystallization technique employed to produce the crystal used (see *Experimental*).



(I)

Fig. 1 presents a view of the asymmetric unit of (I) with its numbering scheme. While the category of δ-keto acids to which (I) belongs encompasses a rich variety of hydrogen-bonding types, the mode here is carboxyl dimerization. The two molecules in this unit, *viz.* (I*A*) and (I*B*), are of identical chirality, but differ in the conformations of their side chains. Hence, despite the centrosymmetry in the space group ($P\overline{1}$), the dimer shown has no symmetry. This is only the third instance we have encountered of the formation of an asymmetric dimer within a centrosymmetric space group (Lalancette *et al.*, 1991, 1996), and surveys have shown that the combination is a very uncommon one (Gavezzotti & Filippini, 1994; Allen *et al.*, 1999), particularly if the survey set is edited to contain only acids capable of packing centrosymmetrically (Sørensen & Larsen, 2003).

In both conformers of (I), the substituent chain extends equatorially from the ring and adopts a standard staggered arrangement about both C1—C7 and C7—C8. However, the staggering constraint still permits three rotational options about each of those bonds, and only conformer (I*A*) adopts a conformation with a fully *anti* arrangement of substituents, which extends into the ring to the ketone C2 atom. By contrast, conformer (I*B*) has an *anti* arrangement about C7′—C8′ but a *gauche* conformation about C1′—C7′. The latter is presumably permitted by the absence of a hindering axial H atom at the ketone C atom. The chains in (I*A*) and (I*B*) differ in their rotation about the C1—C7 bond by almost exactly 120°; in (I*A*), the C6—C1—C7—C8 torsion angle is 60.9 (3)°, while the corresponding angle in (I*B*) is −60.8 (3)°, yielding a difference of 121.7 (4)° for this pair of conformers. The remaining torsion angles within the side chain vary only slightly between (I*A*) and (I*B*), with nearly identical angles for C1—C7—C8—C9 [173.0 (2) and −171.6 (2)°, respectively] and O2—C9—C8—C7 [−6.5 (4) and −8.9 (4)°, respectively]. The result, as to the conformation about the equatorial C1—C7 bond, resembles rotation of a rigid rotor. One consequence of this rotation is that the internal carboxyl *versus* ketone dihedral angle is 0.88 (15)° in (I*A*) but 63.44 (7)° in (I*B*).

Although averaging of C—O bond lengths and C—C—O angles by disorder is common in dimerized carboxyls (Leiserowitz, 1976), neither conformer of (I) displays signifi-

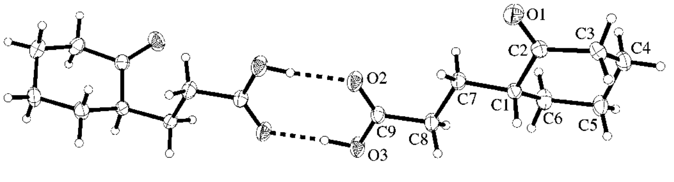


Figure 1
A view of the asymmetric unit of (I) with the atom-numbering scheme for conformer (I*A*). The two halves of the non-centrosymmetric dimer, of identical chirality, differ in conformation by rotation about C1—C7. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arabitrary radii.

cant carboxyl disorder, which may result in part from the complete absence of symmetry in the dimer. In (I*A*), the C—O bond lengths are 1.217 (3) and 1.304 (3) Å, with C—C—O angles of 123.6 (2) and 114.1 (2)°; the corresponding bond lengths for (I*B*) are 1.218 (3) and 1.308 (3) Å, with angles of 124.4 (2) and 113.3 (2)°. Typical values cited for highly ordered dimeric carboxyls are 1.21 and 1.31 Å, and 123 and 112° (Borthwick, 1980). Because of the absence of symmetry, the O···O distances in the dimer are different [2.681 (2) Å for O3···O2′ *versus* 2.654 (2) Å for O3′···O2], although the O—H···O angles are statistically indistinguishable.

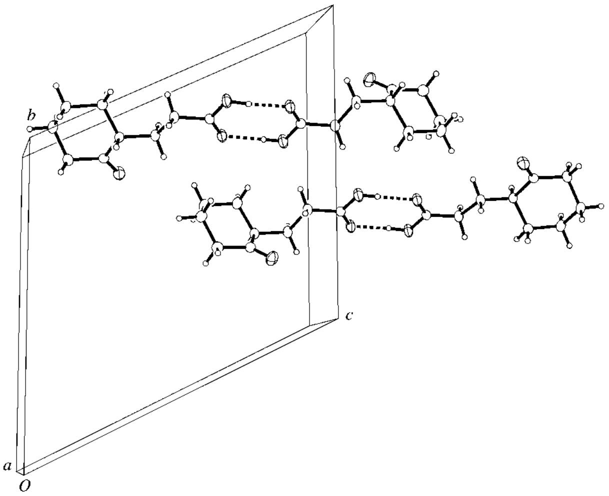


Figure 2
A partial packing diagram for (I), with extra molecules included.

Fig. 2 illustrates the packing of the cell of (I). All the dimers lie bundled with their long axes parallel and lying generally in the *c* direction. Because the dimers lack any symmetry, their centres do not lie on a special position, although they lie quite close to ($\frac{1}{4}$, $\frac{3}{4}$, $\frac{3}{4}$), at (0.23, 0.74, 0.75) (and the corresponding centrosymmetric site). In the packing, two intermolecular C—H···O═C close contacts were found, both involving the ketone group of molecule (I*A*), with a distance of 2.60 Å to atom H8*B* and 2.51 Å to atom H3′*A*, in separate translationally related asymmetric units. These contacts lie within the 2.7 Å range we standardly employ for non-bonded C—H···O packing interactions (Steiner, 1997). Using compiled data for a large number of such contacts, Steiner & Desiraju (1998) have found statistically significant 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.

The solid-state (KBr) IR spectrum of (I) has a single stretching absorption at 1698 cm^{-1} for both C═O functions in both species, typical for acids that have, and unstrained ketones that lack, hydrogen bonding. In $CHCl_3$ solution, this peak appears at 1709 cm^{-1}, broadened by the usual carboxyl-dilution shoulder at *ca* 1750 cm^{-1}.

Experimental

The pyrrolidine enamine of cyclohexanone was alkylated with ethyl acrylate (Stork *et al.*, 1963), yielding the ethyl ester of (I), which was purified by distillation. Saponification followed by recrystallization gave material of melting point 337 K. Exhaustive crystallization trials with numerous solvents and solvent combinations invariably yielded ultrafine needles of (I) unsuitable for X-ray analysis. Usable crystals of (I) (m.p. 340 K) were produced from an aqueous medium by the following technique. Compound (I) was added, with stirring and warming, to an 8 ml vial containing aqueous NaOH (about 4 ml) until the pH of the solution was neutral; the specific gravity of the final solution was 1.03. Additional (I) was added to provide a clot of undissolved keto acid lying in the bottom of the vial, and the vial was tightly capped and placed in a sunlit position providing periodic temperature variation. Over a period of weeks, the solid in the bottom gradually clarified and produced chunky faceted clear projections and extensions, principally on its bottom surface. After several months, the mass was broken up and the liquor removed by pipette and retained in a second vial. The crystals were rinsed with water, gently broken into smaller units and dried. After removal of suitable candidates, unusable crystals were reunited with the retained liquor for further reforming.

Crystal data

$C_9H_{14}O_3$
$M_r = 170.20$
Triclinic, $P\overline{1}$
$a = 5.4302$ (9) Å
$b = 13.370$ (2) Å
$c = 14.075$ (2) Å
$\alpha = 63.198$ (11)°
$\beta = 86.956$ (12)°
$\gamma = 85.297$ (14)°
$V = 908.9$ (3) Å^3
$Z = 4$
$D_x = 1.244$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 34 reflections
$\theta = 3.2$–10.5°
$\mu = 0.09$ mm^{-1}
$T = 296$ (2) K
Parallelepiped, colorless
0.28 × 0.26 × 0.08 mm

Data collection

Siemens *P*4 diffractometer
2θ/θ scans
Absorption correction: numerical (*SHELXTL*; Sheldrick, 1997)
$T_{\min} = 0.96$, $T_{\max} = 0.99$
4166 measured reflections
3104 independent reflections
1995 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.025$
$\theta_{\max} = 25.0°$
$h = -1 \rightarrow 6$
$k = -14 \rightarrow 14$
$l = -16 \rightarrow 16$
3 standard reflections every 97 reflections intensity variation: <1.5%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.052$
$wR(F^2) = 0.145$
$S = 1.02$
3104 reflections
224 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0651P)^2 + 0.1786P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.18$ e Å^{-3}
$\Delta\rho_{\min} = -0.14$ e Å^{-3}
Extinction correction: *SHELXTL* (Sheldrick, 1997)
Extinction coefficient: 0.011 (3)

All H atoms were found in electron-density difference maps. C-bound H atoms were placed in calculated positions (C—H = 0.97 Å

Table 1
Selected geometric parameters (Å, °).

O2—C9	1.217 (3)	O2′—C9′	1.218 (3)
O3—C9	1.304 (3)	O3′—C9′	1.308 (3)
O2—C9—C8	123.6 (2)	O2′—C9′—C8′	124.4 (2)
O3—C9—C8	114.1 (2)	O3′—C9′—C8′	113.3 (2)

Table 2

Hydrogen-bonding geometry (Å, °).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O3—H3$\cdots$O2′	0.94 (3)	1.75 (3)	2.681 (2)	175 (3)
O3′—H3′$\cdots$O2	0.87 (3)	1.79 (3)	2.654 (2)	176 (3)

for methylene H and 0.98 Å for methine H atoms) and allowed to refine as riding models; their displacement parameters were fixed at 120% of those of their respective C atoms. The hydroxyl H atoms were allowed to vary positionally and their displacement parameters were fixed at 150% 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*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1439). Services for accessing these data are described at the back of the journal.

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