trans-4-Acetylcyclohexanecarboxylic acid and (±)-trans-2-acetylcyclohexanecarboxylic acid: hydrogen-bonding patterns in two isomeric keto acids

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Both title compounds, $C_9H_{14}O_3$, display carboxyl-dimer hydrogen-bonding patterns. The 4-acetyl isomer adopts a chiral conformation with negligible disordering of the methyl and carboxyl groups and forms centrosymmetric dimers across the b and c edges of the chosen cell [O···O = 2.667 (3) Å and O—H···O = 175°]. Intermolecular C—H···O close contacts were found for both carbonyl groups. In the 2-acetyl isomer, there is no intramolecular interaction between the carboxyl and acetyl groups and the hydrogen bonding involves centrosymmetric carboxyl dimerization across the ab and ac faces of the chosen cell [O···O = 2.668 (2) Å and O—H···O = 173°]. The carboxyl group is negligibly disordered, but significant rotational disordering was found for the acetyl methyl group. An intermolecular C—H···O close contact was found involving the ketone group.

Comment

Five hydrogen-bonding modes are known for crystalline keto carboxylic acids, these compounds being the subject of a continuing study on our part. Two of these hydrogen-bonding modes have no ketone involvement, reflecting the common pairing and much rarer chain modes seen in simple acids (Leiserowitz, 1976). Acid-to-ketone chains (catemers) constitute a sizable minority of cases, while intramolecular hydrogen bonds and acid-to-ketone dimers are rarely observed. Hydrates with more complex hydrogen-bonding patterns also exist. We have previously provided examples of all of these, along with a discussion of the factors that appear to govern the choice of mode.

We report here the structure and hydrogen-bonding behavior of the title compounds, *viz*. an ε-keto acid, *trans*-4-acetylcyclohexanecarboxylic acid, (I), and its γ-keto isomer, (±)-*trans*-2-acetylcyclohexanecarboxylic acid, (II). Both ε-

and γ-keto acids are rich in hydrogen-bonding types, embracing not only dimers, but catemers of both the homo- and heterochiral types and internal hydrogen bonds, as well as hydrated patterns. Among those keto acids that adopt the catemeric hydrogen-bonding mode, we have identified the lack of conformational flexibility as one of the characteristics they have in common (Lalancette *et al.*, 1999; Barcon *et al.*, 1998, 2002). Compounds (I) and (II) were both of interest to us as part of a group of simple cyclohexane keto acids whose choice of hydrogen-bonding mode appears to correlate strongly with such conformational flexibility, as assessed by the number of fully rotatable bonds.
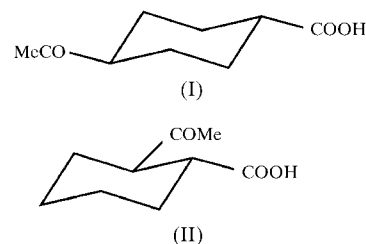

Fig. 1 shows the asymmetric unit of (I) with its atom numbering. Given the expected chair conformation, the only significant rotational options involve the equatorial substituent bonds. The acetyl group is turned roughly orthogonal to the general plane of the cyclohexane ring, so that the O1—C7—C4—C3 torsion angle is −27.0 (5)° (a perfect orthogonal angle would be 60°). The carboxyl carbonyl group is turned slightly toward the opposite face of the ring, so that the O2—C9—C1—C2 torsion angle is −15.2 (4)°. The intramolecular dihedral angle between the carboxyl and ketone planes is 81.1 (2)°.

Although not seen in catemeric hydrogen bonding, full or partial averaging of C—O bond lengths and C—C—O angles through disorder is often observed in dimerically hydrogen-bonded acids (Leiserowitz, 1976). However, no significant averaging is present in (I), where these geometric parameters are 1.222 (4)/1.300 (3) Å and 124.0 (3)/114.5 (3)°, respectively. Our own survey of 56 keto acid structures that are not acid dimers gives average values of 1.200 (10)/1.32 (2) Å and 124.5 (14)/112.7 (17)° for these lengths and angles, in accord with typical values of 1.21/1.31 Å and 123/112° cited for highly
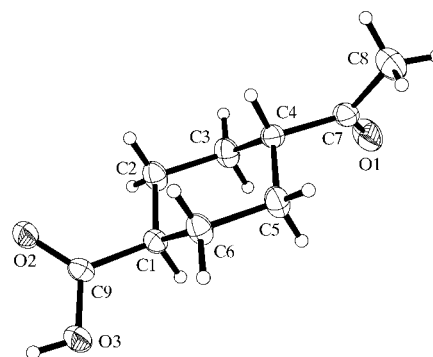
Figure 1
The asymmetric unit of (I), with the atom-numbering scheme. Displacement ellipsoids are set at the 20% probability level.

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ordered dimeric carboxyls (Borthwick, 1980). No rotational disordering of the acetyl methyl group was observed.

Fig. 2 shows the cell packing in (I), which involves formation of centrosymmetric dimers across the *b* and *c* edges of the chosen cell [O···O = 2.667 (3) Å and O—H···O = 175°]. Within the 2.7 Å range we usually employ for non-bonded H···O packing interactions (Steiner, 1997), an intermolecular C—H···O close contact was found for the ketone (2.54 Å to atom H1 in a molecule screw-related in *b*), as well as for the acid (O3···H6*B* = 2.68 Å, in a molecule related through the center of symmetry at the origin). Using compiled data for a large number of C—H···O contacts, Steiner & Desiraju (1998) have found significant statistical directionality 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.

Fig. 3 shows the asymmetric unit for (II) with its atom numbering. As in (I), only the equatorial substituent bonds offer significant rotational options. The acetyl group is turned so that the O1—C7—C2—C1 torsion angle is 13.8 (3)° and the carboxyl group is turned so that the O2—C9—C1—C2 torsion angle is 26.0 (3)°. The intramolecular dihedral angle between the carboxyl and ketone planes in (II) is 74.8 (2)°. A variety of vicinal and other carboxy ketones are known to close internally to form lactols (Chadwick & Dunitz, 1979; Thompson *et al.*, 1985), including the aromatic analog of (II), 2-acetyl-benzoic acid (Dobson & Gerkin, 1996; Valente *et al.*, 1998). Unlike these, compound (II) has no intramolecular interaction between its two functional groups. The carboxyl C—O distances and C—C—O angles found for (II) [1.229 (3)/1.302 (3)° and 122.8 (2)/114.5 (2) Å], like those for (I), indicate a negligible degree of disordering. However, significant

Figure 3
The asymmetric unit of (II), with the atom-numbering scheme. Only the major disorder component [78 (3):22 (3)] of the methyl group is displayed. Displacement ellipsoids are set at the 20% probability level.

rotational disorder was found in the acetyl methyl group; the refinement of partial H atoms found in electron-density difference maps provided a 78 (3):22 (3) population ratio for the two conformers involved, which differ by a rotation of 60°.

Fig. 4 shows the packing arrangement for (II), involving centrosymmetric dimers centered on the *ab* and *ac* faces of the chosen cell [O···O = 2.668 (2) Å and O—H···O = 173°]. For the ketone carbonyl group, a 2.66 Å intermolecular C—H···O close contact was found to atom H2*A* in a neighbor screw-related in *b*.

Among several factors tending to disfavor the kind of standard dimeric carboxyl hydrogen bonding seen in (I) and (II), we have identified low availability of alternative conformations as a major candidate. The flexibility associated with cyclohexane rings is a solution characteristic; in the crystal, the strong preference for chair conformations and equatorial substituents actually leaves systems like (I) and (II) with a diminished repertoire of conformational options. Nevertheless, in both (I) and (II), the fully rotatable bond by which the ketone function is attached allows sufficient flexibility for
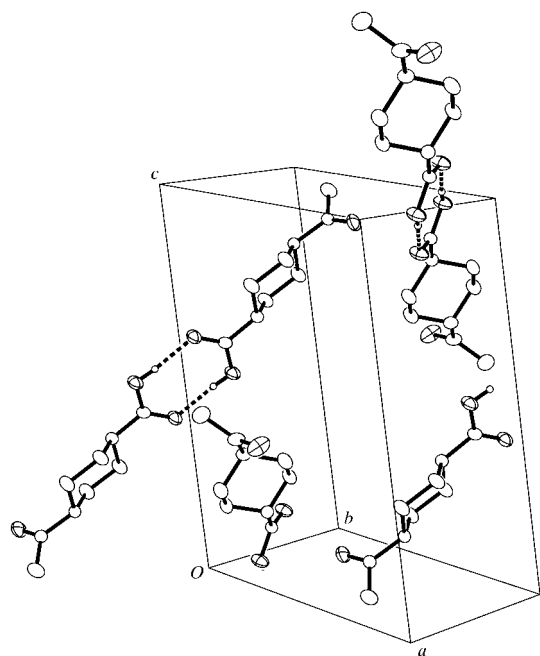

Figure 2
A partial packing diagram for (I), with extracellular molecules to show the dimers centered on the *b* and *c* edges of the chosen cell. All C-bound H atoms have been omitted for clarity. Displacement ellipsoids are set at the 20% probability level.
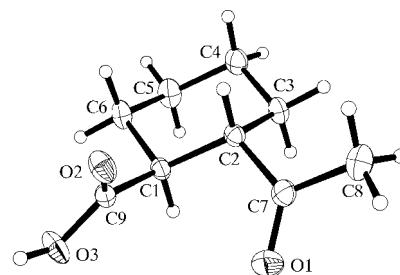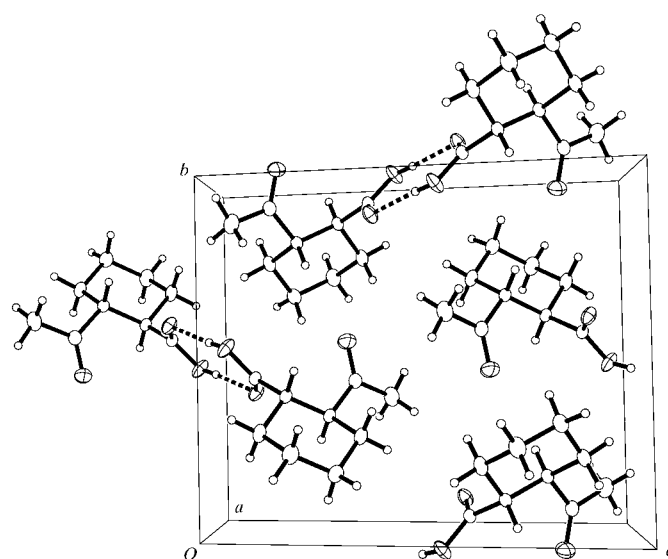

Figure 4
A packing diagram for (II), with extracellular molecules, illustrating the centrosymmetric carboxyl dimers across the *ab* and *ac* faces of the chosen cell. Displacement ellipsoids are set at the 20% probability level.

the system to find a centrosymmetric carboxyl-dimerization arrangement of favorably low energy. This contrasts with the case of several substituted cyclohexanone and cyclopentanone systems we have studied, where incorporation of the ketone into the ring removes that increment of flexibility, resulting in catemeric hydrogen-bonding arrangements (Lalancette *et al.*, 1997; Thompson *et al.*, 1998; Barcon *et al.*, 1998, 2002; Zewge *et al.*, 1998).

The solid-state (KBr) IR spectrum of (I) has separate C=O absorptions at 1712 and 1691 cm^{-1} for the ketone and carboxyl groups, respectively, which coalesce to a single band at 1705 cm^{-1} in CHCl$_3$ solution. Compound (II) in KBr has a single peak at 1695 cm^{-1} for both C=O groups, which shifts to 1707 cm^{-1} in CHCl$_3$. Both solution spectra display typical carboxyl-dilution shoulders around 1735 cm^{-1}.

Experimental

Compound (I) was prepared by a Jones oxidation of the product obtained from the Rh-catalyzed hydrogenation of 4-acetylbenzoic acid; chilled crystallization separated (I) from the non-ketonic hydrogenolyzed material. Crystals of X-ray quality were produced from hexane/diethyl ether (m.p. 384 K). For (II), cyanide addition to 1-acetylcyclohexene, followed by ketone protection, base hydrolysis and deprotection, yielded material suitable for X-ray analysis after recrystallization from cyclohexane/diethyl ether (m.p. 409 K).

Compound (I)

Crystal data

C$_9$H$_{14}$O$_3$	D_x = 1.235 Mg m^{-3}
M_r = 170.20	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 13
a = 9.845 (5) Å	reflections
b = 6.770 (5) Å	θ = 3.0–9.1°
c = 13.994 (8) Å	μ = 0.09 mm^{-1}
β = 101.12 (3)°	T = 296 (2) K
V = 915.2 (10) Å^3	Parallelepiped, colorless
Z = 4	0.38 × 0.24 × 0.20 mm

Data collection

Siemens $P4$ diffractometer	$h = -11 \rightarrow 1$
$2\theta/\theta$ scans	$k = -8 \rightarrow 1$
2253 measured reflections	$l = -16 \rightarrow 16$
1608 independent reflections	3 standard reflections
996 reflections with $I > 2\sigma(I)$	every 97 reflections
R_{int} = 0.034	intensity variation: <4.1%
θ_{max} = 25.0°	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0538P)^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.059	$+ 0.6069P]$where $P =$
$wR(F^2)$ = 0.166	$(F_o^2 + 2F_c^2)/3$
S = 1.04	$(\Delta/\sigma)_{max}$ < 0.001
1608 reflections	$\Delta\rho_{max}$ = 0.19 e Å^{-3}
110 parameters	$\Delta\rho_{min}$ = -0.17 e Å^{-3}
H-atom parameters constrained	Extinction correction: *SHELXL*97
	Extinction coefficient: 0.012 (3)

Table 1
Selected geometric parameters (Å, °) for (I).

O2—C9	1.222 (4)	O3—C9	1.300 (3)
O2—C9—C1	124.0 (3)	O3—C9—C1	114.5 (3)

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

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O3—H3$\cdots$O2^i	0.82	1.85	2.667 (3)	175

Symmetry code: (i) $-x, 1-y, -z$.

Compound (II)

Crystal data

C$_9$H$_{14}$O$_3$	D_x = 1.240 Mg m^{-3}
M_r = 170.20	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 28
a = 6.943 (2) Å	reflections
b = 10.489 (3) Å	θ = 2.5–10.1°
c = 12.778 (4) Å	μ = 0.09 mm^{-1}
β = 101.47 (2)°	T = 296 (2) K
V = 912.0 (5) Å^3	Parallelepiped, colorless
Z = 4	0.36 × 0.32 × 0.14 mm

Data collection

Siemens $P4$ diffractometer	R_{int} = 0.086
$2\theta/\theta$ scans	θ_{max} = 25.0°
Absorption correction: numerical	$h = -8 \rightarrow 8$
(Sheldrick, 1997)	$k = -12 \rightarrow 12$
T_{min} = 0.97, T_{max} = 0.99	$l = -15 \rightarrow 15$
3465 measured reflections	3 standard reflections
1599 independent reflections	every 97 reflections
912 reflections with $I > 2\sigma(I)$	intensity variation: <3%

Refinement

Refinement on F^2	H-atom parameters constrained
$R[F^2 > 2\sigma(F^2)]$ = 0.052	$w = 1/[\sigma^2(F_o^2) + (0.0187P)^2]$
$wR(F^2)$ = 0.104	where $P = (F_o^2 + 2F_c^2)/3$
S = 0.99	$(\Delta/\sigma)_{max}$ < 0.001
1599 reflections	$\Delta\rho_{max}$ = 0.15 e Å^{-3}
112 parameters	$\Delta\rho_{min}$ = -0.13 e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for (II).

O2—C9	1.229 (3)	O3—C9	1.302 (3)
O2—C9—C1	122.8 (2)	O3—C9—C1	114.5 (2)

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O3—H3$\cdots$O2^i	0.82	1.85	2.668 (2)	173

Symmetry code: (i) $1-x, 2-y, 1-z$.

All H atoms in (I) and (II) were found in electron-density difference maps, but were placed in calculated positions (C—H = 0.96 Å for the methyl, 0.97 Å for the methylene, 0.98 Å for the methine and 0.82 Å for the carboxyl H atoms) and allowed to refine as riding models on their respective C and O parent atoms. Their displacement parameters were fixed at 120% of those of the parent C atoms and 150% of the parent O atoms. The methyl group of (II) exhibited significant disorder [population ratio = 78 (3):22 (3)].

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

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1396). Services for accessing these data are described at the back of the journal.

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