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The epimeric 9-oxobicyclo[3.3.1]-nonane-3-carboxylic acids: hydrogen-bonding patterns of the *endo* acid and the lactol of the *exo* acid

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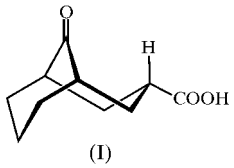
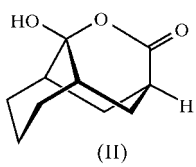
The two δ-keto carboxylic acids of the title, both $C_{10}H_{14}O_3$, are epimeric at the site of carboxyl attachment. The *endo* (3α) epimer, (I), has its keto-acid ring in a boat conformation, with the tilt of the carboxyl group creating conformational chirality. The molecules form hydrogen bonds by centrosymmetric pairing of carboxyl groups across the corners of the chosen cell [O$\cdots$O = 2.671 (2) Å and O—H$\cdots$O = 179 (2)°]. Two close intermolecular C—H$\cdots$O contacts exist for the ketone. The *exo* (3β) epimer exists in the closed ring–chain tautomeric form as the lactol, 8-hydroxy-9-oxatricyclo[5.3.1.0^{3,8}]undecan-10-one, (II). The molecules have conformational chirality, and the hydrogen-bonding scheme involves intermolecular hydroxyl-to-carbonyl chains of molecules screw-related in *b* [O$\cdots$O = 2.741 (2) Å and O—H$\cdots$O = 177 (2)°].

Comment

Keto carboxylic acids, with two hydrogen-bonding receptors and a single donor, constitute a class in which five solid-state hydrogen-bonding modes are known. Three of these engage the ketone function, while the remainder correspond to the common pairing and rare chain modes of simple acids. In our



(I)



(II)

continuing study of the factors governing the choice of hydrogen-bonding mode, we have examined the title compounds, (I) and (II), which belong to the category of δ-keto acids, one generally rich in hydrogen-bonding types.

Fig. 1 shows the asymmetric unit for the 3α or '*endo*' acid, (I), the methyl ester of which was the kinetic but less thermodynamically stable product of our synthesis. Of the four chair–boat permutations available to (I), those having a boat conformation for the ring bearing the carboxyl avoid placing that group on an axial bond and are clearly favored. Thus, the conformation found in the crystal is also the one energetically favored in solution (McEuen *et al.*, 1970), with one boat and one chair. Given that preference, the molecule has no significant conformational flexibility, and the only available rotation involves the bond to the carboxyl group. That group is tilted so that the C2—C3—C10—O2 torsion angle is −8.3 (2)°, producing a net conformational chirality in this otherwise inherently symmetric molecule.

Fig. 2 is a packing diagram showing that the hydrogen bonding in (I) is of the relatively common carboxyl-pairing type, with centrosymmetric dimers across the corners of the chosen cell. Although not seen in catemeric hydrogen bonding, complete or partial averaging of C—O bond lengths and C—C—O angles by disorder is frequent in carboxyl dimers (Leiserowitz, 1976), but is not significantly present in (I). Here, these lengths are 1.222 (2) and 1.320 (2) Å, with angles of 123.67 (18) and 113.94 (17)°. Our own survey of 56 keto acid structures which are not acid dimers gives average values of 1.20 (1) and 1.32 (2) Å, and 124.5 (14) and 112.7 (17)°, respectively, for these lengths and angles, in accord with the typical values of 1.21 and 1.31 Å, and 123 and 112°, cited for highly ordered dimeric carboxyl groups (Borthwick, 1980).

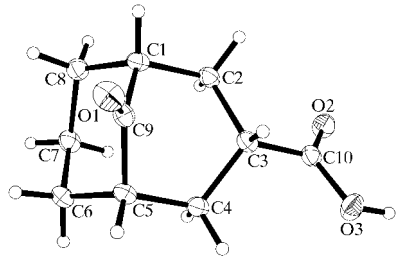


Figure 1
A view of the asymmetric unit of (I). Displacement ellipsoids are set at the 20% probability level and H atoms are shown as small spheres of arbitrary radii.

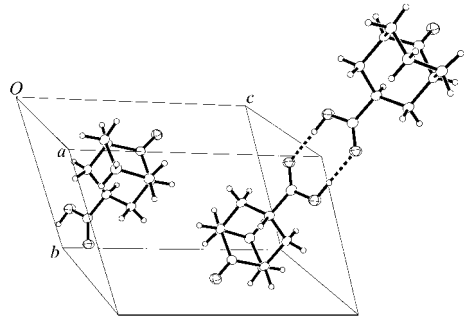


Figure 2
A packing diagram for (I), with an extracellular molecule included to illustrate the centrosymmetric carboxyl pairing across the corners of the chosen cell. Displacement ellipsoids are set at the 20% probability level.

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Within the 2.7 Å range we employ as our standard criterion (Steiner, 1997), two non-bonded intermolecular C—H···O packing interactions were found in (I), both involving the ketone (2.68 Å to atom H3*A* and 2.68 Å to atom H8*A* in two different centrosymmetrically related neighbors). Using compiled data for a large number of C—H···O contacts, Steiner & Desiraju (1998) found significant statistical directionality even as far out as 3.0 Å, and concluded 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 of the 3β '*exo*' diastereomer, (II), obtained *via* base-catalyzed epimerization of the *endo* ester. This material is identical by melting point to that originally identified as the *exo* keto acid by Peters *et al.* (1974), but is found here to exist in the closed lactol form, (II). Based on NMR evidence, the existence of a ring–chain tautomerism for solutions of this compound was later recognized by van Oosterhout *et al.* (1978), but no structural assignment was made for the crystalline form of the compound. Note that the bicyclo[3.3.1] numbering of the *exo* keto acid is retained in the following discussion of (II), rather than the more complex tricyclo[5.3.1.0^{3,8}] alternative, which obscures the parentage of (II) and its relationship to (I).

Such ring–chain tautomerism is relatively common in β- and γ-carboxy ketones and carboxy aldehydes (Chadwick & Dunitz, 1979; Thompson *et al.*, 1985; Dobson & Gerkin, 1996; Valente *et al.*, 1998; Tsao *et al.*, 2003). Although there appears to be some preference for γ- over δ-lactones (Soffer *et al.*, 1950; Jones, 1963), examples of the latter are not lacking. In either case, the open and closed forms often lie so close energetically that small changes in structure or the medium can shift the equilibria appreciably (Valters & Flitsch, 1985), and for (II), the specific source of stability for the δ-lactol form is not obvious. With the carboxyl group in the *exo* position, both rings would appear to be free to adopt chair conformations with no very serious stereochemical disadvantage, as seen in the case of 9-oxobicyclo[3.3.1]nonane-1-carboxylic acid (Thompson *et al.*, 1992). However, in general, incorporating significant rotational constraints and/or substitution on the chain atoms usually shifts equilibria toward the closed form (Valters & Flitsch, 1985), and both of these features are present in (II). The ^{13}C NMR peaks (in C_5D_5N and $CDCl_3$) for both forms of (II) were identified by van Oosterhout *et al.* (1978) and some data on the rates of equilibration were reported, but none on the position of the equilibrium involved. It seems probable that the isolation of (II) represents displacement of the solution equilibrium by selective precipitation.

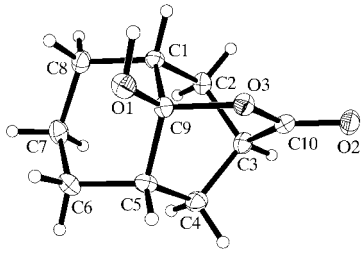

Figure 3
A view of the asymmetric unit of (II); the atom-numbering scheme follows that of the parent keto acid and (I). Displacement ellipsoids are set at the 20% probability level and H atoms are shown as small spheres of arbitrary radii.

Both the open and closed forms of (II) lack chiral centers and are inherently symmetric. However, while (II) is skeletally symmetrical, like (I) it adopts a chiral conformation arising principally from the only free rotation available, in this case that of the hydroxyl. It is well recognized that simple bicyclo[2.2.2]octane systems are not entirely rigid, and the nominally parallel ethylene bridges are often significantly skewed, presumably to relieve eclipsing strain (Deutsch, 1972; Blackstock *et al.*, 1987; Zimmerman *et al.*, 1992). In (II), this tendency is severely curtailed by the presence of the additional ring, which imparts extra rigidity to the bicyclo[2.2.2]-octane portion of the molecule. As a result, the three torsion angles involving the [2.2.2]-bridgeheads all lie very close to 0°; these are C9—C1—C2—C3 [−0.08 (16)°], C9—O3—C10—C3 [−1.13 (16)°] and C9—C5—C4—C3 [−1.43 (16)°].

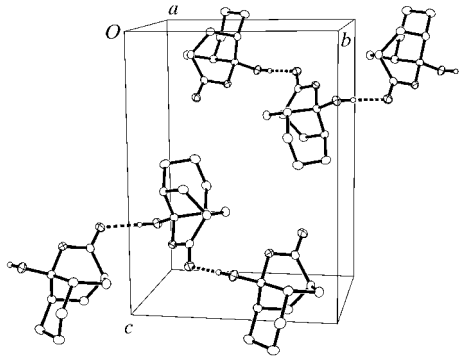

Figure 4
A partial packing diagram for (II) with extracellular molecules, illustrating the hydroxyl-to-carbonyl hydrogen-bonding catemers among molecules screw-related in *b*. All C-bound H atoms have been removed for clarity. Displacement ellipsoids are set at the 20% probability level.

Fig. 4 is a packing diagram showing the hydrogen-bonding scheme for (II). As is seen in other simple lactols, the hydrogen bonding is catemeric, proceeding in the *bc* plane from the hydroxyl of one molecule to the carbonyl of a neighbor, in this case one screw-related in *b*. A second chain, centrosymmetric to the first, runs counterdirectionally. No intermolecular C—H···O contacts were found within 2.7 Å.

The solid-state (KBr) IR spectrum of (I) displays C═O peaks at 1719 and 1702 cm^{-1}. In $CHCl_3$ solution, these bands coalesce and appear at 1712 cm^{-1}. For compound (II), the KBr spectrum displays sharp peaks at 3265 (O—H) and 1714 cm^{-1} (hydrogen-bonded C═O). In $CHCl_3$ solution, peaks appear for both unassociated and associated O—H (3576 and 3323 cm^{-1}), as well as at 1748 cm^{-1} for the lactone C═O, with a shoulder at 1730 cm^{-1}.

Experimental

Compound (I) was synthesized according to the procedure of McEuen *et al.* (1970), as modified by Peters *et al.* (1974), and was recrystallized from methyl acetate–hexane to give crystals suitable for X-ray analysis (m.p. 404 K). The methyl ester of (I) was epimerized with sodium methoxide and saponified to give (II), which was sublimed and recrystallized from ethyl acetate (m.p. 422 K).

Compound (I)

Crystal data

$C_{10}H_{14}O_3$
M_r = 182.21
Triclinic, $P\overline{1}$
a = 6.6170 (10) Å
b = 7.3160 (10) Å
c = 10.421 (2) Å
α = 71.470 (10)°
β = 73.44 (2)°
γ = 77.290 (10)°
V = 453.81 (13) Å^3
Z = 2
D_x = 1.333 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 23 reflections
θ = 3.3–9.9°
μ = 0.10 mm^{-1}
T = 296 (2) K
Pentagonal rod, colorless
0.50 × 0.22 × 0.08 mm

Data collection

Siemens $P4$ diffractometer
$2\theta/\theta$ scans
Absorption correction: analytical (*SHELXTL*; Sheldrick, 1997)
T_{min} = 0.940, T_{max} = 0.980
2040 measured reflections
1588 independent reflections
1141 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 25°
$h = -1 \rightarrow 7$
$k = -8 \rightarrow 8$
$l = -12 \rightarrow 12$
3 standard reflections
every 97 reflections
intensity variation: <1.1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.042
$wR(F^2)$ = 0.108
S = 1.04
1588 reflections
121 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0480P)^2 + 0.0479P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.13 e Å^{-3}
$\Delta\rho_{min}$ = −0.17 e Å^{-3}

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

O2—C10	1.222 (2)	O3—C10	1.320 (2)
O2—C10—C3	123.67 (18)	O3—C10—C3	113.94 (17)

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

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O2^{i}	0.93 (3)	1.74 (3)	2.671 (2)	179 (2)

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

Compound (II)

Crystal data

$C_{10}H_{14}O_3$
M_r = 182.21
Monoclinic, $P2_1/c$
a = 7.331 (4) Å
b = 9.288 (7) Å
c = 12.669 (7) Å
β = 92.64 (2)°
V = 861.7 (9) Å^3
Z = 4
D_x = 1.404 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 30 reflections
θ = 2.8–11.9°
μ = 0.10 mm^{-1}
T = 296 (2) K
Parallelepiped, colorless
0.44 × 0.28 × 0.24 mm

Data collection

Siemens $P4$ diffractometer
$2\theta/\theta$ scans
2946 measured reflections
1512 independent reflections
1239 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 25°
$h = -8 \rightarrow 0$
$k = -11 \rightarrow 11$
$l = -14 \rightarrow 15$
3 standard reflections
every 97 reflections
intensity variation: <1.0%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.033
$wR(F^2)$ = 0.084
S = 1.03
1512 reflections
122 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0326P)^2 + 0.1747P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.16 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}
Extinction correction: *SHELXL*97 in *SHELXTL* (Sheldrick, 1997)
Extinction coefficient: 0.044 (3)

Table 3
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H1···O2^{i}	0.93 (2)	1.81 (2)	2.741 (2)	177 (2)

Symmetry code: (i) $-x, y-\frac{1}{2}, \frac{5}{2}-z$.

All the H atoms of (I) and (II) were found in electron-density difference maps, but C-bound H atoms were placed in calculated positions (0.97 Å for methylene H and 0.98 Å for methine H) and allowed to refine as riding models on their respective C atoms, with their displacement parameters fixed at 120% of those of their respective C atoms. The positional parameters of the O-bound H atoms were allowed to refine, but their displacement parameters were held at 0.08 Å^2.

For both compounds, 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: FR1406). Services for accessing these data are described at the back of the journal.

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