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Two diastereomers of (±)-*cis*-2-(3-oxo-1,3,4,5,6,7-hexahydroisobenzofuran-1-yl)cyclohexanecarboxylic acid

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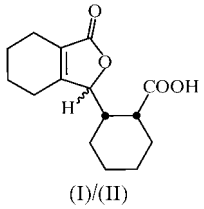
The structures are presented for both diastereomers of the title compound, $C_{15}H_{20}O_4$, produced by base-catalyzed self-condensation of cyclohexane-*cis*-1,2-dicarboxylic anhydride in refluxing triethylamine. Equilibration of either diastereomer under the condensation conditions yielded the same 5:3 mixture. In the crystal, one diastereomer, (II), is ordered, while the other, (I), displays both flexional ring disorder and carboxyl disorder; both aggregate as centrosymmetric hydrogen-bonded dimers [for (I), O···O = 2.680 (2) Å; for (II), O···O = 2.635 (4) Å].

Comment

Our attempts to reproduce a literature synthesis of *cis*-2-acetylcyclohexanecarboxylic acid (Csende & Szabo, 1994) have led us instead to the previously unreported title compound in yields of up to 65%. The wide melting range and overlapping NMR absorptions of the isolated crystalline product (see *Experimental*) indicated that this acidic material was a mixture of diastereomers, which we were then able to separate by fractional crystallization. Independent equilibration of both individual diastereomers, (I) and (II), with refluxing triethylamine led to the same mixture, having a ratio of 5:3. The predominant lower-melting isomer gave the structure whose asymmetric unit is shown as (I).



(I)/(II)

Fig. 1 shows that (I) is a decarboxylated dimeric material, with *cis* stereochemistry derived from the starting anhydride preserved at C8 and C9. Compound (I) is a racemate and for its two enantiomers the stereochemistries at C1, C8 and C9 are *RSR* (illustrated) and *SRS*, respectively. Not surprisingly, the cyclohexane ring adopts a conformation in which the carboxyl group occupies an axial bond, with the larger bicyclic system equatorial. A coupled up–down flexional disorder was found for C5 and C6 in the flattened half-chair cyclohexene ring. Fig. 1 shows both components of this disorder, whose occupancies are in the ratio 65:35 (11). Disorder also appears in the carboxyl group, whose C—O bond lengths and C—C—O angles are partially averaged, with observed lengths of 1.248 (2) and 1.301 (2) Å, and angles of 122.4 (2) and 115.2 (2)°. The packing of (I) involves centrosymmetric carboxyl dimers centered on the *c* edge of the chosen cell [O···O = 2.680 (2) Å]; consistent with the observed disorder, partial carboxyl H atoms were found at appropriate positions and refined to a 69:31 (3) occupancy ratio.

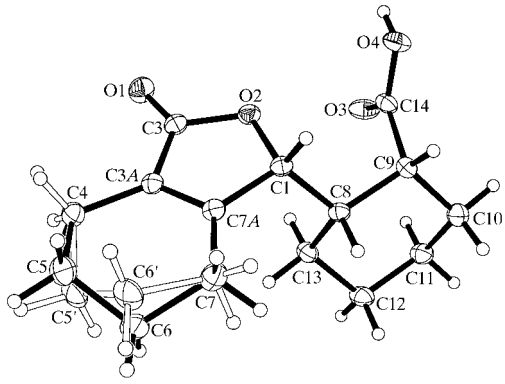


Figure 1
A view of the asymmetric unit of (I) with the atomic numbering scheme. 'Ghost' bonds are used to distinguish the atoms making up the minor component of the C5—C6 disorder [35 (1)% occupancy]. Only the major component [69 (3)% occupancy] of the carboxyl disorder is shown. Ellipsoids are set at 20% probability.

An intermolecular contact was found for (I) between O1 and one of the H atoms attached to C7 of a molecule translationally related in **a** (2.59 Å). This lies within the <2.7 Å range we often employ for non-bonded C—H···O packing interactions (Steiner, 1997). Using compiled data for a large number of such contacts, Steiner & Desiraju (1998) found

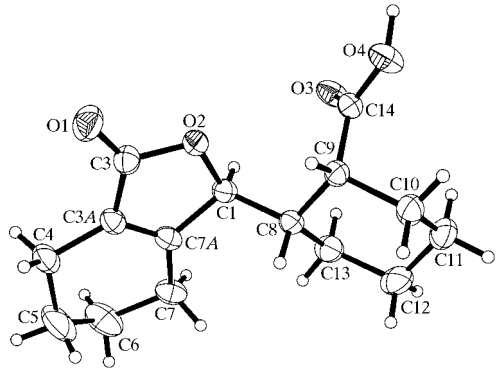


Figure 2
A view of the asymmetric unit of (II). Ellipsoids are set at 20% probability.

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. 2 illustrates the asymmetric unit for (II), which displays the same *cis* stereochemistry at C8 and C9 as does (I), along with the same conformational choice of axial *versus* equatorial cyclohexane substituents. Hence, the observed equilibration, as expected, has involved epimerization only at C1. For the two enantiomers of (II), the stereochemistries at C1, C8 and C9, respectively, are *SSR* (illustrated) and *RRS*. Compound (II) does not display the flexional disorder seen in (I), and no significant disorder was found in its carboxyl group. The C—O bond lengths are 1.231 (5) and 1.315 (5) Å, with C—C—O angles of 125.3 (4) and 113.8 (4)°. Values cited as typical for highly ordered dimeric carboxyls are 1.21 and 1.31 Å, and 123 and 112° (Borthwick, 1980).

The packing for (II) involves centrosymmetric carboxyl dimers centered on the *b* and *c* edges of the chosen cell [O···O = 2.635 (4) Å and O—H···O = 175°]. Close C—H···O contacts were found to a molecule glide-related in **b** for both O1 (2.60 Å to H7*B*) and O4 (2.65 Å to H11*A*). The observed crystal densities of (I) and (II) are identical to within 0.4%.

Compounds (I) and (II) are diastereomeric with a similarly derived compound, (III), whose X-ray structure has been reported by Bayer *et al.* (1985). Compound (III), however, has *trans* stereochemistry in the cyclohexane ring (*RRR* + *SSS*), resulting from equilibration at C8/C9. This evidently arose from the experimental temperature employed (up to 433 K), which in our case was controlled at *ca* 362 K by the reflux point of the excess triethylamine used as solvent. Two earlier reports of high-temperature preparations of (III), cited as the seventh reference in the paper by Bayer *et al.* (1985), present a structure having the double bond misplaced at C8—C9.

Experimental

A mixture of (I) and (II) was obtained in *ca* 39% yield by refluxing cyclohexane-*cis*-1,2-dicarboxylic anhydride with malonic acid in triethylamine for 18 h. A reaction without malonic acid subsequently produced a yield of 65%, from which (I), m.p. 444–446 K, and (II), m.p. 472–476 K, were separated by fractional crystallization. The solid-state (KBr) IR spectra of (I) and (II) differ significantly only in the fingerprint region; (I) has C═O stretch peaks at 1740 (lactone) and 1703 cm^{-1} (acid), with a weak absorption at 1674 cm^{-1}, while the corresponding bands for (II) are at 1743, 1699 and 1668 cm^{-1}. The ^{13}C NMR spectra (125.7 MHz, p.p.m.) also differ only slightly: for (I), δ 179.9, 173.5, 162.8, 127.4, 84.9, 42.7, 40.3, 26.9, 24.2, 24.0, 23.4, 22.7, 21.7, 21.4, 19.9; for (II), δ 179.5, 173.3, 163.4, 126.6, 84.8, 42.7, 40.7, 40.0, 28.4, 25.1, 25.0, 22.1, 21.8, 21.3, 19.9. The ^1H NMR spectrum (500 MHz, p.p.m.) for (I) shows: δ 9.7 (1H, *br*), 5.07 (1H, *s*), 2.90 (1H, *q*, *J* = 5 Hz), 2.15–2.4 (4H, *m*), 2.05–2.15 (2H, *m*), 1.6–1.9 (8H, *m*), *ca* 1.55 (1H, *m*), *ca* 1.45 (1H, *m*), *ca* 1.30 (1H, *m*); for (II), peaks are at δ 10.4 (1H, *br*), 5.03 (1H, *d*, *J* = 8 Hz), 2.96 (1H, *d*, *J* = 3.5 Hz), *ca* 2.36 (2H, *br s*), 2.1–2.3 (3H, *m*), 2.00 (1H, *q*/*d*, *J* = 12, 3.5 Hz), 1.75–1.9 (4H, *m*), *ca* 1.72 (1H, *m*), 1.5–1.65 (5H, *m*), 1.34 (1H, *br s*). The diastereomer ratio can be assessed by means of the paired peaks near δ 5.05 and 2.93 p.p.m.

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

O3—C14	1.248 (2)	O4—C14	1.301 (2)
O3—C14—C9	122.41 (15)	O4—C14—C9	115.16 (15)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O3—H3···O4^{i}	0.82	1.89	2.680 (2)	162
C7—H7*A*′···O1^{ii}	0.96	2.59	3.385 (3)	140

Symmetry codes: (i) $1-x, 2-y, 1-z$; (ii) $x-1, y, z$.

Compound (I)

Crystal data

$C_{15}H_{20}O_4$
M_r = 264.32
Triclinic, $P\overline{1}$
a = 6.652 (2) Å
b = 10.616 (4) Å
c = 11.038 (4) Å
α = 66.180 (10)°
β = 88.200 (10)°
γ = 85.61 (2)°
V = 711.0 (4) Å^3
Z = 2
D_x = 1.235 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 33 reflections
θ = 3.78–13.34°
μ = 0.089 mm^{-1}
T = 293 (2) K
Rectangular prism, colorless
0.60 × 0.18 × 0.16 mm

Data collection

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
Absorption correction: numerical (*XPREP*; Sheldrick, 1997)
T_{min} = 0.98, T_{max} = 0.99
4844 measured reflections
2422 independent reflections
1790 reflections with $I > 2\sigma(I)$
R_{int} = 0.034
θ_{max} = 25°
$h = -7 \rightarrow 7$
$k = -11 \rightarrow 11$
$l = 0 \rightarrow 13$
3 standard reflections
every 97 reflections
intensity variation <1%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.038
$wR(F^2)$ = 0.088
S = 1.01
2422 reflections
192 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0272P)^2 + 0.1159P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.01
$\Delta\rho_{max}$ = 0.14 e Å^{-3}
$\Delta\rho_{min}$ = −0.12 e Å^{-3}

Compound (II)

Crystal data

$C_{15}H_{20}O_4$
M_r = 264.32
Monoclinic, $P2_1/c$
a = 11.372 (7) Å
b = 10.467 (9) Å
c = 11.901 (16) Å
β = 91.11 (7)°
V = 1416 (2) Å^3
Z = 4
D_x = 1.240 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 41 reflections
θ = 1.71–16.72°
μ = 0.089 mm^{-1}
T = 293 (2) K
Rectangular prism, colorless
0.50 × 0.30 × 0.25 mm

Data collection

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
3242 measured reflections
2498 independent reflections
1151 reflections with $I > 2\sigma(I)$
R_{int} = 0.025
θ_{max} = 25°
$h = -13 \rightarrow 13$
$k = 0 \rightarrow 12$
$l = 0 \rightarrow 14$
3 standard reflections
every 97 reflections
intensity variation <3.0%

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

O3—C14	1.231 (5)	O4—C14	1.315 (5)
O3—C14—C9	125.3 (4)	O4—C14—C9	113.8 (4)

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

D—H···A	D—H	H···A	D···A	D—H···A
O4—H4···O3^{i}	1.09 (4)	1.54 (4)	2.635 (4)	175 (3)
C7—H7B···O1^{ii}	0.97	2.60	3.409 (6)	141
C11—H11A···O4^{ii}	0.97	2.65	3.412 (6)	135

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

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.065$
$wR(F^2) = 0.237$
$S = 1.09$
2498 reflections
175 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0941P)^2 + 0.6553P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.42$ e Å^{-3}
$\Delta\rho_{min} = -0.32$ e Å^{-3}

For both (I) and (II), all non-carboxyl H atoms were found in electron-density difference maps, but were replaced in calculated positions and allowed to refine as riding models with displacement parameters set at 120% of their respective C atoms. The H atom distances were held as follows: for methyl, 0.98 Å; for methylene, 0.97 Å. For (I), H atoms were generated for the disordered C5′ and C6′ positions, as well as for the geometric positions on C4 and C7; they were also allowed to ride on their respective C atoms at a distance of 0.97 Å. For (I), the disordered pair of carboxyl H atoms was also found in electron-density difference maps and allowed to refine in idealized positions 0.82 Å from their respective O atoms with isotropic displacement parameters set at 150% of their respective O atoms; their occupancies were allowed to refine [values 0.69:0.31 (3)]. For (II), the carboxyl H-atom position was allowed to refine and its displacement parameter was held constant 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: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1276). Services for accessing these data are described at the back of the journal.

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