

3-Benzoylpropionic Acid: Structure and Hydrogen-Bonding Pattern

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(Received 6 March 1990; accepted 29 October 1990)

Abstract. (I) $C_{10}H_{10}O_3$, $M_r = 178.188$, monoclinic, $P2_1/n$, $a = 12.728$ (6), $b = 5.200$ (3), $c = 14.426$ (6) Å, $\beta = 111.33$ (3)°, $V(235\text{ K}) = 889.4$ (8) Å³, $Z = 4$, $D_m(295\text{ K}) = 1.31$ (1), $D_x[295\text{ K}; V = 891.3$ (6) Å³] = 1.328 g cm^{-3} , $\lambda(\text{Mo K}\alpha) = 0.71069$ Å, $\mu = 1.058\text{ cm}^{-1}$, $F(000) = 376$, $T = 235$ (1) K, $R = 0.058$ for 859 unique observed reflections. Compound (I) adopts a conformation in which all non-H atoms except those in the carboxyl group lie essentially within a single plane. Pairs of molecules of opposite conformational chirality form centrosymmetric dimers by mutual hydrogen bonding of carboxyl groups, leaving the ketone carbonyls uninvolved. Infrared and Raman spectral features consistent with the hydrogen-bonding pattern are discussed.

Introduction. The factors which produce catemeric hydrogen bonding (carboxyl-to-ketone chains) instead of the far more common carboxyl dimer for crystalline keto carboxylic acids are not understood. They are evidently subtle and thus far no pattern has emerged which allows theoretical prediction of solid-state hydrogen-bonding modes. In our exploration of hydrogen bonding in keto acids (Leiserowitz, 1976; Vanderhoff, Thompson & Lalancette, 1986; Lalancette, Slifer & Thompson, 1989; Lalancette, Vanderhoff & Thompson, 1990, 1991; Lalancette, Thompson & Vanderhoff, 1991), we have examined the title compound (I). This material belongs to the class of γ - or 4-keto acids, the major category of simple keto acid in which yet a third pattern, *internal* carboxyl-to-ketone hydrogen bonding, has been demonstrated in the solid state (Griffe, Durant & Pieret, 1972; Sheldrick & Trowitzsch, 1983; Abell, Morris & McKee, 1990). The H-bonding behavior of (I) is of particular interest because this compound constitutes a severely stripped-down model for 4-keto acids, in which no cyclic or unsaturated structures interpose between the acid and ketone, leaving only normal tetrahedral angles as serious conformational constraints.

Experimental. Material (m.p. 384–386 K) prepared by Friedel–Crafts condensation (Somerville & Allen,

1943) was crystallized from benzene by slow evaporation at 295 K; density was measured by flotation in carbon tetrachloride–cyclohexane. An elongated hexagonal platelet with thickness 0.009 mm and edge-to-edge dimensions 0.175, 0.175 and 0.075 mm was mounted on a glass fiber. 15 high-angle reflections were used to calculate the orientation matrix and best cell dimensions, and space group $P2_1/n$ was chosen on the basis of the extinct reflections. Data were collected on a Syntex $P2_1$ diffractometer with a graphite monochromator, using Mo $K\alpha$ radiation. With three standard reflections recorded every 47 reflections ($\pm 1.1\%$), 1559 unique reflections were measured in the θ – 2θ scan mode ($3 < 2\theta < 50^\circ$, $0 \leq h \leq 15$, $0 \leq k \leq 6$, $-17 \leq l \leq 17$); 700 were unobserved [$I < 3\sigma(I)$] and 859 had $I \geq 3\sigma(I)$; the low percentage of reflections observed was due to the low power at which the diffractometer was run during this data cycle. Absorption corrections, based on Howells' analytical expression for polyhedra (Alcock, 1970), were made after accurate measurement of the four pairs of parallel crystal faces, none of which was normal to a principal crystal axis (min. = 1.010, max. = 1.075). The structure was solved using MULTAN80 (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980); all non-H atoms were found from the best E map (CFOM = 3.00) and all H atoms were found in subsequent difference Fourier maps. H-atom positional parameters were not refined and their isotropic thermal parameters were set at $(B + 1)$ Å², where B is the value for the atom to which the H atom is bound. All non-H atoms were refined with anisotropic thermal parameters; $\sum w||F_o| - |F_c||^2$ was minimized; $R = 0.058$, $wR = 0.066$, $S = 1.05$, $w = 1/\sigma^2$ with $\sigma_i = 0.056F_o - 1.281$ for $F_o > 70.0$, $\sigma_i = -0.012F_o + 3.663$ for $F_o \leq 70.0$, last cycle max. $\Delta/\sigma = 0.0052$, av. = 0.0014, final difference Fourier max. = 0.23, min. = 0.06 e Å⁻³. The empirical weighting function was derived from a smoothed plot of the average values of $|\Delta F|/|F_o|$ for various ranges of $|F_o|$. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974, Vol. IV, pp. 72–98) and no anomalous-dispersion corrections were used. The computer programs used have been previously referenced (Lalancette, Vanderhoff & Thompson, 1990).

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Table 1. Fractional atomic coordinates and isotropic thermal parameters for (I)

$$B_{eq} = (4/3)[a^2\beta_{11} + b^2\beta_{22} + c^2\beta_{33} + (2abc\cos\gamma)\beta_{12} + (2accos\beta)\beta_{13} + (2bccos\alpha)\beta_{23}]$$

	x	y	z	$B_{eq}/B_{iso}(\text{\AA}^2)$
O(1)	0.1597 (2)	-0.0060 (6)	0.4773 (2)	6.22 (1)
O(2)	0.3756 (2)	-0.0031 (6)	0.4059 (2)	6.62 (1)
O(3)	0.4370 (2)	0.2802 (6)	0.5270 (2)	6.73 (1)
C(1)	0.3620 (3)	0.1932 (8)	0.4458 (3)	5.38 (2)
C(2)	0.2595 (4)	0.3567 (9)	0.4041 (3)	6.56 (2)
C(3)	0.1584 (3)	0.2111 (8)	0.3337 (3)	5.76 (2)
C(4)	0.1146 (3)	0.0174 (7)	0.3875 (2)	4.54 (1)
C(5)	0.0188 (3)	-0.1488 (7)	0.3304 (2)	4.26 (1)
C(6)	-0.0251 (3)	-0.3177 (9)	0.3803 (2)	5.63 (2)
C(7)	-0.1115 (3)	-0.4812 (10)	0.3301 (3)	6.81 (2)
C(8)	-0.1575 (3)	-0.4761 (10)	0.2267 (3)	6.85 (2)
C(9)	-0.1163 (3)	-0.3047 (10)	0.1765 (3)	6.31 (2)
C(10)	-0.0289 (3)	-0.1402 (8)	0.2267 (2)	5.31 (2)
H(C2)	0.2749	0.4995	0.3701	7.56
H'(C2)	0.2406	0.4282	0.4565	7.56
H(C3)	0.1788	0.1270	0.2844	6.76
H'(C3)	0.1000	0.3293	0.3000	6.76
H(C6)	0.0047	-0.3213	0.4513	6.63
H(C7)	-0.1400	-0.5973	0.3658	7.81
H(C8)	-0.2171	-0.5907	0.1915	7.85
H(C9)	-0.1483	-0.2983	0.1058	7.31
H(C10)	-0.0020	-0.0210	0.1906	6.31
H(O3)	0.5060	0.1700	0.5510	7.73

Discussion. Table 1* lists positional and isotropic thermal parameters and Table 2 lists interatomic distances and angles for (I). Fig. 1 presents a view of the asymmetric unit with its numbering scheme; (I) has no inherent chirality but adopts a chiral conformation. Fig. 1 shows that, apart from the H atoms tetrahedrally attached at C(2) and C(3), the entire molecule is essentially biplanar. The carbonyl bond is not quite coplanar with the aromatic ring but is tilted by $4.3(2)^\circ$ in the direction of the carboxyl group. However, atoms C(2), C(3) and O(1) lie outside the plane of the aromatic ring plus its attached carbon by only 0.05, 0.04 and 0.12 Å, respectively. In contrast, the dihedral angle between that plane [\equiv C(2), O(1), C(9)] and the plane of the carboxyl group is $99.4(4)^\circ$.

Fig. 2 is a partial packing diagram showing the centrosymmetric hydrogen-bonded carboxyl dimers; the ketone is not involved in the hydrogen bonding. The cell is so thin in the *b* dimension [$5.200(3)$ Å] that none of its constituent molecules lie entirely within it. For the two types of carboxyl dimers, those centered on *ac* cell faces *versus* those on *b* cell edges, the carboxyl planes are at dihedral angles of $63.6(5)^\circ$ to each other, while the aromatic rings are at dihedral angles of $87.7(3)^\circ$.

The closest intermolecular approach to either carbonyl O atom, aside from those in the carboxyl

* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 53704 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. Interatomic distances (Å) and angles ($^\circ$) for (I)

E.s.d.'s for the least significant digit are given in parentheses.

C(1)—C(2)	1.488 (6)	C(2)—C(3)	1.520 (6)
C(3)—C(4)	1.497 (5)	C(4)—C(5)	1.477 (5)
C(5)—C(6)	1.377 (5)	C(5)—C(10)	1.396 (4)
C(6)—C(7)	1.370 (5)	C(7)—C(8)	1.391 (6)
C(8)—C(9)	1.367 (6)	C(9)—C(10)	1.381 (6)
O(2)—C(1)	1.215 (4)	O(3)—C(1)	1.295 (4)
O(1)—C(4)	1.216 (4)	O(3)—H(O3)	0.999
O(2)—O(3')	2.650 (4)	H(O3)—O(2')	1.652
C(2)—C(1)—O(2)	122.9 (4)	C(2)—C(1)—O(3)	114.6 (4)
O(2)—C(1)—O(3)	122.5 (4)	C(1)—C(2)—C(3)	113.0 (4)
C(2)—C(3)—C(4)	112.0 (3)	O(1)—C(4)—C(3)	119.9 (3)
O(1)—C(4)—C(5)	120.6 (3)	C(3)—C(4)—C(5)	119.5 (3)
C(4)—C(5)—C(6)	119.4 (3)	C(4)—C(5)—C(10)	121.9 (3)
C(6)—C(5)—C(10)	118.7 (3)	C(5)—C(6)—C(7)	121.3 (3)
C(6)—C(7)—C(8)	119.9 (4)	C(7)—C(8)—C(9)	119.2 (4)
C(8)—C(9)—C(10)	121.1 (3)	C(5)—C(10)—C(9)	119.7 (4)
C(1)—O(3)—H(O3)	112.2	C(1)—O(3)—O(2')	114.2 (3)
O(3)—H(O3)—O(2')	176.5		

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

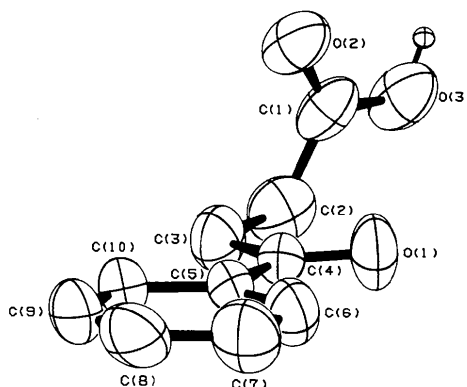


Fig. 1. The asymmetric unit of compound (I), with its numbering scheme, showing the near planarity of C(2), C(3), C(4) and O(1) with the aromatic ring. The slight tilt (4.2°) of the ketone carbonyl group [C(4)—O(1)] out of the ring plane is visible.

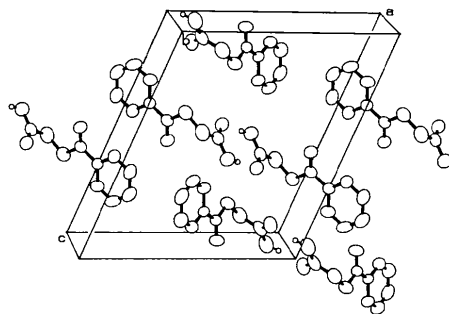


Fig. 2. A partial packing diagram for (I), showing the centrosymmetric hydrogen-bonded carboxyl dimers and their stacking pattern. The dimer near the cell center is actually centered on the front face (*ac*) and has a translational companion, omitted for clarity, centered on the rear face. One extracellular molecule has been included (lower right) to illustrate the carboxyl pairing centered on the *b* cell edge.

pairing, involves O(1) and H(C9). However, at 2.69 Å this is too far beyond the combined van der Waals radii of H and O atoms to justify invoking any special dipolar interactions (Bolton, 1963; Eiland & Pepinsky, 1955).

Although the root causes for the choice of H-bonding mode in solid keto acids remain elusive, a reliable experimental method now exists for ascertaining this pattern in a given sample, short of X-ray structure determination (Vanderhoff, Lalancette & Thompson, 1990). The solid-state (KBr) infrared spectrum of (I) is normal, displaying C=O stretching absorptions at 1684 cm⁻¹ (benzoyl) and 1709 cm⁻¹ (carboxyl). The corresponding Raman frequencies are 1679 cm⁻¹, involving a difference of only 5 cm⁻¹, for the ketone and 1627 cm⁻¹ for the carboxyl group. The frequency difference between infrared and Raman in the latter case, 82 cm⁻¹, is the largest we have observed, the average being about 51 cm⁻¹ for the carboxyl dimers we have studied. This frequency difference is small (typically *ca* 4 cm⁻¹) for carboxyl groups which adopt catemeric hydrogen-bonding patterns and has been shown to be a reliable experimental predictor of H-bonding mode in solid-state keto carboxylic acids (Vanderhoff, Lalancette & Thompson, 1990).

Acta Cryst. (1991). **C47**, 1445–1448

Structure of 5-Methylcytidine

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(Received 10 August 1990; accepted 30 October 1990)

Abstract. 4-Amino-5-methyl-1-β-D-ribofuranosyl-2(1*H*)-pyrimidinone, C₁₀H₁₅N₃O₅, *M_r* = 257.2, monoclinic, *P*2₁, *a* = 5.632 (1), *b* = 14.636 (3), *c* = 13.914 (3) Å, β = 90.57 (1)°, *V* = 1146.9 Å³, *Z* = 4, *D_x* = 1.49 Mg m⁻³, λ(Cu *K*α) = 1.5418 Å, μ = 0.98 mm⁻¹, *F*(000) = 544, *T* = 295 K, *R* = 0.036 for 2025 unique observed reflections with *F* ≥ 3σ(*F*). The bond lengths, bond angles and conformation of the two independent molecules in the asymmetric unit are essentially similar. The cytosine bases are not protonated. Bases are in *anti* conformation, sugars show C(3′)-*endo* pucker (³*E*) and *gg* conformation about the C(4′)—C(5′) bond for both molecules. The structure is stabilized by a number of hydrogen bonds between molecules *A* and molecules *B*. No base-stacking interactions were observed in the

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present structure. This is in agreement with the observation made in a comparison of methylated and unmethylated cytosine structures which showed that methylation at the 5 position of the cytosine base could result in reduced base-stacking interactions.

Introduction. Metabolite activities of 5-methylated cytosine bases with a key role in a variety of biochemical regulation processes have been discussed by Doerfler (1983, 1984), Razin & Riggs (1980), Rideout, Coetzee, Olumi & Jones (1990) and Ehrlich & Wang (1981). The structural and energetic alterations demonstrate that methylation of cytosine in the 5 position may be an important switch mechanism for influencing the B–Z equilibrium and DNA topology in general, thus potentially affecting DNA–