

## Molecular and Crystal Structure of 2-Bromo-1-Hydroxy-1-Phenyl-4,4-Dimethyl-3-Pentanone

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O composto  $C_{13}H_{17}O_2Br$  com  $M_r = 285.22$  é romboédrico, grupo espacial  $R\bar{3}$ , com dimensões de cela unitária  $a = 13.228(7) \text{ \AA}$ ,  $\alpha = 102.97(5)^\circ$ ,  $V = 2104(2) \text{ \AA}^3$ ;  $Z = 6$ ,  $D_{\text{calc}} = 1.35 \text{ Mg m}^{-3}$ ,  $\lambda(\text{MoK}\alpha) = 0.71073 \text{ \AA}$ ,  $\mu = 28.36 \text{ cm}^{-1}$ ,  $F(000) = 876$ ,  $T = 298 \text{ K}$ ,  $R = 10.5\%$  para 371 reflexões observadas com  $I \geq 2.5 \sigma(I)$ . O aspecto interessante desta estrutura é o conjunto de pontes de hidrogênio em torno do eixo de ordem três e através do centro de inversão em  $(1/2, 1/2, 1/2)$ .

The compound  $C_{13}H_{17}O_2Br$  with  $M_r = 285.22$  is rhombohedral, space group  $R\bar{3}$ , with cell dimensions  $a = 13.228(7) \text{ \AA}$ ,  $\alpha = 102.97(5)^\circ$ ,  $V = 2104(2) \text{ \AA}^3$ ;  $Z = 6$ ,  $D_{\text{calc}} = 1.35 \text{ Mg m}^{-3}$ ,  $\lambda(\text{MoK}\alpha) = 0.71073 \text{ \AA}$ ,  $\mu = 28.36 \text{ cm}^{-1}$ ,  $F(000) = 876$ ,  $T = 298 \text{ K}$ ,  $R = 10.5\%$  for 371 observed reflections with  $I \geq 2.5 \sigma(I)$ . The interesting aspect of this structure is the hydrogen bonding around the three-fold symmetry axis and through the inversion center at  $(1/2, 1/2, 1/2)$ .

**Key words:**  $C_{13}H_{17}O_2Br$

### Introduction

The stereoselective synthesis of  $\alpha$ -amino- $\beta$ -hydroxy carbonil compounds has attracted interest by the possible use of the corresponding carboxylic acids as enzyme inhibitors<sup>1-2</sup> and as building blocks in the synthesis of natural products<sup>3</sup> and references cited therein.

$\alpha$ -Bromo- $\beta$ -hydroxy ketones were envisaged as useful synthetic intermediates in the preparation of *anti*  $\alpha$ -amino- $\beta$ -hydroxy ketones and were then stereoselectively prepared through aldol condensation of preformed lithium enolates of bromoketones with aliphatic and aromatic aldehydes (Pilli, Agostini, Grimaldi, Vencato and Mascarenhas, to be published).

<sup>1</sup>H and <sup>13</sup>C-NMR analysis of the  $\alpha$ -bromo- $\beta$ -hydroxy ketones prepared was consistent with the *syn* relative stereochemistry (<sup>3</sup>J<sub>H $\alpha$ -H $\beta$</sub>  = 4 Hz) except<sup>4</sup> for 2-bromo-1-hydroxy-1-phenyl-4,4-dimethyl-3-pentanone (<sup>3</sup>J<sub>H $\alpha$ -HB</sub> = 8 Hz)<sup>4</sup> which was subjected to X-ray diffraction analysis.

### Experimental

Colorless crystals were grown from ligroin. A crystal of approximate dimensions  $0.5 \times 0.4 \times 0.4 \text{ mm}$  was sealed in a thin glass capillary, with unit cell dimensions obtained by a least-squares fit of 25 reflections ( $7.9 < \theta < 14.9^\circ$ ). The intensity data were collected on an Enraf-Nonius CAD-4 single-crystal X-ray diffractometer with graphite-monochromated MoK $\alpha$  radiation, using  $\omega - 2\theta$  scan technique, and scan widths calculated using the expression  $(0.80 + 0.35 \tan \theta)^\circ$ , with a max. time spent on any intensity measurement of 20 s. The range of  $hkl$  was  $-9 \leq h \leq 7$ ;  $-9 \leq k \leq 7$ ;  $0 \leq l \leq 12$  with  $\theta_{\text{max}} = 20^\circ$ . One standard reflection ( $2 \bar{3} 4$ ), measured every 30 min., showed a maximum count variation of 47%. For this reason anisotropic decay correction was applied with max. and min. corrections of 3.5760 and 1.0006, average of 1.6560. A total number of 2419 reflections were measured out of which 1211 were unique and 371 were significant [ $I \geq 2.5 \sigma(I)$ ]. The reflection 113

was omitted from the last refinement cycle. Lp and absorption corrections were applied with max. and min. transmission factors of 1.657 and 0.533 with an average of 0.980, afterwards the equivalent reflections were merged with  $R_{\text{int}} = 8.4\%$ .

The structure was solved using *MULTAN80*<sup>5</sup>. The hydrogen atom H(O1) has been found from a difference electron density map, whereas the remaining H atoms have been placed using an idealized model based on the atoms to which the hydrogen atoms are bonded and were not refined. Due to the low reflections to parameter ratio the C atoms of the ring were refined only with isotropic temperature parameters and fixed geometry. The others non-H atoms were refined with anisotropic thermal parameters. Full-matrix refinement led to an R of 0.105 and  $wR = 0.089$  with the function minimized  $\sum w(|F_o| - |F_c|)^2$ , where  $w = |\sigma(F_o) + (0.000269F_o)|^{-1}$  and  $\sigma(I)$  is based on counting statistics. Maximum shift to estimated standard deviation was 0.42, with the largest feature in the final difference electron map were 1.8 (on the origin) and  $-0.81 e \text{ \AA}^{-3}$ . The number of refined parameters was 103 and the standard deviation of unitary weight was 2.72. Programs from *SHELX76*<sup>6</sup>, Enraf-Nonius SDP<sup>7</sup>; atomic scattering factors from *International Tables for X-ray Crystallography*<sup>8</sup>, drawings made with *ORTEP*<sup>9</sup>. The calculations were performed on a IBM 4341 computer.

### Discussion and Conclusion

The final atomic coordinates are given in Table 1 and bond distances and angles in Table 2. Torsion angles are shown in Table 3. Anisotropic temperature factors and the hydrogen atoms coordinates are given in Tables 4 and 5, respectively. The crystallographic atom numbering and a view of the molecule are shown in Fig. 1. The bond lengths and angles are not significantly different from the expected range. Their large e.s.d.'s may be due to the low value of the data/variable parameter ratio which reflects the poor diffracting quality of the crystal.

The perpendicular displacement ( $\text{\AA}$ ) from the least-squares

plane, defined by the equation  $0.8419 X + 0.1769 Y - 0.5098 Z = 1.7896$  through the ring atoms, of the following atoms are: C(1) =  $-0.09$ ; H(C1) =  $-0.01$ ; O(1) =  $0.86$ ; C(2) =  $-1.50$ ; H(C2) =  $-1.74$ ; C(3) =  $-2.48$ ; O(2) =  $-2.37$ .

The molecule view (Fig. 1) shows the *syn* relative stereochemistry of the two asymmetric centers (torsion angle  $\text{Br-C}(2)-\text{C}(1)-\text{O}(1) = -50^\circ$ ) fully consistent with the relative stereochemistry determined by  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectroscopy for the compounds prepared from aliphatic aldehydes.

The unexpected large coupling constant for H(C1) and H(C2) observed in the title compound can now be rationalized by the Karplus equation<sup>10</sup> assuming that the torsion angle  $\text{H}(C1)-\text{C}(1)-\text{C}(2)-\text{H}(C2)$  (Table 3) observed in the crystalline form is retained in solution.

The interesting feature of this structure is the molecular packing around the threefold symmetry axis through the inversion center at  $(1/2, 1/2, 1/2)$ . The molecules are linked

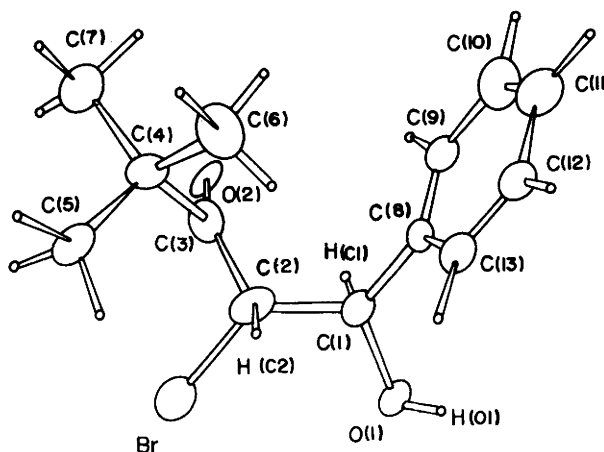


Figure 1. View of the molecule with atom numbering. H atoms treated as isotropic, are on an arbitrary scale.

Table 1. Final positional parameters and equivalent isotropic temperature factors with e.s.d.'s in parentheses

	x	y	z	$B_{\text{eq}}(\text{\AA}^2)^*$
Br	0.4320(4)	0.4183(4)	0.8582(4)	6.7(2)
O(1)	0.453(2)	0.379(2)	0.623(4)	3.8(5)
O(2)	0.278(2)	0.172(2)	0.764(2)	4.9(5)
C(1)	0.372(3)	0.297(3)	0.630(3)	3.8(5)
C(2)	0.321(4)	0.337(3)	0.719(3)	5.6(5)
C(3)	0.254(4)	0.249(4)	0.745(4)	5.4(5)
C(4)	0.143(4)	0.259(4)	0.753(4)	4.9(5)
C(5)	0.154(3)	0.368(4)	0.827(4)	6.2(5)
C(6)	0.069(3)	0.242(4)	0.638(4)	7.1(5)
C(7)	0.086(3)	0.173(4)	0.804(4)	6.3(5)
C(8)	0.293(2)	0.228(2)	0.529(2)	3.6(8)
C(9)	0.263(2)	0.115(2)	0.497(2)	4.4(8)
C(10)	0.181(2)	0.057(2)	0.401(2)	7.0(9)
C(11)	0.128(2)	0.111(2)	0.338(2)	7.9(9)
C(12)	0.158(2)	0.224(2)	0.370(2)	4.6(8)
C(13)	0.240(2)	0.283(2)	0.466(2)	3.8(8)

$$B_{\text{eq}}^* = \frac{4}{3} \sum_i \sum_j T_{ij} B_{ij} \text{ and } \sigma(B_{\text{eq}}) = T_{ij} \sigma(B_{ij})$$

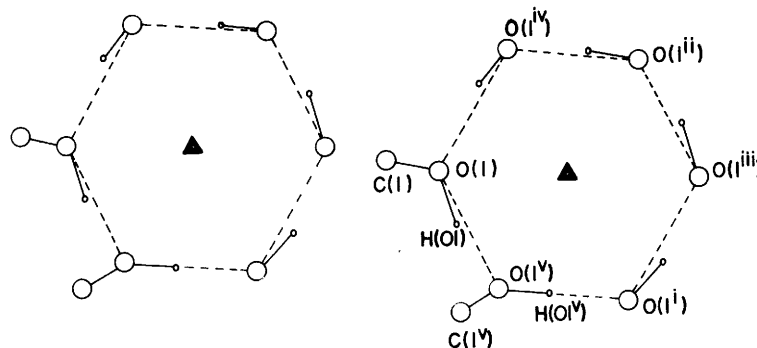
**Table 2.** Bond lengths (Å) and angles (°) with e.s.d.'s in parentheses

Br-C(2)	1.97(4)	C(4)-C(6)	1.56(5)
C(1)-C(2)	1.54(5)	C(4)-C(7)	1.58(6)
C(1)-O(1)	1.38(4)	C(8)-C(9)	1.40
C(1)-C(8)	1.45(4)	C(9)-C(10)	1.40
C(2)-C(3)	1.44(5)	C(10)-C(11)	1.40
C(3)-O(2)	1.20(5)	C(11)-C(12)	1.40
C(3)-C(4)	1.53(5)	C(12)-C(13)	1.40
C(4)-C(5)	1.51(5)	C(13)-C(8)	1.40
Br-C(2)-C(1)	112(3)	C(3)-C(4)-C(7)	113(4)
Br-C(2)-C(3)	104(3)	C(5)-C(4)-C(6)	109(4)
C(1)-C(2)-C(3)	113(4)	C(5)-C(4)-C(7)	105(4)
C(2)-C(1)-C(8)	113(3)	C(6)-C(4)-C(7)	109(4)
C(2)-C(1)-O(1)	112(4)	C(1)-C(8)-C(9)	125(2)
O(1)-C(1)-C(8)	117(4)	C(1)-C(8)-C(13)	115(2)
C(2)-C(3)-O(2)	127(5)	C(8)-C(9)-C(10)	120
C(2)-C(3)-C(4)	116(5)	C(9)-C(10)-C(11)	120
O(2)-C(3)-C(4)	117(5)	C(10)-C(11)-C(12)	120
C(3)-C(4)-C(5)	111(5)	C(11)-C(12)-C(13)	120
C(3)-C(4)-C(6)	109(4)	C(12)-C(13)-C(13)	120
		C(13)-C(8)-C(9)	120

by fairly strong hydrogen bonding between the O(1) atom as a donor of an H bond to O(1<sup>v</sup>) and as an acceptor of O(1<sup>iv</sup>) with the distances and angles O(1) - H(O1) ...O(1<sup>v</sup>) [O(1) - H(O1) 1.02 Å, O(1) ...O(1<sup>v</sup>) 2.64(3) Å, H(O1) ...O(1<sup>v</sup>) 1.77 Å, O(1) - H(O1) ...O(1<sup>v</sup>) 142°] [(v) = 1 - y, 1 - z, 1 - x] and O(1<sup>iv</sup>) - H(O1<sup>iv</sup>) ...O(1) [O(1<sup>iv</sup>) - H(O1<sup>iv</sup>) 1.02 Å, O(1<sup>iv</sup>) ...O(1) 2.64(3) Å, H(O1<sup>iv</sup>) ...O(1) 1.77 Å, O(1<sup>iv</sup>) - H(O1<sup>iv</sup>) ...O(1) 142°] [(iv) = 1 - z, 1 - x, 1 - y]. Only the C(1), C(1<sup>v</sup>), all six O(1) and six H(O1) atoms generated by the space group symmetry are depicted for clarity in the stereoscopic hydrogen bond scheme shown in Fig. 2. The six O(1) atoms interlinked by the H bonds make a six-membered ring with a chair conformation.

### Supplementary Material

List of the observed and calculated structure factors is available from one of the authors (I.V.) upon request.



**Figure 2.** Stereoscopic view of the H-bonding around the threefold-symmetry axis and the inversion center at (1/2, 1/2, 1/2). The symmetry operators are: (i)  $z, x, y$ ; (ii)  $y, z, x$ ; (iii)  $1-x, 1-y, 1-z$ ; (iv)  $1-z, 1-x, 1-y$ ; (v)  $1-y, 1-z, 1-x$ .

**Table 3.** Torsion angles (°). The estimated standard deviation is 3°.

Br-C(2)-C(1)-O(1)	-50
Br-C(2)-C(1)-C(8)	174
Br-C(2)-C(3)-O(2)	-72
Br-C(2)-C(3)-C(4)	106
Br-C(2)-C(1)-H(C1)	69
O(1)-C(1)-C(8)-C(9)	129
O(1)-C(1)-C(8)-C(13)	-56
O(1)-C(1)-C(2)-H(C2)	66
H(C1)-C(1)-C(2)-H(C2)	-175
H(C1)-C(1)-C(8)-C(9)	7
H(C1)-C(1)-C(8)-C(13)	-177
H(C2)-C(2)-C(1)-C(8)	-70
H(C1)-C(1)-C(2)-C(3)	-47
H(C2)-C(2)-C(3)-O(2)	172
H(C2)-C(2)-C(3)-C(4)	-11
O(1)-C(1)-C(2)-C(3)	-167
O(2)-C(3)-C(4)-C(5)	126
O(2)-C(3)-C(4)-C(6)	-111
O(2)-C(3)-C(4)-C(7)	9
C(1)-C(2)-C(3)-O(2)	49
C(1)-C(2)-C(3)-C(4)	-133
C(1)-C(8)-C(9)-C(10)	176
C(1)-C(8)-C(13)-C(12)	-176
C(2)-C(1)-C(8)-C(9)	-98
C(2)-C(1)-C(8)-C(13)	77
C(2)-C(3)-C(4)-C(5)	-51
C(2)-C(3)-C(4)-C(6)	71
C(2)-C(3)-C(4)-C(7)	-169
C(3)-C(2)-C(1)-C(8)	58
C(8)-C(9)-C(10)-C(11)	-1
C(8)-C(13)-C(12)-C(11)	1
C(9)-C(8)-C(13)-C(12)	-1
C(9)-C(10)-C(11)-C(12)	-51
C(10)-C(9)-C(8)-C(13)	1
C(10)-C(11)-C(12)-C(13)	-1

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**Table 4.** Anisotropic temperature factors

Atom	U(1,1)	U(2,2)	U(3,3)	U(2,3)	U(1,3)	U(1,2)
Br	0.082(5)	0.086(5)	0.080(5)	0.024(4)	0.015(4)	0.023(4)
O(1)	0.03(10)	0.06(1)	0.06(1)	0.03(1)	0.02(1)	0.02(1)
O(2)	0.07(1)	0.08(1)	0.07(1)	0.07(1)	0.03(1)	0.04(1)
C(1)	0.04(1)	0.06(1)	0.06(1)	0.03(1)	0.01(1)	0.02(1)
C(2)	0.08(1)	0.07(1)	0.06(1)	0.05(1)	0.00(1)	0.00(1)
C(3)	0.04(1)	0.08(1)	0.09(1)	0.00(1)	0.03(1)	0.04(1)
C(4)	0.05(1)	0.06(1)	0.07(1)	0.02(1)	0.02(1)	0.01(1)
C(5)	0.04(1)	0.09(1)	0.12(1)	0.02(1)	0.05(1)	0.02(1)
C(6)	0.06(1)	0.10(1)	0.12(1)	0.02(1)	0.03(1)	0.06(1)
C(7)	0.06(1)	0.10(1)	0.08(1)	0.04(1)	0.01(1)	0.04(1)

**Table 5.** Hydrogen atoms coordinates and equivalent isotropic temperature factors.

	x	y	z	B <sub>eq</sub> *
H(O1)	0.495	0.347	0.575	3.8
H(C1)	0.406	0.230	0.663	3.8
H(C2)	0.278	0.398	0.692	5.6
H(C5)	0.074	0.387	0.840	6.2
H'(C5)	0.196	0.442	0.812	6.2
H''(C5)	0.198	0.379	0.916	6.2
H(C6)	-0.013	0.249	0.635	7.1
H'(C6)	0.057	0.156	0.591	7.1
H''(C6)	0.104	0.294	0.596	7.1
H(C7)	0.007	0.171	0.807	6.3
H'(C7)	0.139	0.178	0.880	6.3
H''(C7)	0.079	0.090	0.746	6.3
H(C9)	0.301	0.069	0.544	4.4
H(C10)	0.156	-0.033	0.373	7.0
H(C11)	0.063	0.065	0.262	7.9
H(C12)	0.115	0.265	0.321	4.6
H(C13)	0.260	0.368	0.492	3.8

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