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### ***trans*-2-Pivaloylcyclopropanecarboxylic acid**

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**Abstract.** C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>, monoclinic, *P*2<sub>1</sub>/*n* (*Z* = 4), *a* = 5.888 (2), *b* = 16.237 (10), *c* = 10.252 (6) Å, β = 96.56 (4)°, *V* = 973.7 (9) Å<sup>3</sup>, *M<sub>r</sub>* = 170.2. The structure was solved by direct methods and refined by full-matrix least-squares calculations to *R* = 0.047 for 865 observed reflections. These results were compared with those previously obtained by the use of a conformational theoretical study (CNDO/2 method). The conformational similarity found between the solid state (X-ray diffraction) and the gaseous state (quantum calculation) makes it likely that 2-pivaloylcyclopropanecarboxylic acid keeps the same conformation in solution.

**Introduction.** In the field of therapeutic chemistry, a renewal of interest in small cyclic compounds has been stimulated by methods of synthesis developed for pyrethrin-type insecticides. In a general study, Cussac, Pierre, Boucherle & Favier (1975) tried to find out how the cyclopropane ring contributes to pharmacological activity, with the aid of many examples; the often favorable contribution of this structural element suggests that it merits the name 'pharmacophore'.

Bifunctional cyclopropane derivatives have been prepared (Mouzin, Cousse & Bonnaud, 1978); in pharmacology they act particularly on the central

nervous system [as anticonvulsants or muscle relaxants (Lattes, Mouzin, Bonnaud & Cousse, 1977)]. However, the compound that has proved most interesting (Lauressergues, Stenger & Charveron, 1978) is 2-pivaloylcyclopropanecarboxylic acid (Fig. 1), which shows anorexiatic action without noteworthy effects on the central nervous system.

In the case of the anorexiatic amphetamines, this action is accompanied by a stereoselective central one (Goldstein & Anagnoste, 1965). To study further the structure–activity relationships among the cyclopropane derivatives, we have undertaken a crystallographic study to determine their molecular geometry.

We have previously studied their conformations theoretically, using the CNDO/2 methods of quantum chemistry (Crasnier, Labarre, Cousse, Dussourd &

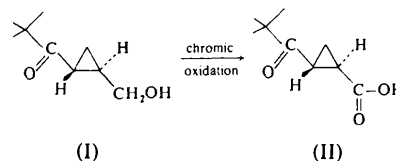


Fig. 1. Synthesis scheme for *trans*-2-pivaloylcyclopropanecarboxylic acid.

Table 1. Atomic coordinates of the carbon and oxygen atoms ( $\times 10^4$ ) and mean isotropic temperature factors,  $B_{\text{eq}}$  ( $\text{\AA}^2$ );  $\sigma(B_{\text{eq}}) = 0.5$

$$B_{\text{eq}} = \frac{8}{3} \pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j$$

	x	y	z	$B_{\text{eq}}$
C(1)	2899 (5)	2821 (2)	5121 (3)	4.8
C(2)	4120 (6)	3489 (2)	5948 (3)	4.6
C(3)	2749 (7)	4141 (2)	6510 (3)	5.1
C(4)	3707 (7)	4480 (2)	7848 (3)	4.6
C(5)	3804 (11)	4977 (3)	6648 (5)	7.6
C(6)	2061 (7)	4710 (2)	8765 (3)	4.5
O(7)	2675 (4)	4519 (2)	9981 (2)	5.3
O(8)	226 (5)	5056 (2)	8579 (2)	6.1
O(9)	6183 (5)	3503 (2)	6167 (3)	6.7
C(10)	1410 (9)	2330 (4)	5998 (6)	7.7
C(11)	1343 (12)	3190 (4)	3991 (5)	9.1
C(12)	4597 (9)	2233 (4)	4638 (6)	8.4

Table 2. Interatomic distances ( $\text{\AA}$ ) and angles ( $^\circ$ )

C(2)–C(1)	1.507 (5)	C(4)–C(3)	1.526 (5)
C(10)–C(1)	1.547 (6)	C(5)–C(3)	1.493 (6)
C(11)–C(1)	1.515 (6)	C(5)–C(4)	1.478 (6)
C(12)–C(1)	1.506 (6)	C(6)–C(4)	1.474 (5)
C(3)–C(2)	1.487 (5)	O(7)–C(6)	1.294 (4)
O(9)–C(2)	1.210 (4)	O(8)–C(6)	1.242 (4)
C(10)–C(1)–C(2)	108.0 (3)	C(5)–C(3)–C(2)	116.5 (4)
C(11)–C(1)–C(2)	110.7 (4)	C(5)–C(3)–C(4)	58.6 (3)
C(11)–C(1)–C(10)	108.3 (4)	C(5)–C(4)–C(3)	59.6 (3)
C(12)–C(1)–C(2)	110.4 (3)	C(6)–C(4)–C(3)	117.6 (3)
C(12)–C(1)–C(10)	107.8 (4)	C(6)–C(4)–C(5)	118.9 (4)
C(12)–C(1)–C(11)	111.4 (4)	C(4)–C(5)–C(3)	61.8 (3)
C(3)–C(2)–C(1)	119.0 (3)	O(7)–C(6)–C(4)	114.9 (3)
O(9)–C(2)–C(1)	121.5 (3)	O(8)–C(6)–C(4)	121.5 (3)
O(9)–C(2)–C(3)	119.4 (3)	O(8)–C(6)–O(7)	123.5 (3)
C(4)–C(3)–C(2)	116.4 (3)		

Table 3. Torsion angles ( $^\circ$ );  $\bar{\sigma} = 1^\circ$

C(10)–C(1)–C(2)–O(3)	–63
C(11)–C(1)–C(2)–C(3)	55
C(12)–C(1)–C(2)–C(3)	180
C(12)–C(1)–C(2)–O(9)	–1
C(2)–C(1)–C(10)–H(C10)	180
C(2)–C(1)–C(11)–H(C11)	177
C(2)–C(1)–C(12)–H(C12)	–177
C(1)–C(2)–C(3)–C(4)	147
O(9)–C(2)–C(3)–C(4)	–33
O(9)–C(2)–C(3)–C(5)	33
O(9)–C(2)–C(3)–H(C3)	–174
C(3)–C(4)–C(6)–O(8)	–39
C(5)–C(4)–C(6)–O(8)	29
H(C4)–C(4)–C(6)–O(7)	0
C(4)–C(6)–O(7)–H(O7)	176

Mouzin, 1975). The acid was obtained by oxidation of the alcohol (Cousse & Mouzin, 1972) according to the reaction scheme shown in Fig. 1.

The configuration of the starting alcohol was assigned by proton magnetic resonance at 250 MHz

(Gey, Perraud, Pierre, Cousse, Dussourd & Mouzin, 1977).

The intensities of 1446 reflections were measured with Mo  $K\alpha$  radiation ( $\lambda = 0.7107 \text{ \AA}$ ) (maximum angle  $2\theta = 47^\circ$ ); of these, 865, which had intensities greater than  $2.5\sigma(I)$ , were considered as observed. The structure was solved with *MULTAN* 78 (Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978). All the heavy atoms were located in the Fourier synthesis corresponding to the most probable set of phases. Full-matrix least-squares refinement was performed with *SHELX* 76 (Sheldrick, 1976). At the end of the anisotropic refinement we obtained a reliability factor,  $R$ , of 0.047.\* The hydrogen atoms were located on a difference Fourier map.

The atomic coordinates are listed in Table 1, the interatomic distances and bond angles in Table 2, and the torsion angles in Table 3.

Fig. 2 is a view of the molecule drawn with the aid of the *PLUTO* program (Motherwell & Clegg, 1978). The arrangement of the molecules in the lattice shows the formation of a dimer by intermolecular hydrogen bonds: O(7)···O(8) 2.623 (6)  $\text{\AA}$ ; O(7)–H(O7)···O(8) 1.43 (5)  $\text{\AA}$ ; symmetry code (i):  $-x, 1-y, 2-z$ . The oxygen atom O(9) is equidistant (2.50  $\text{\AA}$ ) from H(C4) and H(C5).

**Discussion.** There is remarkable agreement between our results and those previously obtained from a theoretical conformational study (CNDO/2 method) performed in 1975 on the basis of a standard geometrical model (Pople & Gordon, 1967) for the acid in the *trans* configuration.

Thus we find here the *tert*-butyl group in the LEM form described previously for compounds of the general formula  $(\text{CH}_3)_3M$ , where  $M = \text{CH, SiH, N, or}$

\* Lists of structure factors, anisotropic temperature factors and H atom positional parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 36547 (8 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

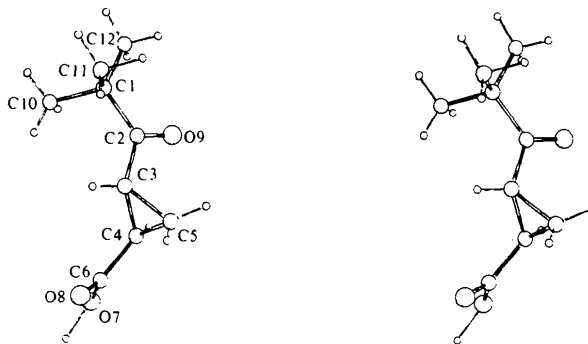


Fig. 2. Stereoscopic view of *trans*-2-pivaloylcyclopropanecarboxylic acid.

P (Corosine, Crasnier, Labarre, Labarre & Leibovici, 1973) with the following values for the torsion angles:  $C(2)-C(1)-C(10)-H(C10) = 180(1)^\circ$ ;  $C(2)-C(1)-C(11)-H(C11) = 177(1)^\circ$ ;  $C(2)-C(1)-C(12)-H(C12) = -177(1)^\circ$ ; where  $180$  and  $-180^\circ$  were predicted in the calculations.

Likewise, the carbonyl group  $C(2)-O(9)$  eclipses the bond  $C(1)-C(12)$ , which corresponds well with the conformation noted (LEM, 60) in the theoretical study and leads to a very short  $C(12)-O(9)$  distance of  $2.692(6) \text{ \AA}$ .

In addition, the carboxylic acid group is in the predicted position, with the same orientation of the hydroxyl  $O(7)-H(O7)$ , defined by the torsion angle  $C(4)-C(6)-O(7)-H(O7)$ ; the crystallographic study gives an angle of  $176(1)^\circ$  where a value of  $180^\circ$  was determined by CNDO/2.

However, a new CNDO/2 calculation performed with the crystallographic data led to an energy (about  $21 \text{ kJ mol}^{-1}$ ) greater than that found from the standard geometry. This may be explained by the fact that in the solid state the molecule exists in the dimer form and the geometrical constraints then observed are not taken into account in a quantum calculation of a molecule described by a regular 'standard' geometry.

The similarity of the conformations found in the solid state and for the free molecule suggests that the general conformation of trans-2-pivaloylcyclopropanecarboxylic acid will remain unchanged in solution and therefore that its activity could be explained from this structure determined by X-ray diffraction.

The trans configuration obtained for this acid is the same as that assigned by NMR to the corresponding alcohol, which indicates that the configuration is indeed retained during the reaction shown in Fig. 1.

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## Hydrogen Bonds in a Dimer of Dimethyl 5-Methyl-2-phenyl-3,4-pyrazolidinedicarboxylate

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**Abstract.**  $C_{14}H_{18}N_2O_4$ , monoclinic,  $P2_1/c$ ,  $a = 10.03(1)$ ,  $b = 14.46(2)$ ,  $c = 20.60(1) \text{ \AA}$ ,  $\beta = 100.24(8)^\circ$ ,  $Z = 8$ ,  $M_r = 278.3$ ,  $D_c = 1.26 \text{ Mg m}^{-3}$ ,  $\mu(\text{Mo } K\alpha) = 0.10 \text{ mm}^{-1}$ . There are two crystallographically independent molecules in the asymmetric

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unit. The structure was solved with *MULTAN*. Full-matrix least-squares refinement converged to  $R = 0.054$  for 2041 observed reflexions. The most interesting feature in the structure is the existence of several hydrogen bonds between the two molecules of the

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