

# The Crystal and Molecular Structure of DL- $\alpha$ -Methyltyrosine

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The crystal structure of DL- $\alpha$ -methyltyrosine has been determined by X-ray diffraction methods using 2095 observed reflections. The crystals are monoclinic, space group  $P2_1/c$ , with four molecules in the unit cell of dimensions  $a = 12.763(2)$  Å;  $b = 5.867(1)$  Å;  $c = 17.653(4)$  Å;  $\beta = 132.12(1)^\circ$ . The structure was solved by Patterson methods and refined to a conventional  $R$ -factor of 0.048. Estimated standard deviation in bond lengths not involving hydrogen atoms is 0.002 Å and in angles 0.1–0.2°. The bond lengths and angles are consistent with those found in L-tyrosine. The conformational angles describing the positions of the amino and carboxyl groups relative to the aromatic ring are nearly identical to those of L-tyrosine and thus different from those reported for  $\alpha$ -methyl-*m*-tyrosine.

DL- $\alpha$ -Methyltyrosine has been examined as a part of the study of structural and conformational characteristics in phenylalanine derivatives in progress in this laboratory. The compound appears interesting both by being biologically active as a specific inhibitor of the enzyme tyrosine 3-hydroxylase<sup>1</sup> thus interfering with the biosynthesis of catecholamines, as well as by offering data in the study of the conformational effect of  $\alpha$  substituents in phenylalanine derivatives.

## EXPERIMENTAL

Crystals of DL- $\alpha$ -methyltyrosine were formed by very slow evaporation of a saturated solution of the compound in formic acid at 60 °C. The specimen used for the X-ray experiments had approximate dimensions 0.15 × 0.30 × 0.35 mm<sup>3</sup>. Oscillation and Weissenberg photographs indicated monoclinic symmetry; systematically absent reflections proved the space group to be  $P2_1/c$ . Unit cell dimensions were determined from diffractometer measurements of 23 general reflections using CuK $\alpha$ -radiation ( $\lambda = 1.3922$  Å).

The intensity data were recorded using a Picker automatic four-circle diffractometer with graphite crystal monochromated MoK $\alpha$  radiation ( $\lambda = 0.71069$  Å). 2710 independent reflections with  $\sin \theta/\lambda < 0.7$  were measured using the  $\omega - 2\theta$  scanning mode. The  $2\theta$  scan speed was 1° min<sup>-1</sup> and the range from 0.8° below  $2\theta(\alpha_1)$  to 0.8° above  $2\theta(\alpha_2)$ , background counts were taken for 30 s at each of the scan range limits. Three standard reflections were measured after every 100 reflections; they showed no systematic variation during the experiment. The standard deviations were taken as  $\sigma(I) = [C_T + (0.02C_N)^2]^{1/2}$  where  $C_T$  is the total number of counts and  $C_N$  the scan count minus background count. 2095 reflections had net intensity larger than  $2\sigma(I)$  and were regarded as observed, whereas the remaining reflections were excluded from the calculations. The intensity data were corrected for Lorentz and polarization effects.

Atomic form factors used were those of Doyle and Turner<sup>2</sup> for oxygen, nitrogen, and carbon atoms, and of Stewart, Davidson and Simpson<sup>3</sup> for hydrogen. A description of the computer programs employed during the structure determination is given in Ref. 6. In the full-matrix least-squares program the quantity minimized was  $\sum w\Delta F^2$  where  $w$  is the inverse of the variance of the observed structure factors.

## CRYSTAL DATA

DL- $\alpha$ -Methyl(4-hydroxyphenyl)alanine ( $\alpha$ -methyltyrosine), C<sub>10</sub>H<sub>13</sub>NO<sub>3</sub>, monoclinic,  $a = 12.763(2)$  Å;  $b = 5.867(1)$  Å;  $c = 17.653(4)$  Å;  $\beta = 132.12(1)^\circ$ , ( $t = 18 \pm 1$  °C).  $V = 980.47$  Å<sup>3</sup>;  $F(000) = 416$ ;  $Z = 4$ ;  $D_{\text{obs}} = 1.30$  g cm<sup>-3</sup>;  $D_{\text{calc}} = 1.322$  g cm<sup>-3</sup>. Absent reflections:  $(0k0)$  for  $k$  odd,  $(h0l)$  for  $l$  odd. Space group  $P2_1/c$  (No. 14).

## STRUCTURE DETERMINATION

The structure was solved by Patterson methods. From a sharpened three-dimensional Pat-

Table 1. Fractional atomic coordinates and thermal parameters with estimated standard deviations ( $\times 10^4$ ). The temperature factor is given by  $\exp -(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl)$ .

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> <sub>11</sub>	<i>B</i> <sub>22</sub>	<i>B</i> <sub>33</sub>	<i>B</i> <sub>12</sub>	<i>B</i> <sub>13</sub>	<i>B</i> <sub>23</sub>
O1	-2643(1)	-616(2)	-3281(1)	98(2)	221(4)	43(1)	-20(4)	55(2)	0(3)
O2	3668(1)	-2098(2)	-430(1)	98(2)	199(3)	44(1)	-40(3)	93(2)	-49(3)
O3	3729(1)	-3711(2)	743(1)	145(2)	136(3)	66(1)	22(4)	144(2)	22(3)
N1	3887(1)	2091(2)	157(1)	85(2)	130(3)	41(1)	9(4)	80(2)	6(3)
C1	1238(1)	468(3)	-338(1)	69(2)	176(4)	40(1)	12(5)	74(2)	-5(3)
C2	623(2)	2175(3)	-1071(1)	84(2)	155(4)	54(1)	1(5)	81(2)	9(4)
C3	-665(2)	1856(3)	-2061(1)	86(2)	179(5)	48(1)	25(5)	82(2)	34(4)
C4	-1377(2)	-191(3)	-2321(1)	75(2)	197(5)	40(1)	11(5)	69(2)	-7(3)
C5	-800(2)	-1894(3)	-1593(1)	88(2)	173(5)	51(1)	-32(5)	84(2)	-3(4)
C6	493(2)	-1560(3)	-618(1)	89(2)	191(5)	44(1)	6(5)	86(2)	23(3)
C7	2676(2)	763(3)	721(1)	80(2)	182(5)	38(1)	2(5)	75(2)	-19(3)
C8	3917(1)	312(2)	777(1)	71(2)	130(4)	31(1)	5(4)	59(2)	5(3)
C9	3757(1)	-2043(3)	327(1)	64(2)	142(4)	39(1)	7(4)	62(2)	-10(3)
C10	5342(2)	487(3)	1865(1)	80(2)	258(5)	37(1)	1(5)	55(2)	-12(4)

Table 2. Fractional atomic coordinates ( $\times 10^3$ ) and *B*-values with estimated standard deviations for hydrogen atoms.

	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i>
HC2	112(2)	366(4)	-89(1)	3.8(4)
HC3	-107(2)	306(4)	-261(2)	4.3(4)
HC5	-127(2)	-335(4)	-175(1)	4.1(4)
HC6	87(2)	-276(3)	-12(1)	3.4(4)
H1C7	182(2)	-34(3)	121(1)	3.2(4)
H2C7	276(2)	228(3)	97(1)	3.1(4)
H1C10	540(3)	-61(5)	230(2)	6.5(6)
H2C10	550(3)	201(5)	213(2)	6.7(7)
H3C10	612(3)	18(4)	190(2)	5.1(5)
H1N	312(2)	190(3)	-55(2)	3.6(4)
H2N	466(2)	196(4)	20(1)	4.6(5)
H3N	383(2)	361(4)	37(2)	5.0(5)
HO1	-294(3)	68(5)	-370(2)	7.3(7)

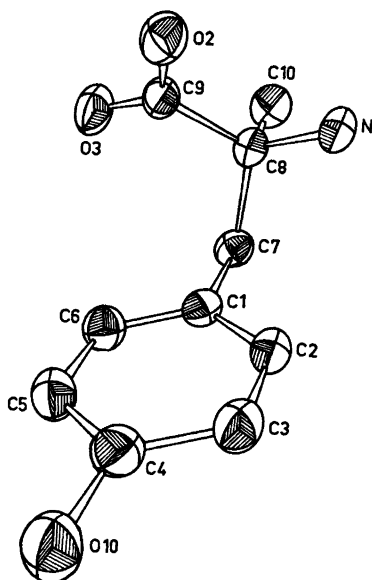
terson map the position and orientation of the molecular fragment comprising the benzene ring and the two non-hydrogen atoms attached to it could be determined. This fragment was sufficient to bring out the positions of the molecular framework in the subsequent Fourier syntheses. The refinement proceeded by full-matrix least-squares calculations. Anisotropic thermal parameters were introduced for non-hydrogen atoms; hydrogen atomic positional parameters (calculated from stereochemical considerations) and isotropic thermal parameters were refined. The refinement converged to a final conventional *R*-factor of 0.048 for the

2095 observed reflections ( $R_w=0.051$ ). The corresponding atomic parameters are listed in Tables 1 and 2. The structure factor list may be obtained from the authors upon request.

The anisotropic thermal parameters were analysed in terms of rigid-body motion both for the whole molecule and for the hydroxybenzyl and alanine parts separately. The latter description was adopted when correcting bond lengths for libration effects. Standard deviations in interatomic distances are calculated from the correlation matrix ignoring uncertainties in cell dimensions.

Table 3. Bond lengths (Å) and bond angles (°). Estimated standard deviations in parentheses.

Bond	(corr)	Angle		
C1-C2	1.390(2)	1.397	C6-C1-C7	120.7(1)
C2-C3	1.392(2)	1.395	C7-C1-C2	121.8(1)
C3-C4	1.385(2)	1.393	C2-C1-C6	117.5(1)
C4-C5	1.387(2)	1.394	C1-C2-C3	121.7(1)
C5-C6	1.384(2)	1.387	C2-C3-C4	119.5(1)
C1-C6	1.391(2)	1.398	C3-C4-C5	119.6(1)
C1-C7	1.514(2)	1.516	C3-C4-O1	122.4(1)
C7-C8	1.542(2)	1.544	O1-C4-C5	117.9(1)
C8-C9	1.538(2)	1.544	C4-C5-C6	120.0(1)
C8-C10	1.524(2)	1.530	C5-C6-C1	121.6(1)
C8-N1	1.494(2)	1.500	C1-C7-C8	113.7(1)
C9-O2	1.263(2)	1.267	C7-C8-C9	110.3(1)
C9-O3	1.239(2)	1.244	C7-C8-C10	112.1(1)
C4-O1	1.368(2)	1.370	C7-C8-N1	108.2(1)
			C9-C8-C10	110.1(1)
			C9-C8-N1	108.6(1)
			C10-C8-N1	107.4(1)
			C8-C9-O2	117.1(1)
			C8-C9-O3	116.7(1)
			O2-C9-O3	126.2(1)
Hydrogen bonds (Å)			Dihedral angles (°)	
O1-O2(-x, ½+y, ½-z)	2.675(2)	C2-C1-C7-C8	278.4	
N-O1(-x, ½+y, ½-z)	2.871(2)	C1-C7-C8-C9	306.5	
N-O2(1-x, -y, -z)	2.821(2)	C1-C7-C8-N	65.2	
N-O3(x, 1+y, z)	2.731(2)	C1-C7-C8-C10	183.4	
		O2-C9-C8-N	1.6	

Fig. 1. Structure of  $\alpha$ -methyltyrosine.

## DISCUSSION

The bond lengths and angles are given in Table 3; Fig. 1 shows an illustration of the molecular structure with the numbering of the atoms. Conformational angles in the molecule and hydrogen bond data are also listed in Table 3. Dihedral angles are given as positive for the clockwise rotation.

The bond lengths and angles found in  $\alpha$ -methyltyrosine are close to those reported for L-tyrosine.<sup>5</sup> Significant differences are found only in the  $\alpha$ -amino acid moiety; in L-tyrosine the C-O2 bond (*cis* relative to the C-N bond) is 1.246 Å and the C-O3 bond 1.260 Å whereas the corresponding bond lengths in  $\alpha$ -methyltyrosine are 1.267 and 1.244 Å, respectively. The difference may be explained by the hydrogen bonding system in the two crystals. In both cases the oxygen atom of the longer C-O bond is acceptor in *two* hydrogen bonds and the other in only one such bond. The C7-C8-N angle in  $\alpha$ -methyltyrosine (108.2°) is smaller

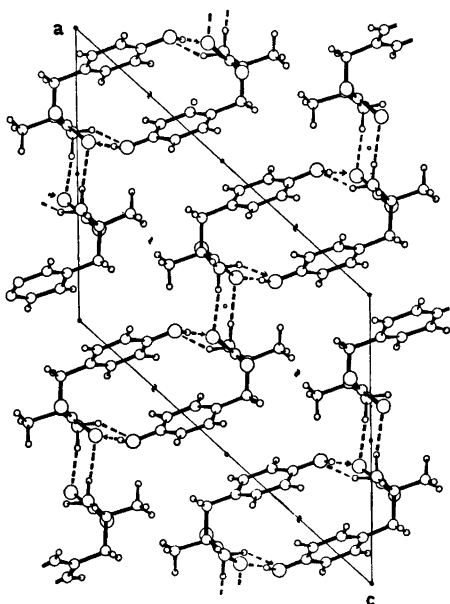


Fig. 2. The crystal structure of  $\alpha$ -methyltyrosine as viewed along the  $b$ -axis.

than the corresponding angle in  $L$ -tyrosine ( $111.3^\circ$ ); this may be a result of the  $\alpha$ -substitution of the more bulky methyl group. The six atoms of the benzene ring are coplanar.

The conformation about the C7–C8 bond of the  $\alpha$ -methyltyrosine molecule corresponds to that found for  $L$ -tyrosine, *i.e.* with the amino and carboxyl groups both in *gauche* positions relative to the phenyl group. The fact that the isomers of these compounds, *m*-tyrosine and  $\alpha$ -methyl-*m*-tyrosine, both appear in the conformation where the carboxyl group is in *trans* position with respect to the aromatic ring in the solid phase<sup>6,7</sup> may indicate that the different conformations are energetically close and mainly determined by crystal forces.

The nitrogen atom in  $\alpha$ -methyltyrosine is situated close to the plane of the carboxyl group, the dihedral angle O2–C9–C8–N is as small as  $1.6^\circ$ .

The crystal structure is characterized by bimolecular layers parallel to (1,0,–2) connected only through van der Waals' forces as illustrated in Fig. 2. Within the layers the molecules are linked together by hydrogen bonds. The nitrogen and phenol oxygen atoms act as hydrogen donors in *four* hydrogen bonds

to other molecules; the phenol oxygen atom (O1) is acceptor in one and the carboxylic oxygen atoms in three such bonds. The molecule is thus linked to other molecules within the double molecular layer by *eight* hydrogen bonds of lengths given in Table 3.

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