THE CRYSTAL AND MOLECULAR STRUCTURE OF 3, 4-DIHYDROXY L-PHENYL-ALANINE

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ABSTRACT

The molecule crystallizes in spacegroup P2₁ with two molecules per unit cell. The unit cell dimensions are \(a = 6.044 \text{ Å}, b = 13.607 \text{ Å}, c = 5.311 \text{ Å}, \gamma = 97.55°\). The density was calculated to be 1.512 g.ml\(^{-1}\) and found to be 1.51 g.ml\(^{-1}\). The major atoms were located by the reliable image method and the hydrogen atoms were located from a difference electron density map. Full-matrix least squares refinement of the parameters yielded an unweighted residual index \(R\) of 0.088.

The bond lengths and angles of the amino acid grouping are consistent with values in other amino acids. The structural parameters of the aromatic system are very similar to those of noradrenaline and dopamine hydrochlorides. The crystal structure is dominated by a three-dimensional intermolecular hydrogen bonding system. The molecular conformation is different from that displayed by any other aromatic amino acid or peptide whose crystal structure is known.

INTRODUCTION

The determination of the structure of 3, 4-dihydroxy L-phenylalanine (L-DOPA) was undertaken as part of a study of the structure and role of melanins and their precursors. The enzymatic oxidation of L-tyrosine to L-DOPA is the first step in the biosynthesis of melanin from L-tyrosine (Evans and Raper, 1937). The compound is of additional interest since it has recently been shown to reduce the symptoms of Parkinson's disease (Sedgewick, 1969).

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The determination was also undertaken as a test of the reliable image method, a new procedure of crystal structure solution based upon Patterson function analysis and employing a minimum of non-crystallographic information.

EXPERIMENTAL

A sample of L-DOPA was obtained from Calbiochem. Corp., and re-crystallized from an ethanol solution by evaporation of solvent at room temperature. The crystals were clear plates, twinned across [010], the largest face. A single crystal was separated from its twin by cleavage and was mounted in a glass capillary. This crystal was $0.35 \times 0.35 \times 0.10$ mm in size and appeared uniform when viewed between crossed polarizers. Weissenberg photographs indicated that the crystal was monoclinic; and the only systematic absences were odd $l$ for the 00$l$ reflections, consistent with only one non-centrosymmetric monoclinic spacegroup, $P2_1$. The crystal was mounted on a Hilger and Watts Y290 computer-controlled four-circle diffractometer for determination of cell constants and collection of intensity data. The crystallographic parameters are:

Spacegroup: $P2_1$, monoclinic.

\[
\begin{align*}
  a & : \quad 6.044 \pm 0.003 \text{Å} \\
  b & : \quad 13.607 \pm 0.008 \text{Å} \\
  c & : \quad 5.311 \pm 0.003 \text{Å} \\
  \gamma & : \quad 97.55 \pm 0.2^\circ \\
  \rho_{\text{calc.}} & : \quad 1.512 \text{ g.ml.}^{-1} \text{ for } Z = 2 \\
  \rho_{\text{obs.}} & : \quad 1.51 \pm 0.02 \text{ g.ml.}^{-1} \text{ (Flotation in } CCl_4\text{-xylene).}
\end{align*}
\]

Radiation: CuK$_\alpha$, $= (\lambda = 1.54051$ Å), reflected from [200] of a doubly-bent LiF crystal monochromator.

The crystal orientation matrix for automatic data collection was calculated from the angular settings of two high-angle reflections. Intensity data were collected automatically using moving crystal-moving counter techniques employing an $\omega-2\theta$ scan. Backgrounds were counted at $\theta \pm 0.36^\circ$ and intensities were measured in 24 steps of $0.03^\circ$ in $\theta$ through each reflection. Equal amounts of time (24 sec.) were spent in counting total background and intensity for each reflection. 798 data were collected with $\theta \leq 70^\circ$. An estimated standard error, $\sigma$, was assigned to each observed reflection by

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\sigma^2 = [I + B + (0.10I)^2 + (0.10B)^2]
\]