

Structure Verification of 4-Hydroxy-2-methylpyrido[2,3-*d*]pyridazin-1-one by Single Crystal Analysis

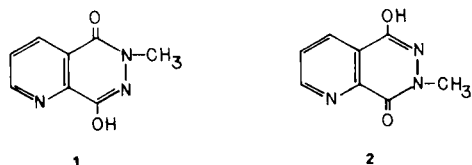
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Sir:

It was observed that the reaction of methylhydrazine with dimethyl 2,3-pyridinedicarboxylate yielded a mixture of two products (1) which were separated by differential solubility in ethyl acetate and identified as the structural isomers of 4-hydroxy-2-methylpyrido[2,3-*d*]pyridazin-1-one (1) and 1-hydroxy-3-methylpyrido[2,3-*d*]pyridazin-4-one (2) or the corresponding keto tautomers. On the



basis of selective chelation characteristics the low melting (204-205°) isomer was tentatively assigned structure 1. Because compounds of similar structures are known for their chemotherapeutic activities as antidepressants and cardiovascular agents, it was deemed desirable to corroborate the structural assignment and to resolve the enol-keto ambiguity by an X-ray single crystal investigation. Also, the low melting isomer has been shown to have mild antineoplastic properties (2), possibly due to its chelating ability since 2 shows no such activity.

The compound is orthorhombic, space group $Pca2_1$, with $a = 16.787$ (1), $b = 5.200$ (1), $c = 8.702$ (1) Å, and $Z = 4$ formula weights per unit cell. Intensity data were collected with a Syntex P2₁ computer-controlled diffractometer using Mo K α ($\lambda = 0.71069$ Å) radiation monochromatized by a graphite crystal. Using the $\theta - 2\theta$ scan technique, in the range $4^\circ < 2\theta < 55^\circ$, 686 independent reflections with $I > 3\sigma(I)$ were measured. The structure was solved by the symbolic addition method and refined by a full-matrix least squares method to a final R value [$R = (\sum ||F_o| - |F_c||) / \sum |F_o|$] of 0.039.

Figure 1 shows the bond distances obtained after the final cycle of refinement and Figure 2 shows the bond angles. It is obvious that the title compound has the skeletal structure previously assigned as 1 and the enol configuration in the solid state. The hydroxyl hydrogen

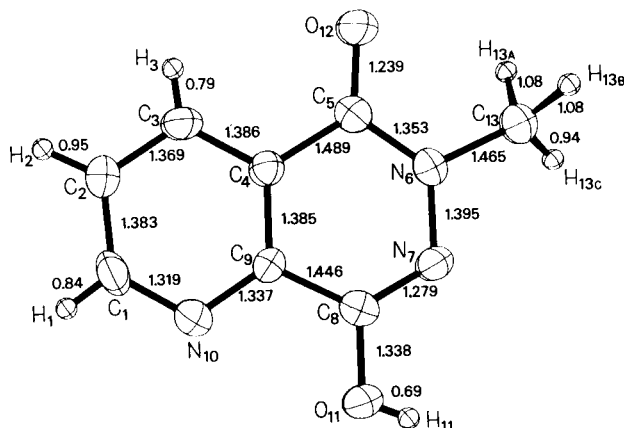


Figure 1. Intermolecular bond lengths (Ångstroms). The standard deviations of the heavy atom bond lengths and of the C-H bond lengths average 0.006 and 0.05 Å, respectively. The numbering of atoms is arbitrary.

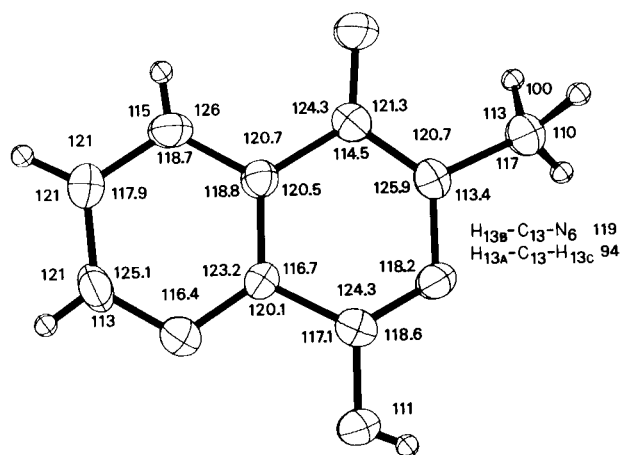


Figure 2. Intramolecular bond angles ($^\circ$). The standard deviations of the C-C-C angles average 0.4° .

(H₁₁) was easily observed in a final difference map and no appreciable electron density was observed in the map at the position a hydrogen would have been found near N₇ if the keto tautomer had been present. The C₅-O₁₂ distance of 1.239 Å is significantly shorter than the enolic C₈-O₁₁ distance of 1.338 Å. There is an intermolecular hydrogen bond between O₁₁ and O'₁₂ with a distance of 2.679 Å (H₁₁ . . . O'₁₂ = 2.02 Å); the angle O₁₁-H₁₁ . . . O'₁₂ is 160 (5)°.

Acknowledgment.

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- (2) Jay Nematollahi, Unpublished results.