5-Acetyl-3,7,8,10-tetramethyl-1,5-dihydroalloxazine: Crystal Structure and Extended Hückel Calculations for different Molecular Geometries

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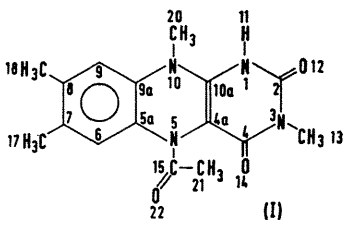
Summary Structure determination and extended Hückel calculations have confirmed the angular form of the reduced state of flavin derivatives.

THE crystal and molecular structure of 5-acetyl-3,7,8,10-tetramethyl-1,5-dihydroalloxazine, $C_{16}H_{18}N_4O_3$ (I), has been determined by *X*-ray diffraction methods in order to obtain accurate, detailed structural information about a flavin derivative in a reduced state and containing only light atoms, *i.e.* carbon, nitrogen, oxygen, and hydrogen.



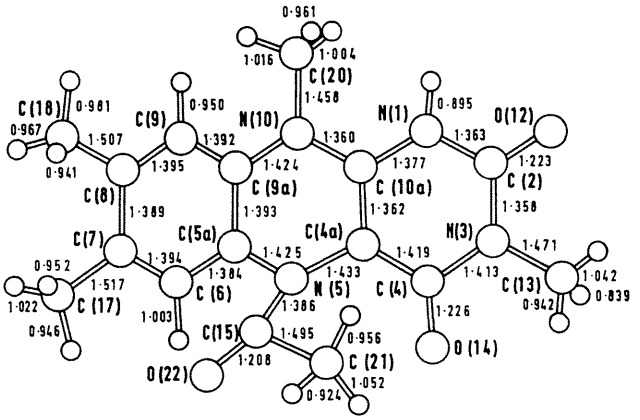
(I)

The crystalline specimen used was prepared by Lajos Maron[1] at this Institute. The symmetry and unit-cell dimensions are: $P2_1/c$, $a = 4{\cdot}687_5$, $b = 18{\cdot}929_6$, $c = 17{\cdot}225_6$ Å, $\beta = 94{\cdot}55 \pm 0{\cdot}02°$, $Z = 4$.

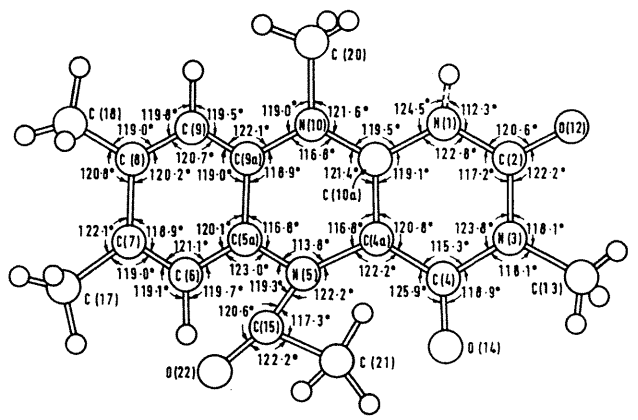
The structure determination was based on 1571 independent, significant reflections registered with Cu-K_α radiation using a Siemens automatic single-crystal diffractometer. The phases of the 250 "strongest" normalized structure factors were obtained by application of the symbolic addition method. From subsequent electron-density calculations and least-squares calculations it was possible to locate all atoms in the structure. The coordinates were refined by full-matrix least-squares techniques including anisotropic thermal parameters for the non-hydrogen atoms and isotropic parameters for the hydrogens. After correction for secondary extinction effects[2] a final R value of 0·039 was obtained.

The dimensions of the molecule are given in Figure 1. The estimated standard deviations are *ca.* 0·003 Å and *ca.* 0·2° for distances and angles involving non-hydrogen atoms and *ca.* 0·04 Å and 1·6° for distances and angles to hydrogens.

The distances C(2)–O(12) and C(4)–O(14) are of lengths



(a)



[b]

FIGURE 1 (a) *Bond lengths within the molecule.*
(b) *Bond angles within the molecule.*

indicating double-bond character. The ring skeleton is bent along a line through N(5) and N(10). The ring atoms deviate less than 0·22 Å for the pyrimidine ring and less than

0·06 Å for the benzene ring from two least-squares planes intersecting at an angle of 148°. This angle is likely to be associated with a high degree of tetrahedral hybridization of the two nitrogens N(5) and N(10). The results confirm the conclusions drawn[3] from spectroscopic observations that reduced flavins adopt the non-planar diketo-form.

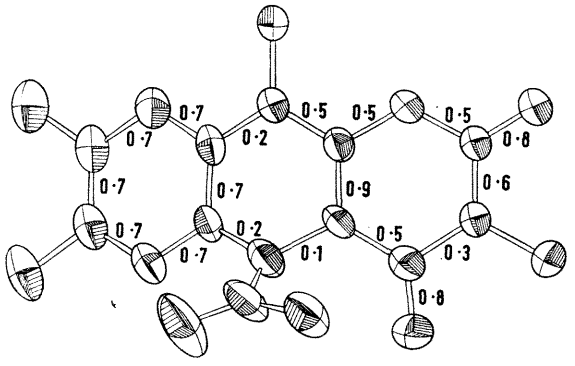


FIGURE 2. *Approximative π-bond-order values.*

Strong hydrogen bonds N(1)–H(1) · · · · · O(12) exist in the structure. The distances N(1)–H(1) and H(1) · · · · · O(12) are 0·90 and 1·92 Å, and the angle at the hydrogen is 172°.

Approximate π-bond orders calculated from correlation functions suggested by several authors[5,6] are in satisfactory agreement with the π-bond scheme [*cf.* (I)] commonly accepted for reduced flavins. The bond order values obtained are given in Figure 2.

Figure 3 illustrates the charge distribution and overlap population obtained for the observed molecular geometry by extended Hückel calculations[7] using a computer program written by Manne and Herman.[8] The Hückel energy calculated for different molecular geometries by varying the angle between the two planar parts of the molecule shows a minimum, at 148°, equal to the observed angle: 20° away from the minimum, on either side, the energy is 3·8 ev greater. Thus, the non-planar molecular form is likely to exist also in solutions.

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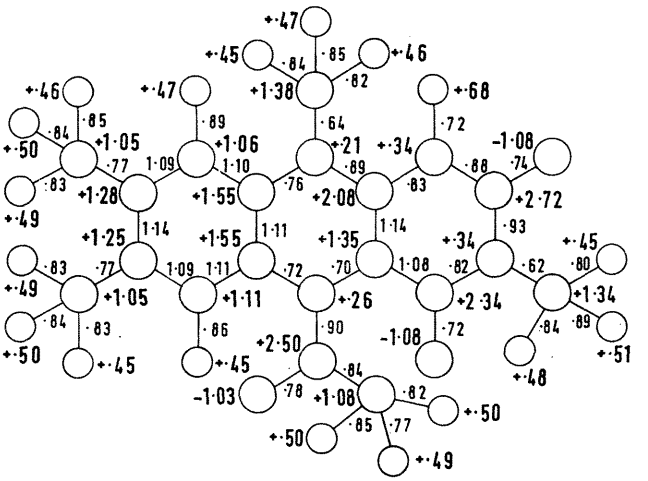

FIGURE 3. *Calculated net charges (values with signs) and overlap populations. All values are given in electron units.*

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