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The Crystal Structure of a Flavin Molecular Complex: 10-Propylisoalloxazine Bis(naphthalene-2,3-diol)

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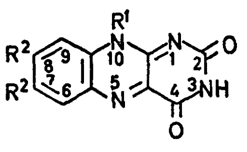
Summary In contrast with lumiflavin or 7,8,10-trimethylisoalloxazine bis(naphthalene-2,3-diol), the 1 : 2 complex of 10-propylisoalloxazine with naphthalene-2,3-diol is orange and contains one flavin–naphthalenediol pair separated by 3·35 Å, suggesting a possible charge-transfer interaction.

ISOALLOXAZINE or flavin, (I), is the redox-active moiety in flavoproteins, and it has been suggested[1] that charge-transfer bonding between the flavin and its substrate may be an initial step in the enzymic reaction. Stable molecular complexes are formed[2a] between flavins and phenols, both in acidic and in neutral solution. The acidic complexes[2] are generally more intensely coloured and therefore more characteristic of charge-transfer complexes but the neutral complexes seem more likely to be of biological significance because of the low basicity of flavins.[3] One such neutral complex, lumiflavin (I, R¹ = R² = Me) bis(naphthalene-2,3-diol), which is nearly the same yellow colour as the component flavin, contains columns of alternating flavin and naphthalenediol molecules, but with a fairly large (3·44 Å) interplanar spacing.[4] The complex described here is orange and seemed likely to reveal a charge-transfer interaction.



(I)

Crystals of 10-propylisoalloxazine bis(naphthalene-2,3-diol), $C_{13}H_{12}O_2N_4 \cdot 2C_{10}H_8O_2$, are monoclinic, space group $A2/a$, with $a = 26{\cdot}69(3)$, $b = 7{\cdot}246(8)$, $c = 29{\cdot}20(4)$ Å,

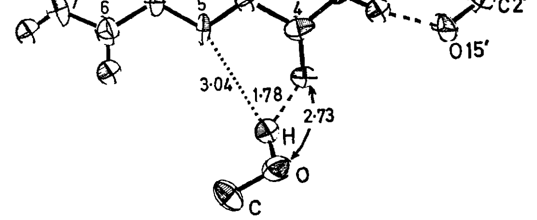


FIGURE 1. *Standard deviations in bond lengths not involving hydrogen are about* 0·013 Å. *For bond lengths involving hydrogen, the standard deviations are about* 0·1 Å. *The primed atoms are derived by a 2-fold axis from the flavin molecule; the other groups of three atoms each are portions of the two independent naphthalenediol molecules.*

(λCu-K_α = 1·5418 Å), β = 102·51(3)°, D_c = 1·39 g cm^{-3}, D_m = 1·40 g cm^{-3}, M = 576·6, U = 5513 Å^3, and Z = 8. A scan of all independent reflections from a small acicular crystal irradiated with Cu-K_α radiation to 2θ = 90°, using a Picker four-circle punched card diffractometer and a Xe-filled proportional counter, yielded 869 observable reflections. The structure was solved by Patterson methods and has been refined to R = 5·4% with all atoms including hydrogen having been located, but only heavy atoms refined† (anisotropically). Within the comparatively large standard deviations, all bond parameters agree with expected values.

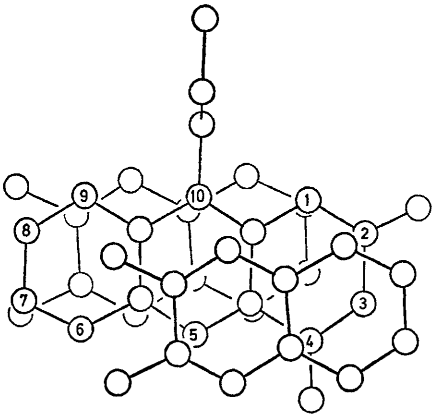


FIGURE 2. *A view of the structure normal to the approximate flavin plane. Hydrogen atoms are omitted for clarity.*

The hydrogen-bonding scheme and propyl configuration are shown in Figure 1. As in every previous flavin structure, NH(3) serves as a hydrogen bond donor, and the "chelate site" CO(4)–N(5) is occupied by a donor group. It is mildly surprising to find the donor at the relatively basic N(1) shared with CO(2) since a similar donor is bound exclusively to N(1) in the lumiflavin complex.

Figure 2 shows the π-overlap of the flavin with two translationally related naphthalenediol molecules. The upper naphthalenediol molecule lies about 3·35 Å from the nearly planar flavin and the lower 3·44 Å. In addition to the one closer contact in comparison with the lumiflavin complex, the position of the hydroxy groups is reversed with respect to the flavin and the naphthalene moiety overlaps the oxo and central rings rather than the opposite end of the flavin. We await the structures of other orange complexes now being studied before interpreting the comparative geometry further.

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† Despite the low observation : parameter ratio of 2·2, anisotropic refinement is significant at better than a 0·005 confidence level according to the Hamilton R-factor ratio test.[5] Isotropic refinement converged at R = 9·3% giving a ratio of 1·7 compared with $R_{388,\,481,\,0\cdot005}$ = 1·24.

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