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Studies on Flavin Derivatives The Crystal and Molecular Structure of 3-Methyl-lumiflavin

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The crystal structure of 3-methyl-lumiflavin (3,7,8,10-tetramethylisoalloxazine), $C_{14}H_{14}N_4O_2$, has been determined by direct methods from three-dimensional diffractometer data taken with Cu $K\alpha$ radiation. The crystals are monoclinic, space group $P2_1/c$, $Z = 4$, $a = 15.509$, $b = 9.624$, $c = 8.865$ Å and $\beta = 107.88^\circ$. The atomic parameters were refined by full-matrix least-squares to a final R of 0.047. The conformation of the molecules confirms that the isoalloxazine ring system in a neutral oxidized flavin derivative is almost planar, as has been suggested by spectroscopic data.

Introduction

Flavin is the trivial name of the prosthetic group of a large class of respiratory enzymes, the flavoproteins, occurring in animals and plants. The simplest flavin compound, lumiflavin, is not known to occur in nature, but is formed from naturally occurring flavin species by photolysis under alkaline conditions. Furthermore, lumiflavin resembles the native coenzyme in its spectral, protolytic and redox properties. The chemistry and biological function of flavins have been reviewed by Penzer & Radda (1967) and by Hemmerich, Nagelschneider & Veeger (1970), *inter alios*.

The present determination of the structure of 3-methyl-lumiflavin, $C_{14}H_{14}N_4O_2$ (Fig. 1), a neutral oxidized flavin derivative, is part of a research project concerning structural studies of flavin derivatives in different states of oxidation and protonation. A survey

of the flavin compounds previously investigated within this project is given by Kierkegaard *et al.* (1970).

Experimental

The faintly yellow crystals used were supplied by L. Maron of this Institute. The selection of a suitable crystal and the determination of the possible space group were performed by X-ray photographic methods (oscillation and Weissenberg techniques). The systematic extinctions are characteristic of the space group $P2_1/c$. The crystal selected for collection of X-ray intensity data measured $0.06 \times 0.10 \times 0.42$ mm, and was mounted along its long axis, parallel to the b axis.

More precise unit cell parameters, $a = 15.509$ (5), $b = 9.624$ (2), $c = 8.865$ (2) Å and $\beta = 107.88$ (3) $^\circ$, were obtained from manual measurements on a Siemens single-crystal X-ray diffractometer. With four formula

Table 3. *Observed and calculated structure factors*

Each group of three columns contains k , $10|F_o|$ and $10|F_c|$, and is headed by the values h and l common to the group. Asterisks following $10|F_c|$ mark reflexions omitted from the final refinement.

h	l	k	$10 F_o $	$10 F_c $
10	10	10	100	100
10	10	11	100	100
10	10	12	100	100
10	10	13	100	100
10	10	14	100	100
10	10	15	100	100
10	10	16	100	100
10	10	17	100	100
10	10	18	100	100
10	10	19	100	100
10	10	20	100	100
10	10	21	100	100
10	10	22	100	100
10	10	23	100	100
10	10	24	100	100
10	10	25	100	100
10	10	26	100	100
10	10	27	100	100
10	10	28	100	100
10	10	29	100	100
10	10	30	100	100
10	10	31	100	100
10	10	32	100	100
10	10	33	100	100
10	10	34	100	100
10	10	35	100	100
10	10	36	100	100
10	10	37	100	100
10	10	38	100	100
10	10	39	100	100
10	10	40	100	100
10	10	41	100	100
10	10	42	100	100
10	10	43	100	100
10	10	44	100	100
10	10	45	100	100
10	10	46	100	100
10	10	47	100	100
10	10	48	100	100
10	10	49	100	100
10	10	50	100	100
10	10	51	100	100
10	10	52	100	100
10	10	53	100	100
10	10	54	100	100
10	10	55	100	100
10	10	56	100	100
10	10	57	100	100
10	10	58	100	100
10	10	59	100	100
10	10	60	100	100
10	10	61	100	100
10	10	62	100	100
10	10	63	100	100
10	10	64	100	100
10	10	65	100	100
10	10	66	100	100
10	10	67	100	100
10	10	68	100	100
10	10	69	100	100
10	10	70	100	100
10	10	71	100	100
10	10	72	100	100
10	10	73	100	100
10	10	74	100	100
10	10	75	100	100
10	10	76	100	100
10	10	77	100	100
10	10	78	100	100
10	10	79	100	100
10	10	80	100	100
10	10	81	100	100
10	10	82	100	100
10	10	83	100	100
10	10	84	100	100
10	10	85	100	100
10	10	86	100	100
10	10	87	100	100
10	10	88	100	100
10	10	89	100	100
10	10	90	100	100
10	10	91	100	100
10	10	92	100	100
10	10	93	100	100
10	10	94	100	100
10	10	95	100	100
10	10	96	100	100
10	10	97	100	100
10	10	98	100	100
10	10	99	100	100
10	10	100	100	100

difference electron density map allowed all the 14 hydrogen atoms to be located. Full-matrix least-squares refinement with anisotropic temperature factors for all the non-hydrogen atoms and isotropic ones for the hydrogen atoms gave an R value ($R = \sum(|F_o| - |F_c|) / \sum|F_o|$) of 0.059 for all the 1538 reflexions used. For the reflexions which ought to be most affected by extinction, $|F_o|$ was usually found to be smaller than $|F_c|$. Accordingly a final full-matrix least-squares refinement was carried out, omitting the 14 reflexions which had the largest calculated secondary extinction correction factors. This refinement gave an R value of 0.047 and slight improvements in the estimated standard deviations of the refined parameters.

In all the refinements Hughes's (1941) weighting scheme with $|F_o|_{\min} = 3.0$ was used. The shifts in the parameters in the last cycle of refinement were all less than 0.1 of their estimated standard deviations. The atomic scattering factors used for carbon, nitrogen, oxygen were those given by Hanson, Herman, Lea & Skillman (1964), for hydrogen that given by Stewart, Davidson & Simpson (1965).

Observed and calculated structure factors are given in Table 3. The reflexions not used in the final refine-

ment are marked with asterisks. In Tables 4, 5 and 6 the coordinates for non-hydrogen atoms, their anisotropic temperature factors, the coordinates and iso-

Table 4. *Atomic fractional coordinates for the nonhydrogen atoms ($\times 10^4$)*

	x	y	z
N(1)	3988 (1)	2180 (2)	5564 (2)
C(2)	4245 (2)	849 (2)	6036 (3)
N(3)	3826 (1)	- 290 (2)	5094 (2)
C(4)	3162 (2)	- 172 (2)	3678 (3)
C(4a)	2898 (1)	1276 (2)	3167 (2)
N(5)	2257 (1)	1476 (2)	1840 (2)
C(5a)	2011 (1)	2825 (2)	1422 (2)
C(6)	1333 (2)	3081 (3)	- 22 (3)
C(7)	1077 (1)	4404 (3)	- 546 (3)
C(8)	1499 (1)	5545 (3)	414 (3)
C(9)	2153 (2)	5315 (2)	1843 (3)
C(9a)	2426 (1)	3966 (2)	2354 (2)
N(10)	3105 (1)	3700 (2)	3750 (2)
C(10a)	3359 (1)	2376 (2)	4217 (2)
O(12)	4823 (1)	620 (2)	7277 (2)
C(13)	4111 (3)	-1699 (3)	5693 (4)
O(14)	2809 (1)	-1183 (2)	2907 (2)
C(17)	392 (2)	4647 (4)	-2134 (4)
C(18)	1244 (2)	7014 (3)	- 111 (4)
C(20)	3571 (2)	4864 (2)	4733 (3)

tropic temperature factors for the hydrogen atoms, respectively, are given. In Tables 7 and 8, the intramolecular bond distances and bond angles are given

Table 5. *Anisotropic thermal parameters for nonhydrogen atoms* ($\times 10^4$)

$$T = \exp [-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl)].$$

	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N(1)	52 (1)	85 (2)	141 (3)	- 3 (2)	34 (3)	- 6 (4)
C(2)	54 (1)	89 (3)	150 (4)	- 4 (3)	62 (4)	5 (4)
N(3)	59 (1)	81 (2)	173 (3)	1 (2)	78 (3)	- 1 (4)
C(4)	57 (1)	86 (2)	169 (4)	-25 (3)	96 (4)	-42 (5)
C(4a)	47 (1)	95 (2)	130 (3)	-20 (3)	60 (3)	-32 (4)
N(5)	50 (1)	112 (2)	147 (3)	-29 (2)	62 (3)	-52 (4)
C(5a)	42 (1)	114 (3)	131 (3)	-21 (3)	50 (3)	-32 (5)
C(6)	45 (1)	144 (3)	141 (4)	-27 (3)	47 (4)	-59 (5)
C(7)	41 (1)	166 (4)	134 (4)	- 3 (3)	41 (3)	- 3 (6)
C(8)	45 (1)	138 (3)	145 (4)	13 (3)	59 (3)	25 (5)
C(9)	47 (1)	107 (3)	134 (3)	- 1 (3)	46 (3)	1 (5)
C(9a)	42 (1)	104 (3)	118 (3)	- 9 (2)	46 (3)	14 (4)
N(10)	47 (1)	84 (2)	122 (3)	-11 (2)	33 (3)	20 (3)
C(10a)	42 (1)	88 (2)	130 (3)	-13 (2)	53 (3)	-16 (4)
O(12)	81 (1)	112 (2)	194 (3)	21 (2)	- 0 (3)	41 (4)
C(13)	79 (2)	80 (3)	254 (6)	9 (4)	112 (6)	11 (6)
O(14)	83 (1)	97 (2)	223 (3)	-42 (2)	85 (3)	- 8 (4)
C(17)	59 (2)	211 (5)	158 (4)	13 (5)	2 (4)	1 (8)
C(18)	60 (2)	157 (4)	191 (5)	38 (4)	37 (5)	61 (7)
C(20)	61 (1)	80 (3)	137 (4)	-15 (3)	17 (4)	-22 (5)

Table 6. *Atomic fractional coordinates* ($\times 10^3$) *for hydrogen atoms and isotropic thermal parameters* (\AA^2)

	x	y	z	B
H(13a)	426 (2)	-218 (3)	487 (4)	7.5 (8)
H(13b)	362 (2)	-213 (4)	584 (4)	8.7 (9)
H(13c)	464 (3)	-162 (5)	658 (5)	12.3 (14)
H(6)	108 (1)	225 (2)	- 60 (3)	4.2 (5)
H(17a)	69 (2)	509 (4)	-283 (4)	9.3 (10)
H(17b)	-9 (2)	525 (3)	-219 (4)	7.9 (9)
H(17c)	16 (2)	374 (4)	-256 (4)	7.9 (8)
H(18a)	133 (2)	719 (3)	-119 (4)	8.4 (8)
H(18b)	61 (2)	717 (3)	- 28 (4)	8.3 (8)
H(18c)	158 (2)	764 (4)	69 (4)	9.1 (9)
H(9)	242 (2)	610 (3)	247 (3)	5.0 (5)
H(20a)	311 (2)	541 (3)	503 (3)	6.8 (7)
H(20b)	383 (2)	555 (3)	410 (3)	6.6 (7)
H(20c)	405 (2)	453 (3)	563 (4)	7.9 (8)

Table 7. *Interatomic distances*

N(1)—C(2)	1.368 (3) \AA	C(9a)—N(10)	1.380 (3) \AA
C(2)—O(12)	1.207 (3)	N(10)—C(20)	1.466 (3)
C(2)—N(3)	1.410 (3)	N(10)—C(10a)	1.360 (3)
N(3)—C(13)	1.473 (3)	C(10a)—N(1)	1.303 (3)
N(3)—C(4)	1.362 (3)	C(6)—H(6)	0.97 (2)
C(4)—C(4a)	1.483 (3)	C(9)—H(9)	0.95 (3)
C(4)—O(14)	1.219 (3)	C(13)—H(13a)	0.96 (3)
C(4a)—C(10a)	1.446 (3)	C(13)—H(13b)	0.91 (4)
C(4a)—N(5)	1.300 (3)	C(13)—H(13c)	0.95 (4)
N(5)—C(5a)	1.372 (3)	C(17)—H(17a)	0.98 (4)
C(5a)—C(9a)	1.405 (3)	C(17)—H(17b)	0.93 (3)
C(5a)—C(6)	1.406 (3)	C(17)—H(17c)	0.98 (4)
C(6)—C(7)	1.371 (4)	C(18)—H(18a)	1.02 (3)
C(7)—C(17)	1.499 (4)	C(18)—H(18b)	0.96 (4)
C(7)—C(8)	1.421 (3)	C(18)—H(18c)	0.96 (4)
C(8)—C(18)	1.502 (4)	C(20)—H(20a)	0.98 (3)
C(8)—C(9)	1.376 (3)	C(20)—H(20b)	1.02 (3)
C(9)—C(9a)	1.397 (3)	C(20)—H(20c)	0.96 (3)

and these are illustrated in Fig. 2. In Table 9 all the intermolecular distances less than 3.45 \AA between nonhydrogen atoms are given. The labelling of the atoms is shown in Fig. 3. The calculations were performed on the IBM 1800 and IBM 360/75 computers.

Discussion

The crystal structure viewed along the a and c axes is shown in Fig. 4. Because of the lack of proper hydrogen donors no conventional hydrogen bonds are formed in the crystal structure. As can be seen in Table 9, most of the intermolecular distances are of the same order as the usual van der Waals distances. The largest deviation from a van der Waals contact distance is between the keto oxygen O(12) of one molecule and the methyl carbon C(20) of another. This distance is only 3.114 \AA rather than the usual 3.4–3.8 \AA. A fairly short contact (3.287 \AA) is also formed between O(12) and the methyl carbon C(13) of an adjacent molecule. Both of these methyl carbon atoms, C(13) and C(20), are bonded to endocyclic nitrogen atoms. Thus, it is probable that these methyl carbon atoms have positive atomic charges and that the short

Table 8. *Intramolecular bond angles*

C(2)—N(1)—C(10a)	118.8 (2)°	C(5a)—C(6)—C(7)	121.9 (2)°
N(1)—C(2)—N(3)	120.5 (2)	C(6)—C(7)—C(8)	118.8 (2)
N(1)—C(2)—O(12)	121.0 (2)	C(6)—C(7)—C(17)	120.8 (3)
N(3)—C(2)—O(12)	118.4 (2)	C(8)—C(7)—C(17)	120.4 (3)
C(2)—N(3)—C(4)	124.1 (2)	C(7)—C(8)—C(9)	120.1 (2)
C(2)—N(3)—C(13)	118.0 (2)	C(7)—C(8)—C(18)	120.8 (2)
C(4)—N(3)—C(13)	117.9 (2)	C(9)—C(8)—C(18)	119.1 (2)
N(3)—C(4)—C(4a)	114.8 (2)	C(8)—C(9)—C(9a)	120.8 (2)
N(3)—C(4)—O(14)	122.2 (2)	C(9)—C(9a)—N(10)	122.3 (2)
C(4a)—C(4)—O(14)	123.0 (2)	C(5a)—C(9a)—C(9)	119.8 (2)
C(4)—C(4a)—N(5)	118.6 (2)	C(5a)—C(9a)—N(10)	117.9 (2)
C(4)—C(4a)—C(10a)	117.1 (2)	C(9a)—N(10)—C(10a)	121.1 (2)
N(5)—C(4a)—C(10a)	124.3 (2)	C(9a)—N(10)—C(20)	119.5 (2)
C(4a)—N(5)—C(5a)	117.2 (2)	C(10a)—N(10)—C(20)	119.4 (2)
N(5)—C(5a)—C(6)	118.7 (2)	N(1)—C(10a)—N(10)	118.7 (2)
N(5)—C(5a)—C(9a)	122.8 (2)	C(4a)—C(10a)—N(10)	116.8 (2)
C(6)—C(5a)—C(9a)	118.6 (2)	N(1)—C(10a)—C(4a)	124.5 (2)

contact distance to the negatively charged keto oxygen is caused by electrostatic forces.

Table 9. Intermolecular distances less than 3.45 Å between nonhydrogen atoms

Code for symmetry related atoms

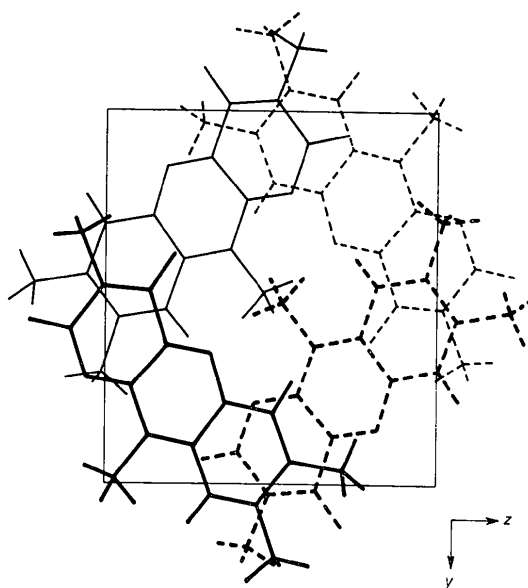
	x	y	z
i	x	$\frac{1}{2}-y$	$\frac{1}{2}+z$
ii	1-x	-y	1-z
iii	x	$\frac{1}{2}-y$	$z-\frac{1}{2}$
iv	1-x	$\frac{1}{2}+y$	$\frac{3}{2}-z$
v	1-x	$y-\frac{1}{2}$	$\frac{3}{2}-z$

N(1)—C(5a ⁱ)	3.378 (3) Å	N(5)—C(20 ⁱⁱⁱ)	3.413 (3) Å
C(2)—C(9a ⁱ)	3.373 (3)	C(5a)—C(10a ⁱⁱⁱ)	3.276 (3)
C(2)—N(10 ⁱ)	3.423 (3)	C(6)—C(10a ⁱⁱⁱ)	3.438 (3)
N(3)—C(9 ⁱ)	3.407 (3)	N(10)—O(12 ⁱ)	3.373 (3)
N(3)—O(12 ⁱⁱ)	3.407 (3)	O(12)—C(13 ^{iv})	3.287 (4)
C(4)—C(8 ⁱ)	3.404 (3)	O(12)—C(20 ⁱ)	3.365 (3)
C(4a)—C(6 ⁱ)	3.353 (3)	O(12)—C(20 ^v)	3.114 (3)
C(4a)—C(7 ⁱ)	3.418 (3)		

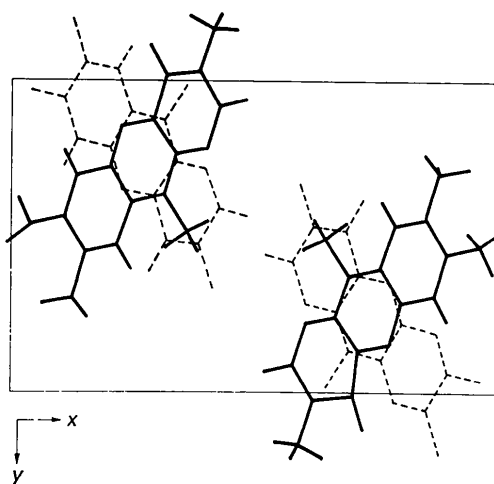
To investigate this possibility, atomic charges were evaluated from semi-empirical molecular orbital calculations of the extended Hückel type. The computer program for the extended Hückel calculations was kindly put at our disposal by Rolf Manne (Quantum Chemistry Group, Uppsala). The atomic charges obtained are given in Table 10. The methyl carbon atoms C(13) and C(20) have the largest positive (+1.35) and the keto oxygen atoms O(12) and O(14) the largest negative atomic charges (-1.03) among the exocyclic atoms. Thus, the charge distribution supports the assumption that a molecular packing in the crystal structure which gives short contact distances between the keto oxygen atom O(12) and the methyl carbon atoms C(13) and C(20) might still be electrostatically favorable. Among the endocyclic atoms, the nitrogen atoms N(1) and N(5) have the largest negative charges (-0.51 and -0.35 respectively). Indeed, in lumiflavinium ions the nitrogen atom N(1) is protonated. The most positive charge (+2.14), except for those of the

keto carbon atoms C(2) and C(4) (+2.78 and 2.45 respectively) is obtained for the carbon atom C(10a).

The almost planar molecules are stacked, with about 3.3 Å separation between parallel molecular planes, along the [20 $\bar{1}$] direction. The shortest interatomic distance, 3.276 Å, between atoms from two different molecules in the stacking occurs between the carbon atoms C(5a) and C(10a). Since the atomic charges on these atoms were calculated to be +1.70 and 2.14, this short contact seems not to be electrostatically favorable. However, the geometry of the molecular packing is favorable for axial π -electron interactions (Foster, 1969). To judge by the faint yellow colour of



(a)



(b)

Fig. 4. Packing diagrams viewed along the *a* axis (a) and the *c* axis (b).

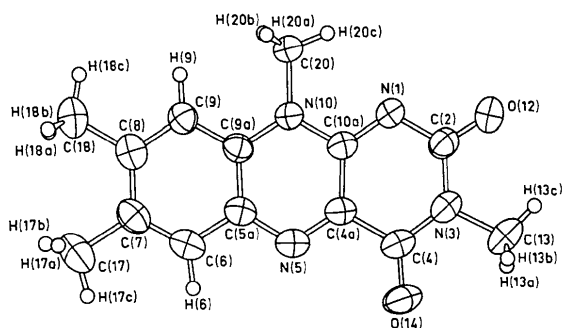


Fig. 3. Molecule conformation observed in the crystal structure of 3-methyl-lumiflavin, with atoms numbered for reference in the text and anisotropic thermal ellipsoids of the nonhydrogen atoms.

the crystalline specimen, such an interaction, if it exists in the structure, must be very weak. Thus, it is doubtful that a weak interaction of this kind can be the cause of this short carbon-carbon contact.

Table 10. Atomic charges calculated by the extended Hückel method

	Atomic charges		Atomic charges
N(1)	-0.51	C(9)	1.07
C(2)	2.78	C(9a)	1.66
N(3)	0.37	N(10)	0.50
C(4)	2.45	C(10a)	2.14
C(4a)	1.71	O(12)	-1.03
N(5)	-0.35	C(13)	1.35
C(5a)	1.70	O(14)	-1.03
C(6)	1.09	C(17)	1.04
C(7)	1.35	C(18)	1.07
C(8)	1.39	C(20)	1.35

As seen from Table 11, the isoalloxazine ring system of the molecule is essentially planar. The estimated standard deviation of the calculated least-squares plane through the atoms forming the ring system is 0.016 Å, while the average of the estimated standard deviations of the positions of the atoms is 0.002 Å. Thus, the ring system is not strictly planar from a statistical point of view (Hamilton, 1965). Calculations of the least-squares planes through the three six-membered rings of the molecules reveal a small distortion of the molecule. Thus, the angle between the normals of the benzenoid and pyrazinoid rings is 1.8°, and the angle between the normals of the pyrazinoid and pyrimidinoid rings is 1.2°.

To visualize the bond scheme consistent with the obtained intramolecular bond distances, approximate π -bond orders were evaluated from the linear π -bond order-bond distance correlation functions suggested by Roos & Skancke (1967) and Fischer-Hjalmars & Sundbom (1968). The π -bond scheme so obtained (Fig. 5) agrees well with the commonly accepted one for the lumiflavin molecule (Fig. 1). The highest π -bond orders, about 0.9, are obtained for the C(10a)-N(1), C(4a)-N(5), C(2)-O(12) and C(4)-O(14) bonds. Thus, the two oxygen atoms O(12) and O(14) are both of keto type and the π -electrons in the pyrazinoid and pyrimidinoid rings are to a large extent localized to the

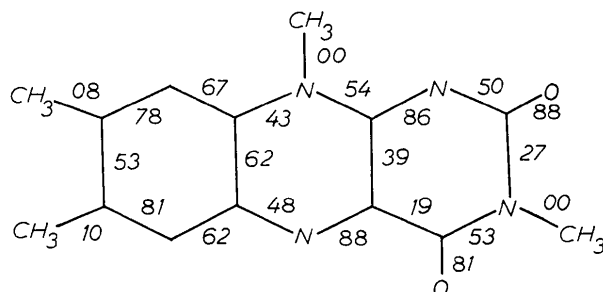


Fig. 5. Estimated π bond orders ($\times 10^2$) in 3-methyl-lumiflavin.

Table 11. Deviations of the atoms from least-squares planes

The planes are expressed as $AX + BY + CZ = D$, where X , Y , and Z are in Å units relative to the axes a^* , b and c . The atoms indicated with asterisks were omitted from the calculations of the least-squares planes.

Plane I	Atom	Deviation
$A = -0.6902$	N(1)	0.002 Å
$B = -0.0345$	C(2)	0.000
$C = 0.7228$	N(3)	0.004
$D = -1.9450$ Å	C(4)	-0.002
	C(4a)	-0.017
	N(5)	0.001
	C(5a)	0.022
	C(6)	0.012
	C(7)	-0.019
	C(8)	-0.017
	C(9)	0.015
	C(9a)	0.015
	N(10)	-0.006
	C(10a)	-0.010
	*O(12)	0.014
	*C(13)	0.045
	*O(14)	0.019
	*C(17)	-0.110
	*C(18)	-0.053
	*C(20)	-0.051

The e.s.d. of the atoms without asterisks from the plane is 0.003 Å.

Plane II	Atom	Deviation
$A = -0.6947$	N(1)	0.005 Å
$B = -0.0312$	C(2)	-0.005
$C = 0.7186$	N(3)	0.001
$D = -1.9796$ Å	C(4)	0.003
	C(4a)	-0.004
	C(10a)	0.000
	*N(5)	0.023
	*N(10)	0.011
	*O(12)	0.001
	*C(13)	0.034
	*O(14)	0.026

The e.s.d. of the atoms without asterisks from the plane is 0.005 Å.

Plane III	Atom	Deviation
$A = -0.6816$	C(4a)	-0.004 Å
$B = -0.0420$	N(5)	-0.001
$C = 0.7305$	C(5a)	0.004
$D = -1.9199$ Å	C(9a)	-0.001
	N(10)	-0.004
	C(10a)	0.007
	*N(1)	0.036
	*C(4)	0.028
	*C(6)	-0.023
	*C(9)	-0.016
	*C(20)	-0.046

The e.s.d. of the atoms without asterisks from the plane is 0.006 Å.

Plane IV	Atom	Deviation
$A = -0.6987$	C(5a)	-0.001 Å
$B = -0.0253$	C(6)	0.008
$C = 0.7149$	C(7)	-0.006
$D = -1.9249$ Å	C(8)	-0.004
	C(9)	0.010
	C(9a)	-0.008
	*N(5)	-0.038
	*N(10)	-0.047
	*C(17)	-0.078
	*C(18)	-0.022

The e.s.d. of the atoms without asterisks from the plane is 0.010 Å.

C(10a)-N(1) and the C(4a)-N(5) bonds. In the benzenoid ring the π -electrons are more delocalized giving π -bond orders ranging from 0.5 to 0.8.

In Table 12 the intramolecular bond distances obtained in the present structure are compared with those obtained by von Glehn, Kierkegaard & Norrestam (1970) for 9-bromo-3-methyl-lumiflavin hydrate and by Trus & Fritchie (1969) for 10-methylalloxazinium bromide dihydrate. The bond distances as evaluated from semi-empirical self-consistent molecular orbital calculations of the Pariser-Parr-Pople type are also given in Table 12. These calculations were performed by use of a computer program kindly put at our disposal by Marianne Sundbom (Institute of Theoretical Physics, University of Stockholm).

The structures of several 9-bromoflavin derivatives have been determined in the last few years (Kierkegaard *et al.*, 1970), and the conclusions drawn from these investigations have partly been based upon the assumption that the 9-bromo substitution does not significantly affect the geometry of the flavin nucleus. From Table 12 it is seen that large bond length differences are obtained for bonds in the vicinity of the bromine substitution. Thus, the bond distances C(8)-C(9), C(9)-C(9a) and C(9a)-N(10) in 9-bromo-3-methyl-lumiflavin are increased by 0.038, 0.025 and 0.038 Å respectively, as compared with the present structure. Since the estimated standard deviations of the bond lengths in 9-bromo-3-methylalumiflavin are about 0.012 Å, the observed differences are about 3σ . Thus it can be stated that the bromine substitution in the 9 position of a flavin nucleus gives only slightly increased bond lengths around the 9 position, and that the conclusions regarding the geometry of the pyrazinoid and pyrimidinoid rings, drawn from structural studies on 9-bromoflavin derivatives, ought to be correct.

A comparison with the molecular structure of the protonated flavin derivative 10-methylalloxazinium bromine dihydrate (Trus & Fritchie, 1969) reveals that upon protonation of the nitrogen atom N(1), the lengths of the intramolecular bonds involving this nitrogen are increased. Thus, the bond lengths N(1)-C(2) and C(10a)-N(1) are in the present study 1.368 and 1.303 Å, while those found in the 10-methylalloxazinium ion are 1.408 and 1.364 Å (estimated standard deviations 0.007 Å). Large differences also occur for the bonds C(4a)-C(10a) and C(10a)-N(10) in such a way that the bond lengths are decreased by about 0.02 Å upon protonation. This suggests increased positive atomic charges at least on the atoms C(4a) and N(10) in the protonated form. The observed differences in the bond lengths of the C(2)-N(3) and N(3)-C(4) bonds between the two structures probably arise from the 3-methyl substitution of the present structure.

Reasonable agreement is found (Table 12) between the bond lengths obtained from molecular orbital calculations of Pariser-Parr-Pople type, and those obtained in the present study. Large differences occur for the lengths of the exocyclic heteropolar bonds. As regards the endocyclic bonds the largest difference, 0.027 Å, occurs for the C(2)-N(3) bond. The average deviation between observed and calculated lengths of these bonds is 0.012 Å.

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Table 12. Comparison of bond distances (in Å) found in 9-bromo-3-methyl lumiflavin hydrate and 10-methylalloxazinium bromide dihydrate

	Observed distances	9-Bromo-3-methyl-lumiflavin hydrate	10-Methylalloxazinium bromide dihydrate	Calculated distances
N(1)—C(2)	1.368	1.387	1.408	1.382
C(2)—N(3)	1.410	1.389	1.379	1.383
N(3)—C(4)	1.362	1.375	1.388	1.364
C(4)—C(4a)	1.483	1.485	1.489	1.468
C(4a)—C(10a)	1.446	1.445	1.422	1.453
C(4a)—N(5)	1.300	1.297	1.299	1.312
N(5)—C(5a)	1.372	1.378	1.376	1.377
C(5a)—C(9a)	1.405	1.420	1.407	1.409
C(5a)—C(6)	1.406	1.398	1.411	1.418
C(6)—C(7)	1.371	1.372	1.348	1.385
C(7)—C(8)	1.421	1.416	1.415	1.414
C(8)—C(9)	1.376	1.414	1.362	1.389
C(9)—C(9a)	1.397	1.422	1.419	1.412
C(9a)—N(10)	1.380	1.418	1.386	1.390
N(10)—C(10a)	1.360	1.356	1.338	1.381
C(10a)—N(1)	1.303	1.324	1.364	1.321
C(2)—O(12)	1.207	1.221	1.209	1.243
N(3)—C(13)	1.473	1.468	—	1.448
C(4)—O(14)	1.219	1.212	1.211	1.243
C(7)—C(17)	1.499	1.508	—	1.491
C(8)—C(18)	1.502	1.509	—	1.488
N(10)—C(20)	1.466	1.489	1.491	1.449

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Molecular Complexes. XII.* The Crystal and Molecular Structure of the 1:1 Complex of Triethyl Phosphate and Benzotrifurazan with Observations on the Structures of the Related Compounds, Trimethyl Phosphate Benzotrifurazan and Tri-isopropyl Phosphate Benzotrifurazan

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The crystal and molecular structure of the 1:1 molecular complex of triethyl phosphate with benzotrifurazan has been determined from three-dimensional data collected on a linear diffractometer at -120°C . The crystals are monoclinic $a = 7.702$, $b = 8.869$, $c = 13.131$ Å, $\gamma = 107.0^{\circ}$; space group $P2_1$. In the crystal the molecules form alternate stacks with the phosphoryl group almost coincident with the threefold axis of the benzotrifurazan molecule. The phosphoryl oxygen atom is 2.51 Å from the benzotrifurazan plane and 2.88 Å (mean) from the carbon atoms of the C_6 ring. The phosphate ester oxygen atoms are 3.05 Å (mean) from a second neighbouring benzotrifurazan molecule. The other complexes named in the title are believed to have similar structures.

Introduction

Benzotrifurazan is reduced (Bailey & Evans, 1967) by some trialkyl phosphites in benzene solution to give colourless crystalline products which are easily purified by sublimation but highly deliquescent. The chemical analyses are consistent with 1:1 complexes of the corresponding phosphate ester and benzotrifurazan. The infrared, visible and ultra-violet spectra are each the sum of the spectra of the components except that slight shifts (-20 cm^{-1}) are observed in the P=O stretching frequency. Molecular weight determinations suggest that the component molecules stay associated in solution.

The structures of the trimethyl, triethyl and triisopropyl phosphate ester complexes with benzotrifurazan

have been investigated. The results for the triethyl phosphate complex, the only analysis that was successfully completed, have been reported briefly (Cameron & Prout, 1968).

Experimental

(i) Preparation

The complexes of $(\text{RO})_3\text{P}=\text{O}$ and benzotrifurazan ($\text{R} = \text{Me}, \text{Et}, \text{isopropyl}$) were prepared by the method described by Bailey & Evans (1967).

Crystals of the triethyl phosphate complex were grown to a size suitable for X-ray photography by alternately raising and lowering the temperature, between 5°C and room temperature, every few hours over a period of three months, of a saturated solution of the complex in 40/60 petroleum ether sealed in contact with a sample of small crystals.

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