

Studies on Flavin Derivatives

The Crystal Structure of 1,3,10-Trimethylisoalloxazinium Iodide

MARIANNE VON GLEHN, PEDER KIERKEGAARD, ROLF NORRESTAM, OWE RÖNNQUIST and PER-ERIK WERNER

Institute of Inorganic and Physical Chemistry, University of Stockholm, Stockholm, Sweden

The crystal structure of 1,3,10-trimethylisoalloxazinium iodide, $C_{13}H_{13}N_4O_2I$, has been determined and refined using three-dimensional X-ray diffractometer data. The unit cell is monoclinic, space group $P2_1/n$ with the constants $a=12.880$, $b=16.076$, $c=6.831$ Å, $\beta=94.04^\circ$. There is one formula unit in the asymmetric unit and all atoms occupy general fourfold positions. The structure was solved by the heavy-atom method and the refinement was carried out by the least-squares procedure. The final R value is 0.043 for 927 observed reflections.

The cations form planar sheets separated by iodide ions located above and below the C(10a)–C(4a) bonds. The isoalloxazinium ring system is essentially planar but the pyrimidine ring is slightly twisted out of this plane. The intra- and intermolecular distances are discussed.

The physical and chemical properties of flavin derivatives in different oxidation states have in the last few years been intensively investigated. Special attention has been paid to the properties of light absorption, electron spin resonance, and binding of metal ions.

A structural investigation of 1,3,10-trimethylisoalloxazinium iodide has been undertaken as part of a research program on flavin compounds.

EXPERIMENTAL

Well-developed crystals of 1,3,10-trimethylisoalloxazinium iodide recrystallized from a methanol solution were kindly supplied by Dr. Franz Müller,¹ who synthesized the substance from 1,3-dimethylalloxazine. The red needle-shaped crystals are stable at room temperature.

Preliminary rotation and Weissenberg photographs established that the crystals are monoclinic and the systematic absences indicated space group $P2_1/n$. Powder photographs were taken in a Guinier-Hägg focusing camera with $CuK\alpha_1$ radiation ($\lambda=1.54056$ Å) and potassium chloride ($a=6.29228$ Å) as an internal standard. The least squares refined unit cell dimensions obtained from the X-ray powder pattern are shown in Table 1.

Three-dimensional intensity data were collected with a General Electric Single-crystal diffractometer XRD6. Ni-filtered CuK radiation was used and the pulse-height analyzer was set to collect 90 % of the $K\alpha$ radiation.

Table 1. Crystal data.

Lattice constants	$a = 12.880 \pm 2 \text{ \AA}$ $b = 16.076 \pm 4 \text{ \AA}$ $c = 6.831 \pm 2 \text{ \AA}$ $\beta = 94.04^\circ \pm 1$
Cell volume	$V = 1418.6 \text{ \AA}^3$
Density (X-ray)	$d = 1.799 \text{ g cm}^{-3}$
Molecules per unit cell	$Z = 4$
Systematic absences	$h0l$ when $h+l = 2n+1$ $0k0$ when $k = 2n+1$
Space group	$P2_1/n$

A crystal with the dimensions $0.04 \times 0.02 \times 0.27 \text{ mm}^3$ was selected and mounted along the c^* -axis. The $\theta-2\theta$ scanning technique was used to measure 2301 independent reflections of which 927 had a net intensity with $\sigma(I)/I < 0.5$. 2θ range of 2° was scanned at a rate of $3^\circ/\text{min}$ and a 20 sec background count was collected at each end of the scan range. Lp and absorption corrections ($\mu = 184.3 \text{ cm}^{-1}$) were applied to the net intensity counts. No extinction effects were observed and thus no correction for extinction was made.

DETERMINATION AND REFINEMENT OF THE STRUCTURE

The position of the iodide ion in the asymmetric unit was found by inspection of the Patterson function. For the heavy atom alone, the reliability index R was 0.21. The plane of the cation was found around $z = 0.22$ in an electron density projection along the a -axis. Three dimensional electron density maps were then calculated and probable positions of the light non-hydrogen atoms were found in sections around $z = 0.22$. All atoms were found to occupy fourfold general positions in $P2_1/n$ [$\pm(x, y, z)$; $\pm(\frac{1}{2} + x, \frac{1}{2} - y, \frac{1}{2} + z)$].

The positional parameters were improved by a series of difference Fourier syntheses. Further refinement was carried out by a full matrix least-squares treatment (World List No. 384).² The scattering factor curves used for oxygen, carbon, and nitrogen were those given by Freeman³ and for the iodide ion that by Cromer and Waber,⁴ corrected by the real part of the anomalous dispersion coefficient. Hughes' weighting scheme was used.⁵

At the first refinement isotropic temperature factors for all atoms except iodine were used. When the R index reached 0.054, all the atoms were given anisotropic thermal parameters. Due to the fact that the program allowed only 156 parameters to vary at the same time it was necessary to do several iterations with 17 atoms varying in each step.

No hydrogen atoms were included in the refinement which was terminated when none of the parameter shifts were greater than 0.2 % of the corresponding standard deviations. At the end of the refinement the reliability factor R [$R = \sum |kF_o| - |F_c| / \sum |kF_o|$] was 0.043 for the reflections listed in Table 2. The calculated values in this table are based on the coordinates and anisotropic thermal parameters given in Table 3. A final difference Fourier synthesis was computed from these structure factors in an attempt to locate the hydrogen atoms.

Table 3. Fractional atomic coordinates, anisotropic temperature parameters and estimated standard deviations. The anisotropic temperature factor $\Gamma = \exp[-h^2B_{11} + k^2B_{22} + l^2B_{33} + 2hkB_{12} + 2hlB_{13} + 2klB_{23}]$.

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
I	0.55961(8)	0.28097(7)	0.7222(2)	0.0061(1)	0.0041(1)	0.163(2)	0.0006(2)	-0.0001(2)	0.0010(3)
N(1)	0.6703(9)	0.2984(8)	0.216(2)	0.004(1)	0.004(1)	0.019(3)	0.000(1)	0.003(3)	0.002(3)
C(10a)	0.5914(12)	0.2427(9)	0.234(2)	0.004(1)	0.003(1)	0.010(3)	0.001(1)	0.000(3)	0.000(2)
C(2)	0.6509(14)	0.3840(11)	0.227(3)	0.007(2)	0.004(1)	0.018(5)	-0.002(2)	0.001(4)	0.005(3)
N(3)	0.5536(11)	0.4117(7)	0.234(2)	0.006(1)	0.004(1)	0.019(3)	0.000(2)	-0.004(3)	-0.002(3)
C(4)	0.4653(12)	0.3637(11)	0.217(2)	0.003(1)	0.005(1)	0.019(5)	0.000(2)	-0.002(3)	0.002(3)
C(4a)	0.4869(11)	0.2716(9)	0.209(2)	0.004(1)	0.002(1)	0.020(4)	0.002(2)	0.004(3)	0.006(3)
N(5)	0.4046(8)	0.2208(10)	0.200(2)	0.005(1)	0.005(1)	0.016(3)	-0.001(2)	0.000(2)	0.000(3)
C(5a)	0.4224(12)	0.1387(11)	0.205(3)	0.005(2)	0.004(1)	0.023(5)	0.000(2)	0.000(4)	0.001(3)
C(6)	0.3355(11)	0.0864(11)	0.190(3)	0.006(2)	0.005(1)	0.021(5)	-0.003(2)	0.003(4)	-0.003(4)
C(7)	0.3533(11)	0.0011(11)	0.201(3)	0.011(2)	0.004(1)	0.026(5)	-0.005(2)	-0.001(5)	0.001(4)
C(8)	0.4487(16)	-0.0315(12)	0.234(2)	0.011(2)	0.005(1)	0.011(4)	0.002(2)	0.000(4)	-0.003(3)
C(9)	0.5409(16)	0.0180(12)	0.260(3)	0.011(2)	0.004(1)	0.019(5)	0.006(2)	0.011(5)	0.005(3)
C(9a)	0.5263(11)	0.1065(9)	0.243(2)	0.005(1)	0.002(1)	0.010(3)	0.003(2)	0.001(3)	0.002(3)
N(10)	0.6081(9)	0.1617(9)	0.267(2)	0.002(1)	0.005(1)	0.017(3)	0.000(2)	0.003(3)	0.000(3)
C(20)	0.7099(12)	0.1325(12)	0.371(3)	0.006(1)	0.007(1)	0.030(5)	0.005(2)	-0.007(4)	0.014(4)
C(11)	0.7731(12)	0.2709(13)	0.139(3)	0.007(1)	0.007(1)	0.036(6)	0.000(2)	0.001(4)	-0.001(5)
O(12)	0.7266(9)	0.4313(8)	0.219(2)	0.005(1)	0.005(1)	0.044(4)	-0.005(2)	-0.001(3)	0.003(3)
C(13)	0.5381(15)	0.5061(9)	0.246(3)	0.010(2)	0.002(1)	0.031(5)	-0.004(2)	-0.004(5)	-0.005(3)
O(14)	0.3782(8)	0.3925(7)	0.214(2)	0.006(1)	0.003(1)	0.055(5)	0.003(1)	-0.003(4)	-0.001(5)

Four peaks were found at the positions expected for the hydrogen atoms attached to C(6), C(7), C(8), and C(9). Some electron-density maxima were also found which might have been assigned to hydrogen atoms in the methyl groups. However, owing to the presence of the heavy iodine atom in the structure all trials to refine hydrogen positions failed.

DESCRIPTION AND DISCUSSION OF THE STRUCTURE

In the following discussion, atoms belonging to different asymmetric units are labelled as follows:

Superscript	Coordinates	Superscript	Coordinates
none	x, y, z	v	$1-x, 1-y, \bar{z}$
'	$x, y, 1+z$	vi	$1-x, 1-y, 1-z$
"	$\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$	vii	$x-\frac{1}{2}, \frac{1}{2}-y, z-\frac{1}{2}$
'''	$1-x, \bar{y}, \bar{z}$	viii	$\frac{1}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$
iv	$1-x, \bar{y}, 1-z$	ix	$\frac{3}{2}-x, y-\frac{1}{2}, \frac{1}{2}-z$

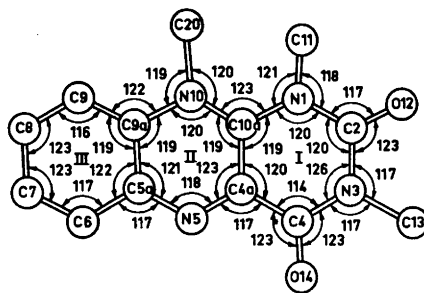
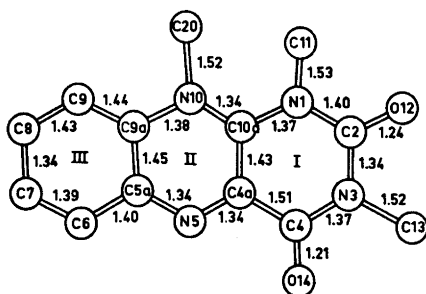


Fig. 1a. Bond lengths (in Å) within the cation of 1,3,10-trimethylisalloxazinium iodide.

Fig. 1b. Bond angles within the cation of 1,3,10-trimethylisalloxazinium iodide.

The bond lengths and bond angles for the cation (Fig. 1) uncorrected for thermal motion were computed from coordinates given in Table 3 and are listed in Table 4. Most of the bond lengths agree, within experimental errors, with accepted values. Owing to the high standard deviation, 0.03 Å, for the C(7)–C(8) bond (1.34 Å), it is not shown that this bond is significantly shorter than the usual C–C bond (1.395 Å⁶) in aromatic compounds. The real deviation of the bond angle C(8)–C(9)–C(9a) from the ideal value might likewise be small or none.

The least-squares planes, A and B, through important regions of the cation and distances of atoms from these planes are given in Table 6 (*cf.* Fig. 2). The dihedral angle between A and B is 8.6°. The distortions are probably mainly due to bending of the axial methyl groups C(20) and C(11) away from each other in order to relieve strain caused by repulsive forces.

Table 4. Interatomic distances and angles in the 1,3,10-trimethylisalloxazinium ion with estimated standard deviations.

N(1) — C(2)	1.40(3) Å	C(4a) — N(5)	1.34(2) Å
N(1) — C(11)	1.53(2)	N(5) — C(5a)	1.34(2)
N(1) — C(10a)	1.37(2)	C(5a) — C(6)	1.40(3)
C(10a) — C(4a)	1.43(2)	C(5a) — C(9a)	1.45(2)
C(10a) — N(10)	1.34(2)	C(6) — C(7)	1.39(3)
C(2) — N(3)	1.34(3)	C(7) — C(8)	1.34(3)
C(2) — O(12)	1.24(3)	C(8) — C(9)	1.43(3)
N(3) — C(4)	1.37(2)	C(9) — C(9a)	1.44(3)
N(3) — C(13)	1.52(2)	C(9a) — N(10)	1.38(2)
C(4) — C(4a)	1.51(3)	N(10) — C(20)	1.52(2)
C(4) — O(14)	1.21(2)		
C(10a) — N(1) — C(2)	120.1(1.3)°	C(10a) — C(4a) — N(5)	123.2(1.4)°
C(10a) — N(1) — C(11)	120.8(1.3)	C(4) — C(4a) — N(5)	116.9(1.3)
C(2) — N(1) — C(11)	117.8(1.3)	C(4a) — N(5) — C(5a)	117.8(1.2)
N(1) — C(10a) — C(4a)	118.6(1.3)	N(5) — C(5a) — C(6)	117.1(1.4)
N(1) — C(10a) — N(10)	122.8(1.3)	N(5) — C(5a) — C(9a)	120.9(1.4)
C(4a) — C(10a) — N(10)	118.6(1.3)	C(6) — C(5a) — C(9a)	121.7(1.6)
N(1) — C(2) — N(3)	120.1(1.5)	C(5a) — C(6) — C(7)	117.4(1.6)
N(1) — C(2) — O(12)	117.1(1.5)	C(6) — C(7) — C(8)	122.6(1.8)
N(3) — C(2) — O(12)	122.8(1.6)	C(7) — C(8) — C(9)	123.3(1.7)
C(2) — N(3) — C(4)	125.8(1.4)	C(8) — C(9) — C(9a)	115.9(1.7)
C(2) — N(3) — C(13)	117.3(1.4)	C(5a) — C(9a) — C(9)	118.9(1.5)
C(4) — N(3) — C(13)	116.7(1.4)	C(5a) — C(9a) — N(10)	118.8(1.3)
N(3) — C(4) — C(4a)	113.6(1.3)	C(9) — C(9a) — N(10)	122.2(1.4)
N(3) — C(4) — O(14)	123.2(1.6)	C(10a) — N(10) — C(9a)	119.7(1.2)
C(4a) — C(4) — O(14)	123.2(1.4)	C(10a) — N(10) — C(20)	120.2(1.3)
C(10a) — C(4a) — C(4)	119.5(1.3)	C(9a) — N(10) — C(20)	118.9(1.3)

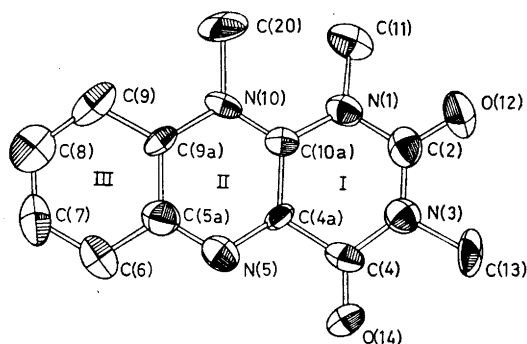


Fig. 2a. The 1,3,10-trimethylisalloxazinium cation.

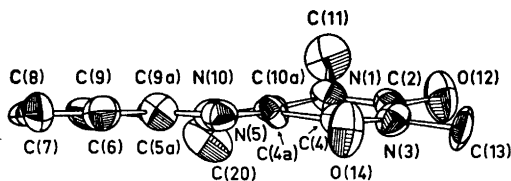


Fig. 2b. The 1,3,10-trimethylisalloxazinium cation (rotated 90° from Fig. 2a).

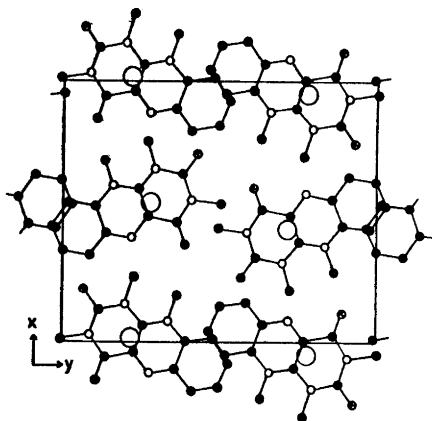


Fig. 3. The structure of 1,3,10-trimethyl-isoalloxazinium iodide. Schematic drawing showing the packing of the ions. Small circles denote carbon atoms (filled ones), nitrogen atoms (open ones), and oxygen atoms (cross marked circles). The large open circles denote iodine atoms.

The packing is illustrated in Fig. 3. The iodide ions distribute themselves between the cations close to the C(10a)–C(4a) bonds. This and the red colour of the crystals might indicate weak charge transfer bonds. Data on the coordination are listed in Table 5.

Table 5. Distances between the iodide ion and the atoms N(1), C(10a), C(4), C(4a), N(5), and N(10), respectively.

I...N(1)	3.84 Å
I...N(1')	3.58
I...C(10a)	3.44
I...C(10a')	3.55
I...C(4)	3.82
I...C(4')	3.91
I...C(4a)	3.57
I...C(4a')	3.52
I...N(5)	4.08
I...N(5')	4.06
I...N(10)	3.74
I...N(10')	4.20

All distances less than 3.80 Å between the cations are tabulated in Table 7. The closest intermolecular C...O distance is as short as 3.106 ± 0.021 Å for C(20)–H...O(14''). The sum of the van der Waals radii of a methyl group and an oxygen atom is 3.40 Å.⁷ It is difficult to explain this considerable shortening of the van der Waals separation. Sim⁸ suggests that short C–H...O contacts may represent situations in which two atoms have been forced closer together than the ideal distance for free atoms in order that the molecules may achieve more favourable packing elsewhere. For crystal structures this should represent configurations of lowest energy for all intermolecular interactions.

However, activation of the CH₃ group here involved is probable since C(20) is attached to the heteroatom N(10). Furthermore, a peak in the final difference

Table 6. Least-squares planes. The planes are described using a vector basis (m, n, p) having $m \parallel a^*$, $n \parallel b$ and $p \parallel c$.

Plane A. $-0.0841 \cdot m + 0.0519 \cdot n + 0.9951 \cdot p = 0.6896$

Plane B. $0.0481 \cdot m - 0.0191 \cdot n + 0.9987 \cdot p = 1.2555$

Plane C. $-0.0011 \cdot m + 0.0273 \cdot n + 0.9996 \cdot p = 1.1497$

The angle between the planes A and B is 8.6°

Plane A		Plane B		Plane C	
Atom	Deviation ^a	Atom	Deviation ^a	Atom	Deviation ^a
C(10a)	-70	C(10a)	96	C(10a)	-161
C(4a)	-9	N(1)	-66	N(1)	-31
N(5)	51	C(2)	-12	C(2)	119
C(5a)	-19	N(3)	55	N(3)	63
C(6)	8	C(4)	-20	C(4)	-52
C(7)	-24	C(4a)	-53	C(4a)	-60
C(8)	-16	I'	3424	N(5)	-78
C(9)	19	I''	3400	C(5a)	-123
C(9a)	6			C(6)	-102
N(10)	53			C(7)	21
I'	3343			C(8)	136
I''	-3457			C(9)	72
				C(9a)	184
				N(10)	10
				O(12)	-134
				O(14)	136
				I'	3389
				I''	3441

I' and I'' (not included into the least-squares planes) situated on opposite sides of the cation.

^a Deviations are given in 10^{-3} Å.

Table 7. Distances less than 3.80 Å between the cations.

N(3) ... C(13 v)	3.66 Å
N(5) ... C(11'')	3.55
C(6) ... O(12 vii)	3.43
C(7) ... C(9'')	3.54
C(7) ... C(20 iv)	3.76
C(7) ... O(12 viii)	3.73
C(7) ... O(14 viii)	3.54
C(8) ... C(8'')	3.69
C(8) ... C(9'')	3.40
C(8) ... C(9 iv)	3.45
C(8) ... C(9a'')	3.51
C(8) ... C(9a iv)	3.76
C(9) ... C(9'')	3.69
C(9) ... C(9 iv)	3.56
C(9) ... O(12 ix)	3.30
C(11) ... O(12 ix)	3.41
C(11) ... O(14'')	3.11
C(14) ... C(13 v)	3.43
C(14) ... C(13 vi)	3.68
C(14) ... O(14 v)	3.77

Fourier synthesis 1.1 Å from C(20) and 2.4 Å from O(14") was also observed. It is notable that in all respects the rules for $\text{CH}_3\cdots\text{O}$ "hydrogen bonds" listed by Sutor⁹ are here fulfilled.

On the other hand, there seems to be no spectroscopic evidence for the existence of $\text{C}-\text{H}\cdots\text{O}$ hydrogen bonds, where the carbon atom belongs to a methyl group (Allerhand and Schleyer).¹⁰ Therefore it remains to investigate whether the $\text{C}(20)-\text{H}\cdots\text{O}(14")$ interaction is repulsive or attractive.

It may be remarked that if the contact is repulsive there are no "hydrogen bonds" at all in the structure and the cations must be linked together by other forces within the sheets.

Because of the wide occurrence of heterocyclic biological molecules, further investigations of short $\text{C}-\text{H}\cdots\text{O}$ contacts in heterocyclic substances would be of vital importance. Therefore we believe that further X-ray crystal structure determinations would be valuable.

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REFERENCES

1. Müller, F. Dissertation, Basel 1964.
2. *IUCr World List of Crystallographic Computer Programs*, 2nd Ed., Cambridge, Mass. 1966, No. 384.
3. Freeman, A. J. *Acta Cryst.* **12** (1959) 261.
4. Cromer, D. T. and Waber, J. T. *Acta Cryst.* **18** (1965) 104.
5. Hughes, E. W. *J. Am. Chem. Soc.* **63** (1941) 1737.
6. *International Tables for X-Ray Crystallography*, Kynoch Press, Birmingham 1959, Vol. III, p. 276.
7. Pauling, L. *The Nature of the Chemical Bond*, 3rd Ed., Cornell Univ. Press, Ithaca 1960, p. 260.
8. Sim, G. A. *Ann. Rev. Phys. Chem.* **18** (1967) 57.
9. Sutor, D. J. *J. Chem. Soc.* 1963 1105.
10. Allerhand, A. and Schleyer, P. von R. *J. Am. Chem. Soc.* **85** (1963) 1715.
11. Johnson, C. K., ORTEP, *A Fortran Thermal-Ellipsoid Plot Program for Crystal-Structure Illustrations*, Oak Ridge National Laboratory, ORNL-3794.

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