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The Crystal and Molecular Structure of 9-Bromo-3,7,8,10-tetramethylisoalloxazine Monohydrate

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The crystal structure of 9-bromo-3,7,8,10-tetramethylisoalloxazine monohydrate, $C_{14}H_{13}BrN_4O_2.H_2O$, an example of a flavin derivative in an oxidized, neutral state, has been determined by three-dimensional X-ray analysis. The symmetry is monoclinic, space group $P2_1/c$, with unit cell constants $a = 13.047(5)$ Å, $b = 7.053(5)$ Å, $c = 17.957(5)$ Å, and $\beta = 120.40(5)°$. There are four molecules in the unit cell. The ring system within the molecule is fairly planar and the molecules are situated in layers normal to the b-axis. The structure was solved by the heavy-atom technique and the parameters obtained were refined by full matrix least squares analysis with a final reliability index, R, of 0.051 for the 1283 most significant observed reflections.

The structure analysis of 9-bromo-3,7,8,10-tetramethylisoalloxazine monohydrate was undertaken as part of a research program of X-ray structural studies of flavin compounds, important in many biological oxidation systems. A survey of the flavin compounds previously investigated within this project is given by Kierkegaard *et al.*[1] The present structure provides information on a flavin derivative in an oxidized nonprotonated state (Fig. 1). A brief description has appeared earlier.[2]

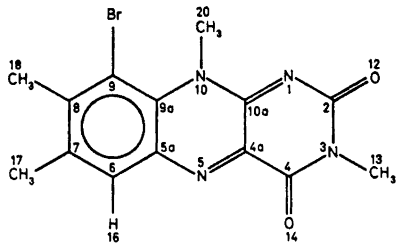

Fig. 1. Schematic drawing of 9-bromo-3,7,8,10-tetramethylisoalloxazine.

EXPERIMENTAL

Suitable single crystals were obtained by crystallization from an acetic acid solution of a specimen prepared by L. Maron [3] at this Institute. A selected single crystal with the dimensions $0.3 \times 0.08 \times 0.02$ mm^3 was indicated by Weissenberg methods to possess the monoclinic symmetry $P2_1/c$. The crystal data are given in Table 1. Three-dimensional

Table 1. Crystallographic data of 9-bromo-3,7,8,10-tetramethylisoalloxazine monohydrate. The estimated standard deviations are given in parentheses.

Lattice constants	$a = 13.047(5)$ Å $b = 7.053(5)$ Å $c = 17.957(5)$ Å $\beta = 120.40(5)°$
Cell volume	$V = 1425.2$ Å^3
Density (X-ray)	$d = 1.7$ g cm^{-3}
Molecules per unit cell	$Z = 4$
Systematically absent reflections	$h0l$ when $l = 2n+1$ $0k0$ when $k = 2n+1$
Space group	$P2_1/c$
Wave length	$\lambda = 0.71069$ Å

X-ray intensity data were collected from a crystal mounted along the b-axis by a Siemens AED (Automatischer Einkristall-Diffraktometer) with Nb-filtered MoK radiation and a scintillation counter, with the pulse height analyzer set to collect about 90 % of the Mo$K\alpha$ radiation. The $\theta - 2\theta$ scan technique was applied to yield integrated intensities. The intensities of 2906 reflections with $\theta \leq 25°$ were determined as the averages of the intensities measured at two different symmetry related reciprocal lattice points. Only the 1283 most significant reflections were included in the further calculations. Lorentz, polarization and absorption corrections ($\mu = 30$ cm^{-1}) [4] were applied to the net intensities.

STRUCTURE DETERMINATION AND REFINEMENT

The position of the bromine atom was determined from a three-dimensional Patterson synthesis and then refined with isotropic thermal parameter in a full matrix least squares refinement to an R-index

$$[R = \sum||kF_o| - |F_c||/\sum|kF_o|]$$

of 0.302. A three-dimensional difference electron density map displayed the atoms in the isoalloxazine ring near a plane $y = 0.6$. Successive three-dimensional difference electron density maps gave well-resolved peaks for the remaining nonhydrogen atoms including the oxygen atom of the water molecule. Full matrix least squares refinement of the atomic positions and the thermal parameters, anisotropic for the bromine atom and isotropic for the other nonhydrogen atoms, reduced the R-value to 0.077. After introduction of anisotropic temperature factors for all the 22 nonhydrogen atoms into the refinement, the R-index fell to 0.060.

Reasonable positions for all non-water hydrogen atoms were then obtained from a three-dimensional difference electron density map. Finally, three cycles of full matrix least squares refinement, with anisotropic temperature factors for all the 22 nonhydrogen atoms and constant isotropic (5 Å^2) ones for the hydrogens, reduced the value of R to 0.051. Refinement was terminated when all shifts in the parameters were less than 5 % of their corresponding standard deviations. A subsequent difference electron density map did not

Table 2. Weight analysis obtained in the final cycle of the least squares refinement of 9-bromo-3,7,8,10-tetramethylisoalloxazine monohydrate. The averages $\overline{w(|F_o|-|F_c|)^2}=\overline{w\Delta^2}$ are normalized. N is the number of independent reflections in each interval.

Interval sin θ	N	$\overline{w\Delta^2}$	Interval F_{obs}	N	$\overline{w\Delta^2}$
0.0 – 0.1973	233	0.9515	0.0 – 14.4	118	1.2247
0.1973 – 0.2485	202	1.0806	14.4 – 16.4	128	1.1049
0.2485 – 0.2845	175	1.1287	16.4 – 18.7	132	1.5215
0.2845 – 0.3131	156	0.7444	18.7 – 21.9	135	1.0459
0.3131 – 0.3373	158	0.8026	21.9 – 24.9	134	0.9258
0.3373 – 0.3585	110	0.8054	24.9 – 29.4	135	1.0770
0.3585 – 0.3774	98	1.1639	29.4 – 33.8	134	0.8165
0.3774 – 0.3945	83	1.2507	33.8 – 42.2	135	0.9311
0.3945 – 0.4103	62	1.3798	42.2 – 57.8	134	0.6263
0.4103 – 0.4250	43	1.1055	57.8 – 304.0	135	0.7671

Table 3. Final positional parameters for the nonhydrogen atoms with estimated standard deviations.

Atom	x	y	z
Br	0.7777(1)	0.5548(2)	0.49550(6)
N(1)	0.3090(7)	0.6316(14)	0.3429(5)
C(2)	0.1872(9)	0.6219(16)	0.2874(6)
N(3)	0.1377(6)	0.6024(13)	0.1989(5)
C(4)	0.2021(8)	0.6053(14)	0.1575(6)
C(4A)	0.3328(7)	0.6183(14)	0.2165(5)
N(5)	0.3987(7)	0.6280(13)	0.1817(4)
C(5A)	0.5203(7)	0.6386(15)	0.2363(6)
C(6)	0.5908(7)	0.6364(13)	0.1978(5)
C(7)	0.7123(8)	0.6363(15)	0.2467(6)
C(8)	0.7668(8)	0.6182(15)	0.3374(6)
C(9)	0.6977(8)	0.6154(14)	0.3776(6)
C(9A)	0.5728(8)	0.6363(15)	0.3274(6)
N(10)	0.4964(6)	0.6526(12)	0.3618(4)
C(10A)	0.3771(8)	0.6303(16)	0.3078(6)
O(12)	0.1219(6)	0.6241(13)	0.3179(5)
C(13)	0.0076(8)	0.5863(19)	0.1444(6)
O(14)	0.1590(5)	0.5907(12)	0.0801(4)
C(17)	0.7833(8)	0.6349(17)	0.2018(6)
C(18)	0.9010(8)	0.6035(18)	0.3922(6)
C(20)	0.5384(9)	0.7216(19)	0.4504(6)
O	0.2989(11)	0.6022(15)	−0.0173(6)

Table 4. Anisotropic thermal parameters for the nonhydrogen atoms and their standard deviations. ($T = \exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$.)

Atom	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Br	0.00583(9)	0.0285(3)	0.00235(4)	−0.00207(28)	0.00159(9)	−0.00241(26)
N(1)	0.0054(7)	0.0270(26)	0.0028(3)	0.0021(21)	0.0045(8)	0.0001(15)
C(2)	0.0061(8)	0.0206(29)	0.0032(4)	0.0052(24)	0.0060(10)	0.0025(17)
N(3)	0.0037(6)	0.0269(29)	0.0033(3)	0.0020(19)	0.0042(8)	0.0035(15)
C(4)	0.0045(7)	0.0155(31)	0.0027(4)	0.0023(21)	0.0035(9)	0.0022(14)
C(4A)	0.0035(7)	0.0153(25)	0.0027(4)	−0.0013(20)	0.0036(8)	−0.0002(15)
N(5)	0.0052(6)	0.0220(23)	0.0015(3)	−0.0004(19)	0.0018(7)	0.0003(12)
C(5A)	0.0024(7)	0.0165(23)	0.0027(4)	0.0018(20)	0.0016(8)	0.0015(15)
C(6)	0.0059(7)	0.0194(21)	0.0020(3)	0.0021(19)	0.0031(7)	−0.0004(13)
C(7)	0.0048(8)	0.0148(24)	0.0037(5)	0.0006(22)	0.0040(10)	0.0030(17)
C(8)	0.0052(8)	0.0140(27)	0.0035(4)	−0.0001(22)	0.0035(10)	−0.0015(16)
C(9)	0.0045(7)	0.0162(26)	0.0029(4)	−0.0016(21)	0.0029(9)	0.0029(16)
C(9A)	0.0048(7)	0.0118(22)	0.0027(4)	−0.0020(21)	0.0039(9)	−0.0001(15)
N(10)	0.0048(6)	0.0173(20)	0.0024(3)	0.0008(19)	0.0036(7)	0.0014(13)
C(10A)	0.0049(8)	0.0198(26)	0.0024(4)	−0.0007(23)	0.0040(9)	−0.0002(15)
O(12)	0.0070(6)	0.0356(26)	0.0051(4)	0.0023(20)	0.0090(9)	0.0005(16)
C(13)	0.0049(7)	0.0254(33)	0.0041(4)	−0.0027(24)	0.0038(8)	−0.0019(19)
O(14)	0.0050(5)	0.0403(29)	0.0020(3)	−0.0072(20)	0.0023(6)	−0.0026(13)
C(17)	0.0062(8)	0.0262(27)	0.0040(4)	−0.0055(24)	0.0070(10)	−0.0054(18)
C(18)	0.0044(6)	0.0352(40)	0.0038(4)	−0.0047(25)	0.0028(7)	−0.0030(20)
C(20)	0.0074(9)	0.0290(36)	0.0035(4)	−0.0041(28)	0.0044(10)	−0.0052(19)
O	0.0244(16)	0.0380(35)	0.0072(6)	0.0182(36)	0.0186(17)	0.0039(22)

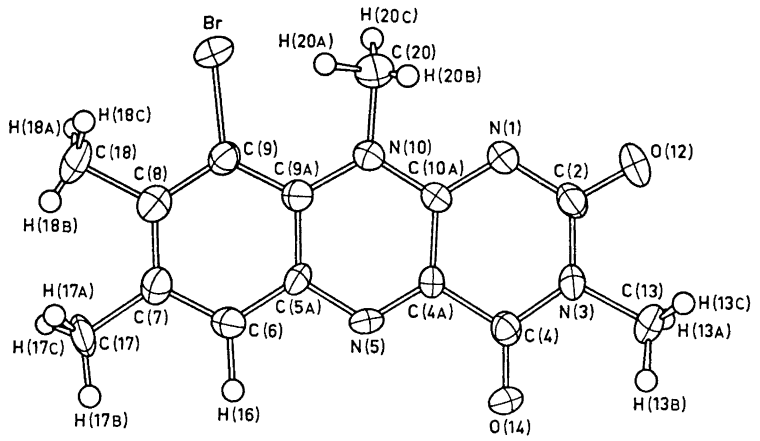

Fig. 2. Molecular conformation observed in the crystal structure of 9-bromo-3,7,8,10-tetramethylisoalloxazine monohydrate with atoms numbered for reference in the text.

reveal the positions of the two remaining hydrogens (bonded to the water oxygen).

The scattering factors for bromine, carbon, nitrogen, and oxygen were taken from Hanson *et al.*[5] and that for hydrogen were given by Stewart *et al.*[6]

Table 5. Atomic coordinates for hydrogen atoms with their standard deviations and isotropic thermal parameters (Å²).

Atom	x	y	z	B
H(16)	0.544(10)	0.621(17)	0.124(8)	5.00
H(13A)	−0.008(9)	0.488(16)	0.149(7)	5.00
H(13B)	−0.022(8)	0.681(14)	0.083(6)	5.00
H(13C)	−0.027(8)	0.706(15)	0.161(6)	5.00
H(17A)	0.835(9)	0.733(15)	0.226(6)	5.00
H(17B)	0.738(8)	0.619(13)	0.135(6)	5.00
H(17C)	0.844(9)	0.499(13)	0.221(6)	5.00
H(18A)	0.926(8)	0.447(14)	0.431(6)	5.00
H(18B)	0.913(9)	0.602(15)	0.353(6)	5.00
H(18C)	0.914(8)	0.705(15)	0.434(6)	5.00
H(20A)	0.613(8)	0.823(15)	0.464(6)	5.00
H(20B)	0.489(9)	0.799(15)	0.441(7)	5.00
H(20C)	0.563(8)	0.594(15)	0.489(6)	5.00

Table 6. Intramolecular bond distances (in Å) and their estimated standard deviations.

Br	−C(9)	1.876(9) Å	N(3)	−C(13)	1.473(11)
N(1)	−C(2)	1.385(12)	C(4)	−O(14)	1.212(10)
C(2)	−N(3)	1.387(12)	C(7)	−C(17)	1.505(13)
N(3)	−C(4)	1.376(11)	C(8)	−C(18)	1.516(13)
C(4)	−C(4A)	1.487(12)	N(10)	−C(20)	1.479(12)
C(4A)	−N(5)	1.295(11)	C(6)	−H(16)	1.14(12)
N(5)	−C(5A)	1.382(11)	C(13)	−H(13A)	0.74(11)
C(5A)	−C(6)	1.403(11)	C(13)	−H(13B)	1.18(10)
C(6)	−C(7)	1.369(12)	C(13)	−H(13C)	1.07(10)
C(7)	−C(8)	1.415(13)	C(17)	−H(17A)	0.91(10)
C(8)	−C(9)	1.411(13)	C(17)	−H(17B)	1.04(10)
C(9)	−C(9A)	1.416(13)	C(17)	−H(17C)	1.18(10)
C(9A)	−N(10)	1.418(11)	C(18)	−H(18A)	1.25(10)
N(10)	−C(10A)	1.363(12)	C(18)	−H(18B)	0.80(10)
C(10A)	−N(1)	1.325(12)	C(18)	−H(18C)	0.98(10)
C(4A)	−C(10A)	1.438(12)	C(20)	−H(20A)	1.13(10)
C(5A)	−C(9A)	1.418(12)	C(20)	−H(20B)	0.79(11)
C(2)	−O(12)	1.224(12)	C(20)	−H(20C)	1.08(10)

Table 7. Intramolecular bond angles (in degrees) with their estimated standard deviations.

Br	−C(9)	−C(9A)	123.1(7)°	C(6)	−C(7)	−C(8)	118.9(8)
Br	−C(9)	−C(8)	116.5(7)	C(6)	−C(7)	−C(17)	118.9(8)
N(1)	−C(2)	−N(3)	122.0(8)	C(7)	−C(8)	−C(9)	120.7(8)
N(1)	−C(2)	−O(12)	118.8(8)	C(7)	−C(8)	−C(18)	119.8(8)
C(2)	−N(3)	−C(13)	118.7(7)	C(8)	−C(9)	−C(9A)	120.0(8)
C(2)	−N(3)	−C(4)	124.0(7)	C(9)	−C(9A)	−N(10)	124.6(8)
N(3)	−C(4)	−O(14)	124.2(8)	C(9A)	−N(10)	−C(20)	122.4(7)
N(3)	−C(4)	−C(4A)	114.2(7)	C(9A)	−N(10)	−C(10A)	118.8(7)
C(4)	−C(4A)	−C(10A)	118.1(7)	C(9A)	−C(5A)	−C(6)	120.9(7)
C(4)	−C(4A)	−N(5)	117.4(8)	N(10)	−C(10A)	−N(1)	117.4(8)
C(4A)	−C(10A)	−N(1)	124.3(8)	C(10A)	−N(1)	−C(2)	117.3(8)
C(4A)	−C(10A)	−N(10)	118.2(8)	C(10A)	−C(4A)	−N(5)	124.4(8)
C(4A)	−N(5)	−C(5A)	117.8(7)	O(12)	−C(2)	−N(3)	119.2(9)
N(5)	−C(5A)	−C(9A)	121.8(7)	C(13)	−N(3)	−C(4)	117.2(7)
N(5)	−C(5A)	−C(6)	117.0(7)	O(14)	−C(4)	−C(4A)	121.5(8)
C(5A)	−C(9A)	−N(10)	117.8(7)	C(17)	−C(7)	−C(8)	121.9(8)
C(5A)	−C(9A)	−C(9)	117.6(8)	C(18)	−C(8)	−C(9)	119.5(8)
C(5A)	−C(6)	−C(7)	121.2(7)	C(20)	−N(10)	−C(10A)	118.1(7)

Table 8. Structure factors. Each of three columns contains k, $10|F_o|$, and $10|F_c|$, and is headed by the values of h and l common to the group.

k	$10\|F_o\|$	$10\|F_c\|$
H= 0	L= 0	
2	856	839
4	1433	1365
6	196	185
H= 0	L= 1	
1	1105	1046
2	3040	2902
3	216	233
6	508	509
H= 0	L= 2	
0	321	387
1	535	472
2	798	782
4	865	812
5	183	156
6	200	205
8	243	251
H= 0	L= 3	
1	859	842
2	323	304
3	695	675
4	164	123
6	206	185
7	145	222
H= 0	L= 4	
0	873	814
1	247	243
2	611	589
4	206	200
5	125	108
H= 0	L= 5	
1	618	600
2	616	605
3	519	532
6	163	178
7	134	152
H= 0	L= 6	
0	1822	1711
1	242	216
2	639	655
3	194	173
4	258	262
5	255	242
H= 0	L= 9	
1	538	537
2	168	178
3	326	415
H= 0	L= 10	
0	741	735
2	553	531
3	183	182
5	162	129
H= 0	L= 11	
1	527	514
3	230	248
4	134	96
H= 0	L= 12	
0	583	585
2	408	397
3	249	225
H= 0	L= 13	
1	342	340
3	186	179
H= 0	L= 14	
0	467	455
2	316	327
3	136	104
H= 0	L= 15	
1	296	286
3	174	153
4	178	151
H= 0	L= 16	
0	384	375
2	172	177
H= 0	L= 17	
1	300	337
H= 0	L= 18	
0	141	179
H= 1	L= 0	
0	401	377
2	656	639
3	184	195
4	276	259
5	375	388
6	205	191
H= 1	L= 1	
1	277	262
2	781	793
4	937	973
5	159	144
6	323	312
H= 1	L= 2	
3	574	595
5	372	409
6	152	160
H= 1	L= 3	
1	117	156
2	1007	1014
4	490	495
6	177	183
H= 1	L= 4	
0	595	650
3	463	469
5	352	366
H= 1	L= 5	
2	355	382
4	475	456
6	206	212
H= 1	L= 6	
0	143	148
1	168	166
3	538	572
5	291	297
7	143	113
H= 1	L= 7	
2	541	535
4	455	473
H= 1	L= 8	
0	127	25
1	213	277
3	617	603
5	337	332
H= 1	L= 9	
1	212	211
2	291	293
4	428	436
6	194	187
H= 1	L= 10	
0	169	201
1	141	139
3	361	377
5	295	277
H= 1	L= 11	
2	392	405
4	338	337
H= 1	L= 12	
1	207	238
3	316	330
5	162	189
H= 1	L= 13	
1	175	194
2	358	326
4	267	264
H= 1	L= 14	
2	137	76
3	174	167
5	195	213
H= 1	L= 15	
2	291	257
4	236	238
H= 1	L= 16	
3	162	178
H= 1	L= 17	
2	151	163
H= 2	L= 0	
0	1668	1526
1	144	150
2	998	1001
4	181	183
5	125	139
6	208	208
H= 2	L= 1	
1	575	570
3	559	558
4	179	157
6	147	173
H= 2	L= 2	
0	1201	1131
1	291	275
2	984	986
3	191	199
6	144	152
8	140	134
H= 2	L= 3	
1	669	633
2	234	251
3	263	327
H= 2	L= 7	
1	723	744
3	304	333
7	139	106
H= 2	L= 8	
0	639	634
1	173	119
2	432	439
4	121	114
6	135	125
H= 2	L= 9	
1	653	647
3	242	250
H= 2	L= 10	
0	684	671
2	338	327
H= 2	L= 11	
1	483	484
3	173	181
H= 2	L= 12	
0	575	565
2	338	338
4	131	75
H= 2	L= 13	
1	422	425
3	152	139
H= 2	L= 14	
0	511	501
2	264	283
H= 2	L= 15	
1	258	268
H= 2	L= 16	
0	360	357
2	229	210
H= 3	L= 0	
0	1033	1050
1	327	325
2	246	267
3	689	694
5	230	258
H= 3	L= 1	
1	259	261
2	767	752
3	200	186
4	501	511
6	169	157
H= 3	L= 2	
0	537	520
2	202	218
3	245	218
4	136	114
5	324	322
7	183	168
H= 3	L= 3	
1	578	550
2	588	592
4	468	477
6	203	209
H= 3	L= 4	
0	499	514
1	219	206
2	162	195
3	332	332
5	324	330
H= 3	L= 5	
1	442	439
2	577	583
4	482	487
6	219	196
H= 3	L= 6	
0	175	197
1	299	290
3	412	415
5	295	302
H= 3	L= 7	
1	221	228
2	518	510
4	430	416
H= 3	L= 8	
1	217	205
3	261	271
5	269	271
H= 3	L= 9	
1	262	236
2	247	235
4	163	165
H= 3	L= 10	
1	295	281
2	182	173
3	387	407
5	233	232
H= 3	L= 11	
2	227	214
4	269	266
H= 3	L= 12	
3	241	255
5	226	187
H= 3	L= 13	
2	241	248
4	281	288
H= 3	L= 14	
3	230	204
H= 4	L= 0	
0	692	649
1	412	375
2	367	359
3	289	282
4	205	187
5	168	158
H= 4	L= 1	
1	642	625
2	502	513
4	384	377
6	146	124
H= 4	L= 2	
0	1188	1162
2	487	483
3	294	295
5	308	297
6	131	132
H= 4	L= 3	
1	422	399
2	116	96
3	344	351
4	262	255
6	162	154
H= 4	L= 4	
0	662	681
1	276	241
2	452	434
3	414	399
4	103	160
5	182	156
H= 4	L= 5	
1	524	507
2	222	239
3	313	327
4	264	268
H= 4	L= 6	
0	610	581
1	280	273
2	488	480
3	336	321
4	172	184
H= 4	L= 7	
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2	515	542
4	154	117
H= 4	L= 8	
0	1306	1318
2	388	363
3	247	211
4	348	375
5	194	205
H= 4	L= 9	
2	594	591
3	244	260
4	178	125
6	285	290
H= 4	L= 10	
0	263	226
2	312	292
3	194	204
4	432	437
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1	367	411
2	414	425
3	196	228
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2	306	287
H= 4	L= 13	
1	304	299
2	241	234
H= 4	L= 14	
0	510	519
1	149	92
2	255	250
H= 5	L= 0	
0	496	499
1	1046	978
2	527	515
3	780	752
6	128	121
H= 5	L= 1	
1	389	317
2	323	291
3	751	728
4	293	288
5	176	198
7	217	182
H= 5	L= 2	
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1	585	559
2	449	461
3	230	208
5	427	448
7	175	171
H= 5	L= 3	
1	972	958
3	131	143
4	331	333
5	246	234
6	197	227
H= 5	L= 4	
0	618	610
1	310	305
2	335	336
3	373	380
5	144	119
H= 5	L= 5	
1	504	510
2	251	255
3	129	127
4	264	265
5	139	142
6	172	180
H= 5	L= 6	
0	688	704
1	337	311
2	316	308
3	478	464
4	219	228
H= 5	L= 7	
2	748	767
3	298	309
4	286	289
H= 5	L= 8	
0	309	288
1	123	164
2	207	224
4	366	401
5	257	248
H= 5	L= 9	
1	472	472
2	179	168
4	328	336
5	155	142
H= 5	L= 10	
0	448	447
1	187	172
3	313	325
4	154	142
5	168	128
H= 5	L= 11	
1	164	181
2	238	232
H= 5	L= 12	
0	185	199
3	214	198
H= 5	L= 13	
1	177	151
H= 5	L= 14	
0	160	155
H= 6	L= 0	
1	146	120
2	219	214
3	410	412
5	321	301
H= 6	L= 1	
1	453	457
2	396	390
3	264	260
4	371	391
7	139	114
H= 6	L= 2	
0	400	394
1	211	206
2	312	320
3	306	304
H= 6	L= 3	
1	316	313
2	275	252
4	304	305
6	170	152
H= 6	L= 4	
0	305	286
2	293	306
3	350	359
5	268	281
H= 6	L= 5	
1	236	238
2	335	340
3	212	235
4	301	298
H= 6	L= 6	
0	392	399
1	222	226
2	278	302
3	318	315
5	178	166
H= 6	L= 7	
1	351	341
2	223	239
4	175	255
H= 6	L= 8	
0	413	399
2	284	309
3	136	140
5	164	158
H= 6	L= 9	
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2	146	-146
3	170	178
H= 6	L= 10	
0	289	-327
1	189	183
2	152	170
3	231	222
H= 6	L= 11	
1	222	260
H= 6	L= 12	
0	211	188
H= 7	L= 0	
0	367	380
1	121	117
2	332	313
3	309	305
H= 7	L= 1	
1	614	595
3	218	205
H= 7	L= 2	
0	591	577
1	164	150
2	364	377
3	218	232
H= 7	L= 3	
1	274	364
3	217	187
4	136	120
H= 7	L= 4	
0	592	600
2	326	343
3	143	108
H= 7	L= 5	
1	414	418
2	127	112
3	139	129
4	165	186
H= 7	L= 6	
0	494	486
2	225	234
3	136	124
H= 7	L= 7	
1	334	346
2	129	146
3	170	136
4	181	129
H= 7	L= 8	
0	374	374
2	226	207
H= 7	L= 9	
1	284	294
4	155	123
H= 7	L= 10	
0	233	238
2	137	161
H= 7	L= 11	
1	268	265
H= 8	L= 0	
0	171	175
1	345	334
3	456	455
5	272	267
H= 8	L= 1	
1	169	182
2	197	189
4	247	260
6	153	129
H= 8	L= 2	
1	241	238
3	361	352
5	198	223
H= 8	L= 3	
1	260	247
2	328	313
4	259	235
6	153	128
H= 8	L= 4	
3	256	214
5	194	175
H= 8	L= 5	
2	275	267
4	250	254
H= 8	L= 6	
0	189	180
3	239	220
H= 8	L= 7	
1	142	125
2	222	213
4	211	202
H= 8	L= 8	
3	207	182
H= 8	L= 9	
2	202	202
H= 8	L= 10	
0	215	204
1	138	105
H= 9	L= 0	
0	536	513
2	342	346
H= 9	L= 1	
1	545	564
H= 9	L= 2	
0	466	465
2	244	262
H= 9	L= 3	
1	462	456
3	159	126
H= 9	L= 4	
0	336	332
2	273	278
H= 9	L= 5	
1	300	292
H= 9	L= 6	
0	327	342
2	222	256
H= 9	L= 7	
1	211	241
H= 9	L= 8	
0	296	294
2	246	244
H= 10	L= 0	
0	374	377
3	263	268
4	221	226
5	155	162
H= 10	L= 1	
2	469	488
4	212	215
H= 10	L= 2	
0	178	177
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H= 10	L= 3	
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H= 10	L= 4	
3	242	247
H= 10	L= 5	
2	138	133
H= 10	L= 6	
1	134	99
H= 11	L= 0	
0	449	492
2	194	201
4	148	102
H= 11	L= 1	
1	288	296
4	140	103
H= 11	L= 2	
2	224	229
H= 11	L= 3	
1	246	269
2	162	156
H= 11	L= 4	
0	312	322
1	136	83
2	222	186
H= 11	L= 5	
1	284	282
H= 12	L= 0	
0	148	149
3	161	145
H= 12	L= 1	
1	154	141
2	135	138
H= 12	L= 2	
0	146	91
H= 12	L= 3	
1	167	119
H= 13	L= 0	
0	231	236
1	151	45
H= 1	L= -1	
1	291	252
2	1594	1546
3	251	247
4	487	507
H= 1	L= -2	
0	1125	1063
1	849	898
2	393	374
3	739	764
4	328	326
5	346	364
H= 1	L= -3	
1	716	666
2	368	356
4	394	395
5	144	111
6	351	330
H= 1	L= -4	
0	312	274
1	548	552
3	475	464
5	377	361
H= 1	L= -5	
1	712	687
2	236	232
3	131	154
4	628	623
6	313	298
H= 1	L= -6	
0	362	359
1	160	155
2	204	181
3	236	219
4	344	350
5	564	560
7	141	138
H= 1	L= -7	
1	227	198
2	770	740
3	556	521
4	408	424
H= 1	L= -8	
0	217	233
1	957	860
3	870	842
H= 1	L= -9	
1	652	824
2	389	519
4	233	339
5	151	168
H= 1	L= -10	
0	250	295
3	176	285
5	211	282
H= 1	L= -11	
1	428	459
2	337	364
3	174	66
4	362	373
H= 1	L= -12	
0	266	284
2	179	177
3	187	248
4	154	118
5	192	174
H= 1	L= -13	
1	221	222
2	335	345
3	130	100
4	294	292
H= 1	L= -14	
0	397	415
2	212	211
3	243	204
5	213	210
H= 1	L= -15	
3	208	227
4	198	224
5	152	97
H= 1	L= -16	
1	248	261
2	189	213
3	360	376
H= 1	L= -17	
1	289	294
2	248	257
H= 1	L= -19	
1	179	181
H= 1	L= -18	
0	182	233
H= 2	L= -1	
1	1242	1152
2	603	587
3	339	333
4	381	374
5	165	151
H= 2	L= -2	
0	585	518
1	276	211
2	676	670
3	575	570
4	194	190
H= 2	L= -3	
1	650	648
3	447	439
4	201	210
6	143	91
7	145	106
H= 2	L= -4	
0	988	994
2	569	574
3	338	364
4	152	158
5	137	174
H= 2	L= -5	
1	929	913
2	167	166
3	232	226
4	153	157
6	206	169
H= 2	L= -6	
0	1315	1243
2	508	487
3	390	402
6	162	154
H= 2	L= -7	
1	956	930
2	127	127
3	321	346
4	194	198
7	189	166
H= 2	L= -8	
0	858	839
1	341	340
2	403	398
3	560	559
5	249	257
6	139	109
H= 2	L= -9	
1	462	443
3	233	199
4	186	190
H= 2	L= -10	
0	877	829
1	221	200
2	357	376
3	318	314
5	187	182
H= 2	L= -11	
1	411	399
2	165	128
3	154	134
4	219	219
6	141	134
H= 2	L= -12	
0	605	599
1	145	170
2	268	272
5	179	163
H= 2	L= -13	
1	440	410
2	248	236
4	154	167
H= 2	L= -14	
0	350	354
1	164	183
2	258	239
3	143	133
H= 2	L= -15	
1	292	304
2	264	299
3	178	183
4	185	170
H= 2	L= -16	
2	170	175
5	214	183
H= 2	L= -17	
1	338	334
H= 2	L= -18	
0	311	334
1	161	132
3	221	210
H= 2	L= -19	
2	166	159
H= 3	L= -1	
1	848	826
2	192	200
4	482	505
6	181	196
H= 3	L= -2	
0	171	170
1	157	190
2	348	341
3	502	513
4	168	185
5	361	369
H= 3	L= -3	
1	424	435
2	480	472
3	302	313
4	460	454
6	176	164
H= 3	L= -4	
0	296	314
1	342	337
2	438	441
3	684	703
4	161	139
5	227	235
H= 3	L= -5	
1	846	841
2	333	345
3	177	167
4	339	354
5	126	141
6	142	156
H= 3	L= -6	
1	318	341
2	399	372
3	516	524

Table 8. Continued.

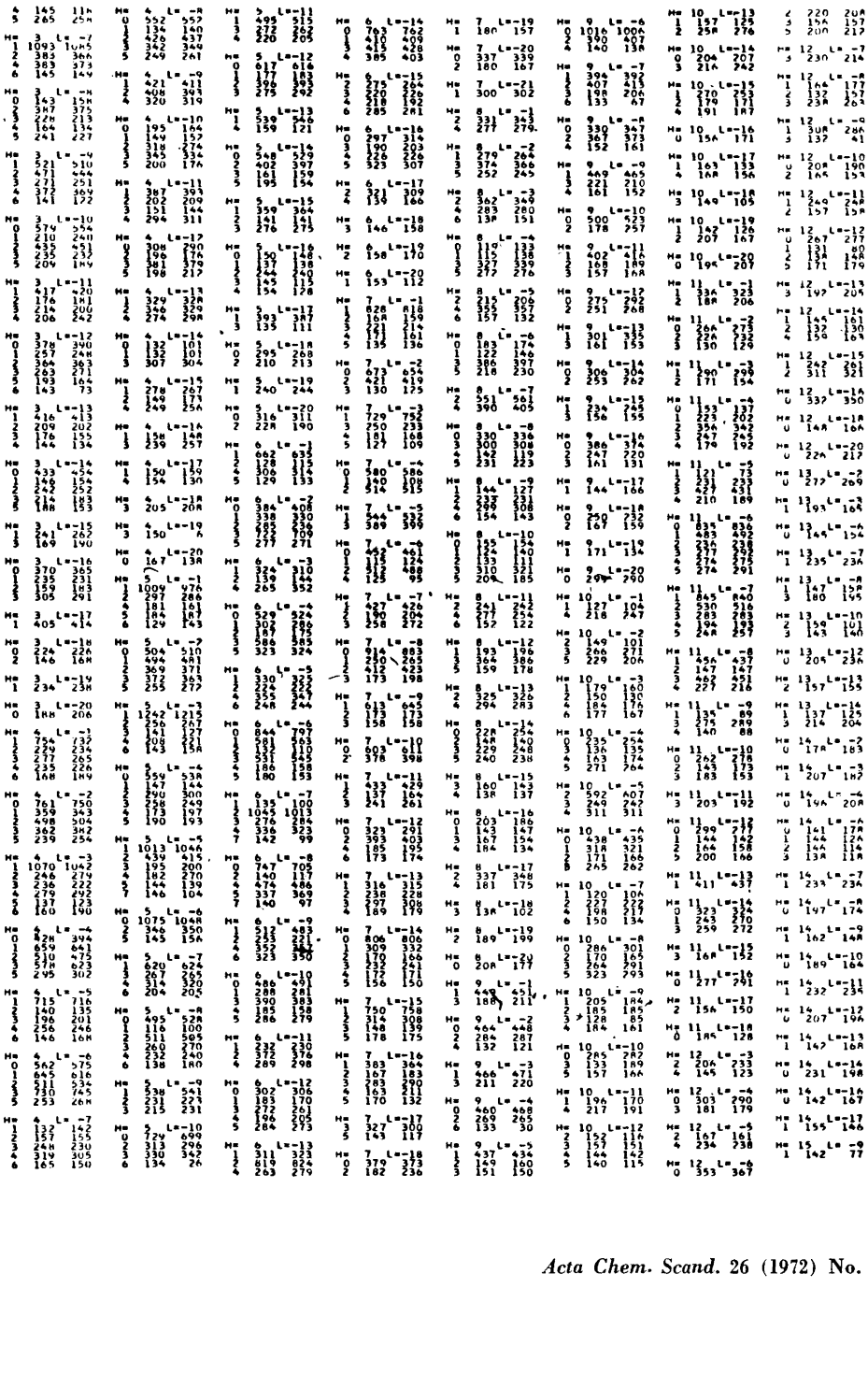

Table 9. Computer programs used for the crystallographic calculations.

Program name and function	Authors
PIRUM. Indexing of powder photographs and least squares refinement of unit cell parameters.	Werner, P.-E.
SIP. Generation of steering paper tape for the SIEMENS AED.	Norrestam, R.
SIMSA. Interpretation of output on paper tape from the SIEMENS AED and evaluation of intensities.	Norrestam, R.
DATA P 2. Lp- and absorption corrections. Preparative calculations for extinction correction.	Coppens P., Leiserowitz, L. & Rabinovich, D. Modified by Olofsson, O., Elfström, M., Brandt, B., Åsbrink, S. & Nord, A.
DATA. Reflection data handling.	Brandt, B.
DRF. Fourier summations and structure factor calculations.	Zalkin, A. Modified by Liminga, R., Lundgren, J.-O., Lindgren, O., Brandt, B. & Nord, A.
LALS. Full matrix least squares refinement of positional and thermal parameters and of scale factors.	Gantzel, P. K., Sparks, R. A. & Trueblood, K. N. Modified by Zalkin, A., Lundgren, J.-O., Liminga, R., Brändén, C.-I., Lindgren, O., Brandt, B. & Nord, A.
DISTAN. Calculation of interatomic distances, and bond angles with estimated standard deviations.	Zalkin, A. Modified by Nord, A. & Brandt, B.
INERT. Calculation of least squares plane and axes of inertia.	Norrestam, R.
ORTEP. Thermal-ellipsoid plot for crystal structure illustrations.	Johnson, C. K. Modified by Carlbom, I.
ACTA. Editing of structure factor tables.	Norrestam, R.
SCF-OPSZDO. Self-consistent field molecular orbital calculations.	Sundbom, M. & Roos, B.

Hughes' [7] weighting scheme was used in all least squares refinements, with $|F_{o,min}| = 10.0$ and $h = 4.0$. The weight analysis obtained in the last cycle is given in Table 2. The positional and thermal parameters (with estimated standard deviations, e.s.d.'s) are given in Tables 3, 4, and 5, intramolecular distances and angles in Tables 6 and 7, and structure factors in Table 8. The atomic labeling is shown in Fig. 2. The computer programs are identified in Table 9; most of the calculations were performed on an IBM-360/75 computer.

DESCRIPTION AND DISCUSSION OF THE STRUCTURE

The molecular packing viewed along the *b* and *c* axes is shown in Figs. 3a and 3b. The crystal structure is built up of an infinite stacking in the [010] direction of almost planar 9-bromo-3,7,8,10-tetramethylisoalloxazine molecules with parallel molecular orientation. The intermolecular distance in the [010] direction is about 3.5 Å, a normal van der Waals separation (usual value 3.5 – 3.7 Å).

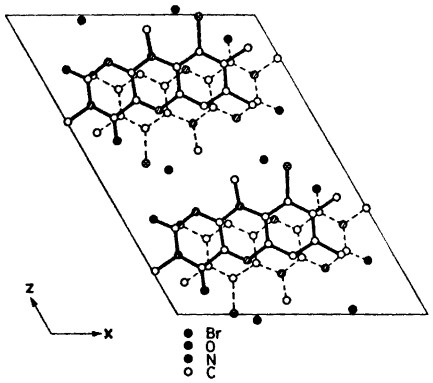

Fig. 3a. A packing diagram, excluding hydrogen atoms, viewed along the *b* axis.

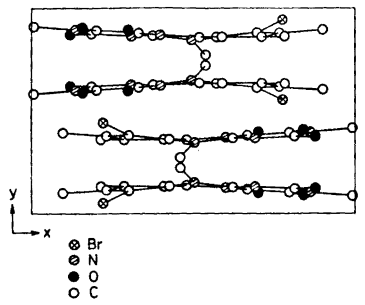

Fig. 3b. A packing diagram, excluding hydrogen atoms, viewed along the *c* axis.

Table 10. Intermolecular distances shorter than 3.6 Å between nonhydrogen atoms and their estimated standard deviations.

Code for symmetry related atoms

Superscript	Atom at			Superscript	Atom at		
None	x	y	z	iii	x	$\frac{3}{2}-y$	$\frac{1}{2}+z$
i	$1-x$	$1-y$	$1-z$	iv	$1-x$	$\frac{1}{2}+y$	$\frac{1}{2}-z$
ii	$1-x$	$-\frac{1}{2}+y$	$\frac{1}{2}-z$	v	$-1+x$	y	z
				vi	$1-x$	$1-y$	$-z$

Br	– O(12 i)	3.177(8) Å
Br	– O(ii)	3.427(11)
N(1)	– O(iii)	3.189(13)
C(2)	– C(17 ii)	3.451(16)
C(4)	– C(8 ii)	3.455(14)
C(4A)	– C(7 ii)	3.569(15)
N(5)	– C(9A ii)	3.500(14)
N(5)	– O	3.130(12)
C(6)	– N(10 ii)	3.585(13)
C(6)	– C(10A iv)	3.516(15)
C(8)	– O(14 iv)	3.576(13)
O(12)	– O(iii)	3.301(13)
C(13)	– C(17 v)	3.577(13)
O(14)	– O	3.103(13)
C(17)	– O(vi)	3.364(14)
C(20)	– O(iv)	3.251(17)

The unit cell contains two molecular stacks related by inversions. Each stack is built up by 9-bromo-3,7,8,10-tetramethylisoalloxazine molecules with alternating orientation, as seen in Fig. 3a. The water molecules, located between the stacks, seem to be involved in several weak hydrogen bonds, linking the flavin molecules together in the [001] direction. Since the positions of the water hydrogens could not be determined it is not possible to draw any firm conclusions regarding the hydrogen bond scheme. The water oxygen forms several contacts less than 3.6 Å (*cf.* Table 10) *viz.* Br – O(ii), N(1) – O(iii), N(5) – O, O(12) – O(iii), O(14) – O, C(17) – O(vi), and C(20) – O(iv). Of these, the first five ranging from 3.10 to 3.43 Å, might be caused by hydrogen bonds. Since the 9-bromo-3,7,8,10-tetramethylisoalloxazine molecule has no suitable donors to hydrogen bonds, the water molecule might serve as a donor to weak hydrogen bonds. Judging from the distances 3.13 and 3.10 Å, respectively, it is likely that the water molecule forms hydrogen bonds (possibly bifurcated) at least to the atoms N(5) and O(14) of the flavin molecule. It is interesting to note that this position of the water molecule relative to the flavin nucleus is the same as that suggested for metal ions in metal flavin complexes from spectroscopical investigations (see, *e.g.*, Hemmerich and Spence [8]). The lack of strong intermolecular contacts of the water molecule is probably the cause of the large temperature vibrations of the water oxygen and the problems of locating its hydrogens.

Apart from the contacts in the [001] direction involving the water molecule given above, there is one remarkably short intermolecular distance, 3.18 Å, between a bromine of one flavin molecule and a keto oxygen, O(12), of another. The occurrence of this short contact might be the reason that no strong hydrogen bonds are formed in the crystal structure, *viz.* if the observed packing is energetically favourable as compared with different packings which allow stronger hydrogen bonds. The shortest intermolecular distance in the [100] direction is 3.58 Å, a resonable van der Waals contact in this direction.

As seen in Fig. 3b the isoalloxazine ring system of the flavin molecule is almost planar and the major deviations from planarity is obtained for the atoms C(20) and Br. Least squares planes calculated through the individual rings of the flavin molecule are given in Table 11. The angle between the normals of the benzenoid and pyrazinoid rings is 7.0°, and the angle between the normals of the pyrazinoid and pyrimidinoid rings is 1.0°. The angle between the planes of the benzenoid and pyrazinoid rings arises from a slight twist of the isoalloxazine ring, attributable to repulsive forces between the bromine atom and the methyl group attached to N(10). Thus the Br – C(20) distance becomes 3.04 Å, equal to the Br – C(18) distance of 3.03 Å. The conclusion that the observed distortion of the isoalloxazine ring in the present study is caused by overcrowding effects (due to the 9-bromo-substitution of the benzenoid ring) is supported by details of the crystal structure of 3-methyl-lumiflavin [9] determined at this Institute.

In Table 12 the intramolecular bond distances found in the present study are compared with those obtained from self-consistent field molecular orbital calculations of the Pariser-Parr-Pople (PPP) type. The molecular orbitals have been evaluated by means of a computer program kindly put at our disposal by Marianne Sundbom (Institute of Theoretical Physics, University of Stock-

Table 11. Deviations of the atoms from least squares planes. The planes are defined by $Ax+By+Cz=D$, where x,y,z are in Å units along 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	Plane III	Atom	Deviation
A = −0.0235	N(1)	0.038 Å	A = −0.0546	C(4A)	−0.032 Å
B = 0.9996	C(2)	0.005	B = 0.9981	N(5)	0.027
C = −0.0156	N(3)	−0.100	C = −0.0302	C(5A	0.022
D = 4.2691 Å	C(4)	−0.078	D = 4.1291 Å	C(9A)	−0.065
	C(4A)	−0.024		N(10)	0.062
	N(5)	0.043		C(10A)	−0.015
	C(5A)	0.083		N(1)*	0.003
	C(6)	0.067		C(4)*	−0.037
	C(7)	0.033		C(6)*	−0.002
	C(8)	−0.129		C(9)*	−0.292
	C(9)	−0.149		C(20)*	0.483
	C(9A)	0.033			
	N(10)	0.150			
	C(10A)	0.028			
	O(12)*	0.022			
	C(13)*	−0.177			
	O(14)*	−0.152			
	C(17)*	0.024			
	C(18)*	−0.270			
	C(20)*	0.606			
	Br*	−0.622			
	O*	−0.067			

Plane II	Atom	Deviation	Plane IV	Atom	Deviation
A = −0.0603	N(1)	−0.004 Å	A = 0.0504	C(5A)	−0.014 Å
B = 0.9970	C(2)	0.019	B = 0.9982	C(6)	−0.029
C = −0.0483	N(3)	−0.023	C = 0.0339	C(7)	0.042
D = 4.0370 Å	C(4)	0.010	D = 4.8325 Å	C(8)	−0.011
	C(4A)	0.004		C(9)	−0.031
	C(10A)	−0.007		C(9A)	0.043
	O(12)*	0.032		N(5)*	−0.164
	C(13)*	−0.042		N(10)*	0.152
	O(14)*	−0.010		C(17)*	0.029
	N(5)*	0.078		C(18)*	−0.036
	N(10)*	0.060		Br*	−0.358

holm). The input atomic coordinates used were derived from those obtained in the present study by assuming a strictly planar conformation of the molecule. The other input parameters used were chosen in accordance with those suggested by Roos and Skancke,[10] Roos,[11] Fischer-Hjalmars and Sundbom,[12] and Jensen and Skancke.[13] The bond lengths were derived from bond order-bond length correlations, *viz.*

$$R_{CC} = 1.517 - 0.180\, p_{CC}$$
$$R_{CN} = 1.458 - 0.180\, p_{CN}$$
$$R_{CO} = 1.365 - 0.180\, p_{CO}$$

Table 12. Calculated π-bond orders with corresponding bond lengths compared with those obtained in the present study.

	π-b. o.	d_{calc}	d_{obs}
N(1) – C(2)	0.42	1.383 Å	1.385 Å
C(2) – N(3)	0.44	1.380	1.387
N(3) – C(4)	0.50	1.368	1.376
C(4) – C(4A)	0.27	1.468	1.487
C(4A) – N(5)	0.82	1.311	1.295
N(5) – C(5A)	0.44	1.379	1.382
C(5A) – C(6)	0.57	1.415	1.403
C(6) – C(7)	0.72	1.388	1.371
C(7) – C(8)	0.60	1.409	1.415
C(8) – C(9)	0.65	1.399	1.411
C(9) – C(9A)	0.58	1.413	1.416
C(9A) – C(5A)	0.59	1.411	1.418
C(9A) – N(10)	0.37	1.391	1.418
N(10) – C(10A)	0.41	1.384	1.363
C(4A) – C(10A)	0.36	1.453	1.438
C(10A) – N(1)	0.77	1.319	1.325
C(2) – O(12)	0.68	1.243	1.224
N(3) – C(13)	0.05	1.449	1.473
C(4) – O(14)	0.68	1.242	1.212
C(7) – C(17)	0.14	1.492	1.506
C(8) – C(18)	0.17	1.486	1.516
N(10) – C(20)	0.05	1.449	1.479

where p is the calculated π-bond order and R the corresponding bond length.

The agreement between the distances found in the crystal structure and those obtained from the molecular orbital calculations is encouraging; the differences among the endocyclic bonds are all less than 0.03 Å, well below three times the estimated standard deviations of the corresponding bond lengths. The main features of the evaluated π-bond order scheme are in accordance with the commonly accepted bonding scheme for an oxidized flavin derivative as given in Fig. 1. Thus the highest π-bond orders within the ring system are those between C(4a) – N(5) (0.82) and N(1) – C(10A) (0.77). It is obvious that both oxygens O(12) and O(14) attached to the pyrimidinoid ring are of keto type.

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