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Studies on Flavin Derivatives. The Crystal and Molecular Structure of a Charge Transfer Complex Between Lumiflavinium Bromide and Hydroquinone

By Ove Tillberg and Rolf Norrestam

Institute of Inorganic and Physical Chemistry, University of Stockholm, S-104 05 *Stockholm, Sweden*

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The crystal structure of a compound consisting of lumiflavinium bromide and hydroquinone in a 2:3 ratio, $C_{22}H_{22}BrN_4O_5$ (space group $P2_1/c$ with $a=8{\cdot}32$, $b=20{\cdot}712$, $c=12{\cdot}400$ Å and $\beta=90{\cdot}22°$), an example of a 1:1 charge transfer complex involving a protonated oxidized flavin derivative, has been determined from three-dimensional X-ray diffractometer data. In the crystal structure an infinite stacking of alternating parallel lumiflavinium and hydroquinone molecules with a molecular plane separation of about 3·3 Å occurs. The molecular stacking shows a new type of charge transfer interaction involving flavinium ions, characterized by the fact that both the benzenoid and the pyrimidinoid rings of the same flavinium molecule participate in the charge transfer complex formation. The observed geometries of the hydroquinone molecules suggest a slight change of the hydroquinone conformation due to charge transfer bonding.

Introduction

According to the observation initially made by Szent-Györgi (1960), molecular complexes of the charge transfer type may be common in biological systems. For a recent review on organic charge transfer complexes see Foster (1969). A charge transfer interaction implies partial oxidation or reduction. Since flavins act as redox prosthetic groups in various widely occuring respiratory enzymes, the role of charge transfer interactions involving flavins has received considerable attention. The role of charge transfer complexes in flavin biochemistry has been discussed *inter alia* by Kosower (1966). The spectral, electrical and magnetic properties of molecular complexes between protonated flavin derivatives and phenols have been investigated by Fleischman & Tollin (1965). They showed that molecular charge transfer complexes occurred and also that observable concentrations of free radicals of the flavin semiquinone type were formed.

The present structural investigation of the complex between lumiflavinium bromide (Fig. 1) and hydroquinone has been undertaken as part of a current research project concerning structural studies of model compounds relevant to flavin biochemistry. A survey of hitherto investigated flavin compounds within this project is given by Kierkegaard *et al.* (1971).

Experimental

A blackish crystalline specimen of the molecular complex between lumiflavinium bromide and hydroquinone was kindly supplied by G. Eriksson (Institute of Biophysics, University of Stockholm). The crystals were examined by X-ray photographic methods (Guinier, oscillation and Weissenberg techniques). The photographs indicated monoclinic symmetry and the systematic absences among the X-ray reflexions were consistent with the space group $P2_1/c$. The crystal finally selected had the dimensions $0{\cdot}09\times0{\cdot}12\times0{\cdot}12$ mm and was mounted on a goniometer head along a prismatic axis parallel to the monoclinic *b* axis. The cell parameters were refined by least squares from diffractometer measurements with Cu *Kα* radiation (1·54184 Å).

Crystal data

Composition of asymmetric unit: $C_{22}H_{22}BrN_4O_5$,
$a=8{\cdot}32$ (1), $b=20{\cdot}712$ (5), $c=12{\cdot}400$ (5) Å,
$V_o=2136{\cdot}8$ Å^3, $D_m=1{\cdot}55$ g.cm^{-3}, $D_c=1{\cdot}56$ g.cm^{-3}
$Z=4$,
Linear absorption coefficient $=31{\cdot}6$ cm^{-1}.
Space group $P2_1/c$.

Three-dimensional X-ray intensity data were collected on a Siemens AED single-crystal diffractometer with Ni-filtered Cu *K* radiation and a scintillation detector. The pulse height discriminator was set to accept about 90% of the characteristic Cu *Kα* radiation. The (approximately 3600) intensities within $\theta<65°$ were measured with the *ω–2θ* scan technique (scan

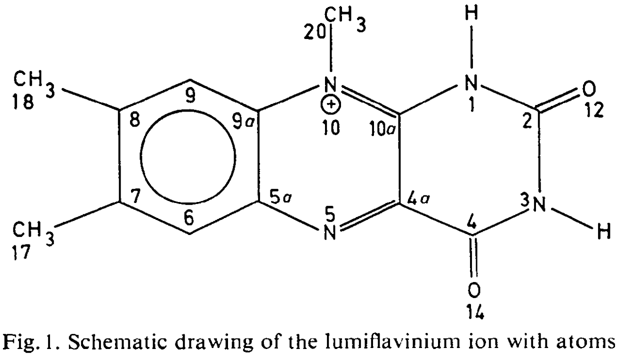


Fig. 1. Schematic drawing of the lumiflavinium ion with atoms numbered for reference in the text.

interval 1·2°) and the background intensity was calculated as the average of the intensities measured at each end of the scan. The 3269 reflexions for which $\sigma(I_{\rm net})/I_{\rm net} < 0{\cdot}25$, were used in the subsequent calculations. The calculations of $\sigma(I_{\rm net})$ was based on conventional counter statistics. The net intensities were corrected for Lorentz, polarization and absorption effects (the transmission factors varied between 0·48 and 0·61).

Structure determination and refinement

The crystal structure was determined by $\sum_1$ and $\sum_2$ direct methods (Hauptman & Karle, 1953). The statistical averages and distributions of the derived normalized structure factors, the $|E|$-values, are given in Table 1.

Table 1. *Statistical averages and distributions of normalized structure factors*

	Experimental	Theoretical (centric)
$\langle \lvert E\rvert \rangle$	0·84	0·798
$\langle \lvert E\rvert^2-1\rangle$	0·87	0·968
$\langle \lvert E\rvert \rangle^2$	1·00	1·000
$\lvert E\rvert > 1$	33·4%	32·0%
$\lvert E\rvert > 2$	3·7%	5·0%
$\lvert E\rvert > 3$	0·2%	0·3%

From the 243 highest $|E|$ values ($|E|$ greater than 1·7), the 934 best triple-product sign-relationships (probabilities greater than 0·985) were derived. Very high $|E|$-values, 3·1 and 2·9, were obtained for the reflexions 480 and 240 respectively. From the simplest sign-relationship of the so called $\sum_1$ type it followed that the sign of 480 was probably positive. By the same argument it followed that the sign of 240 was probably negative, since the reflexion 120 is a very weak one.

To specify the origin in the space group $P2_1/c$ the signs of three properly selected reflexions can be arbitrarily given. The selection of these three reflexions followed a computerized procedure described by Norrestam (1971) to avoid introducing more unknown signs in the basis set than necessary. Thus the signs of the reflexions 6,11,0, $2,17,\bar{3}$ and 1,11,4 were used for origin specification. Together with these three reflexions the reflexions 480 and 240 were used as the basis set for solving the triple relations. The solution yielded the signs of 236 out of the 243 reflexions used for generating the triple relations. After the completion of this structure investigation it was shown that all of the 236 signs were correct. Thus it can be stated that although the present structure can be solved by a straightforward application of the heavy atom technique, direct methods provide a faster and more efficient method of solution.

The E map based on the 236 signed $|E|$ values revealed the position of the bromine atom and of the remaining 31 highest peaks in the map 26 made chemical sense and were tentatively used as non-hydrogen positions. After a few cycles of full-matrix least-squares refinement of the achieved structural model, followed by a difference electron density calculation, the remaining 5 non-hydrogen atoms were located. A subsequent least-squares refinement of the structural parameters, using only the 1184 reflexions with $\sin\theta/\lambda$ less than 0·40, gave an R value ($R=\sum \lvert F_{\rm obs}\rvert-\lvert F_{\rm calc}\rvert / \sum \lvert F_{\rm obs}\rvert$) of 0·087, when the bromine atom was allowed to vibrate anisotropically while the thermal vibrations of the rest of the non-hydrogen atoms were kept isotropic. Upon introduction of anisotropic thermal parameters for all the non-hydrogen atoms, refinement versus the same reflexions as above lowered the R value to 0·073. The resultant structural parameters were used for the calculation of a difference electron density map based on all the 3269 reflexions ($R=$ 0·089). This calculation revealed the locations of 14 of the 22 hydrogen atoms. Another difference electron density calculation, involving these 14 hydrogen atoms, gave reasonable positions for 5 more hydrogen atoms. However, there was no possibility of locating the remaining three hydrogen atoms (all bonded to the oxygen atoms of the hydroquinone molecules). Due to the presence of the fairly 'heavy' bromine atom in the structure, it was considered reasonable to refine only the positions of the hydrogen atoms with isotropic temperature factors held at 6 Å².

Table 2. *Fractional atomic coordinates for non-hydrogen atoms* (× 10⁴).

Estimated standard deviations are given in parertheses.

	x	y	z
Br	276 (1)	1170 (0)	1742 (0)
N(1)	7713 (6)	2457 (2)	3361 (4)
C(2)	6695 (7)	1950 (3)	3158 (4)
N(3)	6334 (6)	1819 (2)	2107 (3)
C(4)	7007 (6)	2116 (3)	1238 (4)
C(4*a*)	8114 (6)	2652 (3)	1488 (4)
N(5)	8760 (6)	2956 (2)	678 (3)
C(5*a*)	9688 (7)	3479 (3)	895 (4)
C(6)	10395 (7)	3807 (3)	35 (5)
C(7)	11424 (7)	4318 (3)	202 (4)
C(8)	11685 (7)	4536 (3)	1277 (5)
C(9)	10973 (7)	4223 (3)	2127 (5)
C(9*a*)	9996 (7)	3686 (3)	1954 (4)
N(10)	9306 (6)	3331 (2)	2800 (3)
C(10*a*)	8395 (7)	2823 (3)	2573 (4)
O(12)	6105 (5)	1644 (2)	3888 (3)
O(14)	6681 (5)	1951 (2)	319 (3)
C(17)	12252 (11)	4636 (4)	−729 (4)
C(18)	12794 (12)	5093 (4)	1494 (4)
C(20)	9642 (10)	3510 (4)	3938 (5)
C′(1)	2934 (8)	2664 (3)	2729 (5)
C′(2)	3849 (8)	3115 (3)	3263 (6)
C′(3)	4820 (8)	3534 (3)	2669 (5)
C′(4)	4846 (7)	3492 (3)	1555 (5)
C′(5)	3902 (8)	3047 (3)	1034 (5)
C′(6)	2956 (8)	2634 (3)	1617 (5)
O′(1)	1973 (6)	2258 (2)	3337 (4)
O′(4)	5832 (6)	3910 (2)	992 (4)
C″(1)	4530 (8)	427 (3)	784 (5)
C″(2)	6123 (8)	343 (3)	573 (5)
C″(3)	6621 (7)	−79 (3)	−238 (5)
O″(1)	4105 (5)	861 (2)	1592 (4)

Table 3. *Anisotropic thermal parameters* ($\times 10^4$)

Estimated standard deviations are given in parentheses. The temperature factor expression used was $\exp[-(h^2b_{11}+k^2b_{22}+l^2b_{33}+hkb_{12}+hlb_{13}+klb_{23})]$

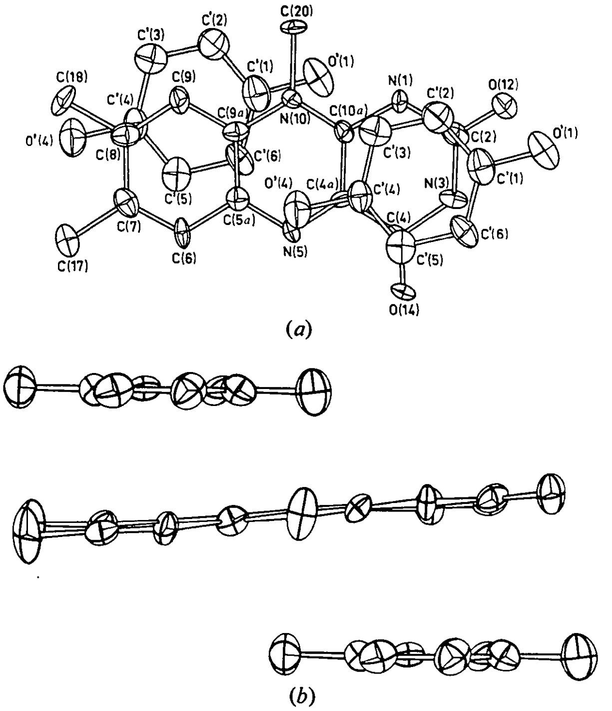
	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
Br	101 (1)	26 (0)	61 (0)	7 (1)	−1 (1)	11 (0)
N(1)	106 (8)	17 (1)	22 (3)	−17 (6)	12 (9)	−3 (3)
C(2)	98 (10)	15 (2)	26 (4)	2 (7)	2 (10)	−3 (4)
N(3)	67 (7)	13 (1)	32 (3)	7 (5)	30 (8)	−5 (3)
C(4)	66 (9)	12 (1)	28 (4)	6 (6)	10 (9)	3 (4)
C(4*a*)	74 (8)	14 (1)	19 (3)	2 (6)	19 (9)	1 (4)
N(5)	76 (7)	15 (1)	28 (3)	−5 (5)	11 (8)	0 (3)
C(5*a*)	86 (9)	13 (1)	29 (4)	5 (6)	−9 (10)	−3 (4)
C(6)	87 (9)	13 (1)	38 (4)	4 (6)	13 (10)	−1 (4)
C(7)	86 (9)	18 (2)	42 (4)	2 (7)	19 (10)	0 (4)
C(8)	90 (9)	16 (2)	47 (4)	−2 (7)	18 (11)	−3 (4)
C(9)	95 (10)	17 (2)	37 (4)	−9 (7)	18 (11)	−12 (4)
C(9*a*)	81 (9)	15 (2)	26 (4)	8 (6)	26 (9)	−1 (4)
N(10)	89 (7)	15 (1)	29 (3)	−4 (5)	3 (8)	−12 (3)
C(10*a*)	73 (9)	14 (1)	23 (4)	6 (6)	17 (9)	−1 (4)
O(12)	137 (7)	20 (1)	34 (3)	−17 (5)	34 (8)	3 (3)
O(14)	114 (7)	18 (1)	22 (3)	−12 (4)	3 (7)	−5 (2)
C(17)	158 (14)	25 (2)	46 (5)	−41 (9)	25 (13)	15 (5)
C(18)	169 (17)	21 (2)	77 (6)	−57 (9)	28 (17)	−10 (6)
C(20)	128 (12)	31 (2)	26 (4)	−54 (9)	31 (12)	−17 (5)
C′(1)	101 (11)	21 (2)	64 (5)	13 (8)	14 (12)	18 (5)
C′(2)	105 (11)	28 (2)	48 (5)	14 (8)	15 (12)	10 (5)
C′(3)	98 (11)	25 (2)	58 (5)	14 (8)	4 (12)	−6 (5)
C′(4)	102 (10)	18 (2)	55 (5)	18 (7)	38 (12)	3 (5)
C′(5)	109 (11)	19 (2)	45 (5)	28 (7)	8 (12)	−3 (5)
C′(6)	93 (10)	20 (2)	49 (5)	−5 (7)	27 (11)	5 (5)
O′(1)	195 (10)	31 (1)	68 (4)	−15 (7)	52 (10)	29 (4)
O′(4)	140 (8)	22 (1)	83 (4)	−22 (5)	91 (9)	4 (4)
C″(1)	124 (11)	17 (2)	45 (4)	0 (7)	0 (11)	−16 (4)
C″(2)	108 (12)	22 (2)	65 (5)	2 (7)	−11 (12)	−25 (5)
C″(3)	70 (10)	19 (2)	67 (5)	−3 (7)	15 (11)	−23 (5)
O″(1)	116 (7)	27 (1)	79 (3)	−16 (5)	55 (9)	−51 (4)

Table 4. *Fractional atomic coordinates for hydrogen atoms* ($\times 10^3$)

Estimated standard deviations are given in parentheses.

H(1)	796 (12)	247 (5)	391 (7)
H(3)	558 (12)	145 (4)	196 (7)
H(6)	015 (11)	130 (4)	433 (7)
H(9)	107 (11)	437 (4)	287 (7)
H(17*a*)	1190 (11)	513 (5)	−73 (6)
H(17*b*)	1354 (13)	461 (4)	−70 (7)
H(17*c*)	1187 (12)	449 (4)	−131 (8)
H(18*a*)	1245 (11)	513 (4)	246 (7)
H(18*b*)	1381 (13)	511 (4)	127 (7)
H(18*c*)	1221 (14)	534 (5)	134 (9)
H(20*a*)	867 (13)	352 (5)	418 (7)
H(20*b*)	975 (12)	312 (5)	438 (8)
H(20*c*)	1075 (13)	367 (4)	394 (7)
H′(2)	388 (11)	299 (4)	407 (8)
H′(3)	568 (11)	398 (4)	303 (6)
H′(5)	363 (11)	301 (4)	32 (7)
H′(6)	273 (12)	240 (4)	115 (7)
H″(2)	735 (11)	61 (4)	89 (6)
H″(3)	759 (11)	−14 (4)	−33 (6)

Thus, the final refinement included all the 32 non-hydrogen positions and anisotropic temperature factors together with the positional parameters for the 19 hydrogen atoms. This refinement was carried out for two cycles using all the 3269 reflexions and gave an R value of 0·069. It was observed that the large observed structure factors were considerably weaker than



(*a*)

(*b*)

Fig. 2. Part of the stacking sequence of alternating lumiflavinium and hydroquinone molecules, viewed perpendicular (*a*) and parallel (*b*) to the molecular planes.

the calculated ones at low sin θ/λ, suggestive of extinction. To reduce the effect of extinction, two more cycles of full-matrix least-squares refinement were performed using only the 3076 reflexions with sin θ/λ greater than 0·2, to yield an R value of 0·062. All the parameter shifts in the last cycle were well below the estimated standard deviations. The difference electron density map based on the final parameters did not reveal the positions of the three remaining hydrogen atoms bonded to the oxygen atoms of the hydroquinones.

Final coordinates and temperature factors are listed in Tables 2, 3 and 4. The atomic labels used are shown in Fig. 2. The bond distances and angles together with their estimated standard deviations are also listed in Tables 5, 6 and 7. No corrections for thermal vibration have been made.

The atomic scattering factors used for carbon, nitrogen and oxygen are those given by Hanson, Herman, Lea & Skillman (1964), for hydrogen that given by Stewart, Davidson & Simpson (1965) and for bromine that given by Cromer & Waber (1965). The real parts of the anomalous dispersion corrections, as given by Cromer (1965), were applied to the atomic scattering factors. In all the least-squares refinements the weights were calculated according to Hughes (1941), using $|F_{\text{obs, min}}| = 15{\cdot}0$.

Table 5. *Intramolecular bond distances within the lumiflavin molecule*

Estimated standard deviations are given in paretheses.

N(1)—C(2)	1·372 (8) Å
C(2)—N(3)	1·363 (7)
N(3)—C(4)	1·364 (7)
C(4)—C(4*a*)	1·474 (8)
C(4*a*)—N(5)	1·304 (7)
N(5)—C(5*a*)	1·356 (7)
C(5*a*)—C(6)	1·396 (8)
C(6)—C(7)	1·376 (8)
C(7)—C(8)	1·423 (8)
C(8)—C(9)	1·375 (8)
C(9)—C(9*a*)	1·394 (8)
C(9*a*)—C(5*a*)	1·404 (7)
C(9*a*)—N(10)	1·405 (7)
N(10)—C(10*a*)	1·326 (7)
C(10*a*)-C(4*a*)	1·410 (7)
C(10*a*)-N(1)	1·363 (7)
C(2)—O(12)	1·211 (7)
C(4)—O(14)	1·219 (6)
C(7)—C(17)	1·499 (10)
C(8)—C(18)	1·499 (11)
N(10)—C(20)	1·484 (8)
N(1)—H(1)	0·71 (10)
N(3)—H(3)	1·01 (9)
C(6)—H(6)	0·93 (9)
C(17)—H(17*a*)	1·07 (10)
C(17)—H(17*b*)	1·07 (11)
C(17)—H(17*c*)	0·84 (10)
C(18)—H(18*a*)	1·23 (9)
C(18)—H(18*b*)	0·89 (10)
C(18)—H(18*c*)	0·73 (11)
C(9)—H(9)	0·97 (9)
C(20)—H(20*a*)	0·86 (11)
C(20)—H(20*b*)	0·98 (10)
C(20)—H(20*c*)	0·98 (11)

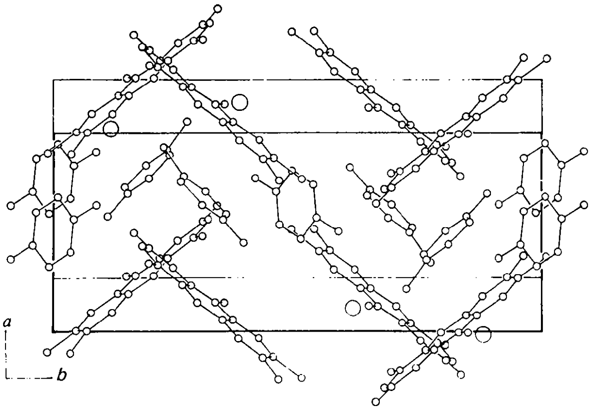


Fig. 3. A packing diagram, excluding hydrogen atoms, viewed perpendicular to the b axis. The a axis has been rotated 10° out of the plane of the paper.

Description and discussion of the structure

The crystal structure viewed along the c axis is shown in Fig. 3. The packing of the molecules along the [120] and [$\bar{1}$20] directions consists of an infinite stacking of alternating lumiflavinium and hydroquinone molecules, with parallel molecular orientations. In Fig. 2 parts of the molecular arrangement of the stacking sequence are shown. The molecular separations be-

Table 6. *Intramolecular bond angles within the lumiflavin molecule*

Only bonds involving non-hydrogen atoms are listed. Estimated standard deviations are given in parentheses.

C(10*a*)-N(1)—C(2)	123·6 (5)°
N(1)—C(2)—O(12)	121·0 (5)
N(1)—C(2)—N(3)	117·5 (5)
O(12)—C(2)—N(3)	121·5 (5)
C(2)—N(3)—C(4)	125·2 (5)
N(3)—C(4)—O(14)	121·5 (5)
N(3)—C(4)—C(4*a*)	115·6 (4)
O(14)—C(4)—C(4*a*)	123·0 (5)
C(4)—C(4*a*)—C(10*a*)	119·4 (5)
C(4)—C(4*a*)—N(5)	117·5 (4)
C(10*a*)-C(4*a*)—N(5)	123·1 (5)
C(4*a*)—N(5)—C(5*a*)	118·1 (4)
N(5)—C(5*a*)—C(9*a*)	122·0 (5)
N(5)—C(5*a*)—C(6)	118·6 (5)
C(9*a*)—C(5*a*)—C(6)	119·3 (5)
C(5*a*)—C(6)—C(7)	121·6 (5)
C(6)—C(7)—C(17)	120·6 (6)
C(6)—C(7)—C(8)	118·6 (5)
C(8)—C(7)—C(17)	120·8 (6)
C(7)—C(8)—C(9)	120·2 (6)
C(7)—C(8)—C(18)	120·3 (6)
C(18)—C(8)—C(9)	119·4 (6)
C(8)—C(9)—C(9*a*)	120·8 (5)
C(9)—C(9*a*)—C(5*a*)	119·5 (5)
C(9)—C(9*a*)—N(10)	122·8 (5)
C(5*a*)—C(9*a*)—N(10)	117·7 (5)
C(9*a*)—N(10)—C(10*a*)	119·4 (4)
C(9*a*)—N(10)—C(20)	120·2 (5)
C(20)—N(10)—C(10*a*)	120·3 (5)
N(10)—C(10*a*)-C(4*a*)	119·5 (5)
N(10)—C(10*a*)-N(1)	121·9 (5)
C(4*a*)—C(10*a*)-N(1)	118·5 (5)

tween the lumiflavinium ions and the hydroquinones are about 3·3 Å (Table 8) while the usual van der Waals distance is 3·5–3·7 Å. This is consistent with the hypothesis that charge-transfer interactions (Foster, 1969), caused by overlap of the π-orbitals in the lumiflavinium and hydroquinone molecules, are present within the molecular stacking in the crystal structure.

Table 7. *Intramolecular bond distances and angles within the hydroquinone molecules*

Estimated standard deviations are given in parentheses.

C'(1)–C'(2)	1·375 (10) Å
C'(2)–C'(3)	1·397 (10)
C'(3)–C'(4)	1·385 (9)
C'(4)–C'(5)	1·371 (9)
C'(5)–C'(6)	1·371 (9)
C'(6)–C'(1)	1·380 (9)
C'(1)–O'(1)	1·385 (8)
C'(4)–O'(4)	1·383 (8)
C'(2)–H'(2)	1·04 (9)
C'(3)–H'(3)	1·25 (9)
C'(5)–H'(5)	0·92 (9)
C'(6)–H'(6)	0·72 (9)
C''(1)–C''(2)	1·363 (10)
C''(2)–C''(3)	1·397 (9)
C''(3)–C''(1$^{\mathrm{vi}}$)	1·374 (9)
C''(1)–O''(1)	1·393 (7)
C''(2)–H''(2)	1·23 (9)
C''(3)–H''(3)	0·82 (10)
C'(1)—C'(2)–C'(3)	119·2 (6)°
C'(2)—C'(3)–C'(4)	119·9 (6)
C'(3)—C'(4)–C'(5)	120·1 (6)
C'(3)—C'(4)–O'(4)	118·5 (6)
O'(4)—C'(4)–C'(5)	121·5 (6)
C'(4)—C'(5)–C'(6)	120·0 (6)
C'(5)—C'(6)–C'(1)	120·6 (6)
C'(6)—C'(1)–C'(2)	120·2 (6)
C'(6)—C'(1)–O'(1)	121·8 (6)
O'(1)—C'(1)–C'(2)	118·1 (6)
C''(1)—C''(2)–C''(3)	120·7 (6)
C''(2)—C''(3)–C''(1$^{\mathrm{vi}}$)	118·3 (6)
C''(3$^{\mathrm{vi}}$)–C''(1)–C''(2)	121·0 (6)
C''(3$^{\mathrm{vi}}$)–C''(1)–O''(1)	120·9 (6)
O''(1)—C''(1)–C''(2)	118·1 (6)

Only $\frac{2}{3}$ of the hydroquinones are involved in the assumed charge-transfer interactions. The remaining $\frac{1}{3}$ of the hydroquinones acts merely in hydrogen bonding.

The ability of phenolic compounds to form charge-transfer complexes with flavins provides support for an interpretation of the binding of flavin to some proteins, and since such interactions are expected to change the redox properties of flavins they may play a role in catalytic processes involving flavoenzymes. Fleischman & Tollin (1965) have also discussed the possibility that charge-transfer reactions are involved in the catalytic processes.

As shown in Fig. 2 both the pyrimidinoid and the benzenoid rings of the same lumiflavinium molecule are involved in charge-transfer interactions with two different hydroquinones on opposite sides of the molecular plane of the flavinium ion.

Table 8. *Intermolecular distances less than* 3·4 Å *between non-hydrogen atoms*

Estimated standard deviations are given in parentheses.

Code for symmetry related atoms

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

Br——O'(1)	3·310 (5)
Br——O''(1)	3·254 (6)
N(1)—N(5$^{\mathrm{ii}}$)	3·119 (6)
N(1)—O(14$^{\mathrm{ii}}$)	2·855 (6)
N(5)—O(12$^{\mathrm{iii}}$)	3·233 (6)
O(12)—C(18$^{\mathrm{v}}$)	3·376 (9)
C(20)—O(14$^{\mathrm{ii}}$)	3·153 (9)
N(1)—C'(3)	3·389 (9)
C(2)—C'(2)	3·384 (9)
N(3)—C'(6)	3·332 (9)
C(4)—C'(4)	3·393 (8)
C(4)—C'(5)	3·232 (9)
C(4*a*)—C'(4)	3·230 (9)
C(4*a*)—O'(4)	3·281 (7)
N(5)—O'(4)	3·161 (7)
C(5*a*)—O'(4)	3·333 (8)
C(5*a*)—C'(6$^{\mathrm{i}}$)	3·352 (9)
C(6)—O'(1$^{\mathrm{iv}}$)	3·324 (8)
C(9*a*)—C'(1$^{\mathrm{i}}$)	3·371 (9)
C(9*a*)—C'(6$^{\mathrm{i}}$)	3·315 (9)
N(10)—C'(1$^{\mathrm{i}}$)	3·322 (9)
N(10)—O'(1$^{\mathrm{i}}$)	3·209 (7)
C(10*a*)–C'(3)	3·321 (9)
C(10*a*)–O'(1$^{\mathrm{i}}$)	3·333 (8)
O(12)—C'(5$^{\mathrm{ii}}$)	3·299 (8)
O(12)—O'(4$^{\mathrm{ii}}$)	2·859 (6)
O(14)—C'(5)	3·362 (8)
C(20)—O'(1$^{\mathrm{i}}$)	3·325 (10)
N(3)—O''(1)	2·789 (7)
O(14)—C''(2)	3·378 (8)

In the crystal structure of the complex between lumiflavinium chloride and hydroquinone, recently determined by Karlsson (1971), only the benzenoid ring appears to be involved in a weaker charge transfer interaction with hydroquinone, with an intermolecular separation of 3·49 Å. In this crystal structure the molecules are associated in pairs separated by usual van der Waals forces. The same kind of molecular pairing has been observed by Langhoff & Fritchie (1970) for the complex between 10-methylisoalloxazinium bromide and naphthalene-2,7-diol (intermolecular separation not given). In the complex between riboflavin and hydroquinone (Bear, Waters & Waters, 1970), two different kinds of molecular pairs have been reported. In one of these pairs interactions occur between the benzenoid ring and hydroquinone and in the other between the pyrimidinoid ring and hydroquinone. The intermolecular separations found in this structure are about 3·3 Å. However, since Bear, Waters & Waters claim that the isoalloxazine nucleus of riboflavin is doubly protonated [at N(1) and N(5)], it is doubtful whether a comparison with the present structure is relevant, especially since no information on the intramolecular bond scheme is given.

Thus it seems that the present flavin hydroquinone compound represents a new type of charge transfer complex involving flavins, characterized by the fact that both the benzenoid and the pyrimidinoid part of the same flavin nucleus are involved in the interactions.

The parallel arrangement of alternating lumiflavinium and hydroquinone molecules in infinite stacks in the present structure is held together by an extensive network of hydrogen bonds involving all of the species of the structure. From Fig. 3 it is seen that there are two differently orientated hydroquinone molecules. Only one of these is involved in the assumed charge transfer arrangement discussed above. The other hydroquinone acts only as a supplier of hydrogen bonds in the structure. Thus each of the oxygen atoms, O″(1) of the hydroquinones not involved in charge transfer interactions is an acceptor in one hydrogen bond from the nitrogen atom N(3) of the lumiflavinium ion and a donor to one presumed hydrogen bond to the bromine atom. In the N(3)–H(3)$\cdots$O″(1) bond, the bond angle is 178 (8)° and the hydrogen–oxygen distance is 1·79 (9) Å. The positions of the hydrogen atoms bonded to the oxygen atoms of the hydroquinones are not known, but since the distance O″(1)$\cdots$Br is as short as 3·225 (6) Å and the angle C″(1)–O″(1)$\cdots$Br is 114·8 (4)°, which is fairly close to the expected tetrahedral value 109·5°, this indicates a normal O–H$\cdots$Br hydrogen bond (Hamilton & Ibers, 1968).

The oxygen atoms, O′(1) and O′(4) of the other hydroquinone molecule, involved in the assumed charge transfer, act as donors in two hydrogen bonds to bromine and to the oxygen atom O(12) of one lumiflavinium ion. As mentioned above, the hydrogen atoms attached to O′(1) and O′(4) have not been located, but the distances O′(1) to Br and O′(4) to O(12) of 3·310 (5) and 2·859 (6) Å respectively, and the angles C′(1)–O′(1)$\cdots$Br and O′(4)–O′(4)$\cdots$O(12) of 109·5 (4)° and 105·0 (4)° respectively, indicate normal hydrogen bonds.

The hydrogen, H(1), on the nitrogen atom N(1) of one lumiflavinium ion, is involved in a possible bifurcated hydrogen bond to the oxygen atom O(14) and the nitrogen N(5) of another ion. The distances H(1)$\cdots$O(14) and H(1)$\cdots$N(5) are 2·38 (10) and 2·46 (10) Å, while the corresponding angles N(1)–H(1)$\cdots$O(14) and N(1)–H(1)$\cdots$N(5) are 126 (10)° and 156 (10)°. The conclusion that these two interatomic contacts represent a bifurcated hydrogen bond is of course uncertain, owing to the fairly large estimated standard deviations of the hydrogen positions.

There is one more short intermolecular distance between the lumiflavinium ions, *viz.* between the methyl carbon C(20) of one ion and the keto oxygen O(14) of another. A possible explanation of this short, 3·153 (9) Å, carbon–oxygen distance is that the probable bifurcated hydrogen bond discussed above, decreases the contact distance between two adjacent lumiflavinium ions. The resulting short intermolecular contact between the methyl group and the keto oxygen atom might also be electrostatically favourable. Thus the methyl carbon atom, when bonded to a nitrogen atom, has generally a positive atomic charge. On the other hand the keto oxygen has a negative charge.

Table 9. *Deviations of the atoms from least-squares planes*

The planes are of the form $AX+BY+CZ=D$, 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		Deviation
$A=$ 0·7900	N(1)	0·051 Å
$B=-$0·6129	C(2)	0·022
$C=$ 0·0166	N(3)	−0·072
$D=$ 1·9686 Å	C(4)	−0·024
	C(4*a*)	0·029
	N(5)	0·050
	C(5*a*)	0·001
	C(6)	0·031
	C(7)	0·062
	C(8)	−0·021
	C(9)	−0·074
	C(9*a*)	−0·038
	N(10)	−0·023
	C(10*a*)	0·018
	O(12)	0·037
	O(14)	−0·048
	*C(17)	0·184
	*C(18)	0·006
	*C(20)	−0·006

The e.s.d. of the atoms without asterisks from this plane is 0·047 Å.

Plane II	C′(1)	0·011 Å
$A=$ 0·7495	C′(2)	−0·005
$B=-$0·6603	C′(3)	−0·007
$C=$ 0·0476	C′(4)	0·000
$D=-$1·6627 Å	C′(5)	−0·010
	C′(6)	−0·002
	O′(1)	0·003
	O′(4)	0·010

The e.s.d. of the atoms from this plane is 0·009 Å.

Plane III	C″(1)	0·007 Å
$A=-$0·0545	C″(2)	−0·011
$B=$ 0·7319	C″(3)	0·011
$C=-$0·6793	C″(1$^{\text{vi}}$)	−0·007
$D=-$0·2134 Å	C″(2$^{\text{vi}}$)	0·011
	C″(3$^{\text{vi}}$)	−0·011
	O″(1)	0·002
	O″(1$^{\text{vi}}$)	−0·002

The e.s.d. of the atoms from this plane is 0·011 Å.

Plane IV	*C′(1)	0·011 Å
$A=$ 0·7518	C′(2)	−0·002
$B=-$0·6578	C′(3)	0·002
$C=$ 0·0457	*C′(4)	0·012
$D=-$1·6512 Å	C′(5)	−0·002
	C′(6)	0·002
	*O′(1)	−0·002
	*O′(4)	0·027

The e.s.d. of the atoms without asterisks from this plane is 0·003 Å.

The flavinium ion is almost planar as shown by the calculations of least squares planes in Table 9. The angles between the planes through the atoms forming the benzenoid and pyrazinoid rings of the lumiflavinium ions is 177·8° and the angle between the pyrazinoid and pyrimidinoid rings is 176·4°. Thus, there are slight distortions from planarity of the alloxazinium ring system. The observed deviation from planarity of the alloxazinium ring system in the crystal structure of 10-methylisoalloxazinium bromide. (Trus & Fritchie, 1969), which is not a charge transfer compound, does not differ remarkably from that found in the present study. Thus, the effect of charge transfer on the conformation of the ring system is probably negligible.

Least-squares planes calculated for the two different hydroquinones show that these are nearly planar, though this is not provable according to the χ^2 test. Since the hydroquinone molecule not involved in the assumed charge transfer interaction possesses an inversion center due to the crystallographic symmetry, any deviation from planarity for this molecule will necessarily lead towards a chair conformation of the benzenoid ring. Calculation of the plane through the atoms C''(2), C''(3) and the inversion centre shows that the atoms C''(1) and O''(1) deviates from this plane (towards a chair conformation) by 0·029 and 0·047 Å respectively. In the crystal structure of γ-hydroquinone (Maartmann-Moe, 1966), the hydroquinones in the crystal structure are located at inversion centres and also show slight deviations from planarity towards chair conformation. As regards the other hydroquinone molecule which is involved in the assumed charge transfer interactions in the present structure, its conformation is not restricted by crystallographic symmetry. A least-squares plane calculation through the atoms C'(2), C'(3), C'(5) and C'(6) of the benzenoid ring (Table 9) shows that the atoms deviate slightly towards a boat conformation of this hydroquinone molecule.

Thus the two hydroquinone molecules deviate slightly from planarity in two different ways, towards boat conformation for the one involved in charge transfer interactions and towards chair conformation of the other. However, the deviations from planarity are so small that there is a possibility that these differences might be caused by systematic errors.

The bond lengths and angles for the two hydroquinone molecules agree closely with those obtained by Maartmann-Moe (1966) for γ-hydroquinone.

Table 10. *Comparison of bond distances within the lumiflavinium and* 10-*methylisoalloxazinium ions*

	Lumiflavinium	10-Methyliso-alloxazinium
N(1)—C(2)	1·372 (8) Å	1·408 (7) Å
C(2)—N(3)	1·363 (7)	1·379 (7)
N(3)—C(4)	1·364 (7)	1·388 (7)
C(4)—C(4*a*)	1·474 (8)	1·489 (7)
C(4*a*)—N(5)	1·304 (7)	1·299 (7)
N(5)—C(5*a*)	1·356 (7)	1·376 (7)
C(5*a*)—C(6)	1·396 (8)	1·411 (7)
C(6)—C(7)	1·376 (8)	1·348 (7)
C(7)—C(8)	1·423 (8)	1·415 (7)
C(8)—C(9)	1·375 (8)	1·362 (7)
C(9)—C(9*a*)	1·394 (8)	1·419 (7)
C(9*a*)—C(5*a*)	1·404 (7)	1·407 (7)
C(9*a*)—N(10)	1·405 (7)	1·386 (7)
N(10)—C(10*a*)	1·326 (7)	1·338 (7)
C(10*a*)-C(4*a*)	1·410 (7)	1·422 (7)
C(10*a*)-N(1)	1·363 (7)	1·364 (7)
C(2)—O(12)	1·211 (7)	1·209 (7)
C(4)—O(14)	1·219 (6)	1·211 (7)
N(10)—C(20)	1·484 (8)	1·491 (7)

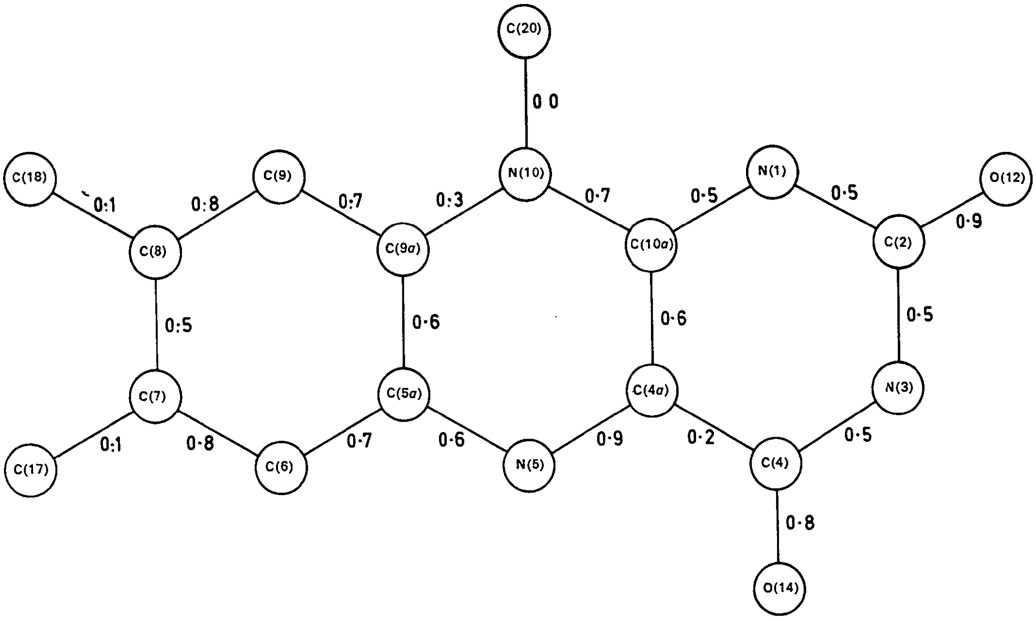


Fig. 4. Estimated π-bond orders in the lumiflavinium ion, obtained from linear bond order – bond distance correlation functions.

Table 11. *Structure factors*

Each group 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.

[illegible]

Table 11 (*cont.*)

[illegible]

The bond lengths and angles obtained for the lumiflavinium ion are in good agreement with those given by Trus & Fritchie (1969) for 10-methylisoalloxazinium bromide dihydrate. A comparison of the bond lengths is given in Table 10. The largest bond length differences are those of the bonds N(1)–C(2), N(3)–C(4), C(6)–C(7) and C(9)–C(9*a*) where the differences are somewhat larger than 3σ. Thus the largest differences occur for the bonds within the pyrimidinoid and the benzenoid rings, both of which are involved in the presumed charge transfer interactions. The average decrease in bond length in the alloxazinium ring system of the present structure as compared with the 10-methylisoalloxazinium ion is 0·006 Å.

To get an approximate overall picture of the π-bond system in the lumiflavinium molecule, estimated π-bond orders have been evaluated (Fig. 4) from the linear π-bond order–bond distance correlation functions suggested by several authors (Roos & Skancke, 1967; Fischer-Hjalmars & Sundbom, 1968). Although these functions were intended for semi-empirical π-electron calculations and are valid only for neutral molecules, the obtained π-bond scheme, as shown in Fig. 4 agrees well with the commonly accepted scheme for the alloxazinium ion (*cf.* Fig. 1). Thus the highest π-bond orders within the pyrazinoid and pyrimidinoid rings are obtained for C(4*a*)–N(5) (0·9) and C(10*a*)–N(10) (0·7). It is also obvious that both of the oxygen atoms, O(12) and O(14), attached to the pyrimidinoid ring are of keto type. The differences of the C–C bond lengths within the benzenoid ring is in accordance with the predictions based on semiempirical π-electron calculations (Grabe, 1969) on different alloxazine species.

Table 11 shows h,k,l, $|F_{\text{obs}}|$ and $|F_{\text{calc}}|$ for all the 3269 reflexions used in this study.

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References

BEAR, C. A., WATERS, J. M. & WATERS, T. N. (1970). *Chem. Commun.* p. 702.

CROMER, D. T. (1965). *Acta Cryst.* **18**, 17.

CROMER, D. T. & WABER, J. T. (1965). *Acta Cryst.* **18**, 17.

FISCHER-HJALMARS, I. & SUNDBOM, M. (1968). *Acta Chem. Scand.* **22**, 607.

FLEISCHMAN, D. E. & TOLLIN, G. (1965). *Biochim. Biophys. Acta.* **94**, 248.

FOSTER, R. (1969). *Organic Charge-Transfer Complexes*, London: Academic Press.

GRABE, B. (1969). Private communication.

HAMILTON, W. C. & IBERS, J. A. (1968). *Hydrogen Bonding in Solids*, New York: Benjamin.

HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040.

HAUPTMAN, H. & KARLE, J. (1953). *Solution of the Phase Problem. I. The Centrosymmetric Crystal.* A.C.A. Monograph No. 3. Pittsburg: Polycrystal Book Service.

HUGHES, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737.

KARLSSON, R. (1971). To be published.

KIERKEGAARD, P., NORRESTAM, R., WERNER, P.-E., CSÖREGH, I., VON GLEHN, M., KARLSSON, R., LEIJONMARCK, M., RÖNNQUIST, O., STENSLAND, B., TILLBERG, O. & TORBJÖRNSSON, L. (1971). *In Flavins and Flavoproteins.* Baltimore: Univ. Park Press.

KOSOWER, E. M. (1966). In *Flavins and Flavoproteins*, Edited by E. C. SLATER. Amsterdam: Elsevier.

LANGHOFF, C. A. & FRITCHIE, JR, C. J. (1970). *Chem. Commun.* p. 20.

MAARTMANN-MOE, K. (1966). *Acta Cryst.* **21**, 979.

NORRESTAM, R. (1970). *Acta Chem. Scand.* **25**, 1040.

ROOS, B. & SKANCKE, P. N. (1967). *Acta Chem. Scand.* **21**, 233.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175.

SZENT-GYÖRGYI, A. (1960). *Introduction to Submolecular Biology.* New York: Academic Press.

TRUS, B. L. & FRITCHIE, JR, C. J. (1969). *Acta Cryst.* **B25**, 1911.