Crystal Structure of a Flavin–Metal Complex, Bis(10-methylisoalloxazine)lead(II) Perchlorate Tetrahydrate

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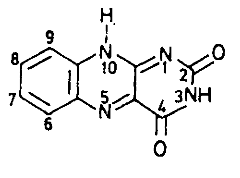
The title complex has been prepared and characterized by *X*-ray techniques. The yellow crystals are monoclinic, space group $P2_1/c$, with lattice constants a = 6·987(2), b = 13·806(7), c = 17·012(5) Å, β = 105·69(3)°, and Z = 4 for $1/2[Pb(ClO_4)_2]C_{11}H_8N_4O_2,2H_2O$. The structure was solved by the heavy-atom method and refined by least-squares to R 8·9%, for 878 counter-measured reflections. The lead ions are disordered in two sites 0·75 Å above and below a plane of four oxygens, two of which are the centrosymmetrically related carbonyl oxygens O(2) of the ligand, [Pb–O 2·46(2) and 2·63(2) Å], the other two being water oxygens [Pb–O 2·38(2) and 2·69(2) Å]. The next nearest atoms to Pb are N(1) of the same flavin at 2·99(2) Å, and another water molecule at 3·12(2) Å. This is the first structure with a metal in the secondary chelate site of the flavin molecule but none in the primary site. Co-ordination of Pb^{2+} to oxygen rather than nitrogen is consistent with its intermediate character on the Pearson hard–soft scale.

ISOALLOXAZINE (I) is the portion of riboflavin co-factors which is active in oxidation–reduction reactions. In many flavoenzymes, the metals molybdenum and iron also participate in these electron-transfer processes. Crystallographic studies of metal–flavin complexes[1-6] have established two common sites of interaction: a primary chelate site consisting of O(4) and N(5) which is the most commonly occupied, and a secondary site consisting of N(1) and O(2) which is occupied when two metal ions co-ordinate to the same flavin. Furthermore, the ion Cu^{II}, intermediate-to-hard in the Pearson hard–soft acid–base scheme[7] binds more closely to the harder base-oxygen in both sites, whereas the softer Ag^I and Cu^I (ref. 8) bind more tightly to the presumably softer nitrogen atoms. These results intimate that, in cases where electrons flow from a reduced soft metal to the oxidized or quinoid flavin, the two nitrogen atoms, and particularly N(5), are likely sites of specific metal–flavin interaction. The structure, described here, which illustrates the interaction of a flavin with the intermediate-to-hard ion Pb^{2+}, supports these general ideas but provides another variant on metal–flavin interactions in which only the secondary chelate site is occupied by a metal ion.



(I)

EXPERIMENTAL

Preparation of the Complex.—The yellow crystals were grown by evaporation of either a concentrated acetic acid solution or a concentrated formic acid solution of 10-methylisoalloxazine and lead perchlorate. They are thin yellow plates on (001) with the longer extension in the

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b direction. The crystals are somewhat unstable in the air and were enclosed in Lindemann glass capillaries for *X*-ray studies.

Crystallographic Data.—$1/2[\mathrm{Pb(ClO_4)_2}]\mathrm{C_{11}H_8N_4O_2,2H_2O}$, M = 467, Monoclinic, a = 6·987(2), b = 13·806(7), c = 17·012(5) Å, β = 105·69(3)°, U = 1580 Å^3, D_m = 1·98 g cm^{-3} (by flotation), Z = 4, D_c = 1·96 g cm^{-3}. Mo-K_α radiation, λ = 0·7107 Å; μ(Mo-K_α) = 55·14 cm^{-1}. Space group $P2_1/c$.

TABLE 1

Positional and anisotropic thermal * parameters

	x	*y*	*z*	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Pb †	0·1139(3)	−0·0084(2)	0·0123(1)	0·0215(3)	0·0047(1)	0·0024(1)	0·0055(7)	0·0037(2)	0·0002(3)
Cl	0·4195(9)	0·1429(5)	0·3474(4)	0·0172(15)	0·0056(4)	0·0039(3)	−0·0002(16)	0·0055(11)	−0·0002(6)
W(1)‡	0·110(3)	0·1000(14)	0·1208(12)	0·057(7)	0·0080(14)	0·0056(10)	0·009(6)	0·017(4)	−0·001(2)
W(2)‡	0·525(4)	0·1424(13)	0·0065(13)	0·084(10)	0·0055(11)	0·0051(9)	0·004(7)	0·001(5)	−0·007(2)
O(A)	0·598(3)	0·1566(15)	0·3242(15)	0·054(5)	0·009(2)	0·0174(15)	0·012(6)	0·048(4)	0·007(3)
O(B)	0·477(3)	0·1002(20)	0·4253(14)	0·048(8)	0·023(3)	0·0067(12)	0·002(9)	0·006(5)	0·015(3)
O(C)	0·284(4)	0·0837(20)	0·2987(18)	0·069(8)	0·023(2)	0·0092(15)	−0·066(6)	0·006(6)	−0·010(3)
O(D)	0·329(4)	0·2324(20)	0·3461(20)	0·050(7)	0·013(2)	0·0231(27)	0·017(7)	0·034(6)	−0·003(4)

* Temperature factors are of the form $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + \beta_{12}hk + \beta_{13}hl + \beta_{23}kl)]$.
† Population factor 0·5.
‡ W = H_2O throughout.

Intensity Measurements.—The single crystal used for data collection, with dimensions 0·22 × 0·067 × 0·5 mm, was mounted along the *b* axis. Intensity measurements were performed on an automatic Picker four-circle diffractometer in the θ—2θ scan mode with zirconium-filtered Mo-K_α radiation. A scintillation counter with pulse-height analyser served as detector. The scan rate was 1° min^{-1}, with the scan range 2° + $\Delta(2\theta)$, where $\Delta(2\theta)$ is the $\alpha_1 - \alpha_2$ separation. All reflections having $2\theta \leqslant 55°$ were measured and the decay occurring during the intensity measurements, as determined by several standard reflections, was <2%. The integrated intensities were corrected for Lorentz and polarization factors. Of 1557 reflections scanned, 878 having $I \geqslant 2\sigma(I)$ were considered statistically reliable. The remainder were omitted from all calculations. The standard deviation $\sigma(I)$ was calculated by $[C + (t_C/2t_B)^2(B_1 + B_2) + p^2I^2]^{\frac{1}{2}}$, where C is the total scan count, t_C is the time of scan, t_B is the time of each background count (20 s), B_1 and B_2 are background counts, and p = 0·02. An absorption correction * was made because of the large value of μ and the greatly anisotropic shape of the crystal.

Determination and Refinement of the Structure.—From the Patterson map the heavy lead atom was found to be disordered. The remainder of the atoms were located by use of Fourier techniques.† Refinement was by least-squares † minimization of the quantity $\Sigma w|F_o - F_c|^2$ with $w = 1/\sigma^2(F)$. Atomic scattering factors used for lead and chlorine were from ref. 9, those for oxygen, nitrogen, and carbon from ref. 10; hydrogen form factors were from ref. 11. Anomalous dispersion corrections were taken from ref. 12 for lead and chlorine. Anisotropic thermal parameters were introduced for some heavy atoms, *i.e.* lead, chlorine, and the perchlorate and water oxygen atoms, but the flavin molecule remained isotropic because of the small number of observed data. With no hydrogen atoms included, the structure refined to R 9·0%. A difference map showed poorly defined positive areas in the regions where ligand hydrogen atoms were expected, as well as much larger peaks near lead (*vide infra*) and the perchlorate ion. The aromatic isoalloxazine hydrogen atoms were introduced in idealized positions and the structure refined to the final value of R 8·9%. Final atomic positions are given in Tables 1 and 2. Observed and calculated structure factors are listed in Supplementary Publication No. SUP 21178 (5 pp., 1 microfiche).‡

TABLE 2

Positional and isotropic thermal parameters

	x	*y*	*z*	B/Å^2
N(1)	0·693(3)	0·4014(14)	0·3257(12)	3·8(5)
C(2)	0·860(4)	0·3548(18)	0·3435(15)	3·6(6)
N(3)	0·911(3)	0·2912(12)	0·2846(11)	2·6(4)
C(4)	0·776(3)	0·2648(17)	0·2174(14)	3·1(5)
C(4a)	0·592(3)	0·3177(15)	0·1949(13)	1·9(5)
N(5)	0·460(3)	0·2981(13)	0·1282(11)	3·1(4)
C(5a)	0·275(3)	0·3449(16)	0·1102(14)	2·6(5)
C(6)	0·137(4)	0·3244(20)	0·0363(16)	4·5(7)
C(7)	−0·050(4)	0·3701(20)	0·0200(16)	4·4(7)
C(8)	−0·092(4)	0·4282(20)	0·0754(16)	4·2(6)
C(9)	0·043(4)	0·4514(19)	0·1472(16)	3·9(6)
C(9a)	0·237(3)	0·4098(17)	0·1669(14)	3·2(6)
N(10)	0·376(3)	0·4216(14)	0·2401(12)	3·8(5)
C(10a)	0·550(3)	0·3858(17)	0·2583(15)	3·1(5)
C(10)	0·336(3)	0·4888(18)	0·3062(15)	4·0(5)
O(2)	0·999(3)	0·3647(13)	0·4093(11)	5·6(5)
O(4)	0·820(2)	0·2082(12)	0·1651(10)	4·7(4)
H(6)	0·168	0·2812	−0·0019	3·0
H(7)	−0·147	0·3593	−0·0306	3·0
H(8)	−0·223	0·4548	0·0647	3·0
H(9)	0·007	0·4954	0·1740	3·0
N(3)H	1·044	0·2681	0·2944	3·0

DESCRIPTION OF THE STRUCTURE AND DISCUSSION

Flavin Geometry.—Figure 1 illustrates the environment of the flavin molecule. As in most flavoquinones, the molecule is nearly planar, with a folding angle of only 1·3° between the two eight-atom planes defined by N(5), N(10), and either the benzenoid or the pyrimidinoid

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* Program ORABS by W. R. Busing, K. O. Martin, and H. A. Levy was used for absorption correction. The absorption factors (for F) varied from 0·546 to 0·840.

† Program LOKI, a local unpublished crystallographic system, was used for Fourier and least-squares calculations.

‡ See Notice to Authors No. 7, in *J.C.S. Dalton*, 1973, Index issue. Iber's program RANGER was used to calculated R over small ranges of either $|F_o|$ or $(\sin\theta/\lambda)$. These tabulations show the usual increase with $(\sin\theta/\lambda)$ and decrease with $|F_o|$, except for anomalously high R in the lowest $(\sin\theta/\lambda)$ range and the largest $|F_o|$ range. A final ΔF synthesis showed peaks of 1·6—2·6 e Å^{-3} near the lead ion. It is likely that even the disordered anisotropic model for lead does not adequately describe its distribution in the crystal.

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rings. Neither of these eight-atom planes fits the atomic positions significantly better than the plane through the entire molecule. A selection of several least-squares planes calculated is given in Table 3. Bond distances and angles within the flavin molecule do not differ significantly from those in 'ideal' flavoquinone.[13] Individual values are listed in Tables 4 and 5.

TABLE 3

Equations of least-squares planes in the form $Am + Bn + Cp = D$, where m, n, and p are dimensions in Å relative to unit orthogonal axes $\boldsymbol{m}\|\boldsymbol{a}$, $\boldsymbol{n}\|\boldsymbol{b}$, and $\boldsymbol{p}\|\boldsymbol{c}^*$. All atoms were given equal weight except that for distances in parentheses the corresponding atom had zero weight

(*a*) Equations

Plane	*A*	*B*	*C*	*D*
(I)	0·49283	0·75980	−0·42405	3·527
(II)	0·49316	0·75592	−0·43056	3·498
(III)	0·50188	0·75137	−0·42844	3·506
(IV)	0·48570	0·76446	−0·42390	3·550

(*b*) Distances (Å) from each plane

	(I)	(II)	(III)	(IV)
N(1)	0·070	0·043	0·051	(0·050)
C(2)	−0·008	−0·033	−0·013	(−0·039)
N(3)	0·043	0·027	0·055	(0·003)
C(4)	−0·078	−0·085	−0·063	(−0·115)
C(4a)	0·049	0·041	0·048	(0·024)
N(5)	0·003	0·003	0·004	−0·019
C(5a)	0·023	0·022		0·012
C(6)	0·014	0·021		0·006
C(7)	−0·002	0·004		0·002
C(8)	−0·046	−0·049		0·034
C(9)	0·003	−0·009		0·012
C(9a)	0·050	0·039		0·047
N(10)	−0·021	−0·040	−0·052	−0·027
C(10a)	0·035	0·016	0·017	(0·019)
C(10)	−0·062	(−0·092)	(−0·112)	(−0·060)
O(2)	−0·030	(−0·063)	−0·035	(−0·065)
O(4)	−0·041	(−0·040)	−0·011	(−0·086)
Pb	(0·188)			
Pb′	(0·922)			
W(1) *	(−0·231)			
W(2) *	(−0·285)			
O(D)	(0·299)			

* Nearest O(4).

TABLE 4

Bond lengths (Å), with standard deviations in parentheses

N(1)–C(2)	1·30(3)	C(9)–C(9a)	1·42(3)
C(2)–N(3)	1·45(3)	C(9a)–N(10)	1·37(3)
N(3)–C(4)	1·32(3)	N(10)–C(10a)	1·27(3)
C(4)–C(4a)	1·44(3)	N(10)–C(10)	1·54(3)
C(4a)–C(10a)	1·53(3)	C(10a)–N(1)	1·32(3)
C(4a)–N(5)	1·28(3)	C(2)–O(2)	1·28(3)
N(5)–C(5a)	1·40(3)	C(4)–O(4)	1·28(3)
C(5a)–C(9a)	1·40(3)	Cl–O(A)	1·42(2)
C(5a)–C(6)	1·39(3)	Cl–O(B)	1·41(2)
C(6)–C(7)	1·41(4)	Cl–O(C)	1·35(2)
C(7)–C(8)	1·33(4)	Cl–O(D)	1·39(2)
C(8)–C(9)	1·37(4)		

Flavin–Metal Interaction.—The metal co-ordination is rather unexpected, since in all other complexes studied where there is one metal per flavin the metal is found in the N(5)–O(4) primary chelate site. However, the binding of Pb^{II} primarily to oxygen rather than to nitrogen is in accord with the interaction being governed largely by the Pearson hard–soft acid–base principle.

TABLE 5

Bond angles (°) with standard deviations in parentheses

N(1)–C(2)–N(3)	121(2)	C(8)–C(9)–C(9a)	120(2)
N(1)–C(2)–O(2)	125(2)	C(9)–C(9a)–C(5a)	116(2)
O(2)–C(2)–N(3)	114(2)	C(5a)–C(9a)–N(10)	119(2)
C(2)–N(3)–C(4)	121(2)	C(9)–C(9a)–N(10)	124(2)
N(3)–C(4)–C(4a)	118(2)	C(9a)–N(10)–C(10)	121(2)
N(3)–C(4)–O(4)	122(2)	C(10)–N(10)–C(10a)	114(2)
O(4)–C(4)–C(4a)	119(2)	C(9a)–N(10)–C(10a)	125(2)
C(4)–C(4a)–C(10a)	117(2)	N(10)–C(10a)–N(1)	127(2)
C(10a)–C(4a)–N(5)	122(2)	N(10)–C(10a)–C(4a)	115(2)
C(4)–C(4a)–N(5)	120(2)	C(4a)–C(10a)–N(1)	118(2)
C(4a)–N(5)–C(5a)	120(2)	C(10a)–N(1)–C(2)	123(2)
N(5)–C(5a)–C(9a)	119(2)	O(A)–Cl–O(B)	106(1)
C(9a)–C(5a)–C(6)	123(2)	O(A)–Cl–O(C)	116(1)
N(5)–C(5a)–C(6)	118(2)	O(A)–Cl–O(D)	108(2)
C(5a)–C(6)–C(7)	118(2)	O(B)–Cl–O(C)	107(2)
C(6)–C(7)–C(8)	120(2)	O(B)–Cl–O(D)	114(2)
C(7)–C(8)–C(9)	123(3)	O(D)–Cl–O(C)	107(1)

The unprimed lead in Figure 1 is 2·46(2) from O(2) of the flavin; the primed lead ion is 2·63(2) away, and N(1)–Pb is 2·99(2) Å.

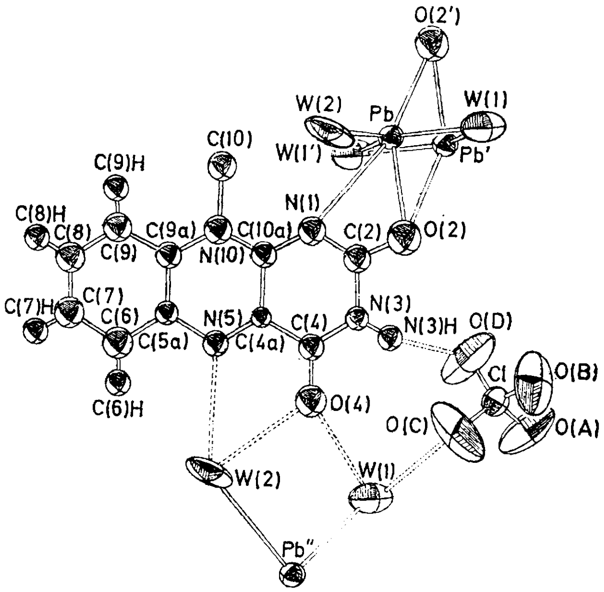

FIGURE 1 Flavin–lead co-ordination and hydrogen bonding

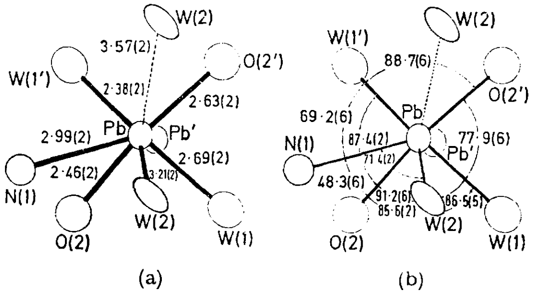

FIGURE 2 The lead co-ordination complex. (a) Interatomic distances. (b) Interligand angles. The unprimed and primed atoms are related by an inversion centre.

The entire co-ordination sphere of Pb^{2+} is illustrated more clearly in Figure 2, which is a projection on the

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[13] M. Wang and C. J. Fritchie, jun., *Acta Cryst.*, 1973, **B29**, 2040.

O(2), O(2′), W(1), W(1′) plane. The nearest neighbours of a given Pb^{2+} ion are these four oxygen atoms, which form the rigorously planar base of an irregular square pyramid having Pb at the apex. Pb is 0·75 Å from the basal plane, and its nearest neighbours above this pyramid are N(1) at 2·99(2), W(2) at 3·21(2), and another, more distant W(2) at 3·57(2) Å. The Pb–N(1) distance is somewhat greater than that found [2·751(6) Å] in the complex of $Pb(SCN)_2$ with the eighteen-membered heterocycle $C_{12}H_{26}N_2O_4$.[14] This latter bond is described as ‘ electrostatic,’ and the Pb^{2+} ion is best described as four-co-ordinate, with the three more distant atoms considered very weakly bound.

The pyramidal four-co-ordination found for Pb^{2+} is quite similar to that in red tetragonal PbO,[15,16] in yellow orthorhombic PbO,[17] and in $PbMnO_2(OH)$.[18] This unusual co-ordination figure has been ascribed to the presence of the inert lone-pair in this ion. The four short Pb–O distances are all 2·30 Å in red PbO, and 2·21(2), 2·22(2), 2·49(1), and 2·49(1) Å in yellow PbO. In $PbMnO_2(OH)$, the Pb–O bond lengths are 2·22(2), 2·31(2), 2·37(2), and 2·76(2) Å. It is reasonable that distances to the neutral water and oxo-oxygens in the flavin complex would be slightly longer than those to oxide or hydroxide ligands. The four interbond angles around the pyramid in this structure are also quite similar to those found in the three purely inorganic compounds, which range from 75 (ref. 15) to 90·4°.[17]

Hydrogen Bonding.—Figures 1 and 3 reveal the extensive hydrogen-bonding network which is present. The primary chelate site contains a water molecule, W(2), which is 3·10(3) from N(5) and 3·06(3) Å from O(4). As Figure 1 illustrates, the thermal parameters of W(2) are consistent with a significant movement of it roughly toward or away from the Pb site, probably depending on whether or not it is occupied in a given cell. The co-ordinates and the bond lengths quoted for this atom are thus probably intermediate between two extreme values actually represented in the crystal. Nevertheless, no other hydrogen-bond receptors are within bonding distance of W(2), and the correct atomic sites cannot be far from the mean. The W(2)–N(5) and W(2)–O(4) distances are similar to those found in two other flavin complexes, 3·08(1) and 3·12(1),[19] and 2·94($1\cdot_6$) and 3·08($1\cdot_6$) Å (ref. 20) respectively.

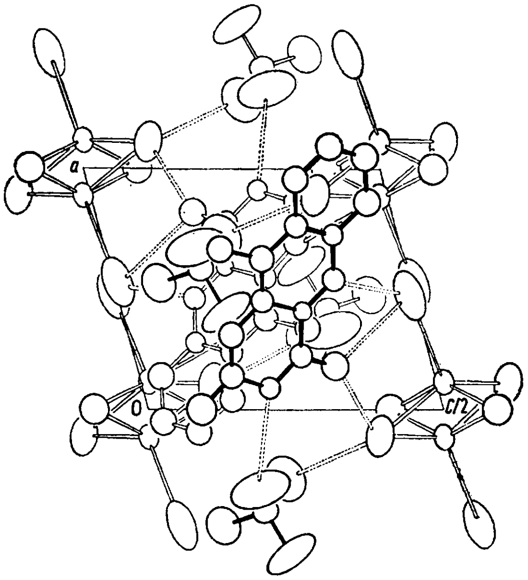

FIGURE 3 Crystal packing and hydrogen bonding. Dashed lines indicate probable hydrogen bonds

O(4) is also bound to a second water, W(1), at 2·78(2) Å, and W(1) apparently uses its second proton in binding to O(C) of the perchlorate group at 2·95(3) Å. The O(4)–W(1)–O(C) angle is 83·7(8)°. Angles subtended at W(1) by the two Pb^{2+} ions and the postulated receptors are: O(4)–W(1)–Pb(nearer) 135·2(9)°, O(4)–W(1)–Pb(further) 100·4(7)°; O(C)–W(1)–Pb(nearer) 131·2(9)°, and O(C)–W(1)–Pb(further) 144·2(9)°. The final hydrogen bond is N(3) · · · O(D), which is 2·89(3) Å.

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[4/1333 *Received, 3rd July*, 1974]

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