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Metal Complexes of Virus Inhibitors. Part II [1]. Coordination Properties of 2-α-methoxybenzylbenzimidazole (= L) and X-ray Crystal Structure of $CoL_2I_2 \cdot$acetone$\cdot 2H_2O$

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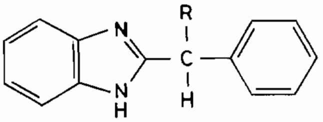
Complexes are described of cobalt(II) and nickel(II) salts with the title ligand (=L). The X-ray crystal structure of $[CoL_2I_2] \cdot$*acetone*$\cdot 2H_2O$ *shows the ligand to be chelating to give distorted* cis-*octahedral geometry. In other complexes the ligand is monodentate through the imidazole nitrogen and an infrared spectral criterion to distinguish these modes of coordination is described. Some of the complexes bind strongly to carbonyl groups, especially of amides. It is suggested that similar binding to proteins may be important in the mode of anti-viral activity.*

Introduction

Benzimidazoles with hydroxy-substituents in the 2-position show a range of antiviral activity, which has been attributed [2] to their ability to complex with metal ions. This was assumed to be by chelation through the tertiary nitrogen and hydroxylic oxygen, as was later shown [3] to occur for 2-α-hydroxybenzylbenzimidazole (I, R = OH).



I

However, the discovery that alkoxy-, as well as hydroxy-compounds, were active, prompted the suggestion that dealkylation may take place *in vivo,* [4] since the ether groups were considered unlikely to coordinate. We report here some metal complexes of 2-α-methoxybenzylbenzimidazole (I, R = OMe) in which chelation involving the methoxy-group is shown to occur in at least some, and probably in the majority, of the compounds.

Experimental

Preparation of Compounds

2-α-Methoxybenzyl-benzimidazole was made by the method of O'Sullivan and Wallis [5]. M.p. 160 °C (lit 160 °C). Metal complexes were made by the following general method: a slight excess over the stoichiometric amount of ligand was dissolved in the minimum quantity of ethanol, acetone or dimethylformamide, and added to a solution of the metal salt in the same solvent. Crystalline solids were formed either on standing or on partial evaporation, and were recrystallised, usually from the same solvent. Several of the complexes formed initially as solvates, especially from acetone and dimethylformamide. In general this solvent could be removed by heating at about 100 °C *in vacuo*, but in some cases desolvation proved very difficult, and resulted in partial decomposition of the complex (see text). Results of microanalyses (Imperial College Analytical Service) are in Table I.

Spectroscopic and Magnetic Measurements

These were carried out as described previously [1].

Single-Crystal X-ray Structure

CoL_2I_2 crystallises from acetone as violet prisms. A specimen of irregular shape and dimensions *ca.* 0.40 × 0.20 × 0.10 mm was used for unit cell and intensity measurements. All determinations were

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TABLE I. Analytical Results for the Complexes.

Compound	Found			Calculated		
	C	H	N	C	H	N
CoL_2Cl_2	59.69	4.95	11.73[a]	59.41	4.65	11.69[a]
CoL_2Br_2	51.67	4.14	7.92	51.82	4.06	8.06
CoL_2I_2	45.55	4.00	7.66	45.65	3.58	7.10
$CoL_2(NO_3)_2$	54.55	4.32	12.84	54.64	4.28	12.75
$CoL_2(NCS)_2$	58.27	4.13	12.89	58.95	4.33	12.89
$CoL_3(ClO_4)_2$	54.94	4.29	8.24[b]	55.56	4.35	8.64[b]
NiL_2Cl_2	58.91	4.98	11.32[a]	59.44	4.66	11.69[a]
NiL_2Br_2	51.90	4.02	7.85	51.84	4.06	8.06
NiL_2I_2	46.34	3.54	6.89	45.65	3.58	7.09
$NiL_2(NCS)_2$	58.28	4.42	13.08	59.00	4.33	12.90
$NiL_2(NO_3)_2$	54.12	4.10	12.20	54.66	4.28	12.75
$NiL_3(ClO_4)_2$	55.68	4.56	18.62[c]	55.58	4.35	18.09[c]

[a] % Chlorine. [b] Found O = 18.55; calcd. O = 18.09%. [c] % Oxygen.

carried out on a Nicolet R3m/Eclipse S140 diffractometer system using graphite-monochromated Cu-Kα radiation. Cell parameters were determined by least-squares refinement of the angular settings of 17 automatically centred reflections.

Crystal Data

Formula $C_{33}H_{38}O_5N_4CoI_2$, M = 883.43, triclinic, $a = 10.619(2)$, $b = 11.934(2)$, $c = 14.940(1)$ Å, $\alpha = 110.39(1)^\circ$, $\beta = 92.45(1)^\circ$, $\gamma = 98.91(2)^\circ$, $U = 1743.7(5)$ Å^3, space group $P\bar{1}$, $Z = 2$, $D_c = 1.68$ g cm^{-1}, $F(000) = 874$, (Cu-Kα) = 184.7 cm^{-1}.

Integrated intensities were collected using the ω scan technique for all the reflections within one hemisphere. Two reflections ($1\bar{1}3$ and $2\bar{1}\bar{1}$) which were monitored every 50 measurements showed no significant variation in their intensities. A total of 4216 unique reflections were collected, of which 3898 with $F > 3\sigma(F)$ were used in the structure analysis. The data were scaled using the check reflections and were corrected for Lorentz and polarisation effects. In the later stages of refinement an empirical absorption correction was also applied [6] based on 36 psi scan measurements for each of 11 representative reflections.

All the calculations and drawings were made using the SHELXTL program system [6], and the atomic scattering factors and anomalous dispersion corrections were taken from ref. 7.

Structure Solution and Refinement

The coordinates of both iodine atoms were readily derived from an initial Patterson map, and the positions of all the other non-H atoms were located in subsequent Fourier maps. Least-squares refinement of the coordinates and isotropic thermal parameters for all the 45 non-hydrogen atoms in the asymmetric unit gave $R = 0.11$. When the atoms were allowed to refine anisotropically the R index was reduced to 0.066, and the application of an absorption correction brought it further down to 0.049.

The hydrogen atoms were either placed in calculated positions or their positions were derived from difference Fourier syntheses. Methyl groups were treated as rigid bodies. During the final stages of refinement one strong low-angle reflection (110) thought to be affected by extinction was omitted, and a weighting scheme was applied so that $w = 1/[(\sigma F_o)^2 + 0.00053\ F_o^2]$. For the last cycle $R = 0.041$ and $R_w = [\Sigma w|\Delta F|^2/\Sigma w|F_o|^2]^{1/2} = 0.044$; the largest shift/e.s.d. ratio for any parameter was 0.064, and the average value was 0.022.

Fractional coordinates of the non-hydrogen atoms are listed in Table II, while the more important bond lengths and bond angles are given in Table III. Complete tables of atomic coordinates for all atoms, the thermal parameters, full lists of bond lengths and bond angles, and lists of F_o/F_c values have been deposited with the Editor as supplementary material.

Results

Cobalt(II) and nickel(II) ions readily form complexes with 2-α-methoxybenzylbenzimidazole (= L), even in the presence of coordinating anions and reasonably polar solvents. The complex CoL_2Cl_2 appears to be essentially tetrahedral, with a magnetic

TABLE II. Fractional Atomic Coordinates with Estimated Standard Deviations in Parentheses.

	x	*y*	*z*
Co	0.2616(1)	0.2126(1)	0.2642(1)
I(1)	0.4233(1)	0.4386(1)	0.3311(1)
I(2)	0.1220(1)	0.2245(1)	0.1075(1)
O(1a)	0.1469(4)	0.0204(3)	0.2327(3)
O(1b)	0.3640(4)	0.1774(4)	0.3916(3)
N(1a)	0.3726(4)	0.0937(4)	0.1795(3)
N(1b)	0.1500(4)	0.2631(4)	0.3793(3)
N(2a)	0.4090(4)	−0.0938(4)	0.1096(3)
N(2b)	0.1223(5)	0.3115(5)	0.5336(3)
C(1a)	0.1827(6)	−0.1915(5)	0.1782(4)
C(2a)	0.1198(7)	−0.3013(6)	0.1096(5)
C(3a)	0.1190(8)	−0.4078(6)	0.1277(6)
C(4a)	0.1783(7)	−0.4050(6)	0.2119(6)
C(5a)	0.2399(7)	−0.2976(7)	0.2791(6)
C(6a)	0.2418(6)	−0.1905(6)	0.2617(5)
C(7a)	0.1908(6)	−0.0734(5)	0.1587(4)
C(8a)	0.3243(6)	−0.0242(5)	0.1504(4)
C(9a)	0.4978(5)	0.0996(5)	0.1521(4)
C(10a)	0.5207(6)	−0.0174(5)	0.1095(4)
C(11a)	0.6371(6)	−0.0412(6)	0.0751(4)
C(12a)	0.7281(6)	0.0557(6)	0.0830(4)
C(13a)	0.7058(6)	0.1742(7)	0.1241(4)
C(14a)	0.5910(6)	0.1998(6)	0.1596(4)
C(15a)	0.0115(7)	−0.0080(6)	0.2358(6)
C(1b)	0.3144(6)	0.1597(6)	0.5447(4)
C(2b)	0.3900(7)	0.1941(7)	0.6299(5)
C(3b)	0.3779(8)	0.1238(10)	0.6864(6)
C(4b)	0.2907(9)	0.0197(9)	0.6592(6)
C(5b)	0.2157(8)	−0.0177(7)	0.5738(7)
C(6b)	0.2263(7)	0.0518(6)	0.5150(5)
C(7b)	0.3256(6)	0.2377(6)	0.4834(4)
C(8b)	0.1979(6)	0.2700(5)	0.4637(4)
C(9b)	0.0309(5)	0.3014(5)	0.3953(4)
C(10b)	0.0154(6)	0.3323(5)	0.4921(4)
C(11b)	−0.0916(7)	0.3755(5)	0.5309(5)
C(12b)	−0.1837(7)	0.3856(6)	0.4683(5)
C(13b)	−0.1714(6)	0.3507(7)	0.3710(5)
C(14b)	−0.0649(6)	0.3090(6)	0.3320(4)
C(15b)	0.4948(7)	0.1637(9)	0.3987(5)
C(1s)	0.2233(10)	0.3242(10)	0.8729(7)
C(2s)	0.1860(7)	0.3638(7)	0.7952(5)
C(3s)	0.2145(15)	0.4932(11)	0.8101(10)
O(1s)	0.1256(6)	0.2912(5)	0.7161(4)
O(1w)	0.4045(6)	0.4328(5)	0.0932(4)
O(2w)	0.4269(6)	0.6594(5)	0.0461(4)

moment of 4.57 and an electronic spectrum (Table IV) typical of a CoN_2Cl_2 chromophore, and quite similar to that of Co(benzimidazole)$_2$Cl$_2$ [8]. The bromide is superficially similar, but its magnetic moment is rather high (4.80) and, in addition to the 3-component $\nu_2(^4A_2 \rightarrow {}^4T_1(F))$ band, the electronic spectrum shows a well-resolved band at 4,600 cm^{-1}, and a shoulder at about 10,400 cm^{-1}. The former is assignable as the $\nu_1(^4A_2 \rightarrow {}^4T_2)$ band, which becomes partially allowed under certain distortions of the tetrahedron. Compared with the chloride, it seems that there is some small perturbation of the CoN_2Br_2 tetrahedron, possibly by 'semi-bonding' of the ether group. Other compounds with a '4 + 2' coordination, such as Co(4,6-dimethylpyrimidinone)$_2$Cl$_2$ show a pronounced shoulder on the high energy side of ν_2 [9].

TABLE III. Selected Bond Lengths (Å) and Bond Angles (°).

Co–I(1)	2.785(1)	Co–I(2)	2.775(1)
Co–O(1a)	2.302(4)	Co–O(1b)	2.345(5)
Co–N(1a)	2.097(5)	Co–N(1b)	2.097(5)
I(1)–Co–I(2)	101.5(1)		
I(1)–Co–O(1a)	169.3(1)	I(2)–Co–O(1b)	172.6(1)
I(1)–Co–N(1a)	104.5(1)	I(2)–Co–N(1b)	106.2(1)
I(1)–Co–O(1b)	85.9(1)	I(2)–Co–O(1a)	89.2(1)
I(1)–Co–N(1b)	92.5(1)	I(2)–Co–N(1a)	93.9(1)
O(1a)–Co–O(1b)	83.4(2)		
O(1a)–Co–N(1a)	74.6(2)	O(1b)–Co–N(1b)	73.2(2)
O(1a)–Co–N(1b)	84.3(2)	O(1b)–Co–N(1a)	84.1(2)
N(1a)–Co–N(1b)	150.6(2)		
Average lengths in L ligands (σ range 0.007–0.015)			
C(7)–O(1)	1.424	C(9)–C(10)	1.385
C(7)–C(1)	1.519	C(10)–C(11)	1.389
C(7)–C(8)	1.493	C(11)–C(12)	1.363
C(8)–N(1)	1.319	C(12)–C(13)	1.389
C(8)–N(2)	1.345	C(13)–C(14)	1.381
C(9)–N(1)	1.410	C(14)–C(9)	1.396
C(10)–N(2)	1.374	C(15)–O(1)	1.429
Phenyl ring (a)	C–C	1.379	
Phenyl ring (b)	C–C	1.376	

The corresponding iodide gives a more complicated system, whose nature depends on the conditions of preparation. The products tended to retain solvent of crystallisation, and gave electronic spectra not readily reconcilable with either octahedral or tetrahedral coordination. The product from acetone gave crystals suitable for X-ray study.

Description of the Structure

The crystal contains molecules of CoL_2I_2 in which the metal ion is coordinated by two *cis* iodine atoms and two bidentate L molecules, together with acetone and water of solvation. The metal ion is therefore 6-coordinate, but the geometry is considerably distorted from octahedral (Fig. 1), apparently due to the combined effect of strain in the chelate rings,

TABLE IV. Reflectance Spectra of the Complexes.

Complex	Absorption maxima (cm^{-1})
CoL_2Cl_2	6200sh, 7150, 8600sh, 15700, 17000sh, 19600sh, 23000sh
CoL_2Br_2	4600, 6000, 6670, 8200sh, 10750sh, 15150, 15600sh, 17100
$CoL_2I_2(DMF)_2$^{a}	6000sh, 6500sh, 7100, 14300sh, 19000, 20600sh
CoL_2I_2(green)	6000sh, 6600, 8000sh, 14300, 15300, 16700, 18100sh
CoL_2I_2 (blue-violet)	4600, 5560, 11800, 14500, 18000
$CoL_2(NO_3)_2$	7700sh, 8600, 12800, 18000, 19200sh
$CoL_2(NCS)_2$acetone$_2$	6850, 7900sh, 14300sh, 18600, 20500
$CoL_2(NCS)_2$ (from acetone)	7200, 8100, 17200, 20400sh
$CoL_2(NCS)_2(DMF)_2$^{a}	7100, 15000sh, 18500, 19600sh, 20400sh
$CoL_2(NCS)_2$ (from DMF)	6450, 17000sh, 18900, 20400sh
$CoL_3(ClO_4)_2$	6400sh, 7400, 14300sh, 16700, 17500sh, 19500sh, 21500
NiL_2Cl_2	7900^{b}, 12500, 13300sh, 17900sh, 22450
NiL_2Br_2	7800^{b}, 12700, 23800
NiL_2I_2	7700, 12900, 20400sh, 23800sh, 27000
$NiL_2(NO_3)_2$	6800, 9000sh, 9500, 13300sh, 14500, 24100
$NiL_2(NCS)_2(DMF)_2$^{a}	7400, 9300sh, 13300sh, 15000, 24400
$NiL_2(NCS)_2$	7300, 9400sh, 13300sh, 14900, 24700
$NiL_3(ClO_4)_2$	8600, 12700sh, 14000, 22000sh, 24700

^{a}DMF = dimethylformamide. ^{b}Broadened to low energy.

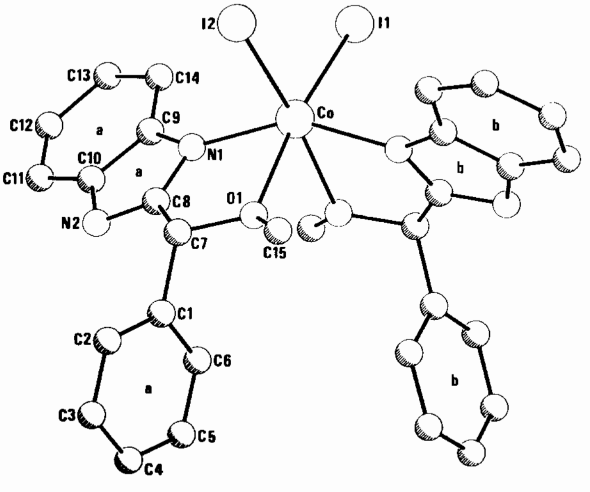

Fig. 1. Molecular structure of Co(2-α-methoxybenzylbenzimidazole)$_2$I$_2$. The two ligands are labelled (a) and (b), and these letters are incorporated in the atom numbers in Tables II and III.

and the large volume of the halogen atoms. The former can be seen in the intraligand N–Co–O angles, which average only 73.9°, compared with the corresponding interligand angles of 84.2°. The second effect not only causes the expected opening of the I–Co–I angle to 101.5°, but also smaller distortions in the I–Co–N angles, due to interactions with the H(14) atoms. The severe distortion of the N–Co–N angle (150.6°) probably results from both effects.

The Co–I distances (mean 2.780 Å) are intermediate between 2.692(6) Å found in $[CoI_2(CNC_6H_4Me)_4]$ [10] and 2.840(5) and 2.853(4) Å in $[CoI_2(CNC_6H_3Et_2)_4]$ [11], and similar to 2.765(2) Å for the terminal bonds [11] of $[I{-}Co(CNC_6H_5)_4{-}I{-}Co(CNC_6H_5)_4{-}I]^+$. However in all these compounds the I atoms are *trans* to one another; we are aware of no diffraction studies on compounds with a *cis*-CoI$_2$ grouping.

The Co–O distances of 2.302(4) and 2.345(5) Å are significantly longer than the average of 2.08 Å found in octahedral Co(II) complexes [12], and correspond to weak interactions as expected for ether oxygens. Comparable values were found in Co(II) complexes with macrocyclic polyether ligands, such as $[Co(12\text{-crown-}4)(NO_3)_2]$ [13] $[Co(15\text{-crown-}5)(H_2O)_2]^{2+}$ [13] and the cryptate-221 $[Co(C_{16}H_{32}O_5N_2)]^{2-}$ [13] in all of which the metal ion is heptacoordinate, these compounds giving a range of 2.096 to 2.347 Å for the Co–O bond lengths. The values for CoL_2I_2 are therefore at the longer end of the range.

Long metal–oxygen distances are also found in complexes containing bidentate NO_3^- groups, where the M–O bonds are severely strained because of

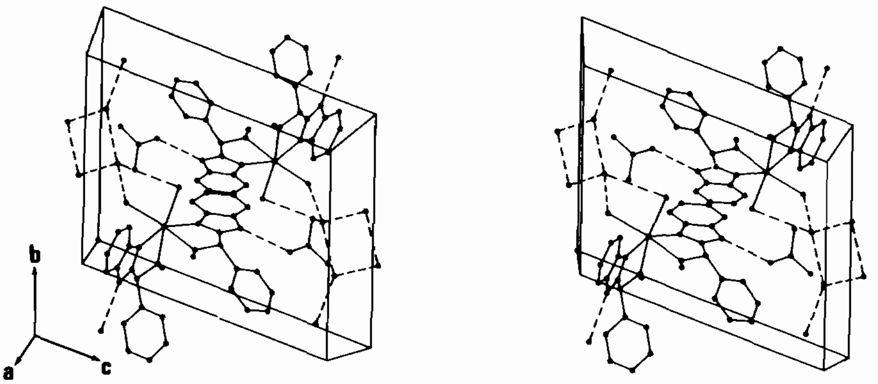

Fig. 2. Stereoscopic drawing of the packing of the various components in the crystal structure of CoL_2I_2·acetone·$2H_2O$.

the small O–M–O angle. For example, in $Co(py)_3(NO_3)_2$, in which the NO_3^- groups are bidentate [14] the lengths are 2.207(9) and 2.311(9) Å. However, it must be pointed out that the bite angle of NO_3^- (*ca.* 56°) is considerably smaller than that of L (av. 73.9°).

All the bond lengths and bond angles in the ligands are within normal values, and the complex has an approximate (non-crystallographic) two-fold axis.

The four phenyl and benzimidazole ring systems all have good planarity, with maximum deviations from mean planes of about 0.02 Å. In each ligand the C(7) atom is coplanar with both ring systems. The five-member chelate rings (Co, O(1), C(7), C(8) and N(1)) have puckered conformations, and here there is a difference between the two ligands. In (a), C(7) is 0.28 Å out of the plane of the other four atoms (rmsd = 0.007 Å), while in (b) it is O(1) which is 0.35 Å out of the plane (rmsd = 0.012 Å).

In the crystal structure there are two water and one acetone molecules of solvation per complex molecule. (There is evidence of some degree of disorder in the acetone molecule). A network of hydrogen bonds of type N–H···O (water), O–H···O(water) and O–H···I links the complex and the water molecules. In the latter bonds O···I distances are 3.53 and 3.65 Å, in good agreement with the average value of 3.53 Å compiled by Pimental and McClellan for this type of bond [15]. In addition, there are bonds of the type N–H···O (acetone). The hydrogen-bond network is two-dimensional, essentially in the *b c* plane. The packing of the various components of the structure is shown as a stereoscopic drawing in Fig. 2.

Effect of Solvent on the Product

Reaction of cobalt iodide with L in dimethylformamide yielded pink crystals containing two moles of the solvent per formula weight. The electronic spectrum was typical of an octahedral cobalt(II) species, with no indication of an approach to tetrahedral geometry or of the low-energy charge-transfer absorption often associated with coordinated iodide. The infrared spectrum suggests that L is chelating, and that the dimethylformamide may be bound to the metal (see below). The solvent is certainly very difficult to remove, some being retained even after prolonged heating at 130 °C *in vacuo,* and also on recrystallisation from acetone.

When attempts are made to remove the dimethylformamide by heating *in vacuo,* the compound rapidly turns green, even though little solvent is lost at this stage. Complete desolvation was achieved by prolonged heating, followed by refluxing in carbon tetrachloride for 3 days, to give a slightly impure green product, essentially CoL_2I_2.

The solution of CoL_2I_2·acetone·$2H_2O$ in acetone is also deep green. Its visible spectrum shows bands near 14300 and 15200 as found for green solid CoL_2I_2, but there are additional bands of similar intensity near 13300 and 13900 cm^{-1}, suggesting some decomposition in solution. However, we believe that the green form of CoL_2I_2 may have a CoN_2I_2 tetrahedral chromophore, similar to that of $Co(benzimidazole)_2I_2$, which absorbs [8] at 14500 and 15200 cm^{-1}.

Infrared Spectra

All of the nickel complexes seem from their electronic spectra and magnetic moments to be essentially octahedral, and for $NiL_3(ClO_4)_2$ it is reasonable to assume that the ligand is chelating. Comparison of the infrared spectra of this compound, and of CoL_2I_2 of known structure, with those of CoL_2Cl_2 and CoL_2Br_2, in which the ligand is monodentate, shows general similarity, but small differences near 1100 and 700–800 cm^{-1}, which seem to depend on the mode of coordination. The most definite difference is the shift of the intense C–O stretch of the ether group, which is at 1110 cm^{-1} in the free ligand, to lower energy (*ca.* 1070–1080 cm^{-1}) on chelation.

Using this criterion, the ligand appears to be chelating in NiL_2Cl_2, which has ν(C–O) at 1072 cm^{-1}, and an electronic spectrum and magnetic moment typical of a nickel ion with 2 strong and 4 weak ligands. The bromide and iodide are very similar. Chelation is almost certainly also present in $NiL_2(NCS)_2$ and in $CoL_2(NCS)_2$ obtained from the dimethylformamide solvate. These are isomorphous, and have electronic spectra typical of these metals in distorted octahedral coordination. Bridging thiocyanate can be ruled out from the position (*ca.* 2060 cm^{-1}) of ν(C≡N).

In $ML_2(NCS)_2(DMF)_2$ however, ν(C–O) of the ether is at 1100 cm^{-1}, and the bands at 700–800 cm^{-1} resemble those of CoL_2Cl_2, suggesting that the ligand is bonded through nitrogen only. It is not clear whether the 6-coordination suggested by the electronic spectra arises from bridging thiocyanate ions or from coordinated dimethylformamide. The ν(C≡N) band, at 2100–2105 cm^{-1}, is considerably raised compared with the unsolvated complexes, but is still rather low for strongly bridging thiocyanate. The ν(C=O) of the dimethylformamide (1657 cm^{-1}) is in a very similar position to that in $CoL_2I_2(DMF)_2$ (1660 cm^{-1}), but a frequency of 1661 cm^{-1} is also observed when dimethylformamide is hydrogen-bonded to a pyrrole NH [16].

The position of the N–C=O deformation has been suggested [17] as a criterion of coordination for dimethylformamide, though the effect of hydrogen bonding, which may well be similar to that of coordination, was not considered. Binding to a divalent ion of the first transition series raises the frequency from 657 to *ca.* 675–696 cm^{-1}, sometimes with splitting, the greater increase being associated with stronger bonding. For $CoL_2I_2(DMF)_2$ a band at 692 cm^{-1} disappears, and one at 672 cm^{-1} is somewhat weakened, on desolvation. For the thiocyanates the corresponding bands, which disappear on heating, are at 670 cm^{-1}. What is clear is that, whether by coordination or by hydrogen bonding, dimethylformamide binds strongly to these complexes.

The complex $CoL_2(NCS)_2$ may also be obtained as an acetone adduct. The solvent is lost on heating *in vacuo*, but the product appears to differ from that obtained from the dimethylformamide adduct. The magnetic moment of 4.60, compared with 4.98 for the product from dimethylformamide, together with the electronic spectrum (Table IV) suggests that the compound from acetone bears more resemblance to a tetrahedron.

Discussion

The structural results for CoL_2I_2 explain the difficulty of assigning an approximate structure from the electronic spectrum. While the metal ion is formally 6-coordinate, the long Co–O distances, and distortion of the bond angles, result in a chromophore which in some ways resembles a tetrahedron almost as much as an octahedron. For example, of the angles within the CoN_2I_2 unit, three are closer to 109 than to 90°. The Co–N distances (2.097(5) Å) are intermediate between the average values of 2.00 and 2.16 Å for tetrahedral and octahedral complexes respectively [12]. The lack of even an approximate centre of symmetry accounts for the high intensity of the electronic spectral bands.

It appears that there is an increasing cobalt–oxygen interaction from the chloro- to the iodo-complex. The nickel–oxygen bonding, on the other hand, is strong throughout the series, and some degree of chelation seems to be normal for this ligand. There is therefore no need to postulate dealkylation to account for the *in vivo* activity.

One interesting feature of the complexes is the strength with which they bind acetone and dimethylformamide. The bonds are difficult to break, and there is considerable reduction of the C=O stretching frequency. It seems possible that the mode of antiviral action involves binding of the complex to protein molecules via the amide C=O.

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