Inorganica Chimica Acta, 46 (1980) 181–184
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Chelation by 1,4,6-Trimethylpyrimidine-2-one with some First Transition Series Metal Ions

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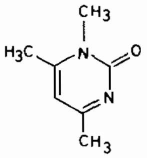
Received February 14, 1980

Preparations are reported of complexes of 1,4,6-trimethylpyrimidine-2-one with the divalent metal ions manganese to zinc. With manganese and nickel salts of weakly coordinating anions, tris-chelate complexes $[ML_3]^{2+}$ *are formed, probably with a facial arrangement of ligands. With the other metal ions, N-bonded pyrimidinones are present. The two modes of coordination may be distinguished by their infrared spectra in the* $\nu(C=O)$ *region.*

Introduction

With the binding of heavy metals to nucleotide bases now well-established, a question of continuing interest is the possibility of interaction between the metal ion and the exocyclic oxygen atom of pyrimidinones. Uracils have recently been shown to bind strongly to metals ions [1] and, when deprotonated, even to chelate [2]. Indeed, such binding may have considerable effect on the conformations of nucleic acids [3]. However, with bases such as cytosine and guanine, which in the uncharged state contain unprotonated ring nitrogen atoms, it is normally the nitrogen, rather than the keto-oxygen, which binds strongly to a metal ion, with, at most, a much weaker metal-oxygen interaction. We now report a series of complexes of 1,4,6-trimethylpyrimidine-2-one (I) with divalent metal ions, some of which contain chelating uncharged pyrimidinones.



I

Experimental

The complexes were prepared by the following general method. The metal salts were dissolved in ethanol, plus some dimethoxypropane, and added to a solution of the pyrimidinone in ethyl acetate. In most cases, precipitates were formed after a few minutes heating, but in a few cases diethylether was added to induce precipitation.

For the iron compounds the preparation was carried out under nitrogen. The complex of cobalt perchlorate could be obtained as above, but better crystals were obtained from pure ethanol, and these were used for the structure determination and all measurements.

The compound $Ni_2L_3Br_4$, made by the general method, was obtained as an oil. This was dissolved in ethanol and evaporated to low bulk. After two further such treatments, crystals were obtained. The complex $NiLCl_2$ was made by refluxing nickel chloride with ligand in a mixture of ethyl acetate and 2,2-dimethoxypropane.

Analytical results for the compounds are given in Table I. Physical measurements were made as described previously [4].

Results and Discussion

The compounds we have prepared are listed in Table I. With manganese and nickel salts of weakly coordinating anions, there is a tendency for complexes with a 3:1 ratio of pyrimidinone (= L) to metal ion to be formed, even when other ratios were used in the preparation. The compound $MnL_3(ClO_4)_2$ gives an X-band e.p.r. spectrum consisting of numerous bands, all below 650 mT, indicative of a D value of less than about 0.10 cm^{-1}. A good simulation of this spectrum may be obtained [5] with $D = 0.05\ cm^{-1}$ and $\lambda = 0.01$. The distortion from octahedral micro-symmetry is therefore very small and comparable with that found in some MnL_6^{2+} systems. The lack of magnetic interaction between adjacent manganese ions strongly suggests a monomeric structure for the complex, and the low distortion indicates a facial, rather than meridional, chelation. Such tris-chelates have been reported [6] with the related ligand 1,4,6-trimethylpyrimidine-2-thione, the manganese complex of which gives a very similar e.p.r. spectrum to the one reported here.

TABLE I. Analytical Results for Complexes of 1,4,6-Trimethylpyrimidinone.

Compound	Colour	% Found			% Calculated		
		C	H	N	C	H	N
$MnL_2Cl_2 \cdot 7H_2O$	Pale Pink	32.02	5.87	10.49	31.83	6.49	10.60
$MnL_2Br_2 \cdot 3H_2O$	Pale Pink	31.02	4.96	10.29	30.84	4.81	10.28
$MnL_4I_2 \cdot 2H_2O$	Pale Pink	37.12	5.19	12.40	37.47	4.94	12.48
$MnL_3(ClO_4)_2$	Pale Pink	37.74	4.41	12.14	37.73	4.52	12.57
FeL_2Cl_2	Yellow	39.50	4.62	13.04	41.72	5.00	13.90
FeL_2Br_2	Yellow	33.80	4.00	10.69	34.18	4.10	11.39
CoL_2Cl_2	Royal Blue	41.06	5.00	14.45	41.40	4.96	13.79
CoL_2Br_2	Royal Blue	34.10	4.10	11.17	33.96	4.07	11.32
CoL_2I_2	Turquoise	30.21	3.56	9.28	28.54	3.42	9.51
$CoL_4(ClO_4)_2$	Cerise	41.80	5.35	13.45	41.49	4.97	13.82
$CoL_2(NO_3)_2$	Cerise	36.29	3.88	18.33	36.61	4.39	18.29
$NiLCl_2$	Salmon	31.67	4.64	10.47	31.40	3.76	10.46
NiL_2Br_2	Red	33.94	4.05	11.27	33.97	4.07	11.32
NiL_2Br_2	Orange	34.03	4.02	11.55	33.97	4.07	11.32
$Ni_2L_3Br_4$	Green	29.67	3.55	9.83	29.62	3.55	9.87
$Ni_2L_3Br_4 \cdot 12H_2O$	Pale Green	23.81	4.49	7.96	23.62	4.91	7.87
NiL_3I_2	Green	34.41	3.88	11.00	34.69	4.16	11.56
$NiL_3(NO_3)_2$	Green	42.25	4.53	18.89	42.22	5.06	18.76
CuL_2Cl_2	Blue-grey	40.65	4.92	13.39	40.93	4.91	13.64
CuL_2Br_2	Yellow-green	33.68	4.16	10.78	33.65	4.03	11.21
$CuL_4(ClO_4)_2 \cdot C_2H_5OH$	Grey-green	41.64	5.03	12.40	41.83	5.38	13.00
ZnL_2Cl_2	White	39.74	4.43	13.17	40.75	4.89	13.58
ZnL_2Br_2	White	33.29	3.96	11.25	33.53	4.02	11.17
ZnL_2I_2	White	29.10	3.48	9.49	28.24	3.38	9.41
$ZnL_4(ClO_4)_2$	White	41.19	4.86	13.74	41.17	4.93	13.72
$ZnL_2(NO_3)_2$	White	36.02	4.47	17.88	36.11	4.33	18.04

TABLE II. Diffuse Reflectance Spectra of Complexes of 1,4,6-Trimethylpyrimidinone.

FeL_2Cl_2	4440vs, 7140vs
FeL_2Br_2	4290vs, 6670vs
CoL_2Cl_2	7380vs, 16390vs, 17860sh, 18350sh, 19160sh, 20830sh
CoL_2Br_2	7300vs, 15750vs, 16670sh, 17700sh
CoL_2I_2	7140vs, 13330sh, 15380vs, 16860sh, 20320sh
$CoL_4(ClO_4)_2$	9300s, 18350vs, 19230sh, 21600sh, 23200sh
$CoL_2(NO_3)_2$	8160sh, 9520s, 18350vs
$NiLCl_2$	6900w, br, 12120m, 13330sh, 19610sh, 22220s
$Ni_2L_3Br_4$	6670†m, 8510sh, 12740s, 14290vs, 19300sh, 21190sh
$Ni_2L_3Br_4 \cdot 12H_2O$	6670w, 8130w, br, 13890w, br, 18520sh, 25000m
NiL_2Br_2 (red)	6490w, br, 11500s, 20790vs
NiL_3I_2	8690ms, 14290ms, 20320sh, 23810*sh
$NiL_3(NO_3)_2$	8700ms, 14490s, 20410sh, 25000vs
CuL_2Cl_2	17240s
CuL_2Br_2	16260s
$CuL_4(ClO_4)_2 \cdot C_2H_5OH$	17700s, br

†Absorption below 5000 cm^{-1}. *Partially obscured by charge-transfer band.

The electronic spectra (Table II) of $NiL_3(NO_3)_2$ and NiL_3I_2 are very similar to one another, showing the three unsplit bands expected for a regular octahedron with $\Delta = ca.$ 8700 cm^{-1}, a reasonable value for an NiN_3O_3 chromophore. The band intensity, however, is somewhat higher than that normally seen for a regular octahedron, suggesting, again, a facial arrangement of ligands.

These two compounds both show a strong band in the infrared spectrum at about 260 cm^{-1}, which we assign to a mode having appreciable metal–ligand stretching character, but necessarily involving also movement of the whole chelate ring. The manganese chelate complex $MnL_3(ClO_4)_2$ shows a similar strong band at 245 cm^{-1}. In the 1600 cm^{-1} region, 1,4,6-trimethylpyrimidine-2-one has a strong, composite band with components at about 1585, 1607 and 1650 cm^{-1}, and a slightly weaker band at 1545 cm^{-1}. In the chelated complexes, the three components of the 1600 cm^{-1} band are much less well resolved. For $MnL_3(ClO_4)_2$ three components can still be seen, at 1573, 1593 and 1613 cm^{-1}, but for the nickel compounds there is only a strong broad band centred on about 1580 cm^{-1} (Fig. 1). The 1545 cm^{-1} band has disappeared in these chelates, presumably having moved either to higher energy, near 1580 cm^{-1}, or to much lower energy. Spectra in KBr discs show strong absorption near 1440 cm^{-1}, but the ligand itself has a band at 1432 cm^{-1}.

With nickel bromide two different compounds are obtained, depending on the ratio of ligand to metal ion used for the preparation. With a 1:1 ratio, the green complex formed has the stoichiometry $NiL_{1.5}Br_2$. Its electronic spectrum shows bands indicative of both an octahedral and a tetrahedral species (Table II). The intense bands are very similar to those of the $NiBr_4^{2-}$ ion [7], while the remaining bands are reasonably consistent with the presence of a $[NiL_3]^{2+}$ chelated cation. The far infrared spectrum is very similar to that of $NiL_3(NO_3)_2$, with the addition of a very strong band at 240 cm^{-1}, assigned as ν(NiBr). This is a little higher than the value reported [8] for the $NiBr_4^{2-}$ ion. The formulation of the compound as NiL_3^{2+} $NiBr_4^{2-}$ seems reasonable.

This compound rapidly picks up water from the atmosphere to give a pale green compound of stoichiometry $Ni_2L_3Br_4 \cdot 12H_2O$. Its electronic spectrum is indicative of $Ni(H_2O)_6^{2+}$ cations, and the far infrared spectrum shows no bands definitely assignable as metal–ligand vibrations. Instead, there is a broad band at about 335 cm^{-1} as commonly found for aqua-ions.

When nickel bromide reacts under anhydrous conditions with the ligand in 1:2 mol ratio, a bright red compound of stoichiometry NiL_2Br_2 is formed. In moist air it quickly becomes orange-brown, and eventually decomposes. The red compound has a magnetic moment of 3.47. The positions of the bands in the electronic spectrum are consistent with the presence of an octahedron of ligands, albeit with a rather weak crystal field (Δ = ca. 6500 cm^{-1}). However, the bands are very intense, resembling, in this respect, the bands of tetrahedral nickel(II) species. An octahedral crystal field with such a low Δ value is normally found only with very weak-field ligands such as halide ions, (e.g., Δ for $NiCl_3^-$ is 6600 cm^{-1} [9]) and the value suggests that perhaps this compound has an N_2Br_4 octahedron, with bridging bromide ions. However, this should give a split $^3A_{2g} \rightarrow {}^3T_{2g}$ transition, whereas the band observed is unsplit. Moreover, the far infrared spectrum shows a very strong band at 225 cm^{-1}, which is most reasonably assigned as due to Ni–Br stretching. This value is intermediate between those normally found for octahedral and tetrahedral complexes with terminal nickel–bromide bonds. It is inconsistent with a chain structure based on bridging bromide ions. What seems most probable is a structure intermediate between an octahedron and a tetrahedron, as found for the cobalt complex of pyrimidine-2-thione [10]. The nickel would then be surrounded by an approximately tetrahedral N_2Br_2 arrangement, with two somewhat weaker Ni–O bonds completing a very distorted *cis*-octahedral array.

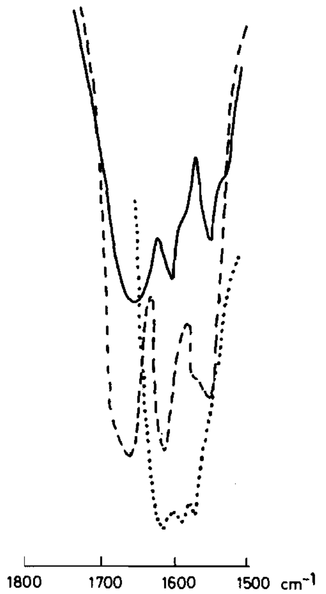


Fig. 1. Infrared spectra (1500–1800 cm^{-1}) of ——— 1,4,6-trimethylpyrimidine-2-one (= L); – – – – $CoL_4(ClO_4)_2$; ········· $MnL_3(ClO_4)_2$.

Despite variations in the ratio of ligand to metal ion, the only complexes obtained from nickel chloride had 1:1 stoichiometry. Under strictly anhydrous conditions, a pink complex $NiLCl_2$ is obtained. Its electronic spectrum indicates an essentially octahedral structure, being similar to that of NiquinolineCl_2. A very strong infrared band at 273 cm^{-1} is then reasonably assigned as ν(Ni–Cl) of a double-stranded chloride-bridged chain structure [11]. This band is broadened to low energy, and could conceal another band near 250 cm^{-1}. Strong bands at 281 and 256 cm^{-1} are reported [11] for NipyridineCl_2.

With the manganese halides, only hydrated complexes were formed. The e.p.r. spectrum of the chloride gives only a $g_{eff} = 2$ signal, indicative of magnetic exchange within the lattice, though whether this is through chloride bridges or hydrogen-bonding interactions is not clear. The bromo-complex, in contrast, gives its strongest line at $g_{eff} = 3.75$, and numerous weaker transitions extending to high field. This is indicative of either an MnL_2Br_2 tetrahedron, or a rhombically distorted octahedron. The low energy infrared spectrum shows no evidence of coordinated water, and is in fact very similar to that of NiL_2Br_2, with ν(M–Br) at slightly lower energy.

In contrast to this tendency to chelation with manganese and nickel, with cobalt tetrahedral complexes are readily formed. Cobalt perchlorate reacts with four moles of ligand in ethanol to yield $CoL_4(ClO_4)_2$, the X-ray structure of which has been determined. Full details will be published elsewhere [12], but it may be noted here that it contains CoL_4^{2+} with a distorted tetrahedron of nitrogen atoms round the cobalt ion. The pyrimidinone oxygen atoms are also fairly close to the metal ion (2.7–2.8 Å) but at this distance any bonding interaction must be quite weak.

With the cobalt halides, complexes CoL_2X_2 are formed, which have normal electronic spectra for CoN_2X_2 chromophores, and ν(Co–X) in the normal range for such species. In the 1600 cm^{-1} region, for these compounds, as for CoL_4^{2+}, three bands are clearly resolved, one near 1550 cm^{-1}, and two very strong bands near 1600 and 1650 cm^{-1} (Fig. 1), affording a reasonably clear distinction from the compounds containing chelating L.

The zinc complexes are very similar to those of cobalt. The stoichiometries are the same throughout the series, the two perchlorates are isomorphous, and the halides give similar infrared spectra in both the 1600 cm^{-1} and the low energy region. On the basis of infrared and electronic spectra, the ferrous complexes also appear to have FeN_2X_2 tetrahedral structures.

The complexes formed with copper(II) ions are similar to those of pyrimidine-2-one and of cytosine. These contain [13, 14] N-bonded ligands, with the carbonyl oxygens in position to form very weak M–O bonds. The infrared spectra of the trimethylpyrimidinone compounds are consistent with essentially N-bonding.

Conclusions

It is clear that under some conditions pyrimidinones can chelate to metal ions, though this tendency is much less dominant than with the thiones. As with the corresponding thiones, chelation is greatly enhanced in 1,4,6-trimethylpyrimidine-2-one compared with pyrimidine-2-one itself.

Amongst the compounds reported here, chelation is limited to compounds of manganese and nickel, and may well be related to the desire of the metal ion to achieve octahedral coordination. Moreover, strong chelation appears only in the tris-chelates ML_3^{2+}, formed in the presence of rather weakly-coordinating, bulky anions. The achievement of an octahedral ligand field without chelation requires either a stoichiometry ML_4X_2, or ML_2X_2 with bidentate (possibly bridging) anions. The first of these would involve very considerable steric crowding, and the second, with anions such as nitrate and bromide, may give lower overall bond energies than those achieved by chelation.

The situation in biological molecules, where it is unlikely that more than one pyrimidinone ligand is coordinated, will be considerably different. However, it is clear that the keto-oxygen is capable of filling a coordination site, especially when steric factors are favourable for this.

Acknowledgements

We thank the SRC for a studenthsip (to K. W. J.) and Dr. J. F. Gibson for the use of computer programs.

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