



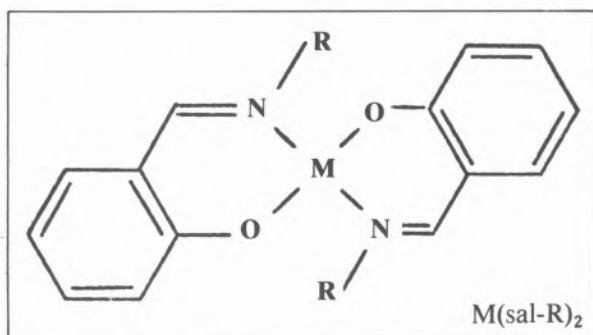
PS5.26 — TH

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KINETICS OF LIGAND SUBSTITUTION IN CHELATE COMPLEXES OF DIVALENT TRANSITION METALS OF BIOLOGICAL IMPORTANCE

The bis chelate complexes $M(\text{sal-R})_2$ of divalent transition metals M^{2+} ($M = \text{Co}, \text{Ni}, \text{Cu}, \text{Zn}$) with various *N*-alkyl salicylaldimines Hsal-R ($R = \text{Et}, n\text{-Pr}, i\text{-Pr}, t\text{-Bu}, \text{neo-Pe}, \text{Ph}$) have been prepared by standard procedures and characterized.



Stopped-flow spectrophotometry has been used to study the reactivity of these complexes towards ligand substitution with acetylacetone (Hacac) in methanol under pseudo first-order conditions ($[\text{Hacac}]_0 \gg [\text{M}(\text{sal-R})_2]_0$) according to (1):



The experimental rate law is a two-term rate law:

$$\text{rate} = (k_S + k_{\text{Hacac}}[\text{Hacac}])[M(\text{sal-R})_2] \quad (2)$$

The substitution of the first ligand in $M(\text{sal-R})_2$ is rate determining, *i.e.*, the conversion

$M(\text{sal-R})(\text{acac}) \rightarrow M(\text{acac})_2$ is a fast consecutive step.

The relative contributions of the terms k_S and $k_{\text{Hacac}}[\text{Hacac}]$ in (2) to the overall rate are mainly controlled by two factors, namely, (i) by the type of the *N*-alkyl group R for a given metal M , and, (ii) by the type of metal M for a given *N*-alkyl group R .

The data obtained for k_S and k_{Hacac} at 25°C for the 24 reactions studied are presented. The rate constants range from $k_S \approx 0$ ($M = \text{Ni}$; $R = \text{Et}, i\text{-Pr}, \text{neo-Pe}$) to $k_S = 18.5 \text{ s}^{-1}$ ($M = \text{Zn}$; $R = \text{Ph}$) and from $k_{\text{Hacac}} \approx 0$ ($M = \text{Cu}, \text{Zn}$; $R = t\text{-Bu}$) to $k_{\text{Hacac}} = 2070 \text{ M}^{-1} \text{ s}^{-1}$ ($M = \text{Ni}$; $R = \text{Et}$). The trends observed for the reactivity of the various complexes are correlated with their coordination geometry (as controlled by the *N*-alkyl group R) and with the intimate mechanism of both the solvent-induced pathway k_S and the ligand-dependent pathway $k_{\text{Hacac}}[\text{Hacac}]$.



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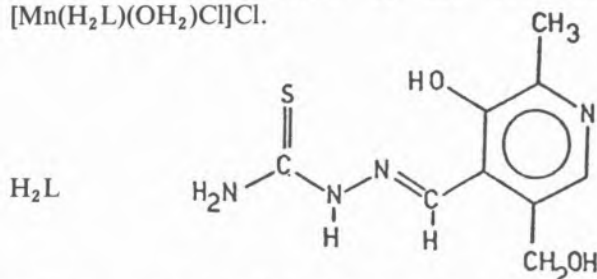
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COORDINATING PROPERTIES OF PYRIDOXAL THIOSEMICARBAZONE IN METAL COMPLEXES

The study of transition metal complexes of thiosemicarbazones is of great interest because of their pharmacological properties [1-3]. As part of a continuing interest in the chelating behaviour of ligands which have biological activities and the

coordinating properties of *S,N*-containing ligands [4], chemical and structural investigations of metal complexes of thiosemicarbazones are now in progress in our laboratory.

The present communication deals with the synthesis and the spectroscopic characterization of a series of Mn, Co, Ni, Cu, and Zn complexes with pyridoxal thiosemicarbazone (H_2L) and the X-ray crystal structure of the complex $[Mn(H_2L)(OH_2)Cl]Cl$.



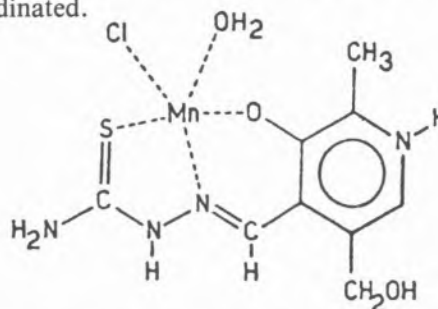
The combination of the pyridoxal moiety, which shows biological activity in several enzymatic reactions, with the thiosemicarbazone system confers to the final product interesting chelating properties.

H_2L was synthesised by the reaction of thiosemicarbazide with pyridoxal in alcoholic medium. Characterization of the ligand was made by IR and 1H NMR spectroscopies and mass spectrometry.

Metal complexes were obtained by reacting H_2L with the equimolar amount of the metal salt (nitrate, chloride or acetate) in ethanol solution. Analytical and spectroscopic data revealed different formulae in connection with the nature of the metal and the inorganic anion. In particular, three types of complexes of formula $M(H_2L)X_2$ ($M=Mn, Zn$; $X=Cl, NO_3$), $M(HL)X$ ($M=Co, Zn$; $X=CH_3COO$; $M=Ni$; $X=NO_3$), and ML ($M=Cu, Ni$) were isolated. Identification of the complexes was mainly made on the basis of the IR spectra, which show bands characteristic of $\nu(NH)$, $\nu(OH)$, $\nu(C=N)$, $\nu(C=S)$. Conspicuous changes were found in the vibrational absorptions of the ligand upon coordination effect. Although definitive assignments for $\nu(C=S)$ vibrations are difficult, the band in the region between 950 and 1050 cm^{-1} is attributable to the stretching vibration of the $C=S$ bond.

In order to gain more information about the structure and stereochemistry of such type of complexes the X-ray crystal structure of

$[Mn(H_2L)(OH_2)Cl]Cl$ was carried out. The crystals are monoclinic, space group $P2_1/n$ with unit-cell dimensions $a=13.902(4)$, $b=9.316(1)$, $c=11.982(3)$ Å, $\beta=107.61(2)^\circ$ and $Z=4$. The structure consists of $[Mn(H_2L)(OH_2)Cl]^+$ cations and Cl^- anions. The ligand behaves as terdentate and the manganese atom is uncommonly five-coordinated.



The cation has a pyramidal tetragonal geometry with a chlorine atom in apical position, the phenolic oxygen atom, a nitrogen atom, the sulphur atom of the organic ligand and the water molecule in the basal plane. This plane shows slight tetrahedral distortion, the manganese atom being 0.59 Å out of the mean basal plane towards the chlorine atom at the apex of the pyramid. The pyridoxal ring corresponds to a dipolar ion, owing to the shift of the proton from the phenolic oxygen atom to the pyridinic nitrogen atom. Bond distances and angles in thiosemicarbazide side chain agree well with those found in various aryl thiosemicarbazones which can be treated as extensively delocalized systems [5]. Packing consists of parallel layers of complex molecules linked by $NH_2...Cl$, $NH...Cl$, $O_w...Cl$, $O_w...OH$ hydrogen bonds. These layers are joined together by other hydrogen bonds of the type $N_{py}...Cl$, $OH...Cl$ to form an intricate network.

Bearing in mind that the nature terdentate of the thiosemicarbazones appears to be a potential feature for antitumor activity, studies on other similar sulphur-ligands and their metal complexes are in progress in our laboratory.

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PS5.28 — TU

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NMR AND SPECTROSCOPIC STUDIES ON THE PYRIDOXAL/GLYCINE/ /DIOXOURANIUM(VI) SYSTEM

In previous communications we have reported some results on formation of dioxouranium(VI) complexes of pyridoxal and pyridoxylideneglycine [1-5].

As it is known, pyridoxal and its derivatives are able to catalyze, in the presence of metal ions, important metabolic reactions of aminoacids through the intermediary formation of Schiff bases metal complexes [6-10].

The pyridoxal/glycine/dioxouranium(VI) system is studied both in the solid state and in solution by IR, electronic, ^1H and ^{13}C NMR spectra.

The results obtained in the solid state are in accord with the formation of a 1:1:1 ternary complex: $\text{UO}_2(\text{C}_{10}\text{H}_{11}\text{N}_2\text{O}_4)\text{XH}_2\text{O}$ (where $\text{X}=\text{CH}_3\text{COO}^-$ or NO_3^-). IR spectra exhibit changes in the regions where the azomethine $\text{C}=\text{N}$ stretching ($\nu_{\text{CN}}=1610\text{ cm}^{-1}$), phenolic $\text{C}=\text{O}$

($\nu_{\text{CO}}=1510\text{ cm}^{-1}$) and the asymmetric carboxyl stretching ($\nu_{\text{COO}^-}=1570\text{ cm}^{-1}$) respectively occur.

The electronic spectra of an equimolar methanol solution of pyridoxal and glycine exhibit bands near 360 nm and 320 nm. Such absorptions markedly increase as a function of time when dioxouranium(VI) is added in equimolar amount and are shifted to 390 nm and 343 nm respectively. Furthermore two isosbestic points are formed at 290 nm and 275 nm. The final spectrum is very near to that of the complex prepared at the solid state. The ^1H and ^{13}C NMR spectra of the pyridoxal/glycine/dioxouranium(VI) system has been then examined in D_2O at pH 3.55 (at higher pH values precipitation occurs) in order to verify the formation of aldimine complexes induced by UO_2^{2+} .

Tables I and II show respectively proton and ^{13}C chemical shifts of pyridoxal and glycine solutions at varying molar ratios with uranyl nitrate. Large chemical shift changes are observed for C-4'-H, C-6-H and 2'- CH_3 pyridoxal protons and for $\alpha\text{-CH}_2$ glycine protons (Table I) upon complex formation and metal ion binding. In order to gain informations on the pyridoxylideneglycine complex, ^1H chemical shifts were measured in DMSO-d_6 . In addition to the remarkable proton chemical shift variation, in particular of the aldehydic C-4'-H hydrogen ($\Delta=1.14\text{ ppm}$), the progressive disappearance of the $-\text{NH}_2$ resonance signal is in accord with the formation of the Schiff base and metal ion complexation. Furthermore, a new signal of intensity one appears at 9.60 ppm, characteristic of a proton bound to the pyrimidine nitrogen donor.

Table I

^1H NMR chemical shifts (δ/ppm)^{a)} of free pyridoxal hydrochloride (HPL)/glycine (Gly) system and UO_2 nitrate solutions in D_2O at pH=3.55

Compound	molar ratio	C-6-H	C-4'-H	5'- CH_2	$\alpha\text{-CH}_2$	2'- CH_3
HPL + Gly	1:1	8.08,1H	6.67,1H	5.22,2H	3.69,2H	2.60,3H
HPL + Gly + UO_2 nitrate	1:1:0.25	8.00,1H	6.62,1H	5.18,2H	3.66,2H	2.60,3H
HPL + Gly + UO_2 nitrate	1:1:0.50	7.90,1H	6.85,1H	5.20,2H	3.60,2H	2.70,3H
HPL + Gly + UO_2 nitrate	1:1:1	7.78,1H	7.30,1H	5.12,2H	3.56,2H	2.87,3H
HPL + Gly + UO_2 nitrate	1:1:2	7.77,1H	7.28,1H	5.28,2H	3.37,2H	2.86,3H
$\Delta\text{ ppm}$	=	-0.31	+0.61	+0.06	-0.32 *	+0.26

a) ^1H NMR chemical shifts are measured downfield from TMS, using dioxane as an internal standard.