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Preparation and Characterization of Iron(III) Complexes of 2-pyridinecarboxaldehyde Thiosemicarbazone

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The iron(III) complexes of 2-pyridinecarboxaldehyde thiosemicarbazone with an appropriate anion such as NO_3^-, Cl^-, N_3^-, NCS^- *and* CN^-, *have been prepared. The data of the elemental analysis, magnetic measurements, infrared spectra and EPR spectra of these complexes have been analysed to characterize the complexes. It has been concluded that the 2-pyridinecarboxaldehyde thiosemicarbazone is coordinated to iron(III) ion in the ratio of 2:1. The anions are associated to the low-spin iron(III) in the polycrystalline complexes. The molar conductances of these complexes in dimethylformamide solution have also been interpreted in terms of some association of anions to iron(III).*

Introduction

Recently, Spingarn and Sartorelli [1] have synthesized several thiosemicarbazones of 2-pyridinecarboxaldehyde and related compounds and evaluated the relative ability of 2-pyridinecarboxaldehyde thiosemicarbazone and related compounds to remove iron from model systems designed to mimic particular aspects of chronic transfusional iron overload. The 2-pyrazinecarboxaldehyde thiosemicarbazone has been found to be more effective in reducing tissue iron levels than the deferoxamine, which is used for removing excess iron accumulated in tissues of patients with Cooley's anemia [2, 3]. The 2-pyridinecarboxaldehyde and 2-pyrazinecarboxaldehyde thiosemicarbazones behave as tridentate ligands, with two nitrogens and one sulphur as donor atoms. The 2-pyridinecarboxaldehyde thiosemicarbazone is simpler in structure than 2-pyrazinecarboxaldehyde thiosemicarbazone because the latter has one additional nitrogen donor in the pyridine ring. The iron(II) complex of 2-pyridinecarboxaldehyde thiosemicarbazone in ratio of 1:2 has been isolated and it shows a substantial inhibitory effect against tumor cells [4, 5]. On the other hand, the iron(III) complex of 2-pyridinecarboxaldehyde thiosemicarbazone is not isolated. Therefore, the synthesis and characterization of several new iron(III) complexes of 2-pyridinecarboxaldehyde thiosemicarbazone in ratios of 1:2 with five anions have been reported here. They are all low-spin iron(III) complexes at room temperature.

Experimental

Materials

Ferric chloride was purchased from Polypharm, India. 2-Pyridinecarboxaldehyde and thiosemicarbazide were purchased from Koch-Light, England, and Fluka AG, Switzerland respectively. All other reagents were of the highest grade commercially avaiable.

2-Pyridinecarboxaldehyde thiosemicarbazone (abbreviated as PT and its anion with −1 charge as PT–H) was prepared by refluxing equimolecular quantities of 2-pyridinecarboxaldehyde and thiosemicarbazide in methanol for one hour. The solution was cooled and the precipitate obtained was filtered. The precipitate was washed with cold methanol. It was recrystallized from ethanol and dried in a dessicator over anhydrous $CaCl_2$ (m.p. 195–196 °C) [6].

$Fe(PT{-}H)_2NO_3$

$FeCl_3$ (1 mmol) was dissolved in water containing a small quantity of dilute HCl. NH_4OH solution in excess was added dropwise to obtain the precipitate of $Fe(OH)_3$. The $Fe(OH)_3$ precipitate was washed with distilled water to remove all chloride ions. This hydroxide precipitate was dissolved in minimum quantity of dilute HNO_3. This solution of iron(III) ions was mixed with a solution of the ligand (2 mmol) in methanol. This mixed solution was first stirred for 3–4 hours and then concentrated at room temperature. Brown crystals were obtained, which were filtered, washed with cold methanol and dried in a dissicator over anhydrous $CaCl_2$. *Anal.* Found: C, 35.1; H, 2.8; N, 26.5. Calcd. for $C_{14}H_{14}N_8S_2Fe(NO_3)$: C, 35.3; H, 2.96; N, 26.46.

$Fe(PT{-}H)_2Cl$

$FeCl_3$ (1 mmol) was dissolved in water containing a minimum quantity of dilute HCl. This solution was mixed with a solution of the ligand (2 mmol) in ethanol. The mixed solution was stirred for 3–4 hours. This solution was concentrated at room temperature. The yellow crystals obtained were washed with cold methanol and dried in a dessicator over

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anhydrous $CaCl_2$. *Anal.* Found: C, 37.1; H, 3.10; N, 24.8. Calcd. for $C_{14}H_{14}N_8S_2Fe(Cl)$: C, 37.38; H, 3.13; N, 24.91.

Fe(PT–H)$_2$N$_3$

$FeCl_3$ (1 mmol) was dissolved in water containing a minimum quantity of dilute HCl. This solution was mixed with the solution of the ligand (2 mmol) in methanol. The mixed solution was stirred for one hour. A concentrated NaN_3 (25 mmol) solution was added to the above solution. The resulting solution was concentrated at room temperature. The black crystals obtained were washed with cold methanol and dried in a dessicator over anhydrous $CaCl_2$. *Anal.* Found: C, 36.7; H, 3.1; N, 33.7. Calcd. for $C_{14}H_{14}N_8S_2Fe(N_3)$: C, 36.85; H, 3.09; N, 33.76.

Fe(PT–H)$_2$NCS

This compound was prepared by following a procedure similar to $Fe(PT–H)_2N_3$, except 25 mmol of KNCS was added in place of NaN_3. The crystals produced were yellow. *Anal.* Found: C, 38.1; H, 2.9; N, 26.6. Calcd. for $C_{14}H_{14}N_8S_2Fe(NCS)$: C, 38.14; H, 2.98; N, 26.68.

Fe(PT–H)$_2$CN

This compound was also prepared by following a procedure similar to $Fe(PT–H)_2N_3$, except 1.2 mmol of KCN was added in place of NaN_3. The crystals produced were brown. *Anal.* Found: C, 40.8; H, 3.3; N, 28.5. Calcd. for $C_{14}H_{14}N_8S_2Fe(CN)$: C, 40.91; H, 3.20; N, 28.62.

Physical Measurements

For magnetic susceptibility measurements, the Gouy method was employed. $Hg[Co(NCS)_4]$ was used as the standard. Diamagnetic corrections were also applied using Pascal's constants from the literature [7]. The electron paramagnetic resonance (EPR) spectra of polycrystalline samples were recorded on a Varian E-112 Spectrometer (X-band) using TCNE (g = 2.00277) as a standard.

Electronic absorption spectra of the complexes and the ligand were recorded on a Perkin-Elmer model 402 spectrophotometer in dimethylformamide (DMF) and methanol in the range 300 to 800 nm. Infrared spectra of the complexes and the ligand were recorded on a Perkin-Elmer model 577 spectrophotometer in Nujol mull or KBr pellet, in the range 4000 to 400 cm^{-1}.

Molar conductances of the complexes in DMF solutions at room temperature (after appropriate incubations) were measured with a Systronics conductivity bridge (Model 305) with platinum cell (cell constant = 0.0843 cm^{-1}).

Results and Discussion

The complexes of the formula $Fe(PT–H)_2X$ (where $X^- = NO_3^-, Cl^-, N_3^-, NCS^-$ and CN^-) were prepared by interacting $FeCl_3$ and 2-pyridinecarboxaldehyde thiosemicarbazone in ratio of 1:2, in methanol–water mixture in presence of an excess of appropriate anion. They are insoluble in NaOH solution, petroleum ether, benzene, carbon tetrachloride, chloroform and diethyl ether, but slightly soluble in acetone. They are soluble in water, methanol and ethanol. They are highly soluble in DMF and dimethylsulphoxide. The molar conductances of these complexes in DMF were measured and they are given in Table I. The results of molar conductances of these complexes vary from 47.0 to 124.3 mhos cm^2 mol^{-1} after 1 hour incubation at room temperature, and from 68.9 to 128.5 mhos cm^2 mol^{-1} after 24 hours incubation at 50 °C. These variations indicate that some of these complexes are weakly associated in DMF [8]. The extent of association is also dependent on the incubation period.

TABLE I. Molar Conductances of $Fe(PT–H)_2X^a$ in DMF at 28 °C.

Complex	Molar conductance in mhos cm^2 mol^{-1} at room temperature^b	
	After one hour incubating at room temperature	After 24 hours incubating at 50 °C
$Fe(PT–H)_2NO_3$	97.2	101 2
$Fe(PT–H)_2Cl$	58.5	68 0
$Fe(PT–H)_2N_3$	47.0	72 0
$Fe(PT–H)_2NCS$	124.3	128.5
$Fe(PT–H)_2CN$	72.5	78.0

$^a X^- = NO_3^-, Cl^-, N_3^-, NCS^-$ and CN^- ^{b}Molar concentration = $10^{-3}M$

TABLE II Magnetic Moments and EPR Data of Polycrystalline $Fe(PT–H)_2X^a$

Complex	Magnetic moment μ_{eff} (BM) (298 K)	EPR data g (77 K)
$Fe(PT–H)_2NO_3$	2.28	2 107 (peak to peak width is 95 G^b)
$Fe(PT–H)_2Cl$	2.14	Diamagnetic
$Fe(PT–H)_2N_3$	2 03	2 121 (peak to peak width is 140 G)
$Fe(PT–H)_2NCS$	2.19	Diamagnetic
$Fe(PT–H)_2CN$	2.12	2.131 (peak to peak width is 155 G)

$^a X^- = NO_3^-, Cl^-, N_3^-, NCS^-$ and CN^-. ^{b}G = gauss.

The magnetic moments (μ_{eff}) of the above polycrystalline complexes (calculated from their magnetic susceptibility data obtained at room temperature) are

TABLE III. Electronic Absorption Maxima of $Fe(PT-H)_2X^a$ in DMF.

Complex	λ_{max} (cm^{-1})	ϵ_{max}
PCT	30303	25460
$Fe(PT-H)_2NO_3$	30514	27978
	17241	408
$Fe(PT-H)_2Cl$	30121	48864
$Fe(PT-H)_2N_3$	28571	4090
	22222	2545
$Fe(PT-H)_2NCS$	30003	33237
	22222	170
$Fe(PT-H)_2CN$	31250	17625
	23805	5362
	16949	460

$^aX^- = NO_3^-, Cl^-, N_3^-, NCS^-$ and $CN^{=}$.

given in Table II. They vary from 2.03 to 2.28 BM. These values can be interpreted in terms of low-spin iron(III) complexes [9]. The g values of these polycrystalline complexes were calculated from their EPR data obtained at liquid nitrogen and they are also given in Table II. The nitrato and azido complexes show broad symmetrical signals which are due to spin–spin relaxation possibly via dipolar interactions [10]. The cyano complex has a broad asymmetric signal which may be due to concentration broadening of the signal of low-spin iron(III) complex having axial or rhombic symmetry. The chlorido and thiocyanato complexes are essentially diamagnetic at liquid nitrogen. These complexes are low-spin iron(III) complexes at room temperature, as discussed above, but at 77 K all spins are paired via exchange coupling through these anions, between two low-spin iron(III) ions [11]. Thus, most of the anions of these complexes in the solid state are interacting with the iron(III) ion.

The electronic absorption maxima of the iron(III) complexes and the ligand were recorded in DMF after incubating the solutions for 2 to 3 hours and they are given in Table III. The dependence of absorption maxima (number, position and extinction coefficient, ϵ_{max}) on the nature of anions clearly indicates that the anions are associated to a different extent in the coordination sphere of the iron(III) complexes in solutions, as is supported by conductivity data given in Table I. The absorption bands observed in the iron(III) complexes can be tentatively assigned. The intense bands above 30.000 cm^{-1} are assigned to $\pi-\pi^*$ transitions. The band at 22.222 cm^{-1} in azide and thiocyanate derivatives may be assigned as charge transfer, probably $d-\pi^*$ and a band around 17.000 cm^{-1} in nitrate and cyanide derivatives may be assigned as d–d transition [12].

The infrared spectra of the iron(III) complexes and the ligand were recorded in the range 4000 to 400 cm^{-1}, and we will only discuss the selective infrared bands. The highest frequency band of the 2-pyridinecarboxaldehyde thiosemicarbazone at 3430 cm^{-1} can be assigned to the asymmetric ν(N–H) vibration of the terminal NH_2 group. The other bands at 3250 and 3150 cm^{-1} may be due to the symmetric ν(N–H) vibrations of the imino and amino groups. The C=N and C=C stretching vibrations are partially overlapping and the band at 1611 cm^{-1} (doublet) is assigned to them. The band at 1589 cm^{-1} can be assigned to δ(N–H) vibration of NH_2 group [13]. The band at 782 cm^{-1} may be due to ν(C=S) + ν (C–N) vibrations [14]. The bands at 609 and 423 cm^{-1} in the ligand are assigned to in plane pyridine ring deformation and out of plane ring deformation respectively [15].

Some infrared bands between 3430 to 3150 cm^{-1} in the iron(III) complexes are broadened due to hydrogen bonding, possibly with lattice water. One band at 3150 cm^{-1} has disappeared, due to enolization of the C=S group on complex formation. The C=N and C=C stretching vibrations are shifted from 1611 cm^{-1} (doublet) to 1620 cm^{-1} (doublet) on complex formation. This shift of 10 cm^{-1} is possibly due to the involvement of C=N group in complex formation. The δ(N–H) vibration of NH_2 group is not shifted at all because it is not involved in bonding. The ν(C=S) + ν(C–N) vibration at 782 cm^{-1} of the ligand is not present in the complexes. This indicates that the enolized form of C=S is involved in the bonding. The band at 609 cm^{-1} in the free ligand is shifted to 620 cm^{-1} and another band at 423 cm^{-1} is shifted to 435 cm^{-1} on complex formation. This indicates that the nitrogen atom of the pyridine group is involved in complex formation [15].

The nitrate ion may be coordinated to iron(III) in the nitrato complex because the infrared bands assigned to ionic $NO_3^-(KNO_3)$ were absent [15]. The metal–chlorine stretch is normally observed between 300 to 200 cm^{-1}, which is outside the range of our measurements. The EPR measurement has already been interpreted in terms of the metal–chloride bonding in the chloro complex. The ν_a(NNN) and ν_s(NNN) vibrations of azide group were observed at 2048 and 1320 cm^{-1} respectively, as compared to the ionic sodium azide values of 2128 and 1358 cm^{-1} [16]. This is interpreted in terms of coordination of azide to the iron(III) in the complex. The ν(CN) vibration of thiocyanate group was observed at 2040 cm^{-1} in the thiocyanato complex, as compared to the ionic thiocyanate value of 2053 cm^{-1}. This can possibly be interpreted in terms of nitrogen atom of thiocyanate coordinated to the iron(III) in the thiocyanato complex [15]. The ν(CN) vibration of the cyanide group was observed at 2040 cm^{-1} as compared to the value 2080 cm^{-1}, which is observed in ionic cyanide ions. The low frequency shift can be interpreted in terms of coordination of cyanide ion to iron(III) in the cyano complex [15].

The low-spin iron(III) complexes of the formula $Fe(PT-H)_2X$, where $X^- = NO_3^-, Cl^-, N_3^-, NCS^-$ and CN^- have been prepared. Some of the anions of these iron(III) complexes are associated in the solid state and in DMF solution and the extent of association depends on the nature of anions.

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