Article

Synthesis, Characterization and Mössbauer Studies of Fe(II) and Fe(III) Complexes of 2-Acetylpyridine Thiosemicarbazone

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Foram obtidos e caracterizados três complexos de ferro da 2-acetilpiridina tiossemicarbazona (2APT): $[Fe(HAPT)(APT)]Cl_2$ (I), $[Fe(HAPT)_2]Cl_2$ (II), e $[Fe(APT)_2]$ (III), nos quais HAPT representa o ligante protonado no nitrogênio N(2') da cadeia lateral e APT⁻ o ligante desprotonado em N(2'). A coordenação ao íon metálico ocorre através do sistema tridentado $N_{py} \cap N(1') \cap (S)$, com a formação de complexos do tipo L:M 2:1. Os parâmetros Mössbauer δ (desvio isomérico) e Δ (desdobramento quadrupolar) são característicos de Fe(III) para o complexo I e de Fe(II) para os complexos II e III, todos de spin baixo e simetria octaédrica. O valor de δ diminui quando se passa do complexo $[Fe(HAPT)_2]Cl_2$ (II, $\delta = 0,264 \pm 0,001$ mm/s) ao complexo $[Fe(APT)_2]$ (III, $\delta = 0,227 \pm 0,001$ mm/s), em razão da maior densidade eletrônica de eletrons s no metal no segundo complexo, resultante do efeito indutivo eletrodoador do grupo metila e da carga negativa no enxofre de tiolato que o tornam um melhor doador sigma do que o enxofre de tiona do primeiro complexo. O desdobramento quadrupolar Δ aumenta quando se passa do complexo protonado, II ($\Delta = 0,537 \pm 0,002$ mm/s) ao desprotonado, III ($\Delta = 0,755 \pm 0,002$ mm/s), provavelmente em razão da diferença na natureza dos dois ligantes, principalmente na ordem das ligações metal-enxofre.

Three iron complexes of 2-acetylpyridine thiosemicarbazone were obtained, namely $[Fe(HAPT)(APT)]Cl_2$ (I), $[Fe(HAPT)_2]Cl_2$ (II), and $[Fe(APT)_2]$ (III), in which HAPT stands for the ligand protonated at the N(2') level in the side chain and APT⁻ for the ligand deprotonated at N(2'). The coordination to the metal ion occurs through the tridentate ligating $N_{py} \cap N(1') \cap (S)$, system with formation of 2:1 ligand-to-metal complexes having meridional stereochemistry. The Mössbauer parameters δ (isomer shift) and Δ (quadrupole splitting) are characteristic of Fe(III) for complex I and of Fe(II) for both complexes II and III, all low spin with octahedral geometry. The isomer shift value decreases in going from $[Fe(HAPT)_2]Cl_2$ (II, $\delta = 0.264 \pm 0.001$ mm/s) to $[Fe(APT)_2]$ (III, $\delta = 0.227 \pm 0.001$ mm/s), due to the higher s electron density of the latter. This results from the electron donor inductive effect of the acetyl methyl group and the negative charge of the thiolate sulfur, which is consequently a better sigma donor than the thione sulfur. The quadrupole splitting increases in going from II ($\Delta = 0.537 \pm 0.002$ mm/s) to III ($\Delta = 0.755 \pm 0.002$ mm/s), probably due to ligand inequivalencies, a significant contribution being attributed to differences in the metal-ligand bond order.

Keywords: *2-acetylpyridine thiosemicarbazone, iron complexes*

Introduction

Thiosemicarbazones are a class of compounds possessing a wide spectrum of medicinal properties[1]. In particular,

thiosemicarbazones derived from 2-acetylpyridine have been shown to present a broad range of chemotherapeutic activities and have been evaluated for their antimalarial, antitumor, antibacterial and antifungal action[2]. The pharmacological activity of these compounds has often been related to their chelating ability with metal ions[3].

In previous works we have undertaken studies on the metal complexes of 2-formylpyridine thiosemicarbazone[4-6]. The present report deals with the preparation, characterization and Mössbauer data of Fe(II) and Fe(III) complexes of 2-acetylpyridine thiosemicarbazone.

The ligand is a tridentate chelating $N_{py} \cap N(1') \cap S$ system (see Fig. 1) that can coordinate metal ions either under the protonated (HAPT) or the deprotonated (APT) form at N(2'). The former contains thione sulfur and the latter thiolate sulfur.

Experimental

Synthesis

The ligand HAPT was prepared according to standard procedures[7]. The complex [Fe(HAPT)(APT)]Cl$_2$ (I) was prepared by adding 1.8 mmole (3.3492 g) of HAPT to a solution containing 0.9 mmol (0.1461 g) of anhydrous FeCl$_3$ dissolved in 35 mL of hot ethanol, acidified at pH 4 with HCl. After 2 h at 70 °C the mixture was cooled and the brown precipitate formed was filtered and washed with ethanol, then ether and dried under vacuum over drierite (yield 45%). The C,H,N,Fe and Cl analysis were compatible with the formula $C_{16}H_{19}N_8S_2FeCl_2$, M = 514.03 g/mole Found: C%:38.86; H%:3.74; N%:22.53; Fe%:11.25; Cl%:13.5. Calcd.: C%:37.35; H%:3.70; N%:21.79; Fe%:10.89; Cl%:13.6.

The complex [Fe(HAPT)$_2$]Cl$_2$ (II) was obtained by the additon of 1.8 mmole (0.3492 g) of HAPT to a hot solution of anhydrous FeCl$_2$ (0.9 mmole, 0.1141 g) in 40 mL of ethanol. After 3 h at 70°C the reaction mixture was cooled and the violet brownish solid was filtered, washed with ethanol and ether and dried under vacuum over drierite (yield 57%). The C,H,N analysis was compatible with the formula $C_{16}H_{20}N_8S_2FeCl_2$, M = 515.03 g/mole Found: C%:37.43; H%:3.94; N%:21.81. Calcd.: C%:37.28; H%:3.88; N%:21.75.
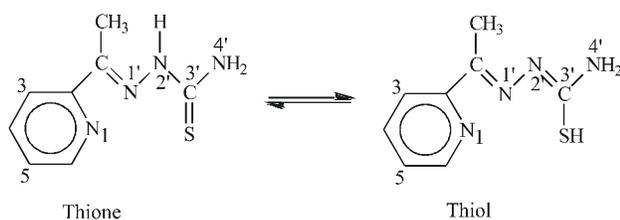
The complex [Fe(APT)$_2$] (III) was obtained by addition of 1.8 mmole (0.3492 g) of HAPT to a hot solution of FeCl$_2$ (0.9 mmole, 0.1141 g) in 35 mL of ethanol. After the addition of the ligand, an equal volume of deionized water and a few drops of concentrated ammonia were added giving a green mixture. After 2 h at 70 °C the reaction mixture was cooled and the brownish green precipitate was filtered, washed with ethanol, followed by ether and dried under vacuum over drierite (yield 23%). The C,H,N analysis was compatible with the formula $C_{16}H_{18}N_8S_2Fe$, M = 442.12 g/mole Found: C%:43.01; H%:3.94; N%:24.95. Calcd.: C%:43.01; H%:3.88; N%:25.34.

All three complexes decompose upon heating: I at 262 °C, II at 197 °C and III at 303 °C.

Apparatus

The atomic absorption spectra were obtained by means of a Varian Techtron AAG spectrometer and the neutronic activation analysis of chloride was obtained by means of a Cambera equipment provided with a 7229 Ge/Li detector. The molar conductance data were obtained by means of a YSI Conductivity Bridge, model 31, equipped with a condutimetric cell of cell constant equal to 0.088 cm^{-1}, using 10^{-4} mol/L solutions in methanol. KCl, KBr, BaCl$_2$ and Mg(NO$_3$)$_2$.6H$_2$0 were used as standards.

IR spectra were run in a Perkin Elmer 283 B instrument, using Nujol mulls.

Mössbauer spectra were obtained using a conventional constant acceleration spectrometer, moving a Co-Rh source at room temperature. All spectra were computer fitted assuming lorentzian line shapes.

Results and Discussion

For all compounds the C,H,N analysis indicated the presence of 1:2 metal to ligand complexes. In the case of complex I this analysis suggested the presence of one protonated and one deprotonated ligand attached to the metal ion (Fe(III)), whereas two protonated and two deprotonated ligands attached to Fe(II) are suggested in the case of complexes II and III respectively. In order to confirm the existence of one protonated and one deprotonated ligand in the same complex, the percentages of the metal and chloride were also determined for complex I, corroborating our assumption. Furthermore, the molar conductance of this complex (148.5 S cm^2 mol^{-1}) indicated that the complex is a 1:2 electrolyte, again confirming our supposition. In fact, some works report the synthesis of 2:1 ligand-to-metal complexes of other thiosemicarbazones having the two ligand molecules in different protonation states[8].

The infrared spectra of the complexes present characteristic features compared to that of the free ligand (Table 1).

Figure 1. Structure of the ligand 2-acetylpyridine thiosemicarbazone under the thione and thiol tautomeric forms.

Table 1. Important I.R. bands and assignements for the ligand (HAPT) and its complexes: [Fe(HAPT)(APT')]Cl$_2$ (I), [Fe(HAPT)$_2$]Cl$_2$ (II) e [Fe(APT)$_2$] (III).

compound	ν CC py + δNH$_2$	ν CN	ν CN + δNH$_2$ (thioamide II)	ν CS + ν NCN	ν $_s$ py (ring breath)	ν CS	δ in plane	δ out of plane	ν MS
HAPT	1605s	1570s	1490s	1135s	985m	835s	630m	390w	320w
		1550m	1465s	1095s	970m	815s	600m	375w	
			1425s	1075s	955m	760s	585m		
I	1620s		1495s	1170s	950w	800w	650m	400w	350w
	1600s		1440s	1150s		760m	625m		325w
				1120s			590m		
II	1625s	1585s	1460s	1165s	1005m	795w	640m	400w	350w
	1605s	1550s	1430s	1150s	985m		595s		315w
				1110m					
III		1590s	1425s	1160s	1000m	790w	635w	410m	350w
		1565m		1150s	975m	765m	600m	390m	305m
		1515m		1115m					

s = strong   m = medium   w = weak

The coordination of the pyridine nitrogen can be evidenced by the shifting of the ligand absorptions at 985 and 970 cm^{-1}, attributed to the ring breath deformation[9] to lower frequencies in the spectra of the complexes. Furthermore, the ligand absorptions at 630 and 375 cm^{-1}, ascribed to the in plane and out of plane ring deformations respectively[10] shift to higher frequencies in the spectra of the complexes. In addition, the band at 1605 cm^{-1}, attributed to the $ν_{CC}$ ring stretching vibration also is shifted to higher frequencies upon complexation[11]. However, the latter normally occurs in the same region as the NH$_2$ deformation (1610-1615 cm^{-1}) or as the $ν_{CN}$ stretching around 1580 cm^{-1} not allowing an unambiguous interpretation of the spectra in this region[12].

The coordination of the azomethine nitrogen N(1') is indicated by the shifting of the ligand absorptions at 1550, 1490 and 1425 cm^{-1}, ascribed to the stretching $ν_{CN}$ or to the $ν_{CN} + δ_{NH2}$ mode (thioamide II), to higher frequencies in the spectra of the complexes[13-15].

A set of three intense bands at 1135, 1095 and 1075 cm^{-1} is believed to have a $ν_{CS}$ contribution[16]. This set of bands is shifted to lower frequencies upon coordination, appearing with lower intensity in the spectra of the complexes, indicating the attachment of the sulfur to the metal in all cases. Moreover, the spectrum of the free ligand exhibits two strong bands at 835 and 815 cm^{-1}, which are usually assigned mainly to the $ν_{CS}$ vibration. These absorptions are shifted 35 to 45 cm^{-1} to lower frequencies with diminution of intensity in the spectra of the complexes, suggesting the coordination of the sulfur[17-18]. Other authors observed a similar shifting of the $ν_{CS}$ vibration

upon complexation[10,15,19]. In fact, when the protonated HAPT is coordinated, the thione sulfur is able to accept electron density from the metal through back π bonding, leading to an increase of the M-S bond order and the concomitant decrease in the C-S bond order. On the other hand, when coordinated as the deprotonated (APT$^-$) form, the tiolate sulfur is not as good a π acceptor[20]. Thus, the CS bond presents a double bond character due to the high delocalization of the negative charge in the ligand's chain, leading again to a strengthening of the M-S bond with the corresponding decrease in the C-S bond order. Therefore, the infrared data do not allow a clear distinction between thione and thiolate sulfur. In conclusion, the IR spectra clearly indicate the coordination of the ligand as a tridentate chelating N$_{py}$ ∩ N(1') ∩ S system.

The Fe-S vibration is assigned to the absorptions in the 340-380 cm^{-1} region, based on reports of other authors[10,21], although the literature also contains reports atributing these bands to the Fe-N vibration and that at 400 cm^{-1} to the Fe-S vibration[22].

In a recent work[23] we reported the visible spectral assignments for complexes I, II and III. In aqueous solution the protonated Fe(II) complex (II), shows a band at 575 nm with a shoulder at 518 nm. Upon deprotonation resulting in the formation of complex III, the maximum at 575 nm shifts to 600 nm and the shoulder to 545 nm. From resonance Raman data obtained previously for the analogous complexes of 2-formypyridine thiosemicarbazone (HFPT), we attributed the spectral maxima to ligand-to-metal charge transfer transitions (LMCT) from a pπ orbital of the thione/thiolate sulfur to a σ* orbital of the

low spin Fe(II). The shoulder was indicated to be due to a vibronic structure corresponding to a transition to an excited vibrational level[11]. The same assignment is suggested for the bands in the visible spectra of complexes II and III (both low spin, as shown by Mossbauer spectroscopy, vide infra). In fact, on deprotonation the energy of this transition decreases due to the the lower energy of the charge transfer from the thiolate sulfur orbital compared to the thione sulfur orbital. This energy difference results because the the thiolate sulfur is more polarizable. That is, the greater p character of the sp^3 hybridization of the thiolate sulfur compared to the sp^2 hybridization of the thione sulfur makes the thiolate a better pπ donor. As we demonstrated before, resonance Raman data as well as the low energy of the absorption maxima in the visible precluded the assignment of the peak to a σ(S)- σ*(M) charge transfer transition[11, 24]. The latter is probably superimposed to the intraligand transitions in the ultraviolet range (Fig. 2).

The visible spectrum of the Fe(III) complex (I) shows a shoulder at 440 nm, which we assigned to a pπ(S)- σ*(M) LMCT, similar to the previously studied Fe(III) complex of HFPT[11]. Because of the larger 10 Dq associated with low spin Fe(III) (Mossbauer data, vide infra) compared to that of low spin Fe(II) resulting from the higher charge[25], the charge transfer transition to σ*(Fe(III)) is higher in energy than to σ*(Fe(II)).

The Mössbauer spectra of complexes I, II and III are shown in Fig. 3. Table 2 gives the Mössbauer experimental

data, as well as those of the Fe(III) complex of the related ligand diacetyl monoxime thiosemicarbazone (IV), studied by other authors[13]. Complex IV is represented by [Fe(DMT-H)(DMT-2H)] in which DMT-H and DMT-2H stand for the ligand diacetyl monoxime thiosemicarbazone containing a thione and a thiolate sulfur respectively (*i.e.*, the other hydrogen is lost from the monoxime moiety).

The Mössbauer spectrum of complex I is an asymmetric doublet, the second line being only 65% as intense as the first one. The narrow band width of the doublet (Γ = 0.242 mm/s) indicates that the most intense line at around 1.25 mmm/s is not due to any impurity but probably to a preferential orientation of the crystals or to vibrational anisotropy of the Mossbauer isotope in the crystal lattice.

The Mossbauer spectrum of complex I was also recorded at room temperature, in which the plane of the sample was rotated by 50° with respect to the γ-ray direction. The parameters obtained were δ = 0.063 ± 0.002 mm/s, Δ = 2.426 ± 0.004 mm/s and Γ = 0.248 ± 0.003 mm/s, that are essentially the same as the ones reported in Table 2, except that now the second line is 98% as intense as the first. This result indicates that the asymmetry of the doublet of complex I depends on the orientation of the crystals in the sample holder, which is characteristic of the texture effect[26]. Therefore, the asymmetric Mossbauer doublet shown by

Figure 2. A simplified molecular orbital diagram illustrating the potential ligand-to-metal charge transfer transitions. Transitions to t$_{2g}$ are absent in the low spin Fe(II) complexes.
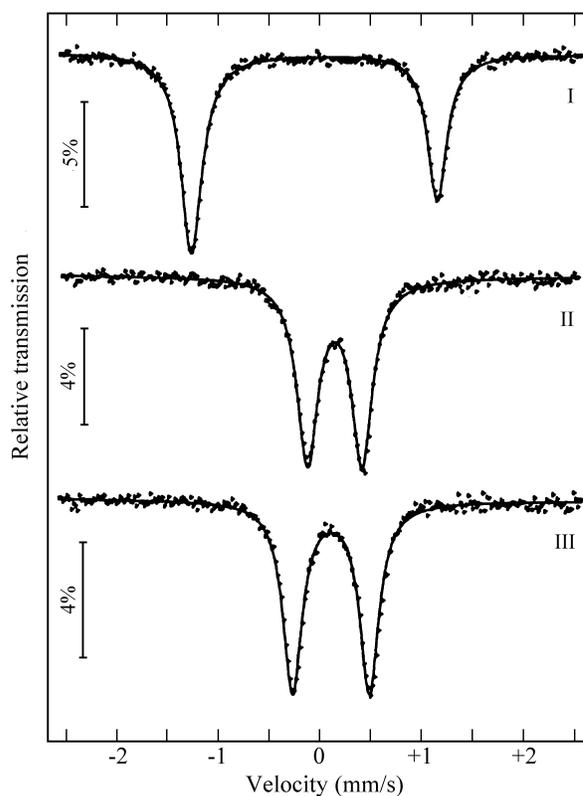
Figure 3. Mössbauer spectra at 298 K of the complexes: [Fe(HAPT)(APT)]Cl$_2$ (I), [Fe(HAPT)$_2$]Cl$_2$ (II) and [Fe(APT)$_2$] (III).

Table 2. Mössbauer parameters at 298 K (δ relative to metallic iron).

Complex	δ (mm/s)	Δ (mm/s)	Γ[#] (mm/s)	Ref.
(I) [Fe(HAPT)(APT)]Cl$_2$	0.065 ± 0.001	2.430 ± 0.002	0.242 ± 0.002	*
(II) [Fe(HAPT)$_2$]Cl$_2$	0.264 ± 0.001	0.537 ± 0.002	0.251 ± 0.002	*
(III) [Fe(APT)$_2$]	0.227 ± 0.001	0.755 ± 0.002	0.232 ± 0.002	*
(IV) [Fe(DMT-H)(DMT-2H)]	0.07	2.2		13

[#] Γ = band width * this work

complex I is mainly due to preferential orientation of the crystals. The spectra of complexes II and III show symmetric doublets.

The isomer shift (δ) relative to metallic iron and the quadrupole splitting (Δ) parameters are characteristic of low spin Fe(III) for complexes I and of low spin Fe(II) for complexes II and III, and all compounds having approximately octahedral geometry. The isomer shift of [Fe(HAPT)$_2$]Cl$_2$ (II, Δ = 0.264 ± 0.001 mm/s) is higher than that of [Fe(APT)$_2$] (III, δ = 0.227 ± 0.001 mm/s, Table 2). The lower δ value of the deprotonated form can be interpreted in terms of an increase in the s electron density at the metal resulting from the negatively charged thiolate sulfur[20]. This greater electron density is also facilitated by the acetyl methyl group's donation via the conjugated system of the anionic thiosemicarbazone ligand. In fact, thiolate sulfur is better a σ as well as a pπ donor to Fe(II) than thione sulfur. Both sulfurs possess vacant dπ orbitals that can be used for dπ-dπ metal-sulfur bonding. Although thione sulfur is less polarizable than thiolate sulfur, it appears to be a better dπ electron acceptor than the negatively charged thiolate sulfur[26]. Therefore, the electronic density at the iron(II) center is lower for the protonated (thione) complex (II) than for the deprotonated (thiolate) complex (III), in accordance with the higher δ value for complex II. Moreover, as we stated before, the energy of the LMCT transition in the electronic spectrum is lower for the deprotonated complex (III), again in accordance with the higher donor ability of the thiolate sulfur.

For the Fe(II) complexes the quadrupole splitting increases appreciably in going from the protonated (II, Δ = 0,537 ± 0.002 mm/s) to the deprotonated (III, Δ = 0.755± 0.002 mm/s) form. In order to explain this variation ligand inequivalencies must be taken into consideration, a significant contribution being attributed to the difference in the Fe-S bond order. Thiolate sulfur is able to form one σ and two π bonds with the metal whereas thione sulfur can only form one π and one σ bonds. Another significant contribution may be ascribed to the negative charge at the thiolate sulfur, the thione sulfur being neutral[20]. Again these results are in perfect agreement with the lower energy of the

thiolate-to-metal charge transfer transition , due to its higher donor ability.

At this stage it is worth noting the similarities of the Mössbauer parameters of the Fe(III) complexes [Fe(HAPT)(APT)]Cl (I, δ = 0.065 ± 0.001 mm/s , Δ = 2.430 ± 0.002 mm/s) and its analog [Fe(DMT-H)(DMT-2H)] (IV, δ = 0.07 mm/s, Δ = 2.2 mm/s). Both the isomer shift and the quadupole splitting of I and IV are comparable, indicating that our formulation of compound I as containing one protonated and one deprotonated ligands is correct.

Acknowledgments

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