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Nickel(II), Copper(I) and Copper(II) Complexes of Bidentate Heterocyclic Thiosemicarbazones

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Complexos de tiossemicarbazonas derivadas de 3- e 4-formilpiridina (H3FPT e H4FPT) e 3- e 4-acetilpiridina (H3APT e H4APT) com níquel(II) e cobre(I) ou cobre(II) foram preparados e caracterizados através de microanálises, medidas de condutividade molar e susceptibilidade magnética e por meio de seus espectros de infravermelho e de R.M.N., no caso dos complexos de cobre(I) e dos complexos diamagnéticos de níquel(II).

Nickel(II) and copper(I) or copper(II) complexes of thiosemicarbazones derived from 3- and 4-formylpyridine (H3FPT and H4FPT) and 3- and 4-acetylpyridine (H3APT and H4APT) have been prepared and characterized by microanalyses, molar conductivity and magnetic susceptibility measurements and by their NMR (in the case of copper(I) and diamagnetic nickel(II) complexes) and IR spectra.

Keywords: heterocyclic thiosemicarbazones, bidentate thiosemicarbazones, nickel(II), copper(I), copper(II)

Introduction

Thiosemicarbazones and their metal complexes are a broad class of biologically active compounds¹. Metal complexes of N-heterocyclic thiosemicarbazones derived from 2-formylpyridine (H2FPT) and 2-acetylpyridine (H2APT) were extensively described in the literature², but very few works deal with those derived from 3- and 4-formylpyridine (H3FPT, H4FPT, Fig. 1) and 3- and 4-acetylpyridine

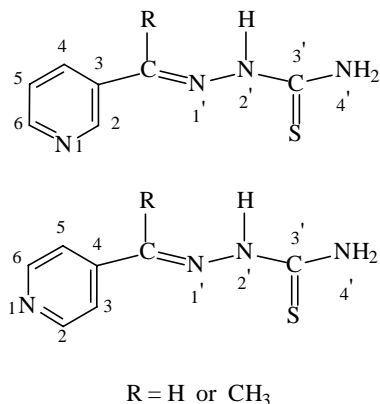


Figure 1. Structures of thiosemicarbazones derived of 3- and 4-formylpyridine and 3- and 4-acetylpyridine.

(H3APT, H4APT, Fig. 1). In some cases, lowering of the thiosemicarbazone's denticity leads to a decrease of activity² but the literature reports examples of biologically significant bidentate thiosemicarbazones. The compound p-acetamidobenzaldehyde thiosemicarbazone, for example, known as thioacetazone, is employed in the clinical treatment of tuberculosis³ and functions as a potential N-S bidentate ligand. In previous works we studied the iron(II), iron(III), copper(II) and zinc(II) complexes of H2FPT and H2APT⁴⁻⁷. In the present article we report the syntheses and characterization of complexes of H3FPT, H4FPT, H3APT and H4APT with nickel(II), and copper(I) or copper(II).

Experimental

IR spectra were recorded by means of a Perkin Elmer 283B spectrometer using Nujol mulls between CsI plates and NMR spectra with a Bruker DRX-400 Avance (400 MHz) spectrometer. The thermogravimetric data were obtained in dynamic air atmosphere at 10 °C/min in the 25 - 750 °C range, by using a Mettler TA 4000 TG50 analyzer. A YSI model 31 conductivity bridge was employed for molar conductivity measurements. The magnetic susceptibilities of the solids were measured at room temperature with a Johnson Matthey Magnetic Susceptibility balance.

Partial elemental analyses were performed using a Perkin Elmer 240 equipment.

H3FPT, H4FPT, H3APT and H4APT were obtained by refluxing an ethanolic solution of 3- or 4-formylpyridine and 3- or 4-acetylpyridine with thiosemicarbazide (all purchased from Aldrich Chemical Company and used without purification) as described in the literature⁸. The complexes were prepared by refluxing ethanolic solutions of the thiosemicarbazone and the metal(II) perchlorate in molar ratio M:L 1:2 during 5-6 h. In the case of H3APT and H4APT the reaction with copper(II) perchlorate gave the copper(I) complexes (*vide infra*). The solids that formed on cooling were filtered off, washed with ethanol then ether and dried. The yields were 50 - 65% in the case of the nickel(II) complexes, 66 - 70% in the case of the copper(I) complexes and 56% in that of the copper(II) complexes.

Results and Discussion

Table 1 lists the colors, partial elemental analyses and molar conductivities of the nickel(II), copper(I) and copper(II) complexes. Thiosemicarbazones can coordinate metal ions as neutral ligands (HTSC) or as anionic species (TSC) upon deprotonation at the N(2')^{4,5,7}.

The C, H, N data indicate that the copper(II) complexes of H3FPT and H4FPT present two anionic bidentate ligands per metal ion, as supported by their behavior as non-electrolytes, and their geometry is probably square planar. In contrast, both H3APT and H4APT form copper complexes in which only one neutral ligand is coordinated to the metal ion and the other coordination positions are occupied by water molecules, as confirmed by the IR

spectra of the complexes (*vide infra*). However, in these cases the compounds are diamagnetic, suggesting reduction of copper(II) to copper(I), consistent with their yellow color and with the presence of one perchlorate as counterion in both complexes. In previous works we demonstrated that H2FPT acts as a reducing agent of its own iron(III) complex⁶. The occurrence of a similar effect may now be suggested. The protonation of the ligand in the complexes was confirmed by the presence of ¹H-NMR signals at $\delta = 10.503$ and $\delta = 11.967$, assigned to the N(2')-H protons hydrogen-bonded to the DMSO solvent molecules⁹ (see Table 2). Also, the acetyl protons which give a signal at $\delta = 2.313$ and $\delta = 2.329$ in the spectra of H3APT and H4APT respectively are shifted to higher frequency ($\delta = 2.391$ and $\delta = 2.484$ respectively) in the spectra of the copper(I) complexes due to coordination through N(1'), as observed in the literature¹⁰. Microanalyses indicate that the copper(I) complex with H3APT presents two coordinated water molecules, whereas that with H4APT presents a total of six water molecules, which are coordinated and crystallization water, as confirmed by the infrared data (*vide infra*), but it is not possible to determine the number of water molecules of each type in that complex. Although the loss of water does not appear separately in the thermograms of both complexes, thermogravimetric data show a residue of CuO corresponding to 18.8% (calcd. 20.3%) and to 18.3% (calcd. 17.1%) for the copper(I) complexes of H3APT and H4APT respectively, in agreement with the proposed formulations. In this case, reoxidation of copper(I) to copper(II) during the thermogravimetric measurements probably occurs.

Table 1. Colors, partial elemental analyses and molar conductivities of the metal complexes of bidentate thiosemicarbazones.

Compound	Color	% C Found (Calcd.)	% H Found (Calcd.)	% N Found (Calcd.)	Λ_M^a
[Ni(H3FPT)(3FPT)]ClO ₄	brown	32.77 (32.49)	2.33 (2.92)	21.95 (21.65)	77
[Cu(3FPT) ₂]	green	41.12 (39.85)	3.04 (3.34)	27.11 (26.55)	32
[Ni(H4FPT)(4FPT)]ClO ₄	green	32.64 (32.49)	2.41 (2.92)	21.82 (21.65)	79
[Cu(4FPT) ₂]	brown	40.44 (39.85)	3.11 (3.34)	27.22 (26.55)	34
[Ni(H3APT) ₂ (3APT)]ClO ₄	brown	39.13 (38.96)	4.01 (3.95)	22.40 (22.72)	87
[Cu(H3APT)(H ₂ O) ₂]ClO ₄	yellow	24.61 (24.50)	3.46 (3.34)	15.02 (14.28)	79
[Ni(H4APT) ₂ (4APT)]ClO ₄	light green	38.04 (38.96)	3.64 (3.95)	21.93 (22.72)	88
[Cu(H4APT)(H ₂ O) _n](ClO ₄).(6-n)H ₂ O ^b	yellow	20.02 (20.64)	3.40 (3.90)	12.14 (12.05)	89

a: *ca.* 10⁻³ M in DMF; b: n = 2, 3 or 4 (see text).

C,H,N analyses suggest that H3FPT and H4FPT form 2:1 ligand-to-metal complexes with nickel(II), in which one of the ligands is neutral and the other anionic, similar to an iron(III) complex of 2-acetylpyridine thiosemicarbazone obtained by us in a previous work¹¹. The molar conductivity measurements indicate that both complexes are 1:1 electrolytes, consistent with the presence of the perchlorate bands in the infrared spectrum (vide infra). The complex [Ni(H4FPT)(4FPT)]ClO₄ is diamagnetic, suggesting square planar geometry but in the case of [Ni(H3FPT)(3FPT)]ClO₄ the measured magnetic susceptibility of 3.0 BM is close to the theoretical value of 2.83 BM of tetrahedral arrangement. The ¹H-NMR spectrum of the former shows a peak at $\delta = 11.398$, assigned to the protonated ligand's N(2')-H hydrogen bonded to DMSO⁹. Also, the signal at $\delta = 7.992$ in the spectrum of H4FPT, assigned to the formyl proton, is shifted to higher frequency ($\delta = 7.998$) upon coordination of the azomethine nitrogen N(1'). H3APT and H4APT form 3:1 ligand-to-metal complexes with nickel(II), of octahedral geometry. Microanalyses of these complexes suggest the presence of two protonated and one deprotonated bidentate ligands, which was also confirmed by the 1:1 electrolyte behavior of both complexes and by the presence of perchlorate absorptions in the IR spectrum. Although the NMR signals are broad for the paramagnetic nickel(II) complexes preventing reliable integration, the presence of resonances at $\delta = 11 - 12$ (data not shown), characteristic of the N(2')-H protons hydrogen bonded to DMSO⁹ confirms that at least one of the ligands is protonated.

The assignments of the IR bands useful for determining the ligand's mode of coordination are listed in Table 3. The bands in the region 3160 - 3440 cm⁻¹, attributed to the symmetrical stretching mode $\nu(\text{NH}_2)$ in the spectra of the ligands, shift to 3460 - 3210 cm⁻¹ in those of the complexes, as a consequence of the coordination of the sulfur from the C=S(NH₂) group, as observed by other authors¹². The $\nu(\text{C}=\text{N})$ bands of the thiosemicarbazones at ca. 1590 cm⁻¹ shift to 1625 - 1565 cm⁻¹ in the spectra of the complexes,

indicating coordination of the azomethine nitrogen N(1') in agreement with previous studies¹³. The uncomplexed thiosemicarbazones show the thioamide IV band, which possesses considerable contribution from $\nu(\text{CS})$, in the 800 - 825 cm⁻¹ range. This band shifts 45 to 110 cm⁻¹ to lower energy when coordination occurs with deprotonation at N(2') and formation of a single C-S bond¹¹. The shift is 5 to 25 cm⁻¹ to lower frequencies when the thiosemicarbazones coordinate the metal in the neutral form¹¹. Bands in the 355 - 395 cm⁻¹ region are assigned to $\nu(\text{M}-\text{S})$ and those at 435 - 485 cm⁻¹ region to $\nu(\text{M}-\text{N})$ vibrations¹³, supporting the coordination of all ligands as bidentate N-S chelating agents. In the spectra of [Cu(H3APT)(H₂O)₂]ClO₄ and [Cu(H4APT)(H₂O)_n]ClO₄·(6-n)H₂O there are bands at 3315, 1630, 605 and 420 cm⁻¹ and at 3420, 1625, 595 and 430 cm⁻¹ respectively, attributable to $\nu(\text{OH})$, $\delta(\text{OH}_2)$, $\pi_w(\text{OH}_2)$ and $\nu_{\text{Cu}-\text{O}}$ of coordinated water¹³. Furthermore, the IR spectrum of [Cu(H4APT)(H₂O)_n]ClO₄·(6-n)H₂O shows broad absorptions in the region 3600 - 3200 cm⁻¹ characteristic of crystallization water¹⁴. Finally, a strong, broad absorption band, which is characteristic of ν_3 of ionic perchlorate¹⁵ is observable in the spectra of [Cu(H3APT)(H₂O)₂]ClO₄, [Ni(H3FPT)(3FPT)]ClO₄ and [Ni(H4FPT)(4FPT)]ClO₄ at about 1070 cm⁻¹. Also, $\nu_4(\text{ClO}_4)$ is present as a sharp shoulder at 620 cm⁻¹ and a weak band at 946 cm⁻¹ may be due to $\nu_1(\text{ClO}_4)$, suggesting that the ionic perchlorate is distorted from tetrahedral symmetry due to lattice effects or hydrogen bonding by the coordinated ligand's NH functions. In contrast, [Cu(H4APT)(H₂O)_n]ClO₄·(6-n)H₂O, [Ni(H3APT)₂(3APT)]ClO₄ and [Ni(H4APT)₂(4APT)]ClO₄ show a much sharper band for $\nu_3(\text{ClO}_4)$, a sharp band for $\nu_4(\text{ClO}_4)$ and no indication of $\nu_1(\text{ClO}_4)$ suggesting minimal distortion from tetrahedral symmetry.

In the present work a variety of metal complexes of heterocyclic bidentate thiosemicarbazones were prepared and characterized. Copper(II) complexes of 3- and 4-formylpyridine thiosemicarbazone present two deprotonated

Table 2. ¹H-NMR spectra (DMSO - d₆) of the thiosemicarbazones and their copper(I) and diamagnetic nickel(II) complexes.

Compound	N(2')-H	C-H	CH ₃
H3FPT	11.558	8.057	-
H4FPT	11.666	7.992	-
H3APT	10.303	-	2.313
H4APT	10.450	-	2.329
[Ni(H4FPT)(4FPT)]ClO ₄	11.398	7.998	-
[Cu(H3APT)(H ₂ O) ₂]ClO ₄	10.503	-	2.391
[Cu(H4APT)(H ₂ O) _n](ClO ₄)·(6-n)H ₂ O ^a	11.967	-	2.484

a: n = 2, 3 or 4.

Table 3. Infrared spectra of the heterocyclic thiosemicarbazones and their metal complexes.

Compound	ν (NH ₂)	ν (C=N)	ν (CS)	ν (MN)	ν (MS)
H3FPT	3320 m 3235 m	1585 s	805 s	-	-
[Ni(H3FPT)(3FPT)]ClO ₄	3440 m 3340 m	1600 m 1525 sh	780 m 695 m	450 m	365 m
[Cu(3FPT) ₂]	3340 m	1605 m	695 m	420 m	360 w
H4FPT	3440 m 3278 m	1600 s	825 s	-	-
[Ni(H4FPT)(4FPT)]ClO ₄	3440 m 3300 m	1625 s	805 m 780 m	480 m	365 m
[Cu(4FPT) ₂]	3360 m 3220 m	1615 s	770 m	455 s	390 w
H3APT	3275 m 3215 sh	1590 m	800 m	-	-
[Ni(H3APT) ₂ (3APT)]ClO ₄	3405 m 3285 m	1575 w	790 m 715 m	480 m	380 w
[Cu(H3APT)(H ₂ O) ₂]ClO ₄ ^a	3410 s 3315 s	1565 s	795 m	430 w	380 w
H4APT	3280 m 3160 m	1590 s	800 m	-	-
[Ni(H4APT) ₂ (4APT)]ClO ₄	3400 m 3220 s	1580 m	795 m 695 m	435 w	395 w
[Cu(H4APT)(H ₂ O) _n](ClO ₄). _(6-n) H ₂ O ^a	3300 s 3210 m	1525 s	775 m	440 w	385 w

a: n = 2, 3 or 4 (see text for the attributions of the vibrational bands of coordinated water).

s = strong; m = medium; w = weak; sh = shoulder.

ligand molecules per metal ion. The reaction of 3- and 4-acetylpyridine thiosemicarbazone with the copper(II) salt leads to the formation of copper(I) complexes in which the thiosemicarbazones coordinate as protonated neutral ligands, in accordance with the lower acidity constant of the acetyl derivatives, due to the electron donor inductive effect of their methyl group⁷. Moreover, 3- and 4-formylpyridine thiosemicarbazone coordinate nickel(II) forming 2:1 ligand-to-metal complexes having one protonated and one deprotonated ligand, of tetrahedral geometry in the first case and of square planar geometry in the latter. The thiosemicarbazones derived from 3- and 4-acetylpyridine form octahedral nickel(II) complexes of the ML₃ type, in which two ligand molecules are protonated and one is deprotonated. At this stage it is worth comparing the structures of the metal complexes of 2-formyl and 2-acetylpyridine thiosemicarbazone with those of the corresponding 3- and 4- analogs. In the former the presence of the tridentate chelating N-N-S system normally favors the formation of 1:1 complexes with copper(II) of approximately square planar geometry². In contrast, the bidentate (3- and 4-) thiosemicarbazones form copper(II) complexes with 2:1 ligand-to-metal ratios. The 2-formyl and 2-ace-

tylpyridine thiosemicarbazones, as well as their 3- and 4- analogs form nickel(II) complexes with a variety of geometries and different ligand-to-metal ratios but only the 2- (*i.e.* α) thiosemicarbazones can form ML₂ complexes of octahedral geometry upon coordination of the tridentate N-N-S ligand¹. To our knowledge the literature does not report many examples of copper(I) complexes of 2-formyl and 2-acetylpyridine thiosemicarbazone for us to establish comparisons with the 3- and 4- analogs.

In conclusion, changing the point of attachment of the lateral chain in relation to the heteroaromatic nitrogen from the 2- (*i.e.* α) to the 3- or 4- (*i.e.* β or γ) positions and the nature of the pyridine starting reagent (formyl or acetyl) may have influence in the structure of the metal complexes obtained and the structural differences probably affect the biological activity of these compounds.

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