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RESEARCH ARTICLE

Synthesis and Characterization of Cu(II), Ni(II) and Co(II) Based 1, 4-Substituted Thosemicarbazone Complexes

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Abstract: Different benzaldehydes and pyridine substitution were used on 1 and 4 ‘*N*’-positions of thiosemicarbazide respectively. This substituted-benzaldehyde-2-aminopyridine-*N*-thiohydrazone ligand was further used to synthesize Co(II), Ni(II) and Co(II) based metal complexes and characterized by FT-IR, Elemental analysis, ESI Mass and elemental analysis. All synthesized compounds were studied for their physical properties, antibacterial and antifungal activity. In this anti-microbial study Cu(II) and Ni(II) metal complexes have shown better anti-bacterial activity. While several synthesized metal complexes have shown comparable activity with standard drugs taken.

Keywords: Thiosemicarbazones, Complexes, Antimicrobial activity, Synthesis

Introduction

Thiosemicarbazones (hydrazine carbothioamides) are a family of compounds with beneficial biological activity[1-2]. They are very good ligands and it has been shown that their biological activity is related with its substitution at its one and forth ‘*N*’-position of thiosemicarbazide[3-5].

Thiosemicarbazones and their metal complexes have been widely explored because of their versatile biological activity and prospective use as drugs[6]. The relationship between structure and biological activity has been covered in several papers[7,8]. Reports show that greater activity is seen in 2-substituted pyridine thiosemicarbazones[9,10]. While Schiff bases are good ligands and shows various activities with thiosemicarbazone derivatives[11-13]. The main aim of present work is to synthesis Cu(II), Ni(II) and Co(II) complexes of thiosemicarbazone derivatives and to study there antimicrobial activity against some strains.

Experimental

The *N*-(pyridin-2-yl)thiosemicarbazide (0.01 M) and substituted aromatic aldehyde (0.01 M) were dissolved in 60 mL methanol in a 100 mL round bottom flask, then add 1 mL gL acetic acid and reflux the resulting reaction mixture for 24 h on boiling-water bath, reaction was monitored by TLC. After completion of the reaction, reaction mixture was poured onto crushed ice. The separated product 1-substituted arylidene-4-(pyridin-2-yl)thiosemicarbazide was filtered wash with sodium bisulphite solution and dried at room temperature (Figure 1).

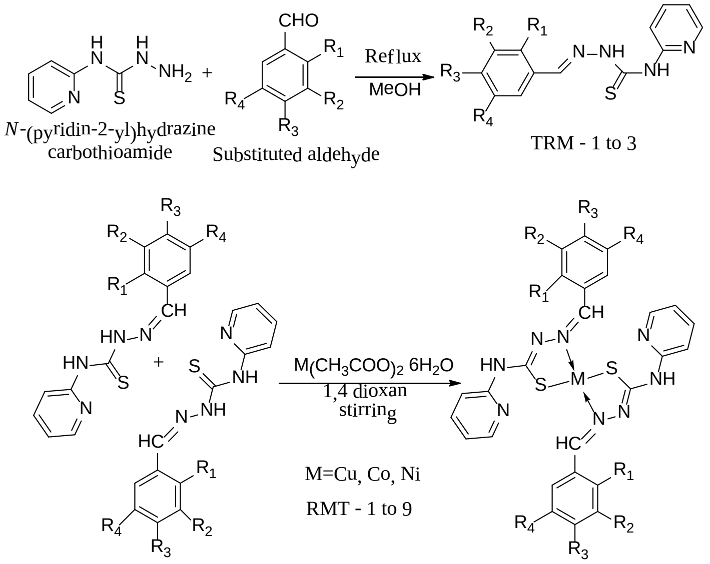

Figure 1. Scheme of synthesis

To a solution of 1-substituted arylidene-4-(pyridin-2-yl)thiosemicarbazide (0.02 mole) in methanol (60 mL) added a solution of M(acetate)$_2$ 4H$_2$O (0.01 mole) in distilled water (5-10 mL). The mixture boiled with stirring for 1 h later stopped heating and reaction mixture stirred for 3 days at room temperature and afterwards 15-20 mL solvent evaporated. On cooling the reaction mixture colored precipitates of 1, 4-substituted thiosemicarbazide collected by filtration, washed thoroughly with cold methanol and dried in a vacuum (Figure 1).

Table 1. Physical properties of ligands and metal complexes

Comp. Code	Metal	R_1	R_2	R_3	R_4	Yield %	M. P. °C
TRM-1		-H	$-OCH_3$	$-OCH_3$	-H	70	110
TRM-2		-H	$-OCH_3$	-OH	-Br	69	140
TRM-3		-Cl	-H	-Cl	-H	76	84
RMT-1	Cu(II)	-H	$-OCH_3$	$-OCH_3$	-H	60	>350
RMT-2	Ni(II)					65	302
RMT-3	Co(II)					71	>350
RMT-4	Cu(II)	-H	$-OCH_3$	-OH	-Br	59	262
RMT-5	Ni(II)					62	>350
RMT-6	Co(II)					55	>350
RMT-7	Cu(II)	-Cl	-H	-Cl	-H	56	212
RMT-8	Ni(II)					59	196
RMT-9	Co(II)					70	240

Results and Discussion

In the elemental analysis of the synthesized ligands and all three metal complexes were shown by found percentages and were matched with calculated (Table 2). In the IR spectra, some significant stretching bands due to -N-H, -N-N- and -C=S were observed in between at 3200-3400 cm^{-1}, 1028-1050 cm^{-1} and 1250-1310 cm^{-1} respectively. The specific band for thiosemicarbazone (-CH=N-) was observed at 1570-1610 cm^{-1}. The aromatic -C-H and -C=C bands due to at 3173-2955 cm^{-1} and 1512 cm^{-1} respectively. The most important bands in the infrared spectra of the metal (II) complex of thiosemicarbazone are along within their tentative assignment (Table 3). Furthermore, in the spectra of all ligands, the strong band observed at 762-829 cm^{-1} was shifted to lower wavenumber by ca 10-15 cm^{-1} in all metal complexes, indicating that thione sulphur participate as a coordinating site. This prediction was confirmed by the presence of a new band at 405-432 cm^{-1}, which can be assigned to ν(M-S). From the IR data, it can be inferred that the ligand involved in the complexation as a bidentate ligand which coordinated with metal ions through their thione sulphur and azomethine N atom.

Table 2. Color, mass and elemental analysis of compounds

Code	Color	M. wt.	%C	%H	%N	%S	% M
TRM-1	White	316.2	56.80 (56.94)	5.00 (5.10)	17.59 (17.71)	10.03 (10.14)	
TRM-2	Brown	380.4	44.02 (44.11)	3.31 (3.44)	14.62 (14.70)	8.30 (8.41)	
TRM-3	Cream	324.2	47.92 (48.01)	3.03 (3.10)	17.11 (17.23)	9.75 (9.86)	
RMT-1	Green	697.0	52.02 (51.90)	4.21 (4.36)	16.19 (16.14)	9.18 (9.24)	9.32 (9.15)
RMT-2	Green	685.6	52.14 (52.26)	4.29 (4.39)	16.37 (16.25)	9.23 (9.30)	8.66 (8.51)
RMT-3	Brown	689.2	52.33 (52.25)	4.47 (4.38)	16.11 (16.25)	9.38 (9.30)	8.43 (8.55)
RMT-4	Brown	821.0	40.93 (40.81)	2.99 (2.94)	13.49 (13.60)	7.65 (7.78)	7.80 (7.71)
RMT-5	Green	815.2	40.91 (41.05)	2.87 (2.95)	13.61 (13.68)	7.92 (7.83)	7.22 (7.83)
RMT-6	Green	820.0	41.16 (41.04)	2.81 (2.95)	13.79 (13.67)	7.95 (7.83)	7.07 (7.19)
RMT-7	Green	715.0	43.99 (43.86)	2.63 (2.55)	15.65 (15.74)	8.87 (9.01)	8.98 (8.93)
RMT-8	Reddish	703.5	44.16 (44.08)	2.44 (2.57)	15.97 (15.85)	9.16 (9.07)	8.22 (8.30)
RMT-9	Brown	705.2	44.05 (44.15)	2.68 (2.56)	15.91 (15.84)	9.00 (9.07)	8.42 (8.33)

Table 3. Selected IR spectral bands of the compounds (in cm^{-1})

Code	ν(C=N)	ν(C=S)	ν(-NH2)	ν(N-N)	ν(M-N)	ν(M-S)
TRM-1	1608	1303	3282	1028		
TRM-2	1599	1288	3339	1045		
TRM-3	1593	1311	3282	1049		
RMT-1	1599	1255	3402	1028	518	412
RMT-2	1589	1259	3421	1037	522	406
RMT-3	1581	1257	3421	1024	505	416
RMT-4	1585	1288	3313	1045	507	406
RMT-5	1577	1236	3281	1031	507	422
RMT-6	1583	1238	3298	1035	513	432
RMT-7	1558	1292	3331	1049	520	410
RMT-8	1585	1280	3362	1051	516	406
RMT-9	1581	1305	3360	1047	486	410

In the ^{1}H NMR spectra of ligands, the signal due to (-CH=N-) proton, present in this compound, appeared near at 8 ppm as a singlet. The, -C-NH and -N-NH protons were observed near at 10 ppm and 12 ppm as a singlet, respectively. All the aromatic protons were observed in the expected regions. In the ^{13}C NMR spectra of ligands the signal due to (-CH=N-) carbon, appeared near at 142 ppm and -C=S carbon appeared near at 177 ppm and all the aromatic carbons were observed in the expected regions. The ^{13}C NMR spectrum provides direct information about the carbon skeleton of ligands.

The electronic spectra of complexes show bands at 310-320 nm and 340-355 nm assigned to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions respectively. All complexes have bands at 410-445 nm due to ligand metal charge transfer transition and very weak and broad bands at 720-756 nm showed d-d transitions. The Cu(II) complexes show the bands near at 744 nm according to $^2B1g \rightarrow {}^2B2g$, $^2Bg \rightarrow {}^2Eg$ and $^2B1g \rightarrow {}^2A1g$ transitions suggesting the square planar geometry for them[14]. The Ni(II) complexes display bands near at 684 nm in the existence of $^3A2g \rightarrow {}^3T1g$ (P), $^3A2g \rightarrow {}^3T1g$ (F) and $^3A2g \rightarrow {}^3T2g$ and the Co(II) complexes exhibits bands near at 748 nm assigned to $^4A2g \rightarrow {}^4T1g$(F) and $^4A2g \rightarrow {}^4T1g$(P) transitions also suggesting the tetrahedral configuration[15,16].

The room temperature magnetic moments for the copper(II), nickel(II) and cobalt(II) complexes correspond to the values normally observed compound (where μ_{eff} is the effective magnetic moment). The molar conductivities of the complexes were measured using a ELICO CM-180 conductivity meter in dimethylformamide solutions (10^{-3} M). Molar conductivity and magnetic moments were taken in room temperature (Table 4).

Table 4. Molar conductivity and effective magnetic moment

Code	Molar cond.(Ω^{-1} cm^2 mol^{-1})	μ_{eff} B.M.
RMT-1	4.18	2.16
RMT-2	4.92	3.34
RMT-3	3.65	4.49
RMT-4	4.56	2.08
RMT-5	3.61	3.54
RMT-6	4.08	4.36
RMT-7	4.51	1.93
RMT-8	4.36	3.18
RMT-9	4.78	4.06

Antimicrobial activity

All the synthesized compounds were tested for their antibacterial and antifungal activity. Minimum Inhibitory concentration of compounds studied *in vitro* by broth dilution method[17]. Three bacteria and four fungal strains were compared with Standard drugs (Table 5 and 6).

Antibacterial study shows that metal complexes (RMT-7 to 9) show better activity compared to its original ligand TRM-3. Similarly, metal complexes (RMT- 7 to 9) shows better activity against fungi compared to its ligand (TRM- 3).While metal complexes named RMT- 4, 6, 7, 8 and 9 have shown comparative activity against bacteria compared to standard drugs. While metal complexes named RMT- 1, 3, 4, 7, 8 and 9 have shown similar activities against fungi compared to standard drugs.

Table 5. MIC against different bacteria (in µg/mL)

Code	*E. Coli* MTCC 443	*S. Epidermidis* MTCC 442	*S. Aureus* MTCC 96
TRM-1	500	250	500
TRM-2	500	250	500
TRM-3	62.5	25	25
RMT-1	1000	250	500
RMT-2	500	250	1000
RMT-3	1000	500	>1000
RMT-4	62.5	31.25	62.5
RMT-5	500	250	1000
RMT-6	62.5	31.25	125
RMT-7	31.25	31.25	62.5
RMT-8	31.25	31.25	31.25
RMT-9	62.5	62.5	125
Ampicillin	100	200	250
Chloramphenicol	50	25	50
Ciprofloxacin	25	50	50

Table 6. MIC against different Fungi (in µg/mL)

Code	*C. Albicans* MTCC 227	*A. Niger* MTCC 282	*S. Cerevisiae* MTCC 170	*E. Floccosum* MTCC 7880
TRM-1	250	500	200	1000
TRM-2	500	250	500	1000
TRM-3	150	200	250	500
RMT-1	500	500	1000	>1000
RMT-2	1000	500	>1000	>1000
RMT-3	500	1000	500	>1000
RMT-4	500	250	500	1000
RMT-5	1000	500	500	>1000
RMT-6	1000	500	>1000	500
RMT-7	250	500	250	1000
RMT-8	150	500	250	500
RMT-9	150	500	500	500
Nystatin	100	100	100	100
Greseofulvin	500	100	500	500

Conclusion

1, 4- Thiosemicarbazone derivatives used as ligands to synthesize Co(II), Ni(II) and Co(II) based metal complexes. Antibacterial and antifungal study indicates that some metal complexes have shown better activity than its ligand while some showed similar activity compared to standard drugs taken.

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