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One-pot synthesis and spectral characterization of 5-Substitutedfuran-2-carbaldehyde N^4-cyclohexyl thiosemicarbazones and their Ni(II) complexes

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Abstract

In this work, the synthesis of thiosemicarbazones (I-V) was carried out using a one-pot method, multicomponent and catalyst-free reaction of cyclohexyl isothiocyanate, hydrazine monohydrate, and 5-substituted-2-furancarbaldehydes in good yields. The chemical structures of 5-substituted-2-furancarbaldehyde thiosemicarbazones were elucidated using UV Vis, IR, ^{1}H NMR, ^{13}C NMR, mass spectra, and elemental analysis. Also, the reaction of $NiCl_2.6H_2O$ with thiosemicarbazones in a 1:2 molar ratio by refluxing gave the nickel (II) complexes (Ia-Va) as binuclear and their structures characterized by UV Vis, IR, and elemental analysis.

Keywords: Thiosemicarbazone, nickel (II) complexes, one pot synthesis

1. Introduction

Thiosemicarbazone derivatives (RNH-CS-NH-NHR') are a large group of thiourea derivatives that have gained attention due to pharmaceutical and medical applications in the last decades [1-3]. They are versatile ligands owing to supply selectivity, coordination tendency, and stability towards metal ions [4,5]. And also, they are a significant group of N, S-donor ligands due to their structural diversity and donor properties [6-8]. Thiosemicarbazones and their transition metal complexes display a wide range of biological activities such as anticancer, antiviral, anti-inflammatory, antidiabetic, antimicrobial, anticonvulsant activities [9-14]. Depending on the type of ketone and aldehyde used, thiosemicarbazones can form monodentate, bidentate, and multidentate chelates with metal ions [15].

Thiosemicarbazones exist in thione-thiol tautomeric form due to intramolecular proton transfer and while coordinating with metals [16]. They can form anionic, cationic, or neutral chelates depending on the pH of the environment, oxidation, and the presence of relative metal ions [17]. For example, depending on the pH of the environment, while benzaldehyde thiosemicarbazone acts as a neutral ligand, it has been found that salicylaldehyde thiosemicarbazone acts as anionic and triangular in metal complexes [18].

Despite these important properties, the current methods used for the synthesis of thiosemicarbazone derivatives are approaches that time, solvent, and energy-consuming as they involve the isolation and purification of each intermediate [19]. Thiosemicarbazones are generally obtained by the condensation reaction between thiosemicarbazides with aldehydes/ketones [20,21].

In recent years, heterocyclic thiosemicarbazones and their transition metal complexes have been extensively studied due to their biological activities and analytical applications [22-26]. The synthesis and spectroscopic studies of heterocyclic and aromatic thiosemicarbazones and their antibacterial, antifungal, antioxidant, cytotoxic, and antiviral activities have reported by our research group [11,12,20,21]. Also, we previously described the synthesis, characterization, antiviral, and cytotoxic activity of thiosemicarbazones derived from 5-substituted thiophene-2-carboxaldehydes and their Pt(II) and Pd(II) complexes [9]. Cyclohexyl thiosemicarbazones (substituted phenyl/thiophene-2-yl/furan-2-yl) were synthesized and screened against HER-2 overexpressed four breast cancer cell lines; SKBr-3, MCF-7, MDA-MB-468, and MDA-MB-231. against breast cancer cells by another research group [27]. On the other hand, especially nickel(II) complexes of

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heterocyclic thiosemicarbazones have attracted attention due to their biological activities [28,29]. For example, a study has been reported the synthesis, spectroscopic characterization, and antifungal activity of 5-methyl-2-furaldehyde thiosemicarbazone and its Ni(II) complex [30].

As a part of our ongoing research, we reported here the catalyst-free synthesis of thiosemicarbazones (I-V) was performed by the multicomponent one-pot reactions of hydrazine monohydrate, cyclohexyl isothiocyanate, and 5-substitutedfuran-2-carbaldehydes. Also, we synthesized their Ni(II) complexes as they can exhibit potent cytotoxic, antiviral, antibacterial, and antifungal activities.

2. Experimental

2.1. Materials and Measurements

All chemicals (cyclohexyl isothiocyanate, 2-furancarbaldehyde, 5-chloro-2-furancarbaldehyde, 5-phenyl-2-furancarbaldehyde, 5-(3-trifluoromethyl)-phenyl-2- furancarbaldehyde, 5-(4-chlorophenyl)-2-furancarbaldehyde, hydrazine monohydrate, and nickel(II) chloride hexahydrate) and solvents were purchased from Sigma Aldrich and used without further purification. The progress of all reactions was followed by thin-layer chromatography (TLC). TLC was performed on silica gel plates (Merck Silica Gel 60, F_{254}, 0.2 mm) using EtOAc/hexane (v/v 1:1) as a solvent system and the plates were visualized by UV light or exposure to iodine vapor.

Melting points of all compounds were determined with an EZ-Melt MPA120 Automated Melting Point apparatus and the results were given uncorrected. UV measurements of all compounds in DMF were performed on a PG Instruments T80+ UV Vis Spectrometer (190-1100 nm). The IR spectra (4000– 400 cm^{-1}) for KBr discs were recorded on a Perkin Elmer 100 FT-IR spectrometer. The ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker Avance-DPX-400 NMR spectrometer in DMSO-d_6 using TMS as the internal standard at room temperature. Chemical shifts (δ) are reported in parts per million (ppm). The splitting of proton resonances in ^{1}H NMR spectra is given as *s*= singlet, *d*= doublet, *t*= triplet, and *m*= multiplet. The mass spectra were obtained using an LC/MS Agilent 1100 MSD series spectrometer in the electrospray mode. Elemental (CHNS) analyses were performed using a VarioMICRO elemental analyzer.

2.2. A General Method for the Synthesis of Thiosemicarbazones (I-V)

To a hot solution of 5-substitutedfuran-2-carbaldehydes (5.20 mmol) in methanol (50 mL) was added hydrazine monohydrate (5.20 mmol) and cyclohexyl isothiocyanate (5.20 mmol). The reaction mixture was refluxed, monitoring the progress of the reaction by TLC (about 24-35 h.) After the reaction mixture was cooled to room temperature, it was filtered and the crude product was recrystallized from methanol [19].

2.2.1. Furan-2-carbaldehyde ^{4}N-cyclohexyl thiosemicarbazone (I)

Yellow solid (methanol). Yield:73%, m.p.: 175-176 °C. Anal. calc. ($C_{12}H_{17}N_3OS$): C, 57.34; H, 6.82; N, 16.72; S, 12.76; found: C, 57.05; H, 6.84; N, 16.47; S, 12.56 %. ES-MS (m/z) 251 [M^+], 252 [$M+H]^+$. UV/Vis λ_{max} (nm): 326, 278. IR ν_{max} (cm^{-1}): 3242, 3120 (N-H); 1614 (C=N); 1087, (C-N); 1052 (N-N); 775 (C=S). ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 11.42 (s, 1H, CSN*H*N); 7.98 (s, 1H, cyclohexyl-N*H*); 7.82 (s, 1H, *H*C=N); 7.70 (d, 1H, *J*=3.52 Hz Ar*H*, C_2 proton of furan); 6.96 (d, 1H, *J*= 3.40 Hz, Ar*H*, C_4 proton of furan); 6.62 (dd, 1H, *J*= 3.39 Hz, Ar*H*, C_3 proton of furan); 4.15 (m, 1H, C*H* proton of cyclohexyl); 1.87-1.10 (m, 10H,-CH_2 protons of cyclohexyl). ^{13}C NMR (DMSO-d_6, 100 MHZ, δ ppm): 176.5 (*C*=S); 149.2 (Ar*C*); 138.3 (H*C*=N); 134.2, 118.0, 112.2 (Ar*C*), 53.4, 32.4, 25.6, 25.2 (*C* atoms of cyclohexyl).

2.2.2. 5-Chlorofuran-2-carbaldehyde ^{4}N-cyclohexyl thiosemicarbazone (II)

Yellow solid (methanol). Yield 68%, m.p.: 158-159 °C. Anal. calc. ($C_{12}H_{16}ClN_3OS$): C, 50.43; H, 5.64; N, 14.70; S, 11.22; found: C, 50.28; H, 5.90; N, 14.36; S, 11.58 %. ES-MS (m/z) 285 [M^+], 286 [$M+H]^+$. UV/Vis λ_{max} (nm): 360, 295. IR ν_{max} (cm^{-1}): 3268, 3126 (N-H); 1627 (C=N); 1089, (C-N); 1055 (N-N); 796 (C=S). ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 11.46 (s, 1H, CSN*H*N); 7.89 (s, 1H, cyclohexyl-N*H*); 7.74 (s, 1H, *H*C=N); 7.05 (d, 1H, *J*=3.54 Hz Ar*H*, C_3 proton of furan); 6.65 (d, 1H, *J*= 3.63 Hz, Ar*H*, C_4 proton of furan); 4.85 (m, 1H, C*H* proton of cyclohexyl); 1.92-1.18 (m, 10H,-CH_2 protons of cyclohexyl). ^{13}C NMR (DMSO-d_6, 100 MHz, δ ppm): 176.8 (*C*=S); 150.5 (Ar*C*); 138.3 (H*C*=N); 132.2, 116.4, 110.6 (Ar*C*); 53.3, 32.5, 25.7 ve 25.5 (*C* atoms of cyclohexyl).

2.2.3. 2-(5-phenyl)furancarbaldehyde ^{4}N-cyclohexyl thiosemicarbazone (III)

Dark yellow solid (methanol). Yield 83%, m.p.: 166-167 °C. Anal. calc. ($C_{18}H_{21}N_3OS$): C, 66.02; H, 6.46; N, 12.83; S, 9.79 found: C, 66.25; H, 6.42; N, 12.51; S, 9.88 %. ES-MS (m/z) 327 [M^+], 328 [$M+H]^+$. UV/Vis λ_{max} (nm): 391, 295. IR ν_{max} (cm^{-1}): 3253, 3126 (N-H); 1628 (C=N); 1090, (C-N); 1059 (N-N); 797 (C=S). ^{1}H NMR (DMSO-d_6, 400 MHz, δ ppm): 11.49 (s, 1H, CSN*H*N); 8.00 (s. 1H, cyclohexyl-N*H*); 7.82 (s, 1H, *H*C=N); 7.80 (d, 2H, *J*=8.62 Hz, Ar*H*, ortho protons); 7.47 (d, 2H, *J*=8.62 Hz, Ar*H*, meta protons); 7.30 (t, 2H, Ar*H* para proton); 7.14 (d, 1H, *J*= 3.60 Hz, Ar*H*, C_4 proton of furan); 7.10 (d, 1H, *J*= 3.62 Hz, Ar*H*, C_3 proton of furan); 4.21 (m, 1H, C*H* proton of

cyclohexyl); 1.91-1.21 (m, 10H,-C*H*$_2$ protons of cyclohexyl). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz, δ ppm): 176.9 (*C*=S); 156.0, 150.3 (Ar*C*); 133.1 (H*C*=N); 130.7, 130.2, 129.5, 125.2, 116.6, 109.5 (Ar*C*); 53.2, 32.5, 25.7, 25.3 (*C* atoms of cyclohexyl).

2.2.4. 2-[5-(3-trifluoromethyl)phenyl]furancarbaldehyde ^{4}N-cyclohexyl thiosemicarbazone (IV)

Yellow solid (methanol). Yield 86%, m.p.: 189-190 °C. Anal. calc. ($C_{19}H_{20}F_3N_3OS$): C, 57.71; H, 5.10; N, 10.63; S, 8.11; found: C, 57.95; H, 5.18; N, 10.49; S, 8.21 %. ES-MS (m/z) 395 [M$^+$], 396 [M+H]$^+$. UV/Vis λ_{max} (nm): 385, 270. IR ν_{max} (cm^{-1}): 3245, 3134 (N-H); 1626 (C=N); 1072, (C-N); 1053 (N-N); 787 (C=S). ^{1}H NMR (DMSO-*d*$_6$, 400 MHz, δ ppm): 11.58 (s, 1H, CSN*H*N); 8.13 (s. 1H, cyclohexyl-N*H*); 8.06 (s, 1H, *H*C=N); 8.02 (s, 1H, Ar*H*, ortho proton to CF_3); 7.90 (s, 1H, Ar*H*, ortho proton to CF_3); 7.71-7.63 (m, 2H, Ar*H*, meta and para protons to CF_3); 7.38 (d, 1H, *J*= 3.63 Hz, Ar*H*, C$_4$ proton of furan); 7.16 (d, 1H, *J*= 3.62 Hz, Ar*H*, C$_3$ proton of furan); 4.18 (m, 1H, C*H* proton of cyclohexyl); 1.92-1.17 (m, 10H,-C*H*$_2$ protons of cyclohexyl). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz, δ ppm): 181.1 (*ipso C* to CF_3); 176.2 (*C*=S); 154.9 ve 153.0 (Ar*C*); 132.4 (H*C*=N); 131.6, 130.7, 129.3, 126.6, 116.2, 111.2 (Ar*C*); 53.4, 32.4, 25.7, 26.6 (*C* atoms of cyclohexyl).

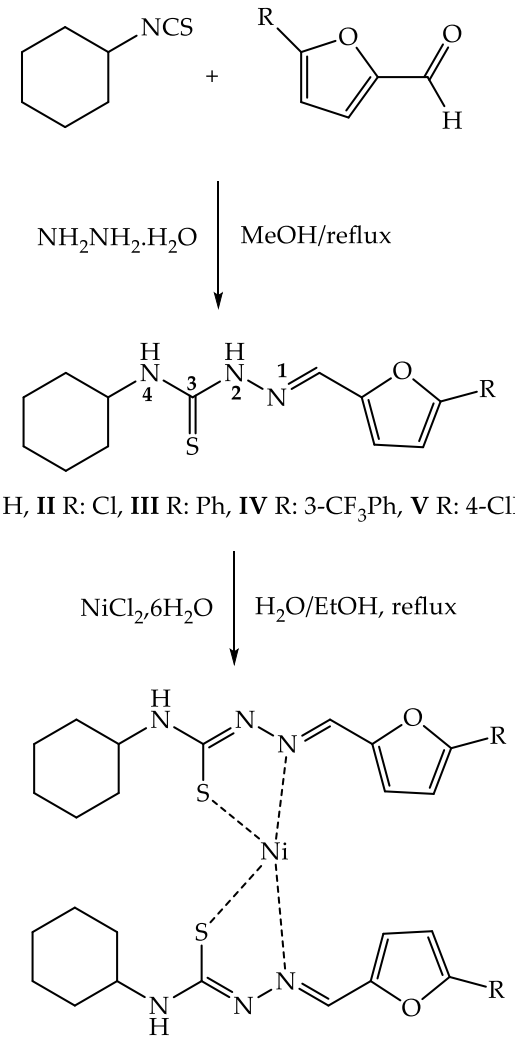
2.2.5. 2-[5-(4-chlorophenyl)]furancarbaldehyde ^{4}N-cyclohexyl thiosemicarbazone (V)

Orange solid (methanol) Yield 76%, m.p.: 198-199 °C. Anal. calc. ($C_{18}H_{20}ClN_3OS$): C, 59.74; H, 5.57; N, 11.61; S, 8.86; found: C, 59.86; H, 5.61; N, 11.55; S, 8.81 %. ES-MS (m/z) 361 [M$^+$], 362 [M+H]$^+$. UV/Vis λ_{max} (nm): 395, 280. IR ν_{max} (cm^{-1}): 3244, 3128 (N-H); 1613 (C=N); 1092, (C-N); 1056 (N-N); 797 (C=S). ^{1}H NMR (DMSO-*d*$_6$, 400 MHz, δ ppm): 11.52 (s, 1H, CSN*H*N); 8.00 (s. 1H, cyclohexyl-N*H*); 7.85 (s, 1H, *H*C=N); 7.82 (d, 2H, *J*=8.57 Hz, Ar*H*, ortho protons); 7.52 (d, 2H, *J*=8.62 Hz, Ar*H*, meta protons); 7.19 (d, 1H, *J*=3.63 Hz, Ar*H*, C$_4$ proton of furan); 7.12 (d, 1H, *J*=3.62 Hz, Ar*H*, C$_3$ proton of furan); 4.25 (m, 1H, C*H* proton of cyclohexyl); 1.91-1.16 (m, 10H,-C*H*$_2$ protons of cyclohexyl). ^{13}C NMR (DMSO-*d*$_6$, 100 MHz, δ ppm): 176.1 (*C*=S); 154.8, 151.0 (Ar*C*); 133.9 (H*C*=N); 132.9, 130.2, 129.6, 126.9, 116.5, 110.2 (Ar*C*), 53.3, 32.5, 25.7, 25.4 (*C* atoms of cyclohexyl).

2.3. A General Method for the Synthesis of Ni(II) complexes (Ia-Va)

To a hot solution of 5-substituted-2-furancarbaldehyde ^{4}*N*-cyclohexyl thiosemicarbazones (5 mmol) in ethanol (10 mL), a hot solution of $NiCl_2.6H_2O$ (2.5 mmol) in distilled water (5 mL) was added slowly dropwise. The reaction mixture was refluxed for 12-24 h. A colored solid was obtained by cooling at room temperature and filtration. The crude product was washed with cold ethanol and finally dried in a vacuum over silica gel [31].

The chemical and physical spectral characteristics of the Ni complexes are given below.



I R: H, **II** R: Cl, **III** R: Ph, **IV** R: 3-CF_3Ph, **V** R: 4-ClPh

Ia R: H, **IIa** R: Cl, **IIIa** R: Ph, **IVa** R: 3-CF_3Ph, **Va** R: 4-ClPh

Scheme 1. Synthetic pathway of ligands and their Ni(II) complexes

2.3.1. Bis(2-furaldehydethiosemicarbazone)nickel(II) [Ni(FTSC)$_2$] (Ia)

Green solid. Yield 64%, m.p.: 256 °C. Anal. calc. ($C_{24}H_{34}N_6NiO_2S_2$): C, 51.35; H, 6.10; N, 14.97; S, 11.42; found: C, 51.26; H, 6.02; N, 14.75; S, 11.48 %. UV/Vis λ_{max}(nm): 380, 340, 270. IR ν_{max}(cm^{-1}, KBr): 3342 (N-H); 1585 (C=N); 1086, (C-N); 1041 (N-N); 747 (C=S); 558 (Ni-N); 439 (Ni-S).

2.3.2. Bis(5-chloro-2-furaldehydethiosemicarbazone)-nickel(II) [Ni(ClFTSC)$_2$] (IIa)

Green solid. Yield 62%, m.p.: 249 °C. Anal. calc. ($C_{24}H_{32}Cl_2N_6NiO_2S_2$): C, 45.73; H, 5.12; N, 13.33; S, 10.17; found: C, 45.82; H, 5.26; N, 13.48; S, 10.34 %. UV/Vis λ_{max}(nm): 381, 340, 269. IR ν_{max}(cm^{-1}, KBr): 3345 (N-H); 1592 (C=N); 1087, (C-N); 1040 (N-N); 752 (C=S); 566 (Ni-N); 437 (Ni-S).

2.3.3. Bis(5-phenyl-2-furaldehydethiosemicarbazone)-nickel(II) [Ni(PhFTSC)$_2$] (IIIa)

Dark brown solid. Yield 46%, m.p.: 241 °C. Anal. calc. ($C_{36}H_{42}N_6NiO_2S_2$): C, 60.59; H, 5.93; N, 11.78; S, 8.99; found: C, 60.88; H, 5.72; N, 11.97; S, 9.05 %. UV/Vis λ_{max}(nm): 410, 390, 294. IR ν_{max}(cm^{-1}, KBr): 3392 (N-H); 1600 (C=N); 1068, (C-N); 1018 (N-N); 758 (C=S); 552 (Ni-N); 438 (Ni-S).

2.3.4. Bis[5-(3-trifluoromethyl)phenyl]-2-furaldehydethiosemicarbazone)nickel(II) [Ni(TFMPhFTSC)$_2$] (IVa)

Dark green solid. Yield 55%, m.p.: 264 °C. Anal. calc. ($C_{38}H_{40}F_6N_6NiO_2S_2$): C, 53.72; H, 4.75; N, 9.89; S, 7.55; found: C, 53.86; H, 4.63; N, 9.92; S, 7.74 %. UV/Vis λ_{max}(nm): 391, 355, 270. IR ν_{max}(cm^{-1}, KBr): 3436 (N-H); 1588 (C=N); 1097, (C-N); 1066 (N-N); 763 (C=S); 563 (Ni-N); 445 (Ni-S).

2.3.5. Bis[5-(4-chlorophenyl)]-2-furaldehydethiosemicarbazone)nickel(II) [Ni(ClPhFTSC)$_2$] (Va)

Brown solid. Yield 47%, m.p.: 238 °C. Anal. calc. ($C_{36}H_{40}Cl_2N_6NiO_2S_2$): C, 55.26; H, 5.15; N, 10.74; S, 8.20; found: C, 55.02; H, 5.36; N, 10.49; S, 8.05 %. UV/Vis λ_{max}(nm): 399, 345, 270. IR ν_{max}(cm^{-1}, KBr): 3423 (N-H); 1567 (C=N); 1092, (C-N); 1065 (N-N); 789 (C=S); 553 (Ni-N); 440 (Ni-S).

3. Results and Discussion

3.1. Synthesis

The one-pot synthesis route of 5-substituted-2-furancarbaldehyde thiosemicarbazones is outlined in Scheme 1. A series of thiosemicarbazones (I-V) were synthesized by refluxing in methanol an equimolar ratio of the 5-substituted-2-furancarbaldehyde, hydrazine monohydrate, and cyclohexyl isothiocyanate without using a catalyst [19]. Furan-2-carbaldehyde 4N-cyclohexyl thiosemicarbazone (I) was synthesized previously [32] but other thiosemicarbazone derivatives (II-V) were firstly synthesized. The chemical structures of 5-substituted-2-furancarbaldehyde thiosemicarbazones were elucidated using UV Vis, IR, ^{1}H NMR, ^{13}C NMR, mass spectra, and elemental analysis. The reaction of $NiCl_2.6H_2O$ with thiosemicarbazones in a 1:2 molar ratio by refluxing gave the nickel complexes (**Ia-Va**) [31]. The analytical and physical data for the thiosemicarbazones and their nickel (II) complexes are given in Table 1. The analytical data of thiosemicarbazones and their Ni(II) complexes showed that the compounds were in good agreement with their empirical formula. The elemental analysis results showed that the percentage of carbon, hydrogen, nitrogen, and sulfur is compatible with their theoretical values and also suggested that the Ni(II) complexes contain 1:2 metals to ligand ratio. All nickel (II) complexes are stable in air, but their low solubility prevented the NMR characterization. Since the complexes were decomposed on heating, a clear melting point was not obtained.

Table 1. Physical data of thiosemicarbazone derivatives and their Ni(II) complexes

Compound No	Molecular Formulae	Color	Yield (%)	Mp/Dec. Temp. (°C)	Found/(Calculated)			
					C	H	N	S
I	$C_{12}H_{17}N_3OS$	Yellow	73	175-176	57.05/(57.34)	6.84/(6.82)	16.47/(16.72)	12.56/(12.76)
Ia	$C_{24}H_{34}N_6NiO_2S_2$	Green	64	256	51.26/(51.35)	6.02/(6.10)	14.75/(14.97)	11.48/(11.42)
II	$C_{12}H_{16}ClN_3OS$	Yellow	68	158-159	50.28/(50.43)	5.90/(5.64)	14.36/(14.70)	11.58/(11.22)
IIa	$C_{24}H_{32}Cl_2N_6NiO_2S_2$	Green	62	249	45.82/(45.73)	5.26/(5.12)	13.48/(13.33)	10.34/(10.17)
III	$C_{18}H_{21}N_3OS$	Dark Yellow	83	166-167	66.25/(66.02)	6.42/(6.46)	12.53/(12.83)	9.88/(9.79)
IIIa	$C_{36}H_{42}N_6NiO_2S_2$	Dark Brown	46	241	60.88/(60.59)	5.72/(5.93)	11.97/(11.78)	9.05/(8.99)
IV	$C_{19}H_{20}F_3N_3OS$	Yellow	86	189-190	57.95/(57.71)	5.18/(5.10)	10.49/(10.63)	8.21/(8.11)
IVa	$C_{38}H_{40}F_6N_6NiO_2S_2$	Dark Green	55	264	53.86/(53.72)	4.63/(4.75)	9.92/(9.89)	7.74/(7.55)
V	$C_{18}H_{20}ClN_3OS$	Orange	76	198-199	59.86/(59.74)	5.61/(5.57)	11.55/(11.61)	8.81/(8.86)
Va	$C_{36}H_{40}Cl_2N_6NiO_2S_2$	Brown	47	238	55.02/(55.26)	5.36/(5.15)	10.49/(10.74)	8.05/(8.20)

3.2. IR Spectral Analysis

Comparison of the IR spectral data of the ligands and their metal complexes provides valuable information on the binding sites of the ligand structure. The most significant vibration bands of the N–H, C=N, and C=S bonds for the thiosemicarbazones and N–H, C=N, C=S, Ni-S, and Ni-N bonds for their complexes are given in the experimental section. Generally, thiosemicarbazones have thione-thiol tautomeric forms in solution due to thioamide groups [33]. The absence of the ν(S–H) band between 2600 and 2800 cm^{-1} and the presence of the ν(N-H) bands at 3120-3128 cm^{-1} and 3242-3268 cm^{-1} and as well as a strong ν(C=S) band at 775-797 cm^{-1} indicates that the ligands remain thione form in the solid phase [34]. The IR spectra reveal the characteristic properties of nickel (II) complexes of thiosemicarbazones. The IR spectra of free ligands and their Ni(II) complexes were compared and given in Table 2. According to the results of this comparison, a different spectral behavior was detected for Ni(II) complexes (**Ia-Va**). It has been observed that when ligands (**I-V**) are coordinated through N, S to the nickel atom, only a strong band ν(NH) occurs at 3342-3436 cm^{-1}. This can be explained by the fact that the ligands deprotonated before coordinating the metal, thus forming a square planar geometry [35]. In all cases, a shift of the ν(C=N) from 1613 cm^{-1} and 1628 cm^{-1} of free ligands (**I-V**), down to 1567 and 1600 cm^{-1} was observed. These shifts prove that

the thiosemicarbazones are coordinated through the N(2) atom [36]. A shift of the ν(C=S) band from 775-797 cm^{-1} of free ligands down to 747-789 cm^{-1} was also observed, corresponding to the coordination of the sulfur atom, with an increase in their thioenol character [37]. In addition, new ν(Ni-S) and ν (Ni-N) bands have emerged in the region 437-445 cm^{-1} and 552-566 cm^{-1}, respectively as further evidence of the coordination of ligands to metal through their bidentate N, S atoms [38].

Table 2. Main characteristic IR vibrational bands of thiosemicarbazones and their nickel(II) complexes

Compound	ν_{max} (cm^{-1})					
	N-H	C=N	N-N	C=S	Ni-N	Ni-S
I	3242	1614	1052	775	-	-
Ia	3342	1585	1041	747	558	439
II	3268	1627	1055	796	-	-
IIa	3345	1592	1040	752	566	437
III	3253	1628	1059	797	-	-
IIIa	3392	1600	1018	758	552	438
IV	3245	1626	1053	787	-	-
IVa	3436	1588	1066	763	563	445
V	3244	1613	1056	797	-	-
Va	3423	1567	1065	789	553	440

3.3. NMR Spectra

When the results of ^{1}H NMR spectra and signal magnitudes are evaluated together with other spectral analysis data, it has been determined that they are a good agreement with the proposed chemical structures. ^{1}H and ^{13}C NMR spectra of the ligands were given in Supplementary Materials. The ^{1}H NMR spectra of all thiosemicarbazones (**I-V**) recorded in DMSO-d_6. In the ^{1}H NMR spectra, two sharp singlet peaks at δ 7.89-8.13 ppm attributed to the N(4) proton and at δ 11.42-11.58 ppm attributed to the N(2) proton, as well as a singlet peak at δ 7.74-8.06 ppm assigned to the HC=N group were observed [38,39]. These signals proved that thiosemicarbazones remain in thione form even in a polar solvent. Furthermore, the ^{13}C NMR spectra of the ligands were recorded in DMSO-d_6. Two important signals at δ 176.1-176.9 and δ 132.4-138.3 ppm attributed to the thioamide (C=S) and imine (C=N) carbons, respectively were observed in ^{13}C NMR of all thiosemicarbazones [40]. The aromatic carbons give resonance signals at 109.5-156.0 ppm. The resonance signals of CH and CH_2 protons for the thiosemicarbazones were assigned at around 53.2-53.4 ppm and 25.2-32.5 ppm, respectively. Since, NMR spectra could not be obtained due to solubility problems of the Ni(II) complexes, the ligands, and their complexes could not be compared.

4. Conclusion

In conclusion, we firstly reported the one-pot synthesis, spectral characterization of 5-substitutedfuran-2-carbaldeyde ^{4}*N*-cyclohexyl thiosemicarbazones (**II-V**) except for furan-2-carbaldehyde ^{4}*N*-cyclohexyl thiosemicarbazone (**I**). The synthesized thiosemicarbazones were characterized by UV Vis, IR, ^{1}H NMR, ^{13}C NMR, ESI-MS, and elemental analysis. On the other hand, we also prepared thiosemicarbazone Ni(II) complexes (**Ia-Va**) as binuclear and their structures characterized by UV Vis, IR, and elemental analysis. Based on the analytical results, the most reasonable structure for the nickel (II) complexes is square planar. In the future, we will study the analytical properties of 5-substitutedfuran-2-carbaldeyde ^{4}N-cyclohexyl thiosemicarbazones and their Ni(II) complexes.

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Supplementary Materials

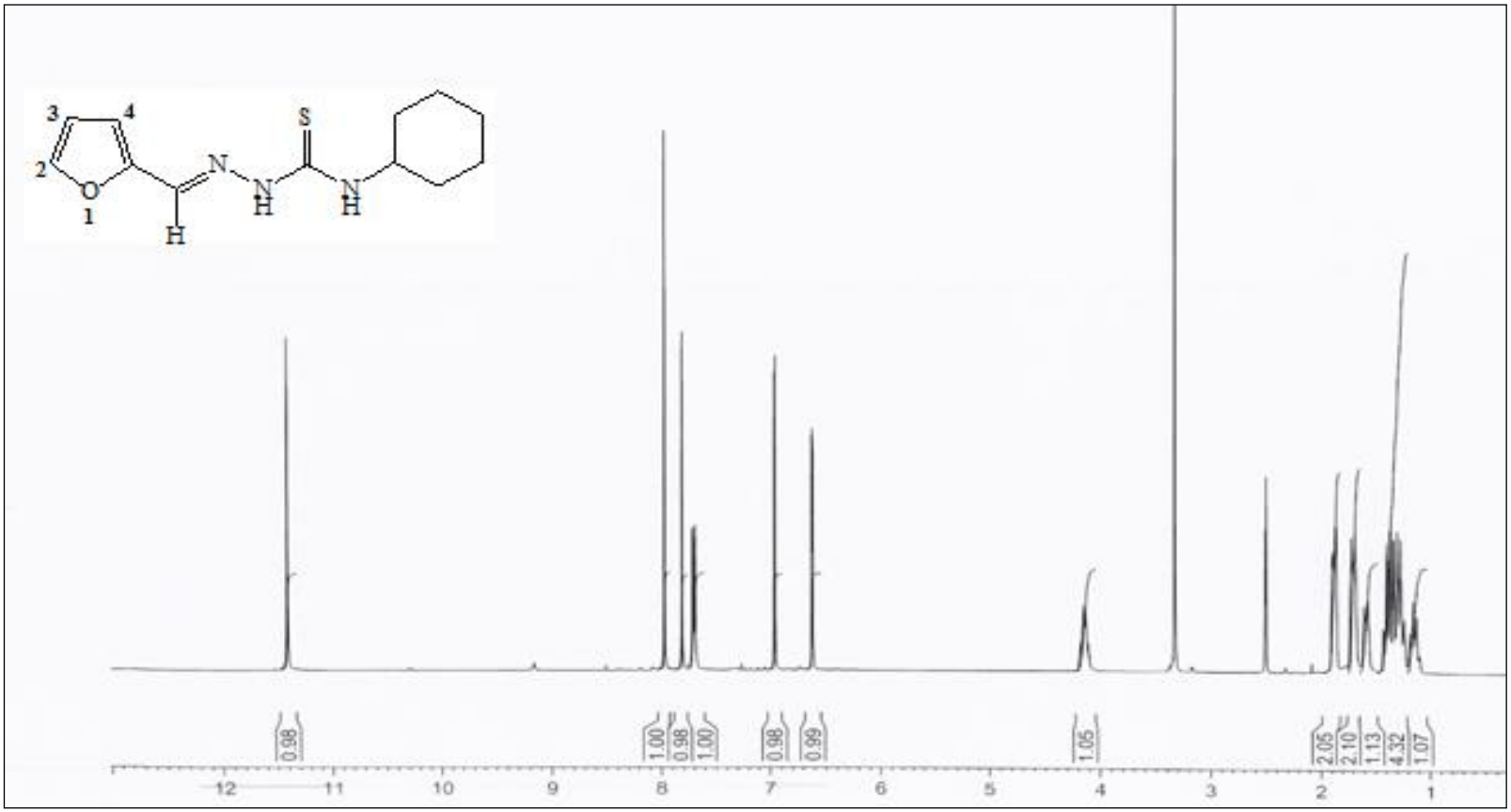


Figure S1. 1H NMR spectrum of compound [I]

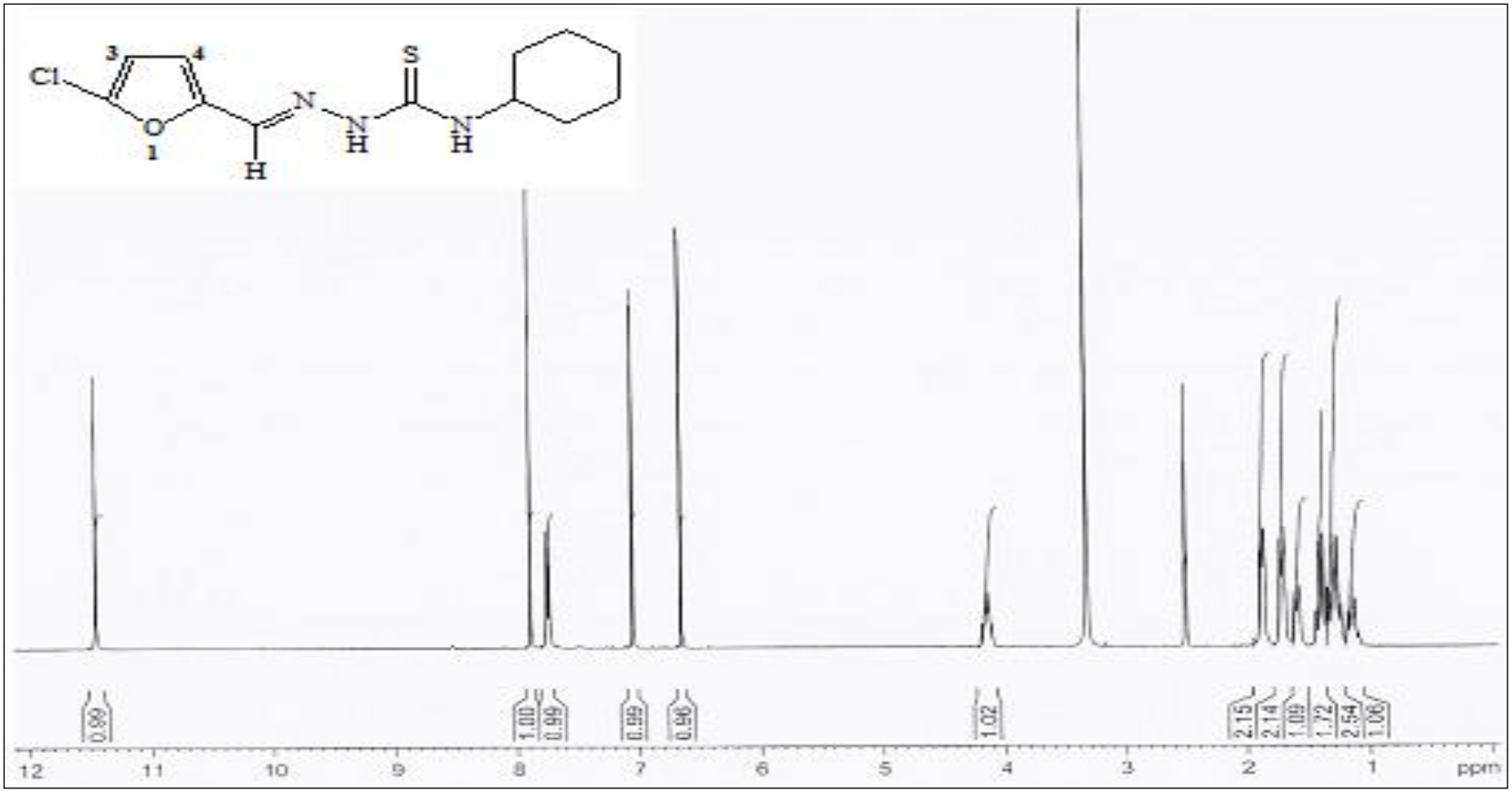
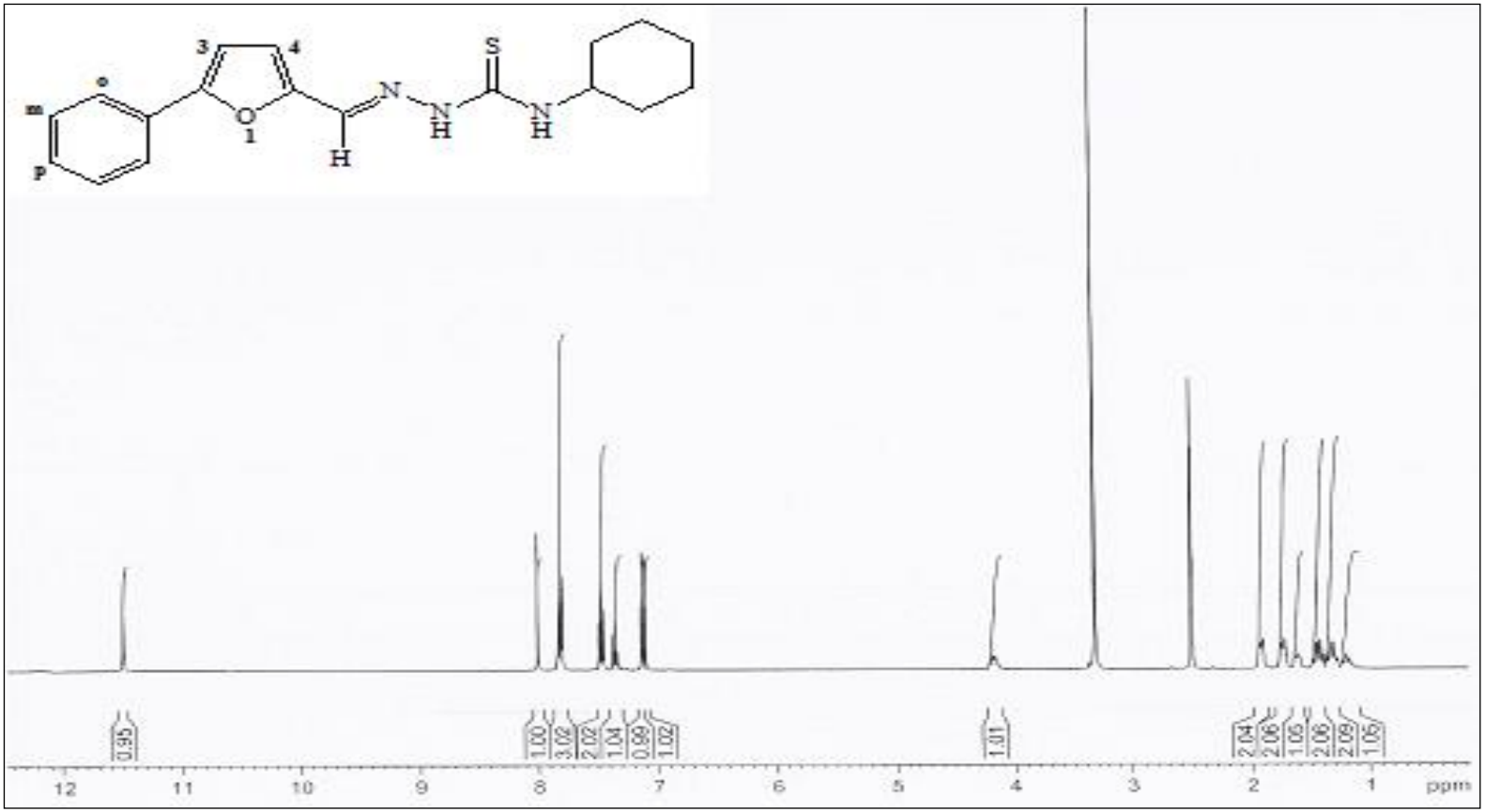


Figure S2. ^{1}H NMR spectrum of compound [II]



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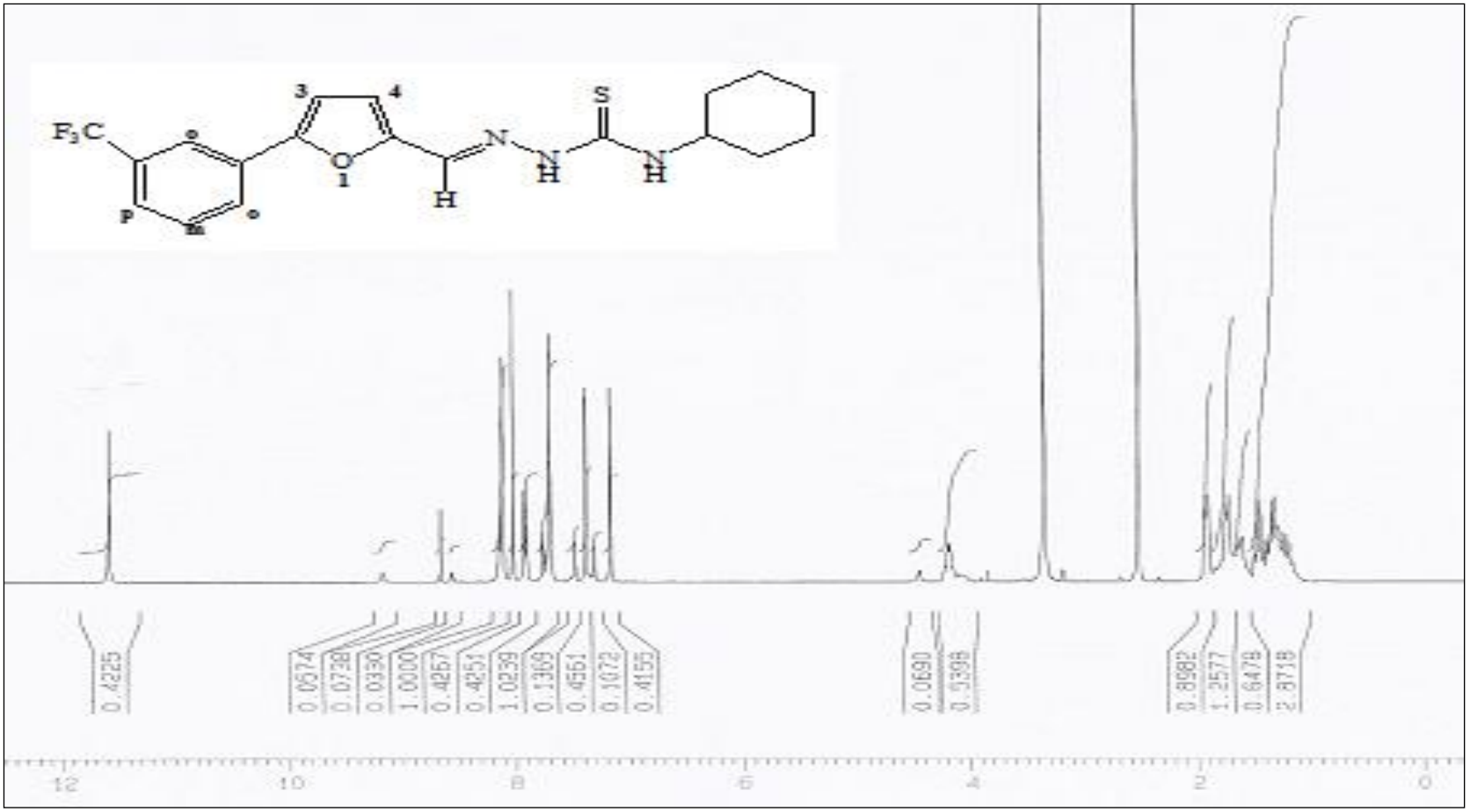

Figure S4. ^{1}H NMR spectrum of compound [IV]

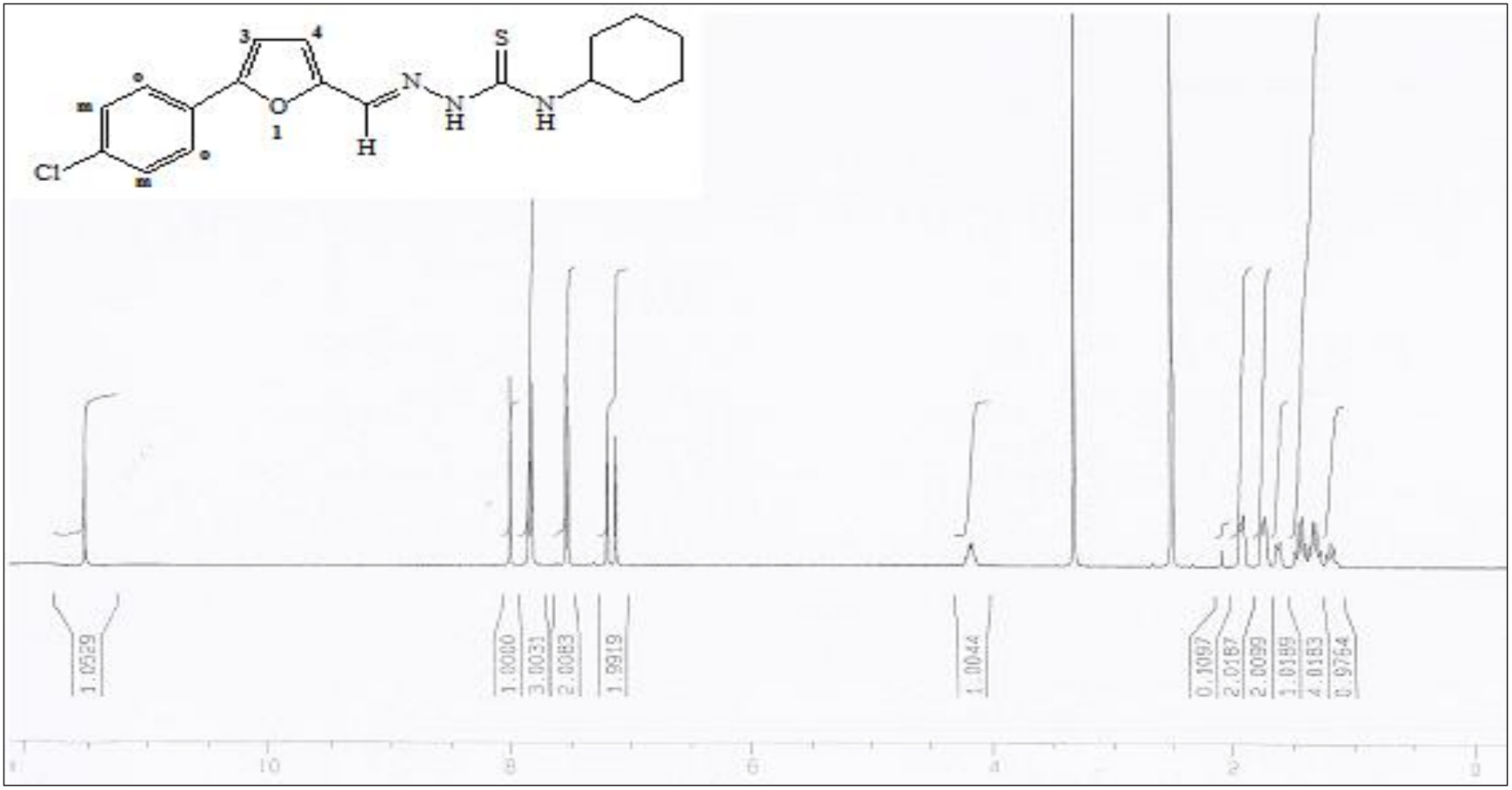

Figure S5. ^{1}H NMR spectrum of compound [V]

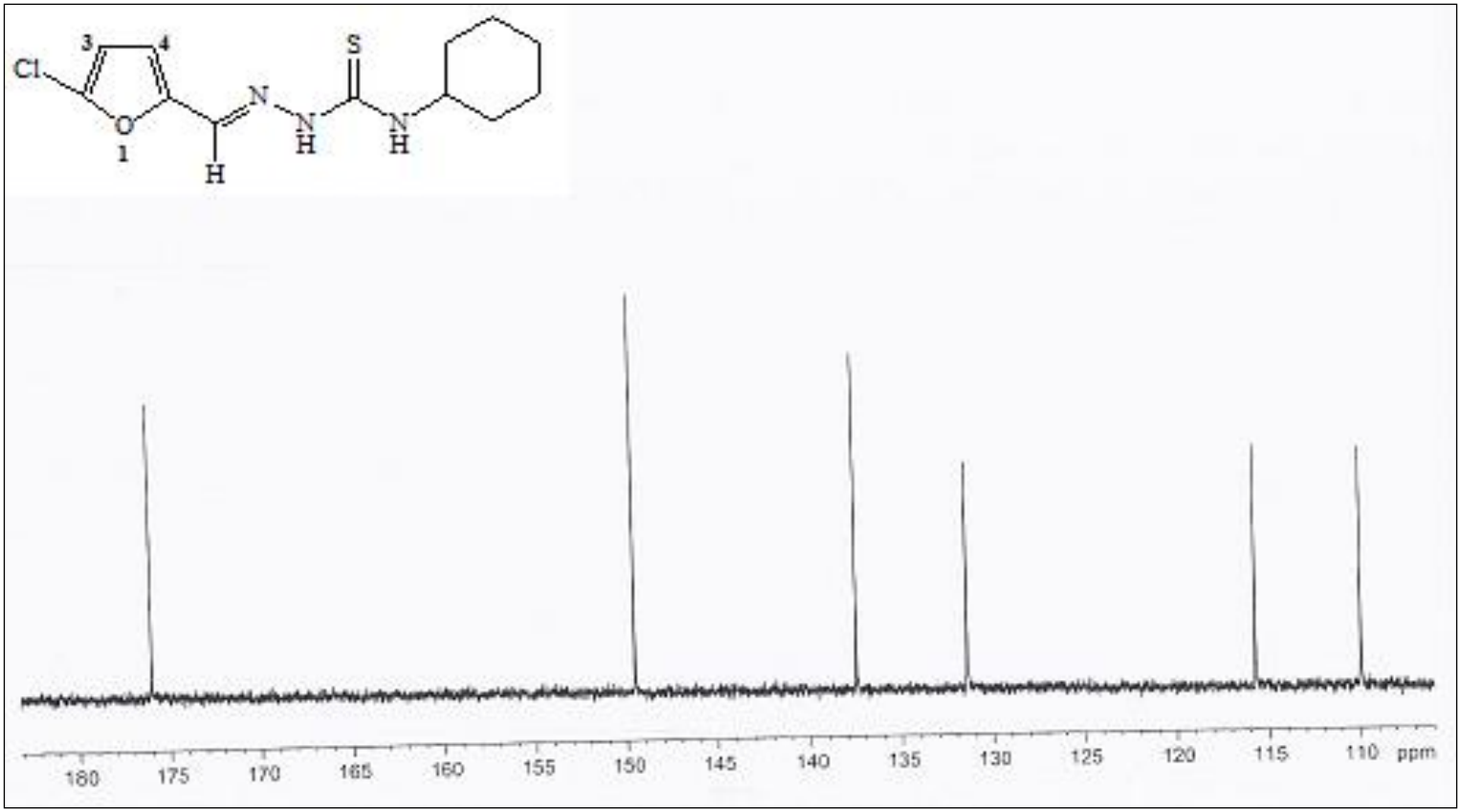

Figure S6. ^{13}C NMR spectrum of compound [II]

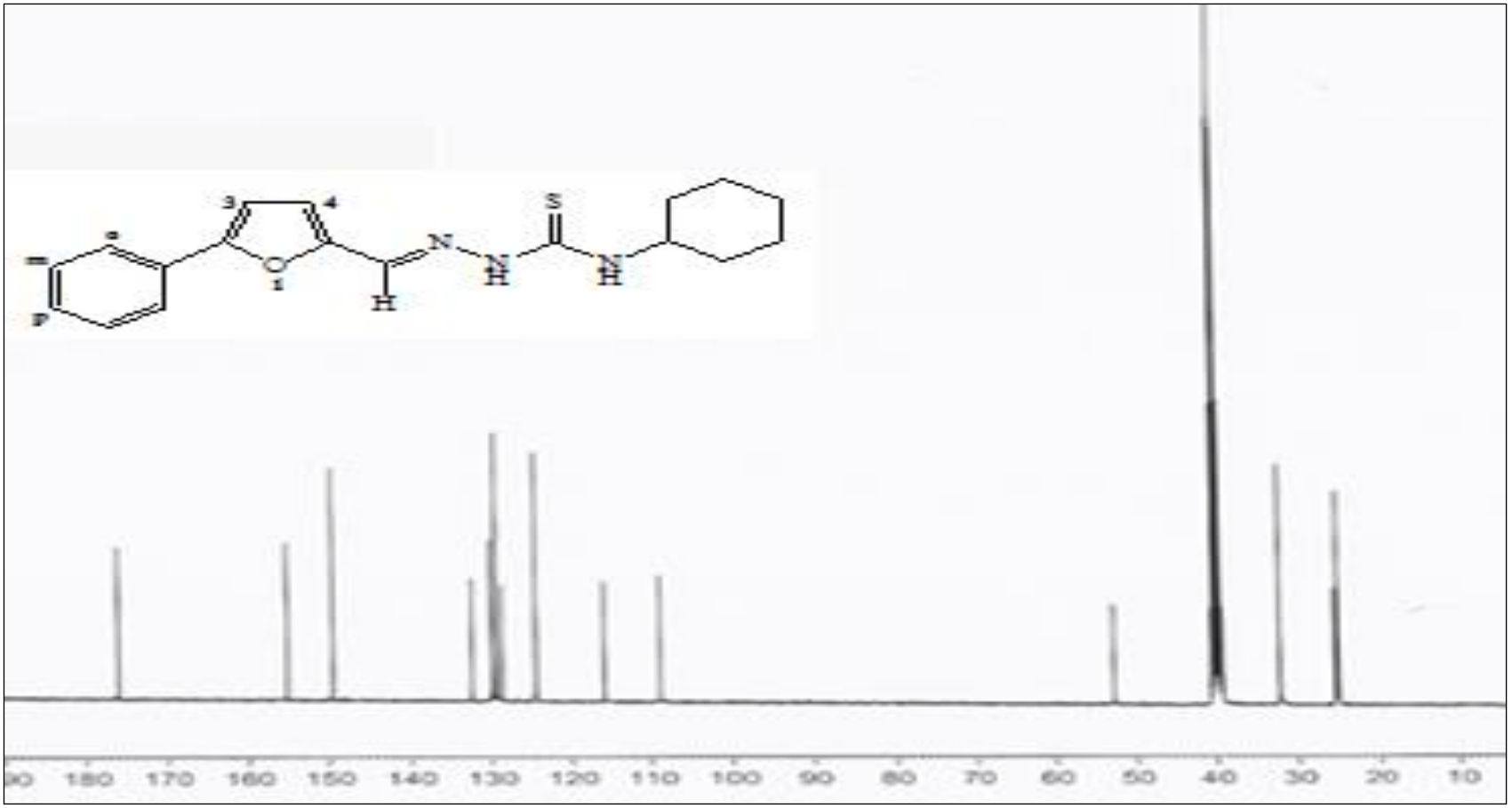

Figure S7. ^{13}C NMR spectrum of compound [III]

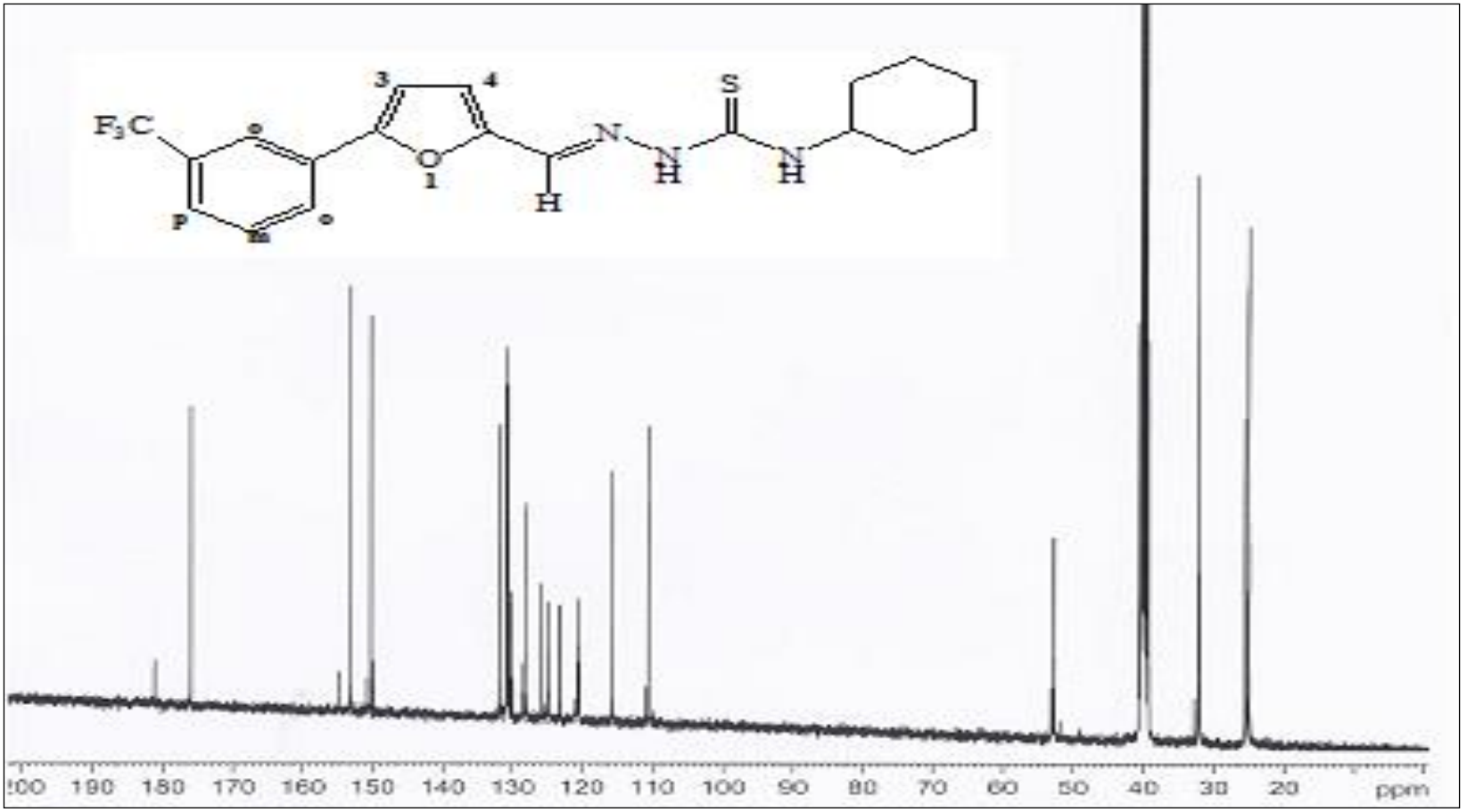

Figure S8. ^{13}C NMR spectrum of compound [IV]

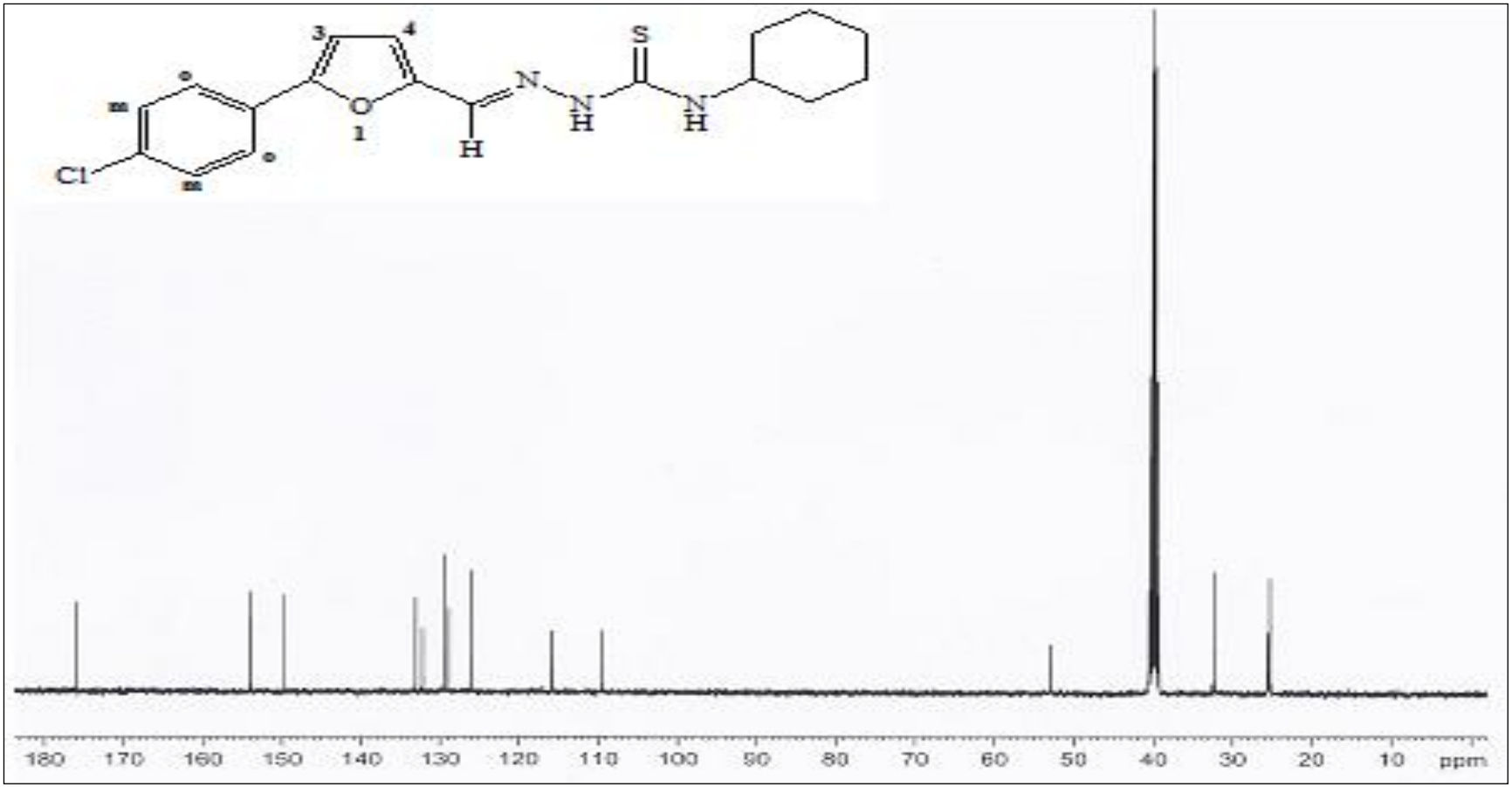

Figure S9. ^{13}C NMR spectrum of compound [V]