

Isothiouronium salts and thienopyridines derived from 7-azacoumarin-3-carboxamides

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Cytotoxicity Assay

Cell lines M-HeLa (epithelioid carcinoma of the cervix. HeLa subline, clone M-HeLa 11), HuTu 80 (adenocarcinoma of the duodenum) and Wi-38 (a human diploid cell line developed from lung cells of a female fetus) were obtained from the collection of the Institute of Cytology of the Russian Academy of Sciences (Russia).

Cytotoxic activity of isothiuronium salts and thienopyridines derivatives on the 7-azacoumarin-3-carboxamide platform was assessed using the MTT reagent. For this purpose, the cells were incubated for 24 hours with the tested compounds and then stained with an MTT solution at a final concentration of 0.5 mg/ml. After 4 hours, the resulting formazan crystals were dissolved in DMSO. Cells not exposed to the compounds were used as a negative control. Sorafenib was used as a comparison drug. IC₅₀ (half-maximal inhibition concentration) was calculated using the online calculator: MLA - "Quest Graph™ IC₅₀ Calculator" [IC₅₀ Calculator. Retrieved June 11, 2024, from: <https://www.aatbio.com/tools/ic50-calculator>].

Experimental Section

¹H and ¹³C NMR spectra were recorded on a Bruker Avance 400 (Bruker, Billerica, Massachusetts, USA) spectrometer (at the frequencies of 400.05 and 100.61 MHz, respectively) and on a Bruker Avance 600 spectrometer (at the frequencies of 600.1 and 150.9 MHz, respectively). Values of the chemical shifts for the ¹H and ¹³C nuclei are reported relative to the residual signals of the solvent (DMSO-d₆). IR spectra were recorded in KBr pellets on a Bruker 3/5 E2_76513 Tensor-27 spectrometer in the range of 400–3600 cm⁻¹. Mass spectra were recorded on an Ultraflex III TOF/TOF Bruker instrument (*p*-nitroaniline as the matrix) and an AmaZon X Bruker instrument. Elemental analysis was performed using a Carlo Erba EA 1108 (Carlo Erba, Cornaredo, Italy) instrument.

Procedures for the Synthesis of Compounds 2a-m, 4a-c

The reaction mixture consisting of 0.055 mmol of the corresponding 5-chloromethyl-7-azacoumarin-3-carboxamide and 0.058 mmol of thiourea (in the case of bisamides 0.116 mmol) was refluxed for four hours in ethyl alcohol. After cooling, the resulting precipitate was filtered off, washed successively with ethanol and diethyl ether. The mixture was dried *in vacuo*. For product **4b**, the precipitate was separated by centrifugation; products **2f,g** were obtained by removing the solvent, washed with diethyl ether.

2-((8-Methyl-2-oxo-3-(*N*-phenylcarbamoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2a

Yield 80%, mp 235-237°C. IR(KBr), ν , cm^{-1} : 534; 697; 768; 792; 886; 917, 1052, 1085, 1153, 1218, 1253, 1322, 1417, 1450, 1493, 1554, 1596, 1645, 1718, 2747, 3018. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 5.02 (2H, s, CH_2), 7.16 (1H, t, $J = 7.4$ Hz, Ph), 7.39 (2H, t, $J = 7.7$ Hz, Ph), 7.74 (2H, d, $J = 8.0$ Hz, Ph), 8.59 (1H, s, CH_{Py}), 8.94 (1H, s, CH), 9.36 (2H, br.s, NH_2), 9.53 (2H, br.s, NH_2), 10.70 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 18.63; 28.48; 119.81; 121.82; 124.43; 125.79; 126.55; 128.99; 137.98; 140.14; 144.50; 147.29; 147.65; 157.94; 159.77; 168.15. Mass spectrum: m/z 368.9 $[\text{M} - \text{Cl}]^+$. Found, %: C 53.49; H 4.33; Cl 8.81; N 13.97; S 8.02. $\text{C}_{18}\text{H}_{17}\text{ClN}_4\text{O}_3\text{S}$. Calculated, %: C 53.40; H 4.23; Cl 8.76; N 13.84; S 7.92.

2-((3-(*N*-(2-Methoxyphenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2b

Yield 73%, mp 245-247°C. IR(KBr), ν , cm^{-1} : 524, 706, 762, 793, 888, 1030, 1048, 1083, 1118, 1153, 1232, 1255, 1291, 1418, 1468, 1486, 1550, 1603, 1645, 1725, 3014, 3236. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 3.92 (3H, s, OCH_3), 5.07 (2H, s, CH_2S), 6.99 (1H, ddd, $J = 8.6, 6.1, 2.7$ Hz, Ph), 7.11-7.15 (2H, m, Ph), 8.44 (1H, d, $J = 8.7$ Hz, Ph), 8.62 (1H, s, CH_{Py}), 9.11 (1H, s, CH), 9.40 (2H, br.s, NH_2), 9.55 (2H, br.s, NH_2), 11.13 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.13, 28.90, 56.64, 111.64, 120.05, 121.22, 122.40, 124.30, 125.31, 126.37, 127.57, 142.74, 145.06, 147.89, 148.27, 149.07, 158.70, 160.00, 168.66. Mass spectrum: m/z 399.0 $[\text{M} - \text{Cl}]^+$. Found, %: C 52.60; H 4.50; Cl 8.31; N 12.97; S 7.45. $\text{C}_{19}\text{H}_{19}\text{ClN}_4\text{O}_4\text{S}$. Calculated, %: C 52.47; H 4.40; Cl 8.15; N 12.88; S 7.37.

2-((3-(*N*-(3-Chlorophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2c

Yield 72%, mp 232-233°C. IR(KBr), ν , cm^{-1} : 479, 536, 686, 791, 868, 1050, 1081, 1151, 1219, 1310, 1414, 1482, 1549, 1593, 1647, 1727, 3049, 3239. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 4.97 (2H, s, CH_2), 7.23 (1H, dd, $J = 8.0, 2.1$ Hz, Ph), 7.43 (1H, t, $J = 8.1$ Hz, Ph), 7.62 (1H, d, $J = 8.2$ Hz, Ph), 7.96 (1H, s, Ph), 8.57 (1H, s, CH_{Py}), 8.94 (1H, s, CH), 9.30 (2H, br.s, NH_2), 9.46 (2H, br.s, NH_2), 10.87 (1H, s, NH), ^{13}C NMR (DMSO- d_6), δ , ppm: 19.16, 29.00, 118.87, 119.85, 122.24, 124.70, 126.32, 127.02, 131.21, 133.77, 139.94, 140.77, 145.00, 147.83, 148.22, 158.10, 160.82, 168.55. Mass spectrum: m/z 403.1 $[\text{M} - \text{Cl}]^+$. Found, %: C 49.24; H 3.71; Cl 16.17; N 12.80; S 7.29. $\text{C}_{18}\text{H}_{16}\text{Cl}_2\text{N}_4\text{O}_3\text{S}$. Calculated, %: C 49.21; H 3.67; Cl 16.14; N 12.75; S 7.30.

2-((3-(*N*-(3-Bromophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2d

Yield 72%, mp 233-235°C. IR(KBr), ν , cm^{-1} : 535, 704, 791, 1051, 1082, 1151, 1217, 1241, 1311, 1479, 1547, 1587, 1646, 1725, 3045, 3237. ^1H NMR (DMSO- d_6), δ ppm: 2.64 (3H, s, CH_3), 4.96 (2H, s, CH_2S), 7.36-7.40 (2H, m, Ph), 7.67 (1H, td, $J = 4.3, 3.9, 2.0$ Hz, Ph), 8.11 (1H, s, Ph), 8.56 (1H, s, CH_{Py}), 8.94 (1H, s, CH), 9.28 (2H, br.s, NH_2), 9.43 (2H, br.s, NH_2), 10.84 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.15, 29.01, 119.26, 122.17, 122.23, 122.71, 126.33, 126.98, 127.58, 131.47, 140.08, 140.75, 145.01, 147.82, 148.20, 158.06, 160.80, 168.59. Mass spectrum: m/z 448.0 $[\text{M} - \text{Cl}]^+$. Found, %: C 44.69; H 3.33; Br 16.52; Cl 7.33; N 11.58; S 6.63. $\text{C}_{18}\text{H}_{16}\text{BrClN}_4\text{O}_3\text{S}$. Calculated, %: C 44.69; H 3.33; Br 16.52; Cl 7.33; N 11.58; S 6.63.

2-((8-Methyl-2-oxo-3-(*N*-(4-sulfamoylphenyl)carbamoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2e

Yield 86%, mp 235-238 °C. IR(KBr), ν , cm^{-1} : 470, 553, 595, 626, 682, 704, 793, 839, 903, 1015, 1051, 1159, 1219, 1318, 1404, 1416, 1542, 1592, 1654, 1722, 3060, 3275. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 5.01 (2H, s, CH_2), 7.34 (2H, s, NH_2), 7.85 (2H, d, $J = 8.8$ Hz, Ph); 7.92 (2H, d, $J = 8.9$ Hz, Ph); 8.59 (1H, s, CH_{Py}); 8.96 (1H, s, CH), 9.34 (2H, br.s, NH_2), 9.52 (2H, br.s, NH_2), 11.03 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 18.63; 28.50; 119.59; 121.75; 125.83; 126.46; 126.86; 139.58; 140.36; 140.81; 144.51; 147.33; 147.70; 157.65; 160.41; 168.12. Mass spectrum: m/z 448.3 $[\text{M} - \text{Cl}]^+$. Found, %: C 44.71; H 3.77; Cl 7.29; N 14.50; S 13.28. $\text{C}_{18}\text{H}_{18}\text{ClN}_5\text{O}_5\text{S}_2$. Calculated, %: C 44.67; H 3.75; Cl 7.33; N 14.47; S 13.25.

2-((3-(*N,N*-Diphenylcarbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2f

Yield 87%, mp 150-152°C. IR(KBr), ν , cm^{-1} : 483, 562, 624, 697, 760, 1051, 1080, 1151, 1206, 1267, 1371, 1415, 1491, 1593, 1652, 1740, 3039, 3187, 3303. ^1H NMR (DMSO- d_6), δ ppm: 2.48 (3H, s, CH_3), 4.89 (2H, s, CH_2), 7.20-7.23 (1H, m, Ph), 7.33 (3H, br.s, Ph), 7.41 (5H, d, $J = 8.4$ Hz, Ph), 7.46 (1H, br.s, Ph), 8.49 (1H, s, CH_{Py}), 8.84 (1H, s, CH), 9.35 (2H, br.s, NH_2), 9.52 (2H, br.s, NH_2). ^{13}C NMR (DMSO- d_6), δ , ppm: 18.95, 29.04, 117.23, 120.11, 121.89, 125.80, 126.99, 127.47, 128.67, 129.36, 129.59, 129.73, 130.04, 130.43, 138.57, 141.84, 142.23, 145.07, 147.30, 148.07, 156.09, 163.73, 168.93. Mass spectrum: m/z 445.1 $[\text{M} - \text{Cl}]^+$. Found, %: C 60.02; H 4.41; Cl 7.29; N 11.58; S 6.63. $\text{C}_{24}\text{H}_{21}\text{ClN}_4\text{O}_3\text{S}$. Calculated, %: C 59.93; H 4.40; Cl 7.37; N 11.65; S 6.67.

2-((3-(*N*-(4-(*N'*-Acetylsulfamoyl)phenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2g

Yield 80%, mp 225-227 °C. IR(KBr), ν , cm^{-1} : 475, 548, 598, 626, 684, 704, 793, 842, 1051, 1090, 1158, 1220, 1339, 1405, 1542, 1590, 1654, 1726, 3401. ^1H NMR (DMSO- d_6), δ ppm: 1.94 (3H, s, CH_3), 2.64 (3H, s, CH_3), 4.97 (2H, s, CH_2), 7.94-7.98 (4H, m, Ph), 8.58 (1H, s, CH_{Py}); 8.96 (1H, s, CH); 9.28 (2H, br.s, NH_2), 9.45 (2H, br.s, NH_2), 11.08 (1H, s, NH), 12.07 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 13.86; 18.42; 23.69; 114.72; 116.91; 121.06; 121.73; 124.23; 129.48; 135.63; 137.61; 139.72; 142.55; 142.94; 152.77; 155.87; 163.25; 163.96. Mass spectrum: m/z 490.2 $[\text{M} - \text{Cl}]^+$. Found, %: C 45.71; H 3.90; Cl 6.69; N 13.28; S 12.10. $\text{C}_{20}\text{H}_{20}\text{ClN}_5\text{O}_6\text{S}_2$. Calculated, %: C 45.67; H 3.83; Cl 6.74; N 13.32; S 12.19.

2-((3-(*N*-(2-Chloro-4-nitrophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2h

Yield 75%, mp 258°C. IR(KBr), ν , cm^{-1} : 426, 469, 516, 566, 592, 694, 745, 775, 792, 845, 836, 893, 930, 965, 1016, 1055, 1084, 1140, 1122, 1220, 1271, 1319, 1343, 1413, 1439, 1463, 1516, 1585, 1602, 1656, 1735, 3028. ^1H NMR (DMSO- d_6), δ ppm: 2.66 (3H, s, CH_3), 5.04 (2H, s, CH_2S), 8.35 (1H, d, $J = 9.6$ Hz, Ph), 8.49 (1H, s, Ph), 8.62 (1H, s, CH_{Py}), 8.79 (1H, d, $J = 9.1$ Hz, Ph), 9.19 (1H, s, CH), 9.28 (2H, br.s, NH_2), 9.43 (2H, br.s, NH_2), 11.57 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.13; 28.89; 121.35; 122.24; 123.52; 124.47; 125.45; 126.60; 140.78; 143.70; 143.97; 145.29; 147.89; 148.46; 160.08, 168.62. Mass spectrum: m/z 448.6 $[\text{M} - \text{Cl}]^+$. Found, %: C 44.71; H 3.30; Cl 14.70; N 14.65; S 6.69. $\text{C}_{18}\text{H}_{15}\text{Cl}_2\text{N}_5\text{O}_5\text{S}$. Calculated, %: C 44.64; H 3.12; Cl 14.64; N 14.46; S 6.62.

2-((3-(*N*-(2-Bromo-4-nitrophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2i

Yield 77%, mp 235°C. IR(KBr), ν , cm^{-1} : 433, 473, 565, 690, 744, 766, 791, 845, 894, 968, 1015, 1040, 1053, 1083, 1118, 1136, 1218, 1314, 1342, 1394, 1413, 1439, 1513, 1549, 1582, 1656, 1731, 3073, 3185, 3398. ^1H NMR (DMSO- d_6), δ ppm: 2.65 (3H, s, CH_3), 5.06 (2H, s, CH_2S), 8.37 (1H, dd, $J = 9.2, 2.6$ Hz, Ph), 8.58 (1H, d, $J = 2.6$ Hz, Ph), 8.63 (1H, s, CH_{Py}), 9.19 (1H, s, CH), 9.33 (2H, s, NH_2), 9.47 (2H, s, NH_2), 11.47 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.12; 28.88; 113.55; 121.57; 122.22; 123.41; 124.80; 126.63; 128.56; 142.08; 143.86; 145.29; 147.89; 148.43; 160.05; 168.64. Mass spectrum: m/z 492.0 $[\text{M} - \text{HCl}]^+$. Found, %: C 40.95; H 3.02; Br 15.13; Cl 6.81; N 13.34; S 6.14. $\text{C}_{18}\text{H}_{15}\text{BrClN}_5\text{O}_5\text{S}$. Calculated, %: C 40.89; H 2.86; Br 15.11; Cl 6.70; N 13.25; S 6.06.

2-((8-Methyl-2-oxo-3-(*N'*-phenylcarbazoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2j

Yield 78%, mp 185°C. IR(KBr), ν , cm^{-1} : 484, 565, 597, 631, 692, 717, 772, 933, 990, 1043, 1084, 1150, 1246, 1282, 1426, 1447, 1483, 1548, 1606, 1656, 1756, 3044, 3384. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 5.13 (2H, s, CH_2S), 7.67 (3H, qd, $J = 8.7, 7.7, 3.6$ Hz, Ph), 8.20 (2H, d, $J = 6.5$ Hz, Ph), 8.60 (1H, s, CH_{Py}), 9.20 (1H, s, CH), 9.37 (2H, br.s, NH_2), 9.61 (2H, br.s, NH_2). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.16, 29.20, 117.28, 121.98, 123.27, 126.41, 127.56, 130.04, 133.06, 140.51, 145.03, 147.91, 148.17, 154.81, 160.45, 165.30, 168.69. Mass spectrum: m/z 412.0 $[\text{M} - \text{Cl}]^+$. Found, %: C 51.04; H 4.21; Cl 8.11; N 15.71; S 7.21. $\text{C}_{19}\text{H}_{18}\text{ClN}_5\text{O}_4\text{S}$. Calculated, %: C 50.95; H 4.05; Cl 7.91; N 15.64; S 7.16.

2-((8-Methyl-2-oxo-3-(*N'*-(pyridin-4-yl)carbazoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2k

Yield 83%, mp 180-183°C. IR(KBr), ν , cm^{-1} : 561, 687, 845, 1062, 1194, 1243, 1293, 1413, 1476, 1545, 1655, 1734, 3187. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 5.01 (2H, s, CH_2S), 7.84 (2H, dd, $J = 4.5, 1.6$ Hz, Py), 8.57 (1H, s, CH_{Py}), 8.80 (2H, dd, $J = 4.4, 1.7$ Hz, Py), 8.95 (1H, s, CH), 9.30 (2H, br.s, NH_2), 9.47 (2H, br.s, NH_2), 10.64 (1H, s, NH), 11.26 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.20, 28.95, 122.02, 122.07, 124.57, 126.35, 139.89, 142.38, 144.93, 148.03, 148.34, 150.80, 158.18, 160.38, 164.05, 168.57. Mass spectrum: m/z 413.0 $[\text{M} - \text{Cl}]^+$. Found, %: C 48.31; H 3.97; Cl 7.99; N 18.92; S 7.11. $\text{C}_{18}\text{H}_{17}\text{ClN}_6\text{O}_4\text{S}$. Calculated, %: C 48.16; H 3.82; Cl 7.90; N 18.72; S 7.14.

2-((8-Methyl-2-oxo-3-(*N*-(prop-2-yn-1-yl)carbamoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2l

Yield 60%, mp 123-126°C. IR(KBr), ν , cm^{-1} : 474, 561, 730, 796, 1071, 1162, 1241, 1407, 1524, 1612, 1721, 3342. ^1H NMR (DMSO- d_6), δ ppm: 2.62 (3H, s, CH_3), 3.17 (1H, t, $J = 2.5$ Hz, CH), 4.13 (2H, dd, $J = 5.6, 2.5$ Hz, CH_2), 4.95 (2H, s, CH_2S), 8.53 (1H, s, CH_{Py}), 8.93 (1H, s, CH), 8.99 (1H, t, $J = 5.6$ Hz, NH), 9.23 (2H, s, NH_2), 9.39 (2H, s, NH_2). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.17, 28.96, 29.40, 73.83, 81.00, 122.22, 124.81, 126.25, 141.93, 144.88, 147.93, 148.23, 158.70, 161.10, 168.60. Mass spectrum: m/z 330.9 $[\text{M} - \text{Cl}]^+$. Found, %: C 49.27; H 4.18; Cl 9.74; N 15.36; S 8.69. $\text{C}_{15}\text{H}_{15}\text{ClN}_4\text{O}_3\text{S}$. Calculated, %: C 49.12; H 4.12; Cl 9.66; N 15.27; S 8.74.

2-((3-(*N*-(2,4-Dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2m

Yield 82%, mp >300°C. IR(KBr), ν , cm^{-1} : 475, 510, 562, 578, 697, 772, 789, 896, 1052, 1083, 1176, 1224, 1254, 1290, 1367, 1415, 1440, 1484, 1558, 1650, 1703, 2837, 3022, 3104, 3201, 3377. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (3H, s, CH_3), 5.01 (2H, s, CH_2S), 8.39 (1H, d, $J = 5.9$ Hz, CH), 8.58 (1H, s, CH_{Py}), 9.02 (1H, s, CH), 9.30 (2H, s, NH_2), 9.44 (2H, s, NH_2), 10.74 (1H, s, NH), 10.85 (1H, d, $J = 6.3$ Hz, NH), 11.69 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.21, 28.89, 113.86, 122.32, 123.57, 126.34, 128.66, 142.49, 145.03, 147.90, 148.32, 149.81, 158.57, 159.68, 160.83, 168.51. Mass spectrum: m/z 402.9 $[\text{M} - \text{Cl}]^+$. Found, %: C 43.84; H 3.52; Cl 8.01; N 19.24; S 7.26. $\text{C}_{16}\text{H}_{15}\text{ClN}_6\text{O}_5\text{S}$. Calculated, %: C 43.79; H 3.45; Cl 8.08; N 19.15; S 7.31.

2,2'-((((1,2-Phenylenebis(azanediyl))bis(carbonyl))bis(8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3,5-diyl))bis(methylene))diisothiuronium dichloride 4a

Yield 64%, mp 225 dec.°C. IR(KBr), ν , cm^{-1} : 476, 699, 758, 793, 1050, 1084, 1150, 1222, 1289, 1314, 1415, 1480, 1547, 1599, 1655, 1726, 3055, 3281. ^1H NMR (DMSO- d_6), δ ppm: 2.64 (6H, s, 2 CH_3), 5.05 (4H, s, 2 CH_2), 7.36 (2H, dd, $J = 6.1, 3.5$ Hz, Ph), 7.90 (2H, dd, $J = 6.1, 3.5$ Hz, Ph), 8.62 (2H, s, 2 CH_{Py}), 9.09 (2H, s, 2CH), 9.34 (4H, br.s, 2 NH_2), 9.51 (4H, br.s, 2 NH_2), 10.69 (2H, s, 2NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.25; 28.90; 122.20; 125.09; 125.21; 126.55; 126.79; 130.94; 142.47; 144.99; 147.96; 148.35; 158.94; 160.39; 168.54. Mass spectrum: m/z 660.1 $[\text{M} - 2\text{Cl}]^+$. Found, %: C 49.29; H 3.92; Cl 9.61; N 15.34; S 8.68. $\text{C}_{30}\text{H}_{28}\text{Cl}_2\text{N}_8\text{O}_6\text{S}_2$. Calculated, %: C 49.25; H 3.86; Cl 9.69; N 15.32; S 8.76.

2,2'-((((Sulfonylbis(4,1-phenylene))bis(azanediyl))bis(carbonyl))bis(8-methyl-2-oxo-2H-pyrano[2,3-c]pyridine-3,5-diyl))bis(methylene))diisothiuronium dichloride 4b

Yield 70%, mp >300 °C. IR(KBr), ν , cm^{-1} : 568, 599, 625, 688, 723, 792, 836, 1049, 1106, 1150, 1217, 1250, 1312, 1404, 1542, 1590, 1655, 1732, 3062, 3285. ^1H NMR (DMSO- d_6), δ ppm: 2.63 (6H, s, 2CH₃), 5.00 (4H, s, 2CH₂), 7.99 (8H, s, 2Ph); 8.58 (2H, s, 2CH_{Py}), 8.95 (2H, s, 2CH), 9.33 (4H, br.s, 2NH₂), 9.51 (4H, br.s, 2NH₂), 11.14 (2H, s, 2NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.15; 28.99; 120.64; 122.20; 126.36; 126.97; 129.19; 136.81; 140.95; 142.94; 145.02; 147.84; 148.23; 158.01; 161.20; 168.56. Mass spectrum: m/z 800.8 $[\text{M} - 2\text{Cl}]^+$. Found, %: C 49.64; H 3.75; Cl 8.01; N 12.94; S 10.97. C₃₆H₃₂Cl₂N₈O₈S₃. Calculated, %: C 49.60; H 3.70; Cl 8.13; N 12.85; S 11.03.

2,2'-((((Sulfonylbis(3,1-phenylene))bis(azanediyl))bis(carbonyl))bis(8-methyl-2-oxo-2H-pyrano[2,3-c]pyridine-3,5-diyl))bis(methylene))diisothiuronium dichloride 4c

Yield 75%, mp >300 °C. IR(KBr), ν , cm^{-1} : 471, 520, 613, 680, 717, 793, 1049, 1084, 1151, 1219, 1303, 1415, 1481, 1543, 1593, 1655, 1734, 3061, 3280. ^1H NMR (DMSO- d_6), δ ppm: 2.62 (6H, s, 2CH₃), 5.01 (4H, s, 2CH₂), 7.68 (2H, t, J = 8.0 Hz, Ph), 7.75 (2H, d, J = 7.9 Hz, Ph), 7.96 (2H, d, J = 8.1 Hz, Ph), 8.53 (2H, s, Ph), 8.59 (2H, s, 2CH_{Py}), 8.97 (2H, s, 2CH), 9.35 (4H, br.s, 2NH₂), 9.54 (4H, br.s, 2NH₂), 11.14 (2H, s, 2NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 18.63, 28.53, 118.00, 121.68, 122.68, 122.99, 124.72, 125.87, 126.43, 130.66, 139.13, 140.39, 141.55, 144.52, 147.32, 147.69, 157.35, 160.65, 168.12. Mass spectrum: m/z 800.8 $[\text{M} - 2\text{Cl}]^+$. Found, %: C 49.58; H 3.69; Cl 8.15; N 12.97; S 11.06. C₃₆H₃₂Cl₂N₈O₈S₃. Calculated, %: C 49.60; H 3.70; Cl 8.13; N 12.85; S 11.03.

General procedure for the preparation of compounds 5a-f

Thiuronium salt **2a-f** (0.445 mmol) was added to a solution of 1.335 mmol of potassium hydroxide in 3 ml of distilled water. The reaction mixture was then refluxed with stirring for one hours. After cooling, it was neutralized (pH 7) with dilute hydrochloric acid. The resulting precipitate was filtered, washed with water, ethyl alcohol and diethyl ether, and dried under vacuum.

2-(7-Hydroxy-6-methyl-1,3-dihydrothieno[3,4-c]pyridin-1-yl)-N-phenylacetamide 5a

Yield 92%, mp 177-178 °C. IR(KBr), ν , cm^{-1} : 507, 535, 575, 694, 757, 792, 838, 879, 907, 1047, 1079, 1178, 1250, 1314, 1383, 1444, 1499, 1549, 1599, 1664, 1720, 2922, 2970, 3060, 3134, 3258. ^1H NMR (DMSO- d_6), δ ppm: 2.40 (3H, s, CH₃), 2.65 (1H, dd, J = 15.8, 10.6 Hz, CH₂), 3.27 (1H, dd, J = 15.8, 3.4 Hz, CH₂), 4.10 (1H, d, J = 14.4 Hz, CH₂), 4.29 (1H, d, J = 14.1 Hz, CH₂), 5.05 (1H, dt, J = 10.6, 2.9 Hz, CH), 7.05 (1H, t, J = 7.4 Hz, Ph), 7.31 (2H, t, J = 7.8 Hz, Ph), 7.59 (2H, d, J = 8.0 Hz, Ph), 7.96 (1H, s, CH_{Py}), 9.98 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.47, 34.08, 43.37, 47.49, 119.64, 123.68, 129.21, 136.57, 138.64, 139.51, 145.17, 169.57. Mass spectrum: m/z 301.0 $[\text{M} + \text{H}]^+$. Found, %: C 64.05; H 5.41; N 9.37; S 10.61. C₁₆H₁₆N₂O₂S. Calculated, %: C 63.98; H 5.37; N 9.33; S 10.67.

2-(7-Hydroxy-6-methyl-1,3-dihydrothieno[3,4-c]pyridin-1-yl)-N-(2-methoxyphenyl)acetamide 5b

Yield 90%, mp 153-154 °C. IR(KBr), ν , cm^{-1} : 475, 575, 715, 755, 798, 851, 871, 937, 1031, 1048, 1117, 1180, 1220, 1255, 1289, 1329, 1383, 1436, 1461, 1488, 1531, 1599, 1679, 2159, 2577, 2834, 2924, 3429. ^1H NMR (DMSO- d_6), δ ppm: 2.39 (3H, s, CH₃), 2.80 (1H, dd, J = 16.0, 10.6 Hz, CH₂), 3.26 (1H, dd, J = 16.1, 3.3 Hz, CH₂), 3.82 (3H, s, OCH₃), 4.07 (1H, d, J = 14.3 Hz, CH₂S), 4.29 (1H, d, J = 14.4 Hz, CH₂S), 5.01 (1H, dt, J = 10.6, 2.9 Hz, CH), 6.91 (1H, td, J = 7.5, 6.9, 1.7 Hz, Ph), 7.01-7.08 (2H, m, Ph), 7.94 (1H, s, CH_{Py}), 7.97 (1H, d, J = 8.2 Hz, Ph), 9.16 (1H, s, NH). ^{13}C NMR (DMSO- d_6), δ , ppm: 19.17, 34.06, 43.09, 47.51, 56.16, 111.71, 120.74, 120.86, 122.37, 124.88, 127.65, 136.03, 136.90, 139.25, 144.91, 147.56, 149.97, 169.74. Mass spectrum: m/z 331.1 $[\text{M} + \text{H}]^+$. Found, %: C 61.97; H 5.57; N 8.64; S 9.58. C₁₇H₁₈N₂O₃S. Calculated, %: C 61.80; H 5.49; N 8.48; S 9.70.

N-(3-Chlorophenyl)-2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-c]pyridin-1-yl)acetamide 5c

Yield 67%, mp 150-154 °C. IR(KBr), ν , cm^{-1} : 442, 483, 573, 683, 703, 738, 781, 874, 906, 997, 1045, 1075, 1098, 1165, 1250, 1327, 1387, 1426, 1481, 1540, 1593, 1649, 3418. ^1H NMR (DMSO- d_6), δ ppm: 2.40 (3H, s, CH₃), 2.65 (1H, dd, J = 15.9, 10.6 Hz, CH₂), 3.28 (1H, dd, J = 15.9, 3.2 Hz, CH₂), 4.10 (1H, d, J = 14.3

Hz, CH₂); 4.29 (1H, d, *J* = 14.4 Hz, CH₂), 5.04 (1H, d, *J* = 10.3 Hz, CH), 7.11 (1H, d, *J* = 7.5 Hz, Ph), 7.34 (1H, t, *J* = 8.0 Hz, Ph), 7.44 (1H, d, *J* = 8.2 Hz, Ph), 7.82 (1H, s, CH_{Py}), 7.96 (1H, s, Ph), 10.19 (1H, s, NH). ¹³C NMR (DMSO-*d*₆), δ, ppm: 19.22, 34.13, 43.30, 47.37, 117.97, 119.08, 123.42, 130.94, 133.59, 136.12, 136.78, 140.89, 144.96, 147.57, 169.93. Mass spectrum: *m/z* 335.1 [M]⁺. Found, %: C 57.46; H 4.71; Cl 10.57; N 8.43; S 9.64. C₁₆H₁₅ClN₂O₂S. Calculated, %: C 57.40; H 4.52; Cl 10.59; N 8.37; S 9.58.

***N*-(3-Bromophenyl)-2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)acetamide 5d**

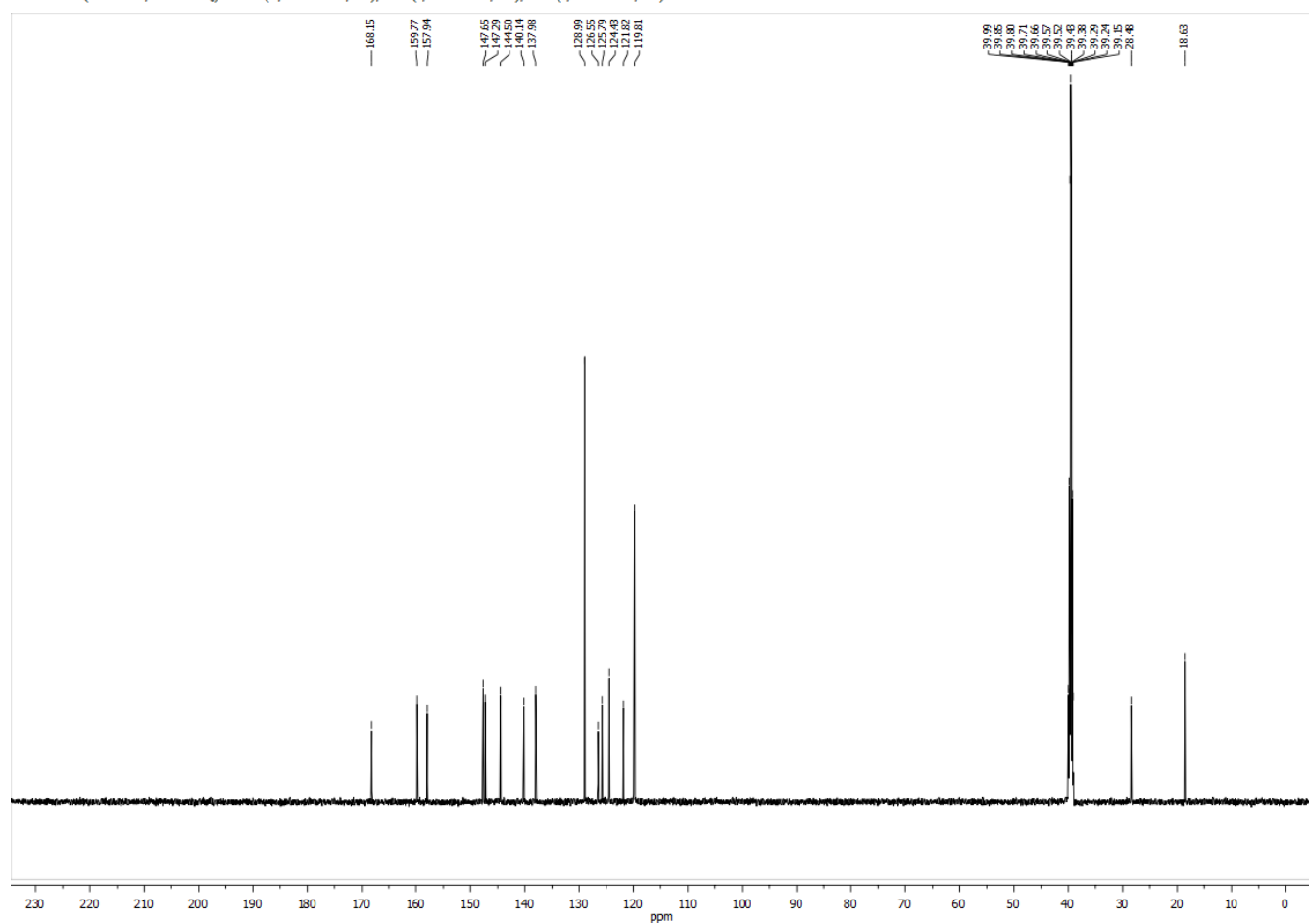
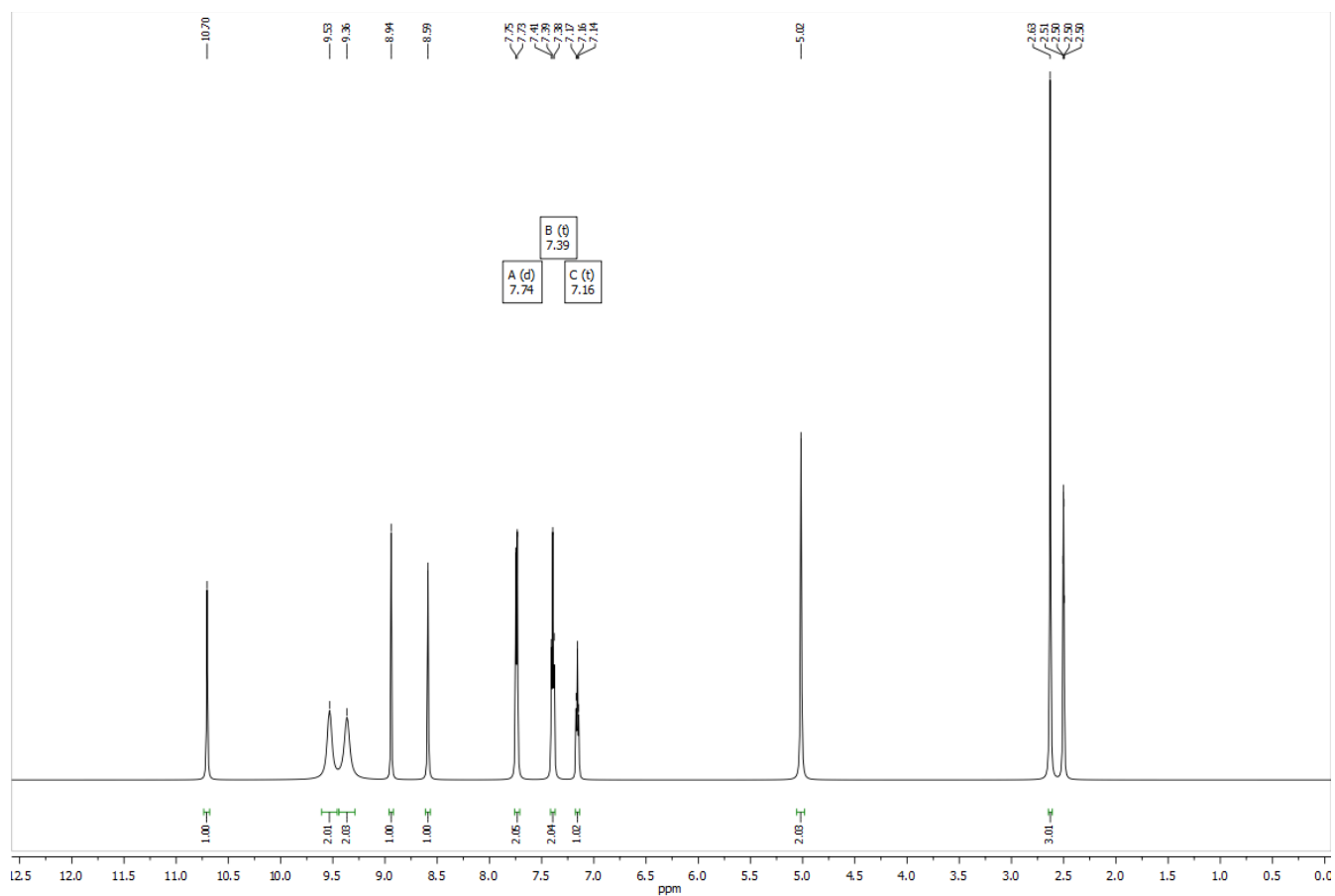
Yield 80%, mp 155-157 °C. IR(KBr), ν, cm⁻¹: 438, 576, 699, 778, 854, 996, 1070, 1326, 1376, 1422, 1477, 1534, 1589, 1648, 3426. ¹H NMR (DMSO-*d*₆), δ ppm: 2.43 (3H, s, CH₃), 2.67 (1H, dd, *J* = 15.8, 10.6 Hz, CH₂), 3.27 (1H, dd, *J* = 16.3, 3.2 Hz, CH₂), 4.11 (1H, d, *J* = 14.4 Hz, CH₂); 4.31 (1H, d, *J* = 14.5 Hz, CH₂), 5.06 (1H, d, *J* = 10.2 Hz, CH), 7.23 - 7.30 (2H, m, Ph), 7.50 (1H, d, *J* = 7.7 Hz, Ph), 7.96 (1H, s, CH_{Py}), 8.00 (1H, s, Ph), 10.24 (1H, s, NH). ¹³C NMR (DMSO-*d*₆), δ, ppm: 19.36, 34.12, 43.33, 47.40, 118.35, 121.93, 122.04, 126.31, 131.23, 136.37, 136.65, 141.06, 145.10, 147.49, 169.95. Mass spectrum: *m/z* 379.0 [M]⁺. Found, %: C 50.63; H 4.15; Br 21.01; N 7.49; S 8.40. C₁₆H₁₅BrN₂O₂S. Calculated, %: C 50.67; H 3.99; Br 21.07; N 7.39; S 8.45.

2-(7-Hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)-*N*-(4-sulfamoylphenyl)acetamide 5e

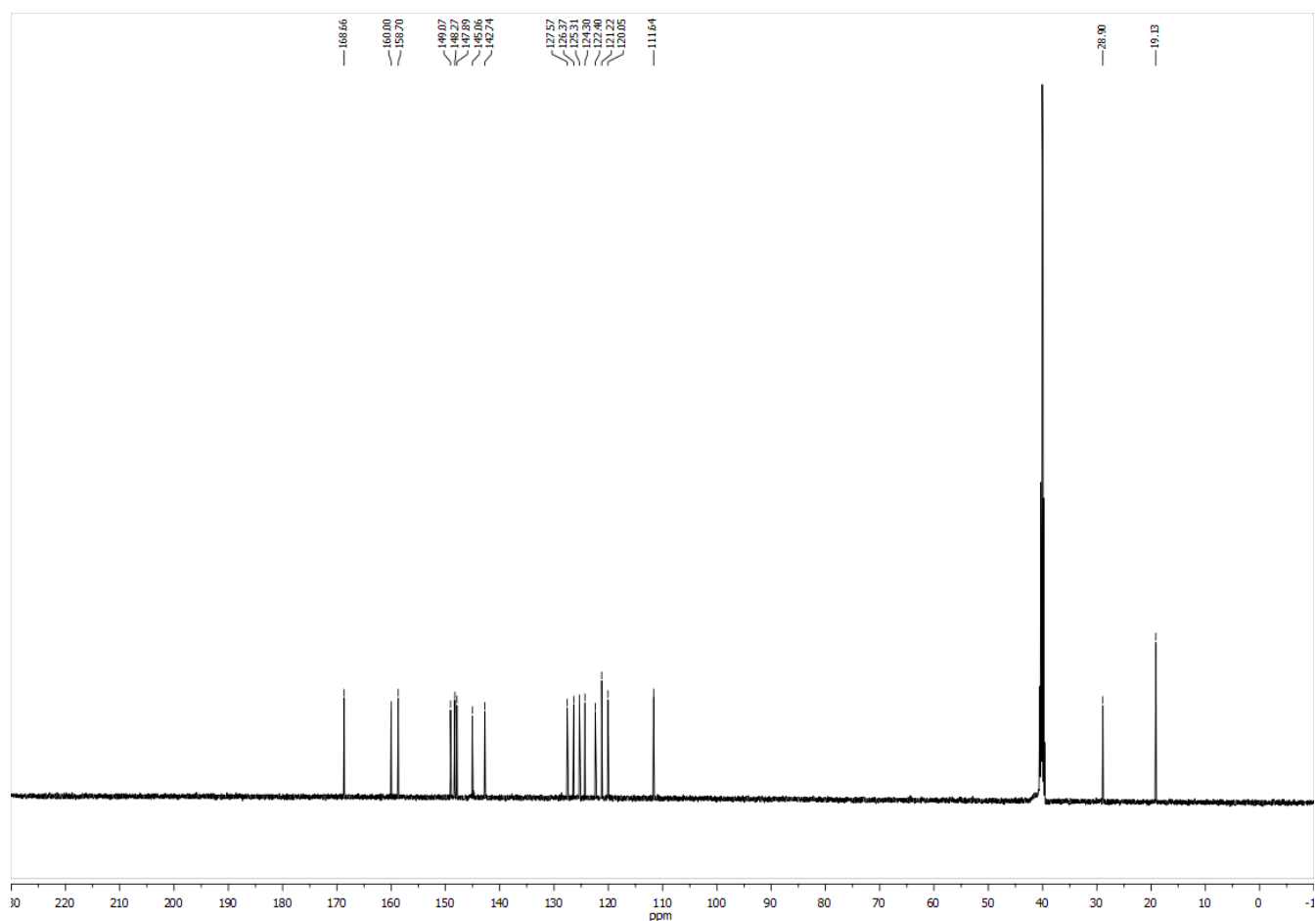
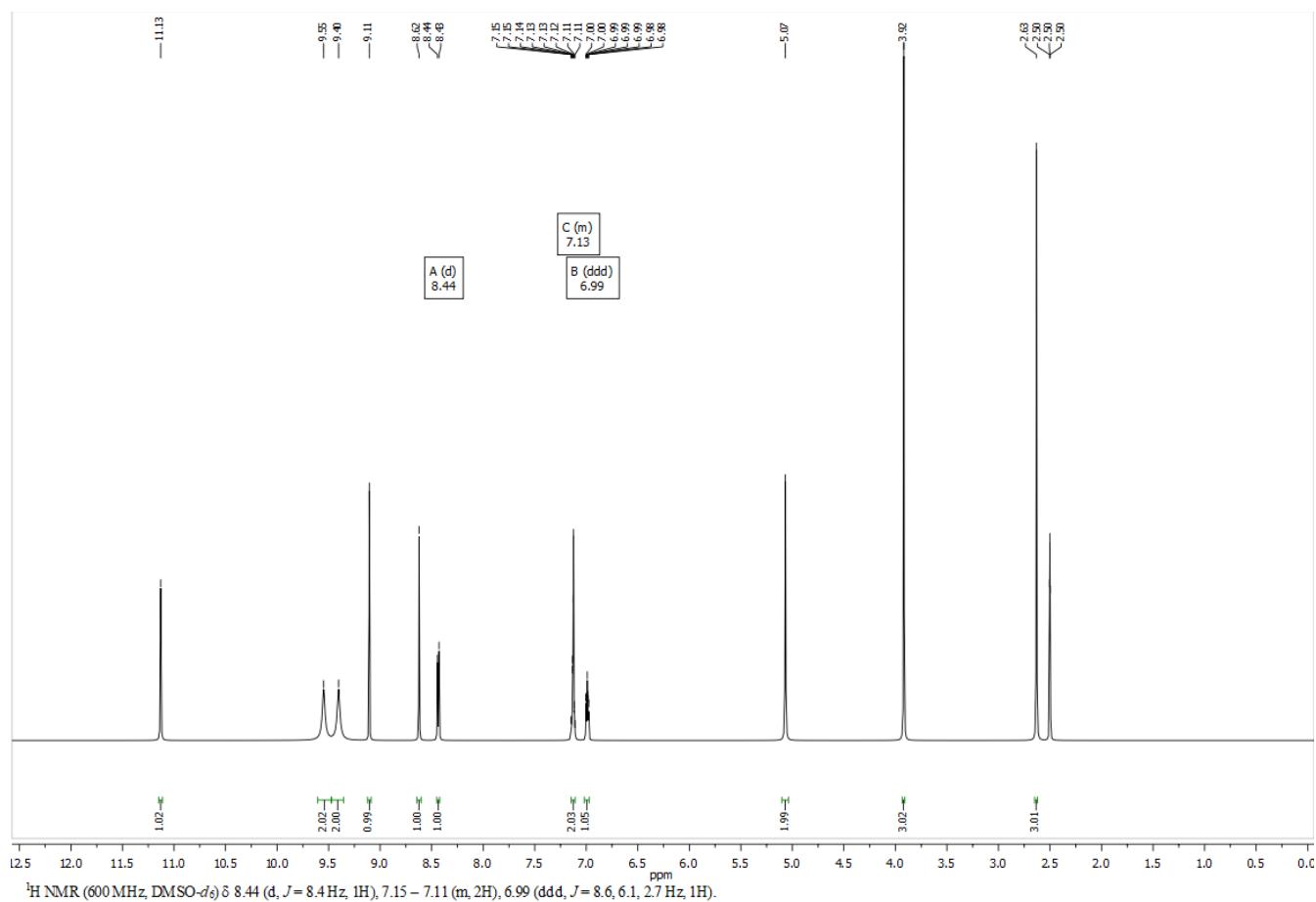
Yield 82%, mp 185-187 °C. IR(KBr), ν, cm⁻¹: 548, 709, 838, 911, 1098, 1157, 1253, 1328, 1403, 1430, 1536, 1593, 1677, 3345. ¹H NMR (DMSO-*d*₆), δ ppm: 2.41 (3H, s, CH₃), 2.69 (1H, dd, *J* = 16.0, 10.6 Hz, CH₂), 3.31 (1H, dd, *J* = 16.0, 3.2 Hz, CH₂), 4.11 (1H, d, *J* = 14.4 Hz, CH₂); 4.30 (1H, d, *J* = 14.4 Hz, CH₂), 5.05 (1H, dt, *J* = 10.6, 2.9 Hz, CH), 7.25 (2H, s, NH₂) 7.72 - 7.85 (4H, m, Ph), 7.97 (1H, s, CH_{Py}), 10.34 (1H, s, NH). ¹³C NMR (DMSO-*d*₆), δ, ppm: 19.05, 34.14, 43.27, 47.32, 112.95, 119.14, 127.23, 127.90, 135.81, 136.96, 138.86, 139.36, 142.32, 144.80, 147.68, 170.07. Mass spectrum: *m/z* 380.0 [M + H]⁺. Found, %: C 50.73; H 4.59; N 11.05; S 17.01. C₁₆H₁₇N₃O₄S₂. Calculated, %: C 50.65; H 4.52; N 11.07; S 16.90.

2-(7-Hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)-*N,N*-diphenylacetamide 5f

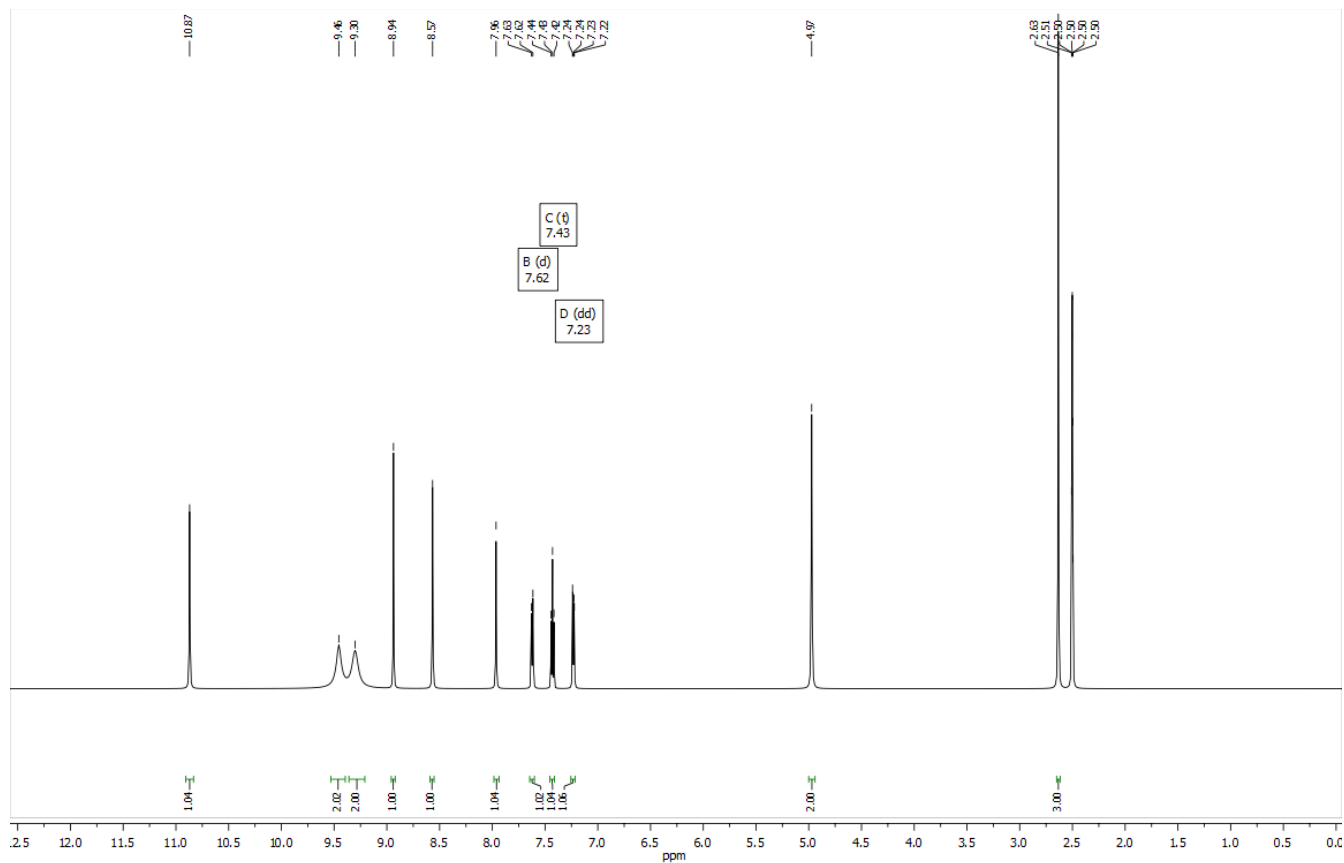
Yield 82%, mp 124-126 °C. IR(KBr), ν, cm⁻¹: 522, 575, 661, 701, 757, 917, 1004, 1029, 1075, 1294, 1379, 1492, 1524, 1593, 1666, 2920, 3061, 3423. ¹H NMR (DMSO-*d*₆), δ ppm: 2.33 (3H, s, CH₃), 2.44 (1H, dd, *J* = 16.5, 10.7 Hz, CH₂), 3.14 (1H, dd, *J* = 16.5, 3.1 Hz, CH₂), 4.03 (1H, d, *J* = 14.3 Hz, CH₂S); 4.17 (1H, d, *J* = 14.3 Hz, CH₂S), 4.98 (1H, dt, *J* = 10.7, 2.9 Hz, CH), 7.21 - 7.40 (10H, m, 2Ph), 7.86 (1H, s, CH_{Py}). ¹³C NMR (DMSO-*d*₆), δ, ppm: 19.17, 33.87, 42.19, 47.91, 117.24, 120.13, 127.44, 129.41, 129.62, 130.36, 136.10, 136.84, 138.74, 144.84, 147.52, 170.57. Mass spectrum: *m/z* 377.1 [M+H]⁺. Found, %: C 70.27; H 5.44; N 7.61; S 8.47. C₂₂H₂₀N₂O₂S. Calculated, %: C 70.19; H 5.35; N 7.44; S 8.52.



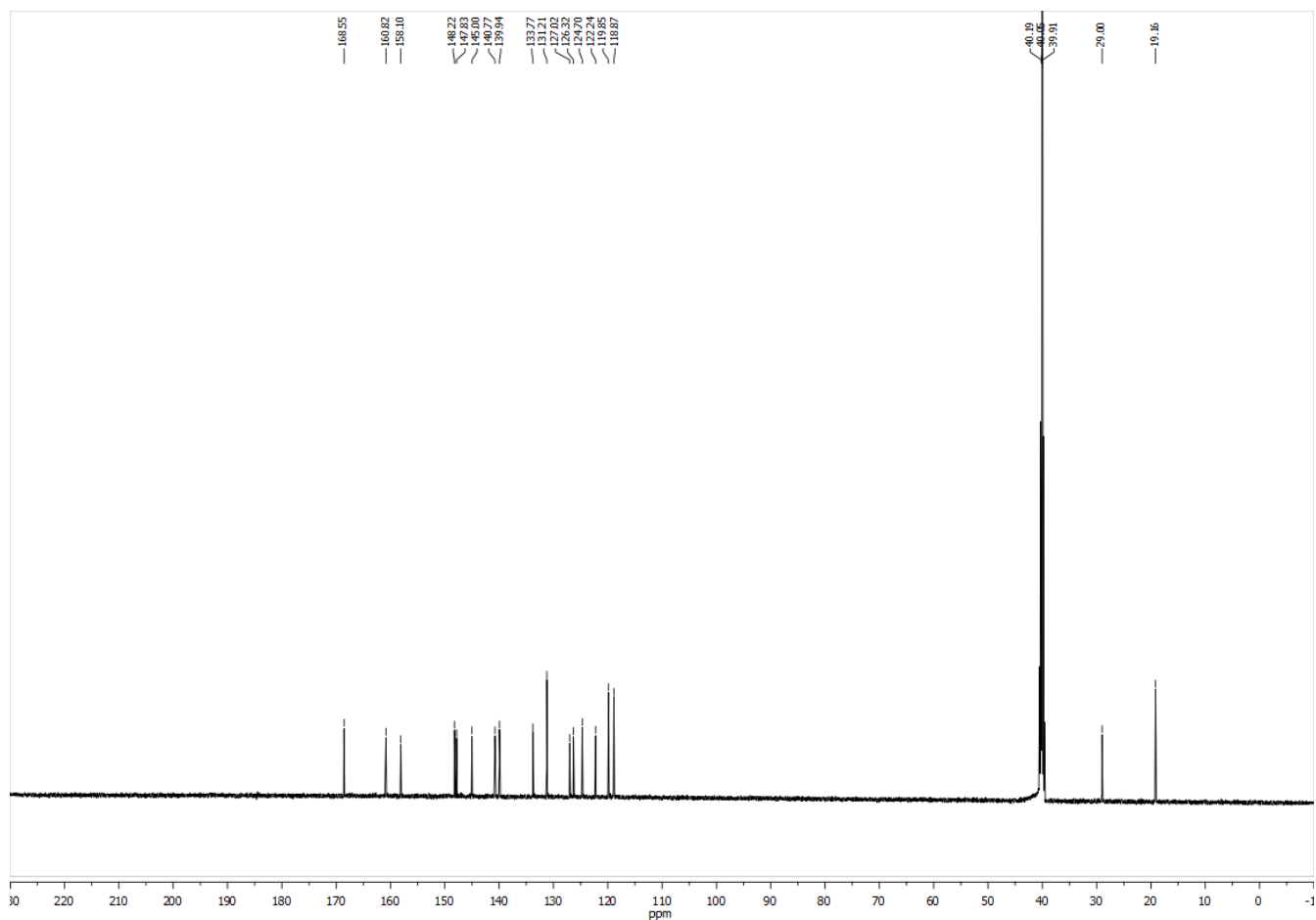
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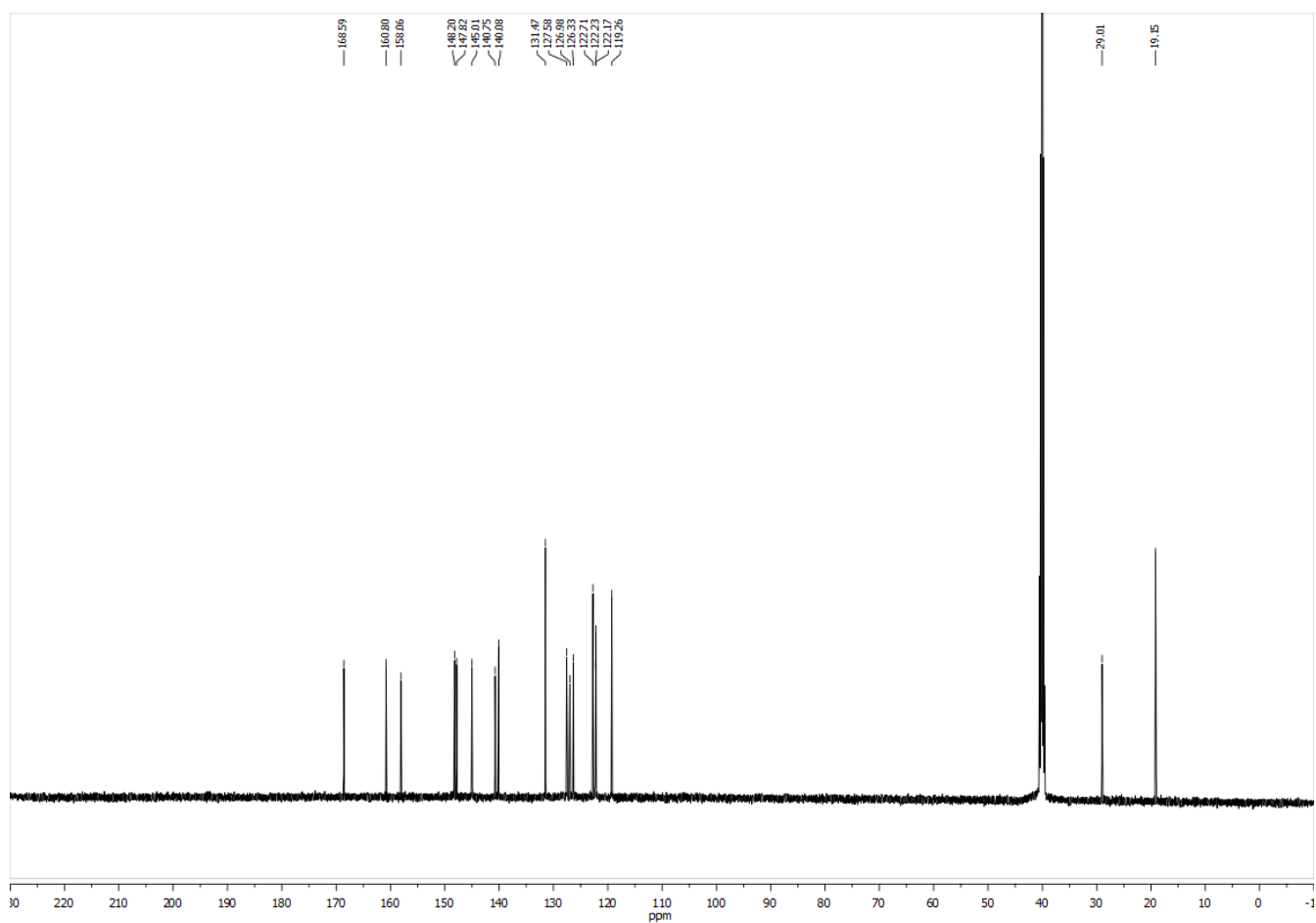
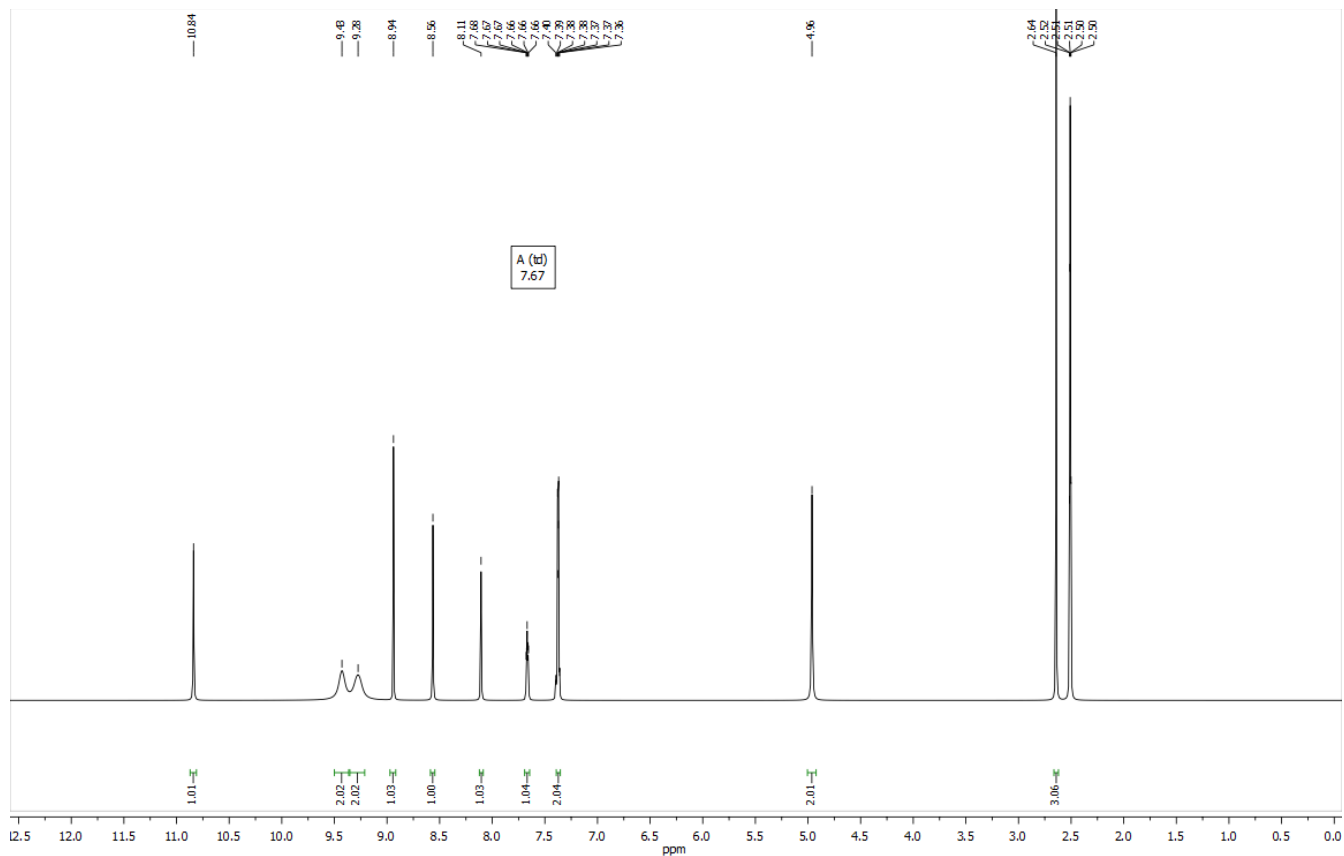
2-((3-(*N*-(2-methoxyphenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2b



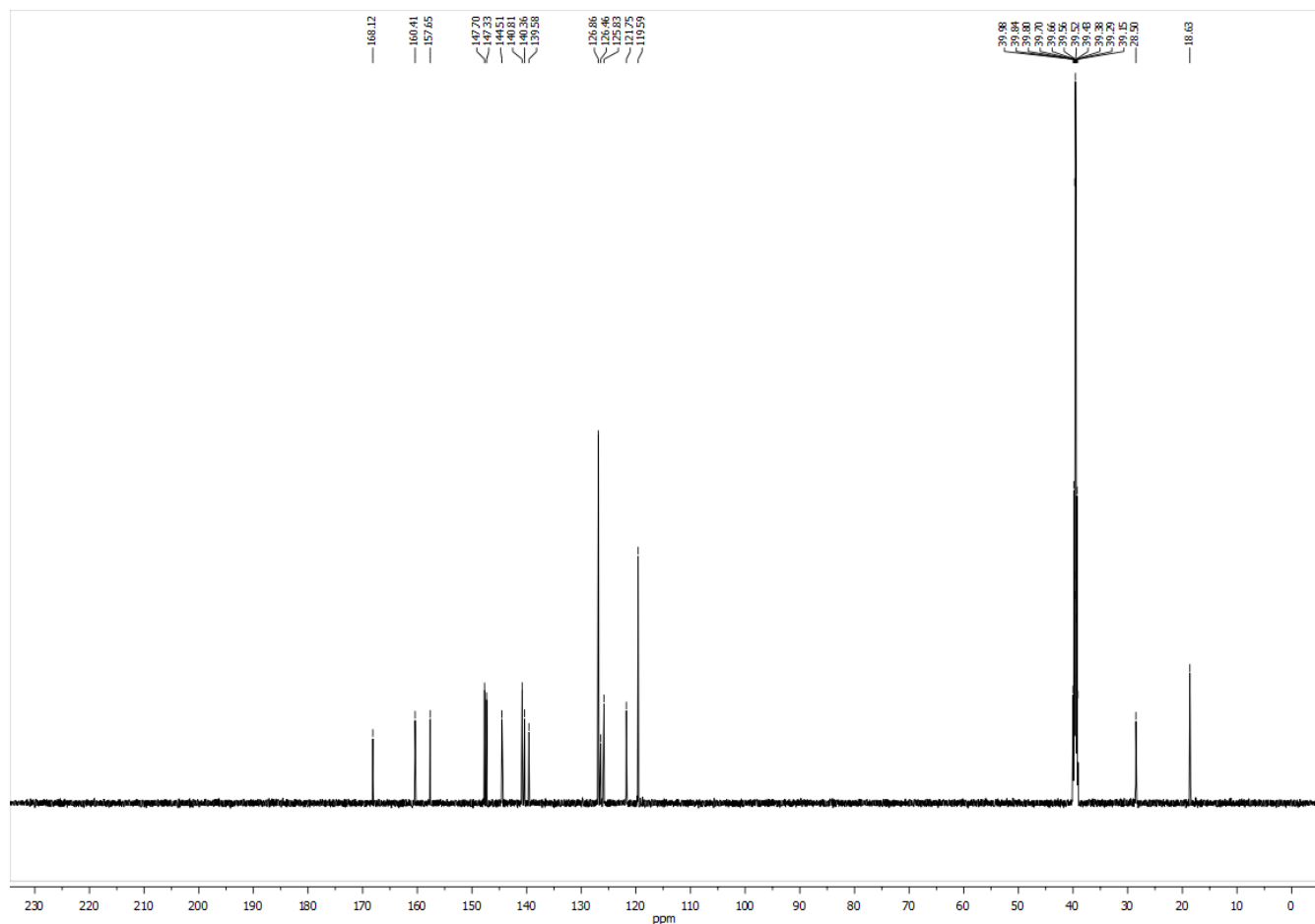
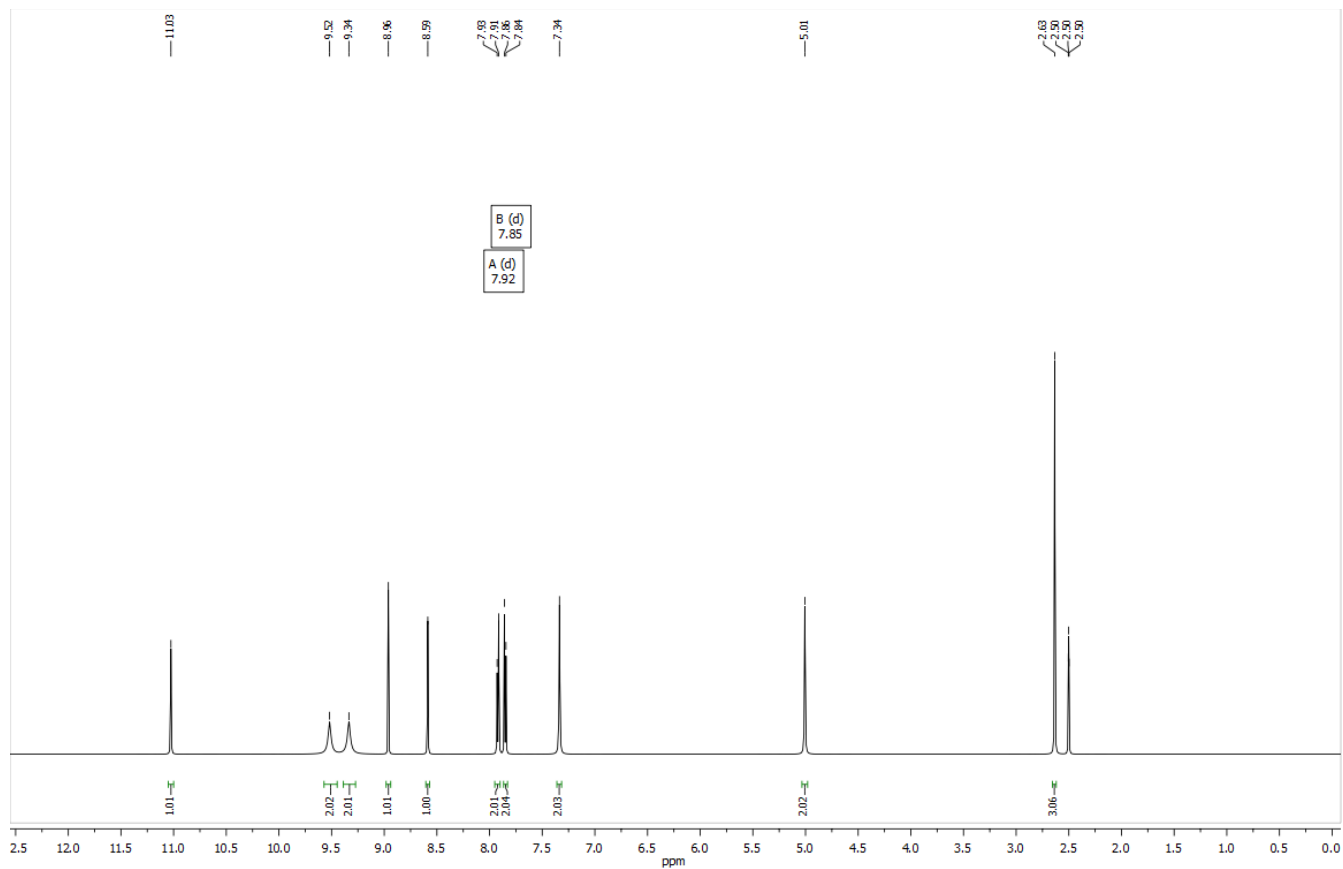
¹H NMR (600 MHz, DMSO-*d*₆) δ 7.62 (d, *J* = 8.2 Hz, 1H), 7.43 (t, *J* = 8.1 Hz, 1H), 7.23 (dd, *J* = 8.0, 2.1 Hz, 1H).



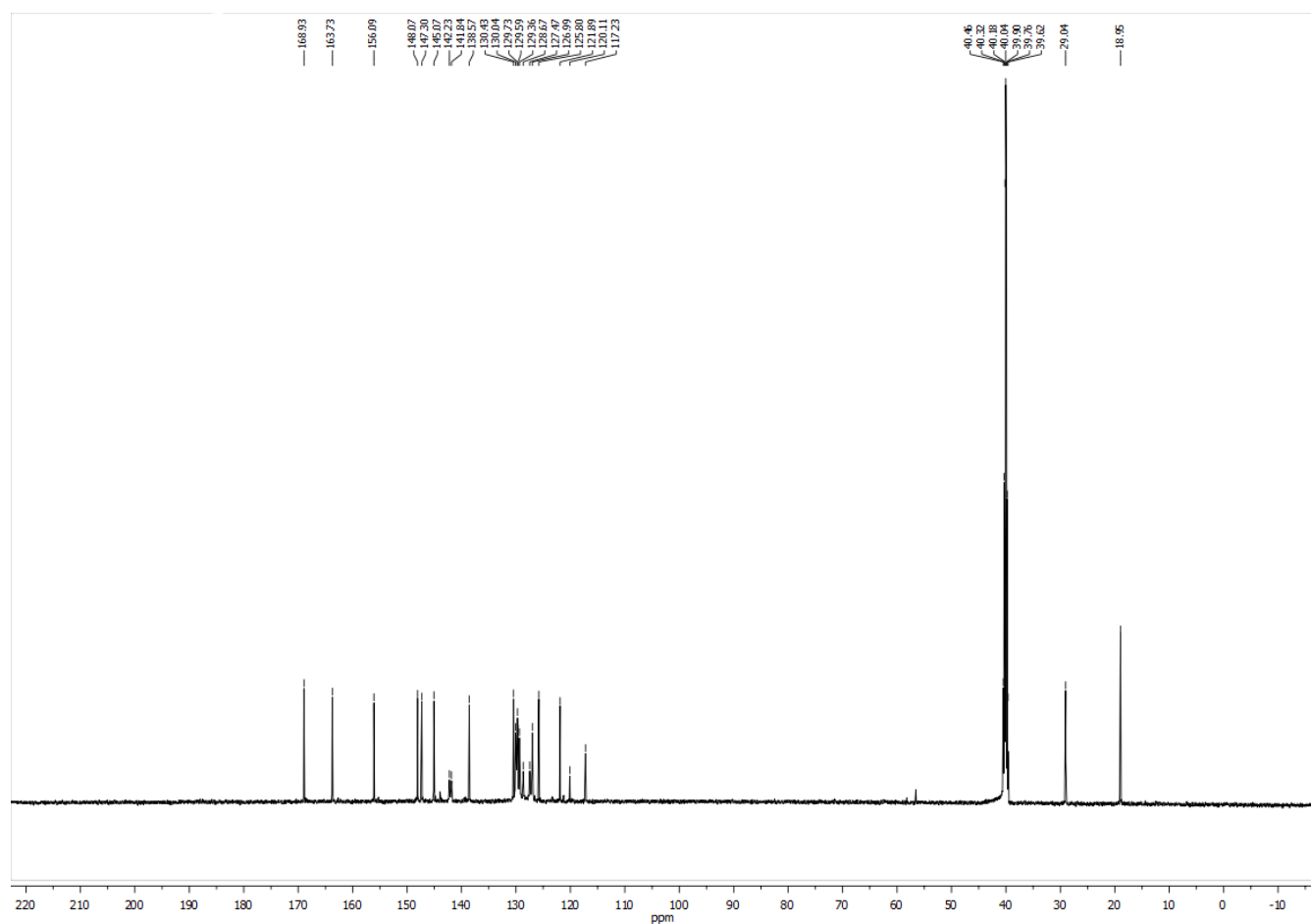
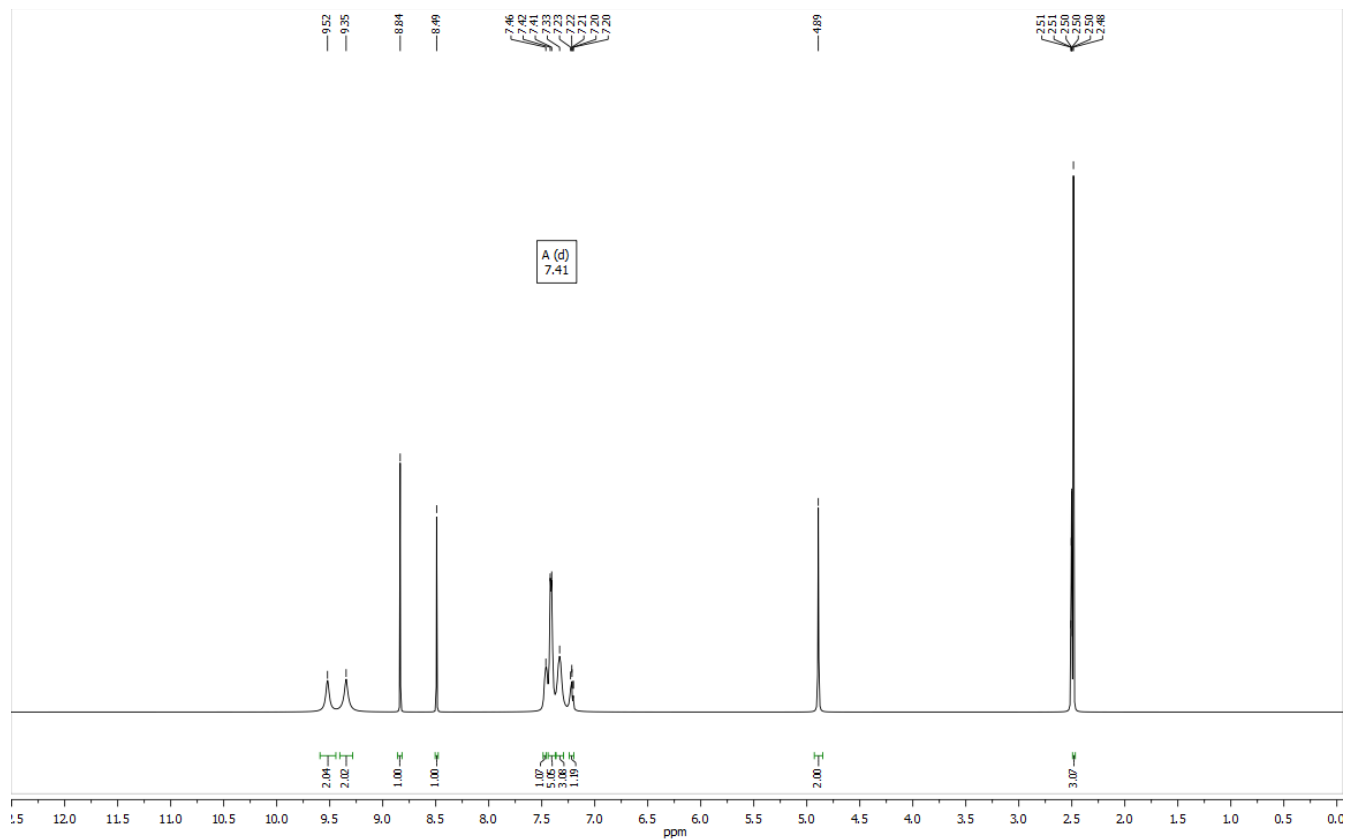
2-((3-(*N*-(3-chlorophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)-isothiuronium chloride 2c



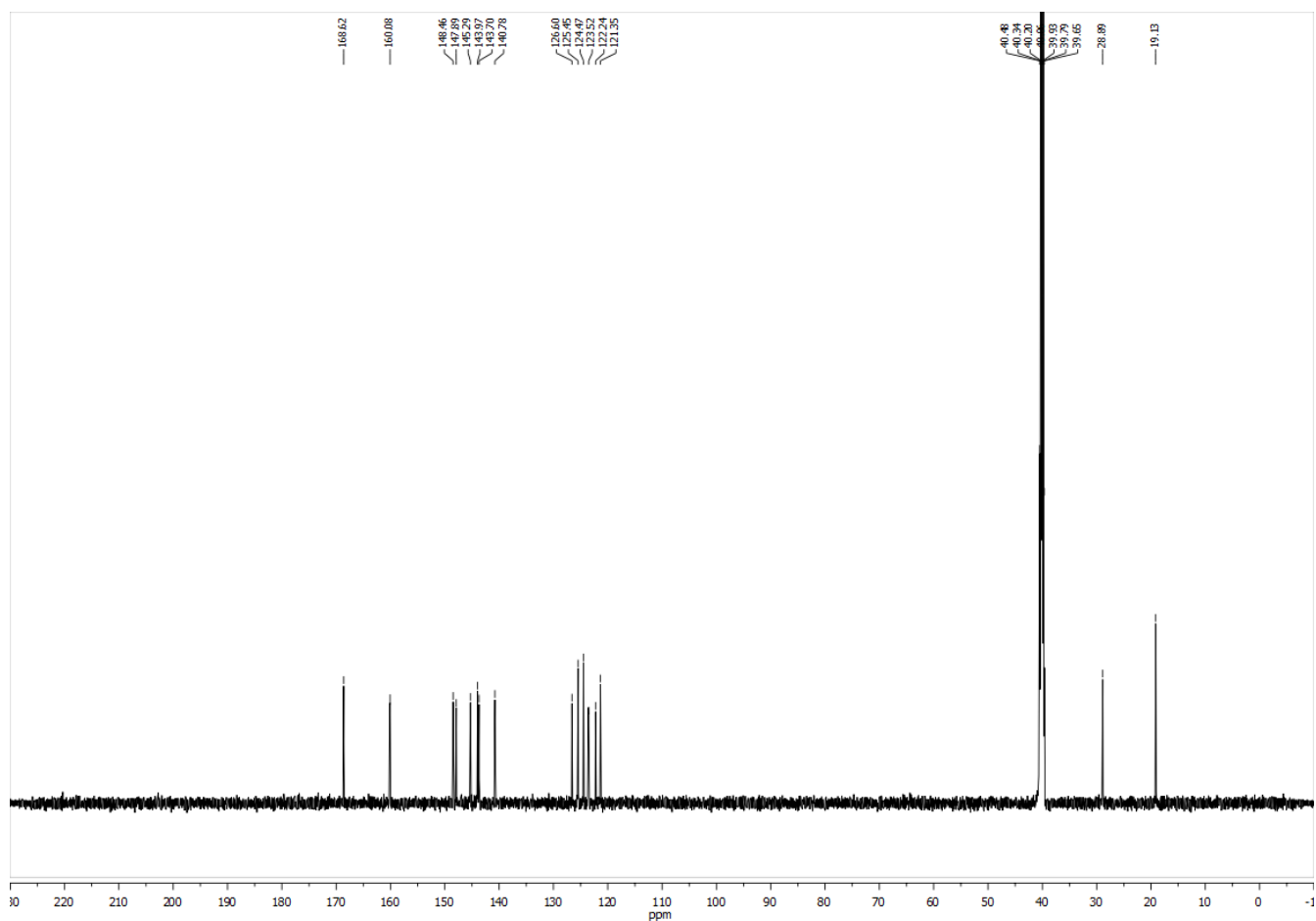
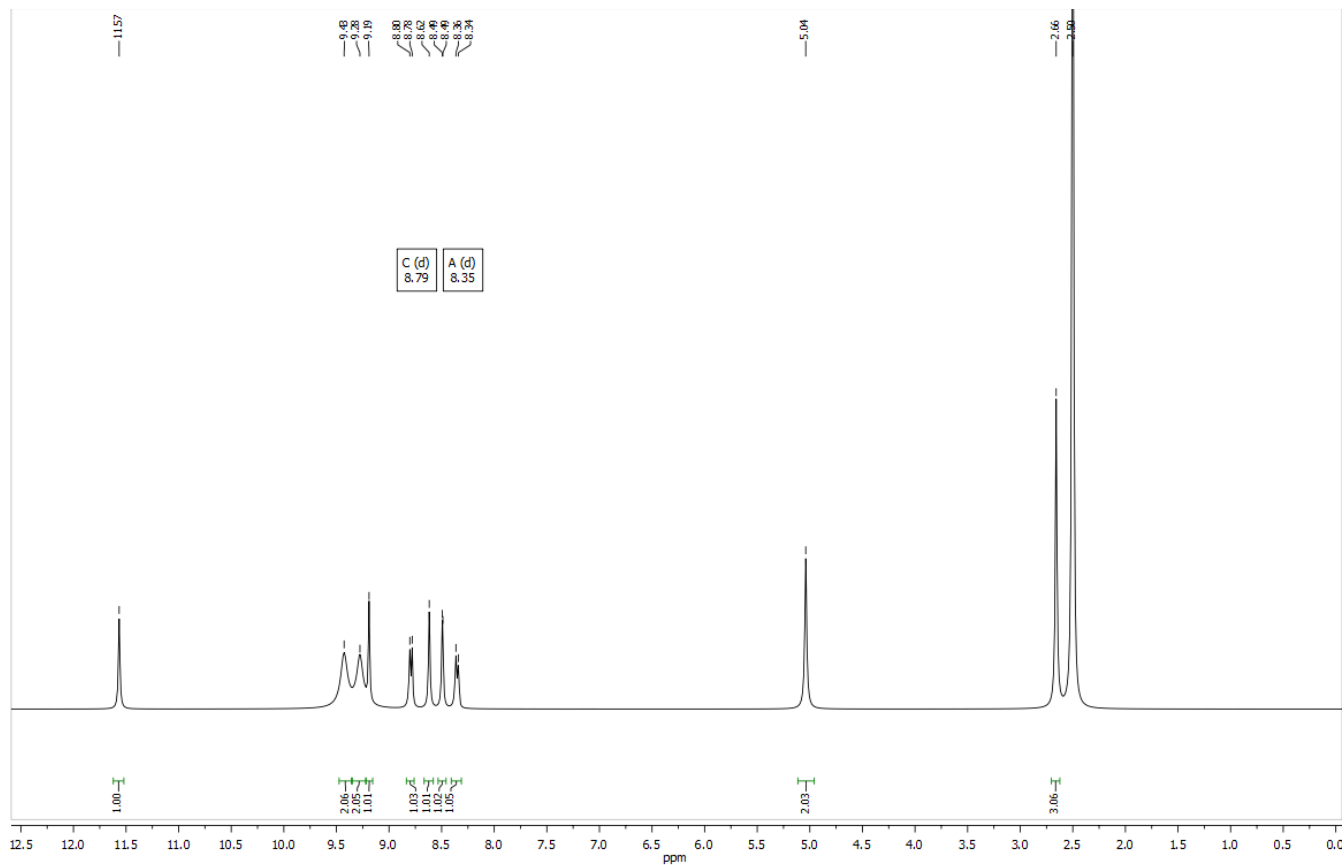
2-((3-(*N*-(3-bromophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)-isothiuronium chloride 2d



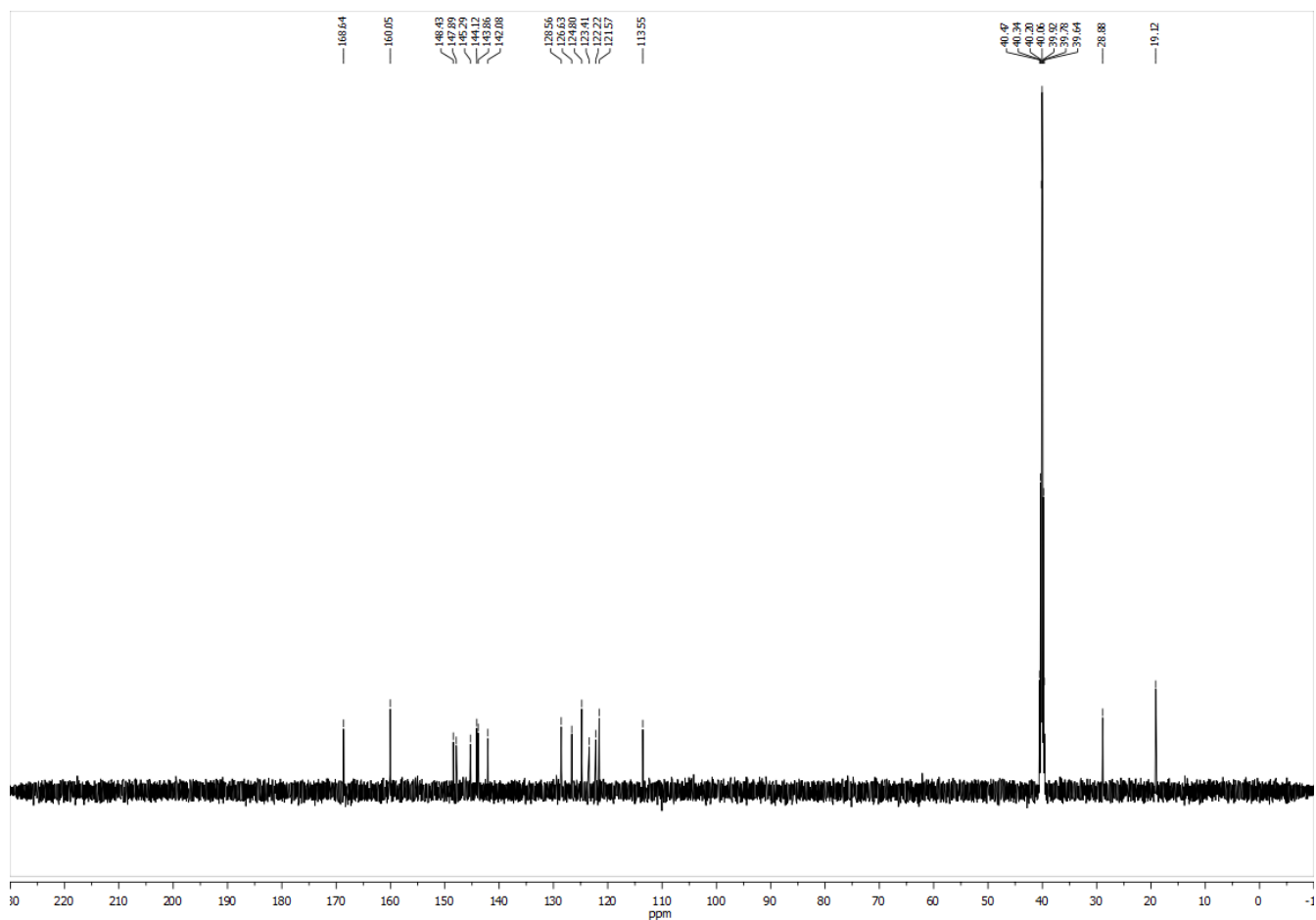
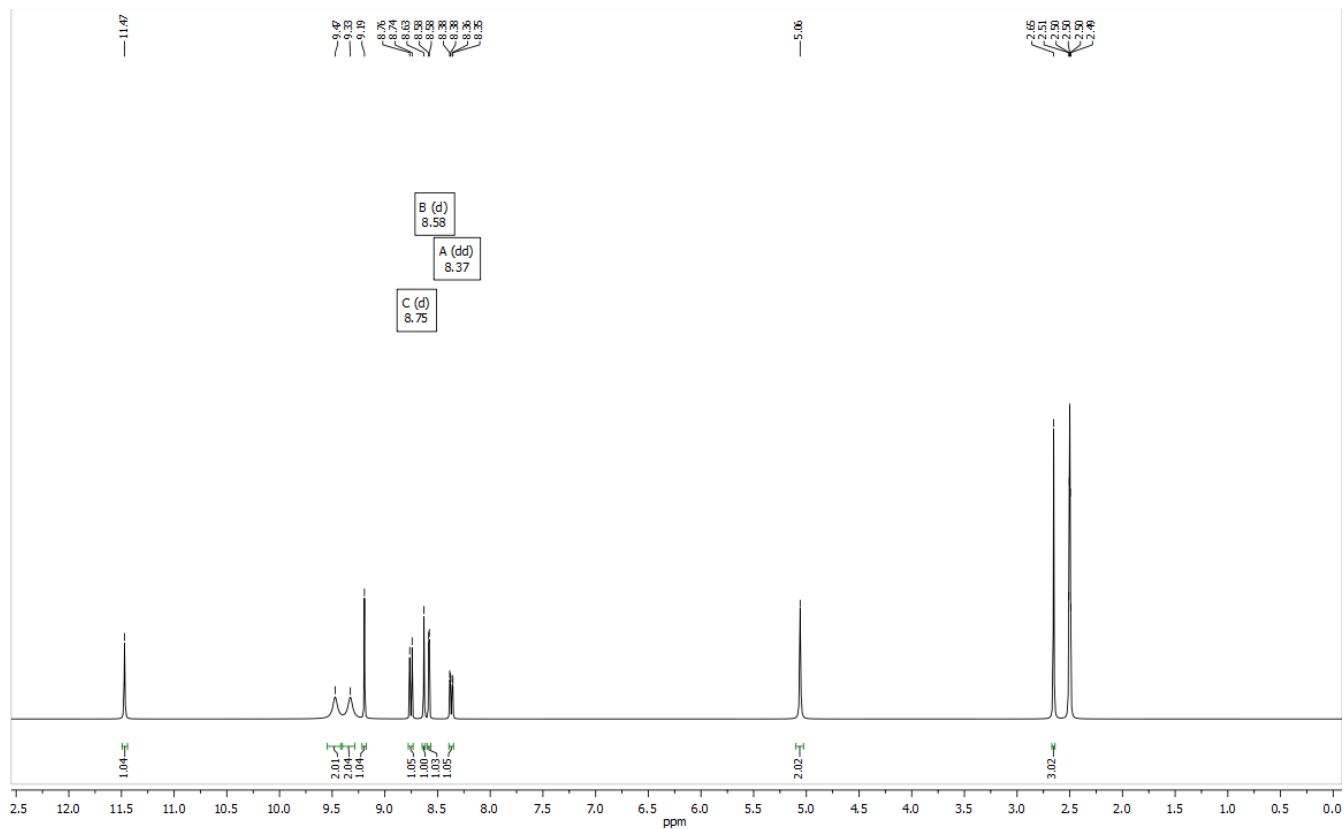
2-((8-methyl-2-oxo-3-(*N*-(4-sulfamoylphenyl)carbamoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)-isothiuronium chloride 2e



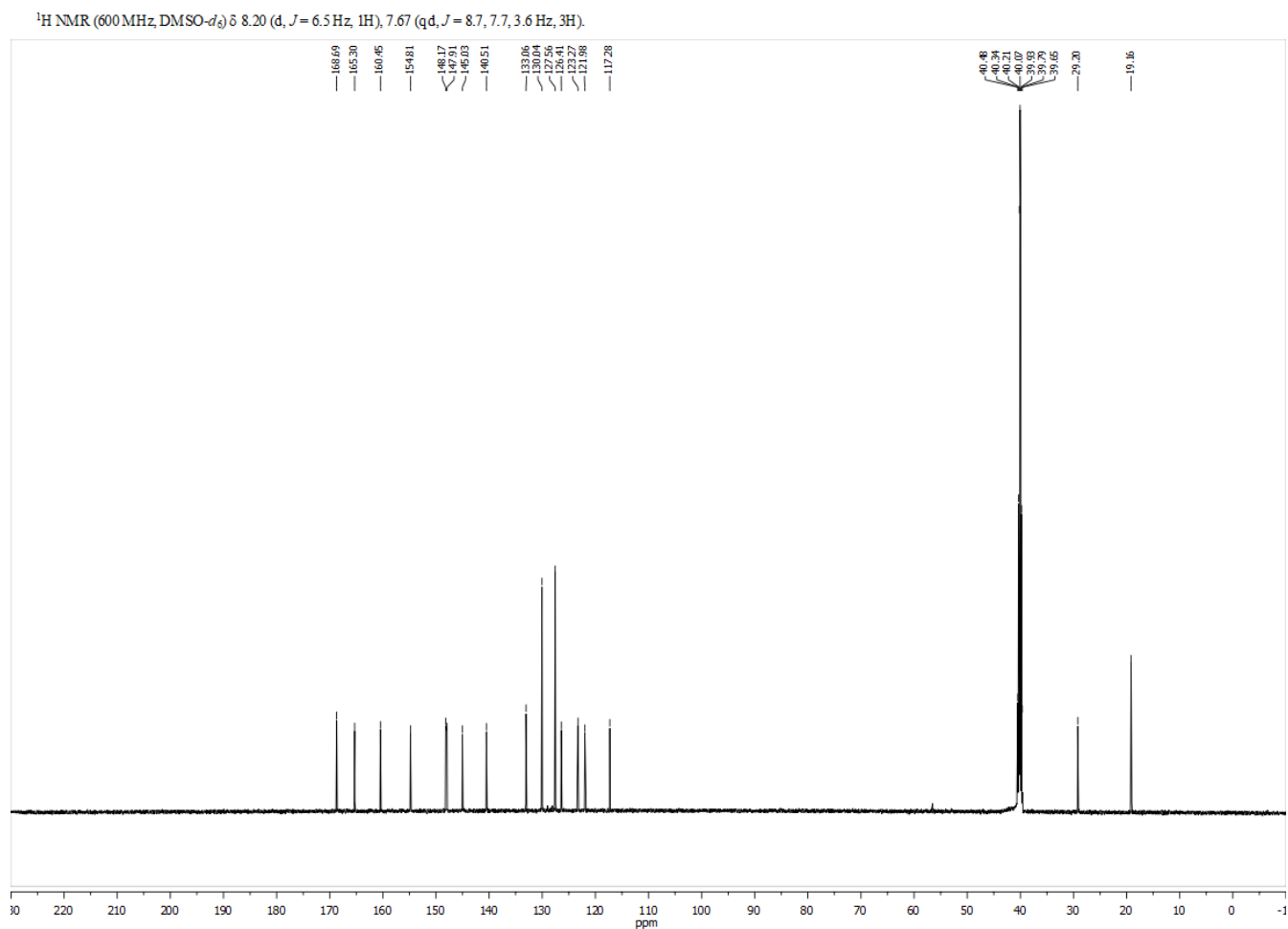
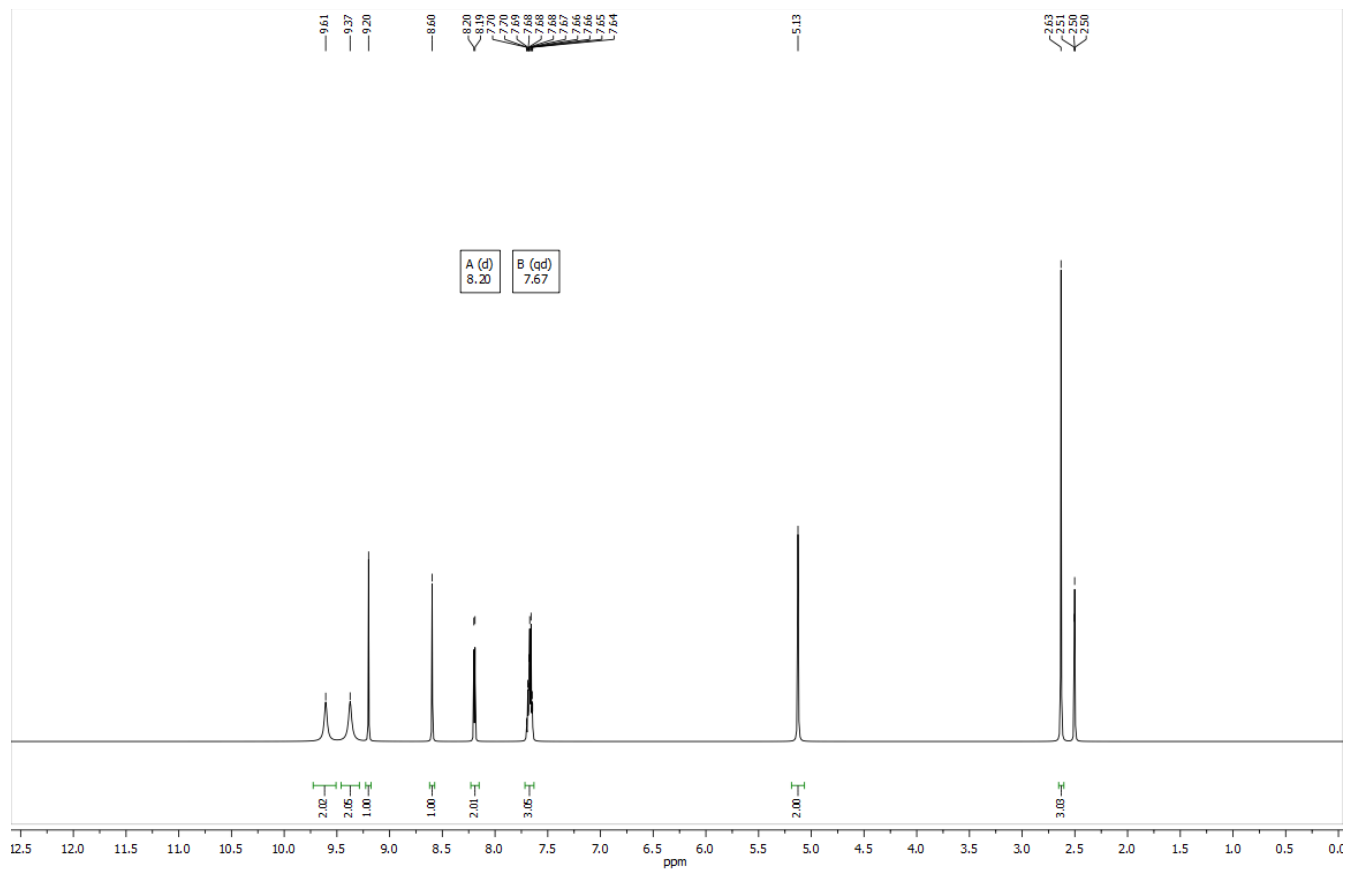
2-((3-(*N,N*-diphenylcarbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2f



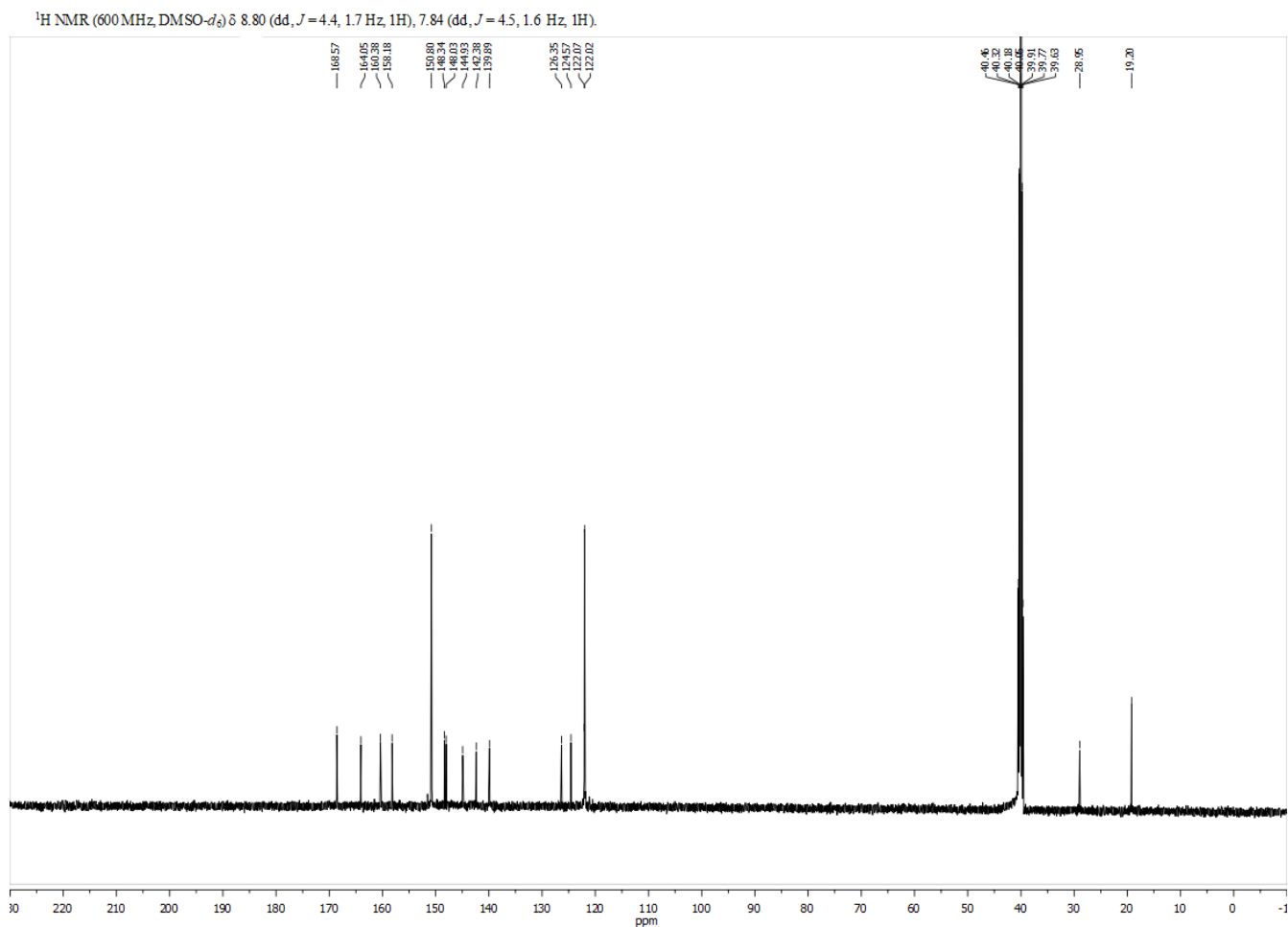
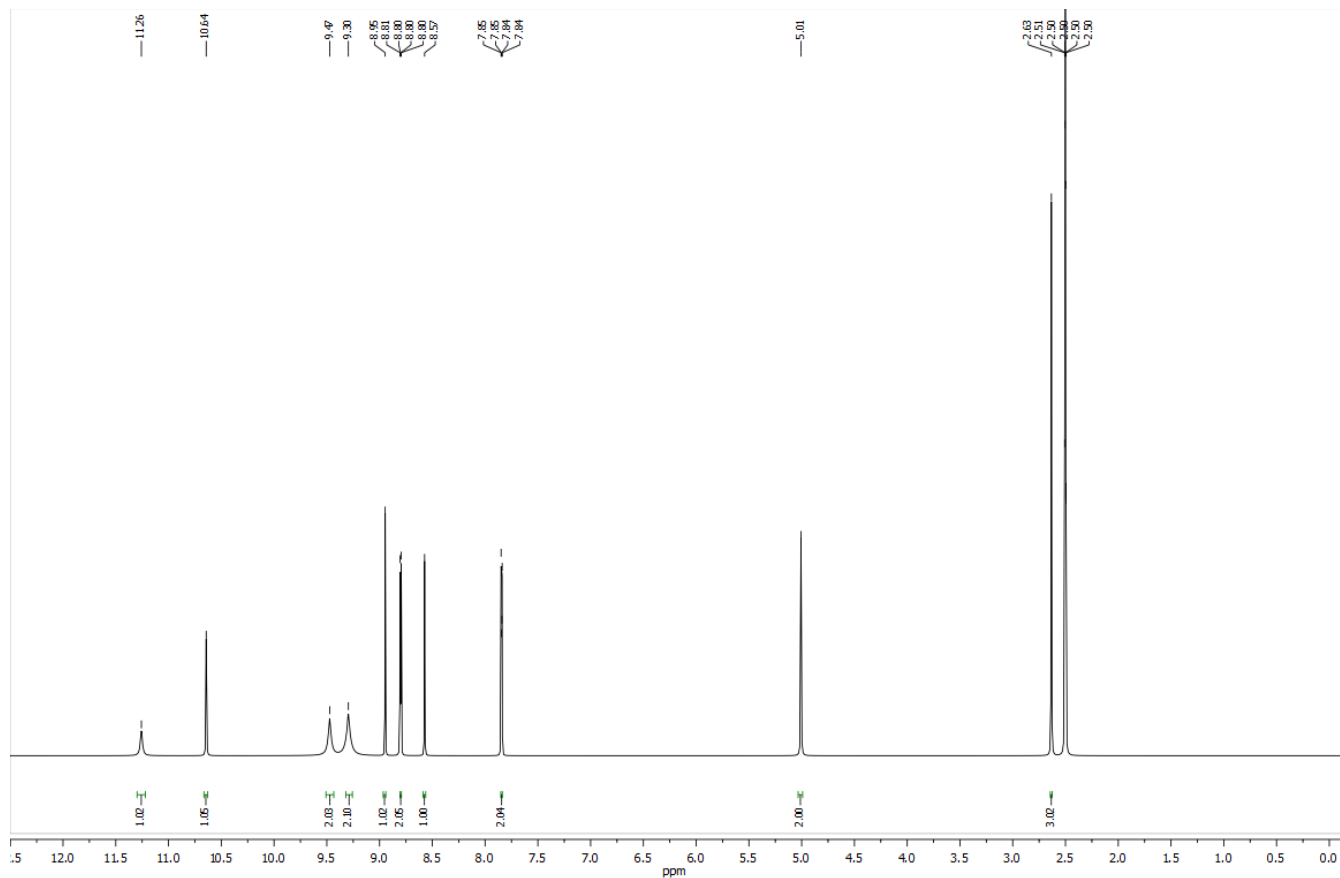
2-((3-(*N*-(2-chloro-4-nitrophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)-isothiuronium chloride 2h



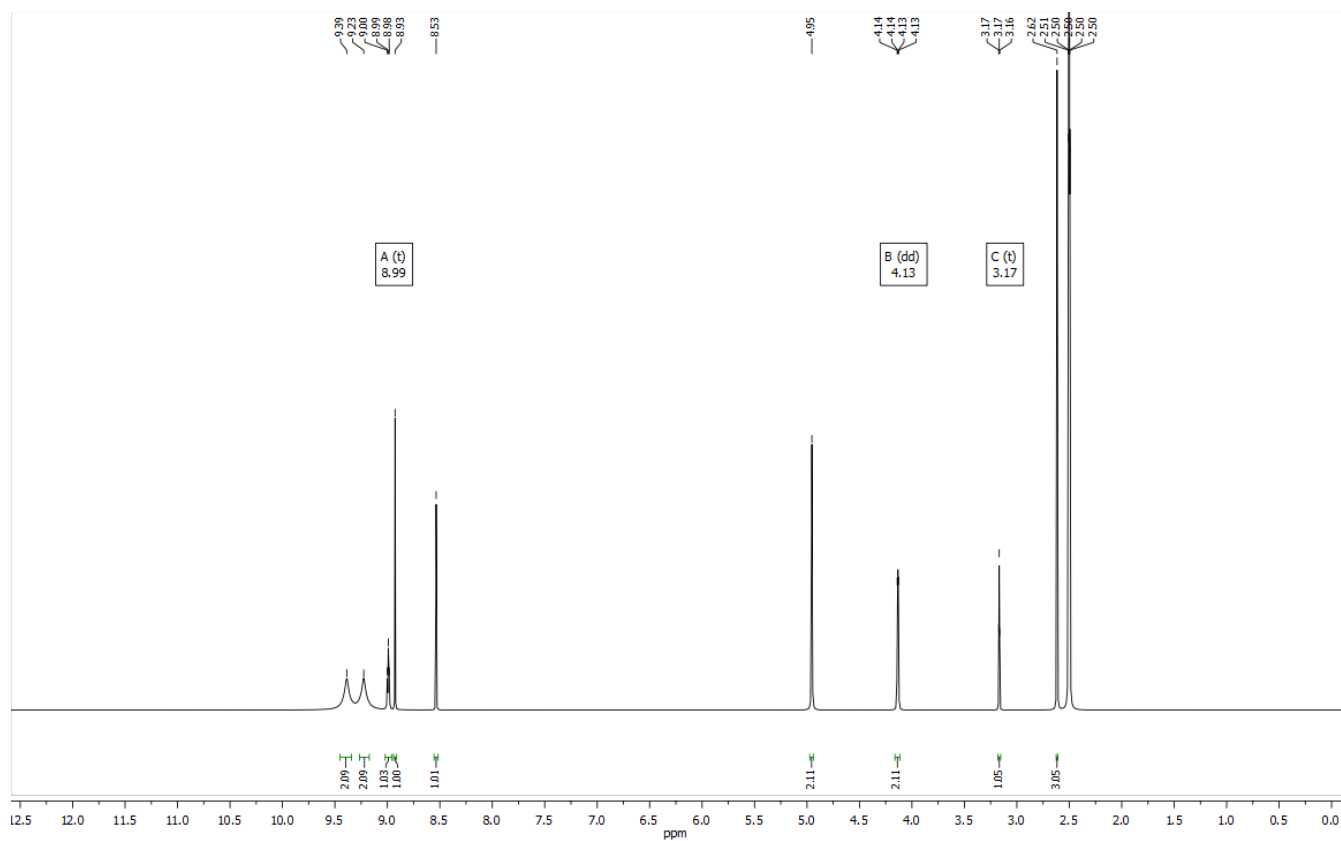
2-((3-(*N*-(2-bromo-4-nitrophenyl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridin-5-yl)-methyl)isothiuronium chloride 2i



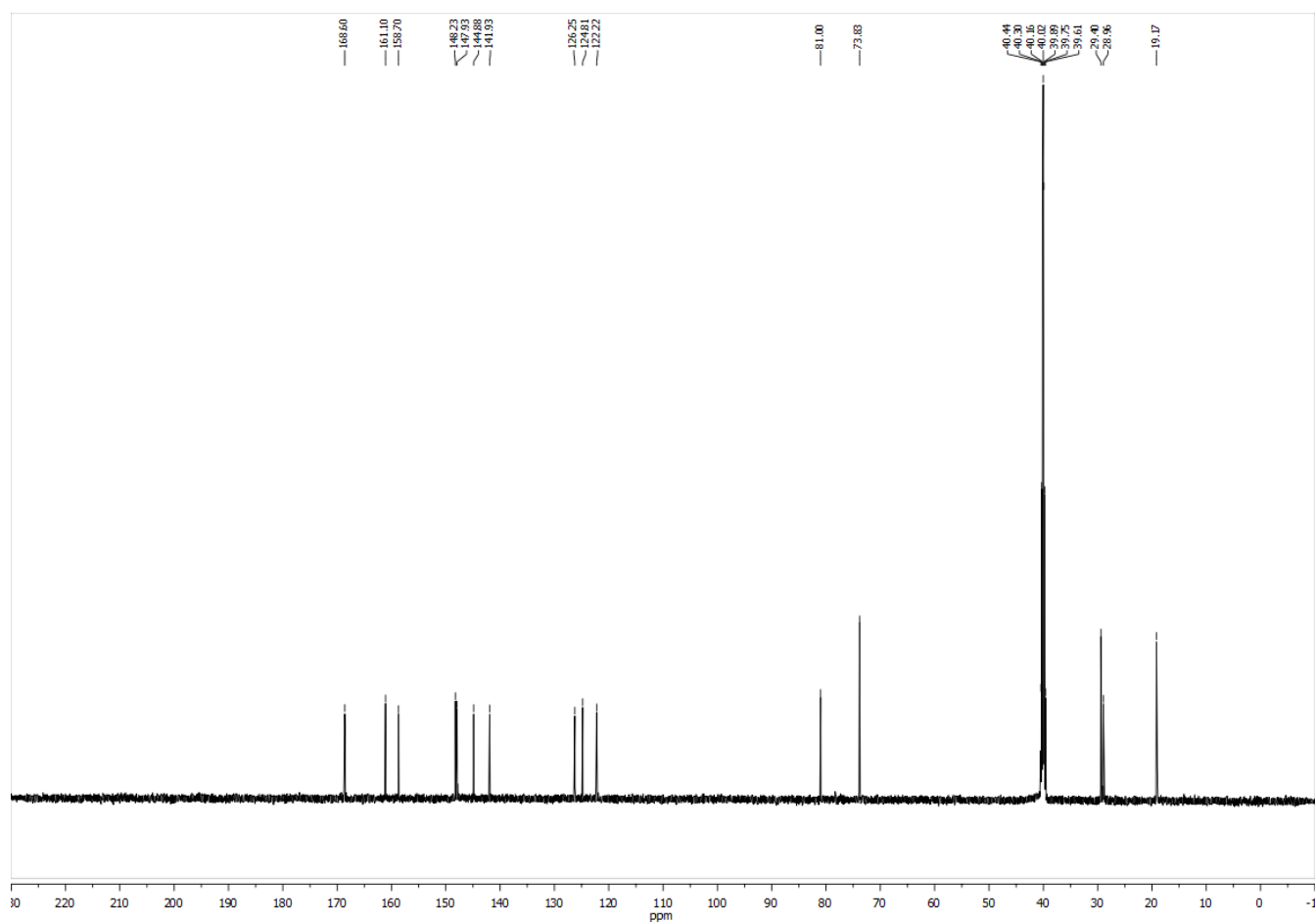
2-((8-methyl-2-oxo-3-(*N*²-phenylcarbazoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)-isothiuronium chloride 2j



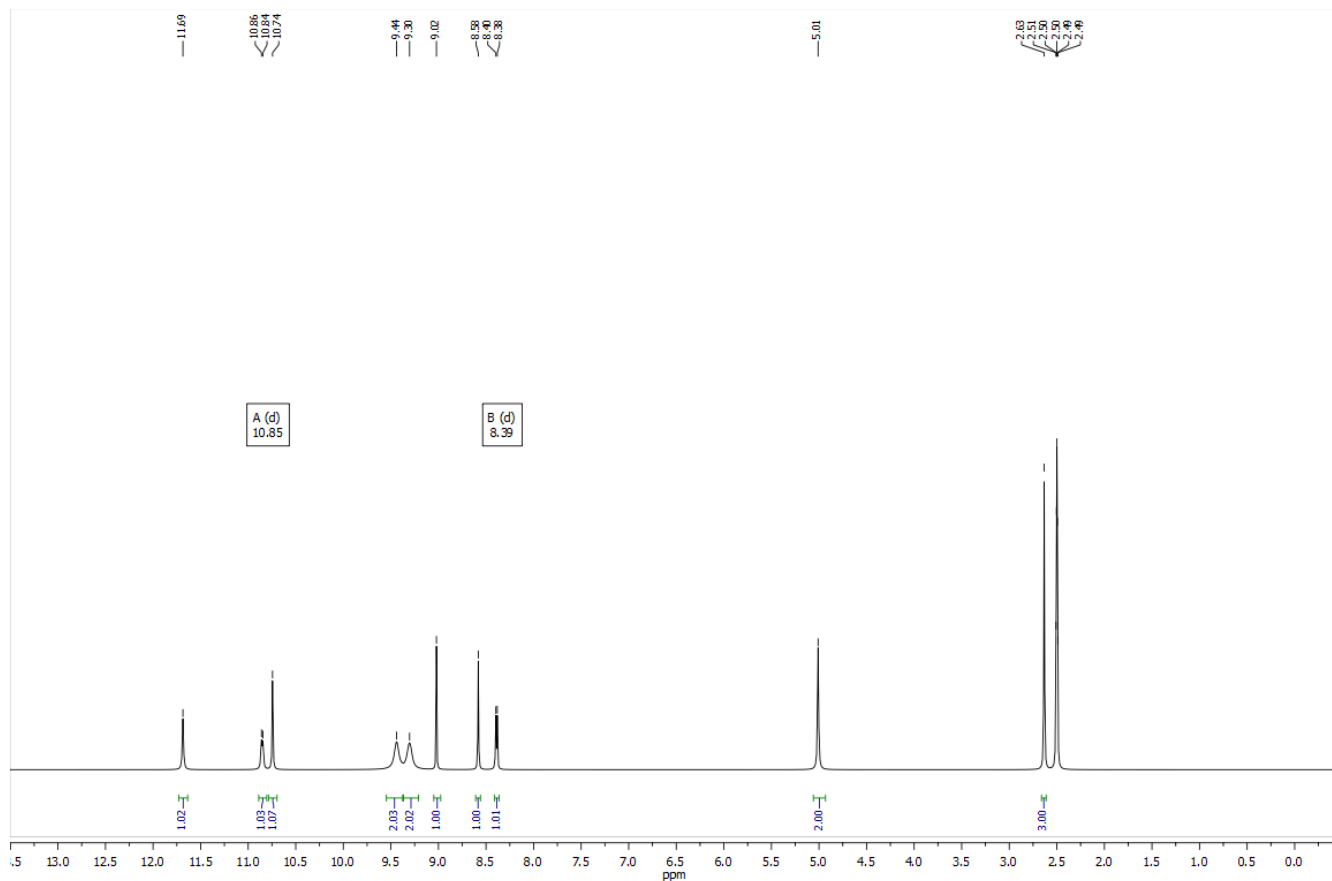
2-((8-methyl-2-oxo-3-(*N*²-(pyridin-4-yl)carbazoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)isothiuronium chloride 2k



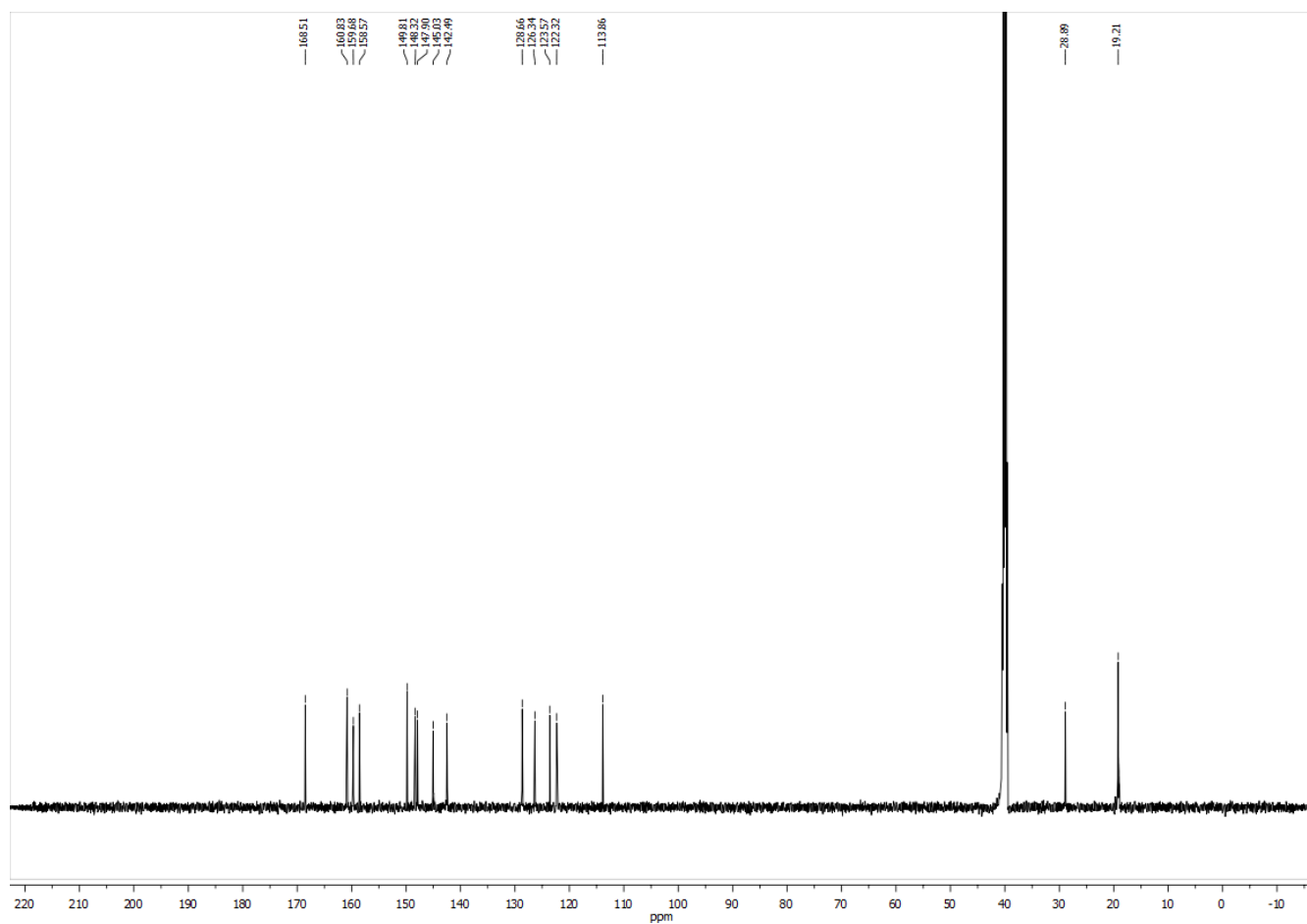
¹H NMR (600 MHz, DMSO-*d*₆) δ 8.99 (t, *J* = 5.6 Hz, 1H), 4.13 (dd, *J* = 5.6, 2.5 Hz, 2H), 3.17 (t, *J* = 2.5 Hz, 1H).



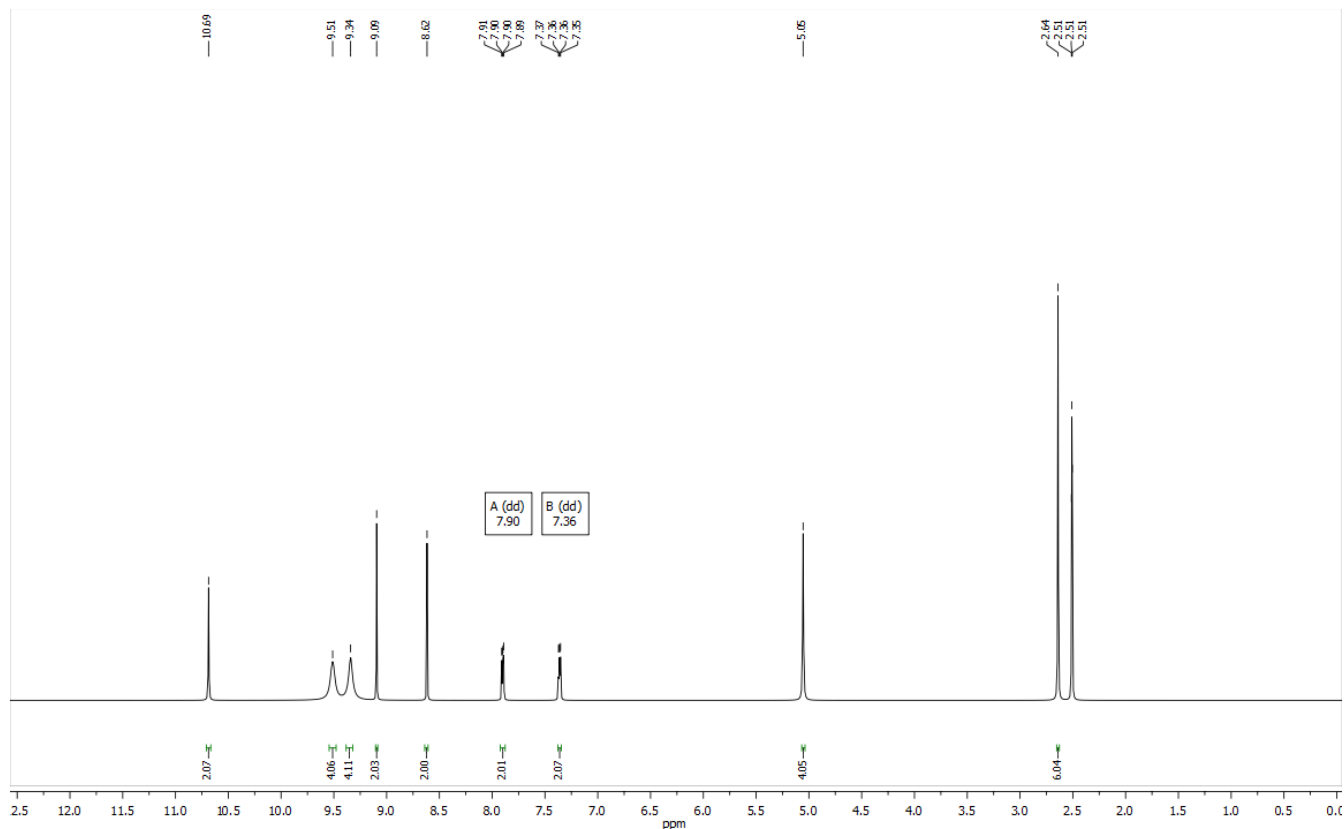
2-((8-methyl-2-oxo-3-(*N*-(prop-2-yn-1-yl)carbamoyl)-2*H*-pyrano[2,3-*c*]pyridin-5-yl)methyl)-isothiuronium chloride 2l



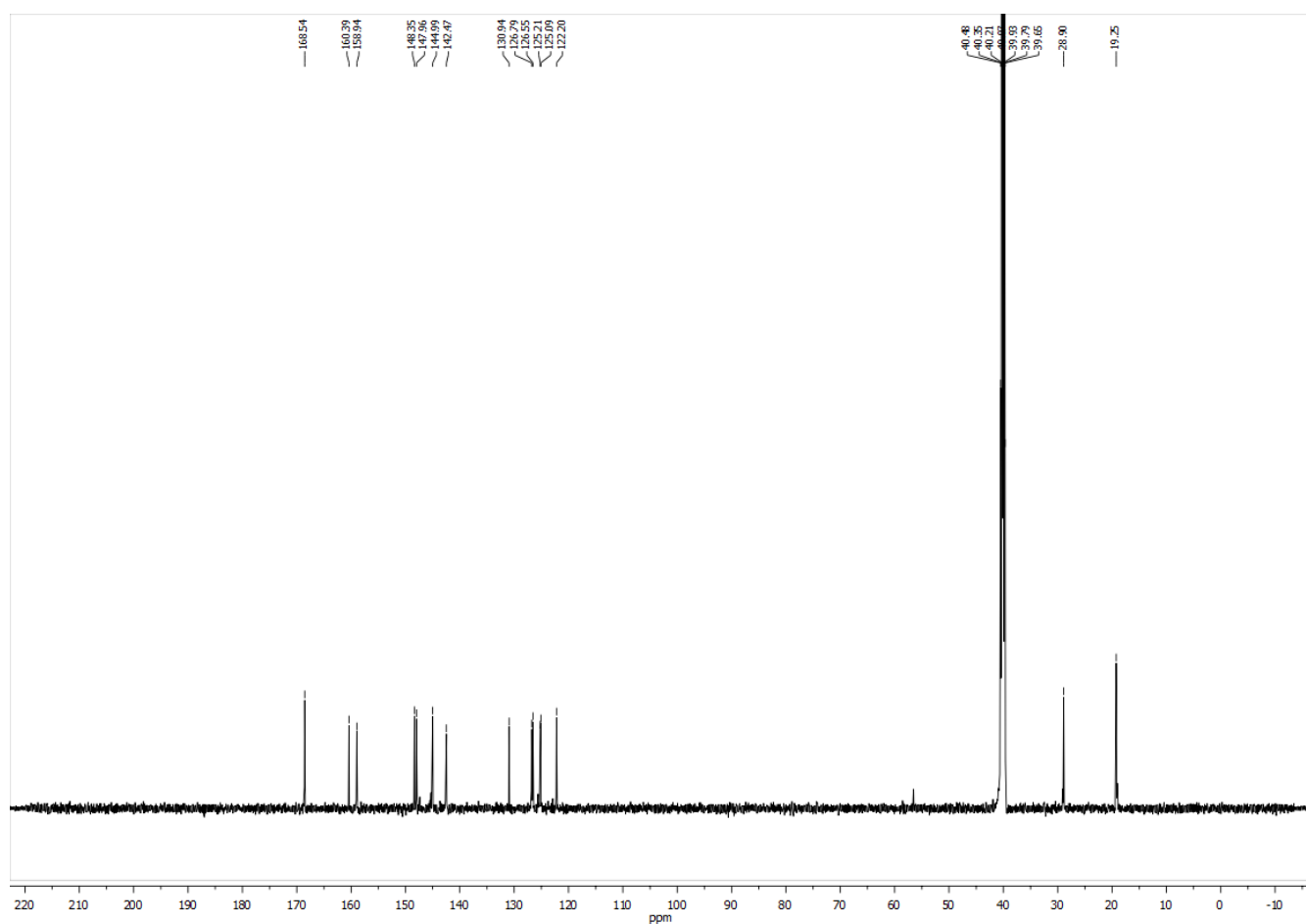
¹H NMR (400 MHz, DMSO-*d*₆) δ 10.85 (d, *J* = 6.3 Hz, 1H), 8.39 (d, *J* = 5.9 Hz, 1H).



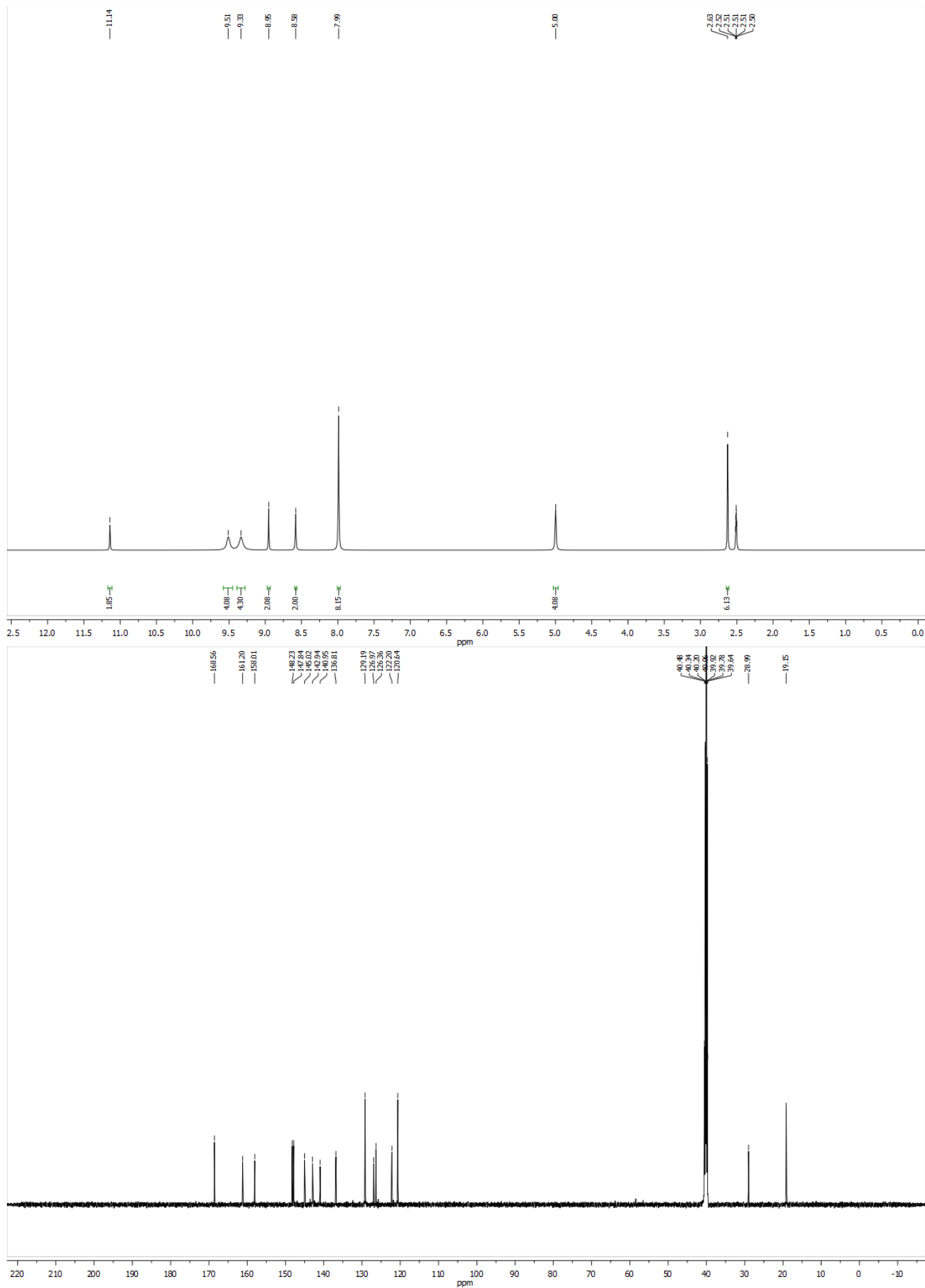
2-((3-(*N*-(2,4-dioxo-1,2,3,4-tetrahydropyrimidin-5-yl)carbamoyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]-pyridin-5-yl)methyl)isothiuronium chloride 2m



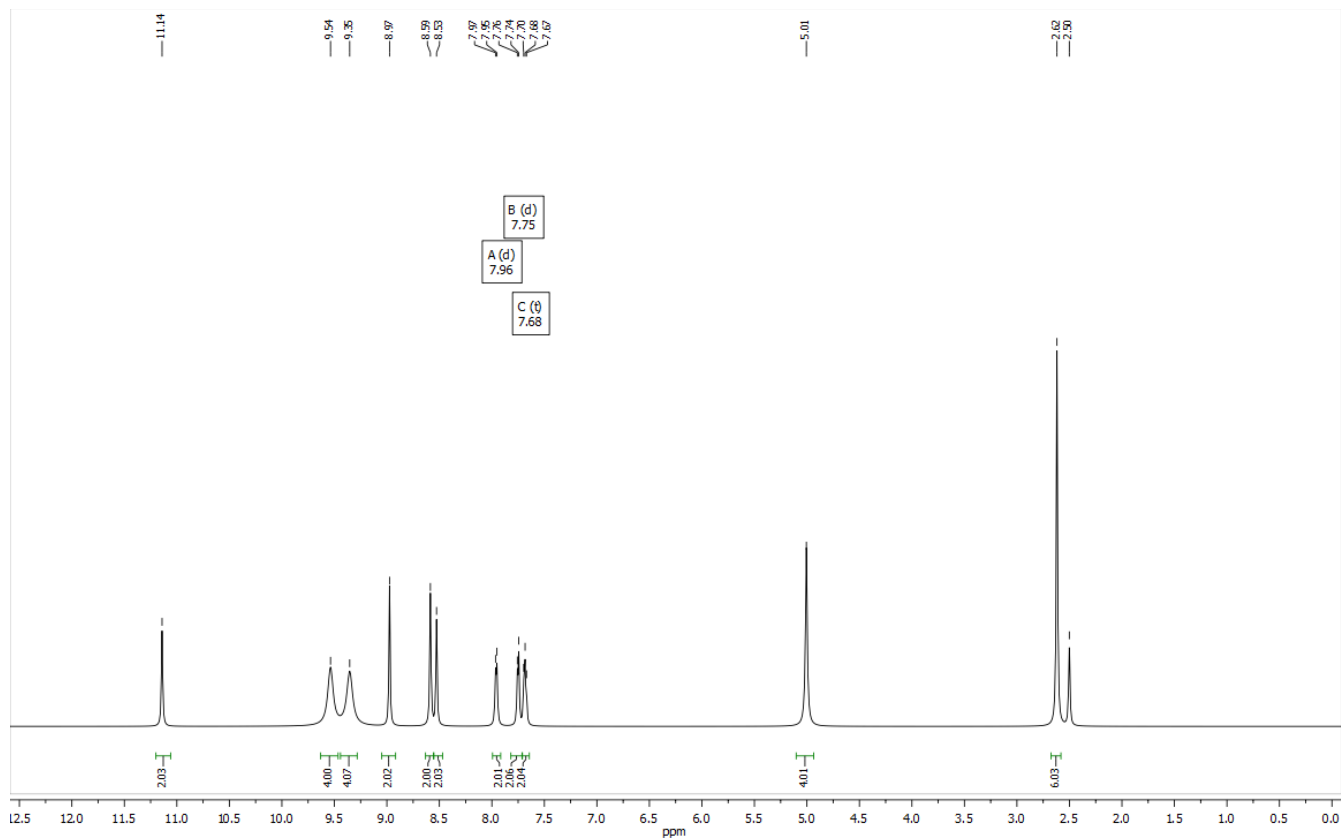
¹H NMR (600 MHz, DMSO-*d*₆) δ 7.90 (dd, *J* = 6.1, 3.5 Hz, 1H), 7.36 (dd, *J* = 6.1, 3.5 Hz, 1H).



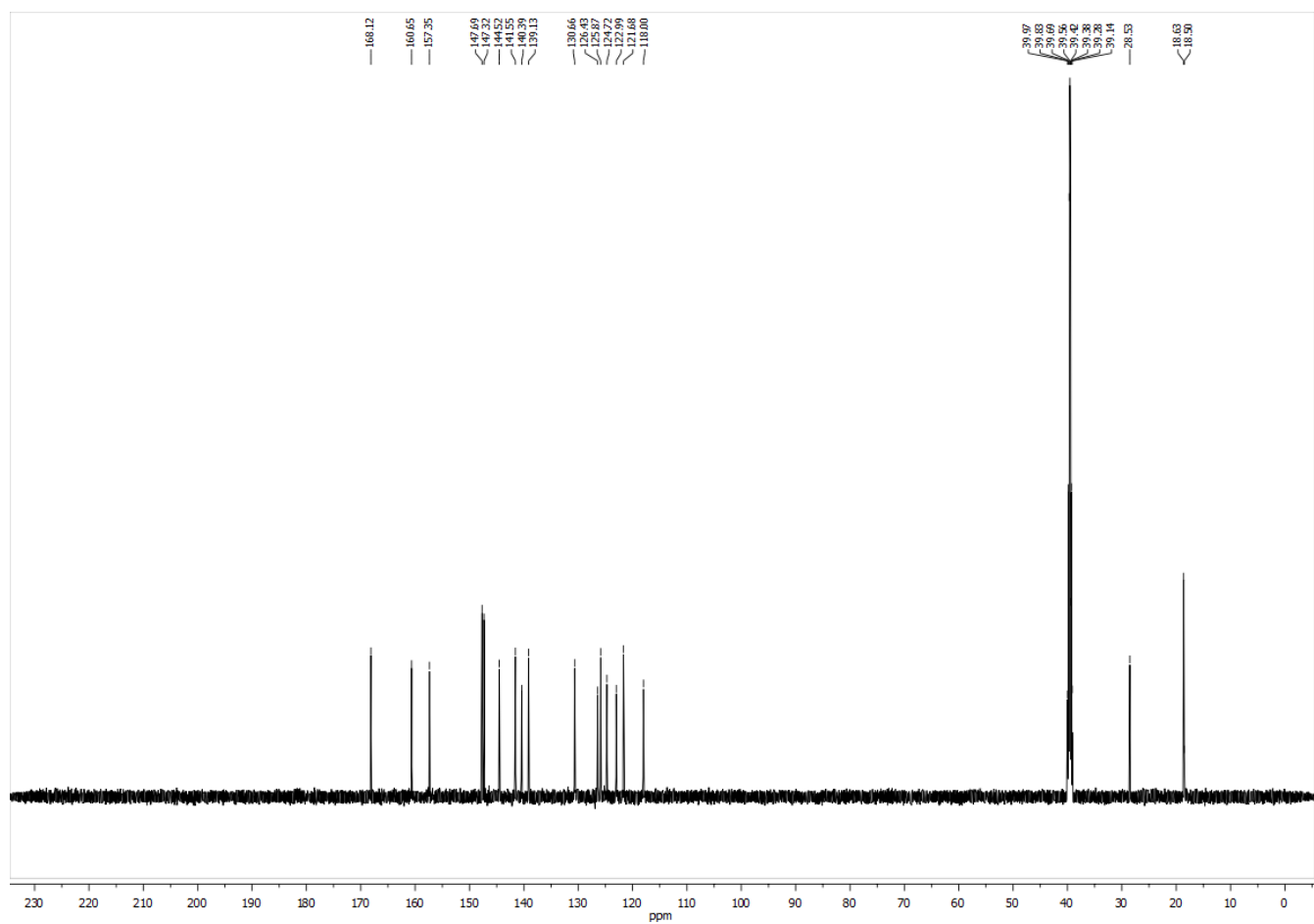
2,2'-((((1,2-phenylenebis(azanediyl))bis(carbonyl))bis(8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3,5-diyl))bis(methylene))diisothiuronium chloride 4a



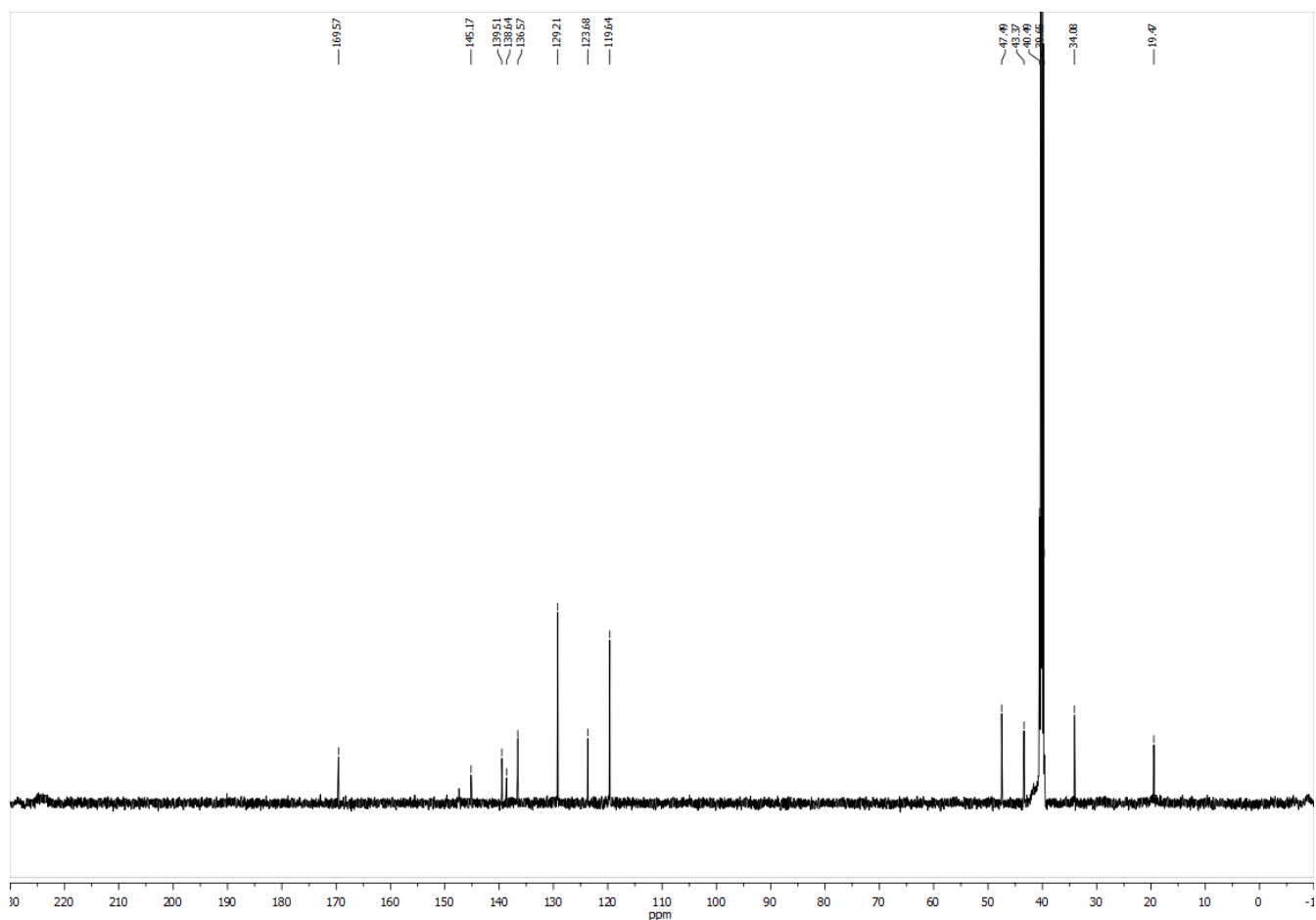
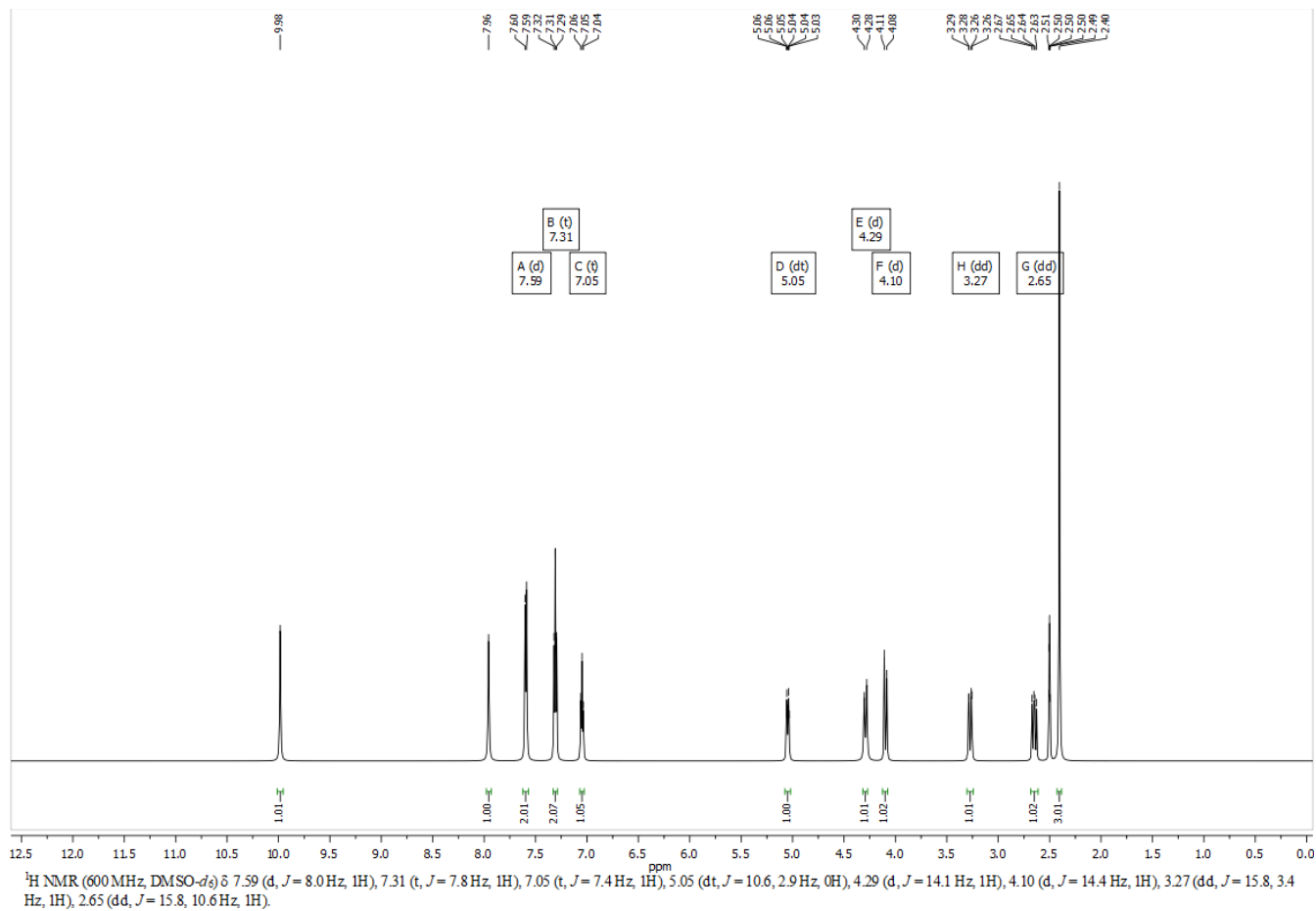
2,2'-((((sulfonylbis(4,1-phenylene))bis(azanediyl))bis(carbonyl))bis(8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3,5-diyl))bis(methylene))diisothiuronium chloride **4b**



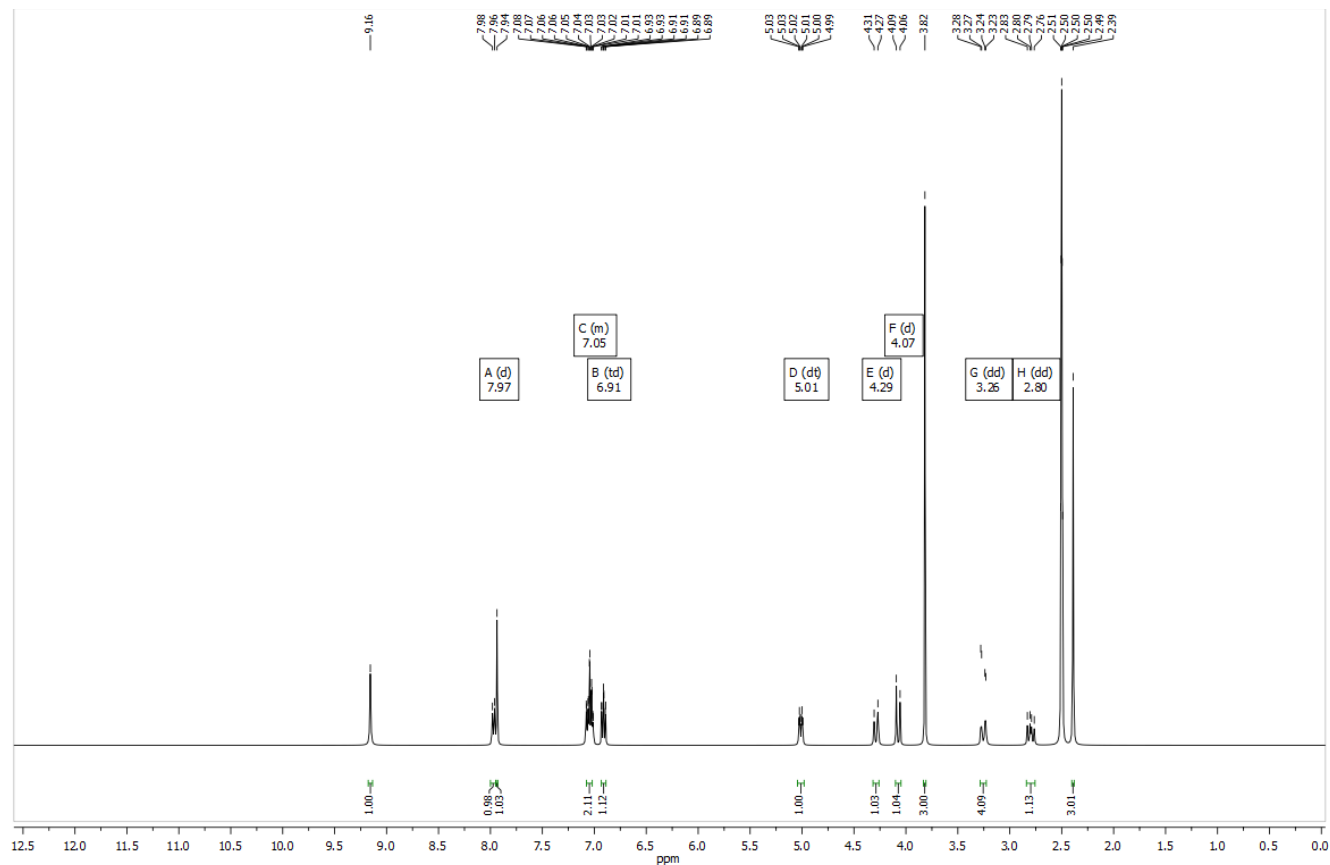
¹H NMR (600 MHz, DMSO-*d*₆) δ 7.96 (d, *J* = 8.1 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 1H).



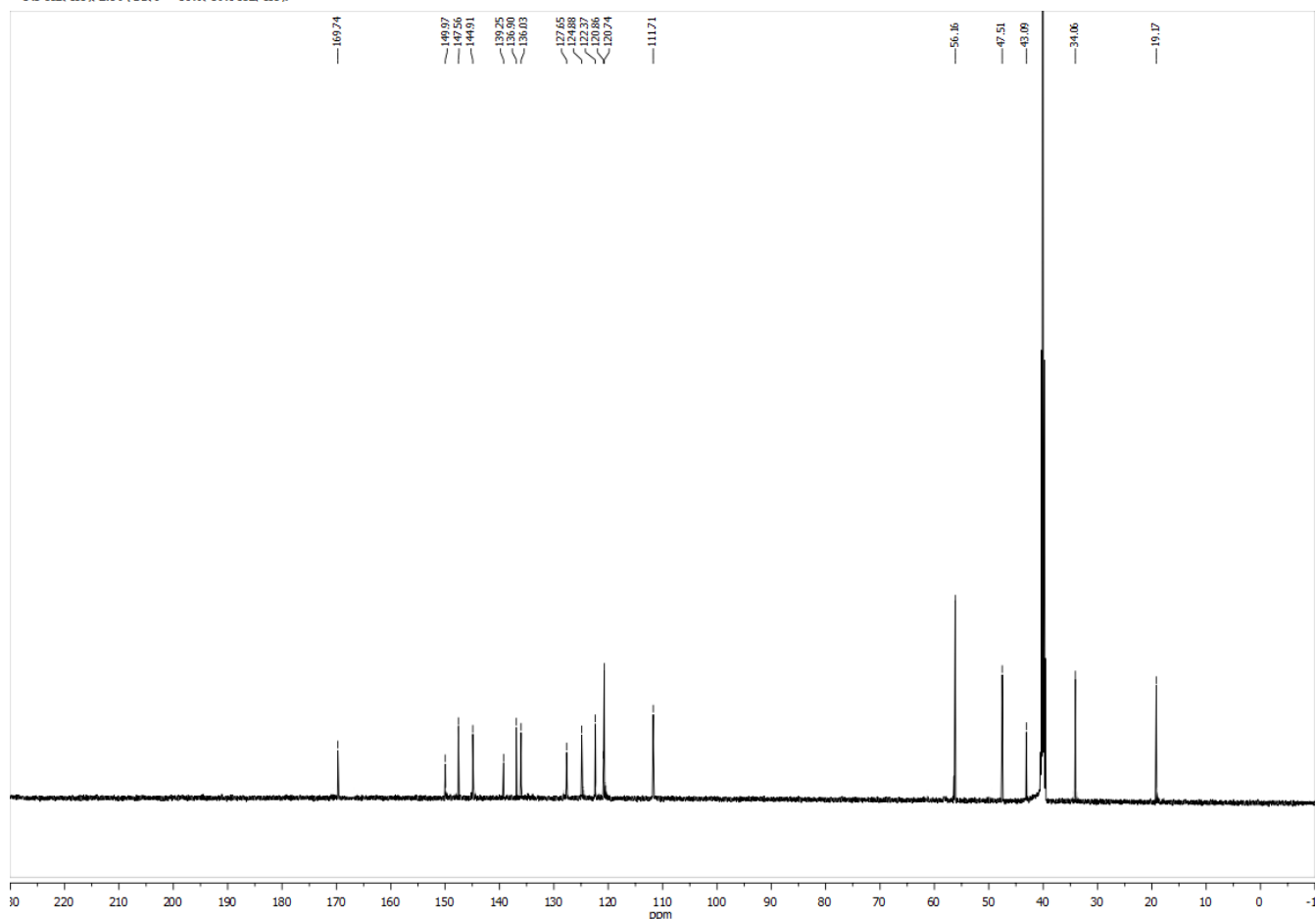
2,2'-((((sulfonylbis(3,1-phenylene))bis(azanediyl))bis(carbonyl))bis(8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3,5-diyl))bis(methylene))diisothiuronium chloride 4c



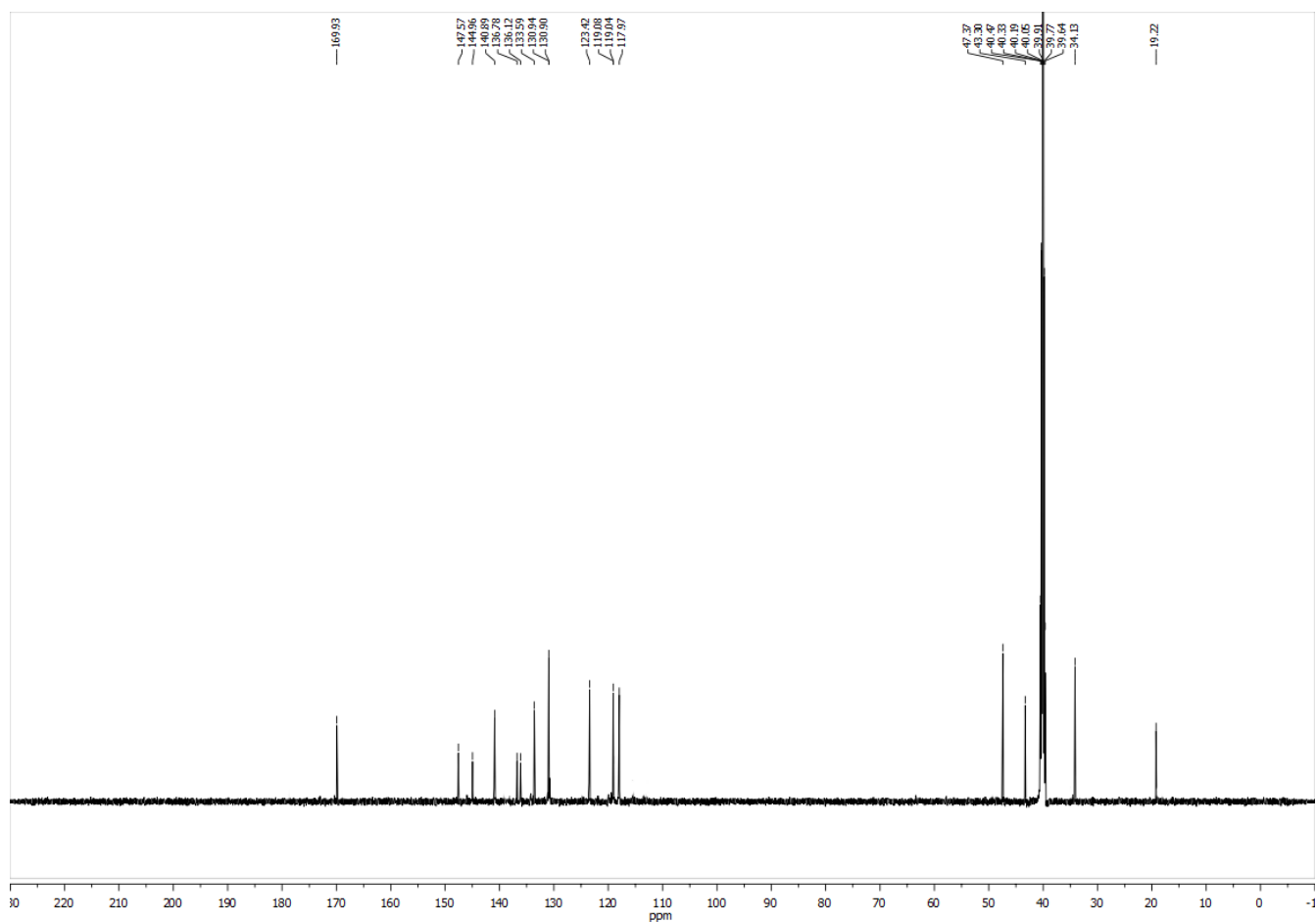
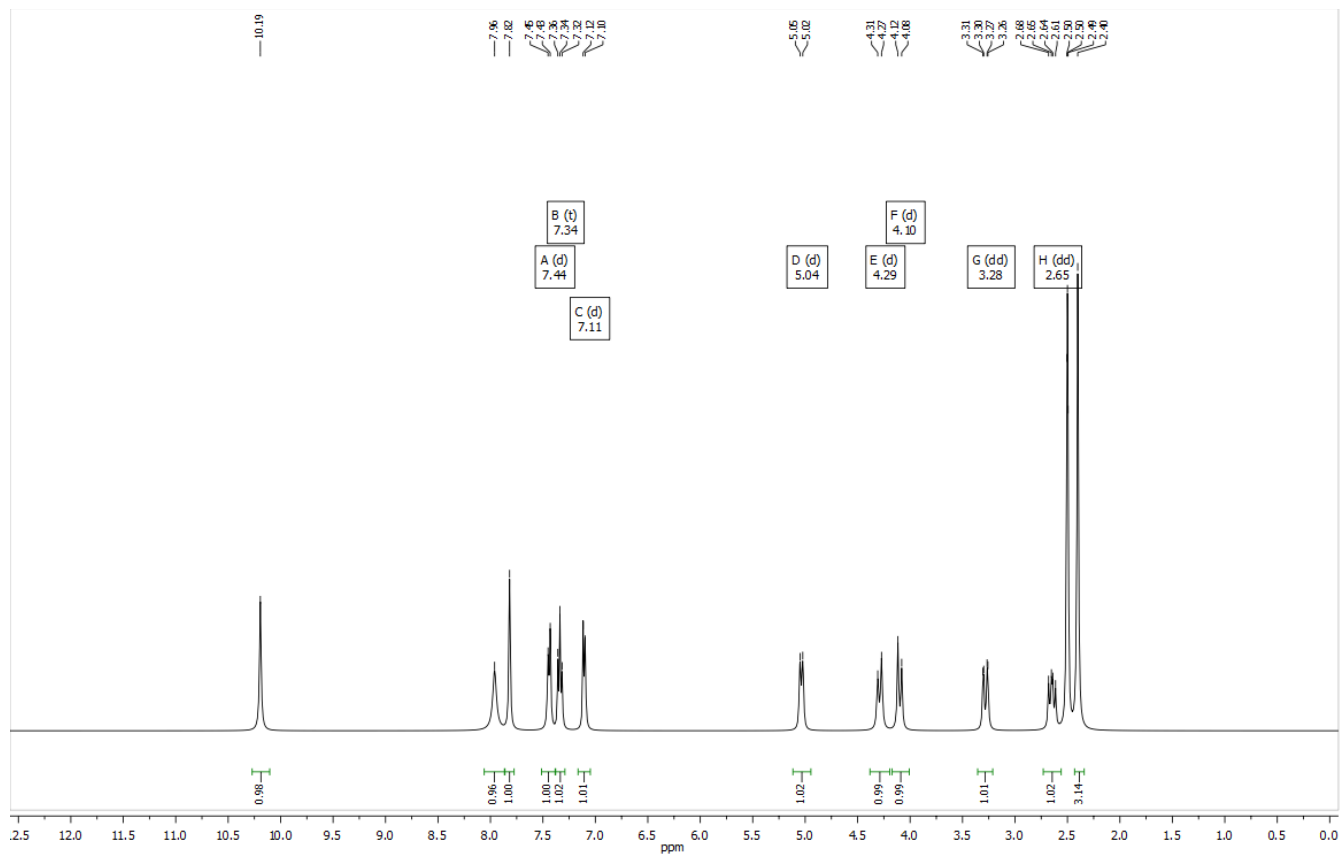
2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)-*N*-phenylacetamide 5a



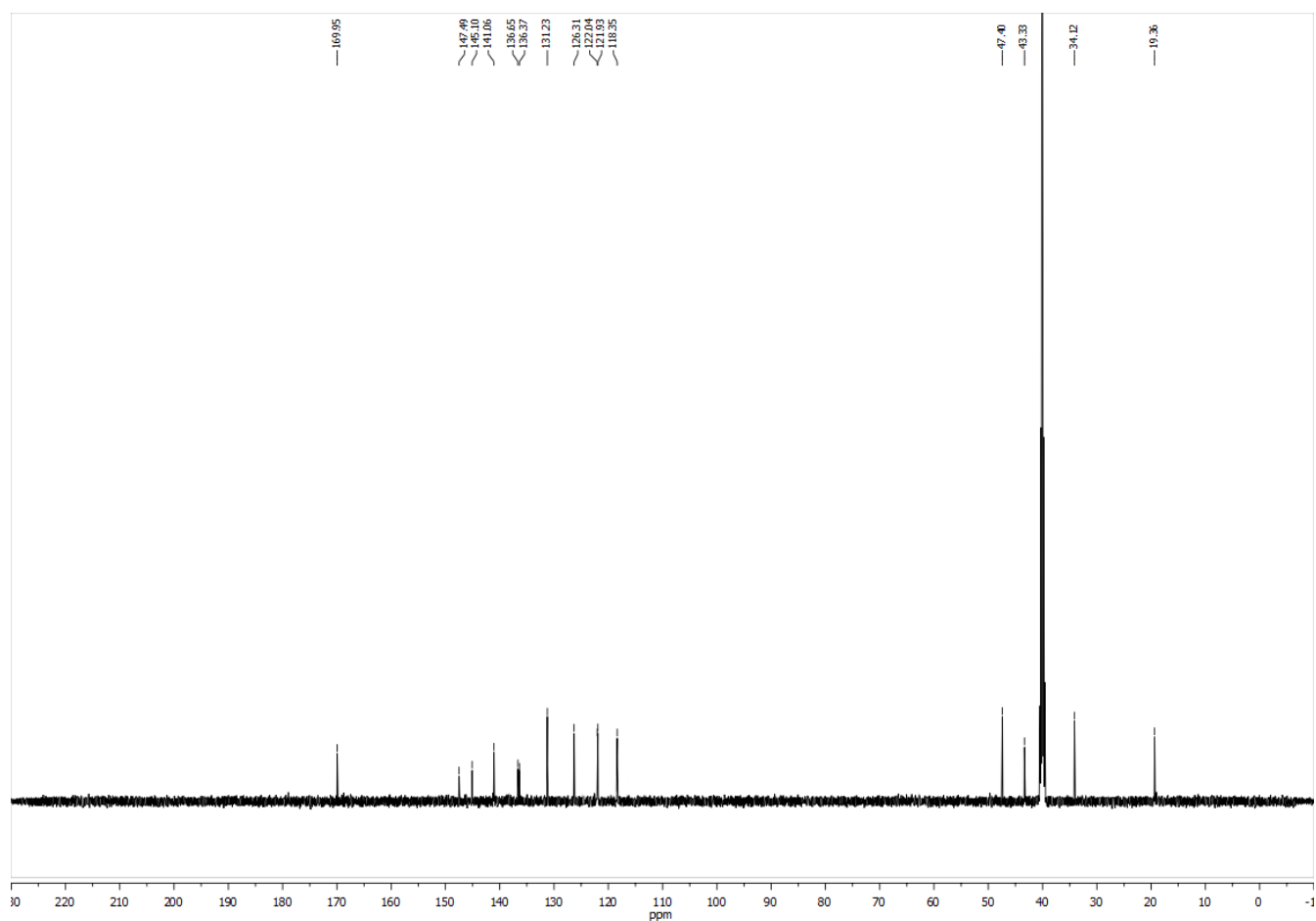
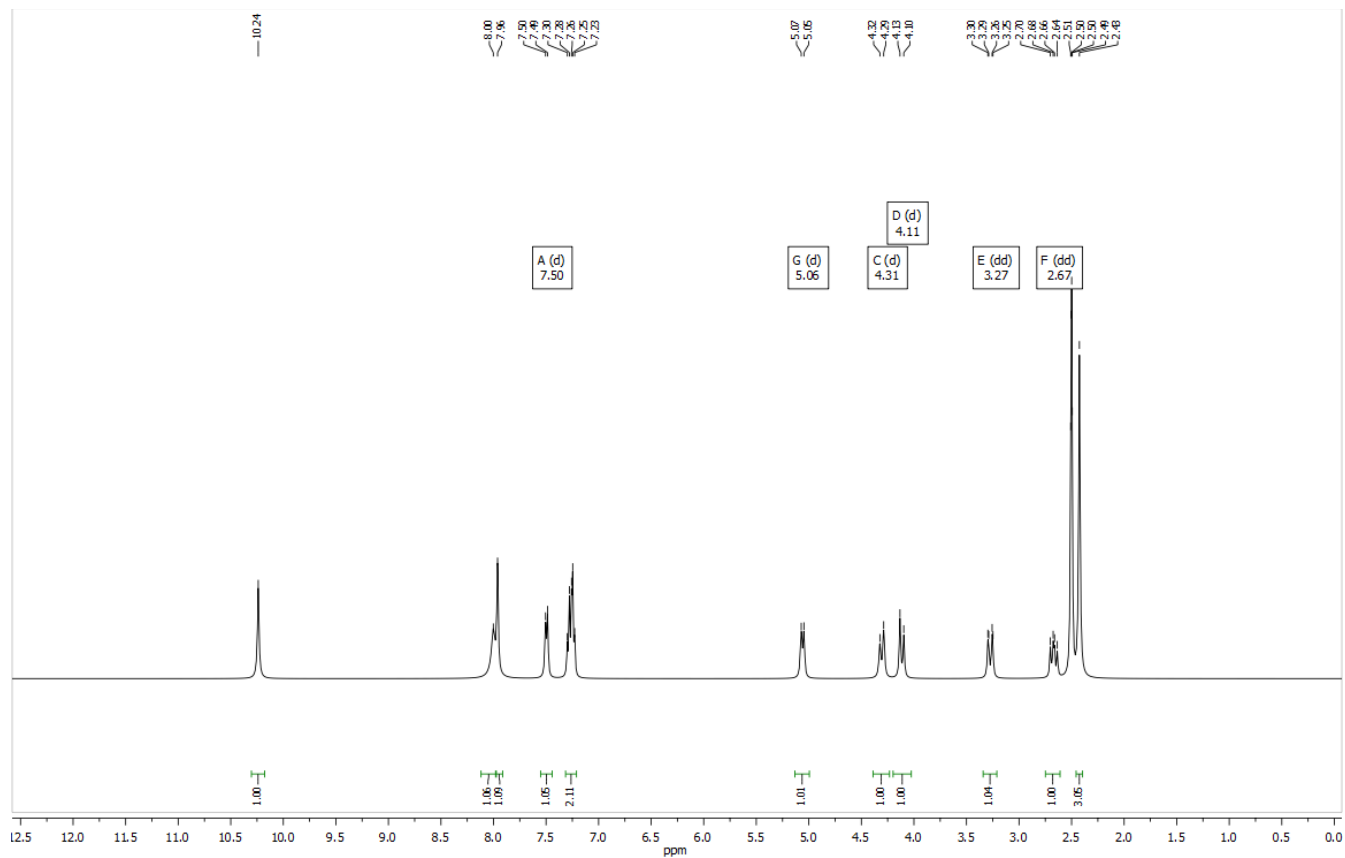
¹H NMR (400 MHz, DMSO-*d*₆) δ 7.97 (d, *J* = 8.2 Hz, 1H), 7.13 – 6.99 (m, 3H), 6.91 (td, *J* = 7.5, 6.9, 1.7 Hz, 1H), 5.01 (dt, *J* = 10.6, 2.9 Hz, 1H), 4.29 (d, *J* = 14.4 Hz, 1H), 4.07 (d, *J* = 14.3 Hz, 1H), 3.26 (dd, *J* = 16.1, 3.3 Hz, 1H), 2.80 (dd, *J* = 16.0, 10.6 Hz, 1H).



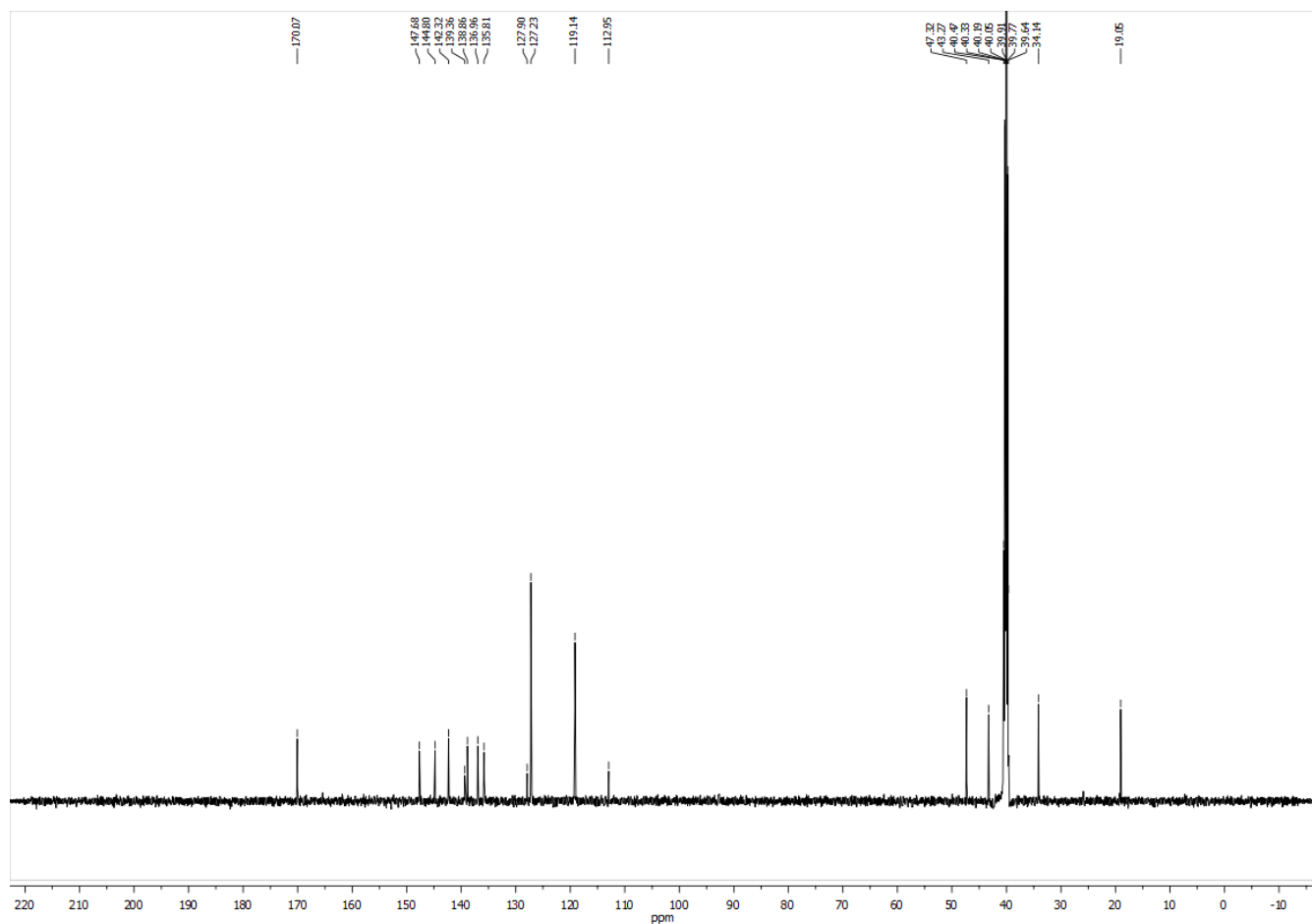
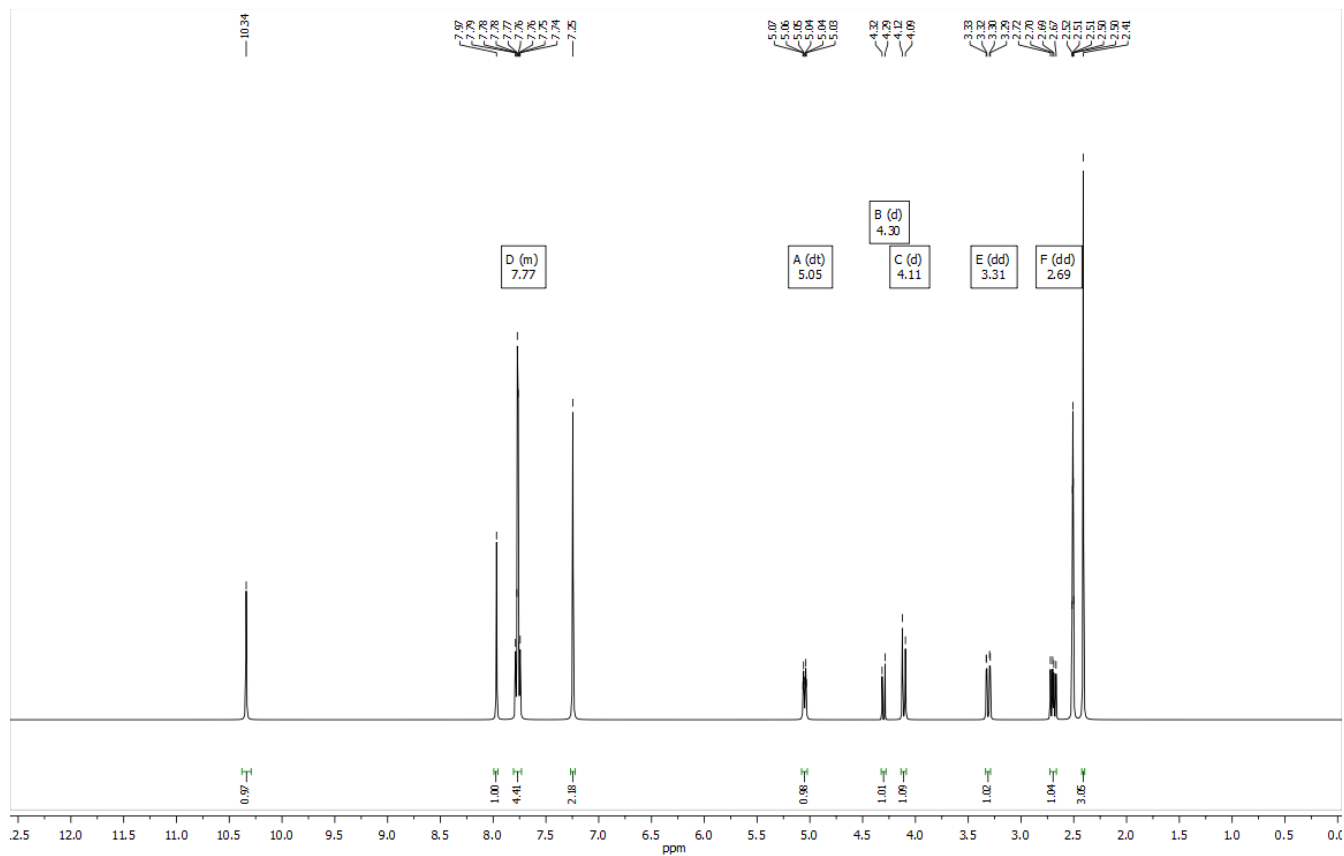
2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)-*N*-(2-methoxyphenyl)acetamide 5b



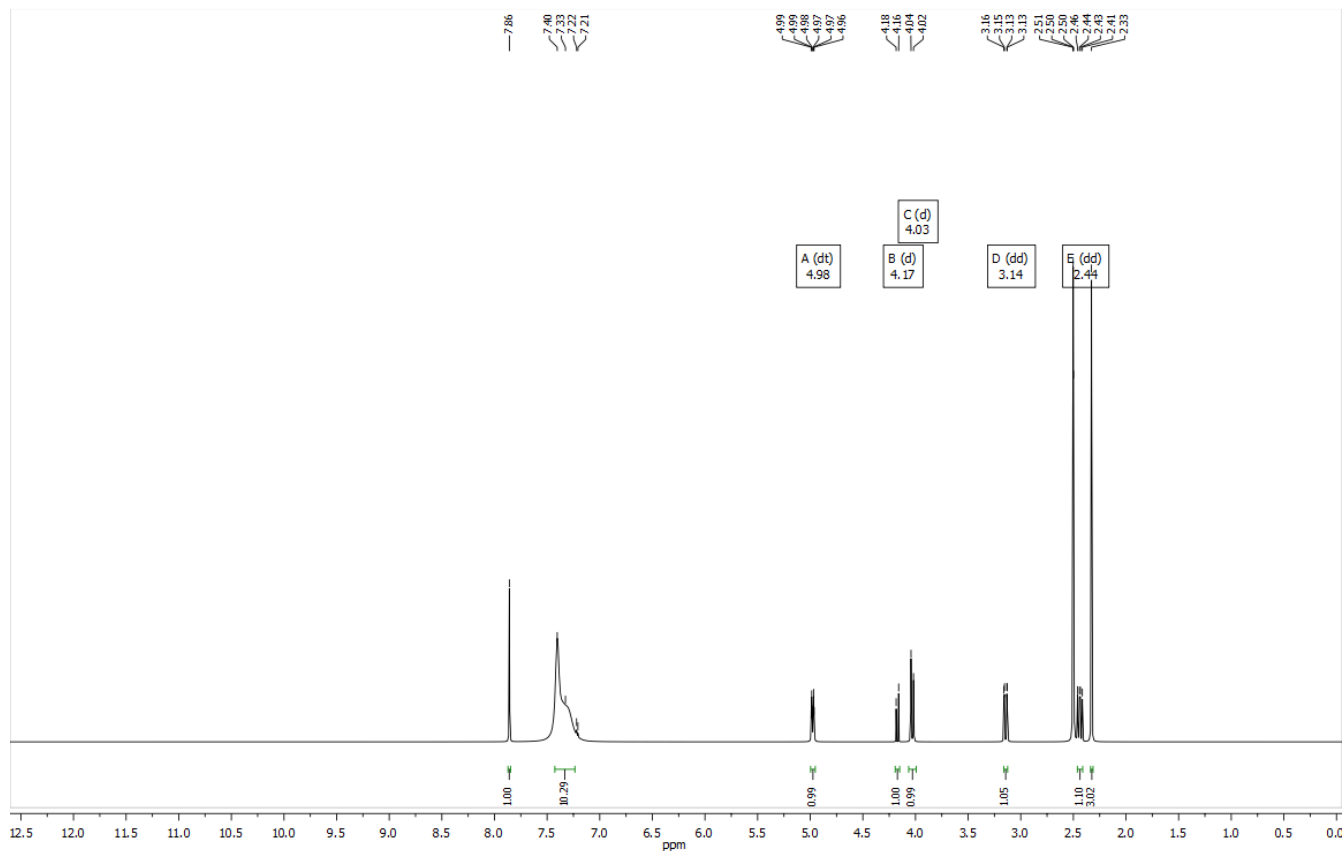
***N*-(3-chlorophenyl)-2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)acetamide 5c**



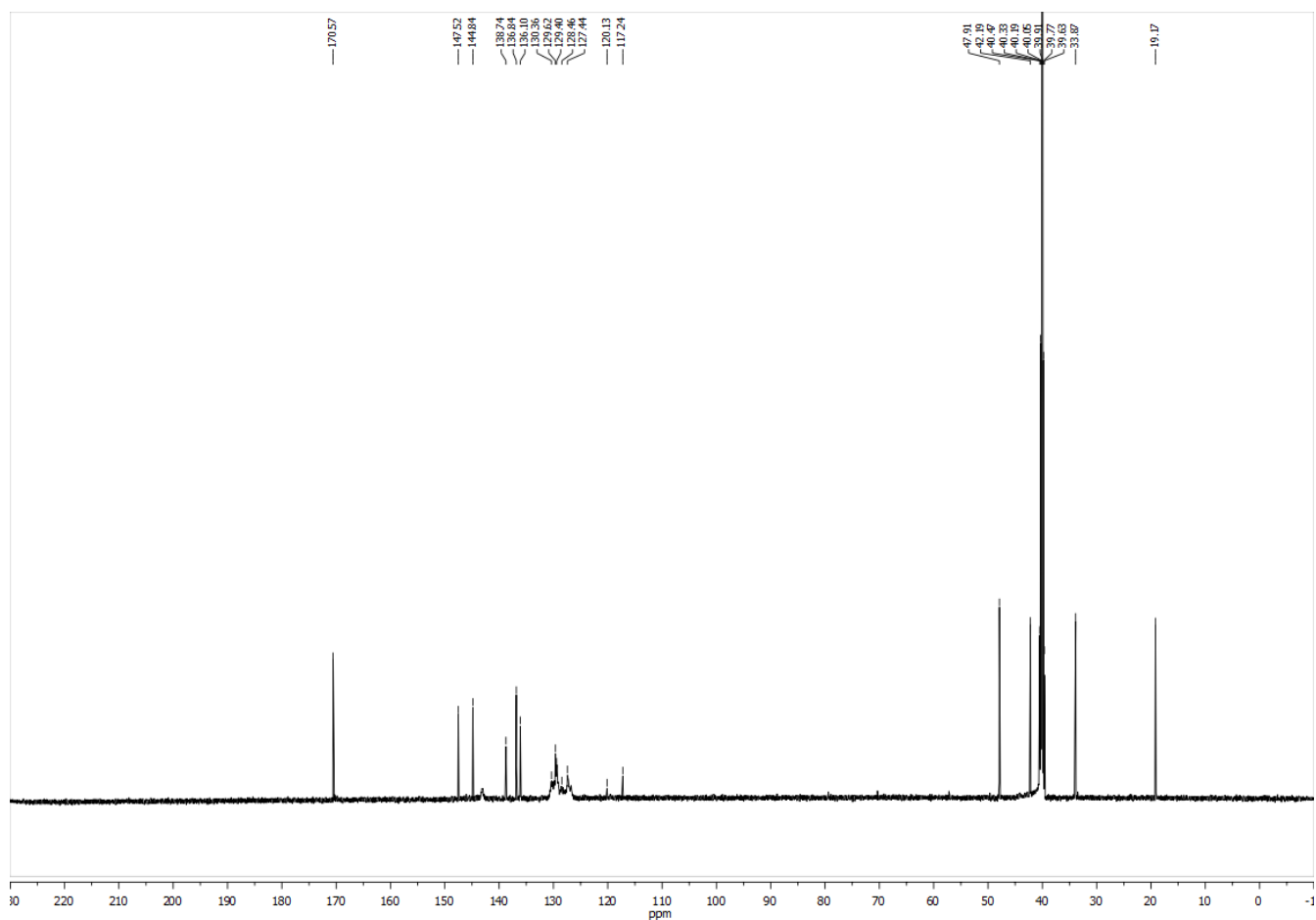
***N*-(3-bromophenyl)-2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-*c*]pyridin-1-yl)acetamide 5d**



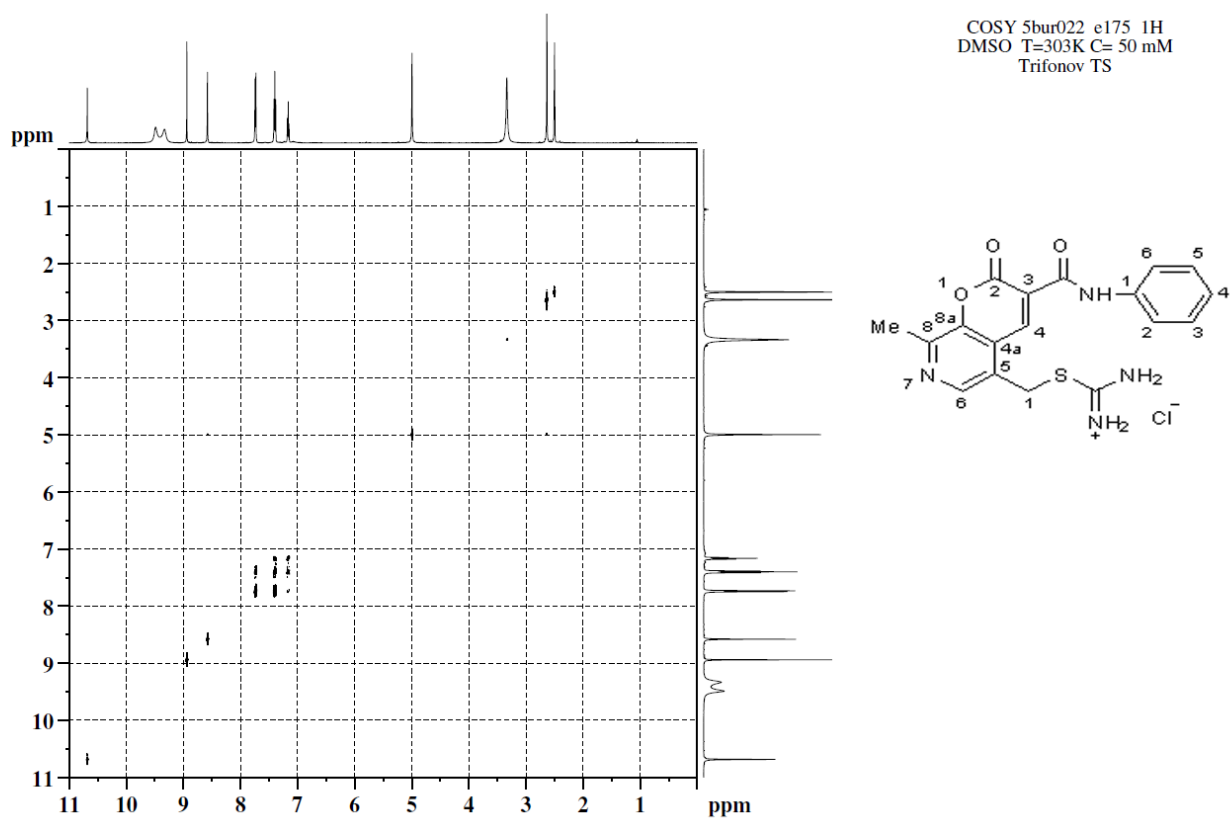
2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-c]pyridin-1-yl)-*N*-(4-sulfamoylphenyl)acetamide 5e



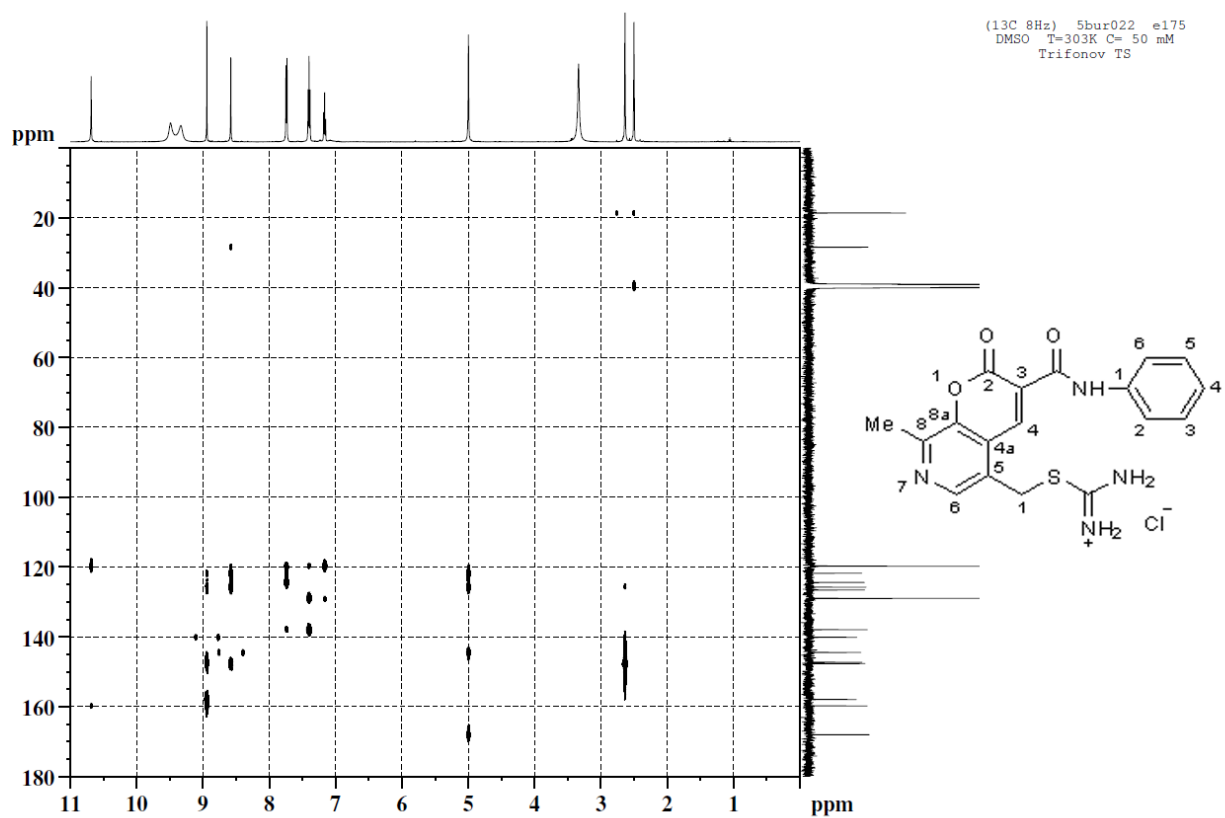
¹H NMR (600 MHz, DMSO-*d*₆) δ 4.98 (dt, *J* = 10.7, 2.9 Hz, 1H), 4.17 (d, *J* = 14.3 Hz, 0H), 4.03 (d, *J* = 14.3 Hz, 1H), 3.14 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.44 (dd, *J* = 16.5, 10.7 Hz, 1H).



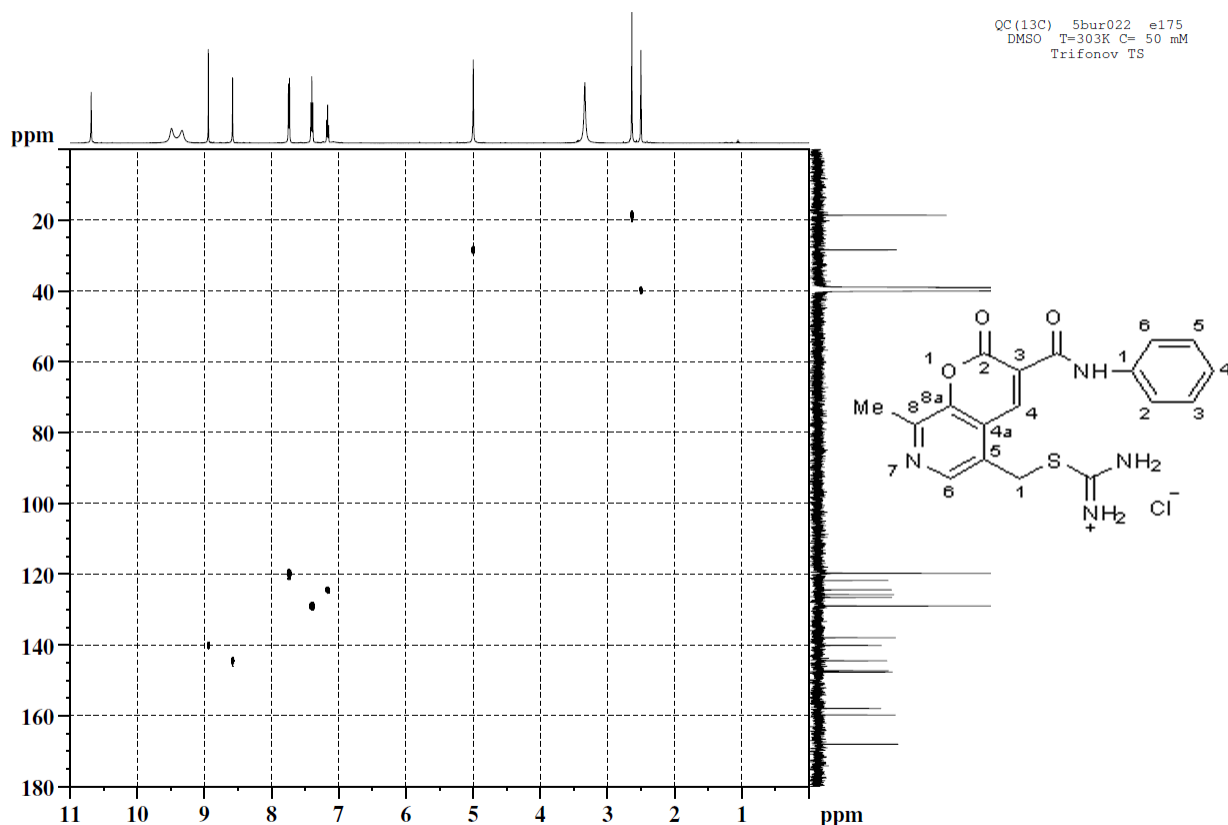
2-(7-hydroxy-6-methyl-1,3-dihydrothieno[3,4-c]pyridin-1-yl)-*N,N*-diphenylacetamide 5f



COSY of 2a



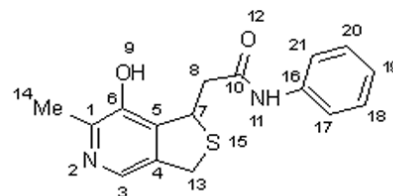
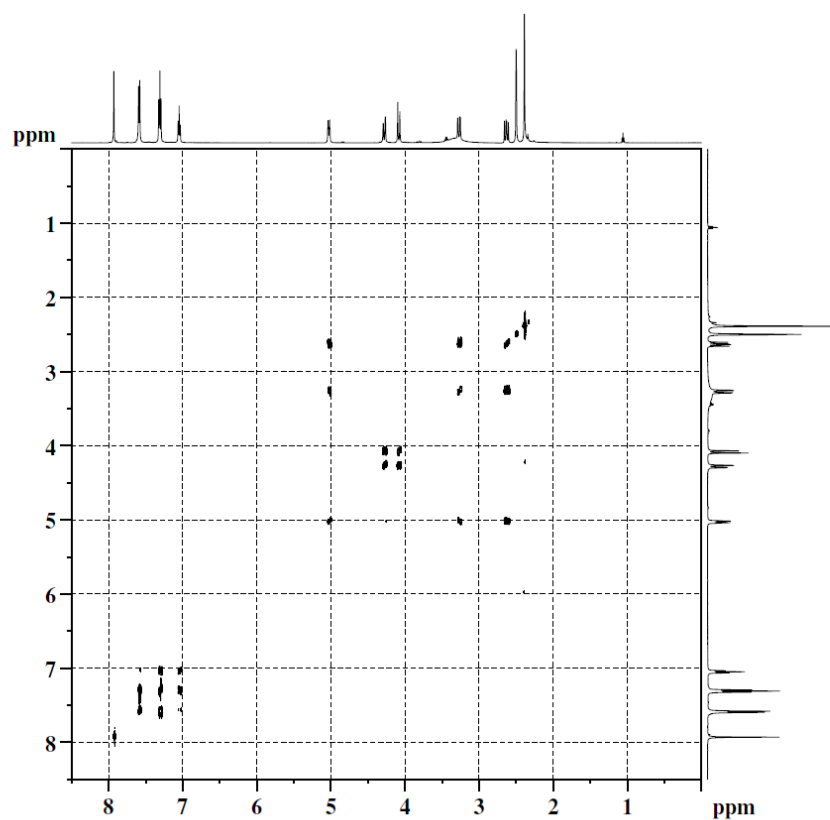
HMBC of 2a



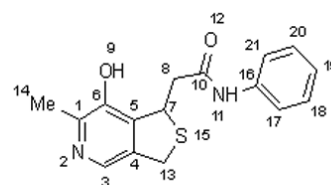
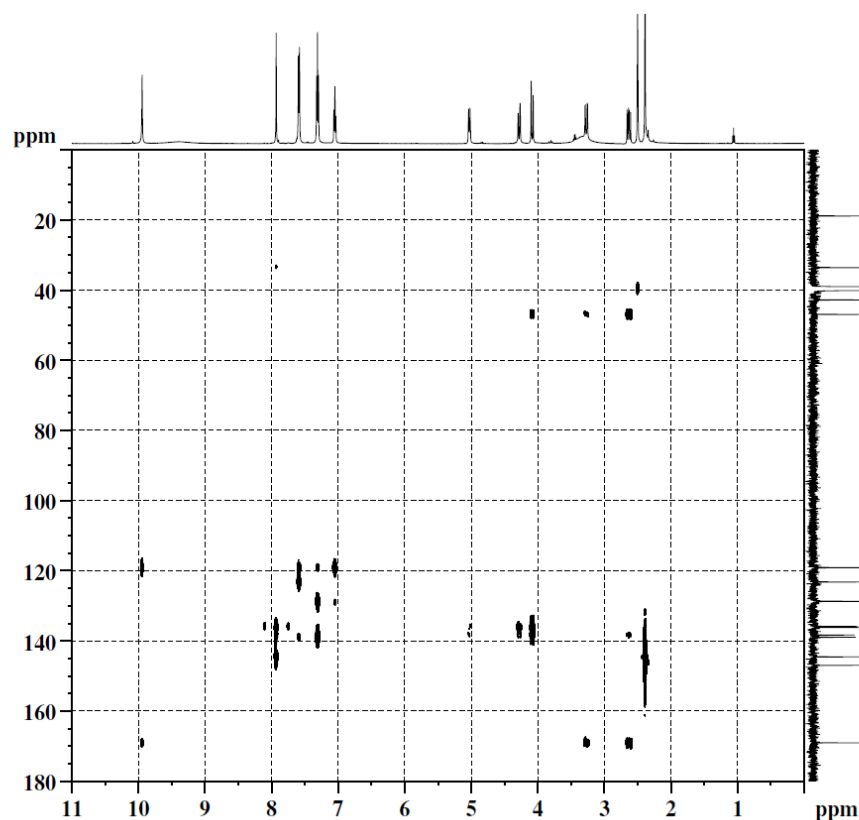
HSQC of 2a

¹H NMR (500 MHz, DMSO-*d*₆): δ 2.634 (s, 3H, H8a), 4.996 (s, 2H, H5a), 7.164 (tr, J = 7.7 Hz, 1H, H4-Ar), 7.400 (tr, J = 7.7 Hz, 2H, H3/H5-Ar), 7.739 (d, J = 7.7 Hz, 1H, H4/H6-Ar), 8.579 (s, 1H, H6), 8.940 (s, 1H, H4), 9.333 (s, 2H, H5d (NH₂)), 9.488 (s, 2H, H5e (N⁺H₂)), 10.684 (s, 1H, H3b (NH)).

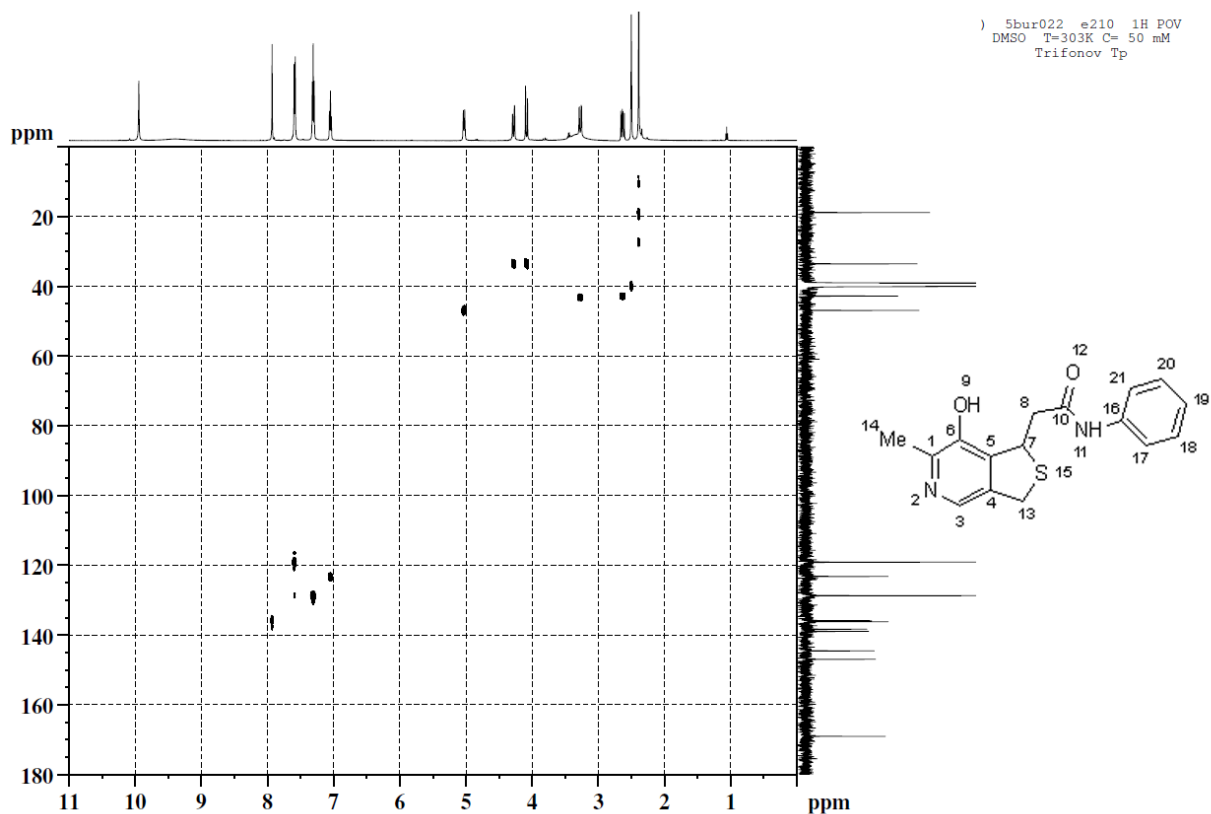
¹³C{¹H} NMR (DMSO-*d*₆, 126 MHz) δ 168.0 (C5c), 159.7 (C3a), 157.9 (C2), 147.6 (C8), 147.3 (C8a), 144.4 (C6), 140.1 (C4), 137.9 (C1-Ar), 129.0 (C3/C5-Ar), 126.6 (C3), 125.7 (C5), 124.4 (C4-Ar), 121.8 (C4a), 119.7 (C2/C6-Ar), 28.4 (C5a), 18.6 (C8a).



COSY of 5a



HMBC of 5a



HSQC of 5a

^1H NMR (500 MHz, DMSO- d_6): δ 2.389 (s, 3H, H14), 2.632 (dd, J = 15.8 Hz, J = 10.7 Hz, 1H, **H8** trans- to H7), 3.271 (dd, J = 15.8 Hz, J = 3.0 Hz, 1H, **H8** cis- to H7), 4.084 and 4.280 (d, J = 14.0 Hz, 2H, H13), 5.028 (dd, J = 10.7 Hz, J = 3.0 Hz, 1H, **H7**), 7.048 (tr, J = 7.9 Hz, 1H, H19 (H4-Ar), 7.308 (tr, J = 7.9 Hz, 2H, H18/H20 H3/H5-Ar), 7.587 (d, J = 7.9 Hz, 1H, H17/H21 H2/H6-Ar), 7.9309 (s, 1H, H3), 9.392 (s, HO, or H9), 9.944 (s, 1H, H11 or (NH)).

$^{13}\text{C}\{^1\text{H}\}$ NMR (DMSO- d_6 , 126 MHz) δ 169.0 (C10), 146.9 (C6), 144.5 (C1), 138.9 (C16 C1-Ar), 138.3 (C5), 136.1 (C4), 135.9 (C3), 128.7 (C18/C20 or C3/C5-Ar), 123.2 (C19 C4-Ar), 119.1 (C17/C21 or C2/C6-Ar), 46.9 (C7), 42.8 (C8), 33.5 (C13), 18.8 (C8a).