

New triazole-containing 7-azacoumarin-3-carboxamides: synthesis and biological properties

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Cytotoxicity Assay

Substances of 5-fluorouracil and sorafenib (Sigma) were used as reference drugs. Human M-HeLa 11 clone (cervical epithelioid carcinoma, HeLa strain, M-HeLa clone), HuTu80 (human duodenal adenocarcinoma), and hepatocyte-like cells (Chang liver) were used in experiments. Human M-HeLa 11 clone and HuTu80 are from the Collection of Type Cultures of the Institute of Cytology, Russian Academy of Sciences; Chang liver is from the collection and the Research Institute of Virology of the Russian Academy of Medical Sciences (Moscow). The cells were cultured on a standard nutrient medium Eagle of the Chumakov Research Institute of Poliomyelitis and Viral Encephalitis (PanEco), supplemented with 10% fetal calf serum and 1% non-essential amino acids. The cytotoxic effect on cells was determined by the colorimetric method of cell proliferation, that is, the MTT test. Cells were seeded on a 96-well Nunc plate at a concentration of $5 \cdot 10^3$ cells per well in a volume of 100 μl of medium and cultured in a CO_2 incubator at 37 °C until a monolayer was formed. The nutrient medium was then removed, and 100 μl of test drug solutions at the specified dilutions, prepared directly in the nutrient medium with the addition of 5% DMSO to improve solubility, were added to the wells. Cytotoxicity analysis was performed in the concentration range (1–100 μM). After 24 h of cell incubation with test compounds, the nutrient medium was removed from the plates, and 100 μl of serum-free nutrient medium containing MTT at a concentration of 0.5 mg ml^{-1} was added and incubated for 4 h at 37 °C. 100 μl of DMSO was added to formazan crystals in each well. Optical density was recorded at 540 nm on an Invitrologic plate reader (Novosibirsk, Russia). IC_{50} (half maximum inhibitory concentration) was calculated using an online tool: MLA – “Quest Graph™ IC_{50} Calculator”. AAT Bioquest, Inc., December 13, 2023, <https://www.aatbio.com/tools/ic50-calculator>. The selectivity index (SI) was calculated as the ratio between the IC_{50} value for normal cells and the IC_{50} value for cancer cells. Experiments were repeated three times. Intact cells cultured together with experimental cells were used as a control.

Antimicrobial Studies

Gram-positive bacteria (*Staphylococcus aureus* ATCC 6538P FDA 209P, *Enterococcus faecalis* ATCC 29212) were used as test objects. As a reference drug for studying antibacterial activity chloramphenicol and norfloxacin were used. Ketoconazole was used as the reference drug for the study of antifungal activity. Bacteriostatic and fungistatic properties were studied by the method of serial dilutions in liquid nutrient media by procedures described in,^{S1,S2} determining MIC, which inhibit the growth and production of the test microorganism. The bactericidal (MBC) and fungicidal activity (MFC), causing complete death of the pathogen was determined according to the previously described procedure.^{S3}

Experimental Section

IR spectra were recorded on a Bruker “Tensor-27” spectrometer in the range 400–3600 cm^{-1} in KBr tablets. ^1H NMR spectra were obtained on Bruker Avance-400 and Bruker Avance-600 spectrometers

with operating frequencies of 400 and 600 MHz, respectively, relative to the signal of residual solvent signals (2.50 ppm for ^1H nuclei in $\text{DMSO}-d_6$). MALDI-TOF mass spectra were obtained on a Bruker Ultraflex III TOF/TOF instrument. For recording, plastic and metal plates were used, the matrix was para-nitroaniline. Elemental analysis was performed on a EuroVector-3000 instrument (C, H, N).

General procedure for the synthesis of compounds 2a-g:

A twofold excess of sodium azide dissolved in a minimal amount of water was added at stirring to a suspension of the corresponding acid amide in 3 mL of acetone at room temperature. The next day, the precipitate was separated and washed with 5 mL of water and then with 5 mL of acetone (in the case of compounds **2a-c**, the reaction mixture was heated at 85 °C for 6.5 hours, then the precipitate was filtered off, washed with 5 mL of water, then with 5 mL of acetone, and dried under reduced pressure).

5-Azidomethyl-8-methyl-2-oxo-*N*-phenyl-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2a)

From 0.30 g (0.9 mmol) of amide and 0.12 g (1.8 mmol) of sodium azide, 0.22 g (71%) of compound **2a** was obtained. Melting point 233-235 °C. IR spectrum (KBr), ν , cm^{-1} : 1595 (Ph), 1672 (C(O)-NH), 1716 (C=O), 2095 (N_3). ^1H NMR spectrum ($\text{DMSO}-d_6$, δ ppm): 2.65 (3H, s, CH_3), 4.93 (2H, s, CH_2), 7.17 (1H, s, Ph), 7.42 (2H, d, $J = 8.3$ Hz, Ph), 7.72 (2H, d, $J = 7.9$ Hz, Ph), 7.86 (2H, tt, $J = 7.1, 1.7$ Hz, Ph), 8.51 (1H, s, CH_{pyr}), 8.78 (1H, s, CH), 10.60 (1H, s, NH). ^{13}C NMR spectrum ($\text{DMSO}-d_6$, δ , ppm): 19.70; 48.56; 120.87; 122.80; 125.51; 127.11; 127.37; 130.06; 138.89; 141.56; 145.20; 148.24; 149.02; 159.29; 160.62. Mass spectrum: m/z 335 $[\text{M}]^+$. Found, %: C 60.93; H 4.01; N 20.74. $\text{C}_{17}\text{H}_{13}\text{N}_5\text{O}_3$. Calculated, %: C 60.89; H 3.91; N 20.89.

5-Azidomethyl-*N*-(2-methoxyphenyl)-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2b)

From 0.30 g (0.8 mmol) of amide and 0.11 g (1.6 mmol) of sodium azide, 0.18 g (58%) of compound **2b** was obtained. Melting point 242-245 °C. IR spectrum (KBr), ν , cm^{-1} : 1598 (Ph), 1671 (C(O)-NH), 1717 (C=O), 2095 (N_3). ^1H NMR spectrum ($\text{DMSO}-d_6$, δ ppm): 2.65 (3H, s, CH_3), 3.93 (3H, s, CH_3), 4.95 (2H, s, CH_2), 7.00 (1H, s, Ph), 7.13 (2H, s, Ph), 7.42 (1H, d, $J = 8.0$ Hz, Ph), 8.44 (1H, d, $J = 8.0$ Hz, Ph), 8.52 (1H, s, CH), 8.95 (1H, s, CH), 11.14 (1H, s, NH). ^{13}C NMR spectrum ($\text{DMSO}-d_6$, δ , ppm): 19.68; 48.70; 57.14; 112.18; 120.64; 121.75; 124.88; 125.81; 127.23; 143.39; 145.13; 148.36; 149.60; 159.23; 160.64. Mass spectrum: m/z 366 $[\text{M}+\text{H}]^+$. Found, %: C 59.13; H 4.08; N 19.25. $\text{C}_{18}\text{H}_{15}\text{N}_5\text{O}_4$. Calculated, %: C 59.18; H 4.14; N 19.17.

5-Azidomethyl-8-methyl-2-oxo-*N,N*-diphenyl-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2c)

From 0.33 g (0.8 mmol) of amide and 0.11 g (1.6 mmol) of sodium azide, 0.28 g (82%) of compound **2c** was obtained. Melting point 233-235 °C. IR spectrum (KBr), ν , cm^{-1} : 1594 (Ph), 1664 (C(O)-NH), 1730 (C=O), 2086 (N_3). ^1H NMR spectrum ($\text{DMSO}-d_6$, δ ppm): 2.51 (3H, d, $J = 2.1$ Hz, CH_3), 4.77 (2H, s, CH_2), 7.14-7.51 (10H, m, Ph), 8.40 (1H, s, CH_{pyr}), 8.55 (1H, s, CH). ^{13}C NMR spectrum ($\text{DMSO}-d_6$, δ , ppm): 19.50; 48.34; 122.33; 126.54; 127.52; 127.93; 129.08; 129.59; 130.10; 130.23; 130.39; 130.86; 139.19; 142.66; 145.26; 147.71; 148.92; 156.70; 164.20. Mass spectrum: m/z 412 $[\text{M}+\text{H}]^+$. Found, %: C 67.13; H 4.28; N 17.14. $\text{C}_{23}\text{H}_{17}\text{N}_5\text{O}_3$. Calculated, %: C 67.15; H 4.17; N 17.02.

5-Azidomethyl-*N'*-benzoyl-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3-carbohydrazide (2d)

From 0.31 g (0.8 mmol) of amide and 0.11 g (1.6 mmol) of sodium azide, 0.18 g (60%) of compound **2c** was obtained. Melting point > 300 °C. IR spectrum (KBr), ν , cm^{-1} : 1643 (C(O)-NH), 1729 (C=O), 1755 (C=O), 2131 (N_3). ^1H NMR spectrum ($\text{DMSO}-d_6$, δ ppm): 2.66 (3H, s, CH_3), 5.00 (2H, s, CH_2), 7.66-7.71 (3H, m, Ph), 8.16 (2H, dd, $J = 8.0, 1.7$ Hz, Ph), 8.42 (1H, s, CH_{pyr}), 8.96 (1H, s, CH), 9.15 (1H, s, NH). ^{13}C NMR spectrum ($\text{DMSO}-d_6$, δ , ppm): 19.68; 48.54; 117.84; 123.82; 127.03; 127.95; 128.49; 129.46; 130.57; 133.55; 140.98; 145.11; 148.35; 149.02; 155.42; 158.84; 160.97; 165.71. Mass spectrum: m/z 379 $[\text{M}+\text{H}]^+$. Found, %: C 57.03; H 3.78; N 22.04. $\text{C}_{23}\text{H}_{17}\text{N}_5\text{O}_3$. Calculated, %: C 57.14; H 3.73; N 22.21.

5-Azidomethyl-8-methyl-2-oxo-*N*-(4-sulfamoylphenyl)-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2e)

From 0.23 g (0.56 mmol) of amide and 0.08 g (1.12 mmol) of sodium azide, 0.15 g (65%) of compound **2e** was obtained. Melting point >300 °C. IR spectrum (KBr), ν , cm^{-1} : 1594 (Ph), 1673 (C(O)-NH), 1730 (C=O), 2151 (N₃). ¹H NMR spectrum (DMSO-*d*₆, δ ppm): 2.64 (3H, s, CH₃), 4.94 (2H, s, CH₂), 7.37(2H, s, NH₂), 7.85(2H, d, *J* = 8.5 Hz, Ph), 7.91 (1H, d, *J* = 8.2 Hz, Ph), 8.51 (1H, s, CH_{pyr}), 8.74 (1H, s, CH), 11.15 (1H, s, NH). ¹³C NMR spectrum (DMSO-*d*₆, δ , ppm): 19.15; 48.04; 120.03; 122.17; 126.61; 126.89; 127.31; 139.99; 140.72; 141.37; 144.60; 147.71; 148.43; 158.19; 160.98. Mass spectrum: *m/z* 461 [M+2Na+H]⁺. Found, %: C 49.23; H 3.48; N 20.14; S 7.62. C₁₇H₁₄N₆O₅S. Calculated, %: C 49.27; H 3.41; N 20.28; S 7.74.

5-Azidomethyl-8-methyl-2-oxo-*N*-{4-[*N*-(thiazol-2-yl)sulfamoyl]phenyl}-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2f)

From 0.30 g (0.61 mmol) of amide and 0.08 g (1.23 mmol) of sodium azide, 0.17 g (57%) of compound **2f** was obtained. Melting point >300 °C. IR spectrum (KBr), ν , cm^{-1} : 1591 (Ph), 1673 (C(O)-NH), 1732 (C=O), 2110 (N₃). ¹H NMR spectrum (DMSO-*d*₆, δ ppm): 2.64 (3H, s, CH₃), 4.92 (2H, s, CH₂), 6.71 (1H, d, *J* = 4.3 Hz, CH), 7.15 (1H, d, *J* = 4.4 Hz, CH), 7.81 (4H, d, *J* = 1.8 Hz, Ph), 8.51 (1H, s, CH_{pyr}), 8.75 (1H, s, CH), 10.88 (1H, s, NH). ¹³C NMR spectrum (DMSO-*d*₆, δ , ppm): 19.67; 48.56; 108.95; 120.45; 122.69; 127.12; 127.37; 128.10; 139.54; 141.43; 141.62; 145.15; 148.23; 148.99; 158.82; 161.29; 169.94. Mass spectrum: *m/z* 498 [M+H]⁺. Found, %: C 48.13; H 3.08; N 19.74; S 12.94. C₂₀H₁₅N₇O₅S₂. Calculated, %: C 48.29; H 3.04; N 19.71; S 12.89.

***N*-[4-(*N*-acetylsulfamoyl)phenyl]-5-azidomethyl-8-methyl-2-oxo-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2g)**

From 0.30 g (0.67 mmol) of amide and 0.09 g (1.38 mmol) of sodium azide, 0.19 g (63%) of compound **2g** was obtained. Melting point >300 °C. IR spectrum (KBr), ν , cm^{-1} : 1593 (Ph), 1674 (C(O)-NH), 1741 (C=O), 2114 (N₃). ¹H NMR spectrum (DMSO-*d*₆, δ ppm): 1.68 (3H, s, CH₃), 2.64 (3H, s, CH₃), 4.93 (2H, s, CH₂), 7.65-7.84(4H, m, Ph), 8.51 (1H, s, CH_{pyr}), 8.77 (1H, s, CH), 10.84 (1H, s, NH). ¹³C NMR spectrum (DMSO-*d*₆, δ , ppm): 19.69; 48.56; 119.75; 122.75; 127.14; 127.30; 128.59; 140.20; 141.55; 142.83; 145.16; 148.24; 148.98; 159.05; 160.95; 176.63. Mass spectrum: *m/z* 457 [M+H]⁺. Found, %: C 50.13; H 3.68; N 18.45; S 7.12. C₁₉H₁₆N₆O₆S. Calculated, %: From 50.00; H 3.53; N 18.41; S 7.02.

General procedure for the synthesis of compounds (3a-g):

To a suspension of the corresponding azide **2** in 3 mL of dry acetonitrile under argon copper sulfate and sodium ascorbate were added a ratio of 1:0.5:1 at stirring, then an equimolar amount of phenylacetylene was added dropwise and the reaction mixture was heated at 90 °C (bath) for 6 hours. The next day, the precipitate was separated, washed with 10 mL of dry acetonitrile, and dried in vacuum.

8-Methyl-2-oxo-*N*-phenyl-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (3a)

From 0.20 g (0.6 mmol) azide, 0.15 g (0.3 mmol) copper sulfate, 0.12 g (0.6 mmol) sodium ascorbate and 0.06 g (0.6 mmol) phenylacetylene, 0.20 g (77%) of compound **3a** was obtained. Melting point 289-292 °C. IR spectrum (KBr), ν , cm^{-1} : 1597 (Ph), 1672 (C(O)-NH), 1721 (C=O). ¹H NMR spectrum (DMSO-*d*₆, δ ppm): 2.65 (3H, s, CH₃), 6.10 (2H, s, CH₂), 7.17 (1H, t, *J* = 7.4 Hz, Ph), 7.33 (1H, d, *J* = 7.4 Hz, Ph), 7.41 (4H, q, *J* = 8.3 Hz, Ph), 7.71 (2H, d, *J* = 7.9 Hz, Ph), 7.81 (2H, d, *J* = 7.6 Hz, Ph), 8.60 (1H, s, CH), 8.64 (1H, s, CH_{pyr}), 9.00 (1H, s, CH), 10.59 (1H, s, NH). ¹³C NMR spectrum (DMSO-*d*₆, δ , ppm): 19.75; 48.01; 120.76; 120.86; 122.59; 122.98; 125.51; 126.18; 127.35; 129.00; 129.89; 130.06; 131.45; 138.87; 141.57; 145.89; 147.73; 149.19; 159.25; 160.53. Mass spectrum: *m/z*

438 $[M+H]^+$. Found, %: C 68.64; H 4.42; N 16.04. $C_{25}H_{19}N_5O_3$. Calculated, %: C 68.64; H 4.38; N 16.01.

***N*-(2-Methoxyphenyl)-8-methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2*H*-pyrano-[2,3-*c*]pyridine-3-carboxamide (3b)**

From 0.07 g (0.2 mmol) azide, 0.02 g (0.1 mmol) copper sulfate, 0.04 g (0.2 mmol) sodium ascorbate and 0.02 g (0.2 mmol) phenylacetylene, 0.09 g (78%) of compound **3b** was obtained. Melting point > 300 °C. IR spectrum (KBr), ν , cm^{-1} : 1601 (Ph), 1670 (C(O)-NH), 1725 (C=O). 1H NMR spectrum (DMSO- d_6 , δ ppm): 2.66 (3H, s, CH₃), 3.92 (3H, s, CH₃), 6.13 (2H, s, CH₂), 7.01 (1H, t, J = 7.1 Hz, Ph), 7.12 – 7.16 (2H, m, Ph), 7.32 (1H, t, J = 7.1 Hz, Ph), 7.42 (2H, t, J = 7.6 Hz, Ph), 7.81 (2H, d, J = 7.8 Hz, Ph), 8.45 (1H, d, J = 7.7 Hz, Ph), 8.62 (1H, s, CH), 8.63 (1H, s, CH_{pyr}), 9.19 (1H, s, CH), 11.12 (1H, s, NH). ^{13}C NMR spectrum could not be taken due to poor solubility in DMSO- d_6 . Mass spectrum: m/z 468 $[M+H]^+$. Found, %: C 66.95; H 4.68; N 44.74. $C_{26}H_{21}N_5O_4$. Calculated, %: C 66.80; H 4.53; N 14.98.

8-Methyl-2-oxo-*N,N*-diphenyl-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2*H*-pyrano-[2,3-*c*]pyridine-3-carboxamide (3c)

From 0.07 g (0.17 mmol) azide, 0.02 g (0.1 mmol) copper sulfate, 0.03 g (0.17 mmol) sodium ascorbate and 0.02 g (0.2 mmol) phenylacetylene, 0.09 g (78%) of compound **3c** was obtained. Melting point 232-235 °C. IR spectrum (KBr), ν , cm^{-1} : 1595 (Ph), 1667 (C(O)-NH), 1746 (C=O). 1H NMR spectrum (DMSO- d_6 , δ ppm): 2.50 (3H, s, CH₃), 5.99 (2H, s, CH₂), 7.12 (3H, br.s, Ph), 7.29-7.38 (7H, m, Ph), 7.46 (3H, t, J = 7.6 Hz, Ph), 7.87 (2H, d, J = 7.6 Hz, Ph), 8.55 (1H, br.s, CH), 8.64 (1H, s, CH_{pyr}), 8.66 (1H, s, CH). ^{13}C NMR spectrum (DMSO- d_6 , δ , ppm): 19.75; 48.01; 120.76; 120.86; 122.59; 122.98; 125.51; 126.18; 127.35; 129.00; 129.89; 130.06; 131.45; 138.87; 141.57; 145.89; 147.73; 149.19; 159.25; 160.53. Mass spectrum: m/z 514 $[M+H]^+$. Found, %: C 72.43; H 4.58; N 13.72. $C_{31}H_{23}N_5O_3$. Calculated, %: C 72.50; H 4.51; N 13.64.

***N'*-Benzoyl-8-methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2*H*-pyrano-[2,3-*c*]pyridine-3-carbohydrazide (3d)**

From 0.20 g (0.57 mmol) azide, 0.07 g (0.3 mmol) copper sulfate, 0.06 g (0.6 mmol) sodium ascorbate and 0.06 g (0.6 mmol) phenylacetylene, 0.26 g (96%) of compound **3d** was obtained. Melting point 237-240 °C (decomposition). IR spectrum (KBr), ν , cm^{-1} : 1605 (Ph), 1620 (C(O)-NH), 1751 (C=O). 1H NMR spectrum (DMSO- d_6 , δ ppm): 2.66 (3H, s, CH₃), 6.16 (2H, s, CH₂), 7.31 (2H, d, J = 7.4 Hz, Ph), 7.41 (3H, t, J = 7.7 Hz, Ph), 7.68 (3H, q, J = 6.9, 5.7 Hz, Ph), 7.82 (2H, d, J = 7.8 Hz, Ph), 8.15 (2H, d, J = 7.2 Hz, Ph), 8.58 (1H, s, CH), 8.68 (1H, s, CH_{pyr}), 9.14 (1H, s, CH). ^{13}C NMR spectrum (DMSO- d_6 , δ , ppm): 19.71; 48.11; 117.92; 122.65; 123.82; 126.17; 126.52; 127.92; 129.01; 129.89; 130.58; 131.43; 133.59; 140.82; 145.73; 147.78; 149.23; 155.25; 160.91; 165.67. Mass spectrum: m/z 481 $[M+H]^+$. Found, %: C 64.83; H 4.18; N 17.44. $C_{26}H_{20}N_6O_4$. Calculated, %: C 64.99; H 4.20; N 17.49.

8-Methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-*N*-(4-sulfamoylphenyl)-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (3e)

From 0.17 g (0.4 mmol) azide, 0.05 g (0.2 mmol) copper sulfate, 0.08 g (0.4 mmol) sodium ascorbate, and 0.04 g (0.4 mmol) phenylacetylene, 0.15 g (72%) of compound **3e** was obtained. Melting point > 300 °C. IR spectrum (KBr), ν , cm^{-1} : 1589 (Ph), 1622 (C(O)-NH), 1716 (C=O). 1H NMR spectrum (DMSO- d_6 , δ ppm): 2.66 (3H, s, CH₃), 6.11 (2H, s, CH₂), 7.33 (3H, m, NH₂ + Ph), 7.43 (2H, t, J = 7.6 Hz, Ph), 7.82 (2H, d, J = 7.7 Hz, Ph), 7.86 (2H, d, J = 8.6 Hz, Ph), 7.90 (2H, d, J = 8.6 Hz, Ph), 8.61 (1H, s, CH), 8.65 (1H, s, CH_{pyr}), 9.02 (1H, s, CH), 10.86 (1H, s, NH). ^{13}C NMR spectrum (DMSO- d_6 , δ , ppm): 19.21; 47.47; 120.15; 122.07; 122.39; 125.65; 126.16; 126.65; 127.39; 128.49; 129.37; 130.90; 140.09; 141.14; 141.38; 145.43; 147.21; 148.73; 158.53; 160.59. Mass spectrum: m/z 517 $[M+H]^+$. Found, %: C 58.21; H 3.88; N 16.24; S 6.21. $C_{25}H_{20}N_6O_4S$. Calculated, %: C 58.13; H 3.90; N 16.27; S 6.21.

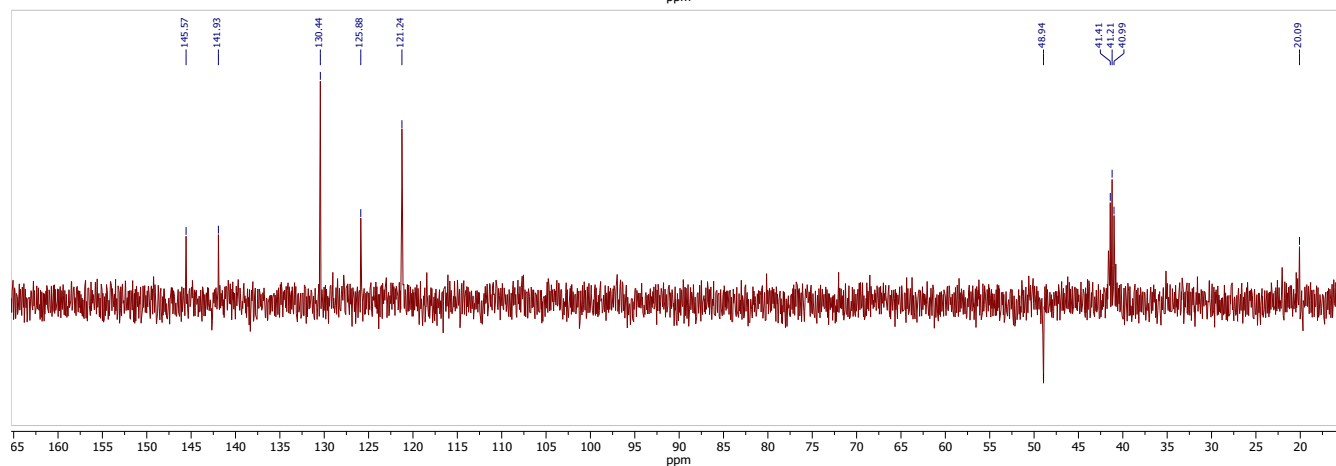
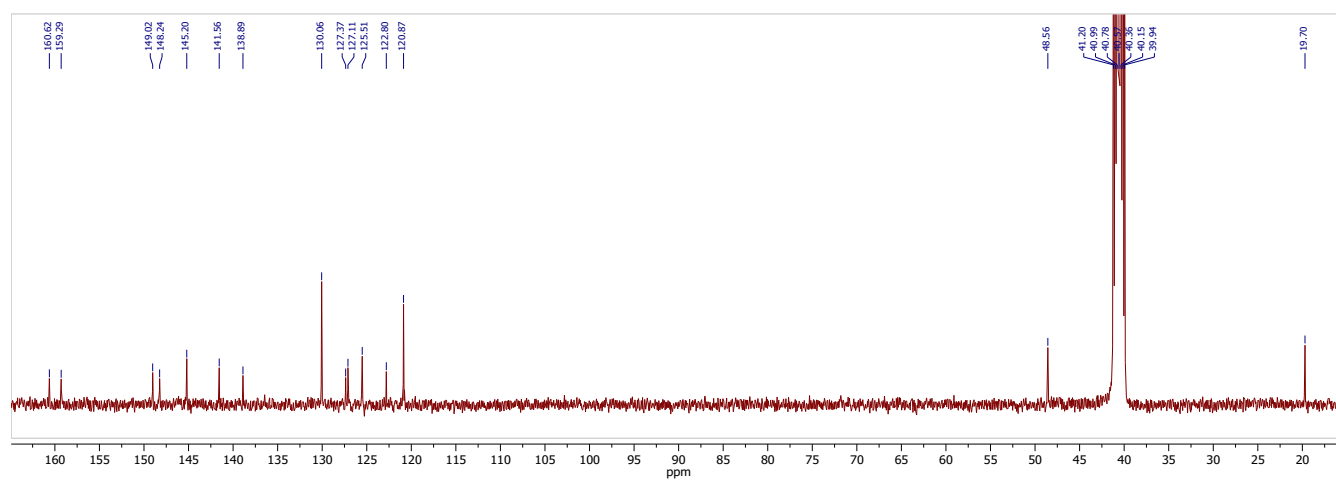
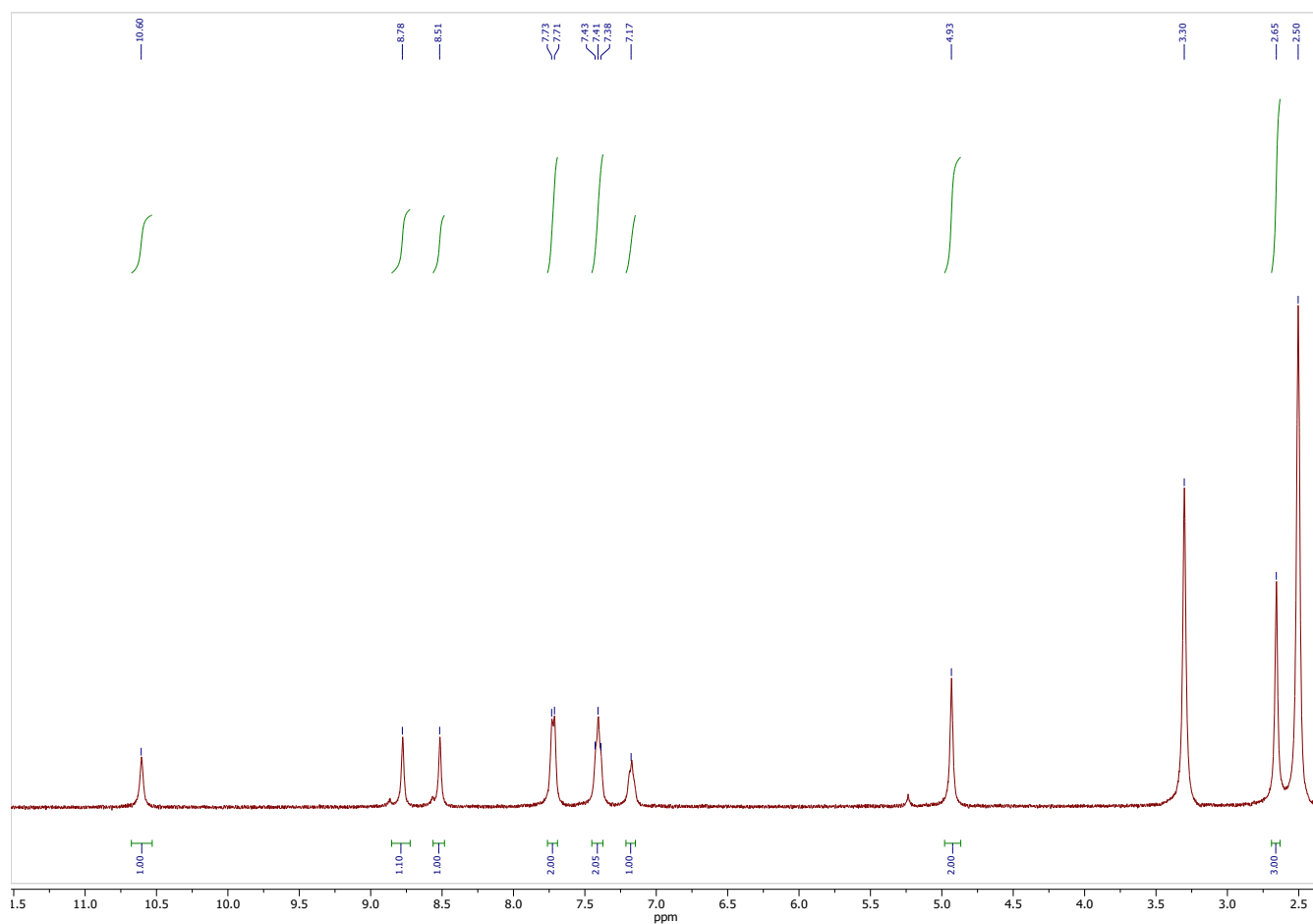
8-Methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-*N*-{4-[*N*-(thiazol-2-yl)sulfamoyl]-phenyl}-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (3f)

From 0.2 g (0.4 mmol) azide, 0.05 g (0.2 mmol) copper sulfate, 0.08 g (0.4 mmol) sodium ascorbate, and 0.04 g (0.4 mmol) phenylacetylene, 0.2 g (83%) of compound **3f** was obtained. Melting point >300 °C. IR spectrum (KBr), ν , cm^{-1} : 1592 (Ph), 1625 (C(O)-NH), 1734 (C=O). ^1H NMR spectrum (DMSO- d_6 , δ ppm): 2.66 (3H, s, CH_3), 6.10 (2H, s, CH_2), 6.78 (1H, br.s, CH), 7.20 (1H, br. s, CH), 7.33 (1H, t, $J = 7.4$ Hz, Ph), 7.43 (2H, t, $J = 7.6$ Hz, Ph), 7.81-7.83 (6H, m, Ph), 8.58 (1H, s, CH), 8.64 (1H, s, CH_{pyr}), 8.99 (1H, s, CH), 10.83 (1H, s, NH). ^{13}C NMR spectrum (DMSO- d_6), δ , ppm: 18.67; 46.92; 119.52; 121.55; 121.85; 125.13; 125.61; 126.26; 127.09; 127.96; 128.84; 130.37; 140.67; 144.86; 146.67; 148.15; 157.92; 160.05. Mass spectrum: m/z 600 $[\text{M}+\text{H}]^+$. Found, %: From 56.11; H 3.78; N 16.24; S 10.81. $\text{C}_{28}\text{H}_{21}\text{N}_7\text{O}_5\text{S}_2$. Calculated, %: From 56.08; H 3.53; N 16.35; S 10.69.

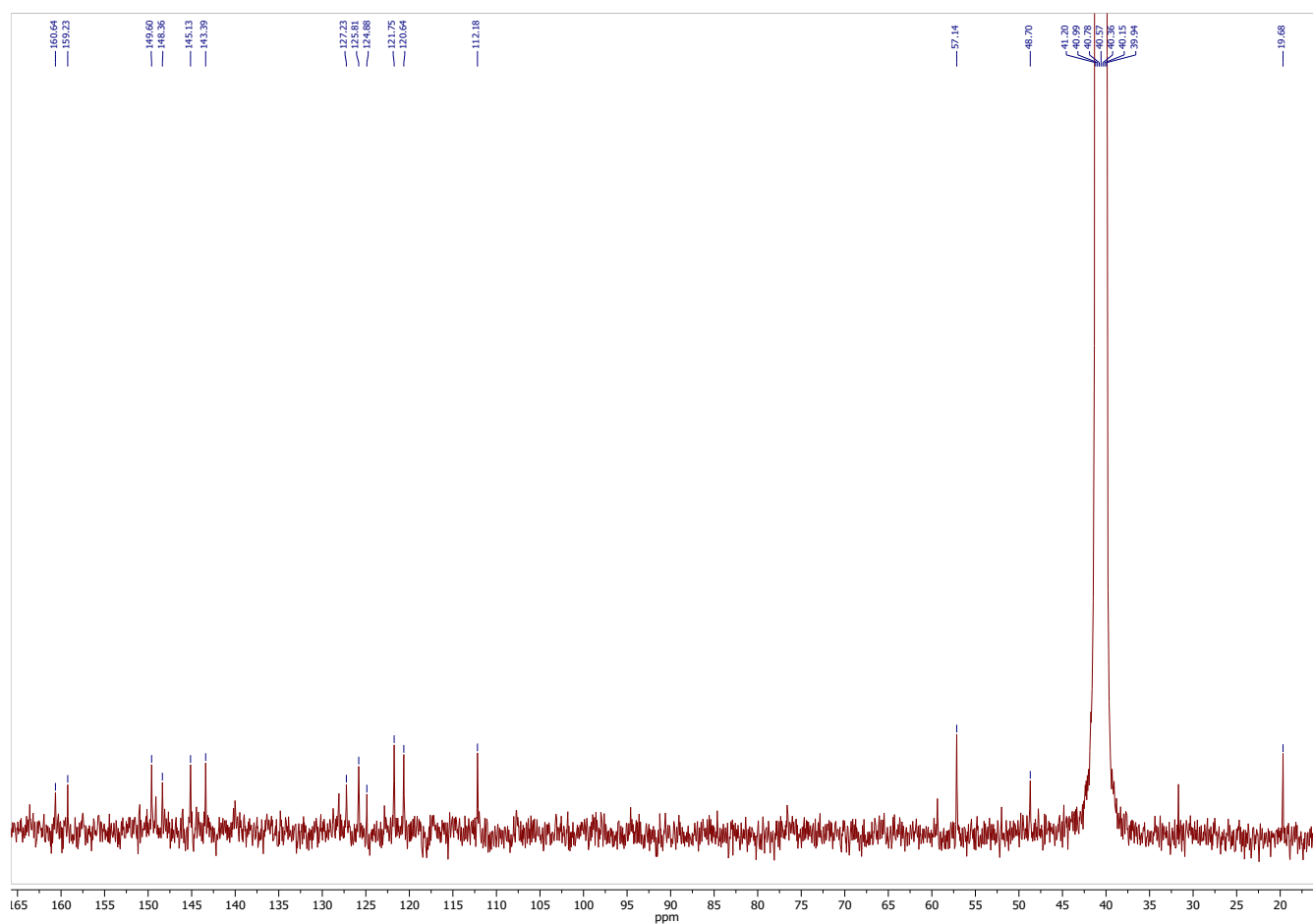
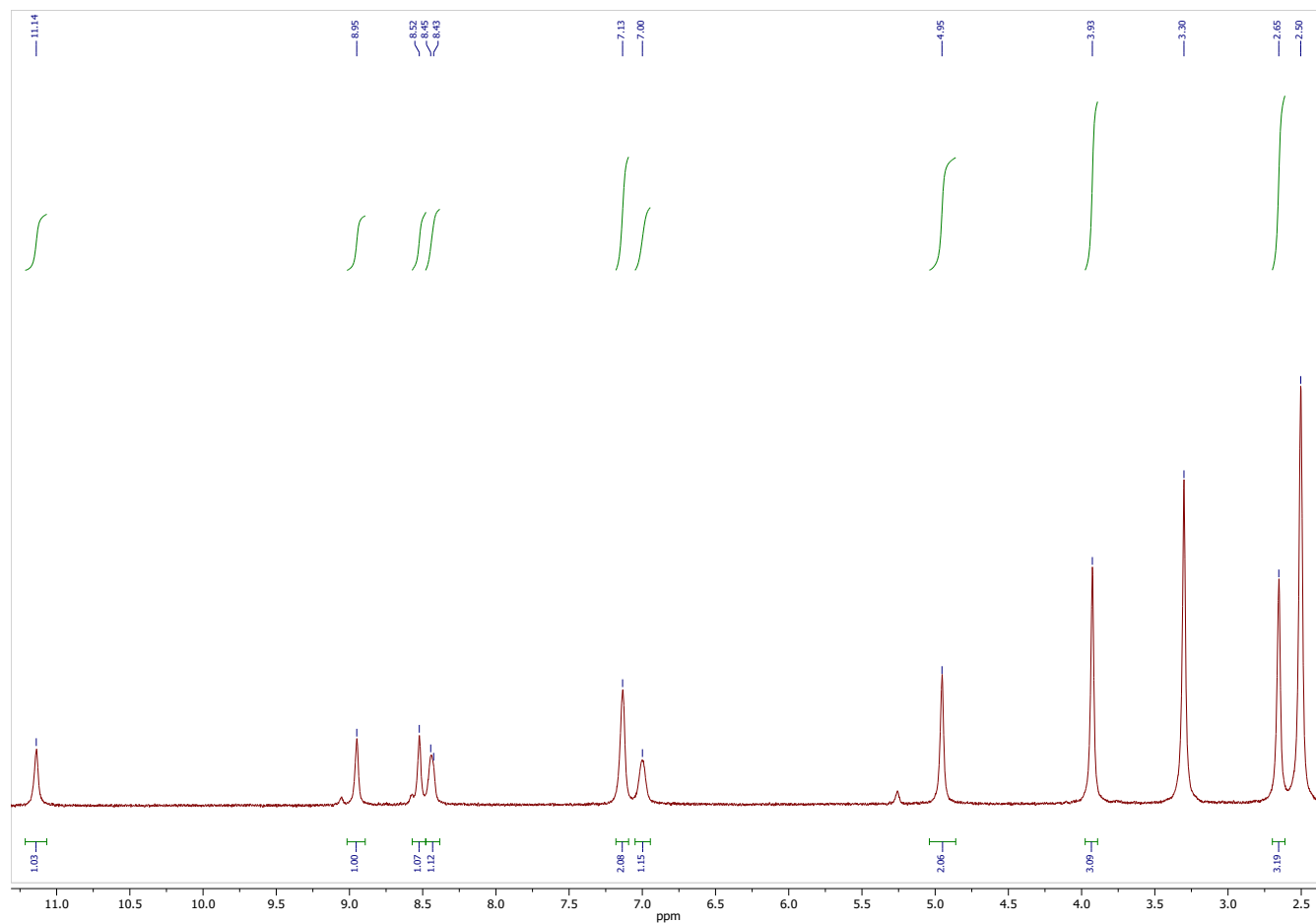
References

- S1 National Committee for Clinical Laboratory Standards, Methods for Dilution Antimicrobial Susceptibility. Tests for Bacteria that Grow Aerobically, Wayne, 2000.
- S2 National Committee for Clinical Laboratory Standards, Reference Method for Broth Dilution Antifungal Susceptibility Testing of Conidium-Forming Filamentous Fungi, Wayne, 1998.
- S3 Amerhanova S., Voloshina A., Sapunova A., Lyubina A., Mikhailov V., Mirgorodskaya A., Zakharova L. European Journal of Clinical Investigation, **2021**, 51, pp. 36.

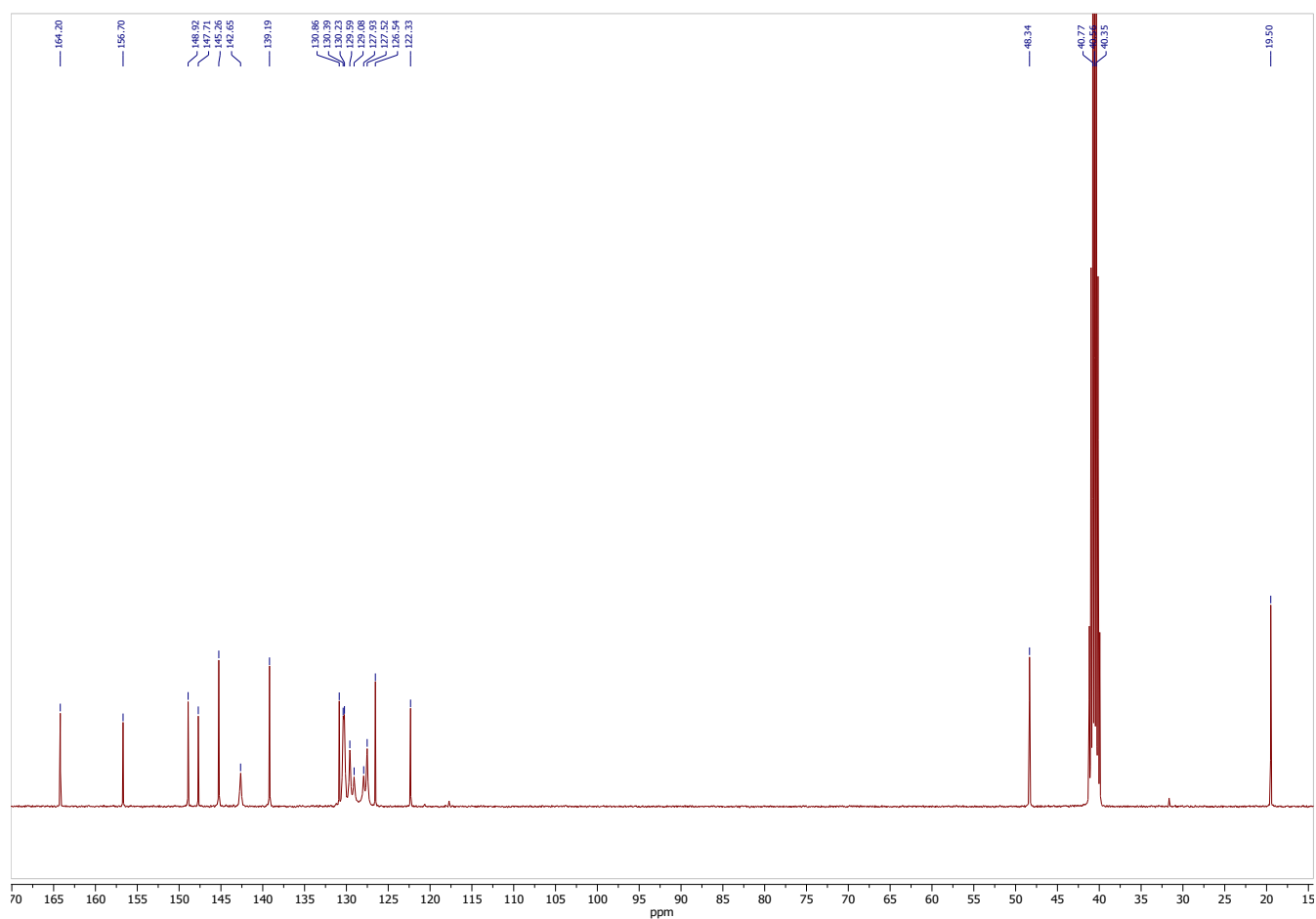
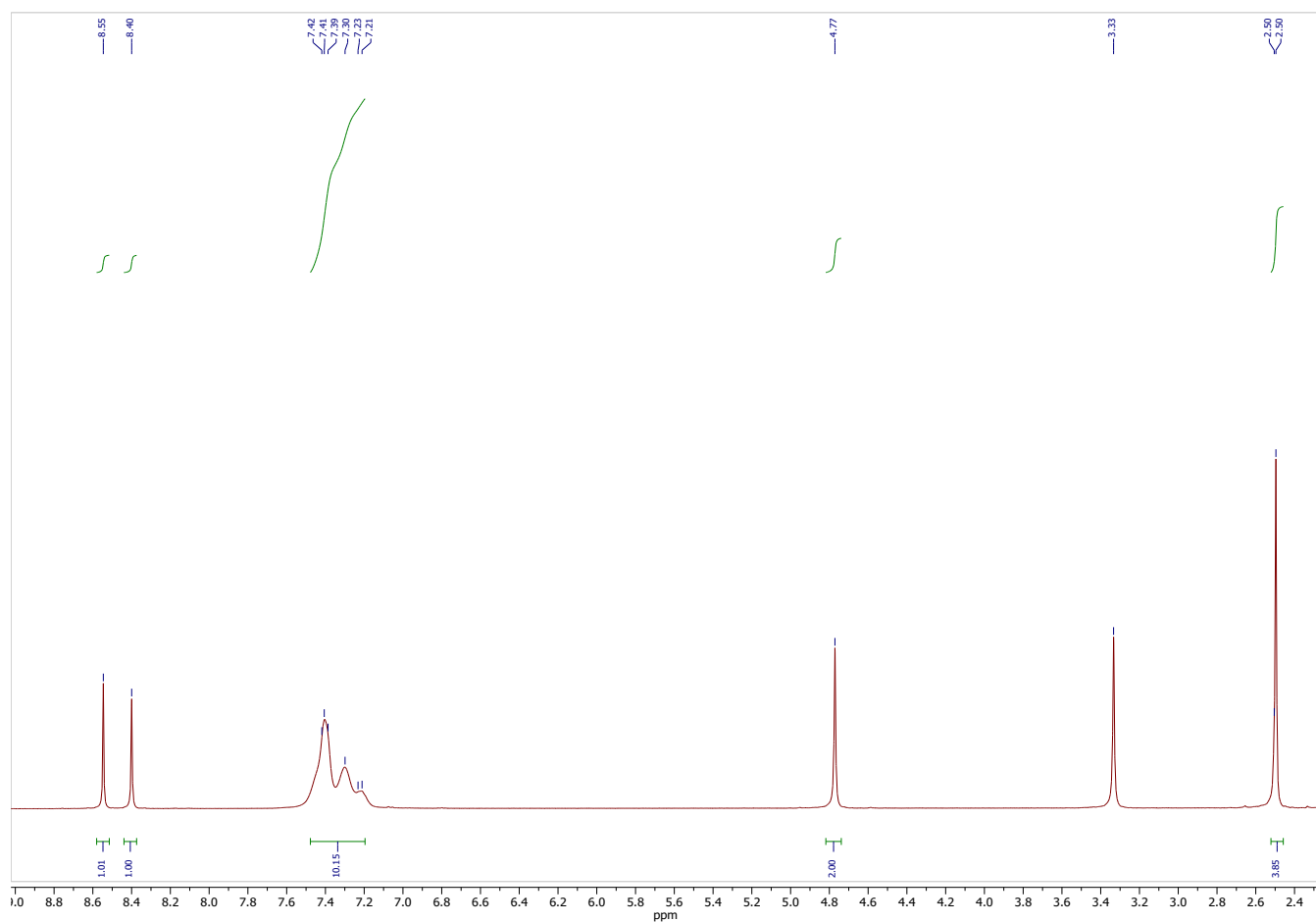
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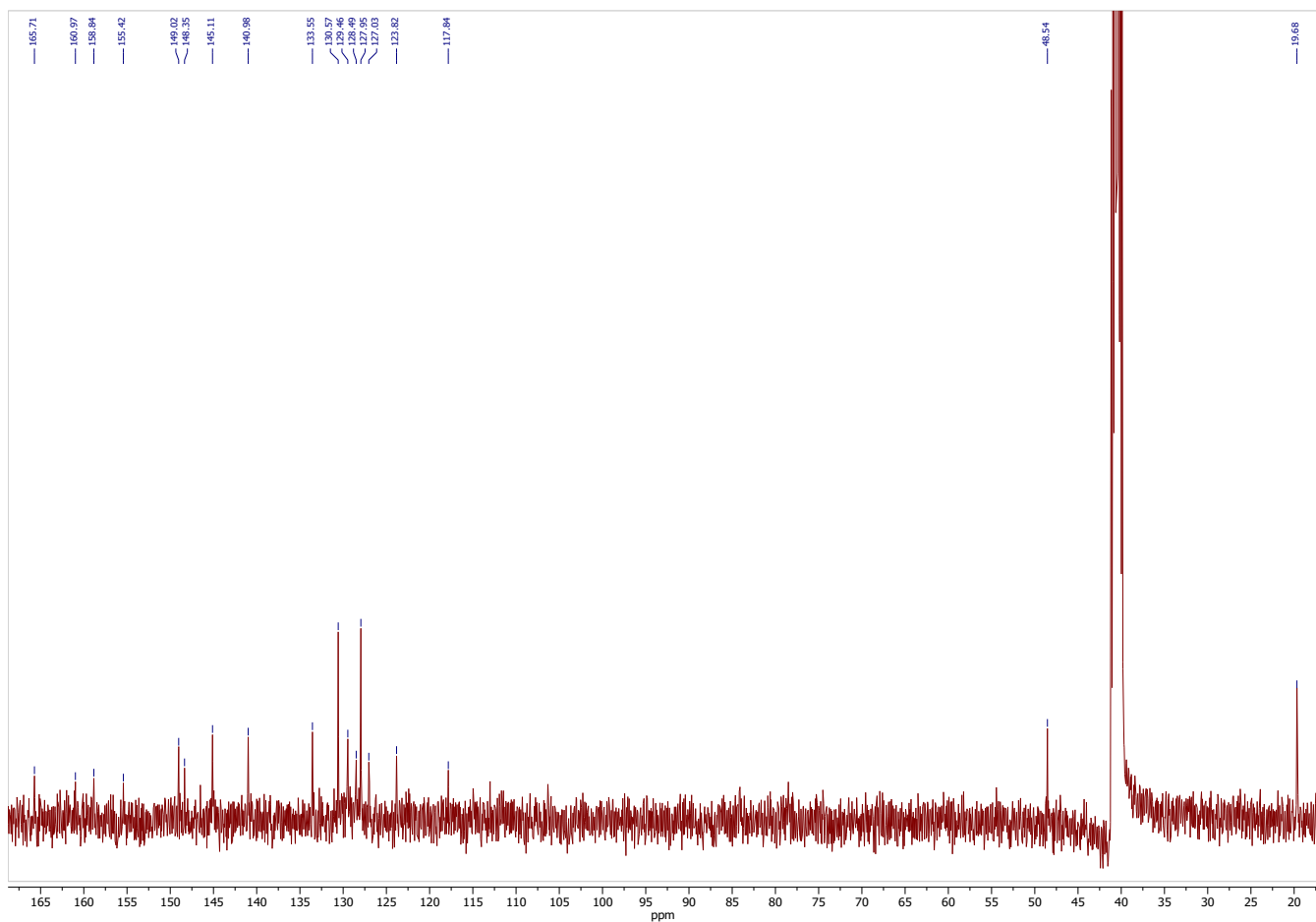
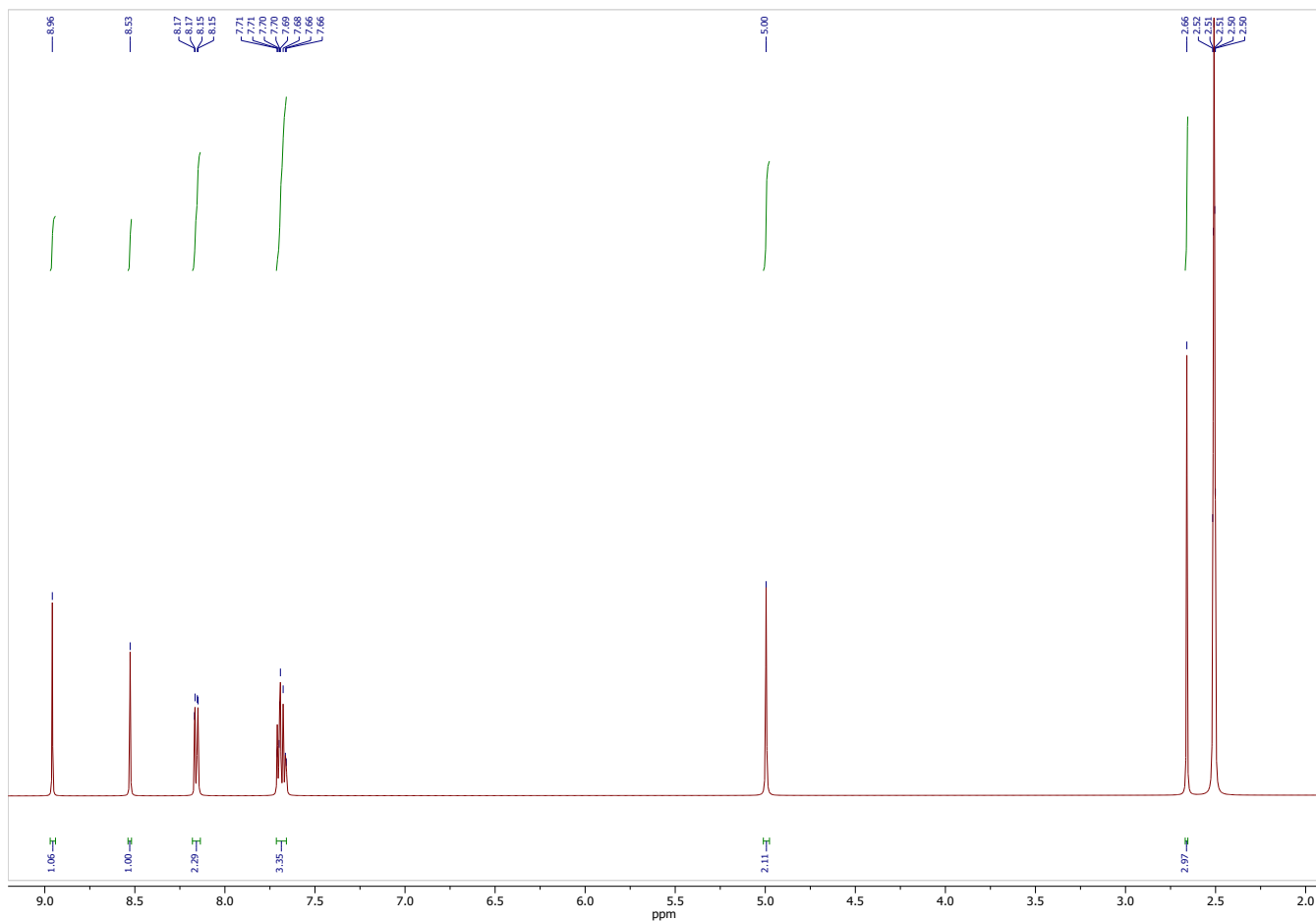
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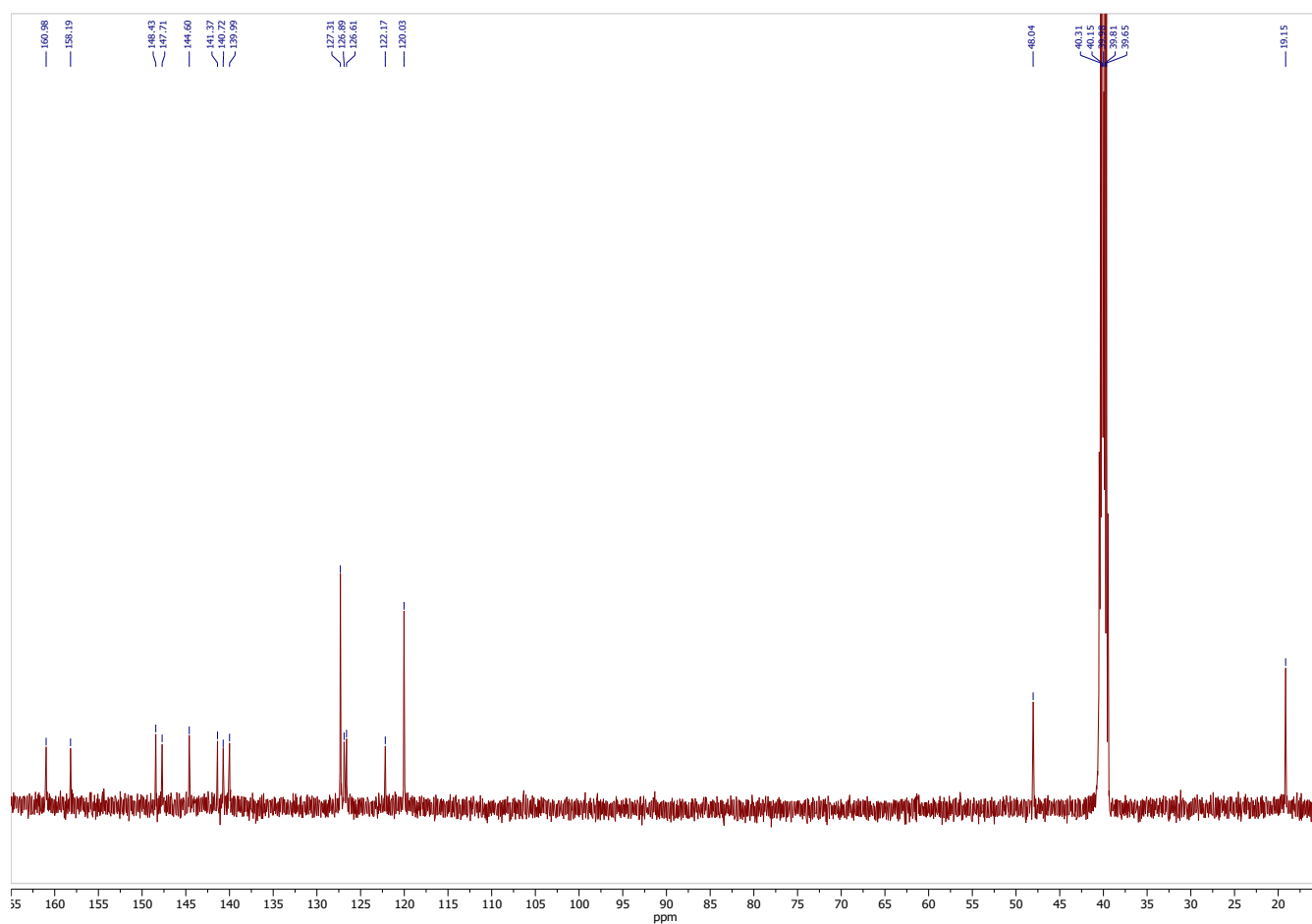
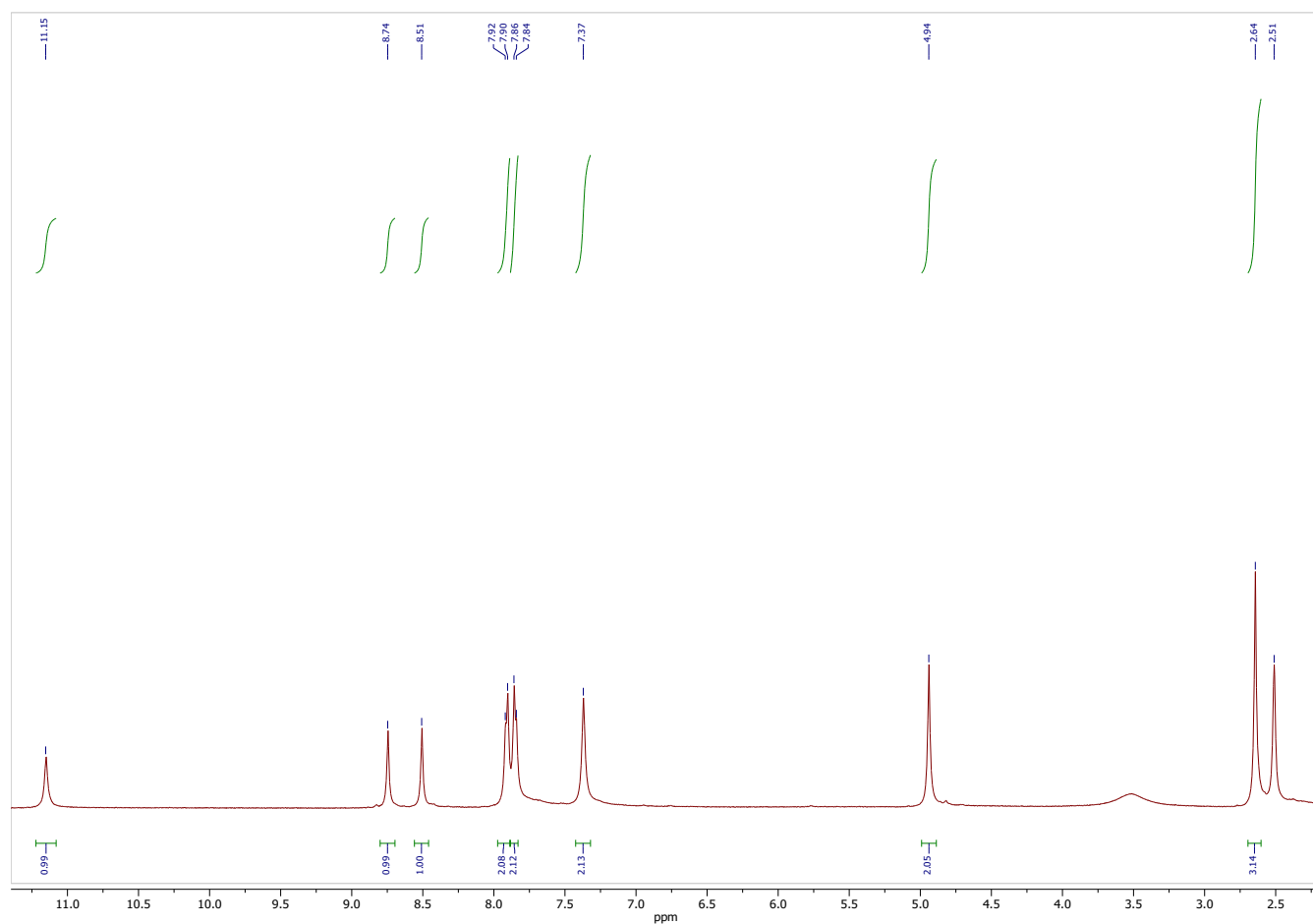
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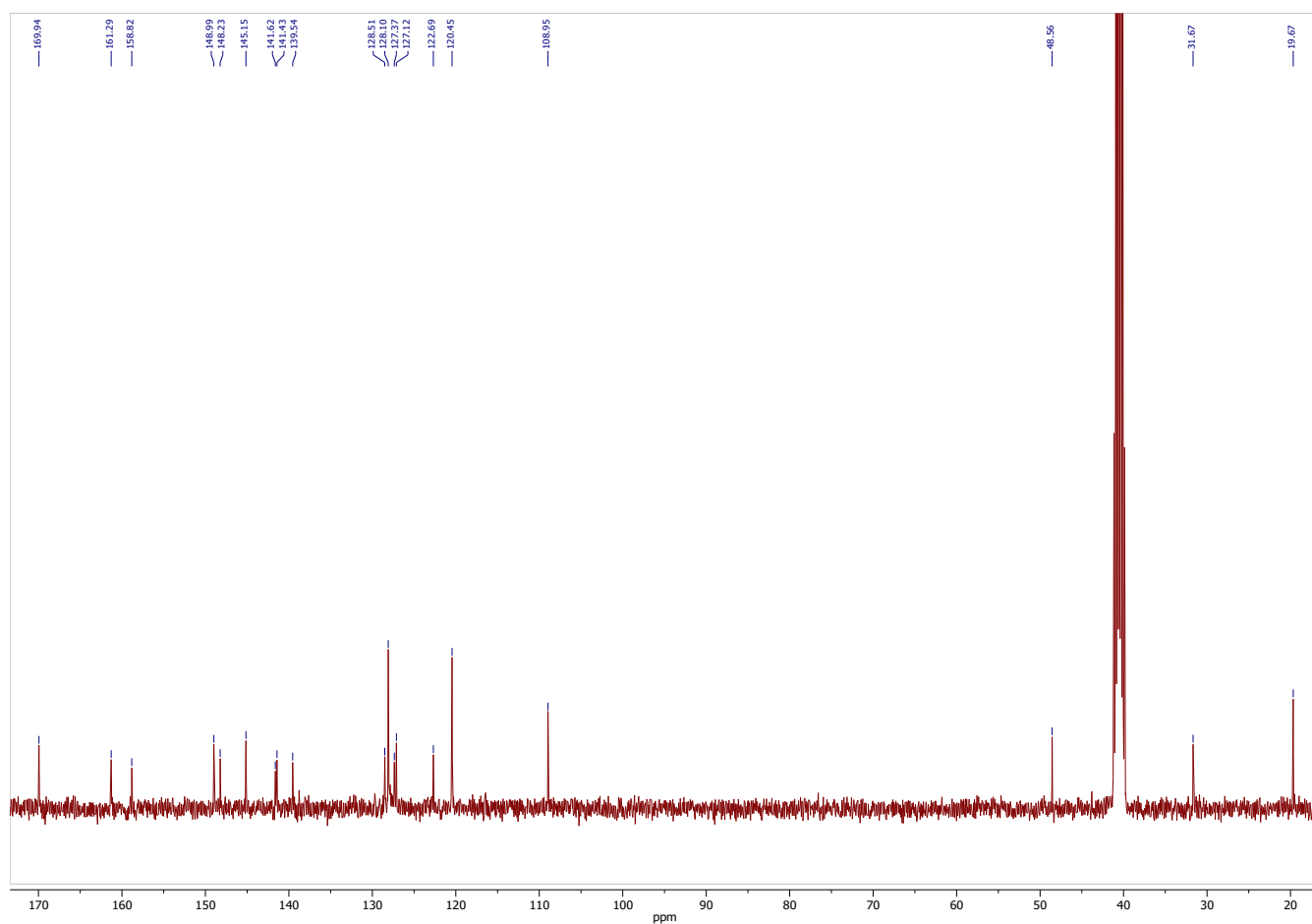
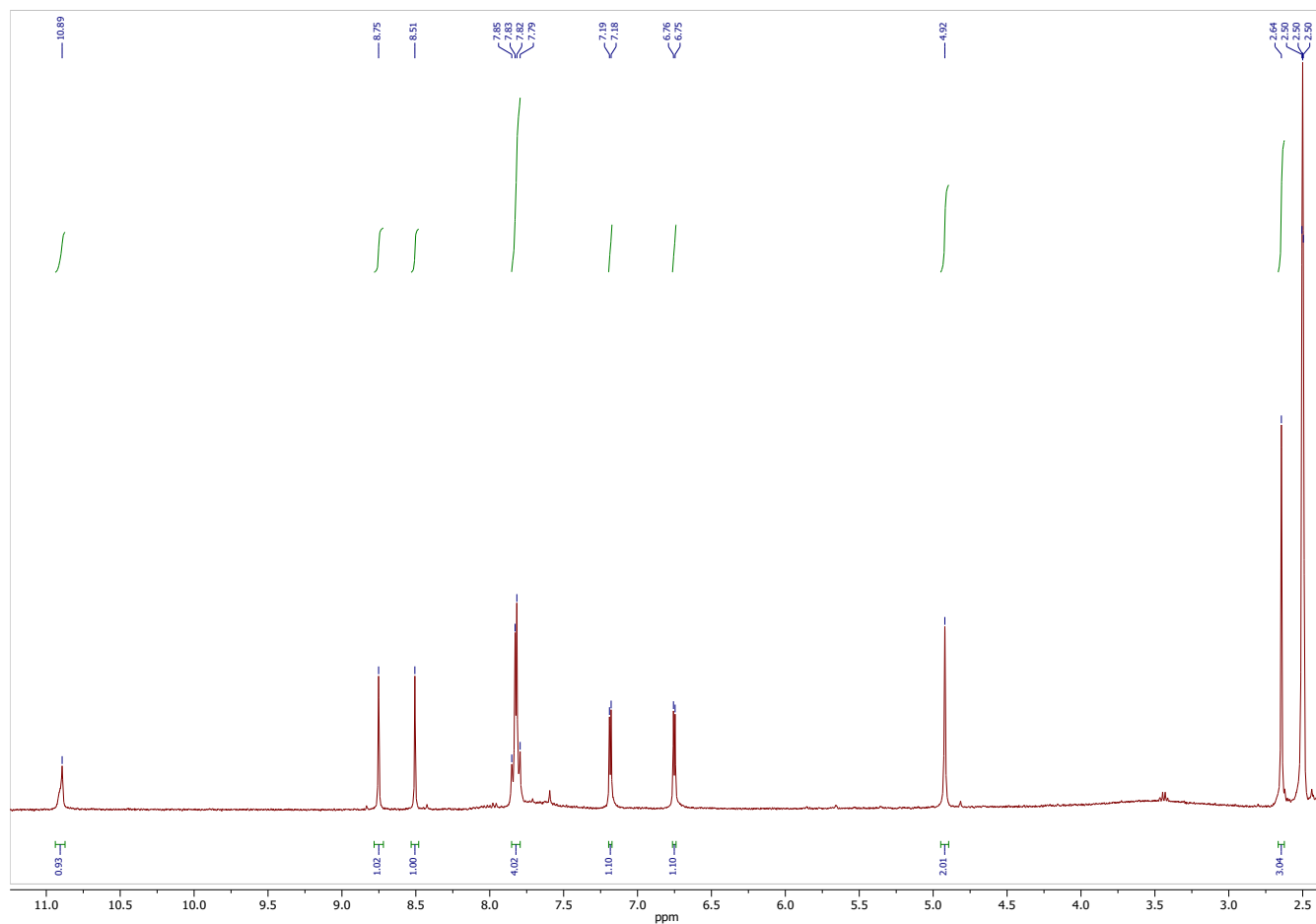
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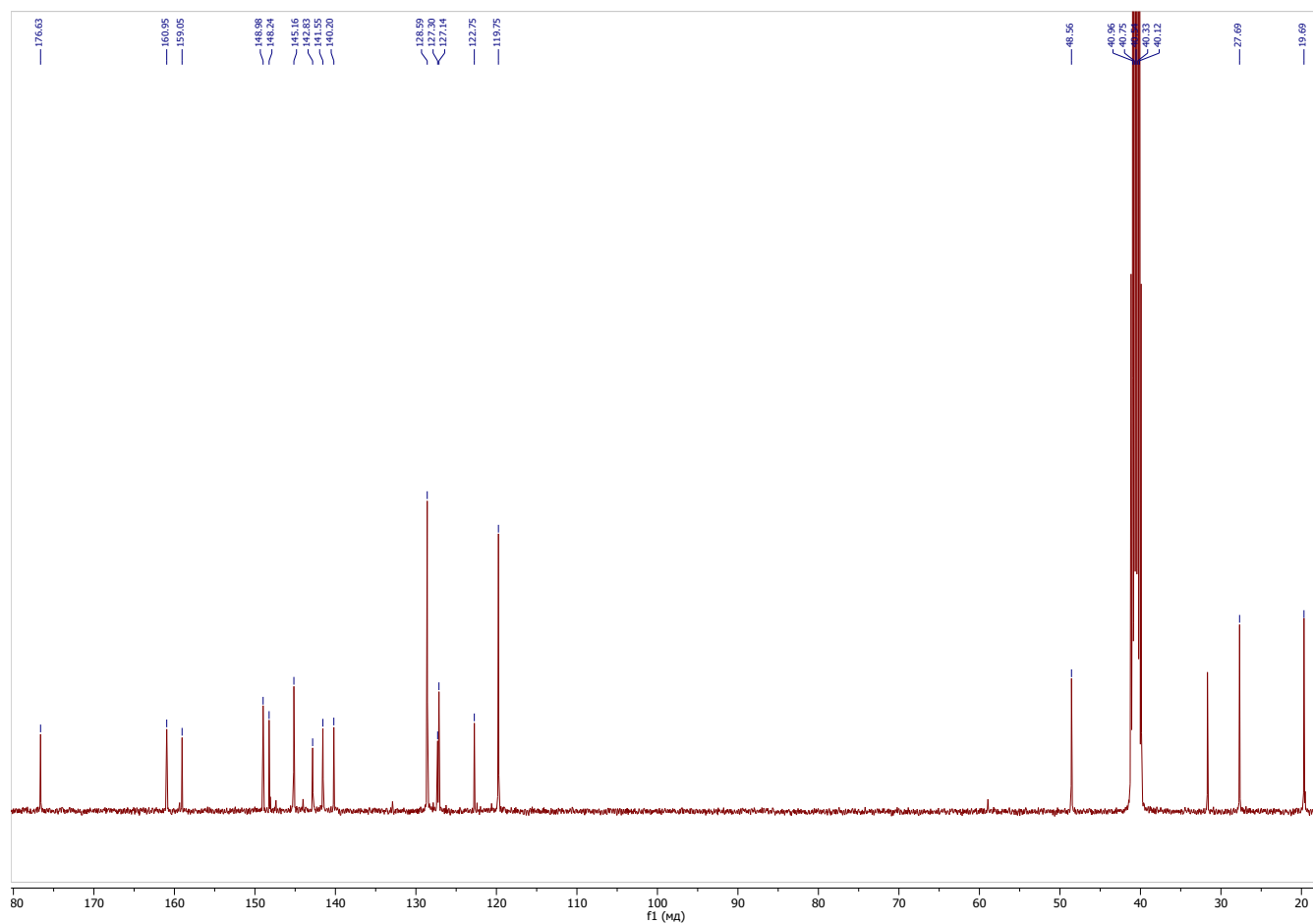
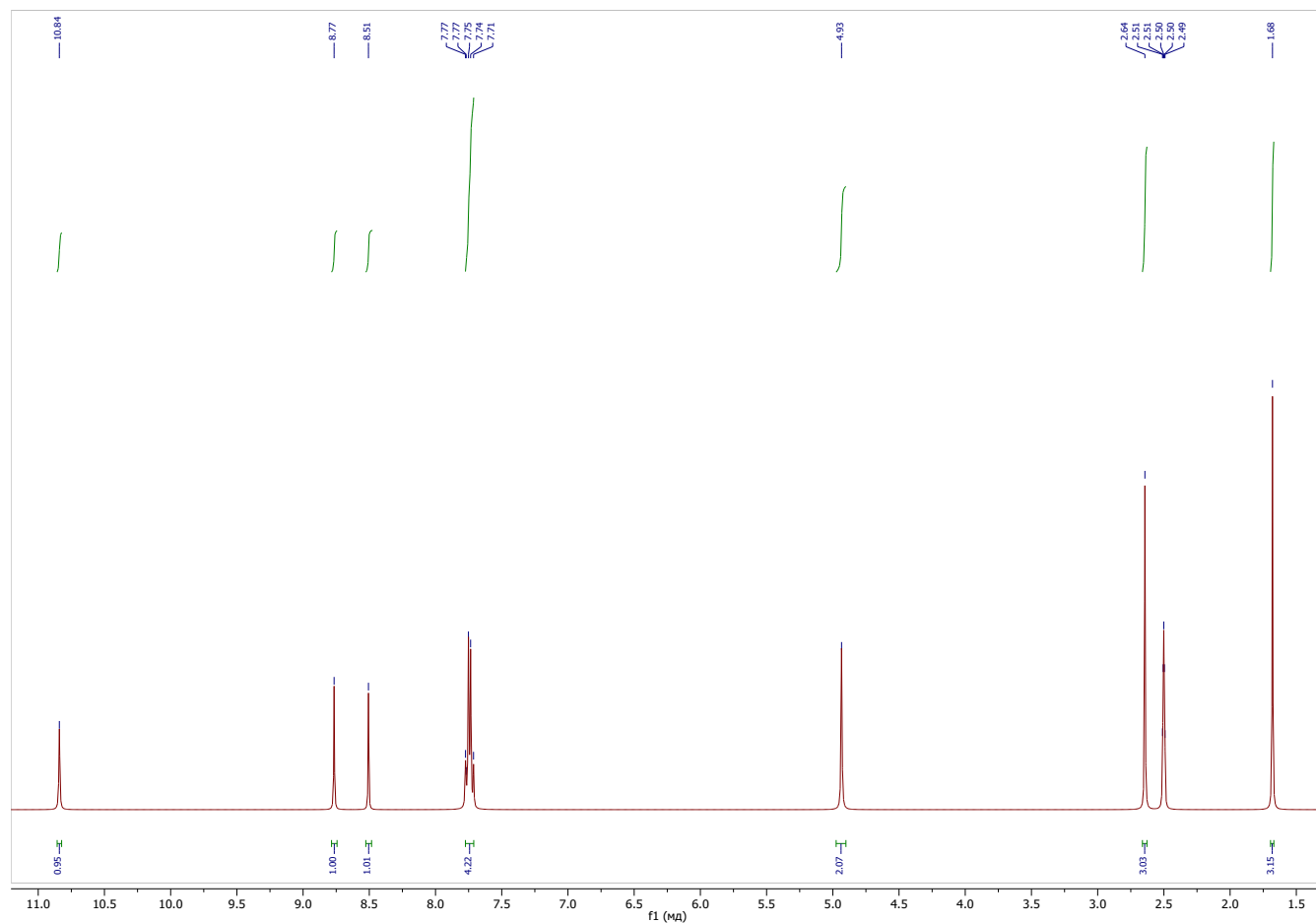
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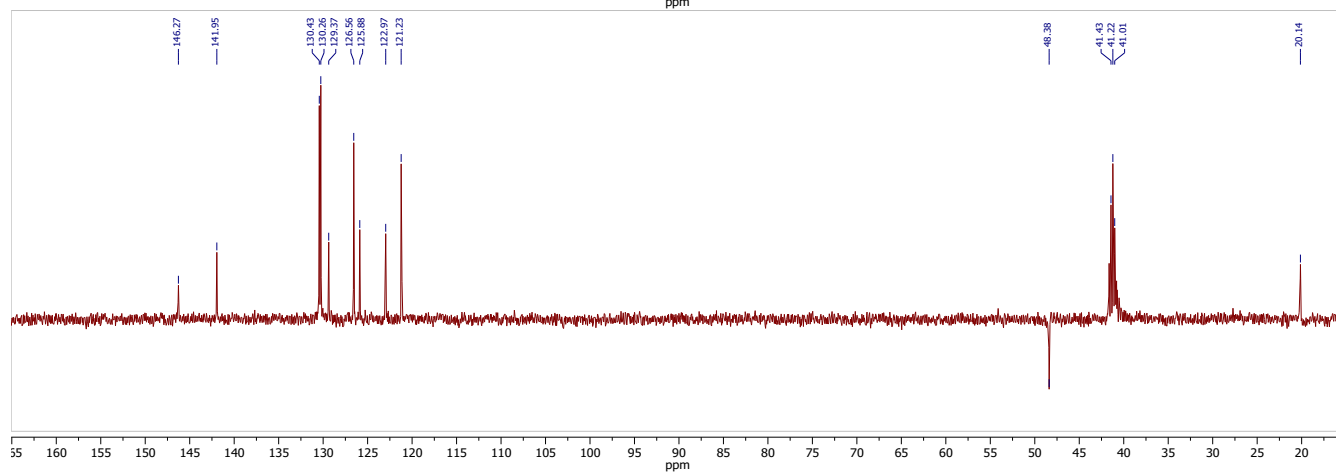
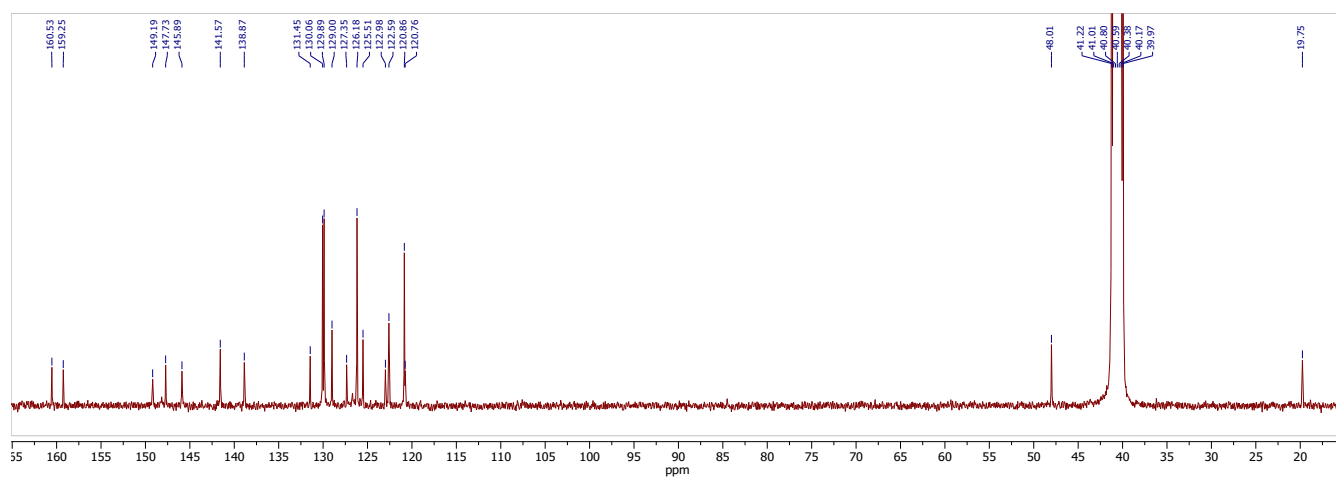
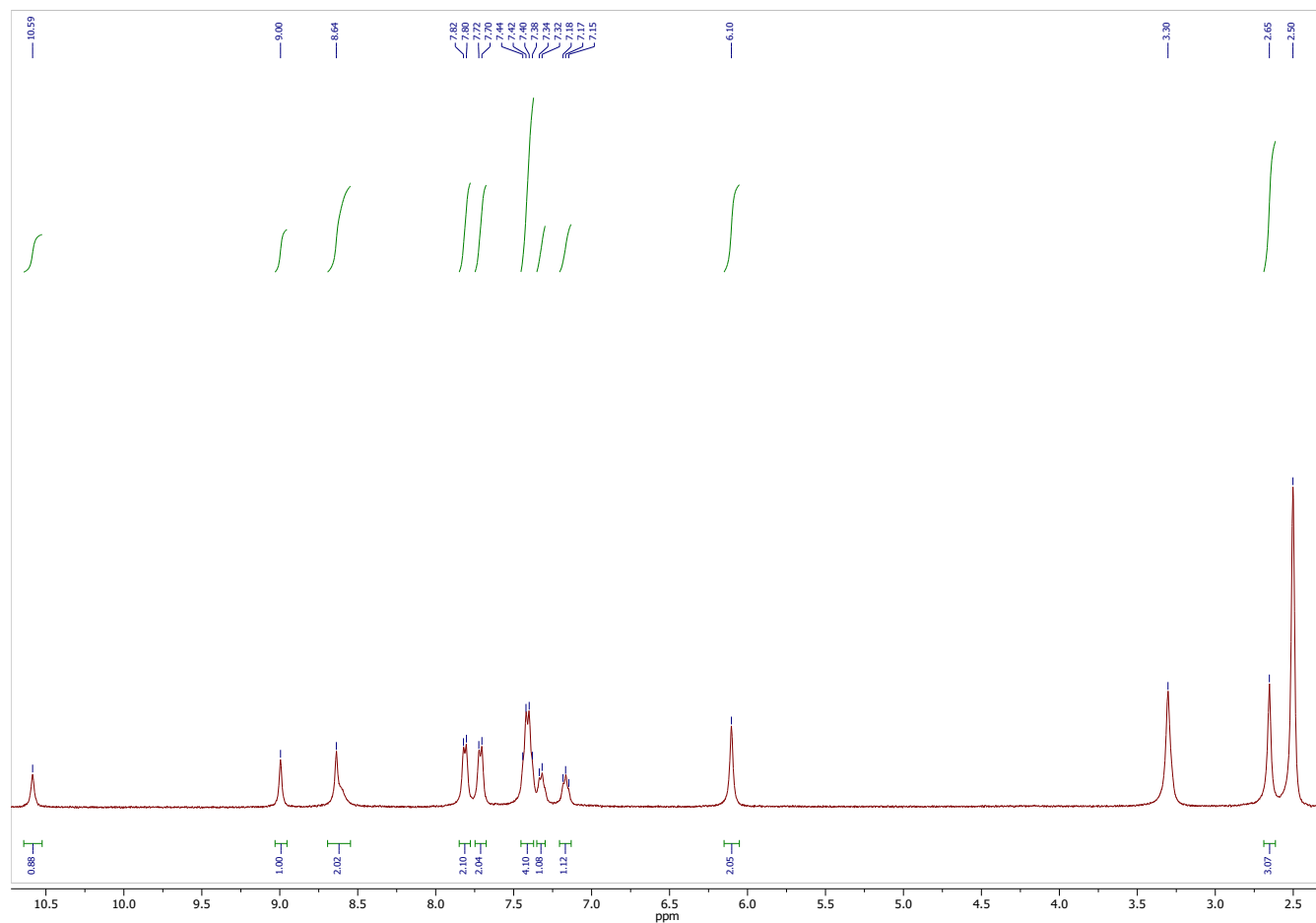
5-Azidomethyl-8-methyl-2-oxo-*N*-[4-(*N*-(thiazol-2-yl)sulfamoyl)phenyl]-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (2f)



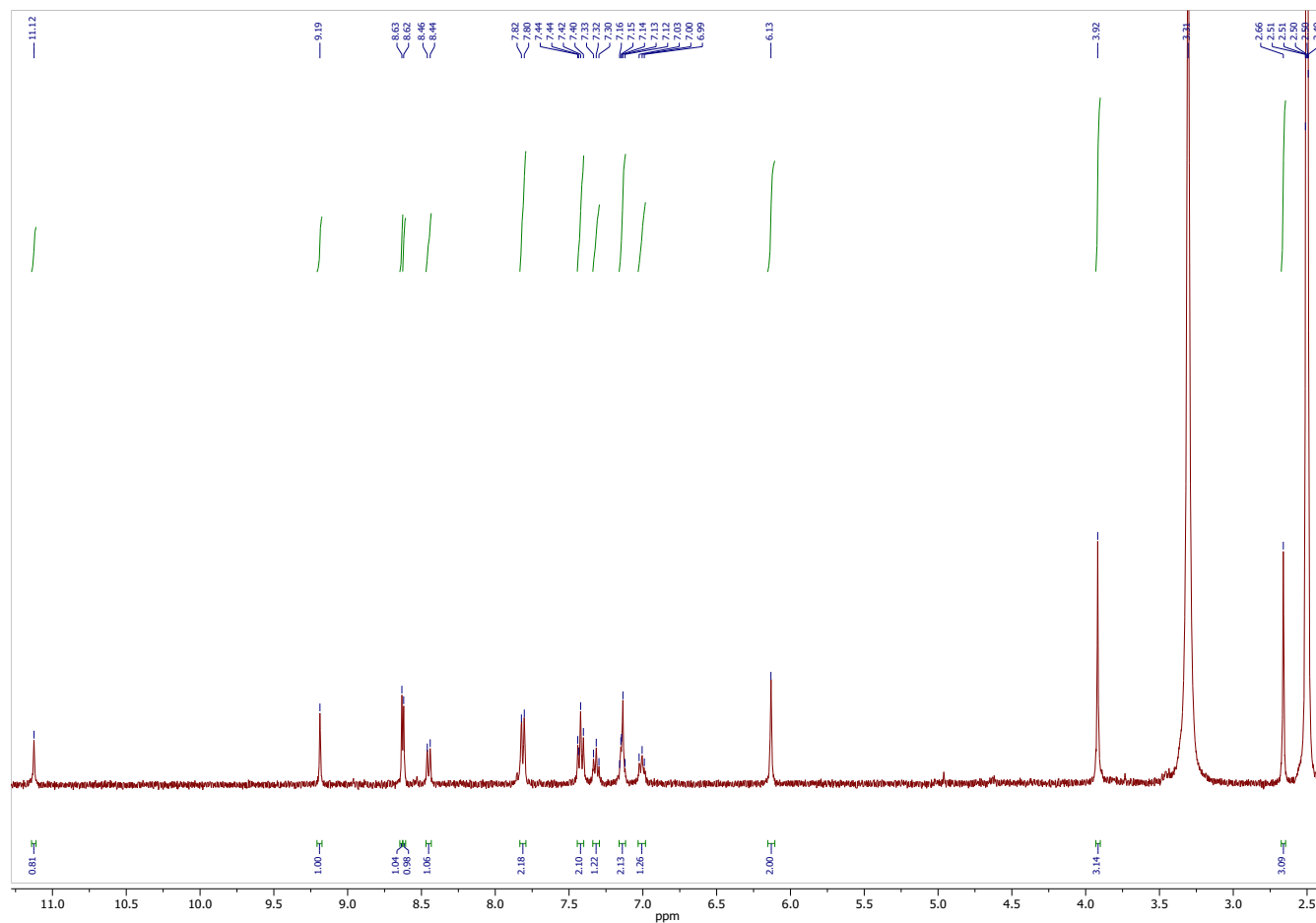
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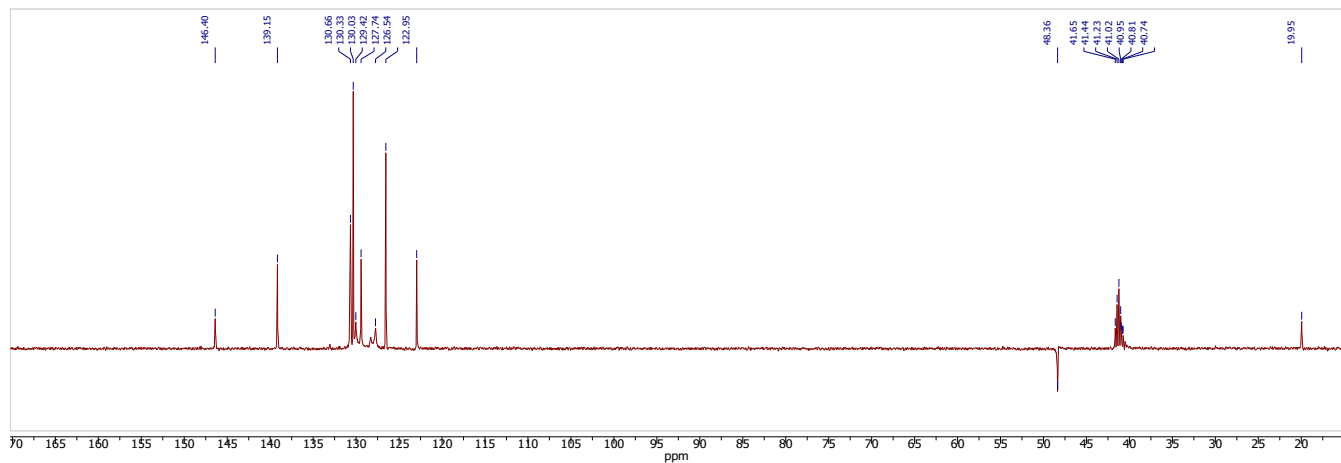
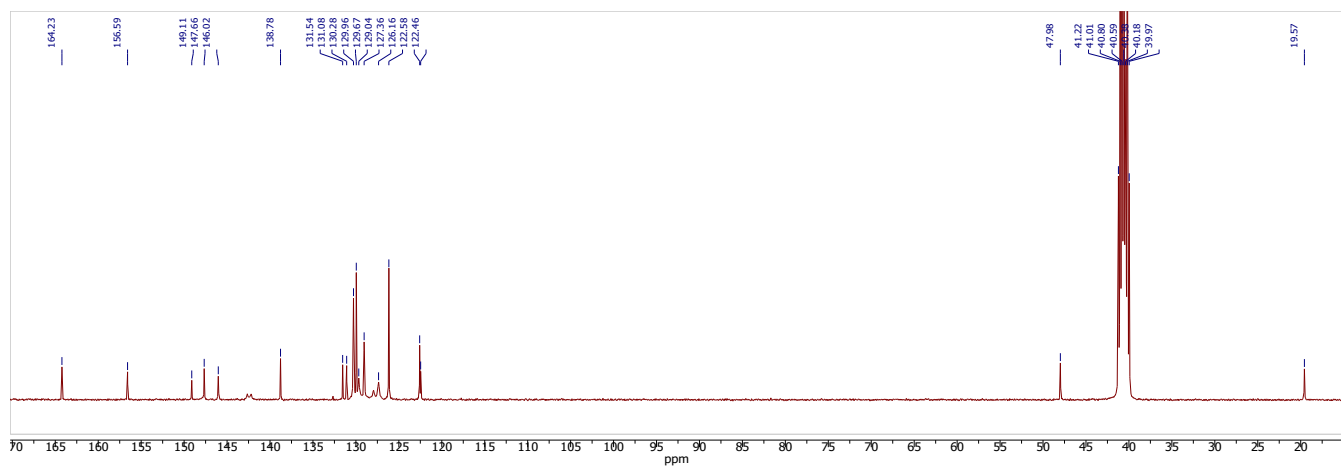
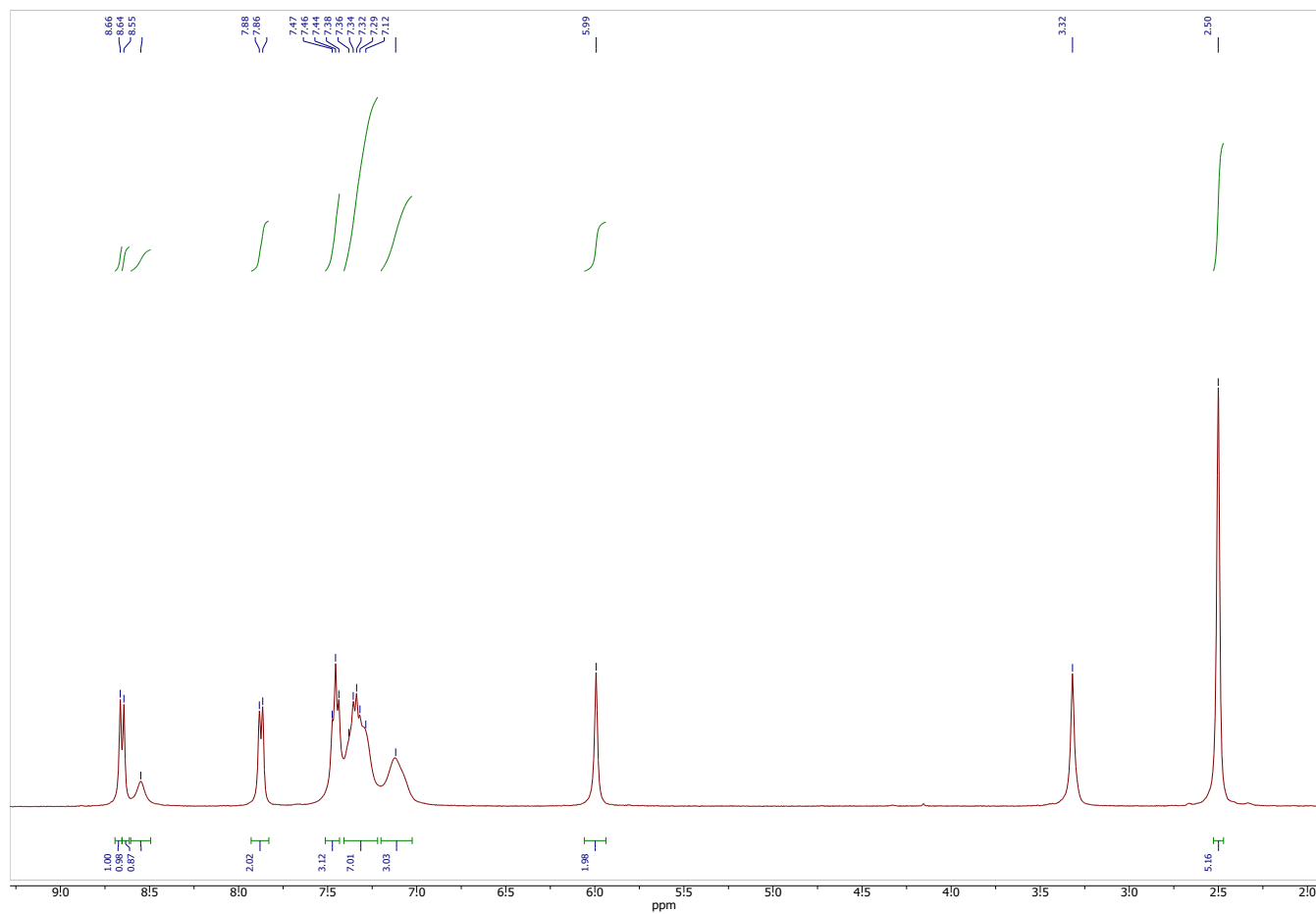
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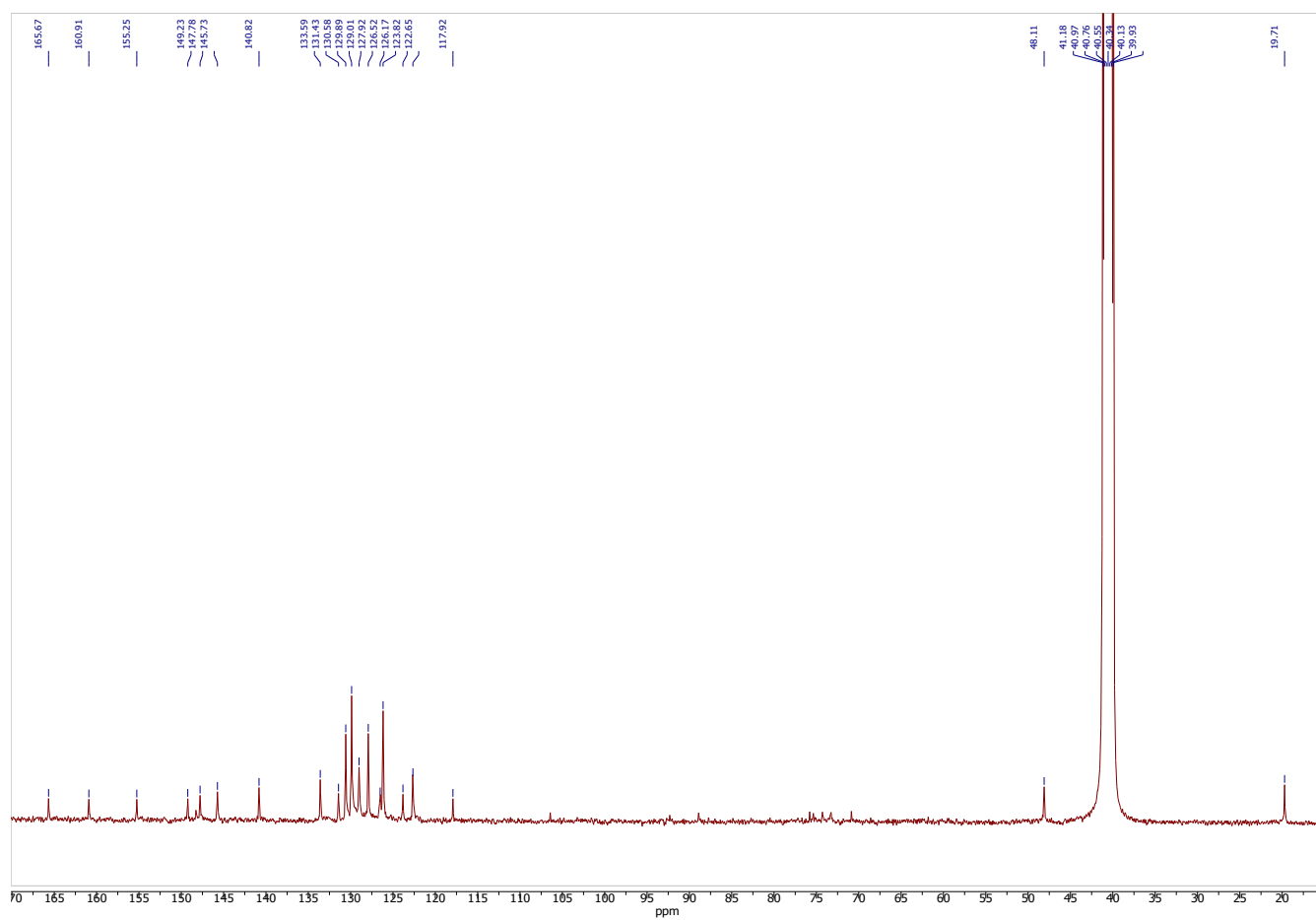
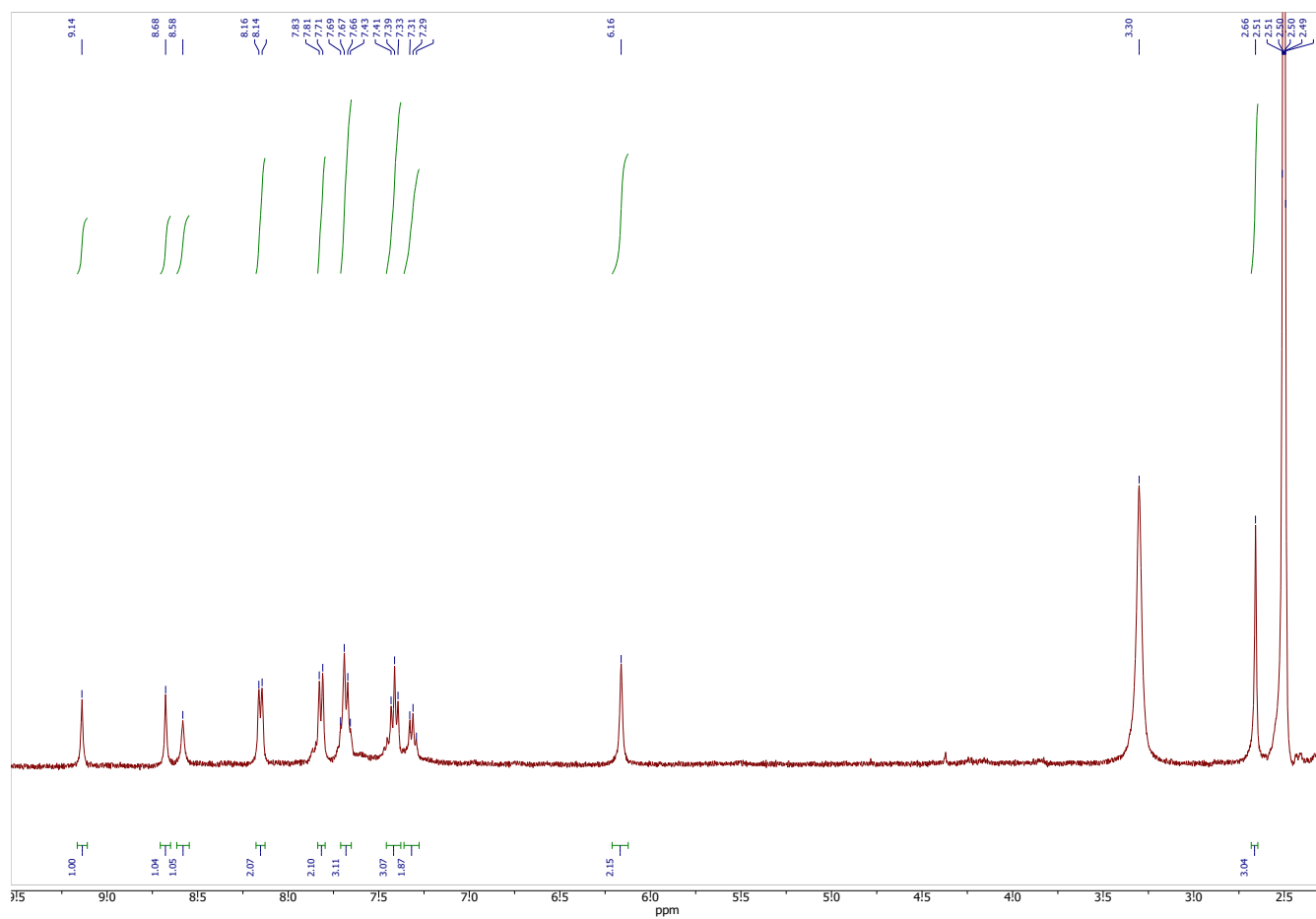
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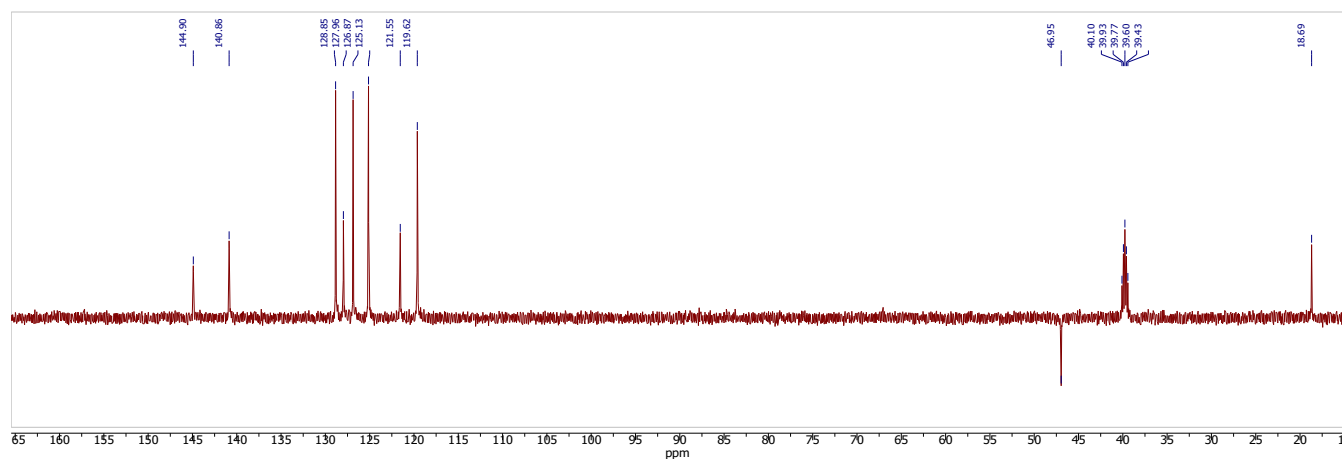
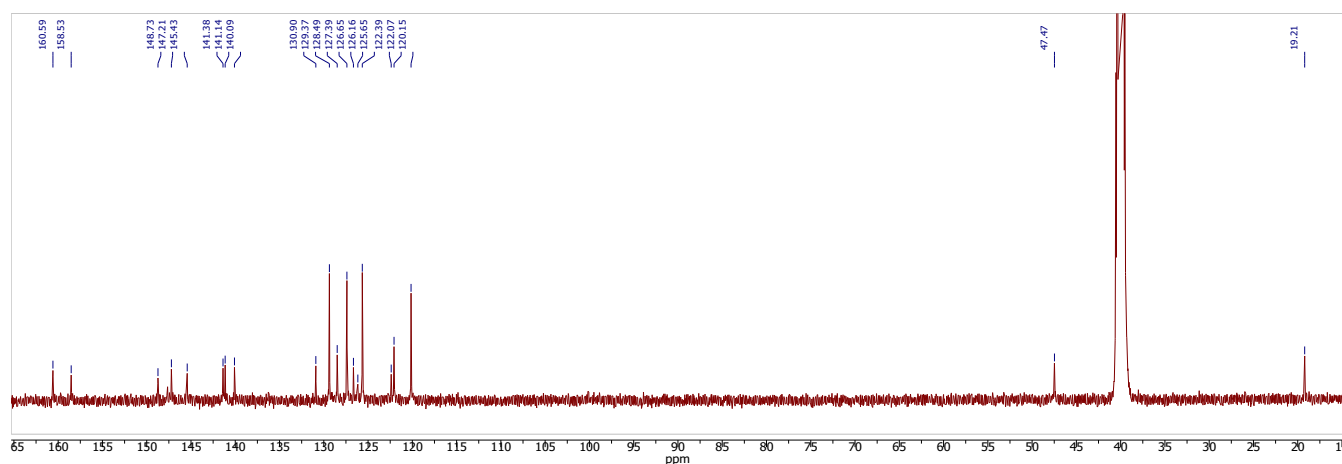
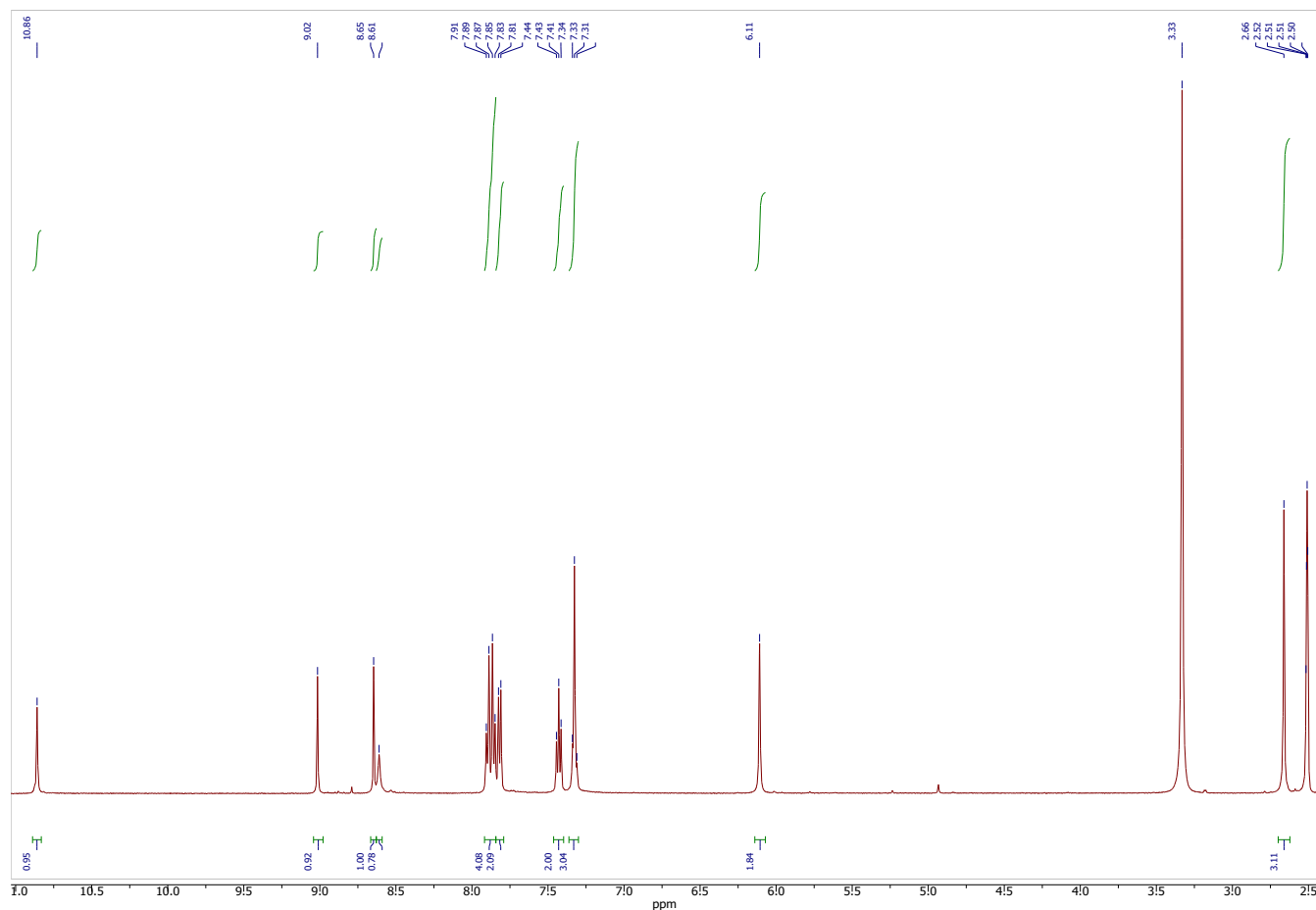
8-Methyl-2-oxo-*N,N*-diphenyl-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (3c)



***N'*-Benzoyl-8-methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-2*H*-pyrano[2,3-*c*]pyridin-3-carbohydrazide (3d)**



8-Methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-*N*-(4-sulfamoylphenyl)-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (3e)



8-Methyl-2-oxo-5-[(4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl]-*N*-{4-[*N*-(thiazol-2-yl)sulfamoyl]phenyl}-2*H*-pyrano[2,3-*c*]pyridine-3-carboxamide (3f)

