Expedited access to thieno[3,2-*c*]quinolin-4(5*H*)-ones and benzo[*h*]-1,6-naphthyridin-5(6*H*)-ones via a continuous flow photocyclization method

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Supplemental Information

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1. General information

^{1}H and ^{13}C NMR spectra were obtained using a 400MHz Bruker NMR spectrometer at 400 and 100 MHz, respectively. TMS or $CDCl_3$ were used as an internal NMR standard for spectral shifts unless otherwise specified. Anhydrous acetone was used as purchased from VWR and all other reagents were used as purchased without further purification.

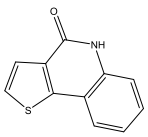
2. Experimental section

2.1 General procedure for the continuous-flow photochemical synthesis of thieno-quinolinones and derivatives

A solution of starting material (corresponding 2-chloro-N-phenylthiophene-3-carboxamide derivative) (0.1 mmol, 0.005 mmol/mL) in acetone (20mL) was passed continuously through the Vapourtec® UV- 150 photochemical flow reactor using a Vapourtec® R2+/R4 flow chemistry system at a rate of 0.100 mL/min (reacting time 100min). The UV-150 reactor uses a medium-pressure pure Hg lamp (lamp power 80%, approximately 112.5 watts), a 10mL FEP reactor coil, and a filter (type 1, quartz, whole-wavelength range). The temperature was set and maintained at 60˚C using the Vapourtec® R4 reactor module, and the UV reactor coil flow stream was passed through an 8 bar back pressure regulator, with the Vapourtec® R2+ pressure limit set at 12 bar. The reaction stream of crude product was collected into a round-bottom flask which was covered by aluminum foil. Solvent acetone was removed by a rotary vacuum and the residue was loaded on silica gel and purified by column chromatography (Teledyne Isco CombiFlash® Rf) using 10% ethyl acetate in hexanes to 50% ethyl acetate in hexanes. The purified product was dried under vacuum and weighed. The product was analyzed by 400 MHz Bruker NMR spectrometer at 400 (^{1}H) and 101 (^{13}C) MHz, respectively, and LC-MS.

2.2 Characterization of thieno-quinolinone(s)and derivatives

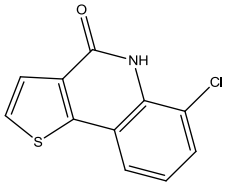
Thieno[3,2-*c*]quinolin-4(5*H*)-one (entry 1)



2-Chloro-*N*-phenylthiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (12.7 mg, 64%) as beige white solid. R_f = 0.27 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.77 (s, 1H, NH), 7.84 (d, *J* = 7.5 Hz, 1H), 7.79 (d, *J* = 5.2 Hz, 1H), 7.59 (d, *J* = 5.2 Hz, 1H), 7.49 (ddd, *J* = 8.3, 7.1, 1.3 Hz, 1H), 7.42 (dd, *J* = 8.3, 0.8 Hz, 1H), 7.27 – 7.21 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.60, 146.02, 136.64, 131.56, 129.81, 127.13, 125.71, 123.82, 122.89, 116.72, 116.61. $C_{11}H_7NOS$.

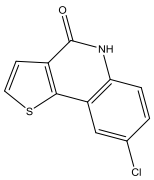
(ESI+, M+1) = 202.05. Known compound: Bhakuni, Bhagat Singh, et al. KO^{t}Bu Mediated Synthesis of Phenanthridinones and Dibenzoazepinones. *Organic letters*, **2012**, 2838-2841.

6-Chlorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 2)



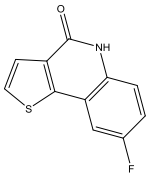
2-Chloro-*N*-(2-chlorophenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (12.7 mg, 54%) as beige white solid. R_f = 0.49 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.93 (s, 1H, NH), 7.85 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.63 (d, J = 6 Hz, 2H), 7.25 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.39, 145.76, 133.04, 132.02, 129.94, 128.50, 125.82, 123.60, 123.07, 119.80, 118.39. $C_{11}H_6ClNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_6ClNNaOS$ 257.9751. Found (ESI+, M+Na): 257.9751.

8-Chlorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 3)



2-Chloro-*N*-(4-chlorophenyl)thiophene-3-carboxamide carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (16.7 mg, 72%) as beige white solid. R_f = 0.31 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.88 (s, 1H, NH), 7.92 (d, *J* = 1.9 Hz, 1H), 7.85 (d, *J* = 5.2 Hz, 1H), 7.60 (d, *J* = 5.2 Hz, 1H), 7.53 (dd, *J* = 8.8, 2.2 Hz, 1H), 7.42 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.38, 144.62, 135.40, 132.27, 129.61, 128.30, 126.77, 125.72, 122.93, 118.45, 117.99. $C_{11}H_6ClNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_6ClNNaOS$ 257.9751. Found (ESI+, M+Na): 257.9748.

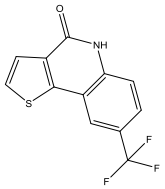
8-Fluorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 4)



2-Chloro-*N*-(4-fluorophenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (14.2 mg, 65%) as beige white solid. R_f = 0.21 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.82 (s, 1H, NH), 7.85 (d, *J* = 5.2 Hz, 1H), 7.74 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.60 (d, *J* = 5.2 Hz, 1H), 7.44 (dd, *J* = 9.0, 5.0 Hz, 1H), 7.39 (td, *J* = 8.8, 2.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.32, 157.76 (d, *J* = 237.5 Hz), 145.03 (d, *J* = 3 Hz), 133.33, 132.27, 128.19, 125.76, 118.48 (d, *J*

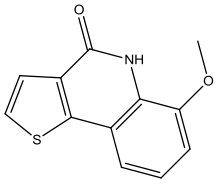
= 9 Hz), 117.58 (d, *J* = 24 Hz), 117.48 (d, *J*= 9 Hz), 109.28 (d, *J* = 23 Hz). $C_{11}H_6FNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_6FNNaOS$ 242.0046. Found (ESI+, M+Na): 242.0051.

8-(Trifluoromethyl)thieno[3,2-*c*]quinolin-4(5*H*)-one (entry 5)



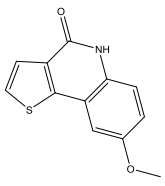
2-Chloro-*N*-(4-(trifluoromethyl)phenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (20.7 mg, 77%) as beige white solid. R_f = 0.46 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.09 (s, 1H, NH), 8.13 (d, *J* = 0.5 Hz, 1H), 7.88 (d, *J* = 5.2 Hz, 1H), 7.79 (dd, *J* = 8.7, 1.6 Hz, 1H), 7.62 (d, *J* = 5.2 Hz, 1H), 7.57 (d, *J* = 8.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.59, 145.11, 139.19, 132.41, 128.55, 125.96 (q, *J* = 3.6 Hz), 125.69, 124.64 (q, *J* = 269.8 Hz), 123.1 (q, *J* = 32 Hz), 121.05 (q, *J* = 4 Hz) 117.54, 116.56. $C_{12}H_6F_3NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_6F_3NNaOS$ 292.0014. Found (ESI+, M+Na): 292.0004.

6-Methoxythieno[3,2-*c*]quinolin-4(5*H*)-one (entry 6)



2-Chloro-*N*-(2-methoxyphenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (11.6 mg, 50%) as beige white solid. R_f = 0.31 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.76 (s, 1H, NH), 7.80 (d, *J* = 5.2 Hz, 1H), 7.61 (d, *J* = 5.2 Hz, 1H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.21 (t, *J* = 7.9 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 1H), 3.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.12, 146.89, 146.03, 131.89, 127.36, 126.45, 125.85, 123.12, 117.07, 115.55, 110.59, 56.56. $C_{12}H_9NO_2S$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_9NNaO_2S$ 254.0246. Found (ESI+, M+Na): 254.0244.

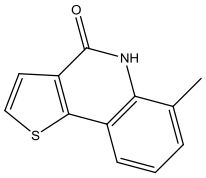
8-Methoxythieno[3,2-*c*]quinolin-4(5*H*)-one (entry 7)



2-Chloro-*N*-(4-methoxyphenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (5.3 mg, 23%) as beige white solid. R_f = 0.16 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.66 (s, 1H, NH), 7.80 (d, *J* = 5.2 Hz, 1H), 7.58 (d, *J* = 5.2 Hz, 1H), 7.36 (d, *J* = 9.0 Hz, 1H), 7.26 (d, *J* = 2.6 Hz, 1H), 7.14 (dd, *J* = 9.0, 2.6 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.20, 155.06, 145.57, 131.87, 130.92, 127.22, 125.81, 118.68, 118.05, 117.26,

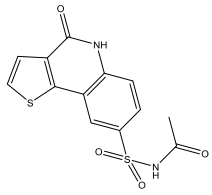
105.70, 56.09. $C_{12}H_9NO_2S$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_9NNaO_2S$ 254.0246. Found (ESI+, M+Na): 254.0240.

6-Methylthieno[3,2-*c*]quinolin-4(5*H*)-one (entry 8)



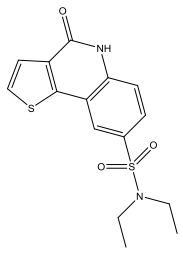
2-Chloro-*N*-(2-methylphenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (8.4 mg, 39%) as beige white solid. R_f = 0.41 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.83 (s, 1H, NH), 7.78 (d, *J* = 5.2 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 5.3 Hz, 1H), 7.34 (d, *J* = 7.3 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H) 2.49 (S, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.90, 146.76, 134.97, 131.29, 131.19, 127.17, 125.73, 125.03, 122.71, 121.84, 116.72, 18.26. $C_{12}H_9NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_9NNaOS$ 238.0297. Found (ESI+, M+Na): 238.0300.

***N*-((4-Oxo-4,5-dihydrothieno[3,2-*c*]quinolin-8-yl)sulfonyl)acetamide (entry 9)**



2-Chloro-*N*-(2-methylphenyl)cyclopenta-1,4-dienecarboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (13.2 mg, 41%) as beige white solid. R_f = 0.51. (Dichloromethane: Methanol = 5: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H, NH), 12.14 (s, 1H), 8.28 (d, *J* = 1.6 Hz, 1H), 7.96 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.92 (d, *J* = 5.2 Hz, 1H), 7.65 (d, *J* = 5.2 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 1.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.38, 158.61, 144.99, 140.02, 132.97, 132.45, 128.65, 128.21, 125.88, 123.91, 117.33, 116.16, 23.74. $C_{13}H_{10}N_2O_4S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{13}H_{10}N_2NaO_4S_2$ 344.9974. Found (ESI+, M+Na): 344.9959.

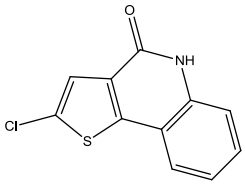
***N,N*-Diethyl-4-oxo-4,5-dihydrothieno[3,2-*c*]quinoline-8-sulfonamide (entry 10)**



2-Chloro-*N*-(4-(*N,N*-diethylsulfamoyl)phenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (9.7 mg, 29%) as white solid. R_f = 0.19 (Hexane: Ethyl acetate = 1:1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H, NH), 8.11 (s, 1H), 7.91 (d, *J* = 5.2 Hz, 1H), 7.88 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.64 (d, *J* = 5.2 Hz, 1H), 7.58 (d, *J* = 8.7 Hz, 1H), 3.20 (q, *J* = 7.0 Hz, 4H), 1.06 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 158.57, 145.09,

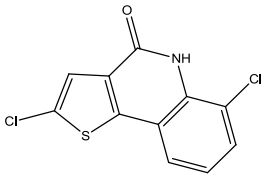
139.27, 133.78, 132.46, 128.60, 127.64, 125.82, 122.48, 117.70, 116.47, 42.32, 14.61. $C_{15}H_{16}N_2O_3S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{15}H_{16}N_2NaO_3S_2$ 359.0495. Found (ESI+, M+Na): 360.3222.

2-Chlorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 11)



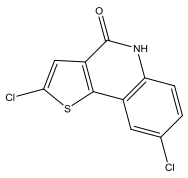
2,5-Dichloro-*N*-phenylthiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (9.7 mg, 41%) as beige white solid. R_f = 0.43 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.87 (s, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 7.54 – 7.49 (m, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.40, 144.99, 136.80, 130.85, 130.35, 129.63, 125.03, 123.76, 123.12, 116.78, 115.77. $C_{11}H_6ClNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_6ClNNaOS$ 257.9751. Found (ESI+, M+Na): 257.9742.

2,6-Dichlorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 12)



2,5-Dichloro-*N*-phenylthiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (8.1 mg, 30%) as beige white solid. R_f = 0.54 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.07 (s, 1H, NH), 7.80 (d, *J* = 7.9 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.66 (s, 1H), 7.27 (t, *J* = 7.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.26, 144.66, 133.23, 131.43, 130.87, 130.48, 125.22, 123.81, 123.06, 119.96, 117.46. $C_{11}H_5Cl_2NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_5Cl_2NNaOS$ 291.9361. Found (ESI+, M+Na): 291.9365.

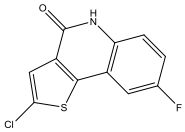
2,8-Dichlorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 13)



2,5-Dichloro-*N*-phenylthiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (12.1 mg, 45%) as beige white solid. R_f = 0.43 (Hexane: Ethyl acetate = 1: 1).^{1}H NMR (400 MHz, DMSO-d_6) δ 12.02 (s, 1H, NH), 7.94 (d, *J* = 2.3 Hz, 1H), 7.61 (s, 1H), 7.56 (dd, *J* = 8.8, 2.3 Hz, 1H), 7.41 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.19, 143.55, 135.57, 131.63, 130.77,

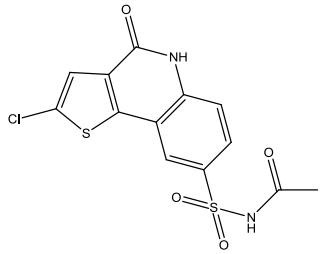
130.16, 127.03, 125.08, 122.98, 118.61, 117.01. $C_{11}H_5Cl_2NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_5Cl_2NNaOS$ 291.9361. Found (ESI+, M+Na): 291.9368.

2-Chloro-8-fluorothieno[3,2-*c*]quinolin-4(5*H*)-one (entry 14)



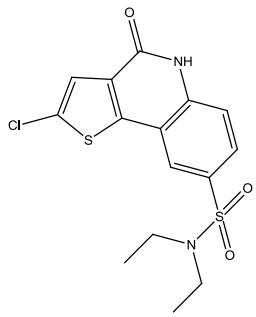
2-Chloro-*N*-(4-fluorophenyl)thiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (6.4 mg, 25%) as beige white solid. R_f = 0.19 (Hexane: Ethyl acetate = 1: 1).^{1}H NMR (400 MHz, DMSO) δ 11.93 (s, 1H), 7.73 (dd, *J* = 9.2, 2.4 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.43 (m, 2H). ^{13}C NMR (101 MHz, DMSO) δ 157.81 (d, *J* = 237.8 Hz), 157.12, 143.94, 133.62 (d, *J* = 3 Hz), 133.53, 131.66, 130.64, 125.12 118.19 (d, *J* = 8.8 Hz), 118.17 (d, *J* = 24.3 Hz), 116.46 (d, *J* = 9.5 Hz), 109.30 (d, *J* = 24.3 Hz) $C_{11}H_5ClFNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_5ClFNNaOS$ 275.9657. Found (ESI+, M+Na): 275.9650.

***N*-((2-Chloro-4-oxo-4,5-dihydrothieno[3,2-*c*]quinolin-8-yl)sulfonyl)acetamide (entry 15)**



N-(4-(*N*-Acetylsulfamoyl)phenyl)- 2,5-dichlorothiophene-3-carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (15.3 mg, 43%) as beige white solid. R_f = 0.57 (Dichloromethane: Methanol = 5: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.28 (s, 1H, NH), 8.17 (d, *J* = 1.8 Hz, 1H), 7.98 (dd, *J* = 8.7, 1.9 Hz, 2H), 7.65 (s, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 1.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.40, 157.39, 143.85, 140.13, 133.31, 131.86, 131.08, 128.64, 125.27, 123.72, 117.52, 115.21, 23.75. $C_{13}H_9ClN_2O_4S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{13}H_9ClN_2NaO_4S_2$ 378.9584. Found (ESI+, M+Na): 378.9577.

2-Chloro-*N,N*-diethyl-4-oxo-4,5-dihydrothieno[3,2-*c*]quinoline-8-sulfonamide (entry 16)



2,5-Dichloro-*N*-(4-(*N,N*-diethylsulfamoyl)phenyl)thiophene-3-carboxamide carboxamide was treated according to the general procedure as starting material. Major product was separated and purified by CombiFlash® Rf, affording the title compound (15.9 mg, 43%) as beige white solid. R_f = 0.30 (Hexane: Ethyl acetate = 1:1) ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.24 (s, 1H, NH), 8.07 (d, *J* = 1.6 Hz, 1H), 7.89 (dd, *J* = 8.7, 1.8 Hz, 1H), 7.65 (s, 1H), 7.57

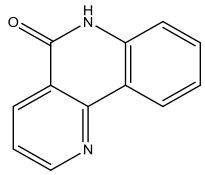
(d, *J* = 8.7 Hz, 1H), 3.20 (q, *J* = 7.1 Hz, 4H), 1.06 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 157.38, 144.03, 139.38, 134.13, 131.86, 131.10, 128.06, 125.14, 122.50, 117.86, 115.57, 42.35, 14.63. $C_{15}H_{15}ClN_2O_3S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{15}H_{15}ClN_2NaO_3S_2$ 393.0105. Found (ESI+, M+Na): 393.0104.

2.3 General procedure for the continuous-flow photochemical synthesis of naphthyridinone(s) and derivatives

A solution of corresponding 2-chloro-N-phenylnicotinamides as starting material (0.1 mmol, 0.005 mmol/mL) in acetone (20 mL) was driven continuously through the Vapourtec® UV- 150 photochemical flow reactor using a Vapourtec® R2+/R4 flow chemistry system at a rate of 0.100 mL/min (reacting time 100min). The UV-150 reactor uses a medium-pressure high-intensity pure Hg lamp (lamp power 80%, approximately 112.5 watts), a 10mL FEP reactor coil, and a filter (type 1, quartz, whole-wavelength range). The temperature was set and maintained at 60˚C using the Vapourtec® R4 reactor module, and the UV reactor coil flow stream was passed through an 8 bar back pressure regulator, with the Vapourtec® R2+ pressure limit set at 12 bar. The reaction stream of crude product was collected into a round-bottom flask which was covered by aluminum foil. Solvent acetone was removed by a rotary vacuum and the residue was absorbed on silica gel and purified by column chromatography (Teledyne Isco CombiFlash® Rf) using 10% to 50% ethyl acetate in hexanes. The cleanest fractions were then combined and the solvent removed, the purified product was dried under vacuum and weighed.

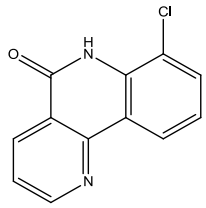
2.4 Characterization of naphthyridinone(s)and derivatives

Benzo[*h*]-1,6-naphthyridin-5(6*H*)-one (entry 17)



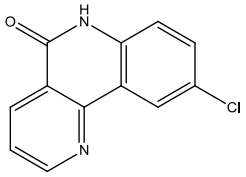
2-Chloro-*N*-phenylnicotinamide was treated according to the general procedure as starting material. Purification by CombiFlash® Rf proved to be difficult and afforded the title compound (10.0, 51%) as a pale yellow crystalline solid. R_f = 0.37 (50% Ethyl acetate/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.88 (s, 1H, NH), 8.63 (td, J = 8, 2 Hz, 2H), 7.72-7.67 (m, 2H), 7.60 (td, J = 15.7, 7.6, 1.6 Hz, 1H), 7.57 (dd, J = 7.6, 7.2 Hz, 1H), 7.33 (td, J= 14.8, 7.2, 0.8 Hz, 1H). The product fractions were found to possess a small portion of starting material by ^{1}H NMR, and possess only moderate purity. Reaction yields were included only as a representative yield in comparison to other examples. Known compound: Cailly, Thomas, Frédéric Fabis, and Sylvain Rault. A new, direct, and efficient synthesis of benzonaphthyridin-5-ones. *Tetrahedron*, **2006**, 5862-5867.

7-Chlorobenzo[*h*]-1,6-naphthyridin-5(6*H*)-one (entry 18)



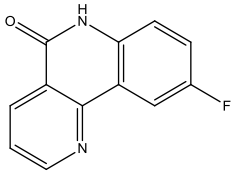
2-Chloro-*N*-(2-chlorophenyl)nicotinamide was treated according to the general procedure as starting material. Purification by CombiFlash® Rf afforded the title compound (10.9 mg, 47%) as a pale yellow crystalline solid. R_f = 0.44 (50% Ethyl acetate/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H, NH), 9.07 (dd, *J* = 4.6, 1.8 Hz, 1H), 8.77 (dd, *J* = 8.0, 1.9 Hz, 1H), 8.73 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.65 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.60 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.07, 154.36, 150.88, 136.52, 133.42, 130.95, 123.91, 123.52, 123.32, 121.47, 121.33, 119.57. $C_{12}H_7ClN_2O$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_7ClN_2NaO$ 253.0139. Found (ESI+, M+Na): 253.0145.

9-Chlorobenzo[*h*]-1,6-naphthyridin-5(6*H*)-one (entry 19)



2-Chloro-*N*-(4-chlorophenyl)nicotinamide was treated according to the general procedure as starting material. Purification by CombiFlash® Rf afforded the title compound (5.5 mg, 24%) as a pale yellow crystalline solid. R_f = 0.28 (50% Ethyl acetate/hexane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H, NH), 9.08 (dd, *J* = 4.6, 1.8 Hz, 1H), 8.62 (dd, *J* = 8.0, 1.8 Hz, 1H), 8.54 (d, *J* = 2.5 Hz, 1H), 7.73 (q, J = 8.0 Hz, 4.8 Hz, 1H), 7.65 (dd, *J* = 8.7, 2.5 Hz, 1H), 7.41 (d, *J* = 8.7 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.16, 154.74, 149.84, 137.15, 136.35, 131.52, 127.11, 124.55, 123.57, 122.03, 120.70, 118.46. $C_{12}H_7ClN_2O$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_7ClN_2NaO$ 253.0139. Found (ESI+, M+Na): 253.0131.

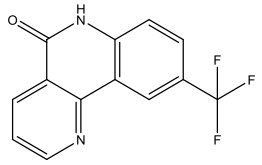
9-Fluorobenzo[*h*]-1,6-naphthyridin-5(6*H*)-one (entry 20)



2-Chloro-*N*-(4-fluorophenyl)nicotinamide was treated according to the general procedure as starting material. Purification by CombiFlash® Rf afforded the title compound (5.5 mg, 26%) as a pale yellow crystalline solid. R_f = 0.22 (50% Ethyl acetate/hexane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H, NH), 9.08 (m, *J* = 8.0, 1.7 Hz, 1H), 8.63 (dd, *J* = 8.0, 1.7 Hz, 1H), 8.28 (dd, *J* = 9.6, 2.8 Hz, 1H), 7.73 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.50 (td, *J* = 8.6, 2.9 Hz, 1H), 7.43 (dd, *J* = 8.9, 4.9 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.03, 158.22 (d, *J* = 237 Hz), 154.62, 136.36, 135.04, 124.47, 123.65, 122.05, 121.87 (d, *J* = 8.1 Hz), 119.47 (d, *J* = 24 Hz), 118.44 (d, *J* = 8.2 Hz),

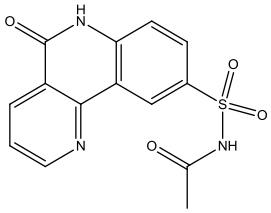
109.61 (d, *J* = 24 Hz). $C_{12}H_7FN_2O$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_7FN_2NaO$ 23.0435. Found (ESI+, M+Na): 237.0441.

9-(Trifluoromethyl)benzo[*h*]-1,6-naphthyridin-5(6*H*)-one (entry 21)



2-Chloro-*N*-(4-(trifluoromethyl)phenyl)nicotinamide was treated according to the general procedure as starting material. Purification by CombiFlash® Rf afforded the title compound (13.2 mg, 50%) as a pale yellow crystalline solid. R_f = 0.23 (50% Ethyl acetate/hexane). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H, NH), 9.10 (dd, J = 4.6 Hz, 1.6 Hz, 1H), 8.86 (d, *J* = 1.5 Hz, 1H), 8.63 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.92 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.75 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.56 (d, *J* = 8.6 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.50, 154.86, 150.02, 141.06, 136.39, 127.96 (q, *J* = 3.4 Hz), 124.85 (q, *J* = 269.6 Hz), 124.73, 123.26 (q, *J* = 32.2 Hz), 122.16, 121.63 (q, *J* = 4.2 Hz), 119.27, 117.53. $C_{13}H_7F_3N_2O$. HRMS m/z (ESI+, M+Na): Calcd for $C_{13}H_7F_3N_2NaO$ 287.0403. Found (ESI+, M+Na): 287.0392.

***N*-((5-Oxo-5,6-dihydrobenzo[h]-1,6-naphthyridin-9-yl)sulfonyl)acetamide (entry 22)**



N-(4-(*N*-Acetylsulfamoyl)phenyl)-2-chloronicotinamide was treated according to the general procedure as starting material. Purification by CombiFlash® Rf afforded the title compound (16.6 mg, 52%) as a pale yellow crystalline solid. R_f = 0.23 (20% DCM/methanol). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.27 (s, 1H, NH), 12.10 (s, 1H), 9.18 (d, *J* = 2.1 Hz, 1H), 9.13 (dd, *J* = 4.5, 1.6 Hz, 1H), 8.64 (dd, *J* = 8.0, 1.6 Hz, 1H), 8.07 (dd, *J* = 8.6, 2.2 Hz, 1H), 7.76 (dd, *J* = 8.0, 4.6 Hz, 1H), 7.56 (d, *J* = 8.7 Hz, 1H), 1.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.24, 161.60, 154.95, 150.01, 141.84, 136.40, 133.34, 130.28, 125.26, 124.80, 122.16, 119.02, 117.11, 23.70. $C_{14}H_{11}N_3O_4S$. HRMS m/z (ESI+, M+Na): Calcd for $C_{14}H_{11}N_3O_4S$ 340.0362. Found (ESI+, M+Na): 340.0350

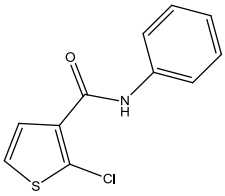
2.5 General procedure of the preparation of *N*-phenylthiophene-3-carboxamides

A round-bottom flask with magnetic stir-bar was cleaned and oven-dried. The carboxylic acid (1 equiv.) was dissolved in dimethylformamide (DMF) (0.5 mL per 0.1mmol reagent) with 1-[bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate

(HATU) (1 equiv.). *N*,*N*-diisopropylethylamine (DIPEA) was added afterward and the resulting solution was stirred for 2 minutes at room temperature. The corresponding aniline (1 equiv.) was added to the solution and the resulting reaction mixture was stirred at room temperature overnight, however, 4 hours was sufficient in most cases. The solvent DMF was removed by vacuum after the residue was absorbed on silica gel. The dry crude product loaded on silica gel was separated and purified by column chromatography (Teledyne Isco CombiFlash® Rf). The cleanest fractions were combined and the solvent was then removed under vacuum and purified product was then dried in the oven.

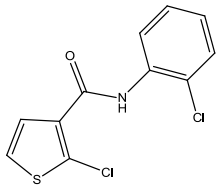
2.6 Characterization of *N*-phenylthiophene-carboxamides

2-Chloro-*N*-phenylthiophene-3-carboxamide (for entry 1)



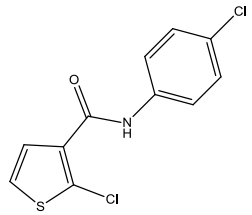
Starting material 2-chlorothiophene-3-carboxylic acid (32.5 mg, 0.2 mmol), HATU (76.1 mg, 0.2 mmol) and aniline (18.7 mg, 0.2 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (36.9 mg, 78%) as a white crystalline solid. R_f = 0.76 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.50 (d, *J* = 5.9 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.19 (m, 1H), 7.17 (d, 8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.50, 137.47, 133.51, 129.27, 129.22, 129.16, 124.82, 123.19, 120.24. $C_{11}H_8ClNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_8ClNNaOS$: 259.9907. Found (ESI+, M+Na): 259.9917.

2-Chloro-*N*-(2-chlorophenyl)thiophene-3-carboxamide (for entry 2)



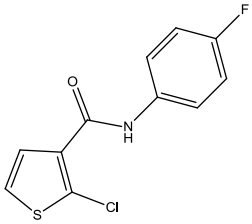
Starting material 2-chlorothiophene-3-carboxylic acid (32.4 mg, 0.2 mmol), HATU (76.1 mg, 0.2 mmol) and 2-chloroaniline (25.6 mg, 0.2 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (27.5 mg, 51%) as a white crystalline solid. R_f = 0.57 (Hexane: Ethyl acetate = 1: 1).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.58 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.53 (d, *J* = 5.9 Hz, 1H), 7.44 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.37 – 7.32 (m, 1H), 7.18 (d, *J* = 5.9 Hz, 1H), 7.11 (td, *J* = 7.7, 1.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.38, 134.66, 133.19, 130.12, 129.38, 129.17, 127.80, 124.91, 123.17, 123.04, 121.80. $C_{11}H_7Cl_2NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_7Cl_2NNaOS$ 293.9518. Found (ESI+, M+Na): 293.9516.

2-Chloro-*N*-(4-chlorophenyl)thiophene-3-carboxamide (for entry 3)



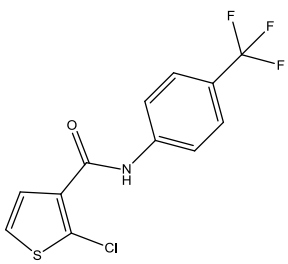
Starting material 2-chlorothiophene-3-carboxylic acid (32.5 mg, 0.2 mmol), HATU (76.1 mg, 0.2 mmol) and 4-chloroaniline (25.5 mg, 0.2 mmol) was treated according to the general procedure. Purification CombiFlash® Rf afforded the title compound (27.3 mg, 50%) as a white crystalline solid. R_f = 0.79 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.64 – 7.58 (m, 2H), 7.48 (d, *J* = 5.9 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.17 (d, *J* = 5.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.48, 136.04, 133.16, 129.80, 129.46, 129.16, 123.32, 121.46. $C_{11}H_7Cl_2NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_7Cl_2NNaOS$ 293.9518. Found (ESI+, M+Na): 293.9510.

2-Chloro-*N*-(4-fluorophenyl)thiophene-3-carboxamide (for entry 4)



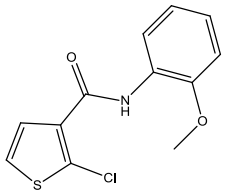
Starting material 2-chlorothiophene-3-carboxylic acid (48.8 mg, 0.3 mmol), HATU (114.0 mg, 0.3 mmol) and 4-fluoroaniline (33.5 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rfafforded the title compound (56.1 mg, 73%) as a white crystalline solid. R_f = 0.76 (Hexane: Ethyl acetate = 1: 1).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.66 – 7.56 (m, 2H), 7.48 (d, *J* = 5.9 Hz, 1H), 7.17 (d, *J* = 5.9 Hz, 1H), 7.12 – 7.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.68 (d, *J* = 243 Hz), 159.54, 133.44 (d, *J* = 3 Hz), 133.26, 129.36, 129.17, 123.26, 122.12 (d, *J* = 8 Hz), 115.82 (d, *J* = 23 Hz) $C_{11}H_7ClFNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_7ClFNNaOS$ 277.9813. Found (ESI+, M+Na): 277.9812.

2-Chloro-*N*-(4-(trifluoromethyl)phenyl)thiophene-3-carboxamide (for entry 5)



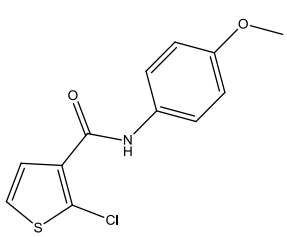
Starting material 2-chlorothiophene-3-carboxylic acid (32.4 mg, 0.2 mmol), HATU (76.0 mg, 0.2 mmol) and 4-(trifluoromethyl)aniline (32.1 mg, 0.2 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (50.7 mg, 55%) as a white crystalline solid. R_f = 0.80 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.79 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.50 (d, *J* = 5.9 Hz, 1H), 7.19 (d, *J* = 5.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.61, 140.52, 132.95, 129.78, 129.18, 126.53 (d, *J* = 3.3 Hz), 126.41 (d, *J* = 3.8 Hz), 124.03 (d, *J* = 269.6 Hz), 123.47, 119.80. $C_{12}H_7ClF_3NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_7ClF_3NNaOS$ 304.9781. Found (ESI+, M+Na): 327.9778.

2-Chloro-*N*-(2-methoxyphenyl)thiophene-3-carboxamide (for entry 6)



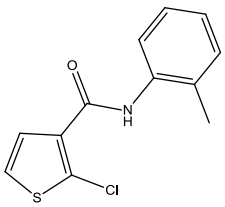
Starting material 2-chlorothiophene-3-carboxylic acid (48.9 mg, 0.3 mmol), HATU (114.2 mg, 0.3 mmol) and 2-methoxyaniline (37.5 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (63 mg, 78%) as a white crystalline solid. R_f = 0.82 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 8.53 (d, *J* = 7.9 Hz, 1H), 7.51 (d, *J* = 5.9 Hz, 1H), 7.15 (d, *J* = 5.9 Hz, 1H), 7.14 – 7.09 (m, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.27, 148.22, 133.88, 129.47, 129.30, 127.61, 124.08, 122.91, 121.22, 120.05, 110.07, 55.94. $C_{12}H_{10}ClNO_2S$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_{10}ClNNaO_2S$ 267.0013. Found (ESI+, M+Na): 290.0007.

2-Chloro-*N*-(4-methoxyphenyl)thiophene-3-carboxamide (for entry 7)



Starting material 2-chlorothiophene-3-carboxylic acid (48.9 mg, 0.3 mmol), HATU (114.2 mg, 0.3 mmol) and 4-methoxyaniline (37.1 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (70.9 mg, 88%) as a white crystalline solid. R_f = 0.73 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.59 – 7.52 (m, 2H), 7.47 (d, *J* = 5.9 Hz, 1H), 7.15 (d, *J* = 5.8 Hz, 1H), 6.96 – 6.89 (m, 2H), 3.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.46, 156.79, 133.55, 130.52, 129.22, 129.05, 123.10, 122.10, 114.27, 55.53. $C_{12}H_{10}ClNO_2S$. HRMS m/z (ESI+, M+Na): $C_{12}H_{10}ClNNaO_2S$ 267.0120. Found (ESI+, M+Na): 290.0007.

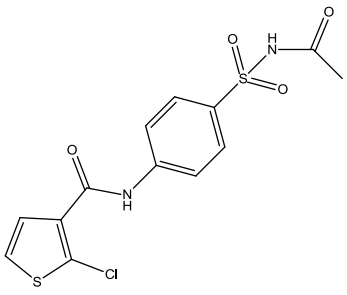
2-Chloro-*N*-(o-tolyl)thiophene-3-carboxamide (for entry 8)



Starting material 2-chlorothiophene-3-carboxylic acid (48.8 mg, 0.3 mmol), HATU (114.0 mg, 0.3 mmol) and *o*-toluidine (32.3 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (74 mg, 98%) as a white crystalline solid. R_f = 0.80 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 7.54 (d, *J* = 5.8 Hz, 1H), 7.32 – 7.24 (m, 2H), 7.18 (d, *J* = 5.9 Hz, 1H), 7.14 (t, *J* = 7.5 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.45, 135.64, 133.71, 130.57, 129.70,

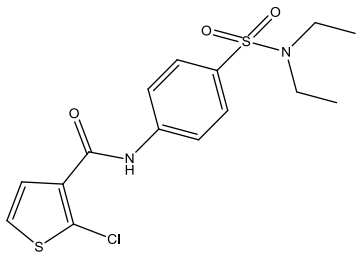
128.89, 128.66, 126.91, 125.28, 123.12, 122.77, 18.24. $C_{12}H_{10}ClNOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_{10}ClNNaOS$ 274.0064. Found (ESI+, M+Na): 274.0060.

_N_-(4-(_N_-Acetylsulfamoyl)phenyl)-2-chlorothiophene-3-carboxamide (for entry 9)



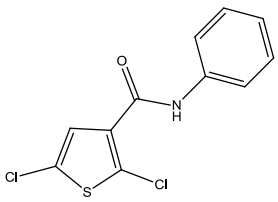
Starting material 2-chlorothiophene-3-carboxylic acid (49.0 mg, 0.3 mmol), HATU (114.2 mg, 0.3 mmol) and _N_-((4-aminophenyl)sulfonyl)acetamide (66.4 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (73.2 mg, 68%) as a white crystalline solid. R_f = 0.72 (Dichloromethane: Methanol = 5: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 10.69 (s, 1H), 7.95 – 7.88 (m, 4H), 7.60 (dd, _J_ = 5.8, 2.7 Hz, 1H), 7.41 (dd, _J_ = 5.8, 2.7 Hz, 1H), 1.92 (d, _J_ = 2.5 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.17, 161.39, 143.74, 134.17, 134.06, 131.21, 129.30, 127.90, 125.45, 119.88, 23.67. $C_{13}H_{11}ClN_2O_4S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{13}H_{11}ClN_2NaO_4S_2$ 380.9741. Found (ESI+, M+Na): 380.9741.

2-Chloro-_N_-(4-(_N_,_N_-diethylsulfamoyl)phenyl)thiophene-3-carboxamide (for entry 10)



Starting material 2-chlorothiophene-3-carboxylic acid (32.4 mg, 0.2 mmol), HATU (76.2 mg, 0.2 mmol) and 4-amino-_N_-(pentan-3-yl)benzenesulfonamide (46.0 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (38.2 mg, 82 %) as a white crystalline solid. R_f = 0.64 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.84 – 7.77 (m, 4H), 7.49 (d, _J_ = 5.9 Hz, 1H), 7.20 (d, _J_ = 5.9 Hz, 1H), 3.26 (q, _J_ = 7.1 Hz, 4H), 1.15 (t, _J_ = 7.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.65, 141.04, 135.87, 132.82, 130.03, 129.09, 128.34, 123.54, 119.87, 42.04, 14.16. $C_{15}H_{17}ClN_2O_3S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{15}H_{17}ClN_2NaO_3S_2$ 395.0261. Found (ESI+, M+Na): 395.0260.

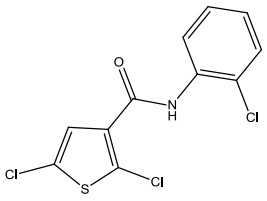
2,5-Dichloro-_N_-phenylthiophene-3-carboxamide (for entry 11)



Starting material 2,5-dichlorothiophene-3-carboxylic acid (60.1 mg, 0.3 mmol), HATU (114.4 mg, 0.3 mmol) and aniline (28.5 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (65 mg, 80%) as a white crystalline solid.

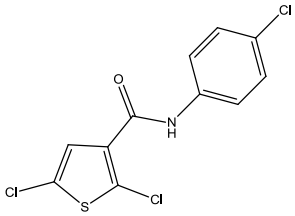
R_f = 0.92 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.31 (s, 1H), 7.23 – 7.17 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.47, 137.15, 133.55, 129.19, 127.89, 127.28, 126.15, 125.06, 120.32. $C_{11}H_7Cl_2NNaOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_7Cl_2NOS$ 293.9518. Found (ESI+, M+Na): 293.9512

2,5-Dichloro-*N*-(2-chlorophenyl)thiophene-3-carboxamide (for entry 12)



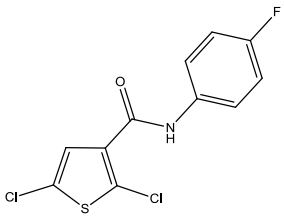
Starting material 2,5-dichlorothiophene-3-carboxylic acid (60.9 mg, 0.3 mmol), HATU (114.1 mg, 0.3 mmol) and 2-chloroaniline (39.0 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (61.6 mg, 67%) as a white crystalline solid. R_f = 0.94 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.54 (dd, J= 8.4 Hz, 0.8 Hz, 1H), 7.44 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.36 (s, 1 Hz), 7.34 (t, J = 6.8 Hz, 1H), 7.12 (td, *J* = 7.8, 1.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.29, 134.39, 133.23, 129.20, 128.06, 127.84, 127.22, 126.91, 125.15, 123.06, 121.83. $C_{11}H_6Cl_3NNaOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_6Cl_3NOS$ 327.9128. Found (ESI+, M+Na): 327.9115.

2,5-Dichloro-*N*-(4-chlorophenyl)thiophene-3-carboxamide (for entry 13)



Starting material 2,5-dichlorothiophene-3-carboxylic acid (59.5 mg, 0.3 mmol), HATU (114.0 mg, 0.3 mmol) and 4-chloroaniline (38.7 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (87.2 mg, 95%) as a white crystalline solid. R_f = 0.94 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.58 (d, *J* = 8.7 Hz, 2H), 7.35 (d, *J* = 8.7 Hz, 2H), 7.30 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.43, 135.71, 133.20, 130.09, 129.22, 127.82, 127.45, 126.34, 121.53. ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.45, 135.64, 133.71, 130.57, 129.70, 128.89, 128.66, 126.91, 125.28, 123.12, 122.77, 18.24. $C_{11}H_6Cl_3NOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_6Cl_3NNaOS$ 327.9128. Found (ESI+, M+Na): 327.9119

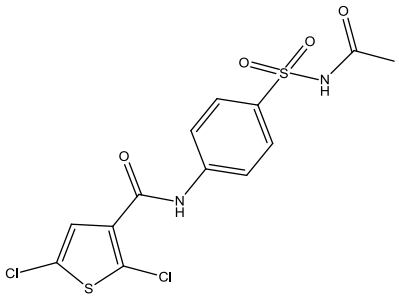
2,5-dichloro-*N*-(4-fluorophenyl)thiophene-3-carboxamide (for entry 14)



Starting material 2.5-dichlorothiophene-3-carboxylic acid (59.3 mg, 0.3 mmol), HATU (114.2 mg, 0.3 mmol) and 4-fluoroaniline (33.3 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (78.9 mg, 91%) as a white

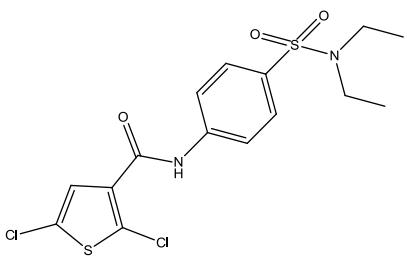
crystalline solid. R_f = 0.64 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.62 – 7.54 (m, 2H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.12 – 7.05 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.83 (d, *J* = 243.1 Hz), 158.46, 133.34, 133.12 (d, *J* = 2.9 Hz), 127.85, 127.39, 126.19, 122.23 (d, *J* = 7.9 Hz), 115.87 (d, *J* = 22.5 Hz) $C_{11}H_7Cl_2FNNaOS$. HRMS m/z (ESI+, M+Na): Calcd for $C_{11}H_7Cl_2FNNaOS$ 311.9423. Found (ESI+, M+Na): 311.9413

_N_-(4-(_N_-Acetylsulfamoyl)phenyl)-2,5-dichlorothiophene-3-carboxamide (for entry 15)



Starting material 2,5-dichlorothiophene-3-carboxylic acid (59.6 mg, 0.3 mmol), HATU (114.2 mg, 0.3 mmol) and *N*-((4-aminophenyl)sulfonyl)acetamide (66.5 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (60.0mg, 50%) as a white crystalline solid. R_f = 0.71 (Dichloromethane: Methanol = 5: 1). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 10.73 (s, 1H), 7.91 (s, 4H), 7.55 (s, 1H), 1.92 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.18, 160.08, 143.47, 134.28, 134.17, 129.35, 128.81, 127.59, 125.95, 119.91, 23.67. $C_{13}H_{11}Cl_2N_2O_4S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{13}H_{11}Cl_2N_2NaO_4S_2$ 414.9351. Found (ESI+, M+Na): 414.9344

2,5-Dichloro-_N_-(4-(_N_,_N_-diethylsulfamoyl)phenyl)thiophene-3-carboxamide (for entry 16)



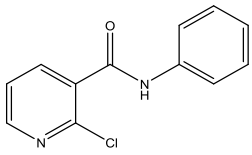
Starting material 2,5-dichlorothiophene-3-carboxylic acid (60.7 mg, 0.3 mmol), HATU (114.2 mg, 0.3 mmol) and 4-amino-*N*-(pentan-3-yl)benzenesulfonamide (68.9 mg, 0.3 mmol) was treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (106.2 mg, 87%) as a white crystalline solid. R_f = 0.94 (Hexane: Ethyl acetate = 1: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.79 (dd, *J* = 22.1, 8.8 Hz, 4H), 7.30 (d, *J* = 11.5 Hz, 1H), 3.26 (q, *J* = 7.1 Hz, 4H), 1.16 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.60, 140.75, 136.21, 132.90, 128.34, 127.68, 126.98, 119.97, 42.04, 14.14. $C_{15}H_{17}Cl_2N_2NaO_3S_2$. HRMS m/z (ESI+, M+Na): Calcd for $C_{15}H_{17}Cl_2N_2O_3S_2$ 428.9872. Found (ESI+, M+Na): 428.9859.

2.7 General procedure of the preparation of *N*-phenylnicotinamides

A round-bottom flask with magnetic stir-bar was cleaned and oven-dried. The corresponding acyl chloride (1.1 equiv.) and aniline (1 equiv.) were dissolved in tetrahydrofuran (THF) (5mL per 1mmol reagent) respectively to make two solutions, one of acyl chloride and one of the aniline. The solution of aniline was introduced to the flask and stirred in ice bath at 0℃ for 5 minutes. Triethylamine (1 equiv.) was added to the solution of aniline followed by addition of the solution of acyl chloride drop by drop at 0℃. The resulting reaction mixture was stirred at r.t. for overnight after removing the ice bath, but in most cases 5 hours was sufficient to produce good yields of product. The resulting product was filtered twice to remove the solid which was washed by THF. THF was then removed from the solution of crude product by vacuum and the residue was absorbed on silica gel, and purified by column chromatography (CombiFlash® Rf). Pure product fraction were carefully selected and the purified product was then dried under vacuum to afford a product that was ready to use in the flow photocyclization reaction.

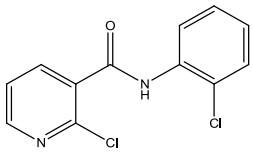
2.8 Characterization of *N*-phenylnicotinamides

2-Chloro-*N*-phenylnicotinamide (for entry 17)



Aniline (93.1 mg, 1 mmol) and 2-chloronicotinoyl chloride (186 mg, 1.05 mmol) were treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (76.2 mg, 23%) as a white crystalline solid. R_f=0.37 (50% Ethyl acetate/hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (dd, *J* = 4.8, 2.0 Hz, 1H), 8.30 (s, 1H), 8.17 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.66 (dd, *J* = 8.5, 1.0 Hz, 2H), 7.41 (m, 3H), 7.25 – 7.19 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.71, 151.29, 146.98, 139.91, 137.15, 131.51, 129.22, 125.32, 122.96, 120.32. Known compound: Cuffini, Silvia, et al. Nine *N*-aryl-2-chloronicotinamides: supramolecular structures in one, two and three dimensions. *Acta Crystallographica Section B: Structural Science*, **2006**, 651-665.

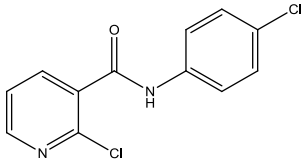
2-Chloro-*N*-(2-chlorophenyl)nicotinamide (for entry 18)



2-Chloroaniline (128 mg, 1 mmol) and 2-chloronicotinoyl chloride (183 mg, 1 mmol) were treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (230 mg, 86%) as a white crystalline solid. R_f=0.44 (50% Ethyl acetate/hexane).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.83 (s, 1H, NH), 8.57 (m, 2H), 8.29 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.46 (m, 2H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.16 (td, *J* = 7.9, 1.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.47, 151.61, 147.06,

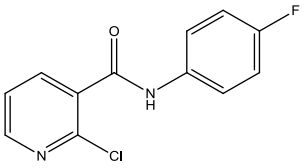
140.43, 134.21, 130.96, 129.31, 127.87, 125.57, 123.47, 123.00, 121.97. $C_{12}H_8Cl_2N_2O$. HRMS m/z (ESI+, M+Na): Calcd for $C_{12}H_8Cl_2N_2NaO$ 288.9906. Found (ESI+, M+Na): 288.9907.

2-Chloro-*N*-(4-chlorophenyl)nicotinamide (for entry 19)



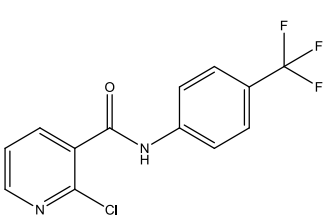
4-Chloroaniline (128 mg, 1 mmol) and 2-chloronicotinoyl chloride (185 mg, 1 mmol) were treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (245 mg, 92%) as a white crystalline solid. R_f=0.25 (50% Ethyl acetate/hexane).^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 4.7, 1.9 Hz, 1H), 8.27 (s, 1H, NH), 8.21 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 2H), 7.42 (dd, *J* = 7.7, 4.8 Hz, 1H), 7.40 – 7.36 (d, J = 8.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.54, 151.49, 146.91, 140.13, 135.70, 131.08, 130.41, 129.28, 123.01, 121.56. Known compound: Cuffini, Silvia, et al. Nine *N*-aryl-2-chloronicotinamides: supramolecular structures in one, two and three dimensions. *Acta Crystallographica Section B: Structural Science,* **2006**, 651-665.

2-Chloro-*N*-(4-fluorophenyl)nicotinamide (for entry 20)



4-Fluoroaniline (111 mg, 1 mmol) and 2-chloronicotinoyl chloride (185 mg, 1 mmol) were treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (200 mg, 80%) as a white crystalline solid. R_f=0.22 (50% Ethyl acetate/hexane).^{1}H NMR (400 MHz, DMSO-d_6) δ 10.69 (s, 1H), 8.55 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.09 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.78 – 7.68 (m, 2H), 7.57 (dt, *J* = 15.9, 7.9 Hz, 1H), 7.27 – 7.17 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 163.92, 160.13, 157.74, 151.03, 146.94, 138.67, 135.55, 135.52, 133.52, 123.65, 121.91, 121.84, 116.08, 115.86. Known compound: Cuffini, Silvia, et al. Nine *N*-aryl-2-chloronicotinamides: supramolecular structures in one, two and three dimensions. *Acta Crystallographica Section B: Structural Science,* **2006**, 651-665.

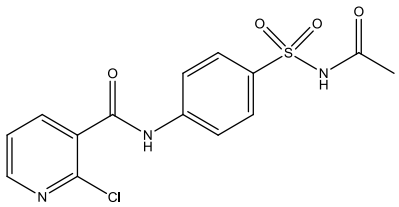
2-Chloro-*N*-(4-(trifluoromethyl)phenyl)nicotinamide (for entry 21)



2-(Trifluoromethyl)aniline (161 mg, 1 mmol) and 2-chloronicotinoyl chloride (184 mg, 1 mmol) were treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (228 mg, 75%) as a white crystalline solid. R_f=0.28 (50% Ethyl acetate/hexane).^{1}H NMR (400 MHz, DMSO-d_6) δ 11.00 (s, 1H,

NH), 8.57 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.13 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.92 (d, *J* = 8.5 Hz, 2H), 7.76 (d, *J* = 8.6 Hz, 2H), 7.60 (dd, *J* = 7.5, 4.8 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.53, 151.26, 146.87, 142.65, 138.76, 133.21, 126.70 (q, *J* = 3.7 Hz), 124.62 (d, *J* = 31.9 Hz), 123.76 (q, *J* = 269.9 Hz) 123.69, 120.04. $C_{13}H_8ClF_3N_2NaO$. HRMS m/z (ESI+, M+Na): Calcd for $C_{13}H_8ClF_3N_2NaO$ 323.0169. Found (ESI+, M+Na): 323.0159.

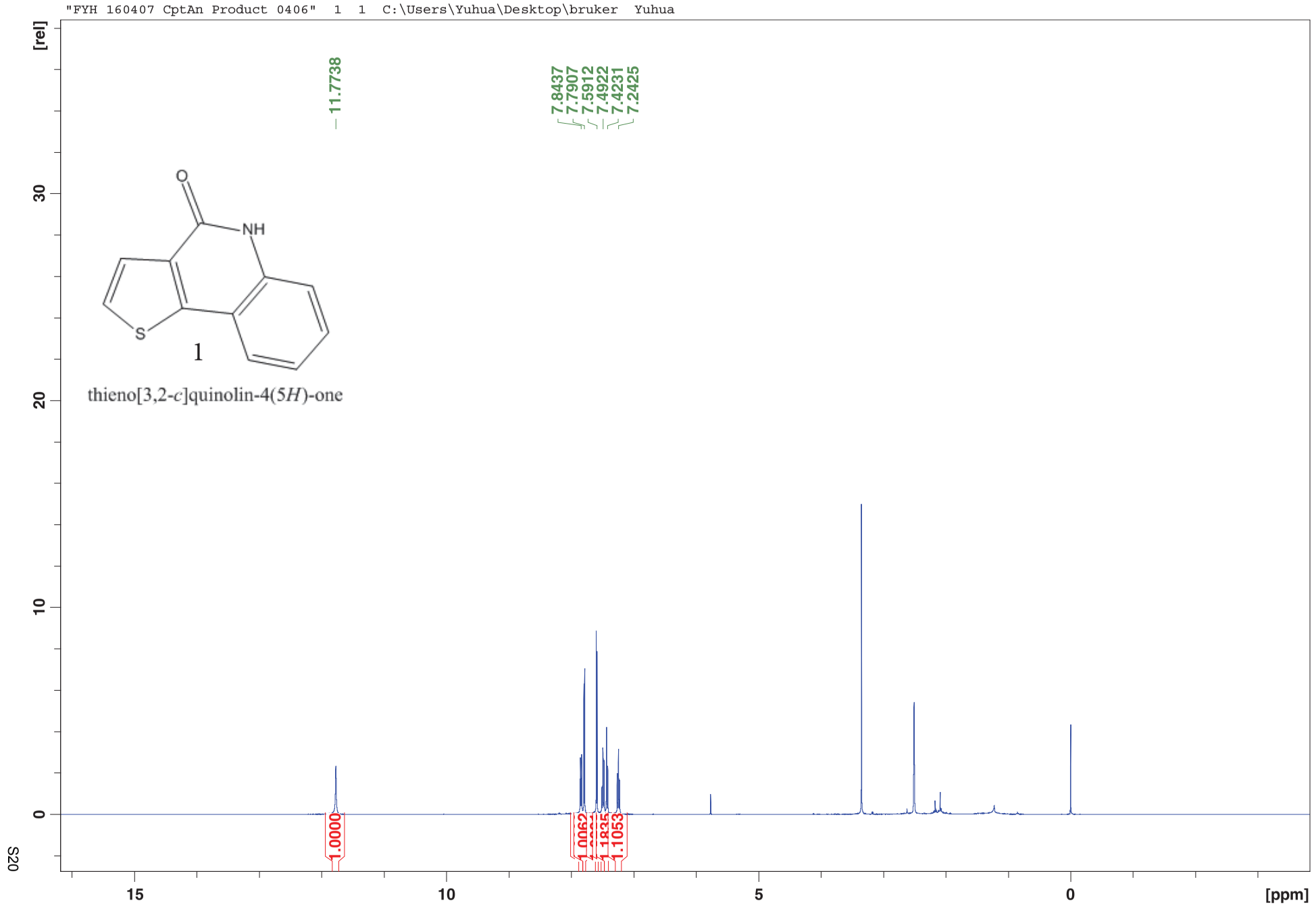
***N*-(4-(*N*-Acetylsulfamoyl)phenyl)-2-chloronicotinamide (for entry 22)**



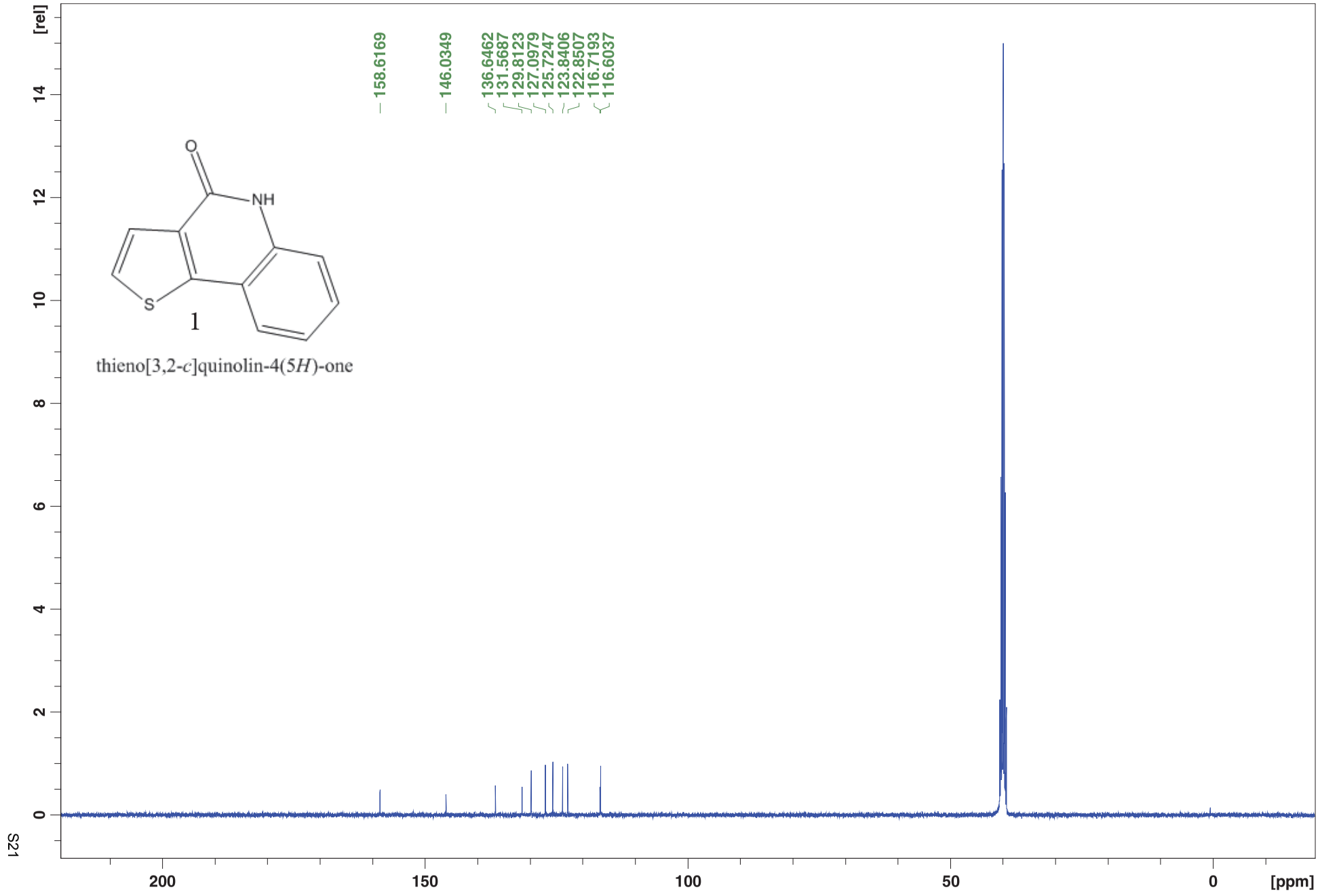
N-((2-Aminobenzyl)sulfonyl)acetamide (229 mg, 1 mmol) and 2-chloronicotinoyl chloride (185 mg, 1 mmol) were treated according to the general procedure. Purification by CombiFlash® Rf afforded the title compound (187 mg, 51%) as a white crystalline solid. R_f=0.66 (20% DCM/methanol).^{1}H NMR (400 MHz, DMSO-d_6) δ 12.01 (s, 1H, NH), 11.09 (s, 1H, NH), 8.61 – 8.53 (m, 1H), 8.12 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.97 – 7.87 (m, 4H), 7.59 (dd, *J* = 7.5, 4.9 Hz, 1H), 1.93 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 169.20, 164.62, 151.29, 146.84, 143.51, 138.76, 134.47, 133.12, 129.48, 123.70, 119.68, 23.65. $C_{14}H_{12}ClN_3NaO_4S$. HRMS m/z (ESI+, M+Na): Calcd for $C_{14}H_{12}ClN_3NaO_4S$ 376.0129. Found (ESI+, M+Na): 376.0117.

3. NMR spectra for listed compounds, ^{1}H and ^{13}C NMR in general order as they appear.

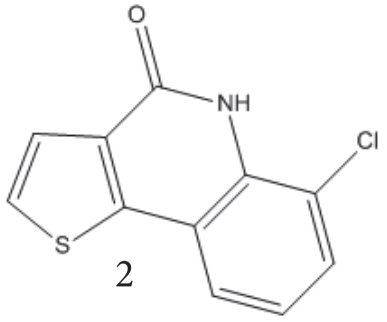
- **a. Title compounds, entries 1 - 22, ^{1}H and ^{13}C NMR**
- **b. Amides for title compounds, entries 1 SM - 22 SM, ^{1}H and ^{13}C NMR**


"FYH 160407 CptAn Product 0406" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
11.7738
7.8437
7.7907
7.5912
7.4922
7.4231
7.2425
O
NH
S
1
thieno[3,2-c]quinolin-4(5H)-one
1.0000
1.0062
1.1835
1.1053
30
20
10
0
15
10
5
0
[ppm]

"FYH 160407 CptAn Product 0406 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



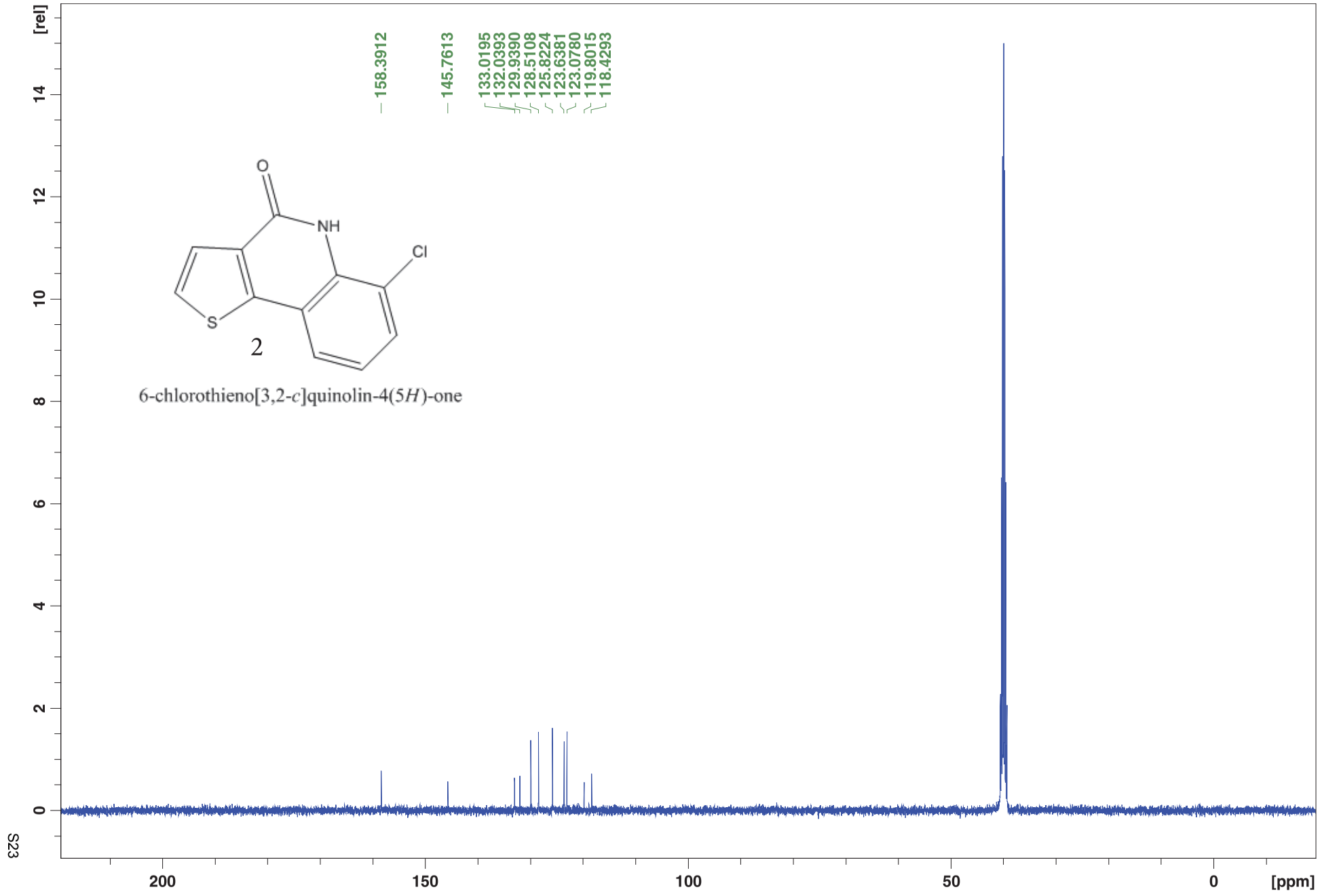
"FYH 160504 CtpCN Product0502" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



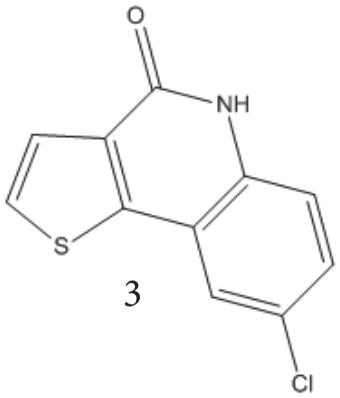
2

6-chlorothieno[3,2-*c*]quinolin-4(5*H*)-one

"FYH 160504 CtpCN Product0502 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



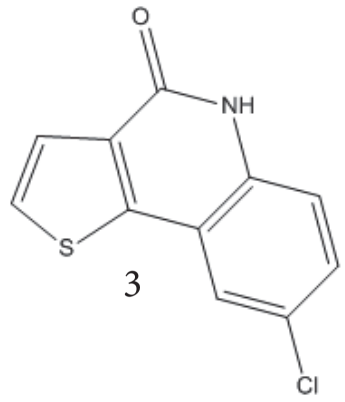
"FYH 160513 CtpAn4Cl Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



3

8-chlorothieno[3,2-*c*]quinolin-4(5*H*)-one

"FYH 160513 CtpAn4Cl Product c13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



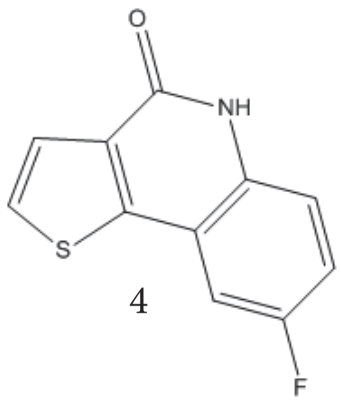
3

8-chlorothieno[3,2-*c*]quinolin-4(5*H*)-one

158.3814
144.6341
135.4086
132.2592
129.6135
128.2939
126.7643
125.7139
122.9303
118.4464
117.9934

[rel]
14
12
10
8
6
4
2
0
200
150
100
50
0
[ppm]

"FYH 160525 CtpAn4F Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



4

8-fluorothieno[3,2-*c*]quinolin-4(5*H*)-one

11.8205

7.8524
7.7404
7.6001
7.4452
7.3858

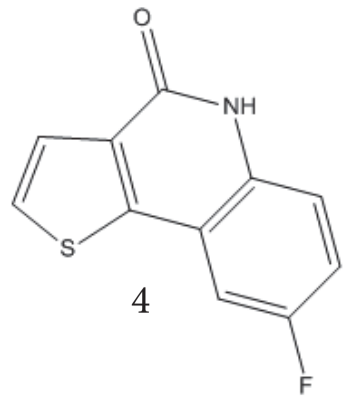
1.0000
1.0344

[rel]

15 10 5 0 [ppm]

"FYH 160525 CtpAn4F Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

158.3380
157.7642
145.0304
133.3235
132.2615
128.1887
125.7577
118.4830
117.5825
117.4779
109.2822



4

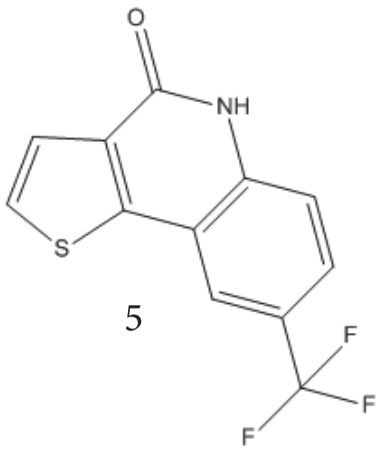
8-fluorothieno[3,2-*c*]quinolin-4(5*H*)-one

[rel]

0 2 4 6 8 10 12 14

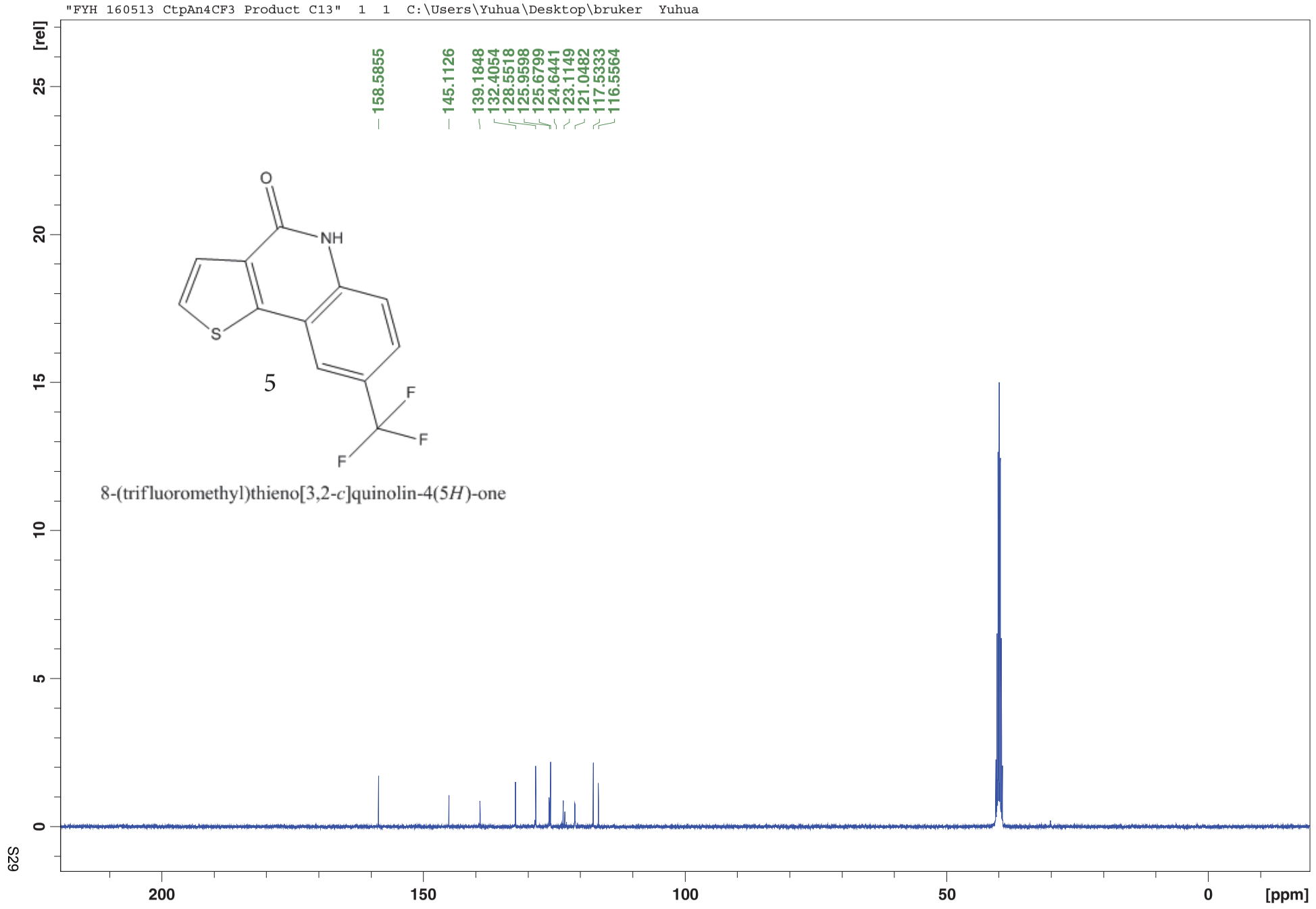
200 150 100 50 0 [ppm]

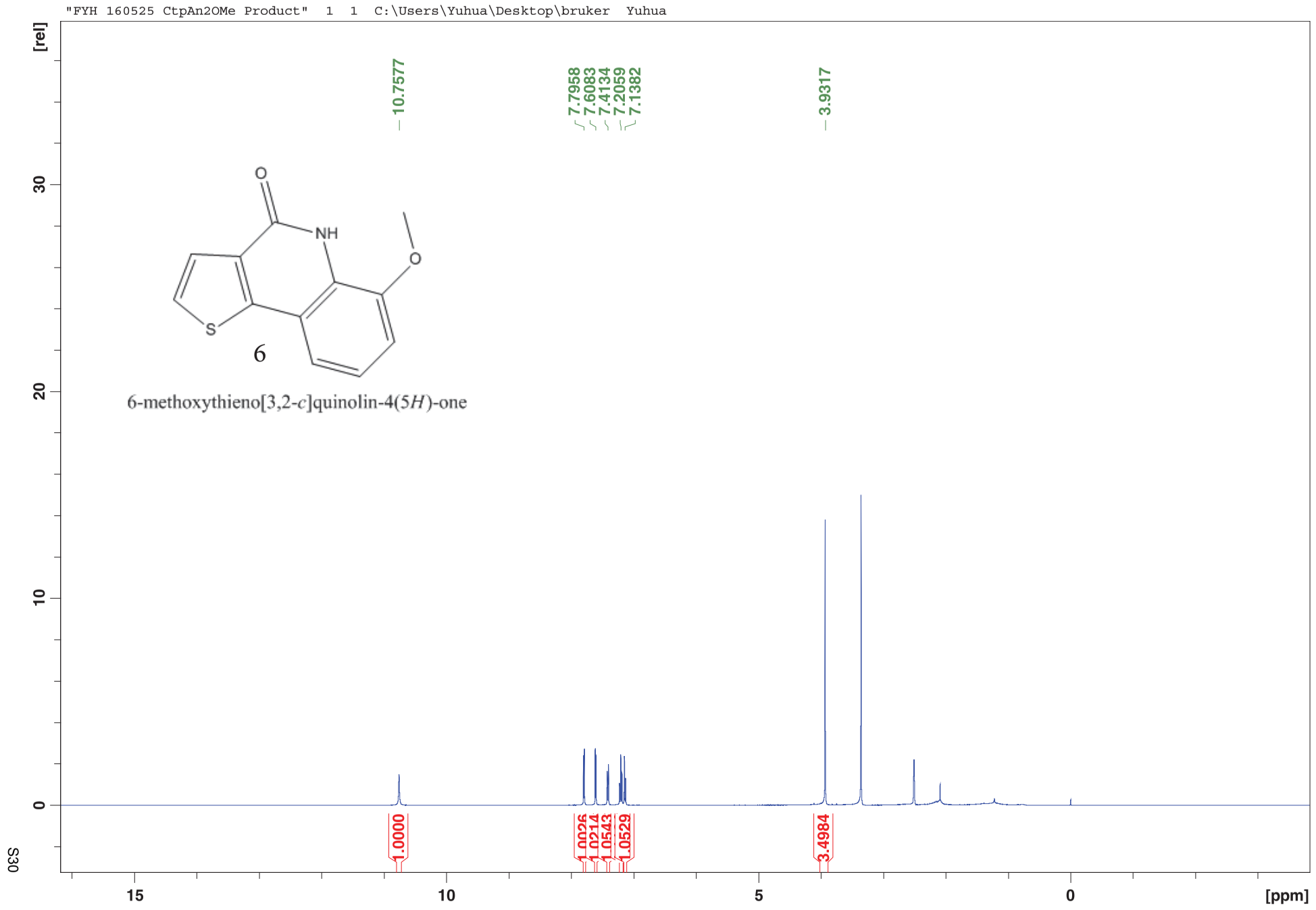
"FYH 160513 CtpAn4CF3 Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



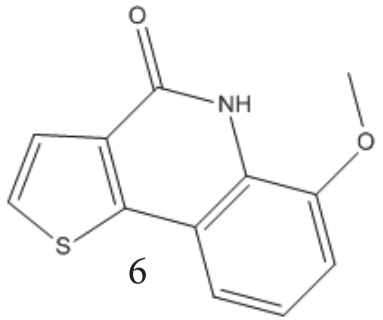
5

8-(trifluoromethyl)thieno[3,2-*c*]quinolin-4(5*H*)-one


"FYH 160513 CtpAn4CF3 Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
158.5855
145.1126
139.1848
132.4054
128.5518
125.9598
125.6799
124.6441
123.1149
121.0482
117.5333
116.5564
O
NH
S
F
F
F
5
8-(trifluoromethyl)thieno[3,2-c]quinolin-4(5H)-one
[rel]
25
20
15
10
5
0
200
150
100
50
0
[ppm]


"FYH 160525 CtpAn2OMe Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
30
20
10
0
10.7577
7.7958
7.6083
7.4134
7.2059
7.1382
3.9317
O
NH
O
S
6
6-methoxythieno[3,2-c]quinolin-4(5H)-one
1.0000
1.0026
1.0214
1.0543
1.0529
3.4984
15
10
5
0
[ppm]

"FYH 160525 CtpAn2OMe Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



6

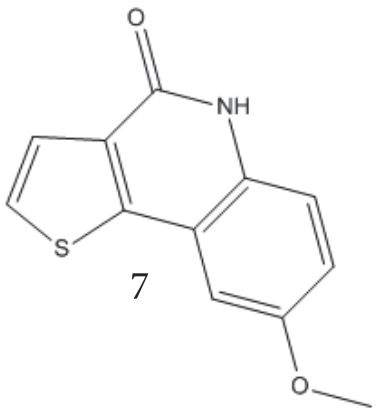
6-methoxythieno[3,2-*c*]quinolin-4(5*H*)-one

146.8867
146.0237
131.9183
127.3802
126.4576
125.9071
123.1396
117.1618
115.6157
110.6337
56.6053

[rel]
0
2
4
6
8
10
12
14

200
150
100
50
0
[ppm]

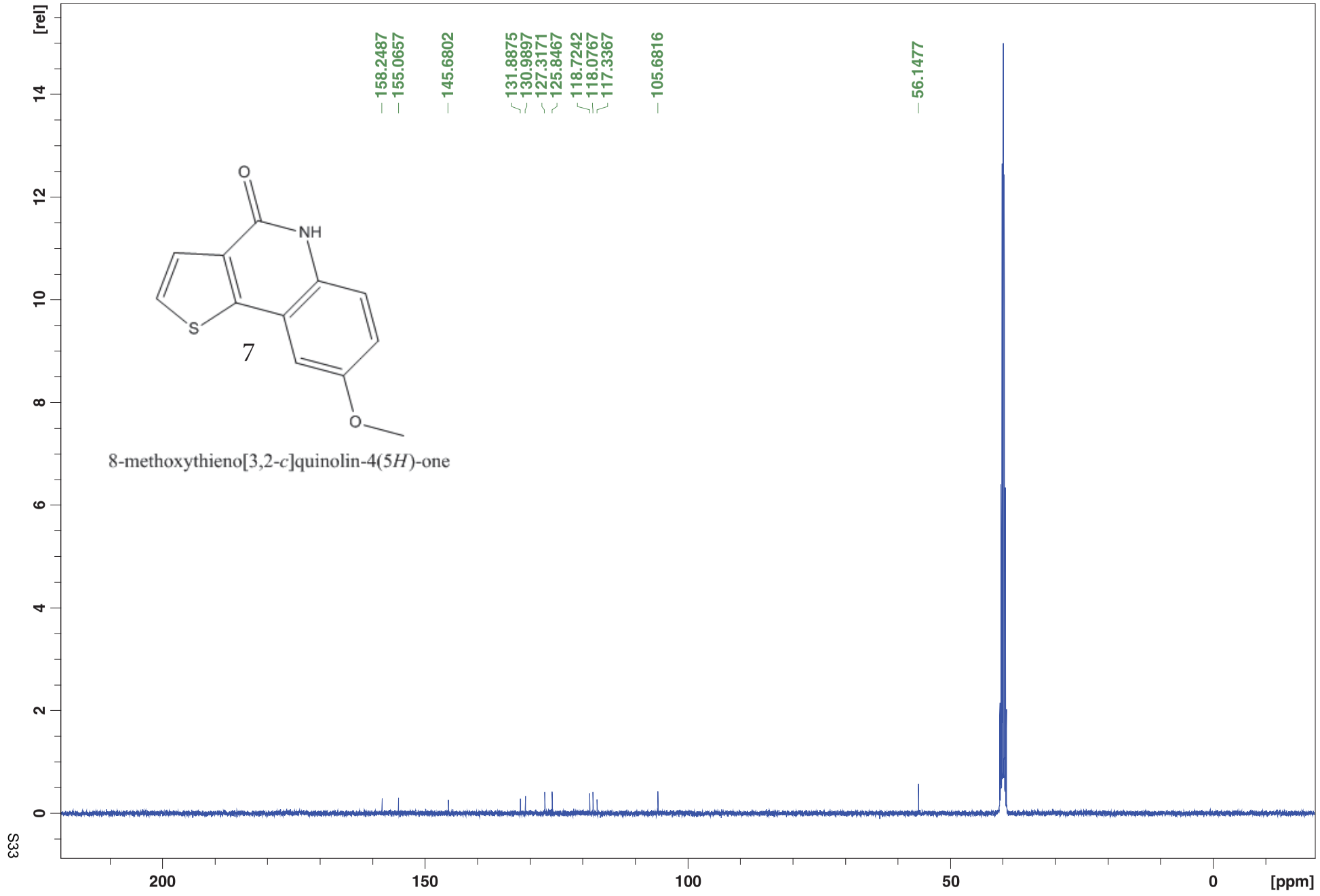
"FYH 160510 CtpAn4OMe Product 0506" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



7

8-methoxythieno[3,2-*c*]quinolin-4(5*H*)-one

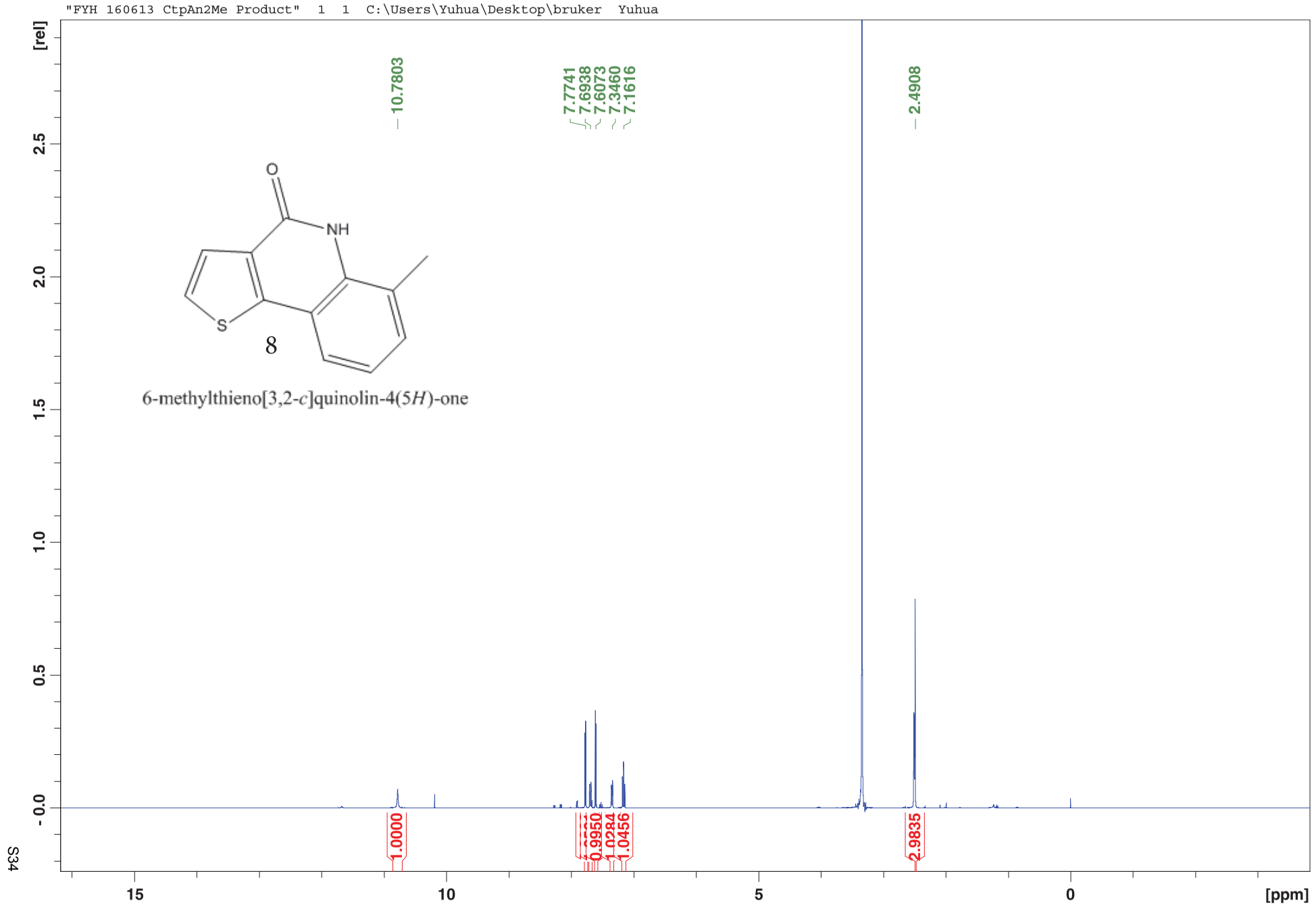
"FYH 160510 CtpAn4OMe Product 0506 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



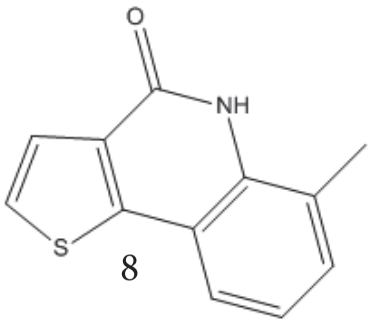
7

8-methoxythieno[3,2-*c*]quinolin-4(5*H*)-one

S33


"FYH 160613 CtpAn2Me Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
2.5
2.0
1.5
1.0
0.5
- 0.0
10.7803
7.7741
7.6938
7.6073
7.3460
7.1616
2.4908
O
NH
S
8
6-methylthieno[3,2-c]quinolin-4(5H)-one
1.0000
0.9950
1.0284
1.0456
2.9835
15
10
5
0
[ppm]

"FYH 160613 CtpAn2Me Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



8

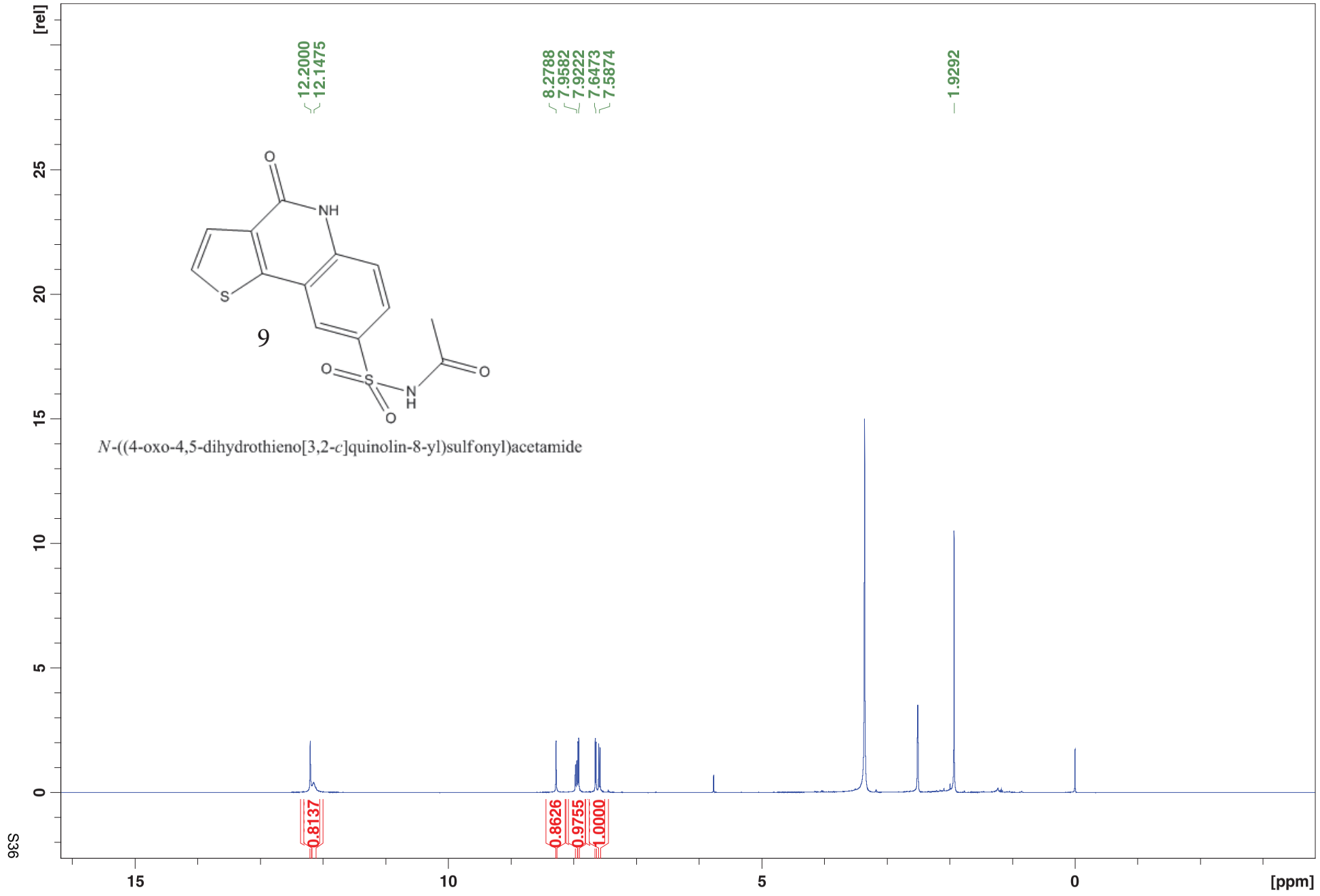
6-methylthieno[3,2-*c*]quinolin-4(5*H*)-one

158.9116
146.7727
134.9909
131.2950
131.1900
127.1387
125.7322
125.0255
122.7165
121.8348
116.7339
18.2206

[rel]
0
2
4
6
8
10
12
14

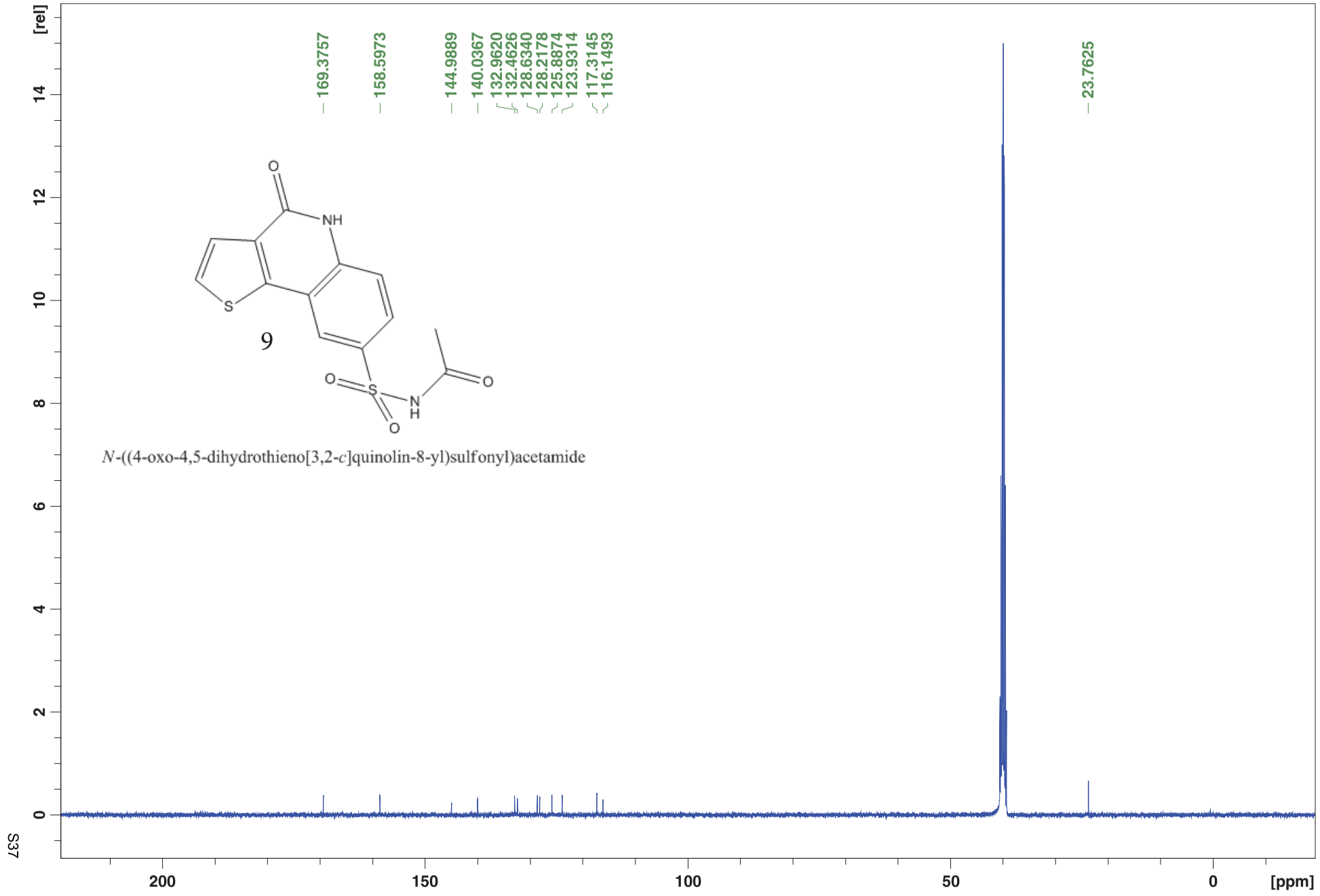
200
150
100
50
0
[ppm]

"FYH 160510 CtpAnSul Product 0506" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



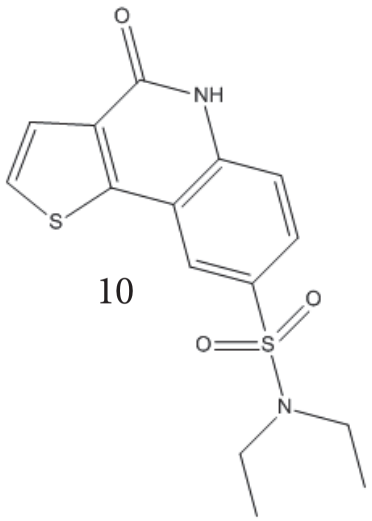
N-((4-oxo-4,5-dihydrothieno[3,2-*c*]quinolin-8-yl)sulfonyl)acetamide

"FYH 160510 CtpAnSul Product 0506 c13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



N-((4-oxo-4,5-dihydrothieno[3,2-*c*]quinolin-8-yl)sulfonyl)acetamide

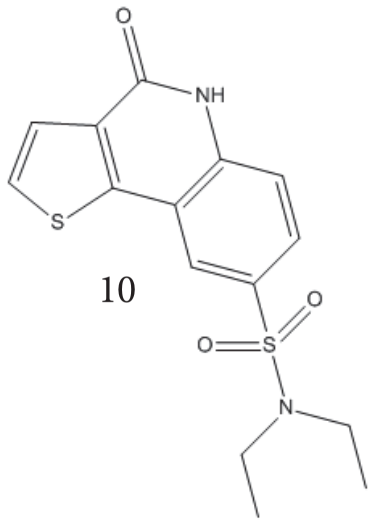
"FYH 160525 CtpAnSfm Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



10

N,*N*-diethyl-4-oxo-4,5-dihydrothieno[3,2-*c*]quinoline-8-sulfonamide

"FYH 160525 CtpAnSfm Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



10

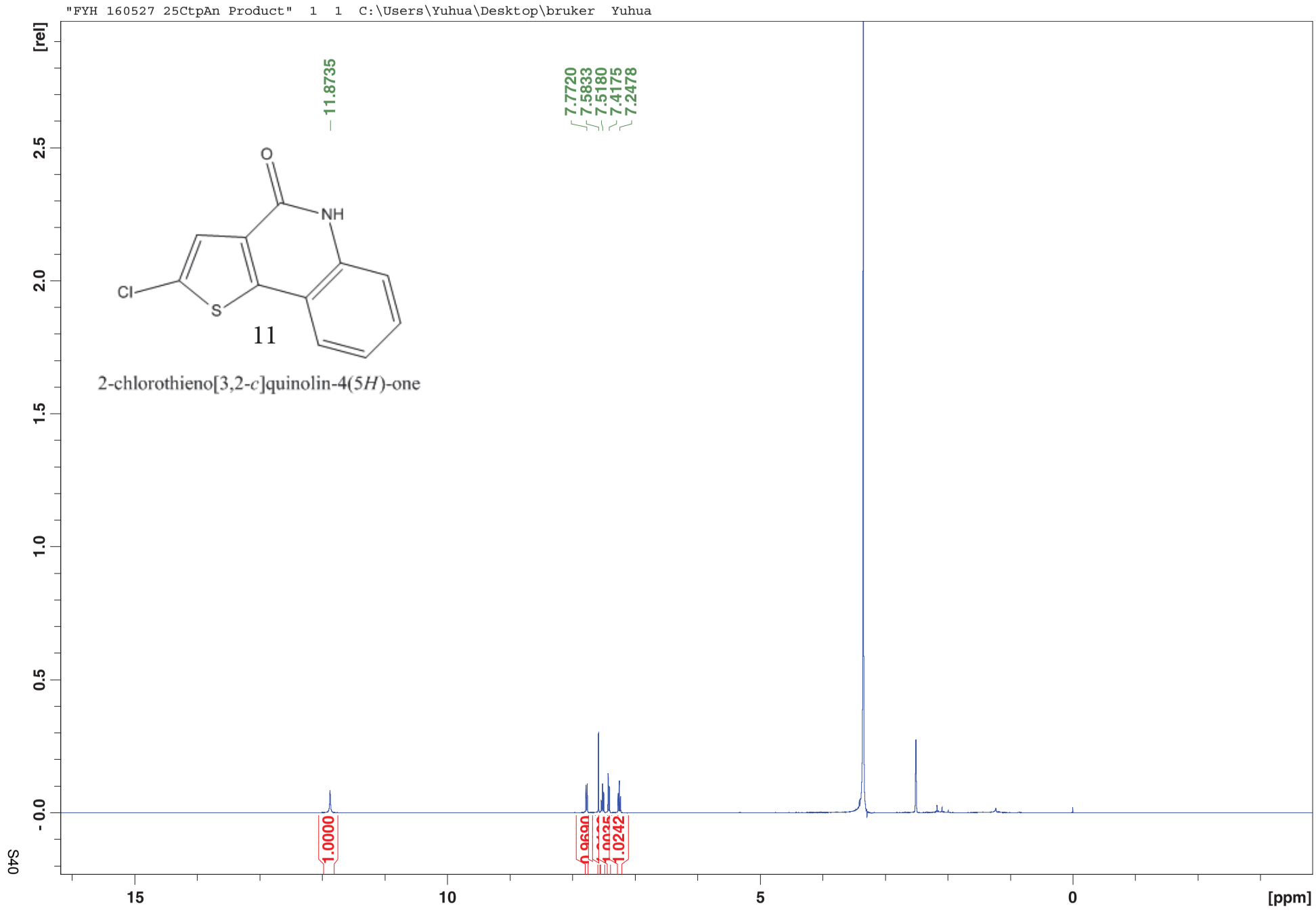
N,*N*-diethyl-4-oxo-4,5-dihydrothieno[3,2-*c*]quinoline-8-sulfonamide

158.5849
145.0777
139.2984
133.8163
132.4953
128.6314
127.6737
125.8243
122.5218
117.7333
116.5444
42.3377
14.6300

[rel]
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]

S39

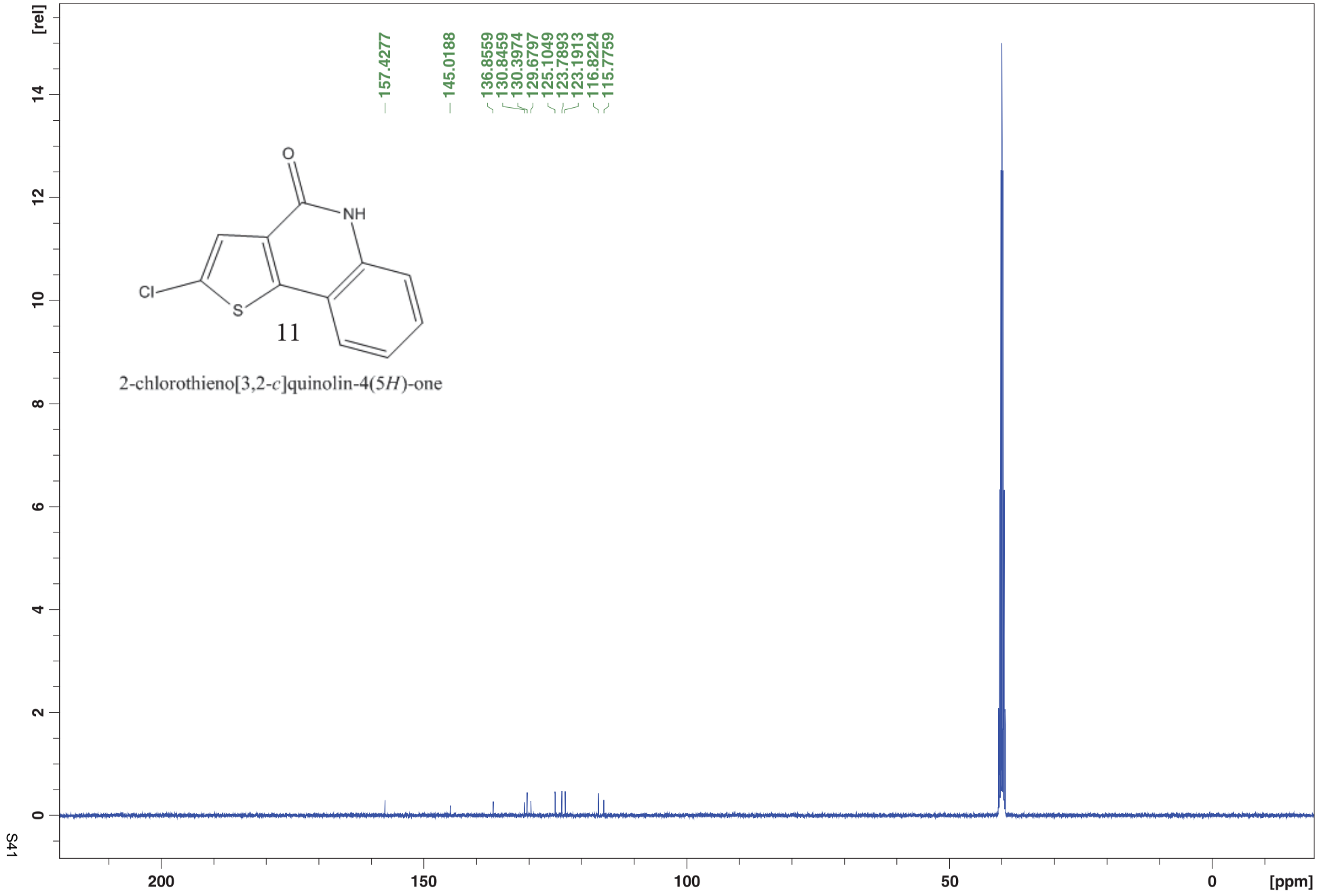
"FYH 160527 25CtpAn Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



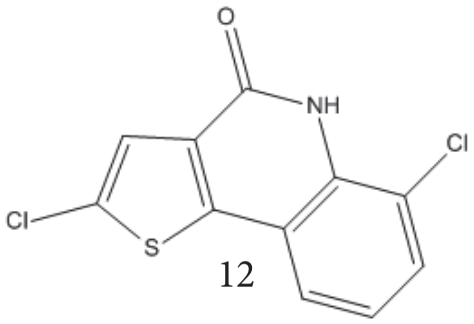
11

2-chlorothieno[3,2-*c*]quinolin-4(5*H*)-one

"FYH 160527 25CtpAn Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



"FYH 160527 25CtpCn Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



12

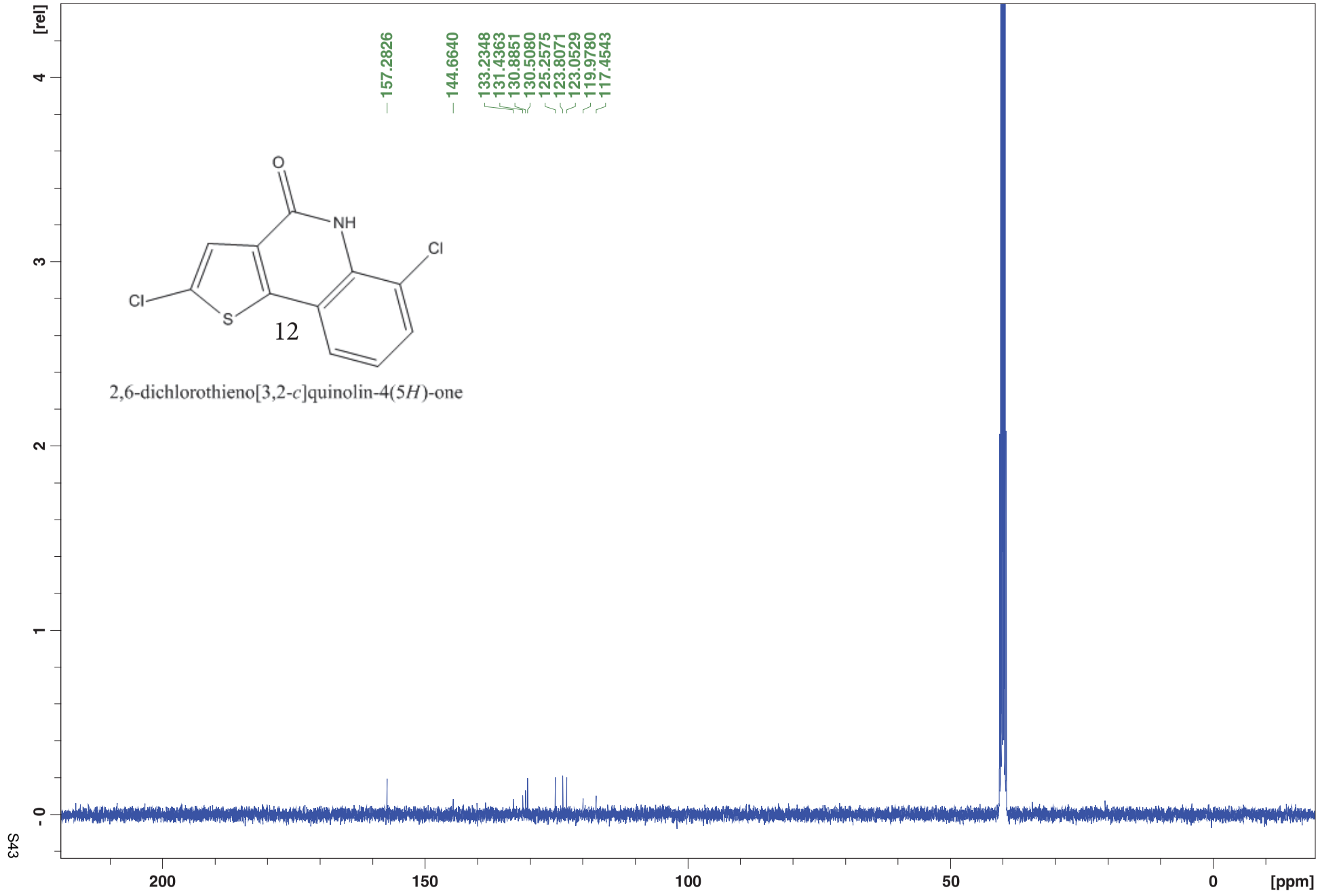
2,6-dichlorothieno[3,2-*c*]quinolin-4(5*H*)-one

11.0746
7.7958
7.6751
7.6575
7.2707

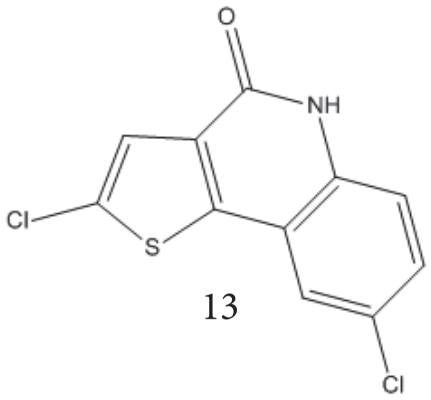
[rel]
4
3
2
1
-0
15
10
5
0
[ppm]

1.0000
1.6730
1.0501

"FYH 160527 25CtpCn Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



"FYH 160525 25CtpAn4Cl Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



13

2,8-dichlorothieno[3,2-*c*]quinolin-4(5*H*)-one

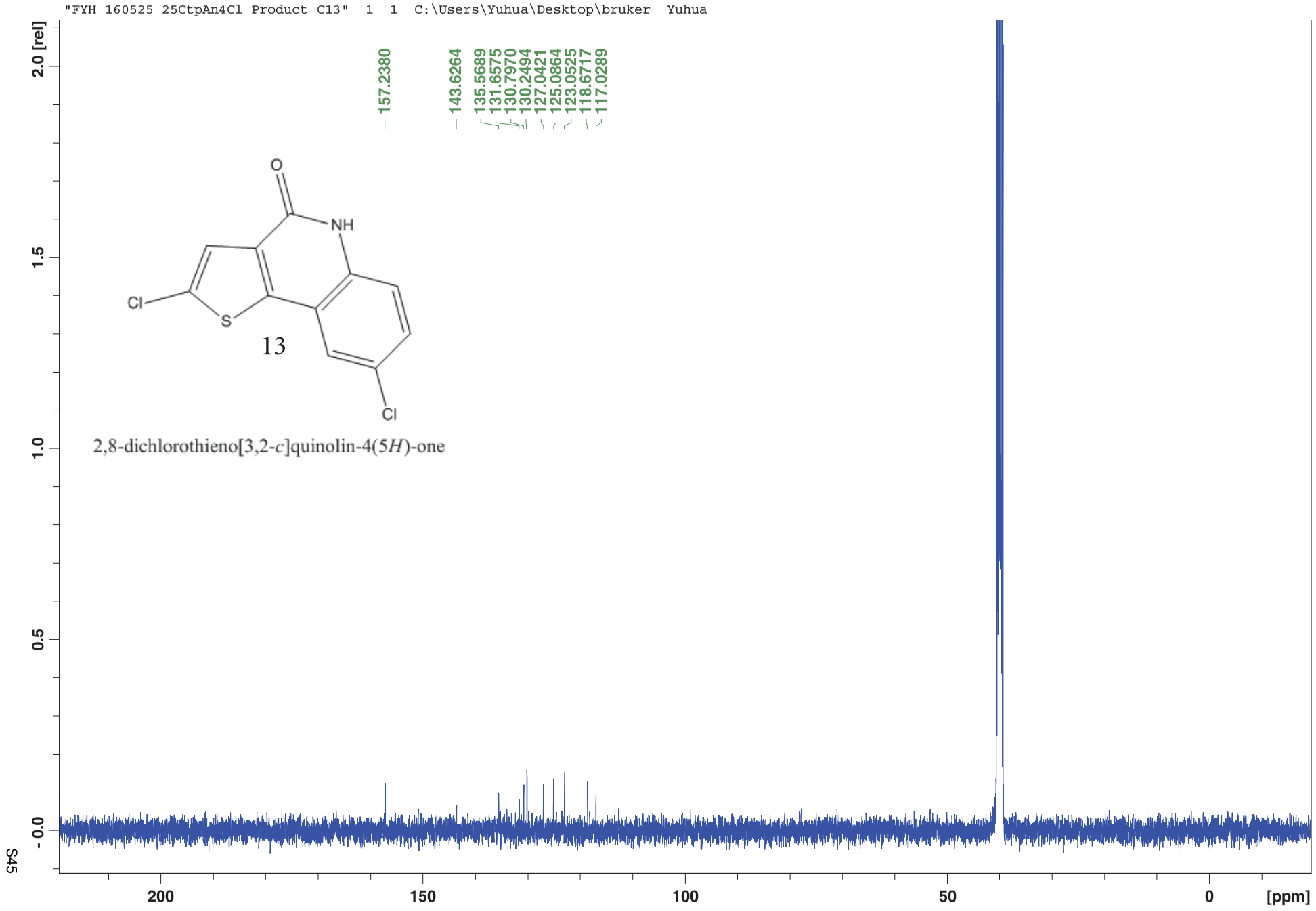
12.0238

7.9381
7.6139
7.5622
7.4126

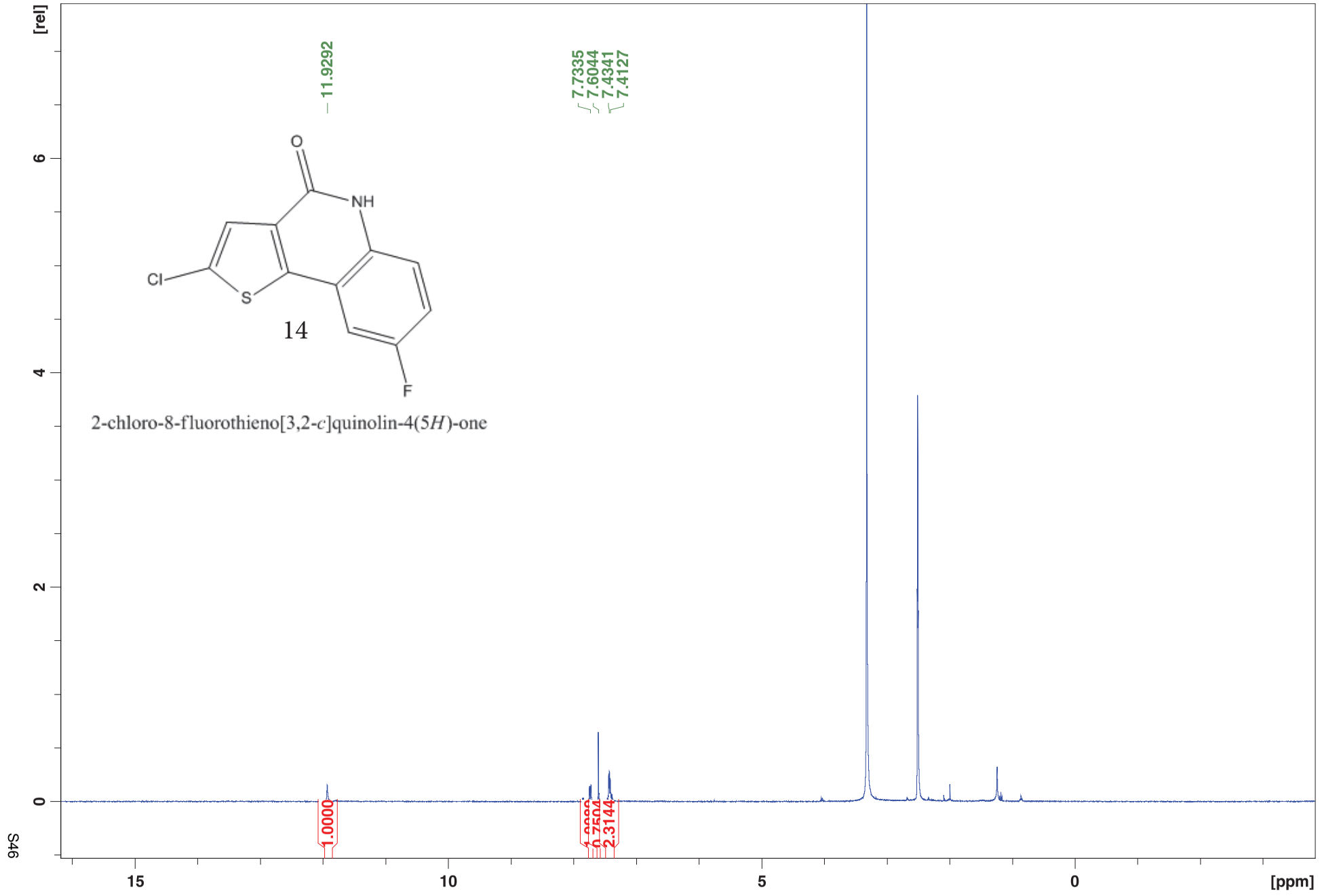
[rel]
3
2
1
-0

1.0567
1.0000
1.1614

15
10
5
0
[ppm]

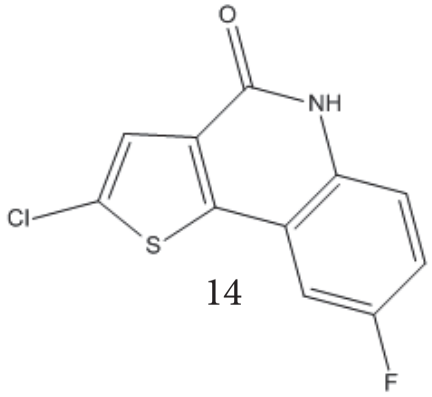

"FYH 160525 25CtpAn4Cl Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
157.2380
143.6264
135.5689
131.6575
130.7970
130.2494
127.0421
125.0864
123.0525
118.6717
117.0289
O
NH
Cl
S
Cl
13
2,8-dichlorothieno[3,2-c]quinolin-4(5H)-one
2.0 [rel]
1.5
1.0
0.5
- 0.0
200
150
100
50
0
[ppm]

"FYH 160708 25CtpAn4F Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



"FYH 160707 25CtpAn4F Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

157.8031
157.1318
133.6110
133.5364
131.6556
130.6301
125.1135
118.6849
118.1717
116.4563
109.2911

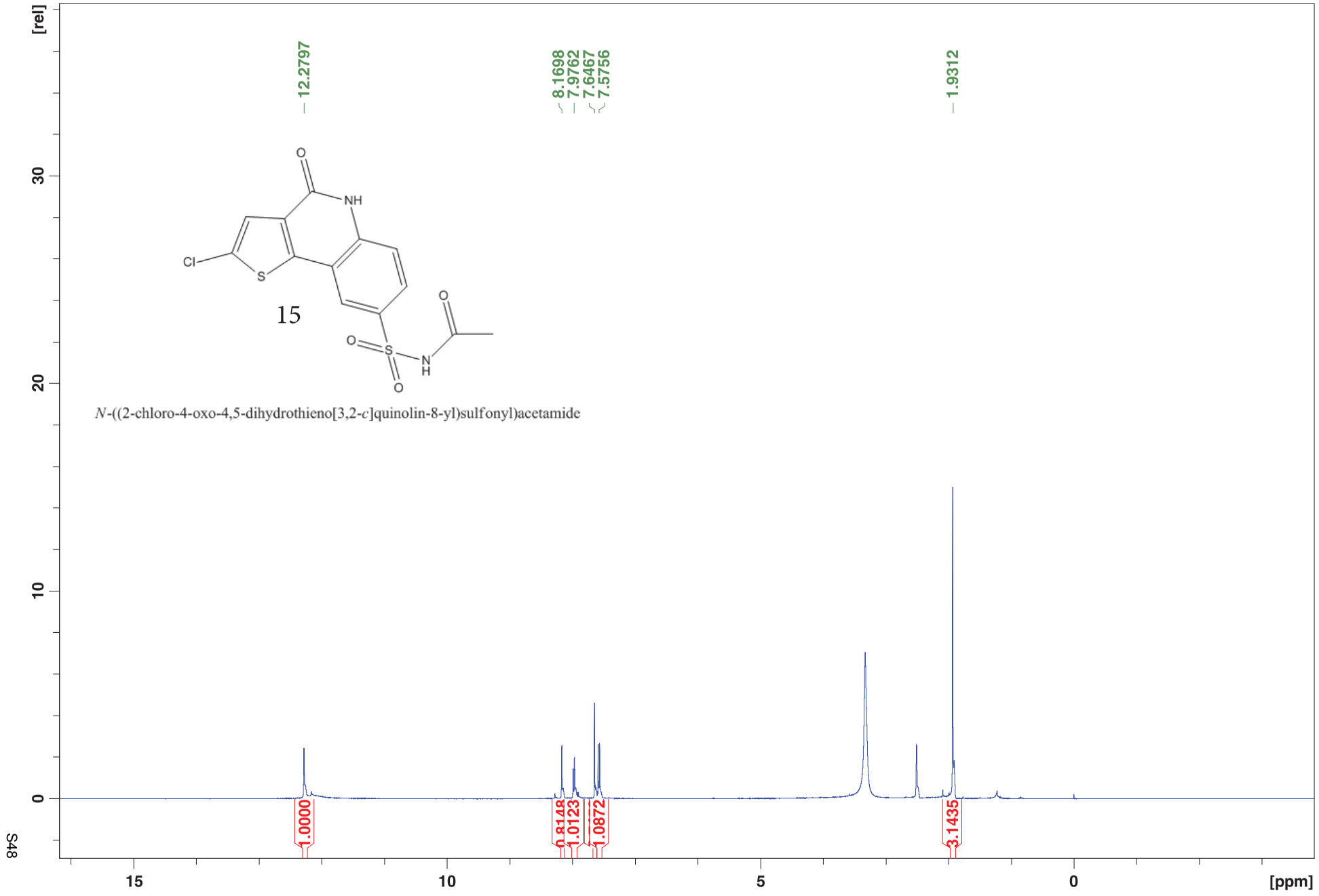


14

2-chloro-8-fluorothieno[3,2-*c*]quinolin-4(5*H*)-one

6 [rel]
5
4
3
2
1
-0
200
150
100
50
0
[ppm]

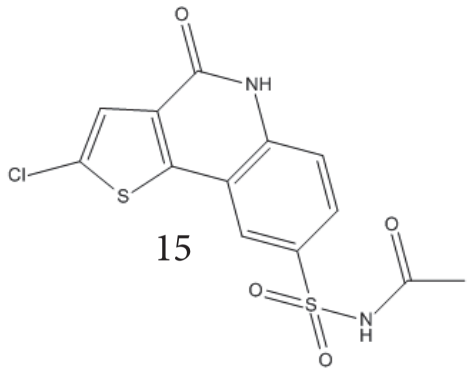
"FYH 160528 25CtpAnSul Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



15

N-((2-chloro-4-oxo-4,5-dihydrothieno[3,2-*c*]quinolin-8-yl)sulfonyl)acetamide

"FYH 160528 25CtpAnSul Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



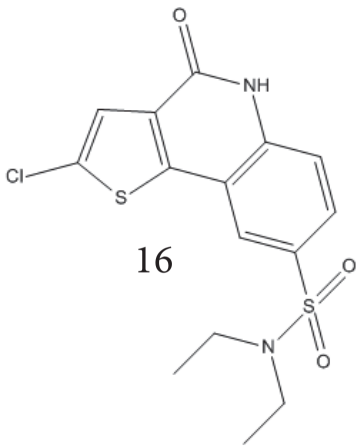
15

N-((2-chloro-4-oxo-4,5-dihydrothieno[3,2-*c*]quinolin-8-yl)sulfonyl)acetamide

169.4488
157.4355
143.8747
140.1689
133.3681
131.9021
131.1284
128.6443
125.3050
123.7575
117.5676
115.2056
23.7416

[rel]
14
12
10
8
6
4
2
0
200
150
100
50
0
[ppm]

"FYH 160527 25CtpAnSfm Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

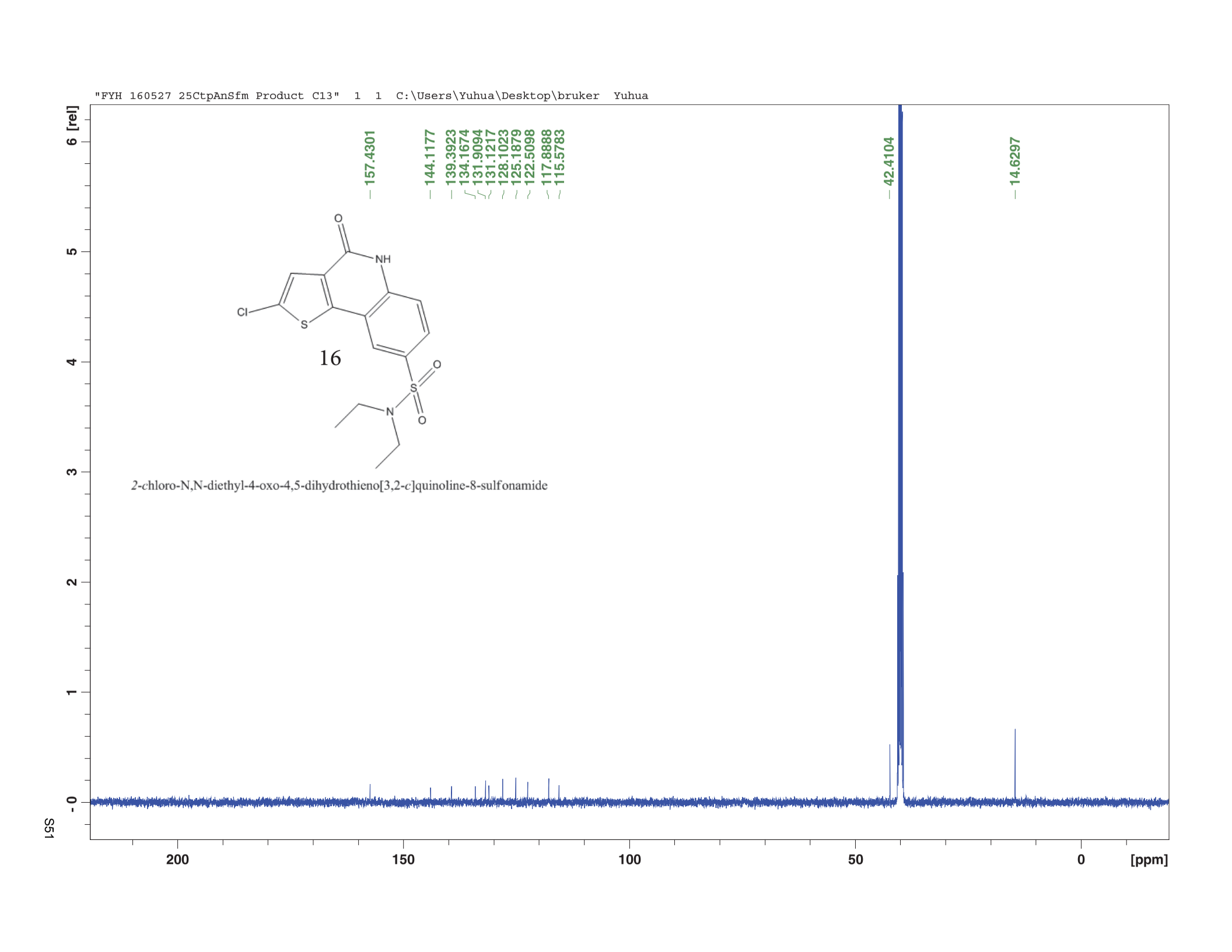


16

*2-c*hloro-N,N-diethyl-4-oxo-4,5-dihydrothieno[3,2-*c*]quinoline-8-sulfonamide

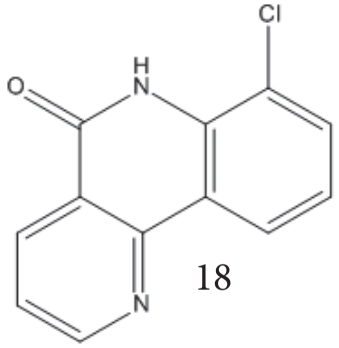
12.2371
8.0670
7.8924
7.6480
7.5679
3.2041
1.0610
0.9748
1.0000
1.1368
1.0698
4.4655
6.5967
[rel]
[ppm]
S50

"FYH 160527 25CtpAnSfm Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



*2-c*hloro-N,N-diethyl-4-oxo-4,5-dihydrothieno[3,2-*c*]quinoline-8-sulfonamide

"FYH CNCCN Product P1.1" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



18

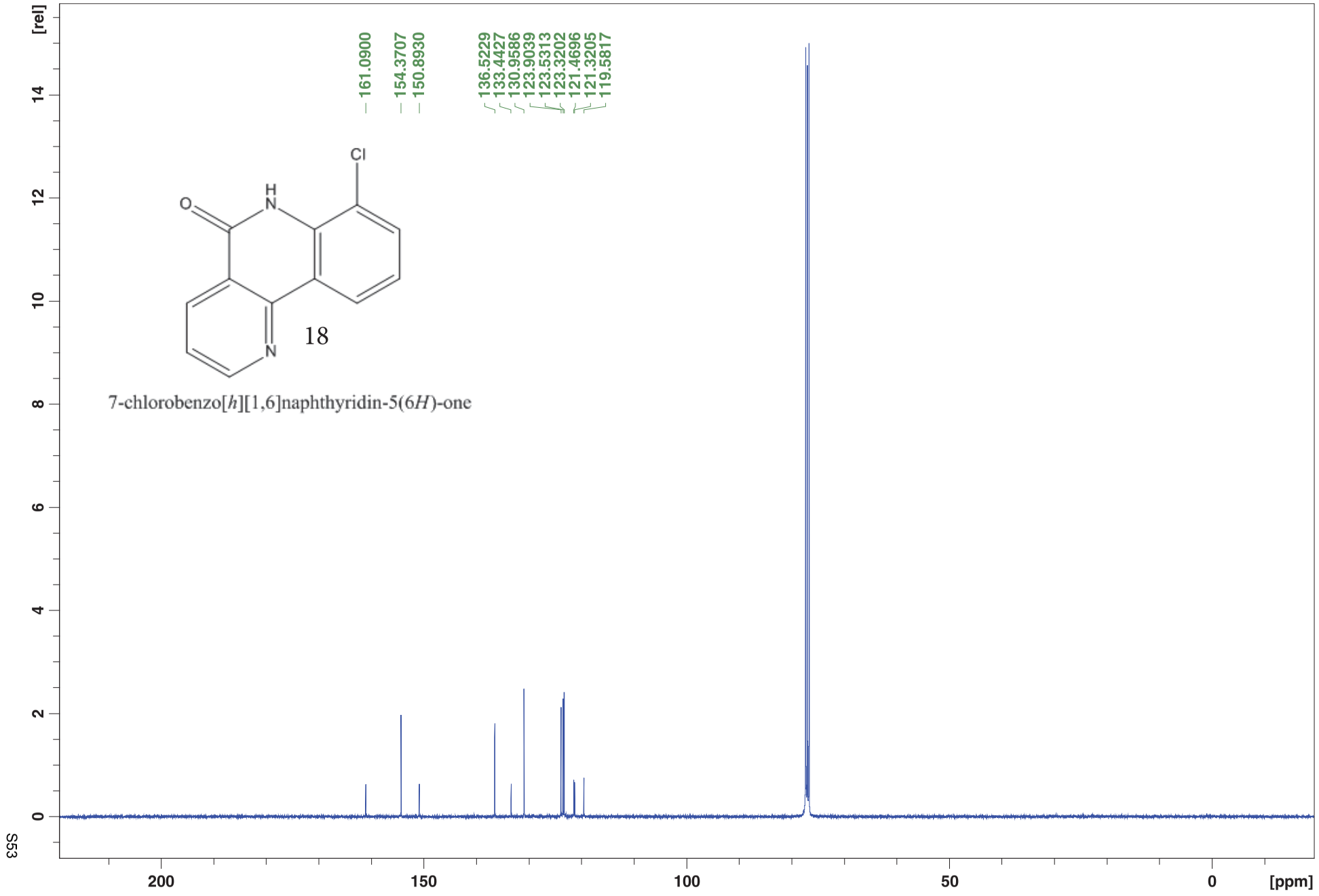
7-chlorobenzo[*h*][1,6]naphthyridin-5(6*H*)-one

9.0832
9.0652
8.7701
8.7332
7.6463
7.5966
7.3222

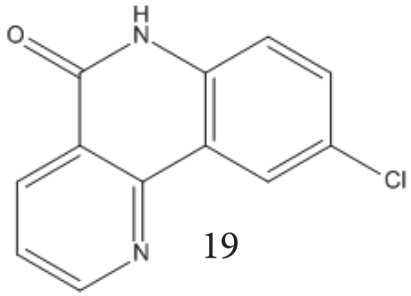
1.6322
0.9570
0.9781
1.0000

[rel]
50
40
30
20
10
0
15
10
5
0
[ppm]

"FYH CNCCN Product P1 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



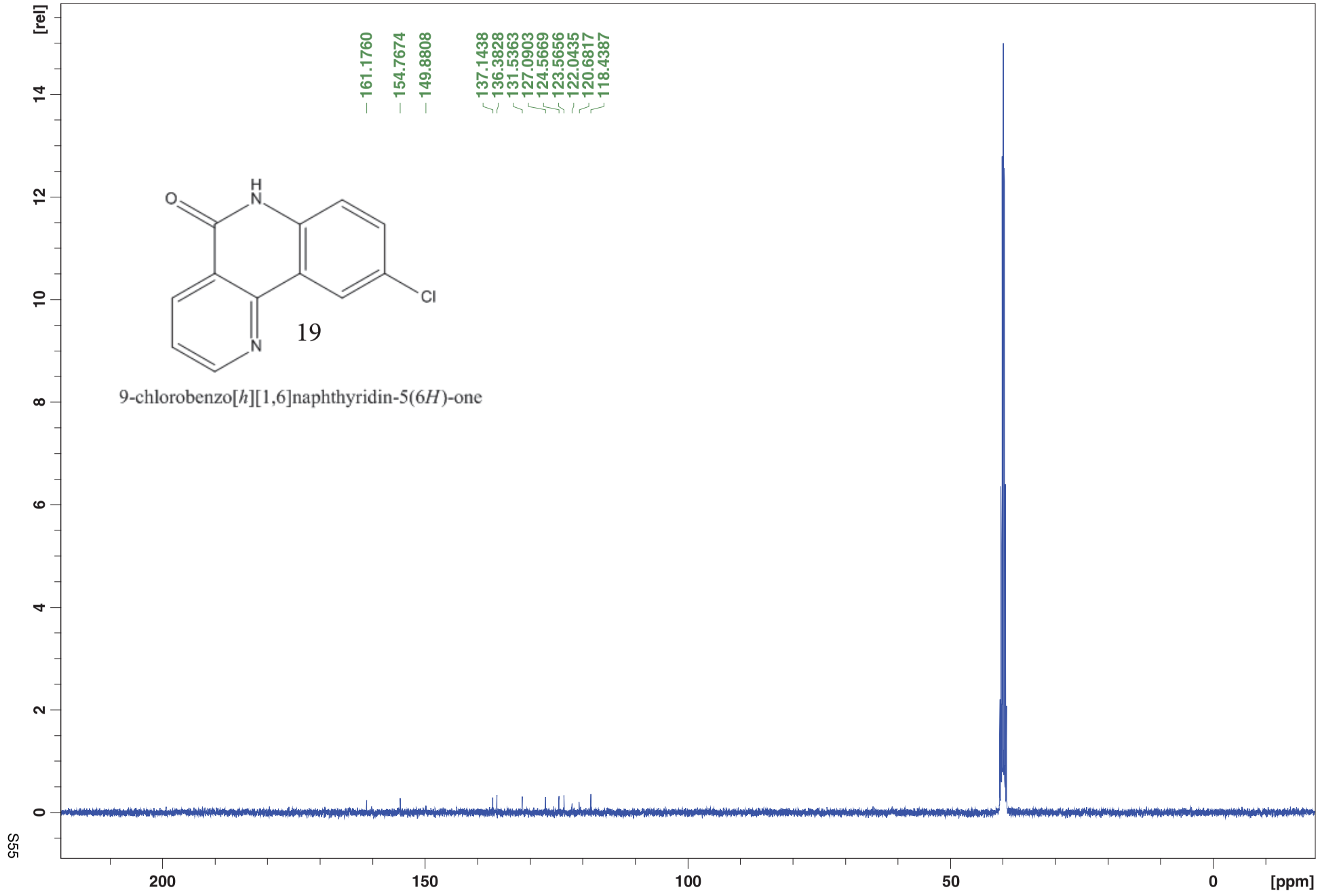
"FYH 151203 CNCAN4Cl Product1130" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



19

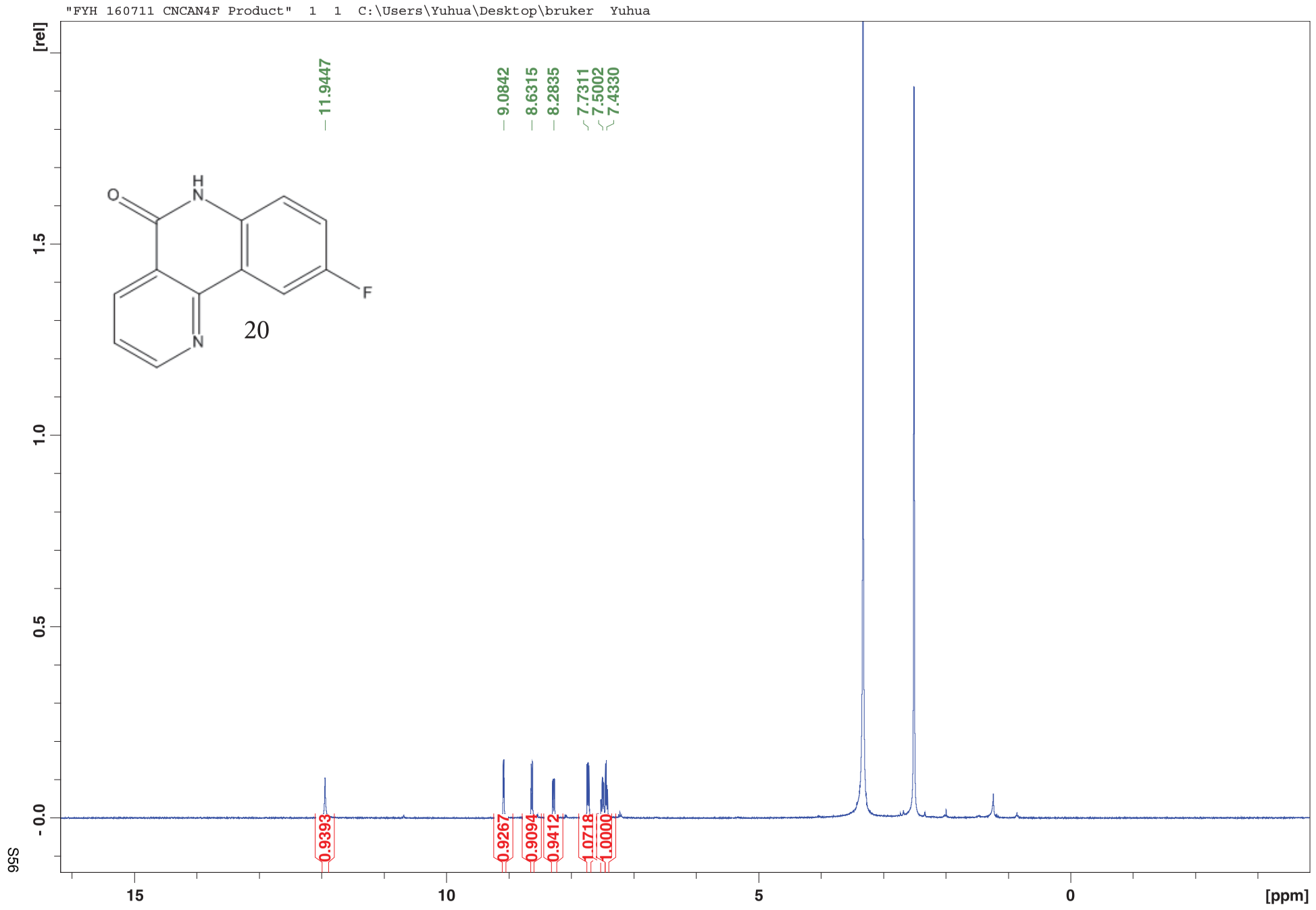
9-chlorobenzo[*h*][1,6]naphthyridin-5(6*H*)-one

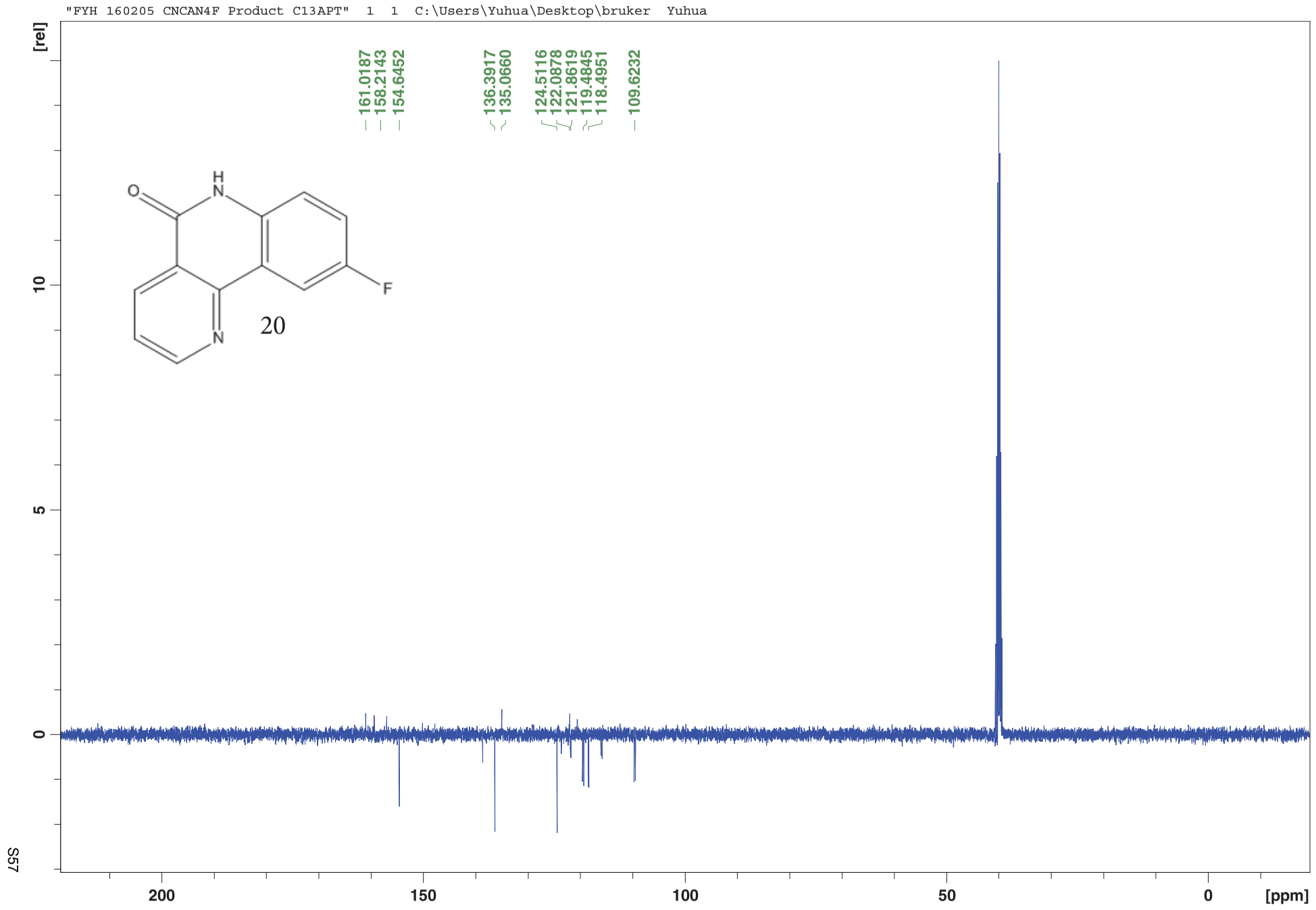
"FYH 151203 CNCAN4Cl Product1130 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

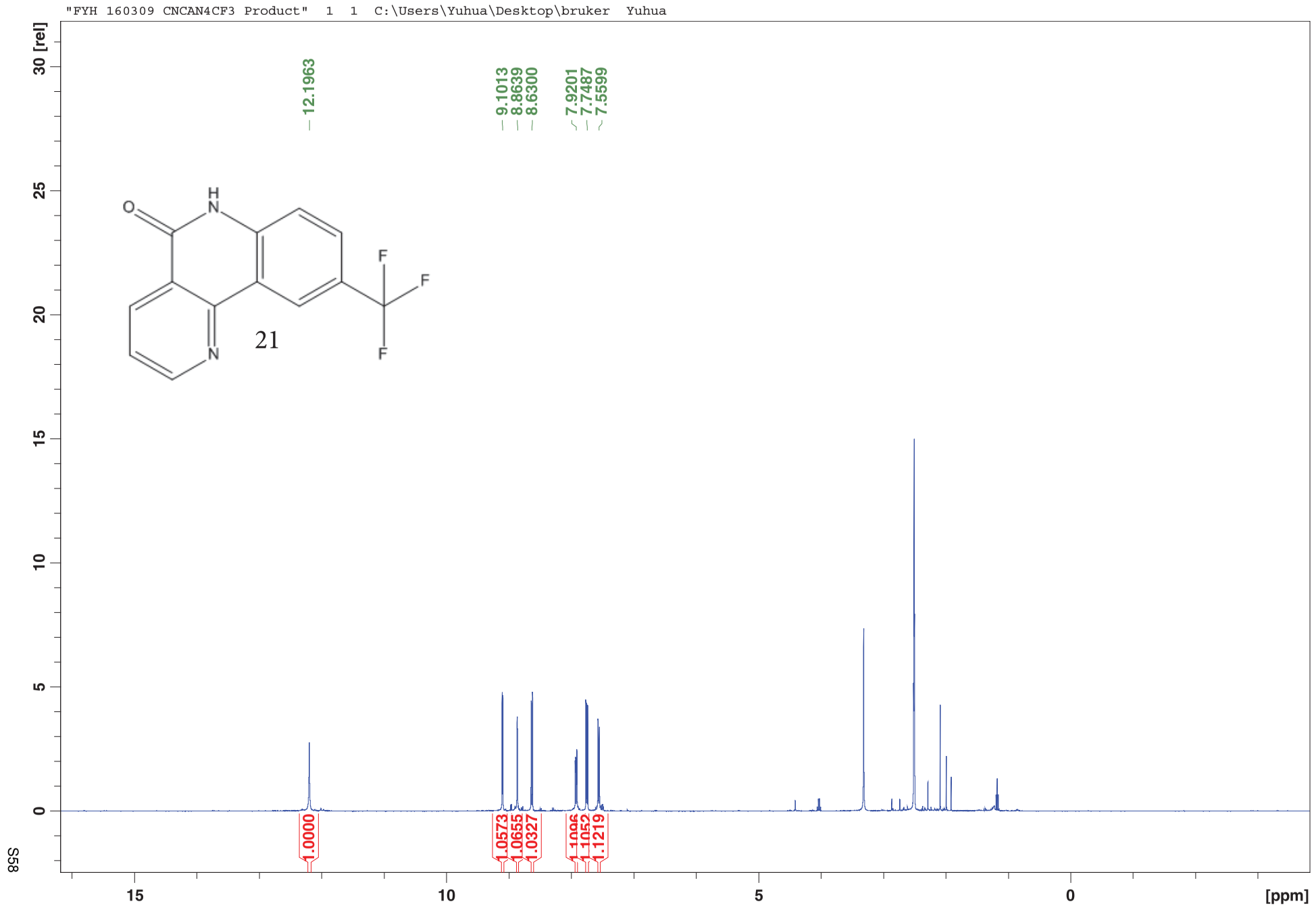


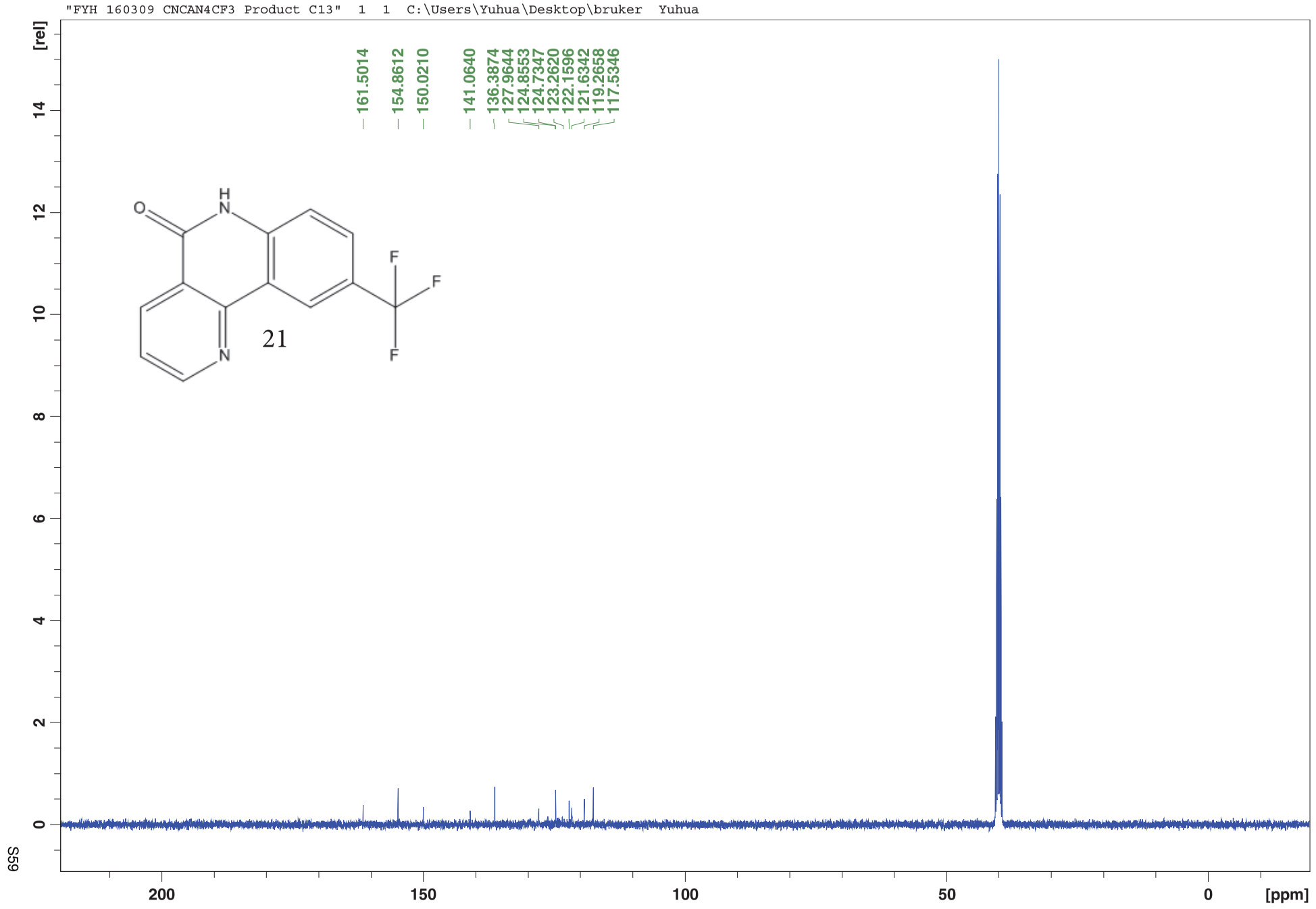
19

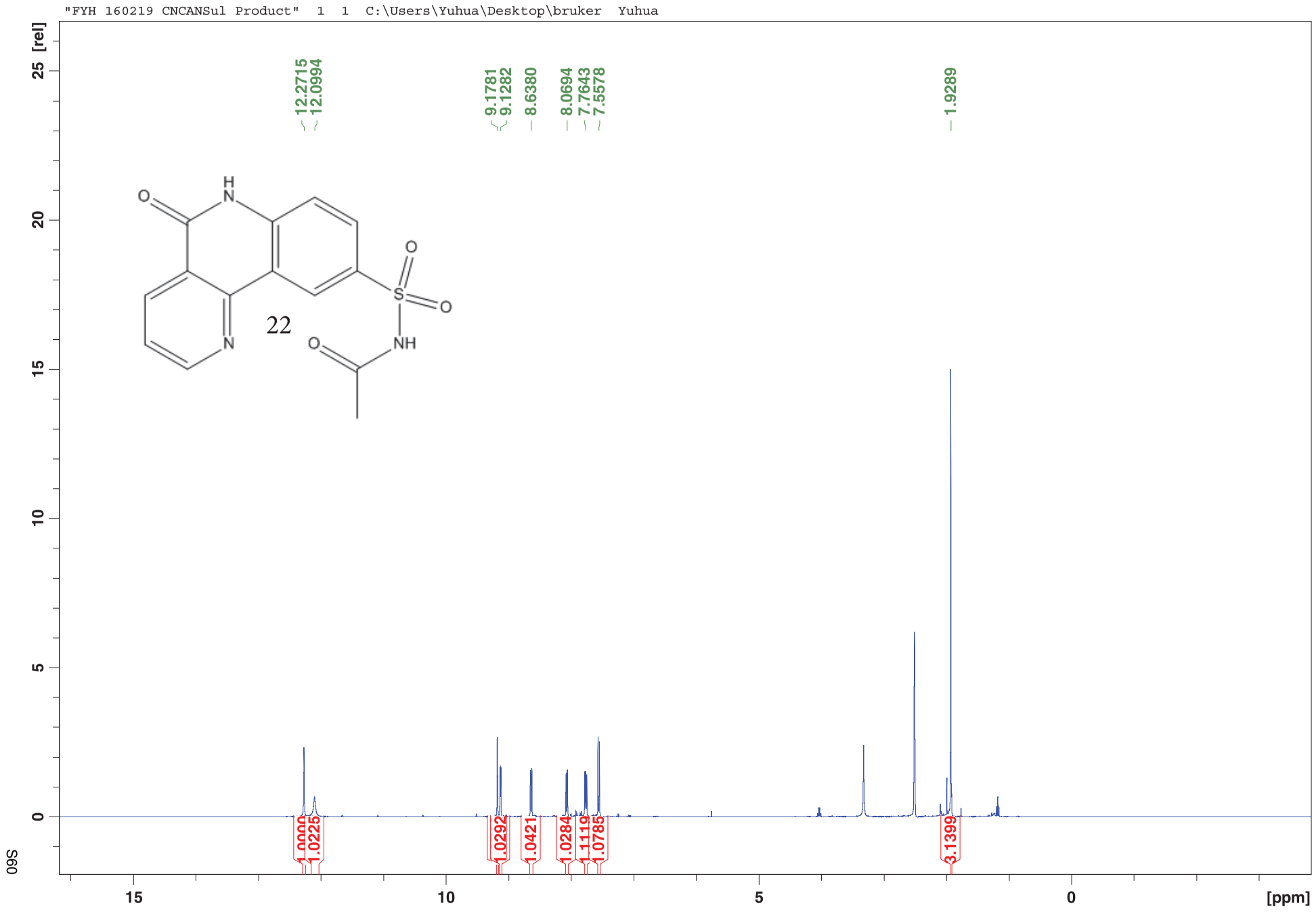
9-chlorobenzo[*h*][1,6]naphthyridin-5(6*H*)-one

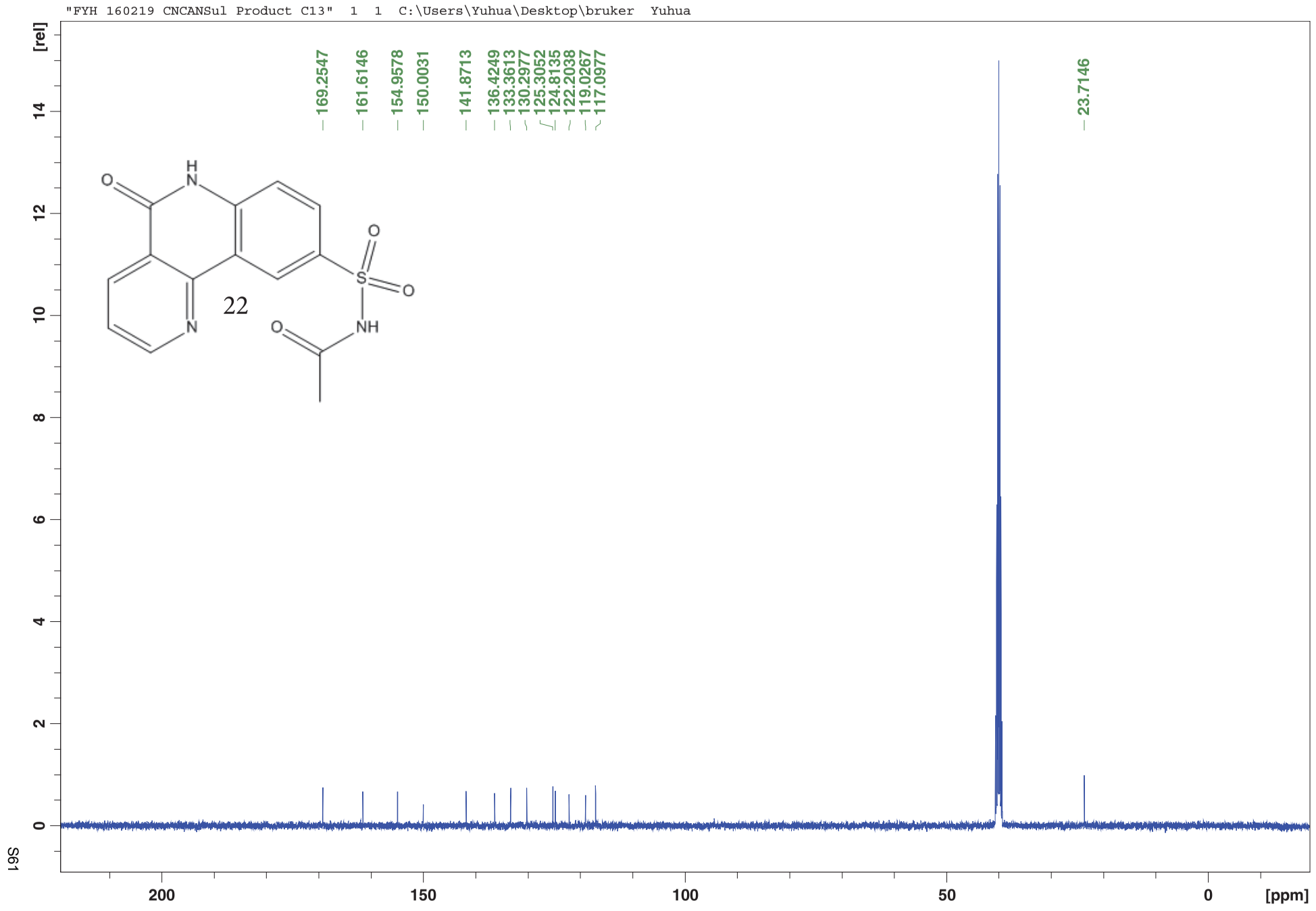

"FYH 160711 CNCAN4F Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
1.5
1.0
0.5
- 0.0
11.9447
9.0842
8.6315
8.2835
7.7311
7.5002
7.4330
O
H
N
F
N
20
0.9393
0.9267
0.9094
0.9412
1.0718
1.0000
15
10
5
0
[ppm]

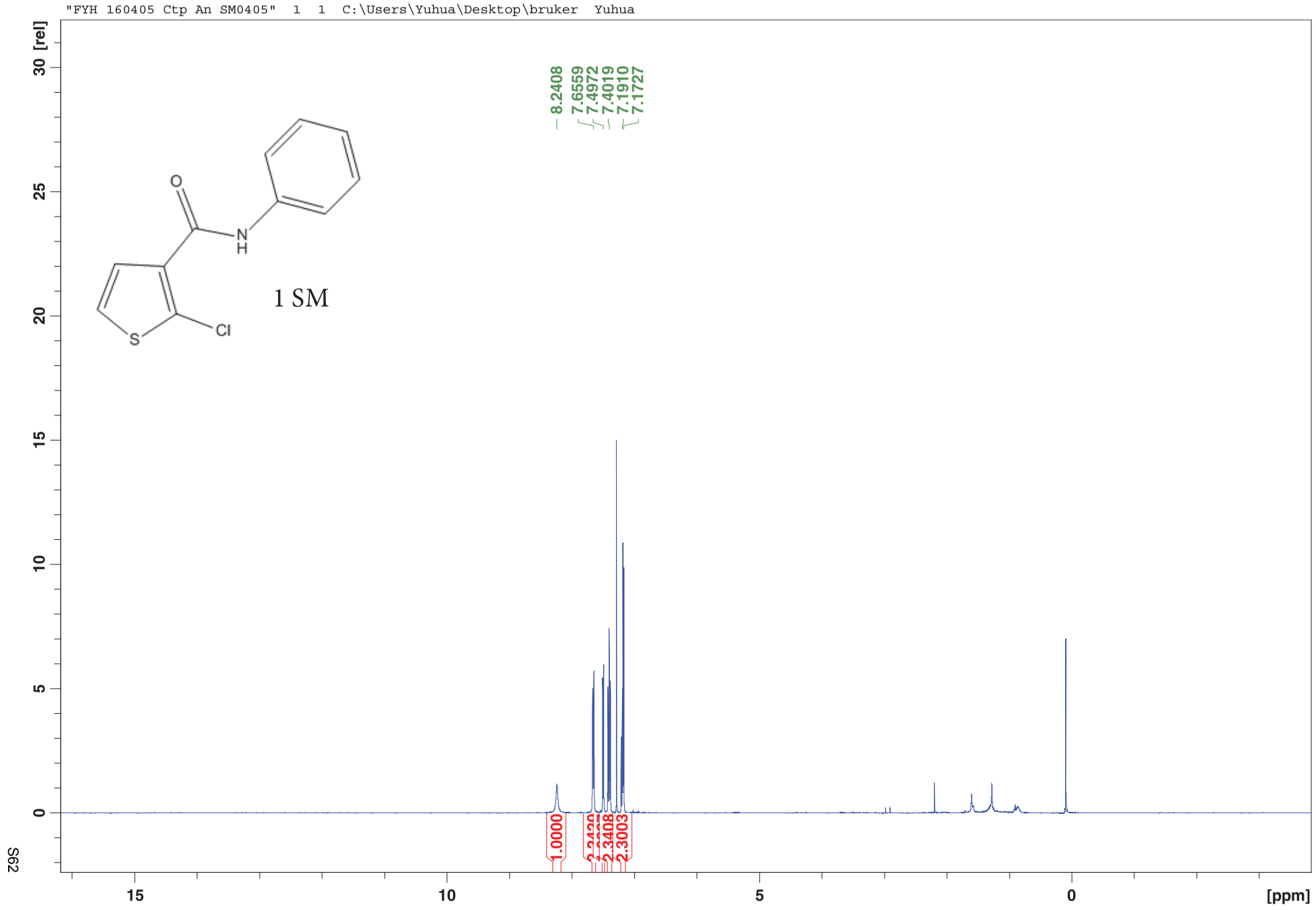

"FYH 160205 CNCAN4F Product C13APT" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
161.0187
158.2143
154.6452
136.3917
135.0660
124.5116
122.0878
121.8619
119.4845
118.4951
109.6232
O
H
N
F
N
20
10
5
0
200
150
100
50
0
[ppm]

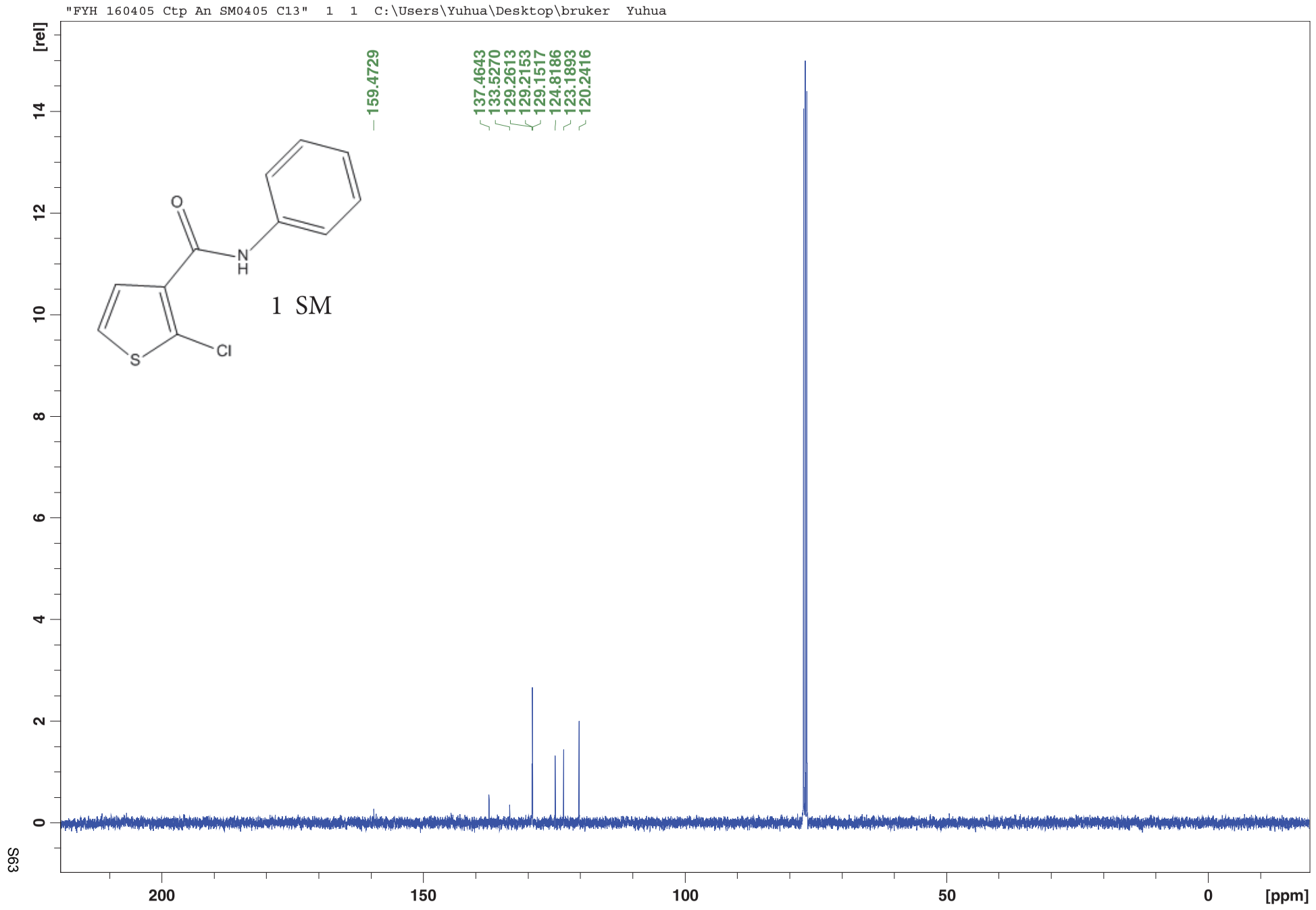

"FYH 160309 CNCAN4CF3 Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
12.1963
9.1013
8.8639
8.6300
7.9201
7.7487
7.5599
21
1.0000
1.0573
1.0655
1.0327
1.1052
1.1219
30 [rel]
25
20
15
10
5
0
15
10
5
0
[ppm]

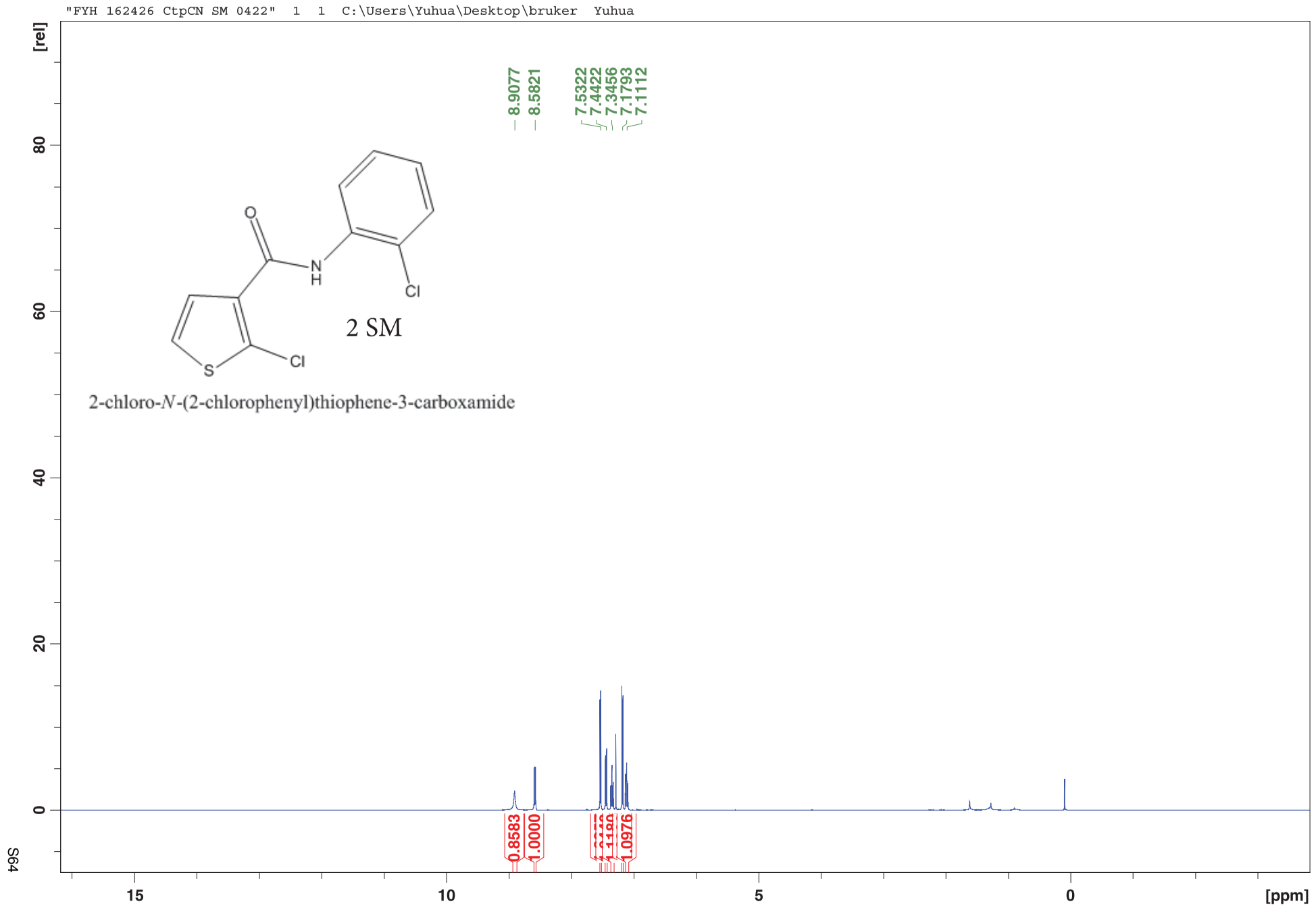

"FYH 160309 CNCAN4CF3 Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
161.5014
154.8612
150.0210
141.0640
136.3874
127.9644
124.8553
124.7347
123.2620
122.1596
121.6342
119.2658
117.5346
O
H
N
F
F
F
N
21
[rel]
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]

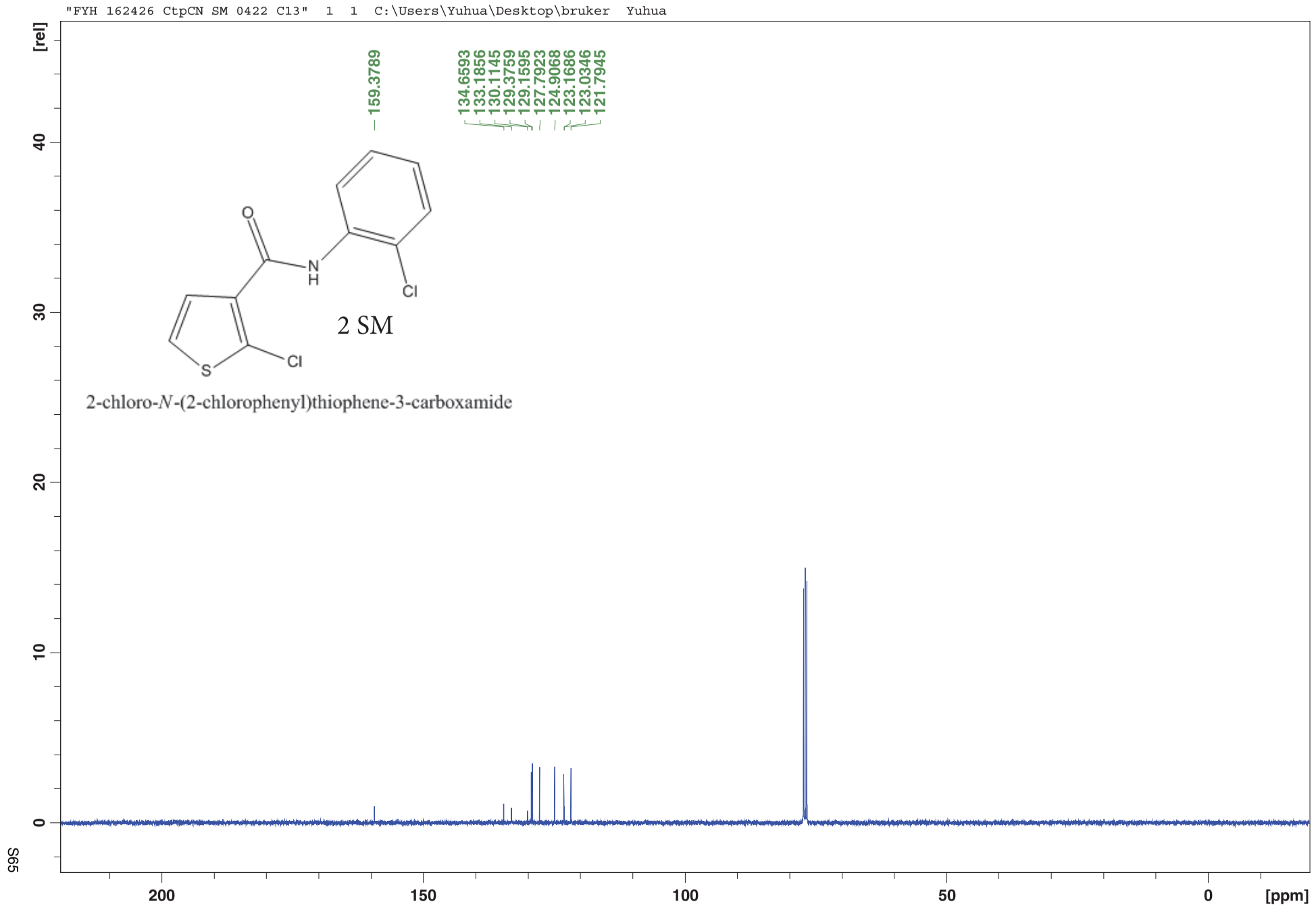

"FYH 160219 CNCANSul Product" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
12.2715
12.0994
9.1781
9.1282
8.6380
8.0694
7.7643
7.5578
1.9289
22
1.0000
1.0225
1.0292
1.0421
1.0284
1.1119
1.0785
3.1399
25 [rel]
20
15
10
5
0
15
10
5
0
[ppm]
S60


"FYH 160219 CNCANSul Product C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
169.2547
161.6146
154.9578
150.0031
141.8713
136.4249
133.3613
130.2977
125.3052
124.8135
122.2038
119.0267
117.0977
23.7146
22
[ppm]

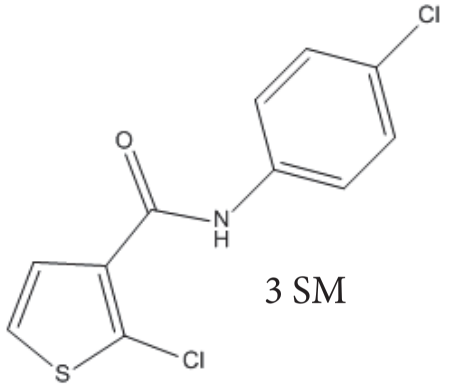

"FYH 160405 Ctp An SM0405" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
8.2408
7.6559
7.4972
7.4019
7.1910
7.1727
1 SM
O
N
H
S
Cl
1.0000
2.3408
2.3003
30 [rel]
25
20
15
10
5
0
15
10
5
0
[ppm]


"FYH 160405 Ctp An SM0405 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
159.4729
137.4643
133.5270
129.2613
129.2153
129.1517
124.8186
123.1893
120.2416
O
N
H
S
Cl
1 SM
[rel]
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]
S63


"FYH 162426 CtpCN SM 0422" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
80
60
40
20
0
8.9077
8.5821
7.5322
7.4422
7.3456
7.1793
7.1112
O
N
H
Cl
S
Cl
2 SM
2-chloro-N-(2-chlorophenyl)thiophene-3-carboxamide
0.8583
1.0000
1.0976
15
10
5
0
[ppm]


"FYH 162426 CtpCN SM 0422 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
159.3789
134.6593
133.1856
130.1145
129.3759
129.1595
127.7923
124.9068
123.1686
123.0346
121.7945
O
N
H
Cl
S
Cl
2 SM
2-chloro-N-(2-chlorophenyl)thiophene-3-carboxamide
0
10
20
30
40
200
150
100
50
0
[ppm]
S65

"FYH 162426 CtpAn4Cl SM 0423" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



3 SM

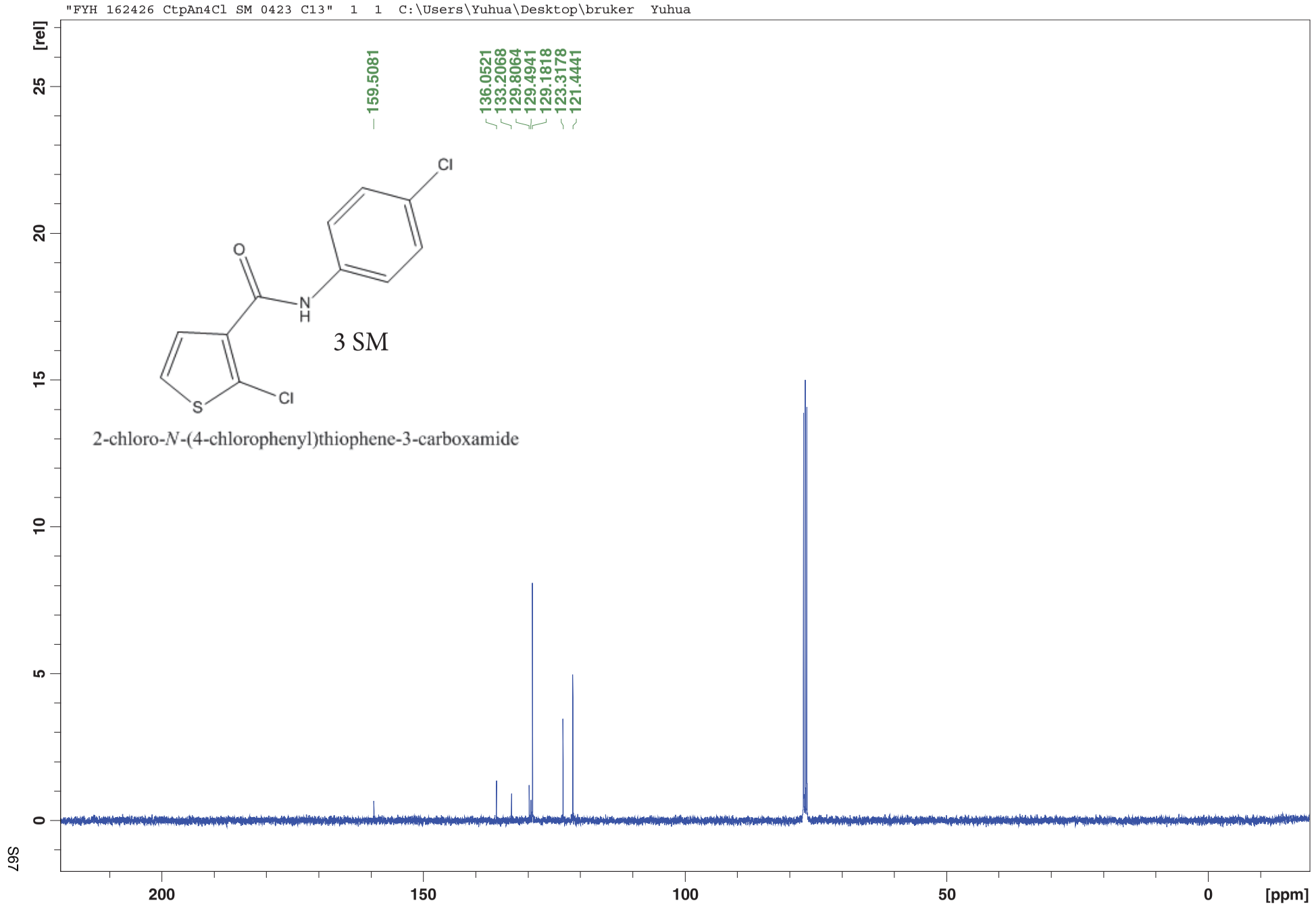
2-chloro-*N*-(4-chlorophenyl)thiophene-3-carboxamide

8.2689
7.6095
7.4766
7.3536
7.1710

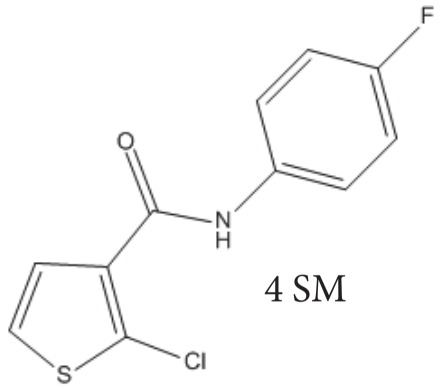
0.8973
0.9997

[rel]
60
50
40
30
20
10
0
15
10
5
0
[ppm]

99S


"FYH 162426 CtpAn4Cl SM 0423 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
159.5081
136.0521
133.2068
129.8064
129.4941
129.1818
123.3178
121.4441
Cl
O
N
H
S
Cl
3 SM
2-chloro-N-(4-chlorophenyl)thiophene-3-carboxamide
[rel]
25
20
15
10
5
0
200
150
100
50
0
[ppm]

"FYH 162426 CtpAn4F SM 0423" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



4 SM

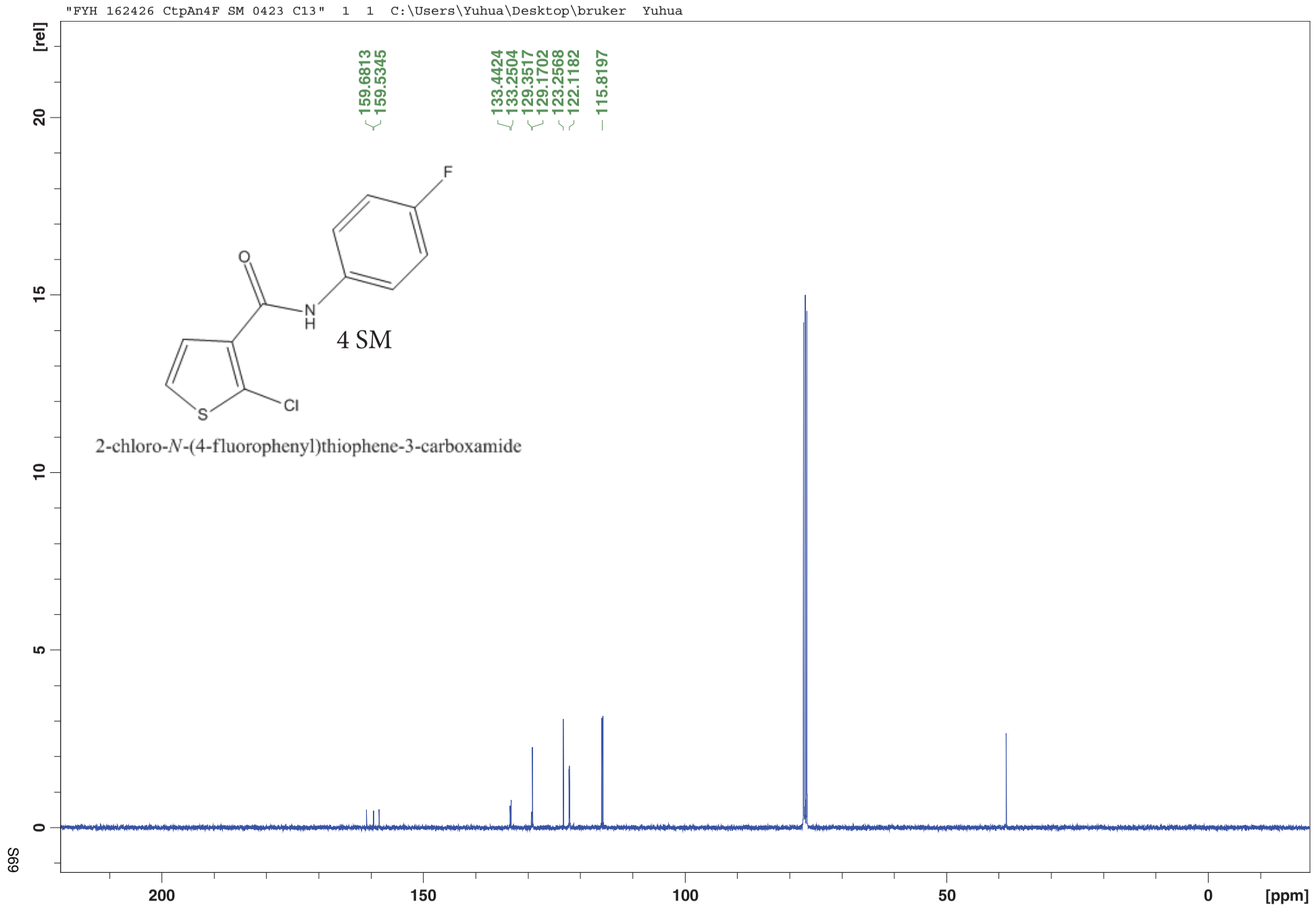
2-chloro-*N*-(4-fluorophenyl)thiophene-3-carboxamide

8.2562
7.6132
7.4778
7.1689
7.0868

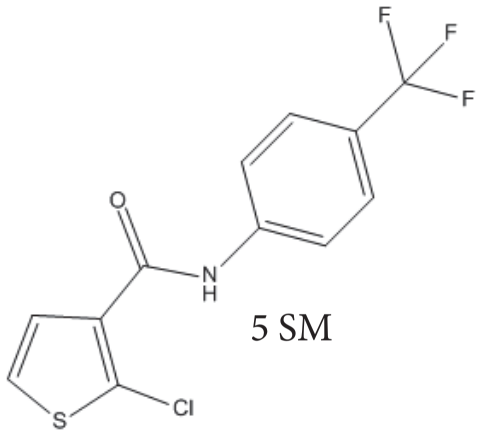
0.8767
1.0000
2.1884

[rel]
[ppm]

S68


"FYH 162426 CtpAn4F SM 0423 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
159.6813
159.5345
133.4424
133.2504
129.3517
129.1702
123.2568
122.1182
115.8197
F
O
N
H
S
Cl
4 SM
2-chloro-N-(4-fluorophenyl)thiophene-3-carboxamide
[ppm]
S69

"FYH 160426 CptAN4CF3 SM0422" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



5 SM

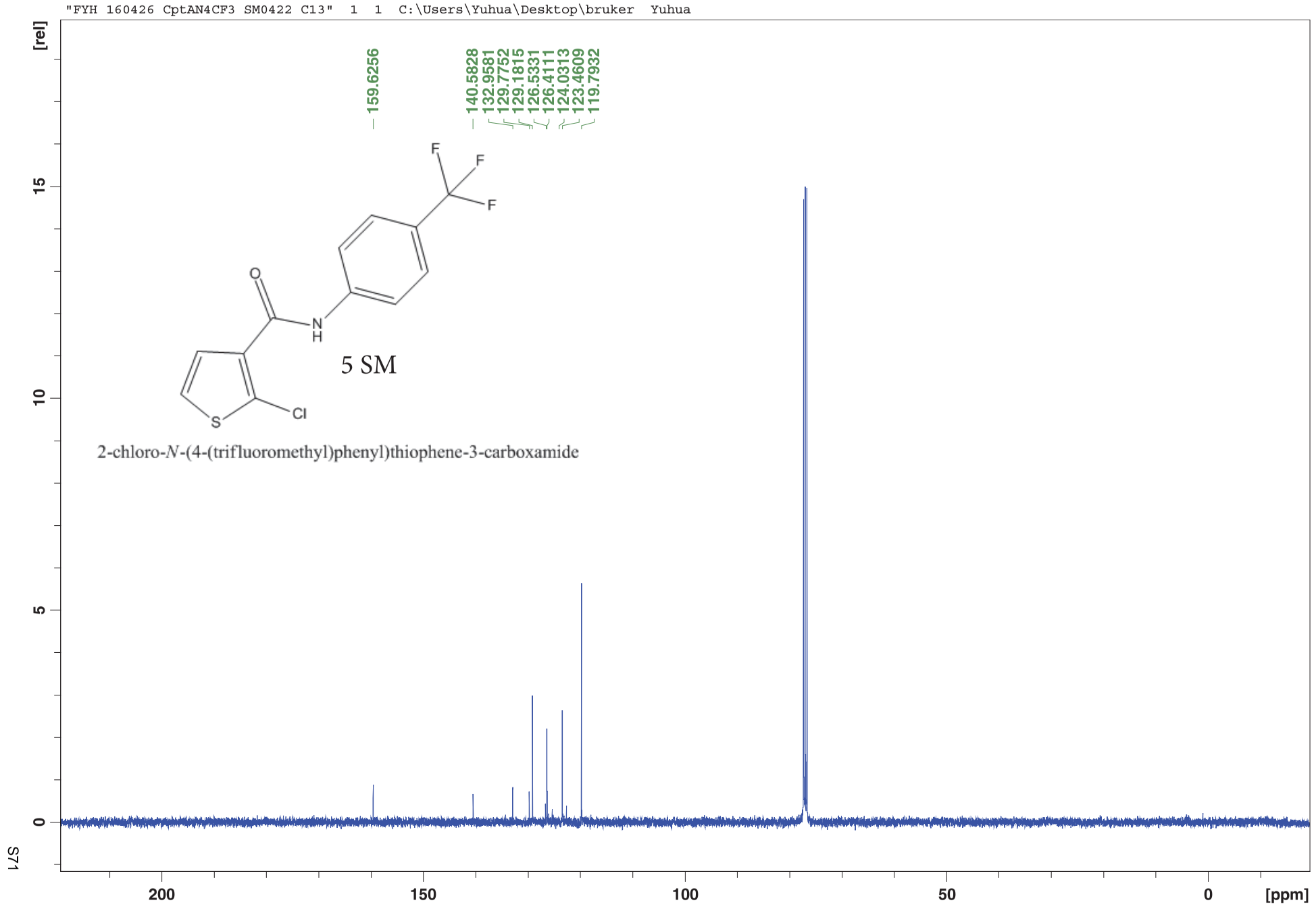
2-chloro-*N*-(4-(trifluoromethyl)phenyl)thiophene-3-carboxamide

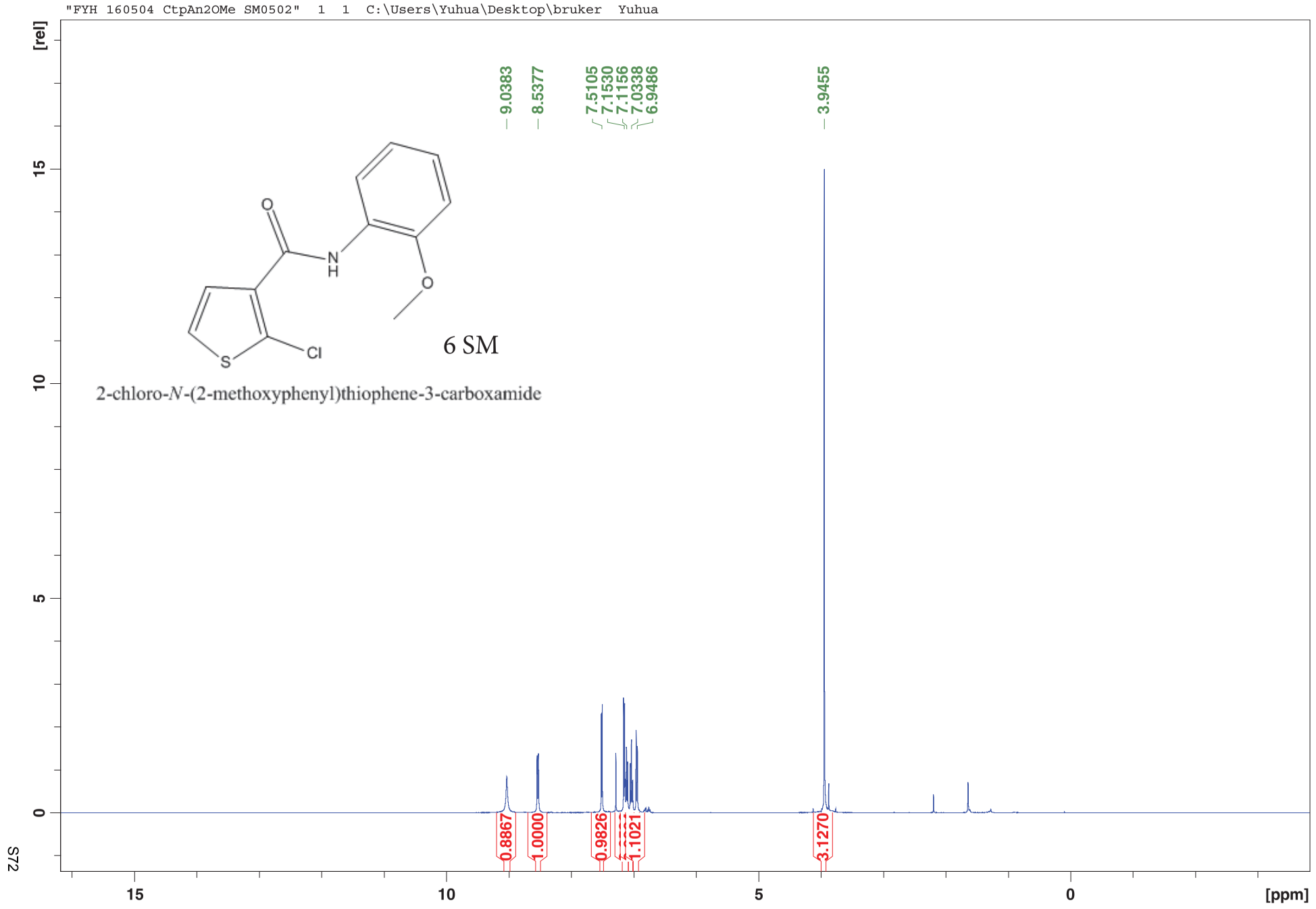
8.4146
7.7899
7.6515
7.4991
7.1944

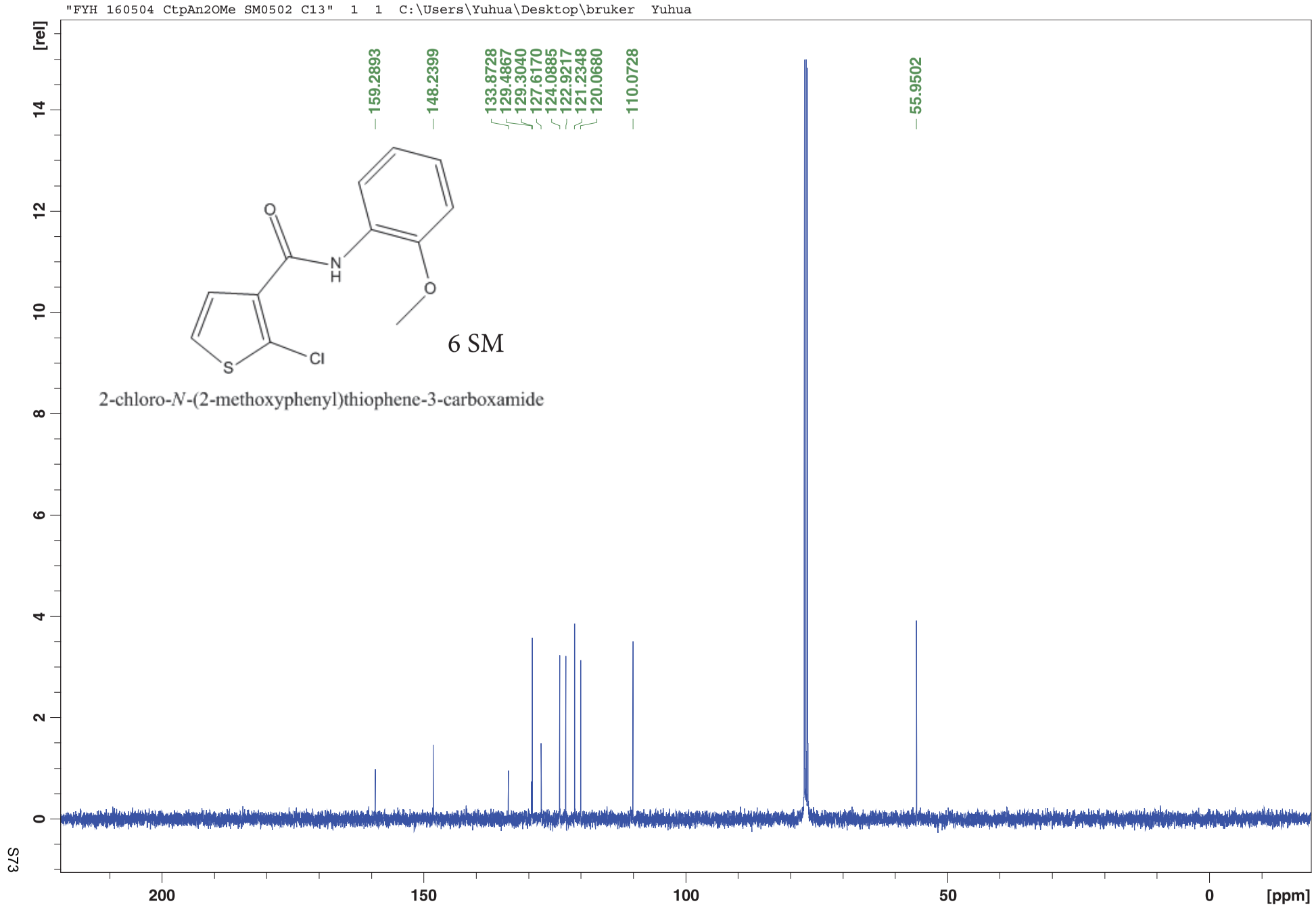
1.0000
1.0712
1.0515

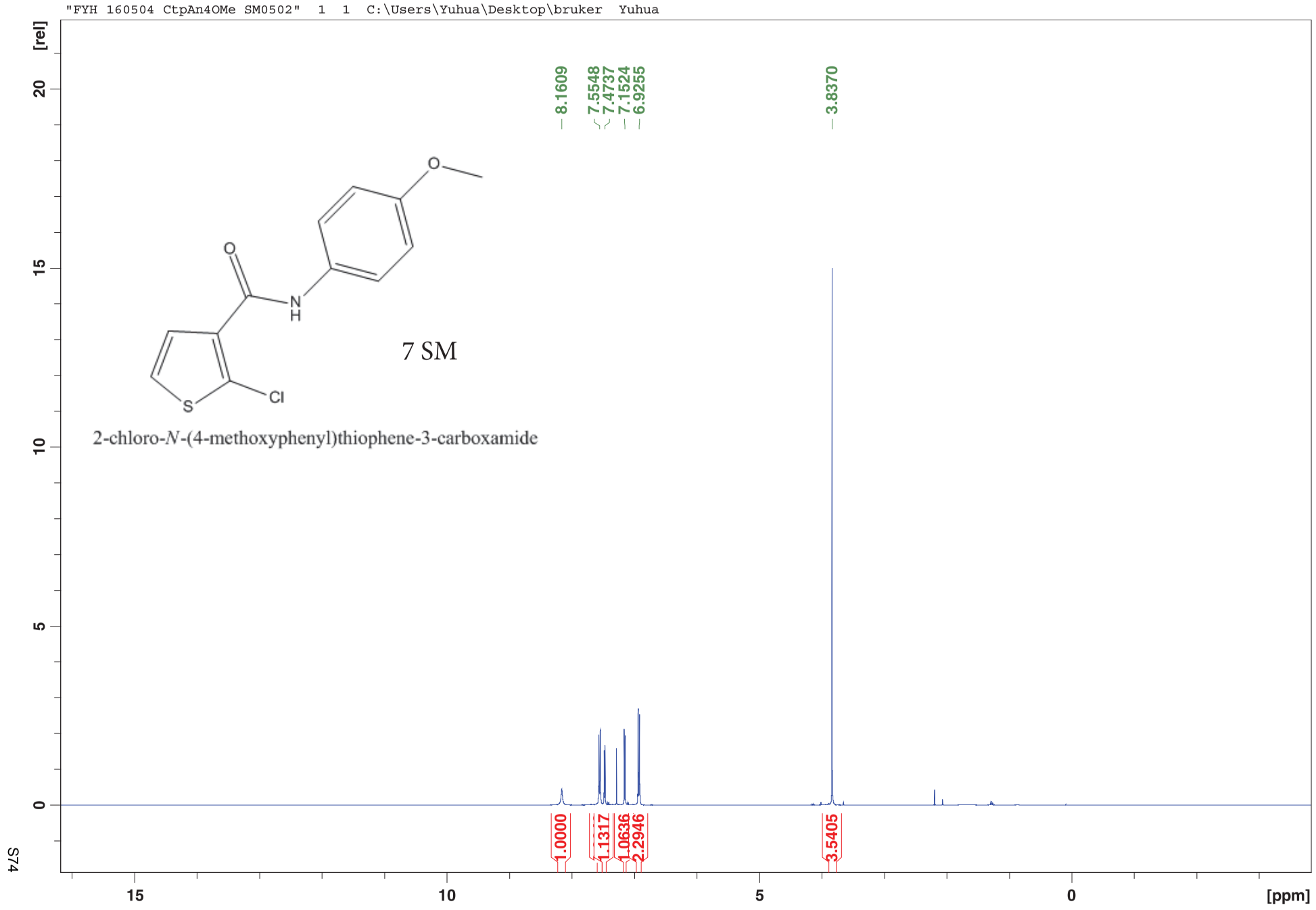
[rel]
60
50
40
30
20
10
0
15
10
5
0
[ppm]

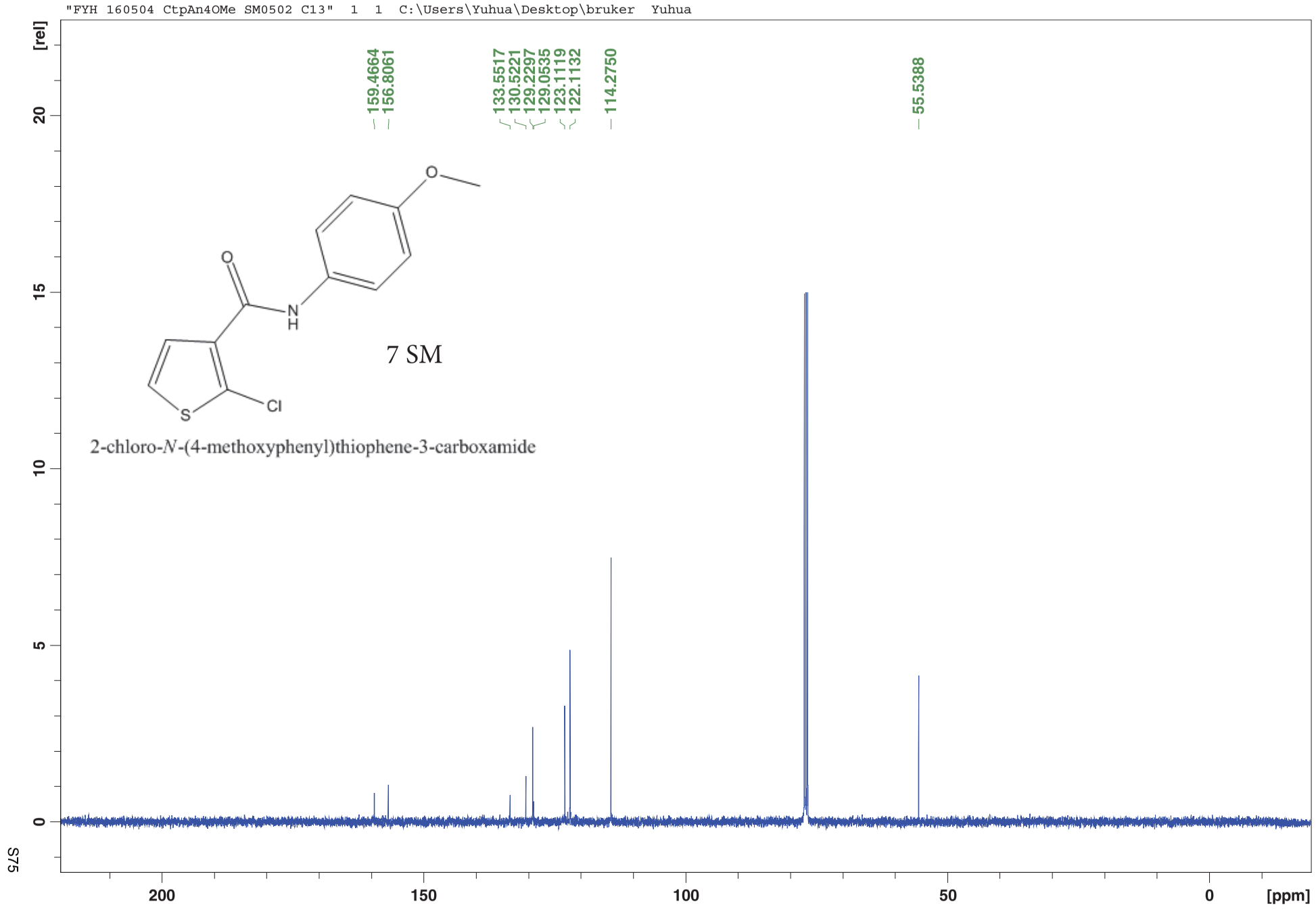
S70

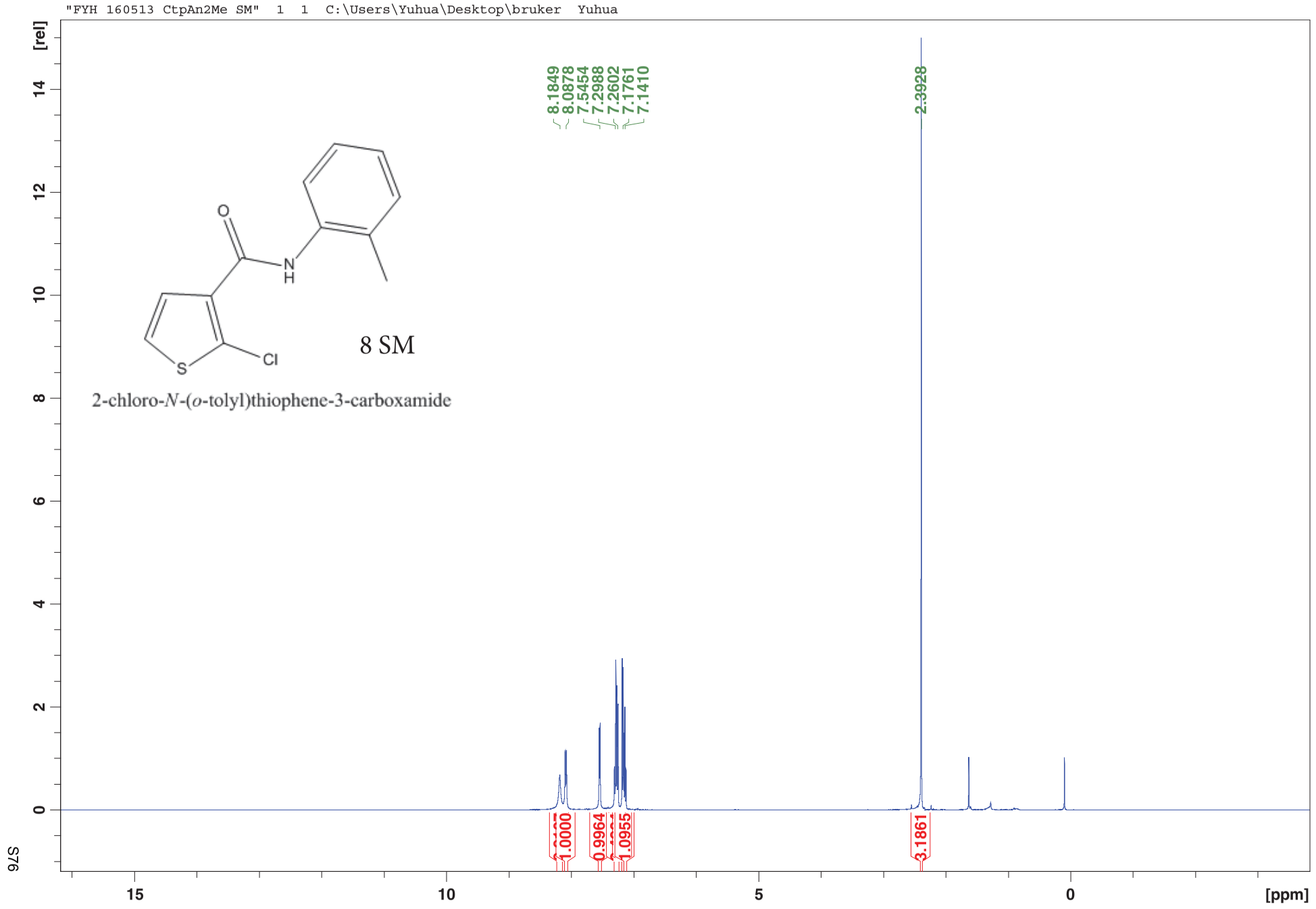

"FYH 160426 CptAN4CF3 SM0422 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
159.6256
140.5828
132.9581
129.7752
129.1815
126.5331
126.4111
124.0313
123.4609
119.7932
F
F
F
O
N
H
S
Cl
5 SM
2-chloro-N-(4-(trifluoromethyl)phenyl)thiophene-3-carboxamide
0
5
10
15
200
150
100
50
0
[ppm]

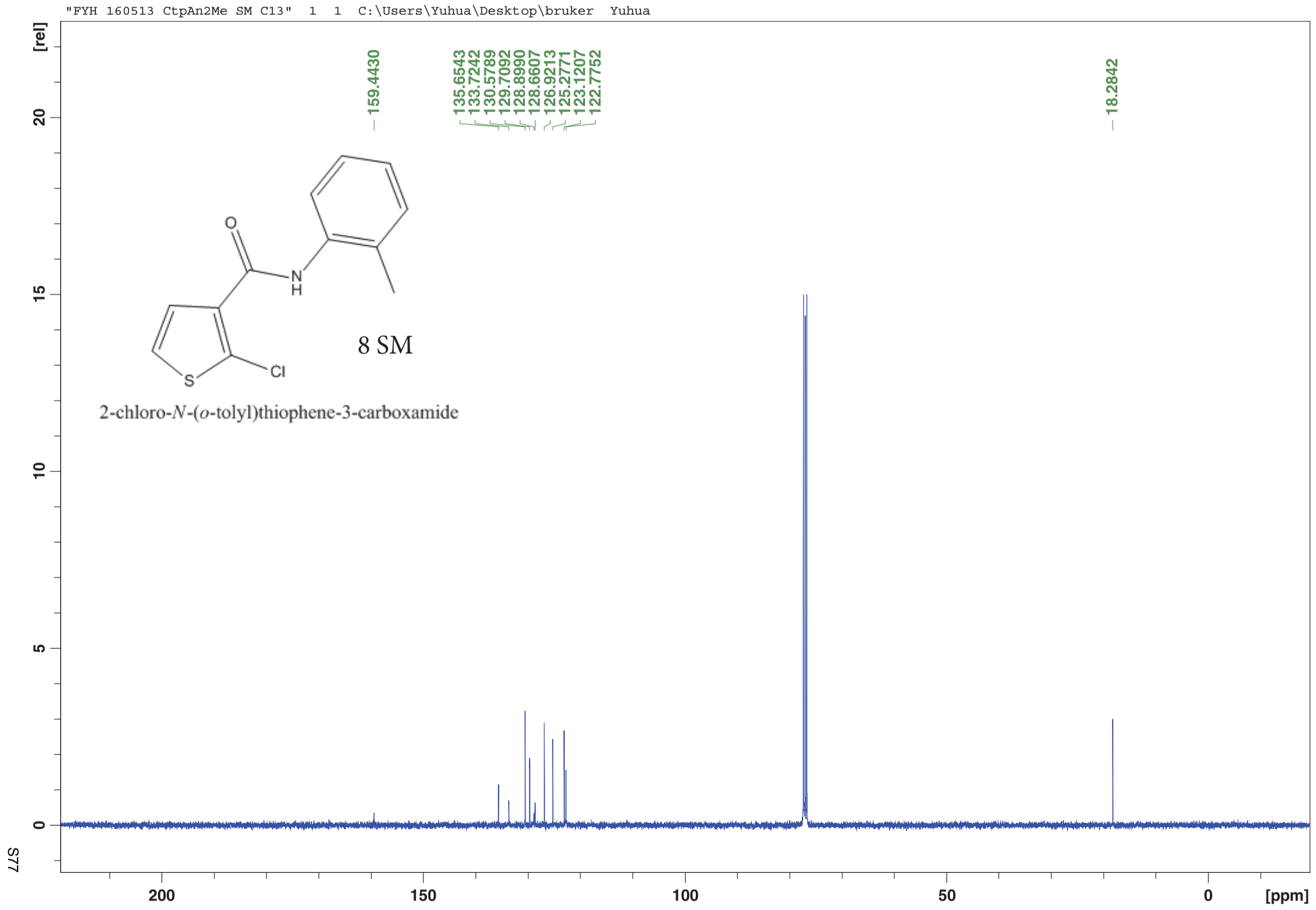

"FYH 160504 CtpAn2OMe SM0502" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
9.0383
8.5377
7.5105
7.1530
7.1156
7.0338
6.9486
3.9455
O
N
H
O
S
Cl
6 SM
2-chloro-N-(2-methoxyphenyl)thiophene-3-carboxamide
0.8867
1.0000
0.9826
1.1021
3.1270
15
10
5
0
[ppm]


"FYH 160504 CtpAn2OMe SM0502 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
159.2893
148.2399
133.8728
129.4867
129.3040
127.6170
124.0885
122.9217
121.2348
120.0680
110.0728
55.9502
O
N
H
O
S
Cl
6 SM
2-chloro-N-(2-methoxyphenyl)thiophene-3-carboxamide
[ppm]

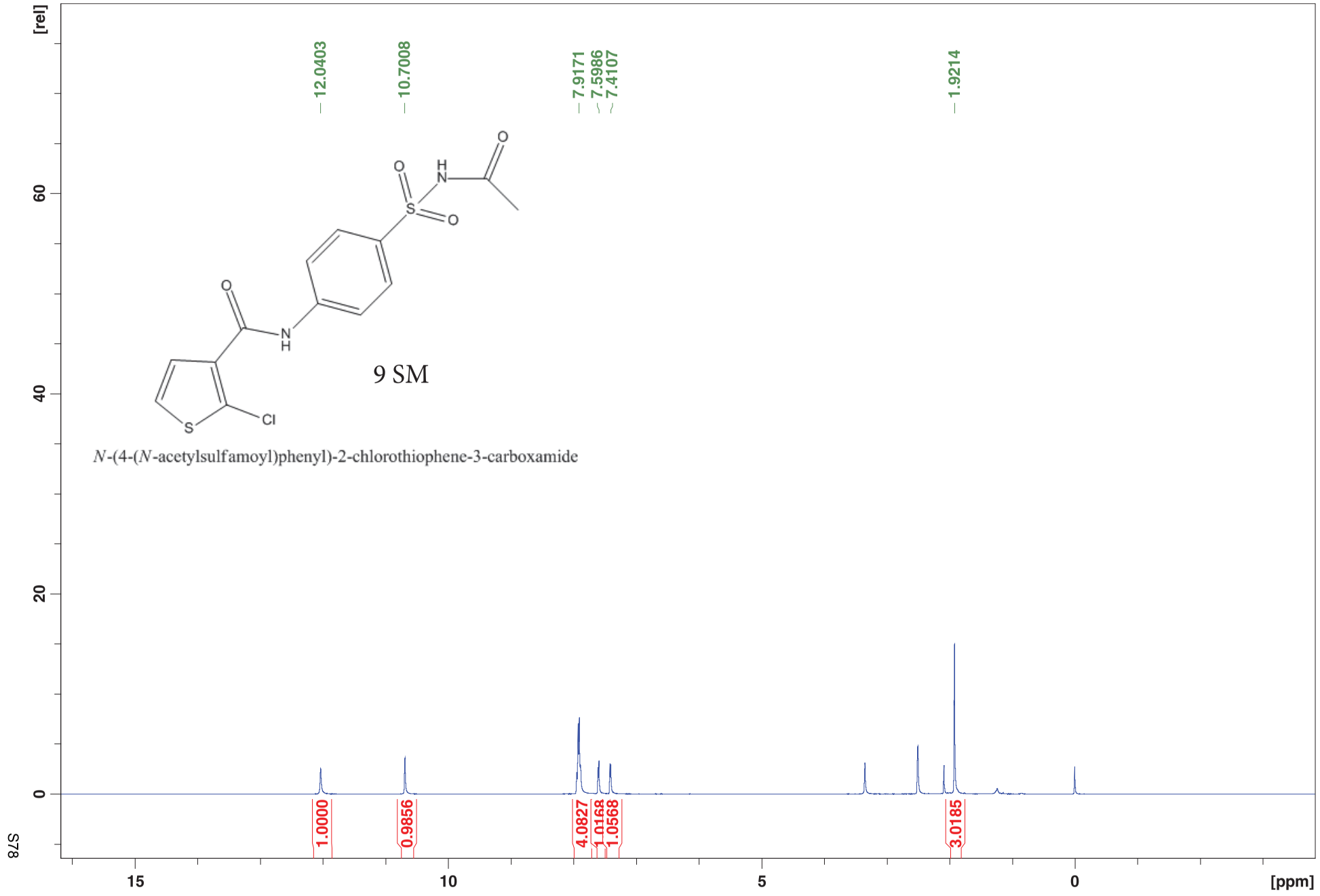

"FYH 160504 CtpAn4OMe SM0502" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
20
15
10
5
0
8.1609
7.5548
7.4737
7.1524
6.9255
3.8370
O
O
N
H
S
Cl
7 SM
2-chloro-N-(4-methoxyphenyl)thiophene-3-carboxamide
1.0000
1.1317
1.0636
2.2946
3.5405
15
10
5
0
[ppm]


"FYH 160504 CtpAn4OMe SM0502 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
159.4664
156.8061
133.5517
130.5221
129.2297
129.0535
123.1119
122.1132
114.2750
55.5388
7 SM
2-chloro-N-(4-methoxyphenyl)thiophene-3-carboxamide
[ppm]

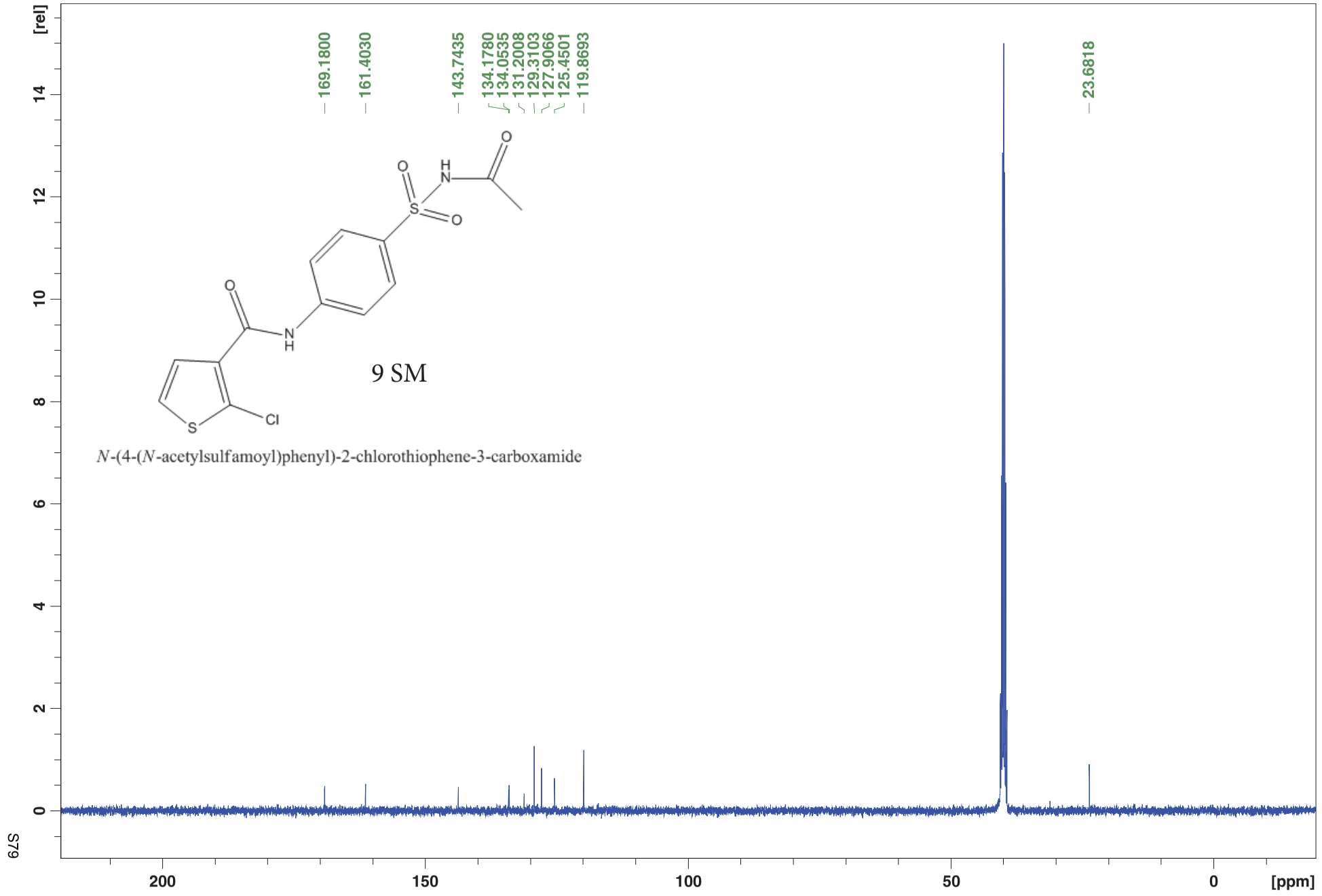

"FYH 160513 CtpAn2Me SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
8.1849
8.0878
7.5454
7.2988
7.2602
7.1761
7.1410
2.3928
O
N
H
S
Cl
8 SM
2-chloro-N-(o-tolyl)thiophene-3-carboxamide
1.0000
0.9964
1.0955
3.1861
[ppm]


"FYH 160513 CtpAn2Me SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
159.4430
135.6543
133.7242
130.5789
129.7092
128.8990
128.6607
126.9213
125.2771
123.1207
122.7752
18.2842
O
N
H
S
Cl
8 SM
2-chloro-N-(o-tolyl)thiophene-3-carboxamide
S77
200
150
100
50
0
[ppm]

"FYH 160504 CtpANSul SM0502" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



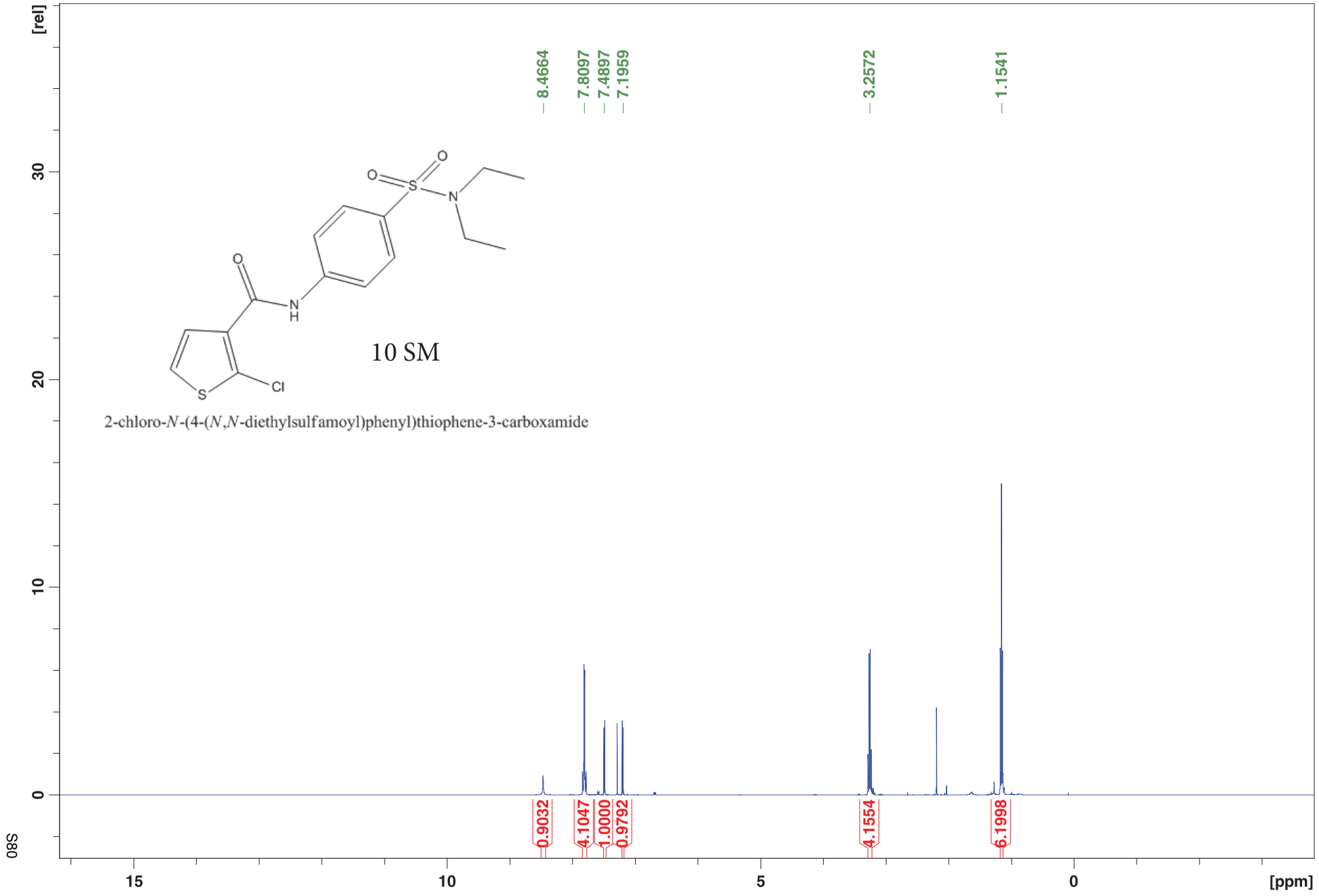
"FYH 160504 CtpANSul SM0502 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



9 SM

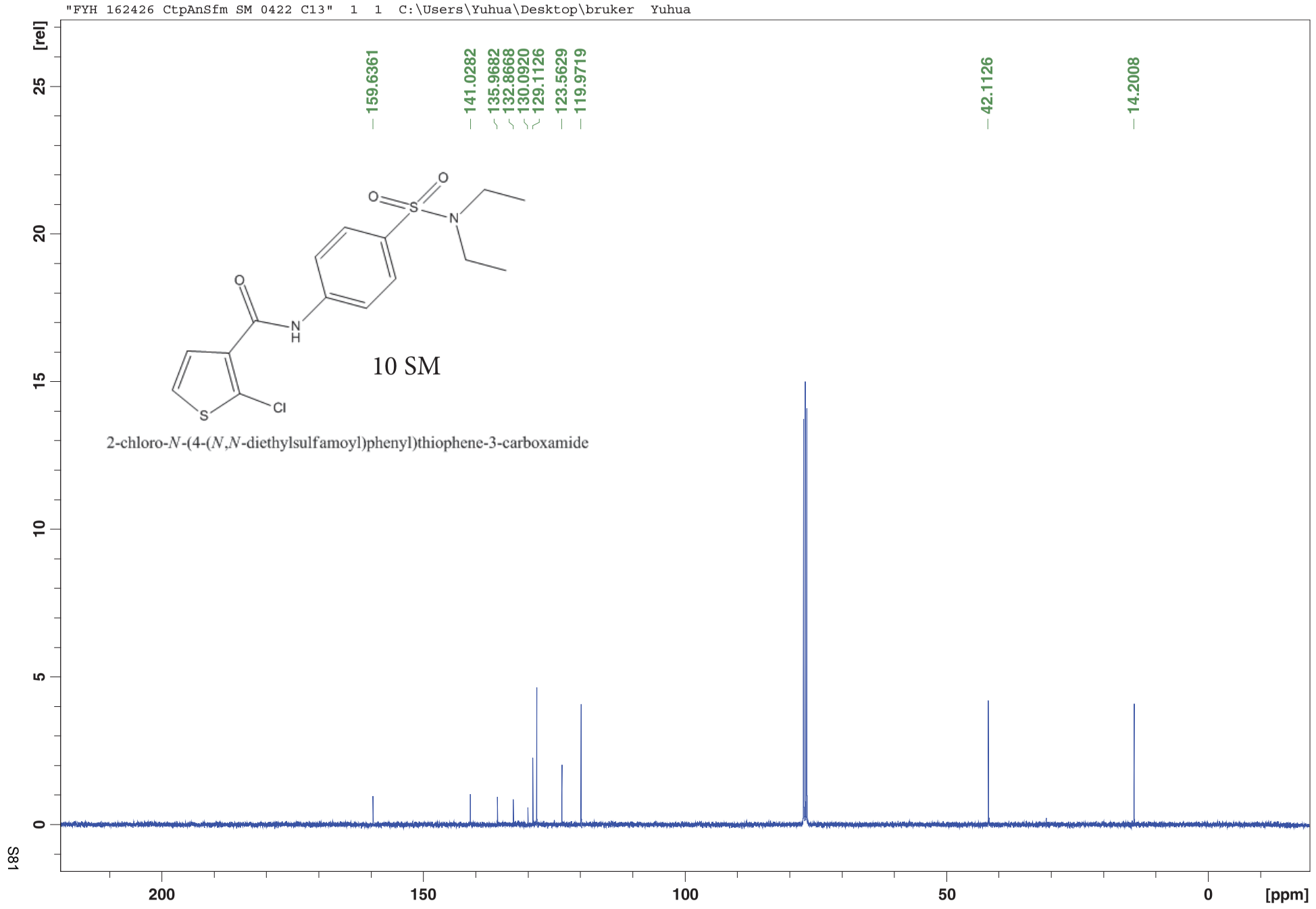
N-(4-(*N*-acetylsulfamoyl)phenyl)-2-chlorothiophene-3-carboxamide

"FYH 162426 CtpAnSfm SM 0422" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

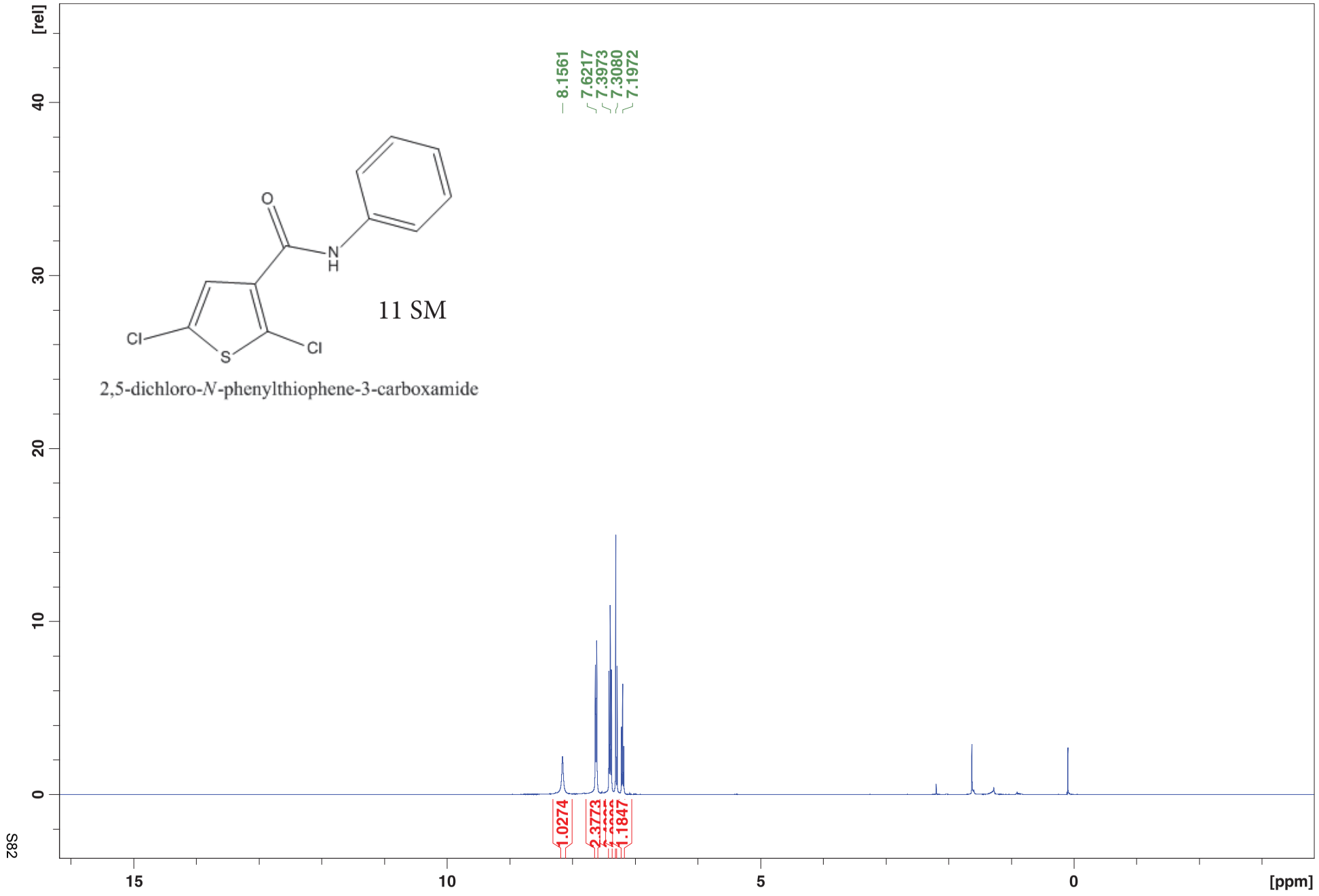


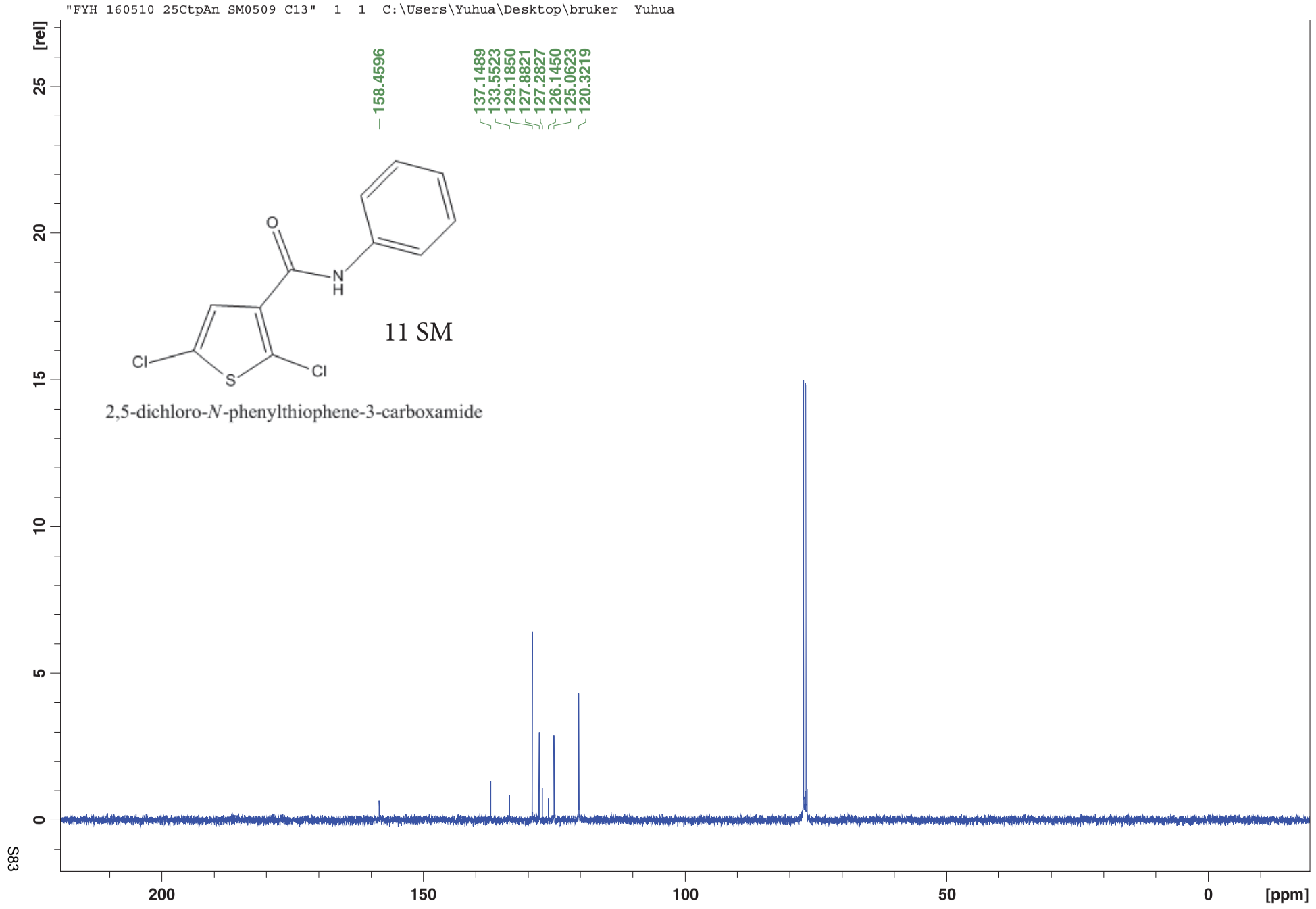
10 SM

2-chloro-*N*-(4-(*N*,*N*-diethylsulfamoyl)phenyl)thiophene-3-carboxamide


"FYH 162426 CtpAnSfm SM 0422 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
25
20
15
10
5
0
159.6361
141.0282
135.9682
132.8668
130.0920
129.1126
123.5629
119.9719
42.1126
14.2008
10 SM
2-chloro-N-(4-(N,N-diethylsulfamoyl)phenyl)thiophene-3-carboxamide
200
150
100
50
0
[ppm]

"FYH 160510 25CtpAn SM0509" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

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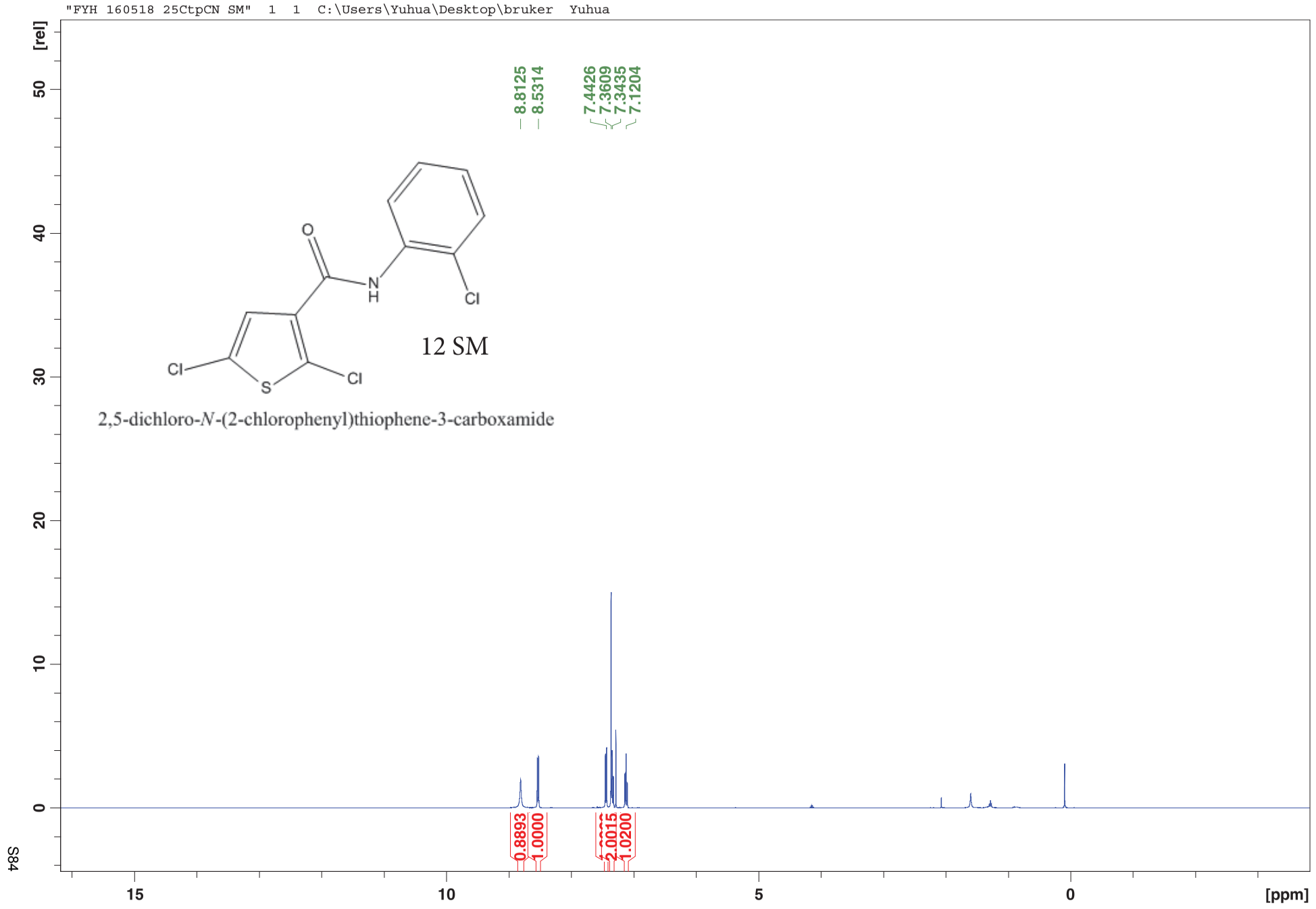
[rel]
25
20
15
10
5
0
158.4596
137.1489
133.5523
129.1850
127.8821
127.2827
126.1450
125.0623
120.3219
O
N
H
Cl
S
Cl
11 SM
2,5-dichloro-N-phenylthiophene-3-carboxamide
200
150
100
50
0
[ppm]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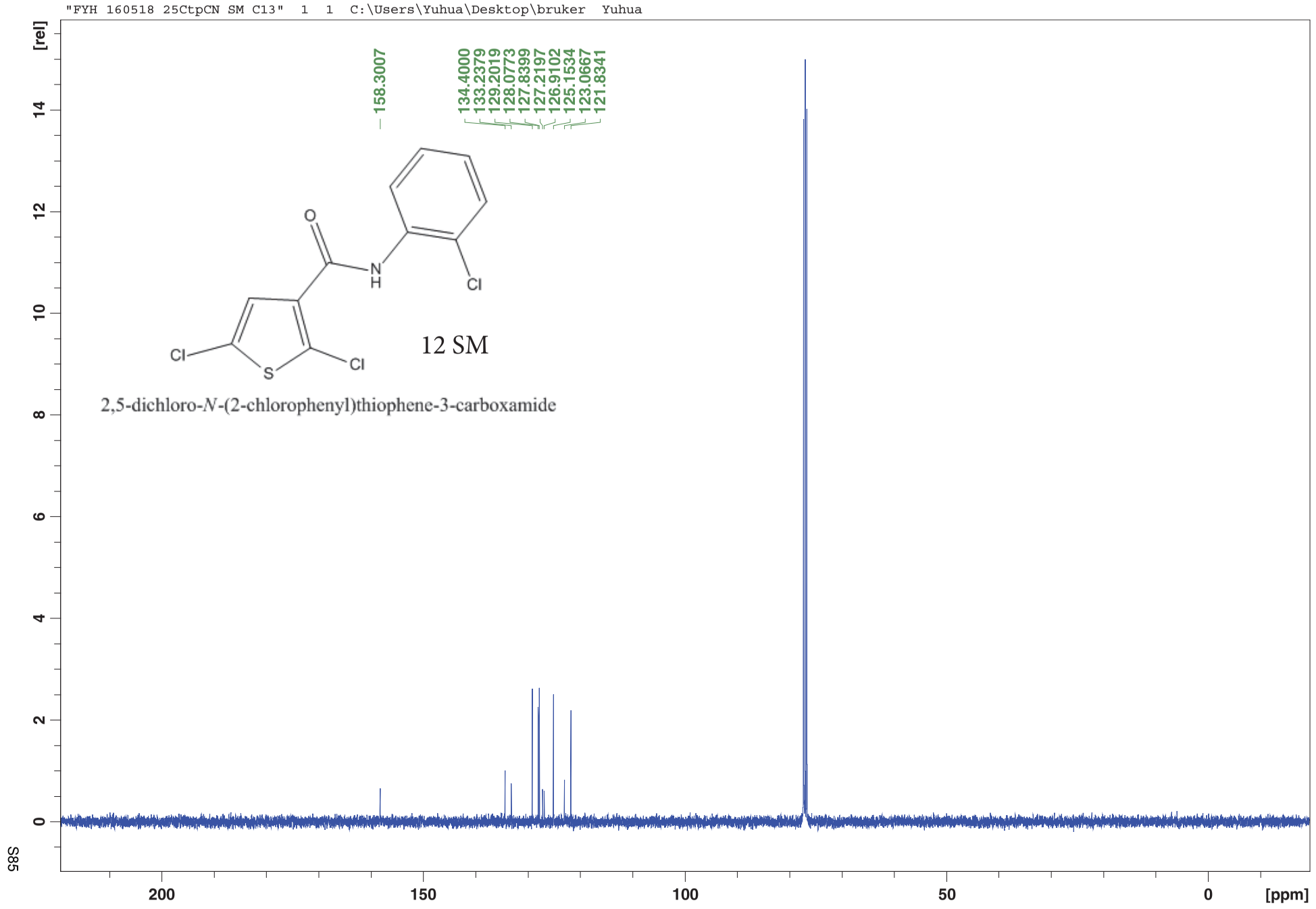
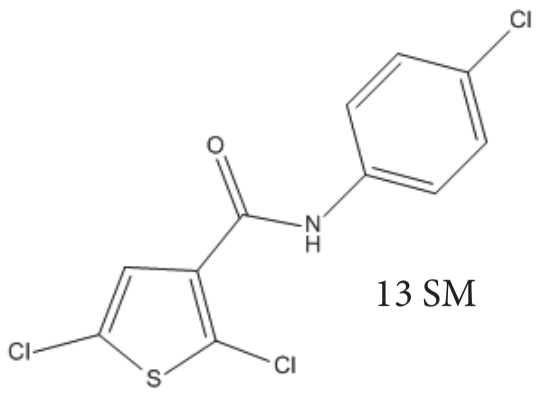
[rel]
50
40
30
20
10
0
8.8125
8.5314
7.4426
7.3609
7.3435
7.1204
O
N
H
Cl
Cl
Cl
S
12 SM
2,5-dichloro-N-(2-chlorophenyl)thiophene-3-carboxamide
0.8893
1.0000
2.0015
1.0200
15
10
5
0
[ppm]


"FYH 160518 25CtpCN SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
158.3007
134.4000
133.2379
129.2019
128.0773
127.8399
127.2197
126.9102
125.1534
123.0667
121.8341
[rel]
14
12
10
8
6
4
2
0
200
150
100
50
0
[ppm]
O
N
H
Cl
Cl
Cl
S
12 SM
2,5-dichloro-N-(2-chlorophenyl)thiophene-3-carboxamide

"FYH 160510 25CtpAn4Cl SM0509" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



13 SM

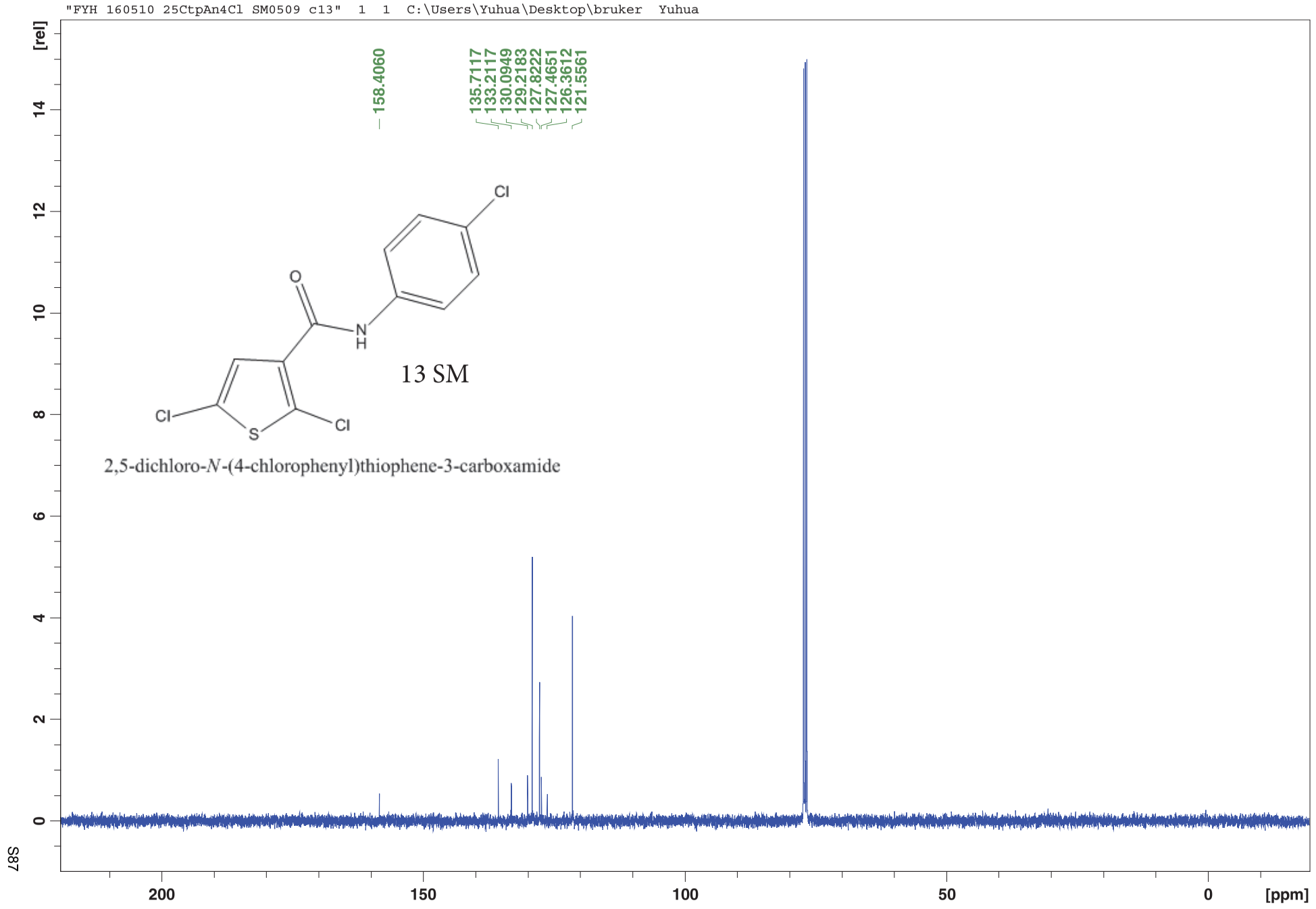
2,5-dichloro-*N*-(4-chlorophenyl)thiophene-3-carboxamide

8.1663
7.5764
7.3525
7.2975

1.0000
2.4775
2.4990

[rel]
50
40
30
20
10
0
15
10
5
0
[ppm]

S86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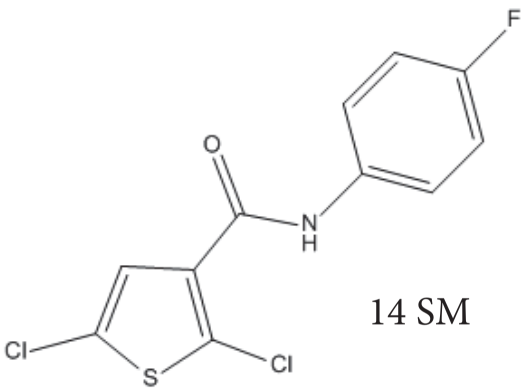
[rel]
158.4060
135.7117
133.2117
130.0949
129.2183
127.8222
127.4651
126.3612
121.5561
Cl
O
N
H
Cl
Cl
S
13 SM
2,5-dichloro-N-(4-chlorophenyl)thiophene-3-carboxamide
200
150
100
50
0
[ppm]

"FYH 160707 25CtpAn4F SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



14 SM

2,5-dichloro-*N*-(4-fluorophenyl)thiophene-3-carboxamide

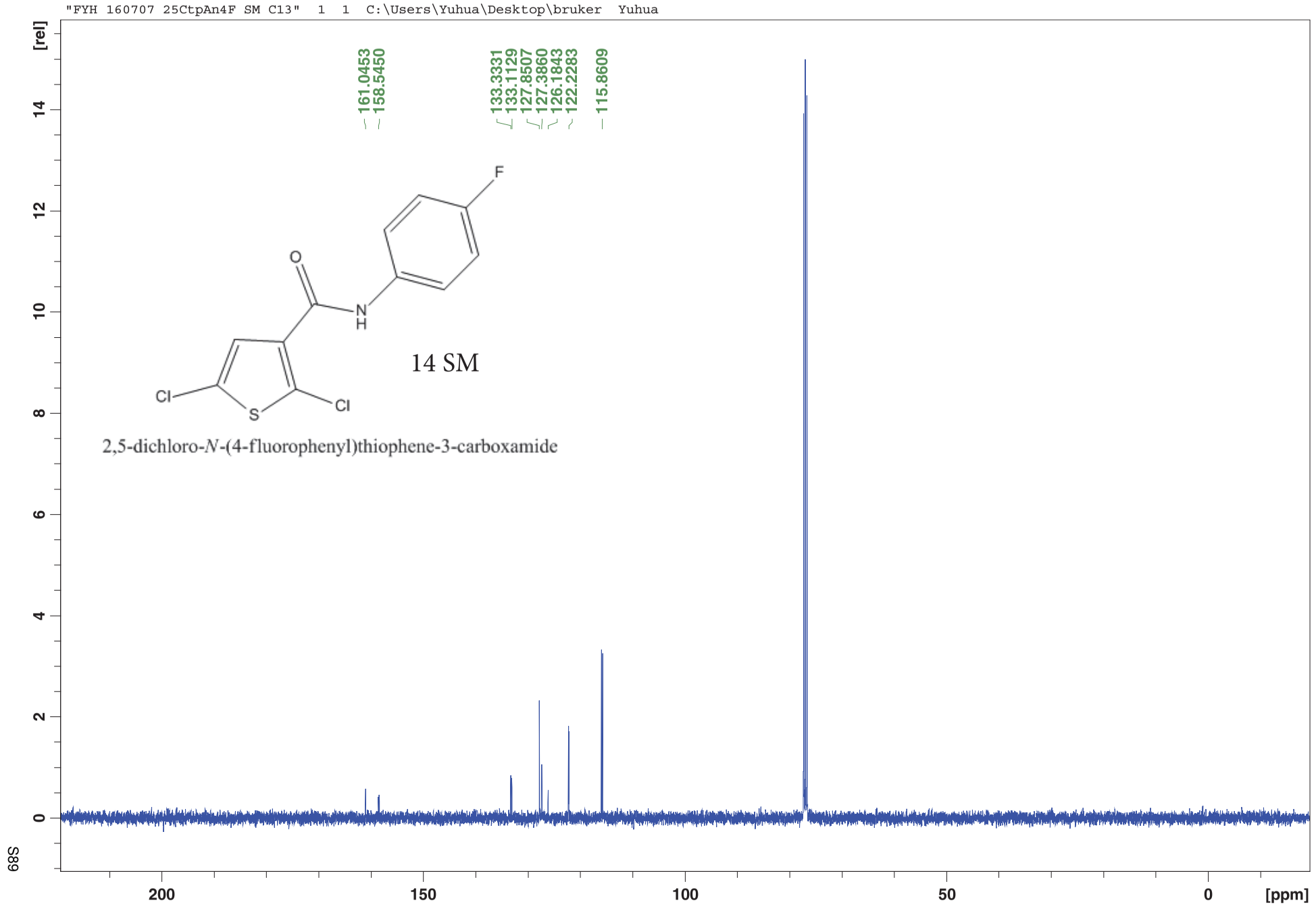
8.1169
7.5798
7.3027
7.0853

1.0000
2.1694
0.9685
2.1910

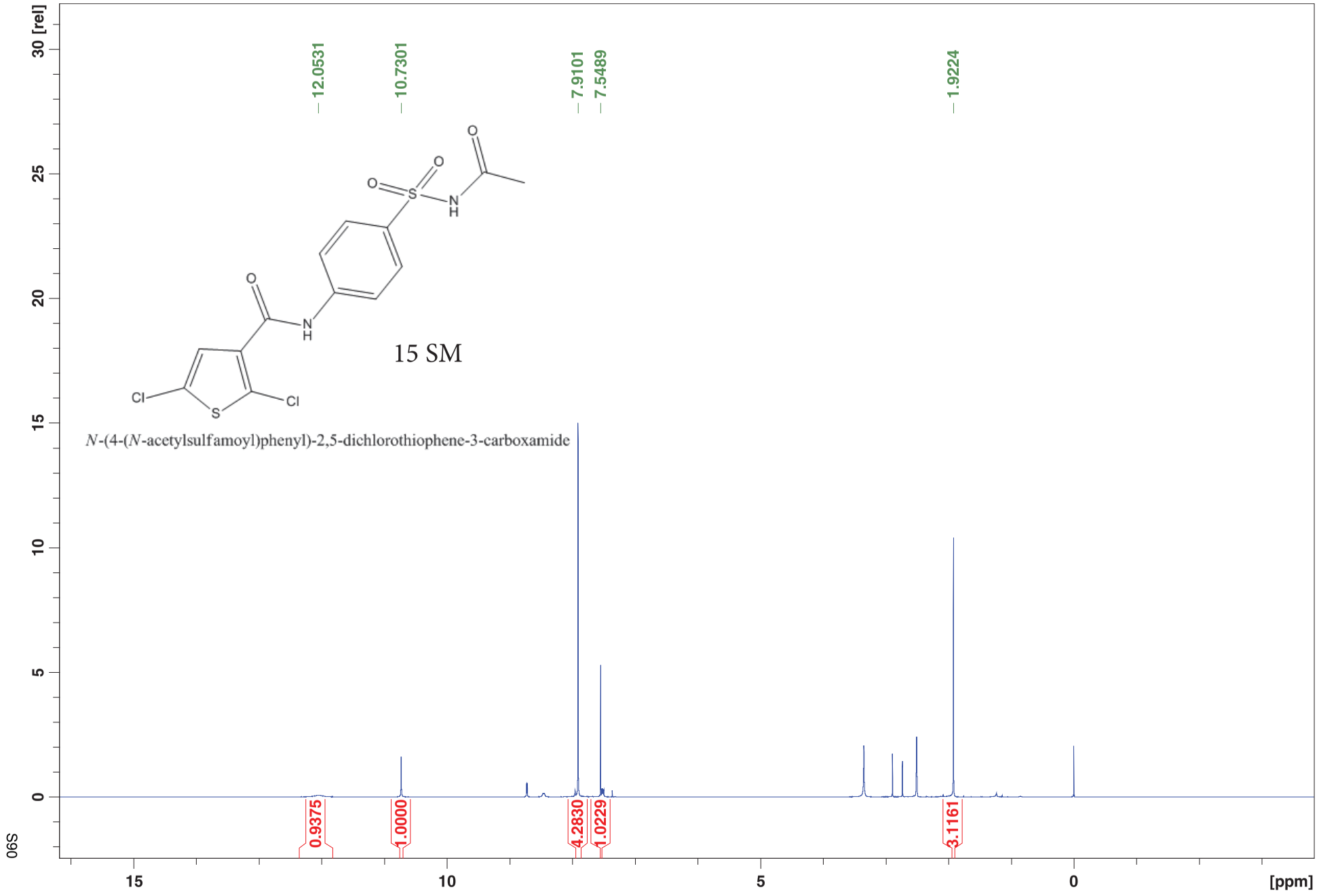
30 [rel]
25
20
15
10
5
0

15
10
5
0
[ppm]

S88

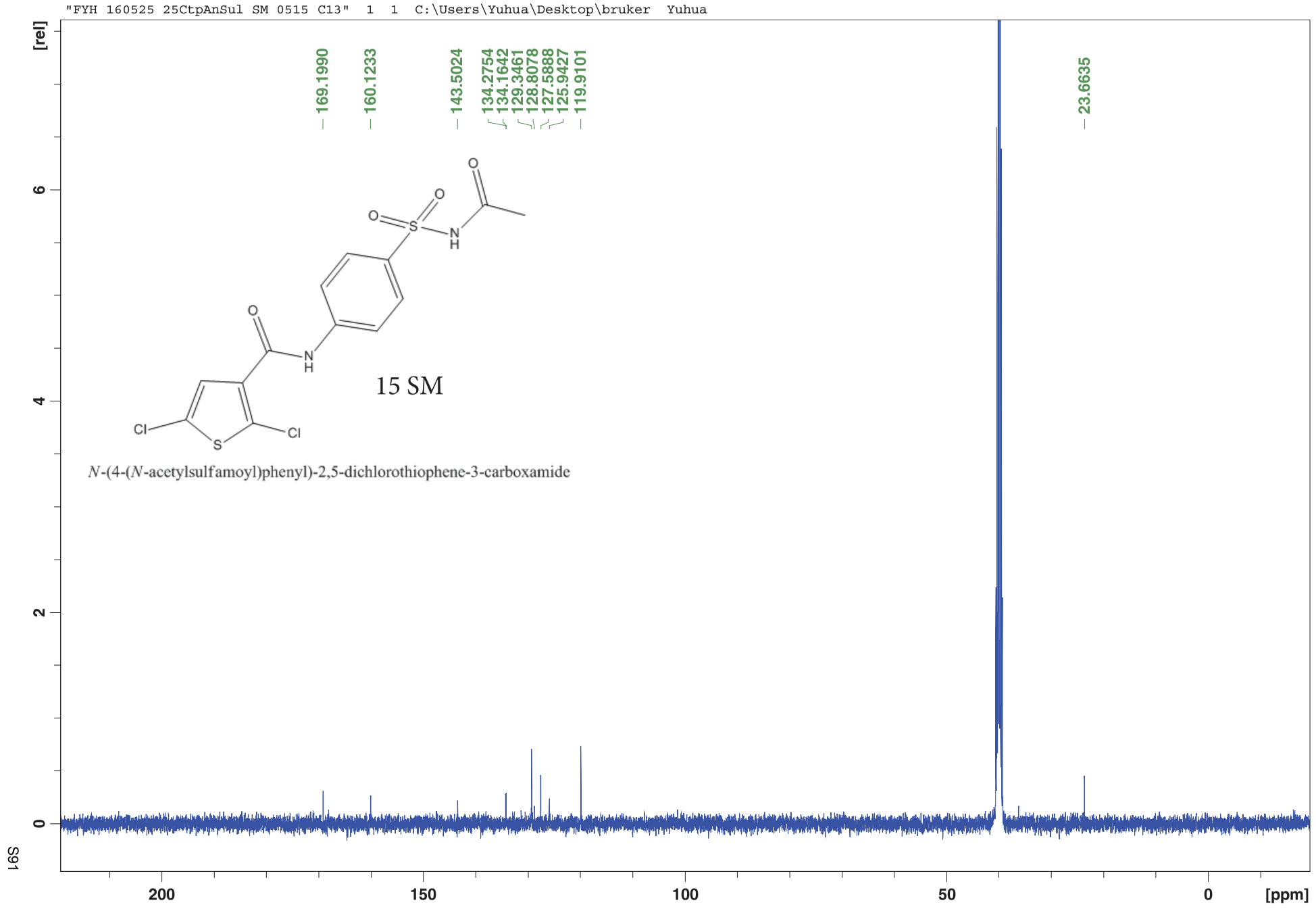

"FYH 160707 25CtpAn4F SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
161.0453
158.5450
133.3331
133.1129
127.8507
127.3860
126.1843
122.2283
115.8609
F
O
N
H
Cl
S
Cl
14 SM
2,5-dichloro-N-(4-fluorophenyl)thiophene-3-carboxamide
[ppm]
200
150
100
50
0
S89

"FYH 160525 25CtpAnSul SM 0515" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

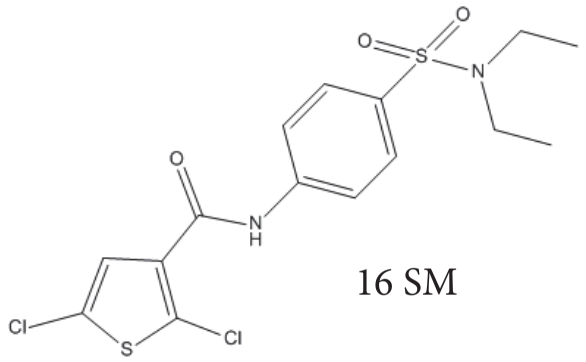


15 SM

N-(4-(*N*-acetylsulfamoyl)phenyl)-2,5-dichlorothiophene-3-carboxamide


"FYH 160525 25CtpAnSul SM 0515 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
169.1990
160.1233
143.5024
134.2754
134.1642
129.3461
128.8078
127.5888
125.9427
119.9101
23.6635
15 SM
N-(4-(N-acetylsulfamoyl)phenyl)-2,5-dichlorothiophene-3-carboxamide
0
2
4
6
200
150
100
50
0
[ppm]

"FYH 160528 25CtpAnSfm SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



16 SM

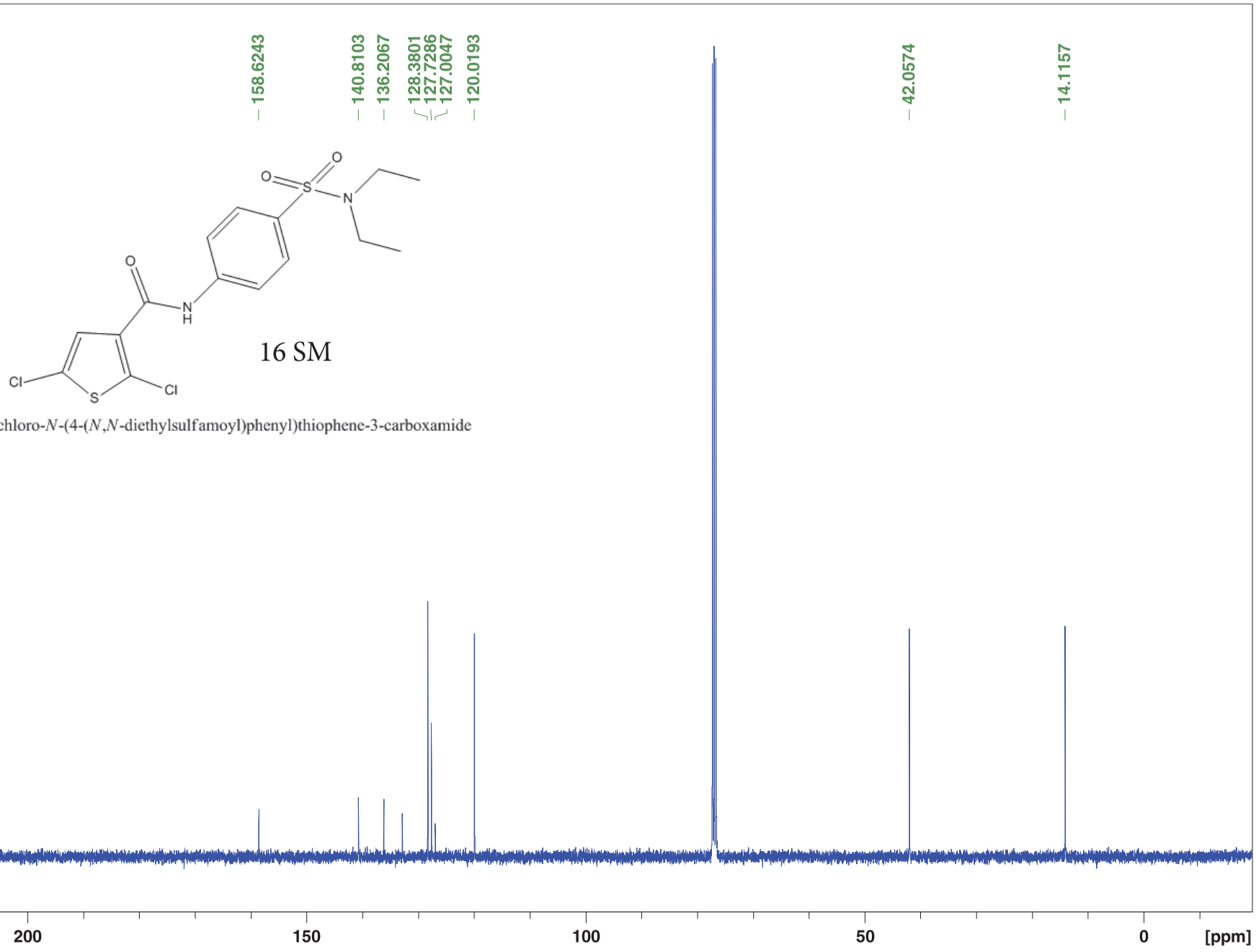
2,5-dichloro-*N*-(4-(*N*,*N*-diethylsulfamoyl)phenyl)thiophene-3-carboxamide

8.3733
7.7928
7.2985
3.2583
1.1577

1.0000
4.5155
1.4699
3.8113
6.2447

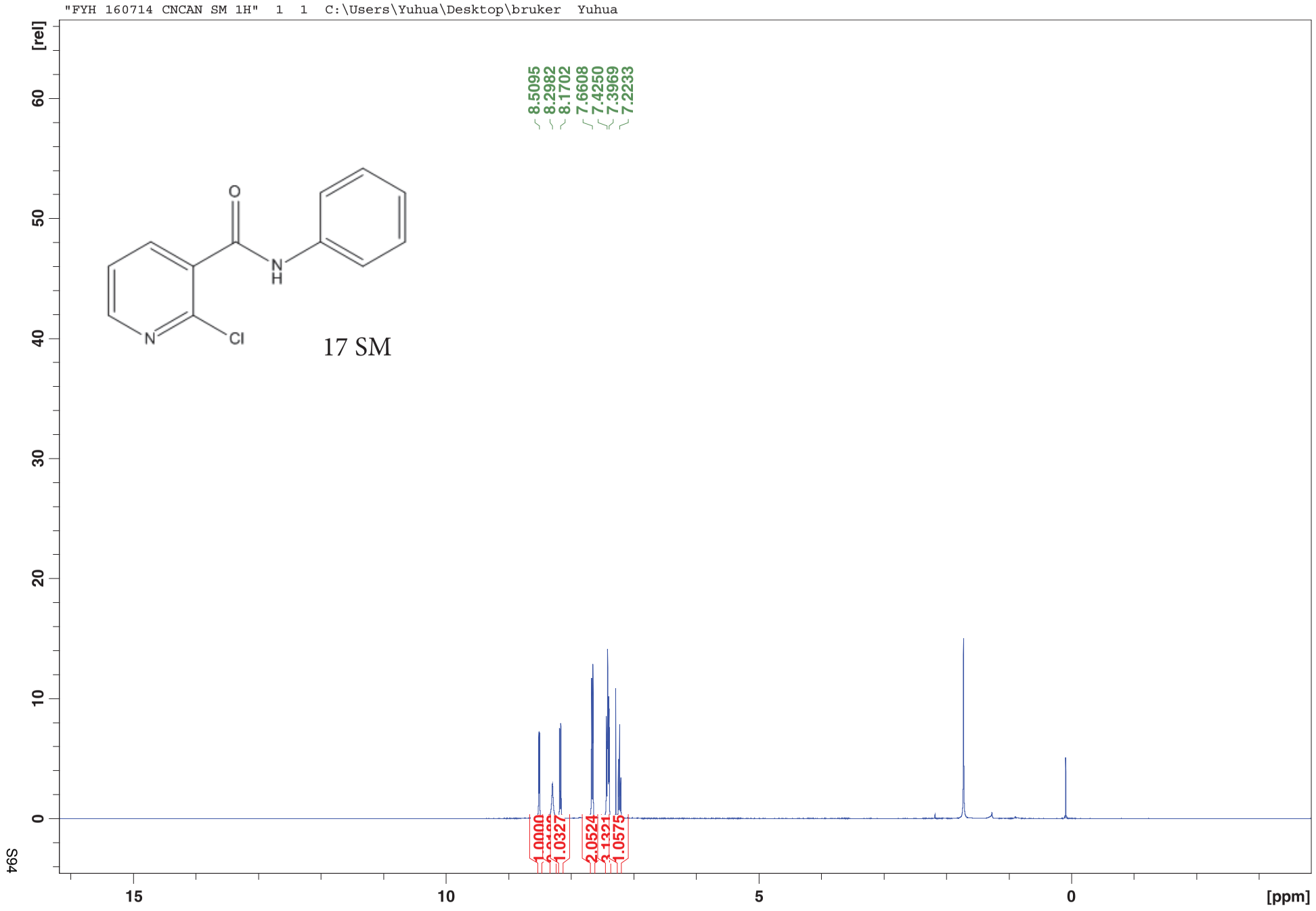
[rel]
40
30
20
10
0
15
10
5
0
[ppm]

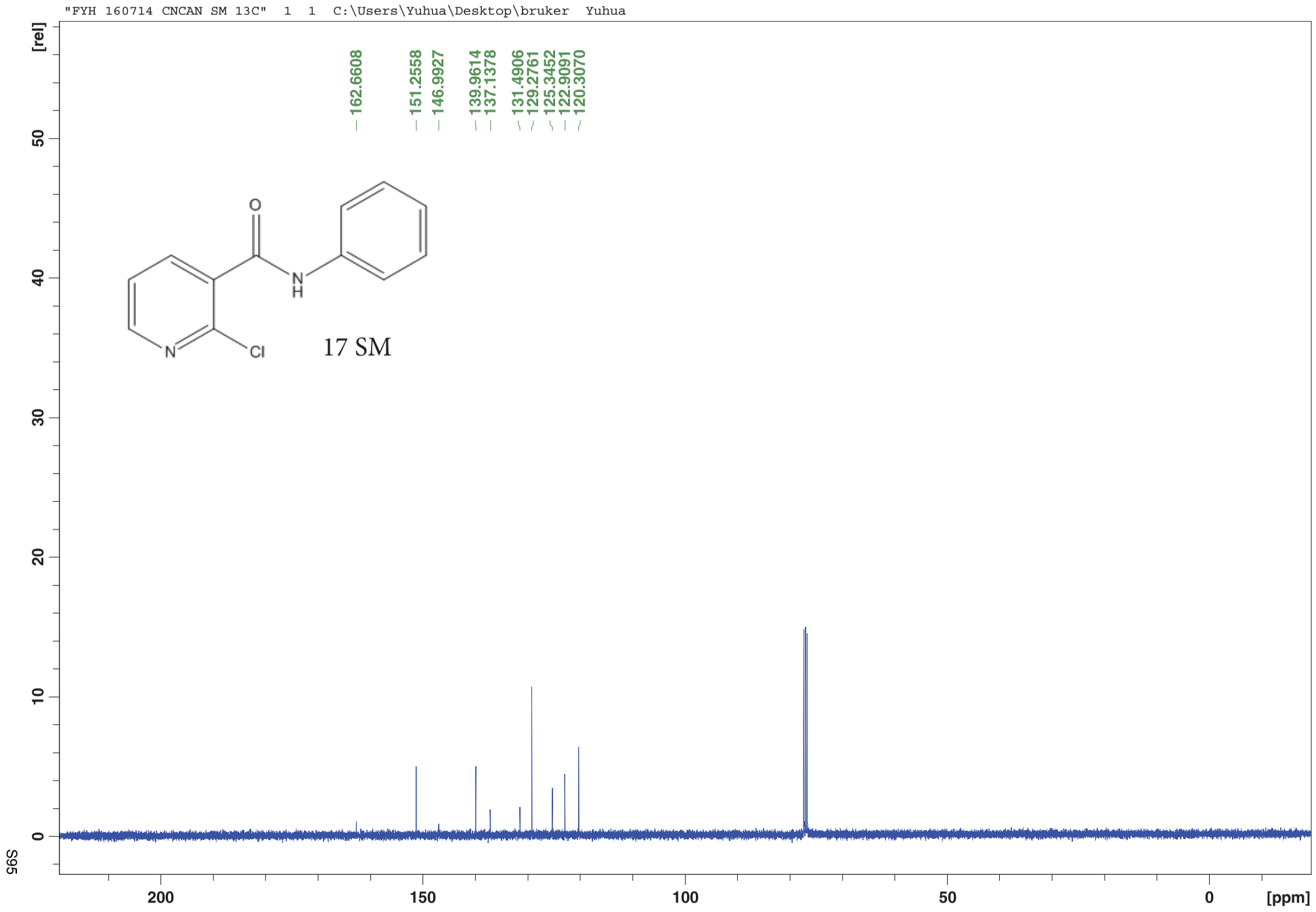
"FYH 160528 25CtpAnSfm SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



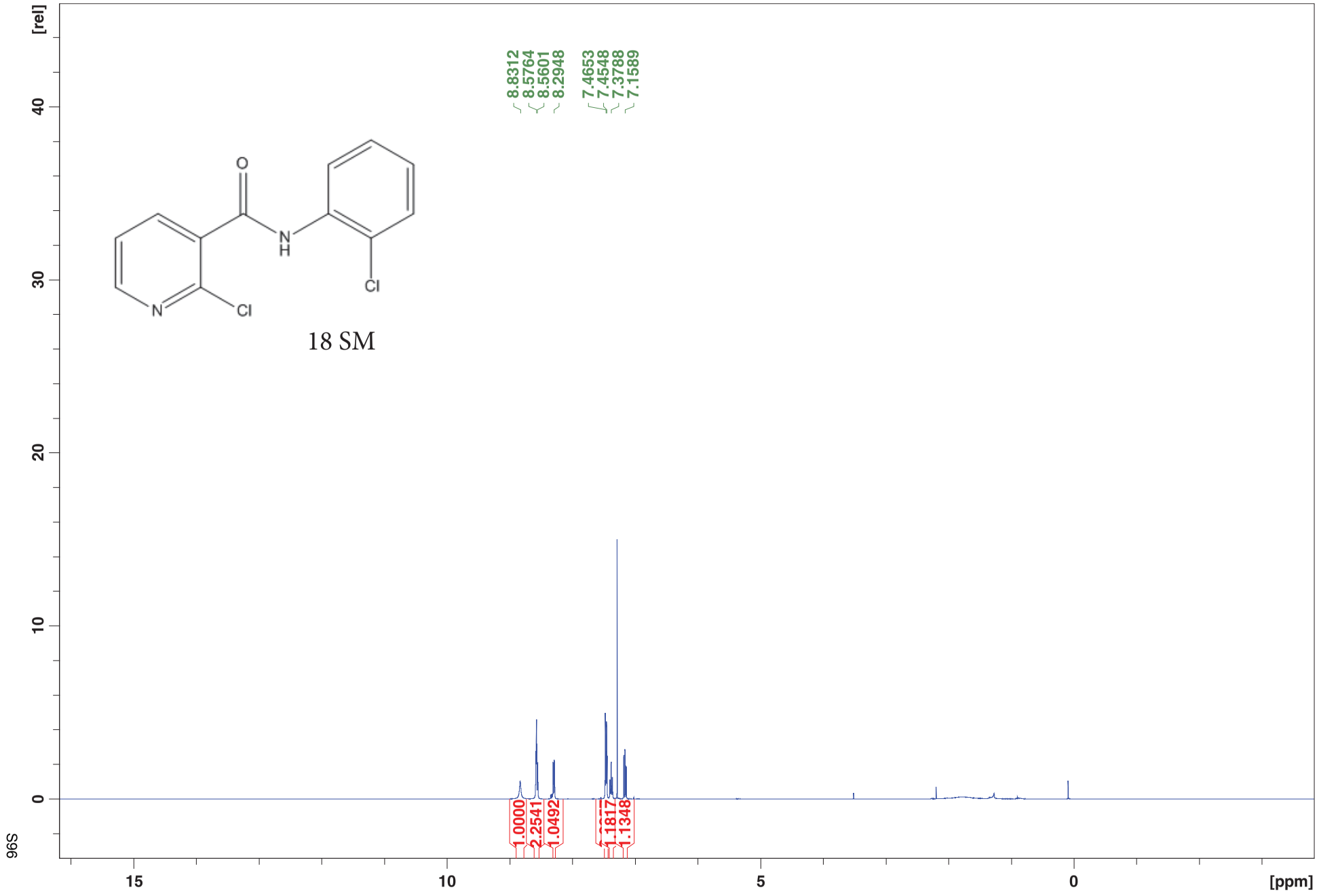
16 SM

2,5-dichloro-*N*-(4-(*N*,*N*-diethylsulfamoyl)phenyl)thiophene-3-carboxamide

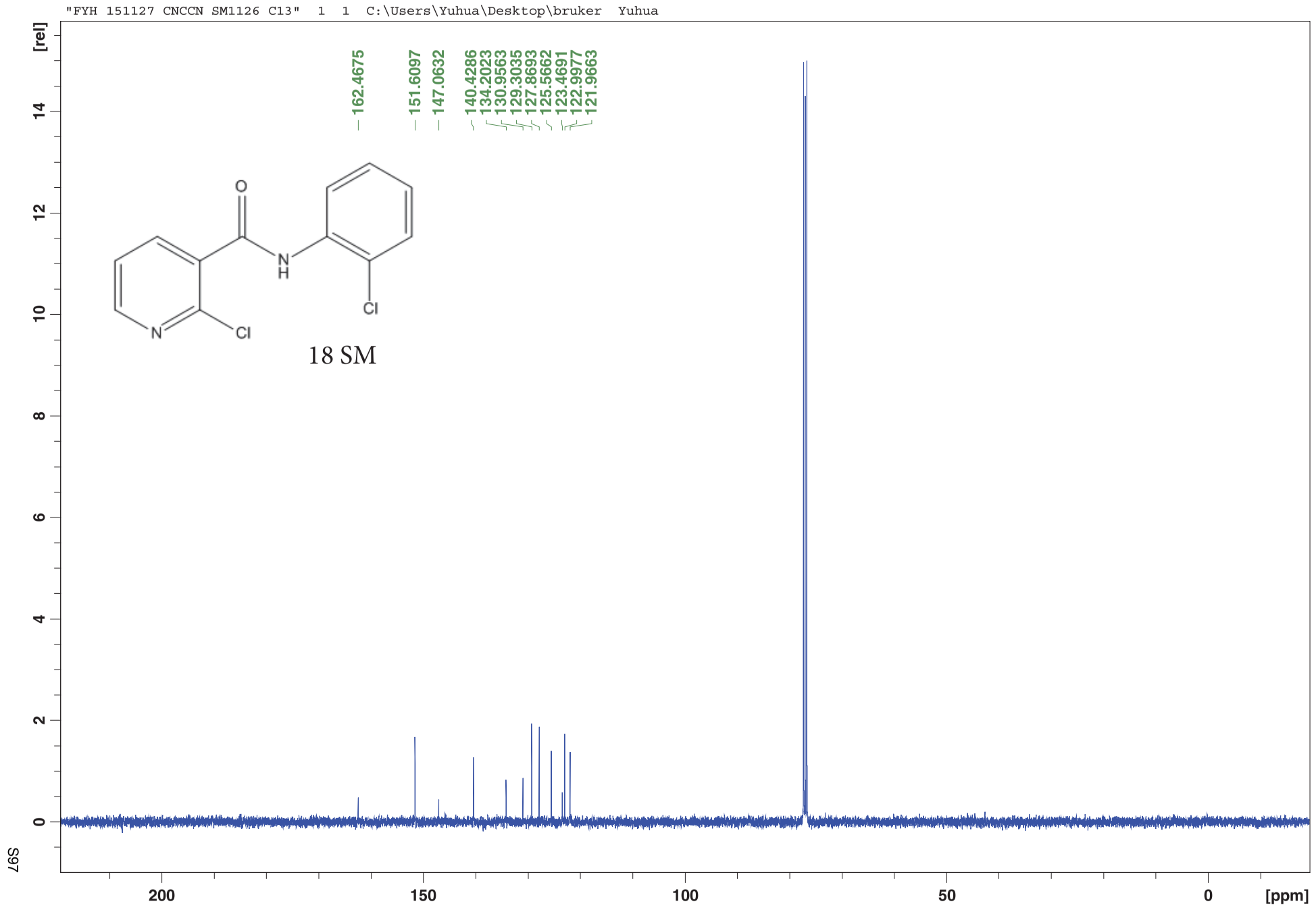

"FYH 160714 CNCAN SM 1H" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
8.5095
8.2982
8.1702
7.6608
7.4250
7.3969
7.2233
O
N
H
N
Cl
17 SM
1.0000
1.0327
2.0524
2.1321
1.0575
15
10
5
0
[ppm]


"FYH 160714 CNCAN SM 13C" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
162.6608
151.2558
146.9927
139.9614
137.1378
131.4906
129.2761
125.3452
122.9091
120.3070
O
N
H
N
Cl
17 SM
0
10
20
30
40
50
200
150
100
50
0
[ppm]

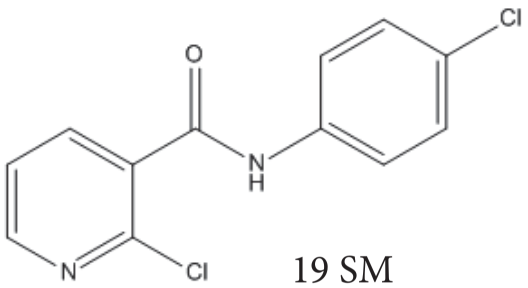
"FYH CNCCN SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua



18 SM


"FYH 151127 CNCCN SM1126 C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
162.4675
151.6097
147.0632
140.4286
134.2023
130.9563
129.3035
127.8693
125.5662
123.4691
122.9977
121.9663
O
N
H
Cl
N
Cl
18 SM
[rel]
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]

"FYH 160613 CNCAN4Cl SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua

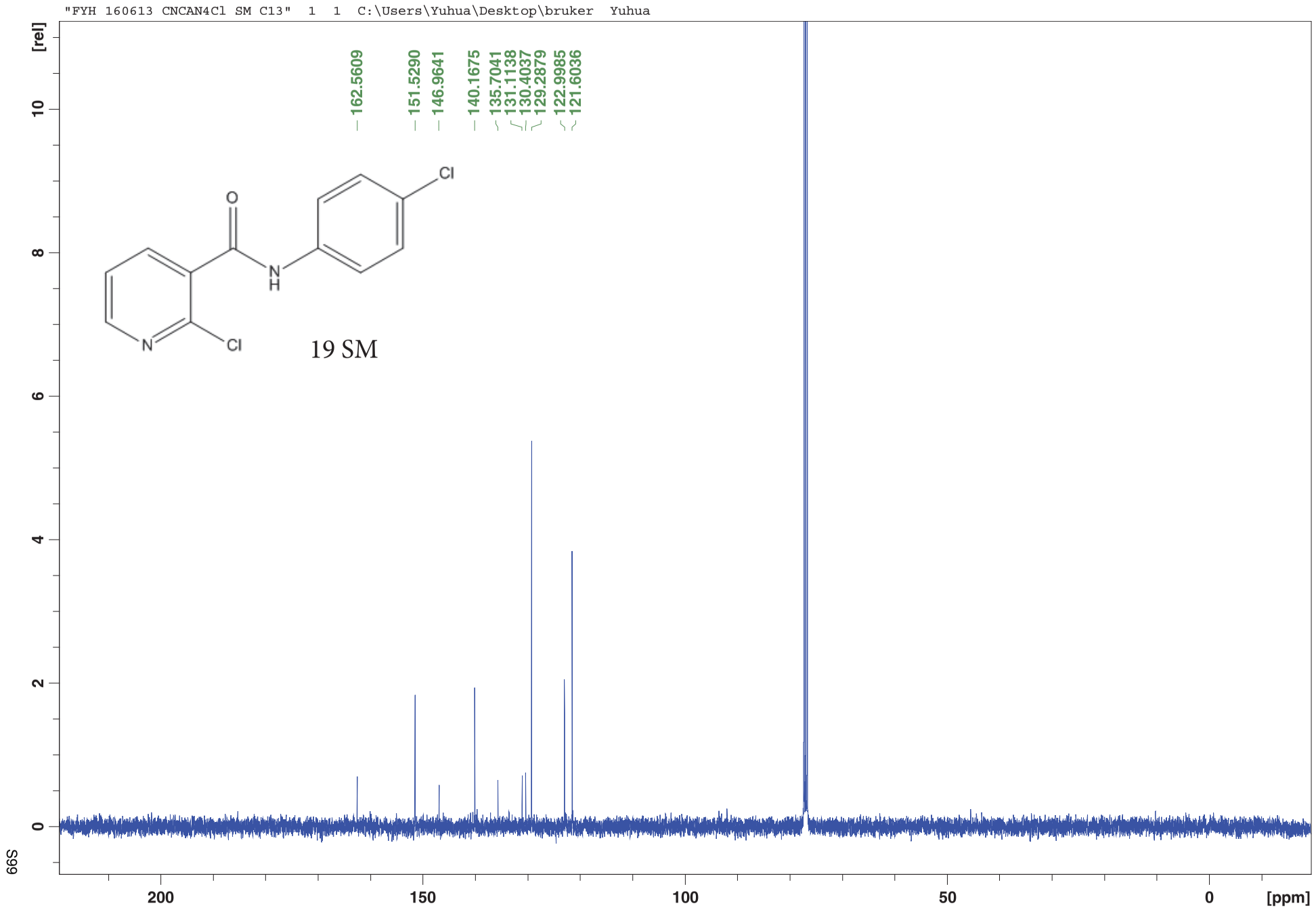


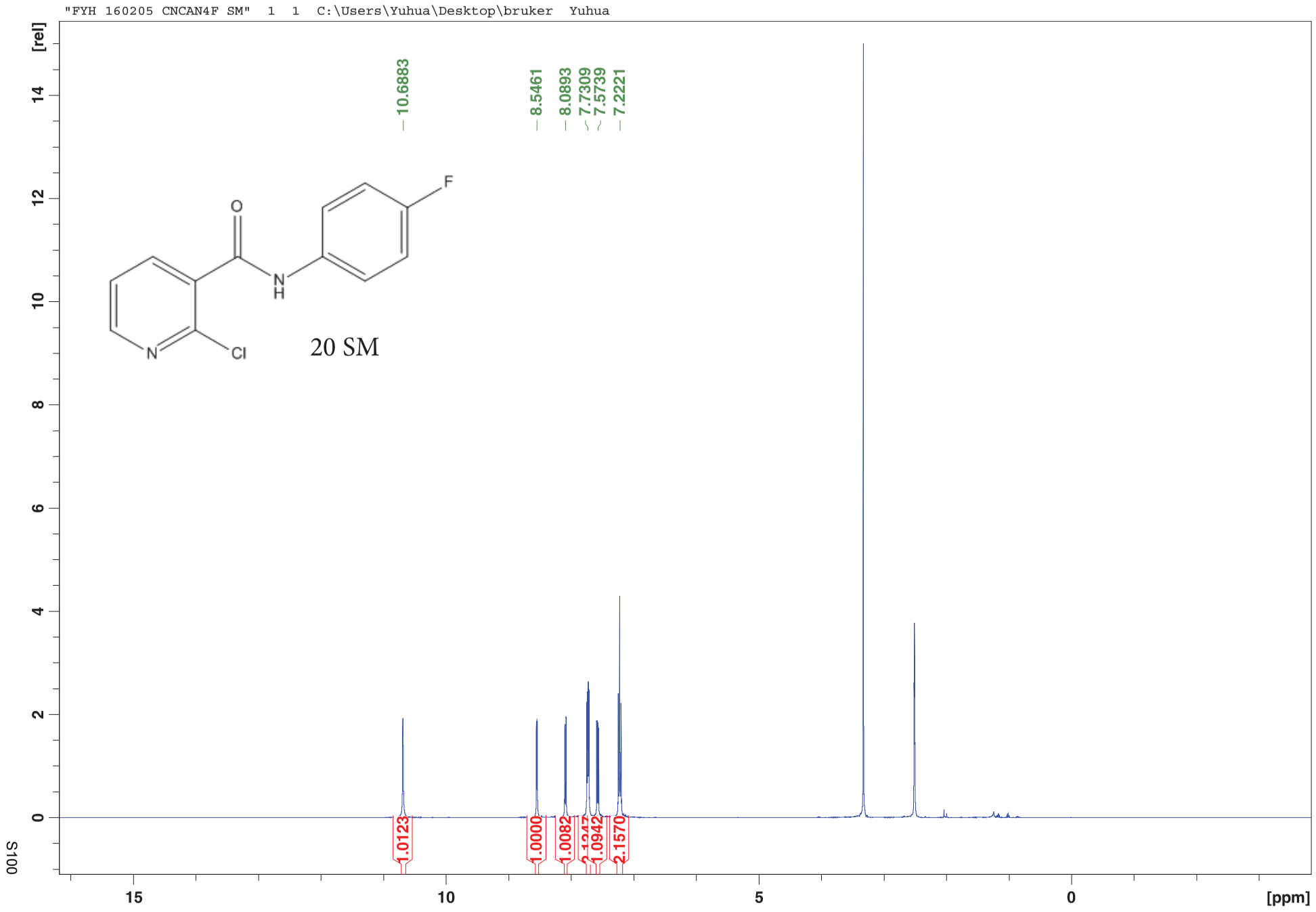
19 SM

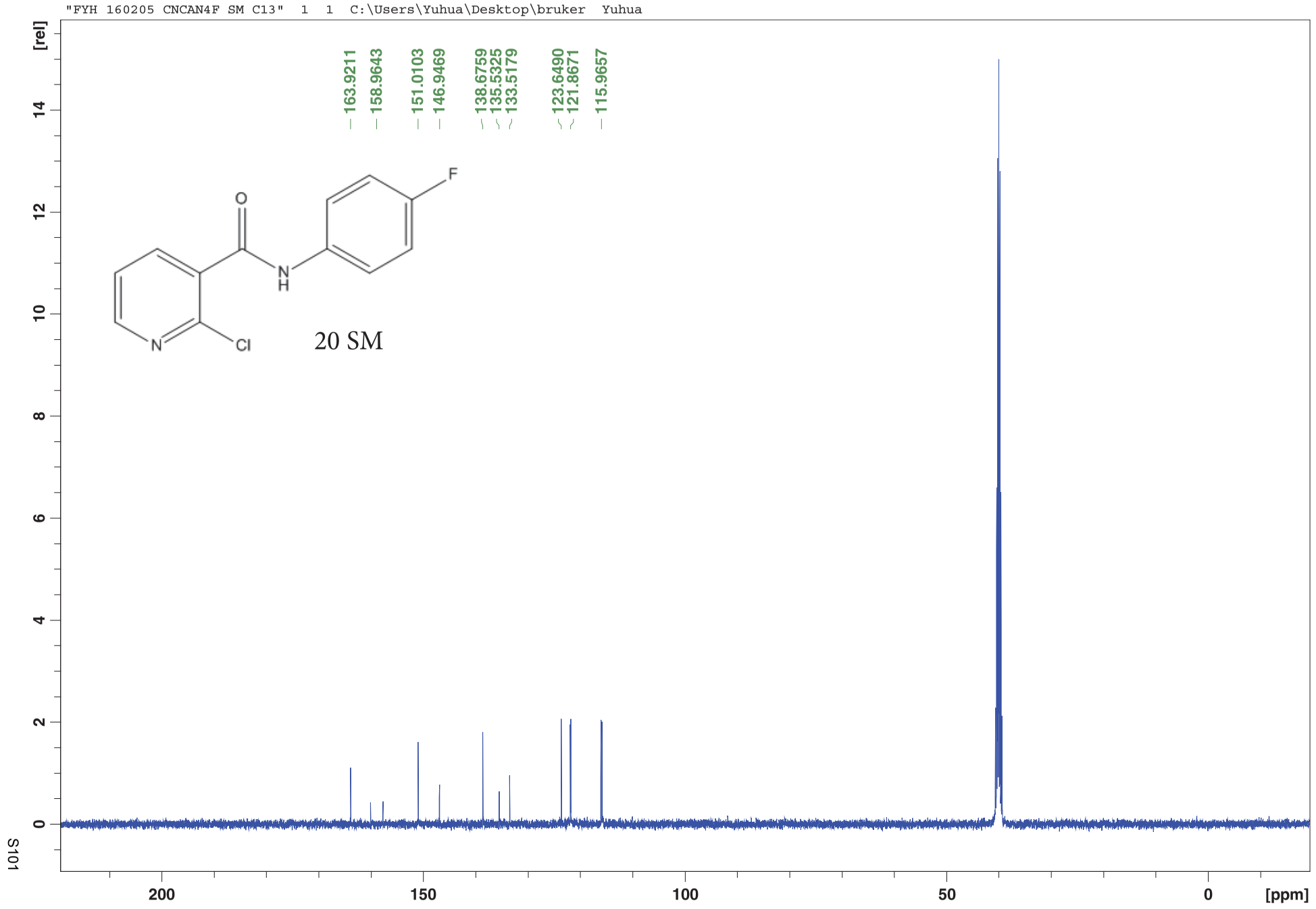
8.5329
8.2715
8.2101
7.6225
7.4225
7.3789

1.0855
1.1327
2.3451
2.2311

[rel]
100
80
60
40
20
0
15
10
5
0
[ppm]


"FYH 160613 CNCAN4Cl SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
162.5609
151.5290
146.9641
140.1675
135.7041
131.1138
130.4037
129.2879
122.9985
121.6036
O
N
H
Cl
N
Cl
19 SM
[rel]
10
8
6
4
2
0
200
150
100
50
0
[ppm]
66S99


"FYH 160205 CNCAN4F SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
10.6883
8.5461
8.0893
7.7309
7.5739
7.2221
F
O
N
H
N
Cl
20 SM
1.0123
1.0000
1.0082
2.1347
1.0942
2.1570
S100
15
10
5
0
[ppm]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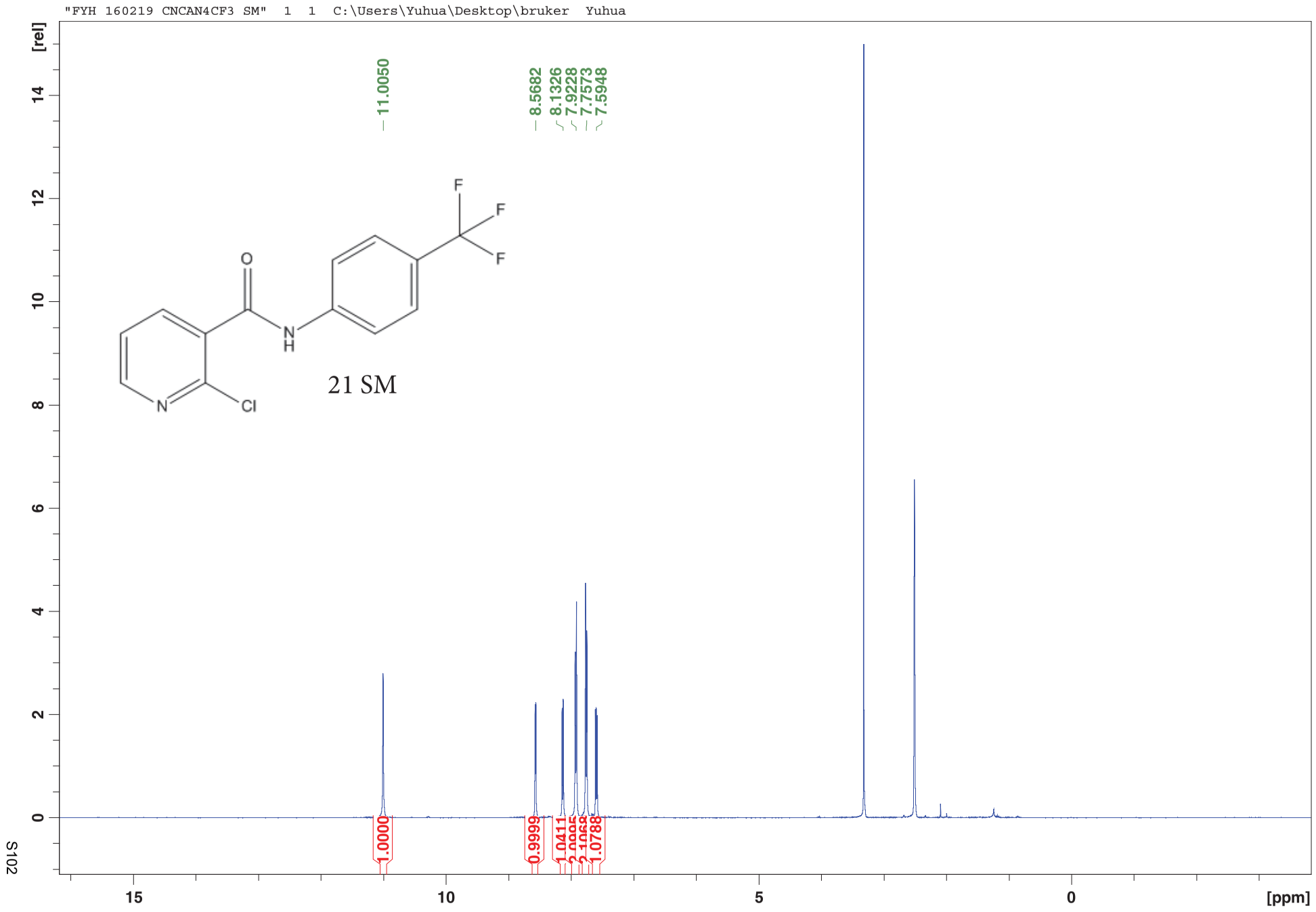
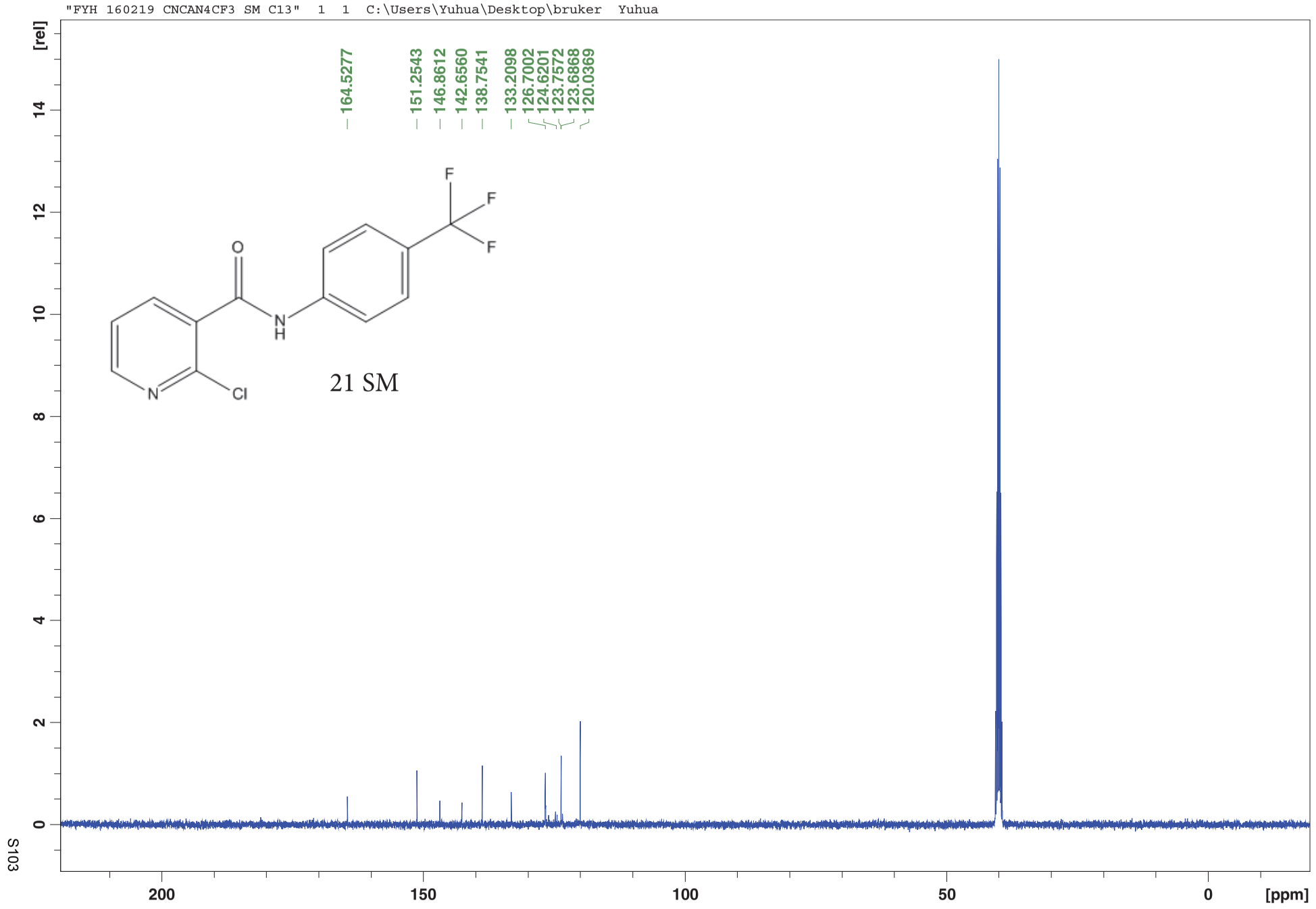
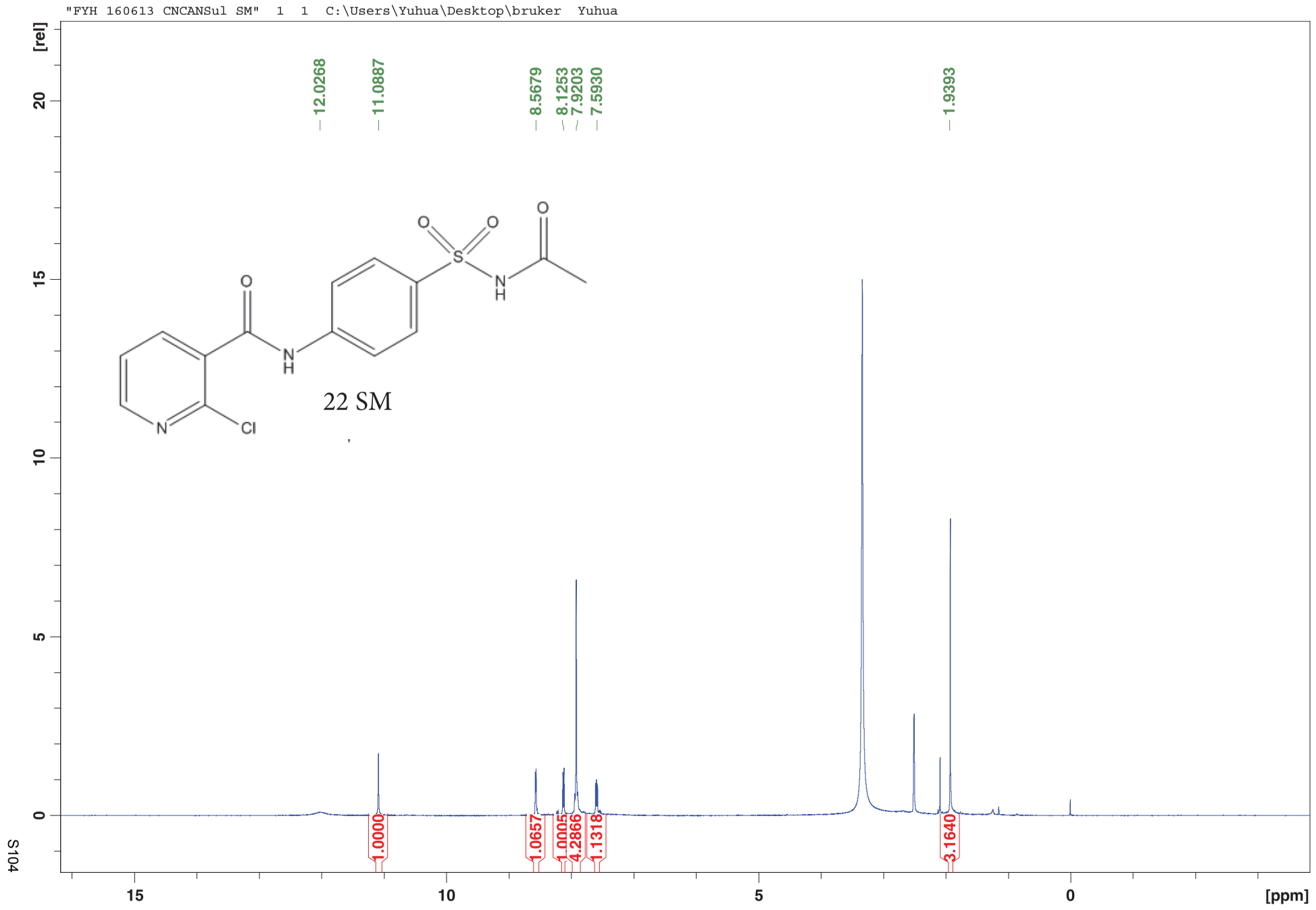
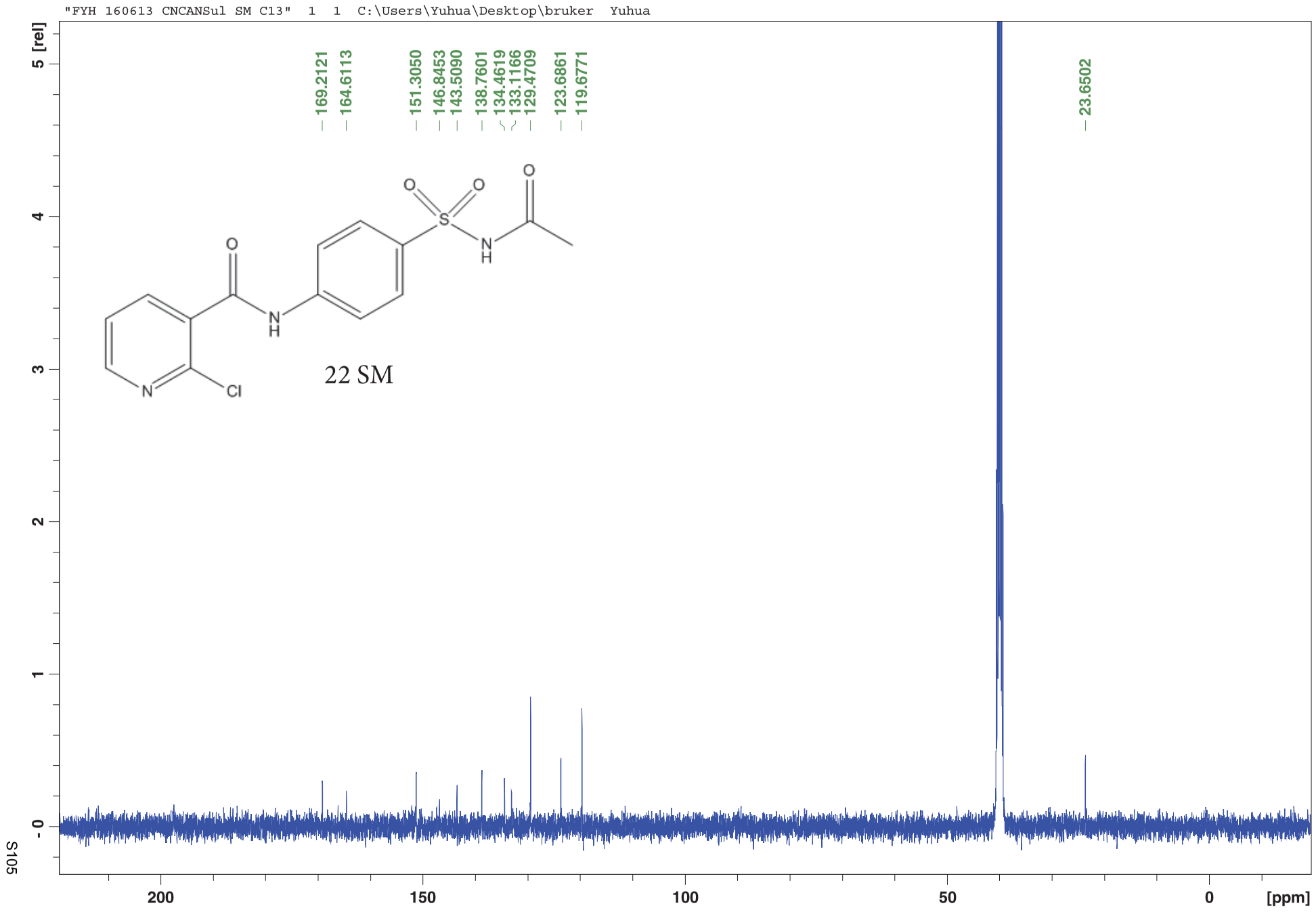
163.9211
158.9643
151.0103
146.9469
138.6759
135.5325
133.5179
123.6490
121.8671
115.9657
O
N
H
F
N
Cl
20 SM
[rel]
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]


"FYH 160219 CNCAN4CF3 SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
11.0050
8.5682
8.1326
7.9228
7.7573
7.5948
21 SM
1.0000
0.9999
1.0411
1.0788
[ppm]


"FYH 160219 CNCAN4CF3 SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
164.5277
151.2543
146.8612
142.6560
138.7541
133.2098
126.7002
124.6201
123.7572
123.6868
120.0369
O
N
H
F
F
F
N
Cl
21 SM
0
2
4
6
8
10
12
14
200
150
100
50
0
[ppm]


"FYH 160613 CNCANSul SM" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
[rel]
20
15
10
5
0
12.0268
11.0887
8.5679
8.1253
7.9203
7.5930
1.9393
O
O
S
O
N
H
O
N
H
N
Cl
22 SM
1.0000
1.0657
1.0005
4.2866
1.1318
3.1640
15
10
5
0
[ppm]


"FYH 160613 CNCANSul SM C13" 1 1 C:\Users\Yuhua\Desktop\bruker Yuhua
169.2121
164.6113
151.3050
146.8453
143.5090
138.7601
134.4619
133.1166
129.4709
123.6861
119.6771
23.6502
22 SM
5 [rel]
4
3
2
1
- 0
200
150
100
50
0
[ppm]