Supplementary Information

Synthesis and Biological Characterization of a 17β Hydroxysteroid Dehydrogenase Type 10 (17β-HSD10) Inhibitor

Louise F. Dow,[1] Rasangi Pathirage,[1] Helen E. Erickson,[1] Edrees Amani,[1] Donald R. Ronning,[1,2,3] and Paul C. Trippier[1,2,3,*]

[1]Department of Pharmaceutical Sciences, College of Pharmacy, University of Nebraska Medical Center, Omaha, Nebraska 68106, United States

[2]Fred & Pamela Buffett Cancer Center, University of Nebraska Medical Center, Omaha, Nebraska 68106, United States

[3]UNMC Center for Drug Design and Innovation, University of Nebraska Medical Center, Omaha, Nebraska 68106, United States

*Corresponding Author; paul.trippier@unmc.edu

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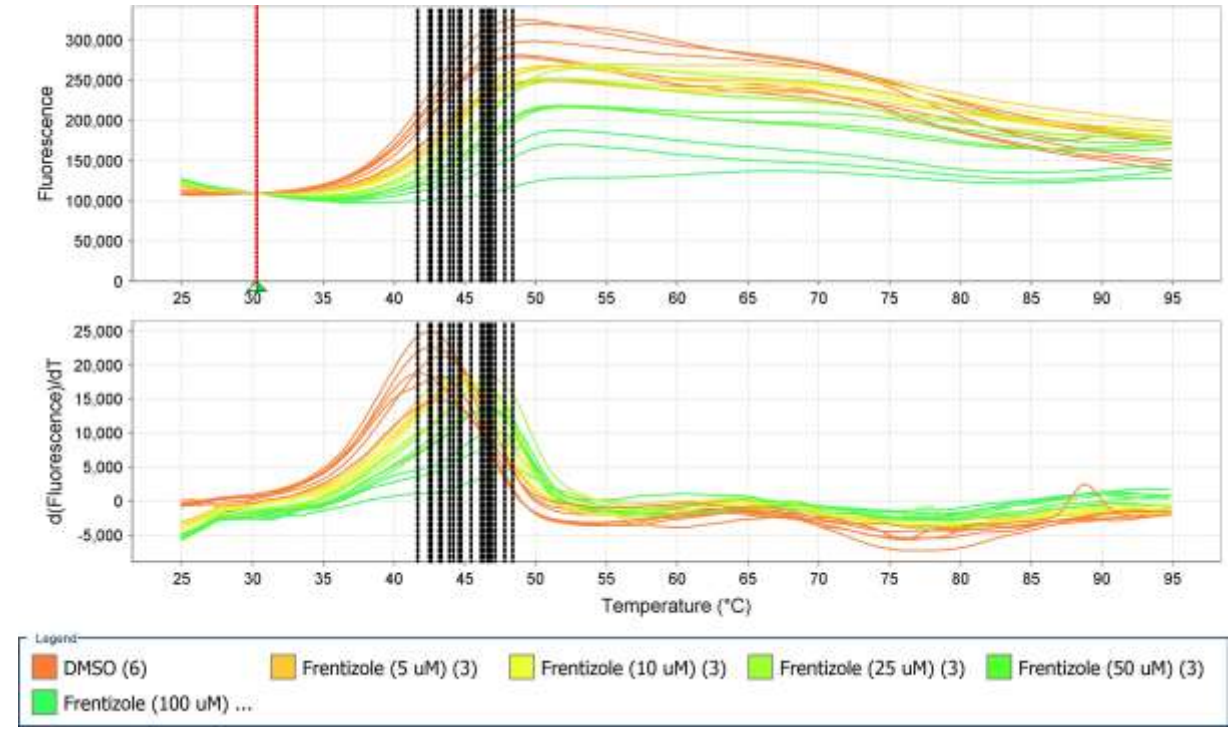
Figure S1A. Melt curve and derivative plot of 17β-HSD10 treated with either DMSO, Frentizole (Top) or **1** (Bottom) at 5, 10, 25, 50 and 100 µM. Conditions: 20 mM Bis-tris pH 6.5, 150 mM NaCl, 0.3 mM TCEP, 10 µM ABAD, 1x dye



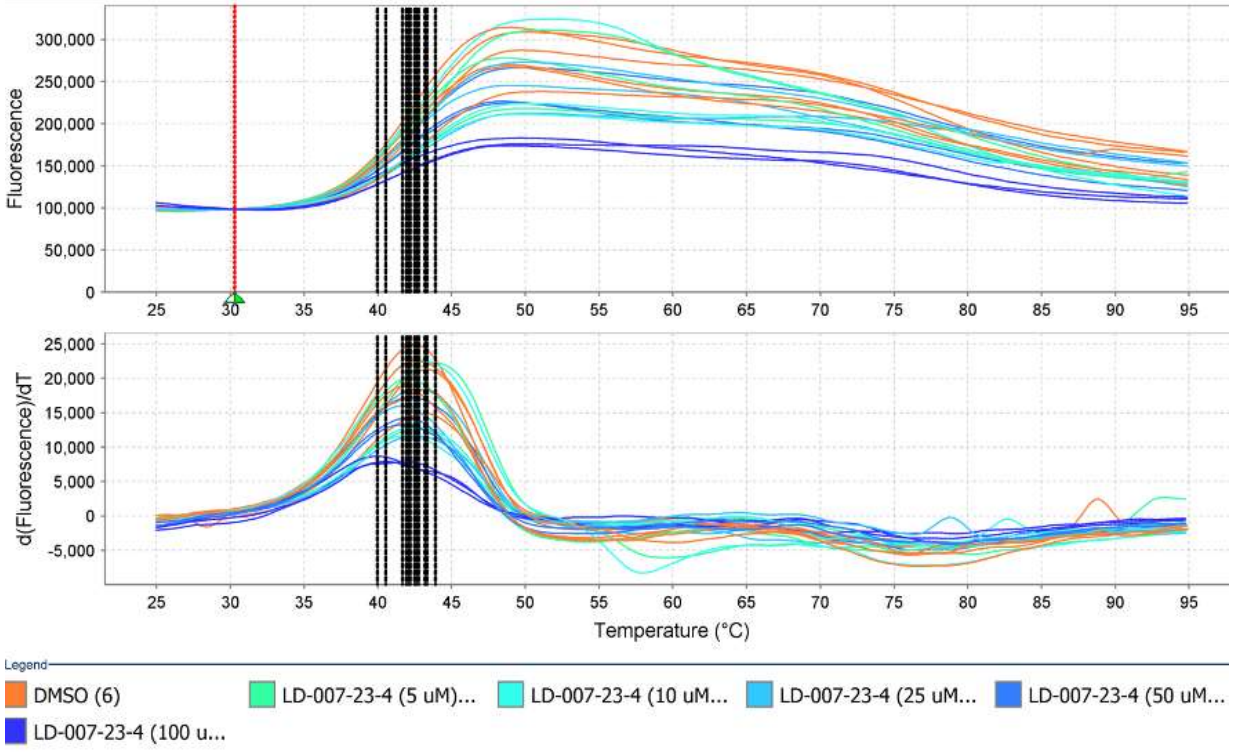
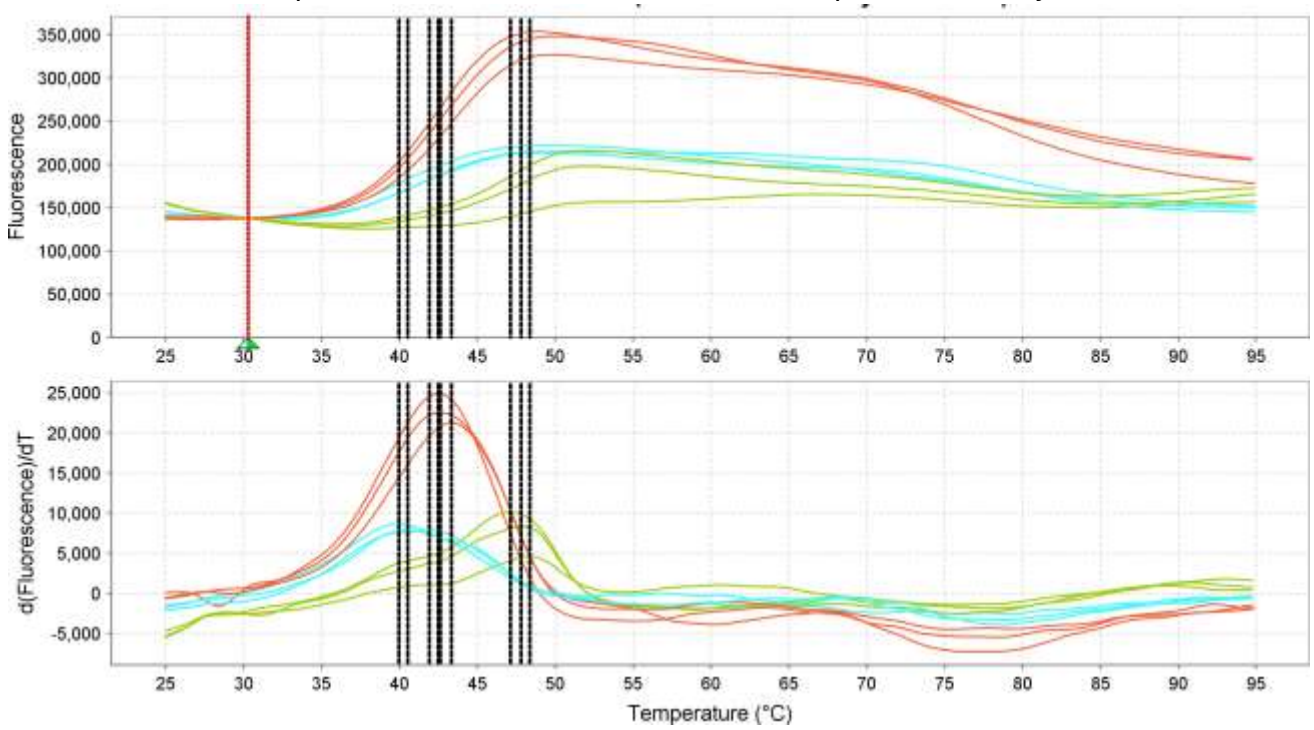
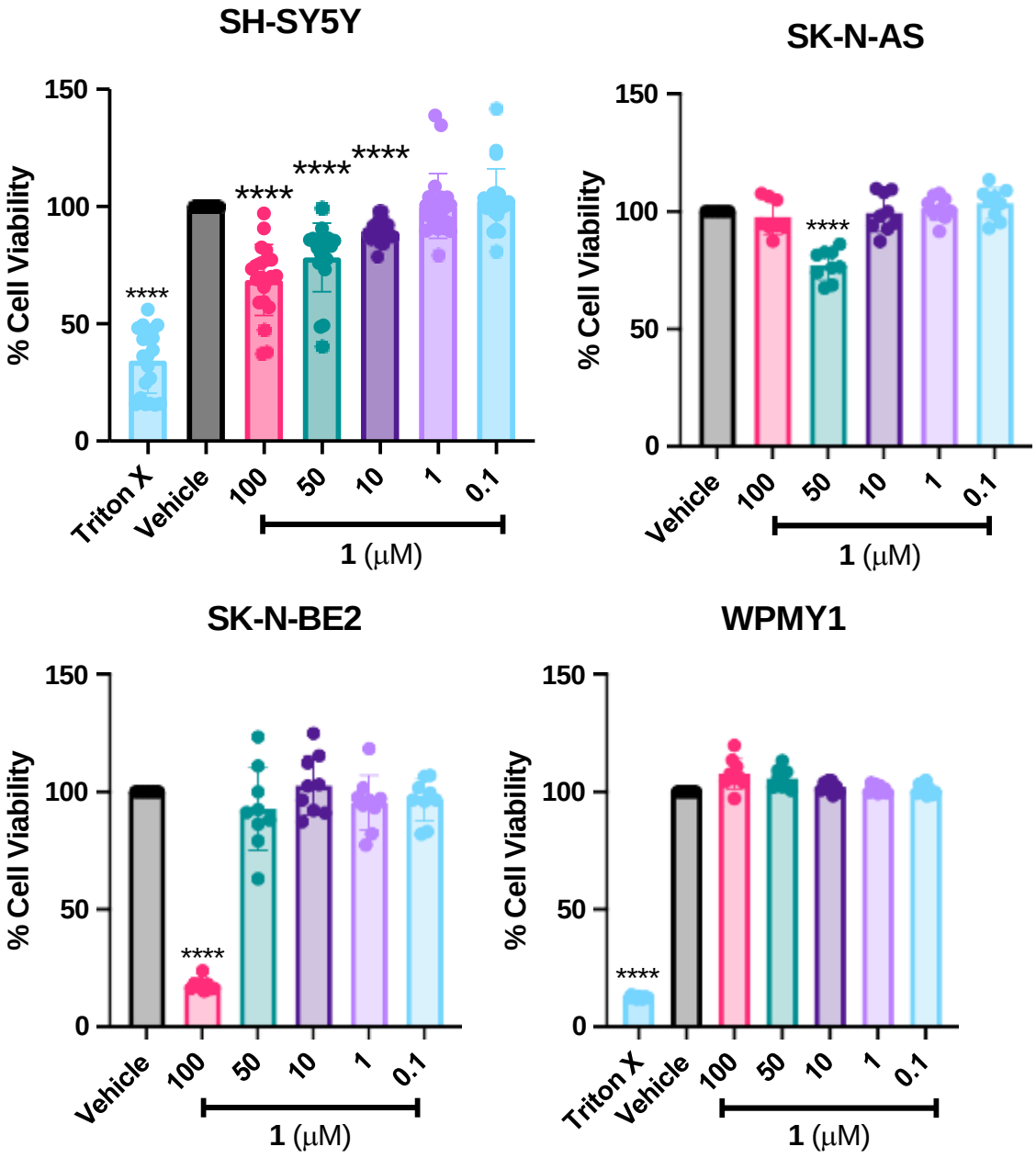


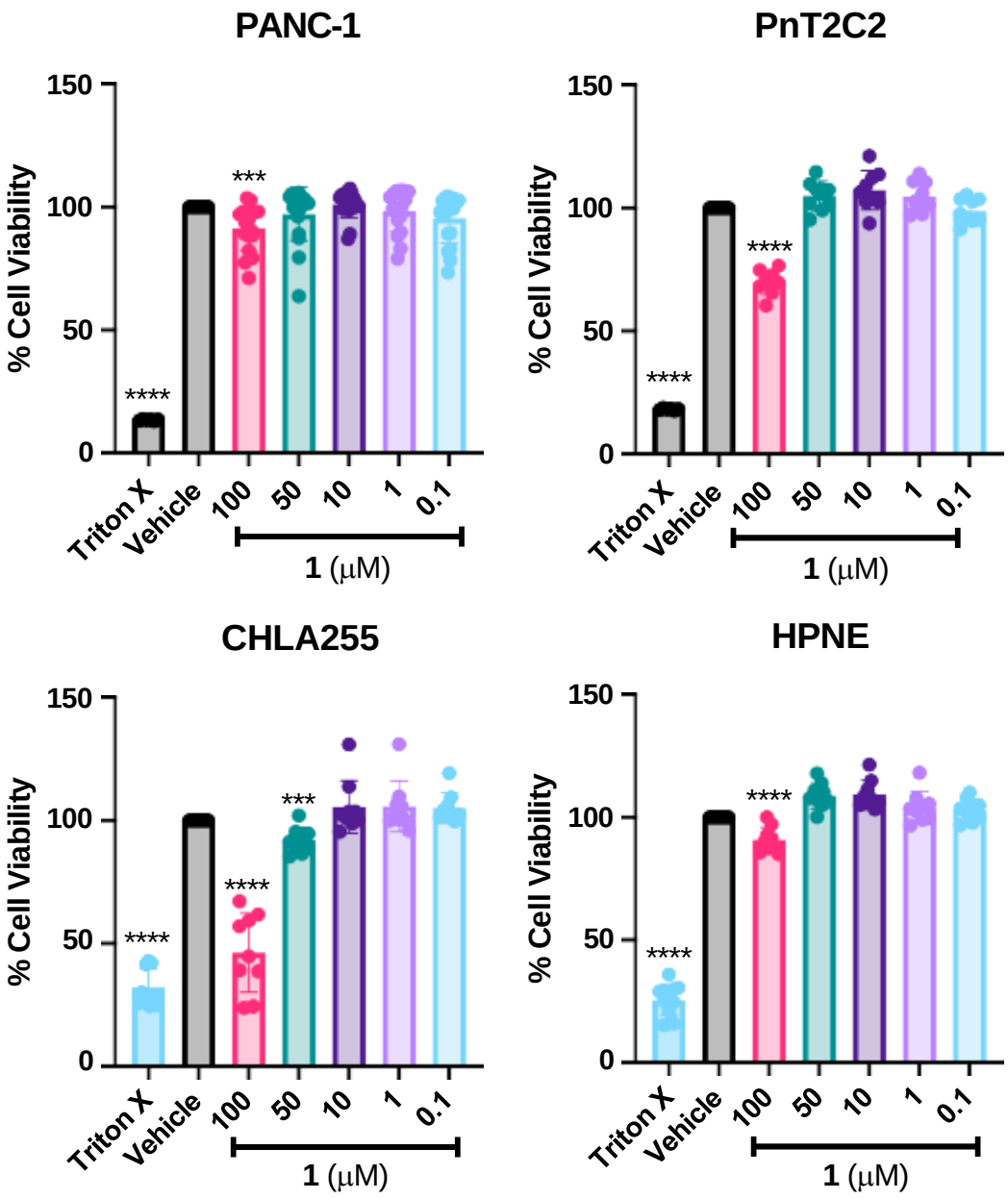
Figure S1B. Melt curve and derivative plot of 17β-HSD10 treated with either DMSO, **1** or Frentizole at 100 µM. Conditions: 20 mM Bis-tris pH 6.5, 150 mM NaCl, 0.3 mM TCEP, 10 µM ABAD, 1x dye.



DMSO **1 (100 µM)** Frentizole (100 µM)

Figure S2. Cell Viability assay measuring the toxicity of **1** at 0.1-100 μM in malignant and non-malignant cell lines.




PANC-1
PnT2C2
CHLA255
HPNE
% Cell Viability
150
100
50
0
****
***
Triton X
Vehicle
100
50
10
1
0.1
1 (μM)

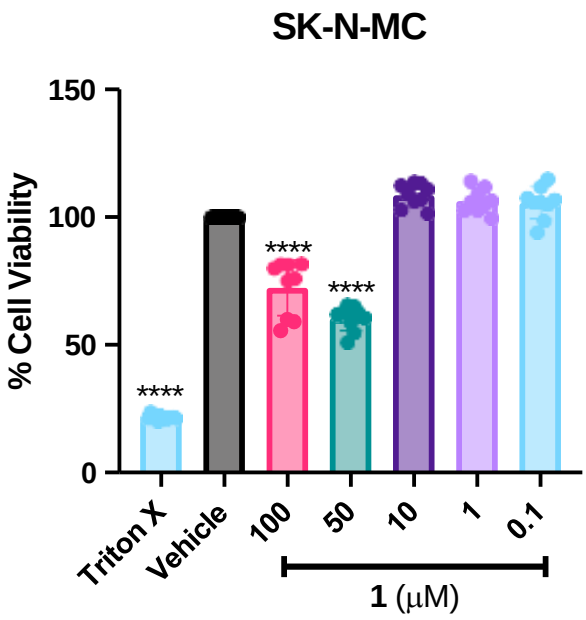
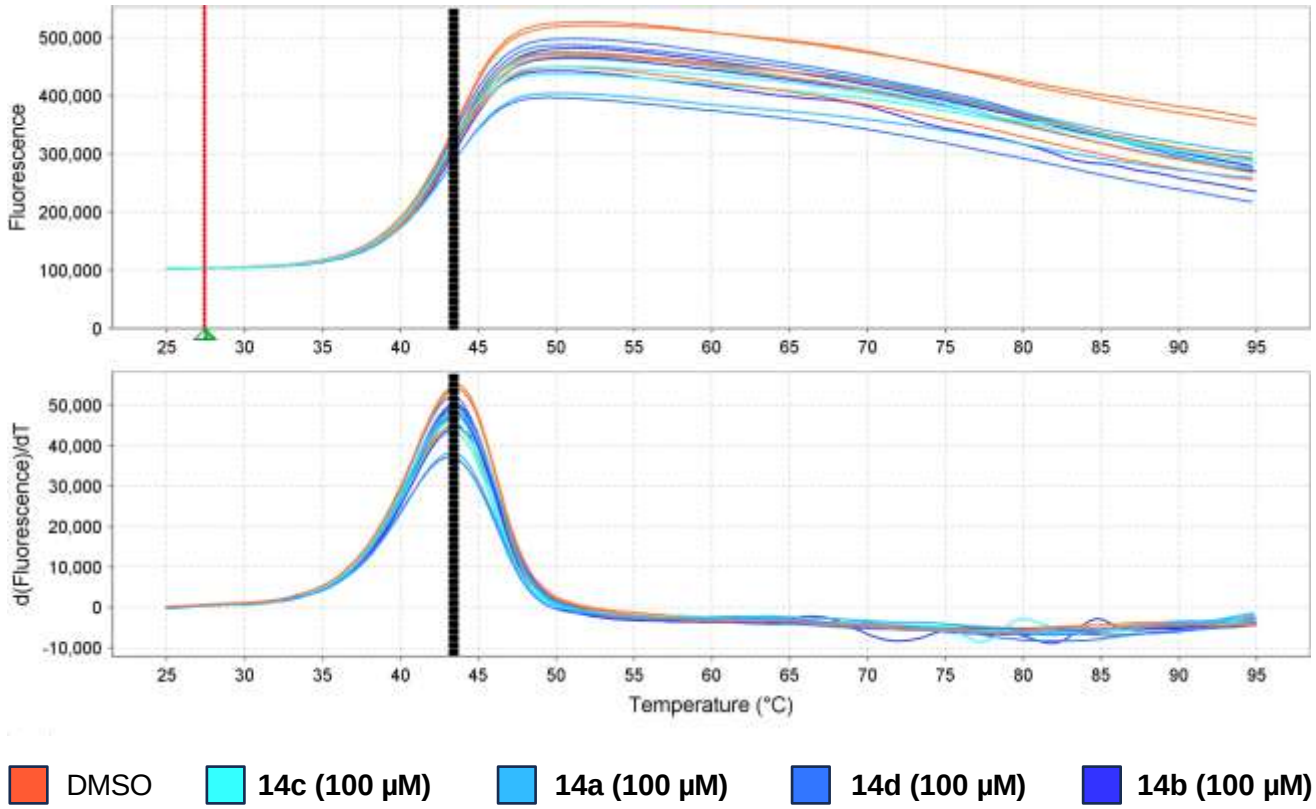

SK-N-MC
% Cell Viability
150
100
50
0
****
****
****
Triton X
Vehicle
100
50
10
1
0.1
1 (μM)

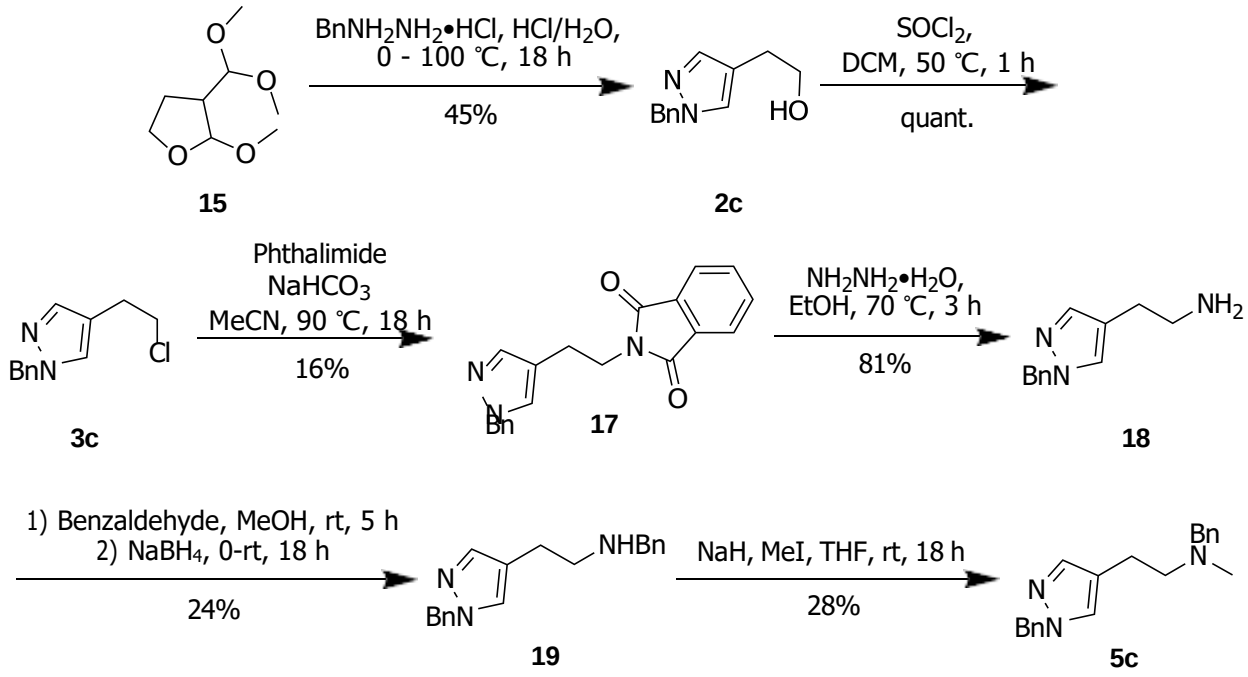
Table S1. Melting temperature (T_m) of 17β-HSD10 in the presence of **1**, Frentizole, **14a**, **14b**, **14c**, and **14d** derived from thermal denaturation curves. a) Both **1** and Frentizole induce dose-dependent shifts in 17β-HSD10 T_m. b) No significant shifts in T_m observed with **14a**, **14b**, **14c**, and **14d**.

		Conc. (μM)	T_m Mean	Std. Error	ΔT_m Mean
a	DMSO		42.78	0.27	-
	Frentizole	5	44.28	0.25	1.49
		10	44.93	0.26	2.15
		25	46.42	0.21	3.64
		50	46.61	0.05	3.83
		100	47.78	0.36	4.99
	1	5	42.32	0.10	- 0.42
		10	42.33	0.12	- 0.41
		25	41.97	0.19	- 0.77
		50	41.67	0.15	- 1.07
		100	40.64	0.28	- 2.1
b	DMSO		43.55	0.06	-
	14a	100	43.40	0.09	- 0.15
	14b	100	43.54	0.05	- 0.01
	14c	100	43.35	0.00	- 0.20
	14d	100	43.35	0.08	- 0.20

Figure S3. Melt curve and derivative plot of 17β-HSD10 treated with either DMSO, **14a**, **14b**, **14c**, or **14d** at 100 µM. Conditions: 20 mM Bis-tris pH 6.5, 150 mM NaCl, 0.3 mM TCEP, 10 µM ABAD, 1x dye.



To the Synthesis of *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)-*N*-methylethan-1-amine (5c)



Synthesis of 2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-ol (2c)

To a cooled solution of 3-(dimethoxymethyl)-2-methoxytetrahydrofuran (16.54 g, 93.8 mmol, 1 equiv.) and benzylhydrazine dihydrochloride (18.3 g, 93.8 mmol, 1 equiv.) in water (4.0 mL) was added hydrochloric acid (12 M) (11.0 mL, 375 mmol, 4 equiv.) dropwise. The reaction was then stirred at 0 °C for 30 minutes and then heated at reflux for 18 h. The reaction was cooled to room temperature, basified by addition of 4 M sodium hydroxide to pH 9 and then diluted with dichloromethane (50 mL). The phases were separated, and the aqueous extracted with dichloromethane (2 x 25 mL); the combined organics were washed with sat. brine (50 mL), dried ($MgSO_4$), and concentrated *in vauco*. The crude material was purified by normal phase chromatography 0-50% ethyl acetate/hexane to afford 2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-ol (8.56 g, 93.8 mmol, 45%) as a colorless oil.

^{1}H NMR (400 MHz, DMSO-D6); δ_H 2.54 (t, *J* = 7.08 Hz, 2H), 3.48-3.56 (m, 2H), 4.60 (t, *J* = 5.2 Hz, 1H), 5.24 (s, 2H), 7.19- 7.23 (m, 2H), 7.24-7.36 (m, 4H), 7.59 (s, 1H).

^{13}C NMR (100 MHz, DMSO-D6): δ_C 22.54, 38.50, 54.57, 116.84, 123.00,127.12, 127.33, 128.35, 128.94, 131.48,134.37, 137.78, 138.69, 167.72.

Synthesis of 1-benzyl-4-(2-chloroethyl)-1*H*-pyrazole hydrochloride (3c)

To a solution of 2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-ol (500 mg, 2.47 mmol, 1 equiv.) in dichloromethane (1.0 mL) was added thionyl chloride (0.90 mL, 12.4 mmol, 5 equiv.) the reaction was stirred at room temperature open to the air for 30 minutes. The reaction was concentrated *in vacuo* to afford 1-benzyl-4-(2-chloroethyl)-1*H*-pyrazole hydrochloride (758 mg, quant.) as an orange solid.

^{1}H NMR (400 MHz, DMSO-D6): δ_H 2.85 (t, *J* = 6.96 Hz, 2H), 3.73 (t, *J* = 7.00 Hz, 2H), 5.30 (s, 2H), 7.19-7.24 (m, 2H), 7.24-7.36 (m, 3H), 7.47 (s, 1H), 7.76 (s, 1H), 11.39 (br.s, 2H).

^{13}C NMR (100 MHz, DMSO-D6): δ_C 27.86, 45.75, 55.08, 117.95, 128.04, 128.11, 128.98, 129.98, 137.84, 138.80.

Synthesis of 2-(2-(1-benzyl-1*H*-pyrazol-4-yl)ethyl)isoindoline-1,3-dione (**17**)

To a solution of 1-benzyl-4-(2-chloroethyl)-1*H*-pyrazole hydrochloride (5.75 g, 22.4 mmol, 1 equiv.) and potassium phthalimide (4.56 g, 24.6 mmol, 1.1 equiv.) in dimethylformamide (25.6 mL) was added sodium bicarbonate (2.82 g, 33.5 mmol, 1.5 equiv.), the reaction was heated at reflux under nitrogen for 72 h. The reaction was filtered, and the solution was concentrated *in vacuo*. The residue was dissolved in water (70 mL) and ethyl acetate (30 mL), the phases were separated, and the aqueous was extracted with ethyl acetate (30 mL). The combined organics were washed with water (30 mL) and sat. brine (30 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The crude material was purified by normal phase chromatography 0-40% ethyl acetate/hexane to afford 2-(2-(1-benzyl-1*H*-pyrazol-4-yl)ethyl)isoindoline-1,3-dione (5.88 g, 17.7 mmol, 79%) as a white solid.

^{1}H NMR (400 MHz, DMSO-D6): δ_H 2.77 (t, *J* = 7.20 Hz, 2H), 3.74 (t, *J* = 7.20 Hz, 2H), 5.22 (s, 2H), 7.04-7.09 (m, 2H), 7.22-7.30 (m, 4H), 7.62 (s, 1H), 7.79-7.95 (m, 4H).

^{13}C NMR (100 MHz, DMSO-D6): δ_C 22.54, 54.57, 116.84, 123.00, 127.12, 127.33, 128.35, 128.94, 131.48, 134.37, 137.79, 138.69, 167.72.

Synthesis of 2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (18)

To a solution 2-(2-(1-benzyl-1*H*-pyrazol-4-yl)ethyl)isoindoline-1,3-dione (500 mg, 1.51 mmol, 1 equiv.) in ethanol (1.0 mL) was added hydrazine hydrate (0.18 mL, 3.03 mmol, 2 equiv.), the reaction was heated at reflux in a

sealed tube for 18 h. The reaction was filtered, and the solution was concentrated *in vacuo*. The crude material was purified by normal phase chromatography 0-5:0.5% methanol:ammonia/dichloromethane to afford 2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (186 mg, 0.92 mmol, 61 %) as a colorless solid.

^{1}H NMR (400 MHz, MeOH-D4): δ_H 2.69 (t, *J* = 7.20 Hz, 2H), 2.90 (t, *J* = 7.20 Hz, 2H), 5.29 (s, 2H), 7.19-7.24 (m, 2H), 7.24-7.7.36 (m, 3H), 7.41 (s, 1H), 7.55 (s, 1H).

^{13}C NMR (100 MHz, MeOH-D4): δ_C 26.72, 42.91, 56.47, 119.65, 128.60, 128.97, 129.74, 130.41, 138.38, 140.04.

Synthesis of *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (19)

To a solution of 2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (500 mg, 2.48 mmol, 1 equiv.) in methanol (5 mL) was added benzaldehyde (0.25 mL, 2.48 mmol, 1 equiv.) and $MgSO_4$ the reaction was stirred at room temperature for 3 h. The reaction was cooled to 0 °C and sodium borohydride (282 mg, 7.45 mmol, 3 equiv.) was added in 2 portions. The reaction was warmed to room temperature and stirred under nitrogen for 18 h. The reaction was concentrated *in vacuo*. The residue was purified by normal phase chromatography 0-5:0.5 methanol:ammonia/dichloromethane to afford *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (176 mg, 0.60 mmol, 24 %) as a colorless oil.

^{1}H NMR (400 MHz, DMSO-D6): δ_H 2.54 (t, *J* = 7.20 Hz, 2H), 2.65 (t, *J* = 6.80 Hz, 2H), 5.70 (s, 2H), 5.24 (s, 2H), 7.15-7.23 (m, 3H), 7.24-7.35 (m, 8H), 7.58 (s, 1H).

ESI-HRMS (m/z): $[M+H]^+$ calc. for $C_{19}H_{21}N_3$, 292.1808; found, 292.2000

Synthesis of *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)-N-methylethan-1-amine (5c)

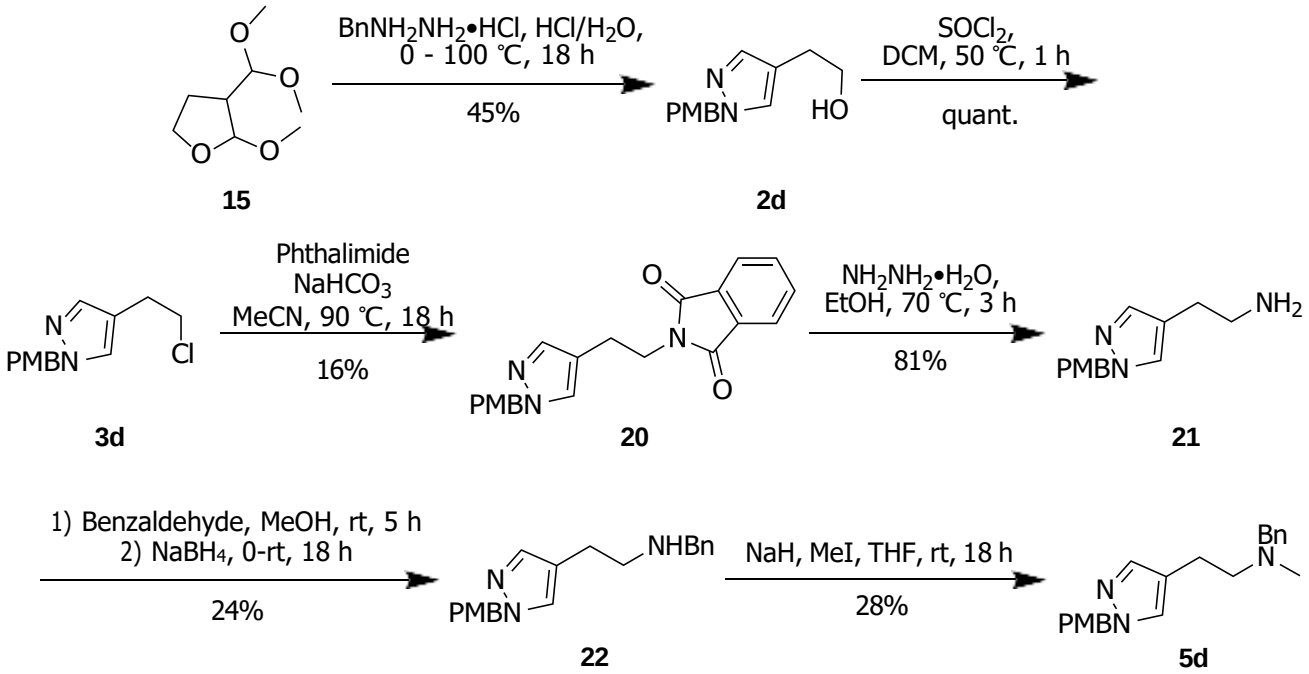
To a solution of *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (1.13 g, 3.86 mmol, 1 equiv.) in tetrahydrofuran (10 mL) was added sodium hydride (60% dispersion in mineral oil) (200 mg, 5.02 mmol, 1.3 equiv.) the reaction was stirred under nitrogen for 30 minutes after which methyl iodide (0.27 mL, 4.24 mmol, 1.1 equiv.) was added and the reaction stirred at room temperature for 18 h. The reaction was quenched with water (20 mL) and diluted with ethyl acetate. The phases separated, and the aqueous extracted with ethyl acetate (2 x 20 mL); the combined organics were washed with water (10 mL) and sat. brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by chromatography 0-2.5:0.25

methanol:ammonia/dichloromethane to afford *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)-*N*-methylethan-1-amine (326 mg, 1.07 mmol, 28 %) as a colorless oil.

^{1}H NMR (500 MHz, MeOH-D4): δ_H 2.25 (s, 3H), 2.59 (t, *J* = 7.95 Hz, 2H), 2.70 (t, *J* = 7.40 Hz, 2H), 3.56 (s, 2H), 5.26 (s, 2H), 7.19 (d, *J* = 7.6 Hz, 2H), 7.22-7.36 (m, 9H), 7.47 (s, 1H).

ESI-HRMS (m/z): $[M+H]^+$ calc. for $C_{20}H_{23}N_3$, 306.1965; found, 306.1972

To the Synthesis of *N*-benzyl-2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)-*N*-methylethan-1-amine (5d)



Synthesis of 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-ol (2d)

To a suspension of (4-methoxybenzyl)hydrazine hydrochloride (28.5 g, 137 mmol, 1 equiv.) and 3-(dimethoxymethyl)-2-methoxytetrahydrofuran (24.2 g, 137mmol, 1 equiv.) in water was added hydrochloric acid (21.0 mL, 687mmol, 5 equiv.) dropwise, the reaction was stirred at room temperature for 30 minutes after which the reaction was heated at reflux for 3 h. The reaction was diluted with tetrahydrofuran (40 mL), and the solid was removed by filtration and washed with diethyl ether (2 x 20 mL). The solution was added slowly to sat. potassium carbonate (200 mL), the phases were separated, and the aqueous was extracted with n-butanol (150 mL), the combined organics were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by normal phase chromatography 0-100% ethyl acetate/hexane to afford 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-ol (4.17 g, 17.9 mmol, 13%) as a yellow oil.

^{1}H NMR (400 MHz, MeOH-D4): δ_H 2.50-2.53 (m, 2H), 3.46-3.51 (m, 2H), 3.72 (s, 3H), 5.89 (t, *J* = 4.8 Hz, 1H), 5.15 (s, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 7.18 (d, *J* = 8.64 Hz, 2H), 7.26 (s, 1H), 7.53 (s, 1H).

^{13}C NMR (100 MHz, MeOH-D4): δ_C 27.71, 54.16, 55.08, 61.82, 113.82, 117.97, 128.15, 129.11, 129.72, 138.55, 158.70.

Synthesis of 4-(2-chloroethyl)-1-(4-methoxybenzyl)-1*H*-pyrazole hydrochloride (3d)

To a solution of 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-ol (3.10 g, 13.3 mmol, 1 equiv.) in dichloromethane (40 mL) was added thionyl chloride (4.87 mL 66.7 mmol, 5 equiv.) the reaction was heated at reflux for 1 h. The reaction was concentrated *in vacuo* and azeotropes with methyl *tert*-butyl ether (2 x 20 mL) to afford crude 4-(2-chloroethyl)-1-(4-methoxybenzyl)-1*H*-pyrazole hydrochloride (3.80 g, 13.2 mmol, 99%) as an orange solid.

^{1}H NMR (600 MHz, DMSO-D6): δ_H 2.84 (t, *J* = 6.5 Hz, 2H), 3.37-3.73 (m, 4H), 5.19 (s, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.39 (s, 1H), 7.66 (s, 1H).

Synthesis of 2-(2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethyl)isoindoline-1,3-dione (20)

To a suspension of 4-(2-chloroethyl)-1-(4-methoxybenzyl)-1*H*-pyrazole hydrochloride (4.49 g, 15.7 mmol, 1 equiv.) and sodium bicarbonate (3.29 g, 15.7 mmol, 1.5 equiv.) in dimethylformamide (40.0 mL) was added potassium phthalimide (3.19 g, 17.2 mmol, 1.1 equiv.) the reaction was heated at reflux under nitrogen for 18 h. The solvent was reduced *in vacuo,* and the residue was partitioned between ethyl acetate (75 mL) and water (200 mL); the aqueous was extracted ethyl acetate (75 mL), and the combined organics washed with water (100 mL), sat. brine (50 mL) dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by normal phase chromatography 0-40% ethyl acetate/hexane to afford 2-(2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethyl)isoindoline-1,3-dione (5.13 g, 14.2 mmol, 91%) as a yellow/brown oil.

^{1}H NMR (600 MHz, MeOH-D4): δ_H 2.87 (t, *J* = 5.90 Hz, 2H), 3.77 (s, 3H), 3.84 (t, *J* = 5.90 Hz, 2H), 5.14 (s, 2H), 6.80 (d, *J* = 7.25 Hz, 2H), 7.03 (d, *J* = 7.20 Hz, 2H), 7.33 (s, 1H), 7.42 (s, 1H), 7.76-7.82 (m, 4H).

^{13}C NMR (150 MHz, MeOH-D4): δ_C 21.92, 37.90, 53.80, 53.97, 113.12, 117.21, 122.19, 127.93, 128.32, 128.44, 131.33, 133.44, 138.19, 1.58.91, 167.73.

Synthesis of 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-amine (21)

A solution of 2-(2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethyl)isoindoline-1,3-dione (3.29 g, 9.10 mmol, 1 equiv.) in methanol (50 mL) was heated at 70 °C after which hydrazine hydrate (2.21 mL, 36.4 mmol, 4 equiv.) was added the reaction was heated at 70 °C for 18 h. The reaction was filtered, and the solution was concentrated *in vacuo*. The solid was dissolved in ethyl acetate (50 mL) and aq sat. K_2CO_3 (50 mL), the phases were separated, and the aqueous was extracted with ethyl acetate (50 mL). The combined organics were washed with sat. aq K_2CO_3 (20 mL) $NaHCO_3$ (20 mL) and sat. brine (20 mL), dried ($MgSO_4$) and concentrated *in vacuo* to afford 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-amine (1.34 g, 5.79 mmol, 64%) as a yellow oil.

^{1}H NMR (400 MHz, DMSO-D6): δ_H 2.44 (t, *J* = 7.20 Hz, 2H), 2.67 (t, *J* = 7.04- Hz, 2H), 3.72 (s, 3H), 5.15 (s, 2H), 6.85-6.91 (m, 2H), 7.14-7.21 (m, 2H), 7.26 (s, 1H), 7.53 (s, 1H).

^{13}C NMR (100 MHz, DMSO-D6): δ_C 18.56, 20.49, 26.94, 42.31, 48.60, 54.20, 55.08, 56.02, 113.83, 118.30, 125.24, 127.96, 128.14, 129.09, 129.68, 132.03, 138.42, 155.55, 158.71.

Synthesis of *N*-benzyl-2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-amine (22)

To a solution of 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-amine (1.34 g, 5.79 mmol, 1 equiv.) in methanol (5.0 ml) was added benzaldehyde (0.59 mL, 5.79 mmol, 1 equiv.) and $MgSO_4$ the reaction was stirred at room temperature for 3 h. The reaction was cooled to 0 ° C, and sodium borohydride (657 mg, 17.4 mmol, 3 equiv.) was added in 3 portions, and the reaction was stirred at room temperature for 18 h. The reaction was concentrated *in vacuo*. The residue was partitioned between 2-methyl tetrahydrofuran (10 mL) and 2M sodium hydroxide (10 mL), the phases were separated, and the aqueous extracted with 2-methyl tetrahydrofuran (2 x 20 mL). The combined organics were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by normal phase chromatography 0-5:0.5 methanol:ammonia/dichloromethan to afford *N*-benzyl-2-(1-benzyl-1*H*-pyrazol-4-yl)ethan-1-amine (355 mg, 1.10 mmol, 19%) as a colorless oil.

^{1}H NMR (500 MHz, DMSO-D6): δ_H 2.52 (t, *J* = 7.25 Hz, 2H), 2.63 (t, *J* = 7.05 Hz, 2H), 3.68 (s, 2H), 3.72 (s, 3H), 5.14 (s, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.16 (d, *J* = 8.7 Hz, 2H), 7.18-7.23 (m, 1H), 7.25 (s, 1H), 7.26-7.30 (m, 4H) 7.52 (s, 1H).

^{13}C NMR (125 MHz, DMSO-D6): δ_C 24.94, 50.45, 53.32, 54.64, 55.55, 114.29, 119.48, 126.92, 128.33, 128.47, 128.53, 129.52, 130.20, 138.84, 159.16.

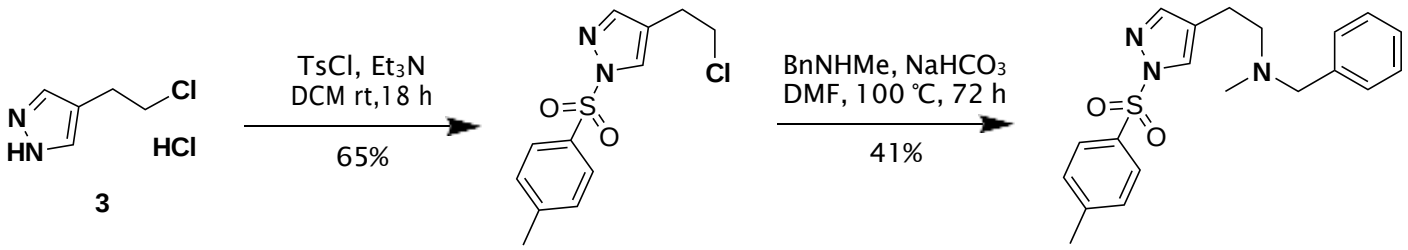
Synthesis of *N*-benzyl-2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)-*N*-methylethan-1-aminium (5d)

To a solution of 2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)ethan-1-amine (355 mg, 1.10 mmol, 1 equiv.), in tetrahydrofuran (3.5 mL) was added sodium hydride (53 mg, 1.33 mmol, 1.2 equiv.) the reaction was stirred at room temperature for 1 h after which methyl iodide (0.11 mL, 1.66 mmol, 1.5 equiv.) was added the reaction was stirred at room temperature in a sealed vial for 18 h. Each reaction vial was quenched into water (20 mL) and extracted with ethyl acetate (2 x 20 mL) the combined organics were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by normal phase chromatography 0-5:0.5 methanol:ammonia/dichloromethane to afford *N*-benzyl-2-(1-(4-methoxybenzyl)-1*H*-pyrazol-4-yl)-*N*-methylethan-1-amine (250 mg, 0.74 mmol, 68%) a colorless oil.

^{1}H NMR (600 MHz, MeOH-D4): δ_H 2.24 (s, 3H), 2.56-2.59 (m, 2H), 2.68 (t, *J* = 7.2 Hz, 2H), 3.55 (s, 2H), 3.76 (s, 3H), 5.17 (s, 2H), 6.87 (d, *J* = 8.4 Hz 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.23-7.30 (m, 5H), 7.32 (s, 1H), 7.41 (s, 1H).

^{13}C NMR (150 MHz, MeOH-D4): δ_C 22.76, 42.22, 55.70, 55.92, 59.35, 62.97, 115.07, 120.96, 128.35, 129.31, 129.79, 130.09, 130.33, 130.59, 139.17, 139.79.

To the synthesis of *N*-benzyl-*N*-methyl-2-(1-tosyl-1*H*-pyrazole-4-yl)ethan-1-amine 5e



Synthesis of 4-(2-chloroethyl)-1-tosyl-1*H*-pyrazole 3e

To a solution of 4-(2-chloroethyl)-1*H*-pyrazole hydrochloride (2.00 g, 11.97 mmol, 1 equiv.) and triethylamine (5.01 mL, 35.92 mmol, 3 equiv.) in dichloromethane (20 mL) was added 4-methylbenzenesulfonyl chloride (3.42 g, 17.96 mmol, 1.5 equiv.) the reaction was stirred at room temperature for 18 h. The reaction was diluted with water (20 ml), and the phases were separated and the aqueous was extracted with dichloromethane (2 x 20

mL); the combined organics were washed with sat. sodium bicarbonate solution (2 x 20mL) and sat brine (20 mL) dried ($MgSO_4$) and concentrated in vacuo. The crude residue was purified by normal phase chromatography 0-30% ethyl acetate/hexane to afford 4-(2-chloroethyl)-1-tosyl-1*H*-pyrazole (2.23 g, 65%, 7.83 mmol) as a colorless oil.

^{1}H NMR (600 MHz, DMSO-D6): δ_H 2.38 (s, 3H), 2.88 (t, *J* = 7.20 Hz, 2H), 3.79 (t, *J* = 7.20 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.83 (s, 1H), 8.34 (s, 1H).

^{13}C NMR (150 MHz, DMSO-D6): δ_C 26.12, 26.82, 44.34, 121.49, 127.57, 130.32, 130.41, 133.50, 146.06, 146.25.

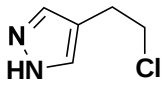
Synthesis of *N*-benzyl-*N*-methyl-2-(1-tosyl-1*H*-pyrazole-4-yl)ethan-1-amine 5e

To a suspension of (4-((4-(2-chloroethyl)-1H-pyrazol-1-yl)sulfonyl)phenyl)methylium (200 mg, 0.71 mmol, 1 equiv.) and sodium bicarbonate (178 mg, 2.11 mmol 3 equiv.) in DMF (2.0 mL) was added N-methyl-1-phenylmethanamine (128 mg, 1.06 mmol, 1.5 equiv.) the reaction was heated in a vial at 100 ^{o}C for 72 h. the reaction was quenched into water (30 mL) and extracted with EtOAc (2 x 10 mL) the combined organics were washed with water (5 x 10 mL) and brine (10 mL), dried ($MgSO_4$) and concentrated *in vacuo*. The crude residue was purified by normal phase chromatography 0-50% ethyl acetate/hexane (1% triethylamine in both phases) to afford *N*-benzyl-*N*-methyl-2-(1-tosyl-1*H*-pyrazole-4-yl)ethan-1-amine (107 mg, 41%, 0.29 mmol) as a colourless solid.

^{1}H NMR (600 MHz, MeOH-D4): δ_H 2.21 (s, 3H), 2.38 (s, 3H), 2.56 (t, *J* = 7.80 Hz, 2H), 2.67 (t, *J* = 7.20 Hz, 2H), 3.50 (s, 2H), 7.19-7.27 (m, 5H), 7.36 (d, *J* = 0.6 Hz, 2H), 7.64 (s, 1H), 7.85 (d, J = 8.4 Hz, 2H), 8.08 (s, 1H).

^{13}C NMR (150 MHz, MeOH-D4): δ_C 21.60, 22.47, 42.12, 58.13, 63.00, 124.80, 128.24, 128.95, 129.28, 130.36, 130.73, 131.12, 135.57, 139.39, 147.18, 147.40.

4-(chloromethyl)-1H-pyrazole hydrochloride



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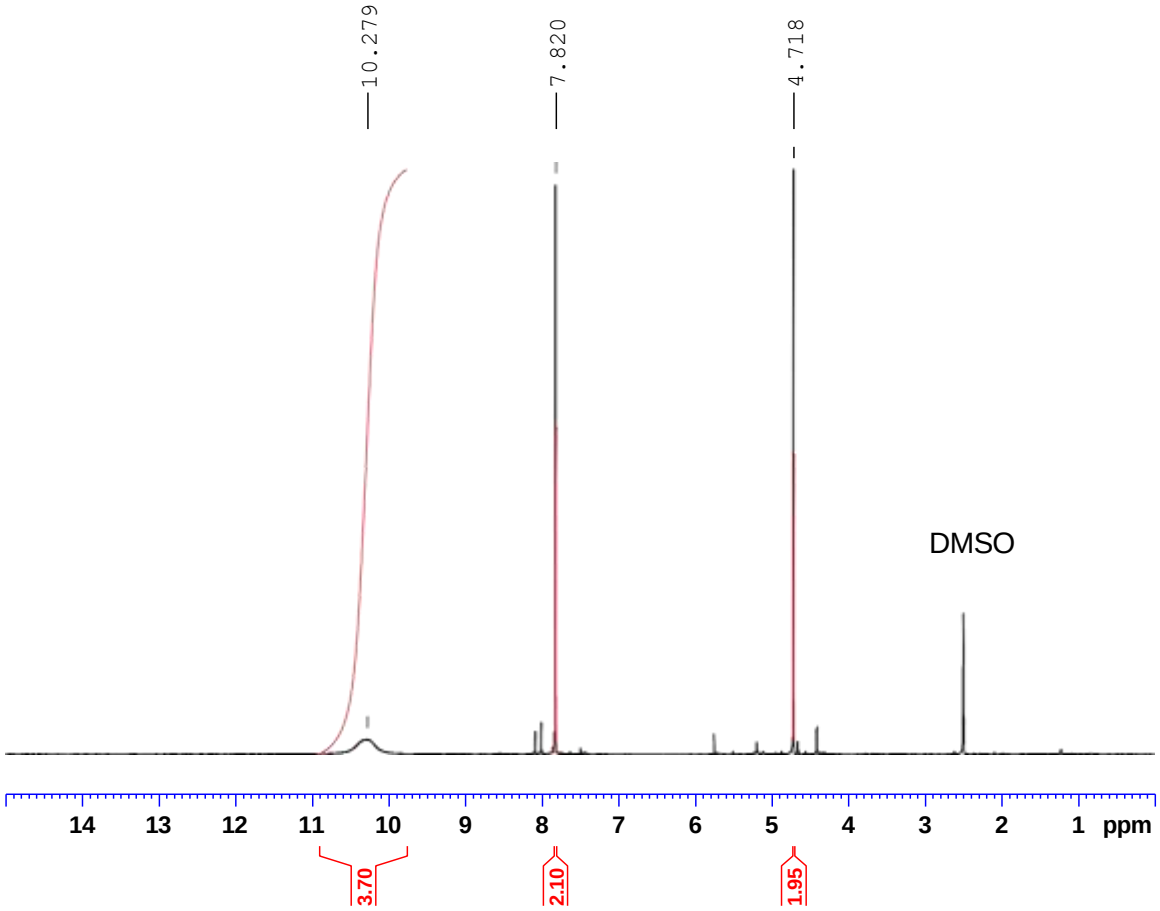
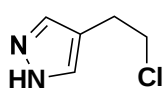


4-(2-chloroethyl)-1H-pyrazole hydrochloride (



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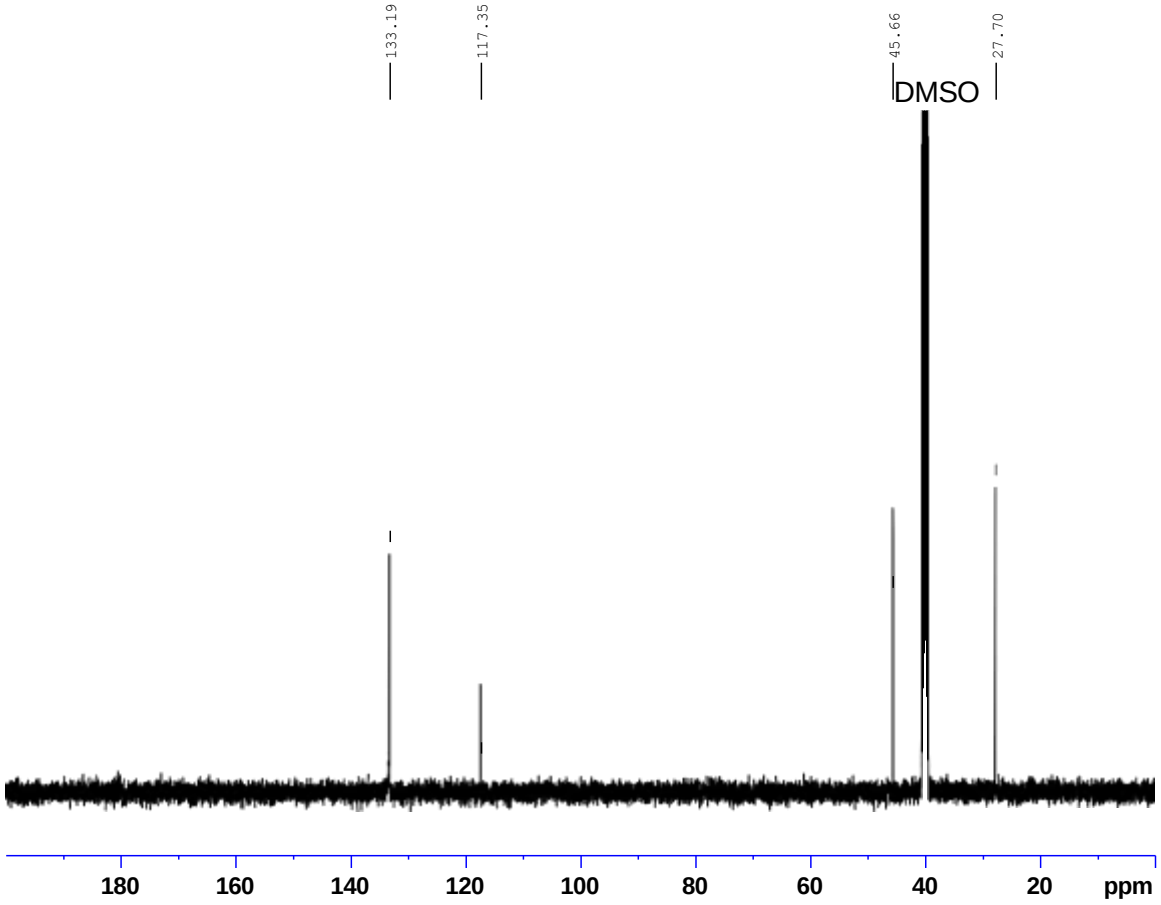
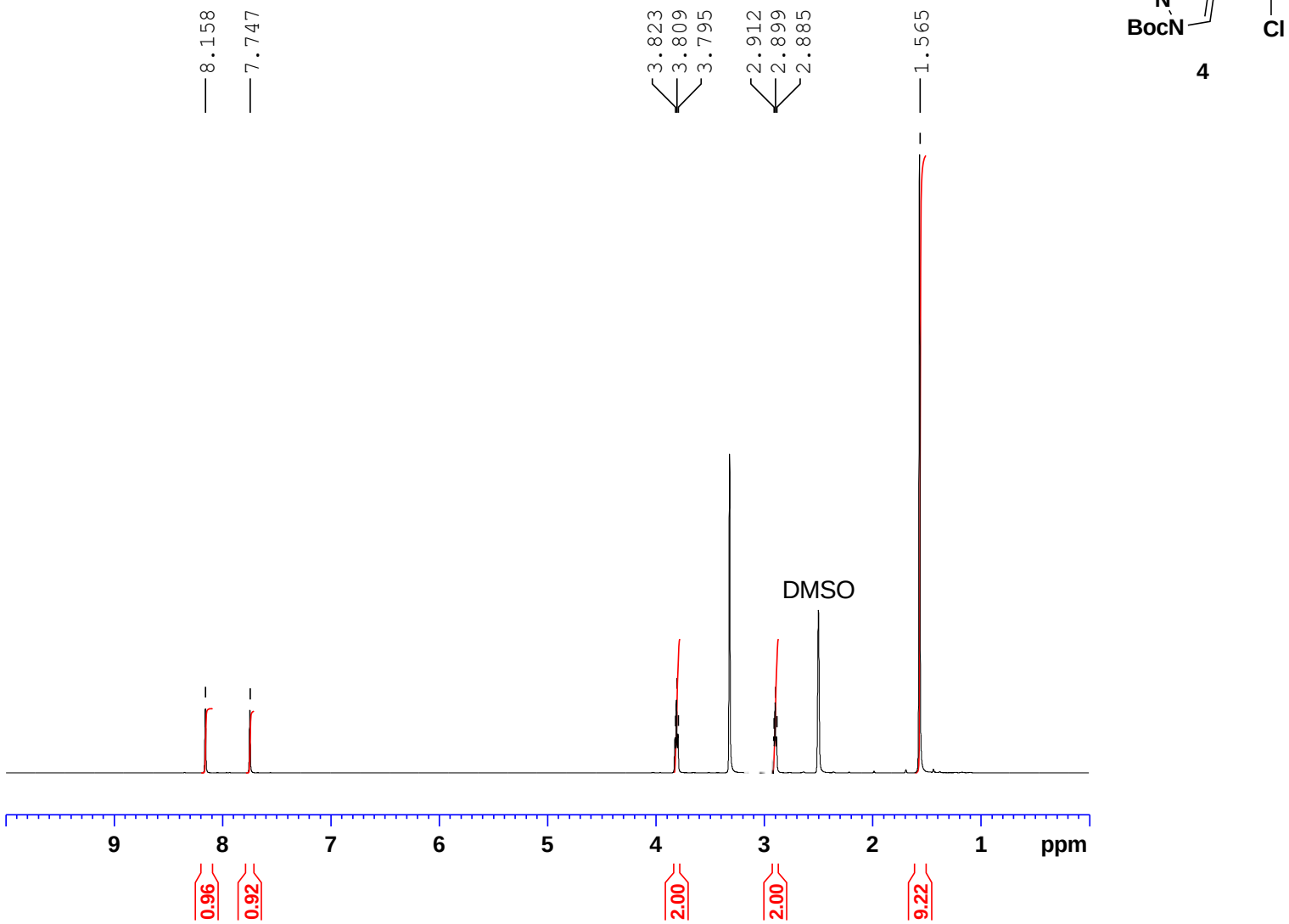


tert-butyl 4-(2-chloroethyl)-1H-pyrazole-1-carboxylate



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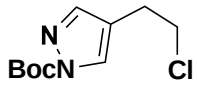
tert-butyl 4-(2-chloroethyl)-1H-pyrazole-1-carboxylate



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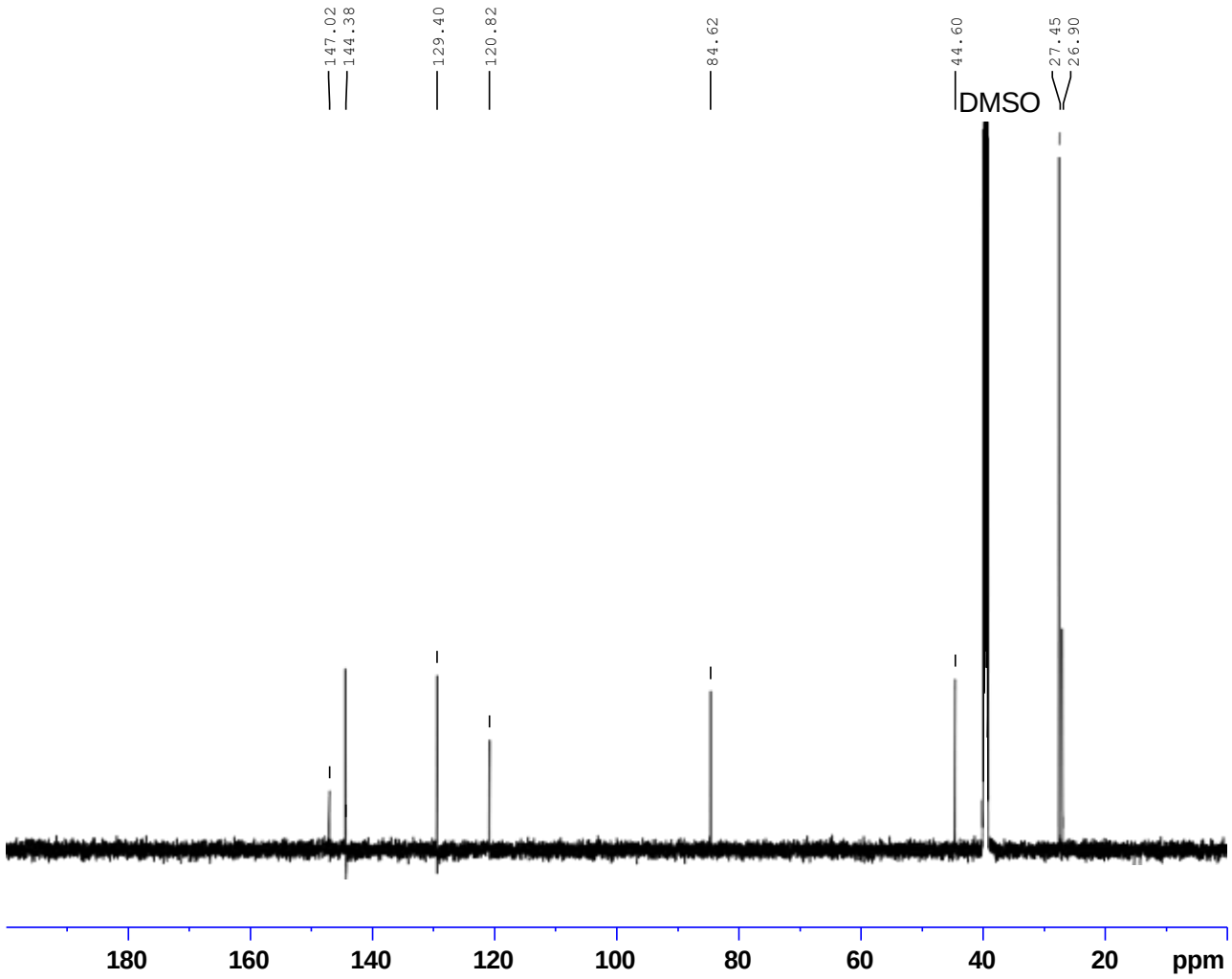
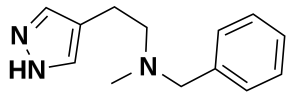


N-benzyl-N-methyl-2-(1H-pyrazol-4-yl)ethan-1-amine



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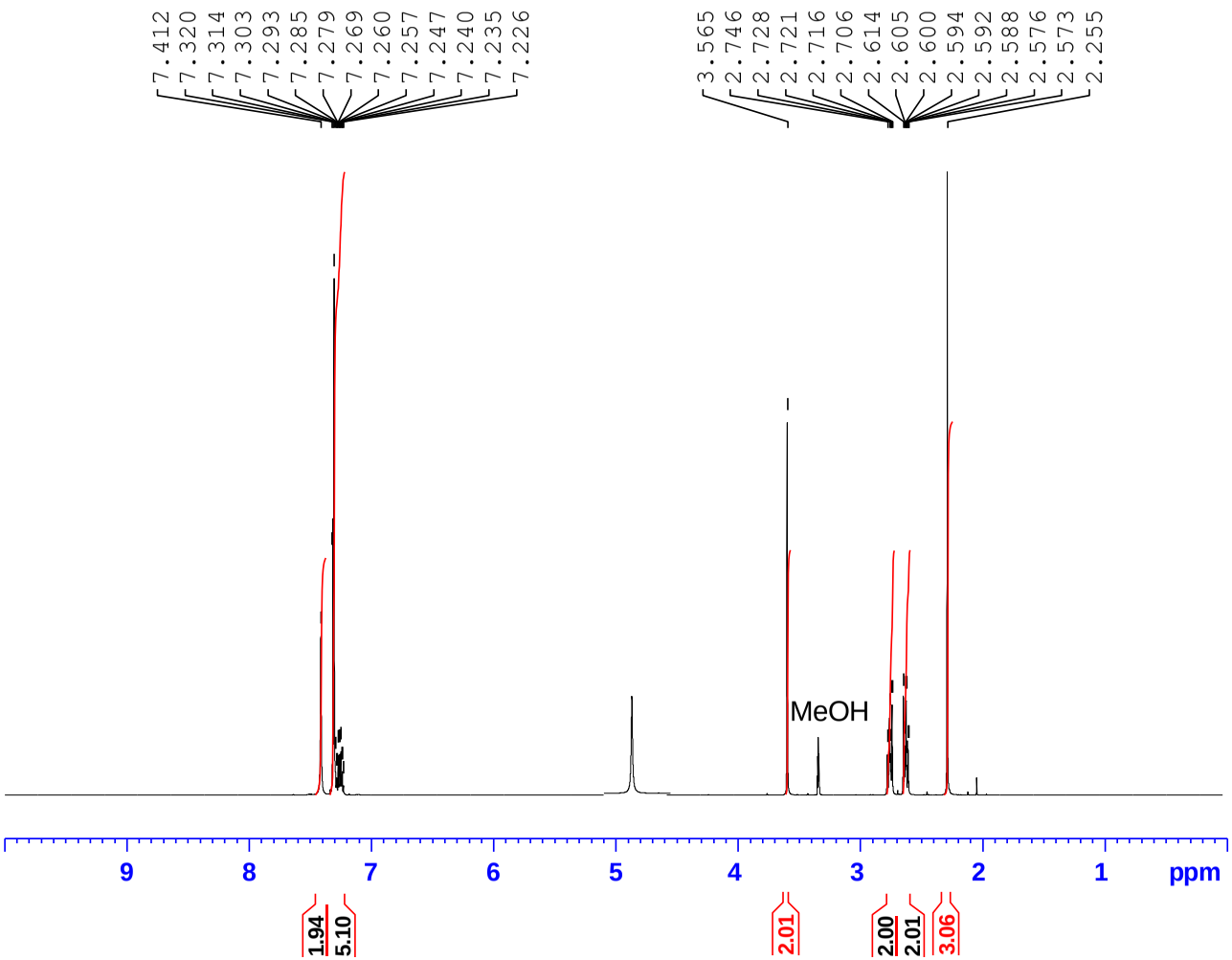
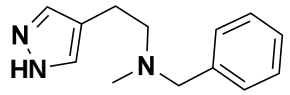


N-benzyl-N-methyl-2-(1H-pyrazol-4-yl)ethan-1-amine



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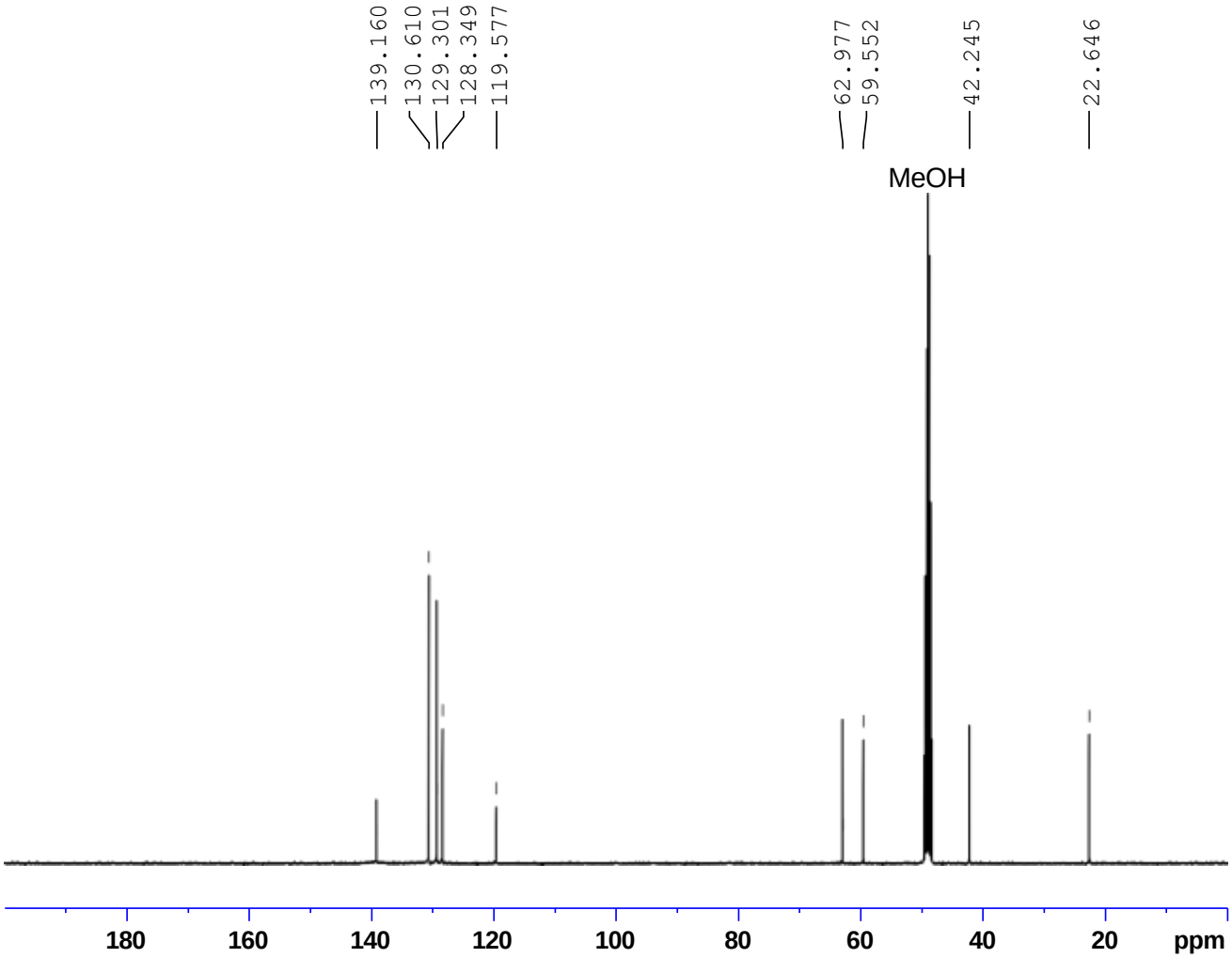
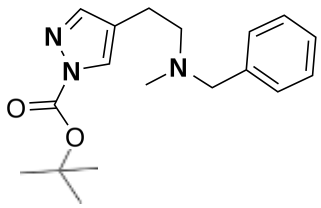


tert-butyl 4-(2-(benzyl(methyl)amino)ethyl)-1H-pyrazole-1-carboxylate



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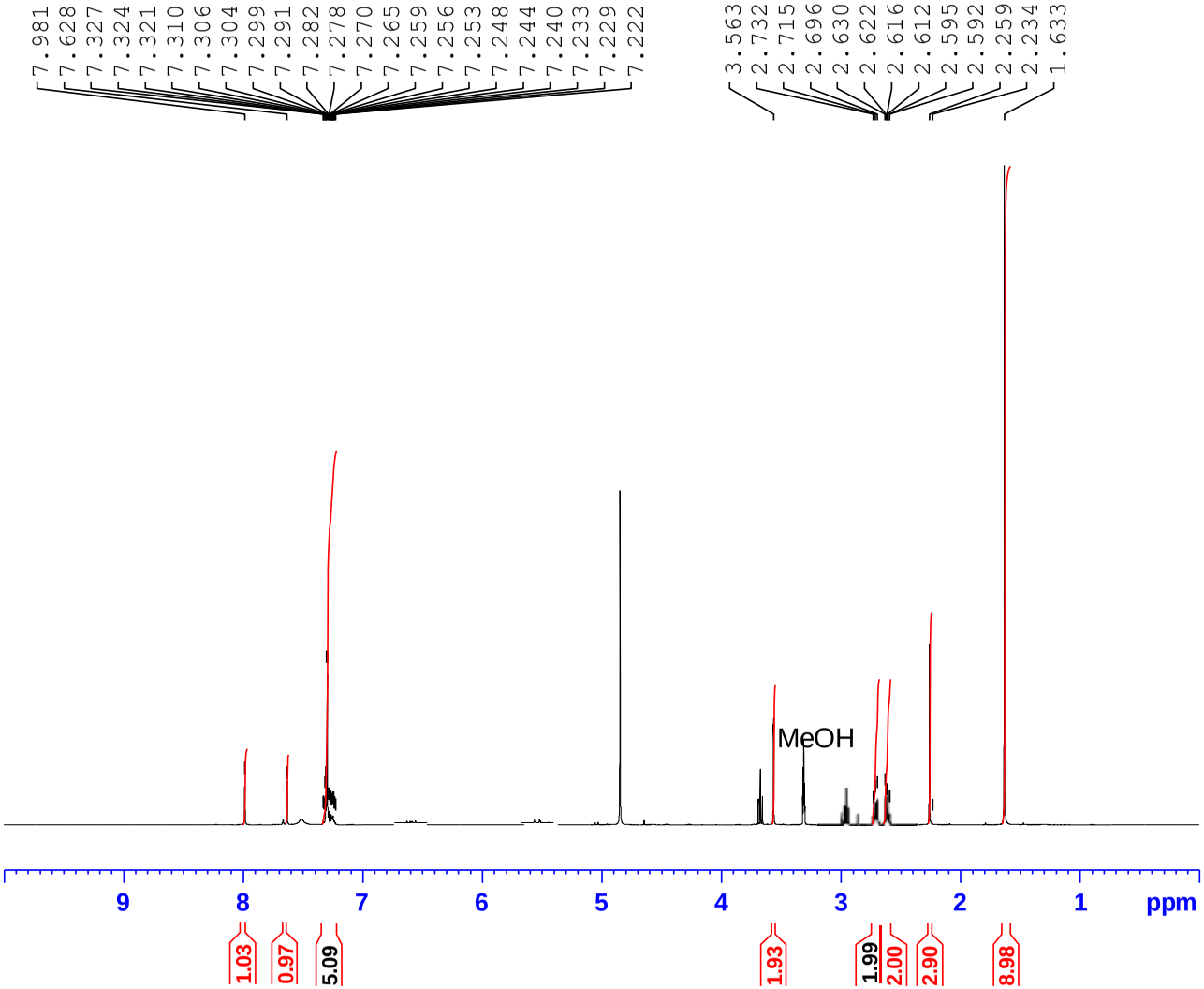

Analysis Report

Agilent | Trusted Answers

Sample Information

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Sample ID		**Acq. Time (Local)**	1/10/2024 6:01:49 PM (UTC-06:00)
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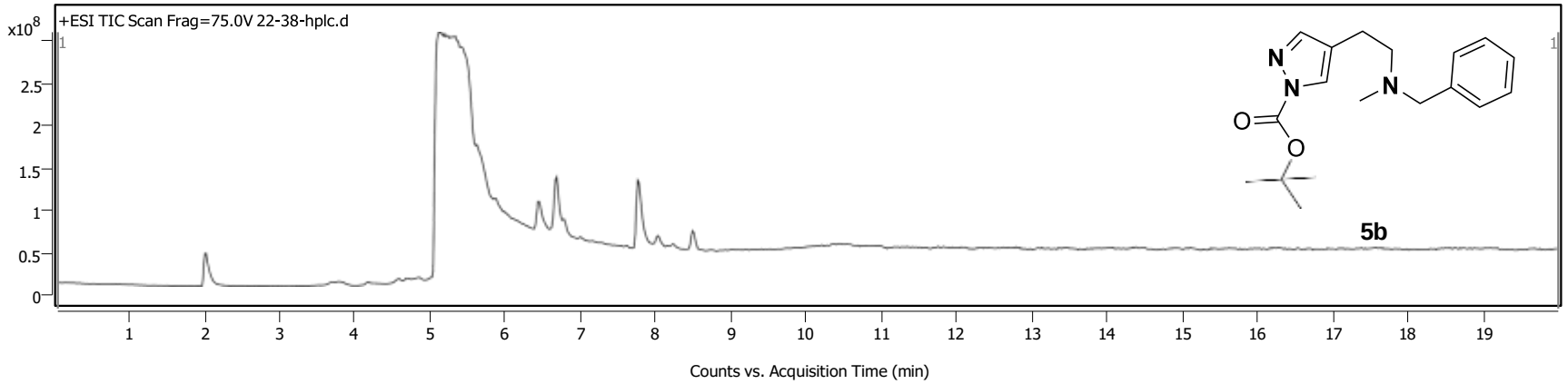
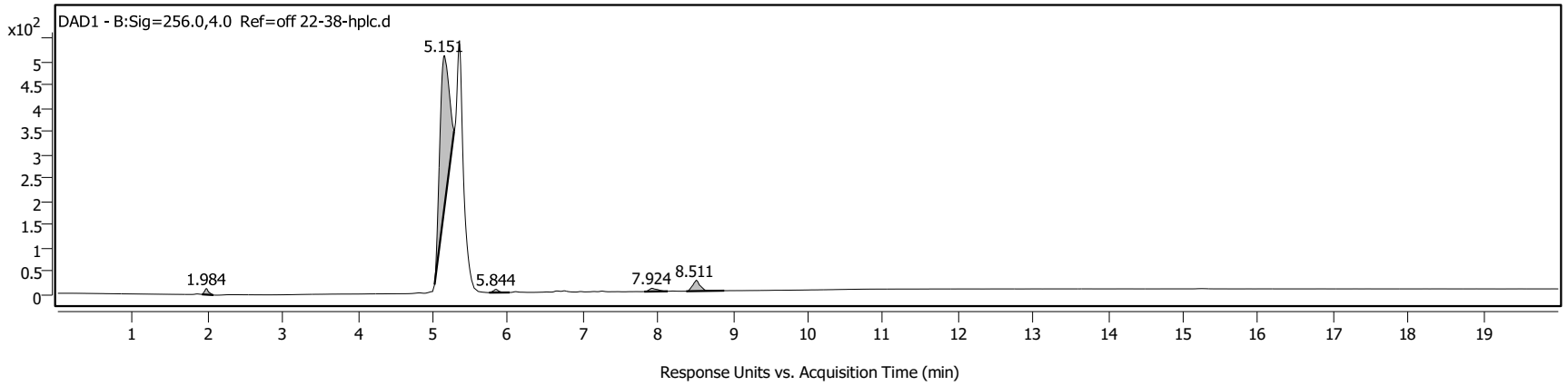
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	10	**IRM Status**	All ions missed
Position	P1-A2	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms





User Spectrum Plot Report

Name	22-38	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	10	Plate Pos.		IRM Status	All ions missed		
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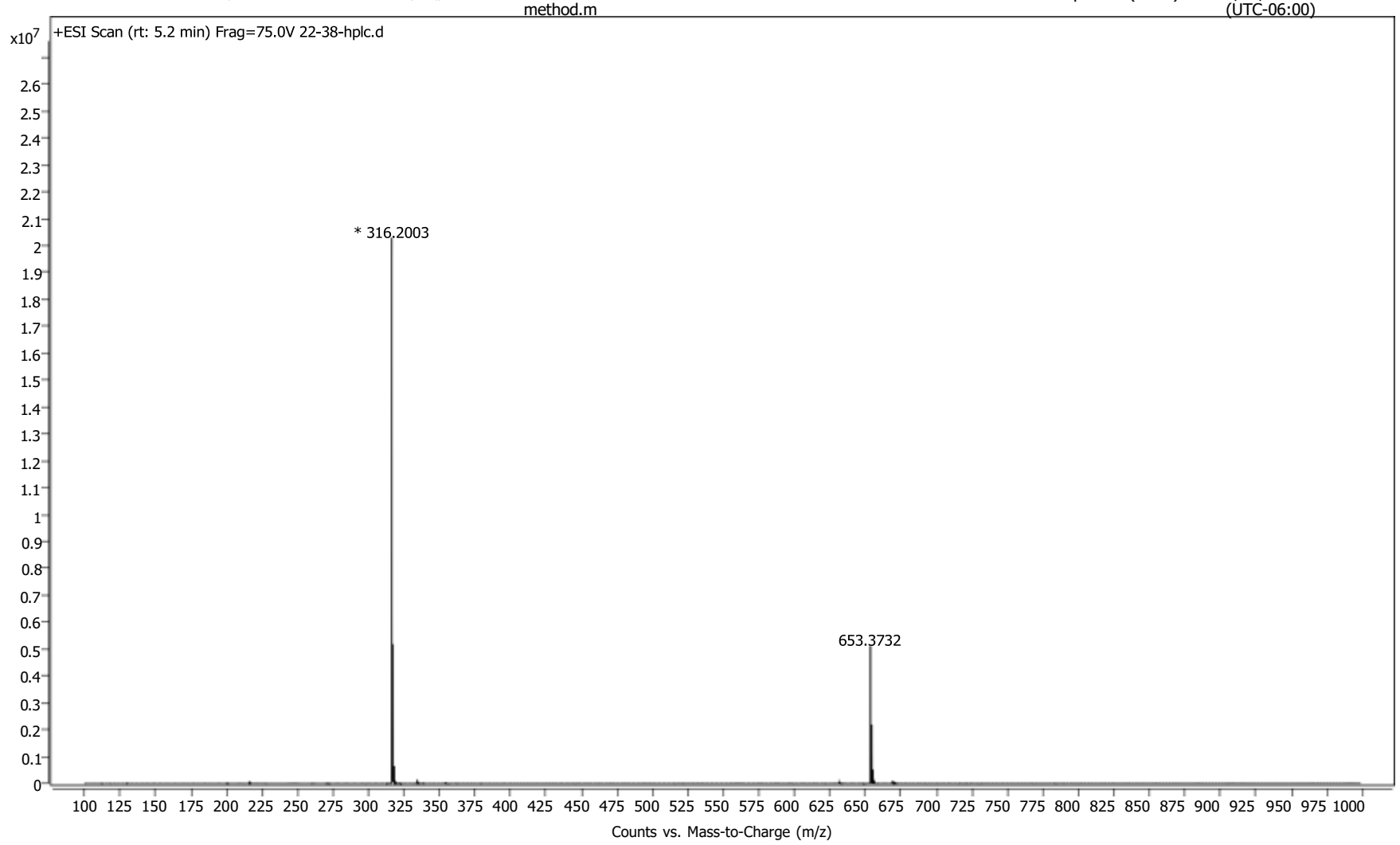
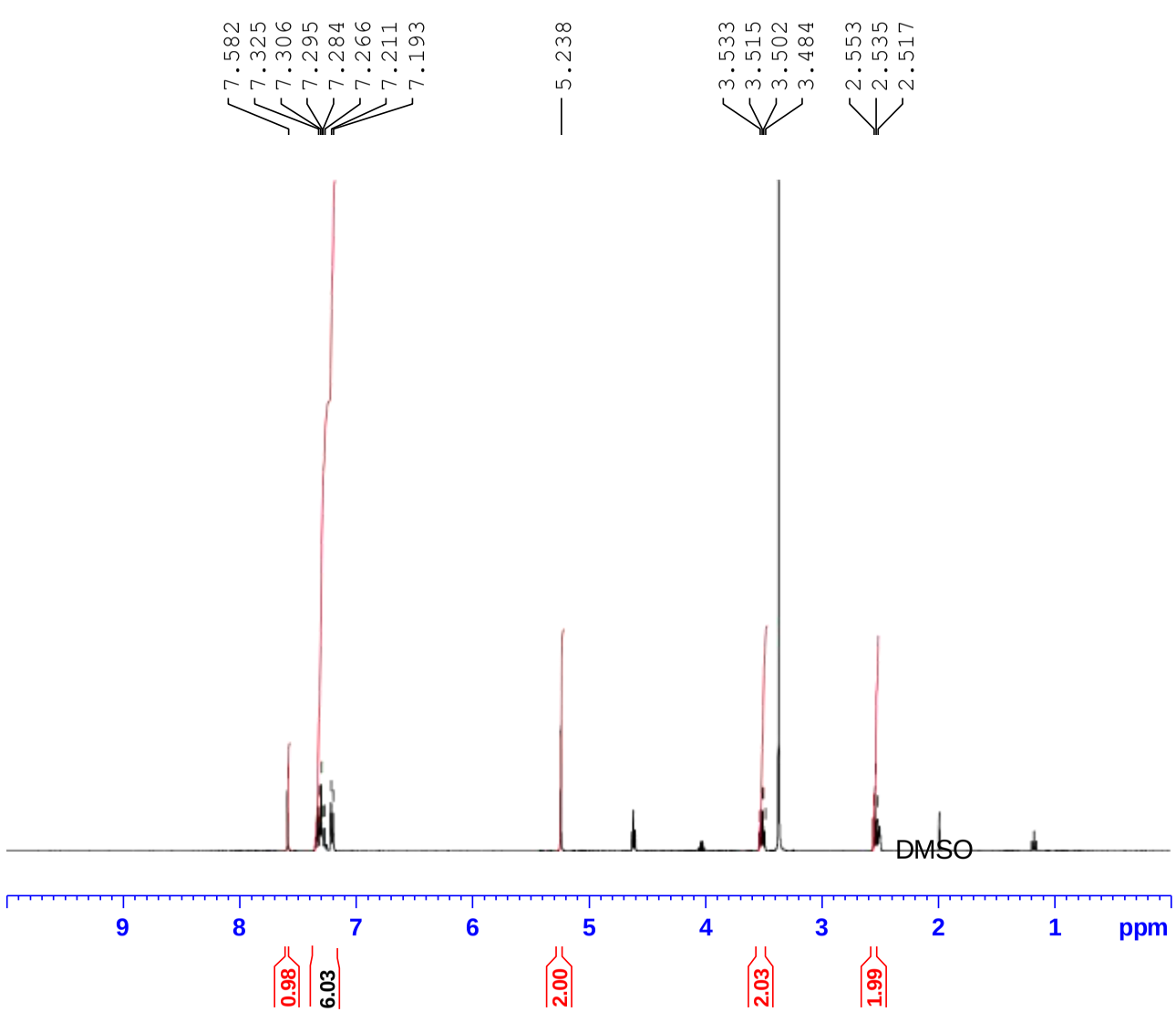
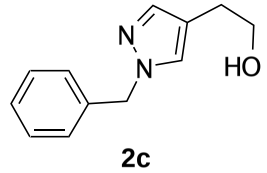


2-(1-benzyl-1H-pyrazol-4-yl)ethan-1-ol





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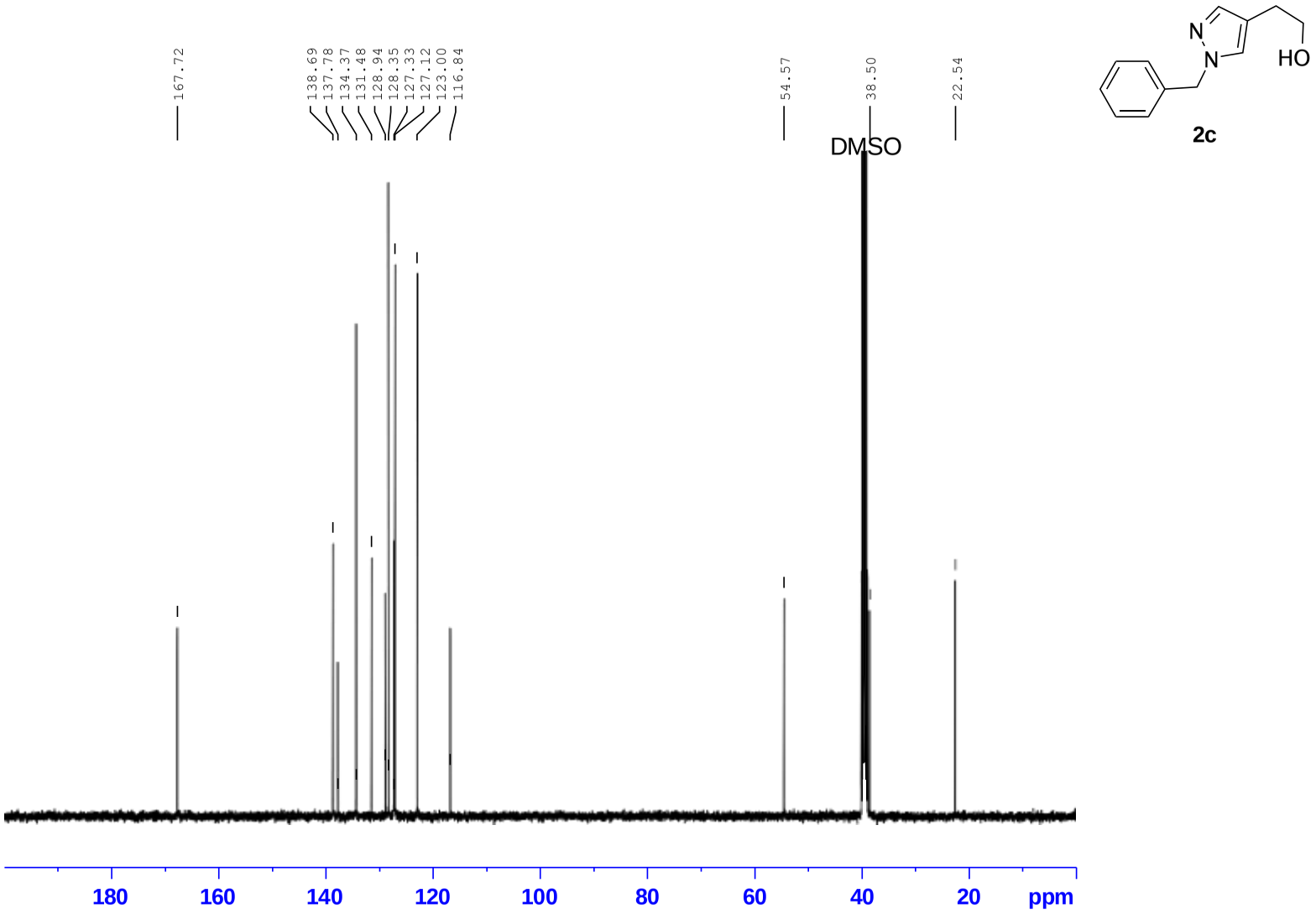
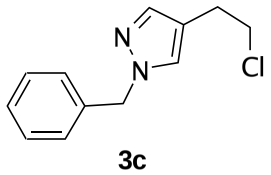


1-benzyl-4-(2-chloroethyl)-1H-pyrazole



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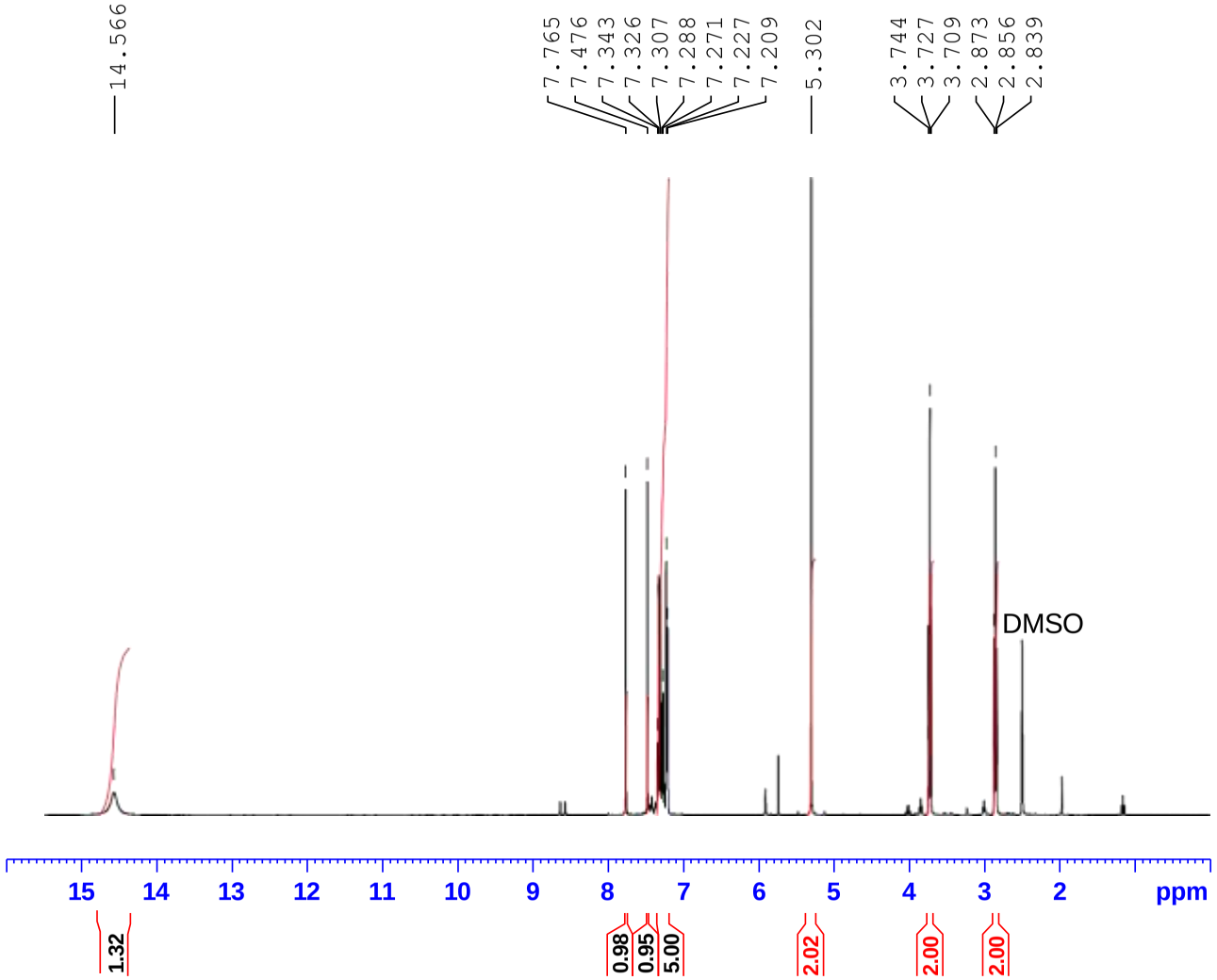
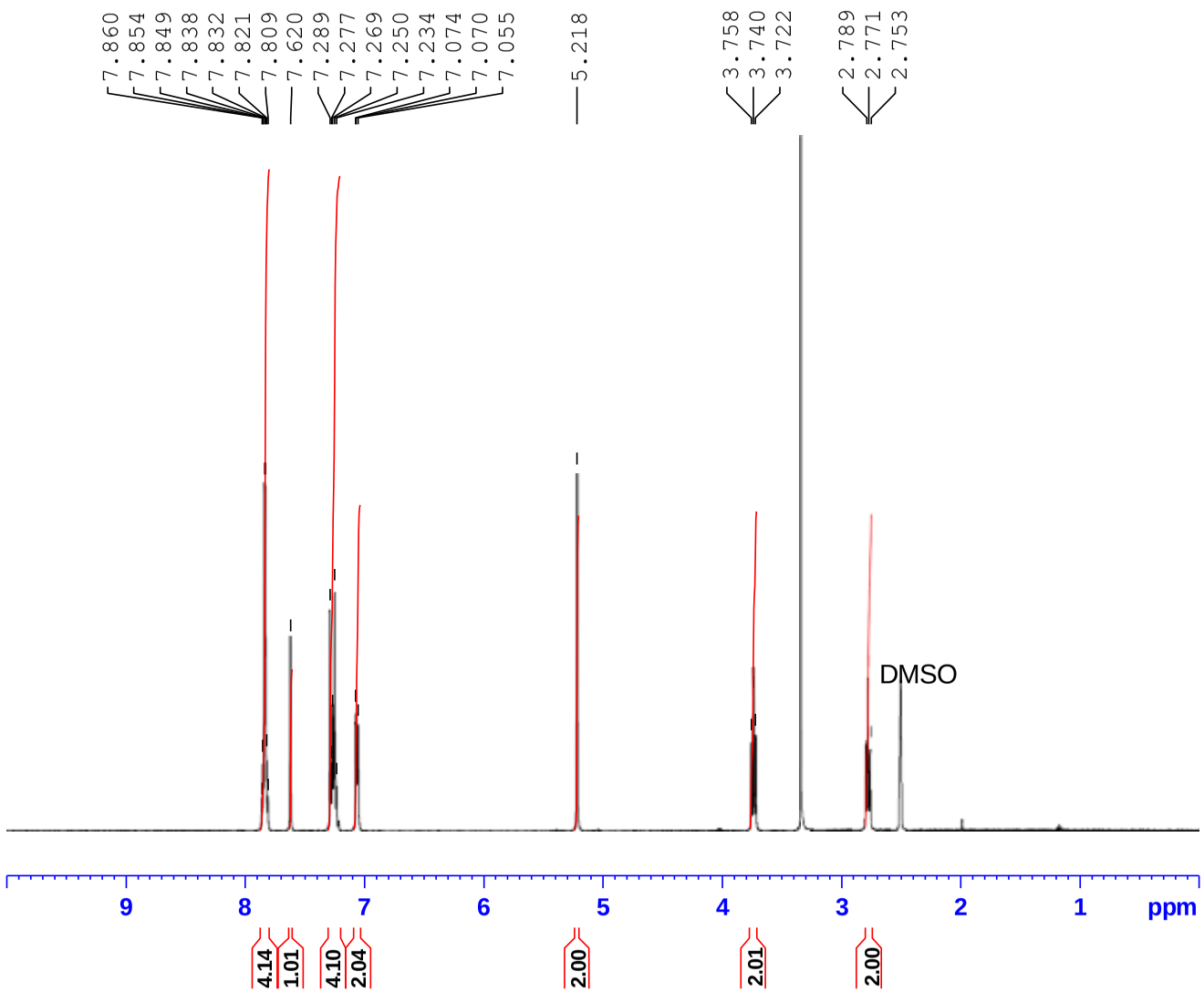
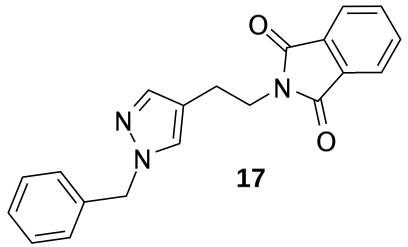
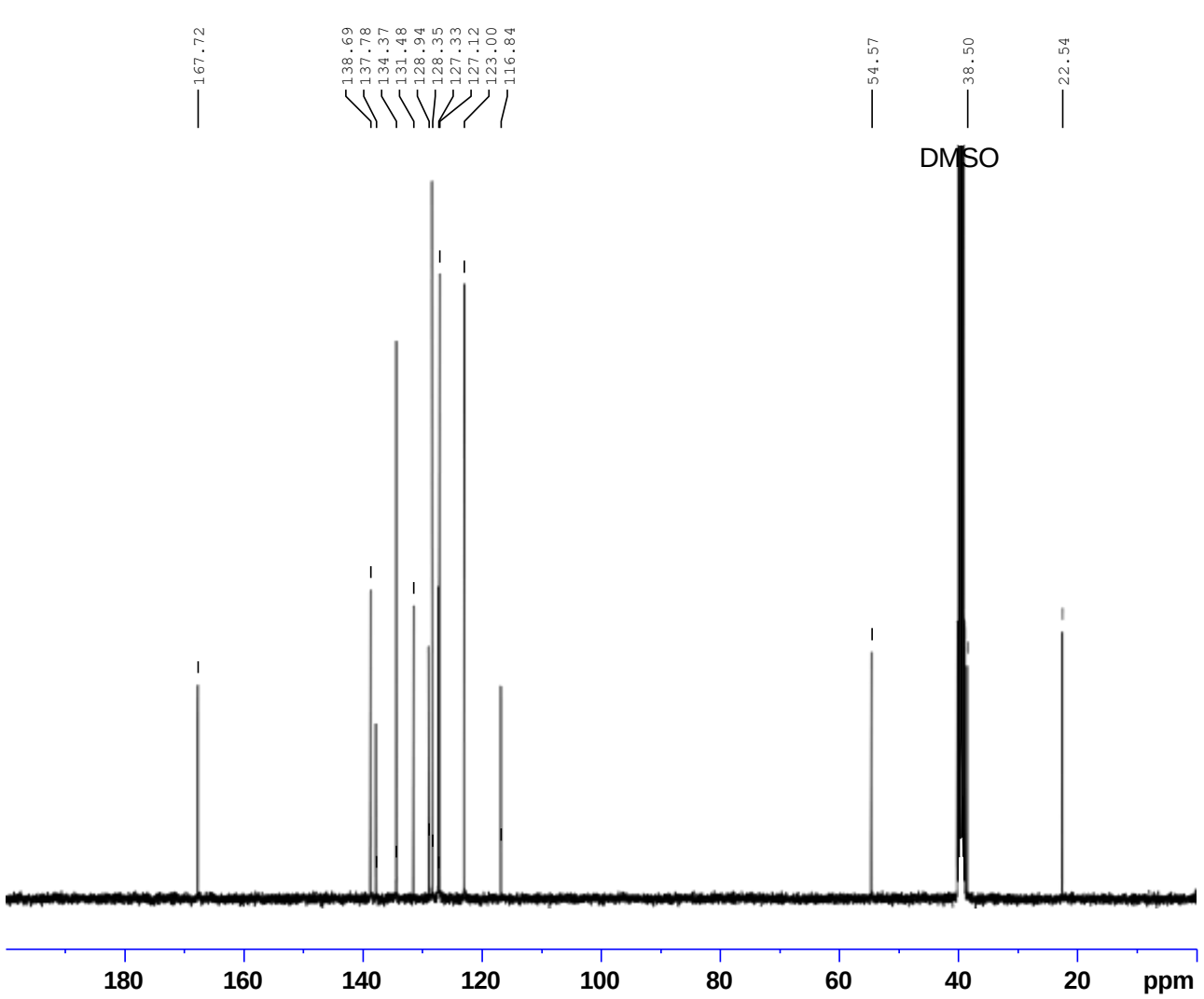


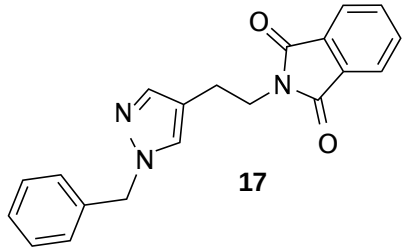
2-(2-(1-benzyl-1H-pyrazol-4-yl)ethyl)isoindoline-1,3-dione





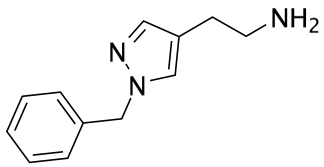
2-(2-(1-benzyl-1H-pyrazol-4-yl)ethyl)isoindoline-1,3-dione





17

2-(1-benzyl-1H-pyrazol-4-yl)ethan-1-amine



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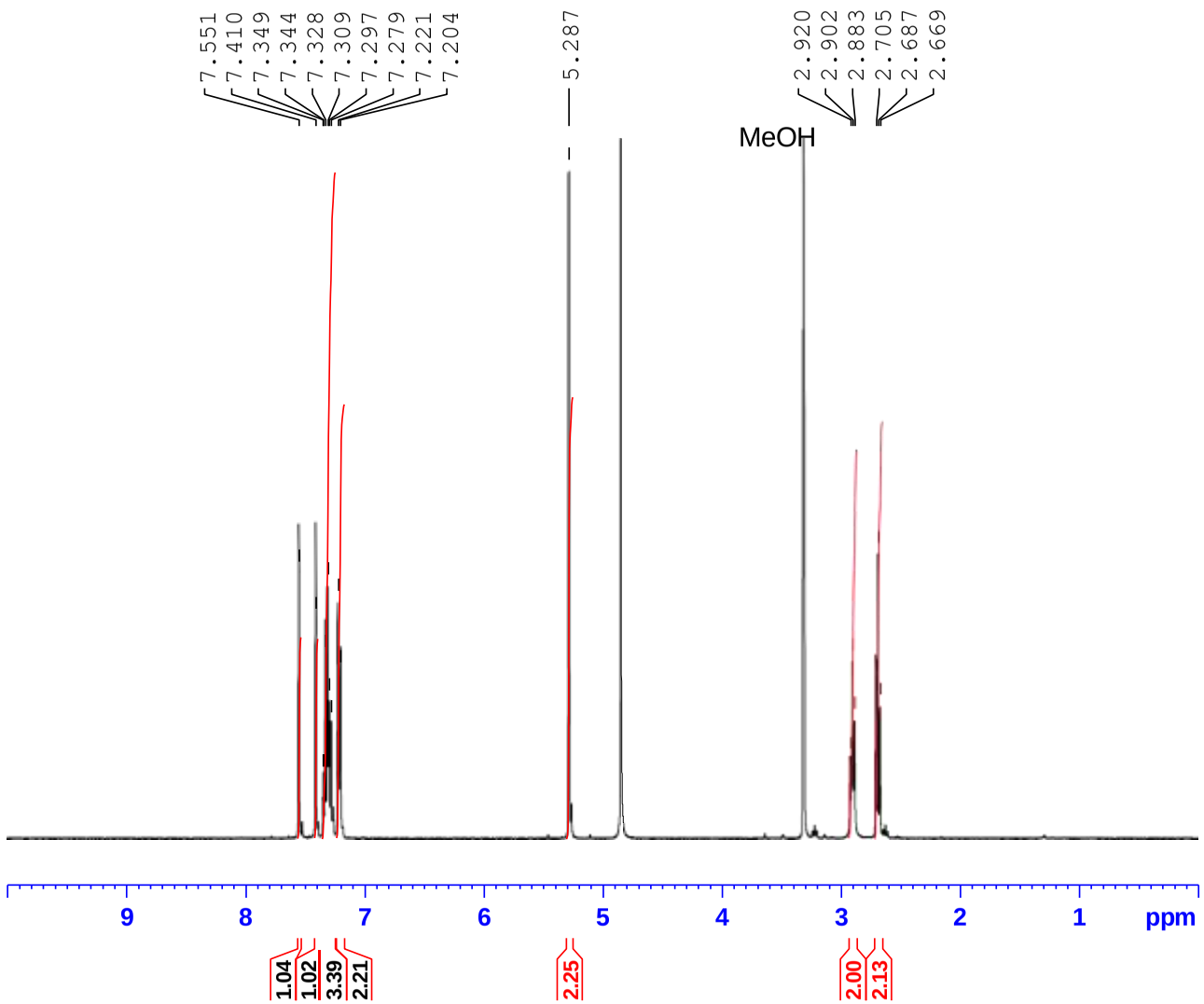
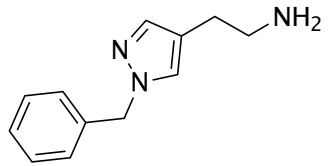


2-(1-benzyl-1H-pyrazol-4-yl)ethan-1-amine



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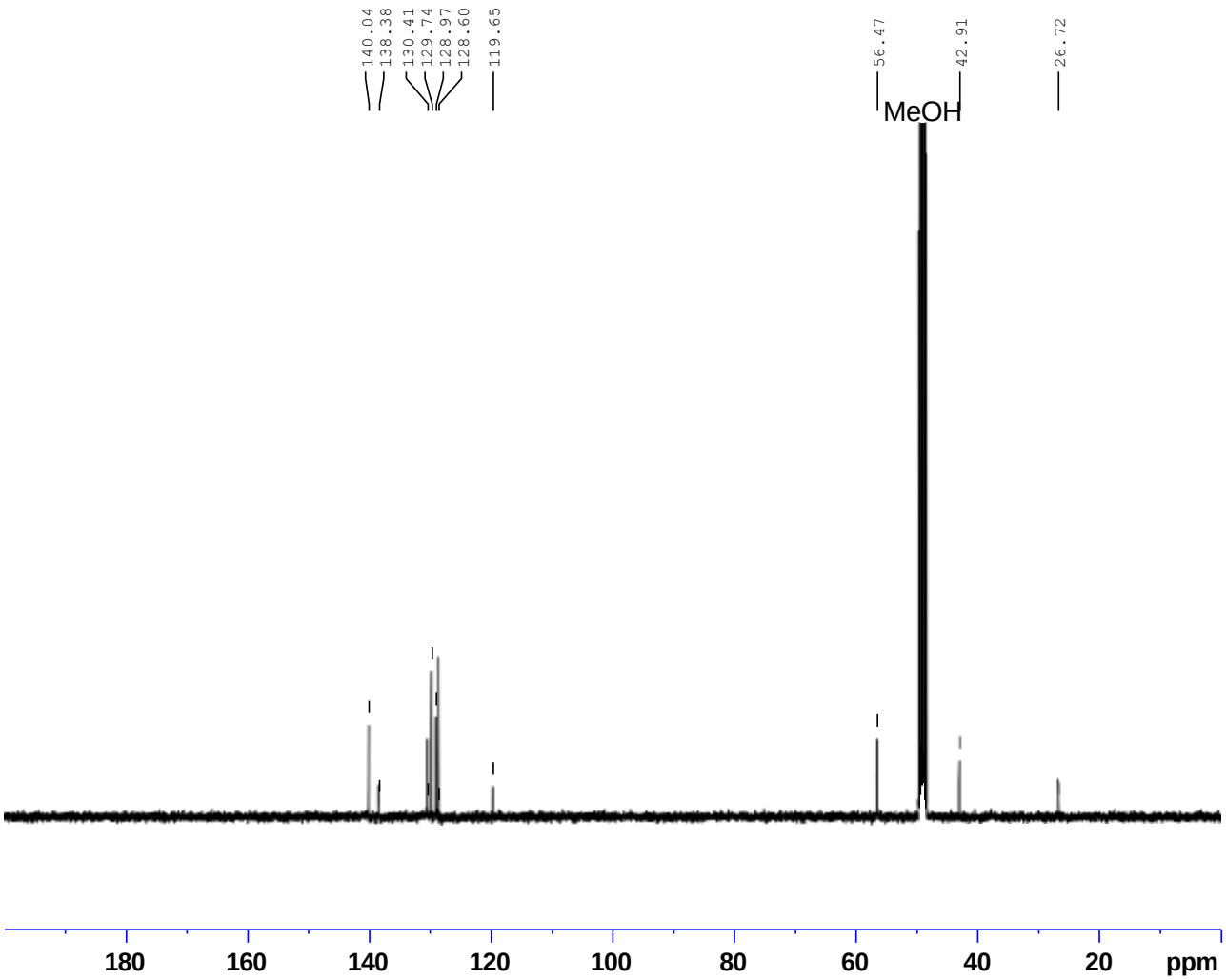
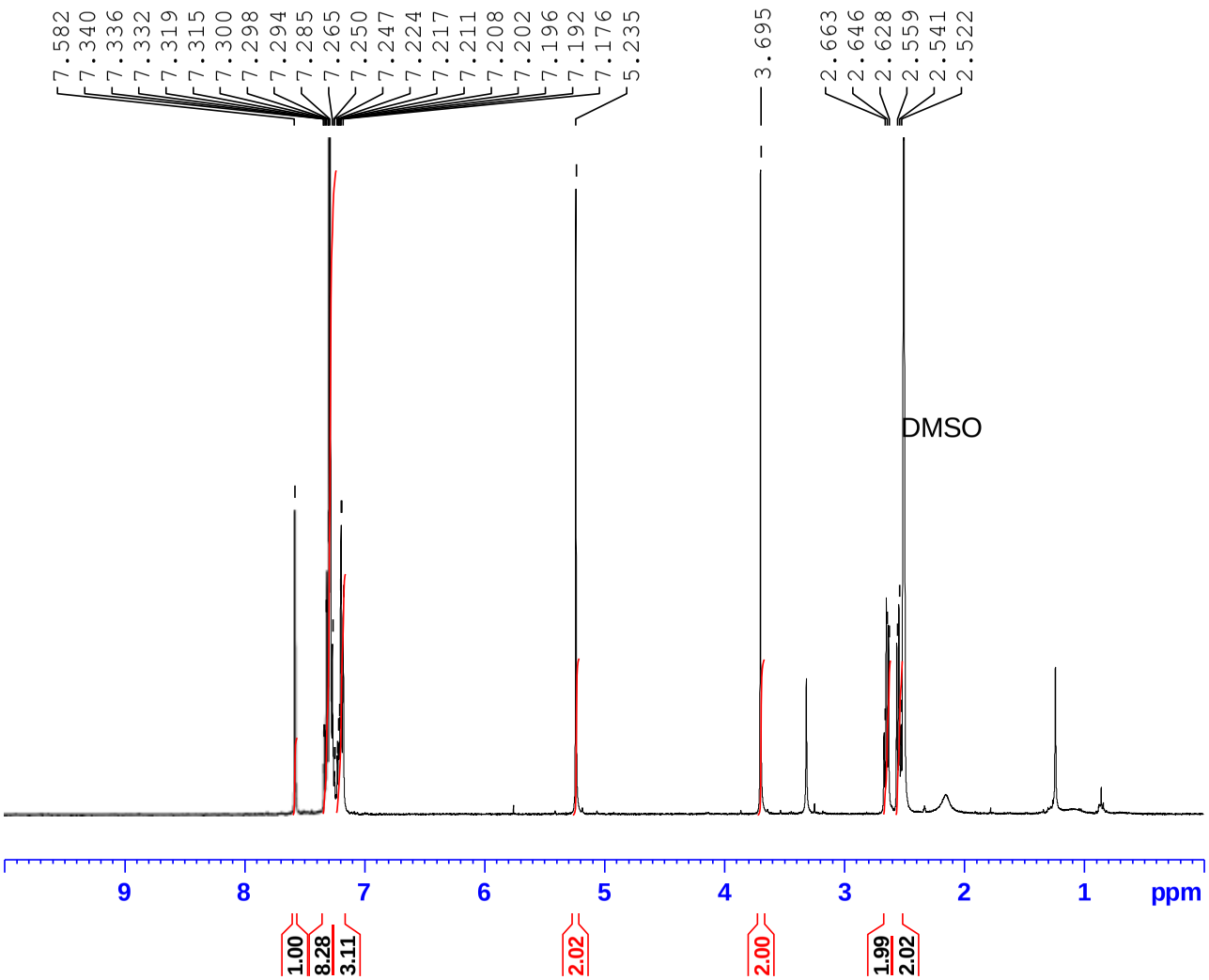
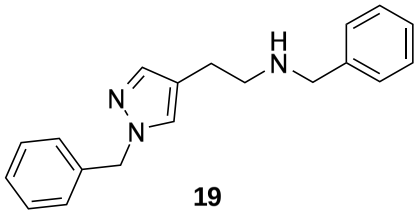


N-benzyl-2-(1-benzyl-1H-pyrazol-4-yl)ethan-1-amine

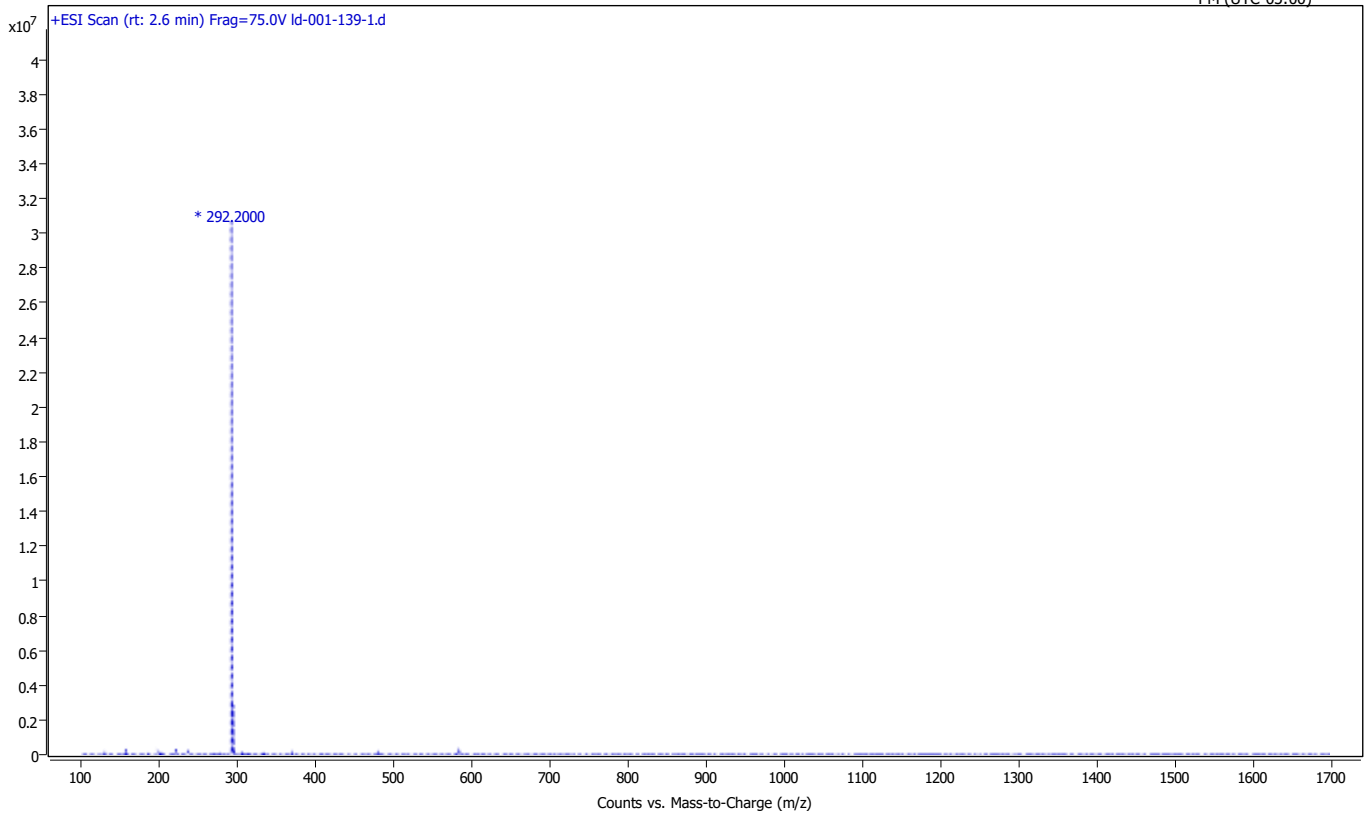




19

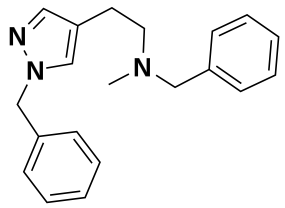
User Spectrum Plot Report

Name		Rack Pos.		Instrument	Operator
Inj. Vol. (ul)		Plate Pos.		IRM Status	Success
Data File	ld-001-139-1.d	Method (Acq)		Comment	Acq. Time (Local)	10/31/2024 2:54:12 PM (UTC-05:00)

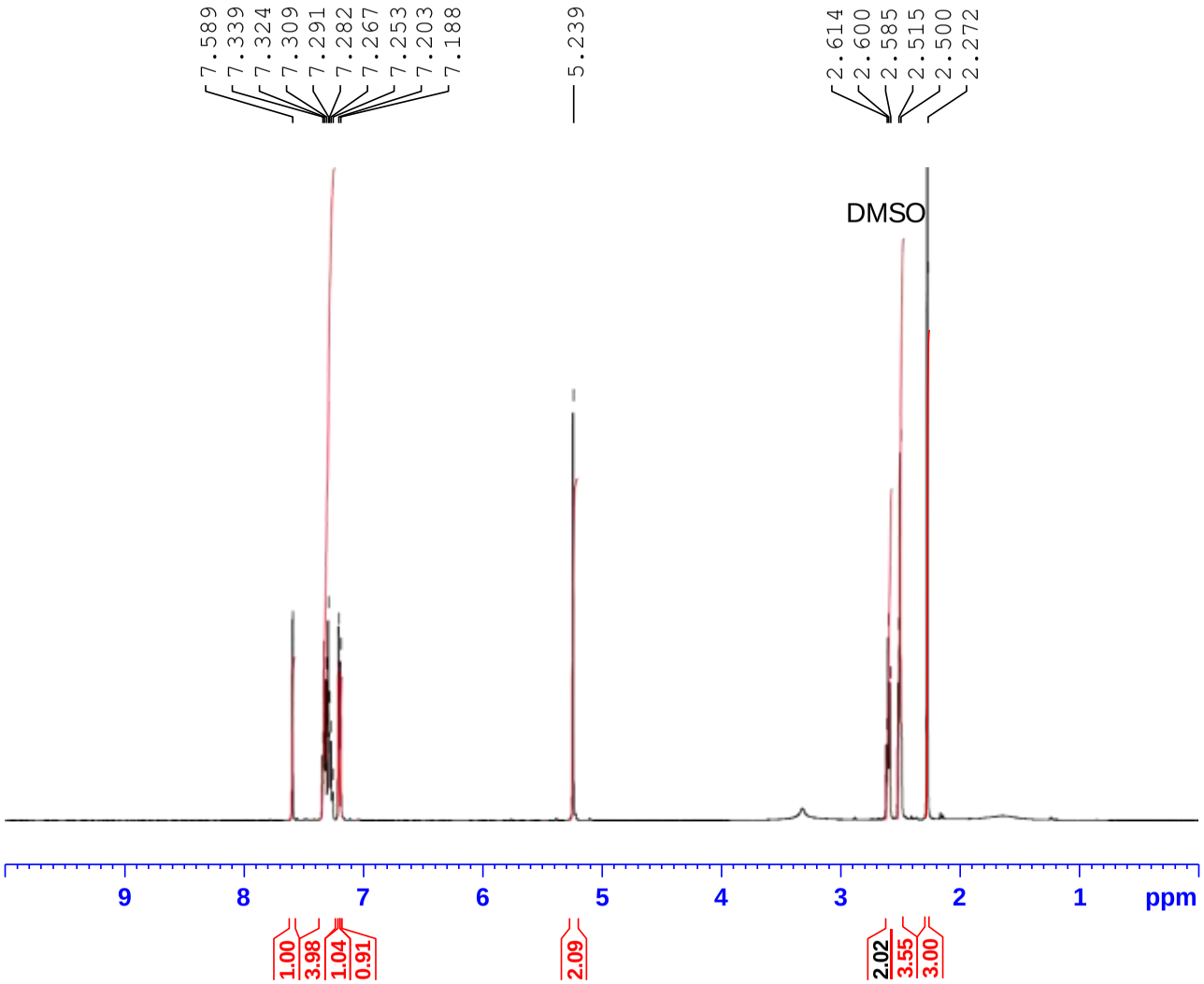


Generated at 3:05 PM on 10/31/2024

2-(1-benzyl-1H-pyrazol-4-yl)-N-methylethan-1-amine



5c



Analysis Report

Agilent | Trusted Answers

Sample Information

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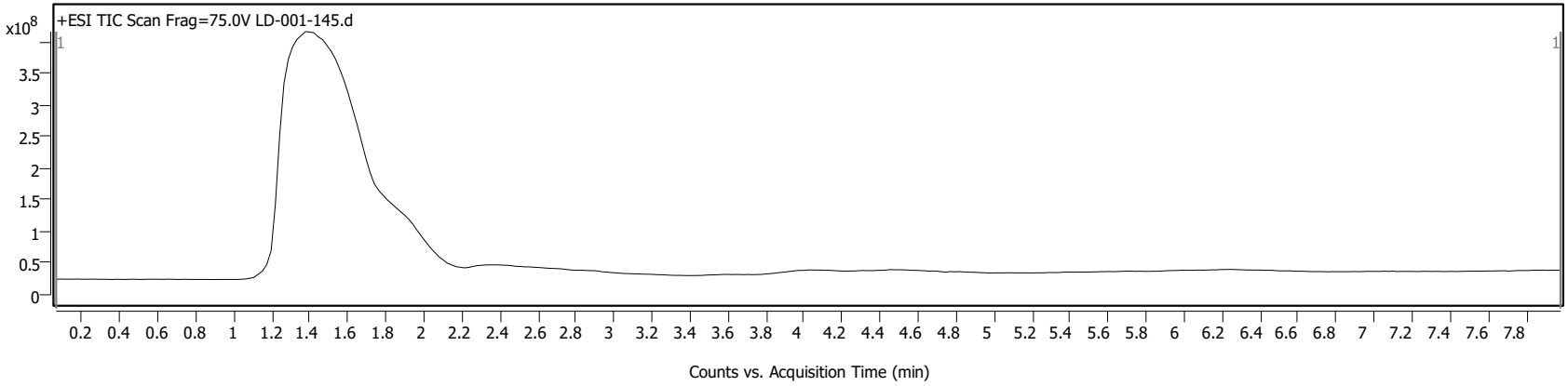
Sample ID		**Acq. Time (Local)**	6/30/2023 2:57:30 PM (UTC-05:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HRMS method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	2	**IRM Status**	Success
Position	P1-A7	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms



MassHunter Qual 10.0
(End of Report)

User Spectrum Plot Report

Name	LD-001-145	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success		
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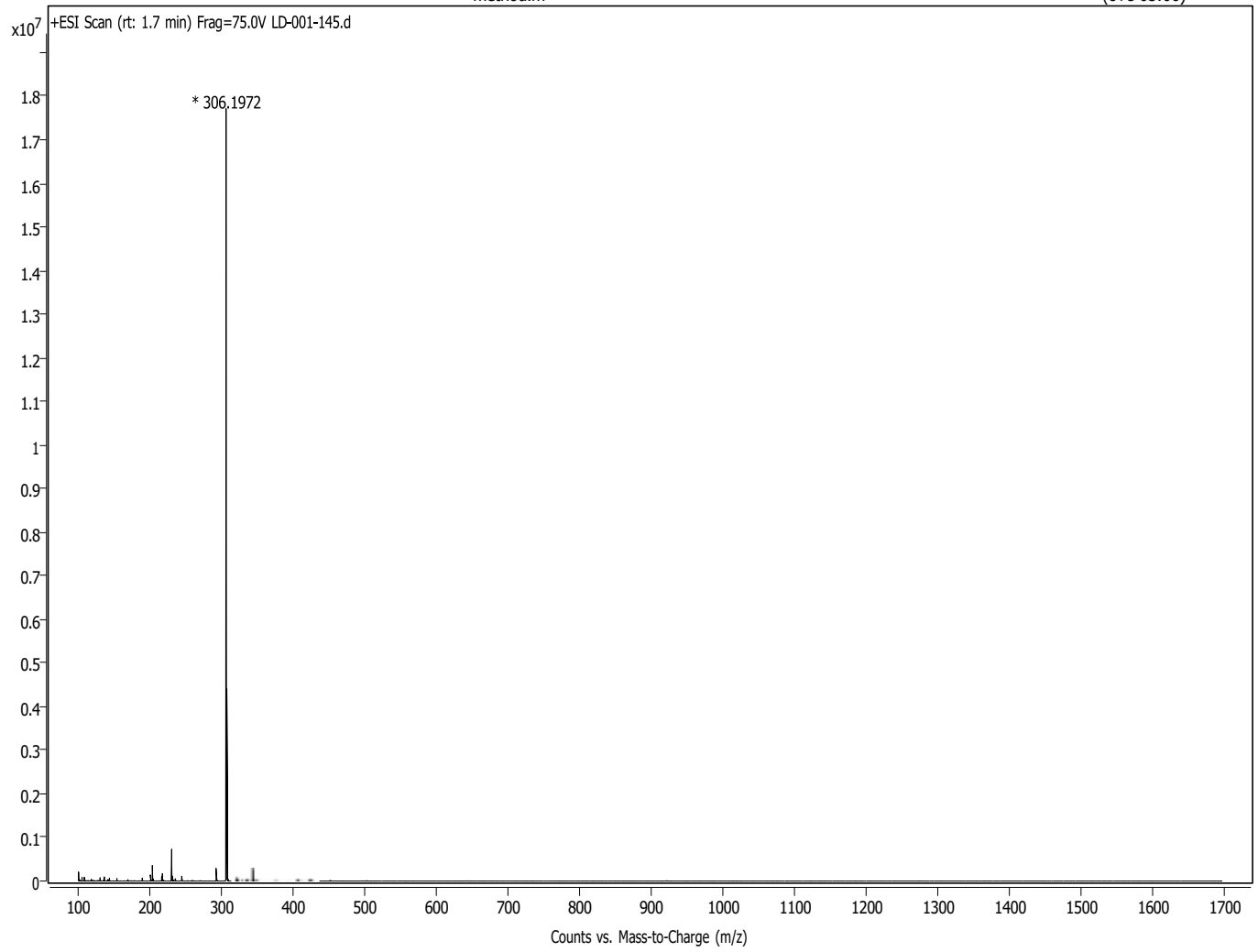

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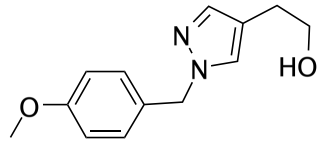

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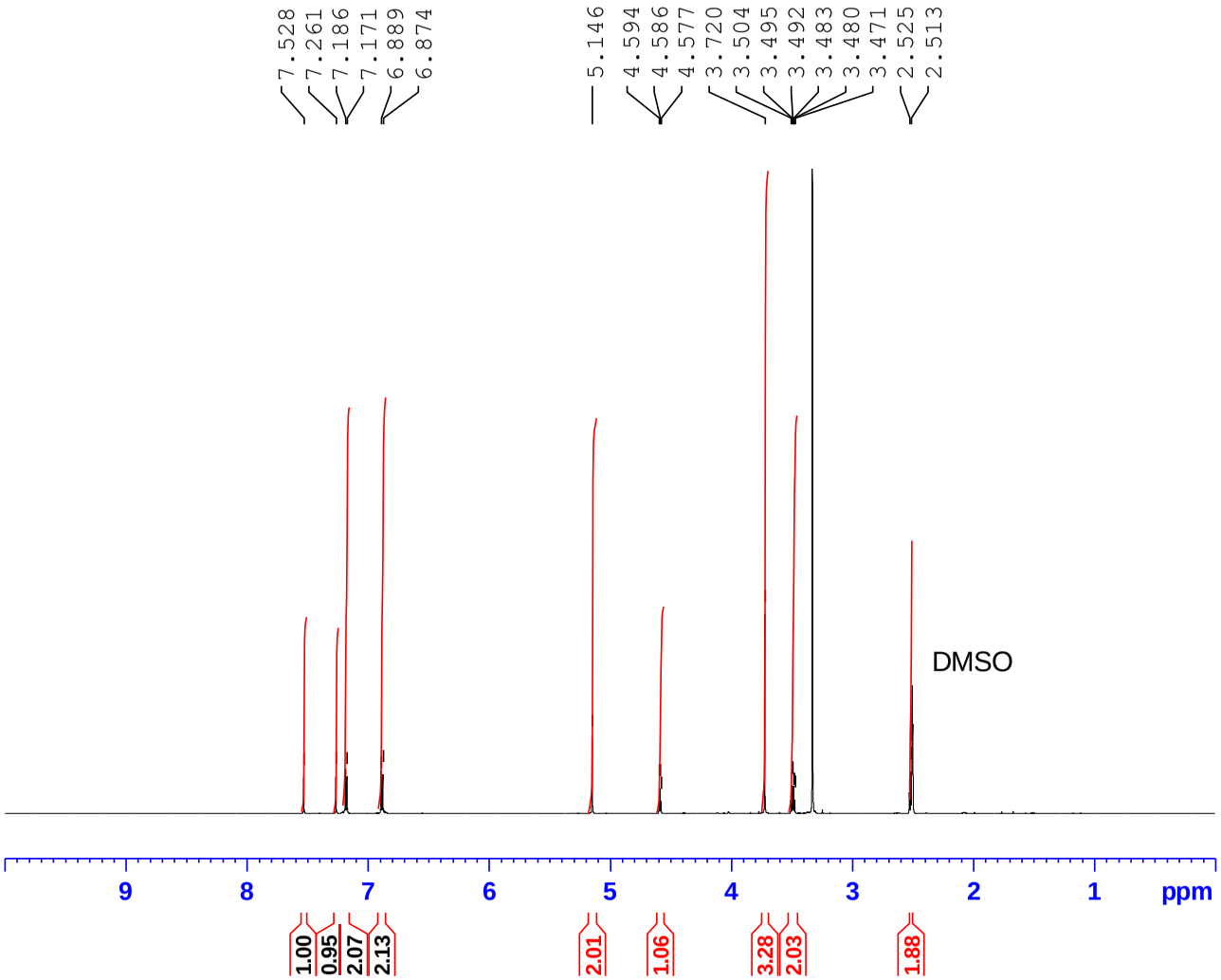
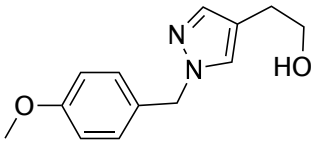
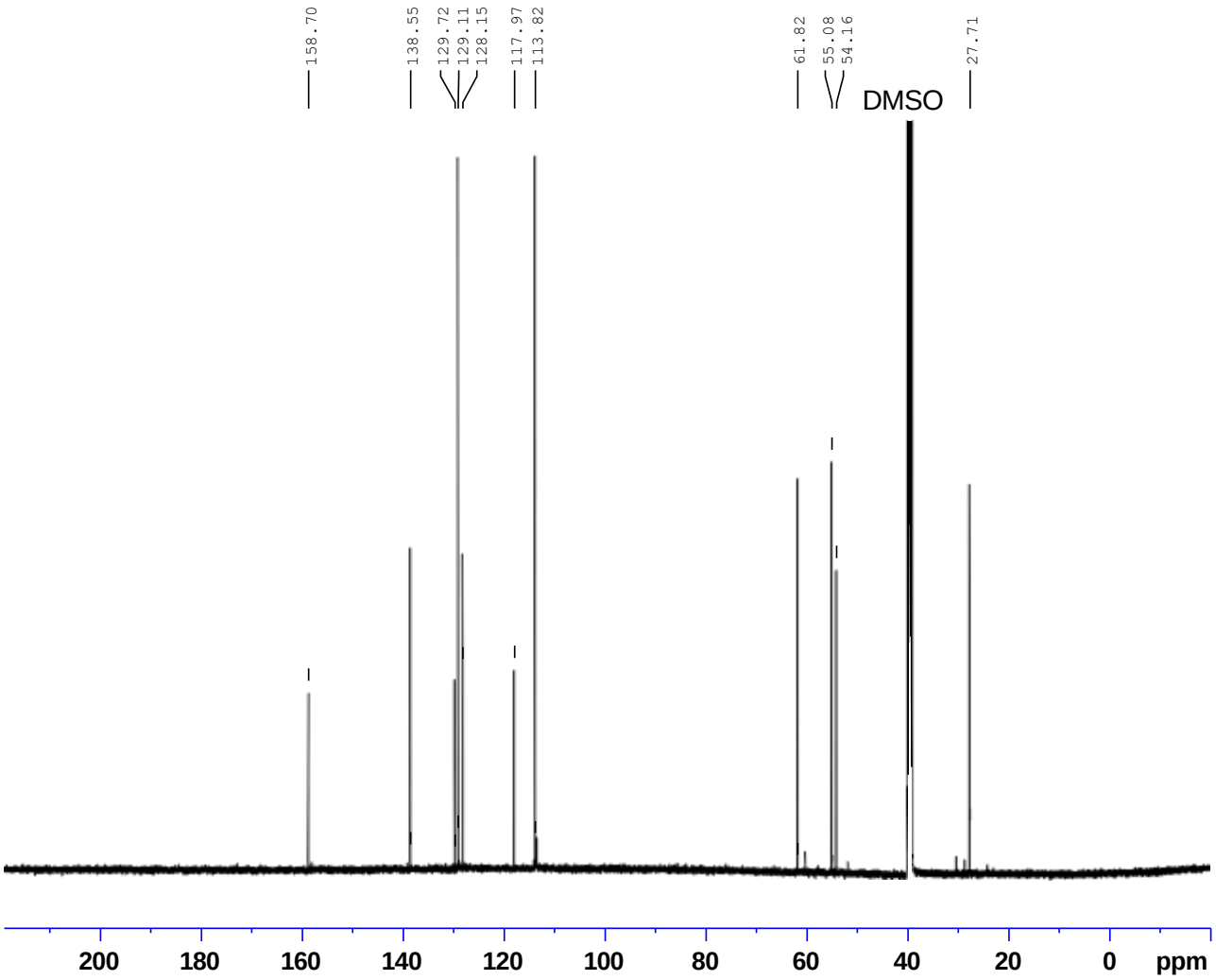


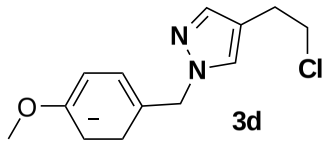
2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethan-1-ol

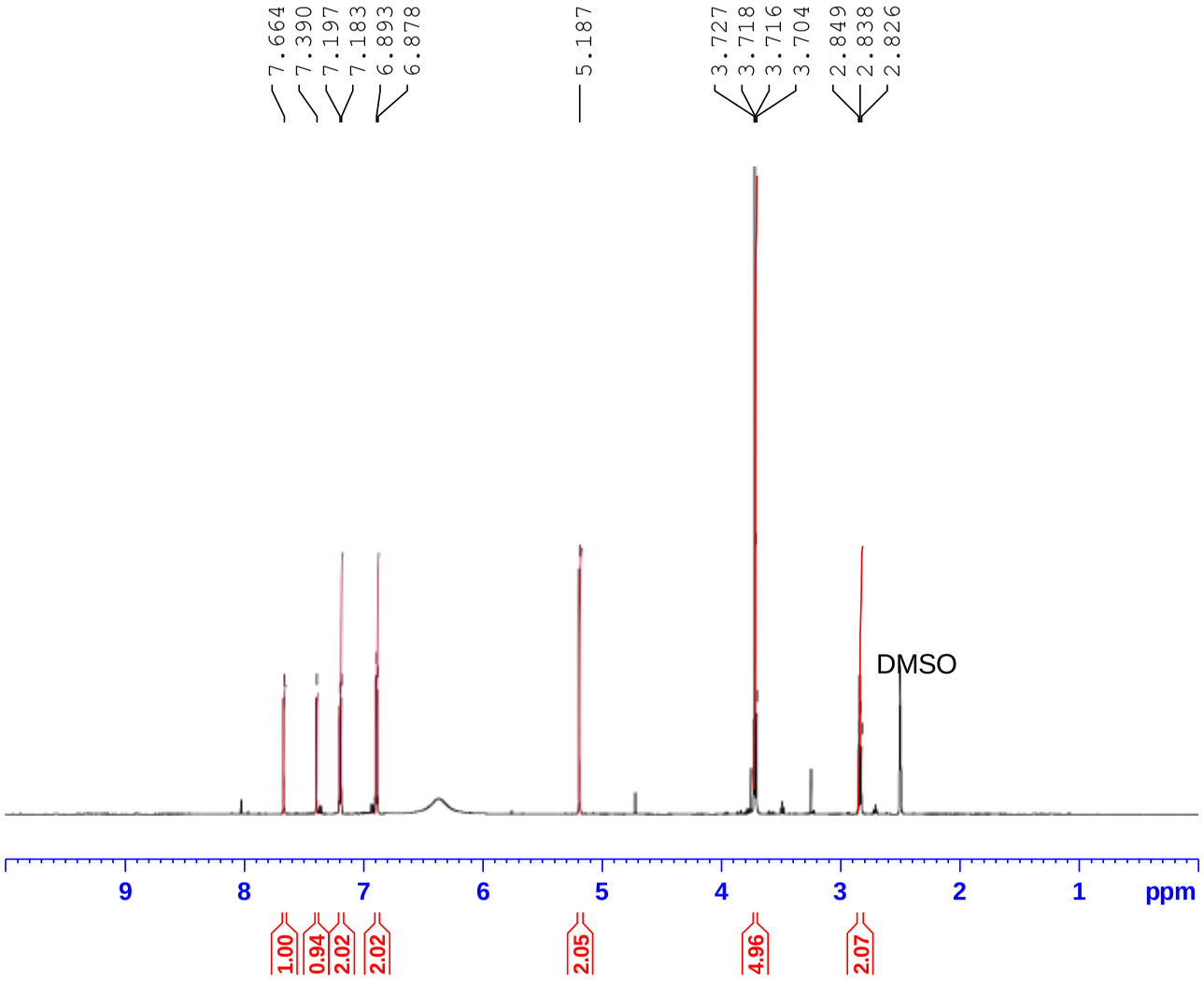


2d

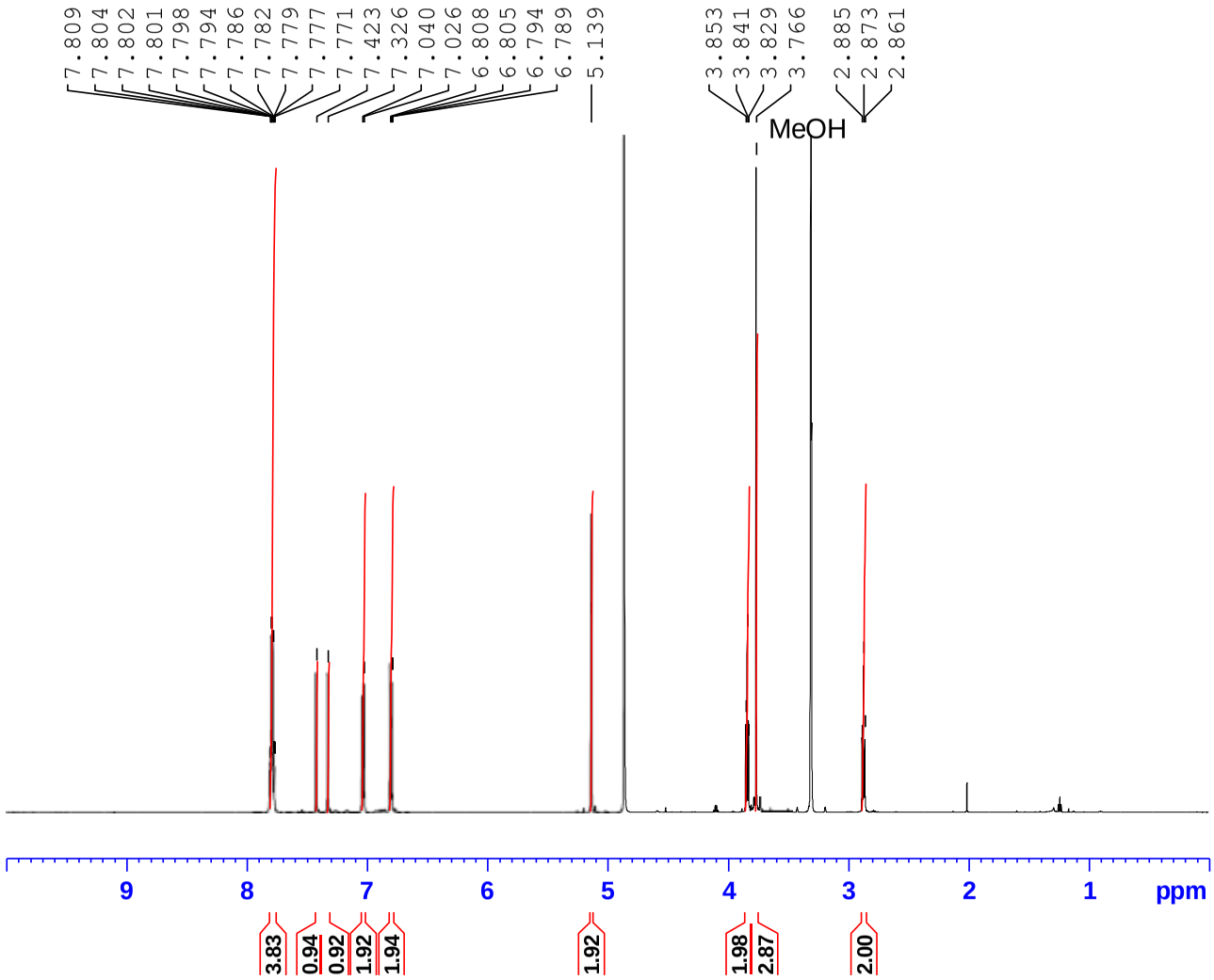


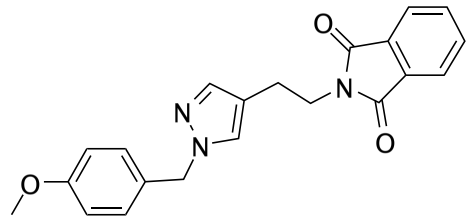
4-(2-Chloroehyl)-1-(4-methoxybenzyl)-1H-pyrazole





2-(2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethyl)isoindoline-1,3-dione





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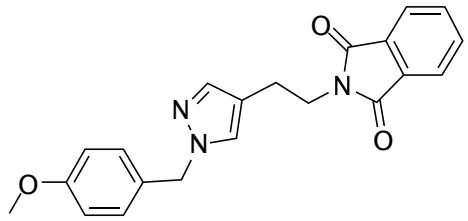
2-(2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethyl)isoindoline-1,3-dione



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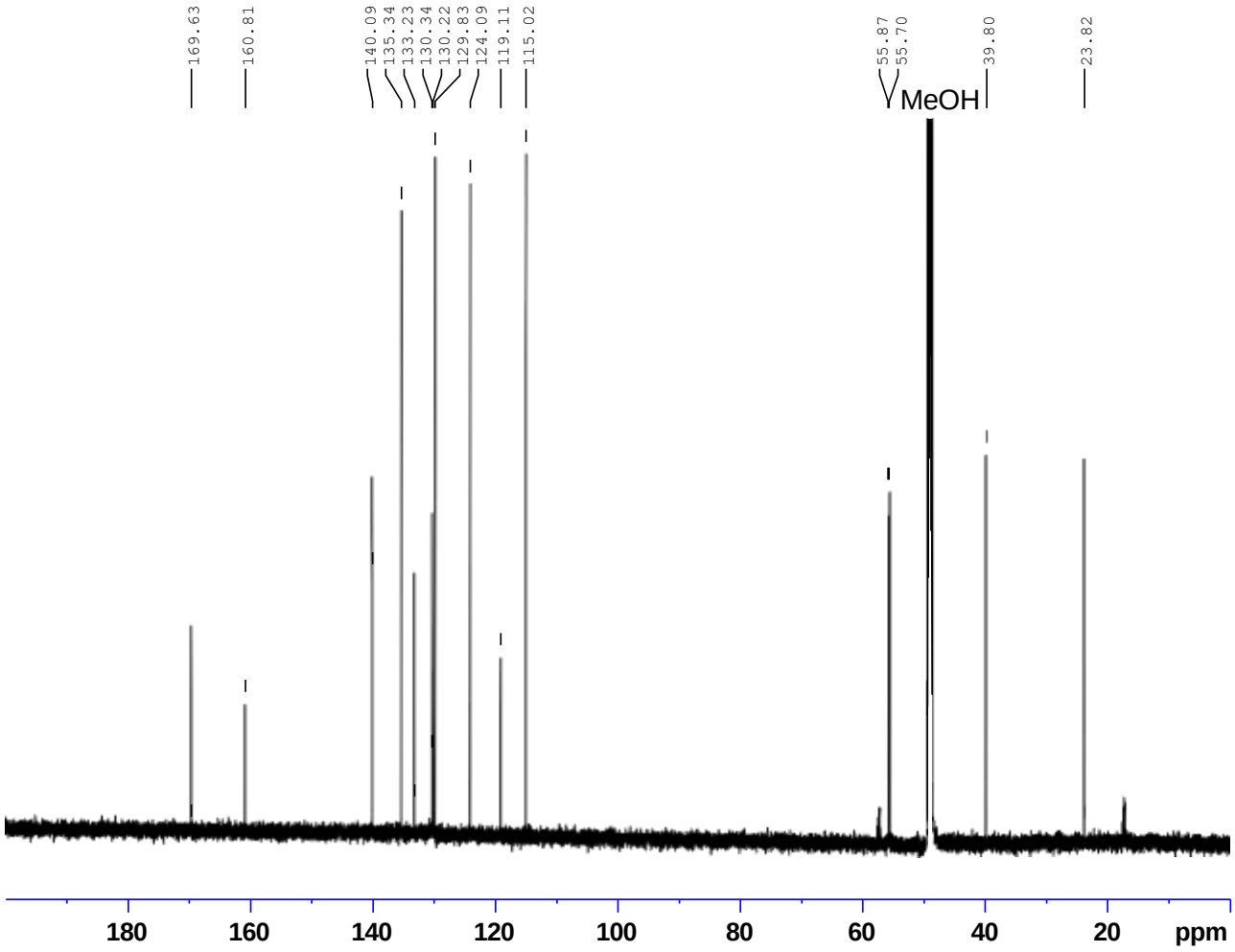
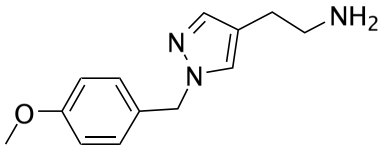


2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethan-1-amine



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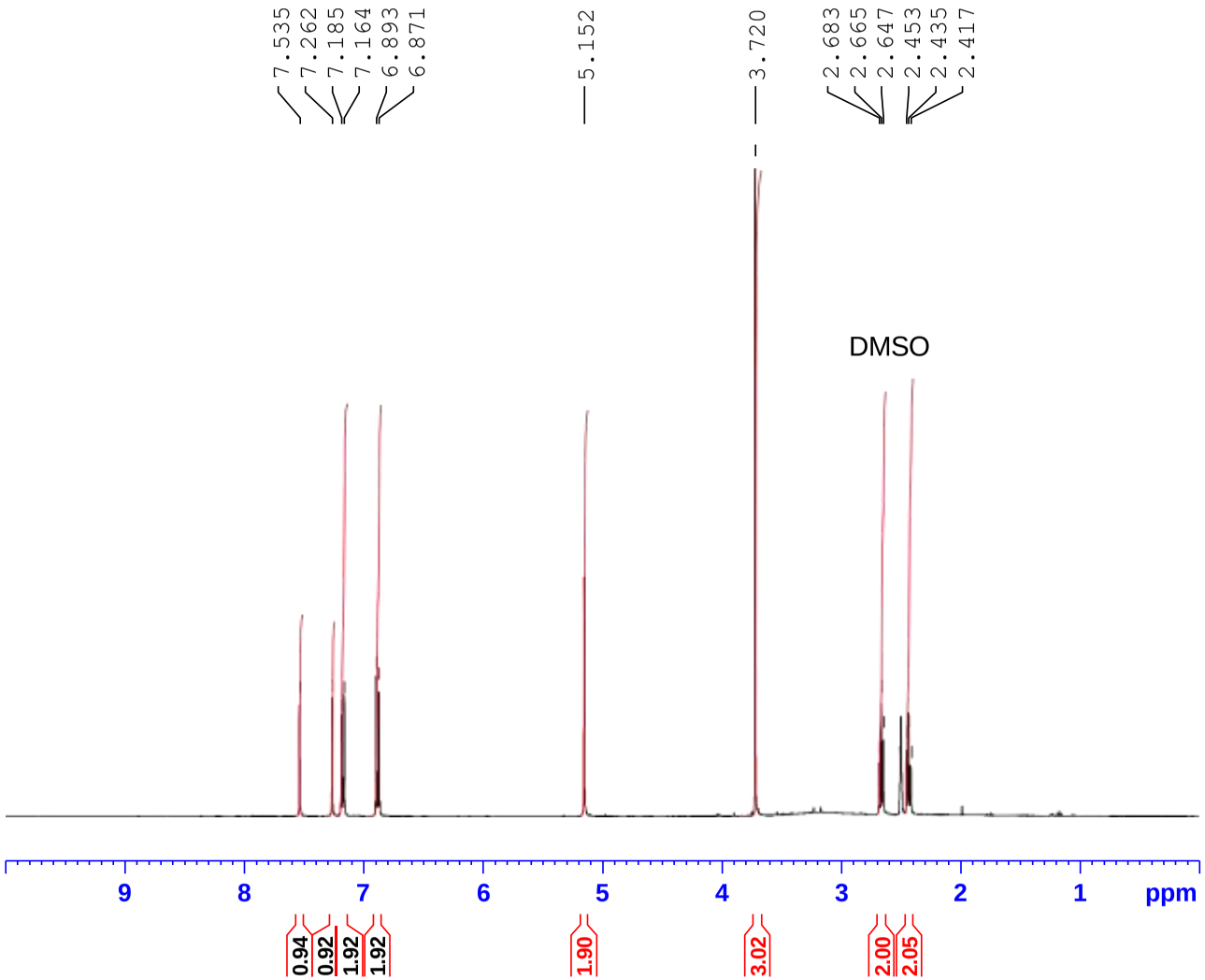
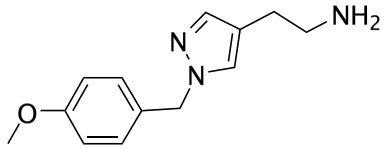


l2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethan-1-amine



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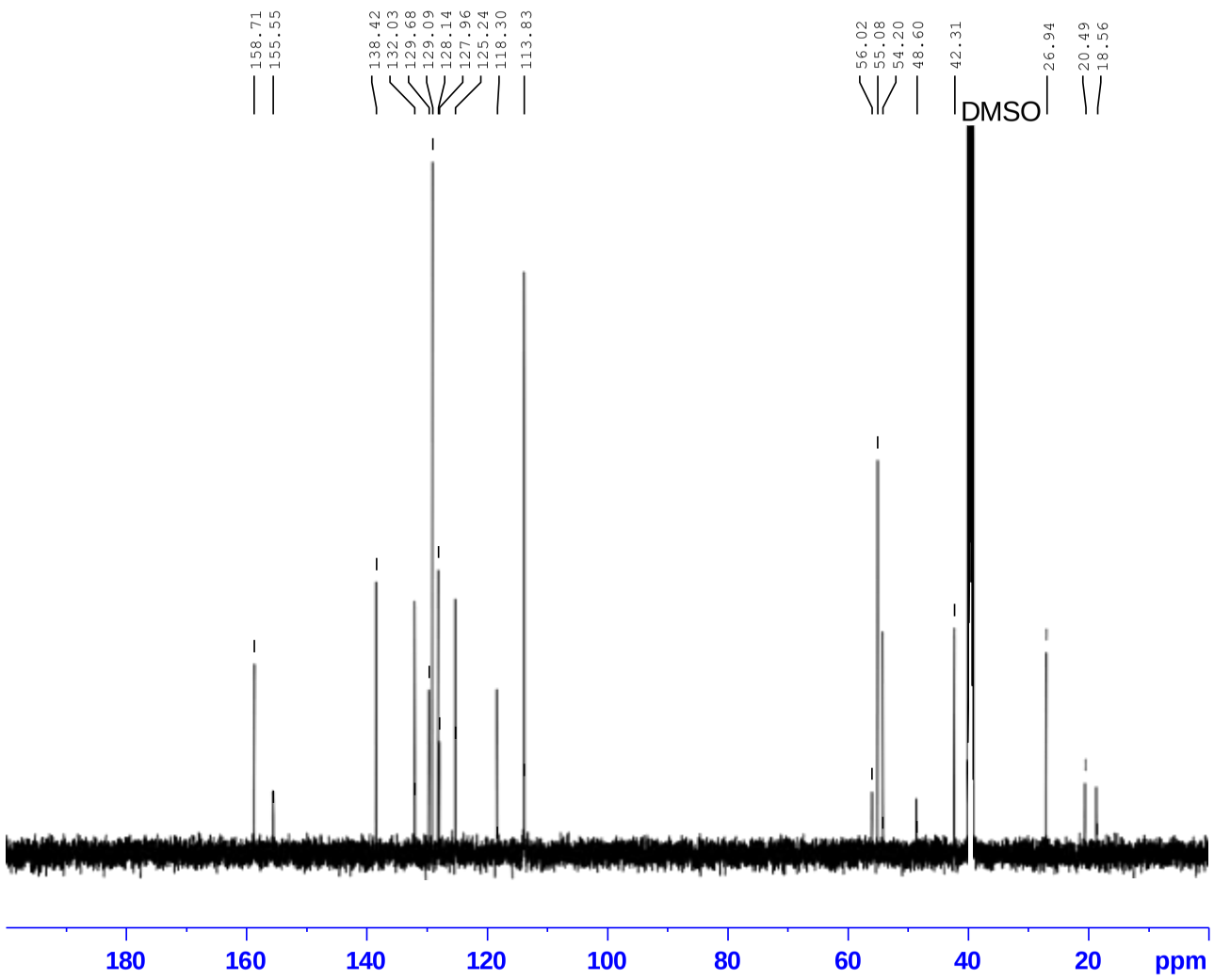
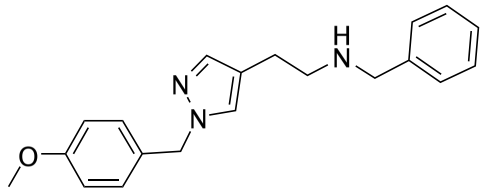


N-benzyl-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethan-1-amine



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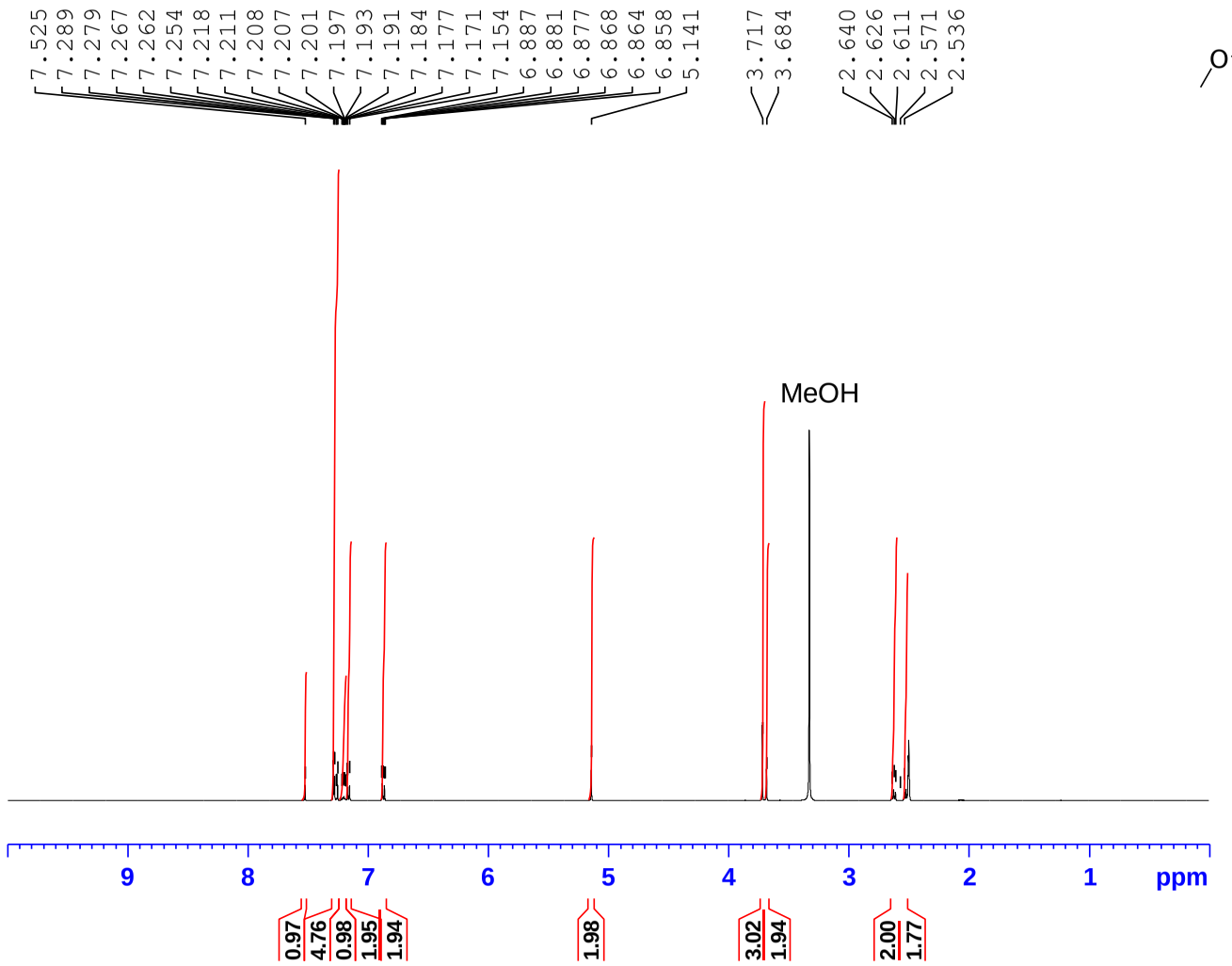
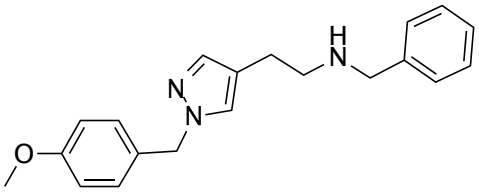


N-benzyl-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)ethan-1-amine



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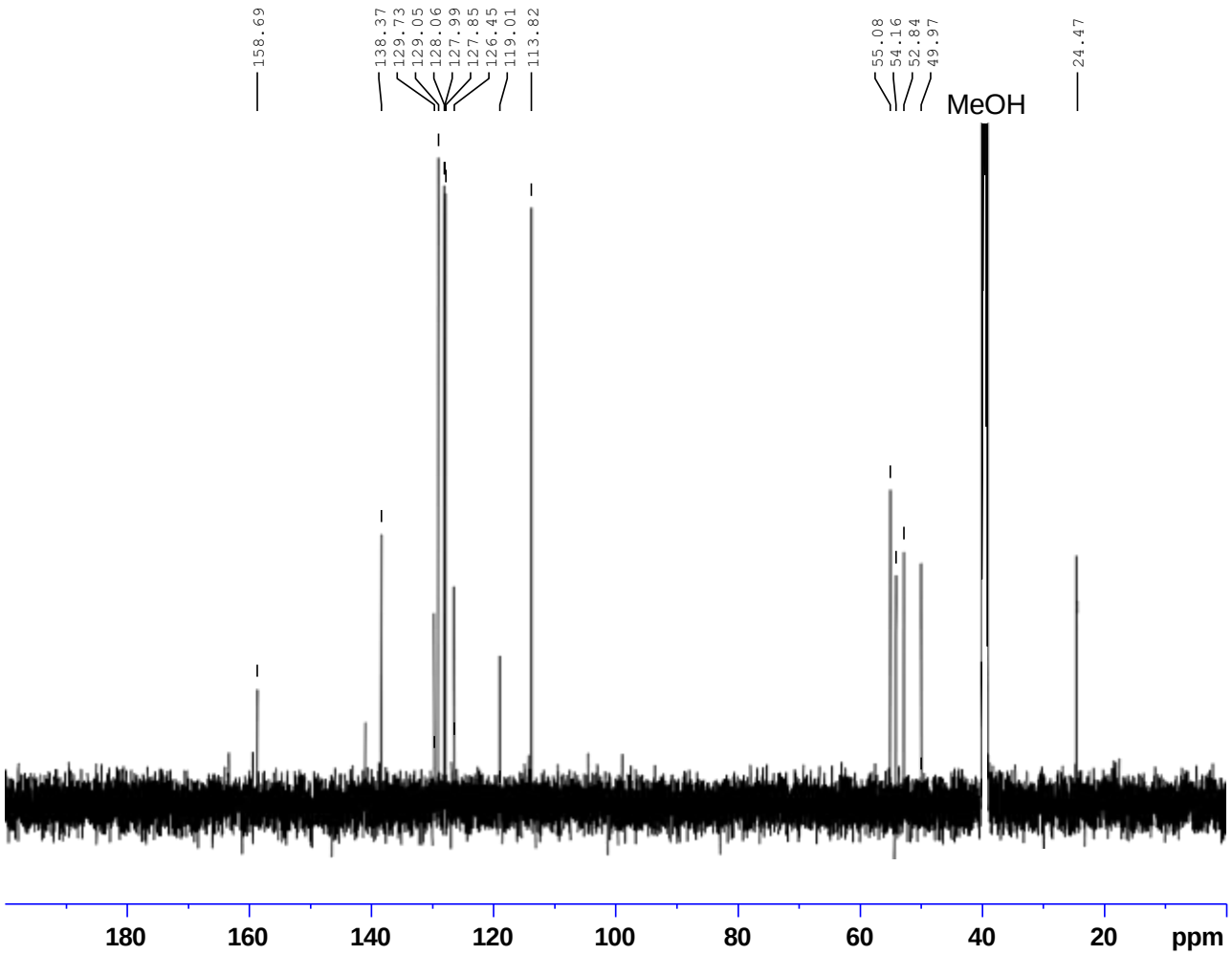
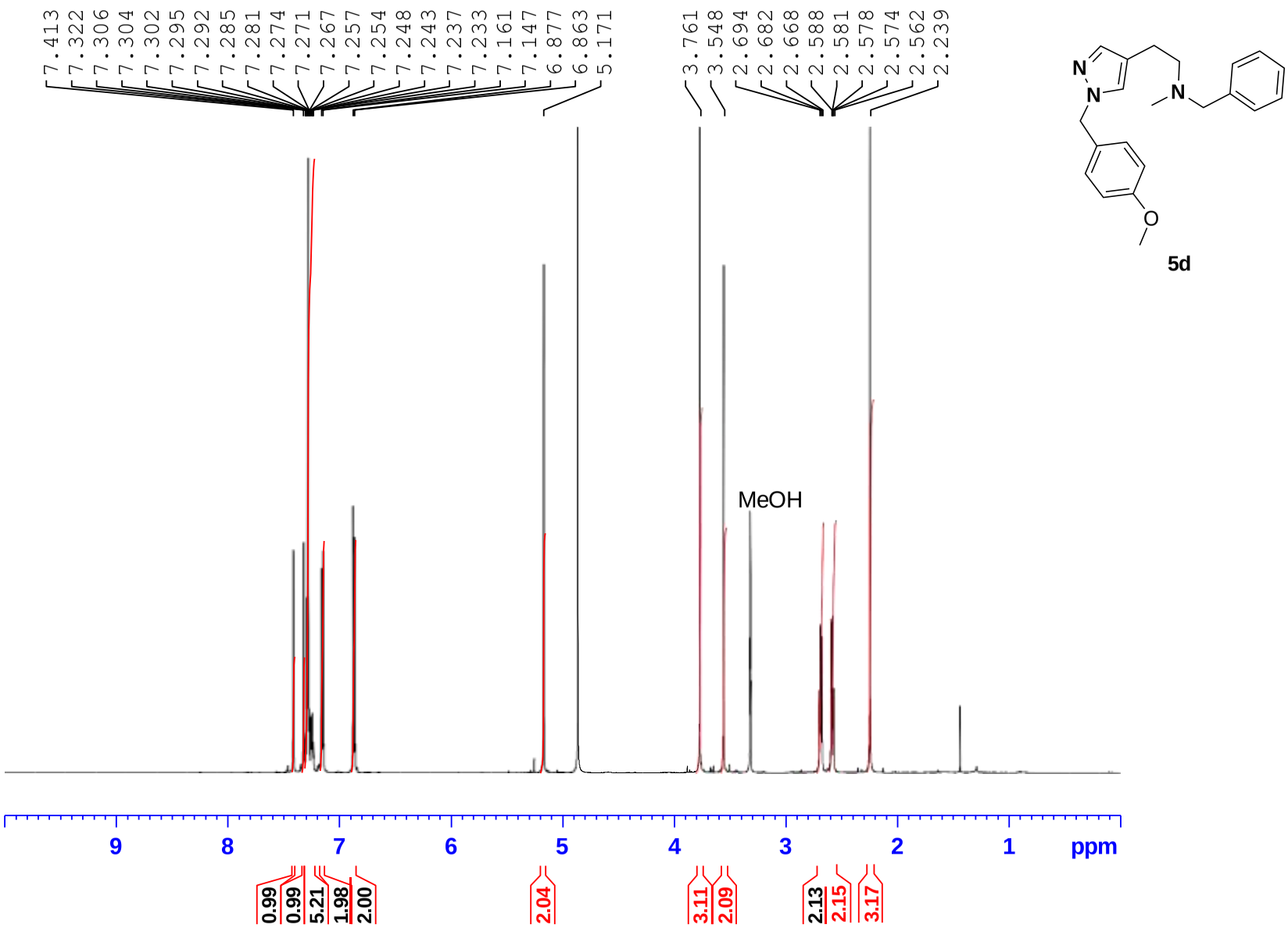
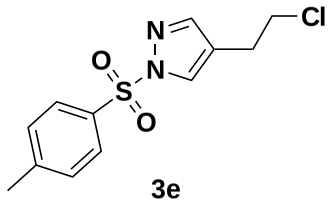


N-benzyl-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-methylethan-1-amine

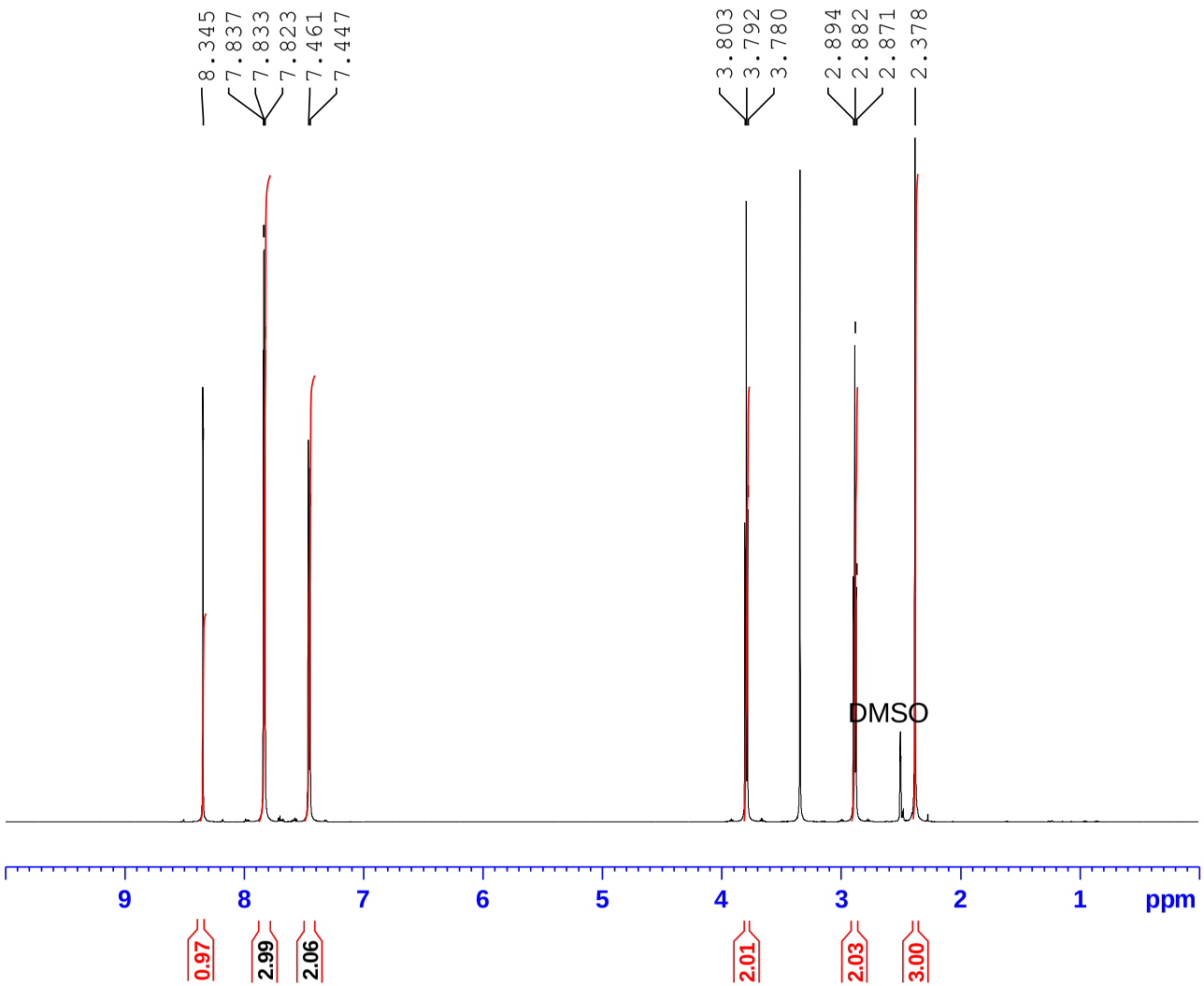


5d

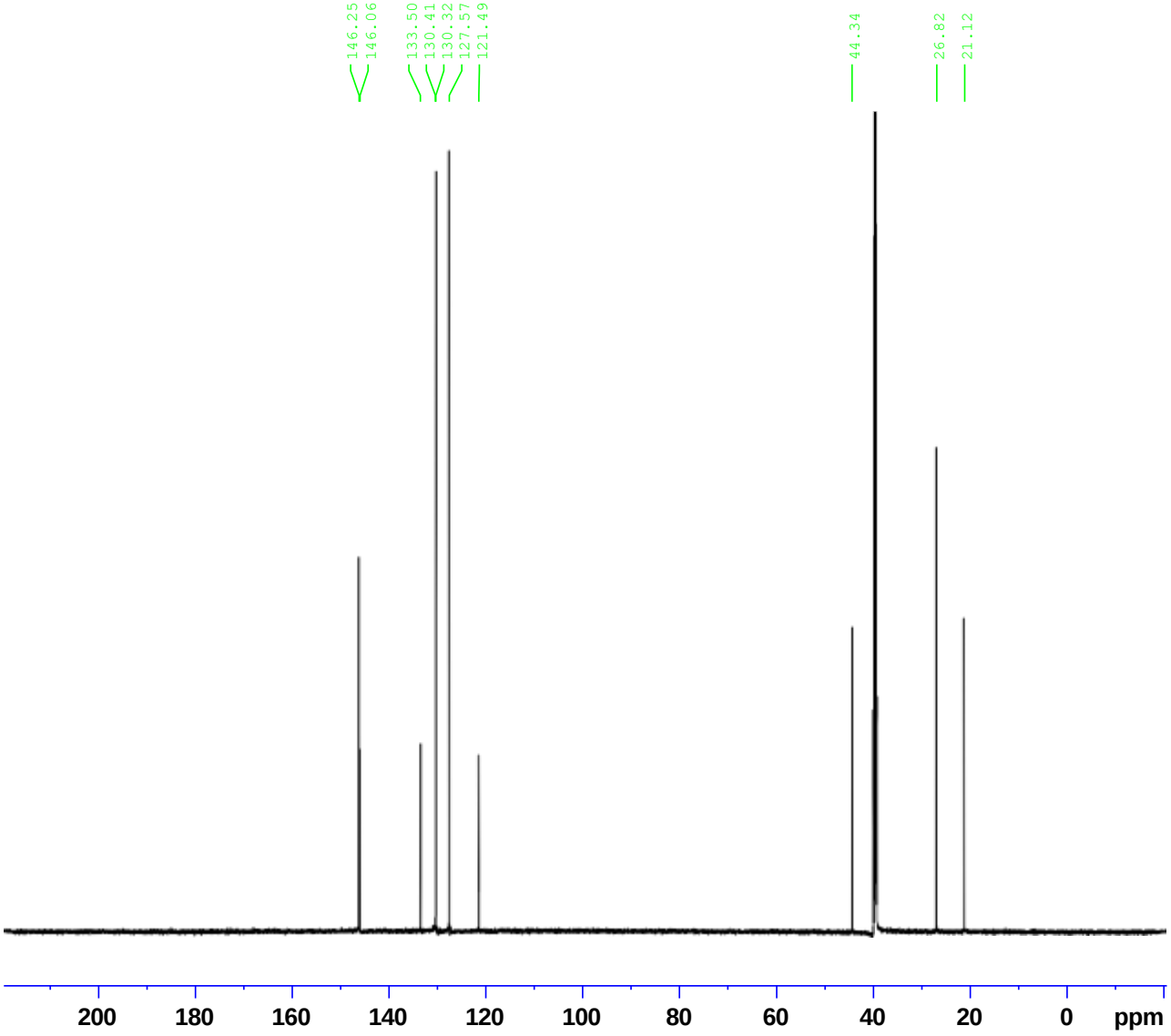
4-(2-chloroethyl)-1-tosy-1H-pyrazole

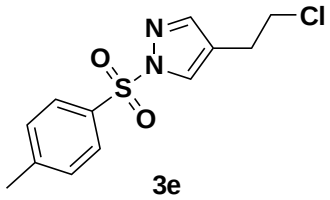


3e



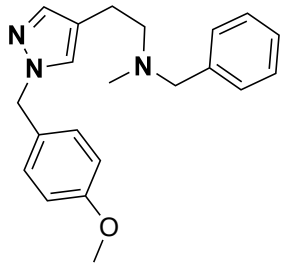
4-(2-chloroethyl)-1-tosy-1H-pyrazole





3e

N-benzyl-2-(1-(4-methoxybenzyl)-1H-pyrazol-4-yl)-N-methylethan-1-amine



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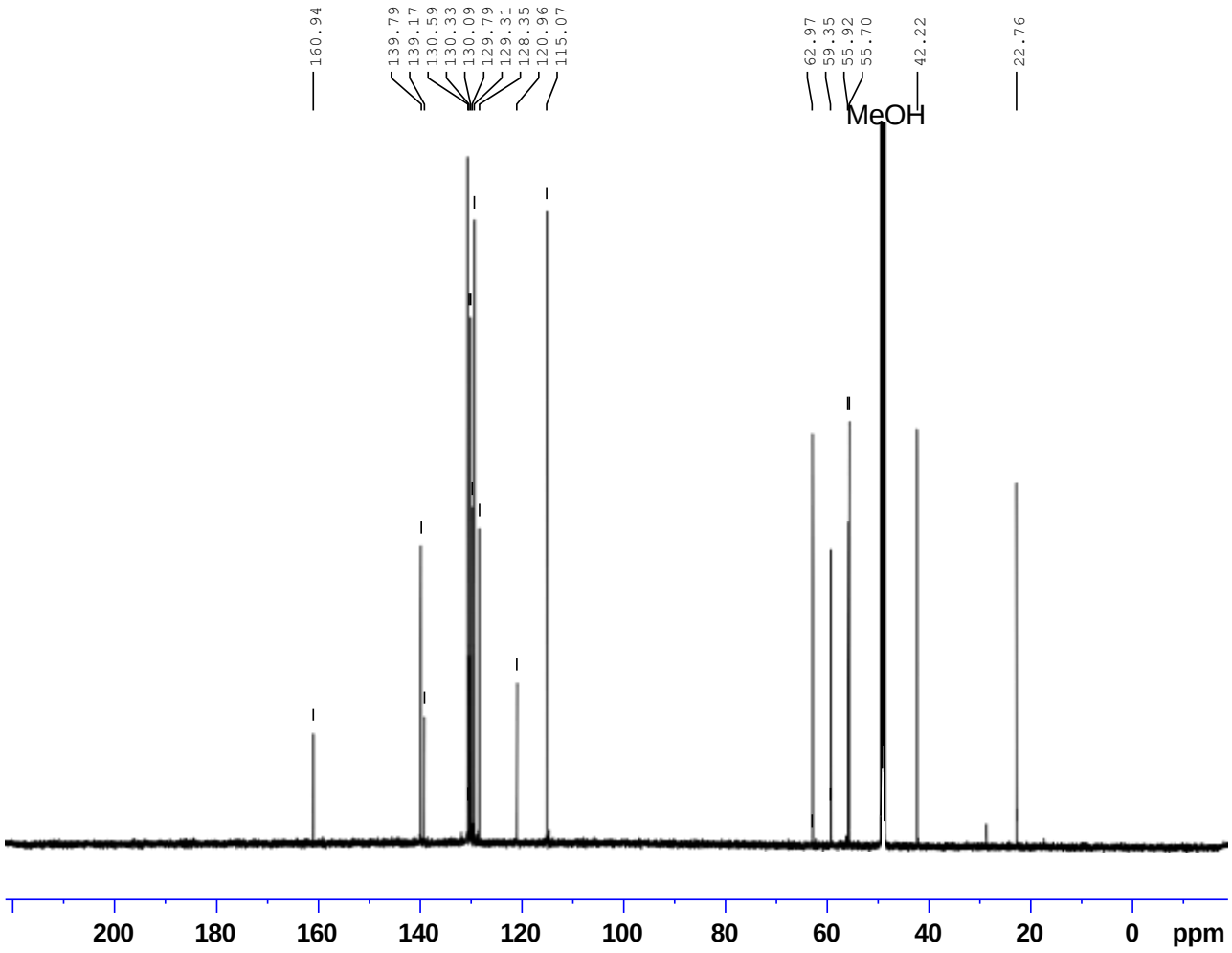
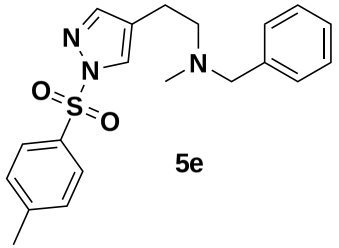
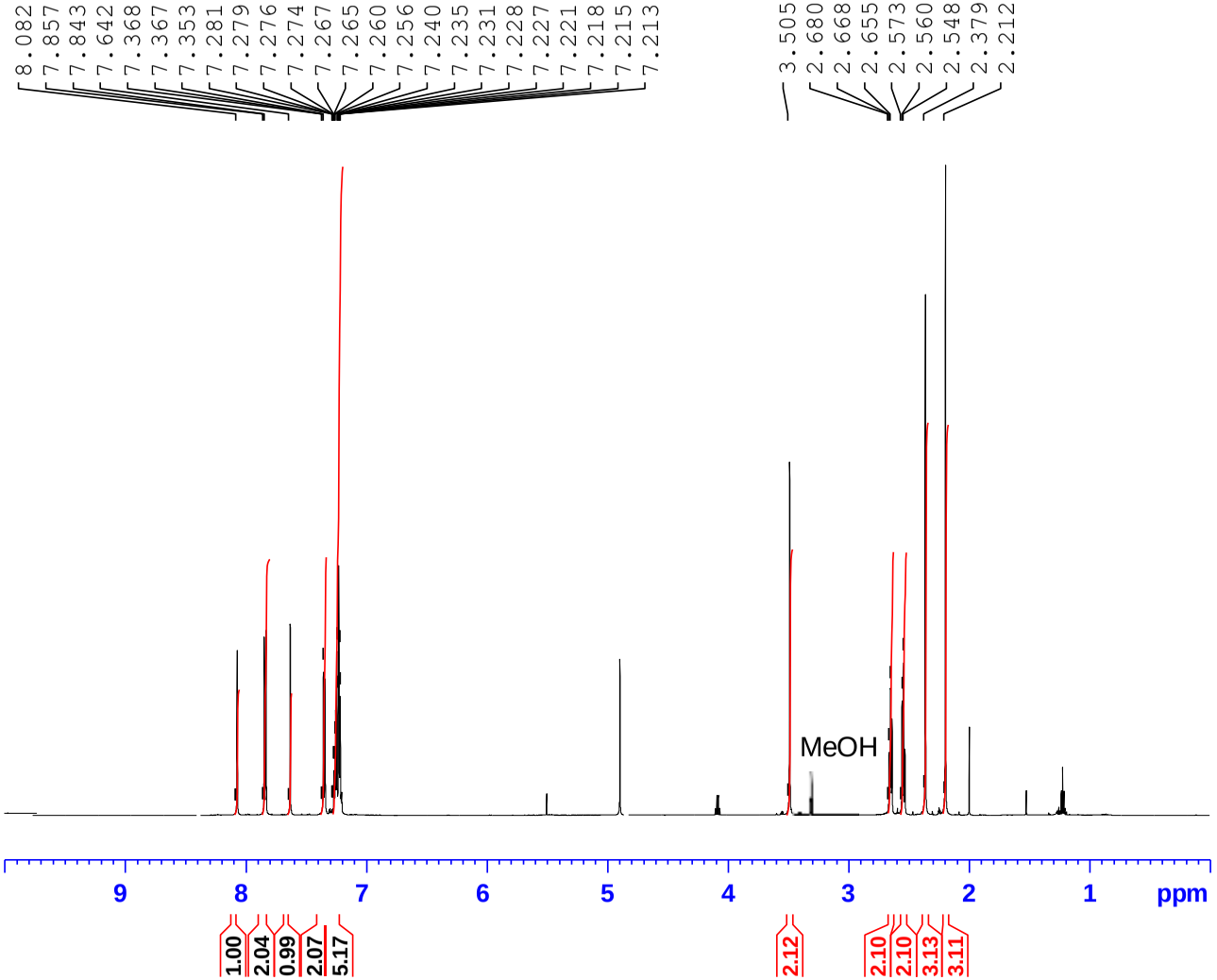


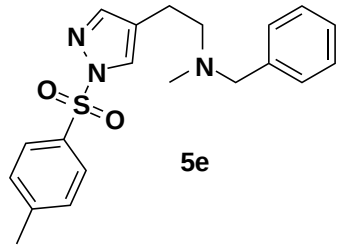
N-benzyl-N-methyl-2-(1-tosyl-1H-pyrazol-4-yl)ethan-1-amine



5e



N-benzyl-N-methyl-2-(1-tosyl-1H-pyrazol-4-yl)ethan-1-amine



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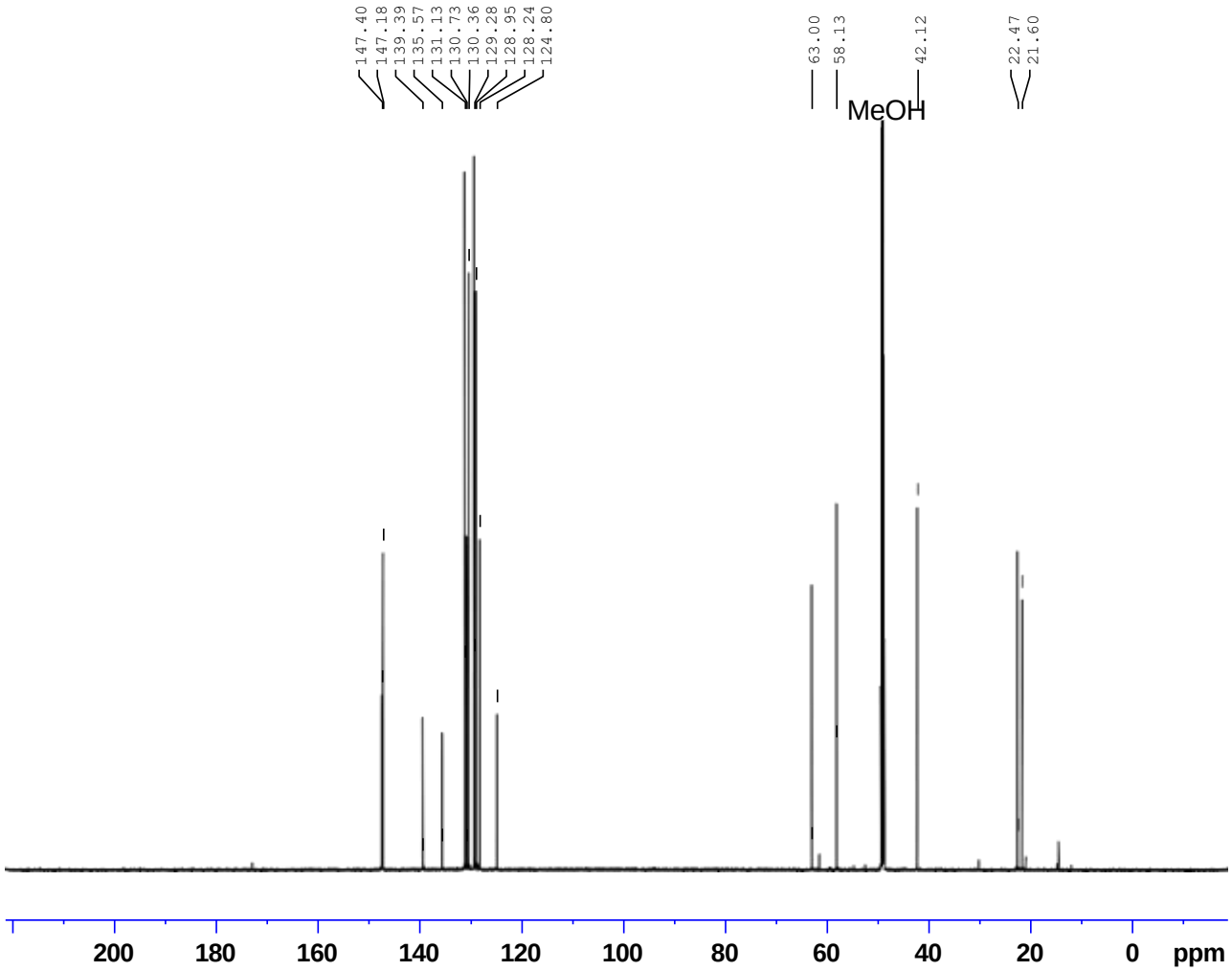
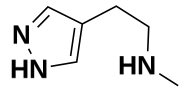


N-methyl-2-(1H-pyrzaol-4-yl)ethan-1-amine



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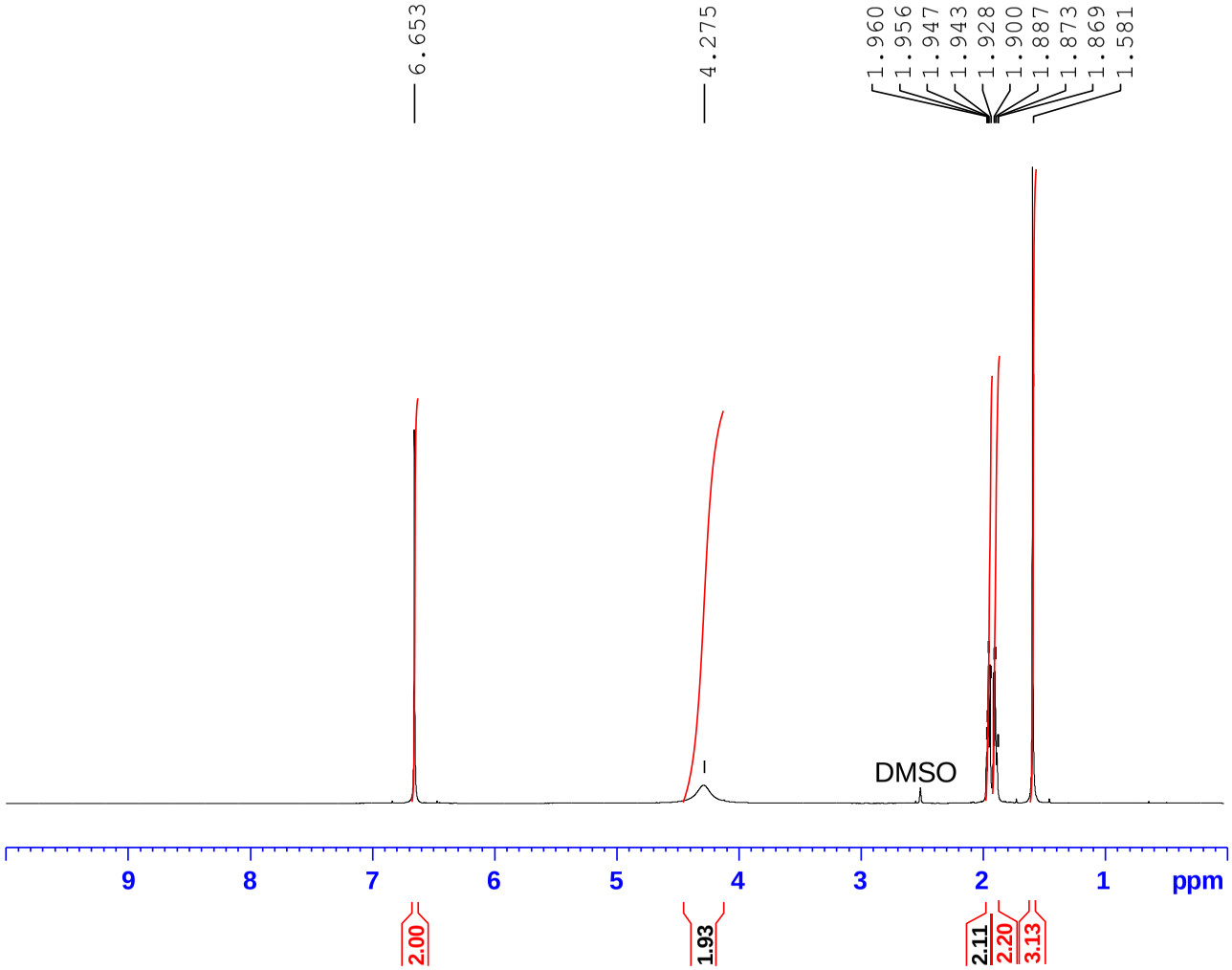
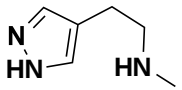


N-methyl-2-(1H-pyrzaol-4-yl)ethan-1-amine



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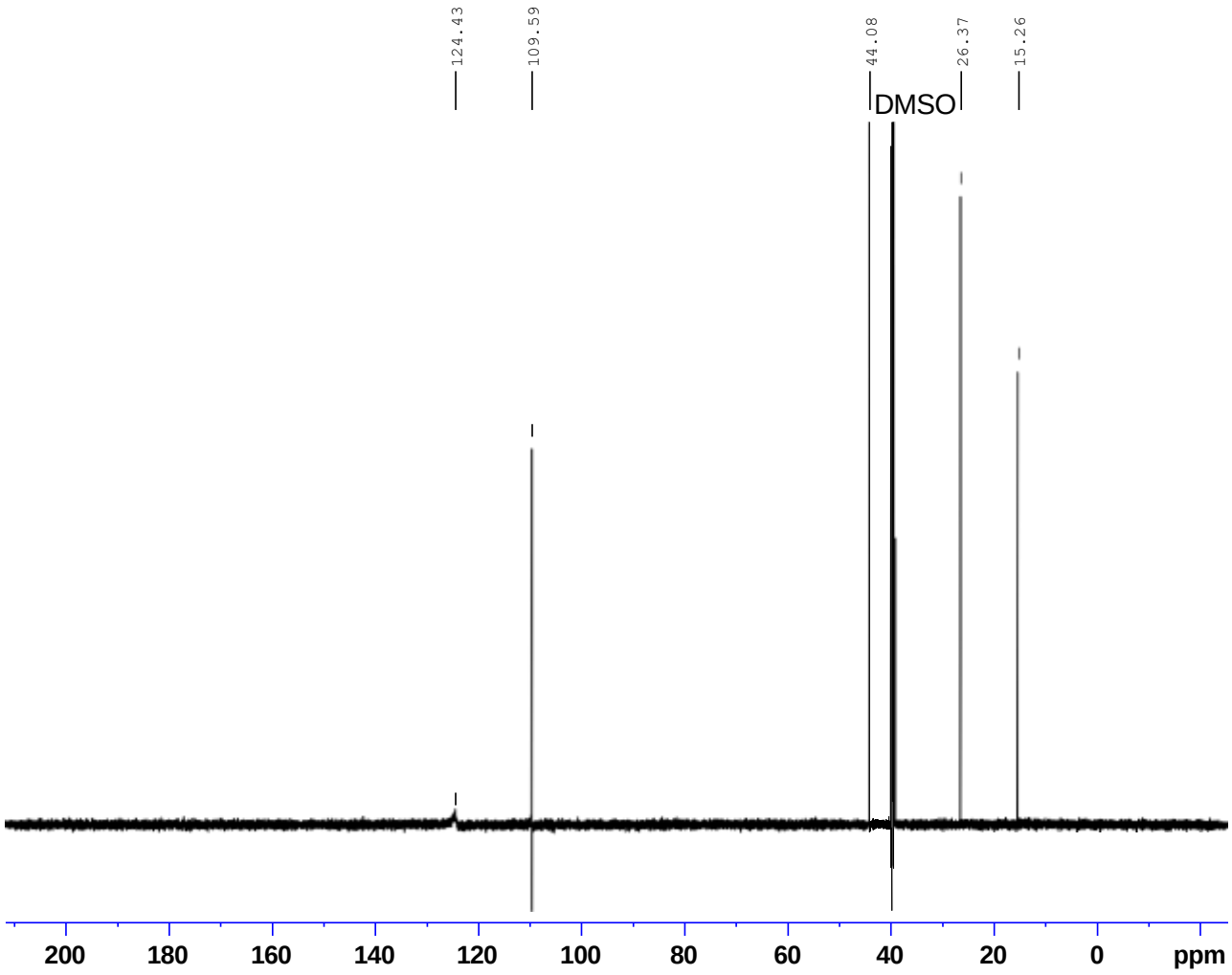
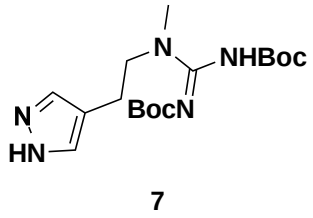


diboc-1-(2-(1H-pyrazol-4-yl)ethyl)-1-methylguanidine



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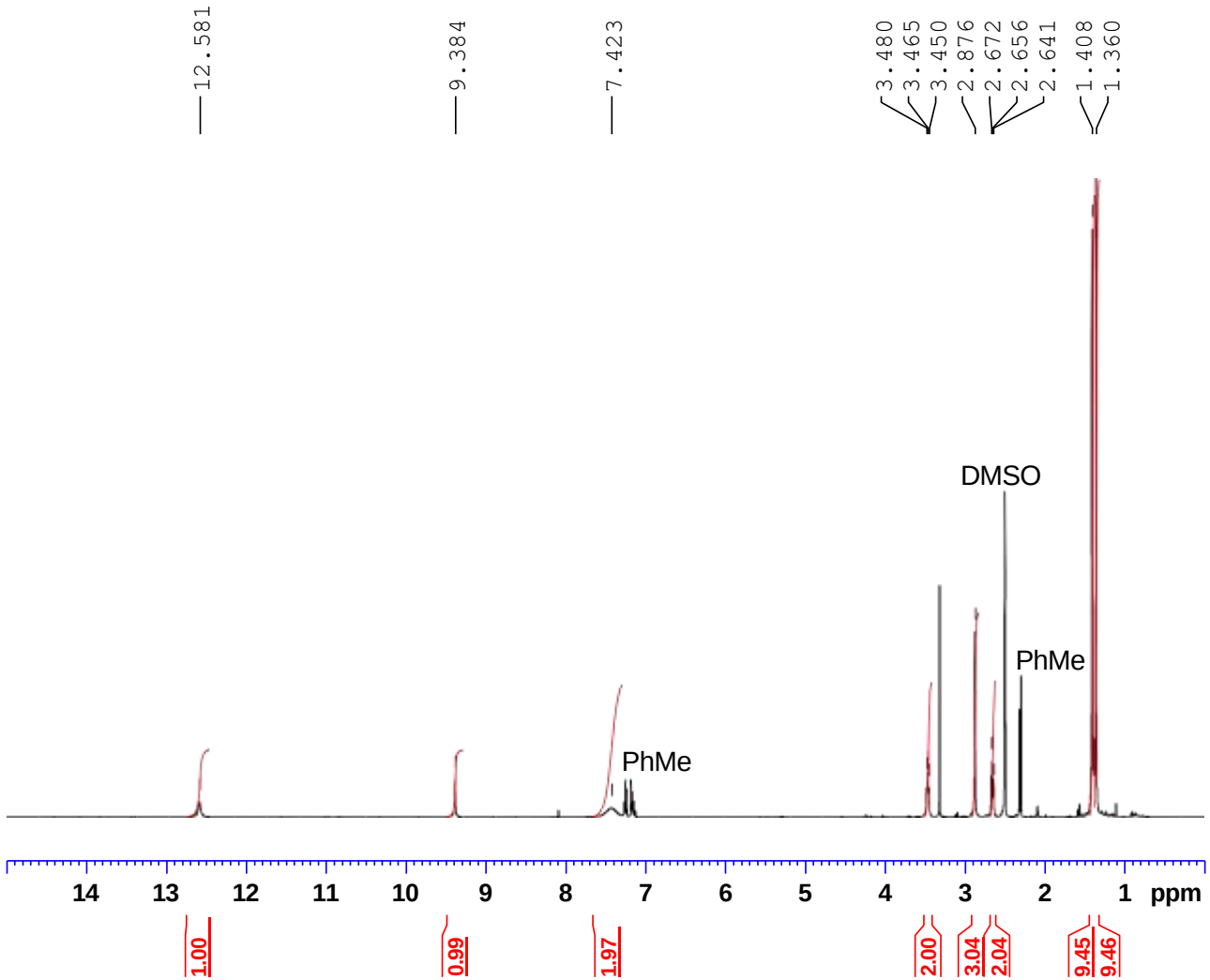
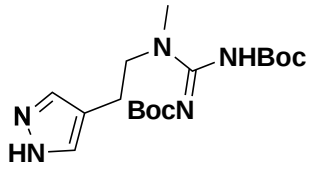


diboc-1-(2-(1H-pyrazol-4-yl)ethyl)-1-methylguanidine



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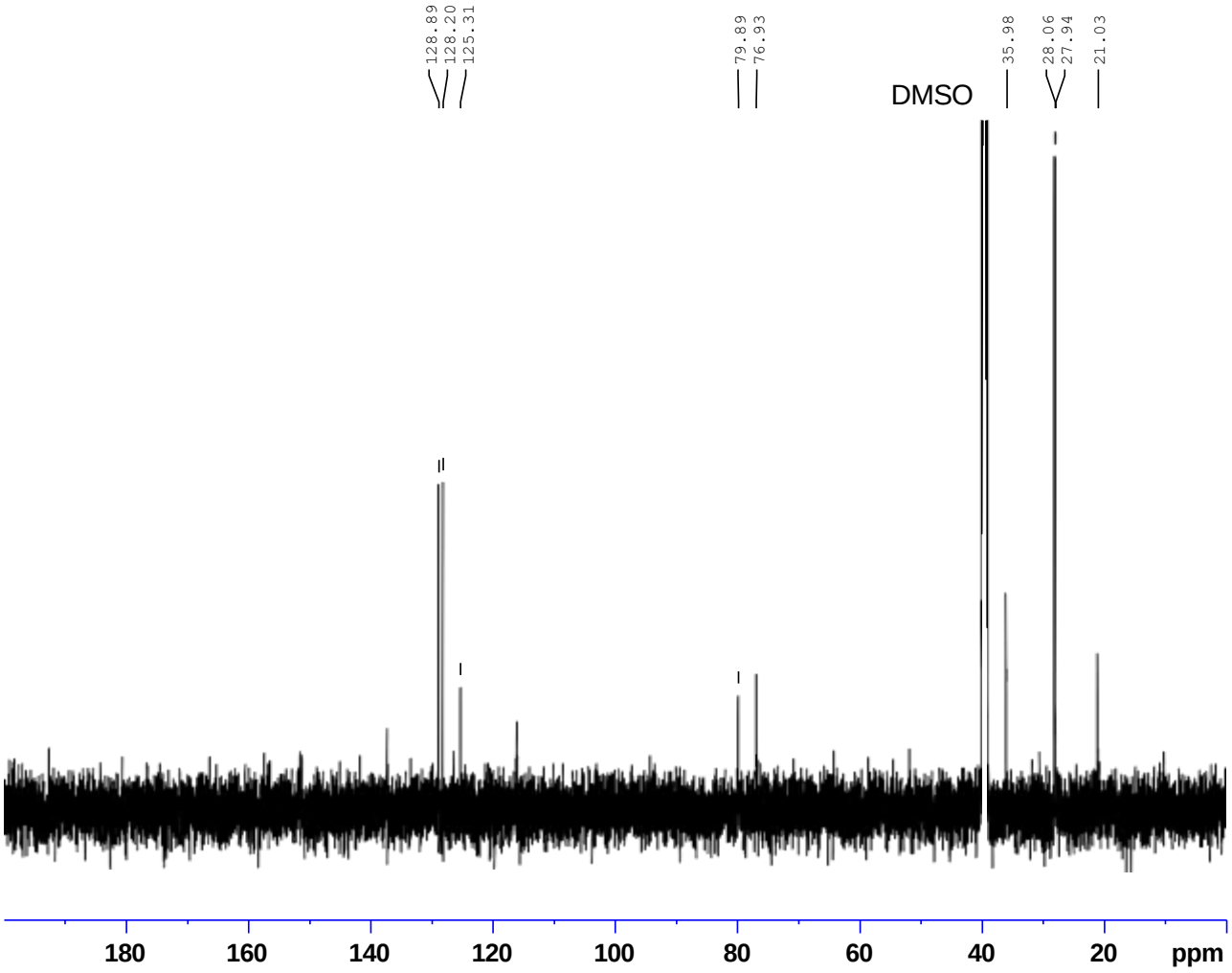
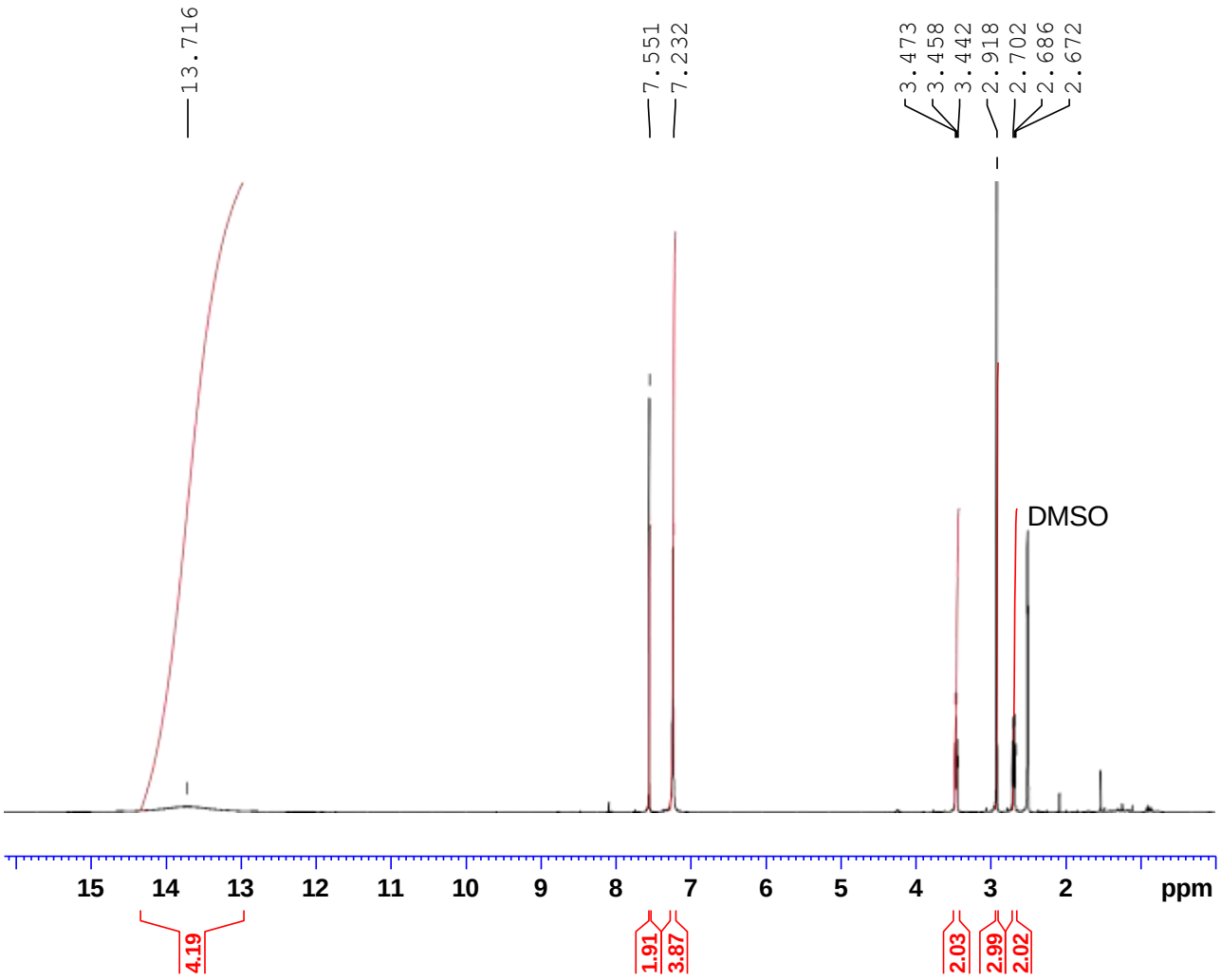
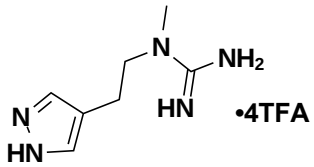


1-(2-(1H-pyrazol-4-yl)ethyl)-1-methylguanadine-2,2,2-trifluoroacetate (1/4)





8

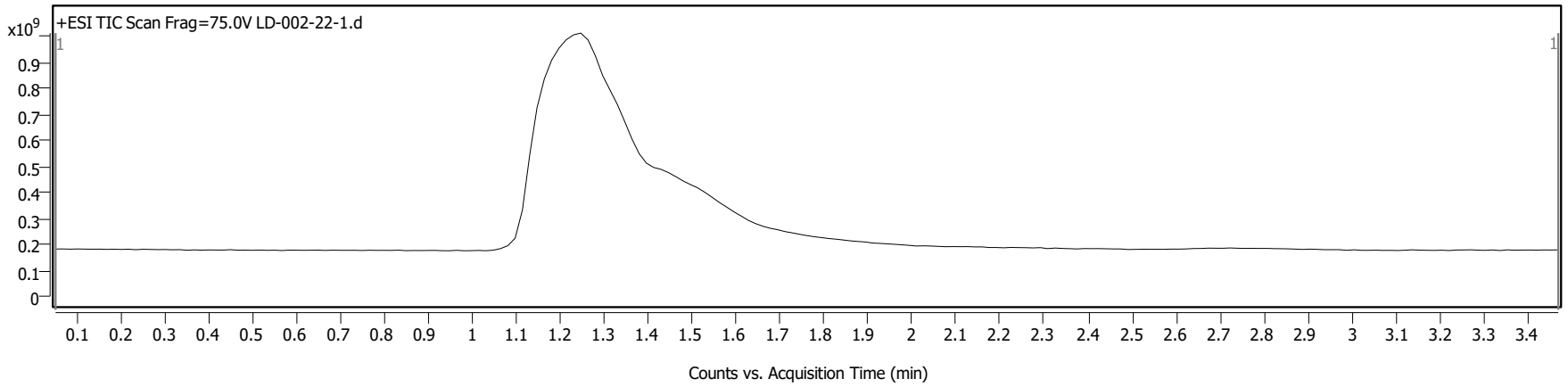
Analysis Report

Agilent | Trusted Answers

Sample Information

Name	LD-002-22-1	**Data File Path**	D:\MassHunter\Data\George\LD-002-22-1.d
Sample ID		**Acq. Time (Local)**	3/7/2023 10:12:00 AM (UTC-05:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\George\George_HRMS.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	2	**IRM Status**	Success
Position	P1-A1	**Method Path (DA)**	D:\MassHunter\Data\George\LD-002-22-1.d\Results\Qual\Version4\Hamdan_HPLC_10_90_15 min.m
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

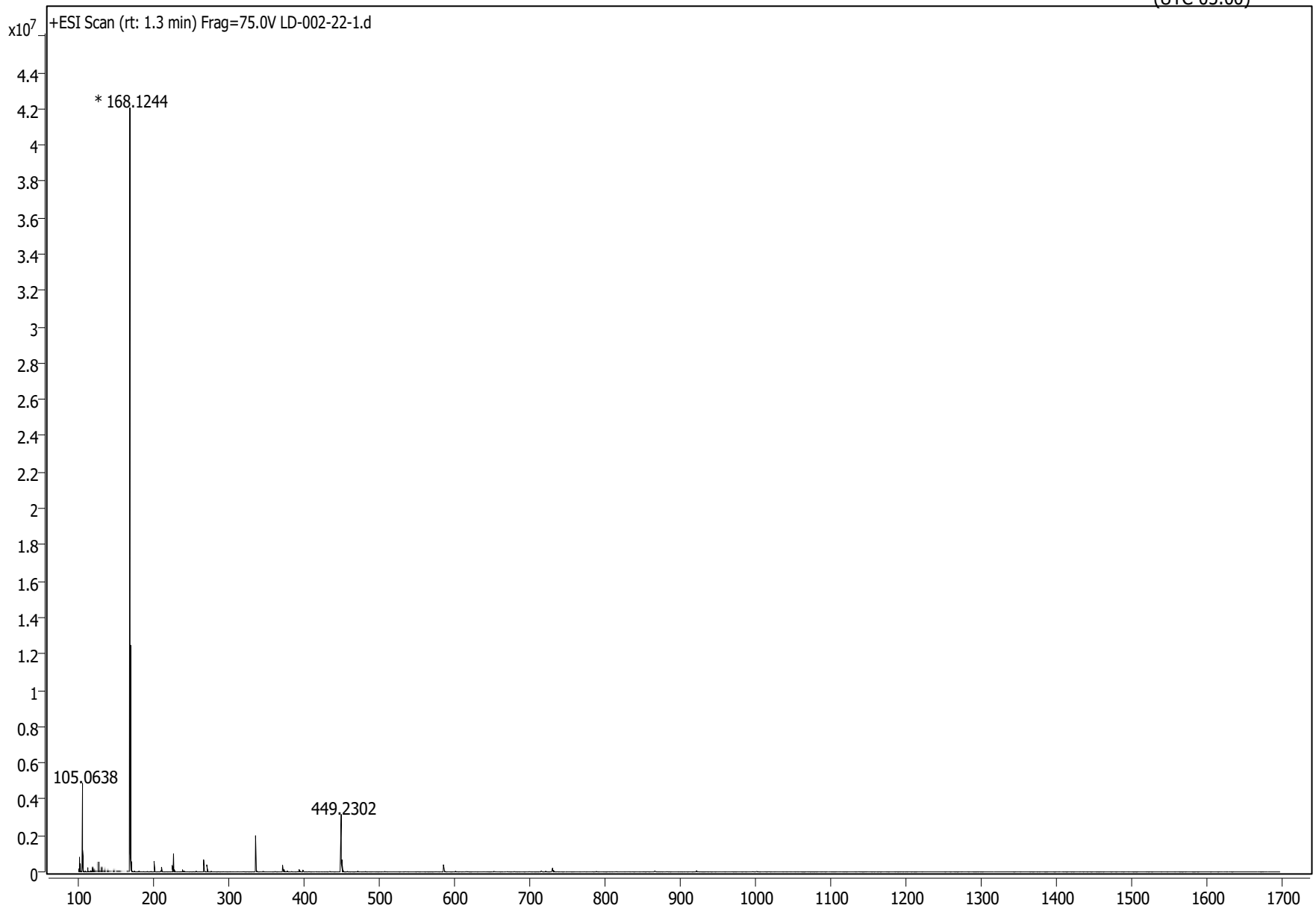
Sample Chromatograms



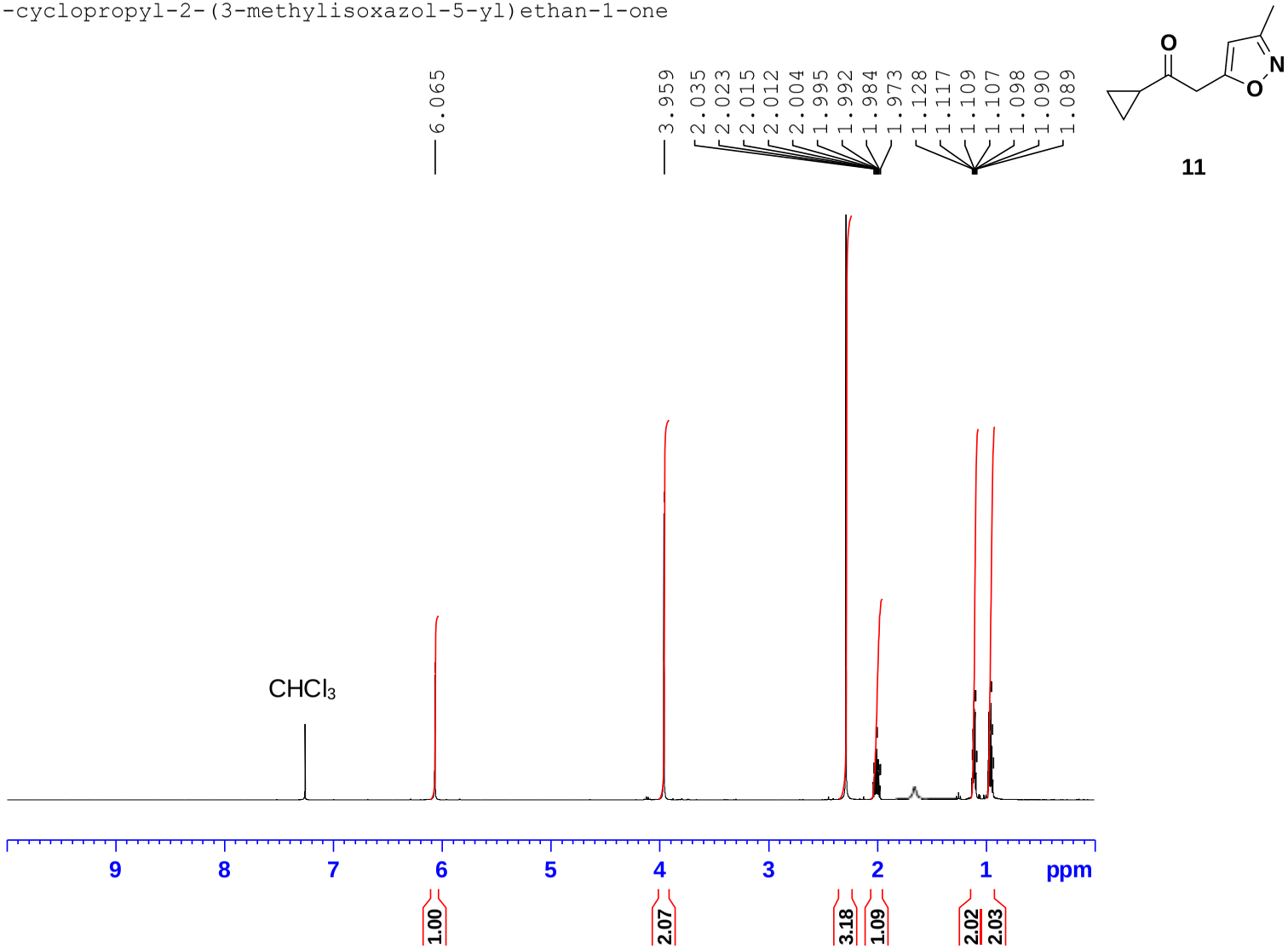
MassHunter Qual 10.0
(End of Report)

User Spectrum Plot Report

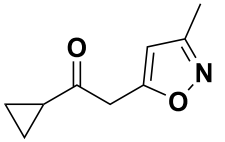
Name	LD-002-22-1	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success		
Data File	LD-002-22-1.d	Method (Acq)	George_HRMS.m	Comment		Acq. Time (Local)	3/7/2023 10:12:00 AM (UTC-05:00)



1-cyclopropyl-2-(3-methylisoxazol-5-yl)ethan-1-one



1-cyclopropyl-2-(3-methylisoxazol-5-yl)ethan-1-one



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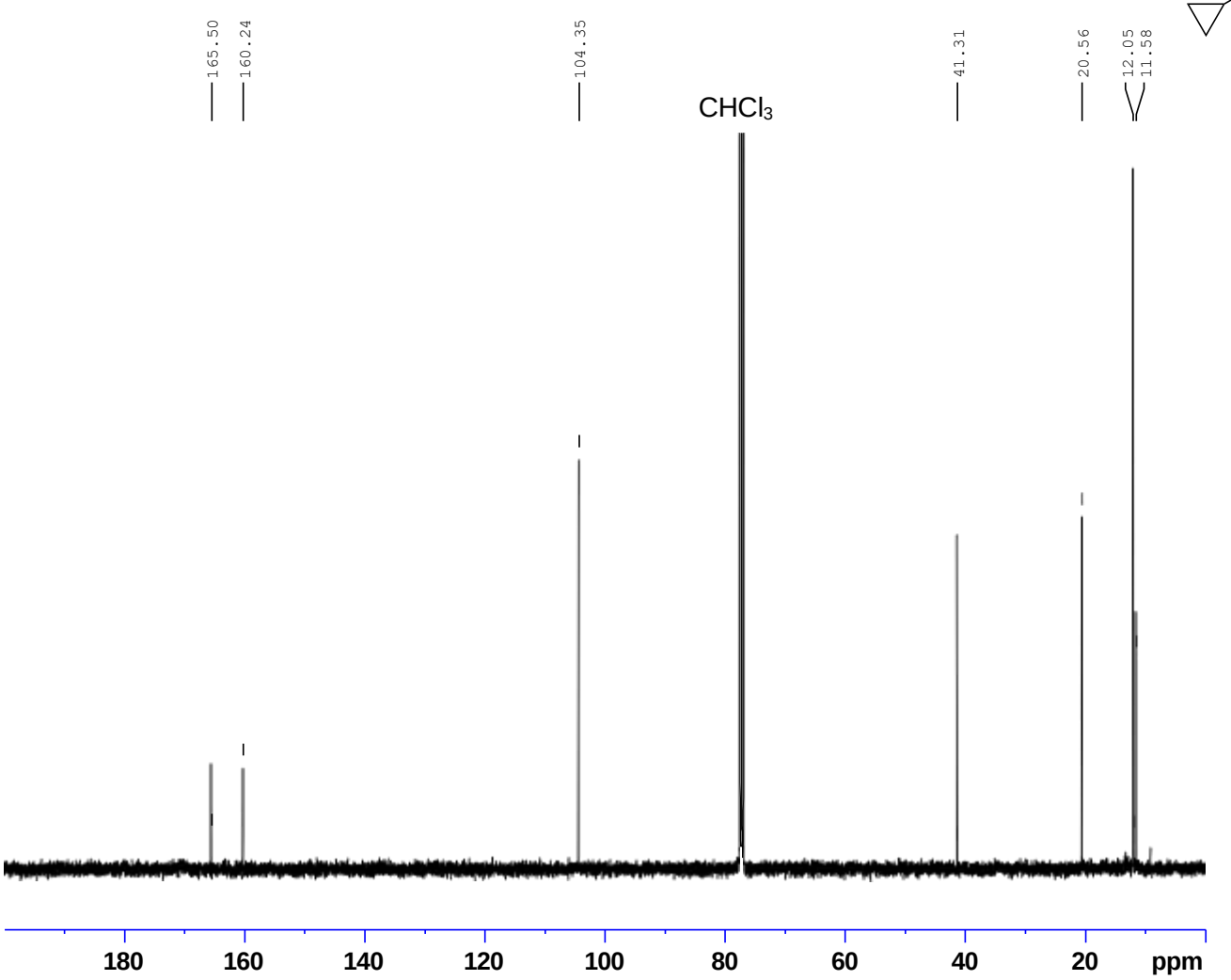
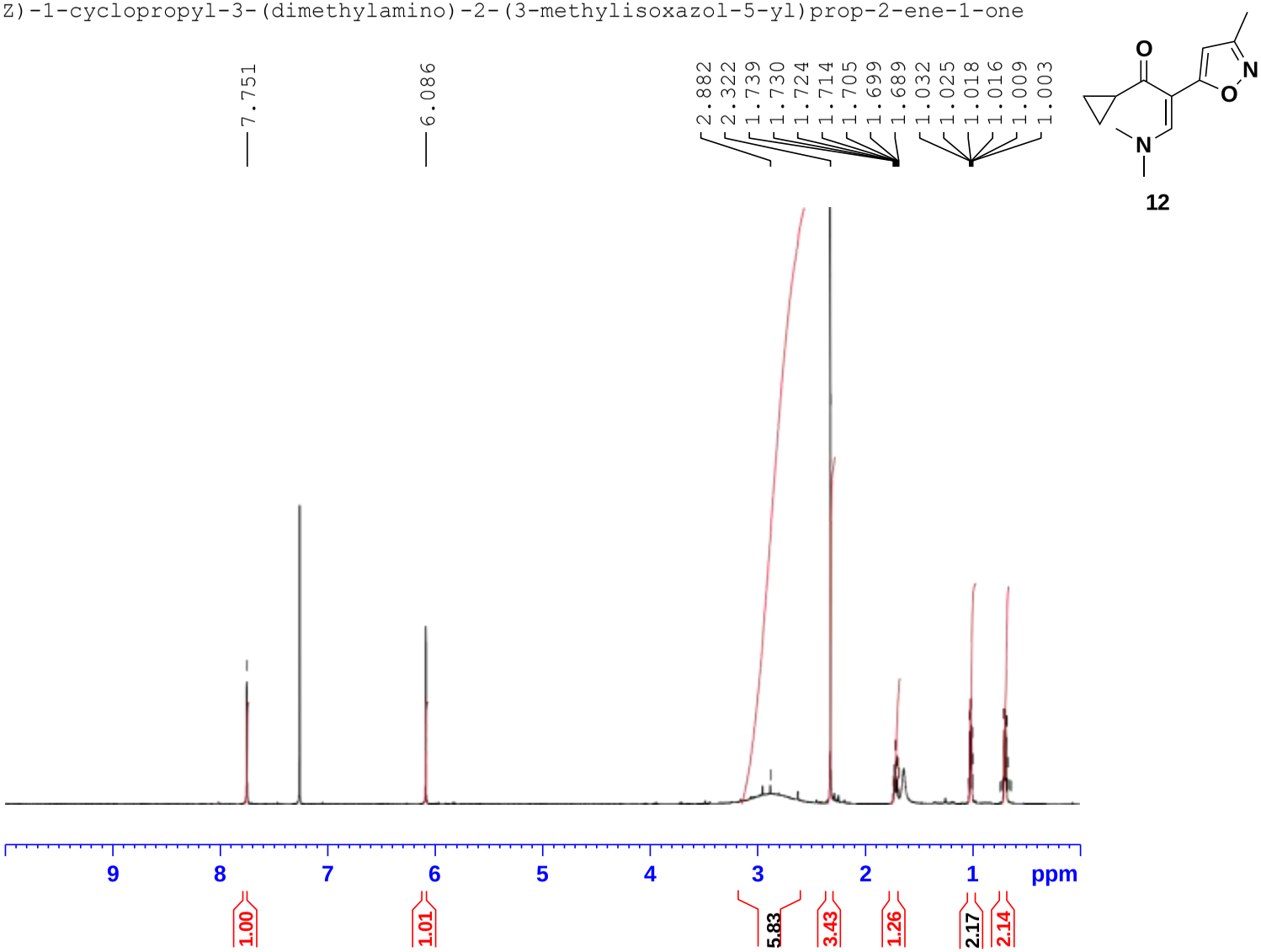


(Z)-1-cyclopropyl-3-(dimethylamino)-2-(3-methylisoxazol-5-yl)prop-2-ene-1-one



12

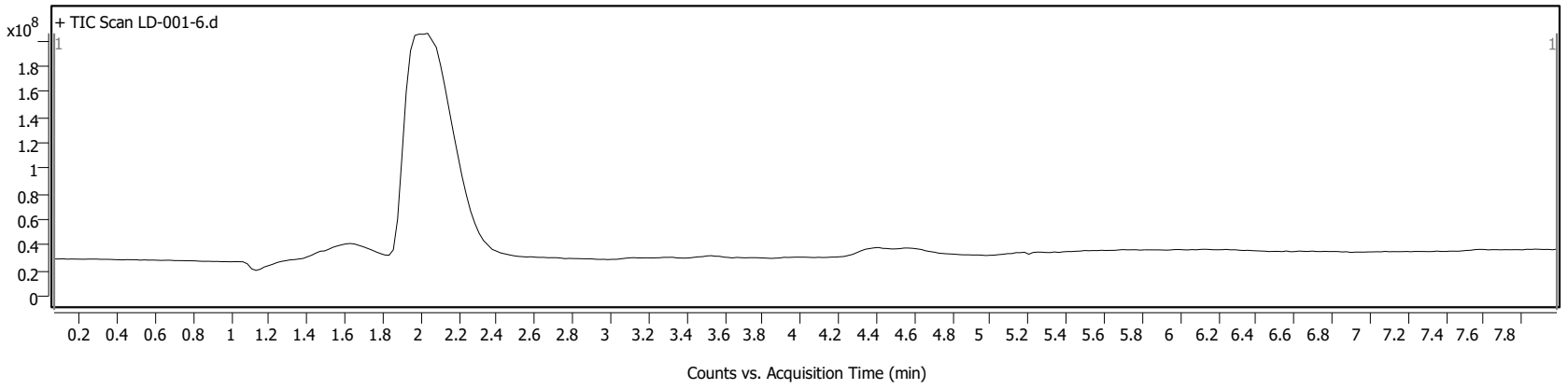
Analysis Report

Agilent | Trusted Answers

Sample Information

Name	LD-001-6	**Data File Path**	D:\MassHunter\Data\Louise\LD-001-6.d
Sample ID		**Acq. Time (Local)**	6/30/2023 1:41:06 PM (UTC-05:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HRMS method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	2	**IRM Status**	Success
Position	P1-A1	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

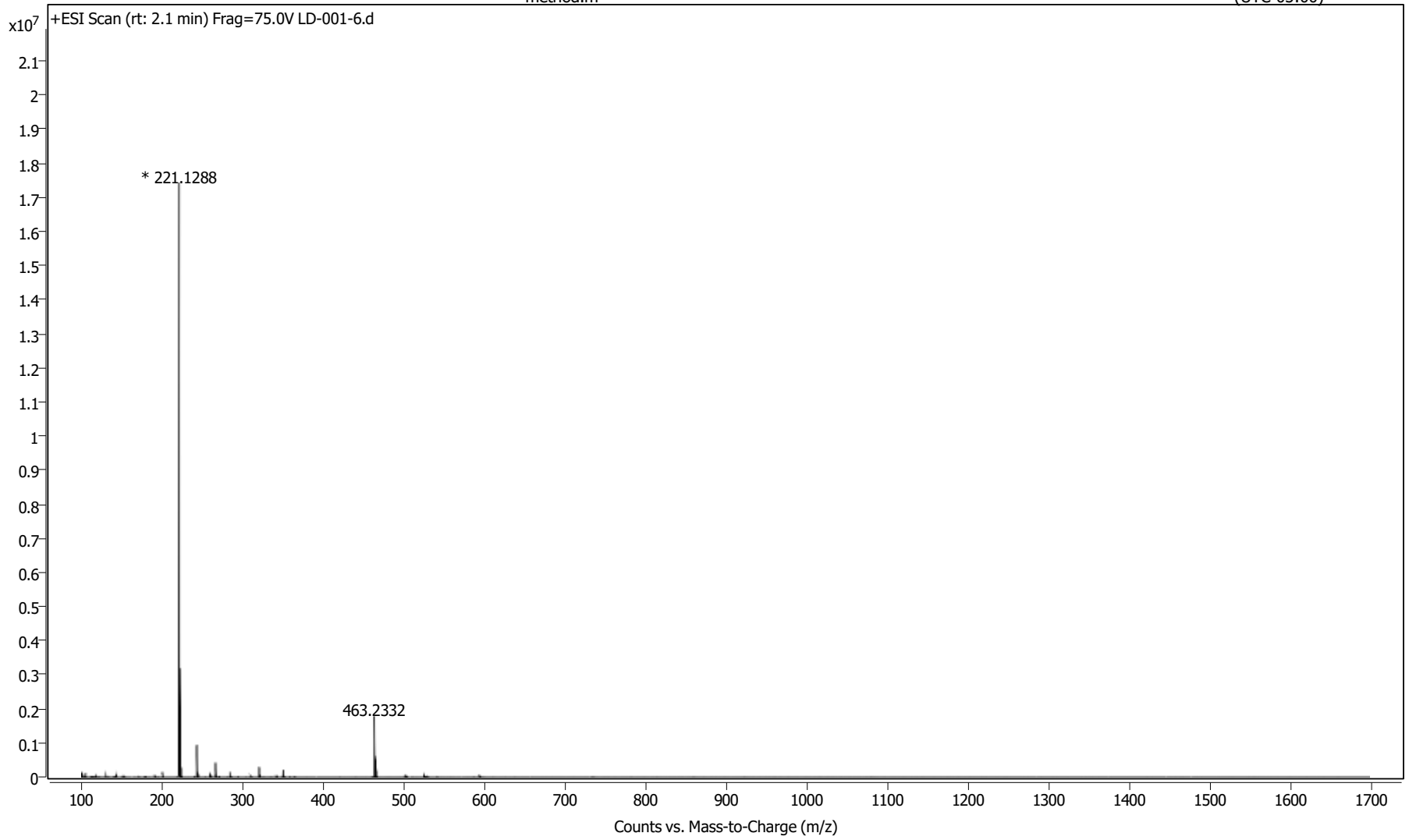
Sample Chromatograms



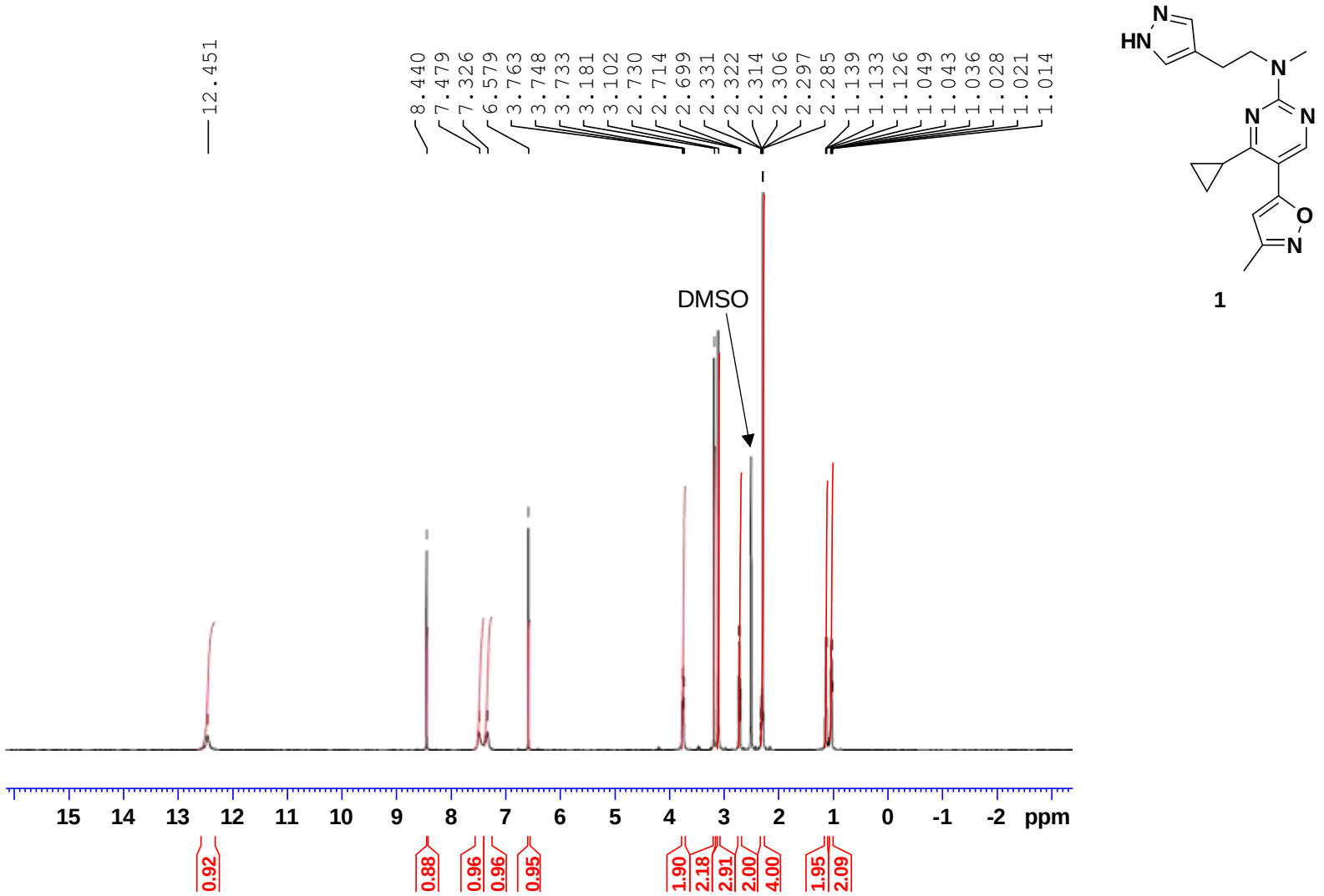
MassHunter Qual 10.0
(End of Report)

User Spectrum Plot Report

Name	LD-001-6	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	Success		
Data File	LD-001-6.d	Method (Acq)	Shafikur_HRMS method.m	Comment		Acq. Time (Local)	6/30/2023 1:41:06 PM (UTC-05:00)

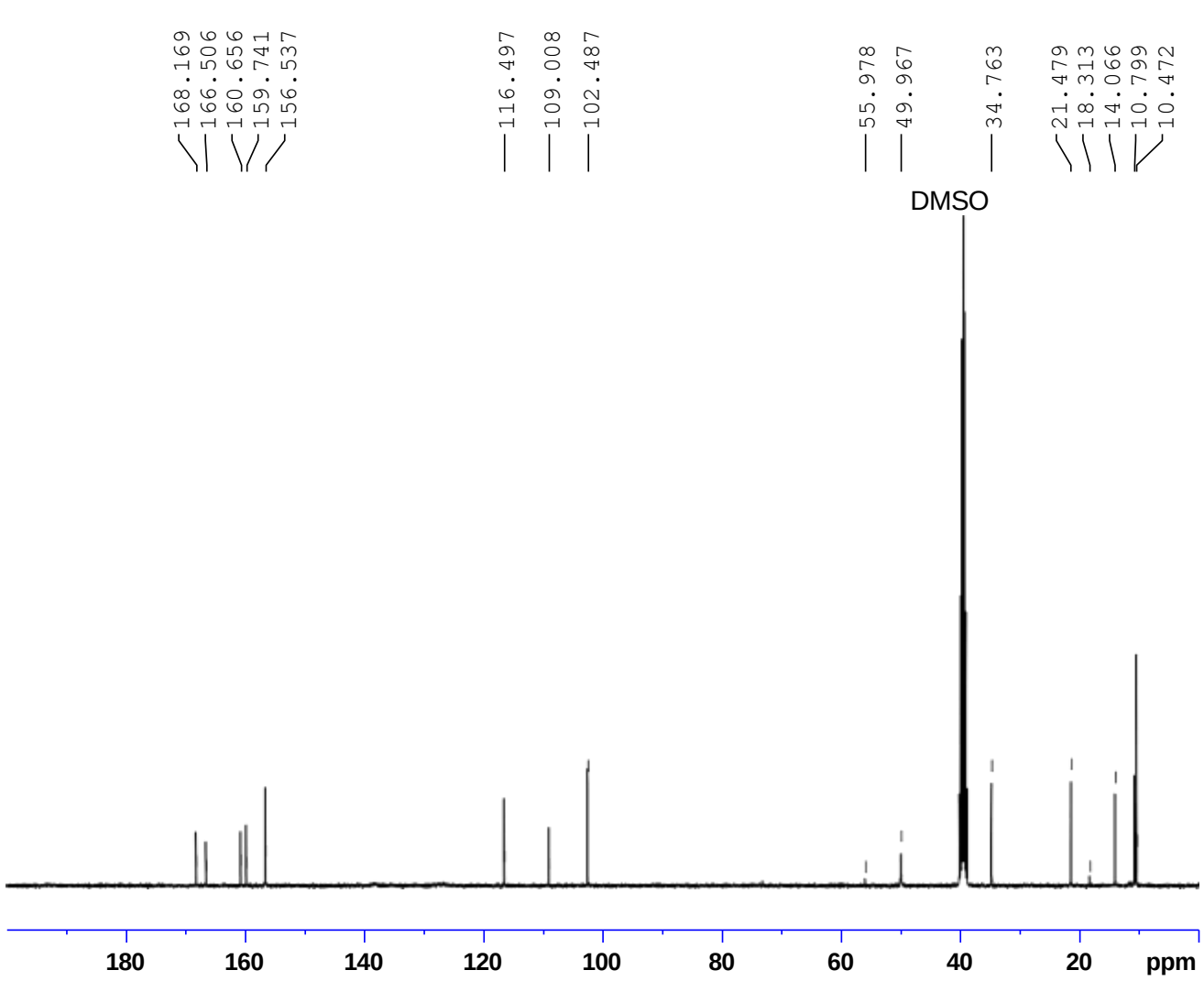


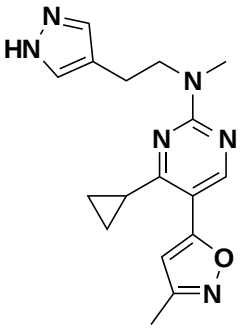
N-(2-(1H-pyrazol-4-yl)ethyl)-4-cyclopropyl-N-methyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine



1

N-(2-(1H-pyrazol-4-yl)ethyl)-4-cyclopropyl-N-methyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine





1

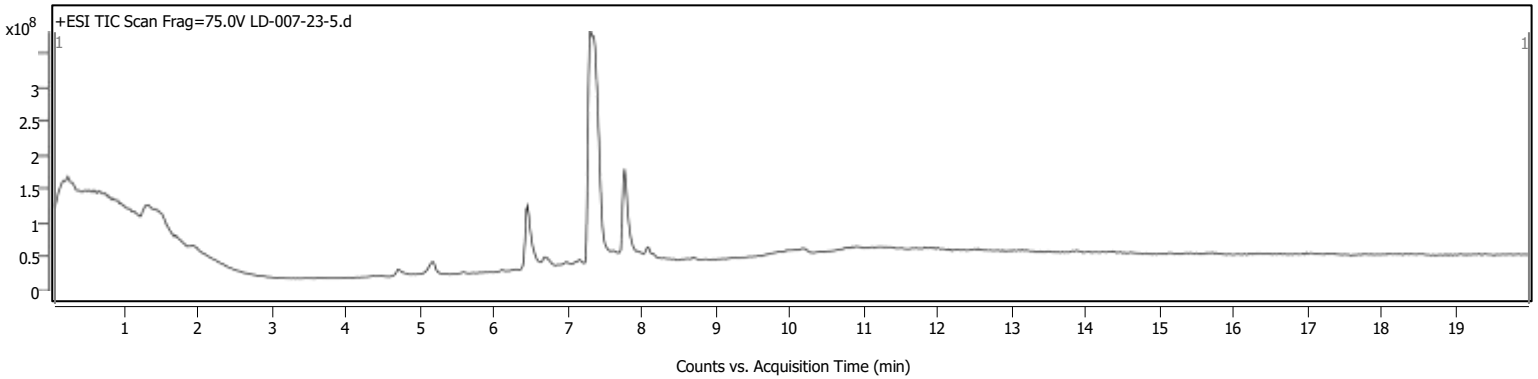
Analysis Report

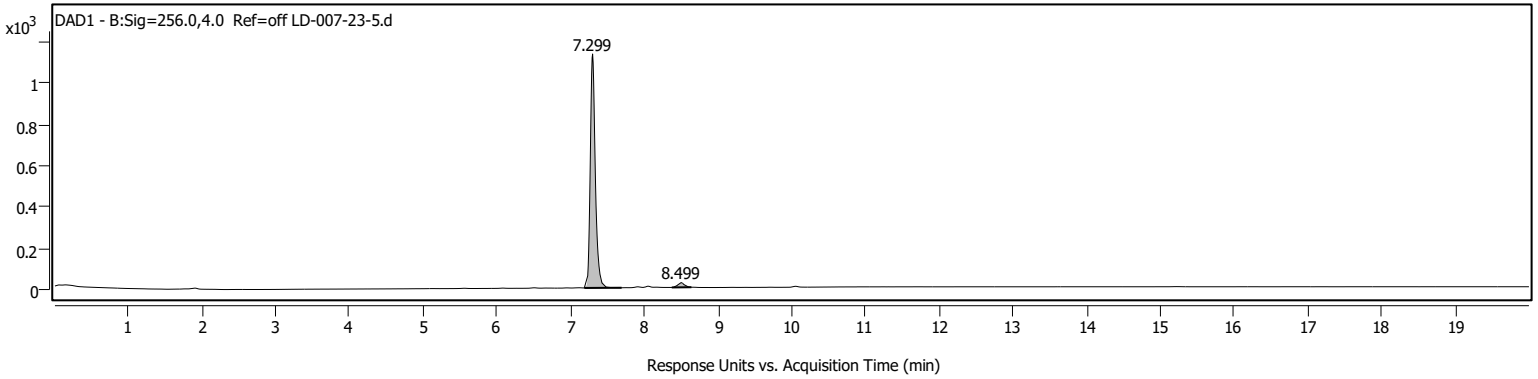
Agilent | Trusted Answers

Sample Information

Name	LD-007-23-5	**Data File Path**	D:\MassHunter\Data\Louise\LD-007-23-5.d
Sample ID		**Acq. Time (Local)**	1/15/2024 9:04:56 AM (UTC-06:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HPLC method\Shafikur_HPLC method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	10	**IRM Status**	All ions missed
Position	P1-A1	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms





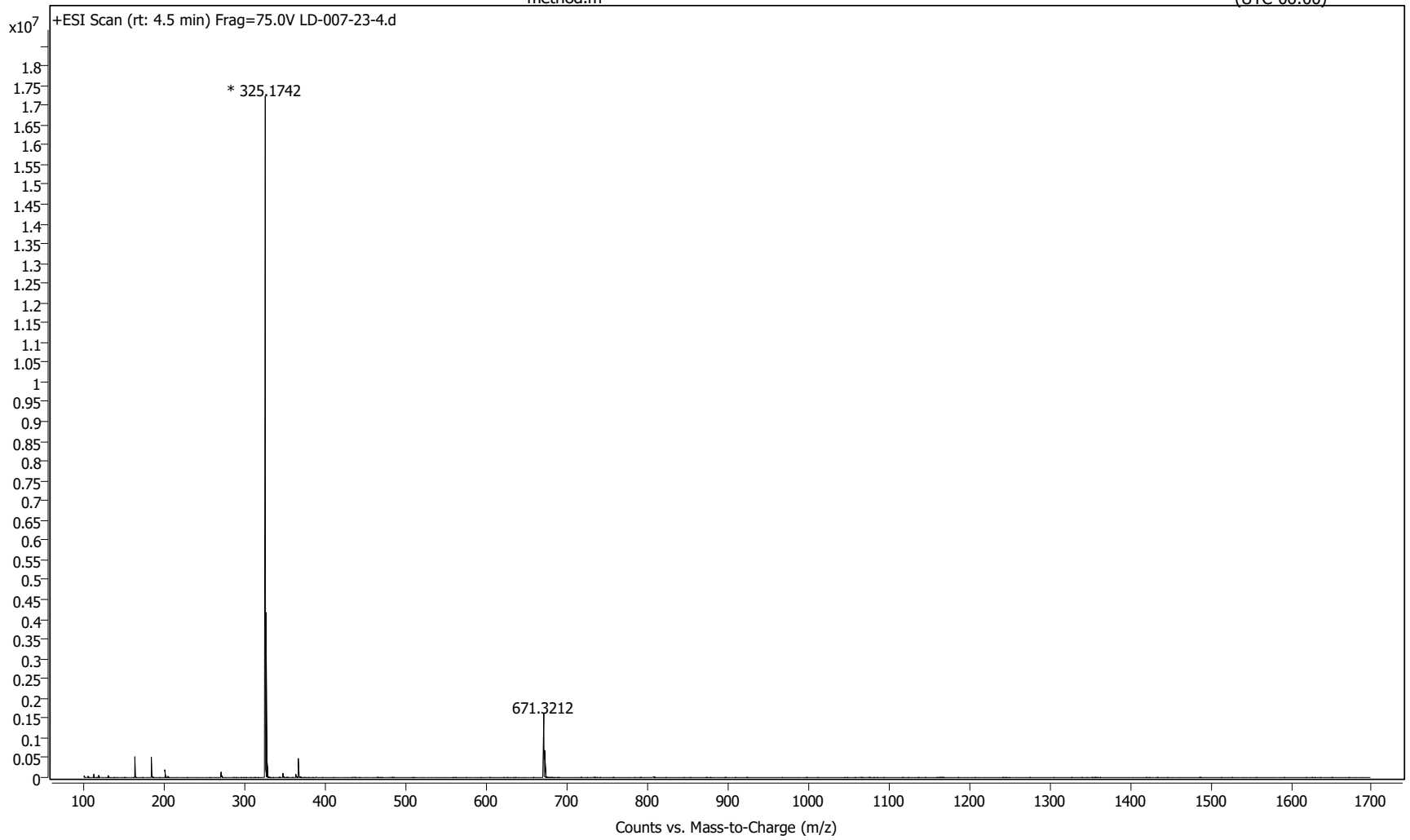
Chromatogram Peaks

Peak	Start	RT	End	Height	Area	Area %	SNR
1	7.186	7.299	7.693	1138	5409	100.00	
2	8.373	8.499	8.639	23	134	2.47	

MassHunter Qual 10.0
(End of Report)

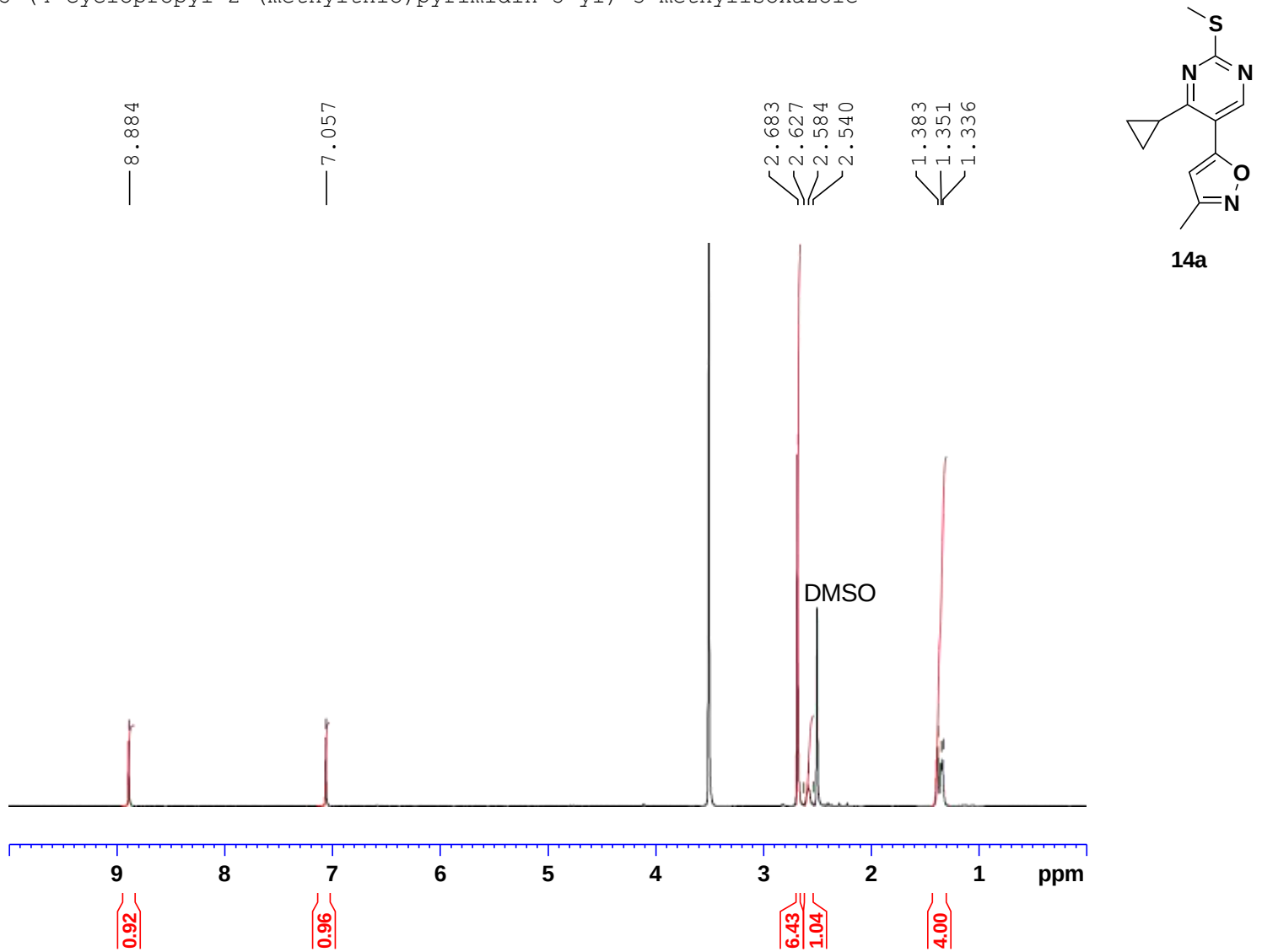
User Spectrum Plot Report

Name	LD-007-23-5	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	All ions missed		
Data File	LD-007-23-4.d	Method (Acq)	Shafikur_HRMS method.m	Comment		Acq. Time (Local)	1/15/2024 9:28:43 AM (UTC-06:00)



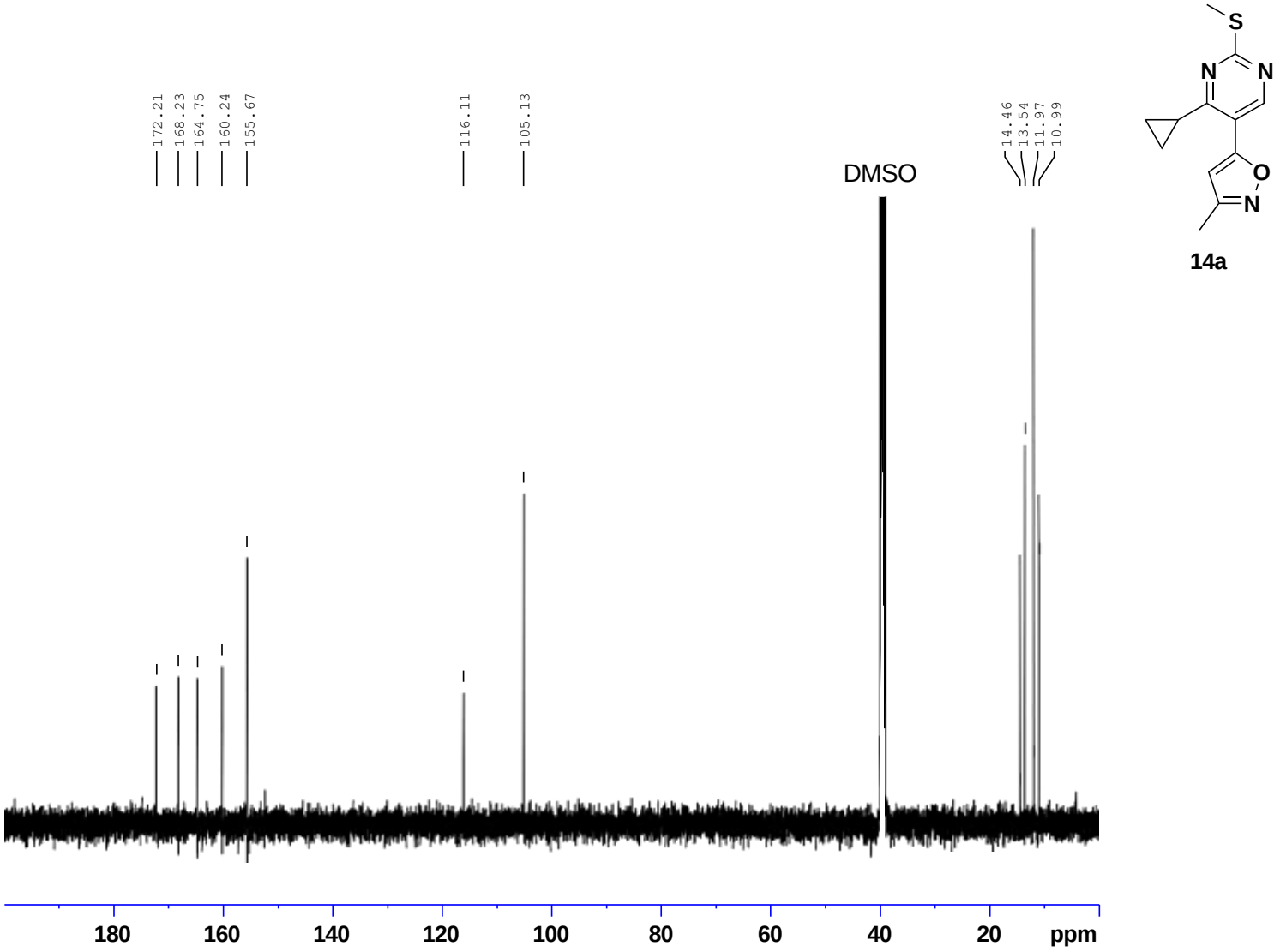
Generated at 9:42 AM on 1/15/2024

5-(4-cyclopropyl-2-(methylthio)pyrimidin-5-yl)-3-methylisoxazole



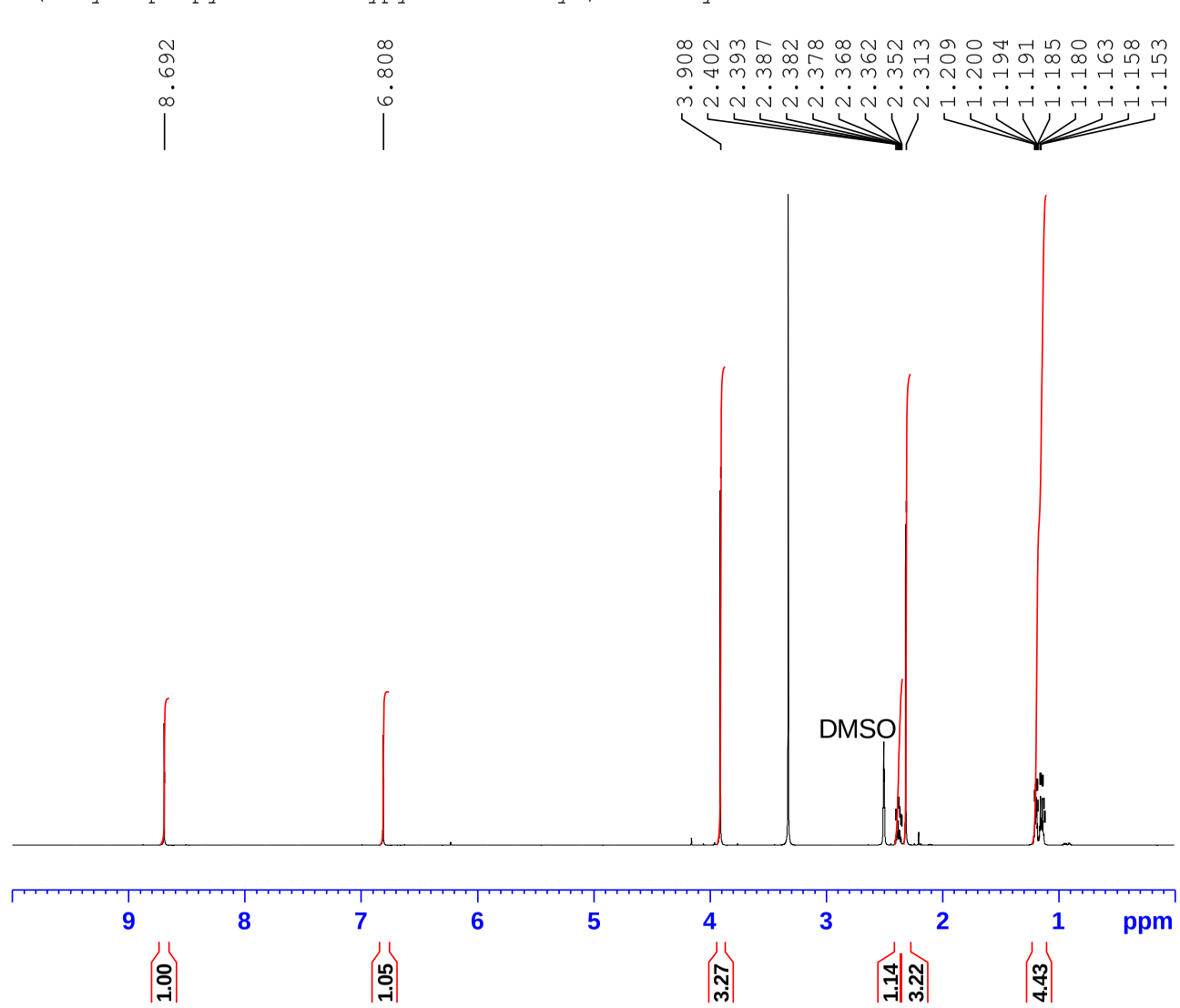
14a

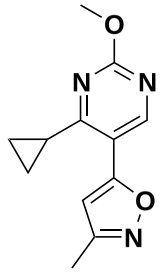
5-(4-cyclopropyl-2-(methylthio)pyrimidin-5-yl)-3-methylisoxazole



14a

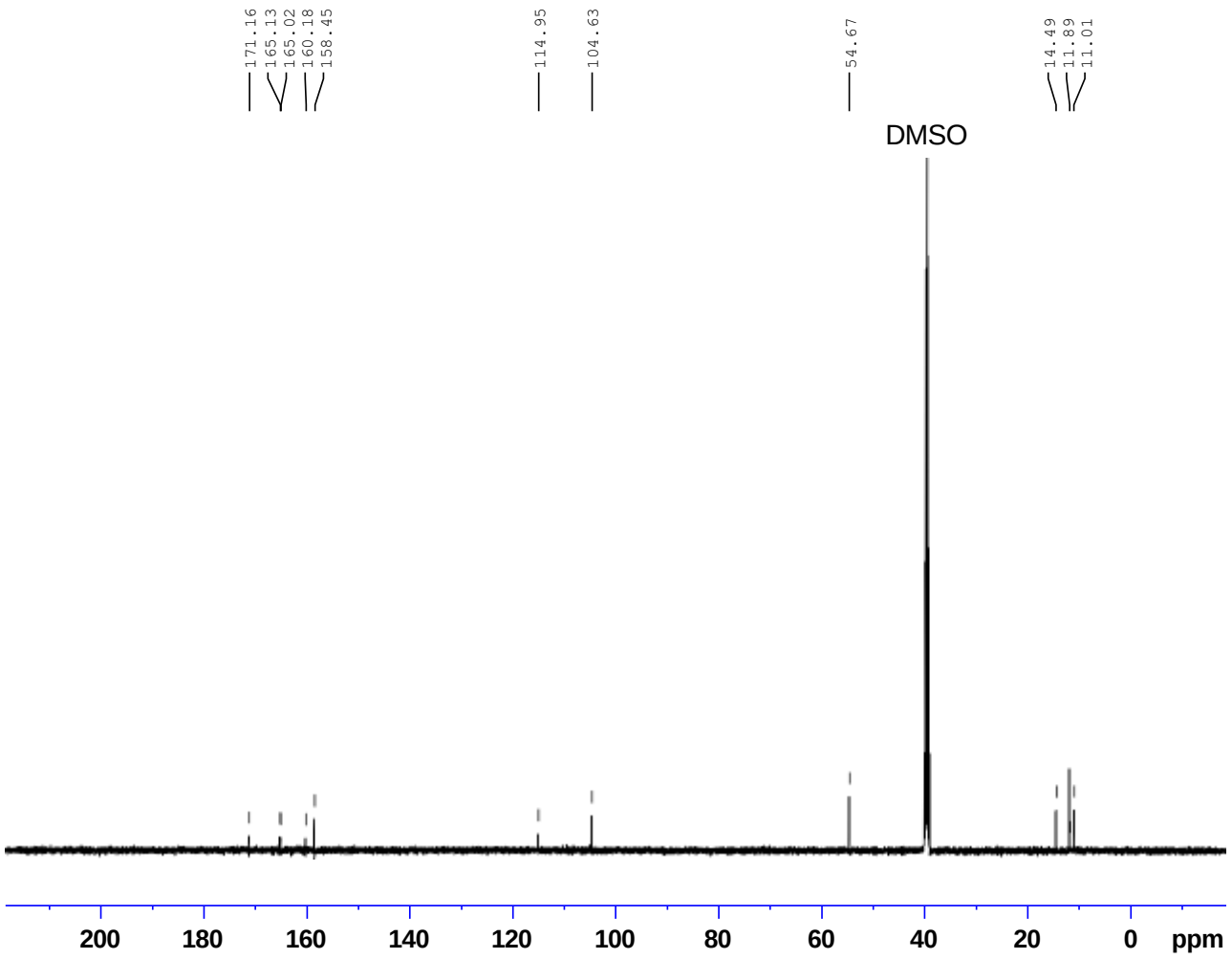
5-(4-cyclopropyl-2-methoxypyrimidin-5-yl)-3-methylisoxazole

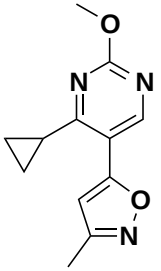




14b

5-(4-cyclopropyl-2-methoxypyrimidin-5-yl)-3-methylisoxazole





14b

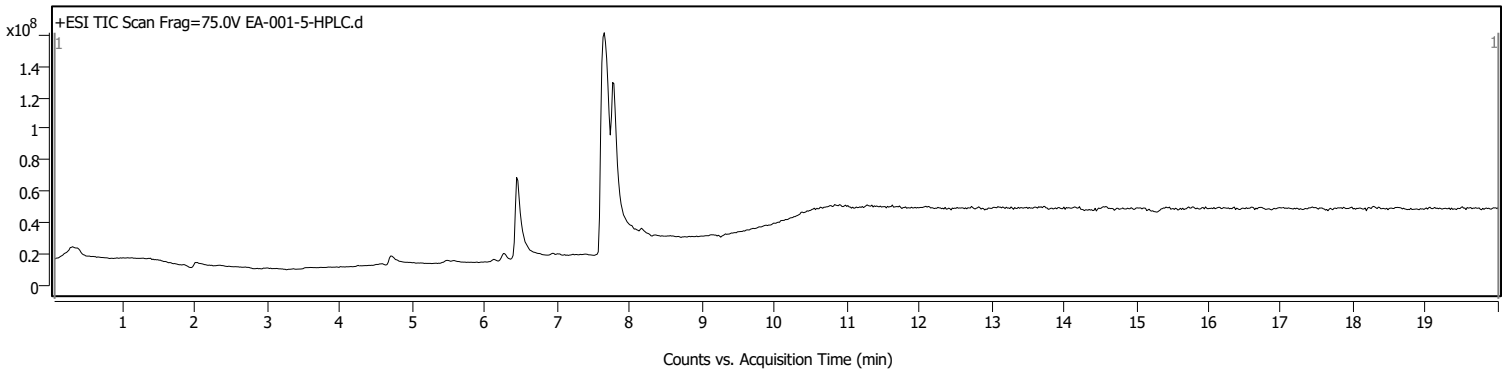
Analysis Report

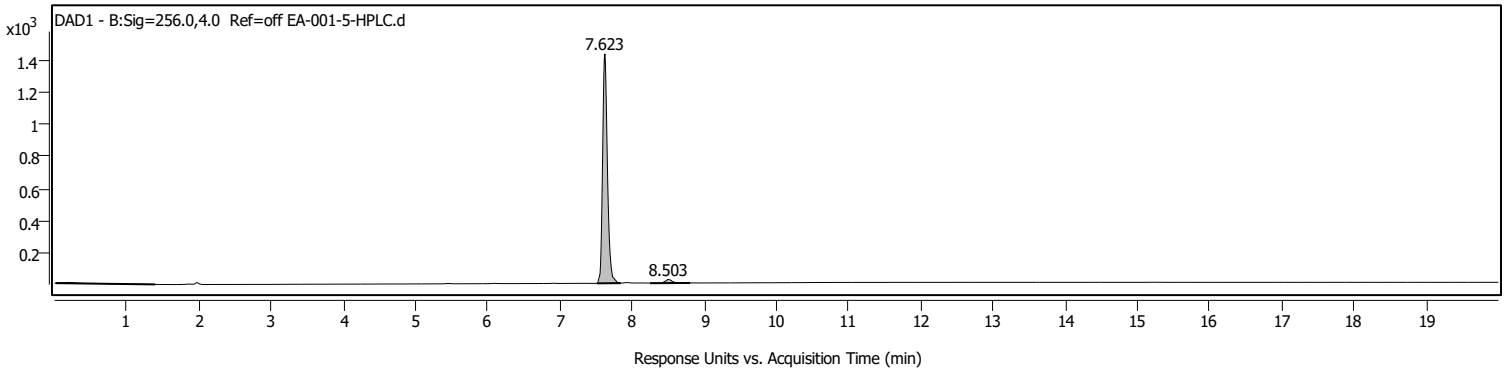
Agilent | Trusted Answers

Sample Information

Name	EA-001-5	**Data File Path**	D:\MassHunter\Data\Louise\EA-001-5-HPLC.d
Sample ID		**Acq. Time (Local)**	1/17/2024 11:51:42 AM (UTC-06:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HPLC method\Shafikur_HPLC method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	10	**IRM Status**	All ions missed
Position	P1-A4	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms





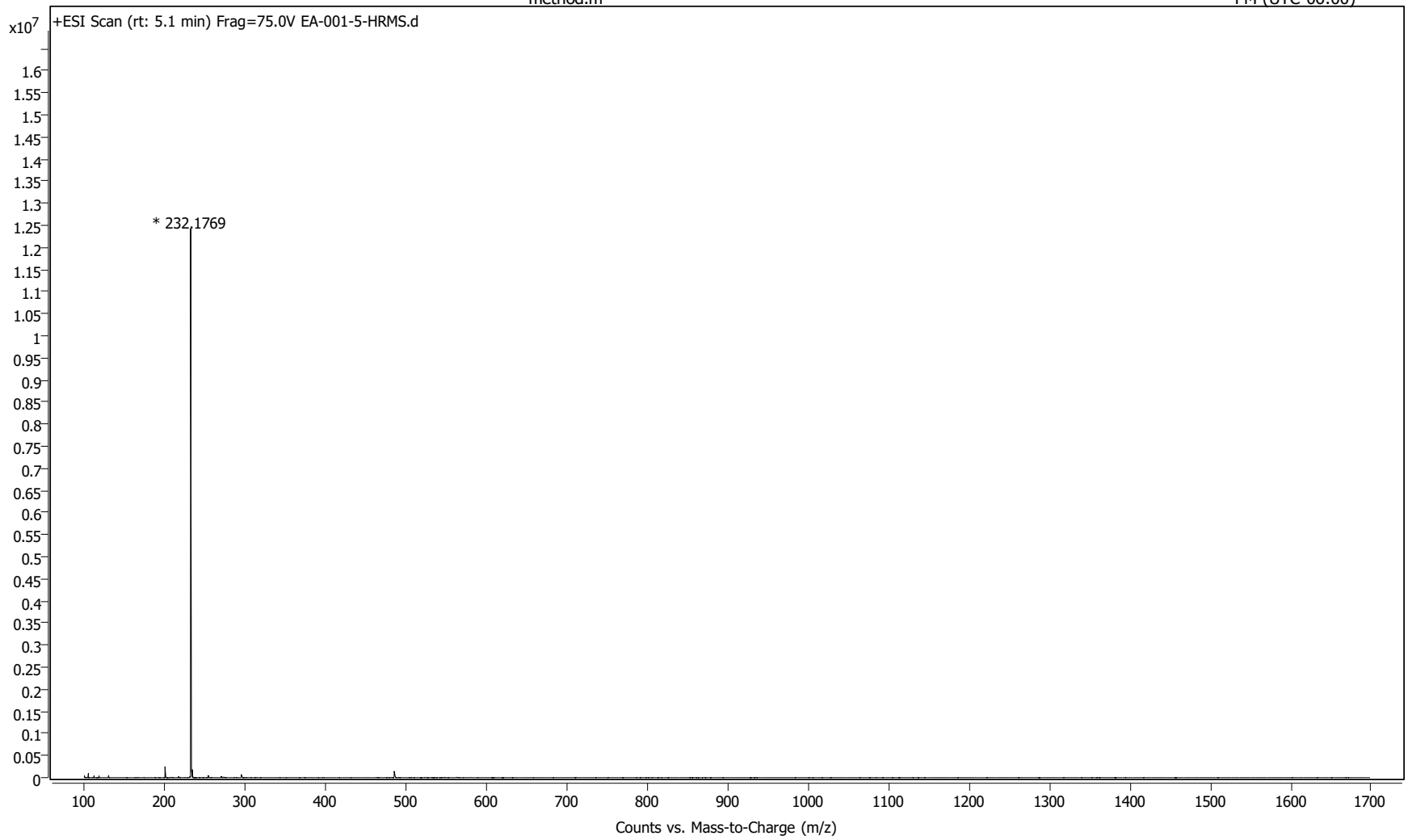
Chromatogram Peaks

Peak	Start	RT	End	Height	Area	Area %	SNR
1	0.016	0.190	1.396	5	123	1.88	
2	7.510	7.623	7.843	1429	6576	100.00	
3	8.250	8.503	8.803	22	136	2.07	

MassHunter Qual 10.0
(End of Report)

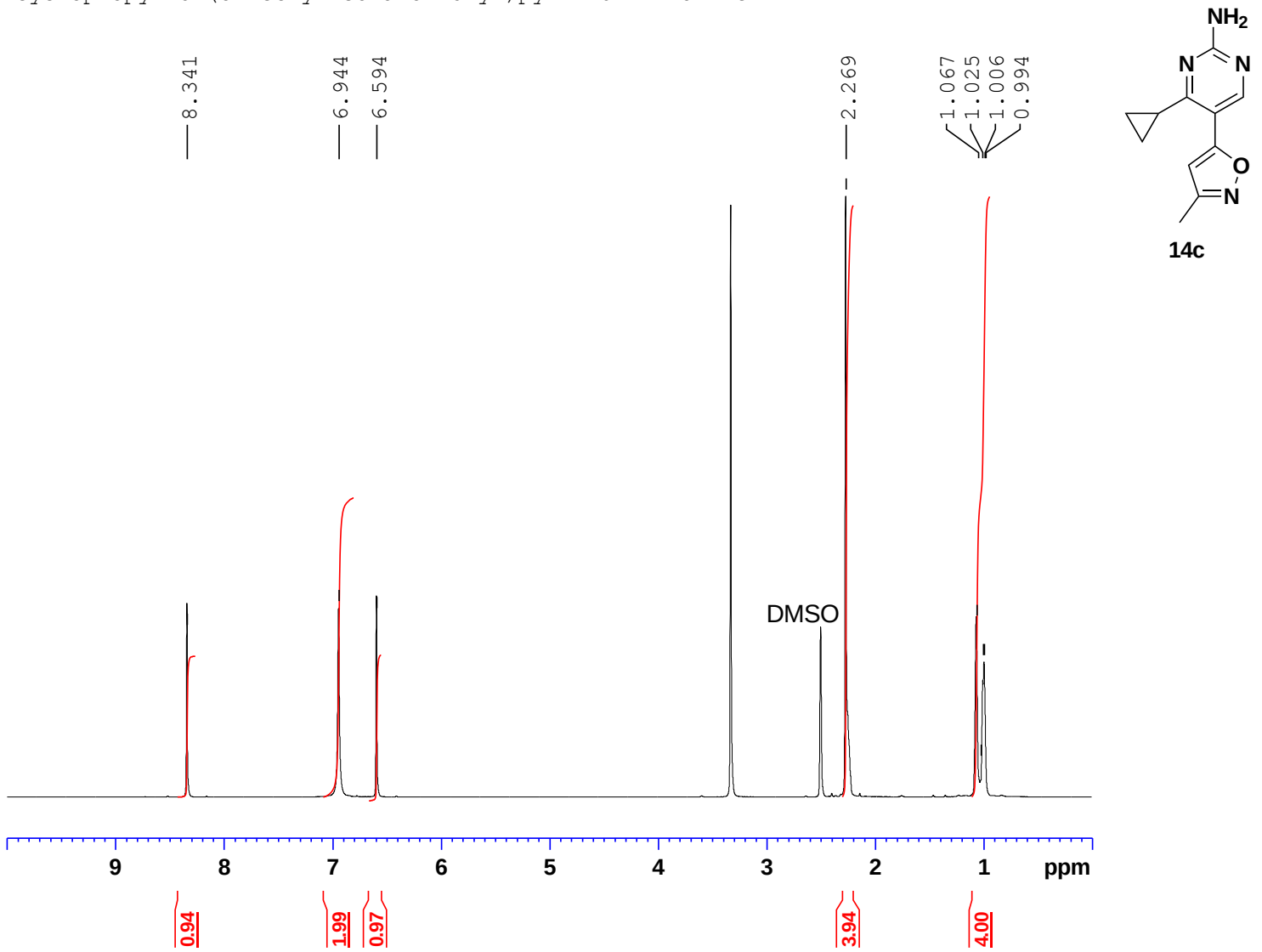
User Spectrum Plot Report

Name	EA-001-5	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	All ions missed		
Data File	EA-001-5-HRMS.d	Method (Acq)	Shafikur_HRMS method.m	Comment		Acq. Time (Local)	1/17/2024 12:15:26 PM (UTC-06:00)



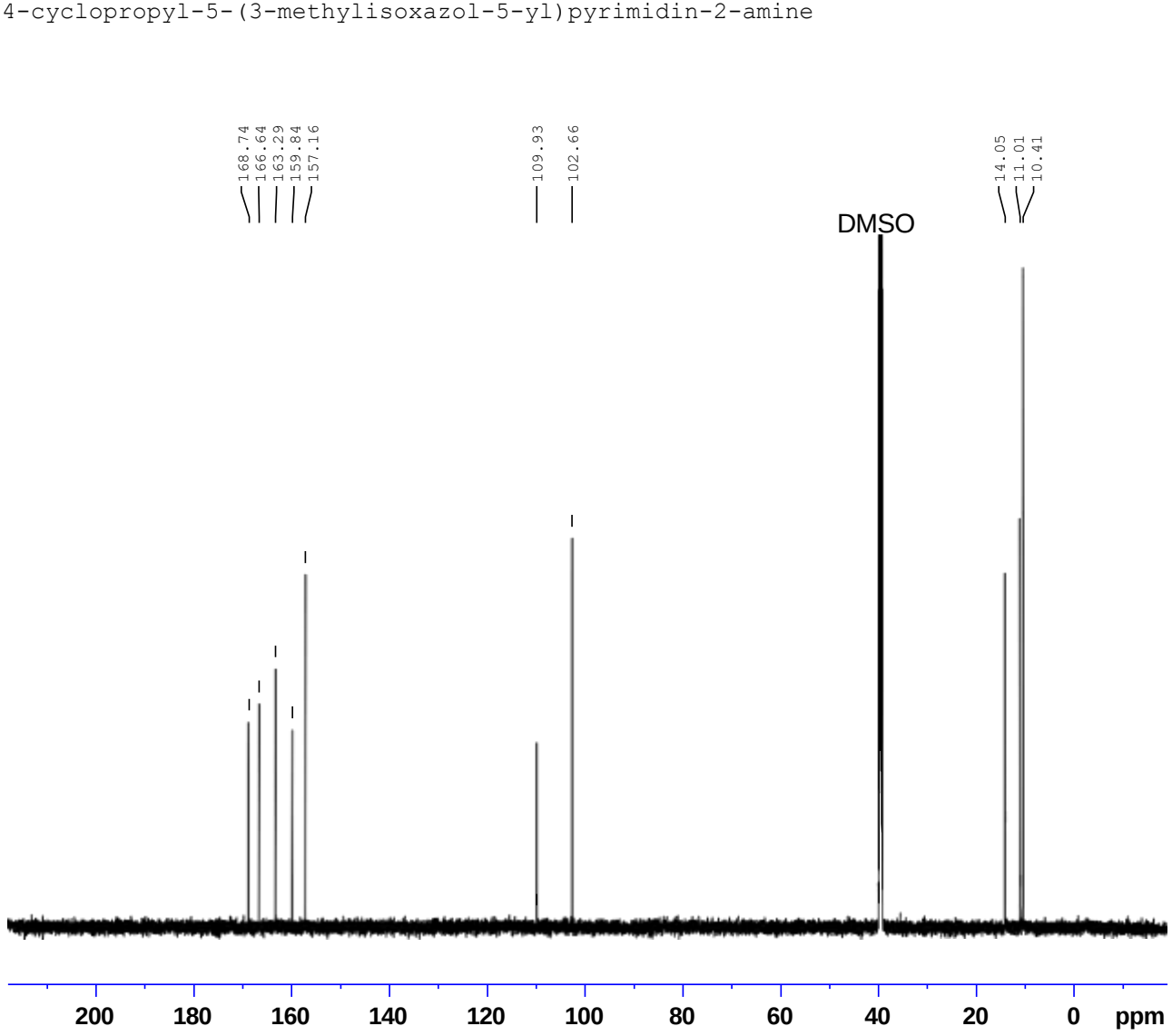
Generated at 12:54 PM on 1/17/2024

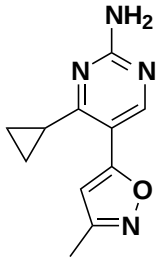
4-cyclopropyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine



14c

4-cyclopropyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine





14c

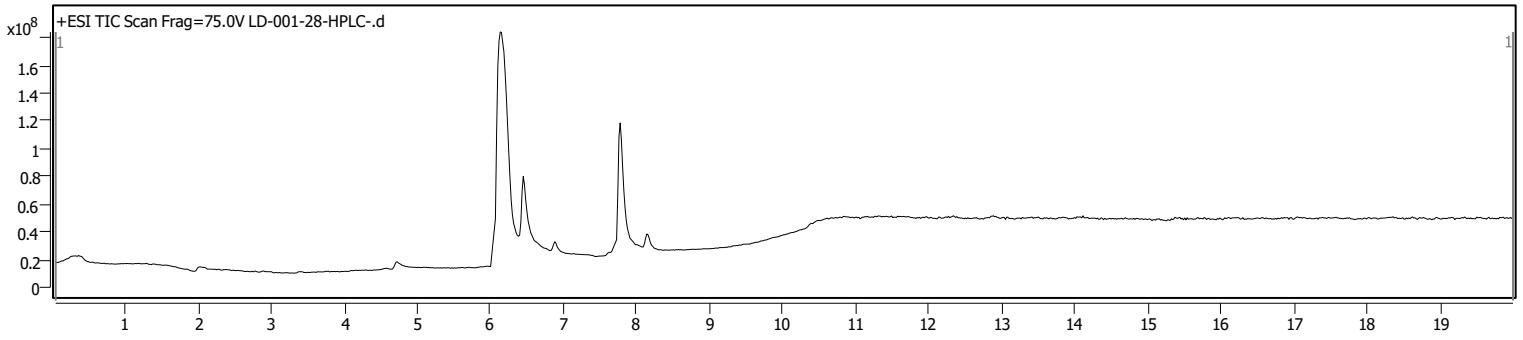
Analysis Report

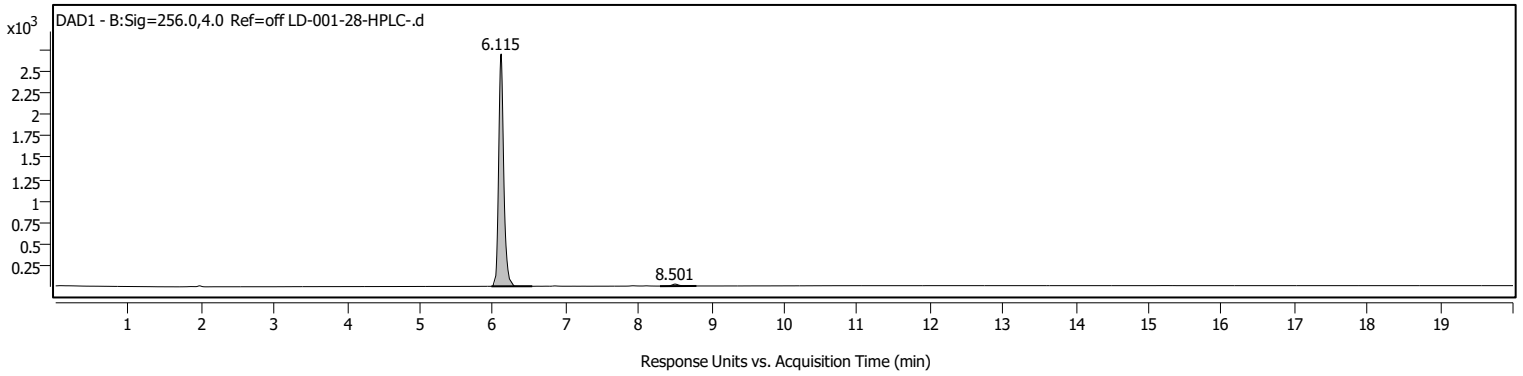
Agilent | Trusted Answers

Sample Information

Name	ld-001-28	**Data File Path**	D:\MassHunter\Data\Louise\LD-001-28-HPLC-.d
Sample ID		**Acq. Time (Local)**	1/17/2024 11:16:10 AM (UTC-06:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HPLC method\Shafikur_HPLC method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	10	**IRM Status**	All ions missed
Position	P1-A3	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms





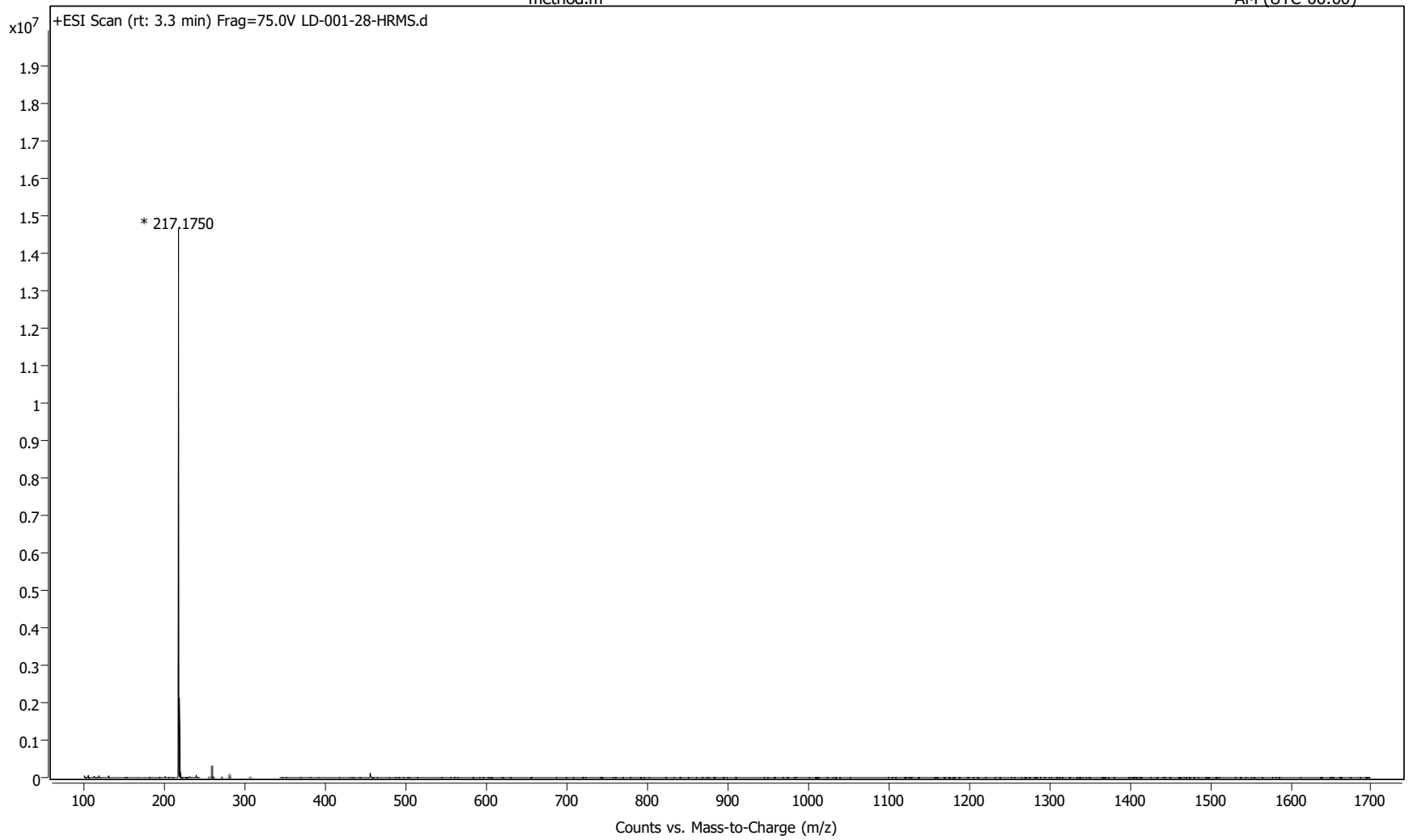
Chromatogram Peaks

Peak	Start	RT	End	Height	Area	Area %	SNR
1	5.981	6.115	6.541	2693	13060	100.00	
2	8.295	8.501	8.795	23	139	1.07	

MassHunter Qual 10.0
(End of Report)

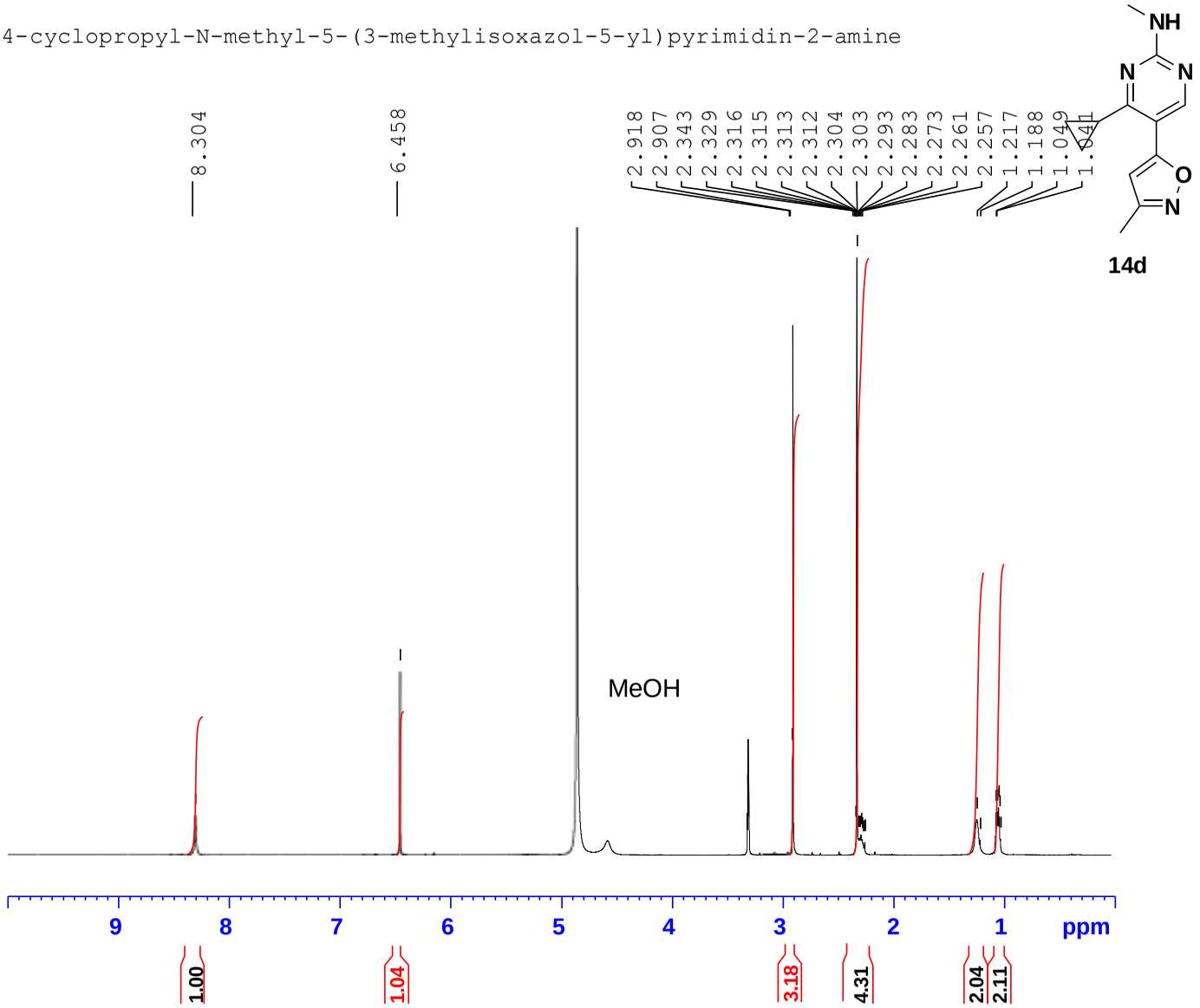
User Spectrum Plot Report

Name	LD-001-28	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	All ions missed		
Data File	LD-001-28-HRMS.d	Method (Acq)	Shafikur_HRMS method.m	Comment		Acq. Time (Local)	1/17/2024 11:39:54 AM (UTC-06:00)



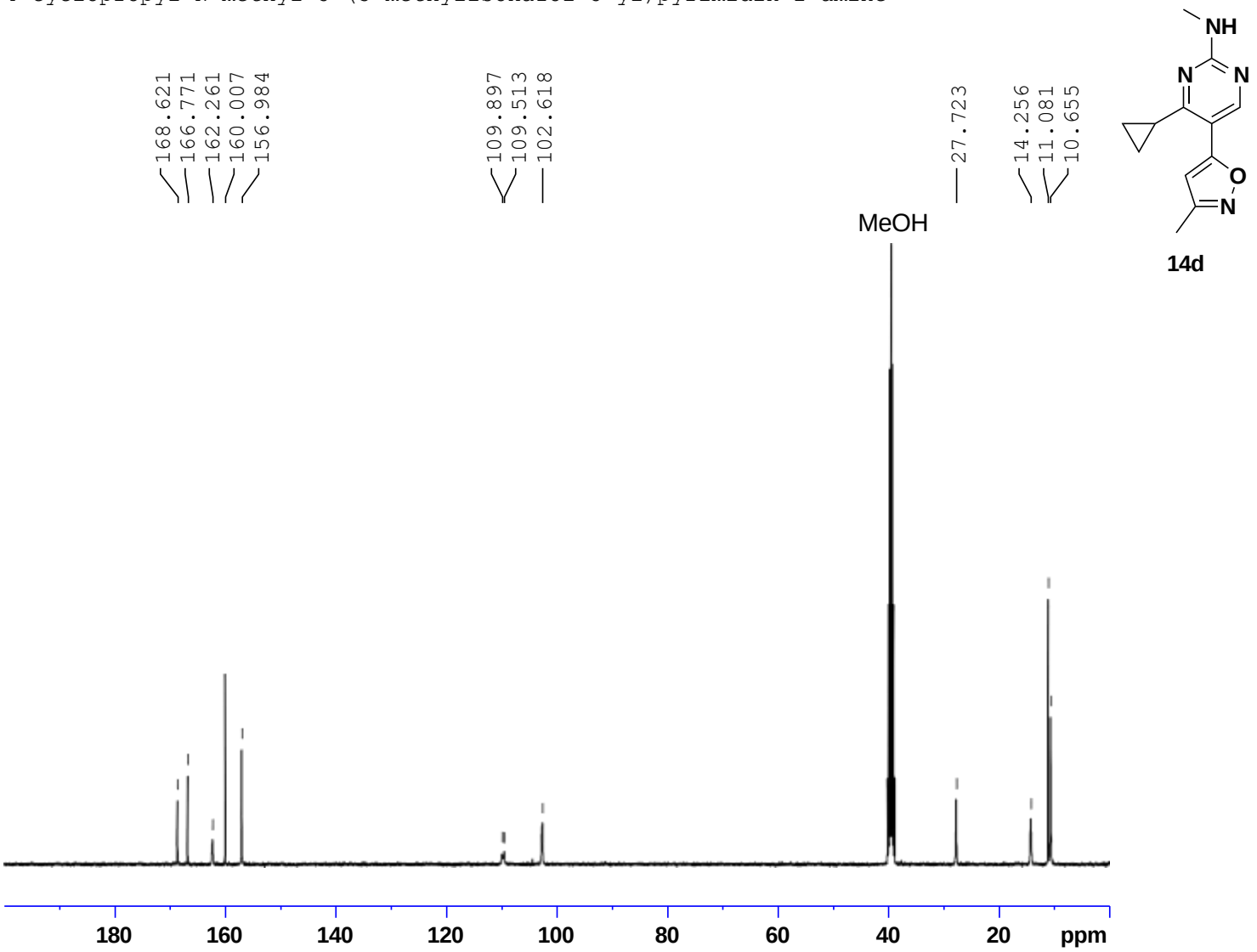
Generated at 12:53 PM on 1/17/2024

4-cyclopropyl-N-methyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine



14d

4-cyclopropyl-N-methyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-amine



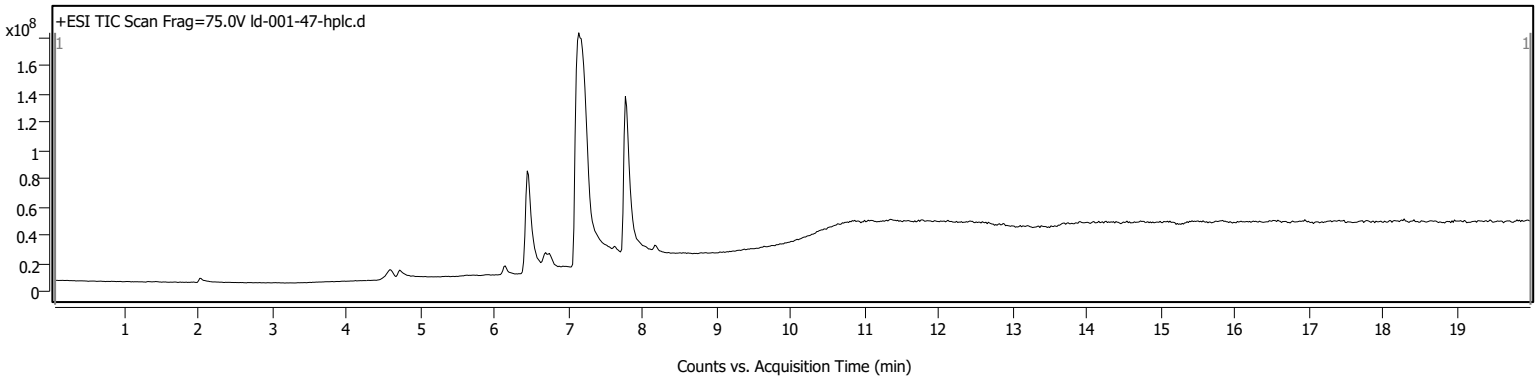
Analysis Report

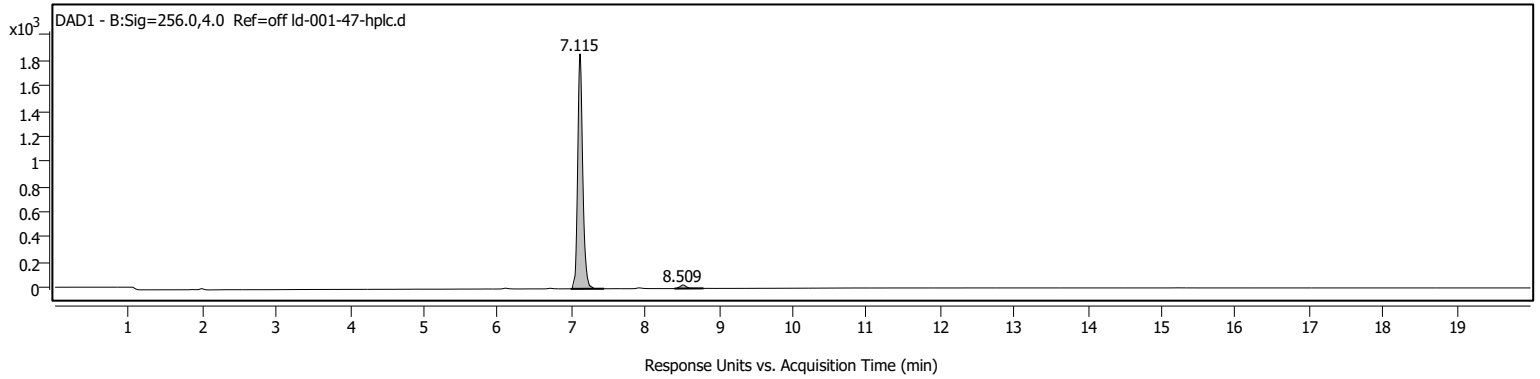
Agilent | Trusted Answers

Sample Information

Name	ld-001-47	**Data File Path**	D:\MassHunter\Data\Louise\ld-001-47-hplc.d
Sample ID		**Acq. Time (Local)**	1/17/2024 10:05:06 AM (UTC-06:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HPLC method\Shafikur_HPLC method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	10	**IRM Status**	All ions missed
Position	P1-A1	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms





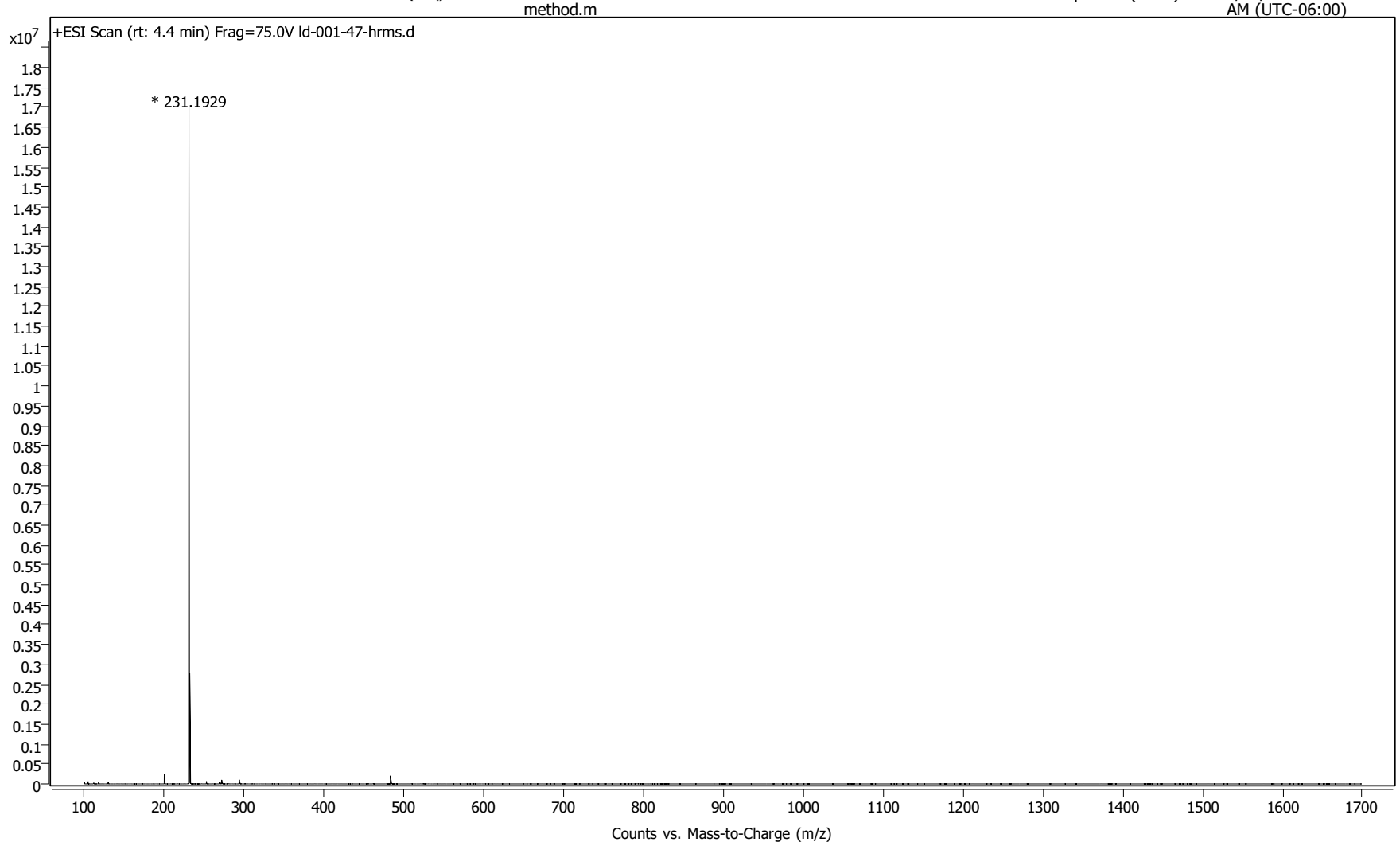
Chromatogram Peaks

Peak	Start	RT	End	Height	Area	Area %	SNR
1	6.989	7.115	7.442	1861	8794	100.00	
2	8.395	8.509	8.789	29	167	1.89	

MassHunter Qual 10.0
(End of Report)

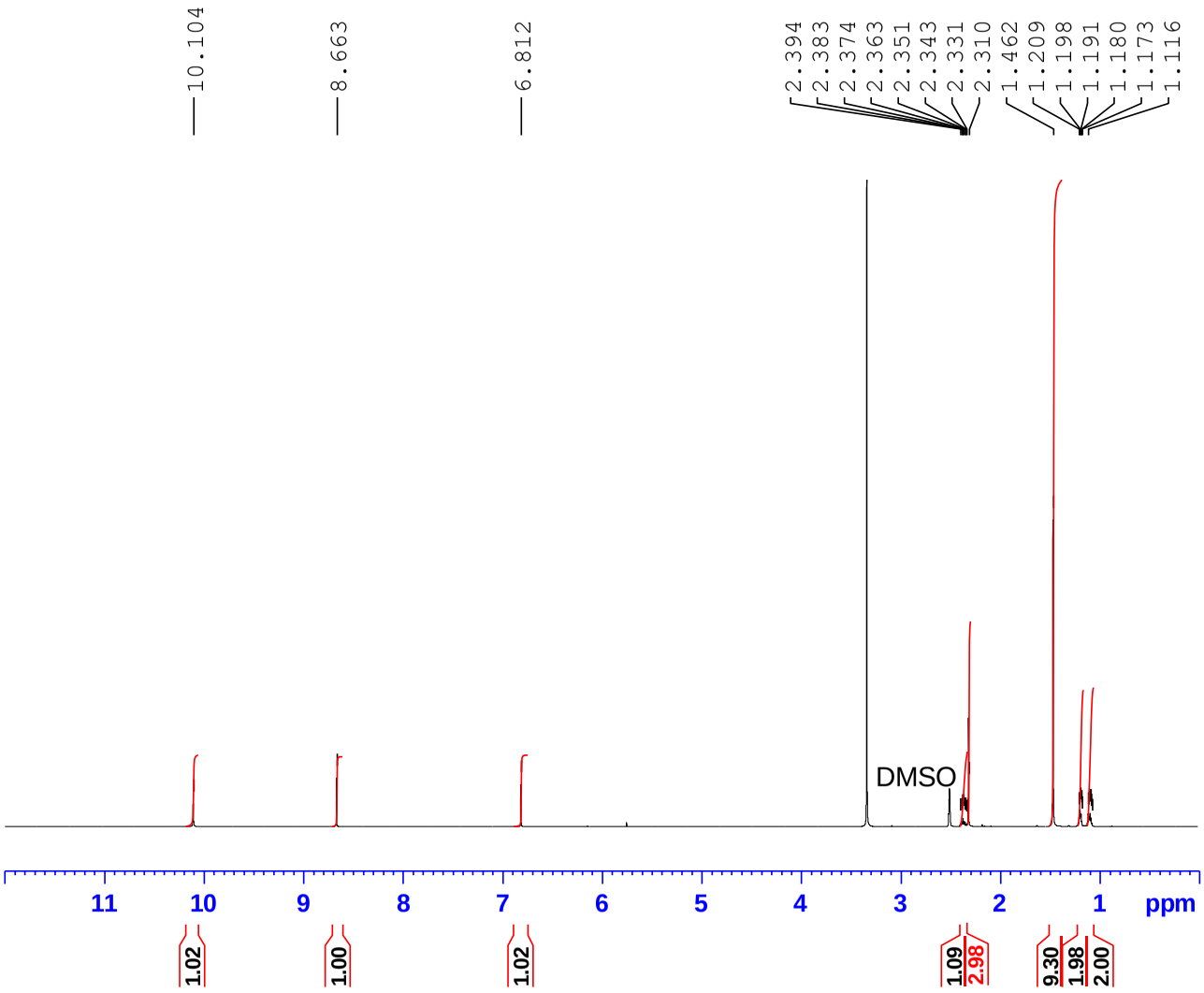
User Spectrum Plot Report

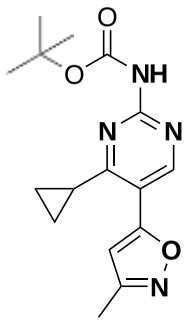
Name	ld-001-47	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	All ions missed		
Data File	ld-001-47-hrms.d	Method (Acq)	Shafikur_HRMS method.m	Comment		Acq. Time (Local)	1/17/2024 10:28:55 AM (UTC-06:00)



Generated at 11:38 AM on 1/17/2024

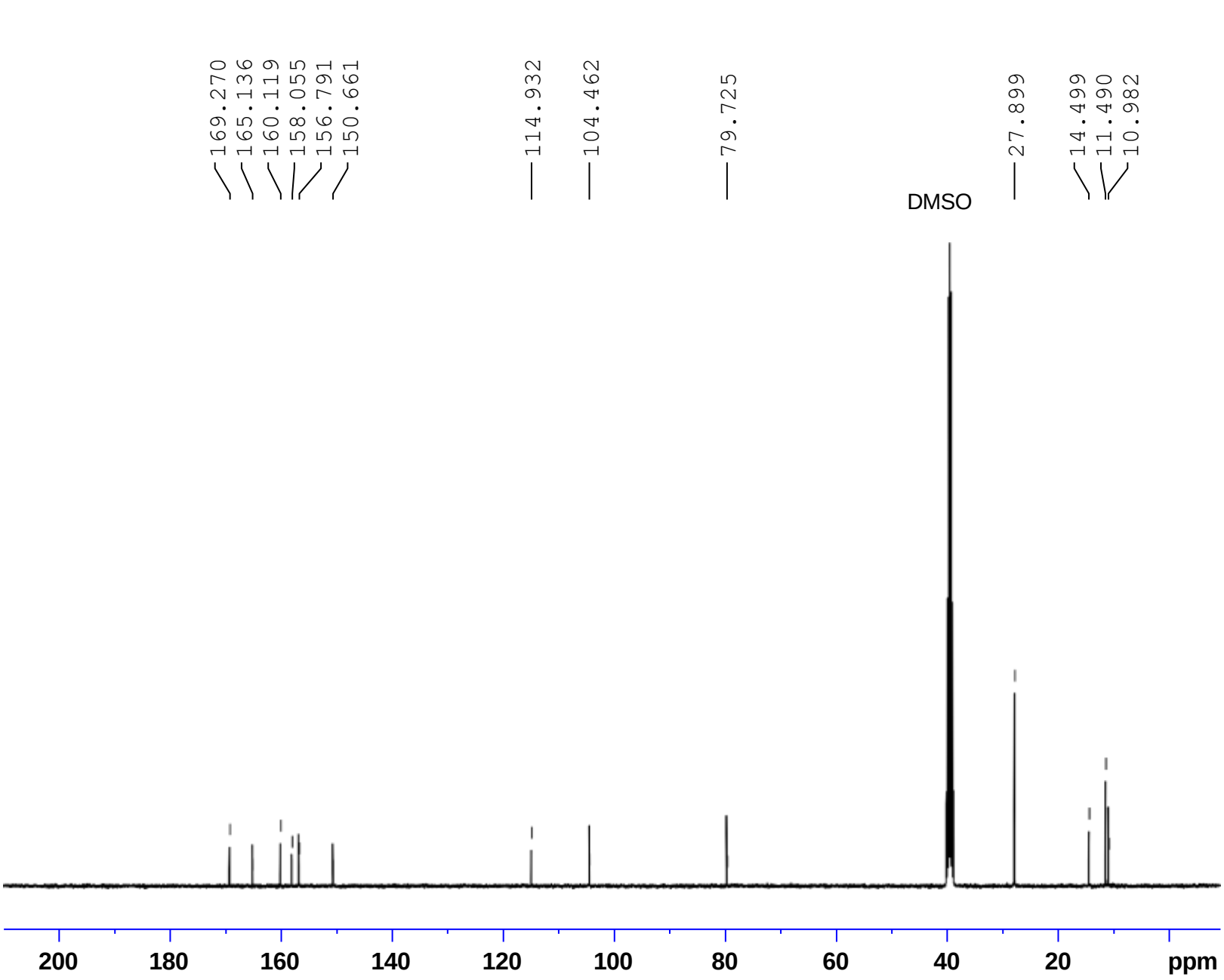
tert-butyl (4-cyclopropyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-yl)carbamate

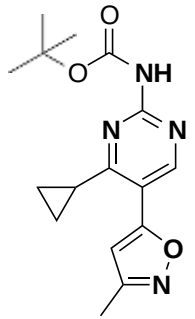




14e

tert-butyl (4-cyclopropyl-5-(3-methylisoxazol-5-yl)pyrimidin-2-yl)carbamate





14e

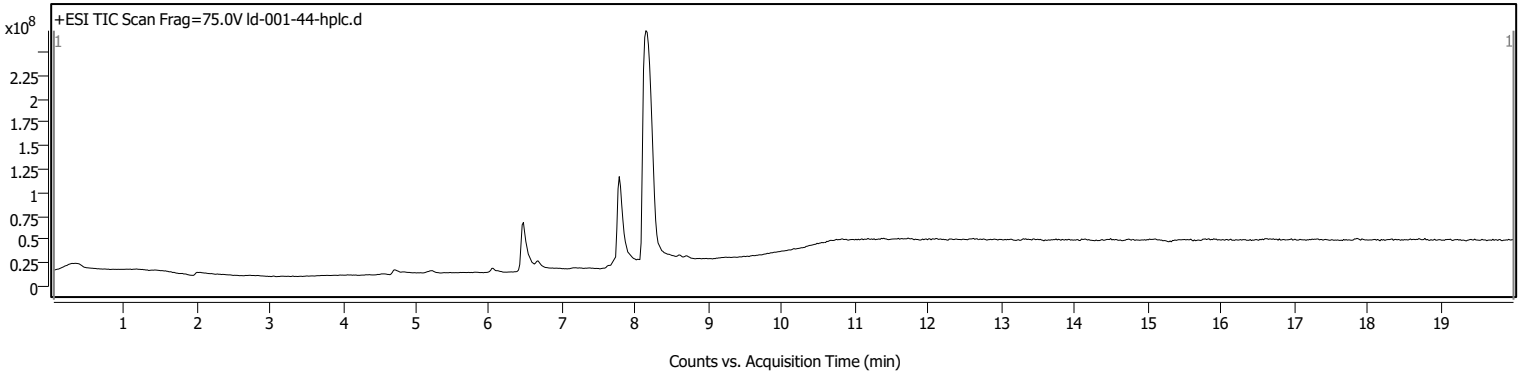
Analysis Report

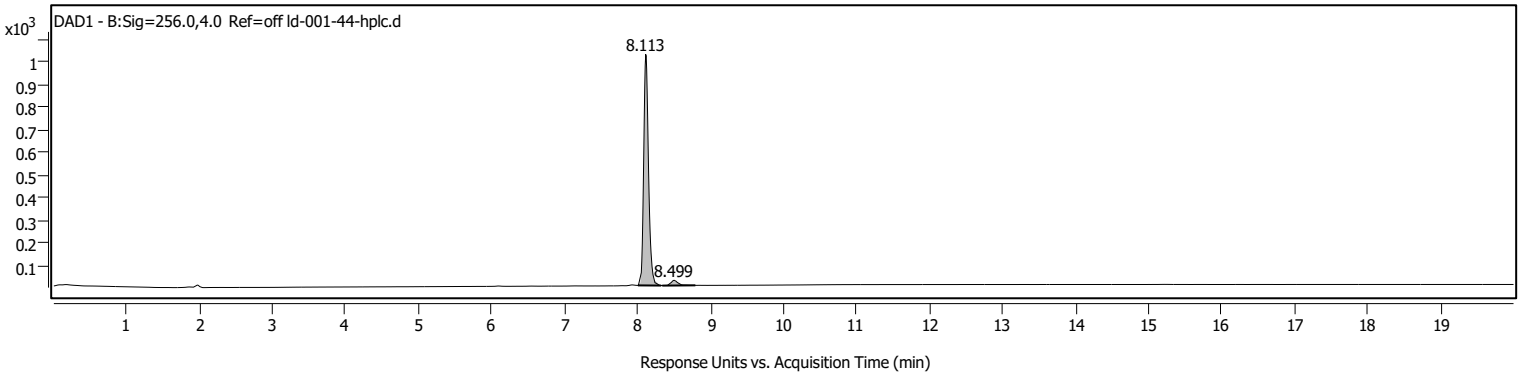
Agilent | Trusted Answers

Sample Information

Name	ld-001-44	**Data File Path**	D:\MassHunter\Data\Louise\ld-001-44-hplc.d
Sample ID		**Acq. Time (Local)**	1/17/2024 10:40:40 AM (UTC-06:00)
Instrument	Instrument 1	**Method Path (Acq)**	D:\MassHunter\Methods\SR\Shafikur_HPLC method\Shafikur_HPLC method.m
MS Type	TOF	**Version (Acq SW)**	6200 series TOF/6500 series Q-TOF 10.1 (48.0)
Inj. Vol. (ul)	10	**IRM Status**	All ions missed
Position	P1-A2	**Method Path (DA)**	
Plate Pos.		**Target Source Path**	
Operator		**Result Summary**	

Sample Chromatograms





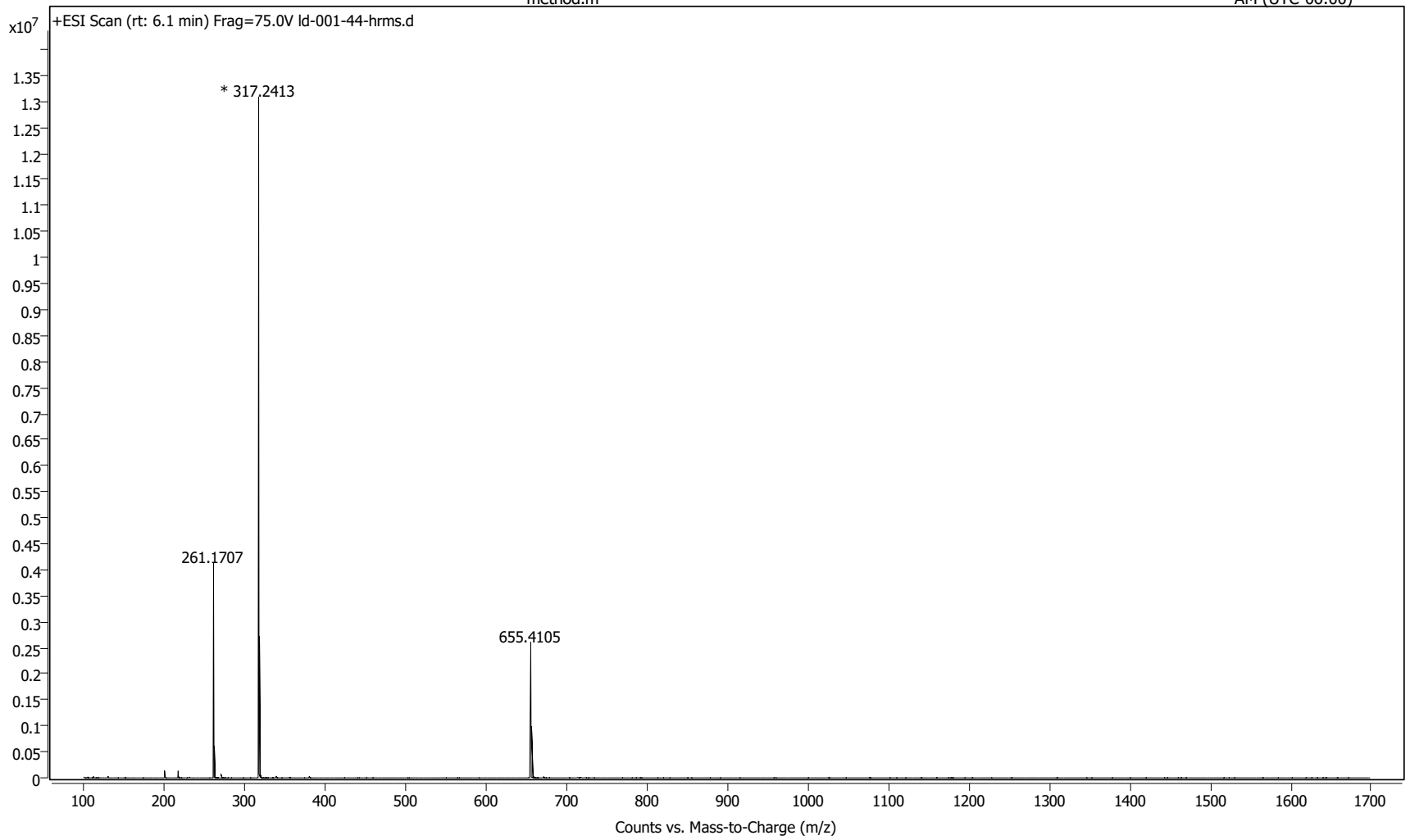
Chromatogram Peaks

Peak	Start	RT	End	Height	Area	Area %	SNR
1	8.006	8.113	8.326	1020	4660	100.00	
2	8.339	8.499	8.793	22	143	3.07	

MassHunter Qual 10.0
(End of Report)

User Spectrum Plot Report

Name	ld-001-44	Rack Pos.		Instrument	Instrument 1	Operator	
Inj. Vol. (ul)	2	Plate Pos.		IRM Status	All ions missed		
Data File	ld-001-44-hrms.d	Method (Acq)	Shafikur_HRMS method.m	Comment		Acq. Time (Local)	1/17/2024 11:04:25 AM (UTC-06:00)



Generated at 11:40 AM on 1/17/2024

SH-SY5Y Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
24.8344371	100	38.1898455	48.6754967	87.196468	89.514349	99.2273732
26.8674699	100	37.5903615	40.6024097	92.4096386	89.6385543	122.409639
32.0359281	100	47.4550898	49.251497	94.760479	138.772455	141.916168
36.4906832	100	59.3167701	76.2422359	88.8198757	90.9937887	89.2857142
38.7791741	100	65.7091561	84.3806104	98.0251346	96.0502693	101.615799
36.2041465	100	59.0111641	73.2057413	84.5295052	108.61244	89.1547045
49.3827157	100	68.148145	86.1728454	86.9135845	93.3333374	96.5432139
49.4033214	100	70.4056995	85.4414895	88.3054537	95.4653495	99.7613008
48.2185167	100	73.3966611	83.1353787	91.9239732	104.038018	97.6246823
47.4025806	100	77.2726912	75.9739957	78.7878439	79.4371964	80.952349
43.5146368	100	75.9414072	77.6150464	84.3096031	90.3765519	90.1673402
56.0975575	100	97.0189682	99.4580007		134.6883	123.848195
43.9252311	100	68.9252311	80.1401868	86.2149558	90.6542085	100.467257
43.4883906	100	69.7674681	85.8139843	92.3256133	100.697674	105.348901
47.0588254	100	70.0980405	90.6862837	98.0392204	103.921539	105.882391
15.949961	100	57.0758407	82.2517594	88.2720879	98.2799069	99.3745115
15.7356413	100	75.6884345	84.3430371	90.9520065	95.8300552	101.966955
18.3742592	100	82.5571549	82.049111	95.0889078	103.979678	105.50381
15.472561	100	77.1341466	85.97561	88.795732	99.314025	101.067073
15.6893819	100	90.7290016	86.2916007	88.4310618	100.396197	103.565768
15.9220147	100	81.4784728	86.4337936	86.9212023	101.218522	103.005686

SK-N-AS Compound Treatment MTS Data

Control	100	50	10	1	0.1
100	104.9729	68.71609	92.72152	91.5009	103.3906
100	107.7249	82.61894	109.4677	97.55064	106.406
100	106.4533	86.12805	108.0793	105.3354	113.6179
100	93.47368	67.49474	93.93684	99.41053	92.92632
100	93.59248	74.11363	87.35583	103.5882	95.30115
100	93.97284	76.14601	100.0424	100.8065	98.89643
100	23.72731	76.40549	98.22931	100.1328	104.8694
100	87.4537	82.68519	95.13889	106.9444	108.8889
100	94.8512	81.5777	109.778	107.8413	107.4634

SK-N-BE2 Compound Treatment MTS Data

Control	100	50	10	1	0.1
100	16.41362	88.01805	115.3878	101.7645	96.0197
100	16.87949	86.31285	91.02155	82.16281	99.60096
100	18.4769	111.0695	112.3179	96.54598	107.1161
100	23.89381	123.4253	124.9349	118.3758	96.56429
100	18.33333	100.0427	103.2051	93.2906	82.05128
100	16.10605	63.03918	92.24377	77.40404	83.22121
100	18.17107	92.58967	87.30784	94.36342	96.64959
100	15.23283	91.35754	102.5257	97.71113	106.7088
100	16.37546	79.15482	96.58675	97.19626	101.7879

SK-N-MC Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
22.1965318	100	55.6069364	65.549133	113.641618	113.988439	105.780347
21.7391304	100	81.6933638	62.9290618	113.157895	111.670481	111.784897
20.0868621	100	80.0217155	58.8490771	101.520087	102.714441	98.6970684
22.1590909	100					
21.3186813	100	81.4285714	63.0769231	110.989011	99.5604396	104.945055
21.5316315	100	81.5760266	65.0388457	112.319645	108.990011	106.770255
21.2606838	100	75.3205128	60.6837607	102.991453	102.67094	94.2307693
21.5285253	100					
21.1991435	100	76.0171306	54.8179871	107.066381	104.925054	105.674518
21.168688	100	59.9779493	51.1576626	106.394708	105.953694	107.607497
23.5772358	100	59.1173055	61.9047619	109.407665	106.387921	114.866434
21.8681319	100					

CHLA255 Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
28.37326608	100	38.72113677	88.72113677	103.6412078	100.7104796	102.3978686
27.30582524	100	44.85049834	85.46511628	100.166113	100	101.4950166
30.22959184	100	39.19382504	94.16809605	101.0291595	101.3722127	109.4339623
28.82653061	100	23.82495948	95.46191248	98.86547812	105.9967585	105.9967585
42.17335058	100	67.17557252	102.0038168	130.9160305	131.0114504	119.2748092
42.91091593	100	24.40622441	86.56838657	113.8411138	106.7977068	101.3104013
41.56479218	100	57.07112971	94.64435146	95.39748954	96.06694561	99.66527197
42.22222222	100	59.32642487	90.41450777	103.626943	109.8445596	104.1450777
24.52606635	100	61.78287732	91.43865843	102.3830538	100.4413063	102.5595763
24.94305239						
25.98607889						
26.37749121						

WPMY-1 Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
11.94105691	100	113.5256	107.0833	102.3077	99.77564	99.48718
12.37998989	100	119.8304	113.2746	100.848	103.8813	104.9902
13.21996709	100	97.23206	109.205	104.9887	103.3151	103.4117
12.70096463	100	105.6299	100.7304	98.3871	101.3086	99.87827
12.65155509	100	104.247	102.0783	101.3855	99.51807	98.34337
13.24903793	100	110.7688	102.9879	104.793	99.75101	102.8945
11.99029126	100	107.7163	102.1556	103.249	101.7182	98.75039
12.43347847	100	106.4118	106.2269	99.75339	99.32182	100.7707
12.47534517	100	104.5923	108.5286	103.9988	102.5305	100.3124
13.60394953						
12.19251337						
13.14223905						

PANC-1 Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
13.65330848	100	103.631291	100.039927	99.8403904	99.6408537	97.4860255
13.95	100	98.2121103	104.185245	104.063374	99.4311214	102.844363
13.80597015	100	102.842103	105.278146	102.923251	99.025583	102.760855
12.94067068	100	90.0245298	101.185609	102.943582	102.902699	101.635323
13.49775785	100	93.9569537	103.311259	103.228476	103.352649	99.2963572
13.2033673	100	95.6896552	105.991379	106.551724	100.560345	103.49138
	100	95.0925927	102.314815	105.925926	106.990741	104.398148
	100	97.0479705	101.52214	104.98155	106.319189	103.597786
	100	98.2175505	104.570384	103.976234	104.021938	102.74223
	100	96.7313585	63.7895812	105.87334	106.690501	98.1103167
	100	89.0489914	101.536984	100.576369	106.48415	103.650336
	100	97.9477611	79.5708955	98.8339552	105.363806	103.311567
	100	71.1840888	89.0841813	89.0379278	79.093432	73.4967622
	100	77.4464119	87.4184529	87.0456663	83.1314072	78.4249767
	100	82.3212537	96.2291871	100.244858	89.8628795	83.1047992
	100	79.3298969	99.2783505	99.2268041	88.1443299	81.9072165
	100	88.4984026	99.8935037	99.4675186	94.9946752	89.6166134
	100	88.2878151	103.203782	107.510504	96.3760504	89.1281513

LNCaP Compound Treatment MTS Data

Enzalutamide 25 µM	Control	100	50	10	1	0.1
88.17204301	100	88.8242895	92.7648579	110.07752	106.007752	102.196382
92.16446858	100		100.571792	89.9618809	106.797967	98.5387557
93.26552087	100	89.9280576	95.4872466	93.852191	103.400915	98.2995422
76.46566164	100	93.0015552	98.289269	104.043545	105.365474	100.311042
66.44250168	100	90.2019446	100.448766	103.066567	101.869858	102.543007
78.54602924	100	87.473002	97.336213	94.1684664	95.4643627	97.5521957
78.21442198	100	84.5833334	91	81.9166667	80.5	77.5416667
84.61869884	100	91.6981132	103.915094	97.4528302	104.716981	89.8584906
77.42812743	100	111.381733	101.358314	102.201405	104.824356	93.0210773
83.77265239						
76.64084794						
91.76470588						

PnT2C2 Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
18.53593015	100	60.48728814	95.33898305	93.75	106.0381356	95.76271186
18.21862348	100		107.6309795	113.667426	114.1230068	105.4669704
17.98611111	100	65.62162162	107.7837838	102.4864865	110.5945946	103.6756757
18.77125368	100	69.70387244	102.0501139	102.3917995	101.7084282	97.72209567
18.36318295	100	68.31896552	99.24568966	106.4655172	103.0172414	95.36637931
17.61505328	100	70.80890973	101.1723329	109.2614302	101.2895662	91.44196952
	100	74.77876106	109.8451327	103.9823009	97.12389381	94.80088496
	100	76.55502392	107.4162679	121.1722488	110.8851675	103.708134
	100	72.52252252	114.6396396	112.3873874	97.52252252	102.5900901

HPNE Compound Treatment MTS Data

Triton X	Control	100	50	10	1	0.1
29.54784437	100	90.09287926	106.3983488	103.3023736	105.5727554	103.5087719
29.00735294	100	87.74193548	113.9784946	108.3870968	105.0537634	104.4086022
35.93220339	100	91.57303371	110.2247191	107.5280899	102.4719101	96.96629213
30.54298643	100	100.1077586	117.9956897	121.4439655	118.2112069	110.1293103
21.74672489	100	87.38916256	107.8817734	105.1231527	99.01477833	102.364532
21.01859337	100	92.6803014	110.9795479	114.9623251	107.9655544	108.073197
25.2553389	100	85.65697091	100.2006018	106.0180542	99.59879639	99.79939819
24.85549133	100	97.22222222	106.2757202	111.4197531	103.7037037	104.9382716
15.2953054	100	85.02512563	104.9246231	105.7286432	96.68341709	97.78894472
15.922539						
29.9196787						
27.6397516						

SH-SY5Y Cells Cotreatment of Compound 1 Aβ MTS Data

Triton	Control	Aβ	100	50	10	1	0.1
15.6626549	100	82.6944418	55.6407634	72.6177725	75.794112	79.29904	79.1895138
15.9142255	100	82.8442412	47.0654626	76.7494284	78.1038358	86.2302495	82.2799116
16.8982825	100	79.822132	49.3607674	74.3746612	77.0428116	85.3807828	83.2684925

SH-SY5Y Cells Pretreatment of Compound 1 Aβ MTS Data

Triton	Control	Aβ (50 μM)	100	50	10	1	0.1
19.7628458	100	94.4664031	24.1106719	56.027668	79.6442687	93.0830039	93.8735178
19.94077	100	89.1411648	26.0612043	57.1569595	70.9772952	90.4244817	96.3474827
20.0604839	100	90.7258065	26.3104839	55.6451613	78.3266129	90.4233871	92.5403226
	100	85.3911405					
	100	95.4864594					
	100	89.2787524					
	100	82.6086957					
	100	81.7796611					
	100	78.9699571					
	100	83.0832196					
	100	75.4789272					
	100	92.4437299					
	100	79.9311927					
	100	88.7978142					
	100	79.3710692					
	100	60.0585938					
	100	65.2173913					
	100	61.6533865					
	100	90.8756748					
	100	88.0025911					
	100	94.4332661					

	100	89.1218876					
	100	94.3396226					
	100	79.6730632					
	100	81.7912659					
	100	80.1101171					
	100	82.0138889					
	100	80.8374734					
	100	82.7191868					
	100	83.6294414					
	100	83.1432189					
	100	82.7191867					
	100	83.6294417					
	100	83.1432193					
	100	90.8756748					
	100	88.0025911					
	100	89.1218876					
	100	94.4332661					

SH-SY5Y Cells Pretreatment of Compound 14b Aβ MTS Data

Control	Aβ	100	50	10	1	0.1
100	94.4664031					
100	89.1411648					
100	90.7258065					
100	85.3911405					
100	95.4864594					
100	89.2787524					
100	82.6086957					
100	81.7796611					
100	78.9699571					
100	83.0832196	79.3997271	83.9017735	78.5811732	81.3096862	84.5839017
100	75.4789272	69.348659	79.6934866	79.6934866	82.247765	87.4840358
100	92.4437299	77.6527331	93.2475884	100.803859	103.054662	109.163987
100	79.9311927					
100	88.7978142					
100	79.3710692					
100	60.0585938					
100	65.2173913					
100	61.6533865					
100	90.8756748					
100	88.0025911					
100	94.4332661					

100	89.1218876					
100	94.3396226					
100	79.6730632					
100	81.7912659					
100	80.1101171					
100	82.0138889					
100	80.8374734					
100	82.7191868					
100	83.6294414					
100	83.1432189					
100	82.7191867					
100	83.6294417					
100	83.1432193					
100	90.8756748	88.4262001	80.4041539	96.9993424	100.91851	97.3668426
100	88.0025911	89.6887118	91.8287867	101.297014	106.485062	109.07907
100	89.1218876	83.7403585	85.4113086	90.8740386	90.2313663	91.2596441
100	94.4332661					

SH-SY5Y Cells Pretreatment of Compound 14c Aβ MTS Data

Control	Aβ	100	50	10	1	0.1
100	94.4664031					
100	89.1411648					
100	90.7258065					
100	85.3911405					
100	95.4864594					
100	89.2787524					
100	82.6086957					
100	81.7796611					
100	78.9699571					
100	83.0832196	73.260573	67.8035471	79.9454297	84.856753	88.8130968
100	75.4789272	52.4904214	70.881226	76.8837803	79.8212005	85.3128991
100	92.4437299	83.9228296	83.6012862	95.3376206	95.3376206	106.109325
100	79.9311927					
100	88.7978142					
100	79.3710692					
100	60.0585938					
100	65.2173913					
100	61.6533865					
100	90.8756748					
100	88.0025911					
100	94.4332661					

100	89.1218876					
100	94.3396226					
100	79.6730632					
100	81.7912659					
100	80.1101171					
100	82.0138889					
100	80.8374734					
100	82.7191868					
100	83.6294414					
100	83.1432189					
100	82.7191867					
100	83.6294417					
100	83.1432193					
100	90.8756748	76.9748873	89.5897034			
100	88.0025911	82.8793708	88.2619919	88.4565451	100.129695	96.4980529
100	89.1218876	66.6452419	95.8868889	97.0437052	93.5732665	96.1439559
100	94.4332661					

SH-SY5Y Cells Pretreatment of Compound 14d Aβ MTS Data

Control	Aβ	100	50	10	1	0.1
100	94.4664031					
100	89.1411648					
100	90.7258065					
100	85.3911405					
100	95.4864594					
100	89.2787524					
100	82.6086957					
100	81.7796611					
100	78.9699571					
100	83.0832196					
100	75.4789272					
100	92.4437299					
100	79.9311927	53.2110092	75.5733945	76.0321101	83.9449541	78.5550459
100	88.7978142	51.0928962	86.2021858	91.3934426	92.3497268	93.715847
100	79.3710692	50.4402516	77.4842767	83.7735849	84.654088	82.2641509
100	60.0585938					
100	65.2173913					
100	61.6533865					
100	90.8756748					
100	88.0025911					
100	94.4332661					

100	89.1218876					
100	94.3396226					
100	79.6730632					
100	81.7912659					
100	80.1101171					
100	82.0138889					
100	80.8374734					
100	82.7191868					
100	83.6294414					
100	83.1432189					
100	82.7191867					
100	83.6294417					
100	83.1432193					
100	90.8756748					
100	88.0025911	104.245974	97.1449488	110.322109	113.250366	
100	89.1218876	86.8283097	91.0222808	108.256881	91.1533425	107.470512
100	94.4332661	96.042924	82.830315	82.3608315	86.3849764	92.8236081

SH-SY5Y Cells Pretreatment of Compound 14e Aβ MTS Data

Control	Aβ	100	50	10	1	0.1
100	94.4664031					
100	89.1411648					
100	90.7258065					
100	85.3911405					
100	95.4864594					
100	89.2787524					
100	82.6086957					
100	81.7796611					
100	78.9699571					
100	83.0832196					
100	75.4789272					
100	92.4437299					
100	79.9311927	86.6972477	82.5688073	77.4082569	84.4036697	83.2568807
100	88.7978142	88.6612022	101.775956	92.3497268	94.8087432	96.7213115
100	79.3710692	85.5345912	86.4150943	85.0314465	90.1886792	91.9496855
100	60.0585938					
100	65.2173913					
100	61.6533865					
100	90.8756748					
100	88.0025911					
100	94.4332661					

100	89.1218876					
100	94.3396226					
100	79.6730632					
100	81.7912659					
100	80.1101171					
100	82.0138889					
100	80.8374734					
100	82.7191868					
100	83.6294414					
100	83.1432189					
100	82.7191867					
100	83.6294417					
100	83.1432193					
100	90.8756748					
100	88.0025911	95.6076135	99.9267936	103.147877	93.7042459	
100	89.1218876	92.1363044	80.0131065	79.9475756	83.5517696	88.3355181
100	94.4332661	84.7753184	85.4460092	93.4942989	88.9336014	100.469483