Supporting Information

Discovery and development of small-molecule inhibitors of glycogen synthase

Buyun Tang[1], Mykhaylo S. Frasinyuk[2,3], Vimbai M. Chikwana[1], Krishna K. Mahalingan[1], Cynthia A. Morgan[1], Dyann M. Segvich[1], Svitlana P. Bondarenko[3], Galyna P. Mrug[2,3], Przemyslaw Wyrebek[4], David S. Watt[4-6], Anna A. DePaoli-Roach[1], Peter J. Roach[1] and Thomas D. Hurley[1]*

[1]Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, Indiana 46202, United States; [2]V. P. Kukhar Institute of Bioorganic Chemistry and Petrochemistry, NAS of Ukraine, Kyiv 02094, Ukraine; [3]National University of Food Technologies, Kyiv 01601, Ukraine; [4]Department of Molecular and Cellular Biochemistry, University of Kentucky, Lexington, Kentucky 40506, United States; [5]Center for Pharmaceutical Research and Innovation, College of Pharmacy, University of Kentucky, Lexington, Kentucky 40536, United States; [6]Lucille Parker Markey Cancer Center, University of Kentucky, Lexington, Kentucky 40536, United States

*Email: thurley@iupui.edu

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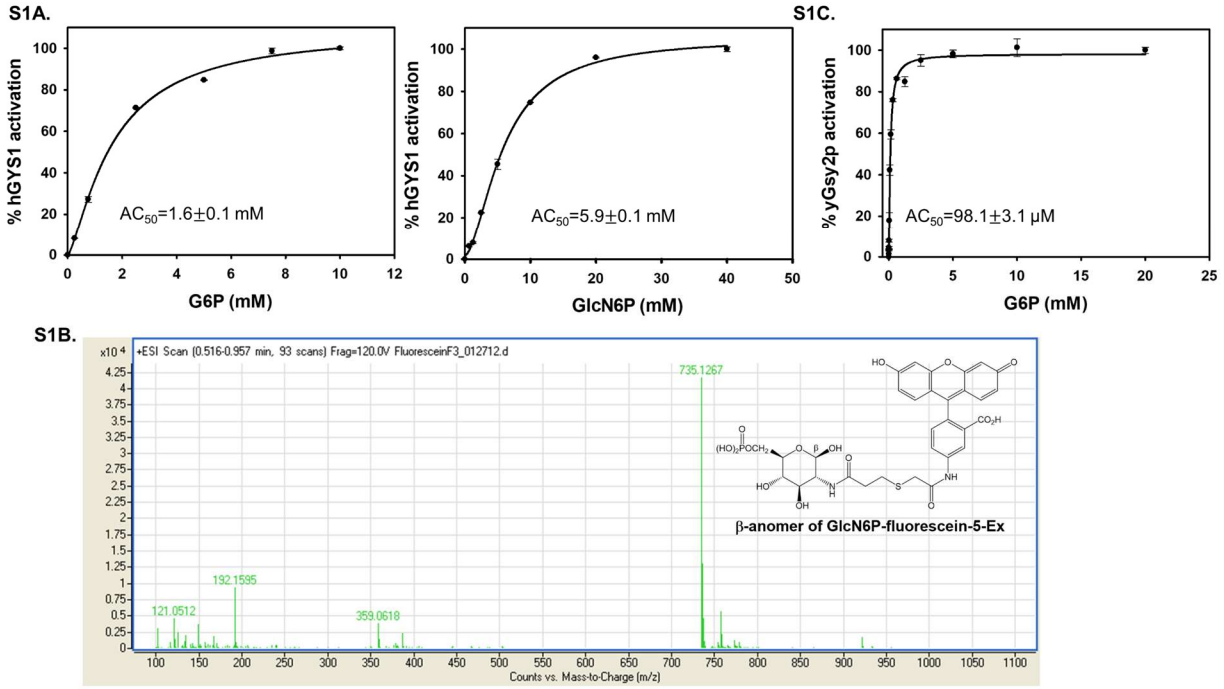


Figure S1. Validation of fluorescence polarization assay. (A) Human GYS1 activation in the presence of varying concentrations of G6P or GlcN6P. The half maximal activation (AC50) of G6P or GlcN6P was determined as 1.6 ± 0.1 and 5.9 ± 0.1 mM, respectively. Averages of triplicate assays ± SEM are shown. (B) The HPLC-purified product of fluorophore coupling reaction was confirmed by mass spectrometry demonstrating *m/z* of 735.1267. (C) Yeast Gsy2p activation in the presence of varying concentrations of G6P. AC50 was determined as 98.1 ± 3.1 µM. Averages of triplicate assays ± SEM are shown. These kinetic analyses are representative experiments from at least three independent experiments.

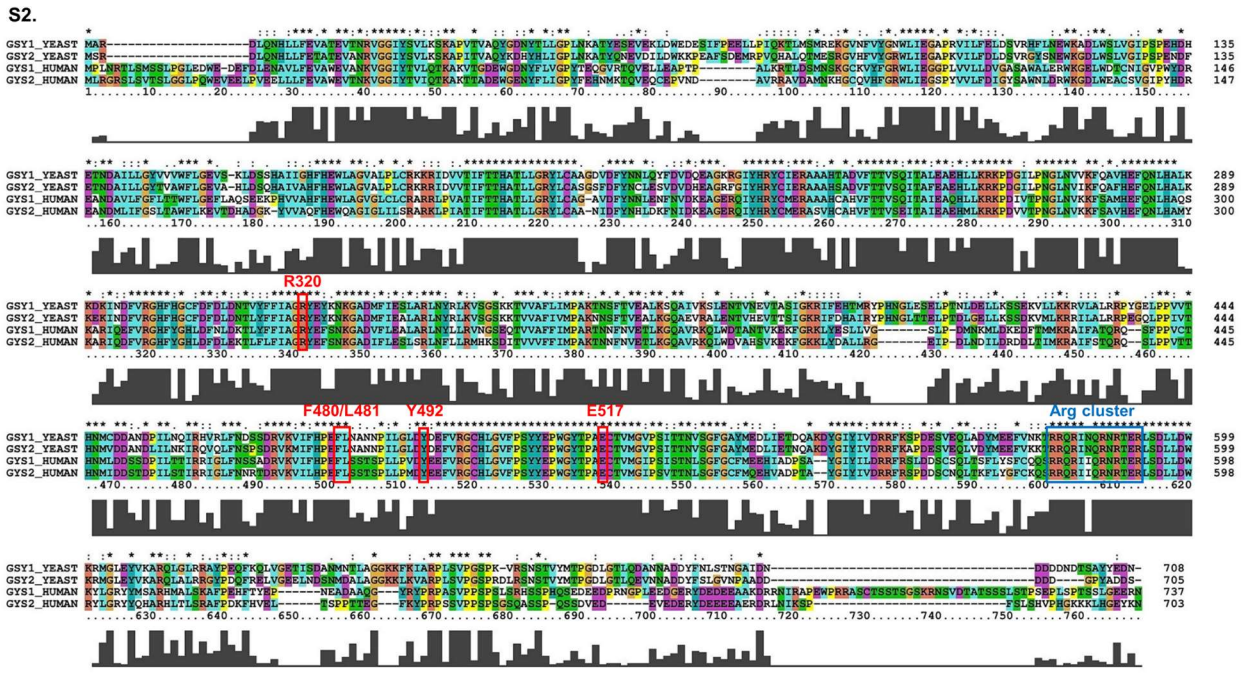


Figure S2. Sequence alignment of yeast and human glycogen synthase. The overall sequence identity between yGsy2p and hGYS1 is around 55%. Residues that form the active site, including R320/F480/L481/Y492/E517 (shown in red box), and G6P binding site (Arg cluster, shown in blue box) are highly conserved across yeast and human species. The sequence alignment was generated using ClustalX.

S3.

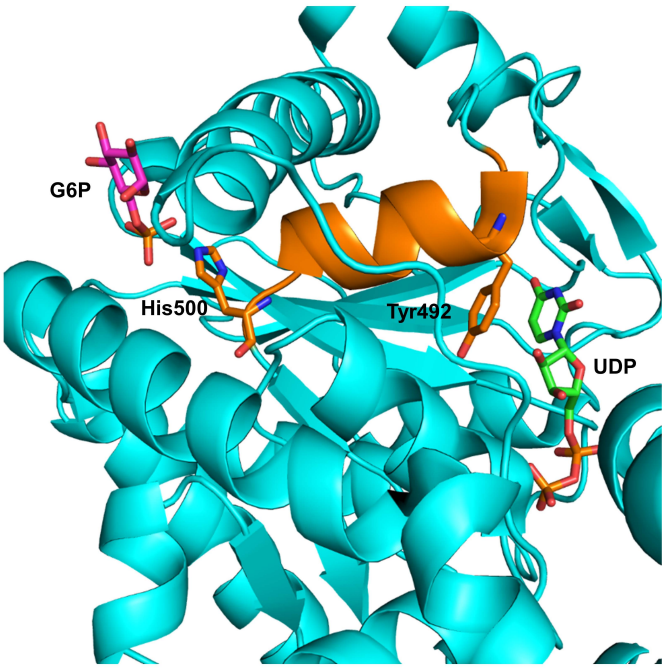
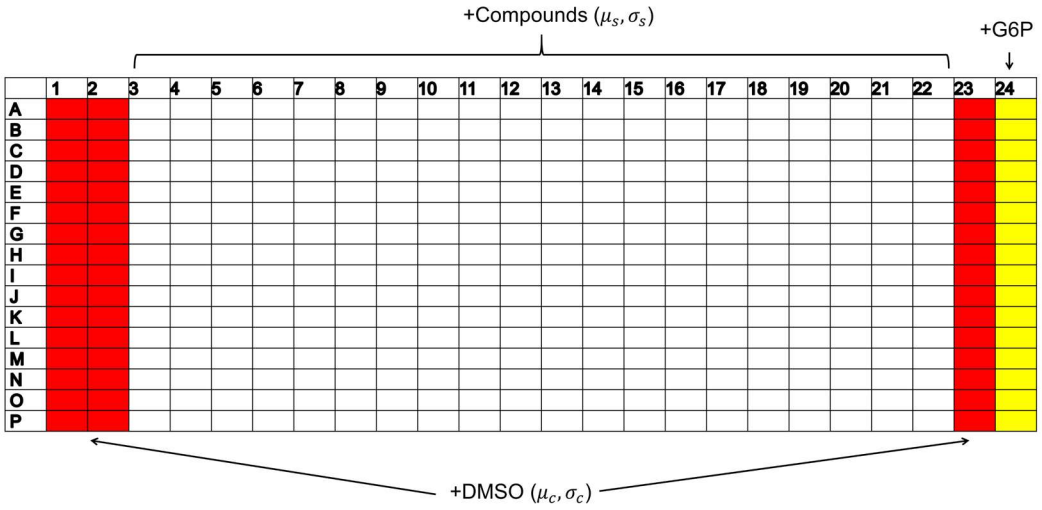


Figure S3. Structural overview of the binding sites for allosteric activator G6P and UDP. The UDP and G6P binding sites lie on opposing ends of the same alpha-helix (orange), with Tyr492 contacting the uracil ring of UDP (green) and His500 contacting the phosphate of G6P (magenta).

Table S1. Small molecule screening data

Category	Parameter	Description
Assay	Type of assay	In vitro
	Target	Gsy2, Saccharomyces cerevisiae
	Primary measurement	Detection of fluorescence polarization
	Key reagents	Purified yeast synthase Gsy2p (3 μM), synthesized and purified fluorophore GlcN6P-fluorescein-5-Ex (20 nM)
	Assay protocol	The fluorescence polarization (FP) experiments were described in methods.
Library	Library size	50,000
	Library composition	The Library is selected from ChemBridge's EXPRESSPick Collection stock of more than 480,000 handcrafted compounds.
	Source	ChemBridge Corporation
Screen	Format	384-well plate
	Concentration tested	10 μM, 1.2 % DMSO
	Plate controls	For the negative controls 10 μL of DMSO (6%) was added and for the positive controls 10 μL of G6P was added for a final concentration of 2 mM to 40 μL reaction mixture in a 384-well plate.
	Reagent/compound dispensing system	Multi-drop 384 liquid dispenser (Titertek)
	Detection instrument	EnVision® Multilabel plate reader (PerkinElmer)
Post-HTS analysis	Assay validation/QC	Plate corrected individual Z'-scores
	Hit criteria	Z'-score threshold of -1, equivalent to a separation of 3 standard deviations between μ_c (means of the control signal) and μ_s (means of the library sample signal)
	Hit rate	0.23%
	Additional assay(s)	Hits were validated using standard ^{14}C-glucose incorporation assay against yGsy2p, using 100 μM compounds in triplicate.
	Confirmation of hit purity and structure	LC/MS or NMR

Table S2. HTS plate layout



Assuming $\sigma_c = \sigma_s$, setting Z'= -1,

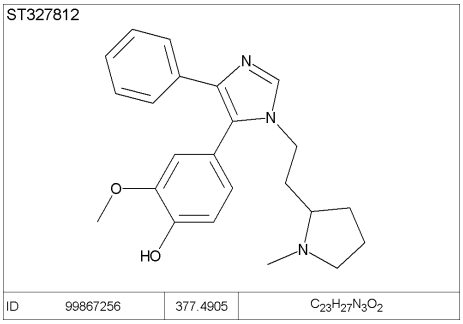
$\because Z' = 1 - \frac{3(\sigma_c+\sigma_s)}{|\mu_c-\mu_s|}$ = -1,

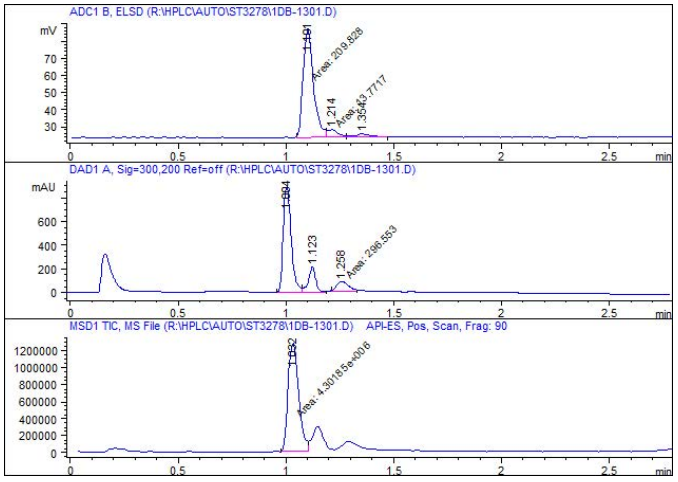
$\therefore \mu_c - \mu_s$=3σ_c.

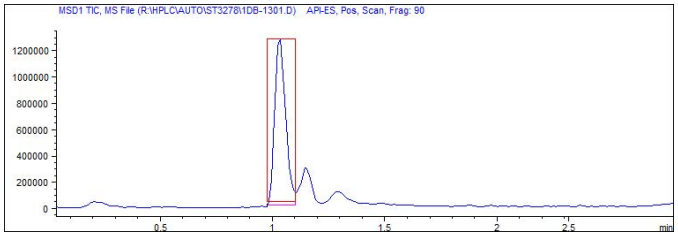
Primary hits were identified if mP < $\mu_c - 3\sigma_c$.

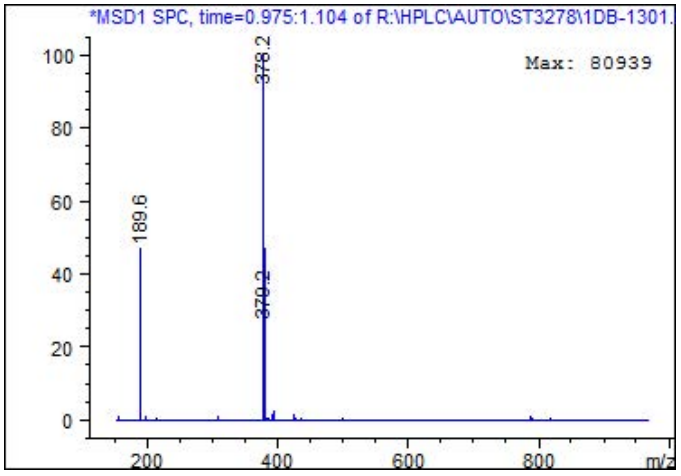
Vendor Supplied Compound Purity

Compound H23 2-methoxy-4-(1-(2-(1-methylpyrrolidin-2-yl)ethyl)-4-phenyl-1H-imidazol-5-yl)phenol









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Column: Onyx C18 50x4.6mm | 3.75ml/min | Columns Reg Valve
Gradient: "A"->@2.2min->"B"(Hold 0.4min)->@0.2min->"A"->PostRun
PMP1, Solvent A : 0.1%TFA, 2.5%AcN in H2O
PMP1, Solvent B : 0.1%TFA in AcN
PMP1, Solvent C : --NOT USED--
PMP1, Solvent D : --NOT USED--
Ionization mode : API-ES Positive

Signal 1: ADC1 B, ELSD

Peak #	RetTime [min]	Type	Width [min]	Area [mV*s]	Height [mV]	Area %
1	1.101	MF	0.0537	209.82787	65.14832	89.8558
2	1.214	FM	0.0556	13.77166	4.12806	5.8975
3	1.354	BB	0.0805	9.91668	1.83537	4.2467
Totals :				233.51620	71.11175	

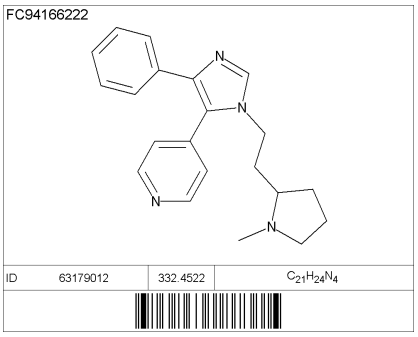
Signal 2: DAD1 A, Sig=300,200 Ref=off

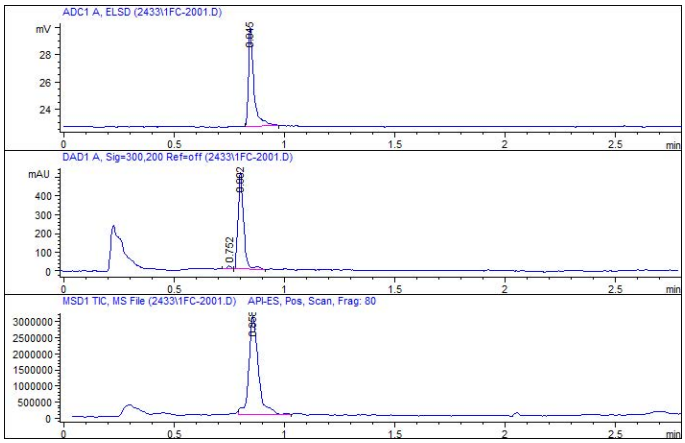
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.004	BV	0.0423	2328.00488	896.85773	74.2856
2	1.123	VB	0.0361	509.29916	211.54639	16.2515
3	1.258	MM	0.0626	296.55338	78.95360	9.4629
Totals :				3133.85742	1187.35771	

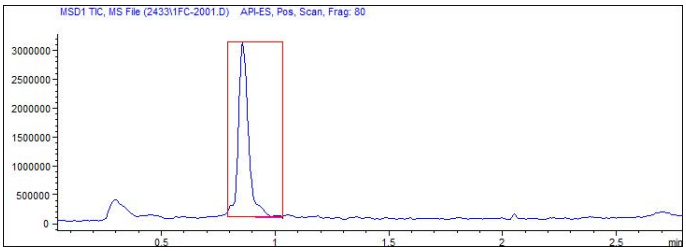
Signal 3: MSD1 TIC, MS File

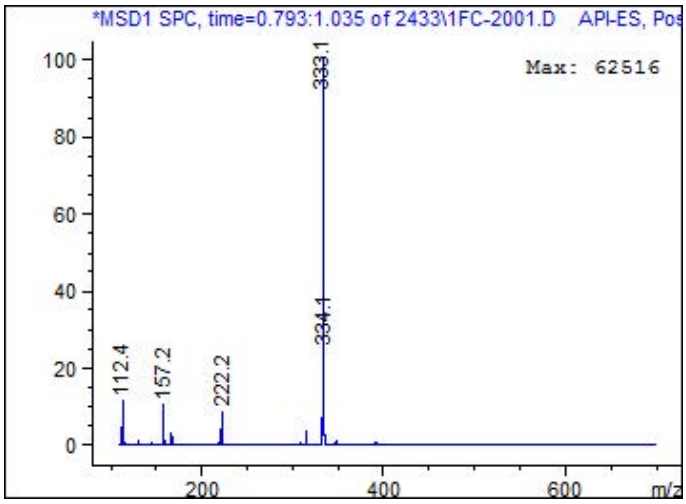
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	1.032	MM	0.0559	4.30185e6	1.28168e6	100.0000
Totals :				4.30185e6	1.28168e6	

Compound 1 4-{1-[2-(1-methylpyrrolidin-2-yl)ethyl]-4-phenyl-1H-imidazol-5-yl}pyridine









Data File D:\DATA\2433\1FC-2001.D
Sample Name: Fc941662P1-F-03
Instrument 1 04/09/2010 00:14:00 #2
Column: Monolithic SpeedROD C18e 50x4.6mm | 3.75ml/min
Gradient: "A"->@2.1min->"B"(Hold 0.8min)->@0.2min->"A"->PostRun
PMP1, Solvent A : 0.1%TFA in MeOH/H2O (2.5:97.5)
PMP1, Solvent B : 0.1% TFA in MeOH
PMP1, Solvent C : 0.1%FA in ACN/H2O (2.5:97.5)
PMP1, Solvent D : 0.1%FA in ACN
Ionization mode : API-ES Positive

Signal 1: ADC1 A, ELSD

Peak #	RetTime [min]	Type	Width [min]	Area [mV*s]	Height [mV]	Area %
1	0.845	PB	0.0266	12.95548	7.32153	100.0000
Totals :				12.95548	7.32153	

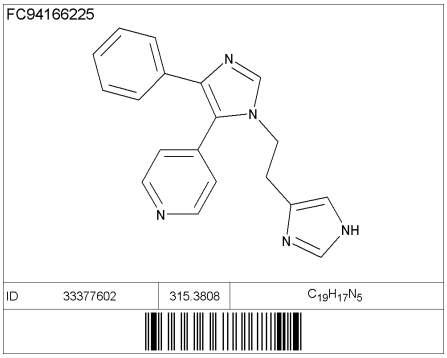
Signal 2: DAD1 A, Sig=300,200 Ref=off

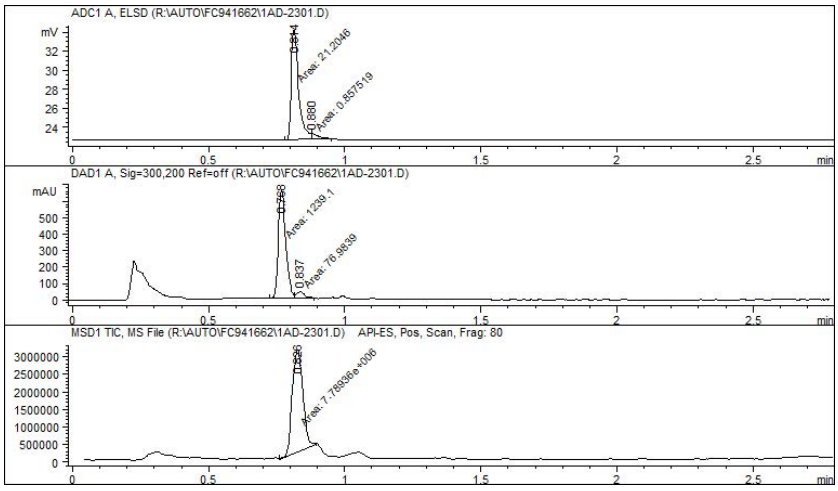
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.752	BV	0.0249	27.03587	17.66420	2.8398
2	0.802	VP	0.0280	925.00928	514.86444	97.1602
Totals :				952.04514	532.52864	

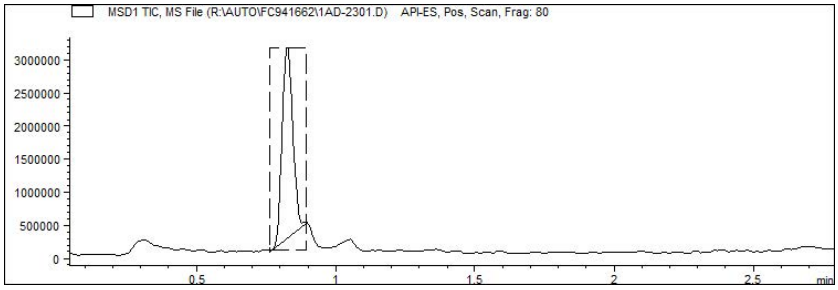
Signal 3: MSD1 TIC, MS File

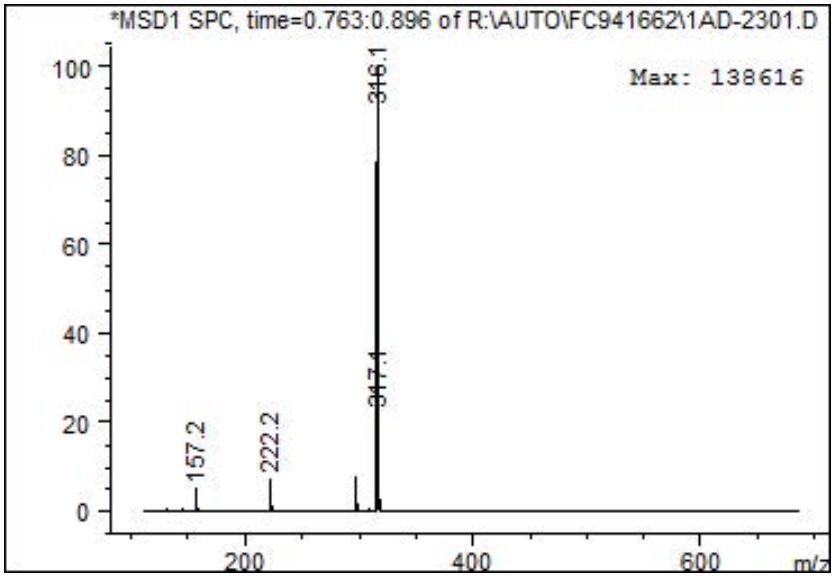
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	0.858	BB	0.0465	9.29456e6	3.04246e6	100.0000
Totals :				9.29456e6	3.04246e6	

Compound 2 4-{1-[2-(1H-imidazol-4-yl)ethyl]-4-phenyl-1H-imidazol-5-yl}pyridine









Data File R:\AUTO\FC941662\1AD-2301.D
Sample Name: Fc941662P1-A-04
Instrument 1 06.09.2010 16:37:40
PMP1, Solvent A : 0.1%TFA in MeOH/H2O (2.5:97.5)
PMP1, Solvent B : 0.1% TFA in MeOH
PMP1, Solvent C : 0.1%FA in ACN/H2O (2.5:97.5)
PMP1, Solvent D : 0.1%FA in ACN
Ionization mode : API-ES Positive

Signal 1: ADC1 A, ELSD

Peak #	RetTime [min]	Type	Width [min]	Area [mV*s]	Height [mV]	Area %
1	0.814	MF	0.0305	21.20461	11.57888	96.1132
2	0.880	FM	0.0252	8.57519e-1	5.67921e-1	3.8868
Totals :				22.06213	12.14680	

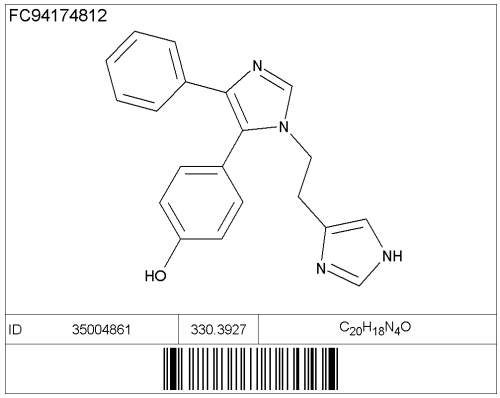
Signal 2: DAD1 A, Sig=300,200 Ref=off

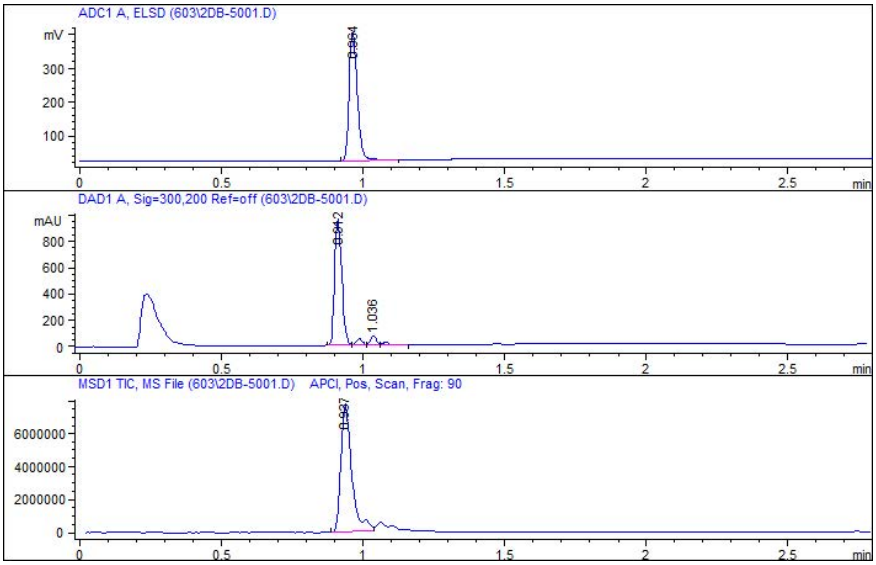
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.768	MF	0.0313	1239.09827	658.82440	94.1505
2	0.837	FM	0.0312	76.98392	41.12902	5.8495
Totals :				1316.08219	699.95342	

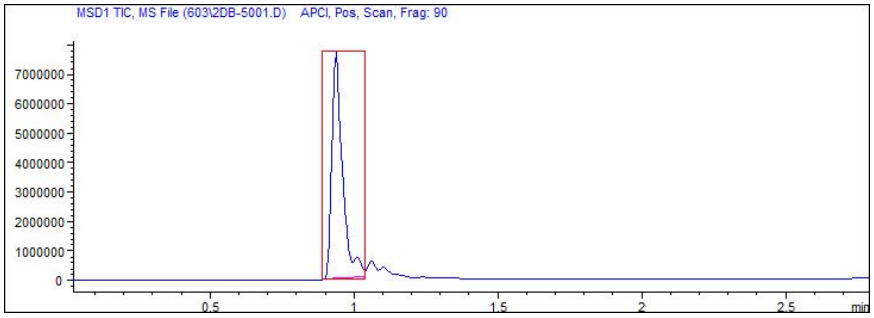
Signal 3: MSD1 TIC, MS File

Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	0.826	MM	0.0442	7.78936e6	2.93575e6	100.0000
Totals :				7.78936e6	2.93575e6	

Compound 3 4-{1-[2-(1H-imidazol-4-yl)ethyl]-4-phenyl-1H-imidazol-5-yl}phenol







Data File D:\DATA\603\2DB-5001.D

Sample Name: Fc941748P2-D-02

Instrument 1 10.09.2010 19:00:13 #6

Column: SpeedROD Rp-18e 50x4.6mm | 3.75ml/min |

Columns Reg Valve

Gradient: "A"->@2.2min->"B"(Hold 0.4min)->@0.2min->"A"->PostRun

PMP1, Solvent A : 0.1%TFA in Acn/H2O (2.5:97.5)

PMP1, Solvent B : 0.1% TFA in AcN

PMP1, Solvent C : 0.1%FA in ACN/H2O (2.5:97.5)

PMP1, Solvent D : 0.1%FA in ACN

Ionization mode : APCI Positive

Signal 1: ADC1 A, ELSD

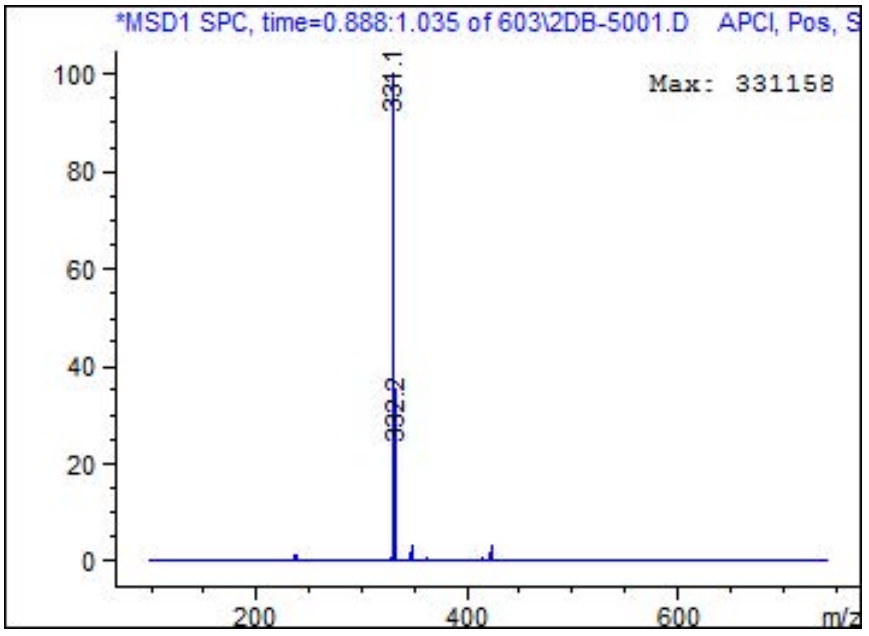
Peak #	RetTime [min]	Type	Width [min]	Area [mV*s]	Height [mV]	Area %
1	0.964	PB	0.0317	768.15430	377.87949	100.0000
Totals :				768.15430	377.87949	

Signal 2: DAD1 A, Sig=300,200 Ref=off

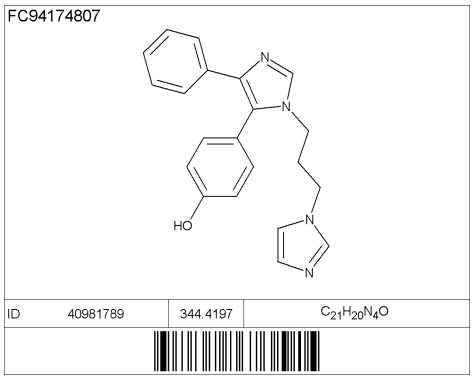
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.912	BV	0.0276	1701.42871	962.96936	88.3473
2	0.987	VV	0.0240	83.76084	54.38354	4.3493
3	1.036	VV	0.0233	104.42519	70.54584	5.4223
4	1.080	VP	0.0258	36.22654	21.31683	1.8811
Totals :				1925.84129	1109.21557	

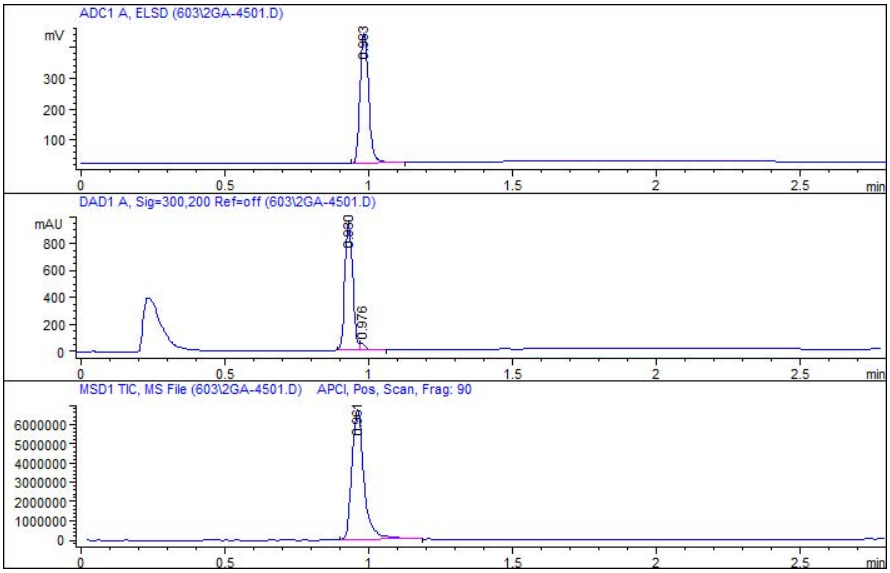
Signal 3: MSD1 TIC, MS File

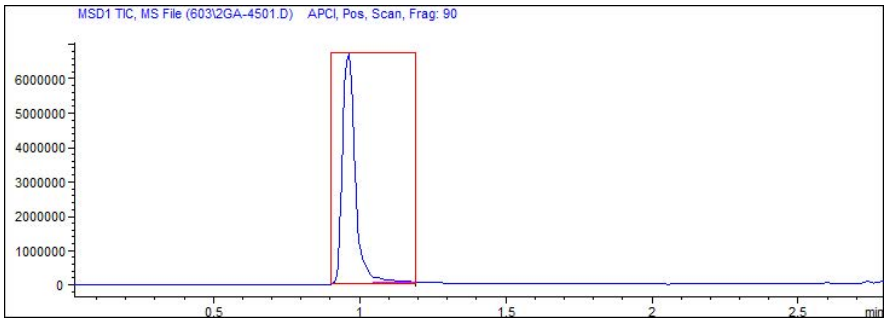
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	0.937	PB	0.0396	2.00729e7	7.70528e6	100.0000
Totals :				2.00729e7	7.70528e6	

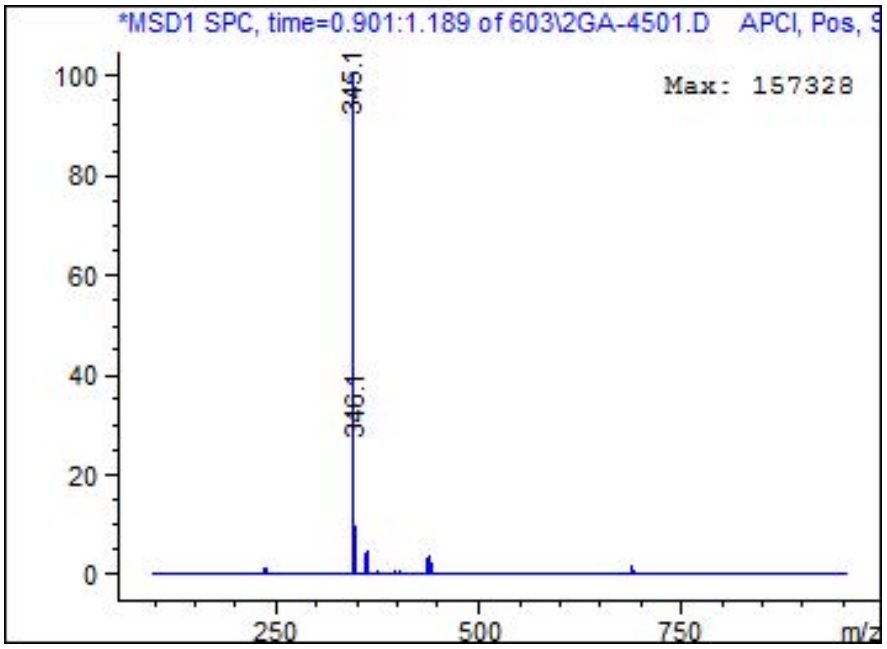


Compound 4 4-{1-[3-(1H-imidazol-1-yl)propyl]-4-phenyl-1H-imidazol-5-yl}phenol









Data File D:\DATA\603\2GA-4501.D

Sample Name: Fc941748P2-G-01

Instrument 1 10.09.2010 18:39:12 #6

Column: SpeedROD Rp-18e 50x4.6mm | 3.75ml/min | Columns Reg Valve

Gradient: "A"->@2.2min->"B"(Hold 0.4min)->@0.2min->"A"->PostRun

PMP1, Solvent A : 0.1%TFA in Acn/H2O (2.5:97.5)

PMP1, Solvent B : 0.1% TFA in AcN

PMP1, Solvent C : 0.1%FA in ACN/H2O (2.5:97.5)

PMP1, Solvent D : 0.1%FA in ACN

Ionization mode : APCI Positive

Signal 1: ADC1 A, ELSD

Peak #	RetTime [min]	Type	Width [min]	Area [mV*s]	Height [mV]	Area %
1	0.983	PB	0.0320	857.73596	417.74936	100.0000
Totals :				857.73596	417.74936	

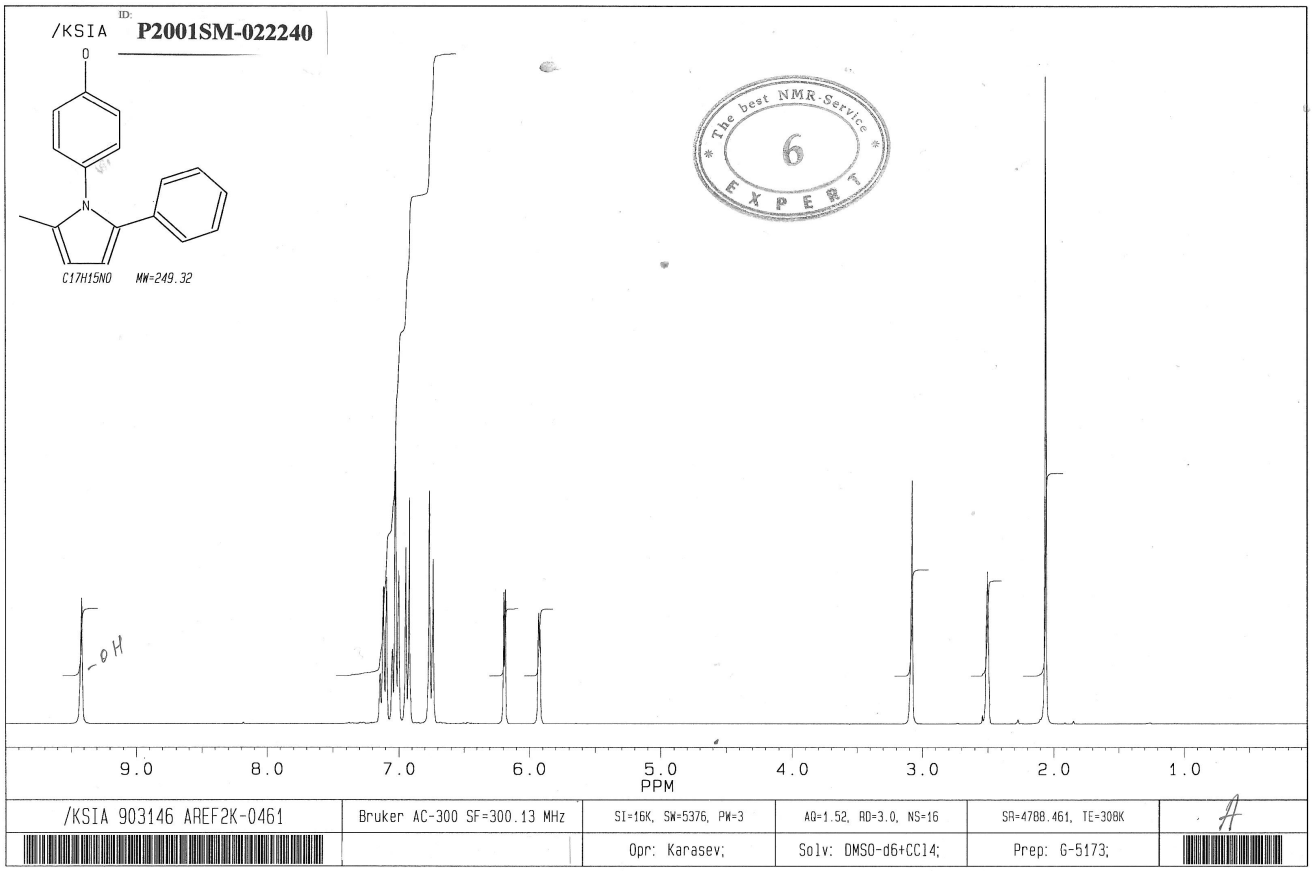
Signal 2: DAD1 A, Sig=300,200 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	0.930	BV	0.0294	1759.64807	958.73767	96.0558
2	0.976	VP	0.0229	72.25453	52.58591	3.9442
Totals :				1831.90260	1011.32358	

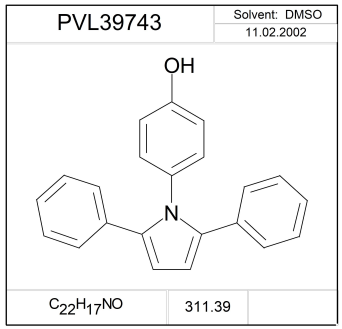
Signal 3: MSD1 TIC, MS File

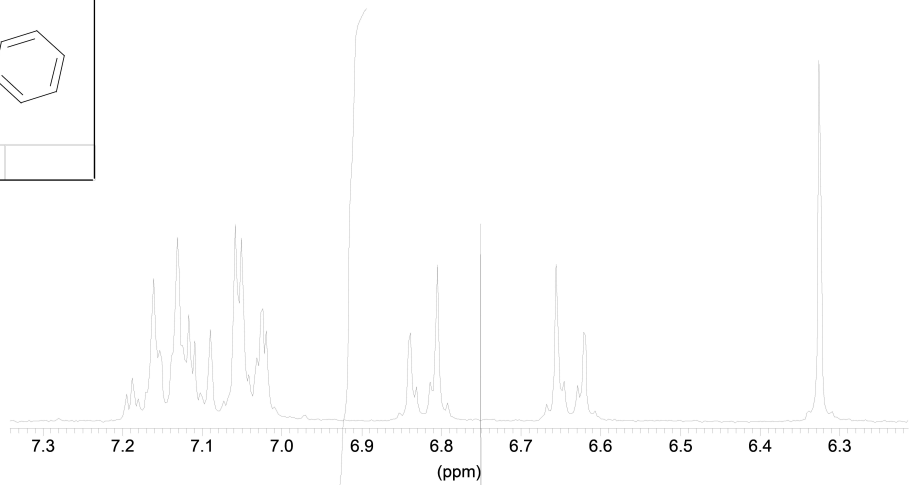
Peak #	RetTime [min]	Type	Width [min]	Area	Height	Area %
1	0.961	PP	0.0464	2.03361e7	6.70778e6	100.0000
Totals :				2.03361e7	6.70778e6	

Compound 5 4-(2-methyl-5-phenyl-1H-pyrrol-1-yl)phenol

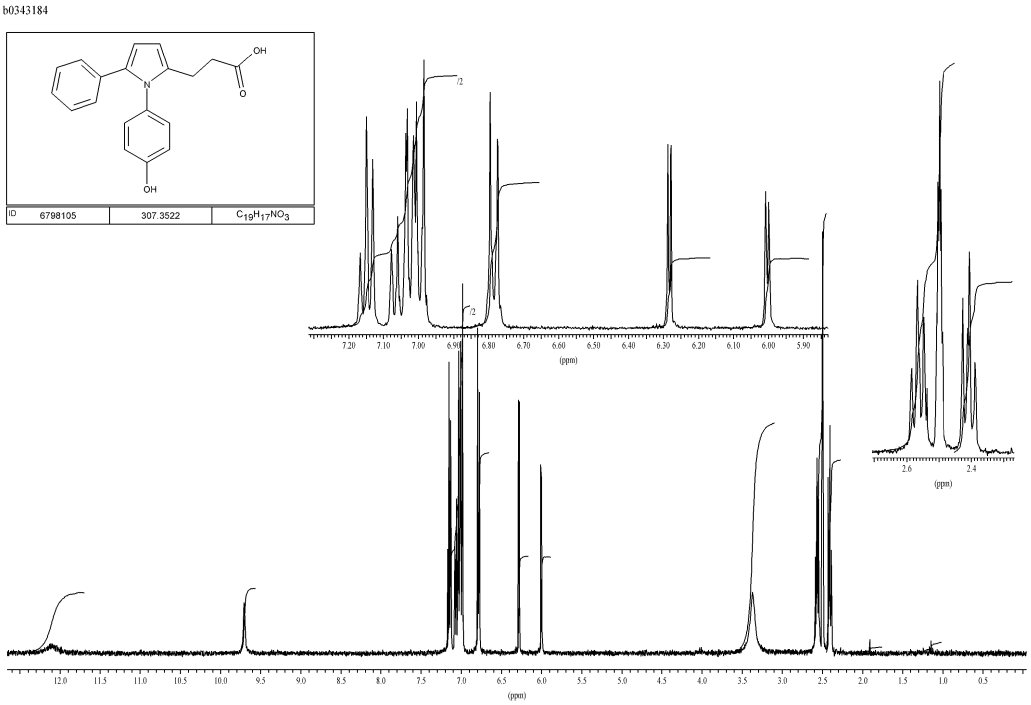


Compound 6 4-(2,5-diphenyl-1H-pyrrol-1-yl)phenol

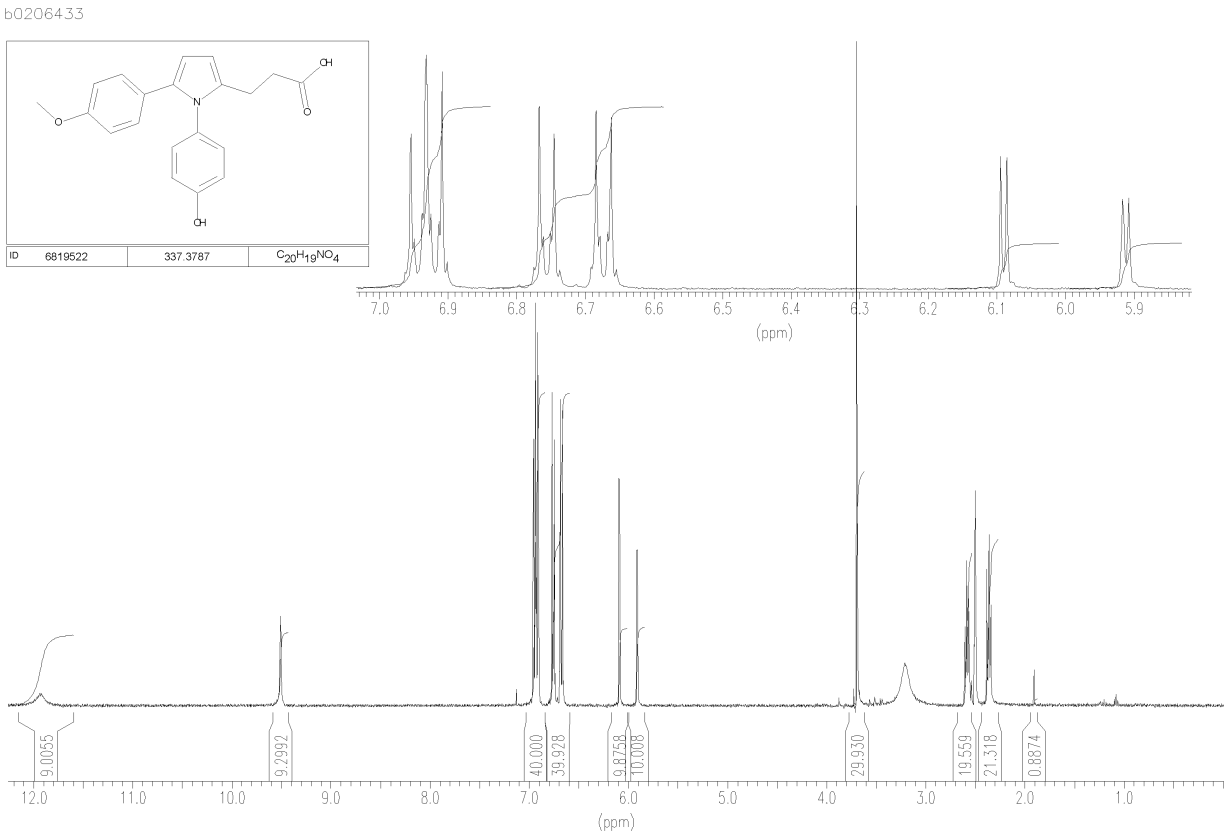




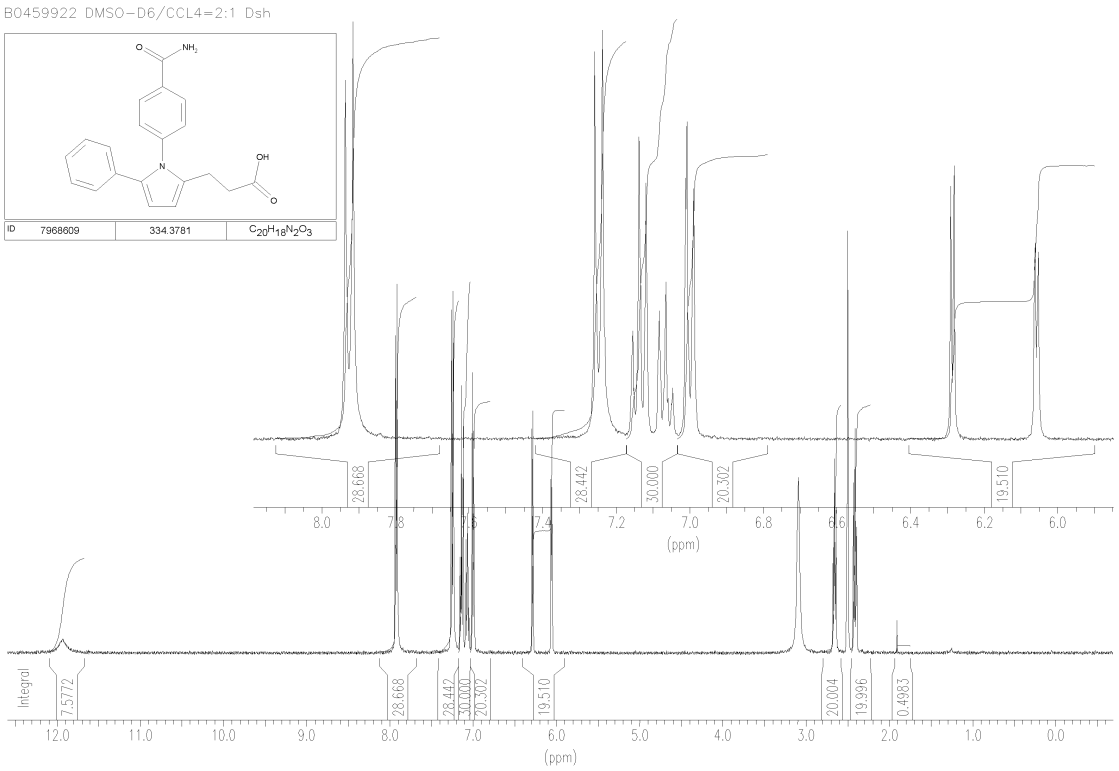
Compound 7 3-[1-(4-hydroxyphenyl)-5-phenyl-1H-pyrrol-2-yl]propanoic acid



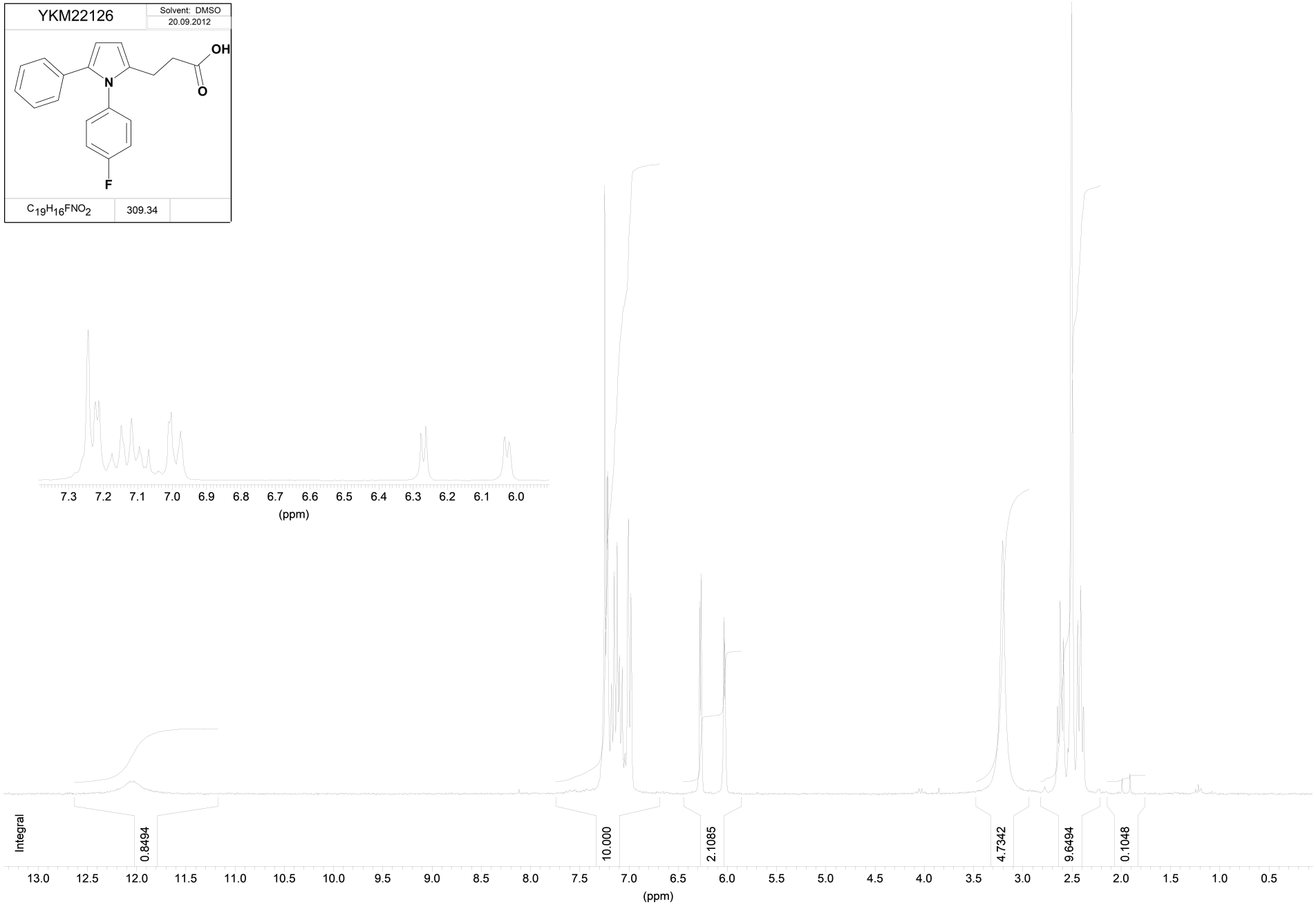
Compound 8 3-(1-(4-hydroxyphenyl)-5-(4-methoxyphenyl)-1H-pyrrol-2-yl)propanoic acid



Compound 9 3-{1-[4-(aminocarbonyl)phenyl]-5-phenyl-1H-pyrrol-2-yl}propanoic acid

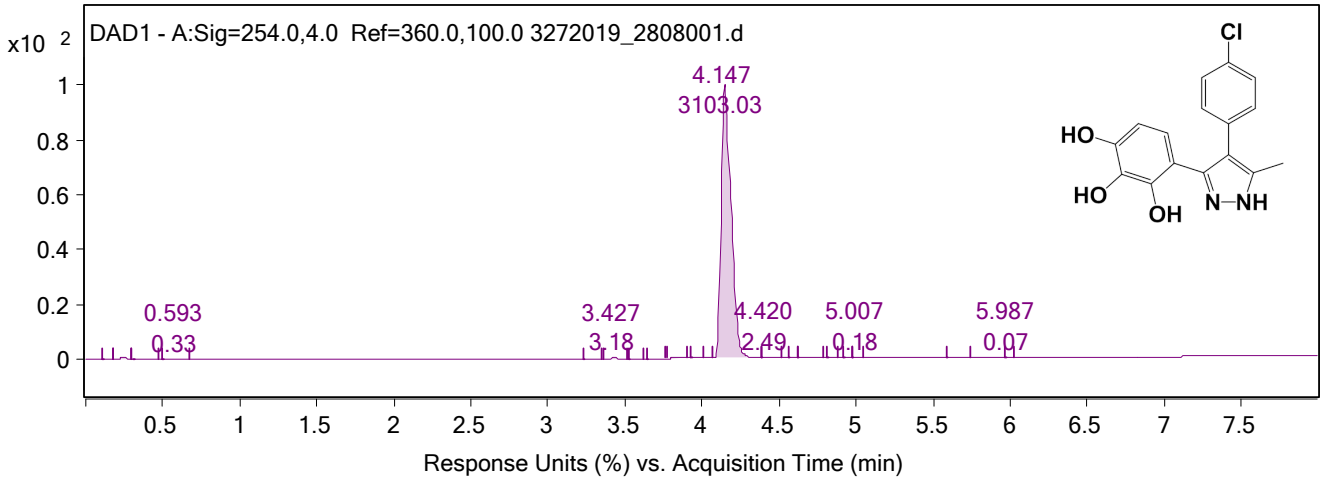


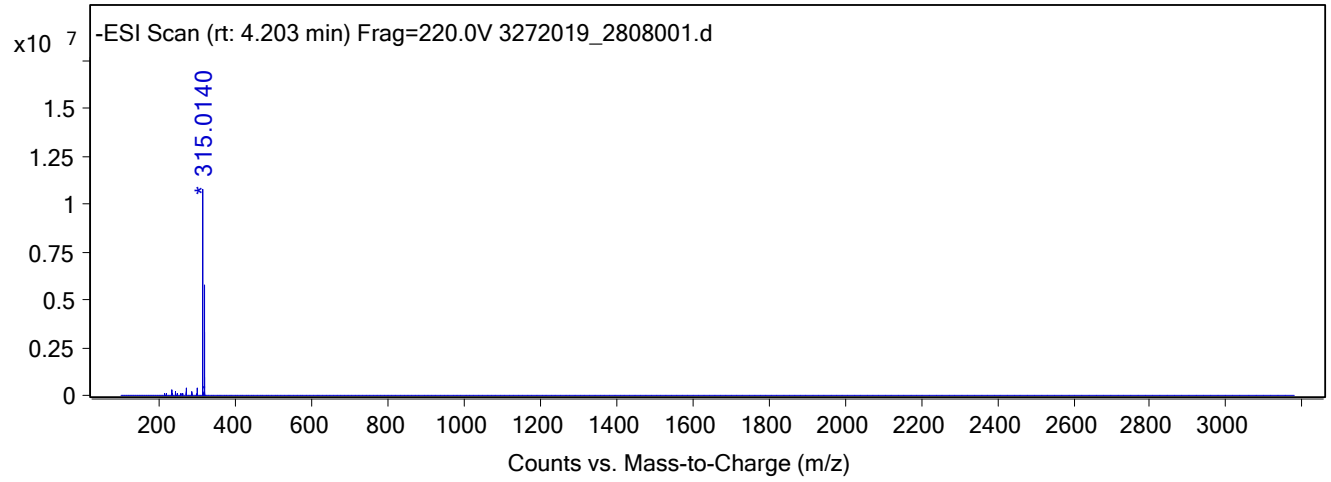
Compound 10 3-(1-(4-fluorophenyl)-5-phenyl-1H-pyrrol-2-yl)propanoic acid



LC/MS and NMR Confirmation of Author Provided Compound Purity

Compound 11 4-(4-(4-chlorophenyl)-5-methyl-1H-pyrazol-3-yl)benzene-1,2,3-triol



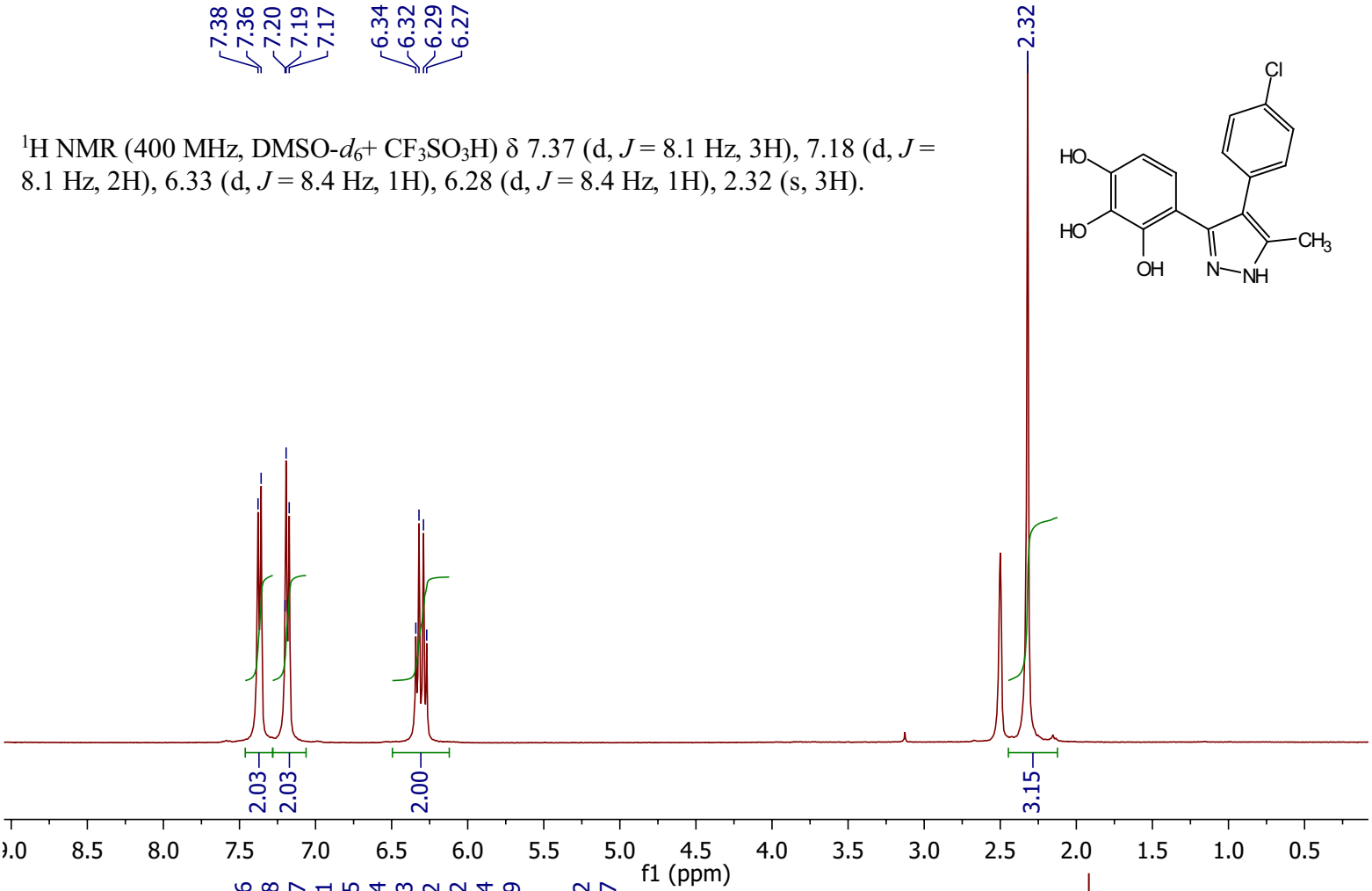


Integration Peak List

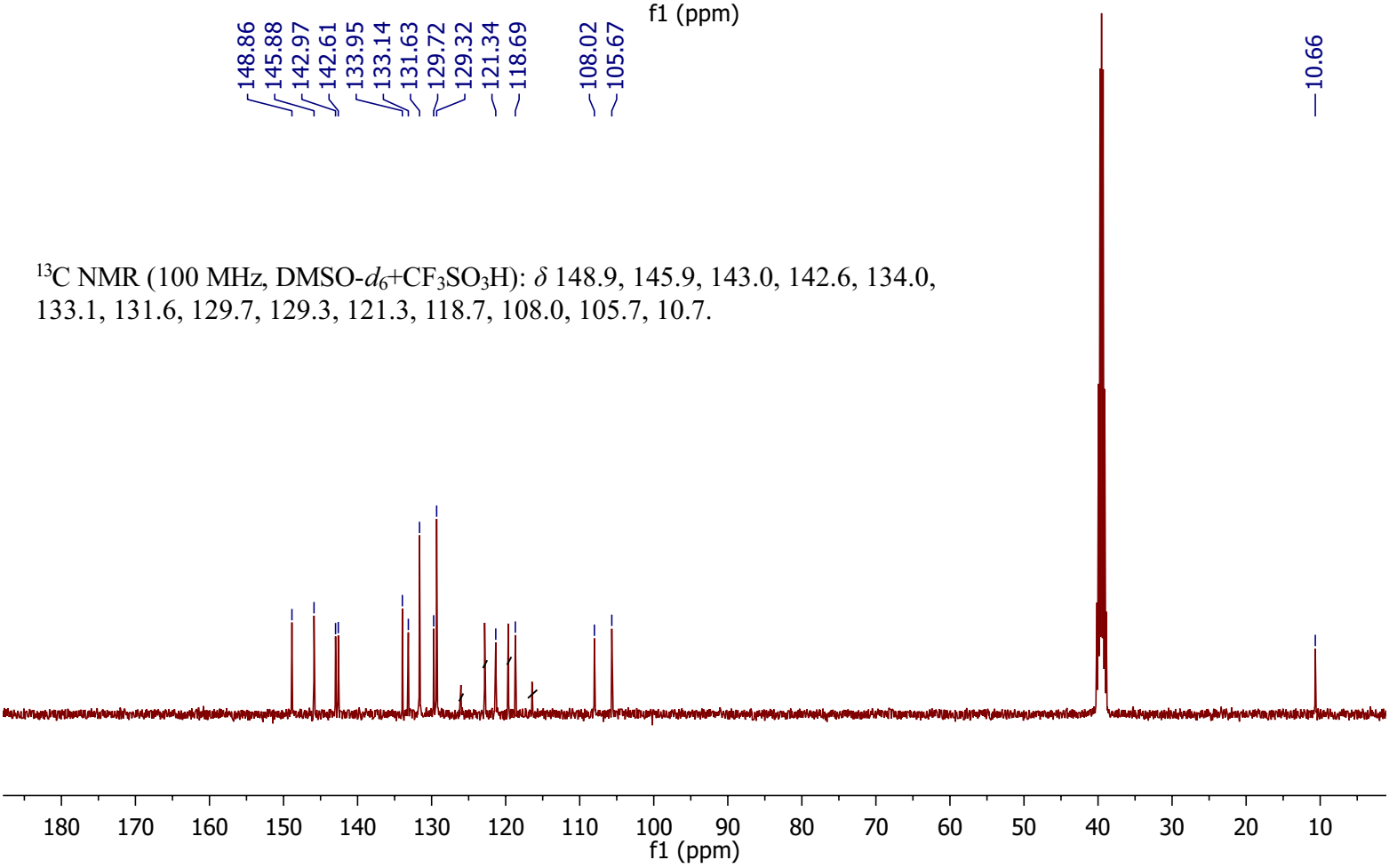
Peak	Start	RT	End	Height	Area	Area %
1	0.107	0.153	0.18	0.05	0.16	0.01
2	0.18	0.247	0.3	7.39	19.61	0.63
3	0.3	0.407	0.473	0.17	1.58	0.05
4	0.493	0.593	0.667	0.05	0.33	0.01
5	3.227	3.287	3.353	0.56	2.16	0.07
6	3.36	3.427	3.513	0.77	3.18	0.1
7	3.52	3.58	3.62	0.07	0.23	0.01
8	3.64	3.74	3.76	0.05	0.57	0.02
9	3.773	3.827	3.907	0.26	1.07	0.03
10	3.927	3.987	4.013	0.07	0.23	0.01
11	4.067	4.147	4.38	685.68	3103.03	100
12	4.38	4.42	4.513	0.69	2.49	0.08
13	4.56	4.613	4.62	0.02	0.17	0.01
14	4.62	4.68	4.787	0.22	0.92	0.03
15	4.813	4.86	4.887	0.03	0.09	0
16	4.92	4.967	4.973	0.05	0.29	0.01
17	4.973	5.007	5.047	0.09	0.18	0.01
18	5.587	5.653	5.74	0.41	1.9	0.06
19	5.967	5.987	6.027	0.05	0.07	0

Peak List

m/z	z	Abund
231.0441		269037.45
241.0264		211992.06
243.0402		190152.64
269.015		371276.01
271.0266		193251.4
297.004		390648.24
315.014	1	11002248.67
316.0132	1	3297760.57
317.0081	1	5859798.24
318.0099	1	991522.15

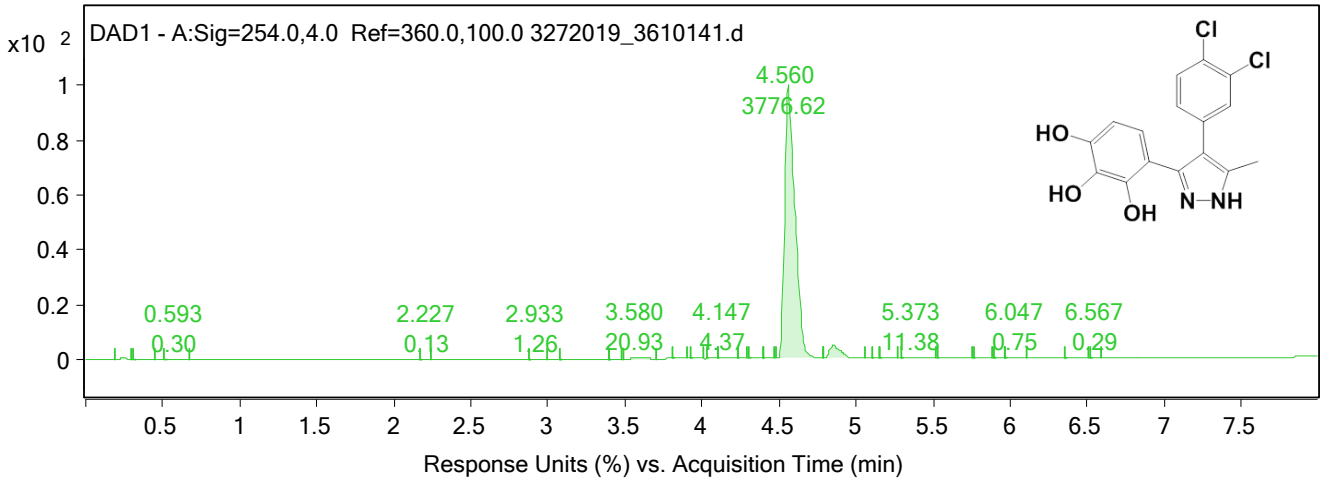


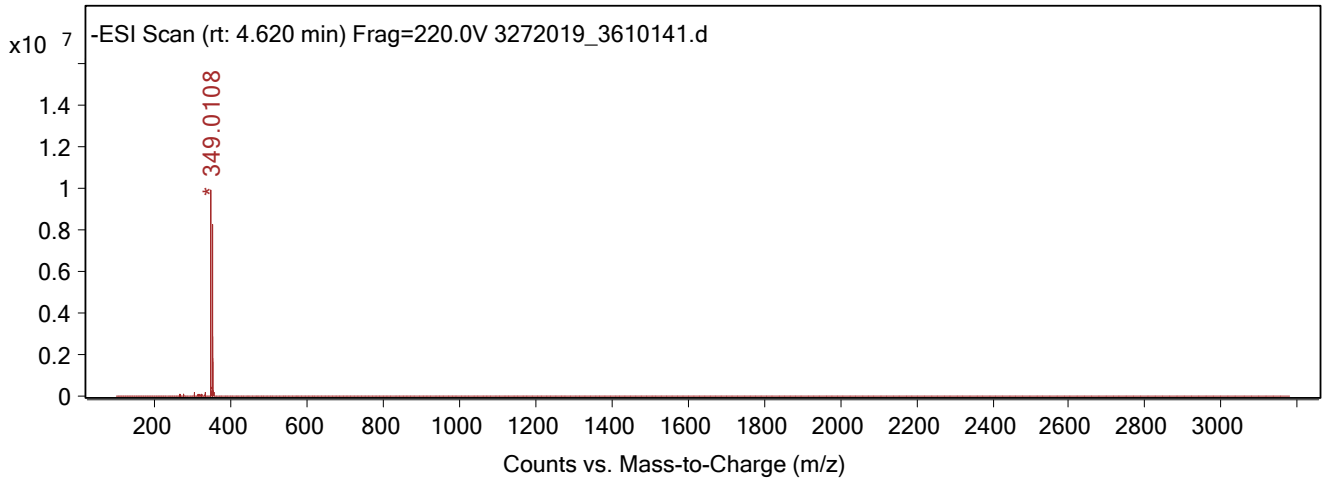
^{1}H NMR (400 MHz, DMSO-d_6+ CF_3SO_3H) δ 7.37 (d, J = 8.1 Hz, 3H), 7.18 (d, J = 8.1 Hz, 2H), 6.33 (d, J = 8.4 Hz, 1H), 6.28 (d, J = 8.4 Hz, 1H), 2.32 (s, 3H).



^{13}C NMR (100 MHz, DMSO-d_6+CF_3SO_3H): δ 148.9, 145.9, 143.0, 142.6, 134.0, 133.1, 131.6, 129.7, 129.3, 121.3, 118.7, 108.0, 105.7, 10.7.

Compound 12 4-(4-(3,4-dichlorophenyl)-5-methyl-1H-pyrazol-3-yl)benzene-1,2,3-triol



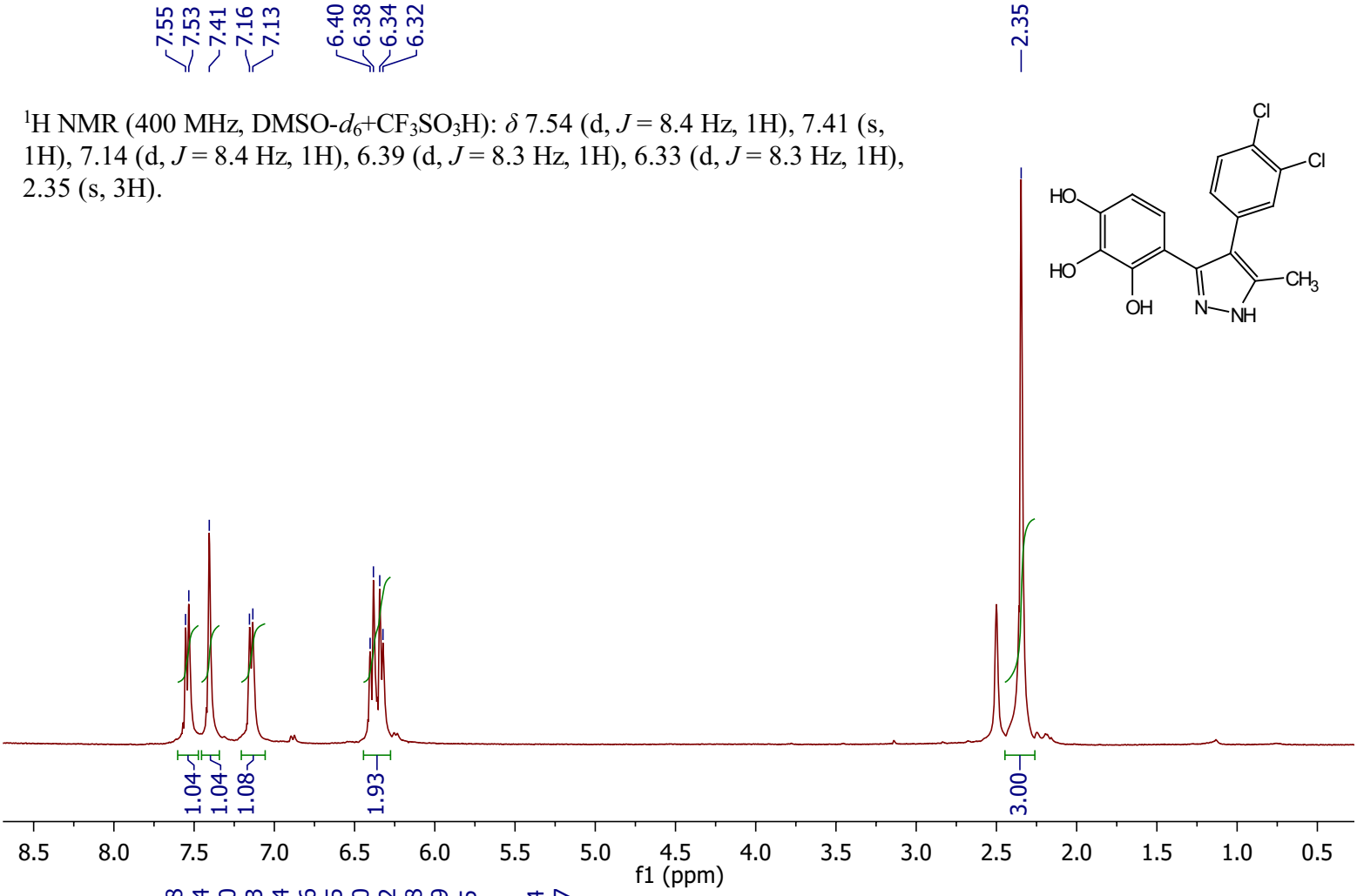


Integration Peak List

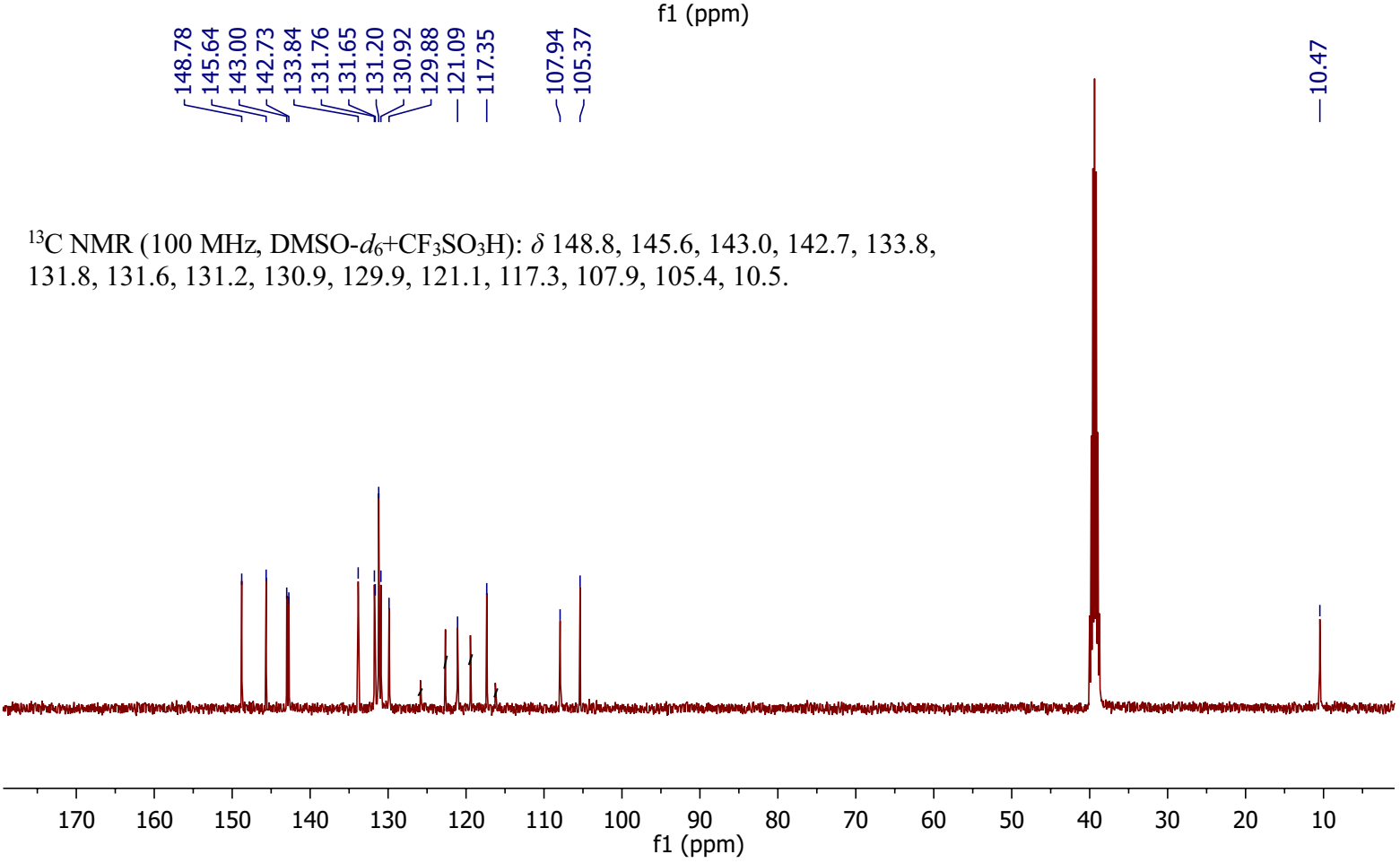
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.3	8.56	22.59	0.6
2	0.307	0.427	0.447	0.06	1.12	0.03
3	0.507	0.593	0.667	0.05	0.3	0.01
4	2.167	2.227	2.24	0.03	0.13	0
5	2.88	2.933	2.993	0.34	1.26	0.03
6	3.08	3.24	3.393	0.55	5.16	0.14
7	3.4	3.453	3.48	0.08	0.29	0.01
8	3.487	3.58	3.7	4.74	20.93	0.55
9	3.807	3.847	3.9	0.72	1.65	0.04
10	3.927	3.967	4.013	0.15	0.38	0.01
11	4.027	4.073	4.1	0.42	1.16	0.03
12	4.1	4.147	4.227	1.23	4.37	0.12
13	4.227	4.26	4.293	0.16	0.32	0.01
14	4.307	4.353	4.393	0.79	2.22	0.06
15	4.393	4.413	4.467	0.17	0.38	0.01
16	4.48	4.56	4.787	819.09	3776.62	100
17	4.787	4.853	5.053	39.34	180.56	4.78
18	5.1	5.147	5.153	0.01	0.1	0
19	5.153	5.193	5.267	0.08	0.28	0.01
20	5.293	5.373	5.513	1.96	11.38	0.3
21	5.527	5.647	5.753	1.36	7.93	0.21
22	5.76	5.84	5.88	0.17	0.68	0.02
23	5.893	5.94	5.96	0.14	0.41	0.01
24	5.967	6.047	6.107	0.21	0.75	0.02
25	6.353	6.413	6.507	0.19	0.76	0.02
26	6.52	6.567	6.593	0.09	0.29	0.01

Peak List

m/z	z	Abund
303.0067		149841.92
330.999		186215.15
332.9958		114189.77
346.9918		150421.24
349.0108	1	10088382.55
350.0103	1	2922728.3
351.0066	1	8262324.06
352.0072	1	1806358.41
353.0019	1	1719293.47
354.0051	1	265719.67

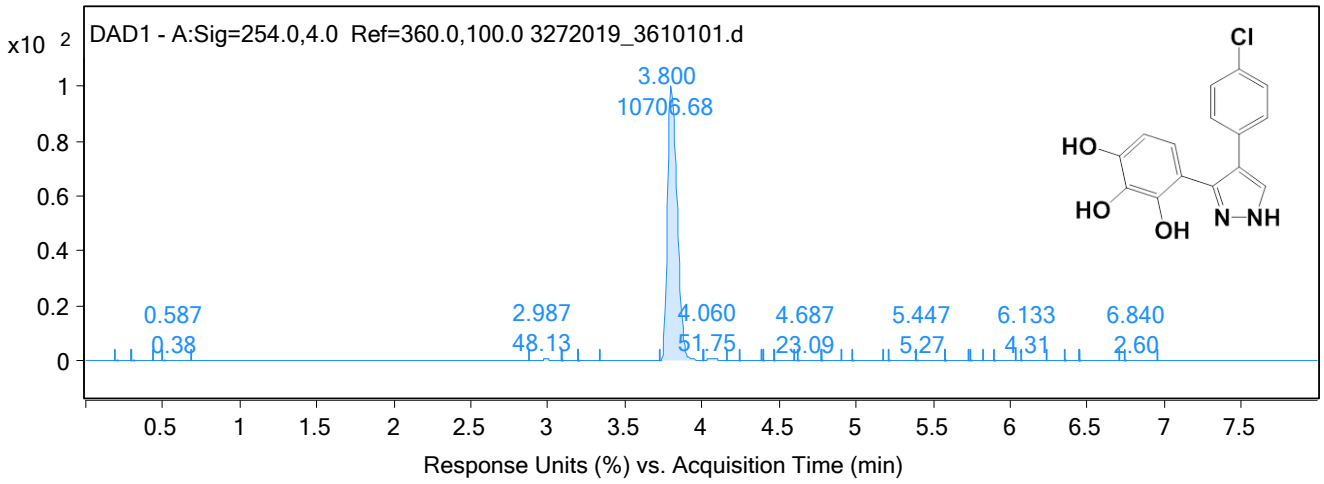


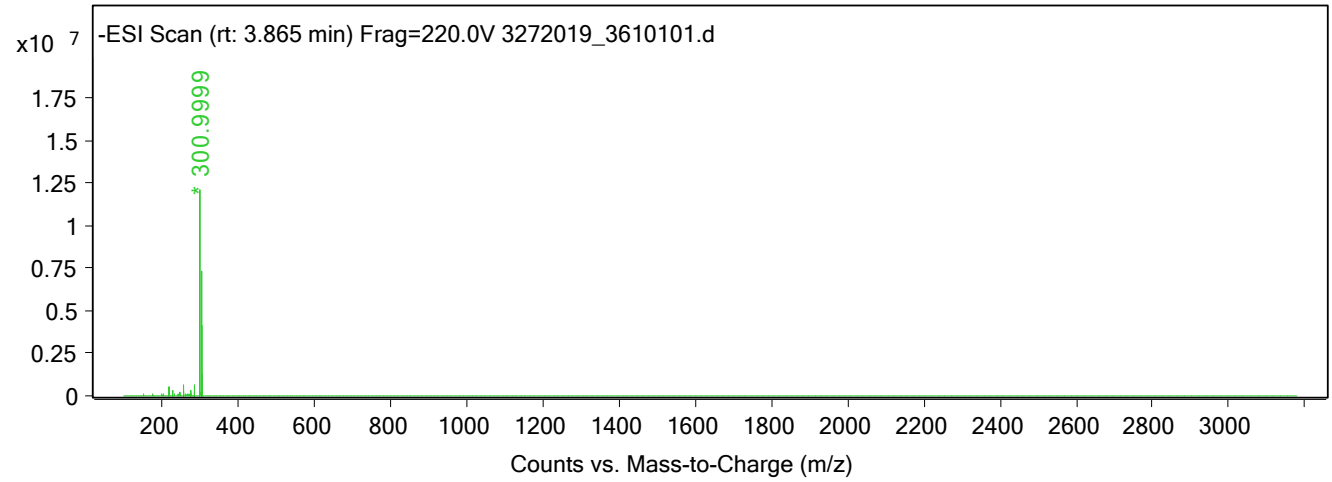
^{1}H NMR (400 MHz, DMSO-d_6+CF_3SO_3H): δ 7.54 (d, J = 8.4 Hz, 1H), 7.41 (s, 1H), 7.14 (d, J = 8.4 Hz, 1H), 6.39 (d, J = 8.3 Hz, 1H), 6.33 (d, J = 8.3 Hz, 1H), 2.35 (s, 3H).



^{13}C NMR (100 MHz, DMSO-d_6+CF_3SO_3H): δ 148.8, 145.6, 143.0, 142.7, 133.8, 131.8, 131.6, 131.2, 130.9, 129.9, 121.1, 117.3, 107.9, 105.4, 10.5.

Compound 13 4-(4-(4-chlorophenyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol



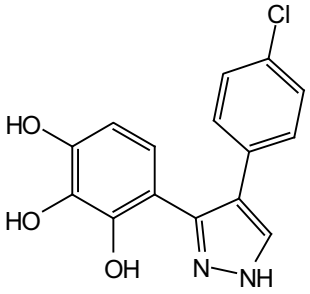


Integration Peak List

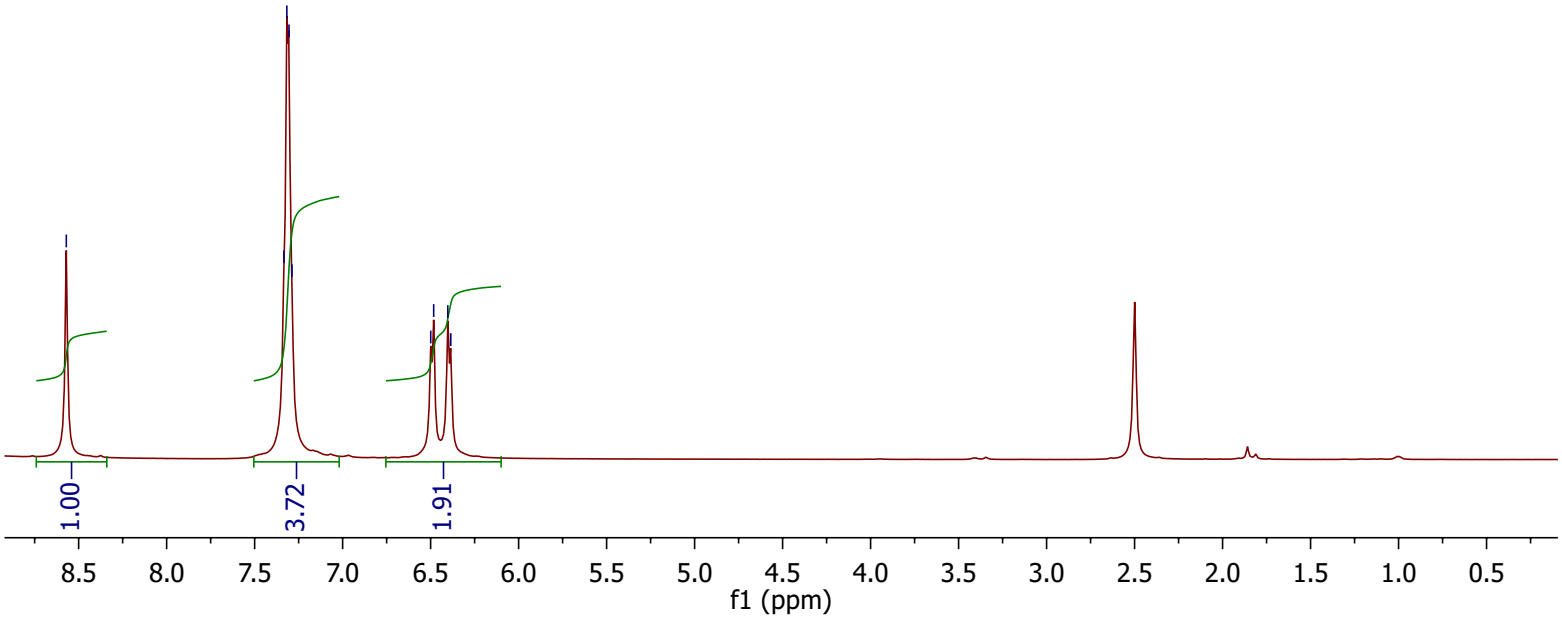
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.3	10.05	26.84	0.25
2	0.3	0.427	0.44	0.04	1.09	0.01
3	0.5	0.587	0.68	0.06	0.38	0
4	2.88	2.987	3.087	13.51	48.13	0.45
5	3.093	3.147	3.2	0.48	1.78	0.02
6	3.2	3.253	3.333	0.74	2.77	0.03
7	3.72	3.8	4.007	2439.48	10706.68	100
8	4.007	4.06	4.167	12.61	51.75	0.48
9	4.24	4.293	4.38	0.34	1.39	0.01
10	4.393	4.44	4.467	1.44	3.97	0.04
11	4.467	4.5	4.6	1.7	5.76	0.05
12	4.627	4.687	4.773	5.83	23.09	0.22
13	4.773	4.813	4.907	1.06	3.39	0.03
14	4.98	5.04	5.173	0.94	4.76	0.04
15	5.213	5.313	5.387	0.33	1.57	0.01
16	5.393	5.447	5.58	1.02	5.27	0.05
17	5.58	5.66	5.727	0.24	1.08	0.01
18	5.747	5.793	5.827	0.24	0.76	0.01
19	5.893	5.947	6.04	0.3	1.29	0.01
20	6.067	6.133	6.233	0.95	4.31	0.04
21	6.353	6.4	6.447	0.09	0.25	0
22	6.453	6.533	6.713	0.36	2.51	0.02
23	6.747	6.84	6.96	0.46	2.6	0.02

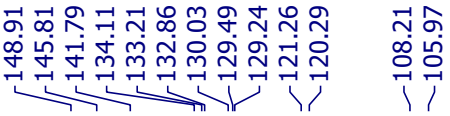
Peak List

m/z	z	Abund
217.0289		538604.84
227.0113		370946.89
229.026		371259.43
254.9999		656336.18
257.0114		346231.5
282.9884		688054.06
300.9999	1	12446481.28
301.9981	1	4232733.55
302.9936	1	7457097.47
303.9947	1	1317845.02

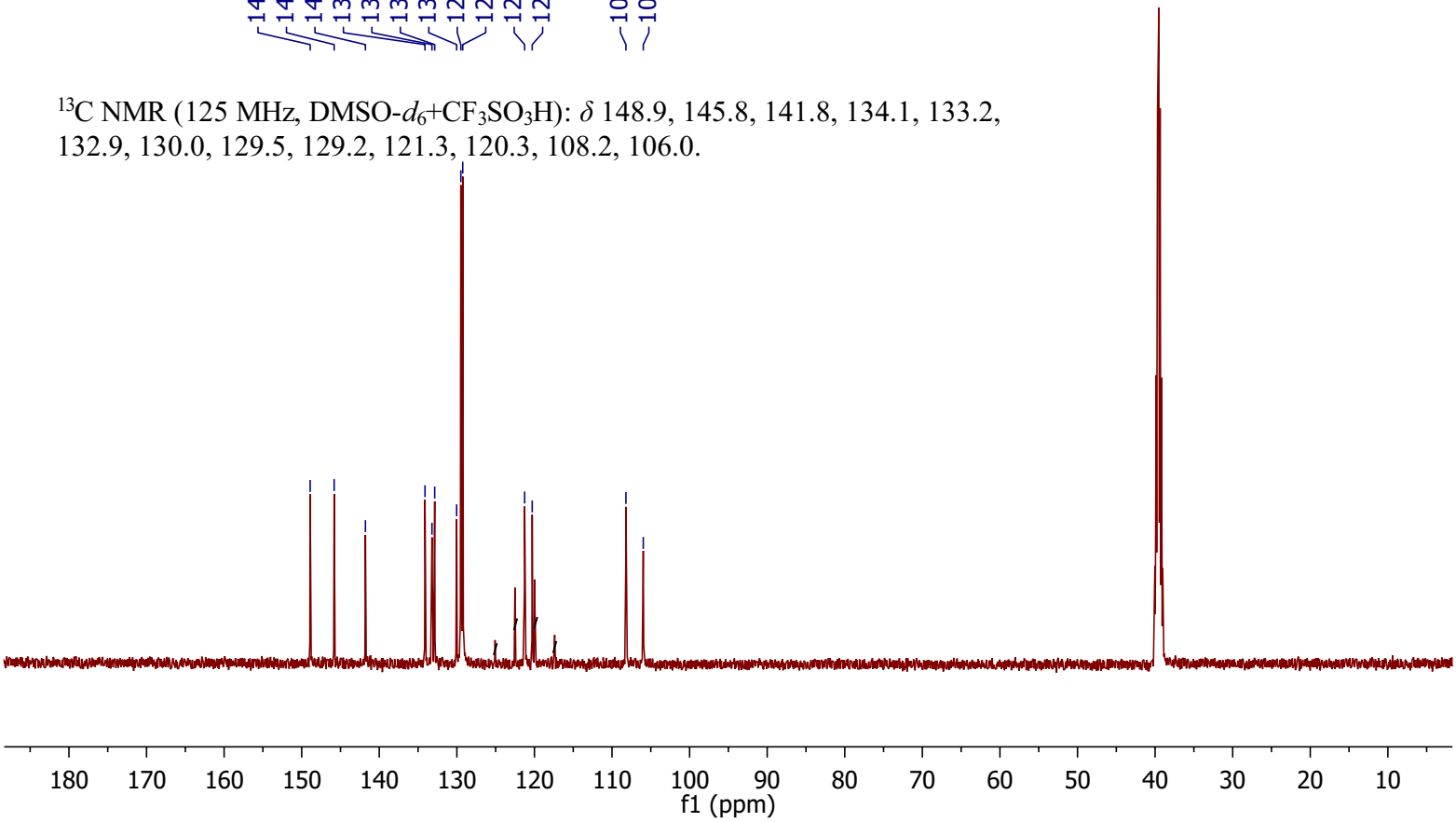


^{1}H NMR (500 MHz, DMSO-d_6+CF_3SO_3H): δ 8.57 (s, 1H), 7.40 – 7.23 (m, 4H), 6.49 (d, J = 8.4 Hz, 1H), 6.39 (d, J = 8.4 Hz, 1H).

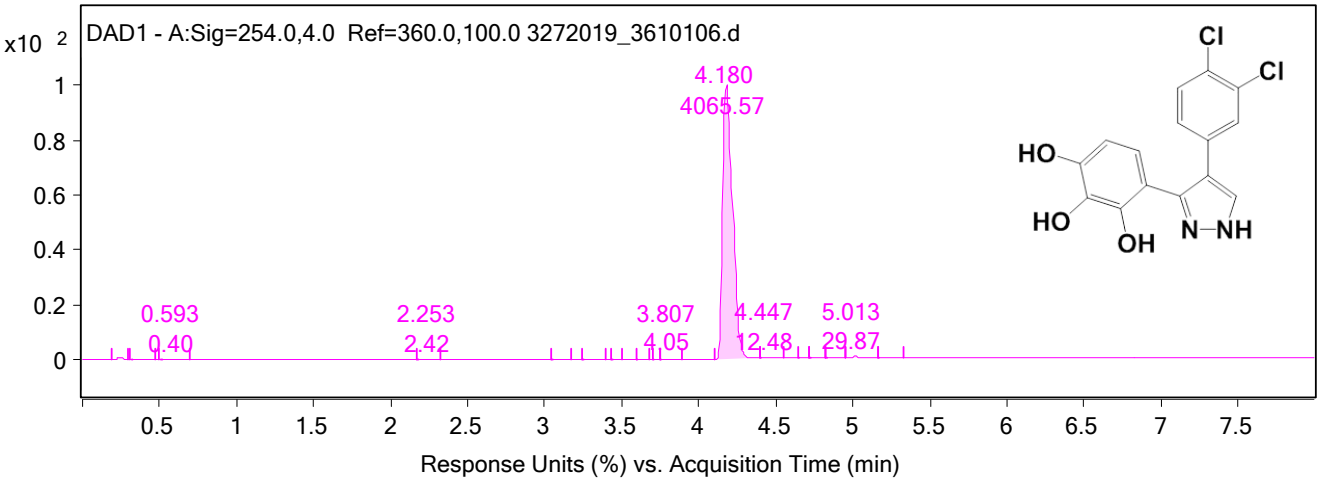


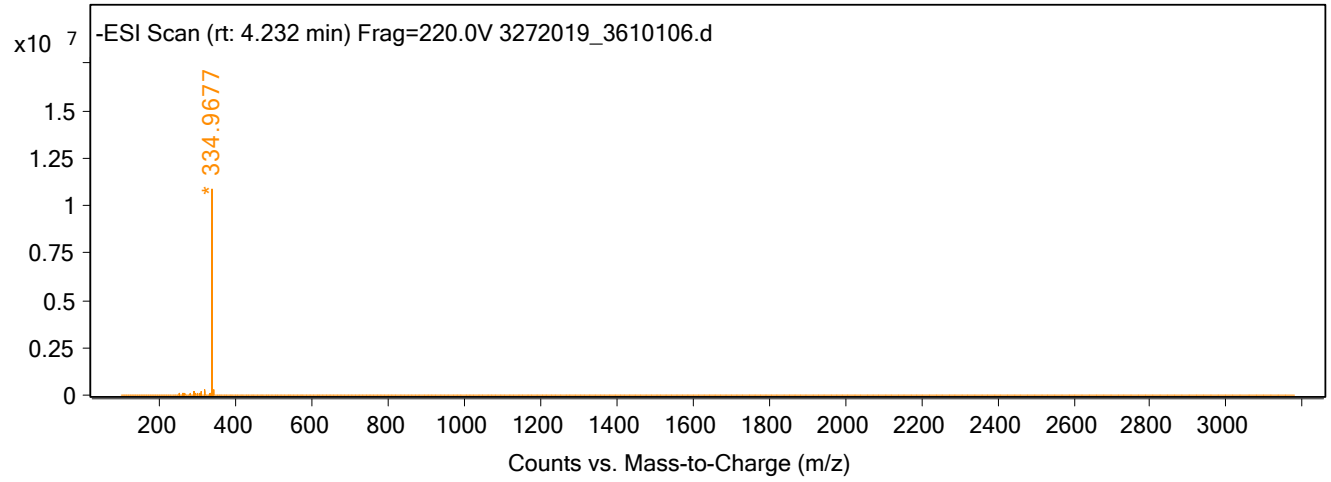


^{13}C NMR (125 MHz, DMSO-d_6+CF_3SO_3H): δ 148.9, 145.8, 141.8, 134.1, 133.2, 132.9, 130.0, 129.5, 129.2, 121.3, 120.3, 108.2, 106.0.



Compound 14 4-(4-(3,4-dichlorophenyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol





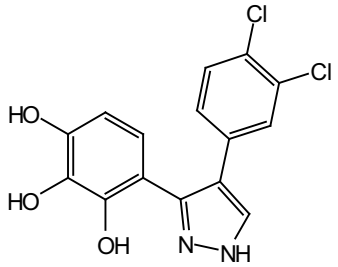
Integration Peak List

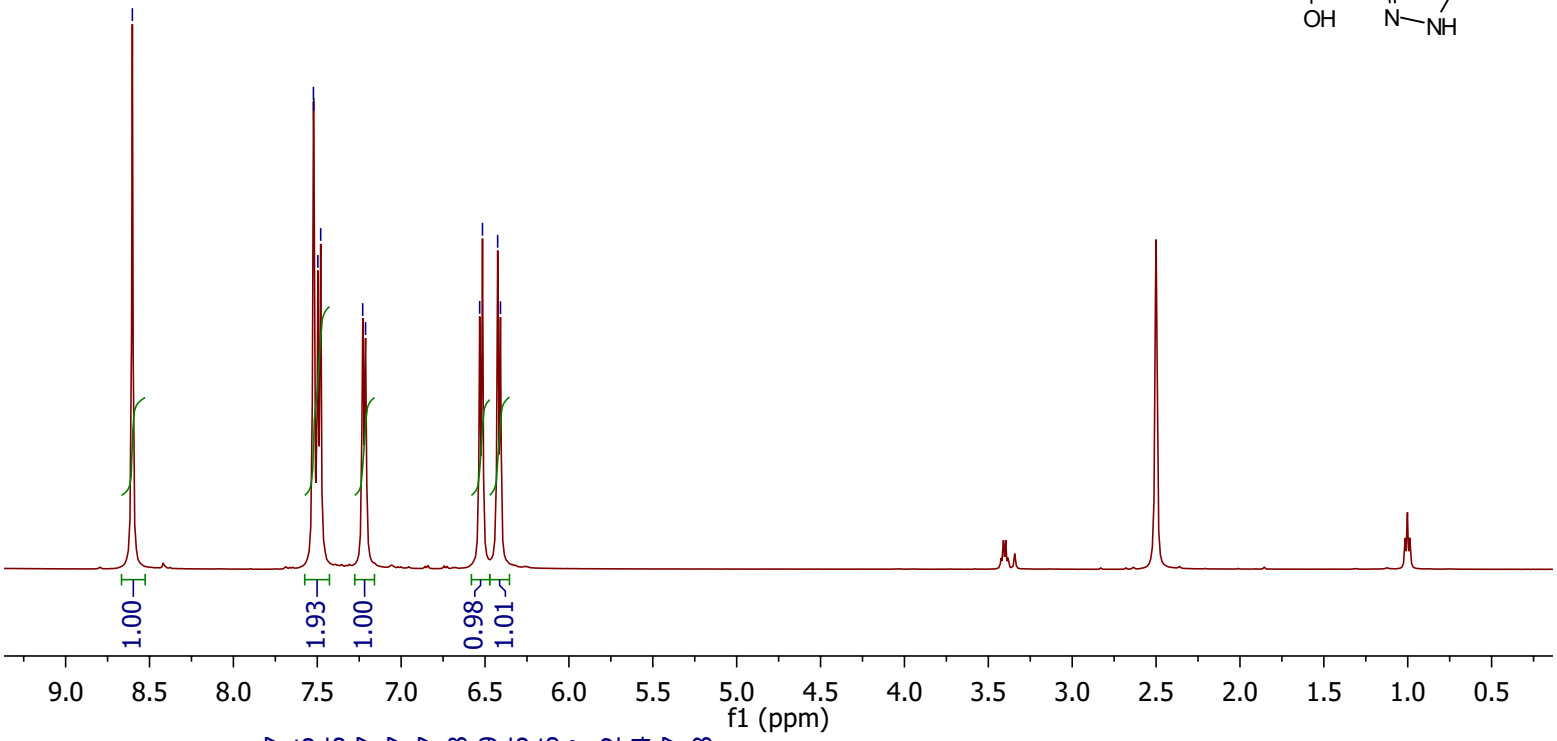
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.3	8.66	22.86	0.56
2	0.307	0.427	0.467	0.11	1.37	0.03
3	0.5	0.593	0.7	0.06	0.4	0.01
4	2.167	2.253	2.32	0.71	2.42	0.06
5	3.047	3.1	3.173	0.32	1.17	0.03
6	3.247	3.307	3.393	1.47	5.4	0.13
7	3.433	3.487	3.507	0.03	0.13	0
8	3.593	3.647	3.68	0.16	0.61	0.02
9	3.7	3.74	3.747	0.03	0.16	0
10	3.747	3.807	3.893	1.06	4.05	0.1
11	4.1	4.18	4.393	915.66	4065.57	100
12	4.393	4.447	4.553	3.07	12.48	0.31
13	4.64	4.687	4.72	0.16	0.47	0.01
14	4.72	4.76	4.82	0.32	0.89	0.02
15	4.827	4.873	4.947	0.13	0.55	0.01
16	4.947	5.013	5.16	6.53	29.87	0.73
17	5.16	5.22	5.333	0.6	2.79	0.07

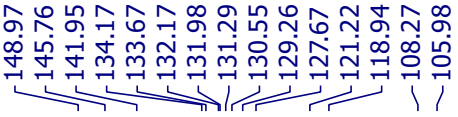
Peak List

m/z	z	Abund
288.9671		228372.93
306.9715		157705.38
316.957		254604.44
318.9535		164198.37
334.9677	1	10928833.84
335.9666	1	3373529.94
336.9633	1	9237528.31
337.9632	1	2099643.52
338.9578	1	2045474.69
339.9609	1	297916.63

^{1}H NMR (500 MHz, DMSO-d_6+CF_3SO_3H): δ 8.60 (s, 1H), 7.54 – 7.51 (m, 1H), 7.49 (d, J = 8.5 Hz, 1H), 7.22 (d, J = 8.5 Hz, 1H), 6.52 (d, J = 8.4 Hz, 1H), 6.42 (d, J = 8.4 Hz, 1H).

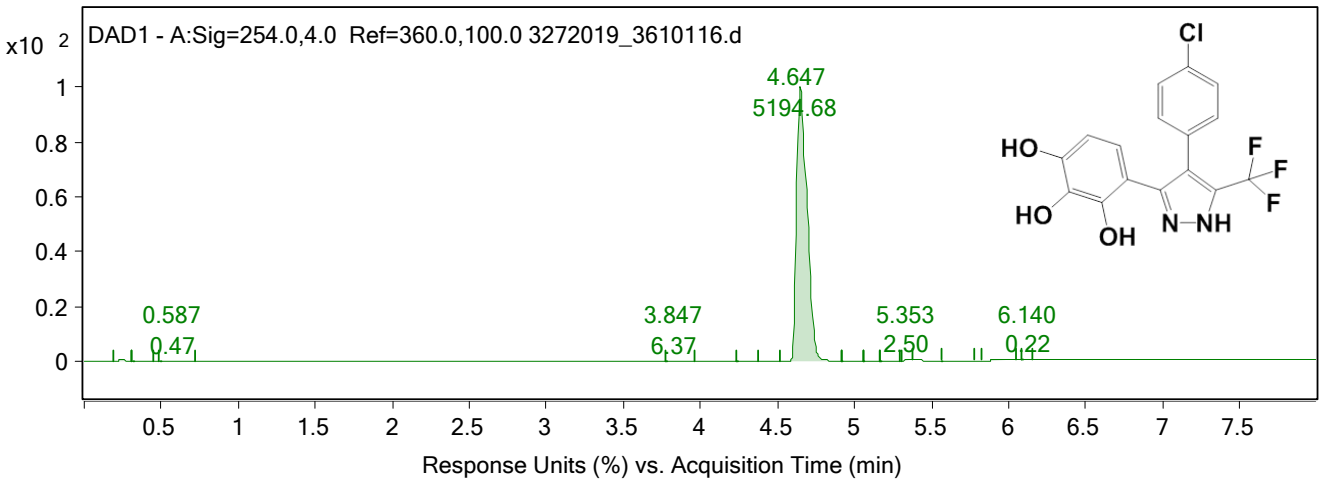


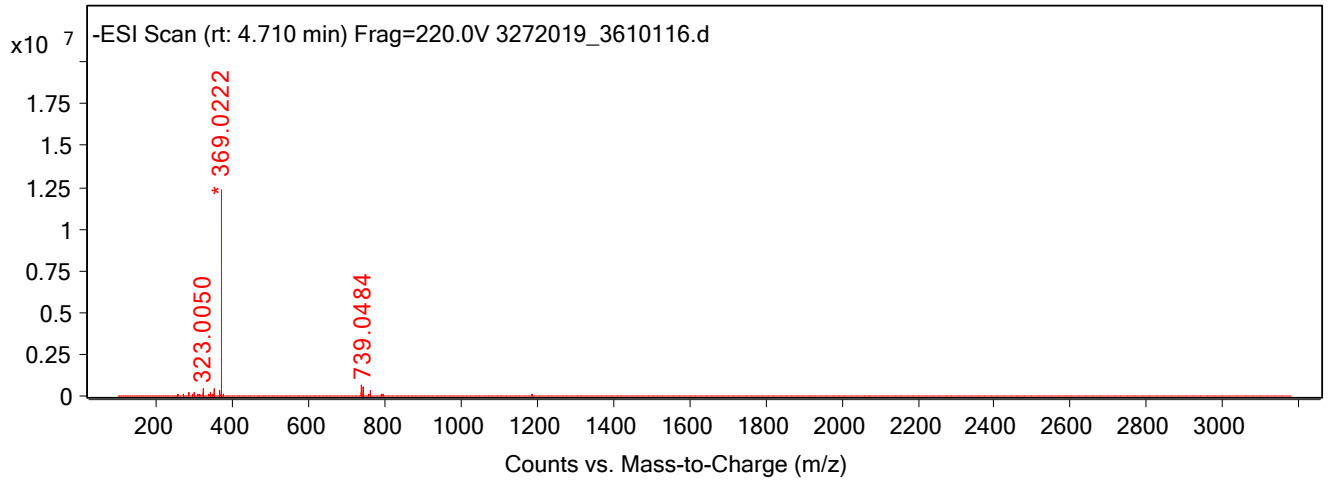




^{13}C NMR (125 MHz, DMSO-d_6+CF_3SO_3H): δ 149.0, 145.8, 142.0, 134.2, 133.7, 132.2, 132.0, 131.3, 130.6, 129.3, 127.7, 121.2, 118.9, 108.3, 106.0.

Compound 15 4-(4-(4-chlorophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol





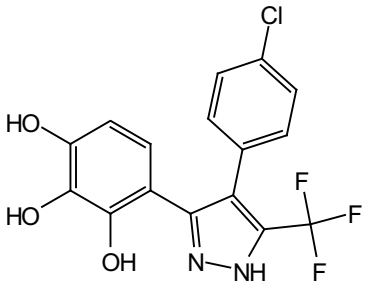
Integration Peak List

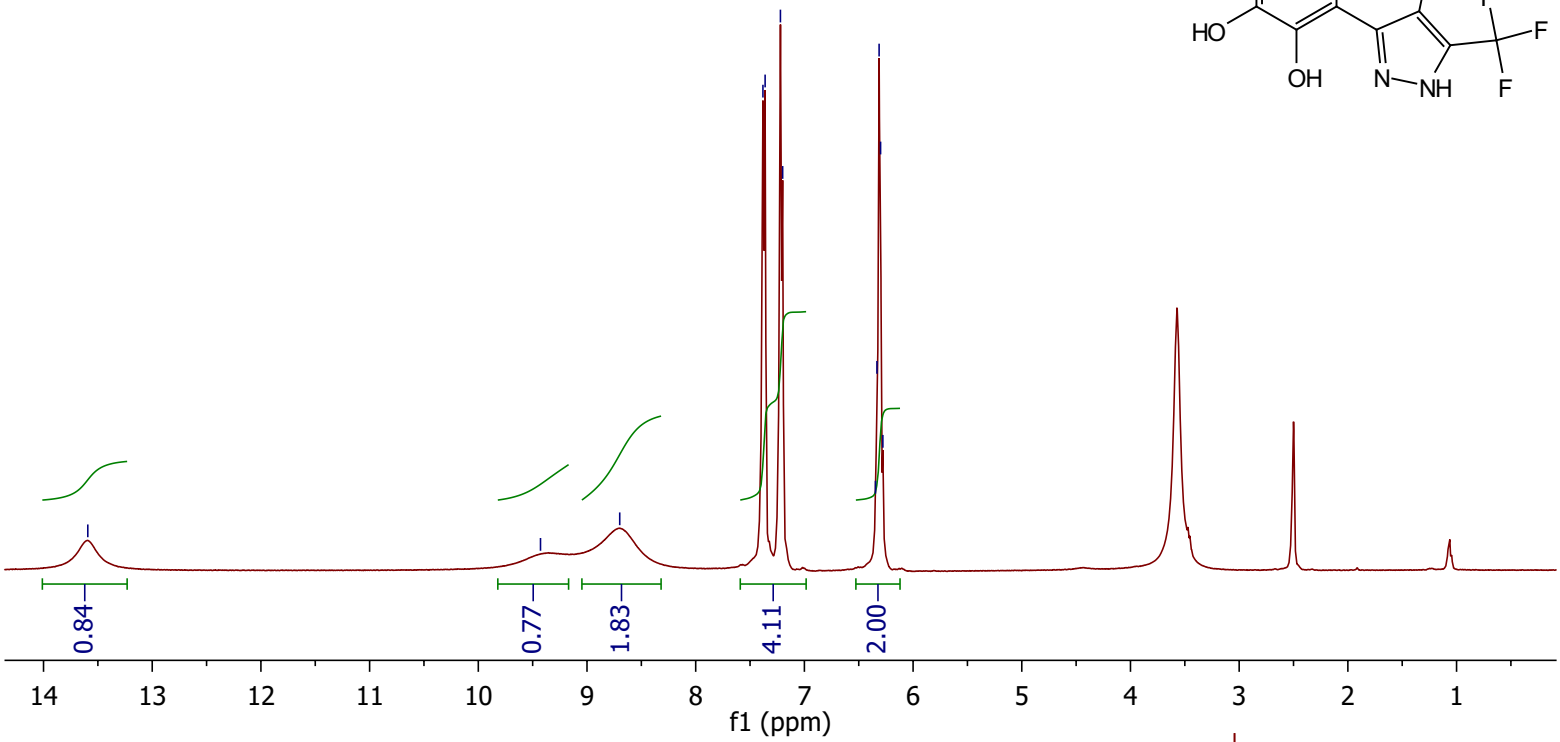
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.307	11.3	30.84	0.59
2	0.307	0.42	0.453	0.07	0.8	0.02
3	0.487	0.587	0.72	0.07	0.47	0.01
4	3.773	3.847	3.967	1.58	6.37	0.12
5	4.233	4.287	4.373	0.27	1.21	0.02
6	4.513	4.647	4.913	1115.08	5194.68	100
7	4.913	4.96	5.053	0.6	2.3	0.04
8	5.053	5.1	5.167	0.25	0.81	0.02
9	5.167	5.213	5.293	0.3	1.19	0.02
10	5.307	5.353	5.38	0.85	2.5	0.05
11	5.56	5.68	5.773	0.23	1.33	0.03
12	5.82	5.947	6.047	0.37	1.94	0.04
13	6.087	6.14	6.16	0.06	0.22	0

Peak List

m/z	z	Abund
323.005		488529.26
351.0001		420835.94
366.9952		309645.48
369.0222		13021154.19
370.0156		7897708.54
371.0121	1	10494937.34
372.011	1	2990711.89
373.0144	1	345631.77
739.0484	1	697510.4
741.0473	1	523211.75

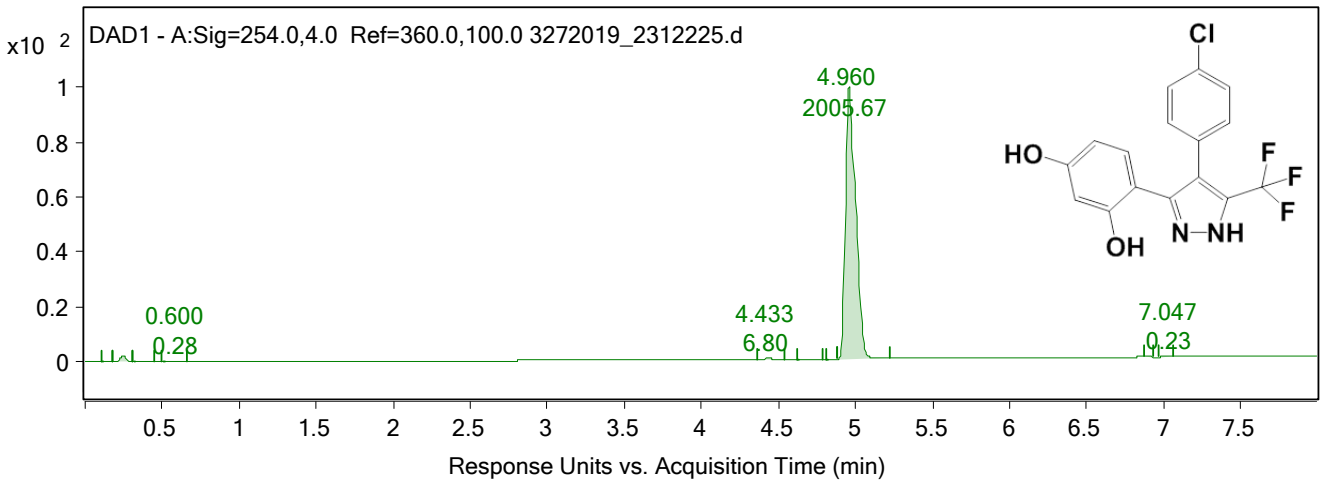
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.59 (s, 1H), 9.43 (s, 1H), 8.70 (s, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 6.36 – 6.26 (m, 2H).

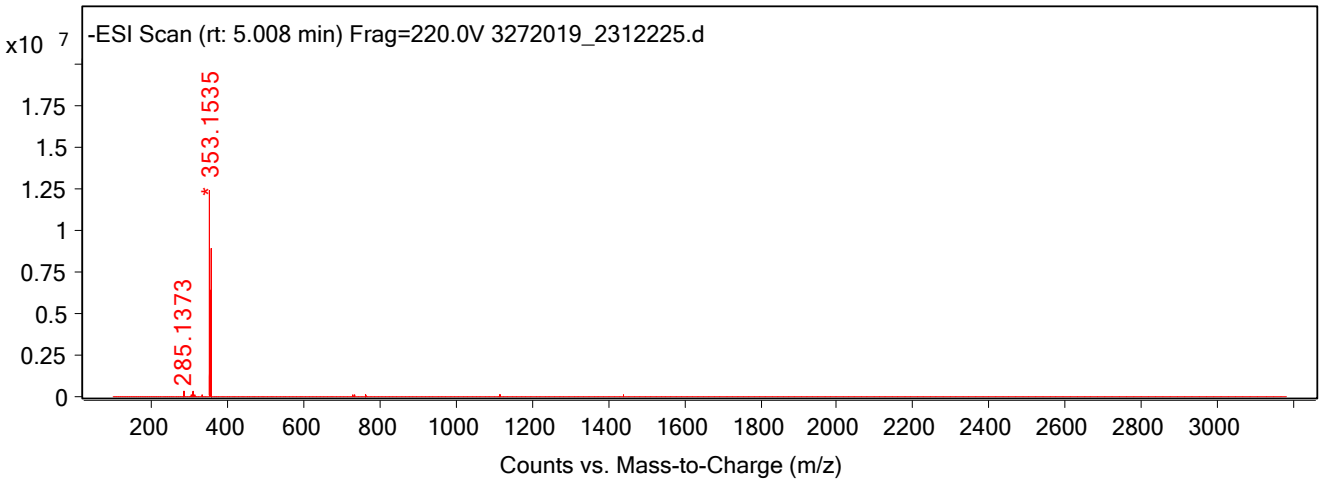




^{13}C NMR (100 MHz, DMSO-d_6): δ 147.3, 145.4, 140.5, 138.3 (q, $J_{C\text{-}F}$ = 36.2 Hz), 133.4, 132.2, 131.5, 130.8, 128.4, 122.5 (q, $J_{C\text{-}F}$ = 251.9 Hz), 121.0, 116.9, 107.4, 107.2.

Compound 16 4-(4-(4-chlorophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,3-diol



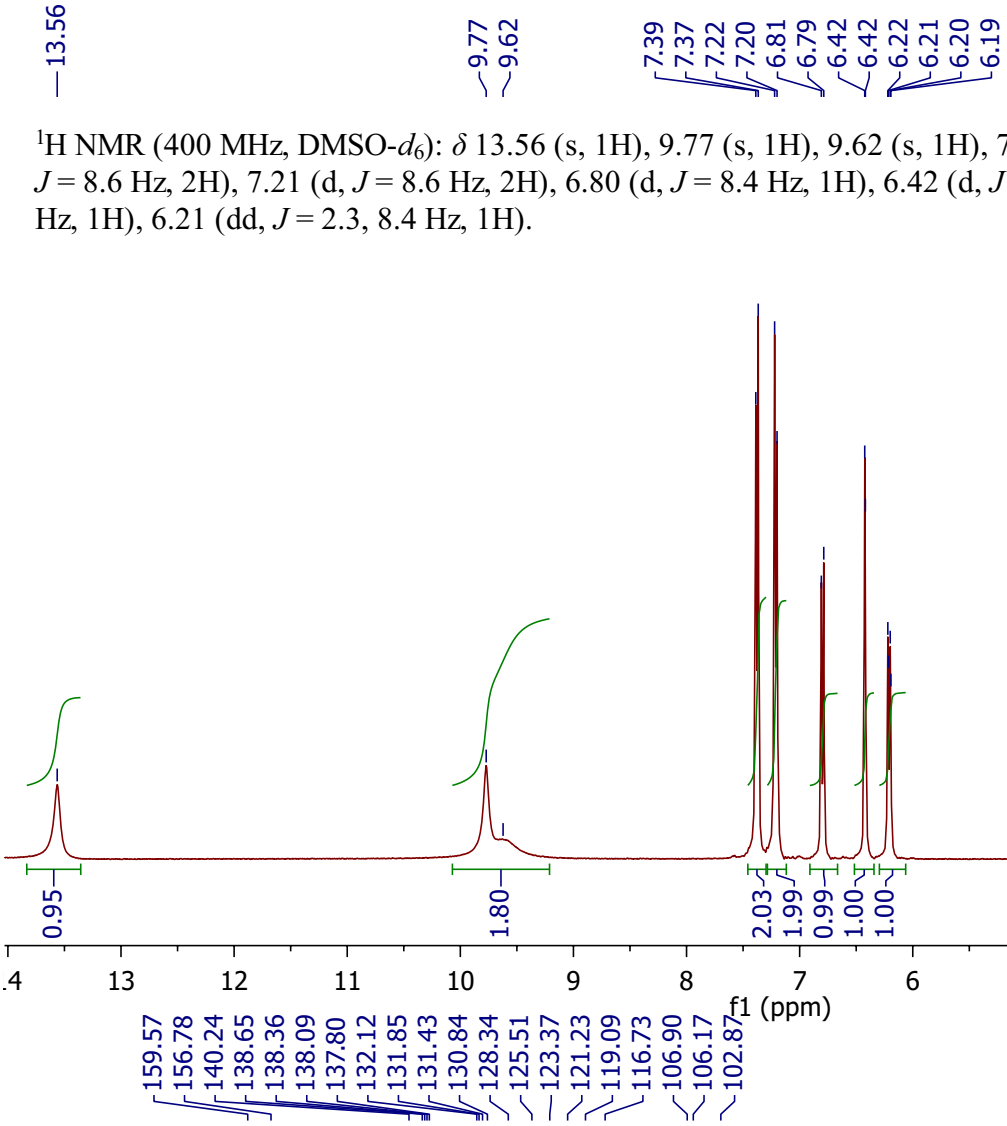


Integration Peak List

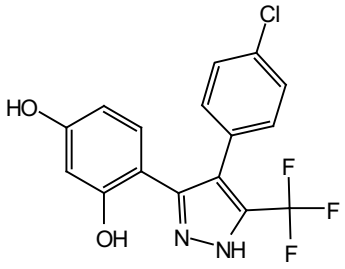
Peak	Start	RT	End	Height	Area	Area %
1	0.107	0.16	0.18	0.04	0.14	0.01
2	0.18	0.247	0.307	9.74	26.17	1.3
3	0.307	0.42	0.453	0.09	1.07	0.05
4	0.5	0.6	0.66	0.04	0.28	0.01
5	4.367	4.433	4.54	1.38	6.8	0.34
6	4.627	4.68	4.787	0.22	0.9	0.04
7	4.813	4.86	4.88	0.17	0.47	0.02
8	4.88	4.96	5.227	429.67	2005.67	100
9	6.873	6.887	6.933	0.02	0.05	0
10	6.967	7.047	7.067	0.04	0.23	0.01

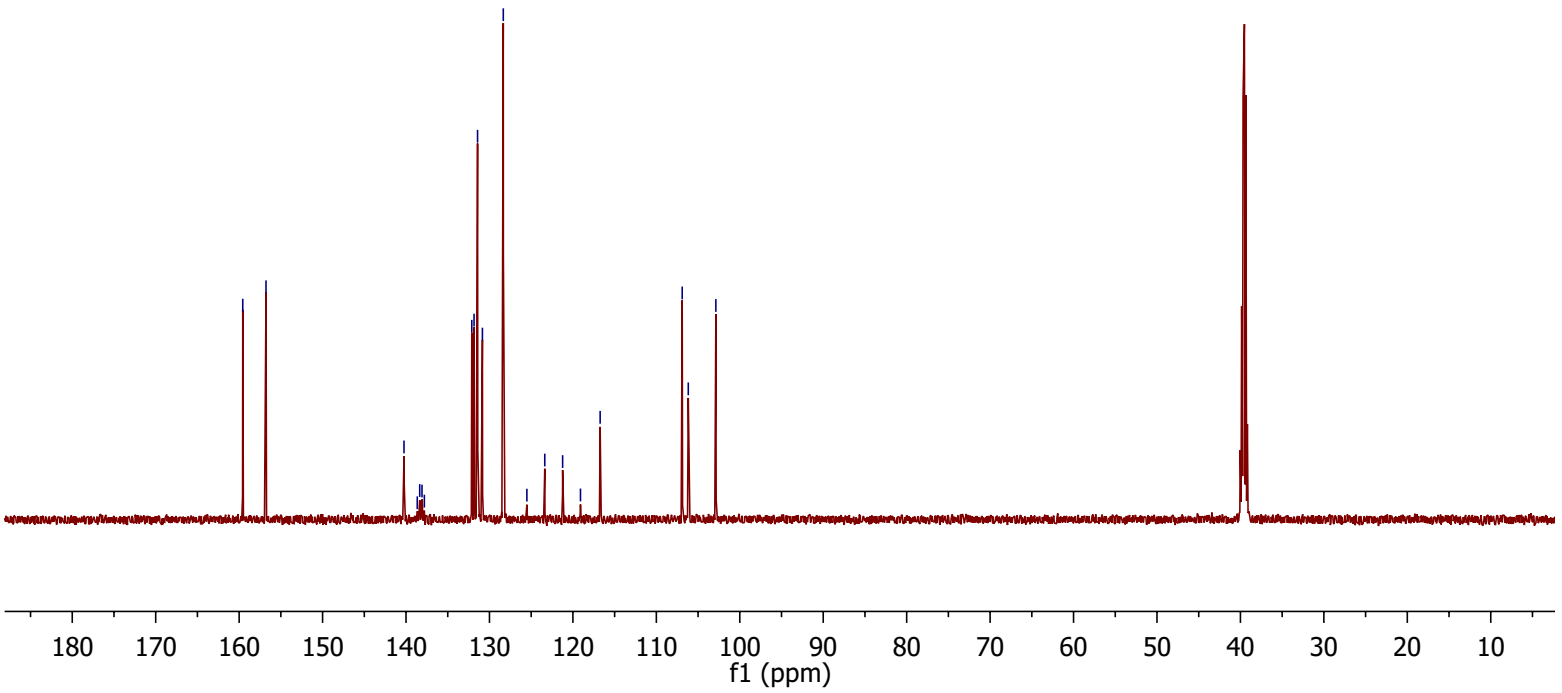
Peak List

m/z	z	Abund
285.1104		327454.33
285.1373		370084.54
309.1447		176622.35
311.1269		353285.21
353.1535		12688231.04
354.1497		6437695.07
355.1461	1	8983528.61
356.1464	1	2152307.59
357.1502	1	213734.47



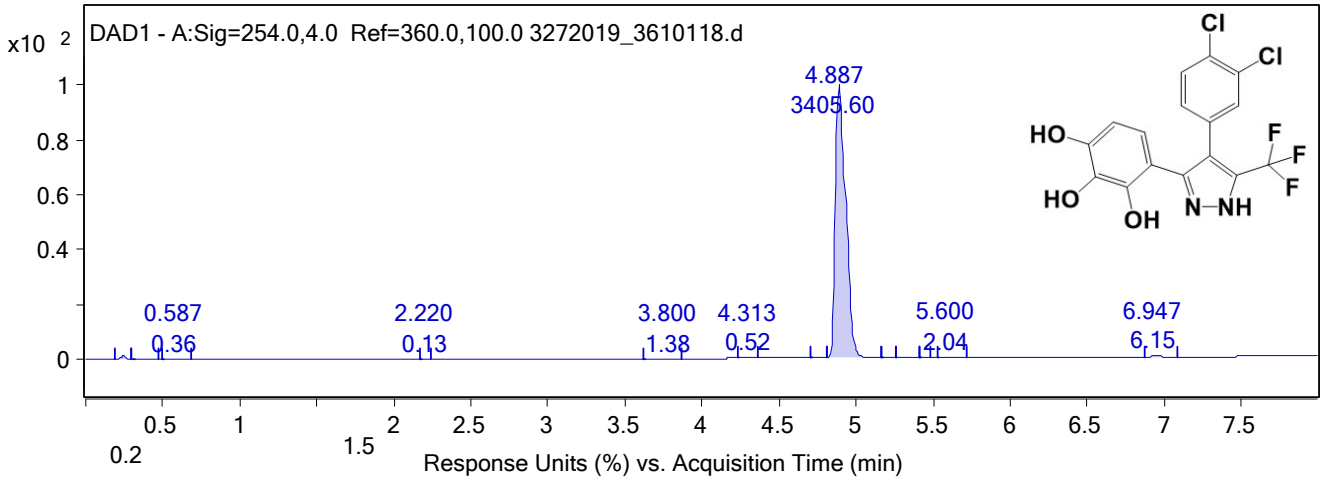
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.56 (s, 1H), 9.77 (s, 1H), 9.62 (s, 1H), 7.38 (d, J = 8.6 Hz, 2H), 7.21 (d, J = 8.6 Hz, 2H), 6.80 (d, J = 8.4 Hz, 1H), 6.42 (d, J = 2.3 Hz, 1H), 6.21 (dd, J = 2.3, 8.4 Hz, 1H).

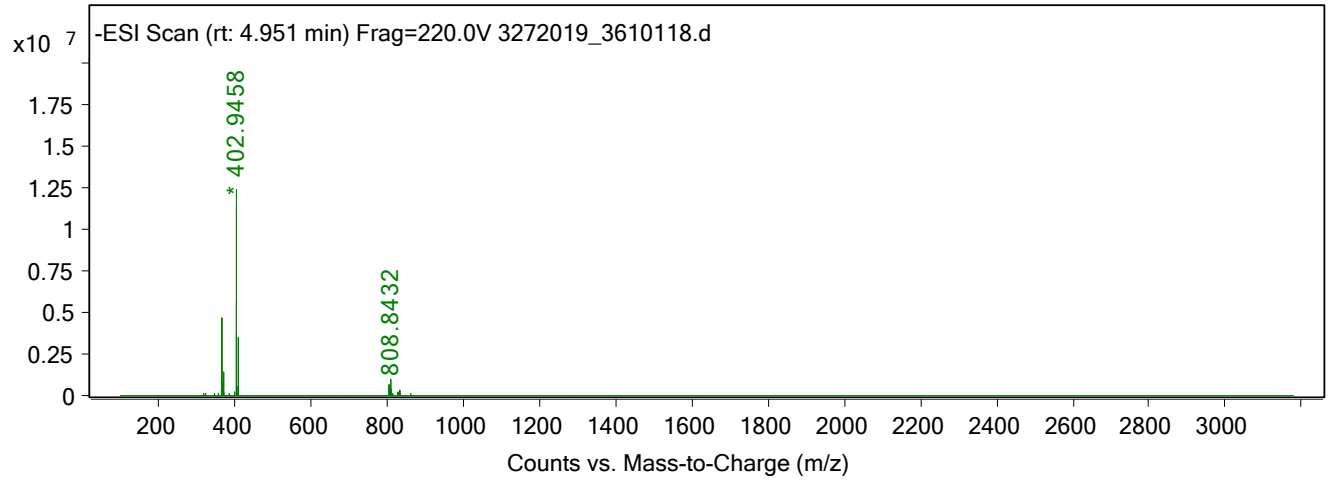




^{13}C NMR (125 MHz, DMSO-d_6): δ 159.6, 156.8, 140.2, 138.2 (q, $J_{C\text{-}F}$ = 34.3 Hz), 132.1, 131.9, 131.4, 130.8, 128.3, 122.3 (q, $J_{C\text{-}F}$ = 269.1 Hz), 116.7, 106.9, 106.2, 102.9.

Compound 17 4-(4-(3,4-dichlorophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol



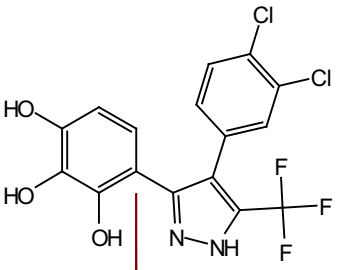


Integration Peak List

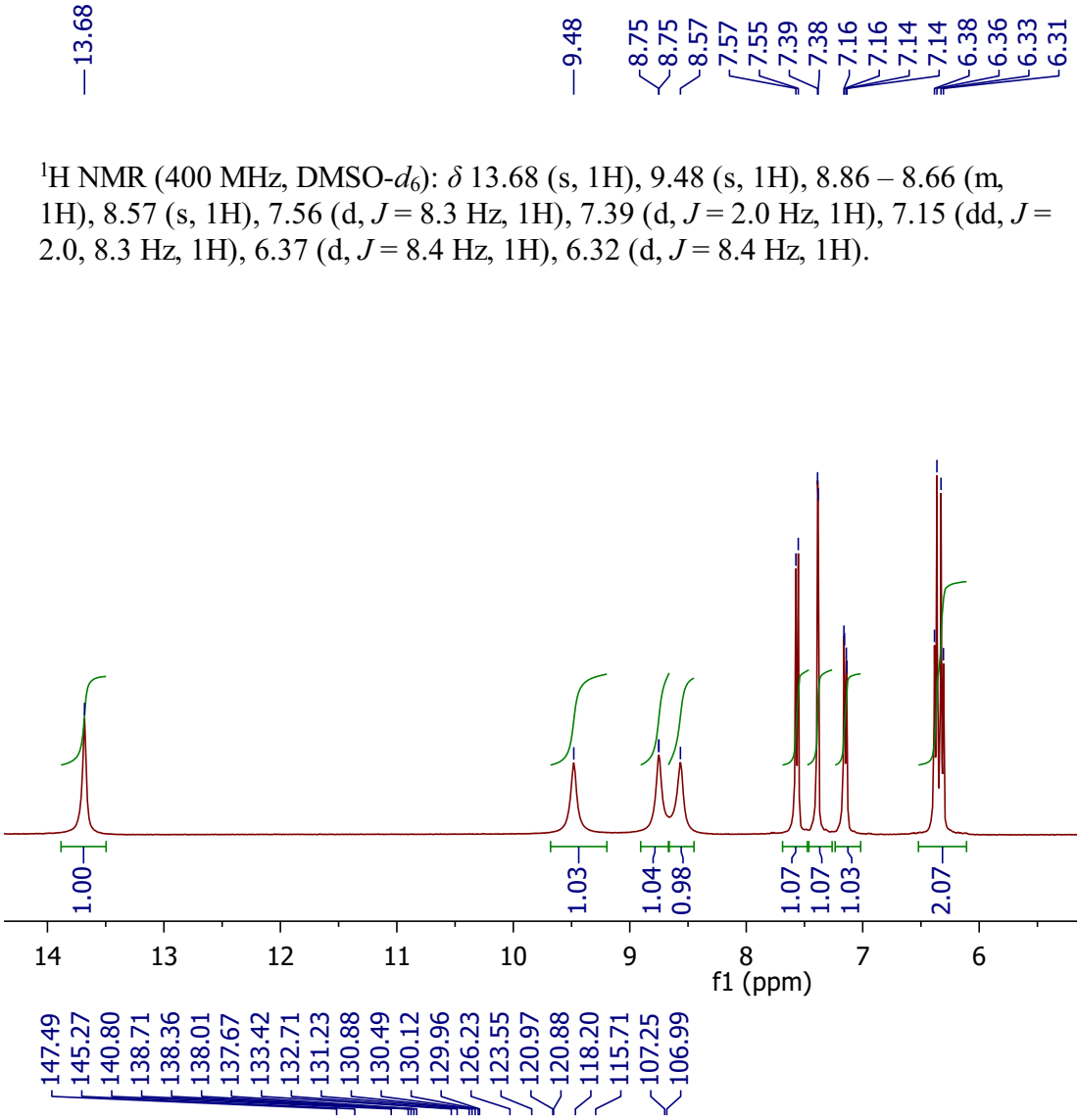
Peak	Start	RT	End	Height	Area	Area %
1	0.187	0.24	0.3	9.15	24.59	0.72
2	0.3	0.413	0.473	0.14	1.45	0.04
3	0.493	0.587	0.687	0.06	0.36	0.01
4	2.167	2.22	2.24	0.03	0.13	0
5	3.62	3.8	3.867	0.14	1.38	0.04
6	4.227	4.313	4.36	0.09	0.52	0.02
7	4.707	4.753	4.813	0.57	1.67	0.05
8	4.813	4.887	5.16	726.45	3405.6	100
9	5.167	5.213	5.253	0.17	0.47	0.01
10	5.253	5.313	5.407	0.1	0.37	0.01
11	5.413	5.46	5.487	0.07	0.19	0.01
12	5.527	5.6	5.72	0.36	2.04	0.06
13	6.873	6.947	7.08	1.26	6.15	0.18

Peak List

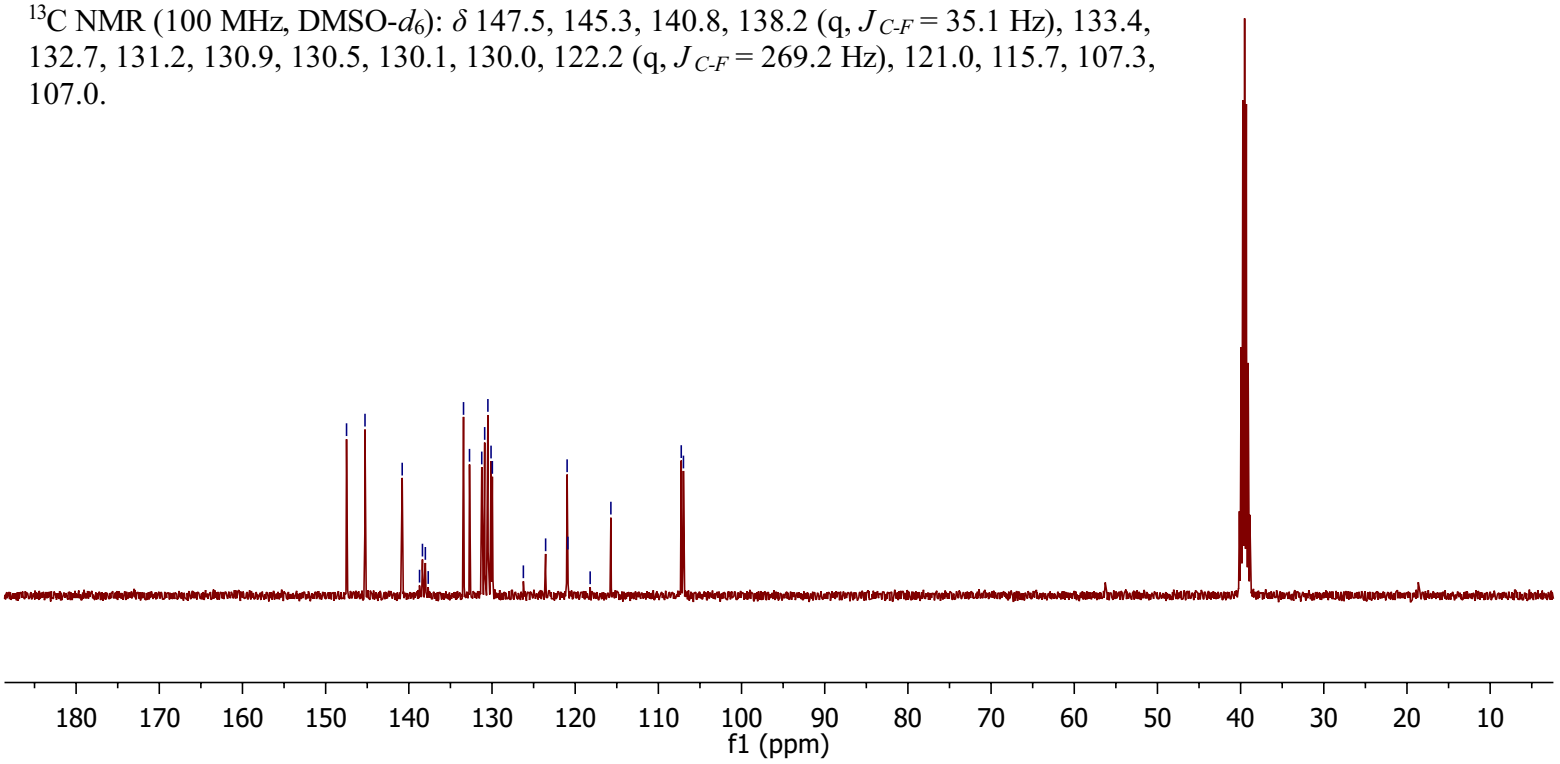
m/z	z	Abund
366.9693	1	4752759.75
367.9719	1	823723.02
368.966	1	1503513.23
402.9458	1	12738211.75
403.9422	1	5774486.97
404.9402	1	11269582.34
405.9384	1	3741349.04
406.9329	1	3503906.36
806.846	1	669865.41
808.8432	1	935041



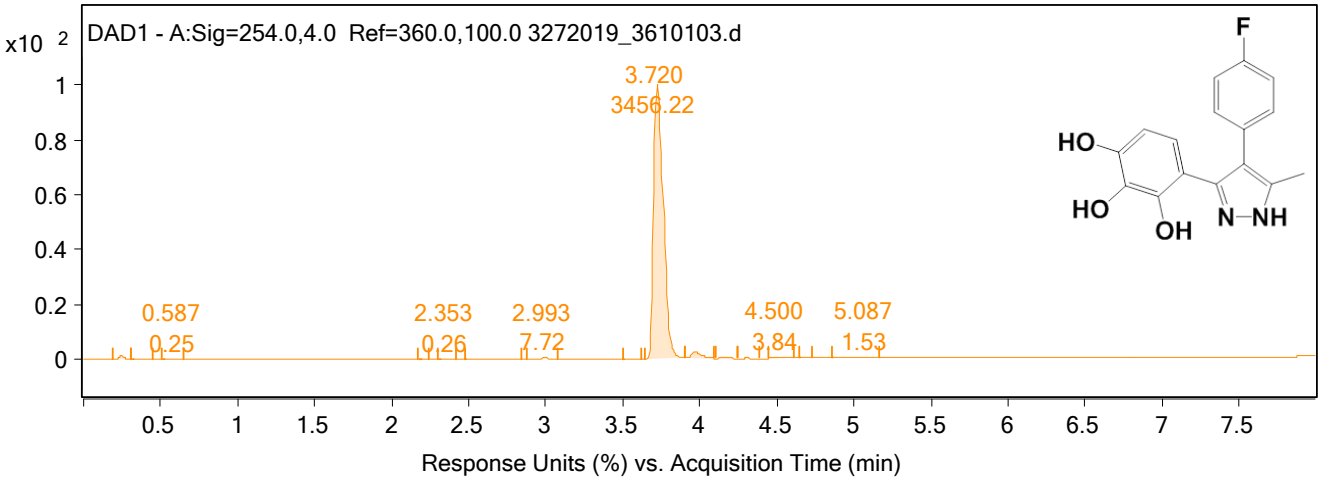
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.68 (s, 1H), 9.48 (s, 1H), 8.86 – 8.66 (m, 1H), 8.57 (s, 1H), 7.56 (d, J = 8.3 Hz, 1H), 7.39 (d, J = 2.0 Hz, 1H), 7.15 (dd, J = 2.0, 8.3 Hz, 1H), 6.37 (d, J = 8.4 Hz, 1H), 6.32 (d, J = 8.4 Hz, 1H).

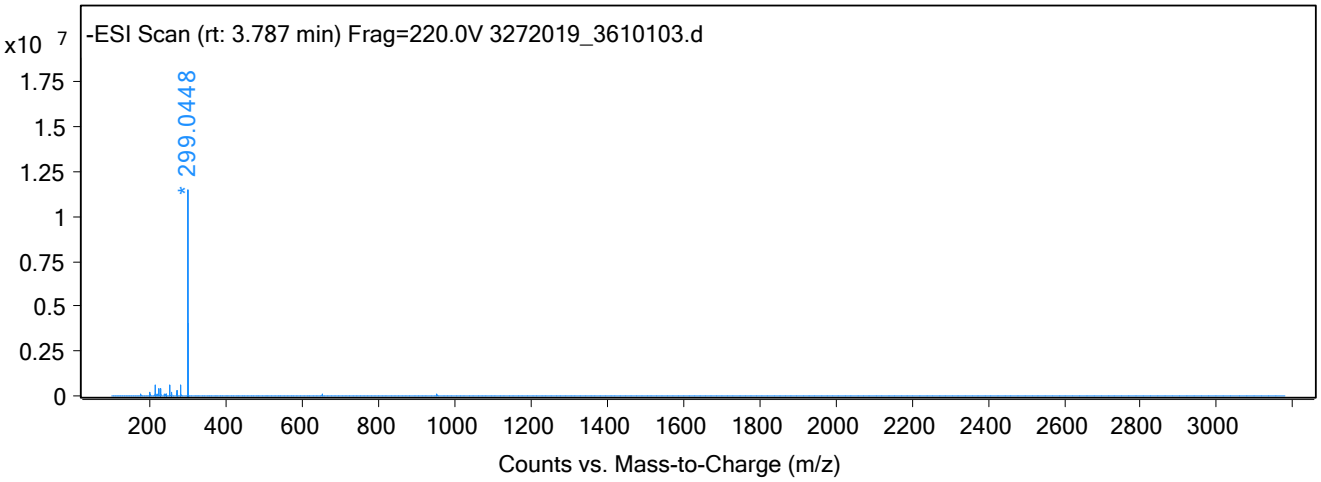


^{13}C NMR (100 MHz, DMSO-d_6): δ 147.5, 145.3, 140.8, 138.2 (q, $J_{C\text{-}F}$ = 35.1 Hz), 133.4, 132.7, 131.2, 130.9, 130.5, 130.1, 130.0, 122.2 (q, $J_{C\text{-}F}$ = 269.2 Hz), 121.0, 115.7, 107.3, 107.0.



Compound 18 4-(4-(4-fluorophenyl)-5-methyl-1H-pyrazol-3-yl)benzene-1,2,3-triol



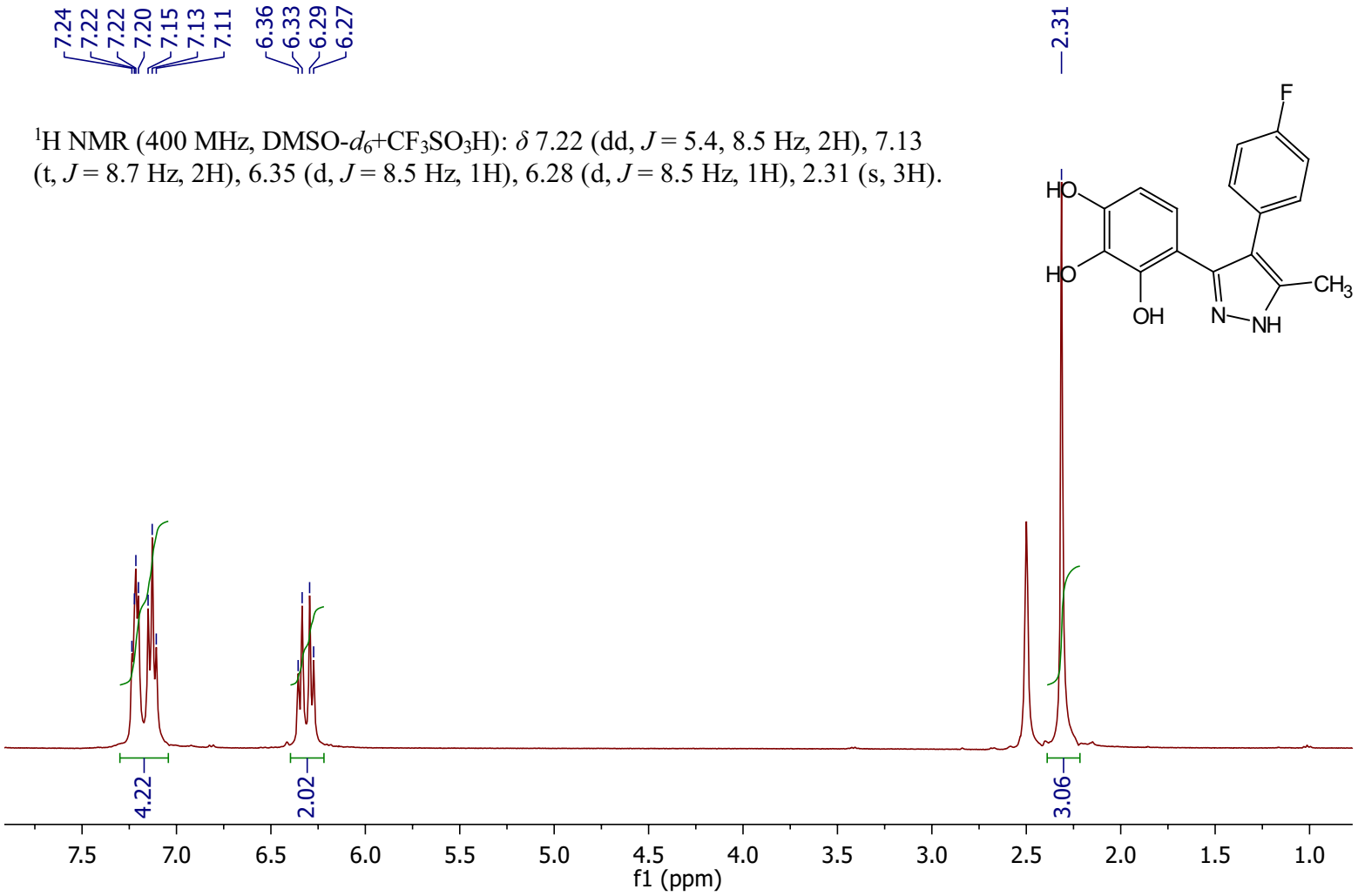


Integration Peak List

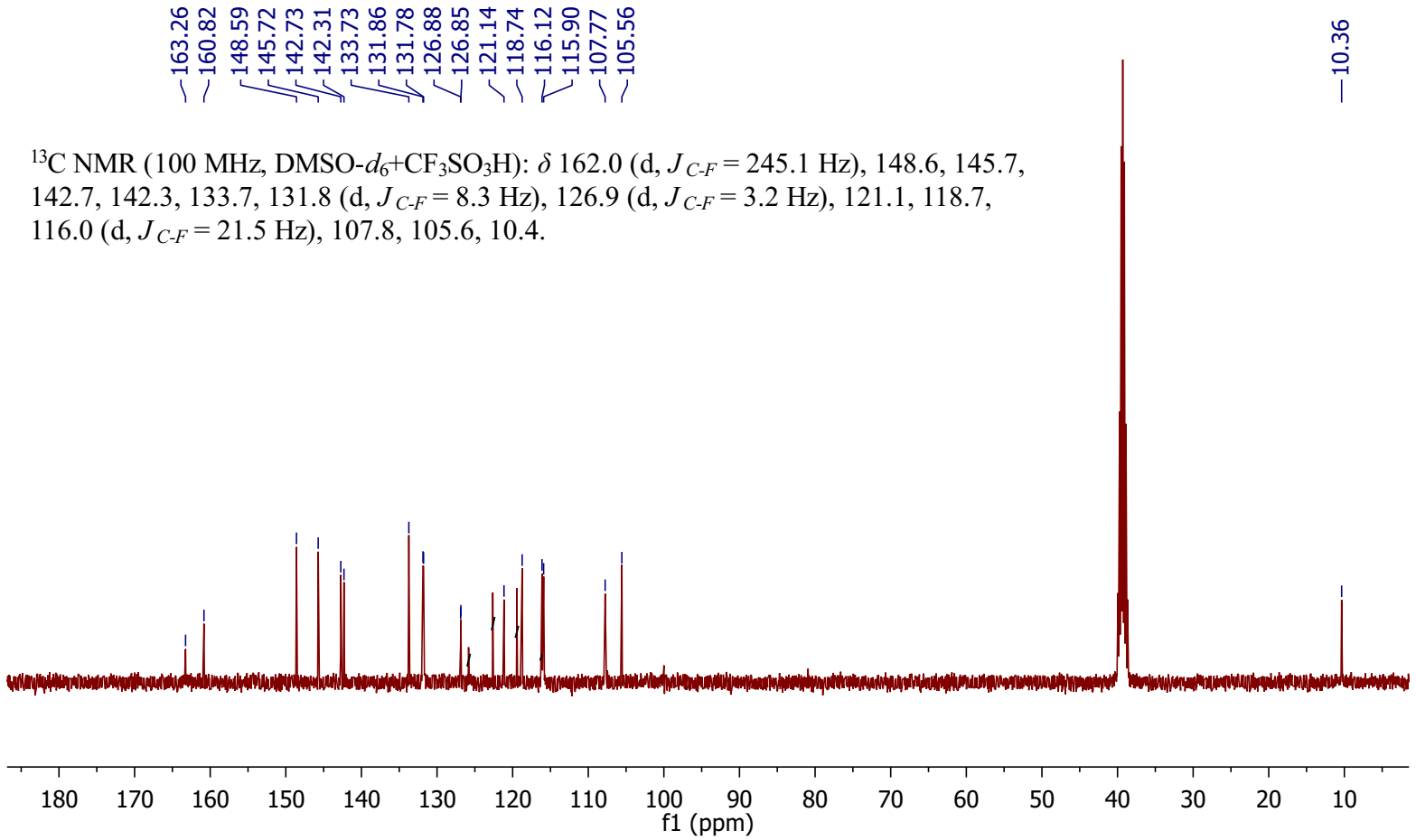
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.307	9.97	26.66	0.77
2	0.307	0.413	0.453	0.1	1.02	0.03
3	0.507	0.587	0.647	0.05	0.25	0.01
4	2.173	2.227	2.24	0.03	0.14	0
5	2.3	2.353	2.413	0.07	0.26	0.01
6	2.473	2.787	2.84	0.16	1.1	0.03
7	2.873	2.993	3.073	2.19	7.72	0.22
8	3.5	3.56	3.62	0.32	1.37	0.04
9	3.64	3.72	3.9	793.61	3456.22	100
10	3.9	3.973	4.093	16.84	71.42	2.07
11	4.107	4.153	4.247	0.47	1.87	0.05
12	4.247	4.3	4.38	0.08	0.36	0.01
13	4.44	4.5	4.607	0.87	3.84	0.11
14	4.64	4.7	4.727	0.13	0.57	0.02
15	4.853	5.087	5.167	0.15	1.53	0.04

Peak List

m/z	z	Abund
215.0747		608449.92
225.057		458540.64
227.0724		375293.79
253.0454		618141.45
255.0608		258330.33
271.0511		280983.23
281.0341	1	639626.81
299.0448	1	11641235.74
300.0436	1	4150325.16
301.0464	1	432038.13

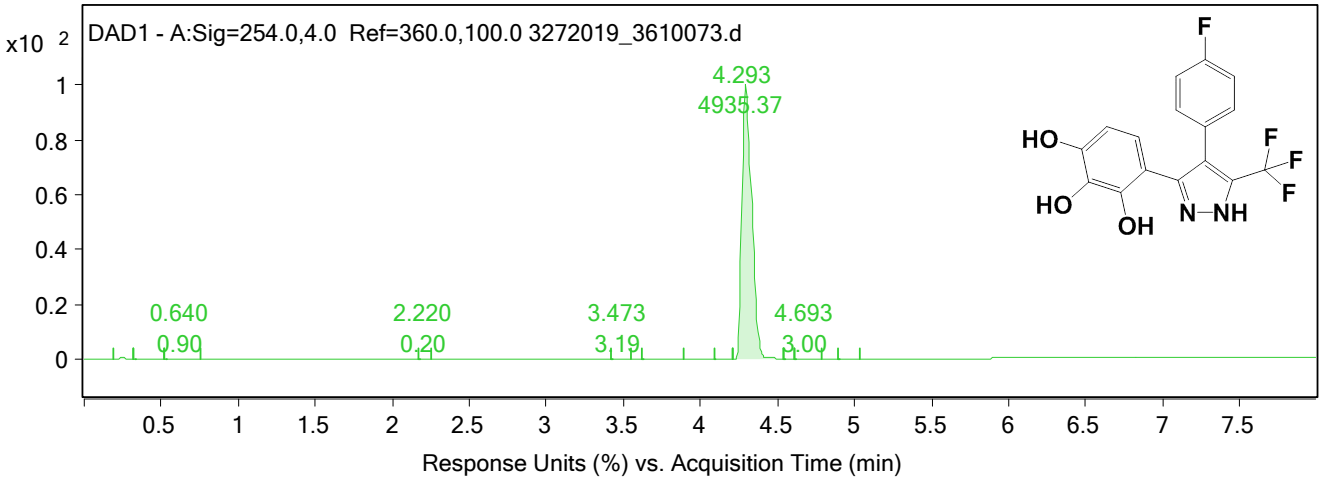


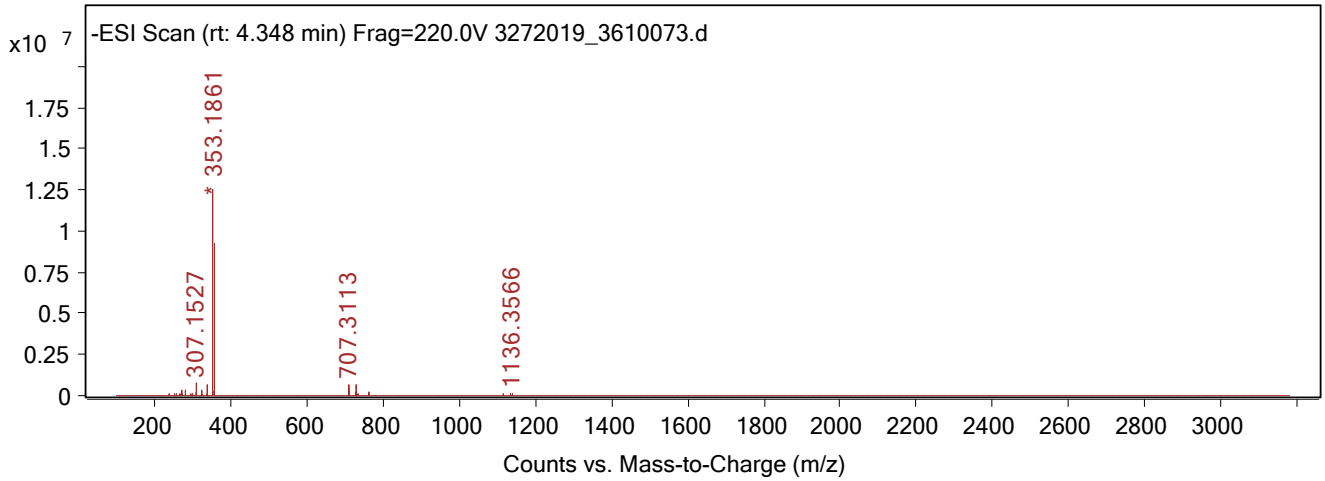
^{1}H NMR (400 MHz, DMSO-d_6+CF_3SO_3H): δ 7.22 (dd, J = 5.4, 8.5 Hz, 2H), 7.13 (t, J = 8.7 Hz, 2H), 6.35 (d, J = 8.5 Hz, 1H), 6.28 (d, J = 8.5 Hz, 1H), 2.31 (s, 3H).



^{13}C NMR (100 MHz, DMSO-d_6+CF_3SO_3H): δ 162.0 (d, $J_{C\text{-}F}$ = 245.1 Hz), 148.6, 145.7, 142.7, 142.3, 133.7, 131.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 126.9 (d, $J_{C\text{-}F}$ = 3.2 Hz), 121.1, 118.7, 116.0 (d, $J_{C\text{-}F}$ = 21.5 Hz), 107.8, 105.6, 10.4.

Compound 19 4-(4-(4-fluorophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol





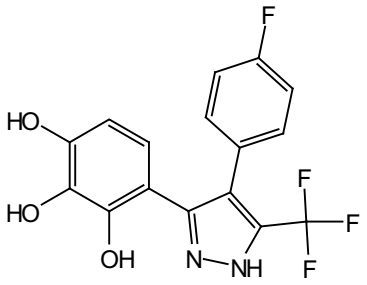
Integration Peak List

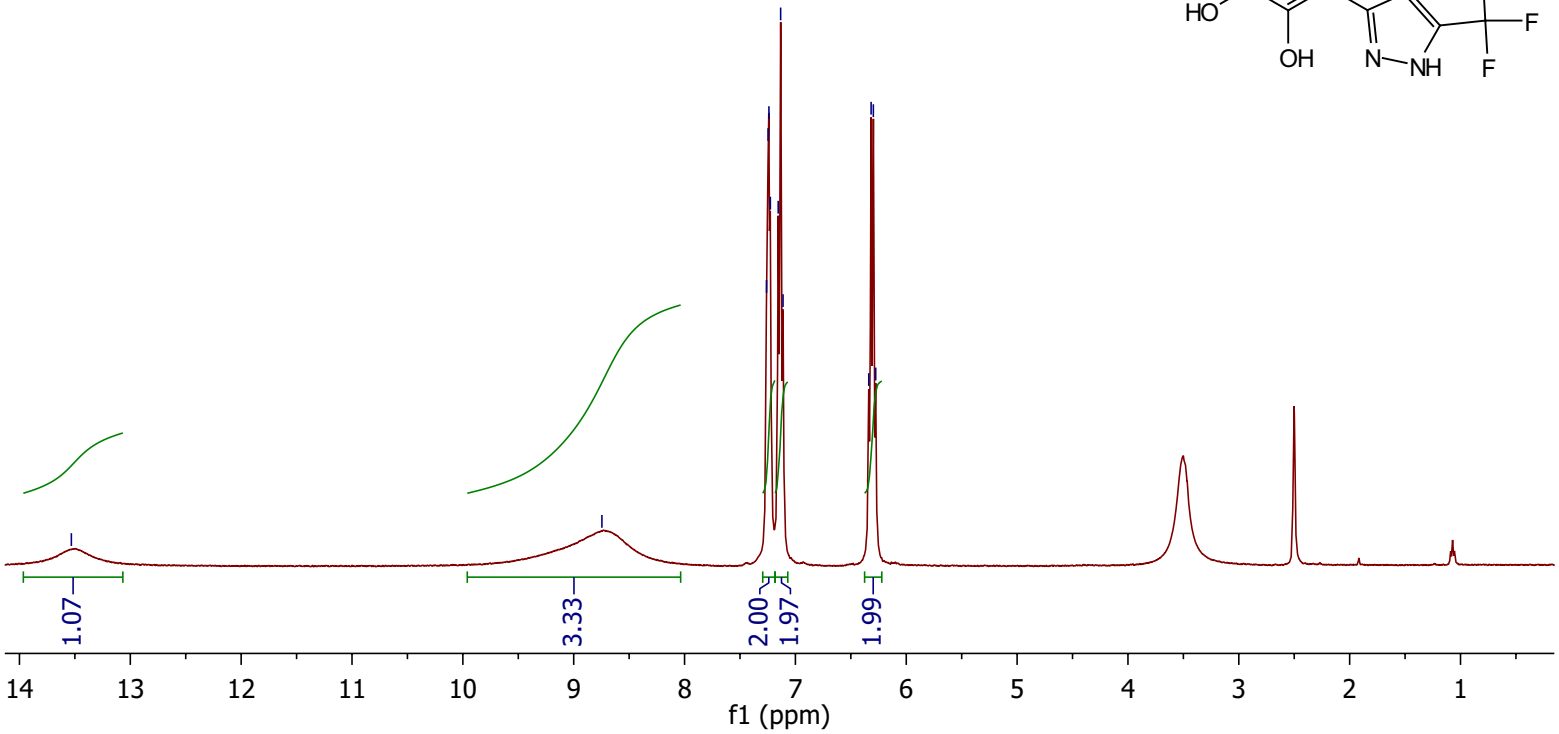
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.313	9.09	25.86	0.52
2	0.32	0.433	0.513	0.13	0.9	0.02
3	0.52	0.64	0.753	0.12	0.9	0.02
4	2.167	2.22	2.247	0.06	0.2	0
5	3.42	3.473	3.553	0.9	3.19	0.06
6	3.62	3.84	3.887	0.07	0.72	0.01
7	4.087	4.147	4.213	0.36	1.52	0.03
8	4.213	4.293	4.54	1102.25	4935.37	100
9	4.54	4.58	4.613	0.22	0.51	0.01
10	4.613	4.693	4.787	0.61	3	0.06
11	4.893	4.953	5.04	0.37	1.59	0.03

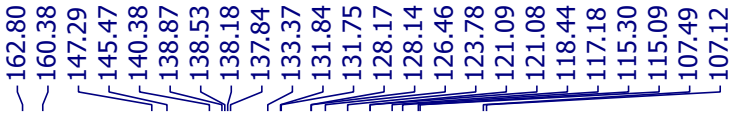
Peak List

m/z	z	Abund
269.1644		351354.43
281.1675		370840.32
307.1527		827917.75
325.1679		402255
335.1545	1	718899.9
353.1861		13100601.37
354.176	1	9218924.82
355.1759	1	1561479.22
707.3113	1	723030.18
729.298	1	693025.55

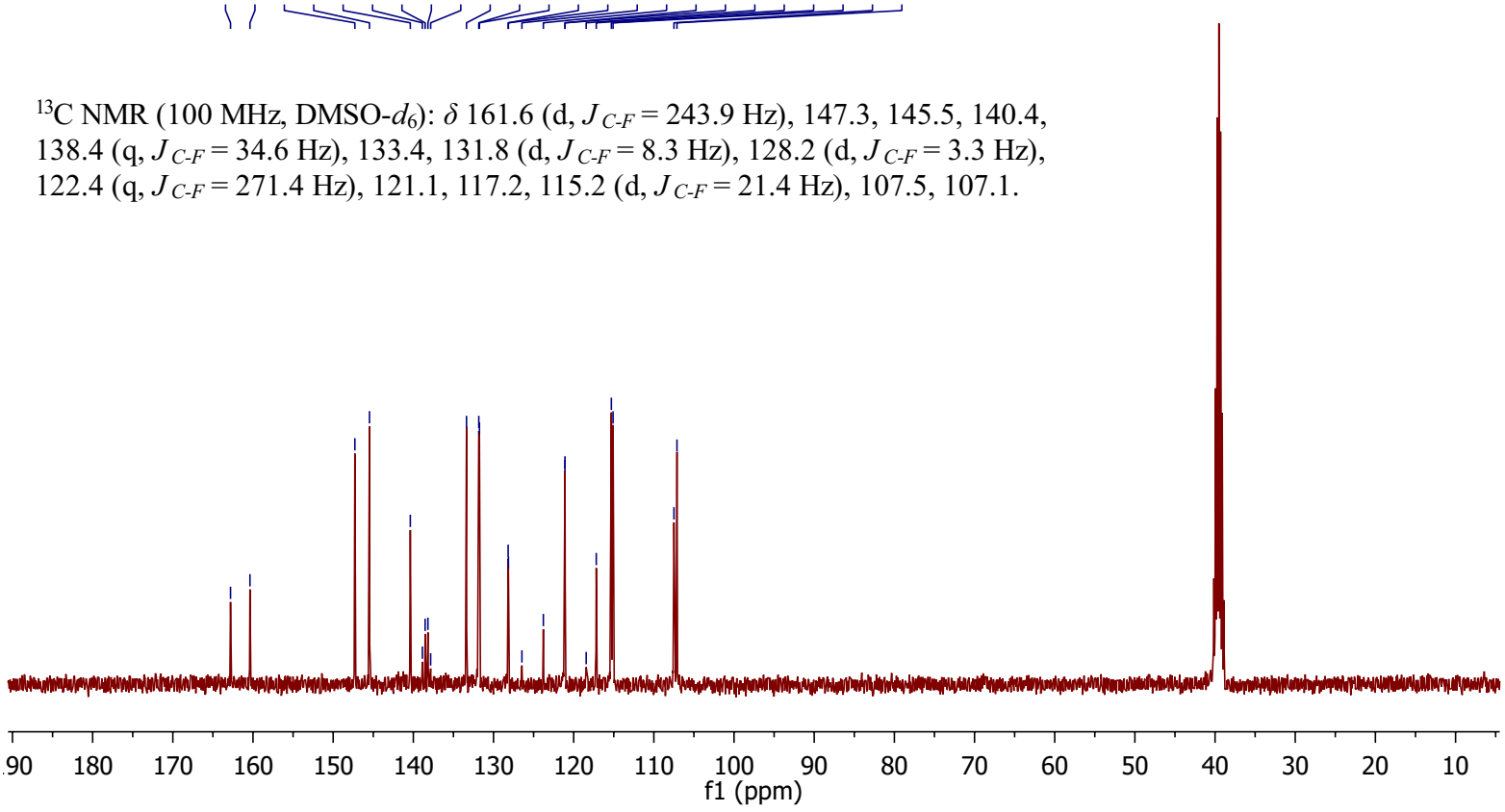
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.53 (s, 1H), 8.75 (s, 3H), 7.24 (dd, J = 5.4, 8.7 Hz, 2H), 7.13 (t, J = 8.7 Hz, 2H), 6.33 (d, J = 8.5 Hz, 1H), 6.29 (d, J = 8.5 Hz, 1H).



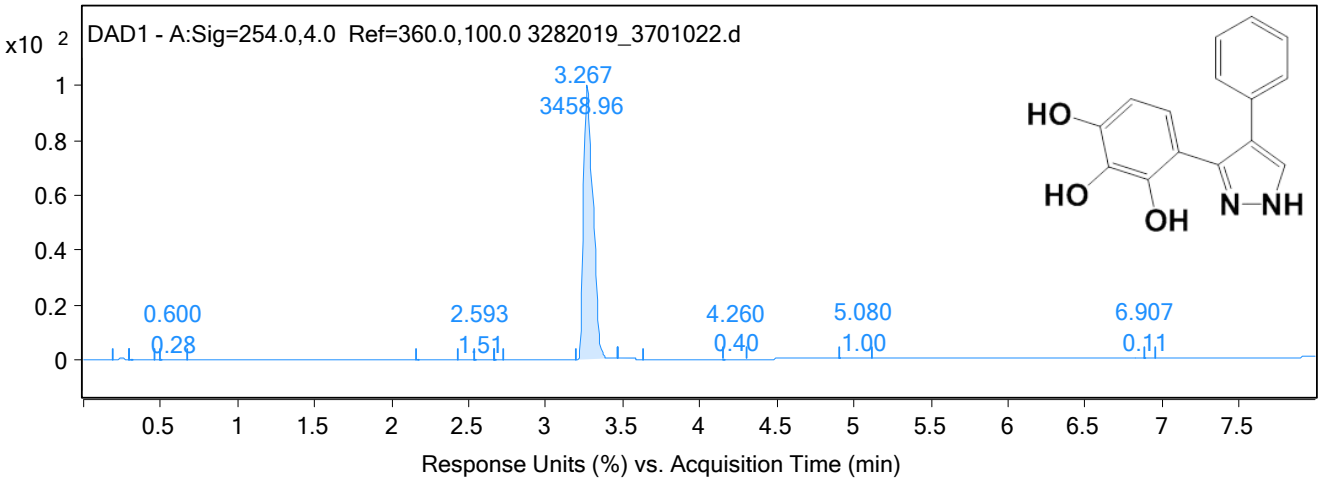


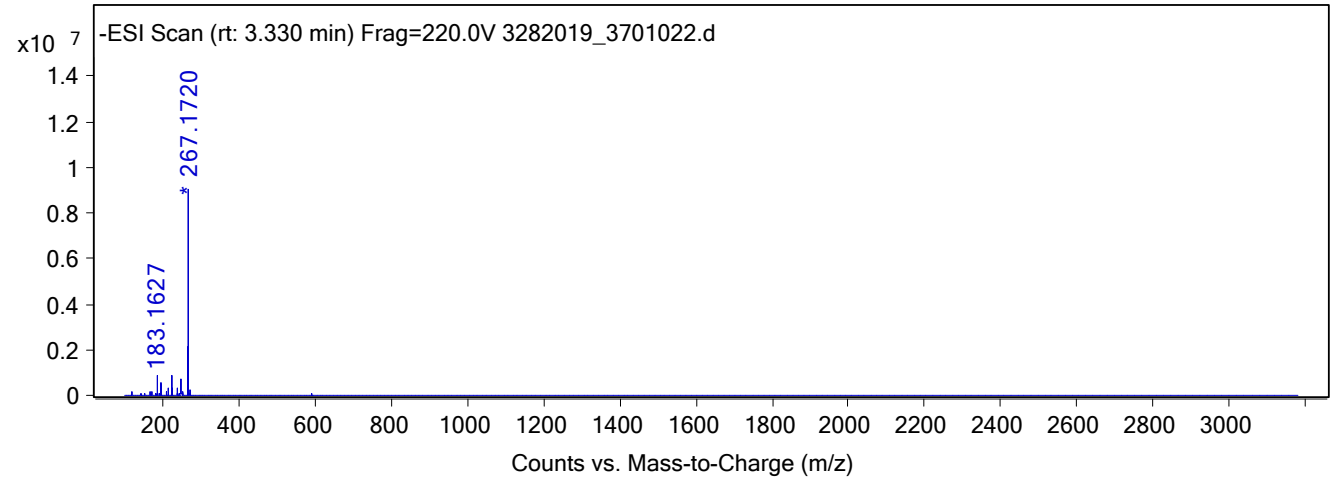


^{13}C NMR (100 MHz, DMSO-d_6): δ 161.6 (d, $J_{C\text{-}F}$ = 243.9 Hz), 147.3, 145.5, 140.4, 138.4 (q, $J_{C\text{-}F}$ = 34.6 Hz), 133.4, 131.8 (d, $J_{C\text{-}F}$ = 8.3 Hz), 128.2 (d, $J_{C\text{-}F}$ = 3.3 Hz), 122.4 (q, $J_{C\text{-}F}$ = 271.4 Hz), 121.1, 117.2, 115.2 (d, $J_{C\text{-}F}$ = 21.4 Hz), 107.5, 107.1.



Compound 20 4-(4-phenyl-1H-pyrazol-3-yl)benzene-1,2,3-triol





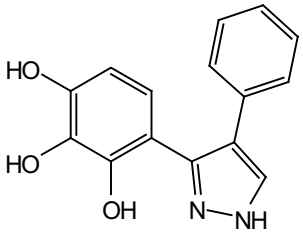
Integration Peak List

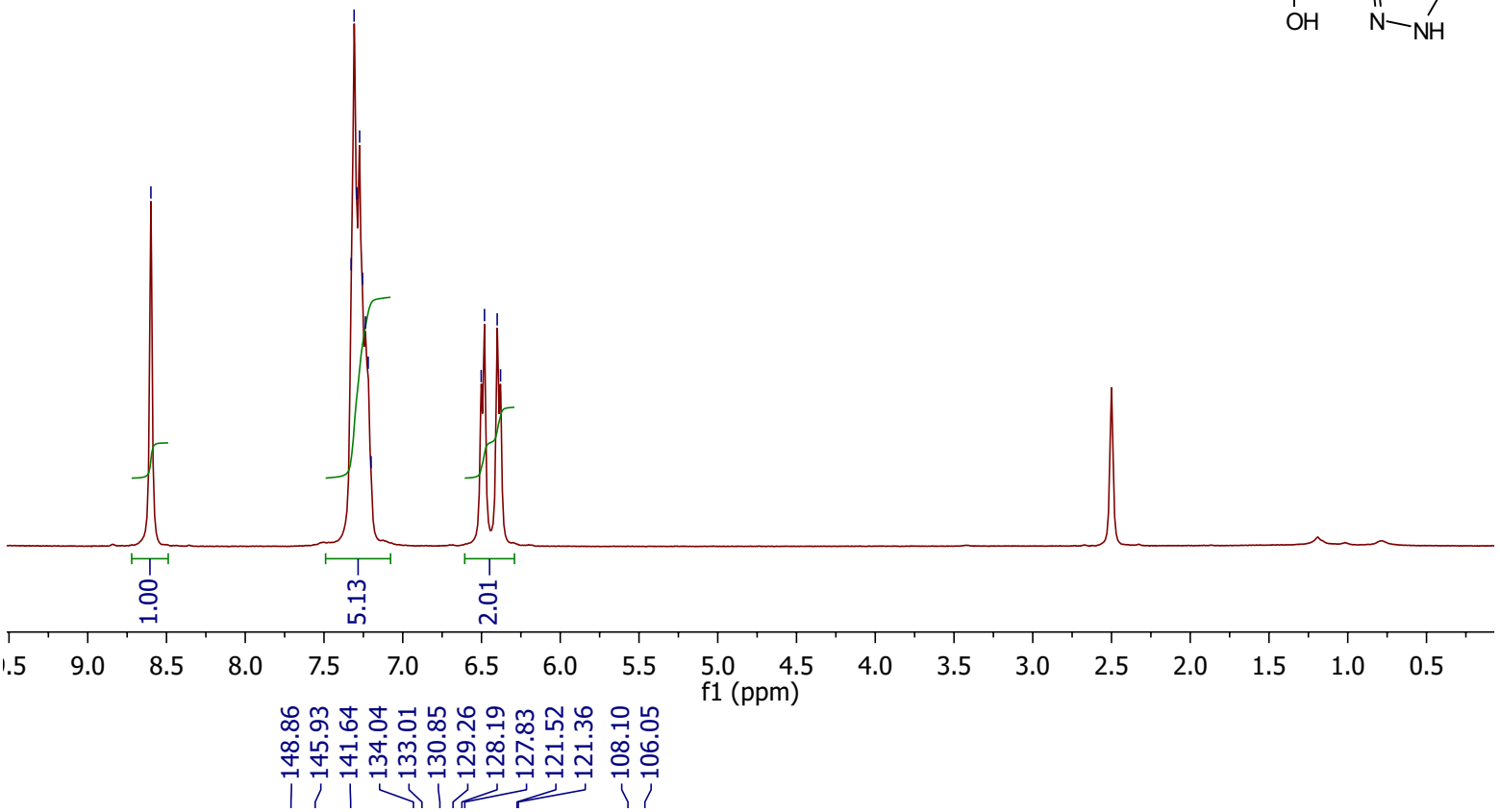
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.293	6.36	16.48	0.48
2	0.3	0.427	0.46	0.11	1.68	0.05
3	0.493	0.6	0.667	0.04	0.28	0.01
4	2.16	2.347	2.433	0.3	1.41	0.04
5	2.533	2.593	2.66	0.42	1.51	0.04
6	2.667	2.72	2.727	0.02	0.13	0
7	3.2	3.267	3.467	819.26	3458.96	100
8	3.467	3.513	3.627	1.49	6.56	0.19
9	4.153	4.26	4.3	0.09	0.4	0.01
10	4.9	5.08	5.12	0.08	1	0.03
11	6.88	6.907	6.953	0.05	0.11	0

Peak List

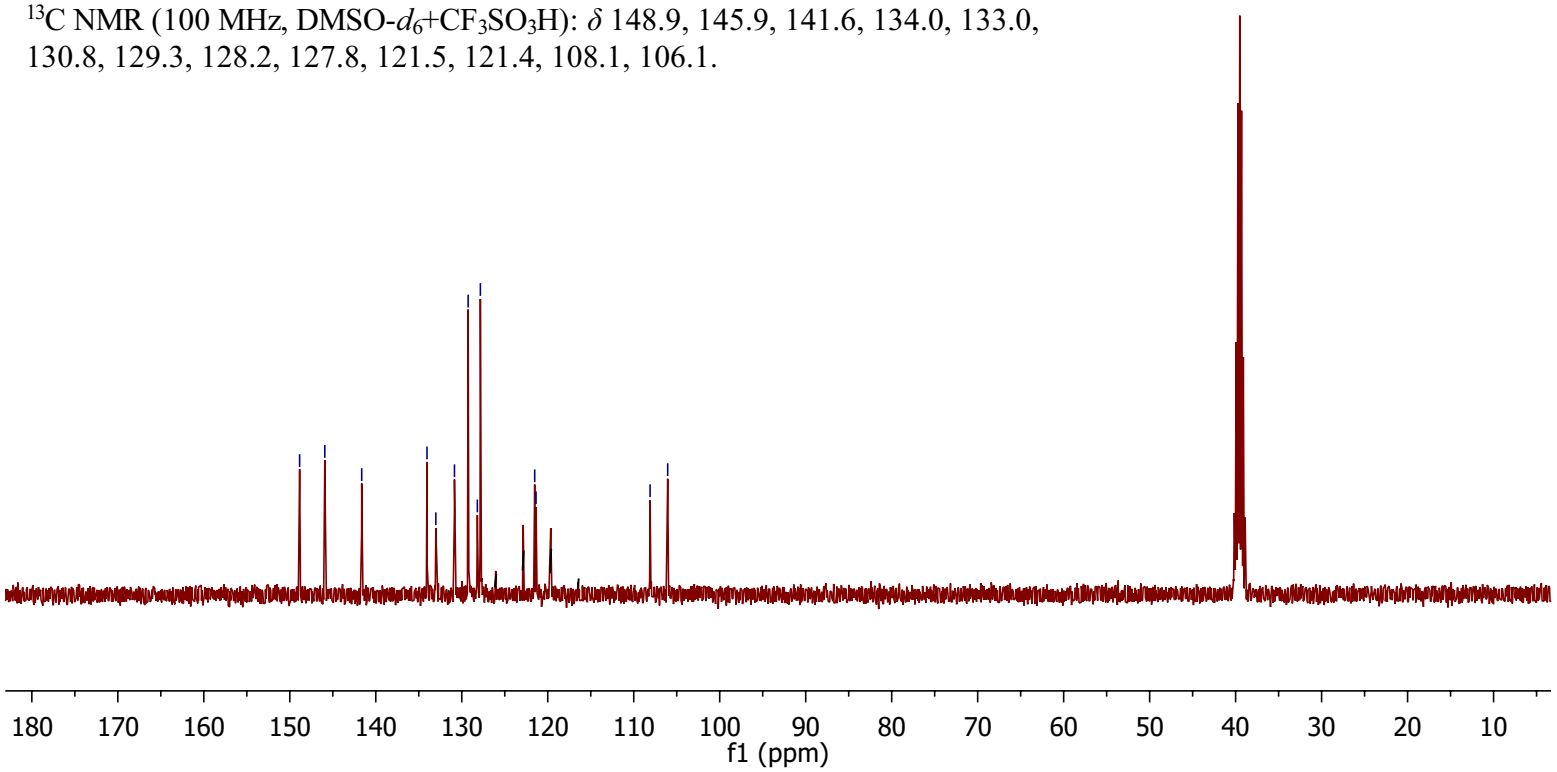
m/z	z	Abund
183.1627	1	918818.04
193.15	1	595205.58
195.1661		500054.65
211.1622		291454.42
221.1519	1	905673.78
223.1687		296932.56
239.1666		320068.5
249.1541	1	749532.53
267.172	1	9068664.97
268.1729	1	2153016.24

^{1}H NMR (400 MHz, DMSO-d_6+CF_3SO_3H): δ 8.60 (s, 1H), 7.41 – 7.12 (m, 5H), 6.49 (d, J = 8.4 Hz, 1H), 6.39 (d, J = 8.4 Hz, 1H).

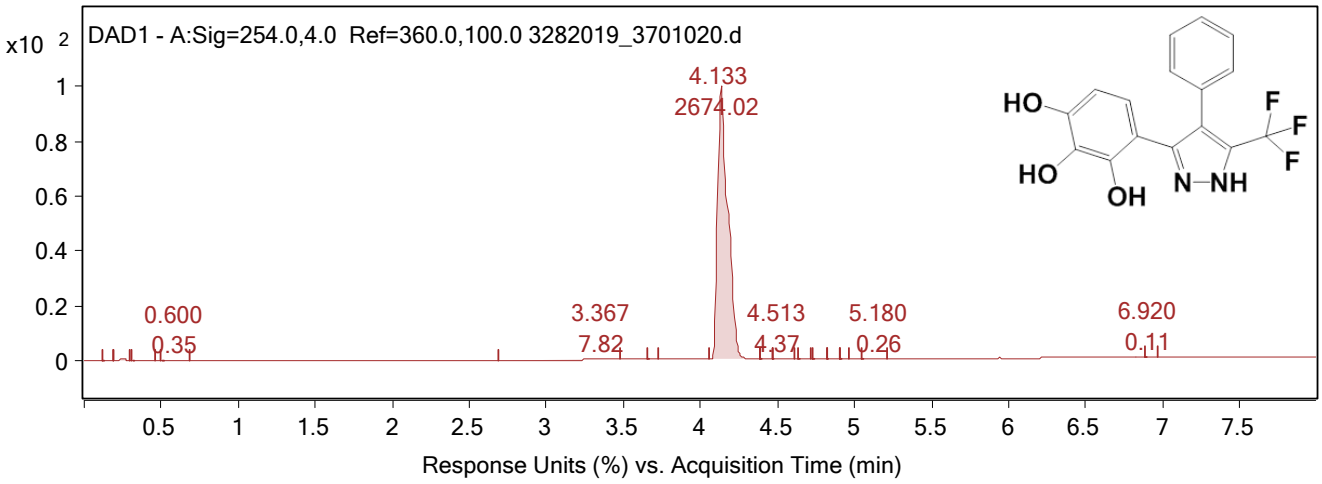


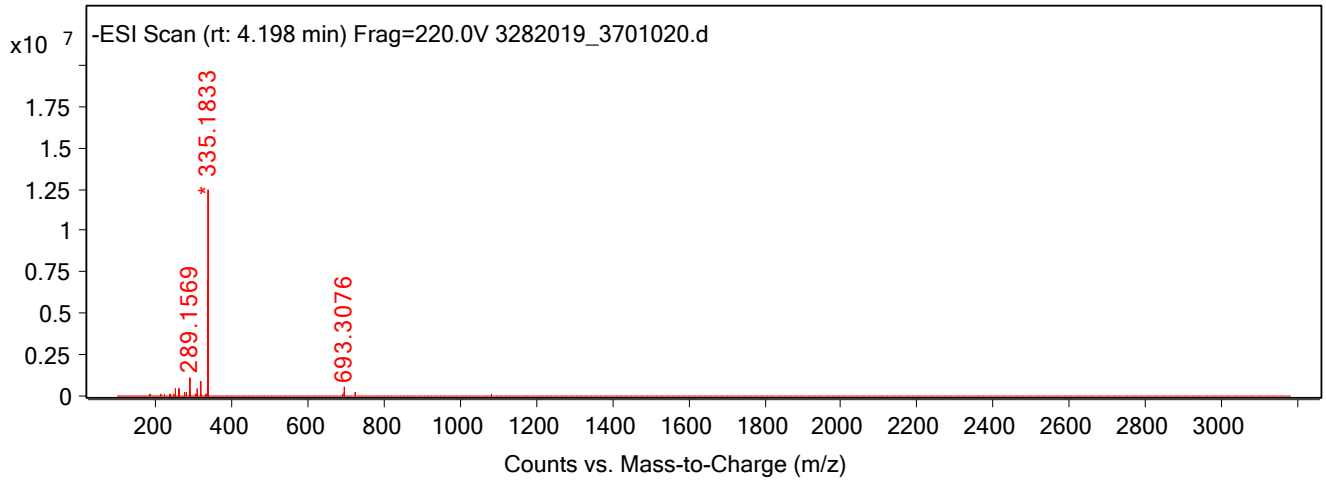


^{13}C NMR (100 MHz, DMSO-d_6+CF_3SO_3H): δ 148.9, 145.9, 141.6, 134.0, 133.0, 130.8, 129.3, 128.2, 127.8, 121.5, 121.4, 108.1, 106.1.



Compound 21 4-(4-phenyl-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol



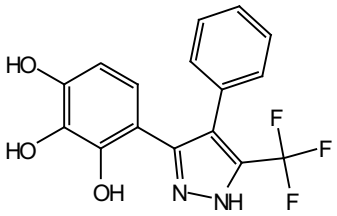


Integration Peak List

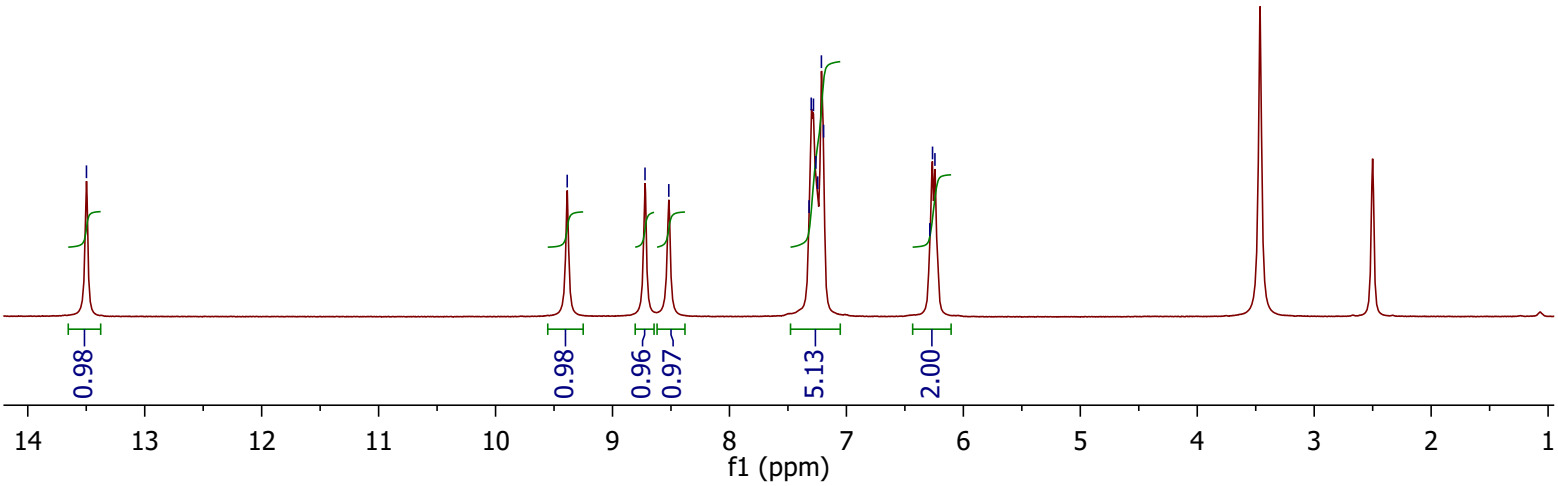
Peak	Start	RT	End	Height	Area	Area %
1	0.12	0.18	0.193	0.03	0.19	0.01
2	0.193	0.253	0.3	6.18	16.21	0.61
3	0.307	0.427	0.46	0.11	1.56	0.06
4	0.5	0.6	0.687	0.05	0.35	0.01
5	2.687	3.367	3.473	1.04	7.82	0.29
6	3.653	3.7	3.727	0.06	0.27	0.01
7	4.053	4.133	4.38	572.55	2674.02	100
8	4.387	4.433	4.467	0.64	1.67	0.06
9	4.467	4.513	4.607	1.19	4.37	0.16
10	4.633	4.687	4.72	0.2	0.64	0.02
11	4.727	4.767	4.82	0.23	0.65	0.02
12	4.82	4.867	4.907	0.37	0.94	0.04
13	4.907	4.92	4.96	0.06	0.09	0
14	5.047	5.18	5.207	0.02	0.26	0.01
15	6.887	6.92	6.967	0.05	0.11	0

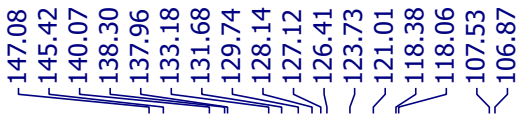
Peak List

m/z	z	Abund
251.1685		482799.42
261.1553		456203.83
263.1713		453563.34
289.1569	1	1127442.04
307.1719		455484.48
317.1586	1	925159.97
335.1833		12852305.54
336.1786	1	7176820.88
337.18	1	885880.22
693.3076	1	537053.86



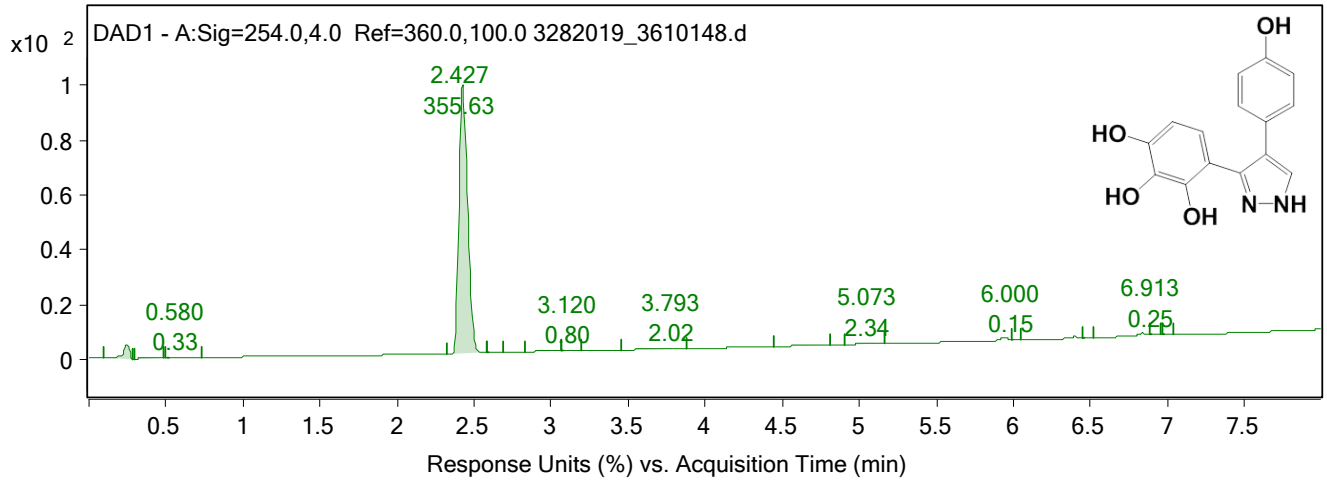
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.50 (s, 1H), 9.39 (s, 1H), 8.72 (s, 1H), 8.52 (s, 1H), 7.37 – 7.15 (m, 5H), 6.28 (d, J = 9.4 Hz, 1H), 6.24 (d, J = 9.4 Hz, 1H).

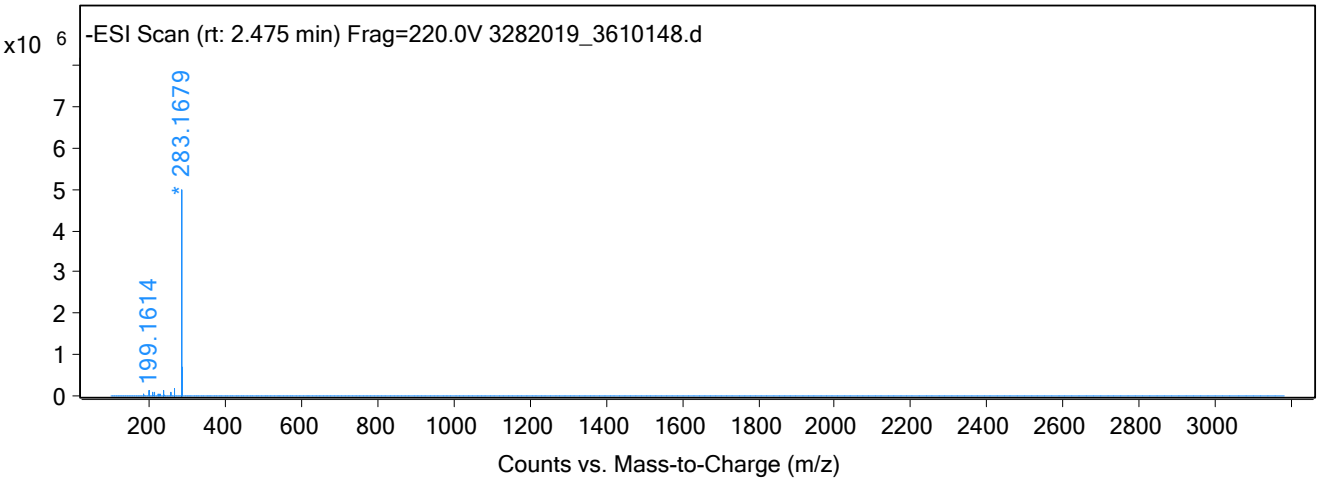




^{13}C NMR (100 MHz, DMSO-d_6) δ 147.1, 145.4, 140.1, 138.1 (q, $J_{C\text{-}F}$ = 34.6 Hz), 133.2, 131.7, 129.7, 128.1, 127.1, 122.40 (q, $J_{C\text{-}F}$ = 269.2 Hz), 121.0, 118.1, 107.51, 106.9.

Compound 22 4-(4-(4-hydroxyphenyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol





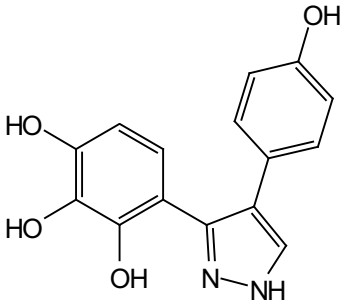
Integration Peak List

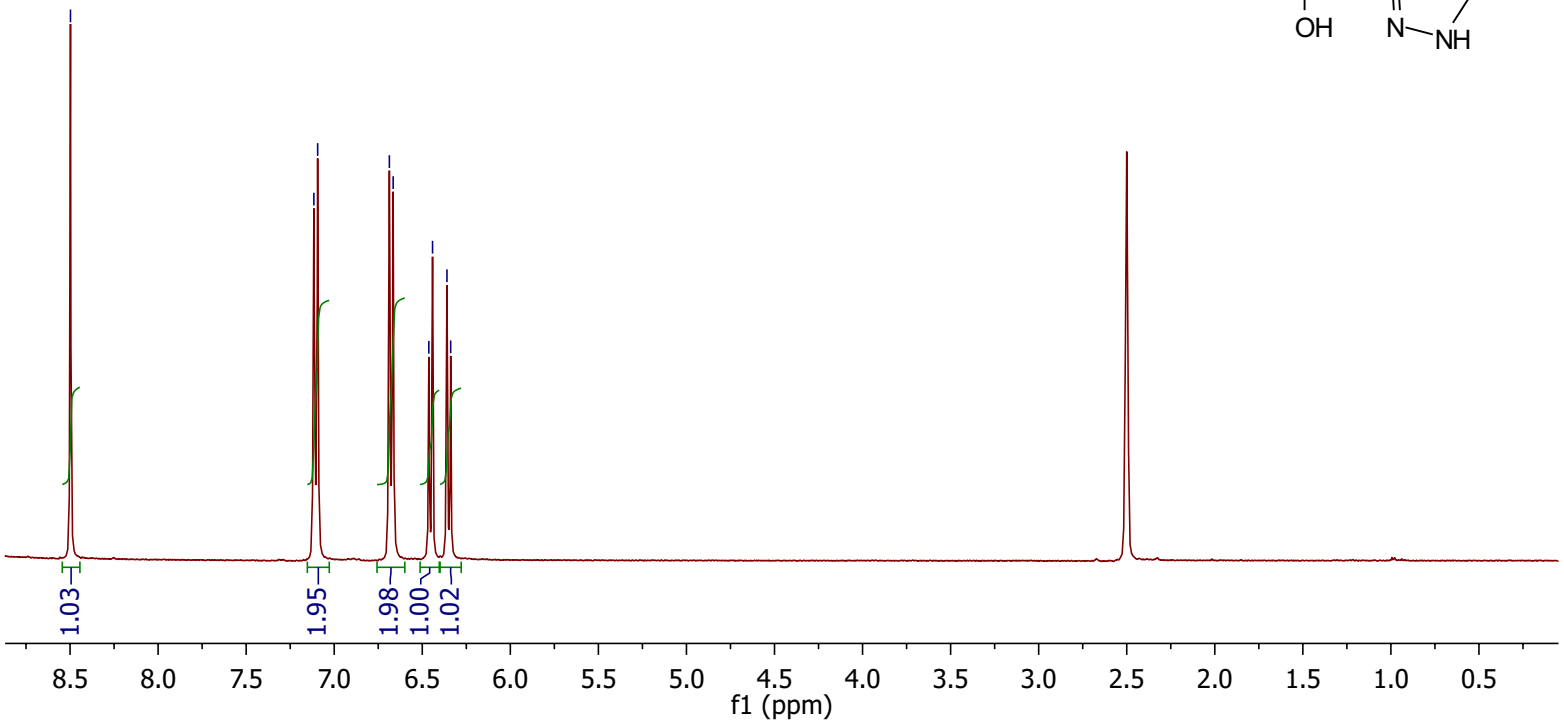
Peak	Start	RT	End	Height	Area	Area %
1	0.093	0.247	0.287	4.82	14.89	4.19
2	0.293	0.4	0.48	0.43	4.04	1.14
3	0.5	0.58	0.727	0.05	0.33	0.09
4	2.32	2.427	2.587	91.39	355.63	100
5	2.587	2.633	2.693	0.07	0.24	0.07
6	2.827	2.967	3.06	0.32	2.16	0.61
7	3.067	3.12	3.193	0.2	0.8	0.22
8	3.46	3.793	3.873	0.1	2.02	0.57
9	4.447	4.68	4.813	0.51	4.52	1.27
10	4.9	5.073	5.16	0.25	2.34	0.66
11	5.987	6	6.053	0.06	0.15	0.04
12	6.453	6.487	6.52	0.04	0.1	0.03
13	6.887	6.913	6.96	0.12	0.25	0.07
14	6.967	7	7.033	0.02	0.03	0.01

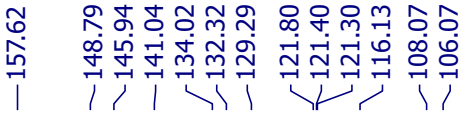
Peak List

m/z	z	Abund
199.1614		133785.14
209.1476		71467.51
211.1645		71605.52
237.1499		139822.99
239.1663		54867.4
255.164		71673.36
265.1525		163328.78
283.1679	1	5025705.41
284.1708	1	765941.57
285.1737	1	79891

^{1}H NMR (400 MHz, DMSO-d_6+CF_3SO_3H): δ 8.50 (s, 1H), 7.10 (d, J = 8.6 Hz, 2H), 6.68 (d, J = 8.6 Hz, 2H), 6.45 (d, J = 8.4 Hz, 1H), 6.35 (d, J = 8.4 Hz, 1H).

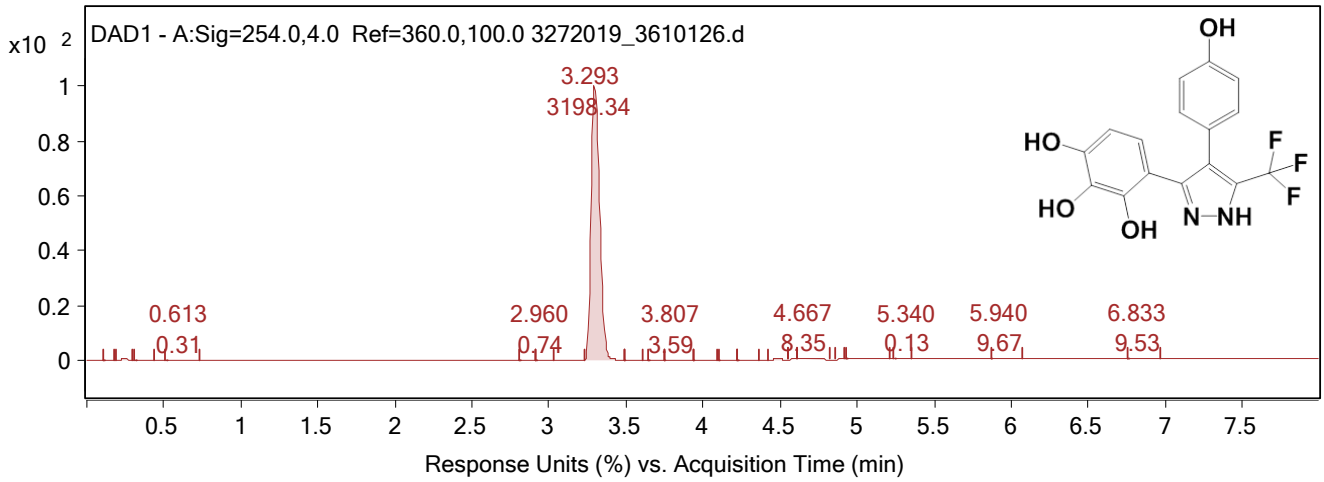


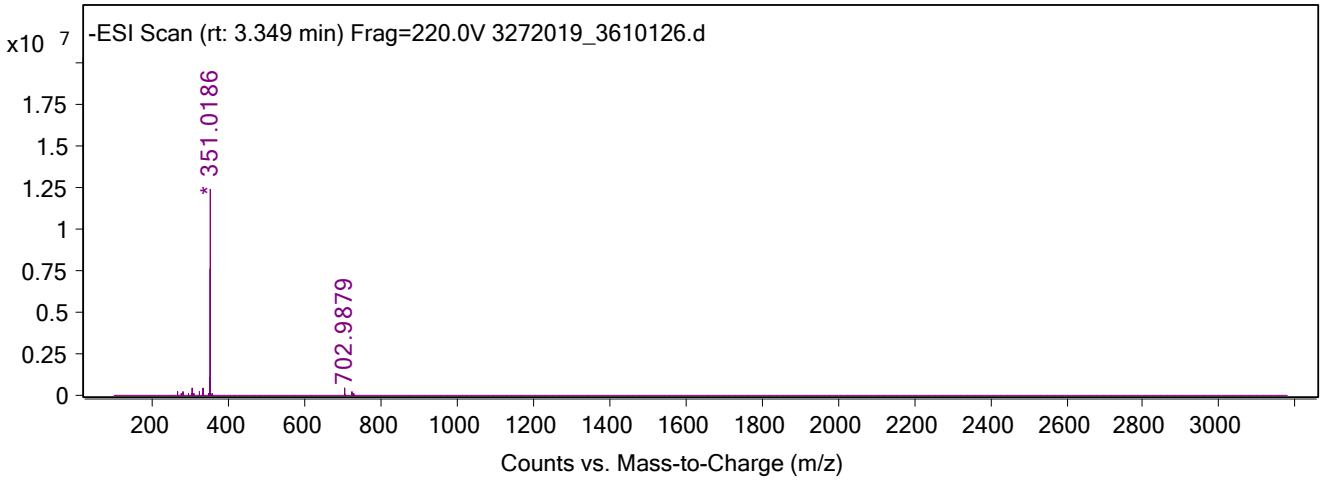




^{13}C NMR (100 MHz, DMSO-d_6+CF_3SO_3H): δ 157.6, 148.8, 145.9, 141.0, 134.0, 132.3, 129.3, 121.8, 121.4, 121.3, 116.1, 108.1, 106.1.

Compound 23 4-(4-(4-hydroxyphenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol



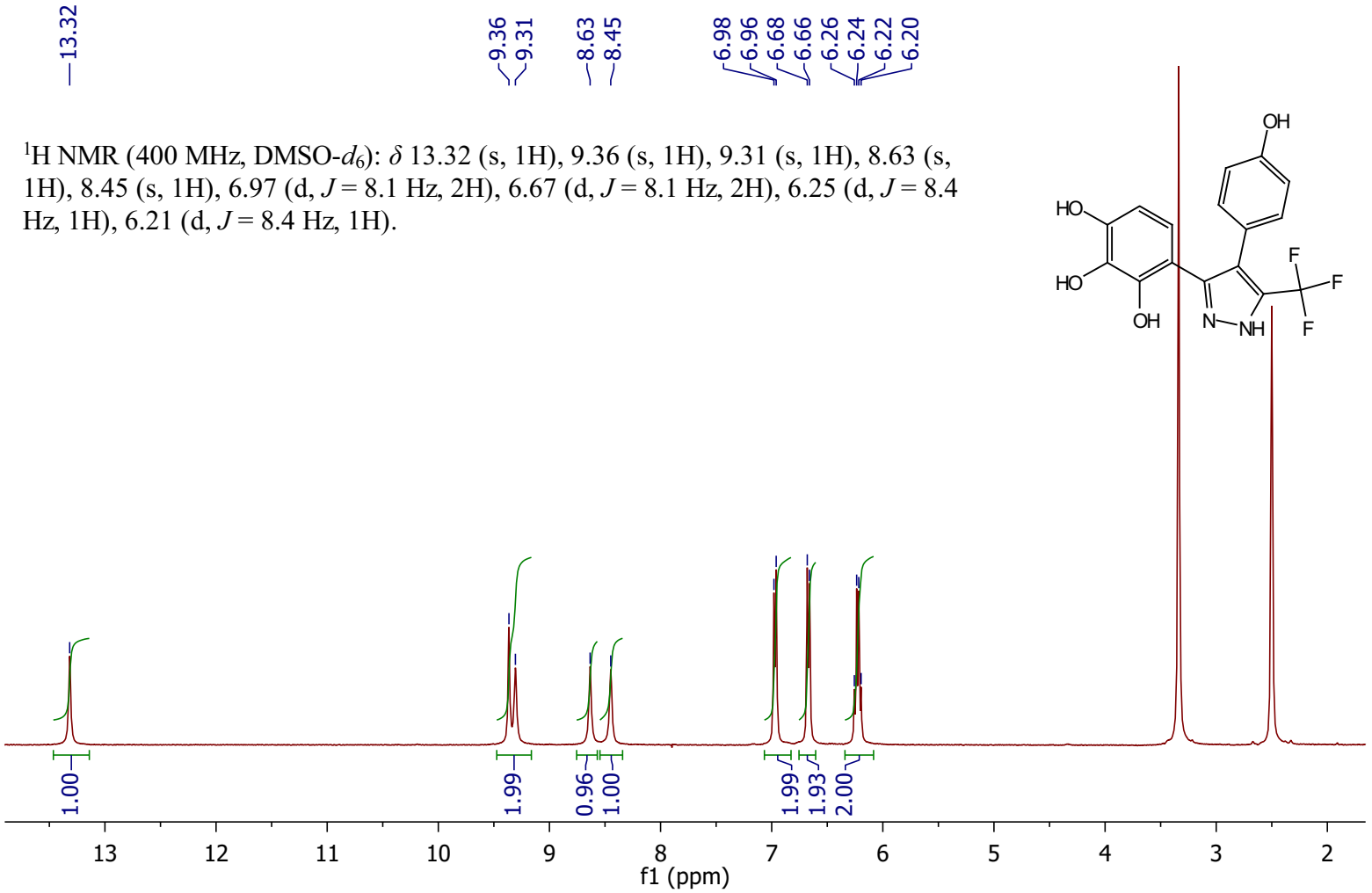


Integration Peak List

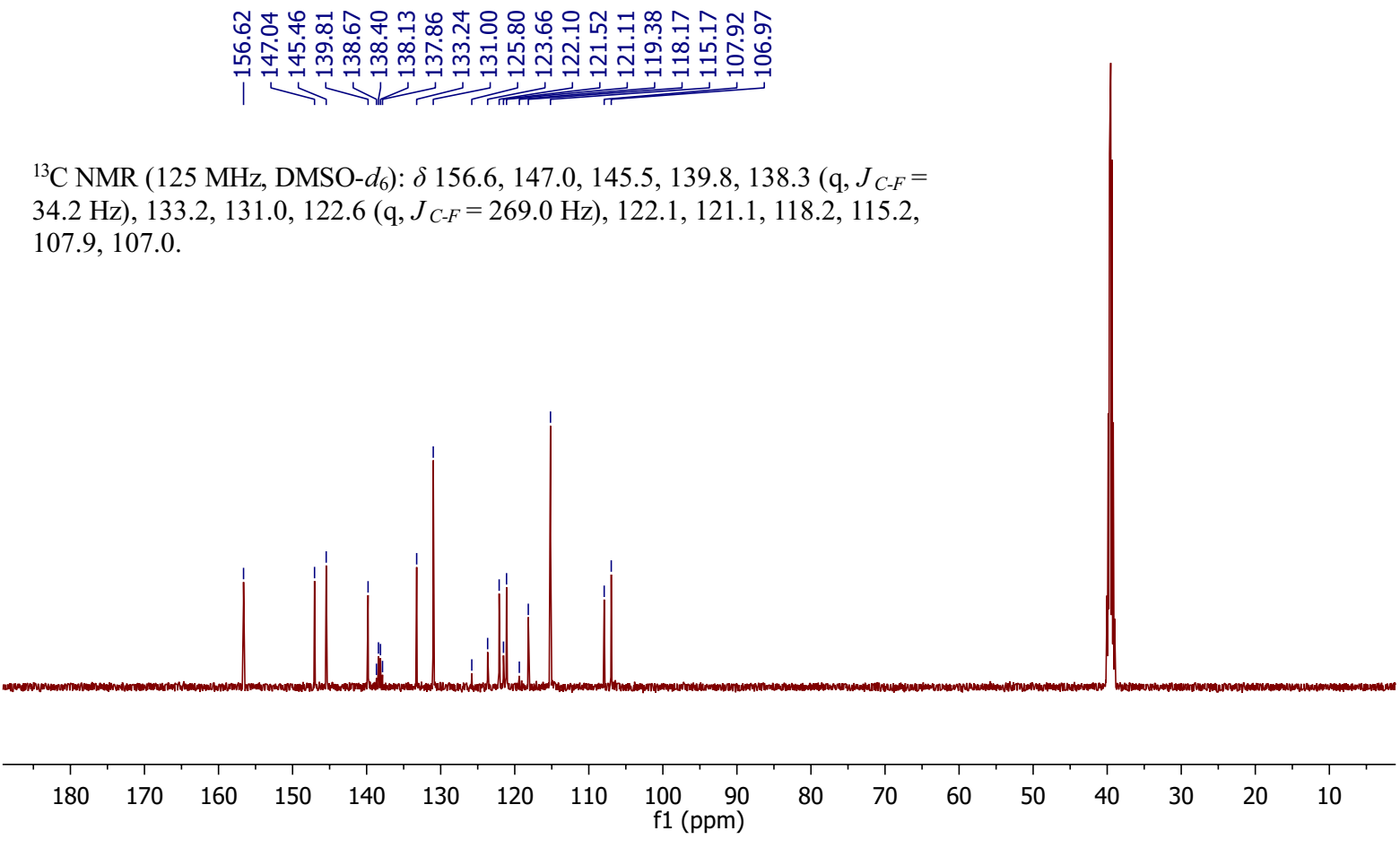
Peak	Start	RT	End	Height	Area	Area %
1	0.107	0.153	0.18	0.04	0.11	0
2	0.187	0.247	0.3	8.93	24.11	0.75
3	0.307	0.4	0.433	0.09	0.83	0.03
4	0.507	0.613	0.727	0.05	0.31	0.01
5	2.807	2.893	2.913	0.1	0.44	0.01
6	2.913	2.96	3.033	0.22	0.74	0.02
7	3.227	3.293	3.487	818.94	3198.34	100
8	3.487	3.52	3.607	0.13	0.55	0.02
9	3.647	3.72	3.747	0.12	0.49	0.02
10	3.747	3.807	3.933	0.71	3.59	0.11
11	3.933	3.987	4.093	0.56	2.32	0.07
12	4.1	4.187	4.22	0.15	0.87	0.03
13	4.22	4.28	4.367	0.16	0.72	0.02
14	4.427	4.48	4.547	0.8	2.85	0.09
15	4.553	4.593	4.607	0.1	0.27	0.01
16	4.607	4.667	4.827	1.64	8.35	0.26
17	4.853	4.907	4.92	0.05	0.2	0.01
18	4.927	5.073	5.207	0.44	2.71	0.08
19	5.24	5.34	5.347	0.01	0.13	0
20	5.867	5.94	6.073	1.88	9.67	0.3
21	6.76	6.833	6.973	1.81	9.53	0.3

Peak List

m/z	z	Abund
267.0419		197900.13
279.0393		175983.54
305.013		480303.1
323.0194		240414.58
333.0017		486855.61
351.0186		13077913.86
352.0125	1	7710646.48
353.0129	1	1082562.77
702.9879	1	446692.75
724.9646		225039.39

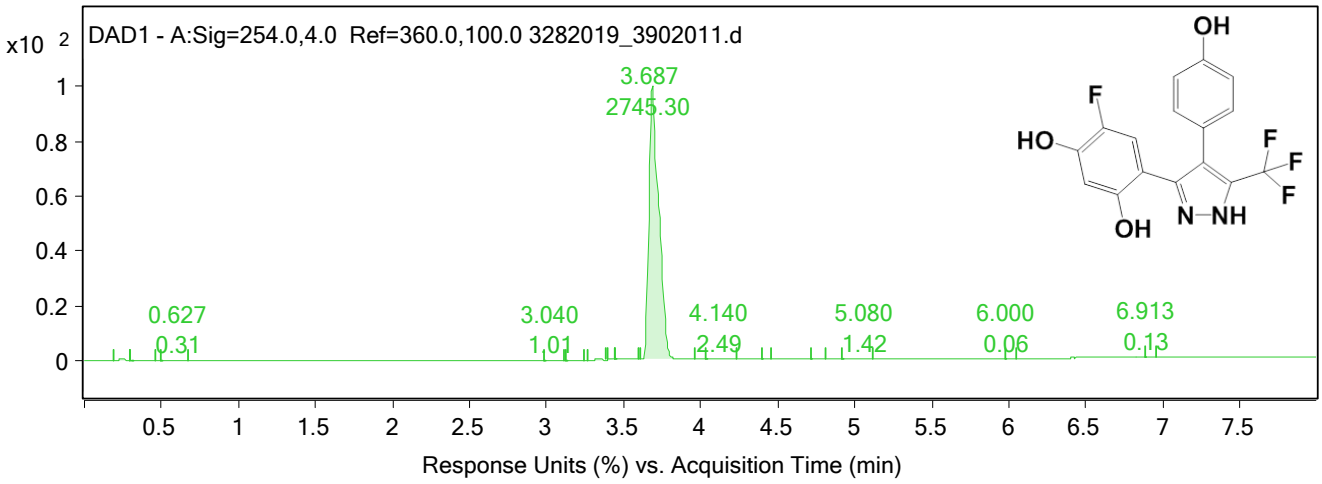


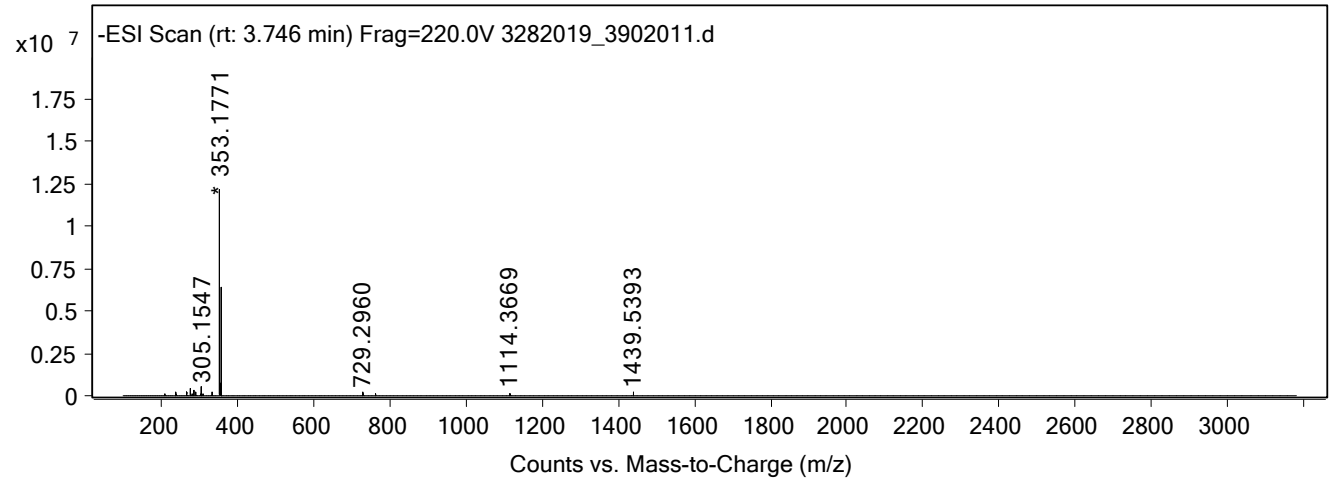
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.32 (s, 1H), 9.36 (s, 1H), 9.31 (s, 1H), 8.63 (s, 1H), 8.45 (s, 1H), 6.97 (d, J = 8.1 Hz, 2H), 6.67 (d, J = 8.1 Hz, 2H), 6.25 (d, J = 8.4 Hz, 1H), 6.21 (d, J = 8.4 Hz, 1H).



^{13}C NMR (125 MHz, DMSO-d_6): δ 156.6, 147.0, 145.5, 139.8, 138.3 (q, $J_{C\text{-}F}$ = 34.2 Hz), 133.2, 131.0, 122.6 (q, $J_{C\text{-}F}$ = 269.0 Hz), 122.1, 121.1, 118.2, 115.2, 107.9, 107.0.

Compound 24 4-fluoro-6-(4-(4-hydroxyphenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,3-diol



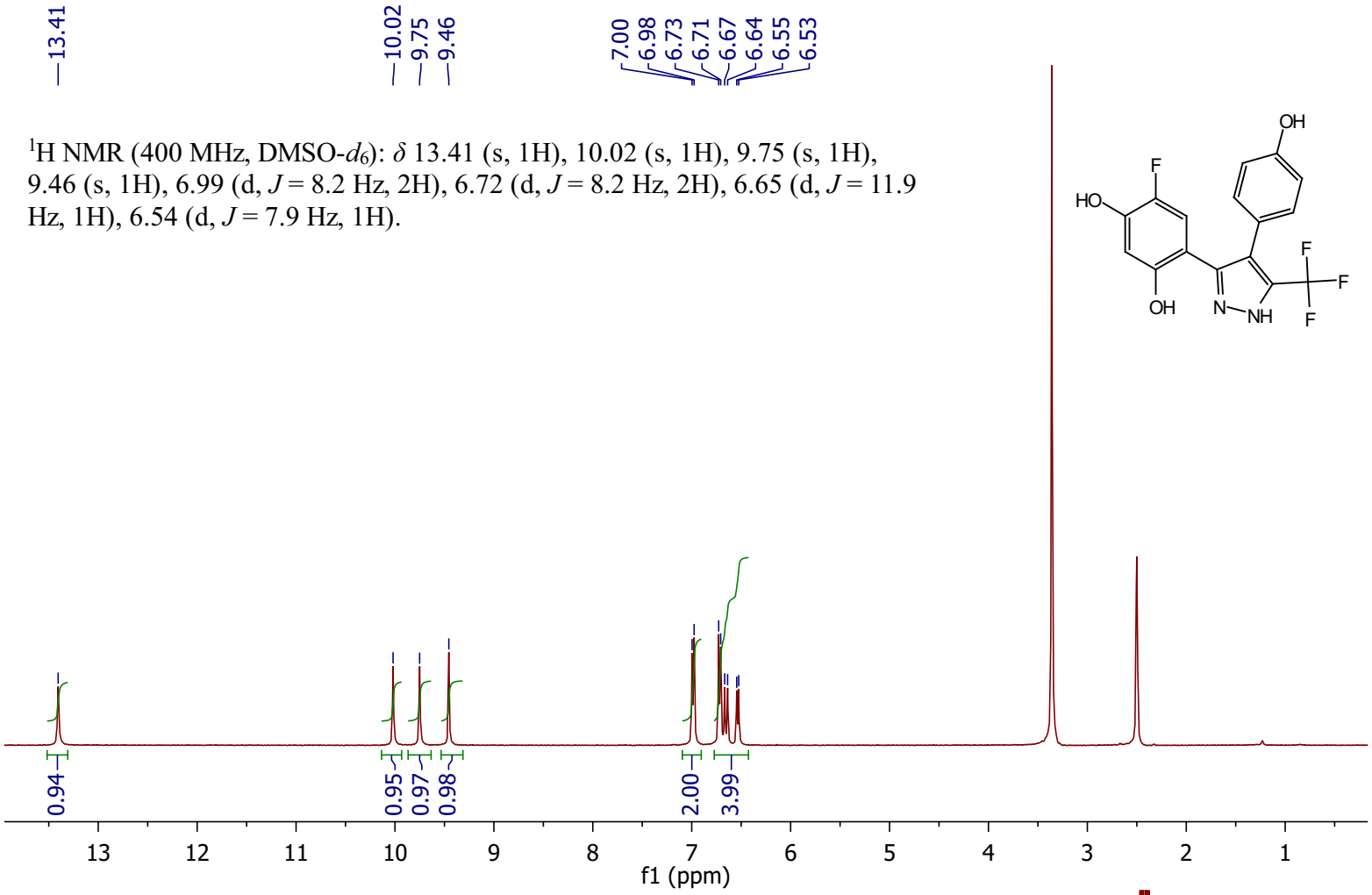


Integration Peak List

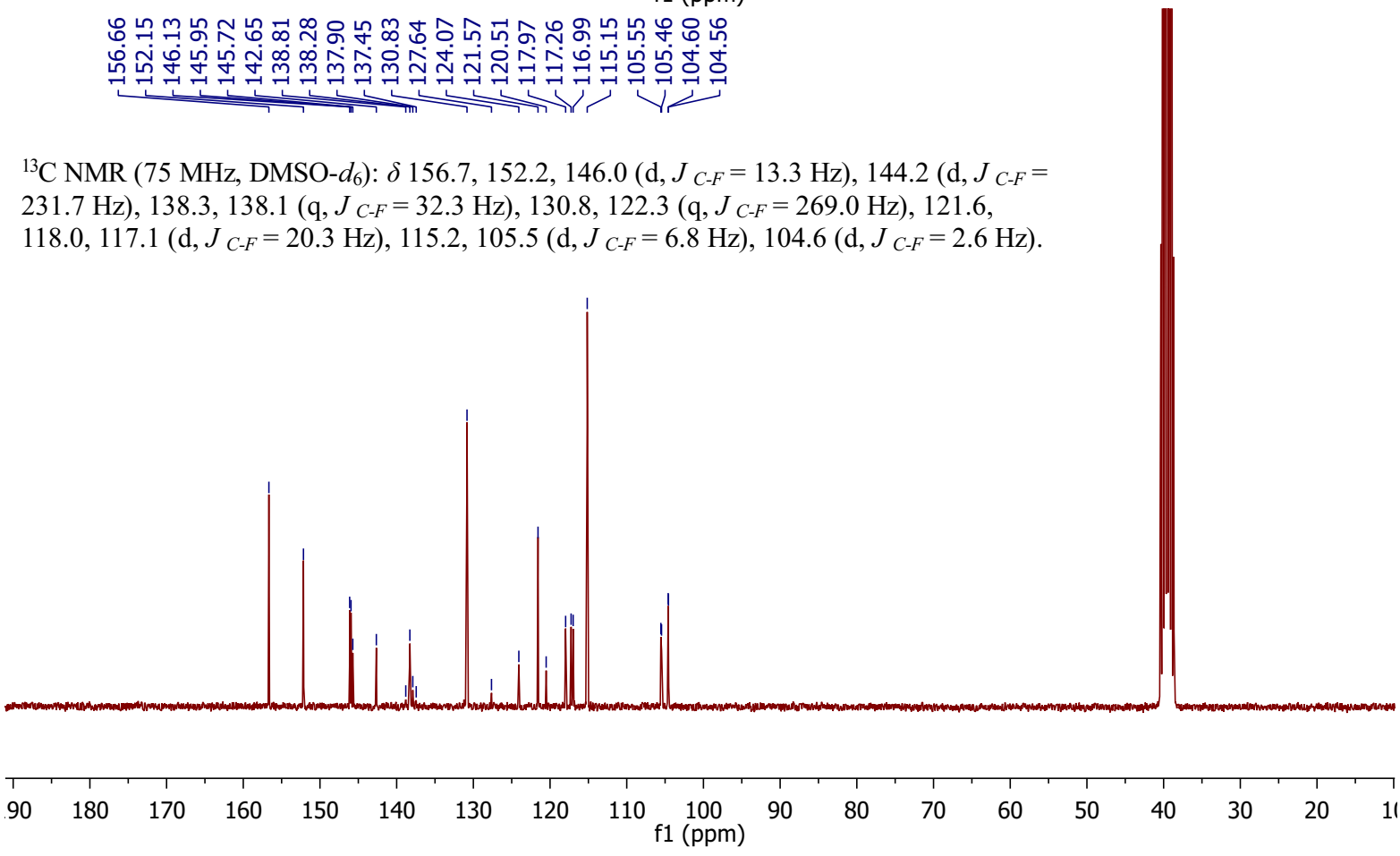
Peak	Start	RT	End	Height	Area	Area %
1	0.193	0.247	0.3	6.3	16.4	0.6
2	0.3	0.433	0.46	0.09	1.57	0.06
3	0.493	0.627	0.667	0.03	0.31	0.01
4	2.987	3.04	3.113	0.28	1.01	0.04
5	3.127	3.22	3.247	0.04	0.33	0.01
6	3.26	3.347	3.387	0.12	0.73	0.03
7	3.393	3.433	3.447	0.08	0.21	0.01
8	3.447	3.493	3.6	1.23	4.91	0.18
9	3.613	3.687	3.96	609.62	2745.3	100
10	4.033	4.14	4.233	0.43	2.49	0.09
11	4.393	4.433	4.453	0.03	0.07	0
12	4.713	4.733	4.807	0.02	0.07	0
13	4.92	5.08	5.113	0.1	1.42	0.05
14	5.973	6	6.047	0.03	0.06	0
15	6.88	6.913	6.96	0.05	0.13	0

Peak List

m/z	z	Abund
265.1224		236298.67
265.1502		280166.26
277.1539		417478.48
285.1344		279586.85
305.1547		535361.23
333.1576		263809.36
353.1771		12163543.26
354.1729	1	6534368.56
355.1747	1	765438.06
729.296		223606.97

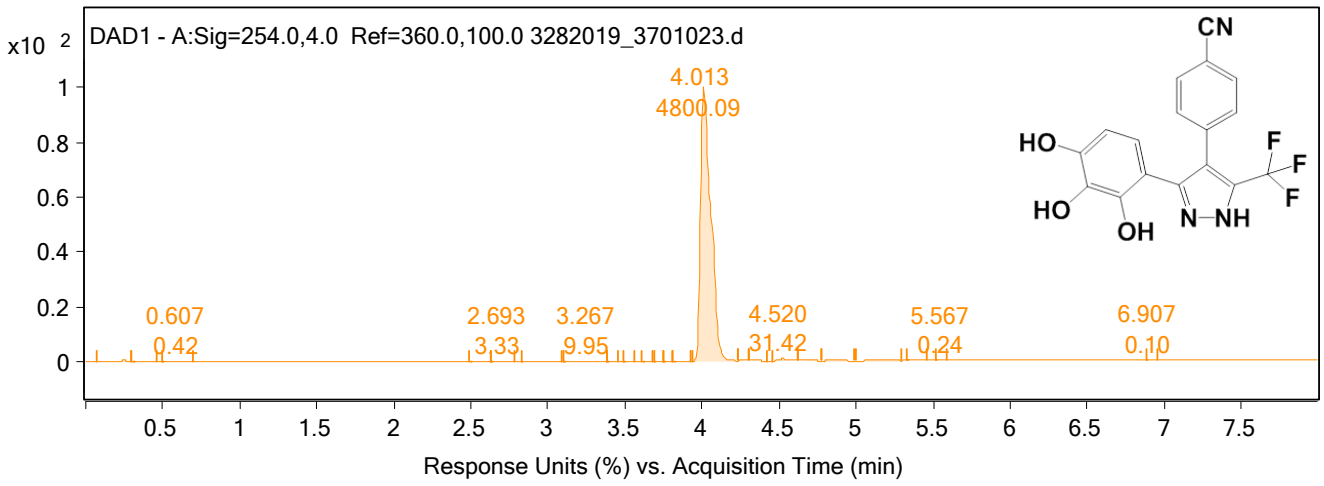


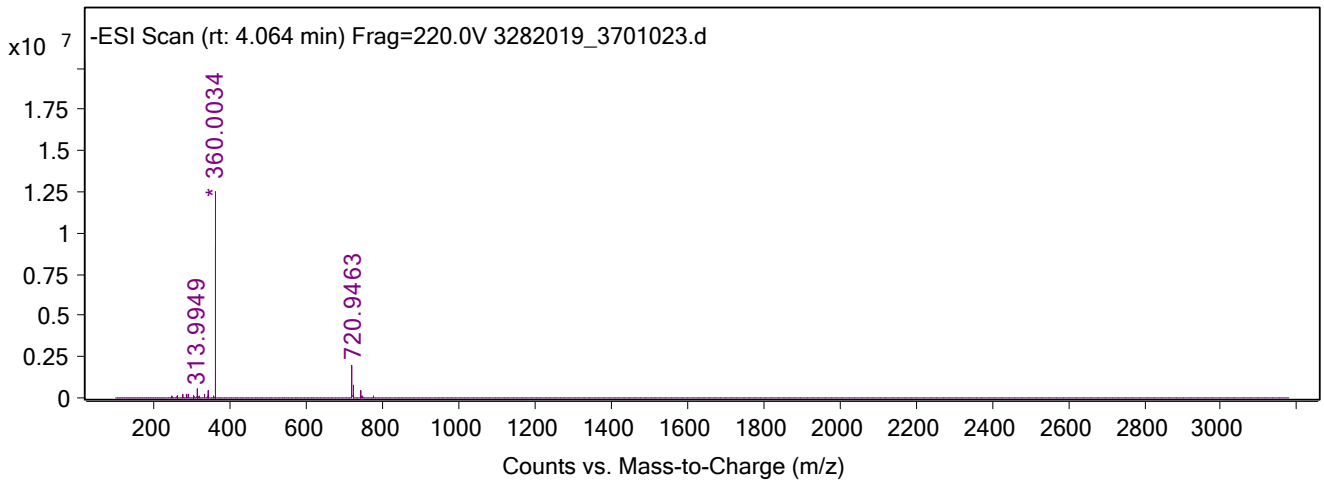
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.41 (s, 1H), 10.02 (s, 1H), 9.75 (s, 1H), 9.46 (s, 1H), 6.99 (d, J = 8.2 Hz, 2H), 6.72 (d, J = 8.2 Hz, 2H), 6.65 (d, J = 11.9 Hz, 1H), 6.54 (d, J = 7.9 Hz, 1H).



^{13}C NMR (75 MHz, DMSO-d_6): δ 156.7, 152.2, 146.0 (d, $J_{C\text{-}F}$ = 13.3 Hz), 144.2 (d, $J_{C\text{-}F}$ = 231.7 Hz), 138.3, 138.1 (q, $J_{C\text{-}F}$ = 32.3 Hz), 130.8, 122.3 (q, $J_{C\text{-}F}$ = 269.0 Hz), 121.6, 118.0, 117.1 (d, $J_{C\text{-}F}$ = 20.3 Hz), 115.2, 105.5 (d, $J_{C\text{-}F}$ = 6.8 Hz), 104.6 (d, $J_{C\text{-}F}$ = 2.6 Hz).

Compound 25 4-(5-(trifluoromethyl)-3-(2,3,4-trihydroxyphenyl)-1H-pyrazol-4-yl)benzonitrile





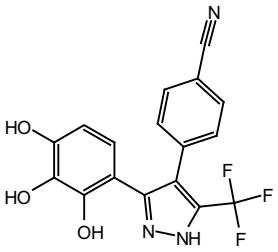
Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	0.067	0.247	0.3	6.59	19.2	0.4
2	0.3	0.42	0.46	0.13	1.58	0.03
3	0.493	0.607	0.7	0.05	0.42	0.01
4	2.493	2.553	2.633	1.07	3.74	0.08
5	2.633	2.693	2.787	0.9	3.33	0.07
6	2.827	3.007	3.087	0.54	2.78	0.06
7	3.1	3.267	3.387	1.88	9.95	0.21
8	3.387	3.433	3.46	0.07	0.18	0
9	3.493	3.547	3.56	0.05	0.21	0
10	3.613	3.66	3.68	0.16	0.44	0.01
11	3.687	3.72	3.747	0.11	0.24	0.01
12	3.753	3.793	3.813	0.15	0.38	0.01
13	3.813	3.853	3.927	0.51	1.53	0.03
14	3.94	4.013	4.227	1034.68	4800.09	100
15	4.233	4.273	4.3	0.93	2.22	0.05
16	4.3	4.333	4.42	1.26	3.69	0.08
17	4.46	4.52	4.62	7.61	31.42	0.65
18	4.62	4.66	4.773	2.1	8.8	0.18
19	4.78	4.833	4.987	2.95	13.66	0.28
20	4.993	5.113	5.293	0.45	2.99	0.06
21	5.333	5.42	5.46	0.07	0.33	0.01
22	5.513	5.567	5.593	0.07	0.24	0
23	6.88	6.907	6.953	0.04	0.1	0

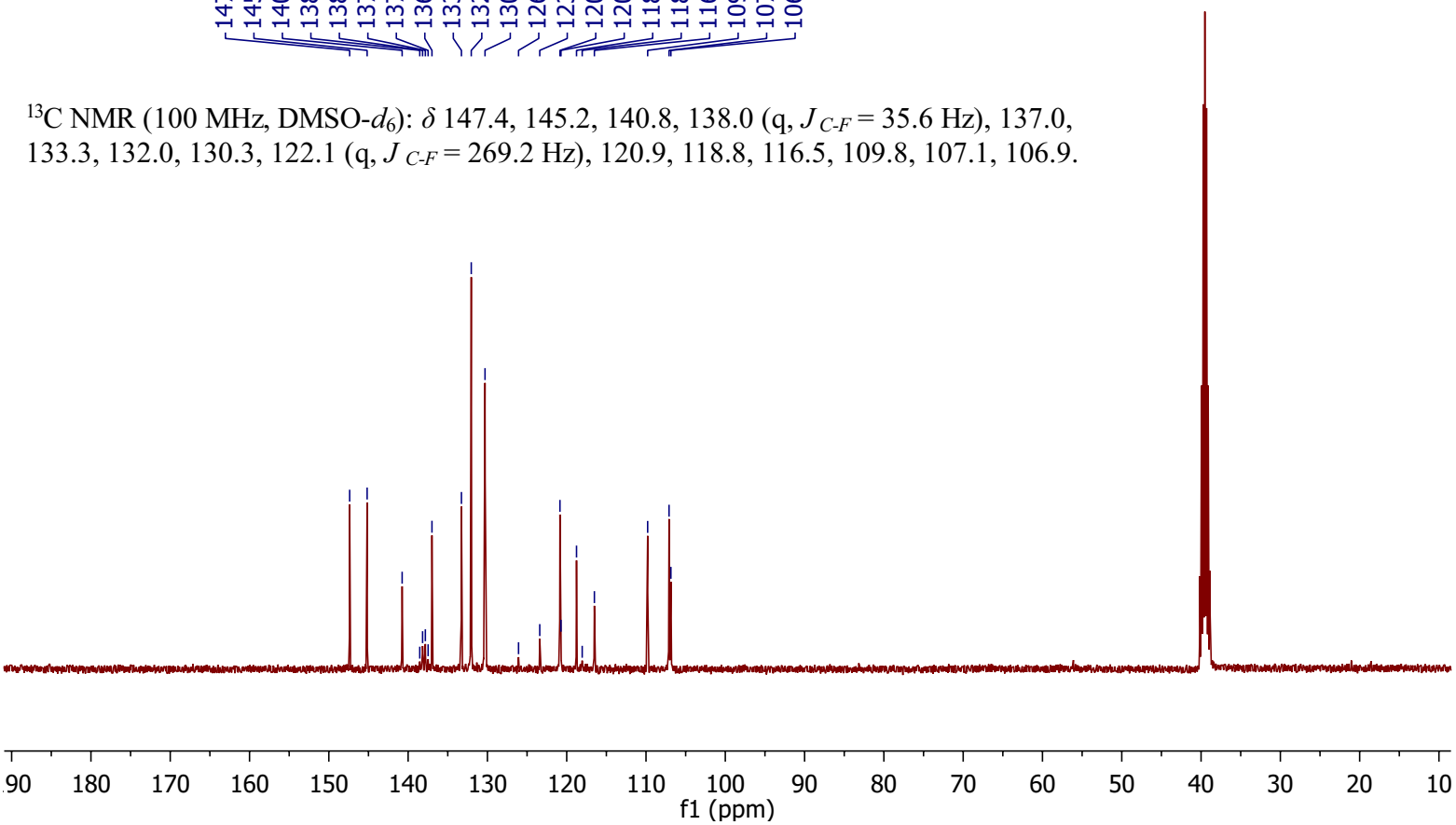
Peak List

m/z	z	Abund
288.0229		227295.06
313.9949		551182.42
332.0006		260601.7
341.9823		433758.65
360.0034		12975079.68
360.9934	1	9351257.86
361.9926	1	1584991.85
720.9463	1	2048183.42
721.9492	1	745496.14
742.9219	1	392500.68

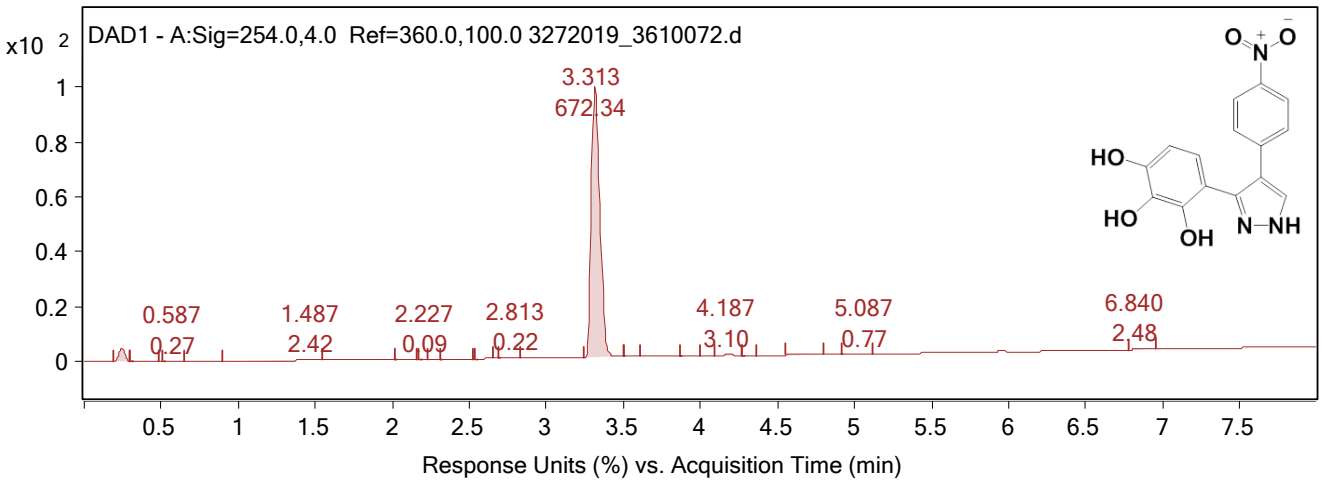
13.70 (s, 1H), 9.44 (s, 1H), 8.71 (s, 1H), 8.52 (s, 1H), 7.78 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.5 Hz, 2H), 6.32 (d, J = 8.4 Hz, 1H), 6.27 (d, J = 8.4 Hz, 1H).

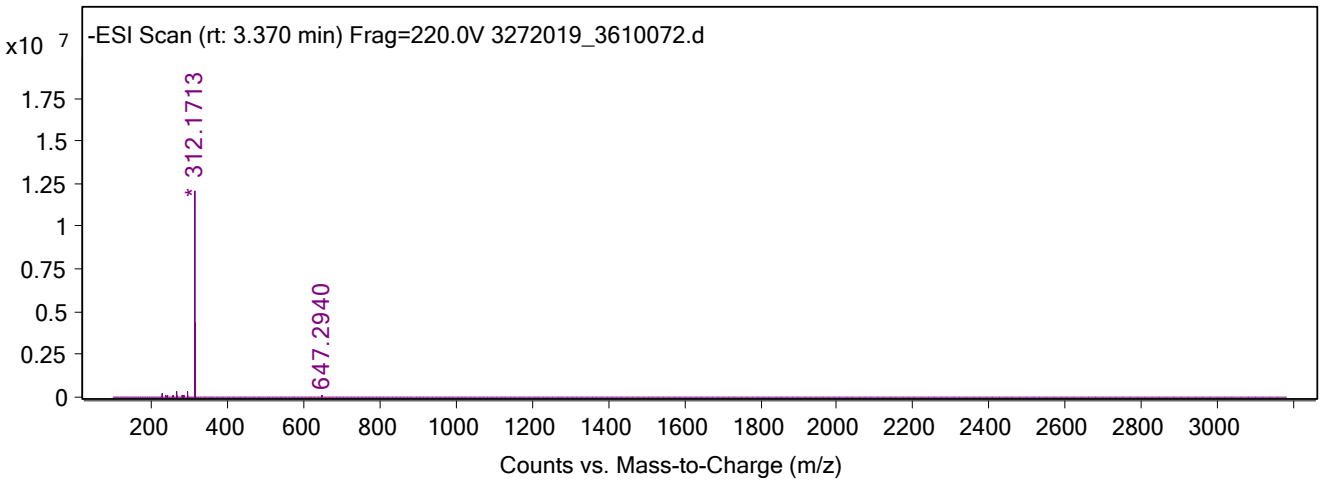


^{13}C NMR (100 MHz, DMSO-d_6): δ 147.4, 145.2, 140.8, 138.0 (q, $J_{C\text{-}F}$ = 35.6 Hz), 137.0, 133.3, 132.0, 130.3, 122.1 (q, $J_{C\text{-}F}$ = 269.2 Hz), 120.9, 118.8, 116.5, 109.8, 107.1, 106.9.



Compound 26 4-(4-(4-nitrophenyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol





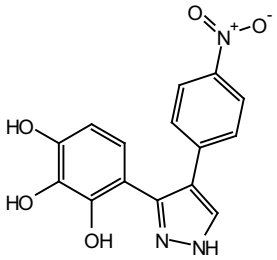
Integration Peak List

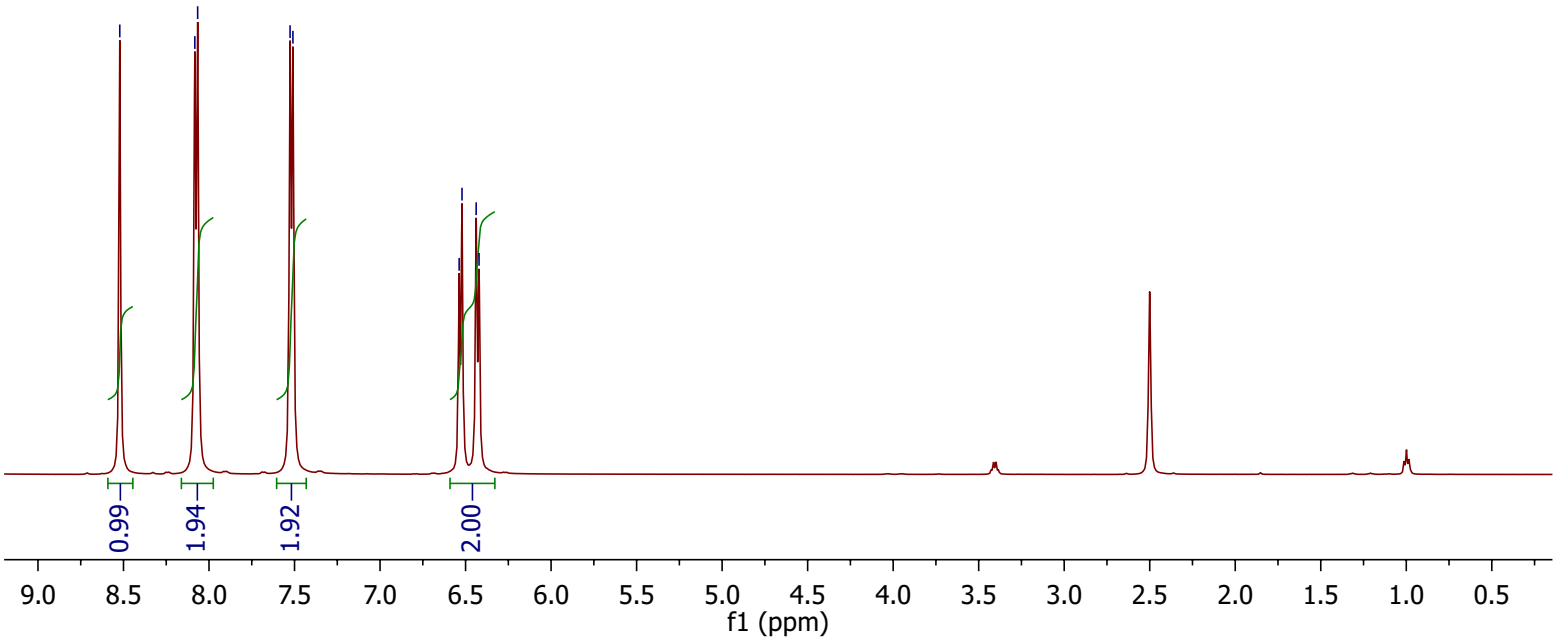
Peak	Start	RT	End	Height	Area	Area %
1	0.187	0.247	0.3	8.66	23.22	3.45
2	0.3	0.447	0.48	0.08	1.49	0.22
3	0.507	0.587	0.653	0.05	0.27	0.04
4	0.9	1.487	1.547	0.18	2.42	0.36
5	2.013	2.12	2.153	0.05	0.33	0.05
6	2.173	2.227	2.233	0.01	0.09	0.01
7	2.307	2.507	2.52	0.01	0.2	0.03
8	2.54	2.64	2.653	0.03	0.27	0.04
9	2.687	2.813	2.833	0.03	0.22	0.03
10	3.24	3.313	3.5	171.78	672.34	100
11	3.5	3.547	3.613	0.05	0.16	0.02
12	3.867	3.92	4	0.23	0.97	0.14
13	4.093	4.187	4.273	0.63	3.1	0.46
14	4.273	4.327	4.36	0.03	0.1	0.01
15	4.553	4.693	4.793	0.29	1.71	0.25
16	4.913	5.087	5.113	0.06	0.77	0.11
17	6.773	6.84	6.953	0.43	2.48	0.37

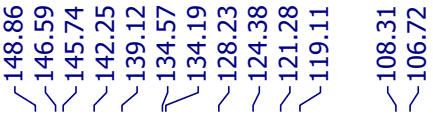
Peak List

m/z	z	Abund
228.1605		186391.07
240.1635		121382.05
266.1552		282896.51
284.1637		142283.46
294.1517		289947.33
312.1713	1	12076097.65
313.1701	1	4416678.09
314.1726	1	563241.03
647.294		142065.8

^{1}H NMR (500 MHz, DMSO-d_6+CF_3SO_3H): δ 8.52 (s, 1H), 8.07 (d, J = 8.3 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H), 6.53 (d, J = 8.4 Hz, 1H), 6.43 (d, J = 8.4 Hz, 1H).

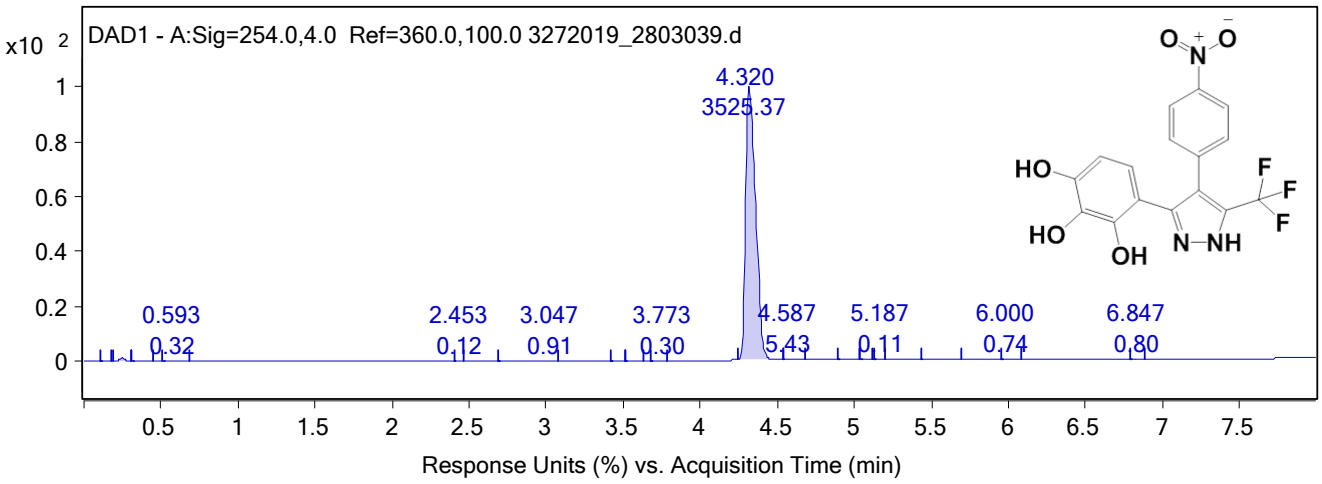


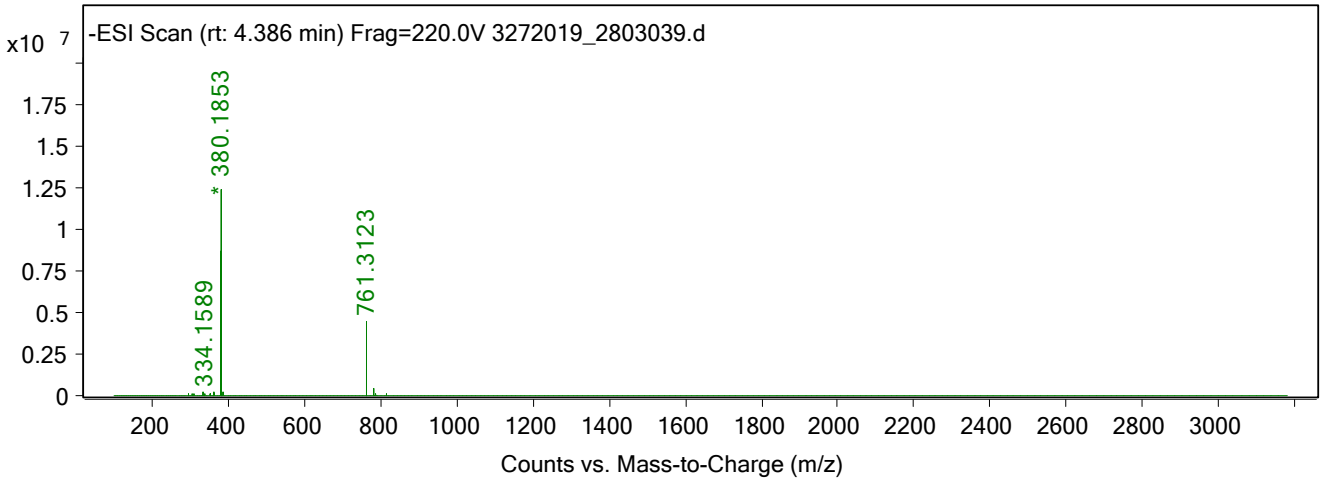




^{13}C NMR (125 MHz, DMSO-d_6+CF_3SO_3H): δ 148.9, 146.6, 145.7, 142.3, 139.1, 134.6, 134.2, 128.2, 124.4, 121.3, 119.1, 108.3, 106.7.

Compound 27 4-(4-(4-nitrophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol





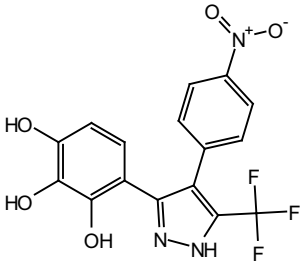
Integration Peak List

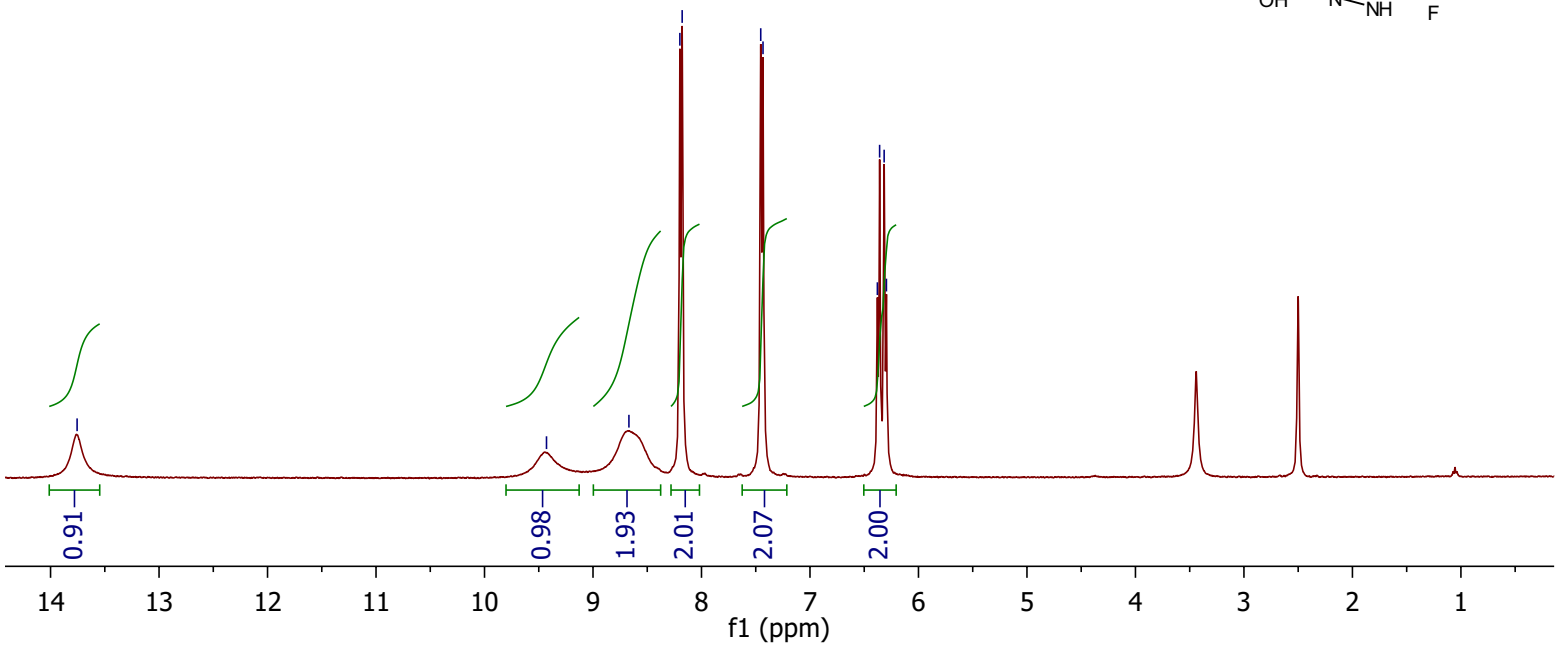
Peak	Start	RT	End	Height	Area	Area %
1	0.107	0.16	0.18	0.04	0.14	0
2	0.193	0.247	0.307	9.68	25.89	0.73
3	0.307	0.427	0.453	0.07	1.09	0.03
4	0.507	0.593	0.68	0.05	0.32	0.01
5	2.4	2.453	2.467	0.02	0.12	0
6	2.687	3.047	3.073	0.04	0.91	0.03
7	3.42	3.473	3.513	0.09	0.46	0.01
8	3.513	3.567	3.633	0.17	0.65	0.02
9	3.68	3.773	3.787	0.02	0.3	0.01
10	4.24	4.32	4.533	776.29	3525.37	100
11	4.533	4.587	4.68	1.42	5.43	0.15
12	4.893	5.013	5.033	0.05	0.63	0.02
13	5.04	5.093	5.113	0.03	0.11	0
14	5.133	5.187	5.2	0.02	0.11	0
15	5.433	5.607	5.693	0.24	1.38	0.04
16	5.953	6	6.087	0.24	0.74	0.02
17	6.793	6.847	6.88	0.23	0.8	0.02

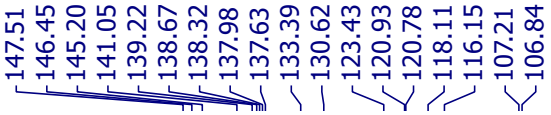
Peak List

m/z	z	Abund
334.1589		274897.12
362.1558		233299.47
380.1853		12706700.53
381.1763	1	8703719.48
382.1761	1	1629723.38
761.3123	1	4636136.39
762.315	1	1694466.15
763.3191	1	349516.15
783.2986	1	474174.55
784.3021	1	169435.35

^{1}H NMR (400 MHz, DMSO-d_6): δ 13.76 (s, 1H), 9.43 (s, 1H), 8.67 (s, 2H), 8.19 (d, J = 8.4 Hz, 2H), 7.44 (d, J = 8.4 Hz, 2H), 6.37 (d, J = 8.4 Hz, 1H), 6.31 (d, J = 8.4 Hz, 1H).

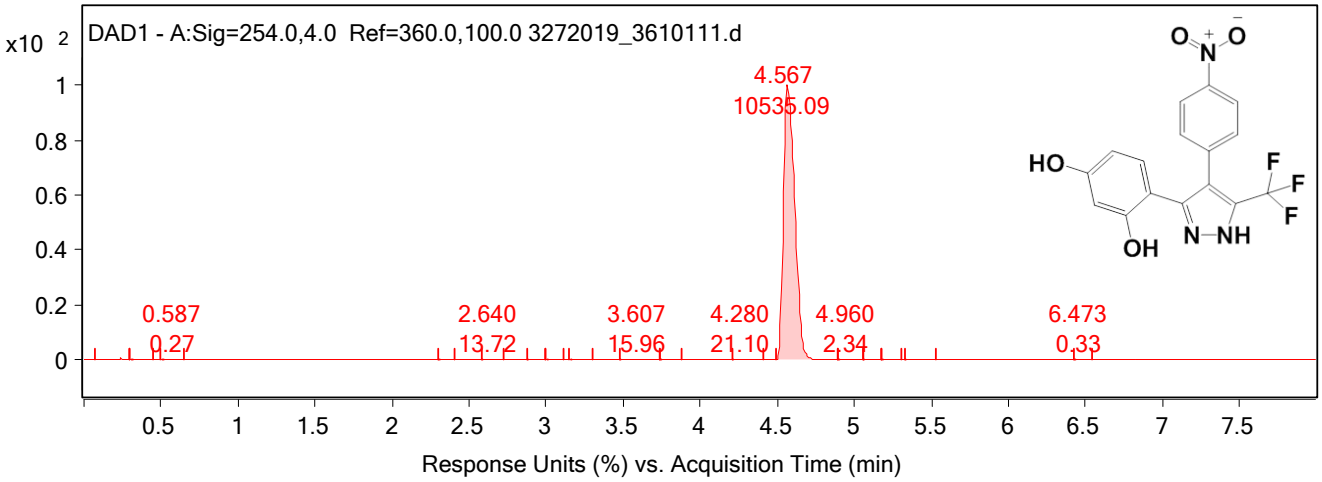


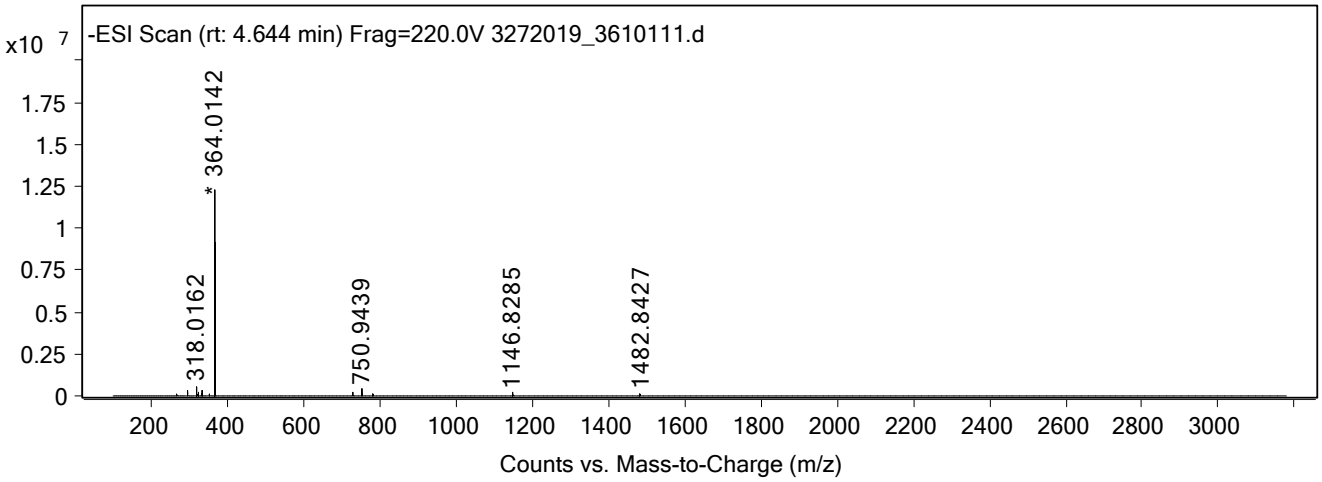




^{13}C NMR (100 MHz, DMSO-d_6): δ 147.5, 146.5, 145.2, 141.1, 139.2, 138.2 (q, $J_{C\text{-}F}$ = 34.7 Hz), 133.4, 130.6, 123.4, 120.9, 119.4 (q, $J_{C\text{-}F}$ = 268.9 Hz), 116.2, 107.2, 106.8.

Compound 28 4-(4-(4-nitrophenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,3-diol





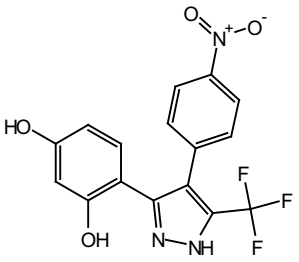
Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	0.067	0.24	0.293	11.45	32.14	0.31
2	0.3	0.413	0.447	0.14	1.79	0.02
3	0.5	0.587	0.653	0.05	0.27	0
4	2.293	2.34	2.407	0.14	0.48	0
5	2.58	2.64	2.727	4	13.72	0.13
6	2.873	2.973	2.993	0.03	0.3	0
7	3	3.053	3.113	0.29	0.91	0.01
8	3.153	3.213	3.3	0.31	1.2	0.01
9	3.473	3.607	3.733	3.71	15.96	0.15
10	3.74	3.813	3.88	0.11	0.49	0
11	4.207	4.28	4.407	4.36	21.1	0.2
12	4.487	4.567	4.893	2066.21	10535.09	100
13	4.893	4.96	5.053	0.54	2.34	0.02
14	5.053	5.133	5.173	0.08	0.38	0
15	5.18	5.227	5.3	0.13	0.5	0
16	5.327	5.467	5.527	0.13	1.18	0.01
17	6.427	6.473	6.547	0.11	0.33	0

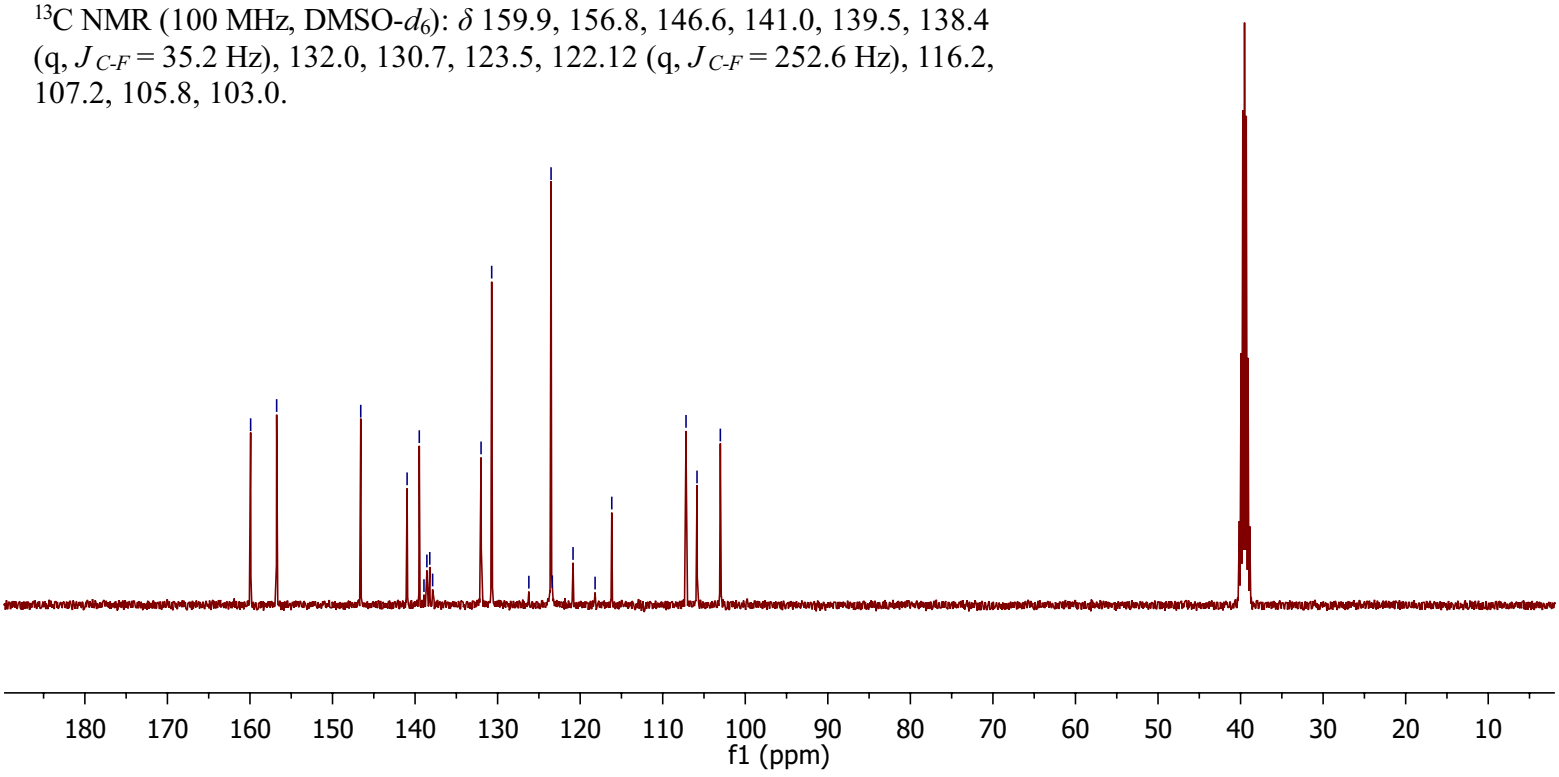
Peak List

m/z	z	Abund
295.9955		206110.03
296.024		369233.21
318.0162		561610.4
322.0002		248081.4
334.0075		354868.81
364.0142		12434473.79
365.0041	1	9120681.28
366.0032	1	1604321.45
750.9439	1	420235.35
1146.8285		197963.2

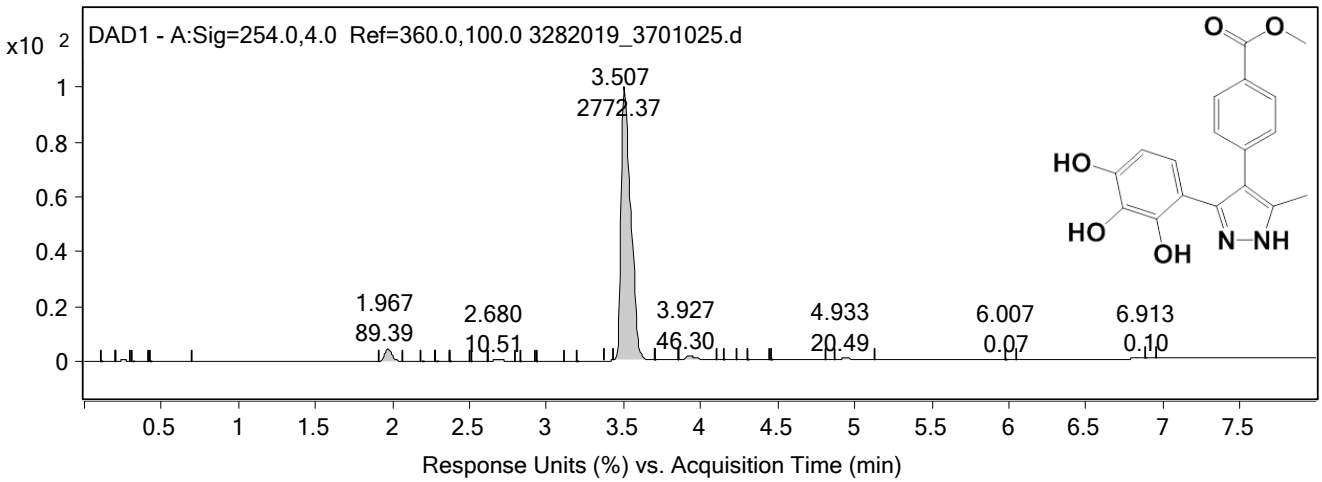
^{1}H NMR (400 MHz, DMSO-d_6): δ 13.76 (s, 1H), 9.77 (s, 1H), 9.67 (s, 1H), 8.19 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.3 Hz, 1H), 6.39 (d, J = 2.2 Hz, 1H), 6.22 (dd, J = 2.3, 8.3 Hz, 1H).

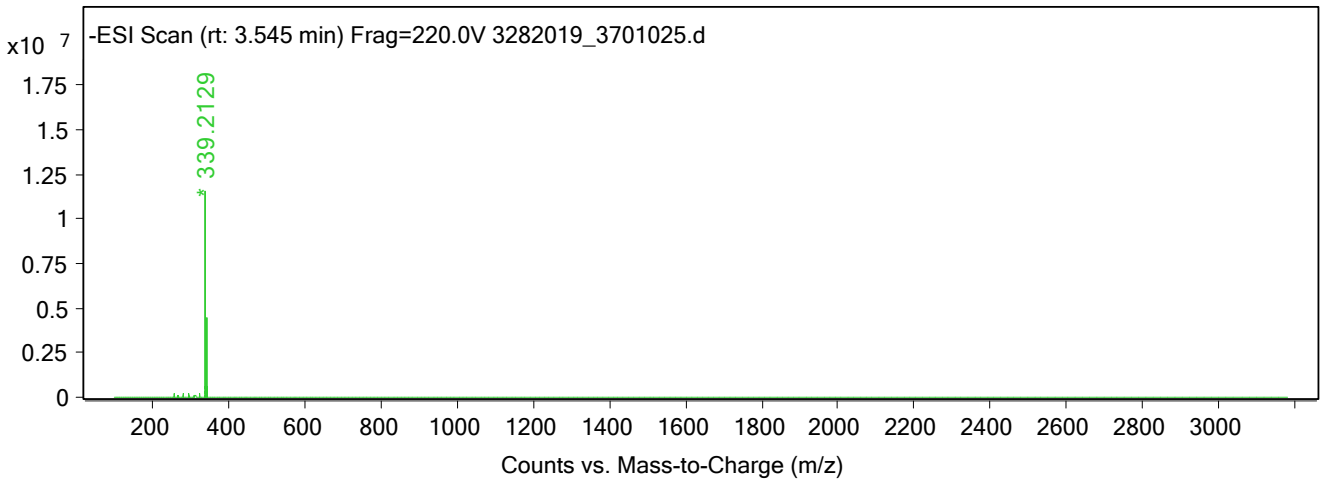


^{13}C NMR (100 MHz, DMSO-d_6): δ 159.9, 156.8, 146.6, 141.0, 139.5, 138.4 (q, $J_{C\text{-}F}$ = 35.2 Hz), 132.0, 130.7, 123.5, 122.12 (q, $J_{C\text{-}F}$ = 252.6 Hz), 116.2, 107.2, 105.8, 103.0.



Compound 29 methyl 4-(5-methyl-3-(2,3,4-trihydroxyphenyl)-1H-pyrazol-4-yl)benzoate



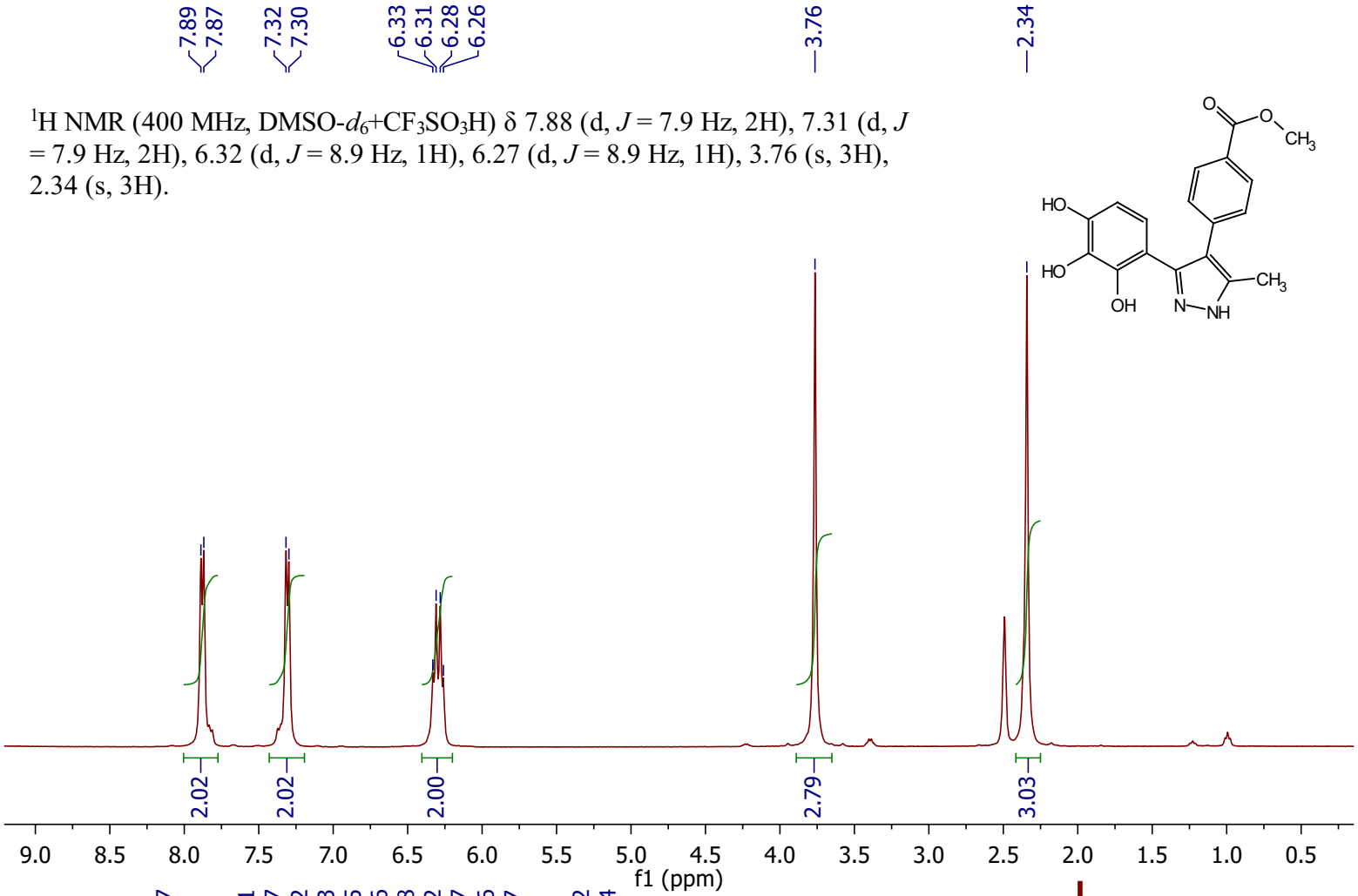


Integration Peak List

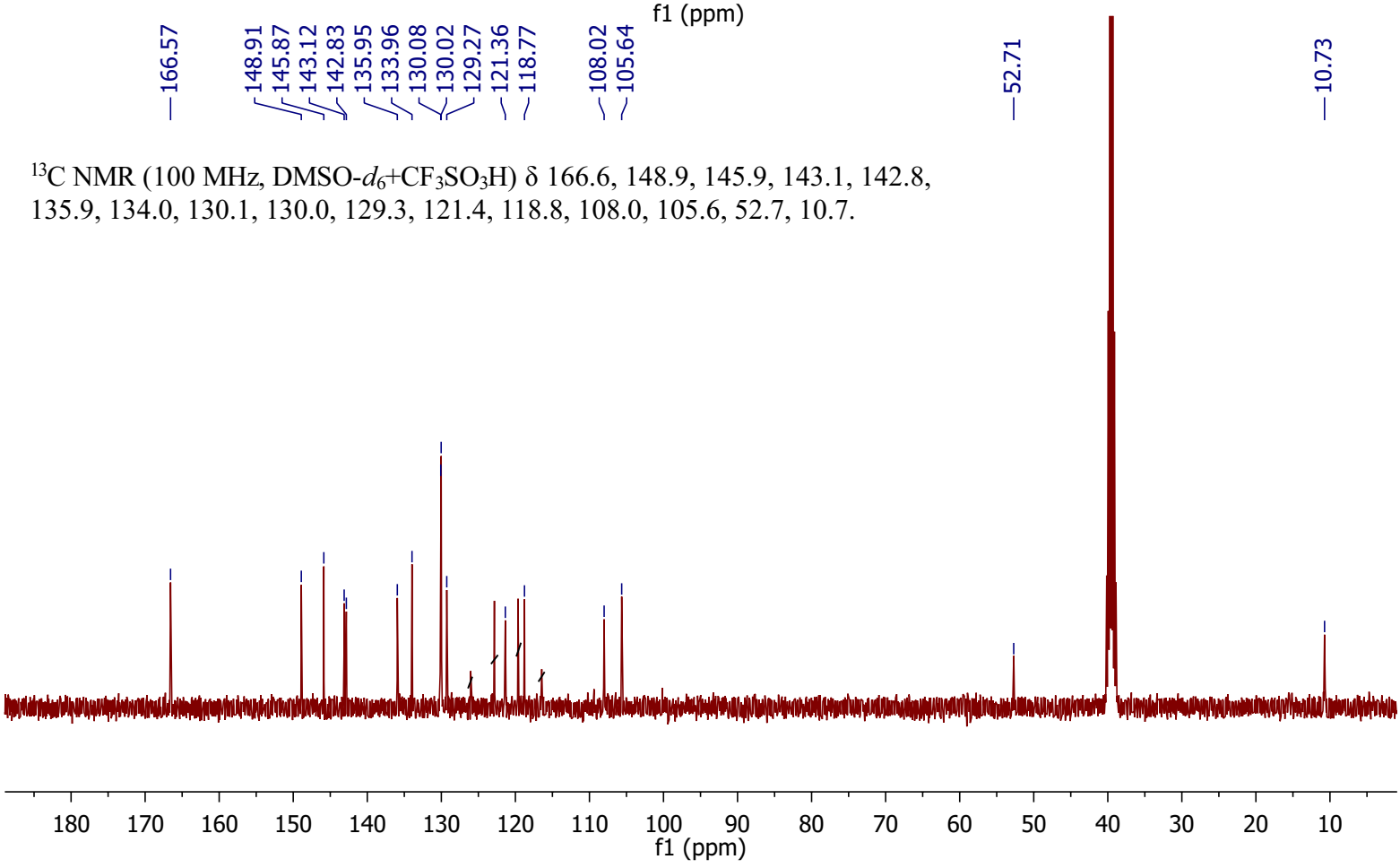
Peak	Start	RT	End	Height	Area	Area %
1	0.107	0.167	0.2	0.12	0.41	0.01
2	0.2	0.253	0.3	4.73	12.14	0.44
3	0.307	0.36	0.413	0.39	1.43	0.05
4	0.42	0.6	0.7	0.08	0.8	0.03
5	1.913	1.967	2.067	28.15	89.39	3.22
6	2.187	2.247	2.28	0.07	0.2	0.01
7	2.28	2.327	2.373	0.1	0.27	0.01
8	2.373	2.427	2.5	1.29	4.3	0.16
9	2.507	2.56	2.613	0.12	0.42	0.02
10	2.62	2.68	2.793	2.69	10.51	0.38
11	2.827	2.893	2.927	0.17	0.69	0.02
12	2.933	3.027	3.107	0.36	1.42	0.05
13	3.2	3.333	3.373	0.08	0.49	0.02
14	3.433	3.507	3.7	635.92	2772.37	100
15	3.7	3.747	3.853	1.42	5.54	0.2
16	3.86	3.927	4.1	10.48	46.3	1.67
17	4.147	4.193	4.227	0.18	0.5	0.02
18	4.307	4.353	4.447	0.09	0.37	0.01
19	4.46	4.693	4.807	0.28	1.82	0.07
20	4.867	4.933	5.133	3.7	20.49	0.74
21	5.98	6.007	6.047	0.04	0.07	0
22	6.88	6.913	6.96	0.04	0.1	0

Peak List

m/z	z	Abund
255.2032		180636.92
265.1898		126923.55
280.1808		163077.06
293.1919		246760.14
321.1938		256158.71
324.1813		122572.63
337.1921		154442.91
339.2129	1	11713325.3
340.2121	1	4426241.05
341.2148	1	596064.5

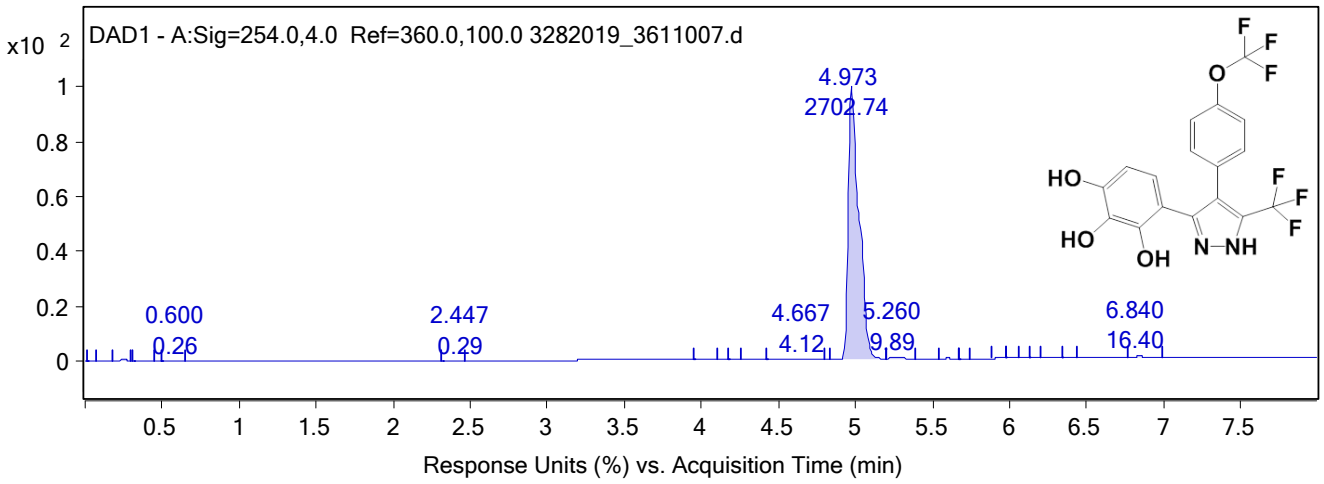


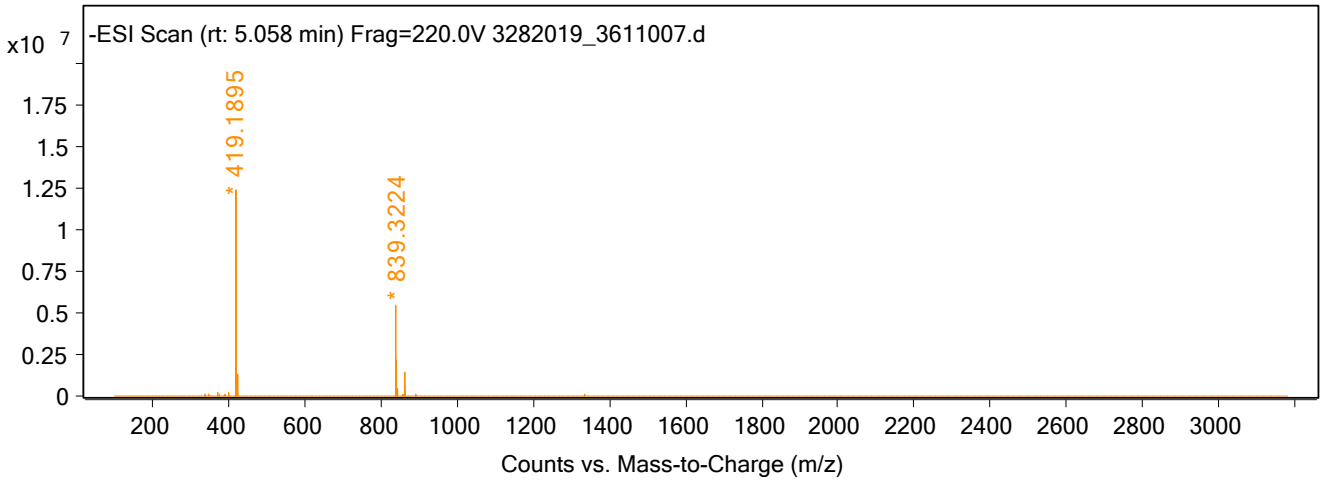
^{1}H NMR (400 MHz, DMSO-d_6+CF_3SO_3H) δ 7.88 (d, J = 7.9 Hz, 2H), 7.31 (d, J = 7.9 Hz, 2H), 6.32 (d, J = 8.9 Hz, 1H), 6.27 (d, J = 8.9 Hz, 1H), 3.76 (s, 3H), 2.34 (s, 3H).



^{13}C NMR (100 MHz, DMSO-d_6+CF_3SO_3H) δ 166.6, 148.9, 145.9, 143.1, 142.8, 135.9, 134.0, 130.1, 130.0, 129.3, 121.4, 118.8, 108.0, 105.6, 52.7, 10.7.

Compound 30 4-(4-(4-(trifluoromethoxy)phenyl)-5-(trifluoromethyl)-1H-pyrazol-3-yl)benzene-1,2,3-triol



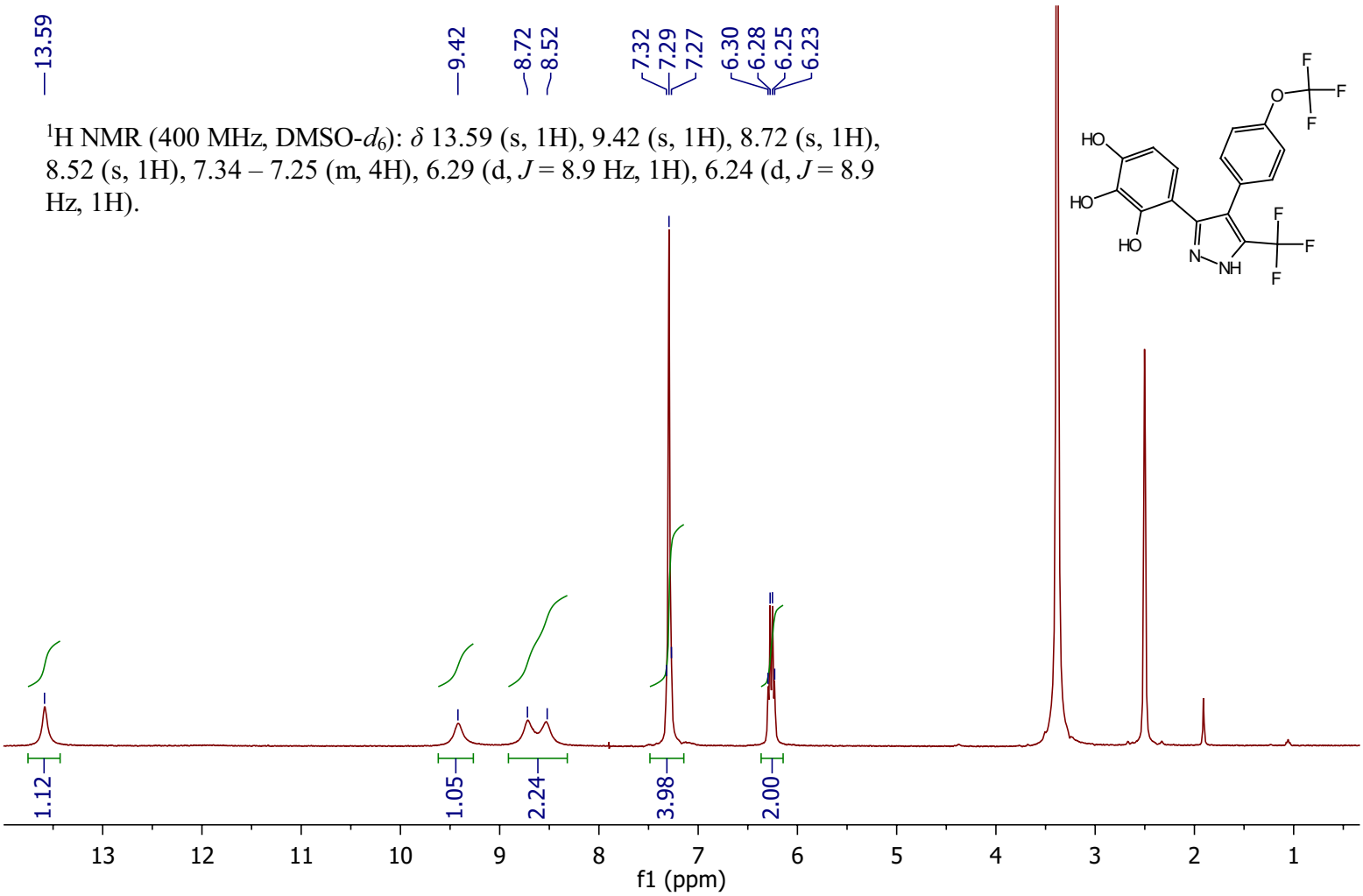


Integration Peak List

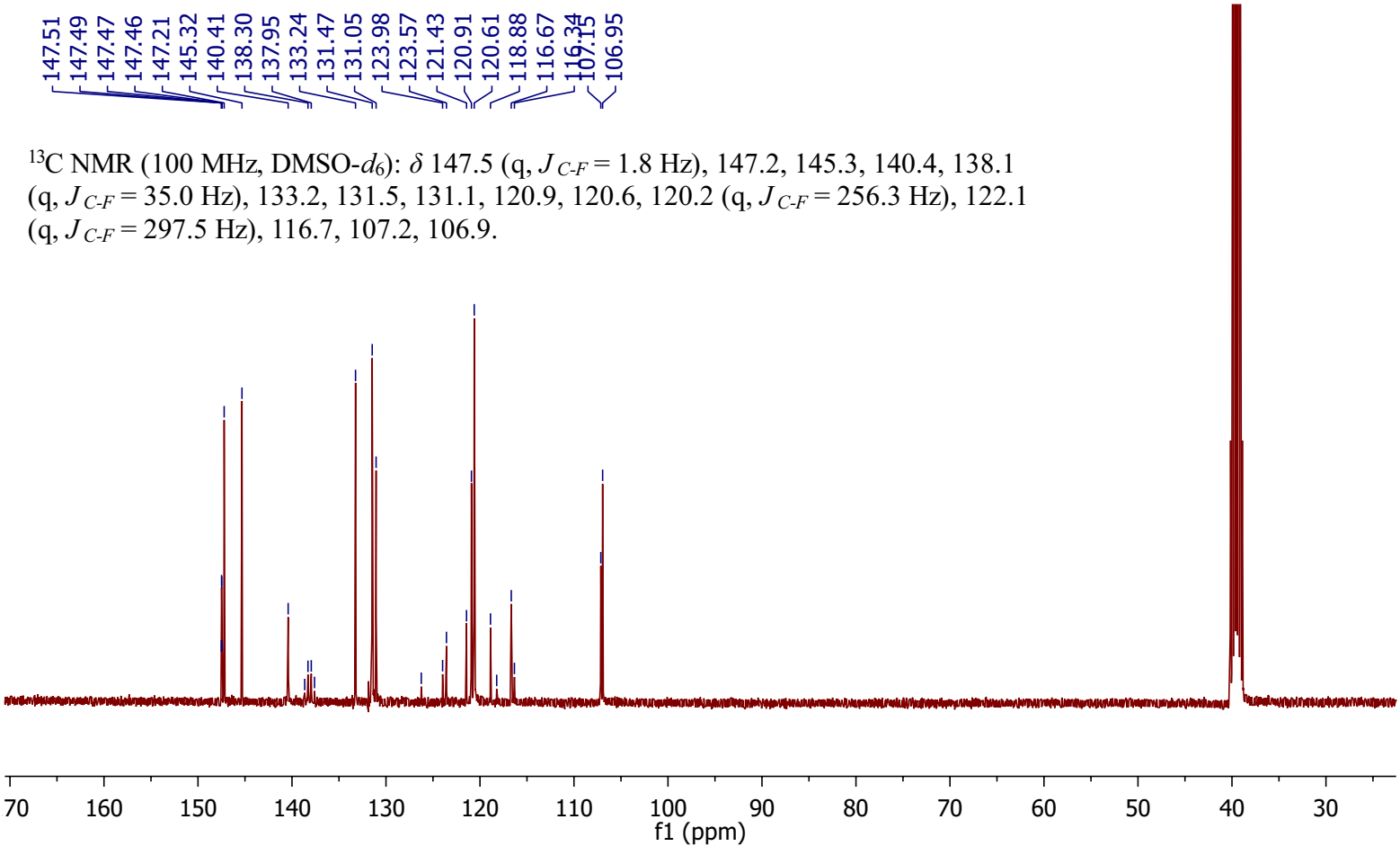
Peak	Start	RT	End	Height	Area	Area %
1	0.013	0.027	0.067	0.04	0.06	0
2	0.18	0.253	0.3	6.17	16.38	0.61
3	0.307	0.433	0.453	0.07	1.46	0.05
4	0.493	0.6	0.653	0.04	0.26	0.01
5	2.313	2.447	2.467	0.03	0.29	0.01
6	3.953	4.053	4.107	0.09	1.12	0.04
7	4.173	4.227	4.253	0.11	0.41	0.02
8	4.42	4.667	4.793	0.65	4.12	0.15
9	4.833	4.973	5.193	561.52	2702.74	100
10	5.193	5.26	5.393	2.08	9.89	0.37
11	5.54	5.6	5.673	0.5	1.91	0.07
12	5.673	5.707	5.74	0.06	0.12	0
13	5.887	5.94	5.973	0.25	0.84	0.03
14	5.973	6.013	6.06	0.09	0.21	0.01
15	6.127	6.173	6.207	0.12	0.35	0.01
16	6.34	6.413	6.44	0.07	0.36	0.01
17	6.767	6.84	6.993	3.21	16.4	0.61

Peak List

m/z	z	Abund
373.1598		187130.78
417.1603		341553.13
419.1895		12683152.94
420.1817	1	8182555.38
421.1819	1	1347142.76
839.3224	1	5581031.84
840.3246	1	2170775.6
841.3283	1	445301.29
861.3074	1	1393080.72
862.3115	1	507471.33



^{1}H NMR (400 MHz, DMSO-d_6): δ 13.59 (s, 1H), 9.42 (s, 1H), 8.72 (s, 1H), 8.52 (s, 1H), 7.34 – 7.25 (m, 4H), 6.29 (d, J = 8.9 Hz, 1H), 6.24 (d, J = 8.9 Hz, 1H).



^{13}C NMR (100 MHz, DMSO-d_6): δ 147.5 (q, $J_{C\text{-}F}$ = 1.8 Hz), 147.2, 145.3, 140.4, 138.1 (q, $J_{C\text{-}F}$ = 35.0 Hz), 133.2, 131.5, 131.1, 120.9, 120.6, 120.2 (q, $J_{C\text{-}F}$ = 256.3 Hz), 122.1 (q, $J_{C\text{-}F}$ = 297.5 Hz), 116.7, 107.2, 106.9.