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Efficient synthesis of tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridines based on the recyclization of *N*-arylitaconimides with aminopyrazoles

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Experimental Section

NMR ^{1}H and ^{13}C spectra were recorded on Bruker AV600 (600.13 and 150.9 MHz, respectively) spectrometer in DMSO-d_6, internal standard was TMS. Melting points were determined on Stuart SMP 30. Control of reagent and products individuality, qualitative analysis of reaction mass was performed by TLC on Merck TLC Silica gel 60 F_{254} chromatographic plate; eluents: methanol, chloroform and their mixtures in various ratios. The chromatograms were visualized by UV or iodine vapor.

Product purity was monitored by high performance liquid chromatography with high resolution mass spectrometric electrospray ionization detection (HPLC-HRMS-ESI) in combination with UV detection. The analyzes were performed on Agilent 1260 Infinity chromatograph (Agilent Technologies, CA, USA) and Agilent 6230 TOF LC/MS high-resolution time-of-flight mass detector. The ionization block was double electrospray; the signals were recorded in positive polarity; nebulizer N_2 20 psig; desiccant gas N_2, 6 ml min^{-1}, 325 °C; mass detection range is 50-2000 Da. Capillary voltage 4.0 kV, fragmentator +191 V, skimmer +66 V, OctRF 750 V. Poroshell 120 EC-C18 column (4.6 x 50 mm; 2.7 μm) was used. Gradient elution: acetonitrile/water (0.1% formic acid); flow rate 0.4 ml min^{-1}. Software for processing research results - MassHunter Workstation/Data Acquisition V.06.00.

Table S1 Yields of 2-(3-methyl-6-oxo-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)-*N*-phenylacetamide **3l** form reactants **1a** and **2e** depending on the reaction medium (reflux, 10 h).

Solvent	Yield, %
AcOH	35
$Pr^{i}OH$ + AcOH, 10:1	65
Toluene + AcOH, 10:1	15
MeOH + AcOH, 10:1	45
Dioxane + AcOH, 10:1	20
DMF + AcOH, 10:1	45

General Procedure.

Synthesis of *N*-aryl-2-(6-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)acetamides 3a-k. A solution of N-arylitaconimide **2a-f** (5 mmol) and 5-aminopyrazole **1a-d** (5 mmol) is boiled in isopropyl alcohol (5 ml) in the presence of catalytic amounts of acetic acid for 8-15 h. The precipitate formed is filtered off and recrystallized from a 2:1 mixture of methanol and DMF.

***N*-(3-Chloro-4-fluorophenyl)-2-(3-methyl-6-oxo-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)acetamide 3a** Yield 70% (1.4 g), light beige powdery compound, m.p. 253-255°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.44 (s, 1H, NH); 10.23 (s, 1H, NH); 7.29-6.95 (m, 8H, Ar); 3.01-3.09 (m, 1H, CH); 2.85 (dd, *J* = 15.6, *J* = 5.8, 1H, CH_2exo); 2.78 (dd, *J* = 15.0, *J* = 7.9, 1H, CH_2endo); 2.49-2.53 (m, 1H, CH_2exo); 2.46 (dd, 1H, *J*= 15.1, *J* = 7.8, CH_2endo); 2.10 (s, 3H, CH_3).^{13}C NMR (δ, ppm): 171.8; 169.9; 152.8 (d, *J* = 230); 145.0; 138.1; 136.4; 129.1; 126.5; 122.4; 120.3; 119.0; 116.9; 116.7 100.2; 37.4; 36.6; 21.9; 11.7; HRMS: m/z calcd: 413.1176; found: 413.1171.

***N*-(3-Chloro-2-methylphenyl)-2-(1-methyl-6-oxo-3-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)acetamide 3b.** Yield 75% (1.5 g), white powdery compound, m.p. 252-254°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.34 (s, 1H, NH); 9.56 (1H, s, NH); 7.50-7.16 (m, 8H, Ar); 3.03-3.09 (m, 1H, CH); 2.91 (dd, *J* = 15.2, *J* = 6.0, 1H, CH_2exo); 2.84 (dd, *J* = 15.1, *J* = 7.1, 1H, CH_2endo); 2.55-2.49 (m, 2H, CH_2exo+CH_2endo); 2.21 (s, 3H, CH_3); 2.25 (s, 3H, CH_3). ^{13}C NMR (δ, ppm): 172.0; 169.8; 145.0; 138.2; 138.1; 139.0; 133.7; 130.5; 129.1; 126.7; 126.5; 125.9; 124.6; 122.4; 100.3; 37.8; 36.0; 22.0; 15.1; 11.8. HRMS: m/z calcd: 409.1427; found: 409.1427.

***N*-(4-Fluorophenyl)-2-(1-methyl-6-oxo-3-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]-pyridin-5-yl)acetamide 3c.** Yield 70% (1.3 g), white powdery compound, m.p. 252-254°C.^{1}H NMR, ((δ, ppm., J/Hz): 10.43 (s, 1H, NH); 10.07 (1H, s, NH); 7.63-7.12 (m, 9H, Ar); 3.07-3.05 (m, 1H, CH); 2.88 (dd, *J* = 15.5, *J* = 5.5, 1H, CH_2exo); 2.82 (dd, *J* = 12.0, *J* = 7.1, 1H, CH_2endo); 2.53-2.46 (m, 2H, CH_2exo+CH_2endo); 2.11(s, 3H, CH_3). ^{13}C NMR (δ, ppm): 172.0; 169.5; 157.8 (d, *J* = 240); 145.1; 138.2-138.1; 135.7; 129.2; 126.6; 122.4; 120.8; 120.7; 115.3; 115.1; 100.3; 37.6; 36.6; 22.0; 11.8. HRMS: m/z calcd: 379.1566; found: 379.1568.

***N*-(4-Chlorophenyl)-2-(1-methyl-6-oxo-3-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]-pyridin-5-yl)acetamide 3d.** Yield 65% (1.3 g), white powdery compound, m.p. 265-267°C.^{1}H NMR, ((δ, ppm., J/Hz): 10.42 (s, 1H, NH); 10.14 (1H, s, NH); 7.63-7.34 (m, 9H, Ar); 3.07-3.05 (m, 1H, CH); 2.90-2.87 (m, 1H, CH_2exo); 2.85-2.82 (m, 1H, CH_2endo); 2.53-2.46 (m, 2H, CH2exo+CH2endo); 2.12(s, 3H, CH3). ^{13}C NMR (δ, ppm): 172.0; 169.8; 145.1; 138.3; 138.2; 138.1; 129.2; 128.6; 126.6; 126.5; 122.5; 120.6; 100.4; 37.5; 36.7; 22.0; 11.9. HRMS: m/z calcd: 395.1270; found: 395.1272.

***N*-(3-Chloro-2-methylphenyl)-2-(6-oxo-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]-pyridin-5-yl)acetamide 3e.** Yield 75% (1.5 g), white powdery compound, m.p. 276-278°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.60 (s, 1H, NH); 9.69 (s, 1H, NH); 7.71-7.18 (m, 13H, Ar); 3.13-3.09 (m, 1H, CH); 3.92-2.89 (m, 2H, CH_2exo + CH_2endo); 2.61-2.50 (m, 2H, CH_2exo + CH_2endo); 2.22 (s, 3H, CH3). ^{13}C NMR (δ, ppm): 171.9; 169.9; 146.9; 139.3; 138.0; 133.7; 133.0; 130.6; 129.3; 128.7; 127.9; 126.7; 126.4; 125.9; 124.7; 123.1; 99. 4;37.8; 35.9; 23.5; 15.1. HRMS: m/z calcd: 409.1427; found: 409.1428.

***N*-(3-Chloro-4-fluorophenyl)-2-(6-oxo-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]-pyridin-5-yl)acetamide 3f.** Yield 75% (1.8 g), white powdery compound, m.p. 228-230°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.59 (s, 1H, NH); 10.29 (s, 1H, NH); 7.93-7.33 (m, 13H, Ar); 3.11-3.17 (m, 2H, CH + CH_2exo); 2.89-2.94 (m, 2H, CH_2exo + CH_2endo); 2.59 (dd, *J* = 15.8, *J* = 6.1, 1H, CH_2 endo). ^{13}C NMR (δ, ppm): 171.8; 169.9; 152.9 (d, *J* = 240); 146.9; 139.3; 137.9; 136.5;

133.0; 129.5; 129.3; 128.7; 128.5; 127.9; 127.3; 126.5; 125.9; 124.7; 123.1; 118.9; 116.9; 116.7; 99.5; 39.0; 36.4; 23.5; 21.6. HRMS: m/z calcd: 475.1332; found: 475.1331.

2-(6-Oxo-1,3-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridine-5-yl)-*N*-phenylacetamide 3g. Yield 65% (1.4 g), white powdery compound, m.p. 265-267°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.57 (s, 1H, NH); 10.00 (s, 1H, NH); 7.68-6.98 (m, 15H, Ar); 3.08-3.15(m, 2H,CH + CH_2exo); 2.89-2.94 (m, 2H,CH_2exo + CH_2endo); 2.54 (dd, *J* = 15.8, *J* = 6.6, 1H, CH_2 endo). ^{13}C NMR (δ, ppm): 171.8; 169.9; 153.9; 151.9; 146.9; 139.3; 137.9; 136.5; 133.0; 129.5; 129.3; 128.7; 128.5; 127.9; 127.3; 126.5; 125.9; 124.7; 123.1; 118.9; 116.9; 116.7; 99.5; 39.0; 36.4; 23.5; 21.6. HRMS: m/z calcd: 423.1817; found: 423.1817

***N*-(4-Methoxyphenyl)-2-[6-oxo-3-phenyl-1-(*p*-tolyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]-pyridine-5-yl]acetamide 3h.** Yield 60% (1.4 g), white powdery compound, m.p. 287-289°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.42 (s, 1H, NH); 9.94 (s, 1H, NH); 7.69-6.86 (m, 13H, Ar); 3.71 (s, 3H CH_3); 3.29-3.12(m, 2H, CH+CH_2exo); 2.89-2.86 (m, 2H, CH_2exo+CH_2endo); 2.59-2.56 (m, 1H, CH_2endo); 2.37 (s, 1H, CH_3);^{13}C NMR (δ, ppm): 171.8; 168.9; 154.9; 149.6; 139.1; 136.6; 135.5; 133.0; 132.5; 129.6; 128.6; 127.7; 126.3; 123.0; 120.5; 113.7; 99.2; 55.0; 37.5; 36.2; 23.5; 20.5. HRMS: m/z calcd: 467.2079; found: 467.2076.

***N*-(3-Chloro-4-fluorophenyl)-2-[6-oxo-1-phenyl-3-(*p*-tolyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl]acetamide 3i.** Yield 65% (1.6 g), white powdery compound, m.p. 245-247°C.^{1}H NMR, ((δ, ppm., J/Hz): 10.56 (s, 1H, NH); 10.25 (s, 1H, NH); 7.92-7.25(m, 12H, Ar); 3.12-3.10 (m, 2H, CH+CH_2exo); 2.92-2.87 (m, 2H, CH_2exo + CH_2endo); 2.59-2.57 (m, 1H, CH_2endo); 2.34 (s, 1H, CH_3). ^{13}C NMR (δ, ppm): 171.8; 169.9; 152.9 (d, *J* = 237); 150.00; 137.9; 137.2; 136.5; 130.2; 129.3; 127.2; 126.4; 123.1; 120.4; 119.2; 119.0; 117.0; 116.8; 37.5; 36.4; 23.5; 20.8. HRMS: m/z calcd: 489.1489; found: 489.1486.

2-[6-Oxo-1-phenyl-3-(*p*-tolyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)-*N*-phenylacetamide 3j. Yield 65% (1.4 g), white powdery compound, m.p. 253-255°C.^{1}H NMR, ((δ, ppm., J/Hz): 10.56 (s, 1H, NH); 10.02 (s, 1H, NH); 7.59-7.02 (m, 14H, Ar);3.13-3.10(m, 2H, CH+CH_2exo); 2.92-2.86 (m, 2H, CH_2endo + CH_2exo); 2.50 (m, 1H, CH_2endo); 2.33 (s, 1H, CH_3). ^{13}C NMR (δ, ppm): 171.9; 169.5; 147.0; 139.2; 138.0; 130.2; 129.3; 128.7; 127.2; 126.7; 123.1; 119.0; 99.3; 37.5; 36.5; 23.5; 20.8. HRMS: m/z calcd: 437.1973; found: 437.1972

***N*-(4-Nitrophenyl)-2-[6-oxo-1-phenyl-3-(*p*-tolyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]-pyridin-5-yl)acetamide 3k.** Yield 70% (1.7 g), yellow powdery compound, m.p. 256-258°C. ^{1}H NMR, ((δ, ppm., J/Hz): 10.65 (s, 1H, NH); 10.56 (s, 1H, NH); 8.22-7.26 (m, 13H, Ar); 3.15-3.12 (m, 2H, CH + CH_2exo); 2.99-2.97 (m, 2H, CH_2endo + CH_2exo); 2.91-2.89 (m, 1H, CH_2endo); 2.33 (s, 1H, CH_3). ^{13}C NMR (δ, ppm): 171.6; 170.6; 146.9; 145.3; 141.9; 139.1; 137.9; 137.1; 129.2; 129.2; 127.1; 126.3; 124.9; 123.0; 118.6; 99.3; 37.3; 36.6; 23.4; 20.7. HRMS: m/z calcd: 482.1824; found: 482.1821.

2-(3-Methyl-6-oxo-1-phenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)-*N*-phenylacetamide 3l. Yield 65% (1,2 g), yellow powdery compound, m.p. 250-253°C.^{1}H NMR, ((δ, ppm., J/Hz): 10.35 (s, 1H, NH); 10.20 (s, 1H, NH); 7.65-7.10 (m, 10H, Ar); 3.00-2.96 (m, 1H, CH); 2.87 (dd, 1H, *J* = 15.3, *J* = 5.7, CH_2exo); 2.78 (dd, 1H, *J* = 15.0, *J* = 7.2, CH_2endo); 2.53-2.44 (m, 2H, CH_2exo + CH_2endo); 2.10 (s, 3H, CH_3). ^{13}C NMR (δ, ppm): 173.2; 170.3; 145.3; 139.9; 139.8; 139.2; 129.5; 129.2; 126.5; 123.4; 122.5; 119.5; 119.4; 100.1; 38.1; 37.8; 26.0; 22.9; 12.4. HRMS: m/z calcd: 361.1660; found: 361.1660.

Qualitative Analysis Report

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Sample Group		**Info.**	
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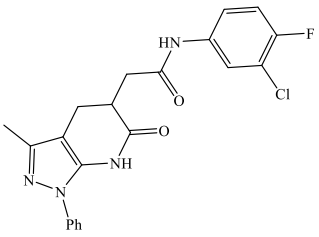
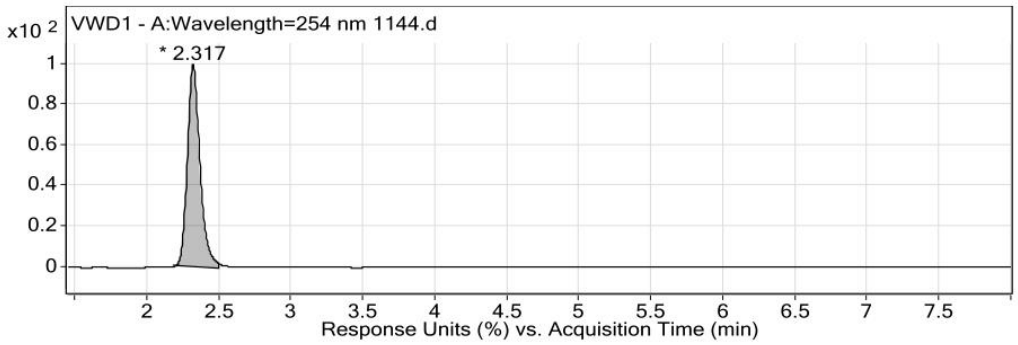


LCMS spectral of compaund 3a

User Chromatograms



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User Spectra

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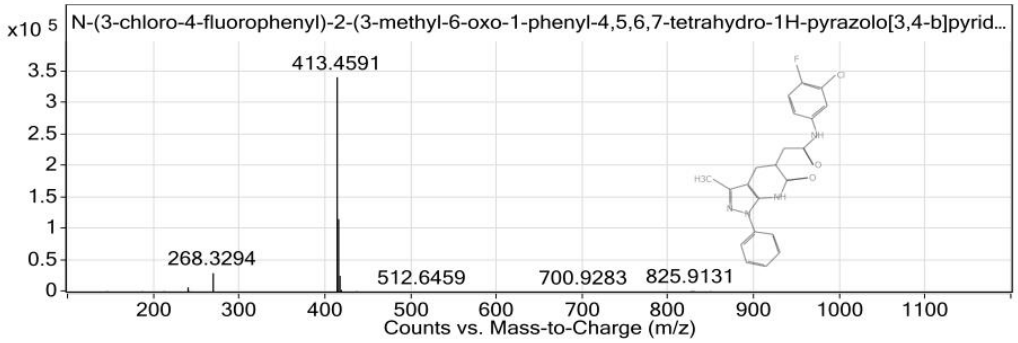

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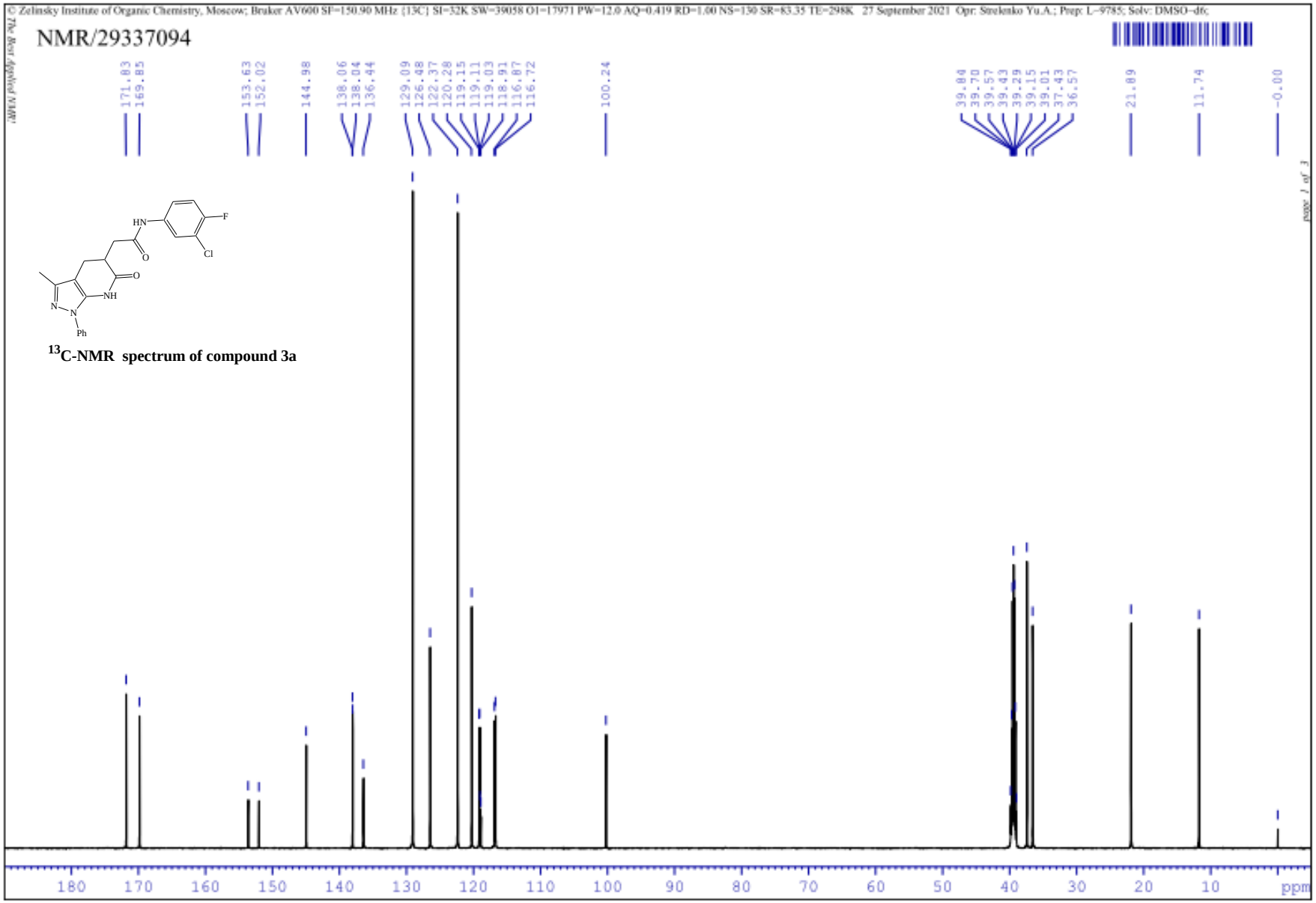

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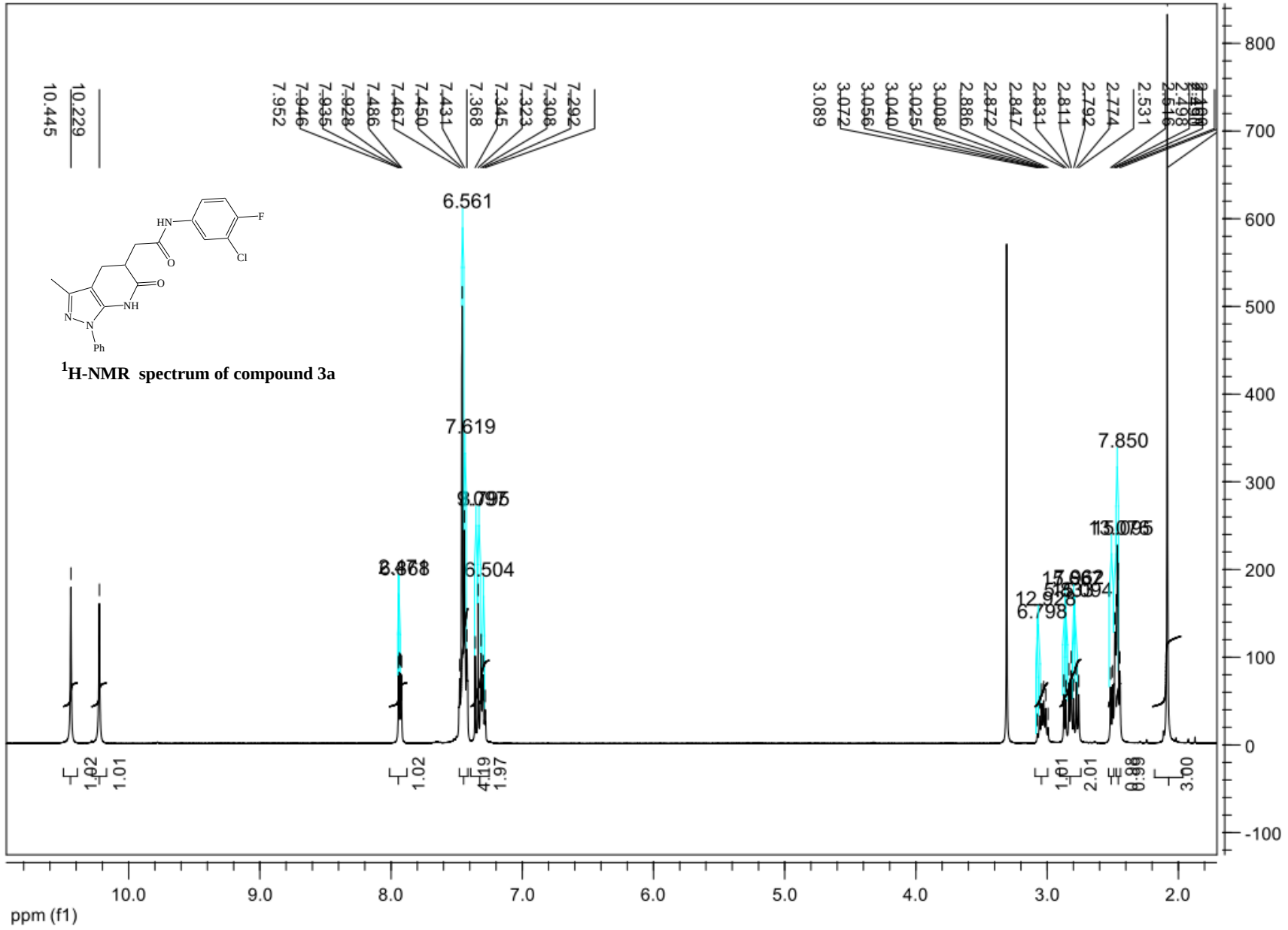

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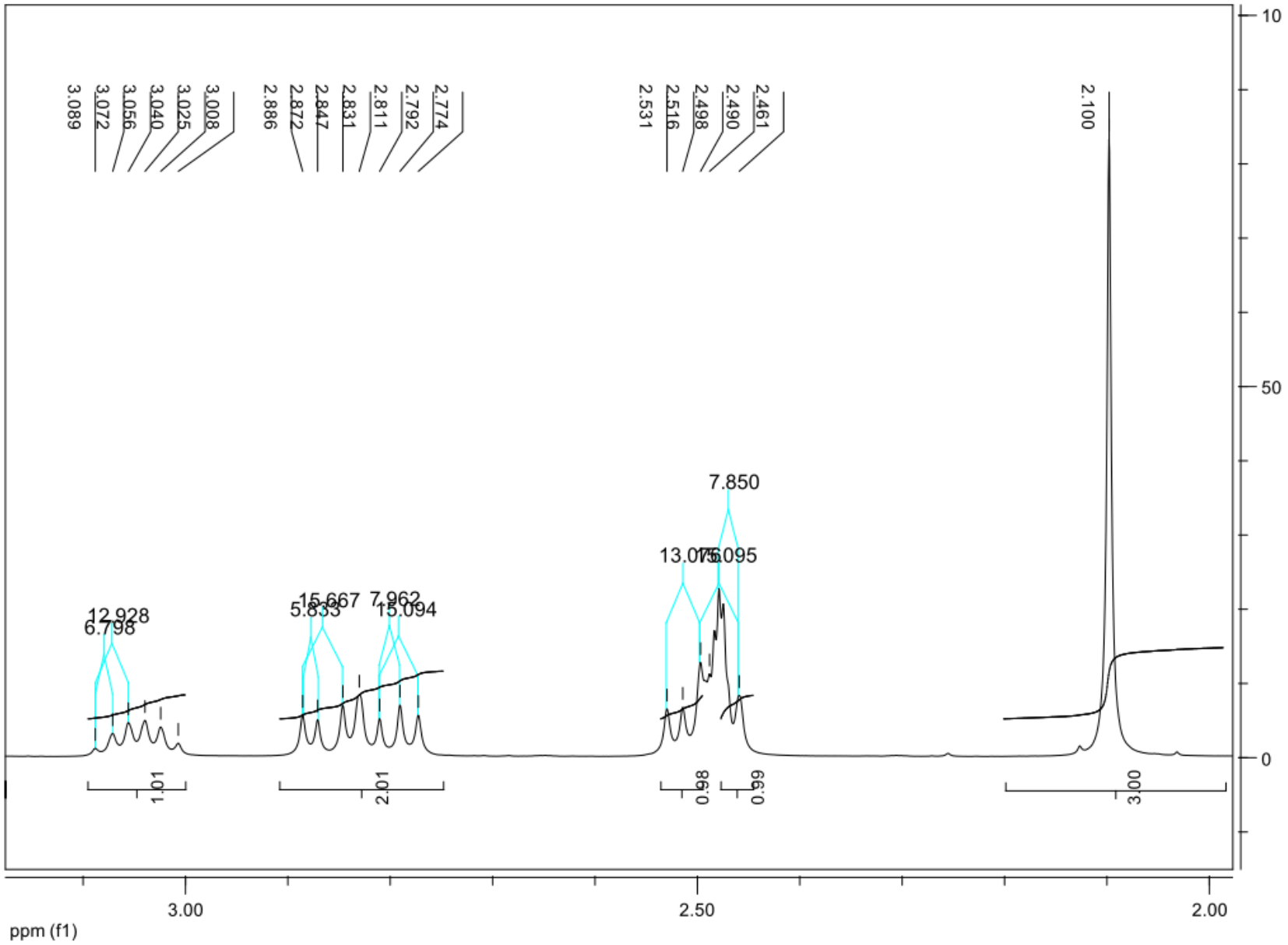
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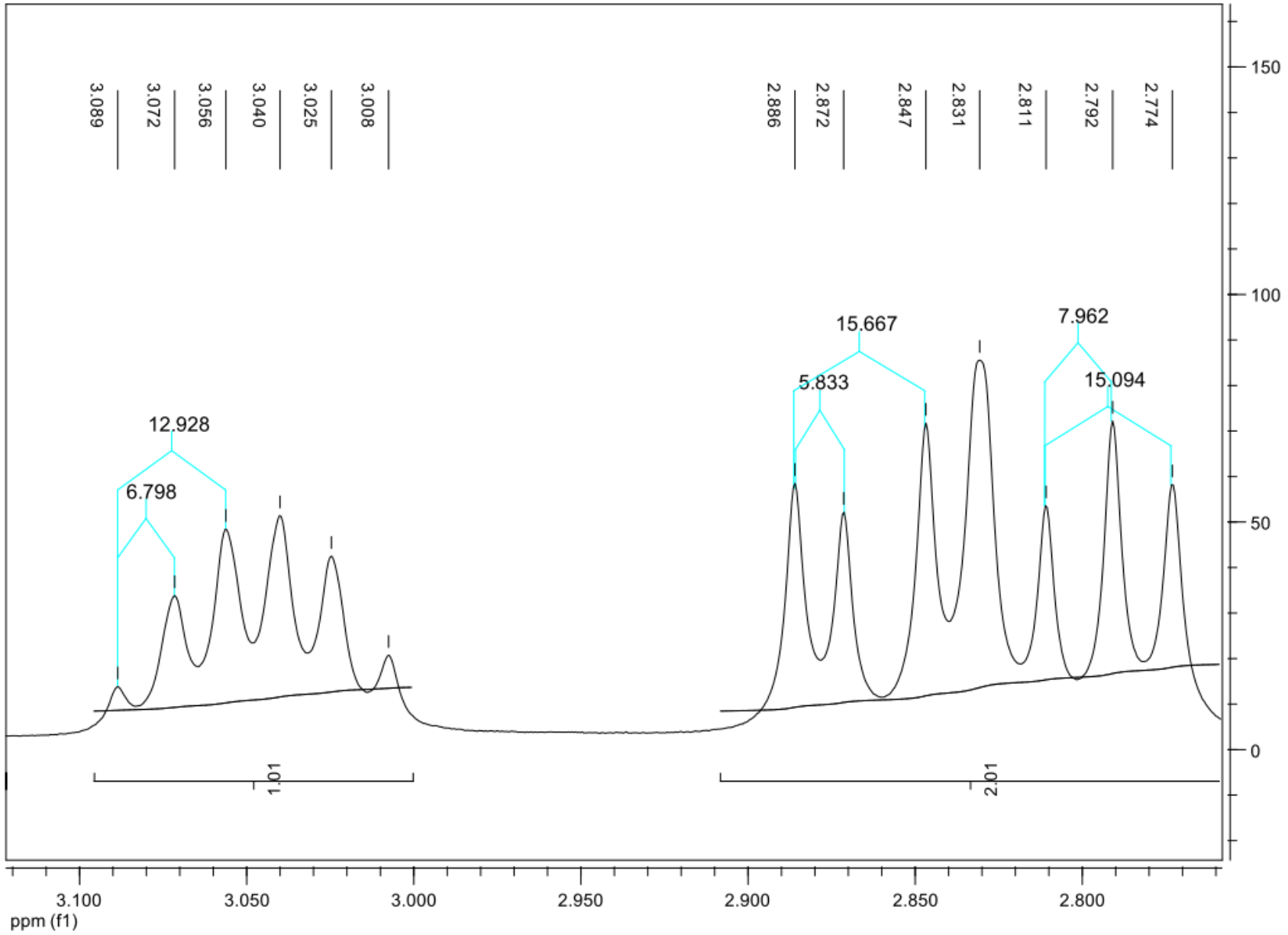
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ppm (f1)

Qualitative Analysis Report

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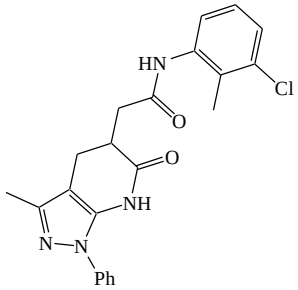
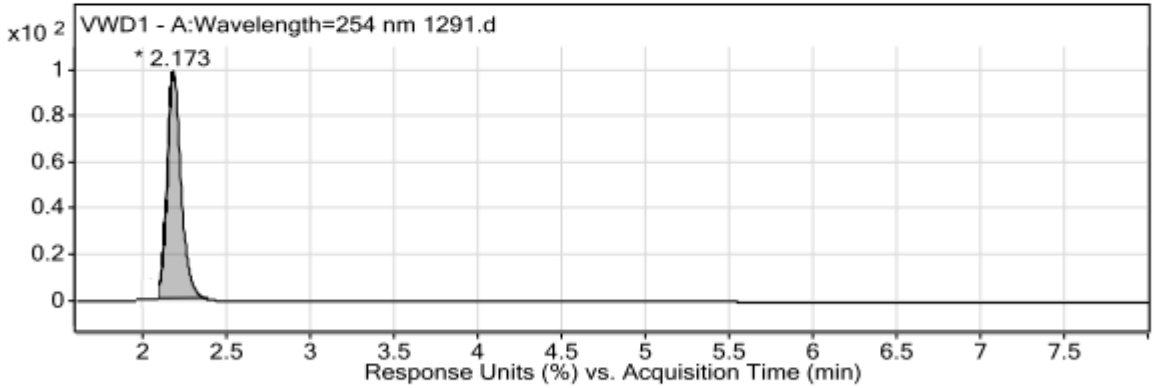


LCMS spectrum of compound 3b

User Chromatograms



Integration Peak List

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User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
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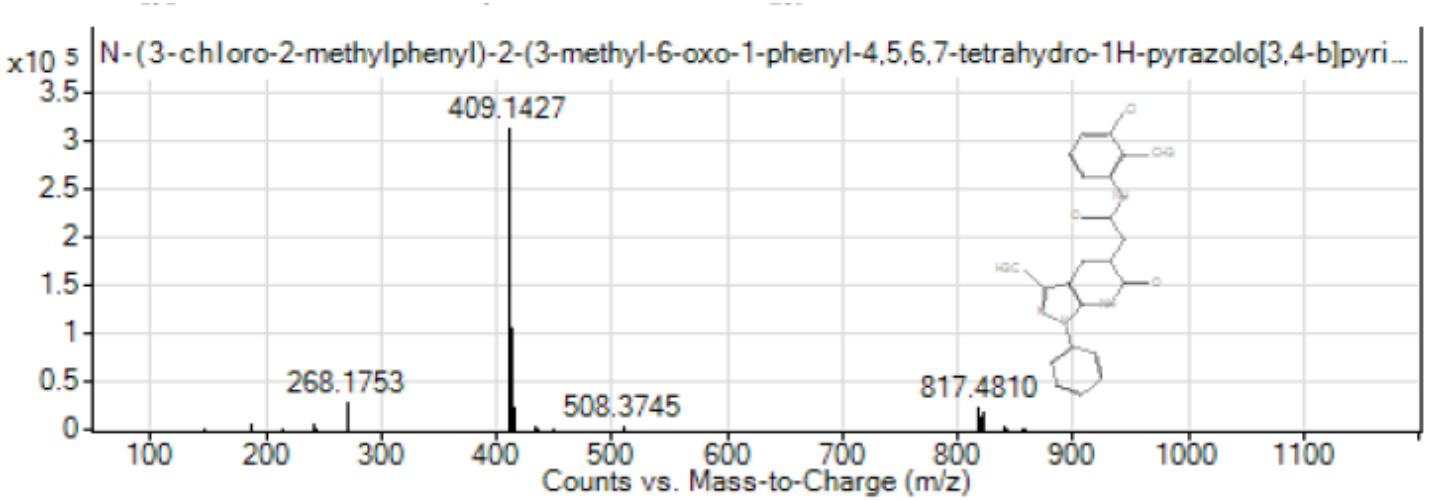

Peak List

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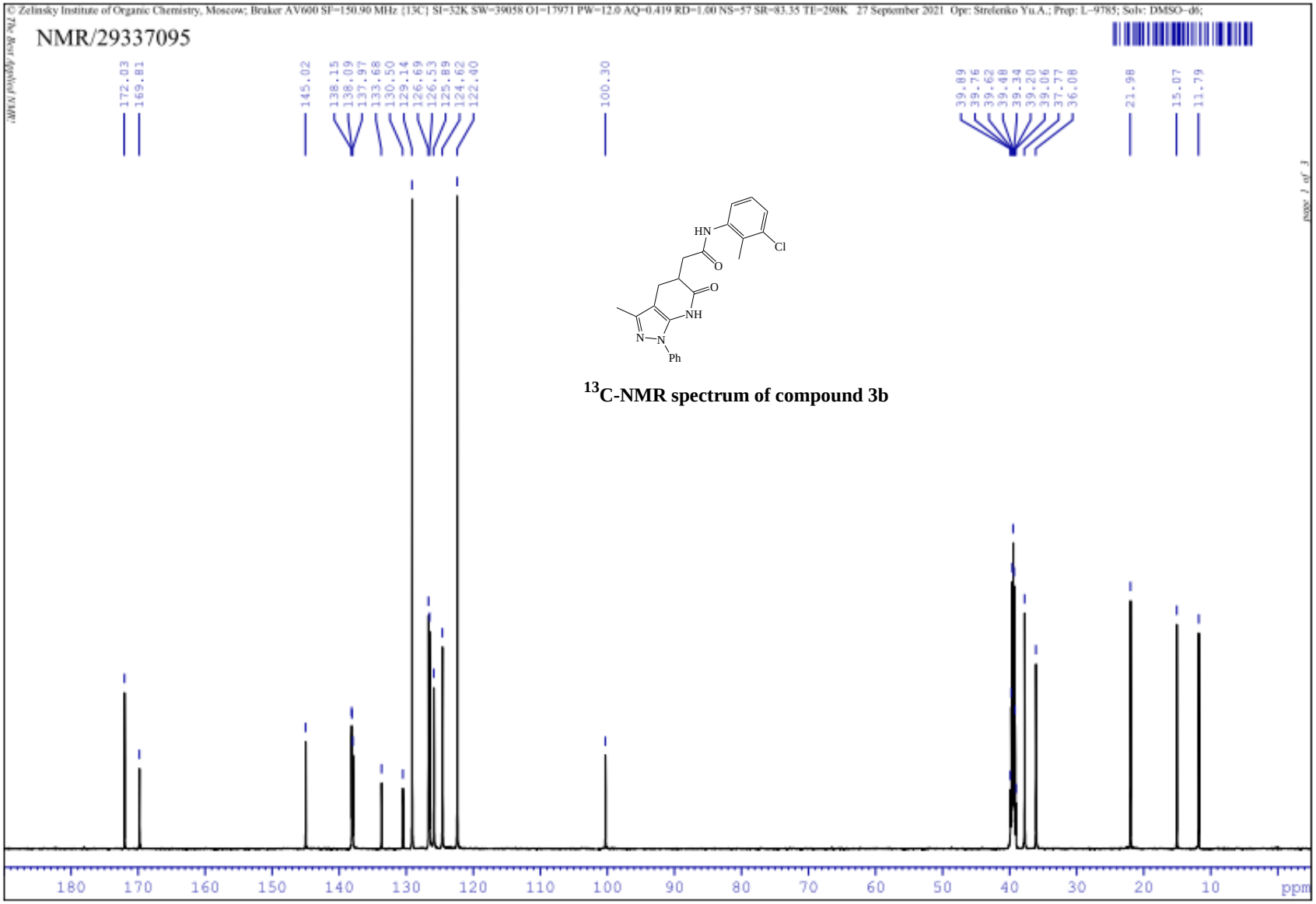
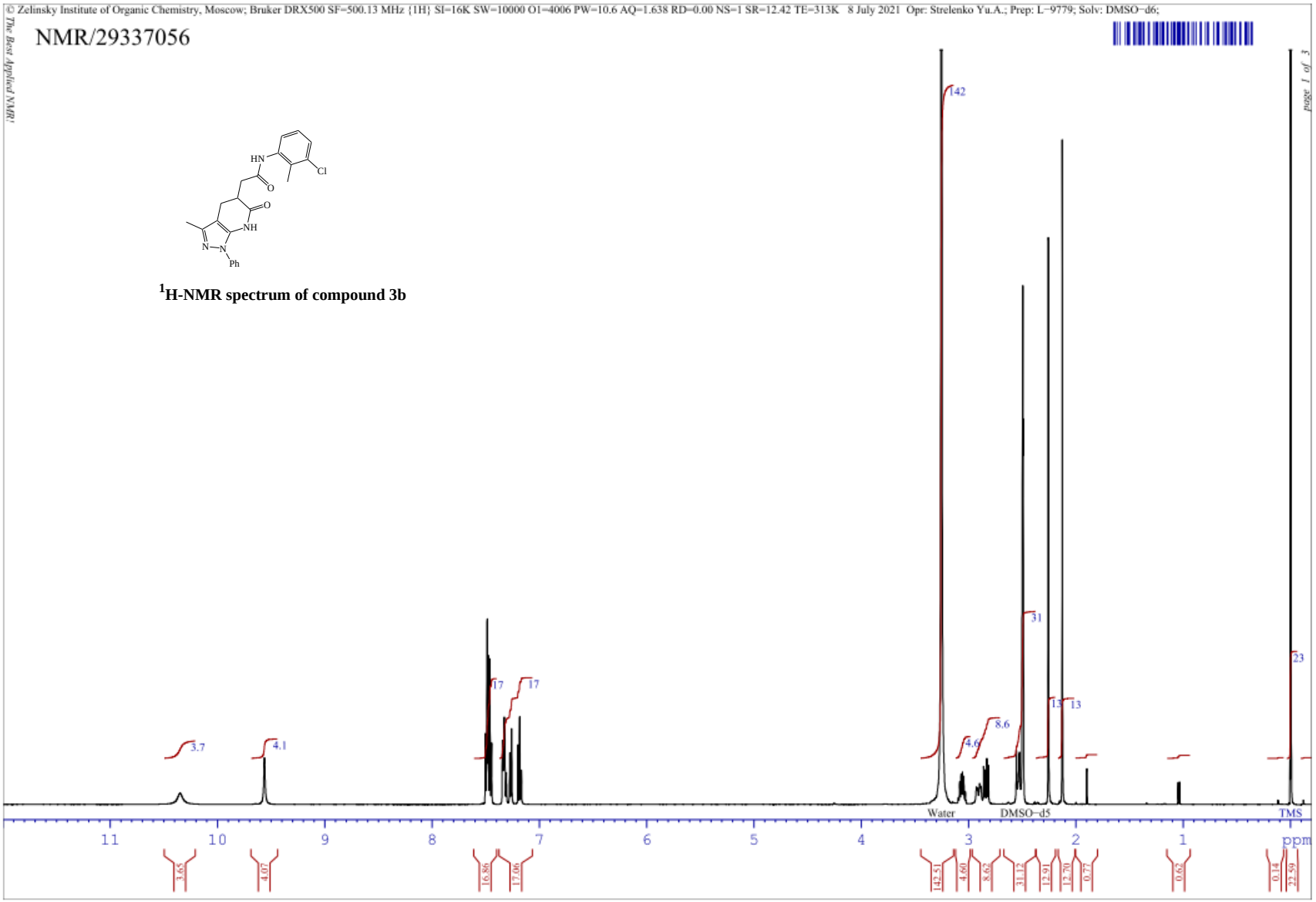
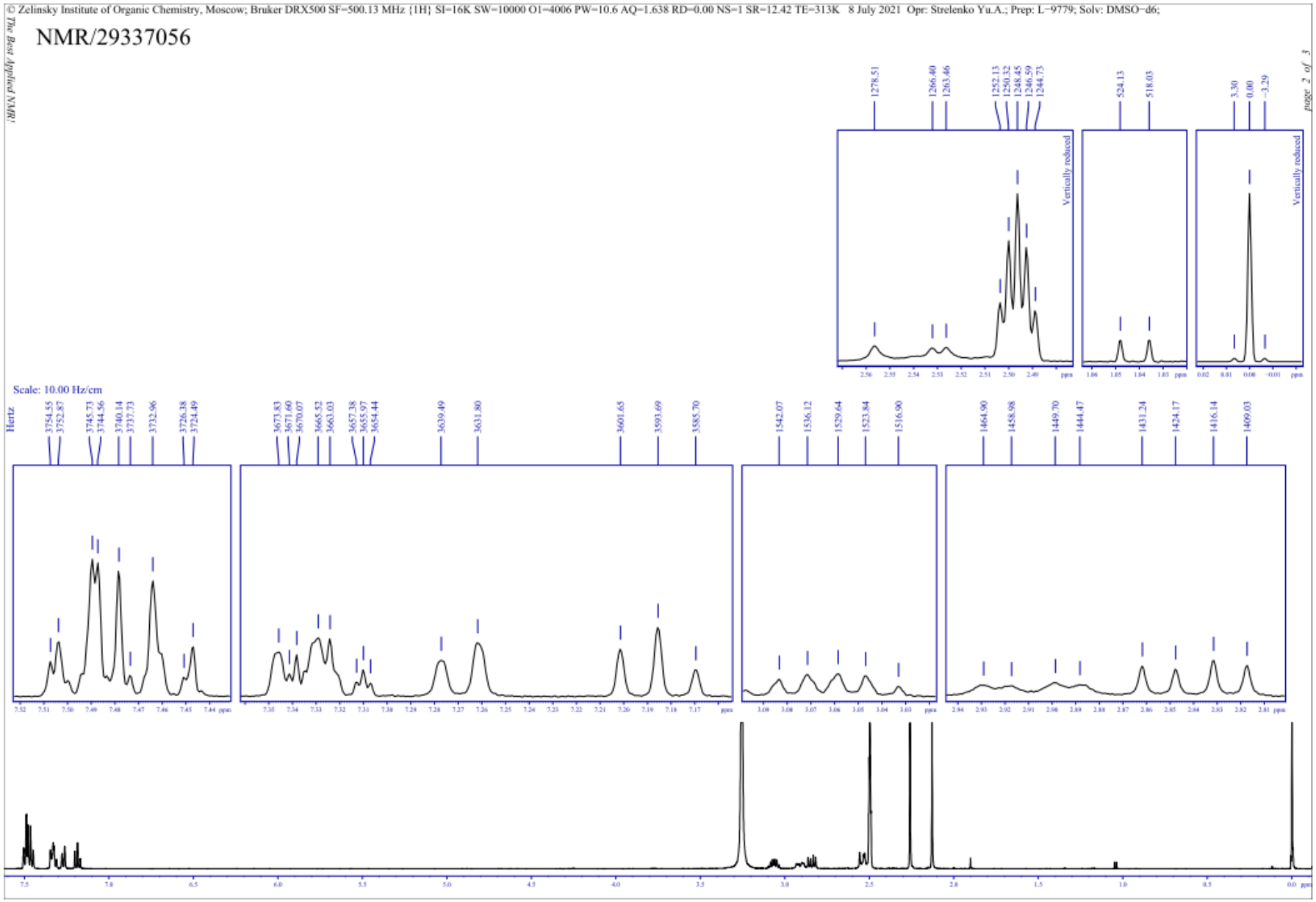


^{13}C-NMR spectrum of compound 3b



^{1}H-NMR spectrum of compound 3b


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz {1H} SI=16K SW=10000 O1=4006 PW=10.6 AQ=1.638 RD=0.00 NS=1 SR=12.42 TE=313K 8 July 2021 Opr: Strelenko Yu.A.; Prep: L−9779; Solv: DMSO−d6;
The Best Applied NMR!
NMR/29337056
page 2 of 3
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Vertically reduced
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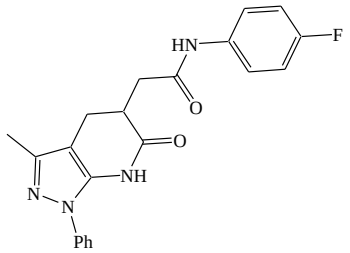
1516.90
1464.90
1458.98
1449.70
1444.47
1431.24
1424.17
1416.14
1409.03

Qualitative Analysis Report

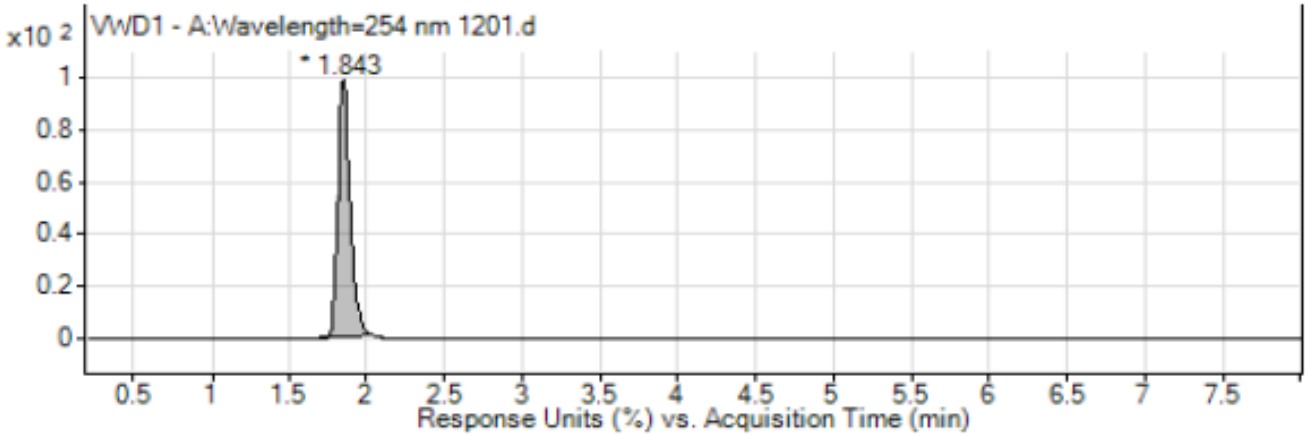
Data Filename	1201.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 13
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	3/10/2021 1:17:41 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



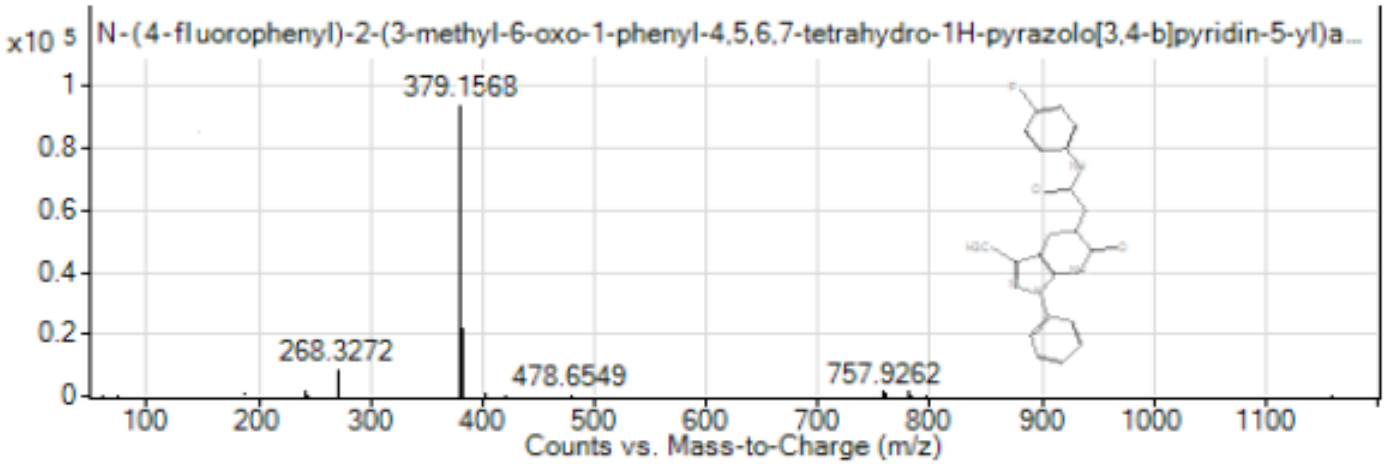
LCMS spectrum of compound 3c

User Chromatograms



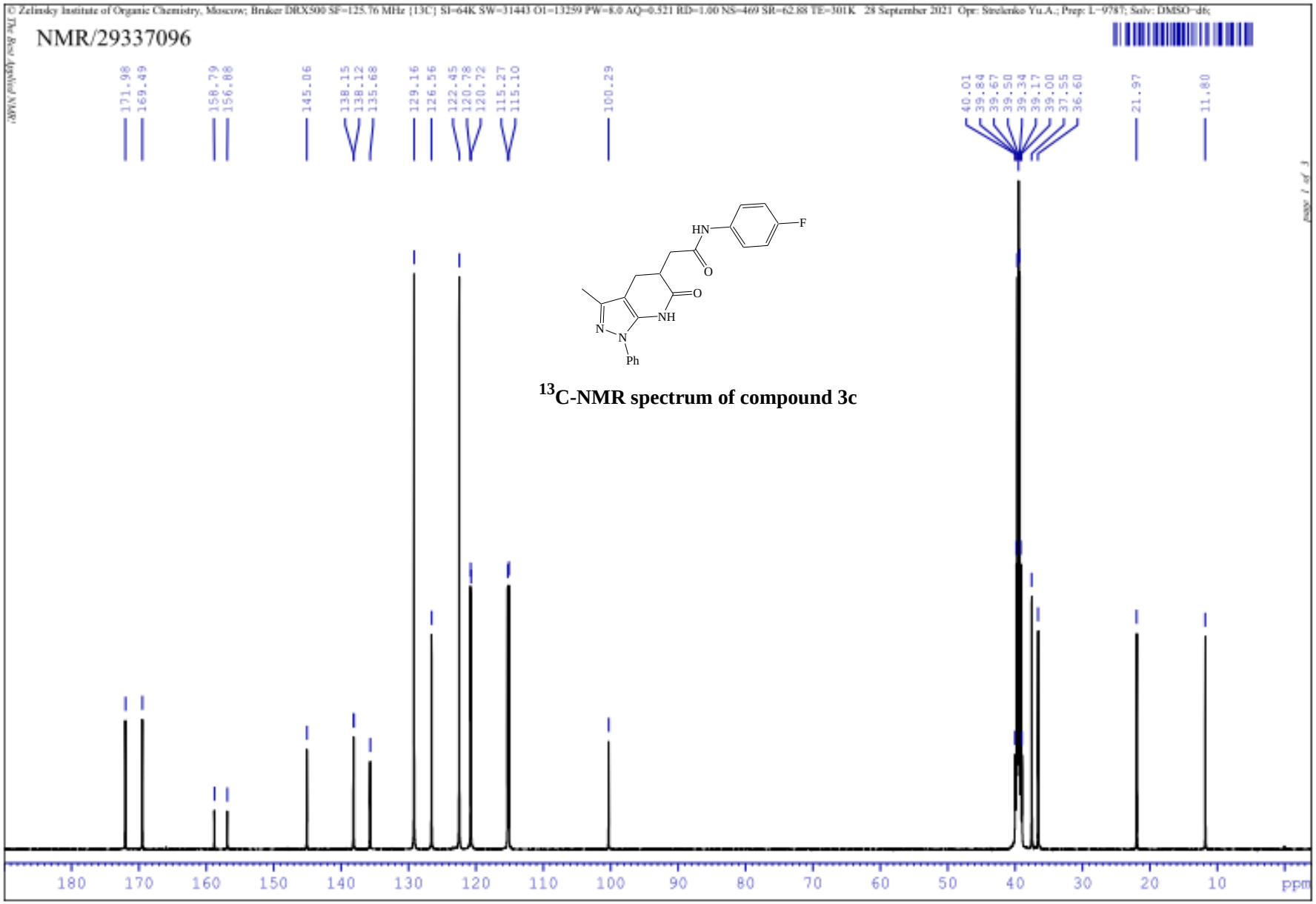
Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	1,7	1,843	2,043	859,27	4715,65	100

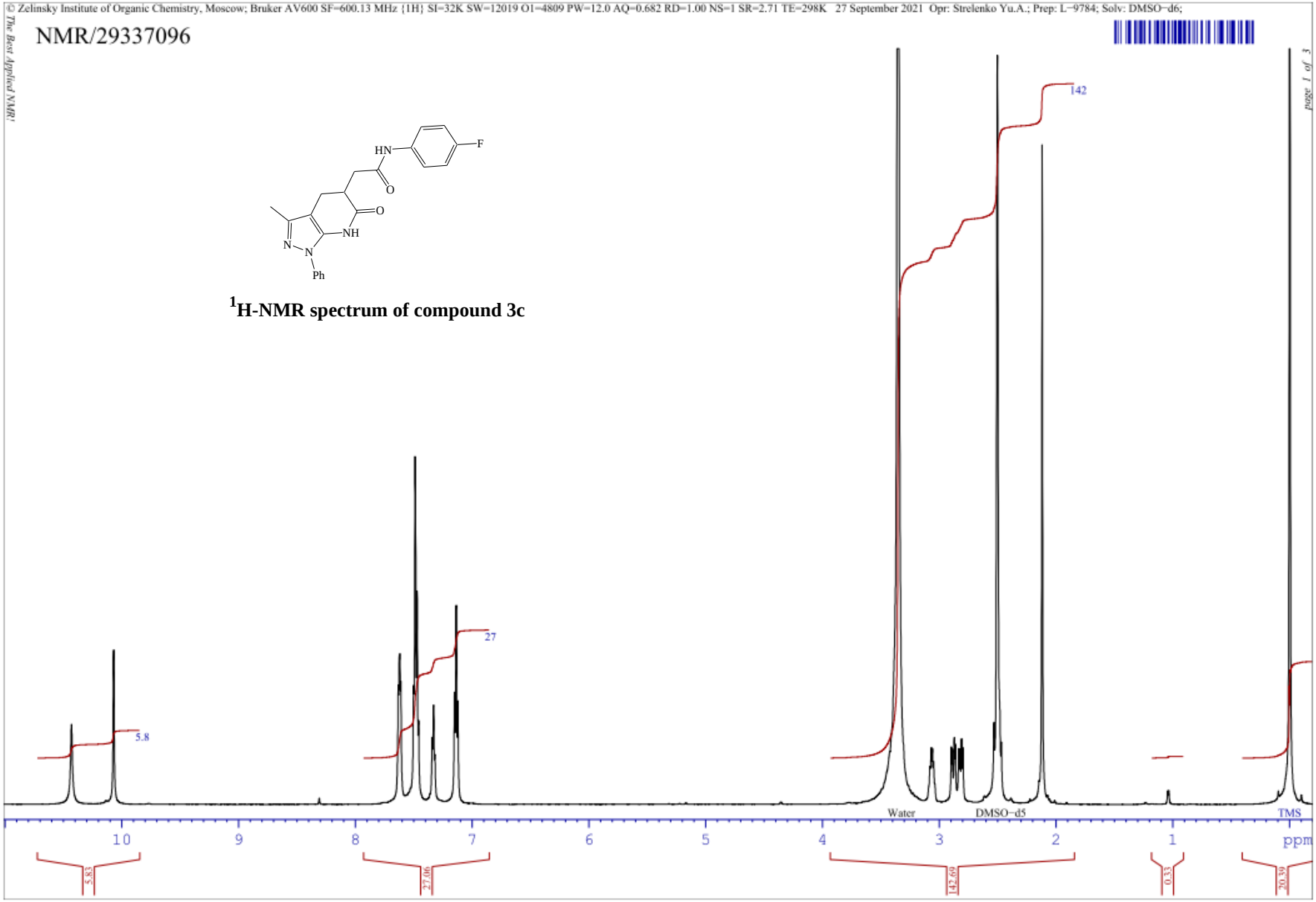


Peak List

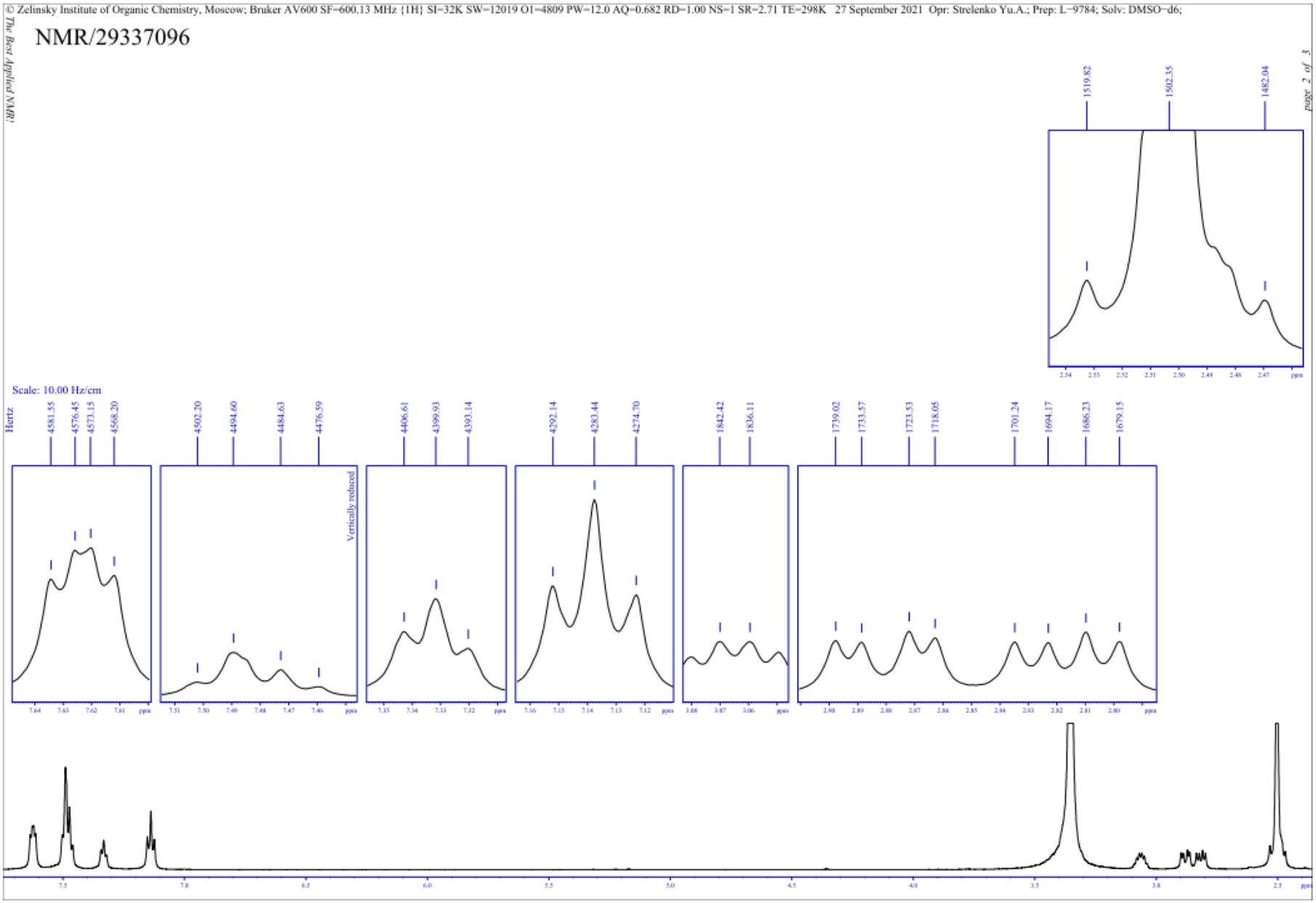
m/z	z	Abund
186,253	1	984,21
240,3099	1	1992,09
268,3272	1	8887,67
269,3296	1	1596,49
379,1568	1	93984,64
380,4693	1	21853,83
381,4741	1	2918,83
401,4641	1	1114,61
757,9262	1	1618,04
779,9289	1	1563,52



^{13}C-NMR spectrum of compound 3c



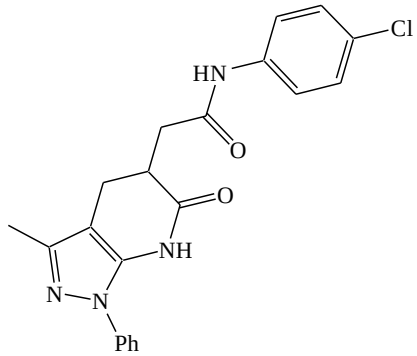
^{1}H-NMR spectrum of compound 3c


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H} SI=32K SW=12019 O1=4809 PW=12.0 AQ=0.682 RD=1.00 NS=1 SR=2.71 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9784; Solv: DMSO−d6;
The Best Applied NMR!
NMR/29337096
page 2 of 3
1519.82
1502.35
1482.04
Scale: 10.00 Hz/cm
Hertz
4581.55
4576.45
4573.15
4568.20
4502.20
4494.60
4484.63
4476.59
Vertically reduced
4406.61
4399.93
4393.14
4292.14
4283.44
4274.70
1842.42
1836.11
1739.02
1733.57
1723.53
1718.05
1701.24
1694.17
1686.23
1679.15

Qualitative Analysis Report

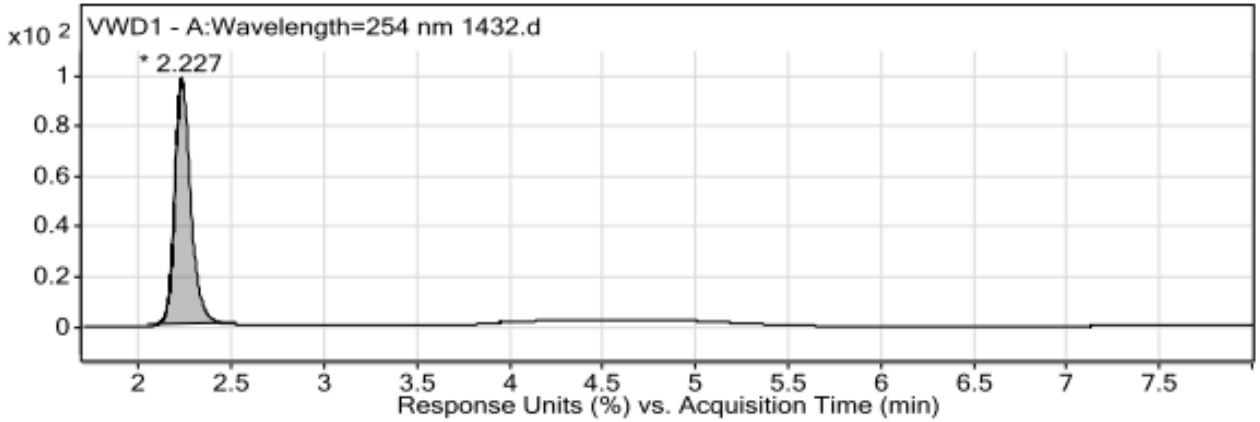
Data Filename	1432.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 13
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	4/9/2021 12:00:04 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



LCMS spectrum of compound 3d

User Chromatograms



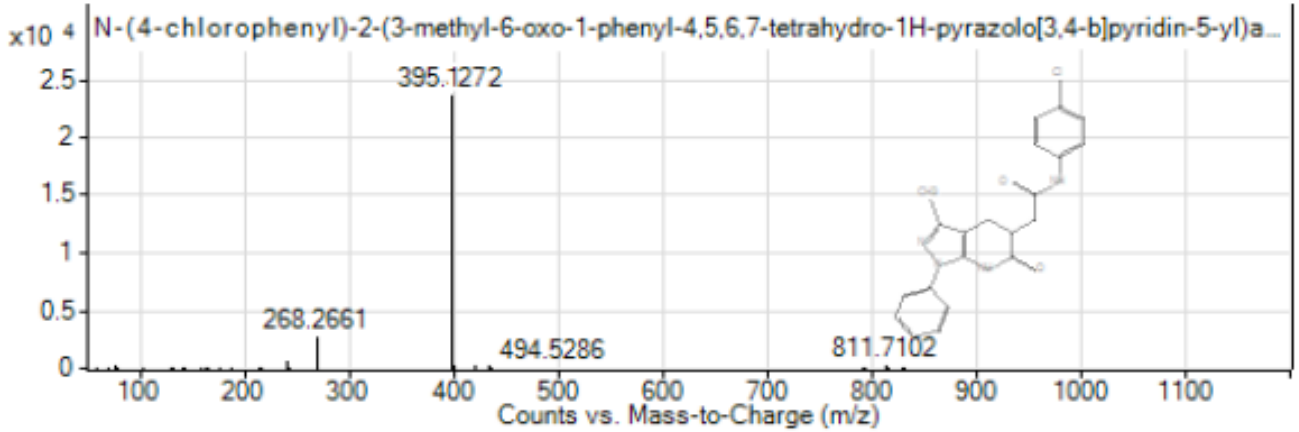
Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	2,047	2,227	2,527	159,99	965,79	100

^{1}H NMR 3c

User Spectra

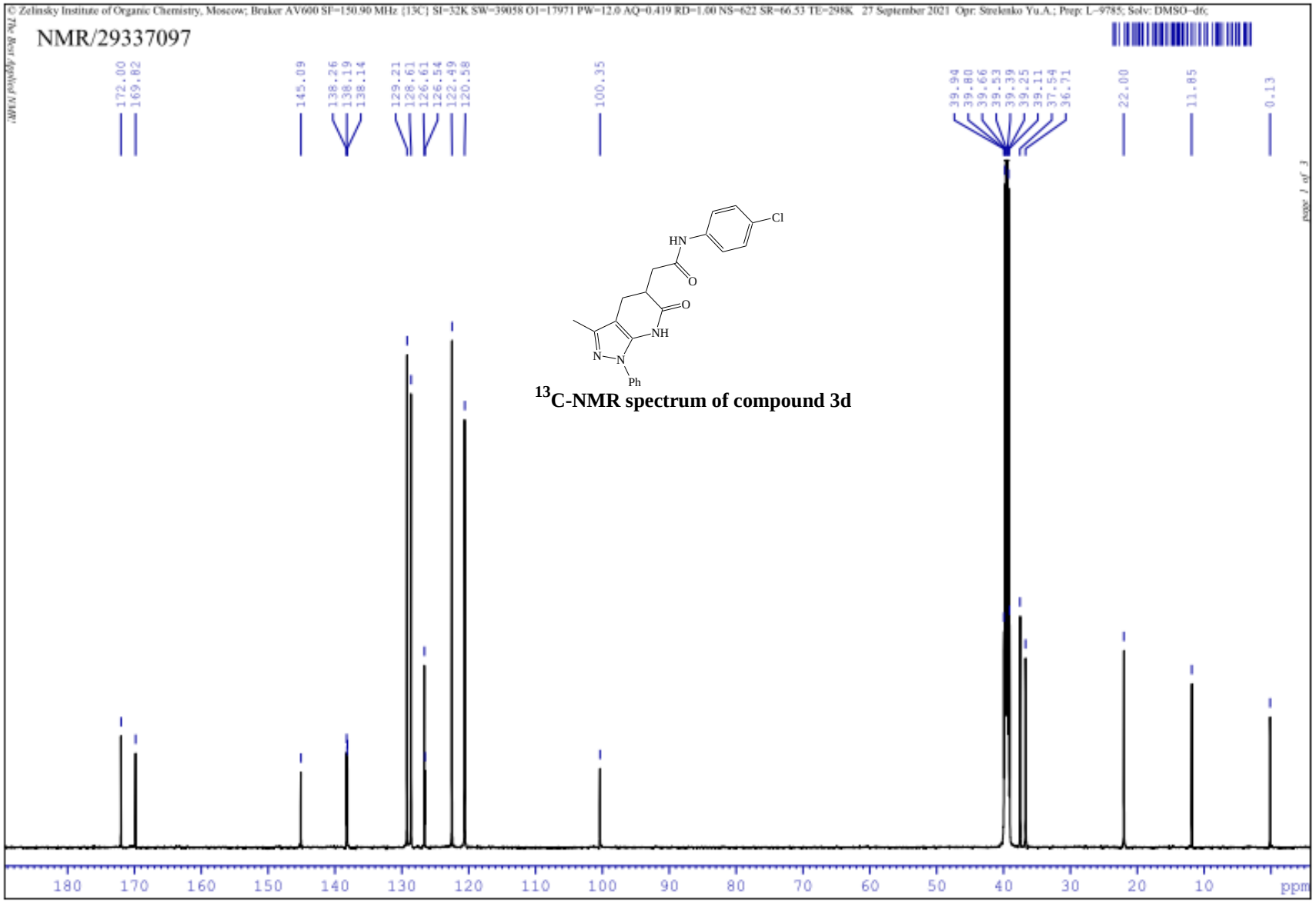
Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI



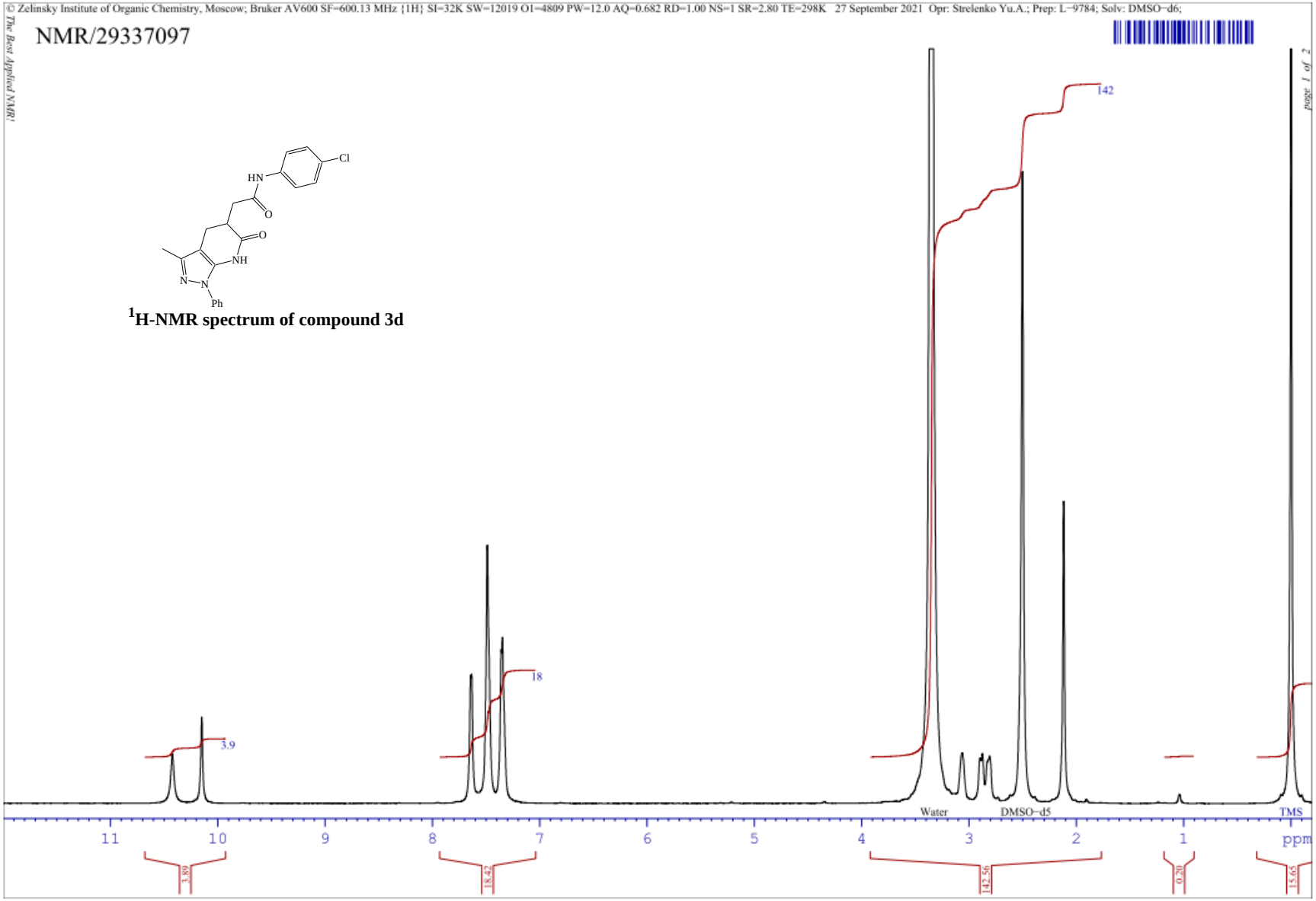
Peak List

m/z	z	Abund
240,2539	1	704,76
268,2661	1	2881,77
269,2689	1	543,37
395,1272	1	23766,57
396,3638	1	5903,62
397,359	1	8053,14
398,3627	1	2093,97
399,3663	1	284,84
417,3593	1	464,4
811,7102	1	293,9

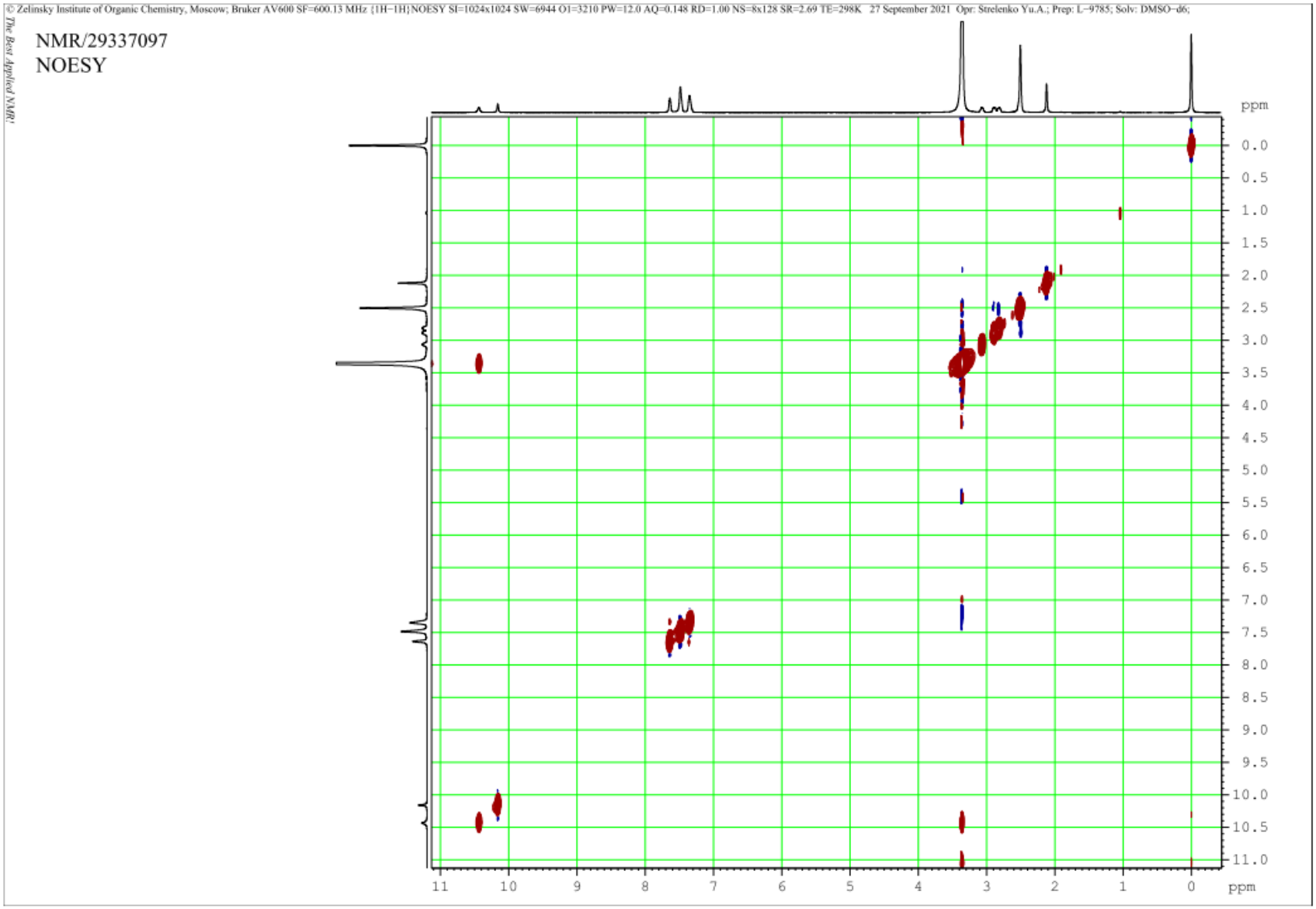
LCMS 3d

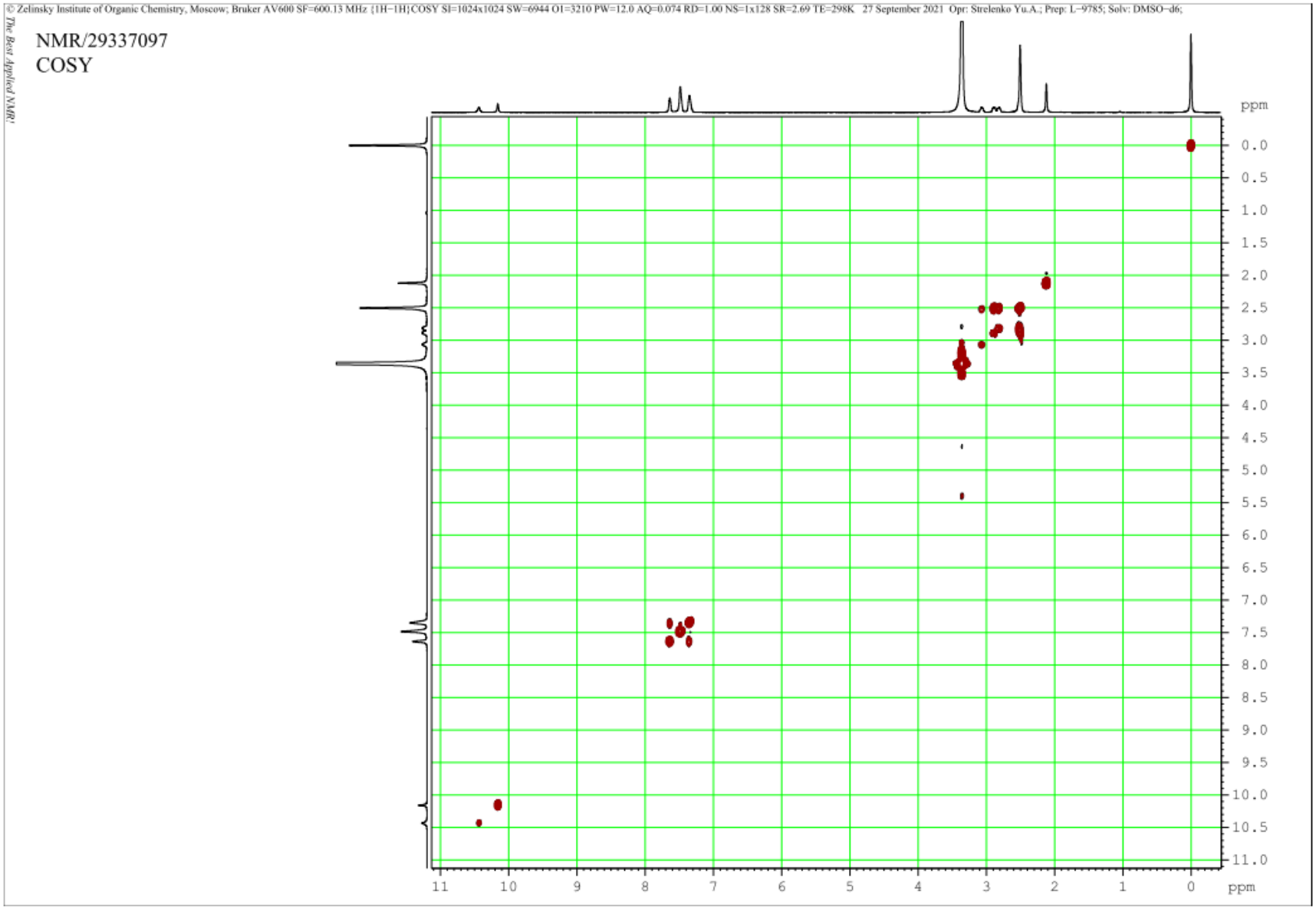


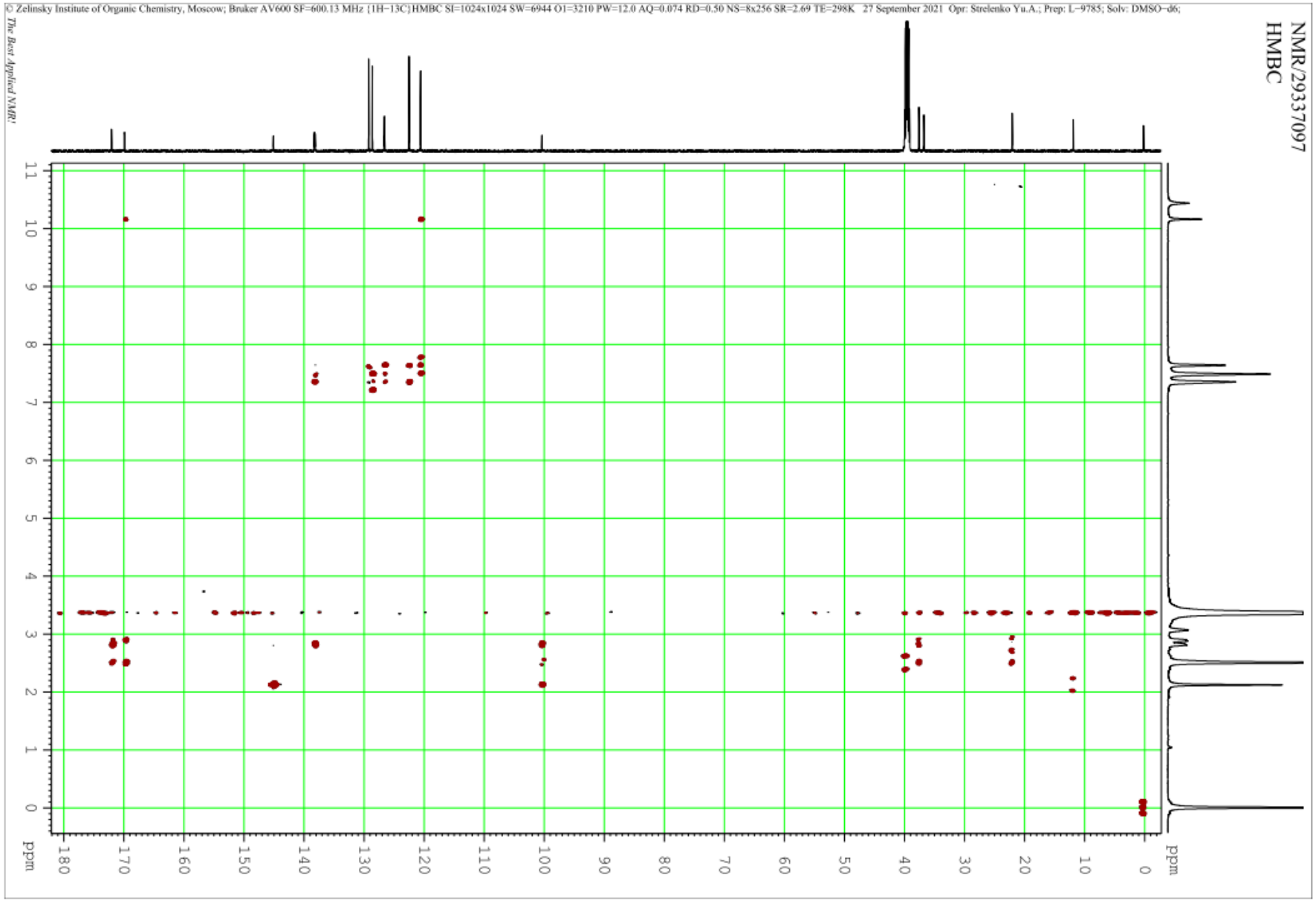
^{13}C-NMR spectrum of compound 3d

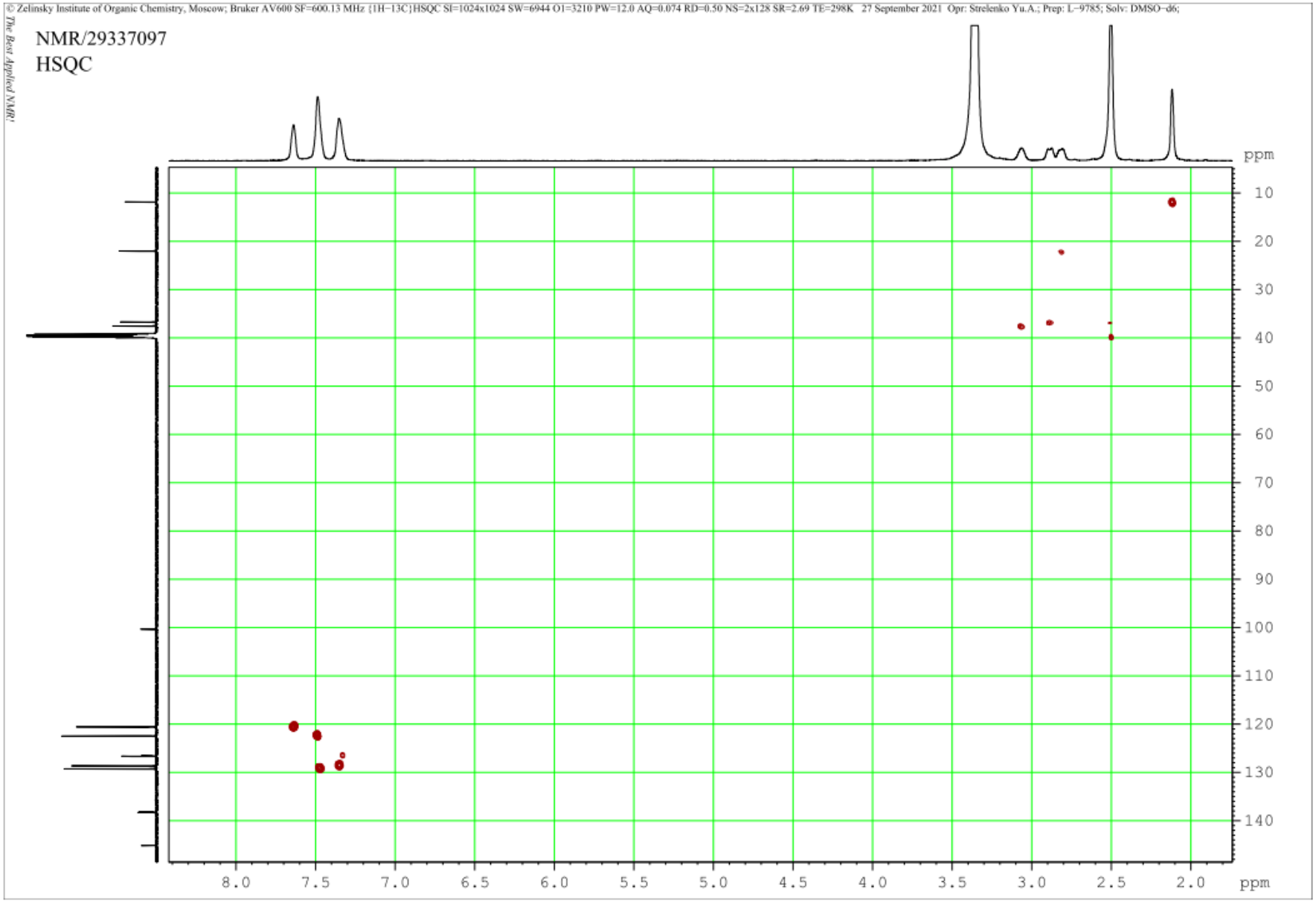


^{1}H-NMR spectrum of compound 3d


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H-1H}NOESY SI=1024x1024 SW=6944 O1=3210 PW=12.0 AQ=0.148 RD=1.00 NS=8x128 SR=2.69 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L-9785; Solv: DMSO-d6;
The Best Applied NMR!
NMR/29337097
NOESY
ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11
10
9
8
7
6
5
4
3
2
1
0
ppm

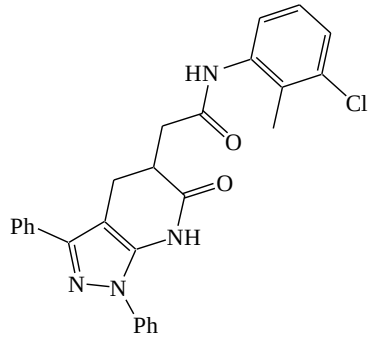

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H-1H}COSY SI=1024x1024 SW=6944 O1=3210 PW=12.0 AQ=0.074 RD=1.00 NS=1x128 SR=2.69 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L-9785; Solv: DMSO-d6;
The Best Applied NMR!
NMR/29337097
COSY
ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
11.0
11
10
9
8
7
6
5
4
3
2
1
0
ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H-13C}HMBC SI=1024x1024 SW=6944 O1=3210 PW=12.0 AQ=0.074 RD=0.50 NS=8x256 SR=2.69 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L-9785; Solv: DMSO-d6;
The Best Applied NMR!
NMR/29337097
HMBC
ppm
ppm


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H−13C}HSQC SI=1024x1024 SW=6944 O1=3210 PW=12.0 AQ=0.074 RD=0.50 NS=2x128 SR=2.69 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9785; Solv: DMSO−d6;
The Best Applied NMR!
NMR/29337097
HSQC
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm

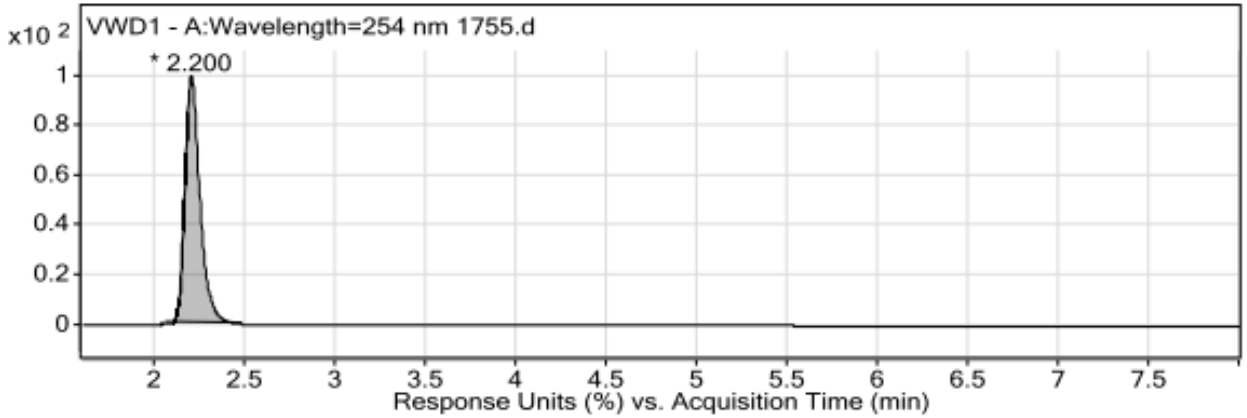
Qualitative Analysis Report

Data Filename	1755.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 58
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	7/2/2021 1:49:49 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			
Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



LCMS spectrum of compound 3e

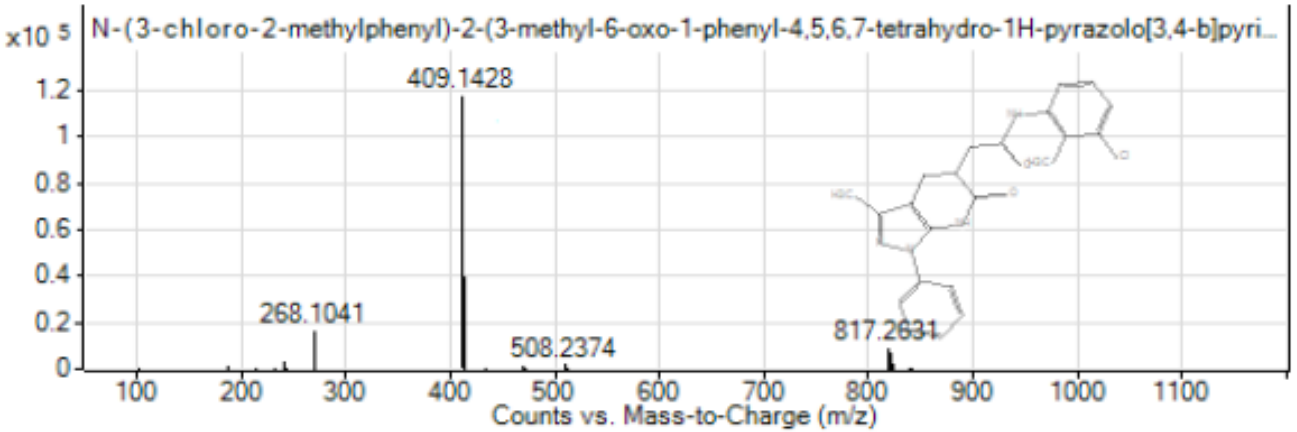
User Chromatograms



Integration Peak List

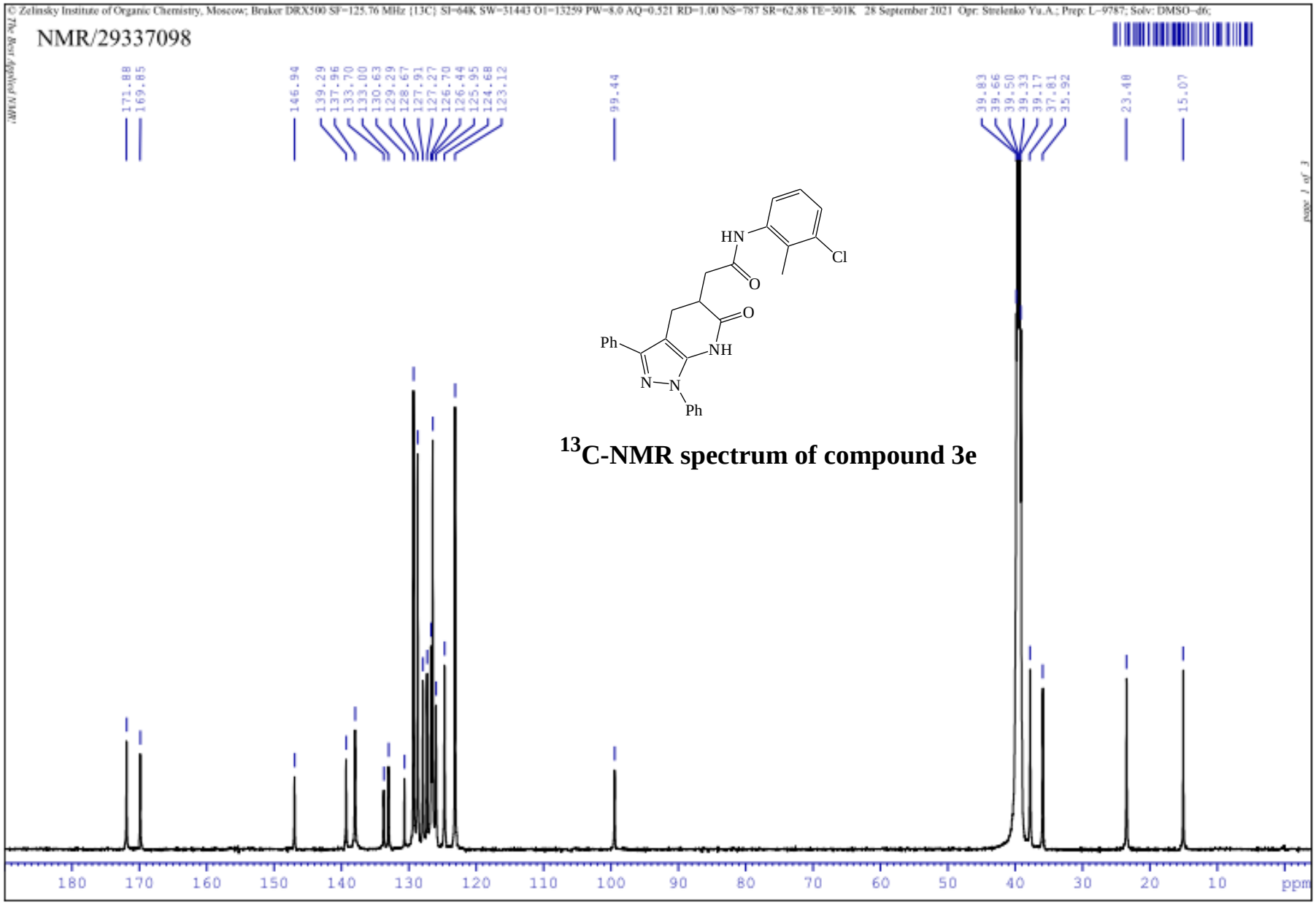
Peak	Start	RT	End	Height	Area	Area %
1	2,06	2,2	2,483	1149,45	6681,75	100

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

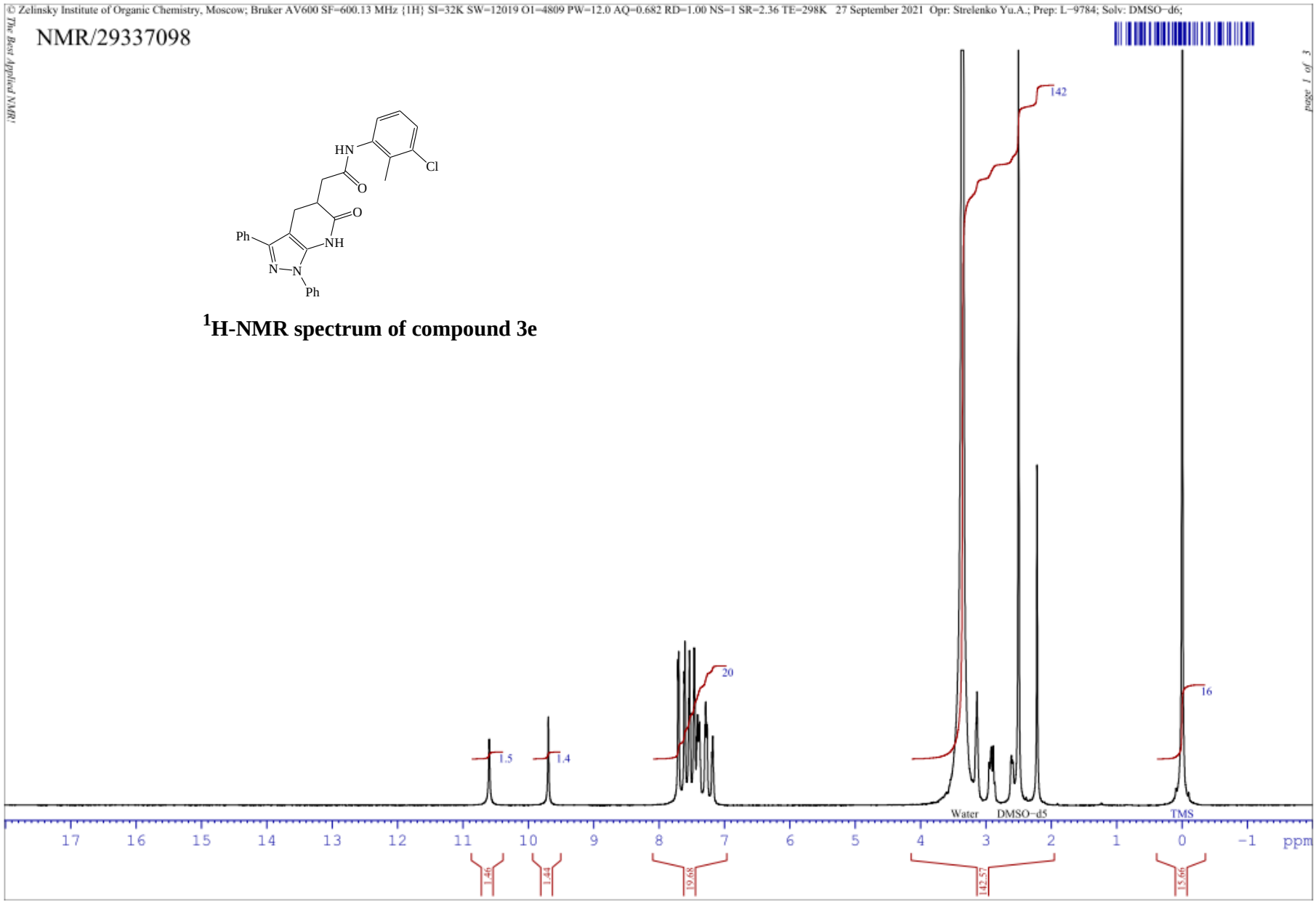


Peak List

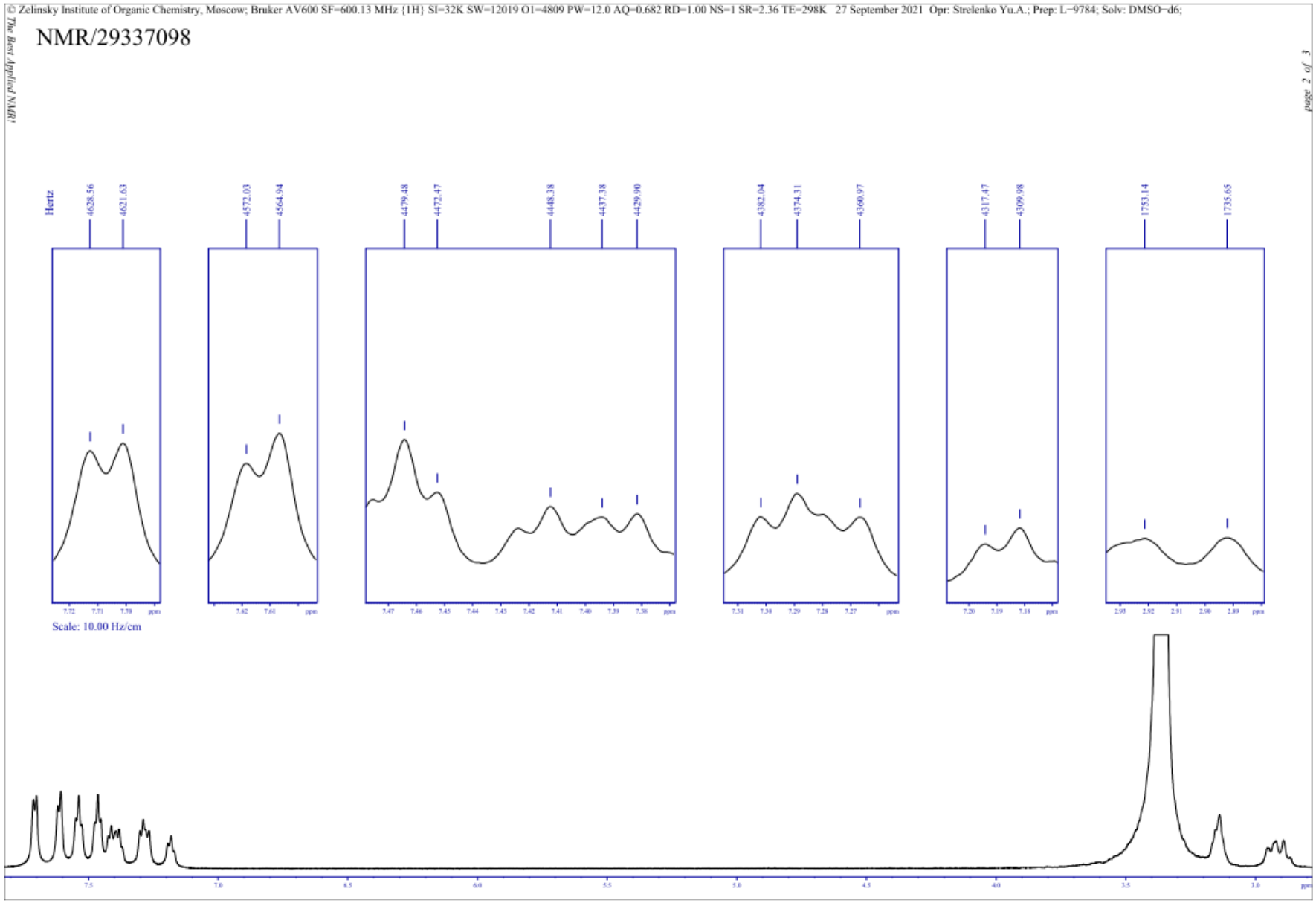
m/z	z	Abund
240,1086	1	3604,96
268,1041	1	16789,77
409,1428	1	118082,42
410,1381	1	29779,83
411,1337	1	40227,45
412,1362	1	9891,49
817,2631	1	9401,82
818,2685	1	5140,34
819,2634	1	7273,96
820,2658	1	3516,77



^{13}C-NMR spectrum of compound 3e



^{1}H-NMR spectrum of compound 3e


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H} SI=32K SW=12019 O1=4809 PW=12.0 AQ=0.682 RD=1.00 NS=1 SR=2.36 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9784; Solv: DMSO−d6;
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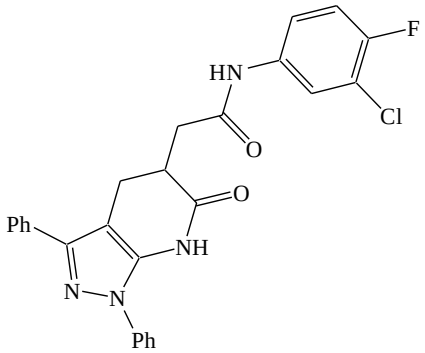
NMR/29337098
page 2 of 3
Hertz
4628.56
4621.63
4572.03
4564.94
4479.48
4472.47
4448.38
4437.38
4429.90
4382.04
4374.31
4360.97
4317.47
4309.98
1753.14
1735.65
Scale: 10.00 Hz/cm

Qualitative Analysis Report

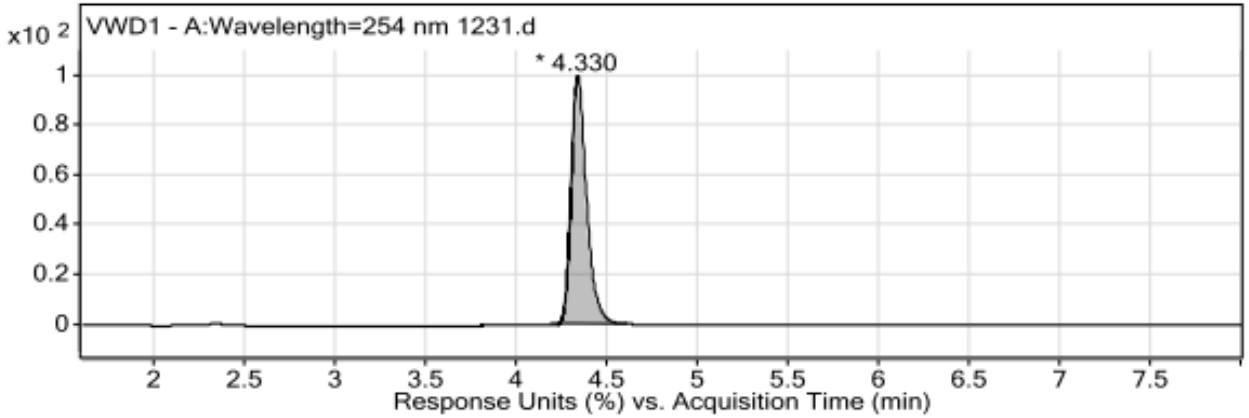
Data Filename	1231.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 78
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	3/15/2021 1:43:45 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



LCMS spectrum of compound 3f

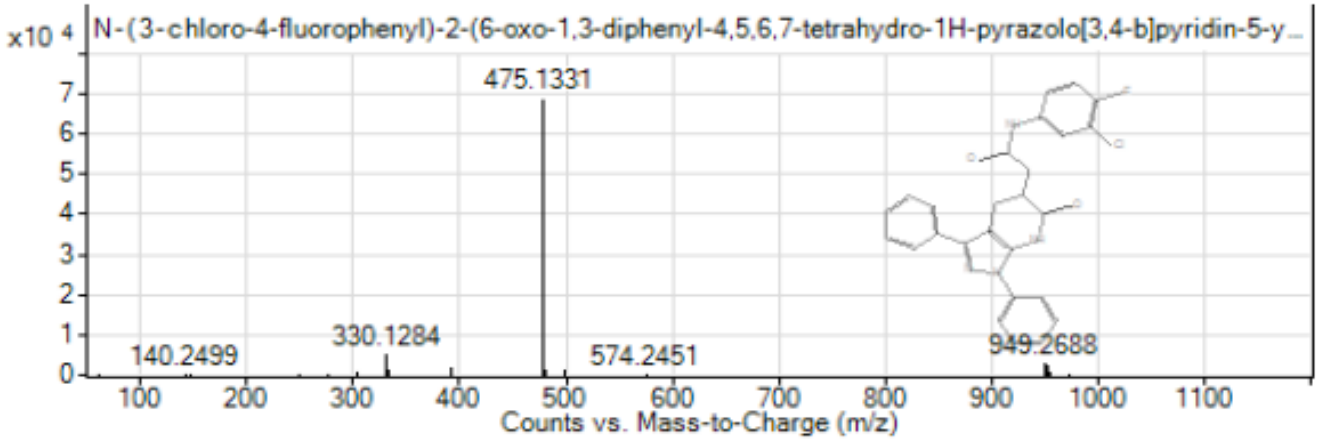
User Chromatograms



Integration Peak List

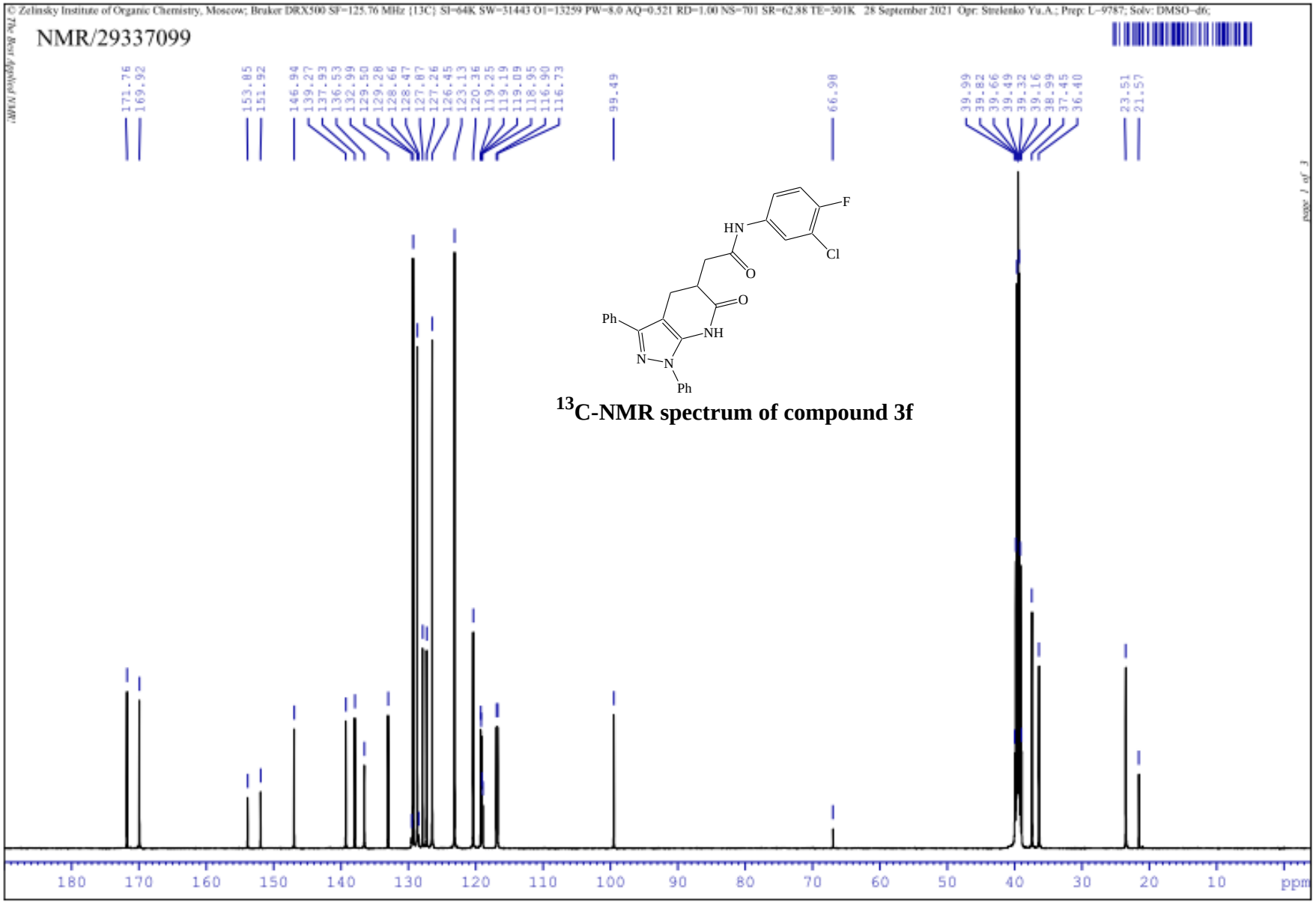
Peak	Start	RT	End	Height	Area	Area %
1	4,187	4,33	4,607	1531,28	9151,55	100

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

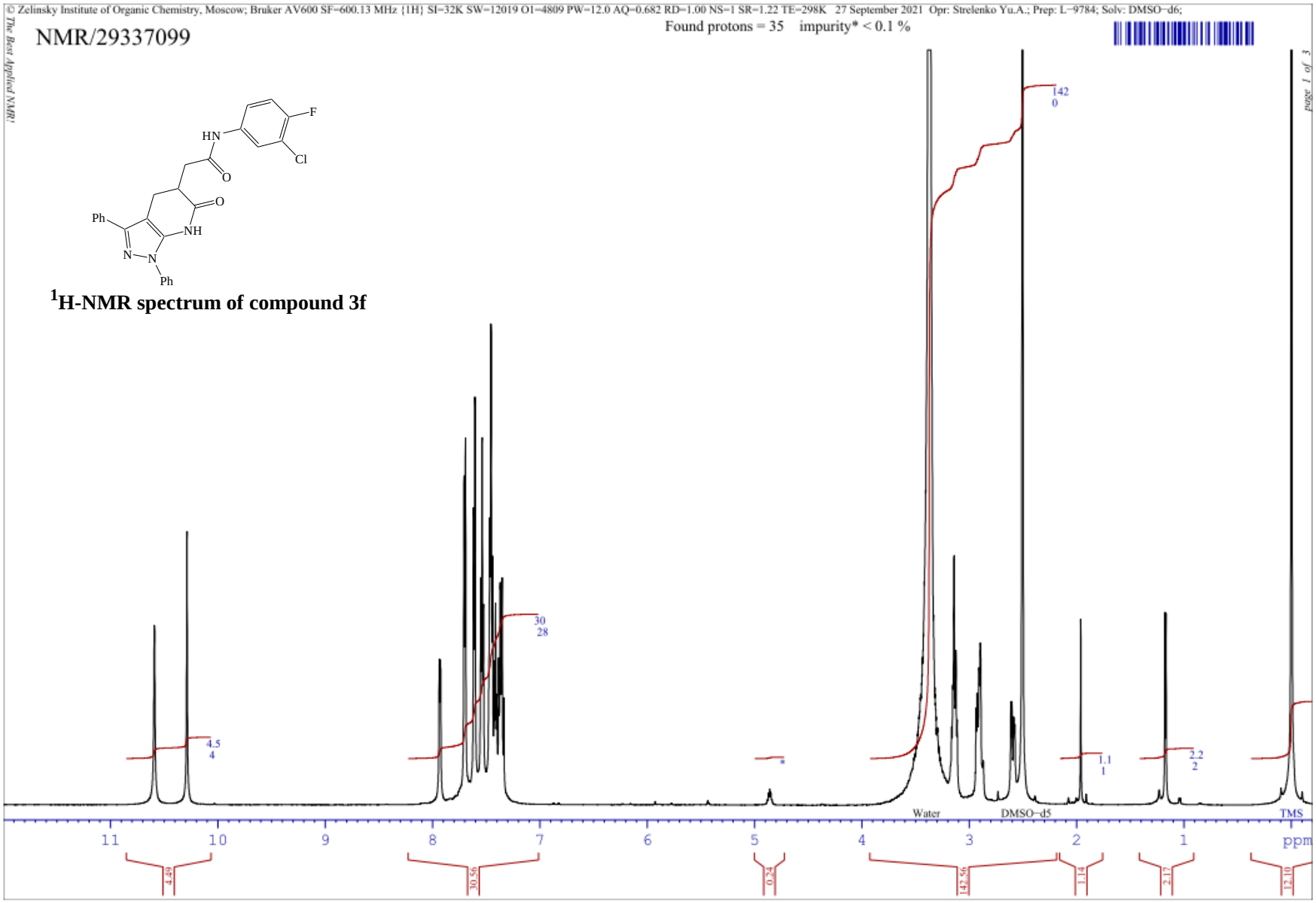


Peak List

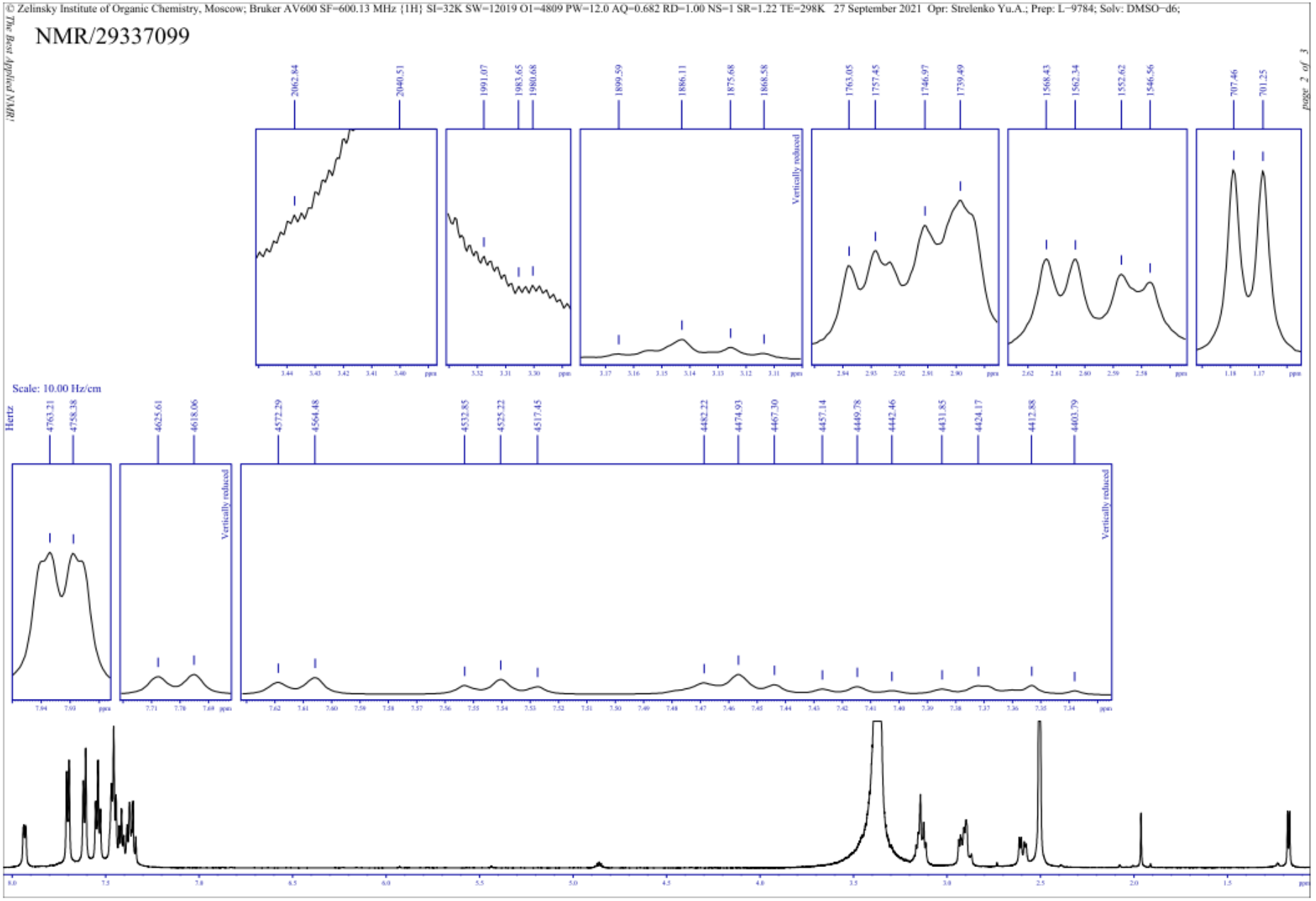
m/z	z	Abund
330,1284	1	5549,97
390,1862	1	2210,04
475,1331	1	69241,83
476,1421	1	20008,65
477,1373	1	24245,66
478,14	1	6830,36
949,2688	1	3162,65
950,2711	1	1922,98
951,269	1	2497,69
952,2722	1	1344,85



^{13}C-NMR spectrum of compound 3f



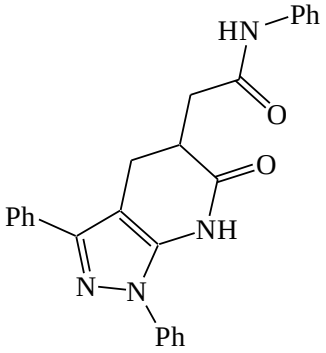
^{1}H-NMR spectrum of compound 3f


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H} SI=32K SW=12019 O1=4809 PW=12.0 AQ=0.682 RD=1.00 NS=1 SR=1.22 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9784; Solv: DMSO−d6;
NMR/29337099
The Best Applied NMR!
page 2 of 3
2062.84
2040.51
1991.07
1983.65
1980.68
1899.59
1886.11
1875.68
1868.58
1763.05
1757.45
1746.97
1739.49
1568.43
1562.34
1552.62
1546.56
707.46
701.25
Vertically reduced
Scale: 10.00 Hz/cm
Hertz
4763.21
4758.38
4625.61
4618.06
4572.29
4564.48
4532.85
4525.22
4517.45
4482.22
4474.93
4467.30
4457.14
4449.78
4442.46
4431.85
4424.17
4412.88
4403.79
Vertically reduced
Vertically reduced

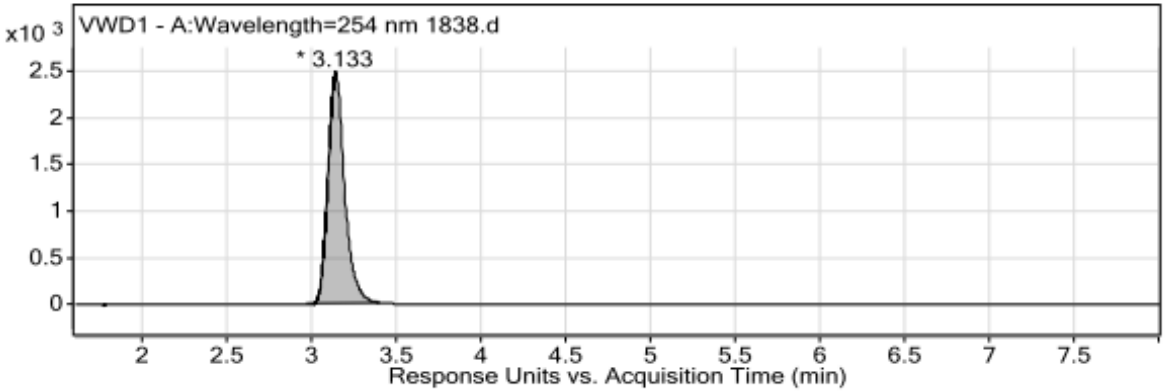
Qualitative Analysis Report

Data Filename	1838.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 14
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	7/20/2021 12:51:04 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



User Chromatograms

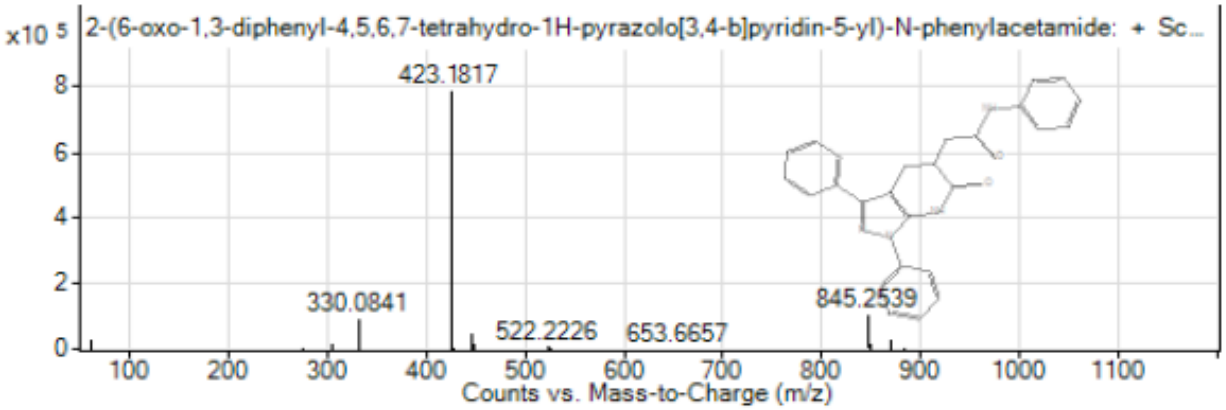


Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	2,967	3,133	3,393	2487,45	17089,6	100

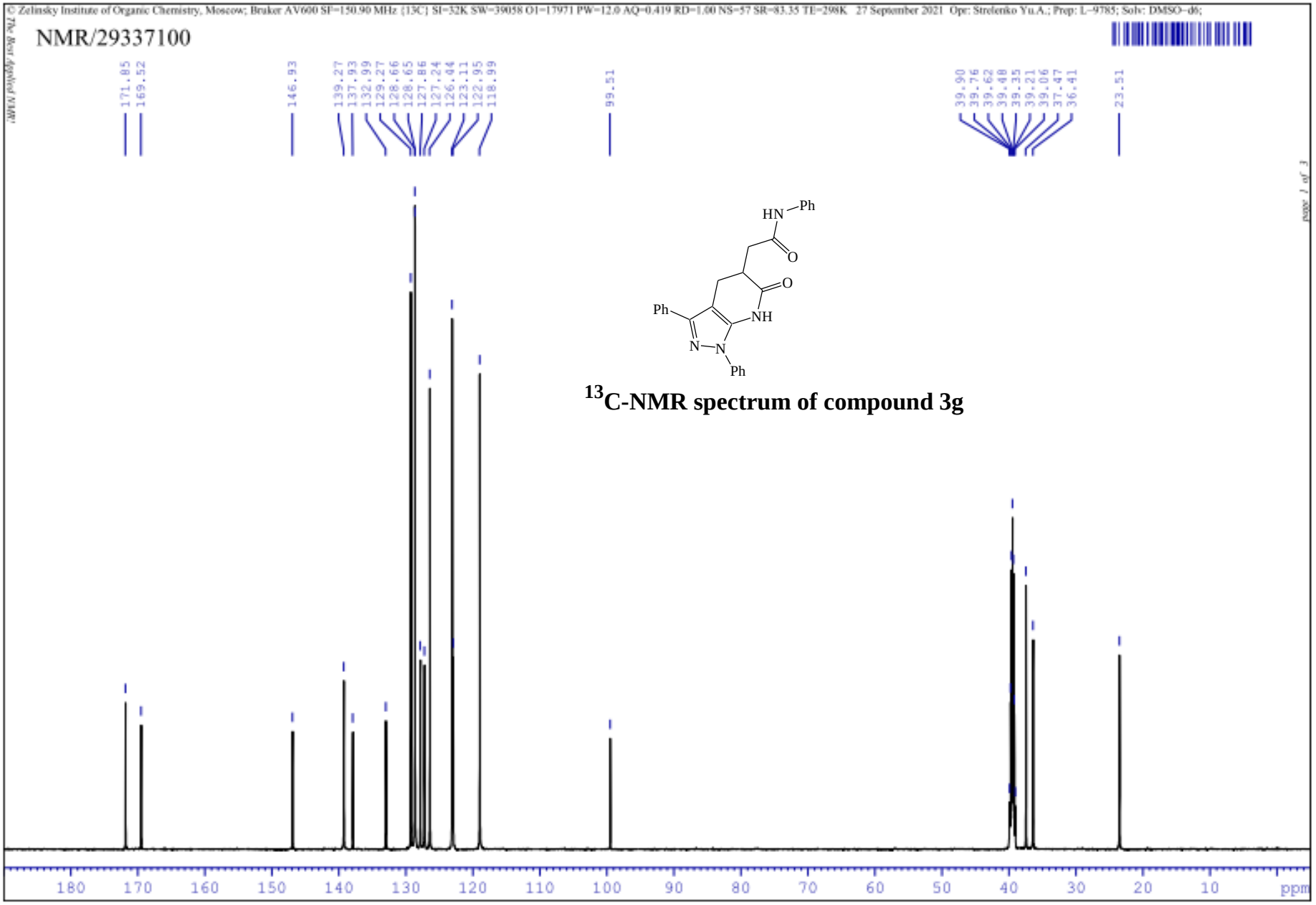
LCMS spectrum of compound 3g

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

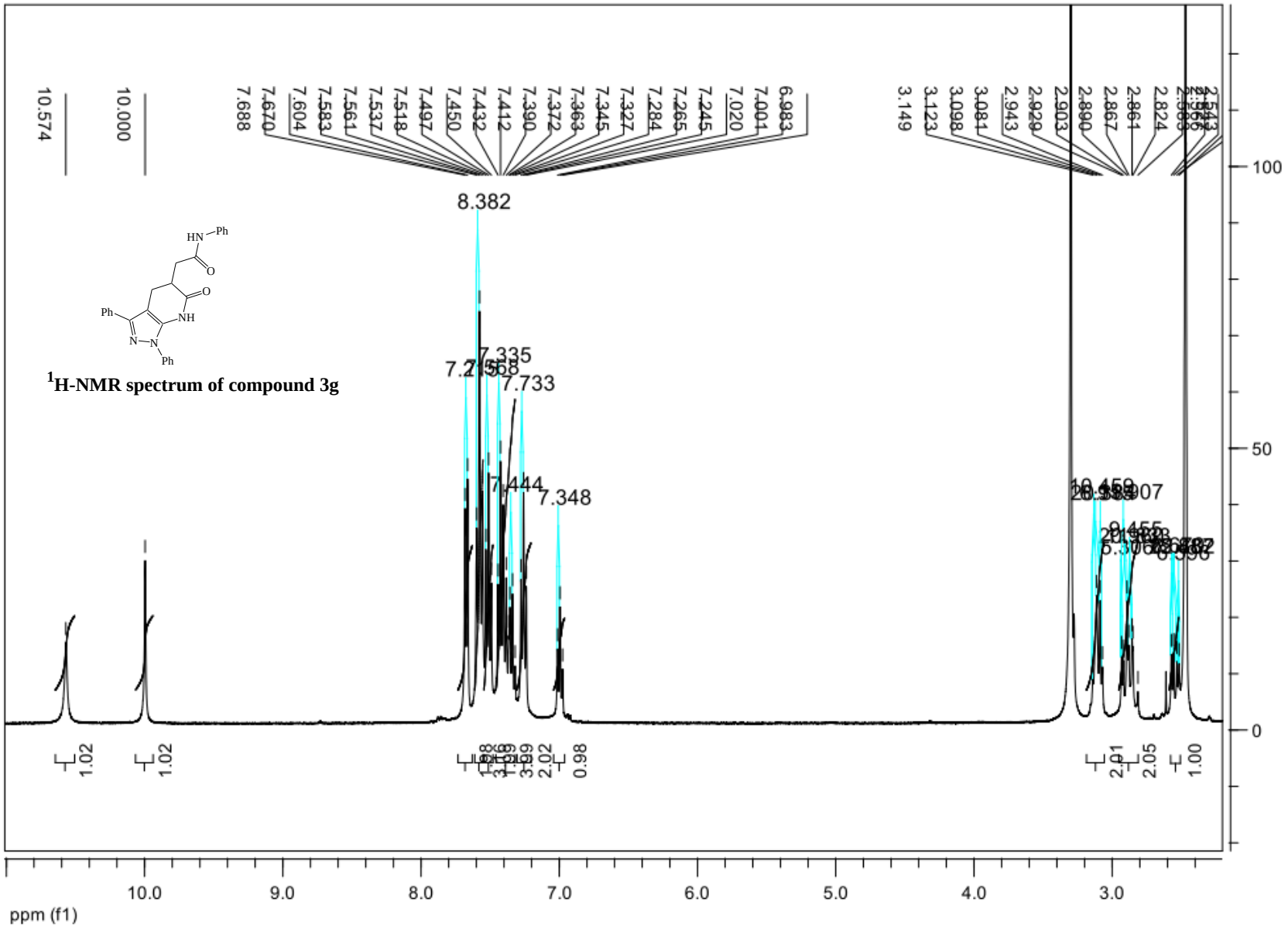


Peak List

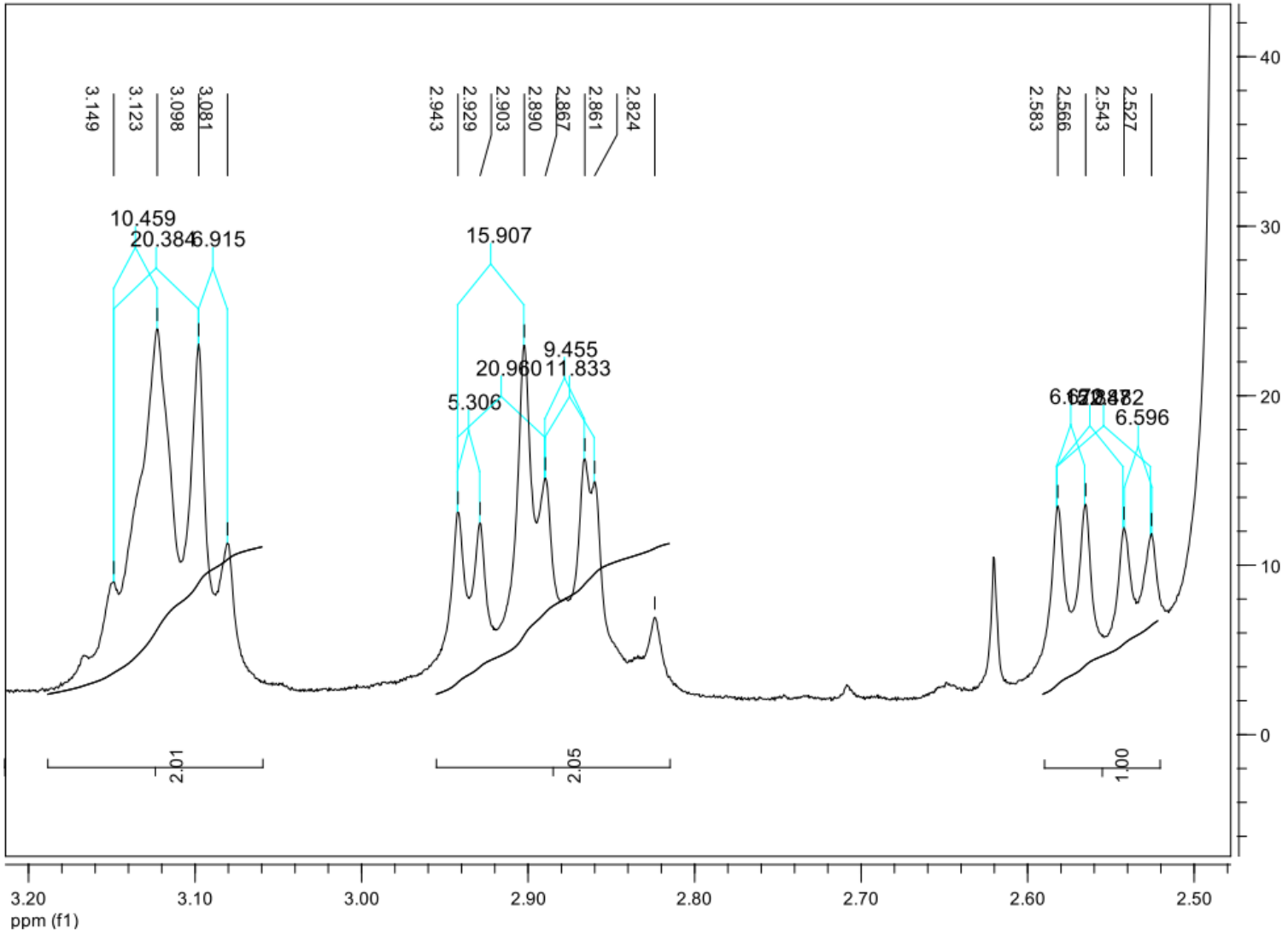
m/z	z	Abund
59,043	1	27825,47
330,084	1	93105,98
331,087	1	22794,01
423,1817	1	788678,25
424,134	1	235123,94
425,136	1	37388,2
445,109	1	52024,36
845,254	1	105343,52
846,257	1	61833,24
867,23	1	27206,44

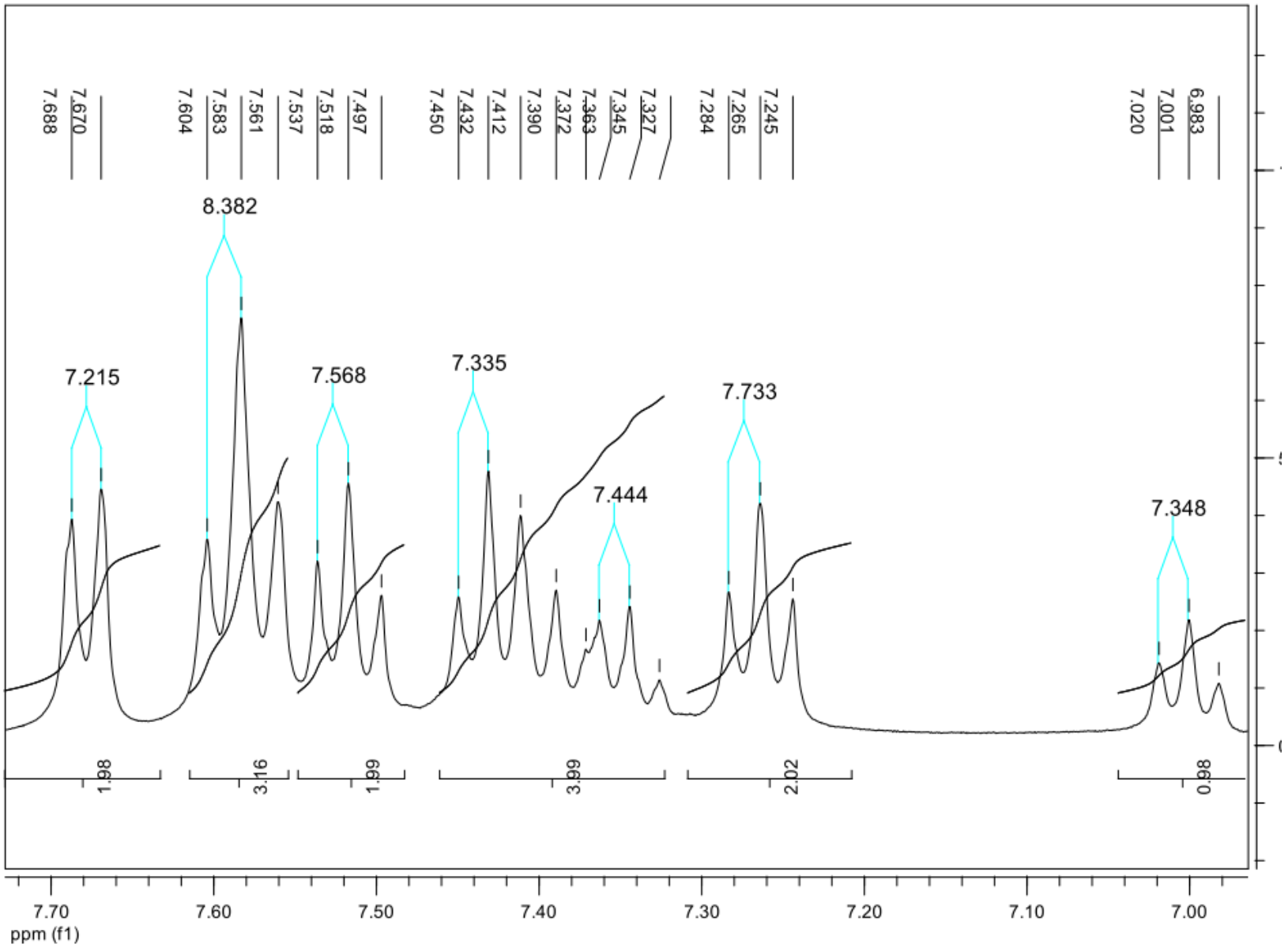


^{13}C-NMR spectrum of compound 3g



^{1}H-NMR spectrum of compound 3g

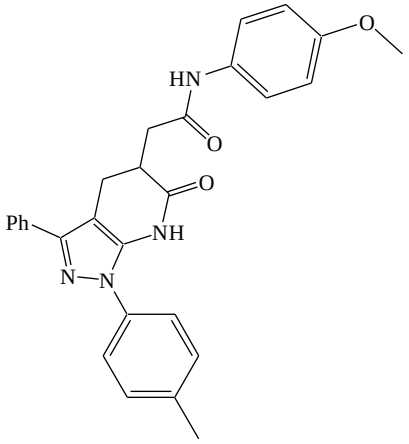

3.149
3.123
3.098
3.081
2.943
2.929
2.903
2.890
2.867
2.861
2.824
2.583
2.566
2.543
2.527
10.459
20.384
6.915
15.907
9.455
20.960
11.833
5.306
6.596
2.01
2.05
1.00
3.20
3.10
3.00
2.90
2.80
2.70
2.60
2.50
ppm (f1)
40
30
20
10
0


7.688
7.670
7.604
7.583
7.561
7.537
7.518
7.497
7.450
7.432
7.412
7.390
7.372
7.363
7.345
7.327
7.284
7.265
7.245
7.020
7.001
6.983
8.382
7.215
7.568
7.335
7.733
7.444
7.348
1.98
3.16
1.99
3.99
2.02
0.98
7.70
7.60
7.50
7.40
7.30
7.20
7.10
7.00
ppm (f1)

Qualitative Analysis Report

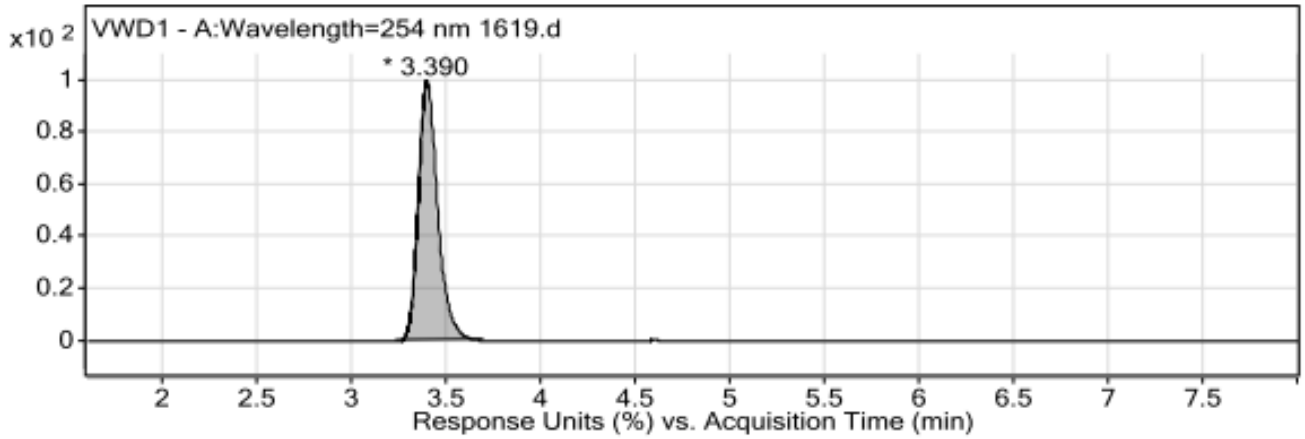
Data Filename	1619.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 54
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	5/31/2021 12:23:00 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



LCMS spectrum of compound 3h

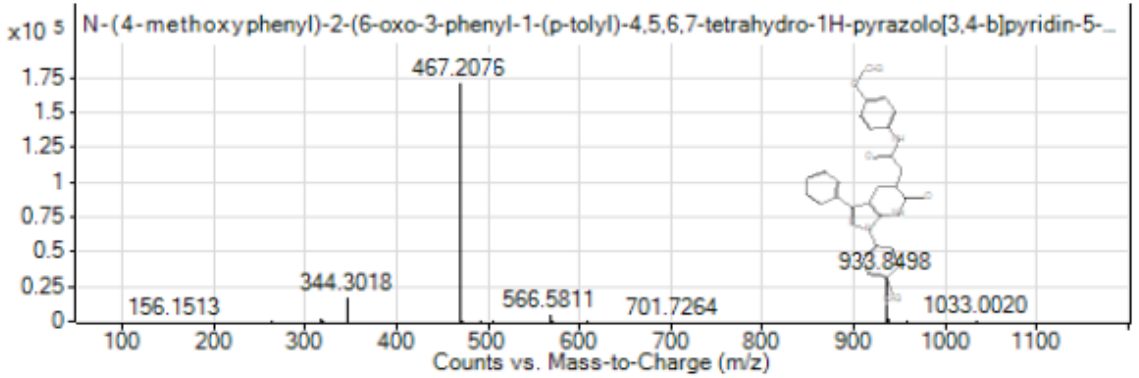
User Chromatograms



Integration Peak List

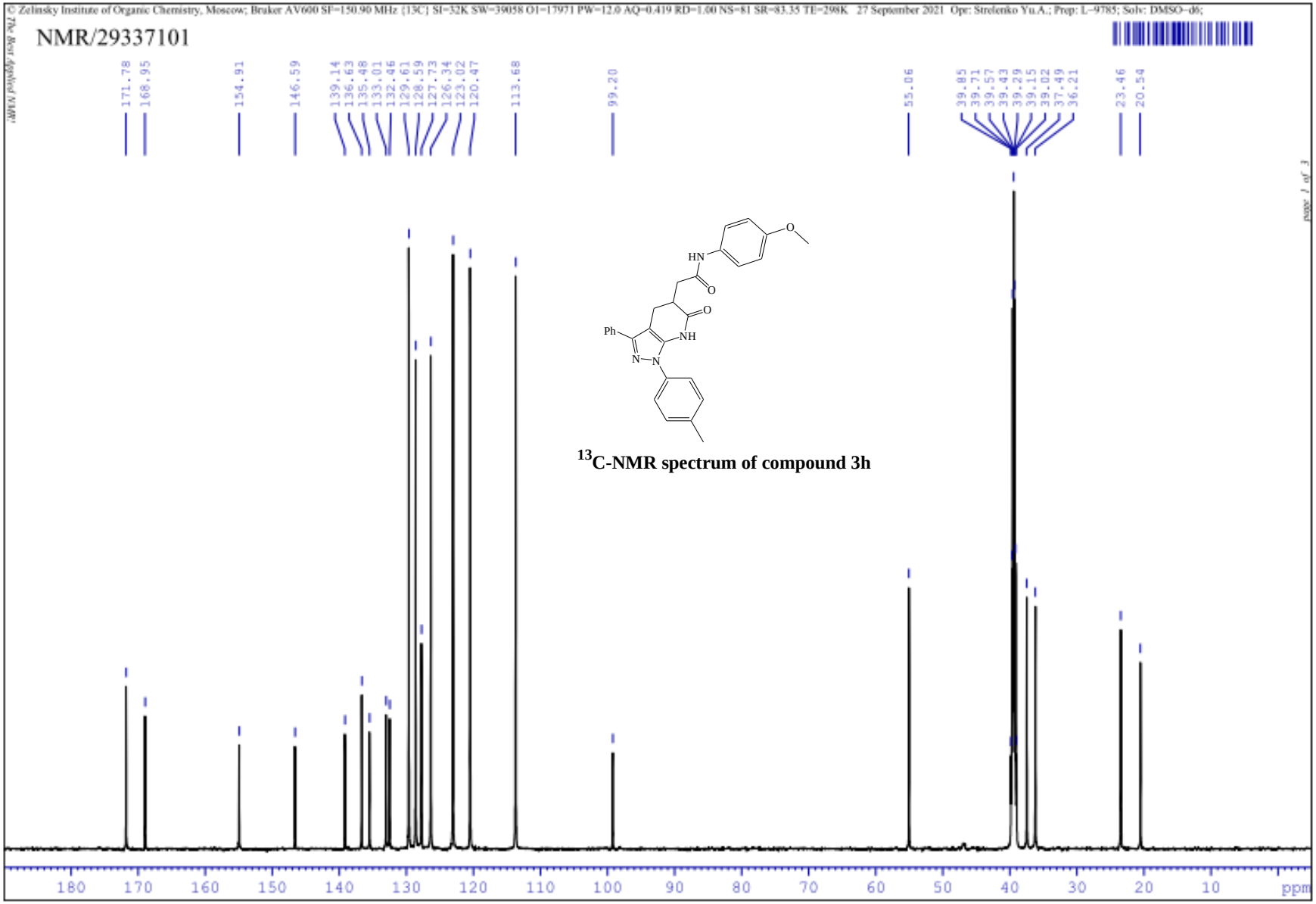
Peak	Start	RT	End	Height	Area	Area %
1	3,23	3,39	3,697	1048,97	7485,15	100

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

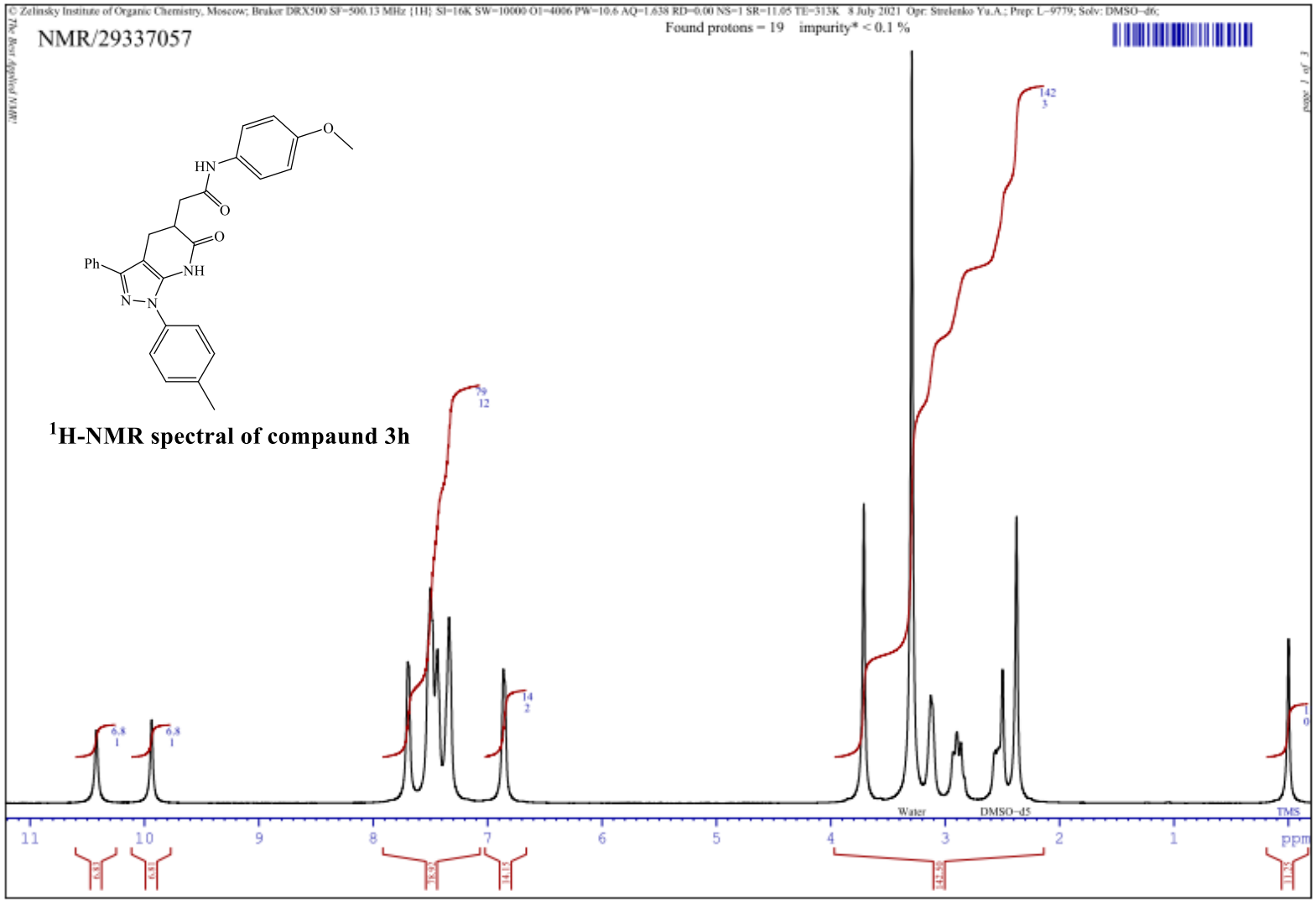


Peak List

m/z	z	Abund
316,2937	1	2882,97
344,3018	1	17158,65
345,3059	1	3996,81
467,2076	1	171969,92
468,4322	1	53052,46
469,4357	1	9066,41
566,5811	1	5565,62
933,8498	1	32823,9
934,854	1	21052,67
935,8571	1	7448,22



^{13}C-NMR spectrum of compound 3h



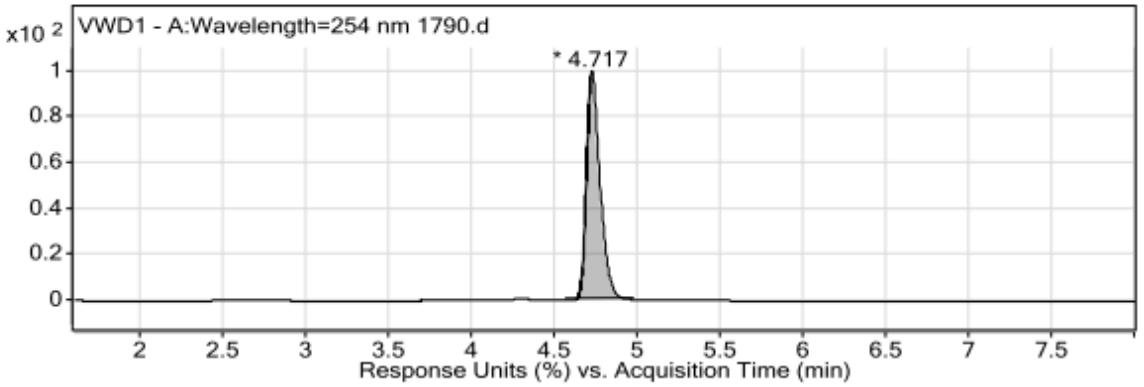
^{1}H-NMR spectral of compaund 3h

Qualitative Analysis Report

Data Filename	1790.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 33
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	7/14/2021 3:07:28 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

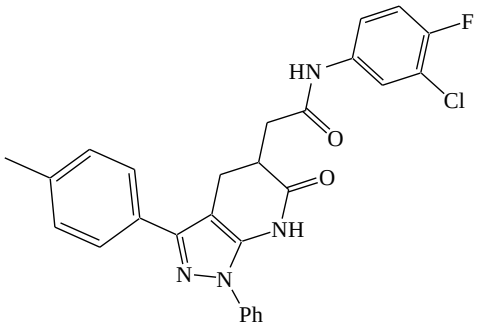
Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)

User Chromatograms



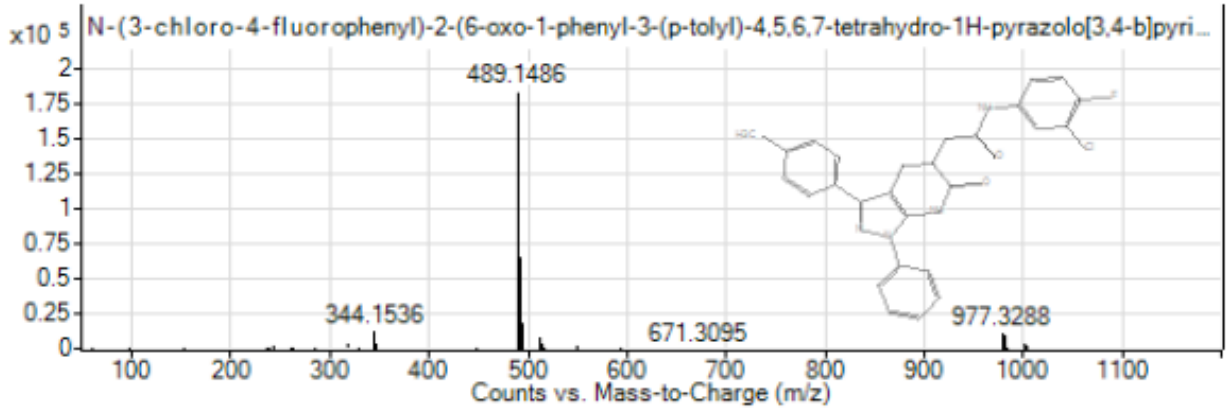
Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	4,563	4,717	4,98	1437,29	8163,49	100



LCMS spectrum of compound 3i

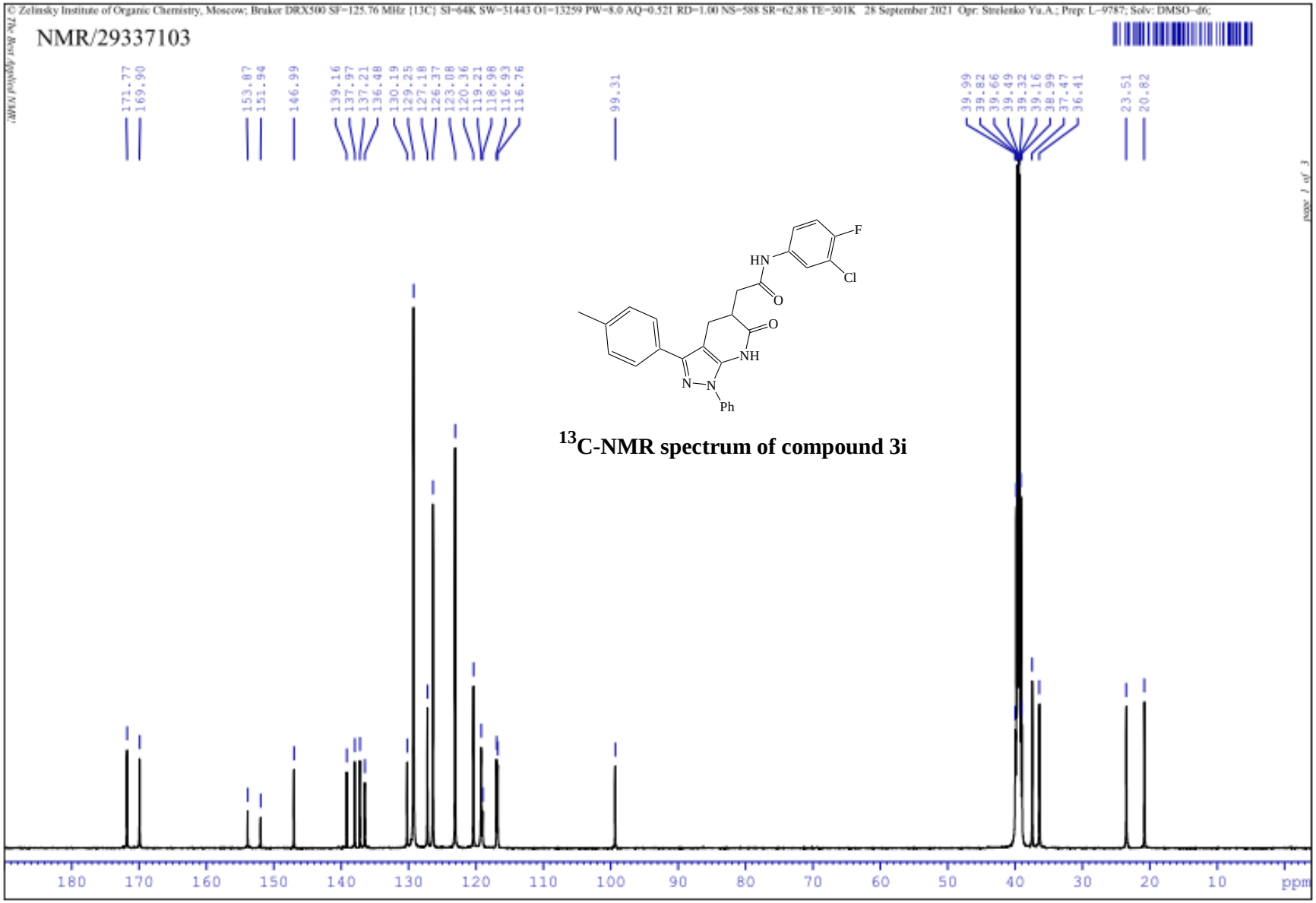
Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI



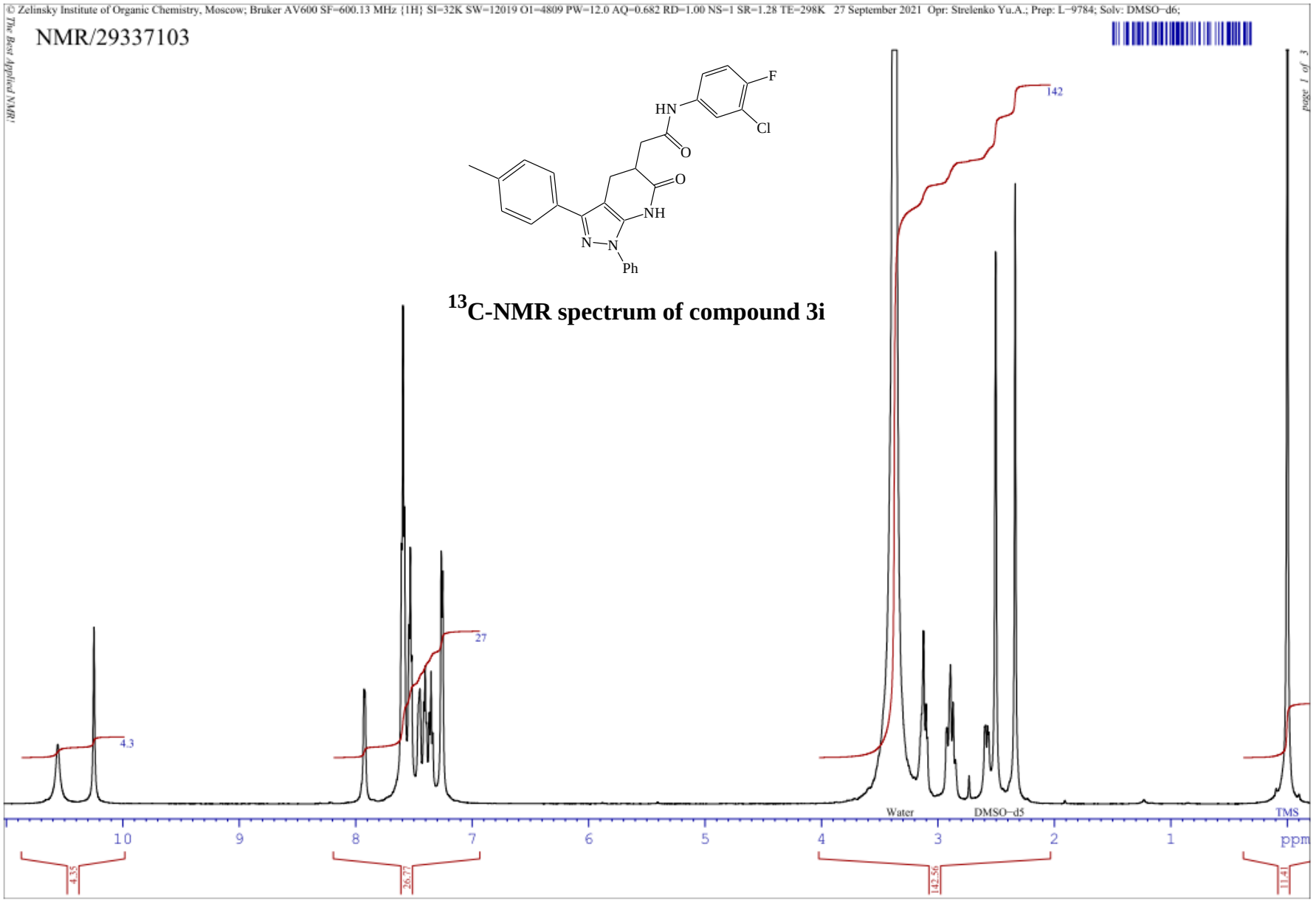
Peak List

m/z	z	Abund
344,1536	1	13079,73
489,1486	1	184877,91
490,1718	1	55792,55
491,1666	1	65792,99
492,1689	1	19139,6
511,1514	1	8823,5
977,3288	1	11314,88
978,3304	1	7312,02
979,3267	1	9857,19
980,3283	1	5173,73

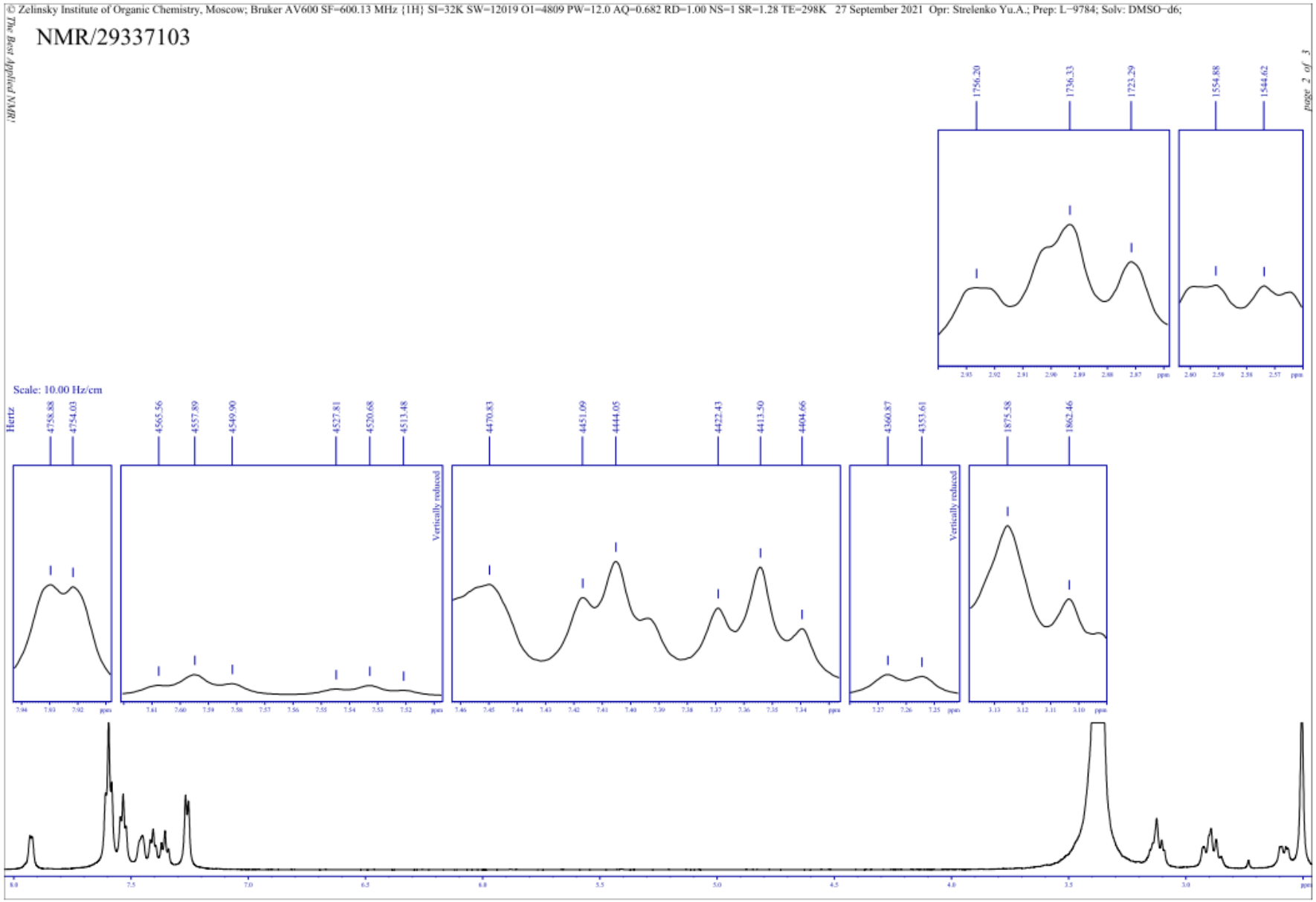
LCMS 3i



^{13}C-NMR spectrum of compound 3i



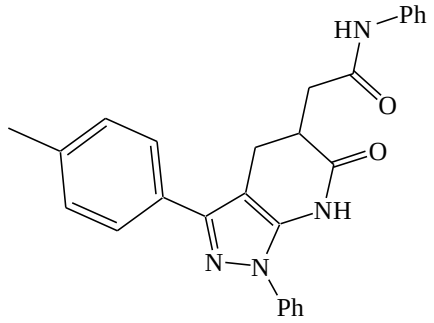
^{13}C-NMR spectrum of compound 3i


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H} SI=32K SW=12019 O1=4809 PW=12.0 AQ=0.682 RD=1.00 NS=1 SR=1.28 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9784; Solv: DMSO−d6;
NMR/29337103
The Best Applied NMR
page 2 of 3
1756.20
1736.33
1723.29
1554.88
1544.62
Scale: 10.00 Hz/cm
Hertz
4758.88
4754.03
4565.56
4557.89
4549.90
4527.81
4520.68
4513.48
4470.83
4451.09
4444.05
4422.43
4413.50
4404.66
4360.87
4353.61
1875.58
1862.46
Vertically reduced
Vertically reduced

Qualitative Analysis Report

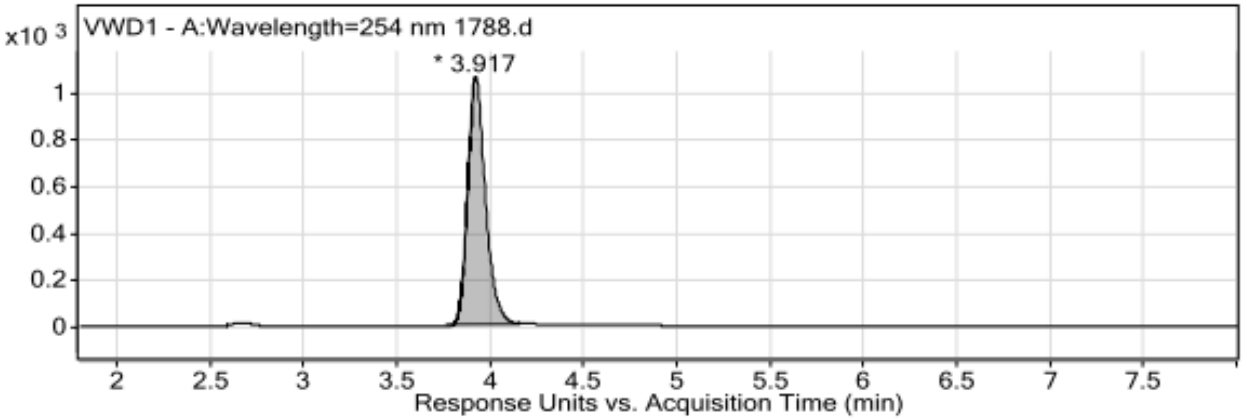
Data Filename	1788.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 31
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	7/14/2021 2:41:27 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



LCMS spectrum of compound 3j

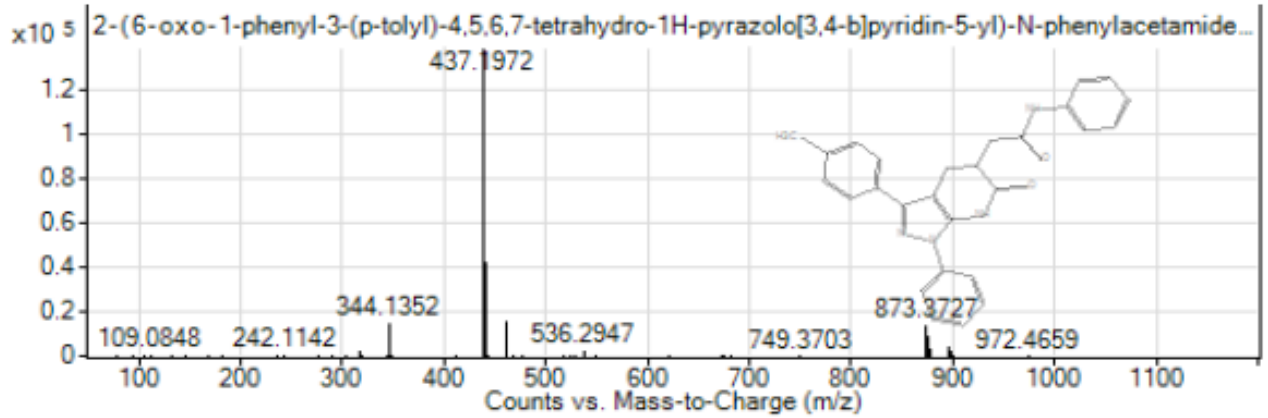
User Chromatograms



Integration Peak List

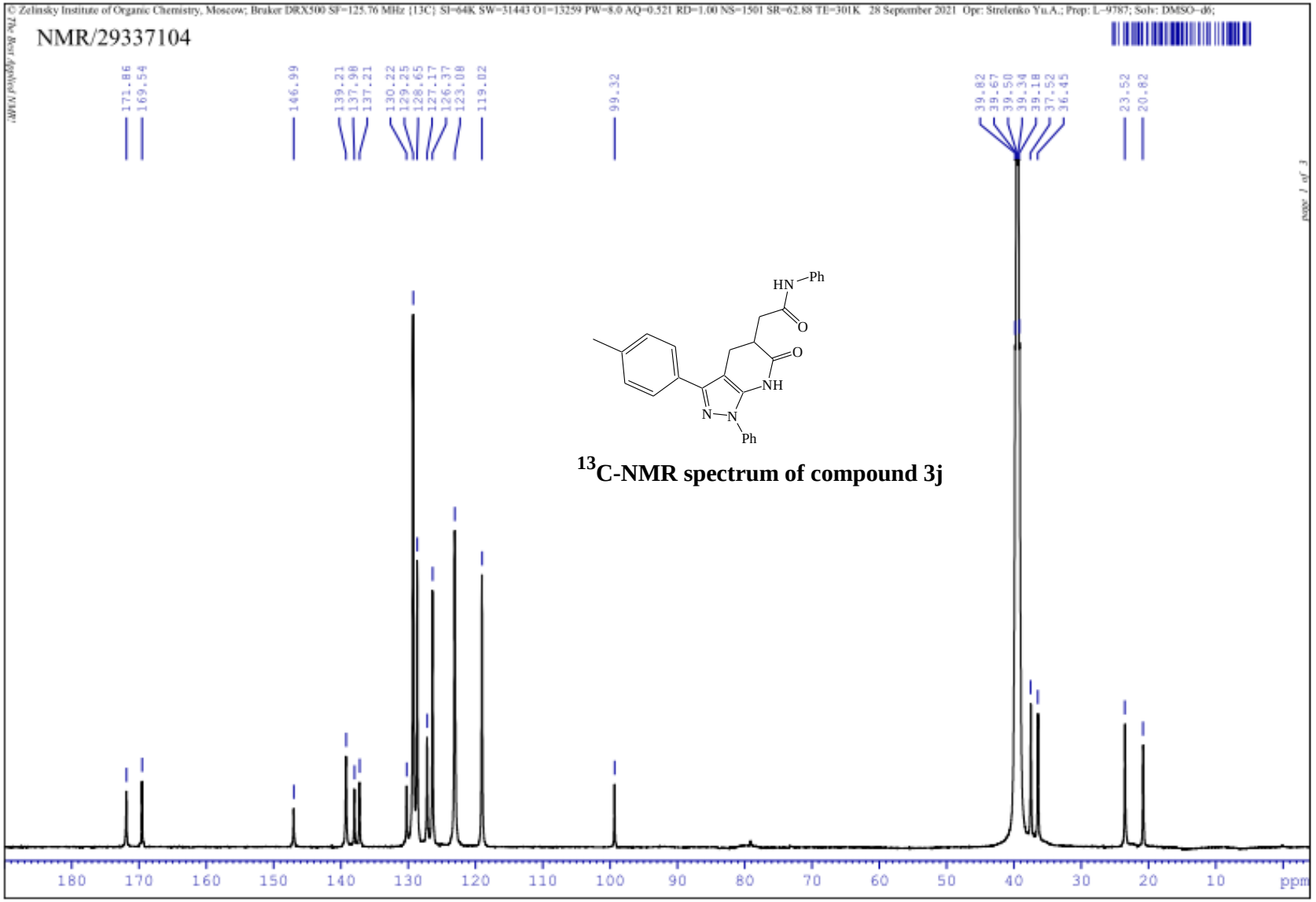
Peak	Start	RT	End	Height	Area	Area %
1	3,763	3,917	4,157	1061,32	7112,32	100

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

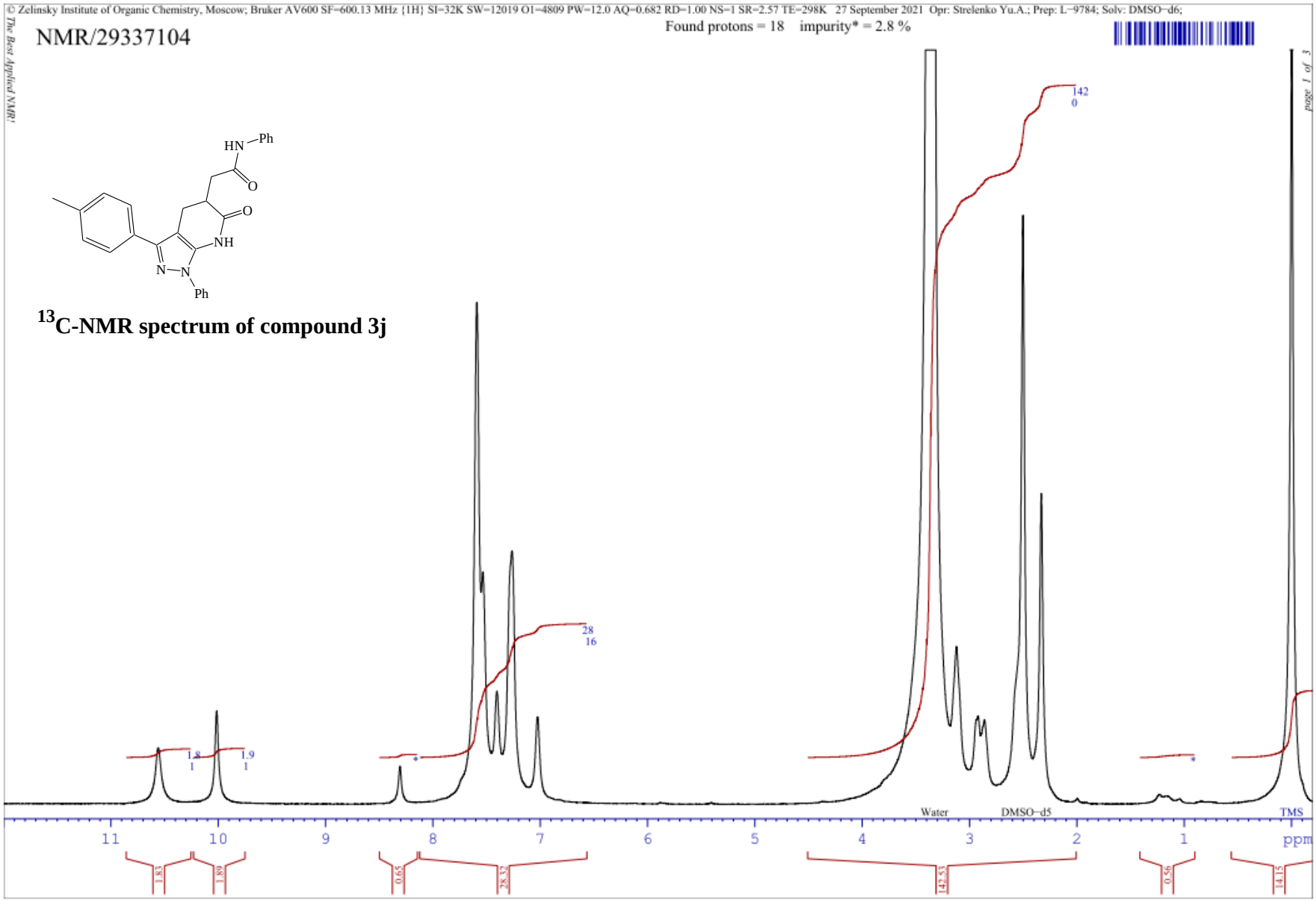


Peak List

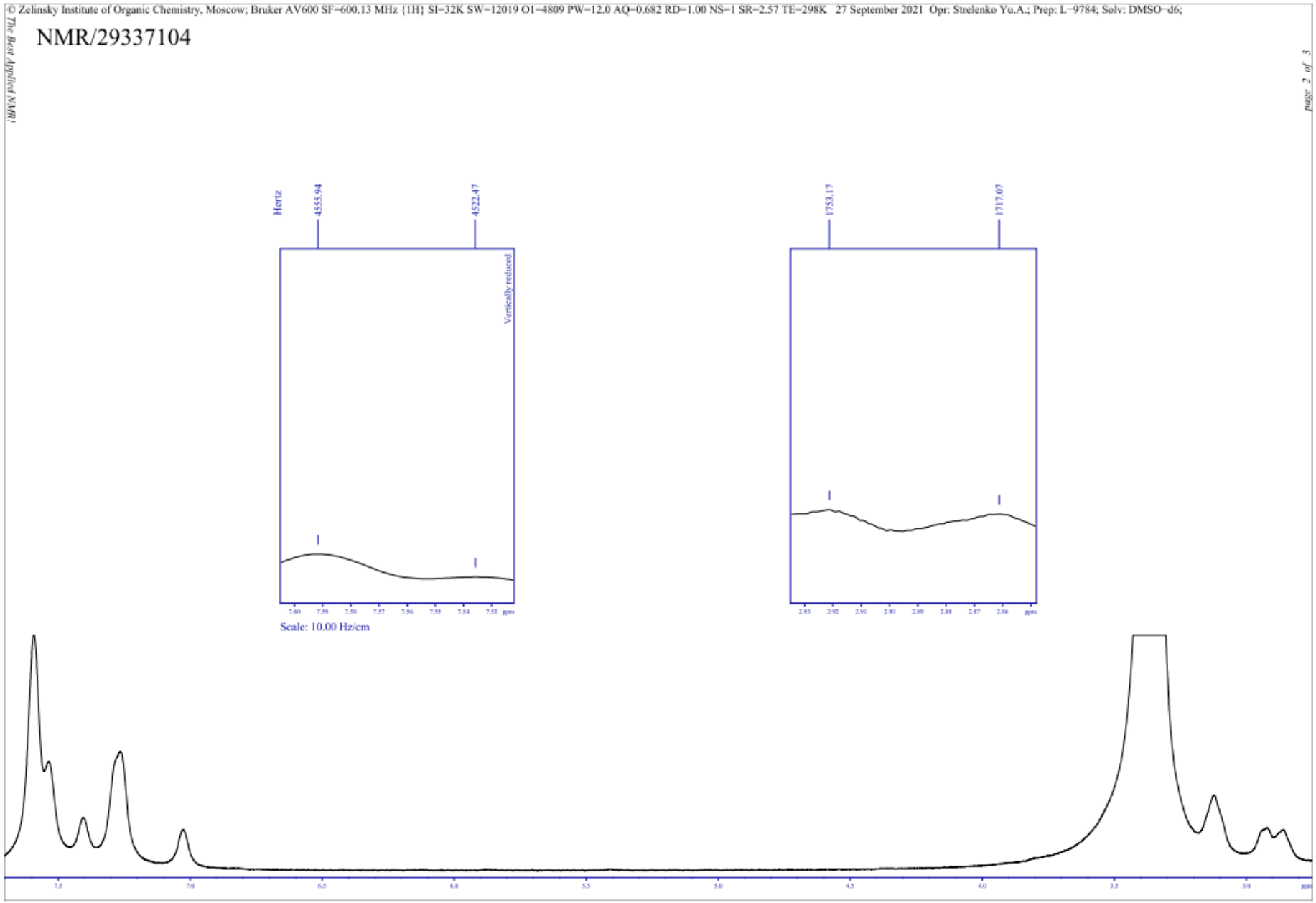
m/z	z	Abund
344,1352	1	15284,29
345,1385	1	4208,39
437,1972	1	138499,69
438,1935	1	42823,87
439,1958	1	6846,86
459,1729	1	15814,7
460,1768	1	4972,42
873,3727	1	14591,69
874,3756	1	9331,35
895,3541	1	4023,48



^{13}C-NMR spectrum of compound 3j



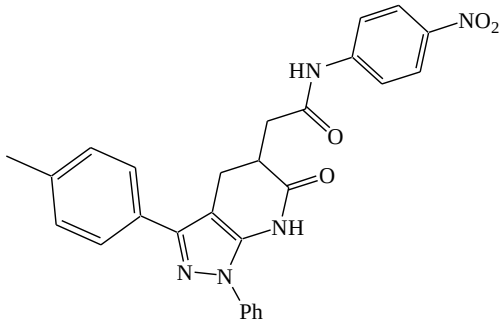
^{13}C-NMR spectrum of compound 3j


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H} SI=32K SW=12019 O1=4809 PW=12.0 AQ=0.682 RD=1.00 NS=1 SR=2.57 TE=298K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9784; Solv: DMSO−d6;
NMR/29337104
The Best Applied NMR!
page 2 of 3
Hertz
4555.94
4522.47
Vertically reduced
1753.17
1717.07
Scale: 10.00 Hz/cm

Qualitative Analysis Report

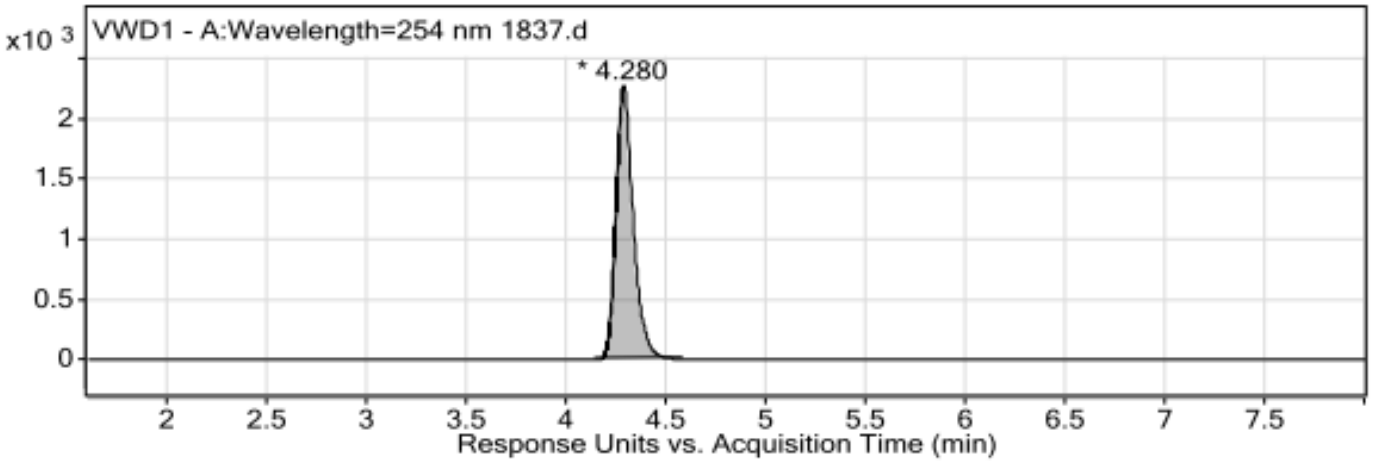
Data Filename	1837.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 13
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	7/20/2021 12:38:05 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



LCMS spectrum of compound 3k

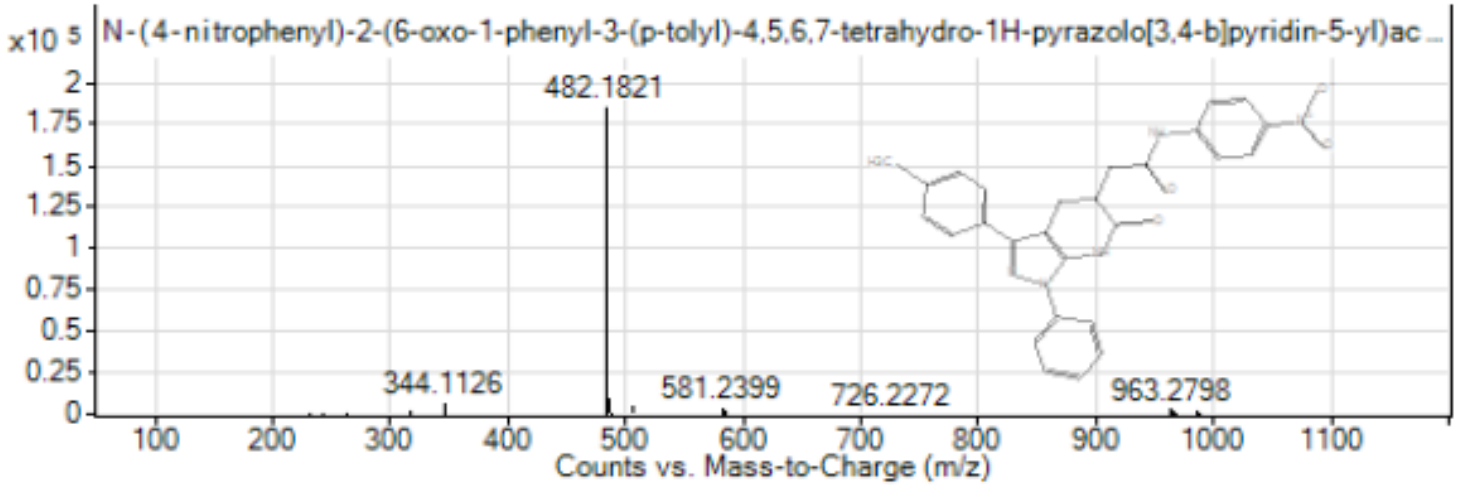
User Chromatograms



Integration Peak List

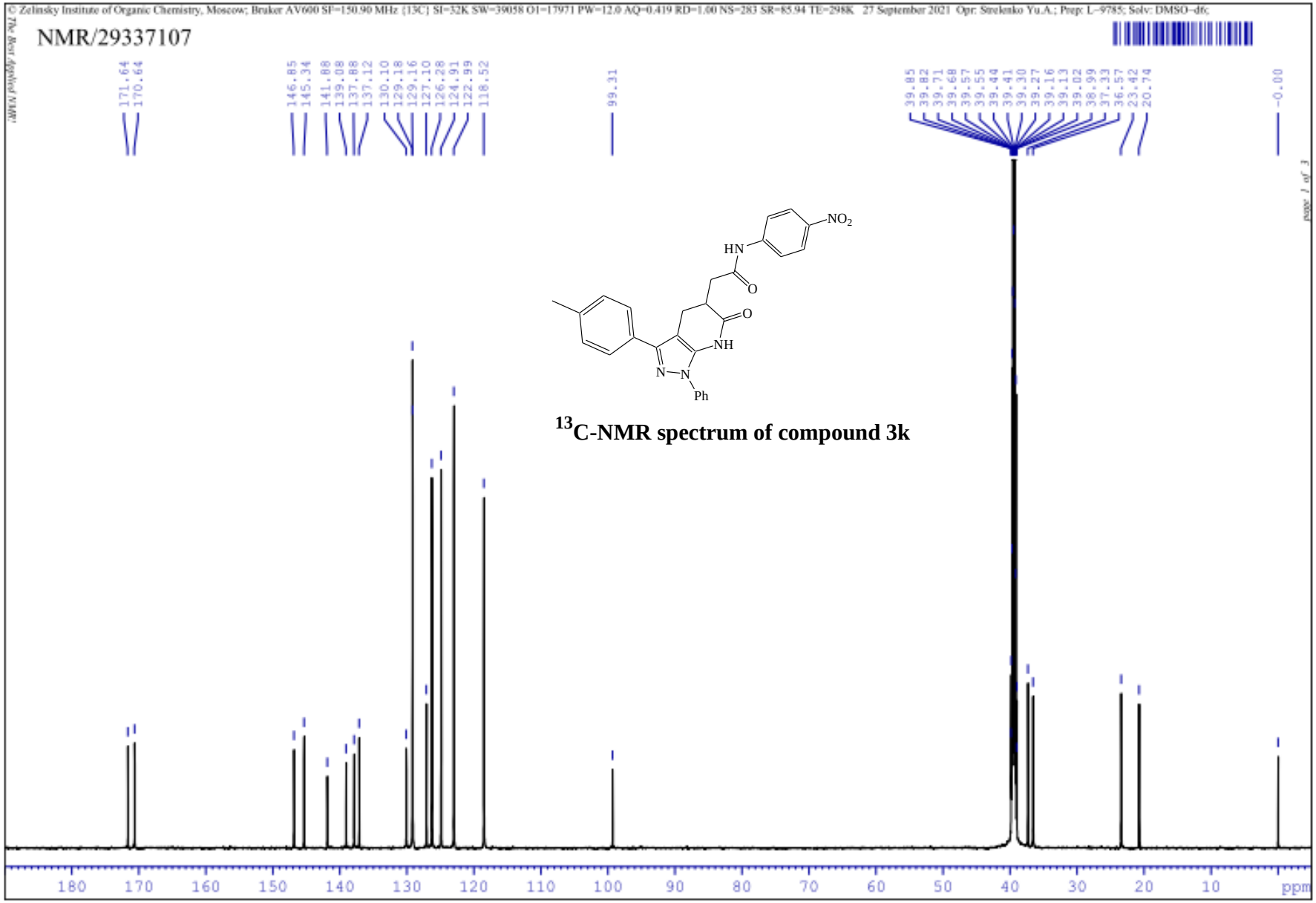
Peak	Start	RT	End	Height	Area	Area %
1	4,14	4,28	4,583	2276,65	13682,13	100

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

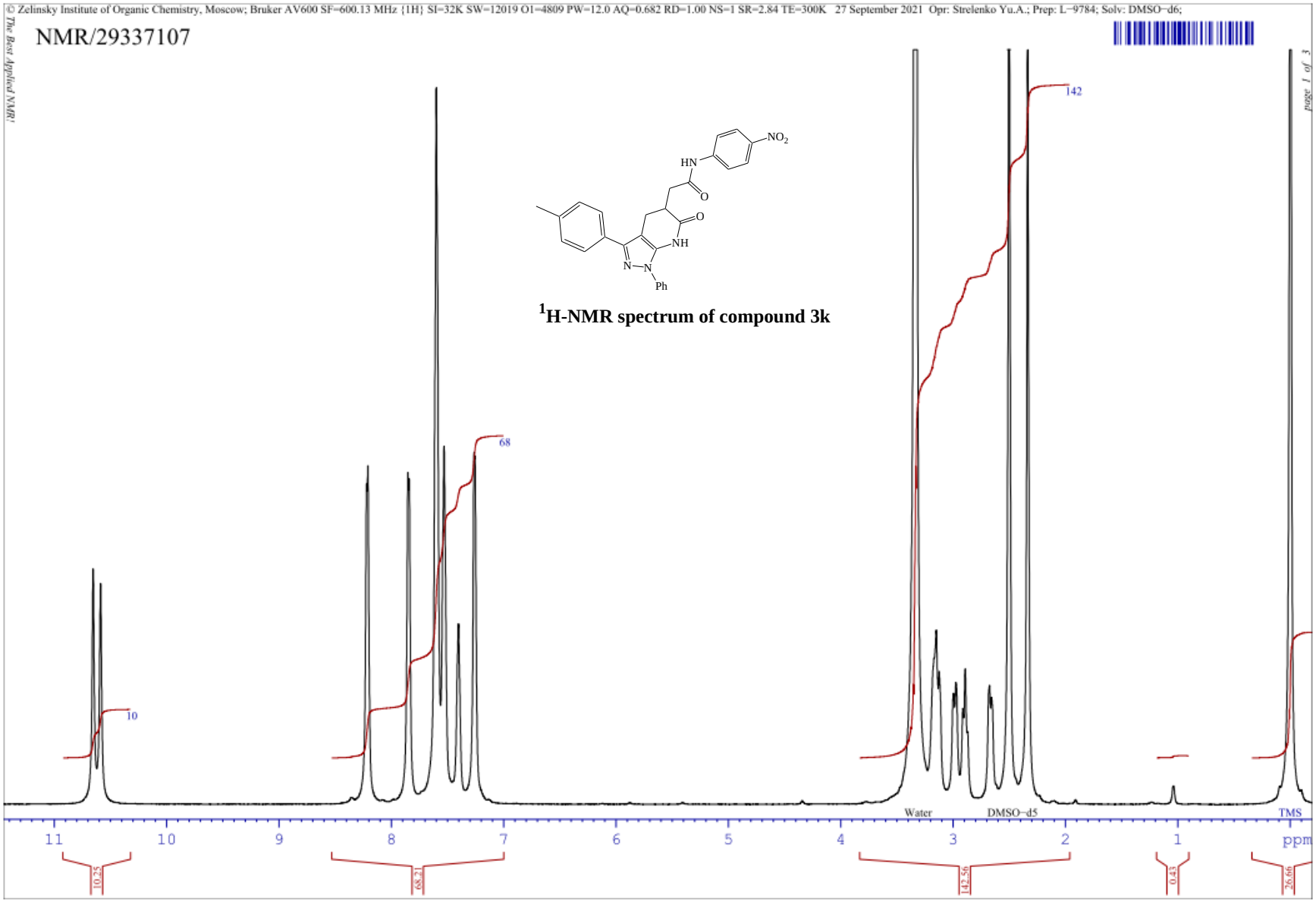


Peak List

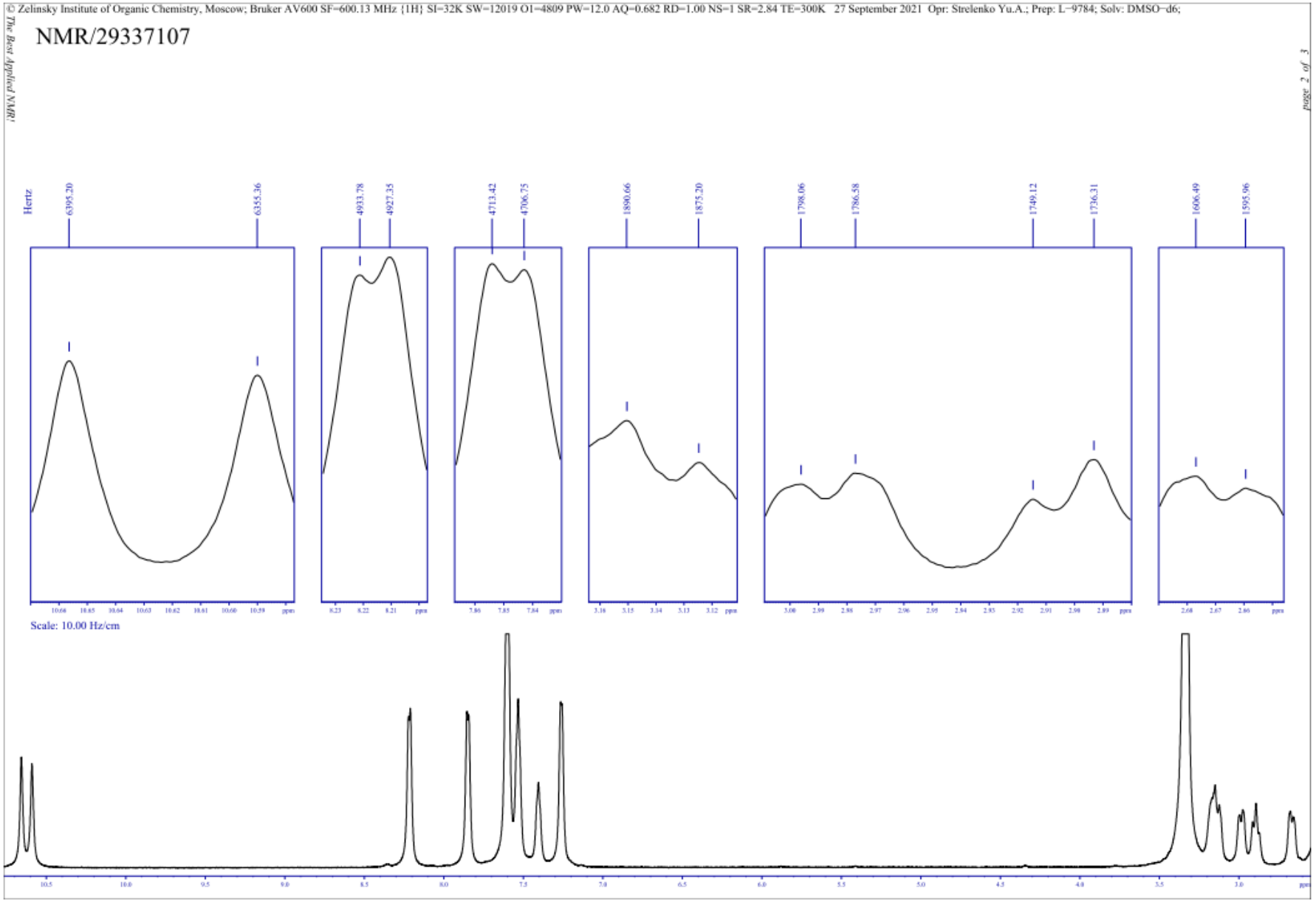
m/z	z	Abund
316,1206	1	2261,46
344,1126	1	8031,42
482,1821	1	185616,97
483,1473	1	57403,89
484,1498	1	10389,05
504,1243	1	4233,63
581,2399	1	4942,11
963,2798	1	3410,86
964,2845	1	2236,6
985,2624	1	2453,66



^{13}C-NMR spectrum of compound 3k



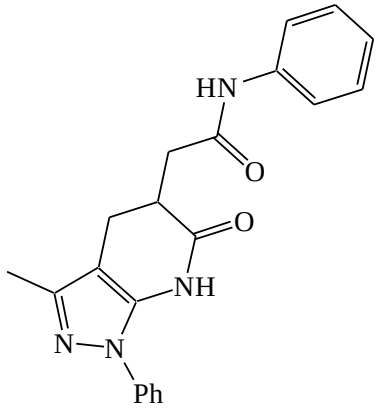
^{1}H-NMR spectrum of compound 3k


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker AV600 SF=600.13 MHz {1H} SI=32K SW=12019 O1=4809 PW=12.0 AQ=0.682 RD=1.00 NS=1 SR=2.84 TE=300K 27 September 2021 Opr: Strelenko Yu.A.; Prep: L−9784; Solv: DMSO−d6;
NMR/29337107
The Best Applied NMR
page 2 of 3
Hertz
6395.20
6355.36
4933.78
4927.35
4713.42
4706.75
1890.66
1875.20
1798.06
1786.58
1749.12
1736.31
1606.49
1595.96
Scale: 10.00 Hz/cm

Qualitative Analysis Report

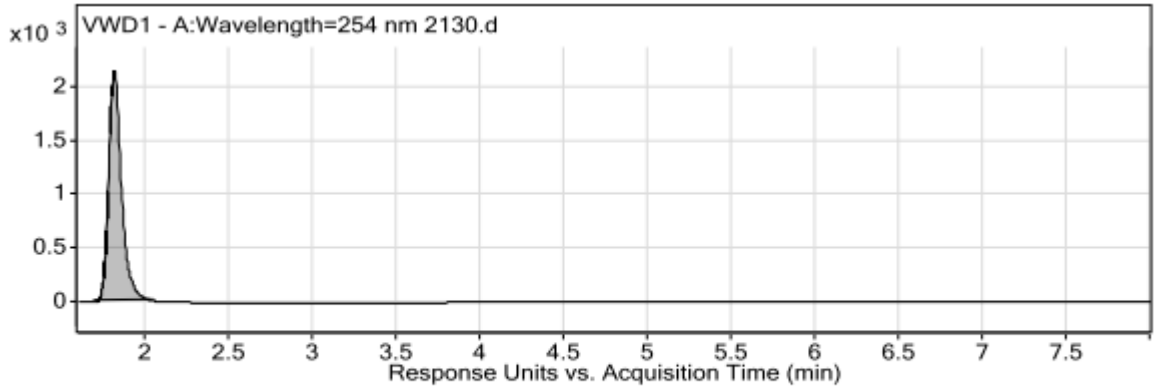
Data Filename	2130.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 91
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	11/25/2021 4:22:09 PM
IRM Calibration Status	Success	**DA Method**	111.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6172 SP1)



User Chromatograms

LCMS spectrum of compound 3l

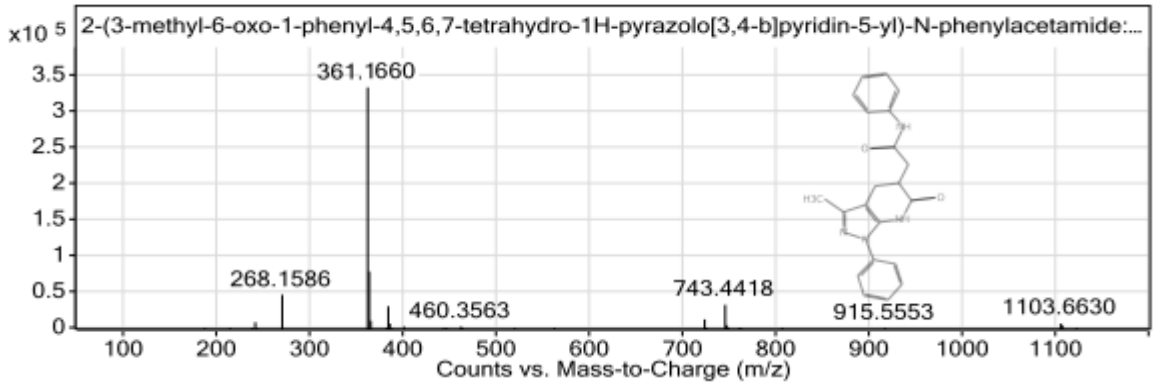


Integration Peak List

Peak	Start	RT	End	Height	Area	Area %
1	1.69	1.813	2.05	2140.17	11489.25	100

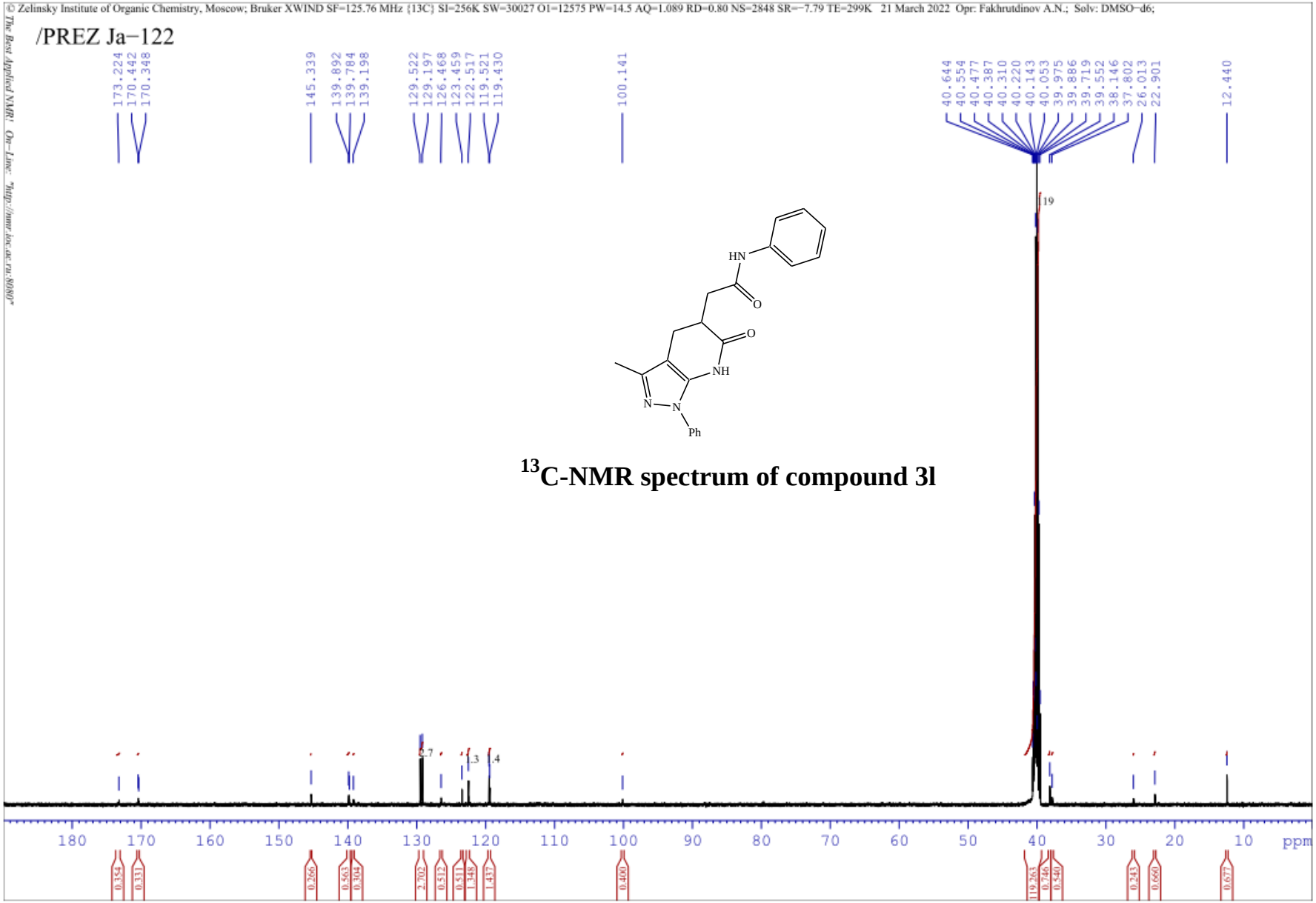
User Spectra

Fragmentor Voltage	Collision Energy	Ionization Mode
191	0	ESI

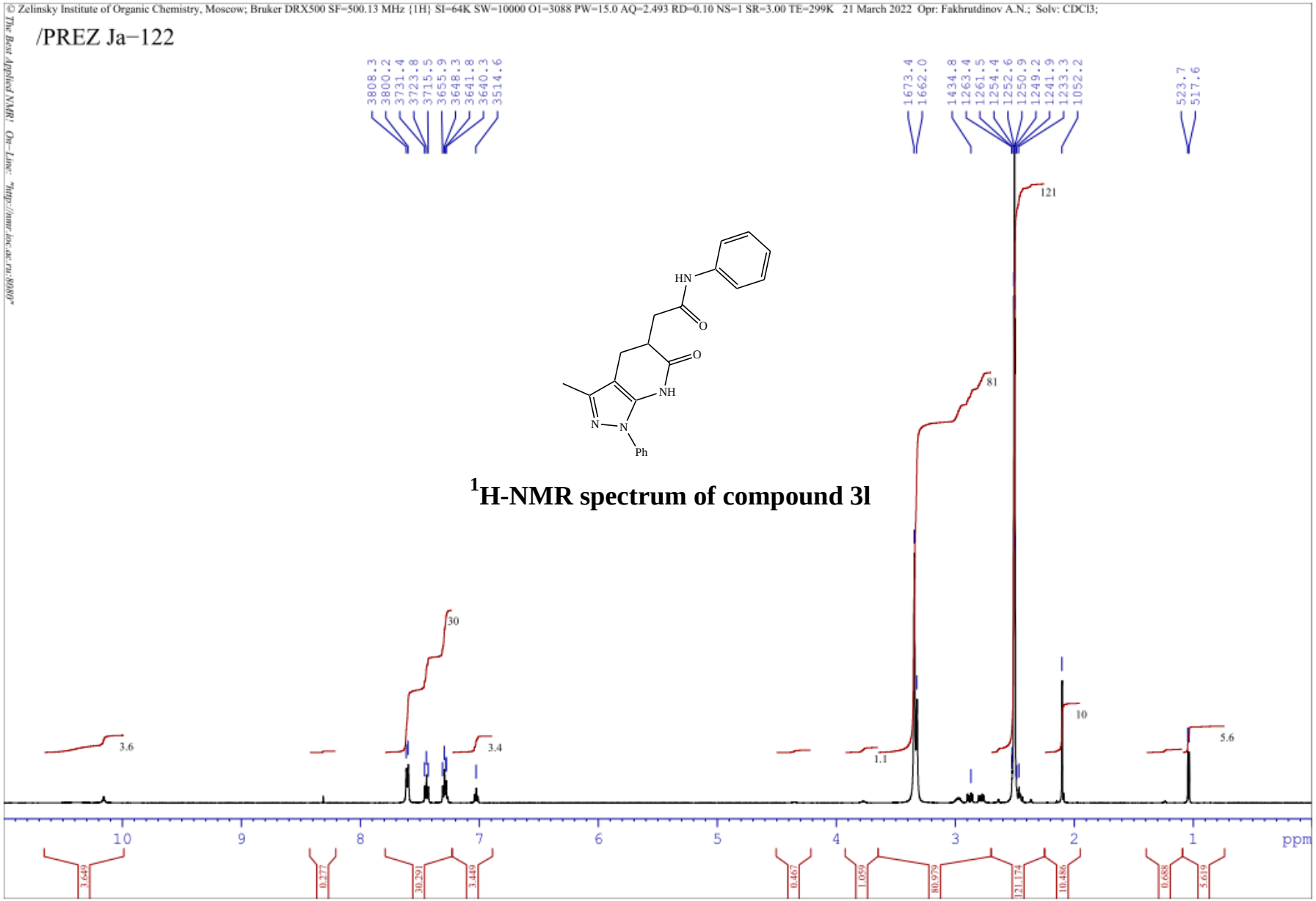


Peak List

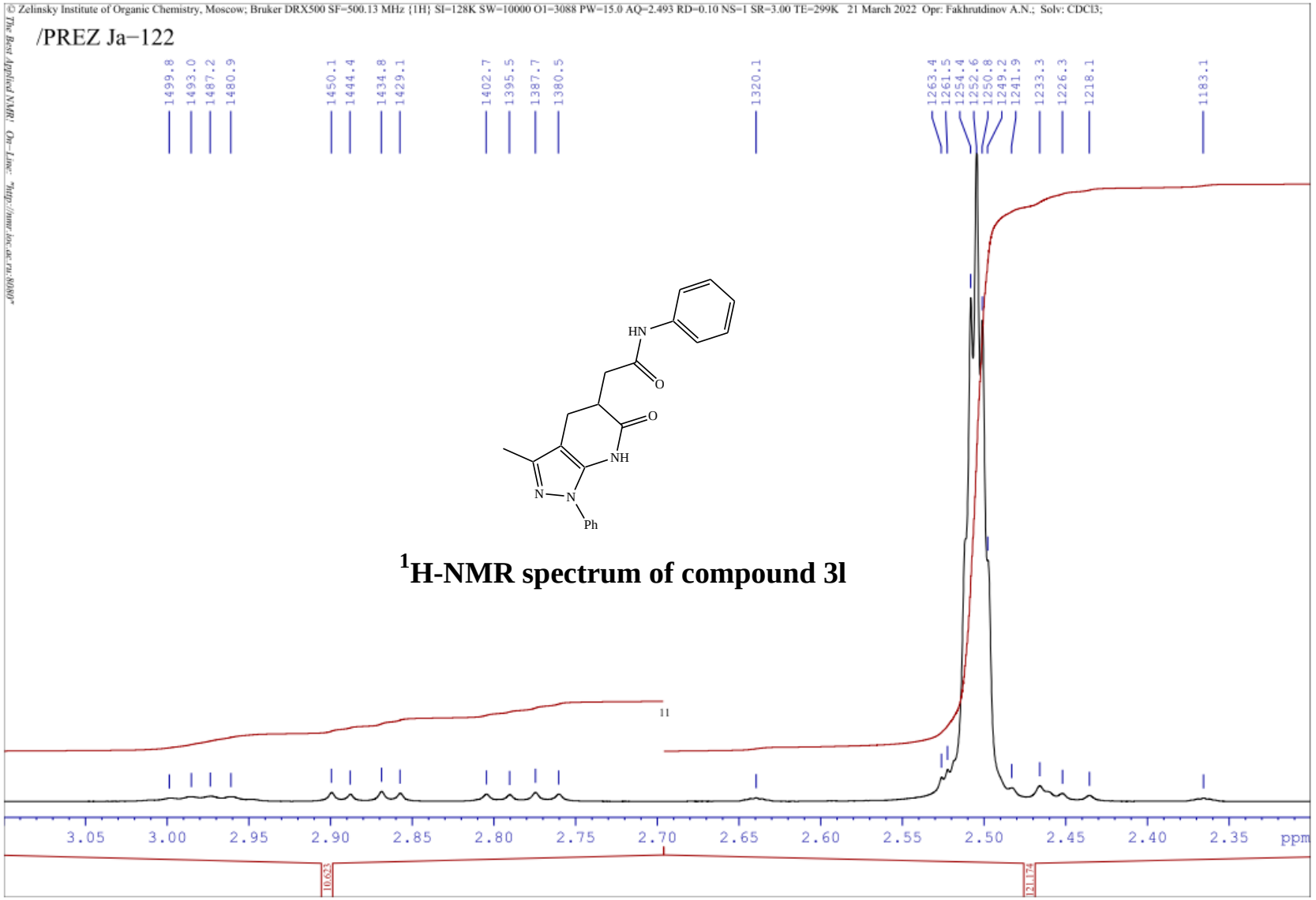
m/z	z	Abund
240.1588	1	9152.57
268.1586	1	47275.59
361.1660	1	334865.94
362.2365	1	79458.05
363.2386	1	11070.13
383.2194	1	32310.91



^{13}C-NMR spectrum of compound 3l



^{1}H-NMR spectrum of compound 3l



^{1}H-NMR spectrum of compound 3l