Electronic supplementary materials *Mendeleev Commun.*, 2021, **31**, 254–256

Synthesis of new tetrahydropyrido[1,2-*a*]benzimidazoles based on recyclization of *N*-arylitaconimides with 2-cyanomethylenebenzimidazole

Yana Yu. Shmoylova, Yuri A. Kovygin, Irina V. Ledenyova, Mikhail A. Prezent, Sergey V. Baranin and Khidmet S. Shikhaliev

Materials and Methods

Instrumentation

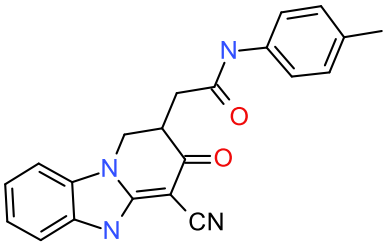
NMR ^{1}H and ^{13}C spectra were registered on Bruker DRX500 (500 and 150.9 MHz, respectively), spectrometer in DMSO-d_6, internal standard is TMS. Melting points were determined on Stuart SMP 30. Control of reagent and products individuality, qualitative analysis of reaction mass was performed by TLC on Merck TLC Silica gel 60 F254 chromatographic plate; eluents: methanol, chloroform and their mixtures in various rations. The chromatograms were developed by UV and 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, 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-C_{18} column (4.6 × 50 mm; 2.7 μm) was used. Gradient elution: acetonitrile/water (0.1% formic acid); flow rate 0.4 ml/min. Software for processing research results - MassHunter Workstation/Data Acquisition V.06.00.

Experimental

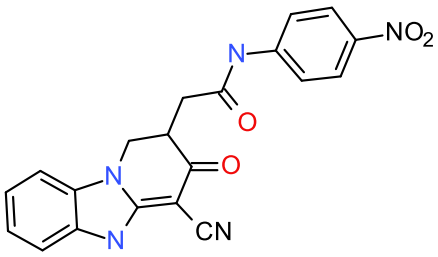
Synthesis of *N*-aryl-2-(4-cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)acetamides 3a-j (*general procedure***):** A solution of substituted itaconimide (0.005 mol) and of 2-cyanomethylbenzimidazole (0.005 mol) in acetic acid (5 ml) was refluxed for 1-2 hours. The crystals formed were filtered off and dried.

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(4-methylphenyl)-acetamide 3a. Yield 0.73 g (41%), white crystals, mp. 314-315 °C**.**



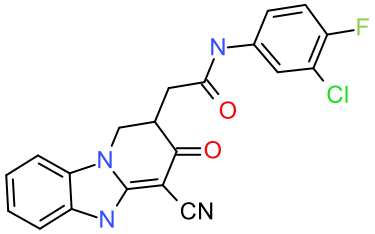
^{1}H NMR, (δ, ppm, *J*, Hz): 12.99 (br s, 1H, NHCO), 9.94 (s, 1H, NH), 7.08-7.51 (m, 8H, Ar-H), 4.55 (dd, *J* 6.6, 12.7 Hz, 1H, H^{1b}), 3.98 (t, *J* 11.8 Hz, 1H, H^{1a}), 3.11-3.17 (m, 1H, CH^{2}), 2.89-2.93 (dd, *J* 4.6, 15.9 Hz, 1H, $CH_{2b}CO$), 2.41 (dd, 1H, $CH_{2a}CO$, *J* 8.3, 15.8 Hz), 2.24 (s, 3H, CH_3). ^{13}C NMR (δ, ppm): 186.4 (C-3), 169.0 (C=O, amide), 152.7 (C-4a), 136.6 (C-1 Ar), 131.8 (C-4 Ar), 131.6 (C-5a), 131.2 (C-9a), 128.9 (C-2,6 Ar), 123.1 (C-9), 123.0 (C-6), 119.0 (C-3,5 Ar), 117.6 (CN), 111.3 (C-8), 109.6 (C-7), 64.4 (C-4), 43.6 (C-1), 34.4 (CH_2-*exo*), 20.3 (CH_3). HRMS (ESI), m/z: 359.1503 $[M+H]^+$. (calc. for $C_{21}H_{18}N_4O_2$, *m/z*: 359.1503).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(4-nitrophenyl)acetamide 3b. Yield 0.78 g (40%), white crystals, mp. 318-319 °C.



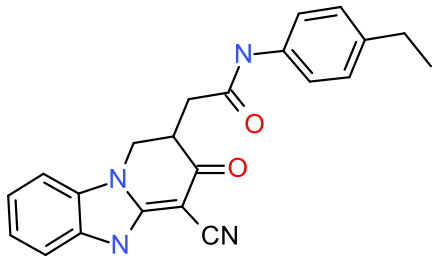
^{1}H NMR, (δ, ppm, *J*, Hz): 13.02 (br s, 1H, NHCO), 10.67 (s, 1H, NH), 7.21-8.23 (m, 8H, H-Ar), 4.61 (dd, *J* 6.7, 12.6 Hz, 1H, H^{3b}), 3.99 (t, *J* 12.3 Hz, 1H, H^{3a}), 3.28-3.23 (m, 1H, H^{2}), 2.98 (dd, *J* 5.2, 16.0 Hz, 1H, $CH_{2b}CO$), 2.41 (dd, 1H, $CH^{2a}CO$, *J* 8.3 Hz, 15.8 Hz). ^{13}C NMR (δ, ppm): 186.1 (C-3), 170.4 (C=O amide), 152.6 (C-4a), 145.3 (C-4 Ar), 141.9 (C-1 Ar), 131.6 (C-5a), 131.1 (C-9a), 124.9 (C-2,6 Ar), 123.1 (C-9), 123.0 (C-6), 118.6 (C-3,5 Ar), 117.5 (CN), 111.3 (C-8), 109.6 (C-7), 64.4 (C-4), 43.5 (C-1), 39.3 (C-2), 34.4 (CH_2-*exo*). HRMS (ESI), m/z: 390.1195 $[M+H]^+$. (calc. for $C_{20}H_{15}N_5O_4$, *m/z*: 390.1197).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(4-fluoro-3-chlorophenyl)acetamide 3c. Yield 0.93 d (47%) white crystals, mp. 320-321 °C.



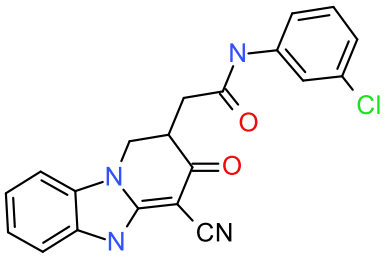
^{1}H NMR, (δ, ppm, *J*, Hz): 13.00 (br s, 1H, NHCO), 10.26 (s, 1H, NH), 7.24-7.96 (m, 7H, H-Ar), 4.58 (dd, *J* 6.5, 12.6 Hz, 1H, H^{3b}), 3.98 (t, *J* 12.3 Hz, 1H, H^{3a}), 3.15-3.19 (m, 1H, CH^{2}), 2.92 (dd, *J* 4.7, 15.8 Hz, 1H, $CH_{2b}CO$), 2,43 (dd, *J* 7.9, 15.8 Hz, 1H, $CH_{2a}CO$). ^{13}C NMR (δ, ppm): 186.8 (C-3), 170.4 (C=O amide), 153.6 (C-4a), 153.2 (C-4 Ar), 137.4 (C-1 Ar), 132.3 (C-3 Ar), 131.8 (C-5a), 128.3 (C-9a), 127.0 (C-2 Ar), 126.2 (C-5 Ar), 125.2 (C-6 Ar), 123.6 (C-9), 123.5 (C-6), 118.0 (CN), 110.1 (C-8), 109.9 (C-7), 65.0 (C-4), 44.0 (C-1), 39.3 (C-2), 34.7 (CH_2-*exo*). HRMS (ESI), m/z: 397.0863 $[M+H]^+$. (calc. for $C_{20}H_{14}CLFN_4O_2$, *m/z*: 397.0863).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(4-ethylphenyl)-acetamide 3d. Yield 0.78 g (42%) white crystals, mp. 311-312 °C.



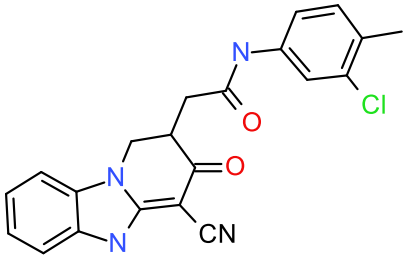
^{1}H NMR, (δ, ppm, *J*, Hz): 13.00 (br s, 1H, NHCO), 9.96 (s, 1H, NH), 7.13-7.50 (m, 8H, H-Ar), 4.55 (dd, *J* 6.6, 12.6 Hz, 1H, H^{3b}); 3.99 (t, *J* 12.3 Hz, 1H, H^{3a}), 3.12-3.18 (m, 1H, H^{2}), 2.92 (dd, *J* 4.5, 15.7 Hz, 1H, $CH_{2b}CO$), 2.55 (q, *J* 7.6, 2H, CH_2CH_3), 2.41 (dd, *J* 8.3, 15.7 Hz, 1H, $CH_{2a}CO$), 1.15 (t, *J* 7.5 Hz, 3H, CH_2CH_3). ^{13}C NMR (δ, ppm): 186.3 (C-3), 169.0 (C=O amide), 152.7 (C-4a), 138.3 (C-1 Ar), 136.8 (C-4 Ar), 131.6 (C-5a), 131.2 (C-9a), 127.7 (C-2,6 Ar), 123.1 (C-9), 123.0 (C-6), 119.1 (C-3,5 Ar), 117.5 (CN), 111.4 (C-8), 109.5 (C-7), 43.6 (C-1), 39.3 (C-2), 34.4 (CH_2-*exo*), 27.5 (CH_2CH_3), 15.6 (CH_3). HRMS (ESI), m/z: 373.1667 $[M+H]^+$. (calc. for $C_{22}H_{20}N_4O_2$, *m/z*: 373.1665).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(3-chlorophenyl)-acetamide 3e. Yield 0.92 g (49%), white crystals, mp. 320-321 °C.



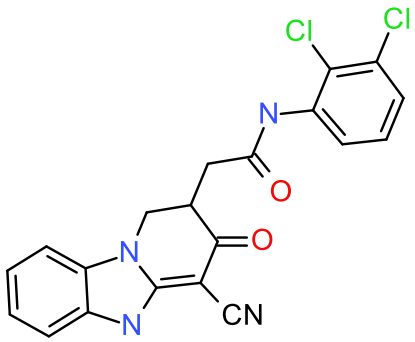
^{1}H NMR, (δ, ppm, *J*, Hz): 12.96 (s, 1H, NHCO), 10.19 (s, 1H, NH), 7.06-7.82 (m, 8H, H-Ar), 4.56 (dd, *J* 6.7, 12.6 Hz, 1H, H^{3b}), 3.97 (t, *J* 12.0 Hz, 1H, H^{3a}), 3.11-3.18 (m, 1H, CH^{2}), 2.92 (dd, *J* 4.8, 15.8 Hz, 1H, $CH_{2b}CO$), 2.43 (dd, *J* 8.0, 15.8 Hz, 1H, $CH_{2a}CO$). ^{13}C NMR (δ, ppm): 186.7 (C-3), 170.2 (C=O amide), 153.2 (C-4a), 141.1 (C-3 Ar), 133.5 (C-1 Ar), 132.2 (C-5a), 131.7 (C-9a), 130.8 (C-2 Ar), 123.6 (C-9), 123.5 (C-6 Ar), 123.2 (C-6), 119.1 (C-4 Ar), 118.0 (C-5 Ar), 117.9 (CN), 112.0 (C-8), 110.2 (C-7), 65.0 (C-4), 44.1 (C-1), 39.3 (C-2), 35.1 (CH_2-*exo*), HRMS (ESI), m/z: 379.0959 $[M+H]^+$. (calc. for $C_{20}H_{14}Cl_2N_4O_2$, *m/z*: 379.0957).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(3-chloro-4-methylphenyl)acetamide 3f. Yield 1.02 g (52%), white crystals, mp. 314-315 °C.



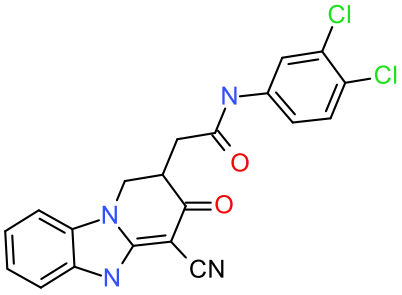
^{1}H NMR, (δ, ppm, *J*, Hz): 13.01 (br s, 1H, NHCO), 10.14 (s, 1H, NH), 7.23-7.83 (m, 7H, H-Ar), 4.57 (dd, *J* 6.6; 12.6 Hz, 1H, H^{3b}), 3.98 (t, *J* 12.1 Hz, 1H, H^{3a}), 3.12-3.18 (m, 1H, H^{2}), 2.92 (dd, *J* 4.7; 15.8 Hz, 1H, $CH_{2b}CO$), 2.42 (dd, *J* 8.1; 15.8 Hz, 1H, $CH_{2a}CO$), 2.27 (s, 3H, CH_3). ^{13}C NMR (δ, ppm): 186.2 (C-3), 169.4 (C=O amide), 152.7 (C-4a), 138.2 (C-1 Ar), 132.8 (C-3 Ar), 131.6 (C-5a), 131.2 (C-9a), 131.0 (C-2 Ar), 129.5 (C-6 Ar), 123.1 (C-9), 123.0 (C-6), 119.0 (C-5 Ar), 117.6 (C-4 Ar), 117.5 (CN), 111.3 (C-8), 109.6 (C-7), 64.4 (C-4), 43.6 (C-1), 39.3 (C-2), 34.4 (CH_2-*exo*), 18.9 (CH_3). HRMS (ESI), m/z: 393.1113 $[M+H]^+$. (calc. for $C_{21}H_{17}ClN_4O_2$, *m/z*: 393,1114).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(2,3-dichloro-phenyl)acetamide 3g. Yield 1.11 g (54%), white crystals, mp. 318-319 °C.



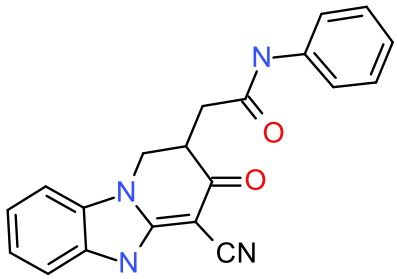
^{1}H NMR, (δ, ppm, *J*, Hz): 13.02 (br s, 1H, NHCO), 9.83 (s, 1H, NH); 7.23-7.76 (m, 7H, H-Ar), 4.56 (dd, *J* 6.5, 12.6 Hz, 1H, H^{3}), 3.99 (t, *J* 12.4 Hz, 1H, H^{3a}); 3.17 (m, 1H, H^{2}); 2.99 (dd, *J* 4.9, 15.7 Hz, 1H, $CH_{2b}CO$); 2.55 (dd, 1H, *J* 8.1 Hz, 15.6, $CH_{2a}CO$), (m, 1H, $CH_{2a}CO$). ^{13}C NMR (δ, ppm): 186.8 (C-3), 170.4 (C=O amide), 152.7 (C-4a), 137.4 (C-1 Ar), 135.2 (C-4 Ar), 132.2 (C-5a) , 131.8 (C-9a), 128.3 (C-2,3 Ar), 127.0 (C-6 Ar), 125.2 (C-5 Ar), 123.6 (C-9), 123.5 (C-6), 118.0 (C-3), 112.0 (C-8), 110.0 (C-7), 65.0 (C-4), 44.0 (C-1), 39.3 (C-2), 34.7 (CH_2-*exo*). HRMS (ESI), m/z: 413.0570 $[M+H]^+$. (calc. for $C_{20}H_{14}Cl_2N_4O_2$, *m/z*: 413.0567).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(3,4-dichloro-phenyl)acetamide 3h. Yield 1.19 g (58%), white crystals, mp. 316-317 °C.



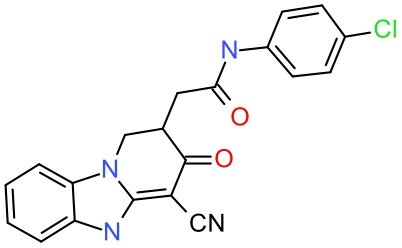
^{1}H NMR, (δ, ppm, *J*, Hz): 12.97 (br s, 1H, NHCO), 10.32 (s, 1H, NH), 7.24-8.00 (m, 7H, H-Ar), 4.56 (dd, *J* 6.7, 12.6 Hz, 1H, H^{3}), 3.96 (t, *J* 12.1 Hz, 1H, H^{3a}), 3.14-3.16 (m, 1H, H^{2}), 2.91 (dd, *J* 4.5, 15.9 Hz, 1H, $CH_{2b}CO$), 2.41 (m, 1H, $CH_{2a}CO$). ^{13}C NMR (δ, ppm): 186.6 (C-3), 170.4 (C=O amide), 156.7 (C-4a), 153.9 (C-1 Ar), 153.2 (C-4 Ar), 139.7 (C-3 Ar), 132.2 (C-6 Ar), 131.4 (C-5a), 131.0 (C-9a), 129.1 (C-2 Ar), 123.6 (C-9), 123.5 (C-6), 119.6 (C-5 Ar), 118.0 (CN), 111.9 (C-8), 110.2 (C-7), 65.0 (C-4), 44.1 (C-1), 39.3 (C-2), 35.1 (CH_2-*exo*). HRMS (ESI), m/z: 413,0567 $[M+H]^+$. (calc. for $C_{20}H_{14}Cl_2N_4O_2$, *m/z*: 413.0567).

2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-phenylacetamide 3i. Yield 0.91 g (53%), white crystals, mp. 314-315 °C.

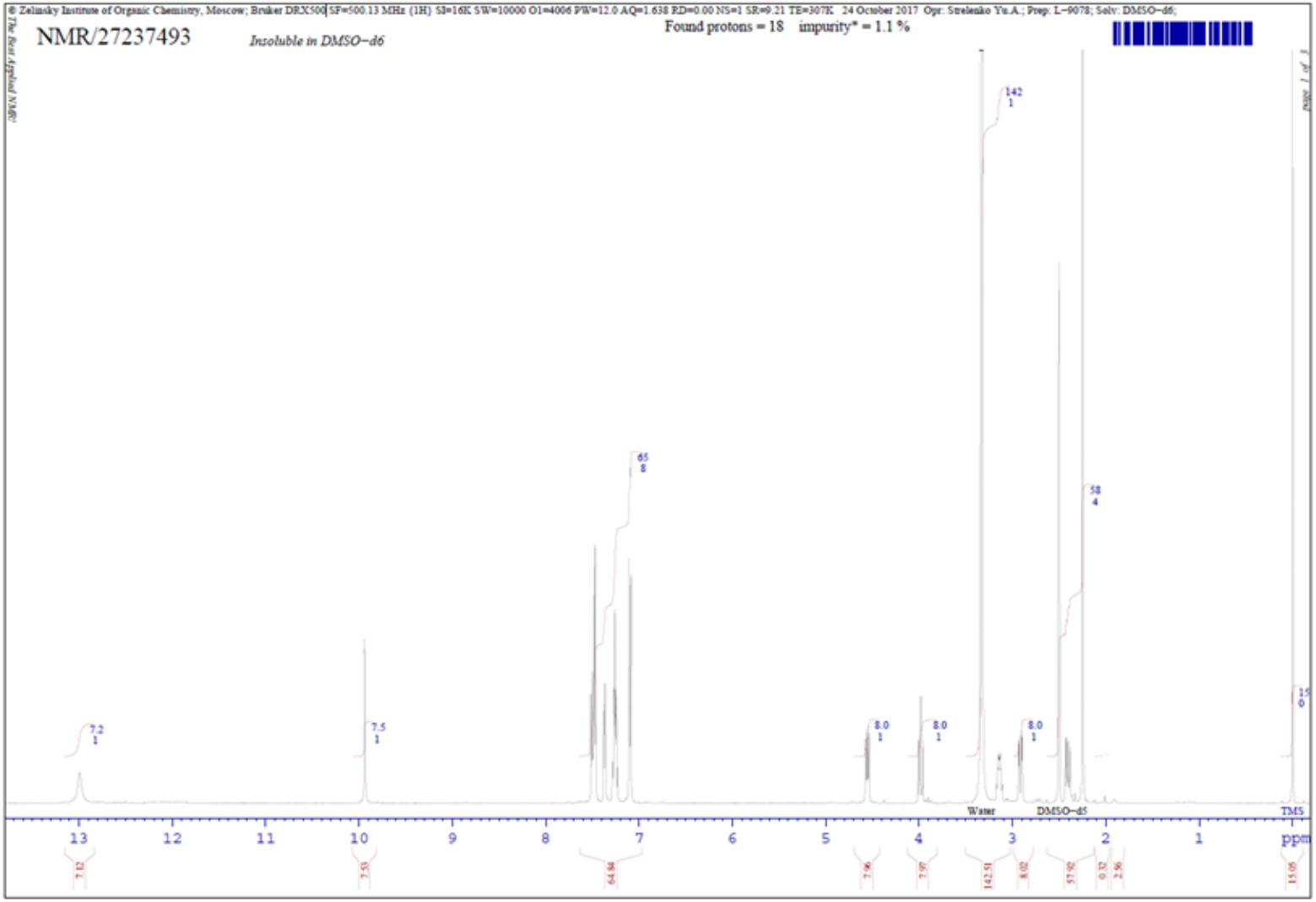


^{1}H NMR, (δ, ppm, *J*, Hz): 13.00 (s, 1H, NHCO), 10.02 (s, 1H, NH), 6.99-7.58 (m, 9H, H-Ar), 4.55 (dd, *J* 6.6, 12.7 Hz, 1H, H^{3b}), 3.97 (t, *J* 11.8 Hz, 1H, H^{3a}), 3.13-3.15 (m, 1H, H^{2}); 2.92 (dd, 1H, *J* 4.6, 15.8 Hz, $CH_{2b}CO$), 2.41 (dd, *J* 8.2, 15.8 Hz, 1H, $CH_{2a}CO$). ^{13}C NMR (δ, ppm): 186.8 (C-3), 169.7 (C=O amide), 156.1 (C-4a), 139.7 (C-1 Ar), 132.2 (C-5a), 131.2 (C-9a), 131.0 (C-4 Ar), 129.1 (C-2,6 Ar), 123.6 (C-9), 123.5 (C-6), 119.6 (C-3,5 Ar), 118.0 (CN), 111.9 (C-8), 110.1 (C7), 65.0 (C-4), 44.1 (C-1), 39.3 (C-2), 35.0 (CH_2-*exo*). HRMS (ESI), m/z: 345.1345 $[M+H]^+$. (calc. for $C_{20}H_{16}N_4O_2$, *m/z*: 345.1347).

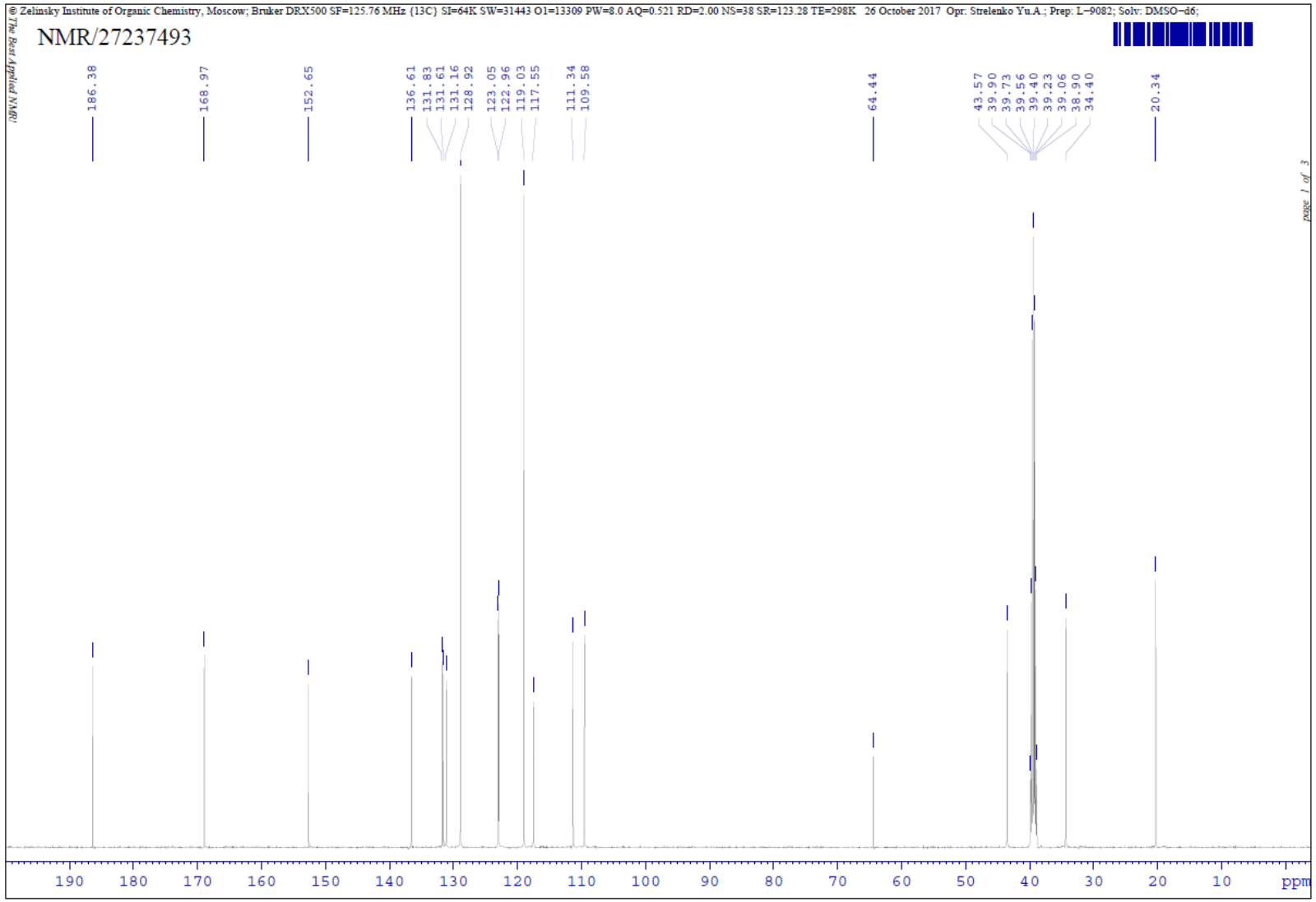
2-(4-Cyano-3-oxo-1,2,3,5-tetrahydropyrido[1,2-*a*]benzimidazol-2-yl)-*N*-(4-chlorophenyl)-acetamide 3j. Yield 0.87 g (46%), white crystals, mp. 312-313 °C.



^{1}H NMR, (δ, ppm, *J*, Hz): 13.00 (br s, 1H, NHCO), 10.26 (s, 1H, NH), 7.24-7.96 (m, 8H, H-Ar), 4.58 (dd, *J* 6.5, 12.6 Hz, 1H, H^{3b}), 3.98 (t, *J* 12.1 Hz, 1H, H^{3a}), 3.13-3.17 (m, 1H, H^{2}); 2.93 (dd, *J* 4.8, 15.8 Hz, 1H, $CH_{2b}CO$); 2.43 (dd, *J* 8.0, 15.8 Hz, 1H, $CH_{2a}CO$). ^{13}C NMR (δ, ppm): 186.4 (C-3), 169.6 (C=O amide), 152.8 (C-4a), 138.2 (C-1 Ar), 131.8 (C-5a), 131.3 (C-9a), 128.9 (C-2,6 Ar), 128.6 (C-4 Ar), 123.2 (C-9), 123.1 (C-6), 120.7 (C-3,5 Ar), 117.7 (CN), 111.5 (C-8), 109.7 (C-7), 64.6 (C-4), 43.7 (C-1), 39.3 (C-2), 34.6 (CH_2-*exo*). HRMS (ESI), m/z: 379.0957 $[M+H]^+$. (calc. for $C_{20}H_{15}ClN_4O_2$., *m/z*: 379.0957).


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz (1H) SI=16K SW=10000 O1=4006 PW=12.0 AQ=1.638 RD=0.00 NS=1 SR=9.21 TE=307K 24 October 2017 Opr: Stvelenko Yu.A.; Prep: L–9078; Solv: DMSO–d6;
NMR/27237493
Insoluble in DMSO–d6
Found protons = 18 impurity* = 1.1 %
7.2
1
7.5
1
6.5
8
8.0
1
8.0
1
14.2
1
8.0
1
5.8
4
Water
DMSO–d5
TMS
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm

^{1}H NMR of **3a**.


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=125.76 MHz {13C} SI=64K SW=31443 O1=13309 PW=8.0 AQ=0.521 RD=2.00 NS=38 SR=123.28 TE=298K 26 October 2017 Opr: Strelenko Yu.A.; Prep: L-9082; Solv: DMSO-d6;
NMR/27237493
186.38
168.97
152.65
136.61
131.83
131.61
131.16
128.92
123.05
122.96
119.03
117.55
111.34
109.58
64.44
43.57
39.90
39.73
39.56
39.40
39.23
39.06
38.90
34.40
20.34
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

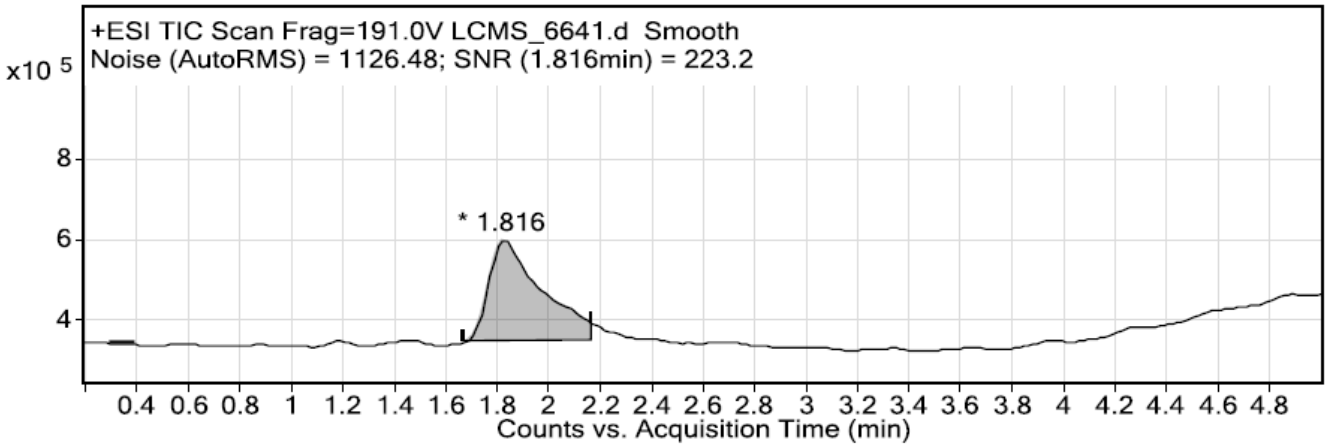
^{13}C NMR of **3a**.

Qualitative Compound Report

Data File	LCMS_6641.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 19
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 12:46:03 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



User Chromatogram Peak List

RT	Height	Height %	Area	Area %	Area Sum %	S/N	Symmetry	Width
1.816	251449.34	100	3683624.92	100	100	223.2	3.22	0.497

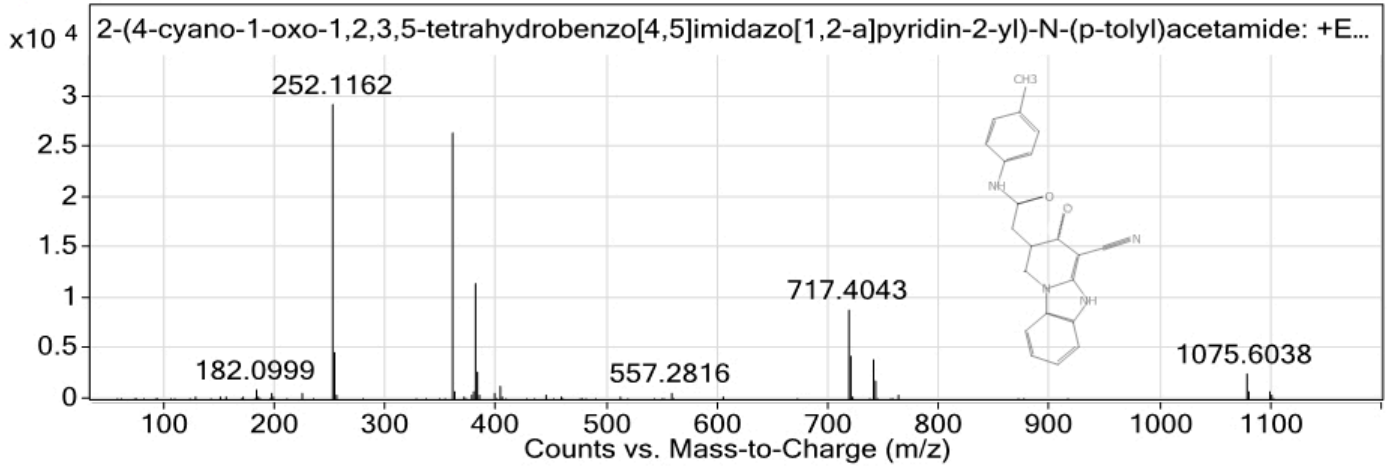
Qualitative Compound Report

Compound Table

Compound Label	RT	Name	Formula	MFG Formula	DB Formula
Cpd 1: 2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(p-tolyl)acetamide	1.816	2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(p-tolyl)acetamide	C21H18N4O2	C21H18N4O2	C21H18N4O2

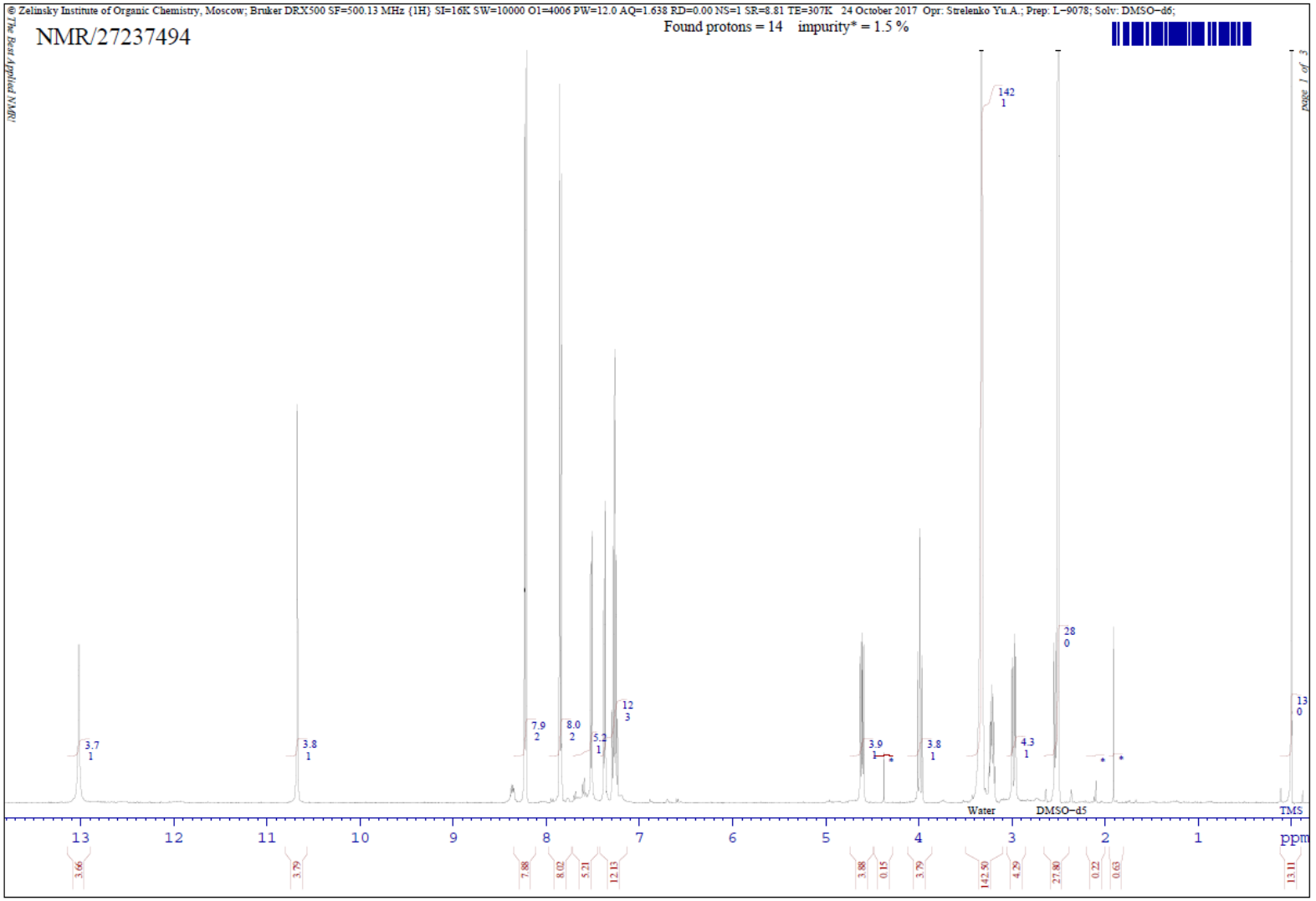
Compound Label	Name	RT	Algorithm
Cpd 1: 2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(p-tolyl)acetamide	**2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(p-**	1.816	Spectrum Extraction

MS Spectrum

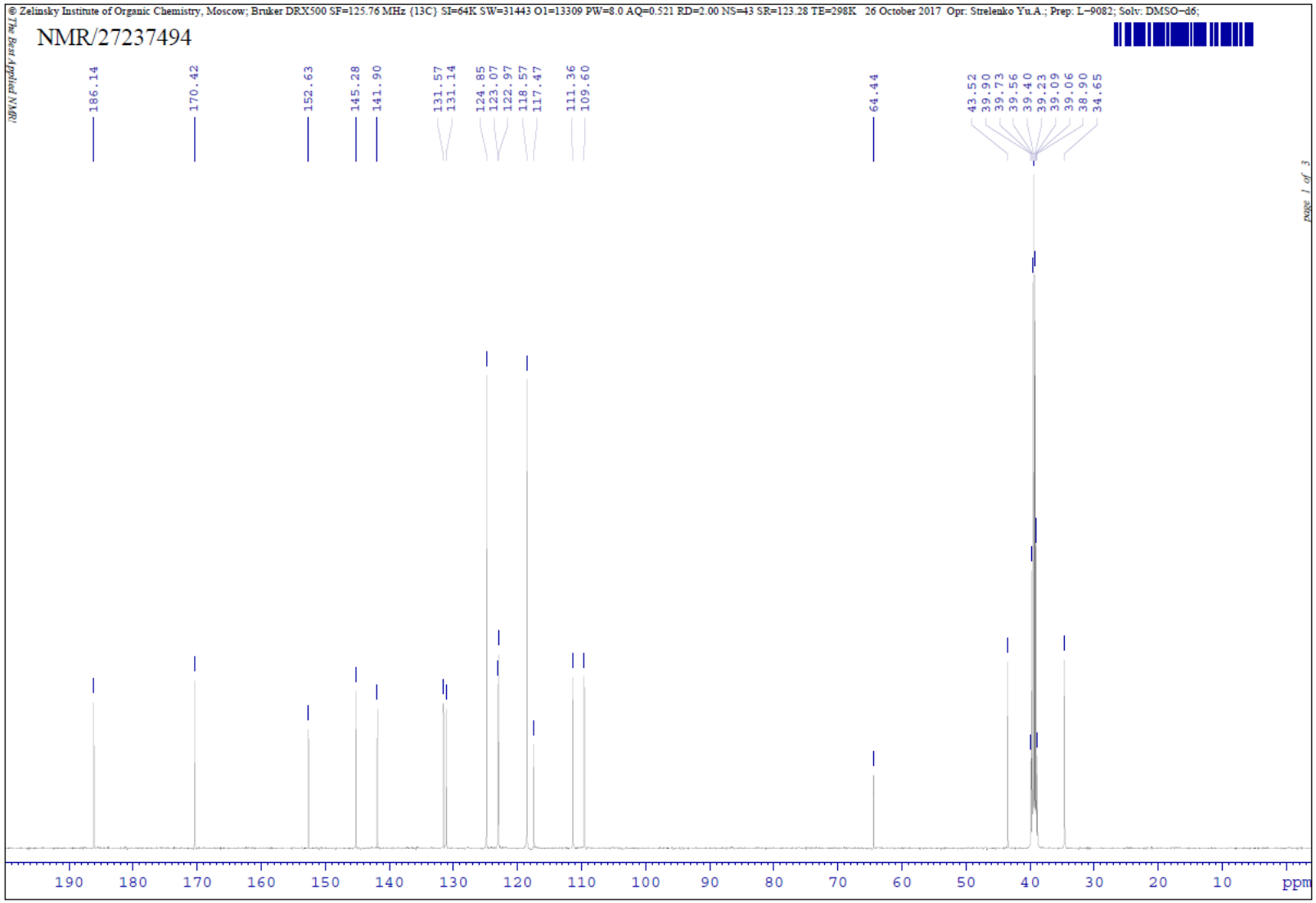


MS Spectrum Peak List

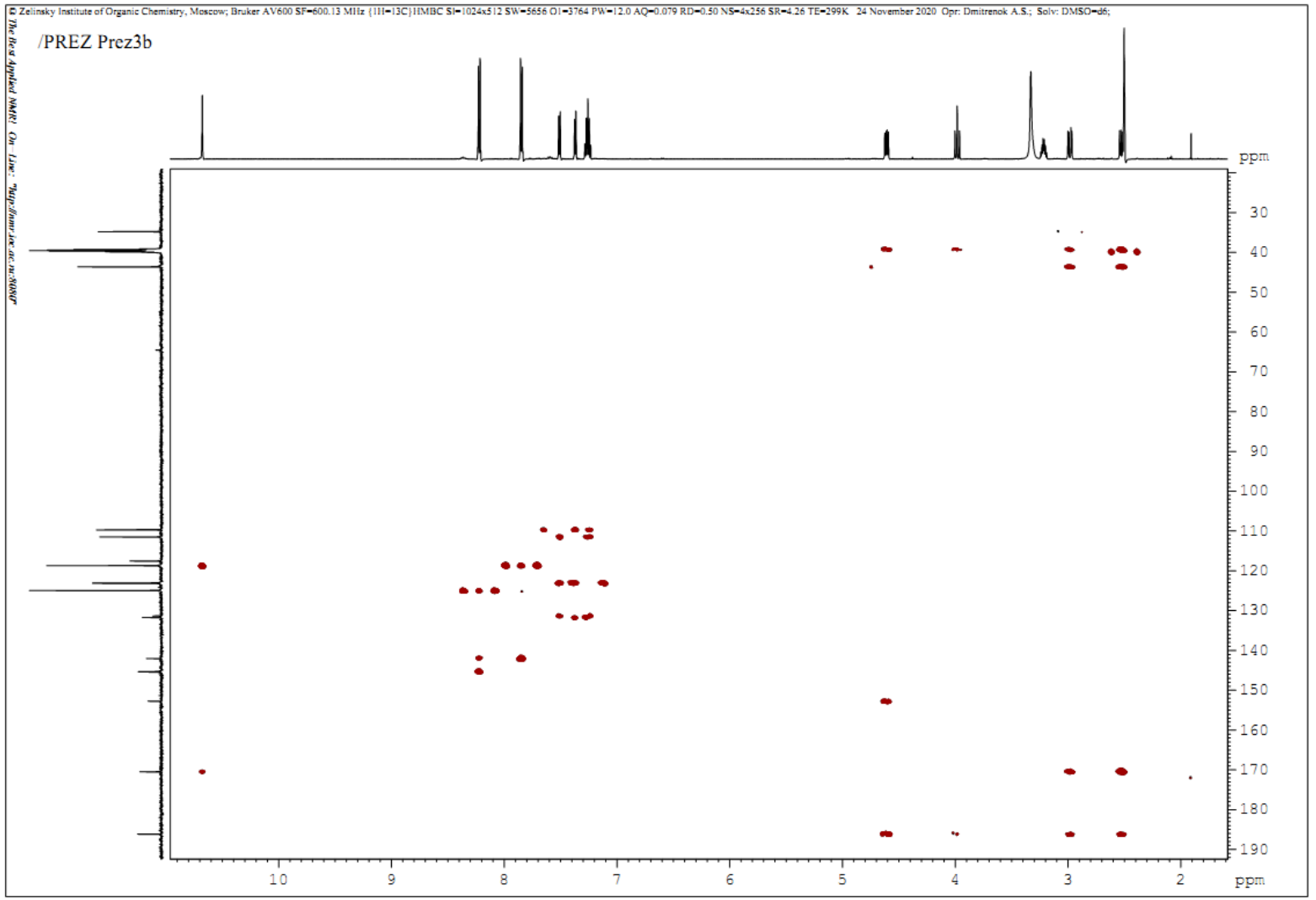
HRMS (ESI) of **3a.**



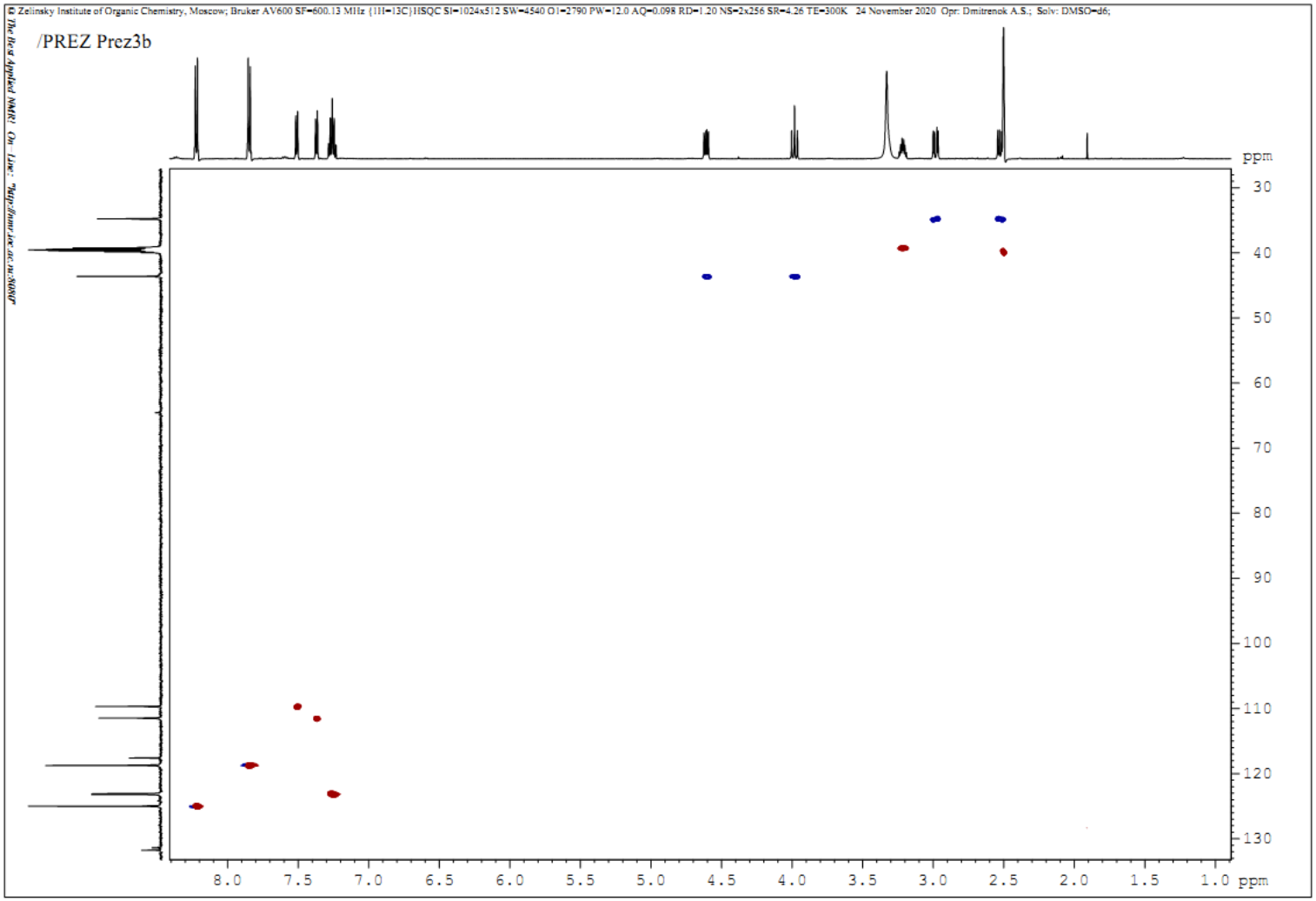
^{1}H NMR of **3b**.


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=125.76 MHz {13C} SI=64K SW=31443 O1=13309 PW=8.0 AQ=0.521 RD=2.00 NS=43 SR=123.28 TE=298K 26 October 2017 Opr: Strelenko Yu.A.; Prep: L-9082; Solv: DMSO-d6;
NMR/27237494
186.14
170.42
152.63
145.28
141.90
131.57
131.14
124.85
123.07
122.97
118.57
117.47
111.36
109.60
64.44
43.52
39.90
39.73
39.56
39.40
39.23
39.09
39.06
38.90
34.65
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

^{13}C NMR of **3b**.



{^{1}H-^{13}C}HMBC of **3b**.

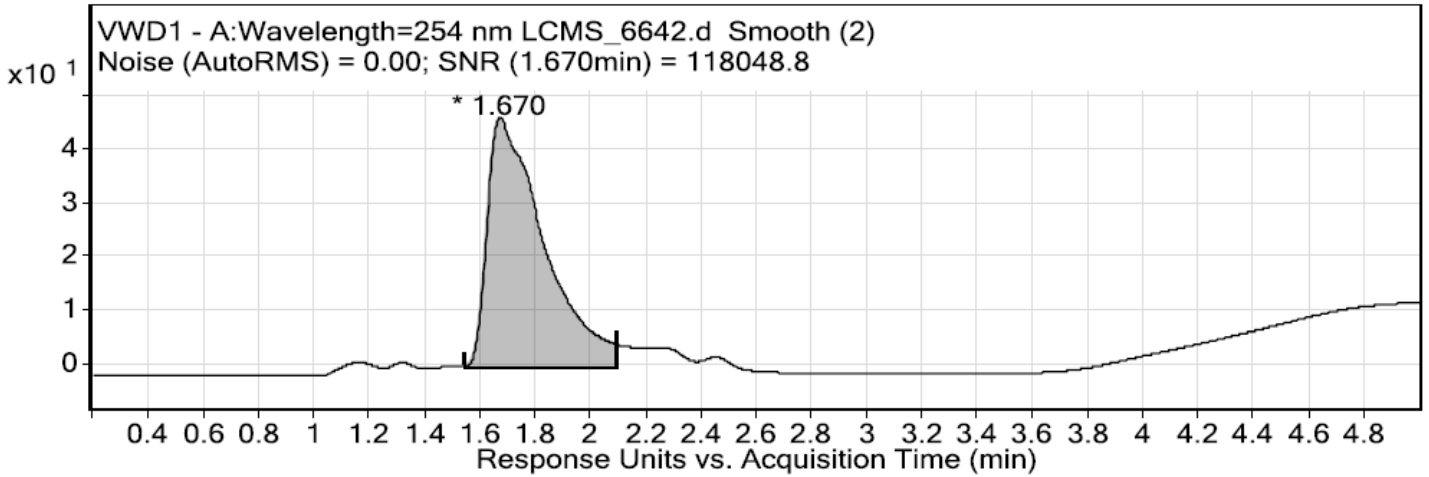


{^{1}H-^{13}C}HSQC of **3b**

Data File	LCMS_6642.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 20
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 12:58:06 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage **Collision Energy** **Ionization Mode**



User Chromatogram Peak List

RT	Height	Height %	Area	Area %	Area Sum %	S/N	Width
1.67	46.67	100	675.26	100	100	118048.8	0.55

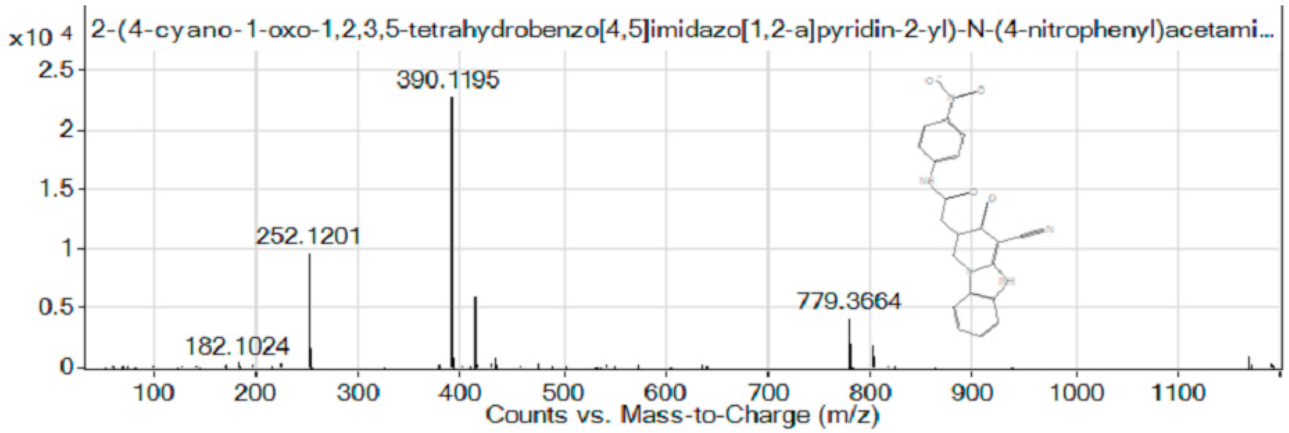
Qualitative Compound Report

Compound Table

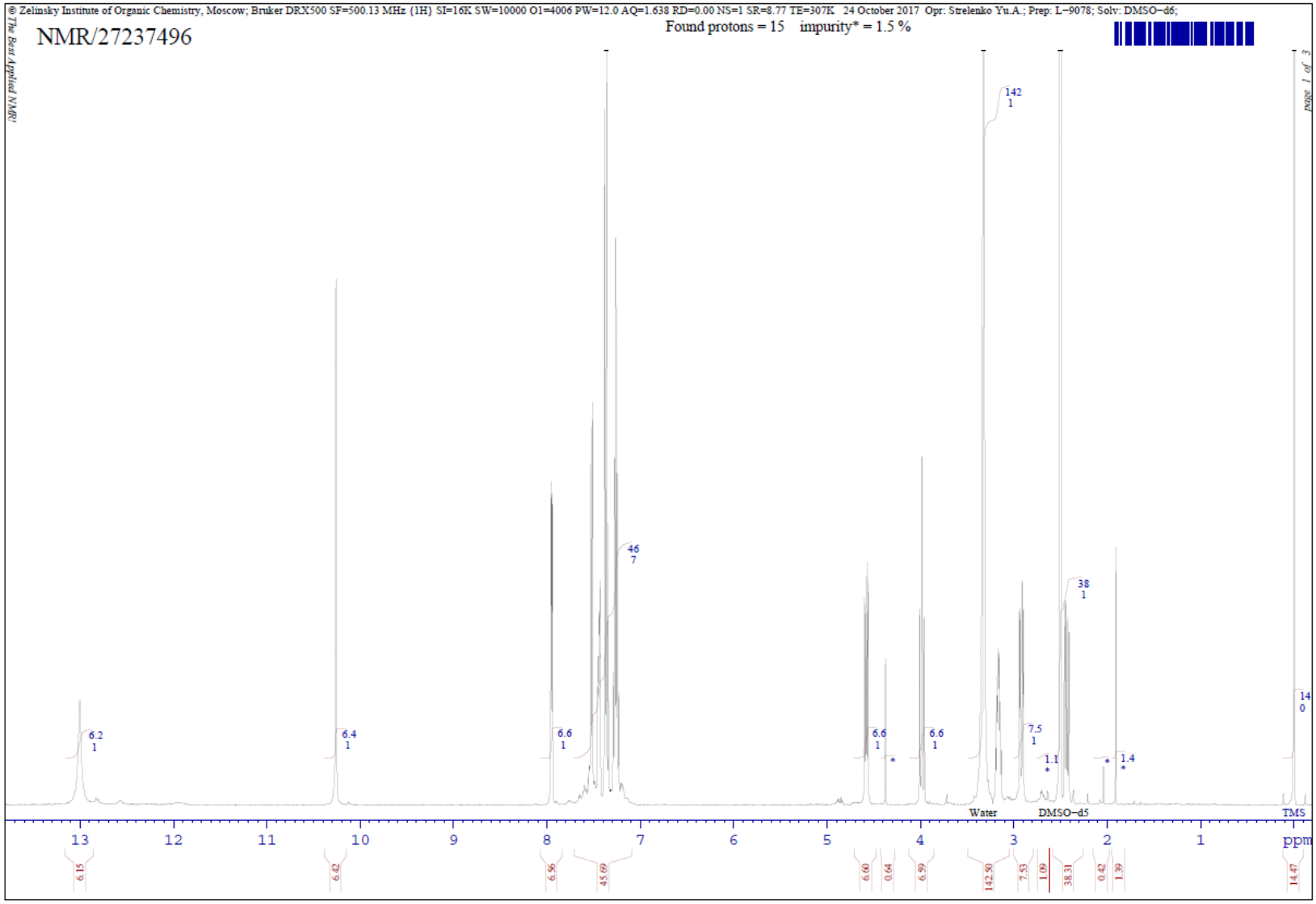
Compound Label	RT	Name	Formula	MFG Formula	DB Formula
Cpd 1: 2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-nitrophenyl)acetamide	1.67	2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-nitrophenyl)acetamide	C20H15N5O4	C20H15N5O4	C20H15N5O4

Compound Label	Name	RT	Algorithm
Cpd 1: 2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-nitrophenyl)acetamide	**2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-**	1.67	Spectrum Extraction

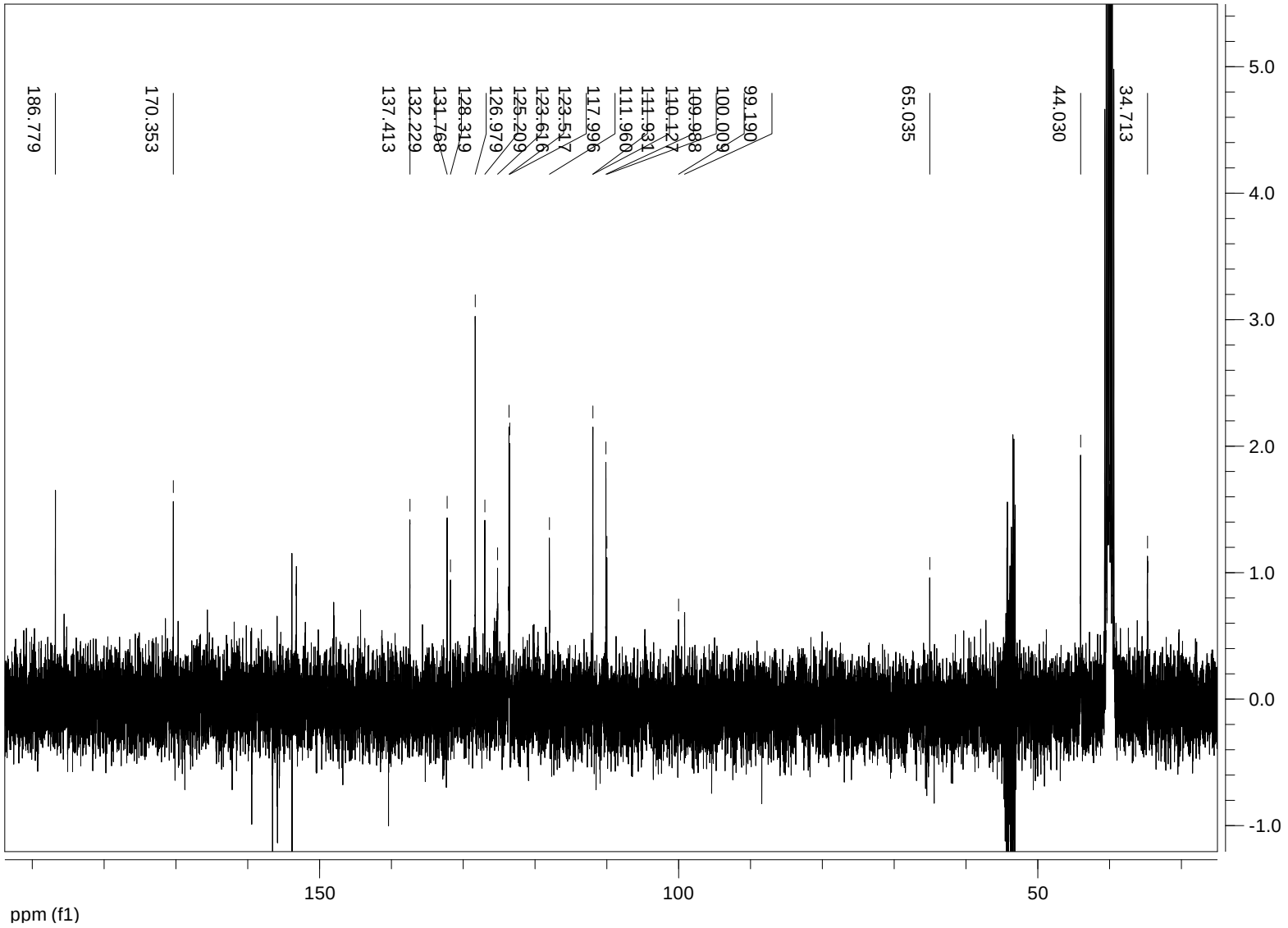
MS Spectrum



HRMS (ESI) of **3b.**


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz (1H) SI=16K SW=10000 O1=4006 PW=12.0 AQ=1.638 RD=0.00 NS=1 SR=8.77 TE=307K 24 October 2017 Opr: Strelenko Yu.A.; Prep: L-9078; Solv: DMSO-d6;
NMR/27237496
Found protons = 15 impurity* = 1.5 %
Water
DMSO-d5
TMS
ppm

^{1}H NMR of **3c**.

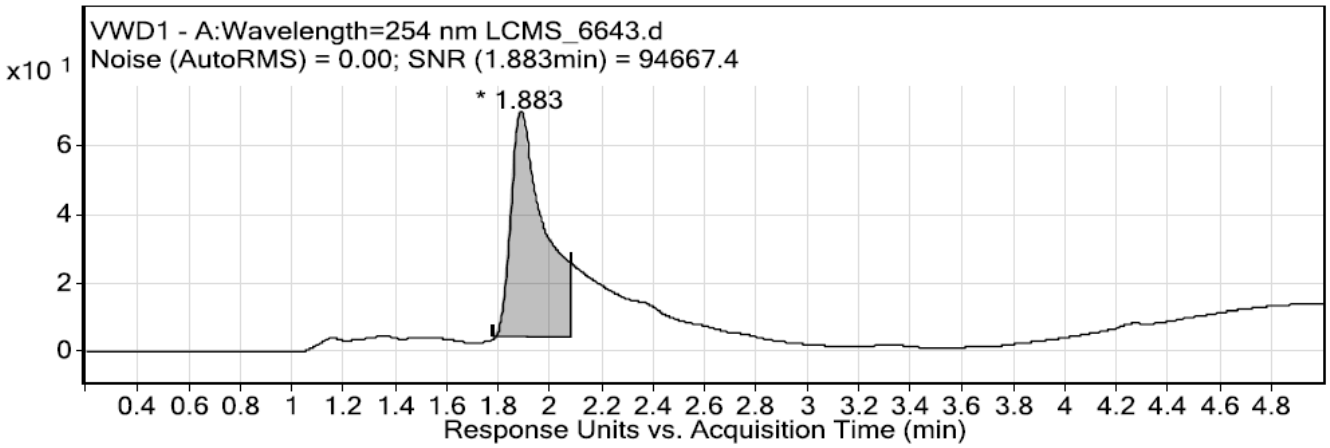

186.779
170.353
137.413
132.229
131.768
128.319
126.979
125.209
123.616
123.517
117.996
111.960
111.931
110.127
109.988
100.009
99.190
65.035
44.030
34.713
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
150
100
50
ppm (f1)

^{13}C NMR of **3c**.

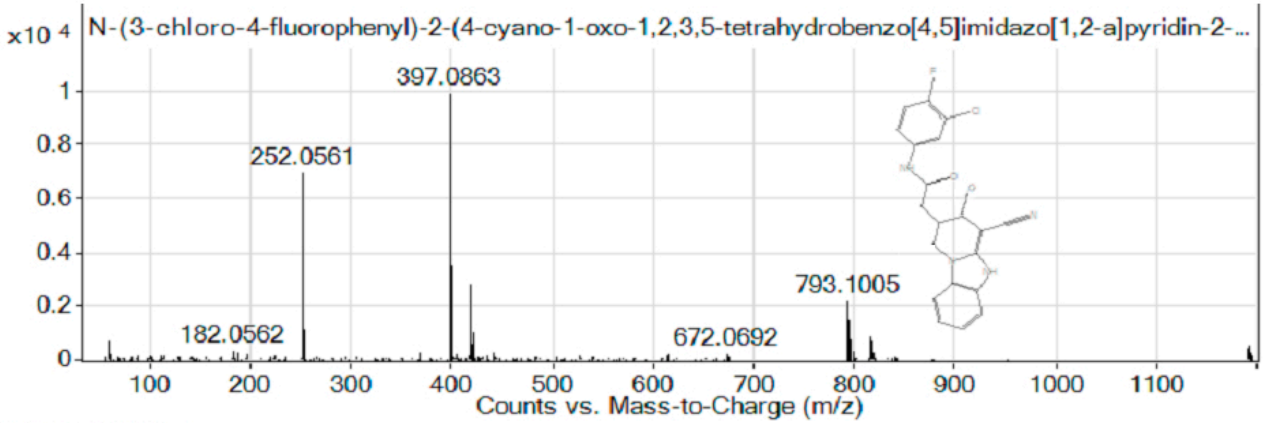
Data File	LCMS_6643.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 21
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 1:10:07 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage **Collision Energy** **Ionization Mode**



Qualitative Compound Report

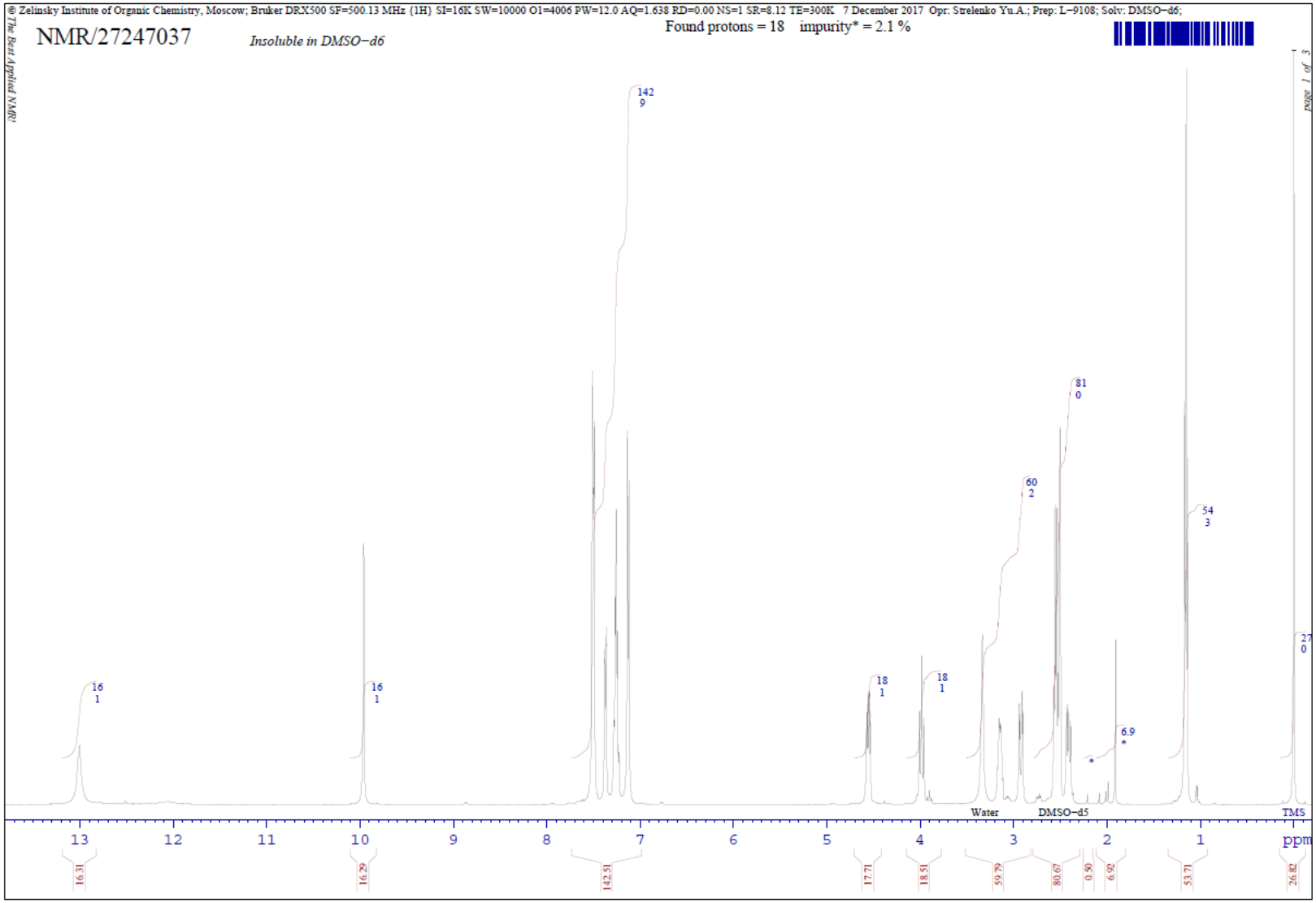


MS Spectrum Peak List

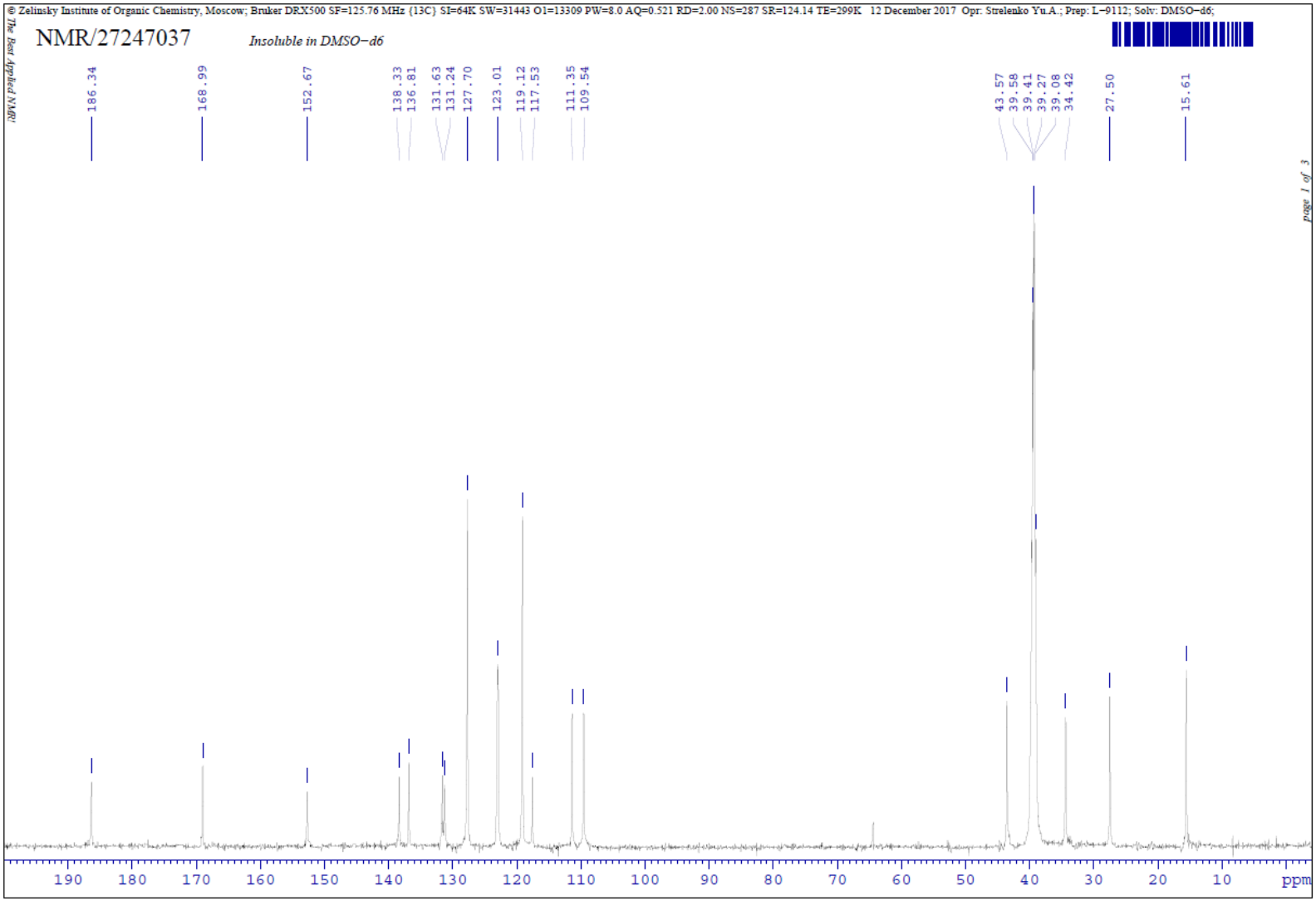
m/z	z	Abund
252.0561	1	6958.45
253.0595	1	1112.45
397.0863	1	9931.48
398.0567	1	2297.59
399.0508	1	3513.16
419.0335	1	2822.99
421.0309	1	1072.35
793.1005	1	2221.85
794.1022	1	963.74
795.0976	1	1548.74

Compound Structure

HRMS (ESI) of **3c.**


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz (1H) SI=16K SW=10000 O1=4006 PW=12.0 AQ=1.638 RD=0.00 NS=1 SR=8.12 TE=300K 7 December 2017 Opr: Strelenko Yu.A.; Prep: L-9108; Solv: DMSO-d6;
NMR/27247037
Insoluble in DMSO-d6
Found protons = 18 impurity* = 2.1 %
The Best Applied NMR
Page 1 of 3
142
9
81
0
60
2
54
3
16
1
16
1
18
1
18
1
6.9
*
27
0
Water
DMSO-d5
TMS
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
16.31
16.29
142.51
17.71
18.51
59.79
80.67
6.90
6.92
53.71
26.82

^{1}H NMR of **3d**.

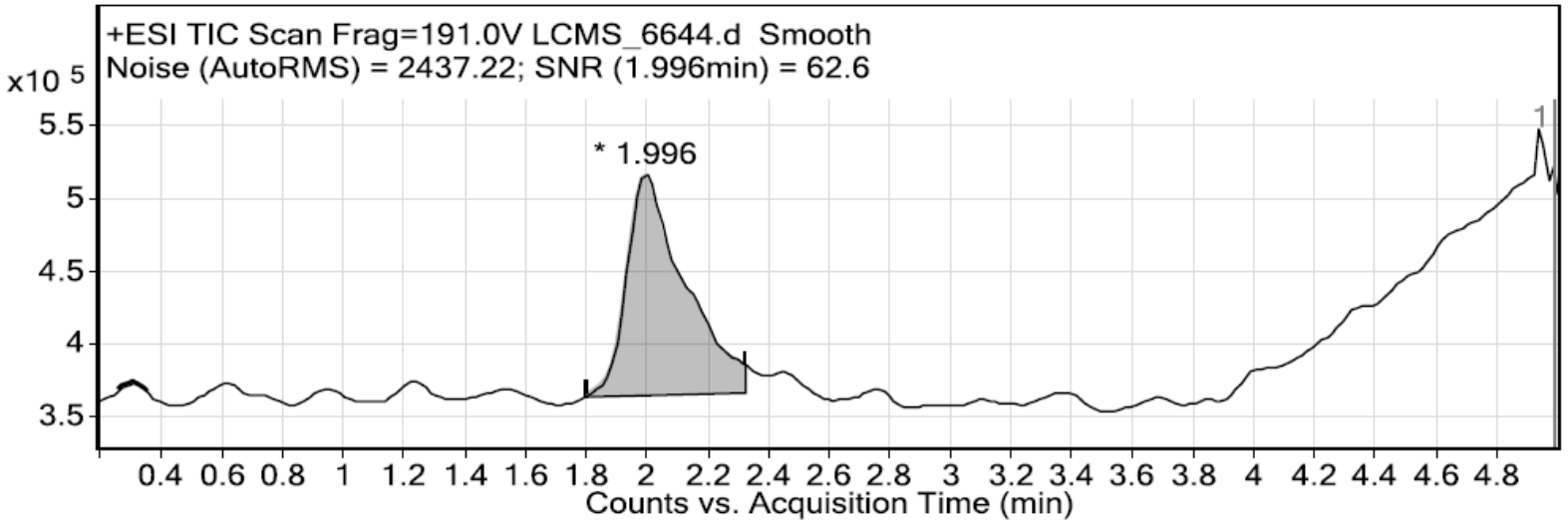

Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=125.76 MHz {13C} SI=64K SW=31443 O1=13309 PW=8.0 AQ=0.521 RD=2.00 NS=287 SR=124.14 TE=299K 12 December 2017 Opr: Strelenko Yu.A.; Prep: L-9112; Solv: DMSO-d6;
NMR/27247037
Insoluble in DMSO-d6
186.34
168.99
152.67
138.33
136.81
131.63
131.24
127.70
123.01
119.12
117.53
111.35
109.54
43.57
39.58
39.41
39.27
39.08
34.42
27.50
15.61
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

^{13}C NMR of **3d**.

Data File	LCMS_6644.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 22
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 1:24:26 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



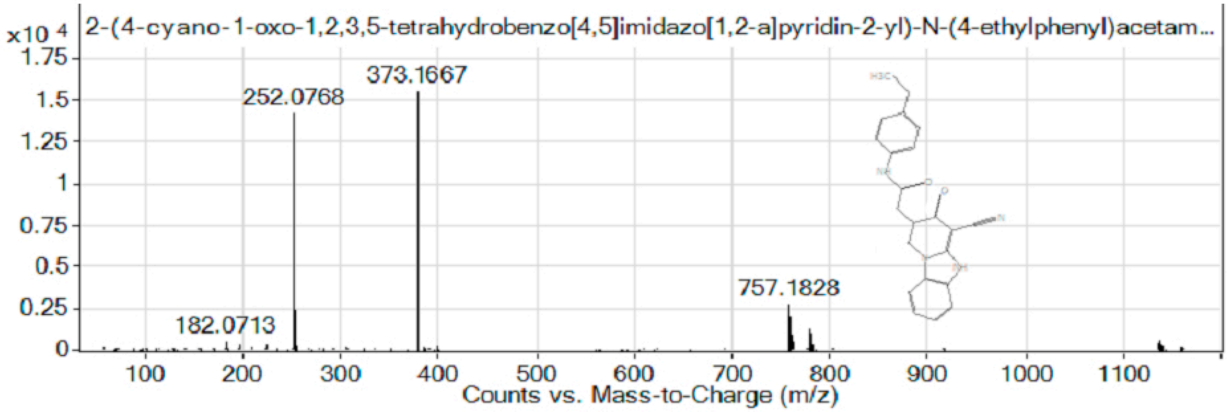
Qualitative Compound Report

Compound Table

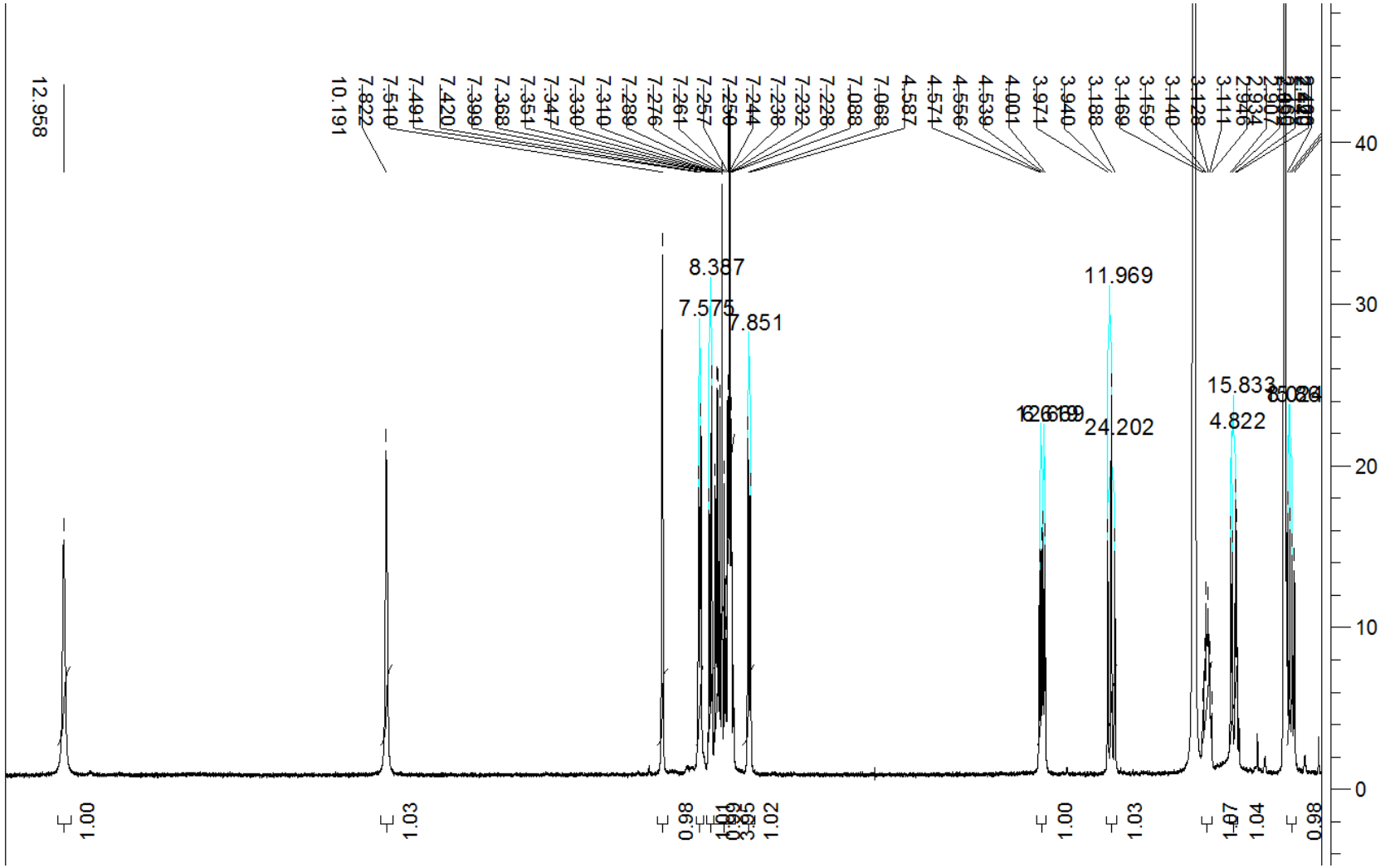
Compound Label	RT	Name	Formula	MFG Formula	DB Formula
Cpd 1: 2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-ethylphenyl)acetamide	1.996	2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-ethylphenyl)acetamide	C22H20N4O2	C22H20N4O2	C22H20N4O2

Compound Label	Name	RT	Algorithm
Cpd 1: 2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-ethylphenyl)acetamide	**2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-(4-**	1.996	Spectrum Extraction

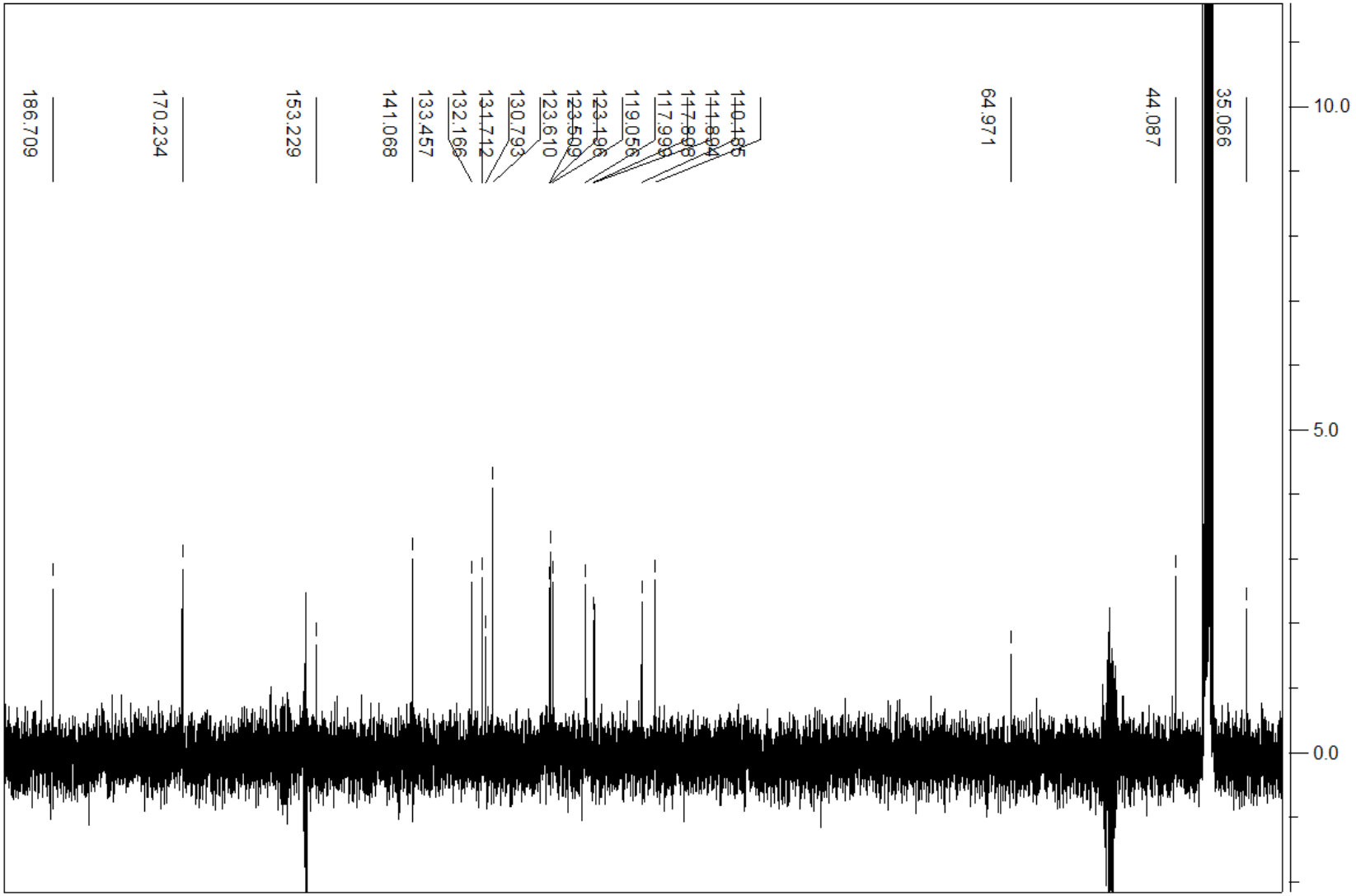
MS Spectrum



HRMS (ESI) of **3d.**


12.958
10.191
8.387
7.575
7.851
11.969
24.202
15.833
4.822
1.00
1.03
1.02
1.00
1.03
1.04
0.98

^{1}H NMR of **3e**.

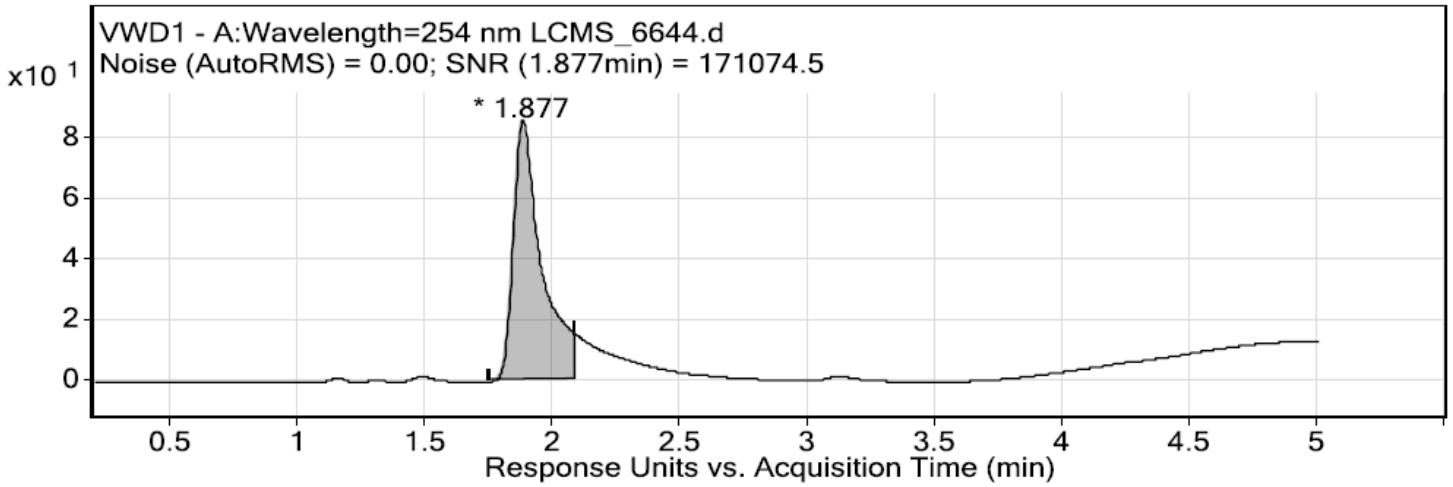

186.709
170.234
153.229
141.068
133.457
132.166
131.712
130.793
123.610
123.509
123.196
119.056
117.998
117.808
111.894
110.185
64.971
44.087
35.066
10.0
5.0
0.0

^{13}C NMR of **3e**.

Data File	LCMS_6644.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 22
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 1:24:26 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage **Collision Energy** **Ionization Mode**



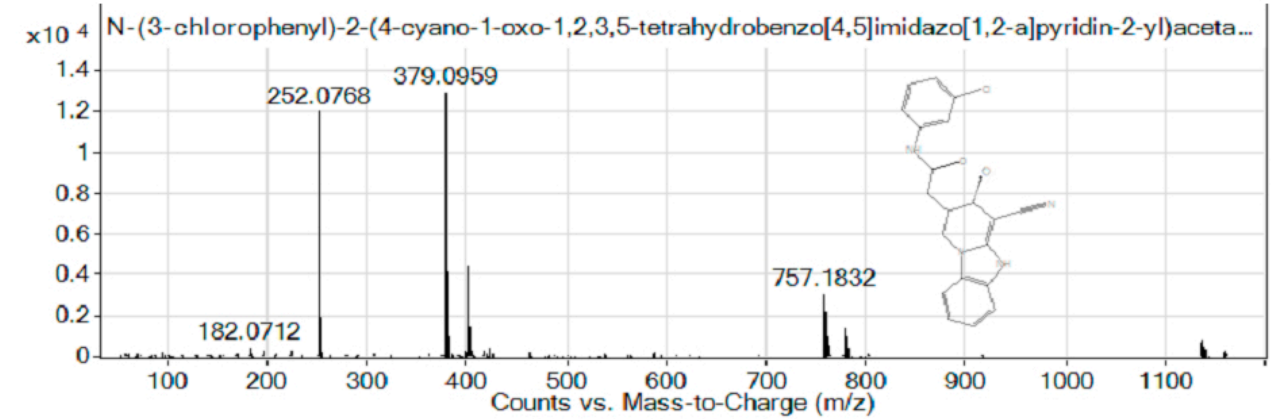
Qualitative Compound Report

Compound Table

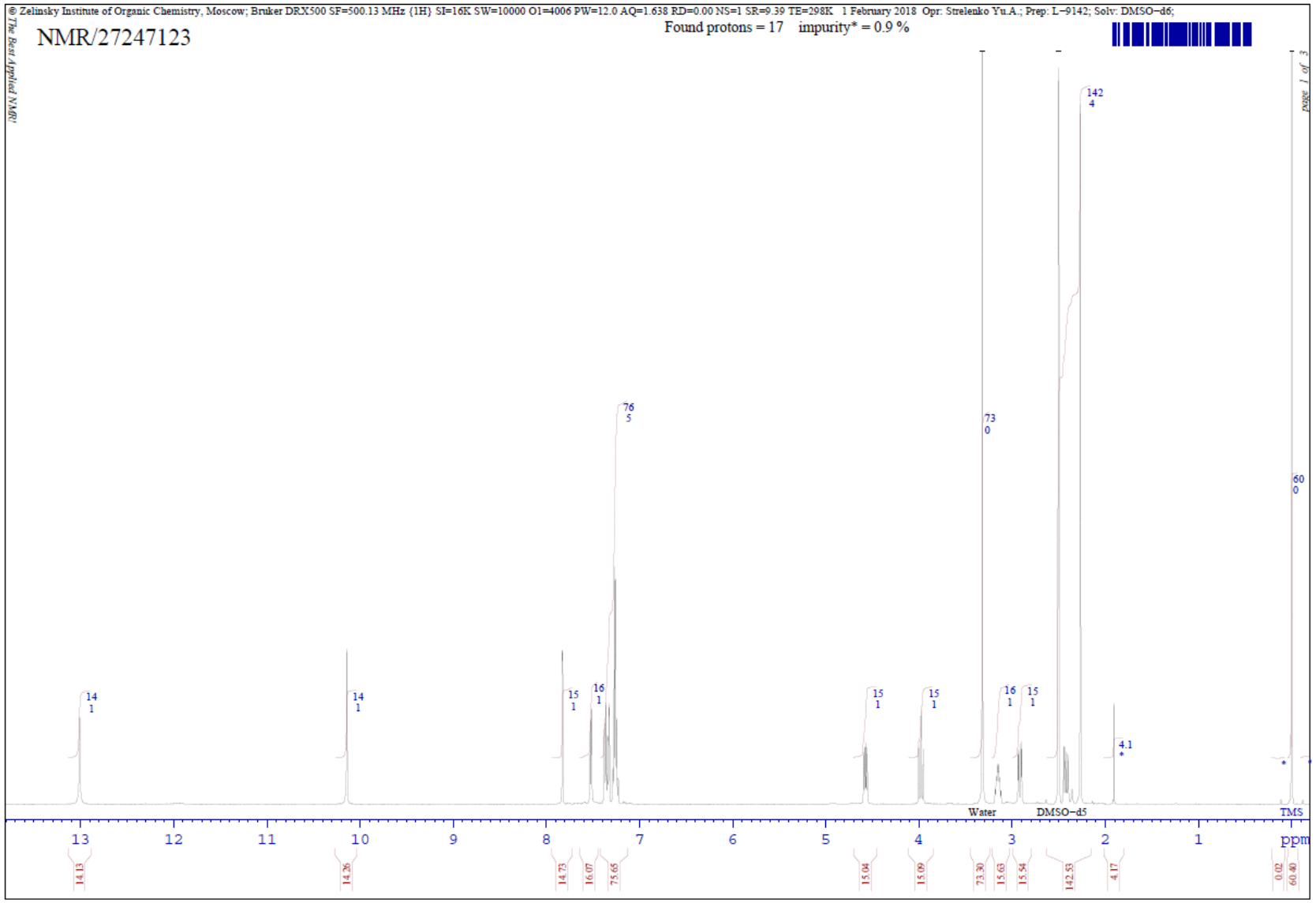
Compound Label	RT	Name	Formula	MFG Formula	DB Formula
Cpd 1: N-(3-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)acetamide	1.877	N-(3-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)acetamide	C20H15ClN4O2	C20H15ClN4O2	C20H15ClN4O2

Compound Label	Name	RT	Algorithm
Cpd 1: N-(3-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)acetamide	**N-(3-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-**	1.877	Spectrum Extraction

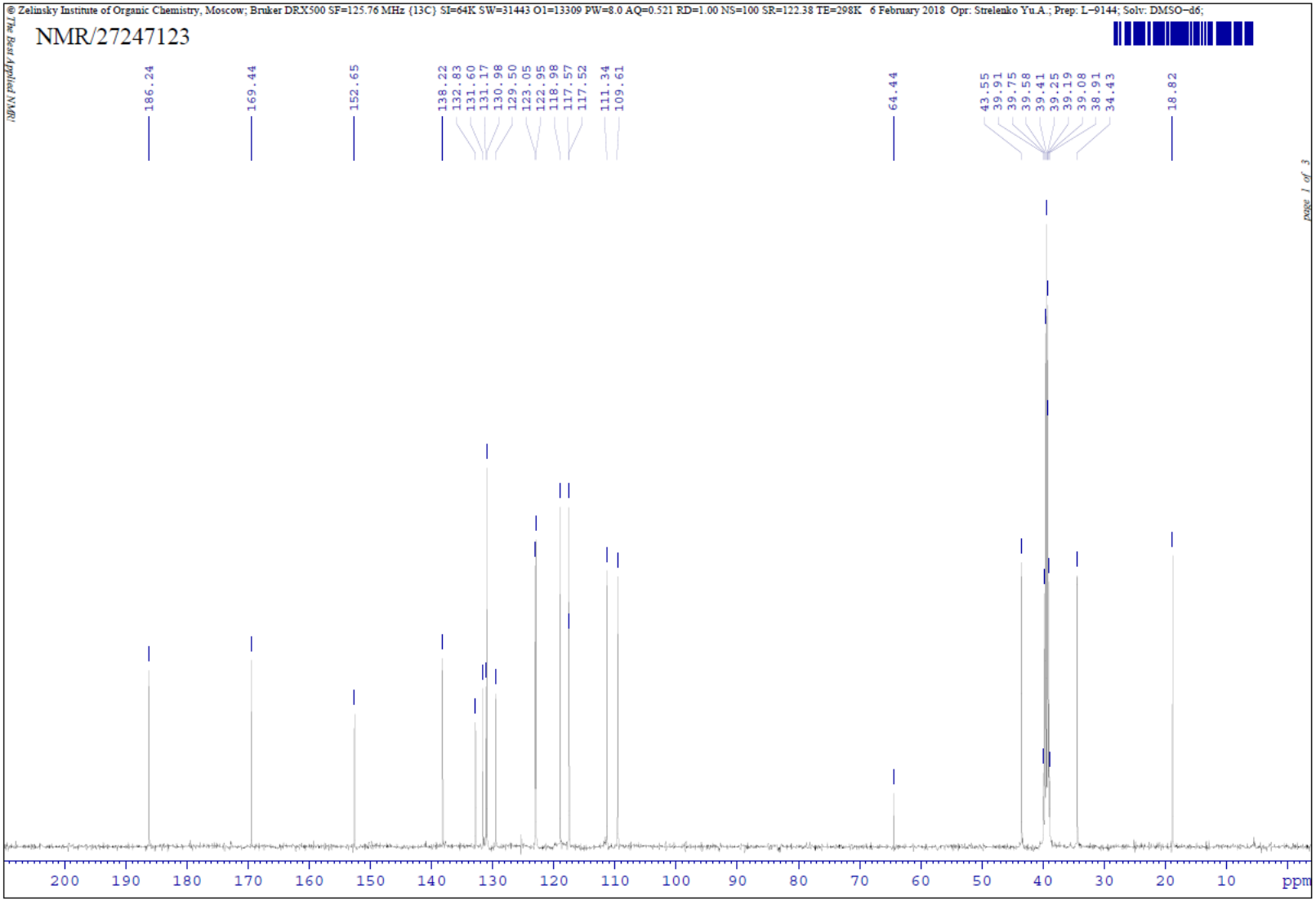
MS Spectrum



HRMS (ESI) of **3e.**


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz {1H} SI=16K SW=10000 O1=4006 PW=12.0 AQ=1.638 RD=0.00 NS=1 SR=9.39 TE=298K 1 February 2018 Opr: Strelenko Yu.A.; Prep: L-9142; Solv: DMSO-d6;
NMR/27247123
Found protons = 17 impurity* = 0.9 %
Water
DMSO-d5
TMS
ppm

^{1}H NMR of **3f**.

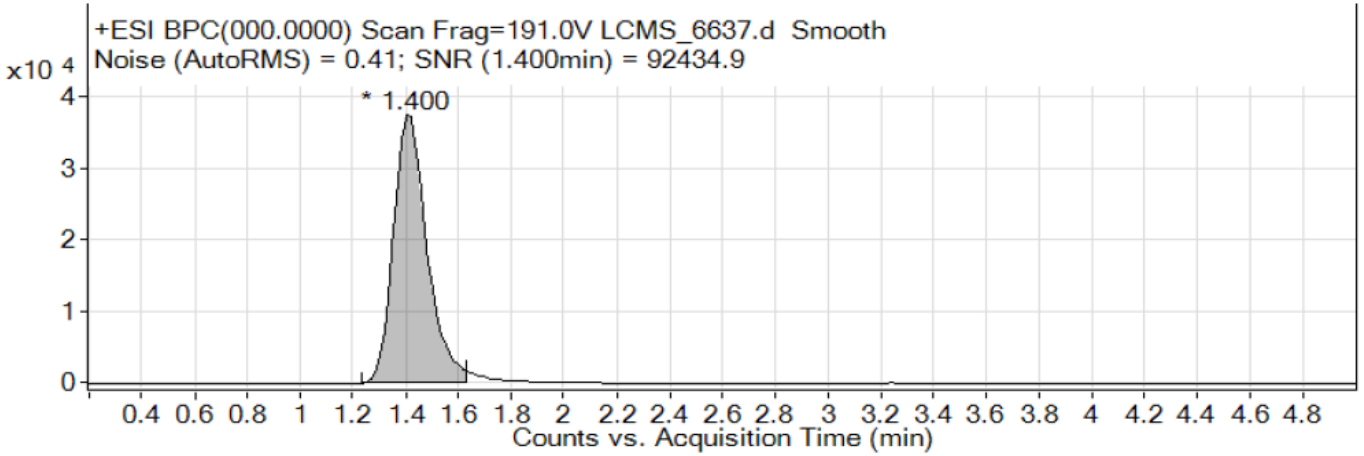

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=125.76 MHz (13C) SI=64K SW=31443 O1=13309 PW=8.0 AQ=0.521 RD=1.00 NS=100 SR=122.38 TE=298K 6 February 2018 Opr: Strelenko Yu.A.; Prep: L-9144; Solv: DMSO-d6;
NMR/27247123
186.24
169.44
152.65
138.22
132.83
131.60
131.17
130.98
129.50
123.05
122.95
118.98
117.57
117.52
111.34
109.61
64.44
43.55
39.91
39.75
39.58
39.41
39.25
39.19
39.08
38.91
34.43
18.82
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

^{13}C NMR of **3f**.

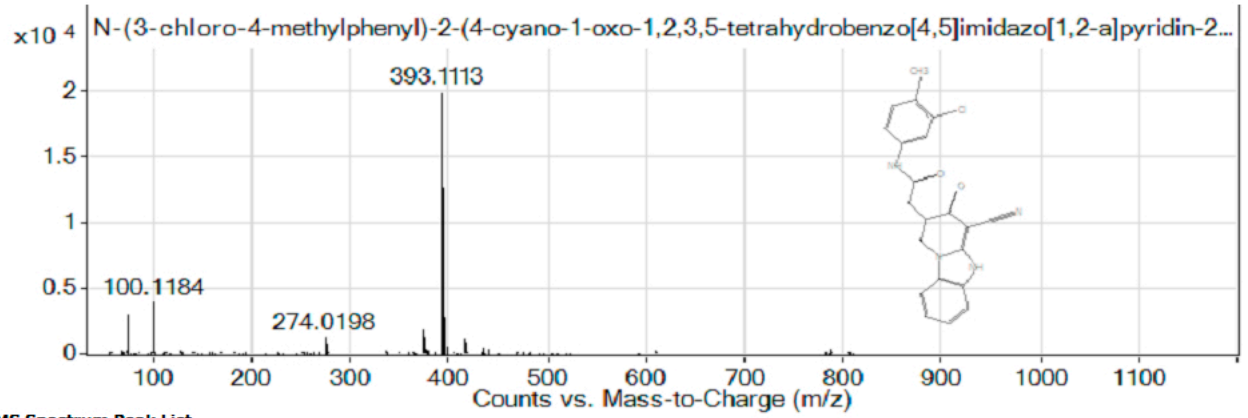
Data File	LCMS_6637.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 15
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 11:57:44 AM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



Qualitative Compound Report



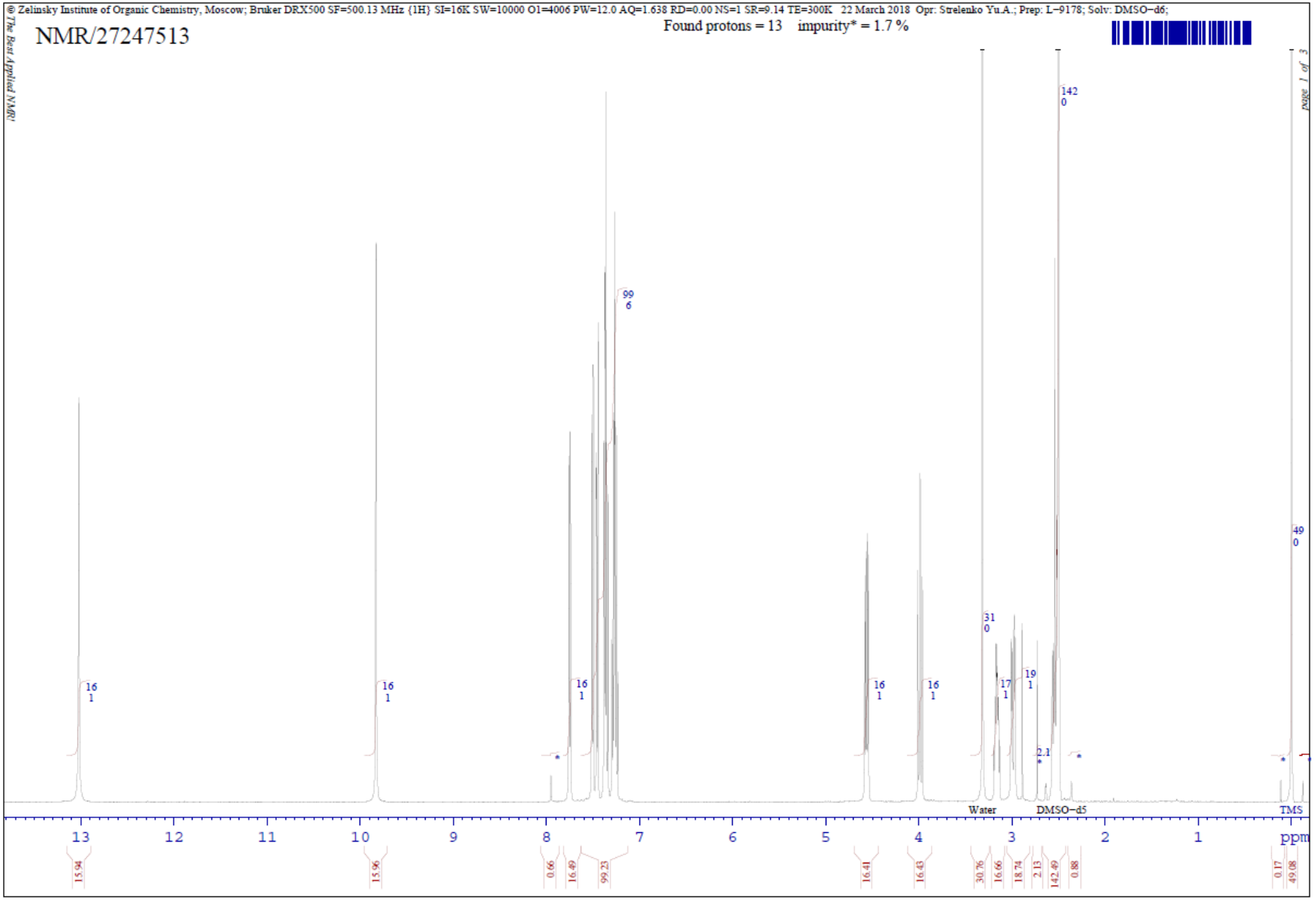
MS Spectrum Peak List

m/z	z	Abund
74.0655		3025.77
100.1184		3870.78
274.0198		1277.11
374.0681	1	1916.48
376.066	1	1252.01
393.1113	1	19900.01
394.0836	1	4132.95
395.0774	1	12793.6

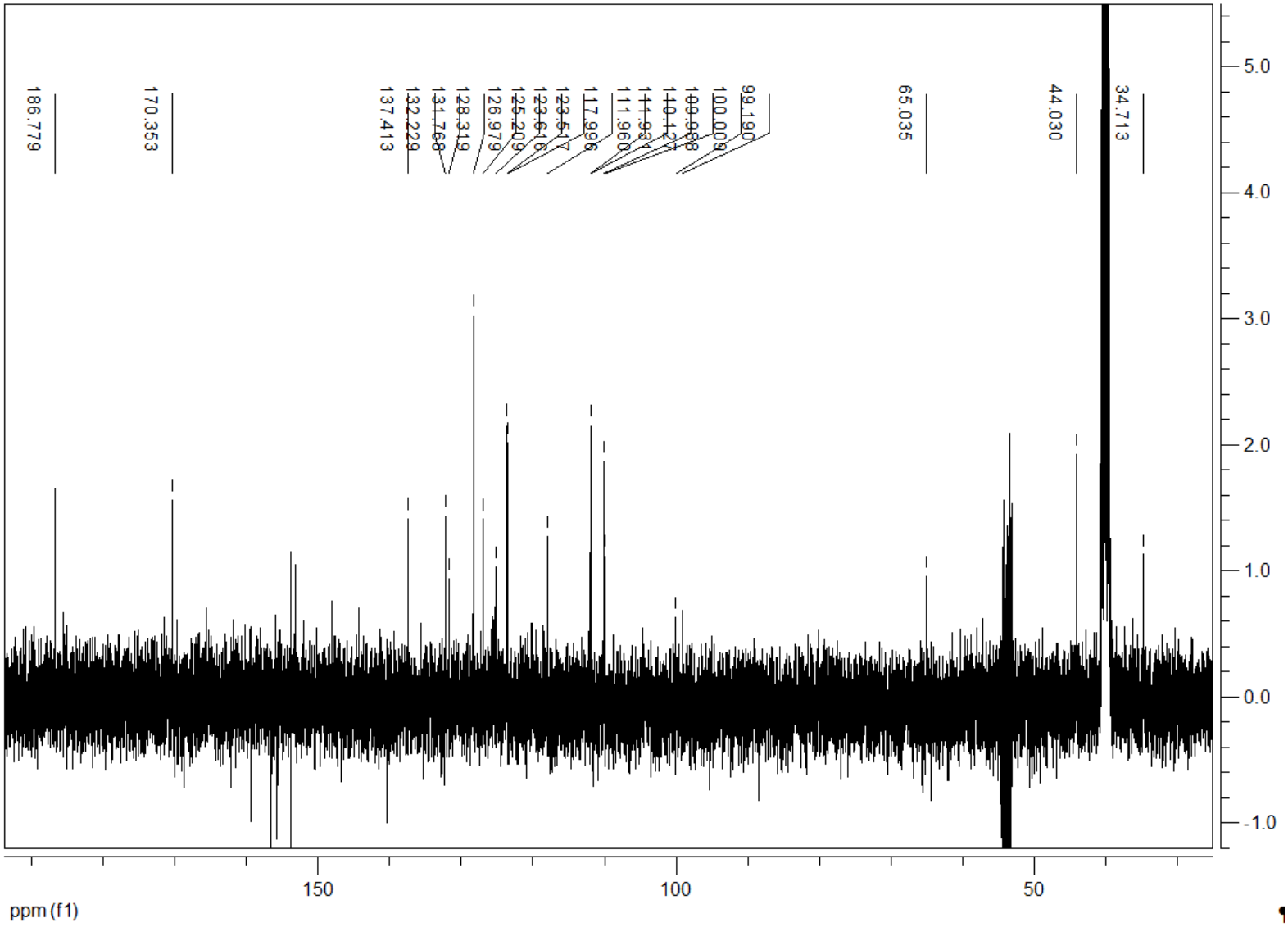
Compound Structure

--- End Of Report ---

HRMS (ESI) of **3f.**


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz {1H} SI=16K SW=10000 O1=4006 PW=12.0 AQ=1.638 RD=0.00 NS=1 SR=9.14 TE=300K 22 March 2018 Opr: Strelenko Yu.A.; Prep: L-9178; Solv: DMSO-d6;
NMR/27247513
Found protons = 13 impurity* = 1.7 %
Water
DMSO-d5
TMS
ppm

^{1}H NMR of **3g**.

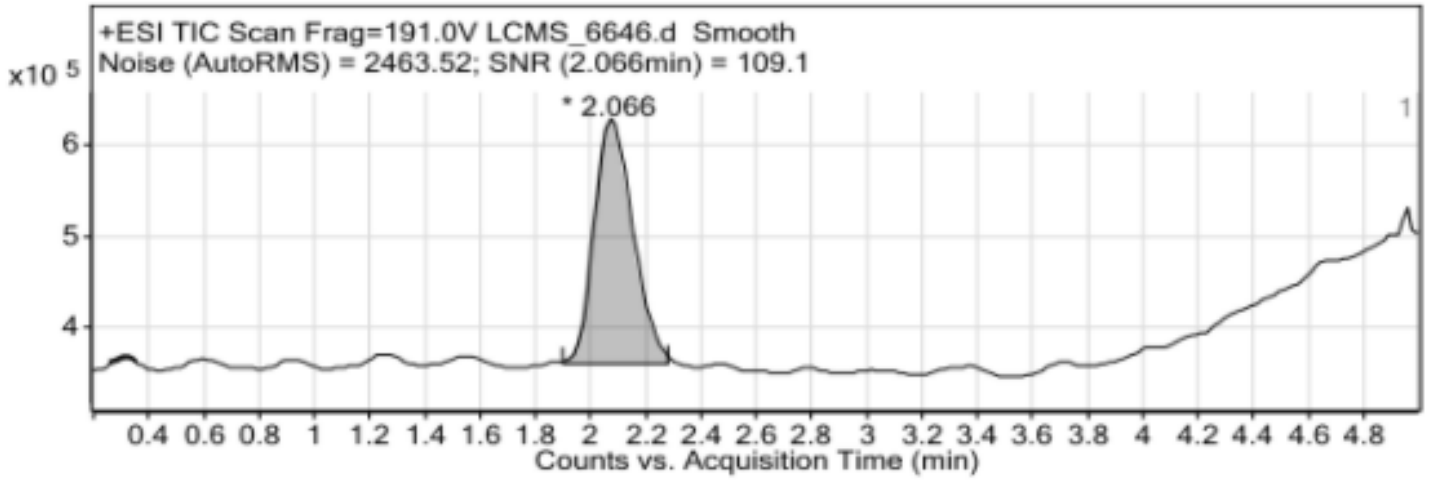

186.779
170.353
137.413
132.229
131.768
128.319
126.979
125.209
123.616
123.517
117.996
111.960
111.931
110.121
109.988
100.009
99.190
65.035
44.030
34.713
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
150
100
50
ppm (f1)

^{13}C NMR of **3g**.

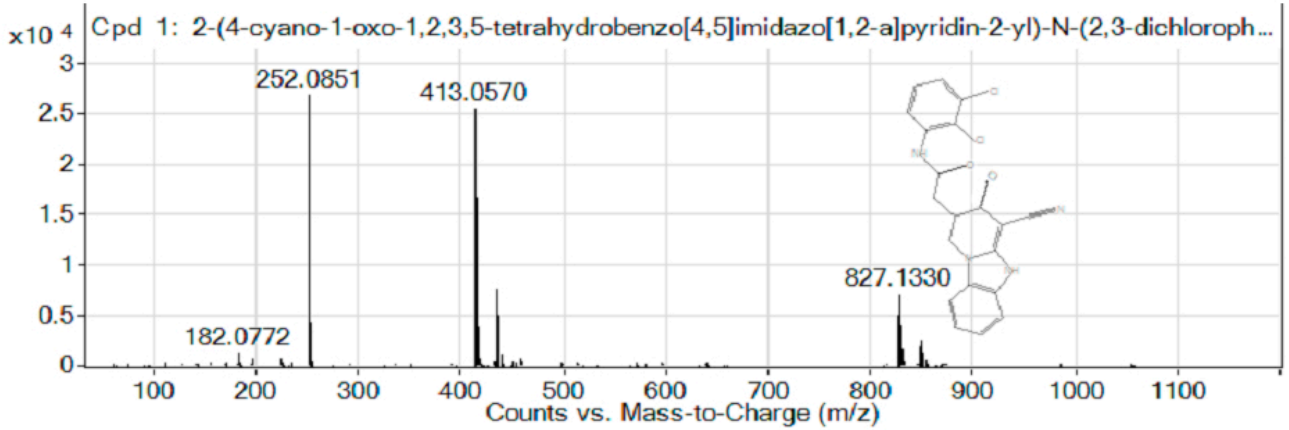
Data File	LCMS_6646.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 24
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 1:44:26 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



Qualitative Compound Report

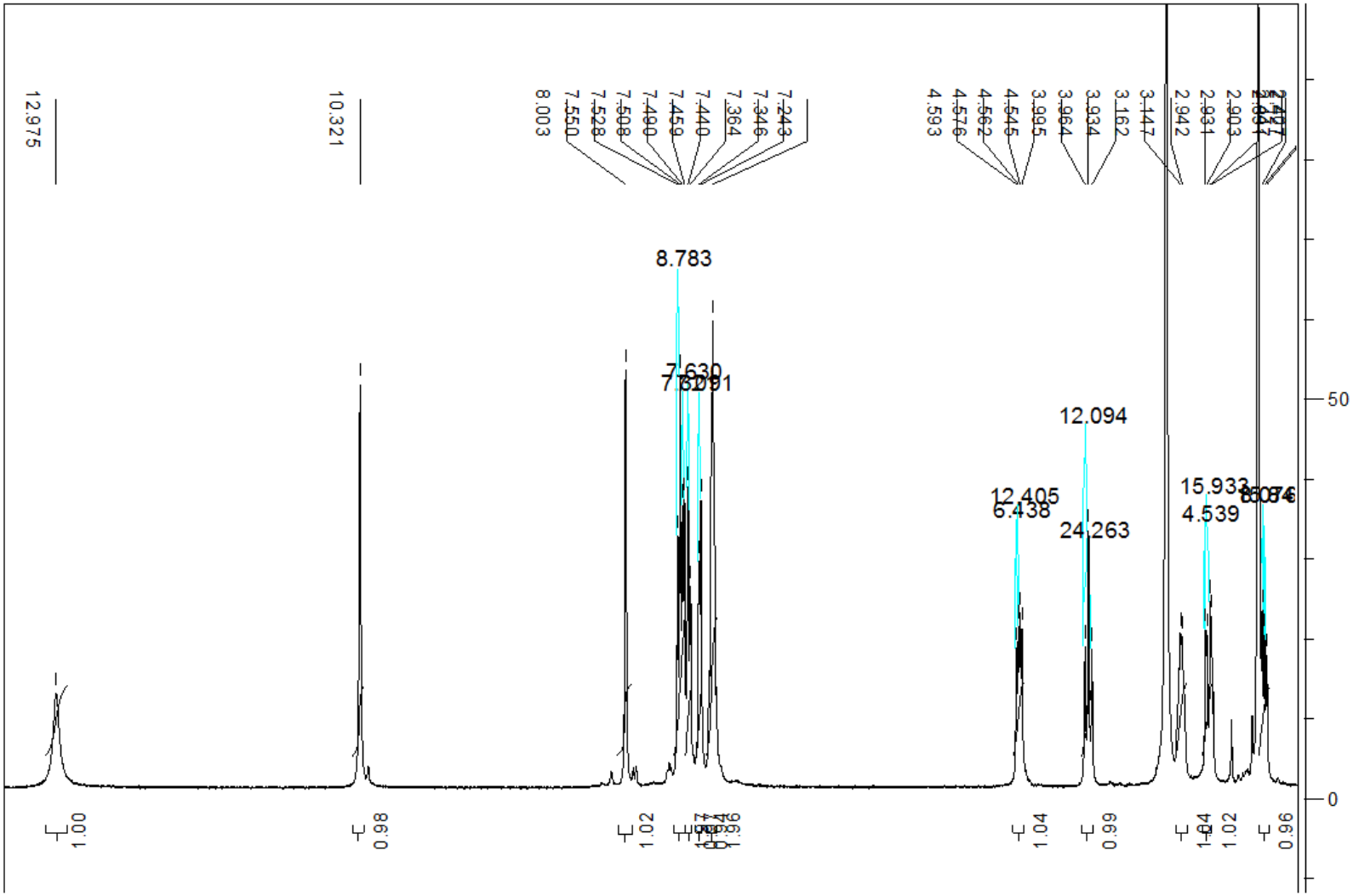


MS Spectrum Peak List

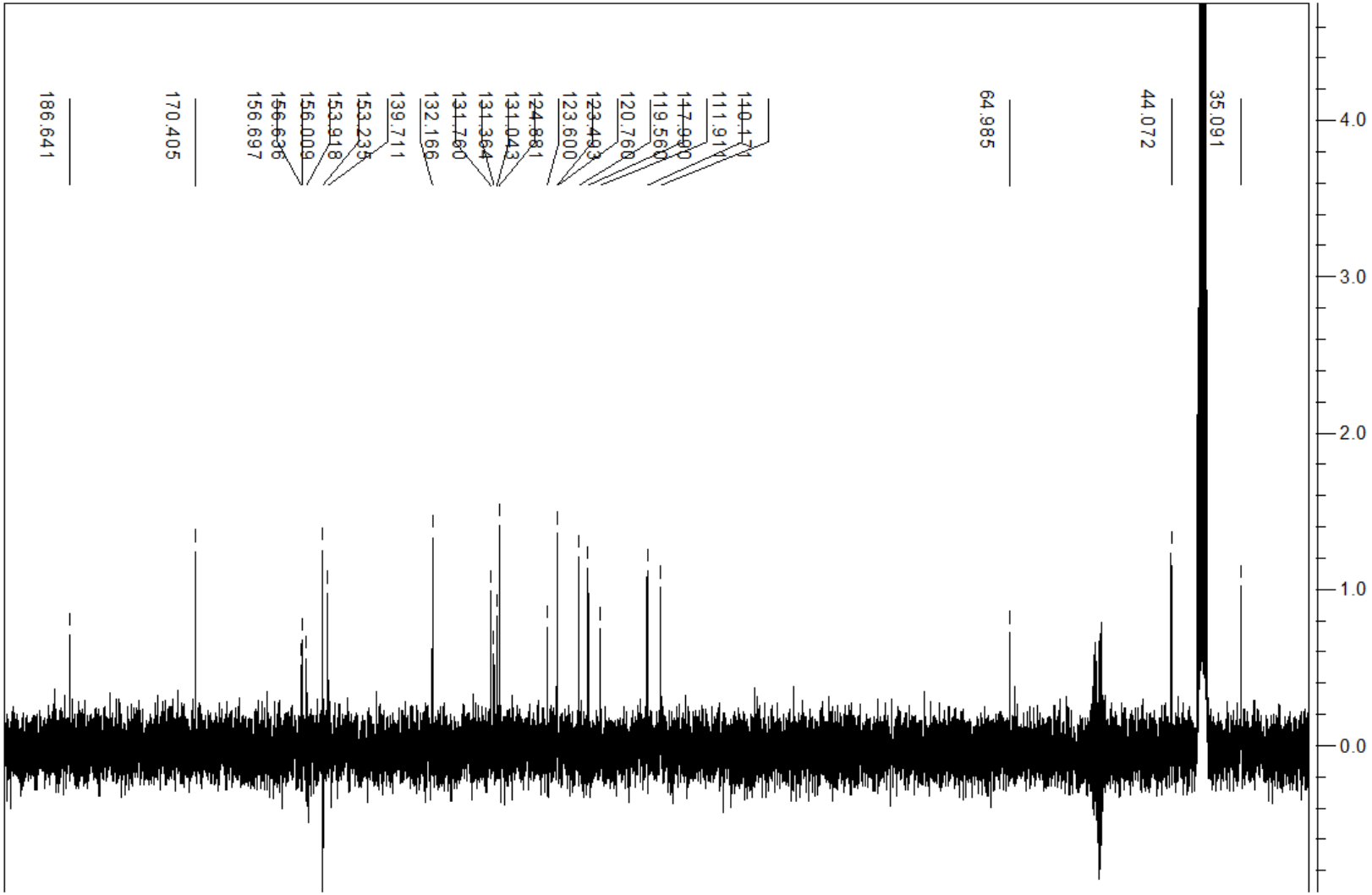
m/z	z	Abund
252.0851	1	26925.42
253.0882	1	4379.56
413.057	1	25530.52
414.0738	1	5958.61
415.0681	1	16763.31
435.0528	1	7777.15
437.0509	1	5155.4
825.134	1	5162.04
827.133	1	7174.09
829.1291	1	4059.65

Compound Structure

HRMS (ESI) of **3g.**


12.975
10.321
8.003
7.550
7.528
7.508
7.490
7.459
7.440
7.364
7.346
7.243
4.593
4.576
4.562
4.545
3.995
3.964
3.934
3.162
3.147
2.942
2.931
2.903
8.783
12.094
12.405
6.438
24.263
15.933
4.539
50
0
1.00
0.98
1.02
1.04
0.99
1.04
1.02
0.96

^{1}H NMR of **3h**.

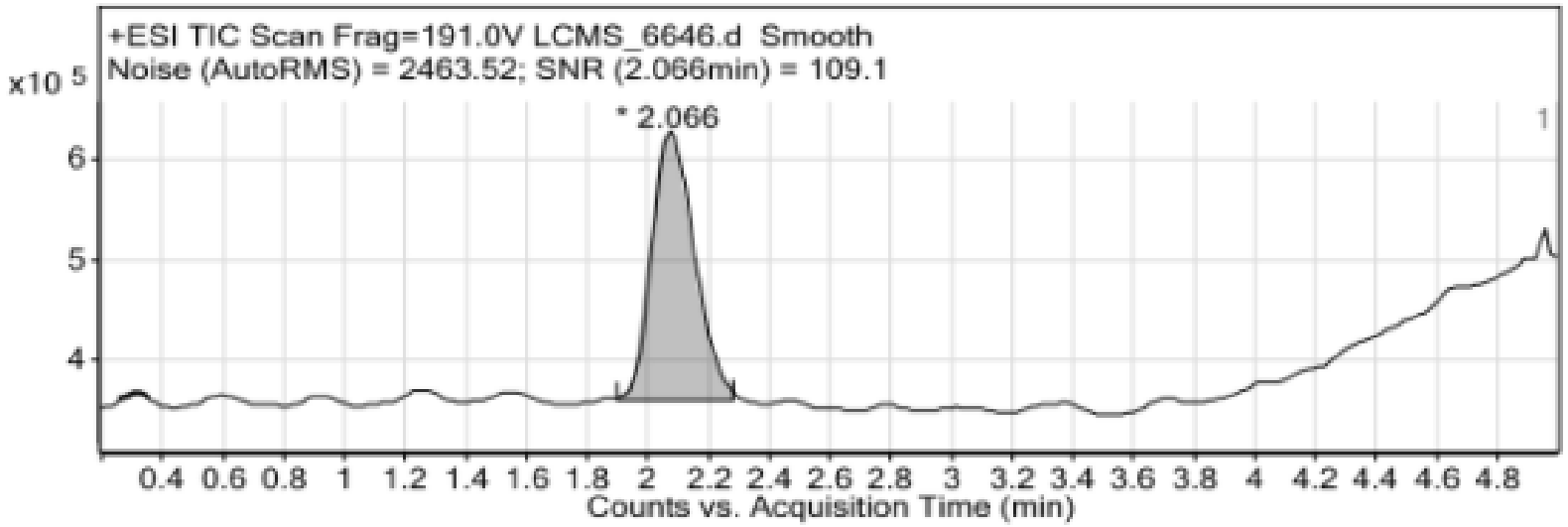

186.641
170.405
156.697
156.636
156.009
153.918
153.235
139.711
132.166
131.760
131.364
131.043
124.881
123.600
123.493
120.760
119.560
117.990
111.911
64.985
44.072
35.091
4.0
3.0
2.0
1.0
0.0

^{13}C NMR of **3h**.

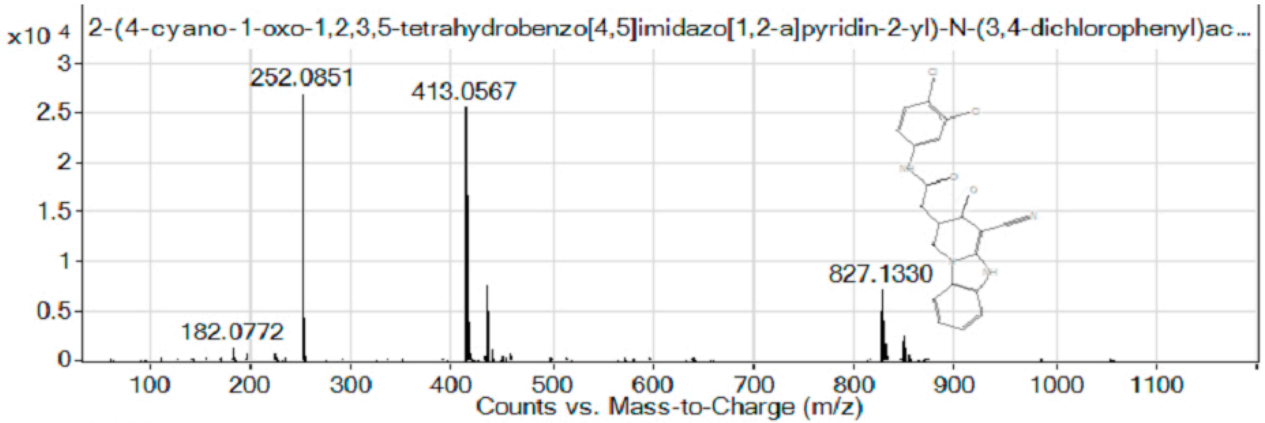
Data File	LCMS_6646.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 24
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 1:44:26 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



Qualitative Compound Report

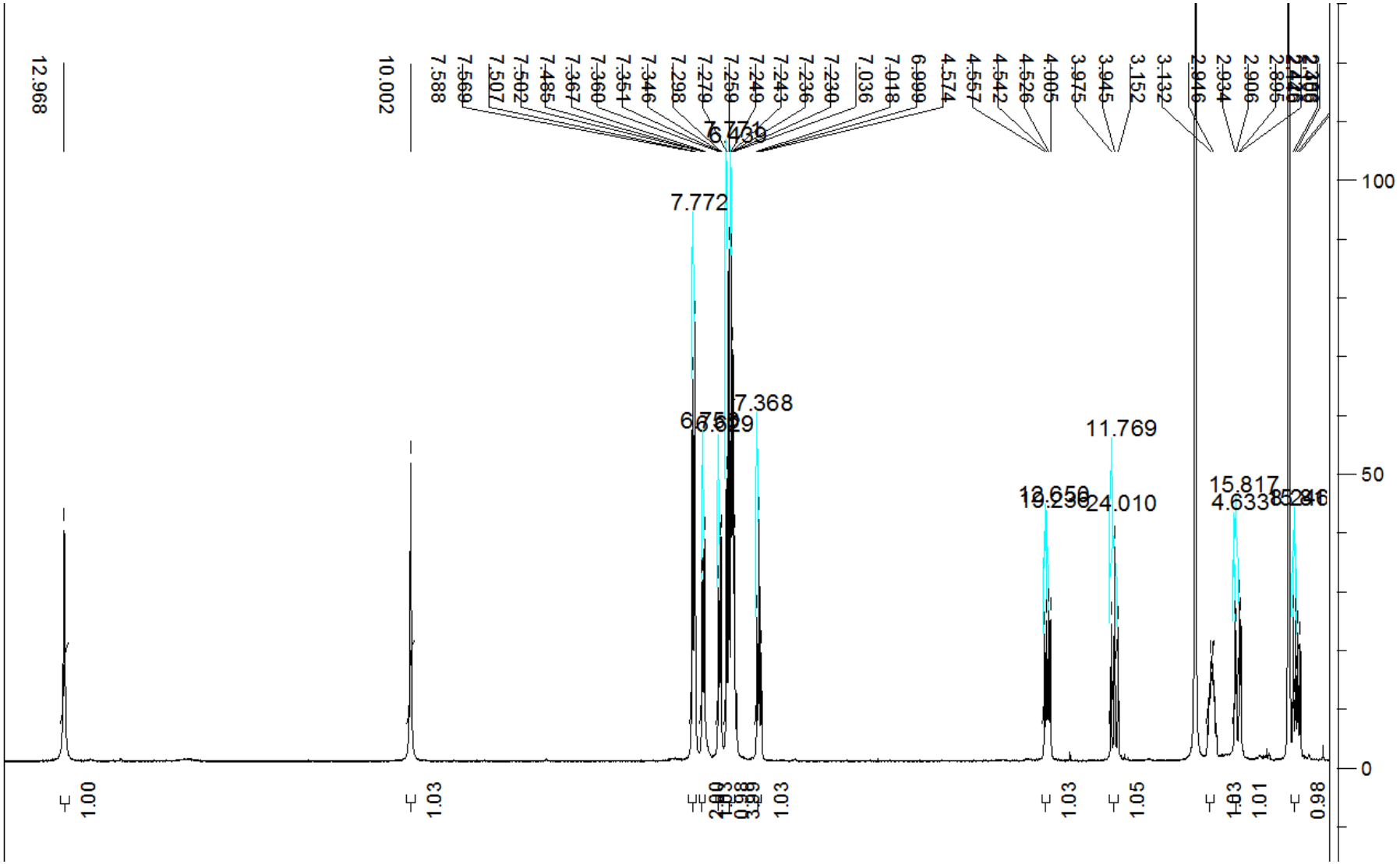


MS Spectrum Peak List

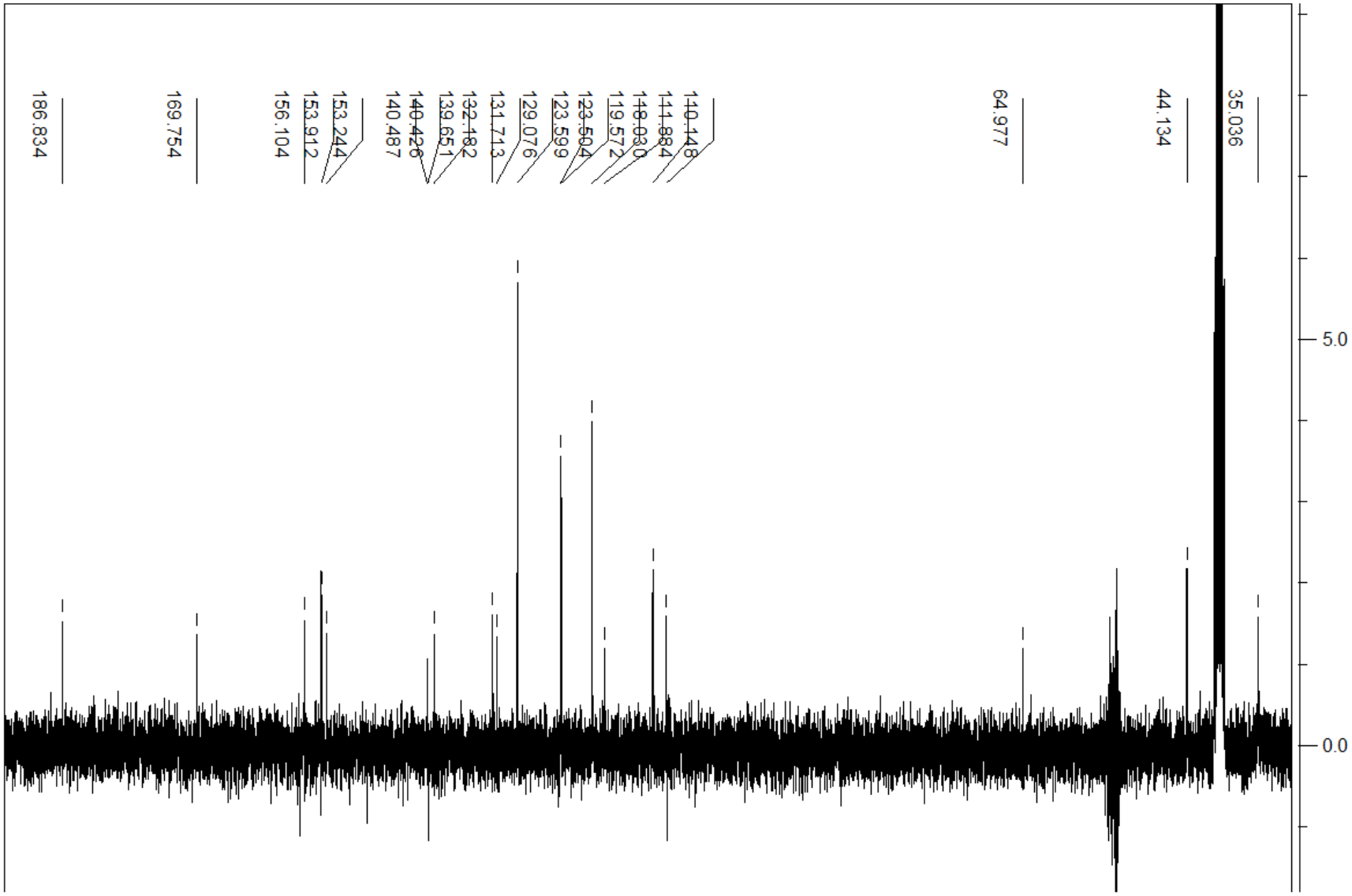
m/z	z	Abund
252.0851	1	26925.42
253.0882	1	4379.56
413.0567	1	25530.52
414.0738	1	5958.61
415.0681	1	16763.31
435.0528	1	7777.15
437.0509	1	5155.4
825.134	1	5162.04
827.133	1	7174.09
829.1291	1	4059.65

Compound Structure

HRMS (ESI) of **3h.**


12.968
10.002
7.588
7.569
7.507
7.502
7.485
7.367
7.360
7.351
7.346
7.298
7.279
7.259
7.249
7.243
7.236
7.230
7.036
7.018
6.999
4.574
4.557
4.542
4.526
4.005
3.975
3.945
3.152
3.132
2.946
2.934
2.906
2.895
7.772
6.439
7.368
11.769
24.010
15.817
4.633
100
50
0
1.00
1.03
1.03
1.03
1.05
1.01
0.98

^{1}H NMR of **3i**.

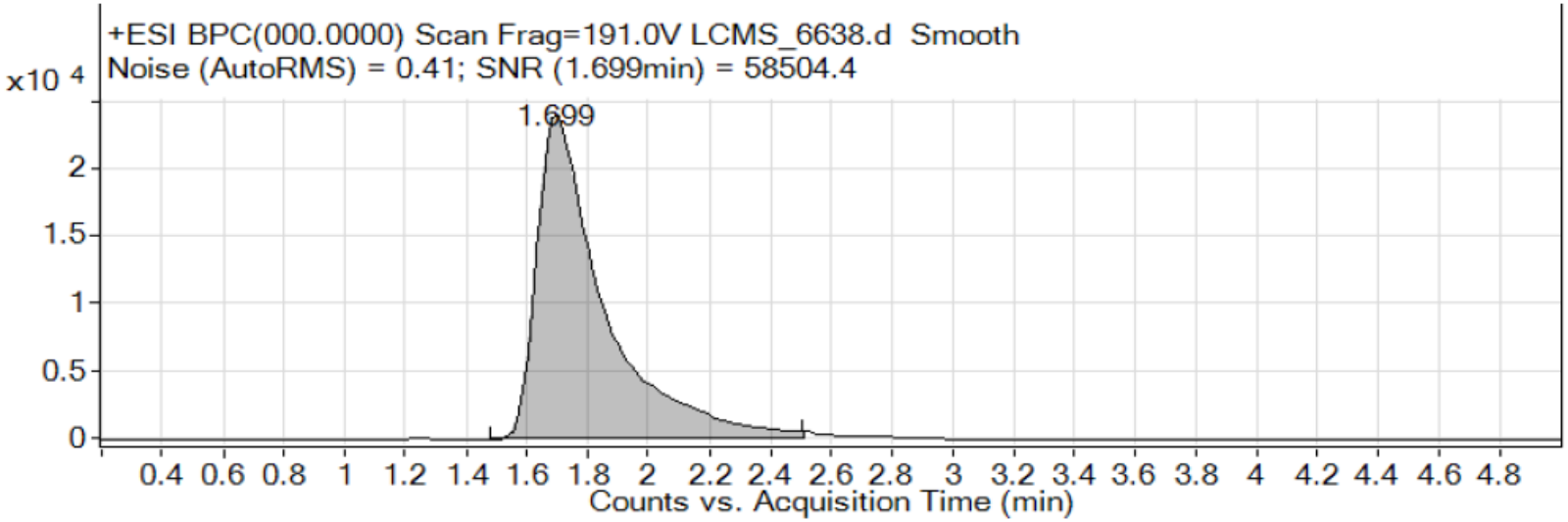

186.834
169.754
156.104
153.912
153.244
140.487
140.426
139.651
132.182
131.713
129.076
123.599
123.504
119.572
118.030
111.884
110.148
64.977
44.134
35.036
5.0
0.0

^{13}C NMR of **3i**.

Data File	LCMS_6638.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 16
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 12:09:41 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



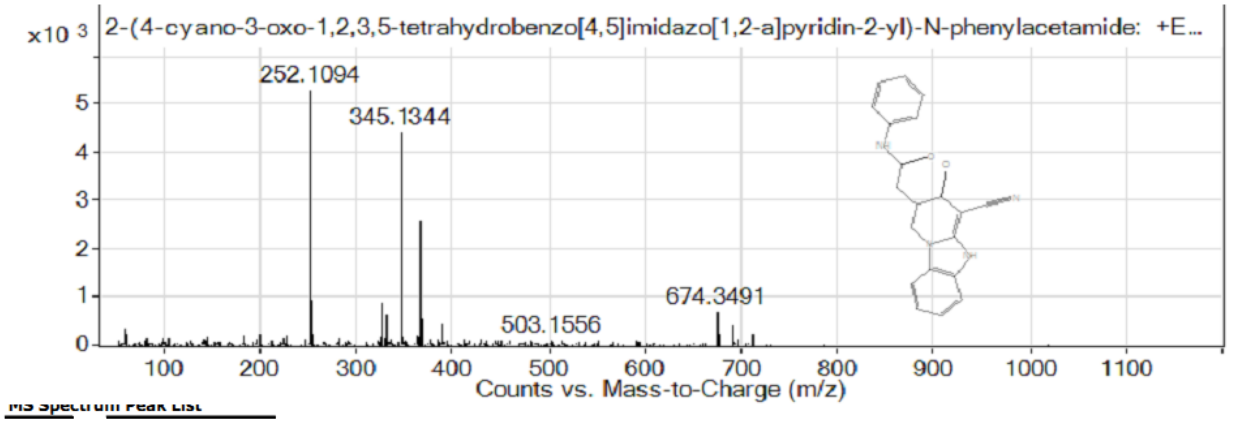
Qualitative Compound Report

Compound Table

Compound Label	RT	Name	Formula	MFG Formula	DB Formula
Cpd 1: 2-(4-cyano-3-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-phenylacetamide	1.684	2-(4-cyano-3-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-phenylacetamide	C20H16N4O2	C20H16N4O2	C20H16N4O2

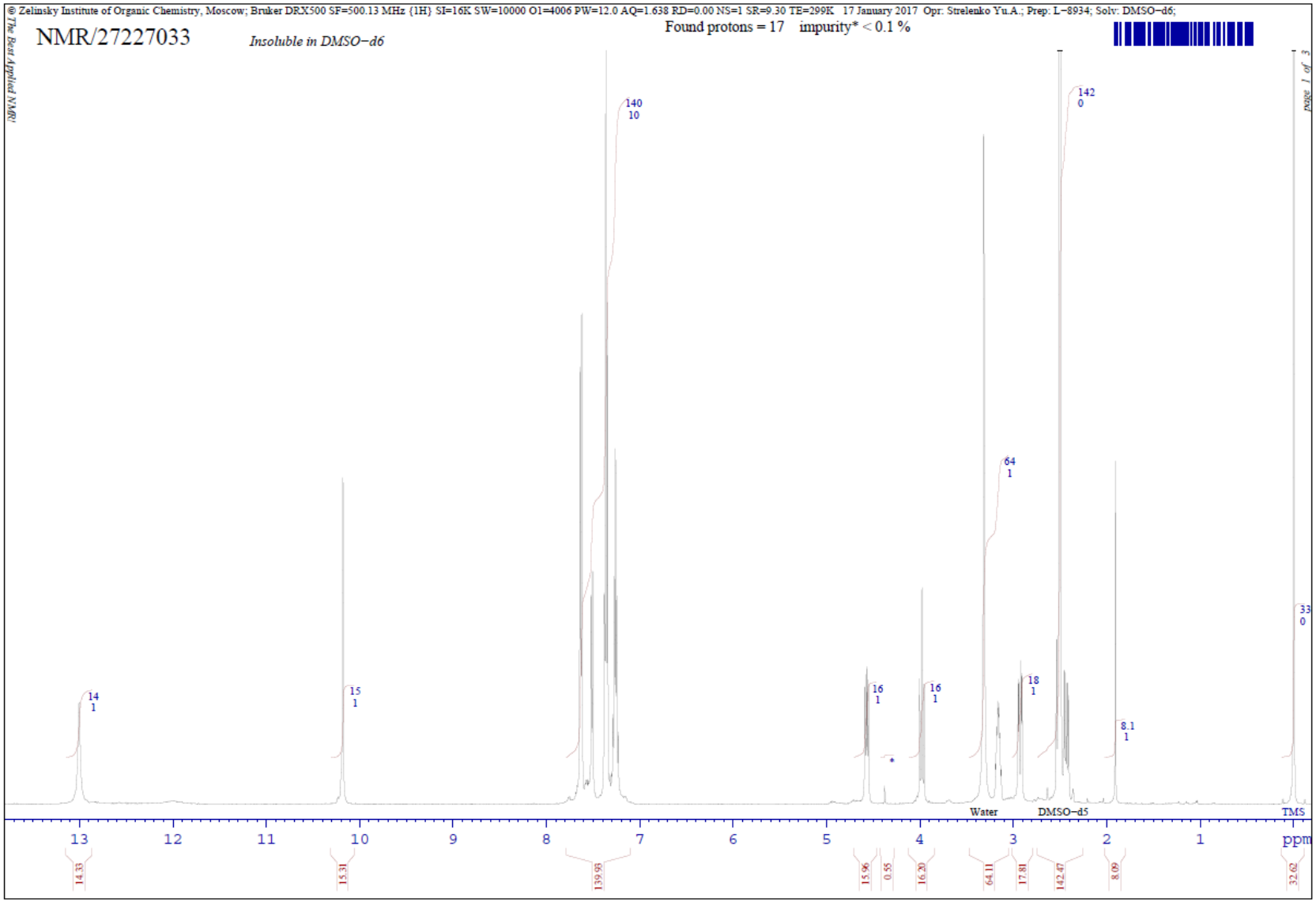
Compound Label	Name	RT	Algorithm
Cpd 1: 2-(4-cyano-3-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-phenylacetamide	**2-(4-cyano-3-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)-N-**	1.684	Spectrum Extraction

MS Spectrum

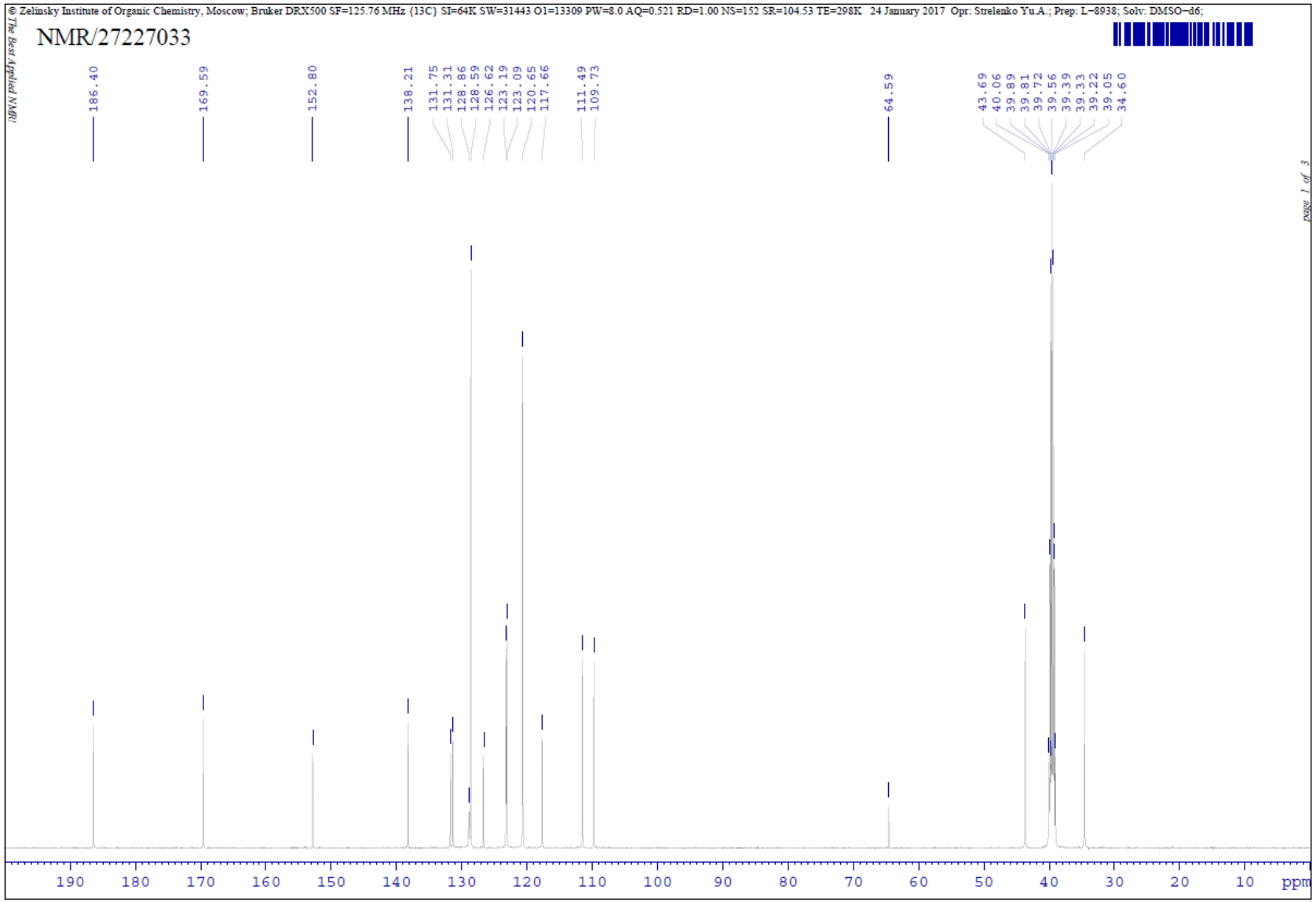


MS Spectrum Peak List

HRMS (ESI) of **3i.**


© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz {1H} SI=16K SW=10000 O1=4006 PW=12.0 AQ=1.638 RD=0.00 NS=1 SR=9.30 TE=299K 17 January 2017 Opr: Strelenko Yu.A.; Prep: L−8934; Solv: DMSO−d6;
The Best Applied NMR!
NMR/27227033
Insoluble in DMSO−d6
Found protons = 17 impurity* < 0.1 %
page 1 of 3
140
10
142
0
64
1
14
1
15
1
16
1
16
1
18
1
8.1
1
33
0
Water
DMSO−d5
TMS
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
14.33
15.31
139.93
15.96
0.55
16.20
64.11
17.81
142.47
8.09
32.62

^{1}H NMR of **3j**.

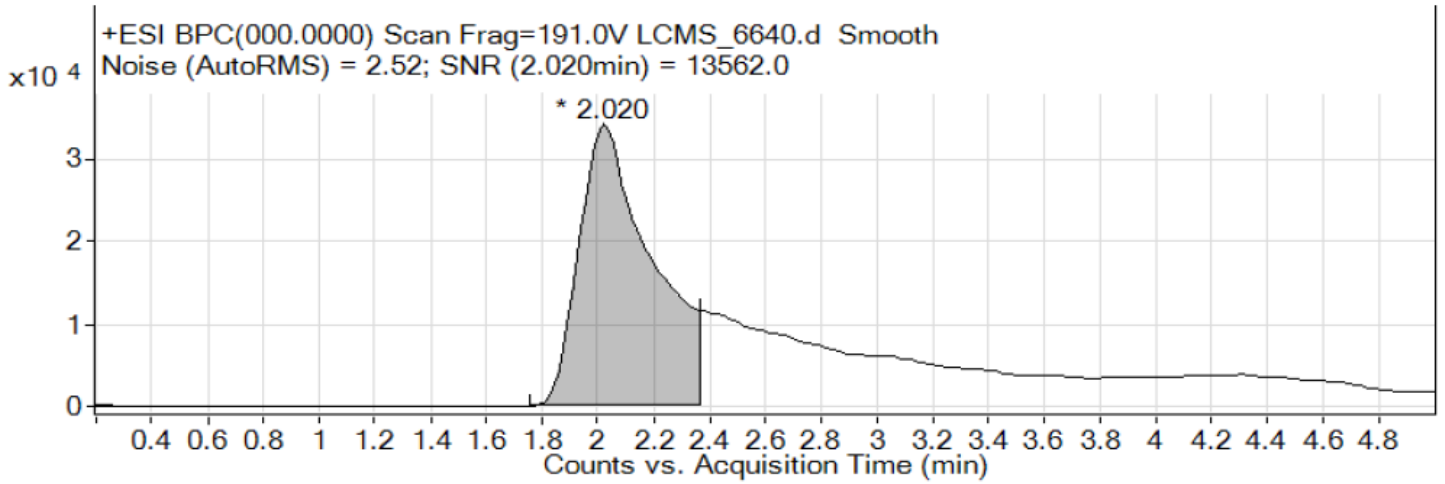

© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=125.76 MHz (13C) SI=64K SW=31443 O1=13309 PW=8.0 AQ=0.521 RD=1.00 NS=152 SR=104.53 TE=298K 24 January 2017 Opr: Strelenko Yu.A.; Prep: L-8938; Solv: DMSO-d6;
NMR/27227033
The Best Applied NMR!
186.40
169.59
152.80
138.21
131.75
131.31
128.86
128.59
126.62
123.19
123.09
120.65
117.66
111.49
109.73
64.59
43.69
40.06
39.89
39.81
39.72
39.56
39.39
39.33
39.22
39.05
34.60
Page 1 of 3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

^{13}C NMR of **3j**.

Data File	LCMS_6640.d	**Sample Name**	
Sample Type	Sample	**Position**	Vial 18
Instrument Name	Instrument 1	**User Name**	
Acq Method	ACN-H2O_60-40.m	**Acquired Time**	16-Jun-20 12:33:42 PM
IRM Calibration Status	Success	**DA Method**	13032017.m
Comment			

Sample Group		**Info.**	
Stream Name	LC 1	**Acquisition SW Version**	6200 series TOF/6500 series Q-TOF B.06.01 (B6157)

Fragmentor Voltage 191 **Collision Energy** 0 **Ionization Mode** ESI



User Chromatogram Peak List

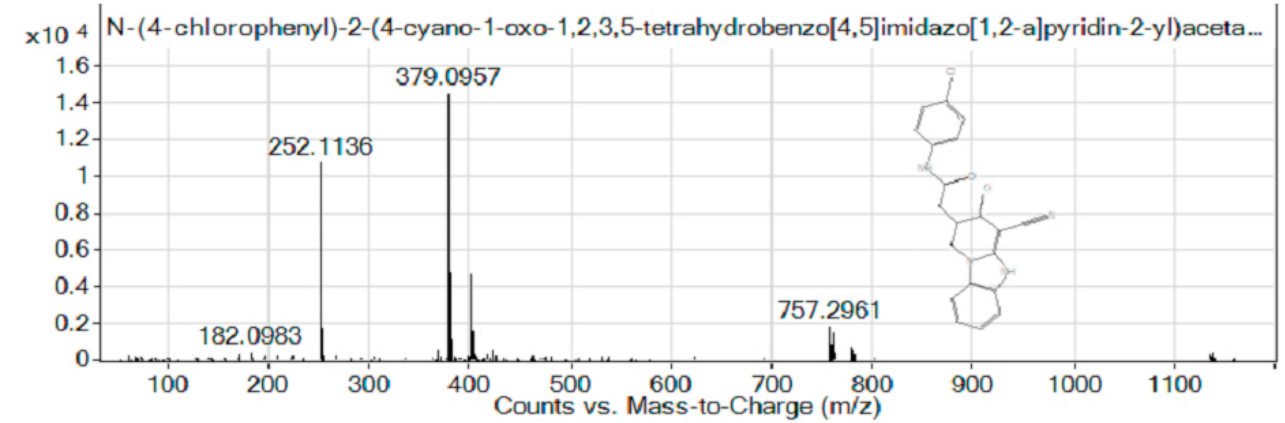
Qualitative Compound Report

Compound Table

Compound Label	RT	Name	Formula	MFG Formula	DB Formula
Cpd 1: N-(4-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)acetamide	2.02	N-(4-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)acetamide	C20H15ClN4O2	C20H15ClN4O2	C20H15ClN4O2

Compound Label	Name	RT	Algorithm
Cpd 1: N-(4-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-2-yl)acetamide	**N-(4-chlorophenyl)-2-(4-cyano-1-oxo-1,2,3,5-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridin-**	2.02	Spectrum Extraction

MS Spectrum



HRMS (ESI) of **3j.**