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# New regio/chemoselective synthesis of hydrogenated imidazo[1,5-*b*]pyridazines

**Dmitriy Yu. Vandyshev, Khidmet S. Shikhaliev, Mikhail Yu. Krysin, Tatiana N. Ilyinova, Daria A. Mangusheva, Oleg E. Sidorenko and Renata R. Iminova**

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## Results of quantum-chemical calculations

Another evidence for the preferred chemoselective heterocyclisation by the ester group was quantum chemical calculations of cyanoacetic ester derivatives using the AM1 and DFT methods[1] (Figures S1-S3). The positive charge on the carbon atom of the ester group significantly exceeded the same of nitrile carbon atom.

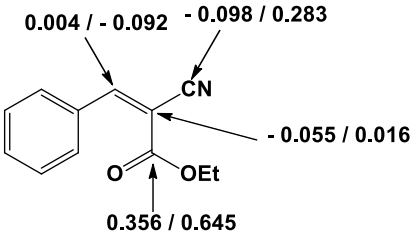



**Figure S1.** Values of charges in reaction centres (AM1/B3LYP)

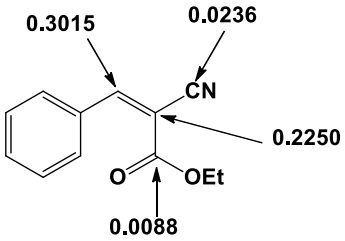
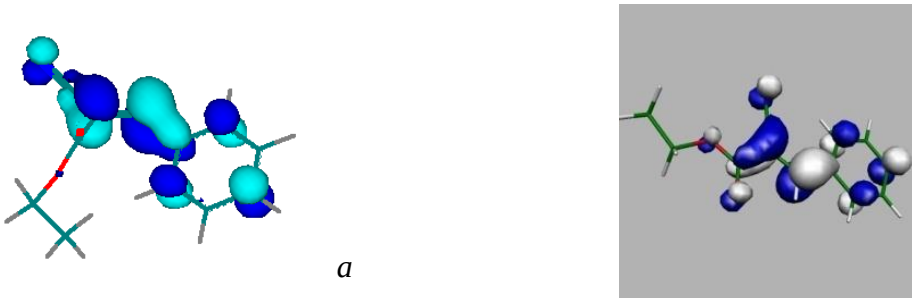



**Figure S2.** Atomic contributions to NBMO (AM1)



*a* *b*

**Figure S3.** NBMO structure of ethyl 2-benzylidene-2-cyanoacetate, (*a*) AM1, (*b*) B3LYP

We also have performed quantum chemical calculations of the initial diaminoimidazole molecule geometry and electronic structure molecule to explain the reaction selectivity based on

density functional theory and the B3LYP exchange-correlation potential, with the 6-31G** basis.[S1] It was shown that the nitrogen atom of the amino group in the second position is most negatively charged, although it is not much different from the hydrazine fragment (Figure S4). However, the molecular electrostatic potential (MEP), which most properly describes the electrostatic interactions between molecules, provided a different result. The MEP near the imidazole molecule showed that the most negative region of the molecule was localised at the endocyclic nitrogen atom. Apparently, this is due to the fact that the remaining nucleophilic centres are associated with positively charged carbon and/or nitrogen atoms, which weakens the electrostatic effect of these centres (Figure S5).

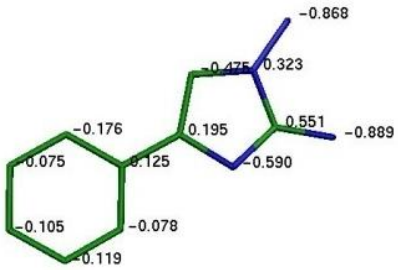



**Figure S4.** Values of charges in the reaction centres of the 1,2-diamino-4-phenylimidazole molecule **1**

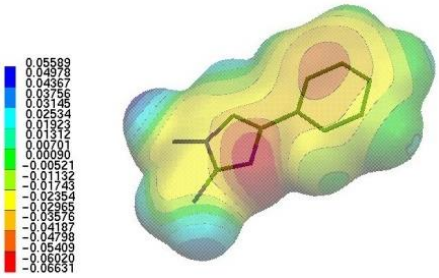



**Figure S5.** Molecular electrostatic potential in the molecule of the initial diamine **1**

However, the charge value is not the only factor that determines electrophilic-nucleophilic interactions. Reactions can also proceed under orbital control. Therefore, we calculated HOMO electron population (Figure S6). The region where the HOMO wave function is not zero and the electron density is high is concentrated on the imidazole cycle, the CH fragment in particular.

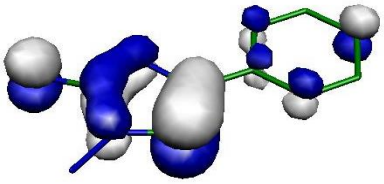


**Figure S6.** HOMO of the 1,2-diamino-4-phenylimidazole molecule

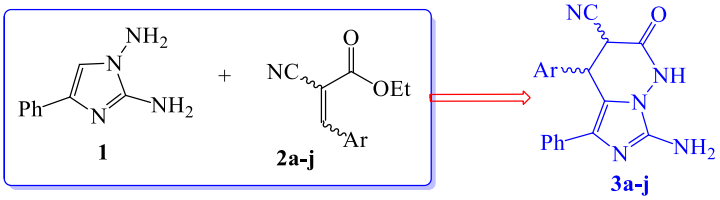
[S1]. M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E.Scuseria, M.A. Robb, J.R. Cheeseman, G. Scalmani, V. Barone, B.Mennucci, G.A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H.P. Hratchian, A.F. Izmaylov, J. Bloino, G. Zheng, J.L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J.A. Montgomery Jr., J.E. Peralta, F. Ogliaro, M. Bearpark, J.J. Heyd, E. Brothers, K.N. Kudin, V.N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J.C. Burant, S.S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J.M. Millam, M. Klene, J.E. Knox, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O.Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, R.L. Martin, K. Morokuma, V.G. Zakrzewski, G.A. Voth, P. Salvador, J.J. Dannenberg, S. Dapprich, A.D. Daniels, O. Farkas, J.B. Foresman, J.V. Ortiz, J. Cioslowski, D.J. Fox, Gaussian 16, Revision B.01; Gaussian, Inc.: Wallingford, CT, **2016**.

## General information (instrumentation)

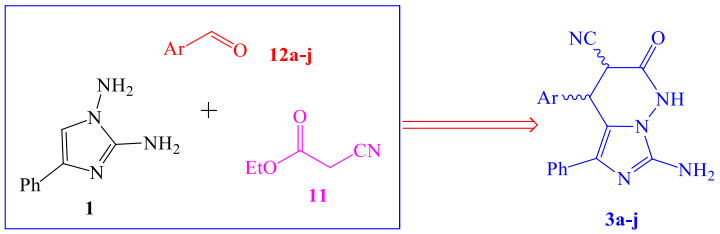
IR spectra were recorded on a Bruker Vertex 70 spectrometer with a Platinum ATR accessory. $^{1}$H NMR, $^{13}$C NMR, NOESY spectra were recorded on Bruker DRX-500 and DRX-600 devices (500.13/600.13 and 125.75 MHz, respectively) in DMSO-$d_6$ and TFA-d with the internal TMS standard. Melting temperatures were taken on a StuartSMP30 device. HPLC/MS spectra were recorded on an Agilent Infinity 1260 chromatograph with MS interface Agilent 6230 TOFLC/MS. Conditions for the separation: mobile phase MeCN/$H_2O$ + 0.1% FA (formic acid), gradient elution, column - Poroshell 120 EC-C18 (4.6 x 50 mm, 2.7 μm), thermostat 23-28°C, flow rate of 0.3-0.4 ml min$^{-1}$. Electrospray ionization (capillary – 3.5 kV; fragmentor + 191V; OctRF + 66V – positive polarity). The reaction progress and purity of the obtained compounds were controlled by TLC on Merck TLC Silica gel 60 F254 plates in a 20:1 $CHCl_3$–MeOH system (visualisation under UV light). The commercially available reagents were purchased from Lancaster.

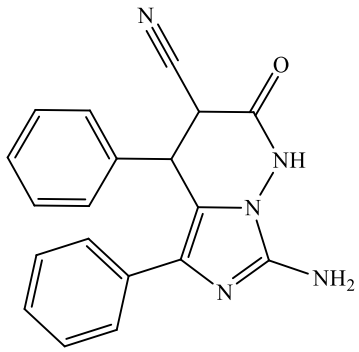
## General procedure for the synthesis of 7-amino -4-aryl-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitriles 3a-j

**Method A.** A mixture of 1,2-diamino-5-phenylimidazole **1** (5 mmol), ethyl 2-arylidene-2-cyanoacetate **2a-j** (5 mmol), and 1,4-dioxane (5 ml) with the addition of acetic acid (5 mol.%) was refluxed. The precipitate formed after 6 hours of boiling was filtered off and recrystallized from a mixture of isopropyl alcohol and DMF (3:1).




**Method B**. A mixture of 1,2-diamino-5-phenylimidazole **1** (5 mmol), ethyl cyanoacetate **11** (5 mmol), aldehyde **12a-j** (5 mmol), and 1,4-dioxane (5 ml) with the addition of acetic acid (5 mol.%) was refluxed. The precipitate formed after 7-8 hours of boiling was filtered and recrystallised from a mixture of isopropyl alcohol and DMF (3:1).



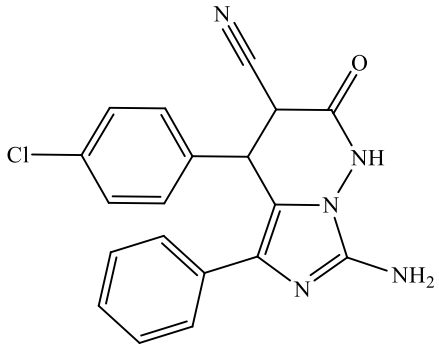



**Molecular formula : $C_{19}H_{15}N_5O$**

**3a**

**7-Amino-2-oxo-4,5-diphenyl-1,2,3,4-tetrahydro-imidazo[1,5-*b*]pyridazine-3-carbonitrile 3a** (mixture of diastereomers 90:1).

Yield: A - 1155 mg (70%); B - 858 mg (52%); white powdery; m.p. > 300 °C. $^1$H NMR (500.13 MHz, DMSO-$d_6$): δ = 3.77, 4.95 (d as br.s and d, $J_{H,H}$ = 3.2 Hz, 1H, CH-4); 4.54, 4.89 (d as br.s and d, $J_{H,H}$ = 5.1 Hz, 1H, CH-3); 6.86, 7.06 (both br.s, 2H, $NH_2$); 7.23-7.40 (m, 10H, H-Ph); 12.50 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 162.2 (CO), 161.7 (CO), 140.9 (C-7), 140.8 (C-7), 137.8 (C-Ar), 137.7 (C-Ar), 128.9 (C-Ar), 128.9 (C-Ar), 128.8 (C-Ar), 128.2 (C-Ar), 128.1 (C-Ar), 127.9 (C-Ar), 127.7 (C-Ar), 127.6 (C-Ar), 127.3 (C-Ar), 125.7 (C-Ar), 125.3 (C-Ar), 118.4 (CN), 117.3 (CN), 115.2 (C-4a), 39.1 (C-3), 39.0 (C-3), 38.9 (C-4), 38.1 (C-4) ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3382 (N-H, $NH_2$ + lactam); 3059, 2661 (br, C-H + H-bond $NH_2$, lactam); 2224 (CN); 1672 (amid I); 1650 (NH); 1552 (C=N imidazole + amid II); 1497 (Ph); 1213 (C-N amin); 766 (C-H Ph); 692 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{19}H_{15}N_5O$: 330.1350 $[M+H]^+$; found 330.1350 (RT 1.337) and 330.1349 (RT 1.767) $[M+H]^+$.

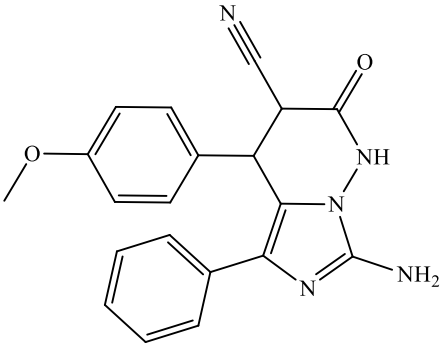



**Molecular formula : $C_{19}H_{14}ClN_5O$**

**3b**

**7-Amino-4-(4-chlorophenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3b** (mixture of diastereomers 3:1).

Yield: A - 1256 mg (69%); B - 874 mg (48%); white powdery; m.p. > 300 °C. $^1$H NMR (500.13 MHz, DMSO-$d_6$): δ = 3.80, 4.96 (d as br.s and d, $J_{H,H}$ = 4.2 Hz, CH-4); 4.54, 4.98 (d as br.s and d, $J_{H,H}$ = 5.7 Hz, 1H, CH-3); 6.84, 7.06 (both br.s, 2H, $NH_2$); 7.21-7.38 (m, 7H, H-Ar); 7.45 (d, $J_{H,H}$ = 8.5 Hz, 2H, H-Ar); 12.60 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 161.7, 161.4, 140.7, 136.7, 136.5, 132.8, 132.6, 130.1, 129.7, 128.9, 128.8, 128.7, 128.7, 127.6, 127.3, 125.8, 125.2, 118.2, 117.2, 116.6, 114.9, 38.5, 37.3 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3378 (N-H, $NH_2$ + lactam); 3035 (br, C-H + H-bond $NH_2$, lactam); 1671 (amid I); 1651 (NH); 1599 (Ar); 1556 (C=N imidazole + amid II); 1492 (Ar); 1209 (C-N amin); 1167 (C-N amin); 812 (p-$C_6H_4$); 766 (C-H Ph); 695 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{19}H_{14}ClN_5O$: 364.0960 $[M+H]^+$; found 364.0960 (RT 1.093) and 364.0963 (RT 1.253) $[M+H]^+$.

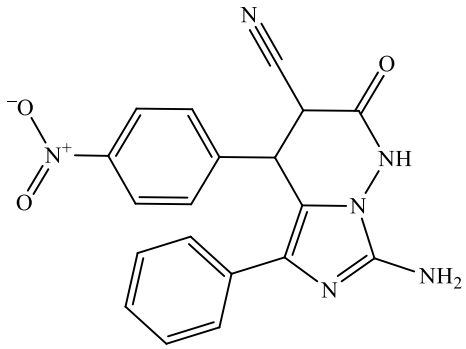


**Molecular formula: $C_{20}H_{17}N_5O_2$**

**3c**

**7-Amino-4-(4-methoxyphenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3c** (mixture of diastereomers 3:2).

Yield: A - 1224 mg (68%); B - 1008 mg (56%); white powdery; m.p. > 300 °C. $^1$H NMR (500.13 MHz, DMSO-$d_6$): δ = 3.70, 4.86 (d as br.s and d, $J_{H,H}$ = 3.2 Hz, 1H, CH-4); 3.73 (s, 3H, $OCH_3$); 4.49, 4.83 (d as br.s and d, $J_{H,H}$ = 5.6 Hz, 1H, CH-3); 6.76, 7.01 (both br.s, 2H, $NH_2$); 6.86, 6.93 (both d, $J_{H,H}$ = 8.6 Hz, 2H, H-Ar), 7.19, 7.24 (both d, $J_{H,H}$ = 8.6 Hz, 2H, H-Ar), 7.25-7.37 (m, 5H, H-Ph); 12.48 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 162.3, 161.8, 158.9, 158.8, 140.9, 140.8, 129.6, 129.5, 129.4, 128.9, 128.8, 128.3, 127.5, 127.3, 125.6, 125.2, 118.4, 117.3, 115.5, 114.3, 114.2, 55.1, 40.2, 38.5, 37.4 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3371 (N-H, $NH_2$ + lactam); 3037 (br, C-H + H-bond $NH_2$, lactam); 2215 (CN); 1672 (amid I); 1648 (NH); 1554 (C=N imidazole + amid II); 1510 (Ar); 1247 (Ar-O-Me); 1211 (C-N amin); 1180 (C-N amin); 821 (p-$C_6H_4$); 769 (C-H Ph); 696 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{20}H_{17}N_5O_2$: 360.1456 $[M+H]^+$; found 360.1456 (RT 1.130) and 360.1451 (RT 1.317) $[M+H]^+$.

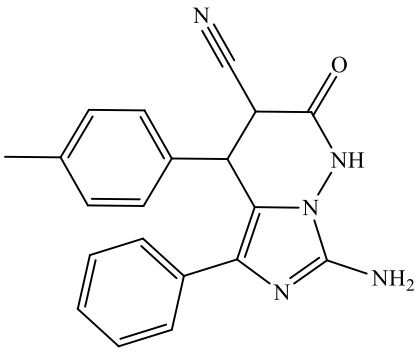


**Molecular formula: $C_{19}H_{14}N_6O_3$**

**3d**

**7-Amino-4-(4-nitrophenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3d** (mixture of diastereomers 15:1).

Yield: A - 1238 mg (66%); B - 956 mg (51%); white powdery; m.p. > 300 °C. $^1$H NMR (500.13 MHz, DMSO-$d_6$): δ = 3.92, 5.18 (d as br.s and d, $J_{H,H}$ = 3.7 Hz, 1H, CH-4); 4.62, 5.17 (d as br.s and d, $J_{H,H}$ = 2.4 Hz, 1H, CH-3); 6.91, 7.08 (both br.s, 2H, $NH_2$); 7.18-7.38 (m, 5H, H-Ph); 7.58, 7.61 (both d, $J_{H,H}$ = 8.7 Hz, 2H, H-Ar), 8.13, 8.26 (both d, $J_{H,H}$ = 8.7 Hz, 2H, H-Ar), 12.58 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 161.4, 161.2, 147.2, 147.0, 145.1, 144.9, 140.9, 140.8, 131.6, 130.6, 129.7, 129.5, 128.9, 128.8, 128.6, 127.7, 127.5, 127.1, 126.0, 125.3, 124.1, 123.9, 123.8, 123.1, 118.0, 117.3, 115.8, 114.5, 38.8, 37.5 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3369 (N-H, $NH_2$ + lactam); 3029 (br, C-H + H-bond $NH_2$, lactam); 2228 (CN); 1673 (amid I); 1648 (NH); 1600 (Ar); 1556 (C=N imidazole + amid II); 1516, 1349 ($NO_2$); 1211 (C-N amin); 857 (p-$C_6H_4$); 771 (C-H Ph); 699 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{19}H_{14}N_6O_3$: 375.1201 $[M+H]^+$; found 375.1201 (RT 1.137) and 375.1204 (RT 1.303) $[M+H]^+$.

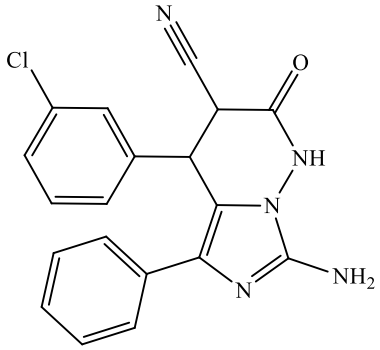



**Molecular formula: $C_{20}H_{17}N_5O$**

**3e**

**7-Amino-4-(4-methylphenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3e** (mixture of diastereomers 5:1).

Yield: A - 1273 mg (74%); B - 791 mg (46%); white powdery; m.p. > 300 °C. $^1$H NMR (500.13 MHz, DMSO-$d_6$): δ = 2.22, 2.23 (both s, 3H, $CH_3$); 3.81, 4.89 (both d, $J_{H,H}$ = 2.9 and 5.7 Hz, 1H, CH-4); 4.58, 4.96 (both d, $J_{H,H}$ = 2.9 and 5.7 Hz, 1H, CH-3) 7.10-7.35 (m, 11H, H-Ar + $NH_2$); 12.52 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 162.3, 161.7, 140.9, 137.3, 137.2, 134.7, 129.4, 128.8, 128.7, 128.0, 127.5, 127.4, 127.2, 125.5, 125.1, 118.4, 117.2, 115.2, 38.7, 37.7, 20.6 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3376 (N-H, $NH_2$ + lactam); 3051 (br, C-H + H-bond $NH_2$, lactam); 2212 (CN); 1673 (amid I); 1649 (NH); 1593 (Ar); 1556 (C=N imidazole + amid II); 1214 (C-N amin); 824 (p-$C_6H_4$); 767 (C-H Ph); 694 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{20}H_{17}N_5O$: 344.1507 $[M+H]^+$; found 344.1507 (RT 1.037) and 344.1503 (RT 1.320) $[M+H]^+$.

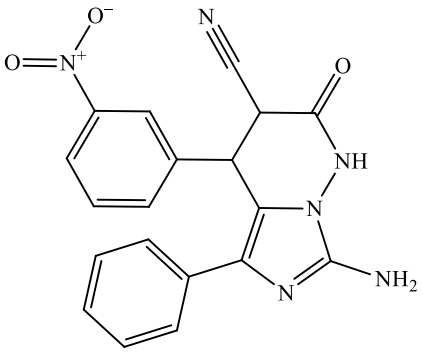



**Molecular formula: $C_{19}H_{14}ClN_5O$**

**3f**

**7-Amino-4-(3-chlorophenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3f** (mixture of diastereomers 5:1).

Yield: A - 1309 mg (70%); B - 430 mg (23%); light yellow powdery; m.p. > 300 °C. $^1$H NMR (600.13 MHz, DMSO-$d_6$): δ = 3.91, 5,00 (d as br.s and d, $J_{H,H}$ = 4.6 Hz, 1H, CH-4); 4.59, 5.03 (d as br.s and d, $J_{H,H}$ = 5.7 Hz, 1H, CH-3); 6.98, 7.15 (both br.s, 2H, $NH_2$); 7.21-7.36 (m, 5H, H-Ar); 7.37 (s, 1H, H-Ar); 7.38-7.43 (m, 3H, H-Ar); 12.62 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 161.5, 161.2, 140.8, 140.1, 139.8, 133.3, 130.6, 130.5, 128.6, 128.5, 128.0, 127.8, 127.7, 127.5, 127.2, 127.0, 126.6, 125.8, 125.2, 118.1, 117.0, 39.1, 38.9, 38.7, 37.4 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3377 (N-H, $NH_2$ + lactam); 3058, 2666 (br, C-H + H-bond $NH_2$, lactam); 2227 (CN); 1673 (amid I); 1654 (NH); 1612 (Ar); 1556 (C=N imidazole + amid II); 1211 (C-N amin); 818 (m-$C_6H_4$); 766 (C-H Ph); 694 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{19}H_{14}ClN_5O$: 364.0960 $[M+H]^+$; found 364.0961 (RT 1.327) and 364.0960 (RT 1.553) $[M+H]^+$.

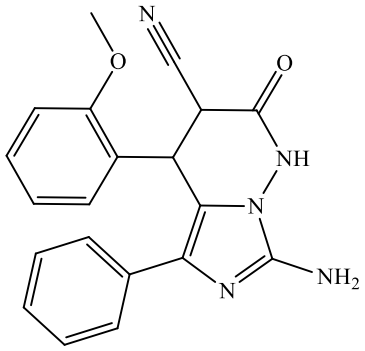


**Molecular formula: $C_{19}H_{14}N_6O_3$**

**3g**

**7-Amino-4-(3-nitrophenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3g** (mixture of diastereomers 25:1).

Yield: A - 1490 mg (82%); B - 782 mg (43%); white powdery; m.p. > 300 °C. $^1$H NMR (600.13 MHz, DMSO-$d_6$): δ = 4.05, 5.17 (d as br.s and d, $J_{H,H}$ = 5.9 Hz, 1H, CH-4); 4.62, 5.26 (d as br.s and d, $J_{H,H}$ = 4.4 Hz, 1H, CH-3); 7.02, 7.12 (both br.s, 2H, $NH_2$); 7.14-7.28 (m, 3H, H-Ar); 7.34 and 7.56 (both t, $J_{H,H}$ = 8.4 Hz, 1H, H-Ar); 7.69-7.75 (m, 2H, H-Ar); 7.82 and 8.06 (both d, $J_{H,H}$ = 8.2 Hz, 1H, H-Ar); 8.17-8.22 (m, 2H, H-Ar); 12.60 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 161.3, 161.2, 147.9, 147.8, 140.7, 139.9, 139.4, 135.1, 134.9, 130.5, 130.1, 128.8, 128.6, 127.6, 127.4, 126.4, 125.3, 123.1, 122.8, 118.0, 117.1, 39.2, 39.0, 38.9, 37.2 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3376 (N-H, $NH_2$ + lactam); 3064, 2661 (br, C-H + H-bond $NH_2$, lactam); 2231 (CN); 1672 (amid I); 1654 (NH); 1612 (Ar); 1555 (C=N imidazole + amid II); 1531, 1352 ($NO_2$); 1213 (C-N amin); 805 (m- $C_6H_4$); 767 (C-H Ph); 695 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{19}H_{14}N_6O_3$: 375.1201 $[M+H]^+$; found 375.1200 (RT 1.097) and 375.1202 (RT 1.323) $[M+H]^+$.

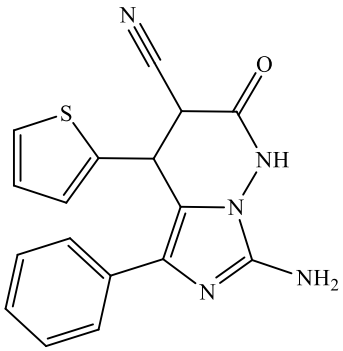


**Molecular formula: $C_{20}H_{17}N_5O_2$**

**3h**

**7-Amino-4-(2-methoxyphenyl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3h** (mixture of diastereomers 7:3).

Yield: A - 1400 mg (78%); B - 305 mg (17%); white powdery; m.p. 240-242 °C. $^1$H NMR (600.13 MHz, DMSO-$d_6$): δ = 3.88, 4.93 (d as br.s and d, $J_{H,H}$ = 3.0 Hz, 1H, CH-4); 3.89 (s, 3H, $OCH_3$); 4.55, 5.28 (d as br.s and d, $J_{H,H}$ = 6.1 Hz, 1H, CH-3); 6.85, 6.88 (both br.s, 2H, $NH_2$); 7.01-7.12 (m, 3H, H-Ar); 7.13-7.18 (m, 3H, H-Ar); 7.23-7.37 (m, 3H, H-Ar); 12.69 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 162.3, 161.9, 156.2, 156.1, 140.7, 129.7, 129.4, 128.8, 128.7, 128.3, 128.1, 127.6, 127.1, 125.9, 125.5, 125.1, 124.6, 121.0, 120.6, 118.4, 117.0, 111.6, 111.4, 55.8, 39.0, 38.9, 36.6, 34.4 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3371 (N-H, $NH_2$ + lactam); 3030, 2755 (br, C-H + H-bond $NH_2$, lactam); 1677 (amid I); 1656 (NH); 1599 (Ar); 1553 (C=N imidazole + amid II); 1251 (Ar-O-Me); 1215 (C-N amin); 754 (o-$C_6H_4$); 696 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{20}H_{17}N_5O_2$: 360.1456 $[M+H]^+$; found 360.1455 (RT 1.127) and 360.1456 (RT 1.330) $[M+H]^+$.

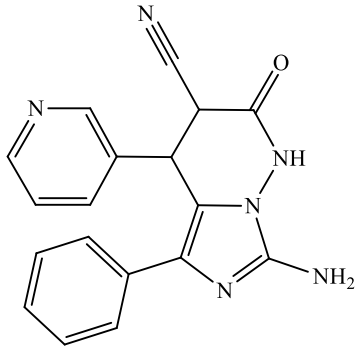


**Molecular formula: $C_{17}H_{13}N_5OS$**

**3i**

**7-Amino-4-(thiophen-2-yl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3i** (mixture of diastereomers 6:1).

Yield: A - 1173 mg (70%); B - 335 mg (20%); white powdery; m.p. > 300 °C. $^1$H NMR (600.13 MHz, DMSO-$d_6$): δ = 3.92, 5.31(d as br.s and d, $J_{H,H}$ = 2.2 Hz, 1H, CH-4); 4.59, 5.34 (d as br.s and d, $J_{H,H}$ = 5.2 Hz, 1H, CH-3); 6.96 (t, $J_{H,H}$ = 4.4 Hz, 1H, H-thiophen ); 7.02 (t, $J_{H,H}$ = 4.1 Hz, 1H, H-thiophen ); 7.06 (both br.s, 2H, $NH_2$); 7.17 (d, $J_{H,H}$ = 2.9 Hz, 1H, H-thiophen ); 7.27-7.32 (m, 2H, H-Ar); 7.37-7.47 (m, 3H, H-Ar); 12.75 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 161.7, 161.0, 140.3, 139.7, 128.7, 128.7, 127.6, 127.2, 127.0, 126.6, 126.4, 126.2, 126.0, 125.5, 125.3, 117.1, 38.9, 38.8, 34.8, 34.0 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3364 (N-H, $NH_2$ + lactam); 3057, 2722 (br, C-H + H-bond $NH_2$, lactam); 2225 (CN); 1671 (amid I); 1652 (NH); 1551 (C=N imidazole + amid II); 1210 (C-N amin); 767 (C-H Ph); 692 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{17}H_{13}N_5OS$: 336.0914 $[M+H]^+$; found 336.0913 (RT 1.233) and 336.0917 (RT 1.593) $[M+H]^+$.



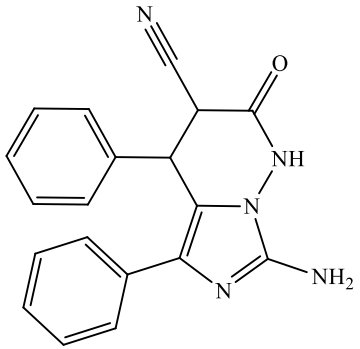
**Molecular formula: $C_{18}H_{14}N_6O$**

**3j**

**7-Amino-4-(pyridin-3-yl)-2-oxo-5-phenyl-1,2,3,4-tetrahydroimidazo[1,5-*b*]pyridazine-3-carbonitrile 3j** (mixture of diastereomers 3:1).

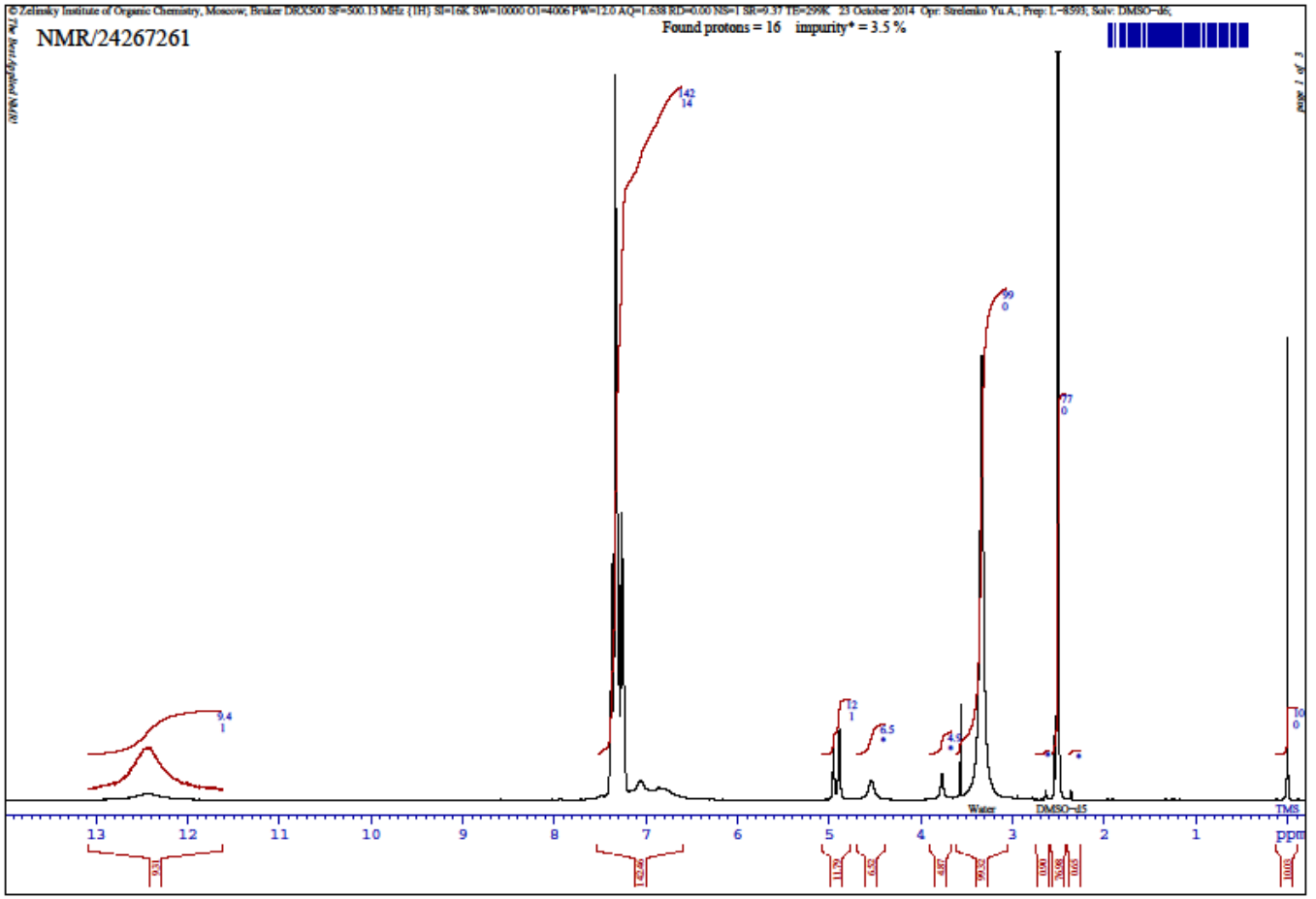
Yield: A - 1172 mg (71%); B - 479 mg (29%); white powdery; m.p. > 300 °C. $^1$H NMR (600.13 MHz, DMSO-$d_6$): δ = 3.94, 5.06 (both d, $J_{H,H}$ = 4.8 and 5.4 Hz, 1H, CH-4); 4.62, 5.00 (d as br.s and d, $J_{H,H}$ = 5.4 Hz, 1H, CH-3); 7.05, 7.19 (both br.s, 2H, $NH_2$); 7.20-7.29 (m, 2H, H-Ar); 7.32-7.41 (m, 2H, H-Ar); 7.65 (d, $J_{H,H}$ = 7.8 Hz, 1H, H-pyridin); 7.70 (d, $J_{H,H}$ = 7.9 Hz, 1H, H-pyridin); 8.42 (d, $J_{H,H}$ = 4.5 Hz, 1H, H-pyridine); 8.52-8.55 (m, 1H, H-Ar); 8.59 (s, 1H, H-pyridin); 12.75 (br.s, 1H, NH) ppm. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): δ = 161.5, 161.4, 149.2, 148.9, 140.9, 140.7, 135.7, 133.5, 133.1, 128.9, 128.5, 128.0, 127.6, 127.4, 126.1, 125.2, 123.9, 123.6, 118.1, 117.2, 116.1, 114.7, 39.1, 39.0, 37.1, 35.6 ppm. IR (FTIR ATR): $\lambda^{-1}$ = 3372 (N-H, $NH_2$ + lactam); 3056, 2663 (br, C-H + H-bond $NH_2$, lactam); 2232 (CN); 1673 (amid I); 1555 (C=N imidazole + amid II); 1212 (C-N amin); 768 (C-H Ph); 697 (C-H Ph + N-H) cm$^{-1}$. HRMS (ESI): *m/z* calcd. for $C_{18}H_{14}N_6O$: 331.1302 $[M+H]^+$; found 331.1302 (RT 1.157) and 331.1300 (RT 1.303) $[M+H]^+$.

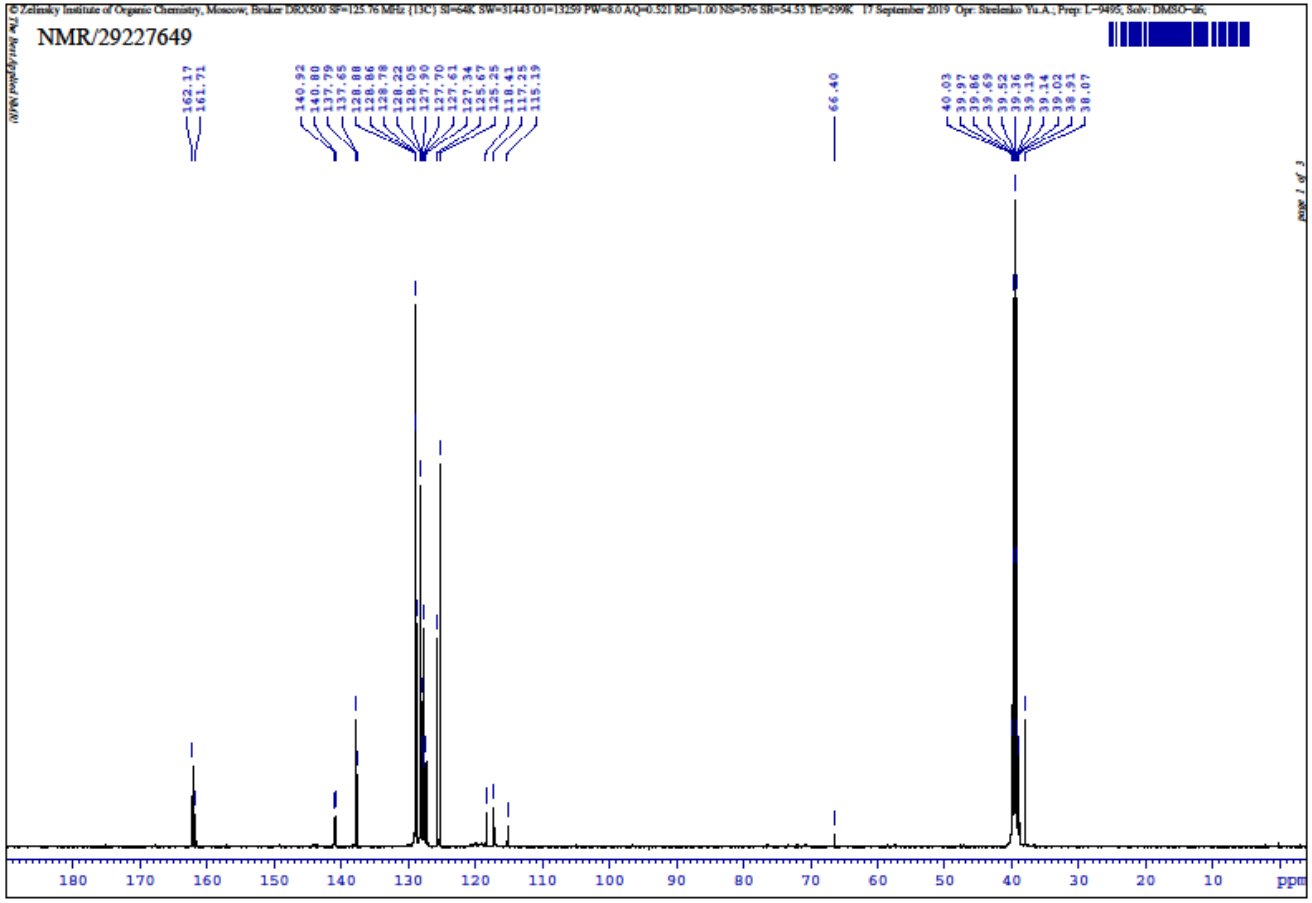
## Table S1. Spectra of isolated compounds 3a-j

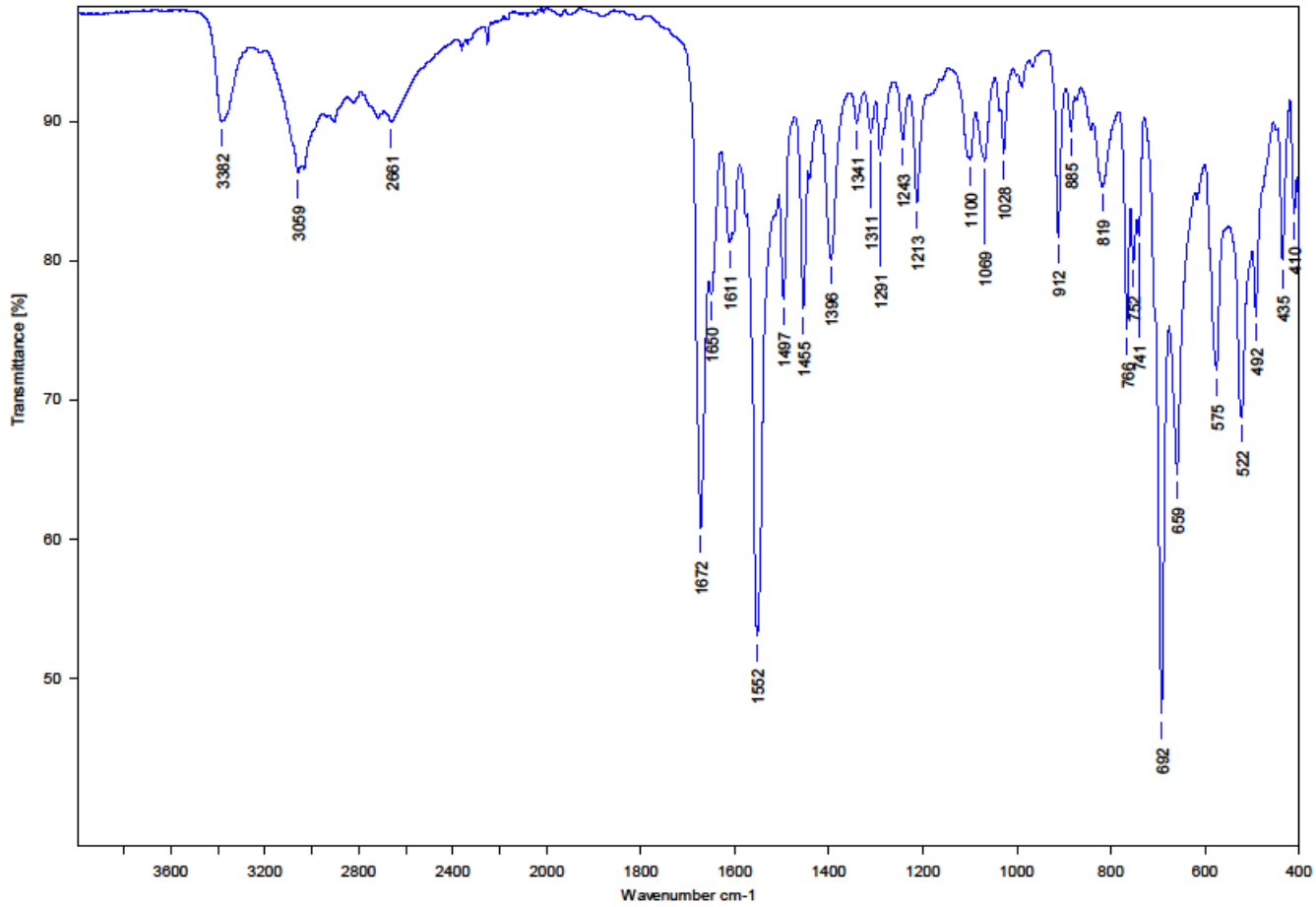



**Molecular formula : $C_{19}H_{15}N_5O$**

**3a**




NMR/29227649
162.17
161.71
140.92
140.80
137.79
137.65
128.88
128.86
128.78
128.22
128.05
127.90
127.70
127.61
127.34
125.67
125.25
118.41
117.25
115.19
66.40
40.03
39.97
39.86
39.69
39.52
39.36
39.19
39.14
39.02
38.91
38.07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

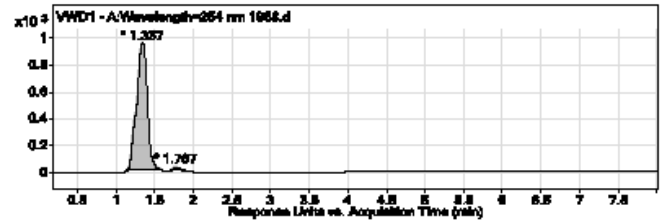

Transmittance [%]
90
80
70
60
50
3382
3059
2661
1672
1650
1611
1552
1497
1455
1396
1341
1311
1291
1243
1213
1100
1069
1028
912
885
819
766
752
741
692
659
575
522
492
435
410
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 1968.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 72 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 9/27/2021 3:48:21 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

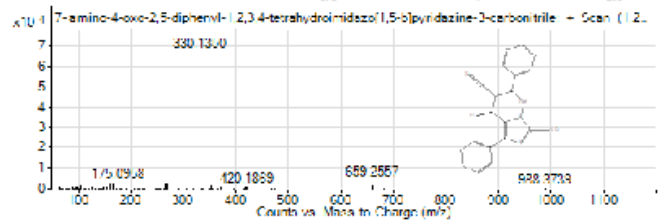



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % | Signal To Noise |
|---|---|---|---|---|---|---|---|
| 1 | 1.14 | 1.337 | 1.607 | 951.38 | 9108.6 | 100 | |
| 2 | 1.703 | 1.767 | 1.893 | 19.23 | 107.86 | 1.18 | |

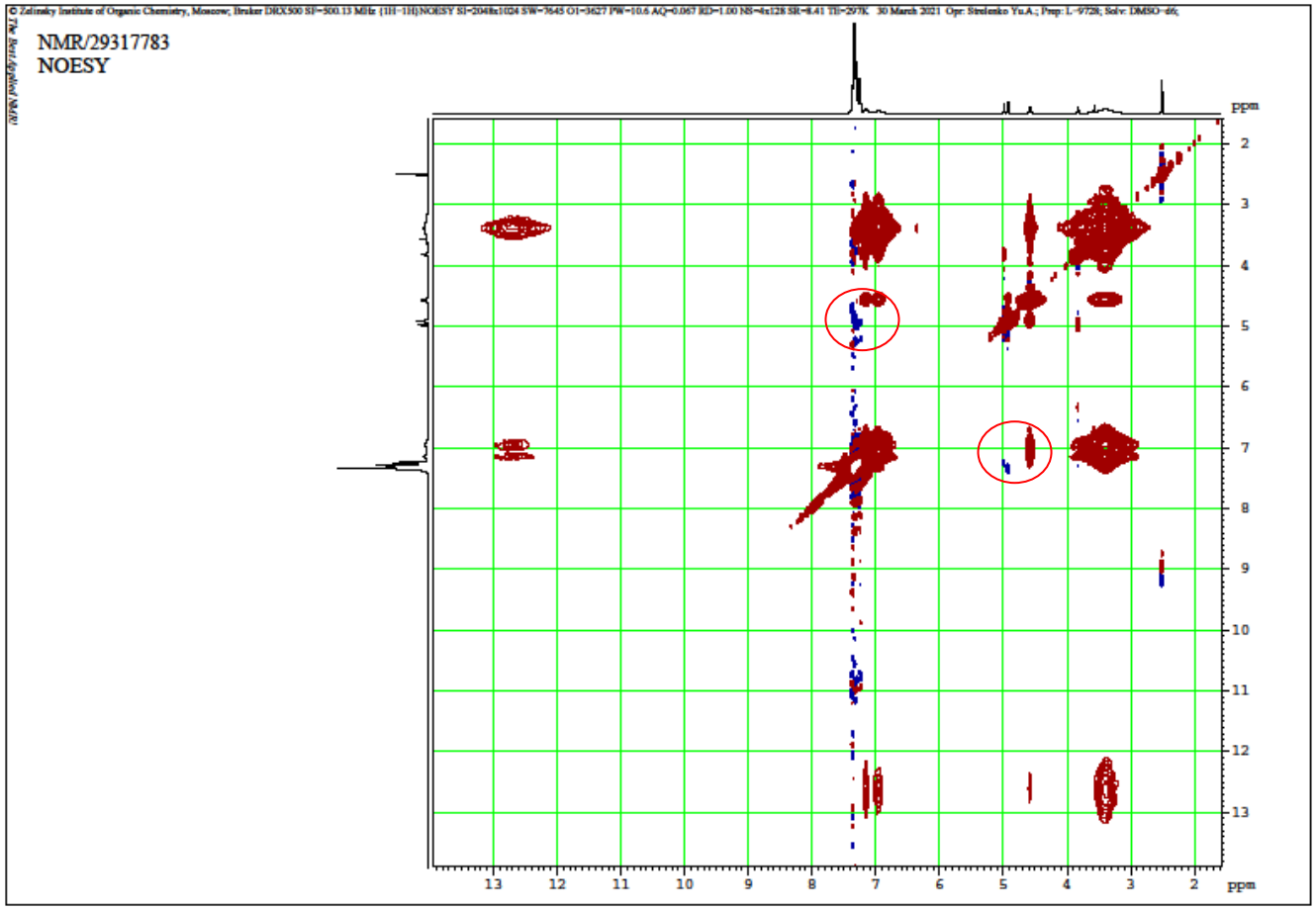
## User Spectra

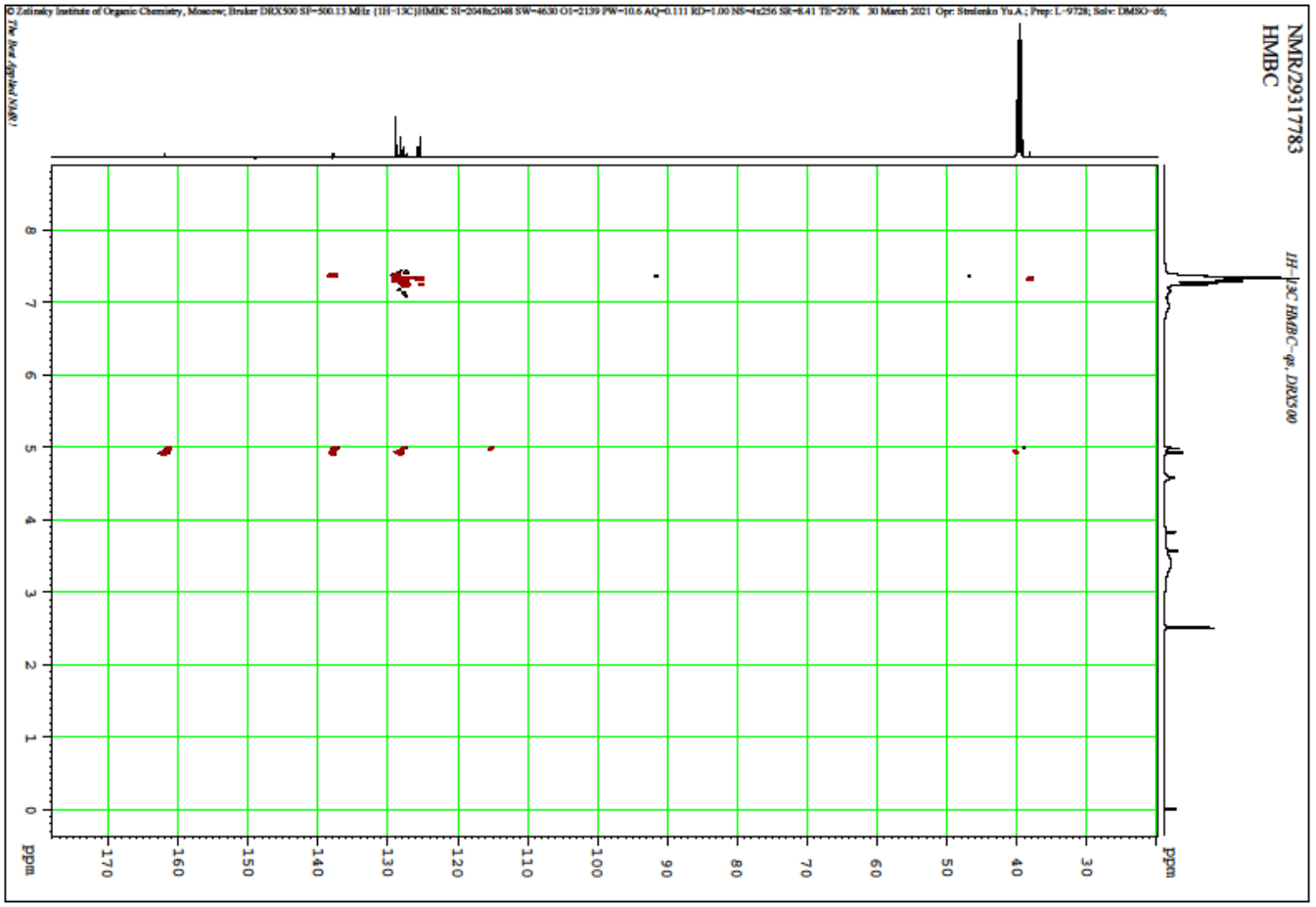
| Spectrum Source | Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|---|
| | 191 | 0 | ESI |

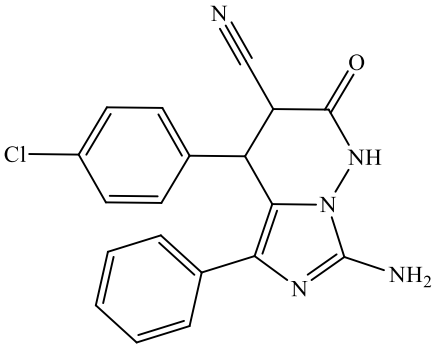



**Peak List**

| m/z | z | Abund |
|---|---|---|
| 76.0738 | | 2122.66 |
| 108.0798 | 1 | 2212.61 |
| 159.0796 | 1 | 2382.14 |
| 163.0958 | 1 | 2800.3 |
| 175.0958 | 1 | 3150.09 |
| 263.1267 | 1 | 2794.83 |
| 268.1182 | 1 | 2377.02 |
| 330.1350 | 1 | 67273.49 |
| 331.135 | 1 | 14767.18 |
| 659.2557 | 1 | 4420.8 |

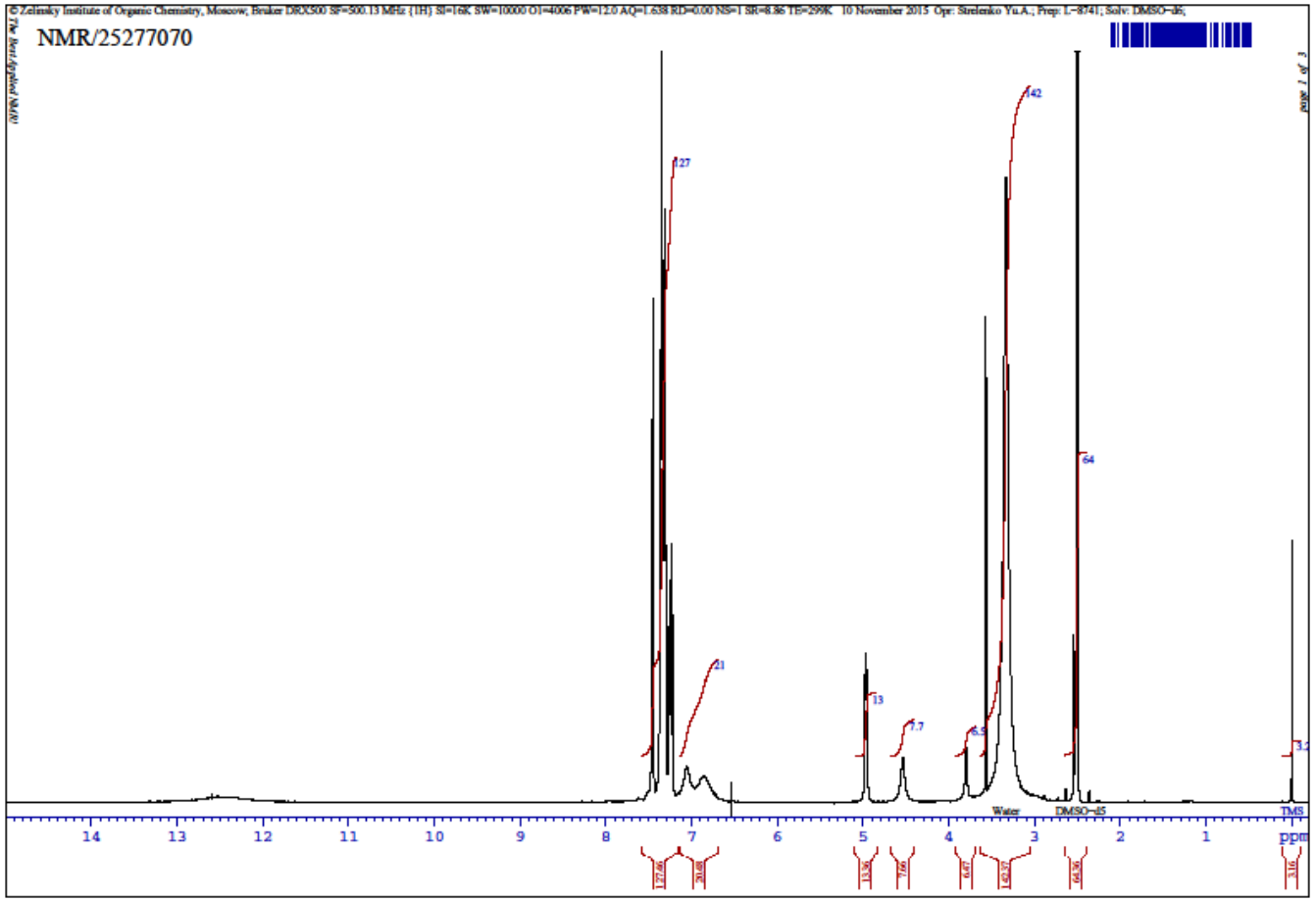

NMR/29317783
NOESY
ppm
13
12
11
10
9
8
7
6
5
4
3
2
ppm

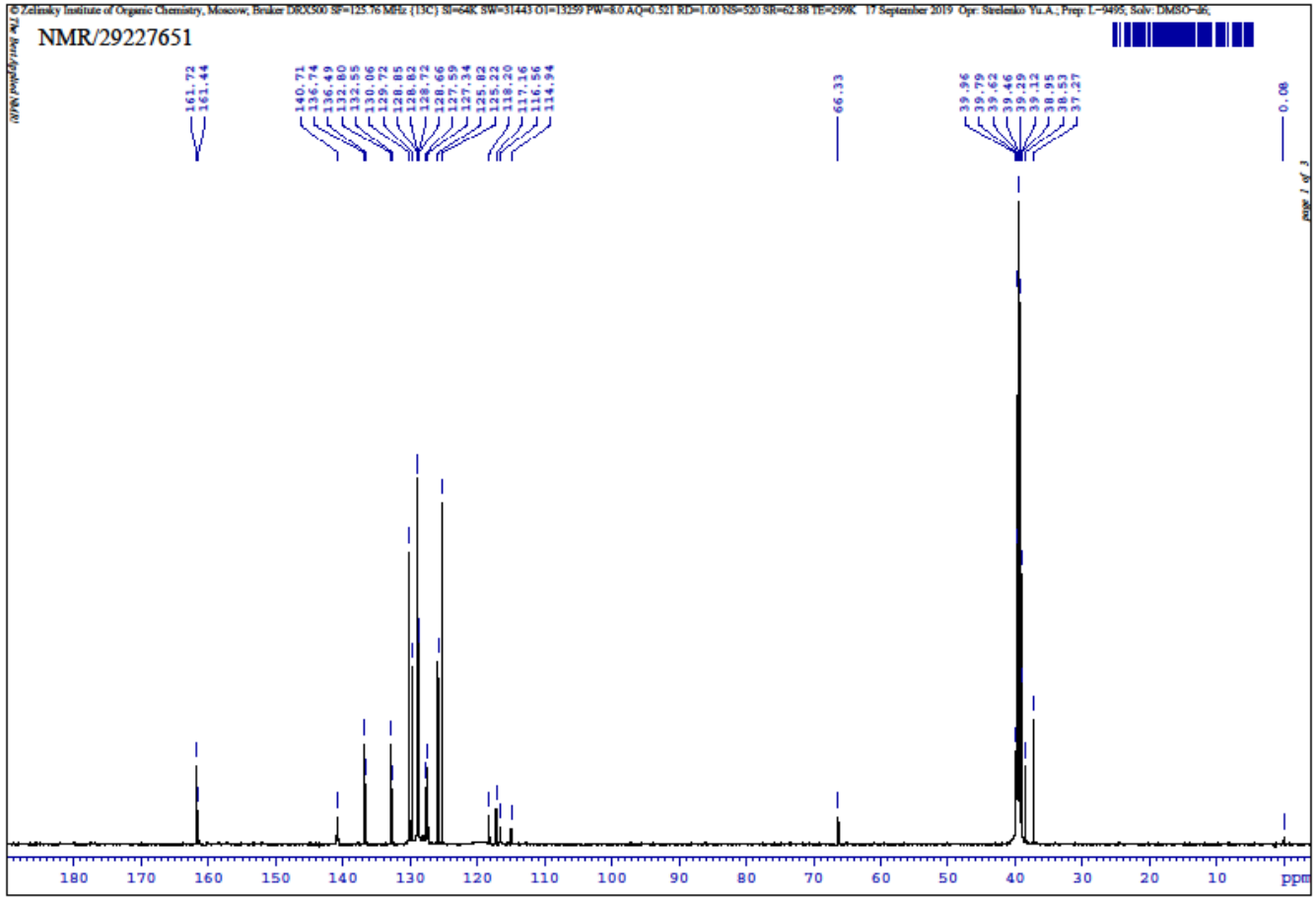

NMR/29317783
HMBC
1H-13C HMBC-qk, DRX500
© Zelinsky Institute of Organic Chemistry, Moscow; Bruker DRX500 SF=500.13 MHz (1H-13C)HMBC SI=2048x2048 SW=4630 O1=2139 PW=10.6 AQ=0.111 RD=1.00 NS=4x256 SR=8.41 TE=297K 30 March 2021 Opr: Strelenko Yu.A.; Prep: L-9728; Solv: DMSO-d6;
The Best Applied NMR!
ppm
ppm

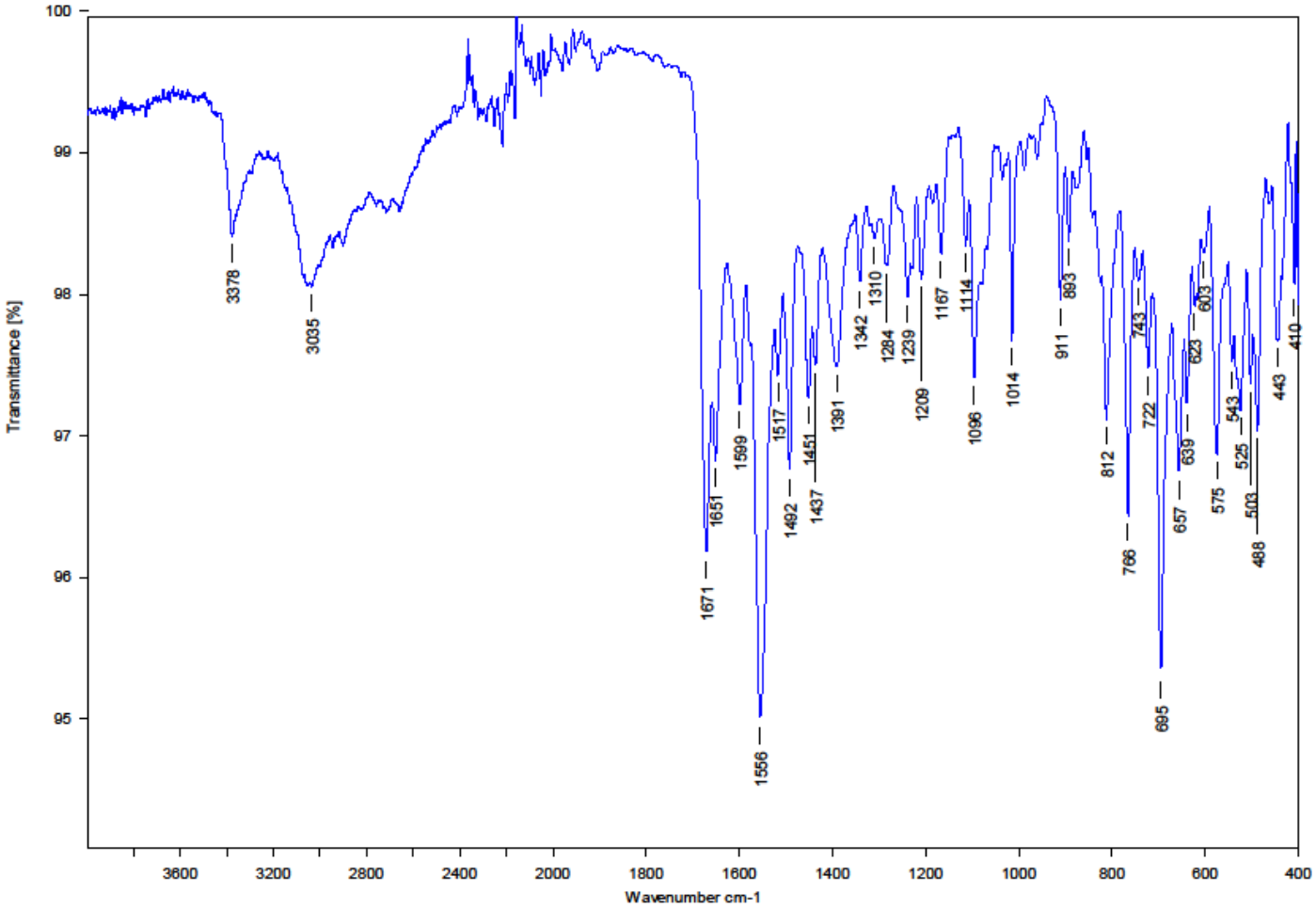



**Molecular formula : $C_{19}H_{14}ClN_5O$**

**3b**



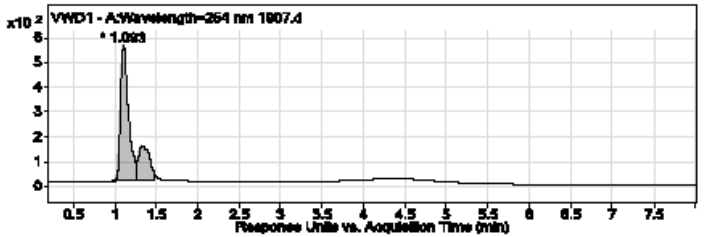

NMR/29227651
161.72
161.44
140.71
136.74
136.49
132.80
132.55
130.06
129.72
128.85
128.82
128.72
128.66
128.59
127.34
125.82
125.20
118.20
117.56
116.56
114.94
66.33
39.96
39.79
39.62
39.46
39.29
39.12
38.95
38.53
37.27
0.08
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Transmittance [%]
100
99
98
97
96
95
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1
3378
3035
1671
1651
1599
1556
1517
1492
1451
1437
1391
1342
1310
1284
1239
1209
1167
1114
1096
1014
911
893
812
766
743
722
695
657
639
623
603
575
543
525
503
488
443
410

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 1907.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 74 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 9/3/2021 12:32:01 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

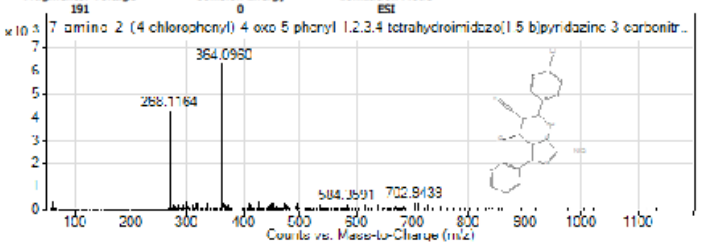



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 0.967 | 1.093 | 1.253 | 547.01 | 3693.46 | 100 |
| 2 | 1.253 | 1.317 | 1.477 | 137.15 | 1310.08 | 35.47 |

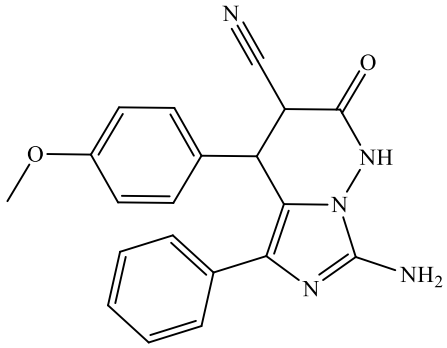
## User Spectra

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



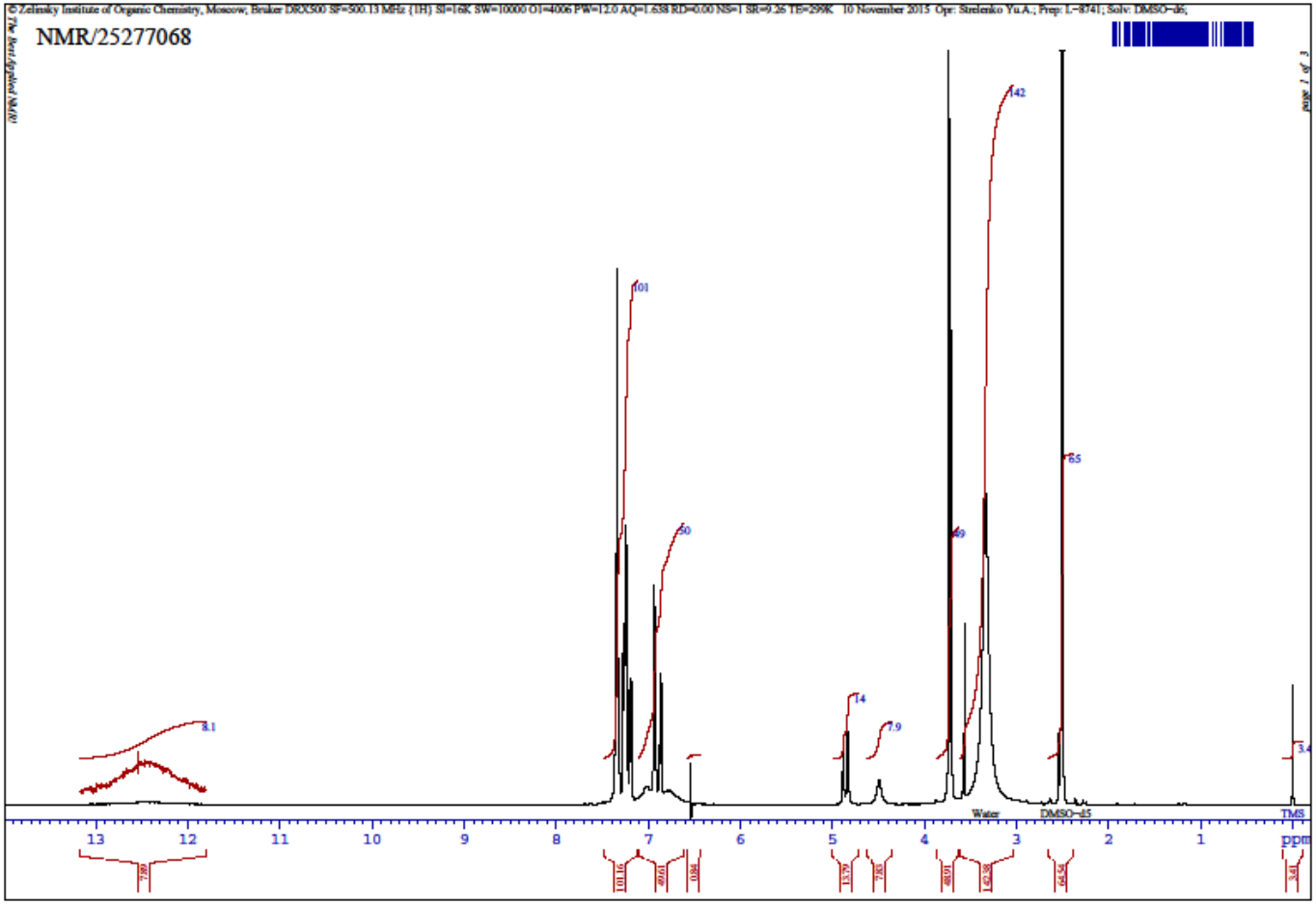

**Peak List**

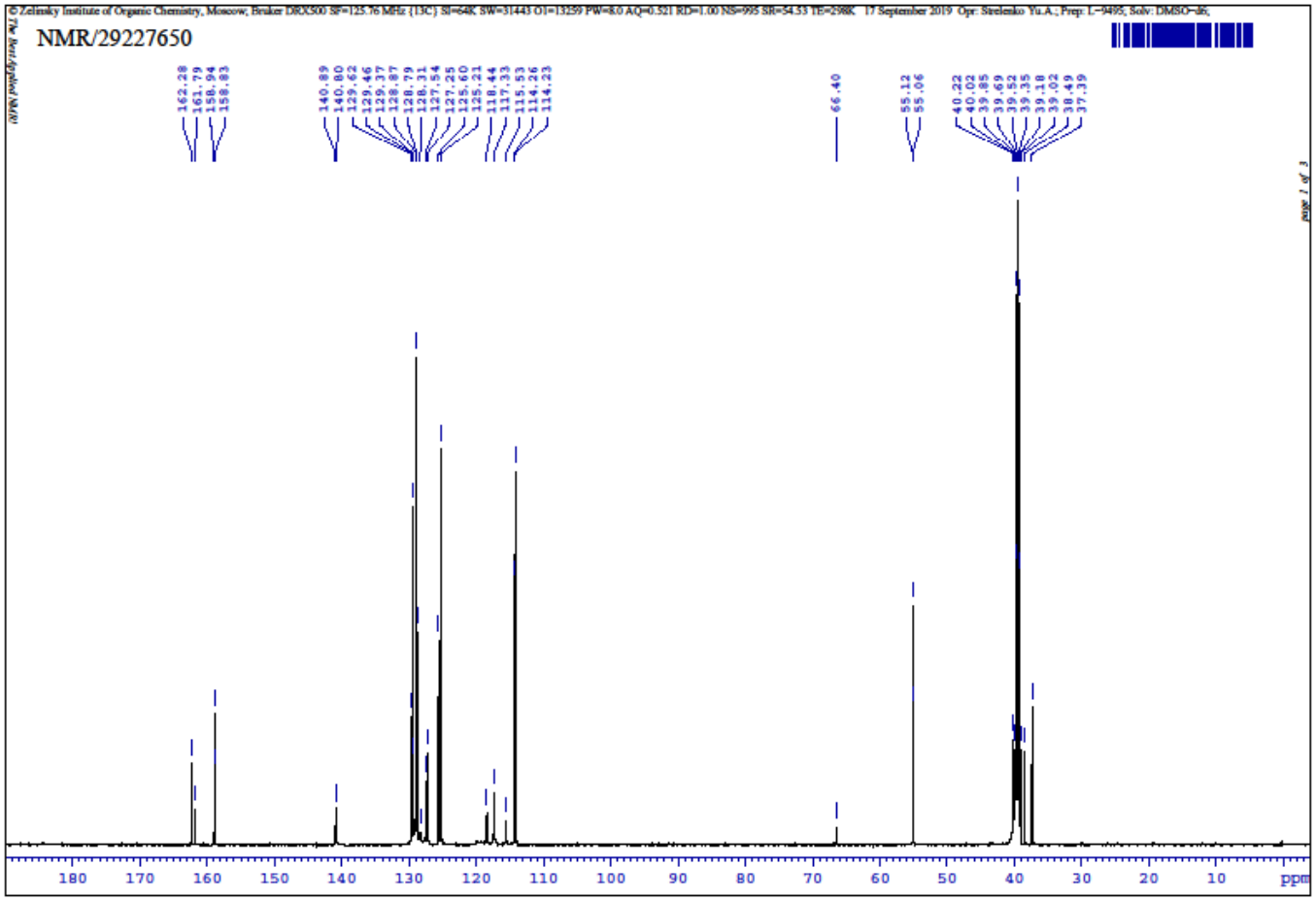
| m/z | z | Abund |
|---|---|---|
| 85.0273 | | 1411.34 |
| 145.0488 | | 1336.44 |
| 158.0724 | | 1590.45 |
| 159.0771 | 1 | 2647.07 |
| 161.0813 | 1 | 1143.44 |




**Molecular formula: $C_{20}H_{17}N_5O_2$**

**3c**




NMR/29227650
162.28
161.79
158.94
158.83
140.89
140.80
129.62
129.46
129.37
128.87
128.79
128.31
127.54
127.25
125.60
125.21
118.44
117.33
115.53
114.26
114.23
66.40
55.12
55.06
40.22
40.02
39.85
39.69
39.52
39.35
39.18
39.02
38.49
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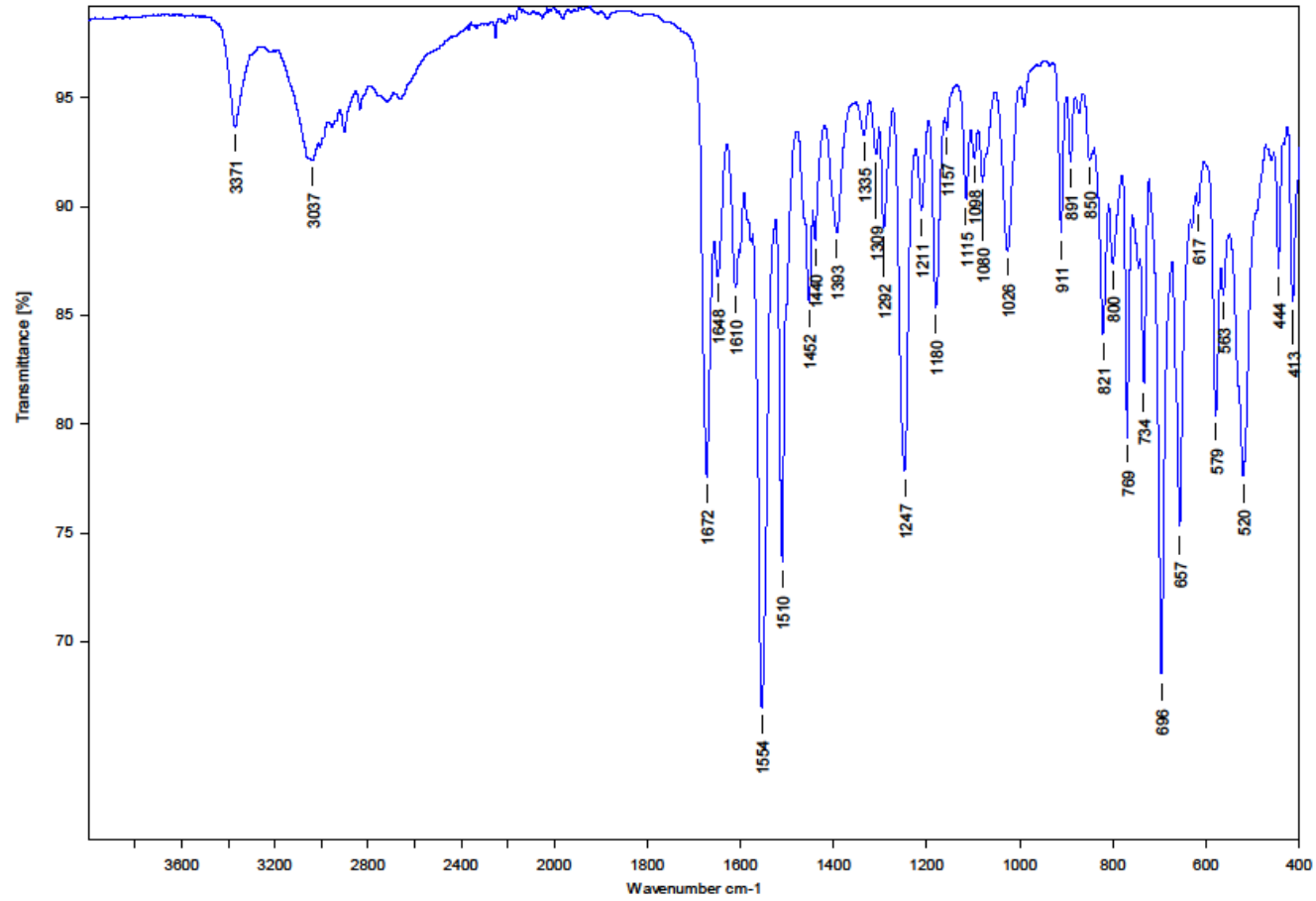
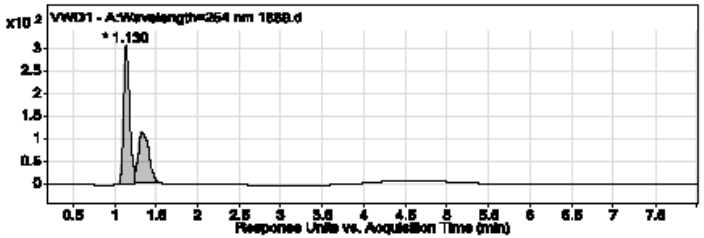
90
80
70
60
50
40
30
20
10
ppm


Transmittance [%]
95
90
85
80
75
70
3371
3037
1672
1648
1610
1554
1510
1452
1440
1393
1335
1309
1292
1247
1211
1180
1157
1115
1098
1080
1026
911
891
850
821
800
769
734
696
657
617
579
563
520
444
413
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 1889.d | **Sample Name** | Unavailable |
| **Sample Type** | Unavailable | **Position** | Unavailable |
| **Instrument Name** | Unavailable | **User Name** | Unavailable |
| **Acq Method** | | **Acquired Time** | Unavailable |
| **IRM Calibration Status** | Success | **DA Method** | 111.m |
| **Comment** | Sample information is unavailable | | |

## User Chromatograms

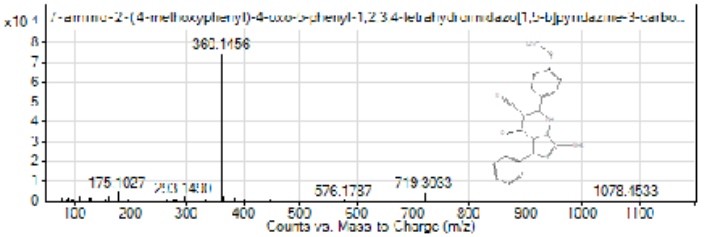



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.033 | 1.13 | 1.237 | 308.12 | 1594.27 | 100 |
| 2 | 1.237 | 1.317 | 1.567 | 112.34 | 997.26 | 62.55 |

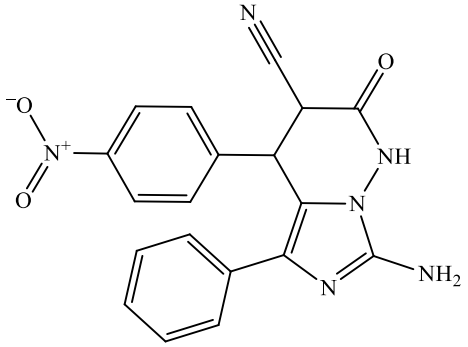
## User Spectra

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



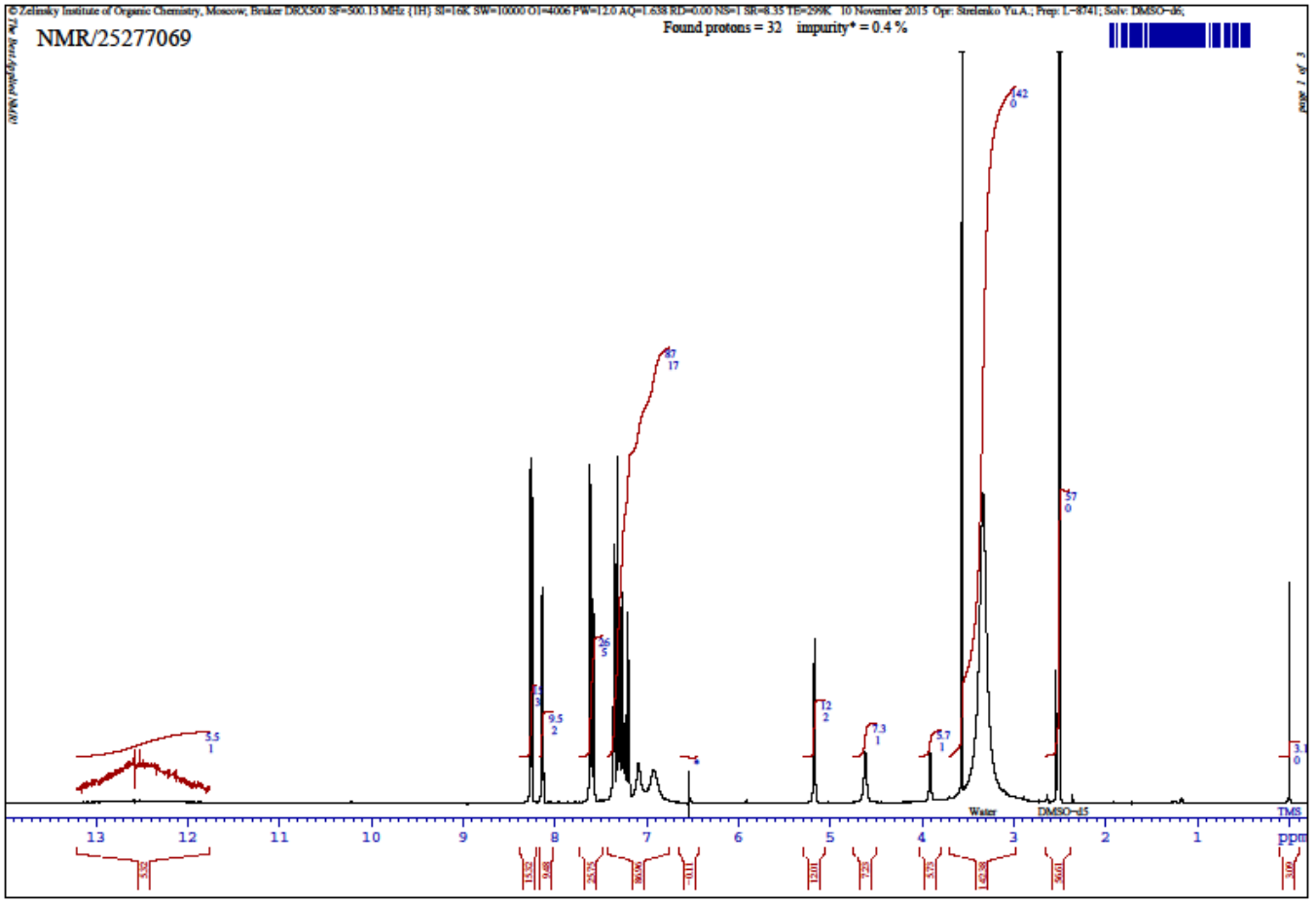

**Peak List**

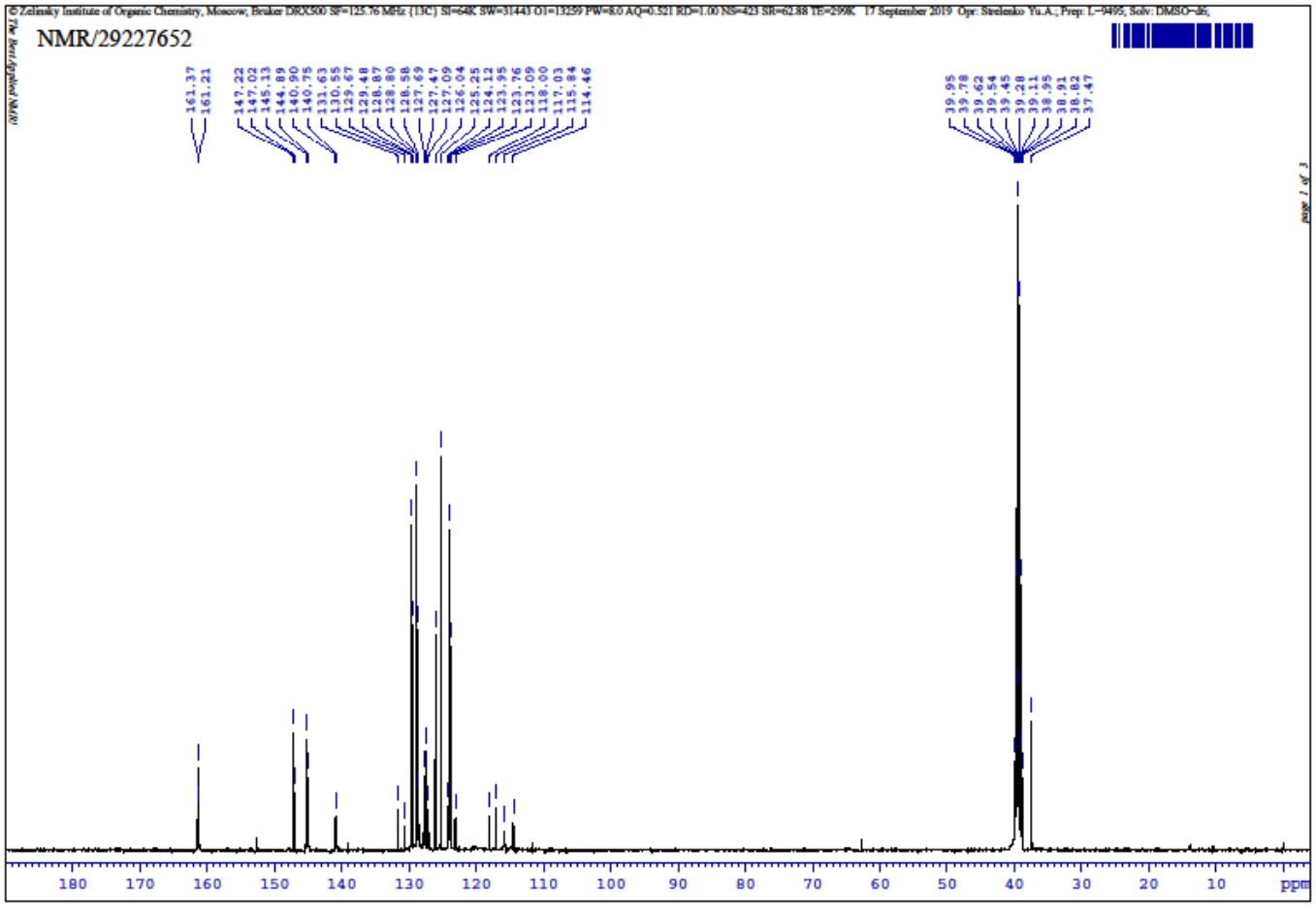
| m/z | z | Abund |
|---|---|---|
| 76.0774 | | 1937.7 |
| 87.096 | | 1945.89 |
| 159.084 | 1 | 2856.04 |
| 175.1027 | 1 | 5014.5 |
| 293.149 | 1 | 2016.04 |
| 360.1456 | 1 | 74375.48 |
| 361.158 | 1 | 17140.55 |
| 362.161 | 1 | 2730.18 |
| 719.3033 | 1 | 4630.56 |
| 720.3101 | 1 | 2482.81 |

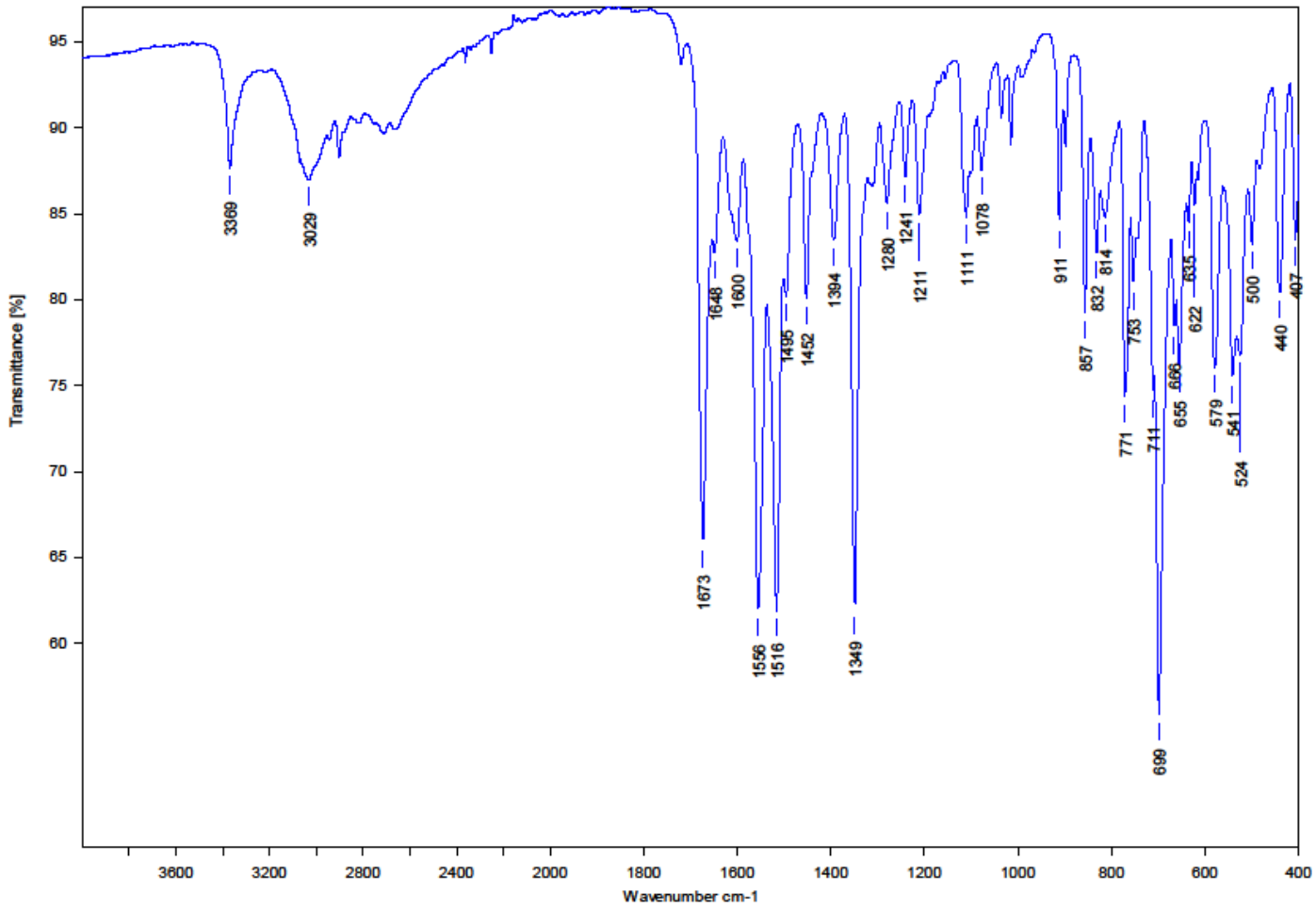


**Molecular formula: $C_{19}H_{14}N_6O_3$**

**3d**




© Zelinsky Institute of Organic Chemistry, Moscow, Bruker DRX500 SF=125.76 MHz {13C} SI=64K SW=31443 O1=13259 PW=8.0 AQ=0.521 RD=1.00 NS=423 SR=62.88 TE=298K 17 September 2019 Opr: Strelenko Yu.A., Prep: L-9495, Solv: DMSO-d6,
NMR/29227652
161.37
161.21
147.22
147.02
145.13
144.89
140.90
140.75
131.63
130.55
129.67
129.48
128.87
128.80
128.58
127.69
127.47
127.09
126.04
125.25
124.12
123.95
123.76
123.09
118.00
117.03
115.84
114.46
39.95
39.78
39.62
39.54
39.45
39.28
39.11
38.95
38.91
38.82
37.47
page 1 of 3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

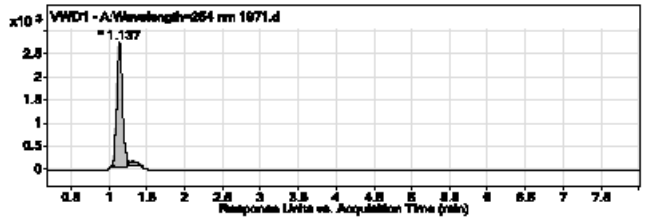

Transmittance [%]
95
90
85
80
75
70
65
60
3369
3029
1673
1648
1600
1556
1516
1495
1452
1394
1349
1280
1241
1211
1111
1078
911
857
832
814
771
753
711
699
666
655
635
622
579
541
524
500
440
407
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 1971.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 75 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 9/27/2021 4:27:20 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

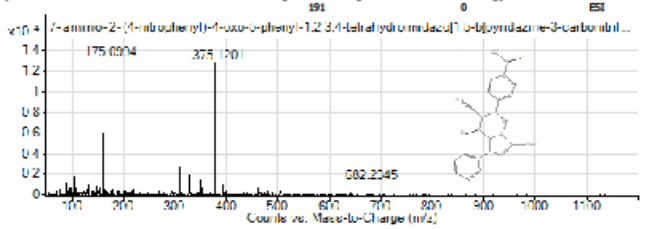



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % | Signal To Noise |
|---|---|---|---|---|---|---|---|
| 1 | 1.023 | 1.137 | 1.247 | 2717.29 | 14401.9 | 100 | |
| 2 | 1.253 | 1.303 | 1.443 | 119.14 | 965.94 | 6.71 | |

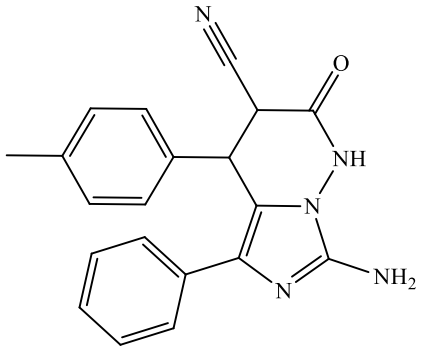
## User Spectra

| Spectrum Source | Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|---|
| | 191 | 0 | ESI |



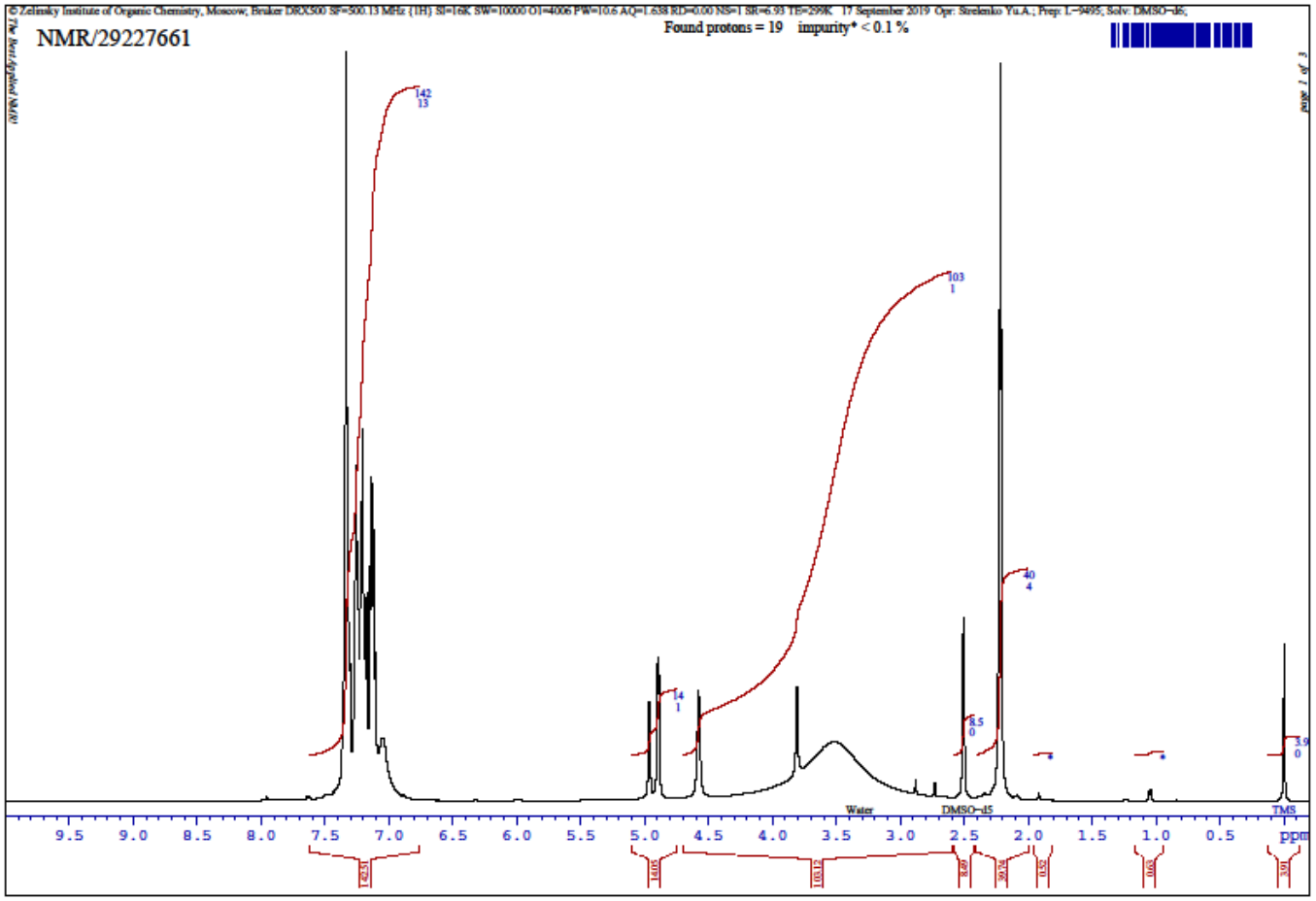

**Peak List**

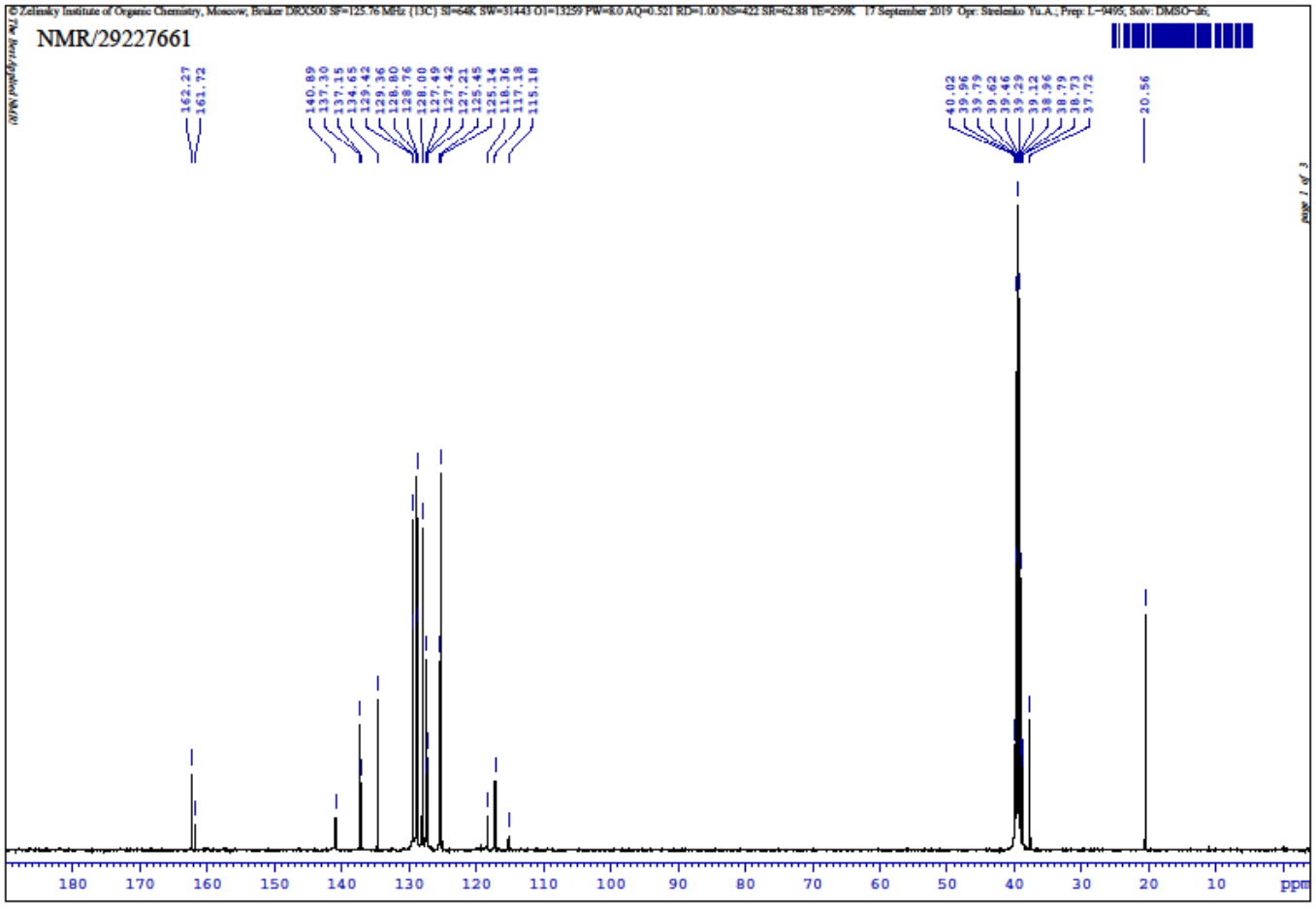
| m/z | z | Abund |
|---|---|---|
| 76.0753 | | 1956.7 |
| 118.1224 | | 2468.51 |
| 158.0912 | | 5483.02 |
| 159.0825 | 1 | 5975.52 |
| 161.084 | 1 | 3786.98 |
| 175.0994 | 1 | 13009.85 |
| 208.0855 | | 2864.5 |
| 308.1171 | 1 | 2741.26 |
| 326.1285 | 1 | 1908.49 |
| 375.1201 | 1 | 12702.27 |

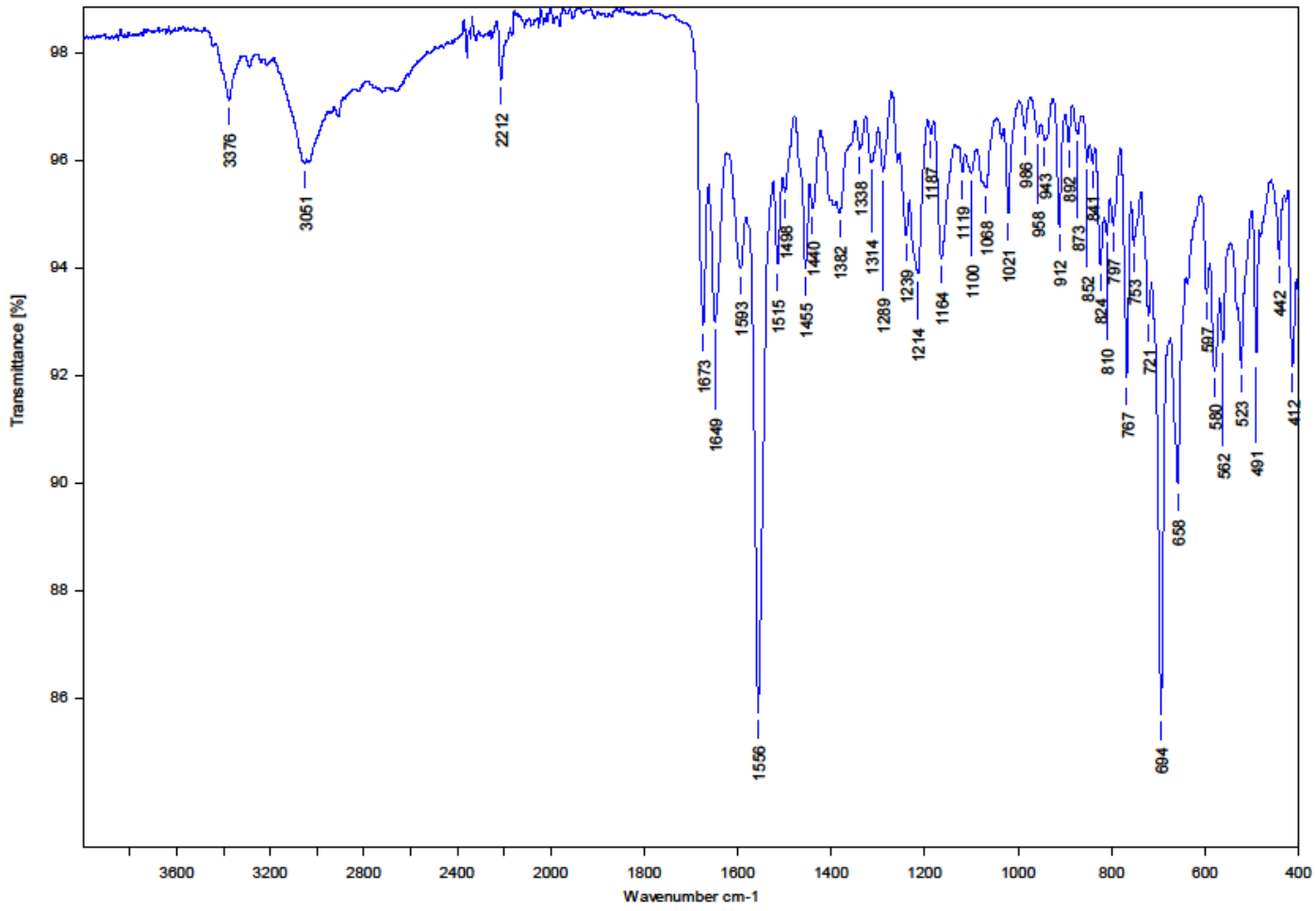



**Molecular formula: $C_{20}H_{17}N_5O$**

**3e**




NMR/29227661
162.27
161.72
140.89
137.30
137.15
134.65
129.42
129.36
128.80
128.76
128.00
127.49
127.42
127.21
125.45
125.14
118.36
117.18
115.18
40.02
39.96
39.79
39.62
39.46
39.29
39.12
38.96
38.79
38.73
37.72
20.56
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

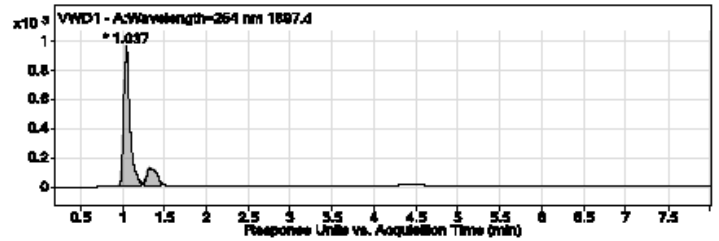

Transmittance [%]
98
96
94
92
90
88
86
3376
3051
2212
1673
1649
1593
1556
1515
1498
1455
1440
1382
1338
1314
1289
1239
1214
1187
1164
1119
1100
1068
1021
986
958
943
912
892
873
852
841
824
810
797
767
753
721
694
658
597
580
562
523
491
442
412
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 1897.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 49 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 8/30/2021 1:30:08 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

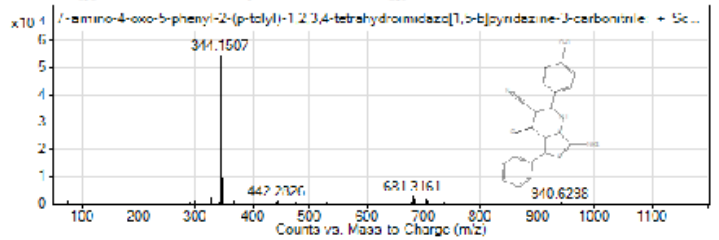



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 0.917 | 1.037 | 1.213 | 956.63 | 4971.58 | 100 |
| 2 | 1.263 | 1.32 | 1.45 | 127.12 | 1047.74 | 21.07 |

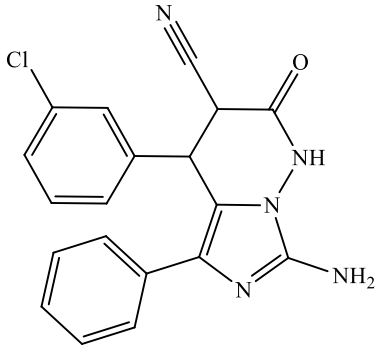
## User Spectra

| Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|
| 191 | 0 | ESI |



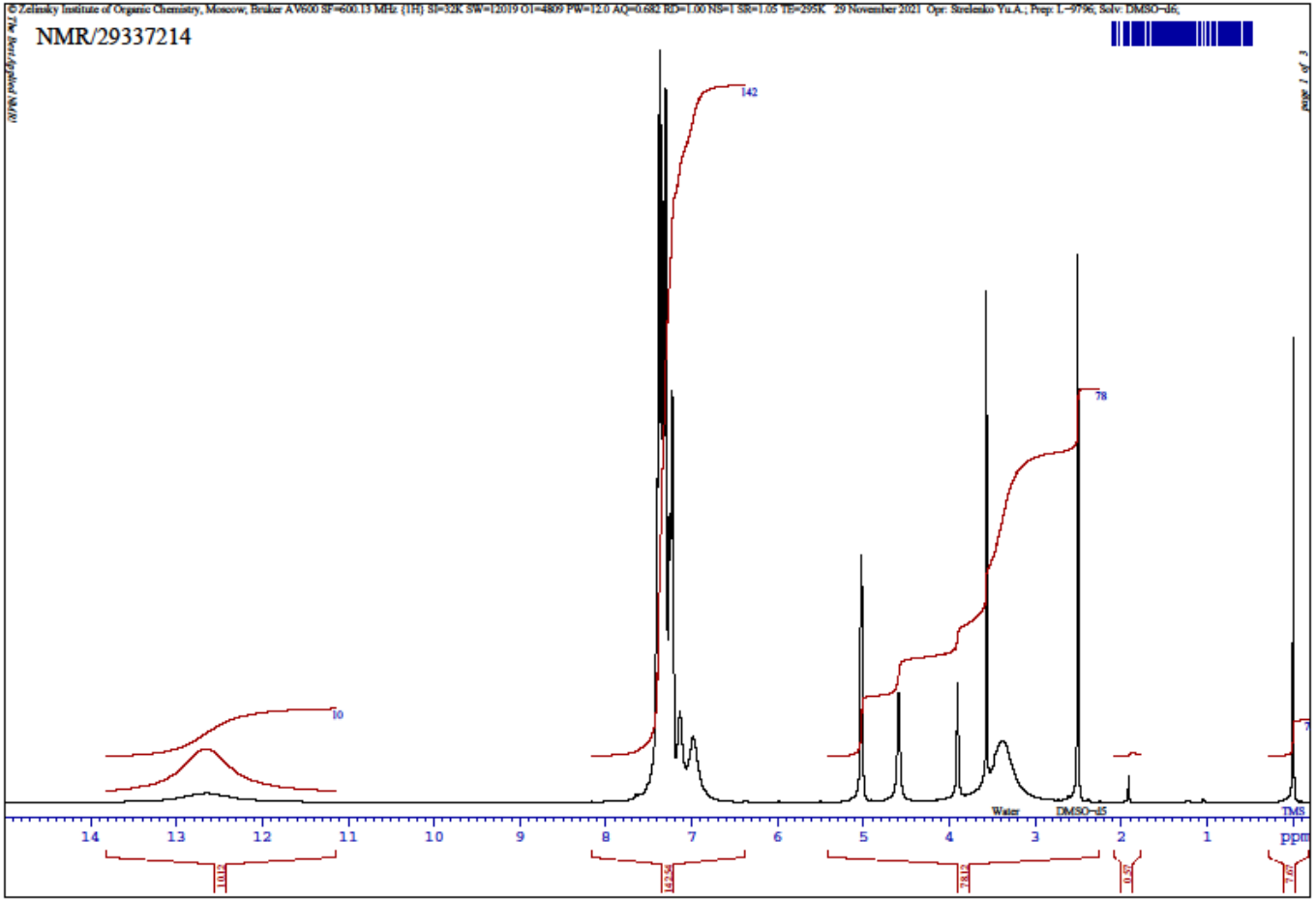

**Peak List**

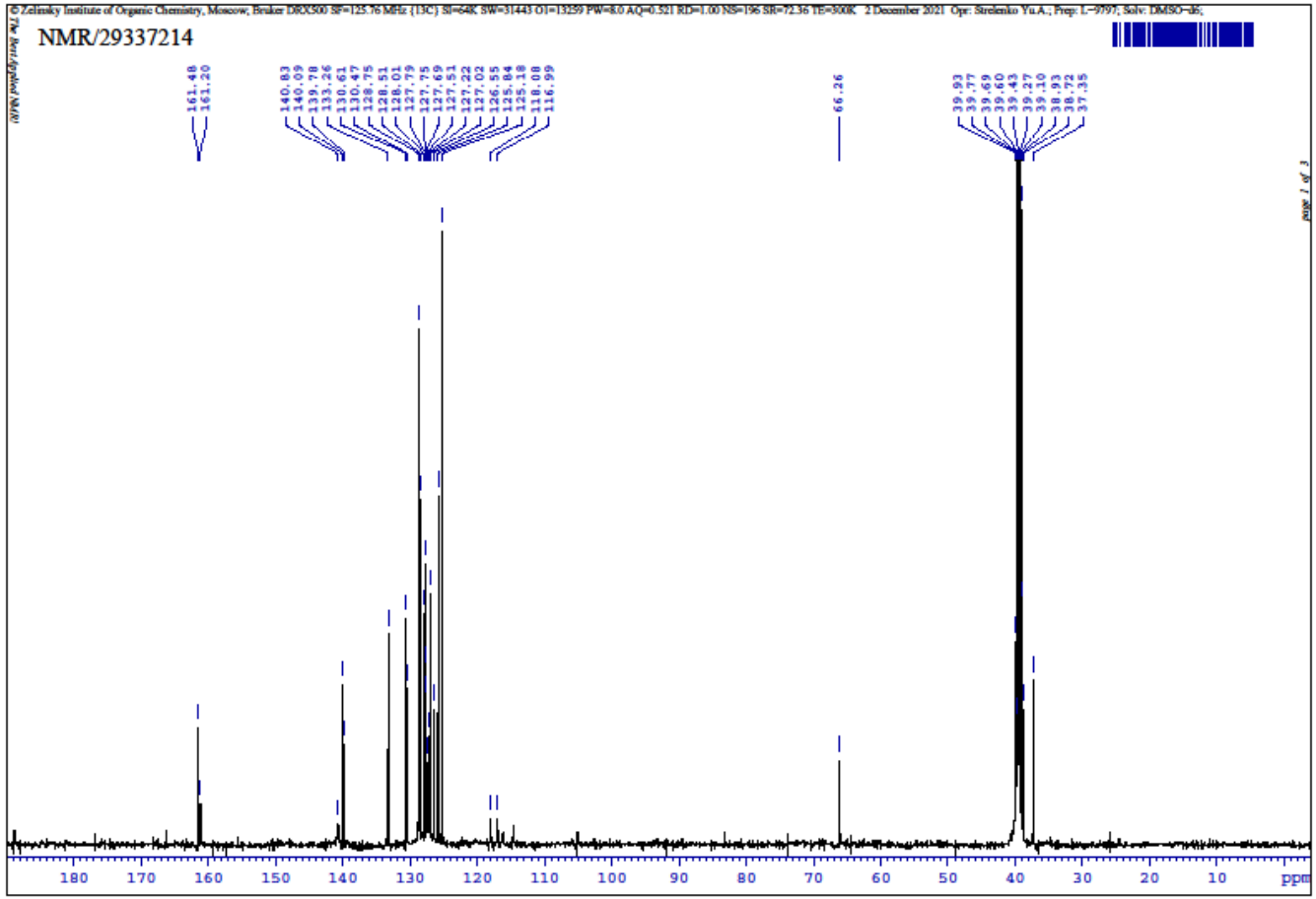
| m/z | z | Abund |
|---|---|---|
| 297.1375 | | 1515.62 |
| 325.132 | | 2205.02 |
| 326.1371 | 1 | 1582.14 |
| 344.1507 | 1 | 54540.62 |
| 345.1652 | 1 | 13655.9 |

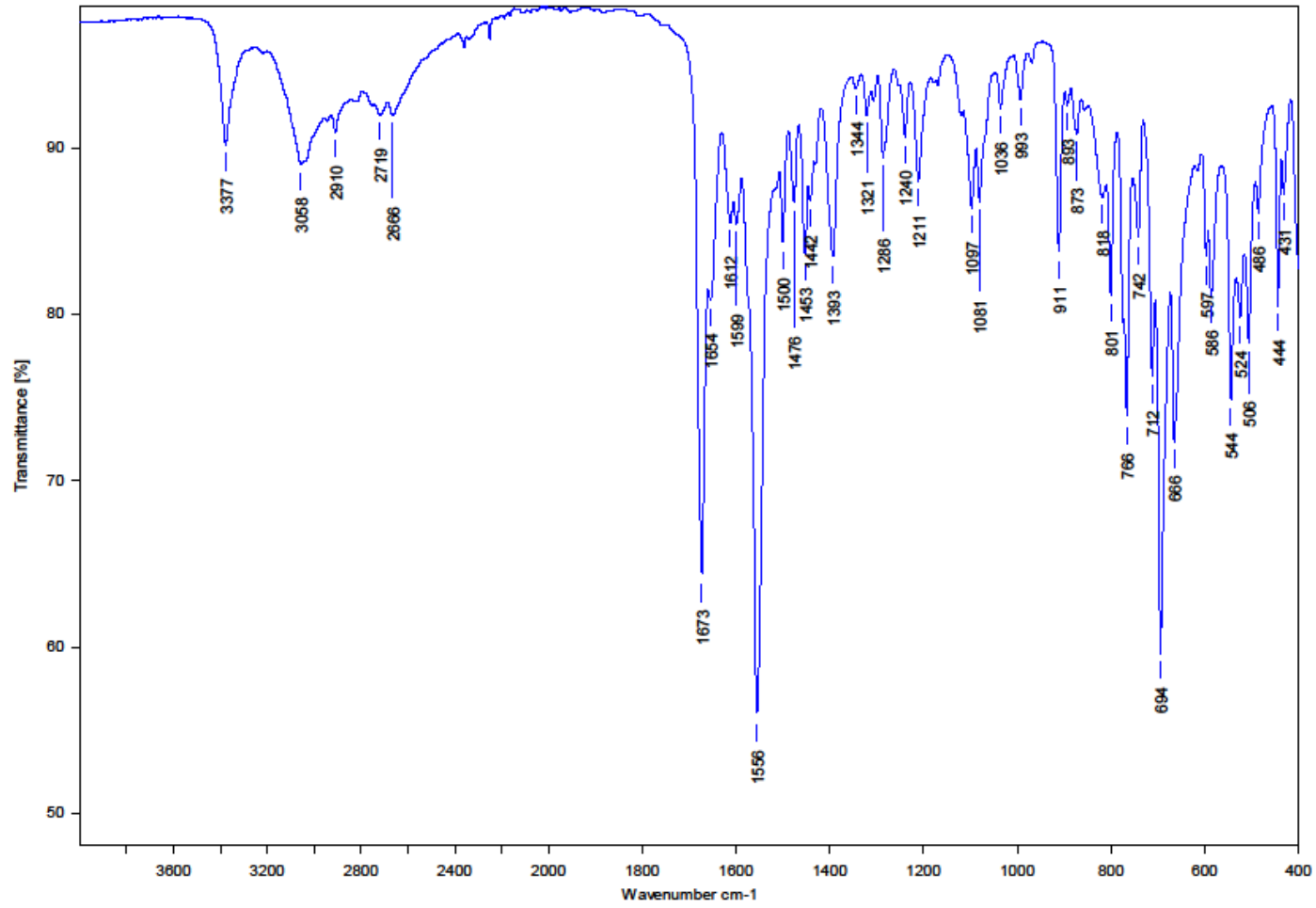



**Molecular formula: $C_{19}H_{14}ClN_5O$**

**3f**



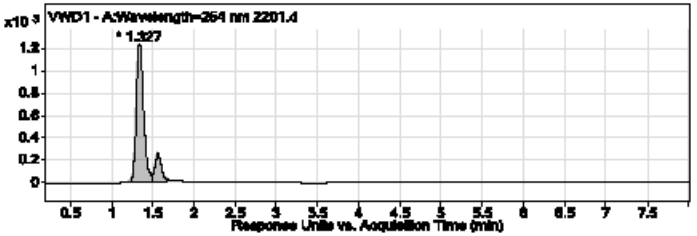

NMR/29337214
161.48
161.20
140.83
140.09
139.78
133.26
130.61
130.47
128.75
128.51
128.01
127.79
127.75
127.69
127.51
127.22
127.02
126.65
126.44
125.18
118.08
116.99
66.26
39.93
39.77
39.69
39.60
39.43
39.27
39.10
38.93
38.72
37.35
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Transmittance [%]
90
80
70
60
50
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1
3377
3058
2910
2719
2666
1673
1654
1612
1599
1556
1500
1476
1453
1442
1393
1344
1321
1286
1240
1211
1097
1081
1036
993
911
893
873
818
801
766
742
712
694
666
597
586
544
524
506
486
444
431

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 2201.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 57 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 12/9/2021 5:24:03 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

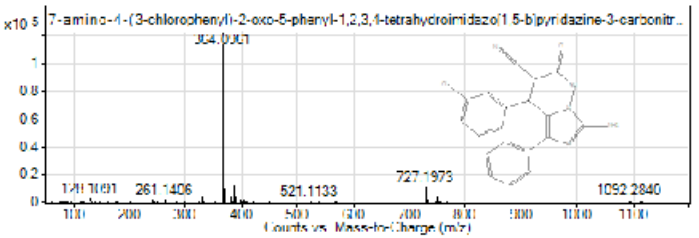



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.163 | 1.327 | 1.493 | 1242.58 | 7736.74 | 100 |
| 2 | 1.493 | 1.553 | 1.673 | 265.04 | 1451.58 | 18.76 |

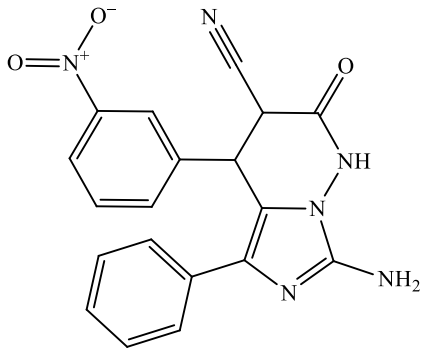
## User Spectra

| Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|
| 191 | 0 | ESI |



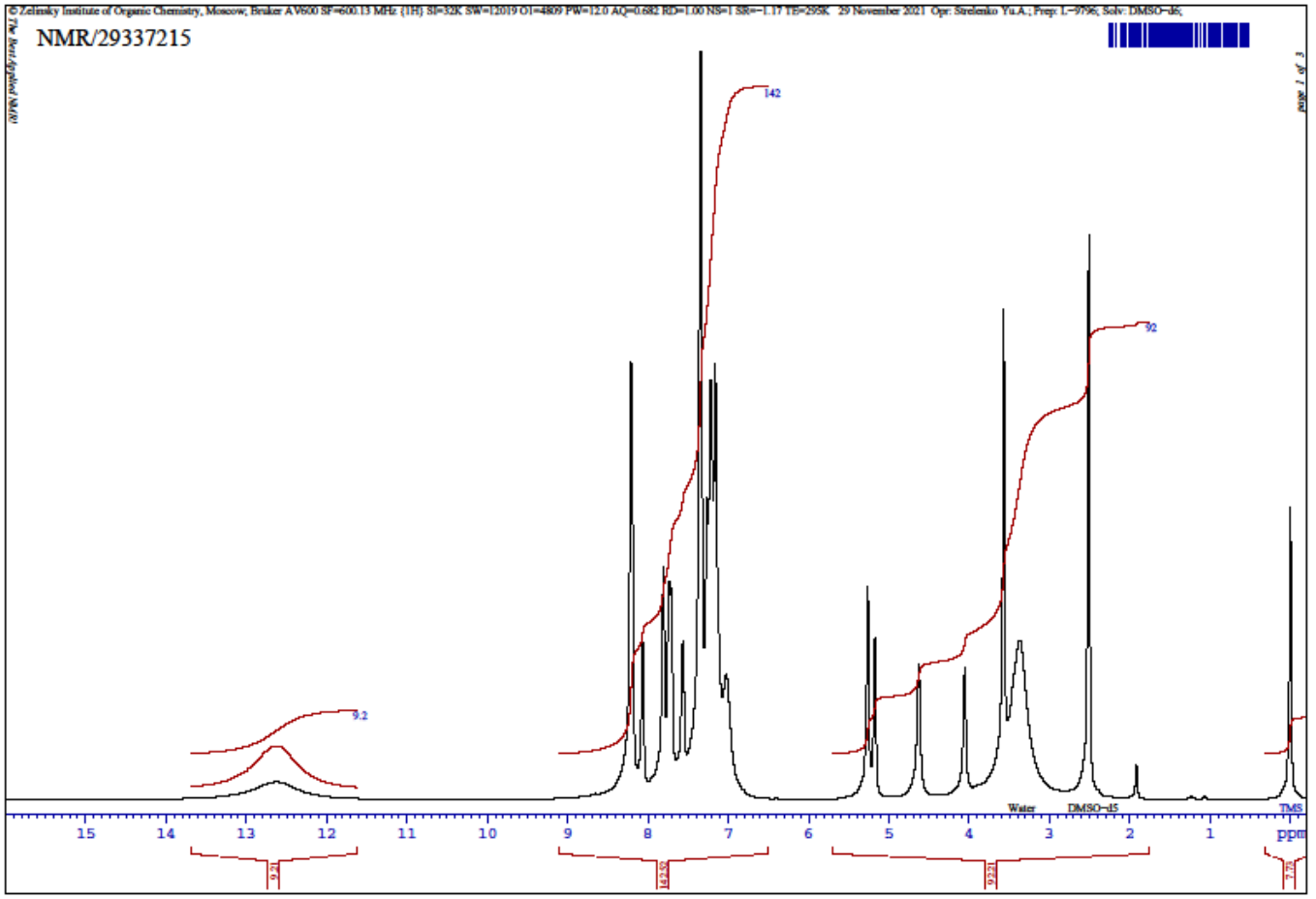

**Peak List**

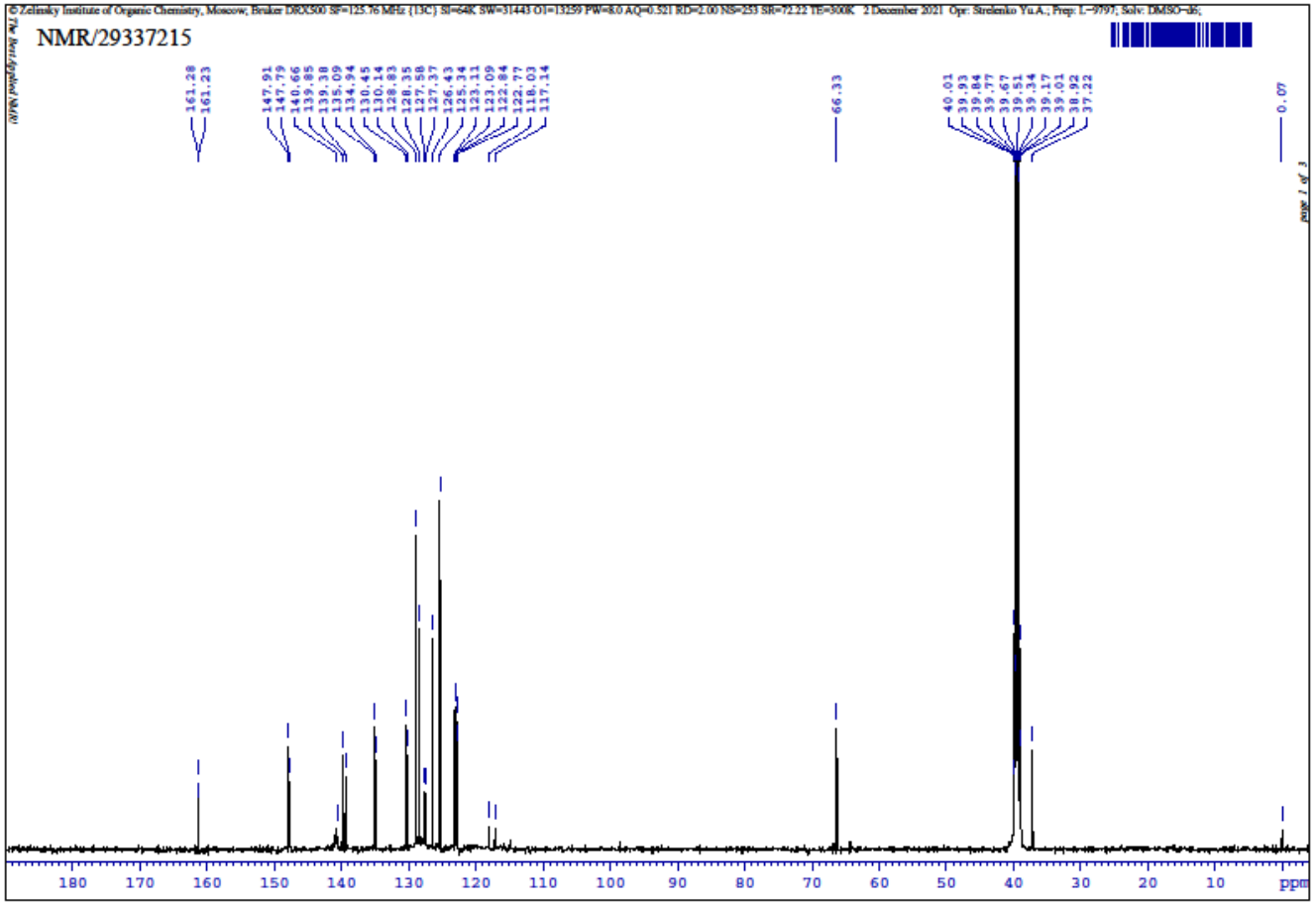
| m/z | z | Abund |
|---|---|---|
| 328.1489 | 1 | 4886.93 |
| 364.0961 | 1 | 122214.42 |
| 365.1059 | 1 | 25584.02 |
| 366.1003 | 1 | 39766.99 |
| 367.1018 | 1 | 9207.93 |

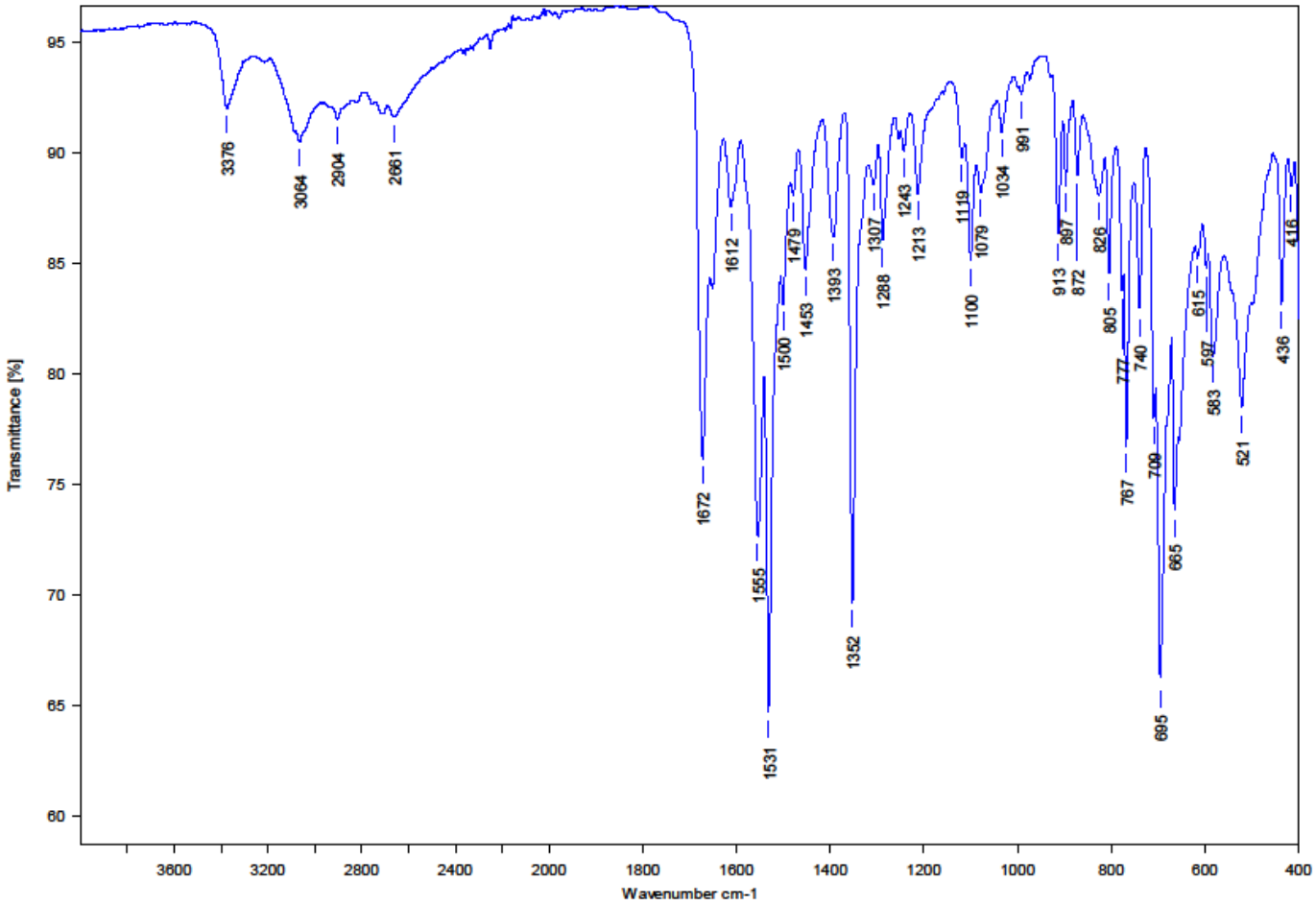


**Molecular formula: $C_{19}H_{14}N_6O_3$**

**3g**



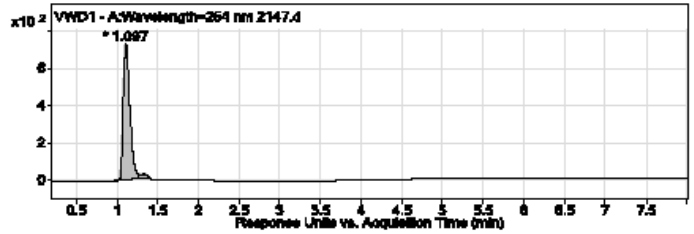

NMR/29337215
161.28
161.23
147.91
147.79
140.66
139.85
139.38
135.09
134.94
130.45
130.14
128.83
128.35
127.58
127.37
126.43
125.34
123.11
123.09
122.84
122.77
118.03
117.14
66.33
40.01
39.93
39.84
39.77
39.67
39.51
39.34
39.17
39.01
38.92
37.22
0.07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm


Transmittance [%]
95
90
85
80
75
70
65
60
3376
3064
2904
2661
1672
1612
1555
1531
1500
1479
1453
1393
1352
1307
1288
1243
1213
1119
1100
1079
1034
991
913
897
872
826
805
777
767
740
709
695
665
615
597
583
521
436
416
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 2147.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 37 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 12/3/2021 2:37:38 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

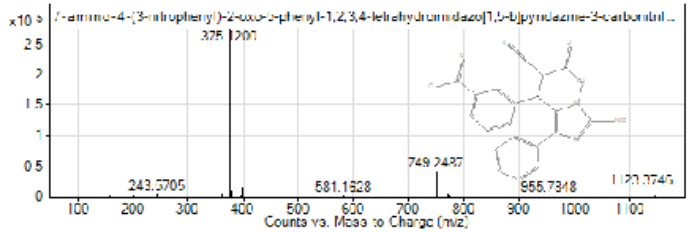



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 0.967 | 1.097 | 1.253 | 729.46 | 4183.99 | 100 |
| 2 | 1.263 | 1.323 | 1.41 | 29.02 | 166.11 | 3.97 |

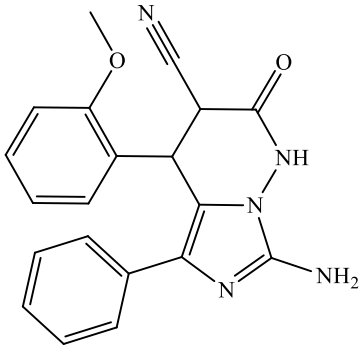
## User Spectra

| Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|
| 191 | 0 | ESI |



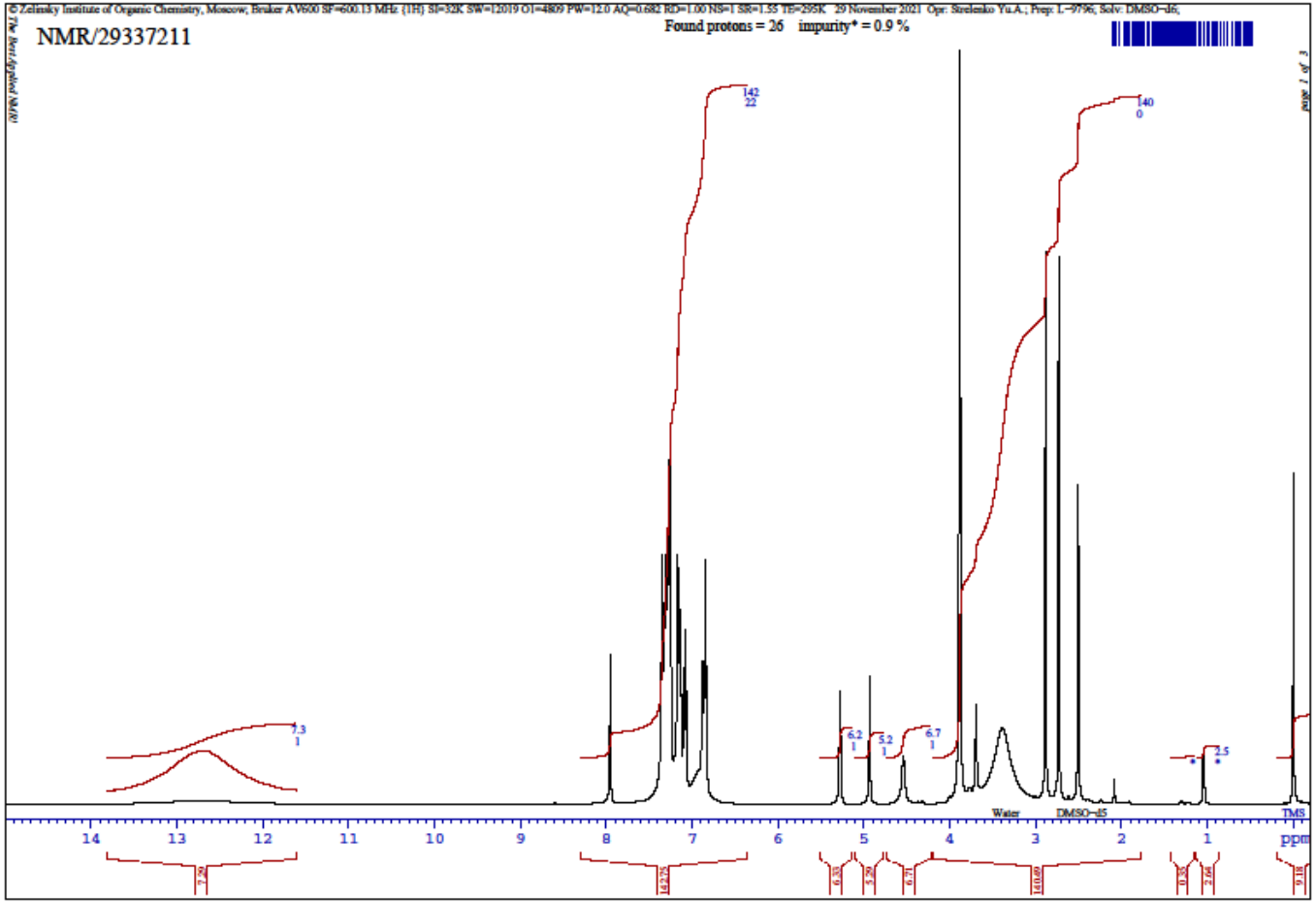

**Peak List**

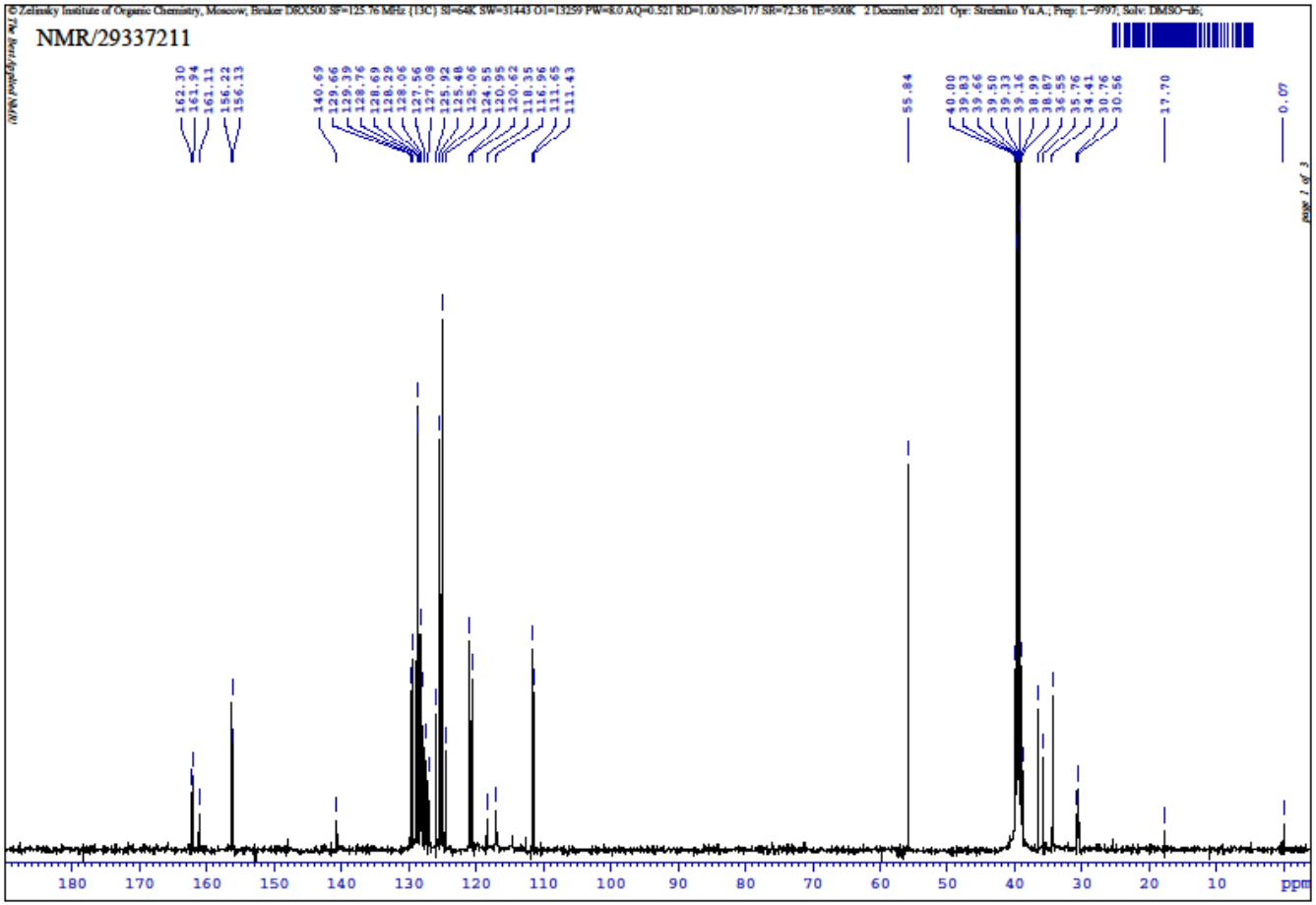
| m/z | z | Abund |
|---|---|---|
| 361.1257 | 1 | 5733.62 |
| 375.1200 | 1 | 275280.69 |
| 376.1216 | 1 | 58567.23 |
| 377.1267 | 1 | 9404.07 |
| 397.1106 | 1 | 15968.42 |

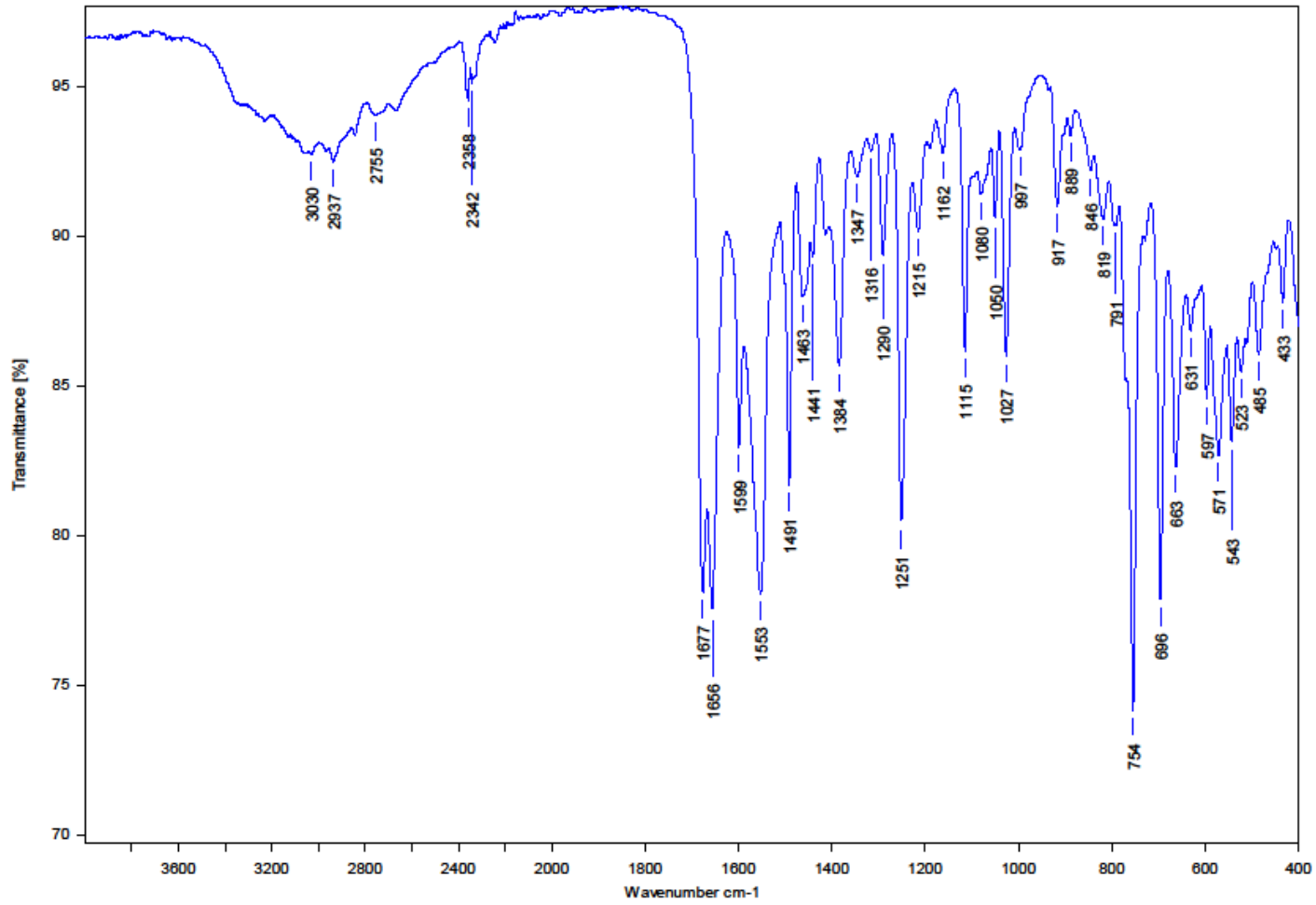



**Molecular formula: $C_{20}H_{17}N_5O_2$**

**3h**




NMR/29337211
162.30
161.94
161.11
156.22
156.13
140.69
129.66
129.39
128.76
128.69
128.29
128.06
127.56
127.08
125.92
125.48
125.06
124.55
120.95
120.62
110.35
116.96
111.65
111.43
55.84
40.00
39.83
39.66
39.50
39.33
39.16
38.99
38.87
36.55
35.76
34.41
30.76
30.56
17.70
0.07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

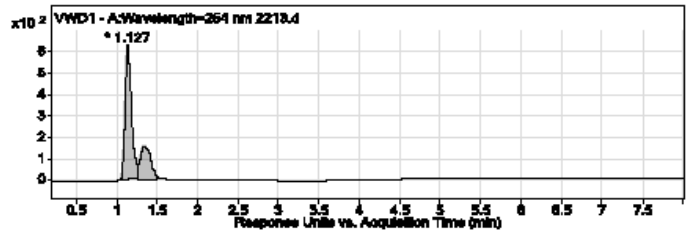

Transmittance [%]
95
90
85
80
75
70
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1
3030
2937
2755
2358
2342
1677
1656
1599
1553
1491
1463
1441
1384
1347
1316
1290
1251
1215
1162
1115
1080
1050
1027
997
917
889
846
819
791
754
696
663
631
597
571
543
523
485
433

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 2213.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 78 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 12/13/2021 1:00:52 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

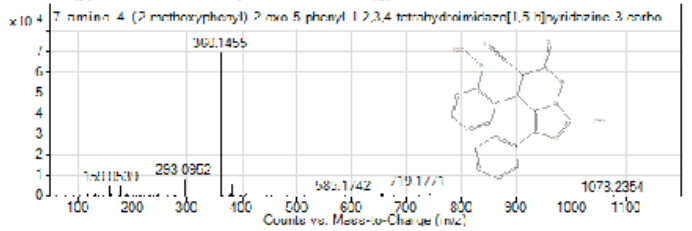



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.033 | 1.127 | 1.253 | 629.26 | 3552.37 | 100 |
| 2 | 1.253 | 1.33 | 1.5 | 165.5 | 1544.09 | 43.47 |

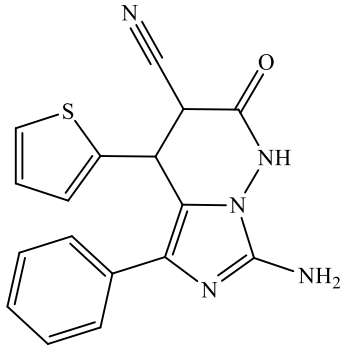
## User Spectra

| Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|
| 191 | 0 | ESI |



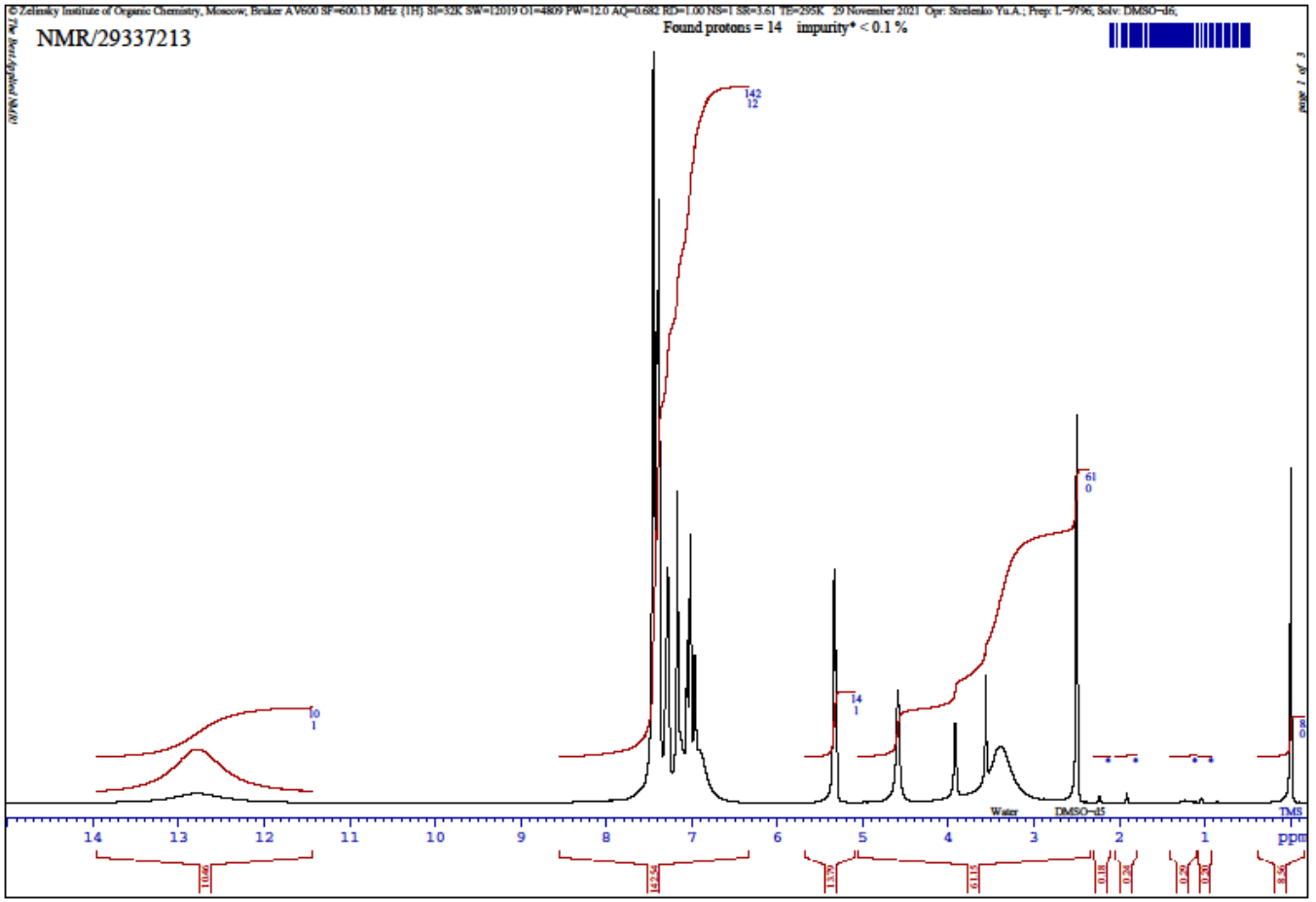

**Peak List**

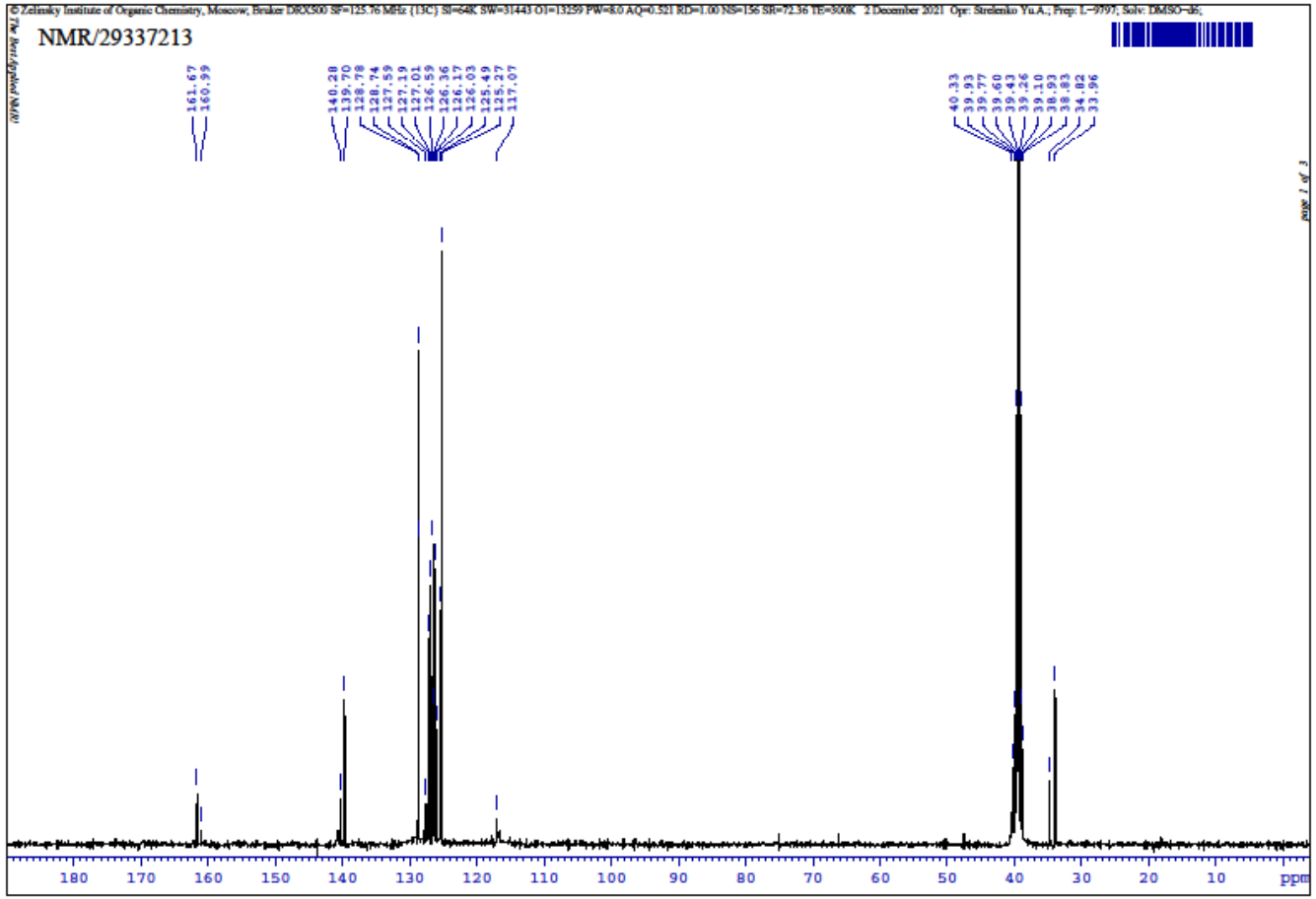
| m/z | z | Abund |
|---|---|---|
| 159.0539 | 1 | 5041.02 |
| 175.075 | 1 | 4484.75 |
| 293.0952 | 1 | 8429.21 |
| 294.0994 | 1 | 2867.3 |
| 360.1455 | 1 | 69495.94 |

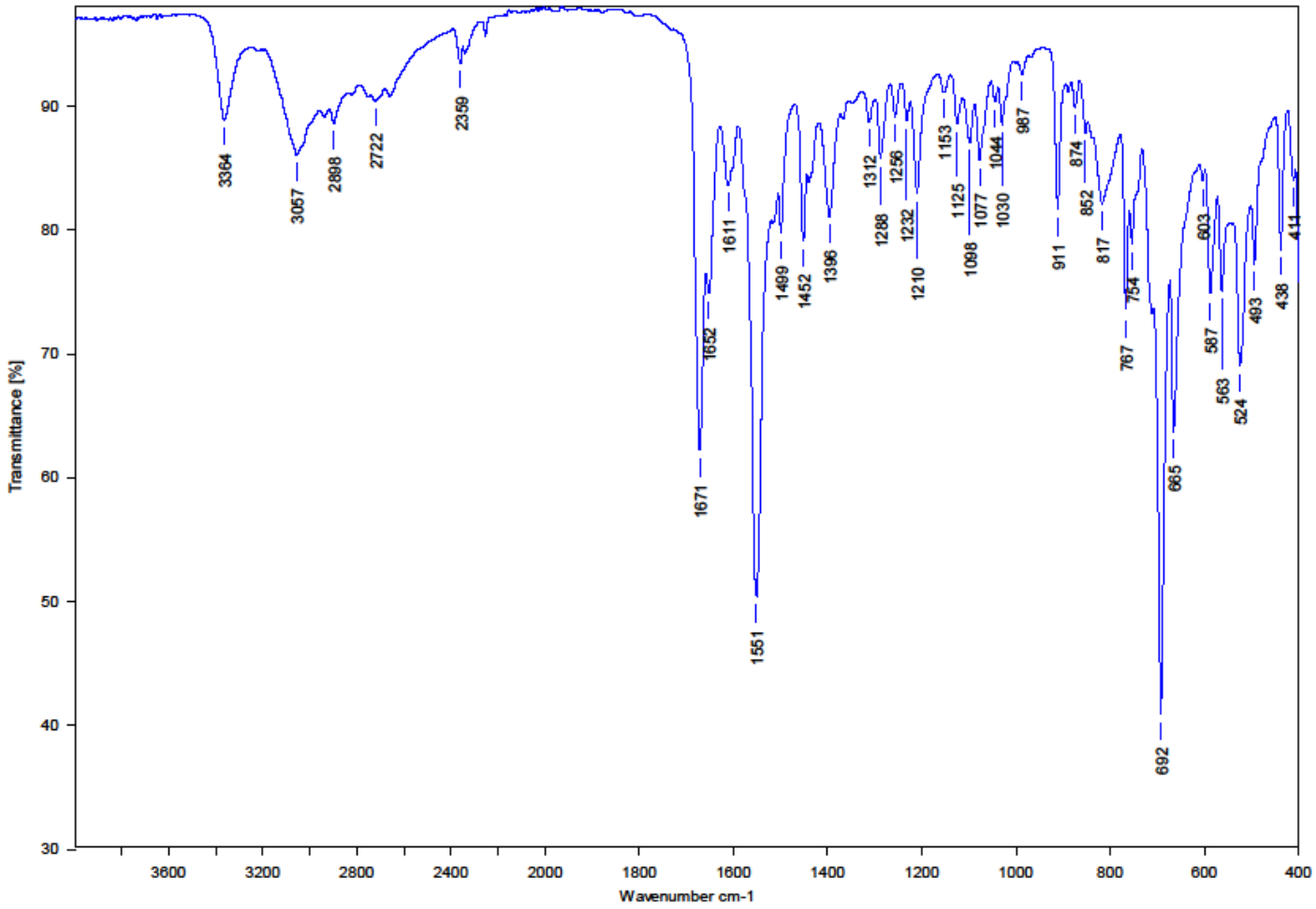



**Molecular formula: $C_{17}H_{13}N_5OS$**

**3i**



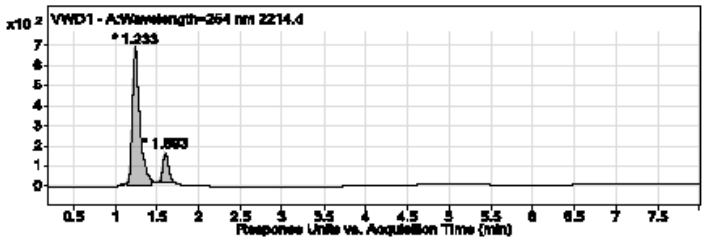

NMR/29337213
161.67
160.99
140.28
139.70
128.78
128.74
127.59
127.19
127.01
126.59
126.36
126.17
126.03
125.49
125.27
117.07
40.33
39.93
39.77
39.60
39.43
39.26
39.10
38.93
38.83
34.82
33.96
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Transmittance [%]
Wavenumber cm-1
3364
3057
2898
2722
2359
1671
1652
1611
1551
1499
1452
1396
1312
1288
1256
1232
1210
1153
1125
1098
1077
1044
1030
987
911
874
852
817
767
754
692
665
603
587
563
524
493
438
411

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 2214.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 79 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 12/13/2021 1:13:53 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

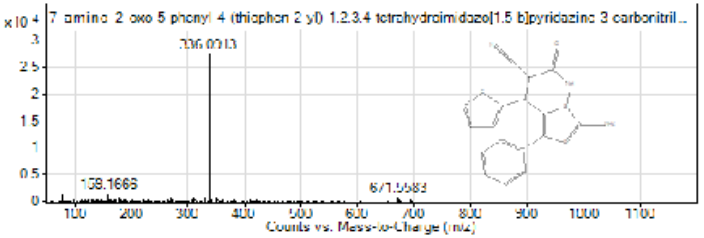



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.067 | 1.233 | 1.433 | 691.18 | 4285.86 | 100 |
| 2 | 1.483 | 1.593 | 1.753 | 149.81 | 750.22 | 17.5 |

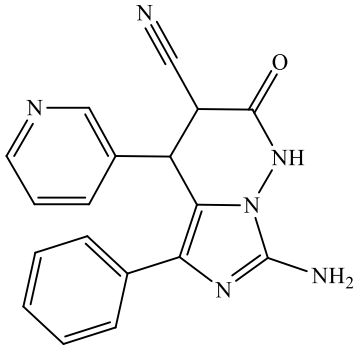
## User Spectra

| Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|
| 191 | 0 | ESI |



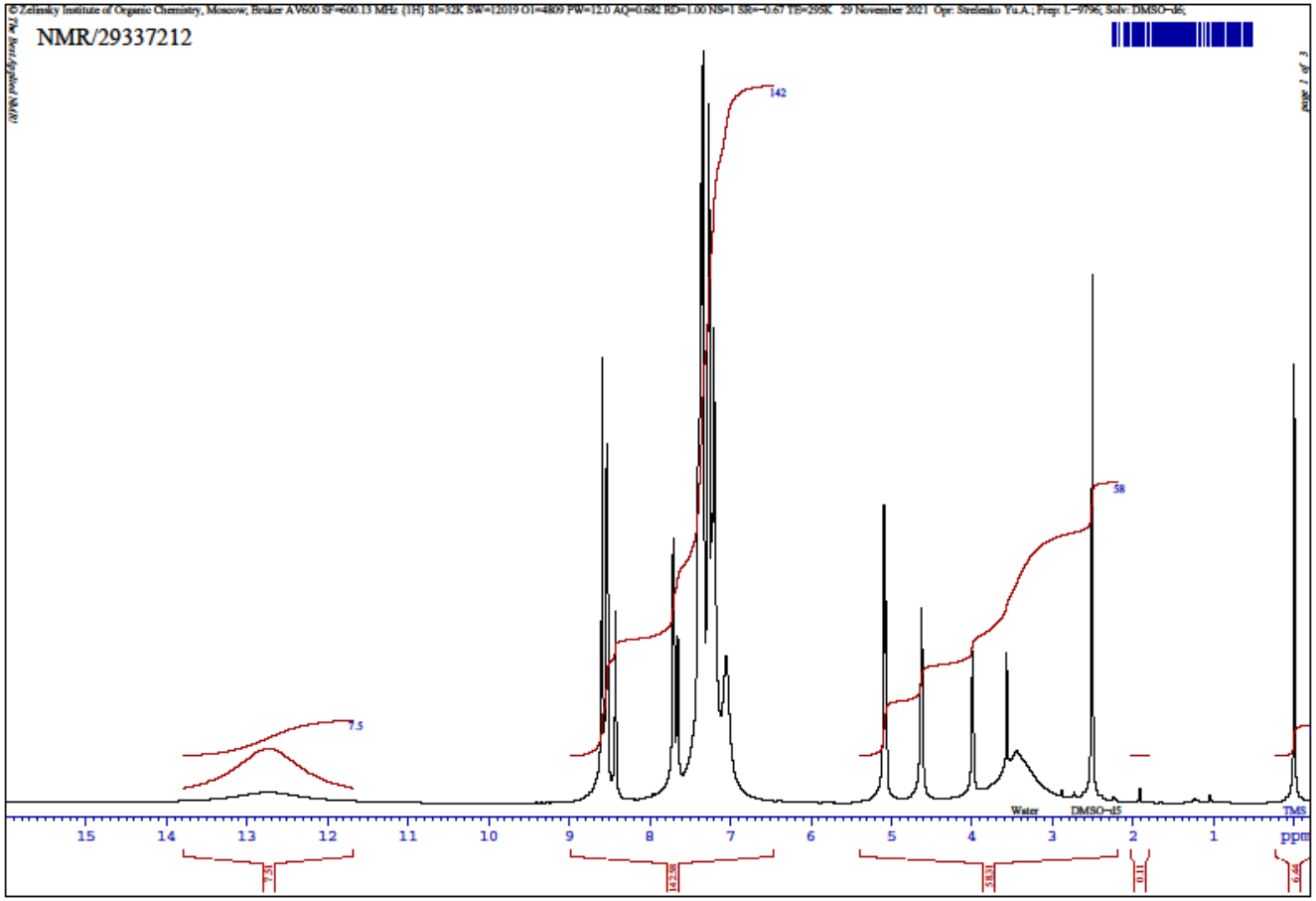

**Peak List**

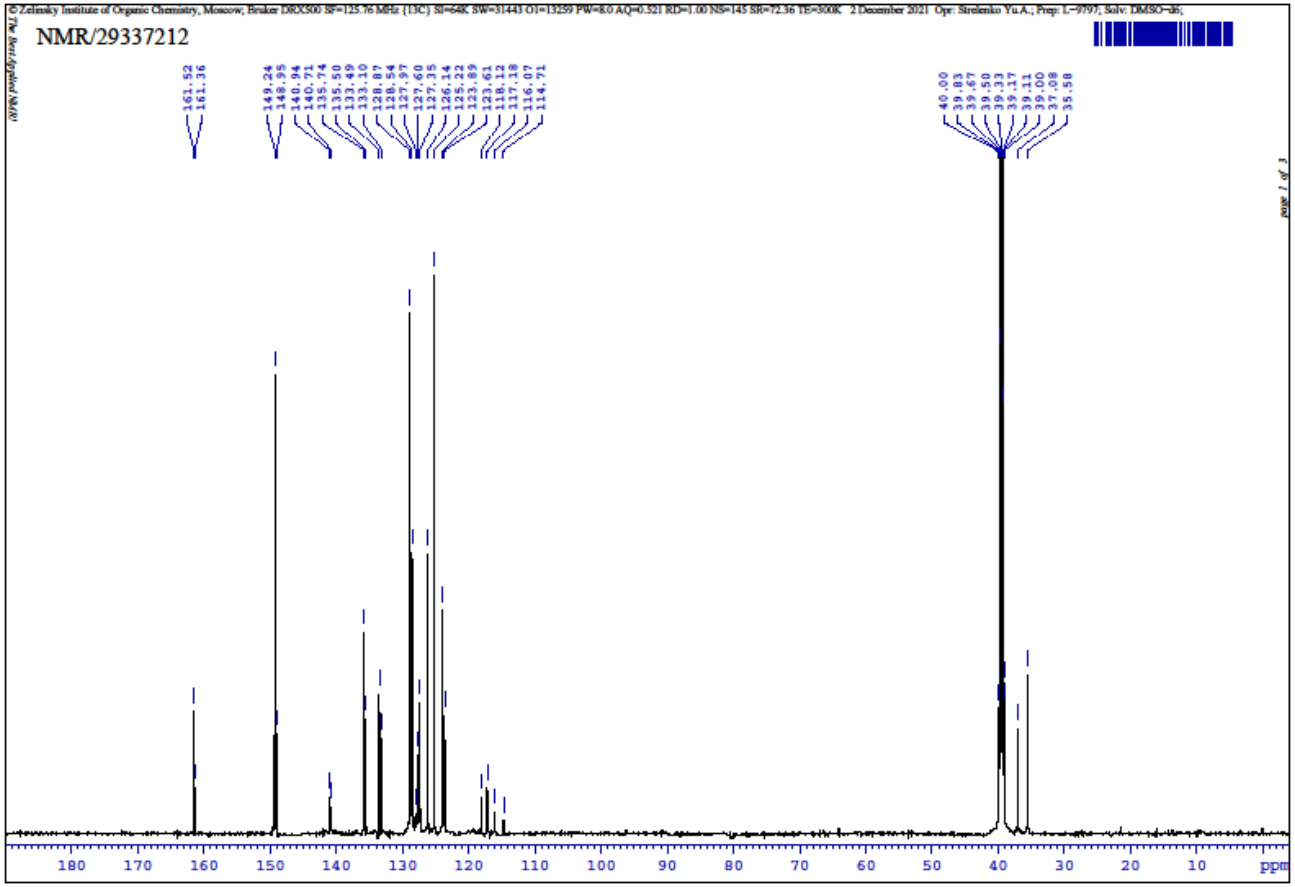
| *m/z* | z | Abund |
|---|---|---|
| 76.1173 | | 1564.25 |
| 159.1666 | 1 | 1450.18 |
| 328.3244 | 1 | 4260.75 |
| 329.3265 | 1 | 901.18 |
| 336.0913 | 1 | 27542.92 |

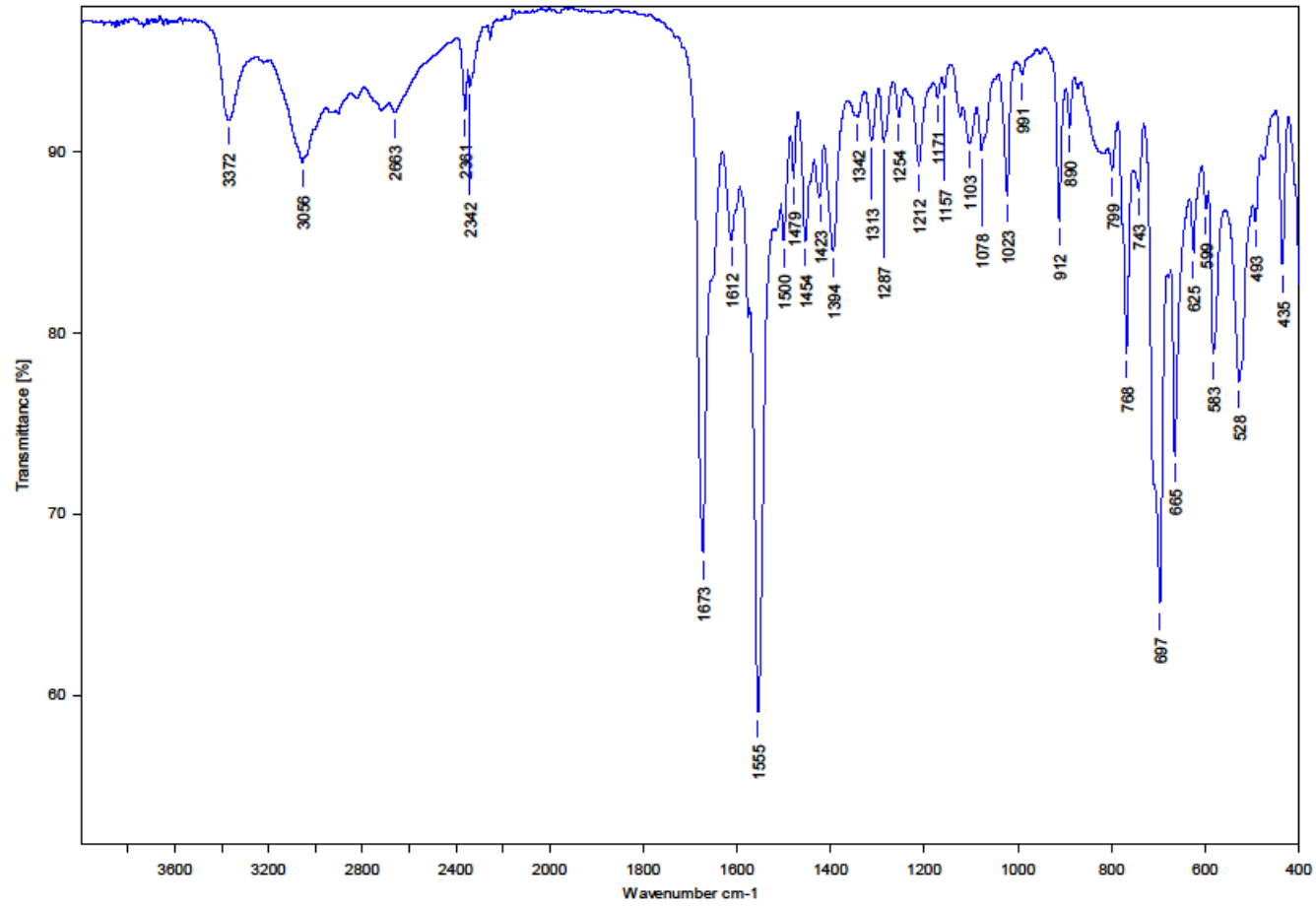



**Molecular formula: $C_{18}H_{14}N_6O$**

**3j**




NMR/29337212
161.52
161.36
149.24
148.95
140.94
140.71
135.74
135.50
133.49
133.10
128.87
128.54
127.97
127.60
127.35
126.14
125.22
123.89
123.61
118.12
117.18
116.07
114.71
40.00
39.83
39.67
39.50
39.33
39.17
39.11
39.00
37.08
35.58
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

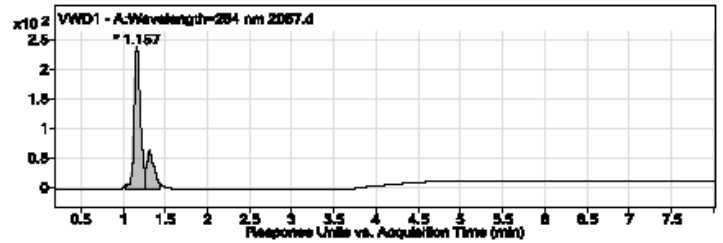

Transmittance [%]
90
80
70
60
3372
3056
2663
2361
2342
1673
1612
1555
1500
1479
1454
1423
1394
1342
1313
1287
1254
1212
1171
1157
1103
1078
1023
991
912
890
799
768
743
697
665
625
599
583
528
493
435
3600
3200
2800
2400
2000
1800
1600
1400
1200
1000
800
600
400
Wavenumber cm-1

# Qualitative Analysis Report

| | | | |
|---|---|---|---|
| **Data Filename** | 2057.d | **Sample Name** | |
| **Sample Type** | Sample | **Position** | Vial 16 |
| **Instrument Name** | Instrument 1 | **User Name** | |
| **Acq Method** | ACN-H2O_60-40.m | **Acquired Time** | 11/8/2021 12:34:01 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

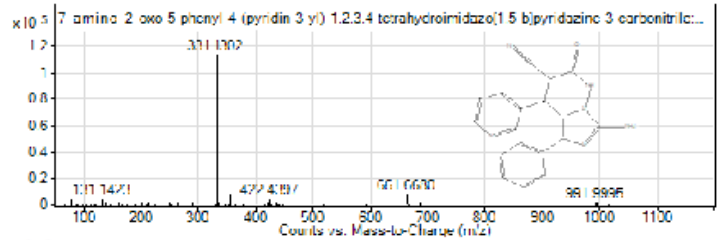



**Integration Peak List**

| Peak | Start | RT | End | Height | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.033 | 1.157 | 1.253 | 241.79 | 1267.33 | 100 |
| 2 | 1.253 | 1.303 | 1.443 | 65.34 | 426.79 | 33.68 |

## User Spectra

| Fragmentor Voltage | Collision Energy | Ionization Mode |
|---|---|---|
| 191 | 0 | ESI |




**Peak List**

| m/z | z | Abund |
|---|---|---|
| 76.1235 | | 3939.41 |
| 104.1145 | | 2413.46 |
| 131.1423 | 1 | 4679.96 |
| 331.1302 | 1 | 113587.13 |
| 332.1403 | 1 | 23339.88 |

**Table S2. Cartesian coordinates 2a for AM 1 and B3LYP/6-31.**

| AM 1 | | | | B3LYP/6-31 | | | |
|---|---|---|---|---|---|---|---|
| C | -2.91675100 | -1.11293700 | 0.99887900 | C | -3.27537000 | -1.67927400 | -0.00016600 |
| C | -3.84383200 | -1.09663700 | -0.04188200 | C | -4.45412500 | -0.92302900 | 0.00007600 |
| C | -3.67501700 | -0.21379800 | -1.11008300 | C | -4.38167400 | 0.47607000 | 0.00024000 |
| C | -2.58518800 | 0.65132000 | -1.13566600 | C | -3.13856800 | 1.10288800 | 0.00015500 |
| C | -1.63925100 | 0.62932600 | -0.09651300 | C | -1.93077900 | 0.35445400 | -0.00004200 |
| C | -1.81631200 | -0.25668000 | 0.97432300 | C | -2.02514300 | -1.05872100 | -0.00021500 |
| C | -0.53162800 | 1.56801900 | -0.15174700 | C | -0.71056900 | 1.15304700 | -0.00010000 |
| C | 0.76144400 | 1.33031900 | 0.14356200 | C | 0.64537800 | 0.92385800 | -0.00009700 |
| C | 1.73510400 | 2.36199100 | 0.03027700 | C | 1.48215000 | 2.09150100 | -0.00021200 |
| C | 1.30110400 | 0.02496100 | 0.59026100 | C | 1.35901400 | -0.37297700 | 0.00002800 |
| O | 1.16628800 | -0.52251600 | 1.68625500 | O | 0.85657200 | -1.50925800 | 0.00009100 |
| O | 2.04942300 | -0.59611900 | -0.36623200 | O | 2.71519700 | -0.18345800 | -0.00006600 |
| C | 2.63742500 | -1.86027700 | 0.00155500 | C | 3.57623400 | -1.39065900 | 0.00000800 |
| C | 3.42279800 | -2.32013900 | -1.20188900 | C | 5.01036100 | -0.89729700 | 0.00019200 |
| N | 2.53176200 | 3.20461100 | -0.06197500 | N | 2.12693900 | 3.07319200 | 0.00001400 |
| H | -3.04900600 | -1.80354000 | 1.84532800 | H | -3.32860500 | -2.76307000 | -0.00032600 |
| H | -4.70877700 | -1.77621600 | -0.02146800 | H | -5.42011900 | -1.41787800 | 0.00015400 |
| H | -4.40573300 | -0.19864700 | -1.93233000 | H | -5.28859500 | 1.07137600 | 0.00038900 |
| H | -2.45758000 | 1.35061400 | -1.97589600 | H | -3.08671900 | 2.18798100 | 0.00025100 |
| H | -1.08675900 | -0.27488500 | 1.80190800 | H | -1.12088000 | -1.64938700 | -0.00042300 |
| H | -0.81409100 | 2.58282400 | -0.49957600 | H | -0.94070500 | 2.21762700 | -0.00015700 |
| H | 3.29193700 | -1.70377500 | 0.89833300 | H | 3.32967900 | -1.98315400 | 0.88609500 |
| H | 1.81371100 | -2.57328900 | 0.26599500 | H | 3.32990000 | -1.98308700 | -0.88619200 |
| H | 3.90289700 | -3.30020100 | -0.96772400 | H | 5.69652500 | -1.75167100 | 0.00015400 |
| H | 2.75196400 | -2.44207900 | -2.08563700 | H | 5.21274200 | -0.28916000 | -0.88617700 |
| H | 4.21402700 | -1.57681900 | -1.46175100 | H | 5.21260100 | -0.28936500 | 0.88673500 |

**Table S3. Cartesian coordinates 1 for AM 1 and B3LYP/6-31.**

| AM 1 | | | | B3LYP/6-31 | | | |
|---|---|---|---|---|---|---|---|
| C | 3.31538000 | -1.18154500 | -0.22656400 | C | 3.38548000 | -1.17492700 | 0.00007000 |
| C | 4.01969800 | 0.00033700 | 0.00225400 | C | 4.03819000 | 0.06468700 | 0.00006900 |
| C | 3.32439900 | 1.18842400 | 0.22467500 | C | 3.27880300 | 1.24114800 | 0.00002500 |
| C | 1.93066900 | 1.20067200 | 0.22199500 | C | 1.88330600 | 1.18299900 | -0.00001600 |
| C | 1.21654200 | 0.01452500 | -0.00463800 | C | 1.21713500 | -0.05795500 | -0.00001900 |
| C | 1.92273000 | -1.17710500 | -0.23207500 | C | 1.99062400 | -1.23581100 | 0.00002700 |
| C | -0.23571000 | 0.00352300 | -0.00165800 | C | -0.24695700 | -0.09490300 | -0.00006700 |
| N | -1.02267200 | 1.15283000 | -0.18276700 | N | -0.99230100 | 1.10635100 | 0.00003800 |
| C | -2.32421700 | 0.74217200 | -0.11109400 | C | -2.26935000 | 0.74345100 | -0.00011300 |
| N | -2.38847200 | -0.67641800 | 0.12365000 | N | -2.39745600 | -0.63665300 | -0.00034500 |
| C | -1.05053300 | -1.12544600 | 0.17801600 | C | -1.09430300 | -1.17871900 | -0.00020000 |
| N | -3.53322200 | -1.40048900 | 0.13746600 | N | -3.62881500 | -1.29272500 | 0.00028600 |
| N | -3.46739400 | 1.56045900 | -0.11902700 | N | -3.36347200 | 1.55509900 | -0.00002800 |
| H | 3.85970600 | -2.12014700 | -0.40568900 | H | 3.96395000 | -2.09404800 | 0.00009500 |
| H | 5.11911200 | -0.00507400 | 0.00561600 | H | 5.12279300 | 0.11156600 | 0.00009300 |
| H | 3.87673700 | 2.12271800 | 0.40357500 | H | 3.77534900 | 2.20701600 | 0.00002800 |
| H | 1.39142500 | 2.14411700 | 0.39814400 | H | 1.28460500 | 2.08611900 | -0.00005500 |
| H | 1.37394800 | -2.11113700 | -0.42157500 | H | 1.49987600 | -2.20475700 | 0.00004700 |
| H | -0.79896300 | -2.16995500 | 0.34415200 | H | -0.93227700 | -2.24276500 | -0.00043200 |
| H | -3.74043500 | -1.66810600 | 1.09526300 | H | -3.81003400 | -1.81214100 | 0.85216300 |
| H | -3.39385500 | -2.25221000 | -0.39527900 | H | -3.81066800 | -1.81262800 | -0.85114300 |
| H | -3.26944700 | 2.47556600 | -0.47095900 | H | -3.23459000 | 2.55016000 | 0.00035500 |
| H | -4.24966000 | 1.13620800 | -0.57396600 | H | -4.28227300 | 1.14715100 | 0.00053800 |