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Thiourea assisted recyclization of 1-(chloromethyl)dihydroisoquinolines: a convenient route to β-(*o*-thiazolylaryl)ethylamines

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1. General Information

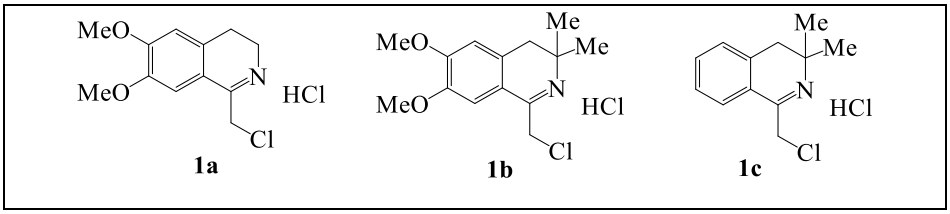
The solvents were purified according to standard procedures. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were recorded in DMSO-d_6 at 30°C on a spectrometer Bruker Avance 600 (600 MHz). Chemical shifts of nuclei ^{1}H and ^{13}C were measured relatively the residual signals of DMSO-d_6 [δ =2.50 (2.49) ppm for protons and 39.09 (39.28) ppm for carbon]. Coupling constants (*J*) are reported in Hertz (Hz). Melting points were determined using Fisher-Johns Melting Point Apparatus (Fisher Scientific) and are uncorrected. High Resolution Mass Spectra were registered on a Bruker UHR-TOF MaxisTM Impact instrument. The reaction course and purity of the obtained compounds (for base) were monitored by TLC (plates with Al_2O_3 III activity grade, eluent $CHCl_3$, development of TLC plates by exposition to iodine vapors in "iodine chamber").

The experimental data for structure **3a** were obtained on an Agilent SuperNova diffractometer by using a microfocus X-ray source with copper anode and an Atlas S2 two-dimensional CCD detector. The reflections were collected, unit cell parameters determined and refined by using the specialized CrysAlisPro 1.171.38.41 software suite (Rigaku Oxford Diffraction, 2018).[S1] The structures were solved by using the ShelXT program (Sheldrick, 2015)[S2] and refined with the ShelXL program (Sheldrick, 2015).[S3] Molecular graphics and presentation of structures for publication were performed with the Olex2 ver. 1.2.10 software suite.[S4] CCDC 2031011 (crystal from mixed solvents (1:1 methanol/propanol)) contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

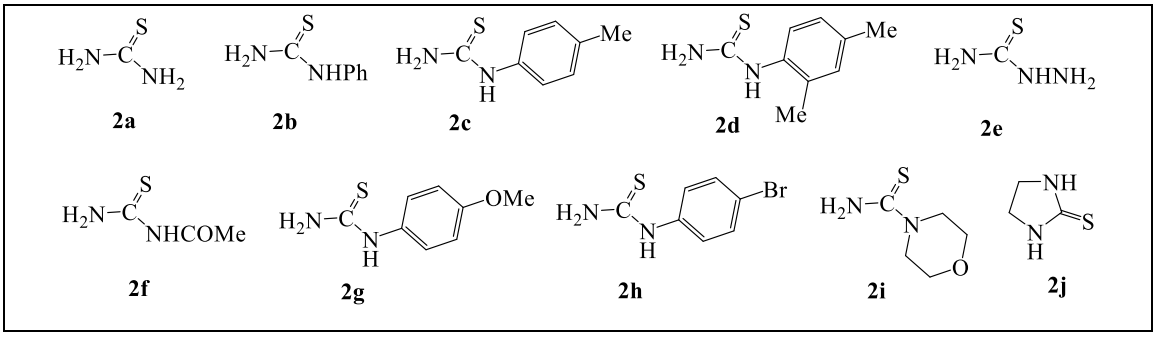
Quantum chemical calculations (BHHLYP/6-311G**) were performed using quantum chemical program package Firefly 8.0[S5], which is partially based on the GAMESS (US)[S6] source code.

2. List of the starting reactants.

Substrates:

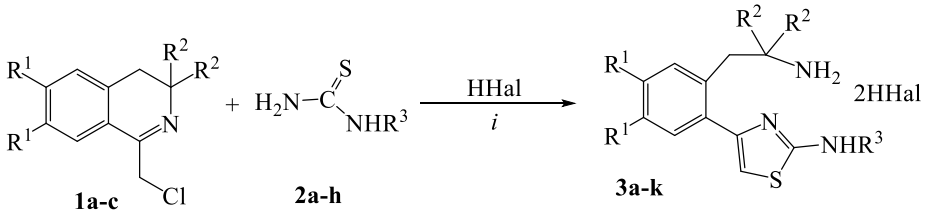


Recyclizing reagents:



The starting dihydroisoquinolines **1a-c** were provided by InterBioscreen Ltd (Russia), thioureas **2a-d, f-j** and thiosemicarbazide (**2e**) are commercially available and used without further purification.

3. General procedure and characterization of compounds 3a-m.

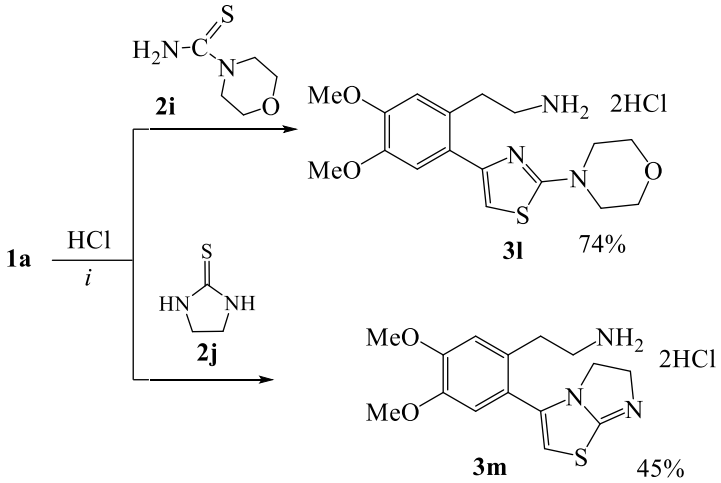


a R^1 = MeO, R^2 = H
b R^1 = MeO, R^2= Me
c R^1 =H, R^2 = Me

a R^3 = H
b R^3 = Ph
c R^3 = 4-MeC_6H_4
d R^3 = 2,4-$Me_2C_6H_3$
e R^3 = NH_2
f R^3 = Ac
g R^3 = 4-$MeOC_6H_4$
h R^3 = 4-BrC_6H_4

a R^1 = MeO, R^2 = H, R^3 = H, Hal = Cl, 92%
b R^1 = MeO, R^2= H, R^3 = Ph, Hal = Cl, 67%
c R^1 = MeO, R^2 = H, R^3 = 4-MeC_6H_4, Hal = Br, 33%
d R^1 = MeO, R^2 = H, R^3 = 2,4-$Me_2C_6H_3$, Hal = Br, 95%
e R^1 = MeO, R^2 = H, R^3 = NH_2, Hal = Cl, 82%
f R^1 = MeO, R^2 = Me, R^3 = H, Hal = Cl, 63%
g R^1 = MeO, R^2 = Me, R^3 = Ac, Hal = Cl, 42%
h R^1 = MeO, R^2 = Me, R^3 = Ph, Hal = Cl, 76%
i R^1 = MeO, R^2 = Me, R^3 = 4-$MeOC_6H_4$, Hal = Br, 95%
j R^1 = MeO, R^2 = Me, R^3 = 4-BrC_6H_4, Hal = Cl, 48%
k R^1 = R^3 = H, R^2 = Me, Hal = Cl, 63%

Scheme 1 *Reagents and conditions: i*, HHal (2 equiv.), PrOH (EtOH for **3b**), reflux, 1 h (0.3 h for **3a**, 2 h for **3b**).



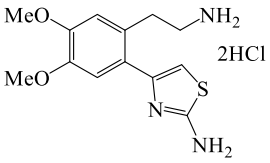
Scheme 2 *Reagents and conditions: i*, HCl (2 equiv.), PrOH reflux 1 h (for **3l**), $MeO(CH_2)_2OH$, reflux, 3 h (for **3m**).

General procedure for synthesis of compounds **3**. A solution of dihydroisoquinoline **1** (5 mmol), thiourea **2** (5 mmol) and HHal (10 mmol) in propanol (ethanol and 2-methoxyethanol are used to synthesize compounds **3b** and **3m**, respectively) is boiled, cooled, filtered off and washed with propanol (3 × 8 ml). Conditions for reaction are also given in Table S1.

Table S1. Reaction conditions and yields of β-[*o*-(thiazol-4-yl)aryl]ethylamines **3a-m**

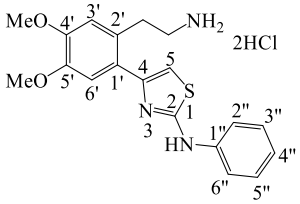
Substrate, reagent	Reaction product	Reaction time h	Yield %
1a, **2a**	**3a**	0.3	92
1a,**2b**	**3b**	2.0	67
1a, **2c**	**3c**	1.0	33
1a,**2d**	**3d**	1.0	95
1a, **2e**	**3e**	1.0	82
1b,**2a**	**3f**	1.0	63
1b, **2f**	**3g**	1.0	42
1b,**2b**	**3h**	1.0	76
1b,**2g**	**3i**	1.0	95
1b,**2h**	**3j**	1.0	48
1c, **2a**	**3k**	1.0	63
1a, **2i**	**3l**	1.0	74
1a, **2j**	**3m**	3.0	45

4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]thiazol-2-amine dihydrochloride (**3a**).



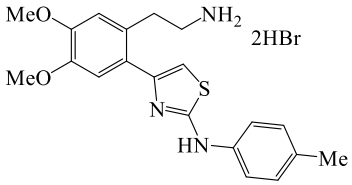
The starting compounds were dihydroisoquinoline **1a** and thiourea **2a**. The yield of **3a** was 1.62 g (92%). Beige crystals with m.p. 220-222 ºC (PrOH). ^{1}H NMR (600 MHz) δ = 9.20 (s, 1H, $^+$NH), 8.25 (t, *J* = 5.6 Hz, 3H, $^+$NH$_3$), 7.01 (s, 1H, H-6′), 7.00 (s, 1H, H-3′), 6.87 (s, 1H, H-5), 3.81-3.77 (m, 8H, 2MeO, NH$_2$), 3.00-2.96 (m, 2H, CH$_2$), 2.93-2.90 (m, 2H, CH$_2$). ^{13}C NMR (150 MHz) δ = 169.55, 149.70, 147.25, 137.40, 128.84, 121.01, 113.43, 113.36, 104.68, 55.71, 55.69, 39.52, 30.02. HRMS (ESI): m/z [M + H]$^+$ calc. for $C_{13}H_{18}N_3O_2S$: 280.1114; found: 280.1105.

4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]-N-phenylthiazol-2-amine dihydrochloride (**3b**).



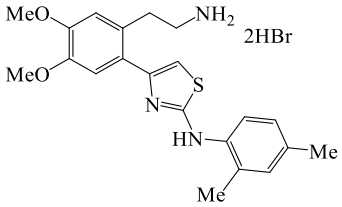
The starting compounds were dihydroisoquinoline **1a** and thiourea **2b**. The yield of **3b** was 1.44 g (67%). Colorless crystals with m.p. 230-232ºC (EtOH). ^{1}H NMR (600 MHz) δ = 10.20 (s, 1H, $^+$NH), 7.68 (s, 3H, $^+$NH$_3$), 7.60-7.58 (m, 2H, H-2", H-6"), 7.33-7.30 (m, 2H, H-3", H-5"), 7.07 (s, 1H, H-6′), 6.95 (t, J = 7.3 Hz, 1H, H-4"), 6.90 (s, 1H, H-3′), 6.89 (s, 1H, H-5), 3.81-3.78 (m, 7H, 2MeO, NH), 3.05-3.00 (m, 4H, CH$_2$). ^{13}C NMR (150 MHz) δ = 162.73, 150.14, 148.53, 147.28, 141.09, 128.99, 127.54, 127.36, 121.24, 116.87, 113.79, 113.57, 104.87, 55.63, 55.58, 39.97, 30.64. HRMS (ESI): m/z [M + H]$^+$ calc. for $C_{19}H_{22}N_3O_2S$: 356.1427; found: 356.1432.

4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl)]-N-(p-tolyl)thiazol-2-amine dihydrobromide (**3c**).



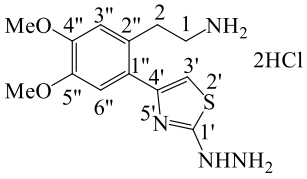
The starting compounds were dihydroisoquinoline **1a** and thiourea **2c**. The yield of **3c** was 0.88 g (33%). Colorless crystals with m.p. 196-198ºC (EtOH). ^{1}H NMR (600 MHz) δ = 10.43 (s, 1H, $^+$NH), 7.85 (s, 3H, $^+$NH$_3$), 7.47-7.45 (m, 2H, H-2", H-6"), 7.15 (d, *J* = 8.2 Hz, 2H, H-3", H-5"), 7.05 (s, 1H, H-6′), 6.95 (s, 1H, H-3′), 6.90 (s, 1H, H-5), 3.81-3.77 (m, 7H, 2MeO, NH), 3.03-3.00 (m, 4H, CH$_2$), 2.25 (s, 3H, Me). ^{13}C NMR (150 MHz) δ = 163.95, 148.78, 147.24, 138.04, 131.39, 129.57, 129.39, 127.79, 126.32, 118.19, 113.77, 113.59, 104.77, 55.70, 55.62, 39.94, 30.49, 20.36. HRMS (ESI): m/z [M + H]$^+$ calc. for $C_{20}H_{24}N_3O_2S$: 370.1584; found: 370.1590.

4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]-N-(2,4-dimethylphenyl)thiazol-2-amine dihydrobromide (**3d**).



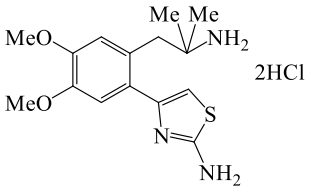
The starting compounds were dihydroisoquinoline **1a** and thiourea **2d**. The yield was 2.59 g (95%). Colorless crystals with m.p. 223-225ºC (EtOH). ^{1}H NMR (600 MHz) δ = 10.47 (s, 1H, $^+$NH), 7.92 (s, 3H, $^+$NH$_3$), 7.48 (d, *J* = 8.0 Hz, 1H, H-6"), 7.14 (d, *J* = 2.1 Hz, 1H, H-3"), 7.11-7.08 (m, 1H, H-5"), 7.02 (s, 1H, H-6′), 6.99 (s, 1H, H-3′), 6.91 (s, 1H, H-5), 3.81-3.76 (m, 7H, 2MeO, NH), 3.02-2.98 (m, 2H, CH$_2$) , 2.92 (dd, *J* = 9.3, 6.0 Hz, 2H, CH$_2$), 2.28 (s, 3H, Me), 2.25 (s, 3H, Me). ^{13}C NMR (150 MHz) δ = 167.84, 149.37, 147.20, 136.08, 134.82, 132.33, 131.69, 131.31, 128.54, 127.66, 124.39, 122.55, 113.71, 113.45, 105.34, 55.74, 55.71, 39.87, 30.21, 20.49, 17.55. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{21}H_{26}N_3O_2S$: 384.1740; found: 384.1745.

2-[2-(2-Hydrazinylthiazol-4-yl)-4,5-dimethoxyphenyl]ethan-1-amine dihydrochloride (**3e**).



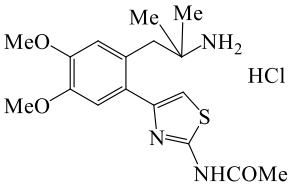
The starting compounds were dihydroisoquinoline **1a** and thiosemicarbazide **2e**. The yield was 1.51 g (82%). Beige crystals with m.p. 199-202ºC (PrOH). ^{1}H NMR (600 MHz) δ = 10.62 (s, 2H, NH$_2$), 10.25 (s, 1H, $^+$NH), 8.54 (t, *J* = 5.6 Hz, 3H, $^+$NH$_3$), 7.14 (s, 1H, H-6′), 7.02 (s, 1H, H-3′), 6.88 (s, 1H, H-5), 3.77-3.79 (m, 7H, 2MeO, NH$_2$), 3.11-3.07 (m, 2H, CH$_2$), 3.01 (dt, *J* = 11.6, 6.2, 5.6 Hz, 2H, CH$_2$). ^{13}C NMR (150 MHz) δ = 165.58, 149.75, 148.73, 147.30, 127.90, 125.99, 114.05, 113.32, 108.17, 55.66, 55.59, 40.00, 30.87. HRMS (ESI): m/z [M + Na]$^+$ calc. for $C_{13}H_{18}N_3O_2SNa$: 317.1043; found: 317.1035.

4-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]thiazol-2-amine dihydrochloride (**3f**).



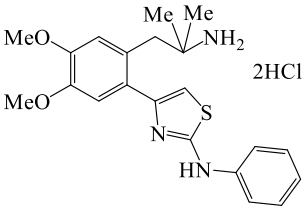
The starting compounds were dihydroisoquinoline **1b** and thiourea **2a**. The yield was 1.69 g (89%). Beige crystals with m.p. 194-196°C (PrOH). ^{1}H NMR (600 MHz) δ = 9.21 (s, 1H, $^+$NH), 8.26 (s, 3H, $^+$NH$_3$), 7.03 (s, 1H, H-6′), 6.98 (s, 1H, H-3′), 6.82 (s, 1H, H-5), 3.81-3.78 (m, 8H, 2MeO, NH$_2$), 3.02 (s, 2H, CH$_2$), 1.08 (s, 6H, Me). ^{13}C NMR (150 MHz) δ = 169.59, 149.18, 147.43, 138.49, 126.91, 122.50, 115.40, 113.80, 104.97, 55.74, 55.62, 54.27, 41.01, 24.91. HRMS (ESI): m/z [M + H]$^+$ calc. for $C_{15}H_{22}N_3O_2S$: 308.1427; found: 308.1418.

N-{4-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]thiazol-2-yl}acetamide hydrochloride (**3g**).



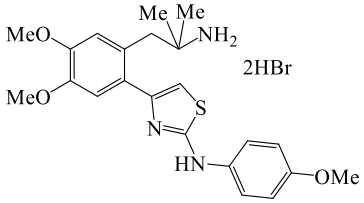
The starting compounds were dihydroisoquinoline **1b** and thiourea **2f**. The yield of **3g** was 0.81 g (42%). Colorless crystals with m.p. 225-227°C (PrOH). ^{1}H NMR (600 MHz) δ = 9.24 (s, 1H, NH), 7.25 (s, 1H, H-6′), 7.16-7.03 (m, 2H, H-3′, H-5), 3.93-3.76 (m, 6H, 2MeO), 3.11 (s, 2H, CH$_2$), 1.41 (s, 6H, Me). ^{13}C NMR (150 MHz) δ = 171.15, 161.61, 156.31, 152.34, 147.69, 134.34, 116.89, 114.55, 112.38, 106.17, 56.46, 56.14, 54.52, 38.14, 25.35, 16.38. HRMS (ESI): m/z [M]$^+$ calc. for $C_{17}H_{23}N_3O_2S$: 332.1427; found: 332.1431.

4-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-N-phenylthiazol-2-amine dihydrochloride (**3h**).



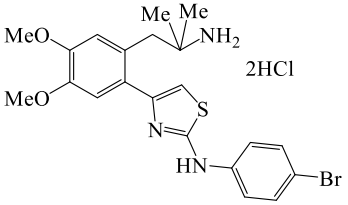
The starting compounds were dihydroisoquinoline **1b** and thiourea **2b**. The yield was 2.03 g (89%). Colorless crystals with m.p. 180-182°C (PrOH). ^{1}H NMR (600 MHz) δ = 10.80 (s, 1H, $^+$NH), 8.13 (s, 3H, $^+$NH$_3$), 7.61-7-58 (m, 2H, H-2", H-6"), 7-34-7.30 (m, 2H, H-3", H-5"), 7.04 (s, 1H, H-6′), 7.03 (s, 1H, H-3′), 7.01-6.97 (m, 1H, H-4"), 6.91(s, 1H, H-5), 3.81-3.78 (m, 7H, 2MeO, NH), 3.29 (m, 2H, CH$_2$), 1.04 (s, 2H, 6Me). ^{13}C NMR (150 MHz) δ = 163.53, 149.04, 148.28, 147.41, 140.69, 129.08, 127.54, 126.17, 122.07, 117.74, 115.90, 113.69, 105.34, 55.74, 55.54, 54.56, 40.92, 25.10. HRMS (ESI): m/z [M + H]$^+$ calc. for $C_{21}H_{26}N_3O_2S$: 384.1740; found: 384.1748.

4-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-N-(4-methoxyphenyl)thiazol-2-amine dihydrobromide (**3i**).



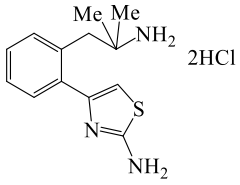
The starting compounds were dihydroisoquinoline **1b** and thiourea **2g**. The yield was 2.73 g (95%). Colorless crystals with m.p. 203-206ºC (PrOH). ^{1}H NMR (600 MHz) δ = 10.45 (s, 1H, $^{+}$NH), 8.89 (s, 3H, $^{+}$NH$_3$), 7.48-7.46 (m, 2H, H-2", H-6"), 7.02 (s, 1H, H-6′), 6.96 (s, 1H, H-3′), 6.95- 6.94 (m, 2H, H-3", H-5"), 6.85 (s, 1H, H-5), 3.81-3.78 (m, 10H, 3MeO, NH), 3.16 (s, 2H, CH$_2$), 1.08 (s, 6H, 2Me). ^{13}C NMR (150 MHz) δ = 165.38, 155.54, 148.44, 147.48, 133.32, 126.92, 126.00, 121.10, 119.19, 115.59, 114.56, 113.81, 104.97, 55.75, 55.57, 55.30, 54.60, 41.13, 25.21. HRMS (ESI): m/z [M + H]$^{+}$ calc. for $C_{22}H_{28}N_3O_3S$: 414.1846; found: 414.1857.

4-[2-(2-Amino-2-methylpropyl)-4,5-dimethoxyphenyl]-N-(4-bromophenyl)thiazol-2-amine dihydrochloride (**3j**).



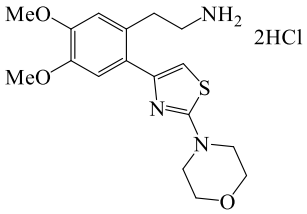
The starting compounds were dihydroisoquinoline **1b** and thiourea **2h**. The yield was 1.29 g (48%). Colorless crystals with m.p. 182-185ºC (PrOH). ^{1}H NMR (600 MHz) δ = 10.78 (s, 1H, $^{+}$NH), 8.06 (s, 3H, $^{+}$NH$_3$), 7.65-7.57 (m, 2H, H-3", H-5"), 7.49- 7.40 (m, 2H, H-2", H-6"), 7.03 (s, 1H, H-6′), 7.02 (s, 1H, H-3′), 6.92 (s, 1H, H-5), 3.81-3.78 (m, 7H, 2MeO, NH), 3.30 (s, 2H, CH$_2$), 1.01 (s, 6H, 2Me). ^{13}C NMR (150 MHz,) δ: 162.45, 150.56, 148.15, 147.43, 140.44, 131.63, 128.30, 126.00, 118.95, 115.95, 113.69, 112.47, 105.78, 55.73, 55.52, 54.57, 40.90, 25.09. HRMS (ESI): m/z [M + H]$^{+}$ calc. for $C_{21}H_{25}BrN_3O_2S$: 462.0845; found: 462.0855.

4-[2-(2-Amino-2-methylpropyl)phenyl]thiazol-2-amine dihydrochloride (**3k**).



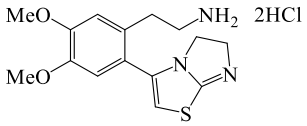
The starting compounds were dihydroisoquinoline **1c** and thiourea **2a**. The yield was 1.01 g (63%). Beige crystals with m.p. 153-156ºC (EtOH). ^{1}H NMR (600 MHz) δ = 9.25 (s, 1H, $^{+}$NH), 8.36 (s, 3H, $^{+}$NH$_3$), 7.47-7.44 (m, 1H, H-6′), 7.40-7.38 (m, 3H, H-3′ - H-5′), 6.86 (s, 1H H-5), 3.00-2.96 (m, 2H, CH$_2$), 3.10 (s, 2H, CH$_2$), 1.01 (s, 6H, 2Me). ^{13}C NMR (150 MHz) δ = 169.71, 138.72, 134.56, 132.12, 130.73, 129.40, 127.33, 105.71, 54.30, 41.34, 40.03, 24.60. HRMS (ESI): m/z [M + H]$^{+}$ calc. for $C_{13}H_{18}N_3S$: 248.1224; found: 248.1214.

4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]-2-(morpholin-4-yl)thiazole dihydrochloride (**3l**).



The starting compounds were dihydroisoquinoline **1a** and morpholine-4-carbothioamide **2i**. The yield was 1.56 g (74%). Colorless crystals with m.p. 174-176ºC (EtOH). ^{1}H NMR (600 MHz) δ = 8.28 (t, *J* = 5.6 Hz, 3H, $^{+}NH_3$), 6.99 (s, 1H, H-6′), 6.97 (s, 1H, H-3′), 6.95 (s, 1H, H-5), 3.80 (s, 3H, MeO), 3.75 (s, 7H, MeO, $2CH_2$), 3.52 (t, J = 4.9 Hz, $2CH_2$), 3.02-2.94 (m, 4H, CH_2). ^{13}C NMR (150 MHz) δ = 170.01, 149.07, 147.14, 146.24, 128.44, 124.90, 113.71, 113.63, 105.13, 65.13, 61.94, 55.96, 55.66, 48.57, 30.68, 18.51, 16.03. HRMS (ESI): m/z $[M + H]^+$ calc. for $C_{17}H_{24}N_3O_3S$: 350.1533; found: 350.1532.

2-[2-(5,6-Dihydroimidazo[2,1-b]thiazol-3-yl)-4,5-dimethoxyphenyl]ethan-1-amine dihydrochloride (**3m**).



The starting compounds were dihydroisoquinoline **1a** and imidazolidine-2-thione **2j**. The yield was 0.85 g (45%). Colorless crystals with m.p. 273-275ºC (EtOH). ^{1}H NMR (600 MHz) δ = 10.63 (s, 1H, ^{+}NH), 8.61 (s, 3H, $^{+}NH_3$), 7.59 (s, 1H, H-6′), 7.38 (s, 1H, H-3′), 6.98 (s, 1H, H-5), 4.34 (t, *J* = 6.4 Hz, 2H, CH_2), 3.82 (s, 3H, MeO), 3.79 (s, 3H, MeO), 3.71 (t, *J* = 5.9 Hz, 2H, CH_2), 3.23-3.18 (m, 2H, CH_2), 3,07 (t, *J* = 6.4 Hz, 2H, CH_2) ^{13}C NMR (150 MHz) δ = 167.51, 150.34, 148.33, 136.62, 125.71, 117.19, 111.13, 108.01, 98.51, 56.01, 55.65, 44.87, 44.10, 37.05, 26.29. HRMS (ESI): m/z $[M + H]^+$ calc. for $C_{15}H_{20}N_3O_2S$: 306.1271; found: 306.1269.

4. Structure and crystal data for compound 3a.

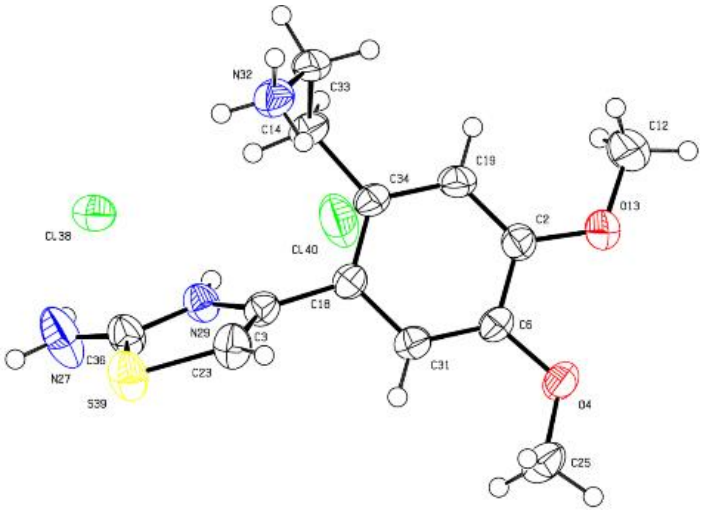


Figure S1. Structure for compound **3a**.

Table S2 Crystal data and structure refinement for compound **3a**.

CCDC Number	2031011
Empirical formula	$C_{13}H_{19}Cl_2N_3O_2S$
Formula weight	352.27
Temperature/K	293
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	14.1345(2)
b/Å	8.83290(10)
c/Å	14.4961(2)
α/°	90
β/°	110.176(2)
γ/°	90
Volume/Å^3	1698.76(4)
Z	4
ρ_{calc}/g cm^{-3}	1.377
μ/mm^{-1}	4.652
F(000)	736.0
Crystal size/mm^3	0.492 × 0.39 × 0.247
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.534 to 152.368
Index ranges	$-17 \le h \le 16$, $-11 \le k \le 7$, $-18 \le l \le 17$
Reflections collected	19797
Independent reflections	3551 [R_{int} = 0.0497, R_{sigma} = 0.0315]
Data/restraints/parameters	3551/0/194
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0401, wR_2 = 0.1102
Final R indexes [all data]	R_1 = 0.0413, wR_2 = 0.1122
Largest diff. peak/hole / e Å^{-3}	0.47/-0.57

5. Quantum chemical data (BHHLYP/6-311**) for the two key stages for the reaction of 1-chloromethyl-3,4-dihydroisoquinoline (1d) with phenylthiourea (2b)

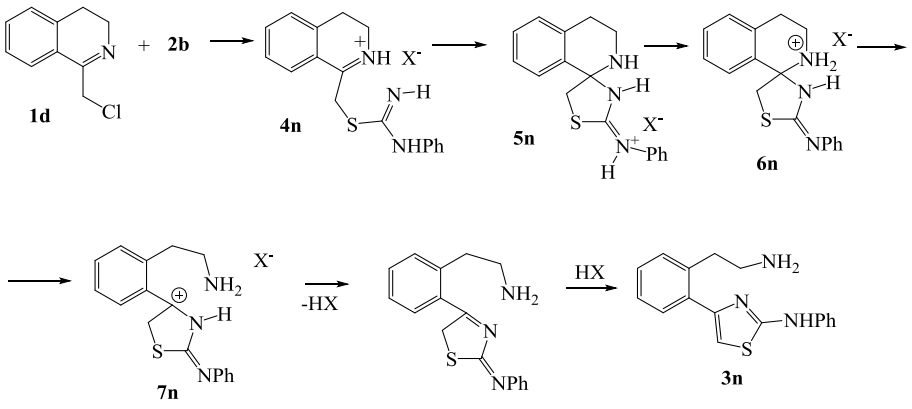
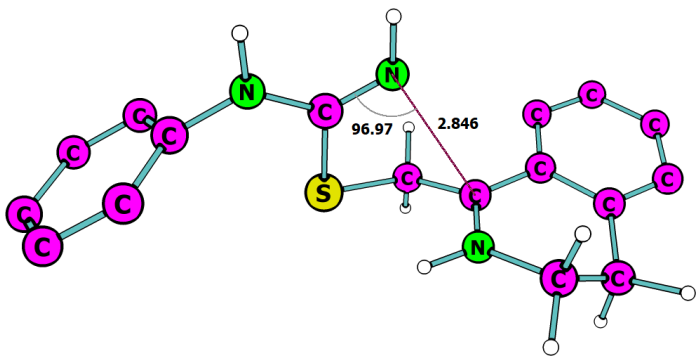


Fig. S2. Cation $4n^+$ (hereinafter, aromatic protons are not shown)

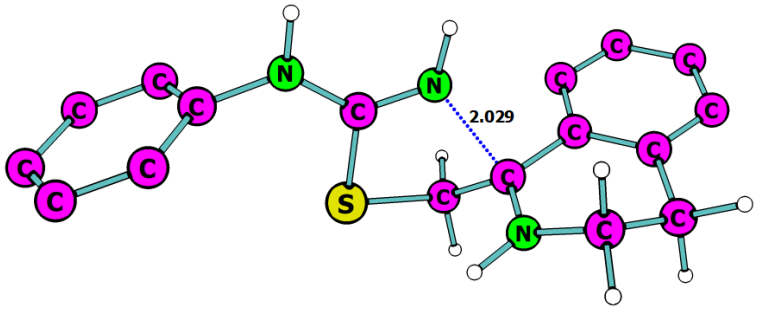


E_{tot} = -1220.600968051 a.u.

39
symmetry c1

C	5.601514494	-1.112859062	-0.085064659
C	5.312352055	0.239570457	-0.124264932
C	4.596031068	-2.042260094	0.117213155
H	6.101326975	0.950631770	-0.284641479
H	4.823470642	-3.090560712	0.134231247
C	4.016853644	0.683163012	0.035629024
C	3.299529788	-1.616947558	0.291578411
H	2.526421887	-2.345765927	0.429001000
C	2.997352208	-0.255682887	0.256916265
H	6.614722029	-1.442619759	-0.218937525
C	3.674996444	2.144989309	0.032282669
C	1.646194889	0.228044227	0.459659673
C	2.282863700	2.355033133	-0.517009340
N	1.357911301	1.444947269	0.154556800
H	4.385686205	2.700408583	-0.564497393
H	2.241402068	2.145621958	-1.580805161
H	3.734124140	2.534393620	1.045324206
H	1.933593222	3.362804837	-0.350065989
C	0.603164770	-0.608133396	1.138979682
H	0.706580695	-1.633963241	0.835676822
H	0.773584330	-0.546978431	2.209289388
S	-1.105420923	-0.098555933	0.872032534
C	-1.208332396	-0.601772407	-0.855337608
N	-2.456204135	-0.524161089	-1.370051586
N	-0.134628921	-0.946052263	-1.424139603
H	-2.549050635	-0.749633211	-2.340489869
H	0.398726692	1.726064196	0.284354256
H	-0.260511458	-1.239879938	-2.380068316
C	-3.647919416	-0.206467857	-0.648343728
C	-4.166994514	1.074709654	-0.718780644
C	-4.295739802	-1.185130888	0.086066363
C	-5.334934287	1.379007758	-0.045650183
C	-5.458957885	-0.874351074	0.763110641
C	-5.978360250	0.406030730	0.696998225
H	-3.659996150	1.819987280	-1.303067814
H	-3.889371891	-2.178540103	0.120410013
H	-5.741725717	2.370956053	-0.102612034
H	-5.962626046	-1.631510259	1.333754602
H	-6.885844600	0.643540939	1.2194921310

Fig. S3. The transition state TS1 for transformation $4n^+$ → $5n^+$:

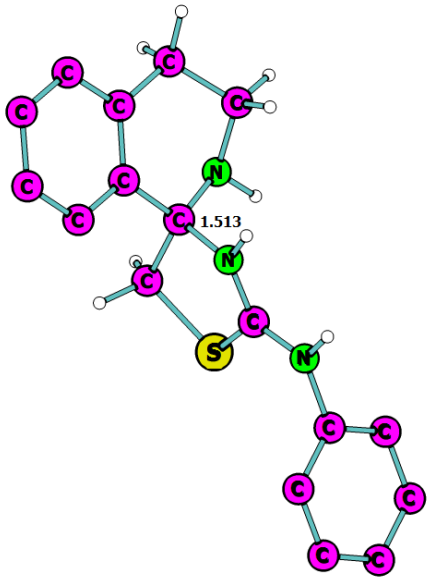


E_{tot} = -1220.595228534 a.u., λ_i = -226 cm^{-1}

39
symmetry c1

C	-5.200455227	1.487909856	-0.397792287
C	-5.100252427	0.112863688	-0.389869029
C	-4.083780261	2.267975566	-0.145152063
H	-5.966499300	-0.487506300	-0.598954556
H	-4.155002682	3.338585788	-0.165658490
C	-3.892454480	-0.511191230	-0.123057244
C	-2.878980098	1.663948856	0.127359023
H	-2.012661108	2.274117244	0.293247775
C	-2.773685225	0.275915715	0.154756824
H	-6.144311990	1.953615435	-0.610518256
C	-3.787513018	-2.009865579	-0.110921010
C	-1.498696624	-0.383514662	0.507570008
C	-2.376936037	-2.437956977	-0.444318772
N	-1.457865806	-1.698773452	0.407242138
H	-4.480452459	-2.438315029	-0.823349898
H	-2.147420994	-2.240962725	-1.487931229
H	-4.060010437	-2.388327769	0.870368775
H	-2.228389043	-3.491127540	-0.258094233
C	-0.603983733	0.217048012	1.563885980
H	-0.745740184	1.281107979	1.621861314
H	-0.843557371	-0.221035177	2.523974092
S	1.144812444	-0.127327664	1.227855802
C	0.970307658	0.241579314	-0.499375767
N	2.088218817	0.341328725	-1.221431781
N	-0.237806100	0.356761050	-0.899548994
H	1.984345516	0.515420752	-2.202008608
H	-0.624069222	-2.157778361	0.717141144
H	-0.413173389	0.553141911	-1.869710430
C	3.419025061	0.237049382	-0.698501096
C	4.042199892	-0.997184572	-0.663564572
C	4.074764277	1.374974120	-0.264361326
C	5.332798069	-1.093269681	-0.178523029
C	5.364684907	1.271850425	0.218674957
C	5.991896265	0.039513769	0.262253311
H	3.522996068	-1.867965491	-1.018183379
H	3.578214355	2.326220788	-0.306686802
H	5.822422040	-2.048102568	-0.149799718
H	5.879059489	2.151005553	0.557434029
H	6.995351601	-0.036917703	0.636378596

Fig. S4. Spiroproduct $5n^+$:

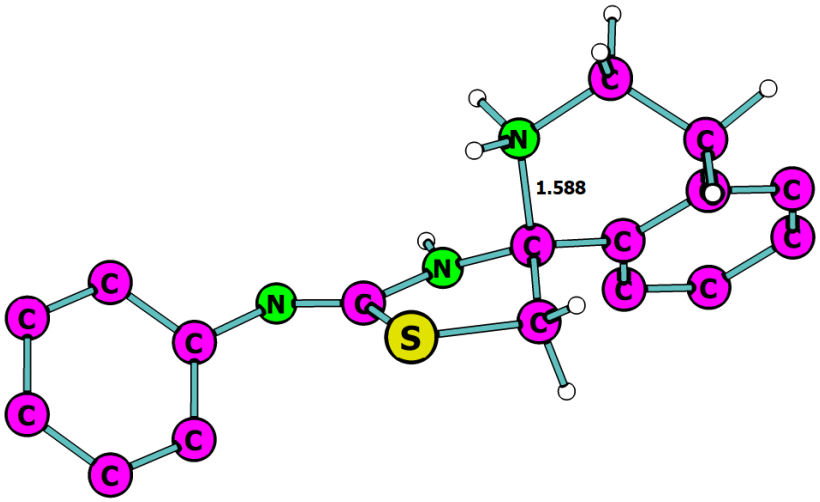


E_{tot} = -1220.609029018 a.u.

39
symmetry c1

C	-4.908061244	1.828853515	-0.332682426
C	-4.952277668	0.456913457	-0.441140757
C	-3.715039044	2.457032943	-0.017410201
H	-5.875255939	-0.027767297	-0.702702142
H	-3.667309862	3.526697758	0.058573760
C	-3.821656207	-0.321978426	-0.227613018
C	-2.587095629	1.698979900	0.199498465
H	-1.663823976	2.197310197	0.433384335
C	-2.631119838	0.310852538	0.113896539
H	-5.795230601	2.409481373	-0.502133650
C	-3.895005919	-1.815591475	-0.376649531
C	-1.365919239	-0.489387319	0.365404626
C	-2.526556877	-2.386111603	-0.668856340
N	-1.614219618	-1.884648015	0.342073312
H	-4.590696850	-2.072457813	-1.166099259
H	-2.217410280	-2.127604816	-1.683815601
H	-4.269671029	-2.254973477	0.542541171
H	-2.539020588	-3.464779990	-0.601321615
C	-0.664584570	-0.124957212	1.684671135
H	-0.865522128	0.887654421	1.989781479
H	-0.968780035	-0.809159576	2.458849607
S	1.137724637	-0.285331802	1.412034186
C	0.915317476	-0.051211214	-0.293417122
N	1.933166186	0.110254283	-1.111462598
N	-0.340957299	-0.066929194	-0.664523684
H	1.744201331	0.187005331	-2.093281684
H	-0.781460344	-2.431585911	0.446307162
H	-0.617464780	0.054904639	-1.619626026
C	3.305767363	0.185450642	-0.685767534
C	4.048426114	-0.976034969	-0.589743233
C	3.861267026	1.420512076	-0.409756289
C	5.371336068	-0.896836464	-0.198036272
C	5.184691592	1.489290150	-0.020446561
C	5.936743576	0.332860597	0.085861119
H	3.600047158	-1.924151746	-0.821096259
H	3.267438305	2.310849805	-0.498936340
H	5.957945145	-1.792148905	-0.119378072
H	5.626941361	2.442692444	0.197086031
H	6.965429861	0.390751338	0.387422806

Fig. S5. Spiroform 6n$^+$:



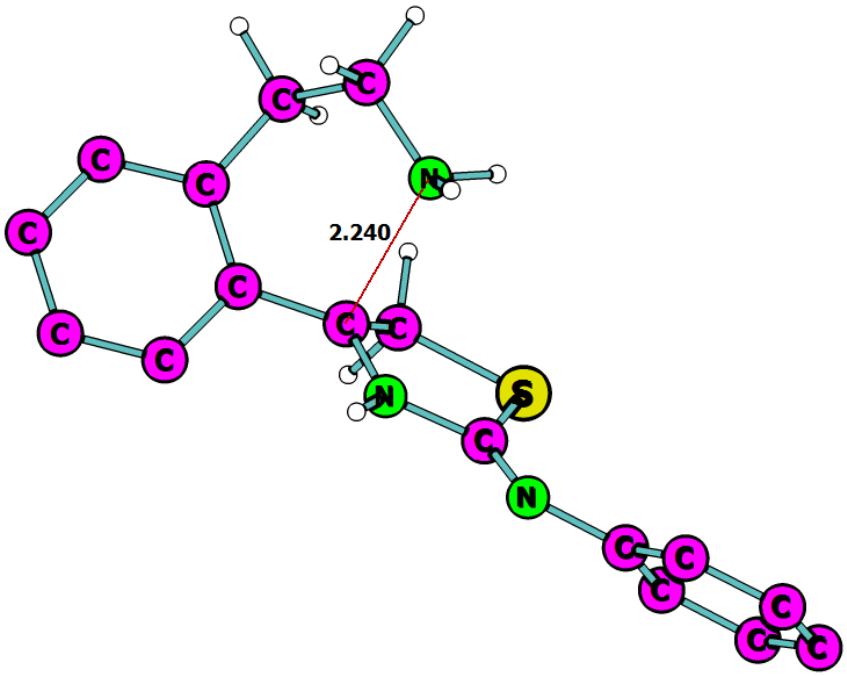
E_{tot} = -1220.583508315 a.u.

39
symmetry c1

C	-5.166428287	-1.551897441	-0.306862964
C	-5.023887212	-0.189757169	-0.122506619
C	-4.049652437	-2.362785128	-0.366886219
H	-5.894836395	0.437930877	-0.078994595
H	-4.155974049	-3.420276516	-0.515921949
C	-3.768138028	0.376943905	-0.000098406
C	-2.789589709	-1.812312051	-0.237184754
H	-1.925281358	-2.444637156	-0.304176064
C	-2.645356918	-0.446994239	-0.046686400
H	-6.147052495	-1.977574138	-0.404785187
C	-3.585103197	1.853785287	0.186875548
C	-1.279857473	0.173814890	0.039935984
C	-2.590548835	2.138232178	1.296353123
N	-1.334511751	1.315832515	1.142283177
H	-4.521668321	2.322185140	0.458544384
H	-3.017469922	1.869894723	2.250693672
H	-3.268165995	2.325856721	-0.736692971
H	-2.301136625	3.178029786	1.328818520
C	-0.789921473	0.837627422	-1.246404509
H	-0.977966511	0.159911069	-2.065024521
H	-1.267522902	1.781955397	-1.454689168
S	0.998496425	1.077927187	-1.022596400
C	1.058101666	-0.316687934	0.115493034
N	2.033970743	-0.863134054	0.652542271
N	-0.249687121	-0.701712163	0.402978902
H	-1.130360017	0.853245320	2.016893701
H	-0.371164025	-1.424393211	1.084802087

H	-0.530439299	1.907400201	0.952371189
C	3.372282515	-0.551696635	0.349393927
C	3.860995804	-0.580555697	-0.949217663
C	4.229640857	-0.271052121	1.403323028
C	5.193101358	-0.297947346	-1.188008850
C	5.554404451	0.022980679	1.153903600
C	6.040415202	0.012685926	-0.141920169
H	3.213788396	-0.850754512	-1.762152097
H	3.848322721	-0.290514535	2.406738309
H	5.568288744	-0.330561640	-2.193723276
H	6.211500313	0.247738462	1.973019758
H	7.074516028	0.229543324	-0.331759084

Fig. S6. The transition state TS2 for transformation $6n^+ \rightarrow 7n^+$:

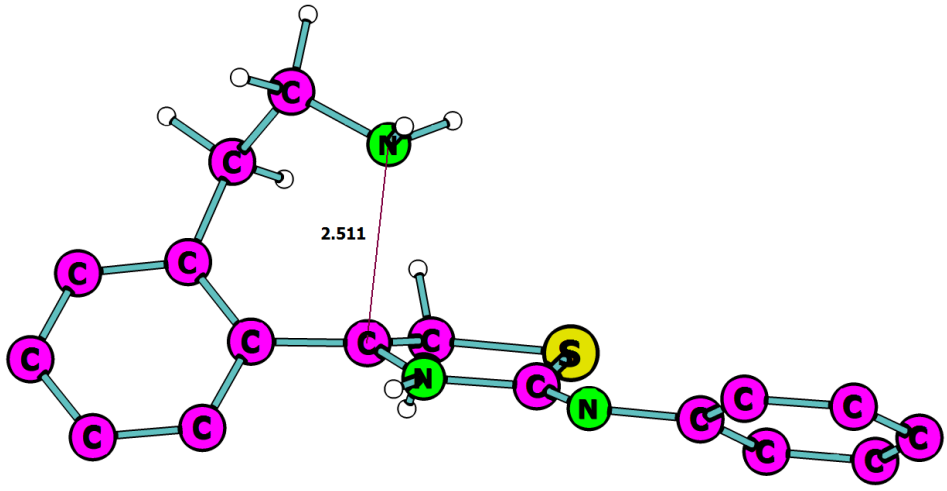


E_{tot} = -1220.574014778 a.u., λ_i = -112 cm^{-1},

39
symmetry c1

C	-5.248935337	1.521847495	-0.3497652720
C	-5.149802160	0.133530845	-0.398808180
C	-4.120003653	2.294676799	-0.063119970
H	-6.025792394	-0.463234835	-0.635762245
H	-4.188565694	3.377023998	-0.039817395
C	-3.933337574	-0.510217852	-0.155089400
C	-2.904209239	1.671522838	0.186943322
H	-2.026350611	2.279042796	0.376736206
C	-2.799083694	0.270133109	0.158545761
H	-6.201879581	2.002569658	-0.546417401
C	-3.831541182	-2.018754237	-0.201881434
C	-1.517207051	-0.408236890	0.485961911
C	-2.409374973	-2.446485240	-0.545850756
N	-1.485076774	-1.737218682	0.343849685
H	-4.529265808	-2.424494883	-0.940002027
H	-2.170025400	-2.212044483	-1.591990786
H	-4.114851956	-2.441775895	0.771250906
H	-2.264211756	-3.517603794	-0.396239970
C	-0.622360997	0.147685195	1.585973798
H	-0.763062163	1.220470106	1.693031424
H	-0.865003351	-0.335354539	2.536476193
S	1.150685851	-0.189255062	1.247283395
C	0.982217695	0.249786922	-0.481903540
N	2.113725903	0.385240385	-1.201606045
N	-0.239817431	0.383869506	-0.887244489
H	2.005679251	0.655592285	-2.172084358
H	-0.638141749	-2.211467804	0.634271528
H	-0.415220616	0.599543959	-1.865415324
C	3.455897868	0.270184409	-0.685657375
C	3.983129887	-0.992392962	-0.400268977
C	4.225143201	1.424123170	-0.513801052
C	5.287742422	-1.095478188	0.084017505
C	5.532691679	1.309480656	-0.044420336
C	6.061661841	0.052574542	0.258808804
H	3.382067192	-1.880255290	-0.568458369
H	3.800021136	2.396514229	-0.741922607
H	5.701539716	-2.072774673	0.309822244
H	6.135587329	2.201611600	0.089701412
H	7.079006129	-0.031394389	0.626988108

Fig. S7. Open-chain form 7n$^+$



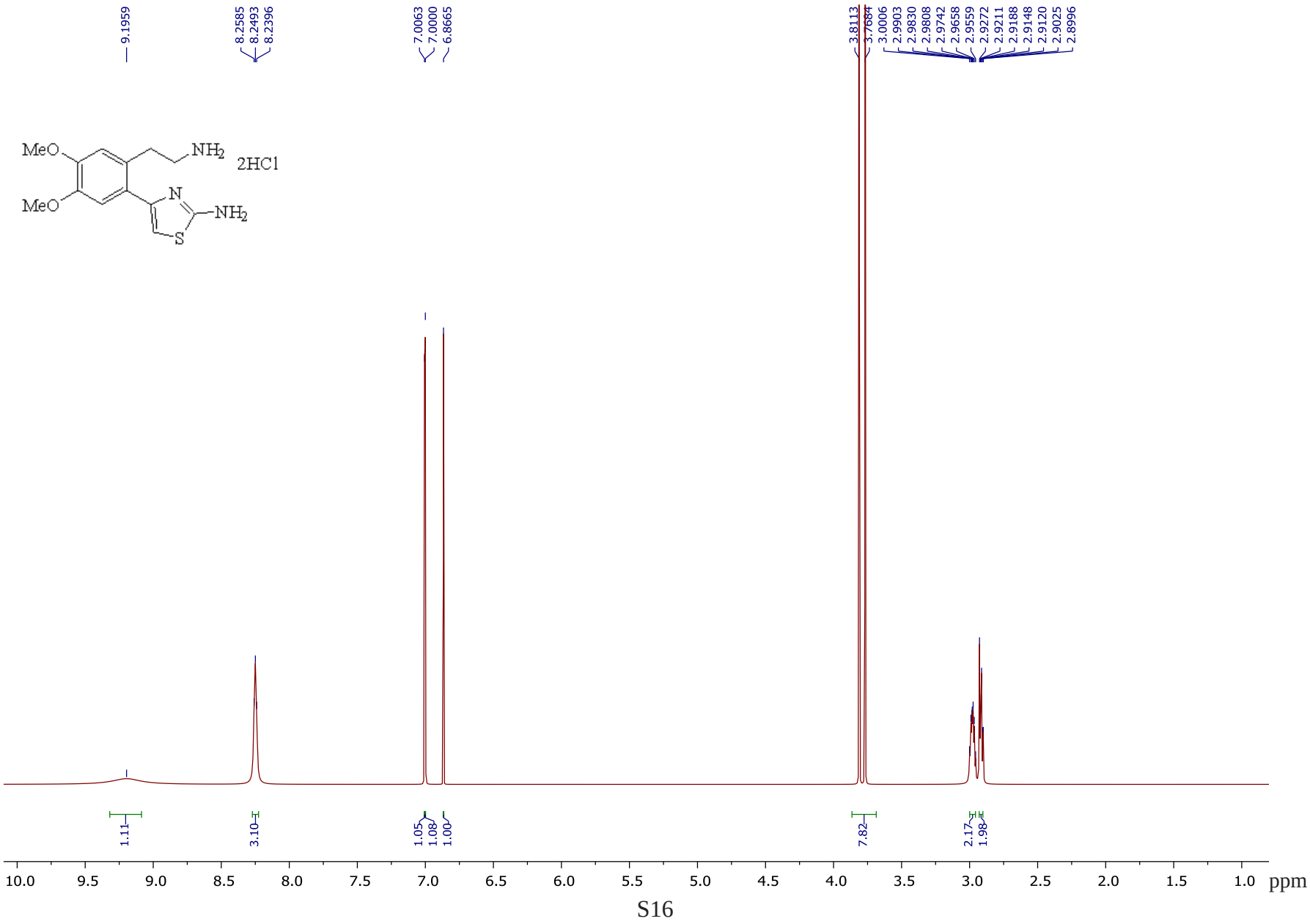
E_{tot} = -1220.574235652

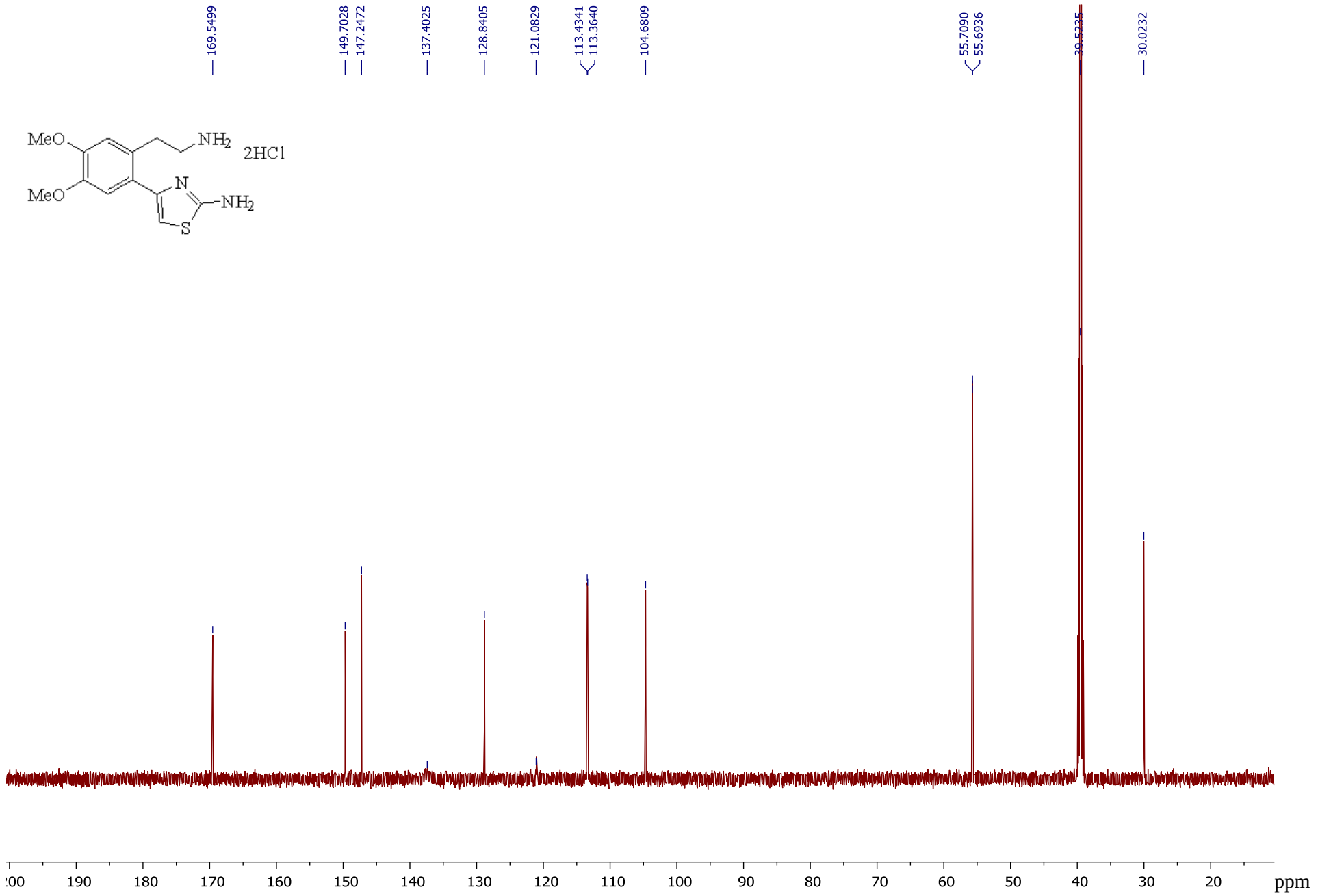
39
symmetry c1

C	-5.1437638270	-1.608869078	0.131194913
C	-4.964923718	-0.239441284	0.141339685
C	-4.056021762	-2.449102315	-0.006045107
H	-5.819873955	0.398425910	0.265831162
H	-4.184128814	-3.514241956	-0.023387853
C	-3.714477249	0.342824710	-0.000368210
C	-2.799682818	-1.904324512	-0.134261514
H	-1.960517428	-2.558777117	-0.280374383
C	-2.613799318	-0.518651538	-0.141750471
H	-6.131808040	-2.017066580	0.231008969
C	-3.605802717	1.836812572	0.127945770
C	-1.247159801	-0.054494021	-0.357130220
C	-2.816025156	2.258646435	1.367167087
N	-1.412022850	1.870439905	1.246270640
H	-4.604420295	2.246874941	0.201100120
H	-3.239048898	1.769703112	2.234864496
H	-3.168520243	2.289062192	-0.754749794
H	-2.928470788	3.327104041	1.515927253
C	-0.829039540	0.858719489	-1.463741449
H	-1.099895877	0.373596828	-2.395328986
H	-1.313721258	1.816250477	-1.424764716
S	0.975813327	1.036926382	-1.360204105
C	1.085446547	-0.272646145	-0.167552848
N	2.021718547	-0.807807588	0.445699717
N	-0.235271568	-0.690692028	0.145072130
H	-1.022763243	1.627809958	2.140309791
H	-0.324190821	-1.381530660	0.869390488
H	-0.854078591	2.627140617	0.888704092
C	3.388824139	-0.540329943	0.310564135
C	3.982643432	-0.083761891	-0.861323461
C	4.175268257	-0.796490777	1.426503319
C	5.345145089	0.136661457	-0.897438145
C	5.532063619	-0.555069659	1.387389824
C	6.120394253	-0.086742181	0.225735681
H	3.403822310	0.060224484	-1.753366512
H	3.705558152	-1.178858222	2.312458727
H	5.801796699	0.477673645	-1.807325928
H	6.132227383	-0.744053414	2.257236641
H	7.178710691	0.090100809	0.191489773

6. NMR and mass spectra of the compounds 3a-m.

4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]thiazol-2-amine dihydrochloride (3a).



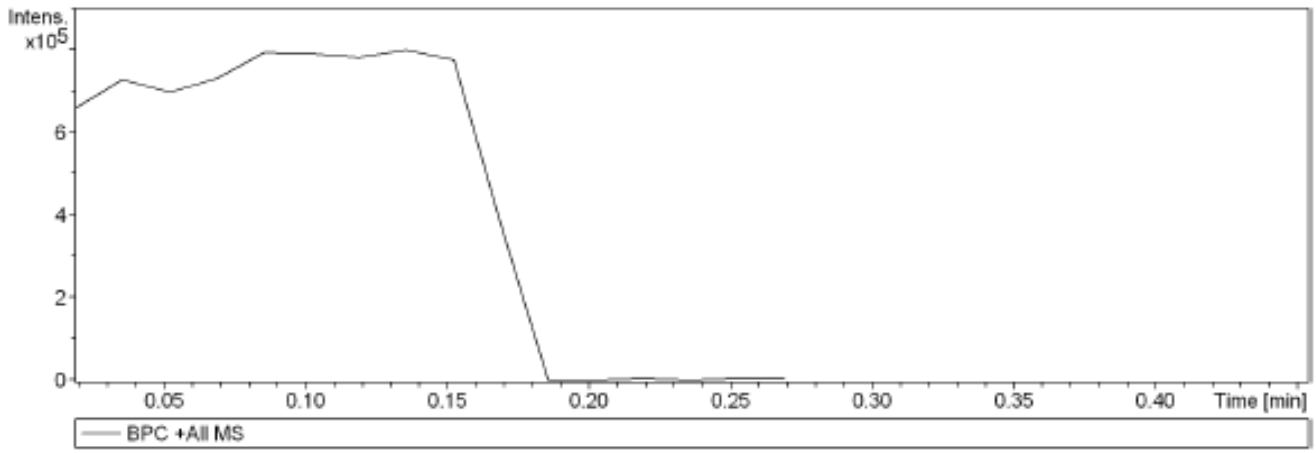

169.5499
149.7028
147.2472
137.4025
128.8405
121.0829
113.4341
113.3640
104.6809
55.7090
55.6936
39.5335
30.0232
MeO
MeO
NH2
2HCl
N
NH2
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

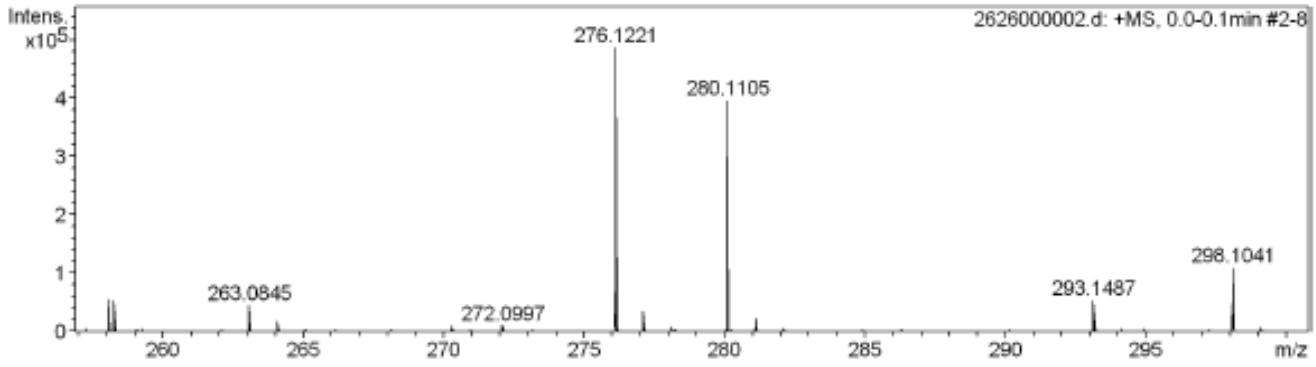
Analysis Info

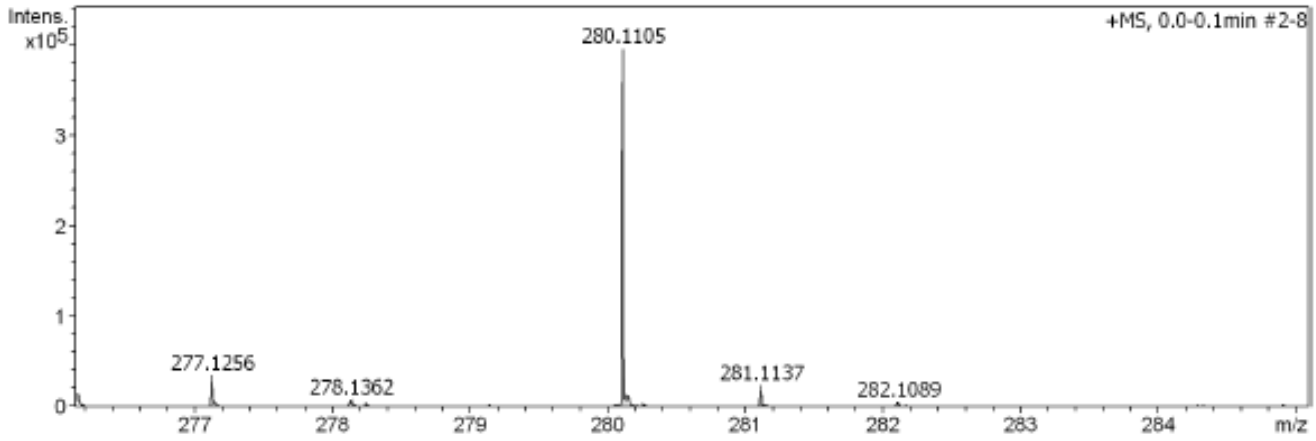
Analysis Name	D:\Data\demidov\2626000002.d	Acquisition Date	11/12/2020 3:46:10 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

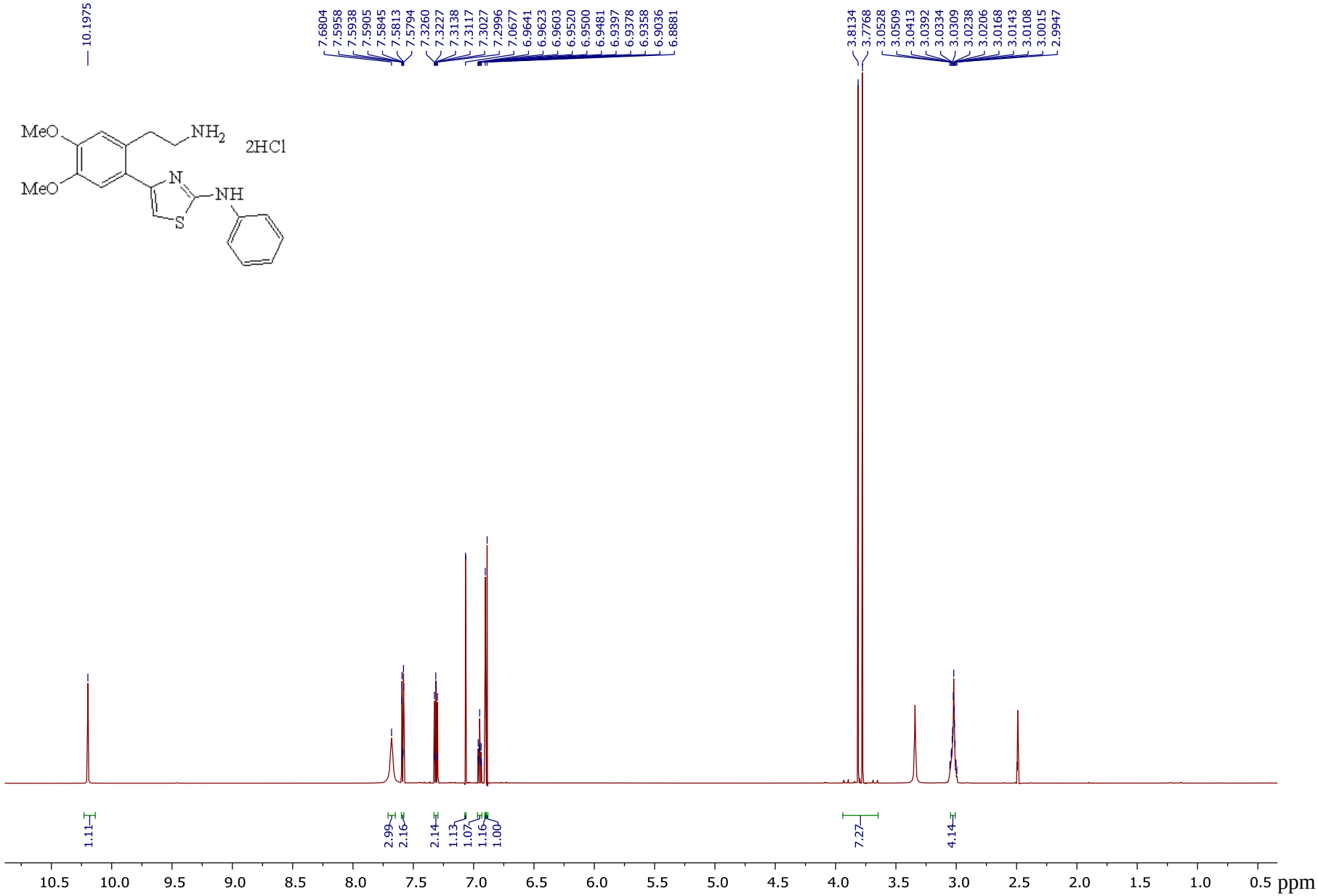
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

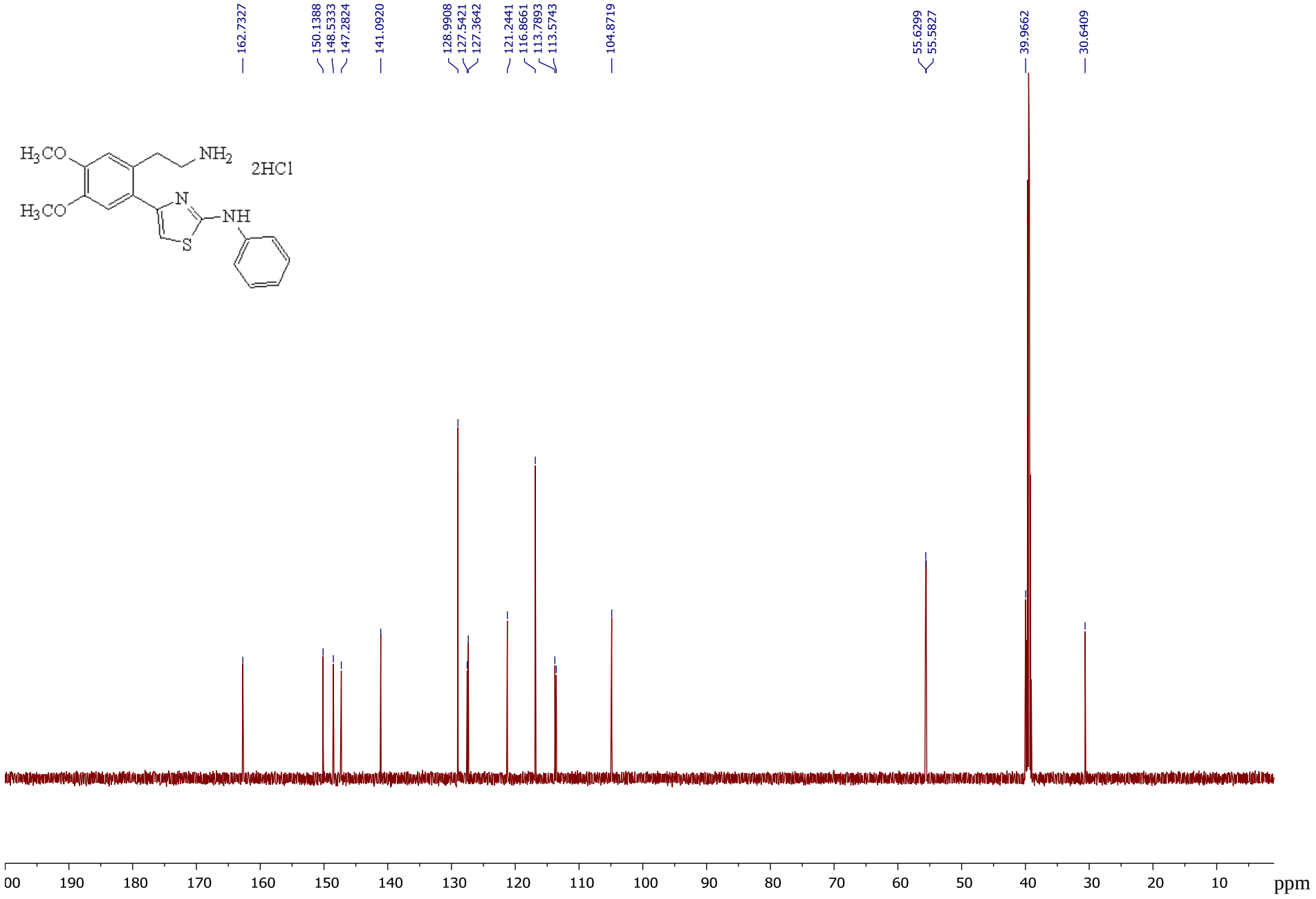






4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]-N-phenylthiazol-2-amine dihydrochloride (3b).



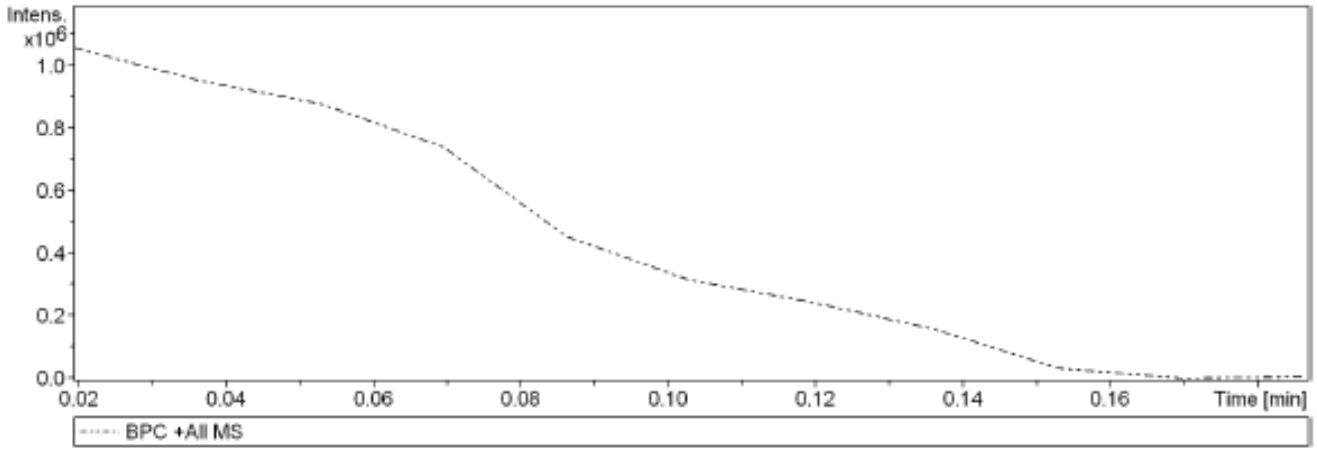

162.7327
150.1388
148.5333
147.2824
141.0920
128.9908
127.5421
127.3642
121.2441
116.8661
113.7893
113.5743
104.8719
55.6299
55.5827
39.9662
30.6409
H3CO
NH2
2HCl
H3CO
N
NH
S
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

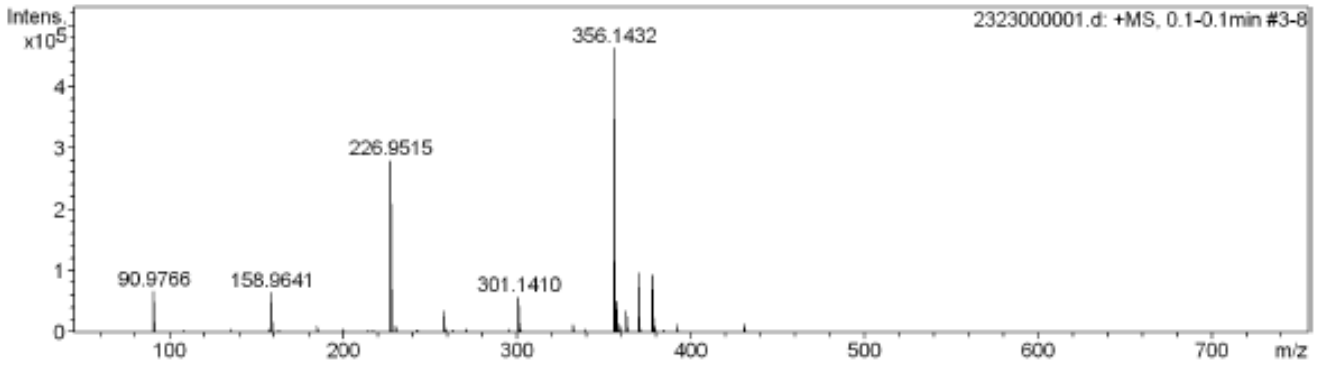
Analysis Info

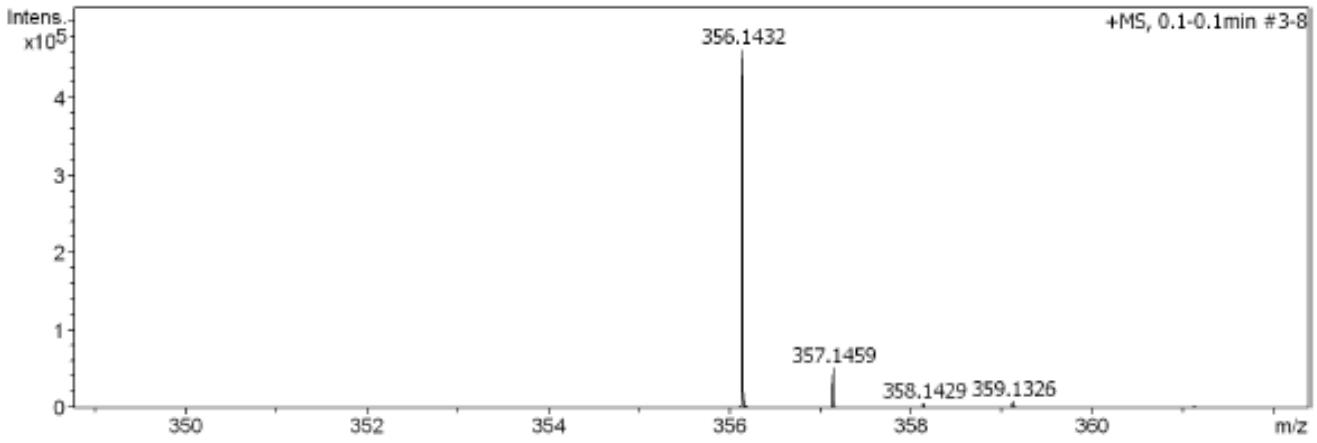
Analysis Name	D:\Data\demidov\2323000001.d	Acquisition Date	11/12/2020 3:02:19 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

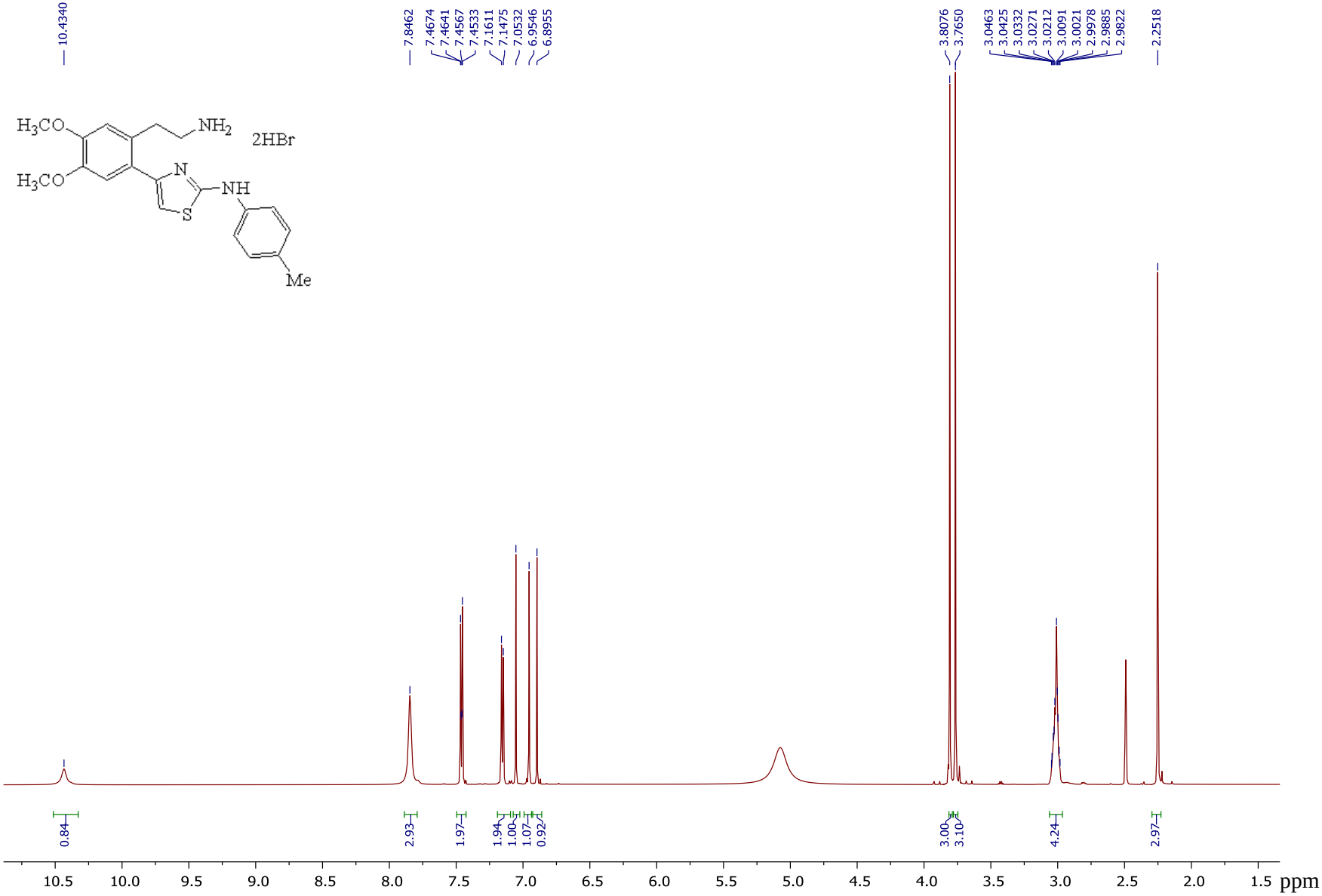
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

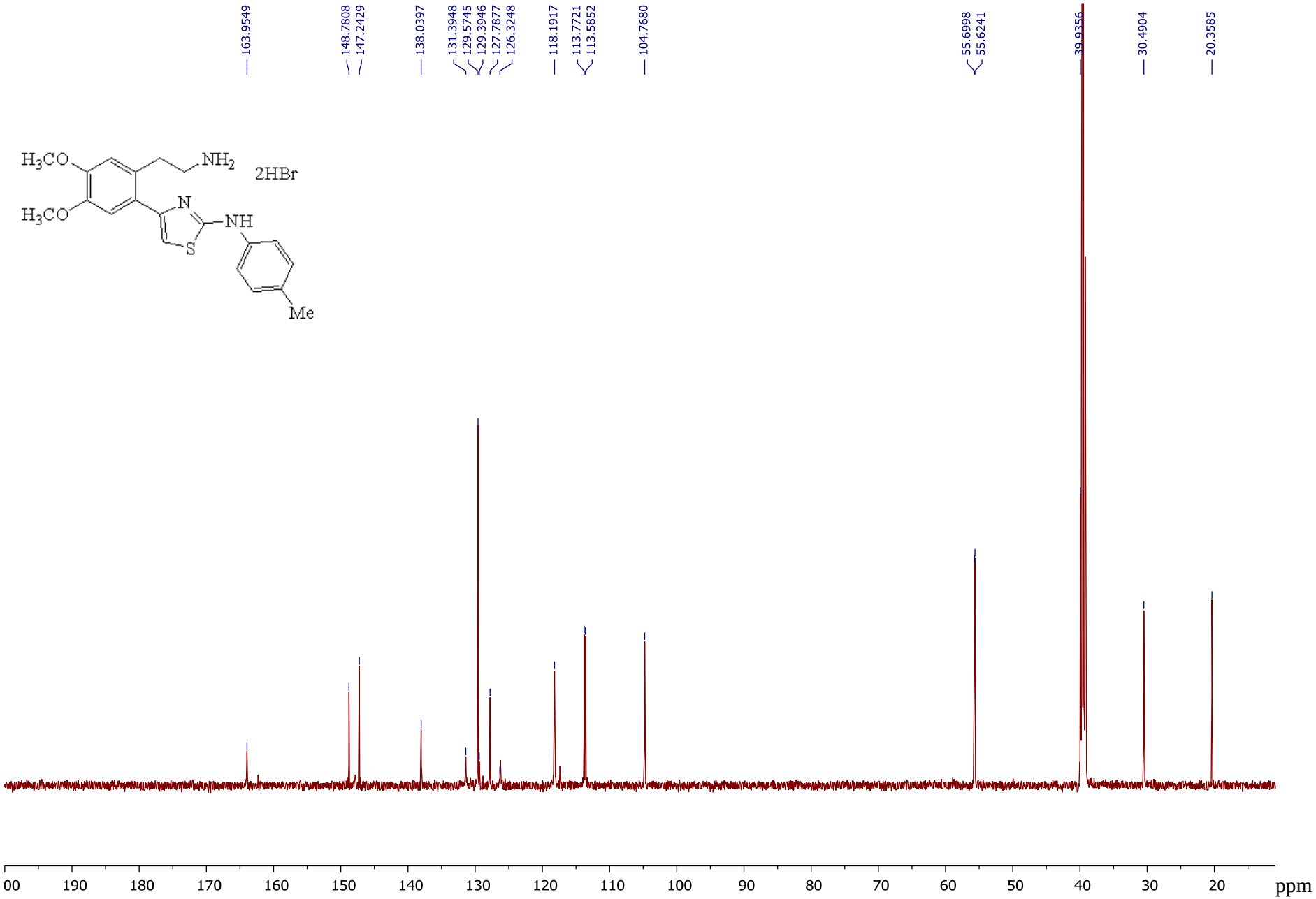






4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl)]-N-(*p*-tolyl)thiazol-2-amine dihydrobromide (3c).



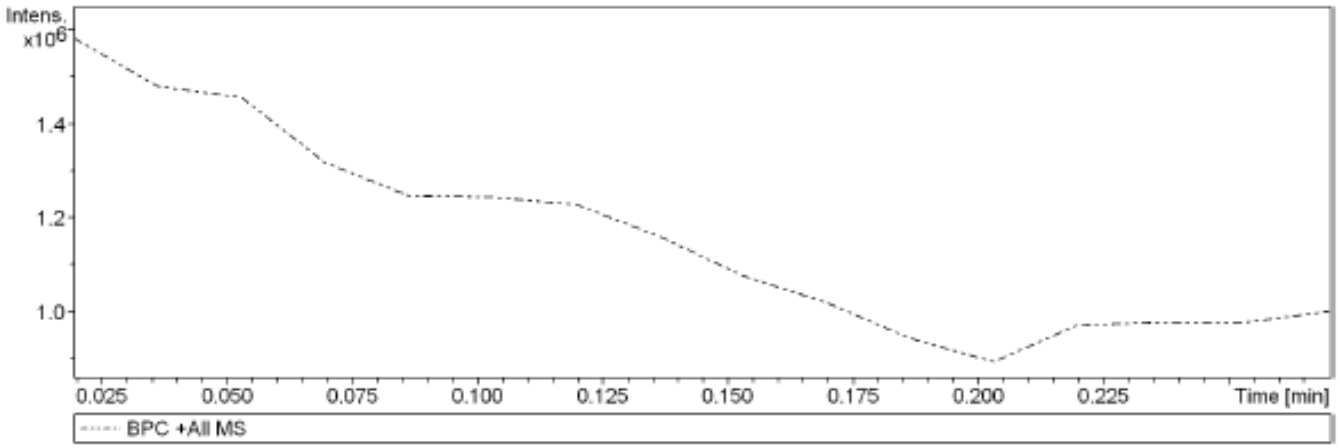

163.9549
148.7808
147.2429
138.0397
131.3948
129.5745
129.3946
127.7877
126.3248
118.1917
113.7721
113.5852
104.7680
55.6998
55.6241
39.9356
30.4904
20.3585
H3CO
NH2
2HBr
H3CO
N
NH
S
Me
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

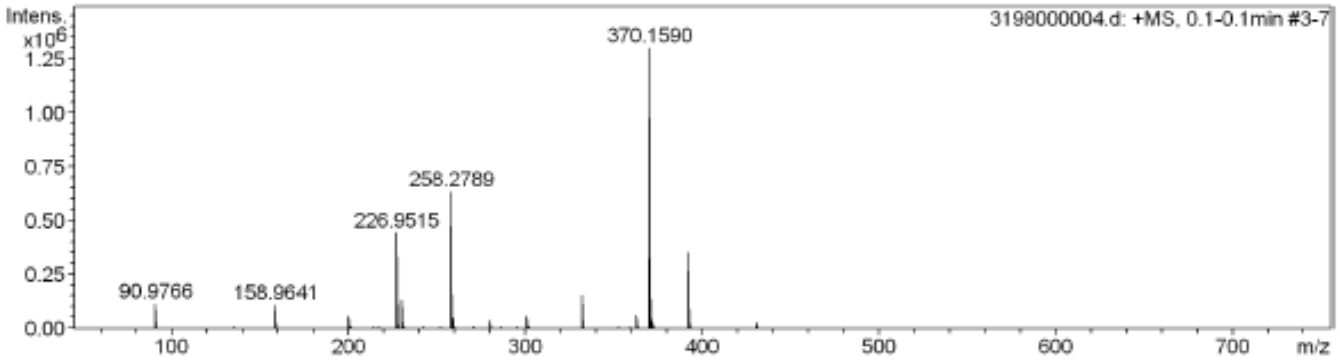
Analysis Info

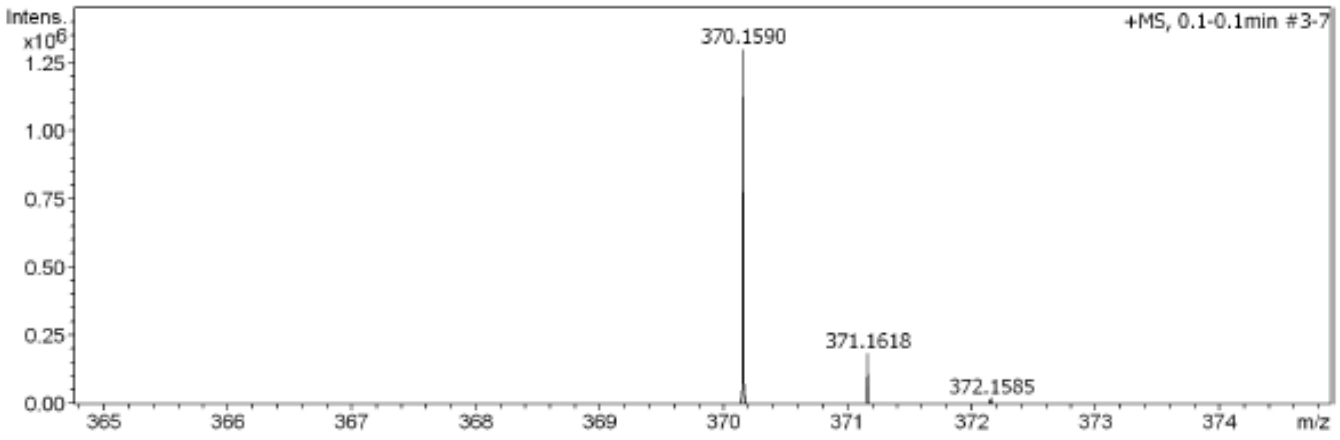
Analysis Name	D:\Data\demidov\3198000004.d	Acquisition Date	11/12/2020 3:01:05 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

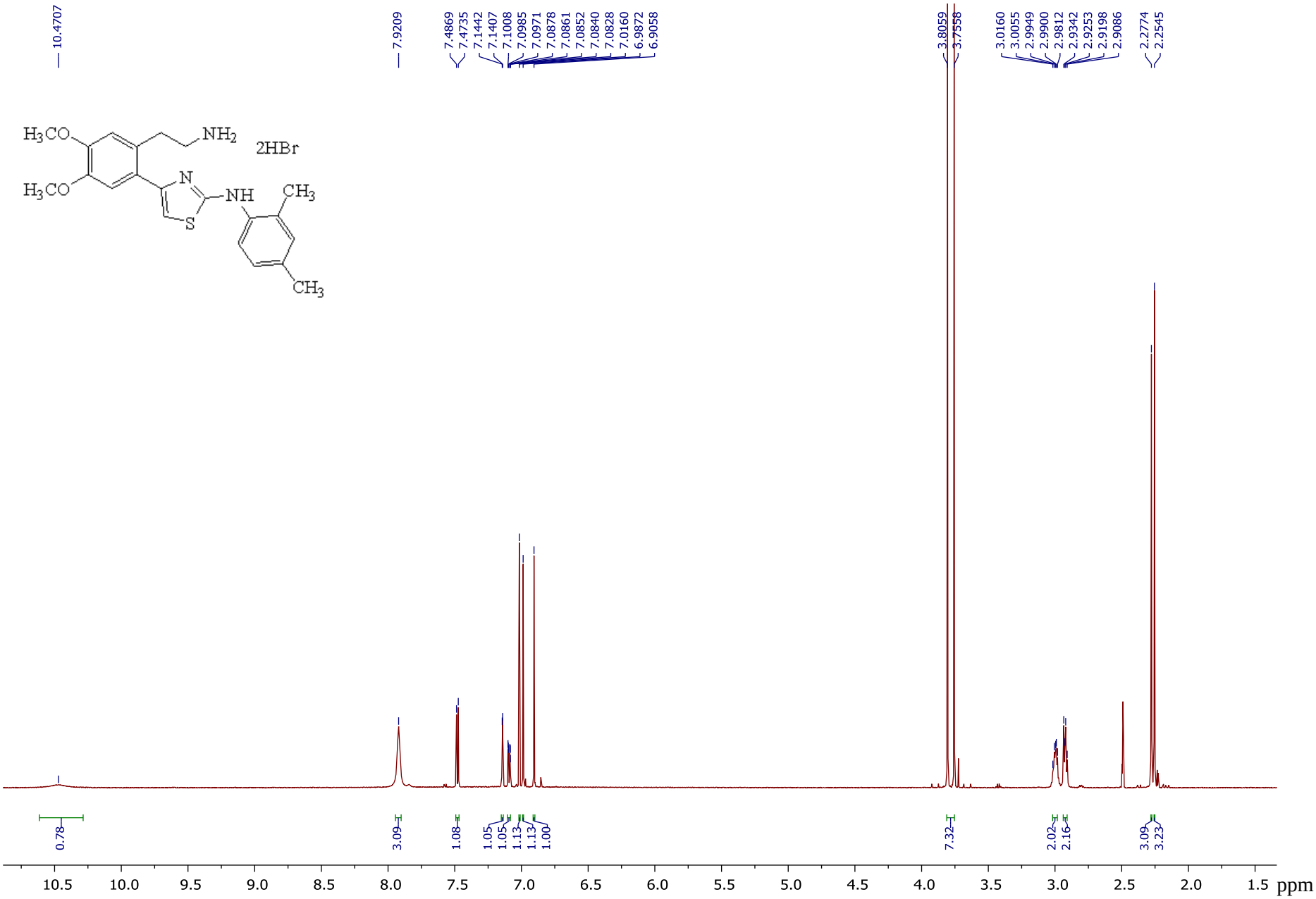
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

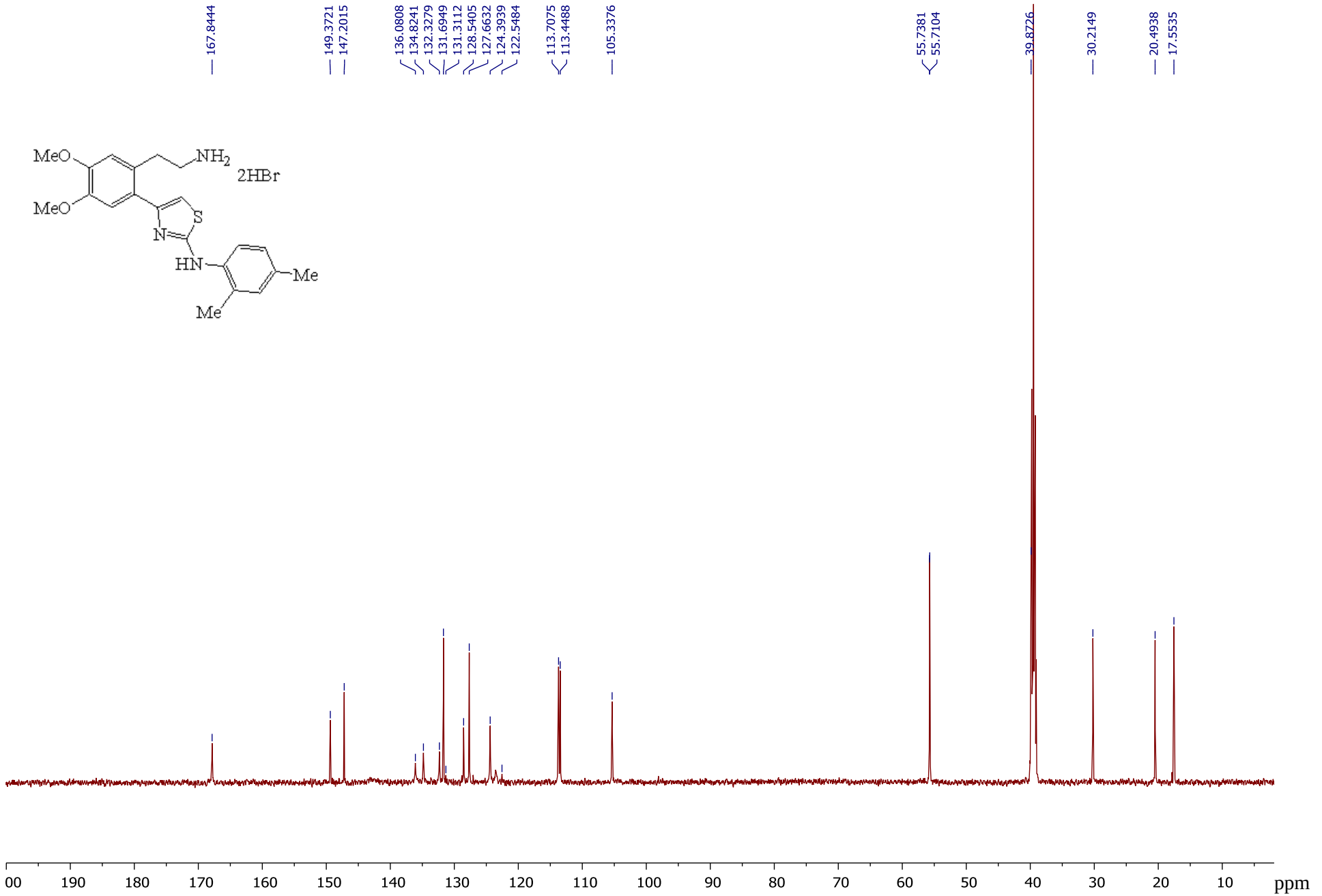






4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]-N-(2,4-dimethylphenyl)thiazol-2-amine dihydrobromide (3d).




167.8444
149.3721
147.2015
136.0808
134.8241
132.3279
131.6949
131.3112
128.5405
127.6632
124.3939
122.5484
113.7075
113.4488
105.3376
55.7381
55.7104
39.8726
30.2149
20.4938
17.5535
MeO
MeO
NH2
2HBr
S
N
HN
Me
Me
00
190
180
170
160
150
140
130
120
110
100
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80
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60
50
40
30
20
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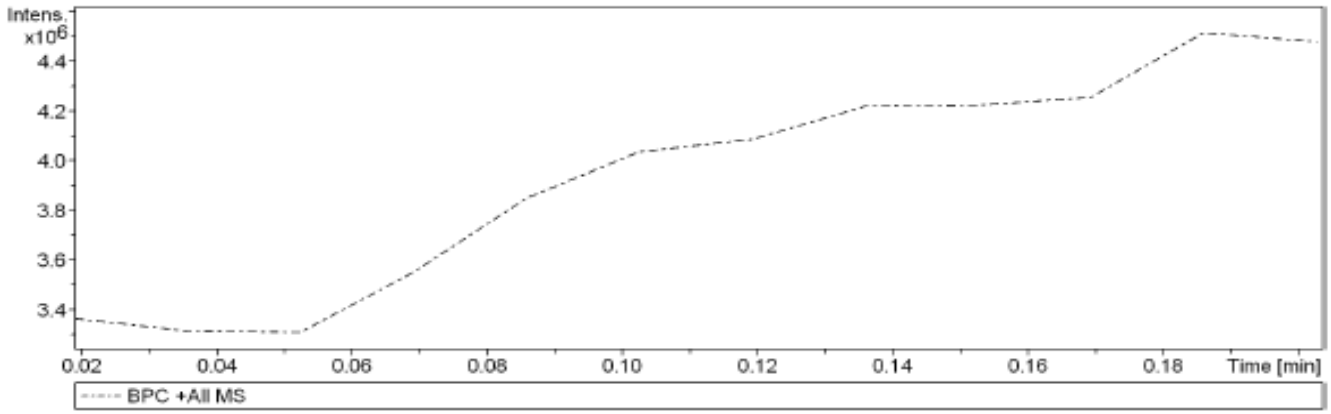
ppm

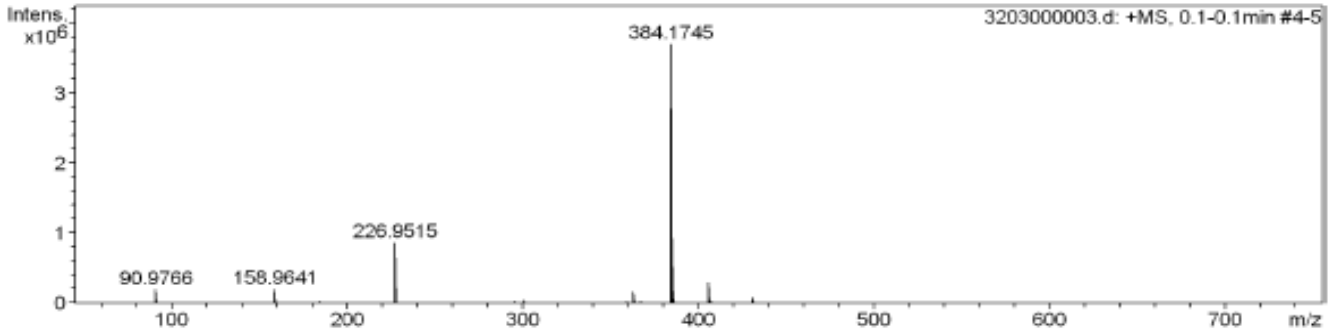
Analysis Info

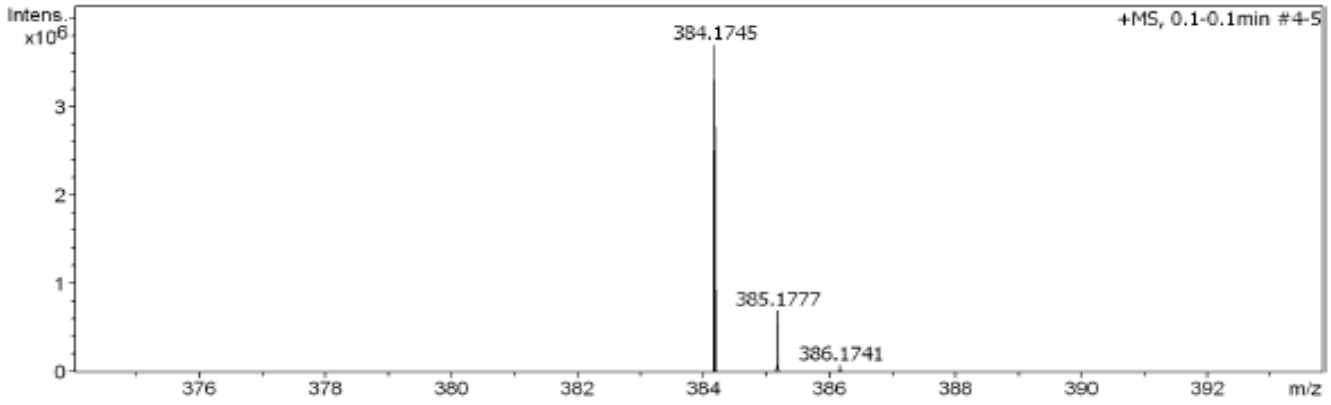
Analysis Name	D:\Data\demidov\3203000003.d	Acquisition Date	11/12/2020 2:58:00 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

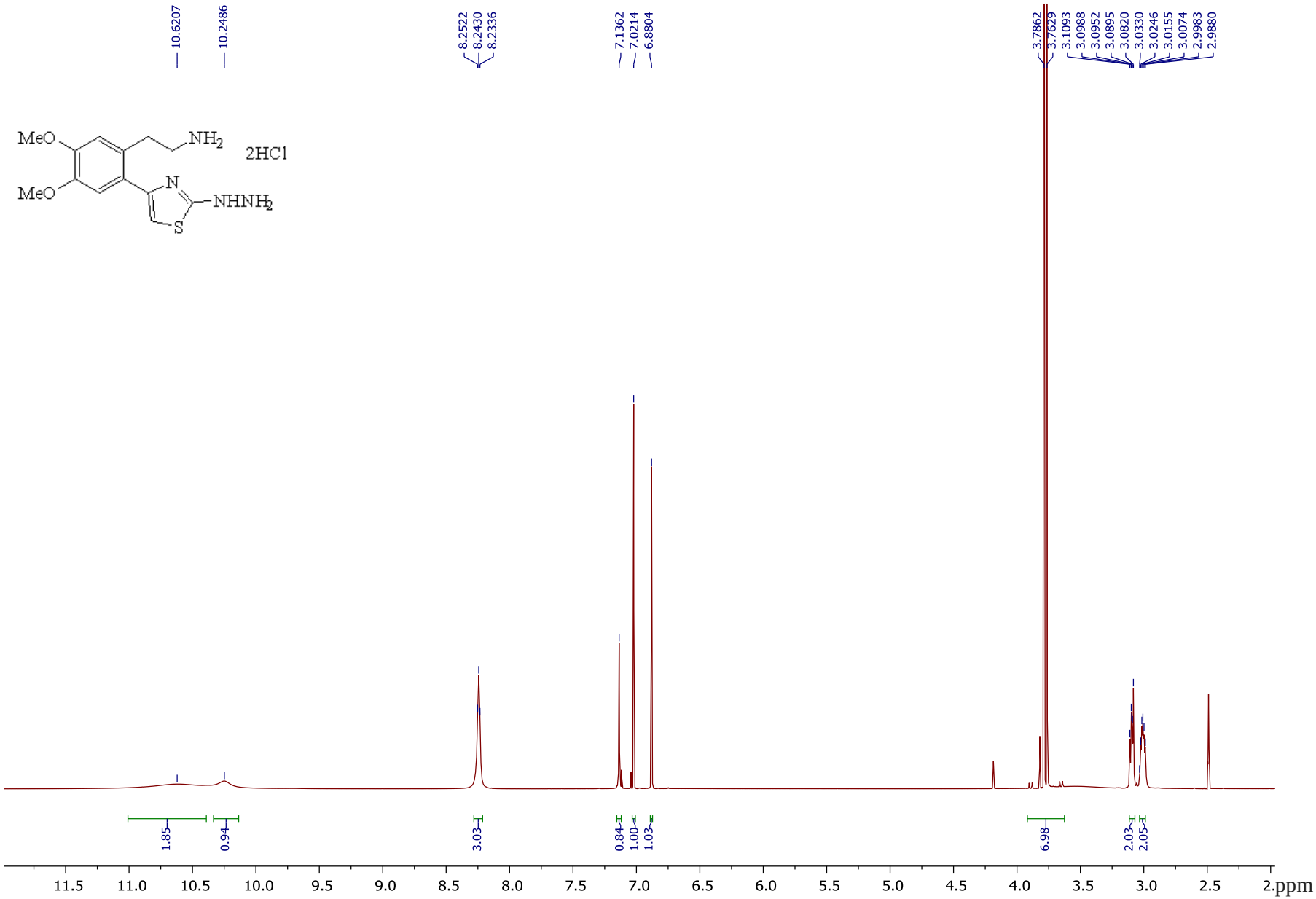
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

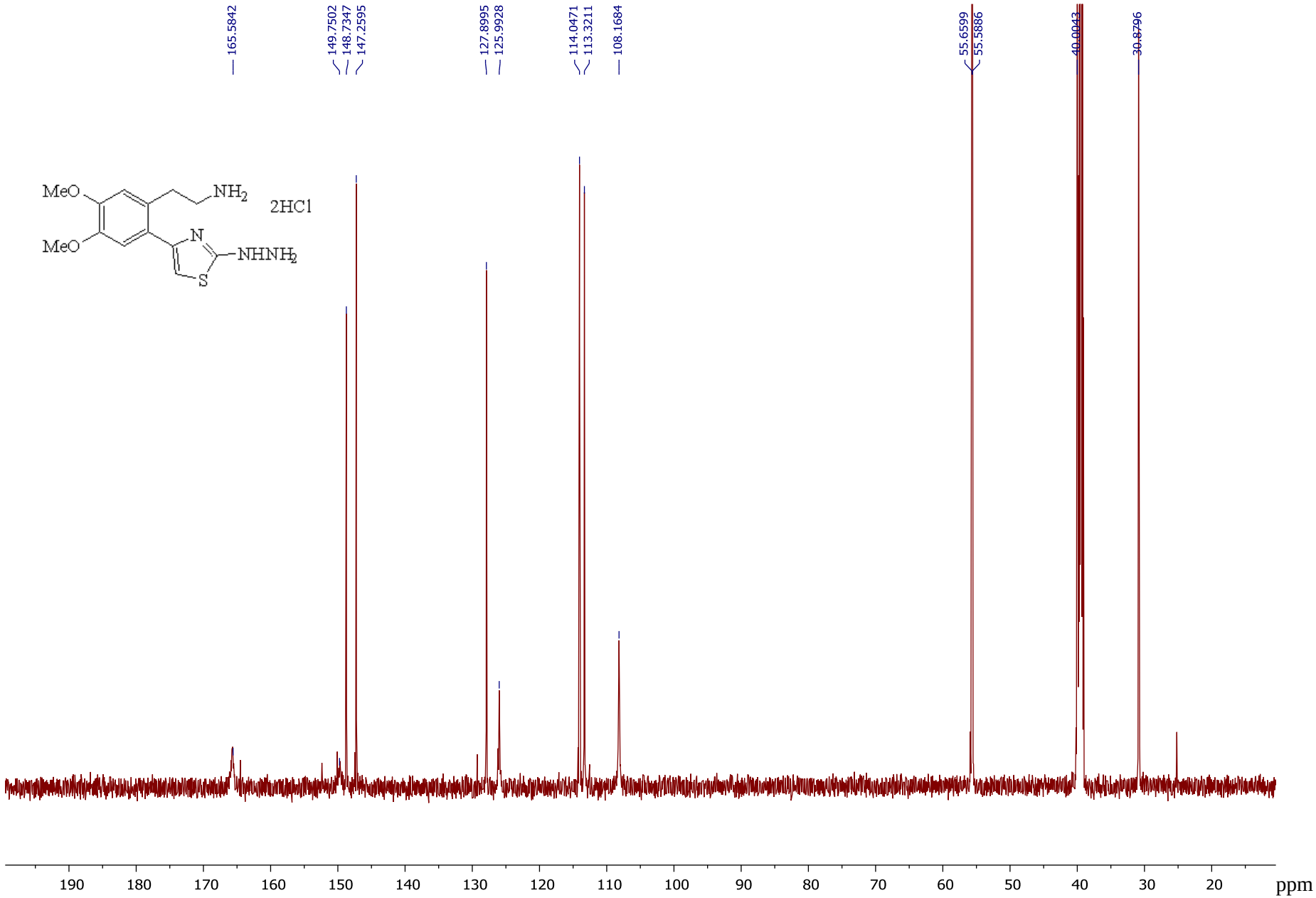






2-[2-(2-Hydrazineylthiazol-4yl)-4,5-dimethoxyphenyl]ethan-1-amine dihydrochloride (3e).

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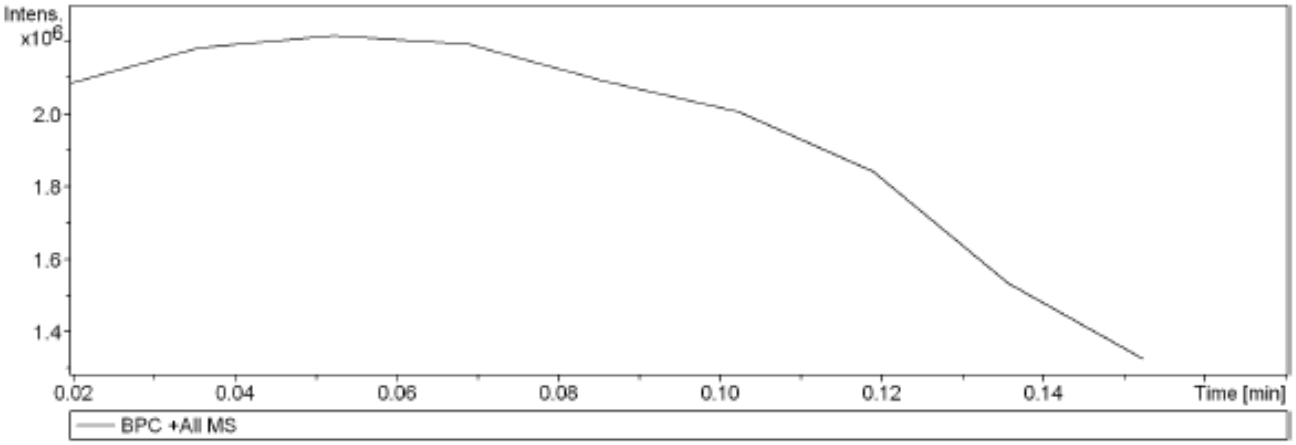
148.7347
147.2595
127.8995
125.9928
114.0471
113.3211
108.1684
55.6599
55.5886
40.0043
30.8796
MeO
MeO
NH2
2HCl
N
NHNH2
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

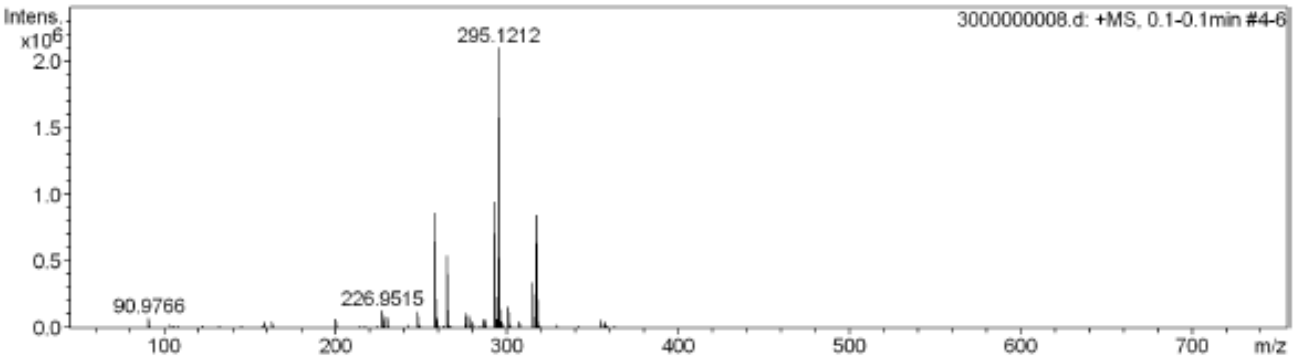
Analysis Info

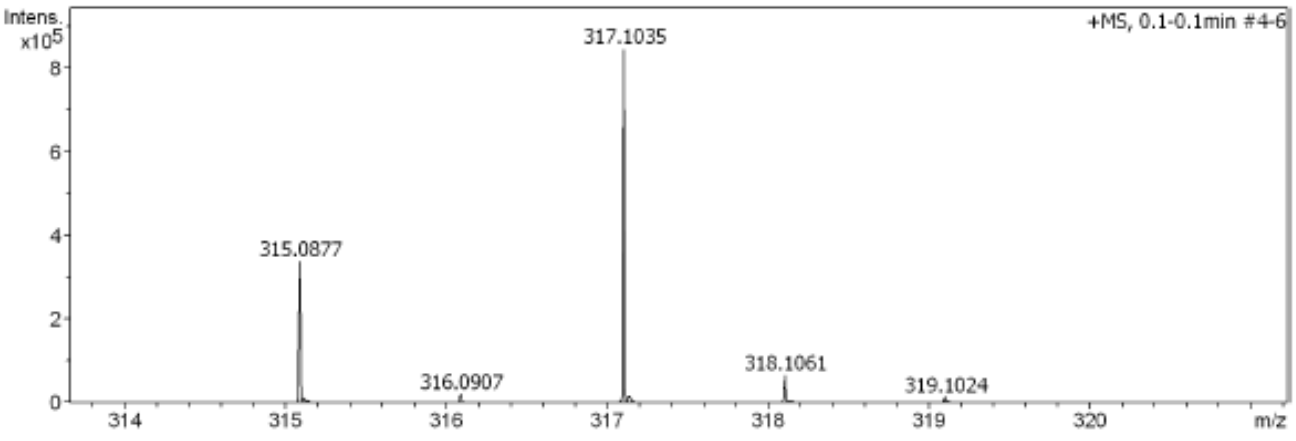
Analysis Name	D:\Data\demidov\3000000008.d	Acquisition Date	11/12/2020 3:13:14 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

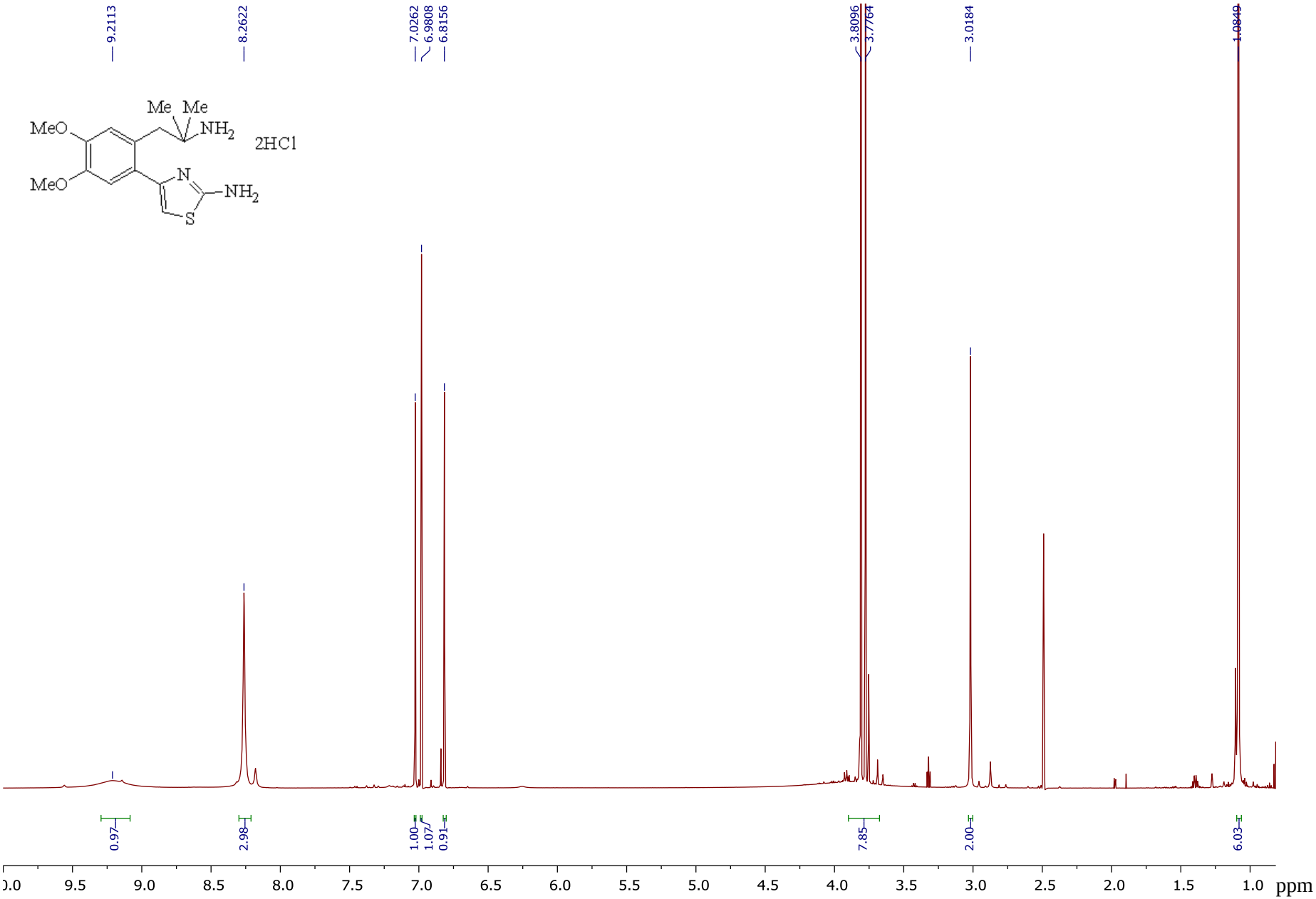
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

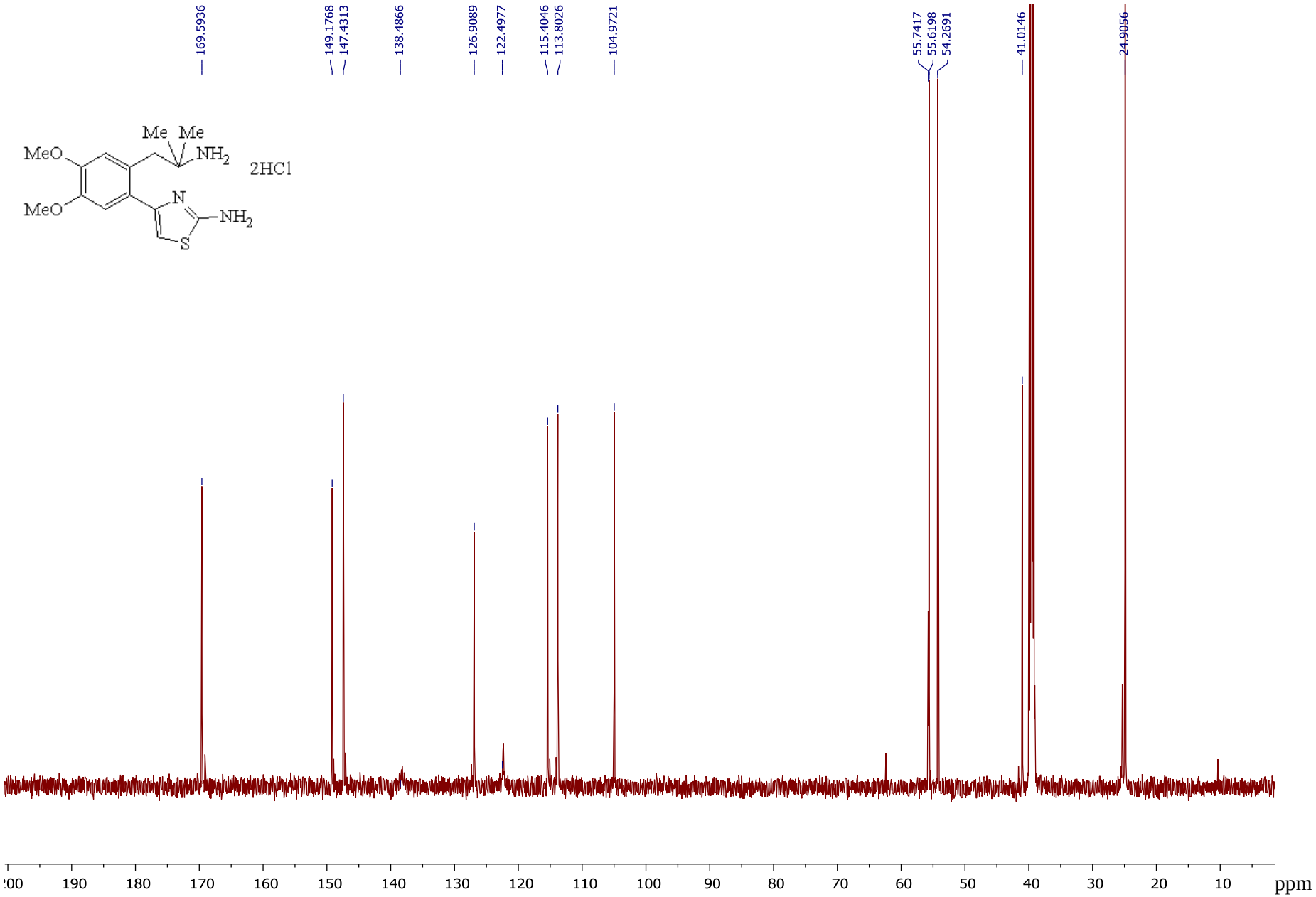






4-[2-(1-Amino-2-methylpropan-2-yl)-4,5-dimethoxyphenyl]thiazol-2-amine dihydrochloride (3f).

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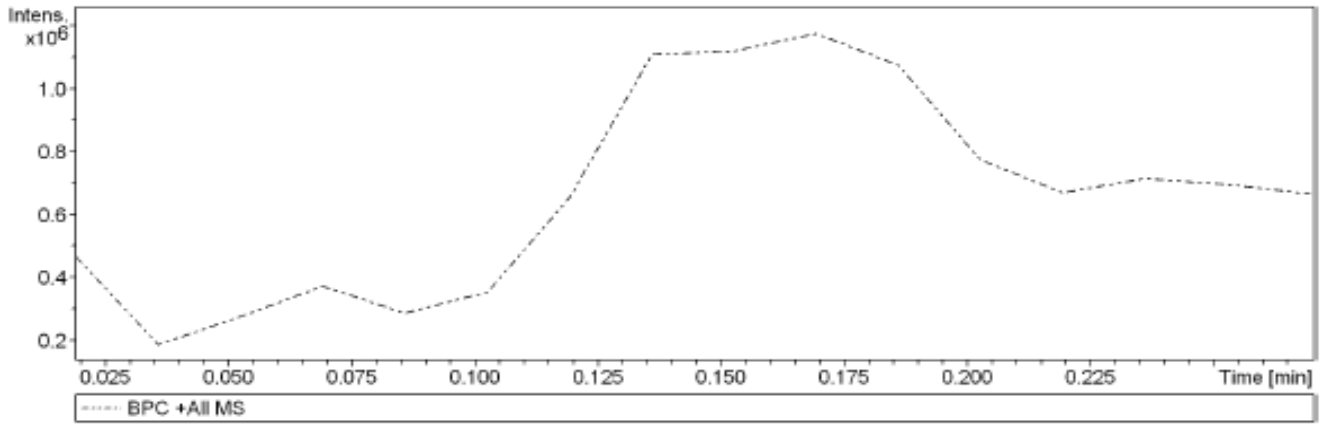
147.4313
138.4866
126.9089
122.4977
115.4046
113.8026
104.9721
55.7417
55.6198
54.2691
41.0146
24.9056
Me Me
NH2
MeO
MeO
2HCl
N
NH2
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

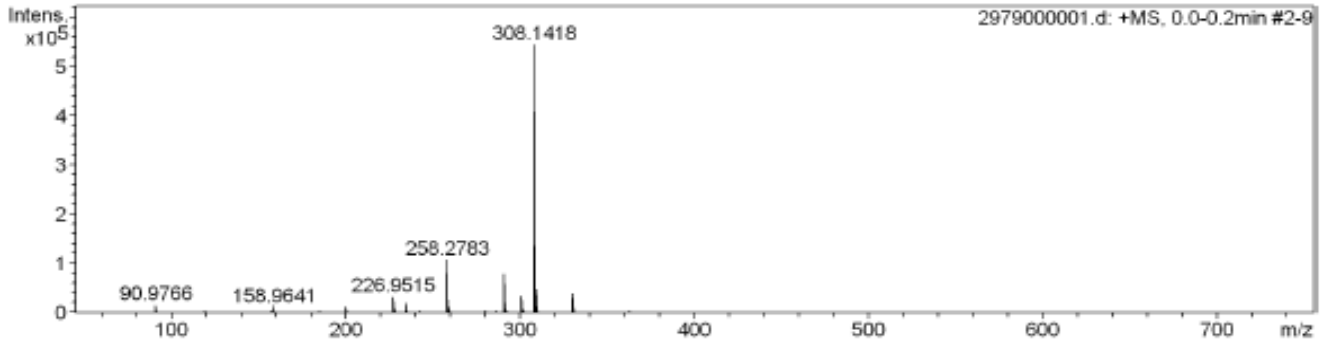
Analysis Info

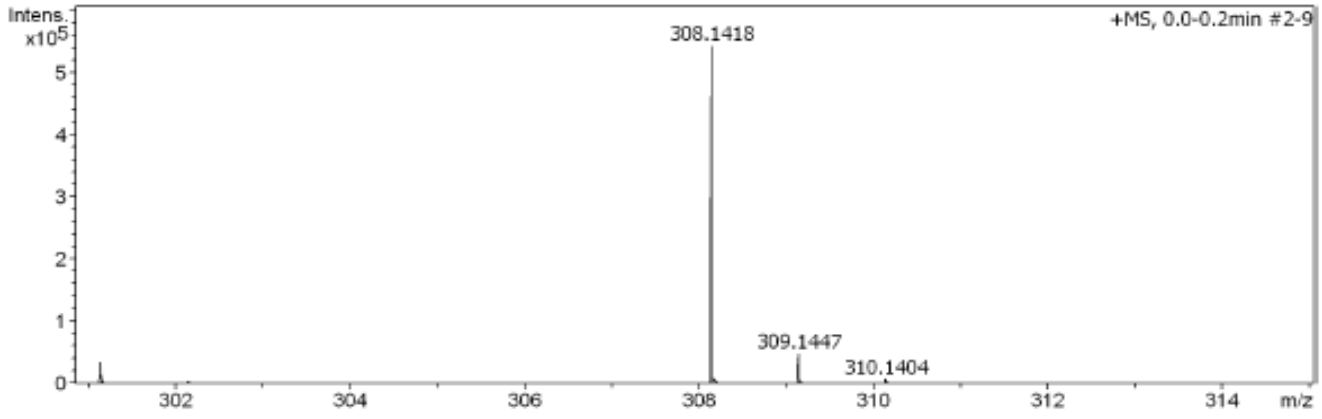
Analysis Name	D:\Data\demidov\2979000001.d	Acquisition Date	11/12/2020 3:06:24 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

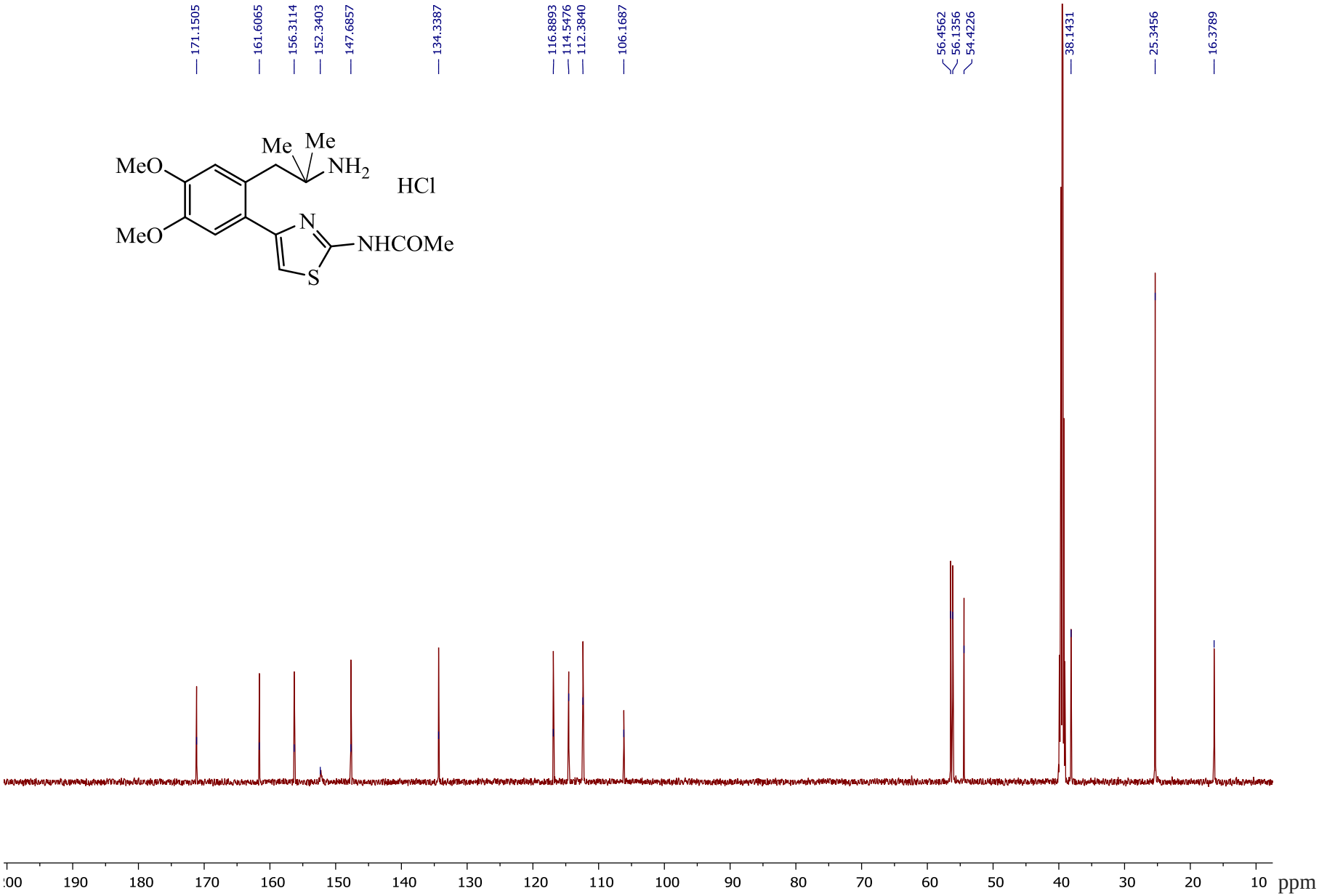
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

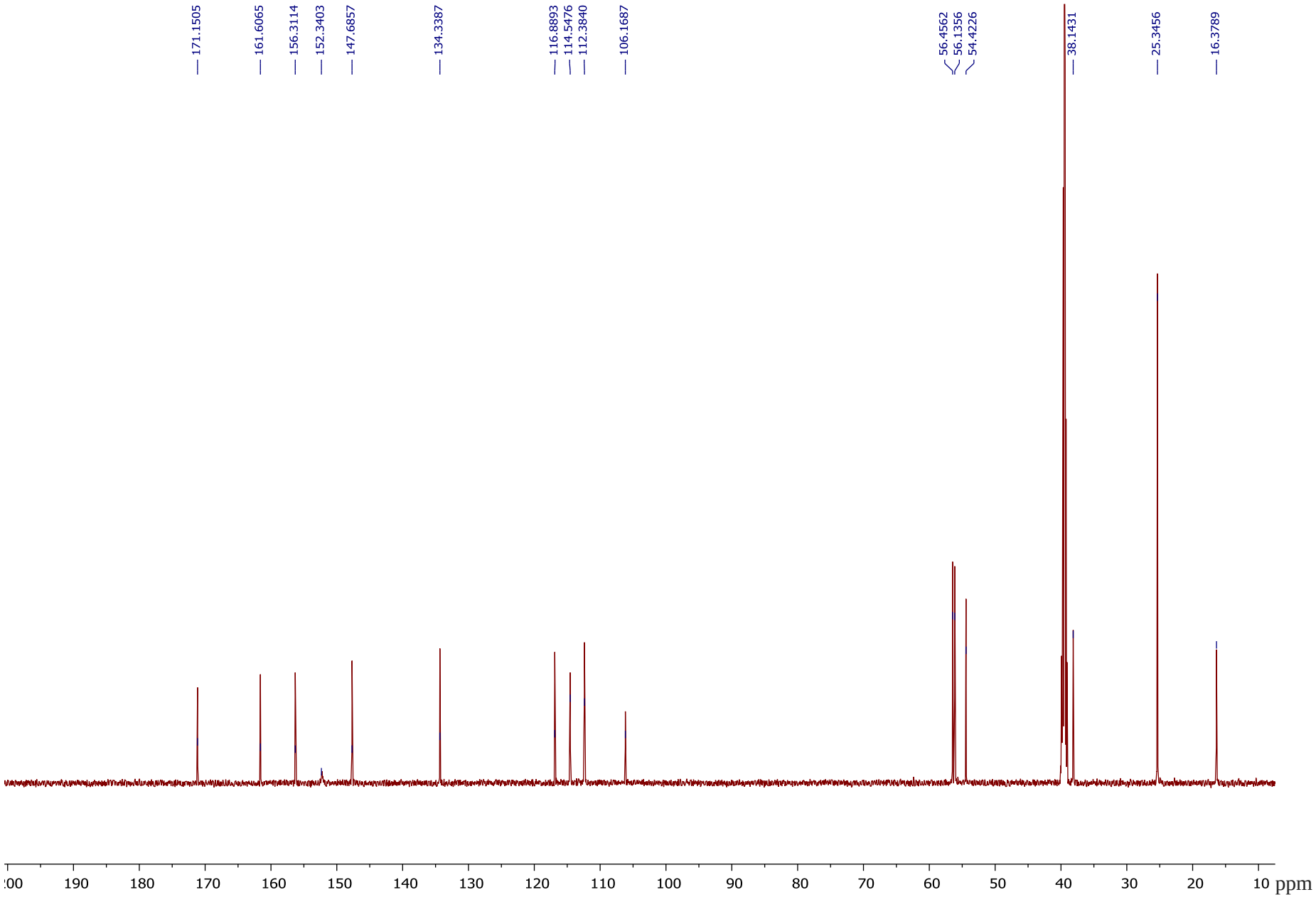






N-{4-[2-(2-amino-2-methylpropyl)-4,5-dimethoxyphenyl]thiazol-2yl}-acetamidedihydrochloride (3g).

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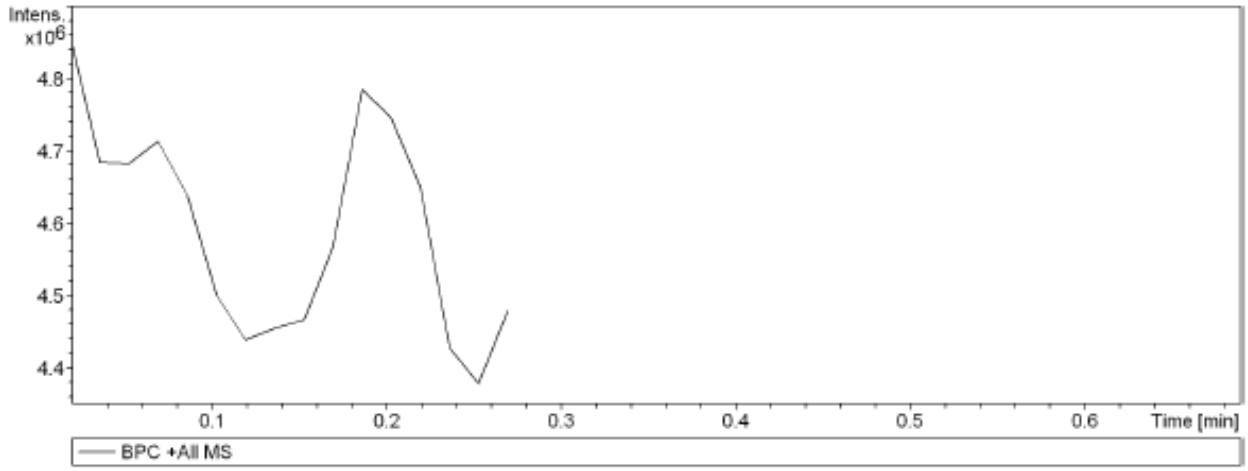
156.3114
152.3403
147.6857
134.3387
116.8893
114.5476
112.3840
106.1687
56.4562
56.1356
54.4226
38.1431
25.3456
16.3789
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

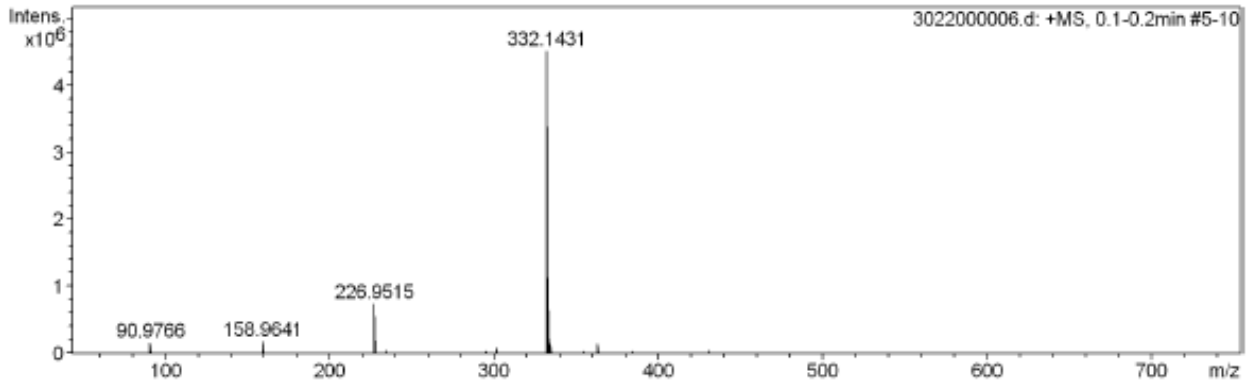
Analysis Info

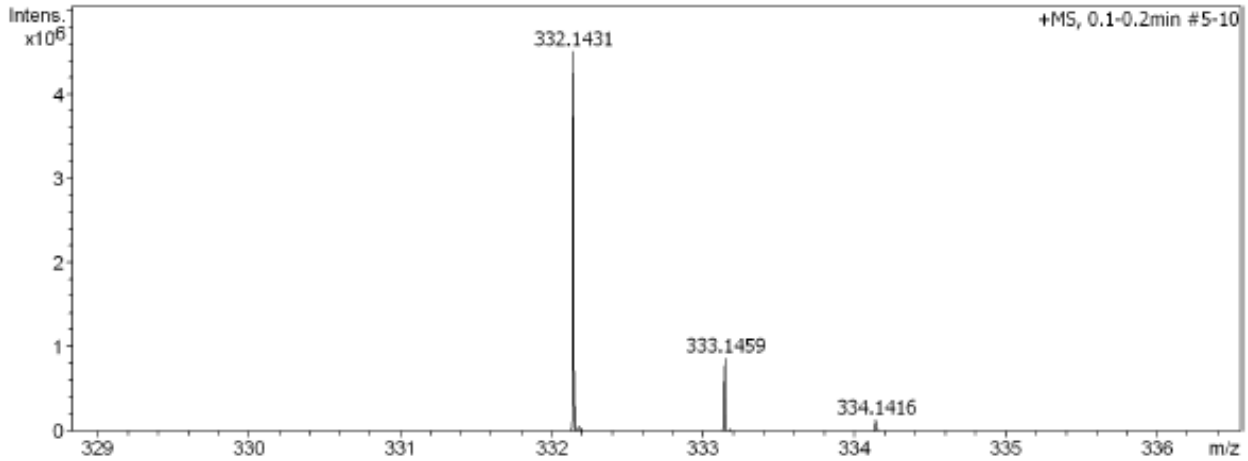
Analysis Name	D:\Data\demidov\3022000006.d	Acquisition Date	11/12/2020 2:59:59 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

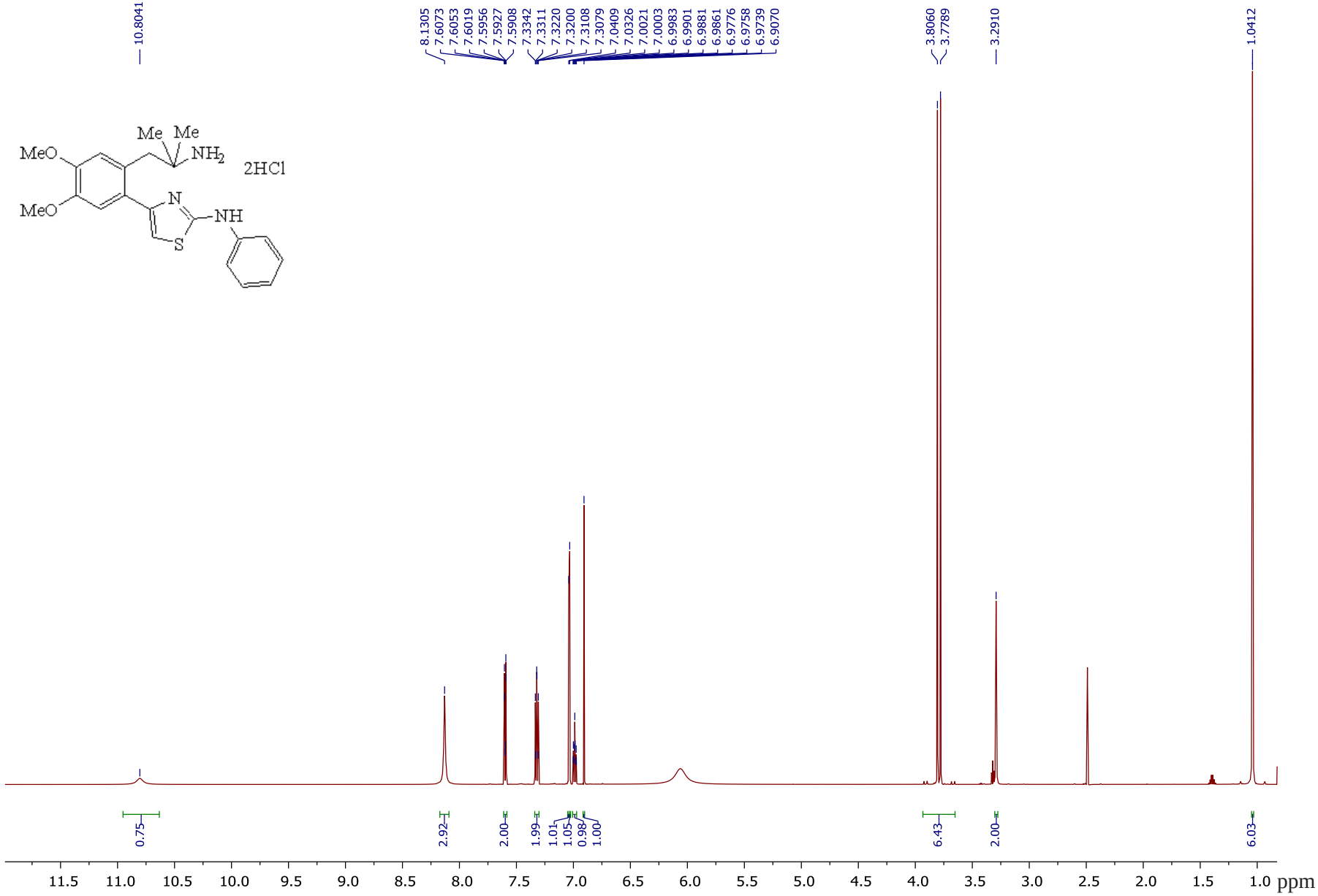
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

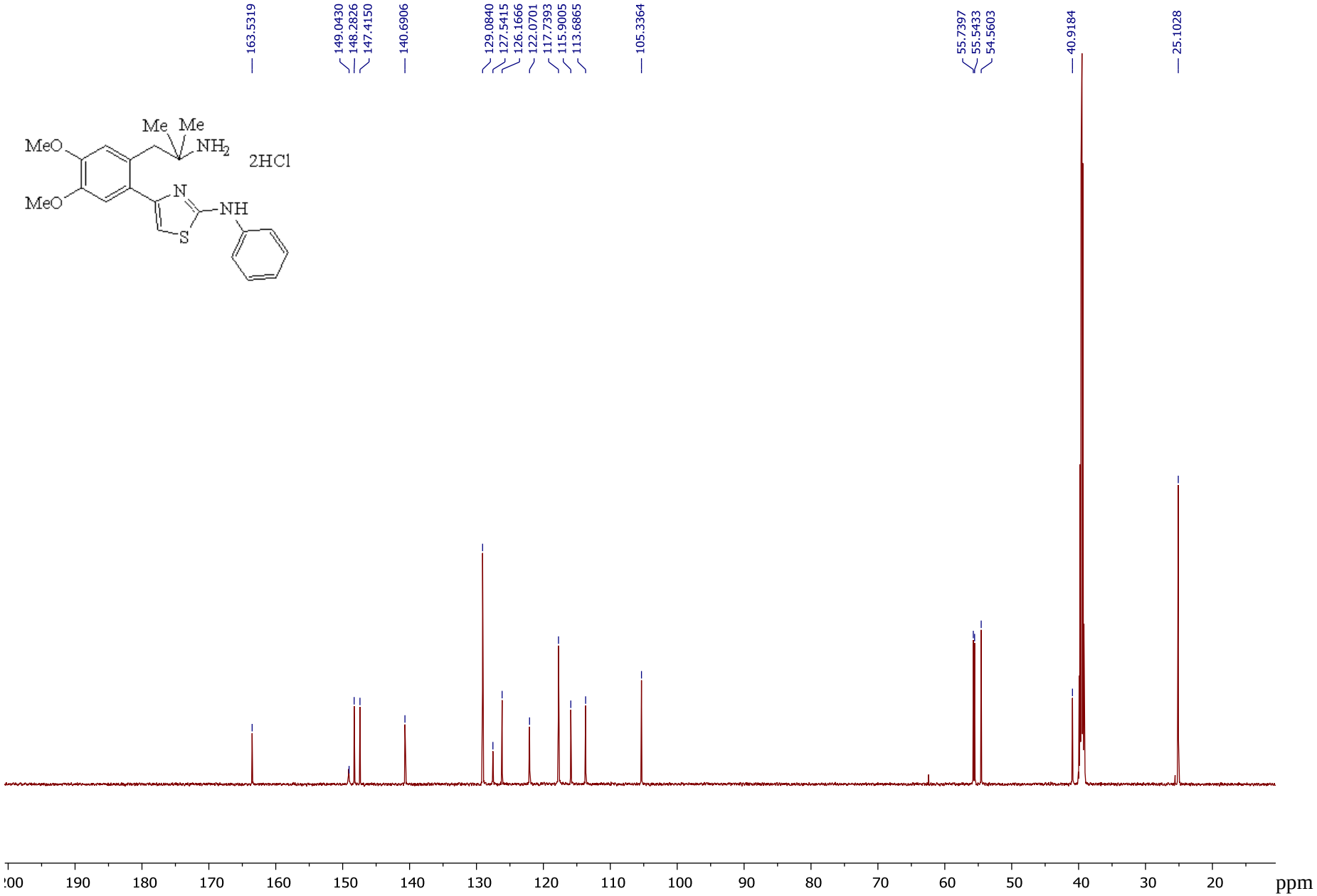






4-[2-(1-Amino-2-methylpropan-2-yl)-4,5-dimethoxyphenyl]-N-phenylthiazol-2-amine dihydrochloride (3h).

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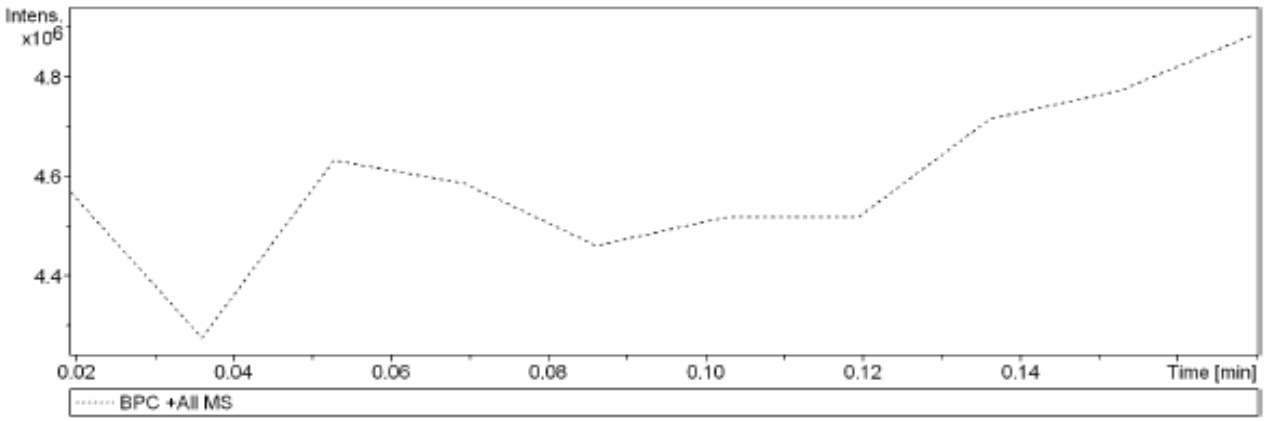
149.0430
148.2826
147.4150
140.6906
129.0840
127.5415
126.1666
122.0701
117.7393
115.9005
113.6865
105.3364
55.7397
55.5433
54.5603
40.9184
25.1028
Me
Me
NH2
MeO
MeO
2HCl
N
NH
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

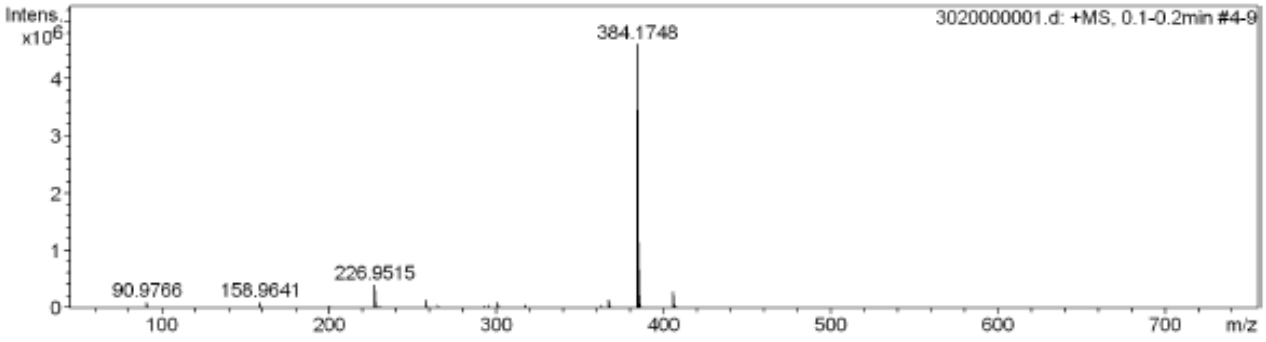
Analysis Info

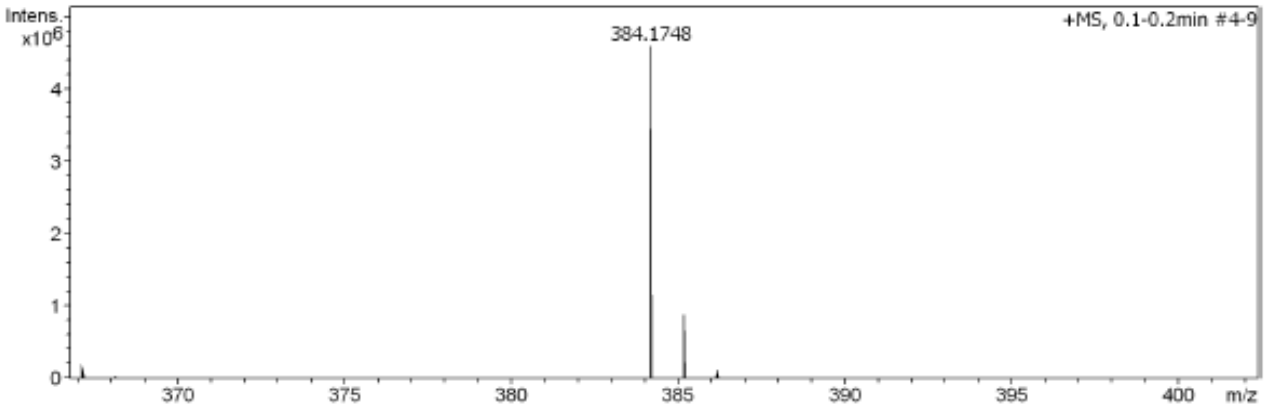
Analysis Name	D:\Data\demidov\3020000001.d	Acquisition Date	11/12/2020 3:14:24 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

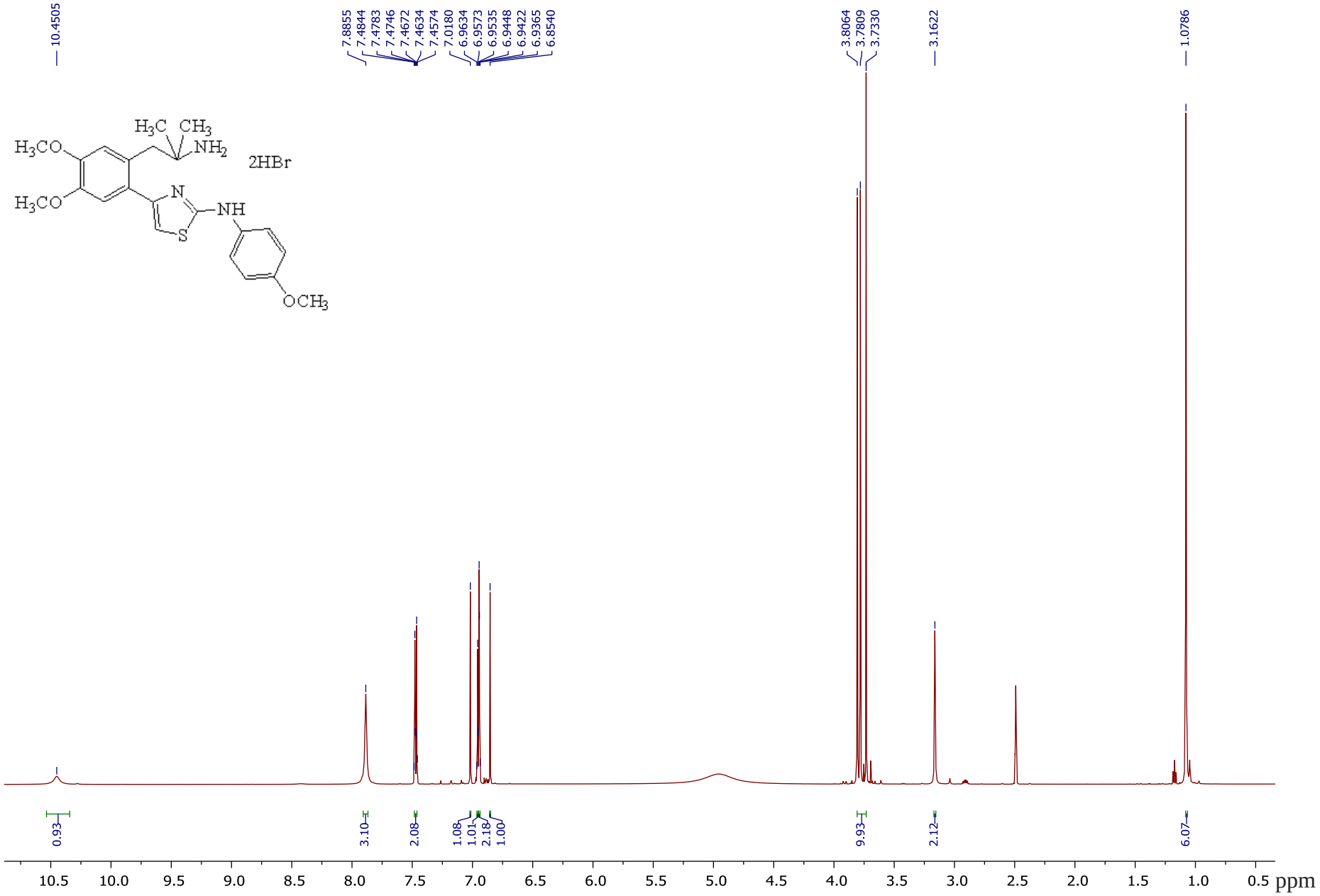
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

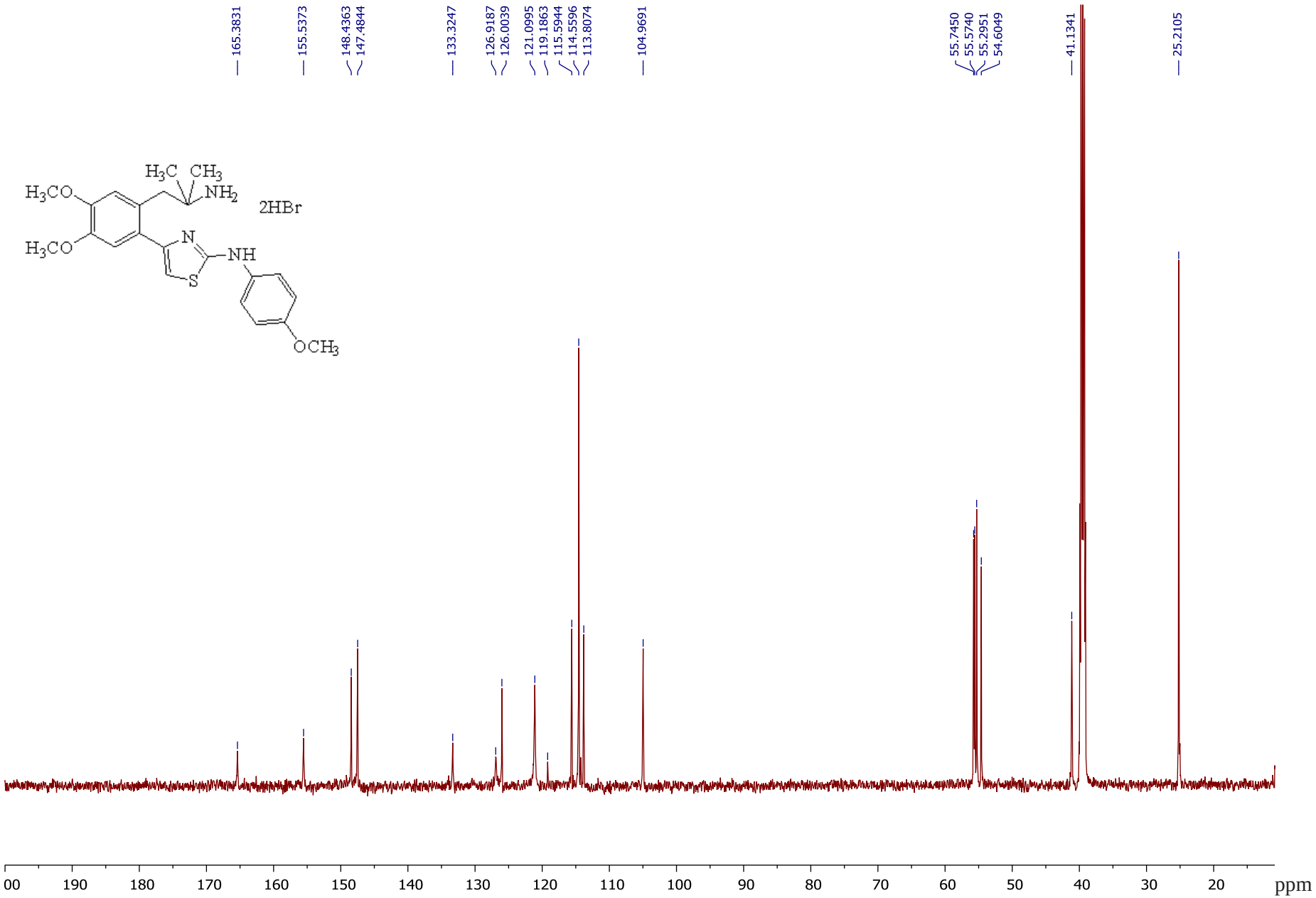






4-[2-(1-Amino-2-methylpropan-2-yl)-4,5-dimethoxyphenyl]-N-(4-methoxyphenyl)thiazol-2-amine dihydrobromide (3i).



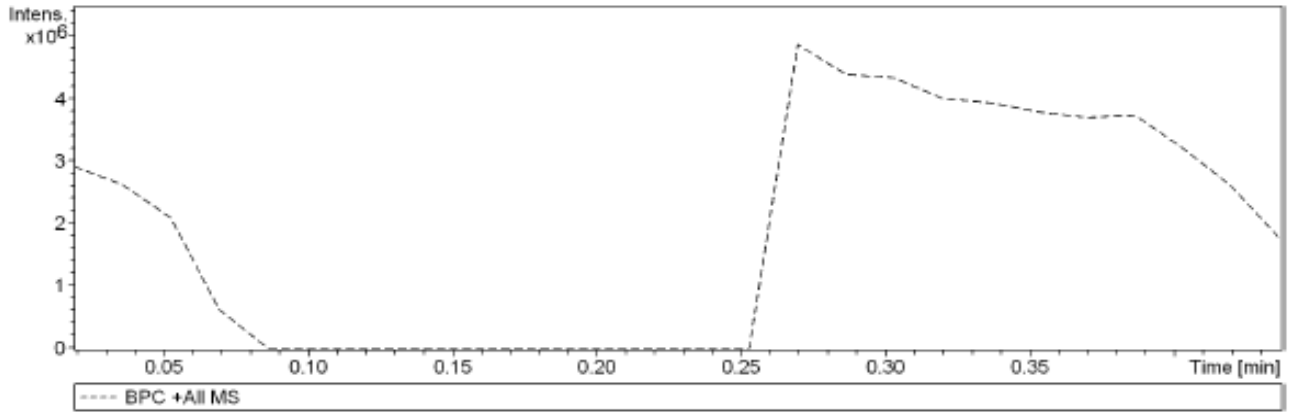

165.3831
155.5373
148.4363
147.4844
133.3247
126.9187
126.0039
121.0995
119.1863
115.5944
114.5596
113.8074
104.9691
55.7450
55.5740
55.2951
54.6049
41.1341
25.2105
H3C CH3
H3CO
NH2
2HBr
H3CO
N
NH
S
OCH3
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

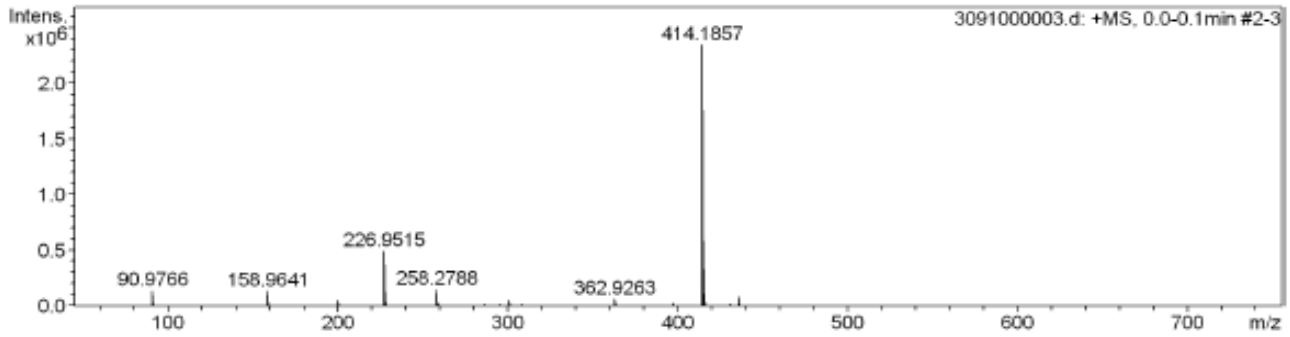
Analysis Info

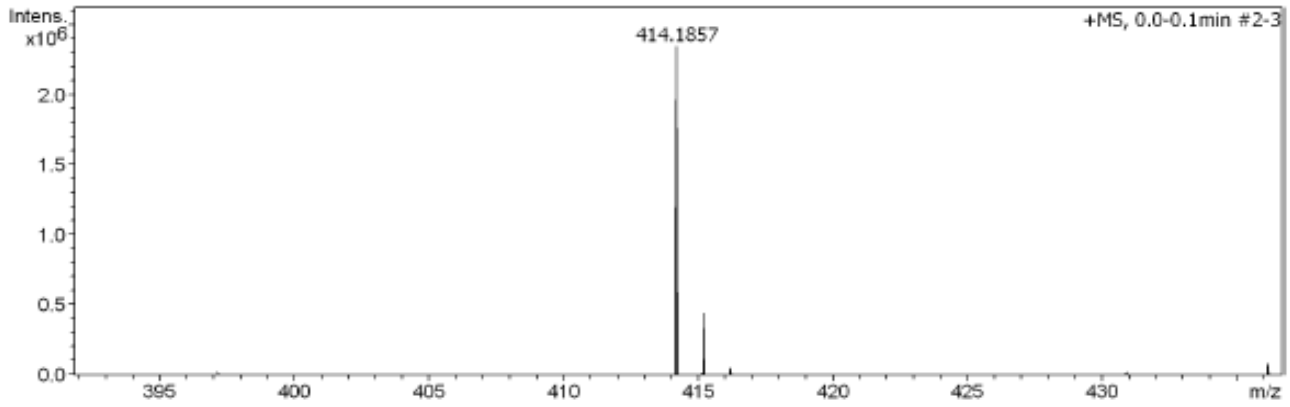
Analysis Name	D:\Data\demidov\3091000003.d	Acquisition Date	11/12/2020 3:07:31 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

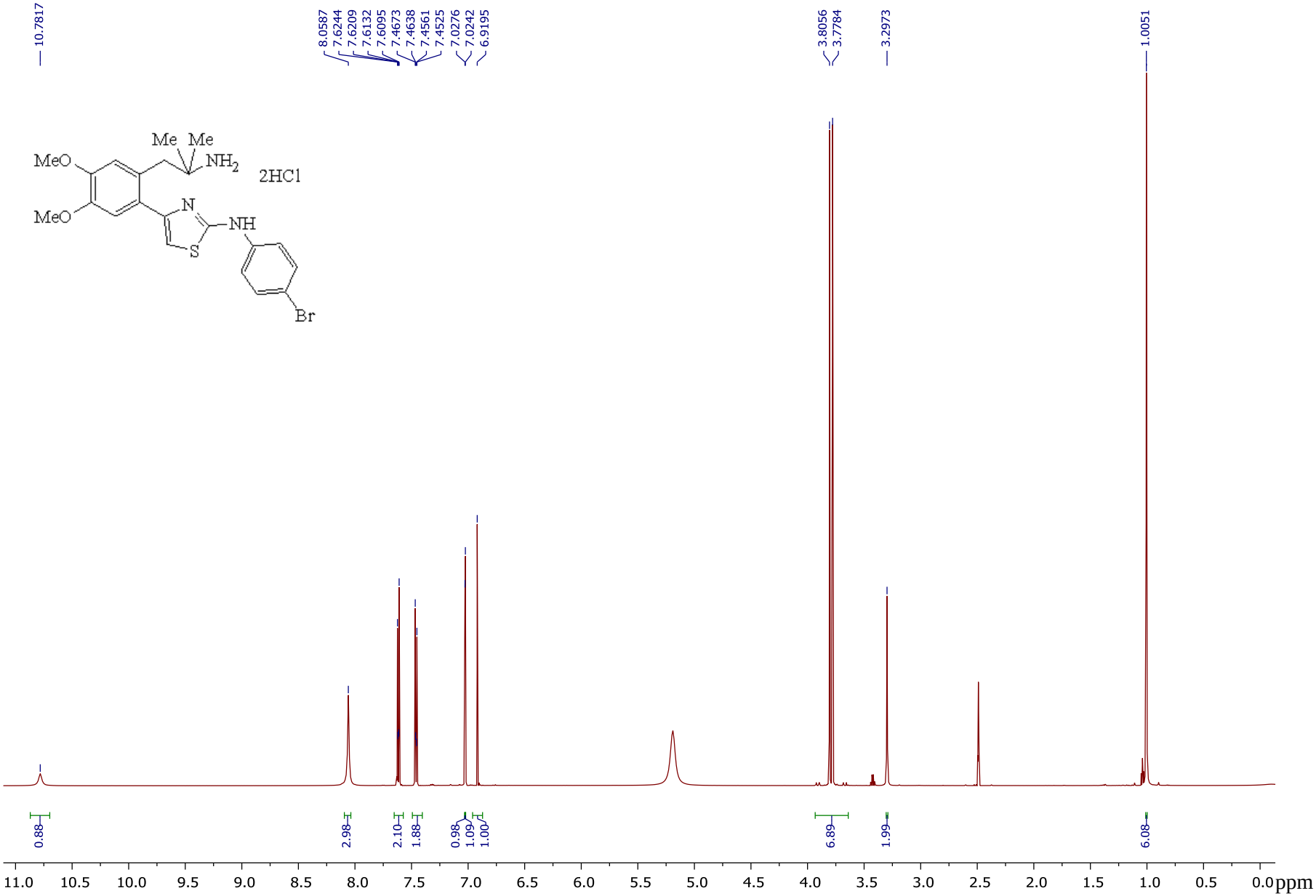
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

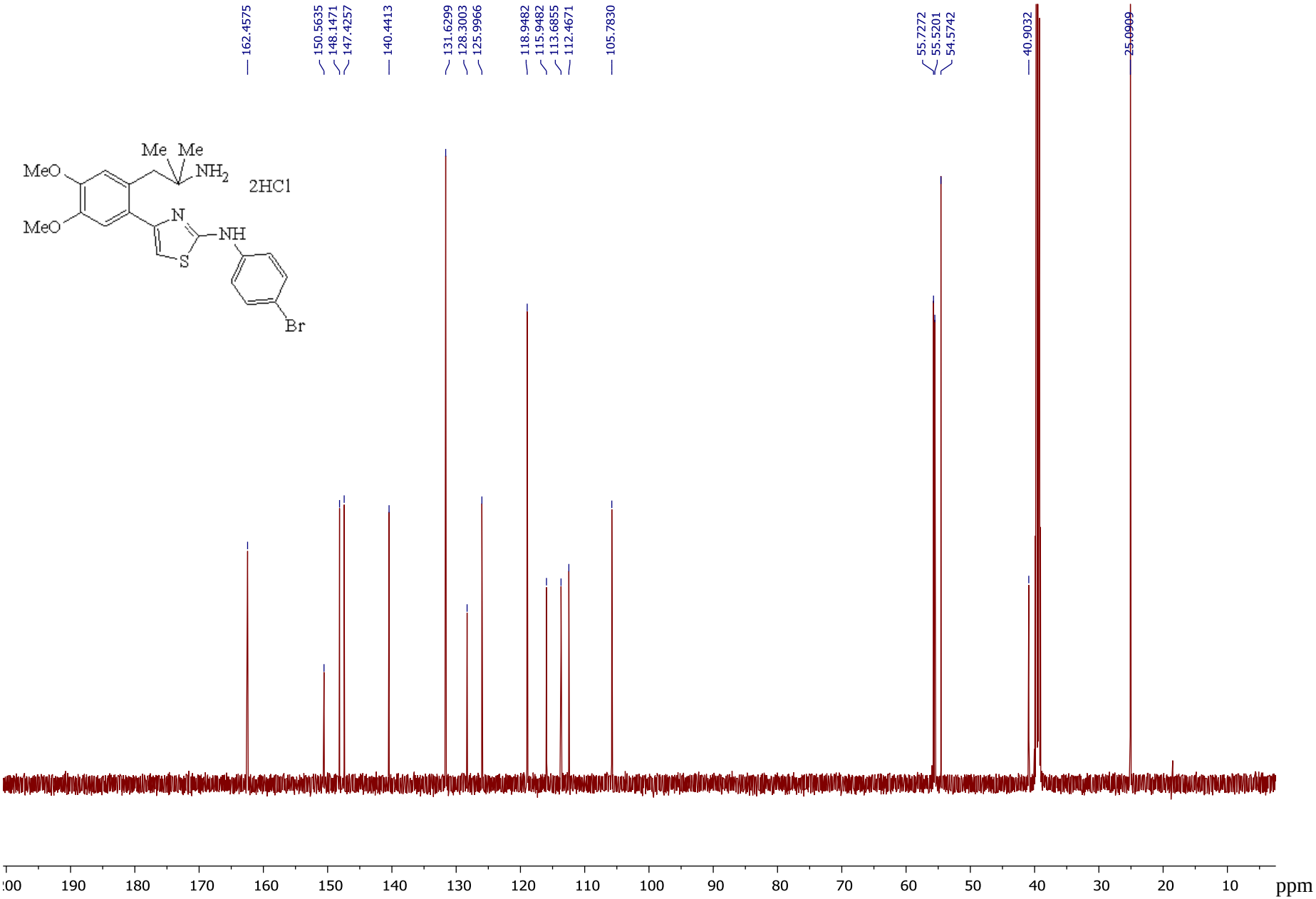






4-[2-(2-Amino-2-methylpropan-2-yl)-4,5-dimethoxyphenyl]-N-(4-bromophenyl)thiazol-2-amine dihydrochloride (3j).

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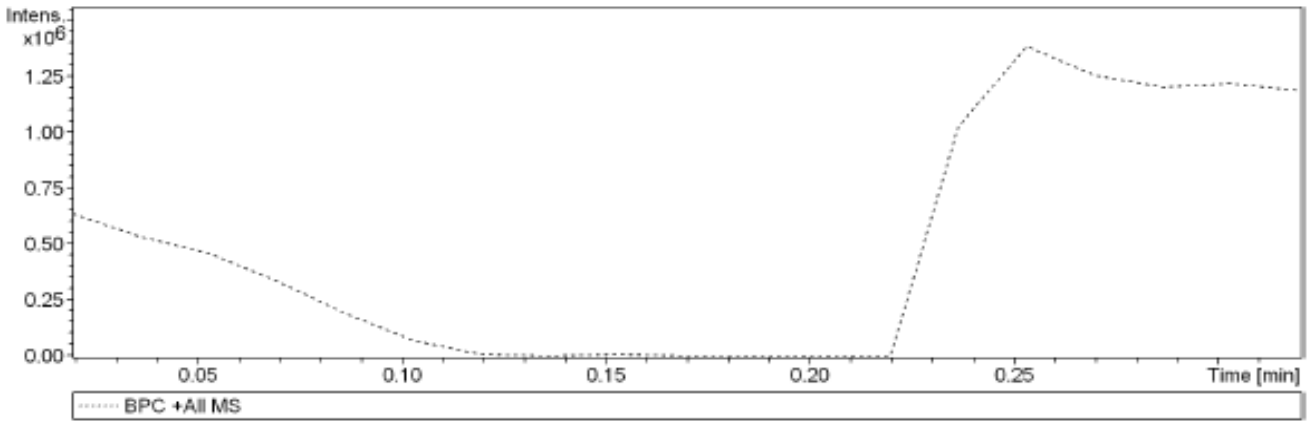
148.1471
147.4257
140.4413
131.6299
128.3003
125.9966
118.9482
115.9482
113.6855
112.4671
105.7830
55.7272
55.5201
54.5742
40.9032
25.0909
Me Me
NH2
MeO
MeO
2HCl
N
NH
S
Br
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

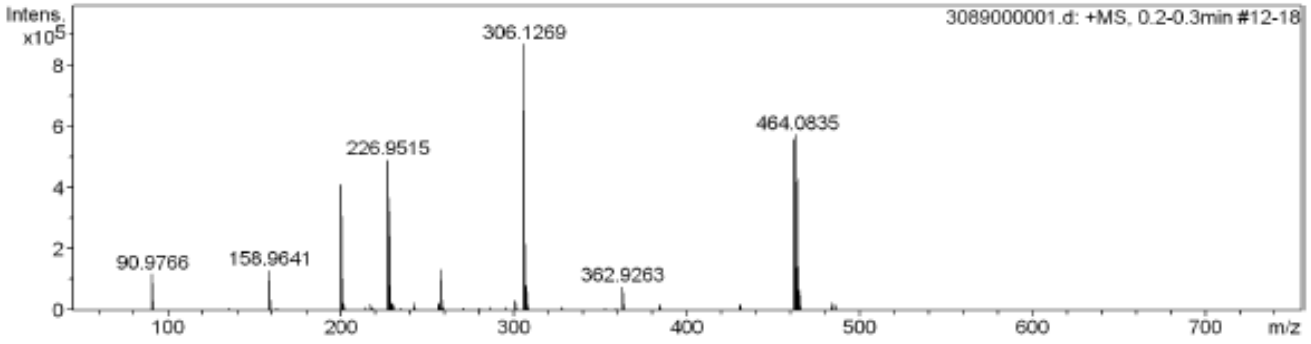
Analysis Info

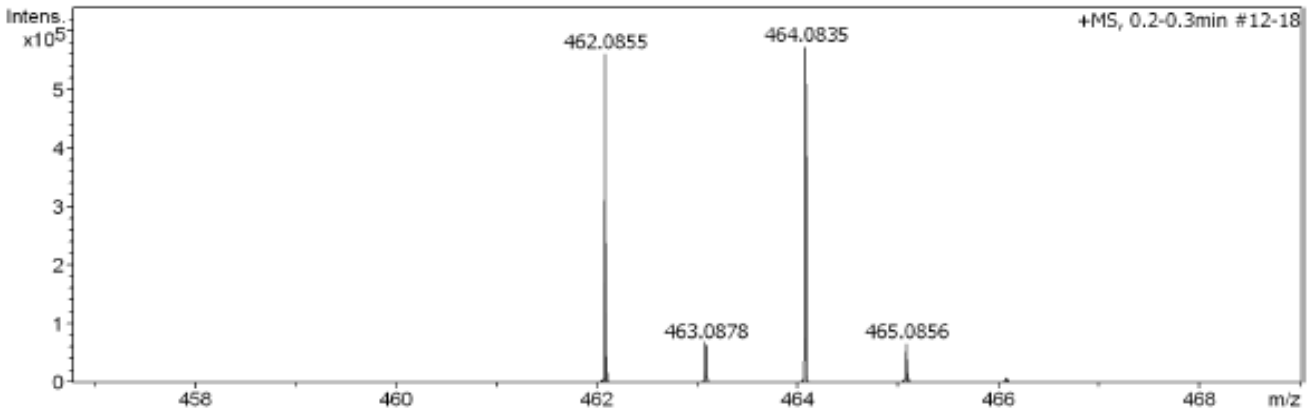
Analysis Name	D:\Data\demidov\3089000001.d	Acquisition Date	11/12/2020 3:09:46 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

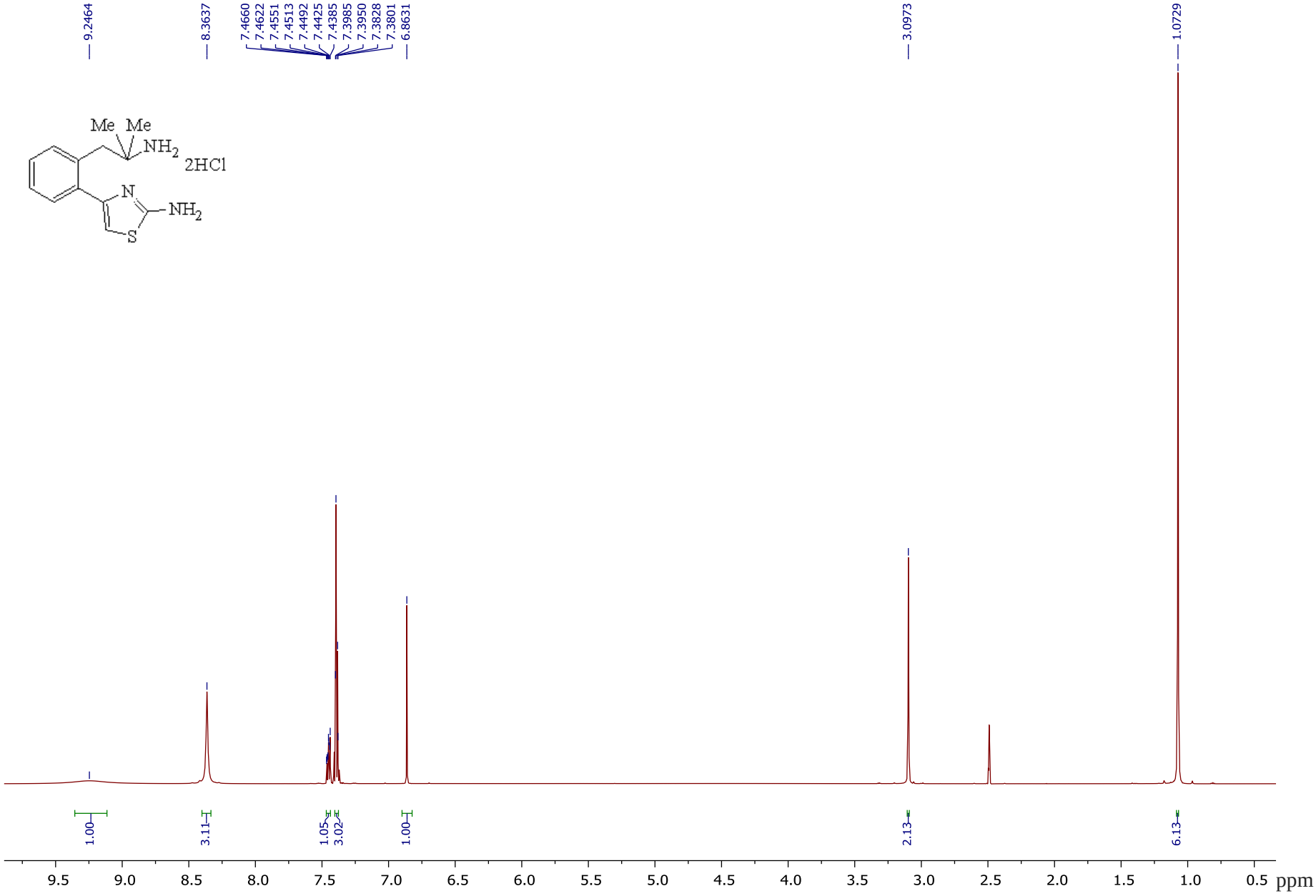
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

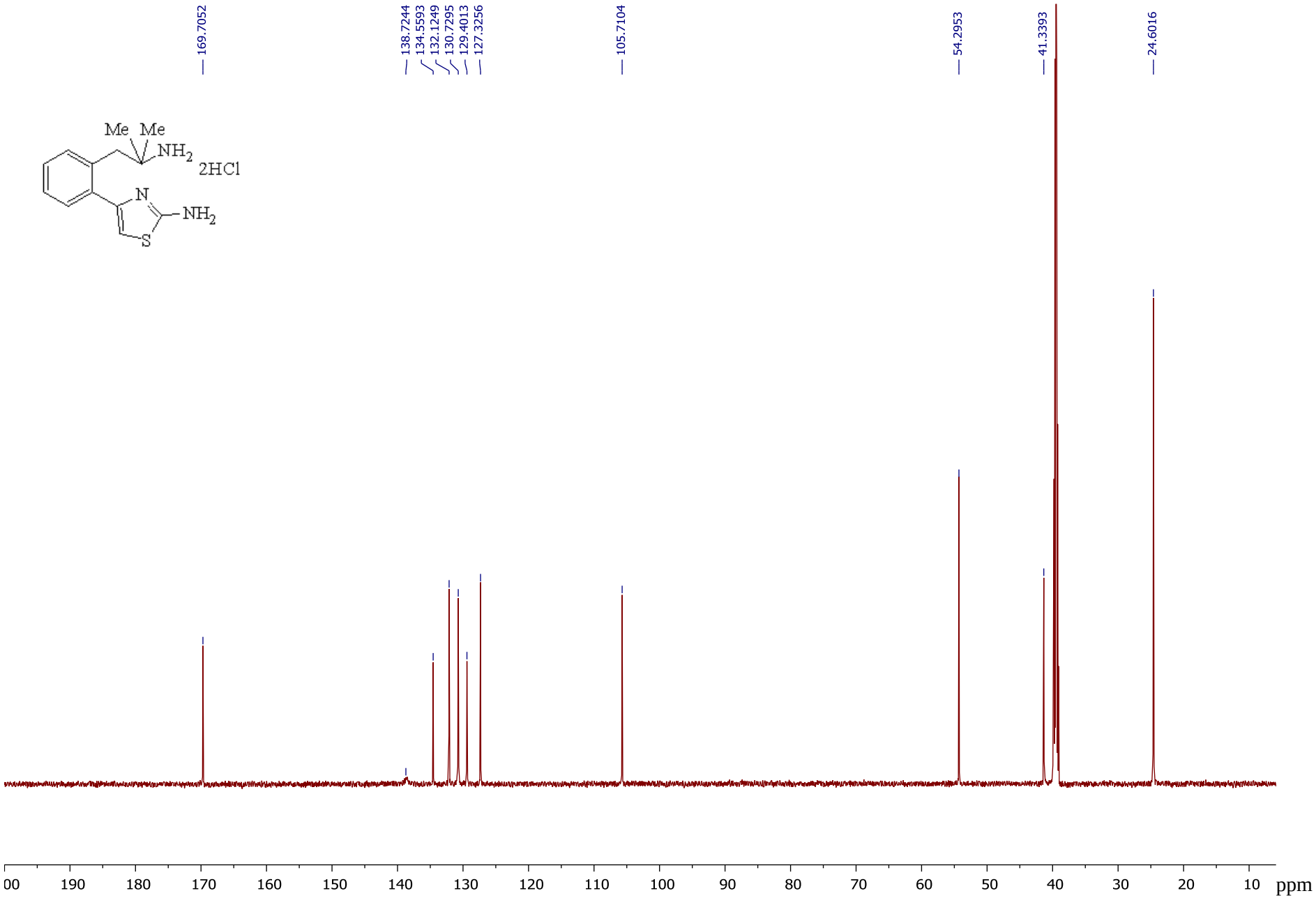






4-[2-(2-Amino-2-methylpropyl)phenyl]thiazol-2-amine dihydrochloride (3k).



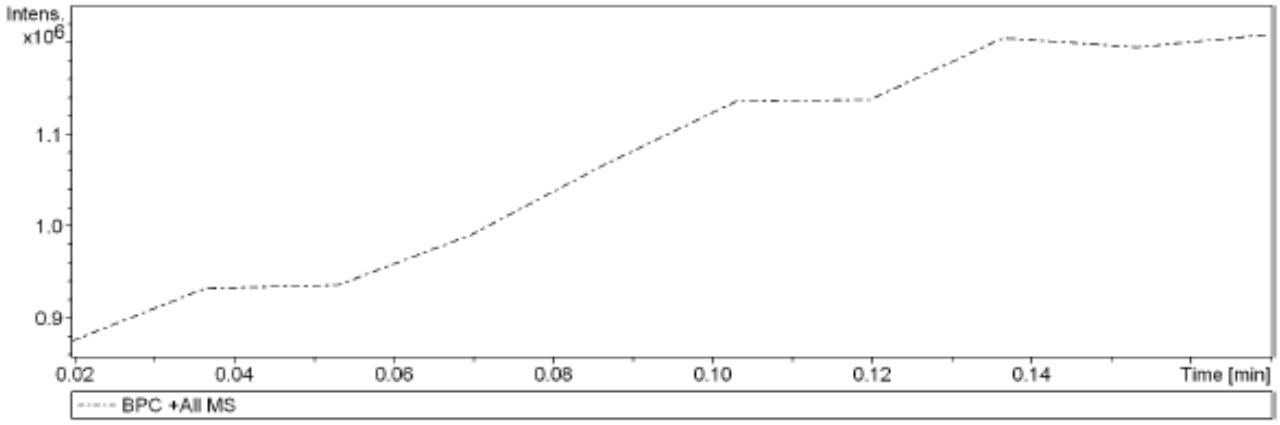

169.7052
138.7244
134.5593
132.1249
130.7295
129.4013
127.3256
105.7104
54.2953
41.3393
24.6016
Me
Me
NH2
2HCl
N
NH2
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

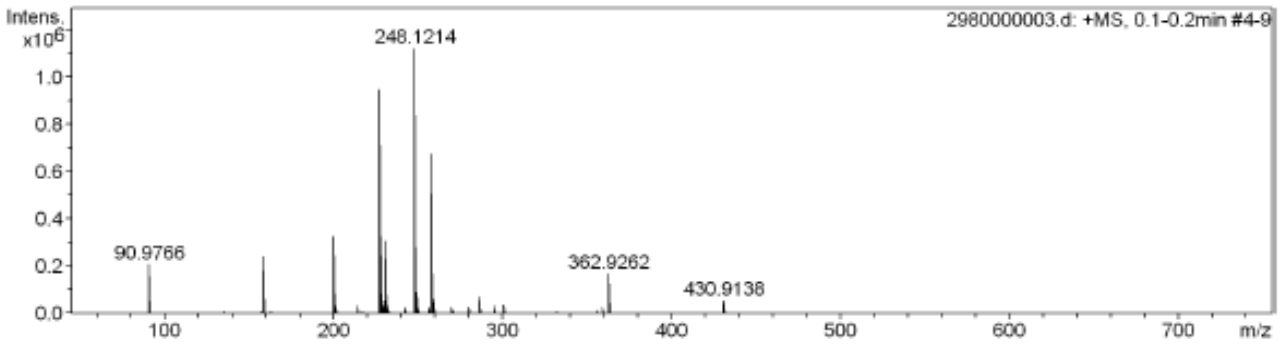
Analysis Info

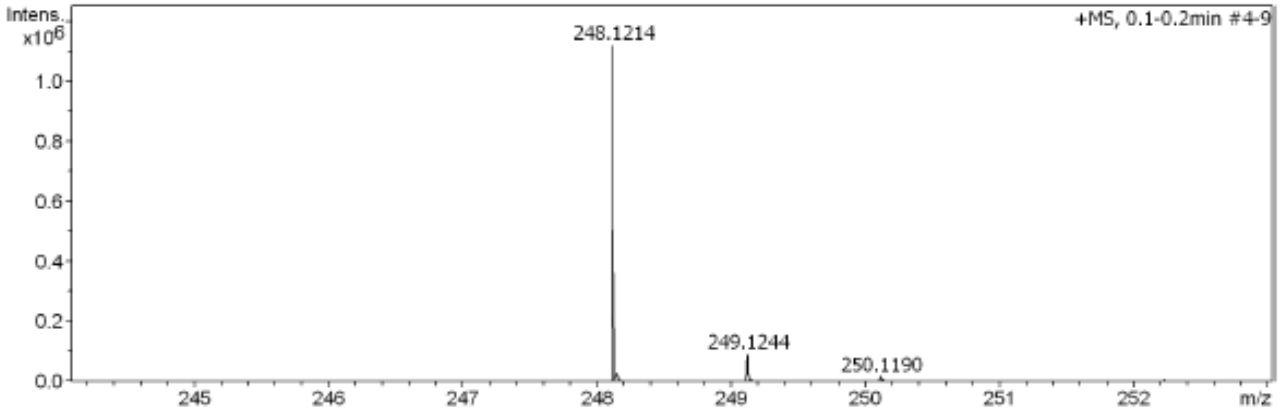
Analysis Name	D:\Data\demidov\2980000003.d	Acquisition Date	11/12/2020 3:03:25 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

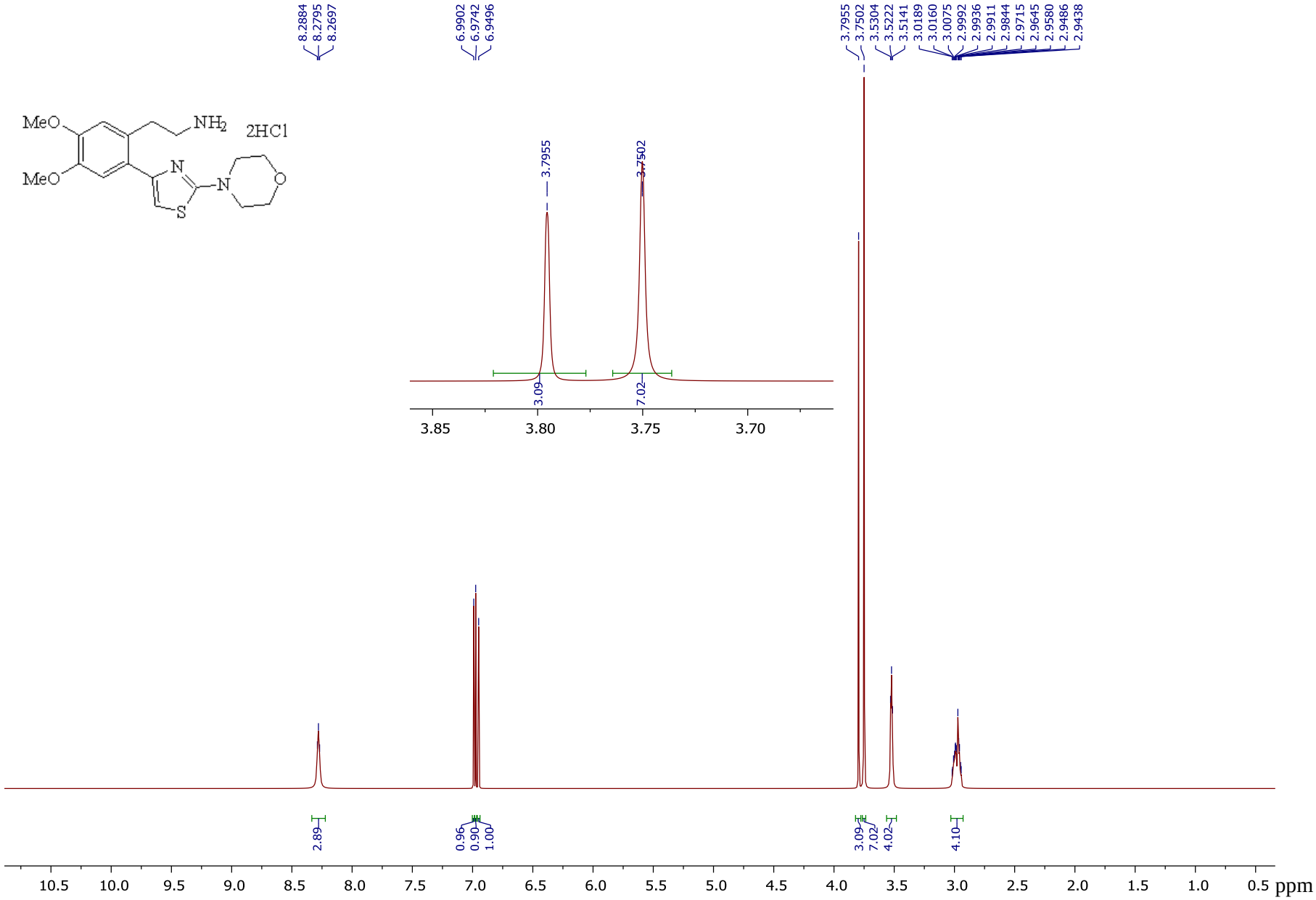
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

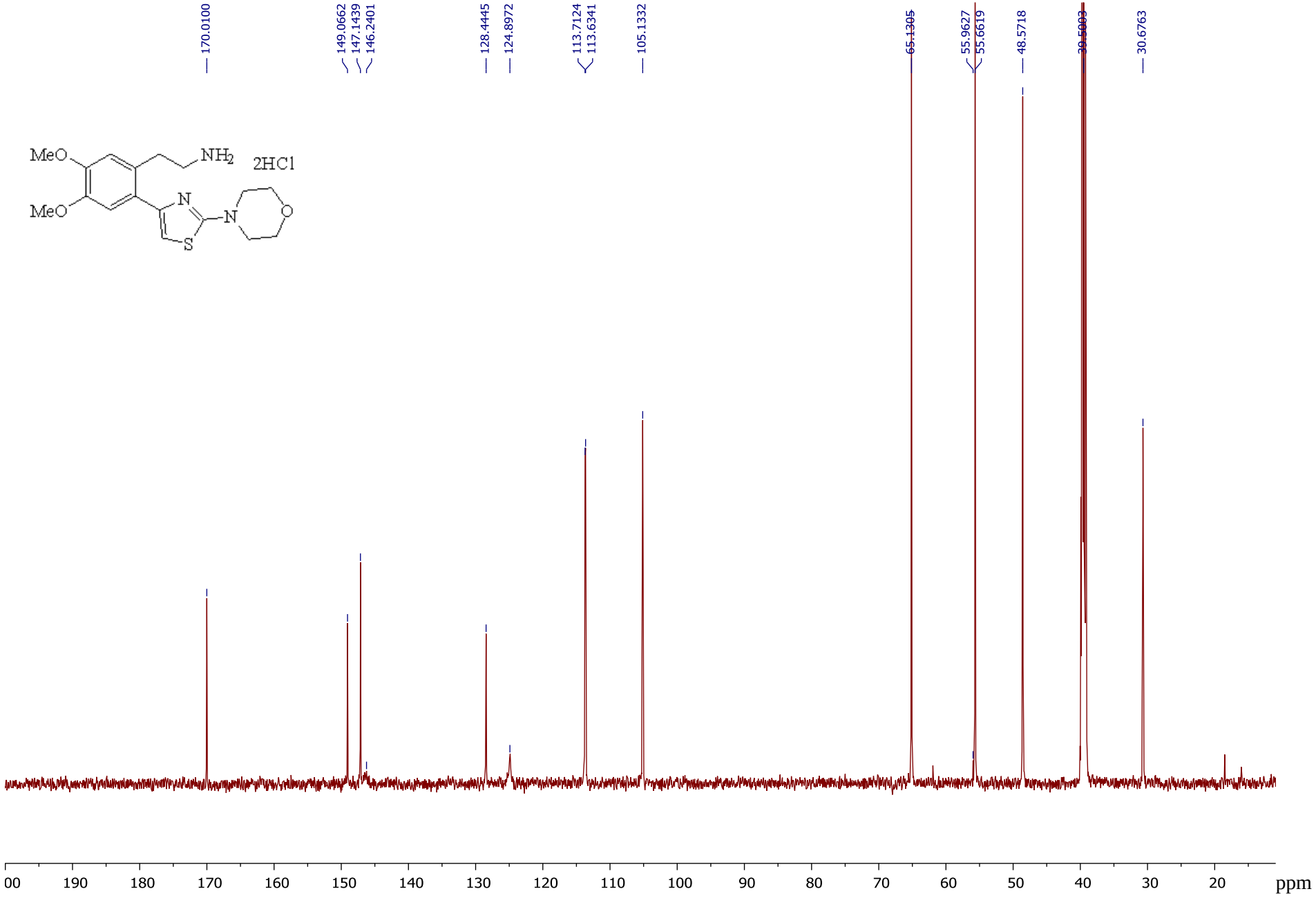






N-{4-[2-(2-Aminoethyl)-4,5-dimethoxyphenyl]thiazol-2-yl}morpholin-4-amine dihydrochloride (3l).

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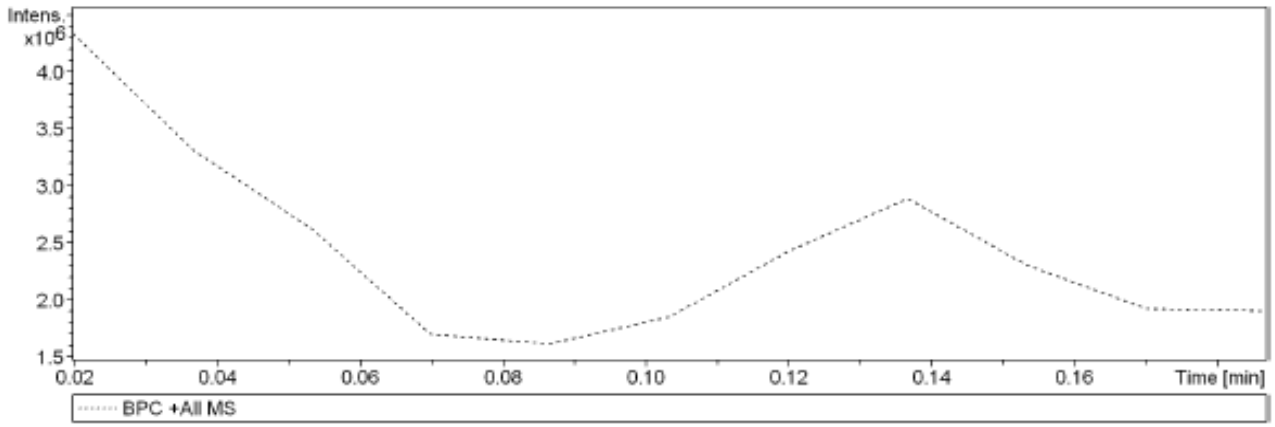
149.0662
147.1439
146.2401
128.4445
124.8972
113.7124
113.6341
105.1332
65.1305
55.9627
55.6619
48.5718
39.5003
30.6763
MeO
MeO
NH2
2HCl
N
N
S
O
ppm

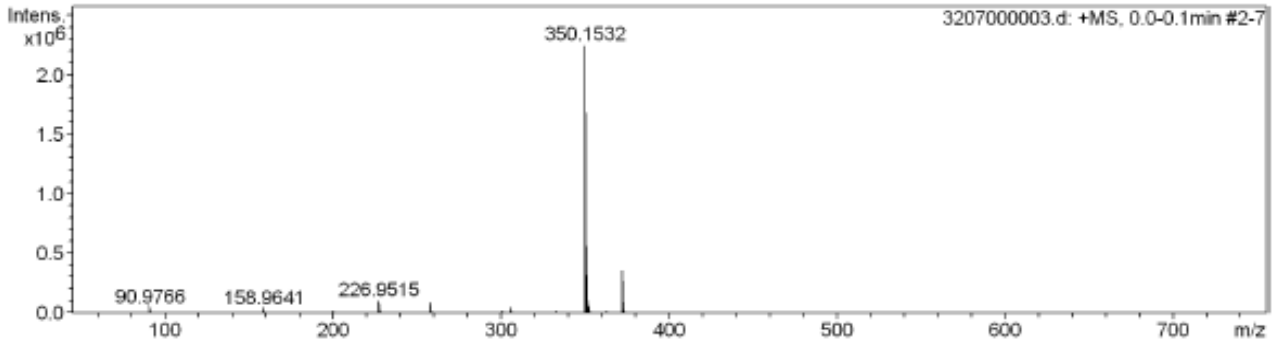
Analysis Info

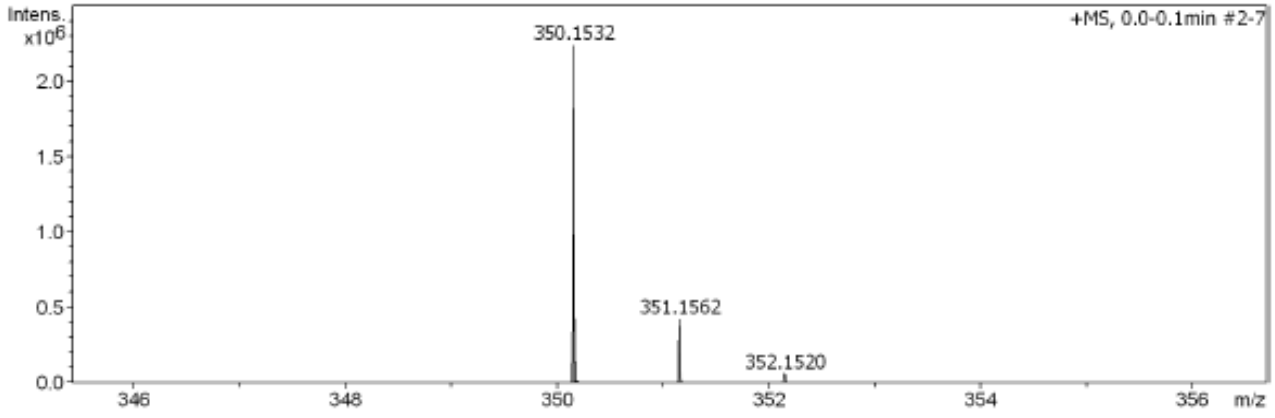
Analysis Name	D:\Data\demidov\3207000003.d	Acquisition Date	11/12/2020 3:10:54 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

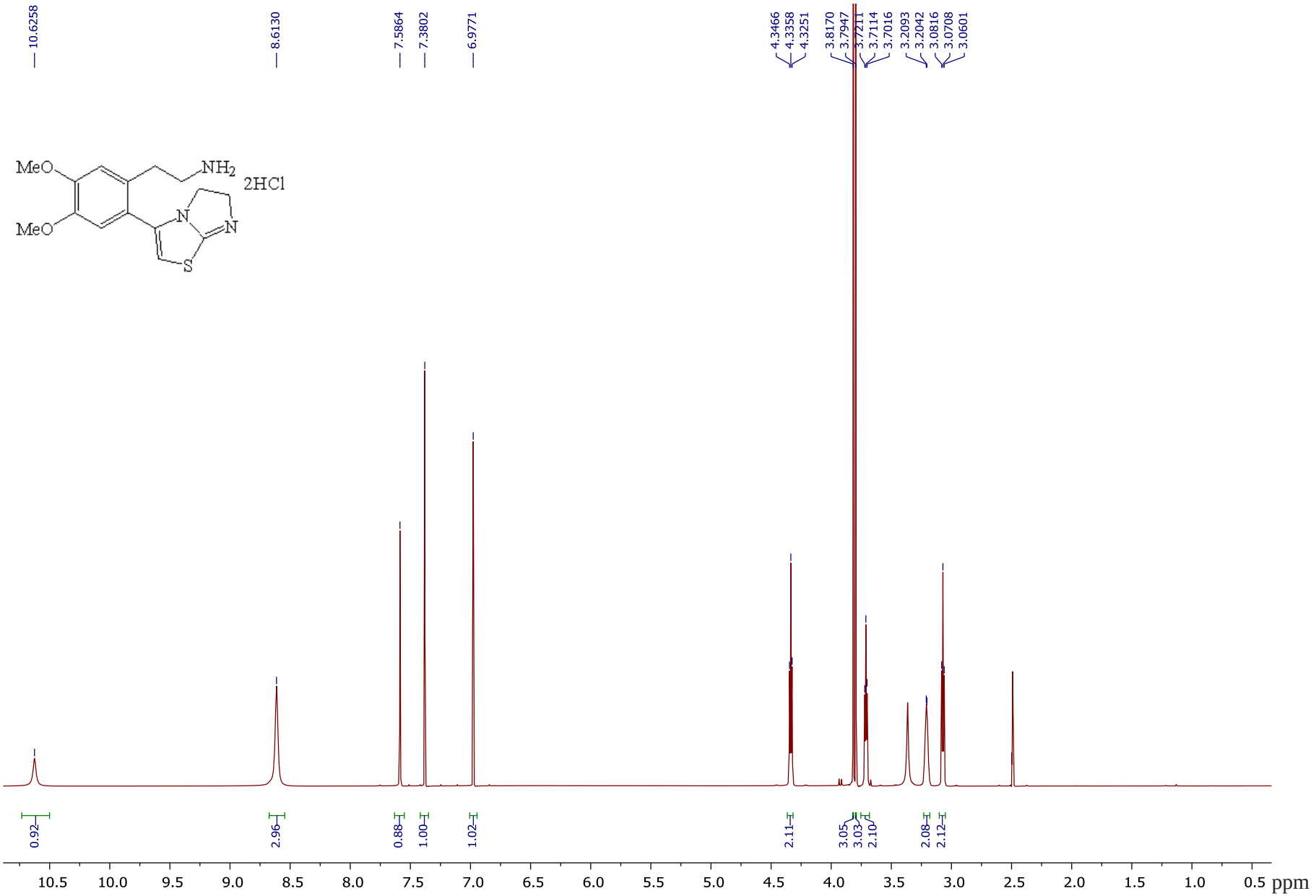
Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source

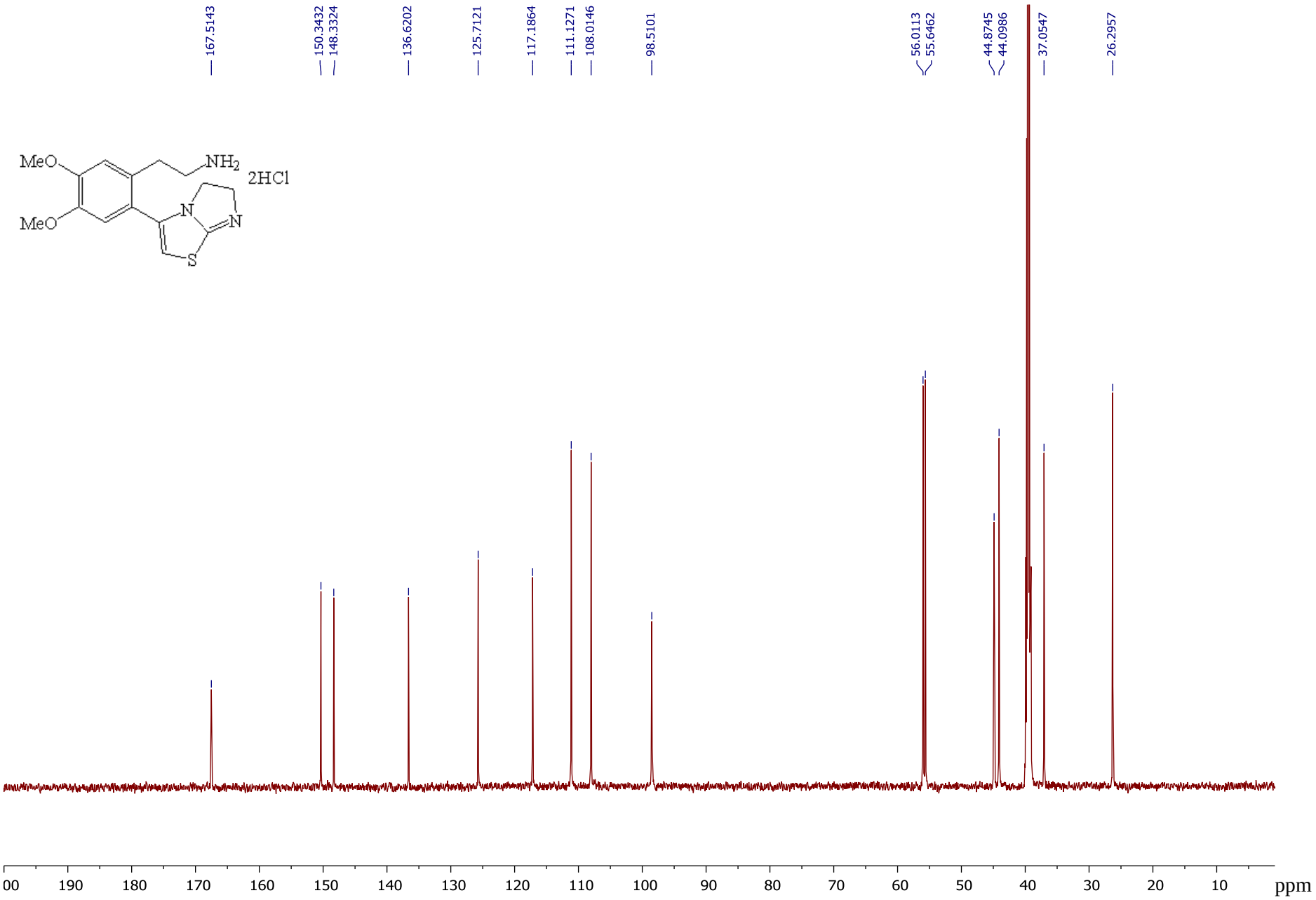






2-[2-(5,6-Dihydroimidazo[2,1-*b*]thiazol-3-yl)-4,5-dimethoxyphenyl]ethan-1-amine dihydrochloride (3m).



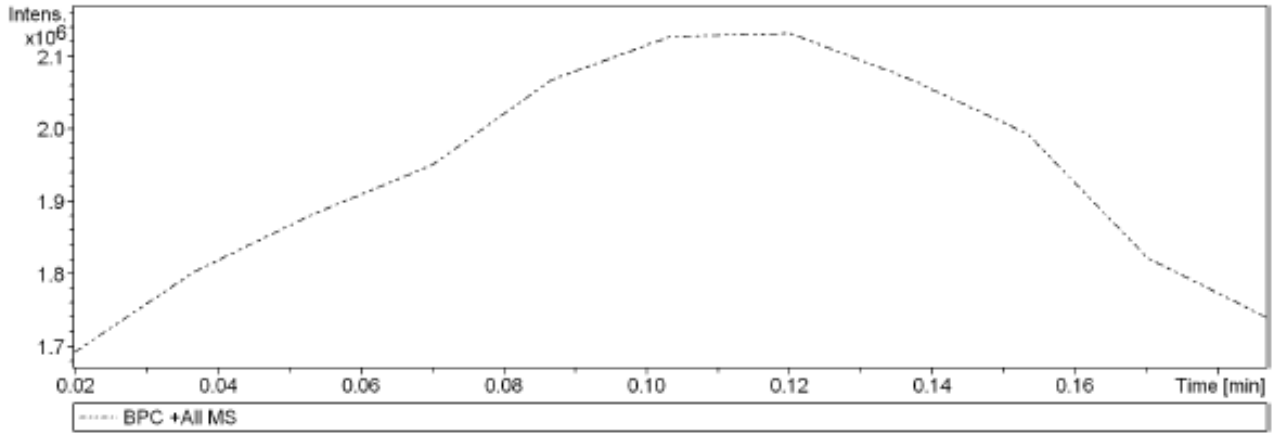

167.5143
150.3432
148.3324
136.6202
125.7121
117.1864
111.1271
108.0146
98.5101
56.0113
55.6462
44.8745
44.0986
37.0547
26.2957
MeO
MeO
NH2
2HCl
N
N
S
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

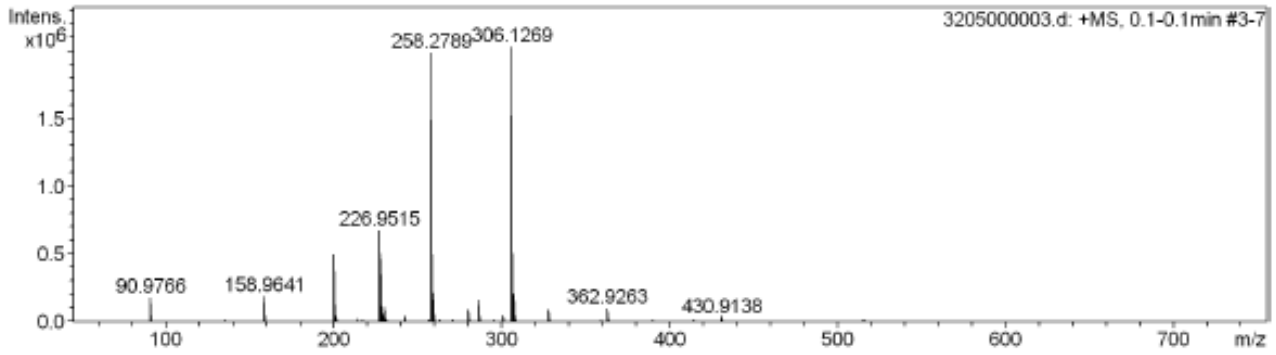
Analysis Info

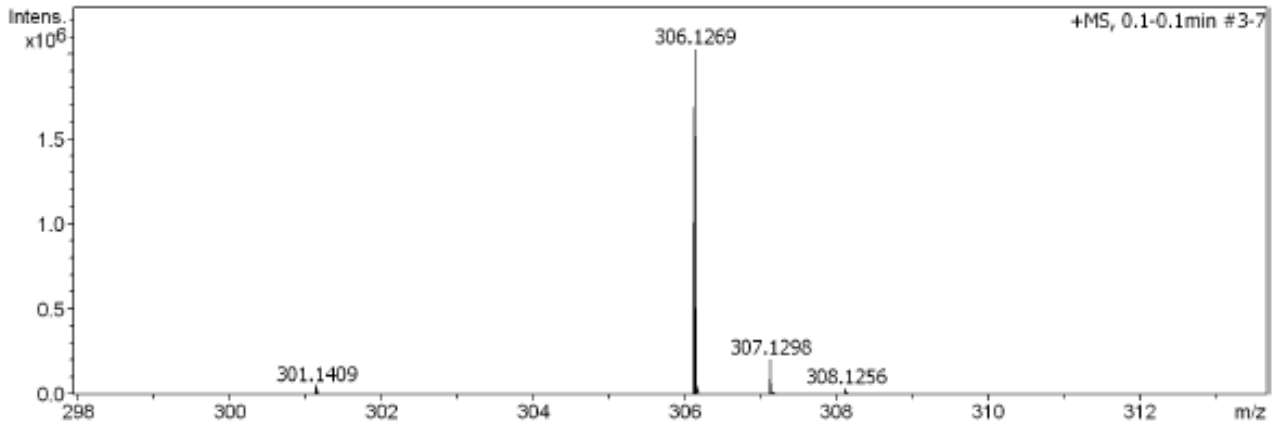
Analysis Name	D:\Data\demidov\3205000003.d	Acquisition Date	11/12/2020 3:08:37 PM
Method	Direct_Infusion_50-500_2018.m	Operator	Demidov
Sample Name	322	Instrument	maXis impact 282001.00109
Comment			

Acquisition Parameter

Source Type	ESI	Ion Polarity	Positive	Set Nebulizer	0.3 Bar
Focus	Active	Set Capillary	3500 V	Set Dry Heater	180 °C
Scan Begin	50 m/z	Set End Plate Offset	-500 V	Set Dry Gas	4.0 l/min
Scan End	750 m/z	Set Collision Cell RF	450.0 Vpp	Set Divert Valve	Source







7. Reference

S1 *CrysAlisPro, version 1.171.38.41*, *Rigaku Oxford Diffraction*, Oxford, 2015.

S2 G. M. Sheldrick, *Acta Crystallogr.*, *Sect. A*: *Found. Adv*., 2015, **71**, 3.

S3 G. M. Sheldrick, *Acta Crystallogr.*, *Sect. C*: *Struct. Chem*., 2015, **71**, 3.

S4 O. V. Dolomanov, L. J. Bourhis,; R. J. Gildea, J. A. K. Howard and H. J. Puschmann, *Appl. Crystallogr.*, 2009, **42**, 339.

S5 A. A. Granovsky, *Firefly version 8,* http://classic.chem.msu.su/gran/firefly/index.html.

S6 M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis and J. A. Montgomery, *J. Comput. Chem*., 1993, **14**, 1347.