Supplementary Information

Structure-Guided Design of *N*-Methylpropargylamino-Quinazoline Derivatives as Multipotent Agents for the Treatment of Alzheimer's Disease

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1. Physiochemical Properties and Drug-likeness of Final Compounds

For the prediction of physiochemical properties (**Table S1**) was used MarvinSketch 20.4.0, ChemAxon Ltd. Drug-likeness of designed derivatives was evaluated by SwissADME online tool [1].

Table S1. Physiochemical parameters of compounds **I-III/6a-6h** THA and Memantine.

Compound	MW	pKa	logP	HBA	HBD	TPSA
I-6a	212.25	6.55	2.21	2	1	55.04
I-6b	226.28	6.45	2.51	2	1	41.05
I-6c	240.30	6.42	2.86	2	1	41.05
I-6d	254.33	6.40	3.28	2	1	41.05
I-6e	268.36	6.42	3.83	2	1	41.05
I-6f	270.33	6.40	2.46	3	1	50.28
I-6g	252.31	6.39	2.97	2	1	41.05
I-6h	294.39	6.39	4.31	2	1	41.05
II-6a	246.70	5.82	2.81	2	1	55.04
II-6b	260.72	5.72	3.11	2	1	41.05
II-6c	304.77	5.67	3.06	3	1	50.28
II-6d	288.78	5.67	3.88	2	1	41.05
II-6e	302.80	5.69	4.44	2	1	41.05
II-6f	304.77	5.67	3.06	3	1	50.28
II-6g	286.76	5.66	3.58	2	1	41.05
II-6h	328.84	5.66	4.91	2	1	41.05
III-6a	242.28	6.60	2.05	3	1	64.27
III-6b	256.30	6.51	2.35	3	1	50.28
III-6c	270.33	6.48	2.71	3	1	50.28
III-6d	284.36	6.48	3.12	3	1	50.28
III-6e	298.38	6.48	3.67	3	1	50.28
III-6f	300.36	6.46	2.30	4	1	59.51
III-6g	282.34	6.45	2.82	3	1	50.28
III-6h	324.42	6.45	4.15	3	1	50.28
THA	198.26	8.95	2.63	2	1	38.91
Memantine	179.30	10.70	2.07	1	1	26.02

MW = molecular weight, pKa = acid dissociation constant, logP = partition coefficient, HBA = hydrogen bond acceptor, HBB = hydrogen bond donor, TPSA = topological polar surface area

Table S2. Drug-likeness of derivatives **I-III/6a-6h**; THA and memantine.

Compound	Drug-likeness				
	Lipinski [a]	**Ghose** [b]	**Veber** [c]	**Egan** [d]	**Muegge** [e]
I-6a	Yes	Yes	Yes	Yes	Yes
I-6b	Yes	Yes	Yes	Yes	Yes
I-6c	Yes	Yes	Yes	Yes	Yes
I-6d	Yes	Yes	Yes	Yes	Yes
I-6e	Yes	Yes	Yes	Yes	Yes
I-6f	Yes	Yes	Yes	Yes	Yes
I-6g	Yes	Yes	Yes	Yes	Yes
I-6h	Yes	Yes	Yes	Yes	Yes
II-6a	Yes	Yes	Yes	Yes	Yes
II-6b	Yes	Yes	Yes	Yes	Yes
II-6c	Yes	Yes	Yes	Yes	Yes
II-6d	Yes	Yes	Yes	Yes	Yes
II-6e	Yes	Yes	Yes	Yes	Yes
II-6f	Yes	Yes	Yes	Yes	Yes
II-6g	Yes	Yes	Yes	Yes	Yes
II-6h	Yes	Yes	Yes	Yes	Yes
III-6a	Yes	Yes	Yes	Yes	Yes
III-6b	Yes	Yes	Yes	Yes	Yes
III-6c	Yes	Yes	Yes	Yes	Yes
III-6d	Yes	Yes	Yes	Yes	Yes
III-6e	Yes	Yes	Yes	Yes	Yes
III-6f	Yes	Yes	Yes	Yes	Yes
III-6g	Yes	Yes	Yes	Yes	Yes
III-6h	Yes	Yes	Yes	Yes	Yes
THA	Yes	Yes	Yes	Yes	No [f]
Memantine	Yes	Yes	Yes	Yes	No [g]

[a] Lipinski represent [2], MW < 500 Da, logP <5, HBD <5, HBA <10; [b] Ghose [3], MW = 180 – 480, MR (molar refractivity) = 40 – 130, logP = -0.4 – +5.6, number of atoms = 20 – 70; [c] Veber [4], rotatable bonds <10, TPSA <140; [d] Egan [5], TPSA <132, logP <5.88; [e] Muegge [6], MW = 200 – 500, log P = -2 -+5, HBD <5, HBA <10, MR = 40 – 130, rotatable bonds <8, heavy atoms = 20 – 70, TPSA <120, net charge -2 -+2; [f] 1 violation, [g] 2 violations.

2. Cholinesterase Inhibitory Activity

Table S3. The inhibitory activities of compounds **I-III/6a-6h** for human acetylcholinesterase (*h*AChE) and human butyrylcholinesterase (*h*BChE).

Compound	% of AChE inhibition 10^{-6} M	% of BChE inhibition 10^{-6} M
I-6a	5	0
I-6b	5	3
I-6c	4	0
I-6d	4	1
I-6e	3	4
I-6f	5	1
I-6g	4	2
I-6h	4	0
II-6a	7	2
II-6b	15	2
II-6c	4	0
II-6d	1	3
II-6e	9	0
II-6f	9	2
II-6g	4	0
II-6h	3	3
III-6a	9	1
III-6b	4	1
III-6c	7	2
III-6d	2	2
III-6e	8	1
III-6f	6	1
III-6g	5	0
III-6h	3	2
THA	59	14
7-MEOTA	91	18

3. Anti-MAOs Activity Screening

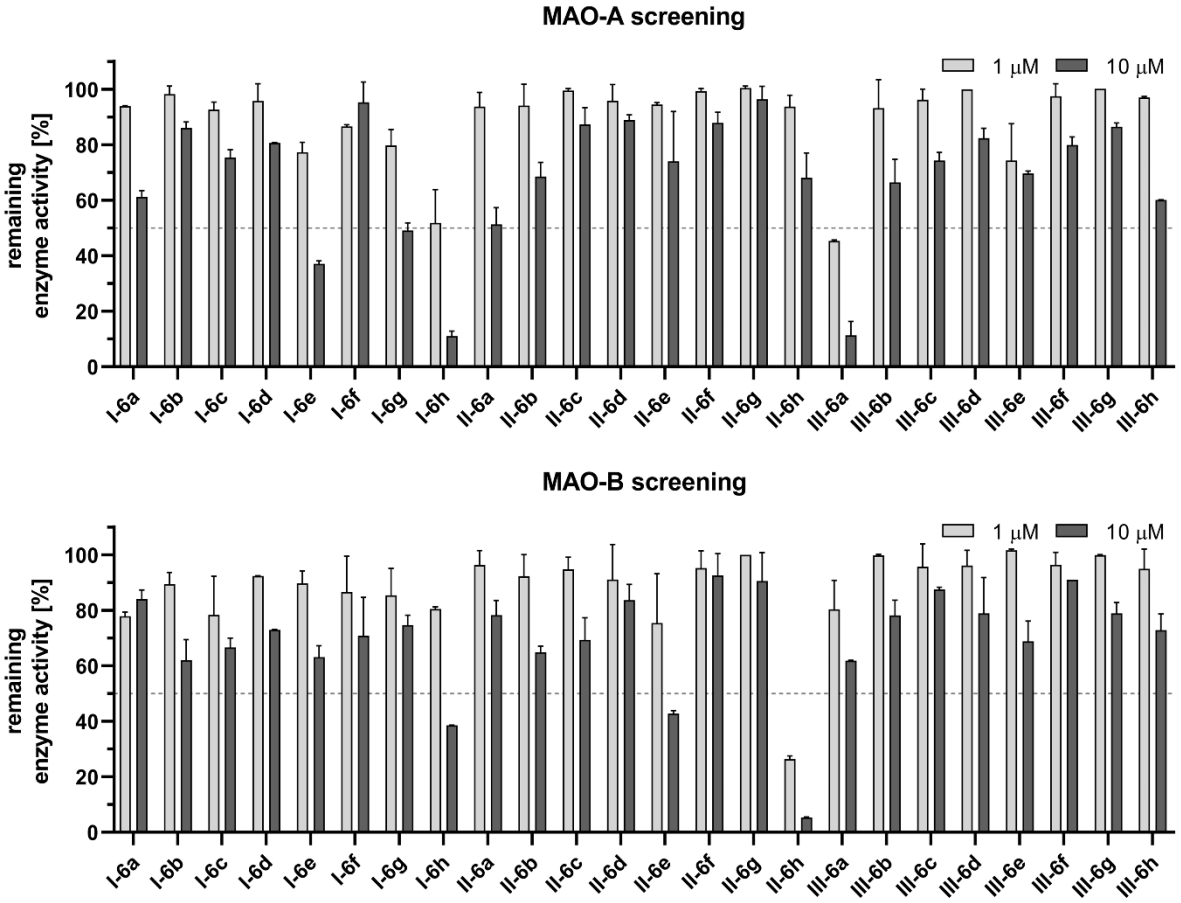


Figure S1. Screening MAO-A/B.

4. ^{1}H and ^{13}C NMR Spectra

Fig. S2. ^{1}H NMR of 2-chloroquinazolin-4-amine (I-5a)

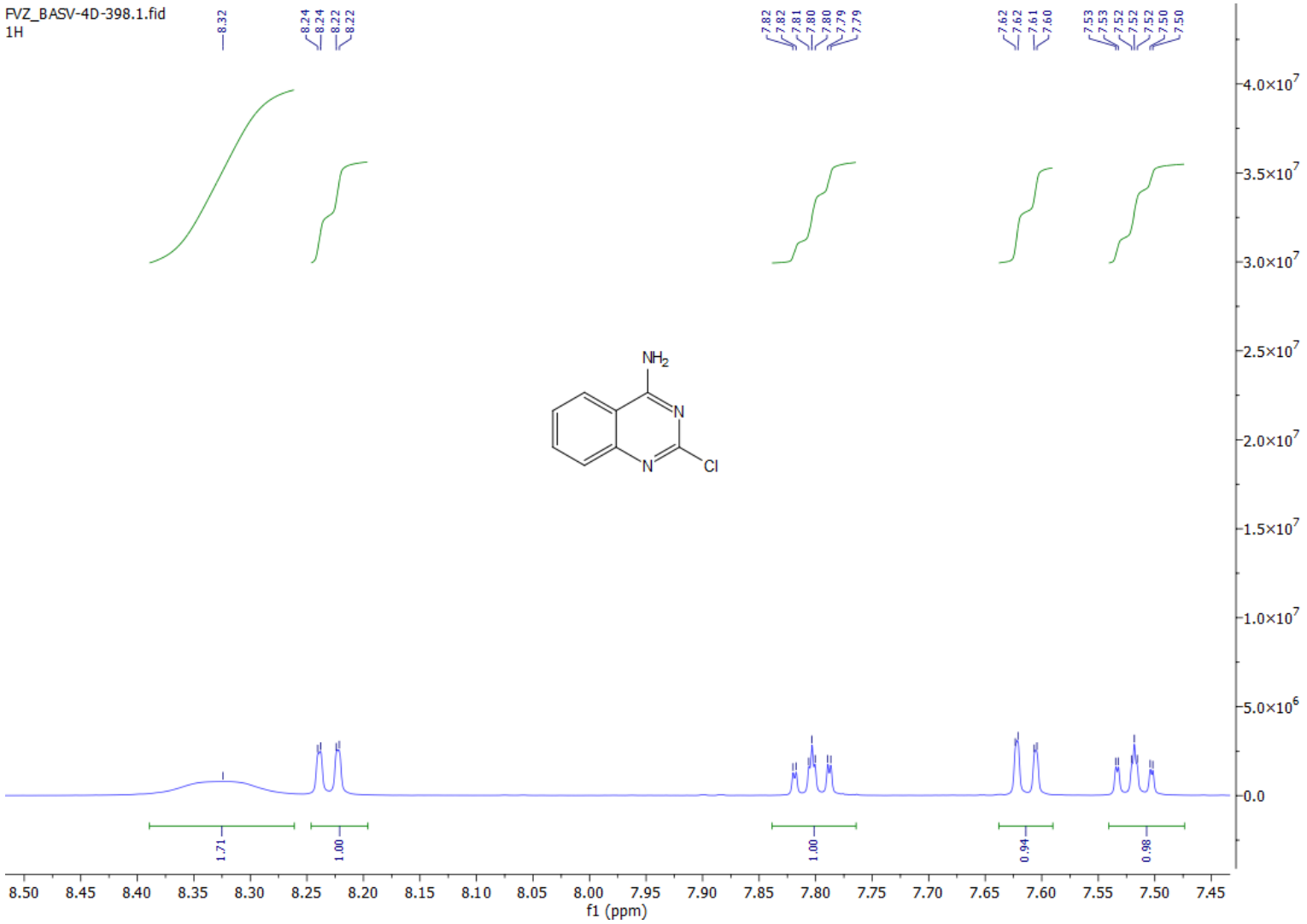


Fig. S3. ^{13}C NMR of 2-chloroquinazolin-4-amine (I-5a)

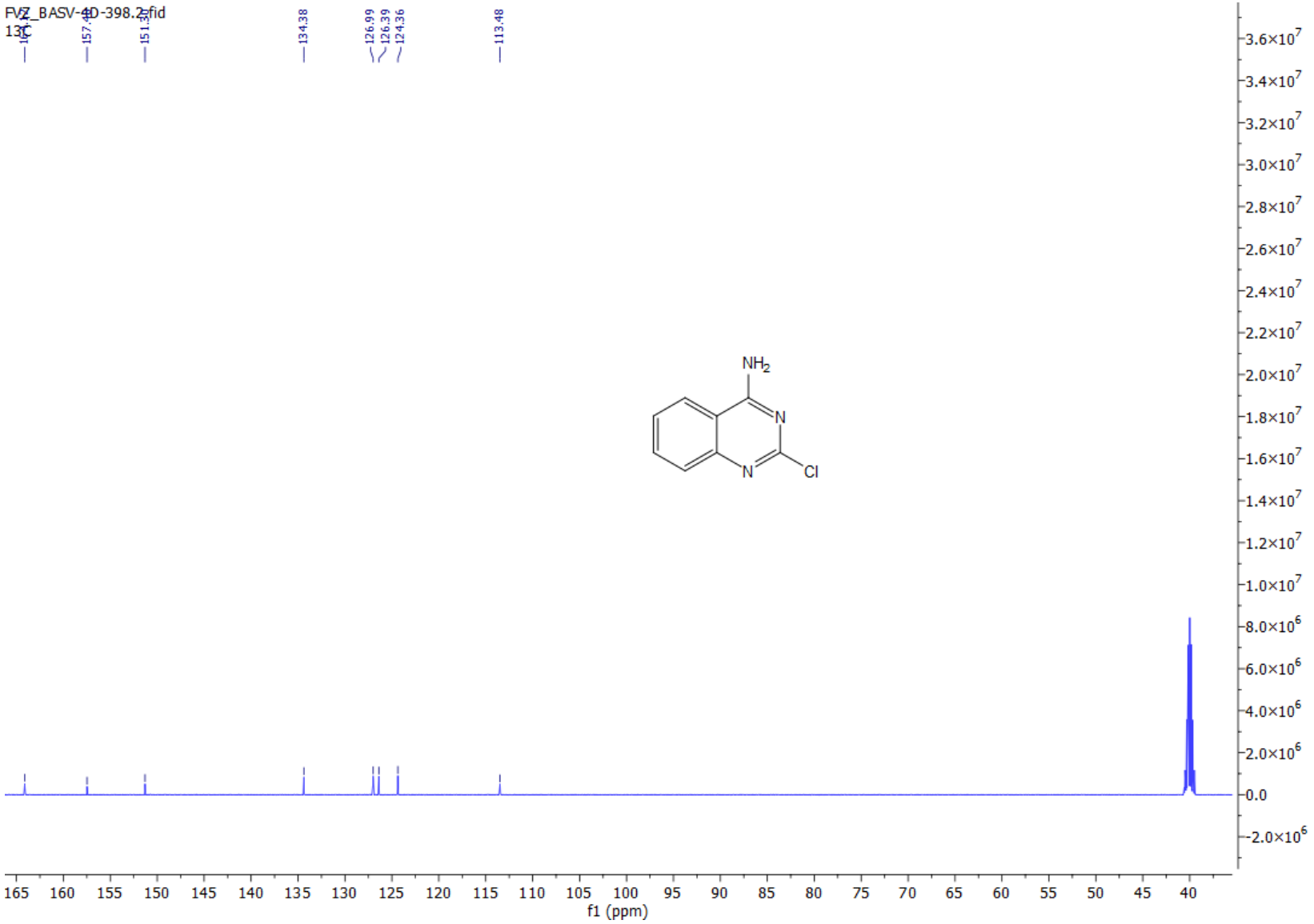


Fig. S4. ^{1}H NMR of 2-chloro-*N*-methylquinazolin-4-amine (I-5b)

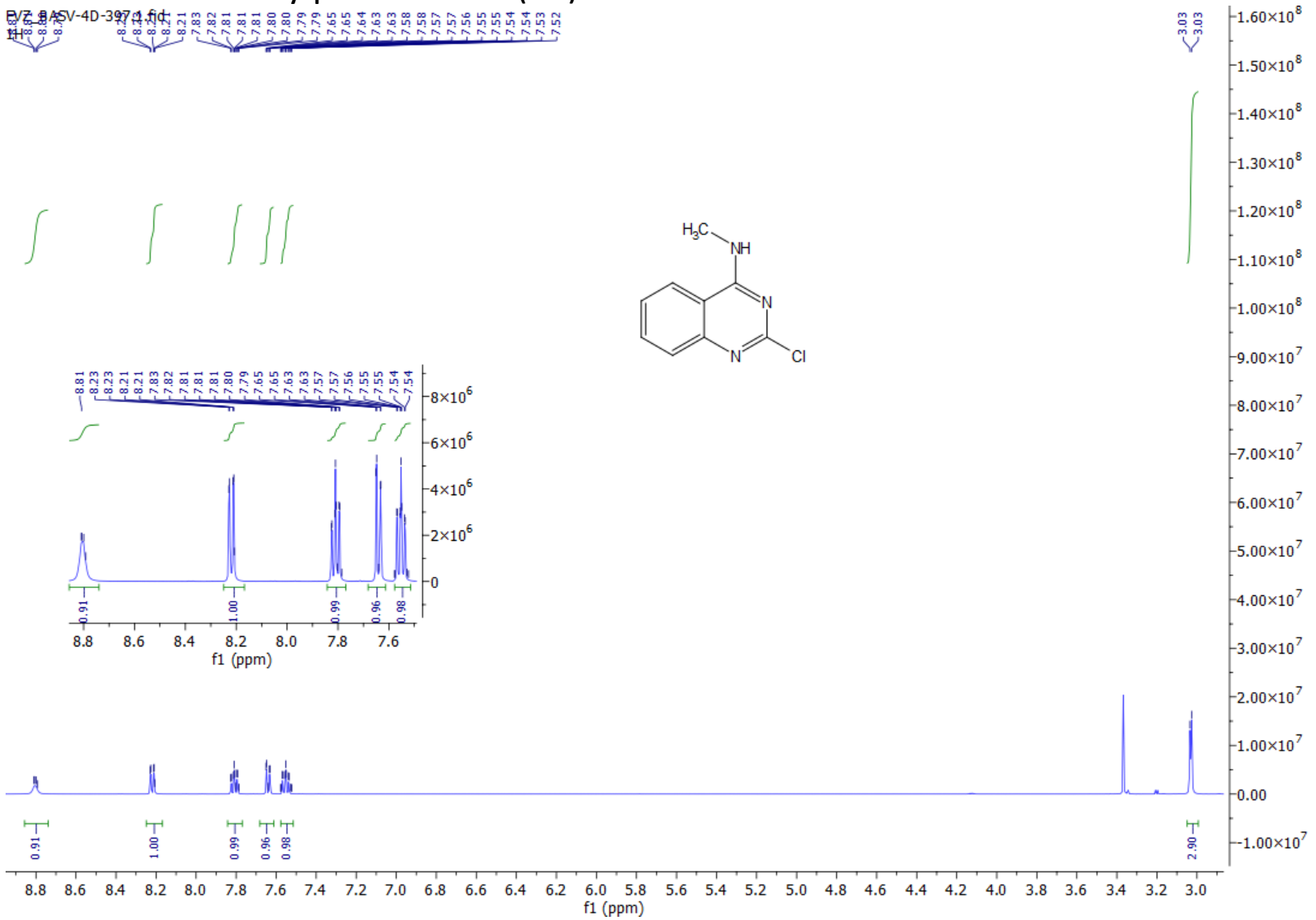


Fig. S5. ^{13}C NMR of 2-chloro-*N*-methylquinazolin-4-amine (I-5b)

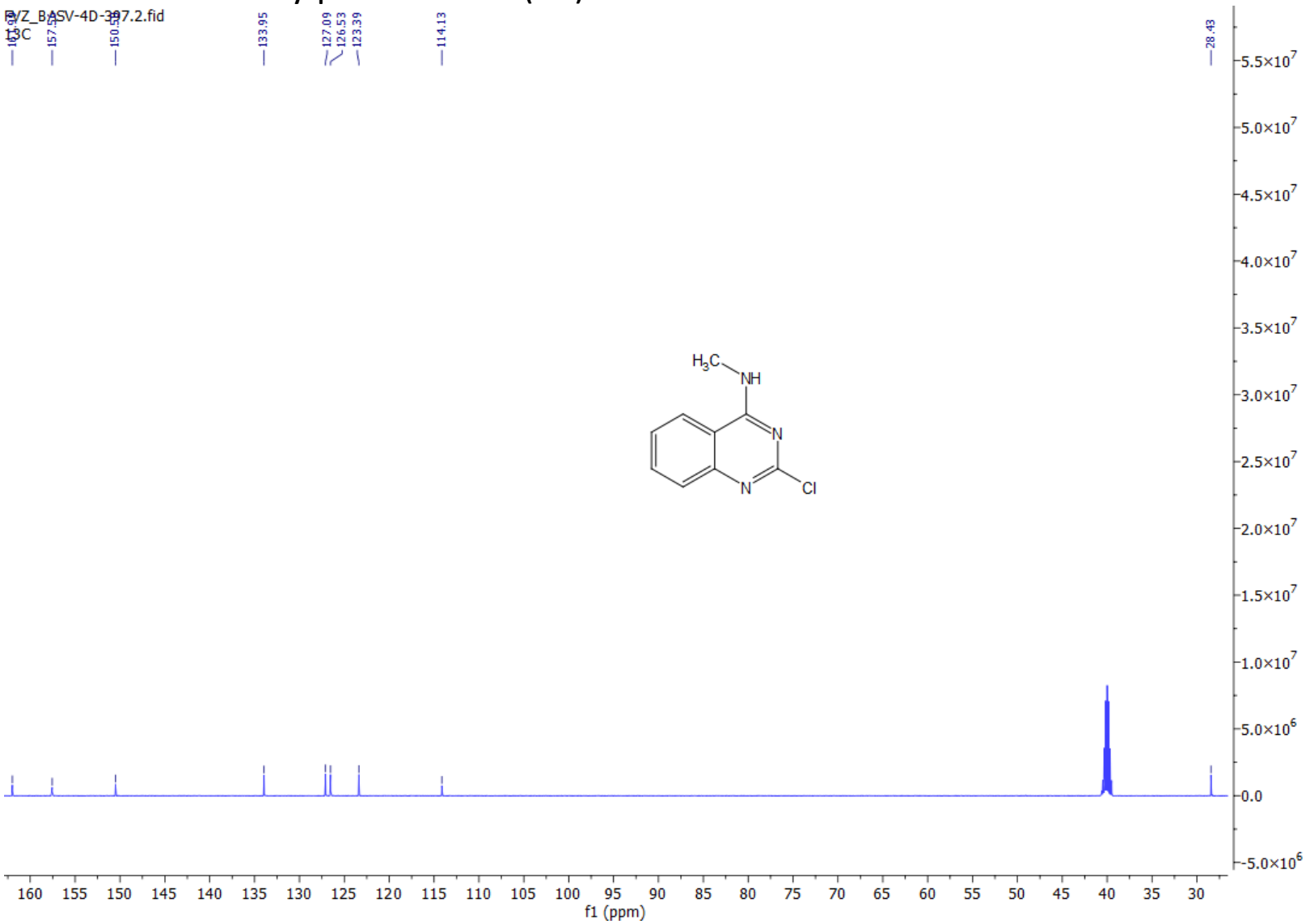


Fig. S6. ^{1}H NMR of 2-chloro-*N*-ethylquinazolin-4-amine (I-5c)

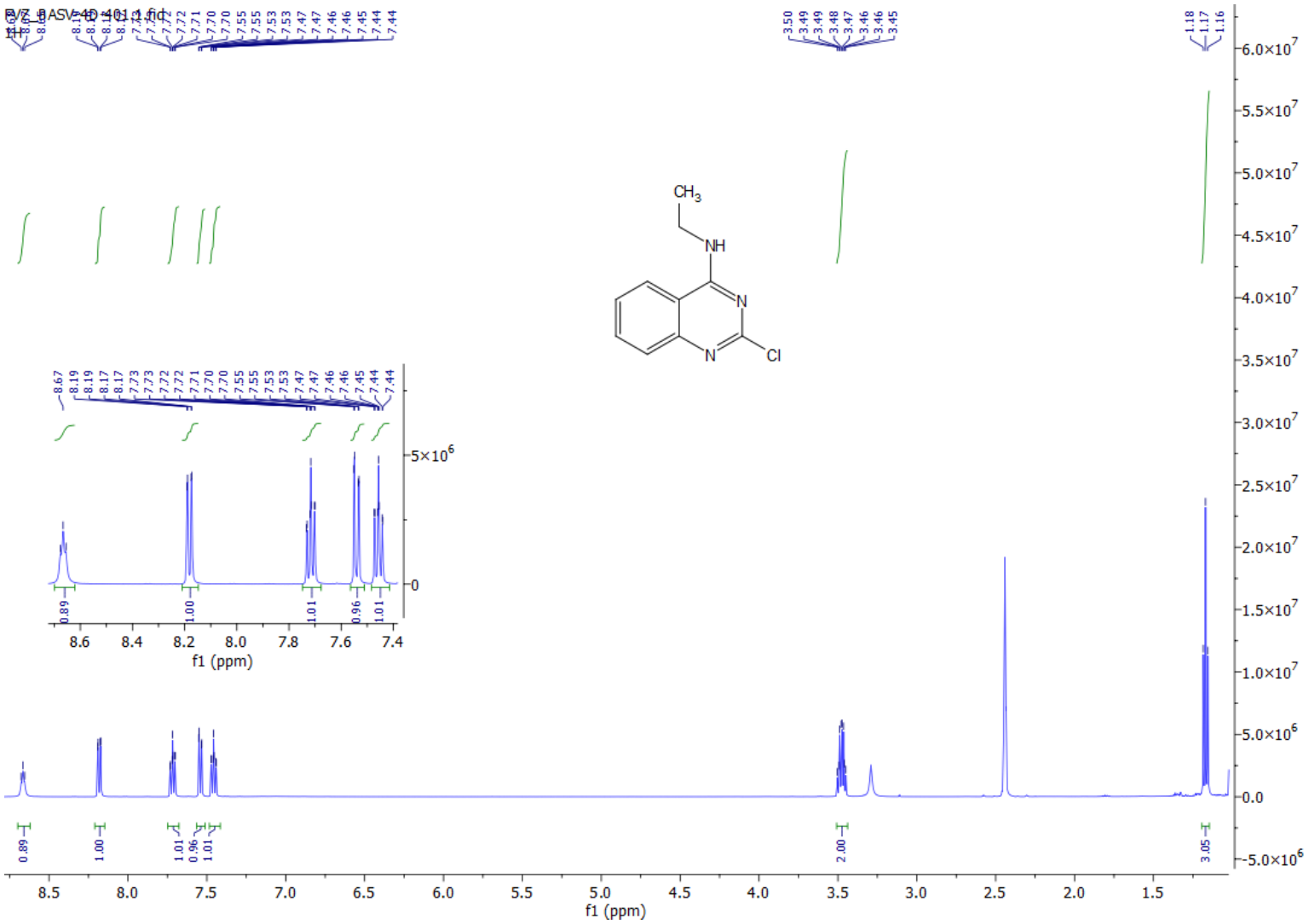


Fig. S7. ^{13}C NMR of 2-chloro-*N*-ethylquinazolin-4-amine (I-5c)

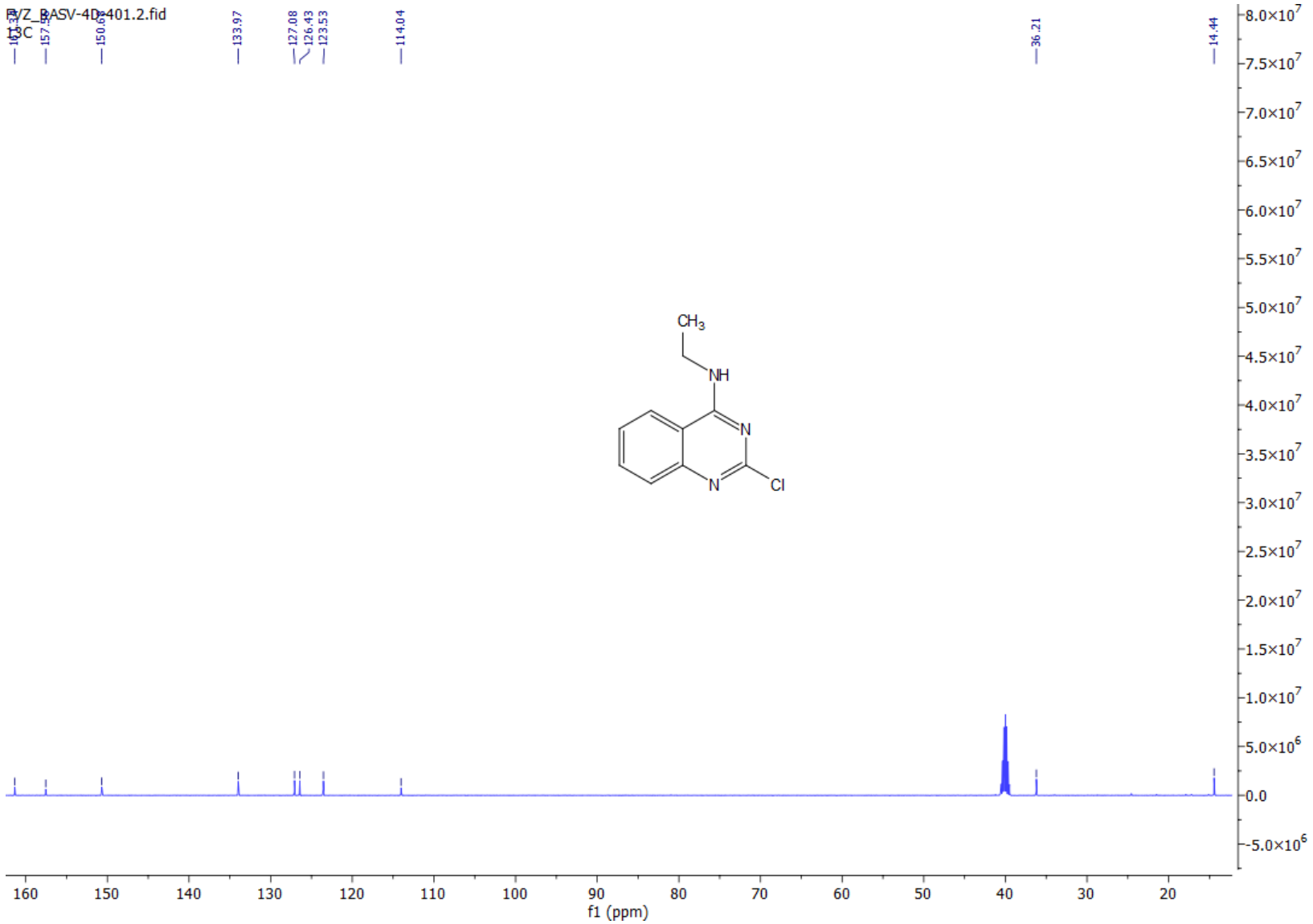


Fig. S8. ^{1}H NMR of 2-chloro-*N*-(propan-2-yl)quinazolin-4-amine (I-5d)

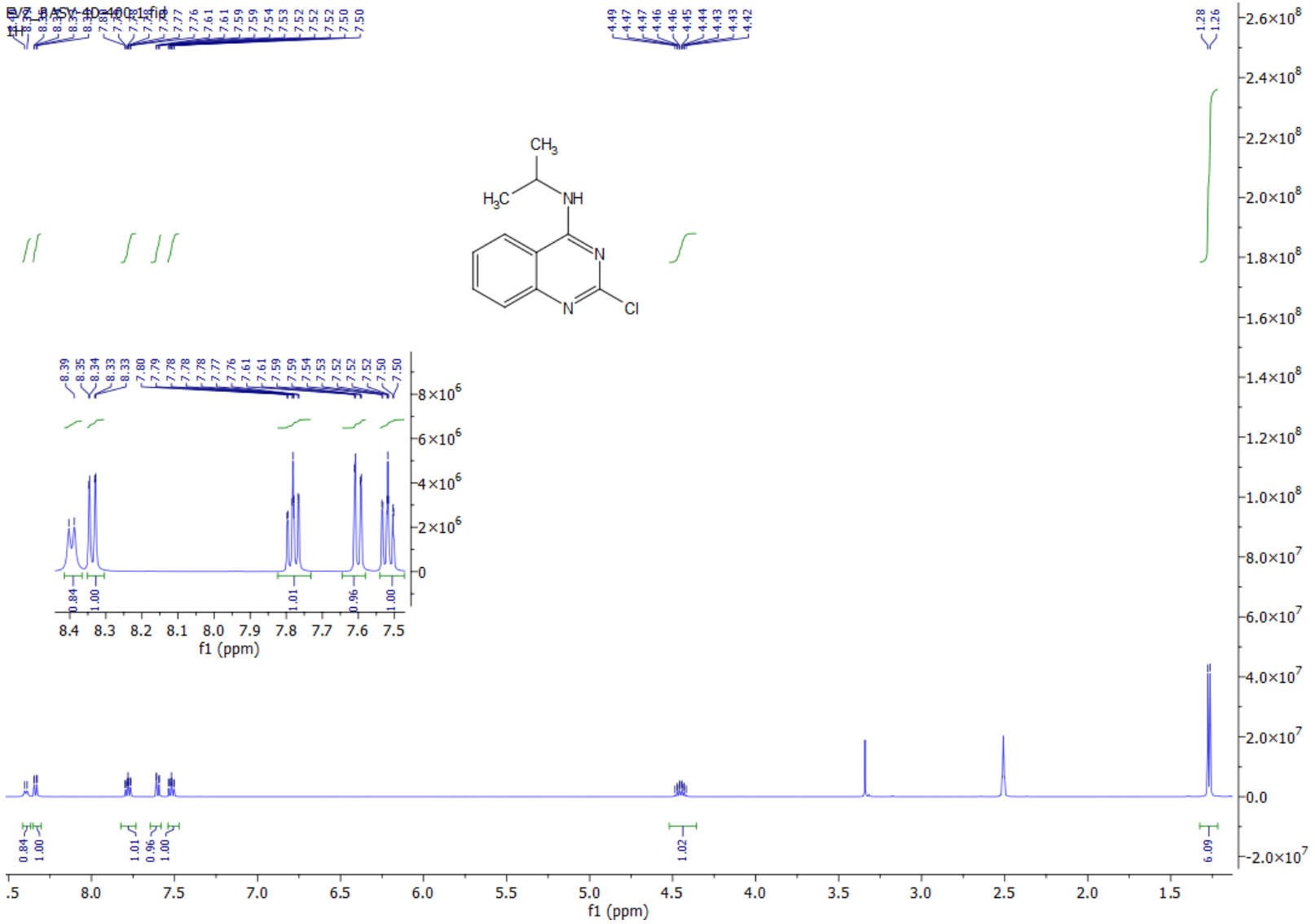


Fig. S9. ^{13}C NMR of 2-chloro-*N*-(propan-2-yl)quinazolin-4-amine (I-5d)

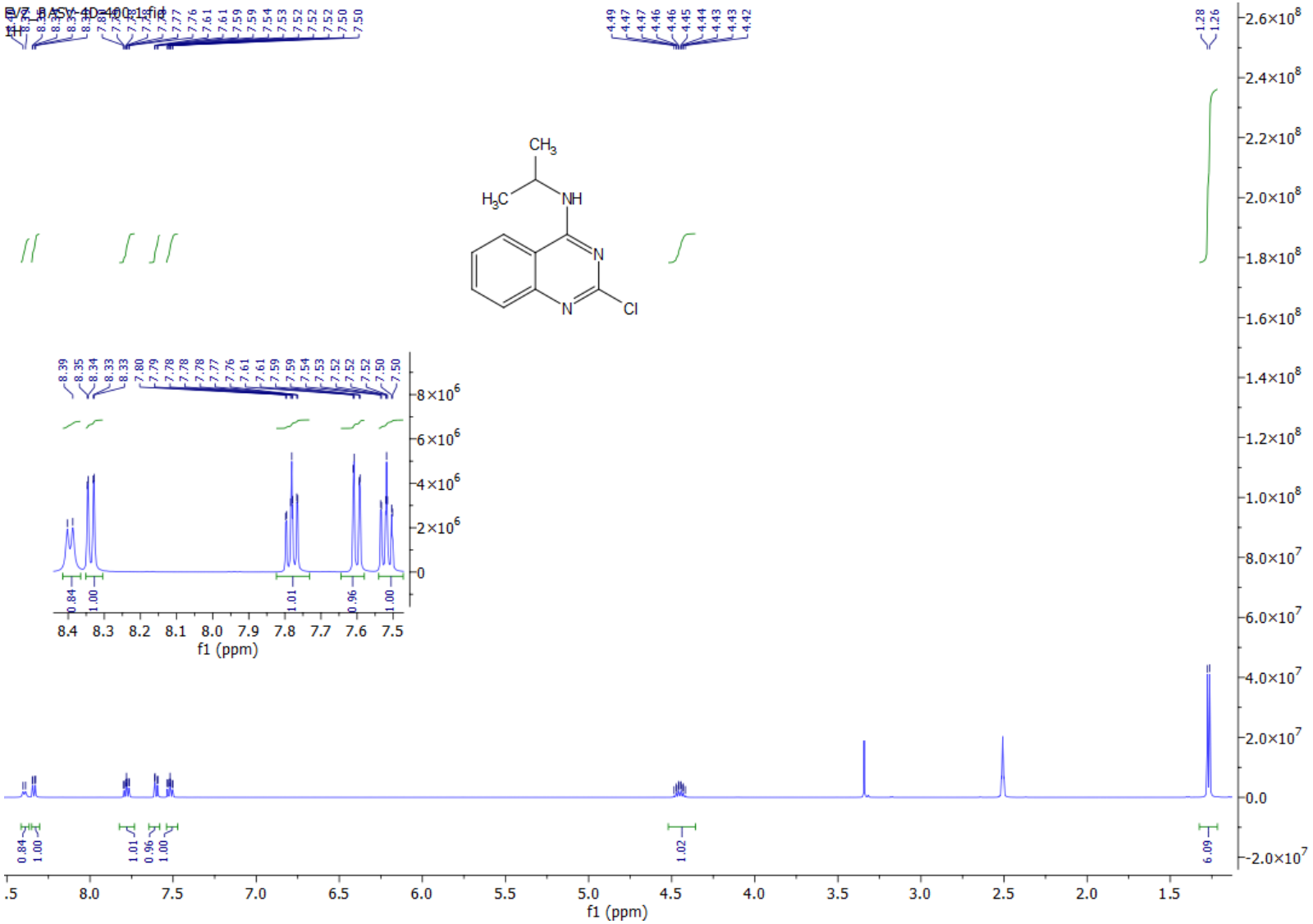


Fig. S10. ^{1}H NMR of *N*-butyl-2-chloroquinazolin-4-amine (I-5e)

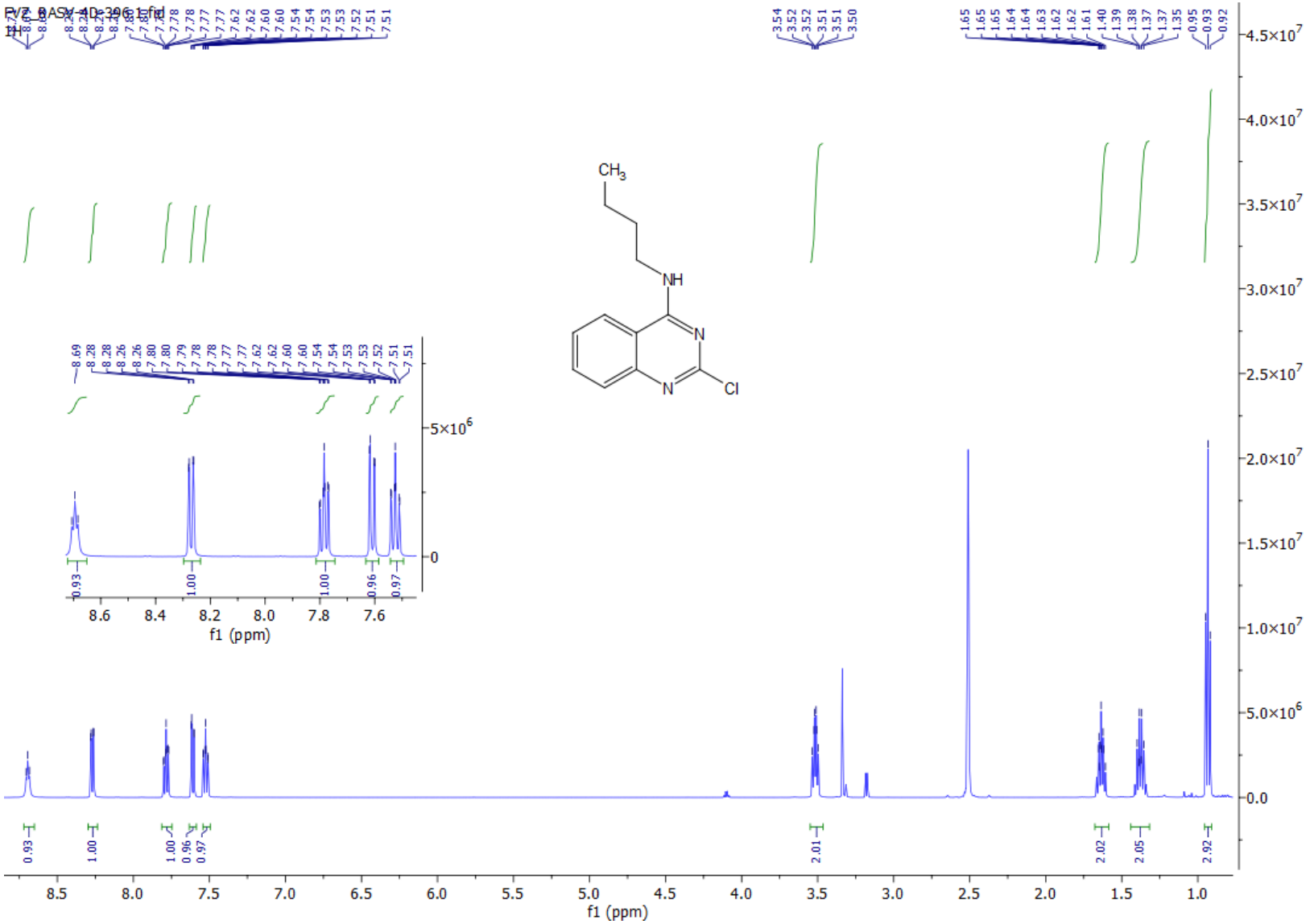


Fig. S11. ^{13}C NMR of *N*-butyl-2-chloroquinazolin-4-amine (I-5e)

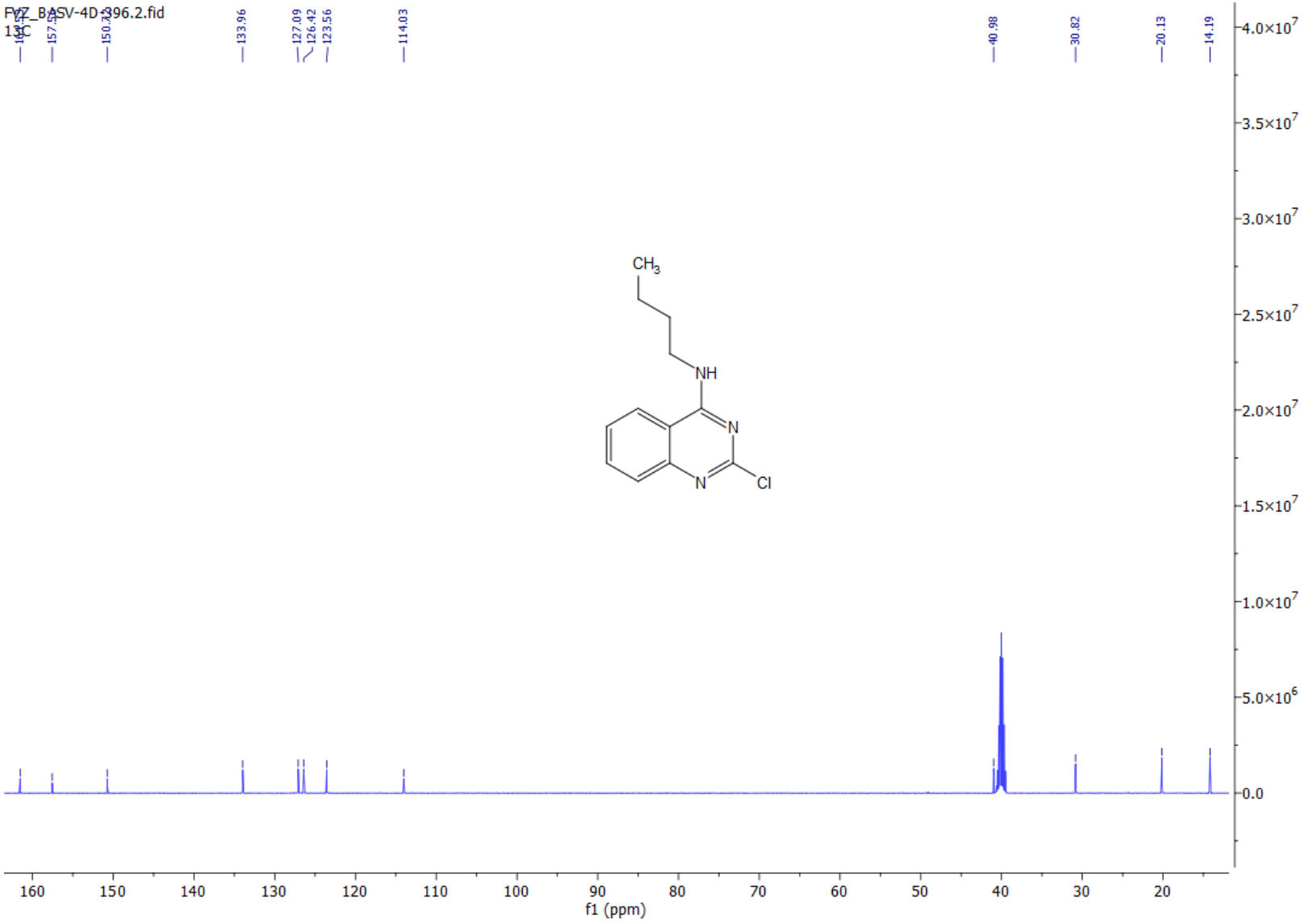


Fig. S12. ^{1}H NMR of 2-chloro-*N*-(2-methoxyethyl)quinazolin-4-amine (I-5f)

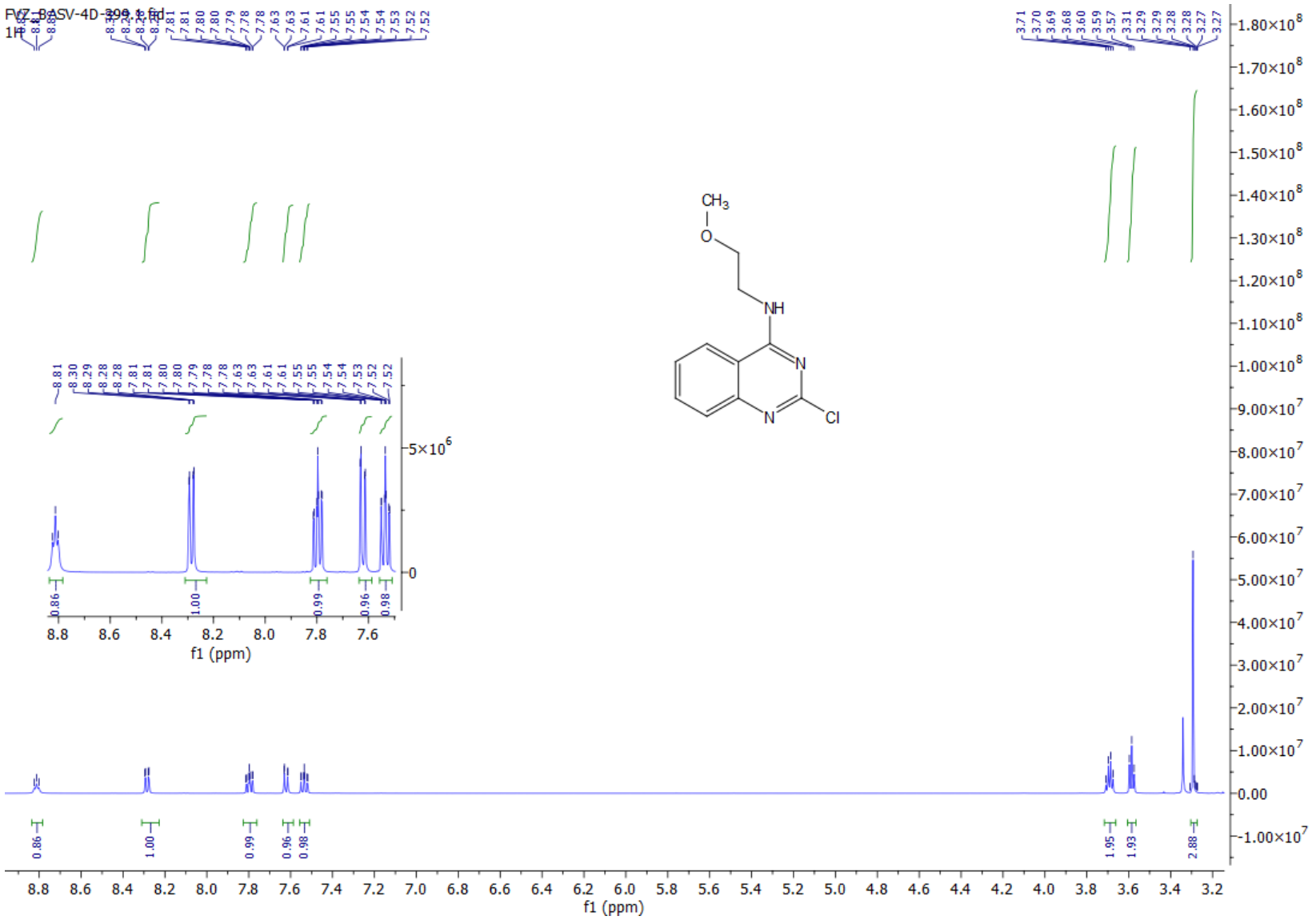


Fig. S13. ^{13}C NMR of 2-chloro-*N*-(2-methoxyethyl)quinazolin-4-amine (I-5f)

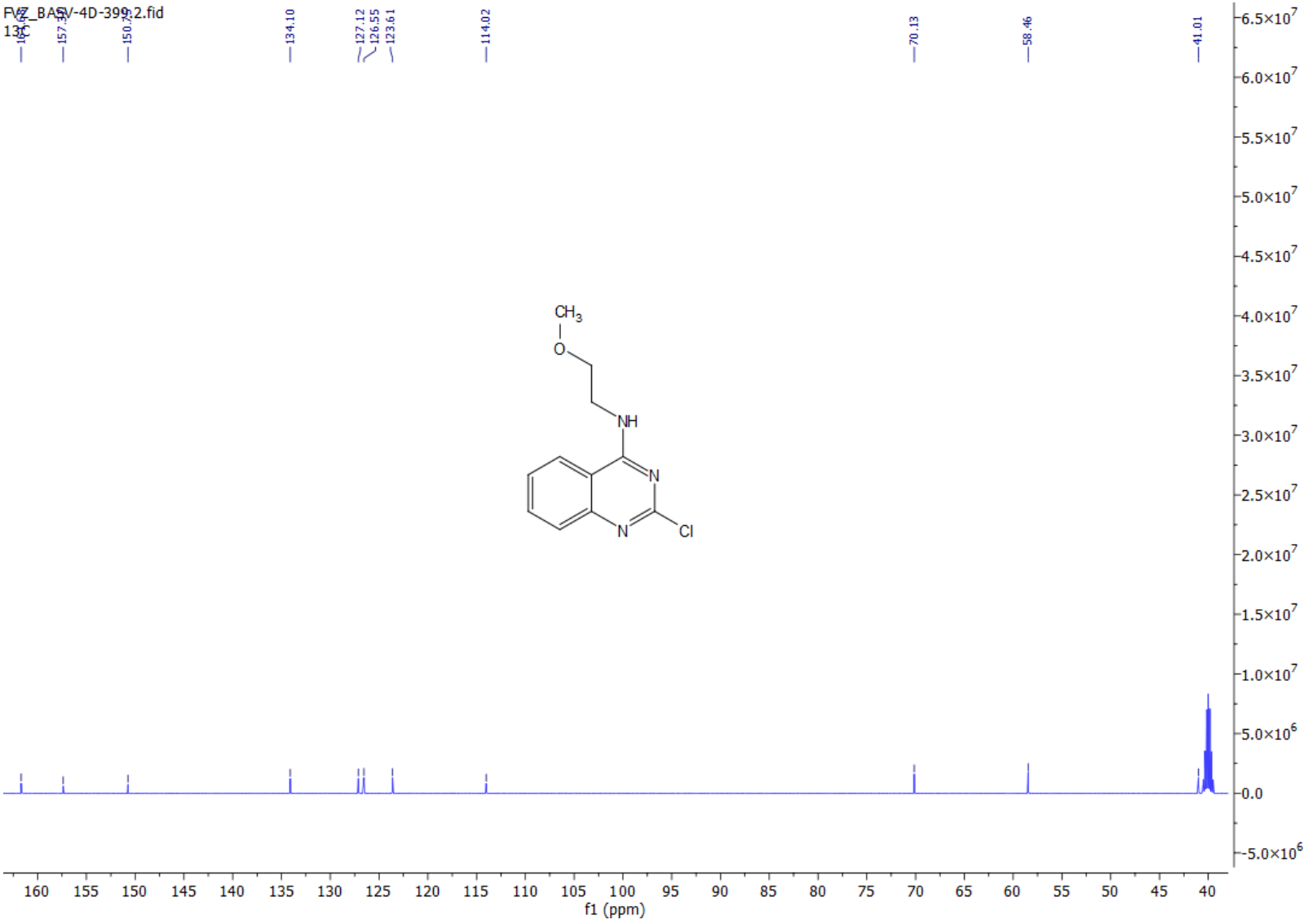


Fig. S14. ^{1}H NMR of 2,7-dichloroquinazolin-4-amine (II-5a)

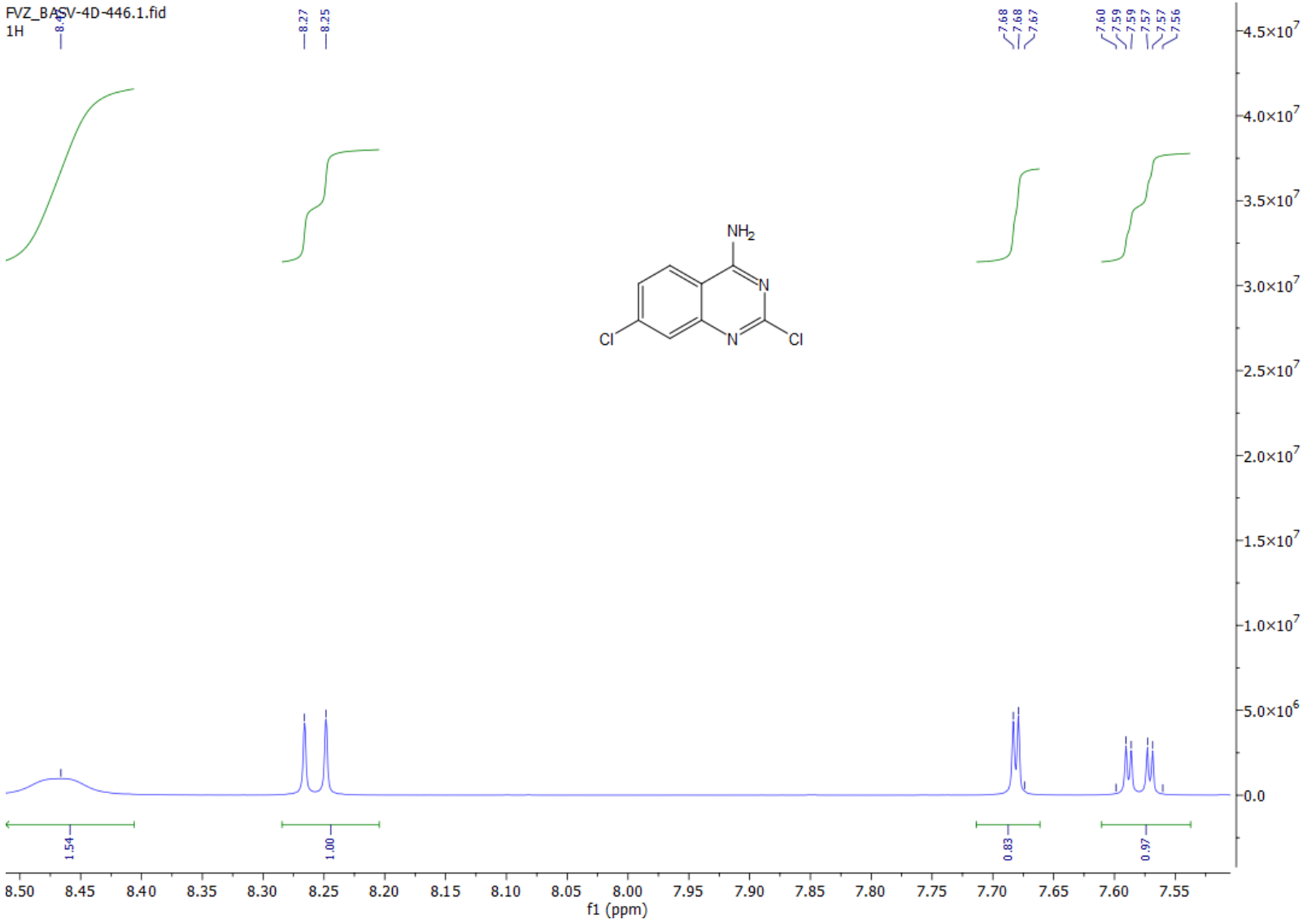


Fig. S15. ^{13}C NMR of 2,7-dichloroquinazolin-4-amine (II-5a)

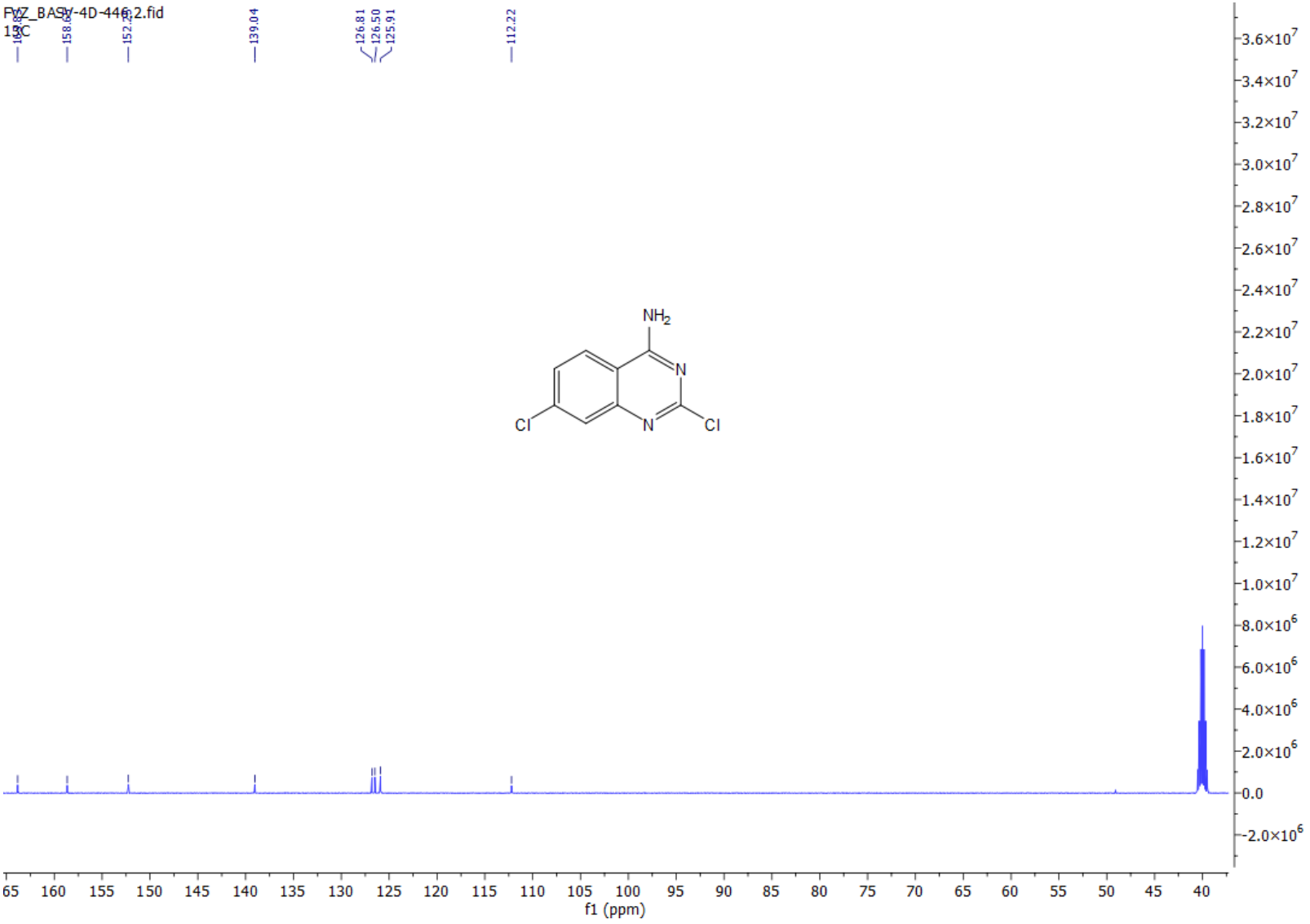


Fig. S16. ^{1}H NMR of 2,7-dichloro-*N*-methylquinazolin-4-amine (II-5b)

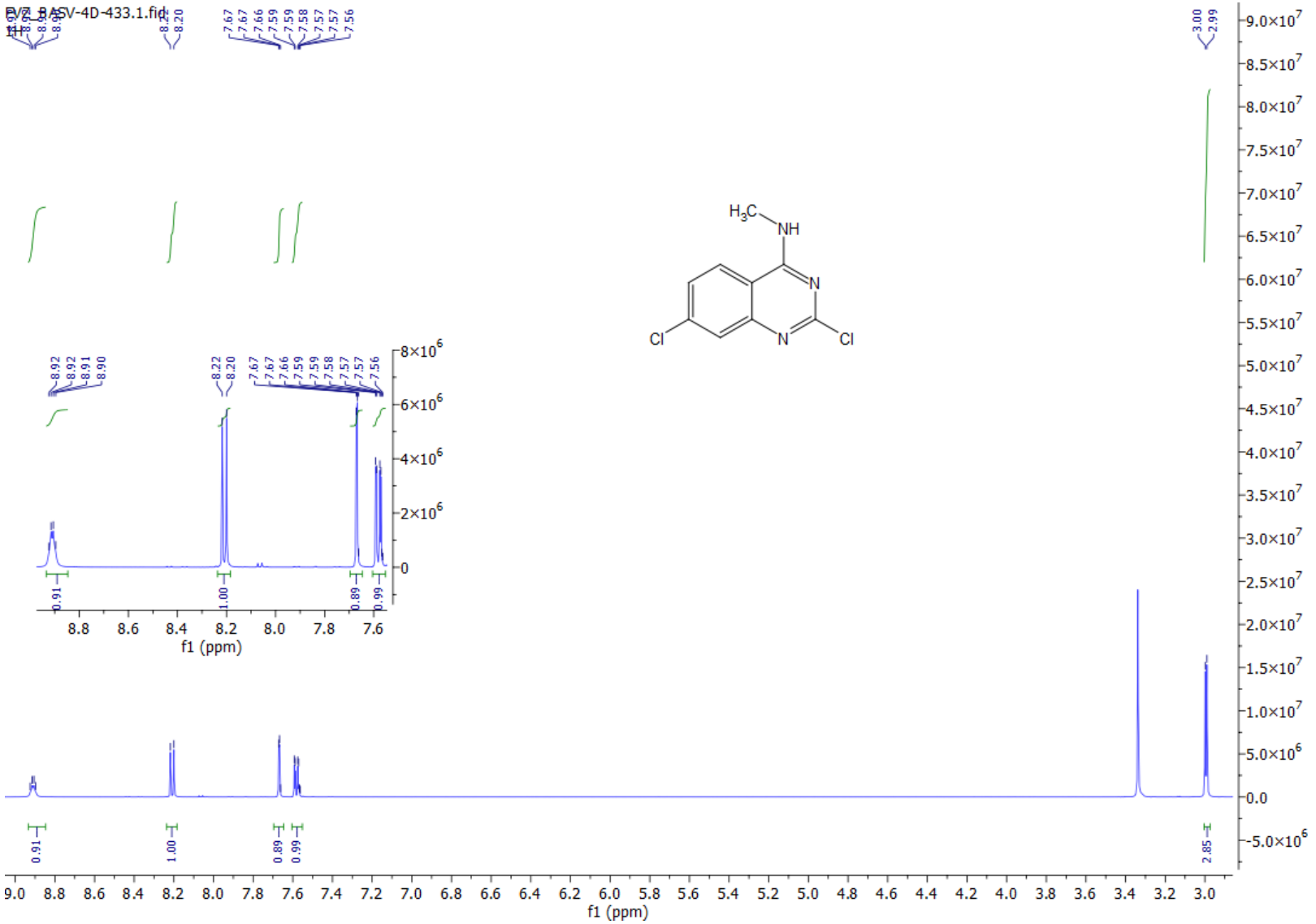


Fig. S17. ^{13}C NMR of 2,7-dichloro-*N*-methylquinazolin-4-amine (II-5b)

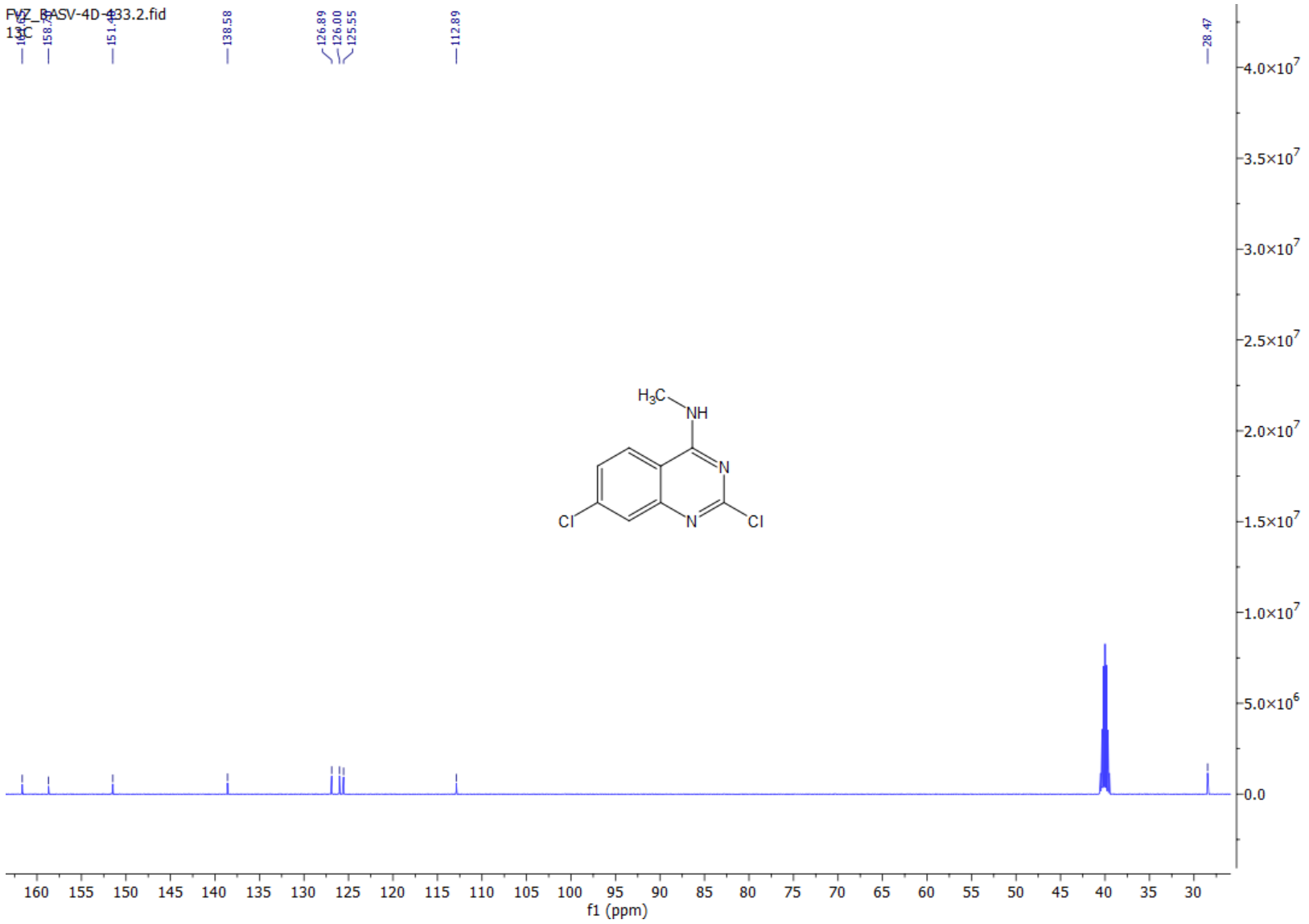


Fig. S18. ^{1}H NMR of 2,7-dichloro-*N*-ethylquinazolin-4-amine (II-5c)

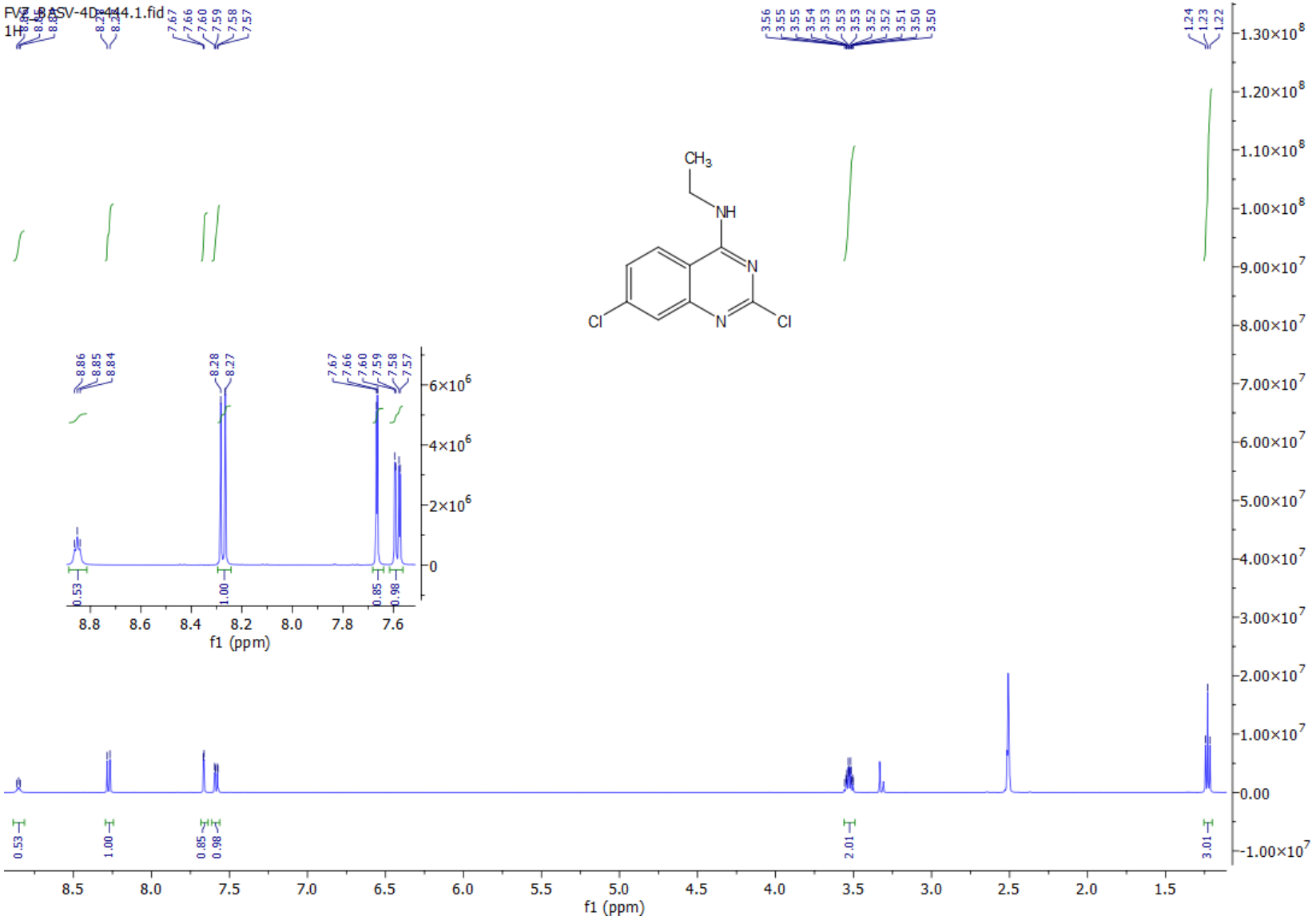


Fig. S19. ^{13}C NMR of 2,7-dichloro-*N*-ethylquinazolin-4-amine (II-5c)

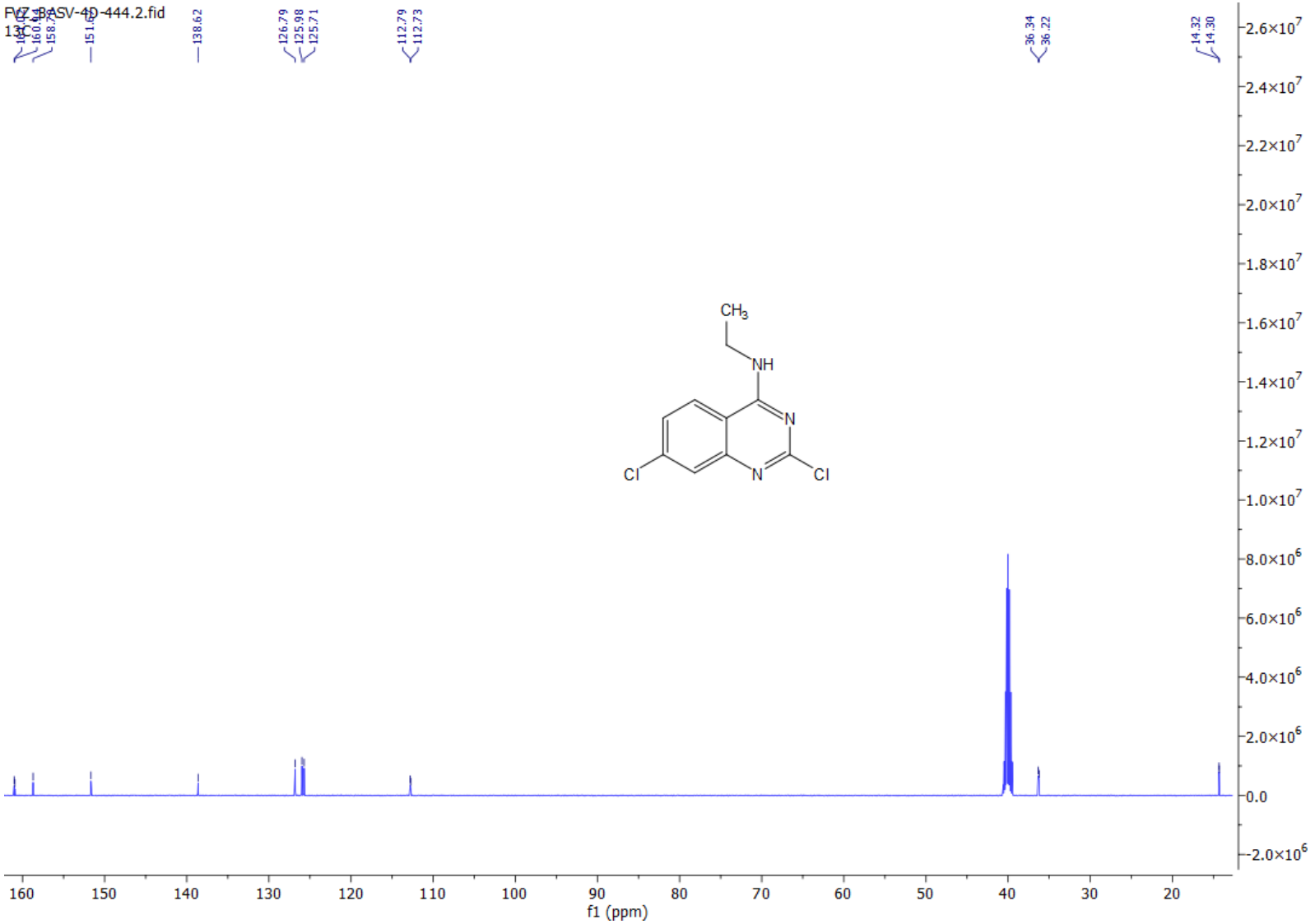


Fig. S20. ^{1}H NMR of 2,7-dichloro-*N*-(propan-2-yl)quinazolin-4-amine (II-5d)

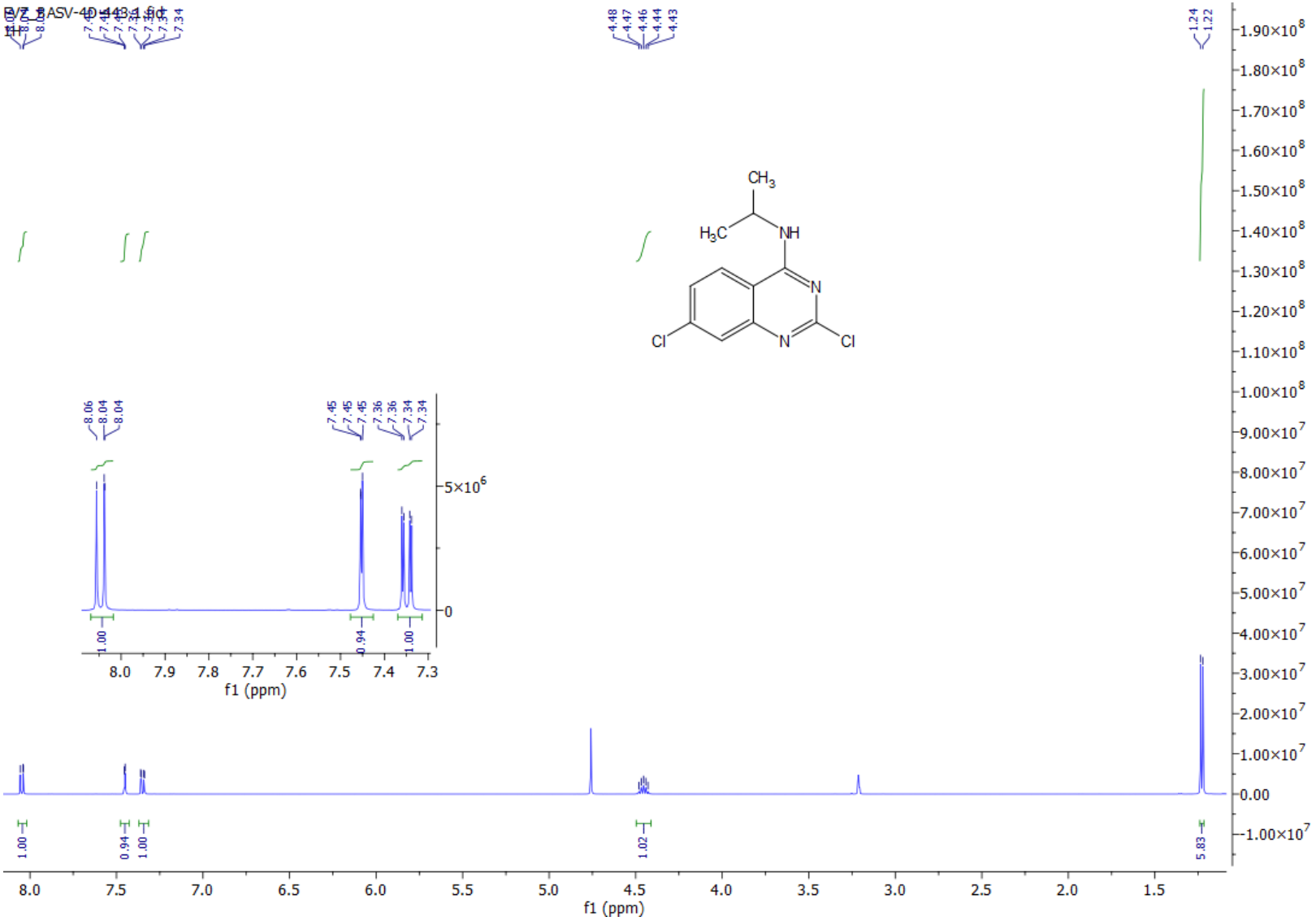


Fig. S21. ^{13}C NMR of 2,7-dichloro-*N*-(propan-2-yl)quinazolin-4-amine (II-5d)

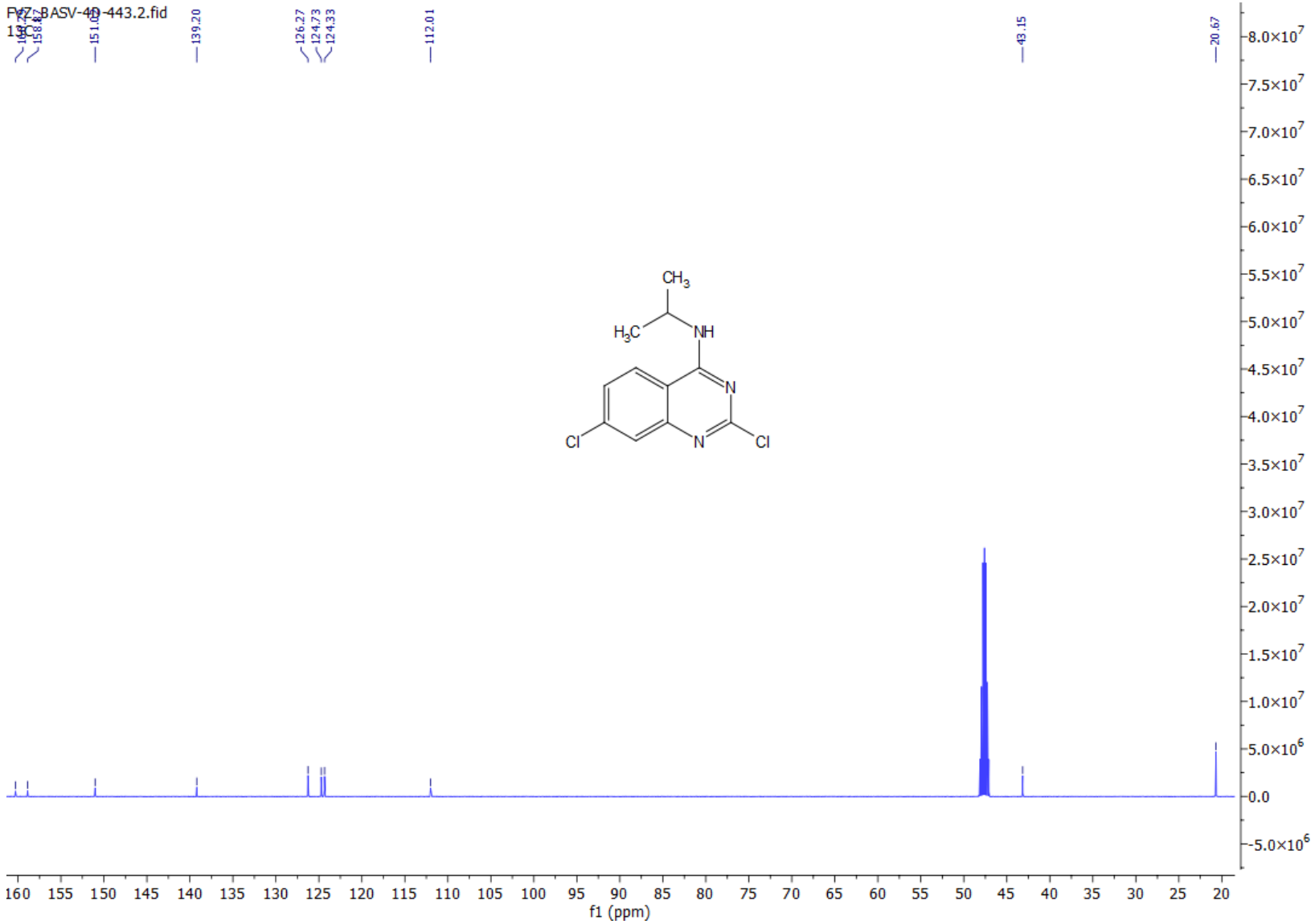


Fig. S22. ^{1}H NMR of *N*-butyl-2,7-dichloroquinazolin-4-amine (II-5e)

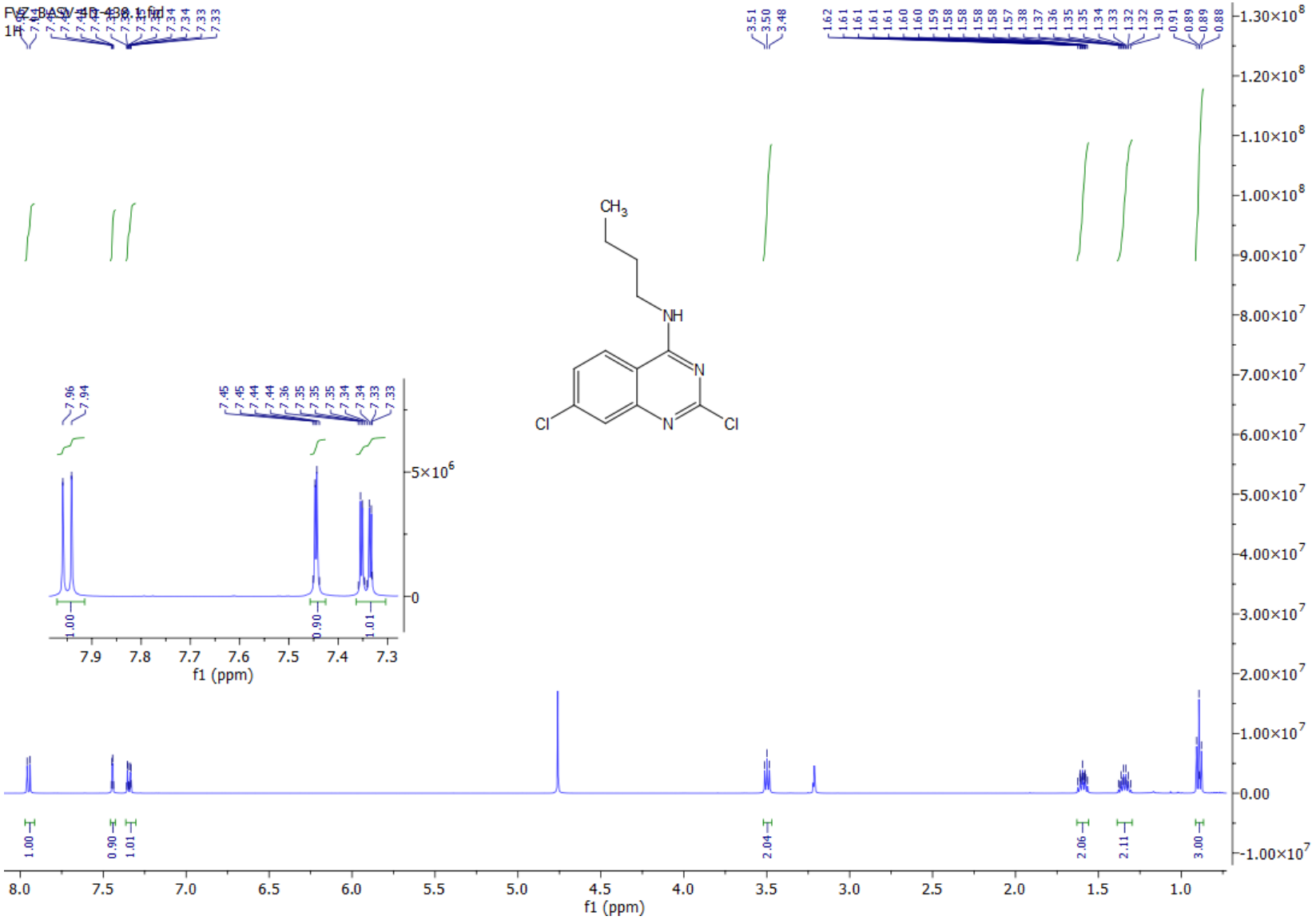


Fig. S23. ^{13}C NMR of *N*-butyl-2,7-dichloroquinazolin-4-amine (II-5e)

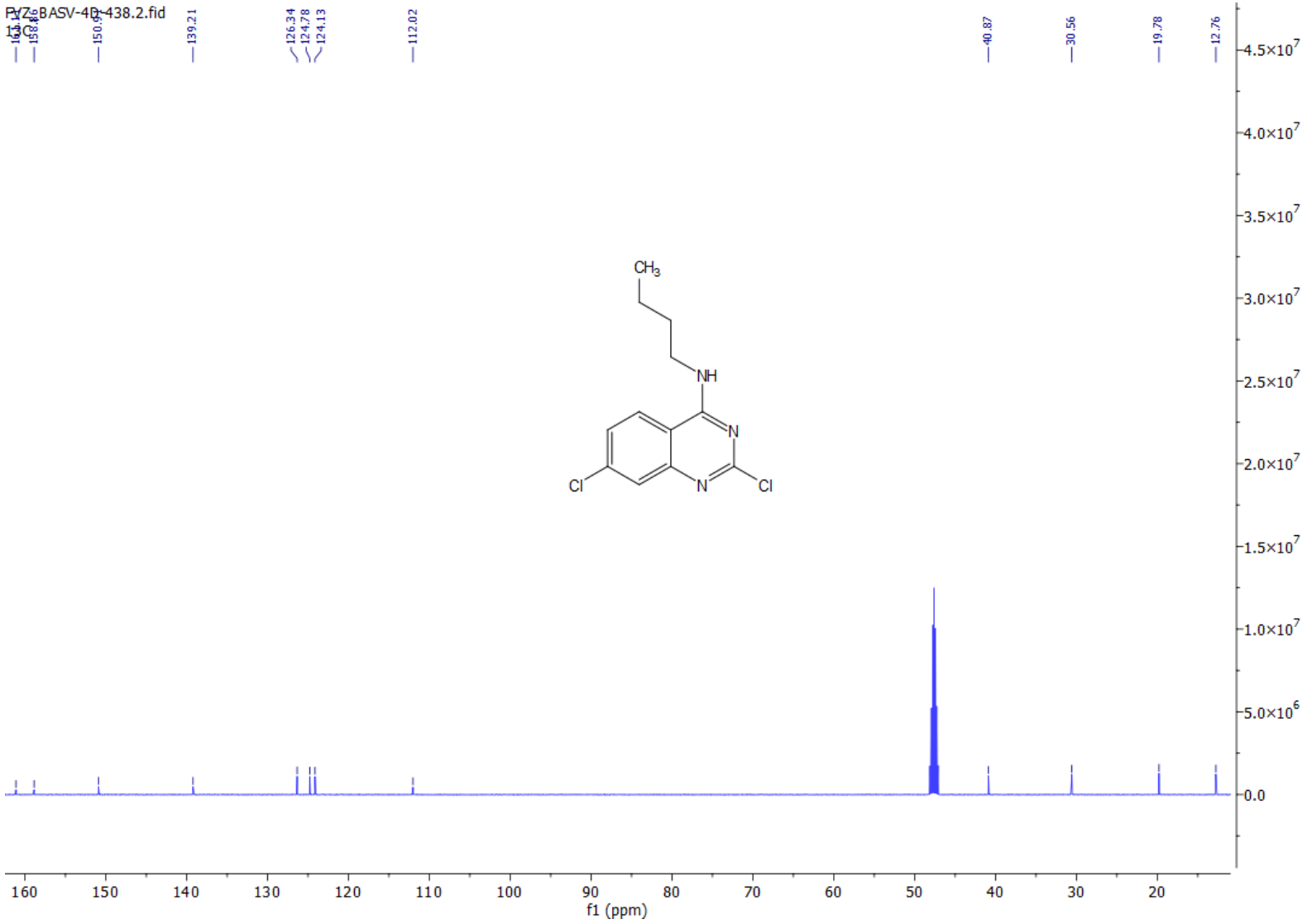


Fig. S24. ^{1}H NMR of 2,7-dichloro-*N*-(2-methoxyethyl)quinazolin-4-amine (II-5f)

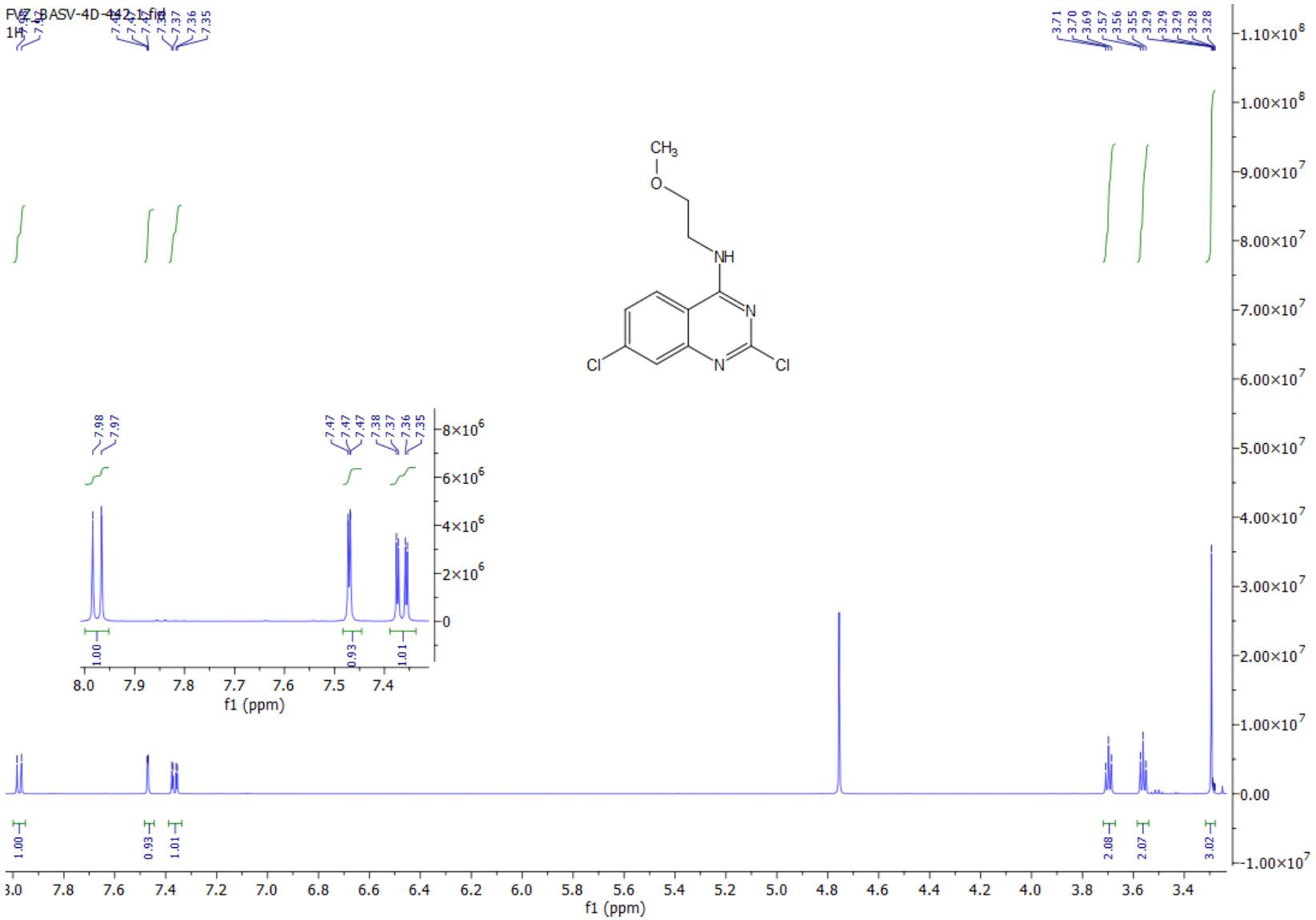


Fig. S25. ^{13}C NMR of 2,7-dichloro-*N*-(2-methoxyethyl)quinazolin-4-amine (II-5f)

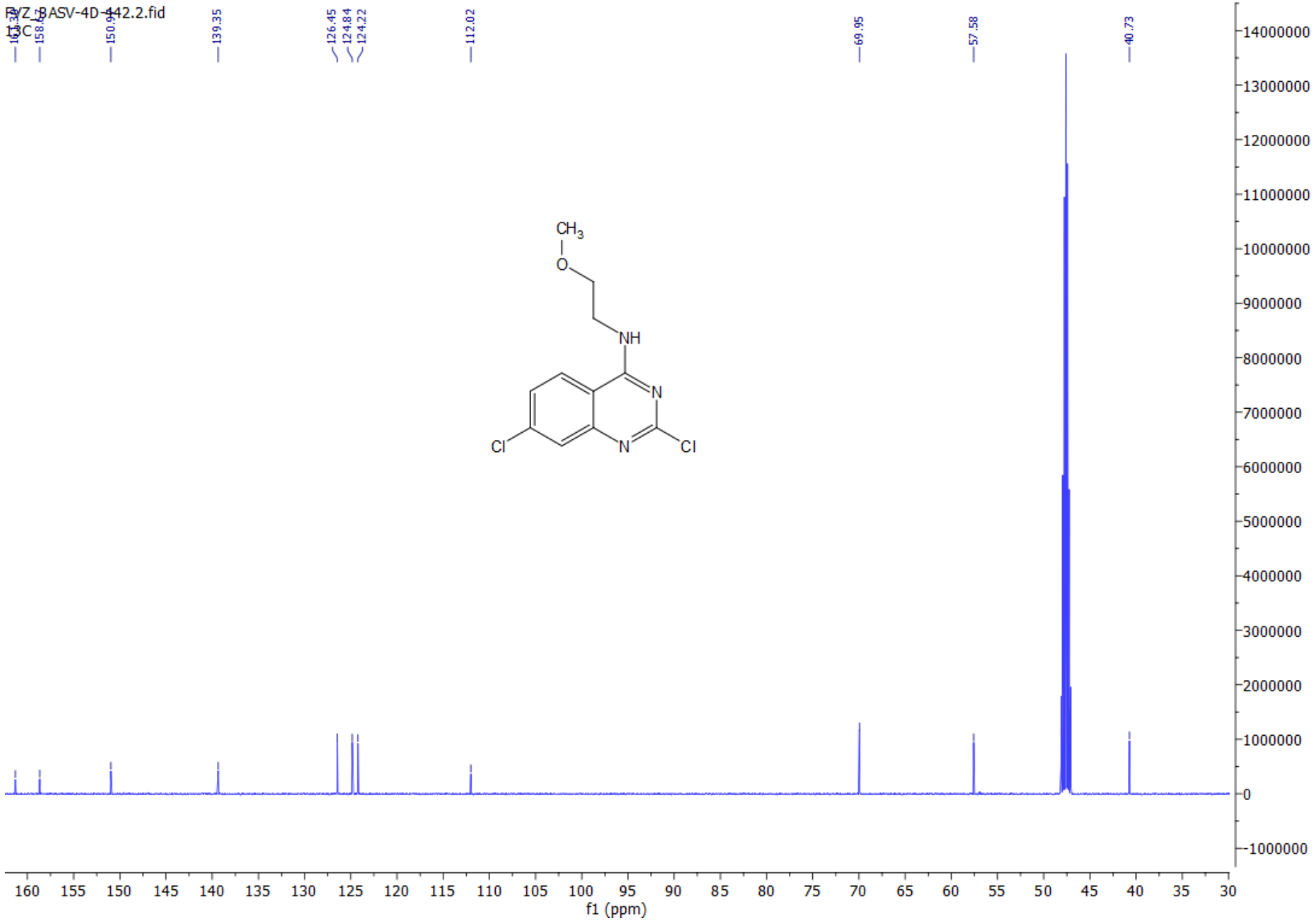


Fig. S26. ^{1}H NMR of 2,7-dichloro-*N*-cyclohexylquinazolin-4-amine (II-5h)

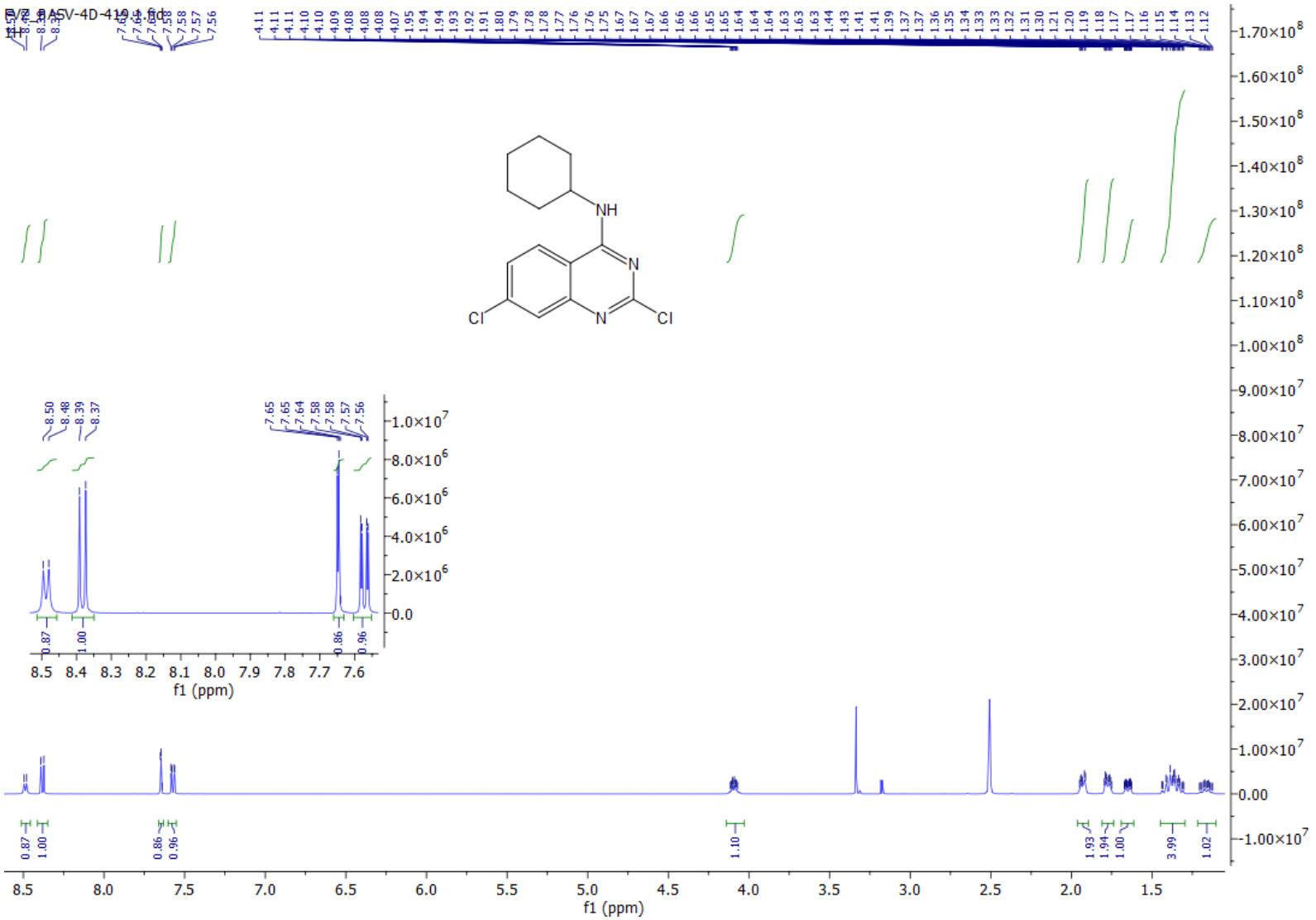


Fig. S27. ^{13}C NMR of 2,7-dichloro-*N*-cyclohexylquinazolin-4-amine (II-5h)

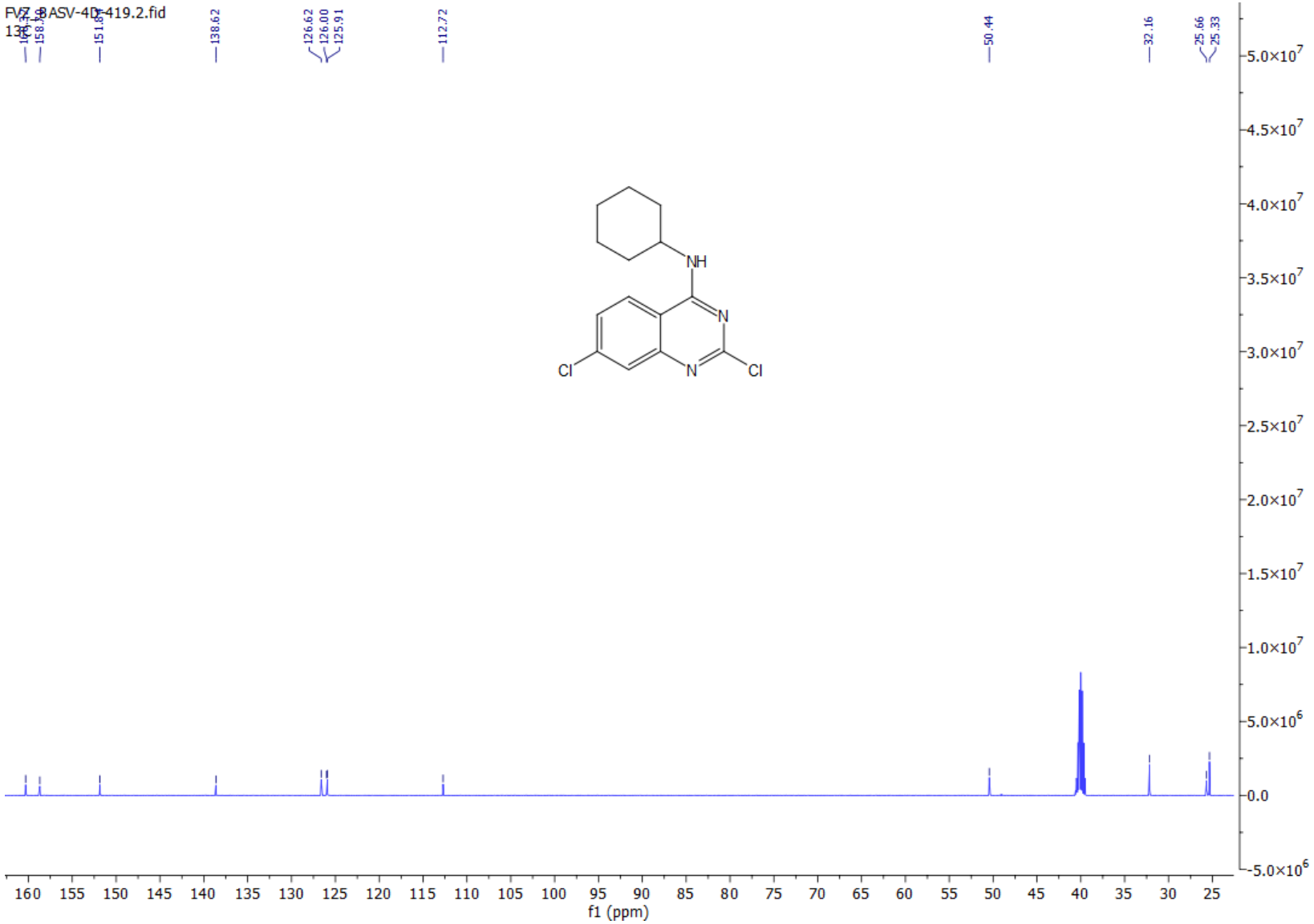


Fig. S28. ^{1}H NMR of 2-chloro-6-methoxyquinazolin-4-amine (III-5a)

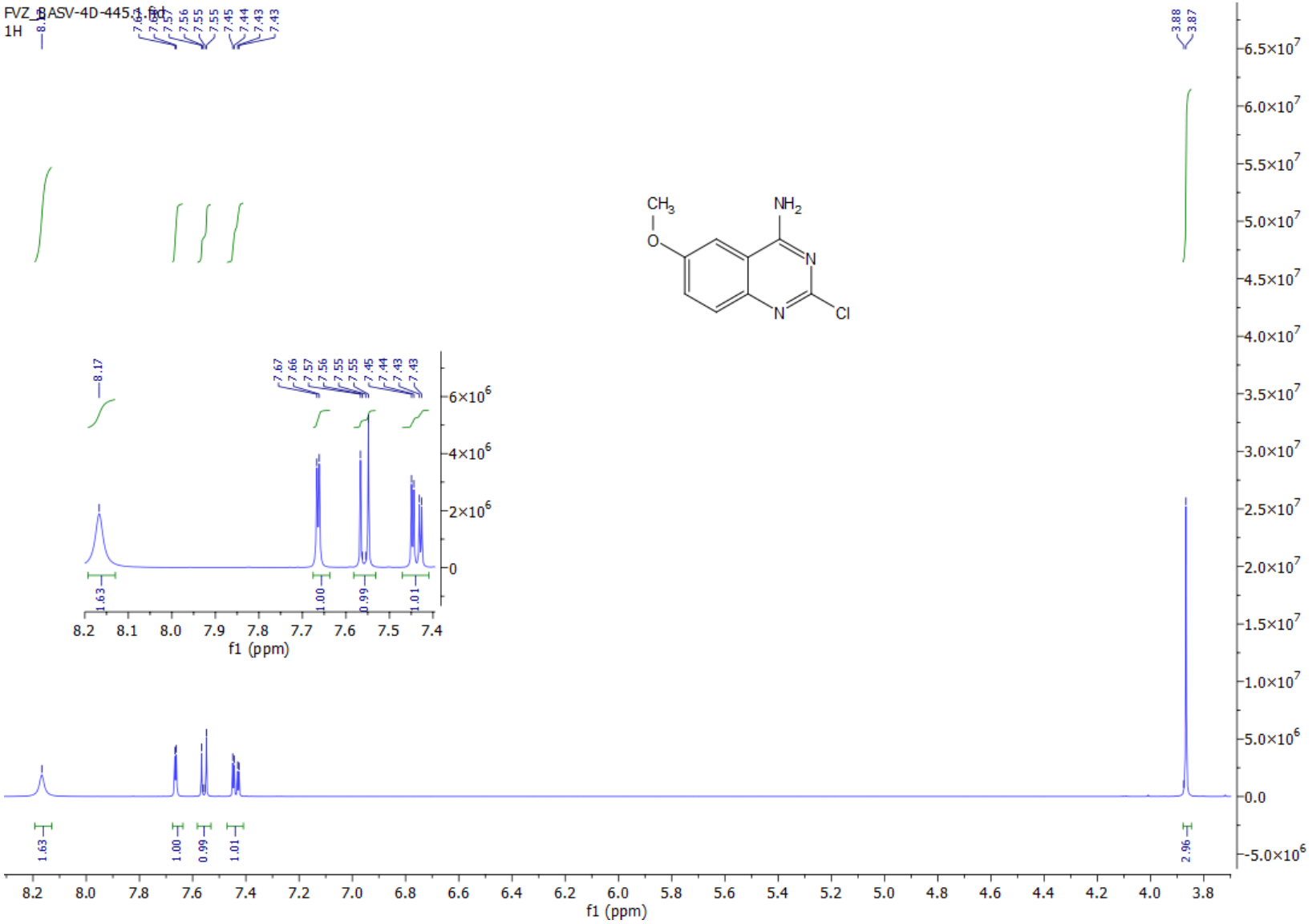


Fig. S29. ^{13}C NMR of 2-chloro-6-methoxyquinazolin-4-amine (III-5a)

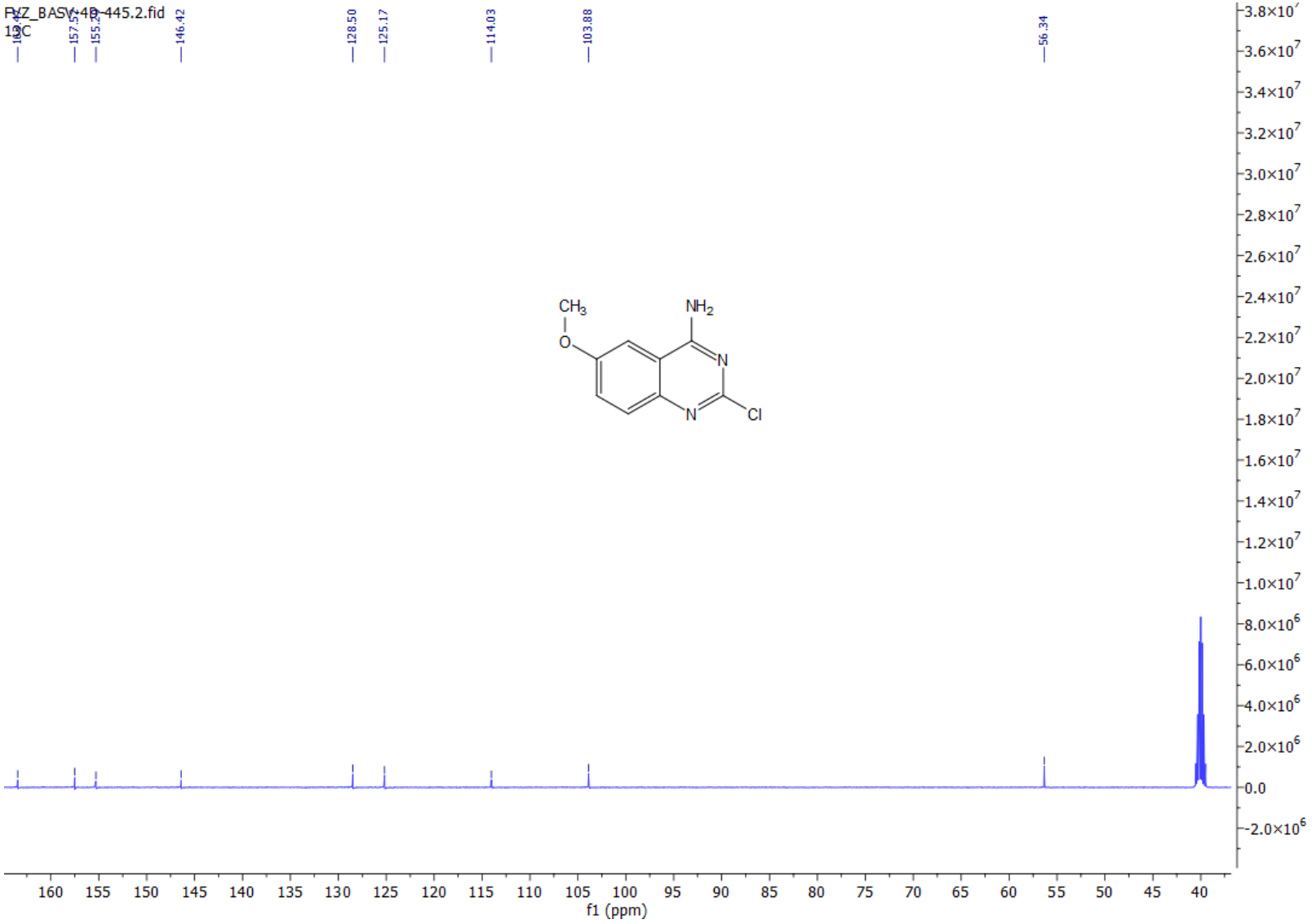


Fig. S30. ^{1}H NMR of 2-chloro-6-methoxy-*N*-methylquinazolin-4-amine (III-5b)

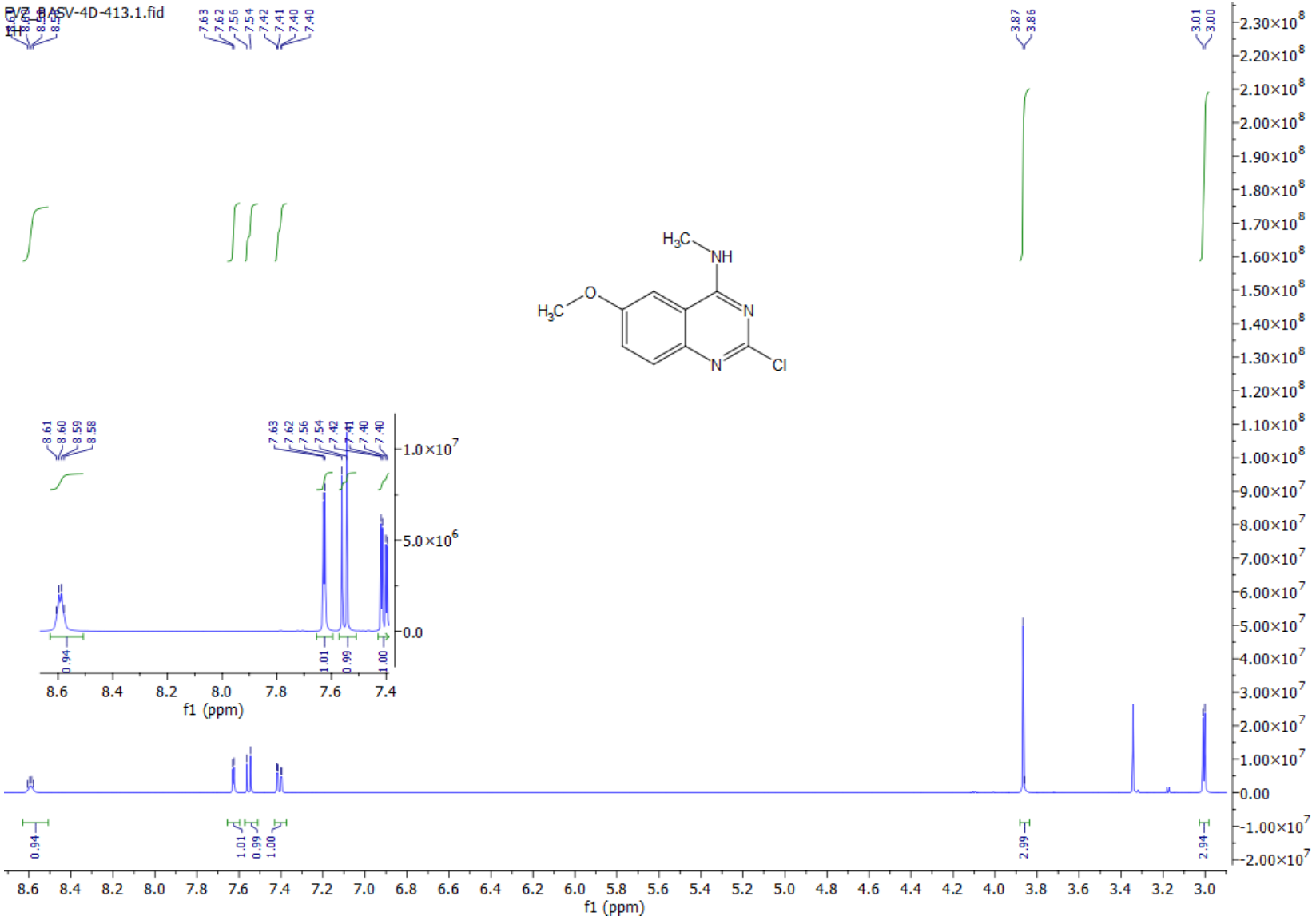


Fig. S31. ^{13}C NMR of 2-chloro-6-methoxy-*N*-methylquinazolin-4-amine (III-5b)

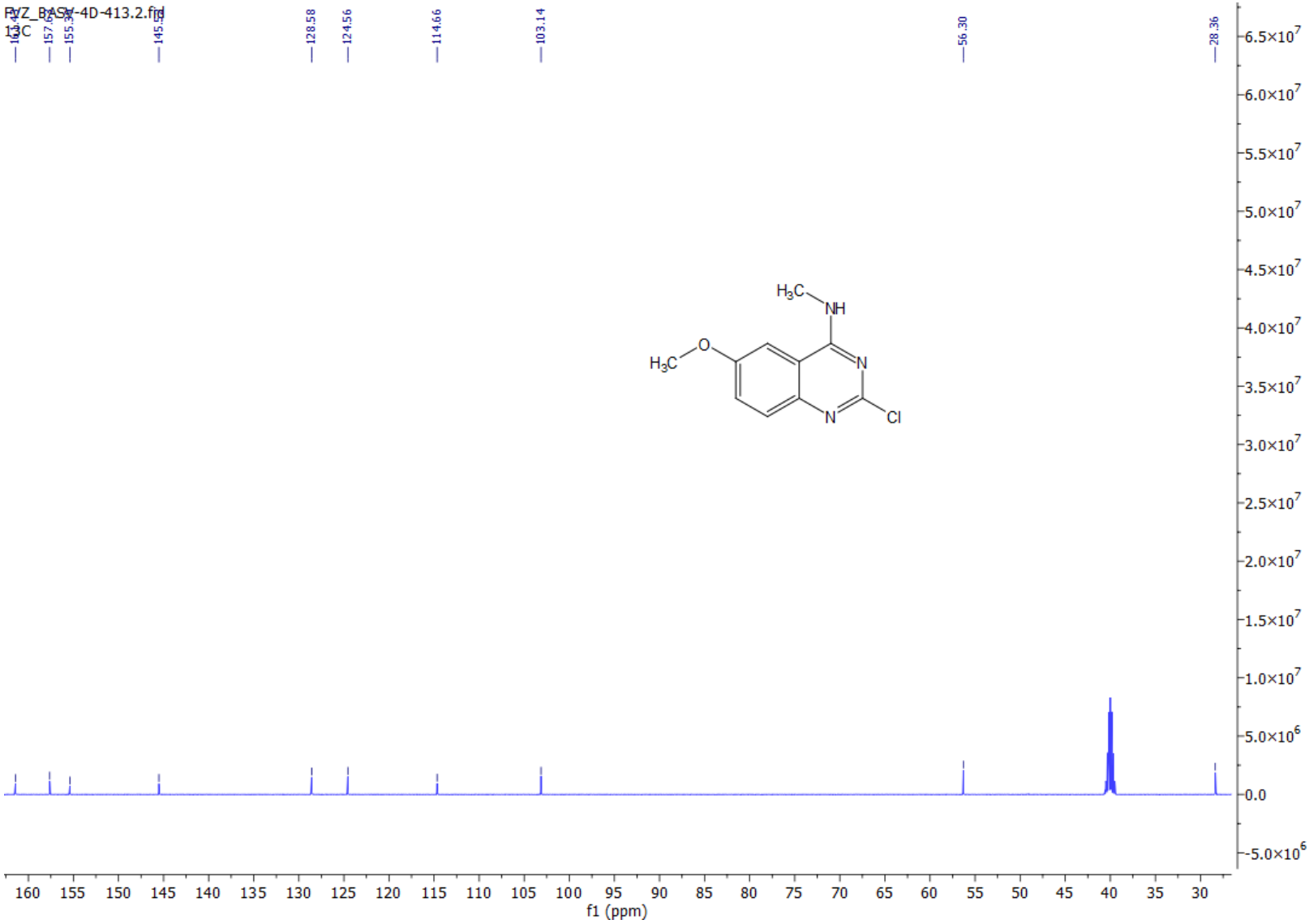


Fig. S32. ^{1}H NMR of 2-chloro-*N*-ethyl-6-methoxyquinazolin-4-amine (III-5c)

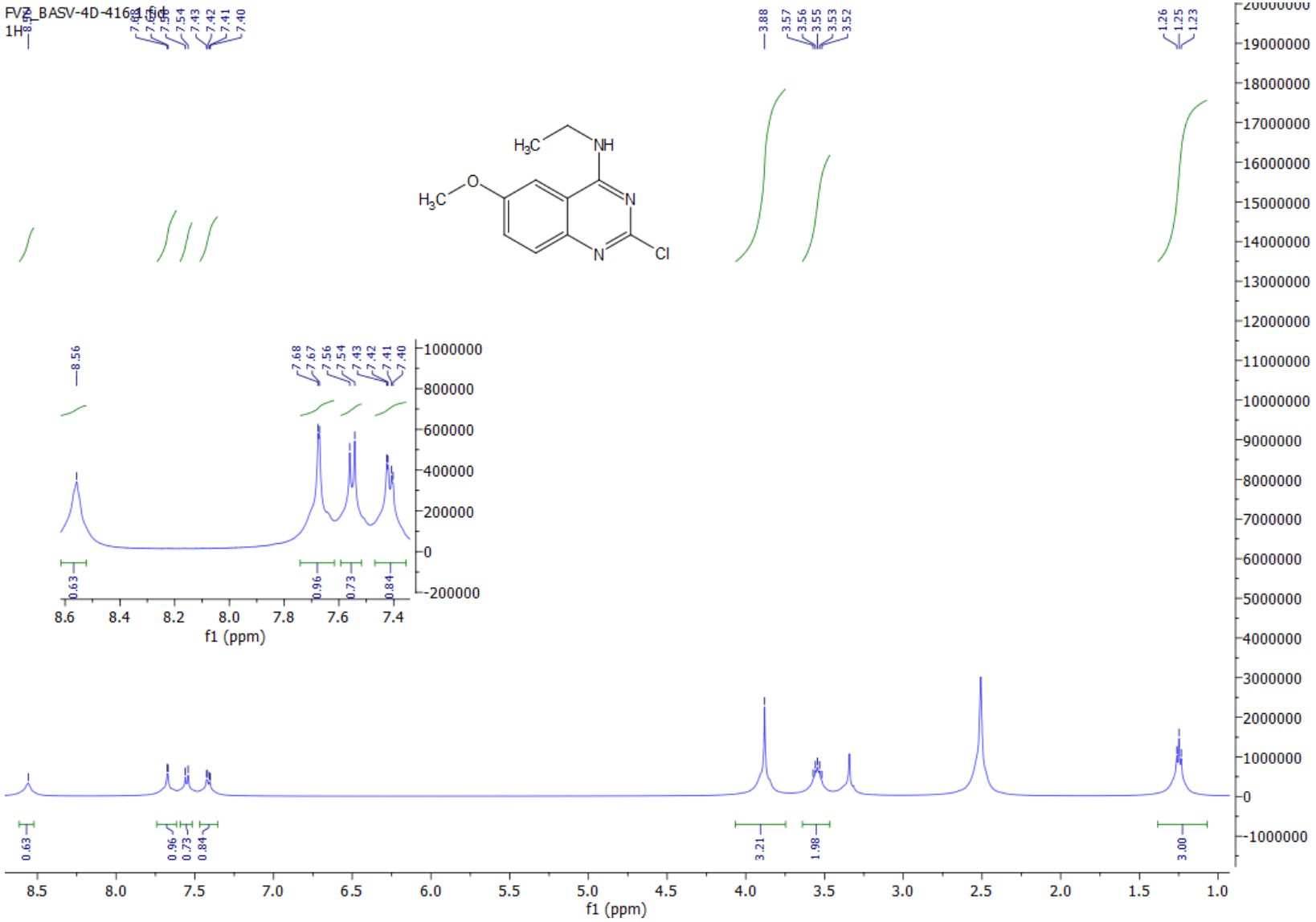


Fig. S33. ^{13}C NMR of 2-chloro-*N*-ethyl-6-methoxyquinazolin-4-amine (III-5c)

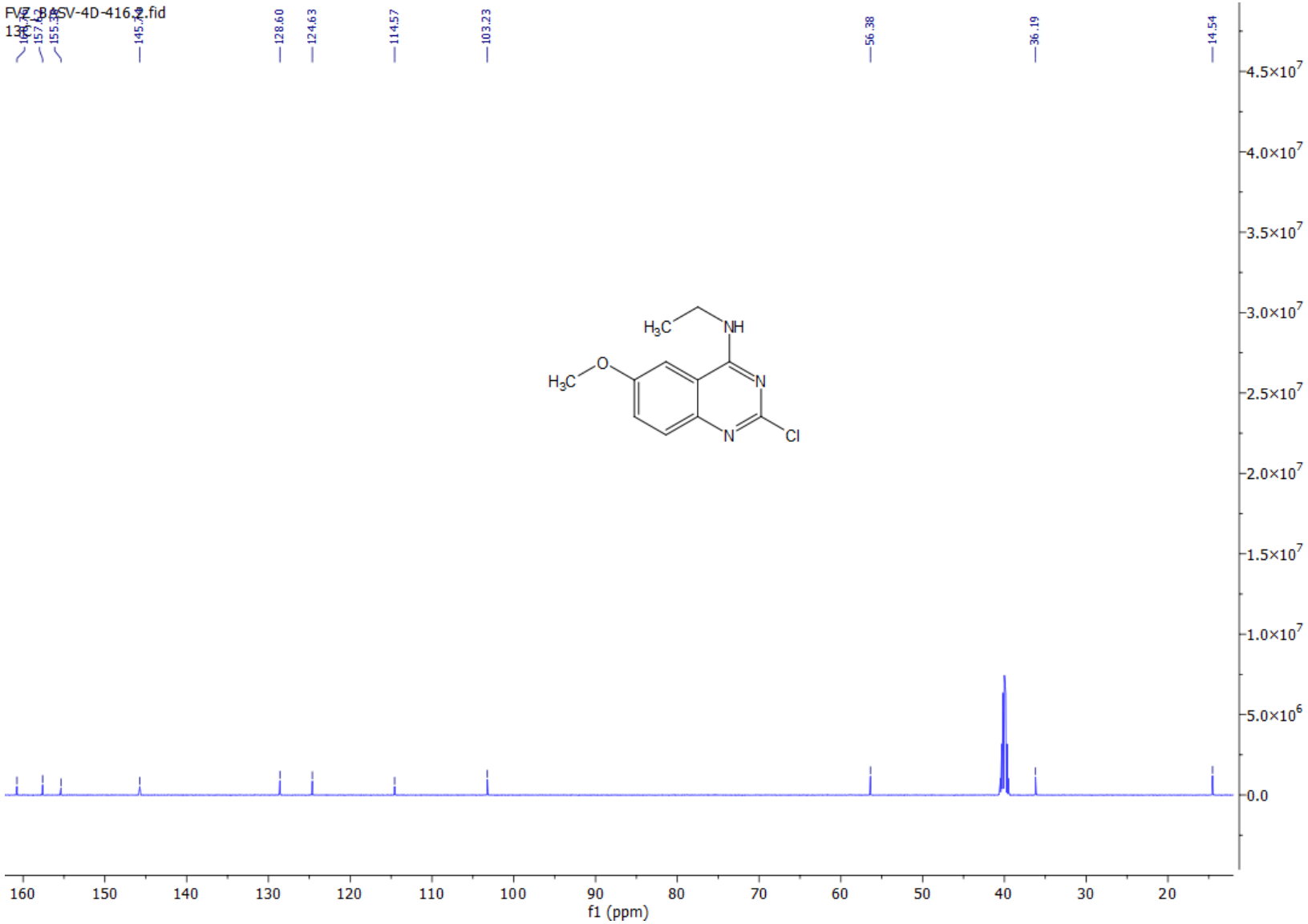


Fig. S34. ^{1}H NMR of 2-chloro-6-methoxy-*N*-(propan-2-yl)quinazolin-4-amine (III-5d)

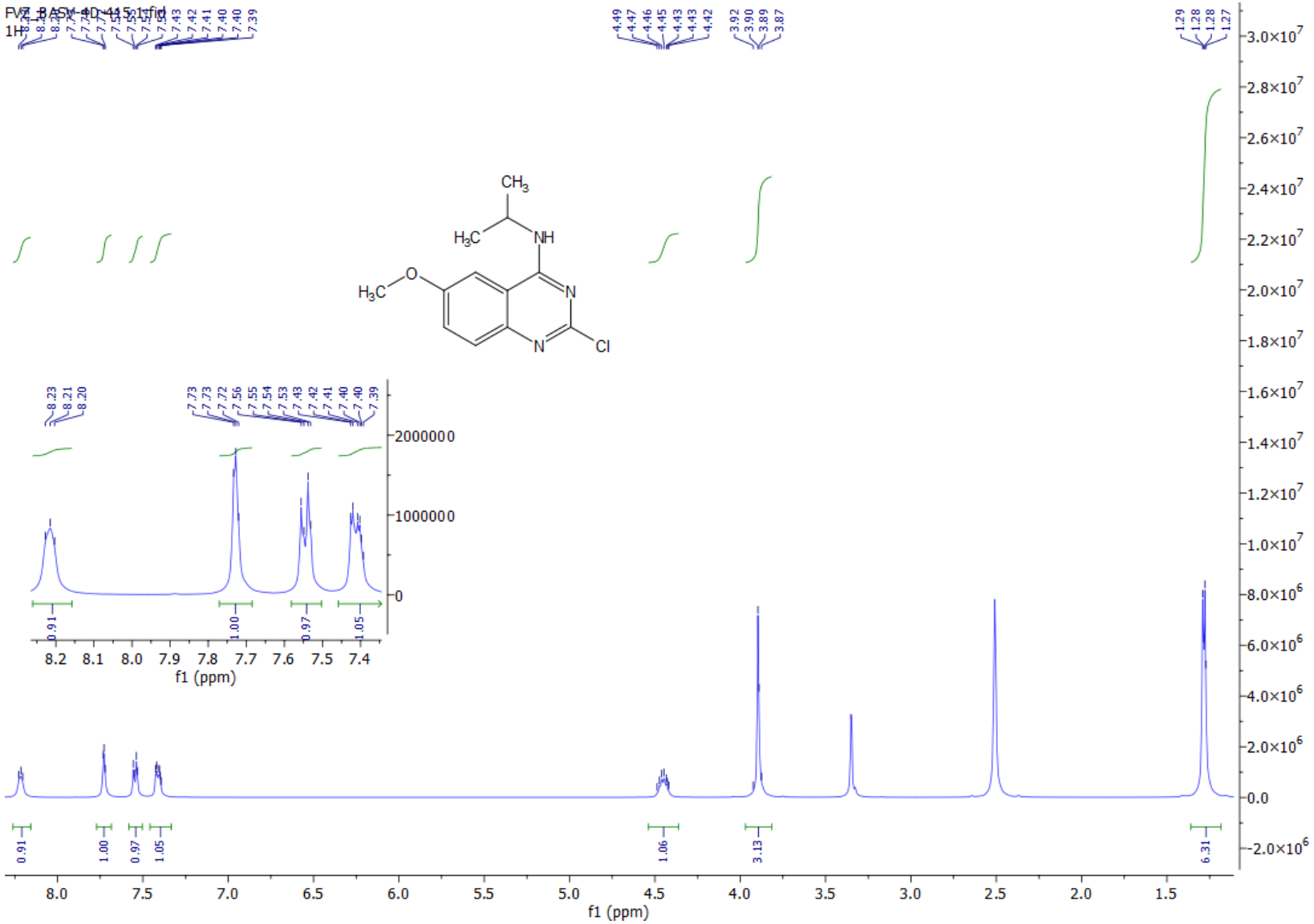


Fig. S35. ^{13}C NMR of 2-chloro-6-methoxy-*N*-(propan-2-yl)quinazolin-4-amine (III-5d)

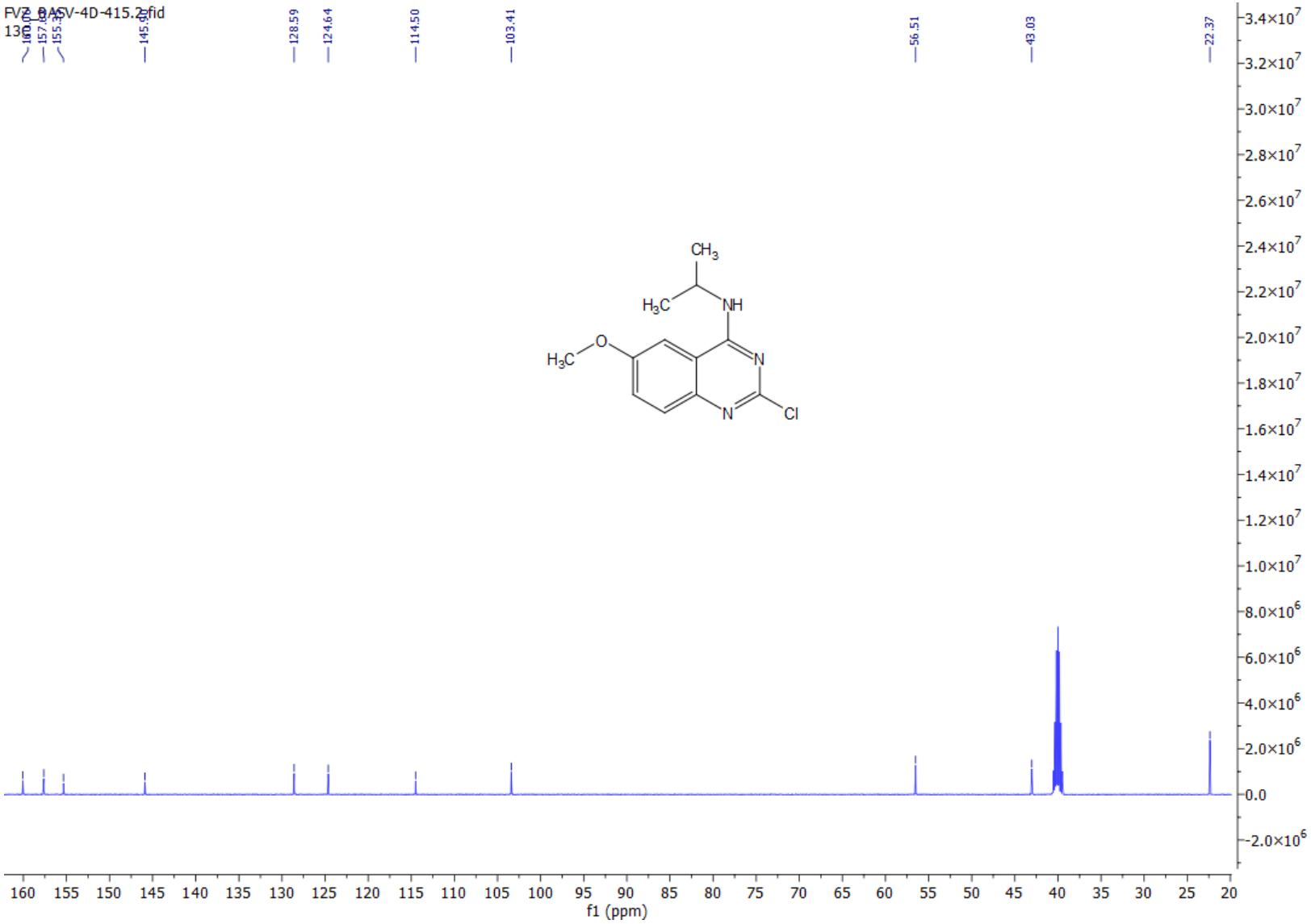


Fig. S36. ^{1}H NMR of *N*-butyl-2-chloro-6-methoxyquinazolin-4-amine (III-5e)

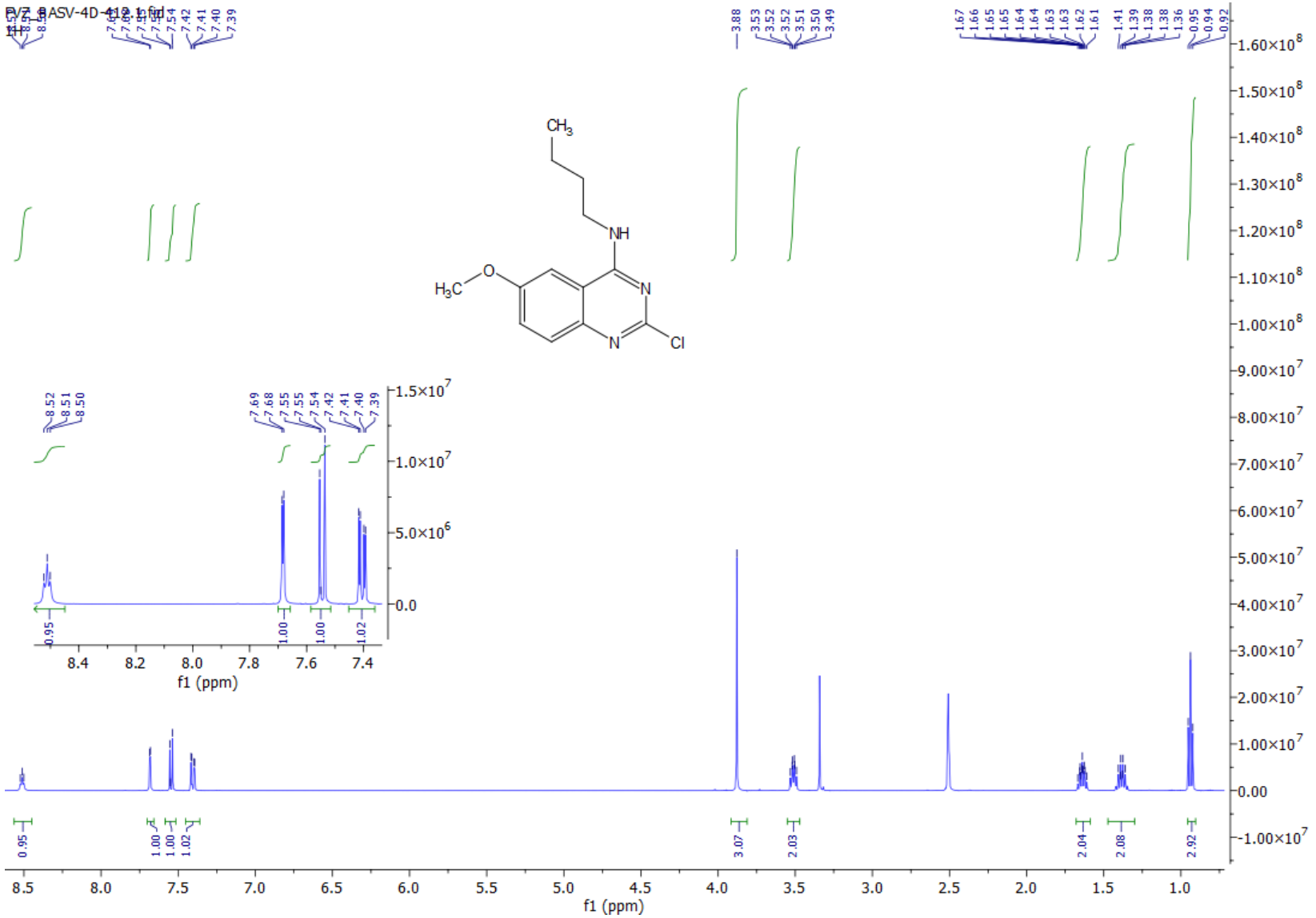


Fig. S37. ^{13}C NMR of *N*-butyl-2-chloro-6-methoxyquinazolin-4-amine (III-5e)

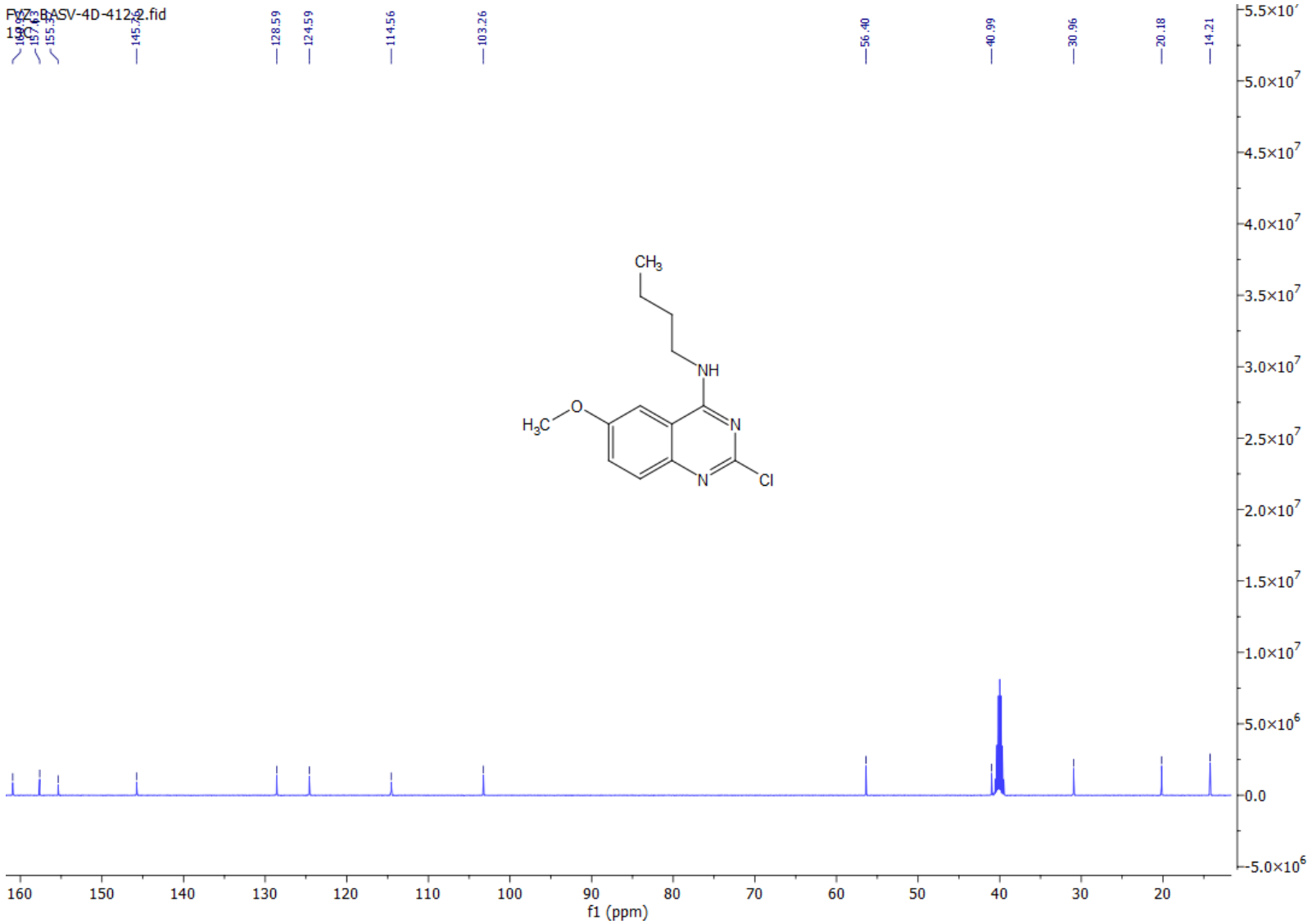


Fig. S38. ^{1}H NMR of 2-chloro-*N*-cyclopropyl-6-methoxyquinazolin-4-amine (III-5g)

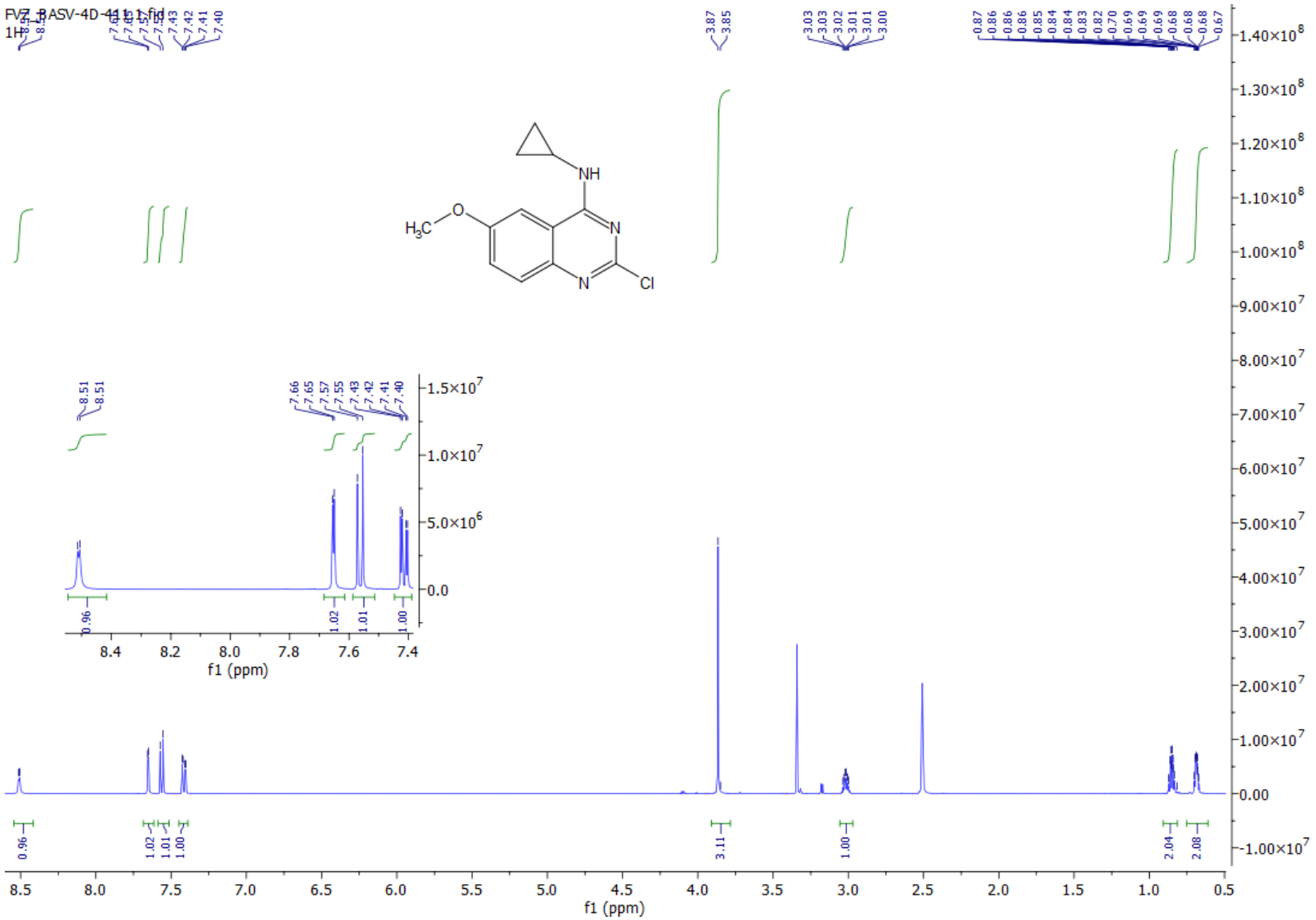


Fig. S39. ^{13}C NMR of 2-chloro-*N*-cyclopropyl-6-methoxyquinazolin-4-amine (III-5g)

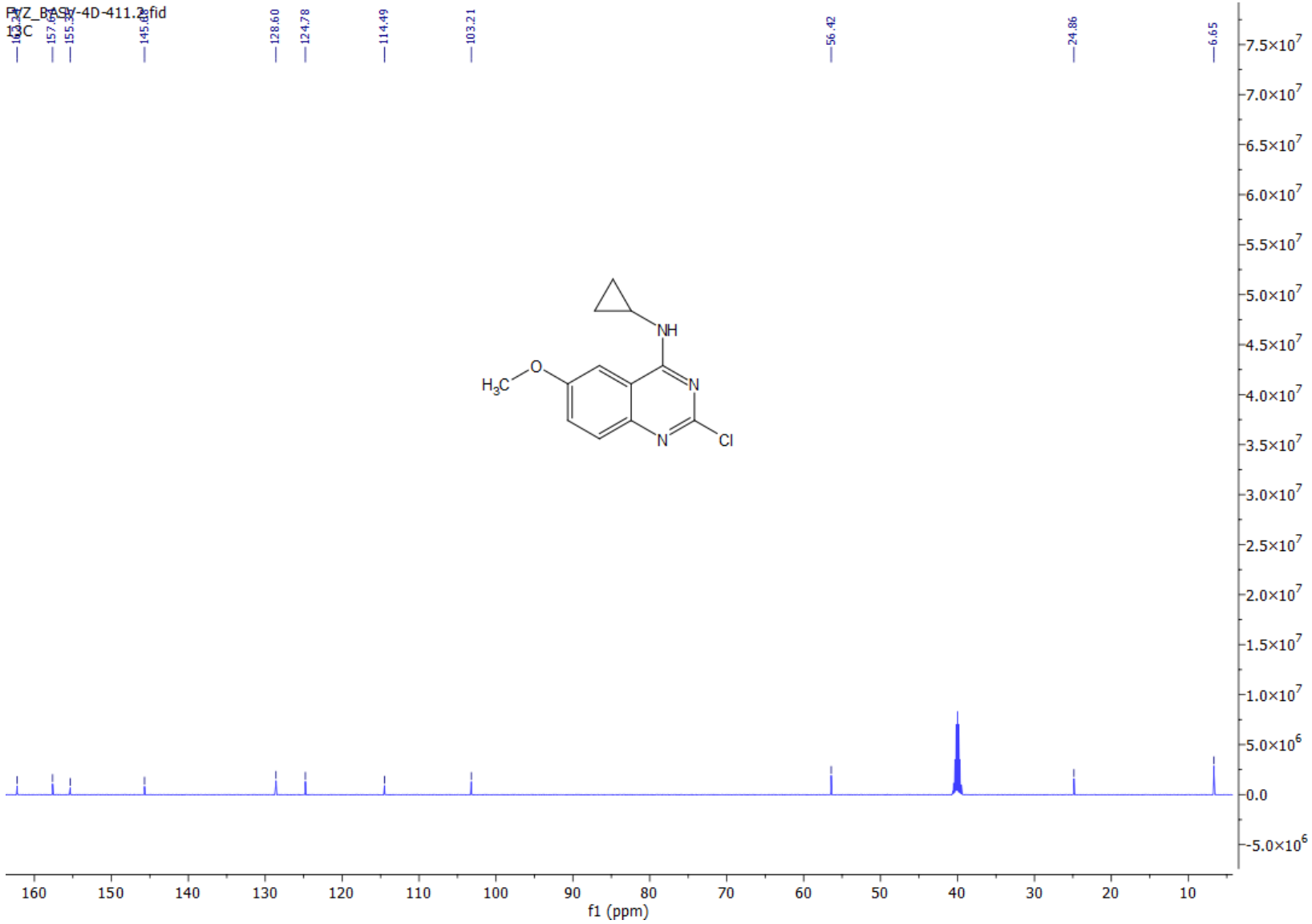


Fig. S40. ^{1}H NMR of 2-chloro-*N*-cyclohexyl-6-methoxyquinazolin-4-amine (III-5h)

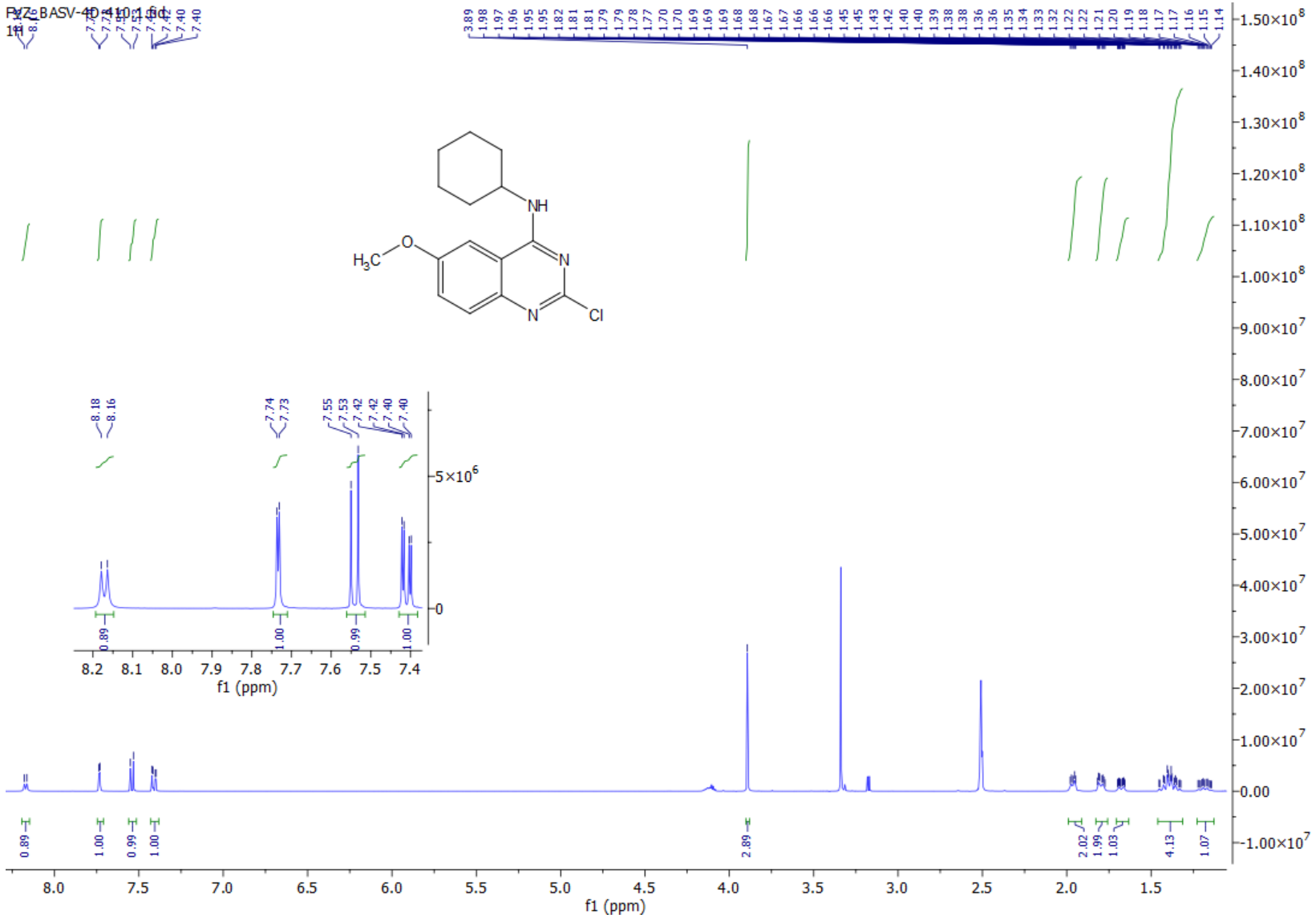


Fig. S41. ^{13}C NMR of 2-chloro-*N*-cyclohexyl-6-methoxyquinazolin-4-amine (III-5h)

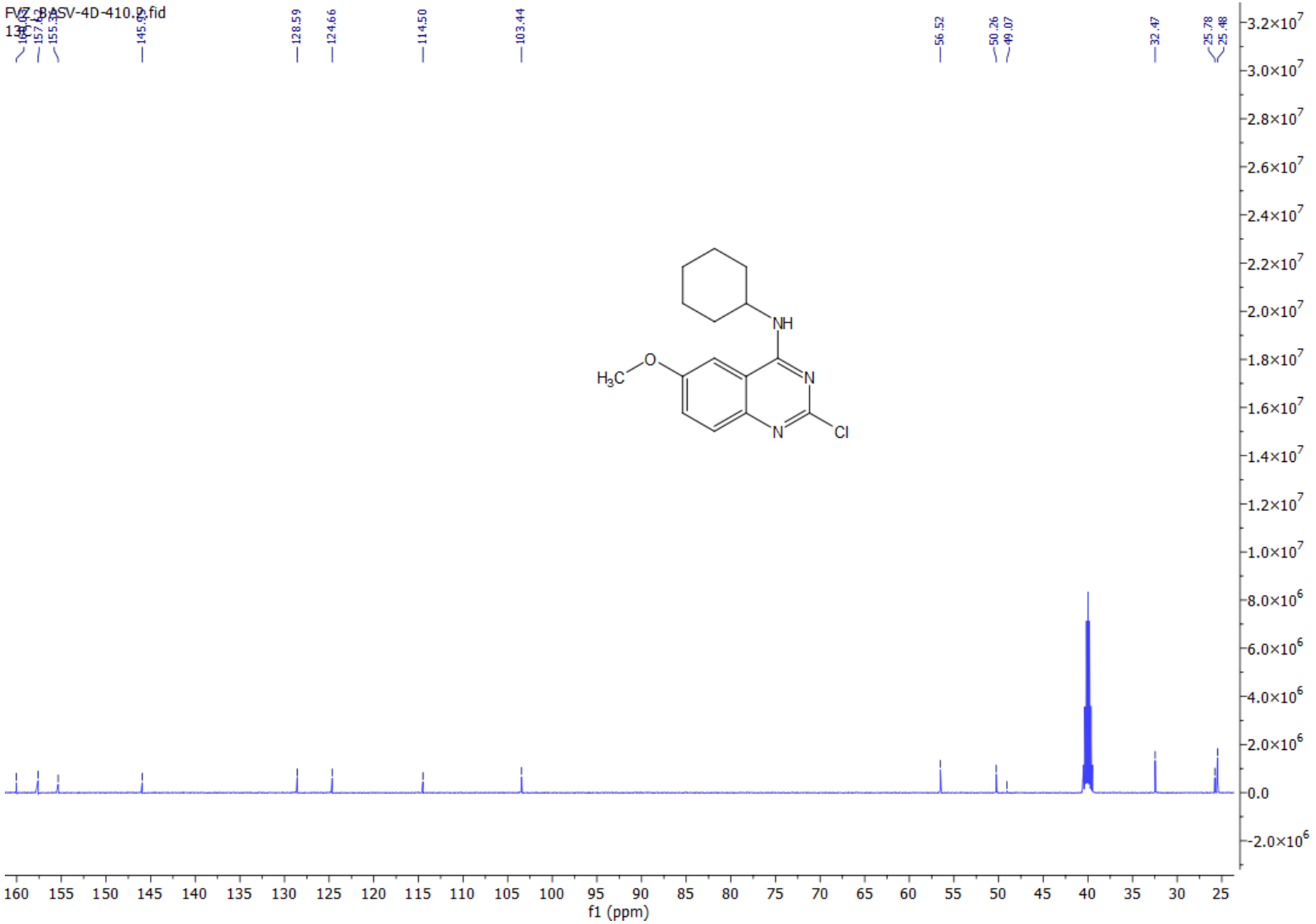


Fig. S42. ^{1}H NMR of *N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6a)

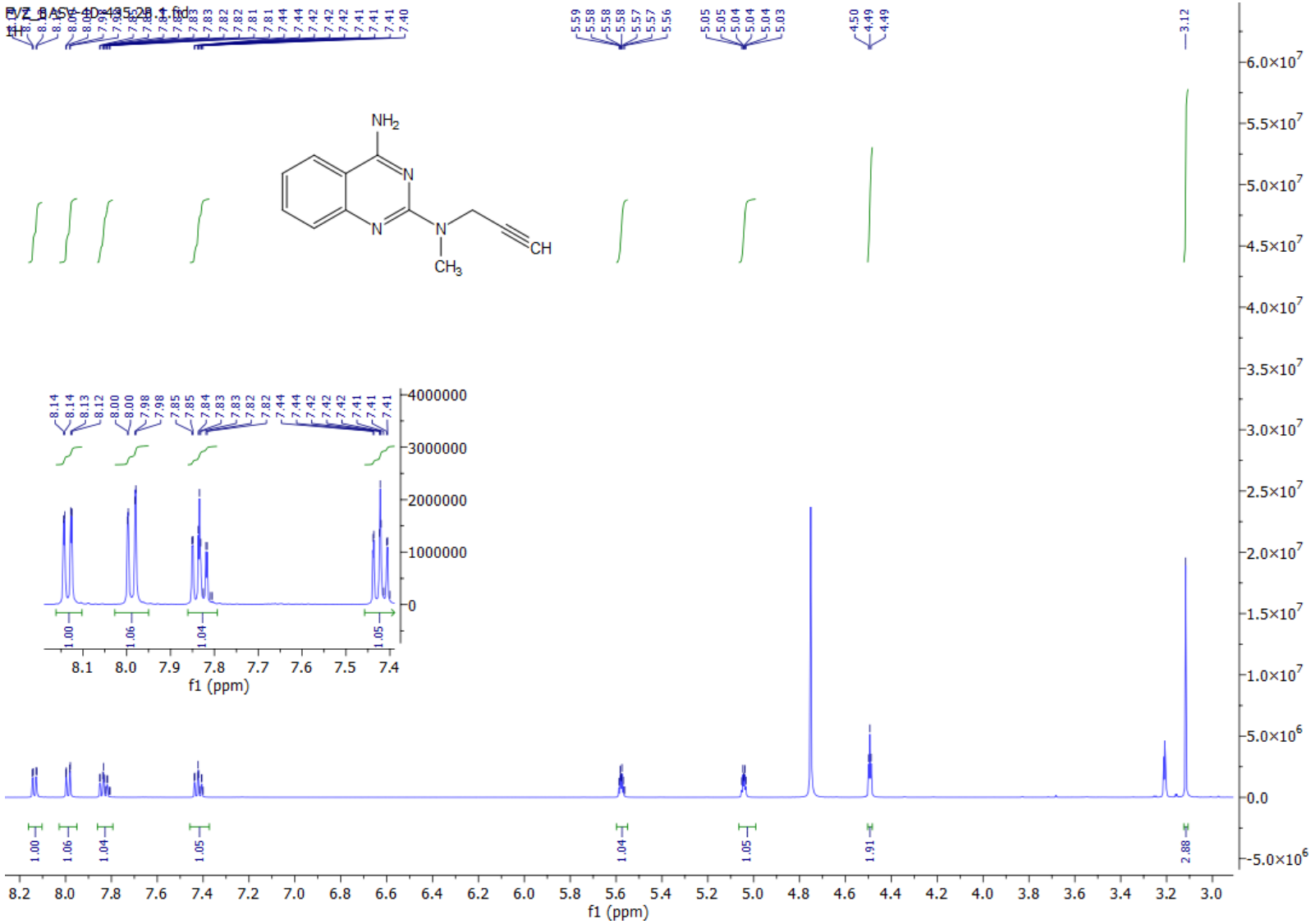


Fig. S43. ^{13}C NMR of *N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6a)

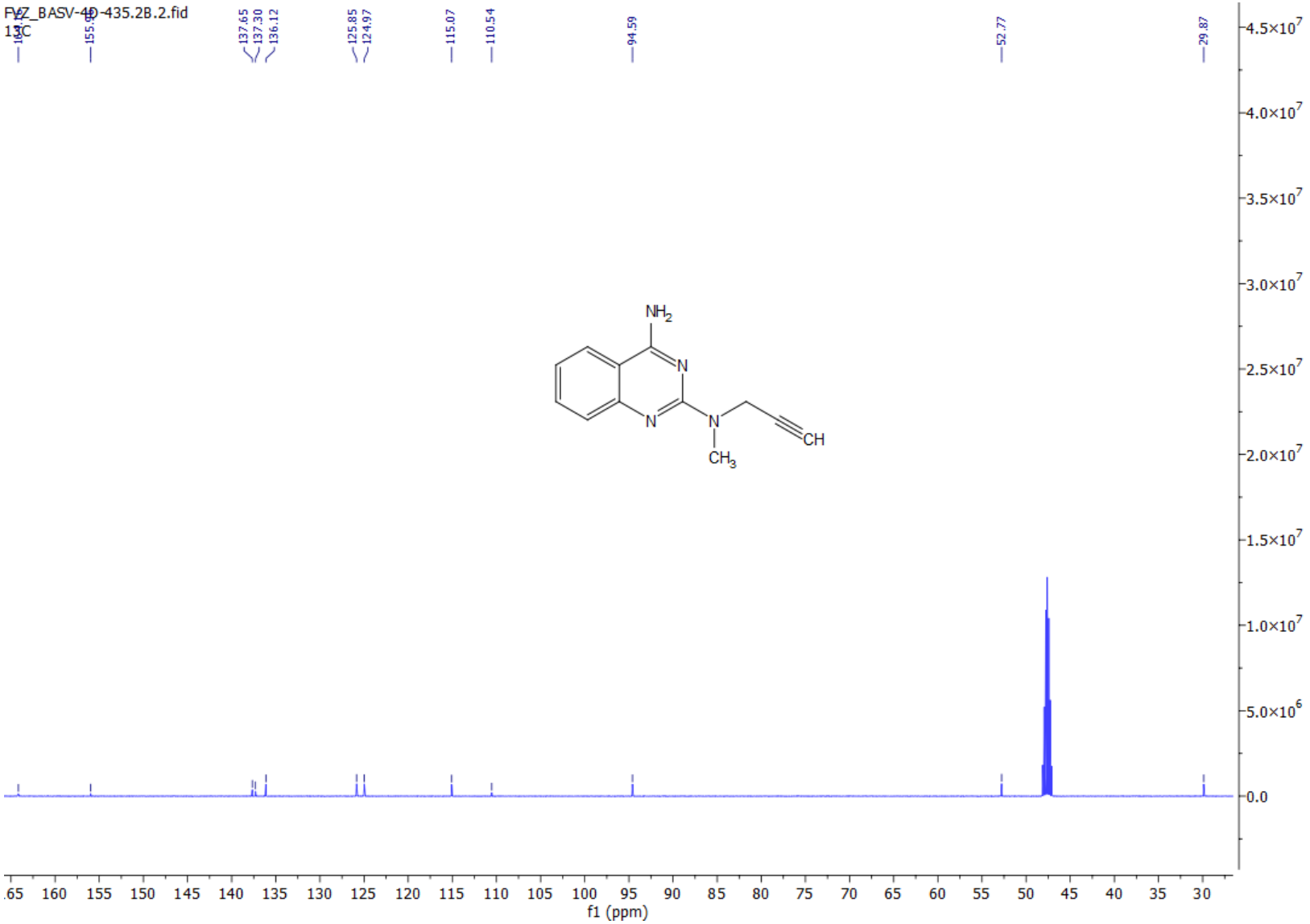


Fig. S44. ^{1}H NMR of *N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6b)

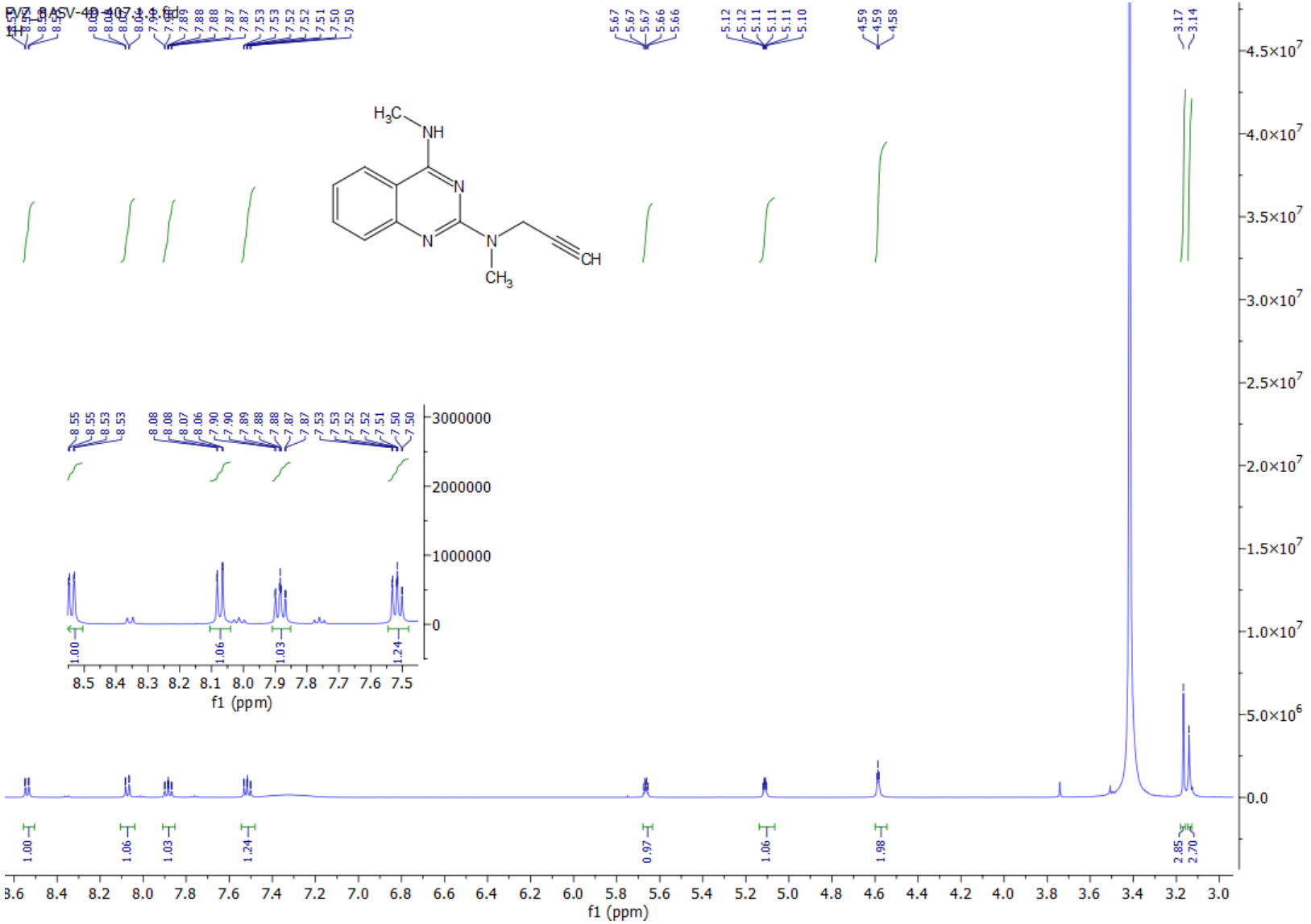


Fig. S45. ^{13}C NMR of *N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6b)

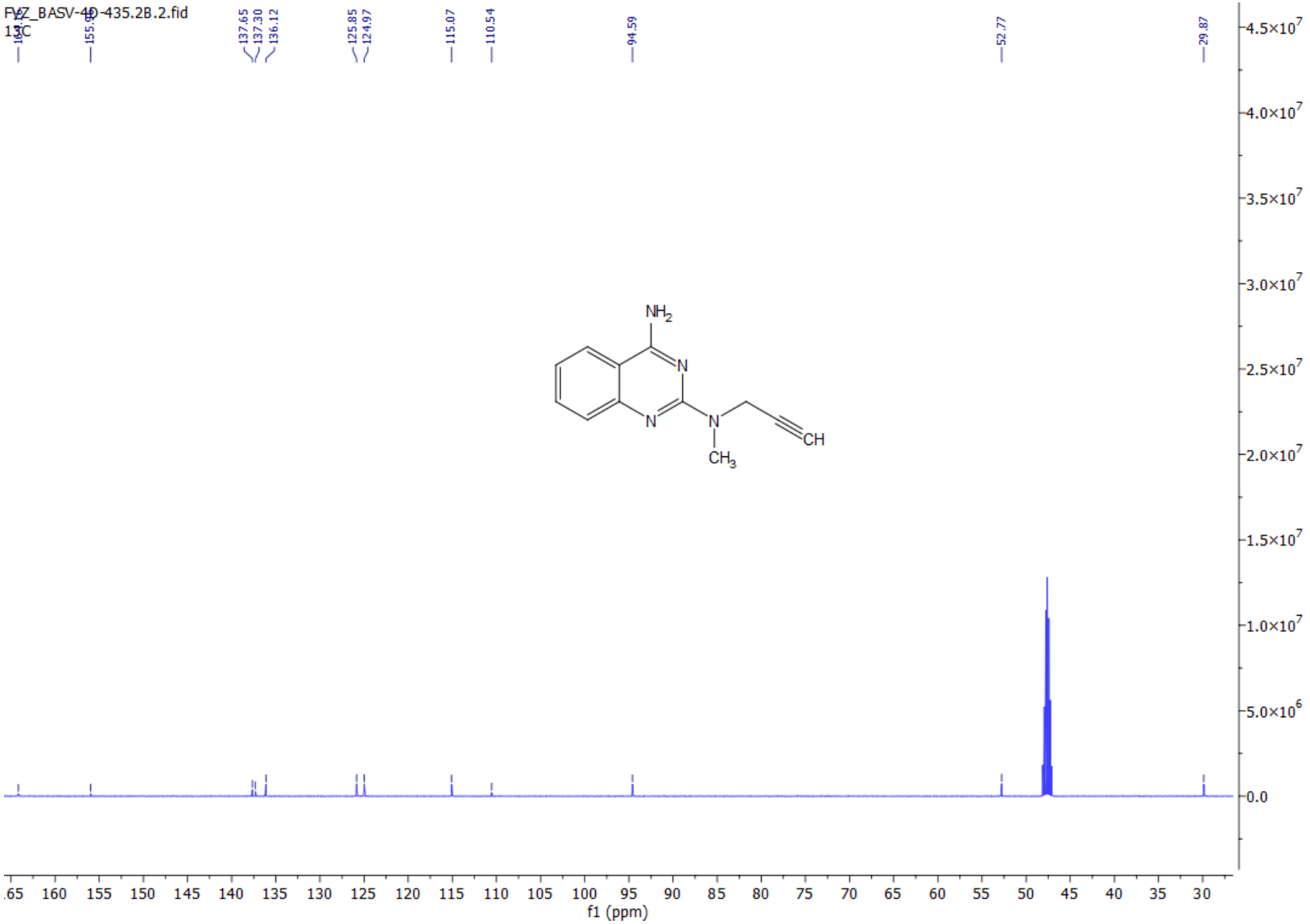


Fig. S46. ^{1}H NMR of *N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6c)

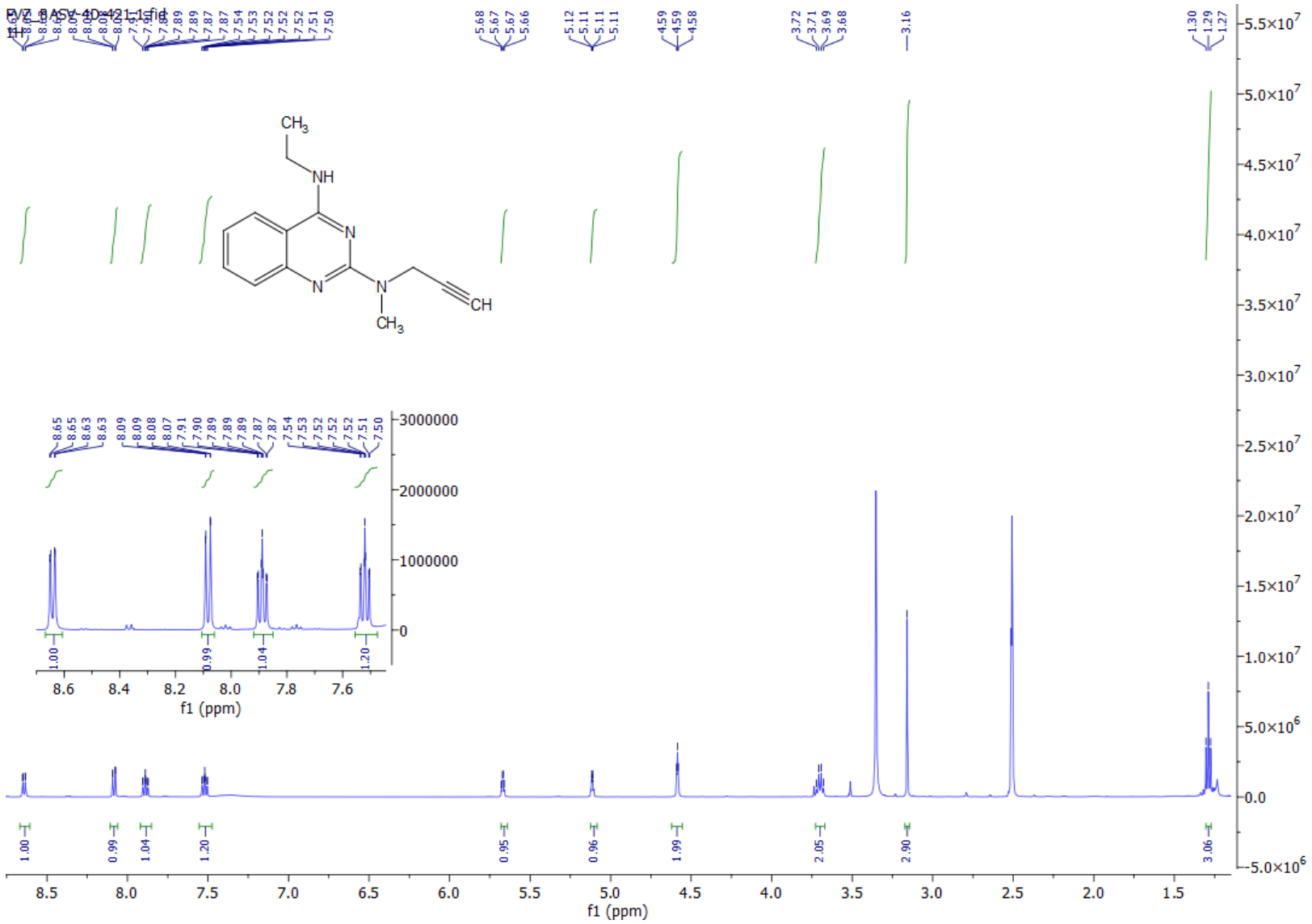


Fig. S47. ^{13}C NMR of *N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6c)

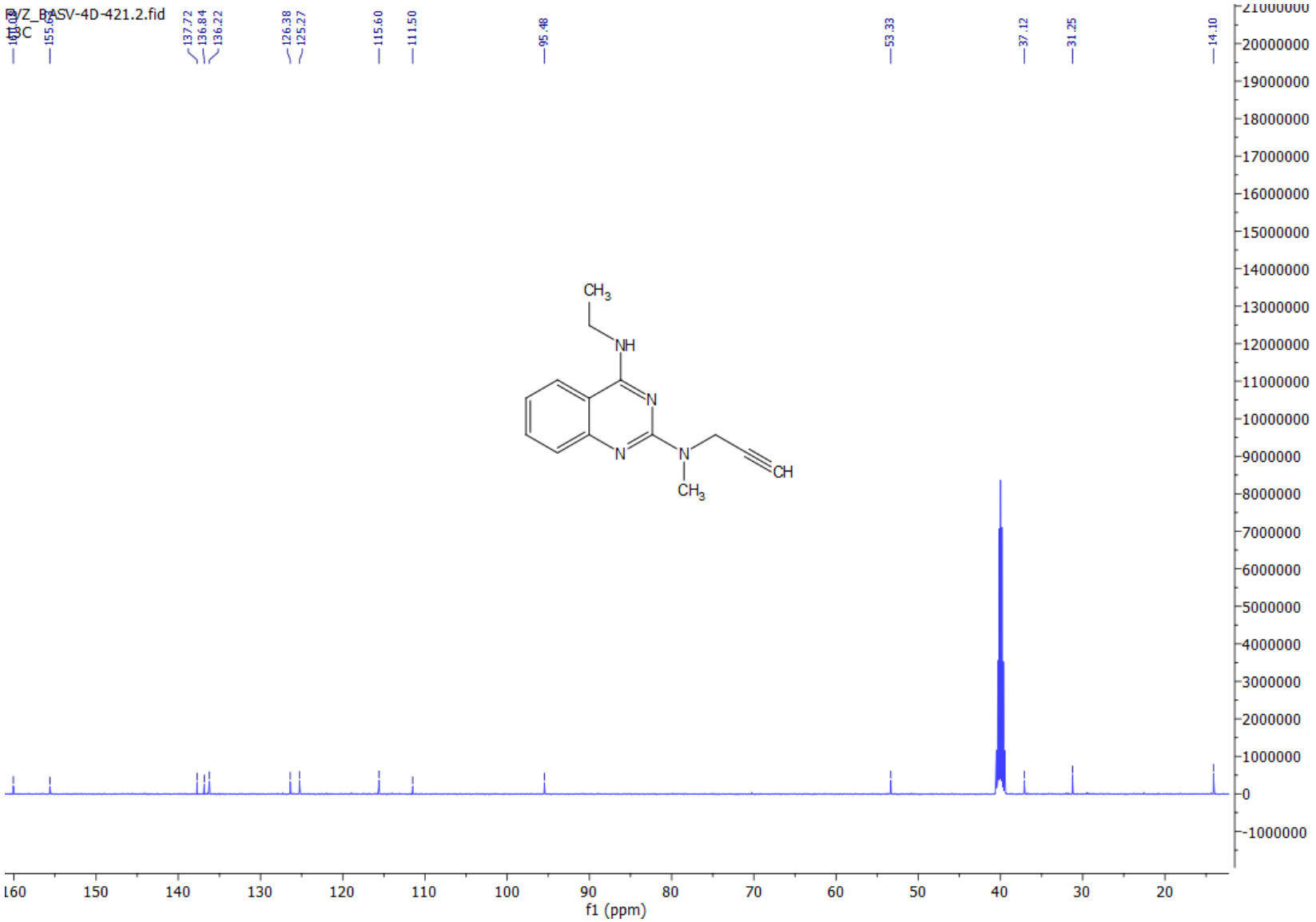


Fig. S48. ^{1}H NMR of *N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (I-6d)

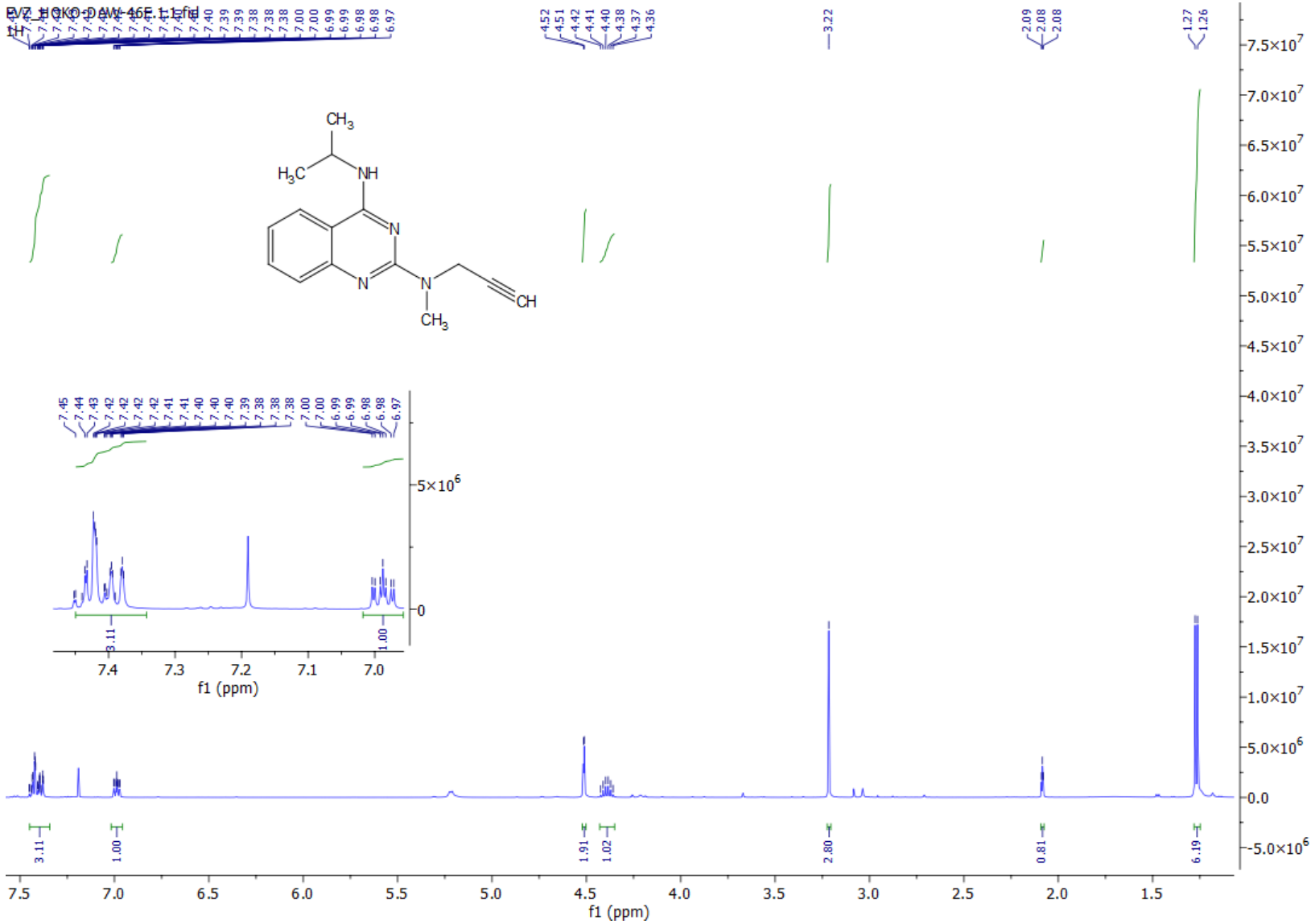


Fig. S49. ^{13}C NMR of *N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (I-6d)

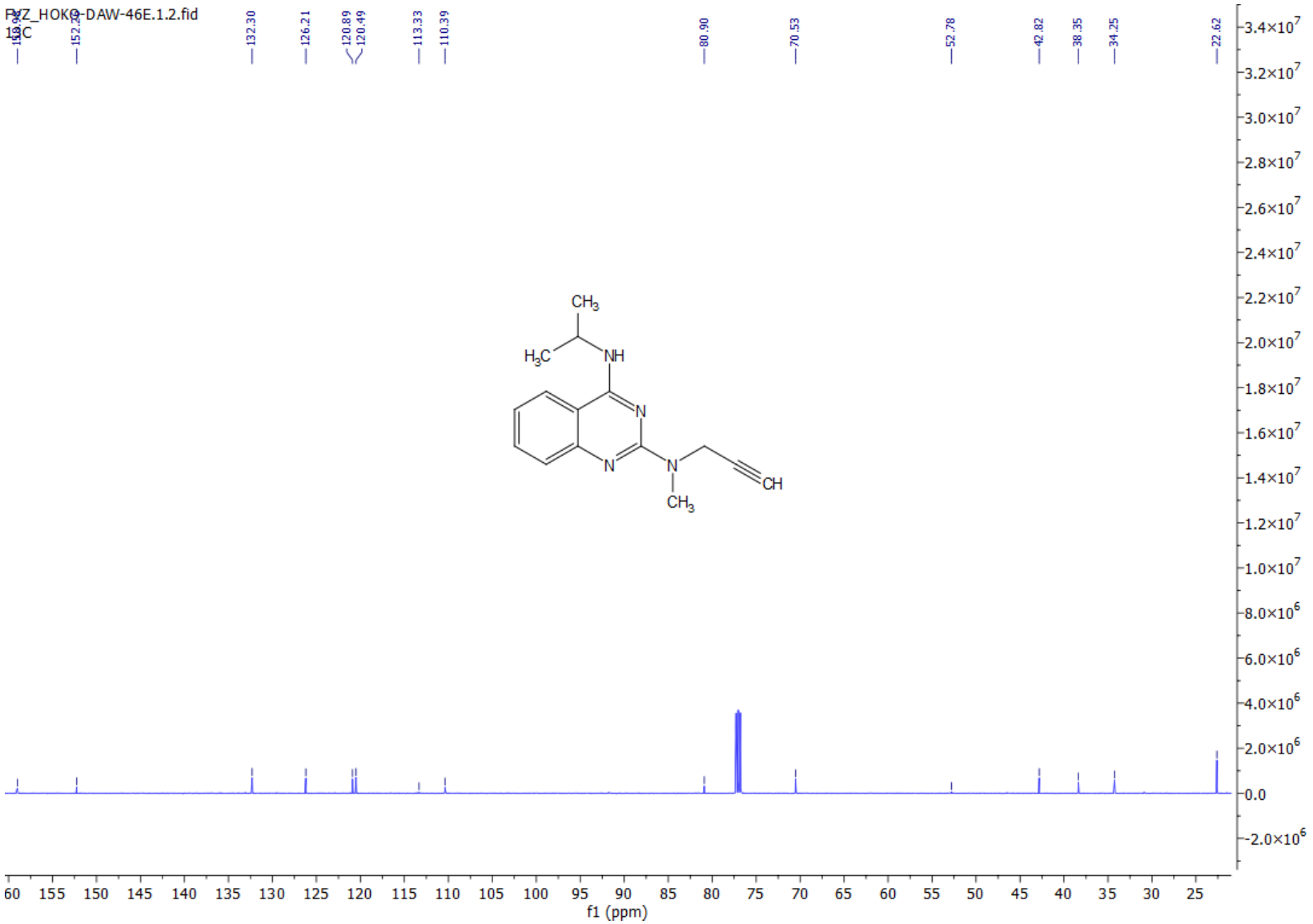


Fig. S50. ^{1}H NMR of *N4*-butyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6e)

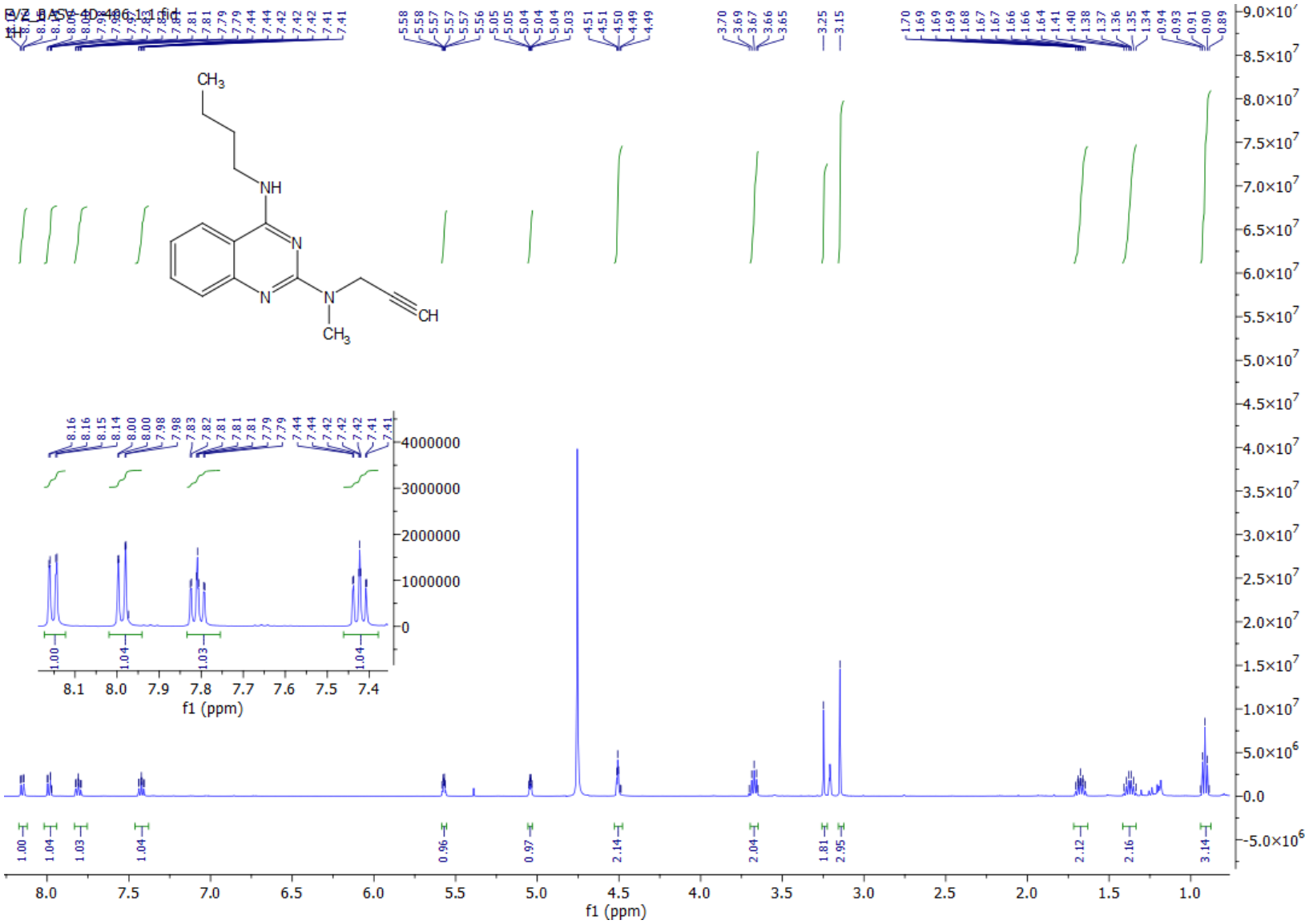


Fig. S51. ^{13}C NMR of *N4*-butyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6e)

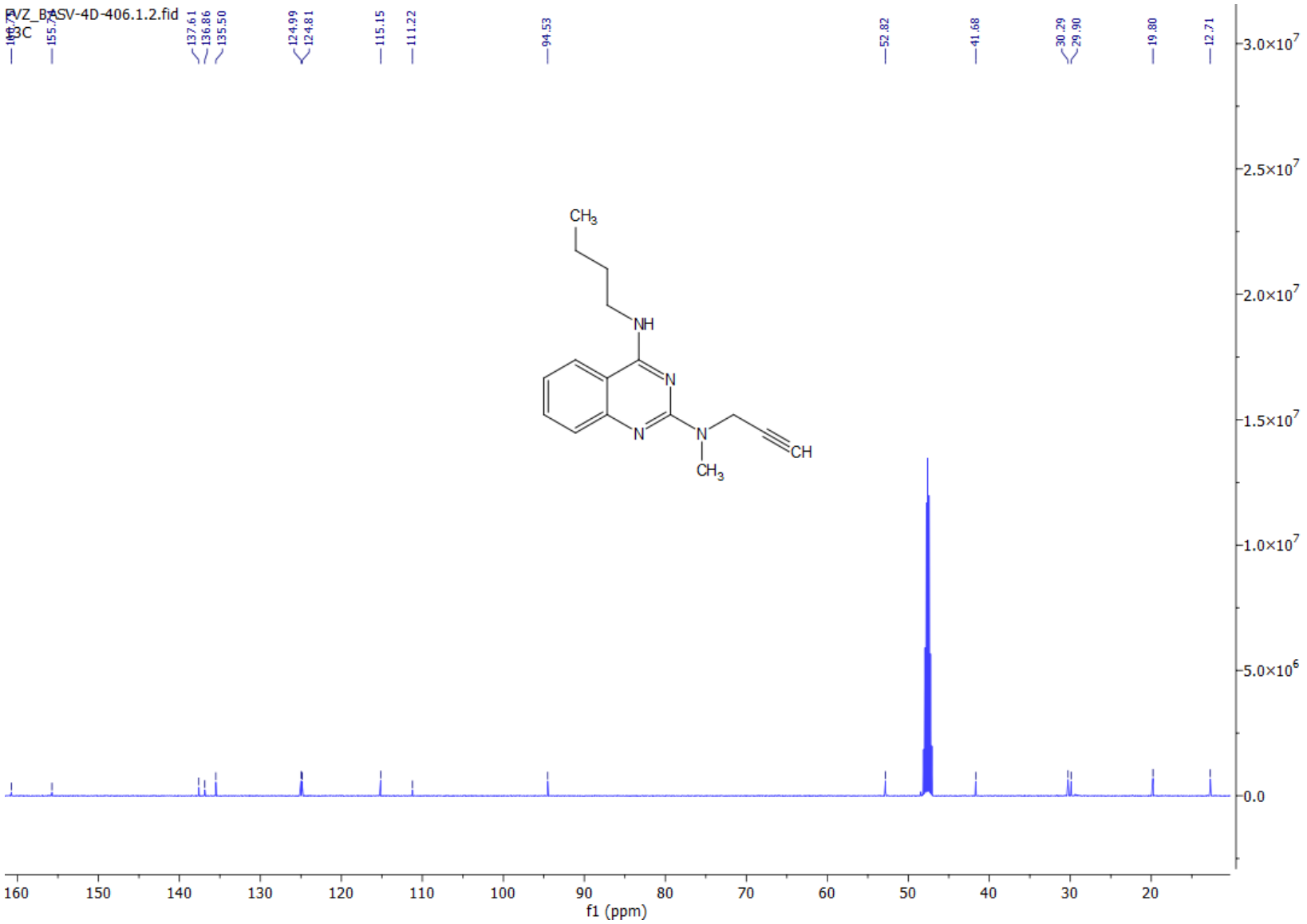


Fig. S52. ^{1}H NMR of *N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6f)

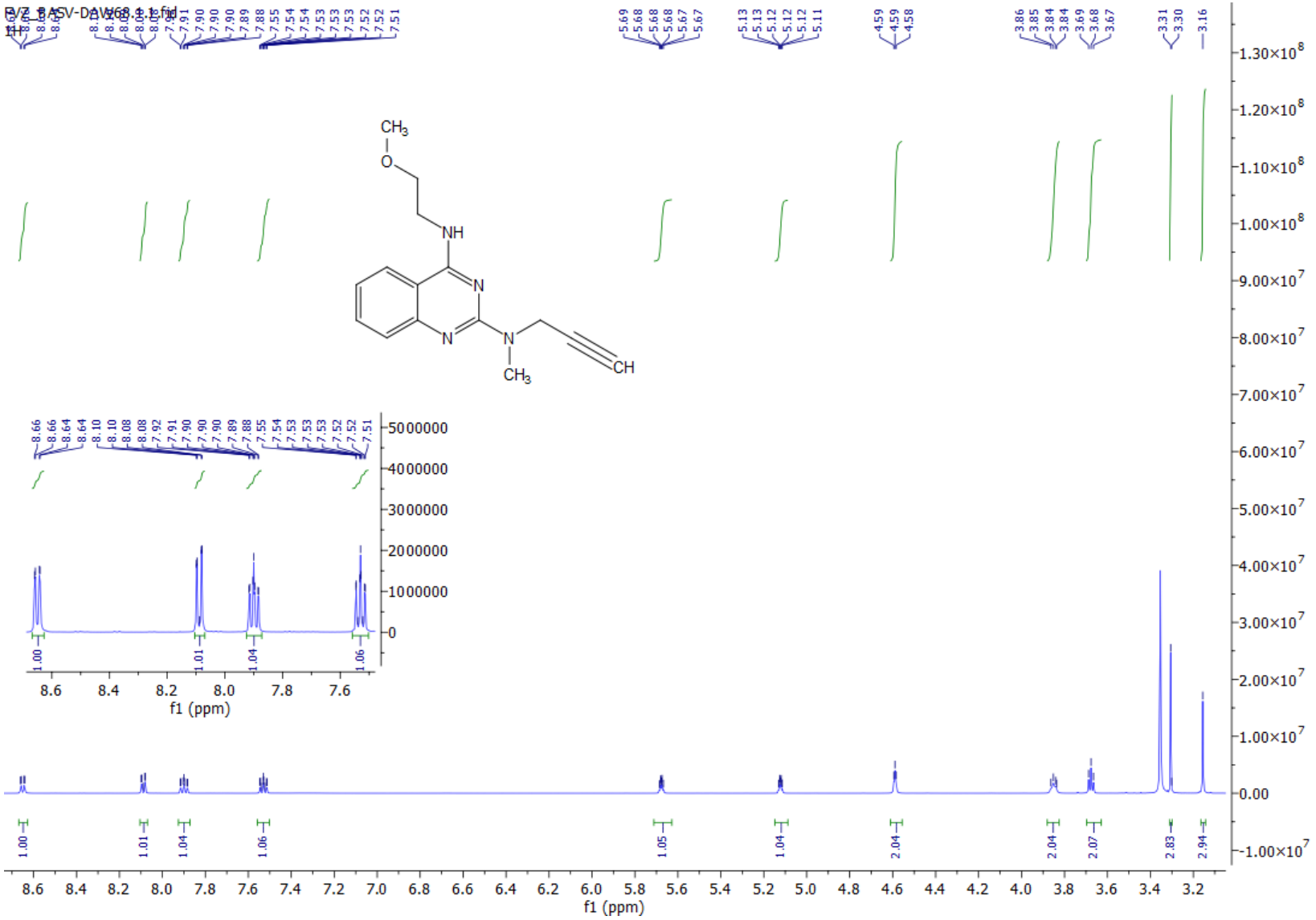


Fig. S53. ^{13}C NMR of *N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6f)

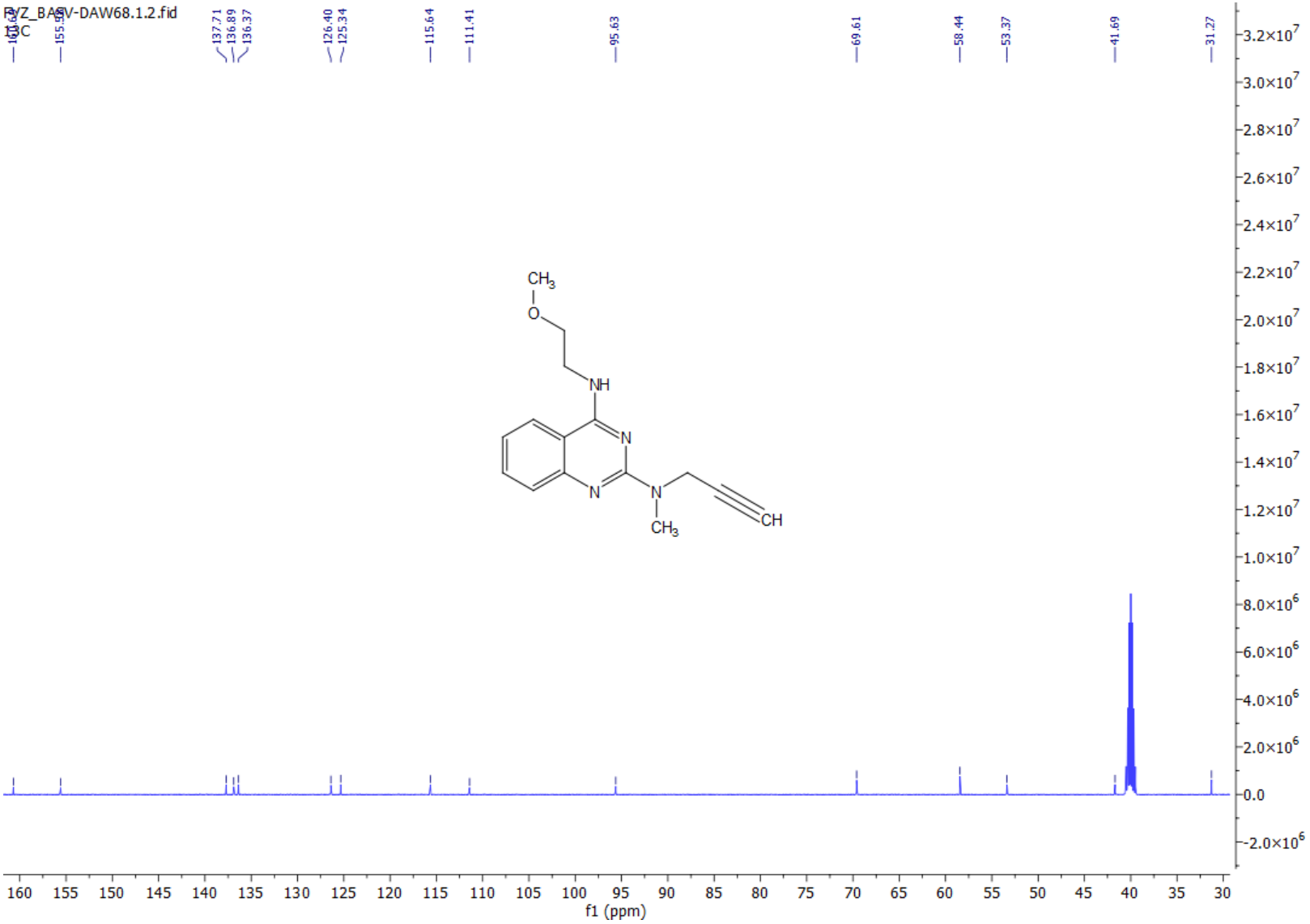


Fig. S54. ^{1}H NMR of *N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6g)

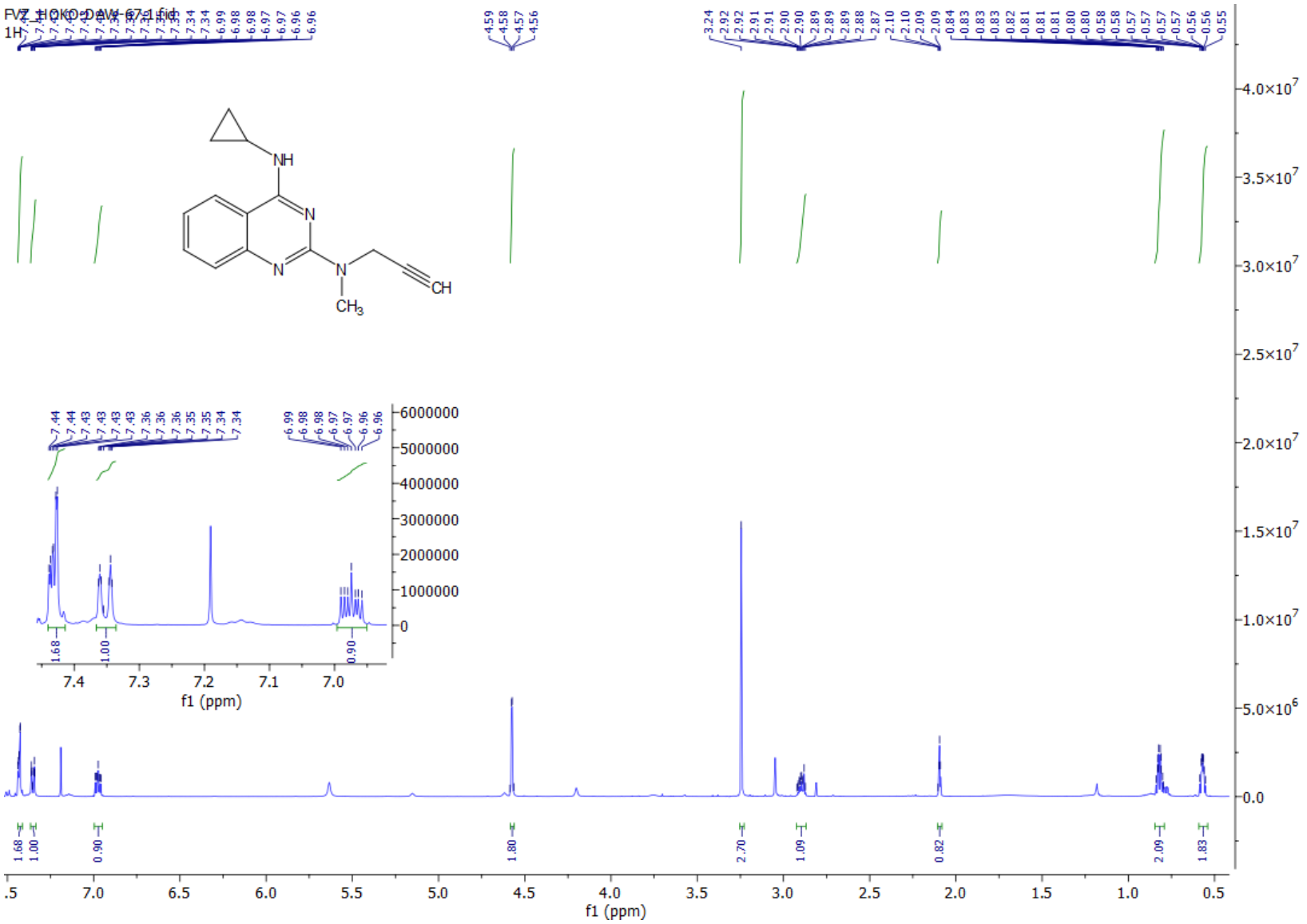


Fig. S55. ^{13}C NMR of *N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6g)

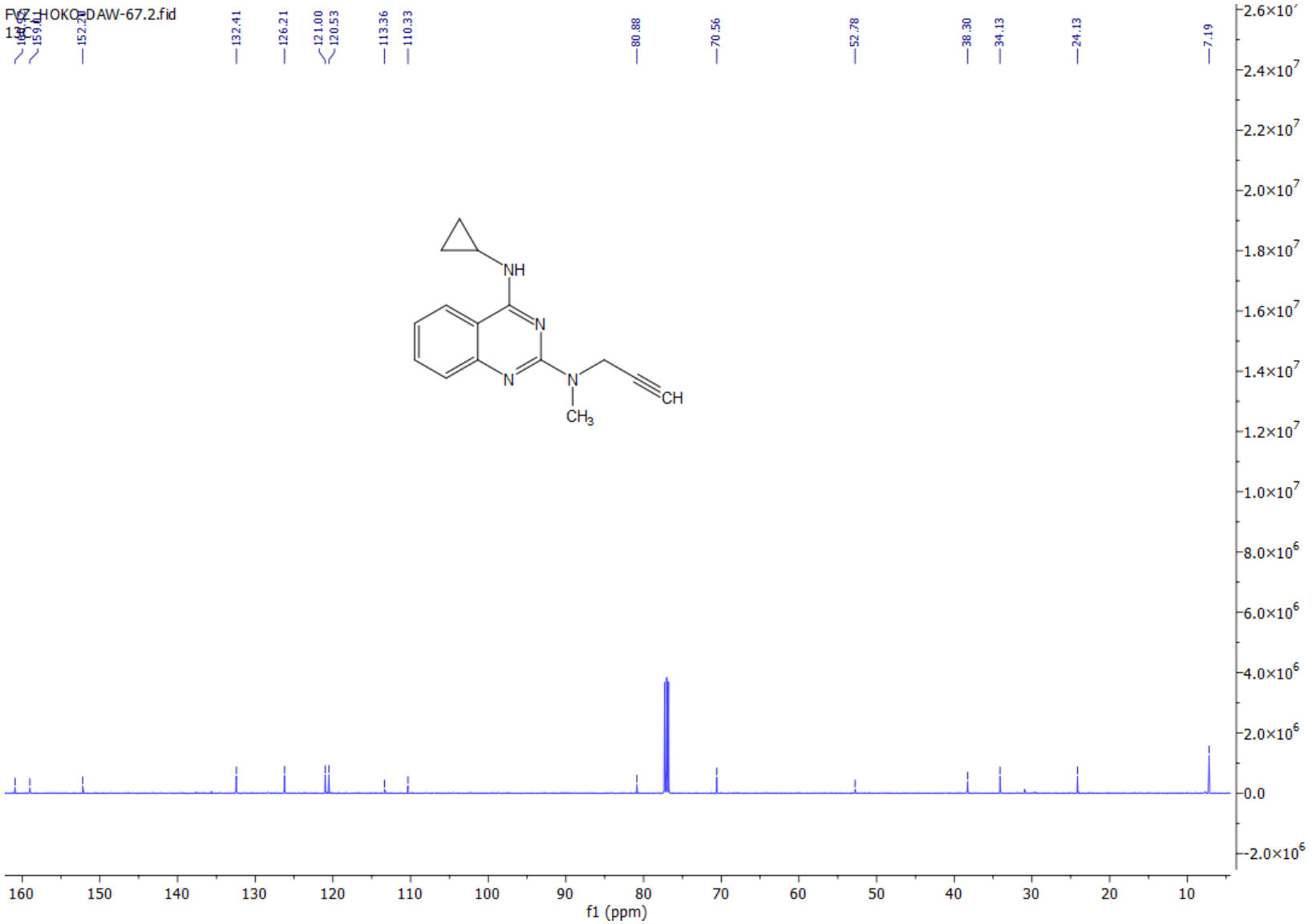


Fig. S56. ^{1}H NMR of *N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6h)

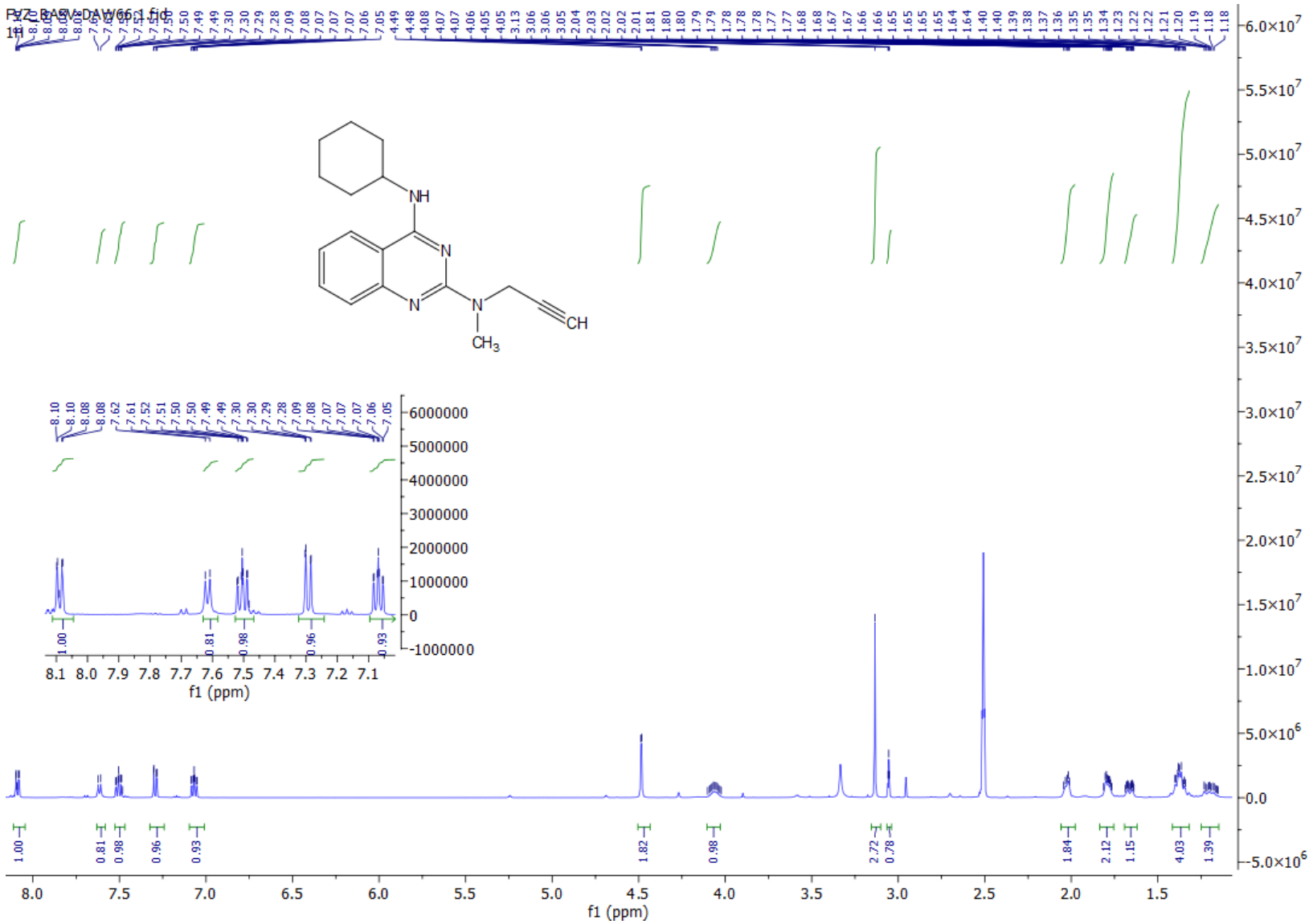


Fig. S57. ^{13}C NMR of *N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6h)

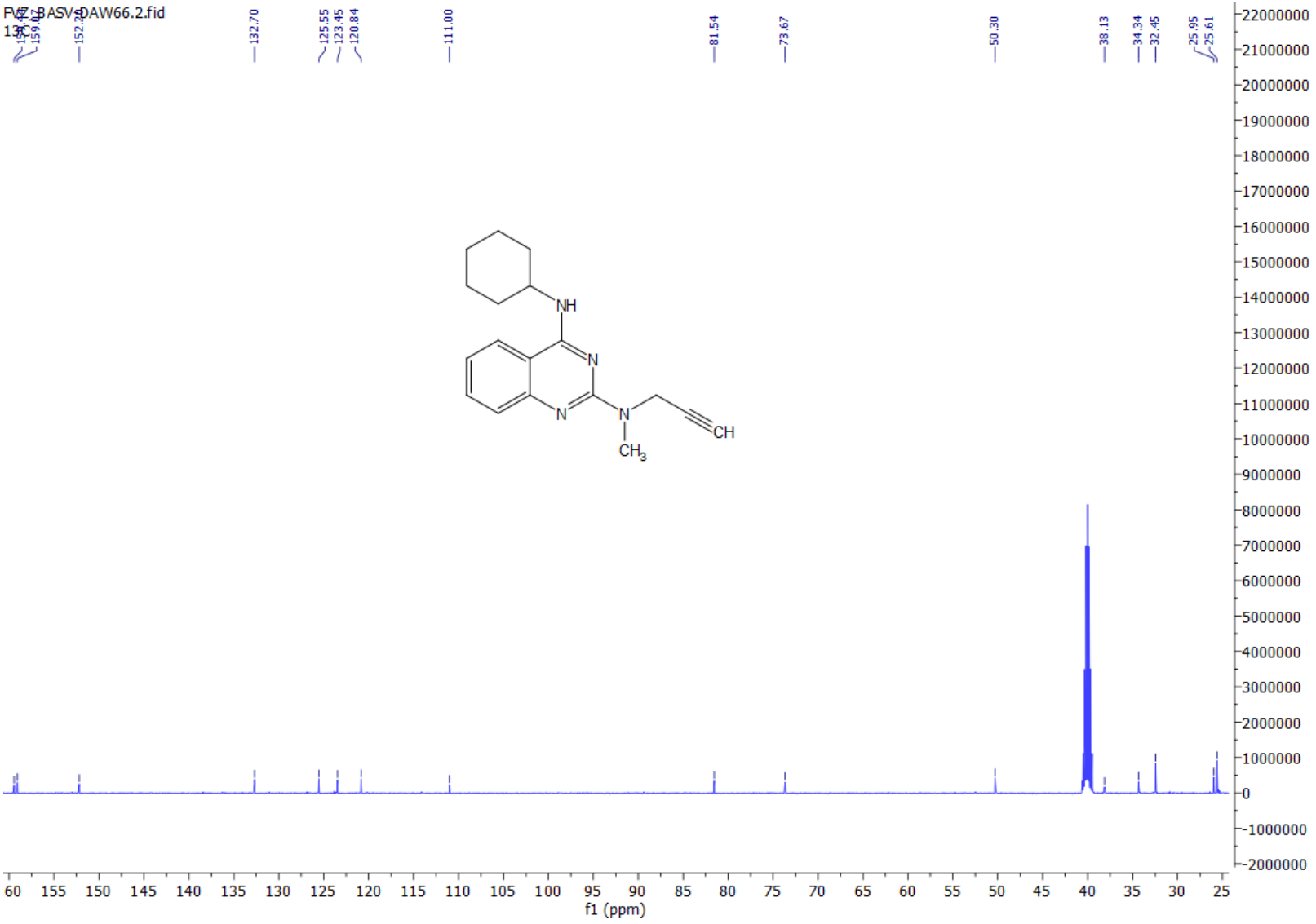


Fig. S58. ^{1}H NMR of 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6a)



Fig. S59. ^{13}C NMR of 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6a)

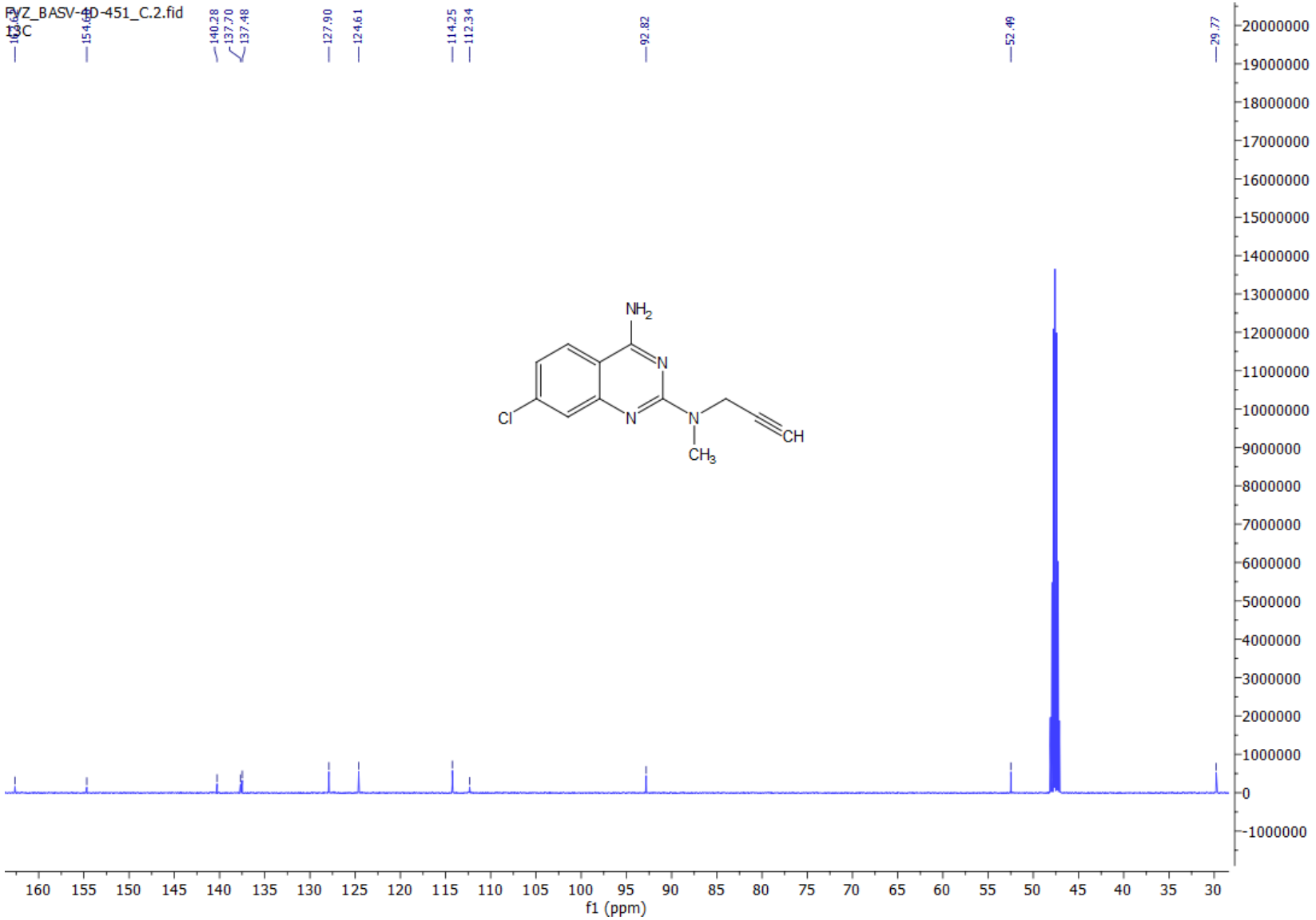


Fig. S60. ^{1}H NMR of 7-chloro-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6b)

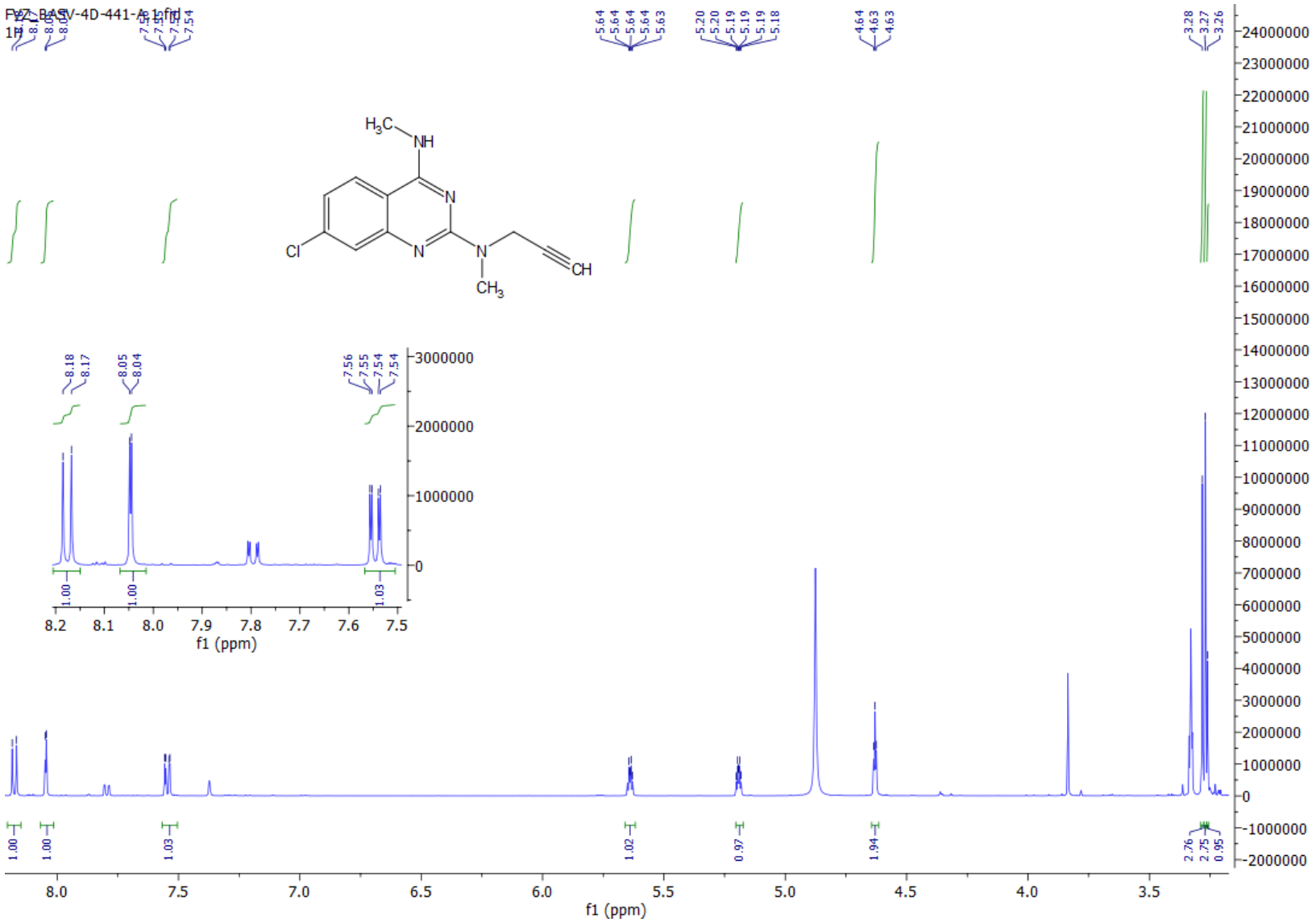


Fig. S61. ^{13}C NMR of 7-chloro-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6b)

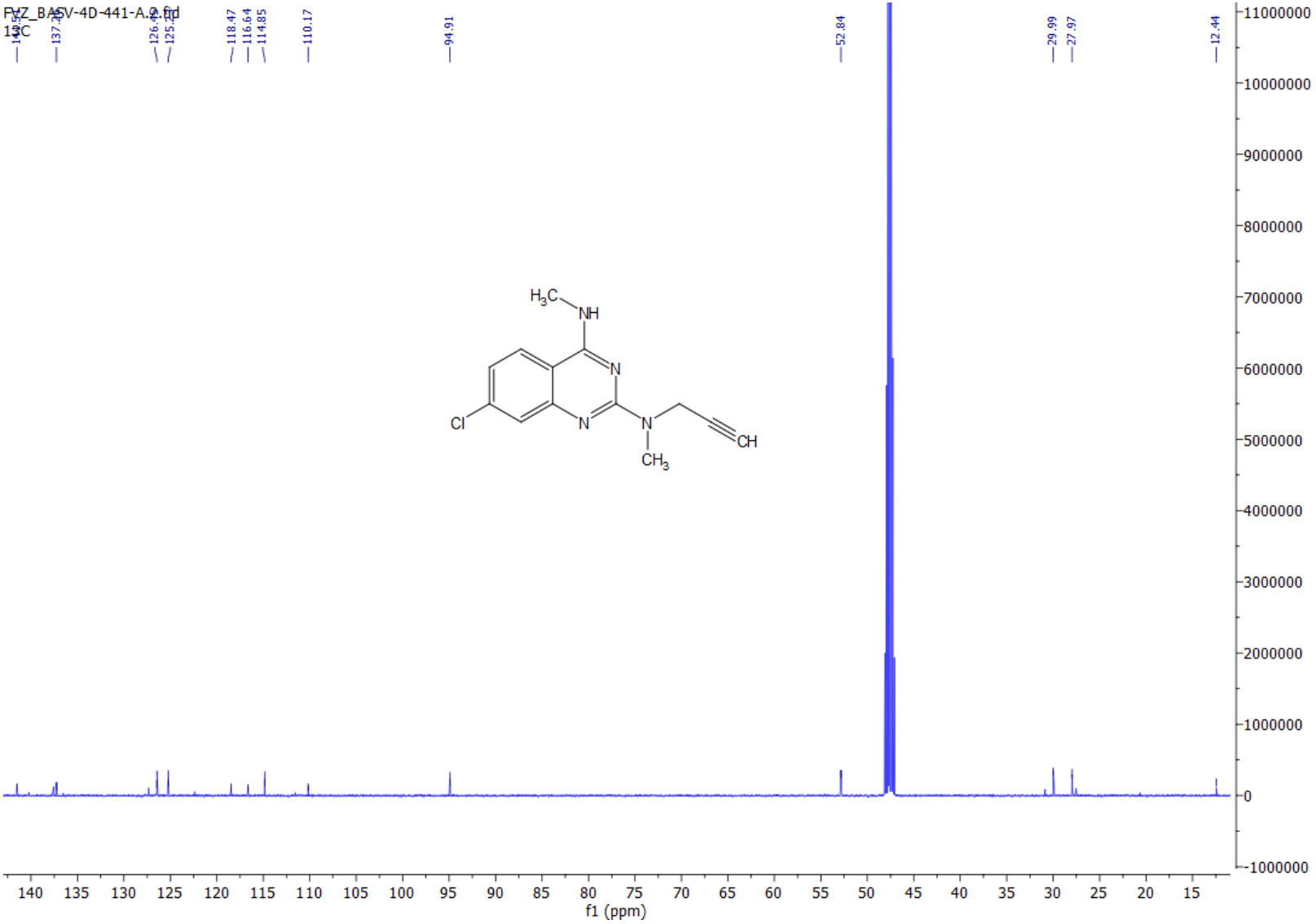


Fig. S62. ^{1}H NMR of 7-chloro-*N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6c)

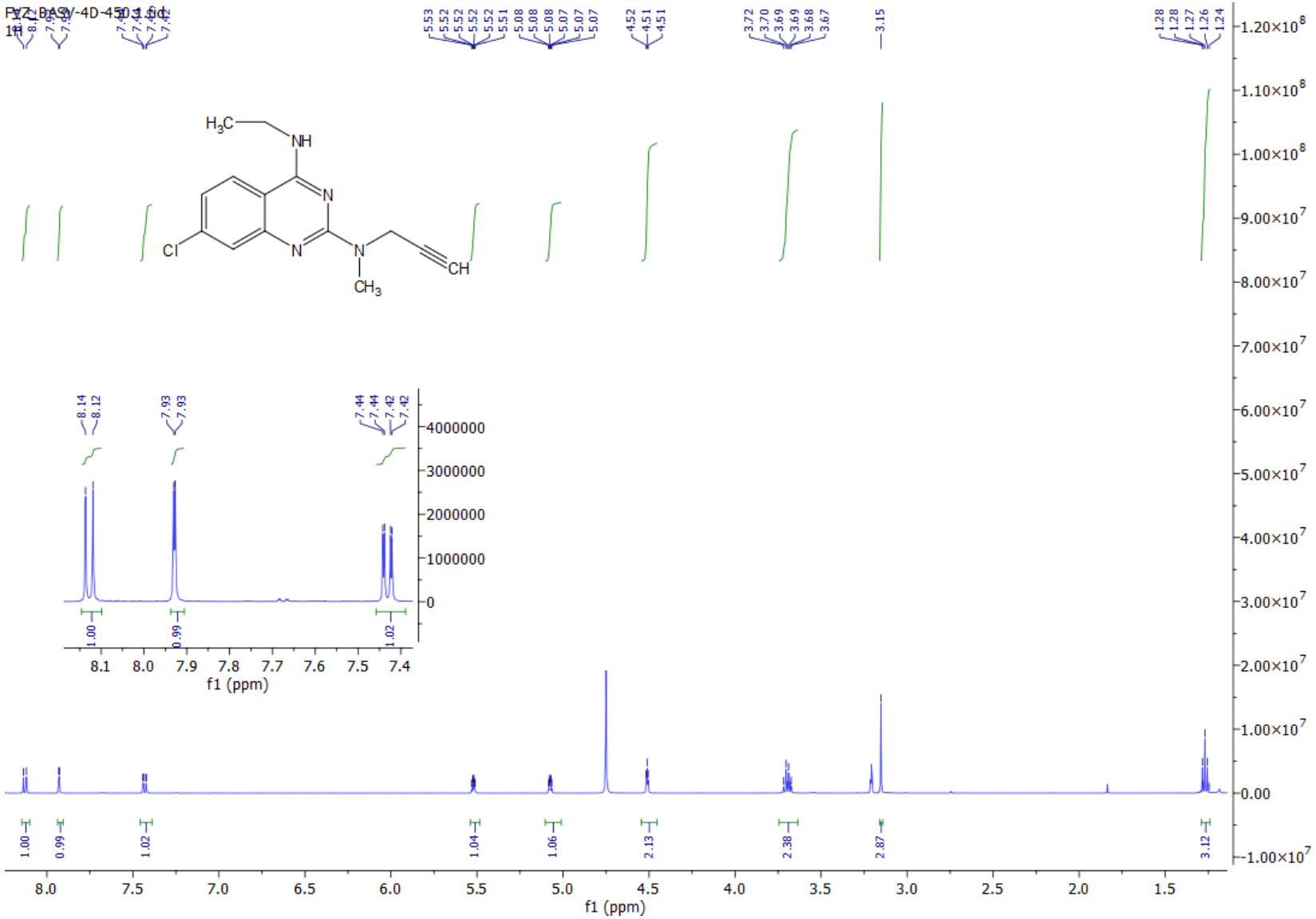


Fig. S63. ^{13}C NMR of 7-chloro-*N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6c)

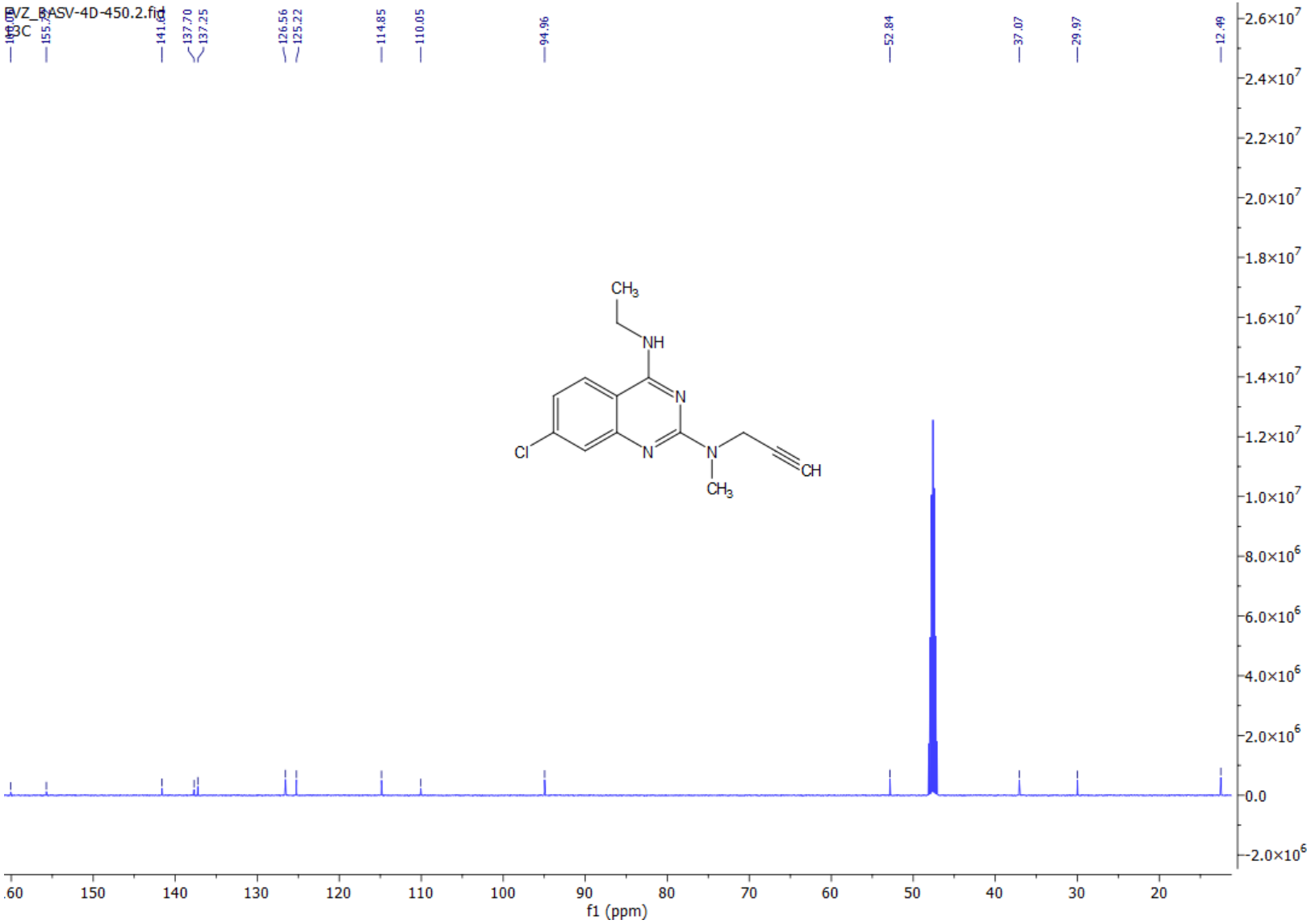


Fig. S64. ^{1}H NMR of 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (II-6d)

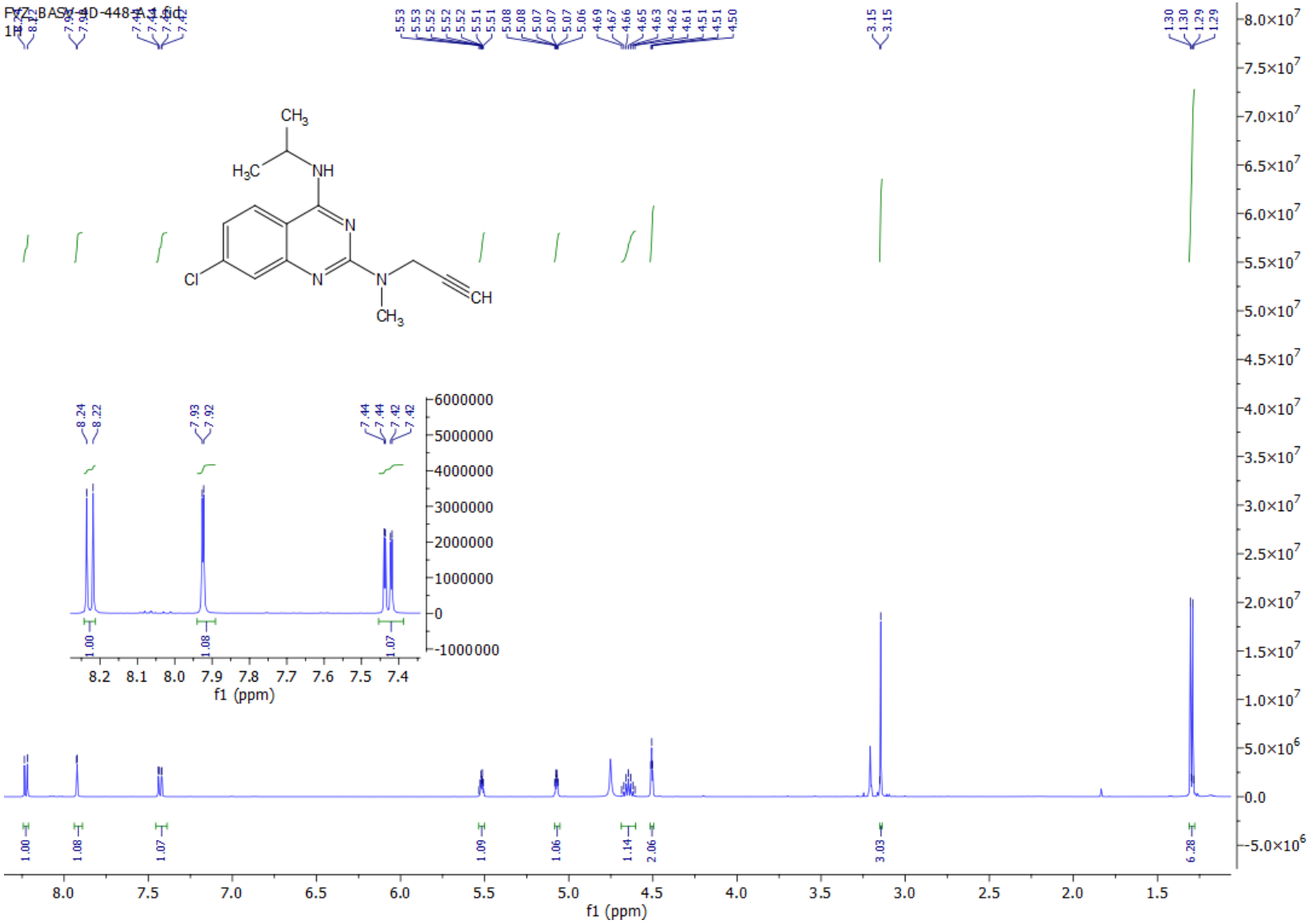


Fig. S65. ^{13}C NMR of 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (II-6d)

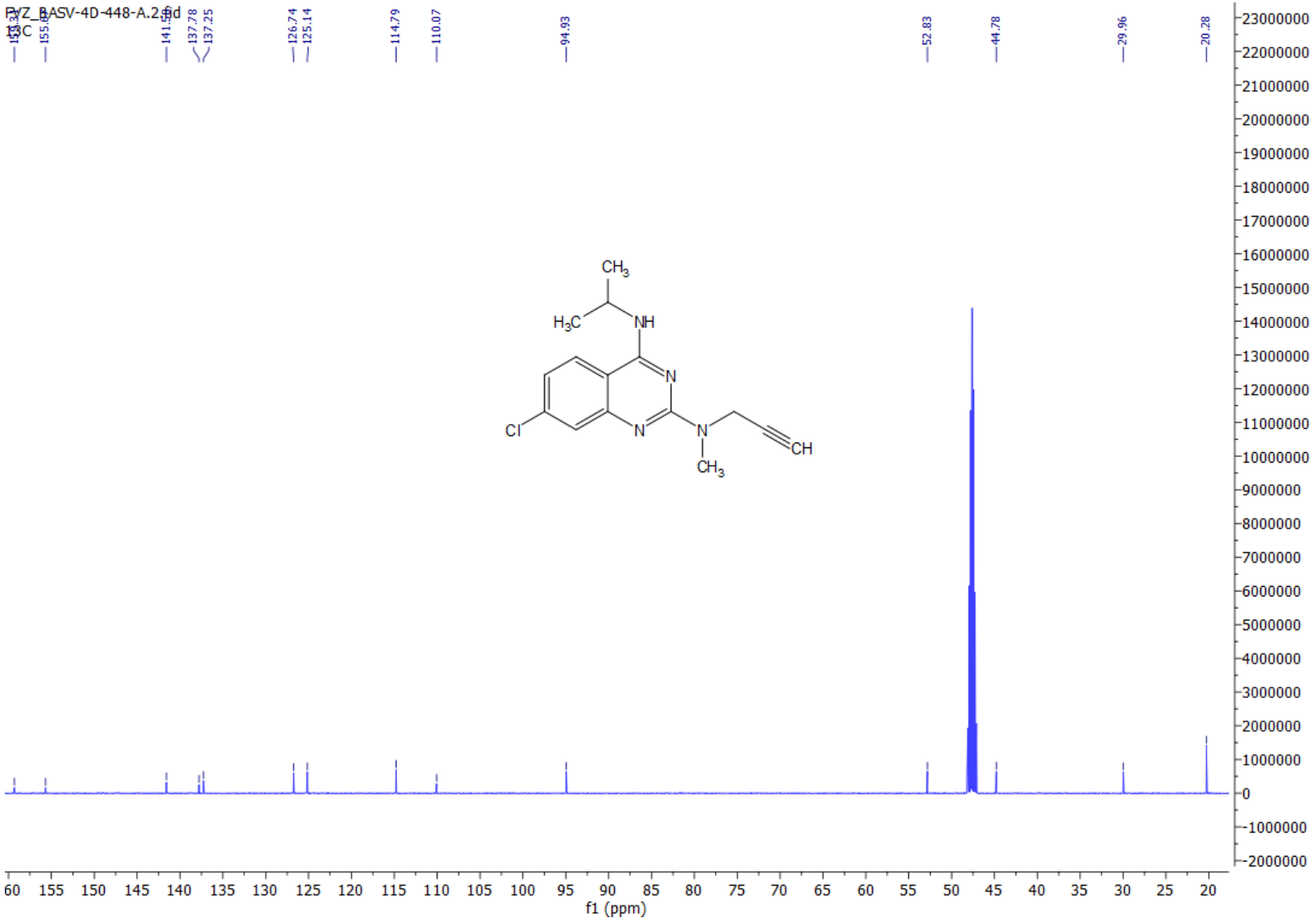


Fig. S66. ^{1}H NMR of *N4*-butyl-7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6e)

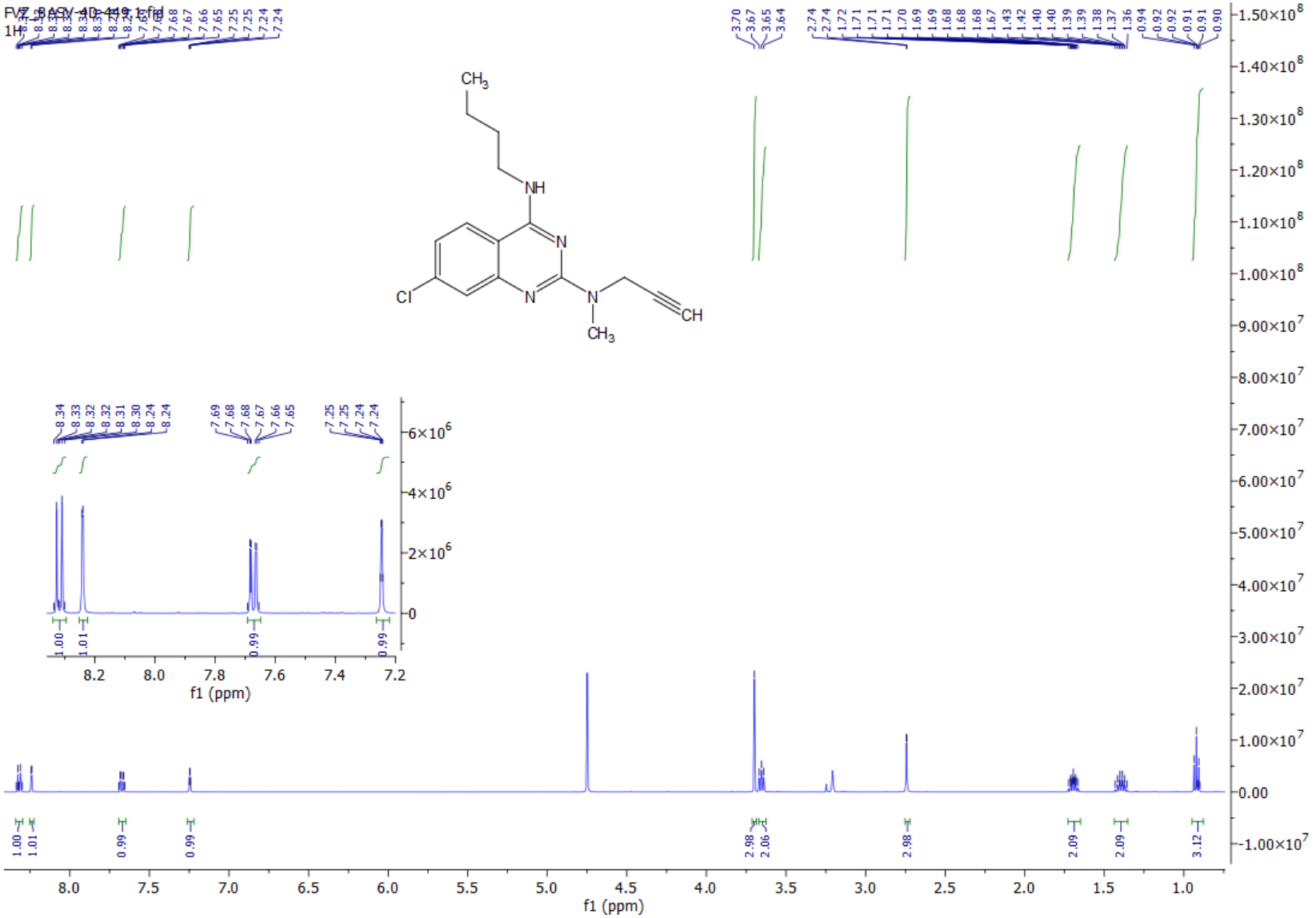


Fig. S67. ^{13}C NMR of *N4*-butyl-7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6e)

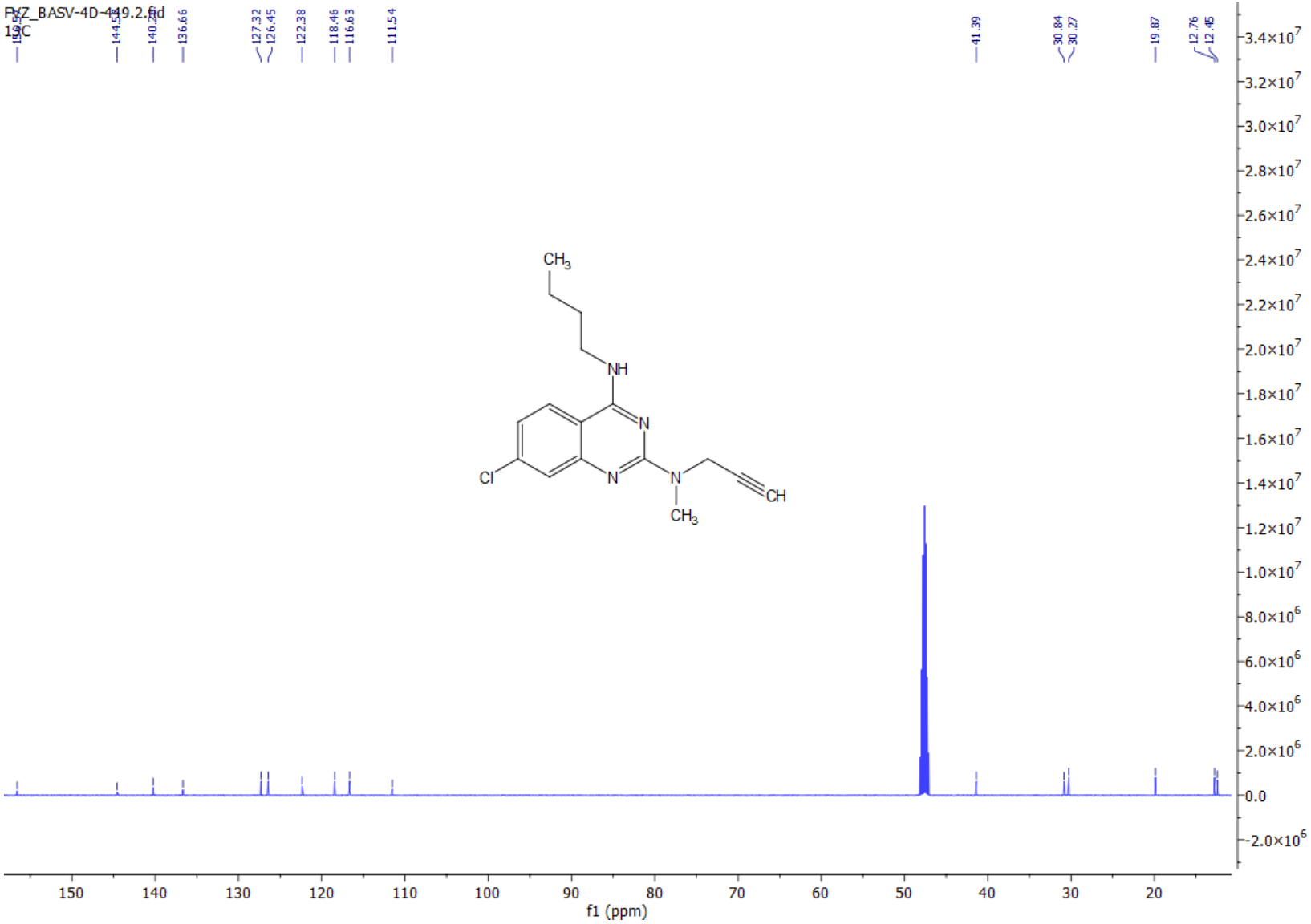


Fig. S68. ^{1}H NMR of 7-chloro-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6f)

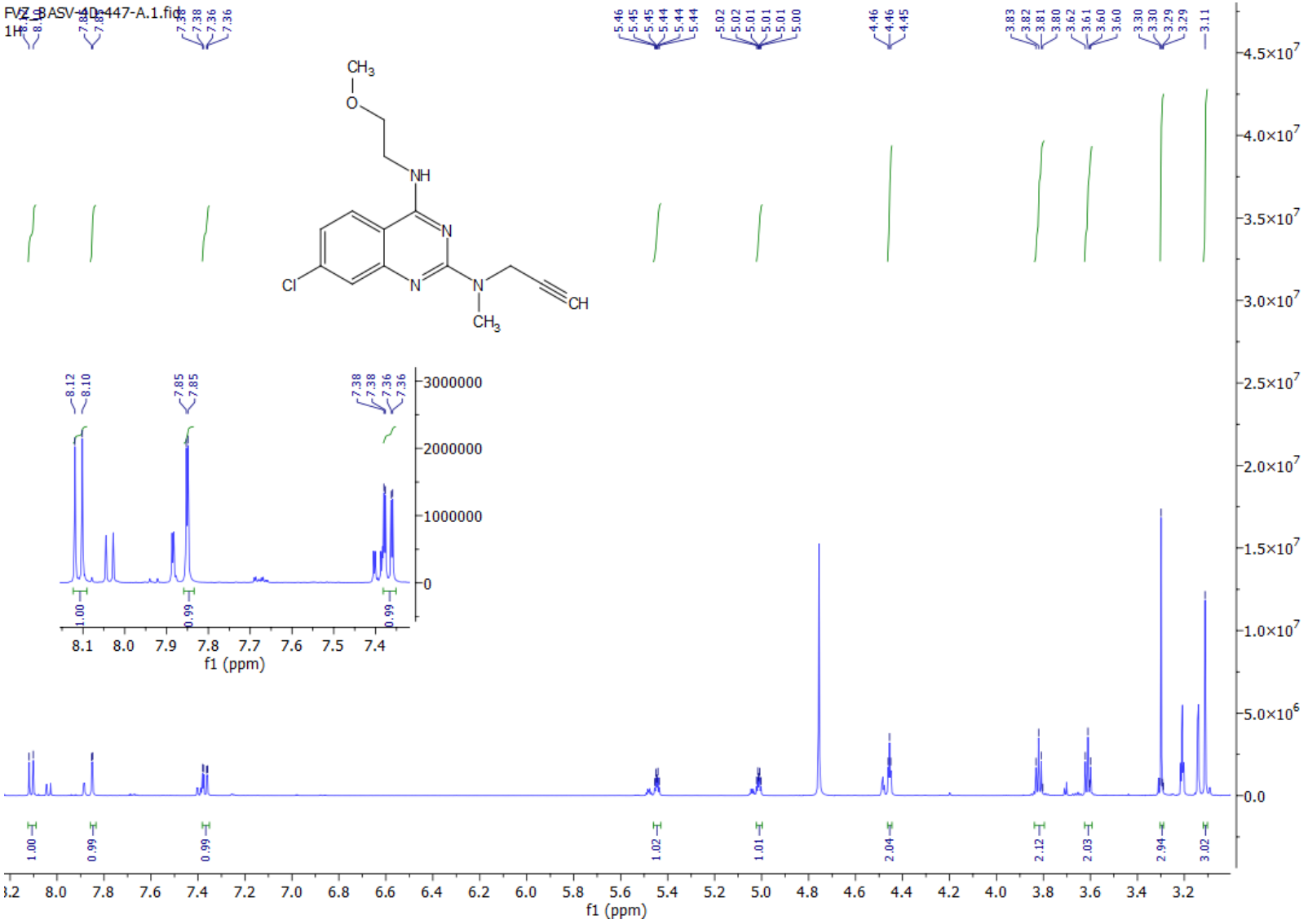


Fig. S69. ^{13}C NMR of 7-chloro-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6f)

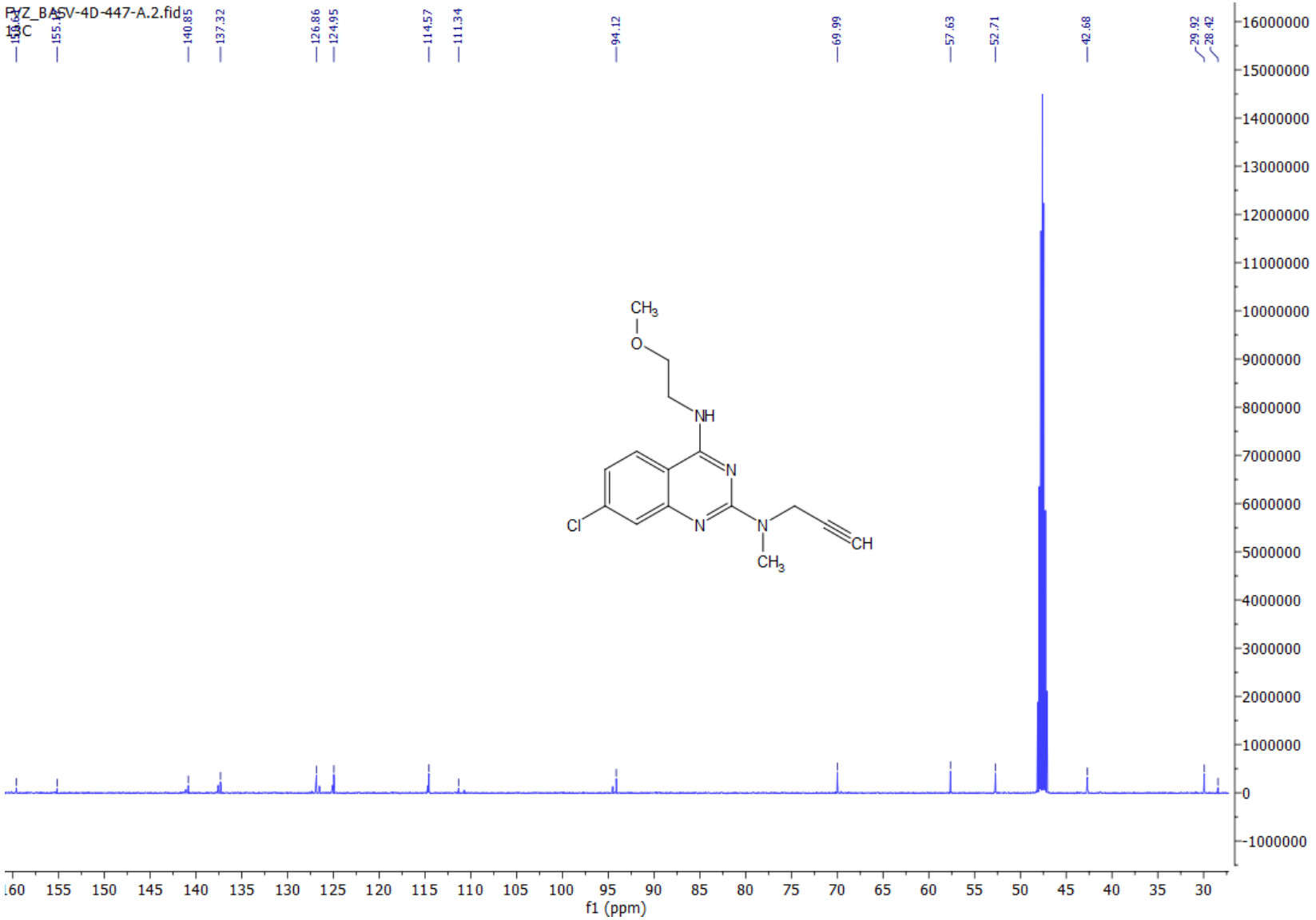


Fig. S70. ^{1}H NMR of 7-chloro-*N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6g)

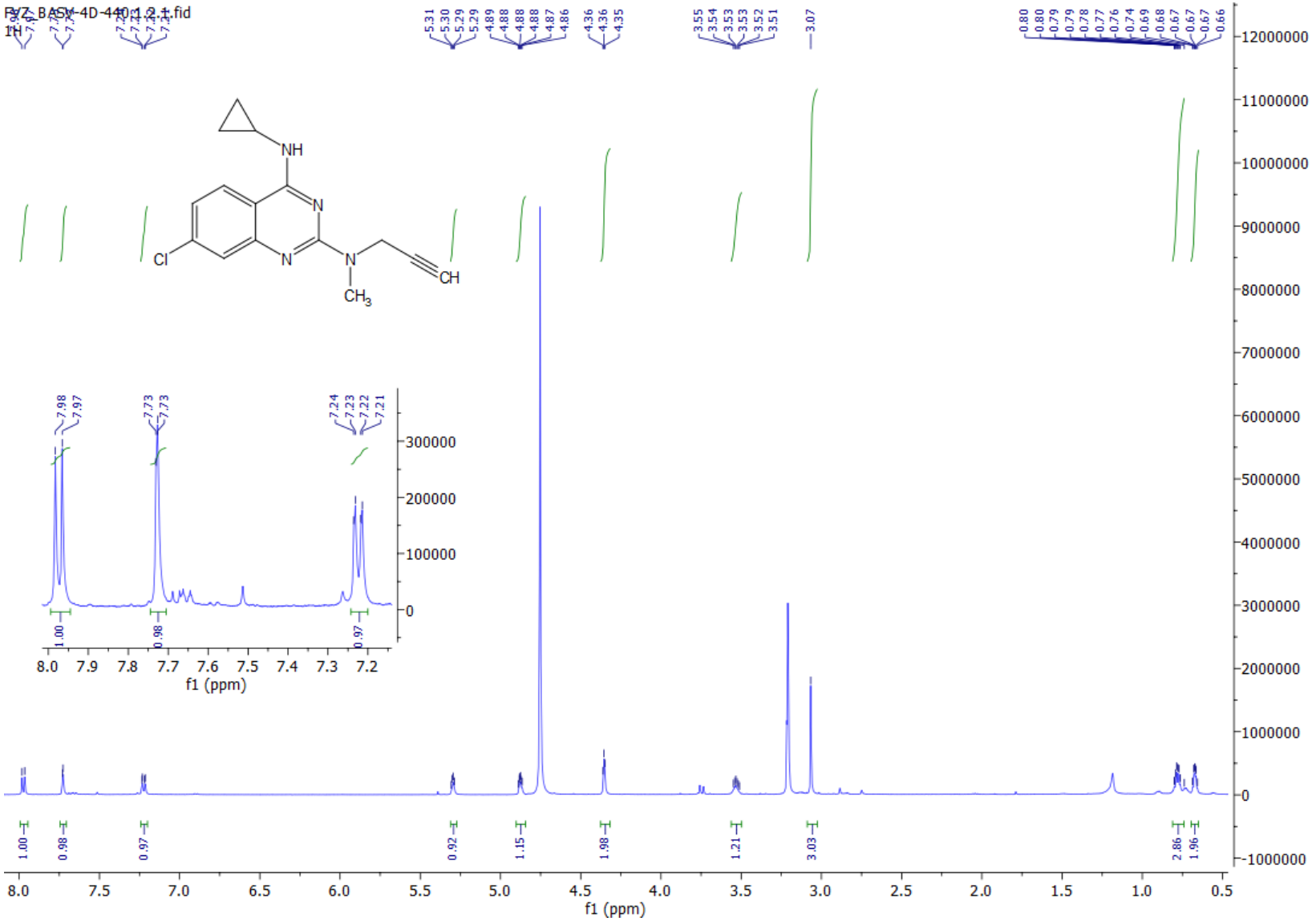


Fig. S71. ^{13}C NMR of 7-chloro-*N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6g)

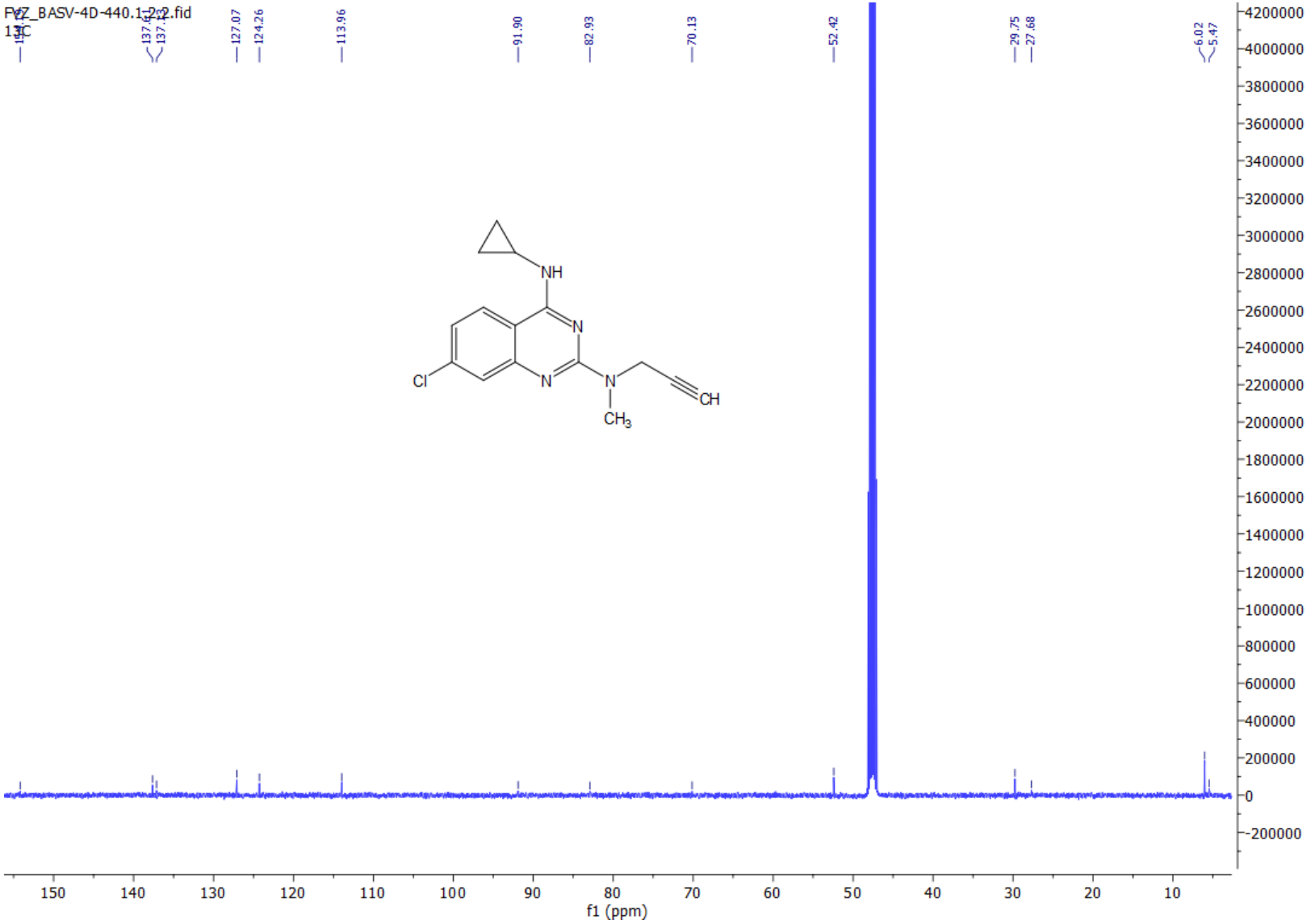


Fig. S72. ^{1}H NMR of 7-chloro-*N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6h)

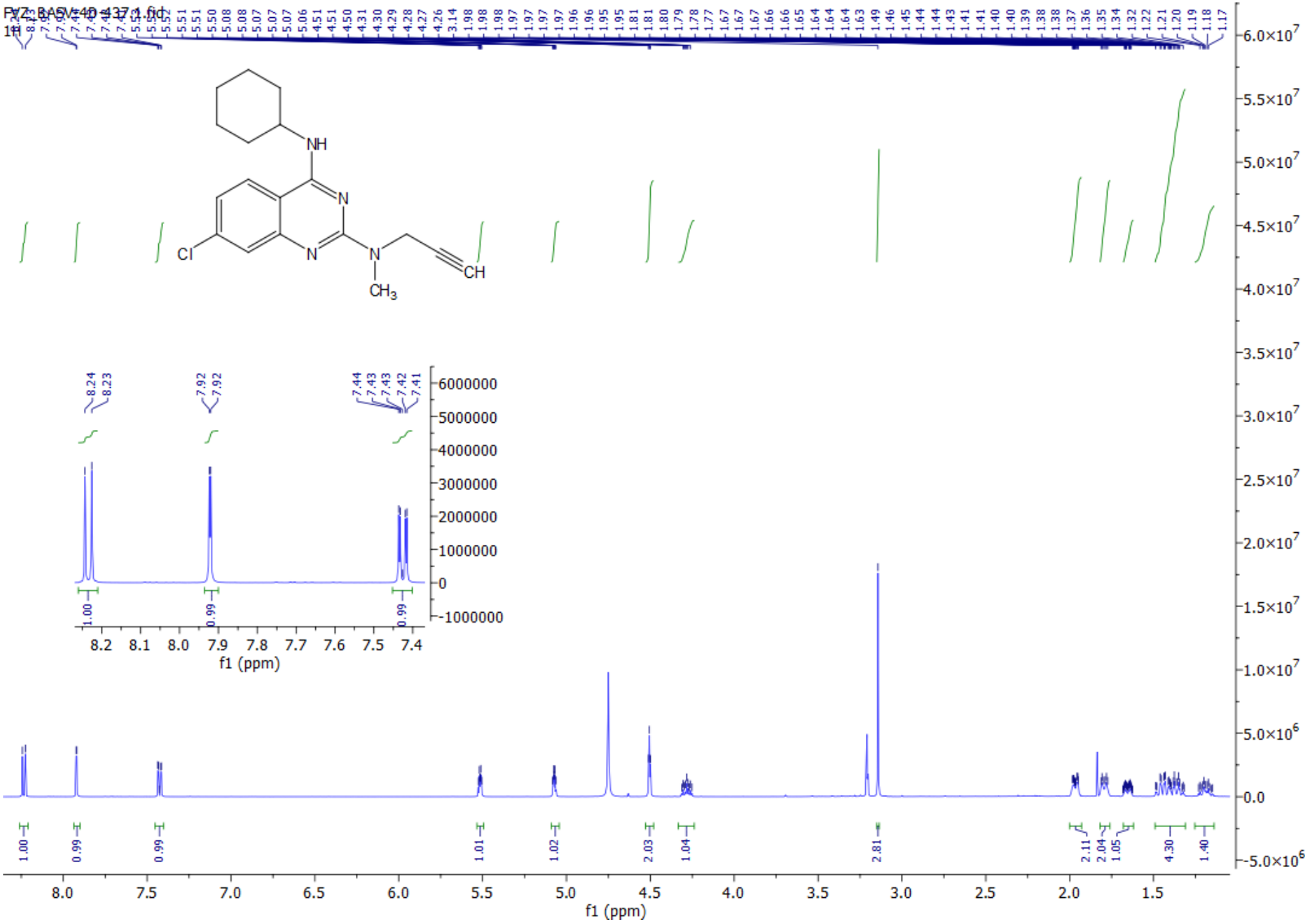


Fig. S73. ^{13}C NMR of 7-chloro-*N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6h)

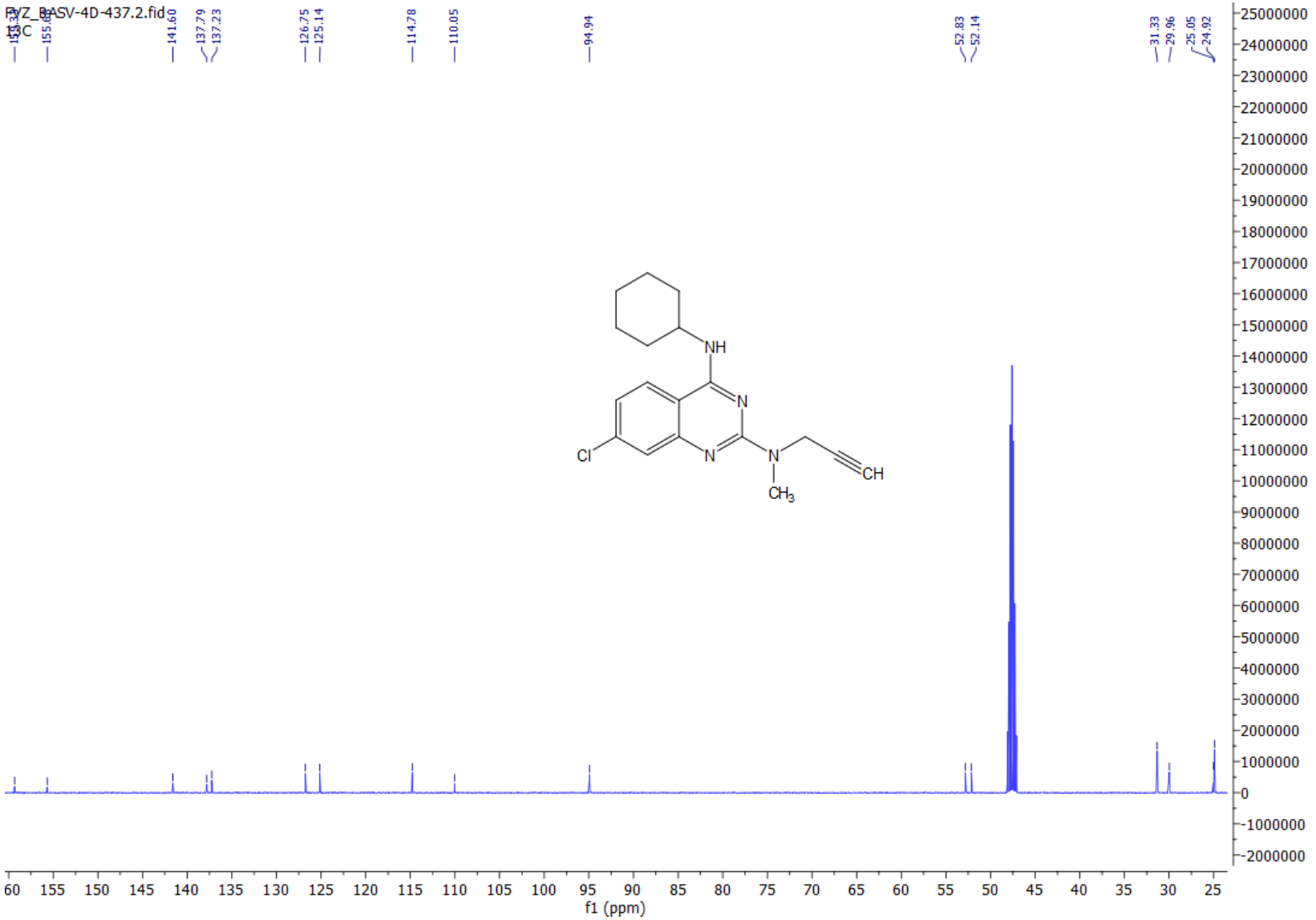


Fig. S74. ^{1}H NMR of 6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6a)

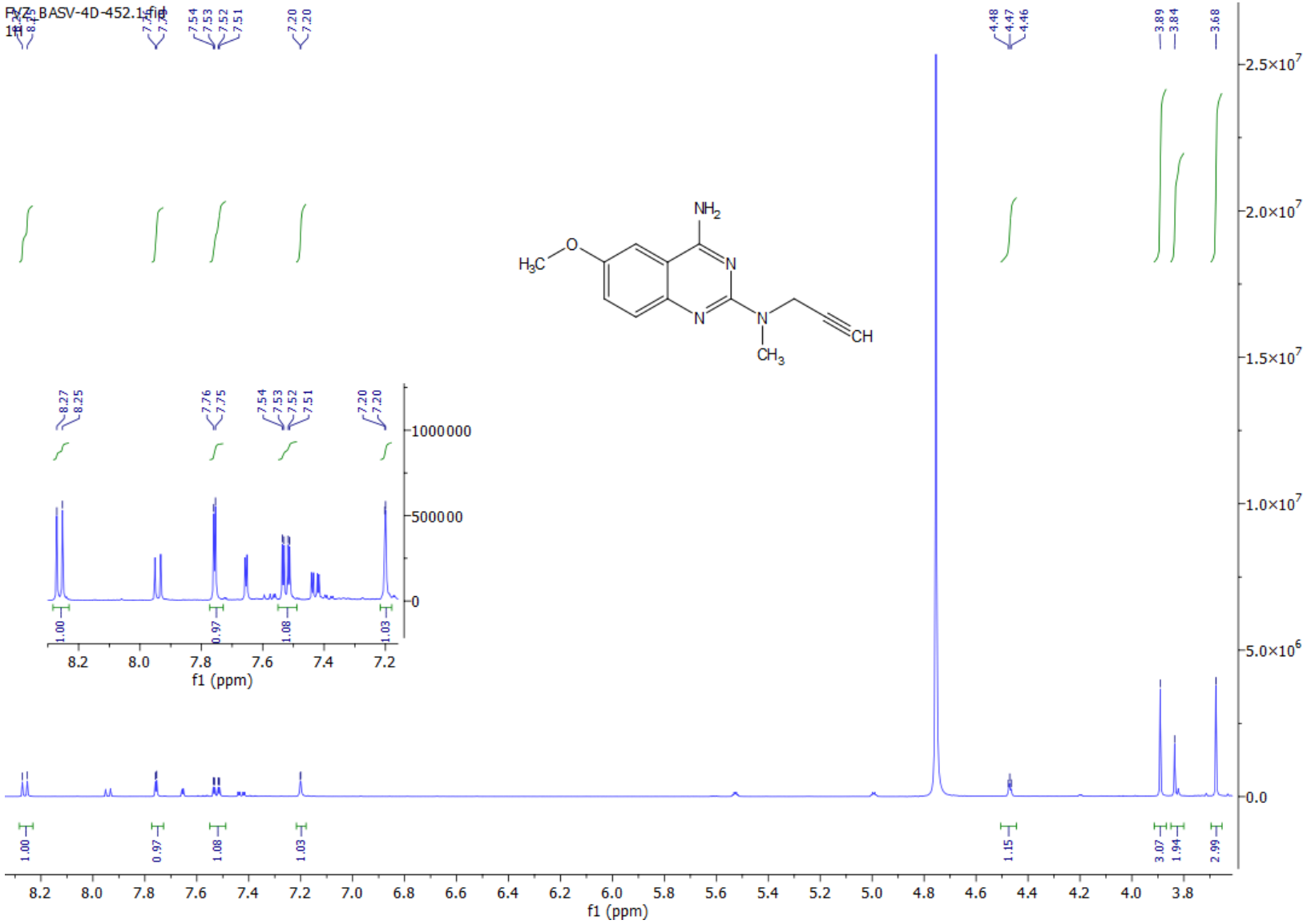


Fig. S75. ^{13}C NMR of 6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6a)

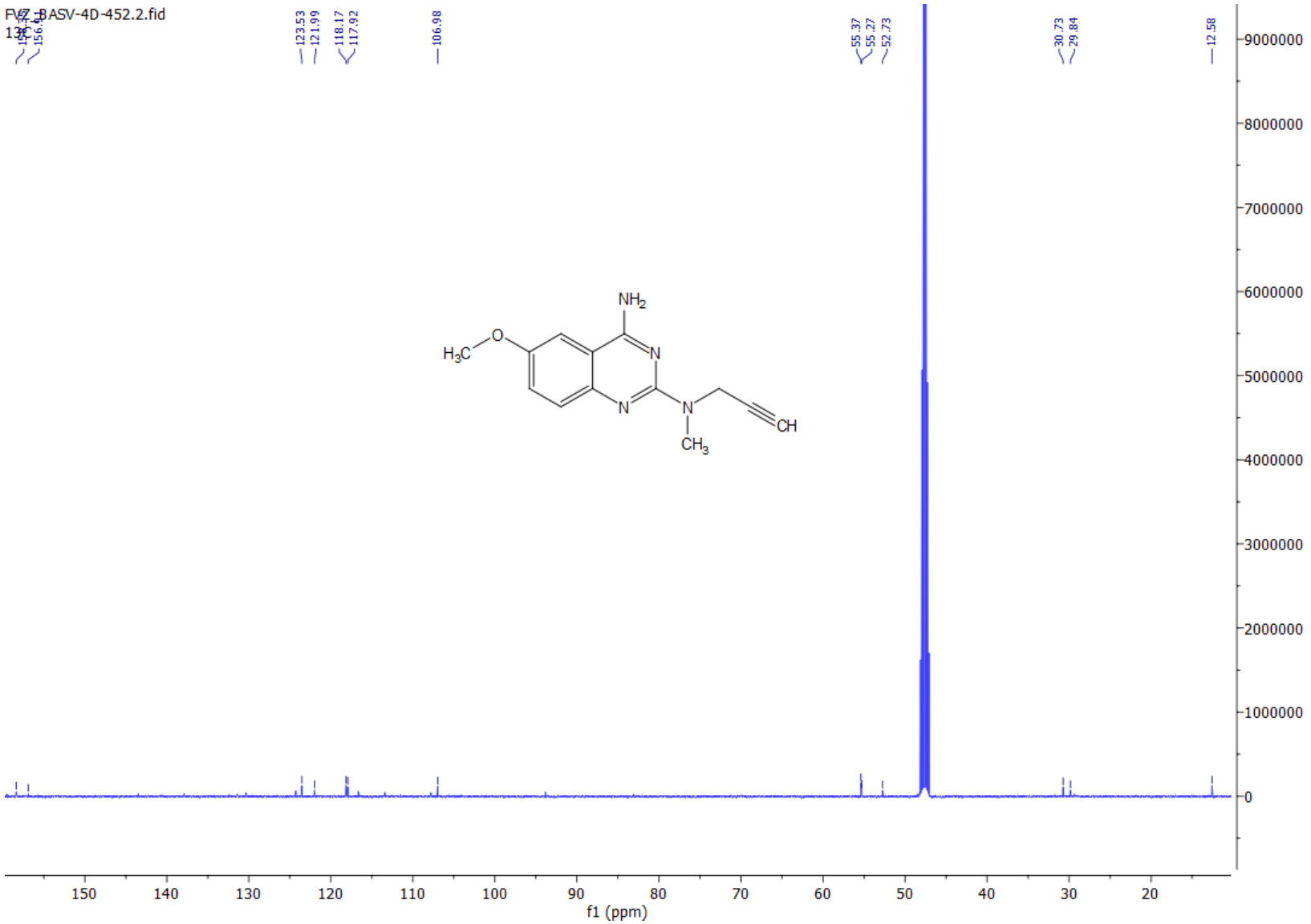


Fig. S76. ^{1}H NMR of 6-methoxy-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6b)

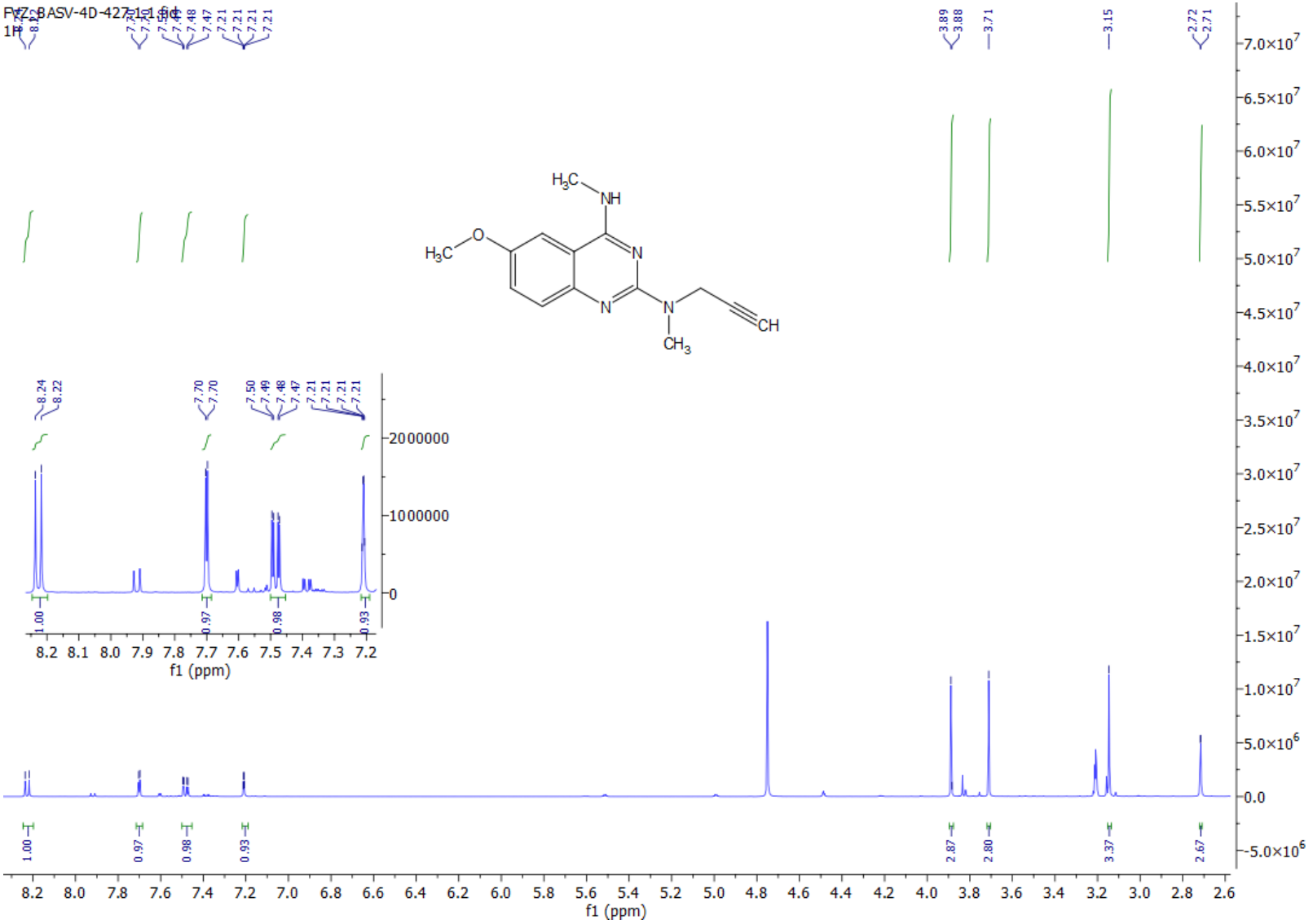


Fig. S77. ^{13}C NMR of 6-methoxy-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6b)

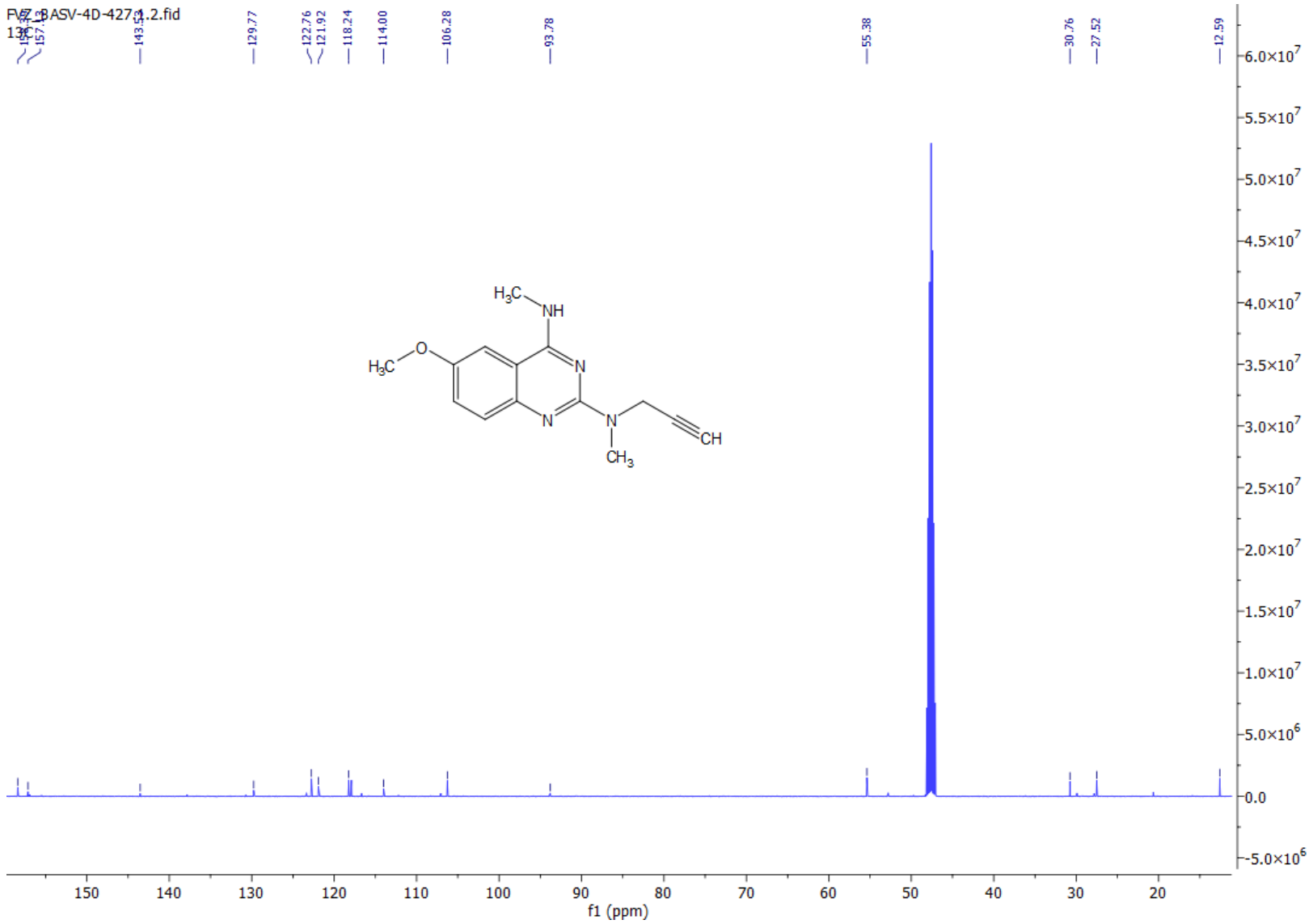


Fig. S78. ^{1}H NMR of *N4*-ethyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6c)

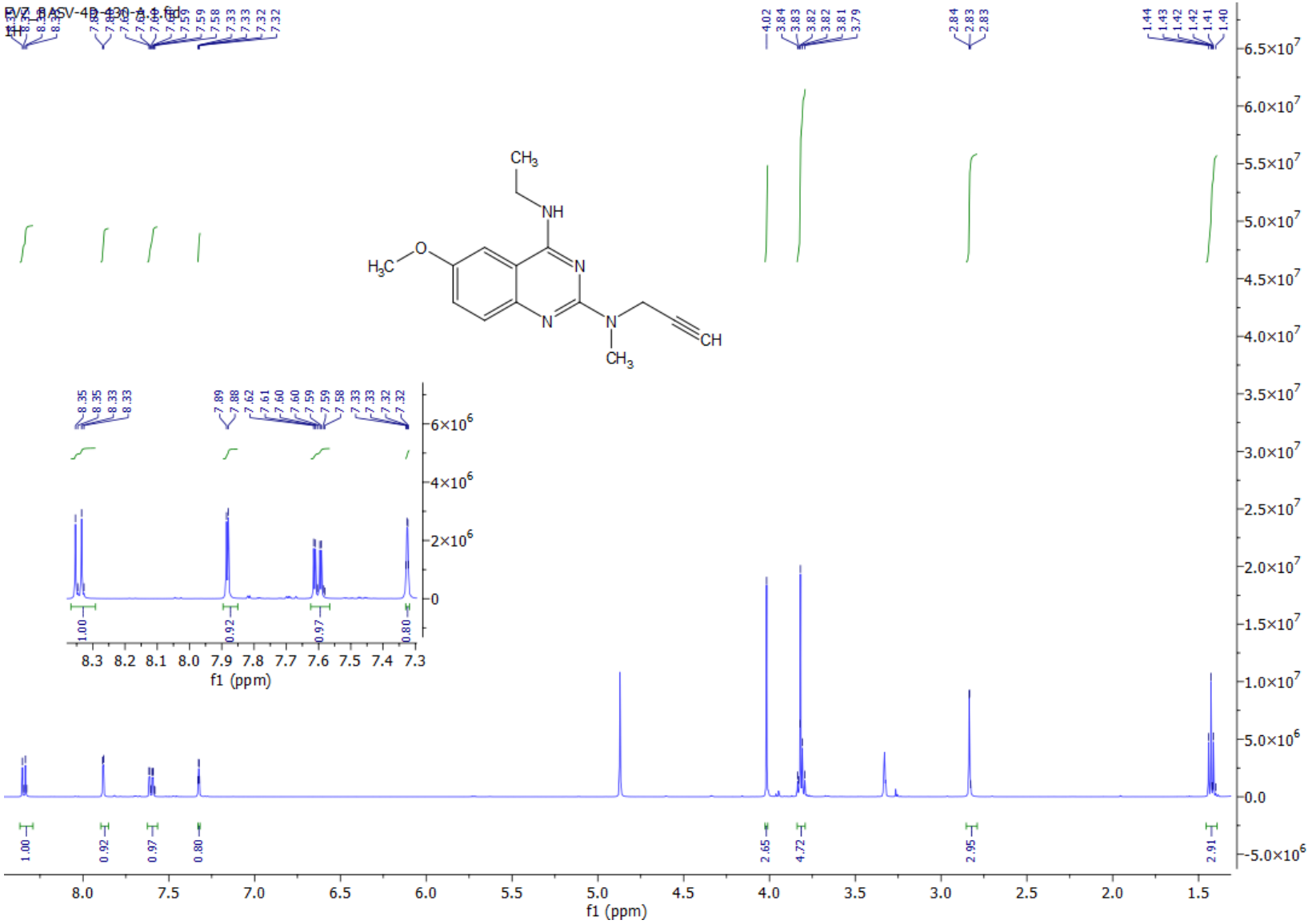


Fig. S79. ^{13}C NMR of *N4*-ethyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6c)

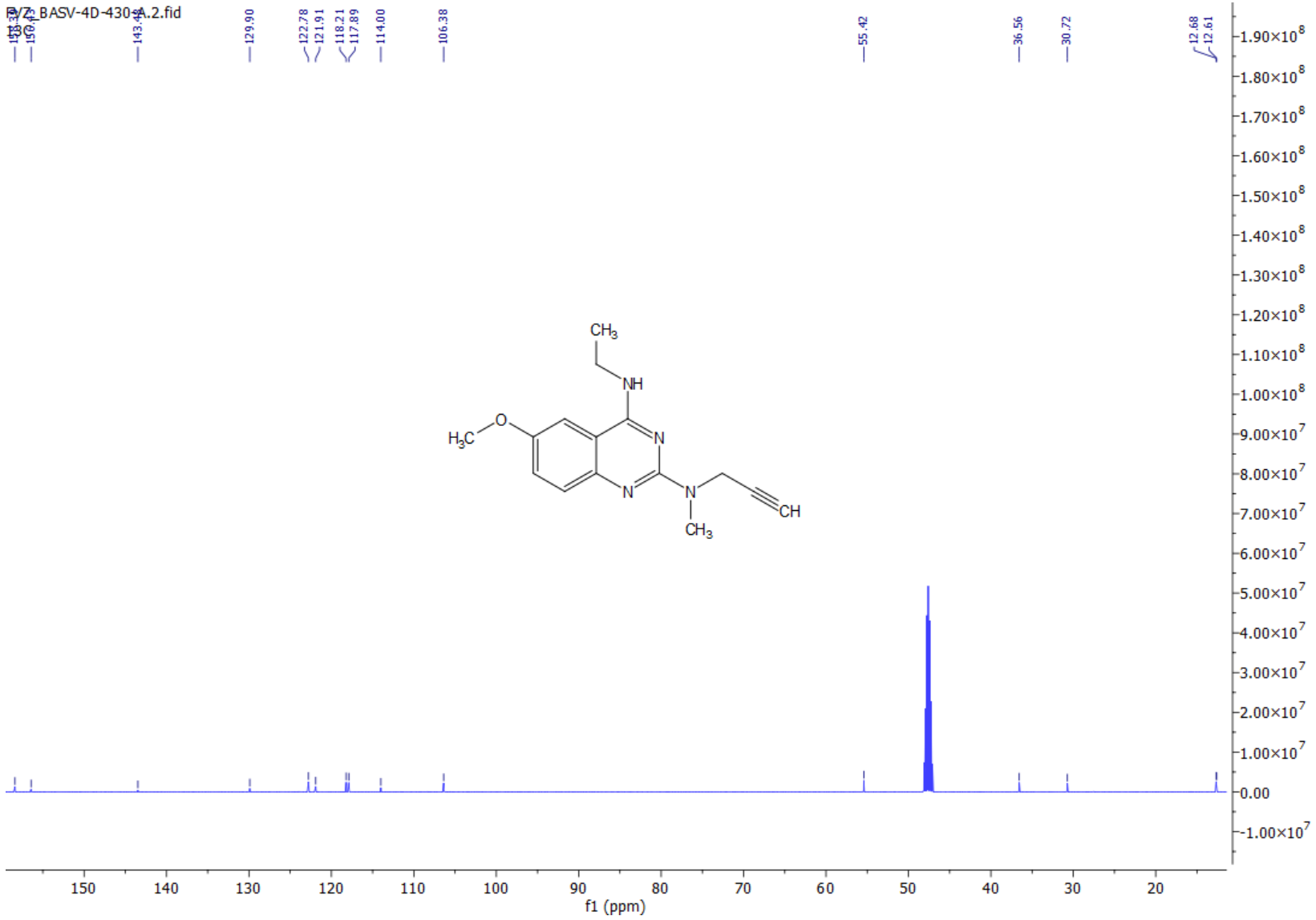


Fig. S80. ^{1}H NMR of -methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (III-6d)

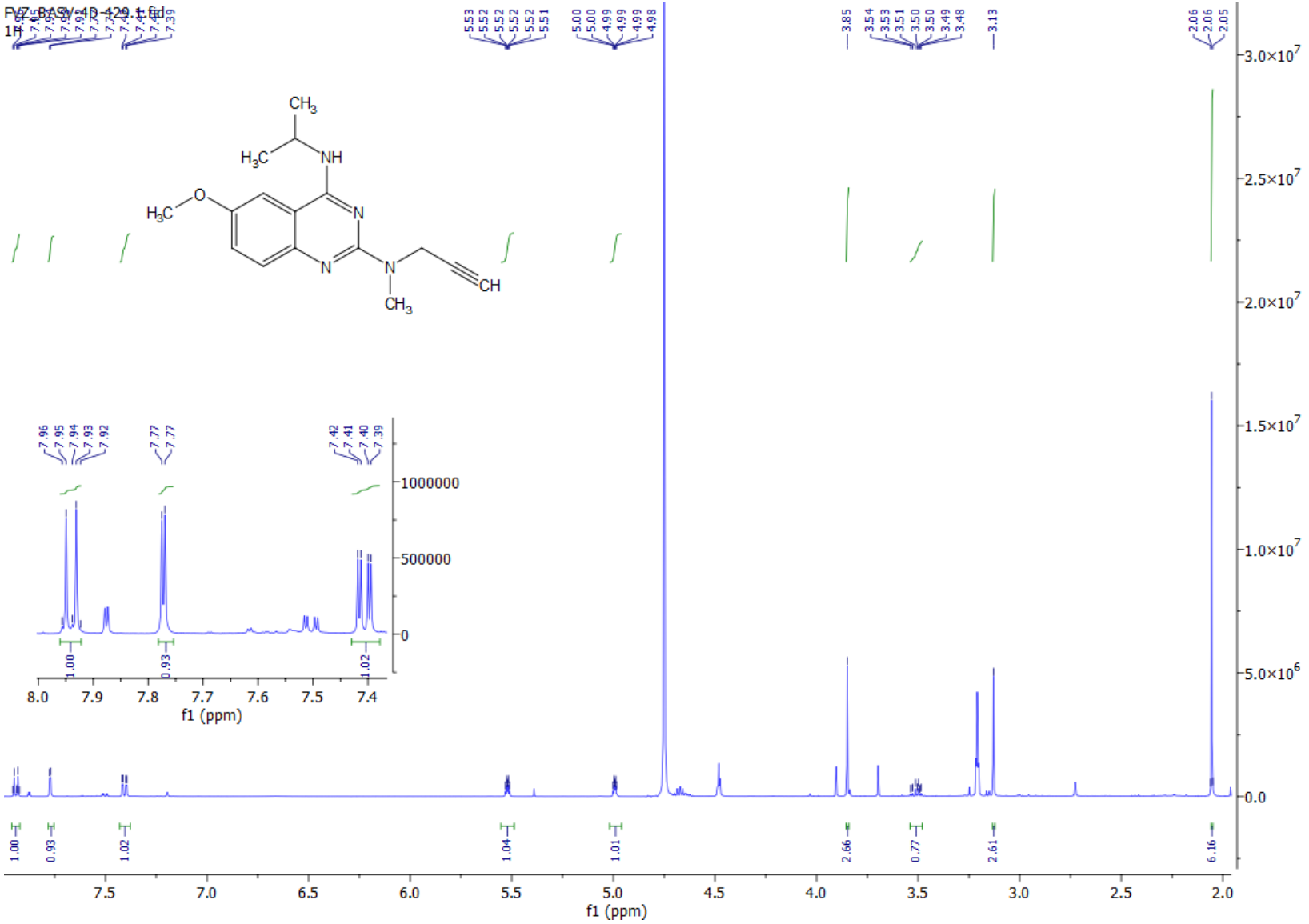


Fig. S81. ^{13}C NMR of -methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (III-6d)

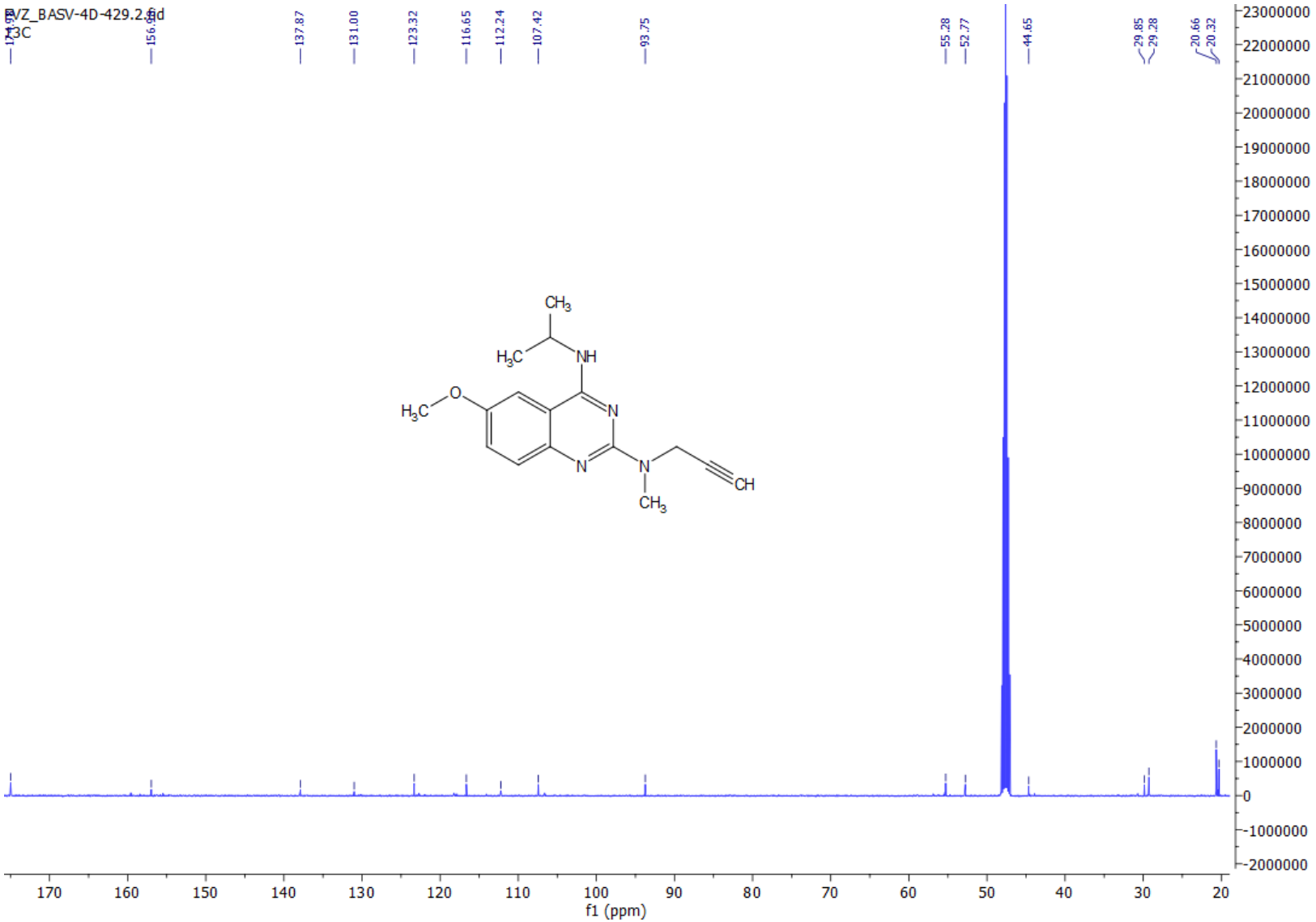


Fig. S82. ^{1}H NMR of *N4*-butyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6e)

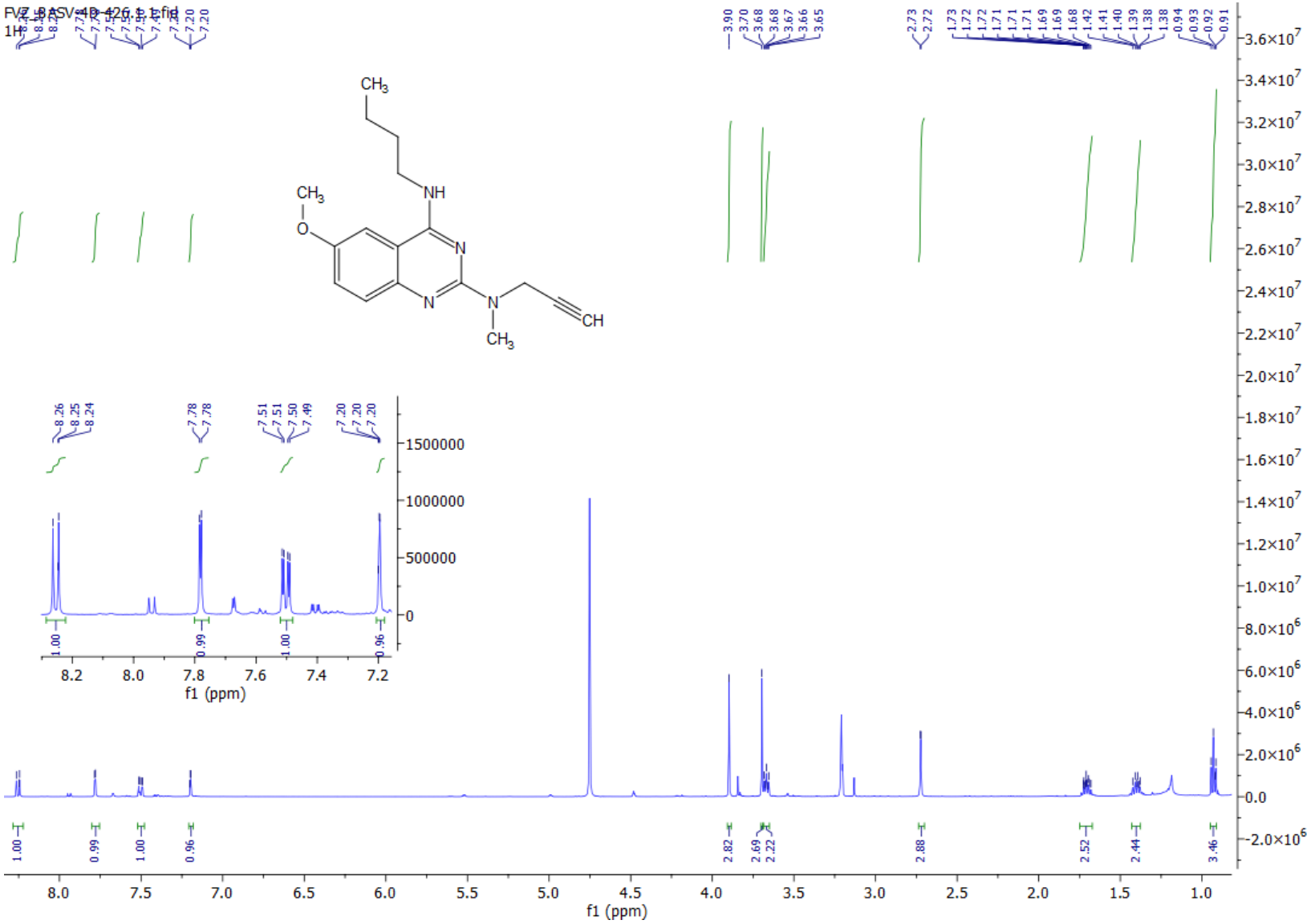


Fig. S83. ^{13}C NMR of *N4*-butyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6e)

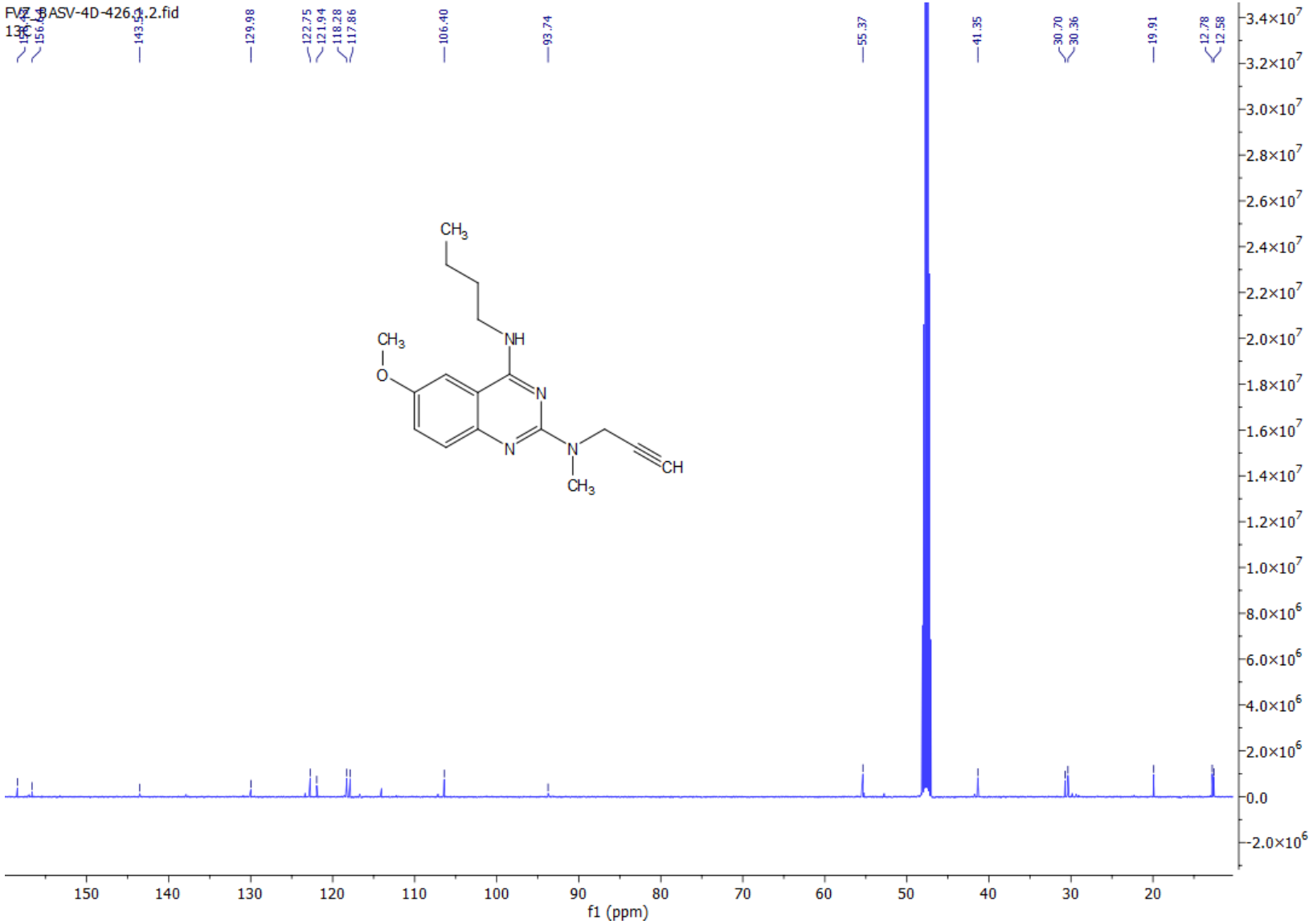


Fig. S84. ^{1}H NMR of 6-methoxy-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6f)

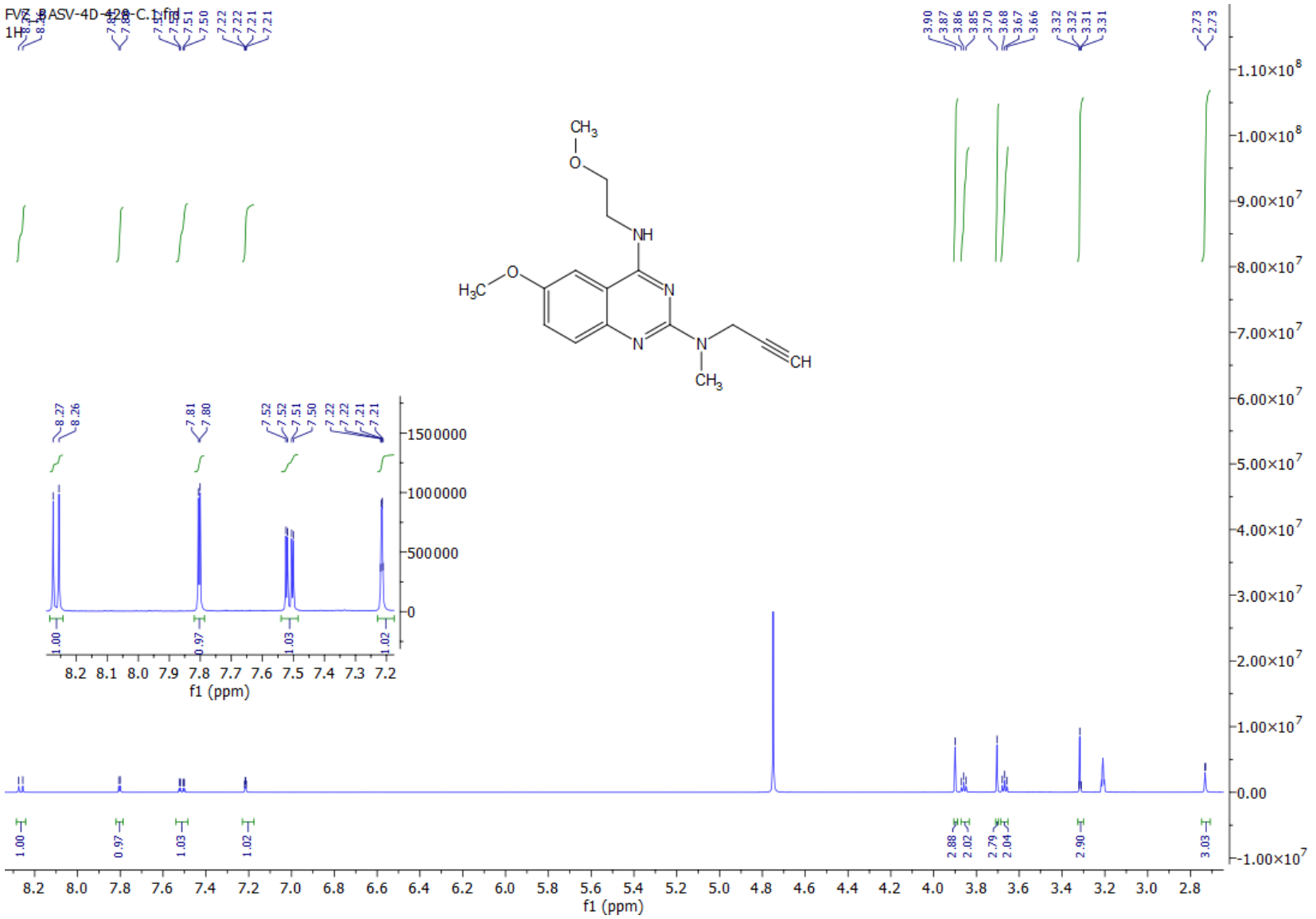


Fig. S85. ^{13}C NMR of 6-methoxy-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6f)

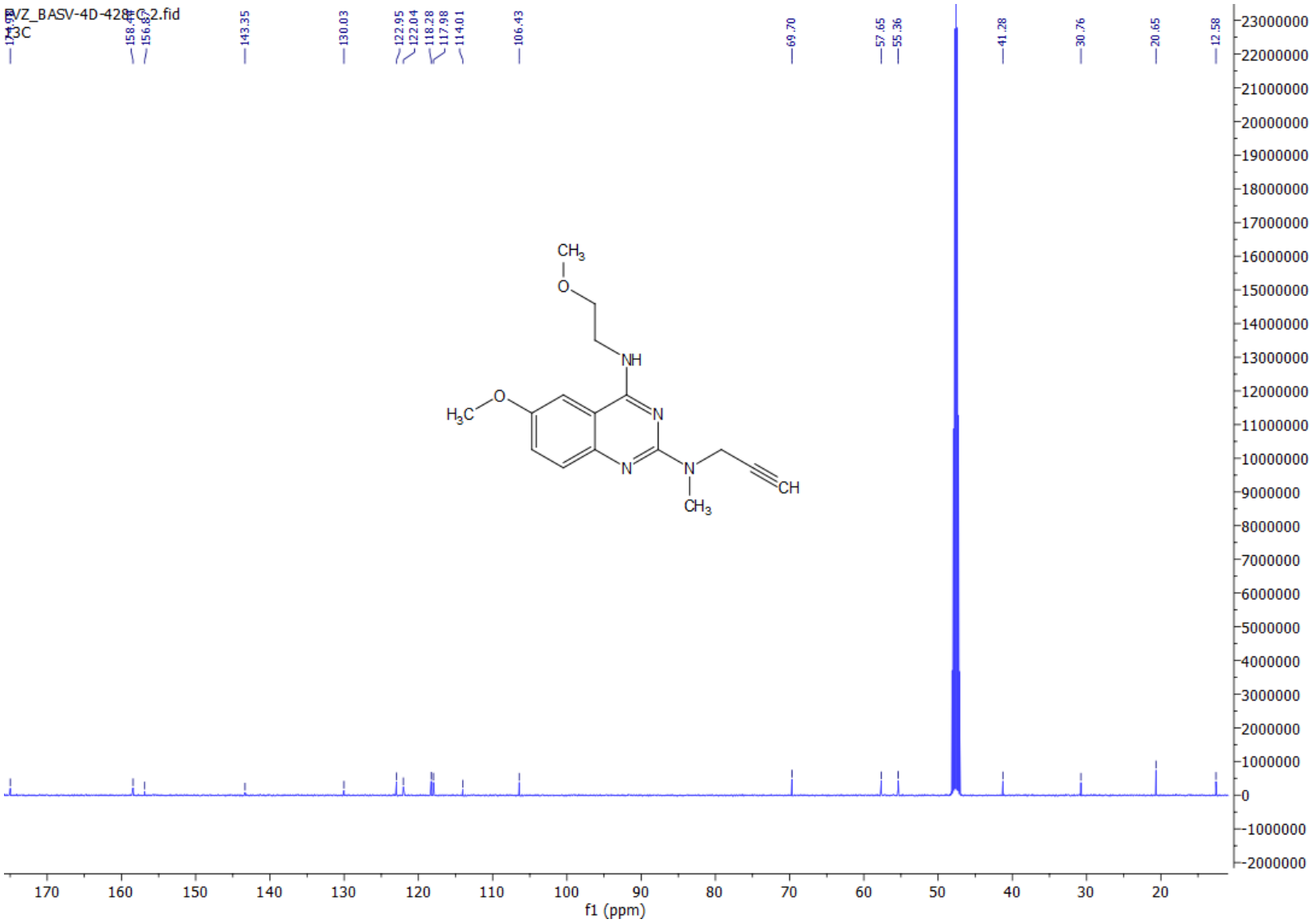


Fig. S86. ^{1}H NMR of *N4*-cyclopropyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6g)

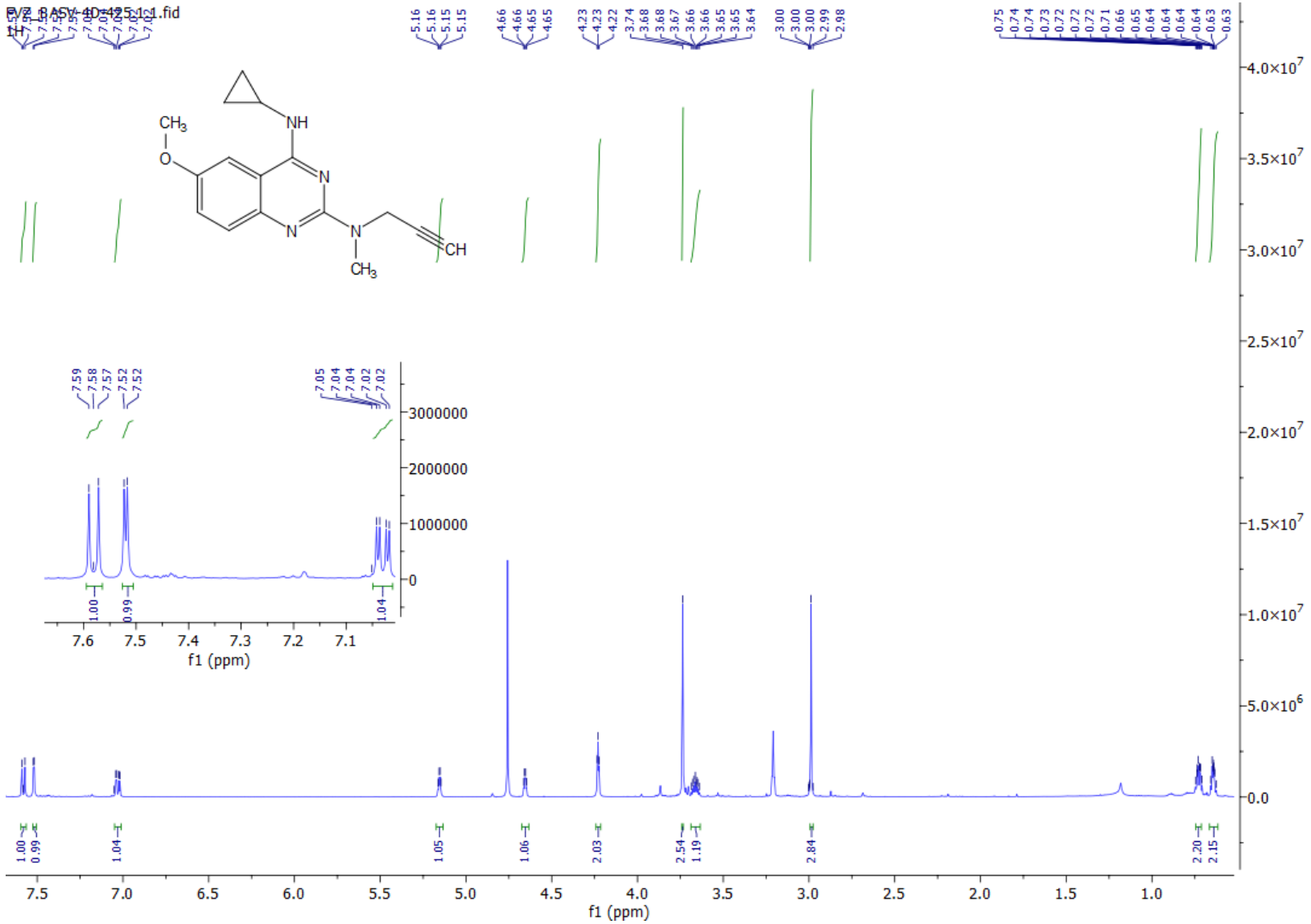


Fig. S87. ^{13}C NMR of *N4*-cyclopropyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6g)

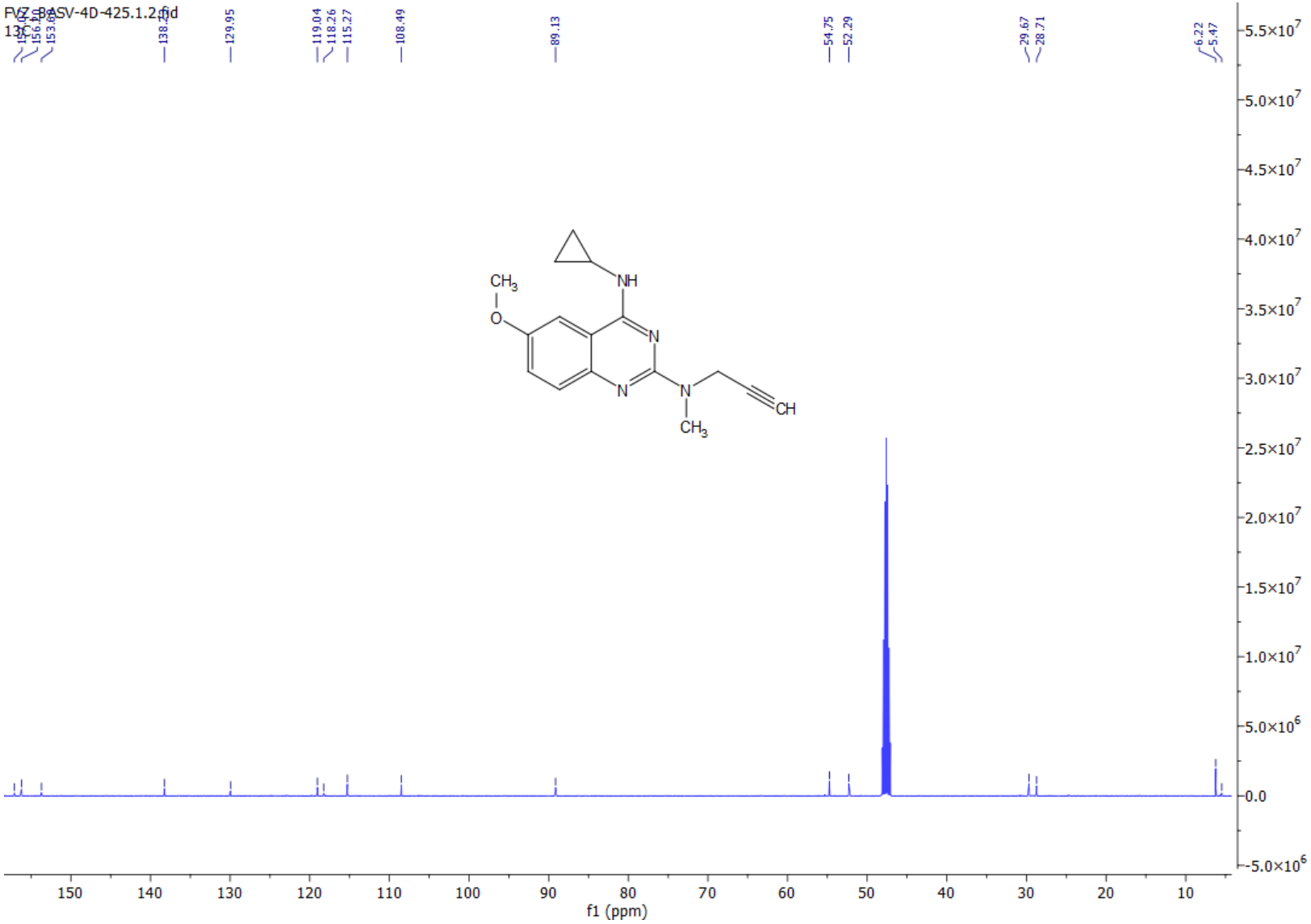


Fig. S88. ^{1}H NMR of *N4*-cyclohexyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6h)

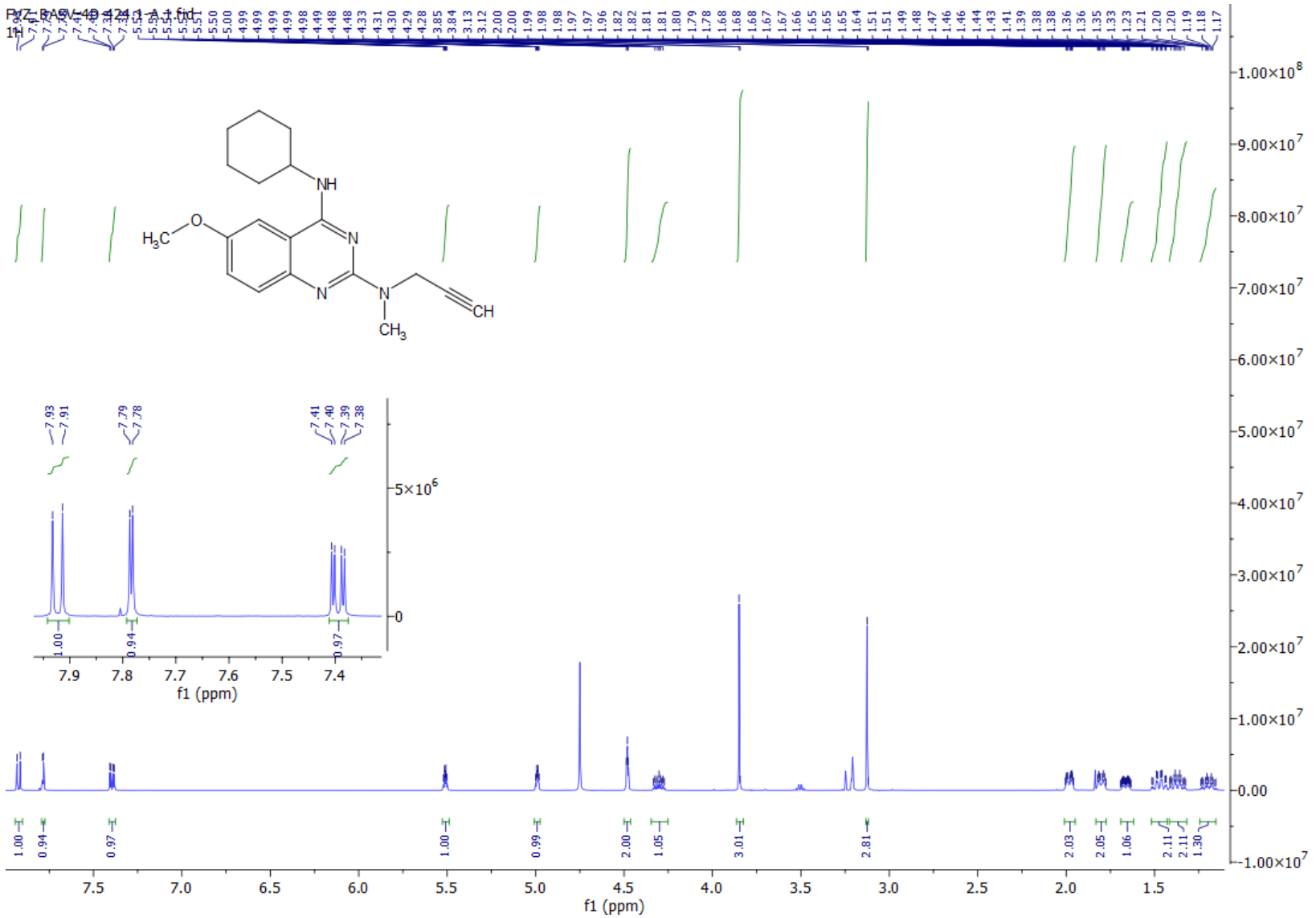
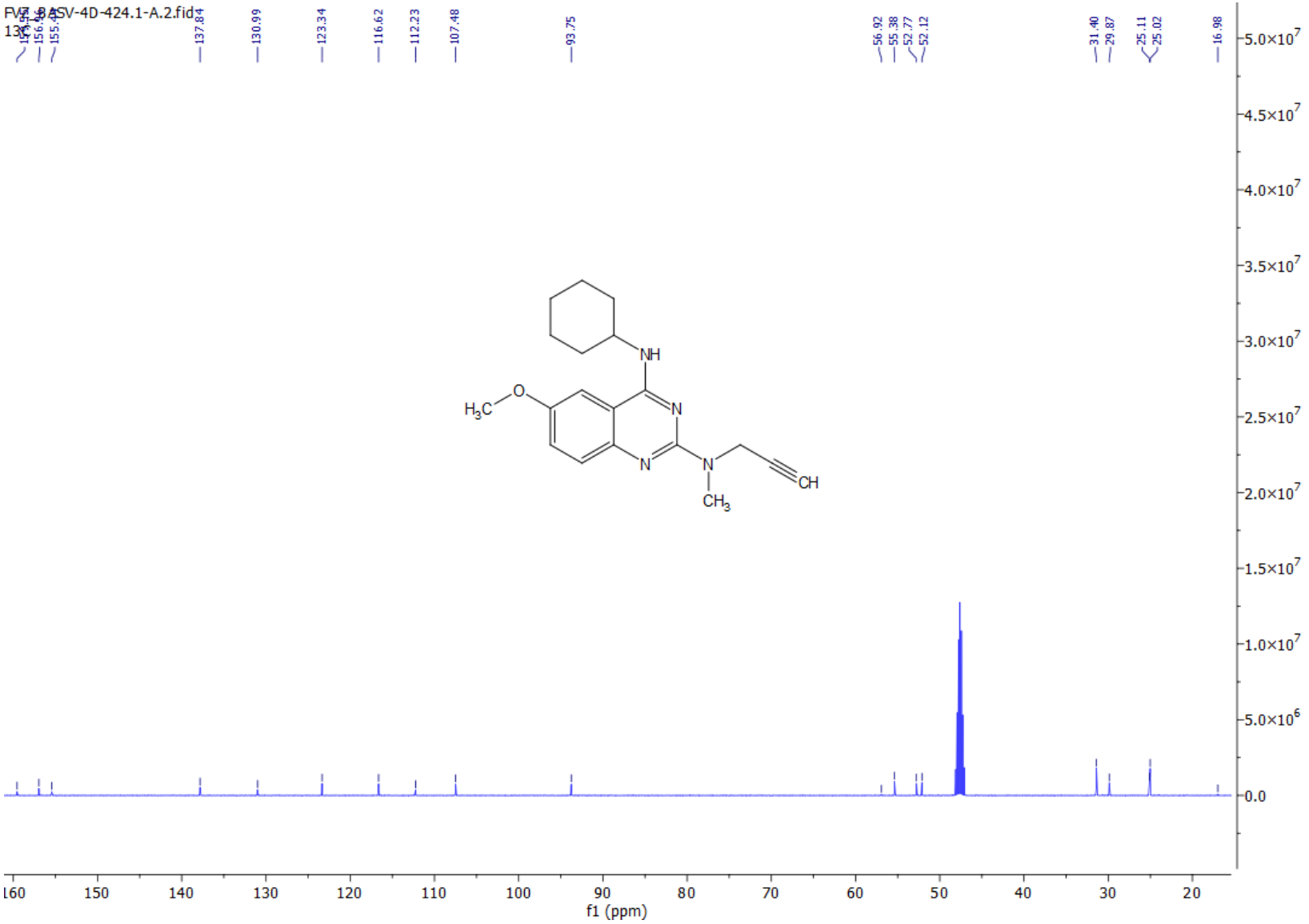


Fig. S89. ^{13}C NMR of *N4*-cyclohexyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6h)



5. HPLC Analysis of Compounds

High performance liquid chromatography (HPLC) with mass spectrometry (MS) was used to determine high resolution mass spectra (HRMS) and purity of compounds.

LC-MS Instrumentation

The system used in this study was Dionex Ultimate 3000 UHPLC: RS LPG quaternary Pump, RS Column Compartment, RS Autosampler, Diode Array Detector, Chromeleon (version 7.2.9 build 11323) software with Q Exactive Plus Orbitrap mass spectrometer with Thermo Xcalibur (version 4.3.73.11) software (Thermo Fisher Scientific, Waltham, MA, USA). Settings of heated electrospray source were: Spray voltage 3.5 kV, Capillary temperature: 260 °C, Sheath gas: 50 arbitrary units, Auxiliary gas: 12.5 arbitrary units, Spare gas: 2.5 arbitrary units, Probe heater temperature: 300 °C, Max spray current: 100 μA, S-lens RF Level: 50.

HRMS and purity determination

High resolution mass spectra and sample purities were obtained by HPLC gradient method with detection by UV and MS. C18 column (Kinetex EVO C18, 2.1x50 mm, 1.7 μm, Phenomenex, Torrance, CA, USA) was used in this study. Mobile phase A was ultrapure water of ASTM I type (resistance 18.2 MΩ.cm at 25°C) prepared by Barnstead Smart2Pure 3 UV/UF apparatus (Thermo Fisher Scientific, Waltham, MA, USA) with 0.1 % (v/v) formic acid (LC-MS grade, VWR, Radnor, PA, USA); mobile phase B was acetonitrile (MS grade, VWR, Radnor, PA, USA) with 0.1 % (v/v) of formic acid. The flow was constant at 0.4 ml/min. Method started with 0.3 minute of isocratic flow of 5 % B, then the gradient of B rose to 100 % B in 3 min and remained constant at 100 % B for 0.7 min. Then the composition went back to 5 % B and equilibrated for 3.5 min. Samples were dissolved in methanol (LC-MS grade, VWR, Radnor, PA, USA) with concentration 1 mg/mL and sample injection was 1 μL. Purity was determined from UV spectra measured at wavelength 254 nm. HRMS was determined in total ion current spectra from mass spectrometer in positive mode.

Fig. S90. HRMS spectrum for *N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6a)

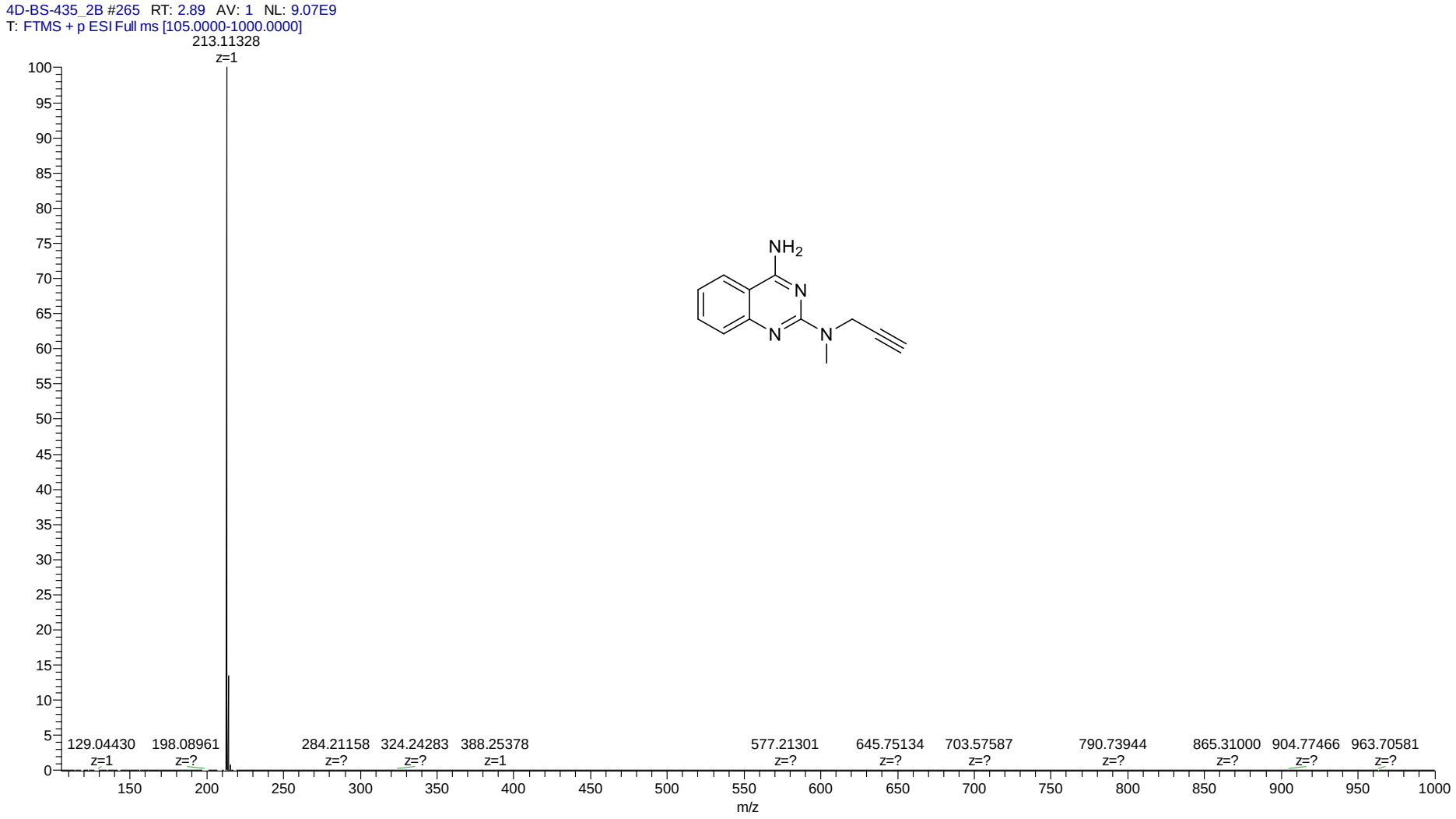


Fig. S91. LC-UV chromatogram for *N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6a)

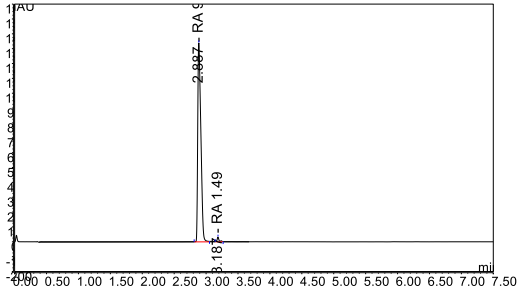


Fig. S92. HRMS spectrum for *N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6b)

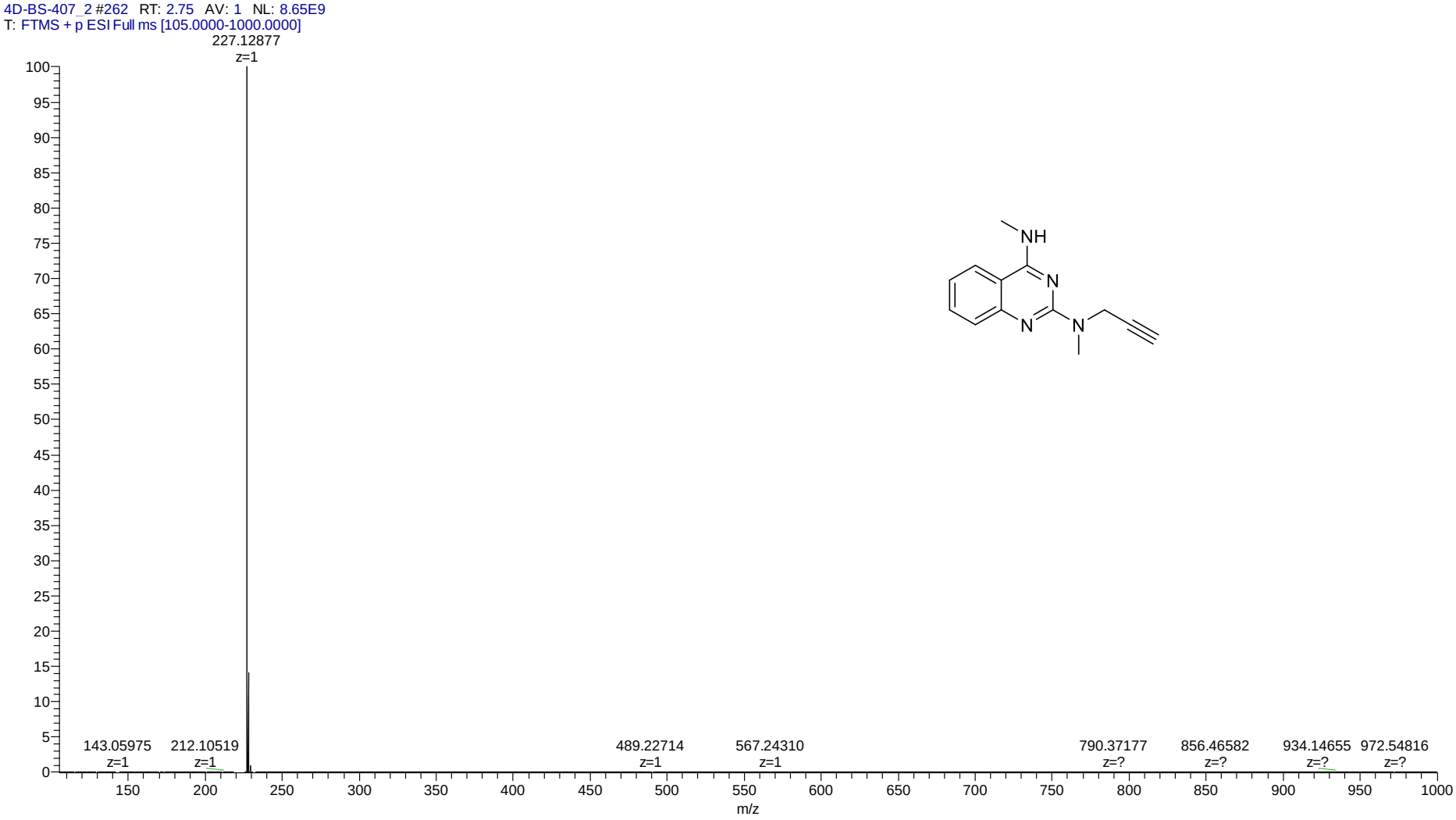


Fig. S93. **LC-UV chromatogram for *N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6b)**

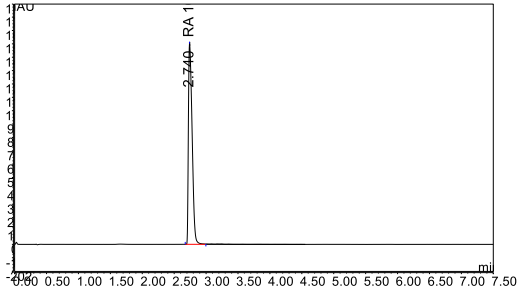


Fig. S94. HRMS spectrum for *N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6c)

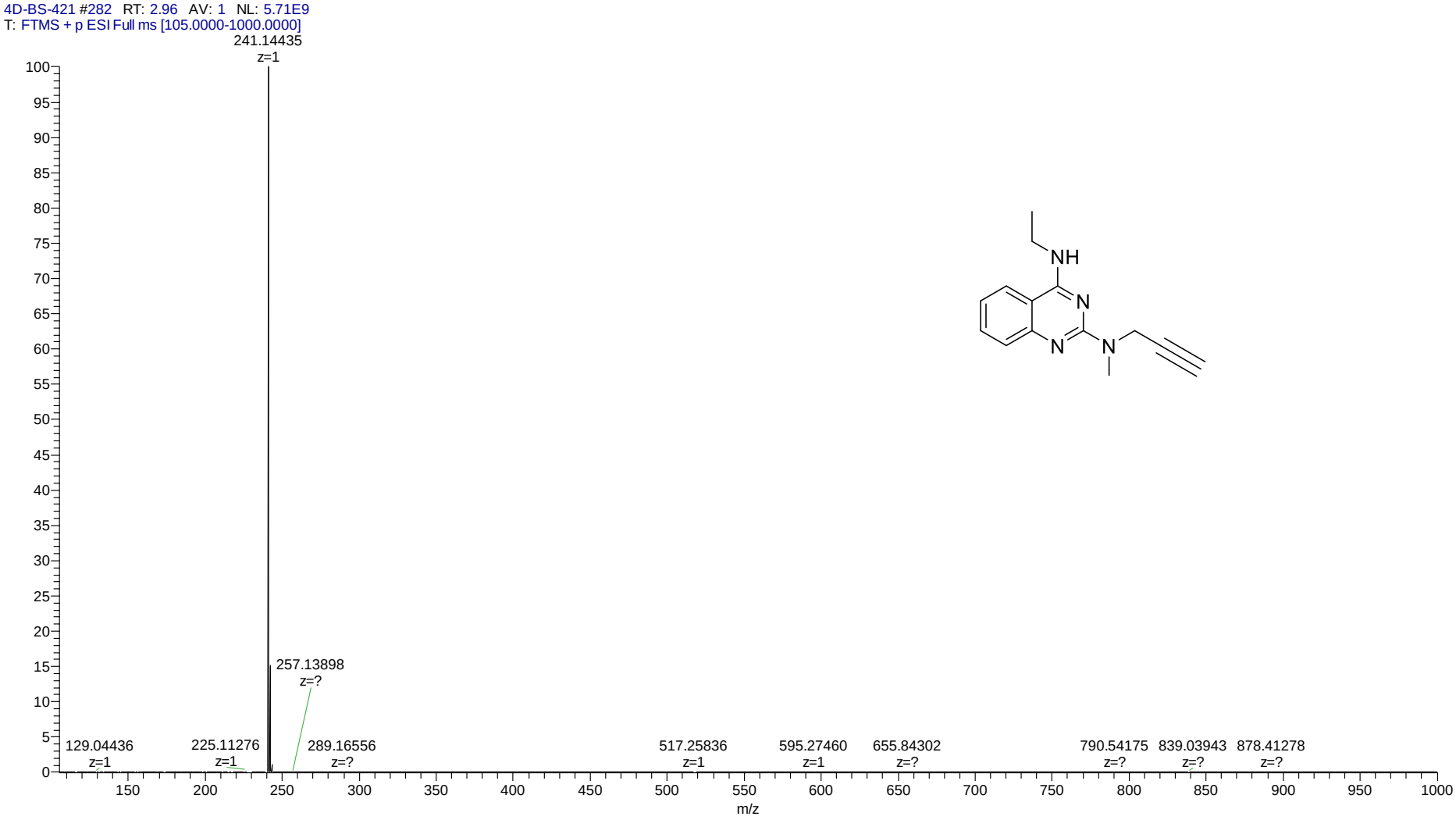


Fig. S95. LC-UV chromatogram for *N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6c)

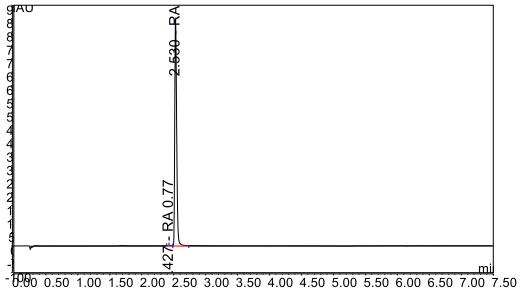


Fig. S96. HRMS spectrum for *N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (I-6d)

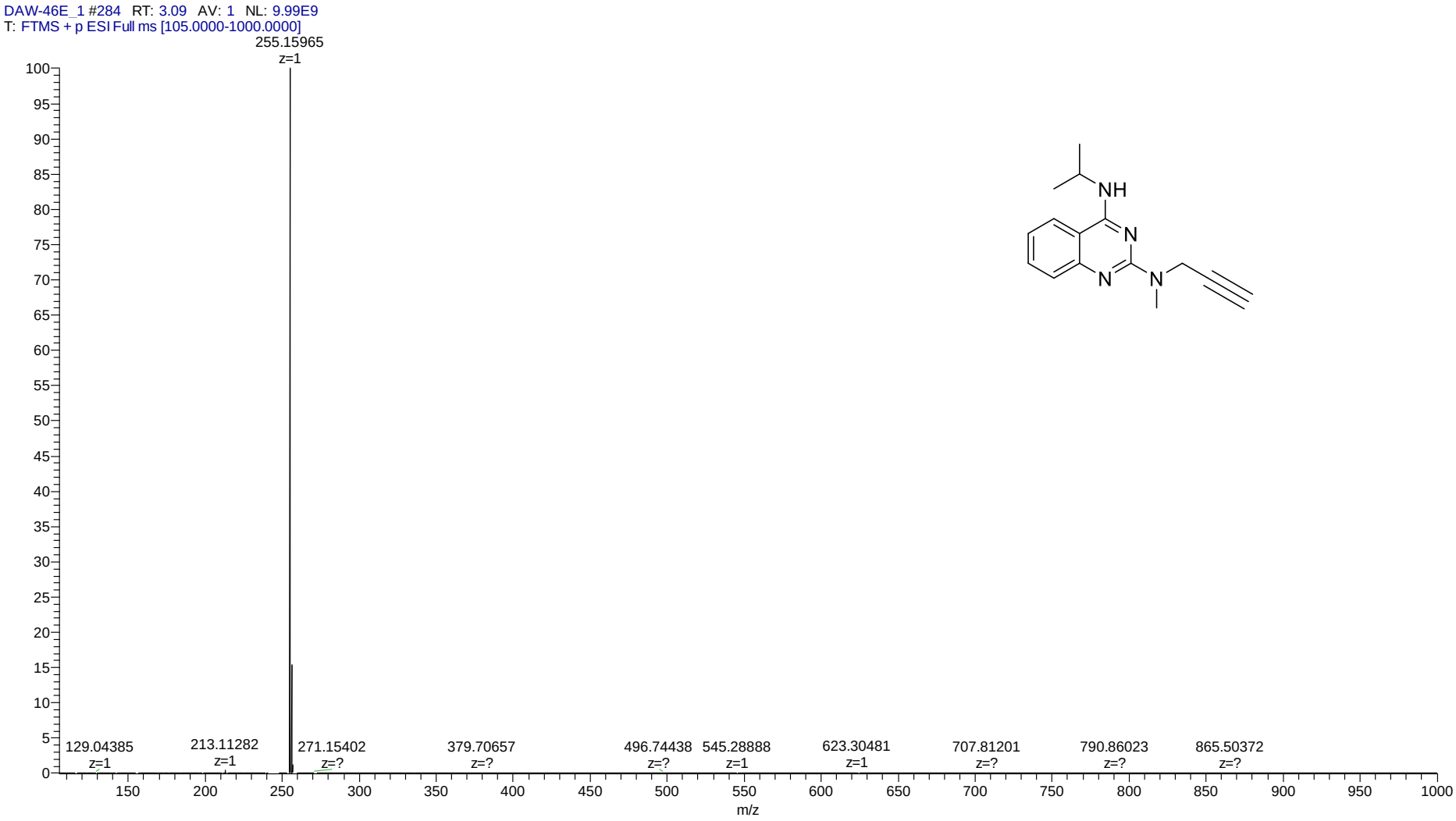


Fig. S97. **LC-UV chromatogram for *N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (I-6d)**

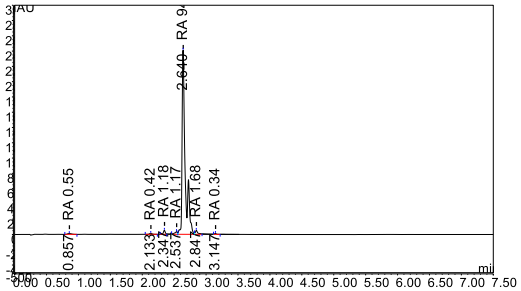


Fig. S98. HRMS spectrum for *N4*-butyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6e)

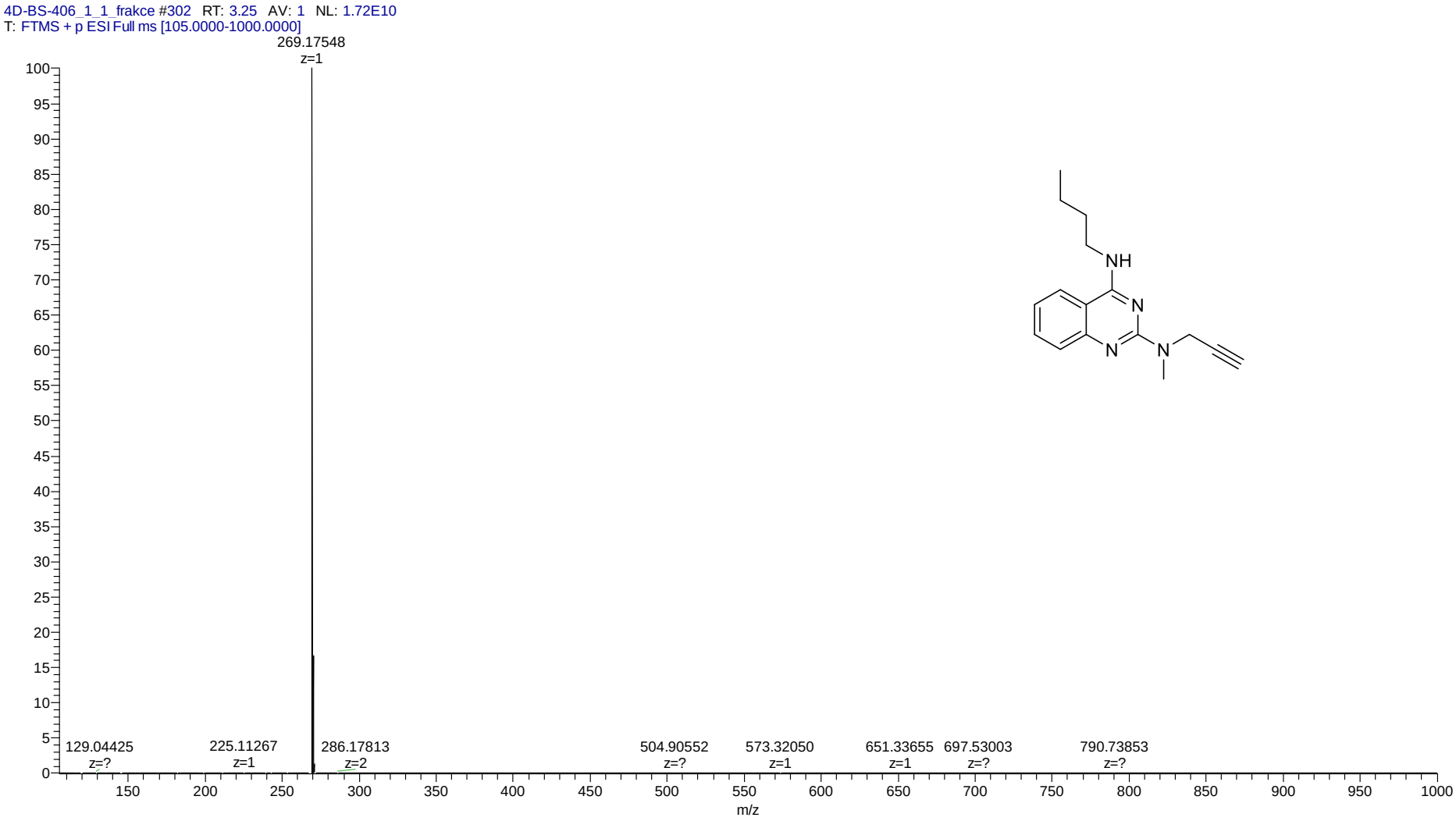


Fig. S99. LC-UV chromatogram for *N4*-butyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6e)

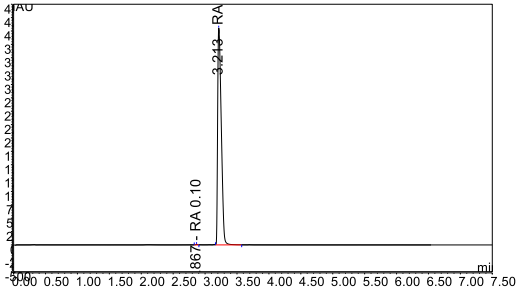


Fig. S100. HRMS spectrum for *N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6f)

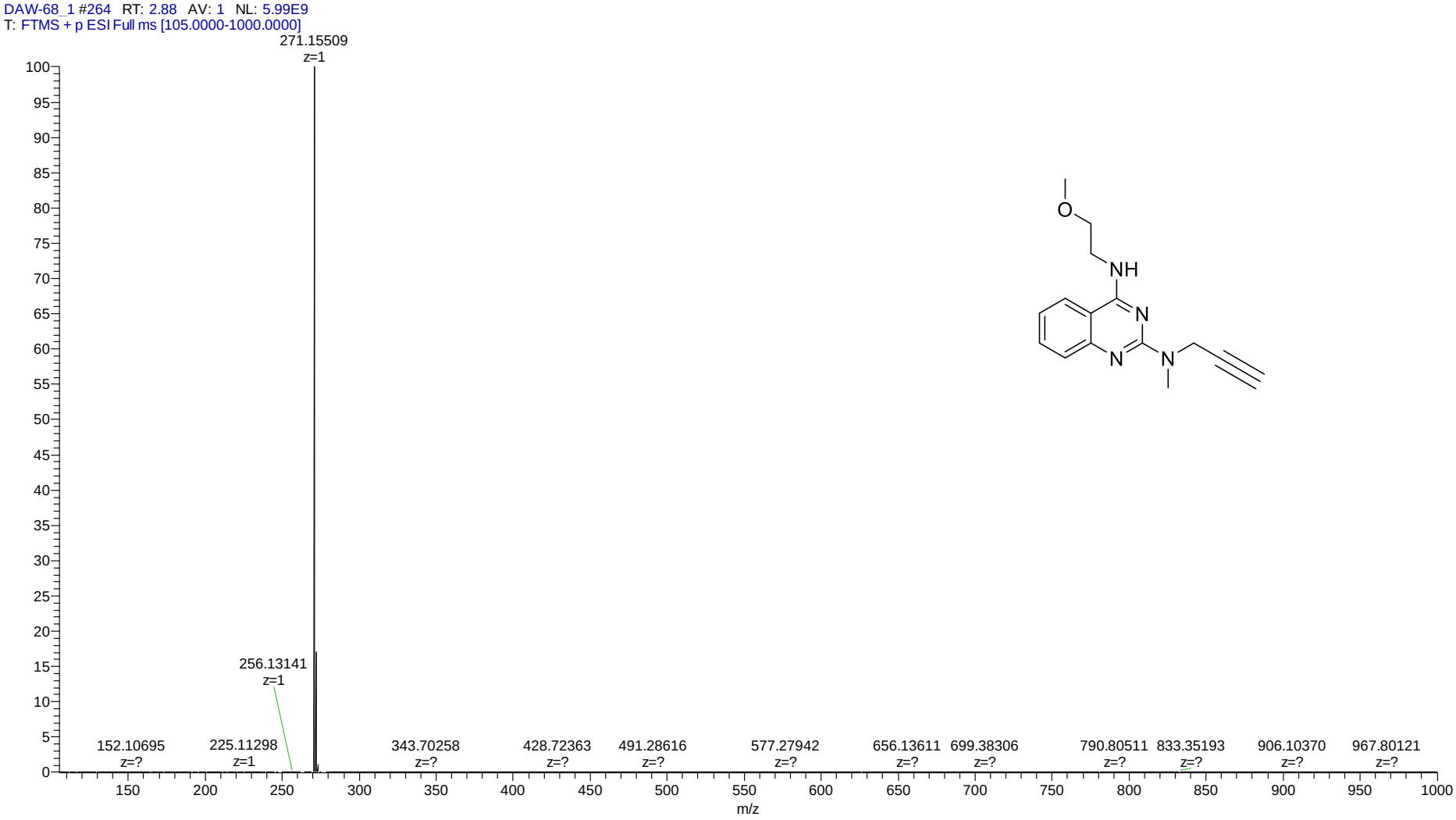


Fig. S101. LC-UV chromatogram for *N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6f)

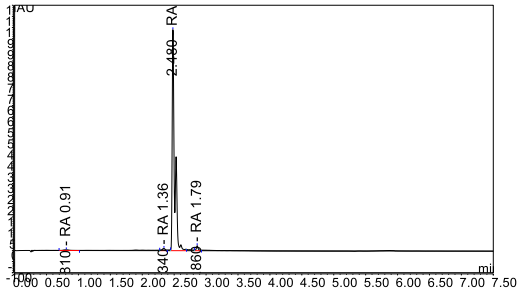


Fig. S102. HRMS spectrum for *N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6g)

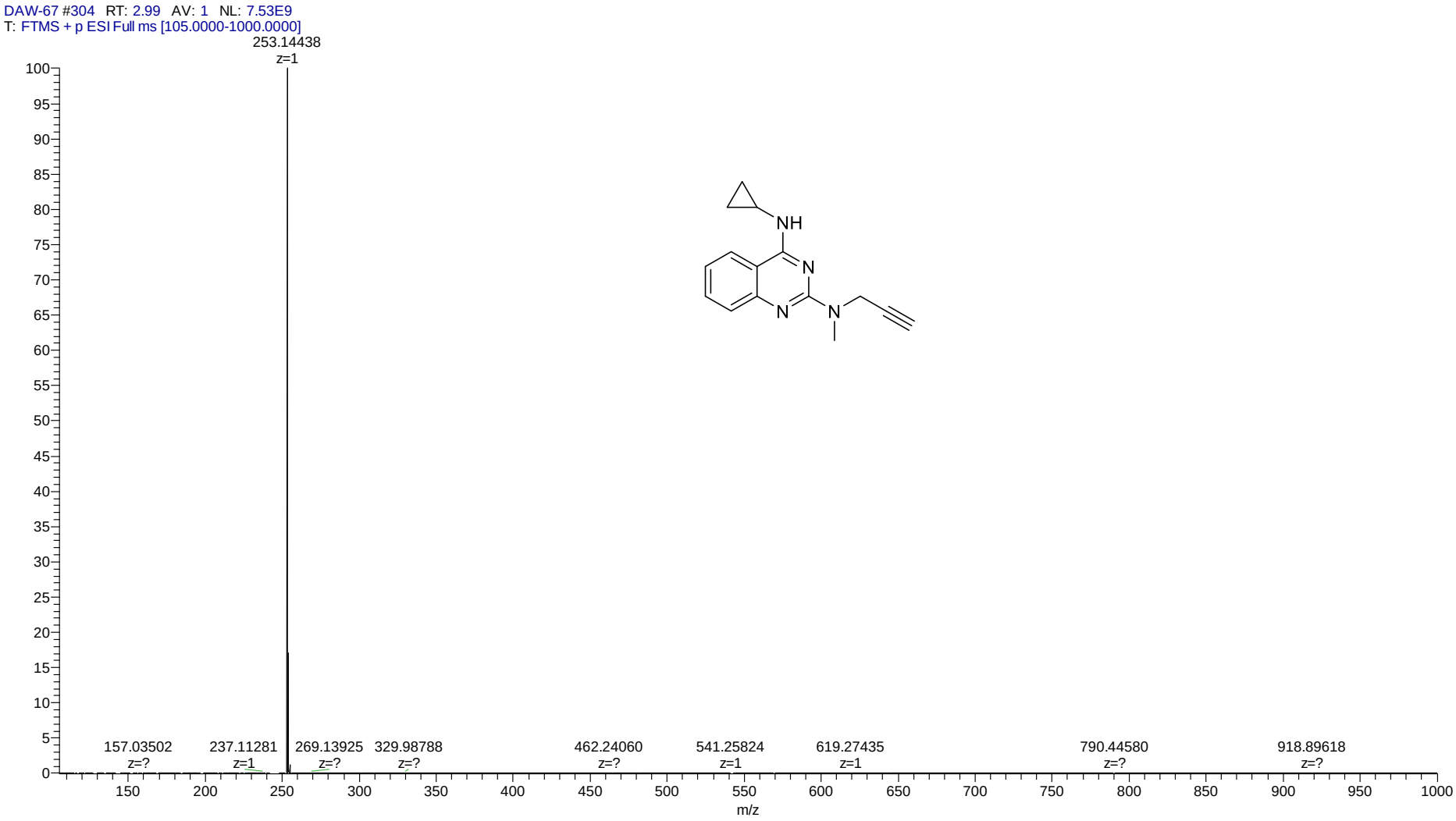


Fig. S103. **LC-UV chromatogram for *N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6g)**

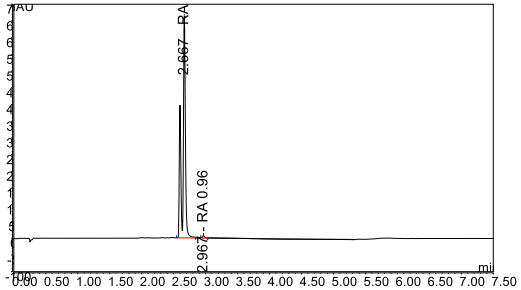


Fig. S104. HRMS spectrum for *N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6h)

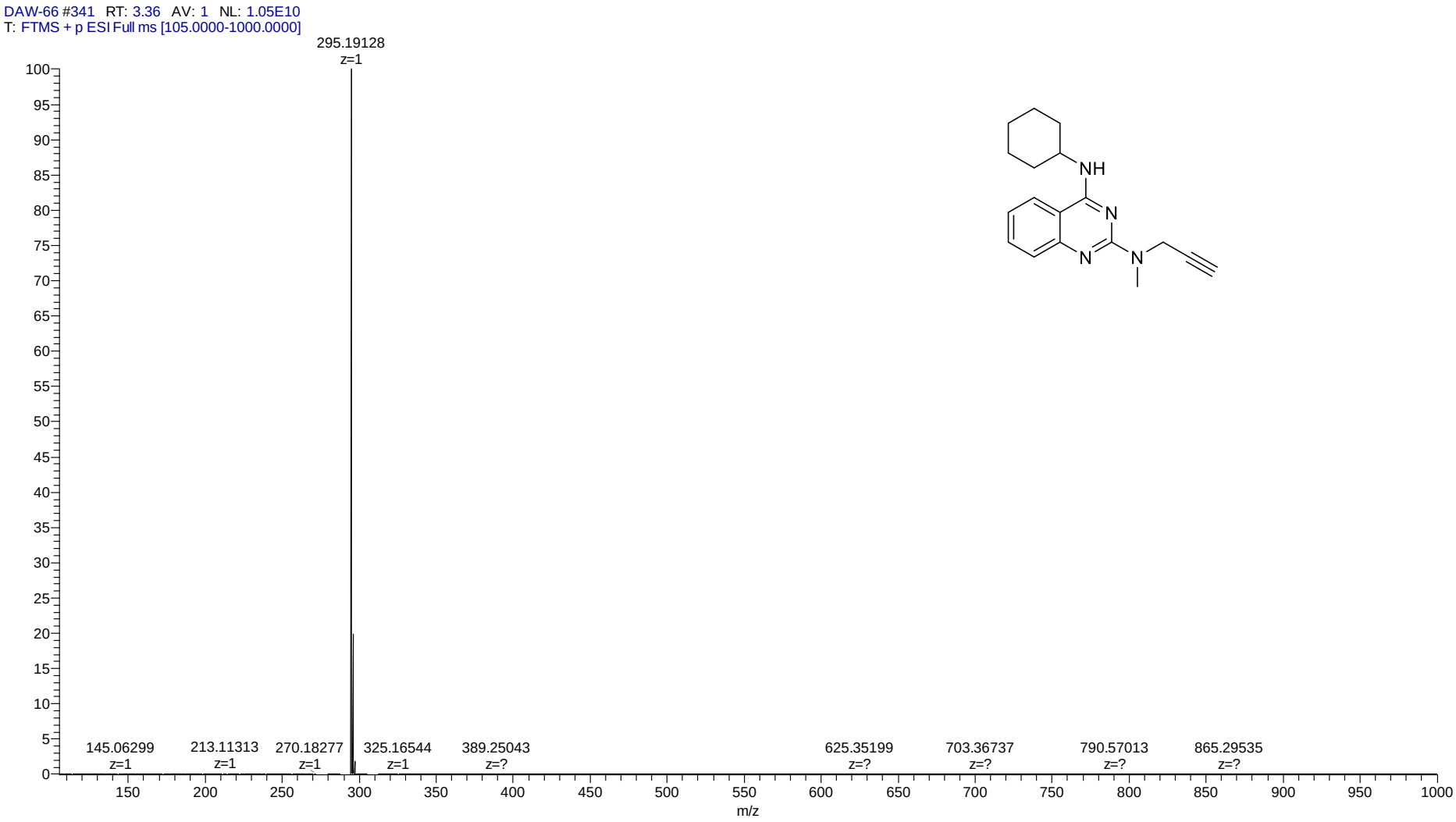


Fig. S105. LC-UV chromatogram for *N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (I-6h)

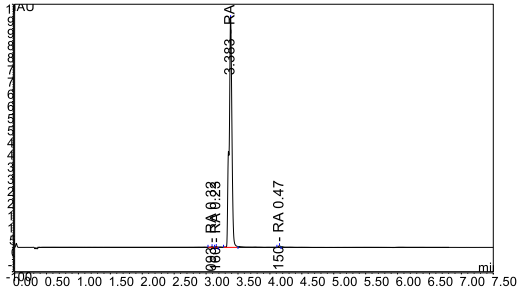


Fig. S106. HRMS spectrum for 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6a)

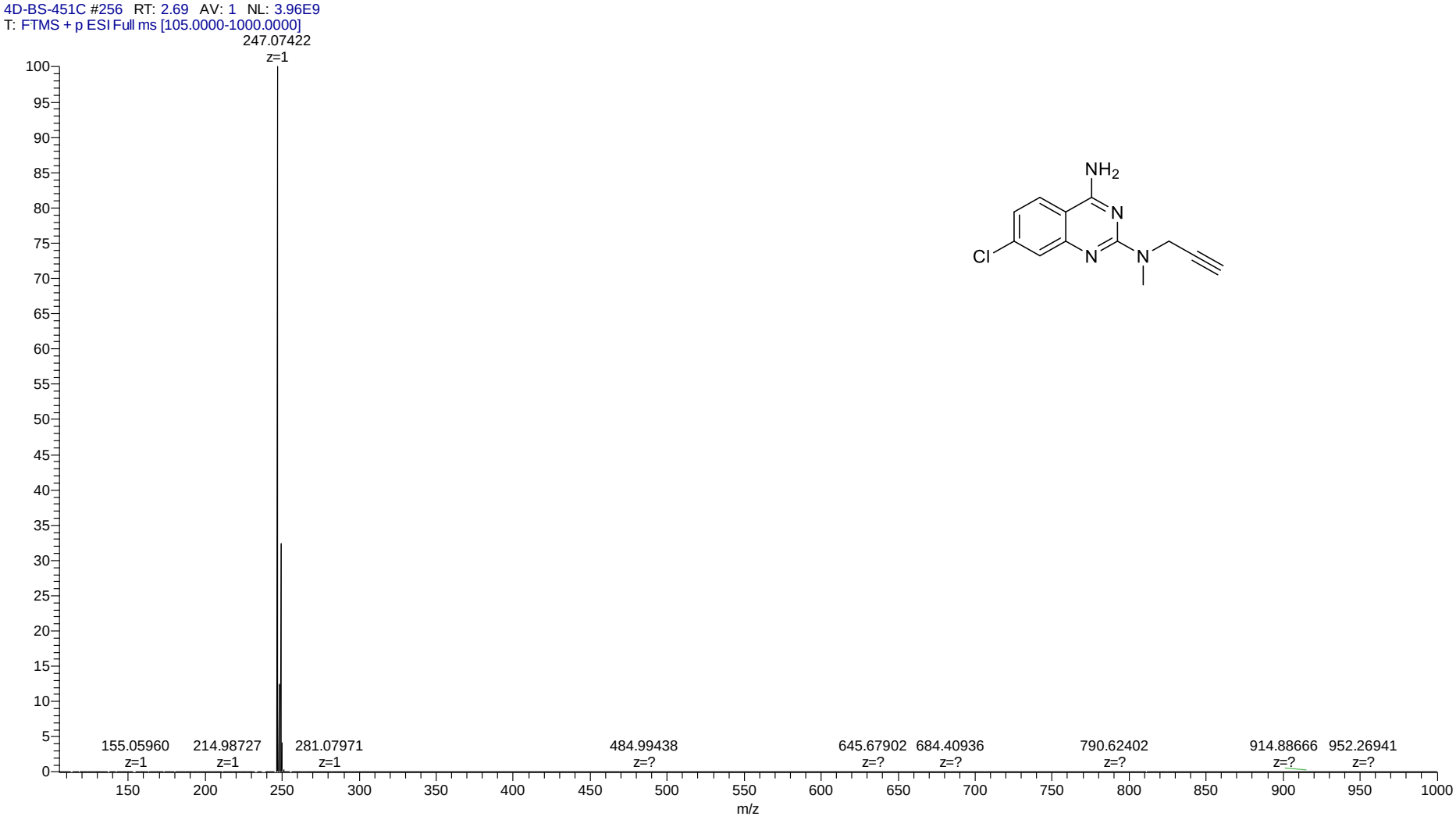


Fig. S107. **LC-UV chromatogram for 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6a)**

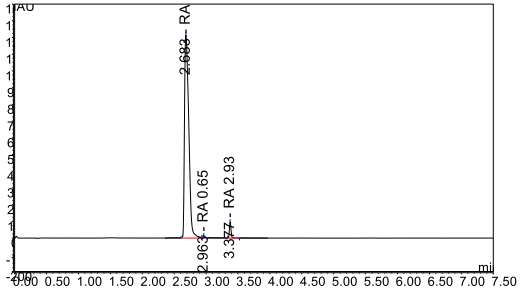


Fig. S108. HRMS spectrum for 7-chloro-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6b)

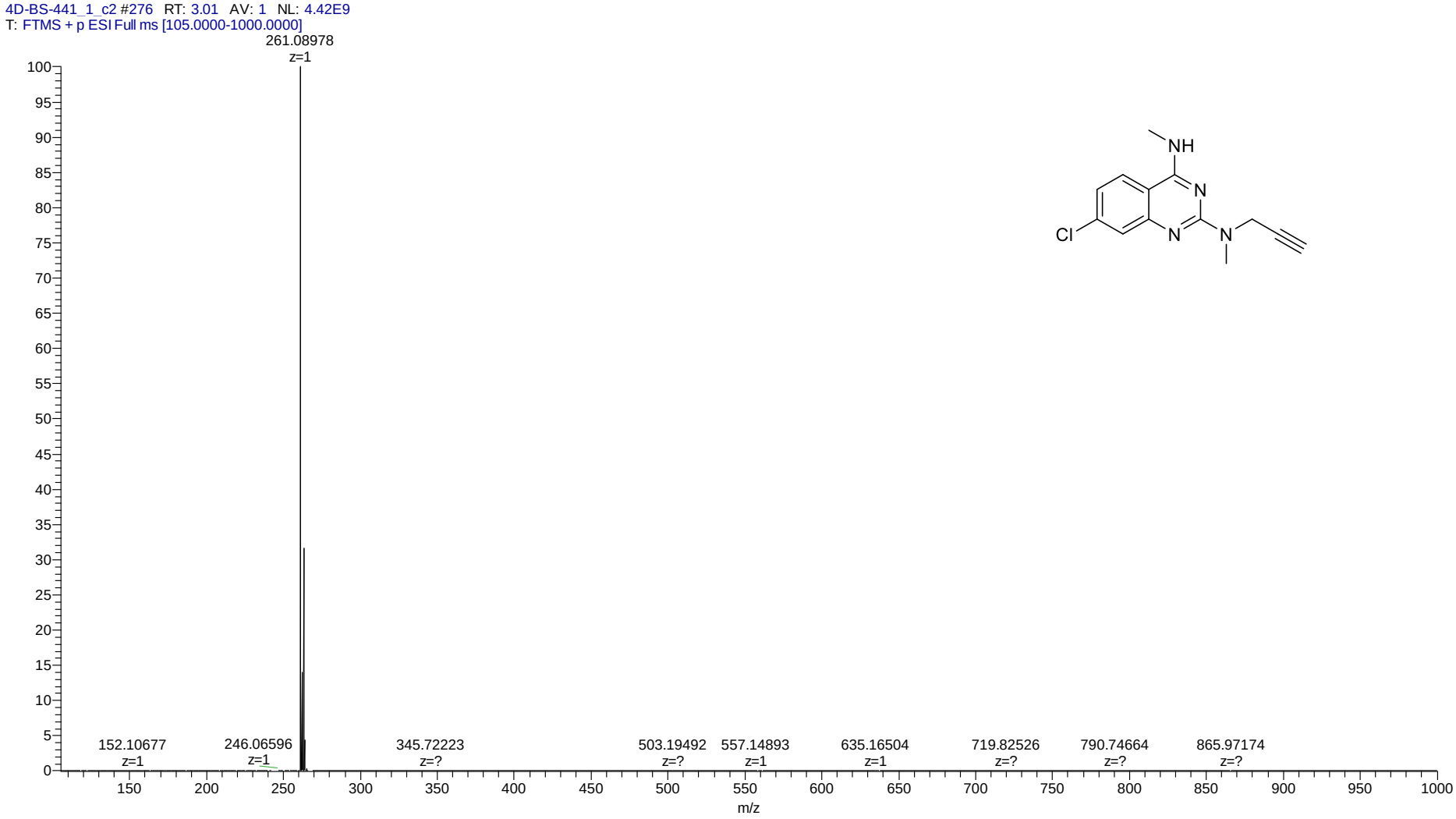


Fig. S109. **LC-UV chromatogram for 7-chloro-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6b)**

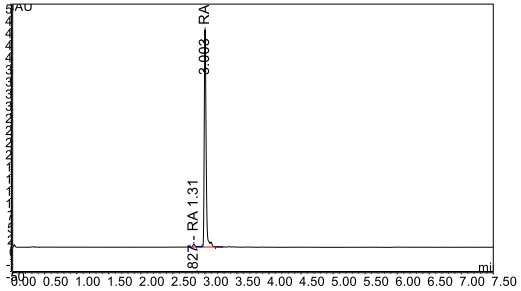


Fig. S110. HRMS spectrum for 7-chloro-*N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6c)

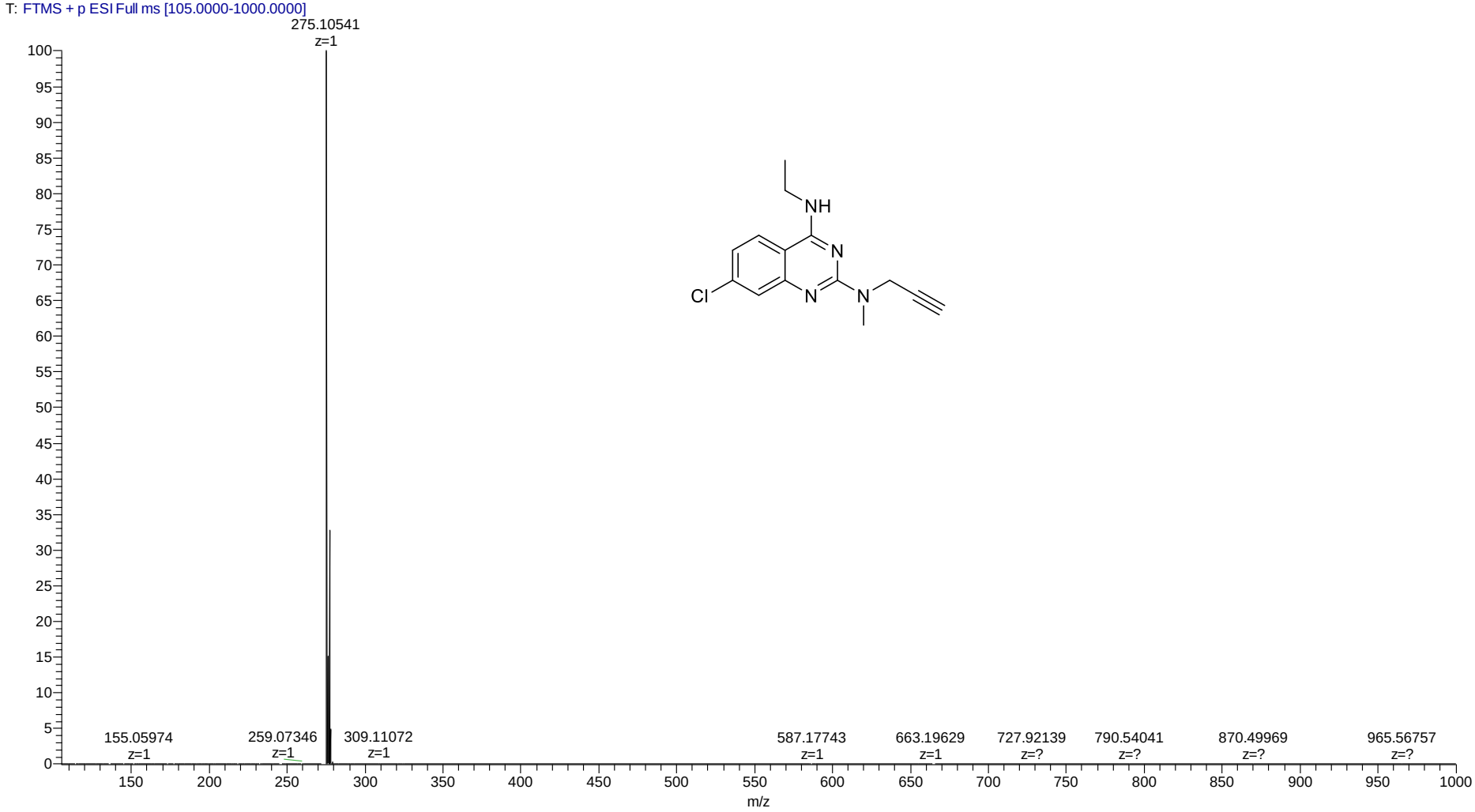


Fig. S111. LC-UV chromatogram for 7-chloro-*N4*-ethyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6c)

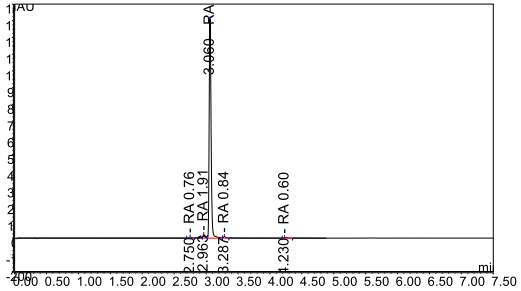


Fig. S112. HRMS spectrum for 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (II-6d)

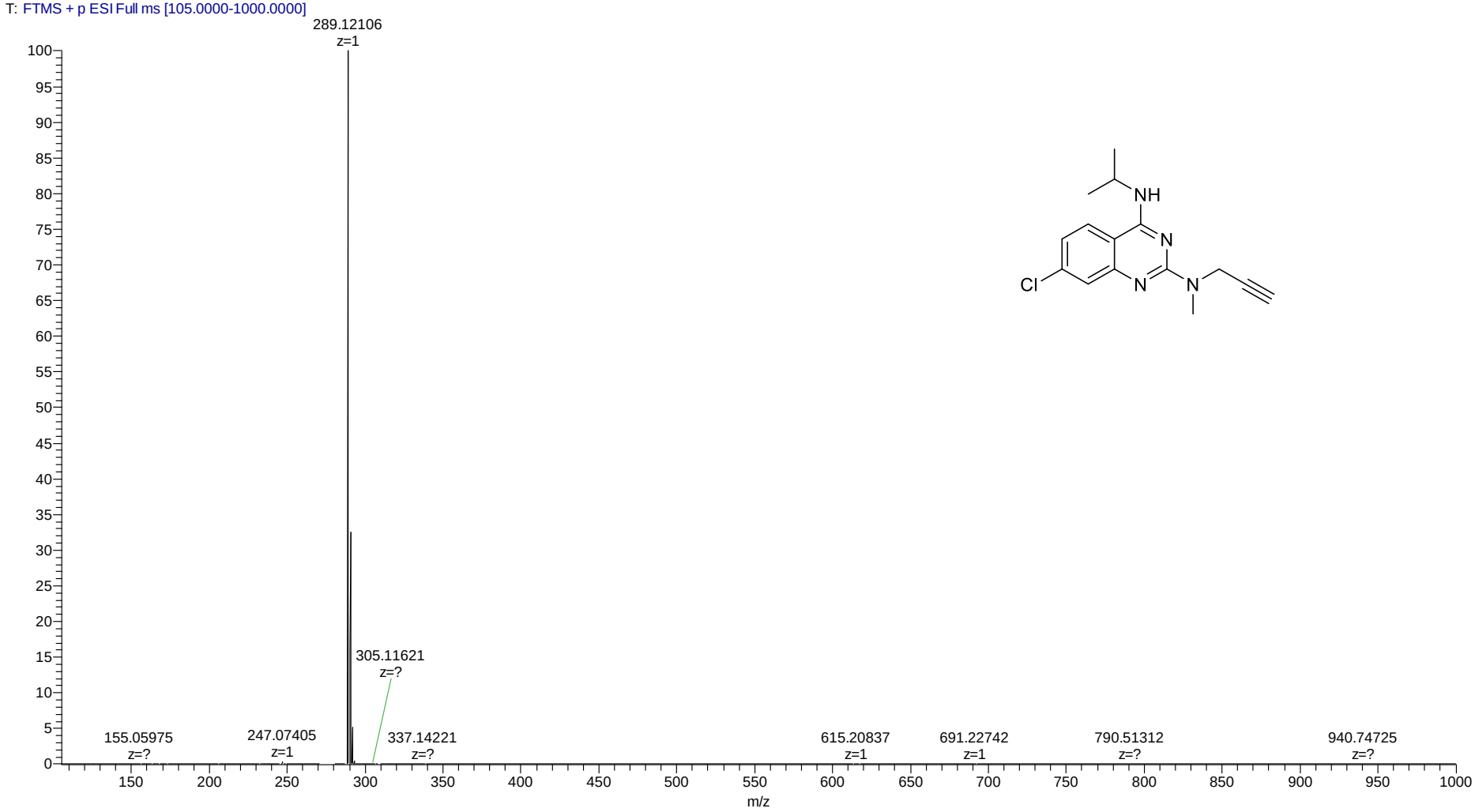


Fig. S113. **LC-UV chromatogram for 7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (II-6d)**

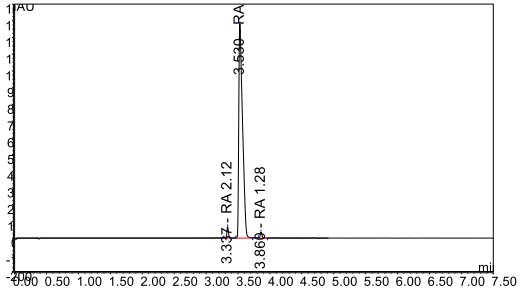


Fig. S114. HRMS spectrum for *N4*-butyl-7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6e)

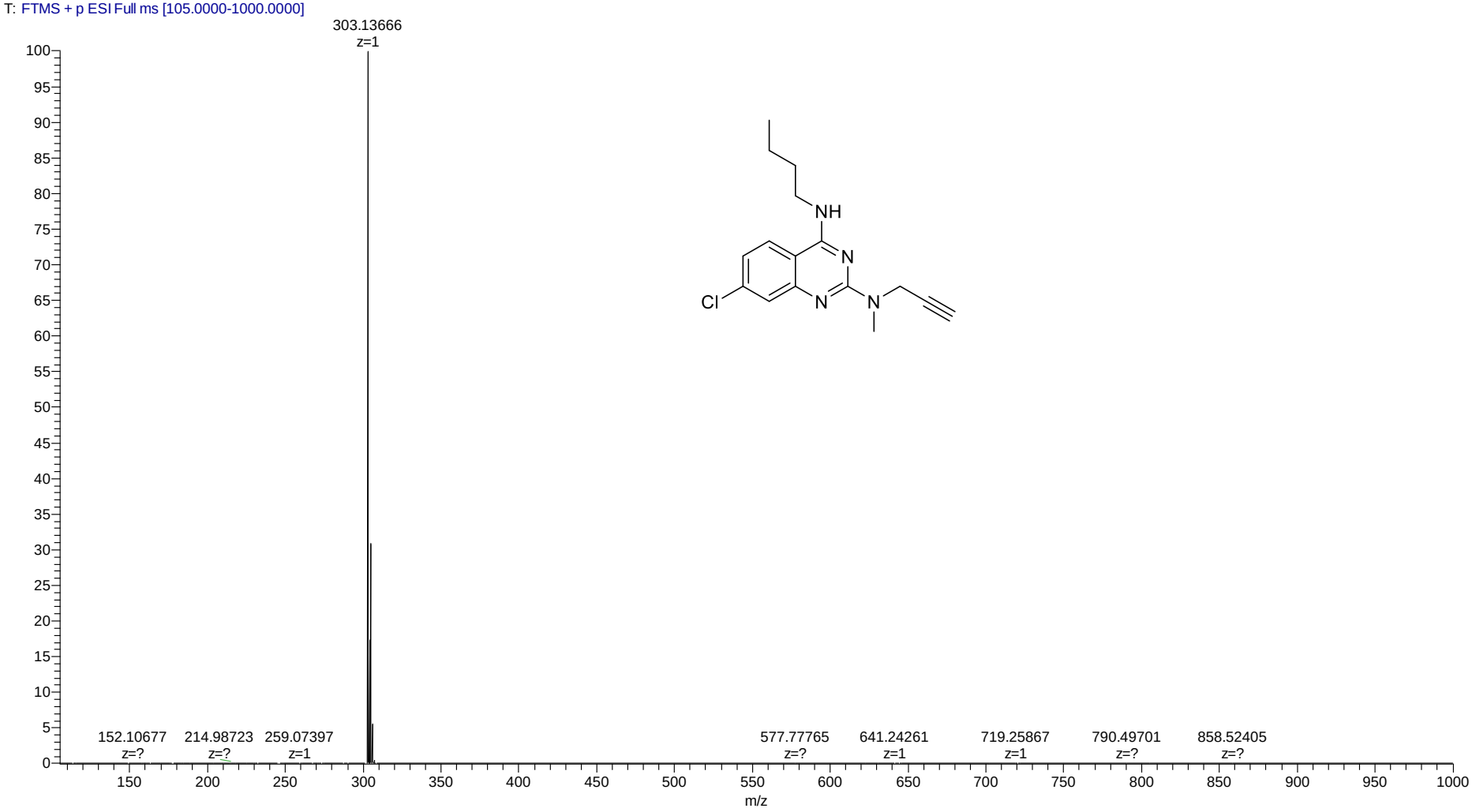


Fig. S115. **LC-UV chromatogram for *N4*-butyl-7-chloro-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6e)**

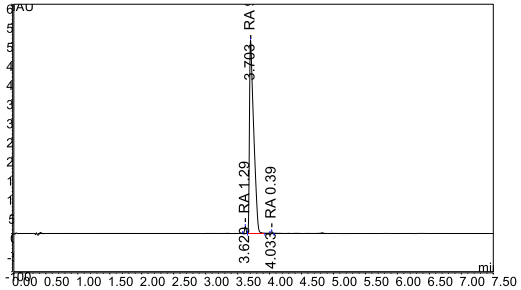


Fig. S116. HRMS spectrum for 7-chloro-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6f)

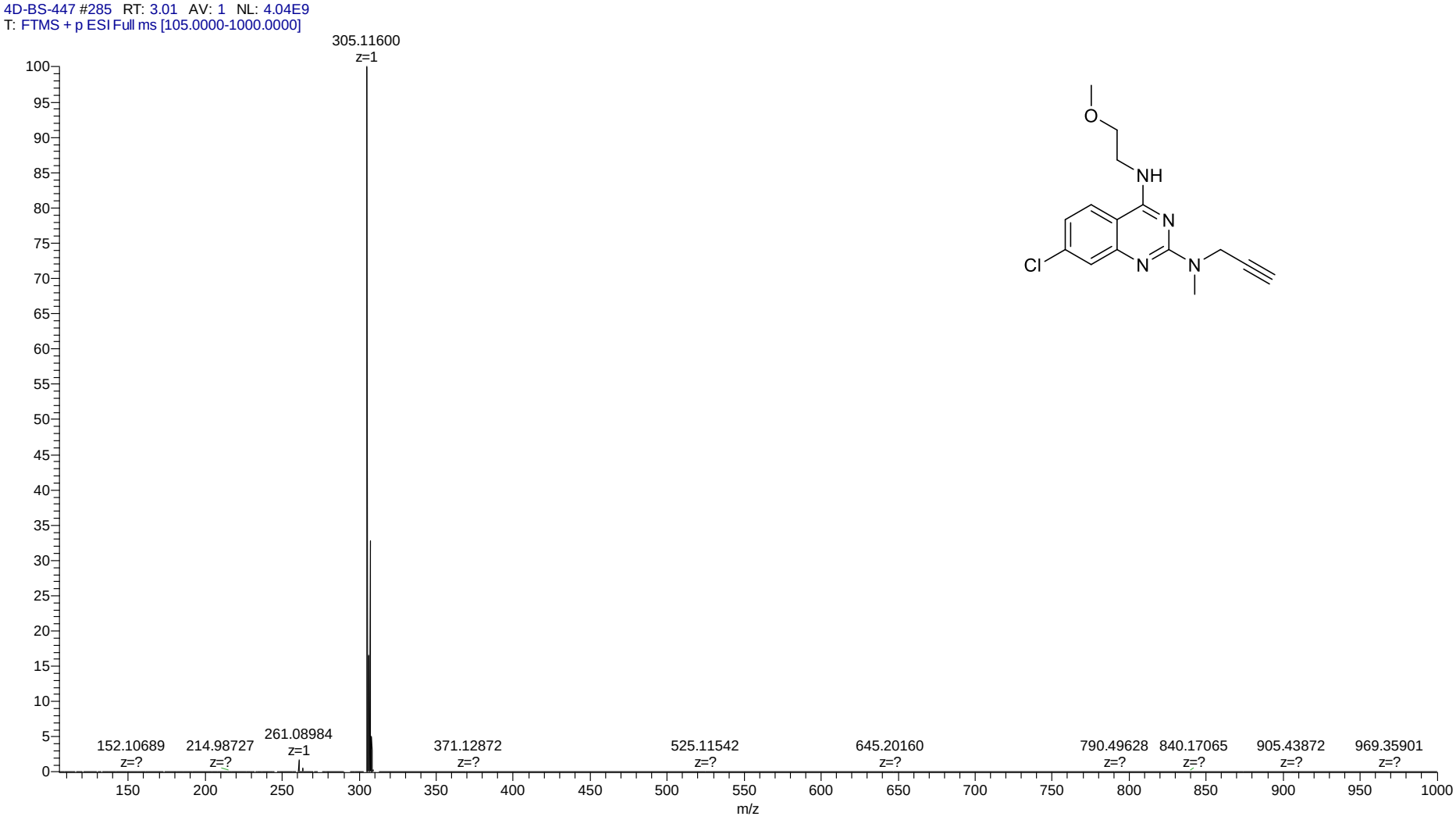


Fig. S117. **LC-UV chromatogram for 7-chloro-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6f)**

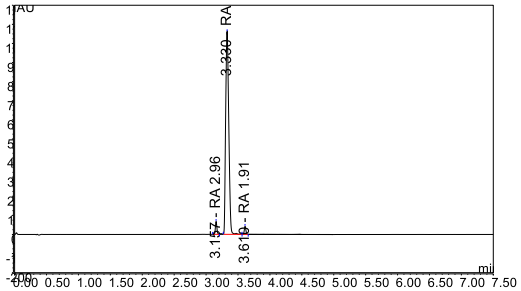


Fig. S118. HRMS spectrum for 7-chloro-*N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6g)

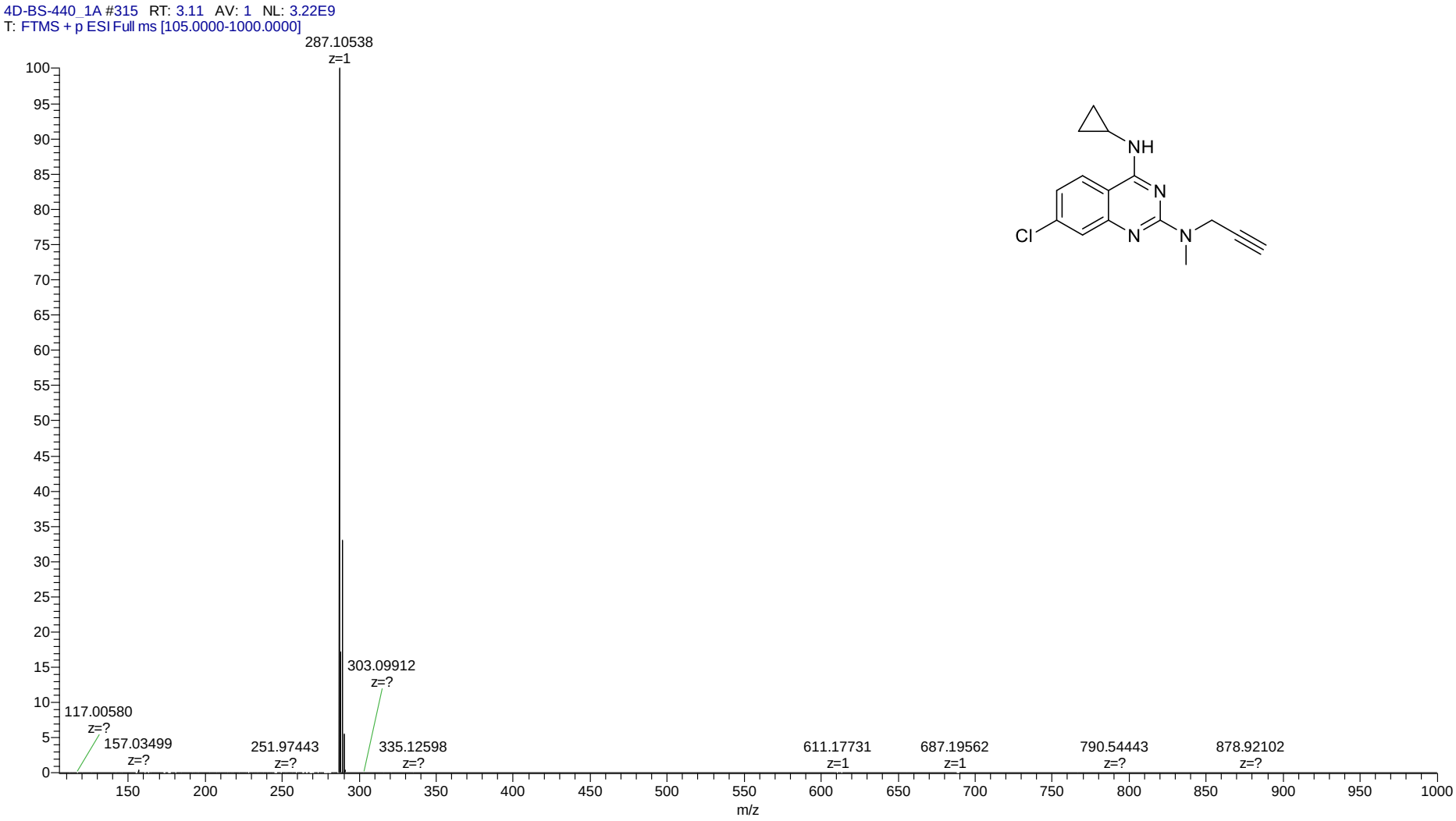


Fig. S119. **LC-UV chromatogram for 7-chloro-*N4*-cyclopropyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6g)**

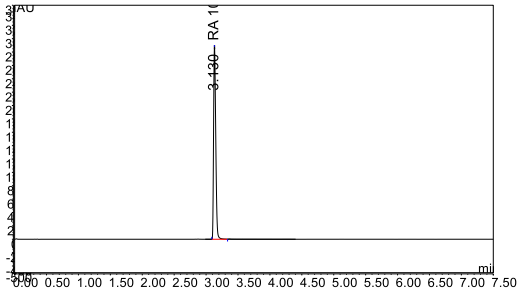


Fig. S120. HRMS spectrum for 7-chloro-*N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6h)

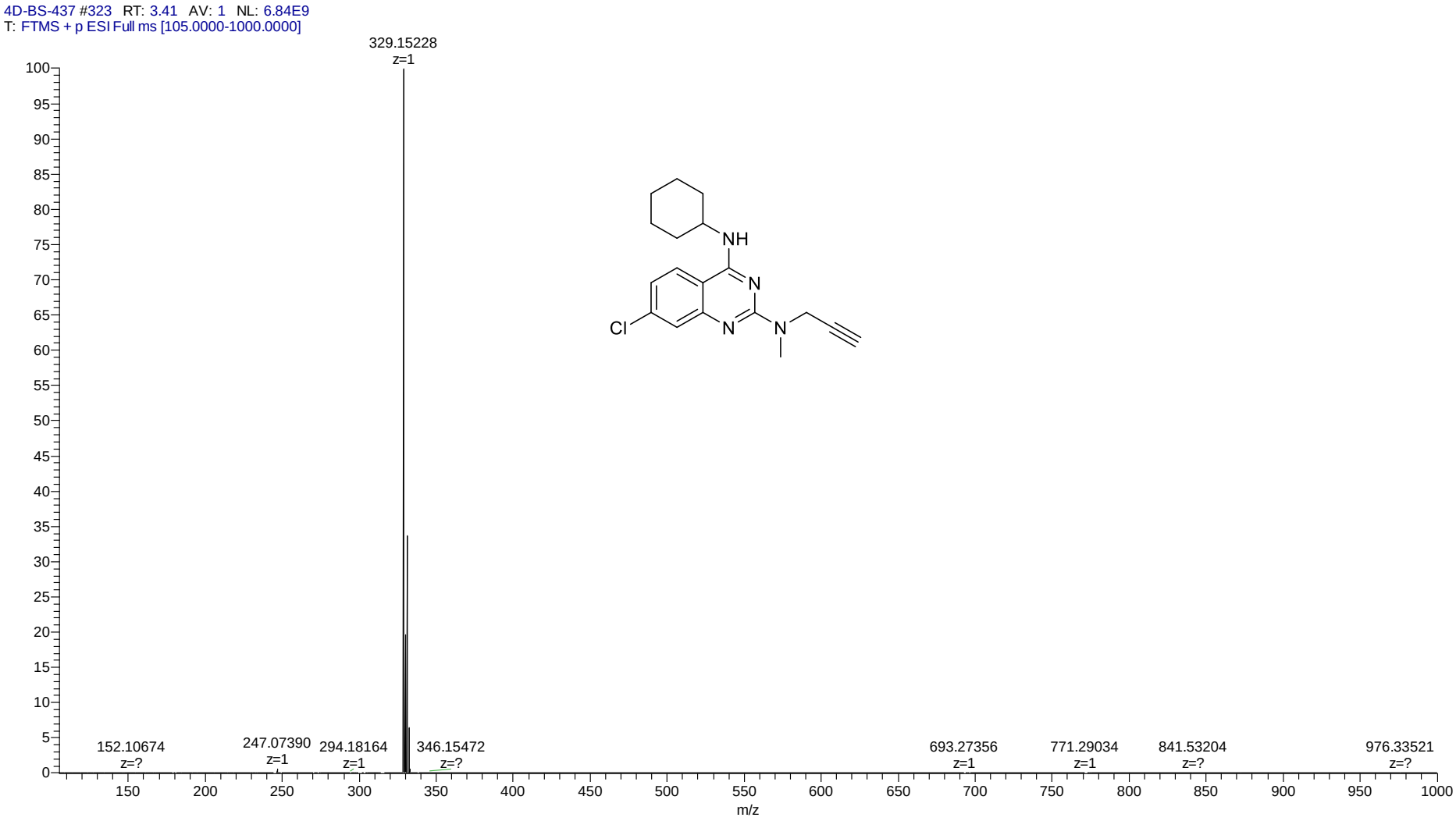


Fig. S121. LC-UV chromatogram for 7-chloro-*N4*-cyclohexyl-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (II-6h)

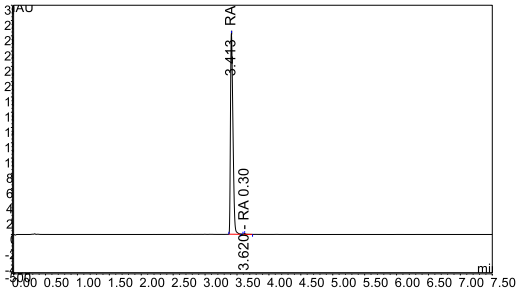


Fig. S122. HRMS spectrum for 6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6a)

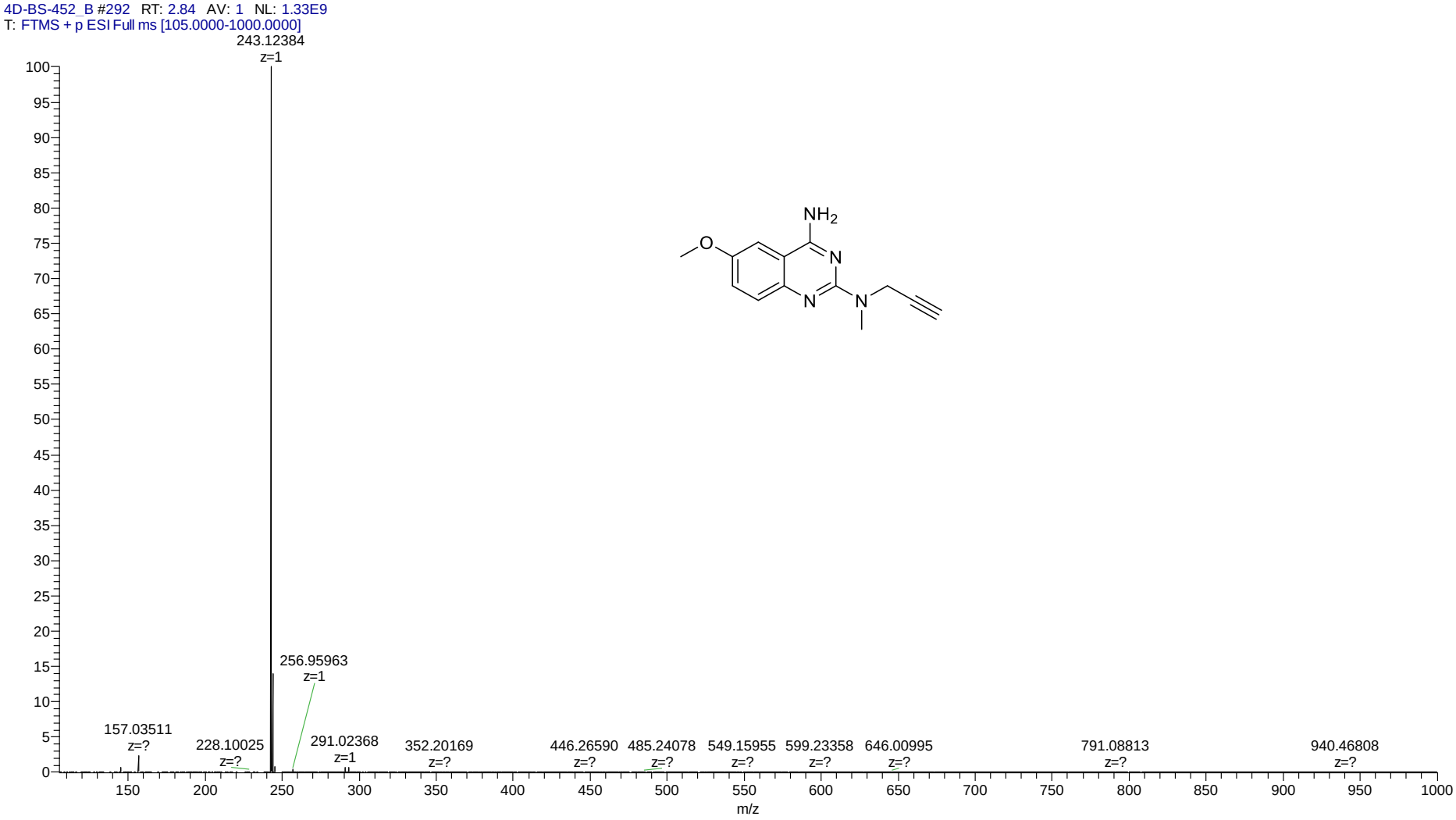


Fig. S123. **LC-UV chromatogram for 6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6a)**

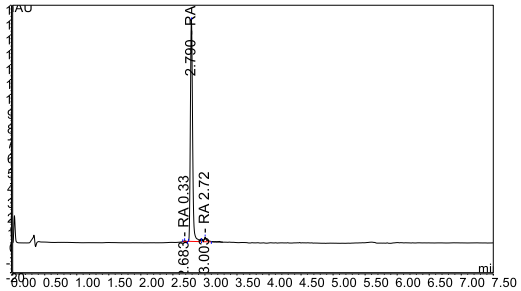


Fig. S124. HRMS spectrum for 6-methoxy-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6b)

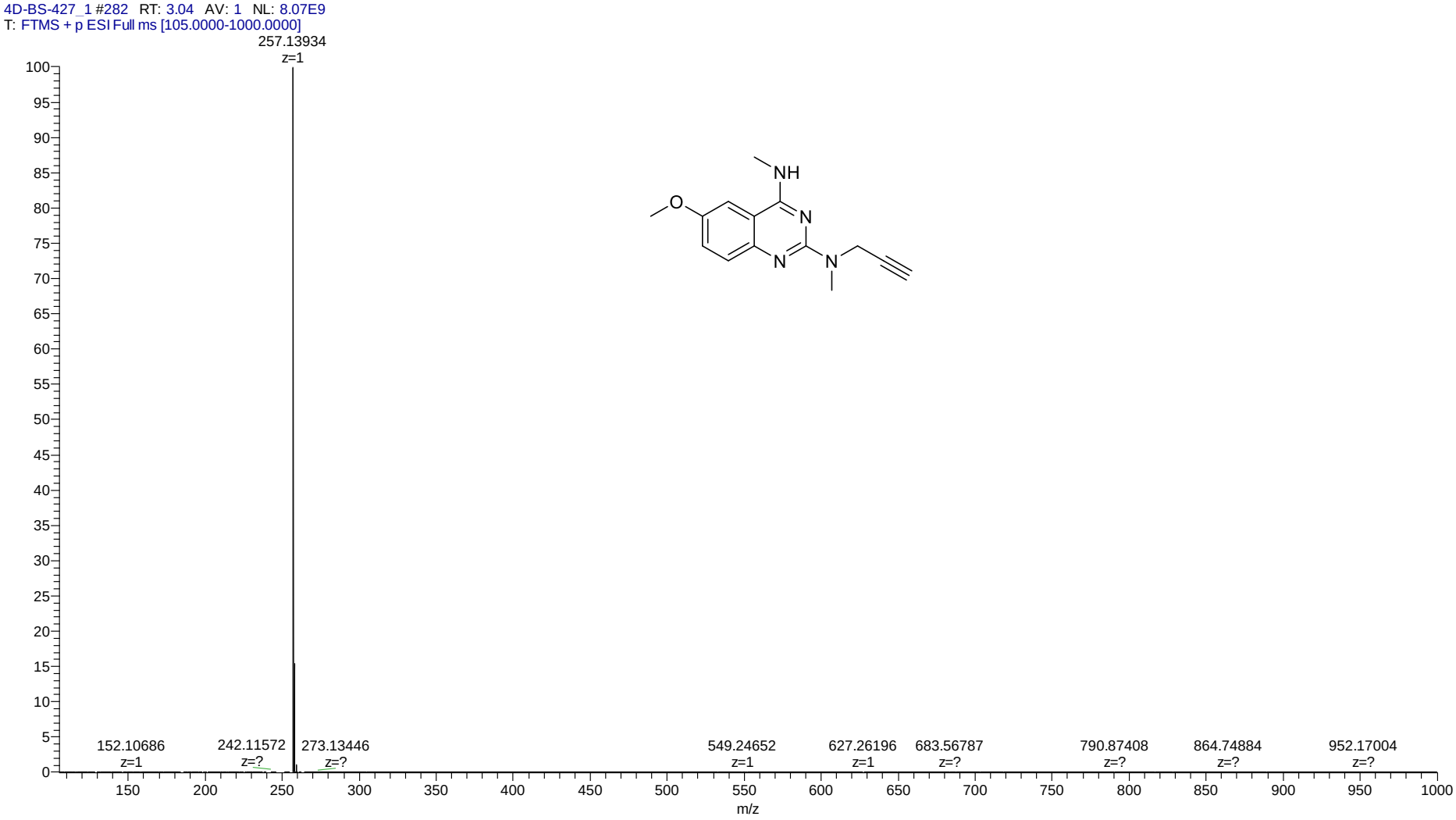


Fig. S125. LC-UV chromatogram for 6-methoxy-*N2*,*N4*-dimethyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6b)

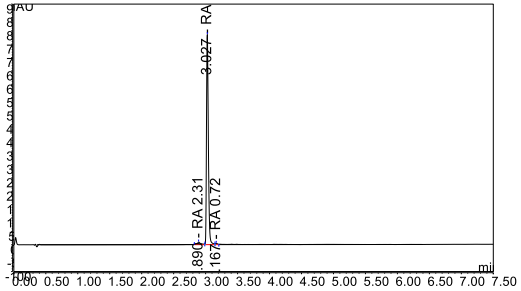


Fig. S126. HRMS spectrum for *N4*-ethyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6c)

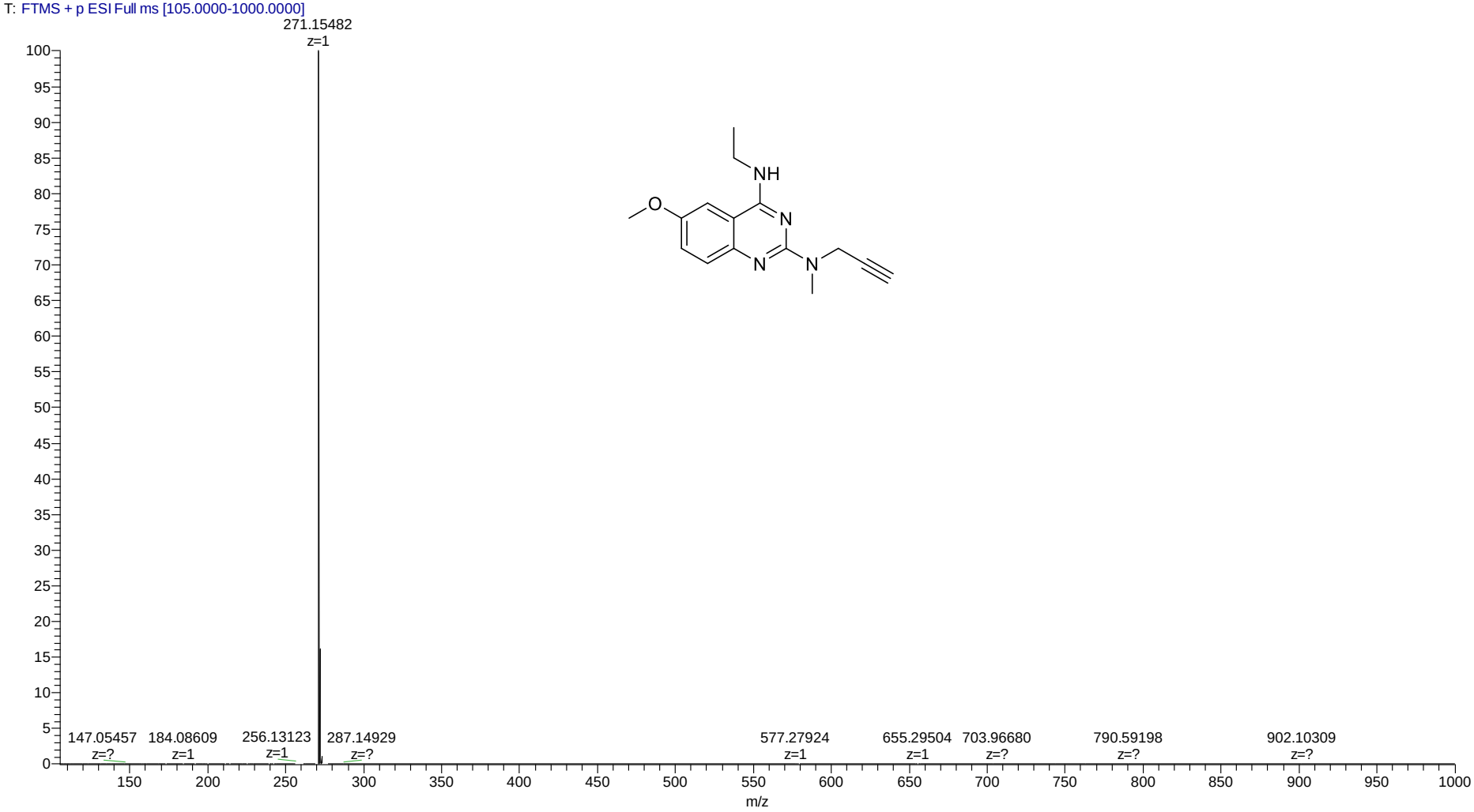


Fig. S127. **LC-UV chromatogram for *N4*-ethyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6c)**

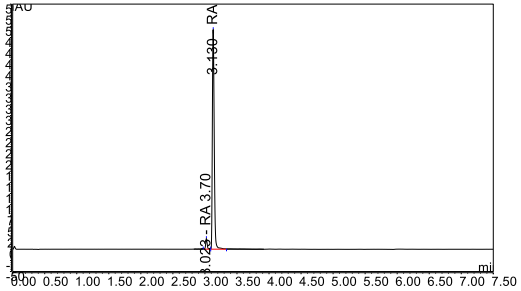


Fig. S128. HRMS spectrum for 6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (III-6d)

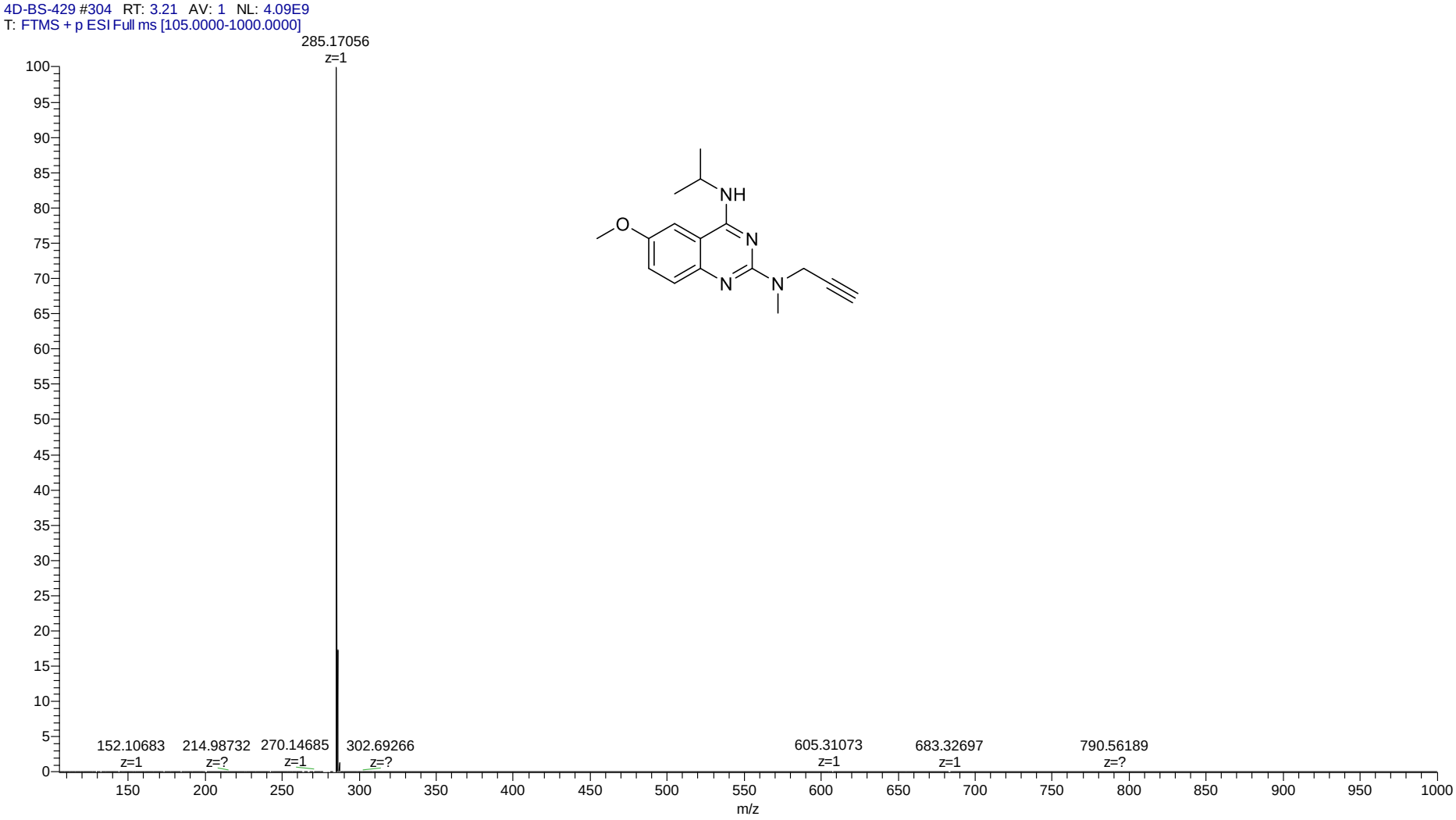


Fig. S129. **LC-UV chromatogram for 6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)-*N4*-(propan-2-yl)quinazoline-2,4-diamine (III-6d)**

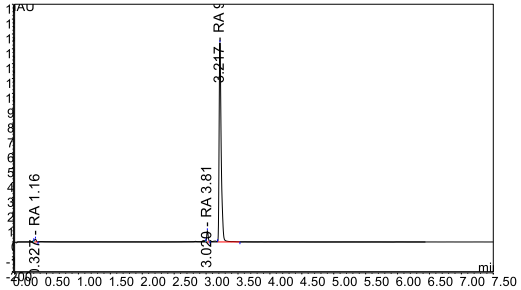


Fig. S130. HRMS spectrum for *N4*-butyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6e)

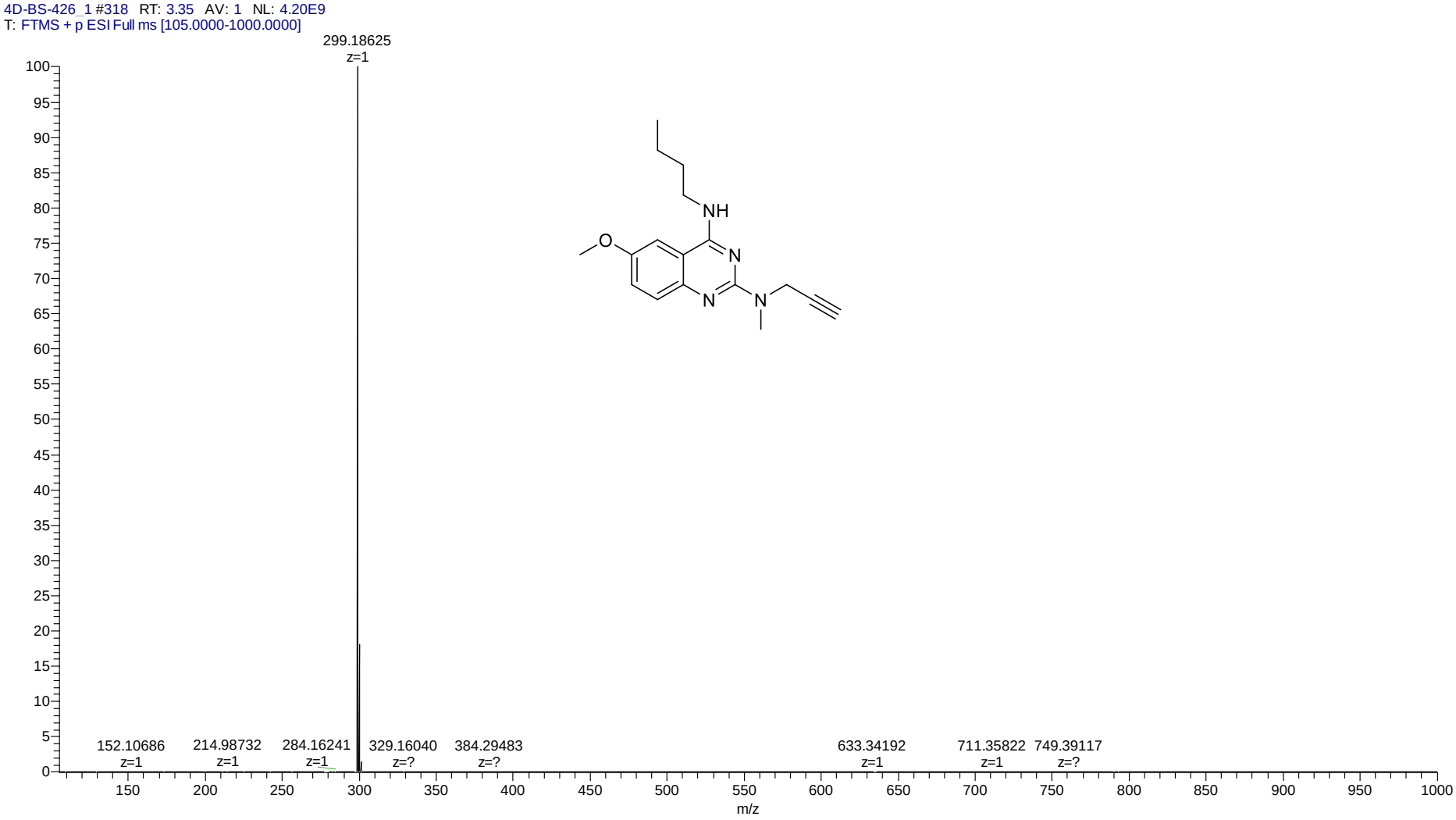


Fig. S131. **LC-UV chromatogram for *N4*-butyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6e)**

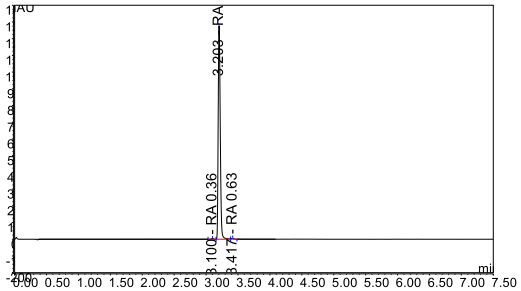


Fig. S132. HRMS spectrum for 6-methoxy-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6f)

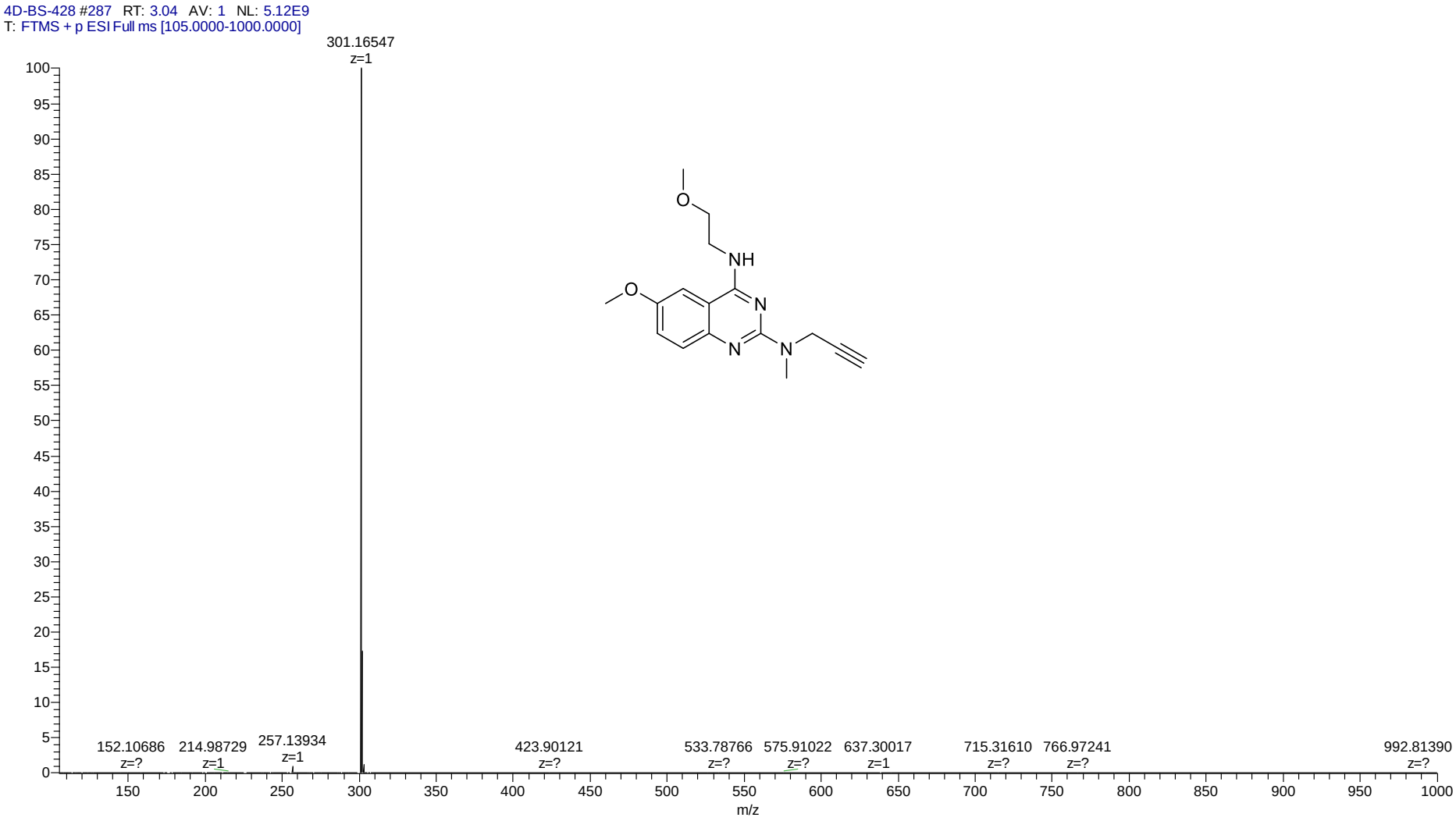


Fig. S133. **LC-UV chromatogram for 6-methoxy-*N4*-(2-methoxyethyl)-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6f)**

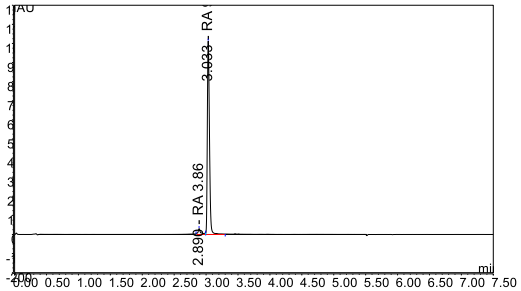


Fig. S134. HRMS spectrum for *N4*-cyclopropyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6g)

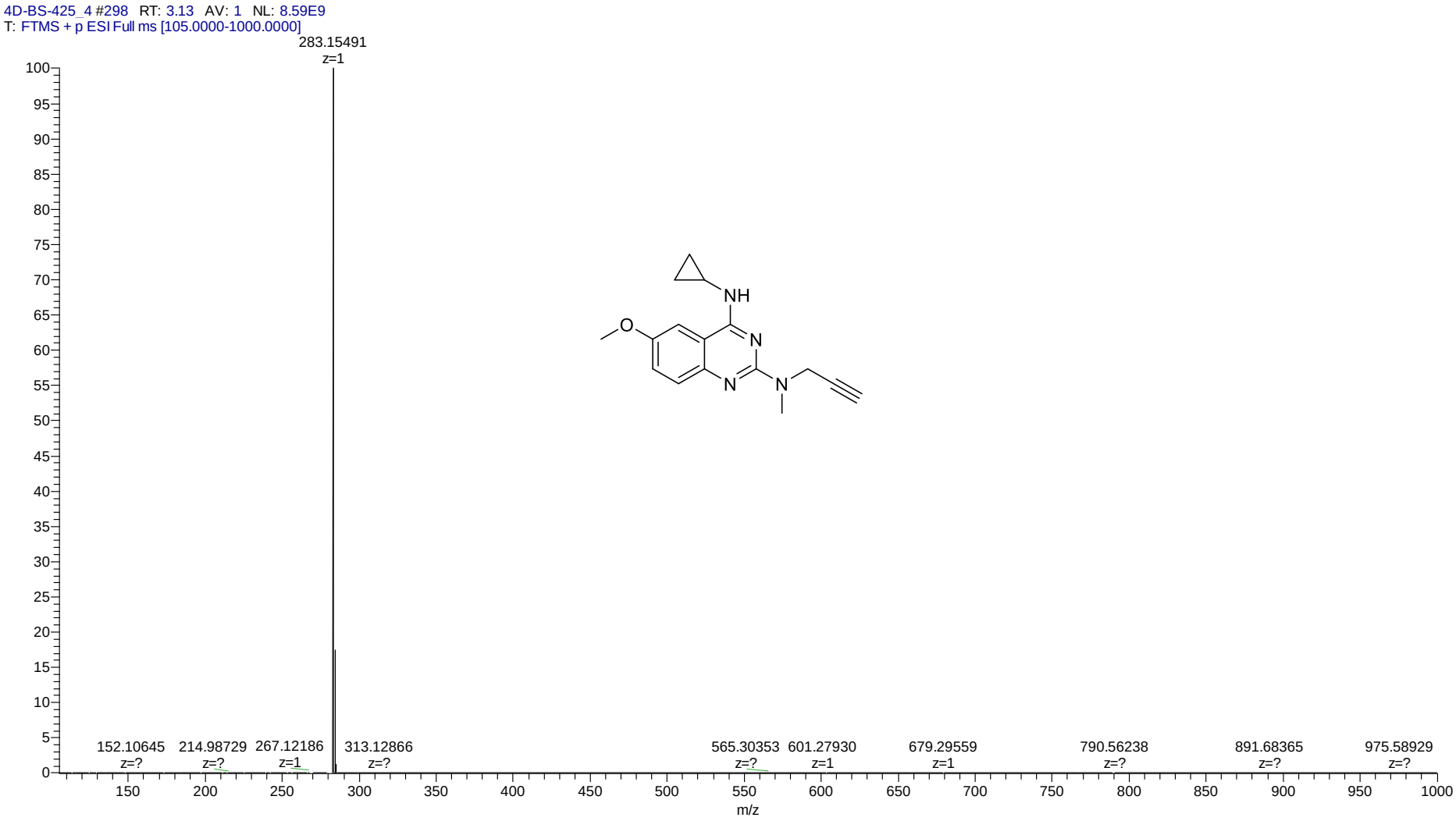


Fig. S135. **LC-UV chromatogram for *N4*-cyclopropyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6g)**

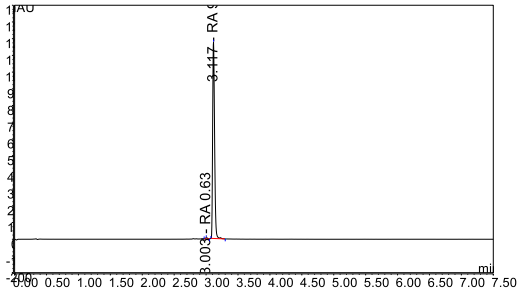


Fig. S136. HRMS spectrum for *N4*-cyclohexyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6h)

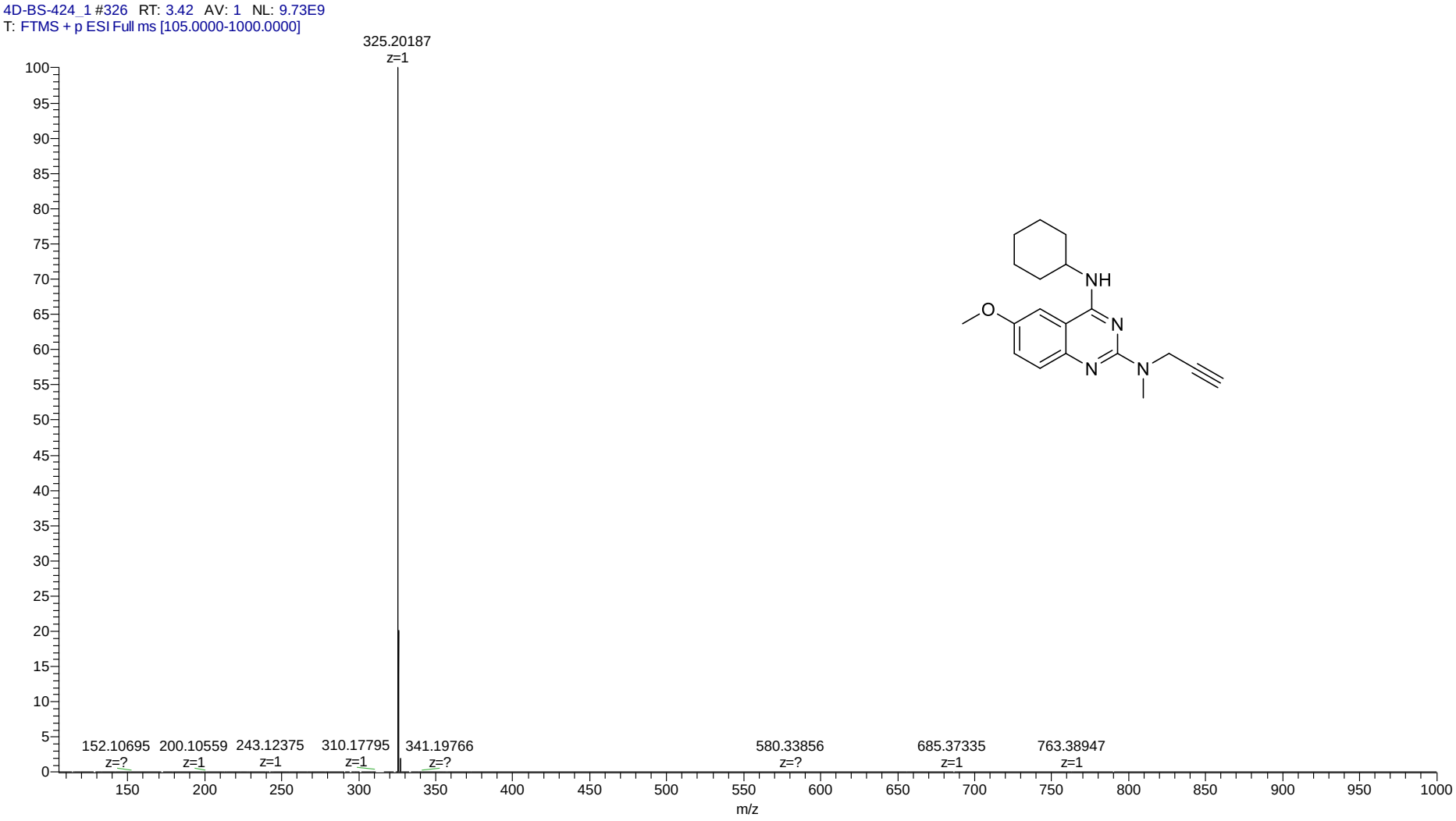
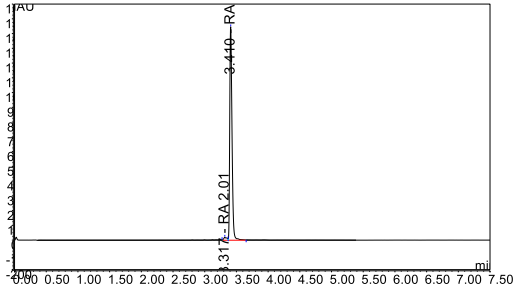


Fig. S137. **LC-UV chromatogram for *N4*-cyclohexyl-6-methoxy-*N2*-methyl-*N2*-(prop-2-yn-1-yl)quinazoline-2,4-diamine (III-6h)**



6. References

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