Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

Copper catalyzed synthesis of aryloxy tethered symmetrical 1,2,3-triazoles as potential antifungal agents targeting 14 α-demethylase

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Experimental section: General method, General procedures

Spectral Data: ^{1}H NMR, ^{13}C NMR, MS/ LCMS

Experimental section

General method

All the chemicals were of laboratory grade, purchased from commercial suppliers Spectrochem, Alfa Aesar and Sigma Aldrich and were used without further purification. Purity and completion of reaction time of all the synthesized compounds were monitored by thin layer chromatography (TLC) using silica gel 60-F_{254} pre-coated on aluminium sheets as an adsorbent, Merck, Germany and visualization was accomplished by iodine/ultraviolet light. Melting points of all the synthesized compounds were determined in an open capillary tube method and are uncorrected. The IR spectra were recorded on Brukar FT-IR spectrometer. ^{1}H NMR spectra were recorded on a Brukar DRX-400 and 400/500 MHz NMR spectrometer using tetramethylsilane (TMS) as an internal standard and chemical shifts are in δ(ppm). The splitting pattern abbreviations are designed as singlet (s); doublet (d); double doublet (dd); triplet (t) and multiplet (m). ^{13}C NMR spectra were recorded on a Brukar DRX-75 and 100/125 MHz NMR in DMSO-d_6/ $CDCl_3$. mass spectra (MS/LCMS) were obtained using MALDI-TOF-Mass spectrometer / LC-MS instrument.

General procedure for the synthesis of azide derivatives (4a-m)

General procedure for synthesis 2-chloro-*N*-phenylacetamide derivatives (3a-m)

In a round bottom flask, anilines (**1a-m**) (0.1 mol) and triethyl amine base were dissolved in chloroform and stirred at 0 °C temperature in ice bath. The 2-chloroacetyl chloride (**2**) (0.1 mol) was added to reaction mixture drop wise with continuous stirring on magnetic stirrer. After this addition, the ice bath was removed and the reaction mixture was stirred at room temperature for 4 h. The progress of the reaction was monitored by TLC using ethyl acetate: hexane (1:9) as a solvent system. After completion of the reaction, the reaction mixture was poured on crushed ice and neutralised by adding acetic acid to it. The obtained solid intermediates of respective amines were filtered, dried and crystallised in ethanol. The melting points of all the compounds shows good agreement with the reported.[1,2]

General procedure for synthesis of 2-azido-*N*-phenylacetamide derivatives (4a-m)

The freshly synthesized intermediates of 2-chloro-*N*-phenylacetamide derivatives (**3a-m**) were refluxed with aqueous solution of sodium azide (0.1 mol) in toluene for 6 h. The progress of the reaction was monitored by TLC using ethyl acetate: hexane (1:9) as a solvent system. After completion of the reaction, the reaction mixture was poured on crushed ice. All the synthesized azides (**4a-m**) were obtained as solid compounds except azide (**4e**) which was obtained in liquid state from o-anisidine. This azide (**4e**) was extracted in organic layer using ethyl acetate and solvent is removed under reduced pressure. After this, it was used for further reaction without any purification. The compounds were filtered, dried and crystallised in ethanol and then used for further reaction. The melting points of all freshly synthesized azides (**4a-m**) were in good agreement with the reported.[1,2]

General procedure for synthesis of bis(prop-2-yn-1-yloxy)benzene derivatives (6a-b)

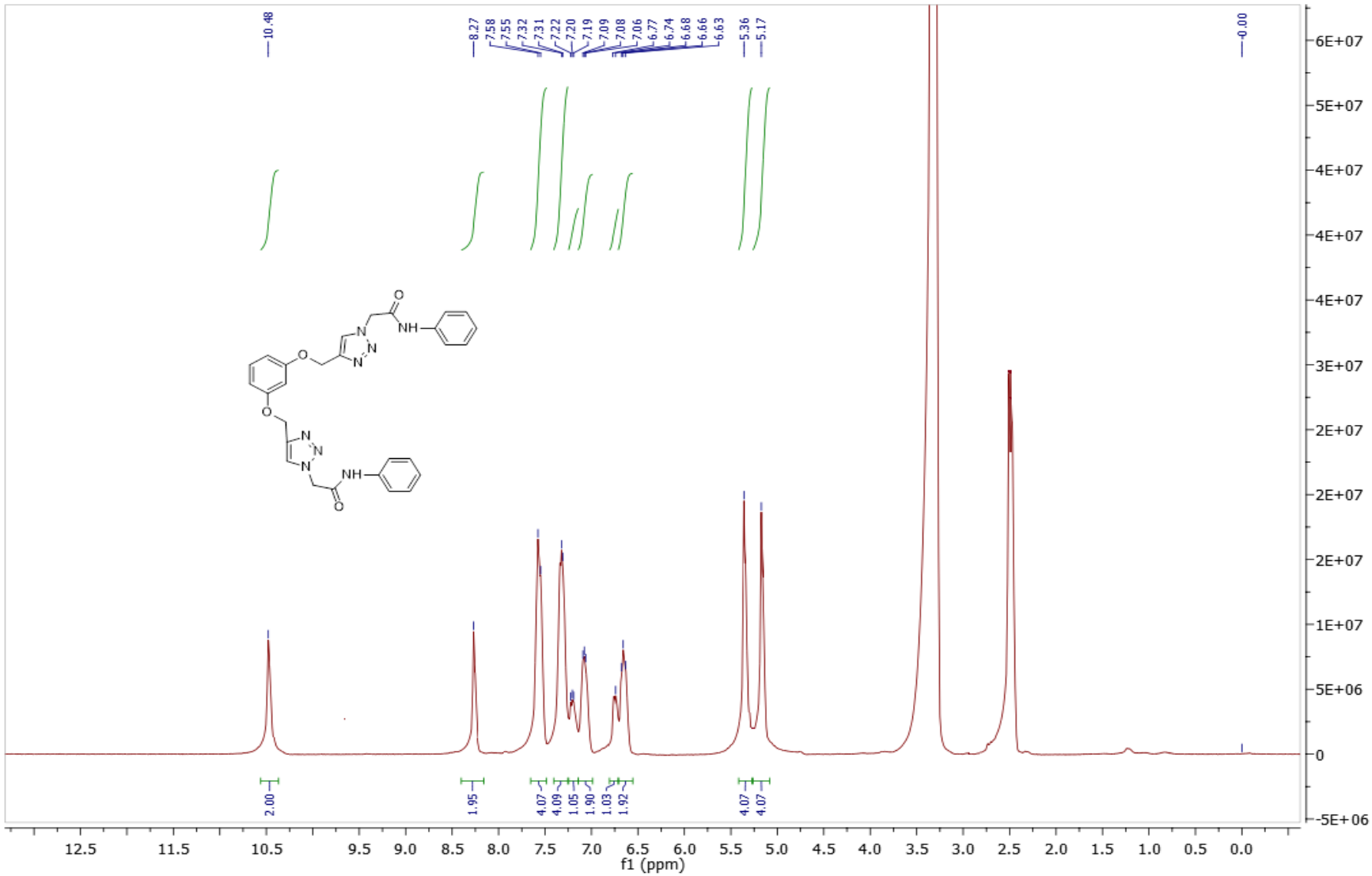
In a round bottom flask resorcinol (**5a**) or catechol (**5b**) (0.01 mol) were allowed to react with propargyl bromide (0.02 mol) in presence of K_2CO_3 base dissolved in DMF and stirred at room temperature for 2 h. The progress of the reaction was monitored by TLC using ethyl acetate: hexane (1:9) as a solvent system. After completion of the reaction, the reaction mixture was poured on crushed ice. Ethyl acetate was added to the mixture and the organic layer was separated. The aqueous layer was extracted with 3 x 10 mL of ethyl acetate. Solvent was removed under reduced pressure, and the brownish liquids of 1,3-bis(prop-2-yn-1-yloxy)benzene (**6a**) and 1,2-bis(prop-2-yn-1-yloxy)benzene (**6b**) were obtained from resorcinol and catechol, respectively. The melting points were in good agreement with the reported.[1,3,4]

Spectral data of the synthesized compounds (8a-z)

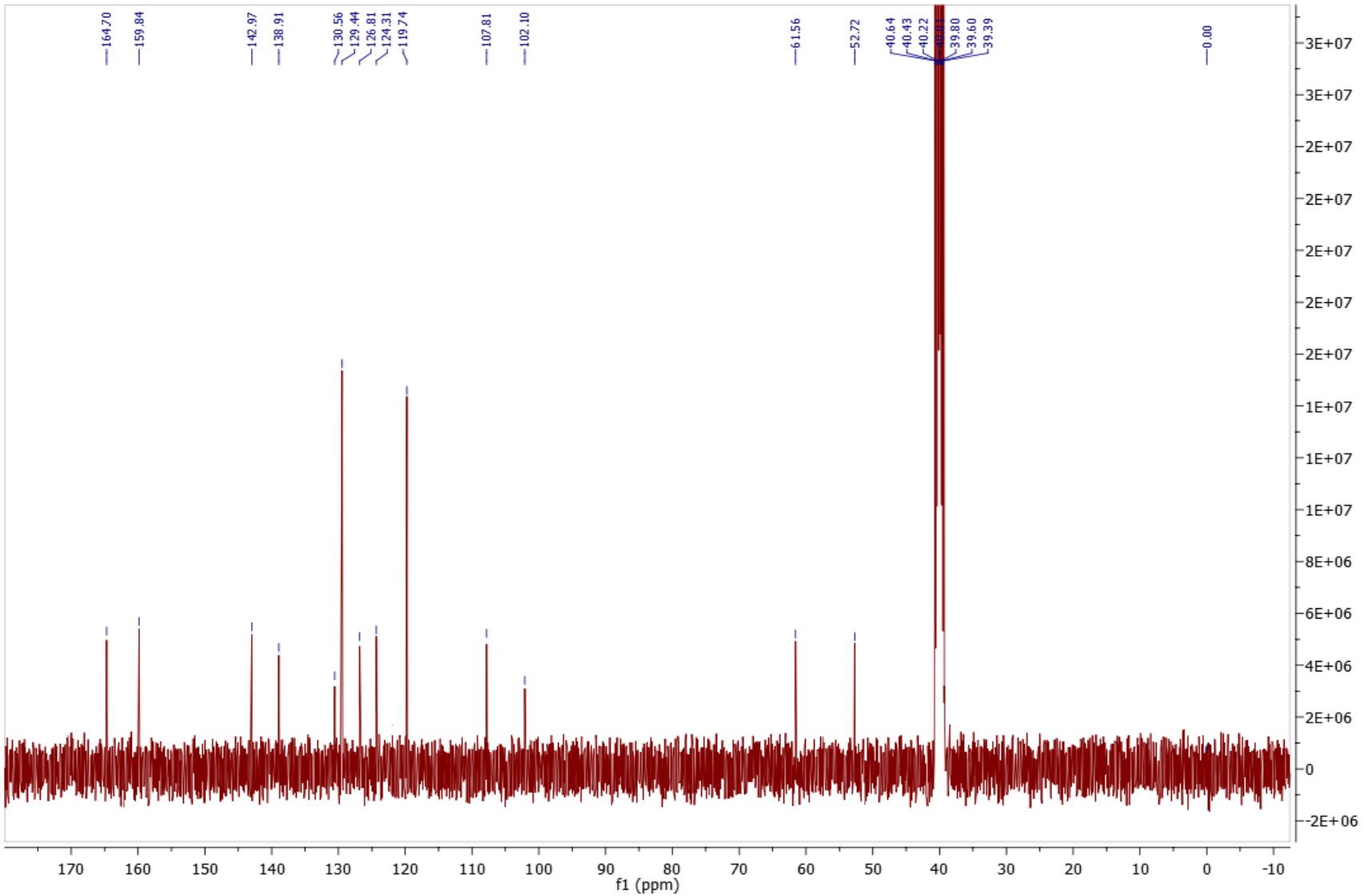
^{1}H NMR

^{13}C NMR

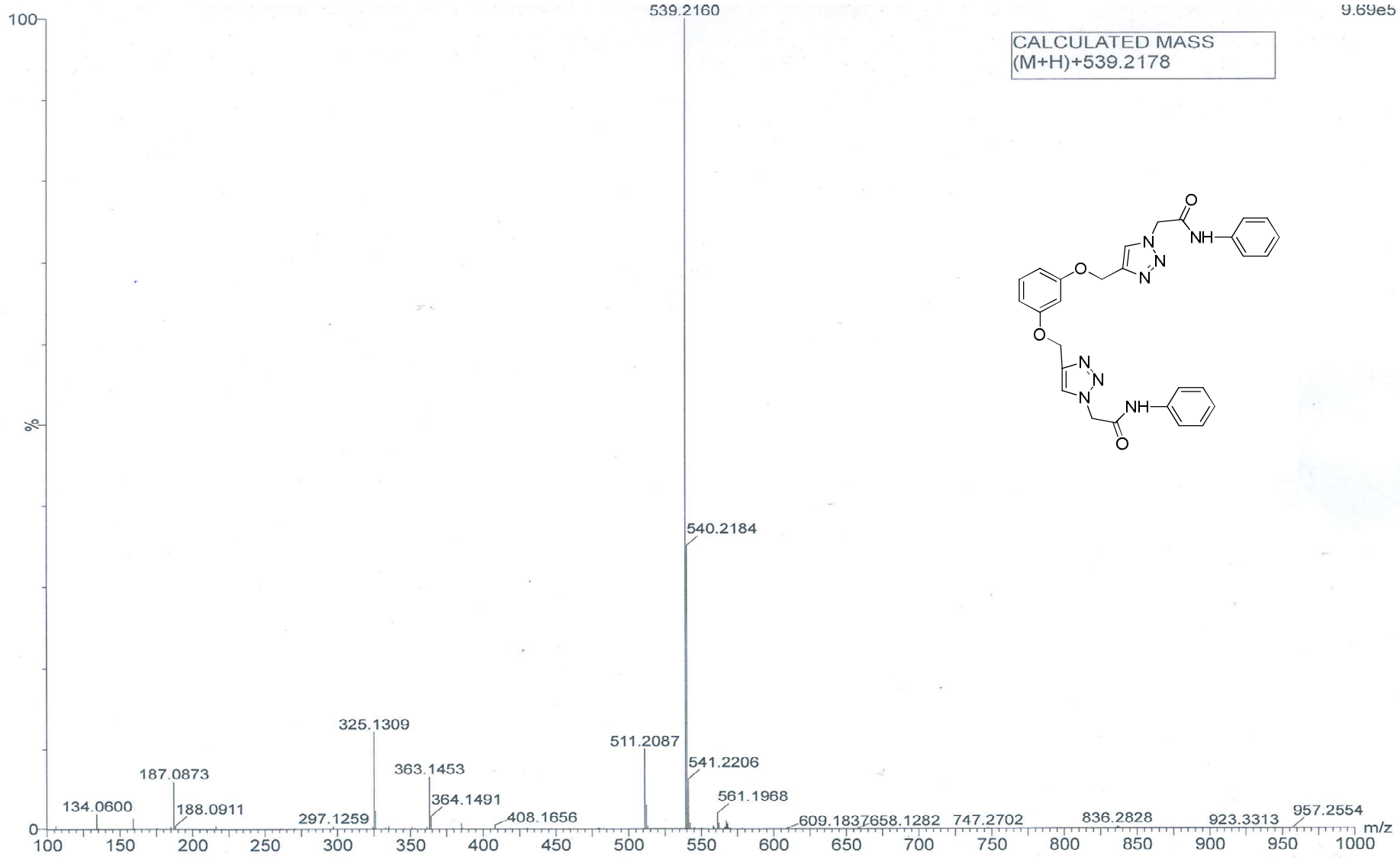
MS/ LCMS



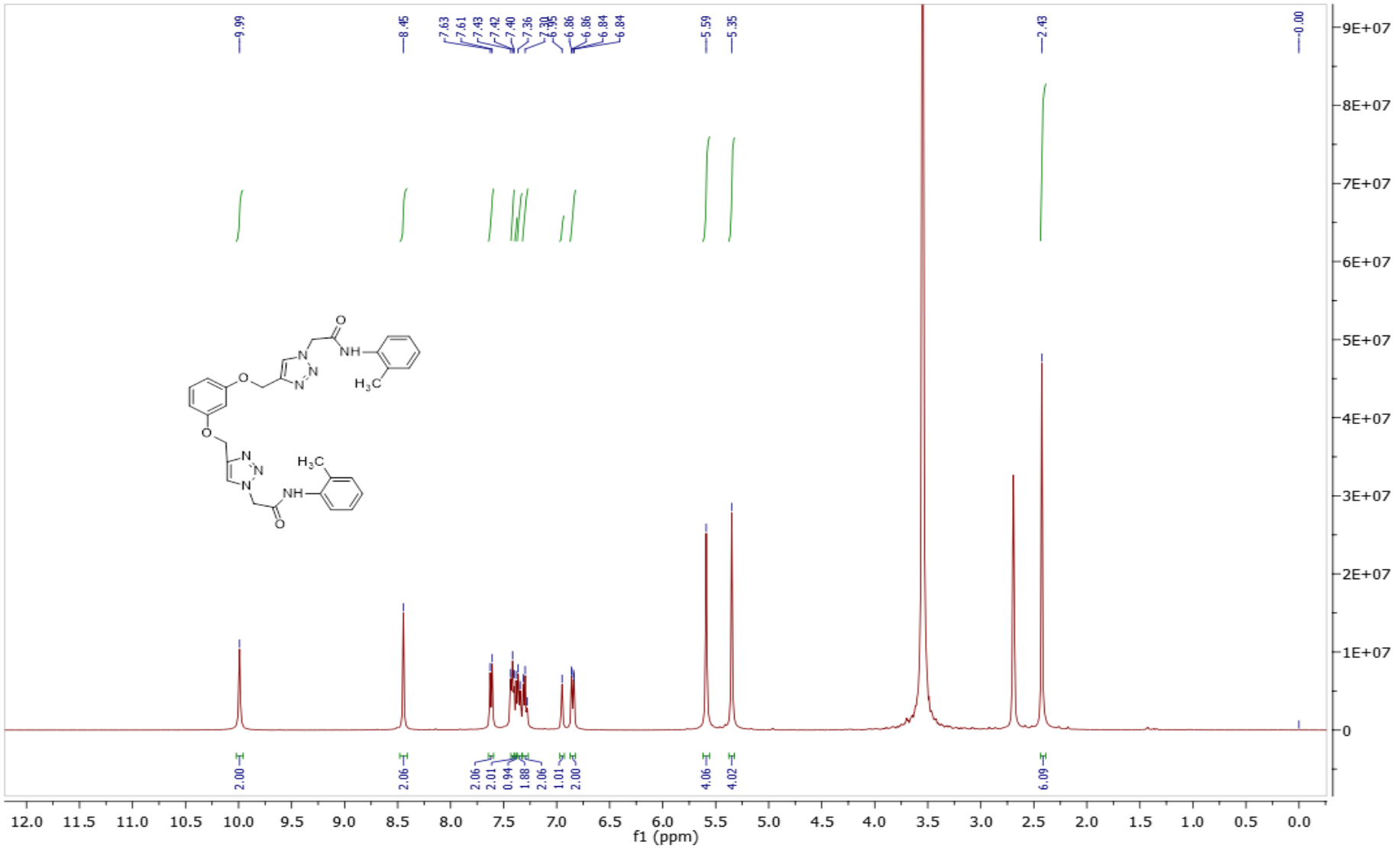
8a: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



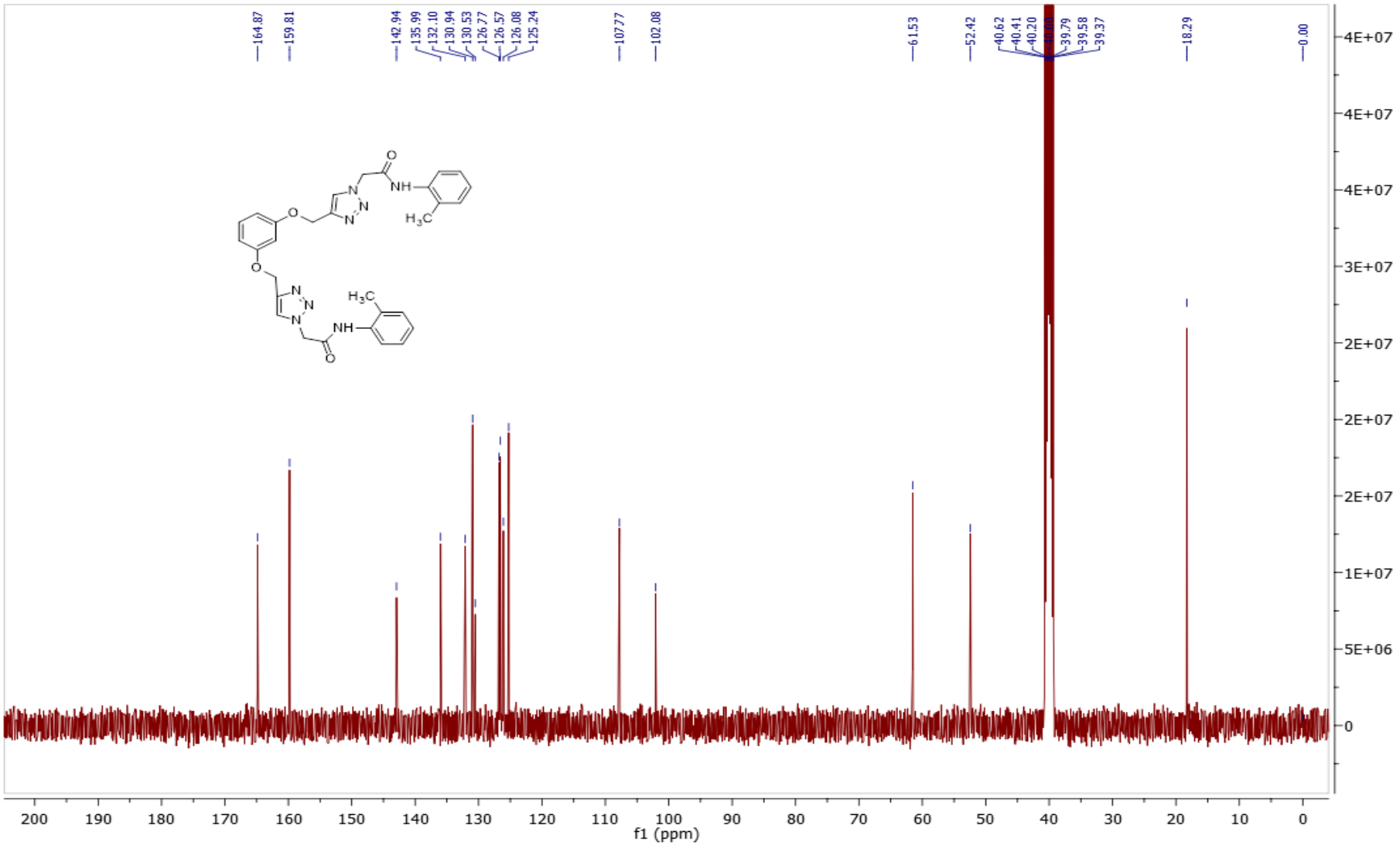
8a: ^{13}C NMR (100 MHz, $CDCl_3$, ppm)



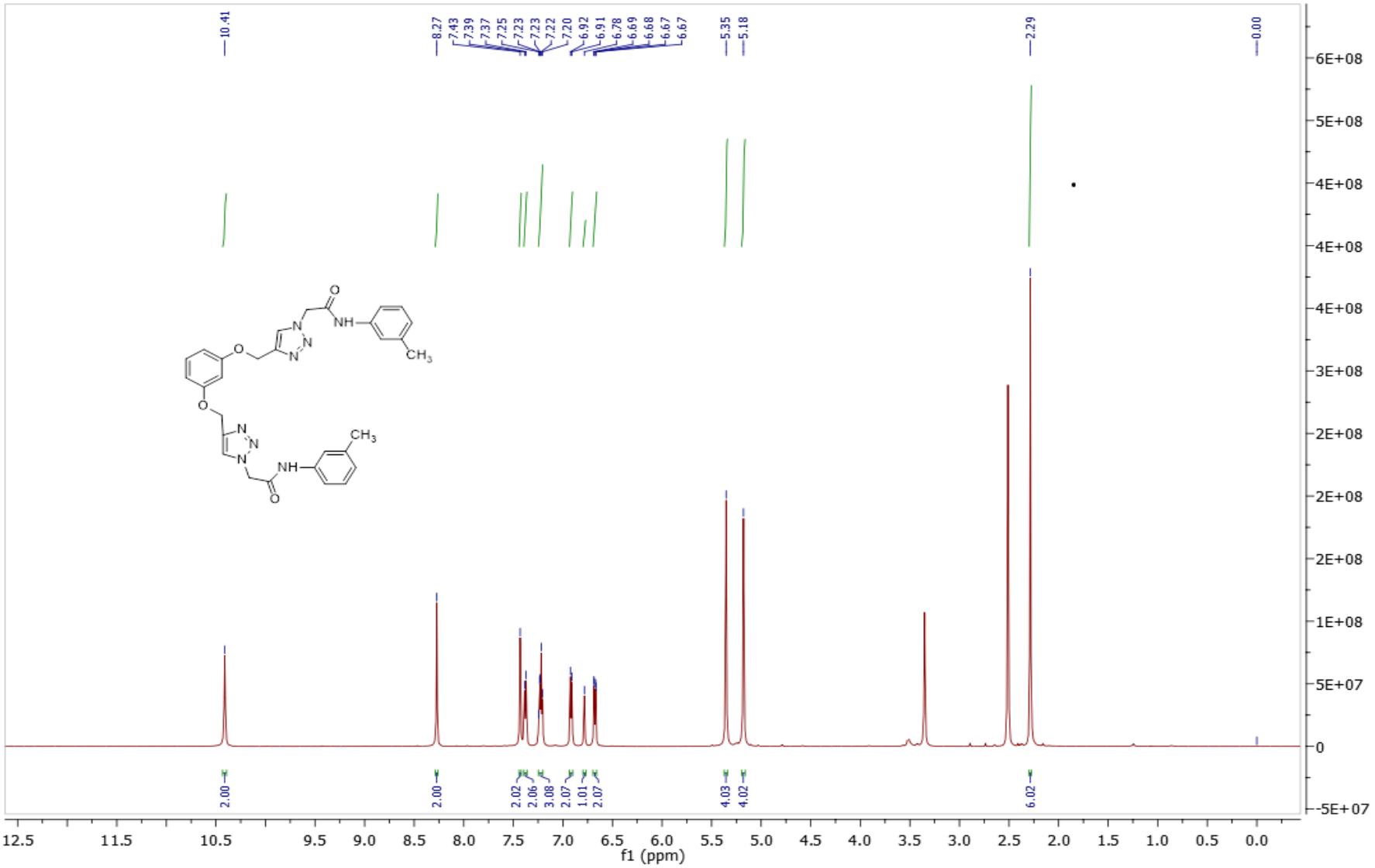
8a: MS (MALDI-TOF) calcd. For $C_{28}H_{27}N_8O_4$ $[M+H]^+$: 539.2155; found: 539.2160.



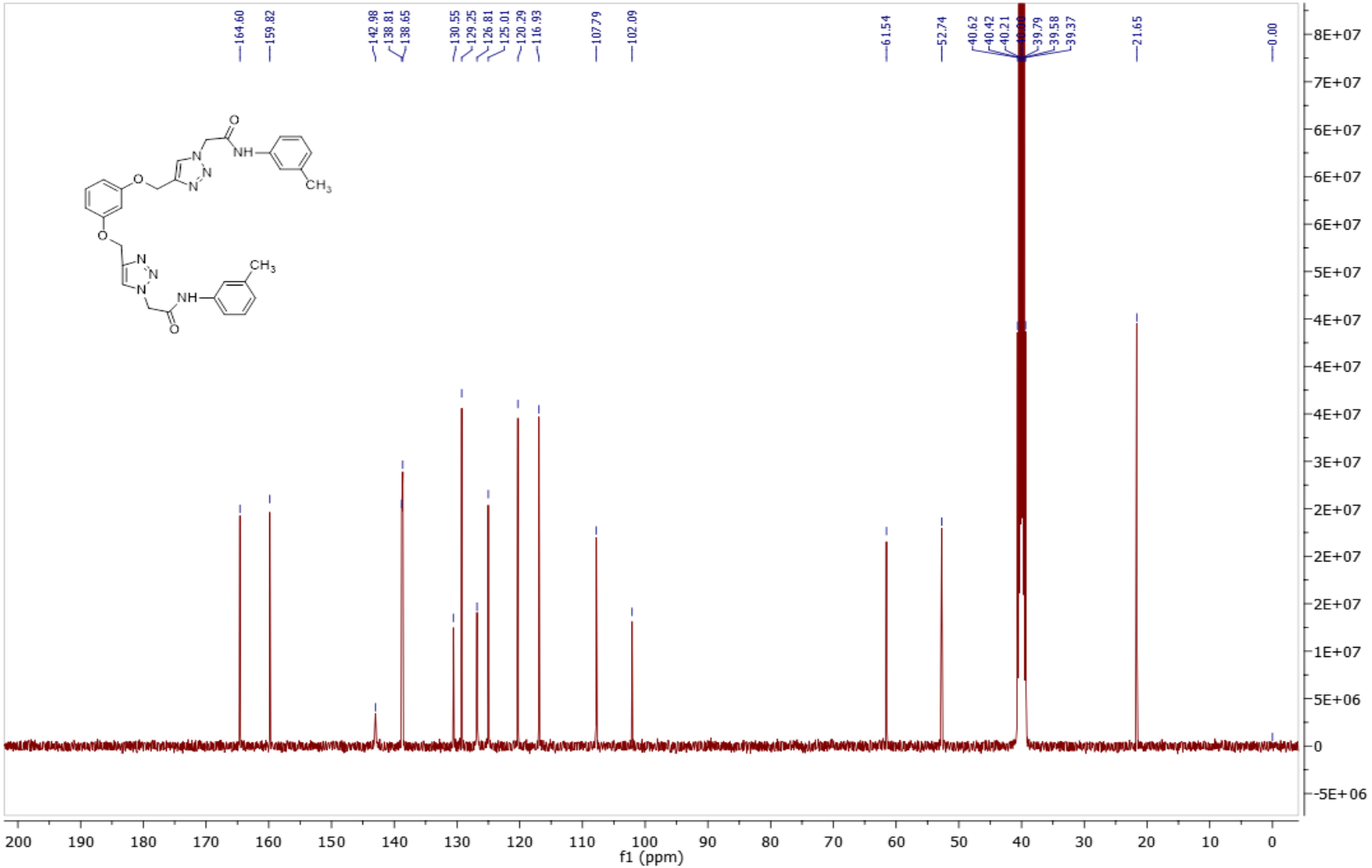
8b: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



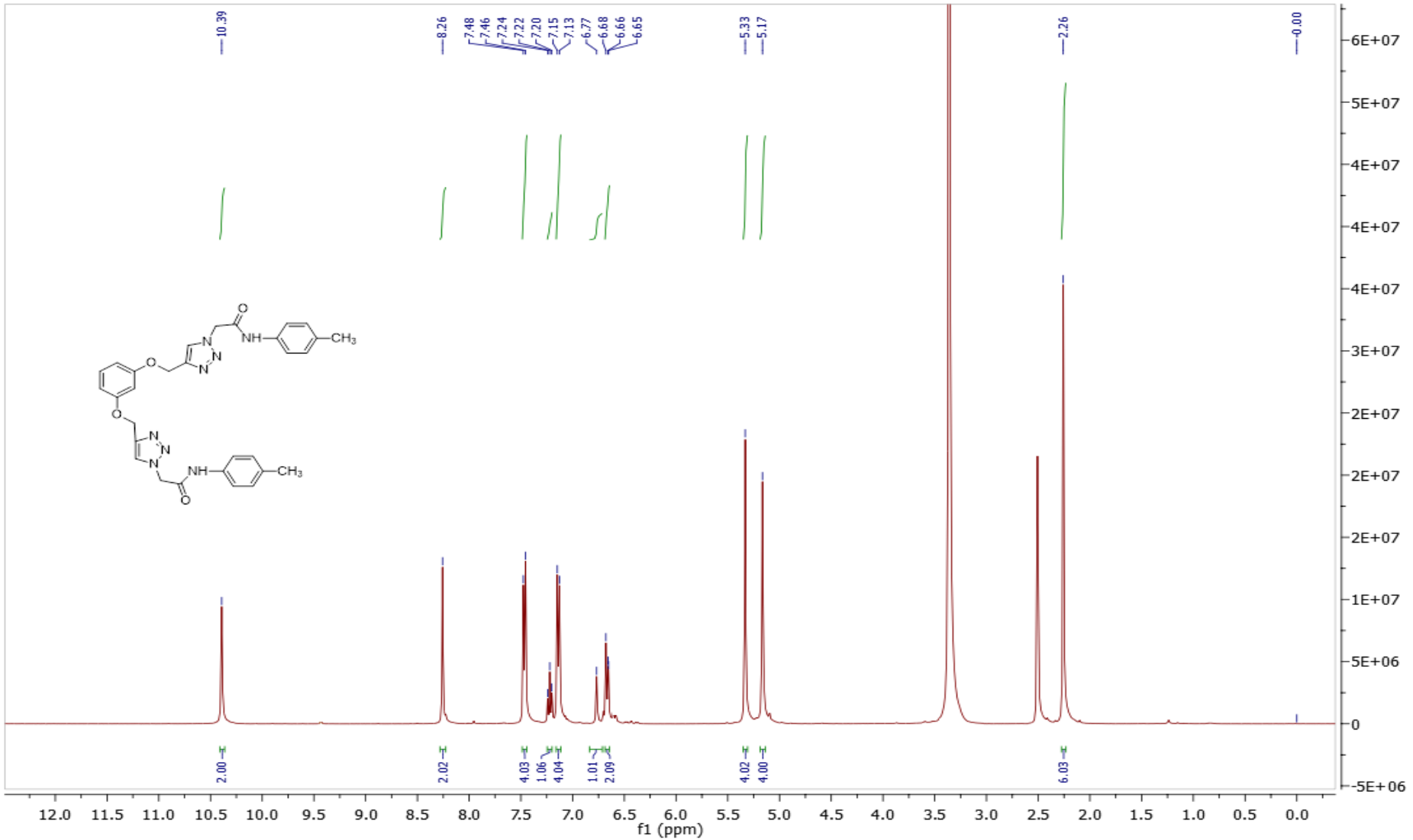
8b: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



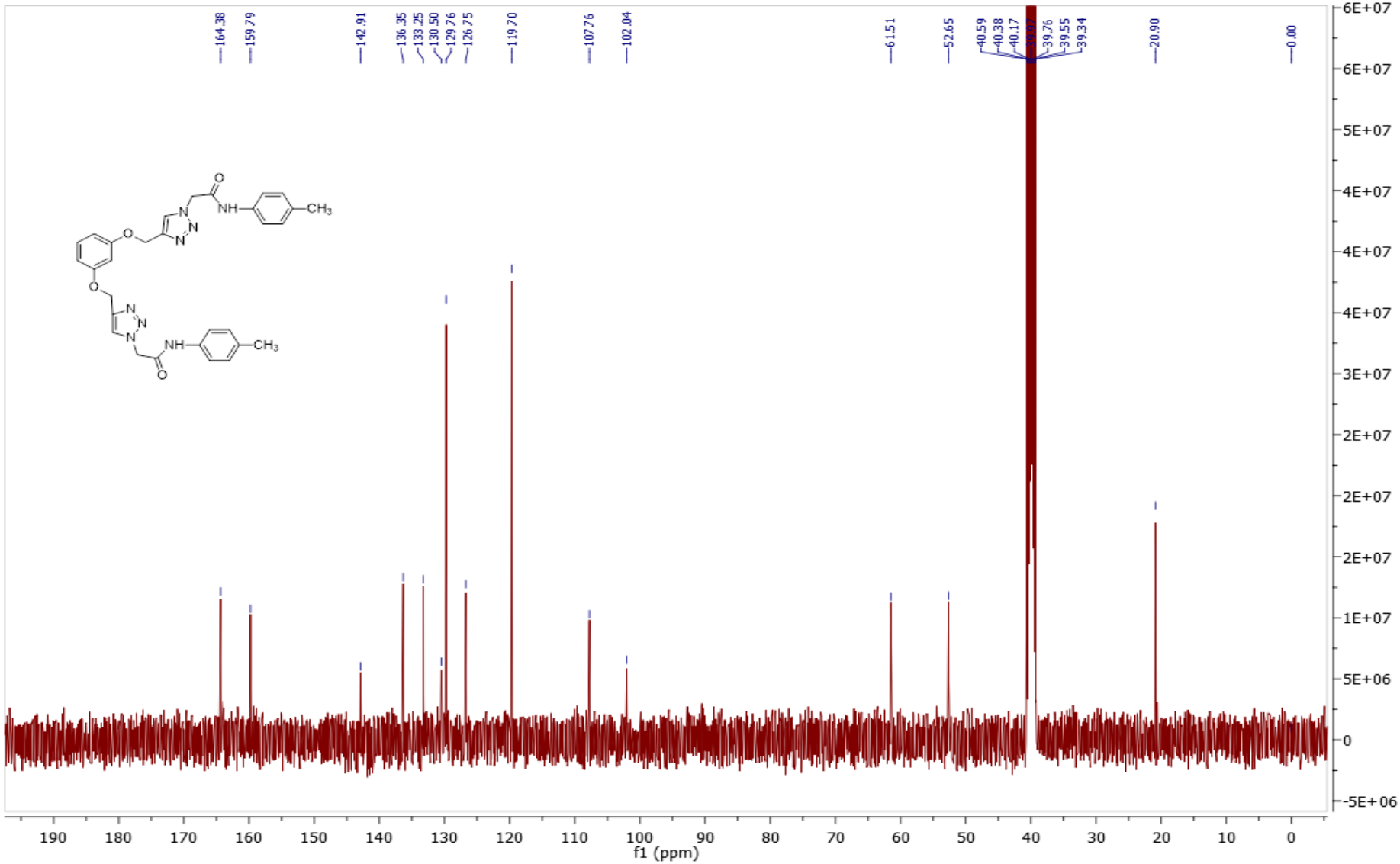
8c: ^{1}H NMR (500 MHz, DMSO-d_6, ppm)



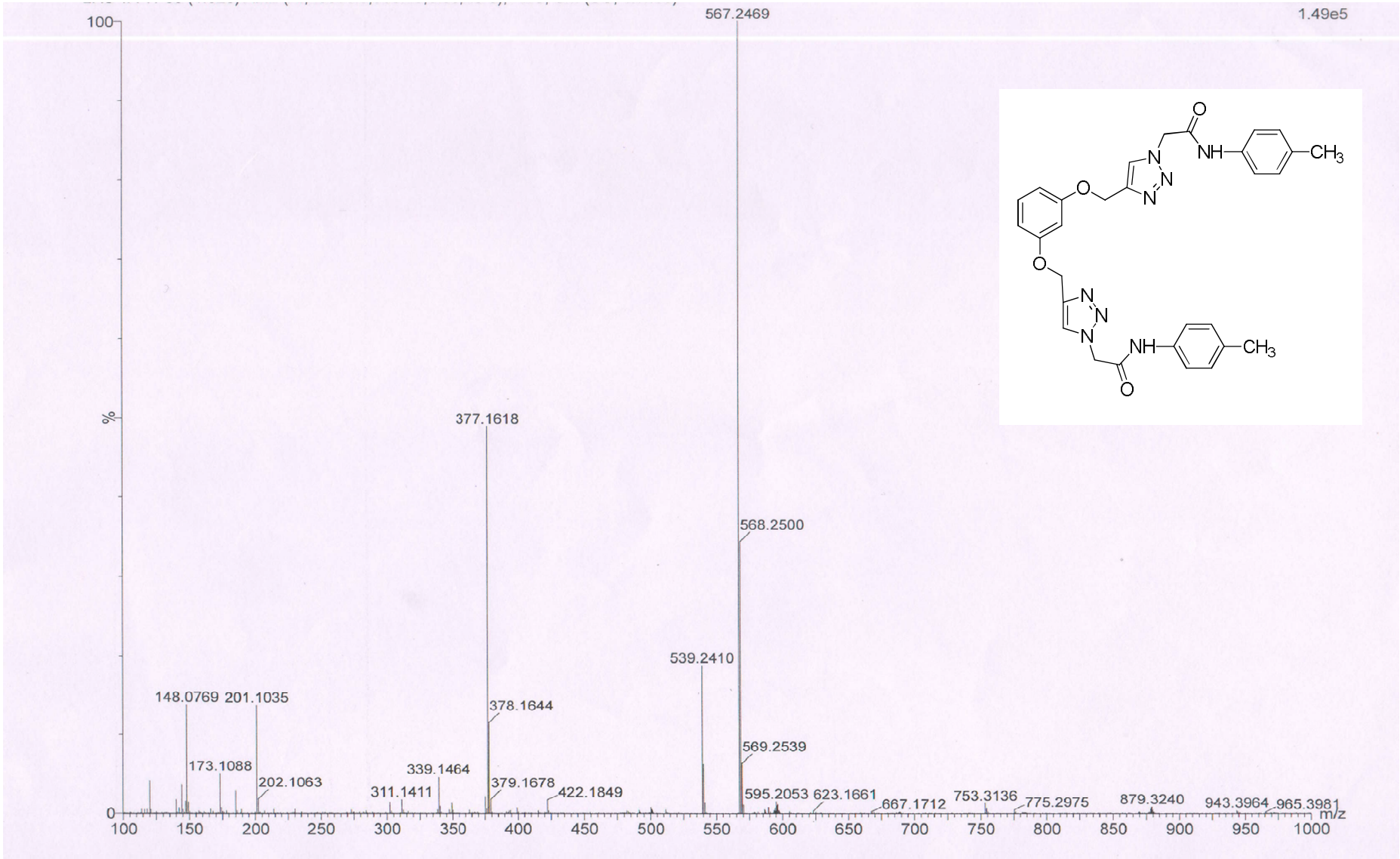
8c: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



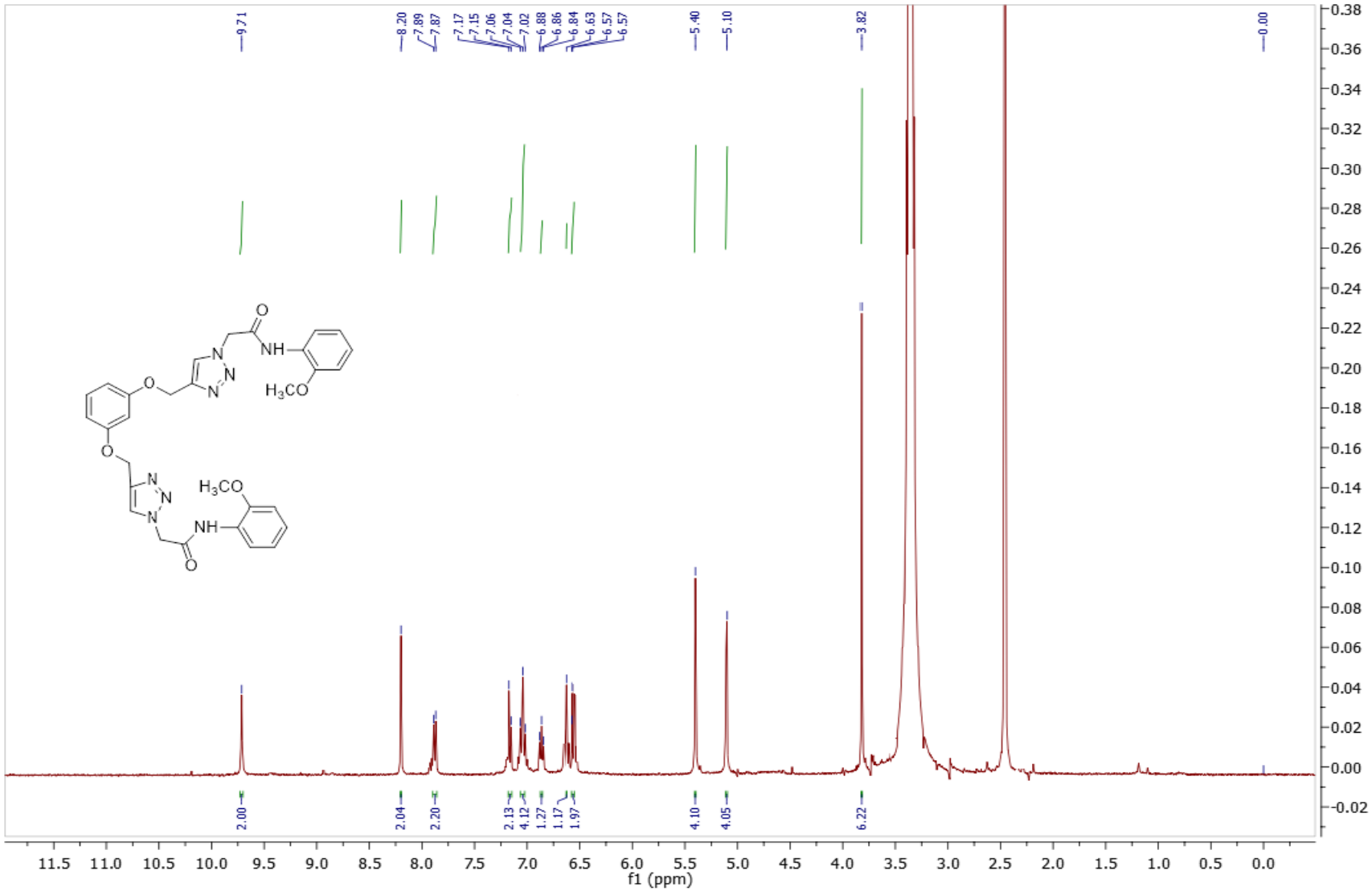
8d: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



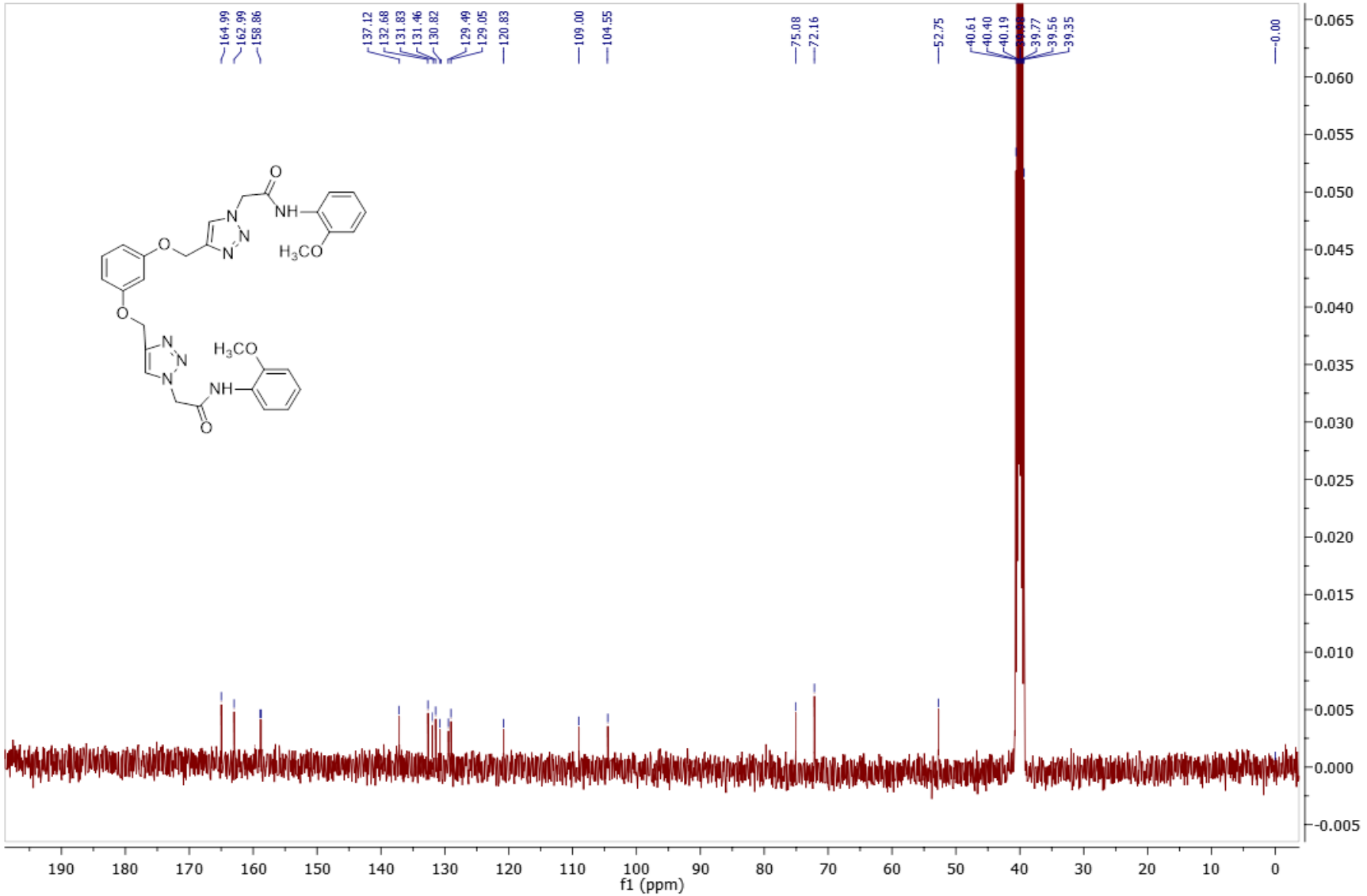
8d: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



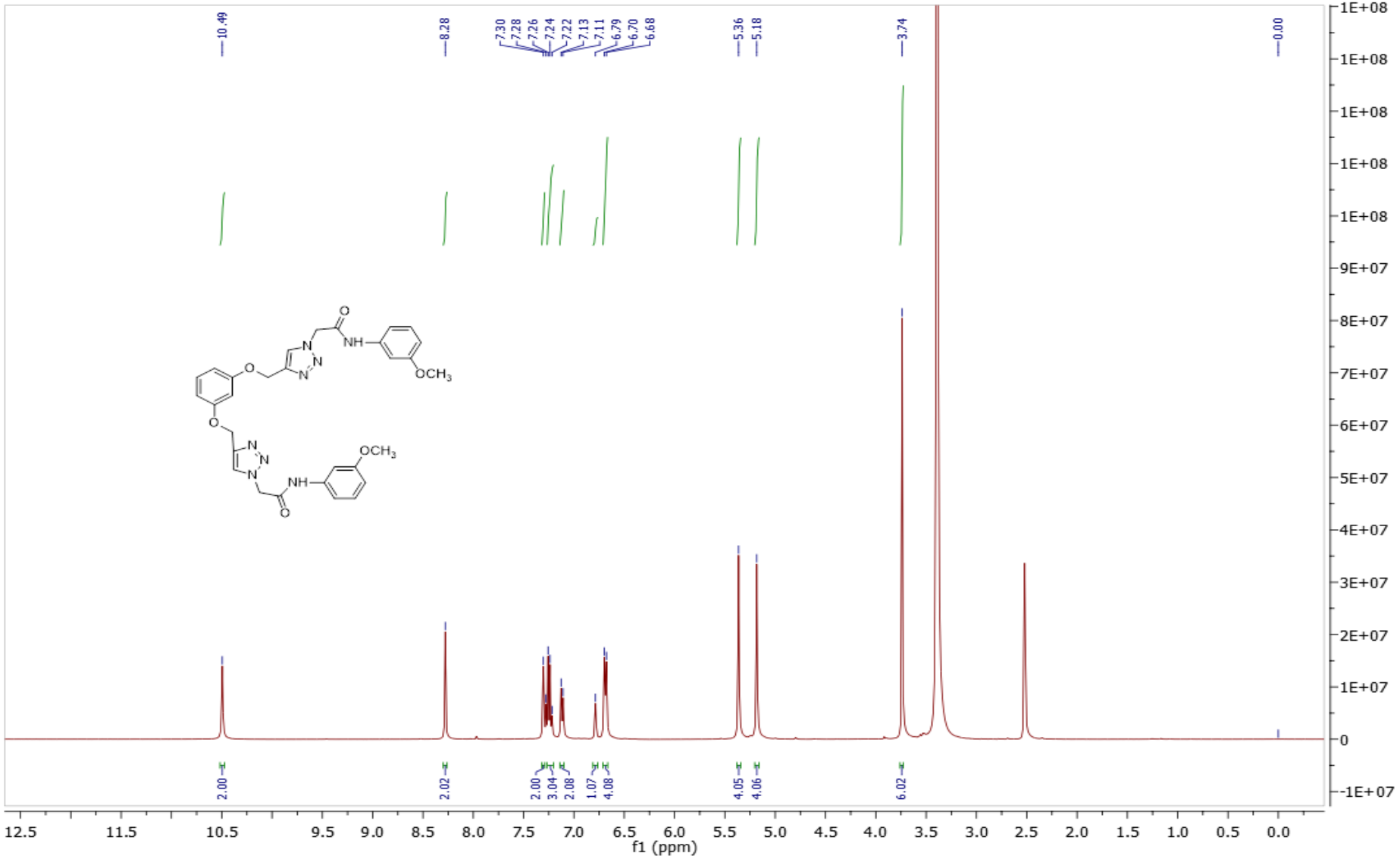
8d: MS (MALDI-TOF) calcd. For $C_{30}H_{31}N_8O_4$ $[M+H]^+$: 567.2468; found: 567.2469.



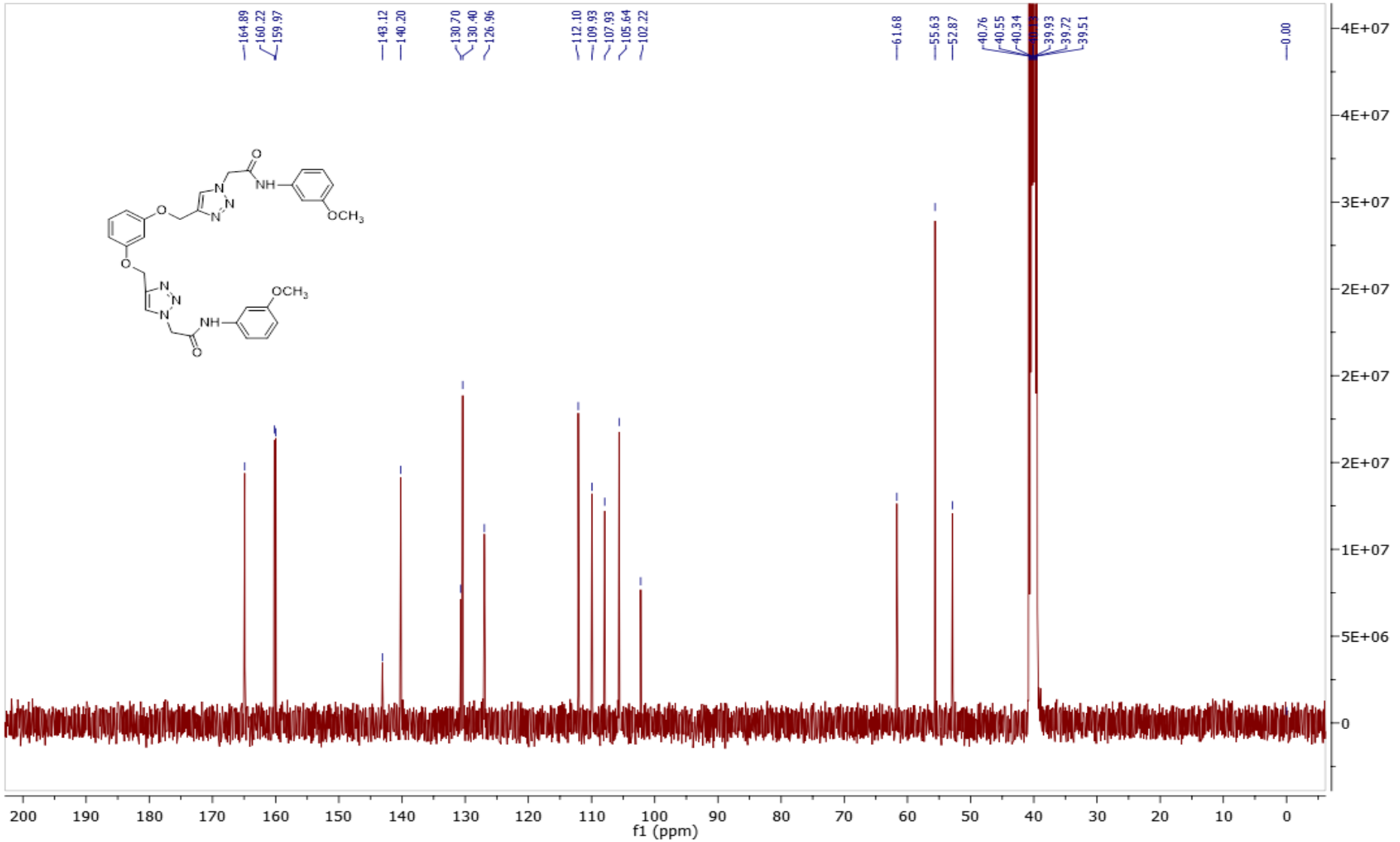
8e: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



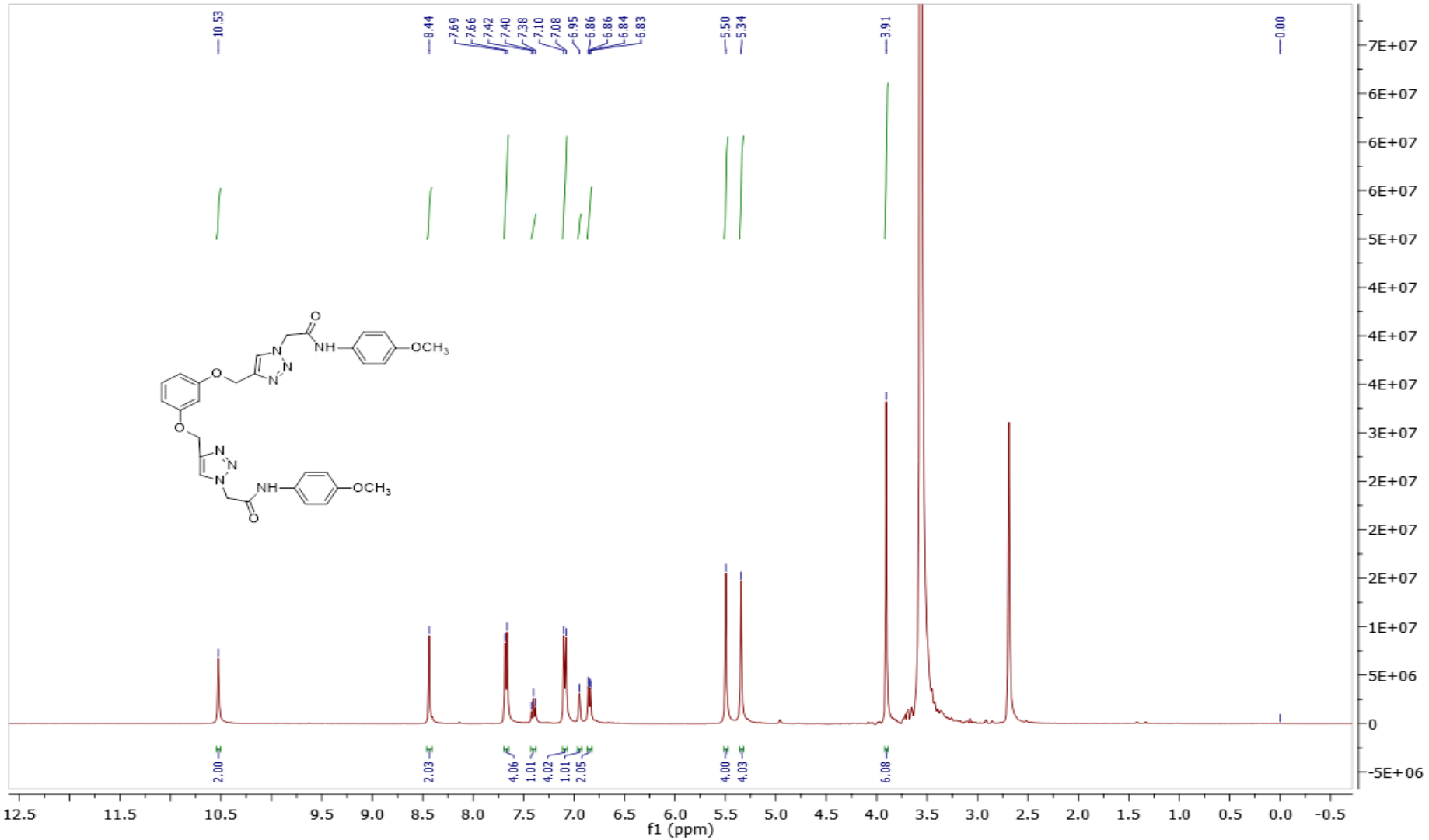
8e: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



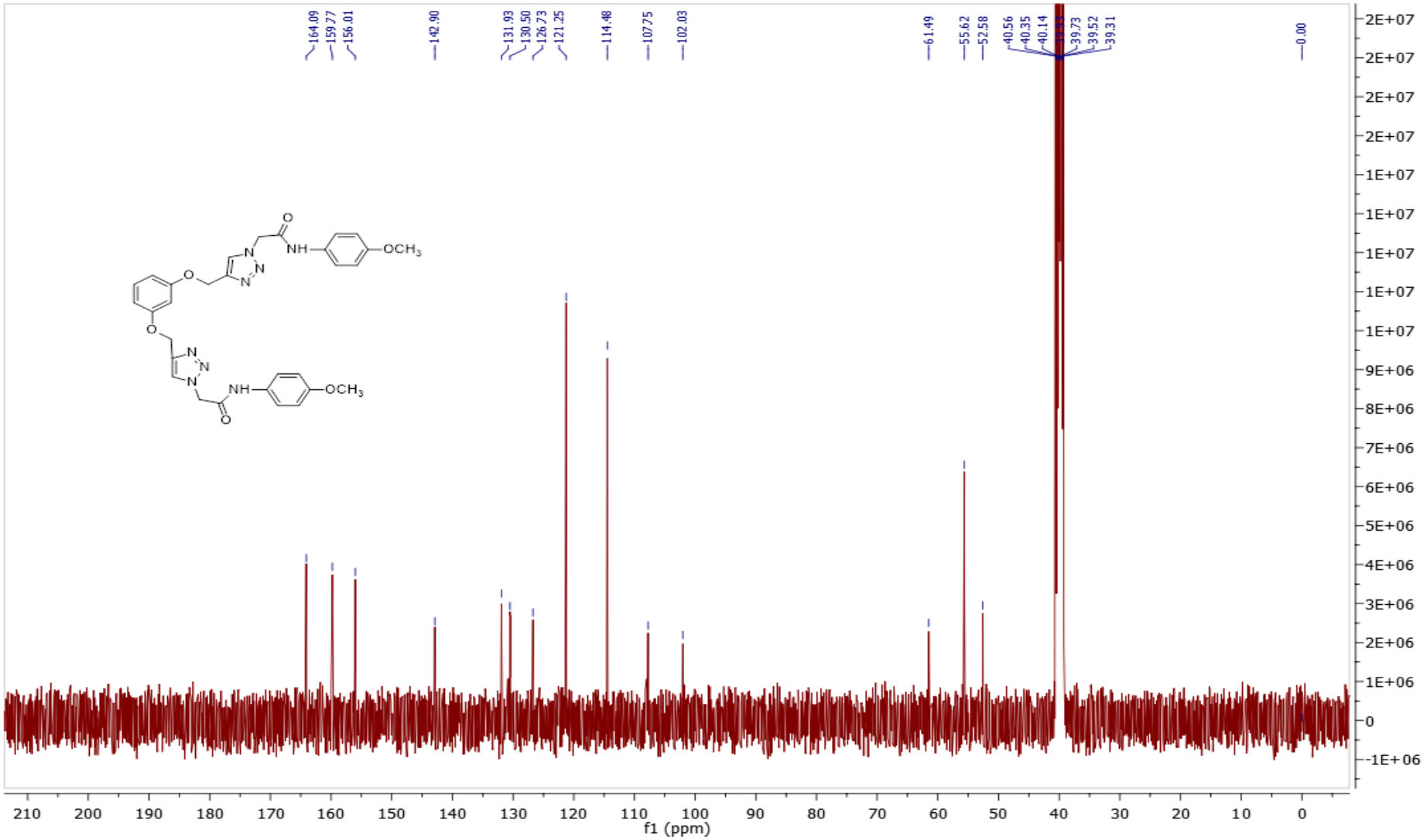
8f: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



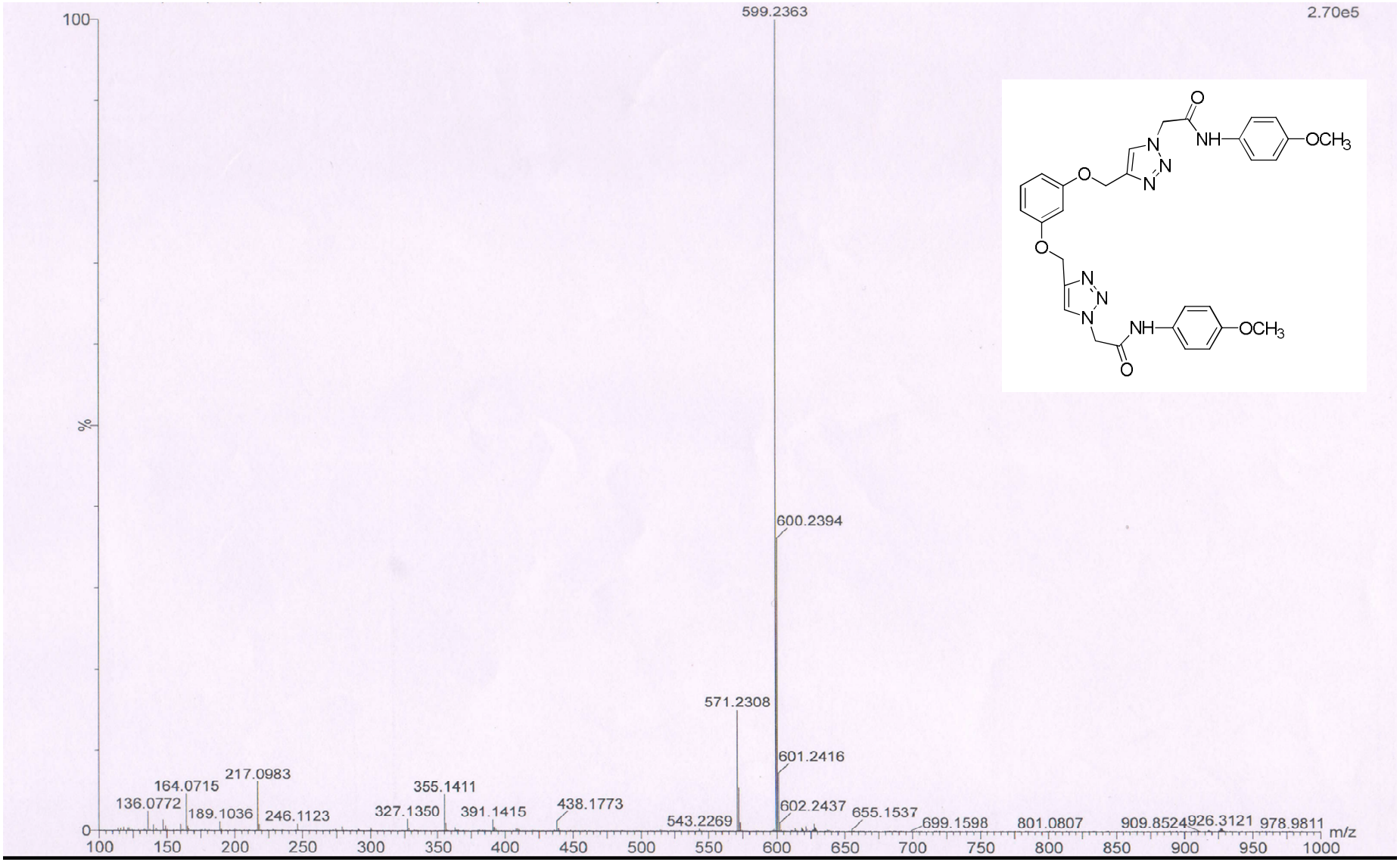
8f: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



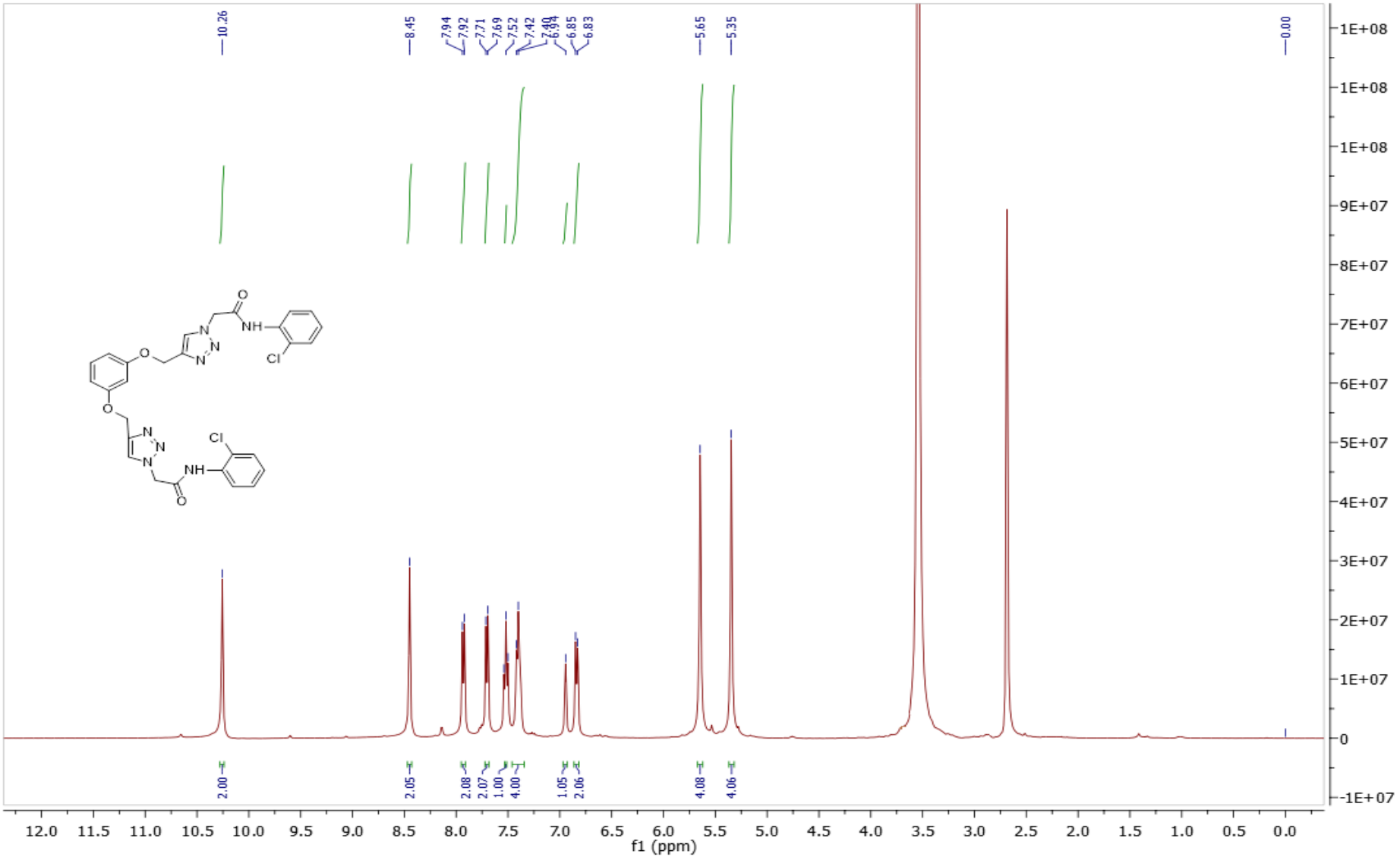
8g: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



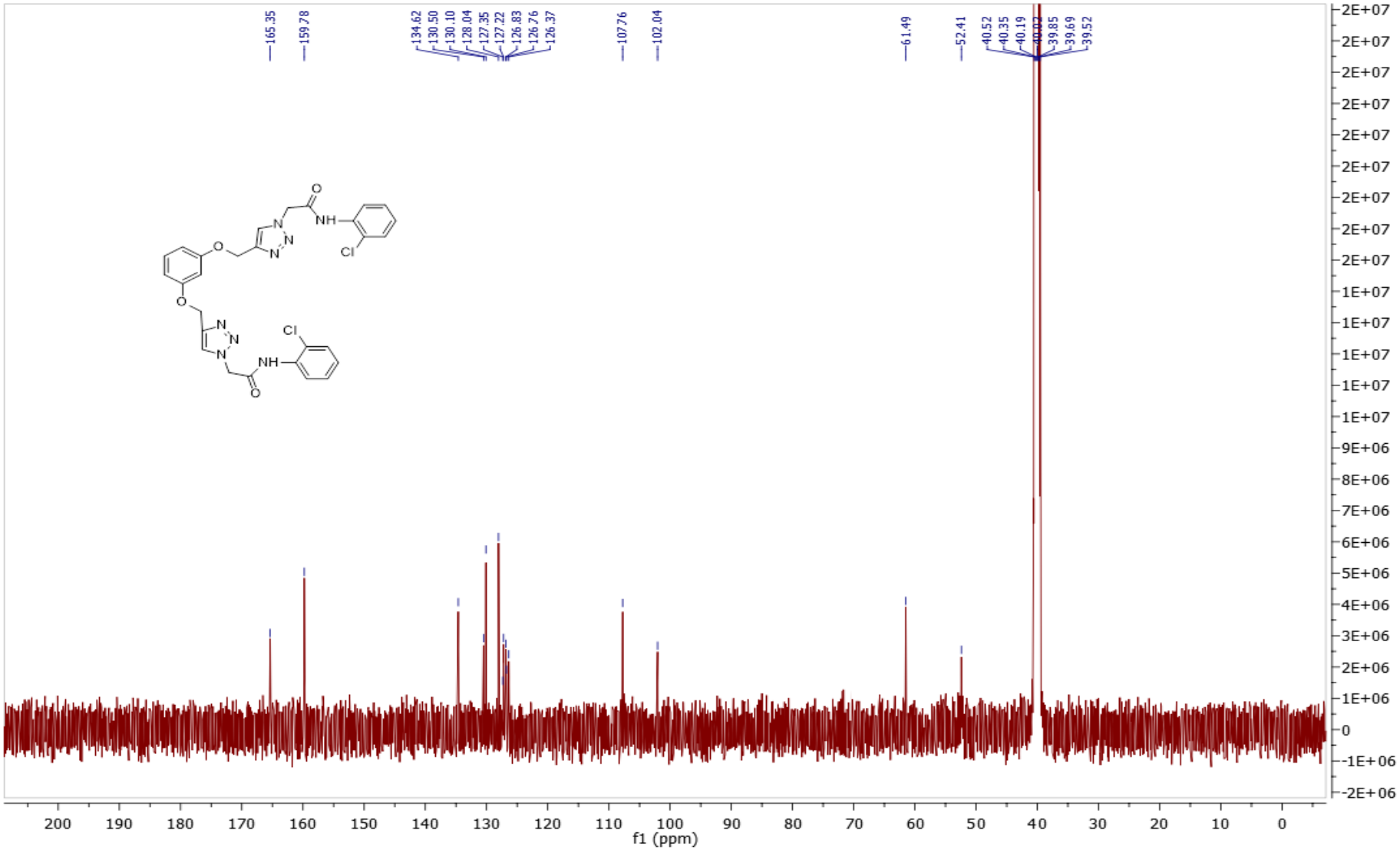
8g: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



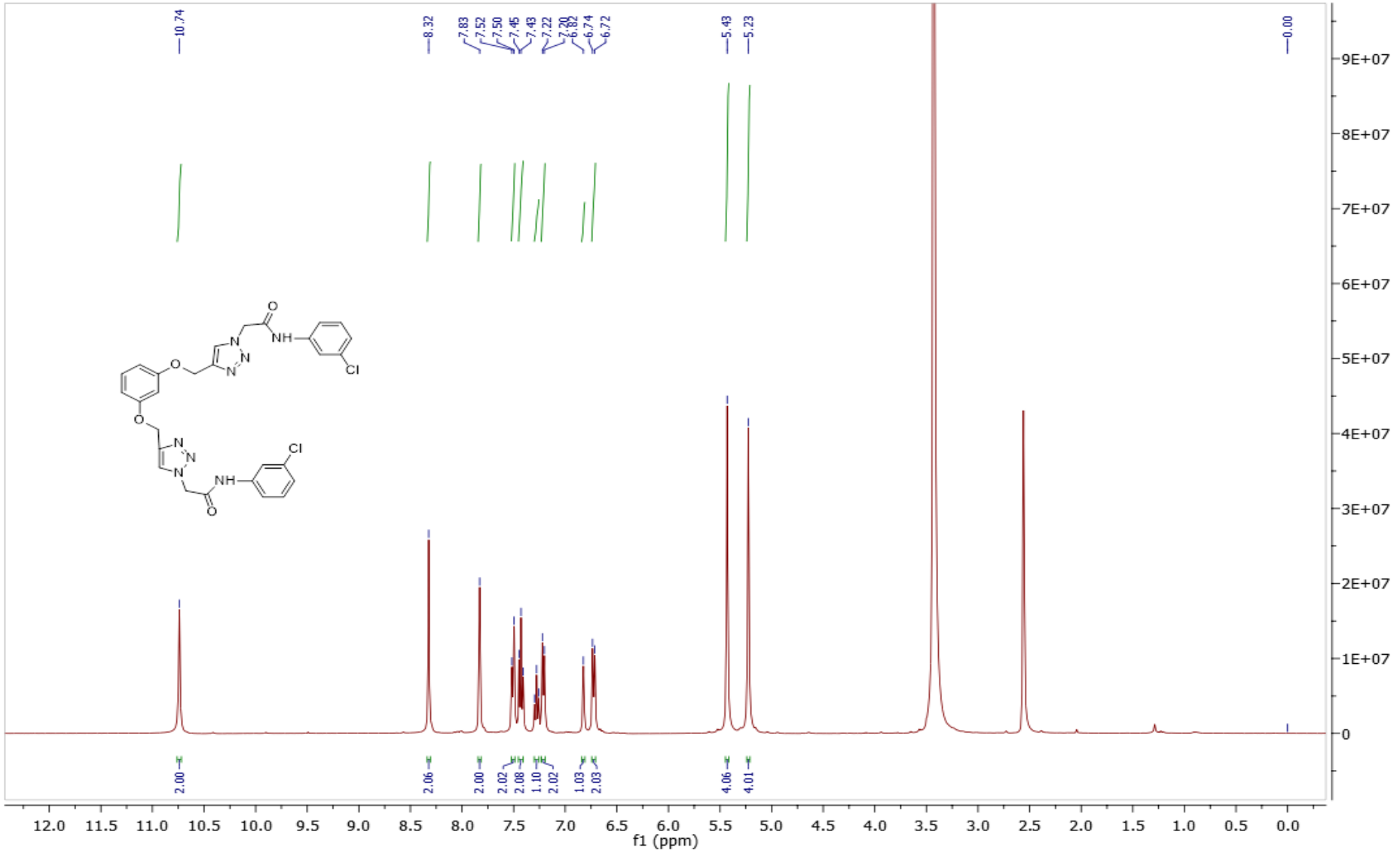
8g: MS (MALDI-TOF) calcd. For $C_{30}H_{31}N_8O_6$ $[M+H]^+$: 599.2367; found: 599.2363.



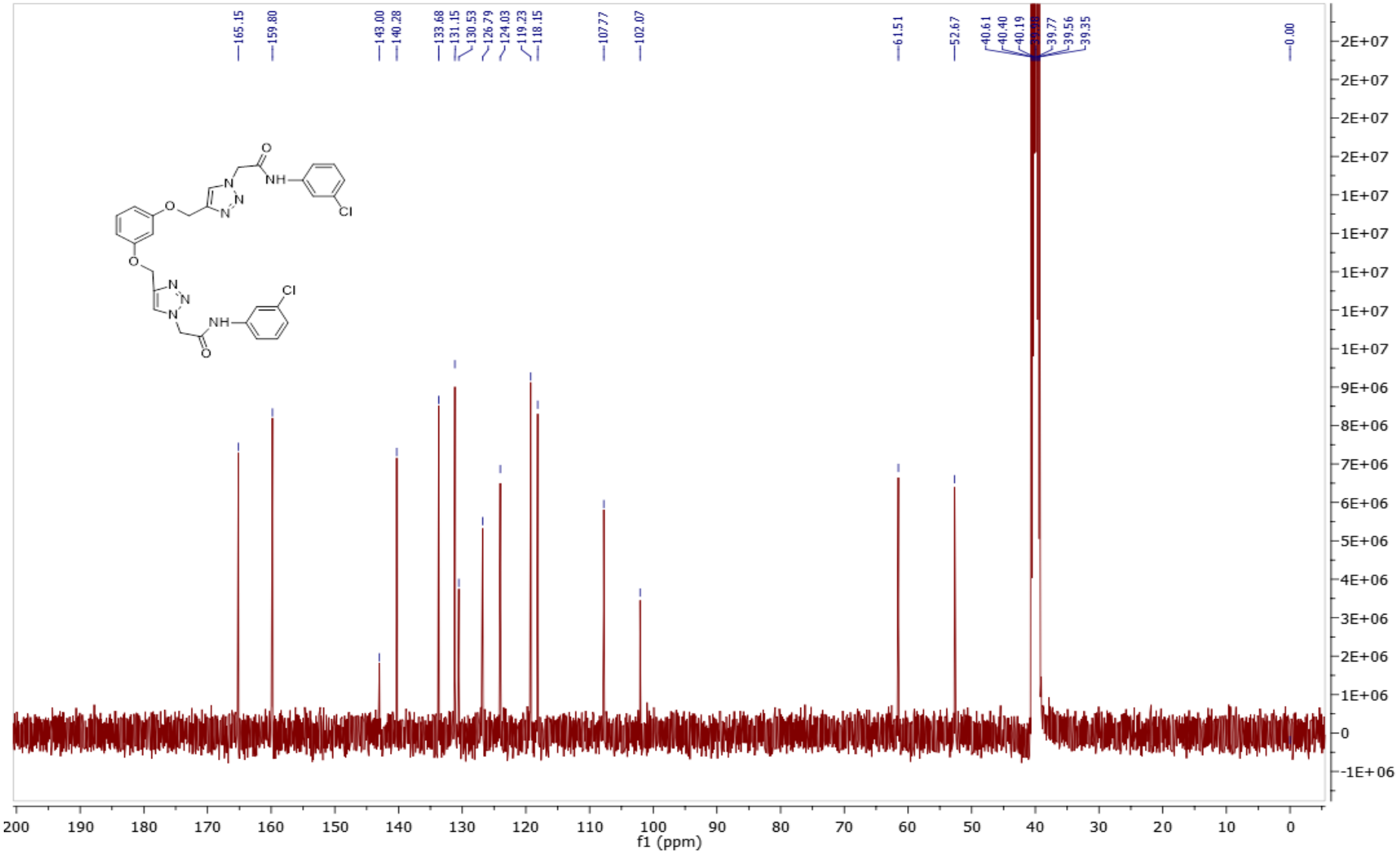
8h: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



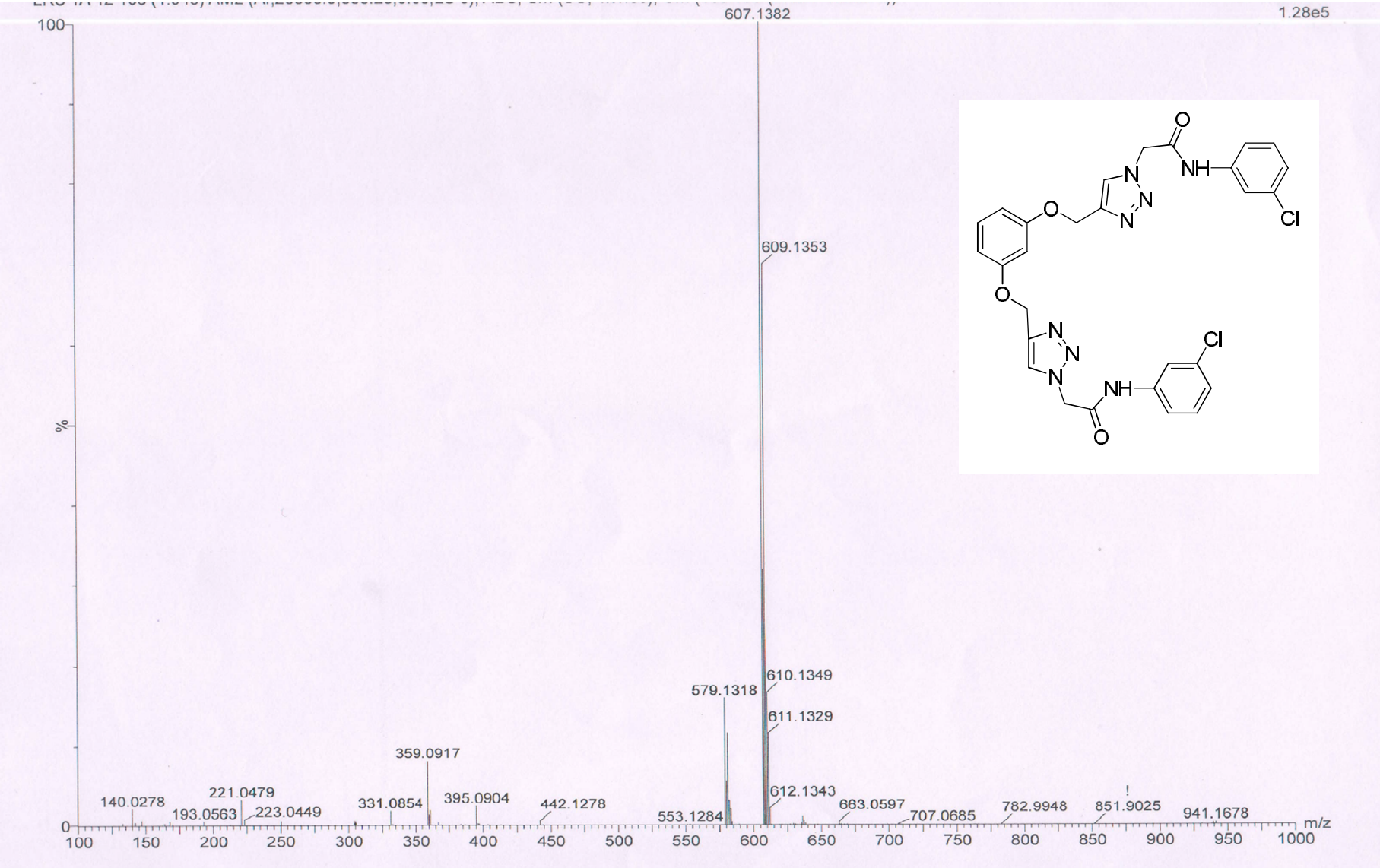
8h: ^{13}C NMR (125 MHz, DMSO-d_6, ppm)



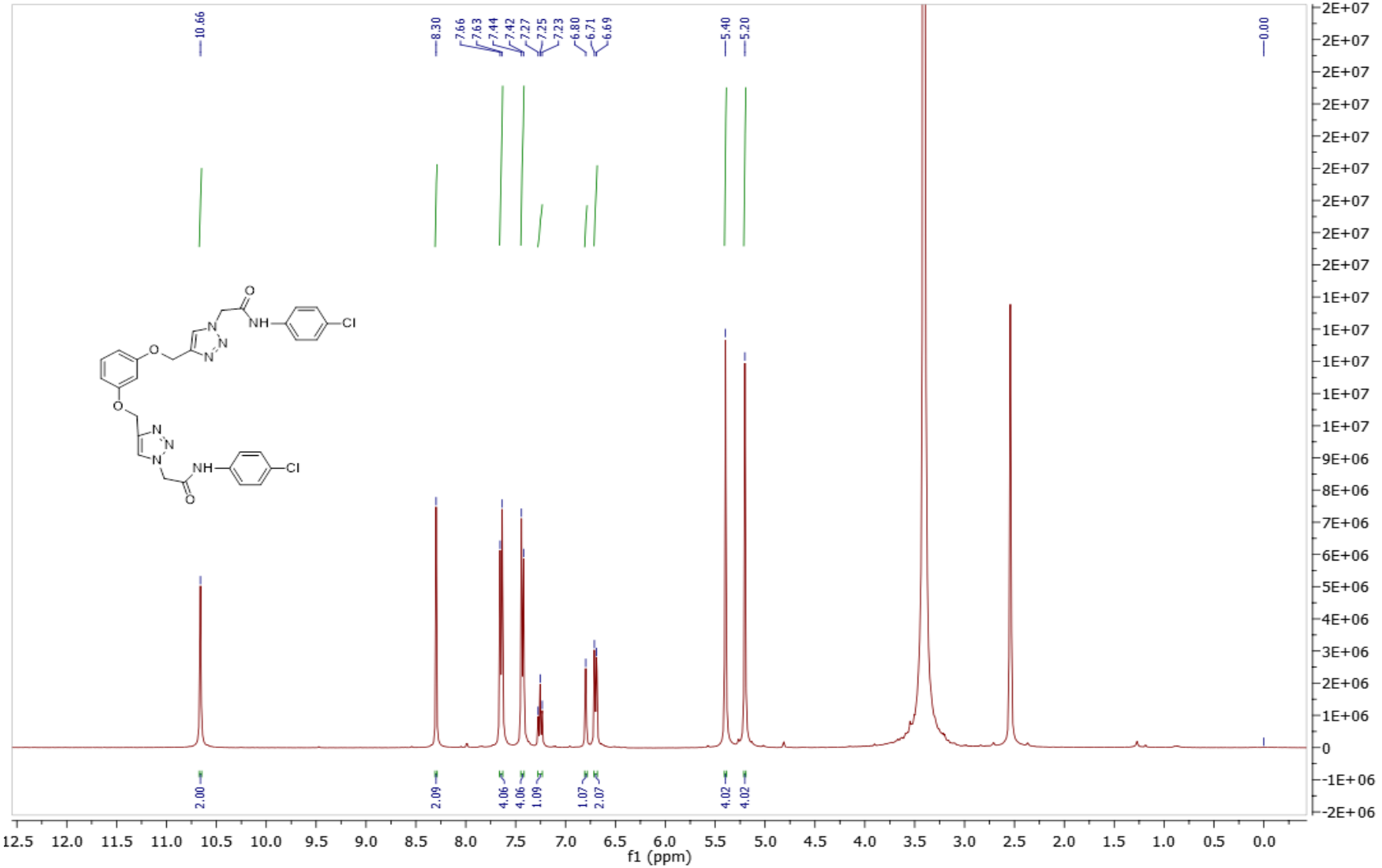
8i: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



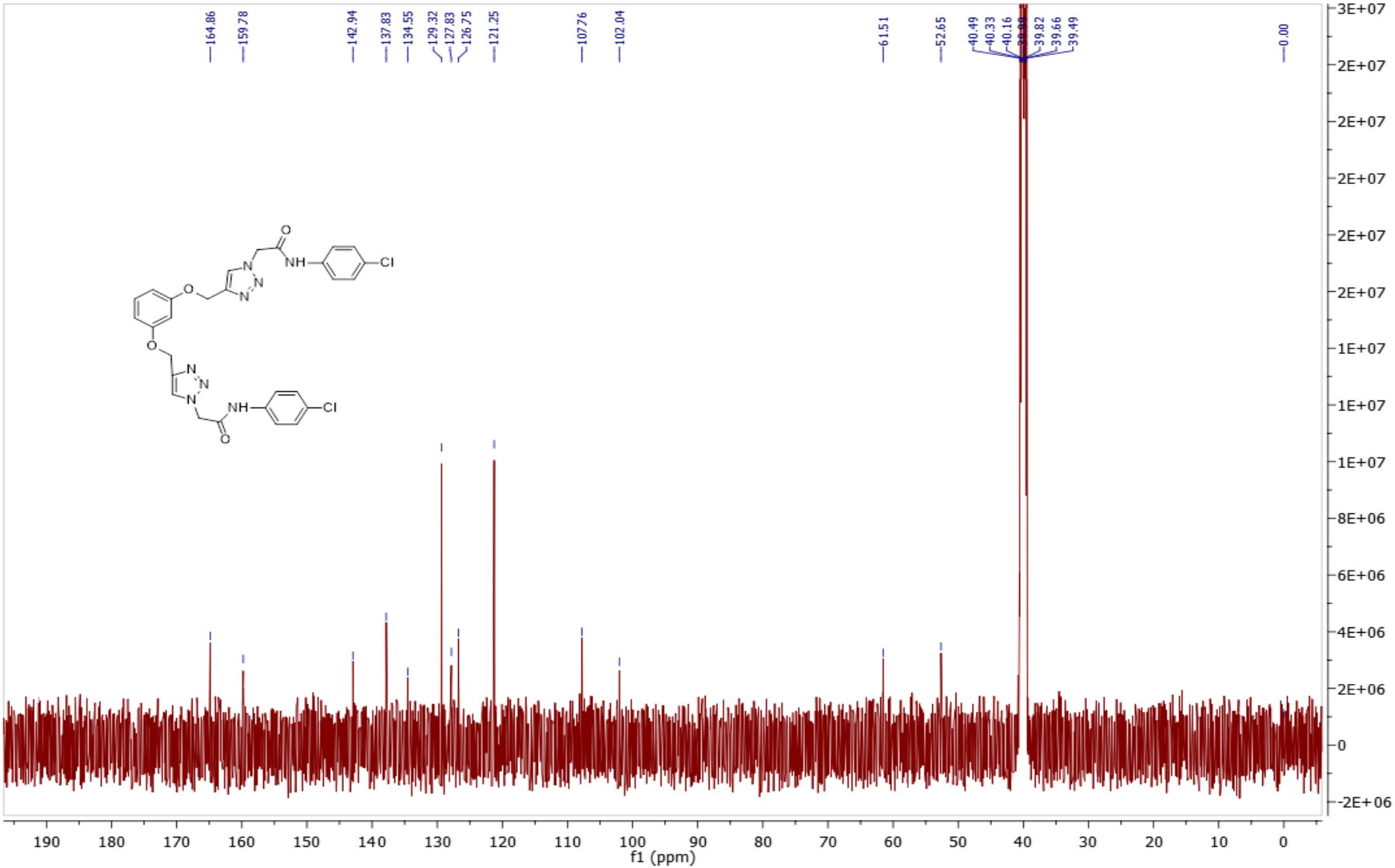
8i: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



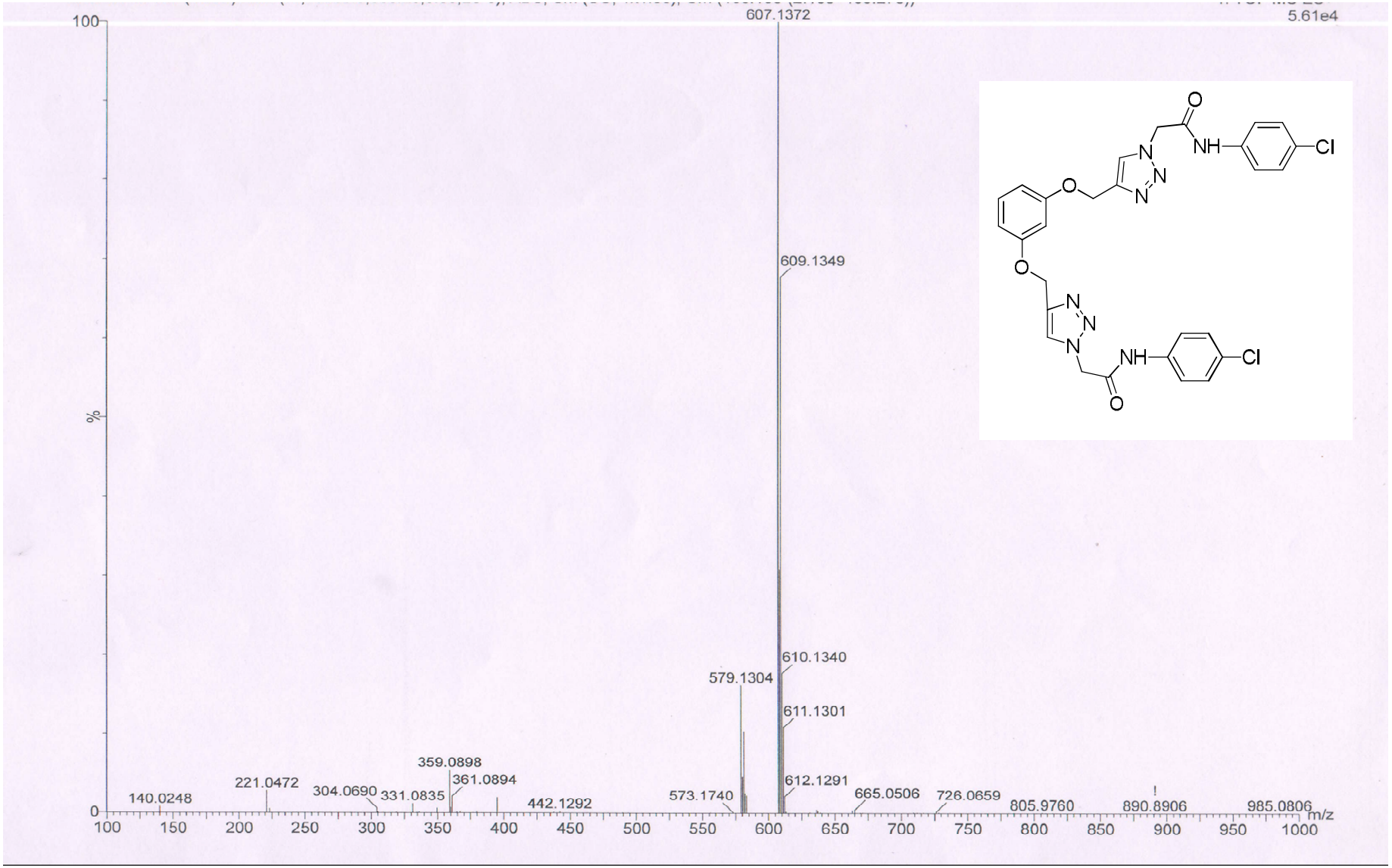
8i: MS (MALDI-TOF) calcd. For $C_{28}H_{25}Cl_2N_8O_4$ $[M+H]^+$: 607.1376; found: 607.1382.



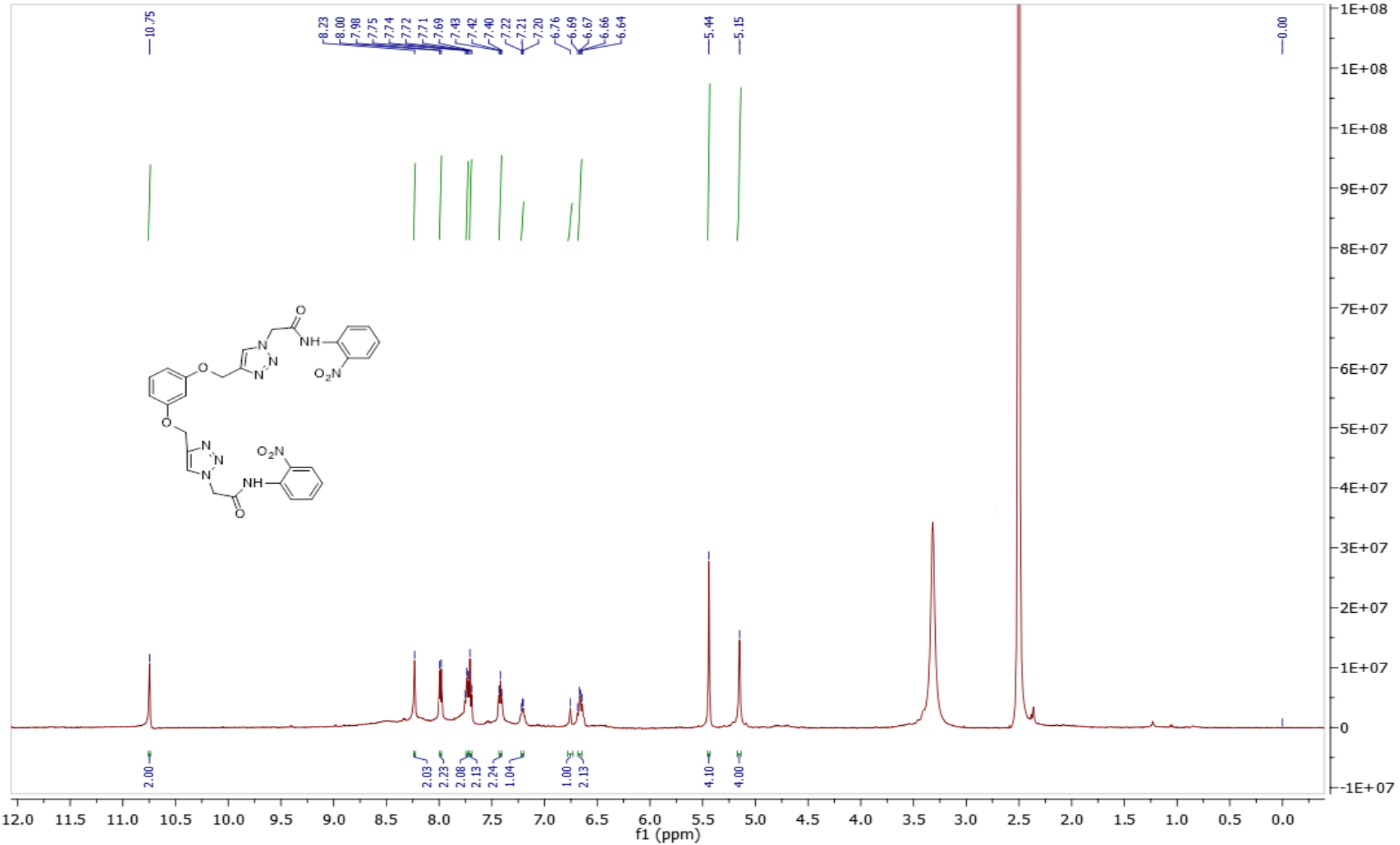
8j: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



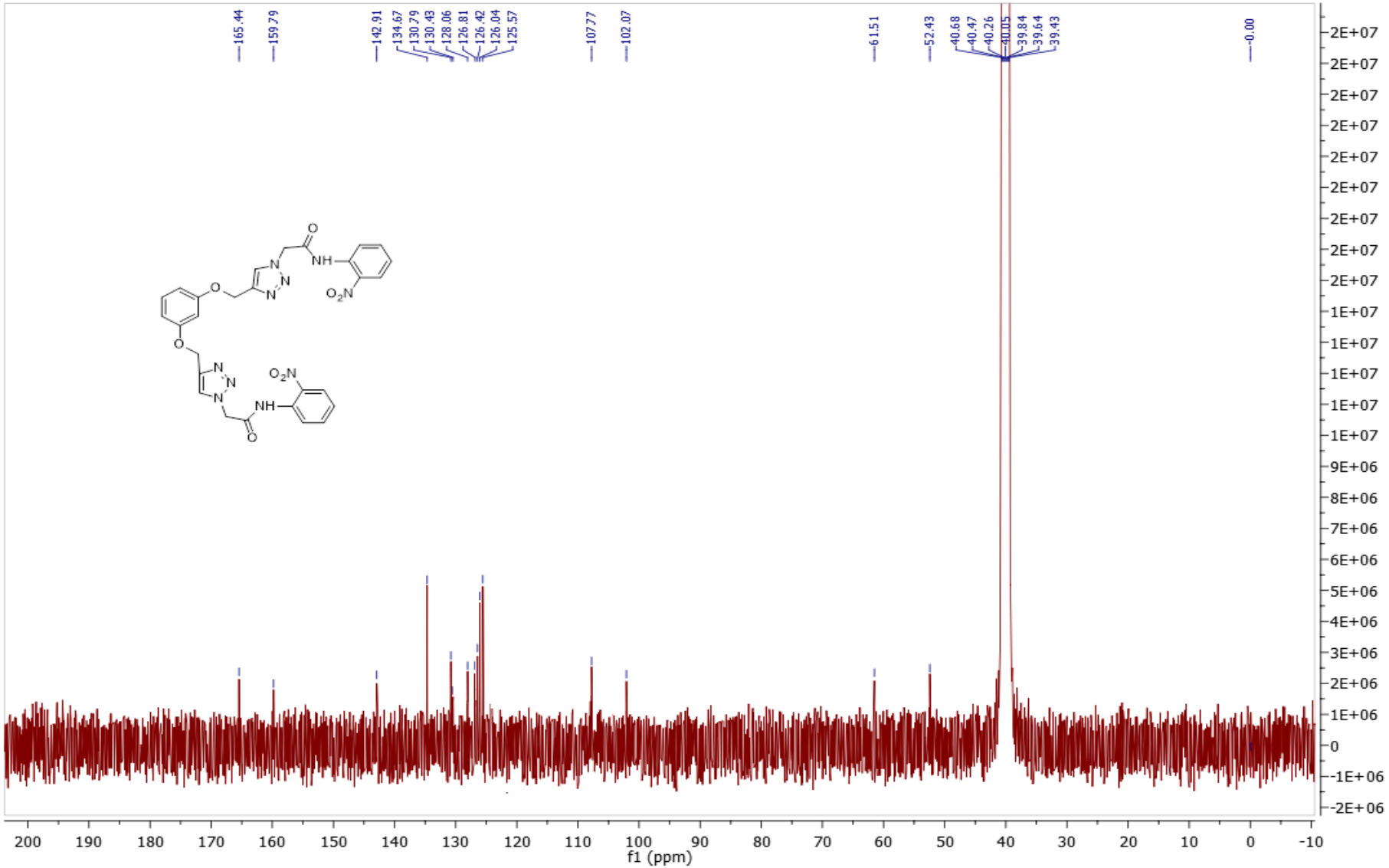
8j: ^{13}C NMR (125 MHz, DMSO-d_6, ppm)



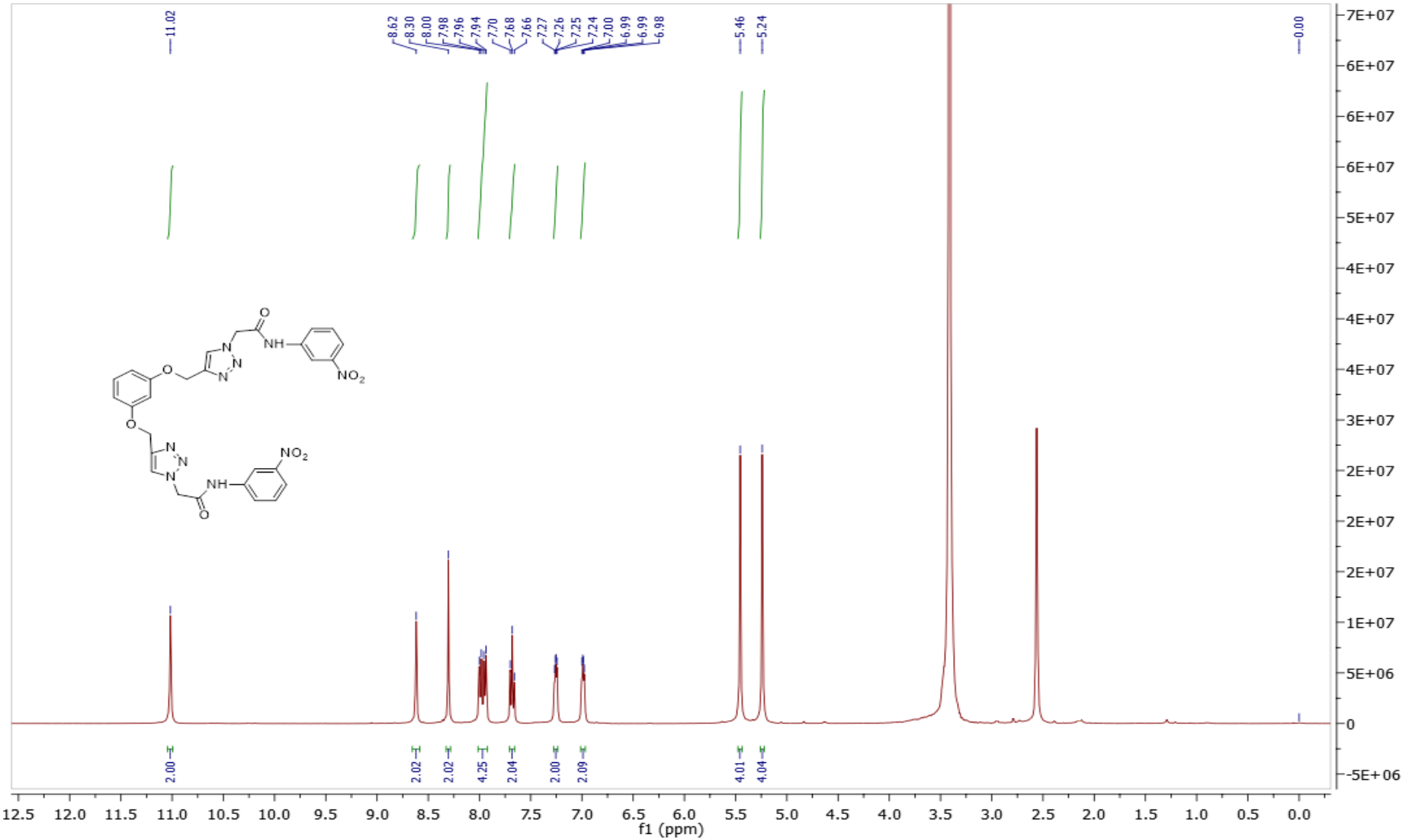
8j: MS (MALDI-TOF) calcd. For $C_{28}H_{25}Cl_2N_8O_4$ $[M+H]^+$: 607.1376; found: 607.1372.



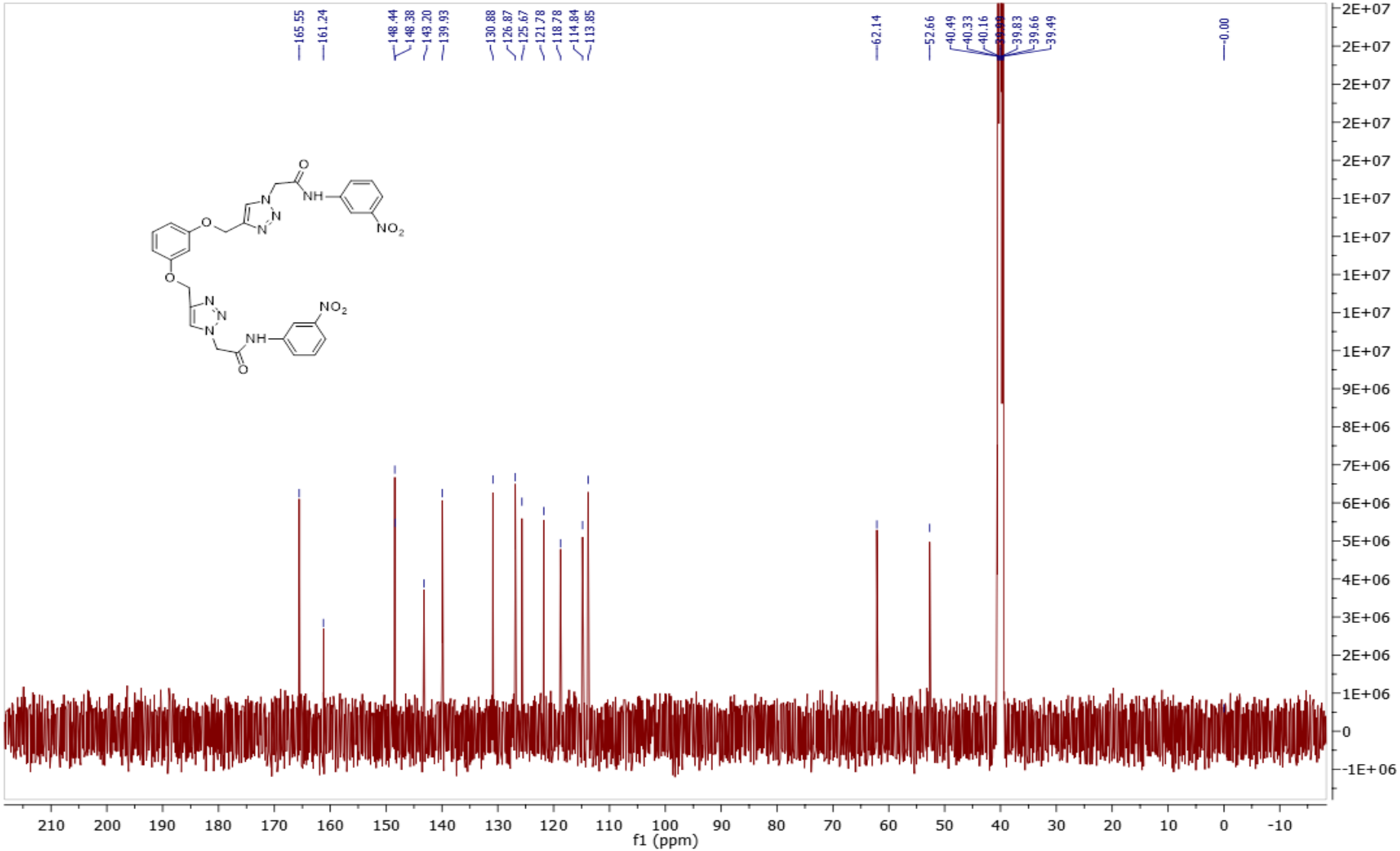
8k: ^{1}H NMR (500 MHz, DMSO-d_6, ppm)



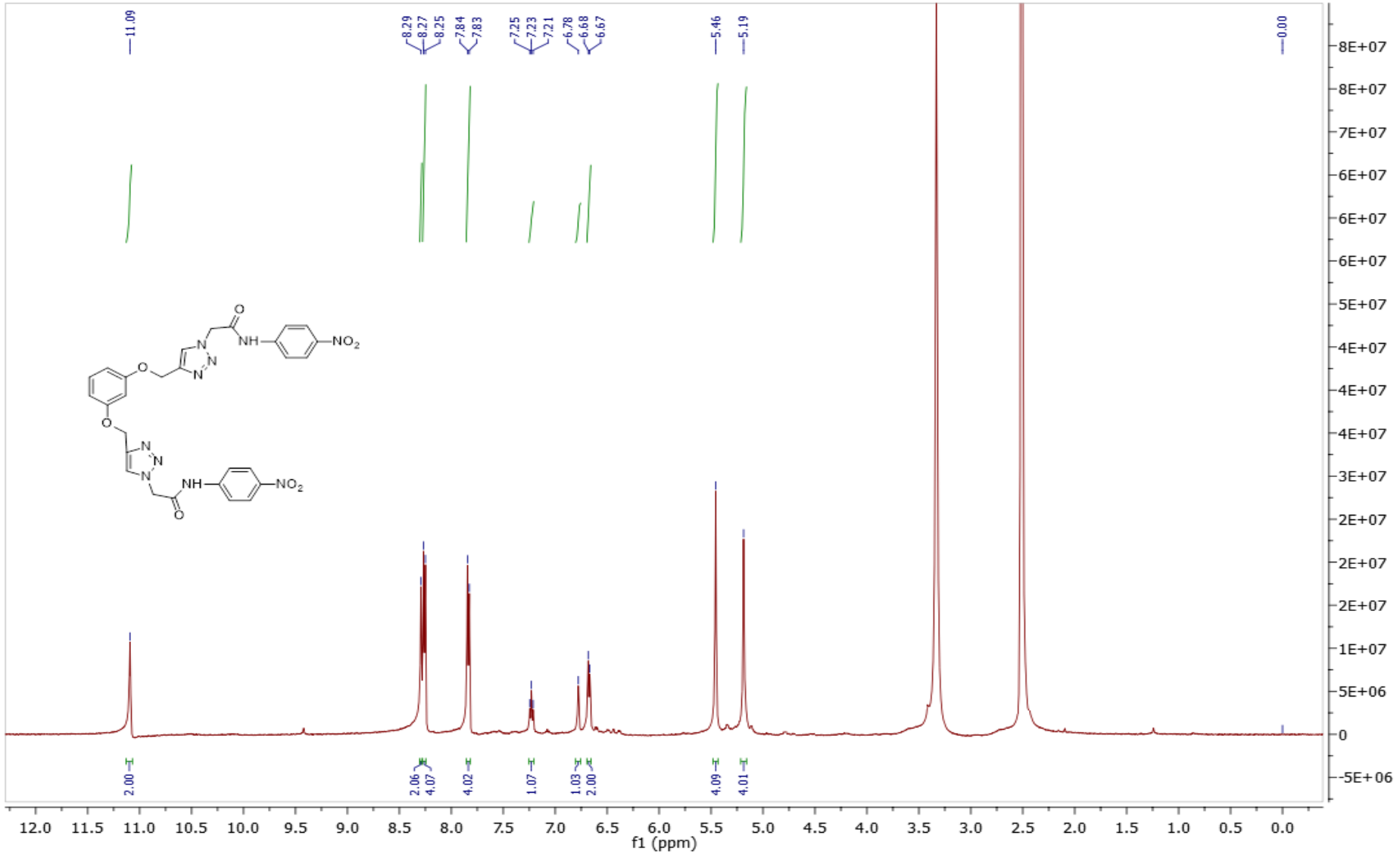
8k: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



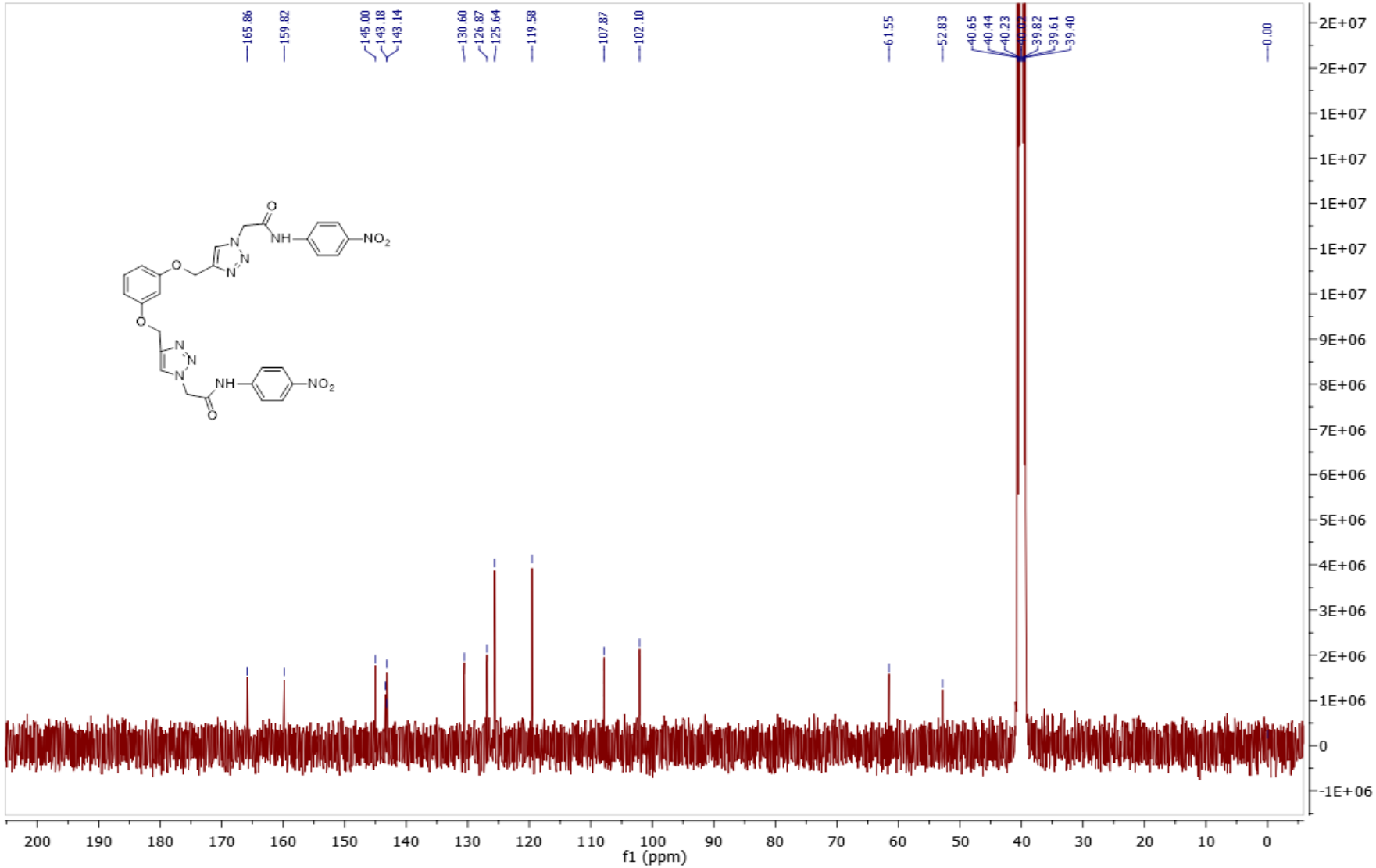
8l: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



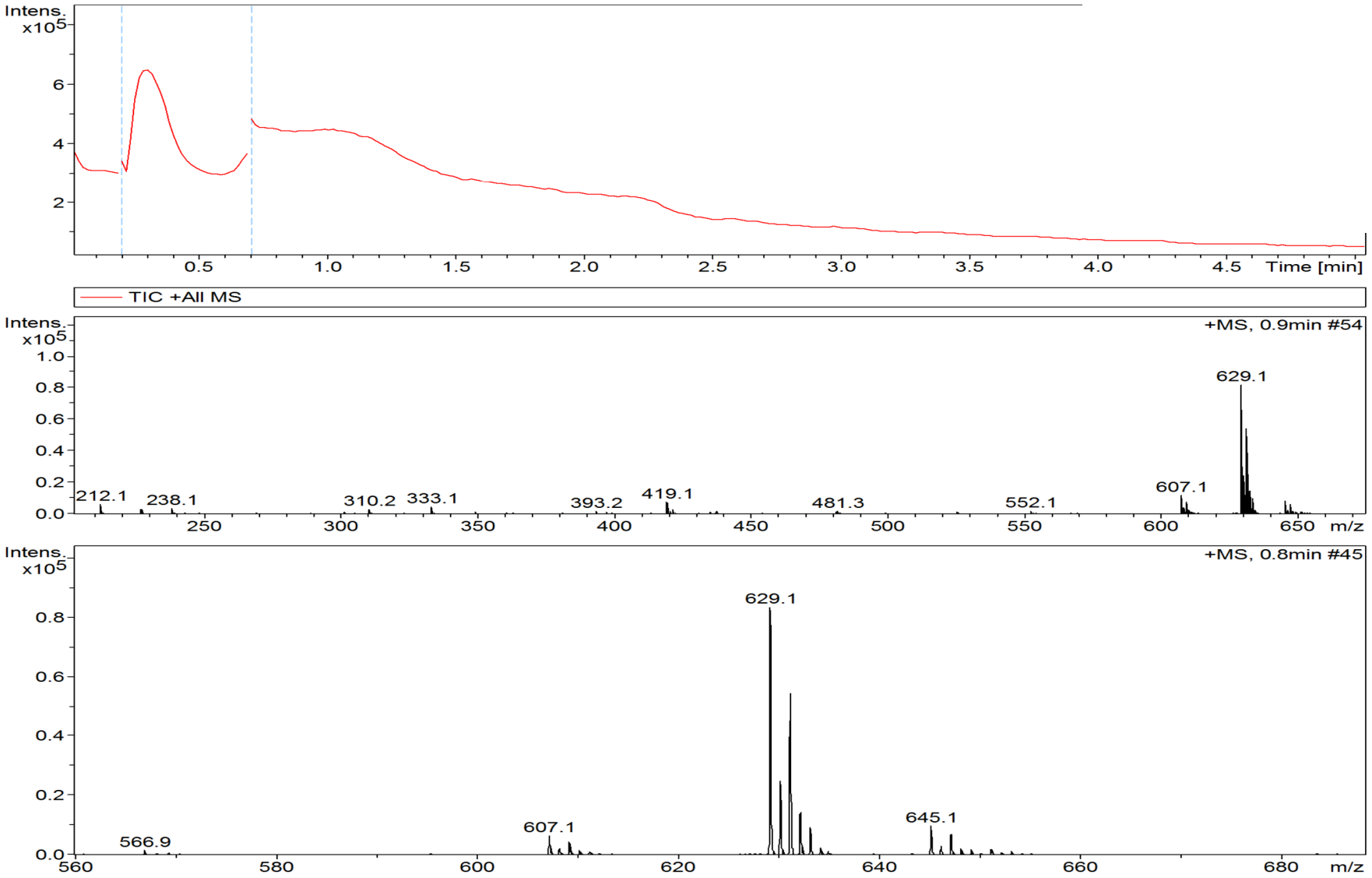
8l : ^{13}C NMR (125 MHz, DMSO-d_6, ppm)



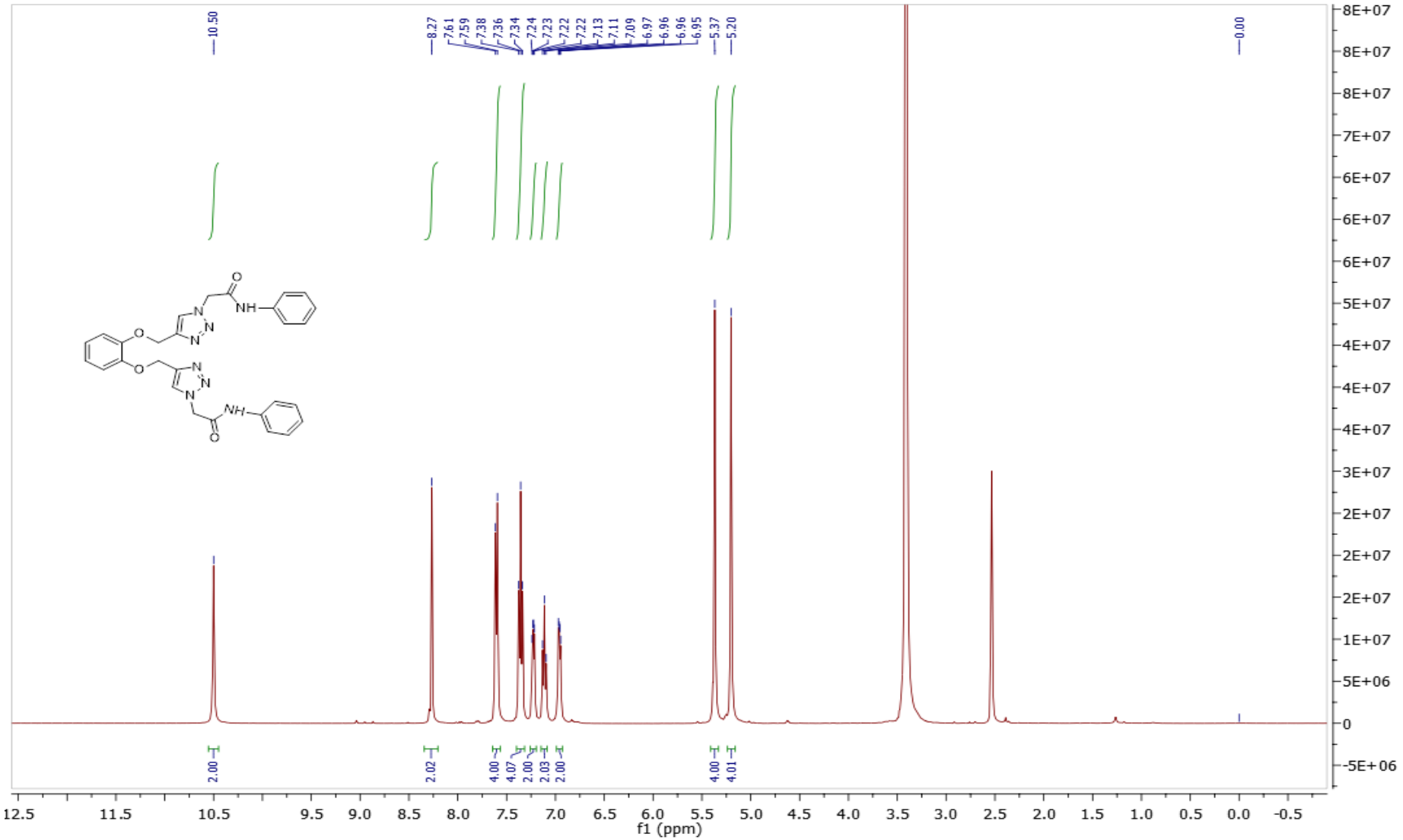
8m: ^{1}H NMR (500 MHz, DMSO-d$_6$, ppm)



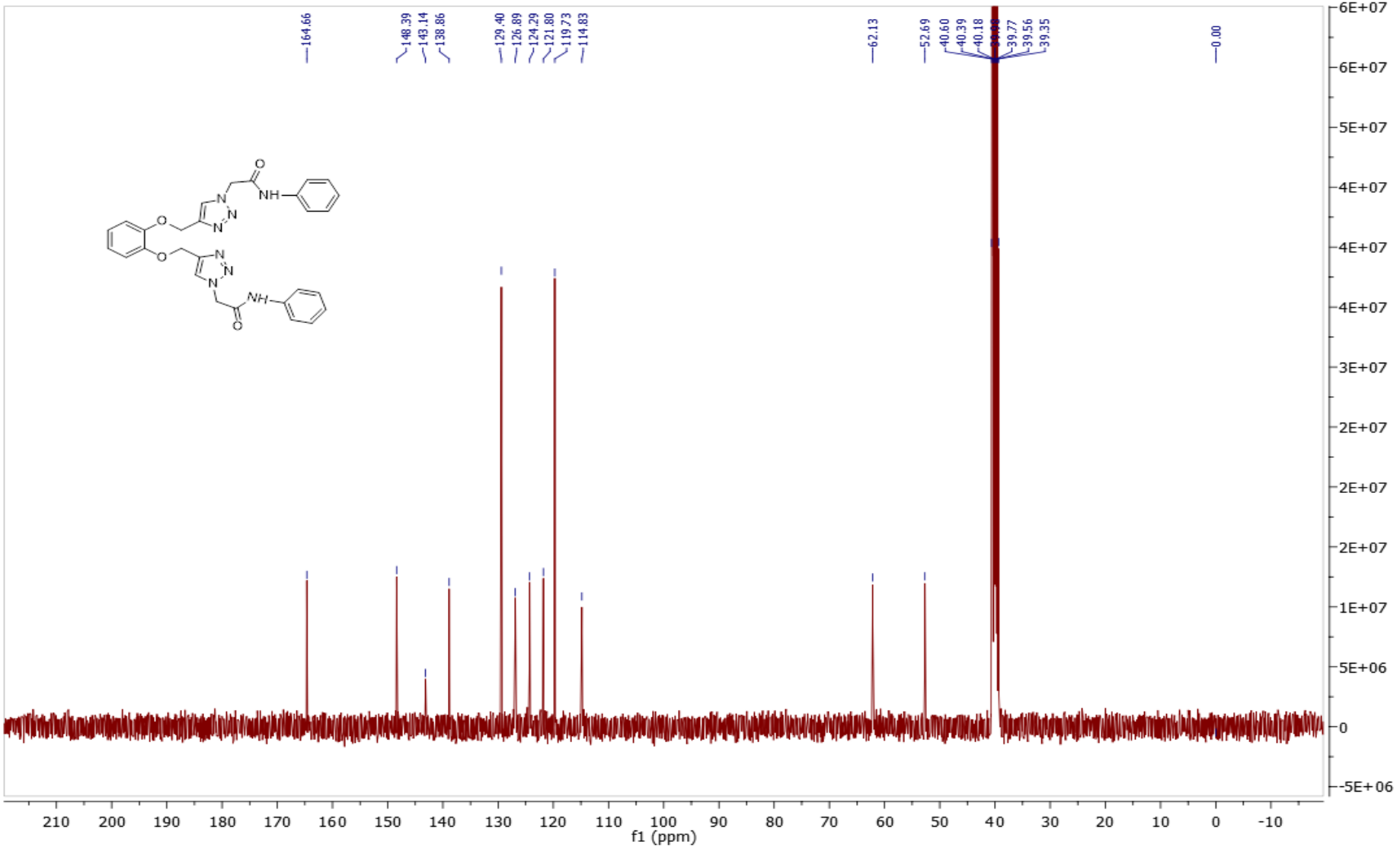
8m: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



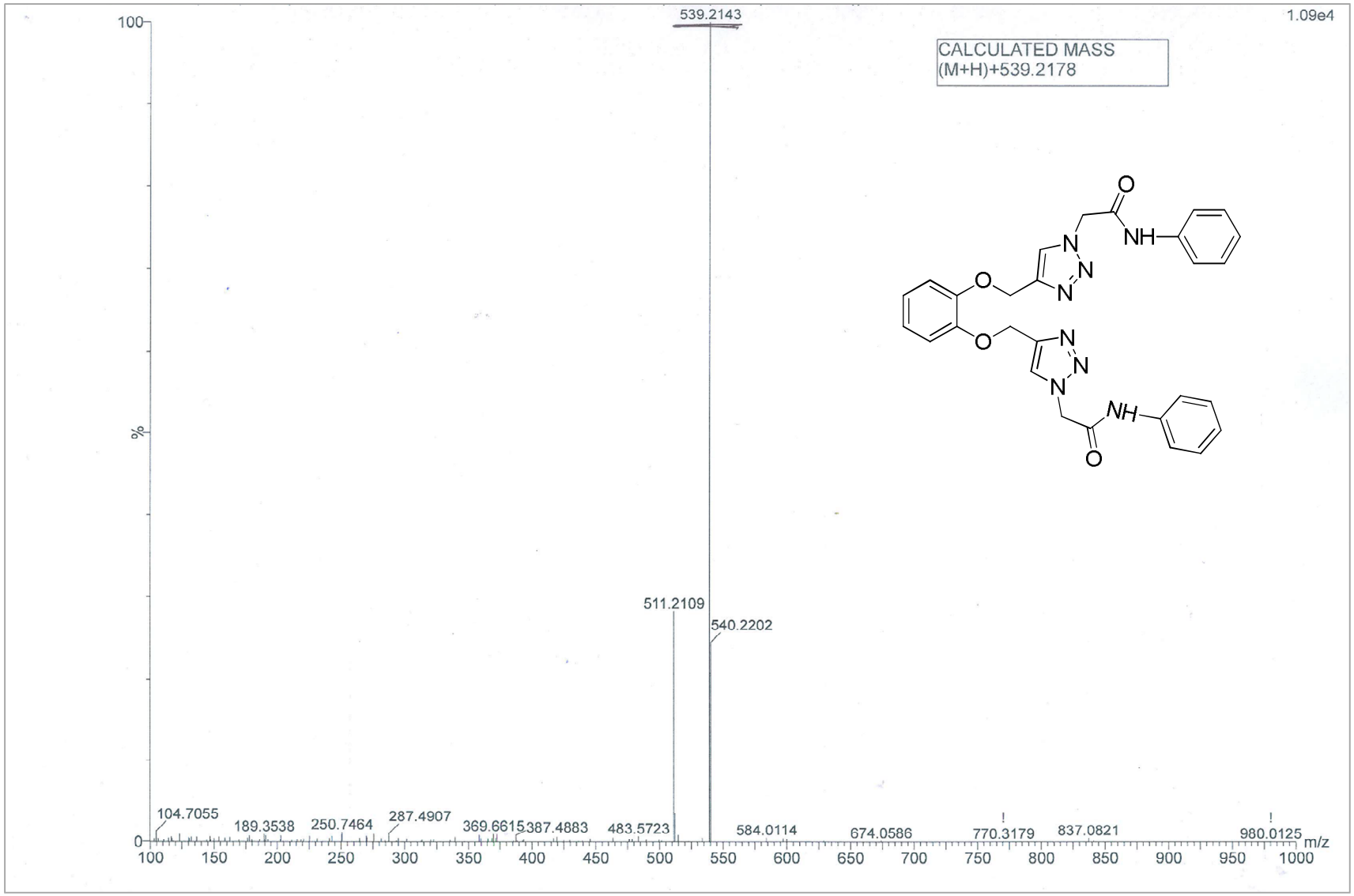
8m: LCMS (ESI) calcd. For $C_{28}H_{25}N_{10}O_8$ $[M+H]^+$: 629.1857; found: 629.1.



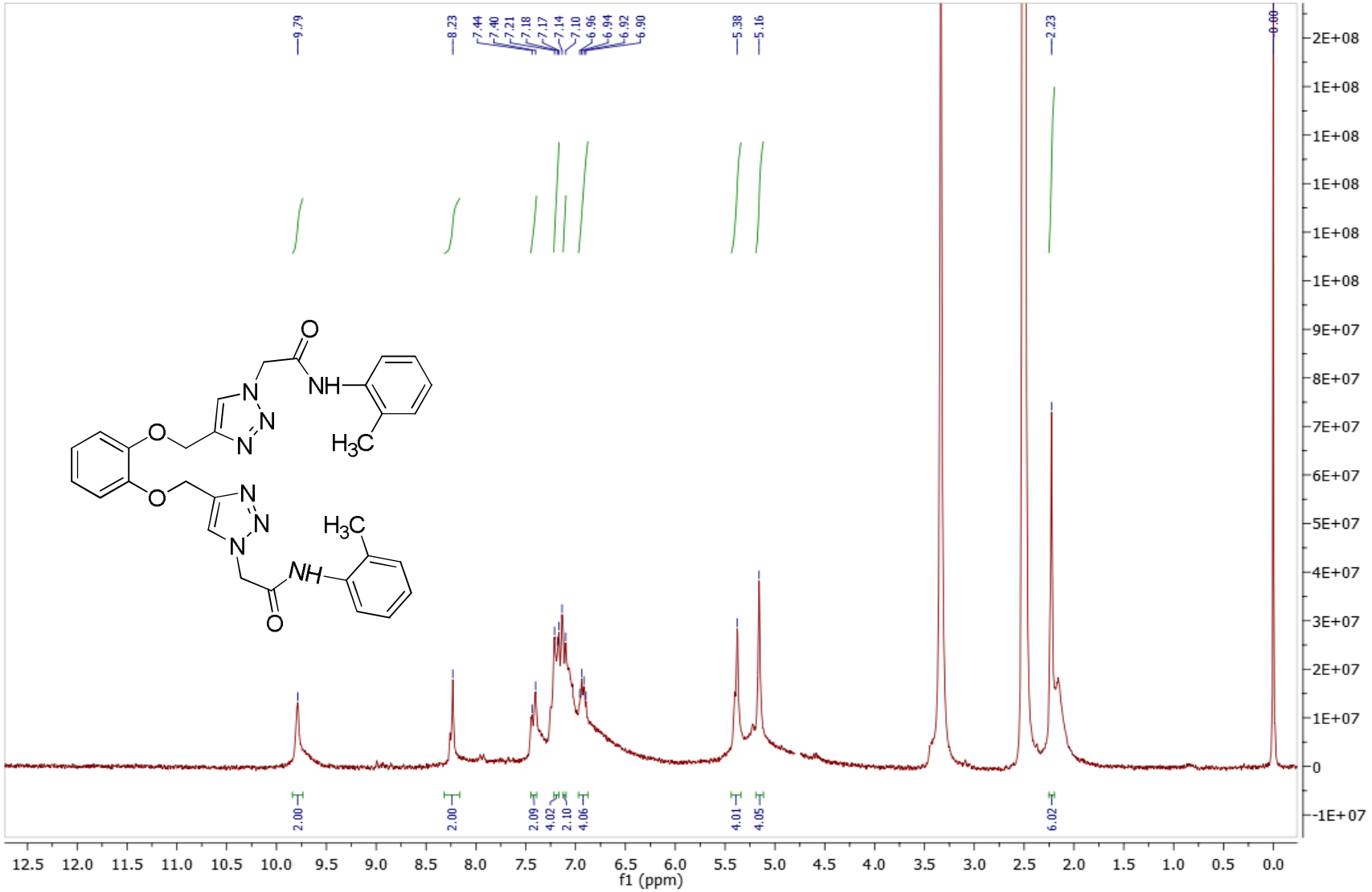
8n: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



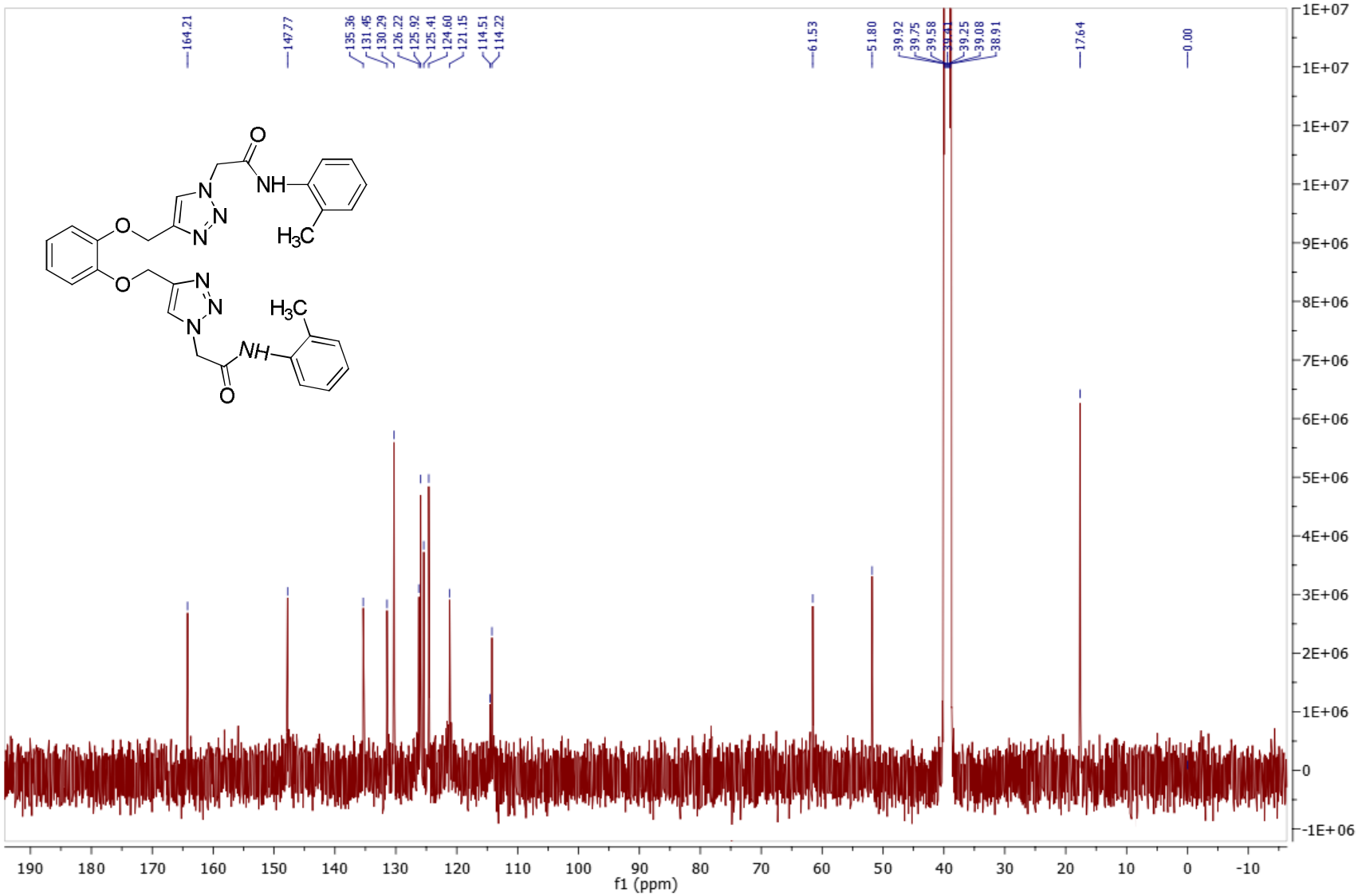
8n: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



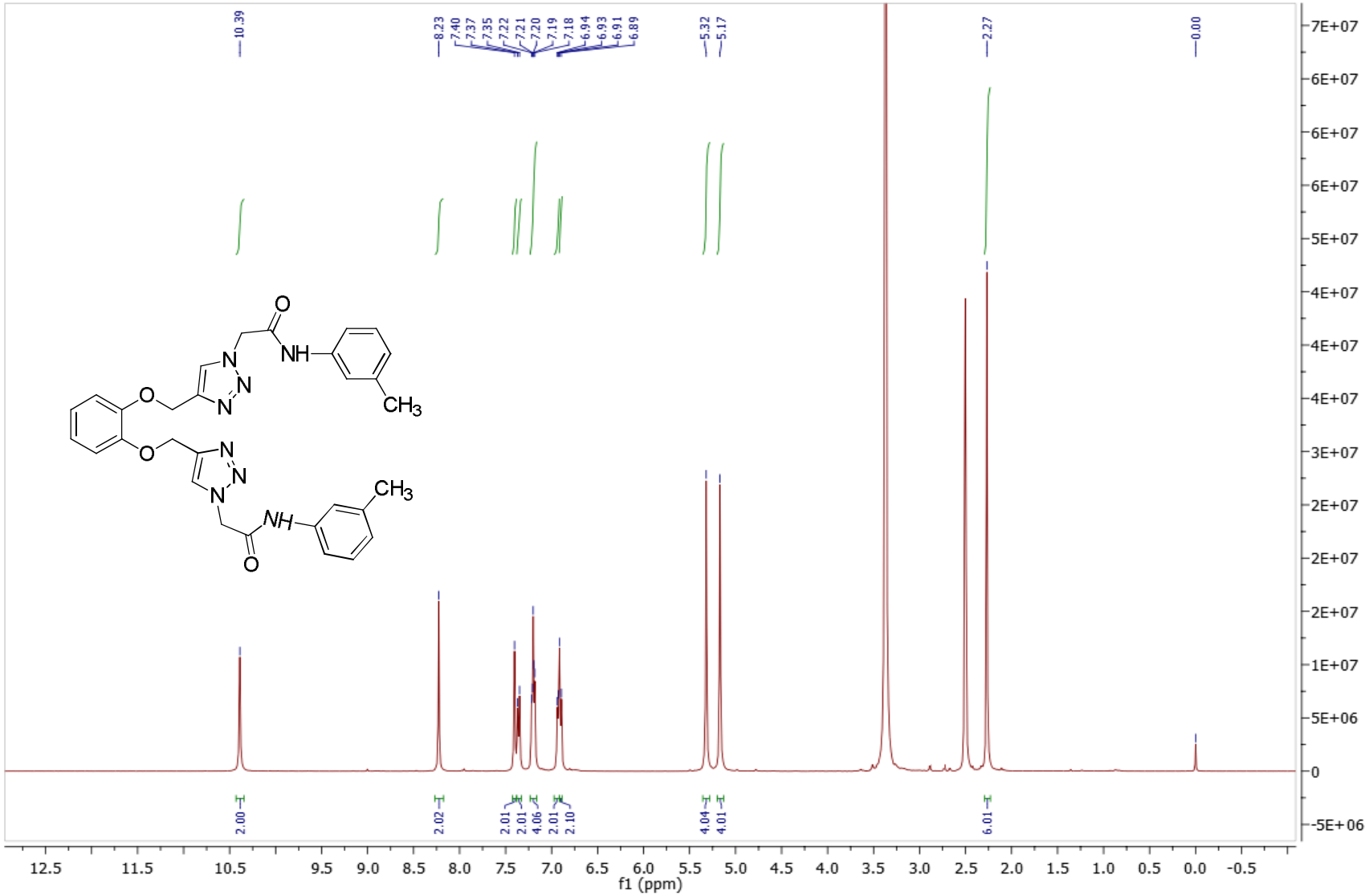
8n: MS (MALDI-TOF) calcd. For $C_{28}H_{27}N_8O_4$ $[M+H]^+$: 539.2155; found: 539.2143.



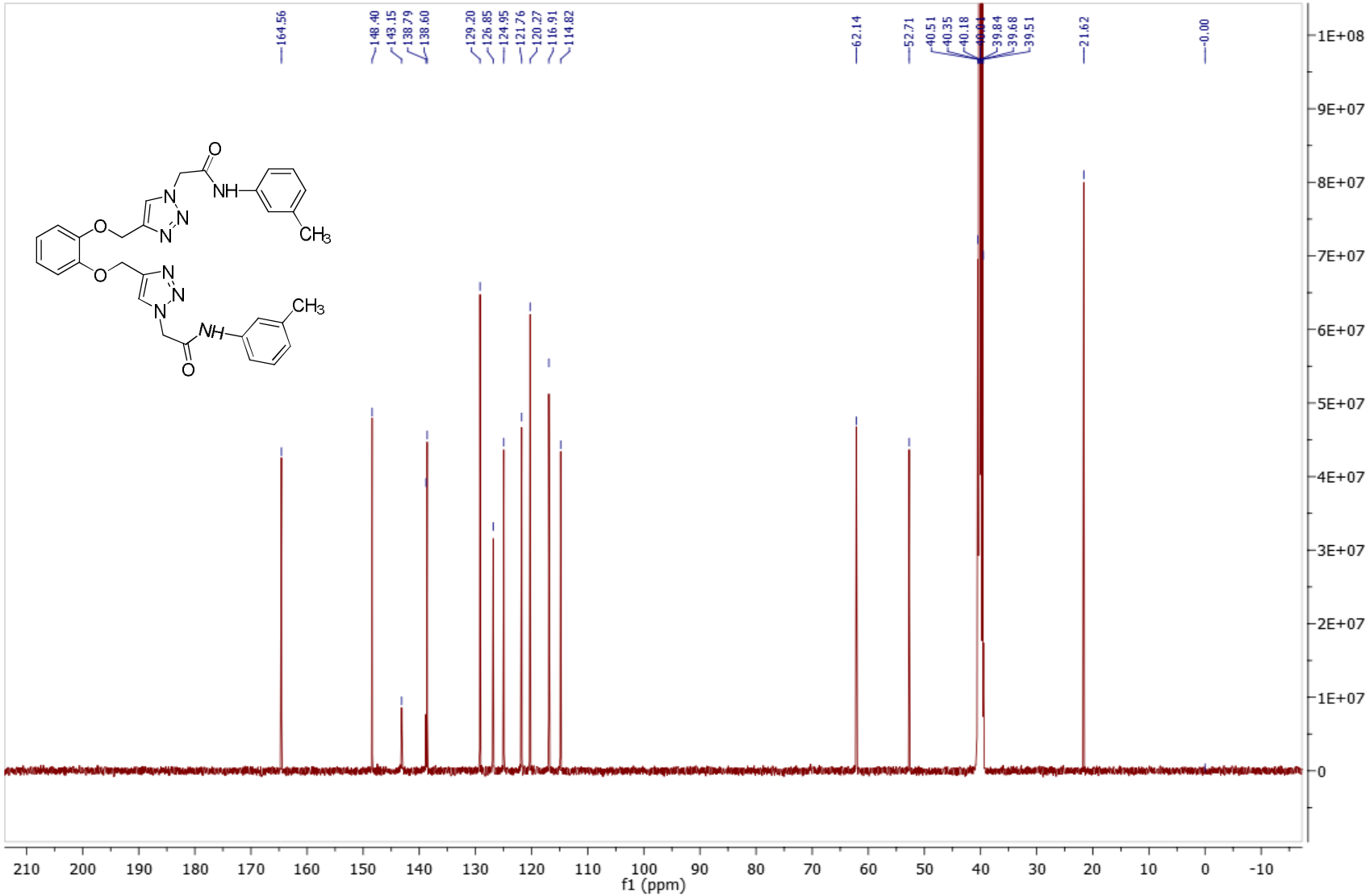
8o: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



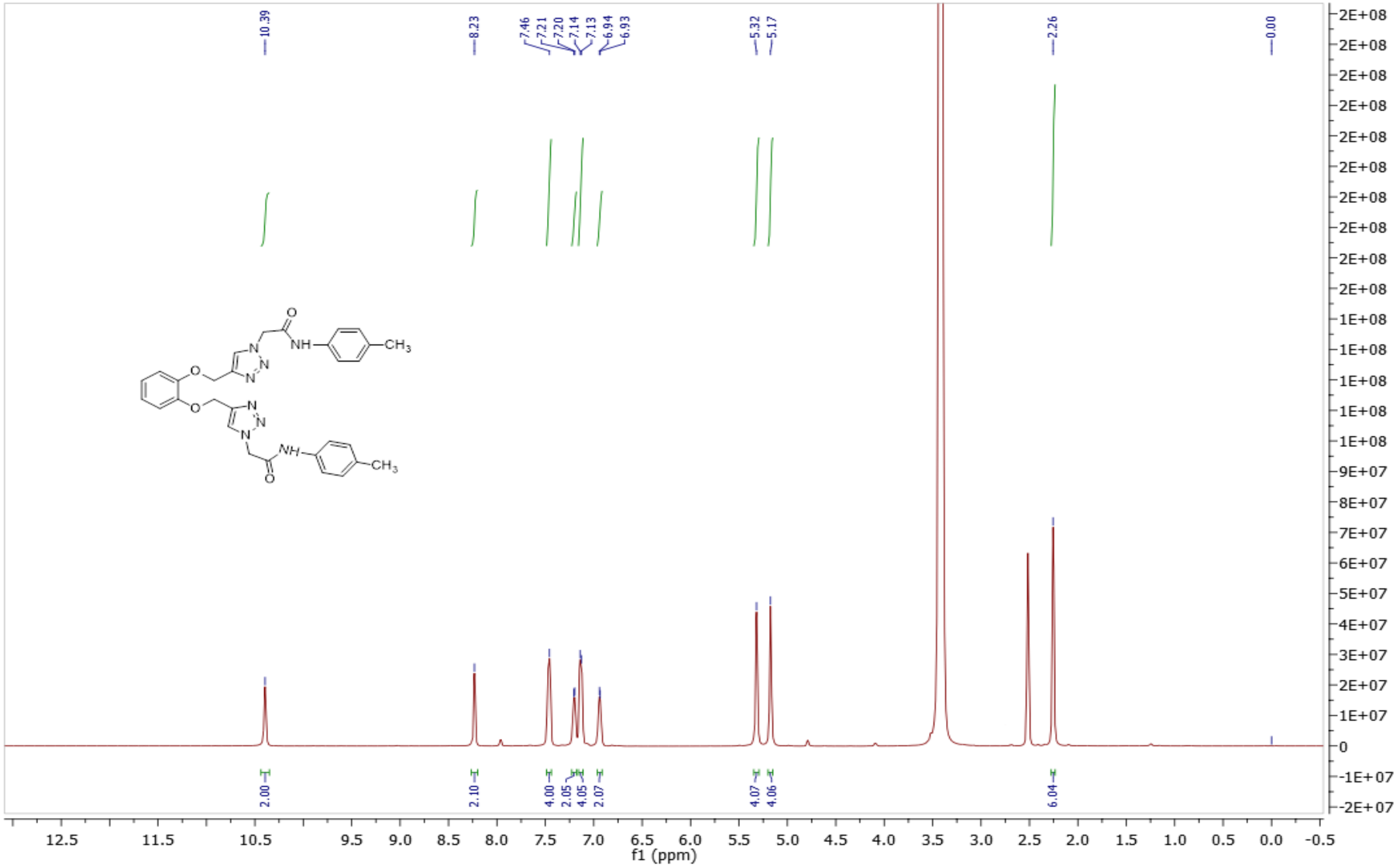
8o: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



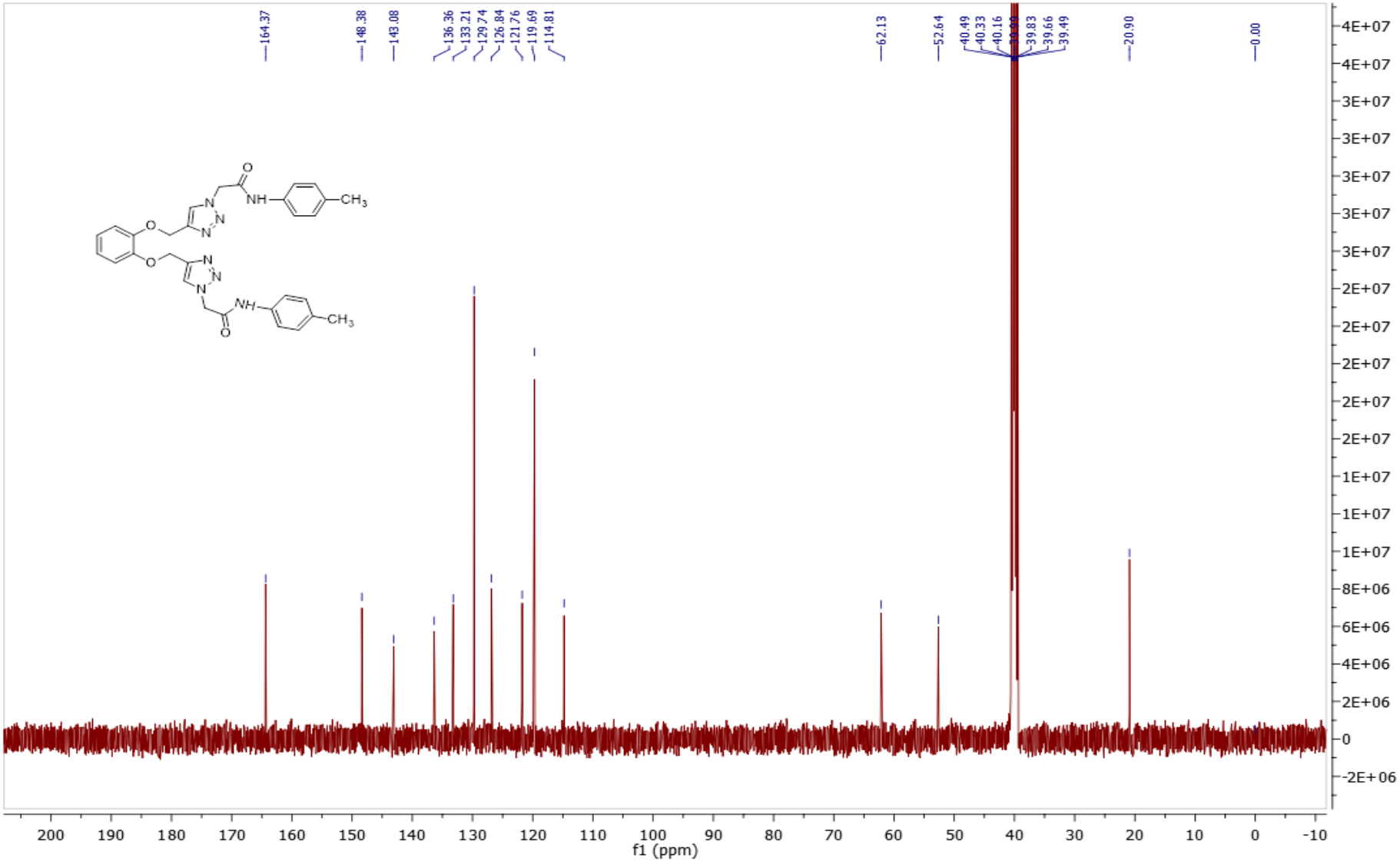
8p: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



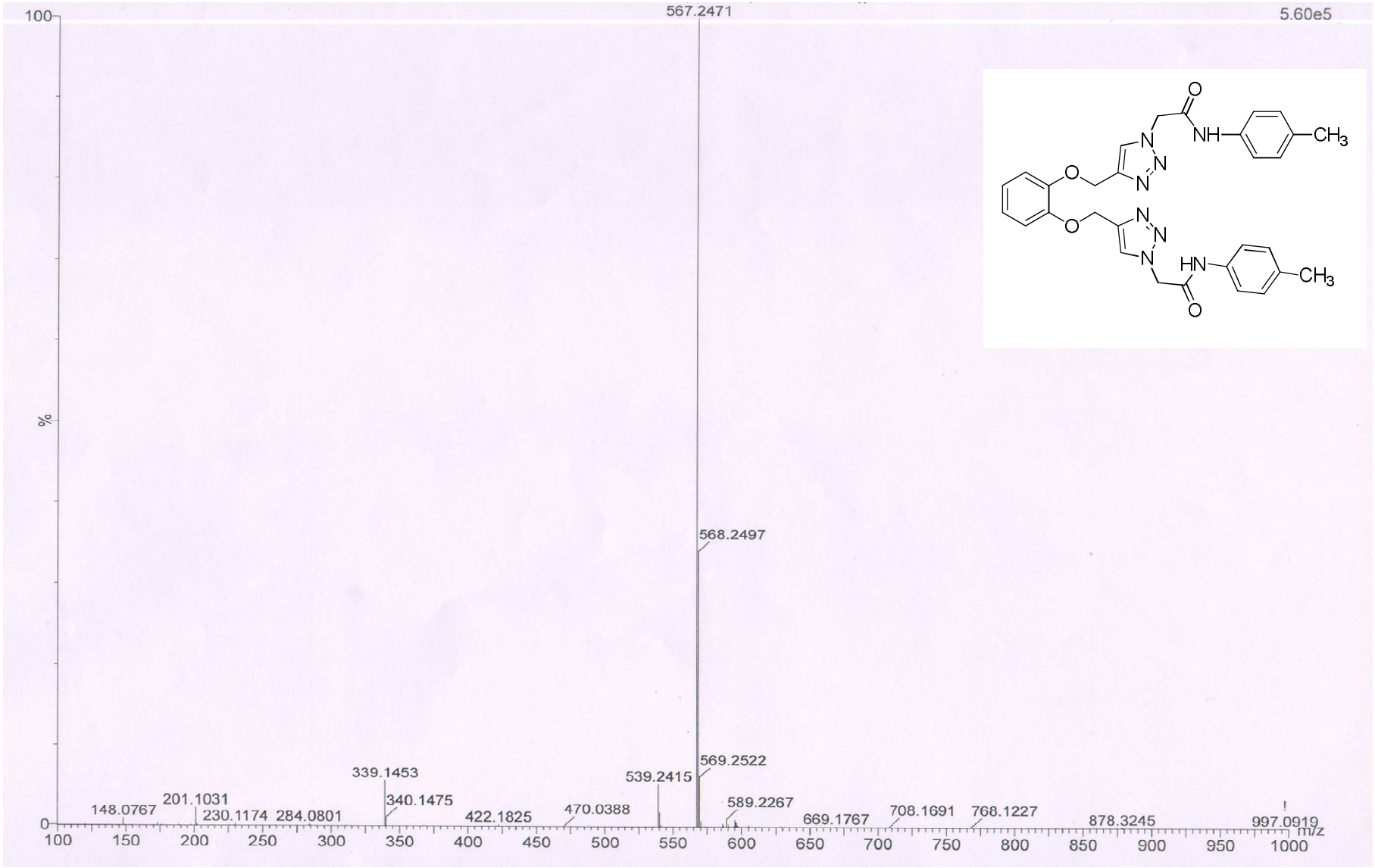
8p: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



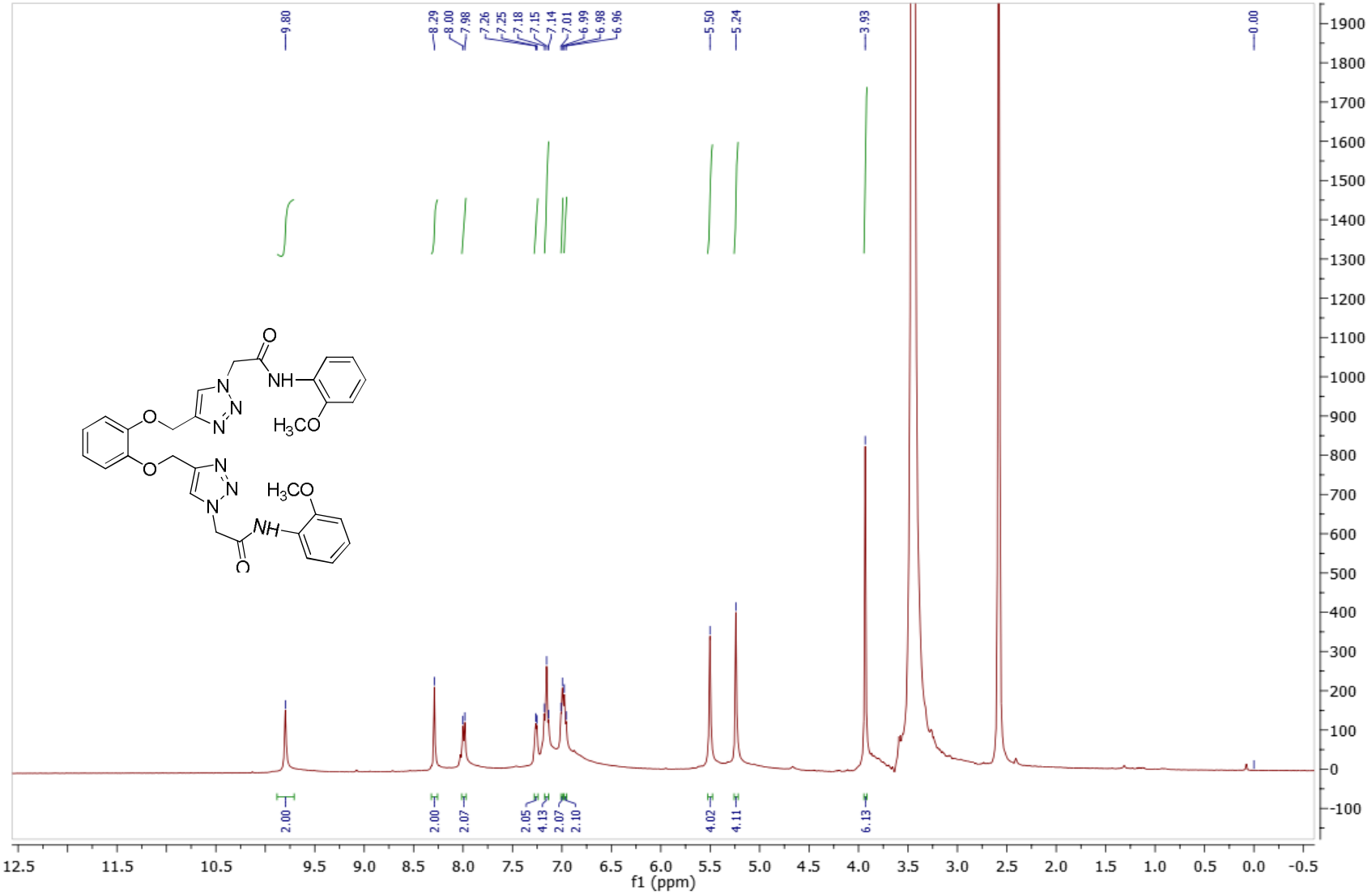
8q: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



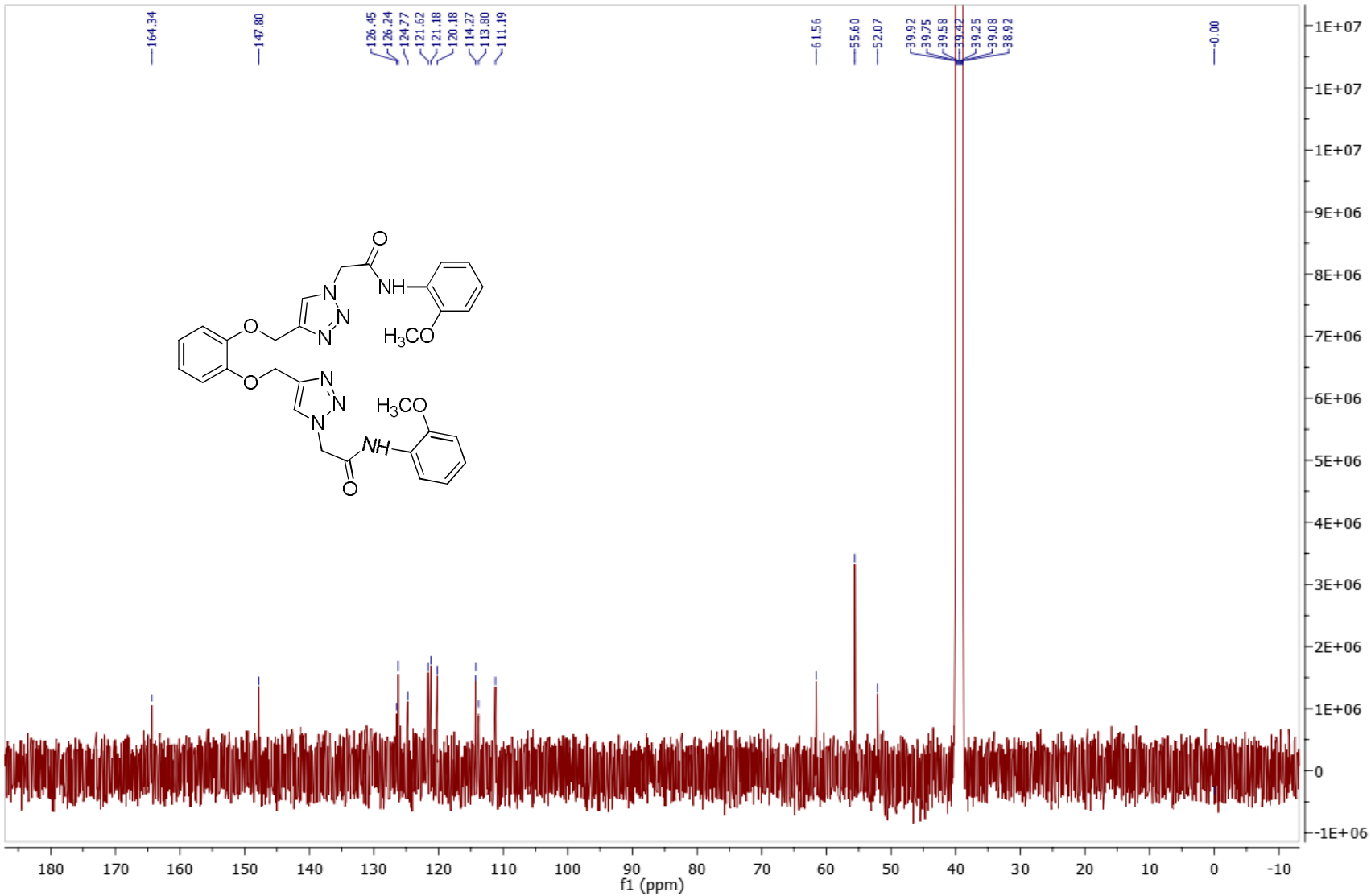
8q: ^{13}C NMR (125 MHz, DMSO-d_6, ppm)



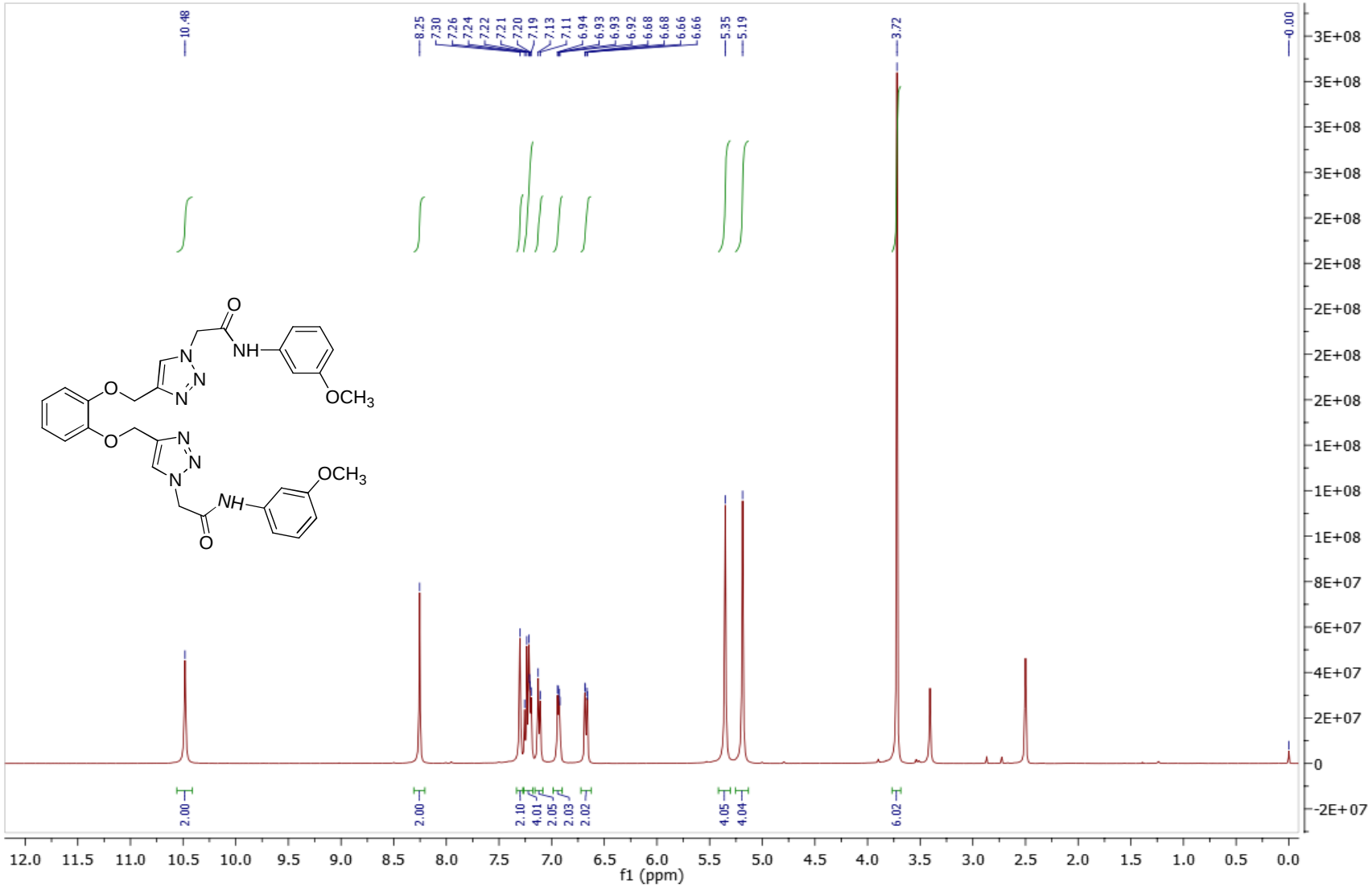
8q: MS (MALDI-TOF) calcd. For $C_{30}H_{31}N_8O_4$ $[M+H]^+$: 567.2468; found: 567.2471.



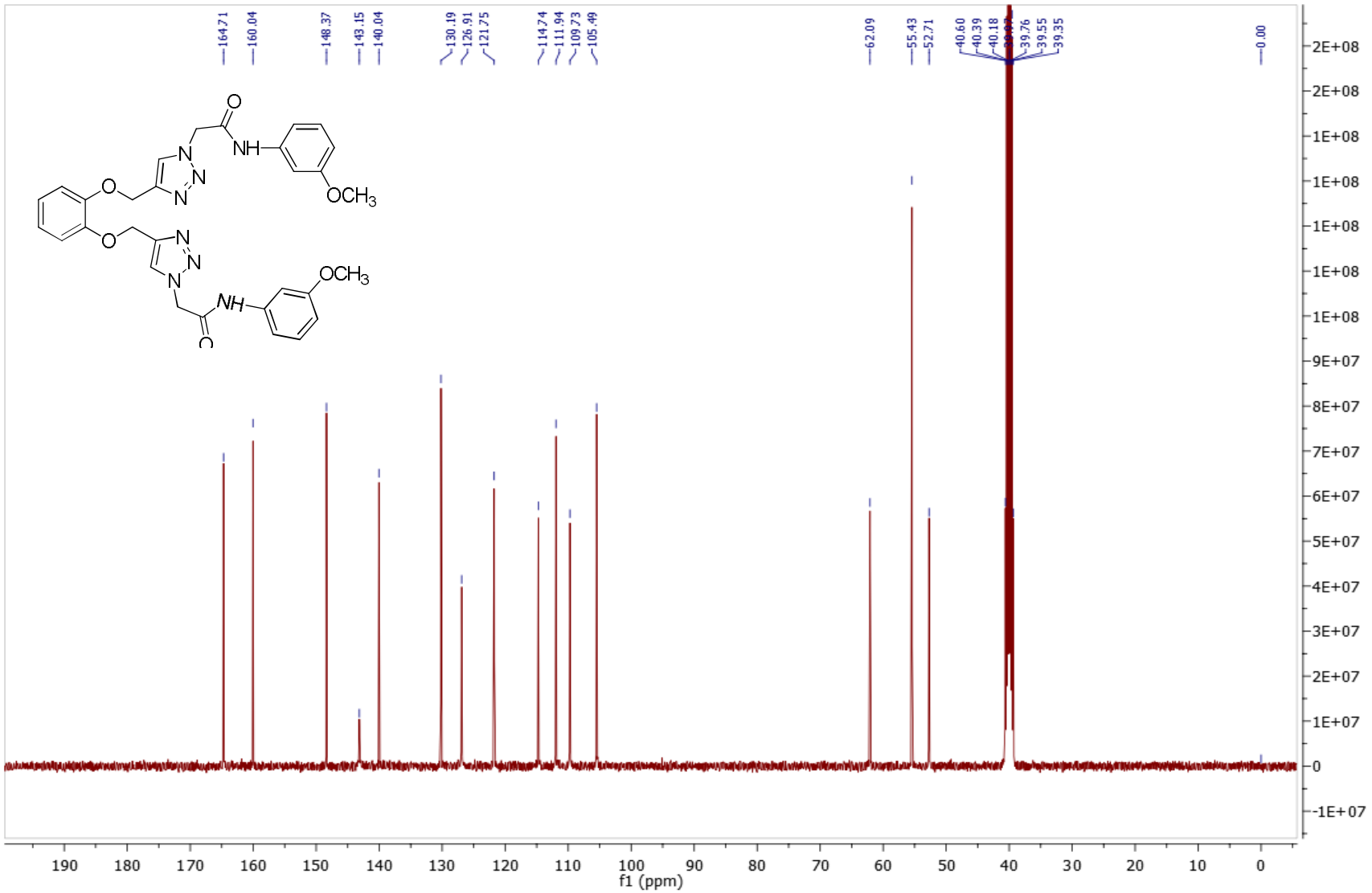
8r: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



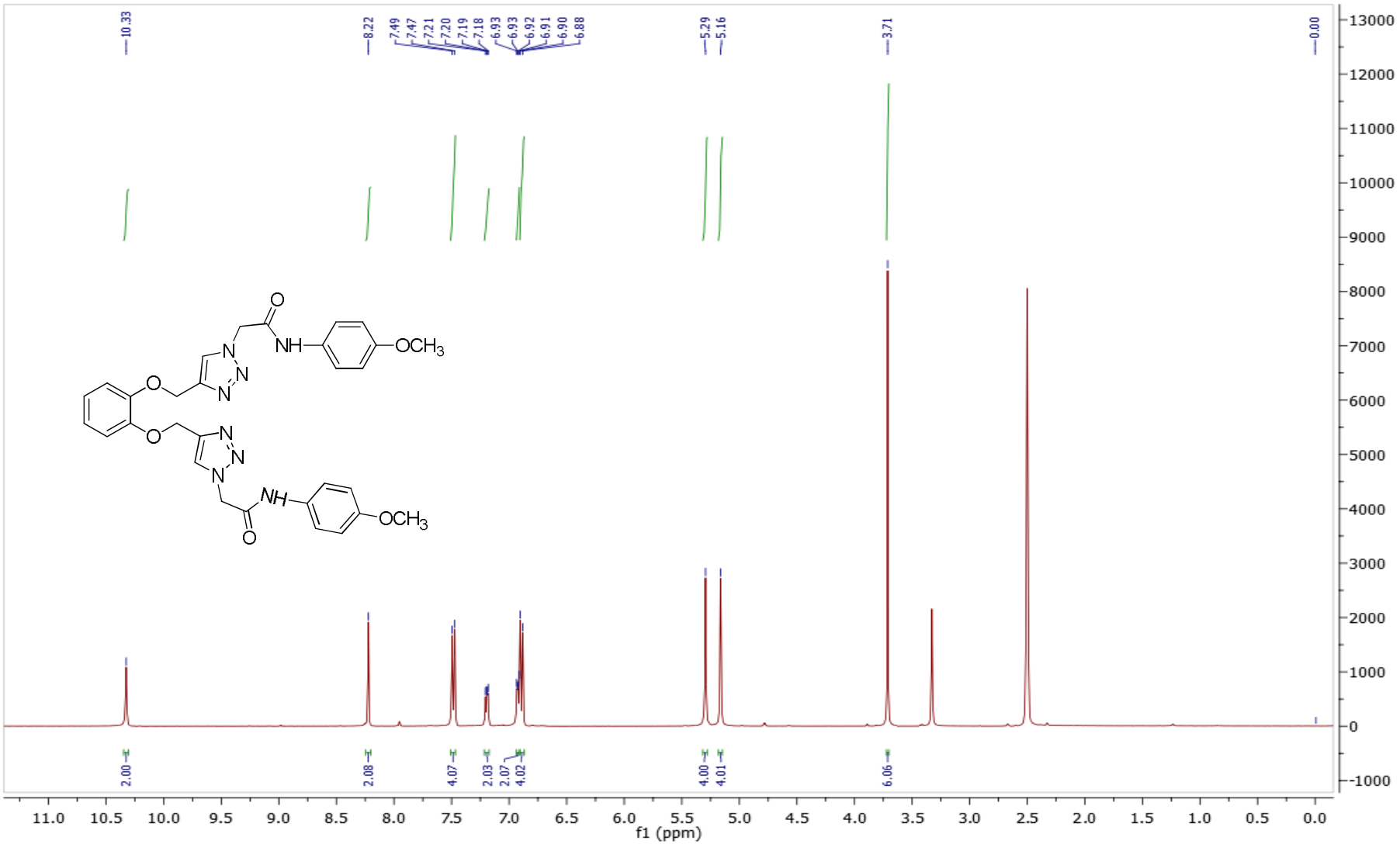
8r: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



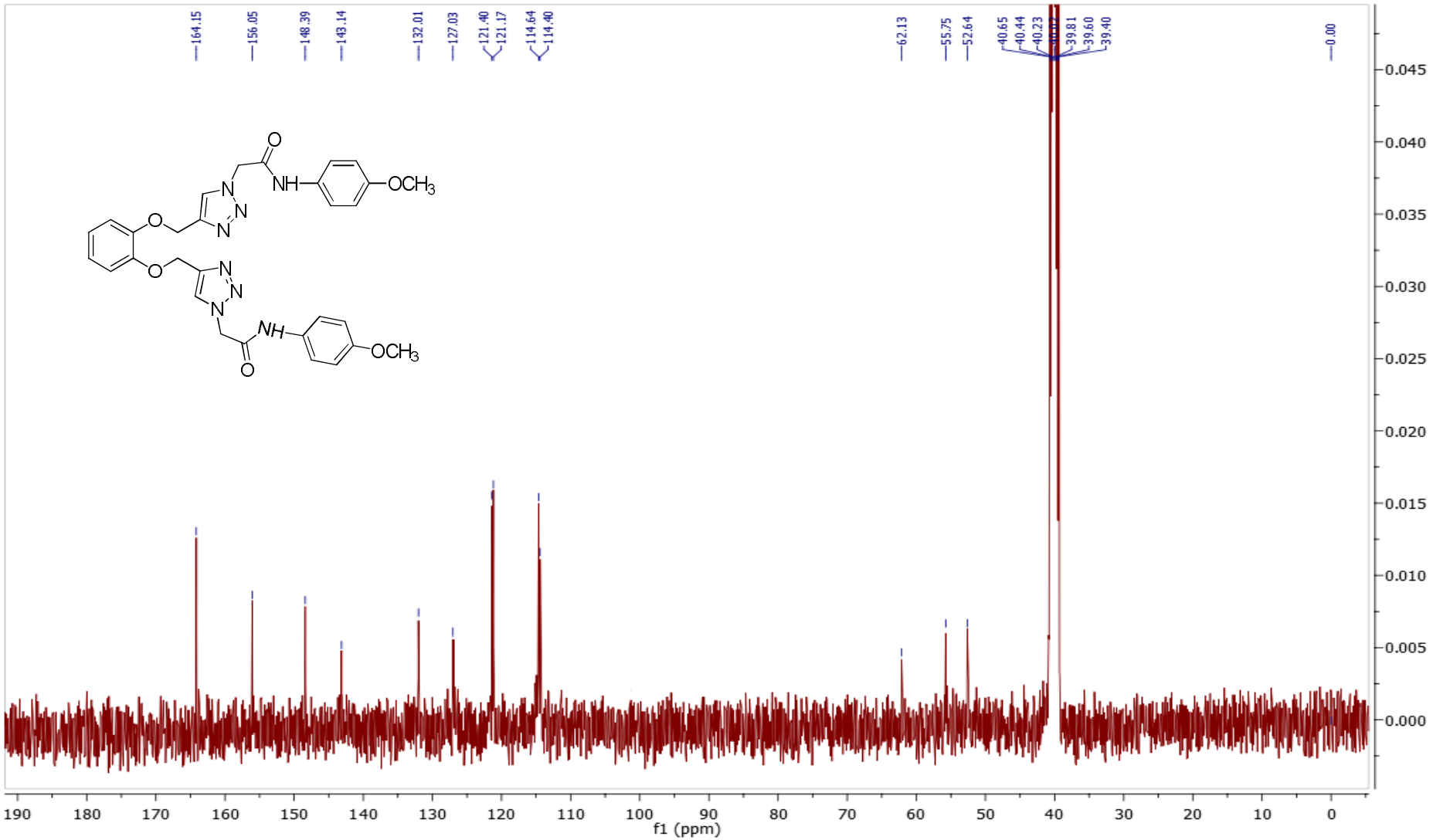
8s: ^{1}H NMR (400 MHz, DMSO-d$_6$, ppm)



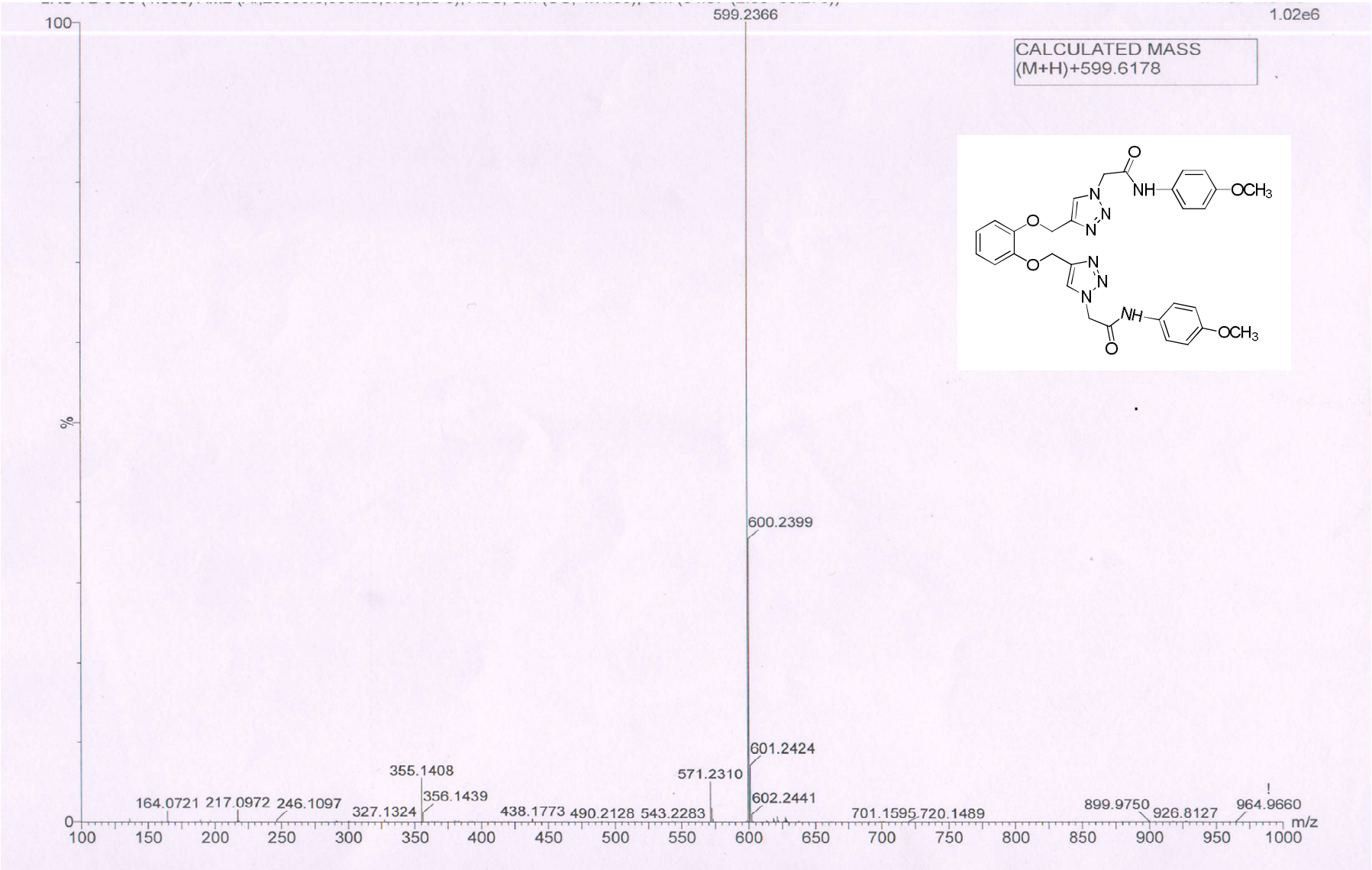
8s: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



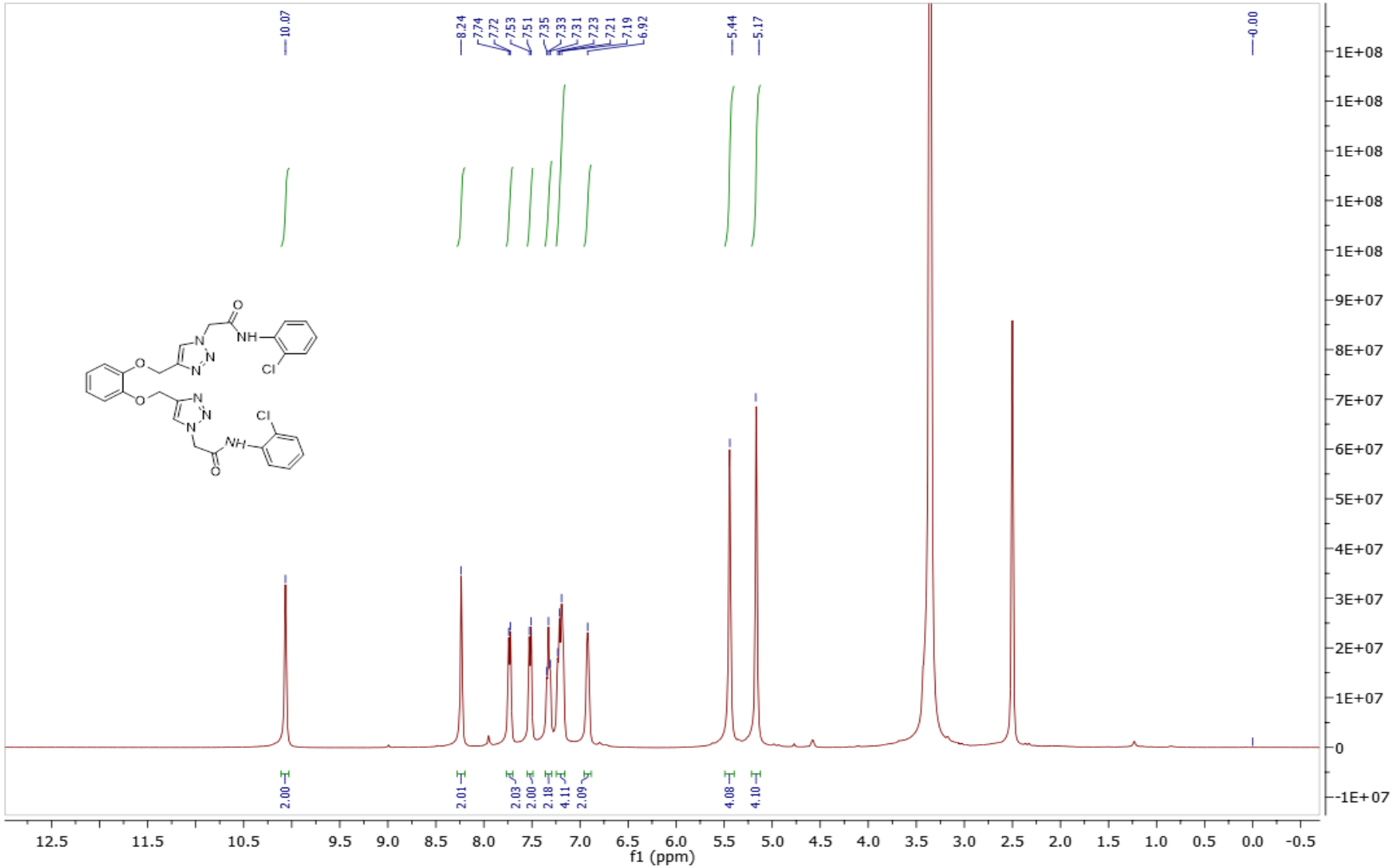
8t: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



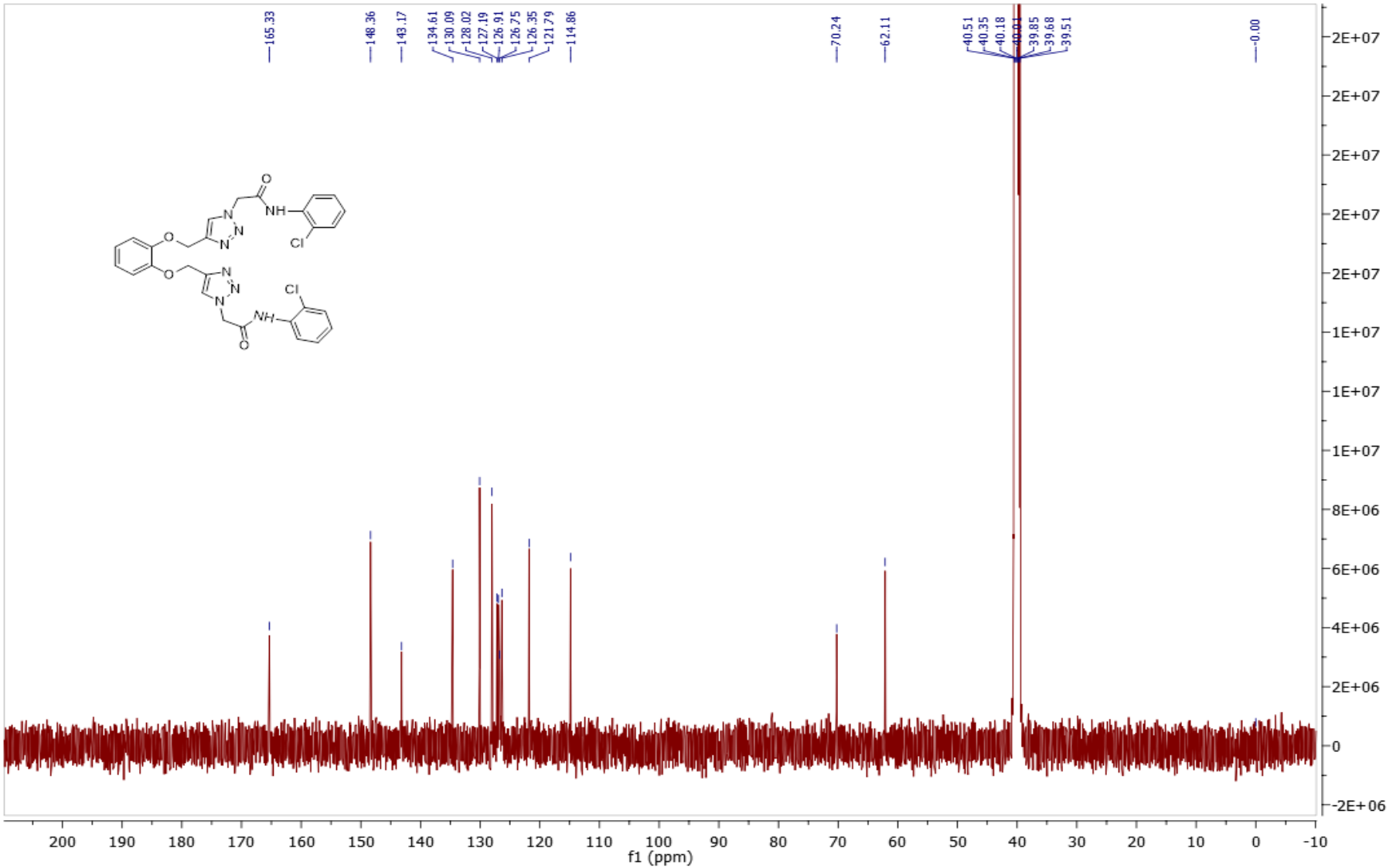
8t: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



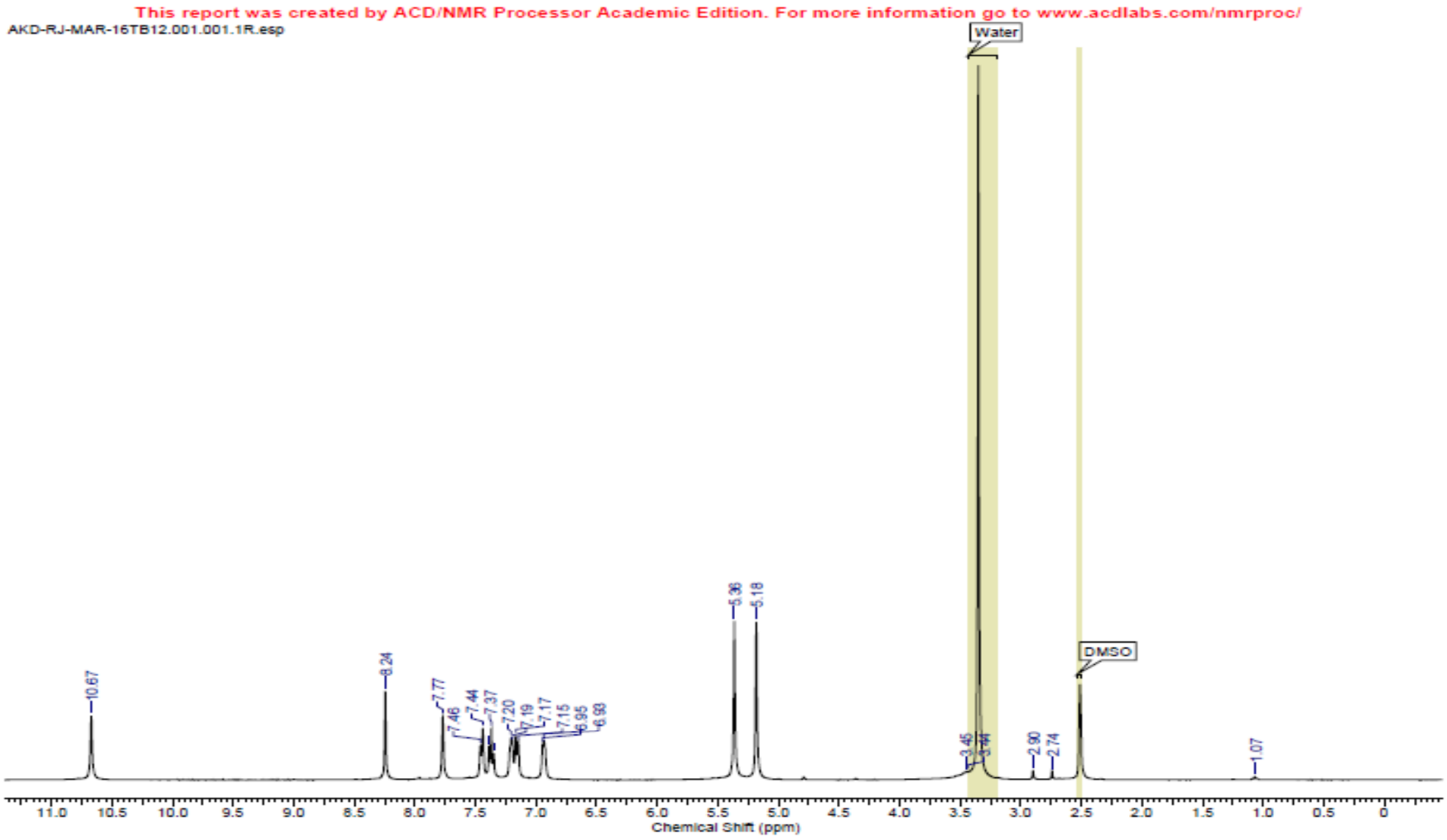
8t: MS (MALDI-TOF) calcd. For $C_{30}H_{31}N_8O_6$ $[M+H]^+$: 599.2367; found: 599.2366.



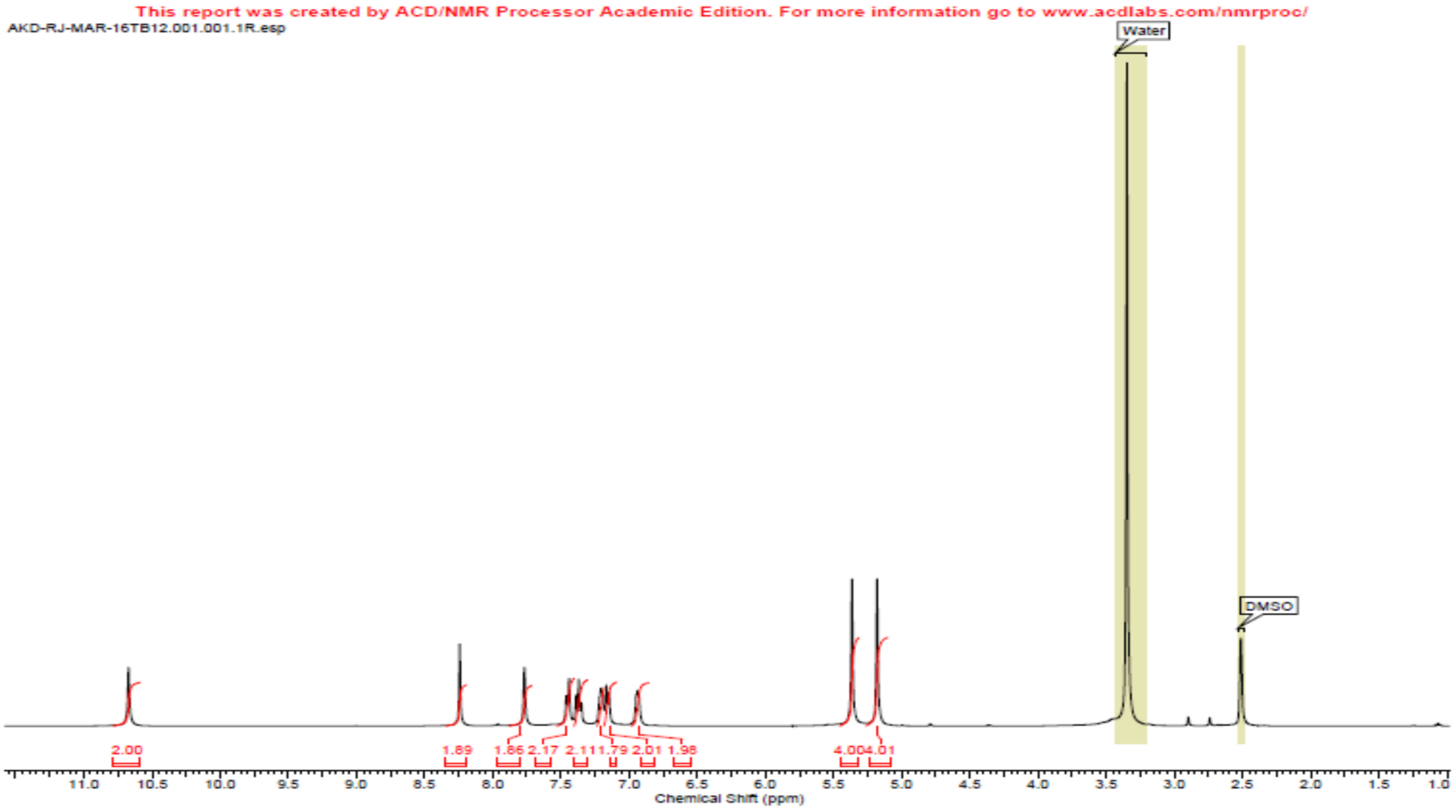
8u: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



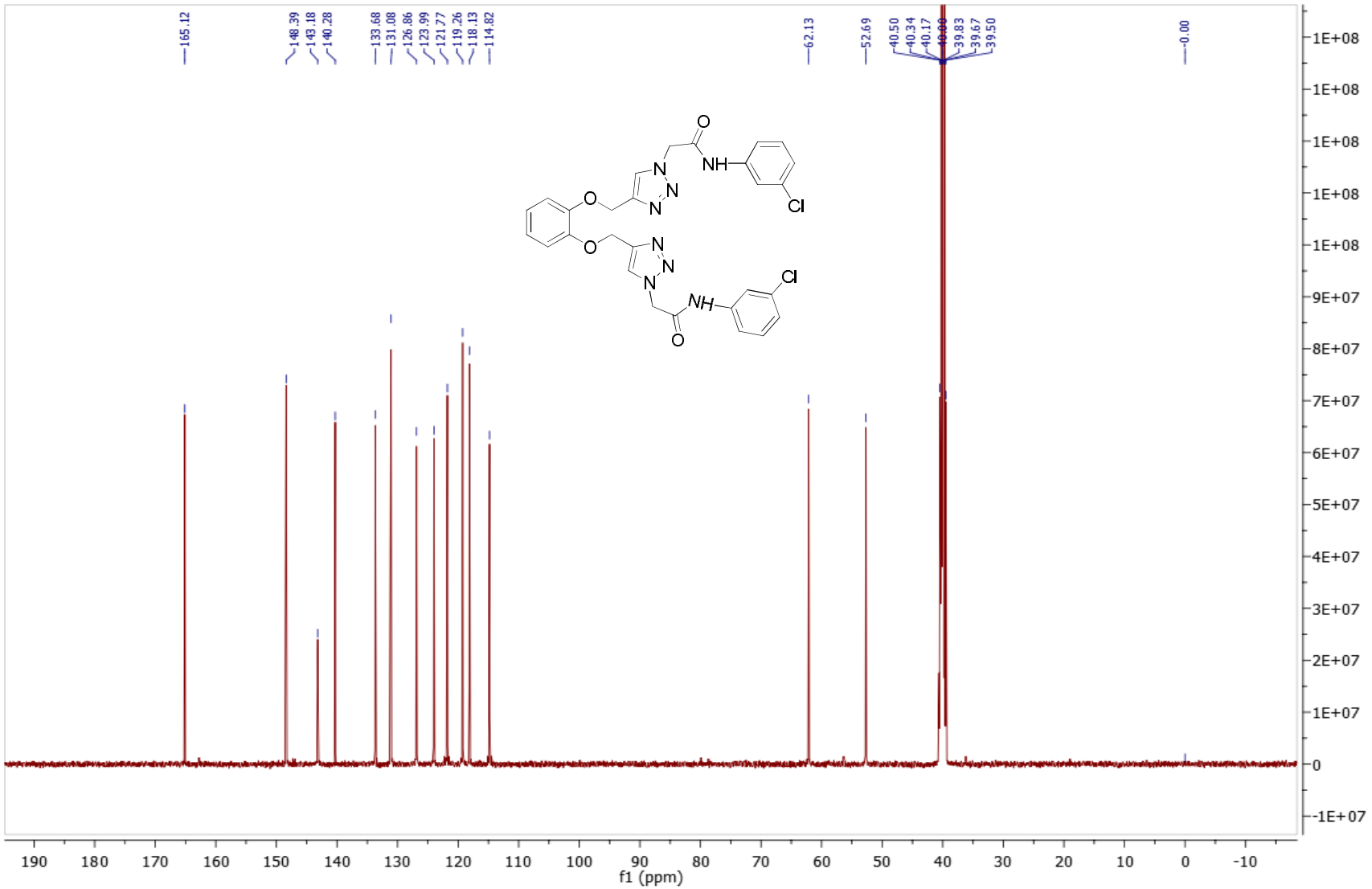
8u: ^{13}C NMR (125 MHz, DMSO-d_6, ppm)



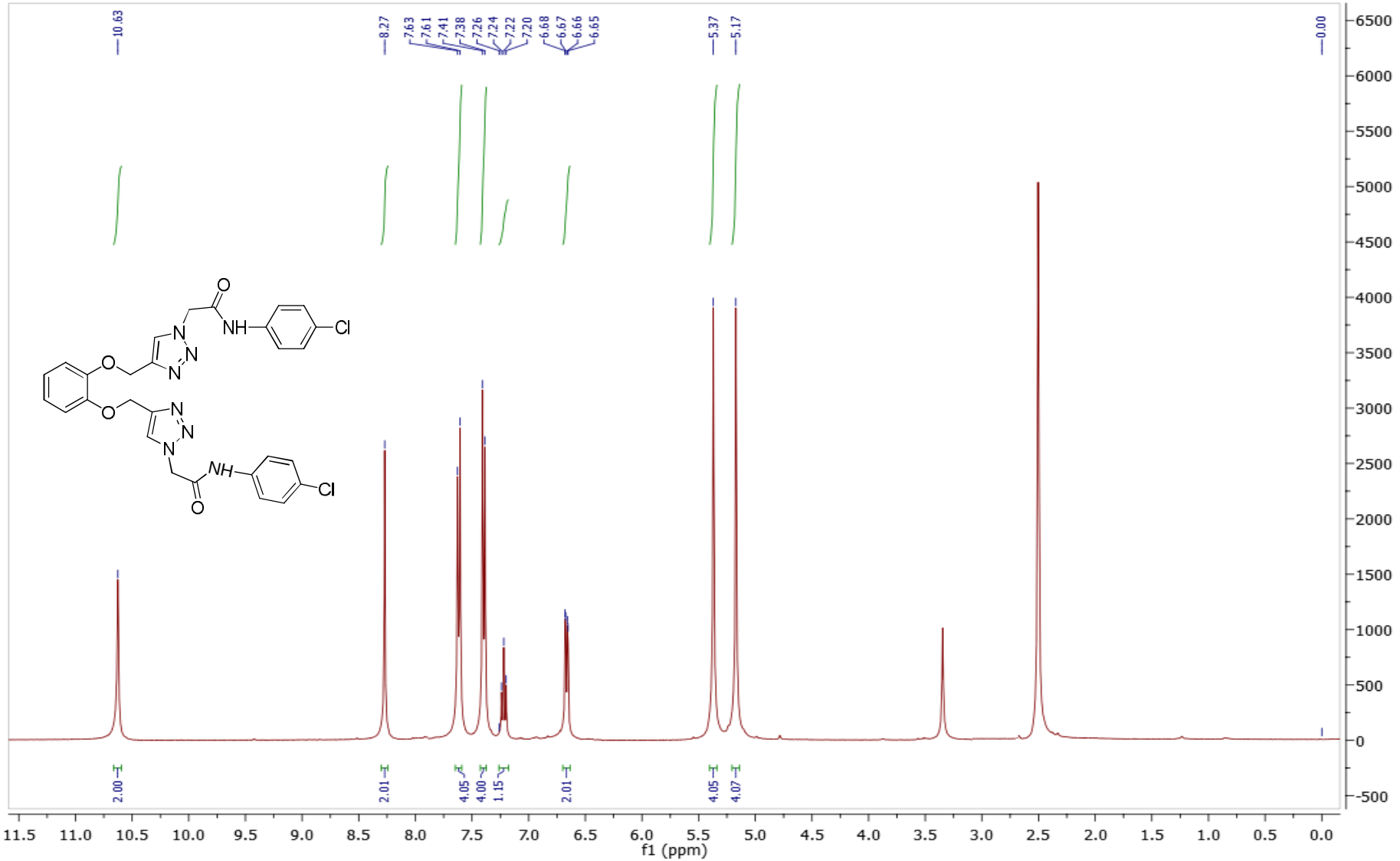
8v: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



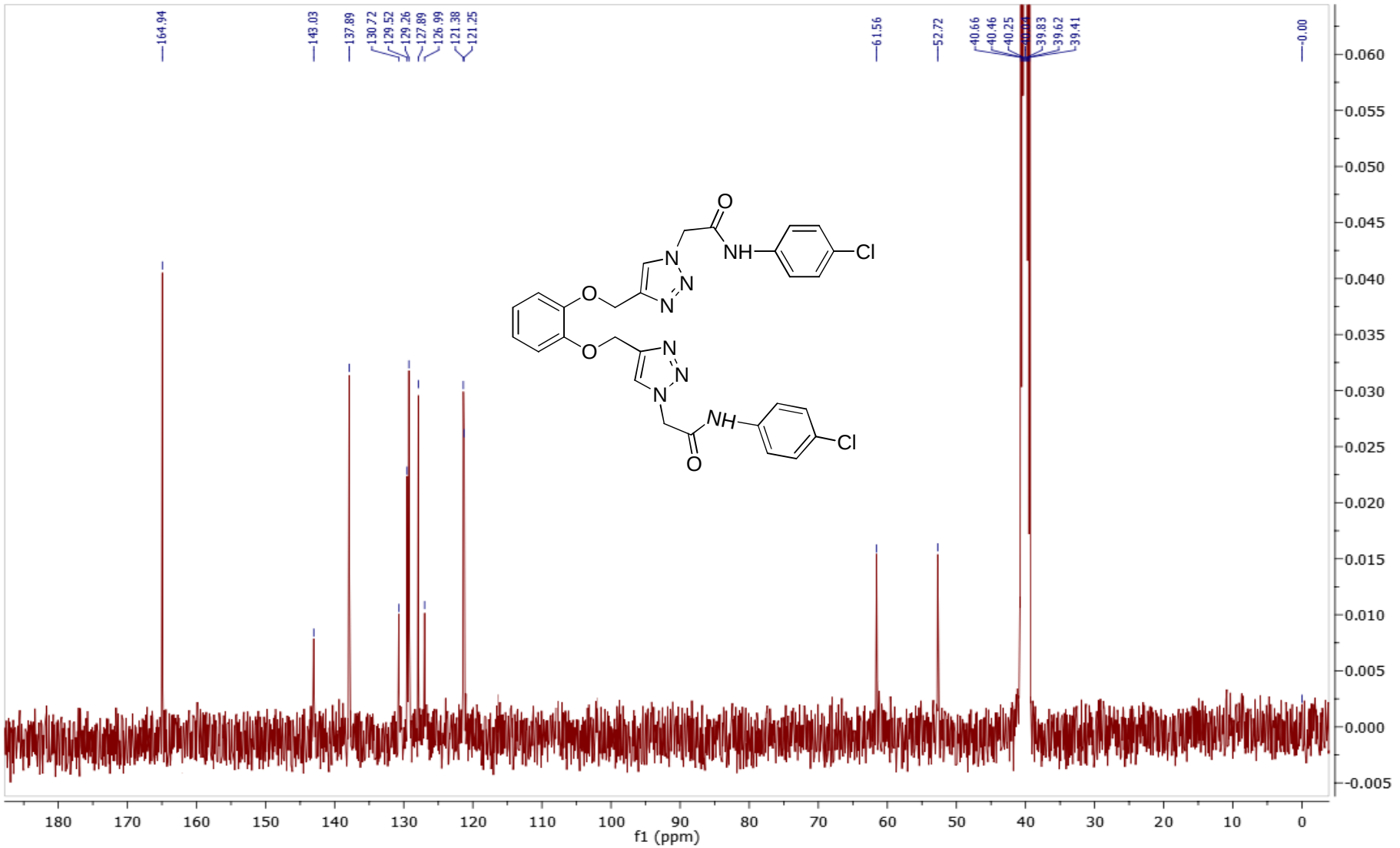
8v: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



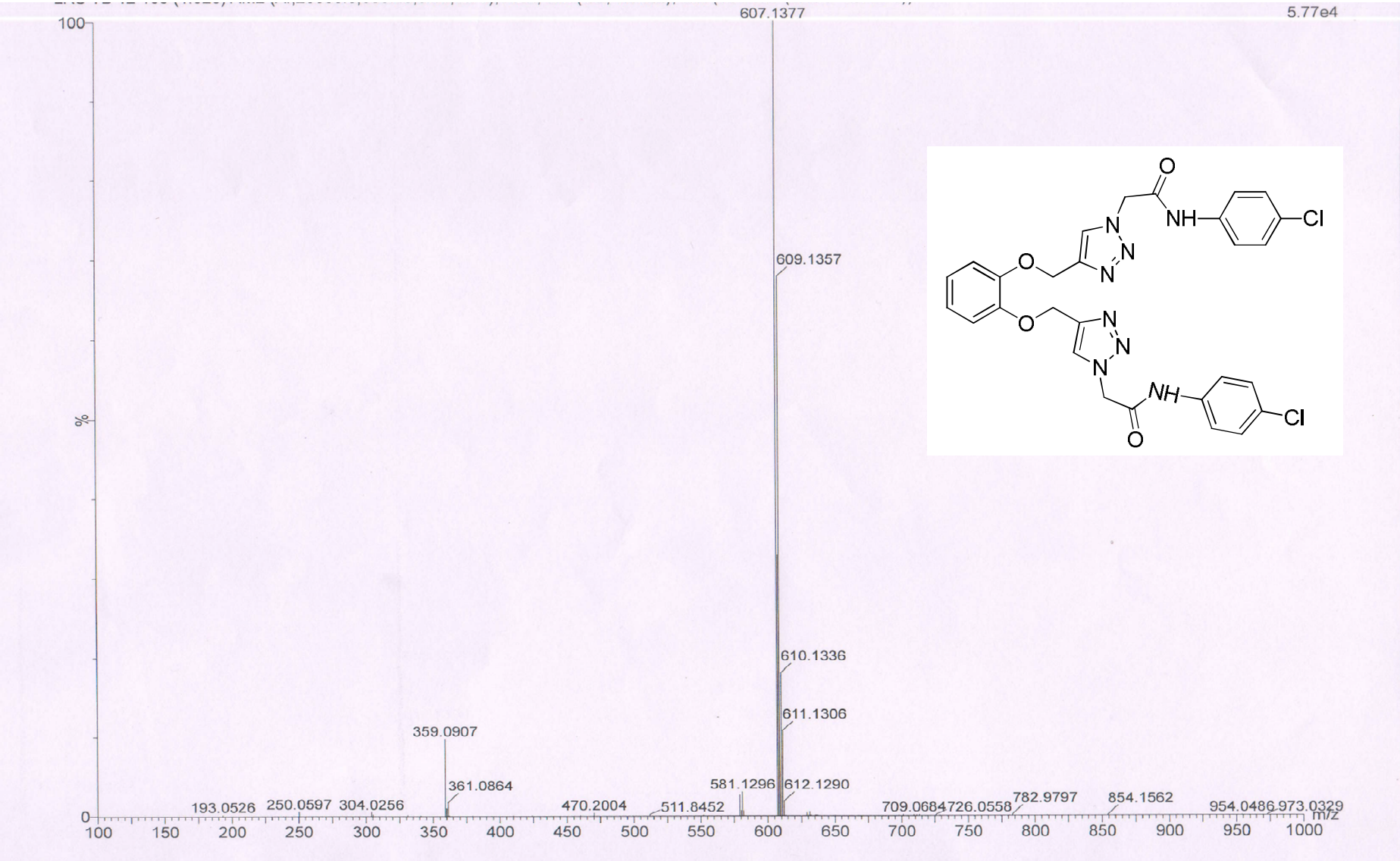
8v: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



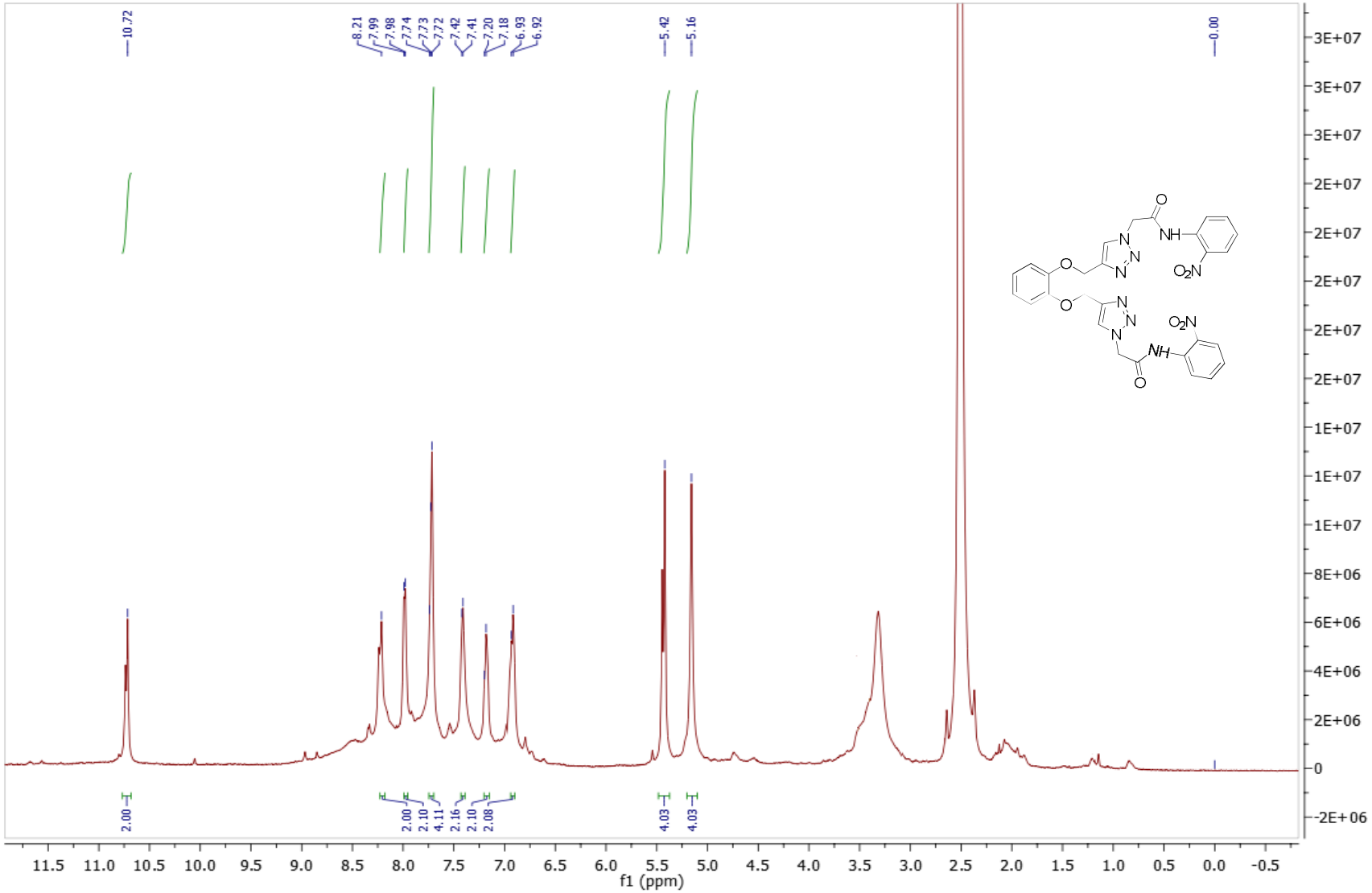
8w: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



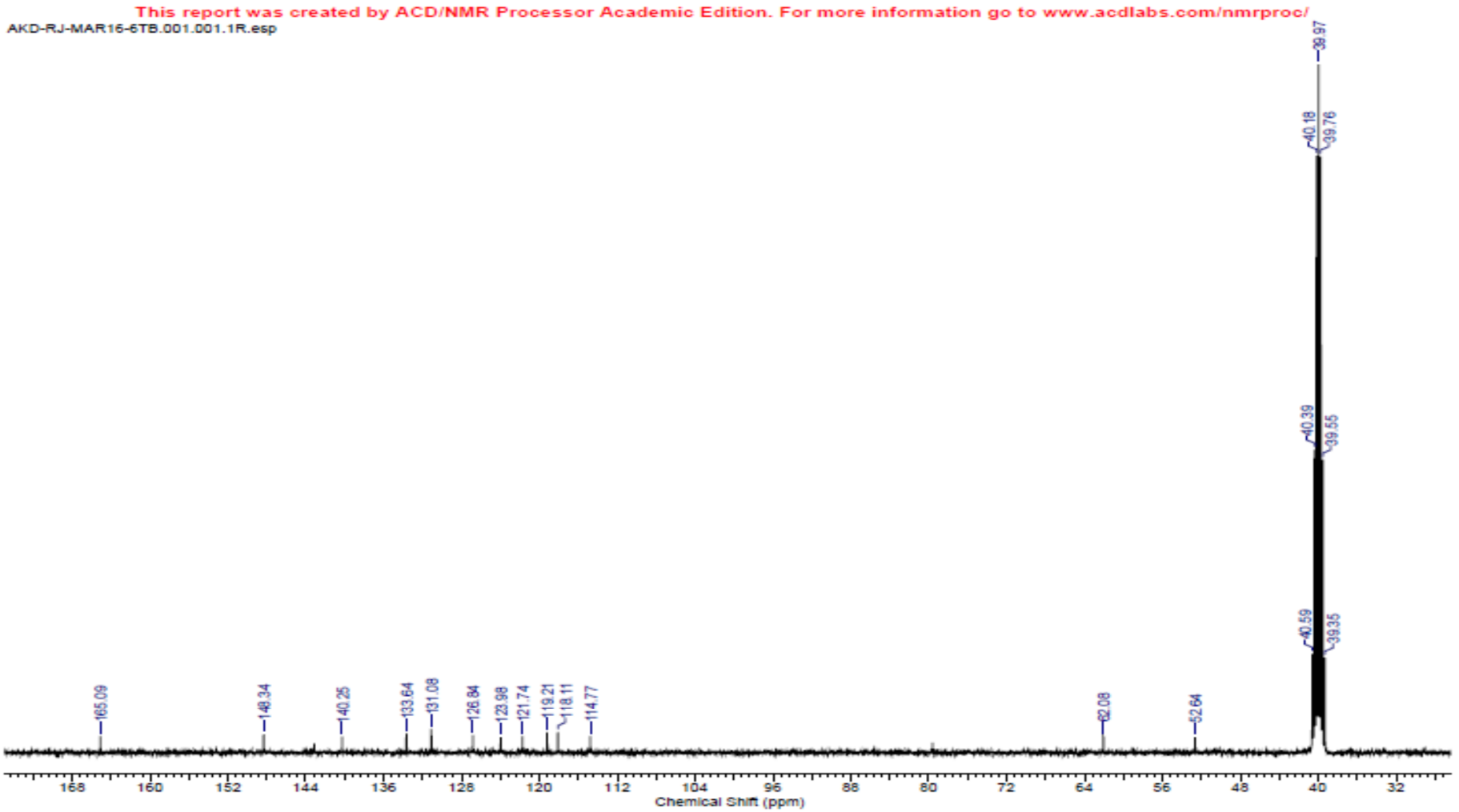
8w: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



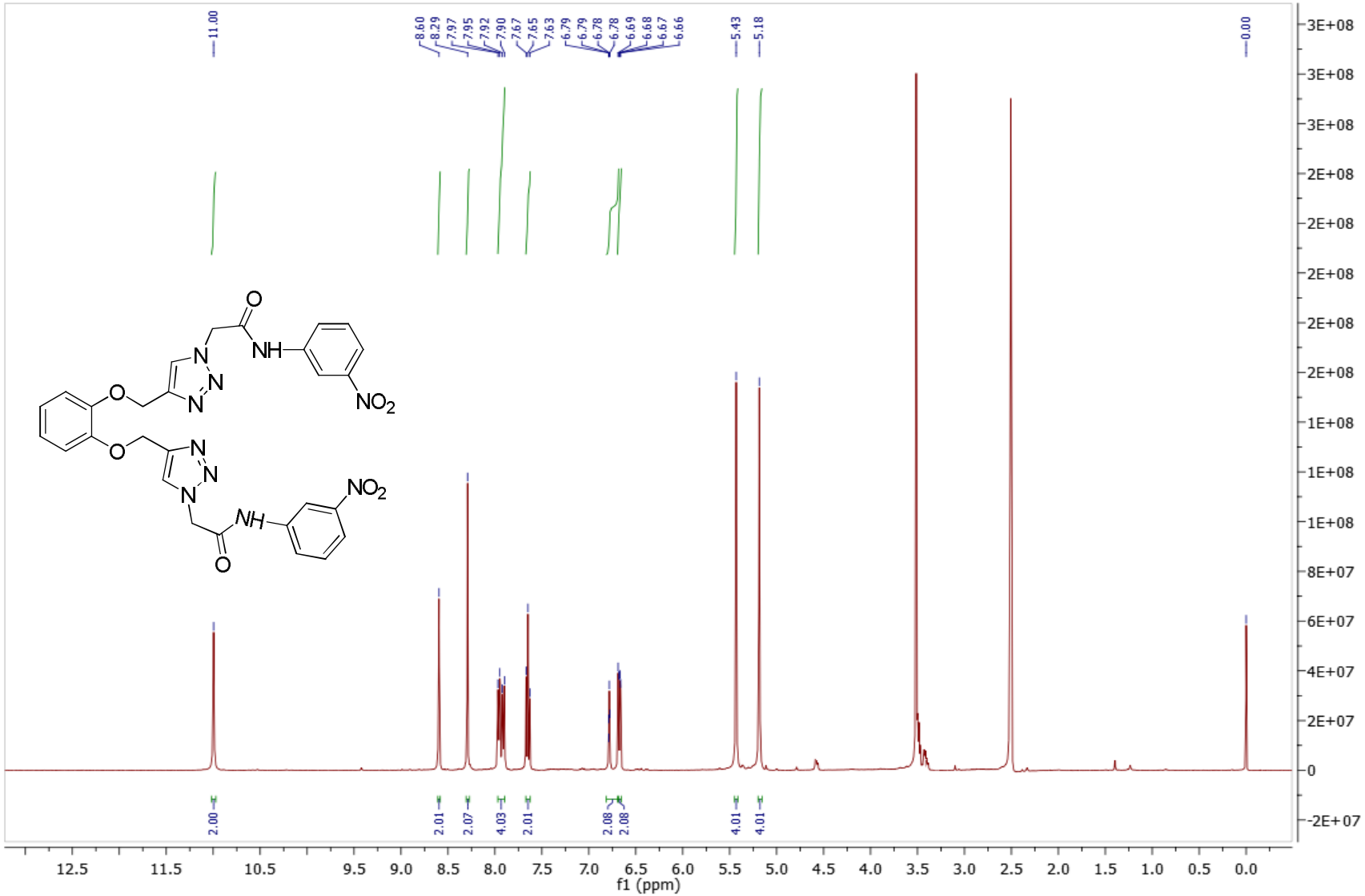
8w: MS (MALDI-TOF) calcd. For $C_{28}H_{25}Cl_2N_8O_4$ $[M+H]^+$: 607.1376; found: 607.1377.



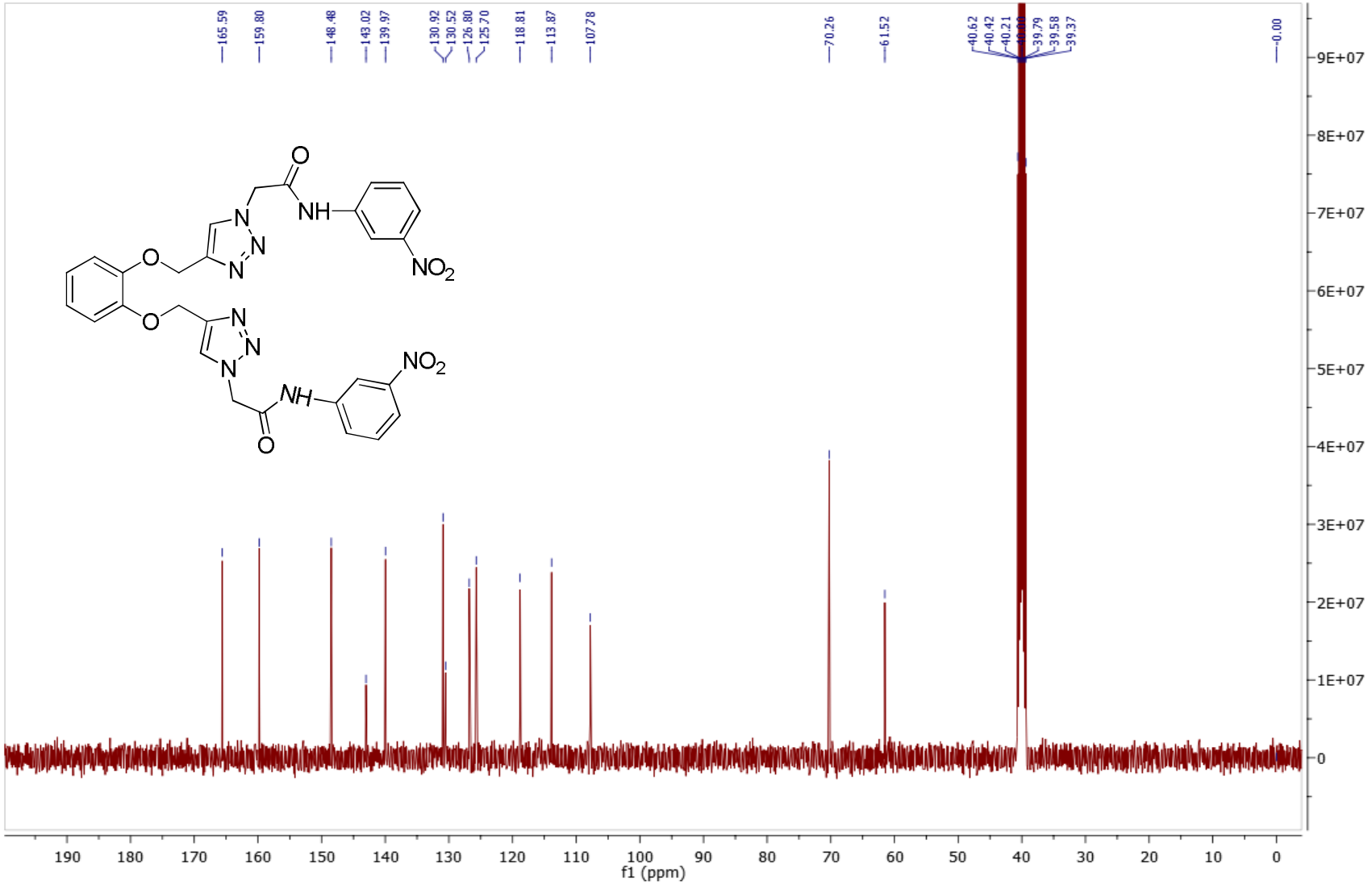
8x: ^{1}H NMR (500 MHz, DMSO-d_6, ppm)



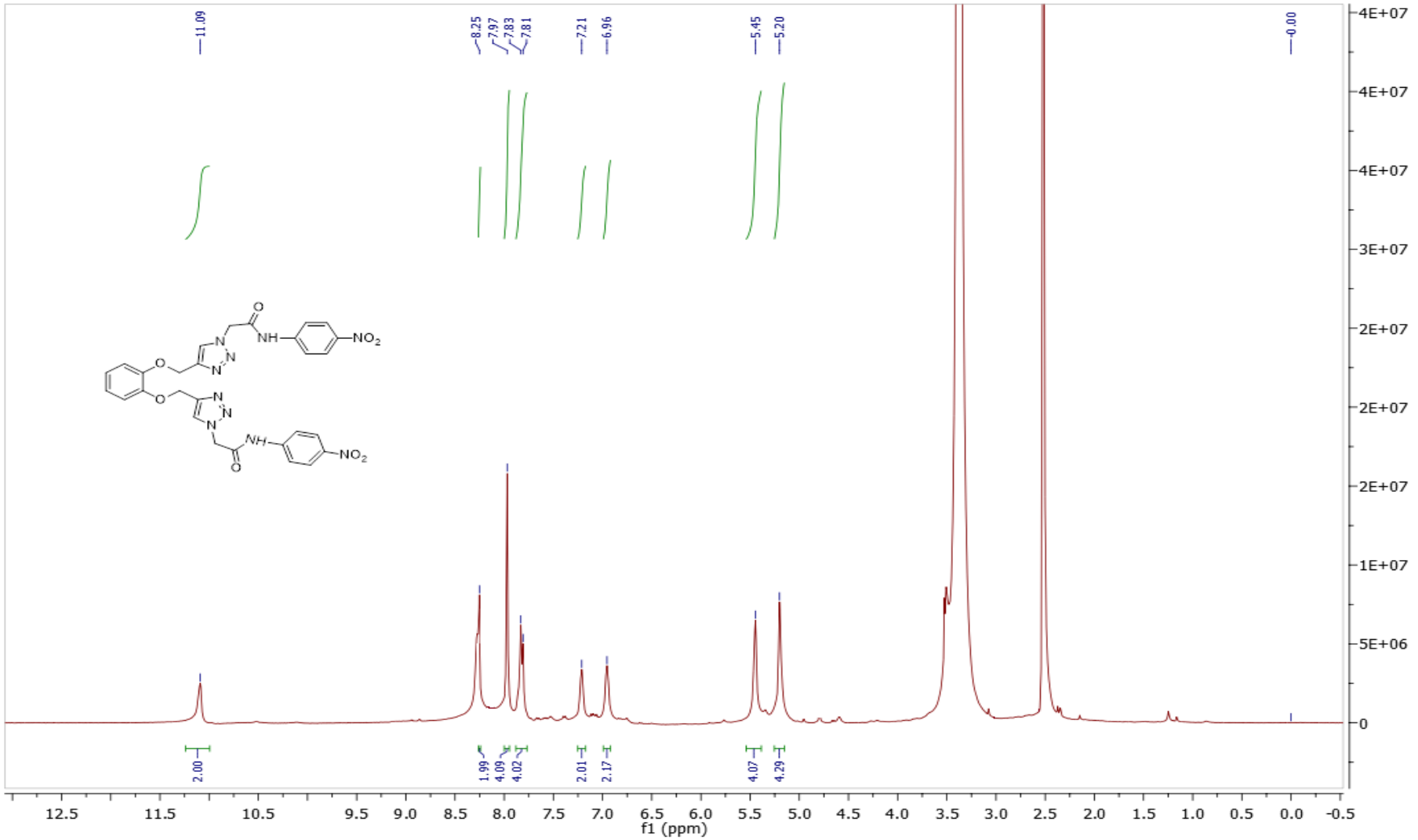
8x: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



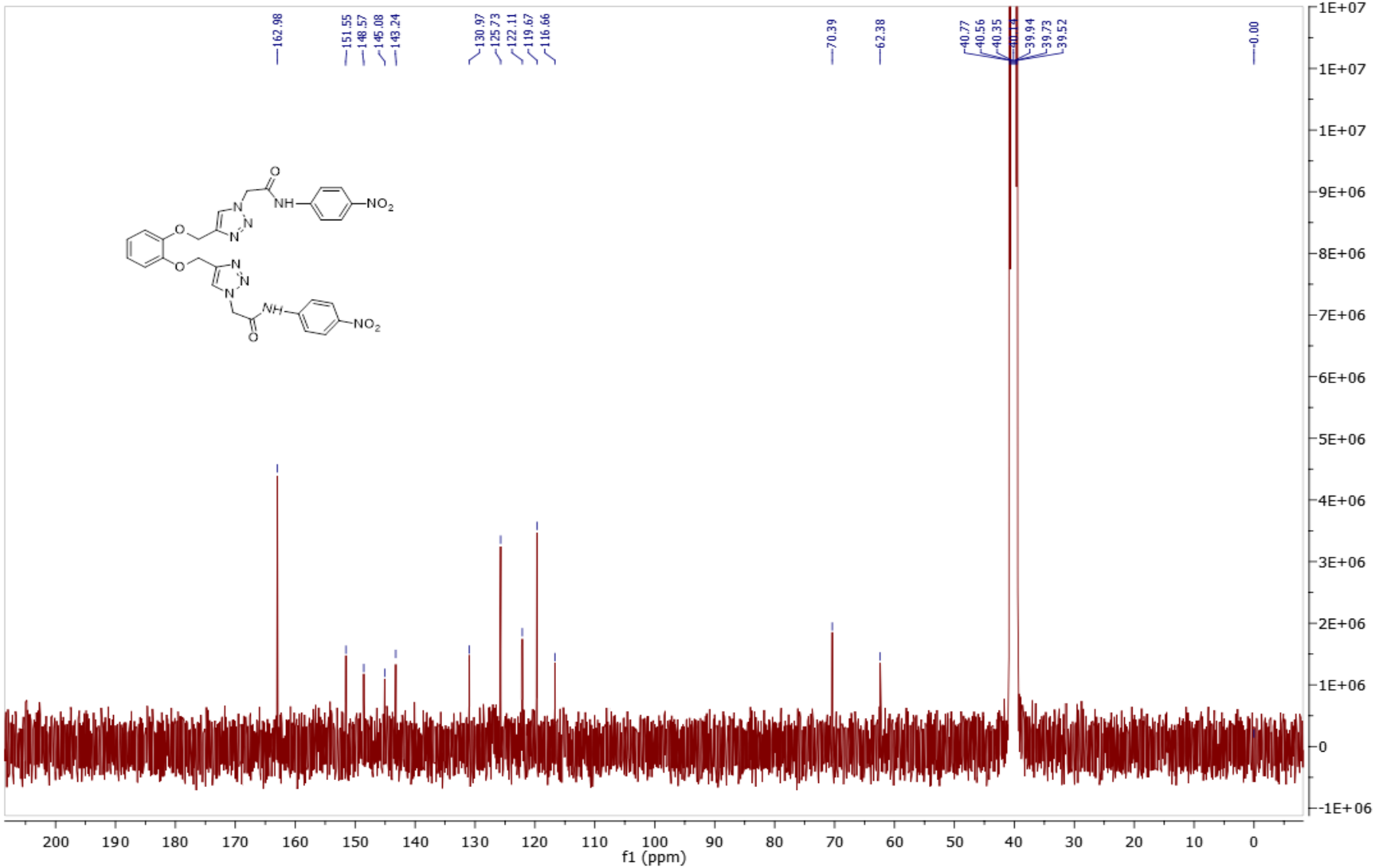
8y: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



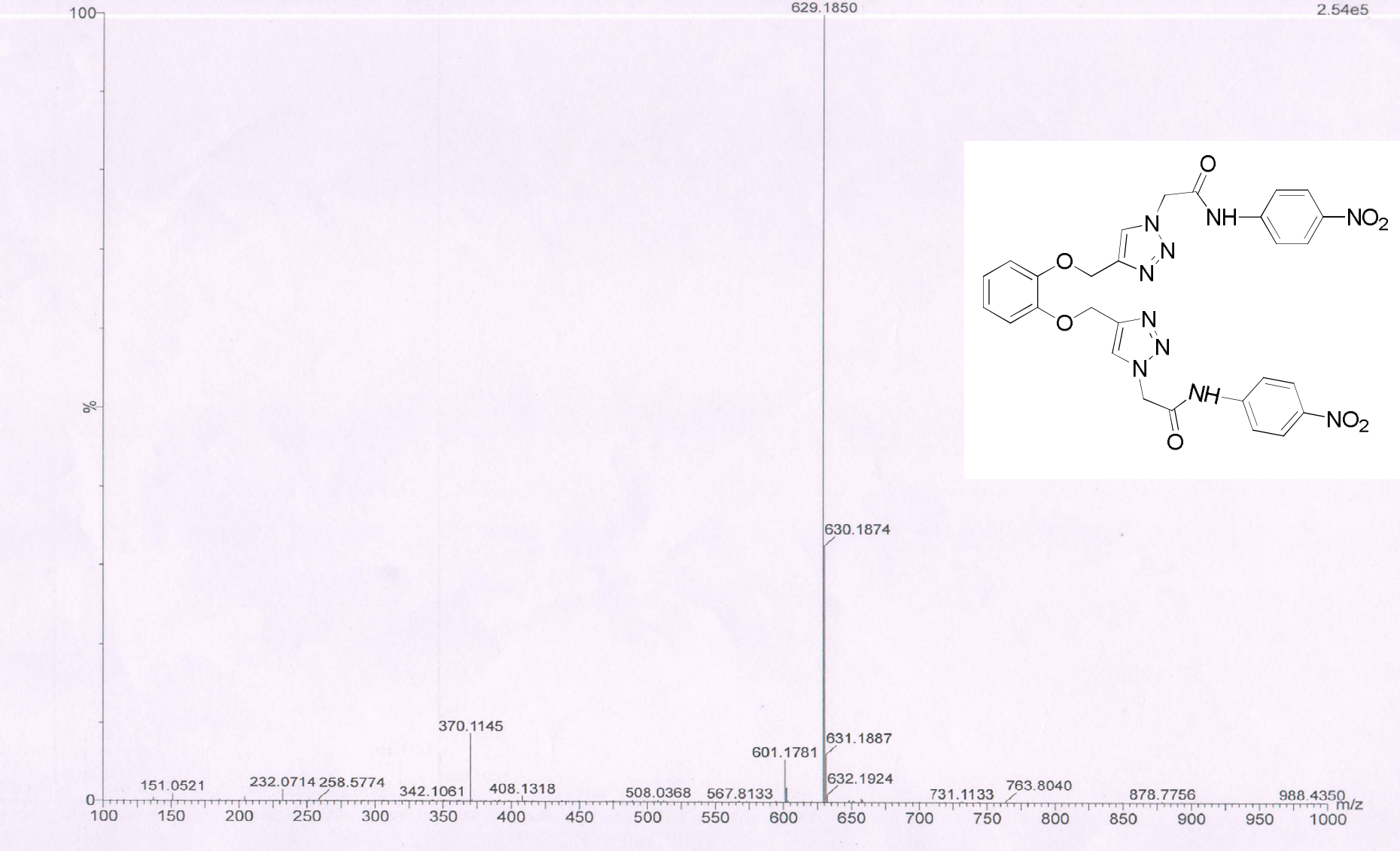
8y: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



8z: ^{1}H NMR (400 MHz, DMSO-d_6, ppm)



8z: ^{13}C NMR (100 MHz, DMSO-d_6, ppm)



8z: MS (MALDI-TOF) calcd. For $C_{28}H_{25}N_{10}O_8$ $[M+H]^+$: 629.1857; found: 629.1850.

References

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4. A. Anand, R. J. Naik, H. M. Revankar, M. V. Kulkarni, S. R Dixit and S. D. Joshi. *Eur. J. Med. Chem*., 2015, 105, 194-207.