Supporting Information

Synthesis of propargylamines via A³ multicomponent reaction and biological evaluation as potential anticancer agents

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1. General Information

Unless the preparation procedure is indicated, the compounds used were obtained from commercial sources and employed without further purification. Wang resins used were commercial brands Novabiochem (San Diego, CA, U.S.A.) and Aldrich (Saint Louis, MO, USA). Solvents used as eluents in chromatographic techniques (CCD or column chromatography) were purified by distillation.

2. Instruments and conditions

Nuclear Magnetic Resonance: NMR spectra were recorded with Bruker spectrometer brand model Avance-300 DPX at 300 MHz for ^{1}H NMR (using the Me_4Si signal as internal reference standard, δ = 0.00 ppm) and at 75 MHz for ^{13}C NMR (using the solvent signal as internal reference standard) both conventional and gel-phase. Measurements were made with sample dissolved in $CDCl_3$. ^{1}H NMR spectra are informed indicating the chemical shifts of the signals (δ) and then, in parentheses, the multiplicity of the signal, the coupling constants (*J*) and integration. The ^{13}C NMR spectra are reported indicating the chemical shifts of the signals. Abbreviations used to indicate the multiplicities of the signals were s: singlet; brs: broad singlet; d: doublet; dd: doublet of doublets; td: triplet of doublets; dt: doublet of triplets; t: triplet; sept: septet and m: multiplet.

Samples for ^{13}C NMR phase gel were prepared as follows: 50-80 mg of resin were placed in a conventional NMR tube and 0.5 mL of $CDCl_3$ was added slowly in order to obtain a gel, which is homogenized by sonication. Spectra were made according to the literature.[1]

Mass Spectrometry: HRMS spectra were performed at the Mass Spectrometry Laboratory of the Rosario Scientific and Technological Center, at the Unit of Microanalysis and Physical Methods Applied to Organic Chemistry (UMYMFOR-UBA) or Mass Spectrometry Service at Córdoba Food Science and Technology Institute (ICYTAC), using a Bruker mass spectrometer micrOTOF-Q II. The detection of ions was carried out by electrospray ionization (ESI), positive mode.

Chromatography: TLCs were performed on commercial aluminum plates covered with Merck silica gel (60 F_{254}). Chromatographic plates were analyzed by UV radiation (254 nm) and/or spraying with irreversible development methods.

Preparative separations were carried out by liquid column chromatography using Merck 60 H silica gel (230-400 mesh).

[1] Giralt, E., Rizo, J., and Pedroso, E. (1984) Application of gel-phase ^{13}C-NMR to monitor solid phase peptide synthesis. *Tetrahedron 40*, 4141–4152

3. Selected NMR spectra

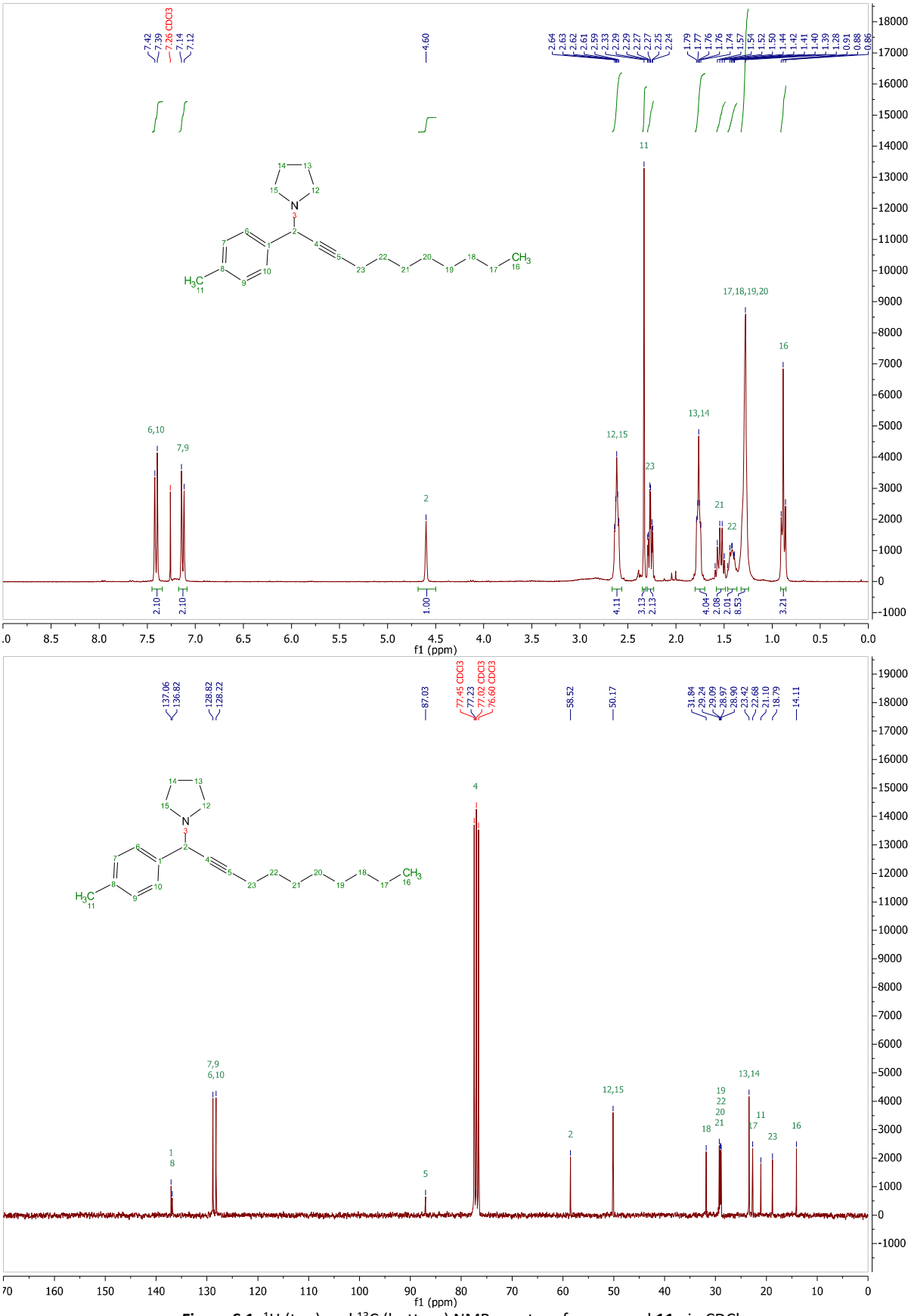

Figure S 1. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11a** in $CDCl_3$.

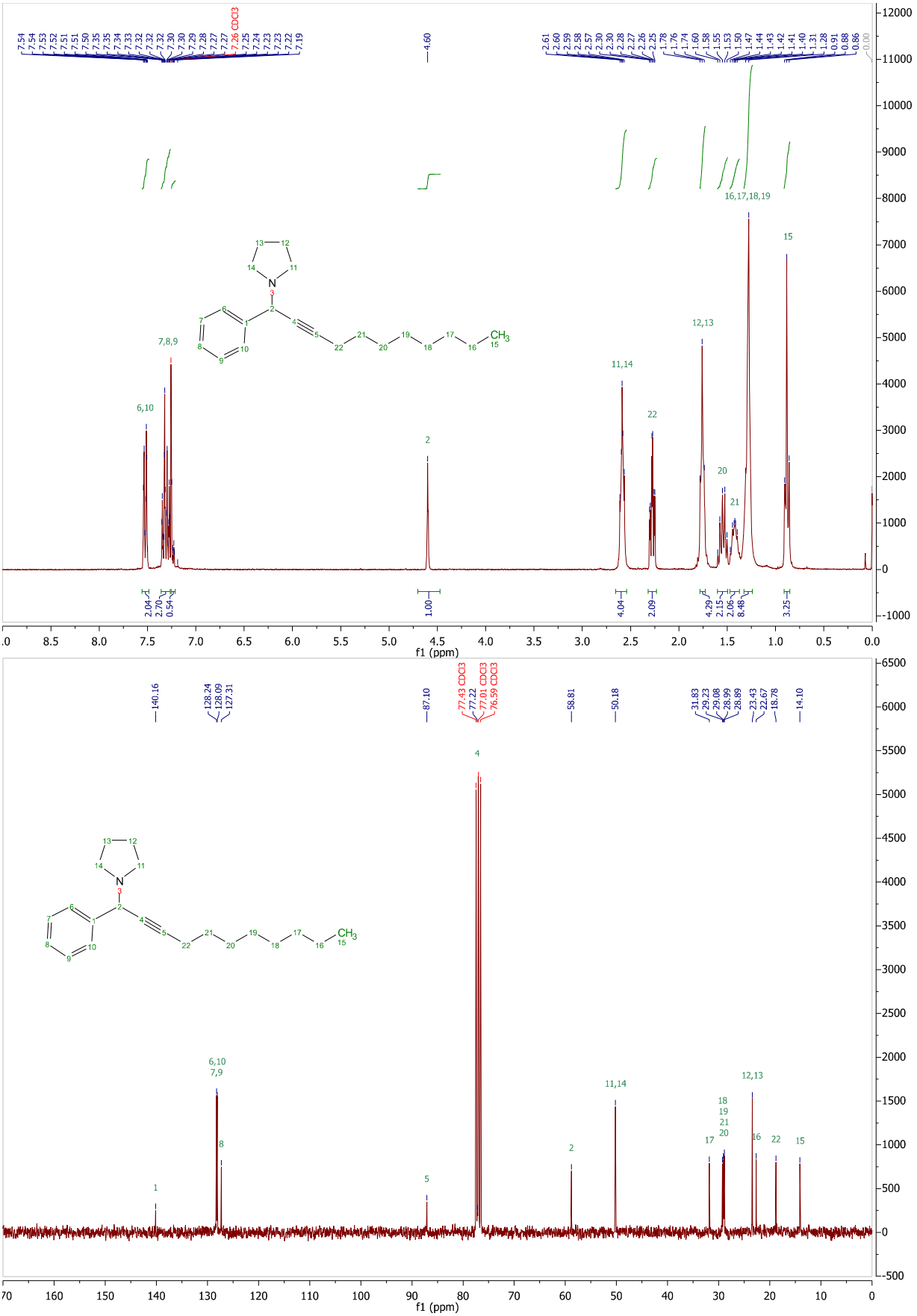

Figure S 2. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11b** in $CDCl_3$.

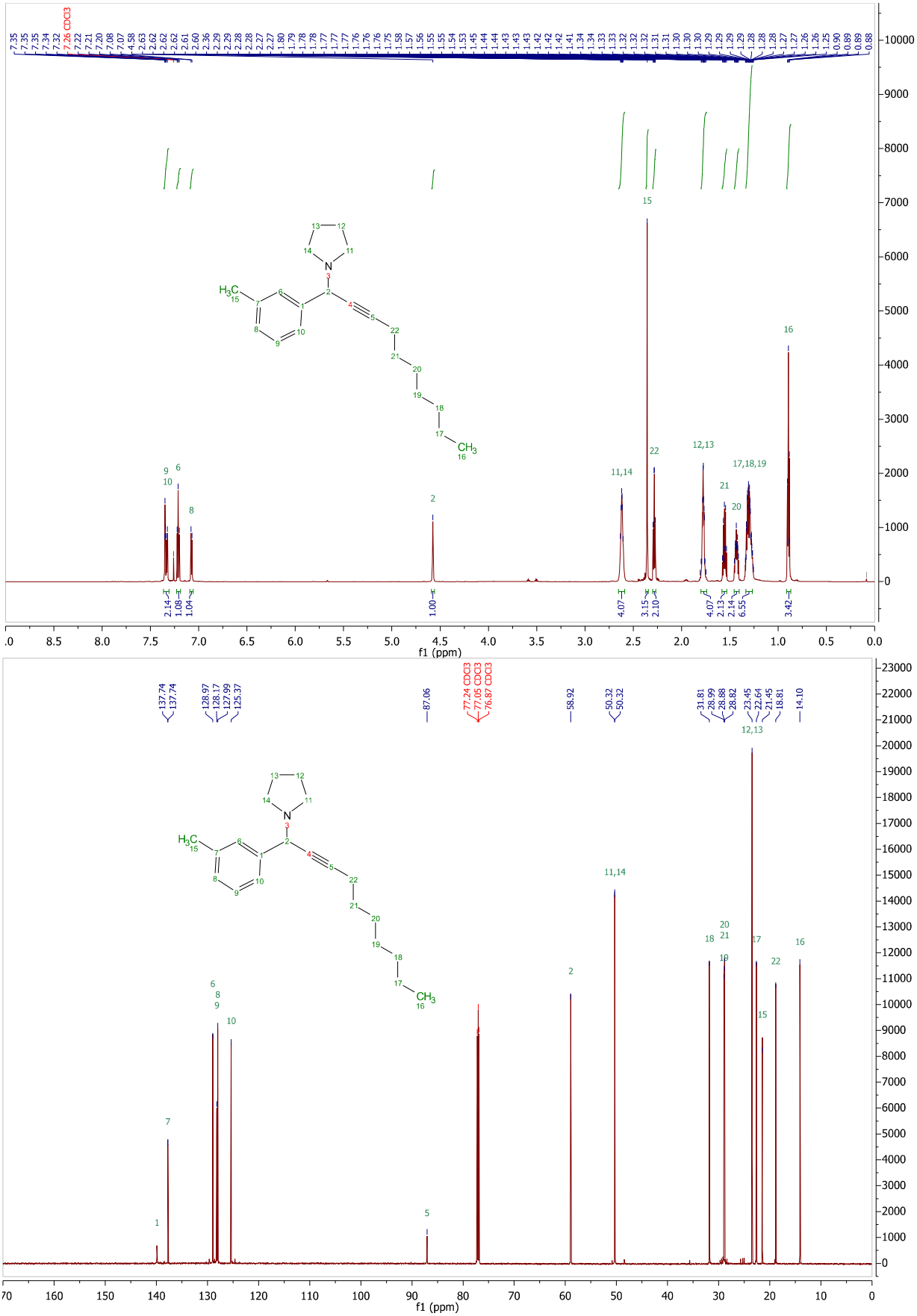

Figure S 3. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11c** in $CDCl_3$.

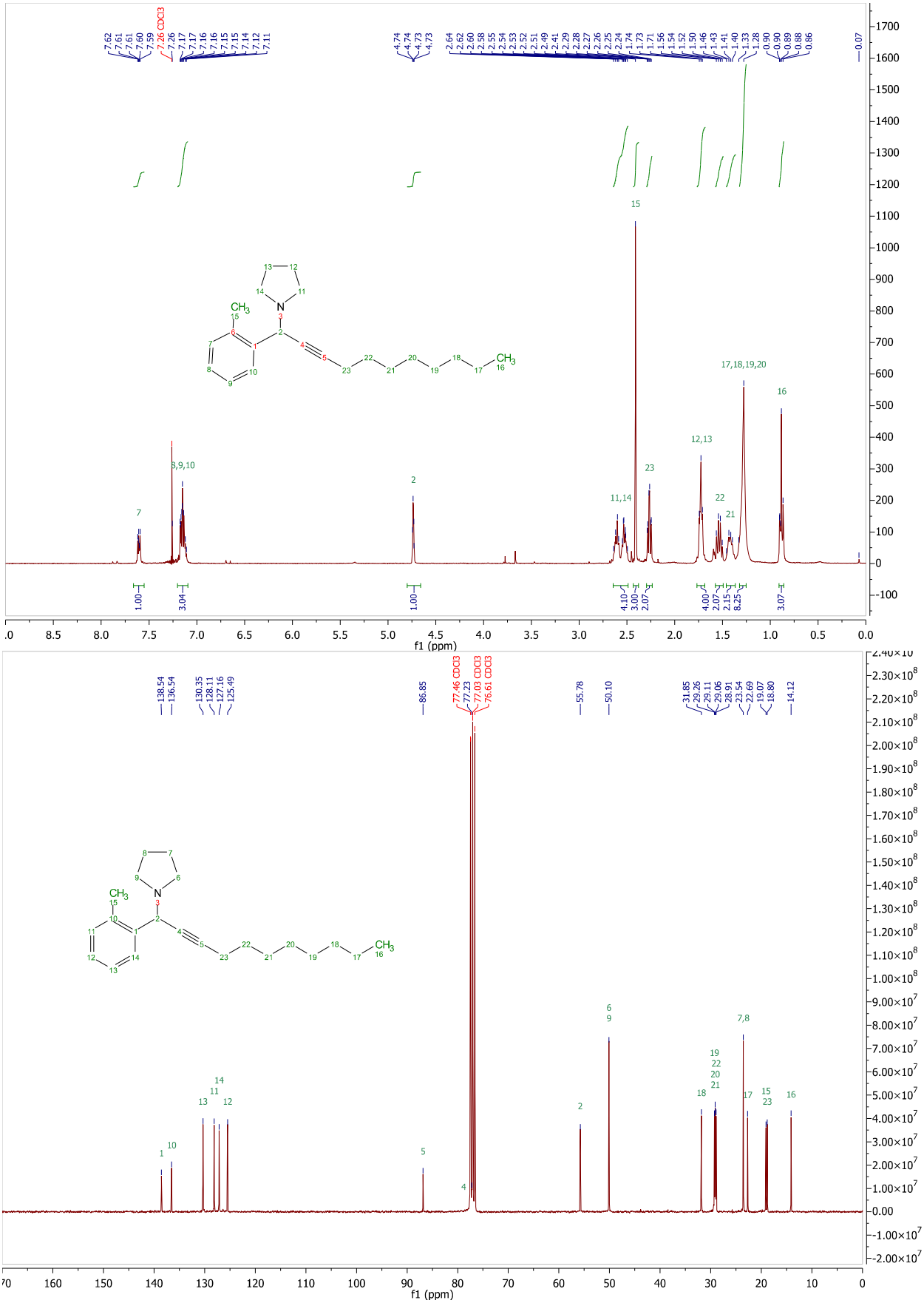

Figure S 4. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11d** in $CDCl_3$.

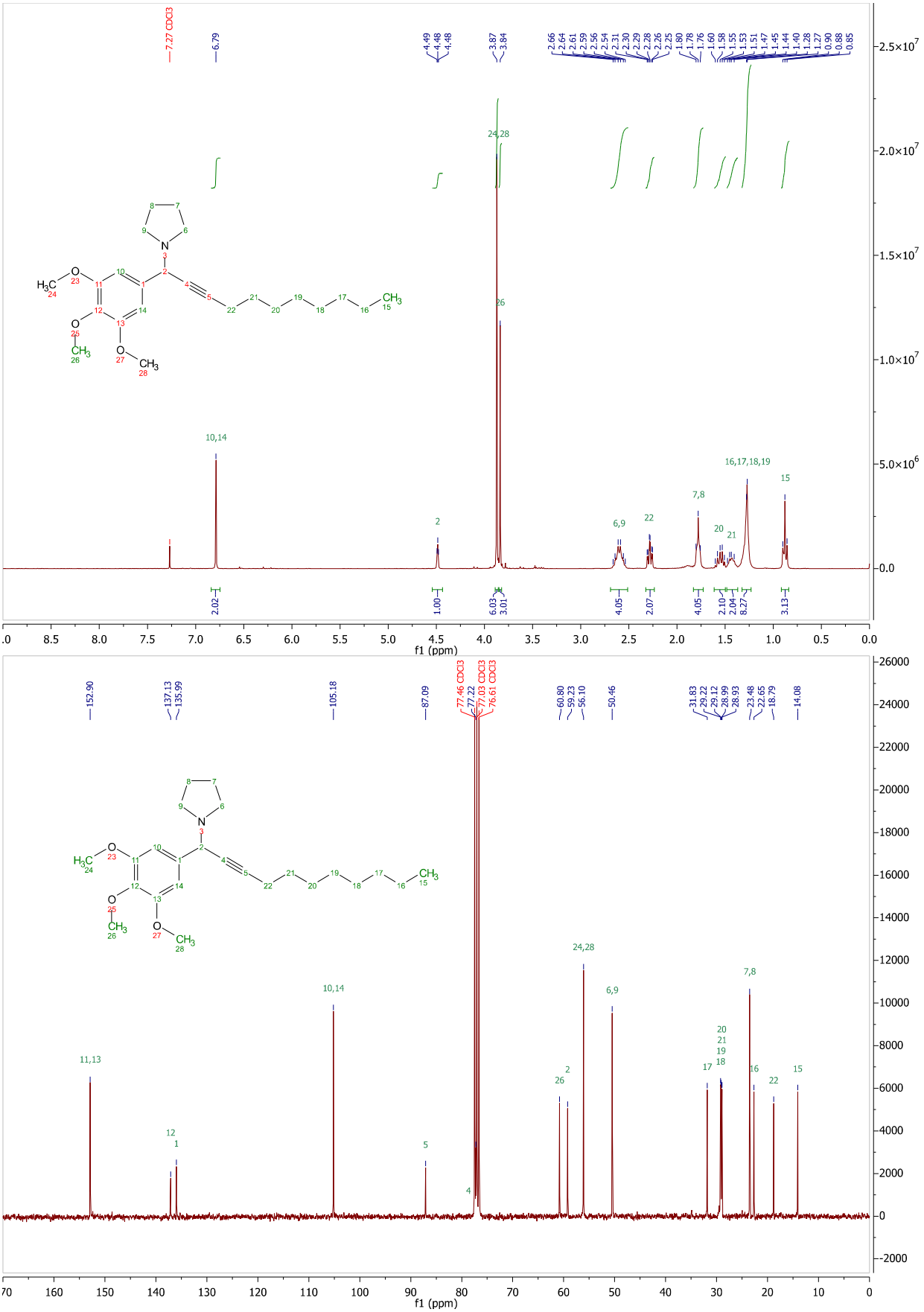

Figure S 5. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11e** in $CDCl_3$.

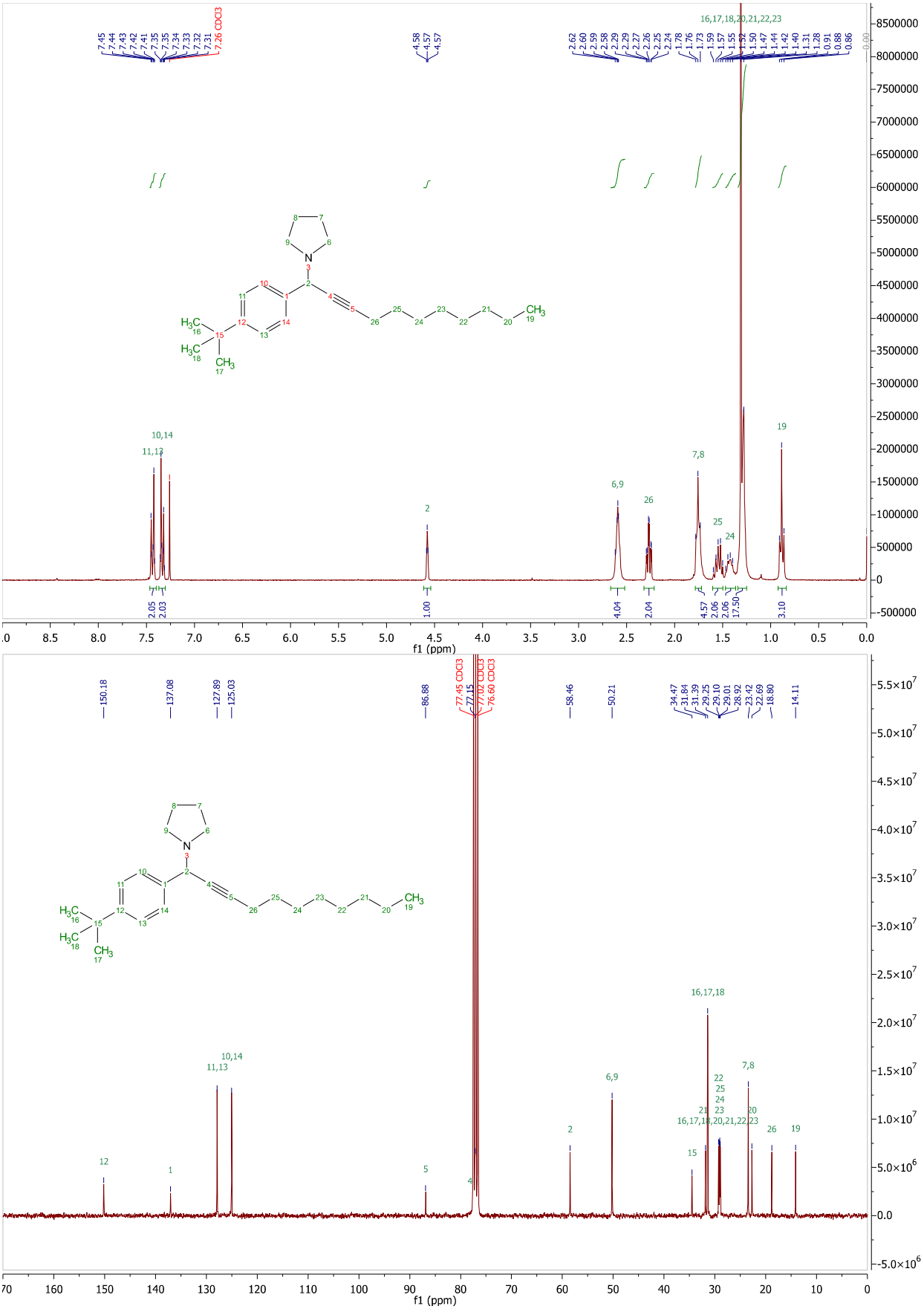

Figure S 6. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11f** in $CDCl_3$.

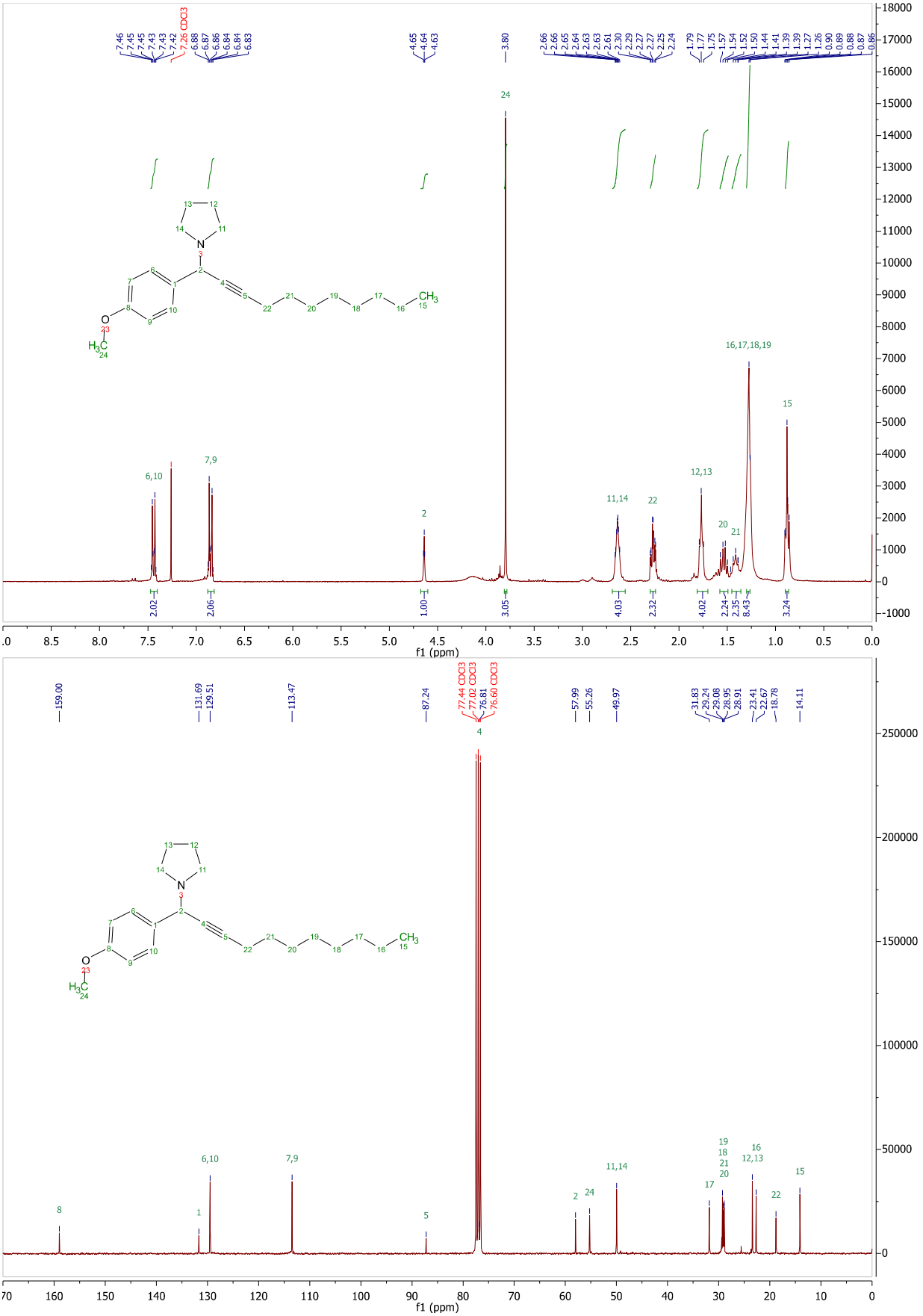

Figure S 7. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11g** in $CDCl_3$.

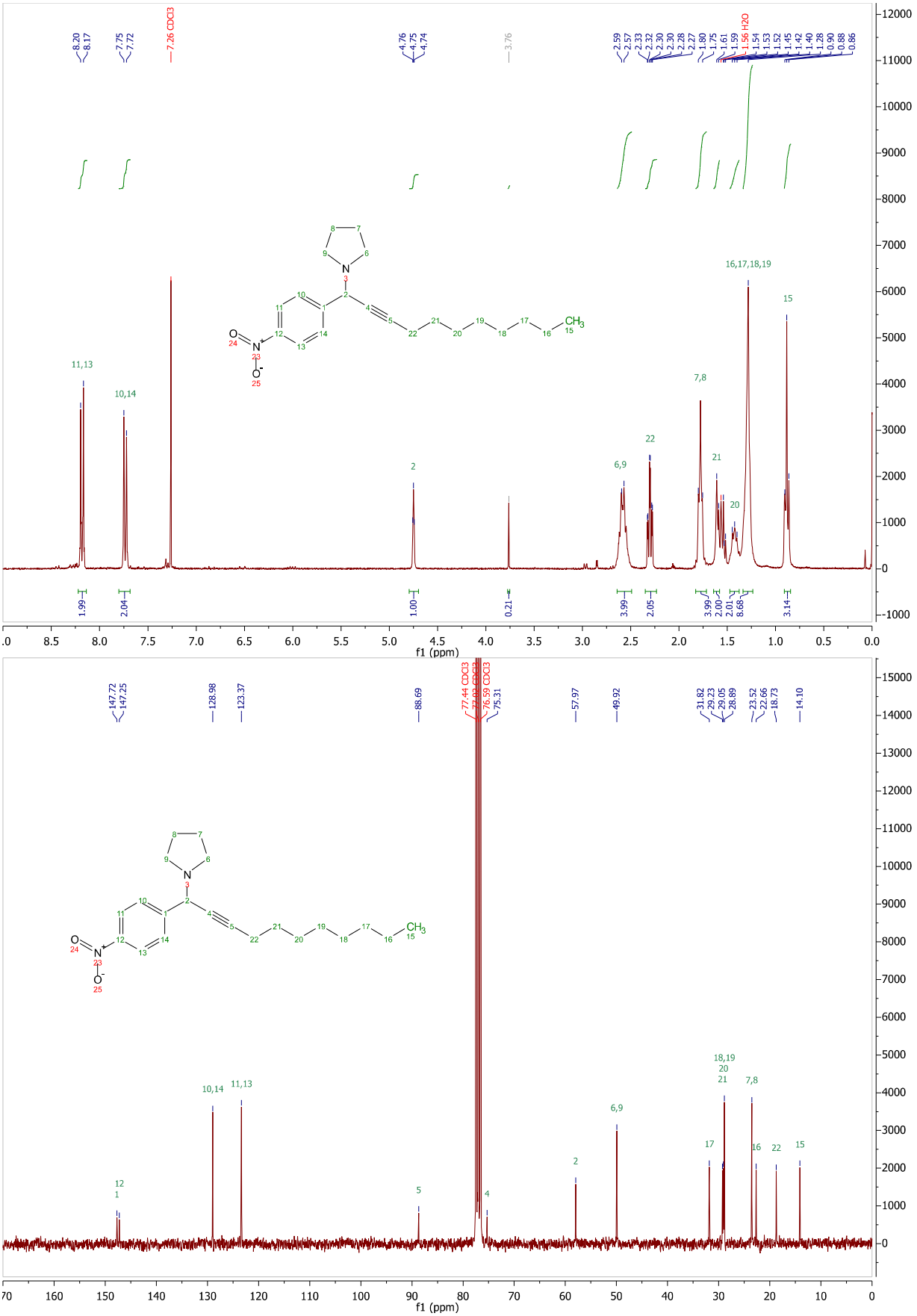

Figure S 8. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11h** in $CDCl_3$.

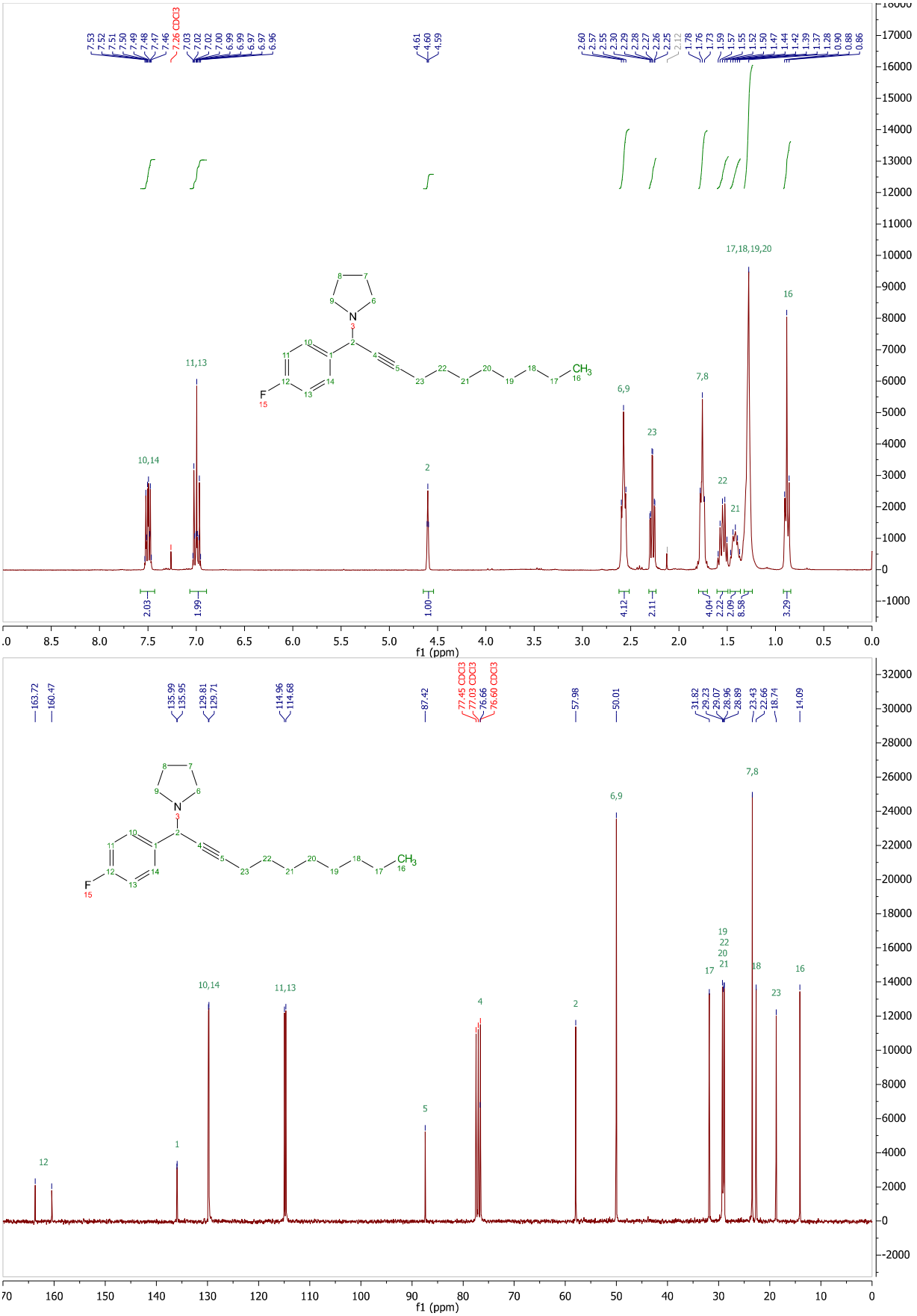

Figure S 9. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11i** in $CDCl_3$.

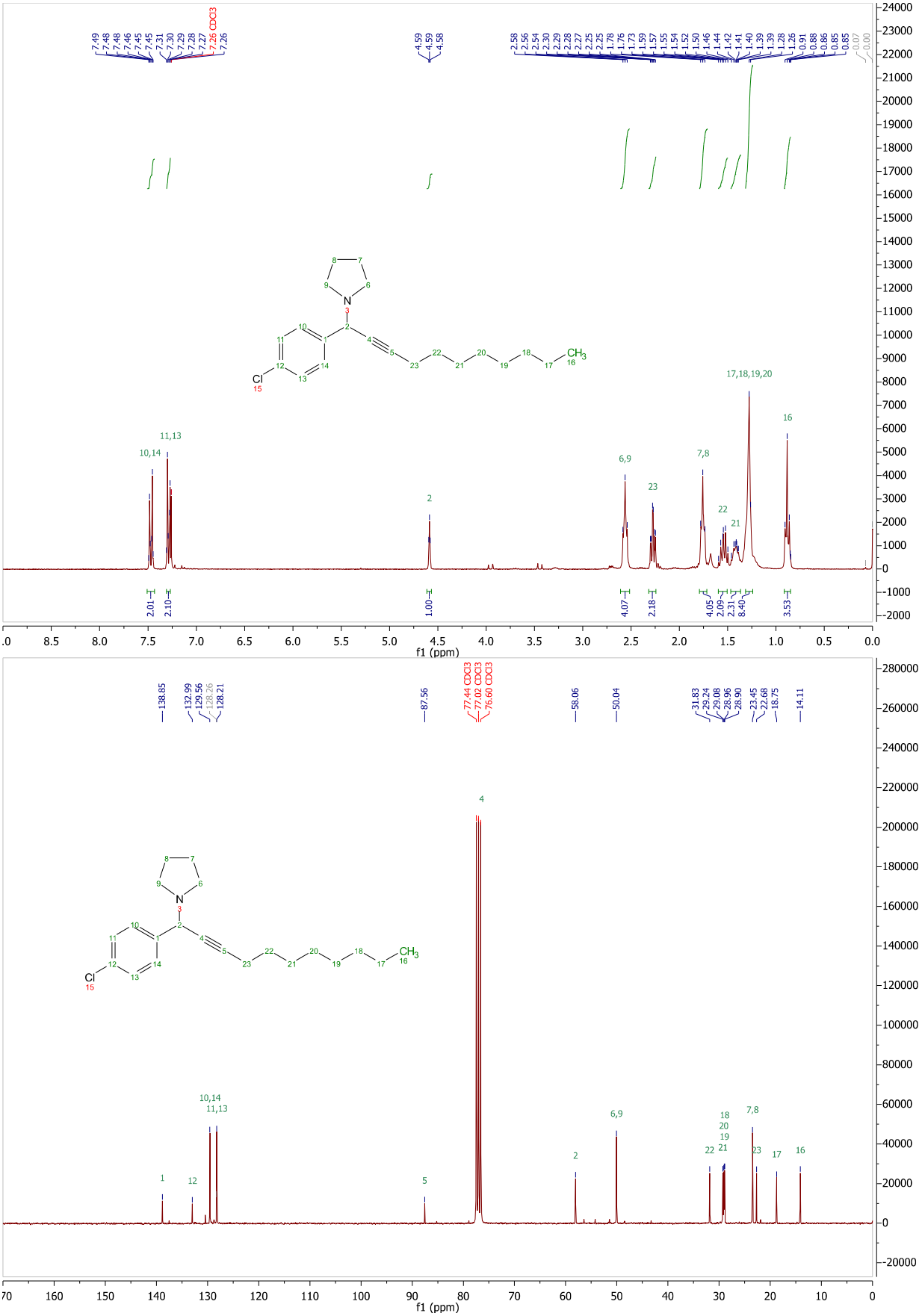

Figure S 10. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11j** in $CDCl_3$.

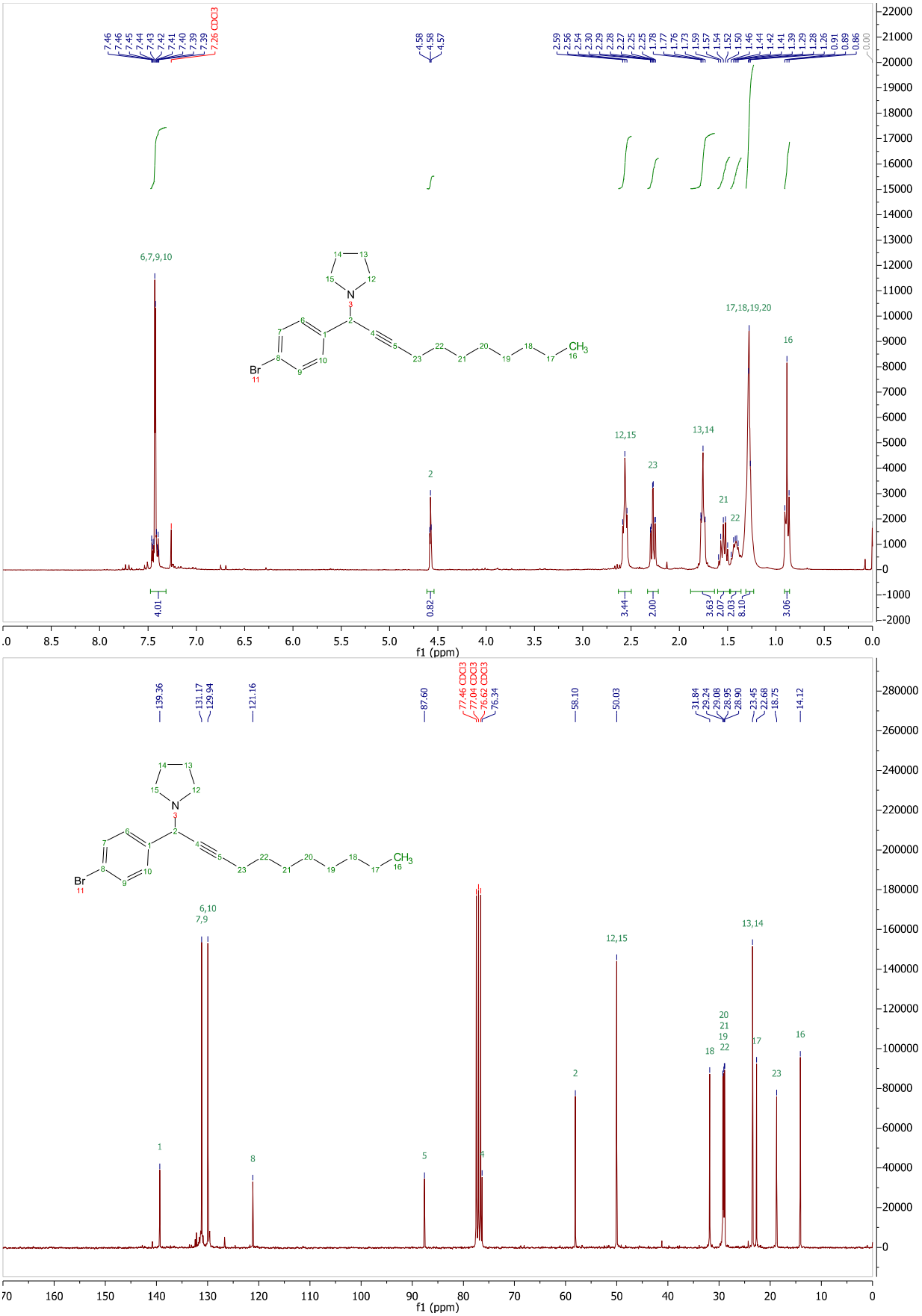

Figure S 11. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11k** in $CDCl_3$.

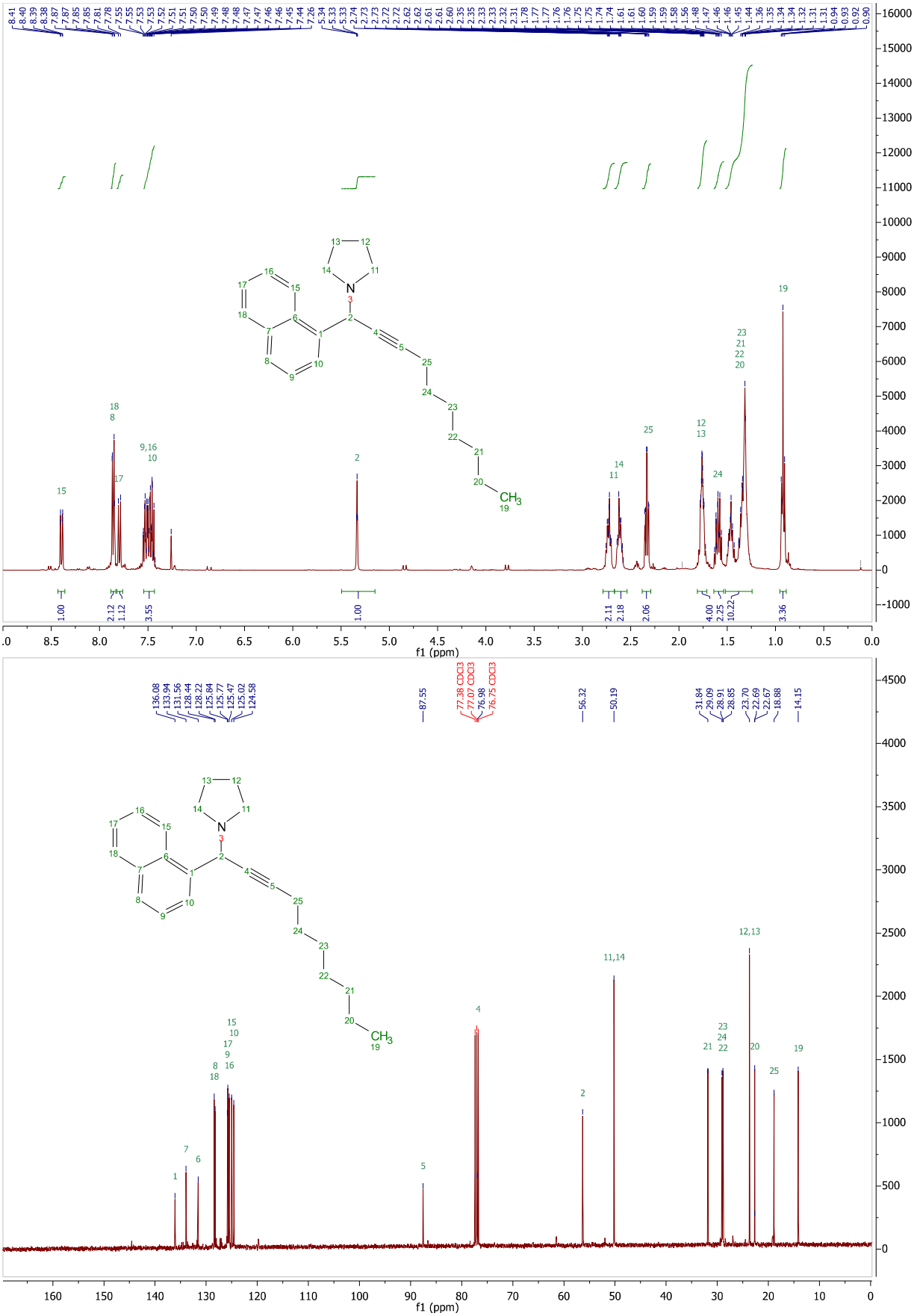

Figure S 12. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11l** in $CDCl_3$.

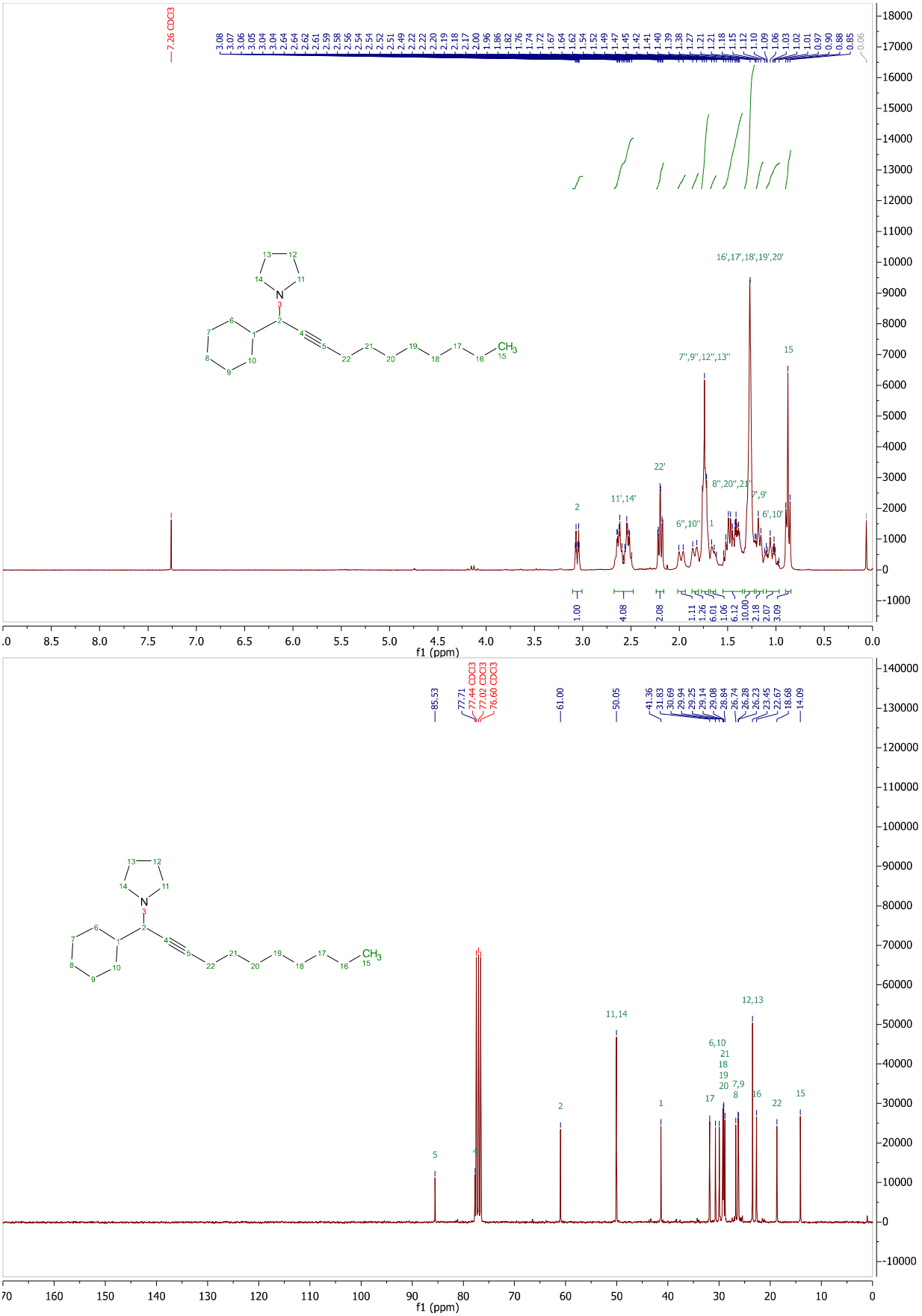

Figure S 13. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11m** in $CDCl_3$.

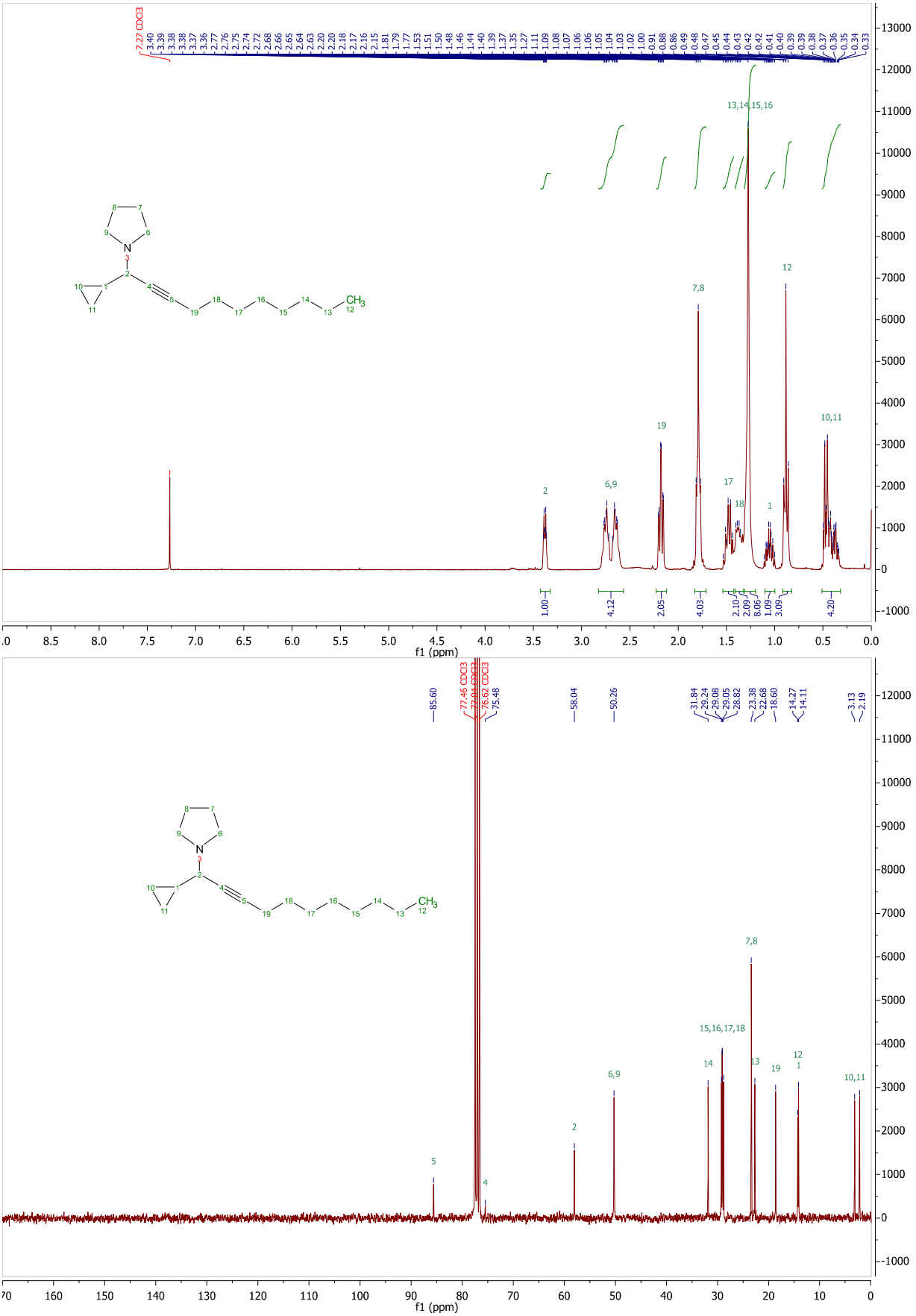

Figure S 14. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11n** in $CDCl_3$.

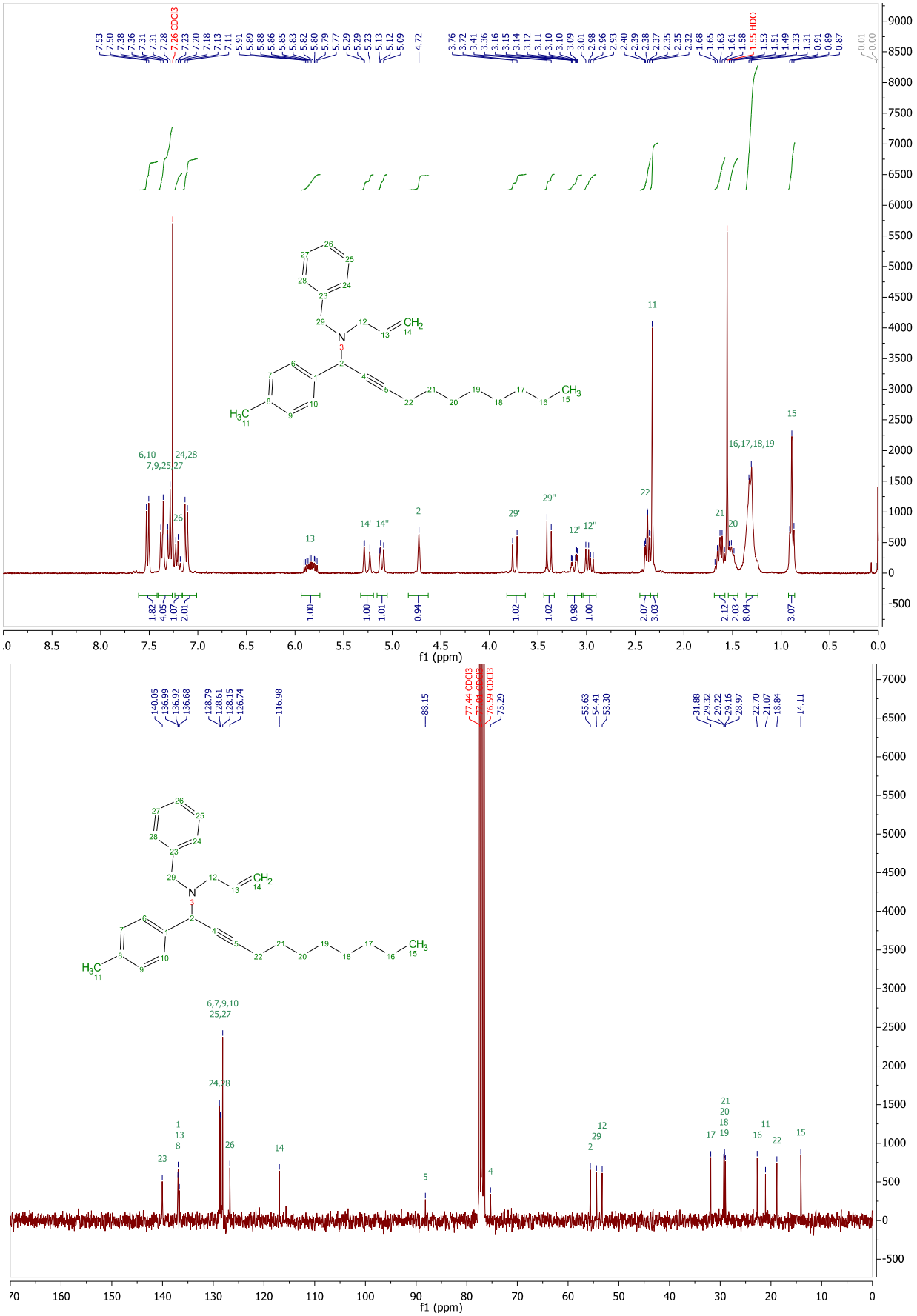

Figure S 15. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11o** in $CDCl_3$.

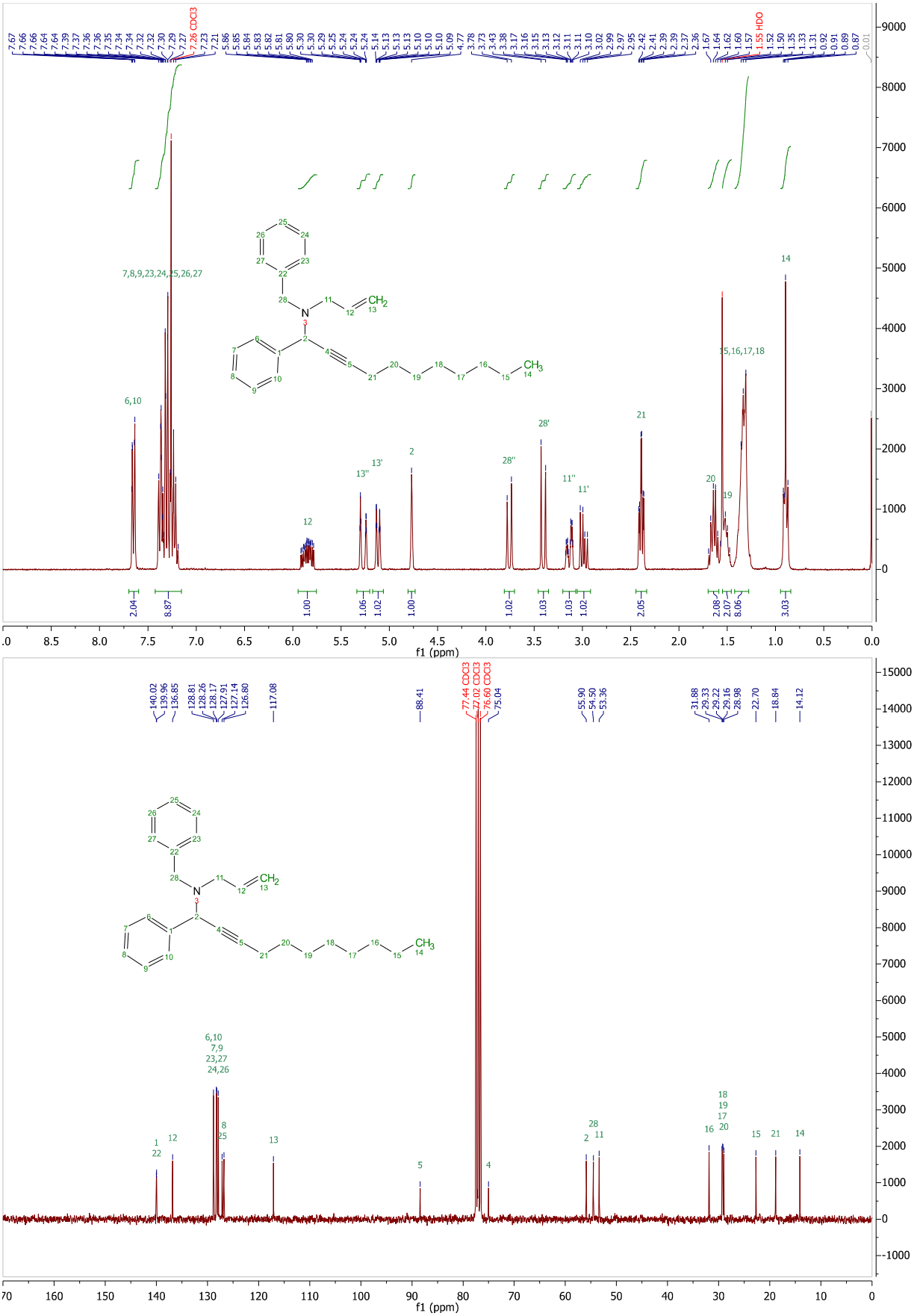

Figure S 16. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11p** in $CDCl_3$.

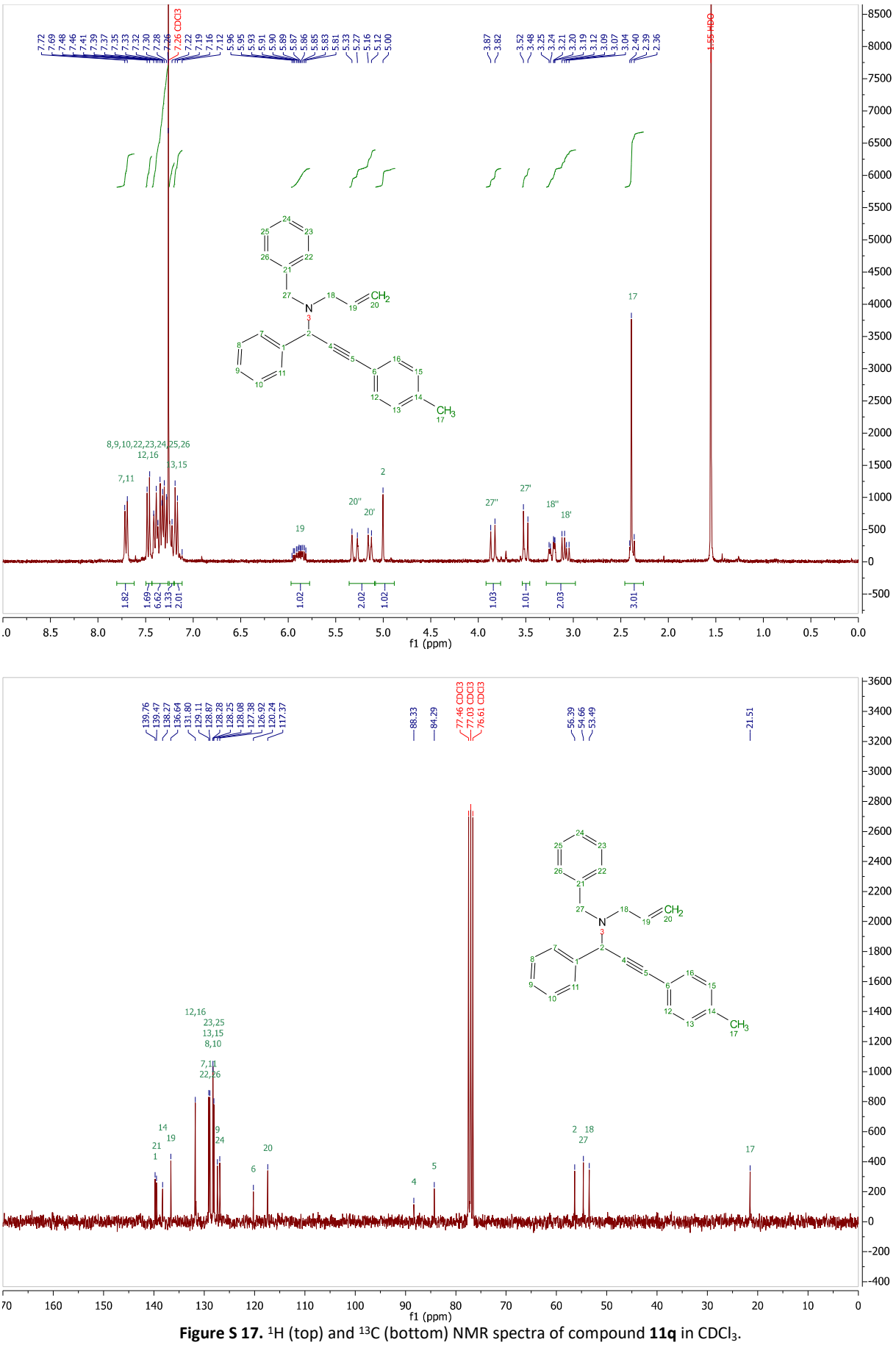

Figure S 17. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11q** in $CDCl_3$.

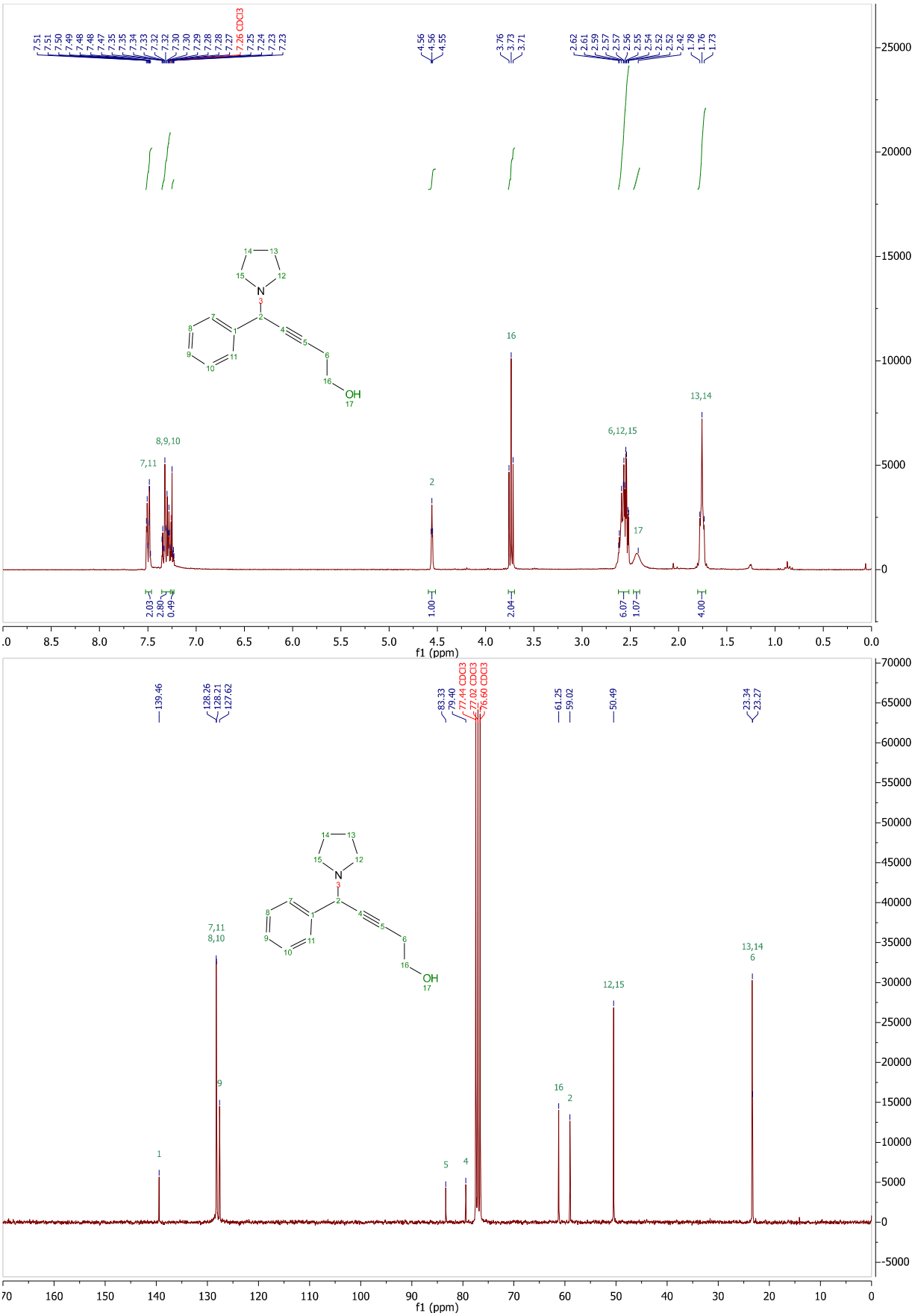

Figure S 18. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11r** in $CDCl_3$.

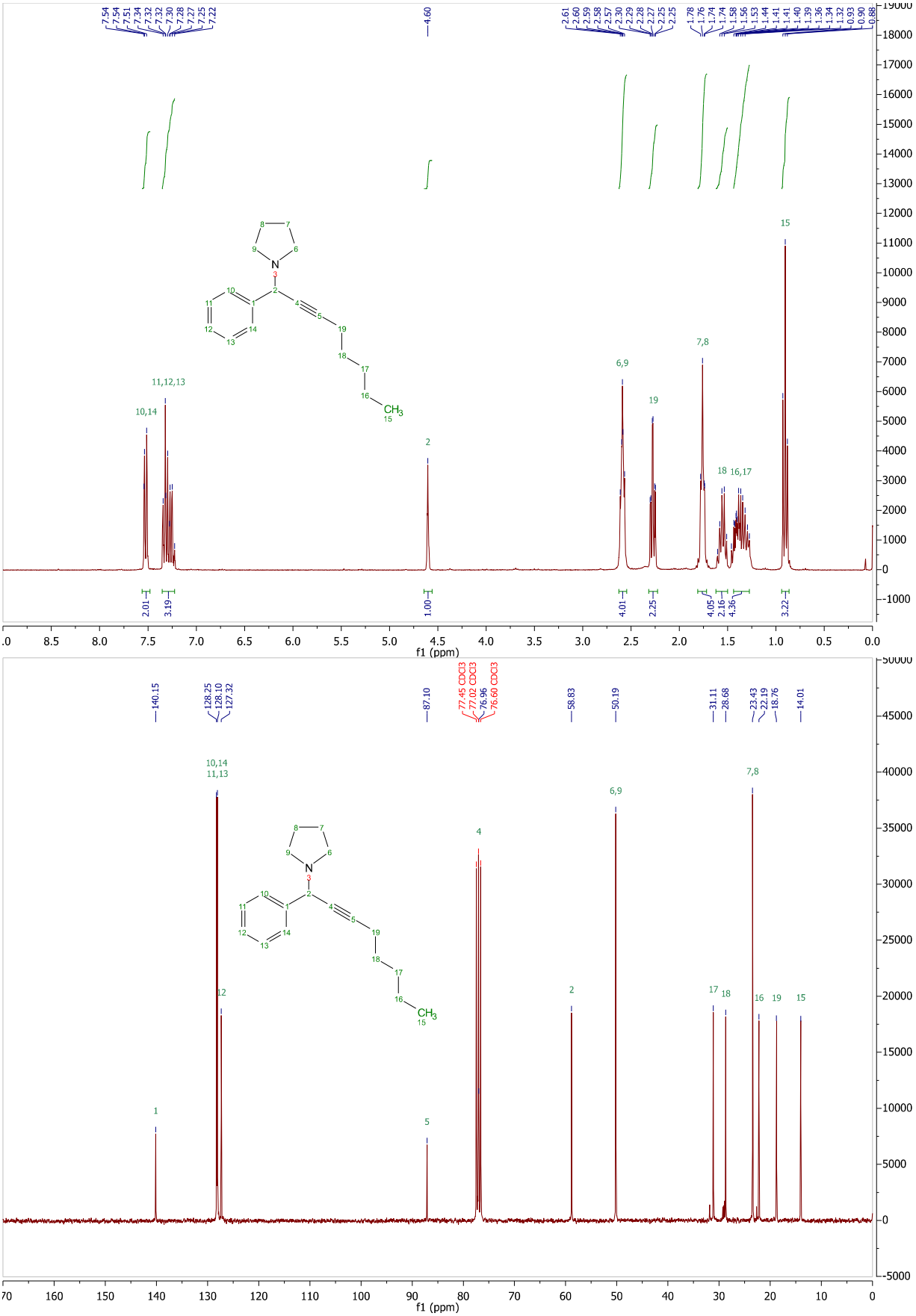

Figure S 19. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11s** in $CDCl_3$.

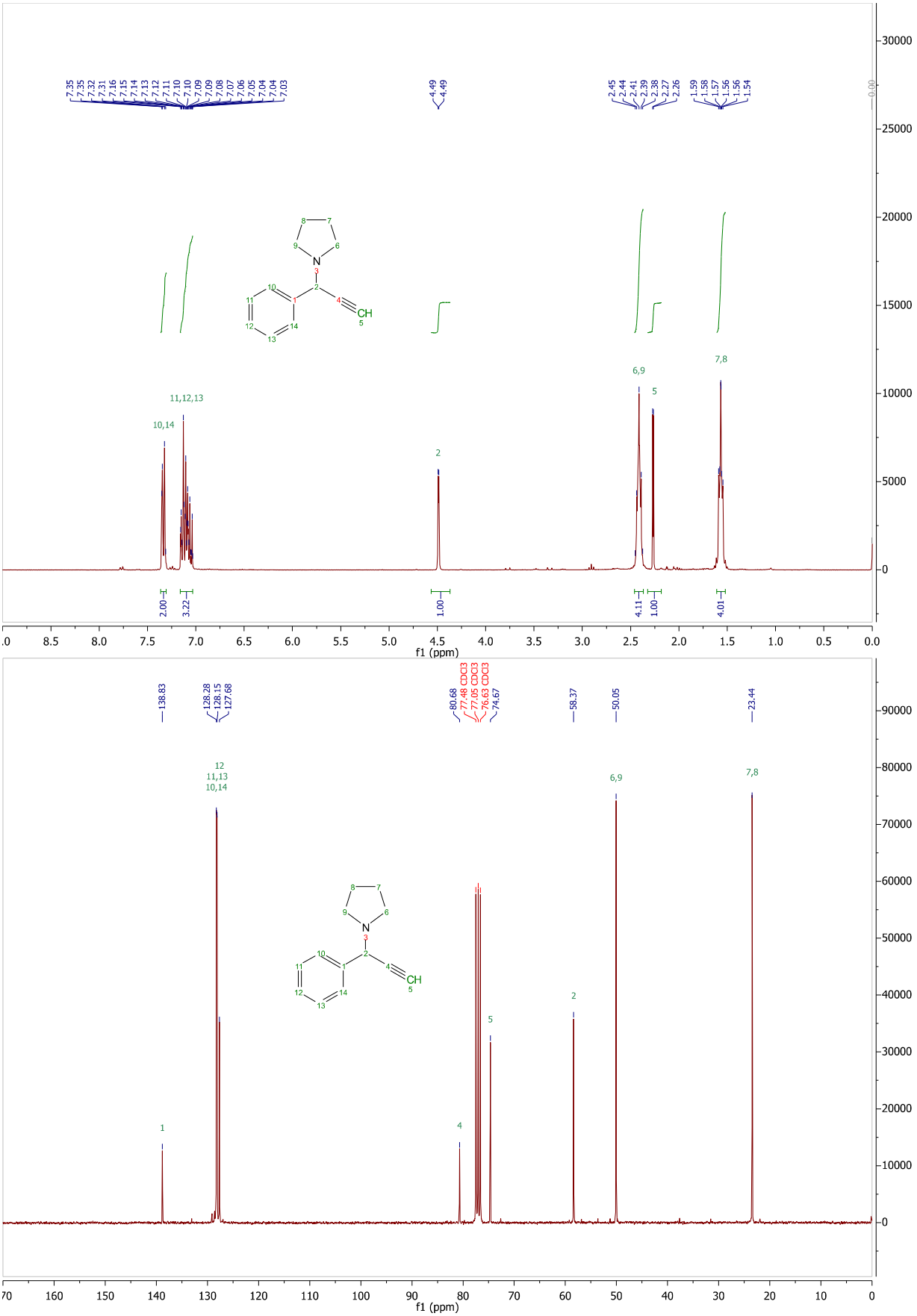

Figure S 20. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11t** in $CDCl_3$.

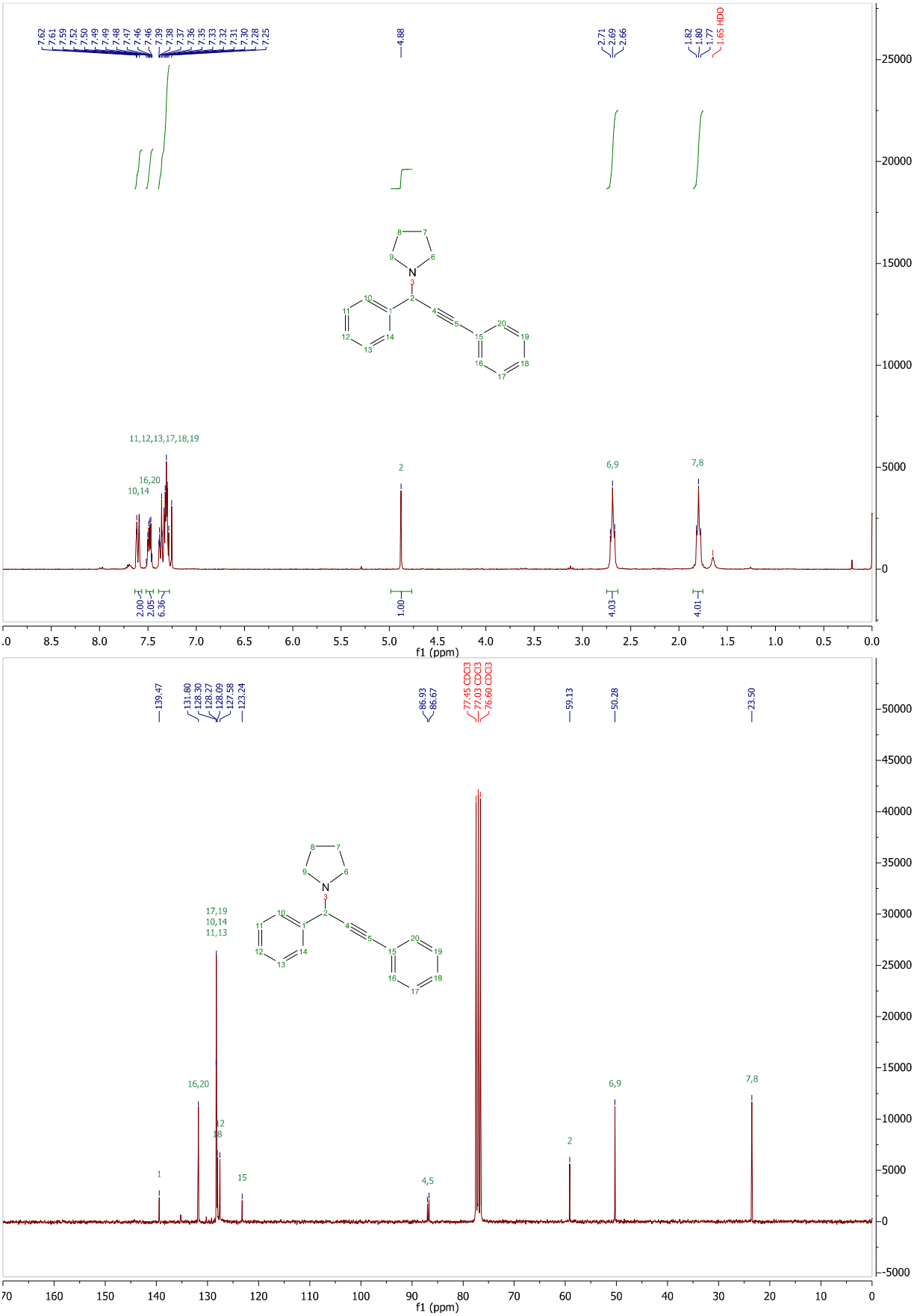

Figure S 21. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **11u** in $CDCl_3$.

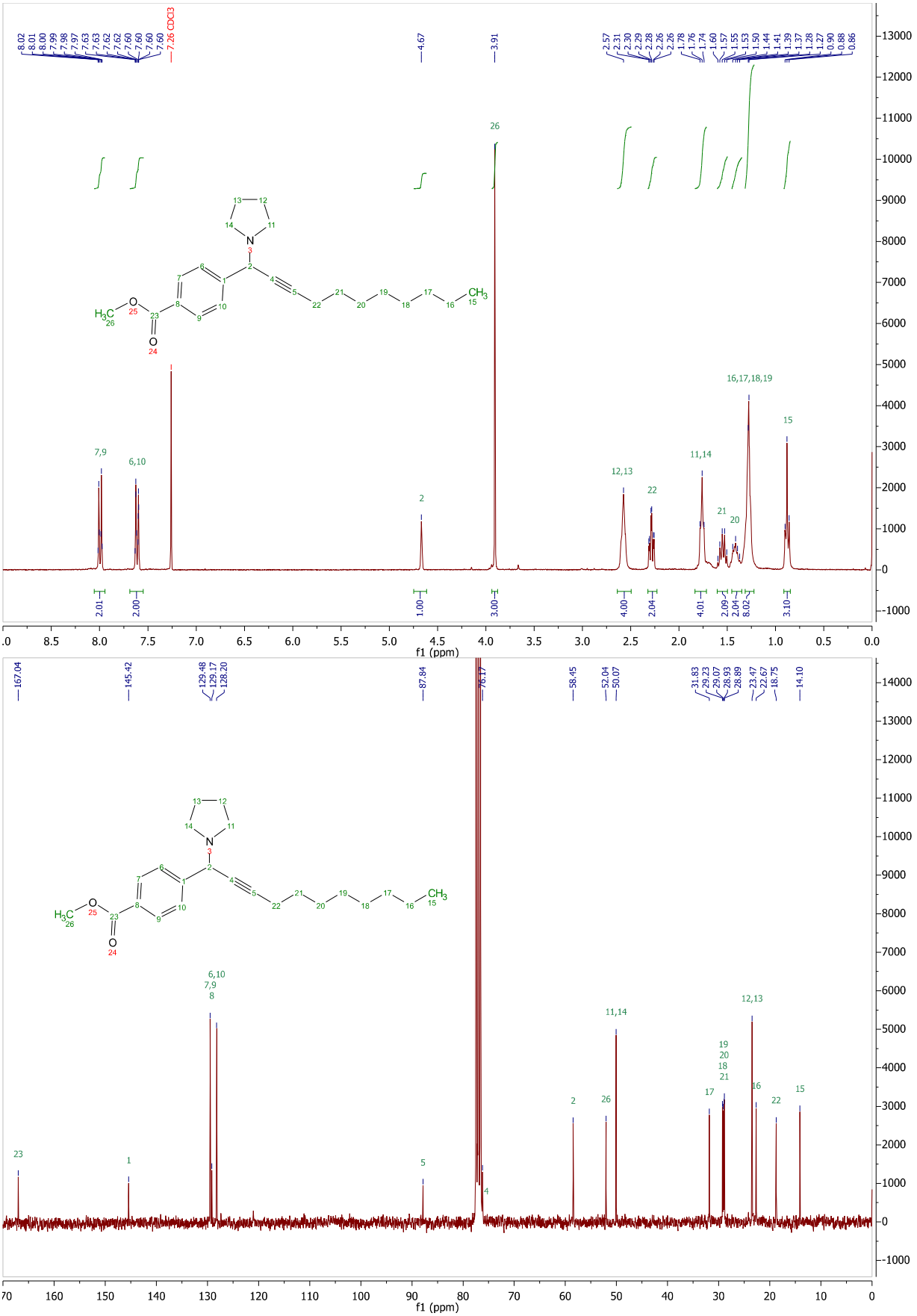

Figure S 22. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **18a** in $CDCl_3$.

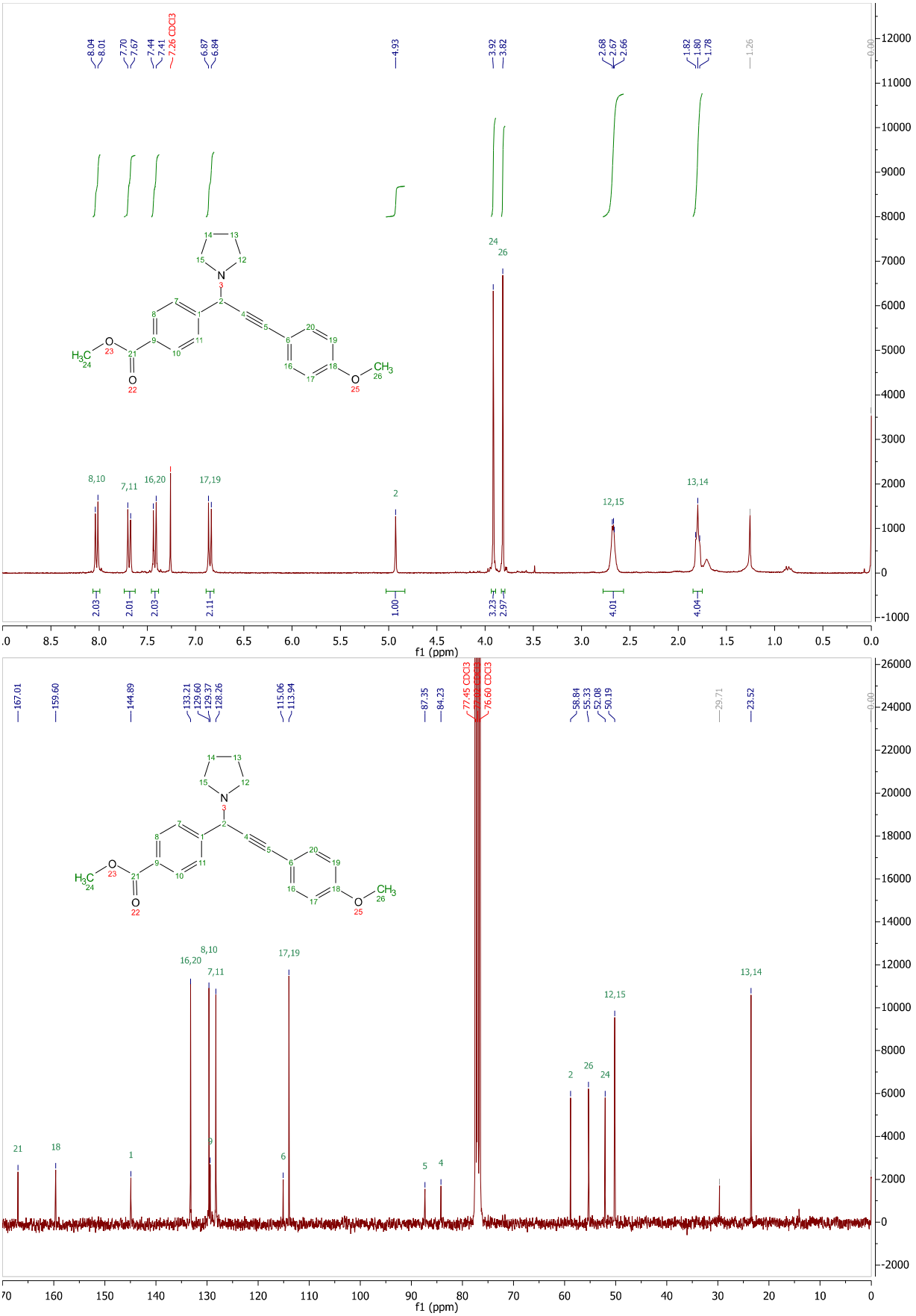

Figure S 23. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **18b** in $CDCl_3$.

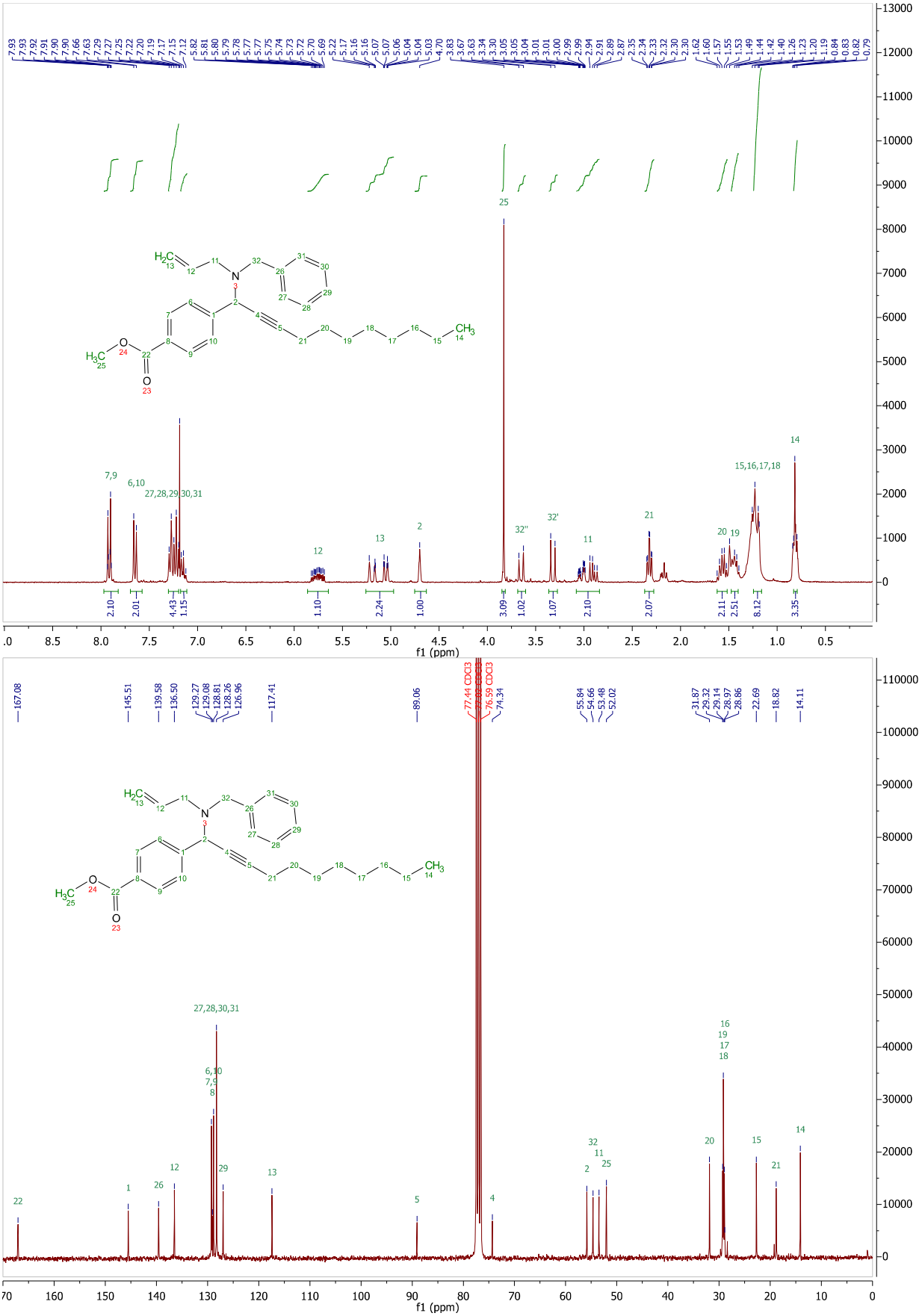

Figure S 24. . ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **18c** in $CDCl_3$.

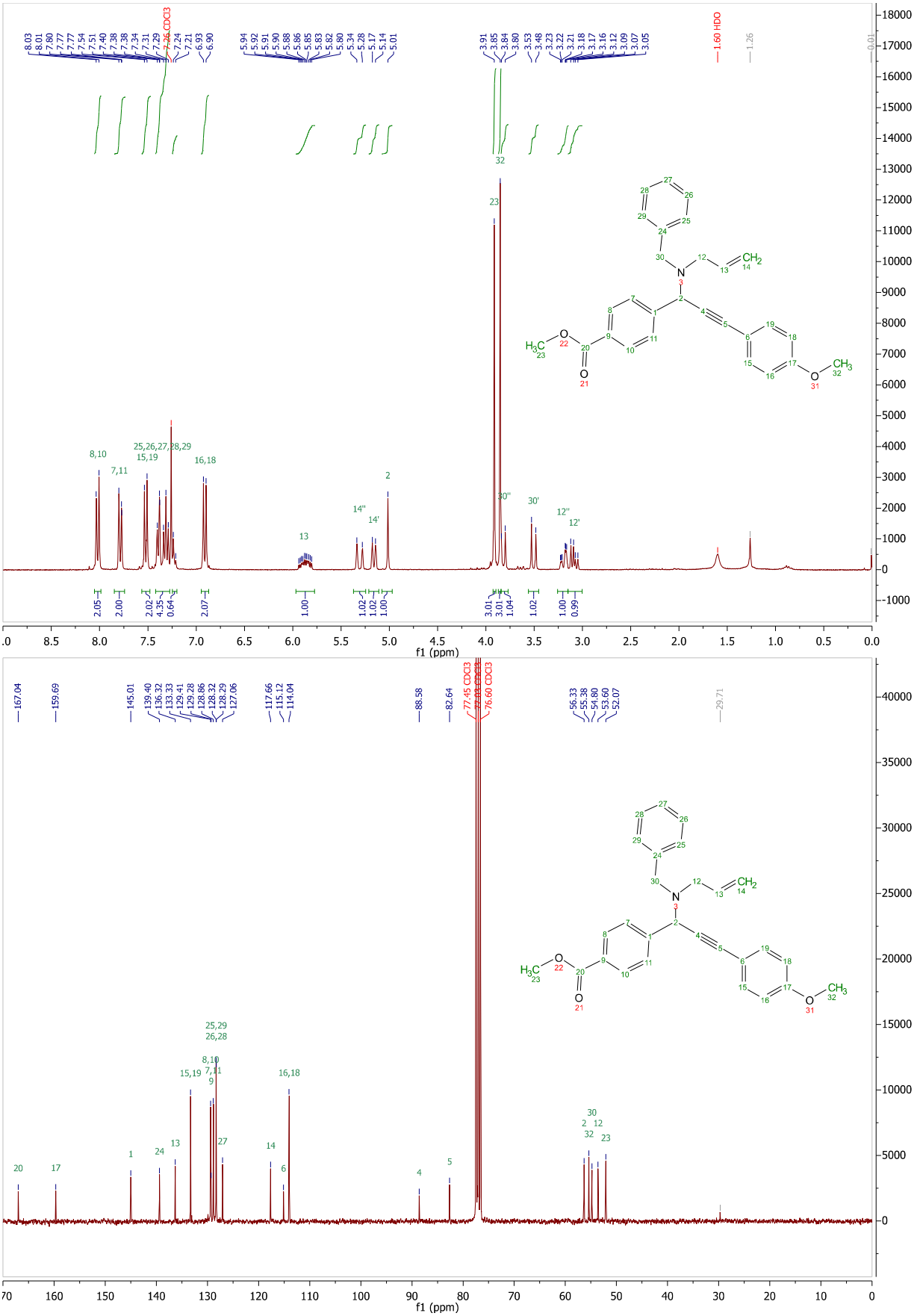

Figure S 25. ^{1}H (top) and ^{13}C (bottom) NMR spectra of compound **18d** in $CDCl_3$.

4. Cell Viability values of the propargylamines on 4T1, PANC-1 and MC3T3-E1

COMPOUND	CELL VIABILITY (%)		
	4T1	PANC-1	MC3T3-E1
CONTROL	100.0±4.009	100.0±6.628	100.0±2.233
11a	7.068±2.153	-12.75±6.412	5.092±2.678
11b	-3.287±1.219	8.375±2.565	74.72±2.446
11f	17.47±1.142	32.61±2.199	73.74±7.715
11g	11.65±1.014	12.72±1.206	-24.39±0,3565
11h	-0.485±0.08713	39,69±2.715	-21.83±0.3262
11i	19.87±2.233	45.52±3.113	82.66±10.41
11j	22.24±1.686	35.23±3.656	94.91±4.355
11k	42.73±3.943	18.47±1.488	6.660±3.536
11m	24.53±2.631	11.33±2.873	0.04826±3.049
11n	15.88±1.047	-0.6206±0.3199	63.43±8.206
11o	124.5±1.533	91.29±0.2186	96.18±3.395
11p	93.81±6.072	88.20±6.767	22.30±2.054
11q	72.57±2.946	44.50±4.440	38.80±10.15
11r	104.1±7.002	72.44±8.389	54.21±2.998
11s	30.02±5.775	30.53±3.000	40.52±10.87
11t	99.31±7.339	61.73±2.109	58.21±15.79
11u	74.58±1.947	92.06±7.261	51.94±24.13
17a	95.20±3.614	80.28±16.45	33.83±1.641
18a	30.73±0.6178	7.011±4.448	73.78±2.225
18b	27.43±3.066	64.61±4.541	22.22±6.298

5. Viability essays of 11b and 18a on MDA MB 231, PANC-1 and MC3T3-E1

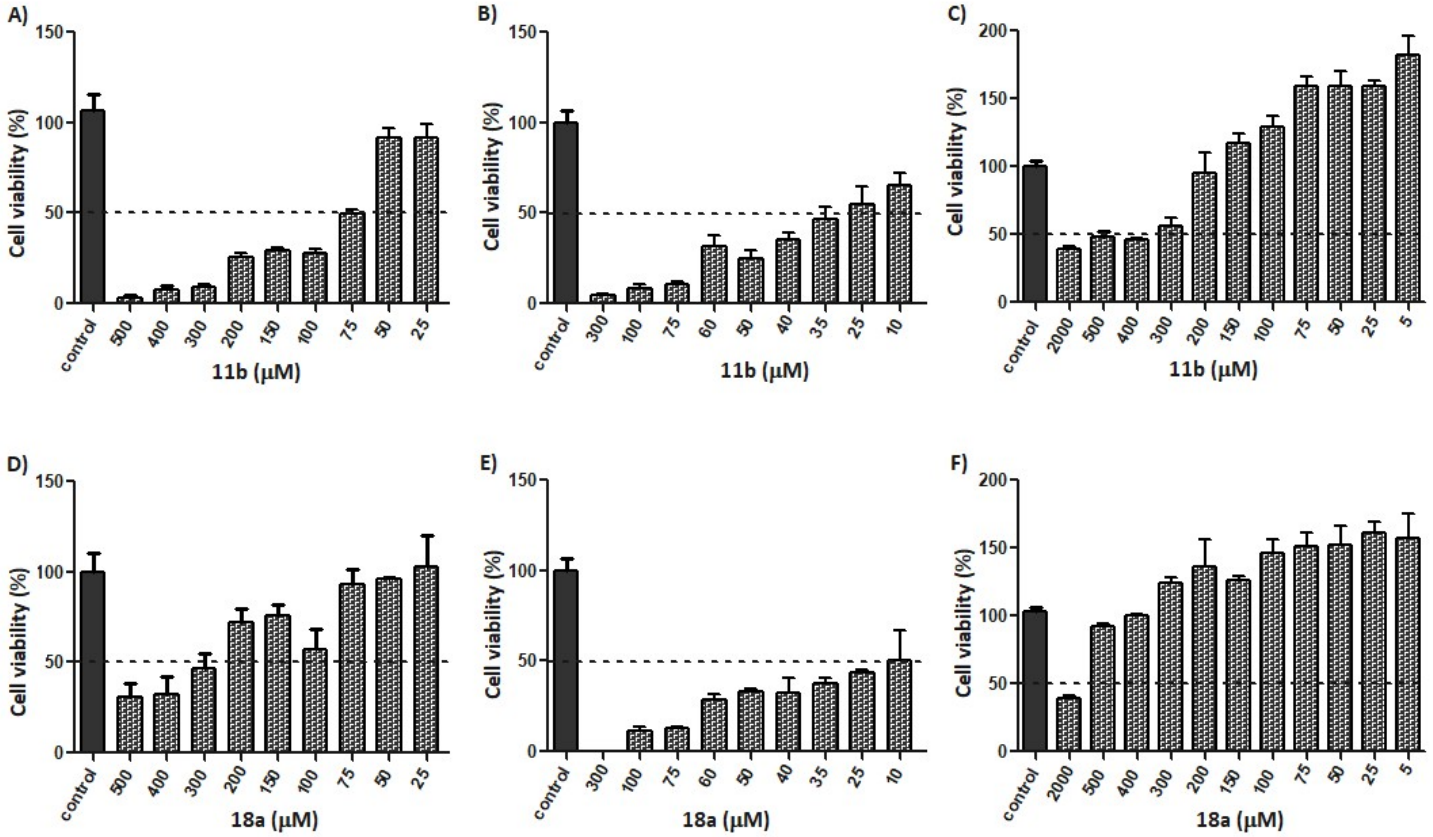

Figure S 26. Effect of **11b** on MDA MB 231 (500-25 µM) (A), PANC-1 (300-10 µM) (B) and MC3T3-E1 (C) on cells viability. Cells were incubated for 36 h in complete medium with **11b**. Viable cell number was evaluated with WST-1. Effect of **18a** on MDA MB 231 (500-25 µM) (D), PANC-1 (300-10 µM) (E) and MC3T3-E1 (F) on cells viability. Cells were incubated for 36 h in complete medium with **18a**. Viable cell number was evaluated with WST-1. Results are shown as percentage of cell viability relative to control (100%) and are expressed as mean ± SEM. Experiments were performed in triplicate.