Efficient NQO1 Substrates are Potent and Selective Anticancer Agents

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Supplemental Information

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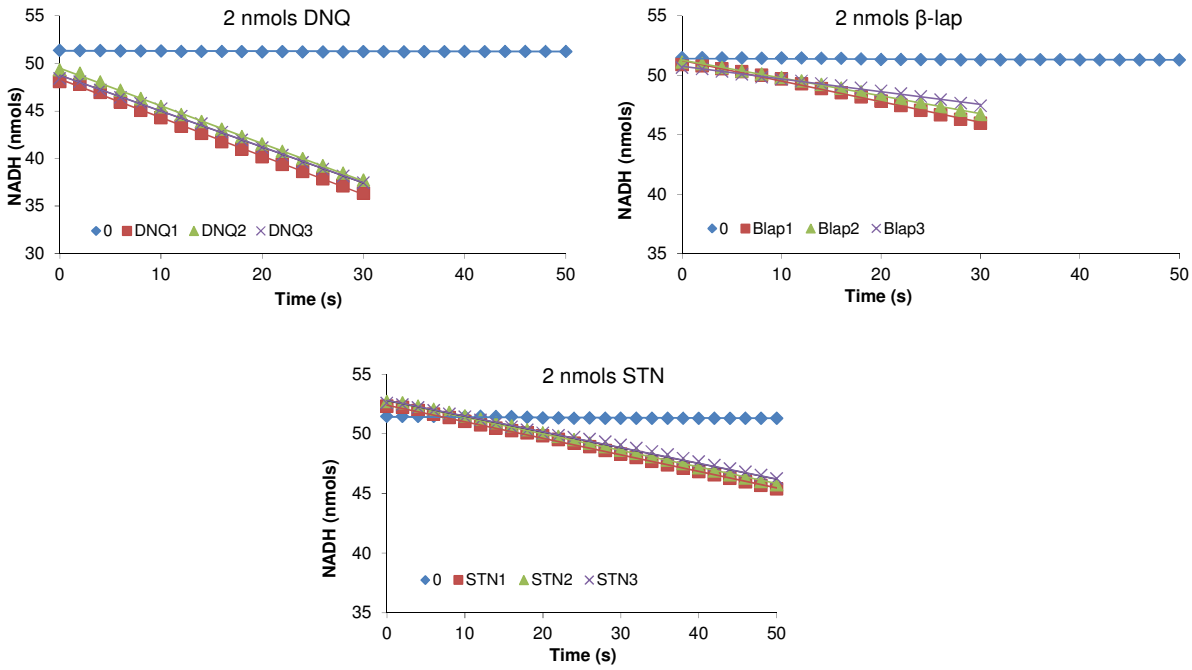
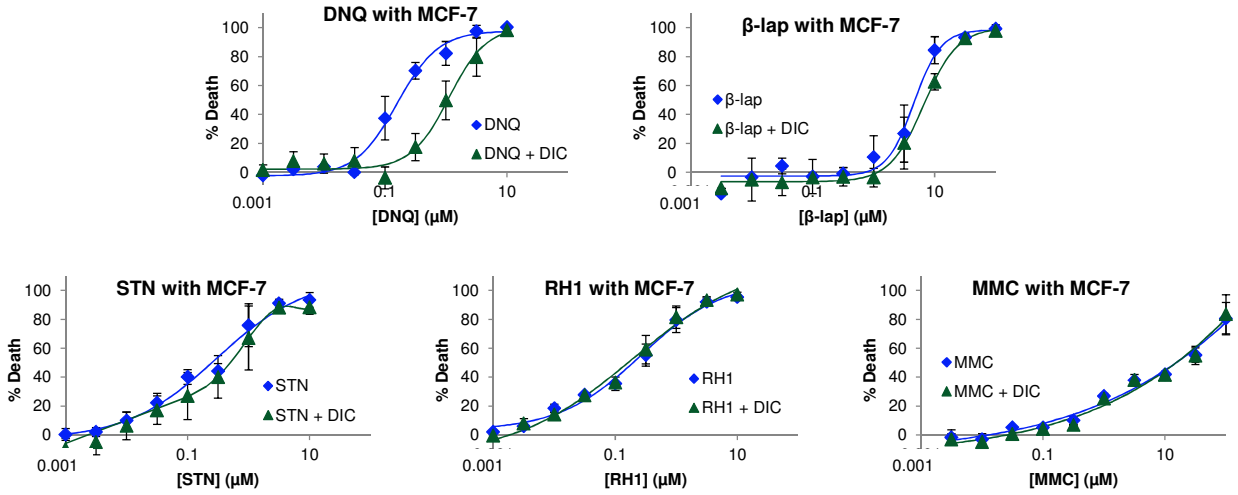
Supplemental Figure 1. Redox cycling of DNQ, β-lap, and STN. This experiment is performed as described in the in vitro NQO1 assay. 10 µM compound was incubated with NADH (400 µM) and recombinant NQO1 (1.4 µg/mL) in a 96 well plate (total volume = 200 µL). Upon incubation with purified human NQO1 and NADH, each compound utilizes >1 equivalent of NADH (assessed by the absorbance of NADH at A_{340nm}). Shown is representative data in which 2 nmols of DNQ, β-lap, or STN results in the reduction of ~10 nmols of NADH (control = blue, 3 replicates of each compound at 10 µM each = red, green, and purple).

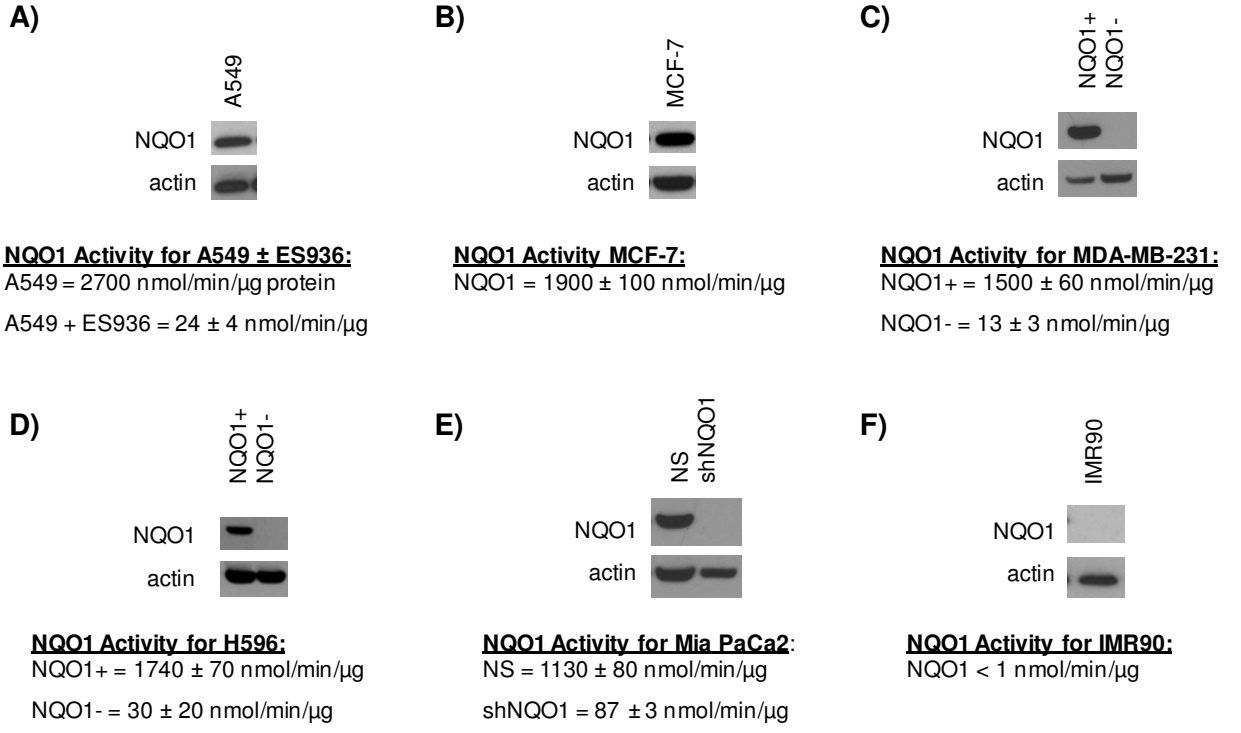


Supplemental Figure 2. MCF-7 sensitivity to quinones and protection by the NQO1 inhibitor dicoumarol (DIC). Cells were plated at 5000 cells/well in 96 well plates and allowed to attach overnight. They were then treated with quinone ± 25 µM DIC for 2 h. The media was replaced and the cells were allowed to recover for 72 h. Cell death was assessed by the sulforhodamine B assay SRB. DIC = dicoumarol, DNQ = deoxynyboquinone, β-lap = β-lapachone, STN = streptonigrin, MMC = mitomycin C.



Compound	IC_{50} (µM)	IC_{50} with 25 µM DIC (µM)	Fold Protection
DNQ	0.13	1.8	14
β-lap	3.7	7.9	2.1
STN	0.31	0.5	1.6
RH1	0.21	0.18	0.86
MMC	14.3	14.6	1.0

Supplemental Figure 3. NQO1 expression and activity in cell lines utilized in the paper. A) the non-small cell lung cancer cell line A549 and A549 cells which were pre-treated for 2h with 100 nM ES936. B) the breast cancer cell line MCF-7 cells, C) the breast cancer cell line MDA-MB-231 transfected with empty vector (NQO1-) or with the gene for NQO1 (NQO1+), D) the non-small cell lung cancer cell line H596 transfected with empty vector (NQO1-) or with the gene for NQO1 (NQO1+), E) the pancreatic cancer cell line Mia PaCa-2 with scrambled control (NS) or with shRNA for NQO1 (shNQO1) , and F) the normal lung fibroblast cell line (IMR90).



NQO1 Activity for A549 ± ES936:
A549 = 2700 nmol/min/µg protein
A549 + ES936 = 24 ± 4 nmol/min/µg

NQO1 Activity MCF-7:
NQO1 = 1900 ± 100 nmol/min/µg

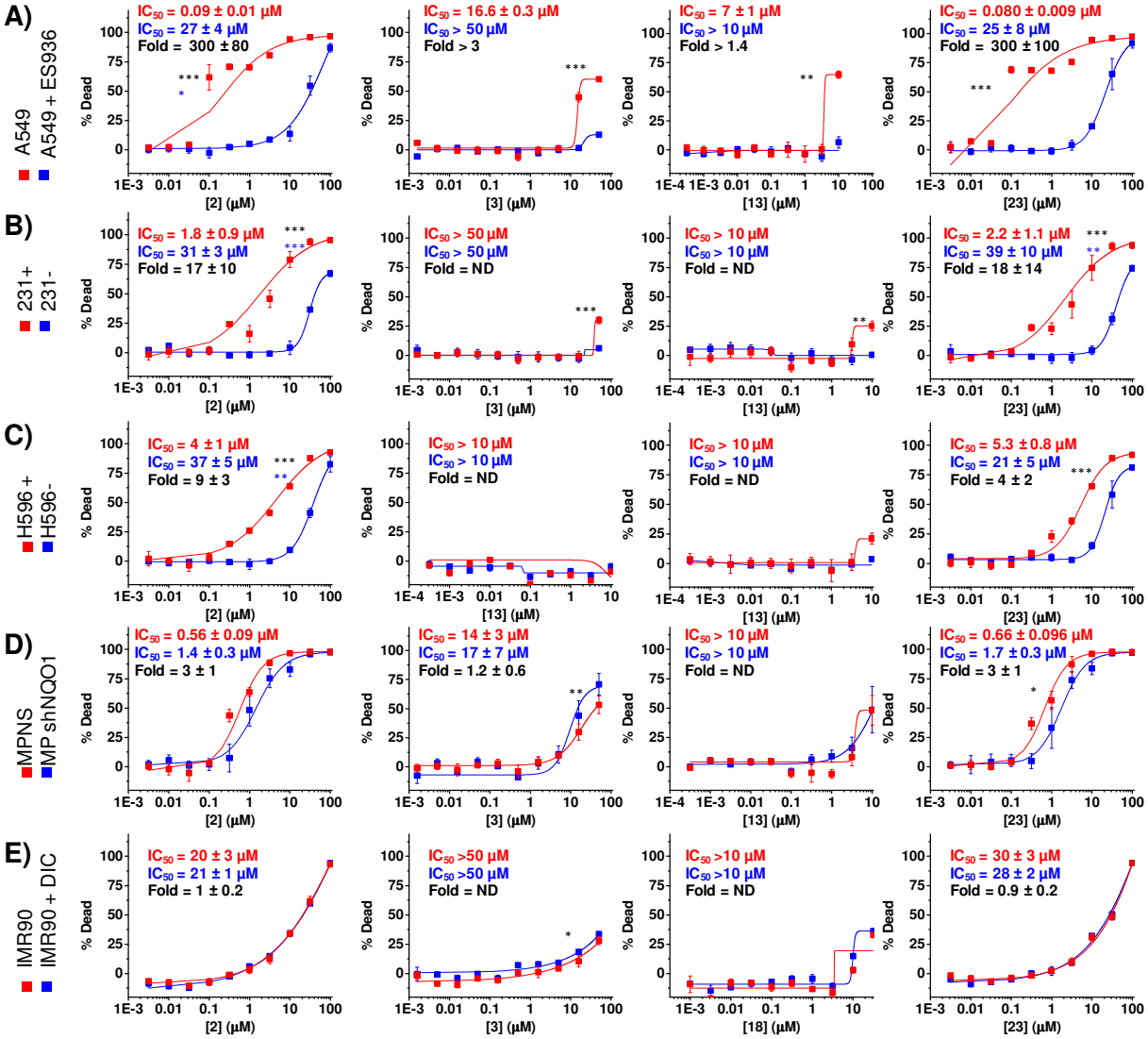
NQO1 Activity for MDA-MB-231:
NQO1+ = 1500 ± 60 nmol/min/µg
NQO1- = 13 ± 3 nmol/min/µg

NQO1 Activity for H596:
NQO1+ = 1740 ± 70 nmol/min/µg
NQO1- = 30 ± 20 nmol/min/µg

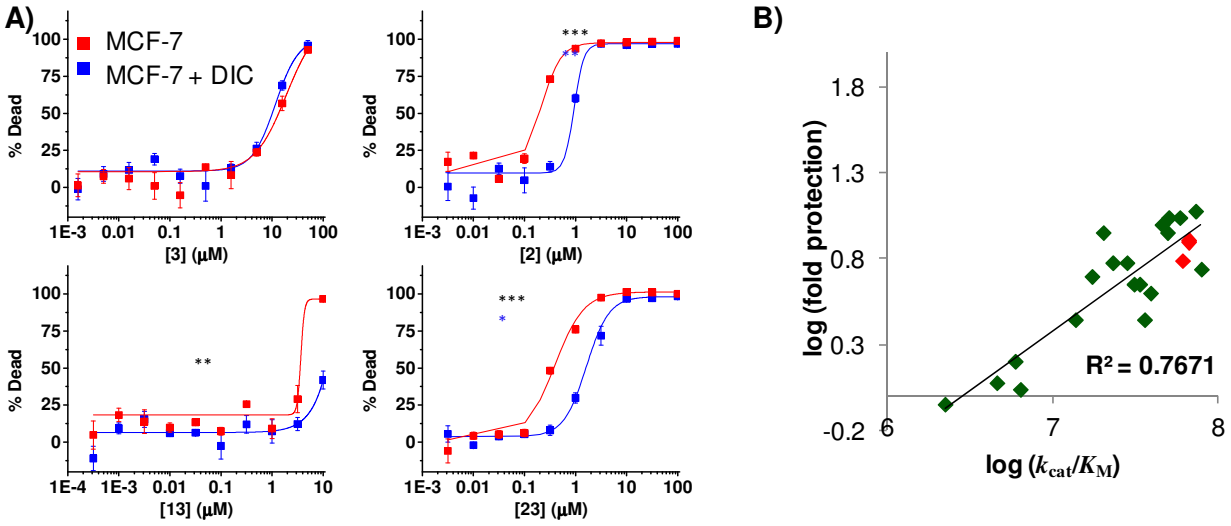
NQO1 Activity for Mia PaCa2:
NS = 1130 ± 80 nmol/min/µg
shNQO1 = 87 ± 3 nmol/min/µg

NQO1 Activity for IMR90:
NQO1 < 1 nmol/min/µg

Supplemental Figure 4. A) Cell death curves of 2, 3, 13, or 23 against A) A549 cells treated for 2h in the presence or absence of the NQO1 inhibitor ES936 (100 nM), B) MDA-MB-231 cells that express (NQO1+) or do not express (NQO1-) NQO1, C) H596 cells that express (NQO1+) or do not express (NQO1-) NQO1, D) MIA PaCa-2 cells that have stably express nonsense (NS) or NQO1 (shNQO1) shRNA, and E) the lung fibroblast cell line IMR-90 treated with or without the NQO1 inhibitor dicoumarol (25 µM).



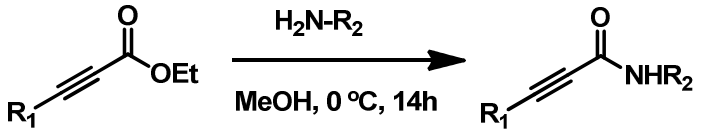
Supplemental Figure 5. MCF-7 sensitivity to quinones and protection by the NQO1 inhibitor dicoumarol (DIC). Cells were plated at 5000 cells/well in 96 well plates and allowed to attach overnight. They were then treated with quinone ± 25 µM DIC for 2 h. The media was replaced and the cells were allowed to recover for 72 h. Cell death was assessed by the sulforhodamine B assay SRB. DIC = dicoumarol. A) Cell death curves for DNQ derivatives 2, 3, 13, and 23. B) Correlation between catalytic efficiency of a quionones and the fold protection provided by DIC when treating MCF-7 cells. Red points are DNQ and IB-DNQ.



Materials and Methods

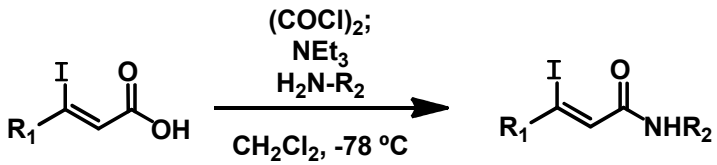
General chemical reagents were purchased from Sigma Aldrich. Metal catalysts and ligands were purchased from Strem Chemicals Inc. (Newburyport, MA). Alkynes were purchased from GFS Chemicals (Powell, OH) and bis-pinacolboronate was purchased from Frontier Scientific (Logan, UT). All reagents were used without further purification unless otherwise noted. Solvents were dried by passage through columns packed with activated alumina (THF, CH_2Cl_2, diethyl ether) or activated molecular sieves (DMSO). Amines were freshly distilled over CaH_2 under a nitrogen atmosphere. Reactions involving n-BuLi were performed using standard Schlenk techniques under argon

^{1}H-NMR and ^{13}C-NMR spectra were recorded on Varian Unity spectrometers at 500 MHz and 125 MHz, respectively. Spectra generated from a solution of $CDCl_3$ were referenced to residual chloroform (^{1}H: δ 7.26 ppm, ^{13}C: δ 77.16 ppm). Spectra generated in mixtures of $CDCl_3$ and CD_3OD were referenced to CD_3OD (^{1}H: δ 3.31 ppm, ^{13}C: δ 49.0 ppm). Spectra generated from d-TFA were referenced to residual H (^{1}H: δ 11.50 ppm) or F_3CCO_2D (^{13}C: δ 164.2 ppm).



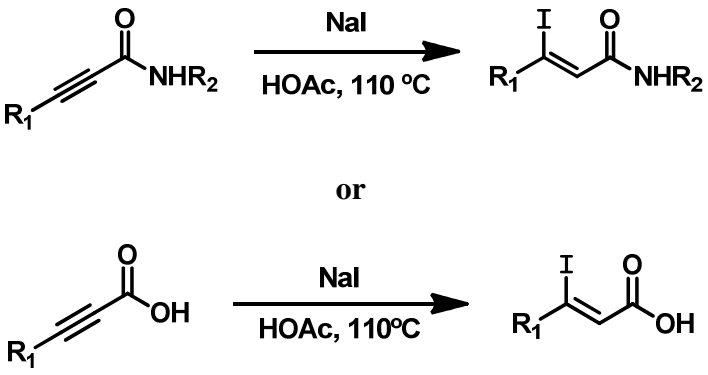
General protocol A: Amidation of ester

To a solution of alkynyl ester (1 equiv.) in methanol (1 M), chilled in an ice-water bath was added alkyl amine (1.2 equiv.). The reaction was stirred at 0 ºC for 14h. The solvent was evaporated directly from the flask and the residue was separated by silica gel chromatography (9:1 hexanes:ethyl acetate to 1:1 hexanes:ethylacetate) to yield the desired alkynyl amide as a mixture of rotamers.



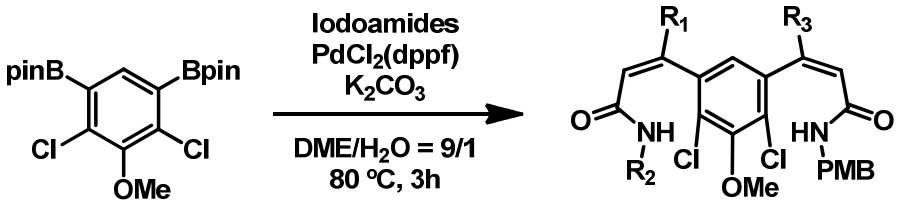
General protocol B: Amidation of acid chloride

To an oven-dried Schlenk flask with a stirbar was added the iodoacid and the flask was evacuated and backfilled with argon. Dry CH_2Cl_2 (0.4 M iodoacid) was added and the solution was chilled on an ice-water bath. Oxalyl chloride (3 equiv.) was added by syringe and the cold bath was removed. After 5h at room temperature the volatile components were evaporated directly from the flask. Dry CH_2Cl_2 (0.5 M) was added to the residual oil and the vial was chilled on a dry ice/isopropanol bath. Freshly distilled p-methoxybenzyl amine (1.1 equiv.) was added dropwise by syringe followed by NEt_3 (1.2 equiv.). The mixture was stirred for 10 minutes then was allowed to warm to RT. 1 M HCl (1.5 mL per mmol) was added and the solution was poured into a separatory funnel with CH_2Cl_2 (1.5 mL per mmol), shaken and separated. The aqueous fraction was extracted with CH_2Cl_2 (0.8 mL per mmol, 3 times) then dried over $MgSO_4$ and evaporated. The residue was purified by silica gel chromatography.



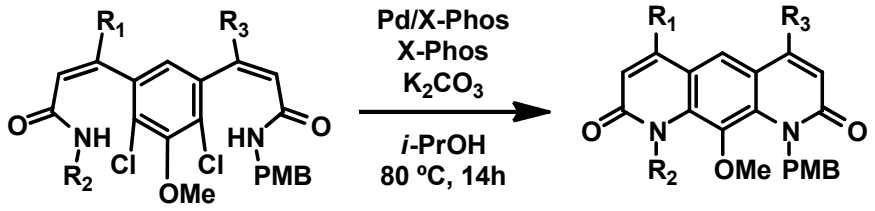
General protocol C: Hydroiodination

Alkynyl amide (1 equiv.), NaI (2 equiv.), and acetic acid (10 equiv.) were combined and heated to 110 ºC for 8h. Reaction completion was determined by removing aliquots for ^{1}H-NMR analysis. The deep red reaction mixture was diluted with water (1-2 mL per mmol alkyne) and CH_2Cl_2 (3-4 mL per mmol alkyne), treated with $NaHSO_3$ until colorless, and carefully neutralized with a saturated aqueous solution of $NaHCO_3$. This mixture was poured into a separatory funnel with CH_2Cl_2, shaken and separated. The aqueous fraction was extracted with CH_2Cl_2 (4-5 mL per mmol alkyne, 2 times). The combined organic fractions were washed with brine, dried over $MgSO_4$, and evaporated to yield the desired iodoamide.



General protocol D: Suzuki cross-coupling

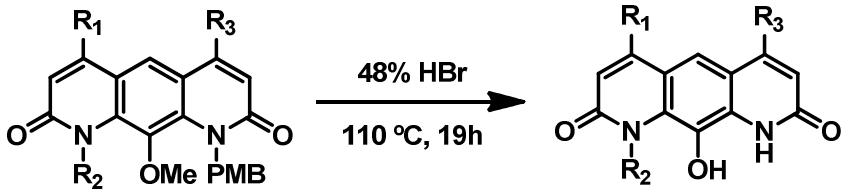
To a Schlenk flask with a stir bar was added pure (recrystallized) 2,6-dichloro-3,5-bis(pinacolboronato)anisole (**70**)[1] (1 equiv.), $PdCl_2$(dppf) (20 mol%), K_2CO_3 (6 equiv.), and both desired iodoamides (1.3 equiv. of amide bearing PMB, 1.5 equiv. of *N*-alkyl amide) and the flask was evacuated and backfilled with argon three times. Water (1 mL per mmol bispinacolboronate) and DME (9 mL per mmol bispinacolboronate) were added by syringe after degassing the solvents by bubbling with argon for 45 minutes. The flask was plunged into an oil bath at 80 ºC for 3h. The mixture was poured into a separatory funnel and diluted with water (12-13 mL per mmol bispinacolboronate). The mixture was extracted with EtOAc (12-13 mL per mmol bispinacolboronate, 2 times). The combined organic extracts were dried over $MgSO_4$, filtered and evaporated to a deep red oil. The crude product was dissolved in CH_2Cl_2 and separated by silica gel chromatography (100:0 to 70:30 to 30:70 to 0:100 hexanes:ethyl acetate). The purity of the diamide product was highly variable and the product was subjected to intramolecular amidation without further purification.



General protocol E: Intramolecular aryl amidation

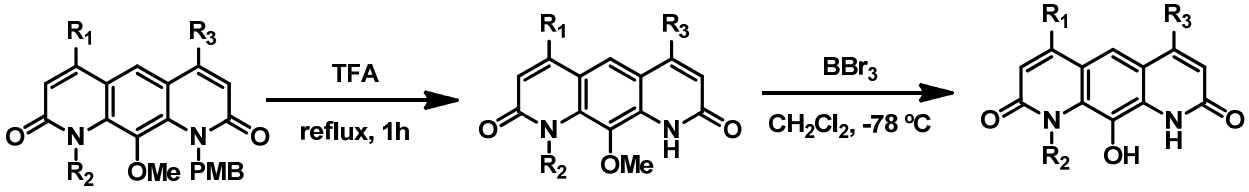
In a Schlenk flask or a vial with a Teflon-lined cap were combined the diamide starting material, K_2CO_3 (6 equiv.), Pd/X-Phos (10 mol%), and X-Phos (10 mol%). The flask was cycled between vacuum and argon three times and argon-sparged *i*-PrOH (20-30 mL per mmol diamide) was added by syringe. The mixture was heated to 80 ºC with stirring for 14h. Insoluble materials

were removed by filtration through Celite and rinsed with CH_2Cl_2. The filtrate was evaporated and the residue was used directly in the next step.



General protocol F: HBr deprotection

The crude diazaanthracene was dissolved in 48% HBr (12-13 mL per mmol diazaanthracene) and heated to 110 ºC. After 19 hours the reaction was removed from heat. The mixture was cooled on an ice bath and was carefully rendered basic by adding 10 M NaOH. The residual solid was removed by filtration through hardened filter paper and discarded. The filtrate was rendered acidic with 1 M HCl, whereupon a colloidal precipitate formed. The mixture was then centrifuged (3220 x g for 5 minutes). The resulting semi-compact gelatinous solid was collected by filtration through hardened filter paper and dried to a constant mass under vacuum to yield the desired diazaanthracenol in frequently high purity as assessed by NMR.



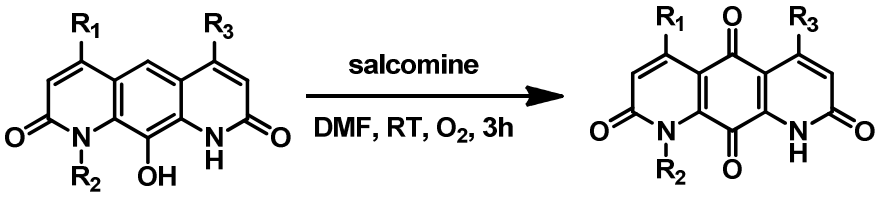
General protocol G: TFA and BBr_3 deprotection

For substrates that proved sensitive to global deprotection by HBr, the following protocol was employed.

The product of intramolecular amidation (General Protocol E) was dissolved in TFA (15-20 mL per mmol) and heated to reflux for 1h. The solvent was then evaporated and the residue was purified by silica gel chromatography (DCM, 0-5% MeOH).

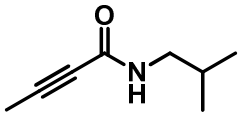
In a Schlenk flask containing the PMB-deprotected material under Ar was added DCM (70 mL per mmol) and the solution was cooled in a dry ice/isopropanol bath. BBr_3 (6 equiv.) was added

by syringe and the solution was stirred until starting material was consumed as shown by TLC. Residual BBr_3 was quenched by the addition of conc. $NaHCO_3$ solution until pH neutral. The solvents were evaporated. The residue was taken directly to oxidation (General Protocol H) without further purification.



General protocol H: Oxidation

To a flask containing the diazaanthracenol starting material was added salcomine (10 mol%) and DMF (~0.02 to 0.04 mL per mg of impure diazaanthracenol). A balloon containing O_2 was fitted over the mouth of the flask and the slurry was stirred at room temperature. The solid dissolved after about 30 minutes. After 3h stirring, the mixture was diluted with one volume each of DCM and hexanes and loaded directly onto a chromatography column consisting of a layer of basic alumina (5 cm) under a layer of silica gel (5 cm) prepared in DCM. The column was flushed with increasing amounts of methanol (0-2%) in DCM until the red product band entered the alumina layer which retained the product, allowing coeluting impurities to be removed. The product was then released from the basic alumina by adding 1% HOAc to the mobile phase. The red fractions were evaporated and purified by chromatography through silica gel (0-5% MeOH in DCM) to yield the desired DNQ derivative as an orange, red, or red-pink solid.



27

Synthesized from ethyl-2-butynoate and isobutylamine by General Protocol A. 50% yield. Compound is a light yellow oil at rt.

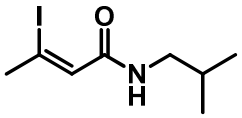
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.78 (bs, 1H, major rotamer, N*H*), 3.21 (t, 2H, *J* = 6.5 Hz, minor rotamer, NCH_2), 3.10 (t, 2H, *J* = 6.5 Hz, major rotamer, NCH_2), 2.01 (s, 3H, minor rotamer, allylic CH_3), 1.93 (s, 3H, major rotamer, allylic CH_3), 1.78 (sept, 1H, *J* = 6.5 Hz, major rotamer, C*H*), 0.94 (d, 6H, *J* = 7.0 Hz, minor rotamer CH(CH_3)$_2$), 0.91 (d, 6H, *J* = 6.5 Hz, major rotamer, CH(CH_3)$_2$)

^{13}C-NMR ($CDCl_3$, 125 MHz) δ 153.68 (major), 83.17 (major), 75.11 (major), 50.90 (minor), 47.15 (major), 29.56 (minor), 28.50 (major), 20.16 (major), 19.96 (minor), 4.13 (minor), 3.80 (major)

HRMS (ESI) calcd for $C_8H_{14}NO$ $(M+H)^+$: 140.1075, found: 140.1070.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in CCl_4): 3450 (w), 3292 (b, m), 3062 (b, w), 2962 (m), 2254 (m), 1654 (s), 1544 (s), 1468 (m) 1275 (m), 1006 (w).



28

Synthesized from **27** by General Protocol C. 95% yield. Compound is a yellow/orange solid.

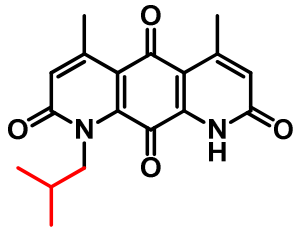
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.25 (q, 1H, *J* = 1.0 Hz, vinyl C*H*), 5.75 (bs, 1H, N*H*), 3.17 (t, 2H, *J* = 6.5 Hz, NCH_2), 2.66 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.85 (sept, 1H, *J* = 6.5 Hz, C*H*), 0.95 (d, 6H, *J* = 6.5 Hz, CH(CH_3)$_2$)

^{13}C-NMR ($CDCl_3$, 125 MHz) δ 165.00, 129.73, 105.42, 46.97, 35.78, 28.50, 20.37.

HRMS (ESI-TOF) calcd for $C_8H_{15}NOI$ $(M+H)^+$: 268.0198, found: 268.0197.

Melting Point: 49.3-51.2 °C

IR (cm^{-1}, thin film in $CHCl_3$): 3450 (m), 3280 (b, m), 3060 (b, w), 2962 (m), 1650 (s), 1620 (m), 1430 (w), 1410 (w), 1370 (w), 1330 (w), 1230 (w), 1160 (m).



2

Synthesized from **70**,[1] (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide,[1] and **28** by General Protocols D, E, F, and H. 9% yield over 4 steps. Compound is an orange/red solid at rt.

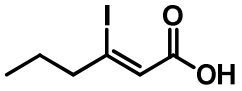
^{1}H-NMR ($CDCl_3$ 500 MHz): δ 6.78 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.67 (d, 1H, *J* = 1.5 Hz, vinyl C*H*), 4.64 (d, 2H), 2.62 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.60 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.88 (sept, 1H, *J* = 7.0 Hz, C*H*), 0.93 (d, 6H, *J* = 6.5 Hz, CH(CH_3)$_2$).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.71, 175.38, 161.47, 160.73, 151.21, 149.01, 138.99, 137.93, 128.64, 128.35, 120.11, 114.49, 50.58, 29.83, 23.49, 22.33, 20.07.

HRMS (ESI-TOF) calcd for $C_{18}H_{19}N_2O_4$ $(M+H)^+$: 327.1345, found: 327.1347.

Melting Point >250 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1676 (m), 1653 (b, s), 1607 (m), 1592 (m), 1467 (w), 1401 (w), 1376 (m), 1350 (w), 1290 (m), 1203 (w), 1101 (w).



29

Synthesized from 2-hexynoic acid by General Protocol C. 83% yield. Compound is an off-white solid at rt.

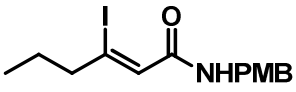
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.40 (t, 1H, *J* = 1.2 Hz, vinyl C*H*), 2.71 (dt, 2H, *J* = 1.2 Hz, 7.2 Hz, allylic CH_2), 1.65 (sext, 2H, *J* = 7.2 Hz, CH_2CH_2), 0.93 (t, 3H, *J* = 7.2 Hz, CH_2CH_3)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 169.78, 125.11, 124.62, 50.35, 22.69, 12.83.

HRMS (ESI-TOF) calcd for $C_6H_{11}NOI$ $(M+Na)^+$: 262.9545, found: 262.9555.

Melting Point: 55.2-55.8 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 2964 (b, s), 2709 (m), 2596 (m), 1704 (s), 1616 (s), 1464 (m), 1405 (s), 1311 (s), 1240 (s), 1212 (s).



30

Synthesized from **29** and 4-methoxybenzylamine by General Protocol B. 99% yield. Compound is an off-white solid.

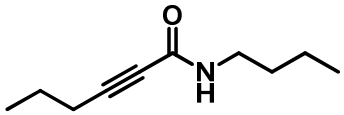
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.23 (d, 2H, *J* = 8.8 Hz, aryl C*H*), 6.84 (d, 2H, *J* = 8.8 Hz, aryl C*H*), 6.26 (s, 1H, vinylic C*H*), 5.96 (bs, 1H, N*H*), 4.42 (d, 2H, *J* = 5.6 Hz, NCH_2), 3.77 (s, 3H, OCH_3), 2.54 (t, 2H, *J* = 7.2 Hz, allylic CH_2), 1.57 (sext, 2H, *J* = 7.2 Hz), 0.88 (t, 3H, *J* = 7.2 Hz)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.85, 159.10, 129.96, 129.49, 128.40, 114.42, 114.10, 55.36, 49.06, 43.15, 22.49, 12.84.

HRMS (ESI-TOF) calcd for $C_{14}H_{19}NO_2I$ $(M+H)^+$: 360.0461, found: 360.0471.

Melting Point: 57.2-59.2 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3421 (b, s), 3262 (s), 3033 (m), 2959 (s), 2835 (w), 1618 (s), 1514 (s), 1460 (m), 1303 (w), 1237 (m), 1177 (w), 1038 (w).



31

Synthesized by from ethyl-2-hexynoate and butylamine by General Protocol A. 68% yield. Compound is a pale yellow oil.

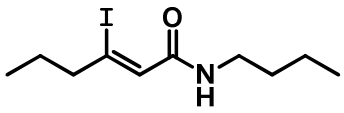
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.07 (s, 1H, minor rotamer, N*H*), 5.95 (s, 1H, major rotamer, N*H*), 3.35 (dq, 2H, minor rotamer, *J* = 7.0 Hz, 2.0 Hz, NCH_2), 3.24 (dq, 2H, major rotamer, *J* = 7.0 Hz, 2.0 Hz, NCH_2), 2.22 (dt, 2H, *J* = 7.0 Hz, 2.0 Hz, allylic CH_2), 1.54 (dq, 2H, *J* = 7.0 Hz, 2.0 Hz), 1.46 (quint, 2H, *J* = 7.0 Hz), 1.32 (sext, 2H, *J* = 7.5 Hz), 0.96 (dt, 3H, *J* = 7.0 Hz, 2.0 Hz), 0.88 (dt, 3H, *J* = 7.5 Hz, 2.0 Hz)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 153.68 (major), 93.69 (minor), 86.89 (major), 75.87 (major), 73.56 (minor), 43.14 (minor), 39.59 (major), 32.71 (minor), 31.45 (major), 21.37 (major), 20.60 (major), 20.08 (major), 19.76 (minor), 13.73 (major), 13.56 (major).

HRMS (ESI) calcd for $C_{10}H_{15}NO$ $(M+H)^+$: 168.1388, found: 168.1382.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in CCl_4): 3588 (m), 3294 (b, m), 3060 (b, w), 2964 (m), 2247 (m), 2221 (m), 1637 (s), 1515 (s), 1460 (m), 1278 (m), 1095 (w).



32

Synthesized from **31** by General Protocol C. 98% yield. Compound is a yellow/brown oil.

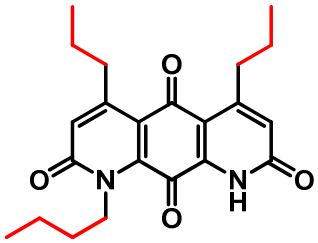
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.26 (s, 1H, vinyl C*H*), 3.25 (q, 2H, *J* = 7.0 Hz), 2.51 (t, 2H, *J* = 7.5 Hz), 1.54 (sext, 2H, *J* = 7.5 Hz), 1.48 (pent, 2H, *J* = 7.5 Hz), 1.32 (sext, 2H, *J* = 8.0 Hz), 0.86 (t, 3H, *J* = 7.0 Hz), 0.85 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 165.13, 128.87, 113.51, 49.01, 39.36, 31.54, 22.51, 20.27, 13.81, 12.83.

HRMS (ESI-TOF) calcd for $C_{10}H_{19}NOI$ $(M+H)^+$: 296.0511, found: 296.0503.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3439 (m), 3324 (b, m), 3073 (w), 2965 (m), 1655 (s), 1621 (m), 1467 (m), 1335(w), 1283 (w), 1239 (w), 1204 (w), 1087 (w).



3

Synthesized from **70**, **30**, and **32** by General Protocols D, E, F, and H. 13% yield over 4 steps. Compound is a red/pink solid.

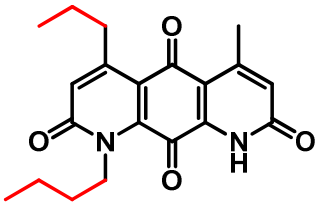
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.67 (s, 1H, N*H*), 6.77 (s, 1H, vinyl C*H*), 6.68 (s, 1H, vinyl C*H*), 4.49 (m, 2H), 2.98 (t, 2H, *J* = 7.0 Hz, allylic CH_2), 2.95 (t, 2H, *J* = 7.0 Hz, allylic CH_3), 1.69 (pent, 2H, *J* = 8.5 Hz, C*H*), 1.72-1.65 (m, 2H), 1.65-1.55 (m, 4H), 1.47 (sext, 2H, *J* = 7.5 Hz), 1.03 (t, 3H, *J* = 7.0 Hz), 1.03 (t, 3H, *J* = 7.5 Hz), 1.00 (t, 3H, *J* = 7.5 Hz, CH_3).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ□181.70, 175.33, 161.47, 160.79, 155.34, 153.19, 139.15, 138.01, 127.93, 127.62, 120.10, 114.69, 46.31, 37.09, 36.23, 31.41, 23.25, 22.98, 20.40, 14.28, 14.14, 13.93.

HRMS (ESI-TOF) calcd for $C_{22}H_{27}N_2O_4$ $(M+H)^+$: 383.1971, found: 383.1969.

Melting Point: >200 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 2940 (b, w), 1649 (b, s), 1587 (w), 1382 (w), 1299 (w), 1281 (w), 1254 (w).



4

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **32** by General Protocols D, E, F, and H. 6.3% yield over 4 steps. Compound is a pink/red solid at rt.

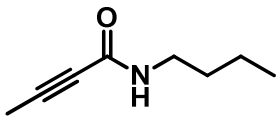
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.46 (s, 1H, N*H*), 6.77 (s, 1H, vinyl C*H*), 6.67 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.50 (m, 2H), 2.97 (t, 2H, *J* = 7.5 Hz, allylic CH_2), 2.61 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.69 (pent, 2H, *J* = 8.0 Hz), 1.60 (sext, 2H, *J* = 7.5 Hz), 1.47 (sext, 2H, *J* = 8.0 Hz), 1.03 (t, 3H, *J* = 7.5 Hz, CH_3), 0.99 (t, 3H, *J* = 7.5 Hz, CH_3).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.73, 175.37, 161.47, 160.91, 153.23, 151.31, 139.49, 137.78, 128.40, 127.82, 119.67, 114.98, 46.35, 39.15, 31.40, 23.14, 22.40, 20.40, 14.28, 13.93.

HRMS (ESI-TOF) calcd for $C_{20}H_{23}N_2O_4$ $(M+H)^+$: 355.1658, found: 355.1655.

Melting Point: >270 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1680 (m), 1651 (s), 1608 (m), 1535 (w), 1458 (w), 1396 (w), 1368 (w), 1281 (w), 1153 (w), 1108 (w).



33

Synthesized from ethyl-2-butynoate and butylamine by General Protocol A. 78% yield. Compound is a clear, colorless oil at rt.

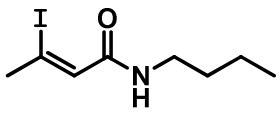
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.01 (bs, 1H), 3.34 (q, 2H, *J* = 7.0 Hz, minor rotamer NCH_2), 3.23 (q, 2H, *J* = 6.0 Hz, major rotamer NCH_2), 1.98 (s, 3H, minor rotamer allylic CH_3), 1.89 (s, 3H, major rotamer allylic CH_3), 1.46 (pent, 2H, *J* = 7.0 Hz), 1.31 (sext, 2H *J* = 7.5 Hz), 0.88 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 153.71 (major), 89.96 (major), 75.13 (major), 45.15 (minor), 41.57 (major), 23.92 (minor), 22.69 (major), 11.39 (major), 11.18 (minor), 3.69 (major).

HRMS (ESI-TOF) calcd for $C_8H_{14}NO$ $(M+H)^+$: 140.1075, found: 140.1071.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film, neat): 3512 (b, w), 3271 (m), 3066 (w), 2954 (m), 2878 (m), 2257 (m), 2216 (w), 1651 (s), 1538 (s), 1285 (m), 1226 (w), 1150 (w).



34

Synthesized from **33** by General Protocol C. 97% yield. Compound is a light yellow/brown oil.

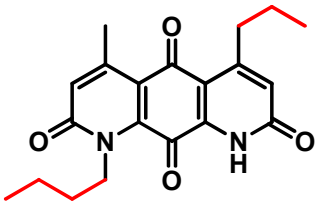
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.23 (d, 1H. *J* = 1.5 Hz, vinyl C*H*), 3.26 (q, 2H, *J* = 7.0 Hz, NCH_2), 2.59 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.48 (p, 2H, *J* = 7.5 Hz), 1.32 (sext, 2H, *J* = 7.5 Hz), 0.87 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.93, 129.47, 105.41, 39.35, 35.75, 31.55, 20.26, 13.83.

HRMS (ESI-TOF) calcd for $C_8H_{15}NOI$ $(M+H)^+$: 268.0198, found: 268.0197.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3441 (m), 3324 (b,m), 3073 (b, w), 2965 (m), 1653 (s), 1628 (s), 1515 (s), 1435 (m), 1331 (w), 1269 (w), 1232 (m), 1154 (w), 1080 (w).



5

Synthesized from **70**, **30**, and **34** by General Protocols D, E, F, and H. 6.7% yield over 4 steps. Compound is a pink/red solid at rt.

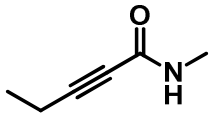
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.52 (s, 1H, N*H*), 6.77 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.68 (s, 1H, vinyl C*H*), 4.52-4.49 (m, 2H), 2.99 (t, 2H, *J* = 7.5 Hz, allylic CH_2), 2.59 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.68 (pent, 2H, *J* = 7.5 Hz), 1.61 (sext, 2H, *J* = 8.0 Hz, $CH_2CH_2CH_3$), 1.47 (sext, 2H, *J* = 8.0 Hz, $CH_2CH_2CH_3$), 1.04 (t, 3H, *J* = 7.5 Hz, CH_3), 1.00 (t, 3H, *J* = 7.5 Hz, CH_3).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.67, 175.28, 161.28, 160.96, 155.41, 149.27, 138.84, 138.25, 128.69, 127.59, 120.12, 114.40, 46.20, 36.30, 31.40, 23.53, 22.88, 20.39, 14.13, 13.92.

HRMS (ESI-TOF) calcd for $C_{20}H_{23}N_2O_4$ $(M+H)^+$: 355.1658, found: 355.1658.

Melting Point: >270 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 1677 (w), 1651 (b, s), 1604 (w), 1555(w), 1455 (w), 1399 (w), 1306 (w), 1285 (w), 1212 (w), 1108 (w).



35

Synthesized from ethyl-2-pentynoate and methylamine by General Protocol A. 78% yield. Compound is a yellow oil at rt.

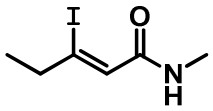
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.95 (bs, 1H), 2.99 (d, 3H, *J* = 5.0 Hz, minor rotamer), 2.82 (d, 3H, *J* = 5.0 Hz, major rotamer), 2.37 (t, 2H, *J* = 7.0 Hz, minor rotamer), 2.27 (t, 2H, *J* = 7.0 Hz, major rotamer), 1.20 (t, 3H, *J* = 7.5 Hz, minor rotamer), 1.15 (t, 3H, *J* = 7.5 Hz, major rotamer).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 157.11 (minor), 154.40 (major), 95.38 (minor), 87.96 (major), 74.62 (major), 72.25 (minor), 29.56 (minor), 26.17 (major), 12.66 (minor), 12.58 (major), 12.33 (minor), 12.40.

HRMS (ESI-TOF) calcd for $C_6H_{10}NO$ $(M+H)^+$: 112.0762, found: 112.0765.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3501 (w), 3282 (b, m), 3069 (w), 2981 (m), 2259 (m), 2223 (m), 1629 (s), 1540 (s), 1413 (m), 1317 (m), 1286 (m), 1162 (w).



36

Synthesized from **35** by General Protocol C. 92% yield. Compound is a yellow/brown oil.

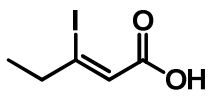
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.28 (q, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.9 (bs, 1H, N*H*), 2.88 (d, 3H, *J* = 5.0 Hz, NCH_3), 2.62 (dq, 2H, *J* = 1.5 Hz, 7.5 Hz, allylic CH_2), 1.11 (t, 3H, *J* = 7.5 Hz, -CH_3).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 166.14, 127.91, 115.56, 40.94, 26.39, 14.67.

HRMS (ESI-TOF) calcd for $C_6H_{11}NOI$ $(M+H)^+$: 239.9885, found: 239.9885.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3455 (m), 3323 (b, m), 3082 (b, w), 2978 (m), 1653 (s), 1626 (m), 1524 (m), 1411 (w), 1342 (w), 1292 (w), 1220 (m), 1161 (w), 1069 (w).



37

Synthesized from 2-pentynoic acid by General Protocol C. 91% yield. Compound is an off-white solid.

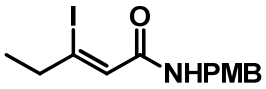
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.40 (t, 1H, *J* = 1.0 Hz, vinyl C*H*), 2.78 (dq, *J* = 7.5 Hz, 1.0 Hz, 2H, allylic CH_2), 1.16 (t, 3H, *J* = 7.5 Hz, CH_2CH_3)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 169.66, 126.56, 123.62, 42.36, 14.72.

HRMS (ESI-TOF) calcd for C_5H_7NOI $(M+H)^+$: 225.9491, found: 225.9507.

Melting Point: 67.0-67.9 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3233 (b, m), 2703 (w), 2578 (w), 1694 (s), 1626 (s), 1455 (m), 1418 (w), 1310 (w), 1237 (m), 1077 (w).



38

Synthesized from **37** and 4-methoxybenzylamine by General Protocol B. 84% yield. Compound is an off-white/light yellow solid.

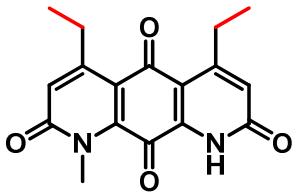
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 7.23 (d, 2H, *J* = 8.4 Hz, aryl C*H*), 6.83 (d, 2H, *J* = 8.8 Hz, aryl C*H*), 6.26 (s, 1H, vinylic C*H*), 6.01 (bs, 1H, N*H*), 4.42 (d, 2H, *J* = 5.6 Hz, NCH_2), 3.76 (s, 3H, OCH_3), 2.61 (q, 2H, *J* = 7.6 Hz, allylic CH_2), 1.08 (t, 3H, *J* = 7.2 Hz)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ165.00, 159.04, 129.95, 129.44, 127.41, 115.90, 114.06, 55.34, 43.11, 40.91, 14.55.

HRMS (ESI-TOF) calcd for $C_{13}H_{17}NO_2I$ $(M+H)^+$: 346.0304, found: 346.0308.

Melting Point: 60.7-63.3 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3519 (w), 3283 (b, s), 3059 (m), 2970 (m), 2834 (m), 1651 (s), 1505 (s), 1455 (m), 1250 (m), 1175 (m), 1033 (m).



6

Synthesized from **70**, **36**, and **38** by General Protocols D, E, F, and H. 17% yield over 4 steps. Compound is a pink amorphous solid.

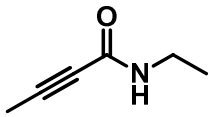
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 10.28 (bs, 1H), 6.83 (s, 1H, vinyl C*H*), 6.75 (s, 1H, vinyl C*H*), 3.93 (s, 3H), 3.07 (dq, 2H, *J* = 7.5 Hz, 1.0 Hz), 3.04 (dq, 2H, *J* = 7.5 Hz, 1.0 Hz), 1.25 (t, 3H, *J* = 7.5 Hz), 1.24 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ 181.29, 175.34, 162.29, 162.15, 157.28, 155.52, 140.00, 138.78, 33.96, 27.90, 27.27, 13.62, 13.34.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+H)^+$: 313.1188, found: 313.1193.

Melting Point: >280 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1684 (w), 1648 (s), 1604 (w), 1580 (w), 1507 (w), 1406 (w), 1363 (w), 1289 (w), 1153 (w), 1101 (w).



39

Synthesized from ethyl-2-butynoate and ethylamine by General Protocol A. 83% yield. Compound is a pale yellow oil.

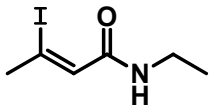
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.25 (bs, 1H), 3.35 (pent, 2H, *J* = 7.0 Hz, minor rotamer NCH_2), 3.23 (pent, 2H, *J* = 7.5 Hz, major rotamer), 1.95 (s, 3H, minor rotamer), 1.85 (s, 3H, major rotamer), 1.12 (t, 3H, *J* = 7.5 Hz, minor rotamer), 1.08 (t, 3H, *J* = 7.0 Hz, major rotamer).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 153.58 (major), 82.80 (major), 75.05 (major), 38.20 (minor), 34.66 (major), 15.91 (minor), 14.51 (major), 3.93 (minor), 3.59 (major).

HRMS (ESI) calcd for $C_6H_{10}NO$ $(M+H)^+$: 112.0762, found: 112.0764.

Melting Point Not determined (oil).

IR (cm^{-1}, neat): 3438 (m), 3291 (b, m), 3066 (b, w), 2983 (m), 2240 (m), 2209 (m), 1641 (s), 1520 (s), 1437 (m), 1379 (w), 1283 (m), 1149 (w).



40

Synthesized from **39** by General Protocol C. 98% yield. Compound is a pale yellow/brown oil.

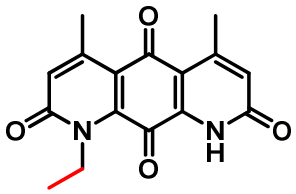
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.28 (bs, 1H, N*H*), 6.22 (s, 1H, vinyl C*H*), 3.30 (pent, 2H, *J* = 7.5 Hz, NCH_2), 2.59 (s, 3H, allylic CH_3), 1.12 (s, 3H).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.85, 129.28, 105.58, 35.75, 34.45, 14.74.

HRMS (ESI-TOF) calcd for $C_6H_{11}NOI$ $(M+H)^+$: 139.9885, found: 139.9884.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3441 (m), 3322 (b, m), 3073 (b,w), 2976 (m), 1653 (s), 1626 (m), 1515 (m), 1432 (m), 1375 (w), 1326 (w), 1269 (w), 1211 (m), 1152 (w), 1080 (m).



7

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **40** by General Protocols D, E, F, and H. 13% yield over 4 steps. Compound is a red/orange solid at rt.

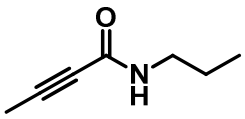
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.76 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.67 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.51 (q, 2H, *J* = 8.0 Hz), 2.36 (m, 6H, allylic CH_3), 1.45 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 182.06, 175.64, 162.52, 162.29, 152.29, 150.66, 140.21, 139.27, 127.93, 127.71, 119.94, 115.35, 42.97, 23.42, 22.39, 14.36.

HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_4$ $(M+H)^+$: 299.1032, found: 299.1034.

Melting Point: >280 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 1680 (w), 1647 (b, s), 1601 (w), 1580 (w), 1374 (m), 1292 (m), 1161 (m).



41

Synthesized from ethyl-2-butynoate and propylamine by General Protocol A. 71% yield. Compound is a clear, colorless oil.

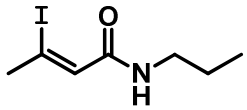
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.99 (bs, 1H), 3.35 (q, 2H, *J* = 7.0 Hz, minor rotamer NC*H*$_2$), 3.24 (q, 2H, *J* = 7.5 Hz, major rotamer NC*H*$_2$), 2.02 (s, 3H, minor rotamer allylic C*H*$_3$), 1.93 (s, 3H, major rotamer allylic C*H*$_3$), 1.53 (sext, 2H, *J* = 7.5 Hz), 0.93 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 156.60 (minor), 153.62 (major), 89.57 (minor), 82.71 (major), 74.90 (major), 72.54 (minor), 44.97 (minor), 41.34 (major), 23.68 (minor), 22.43 (major), 11.21 (major), 10.98 (minor), 3.83 (minor), 3.50 (major).

HRMS (ESI-TOF) calcd for $C_7H_{12}NO$ $(M+H)^+$: 126.0919, found: 126.0914

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3441 (m), 3300 (b, m), 3066 (b, w), 2967 (m), 2249 (s), 2224 (m), 1649 (s), 1517 (s), 1440 (w), 1272 (m), 1162 (w).



42

Synthesized from **41** by General Protocol C. 98% yield. Compound is a clear, colorless oil.

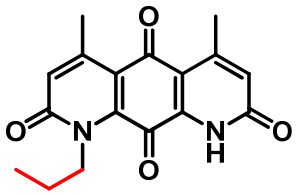
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.23 (d, 1H. *J* = 1.5 Hz, vinyl C*H*), 6.22 (bs, 1H, N*H*), 3.23 (d, 2H, *J* = 7.0 Hz, NCH_2), 2.60 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.53 (sext, 2H, *J* = 7.0 Hz), 0.90 (t, 3H, 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.98, 129.47, 105.47, 41.34, 35.76, 22.77, 11.61.

HRMS (ESI-TOF) calcd for $C_7H_{13}NOI$ $(M+H)^+$: 254.0042, found: 254.0044.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3437 (m), 3324 (b, m), 3073 (b, w), 2967 (m), 1654 (s), 1628 (m), 1513 (m), 1455 (w), 1428 (w), 1377 (w), 1338 (w), 1283 (w), 1154 (w), 1080 (w).



8

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **42** by General Protocols D, E, F, and H. 13% yield over 4 steps. Compound is a red/orange solid.

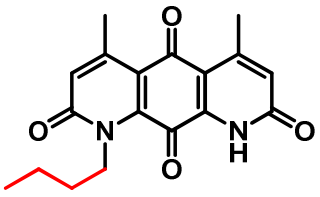
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.77 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.68 (d, 1H, *J* = 1.5 Hz, vinyl C*H*), 4.60 (m, 2H), 2.62 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 2.60 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.73 (sext, 2H, *J* = 8.0 Hz, C*H*), 1.04 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 182.08, 175.69, 162.52, 162.38, 152.31, 150.63, 140.01, 139.25, 127.94, 127.73, 120.05, 115.39, 48.50, 23.45, 22.77, 22.38, 11.29.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+H)^+$: 313.1188, found: 313.1192.

Melting Point: >260 °C.

IR (cm^{-1}, thin film in $CDCl_3$:MeOH, 2:1): 1651 (b, s), 1557 (w), 1535 (w), 1401 (w), 1289 (w), 1153 (w), 1094 (w).



9

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **34** by General Protocols D, E, F, and H. 9.9% yield over 4 steps. Compound is a red solid.

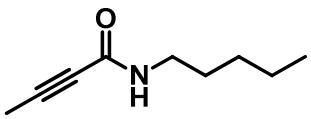
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.54 (bs, 1H), 6.77 (q, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.68 (q, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.53-4.50 (m, 2H), 2.62 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.60 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.68 (pent, 2H, *J* = 7.5 Hz), 1.47 (sext, 2H, *J* = 7.5 Hz), 1.00 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ ^{13}C NMR (126 MHz, CD_3OD) δ 181.79, 175.38, 162.20, 162.06, 152.03, 150.29, 139.65, 138.89, 127.71, 127.50, 119.82, 115.11, 48.76, 31.16, 29.76, 23.20, 22.14, 20.27, 13.61.

HRMS (ESI-TOF) calcd for $C_{18}H_{19}N_2O_4$ $(M+H)^+$: 327.1345, found: 327.1358.

Melting Point: >270 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1670 (m), 1651 (b, s), 1609 (w), 1587 (w), 1466 (w), 1401 (w), 1375 (w), 1289 (w), 1157 (w), 1100 (w), 1046 (w).



43

Synthesized from ethyl-2-butynoate and pentylamine by General Protocol A. 86% yield. Compound is a clear, colorless oil.

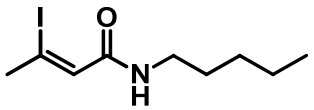
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.91 (bs, 1H), 3.35 (q, 2H, minor rotamer, *J* = 6.8 Hz, NC*H*$_2$), 3.24 (q, 2H, major rotamer, *J* = 6.8 Hz, NC*H*$_2$), 1.99 (s, 3H, minor rotamer, allylic C*H*$_3$), 1.90 (s, 3H, major rotamer, allylic C*H*$_3$), 1.48 (quint, 2H, *J* = 7.2 Hz), 1.28 (m, 4H), 0.86 (t, 3H, *J* = 6.8 Hz)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 156.37 (minor), 153.54 (major), 89.39 (minor), 82.51 (major), 74.86 (major), 72.49 (minor), 43.15 (minor), 39.57 (major), 30.01 (minor), 28.82 (major), 28.74 (major), 28.45 (minor), 22.13 (major), 22.05 (minor), 13.75 (major), 3.71 (minor), 3.39 (major) .

HRMS (ESI) calcd for $C_9H_{16}NO$ $(M+H)^+$: 154.1232, found: 154.1231.

Melting Point: Not determined (oil).

IR (cm^{-1}, thin film in $CDCl_3$): 3498 (m), 3270 (b, s), 3063 (m), 2933 (s), 2861 (m), 2256 (m), 2216 (m), 1651 (s), 1539 (s), 1455 (m), 1373 (m), 1288 (m), 1211 (w), 1149 (w).



44

Synthesized from **43** by General Protocol C. 81% yield. Compound is a pale yellow/brown oil.

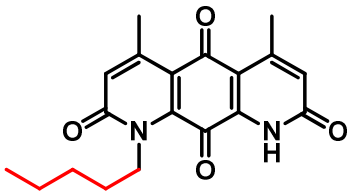
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.22 (d, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.77 (bs, 1H, N*H*), 3.32 (q, 2H, *J* = 7.0 Hz, NC*H*$_2$), 2.64 (d, 3H, *J* = 1.5 Hz, allylic C*H*$_3$), 1.55 (pent, 2H, *J* = 7.0 Hz), 1.35-1.30 (m, 4H), 0.89 (t, 3H, *J* = 7.0 Hz)

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.60, 128.78, 105.36, 39.36, 35.62, 29.00, 28.92, 22.19, 13.87.

HRMS (ESI-TOF) calcd for $C_9H_{17}NOI$ $(M+H)^+$: 282.0355, found: 282.0356.

Melting Point: Not determined (oil).

IR (cm^{-1}, thin film in $CDCl_3$): 3498 (m), 3288 (b, s), 3072 (m), 2928 (s), 2859 (s), 1651 (s), 1618 (s), 1557 (s), 1434 (m), 1374 (m), 1337 (m), 1228 (m), 1149 (w), 1087 (m).



10

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **44** by General Protocols D, E, F, and H. 11% yield over 4 steps. Compound is a red amorphous solid.

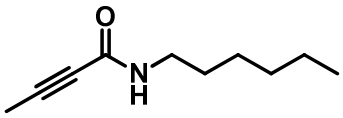
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.76 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.67 (d, 1H, *J* = 1.5 Hz, vinyl C*H*), 4.48-4.43 (m, 2H), 2.63 (d, 3H, *J* = 1.5 Hz, allylic C*H*$_3$), 2.63 (d, 3H, *J* = 1.0 Hz, allylic C*H*$_3$), 1.77 (pent, 2H, *J* = 7.5 Hz), 1.48-1.40 (m, 4H), 0.95 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ 181.47, 175.05, 161.83, 161.68, 151.66, 149.89, 139.31, 138.53, 127.40, 127.19, 119.45, 114.75, 28.82, 28.48, 22.87, 22.07, 21.81, 13.58.

HRMS (ESI-TOF) calcd for $C_{19}H_{21}N_2O_4$ $(M+H)^+$: 341.1501, found: 341.1496.

Melting Point: >250 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1683 (m), 1651 (b, s), 1613 (m), 1591 (w), 1471 (w), 1399, (w), 1368 (w), 1290 (w), 1160 (w), 1053 (w).



45

Synthesized from ethyl-2-butynoate and hexylamine by General Protocol A. 79% yield. Compound is a white crystalline solid.

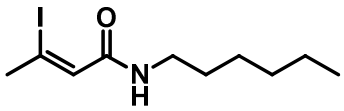
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.95 (bs, 1H, major rotamer N*H*), 3.34 (q, 2H, *J* = 7.0 Hz, minor rotamer), 3.23 (q, 2H, *J* = 7.0 Hz, major rotamer), 1.98 (s, 3H, minor rotamer), 1.89 (s, 3H, major rotamer), 1.47 (pent, 2H, *J* = 7.0 Hz), 1.33-1.23 (m, 6H), 0.84 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz) δ 153.58 (major), 82.92 (major), 75.05 (major), 43.37 (minor), 39.85 (major), 31.49 (major), 30.56 (minor), 29.33 (major), 26.57 (major), 26.22 (minor), 22.59 (major), 14.06 (major), 3.69 (major).

HRMS (ESI) calcd for $C_{10}H_{18}NO$ $(M+H)^+$: 168.1388, found: 168.1391.

Melting Point: 39.0-39.8 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3540 (b, s), 2957 (m), 2858 (w), 2252 (w), 2222 (w), 1635 (s), 1541 (m), 1458 (w), 1291 (w).



46

Synthesized from **45** by General Protocol C. 98% yield. Compound is a light yellow/brown oil.

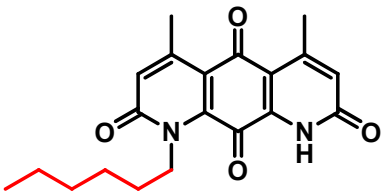
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.22 (q, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.73 (bs, 1H, N*H*), 3.32 (q, 2H, *J* = 7.0 Hz), 2.64 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.55 (pent, 2H, *J* = 7.0 Hz), 1.38-1.27 (m, 6H), 0.88 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz) δ 164.51, 128.65, 105.27, 39.35, 35.58, 31.27, 29.14, 26.49, 22.33, 13.83.

HRMS (ESI-TOF) calcd for $C_{10}H_{19}NOI$ $(M+H)^+$: 296.0511, found: 296.0510.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CDCl_3$): 3291 (b, s), 3070 (m), 2954 (s), 2857 (s), 1654 (s), 1625 (m), 1542 (m), 1458 (m), 1437 (m), 1375 (w), 1339 (w), 1226 (m), 1078 (w).



11

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **46** by General Protocols D, E, F, and H. 12% yield over 4 steps. Compound is a pink/red solid.

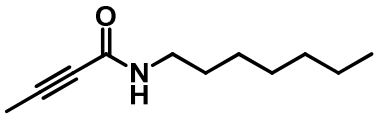
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.76 (s, 1H), 6.67 (s, 1H), 4.45 (m, 2H), 2.63 (d, 3H, *J* = 1.0 Hz, allylic C*H*$_3$), 2.63 (d, 3H, *J* = 1.0 Hz, allylic C*H*$_3$), 1.76 (pent, 2H, *J* = 7.5 Hz), 1.46 (pent, 2H, *J* = 7.0 Hz), 1.40-1.34 (m, 4H), 0.92 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ181.46, 175.04, 161.82, 161.66, 151.65, 149.88, 139.30, 138.53, 127.40, 127.20, 119.44, 114.74, 46.57, 31.18, 28.76, 26.36, 22.87, 22.35, 21.81, 13.58.

HRMS (ESI-TOF) calcd for $C_{20}H_{23}N_2O_5$ $(M+H)^+$: 355.1658, found: 355.1660.

Melting Point: >250 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1677 (m), 1651 (b, s), 1613 (m), 1586 (m), 1469 (w), 1434 (w), 1402 (m), 1386 (m), 1328 (w), 1291 (m), 1150 (w), 1102 (m), 1060 (w).



47

Synthesized from ethyl-2-butynoate and heptylamine by General Protocol A. 72% yield. Compound is white crystalline solid.

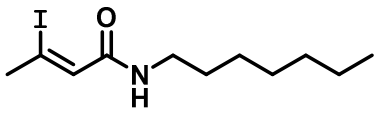
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.95 (bs, 1H, N*H*), 3.34 (q, 2H, *J* = 7.0 Hz, minor rotamer NC*H*$_2$), 3.22 (dt, 2H, *J* = 7.0 Hz, major rotamer), 1.98 (s, 3H, minor rotamer), 1.89 (s, 3H, major rotamer), 1.47 (pent, 2H, *J* = 7.5 Hz), 1.30-1.20 (m, 8H), 0.84 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 156.51 (minor), 153.65 (major), 89.75 (minor), 82.97 (major), 75.14 (major), 72.80 (minor), 43.44 (minor), 39.93, (major), 31.84 (major), 30.67 (minor), 29.44 (major), 29.04 (major), 28.97 (minor), 26.94 (major), 26.59 (minor), 22.69 (major).

HRMS (ESI-TOF) calcd for $C_{11}H_{20}NO$ $(M+H)^+$: 182.1545, found: 182.1550.

Melting Point: 50.1-52.2 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3449 (b, s), 2960 (m), 2250 (w), 2202 (w), 1636 (s), 1278 (m).



48

Synthesized from **47** by General Protocol C. 86% yield. Compound is a pale yellow oil.

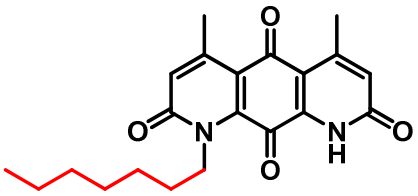
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.24 (q, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.73 (bs, 1H, N*H*), 3.33 (q, 2H, *J* = 6.5 Hz), 2.65 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.55 (pent, 2H, *J* = 7.0 Hz), 1.38-1.23 (m, 8H), 0.88 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.72, 129.06, 105.40, 39.52, 35.68, 31.68, 29.37, 28.92, 26.95, 22.52, 14.02.

HRMS (ESI-TOF) calcd for $C_{11}H_{21}NOI$ $(M+H)^+$: 310.0668, found: 310.0654.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3289 (b, s), 3069 (m), 2926 (s), 2855 (s), 1651 (b, s), 1539 (s), 1435 (m), 1229 (m), 1077 (w).



12

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **48** by General Protocols D, E, F, and H. 10% yield over 4 steps. Compound is an orange solid.

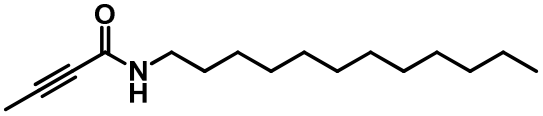
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.76 (q, 1H, *J* = 1.5 Hz, vinyl C*H*), 6.66 (q, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.47-4.44 (m, 2H), 2.63 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.63 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.77 (bpent, 2H, *J* = 8.0 Hz), 1.46 (bpent, 2H, *J* = 8.0 Hz), 1.42-1.26 (m, 6H), 0.90 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 182.01, 175.59, 162.40, 162.24, 152.24, 150.46, 139.86, 139.09, 127.95, 127.73, 120.01, 115.32, 47.14, 32.13, 29.39, 29.26, 27.23, 23.43, 22.89, 22.37, 14.20.

HRMS (ESI-TOF) calcd for $C_{21}H_{25}N_2O_4$ $(M+H)^+$: 369.1814, found: 369.1811.

Melting Point: >220 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 1651 (b, s), 1611 (m), 1587 (w), 1397 (w), 1323 (w), 1292 (w), 1177 (w), 1102 (w).



49

Synthesized from ethyl-2-butynoate and dodecylamine by General Protocol A. 72% yield. Compound is a white amorphous solid.

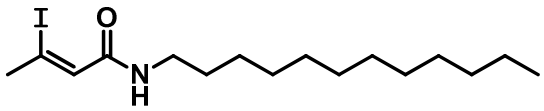
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.72 (bs, 1H, major rotamer N*H*), 5.64 (bs, 1H, minor rotamer N*H*), 3.37 (q, 2H, *J* = 7.0 Hz, minor rotamer NCH_2), 3.26 (q, 2H, *J* = 7.0 Hz, major rotamer NCH_2), 2.01 (d, 3H, *J* = 1.0 Hz, minor rotamer allylic CH_3), 1.93 (d, 3H, *J* = 1.0 Hz, major rotamer allylic CH_3), 1.50 (pent, 2H, *J* = 7.0 Hz), 1.34-1.20 (m, 18H), 0.87 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 153.61 (major), 82.73 (major), 75.05 (major), 43.36 (minor), 39.81 (major), 31.92 (major), 30.55 (minor), 29.66 (major), 29.64 (major), 29.61(major), 29.56 (major), 29.37 (major), 29.31 (2C, major), 26.90 (major), 26.53 (minor), 22.69 (major), 14.12 (major), 3.95 (minor), 3.62 (major).

HRMS (ESI-TOF) calcd for $C_{16}H_{30}NO$ $(M+H)^+$: 252.2327, found: 252.2327.

Melting Point: 63.4-64.6 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3300 (b, w), 3273 (m), 3059 (w), 2956 (w), 2918 (m), 2848 (m), 2258 (w), 2216 (w), 1645 (w), 1615 (s), 1541 (m), 1474 (m), 1296 (w).



50

Synthesized from **49** by General Protocol C. 98% yield. Compound is an off-white solid.

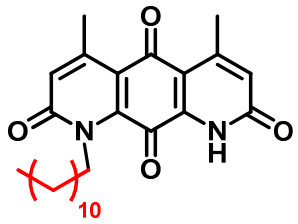
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.22 (q, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.93 (bs, 1H, N*H*), 3.29 (q, 2H, *J* = 6.0 Hz), 2.62 (d, 3H, *J* = 1.5 Hz, NCH_3), 1.52 (pent, 2H, *J* = 7.5 Hz), 1.35-1.20 (m, 18H), 0.85 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.97, 129.73, 105.42, 39.74, 35.80, 32.07,29.80, 29.79, 29.74, 29.71, 29.59, 29.50, 29.46, 27.20, 22.84, 14.27.

HRMS (ESI-TOF) calcd for $C_{16}H_{31}NOI$ $(M+H)^+$: 380.1450, found: 380.1452.

Melting Point: 51.9-53.6 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3512 (b, s), 3308 (s), 3094 (m), 2916 (s), 2850 (s), 1651 (s), 1632 (s), 1557 (s), 1470 (m), 1431 (w), 1372 (w), 1337 (w), 1237 (m), 1157 (w), 1076 (w).



13

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **50** by General Protocols D, E, F, and H. 15% yield over 4 steps. Compound is an orange solid.

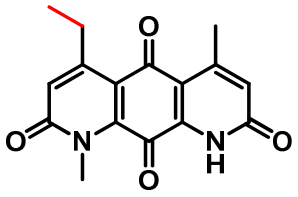
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 10.3 (bs, 1H, N*H*), 6.75 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.68 (s, 1H, vinyl C*H*), 4.48 (t, 2H, *J* = 8.0 Hz, NC*H*$_2$), 2.61 (d, 3H, *J* = 0.5 Hz, allylic C*H*$_3$), 2.59 (d, 3H, *J* = 1.0 Hz, allylic C*H*$_3$), 1.69 (pent, 2H, *J* = 7.5 Hz, NCH_2CH_2-), 1.42 (pent, 2H, *J* = 7.5 Hz, $NCH_2CH_2CH_2$-), 1.38-1.18 (m, 16H), 0.86 (t, 3H, *J* = 7.0 Hz, -CH_2CH_3).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ181.78, 175.27, 161.27, 130.99, 151.38, 149.30, 139.13, 137.98, 128.64, 128.40, 119.69, 114.66, 46.50, 32.12, 29.87, 29.85, 29.81, 29.80, 29.55, 29.44, 29.39, 27.14, 23.55, 22.88, 22.44, 14.32.

HRMS (ESI-TOF) calcd for $C_{26}H_{35}N_2O_4$ $(M+H)^+$: 439.2597, found: 439.2595.

Melting Point: >180 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 2919 (m), 2850 (m), 1680 (m), 1651 (b, s), 1613 (m), 1557 (w), 1470 (w), 1401 (m), 1302 (m), 1157 (w), 1052 (w).



14

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **36** by General Protocols D, E, F, and H. 7.4% yield over 4 steps. Compound is a red solid.

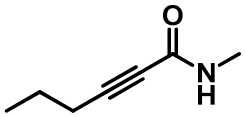
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.81 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.67 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 3.92 (s, 3H), 3.09 (dq, 2H, *J* = 7.0, 0.5 Hz, allylic CH_2), 2.64 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.26 (t, 3H, *J* = 7.5 Hz, C*H3*).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ181.33, 175.31, 162.29, 161.90, 155.57, 151.68, 140.24, 138.50, 127.15, 125.27, 118.83, 115.06, 33.98, 27.88, 21.83, 13.55.

HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_4$ $(M+H)^+$: 299.1032, found: 299.1034.

Melting Point: >290 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3024 (w), 2905 (w), 1684 (m), 1653 (b, s), 1607 (m), 1583 (w), 1458 (w), 1399 (m), 1363 (m), 1291 (m), 1264 (w), 1165 (w), 1035 (w).



51

Synthesized from ethyl-2-hexynoate and methylamine by General Protocol A. 92% yield. Compound is a pale yellow oil.

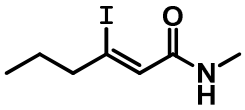
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.04 (bs, 1H, major rotamer N*H*), 5.89 (bs, 1H, minor rotamer), 2.99 (d, 3H, *J* = 5.0 Hz, minor rotamer), 2.81 (d, 3H, *J* = 5.0 Hz, major rotamer), 2.33 (t, 2H, *J* = 7.0 Hz, minor rotamer), 2.22 (t, 2H, *J* = 7.0 Hz, major rotamer), 1.59 (sext, 2H, *J* = 7.0 Hz, minor rotamer), 1.54 (sext, 2H, *J* = 7.0 Hz, major rotamer), 0.99 (t, 3H, *J* = 7.5 Hz, minor rotamer), 0.96 (t, 3H, *J* = 7.5 Hz, major rotamer).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 54.47 (major), 87.18 (major), 75.76 (major), 29.87 (minor), 26.58 (major), 21.43 (major), 20.97 (minor), 20.65 (major), 13.60 (major).

HRMS (ESI) calcd for $C_7H_{12}NO$ $(M+H)^+$: 126.0919, found: 126.0920.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3455 (m), 3307 (b, m), 3070 (b, w), 2967 (m), 2251 (m), 2217 (m), 1649 (s), 1520 (m), 1411 (w), 1267 (m), 1163 (w).



52

Synthesized from **51** by General Protocol C. 96% yield. Compound is a yellow/brown oil.

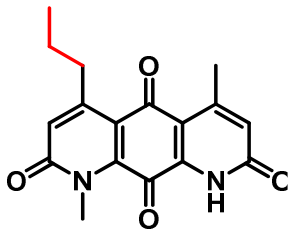
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.40 (bs, 1H, N*H*), 6.30 (s, 1H, vinyl C*H*), 2.82 (d, 3H, *J* = 5.0 Hz, NCH_3), 2.53 (t, 2H, *J* = 7.0 Hz, allylic CH_2), 1.54 (sext, 2H, *J* = 7.5 Hz), 0.86 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 165.86, 128.49, 114.01, 49.03, 26.30, 22.52, 12.82.

HRMS (ESI-TOF) calcd for $C_7H_{13}NOI$ $(M+H)^+$: 254.0042, found: 254.0045.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3455 (m), 3328 (b, m), 3080 (b, w), 2965 (m), 1658 (s), 1624 (m), 1524 (m), 1414 (m), 1333 (w), 1285 (w), 1237 (w), 1165 (w), 1087 (w).



15

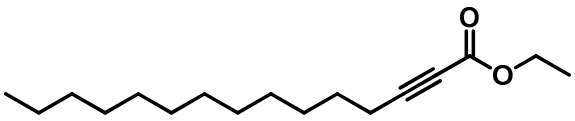
Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **52** by General Protocols D, E, F, and H. 3.4% yield over 4 steps. Compound is a red/orange solid.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.80 (s, 1H, vinyl C*H*), 6.68 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 3.93 (s, 3H), 2.98 (t, 2H, *J* = 7.5 Hz, allylic CH_2), 2.62 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.61 (q, 2H, *J* = 7.5 Hz), 1.03 (t, 3H, *J* = 7.5 Hz, CH(CH_3)$_2$).

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+H)^+$: 313.1188, found: 313.1189.

Melting Point: >220°C.

IR (cm^{-1}, thin film in $CDCl_3$): 2954 (w), 2912 (w), 2850 (w), 1651 (b, s), 1542 (s), 1632 (m), 1557 (w), 1538 (w), 1505 (w), 1455 (w), 1399 (w), 1288 (m), 1163 (w).



53

To an oven-dried Schlenk flask was added 1-tetradecyne (0.748 g, 3.85 mmol) and THF (10 mL). Chilled to -78 ºC. Added n-BuLi (2.7 mL, 4.32 mmol) dropwise then stirred for 10 minutes. Added ethyl chloroformate (0.56 mL, 5.86 mmol) then allowed the reaction to warm to RT. The solvent was evaporated and the residue was purified by silica gel chromatography. Product was collected as a colorless oil (1.01 g, 3.79 mmol, 98.5% yield). Compound is a clear, colorless oil.

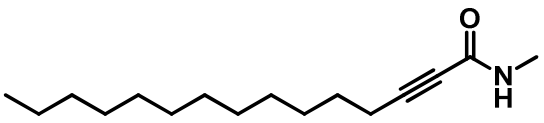
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 4.19 (q, 2H, *J* = 7.5 Hz), 2.30 (t, 2H, *J* = 7.5 Hz), 1.56 (pent, 2H, *J* = 7.5 Hz), 1.37 (bpent, 2H, *J* = 8.0 Hz), 1.29 (t, 3H, *J* = 7.5 Hz), 1.28-1.21 (m, 16H), 0.86 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 154.06, 89.66, 73.33, 61.91, 32.10, 29.82, 29.81, 29.77, 29.60, 29.53, 29.21, 29.04, 27.73, 22.87, 14.29, 14.21.

HRMS (ESI-TOF) calcd for $C_{17}H_{31}O_2$ $(M+H)^+$: 267.2324, found: 267.2327.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film, neat): 2952 (s), 2855 (s), 2320 (w), 2235 (s), 1714 (b, s), 1464 (m), 1366 (m), 1248 (s), 1073 (s).



54

Synthesized from **53** and methylamine by General Protocol A. 66% yield. Compound is a white amorphous solid.

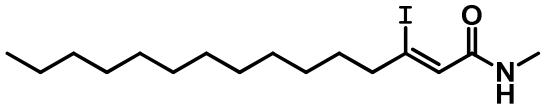
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.42 (bs, 1H, major rotamer N*H*), 6.24 (bs, 1H, minor rotamer N*H*), 2.93 (d, 3H, *J* = 5.0 Hz, minor rotamer NCH_3), 2.75 (d, 3H, *J* = 5.0 Hz, major rotamer NCH_3), 2.29 (t, 2H, *J* = 7.0 Hz, minor rotamer allylic CH_2), 2.18 (t, 2H, *J* = 7.0 Hz, *J* = 7.0 Hz, major rotamer allylic CH_2), 1.50 (pent, 2H, *J* = 7.0 Hz, minor rotamer), 1.45 (pent, 2H, *J* = 7.5 Hz, major rotamer), 1.29 (bpent, 2H, *J* = 7.5 Hz, major rotamer), 1.25-1.13 (m, 16H), 0.79 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 157.35 (minor), 154.47 (major), 94.59 (minor), 87.17 (major), 75.50 (major), 73.14 (minor), 31.92 (major), 29.66 (major), 29.64 (2C, major), 29.48 (major), 29.36 (major), 29.10 (major), 28.90 (major), 27.83 (major), 26.43 (major), 22.69 (major), 18.57 (major), 14.11 (major).

HRMS (ESI-TOF) calcd for $C_{16}H_{30}NO$ $(M+H)^+$: 252.2327, found: 252.2327.

Melting Point: 49.2-50.2 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3428 (b, m), 3290 (s), 2958 (m), 2920 (s), 2849 (m), 2250 (w), 2221 (w), 1625 (s), 1557 (m), 1469 (m), 1414 (w), 1292 (w), 1160 (w).



55

Synthesized from **54** by General Protocol C. 100% yield. Compound is a yellow solid.

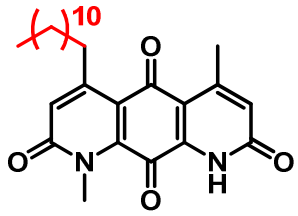
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.27 (s, 1H, vinyl C*H*), 5.74 (bs, 1H, N*H*), 2.89 (d, 3H, *J* = 4.5 Hz), 2.59 (t, 2H, *J* = 7.5 Hz), 1.56 (bt, 2H, *J* = 7.0), 1.33-1.22 (m, 18H), 0.88 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 165.96, 128.50, 114.45, 47.23, 32.07, 29.81, 29.80, 29.77, 29.66, 29.51, 29.50, 29.36, 28.44, 26.36, 22.84, 14.29.

HRMS (ESI-TOF) calcd for $C_{16}H_{31}NOI$ $(M+H)^+$: 380.1450, found: 380.1451.

Melting Point: 45.1-48.8 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3470 (b, w), 3291 (m), 3080 (w), 2924 (s), 2853 (s), 1651 (s), 1618 (m), 1557 (m), 1464 (w), 1410 (w), 1350 (w), 1234 (w), 1161 (w), 1091 (w).



16

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **55** by General Protocols D, E, F, and H. 7.0% yield over 4 steps. Compound is a peach solid.

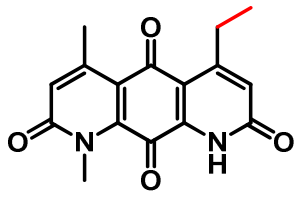
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.78 (s, vinyl C*H*), 6.67 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 3.91 (s, 3H), 3.03 (t, *J* = 8.0 Hz), 2.64 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.58 (p, 2H, *J* = 7.5 Hz), 1.44 (p, 2H, *J* = 7.5 Hz), 1.27-1.4 (m, 16H), 0.89 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR (d-TFA, 125 MHz): δ182.13, 176.16, 166.58 (bs), 163.92 (bs), 160.66, 141.89, 139.75, 128.19 (bs), 126.92, 125.93, 120.93, 38.25, 37.45, 33.96, 32.05, 31.63 (2C), 31.57, 31.52, 31.41, 31.36, 31.15, 24.53, 23.41, 14.85.

HRMS (ESI-TOF) calcd for $C_{26}H_{35}N_2O_4$ $(M+H)^+$: 439.2597, found: 439.2600.

Melting Point: >220 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3066 (w), 2916 (m), 2849 (m), 1662 (b, s), 1612 (w), 1583 (w), 1469 (w), 1399 (m), 1297 (m), 1257 (w), 1163 (w), 1095 (w).



17

Synthesized from **70**, (Z)-3-iodo-N-methylbut-2-enamide,[1] and **38** by General Protocols D, E, F, and H. 6.2% yield over 4 steps. Compound is a red solid at rt.

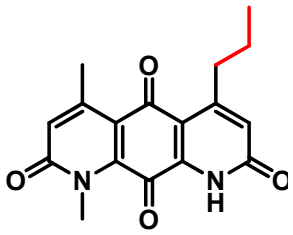
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.78 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.70 (s, 1H, vinyl C*H*), 3.92 (s, 3H), 3.09 (qd, 2H, *J* = 7.5, 1.0 Hz), 2.64 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.26 (t, 3H, *J* = 7.5 Hz, CH(CH_3)$_2$).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ 181.96, 175.93, 162.89, 162.72, 158.05, 150.81, 140.47, 139.74, 127.48, 125.97, 119.98, 115.12, 34.49, 27.94, 23.36, 13.93.

HRMS (ESI-TOF) calcd for $C_{16}H_{15}N_2O_4$ $(M+H)^+$: 299.1032, found: 299.1041.

Melting Point: >290 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3036 (w), 2968 (w), 2926 (w), 1680 (m), 1651 (b, s), 1601 (m), 1583 (m), 1397 (w), 1375 (w), 1348 (m), 1287 (w), 1156 (w), 1100 (w).



18

Synthesized from **70**, (Z)-3-iodo-N-methylbut-2-enamide, and **30** by General Protocols D, E, F, and H. 11% yield over 4 steps. Compound is an orange solid.

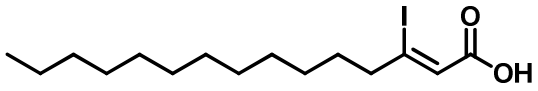
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.48 (bs, 1H, N*H*), 6.79 (d, 1H, *J* = 1.5 Hz, vinyl C*H*), 6.69 (s, 1H, vinyl C*H*), 3.93 (s, 3H), 3.00 (t, 2H, *J* = 7.5 Hz) 2.61 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.62 (sext, 2H, *J* = 7.5 Hz), 1.04 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.55, 175.57, 162.35, 156.13, 150.44, 140.04, 139.38, 127.23, 126.62, 119.70, 114.83, 36.32, 34.18, 23.08, 22.95, 13.83.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+H)^+$: 313.1188, found: 313.1187.

Melting Point: >280 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3031 (w), 2961 (w), 2912 (w), 1680 (m), 1651 (b, s), 1604 (w), 1583 (w), 1455 (w), 1398 (w), 1350 (m), 1289 (m), 1261 (w), 1160 (w), 1105 (w).



56

To an oven-dried Schlenk flask was added 1-tetradecyne (0.748 g, 3.85 mmol) and THF (10 mL). Chilled to -78 ºC. Added n-BuLi (2.7 mL, 4.32 mmol) dropwise then stirred for 10 minutes. Added a large excess of solid carbon dioxide then allowed the reaction to warm to RT. The solvent was evaporated and the residue was purified by silica gel chromatography. Product was collected as a colorless oil (1.01 g, 3.79 mmol, 88% yield). Followed by General Protocol C, 71% yield.

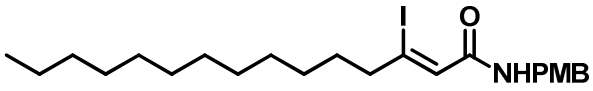
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.39 (s, 1H, vinyl C*H*), 2.72 (t, 2H, *J* = 7 Hz), 1.60 (bp, 2H, *J* = 7.0), 1.33-1.22 (m, 18H), 0.88 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 168.90, 125.50, 124.24, 48.54, 32.07, 29.79, 29.78, 29.74, 29.61, 29.50, 29.46, 29.44, 28.39, 22.85, 14.29.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+Na)^+$: 389.0954, found: 389.0950.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3533 (b, s), 3295 (s), 3080 (m), 2954 (m), 2864 (m), 1651 (s), 1633 (m), 1557 (s), 1538 (m), 1431 (w), 1365 (w), 1330 (w), 1228 (w), 1208 (w).



57

Synthesized from **56** and 4-methoxybenzylamine by General Protocol B. 90% yield. Compound is an off-white solid.

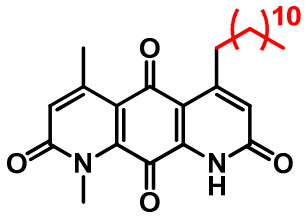
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.11 (d, 2H, *J* = 8.5 Hz, aryl C*H*), 6.72 (d, 2H, *J* = 8.5 Hz, aryl C*H*), 6.31 (s, 1H, vinylic C*H*), 4.251 (d, 2H, *J* = 5.5 Hz, NCH_2), 3.66 (s, 3H, OCH_3), 2.49 (t, 2H, *J* = 7 Hz), 1.47 (bp, 2H, *J* = 7.0), 1.33-1.22 (m, 18H), 0.83 (t, 3H, *J* = 7.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.88, 159.12, 129.96, 129.50, 128.16, 114.77, 114.11, 55.41, 55.37, 55.32, 55.28, 47.25, 43.18, 31.99, 29.70, 29.56, 29.42, 29.30, 28.38, 22.77, 14.22.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+H)^+$: 486.1869, found: 486.1862.

Melting Point: 50.2-55.0 °C

IR (cm^{-1}, thin film in $CHCl_3$): 3417 (b, s), 3303 (s), 3066 (m), 2925 (s), 2853 (m), 1651 (s), 1621 (s), 1540 (m), 1513 (s), 1464 (m), 1337 (w), 1302 (2), 1248 (m), 1175 (m), 1084 (w).



19

Synthesized from **70**, (Z)-3-iodo-N-methylbut-2-enamide, and **57** by General Protocols D, E, F, and H. 20% yield over 4 steps. Compound is an orange solid.

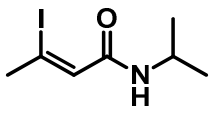
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.78 (s, vinyl C*H*), 6.67 (s, 1H), 3.92 (s, 3H), 3.03 (t, *J* = 7.5 Hz), 2.64 (d, 3H, *J* = 1.0 Hz, allylic C*H*$_3$), 1.58 (p, 2H, *J* = 7.5 Hz), 1.44 (p, 2H, *J* = 7.5 Hz), 1.27-1.4 (m, 16H), 0.89 (t, 3H, *J* = 7.5 Hz).

^{13}C-NMR (d-TFA, 125 MHz): δ182.21, 176.18, 166.64, 166.55, 165.56, 158.87, 141.347, 140.27, 128.14, 127.13, 126.09, 120.54, 37.93, 36.73, 33.95, 31.84, 31.61 (2H), 31.54, 31.42, 31.38, 31.34, 31.13, 24.50 24.37, 14.79.

HRMS (ESI-TOF) calcd for $C_{26}H_{35}N_2O_4$ $(M+H)^+$: 439.2597, found: 439.2590.

Melting Point: >230 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 2954 (w), 2918 (m), 2850 (m), 1677 (s), 1651 (s), 1639 (s), 1587 (w), 1505 (w), 1408 (w), 1352 (w), 1290 (w), 1254 (w), 1160 (w), 1087 (w).



58

Synthesized from (Z)-3-iodobut-2-enoic acid[1] and isopropylamine by General Protocols B. 74% yield over 4 steps. Compound is a off-white solid.

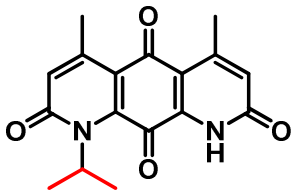
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.19 (d, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.52 (bs, 1H, N*H*), 4.18 (sextet, 1H, *J* = 7.5 Hz), 2.64 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.20 (d, 6H, *J* = 7.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.85, 129.28, 105.58, 35.75, 34.45, 14.74. 25Oct11_8-167-1_VXR500

HRMS (ESI-TOF) calcd for $C_7H_{13}NOI$ $(M+H)^+$: 254.0042, found: 254.0043.

Melting Point: 68.8-71.3 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3248 (m), 3060 (w), 2965 (m), 1642 (m), 1628 (s), 1557 (s), 1466 (w), 1347 (w), 1333 (w), 1240 (m), 1163 (w), 1073 (w).



20

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **58** by General Protocols D, E, G, and H. 20% yield over 4 steps. Compound is a yellow/orange oily solid.

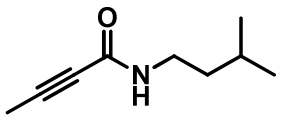
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.74 (bs, 1H, N*H*), 6.67 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.62 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 5.00 (sept, 1H, J = 7.0 Hz), 2.61 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.56 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.67 (d, 6H, *J* = 7.0 Hz, CH(CH_3)$_2$).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ 181.83, 176.18, 163.26, 162.57, 152.34, 149.75, 143.05, 139.79, 129.12, 127.42, 120.40, 115.16, 55.91, 23.01, 22.32, 20.29.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_4$ $(M+H)^+$: 313.1188, found: 313.1197.

Melting Point: >280 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 2982 (b, w), 1677 (w), 1647 (b, s), 1611 (m), 1587 (w), 1396 (w), 1344 (w), 1288 (w).



59

Synthesized from ethyl-2-butynoate and isoamylamine by General Protocol A. 73% yield. Compound is a white crystalline solid.

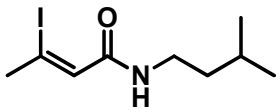
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.84 (bs, 1H, major rotamer, N*H*), 3.37 (q, 2H, *J* = 7.0 Hz, minor rotamer, NCH_2), 3.27 (q, 2H, *J* = 7.0 Hz, major rotamer, NCH_2), 1.99 (d, 3H, *J* = 1.5 Hz, minor rotamer, allylic CH_3), 1.90 (d, 3H, *J* = 1.5 Hz, major rotamer, allylic CH_3), 1.59 (sept, 1H, *J* = 6.5 Hz, major rotamer, C*H*), 1.38 (q, 2H, *J* = 7.5 Hz, major rotamer CH_2CH_2CH), 0.91 (d, 6H, *J* = 6.5 Hz, minor rotamer $CH(CH_3)_2$), 0.88 (d, 6H, *J* = 6.5 Hz, major rotamer, $CH(CH_3)_2$)

^{13}C-NMR ($CDCl_3$, 125 MHz) δ 156.19 (minor), 153.45 (major), 89.12 (minor), 82.24 (major), 74.74 (major), 72.37 (minor), 41.28 (minor), 39.12 (minor), 37.70 (major), 37.63 (major), 25.40 (major), 25.05 (minor), 22.02 (major), 3.50 (minor), 3.22 (major).

HRMS (ESI) calcd for $C_9H_{16}NO$ $(M+H)^+$: 154.1232, found: 154.1233.

Melting Point: 42.2-43.3 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3626 (b, s), 3303 (s), 3073 (m), 2955 (m), 2871 (w), 2256 (w), 2219 (w), 1651 (s), 1557 (m), 1470 (w), 1455 (w), 1368 (w), 1299 (w), 1230 (w), 1158 (w).



60

Synthesized from **59** by General Protocol C. 95% yield. Compound is a light gold oil.

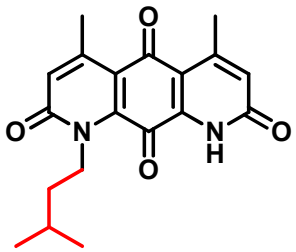
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.22 (q, 1H, *J* = 1.5 Hz, vinyl C*H*), 5.82 (bs, 1H, N*H*), 3.33 (dq, 2H, *J* = 7.5, 1.0 Hz), 2.63 (d, 3H, *J* = 1.5 Hz, allylic CH_3), 1.64 (sept, 1H, *J* = 6.5 Hz), 1.43 (q, 2H, *J* = 7.0 Hz), 0.91 (d, 6H, *J* = 6.5 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz) δ 165.02, 129.91, 105.08, 50.64, 35.74, 31.98, 27.43, 27.20.

HRMS (ESI-TOF) calcd for $C_9H_{17}NOI$ $(M+H)^+$: 282.0355, found: 282.0351.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in $CDCl_3$): 3519 (b, w), 3307 (s), 3074 (m), 2957 (s), 1651 (s), 1633 (s), 1538 (s), 1470 (m), 1455 (m), 1434 (w), 1367 (w), 1231 (w), 1090 (w).



21

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **60** by General Protocols D, E, F, and H. 12% yield over 4 steps. Compound is a red solid.

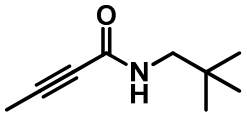
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.76 (q, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.67 (q, 1H, *J* = 1.5 Hz, vinyl C*H*), 4.52-4.49 (m, 2H), 2.64 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.63 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.81 (sept, 1H, *J* = 7.0 Hz, C*H*), 1.68-1.63 (m, 2H, CH_2CH_2CH), 1.03 (d, 6H, *J* = 6.5 Hz, $CH(CH_3)_2$).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ 181.48, 175.02, 161.83, 161.65, 151.69, 149.89, 139.30, 138.50, 127.42, 127.23, 119.52, 114.77, 45.45, 37.28, 26.49, 22.89, 22.02, 21.83.

HRMS (ESI-TOF) calcd for $C_{19}H_{21}N_2O_4$ $(M+H)^+$: 341.1501, found: 341.1507.

Melting Point: >280 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1684 (m), 1651 (b, s), 1611 (m), 1590 (m), 1469 (w), 1402 (w), 1290 (w), 1261 (w), 1157 (w), 1056 (w).



61

Synthesized from ethyl-2-butynoate and neopentylamine by General Protocol A. 38% yield. Compound is a white crystalline solid.

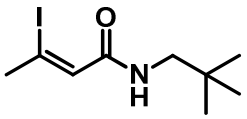
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.75 (bs, 1H, major rotamer N*H*), 3.17 (d, 2H, *J* = 7.0 Hz, minor rotamer NCH_2), 3.09 (d, 2H, *J* = 6.5 Hz, major rotamer NCH_2), 2.01 (s, 3H, minor rotamer allylic CH_3), 1.94 (s, 3H, major rotamer allylic CH_3), 0.93 (s, 9H, minor rotamer), 0.92 (s, 9H, major rotamer).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 156.81, 153.77, 89.95, 83.20, 75.08, 72.77, 55.08, 50.77, 32.22, 31.99, 27.19, 27.07, 4.01, 3.72.

HRMS (ESI) calcd for $C_9H_{16}NO$ $(M+H)^+$: 154.1232, found: 154.1233.

Melting Point: 76.5-78.5 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3310 (b, s), 1961 (m), 2248 (m), 2213 (m), 1651 (s), 1574 (m), 1434 (w), 1366 (w), 1281 (m), 1211 (w).



62

Synthesized from **61** by General Protocol C. 96% yield. Compound is white amorphous powder.

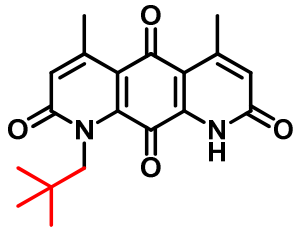
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.29 (q, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.78 (bs, 1H, N*H*), 3.16 (d, 2H, *J* = 6.0 Hz), 2.66 (d, 3H, *J* = 1.0 Hz), 0.96 (s, 9H).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 165.02, 129.91, 105.08, 50.64, 35.74, 31.98, 27.43, 27.20.

HRMS (ESI-TOF) calcd for $C_9H_{17}NOI$ $(M+H)^+$: 282.0355, found: 282.0354.

Melting Point: 92.3-94.5 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3442 (b, m), 3298 (s), 3080 (w), 2956 (m), 1652 (s), 1633 (s), 1557 (m), 1463 (w), 1428 (w), 1365 (w), 1228 (m), 1208 (m), 1063 (w).



22

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **62** by General Protocols D, E, F, and H. 10% yield over 4 steps. Compound is a red solid.

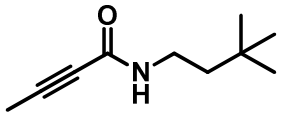
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.75 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.67 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.95 (bs, 1H), 4.86 (bs, 1H), 2.64 (s, 6H, allylic CH_3), 0.87 (s, 9H, (CH_3)$_3$).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ181.20, 176.32, 162.40, 149.55, 141.41, 139.05, 127.31, 127.19, 119.33, 114.87, 51.10, 34.31, 27.58, 22.80, 21.67.

HRMS (ESI-TOF) calcd for $C_{19}H_{21}N_2O_4$ $(M+H)^+$: 341.1501, found: 341.1498.

Melting Point: >270 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 1663 (s), 1651 (s), 1628 (s), 1462 (w), 1396 (w), 1367 (w), 1301 (w), 1106 (w), 1073 (w).



63

Synthesized ethyl-2-butynoate and 3,3-dimethylbutan-1-amine by General Protocol A. 76% yield. Compound is a white amorphous solid.

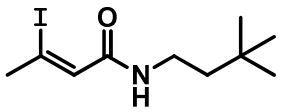
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.00 (bs, 1H, minor rotamer N*H*), 5.60 (bs, 1H, major rotamer N*H*), 3.39 (m, 2H, minor rotamer NCH_2), 3.29 (m, 2H, major rotamer NCH_2), 2.02 (s, 3H, minor rotamer allylic CH_3), 1.93 (s, 3H, major rotamer allylic CH_3), 1.46 (m, 2H, minor rotamer), 1.42 (m, 2H, major rotamer), 0.94 (s, 9H, minor rotamer), 0.92 (s, 9H, major rotamer).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 153.56, 82.97, 75.14, 43.10, 36.64, 30.04, 29.49, 3.78.

HRMS (ESI) calcd for $C_{10}H_{18}NO$ $(M+H)^+$: 168.1388, found: 168.1387.

Melting Point: 70.5-72.0 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 3289 (b, m), 3064 (w), 2955 (s), 2255(m), 2216 (m), 1636 (s), 1540 (s), 1473 (m), 1365 (m), 1309 (m), 1286 (m), 1189 (w), 1075 (w).



64

Synthesized from **63** by General Protocol C. 93% yield. Compound is a pale brown oil.

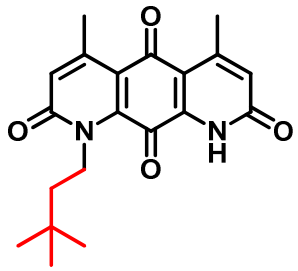
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.21 (q, 1H, *J* = 1.5 Hz, vinyl C*H*), 6.02 (bs, 1H, N*H*), 3.31-3.27 (m, 2H), 2.61 (d, 3H, *J* = 1.5 Hz, NCH_3), 1.44-1.41 (m, 2H), 0.89 (s, 9H).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.78, 129.39, 105.53, 43.17, 36.31, 35.77, 30.02, 29.50.

HRMS (ESI-TOF) calcd for $C_{10}H_{19}NOI$ $(M+H)^+$: 296.0511, found: 296.0513.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film, neat): 3289 (b, m), 3073 (w), 2955 (s), 2857 (m), 1653 (s), 1621 (m), 1541 (s), 1474 (w), 1431 (w), 1364 (w), 1333(w), 1229 (m), 1074 (w).



23

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **64** by General Protocols D, E, F, and H. 17% yield over 4 steps. Compound is a red solid.

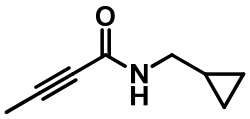
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.75 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.66 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.57-4.53 (m, 2H), 2.63 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.62 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.66 (m, 2H, $CH_2CH_2C(CH_3)_3$, 1.07 (s, 9H, $C(CH_3)_3$).

^{13}C-NMR (2:1 $CDCl_3$:CD_3OD, 125 MHz): δ 181.46, 174.98, 161.81, 161.60, 151.64, 149.82, 139.35, 138.45, 127.38, 127.21, 119.53, 114.74, 43.73, 41.45, 29.97, 28.87, 22.88, 21.81.

HRMS (ESI-TOF) calcd for $C_{20}H_{23}N_2O_4$ $(M+H)^+$: 355.1658, found: 355.1664.

Melting Point: >290 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 2940 (w), 1652 (b, s), 1614 (w), 1583 (w), 1386 (w), 1372 (w), 1331 (w), 1293 (w), 1177 (w), 1108 (w).



65

Synthesized from ethyl-2-butynoate and cyclopropylmethanamine by General Protocol A. 94% yield. Compound is a clear, colorless oil.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.94 (bs, 1H, major rotamer N*H*), 5.91 (bs, 1H, minor rotamer N*H*), 3.25 (dd, 2H, *J* = 5.5 and 1.5 Hz, minor rotamer NCH_2CH), 3.13 (dd, 2H, *J* = 5.5 Hz and 1.5 Hz, major rotamer NCH_2CH), 1.99 (s, 3H, minor rotamer CH_3), 1.92 (s, 3H, major rotamer

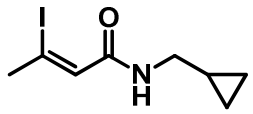
C*H*$_3$), 0.92 (m, 1H, *J* = 0.9 Hz, NCH$_2$C*H*(CH$_2$)$_2$), 0.48 (m, 2H, NCH$_2$CH(C*H*$_2$)$_2$), 0.19 (m, 2H, NCH$_2$CH(C*H*$_2$)$_2$).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 153.47 (major), 83.15 (major), 76.90 (major), 48.22 (minor), 44.66 (major), 11.52 (minor), 10.55 (major), 3.73 (major), 3.52 (major).

HRMS (ESI) calcd for $C_8H_{12}NO$ $(M+H)^+$: 138.0919, found: 138.0916.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film in CCl_4): 3276 (b, m), 3080 (b, w), 2964 (w), 2253 (m), 2217 (m), 1632 (s), 1536 (s), 1437 (m) 1287 (s), 1168 (w).



66

Synthesized from **65** by General Protocol C. 65% yield. Compound is a yellow/orange oily solid.

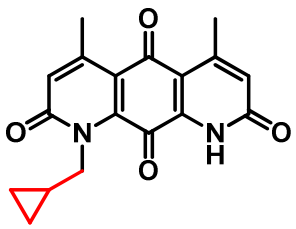
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.24 (d, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.80 (bs, 1H, N*H*), 3.20 (dd, 2H, *J* = 5.5 and 1.0 Hz, NC*H*$_2$CH), 2.66 (d, 3H, *J* = 1.5 Hz, allylic C*H*$_3$), 1.01 (m, 1H, NCH$_2$C*H*(CH$_2$)$_2$), 0.53 (m, 2H, NCH$_2$CH(C*H*$_2$)$_2$), 0.24 (m, 2H, NCH$_2$CH(C*H*$_2$)$_2$).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.81, 129.47, 105.71, 44.41, 35.76, 10.63, 3.64.

HRMS (ESI-TOF) calcd for $C_8H_{13}NOI$ $(M+H)^+$: 266.0042, found: 266.0041.

Melting Point Not determined.

IR (cm^{-1}, thin film in $CHCl_3$): 3438 (w), 2960 (w), 1655 (s), 1620 (m), 1560 (w), 1508 (m) 1466 (m), 1381 (w), 1208 (w), 1094 (w).



24

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **66** by General Protocols D, E, G, and H. 16% yield over 4 steps. Compound is an orange solid.

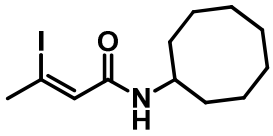
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.78 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.69 (d, 1H, *J* = 1.5 Hz, vinyl C*H*), 4.61 (d, *J* = 7.0 Hz, 2H), 2.62 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.61 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.19 (sept, 1H, *J* = 6.5 Hz, C*H*), 0.50 (d, *J* = 6.5 Hz 4H, CH(CH_2)$_2$).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.73, 175.33, 161.55, 160.55, 151.25, 149.24, 138.83, 137.76, 128.96, 128.46, 119.99, 114.54, 49.24, 23.51, 22.37, 11.54, 4.35. 6-29-11_BIP2-77_13C_u500

HRMS (ESI-TOF) calcd for $C_{18}H_{17}N_2O_4$ $(M+H)^+$: 325.1188, found: 325.1181.

Melting Point: >260 °C.

IR (cm^{-1}, thin film in $CDCl_3$): 1677 (w), 1651 (s), 1632 (w), 1604 (w), 1392 (w), 1375 (w), 1358 (w), 1293 (w), 1205 (w), 1167 (w), 1098 (w).



67

Synthesized from (Z)-3-iodobut-2-enoic acid and cyclooctylamine by General Protocols B. 92% yield. Compound is a yellow/brown oil.

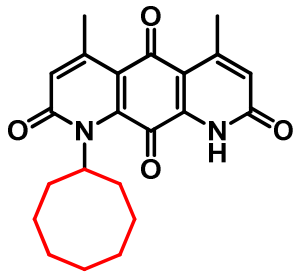
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.19 (d, 1H. *J* = 1.5 Hz, vinyl C*H*), 5.81 (bs, 1H, N*H*), 4.06 (m, 1H, NC*H*), 2.61 (d, 3H, *J* = 1.5 Hz, allylic CH_3) 1.86 (m, 2H), 1.65 (m, 2H), 1.54 (m, 10H).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 163.76, 129.87, 105.07, 49.56, 35.67, 32.05, 27.27, 25.46, 23.76.

HRMS (ESI-TOF) calcd for $C_{12}H_{21}NOI$ $(M+H)^+$: 322.0668, found: 322.0667.

Melting Point: Not determined (oil).

IR (cm^{-1}, thin film in $CHCl_3$): 3424 (w), 3293 (b, m), 3060 (w), 2923 (w), 1649 (s), 1624 (s), 1539 (s), 1473 (m), 1447 (m), 1426 (m), 1375 (w), 1351 (w), 1226 (s), 1128 (w), 1081 (m).



25

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **67** by General Protocols D, E, G, and H. 4% yield over 4 steps. Compound is a yellow/orange oily solid.

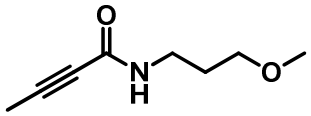
^{1}H-NMR ($CDCl_3$, 400 MHz): δ 6.65 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.63 (d, 1H, *J* = 1.5 Hz, vinyl C*H*), 5.02 (m, 1H), 2.60 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.55 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 1.79 (m, 14 HCH_2)$_7$),

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.71, 175.87, 161.81, 161.07, 151.51, 148.69, 141.52, 138.64, 129.80, 128.02, 120.01, 114.55, 32.97, 26.60, 26.56, 26.31, 23.24, 22.42.

HRMS (ESI-TOF) calcd for $C_{22}H_{25}N_2O_4$ $(M+H)^+$: 381.1814, found: 381.1820.

Melting Point: >250 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 2925 (m), 1666 (s), 1651 (s), 1611 (m), 1587 (w), 1470 (w), 1397 (w), 1375 (w), 1354 (w), 1295 (w), 1170 (w), 1110 (w).



68

Synthesized from ethyl-2-butynoate and 3-methoxypropan-1-amine by General Protocol A. 65% yield. Compound is a clear, colorless oil.

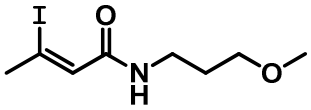
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.27 (bs, 1H, major rotamer N*H*), 6.02 (bs, 1H, minor rotamer N*H*), 3.46 (t, 2H, *J* = 6.0 Hz), 3.38 (q, 2H, *J* = 6.5 Hz), 3.34 (s, 3H), 1.92 (s, 3H), 1.77 (pent, 2H, *J* = 6.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 156.37 (minor), 153.62 (major), 89.82 (minor), 82.95 (major), 75.00 (major), 72.58 (minor), 71.28 (major), 70.45 (minor), 58.77 (major), 41.34 (minor), 38.04 (major), 30.15 (minor), 28.87 (major), 3.97 (minor), 3.64 (major).

HRMS (ESI-TOF) calcd for $C_8H_{14}NO_2$ $(M+H)^+$: 156.1025, found: 156.1029.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film, neat): 3491 (b, m), 3273 (s), 3064 (w), 2928 (s), 2829 (w), 2255 (m), 2222 (m), 1651 (s), 1539 (s), 1446 (m), 1391 (w), 1287 (m), 1225 (w), 1191 (w), 1114 (m), 1029 (w).



69

Synthesized from **68** by General Protocol C. 96% yield. Compound is a light yellow oil.

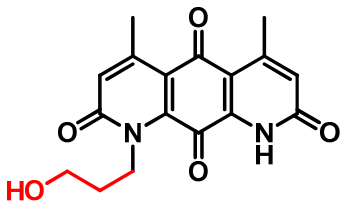
^{1}H-NMR ($CDCl_3$, 500 MHz): δ 6.26 (bs, 1H, N*H*), 6.21 (d, 1H. *J* = 1.0 Hz, vinyl C*H*), 3.49 (t, 2H, *J* = 6.0 Hz), 3.42 (q, 2H, *J* = 6.5 Hz), 3.34 (s, 3H), 2.64 (d, 3H, *J* = 1.5 Hz), 1.81 (pent, 2H, *J* = 6.0 Hz).

^{13}C-NMR ($CDCl_3$, 125 MHz): δ 164.90, 129.40, 105.51, 71.65, 58.93, 38.02, 35.78, 29.07.

HRMS (ESI-TOF) calcd for $C_8H_{15}NO_2I$ $(M+H)^+$: 284.0148, found: 284.0147.

Melting Point Not determined (oil).

IR (cm^{-1}, thin film, neat): 3491 (m), 3290 (s), 3069 (m), 2927 (s), 2872 (s), 1651 (s), 1538 (s), 1434 (m), 1374 (w), 1336 (w), 1229 (s), 1190 (m), 1080 (m), 1031 (w).



26

Synthesized from **70**, (Z)-3-iodo-N-(4-methoxybenzyl)but-2-enamide, and **69** by General Protocols D, E, G, and H. 22% yield over 4 steps. Compound is an orange solid.

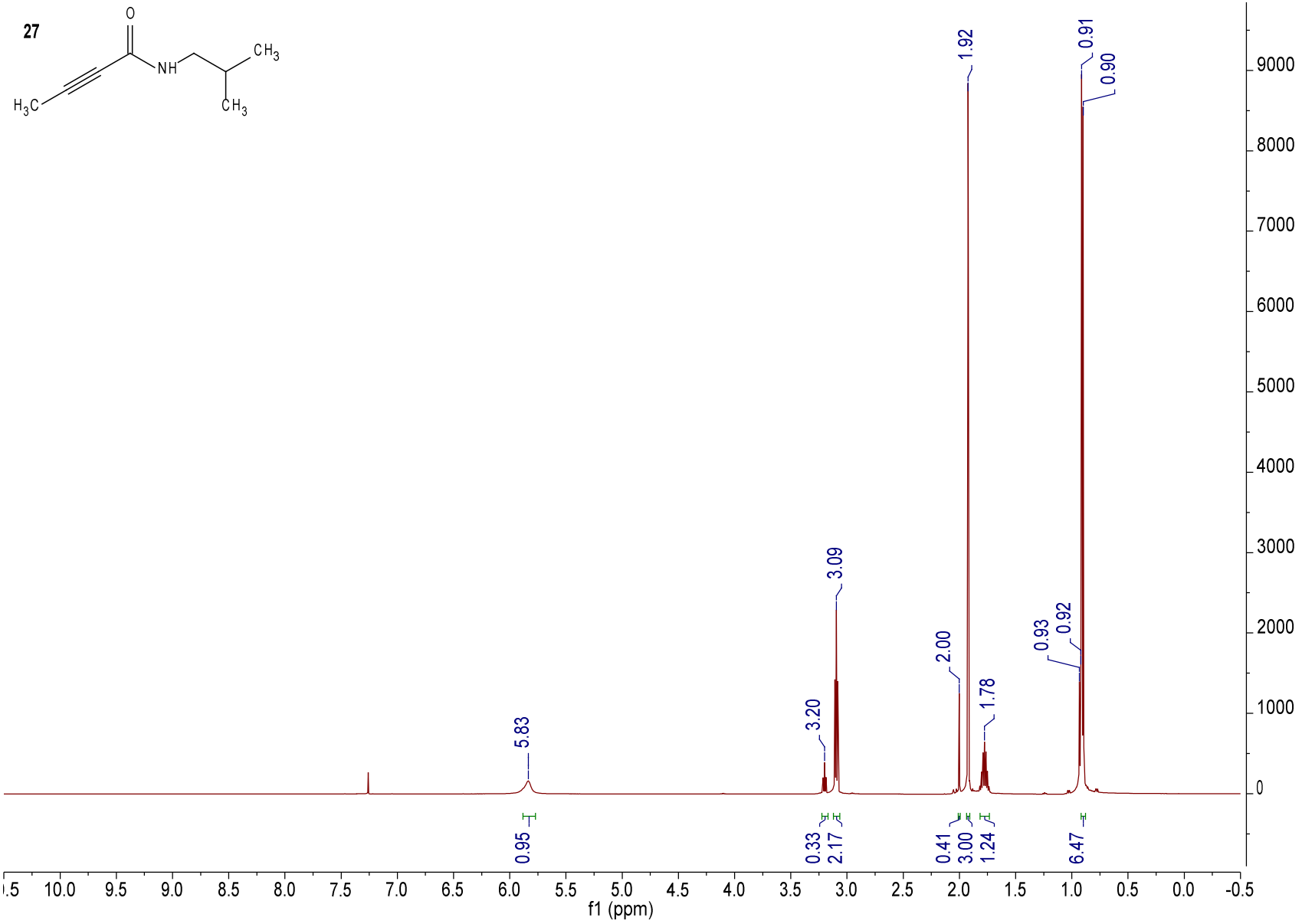
^{1}H-NMR (2:1 $CDCl_3$:CD_3OD, 500 MHz): δ 6.76 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 6.65 (d, 1H, *J* = 1.0 Hz, vinyl C*H*), 4.58 (t, 2H, *J* = 7.5 Hz), 3.70 (t, 2H, *J* = 6.0 Hz), 2.63 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.63 (d, 3H, *J* = 1.0 Hz, allylic CH_3), 2.06-2.01 (m, 2H).

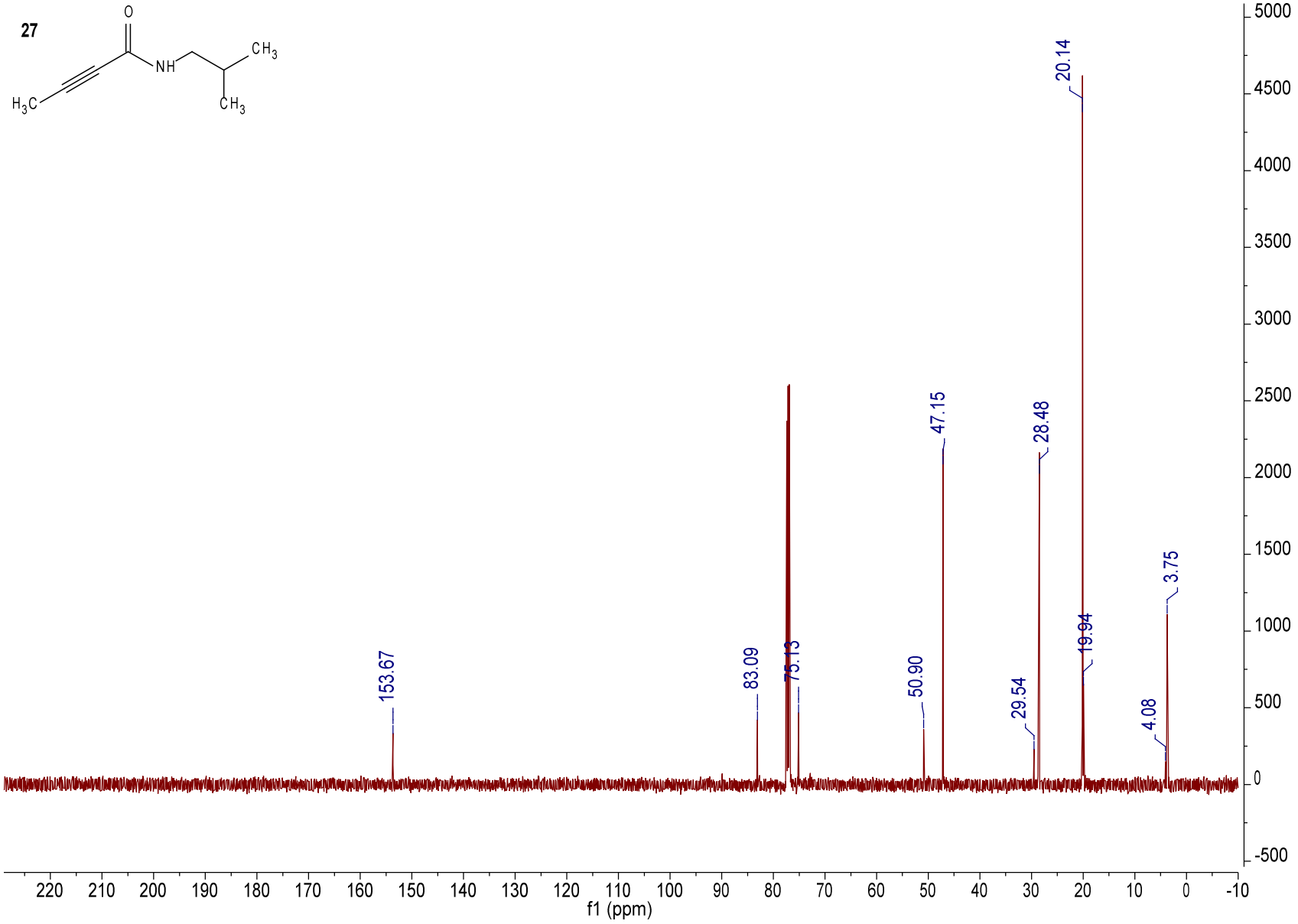
^{13}C-NMR ($CDCl_3$, 125 MHz): δ 181.76, 175.59, 162.35, 151.91, 150.60, 140.16, 139.33, 127.45, 127.40, 119.76, 115.06, 59.79, 44.48, 31.66, 23.21, 22.15.

HRMS (ESI-TOF) calcd for $C_{17}H_{17}N_2O_5$ $(M+H)^+$: 329.1137, found: 329.1129.

Melting Point: >270 °C.

IR (cm^{-1}, thin film in $CHCl_3$): 3446 (b, s), 1646 (s), 1642 (s), 1635 (s), 1392 (w), 1373 (w), 1306 (w), 1292 (w).


27
O
NH
CH3
H3C
CH3
5.83
3.20
3.09
2.00
1.92
1.78
0.93
0.92
0.91
0.90
0.95
0.33
2.17
0.41
3.00
1.24
6.47
f1 (ppm)


27
O
NH
CH3
CH3
H3C
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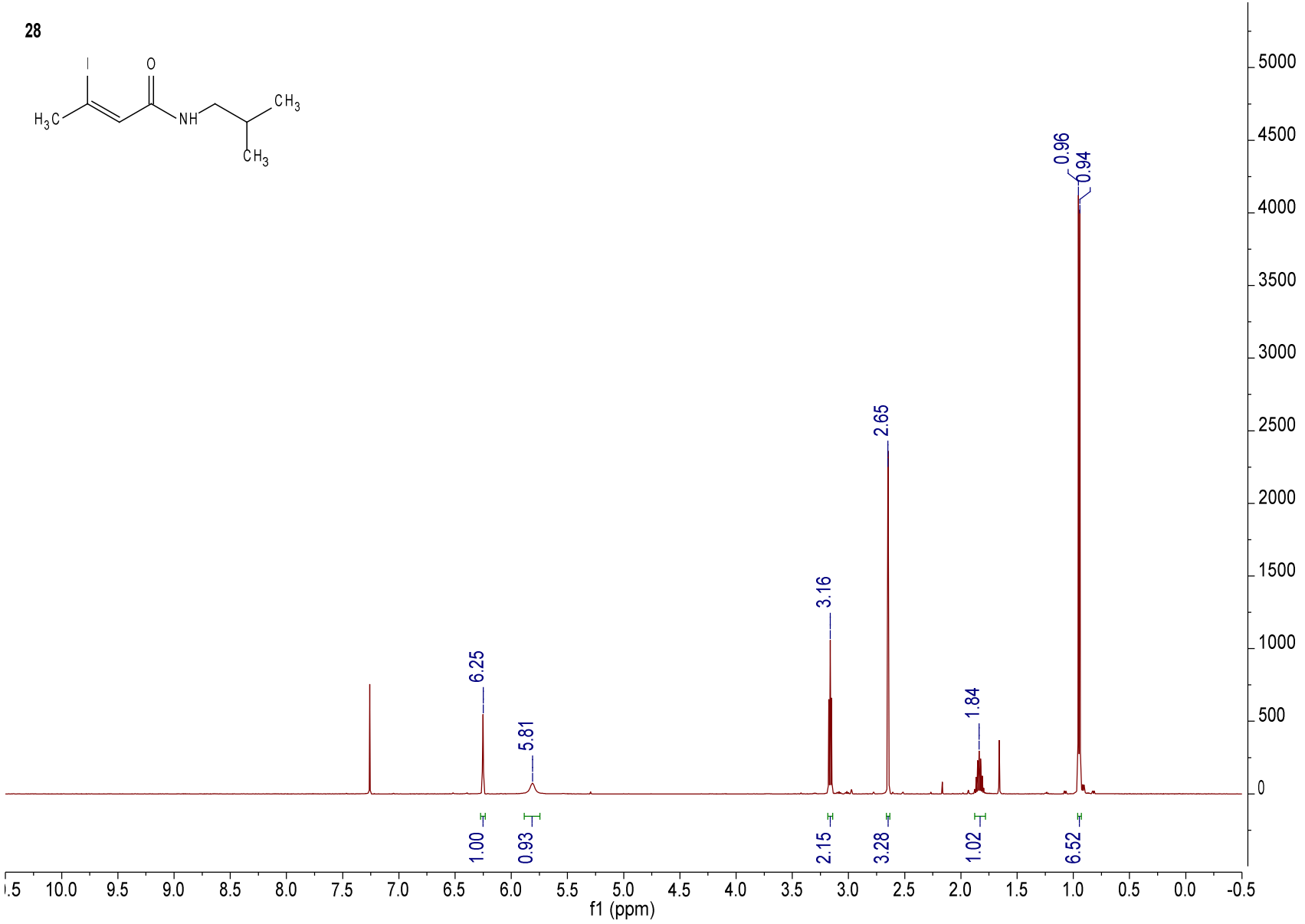
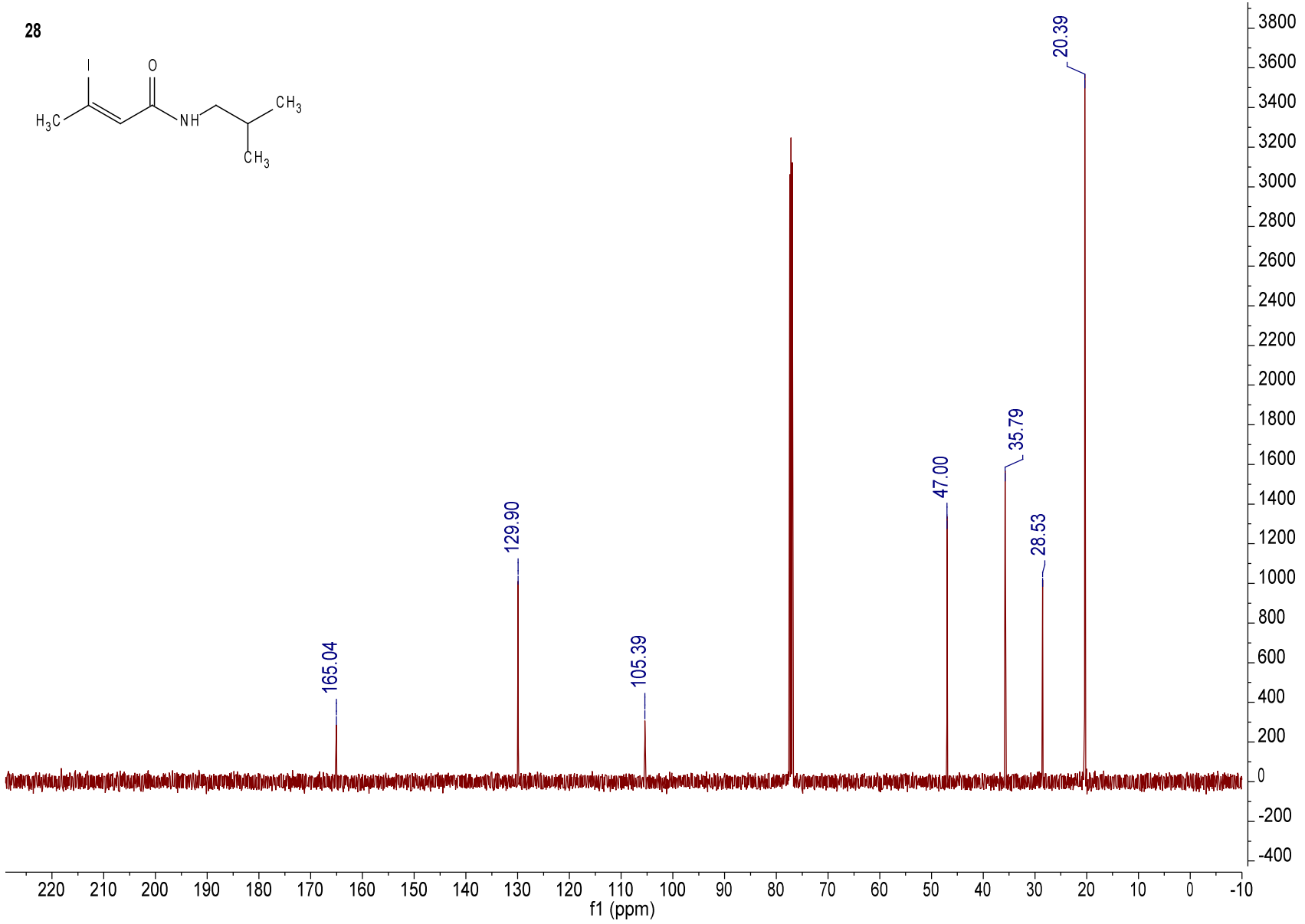
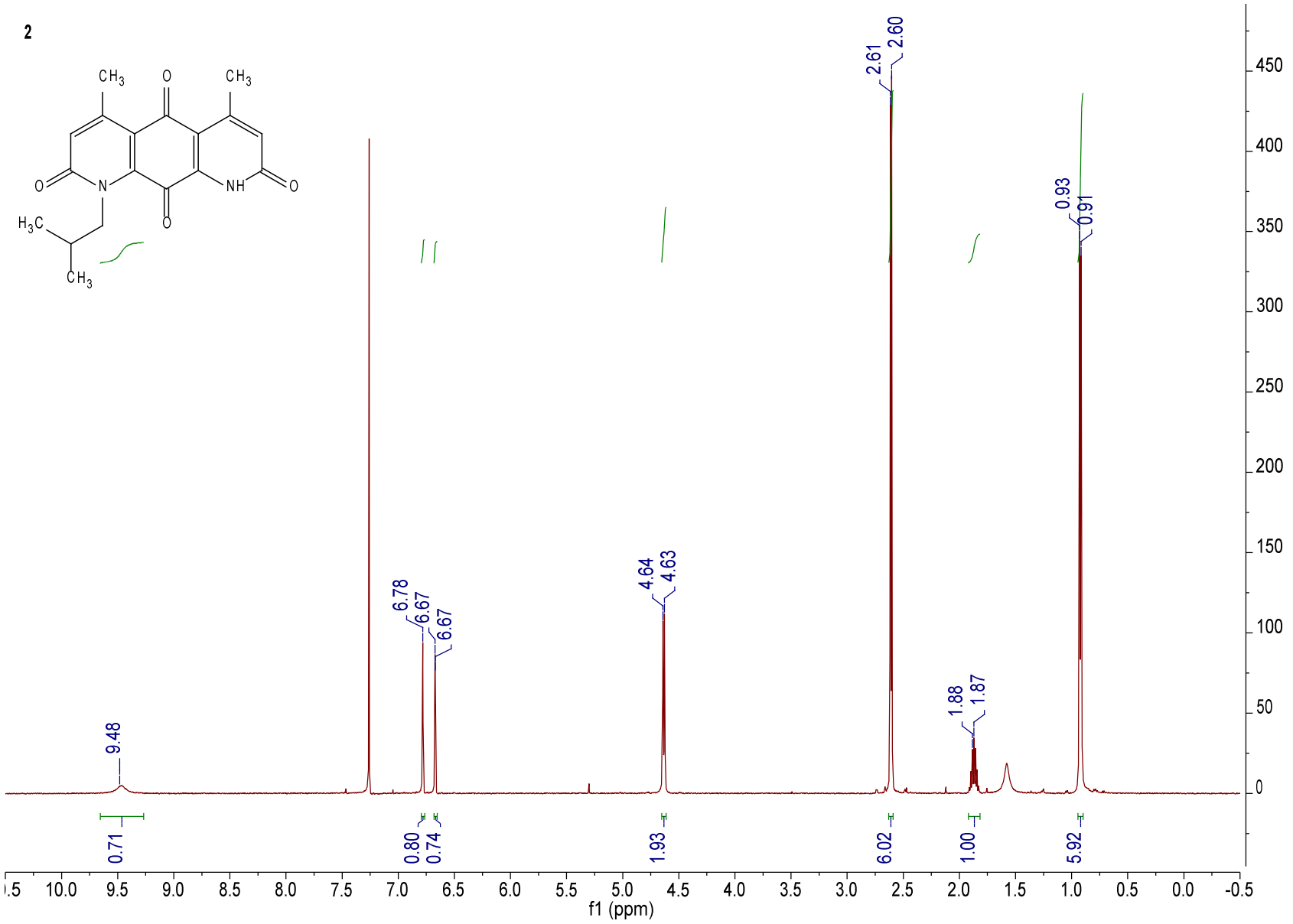
83.09
75.13
50.90
47.15
29.54
28.48
20.14
19.94
4.08
3.75
f1 (ppm)


28
O
NH
CH3
CH3
H3C
6.25
5.81
3.16
2.65
1.84
0.96
0.94
1.00
0.93
2.15
3.28
1.02
6.52
f1 (ppm)


28
I
O
H_3C
NH
CH_3
CH_3
165.04
129.90
105.39
47.00
35.79
28.53
20.39
f1 (ppm)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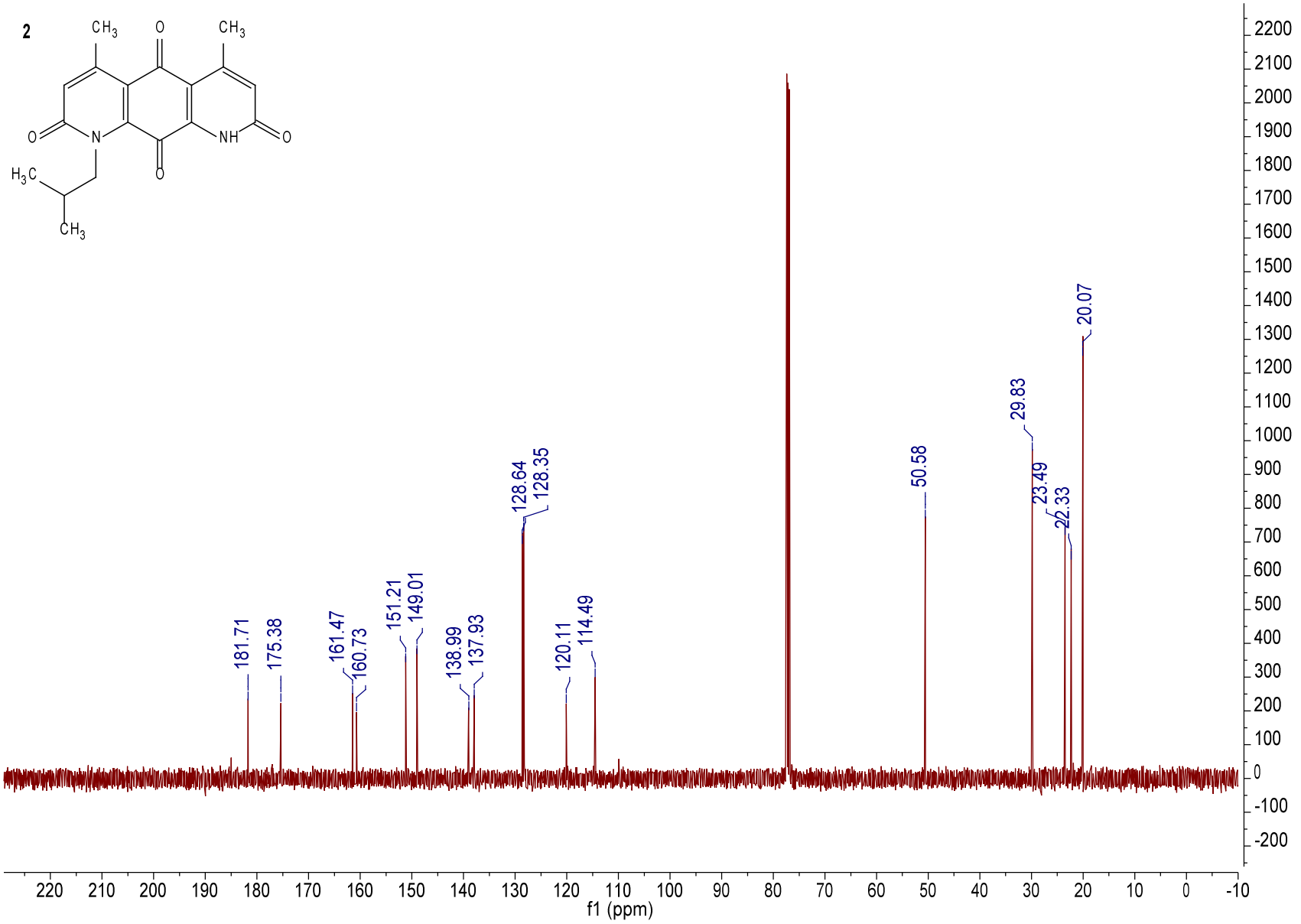
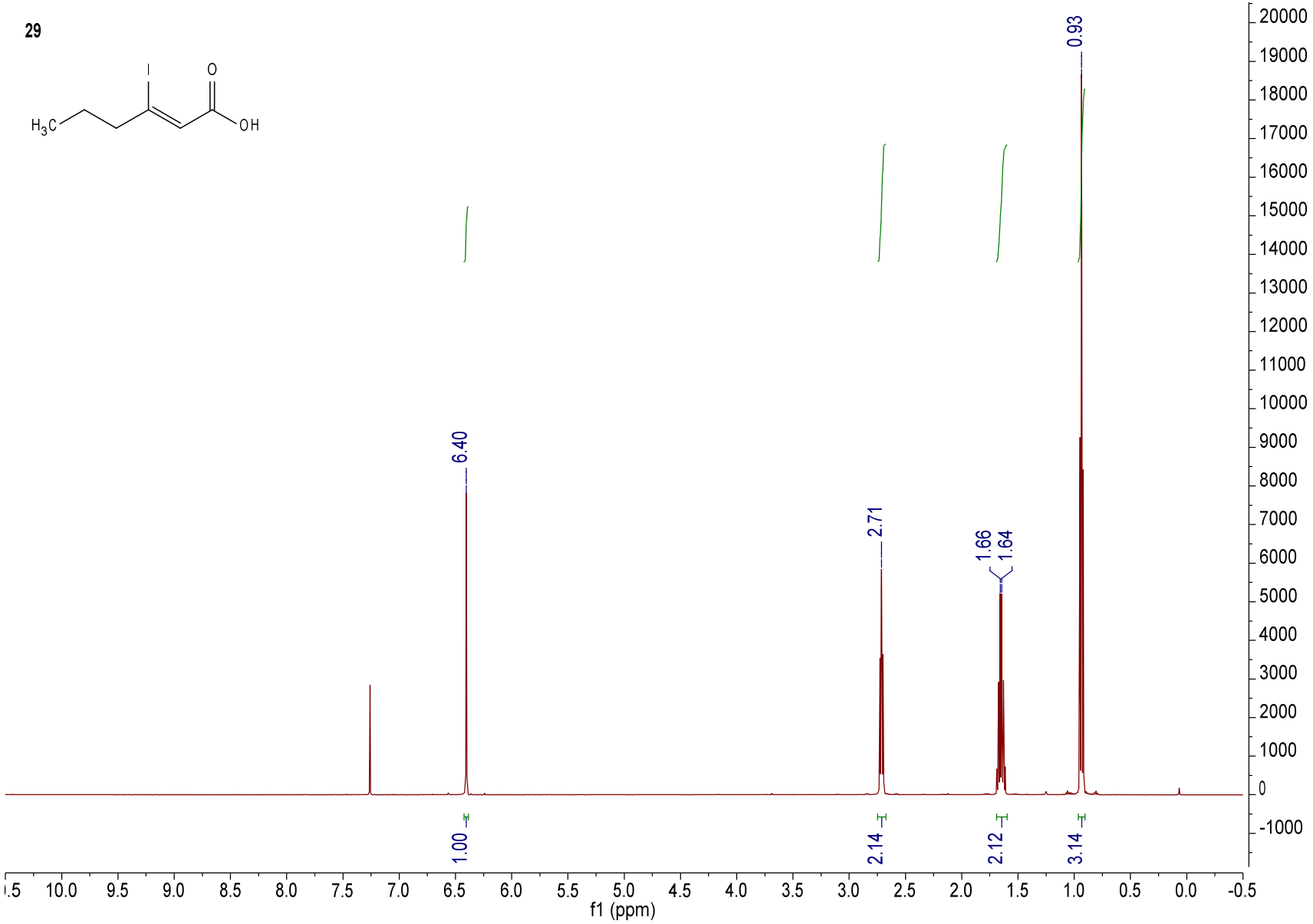
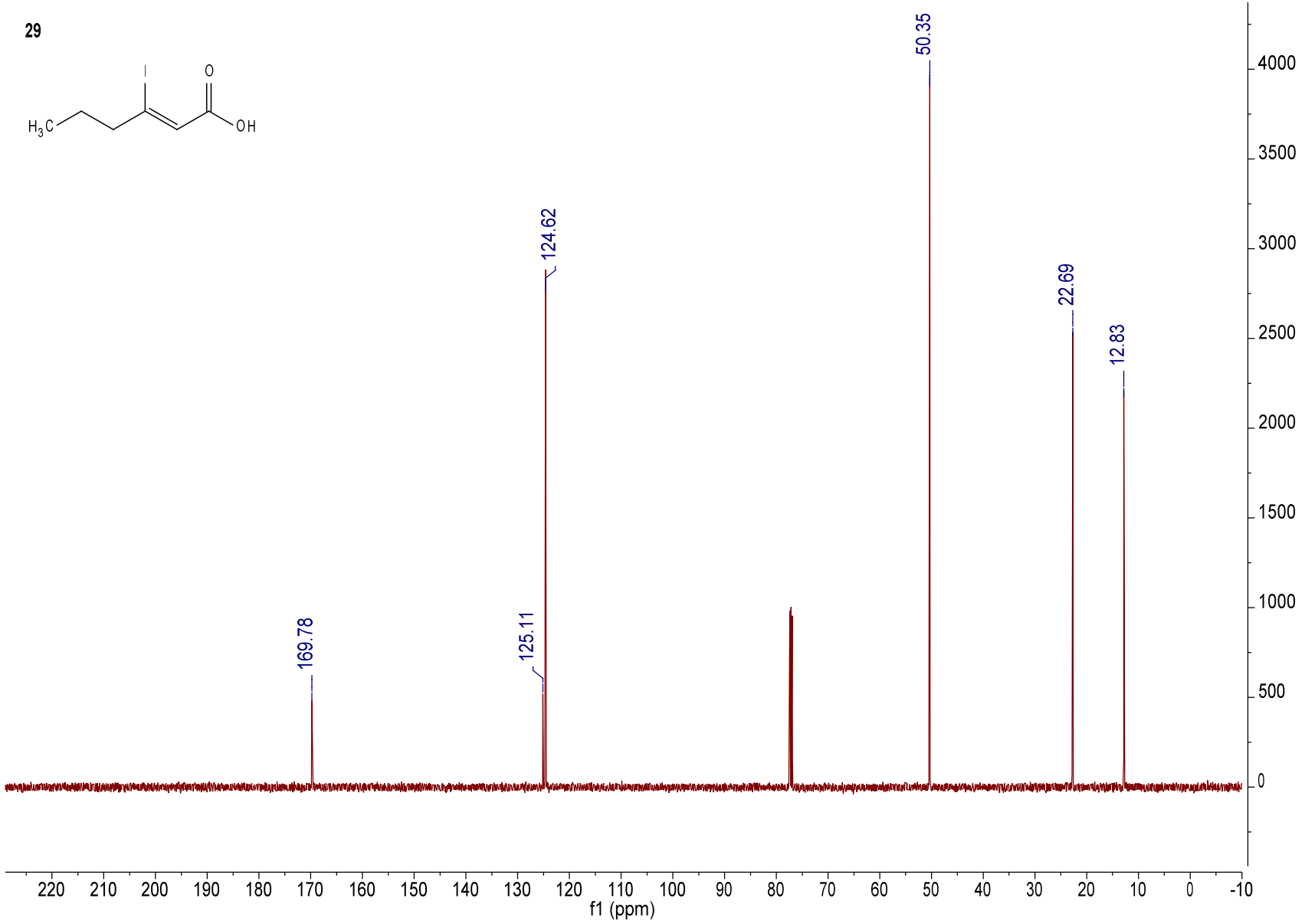
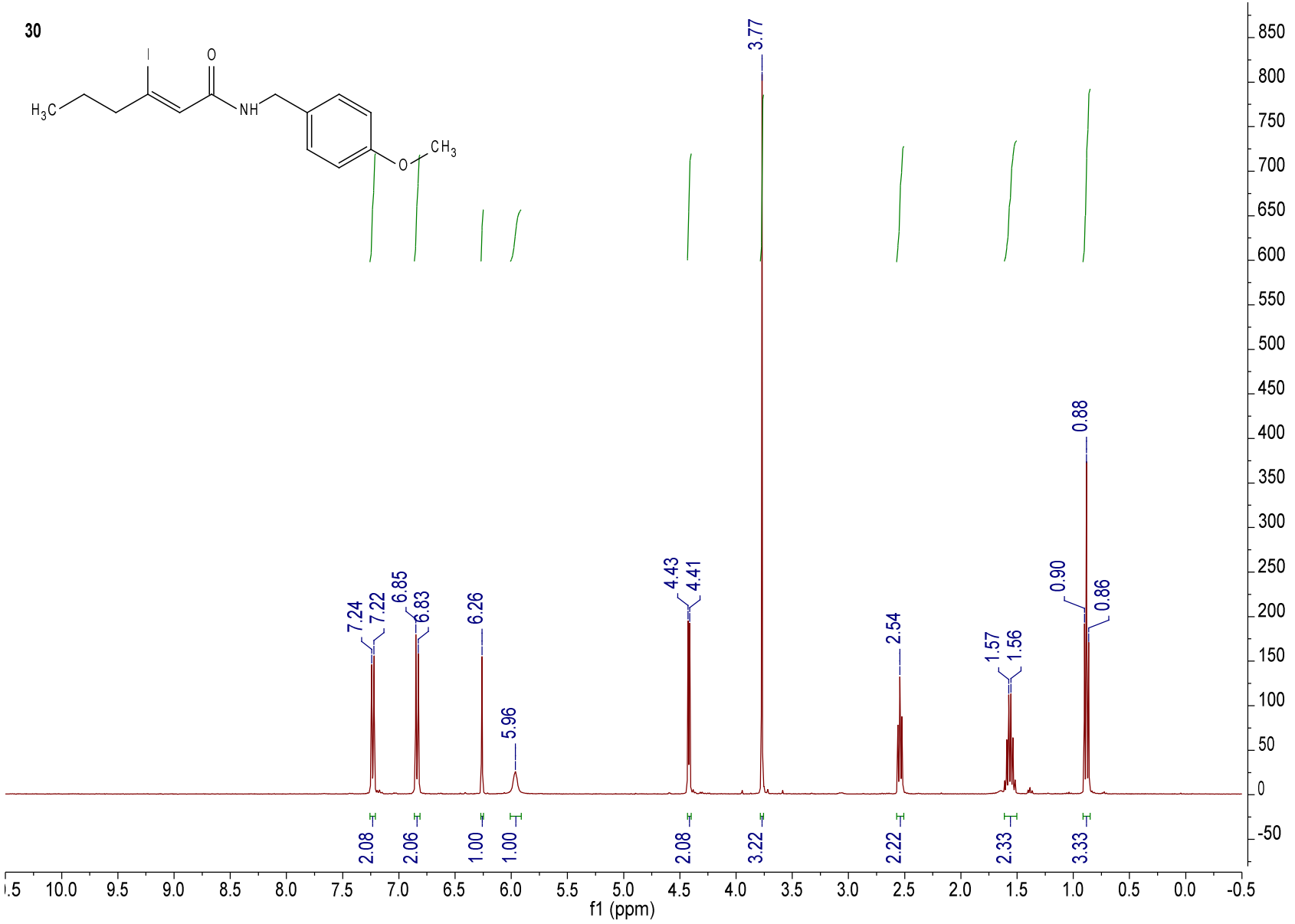
CH3
O
CH3
O
N
NH
O
O
H3C
CH3
9.48
6.78
6.67
6.67
4.64
4.63
2.61
2.60
1.88
1.87
0.93
0.91
0.71
0.80
0.74
1.93
6.02
1.00
5.92
f1 (ppm)


2
CH3
O
CH3
O
N
NH
O
O
H3C
CH3
181.71
175.38
161.47
160.73
151.21
149.01
138.99
137.93
128.64
128.35
120.11
114.49
50.58
29.83
23.49
22.33
20.07
f1 (ppm)


29
I
O
H3C
OH
6.40
2.71
1.66
1.64
0.93
1.00
2.14
2.12
3.14
f1 (ppm)


29
I
O
H3C
OH
50.35
124.62
22.69
12.83
169.78
125.11
4000
3500
3000
2500
2000
1500
1000
500
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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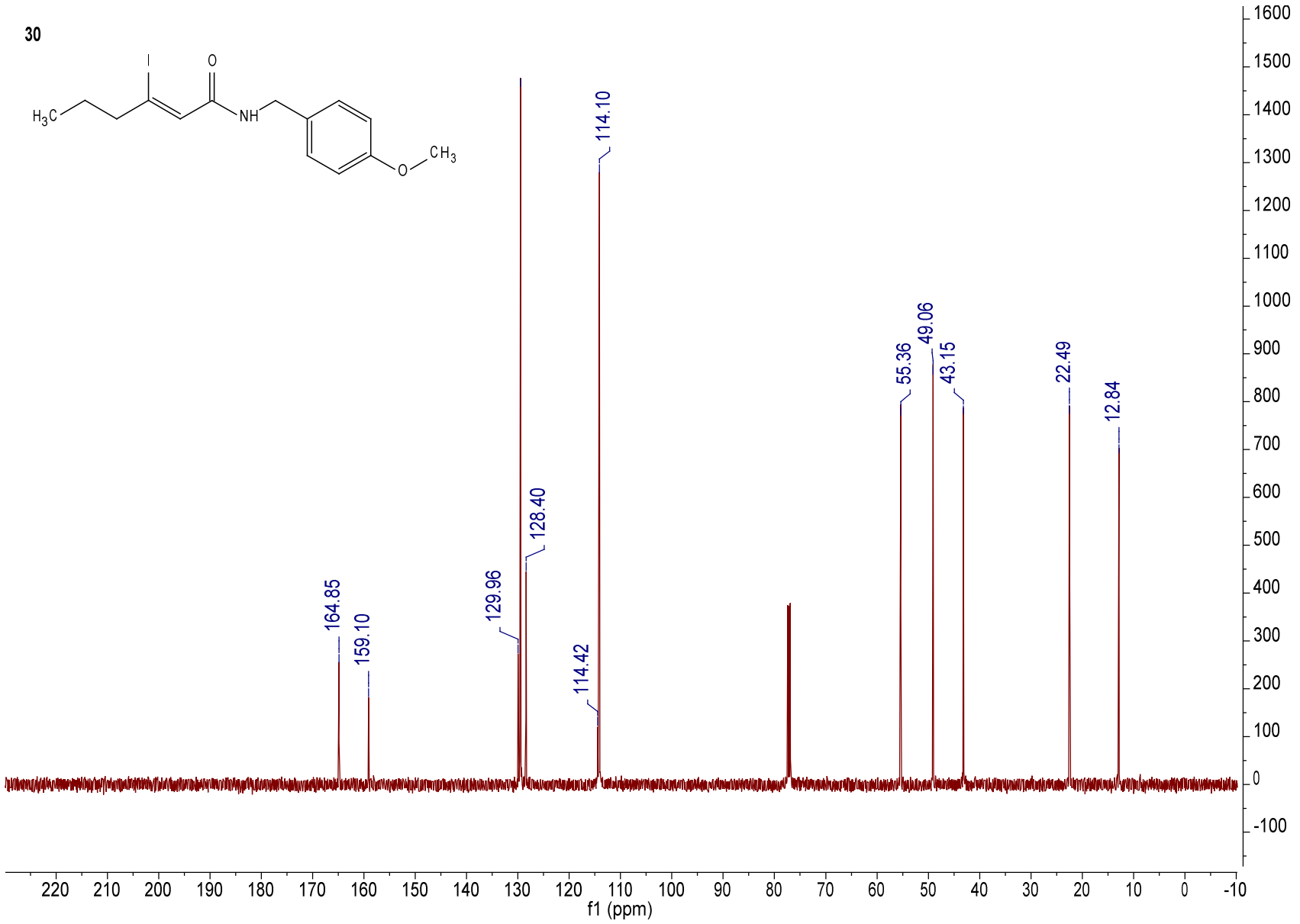
I
O
H_3C
NH
CH_3
O
7.24
7.22
6.85
6.83
6.26
5.96
4.43
4.41
3.77
2.54
1.57
1.56
0.90
0.88
0.86
2.08
2.06
1.00
1.00
2.08
3.22
2.22
2.33
3.33
f1 (ppm)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H3C
I
O
NH
O
CH3
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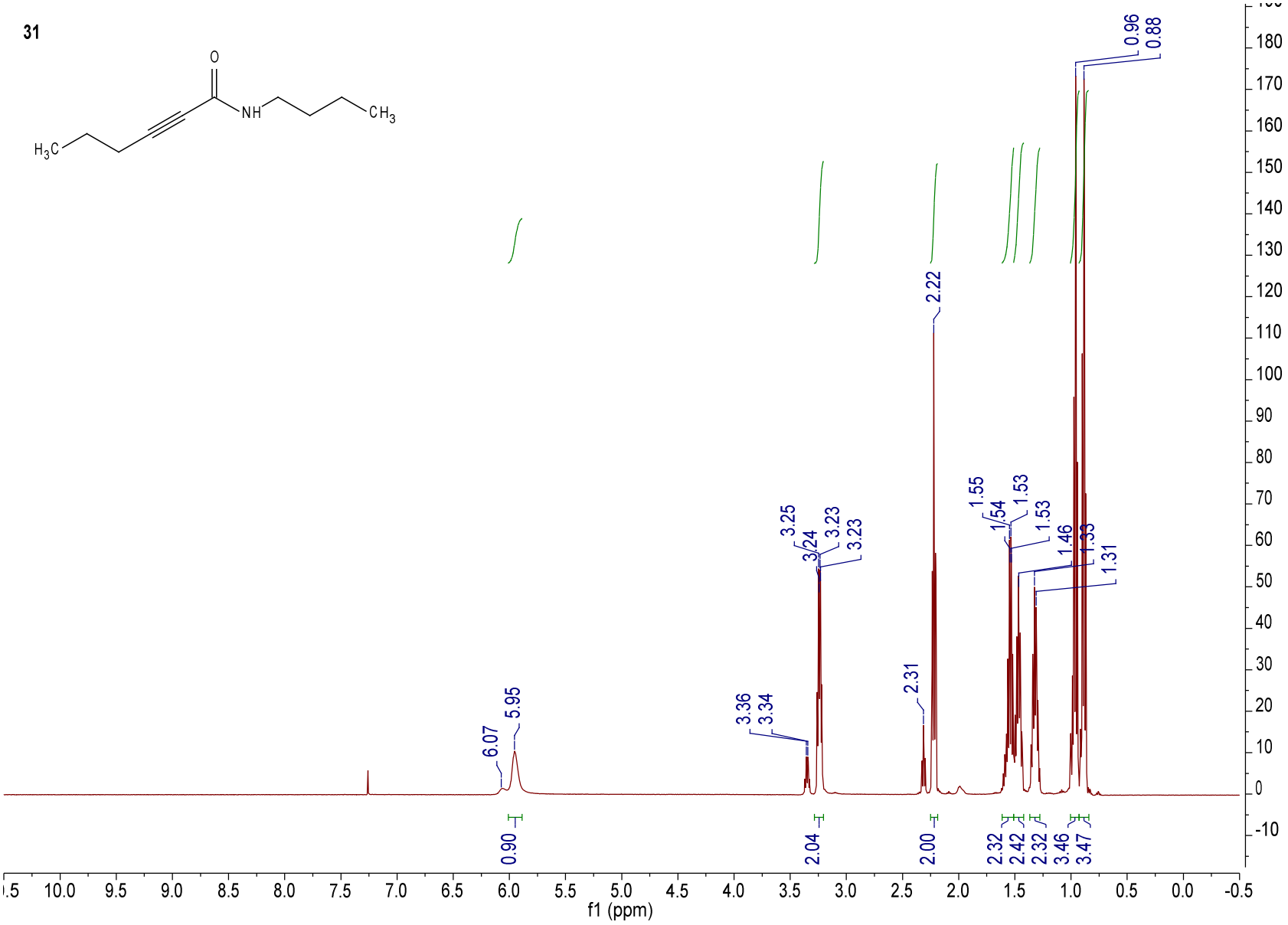
159.10
129.96
128.40
114.42
114.10
55.36
49.06
43.15
22.49
12.84
f1 (ppm)


31
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NH
CH_3
H_3C
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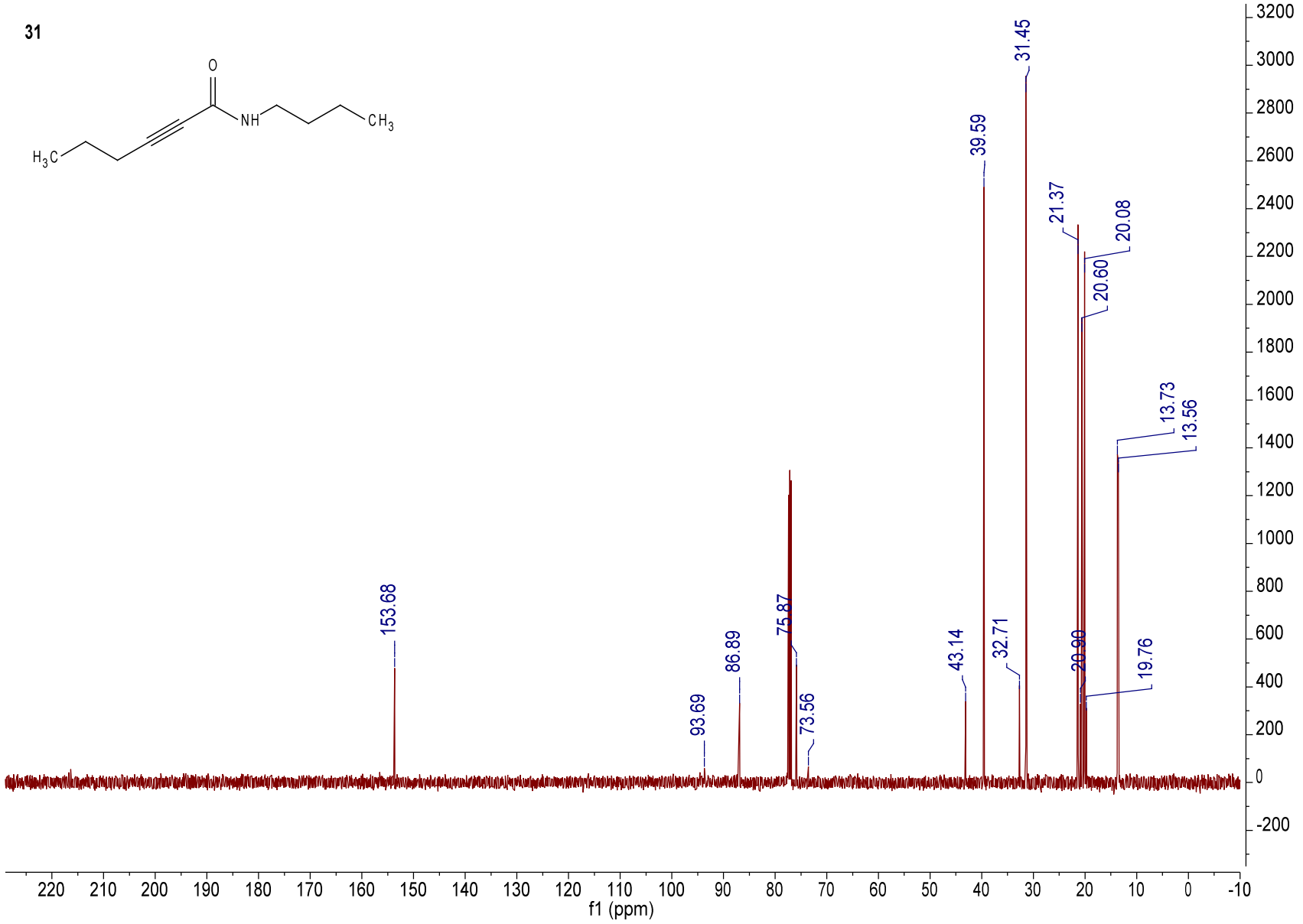
0.88
2.22
1.55
1.54
1.53
1.53
1.46
1.33
1.31
3.25
3.24
3.23
3.23
2.31
3.36
3.34
6.07
5.95
0.90
2.04
2.00
2.32
2.42
2.32
3.46
3.47
f1 (ppm)


31
O
NH
CH3
H3C
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93.69
86.89
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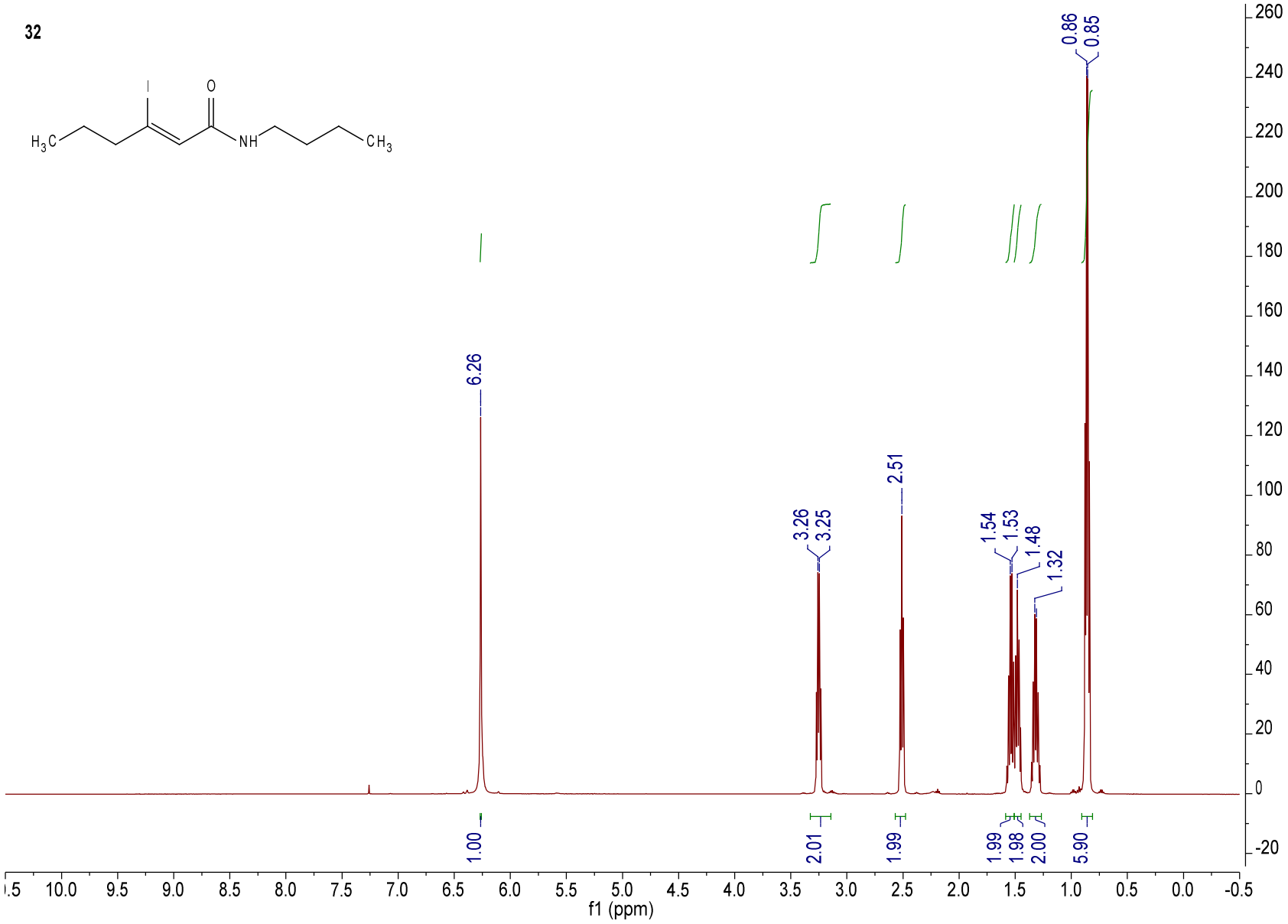
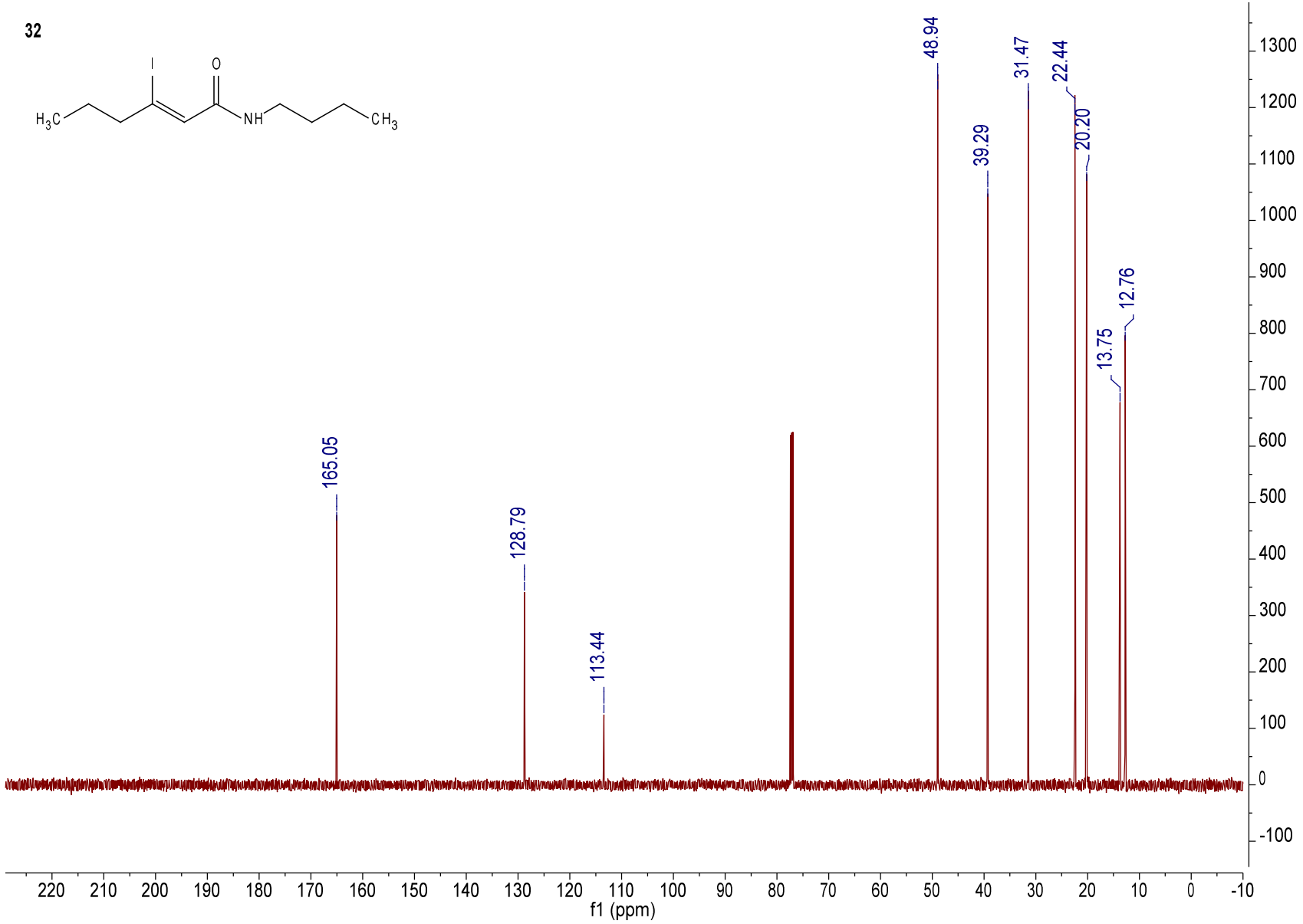
73.56
43.14
39.59
32.71
31.45
21.37
20.90
20.60
20.08
19.76
13.73
13.56
f1 (ppm)


32
I
O
H3C
NH
CH3
6.26
3.26
3.25
2.51
1.54
1.53
1.48
1.32
0.86
0.85
1.00
2.01
1.99
1.99
1.98
2.00
5.90
f1 (ppm)


32
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O
H3C
NH
CH3
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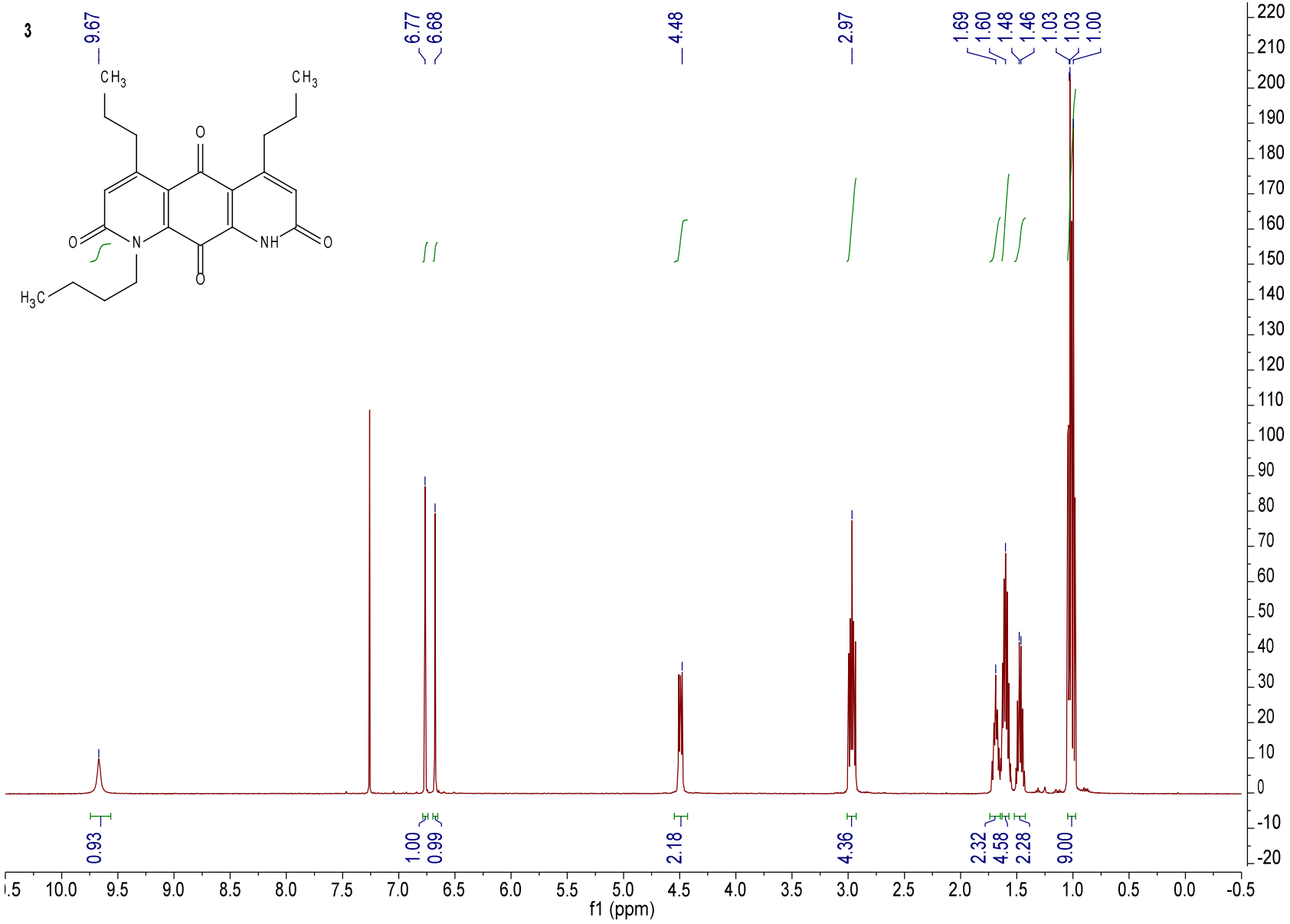
22.44
20.20
13.75
12.76
165.05
128.79
113.44
f1 (ppm)


3
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6.77
6.68
4.48
2.97
1.69
1.60
1.48
1.46
1.03
1.03
1.00
CH3
CH3
O
O
N
NH
O
O
H3C
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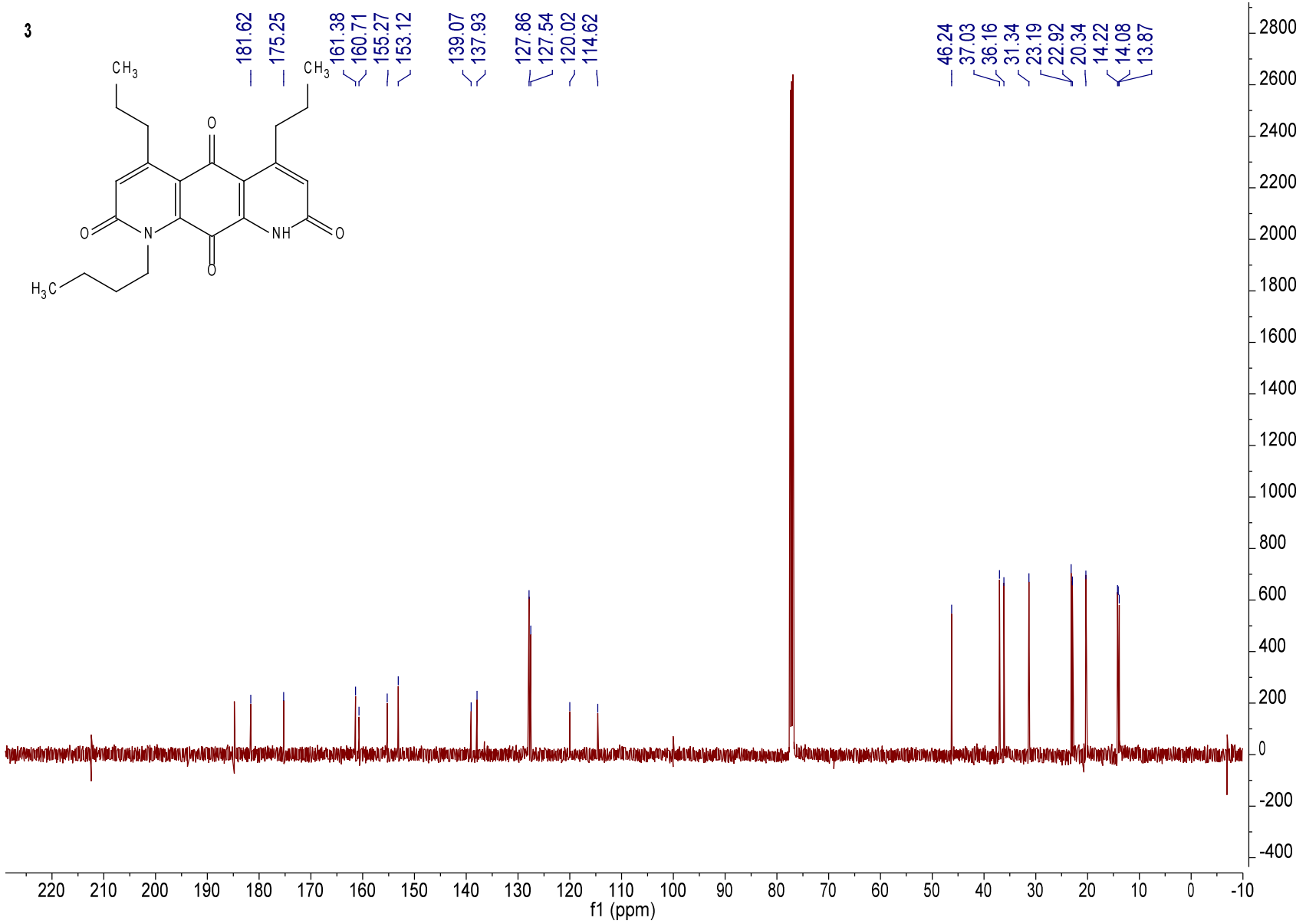
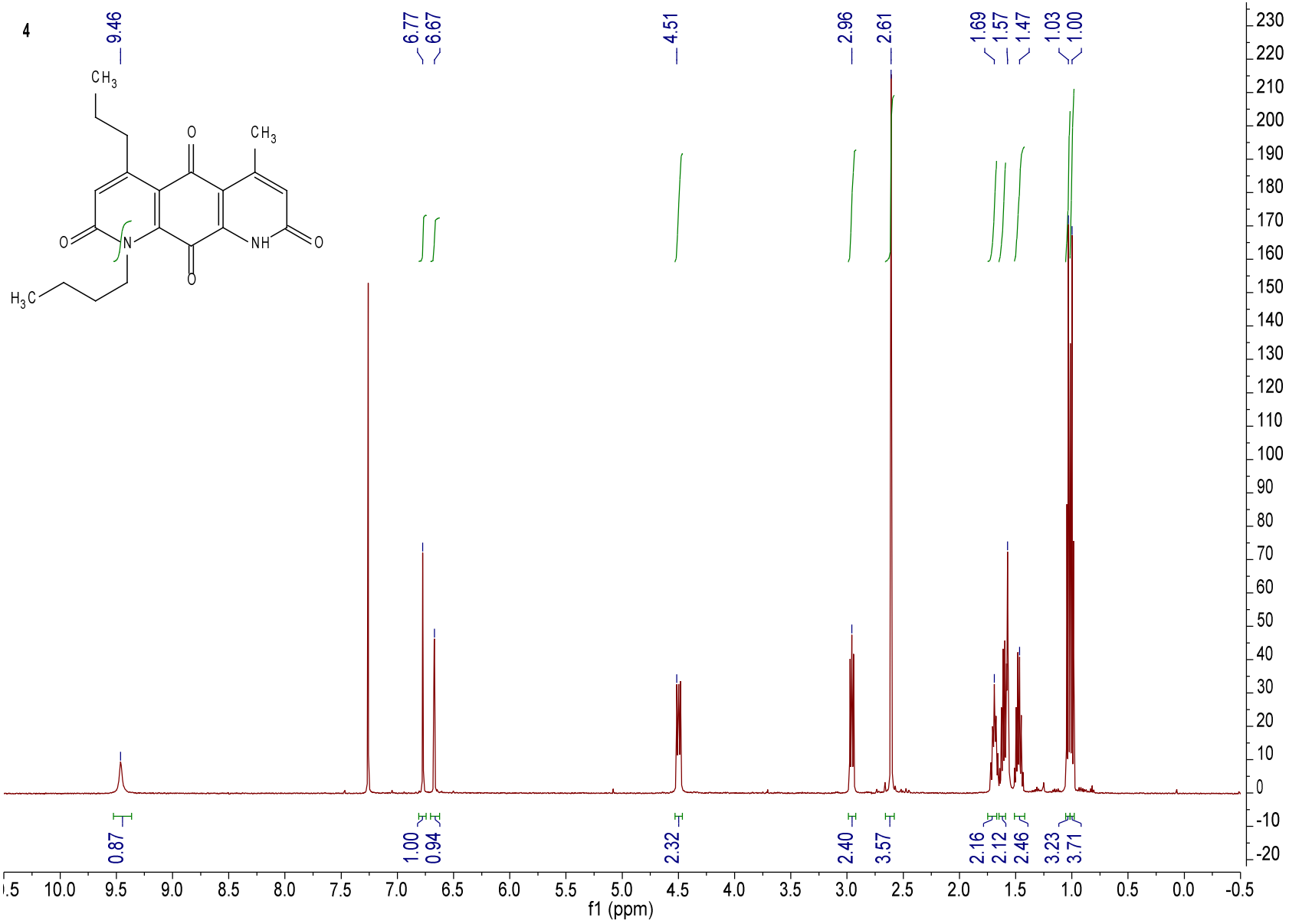
1.00
0.99
2.18
4.36
2.32
4.58
2.28
9.00
f1 (ppm)


3
181.62
175.25
161.38
160.71
155.27
153.12
139.07
137.93
127.86
127.54
120.02
114.62
46.24
37.03
36.16
31.34
23.19
22.92
20.34
14.22
14.08
13.87
f1 (ppm)


4
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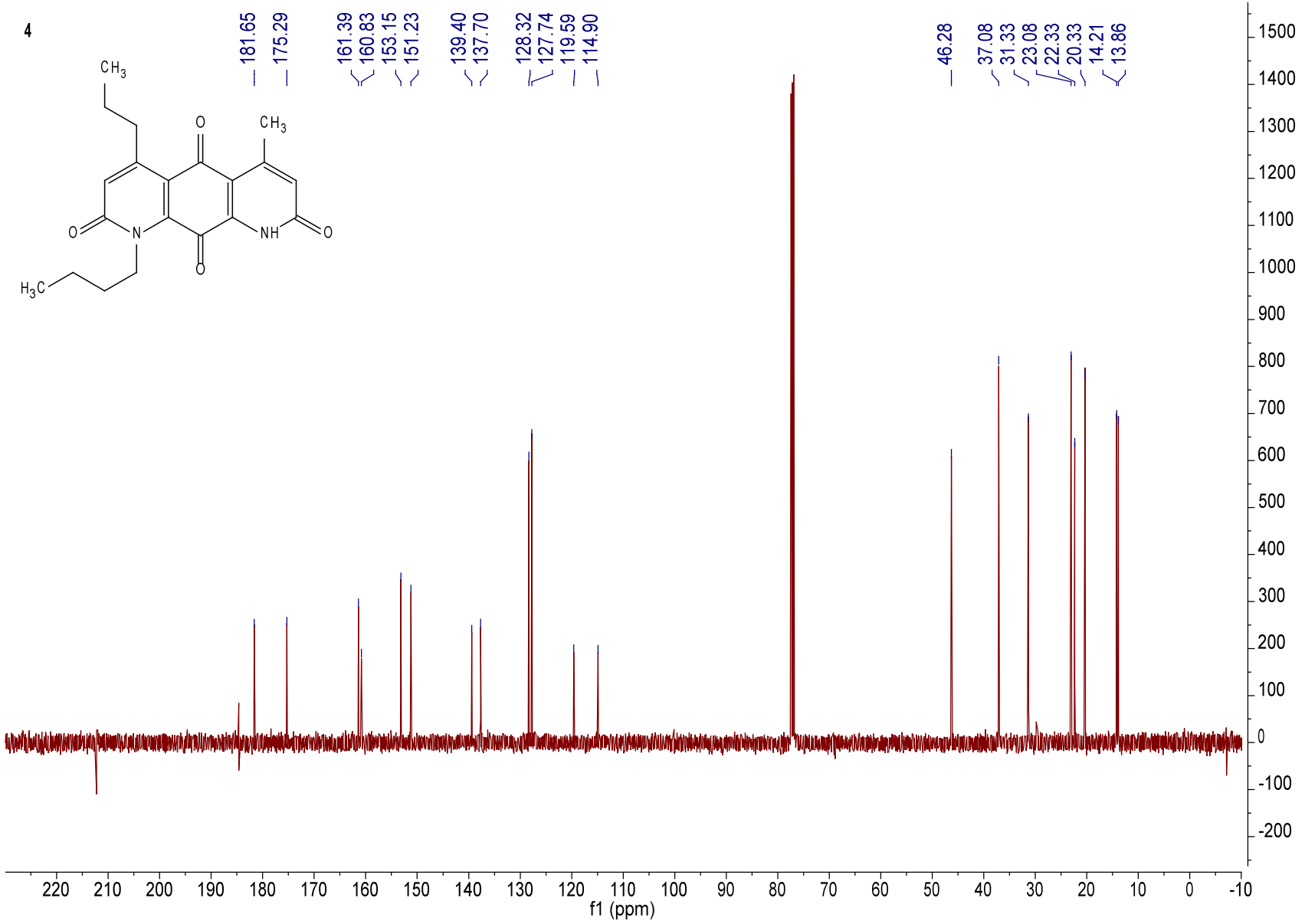
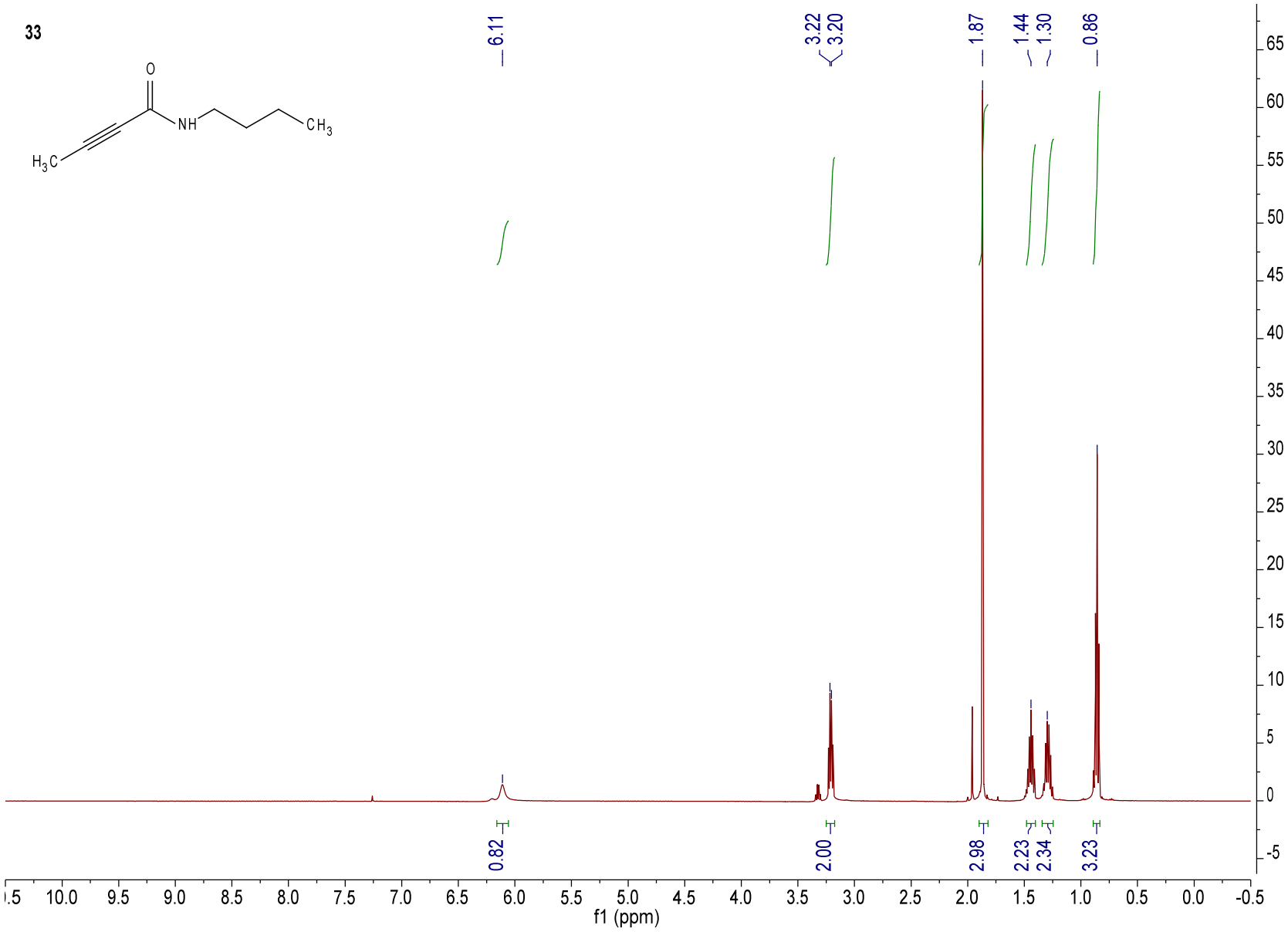
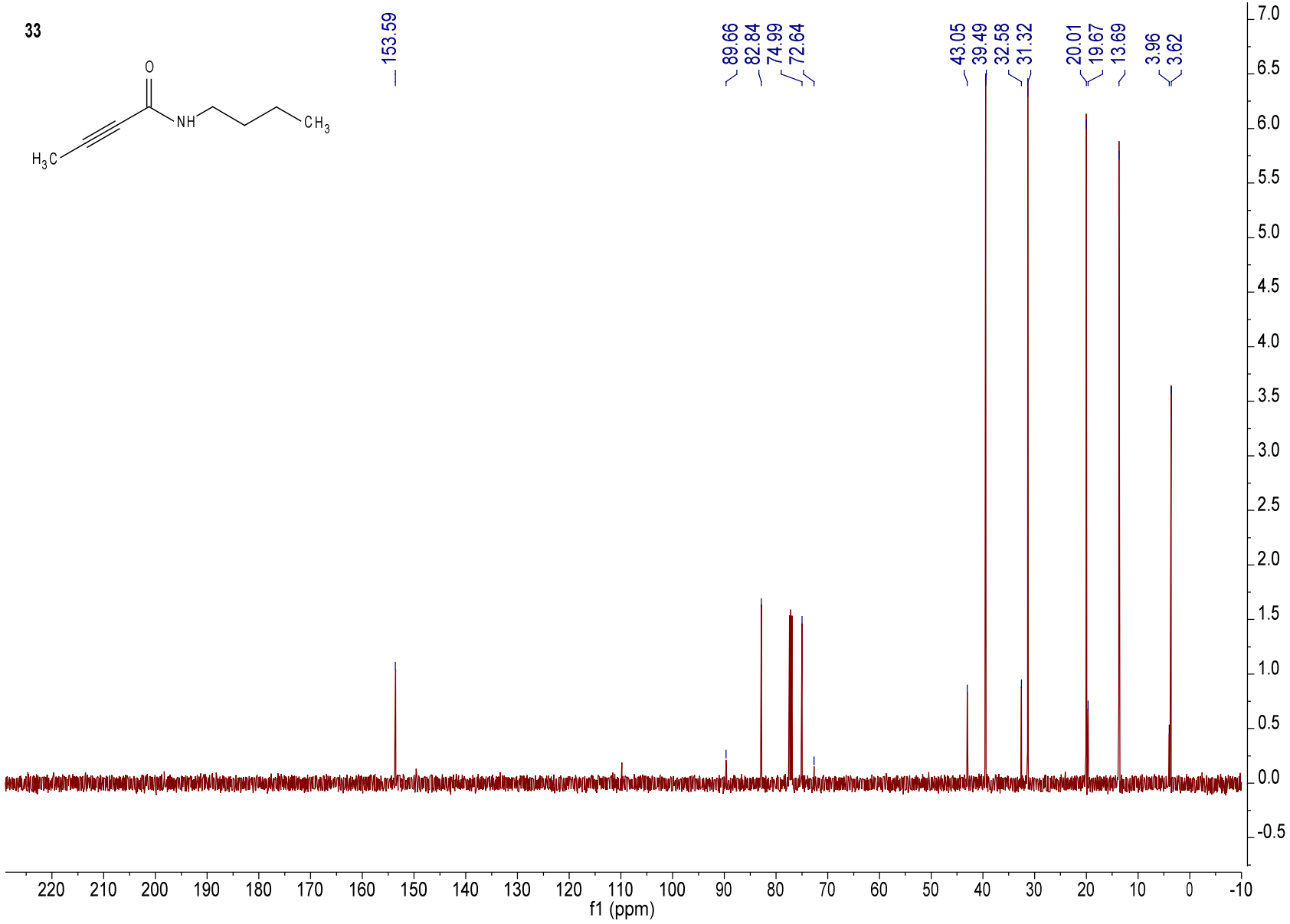
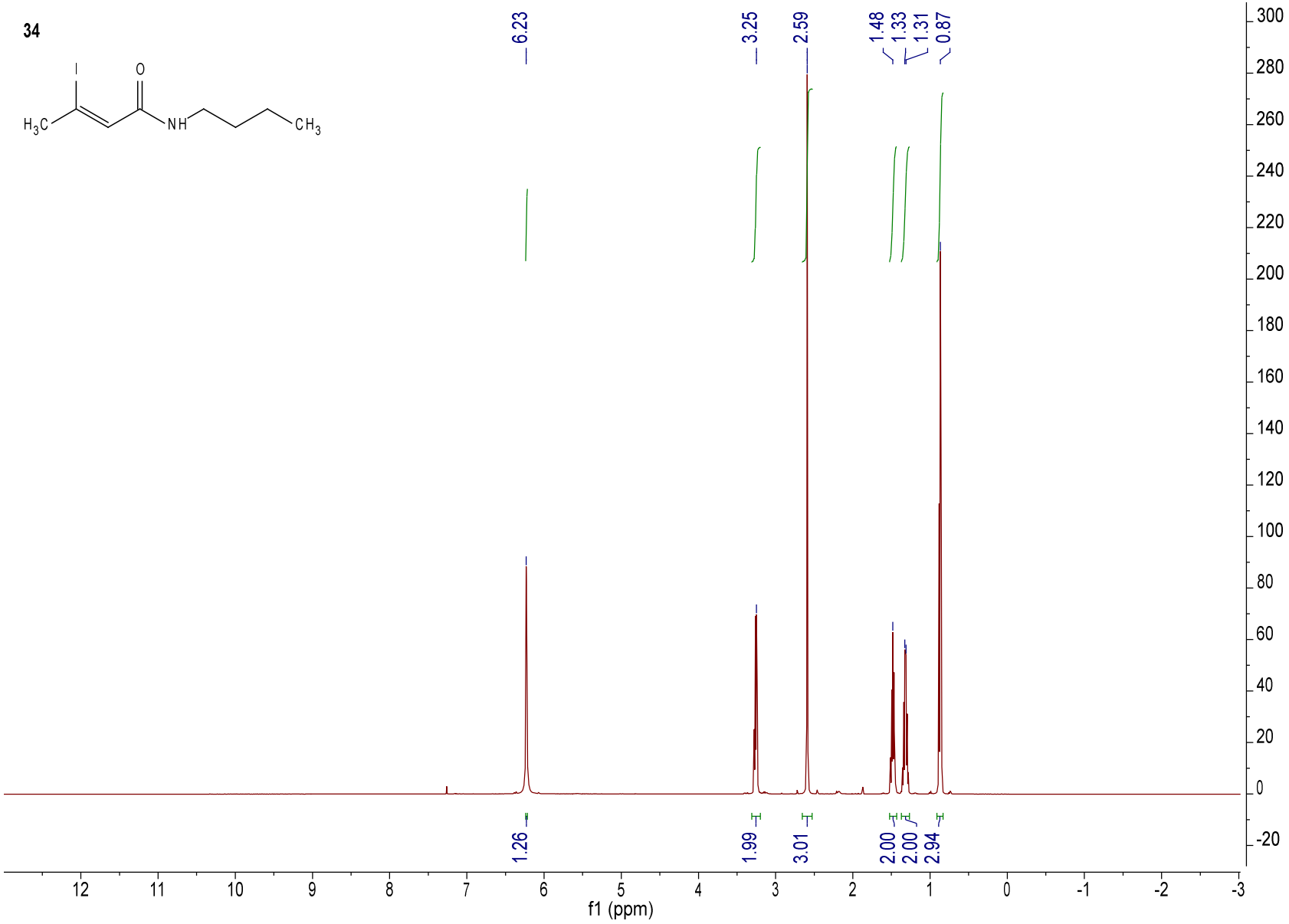
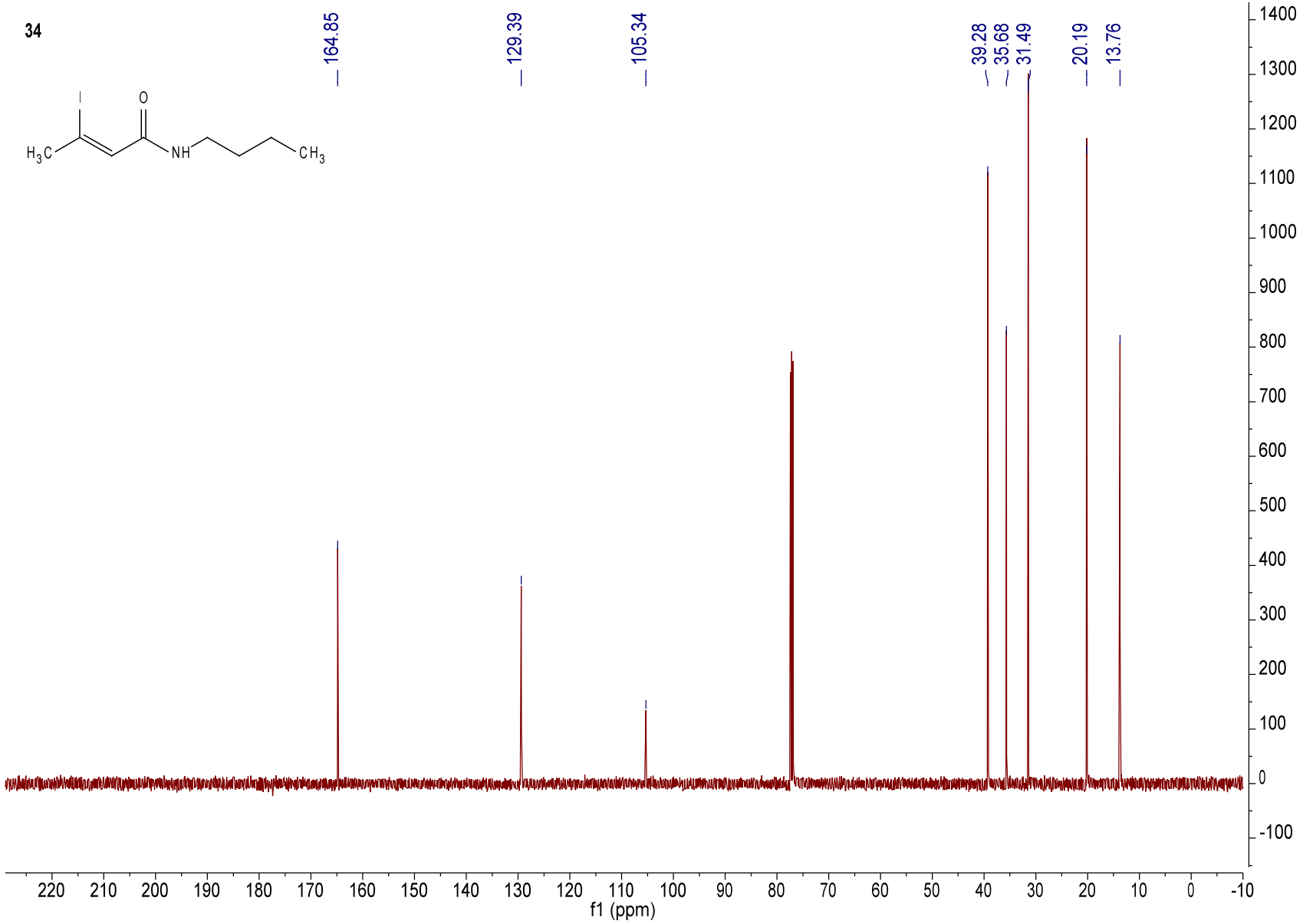
2.96
2.61
1.69
1.57
1.47
1.03
1.00
0.87
1.00
0.94
2.32
2.40
3.57
2.16
2.12
2.46
3.23
3.71
f1 (ppm)

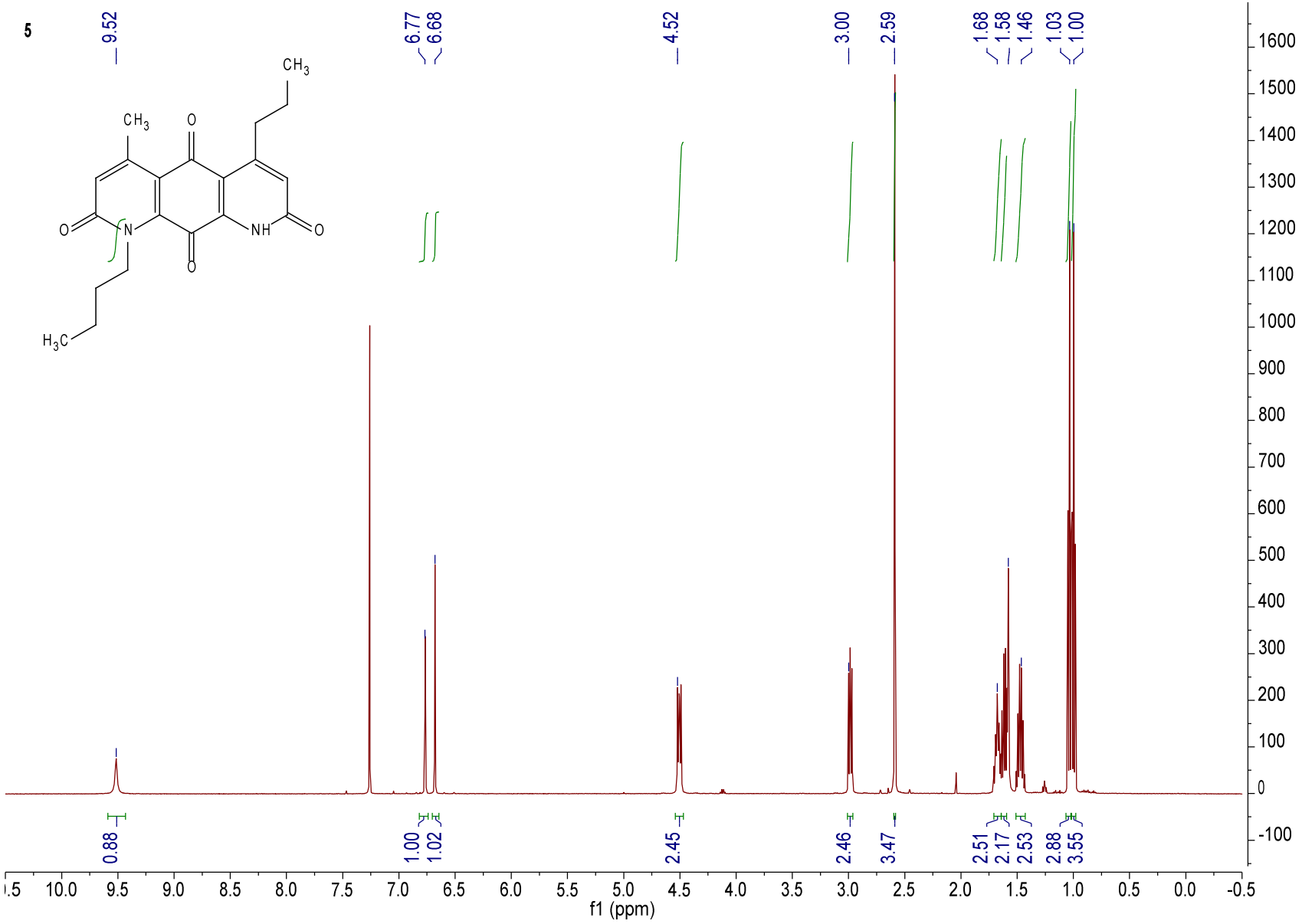

4
181.65
175.29
161.39
160.83
153.15
151.23
139.40
137.70
128.32
127.74
119.59
114.90
46.28
37.08
31.33
23.08
22.33
20.33
14.21
13.86
f1 (ppm)

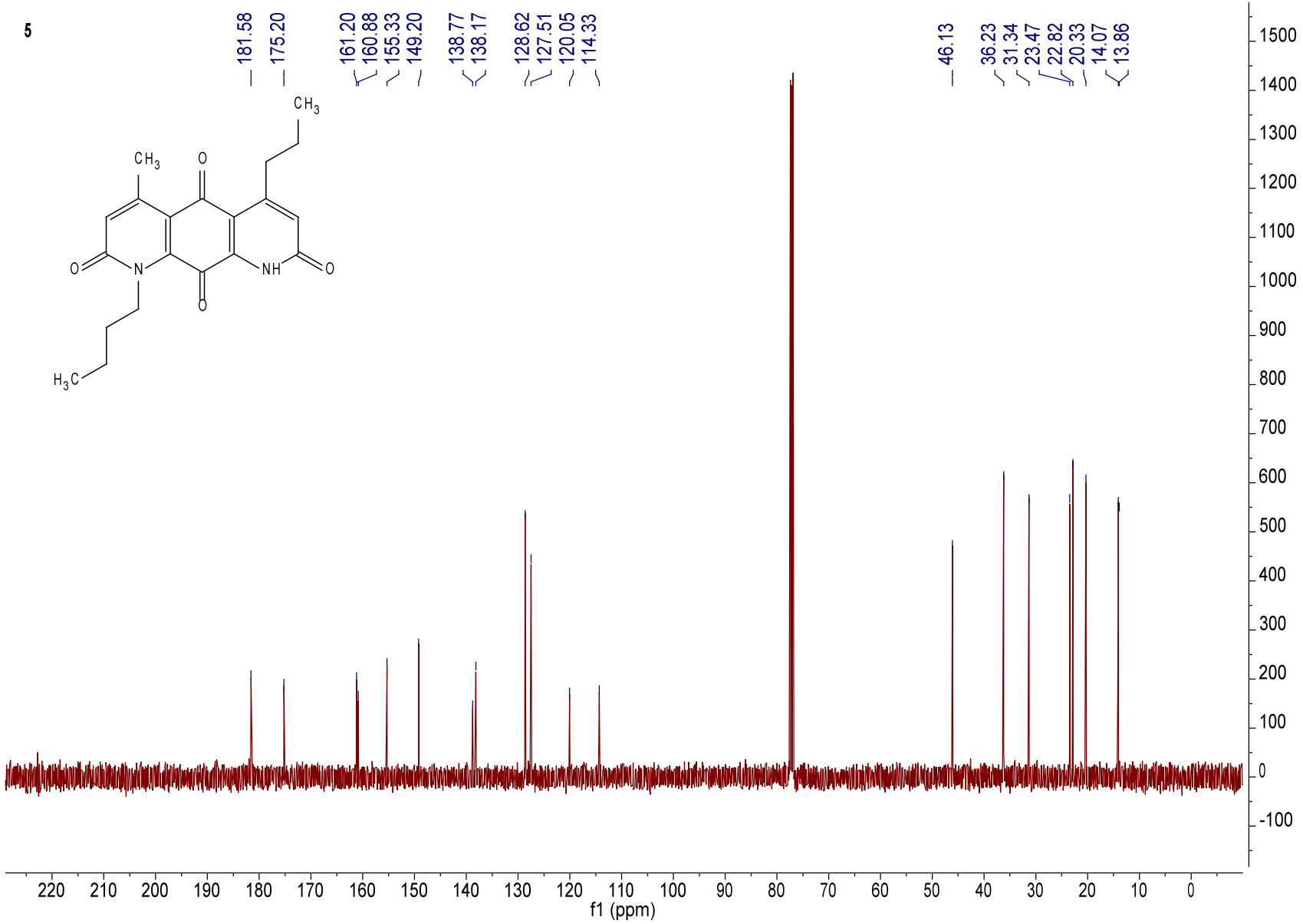

33
O
NH
CH3
H3C
6.11
3.22
3.20
1.87
1.44
1.30
0.86
0.82
2.00
2.98
2.23
2.34
3.23
f1 (ppm)

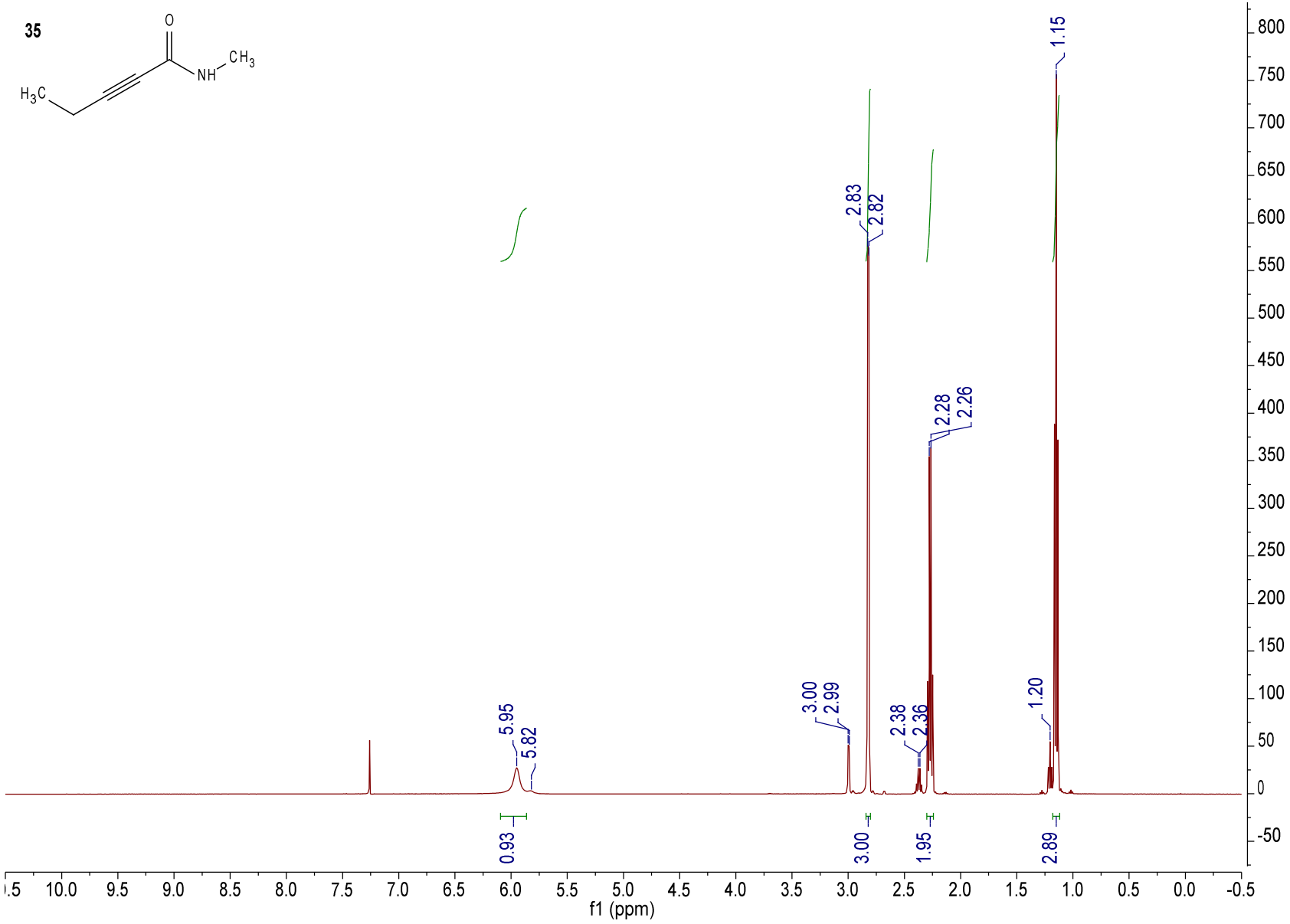

33
O
NH
CH3
H3C
153.59
89.66
82.84
74.99
72.64
43.05
39.49
32.58
31.32
20.01
19.67
13.69
3.96
3.62
f1 (ppm)

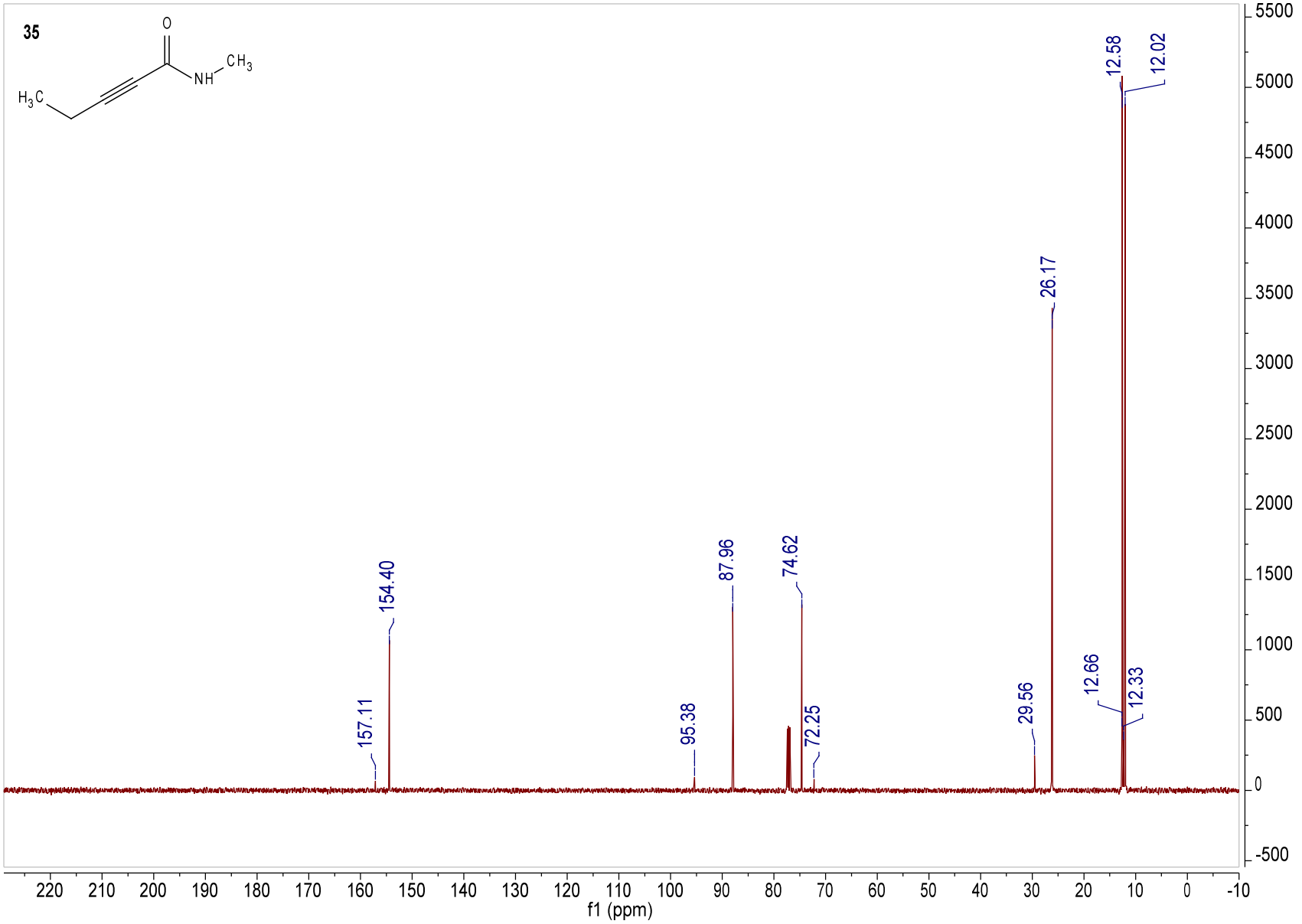

34
I
O
H3C
NH
CH3
6.23
3.25
2.59
1.48
1.33
1.31
0.87
1.26
1.99
3.01
2.00
2.00
2.94
f1 (ppm)

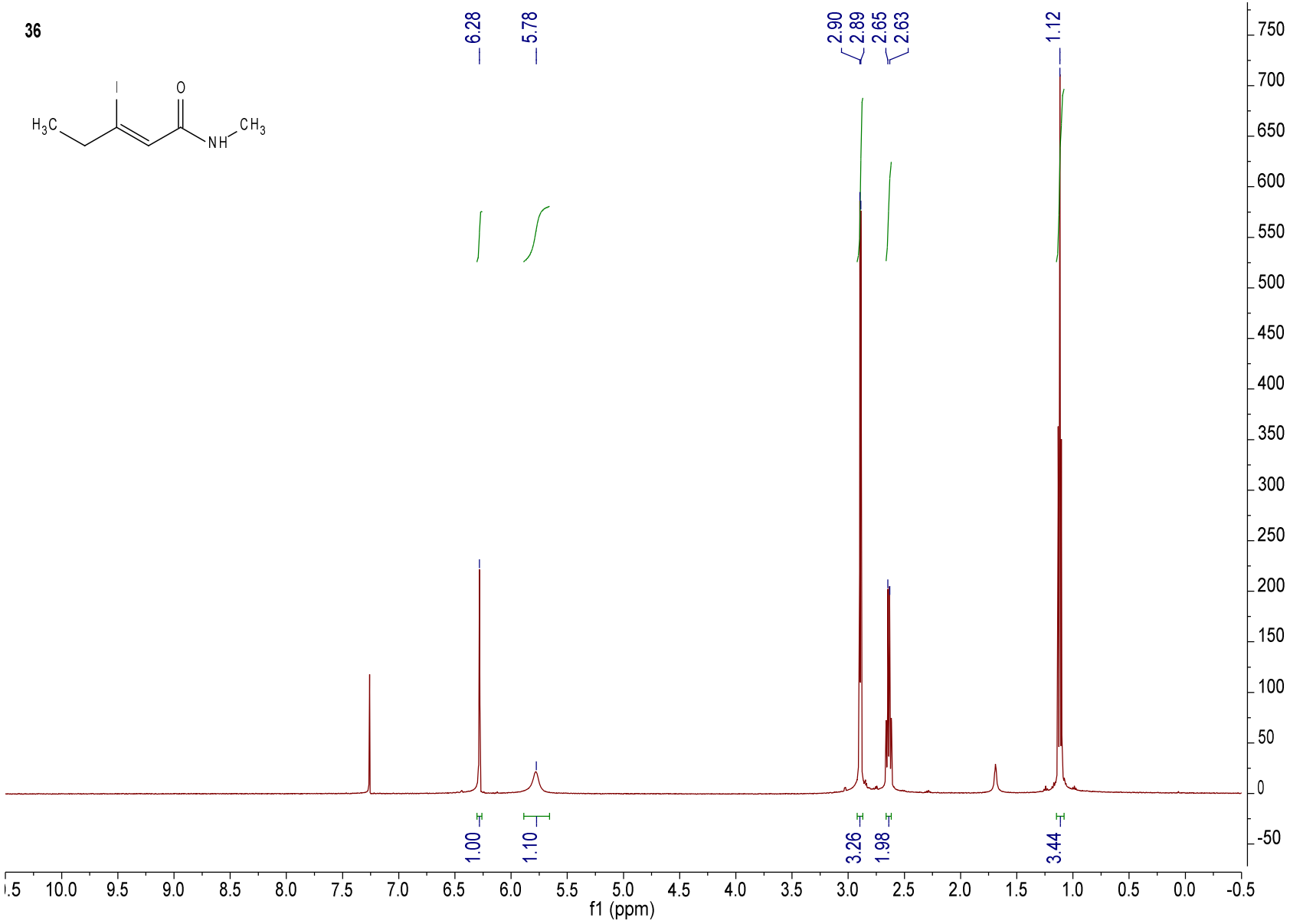

34
164.85
129.39
105.34
39.28
35.68
31.49
20.19
13.76
I
O
H3C
NH
CH3
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

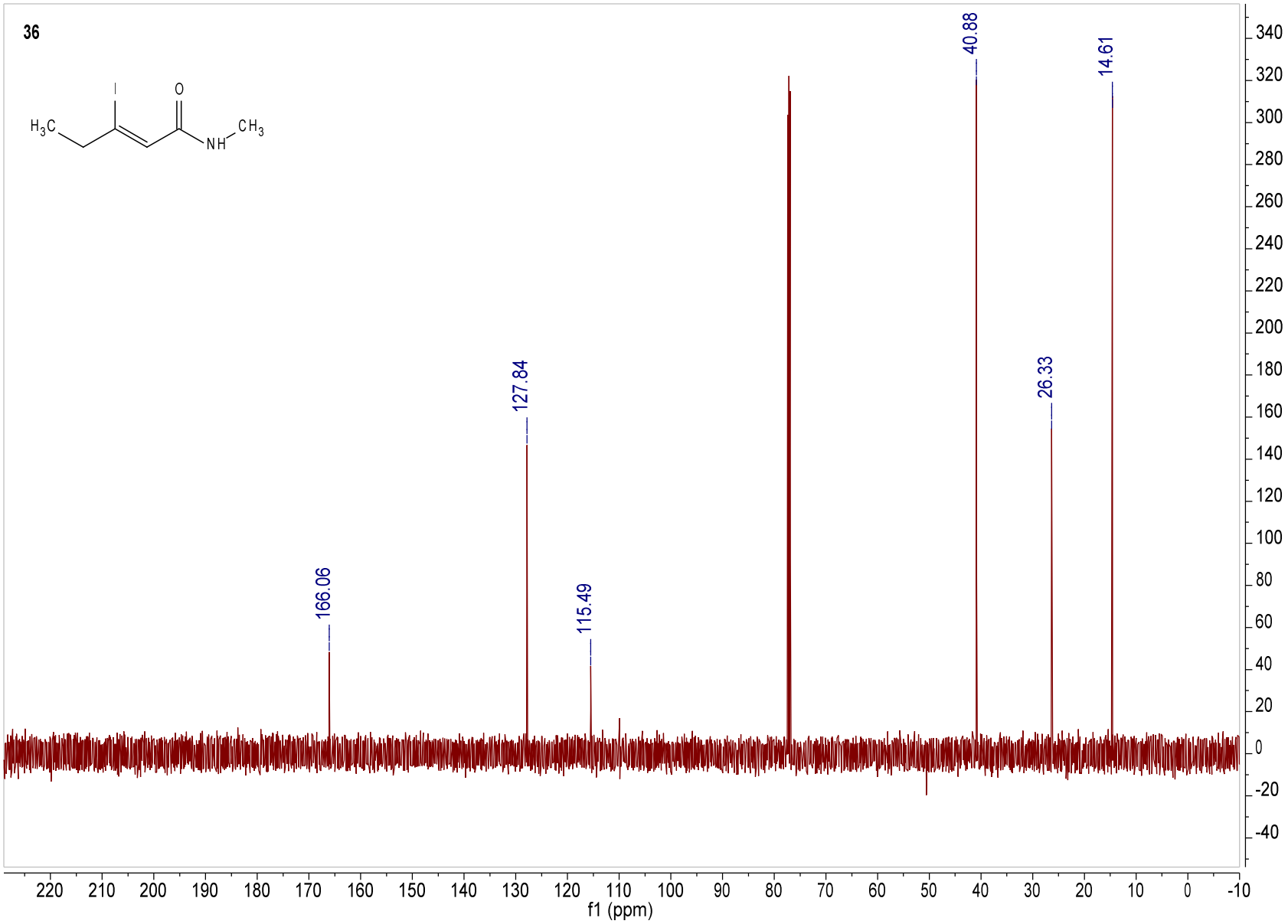

5
9.52
6.77
6.68
4.52
3.00
2.59
1.68
1.58
1.46
1.03
1.00
CH3
CH3
O
O
O
N
NH
O
O
H3C
0.88
1.00
1.02
2.45
2.46
3.47
2.51
2.17
2.53
2.88
3.55
f1 (ppm)

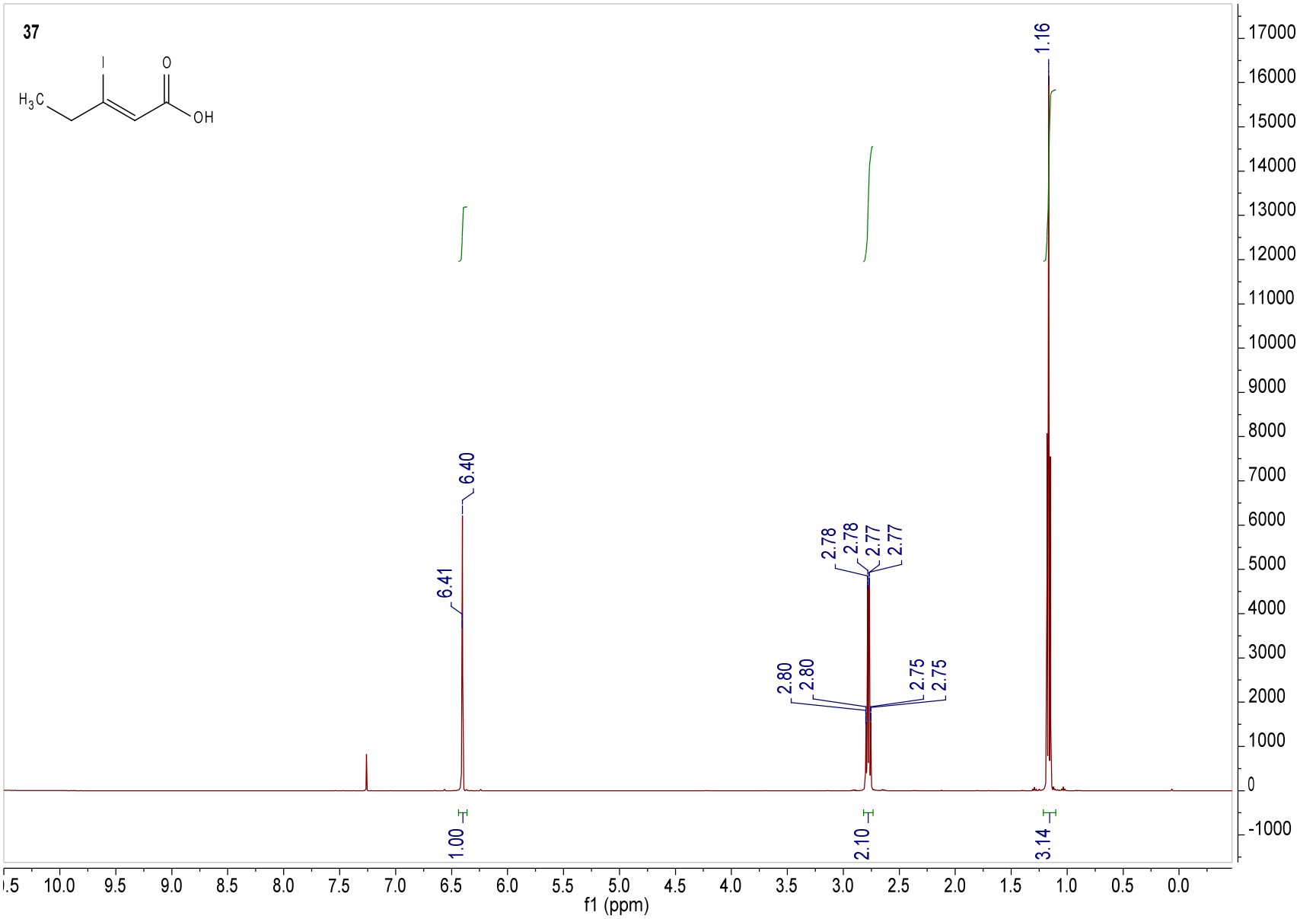

5
181.58
175.20
161.20
160.88
155.33
149.20
138.77
138.17
128.62
127.51
120.05
114.33
46.13
36.23
31.34
23.47
22.82
20.33
14.07
13.86
CH3
O
N
NH
O
O
CH3
H3C
f1 (ppm)

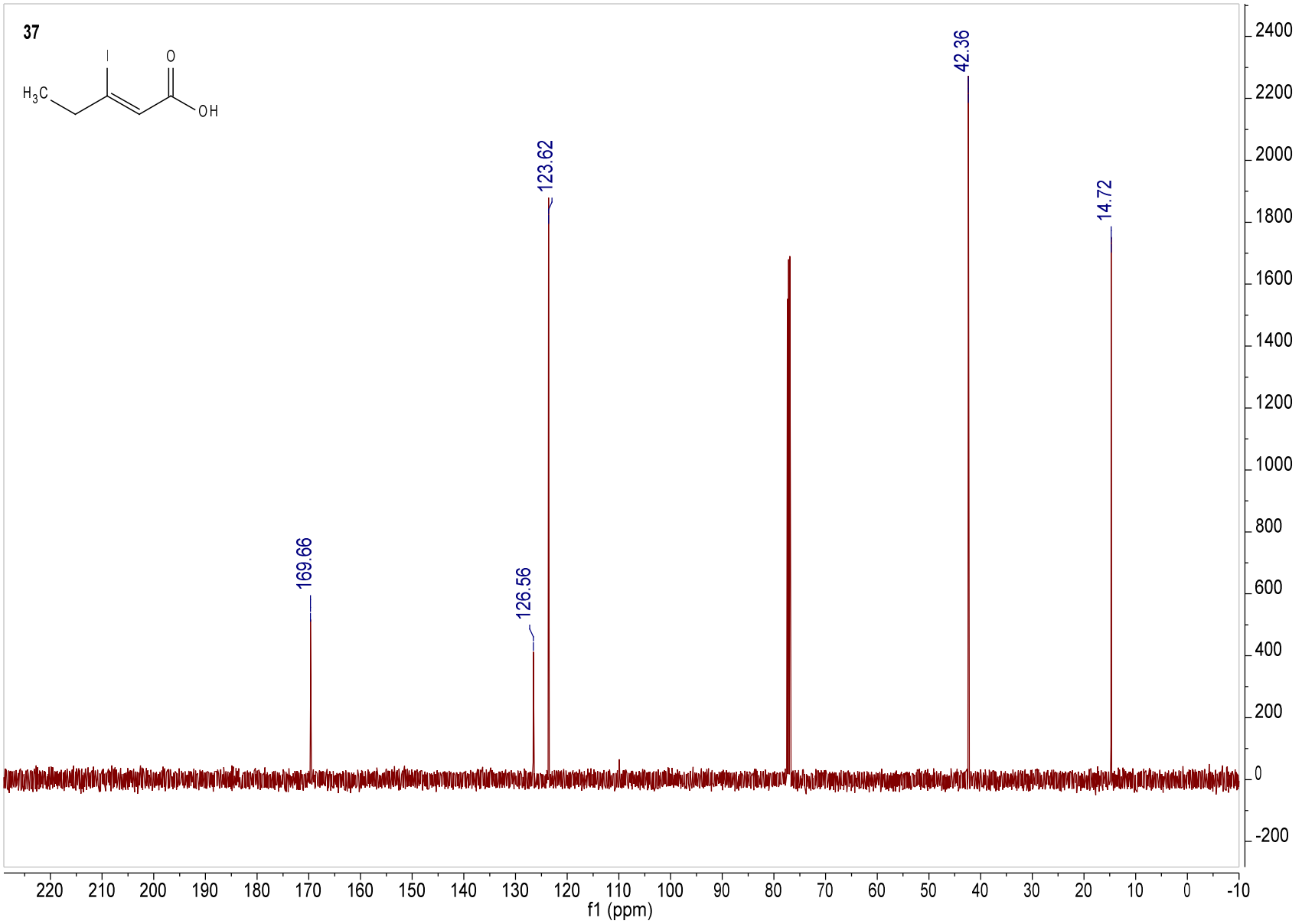

35
O
NH
CH3
H3C
5.95
5.82
3.00
2.99
2.83
2.82
2.38
2.36
2.28
2.26
1.20
1.15
0.93
3.00
1.95
2.89
f1 (ppm)

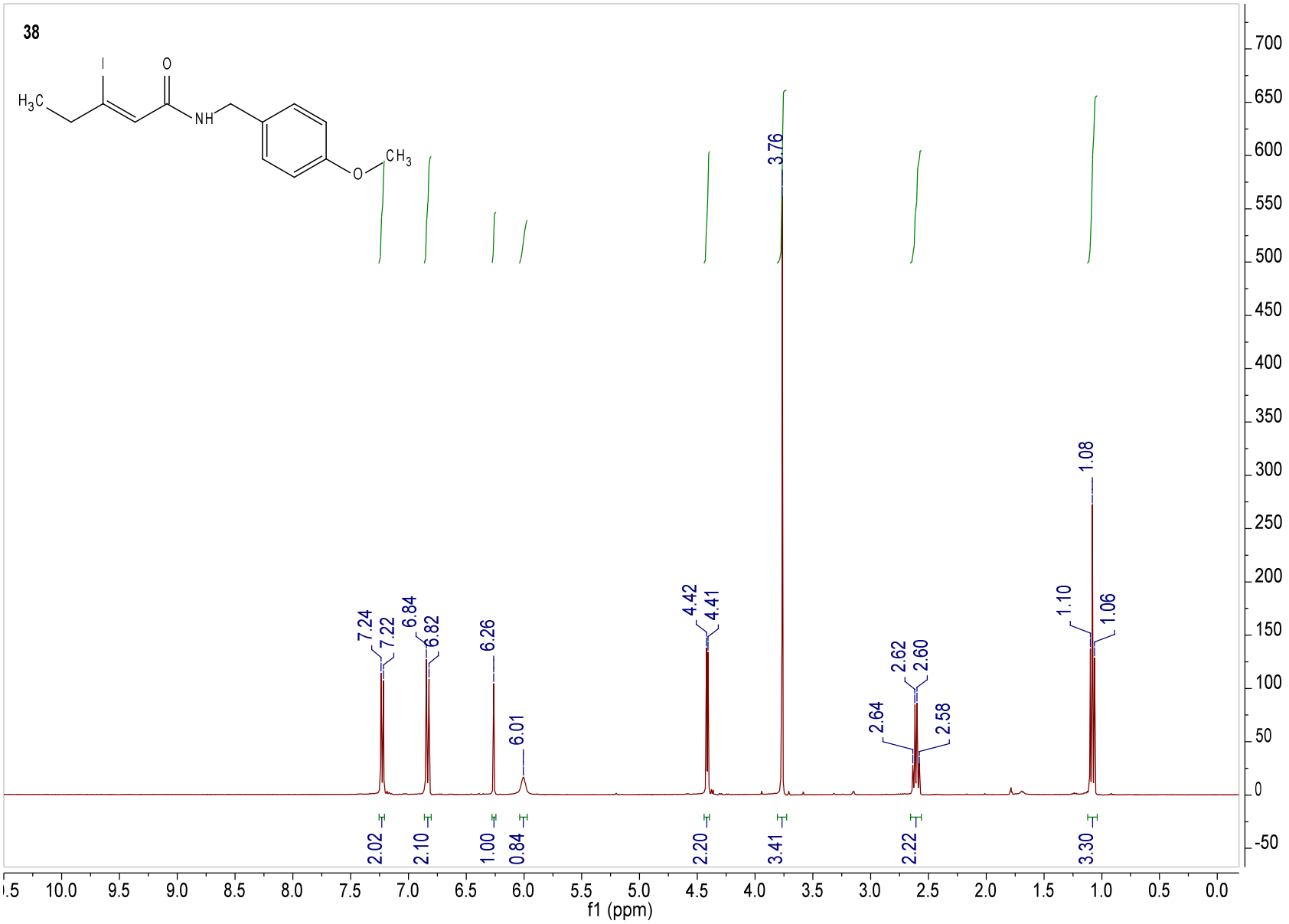

35
O
NH
CH3
H3C
157.11
154.40
95.38
87.96
74.62
72.25
29.56
26.17
12.66
12.58
12.33
12.02
f1 (ppm)

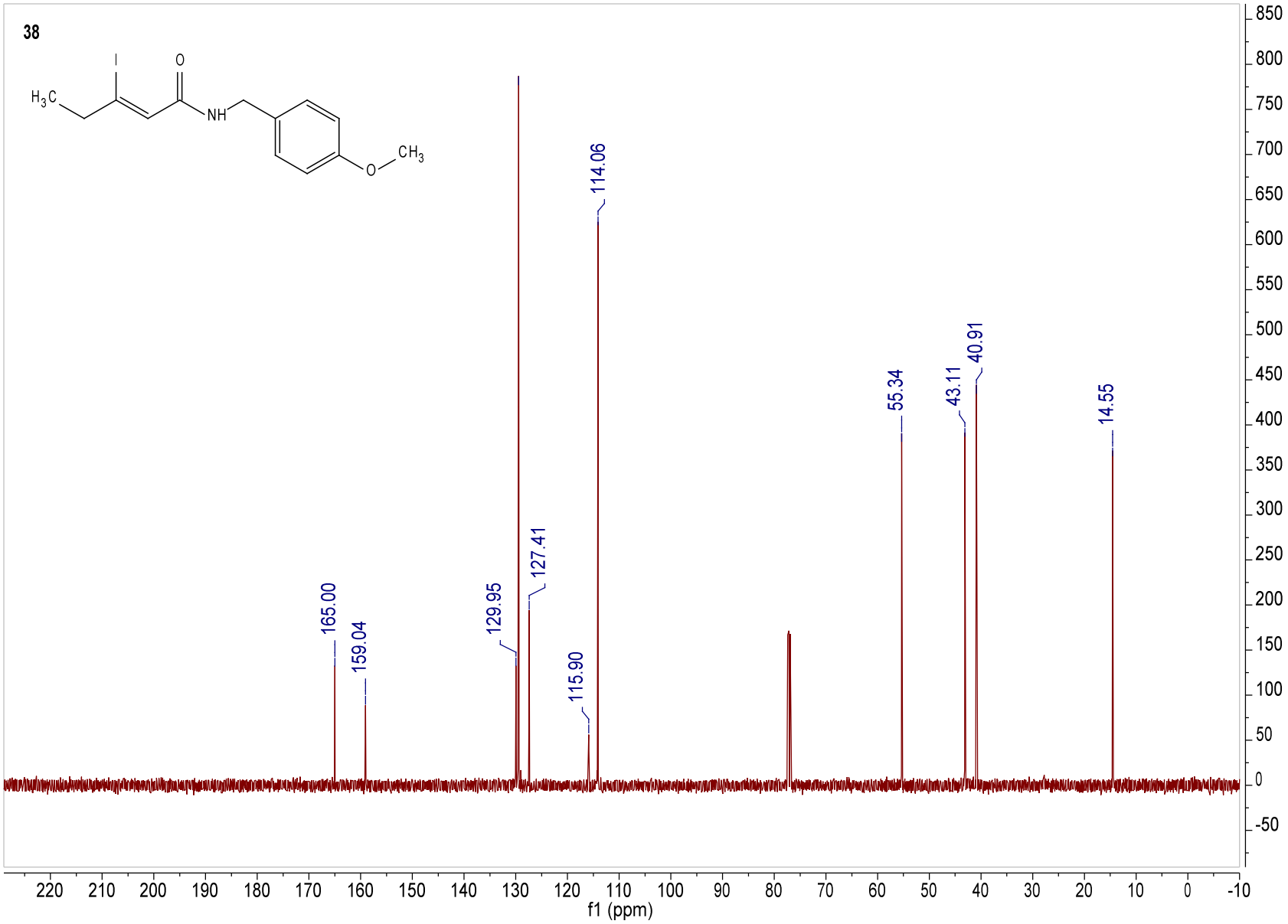

36
6.28
5.78
2.90
2.89
2.65
2.63
1.12
1.00
1.10
3.26
1.98
3.44
f1 (ppm)

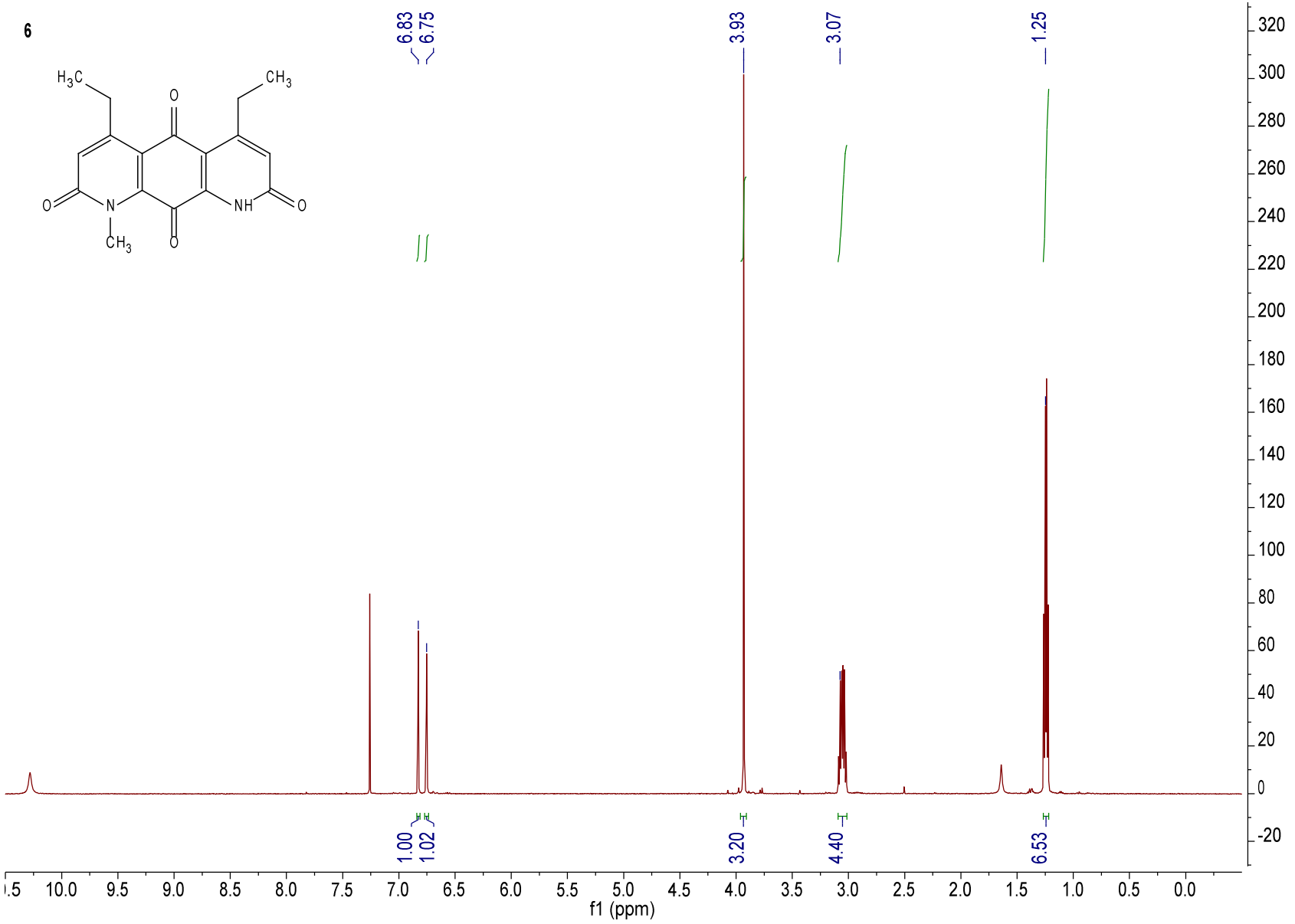

36
I
O
H3C
NH
CH3
166.06
127.84
115.49
40.88
26.33
14.61
f1 (ppm)

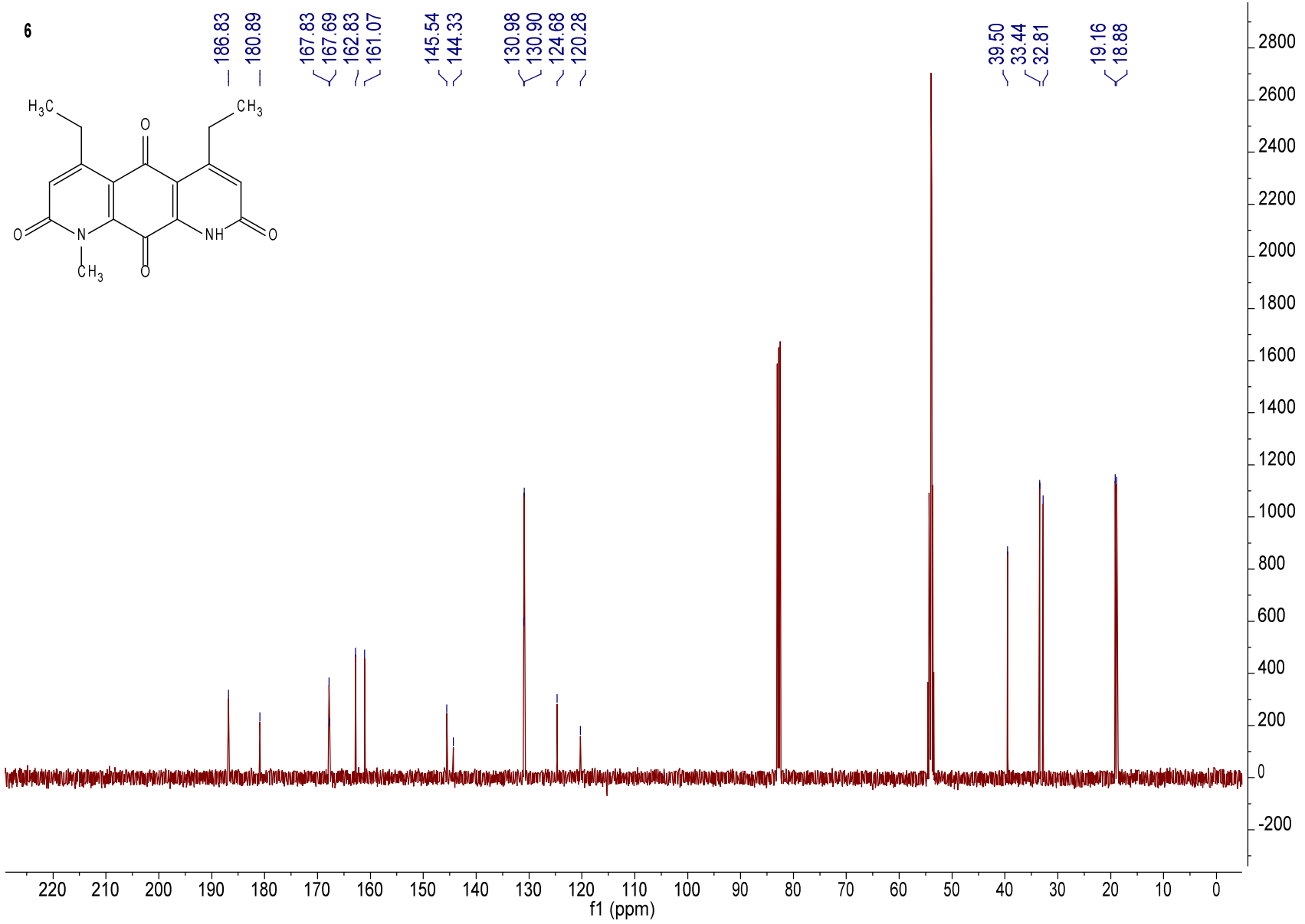

37
I
O
H3C
OH
1.16
6.40
6.41
2.78
2.78
2.77
2.77
2.80
2.80
2.75
2.75
1.00
2.10
3.14
f1 (ppm)

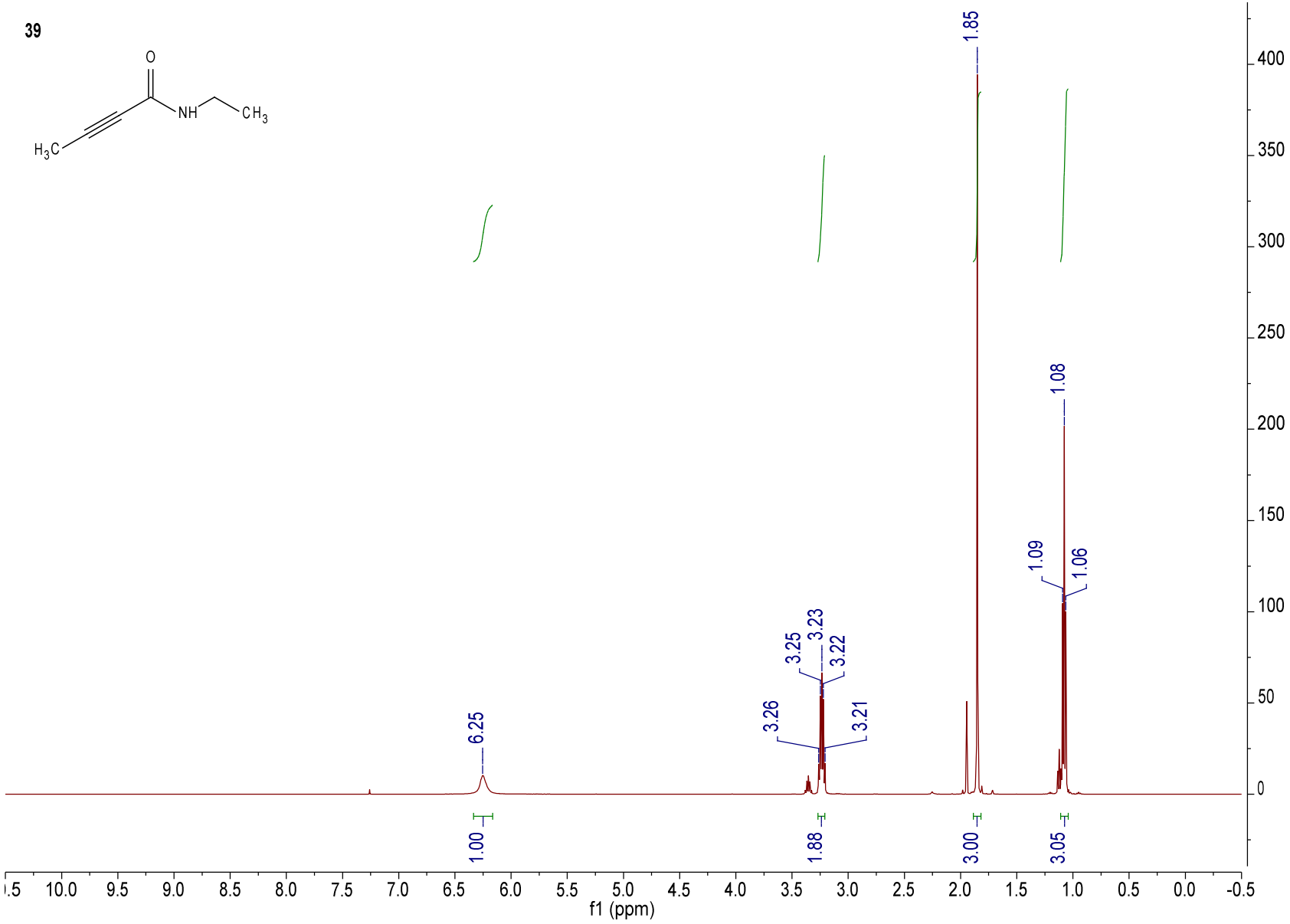

37
I
O
H3C
OH
169.66
126.56
123.62
42.36
14.72
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

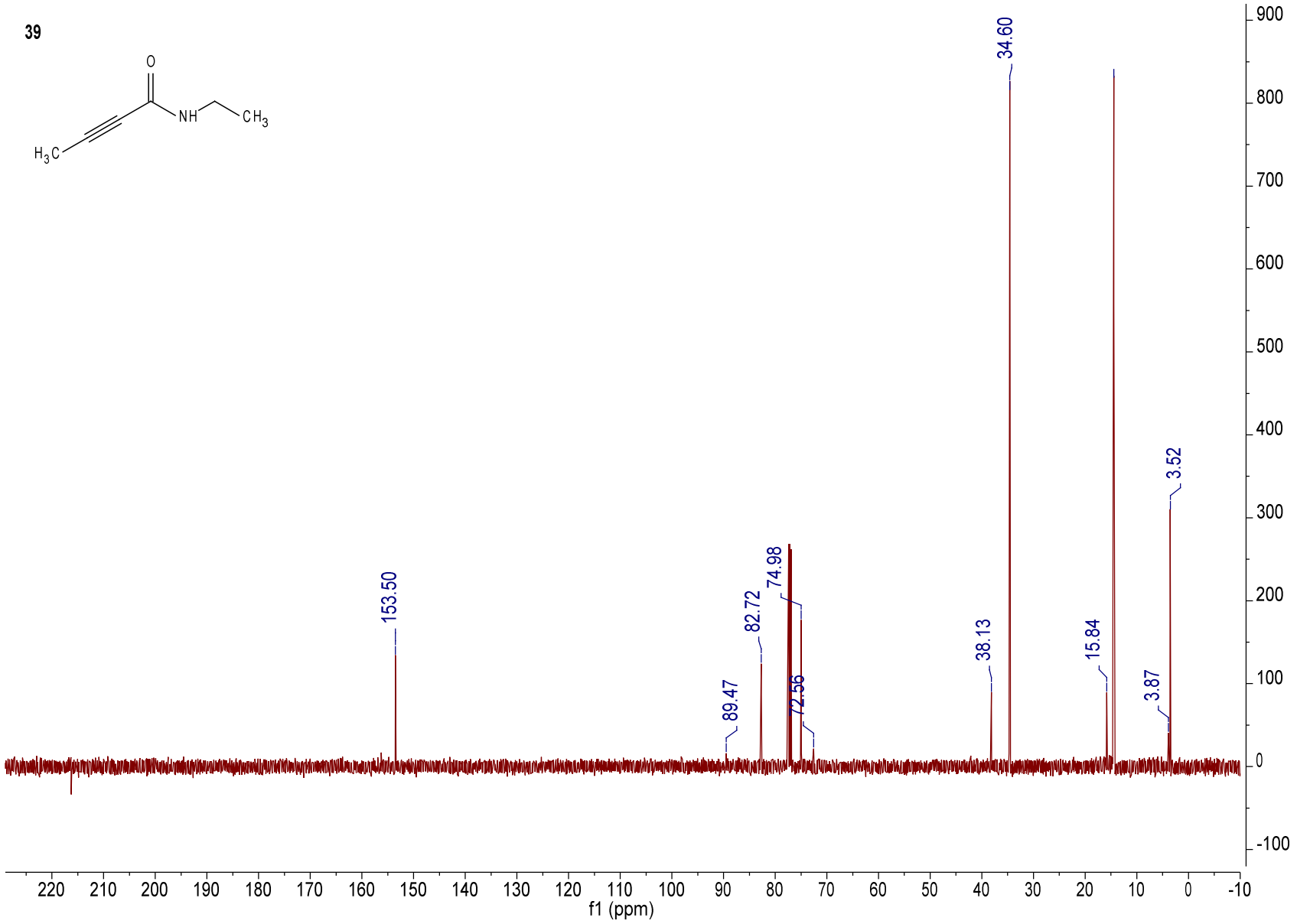

38
I
O
H3C
NH
CH3
O
7.24
7.22
6.84
6.82
6.26
6.01
4.42
4.41
3.76
2.64
2.62
2.60
2.58
1.10
1.08
1.06
2.02
2.10
1.00
0.84
2.20
3.41
2.22
3.30
f1 (ppm)

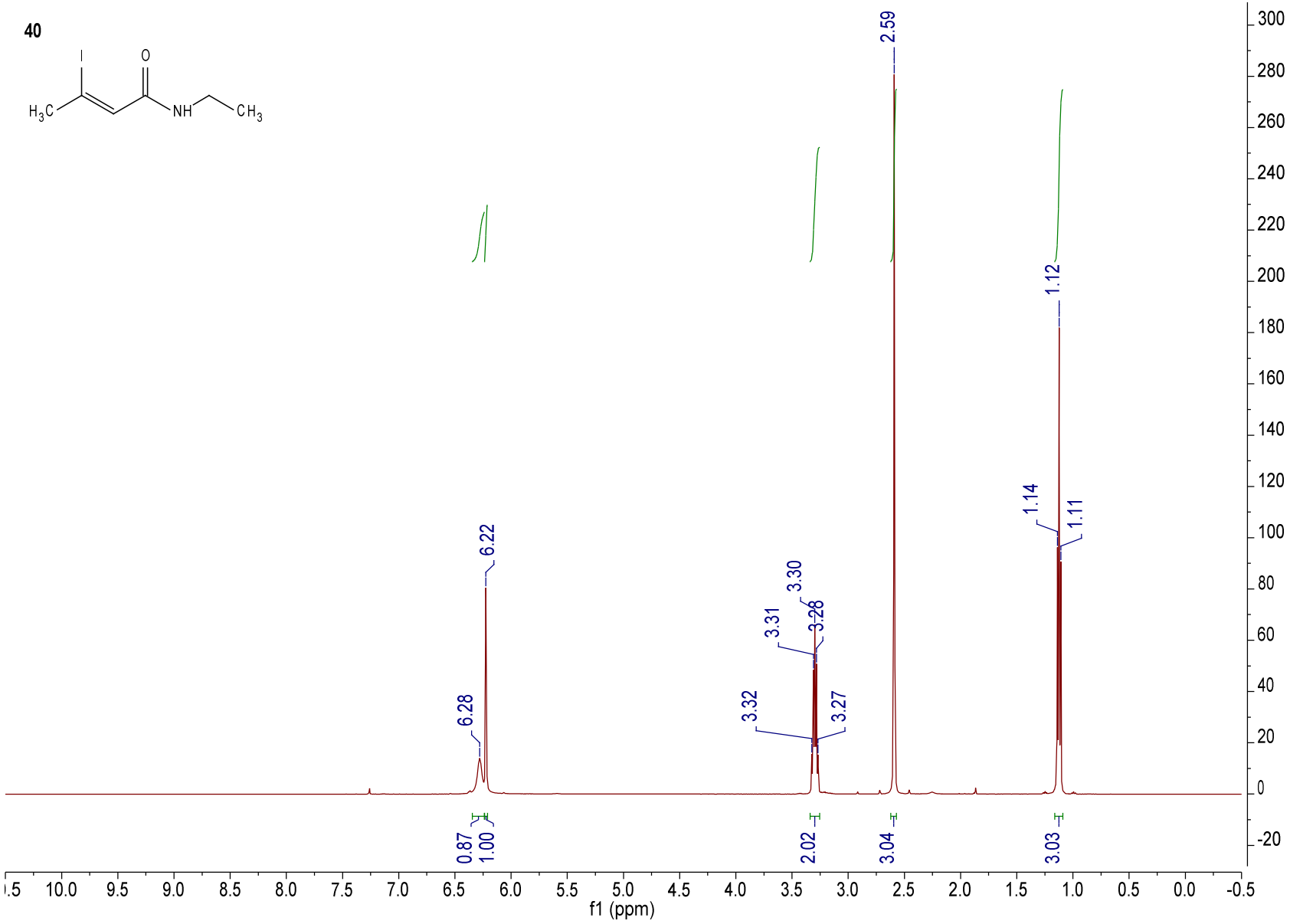

38
I
O
H_3C
NH
O
CH_3
165.00
159.04
129.95
127.41
115.90
114.06
55.34
43.11
40.91
14.55
850
800
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

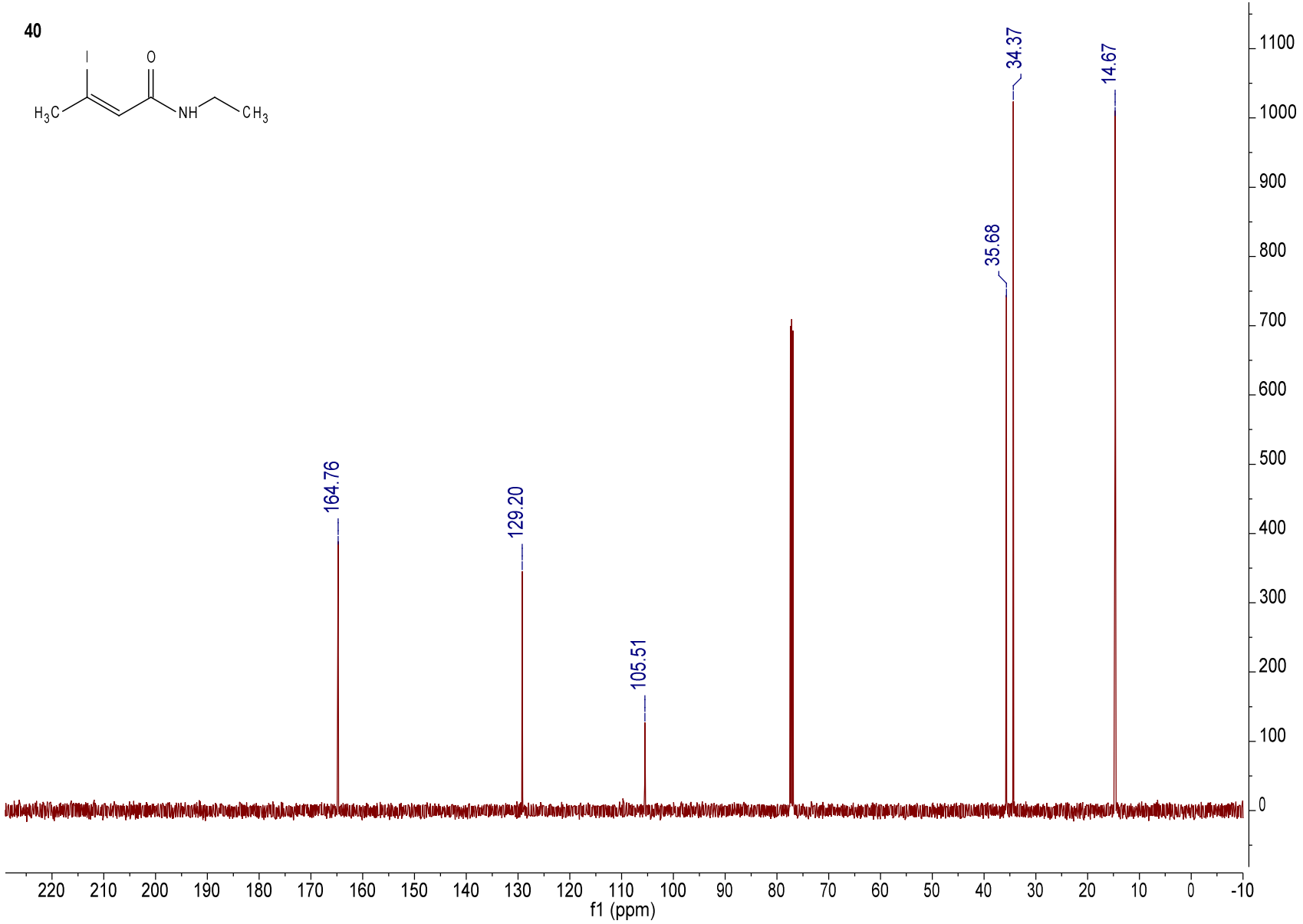

6
6.83
6.75
3.93
3.07
1.25
1.00
1.02
3.20
4.40
6.53
f1 (ppm)

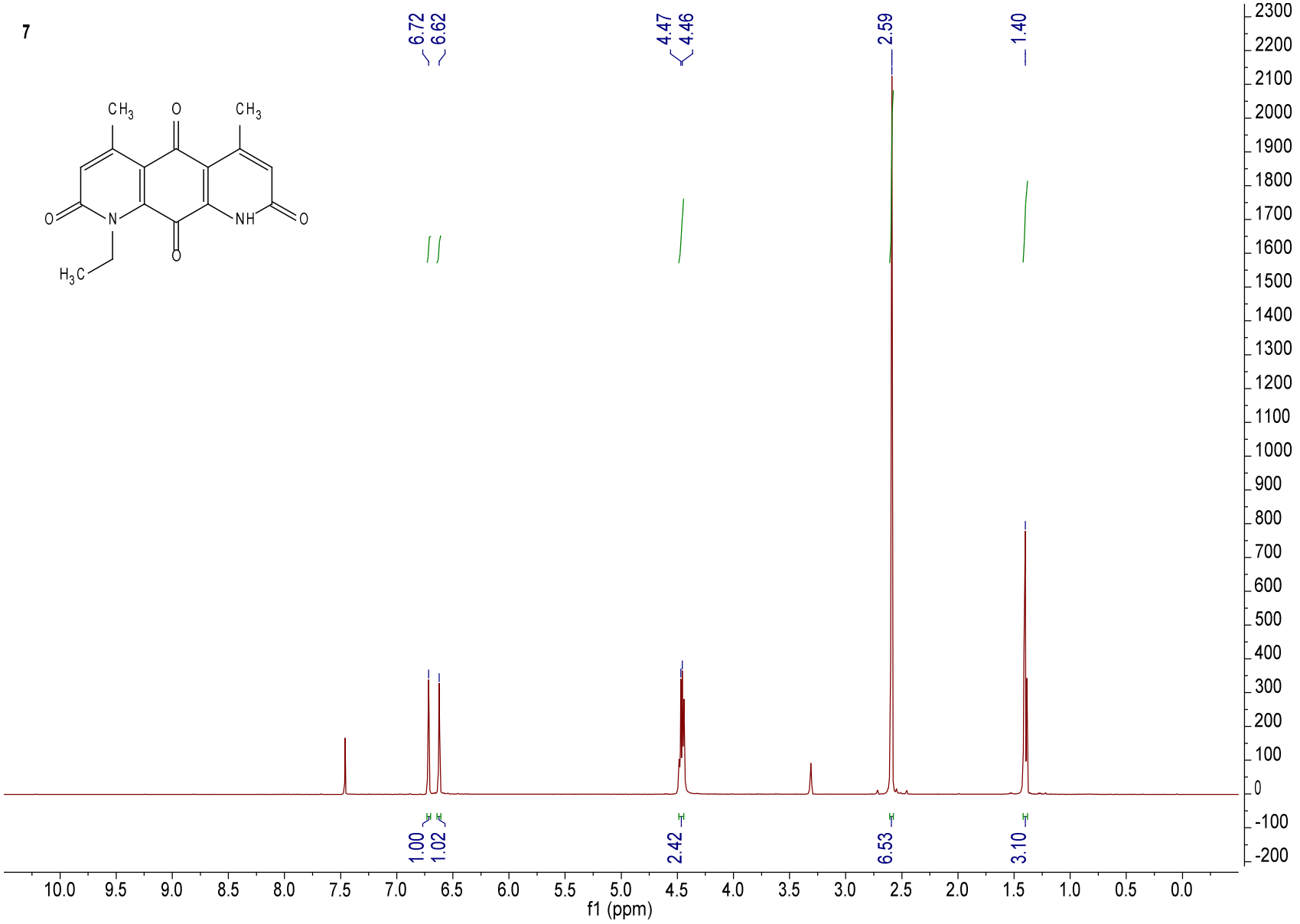

6
186.83
180.89
167.83
167.69
162.83
161.07
145.54
144.33
130.98
130.90
124.68
120.28
39.50
33.44
32.81
19.16
18.88
H3C
CH3
O
O
N
NH
O
CH3
O
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

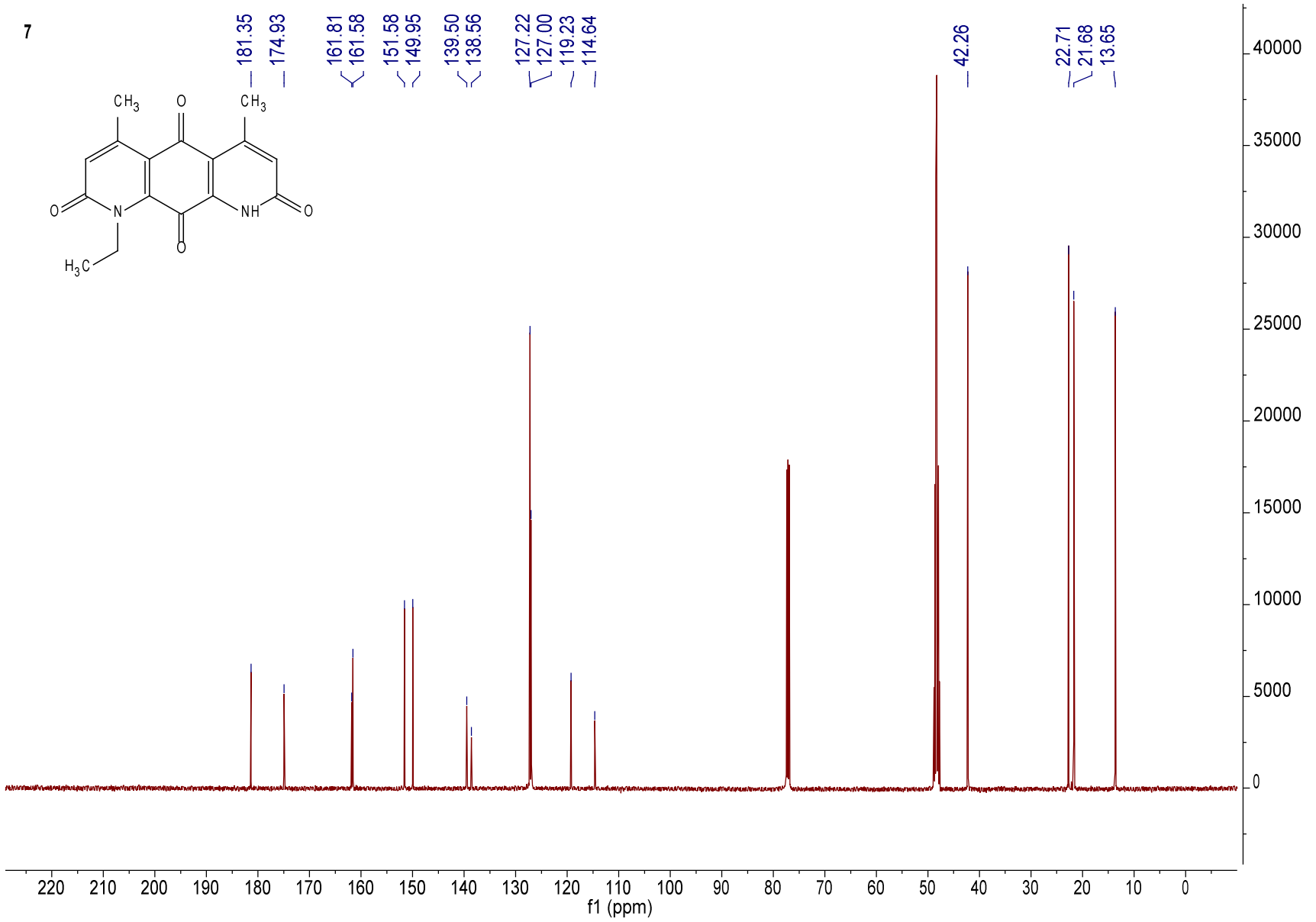

39
O
NH
CH3
H3C
1.85
1.08
1.09
1.06
3.25
3.23
3.22
3.26
3.21
6.25
1.00
1.88
3.00
3.05
f1 (ppm)

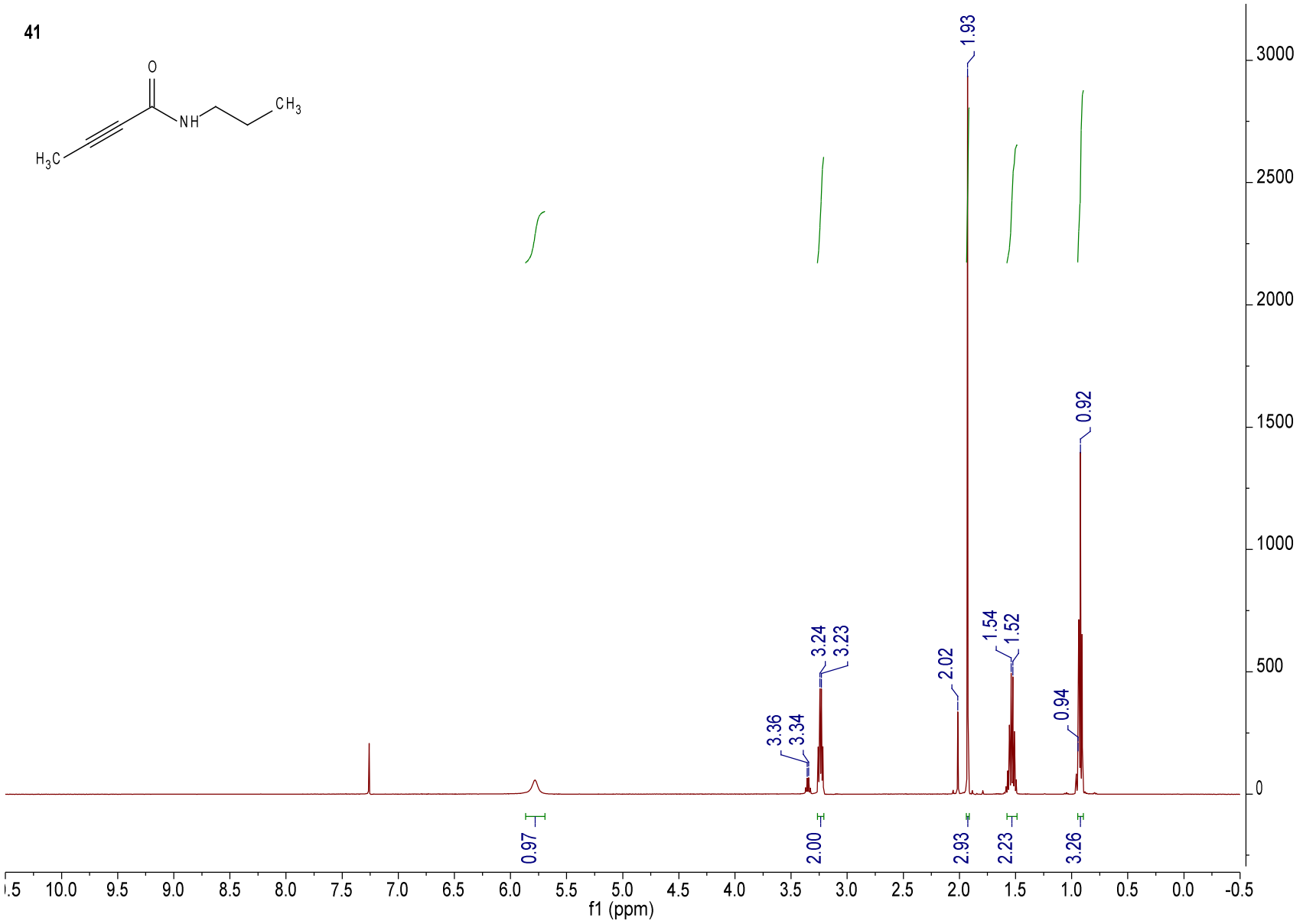

39
O
NH
CH3
H3C
153.50
89.47
82.72
74.98
72.56
38.13
34.60
15.84
3.87
3.52
f1 (ppm)

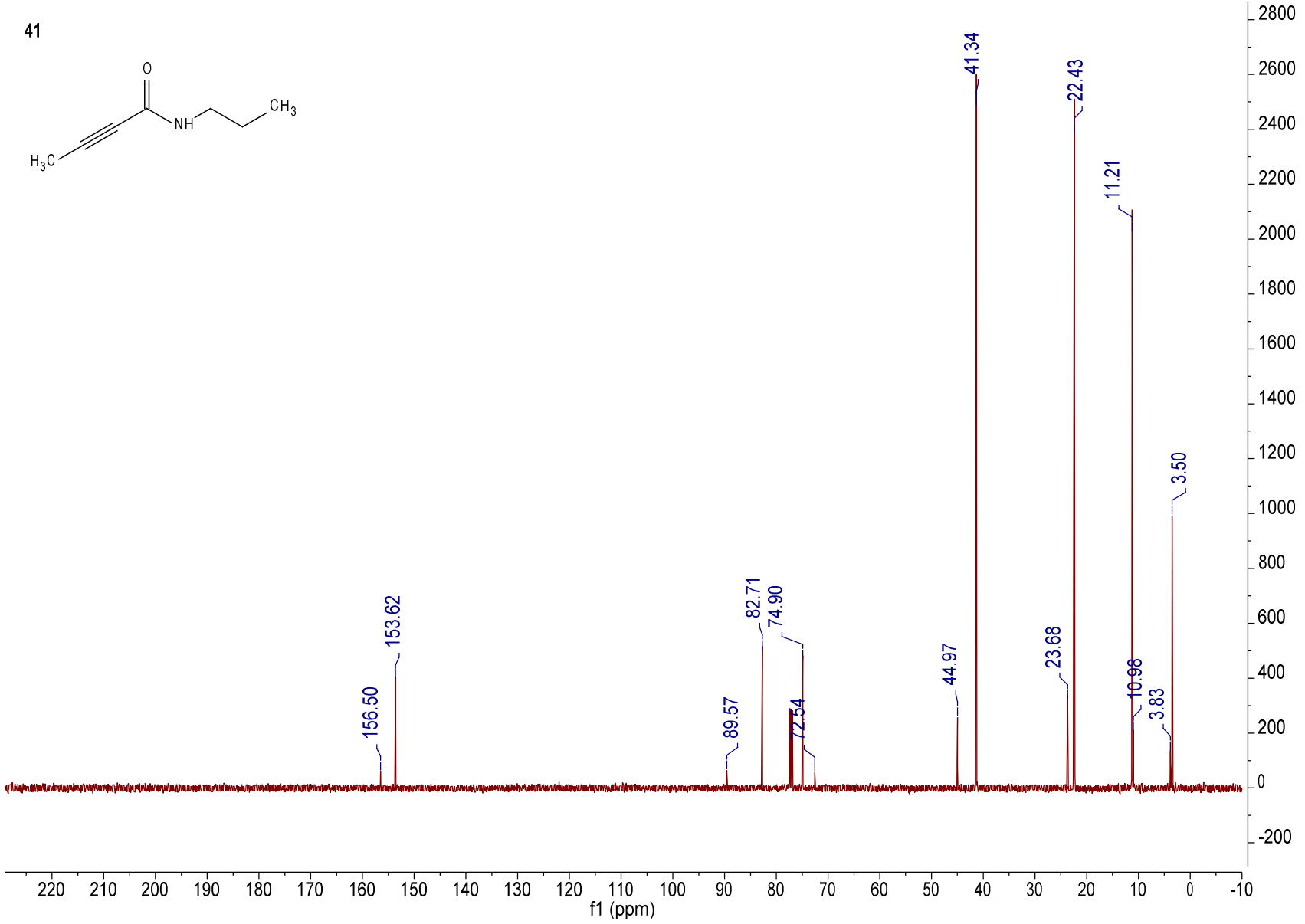

40
I
O
H3C
NH
CH3
6.28
6.22
3.32
3.31
3.30
3.28
3.27
2.59
1.14
1.12
1.11
0.87
1.00
2.02
3.04
3.03
f1 (ppm)

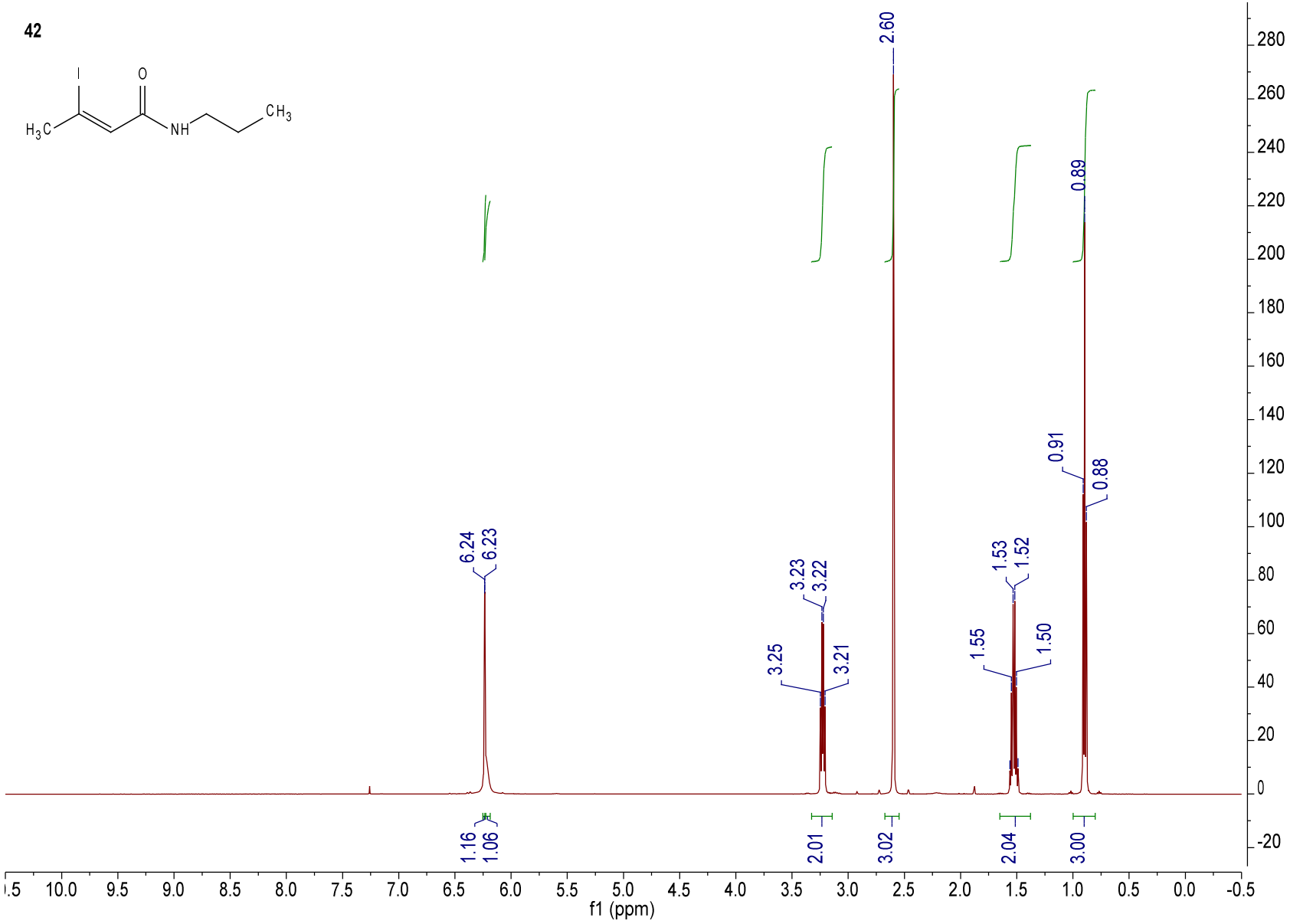

40
I
O
H_3C
NH
CH_3
164.76
129.20
105.51
35.68
34.37
14.67
f1 (ppm)

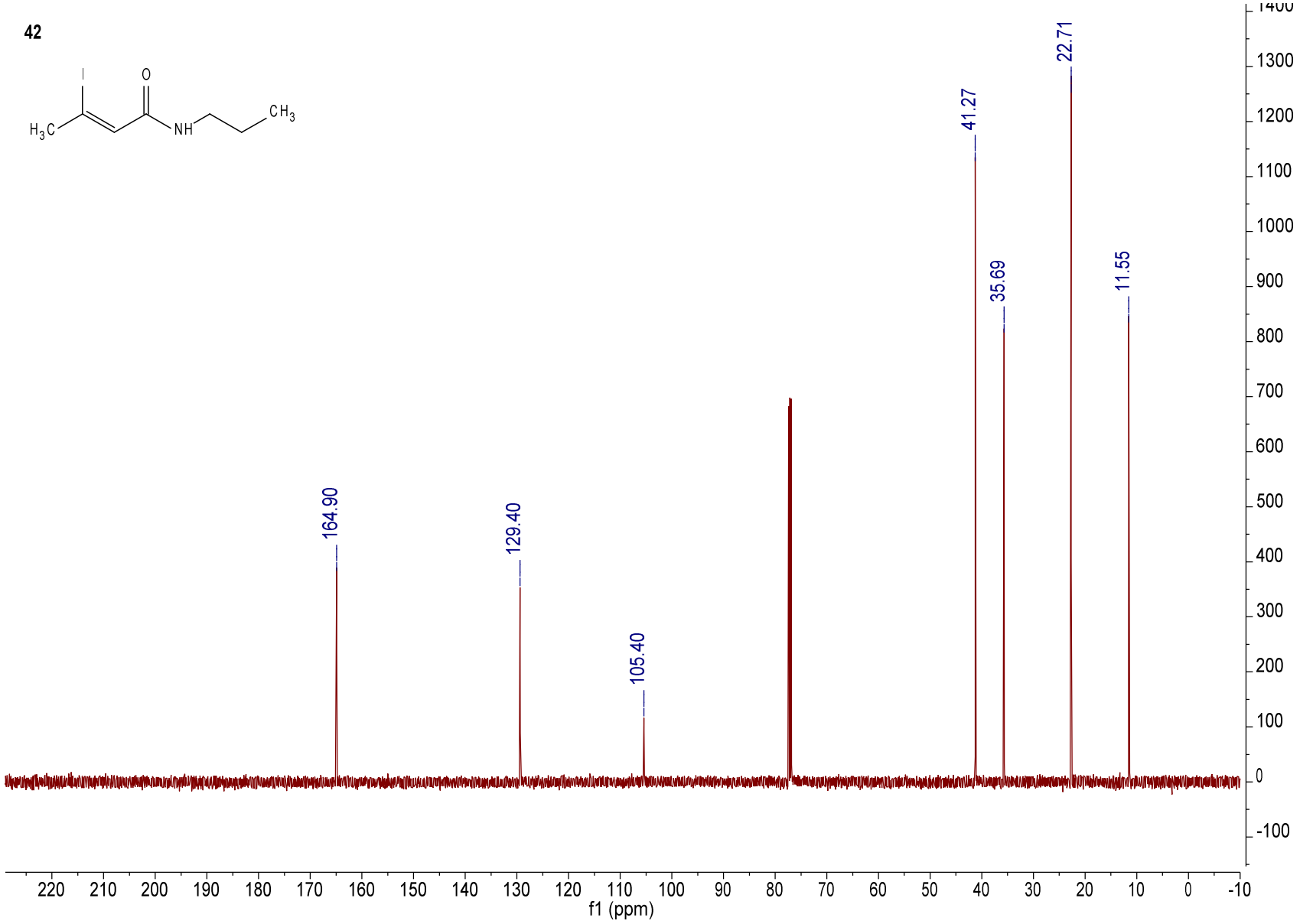

7
6.72
6.62
4.47
4.46
2.59
1.40
CH3
O
CH3
O
N
NH
O
O
H3C
1.00
1.02
2.42
6.53
3.10
f1 (ppm)

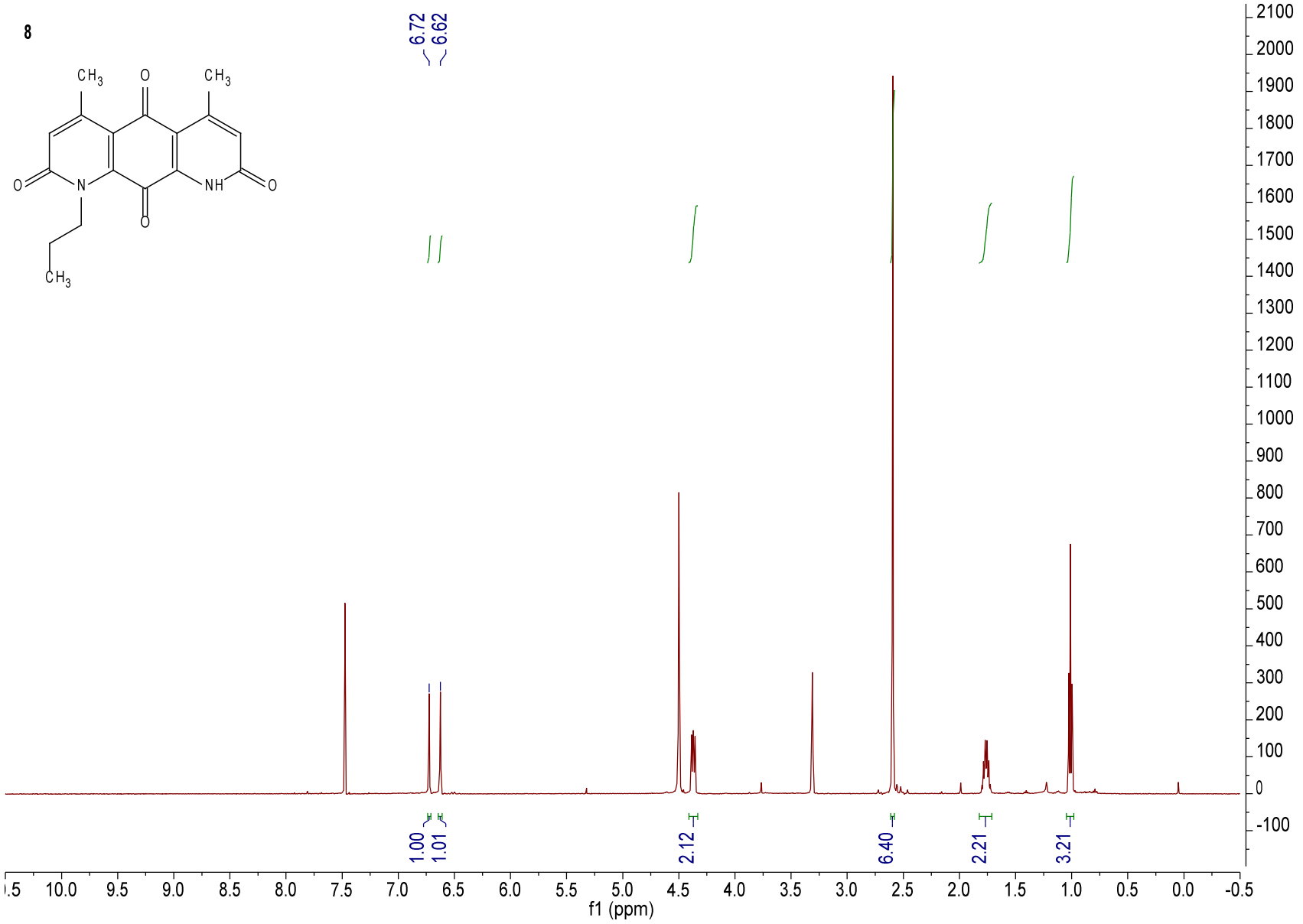

7
181.35
174.93
161.81
161.58
151.58
149.95
139.50
138.56
127.22
127.00
119.23
114.64
42.26
22.71
21.68
13.65
CH3
O
CH3
O
N
NH
O
O
H3C
40000
35000
30000
25000
20000
15000
10000
5000
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

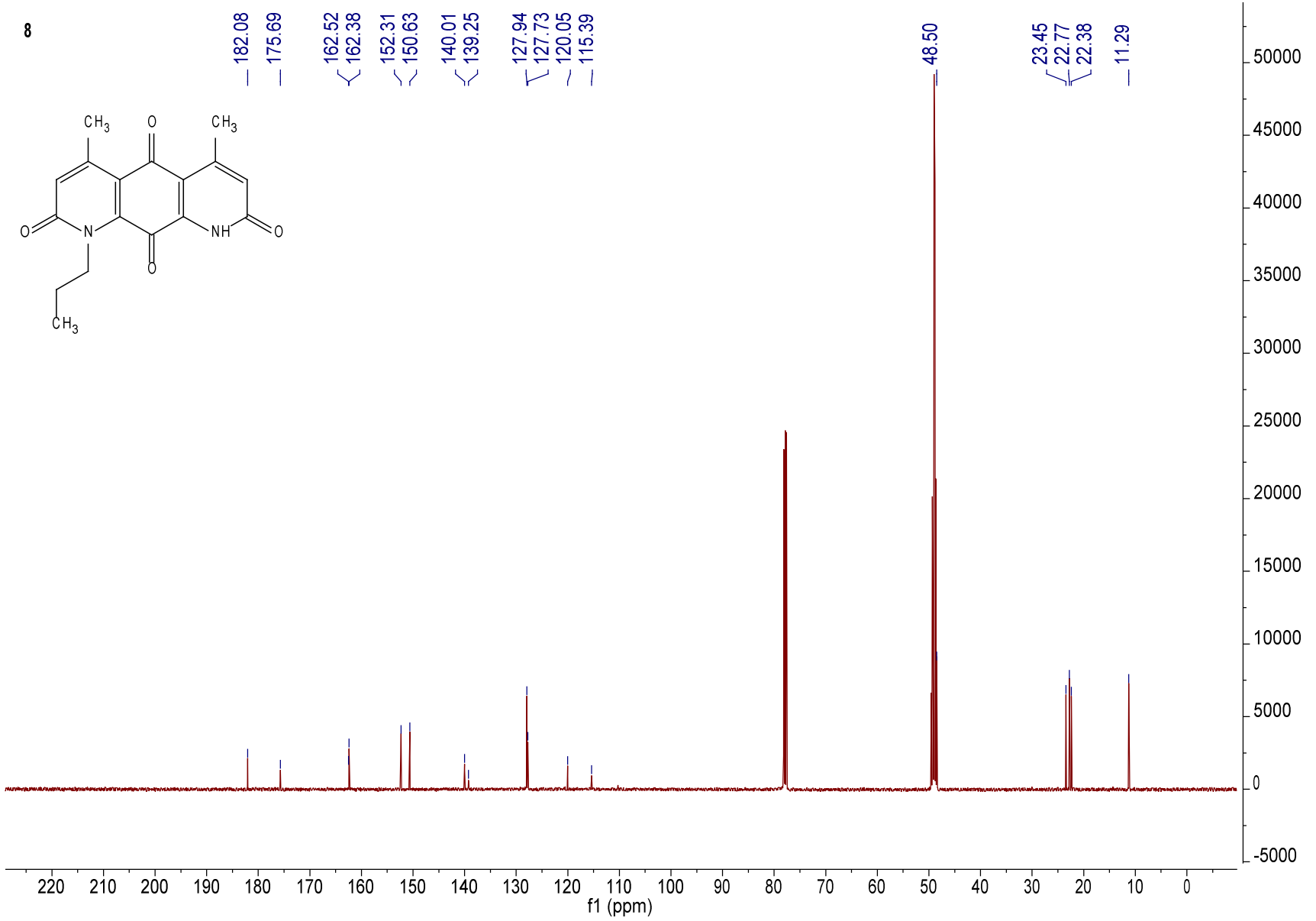

41
O
NH
CH3
H3C
1.93
0.92
3.24
3.23
3.36
3.34
2.02
1.54
1.52
0.94
0.97
2.00
2.93
2.23
3.26
f1 (ppm)

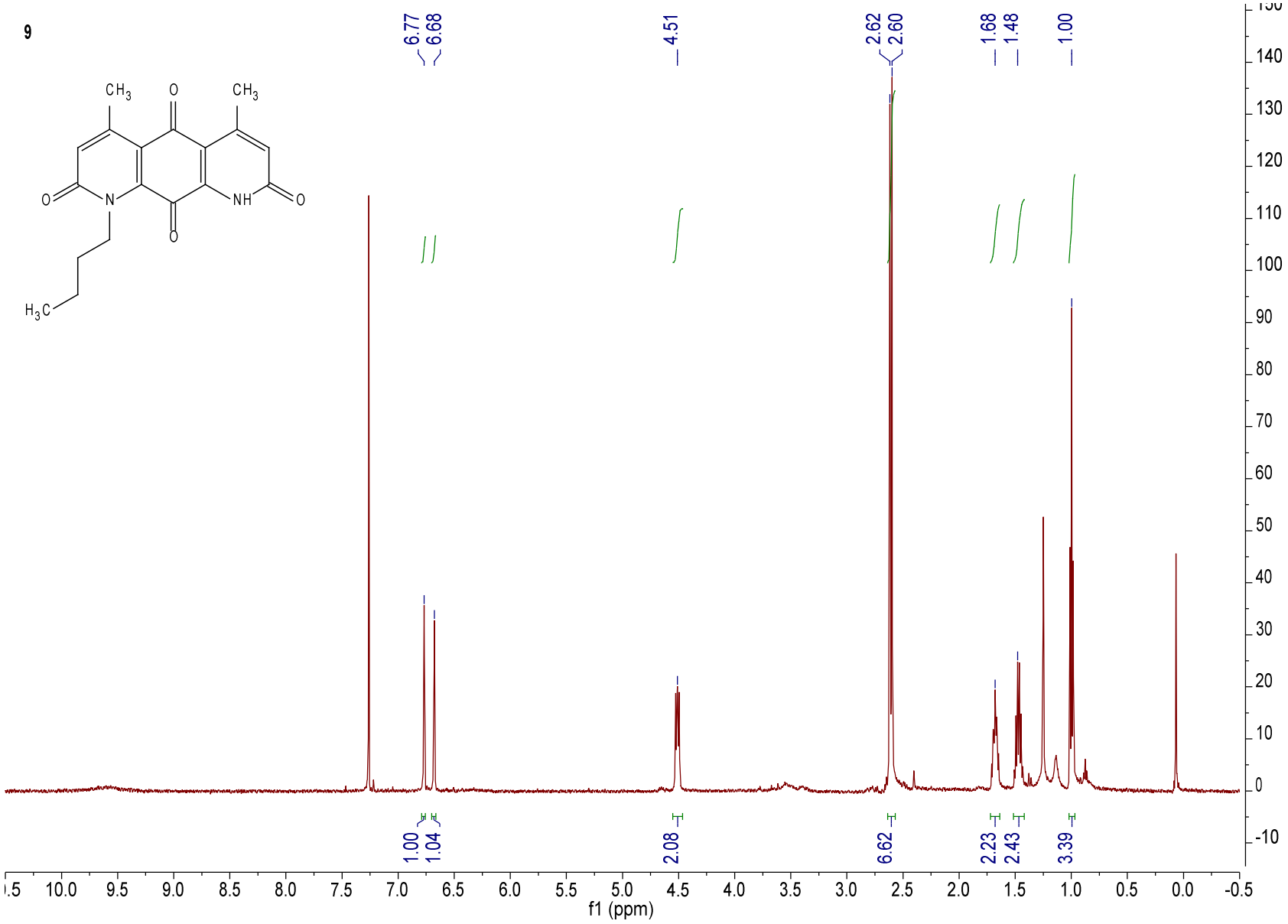

41
O
NH
CH3
H3C
156.50
153.62
89.57
82.71
74.90
72.54
44.97
41.34
23.68
22.43
11.21
10.98
3.83
3.50
f1 (ppm)

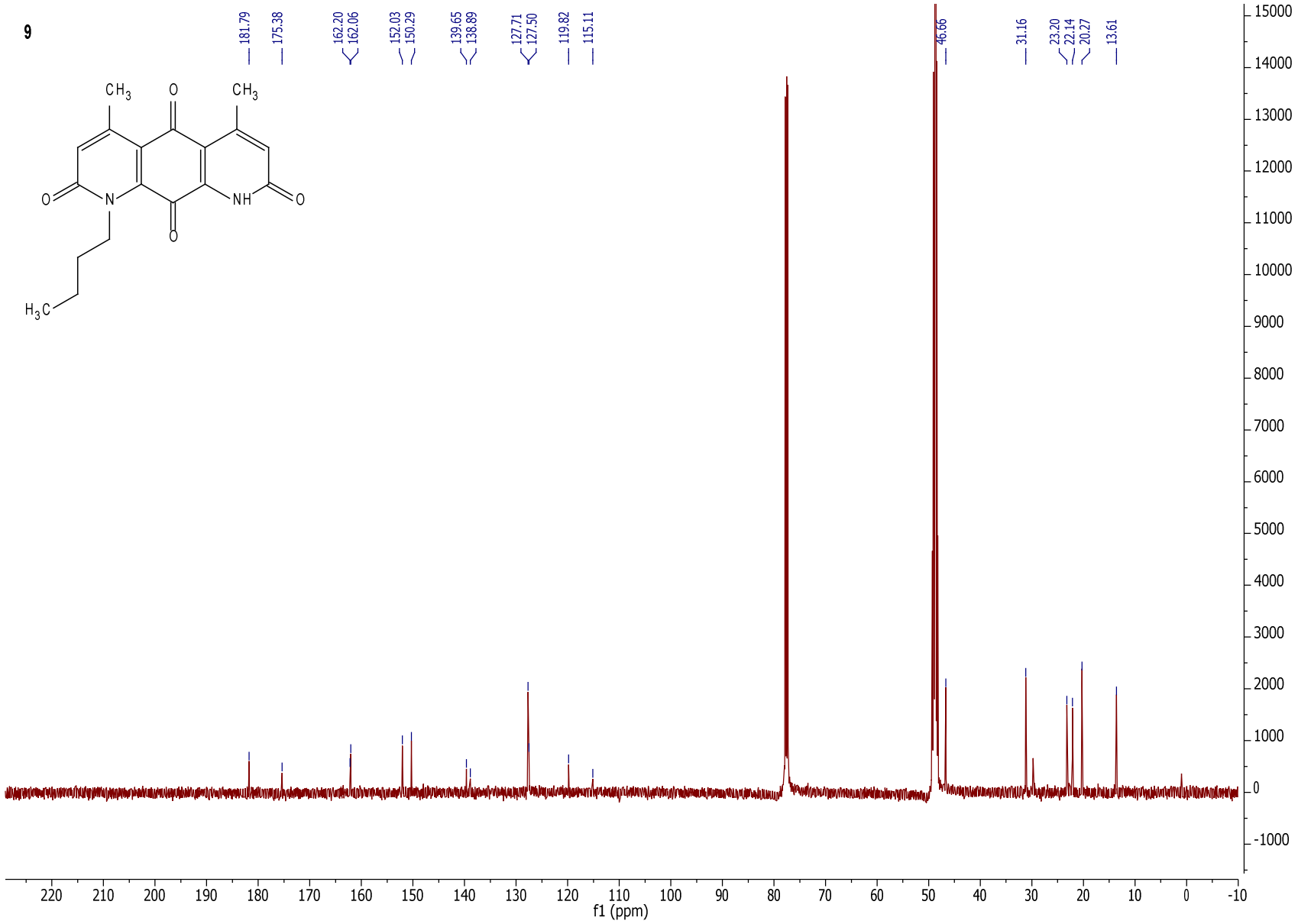

42
I
O
H_3C
NH
CH_3
6.24
6.23
3.25
3.23
3.22
3.21
2.60
1.55
1.53
1.52
1.50
0.91
0.89
0.88
1.16
1.06
2.01
3.02
2.04
3.00
f1 (ppm)

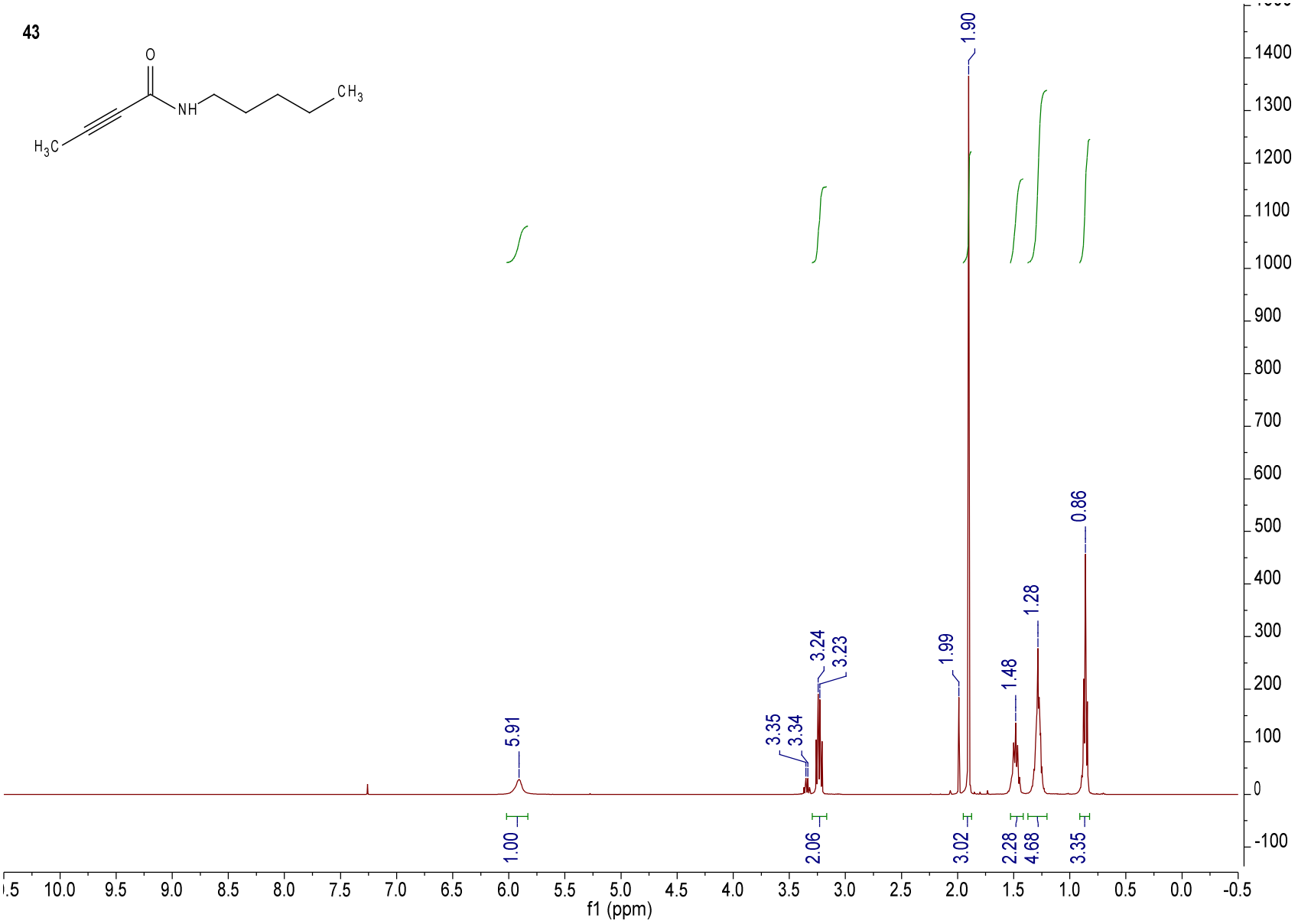

42
O
NH
CH3
H3C
164.90
129.40
105.40
41.27
35.69
22.71
11.55
f1 (ppm)

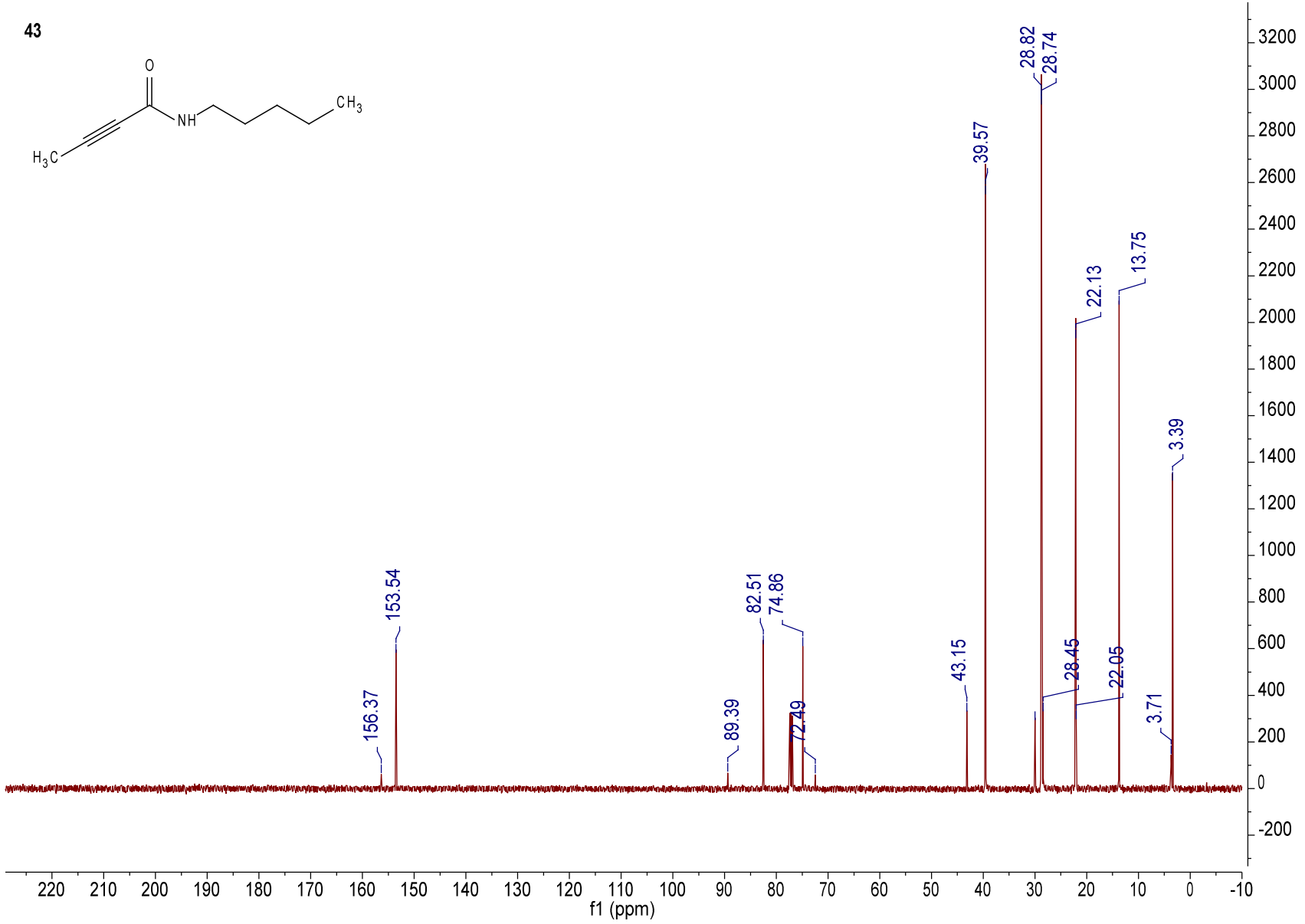

8
6.72
6.62
1.00
1.01
2.12
6.40
2.21
3.21
f1 (ppm)

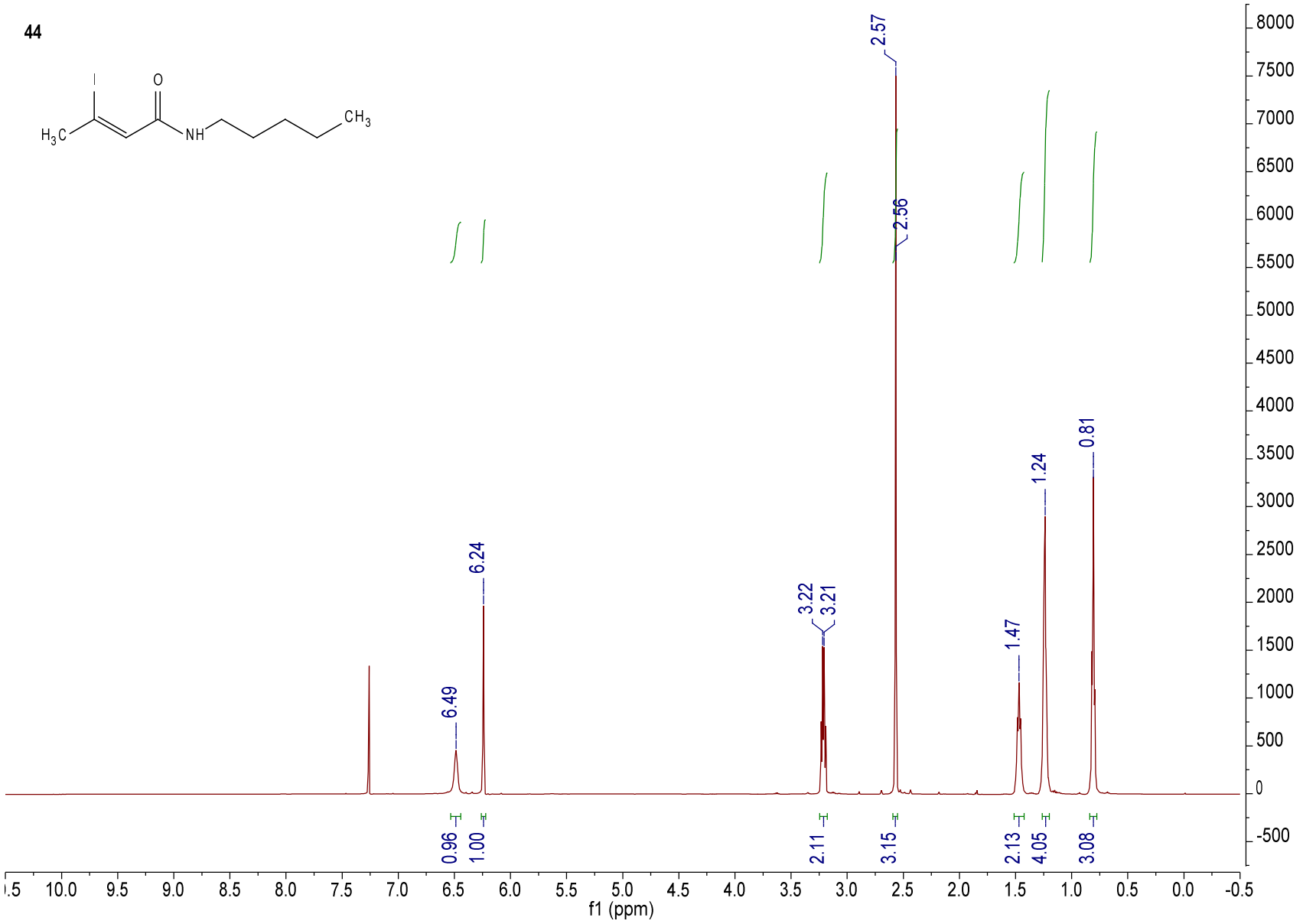

8
182.08
175.69
162.52
162.38
152.31
150.63
140.01
139.25
127.94
127.73
120.05
115.39
48.50
23.45
22.77
22.38
11.29
CH3
O
CH3
O
N
NH
O
O
CH3
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

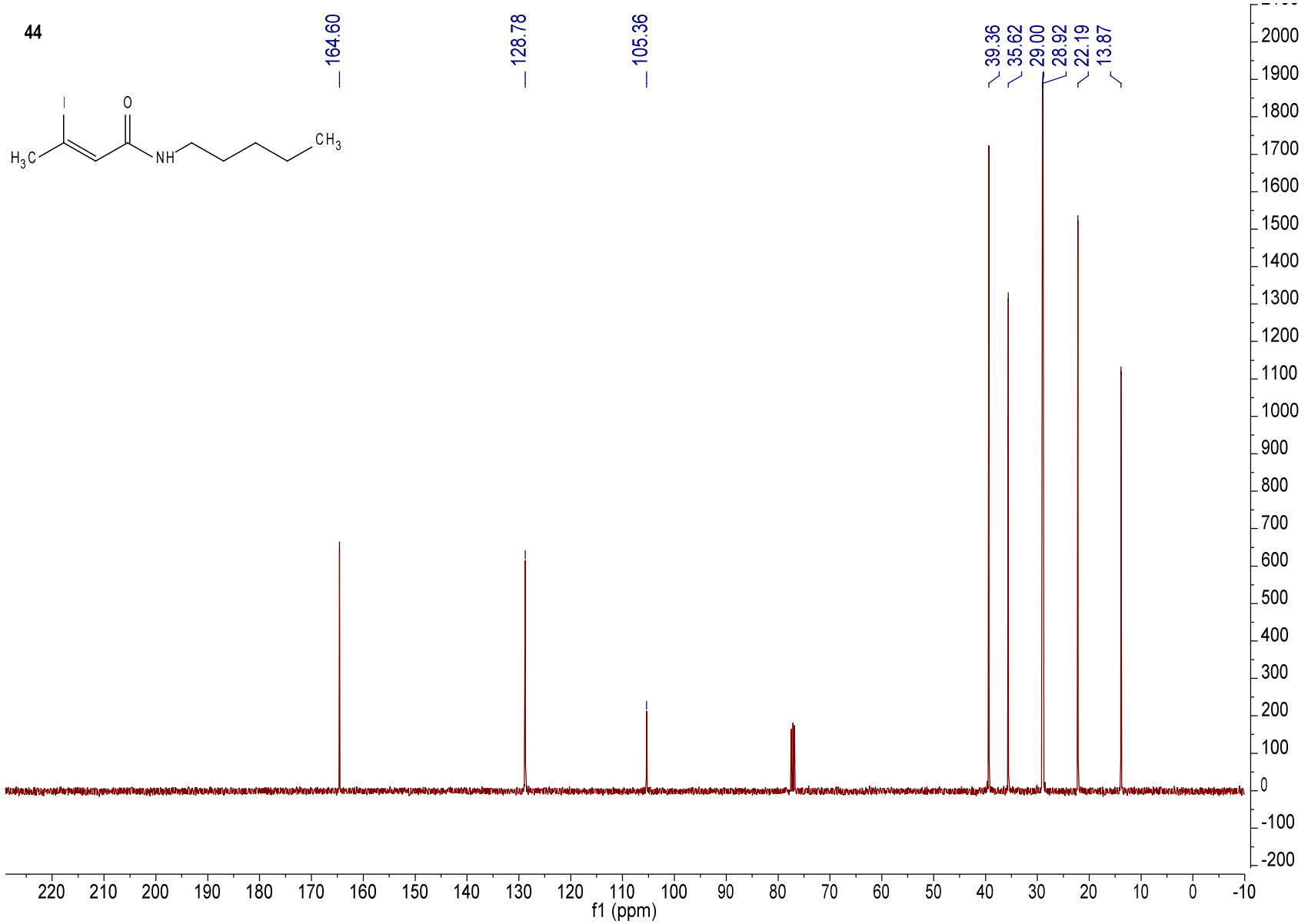

9
6.77
6.68
4.51
2.62
2.60
1.68
1.48
1.00
1.00
1.04
2.08
6.62
2.23
2.43
3.39
f1 (ppm)

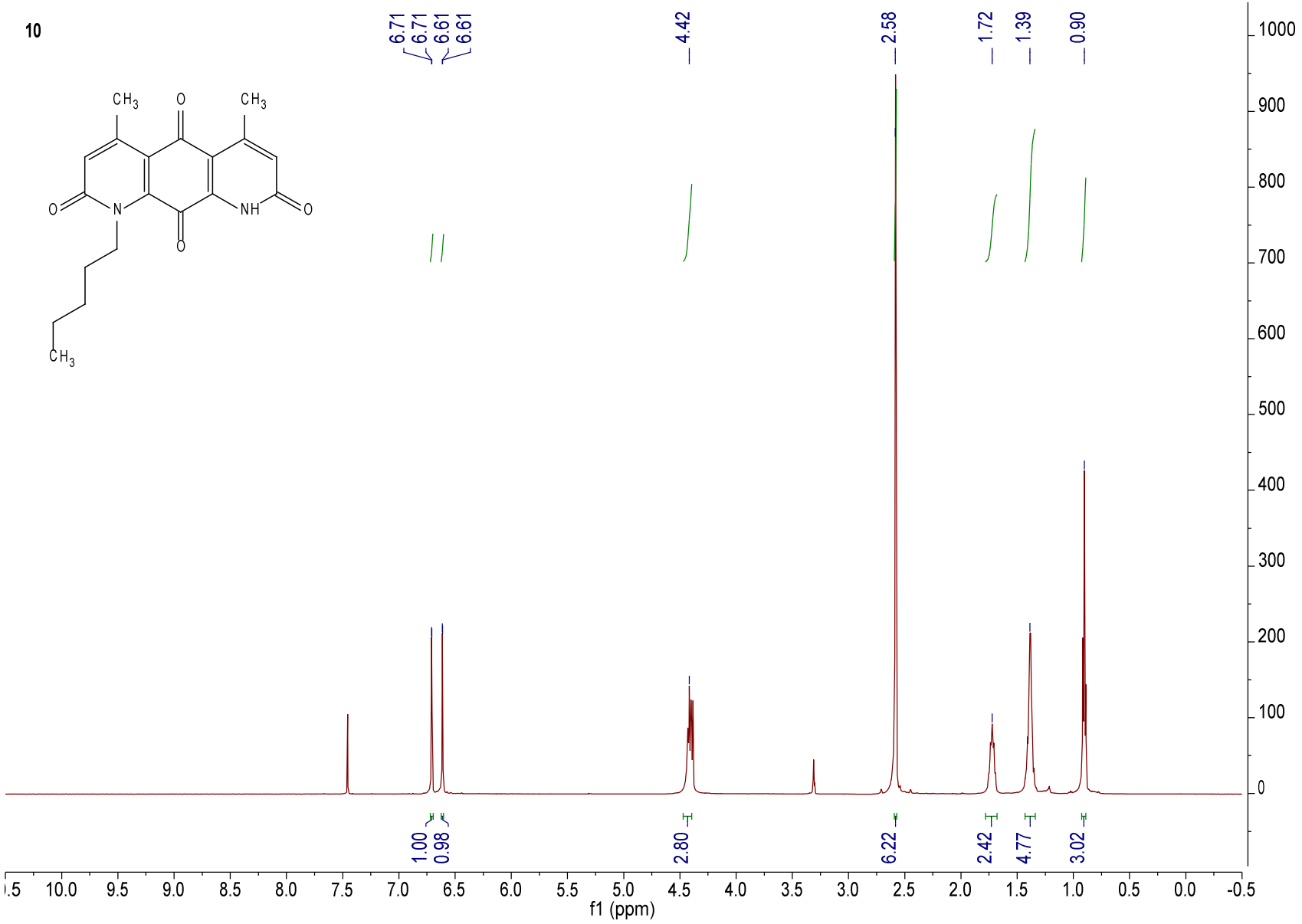

9
181.79
175.38
162.20
162.06
152.03
150.29
139.65
138.89
127.71
127.50
119.82
115.11
46.66
31.16
23.20
22.14
20.27
13.61
CH3
O
CH3
O
N
NH
O
O
H3C
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

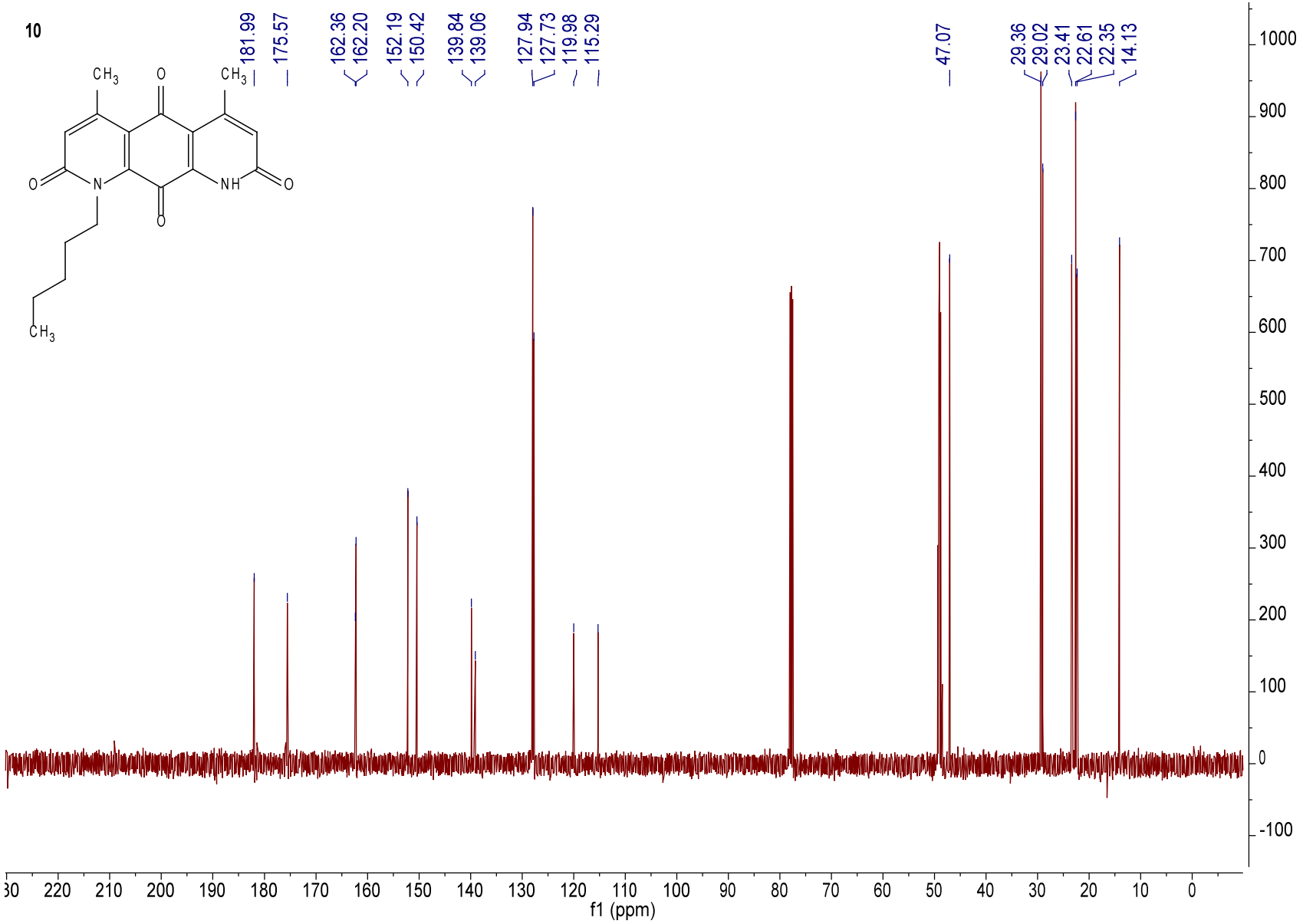

43
O
NH
CH3
H3C
1.90
5.91
3.35
3.34
3.24
3.23
1.99
1.48
1.28
0.86
1.00
2.06
3.02
2.28
4.68
3.35
f1 (ppm)

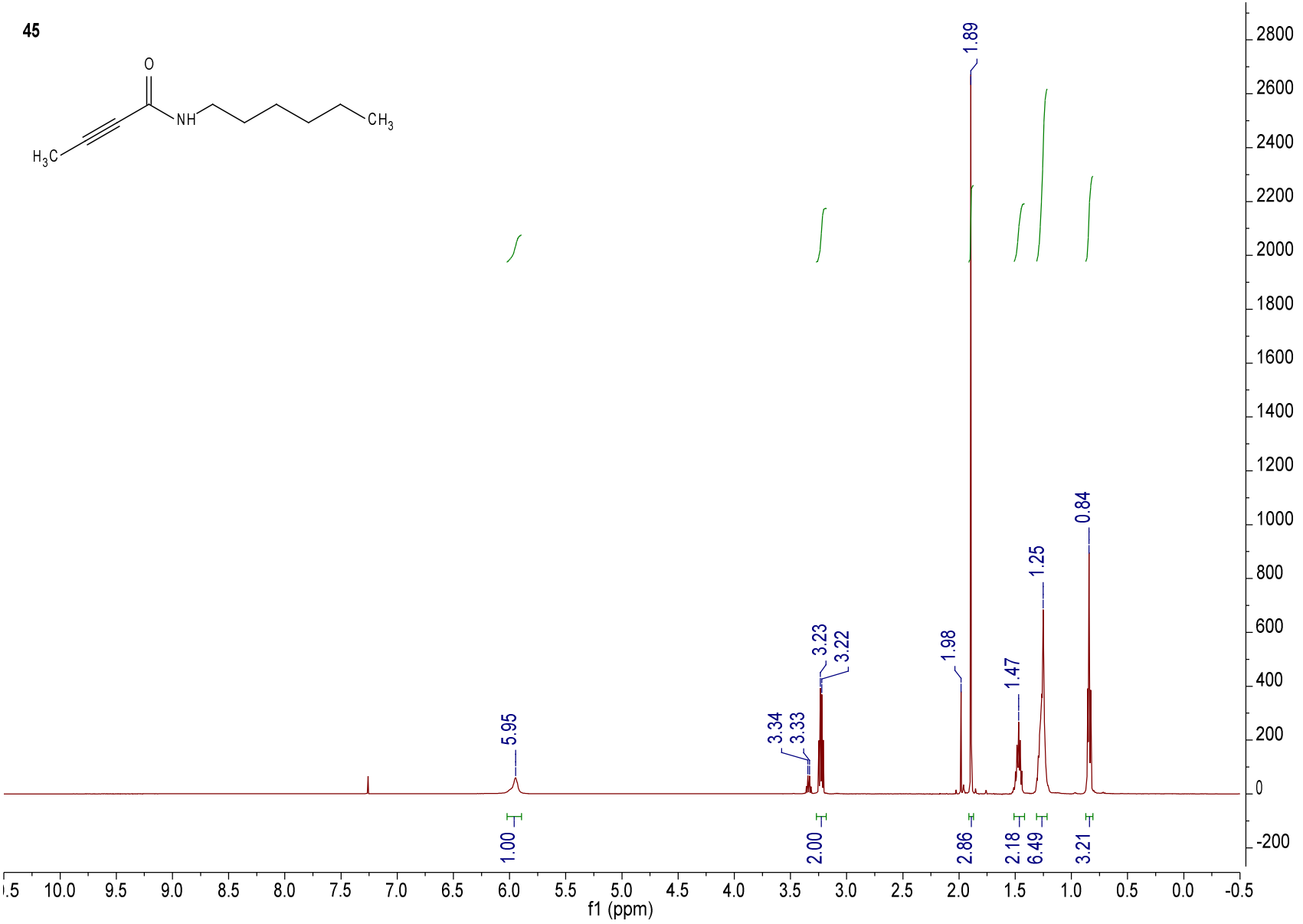

43
O
NH
CH3
H3C
156.37
153.54
89.39
82.51
74.86
72.49
43.15
39.57
28.82
28.74
28.45
22.13
22.05
13.75
3.71
3.39
f1 (ppm)

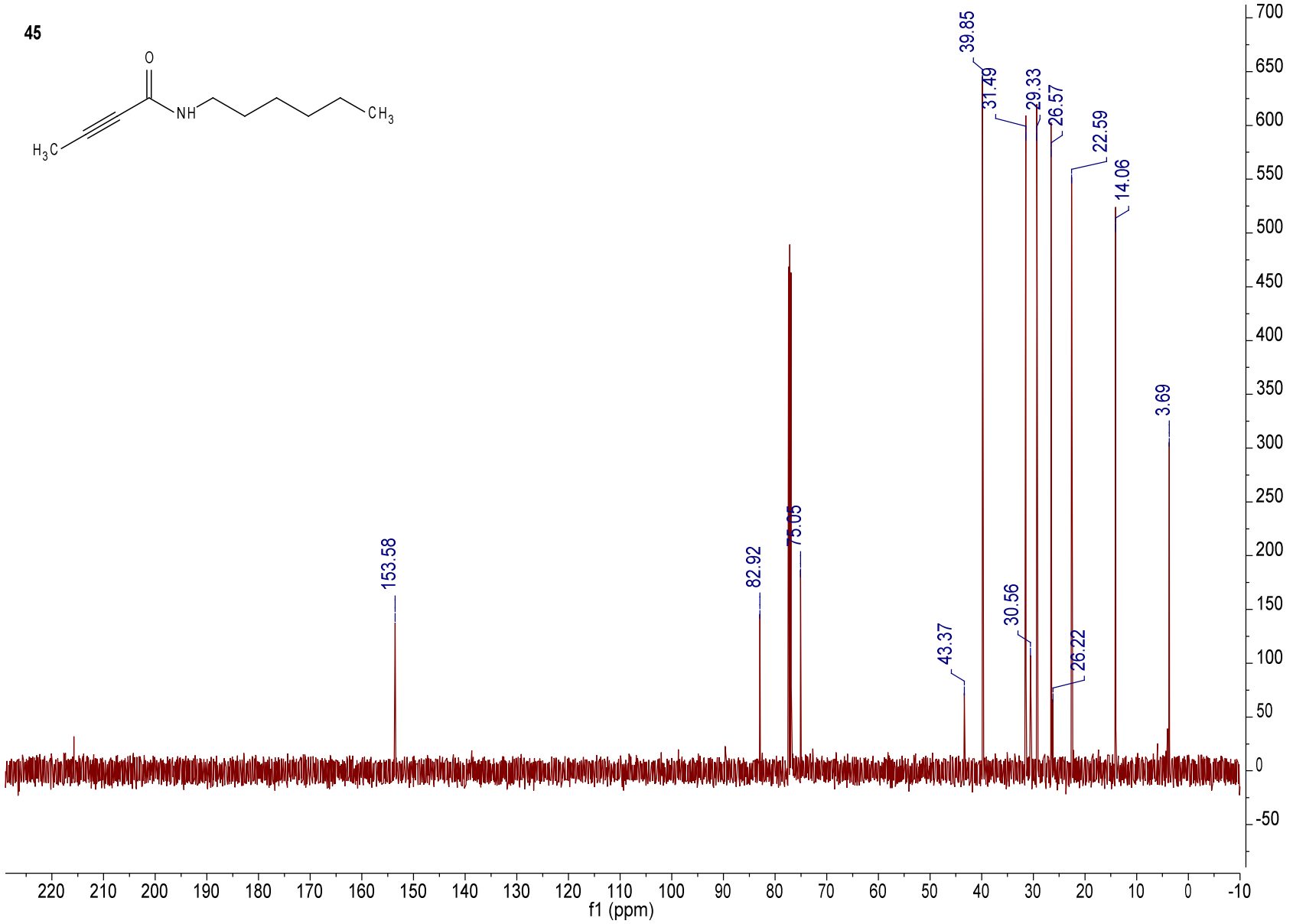

44
O
NH
CH3
H3C
2.57
2.56
6.24
6.49
3.22
3.21
1.47
1.24
0.81
0.96
1.00
2.11
3.15
2.13
4.05
3.08
f1 (ppm)

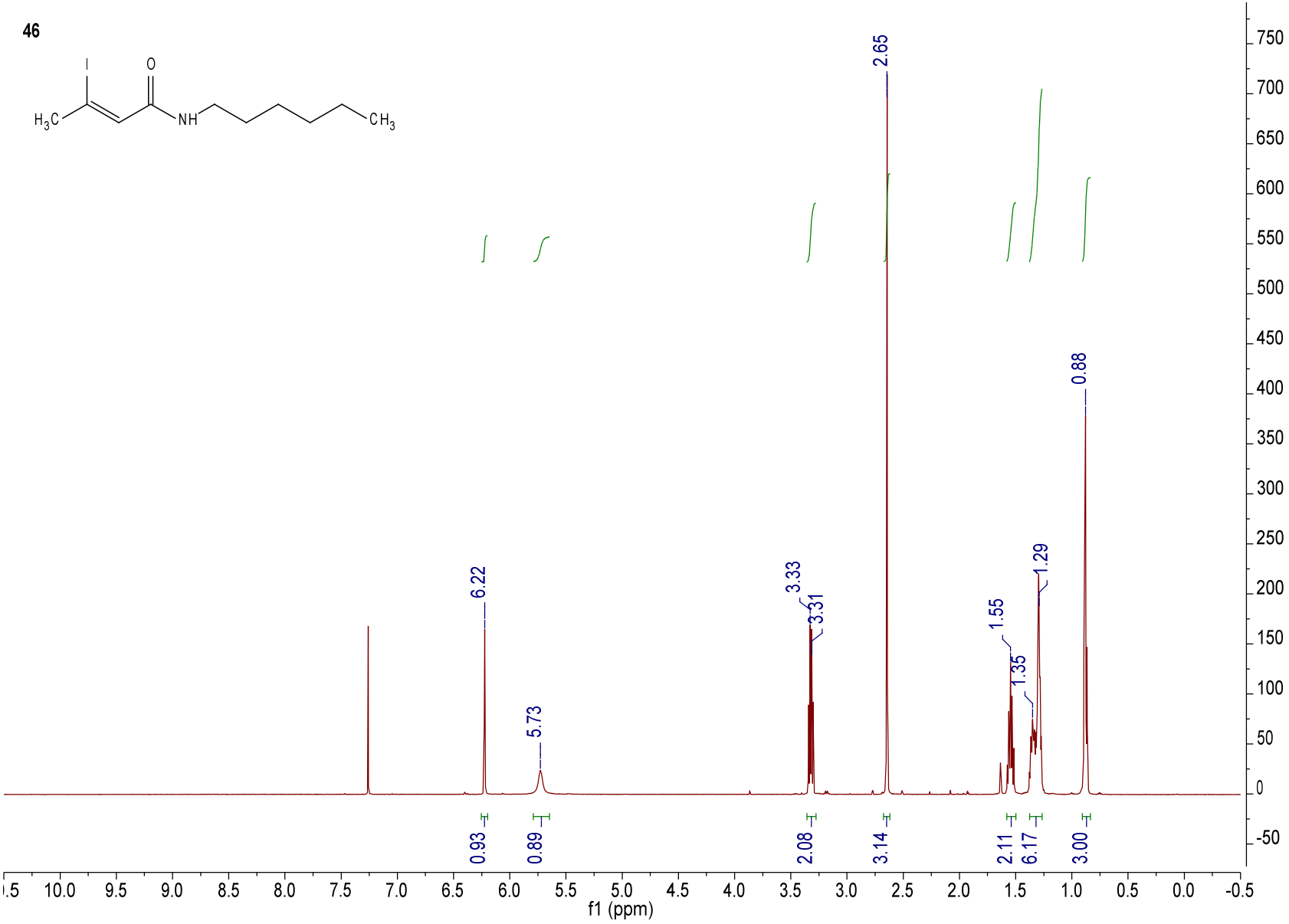

44
164.60
128.78
105.36
39.36
35.62
29.00
28.92
22.19
13.87
O
NH
H_3C
CH_3
f1 (ppm)

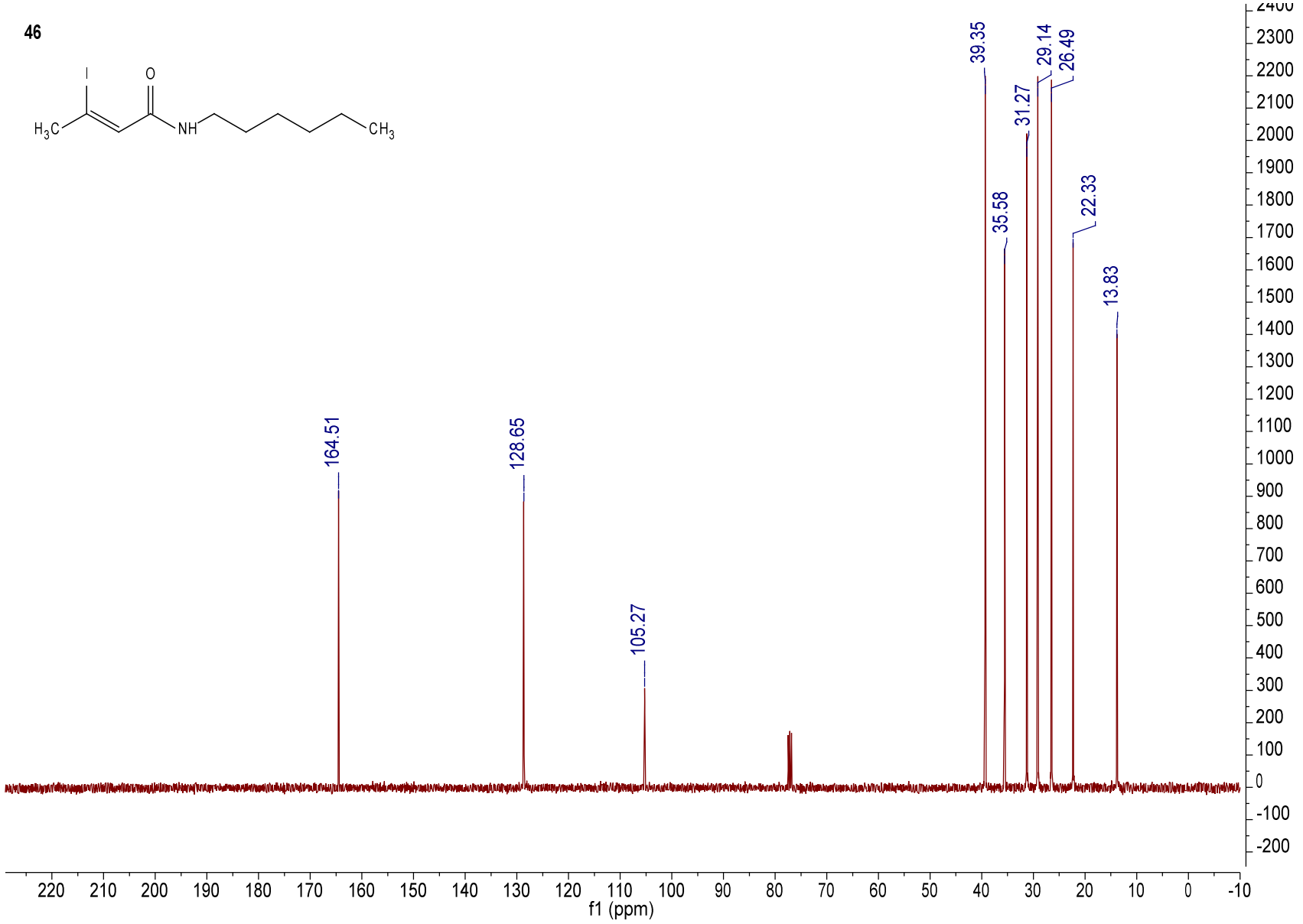

10
6.71
6.71
6.61
6.61
4.42
2.58
1.72
1.39
0.90
1.00
0.98
2.80
6.22
2.42
4.77
3.02
f1 (ppm)

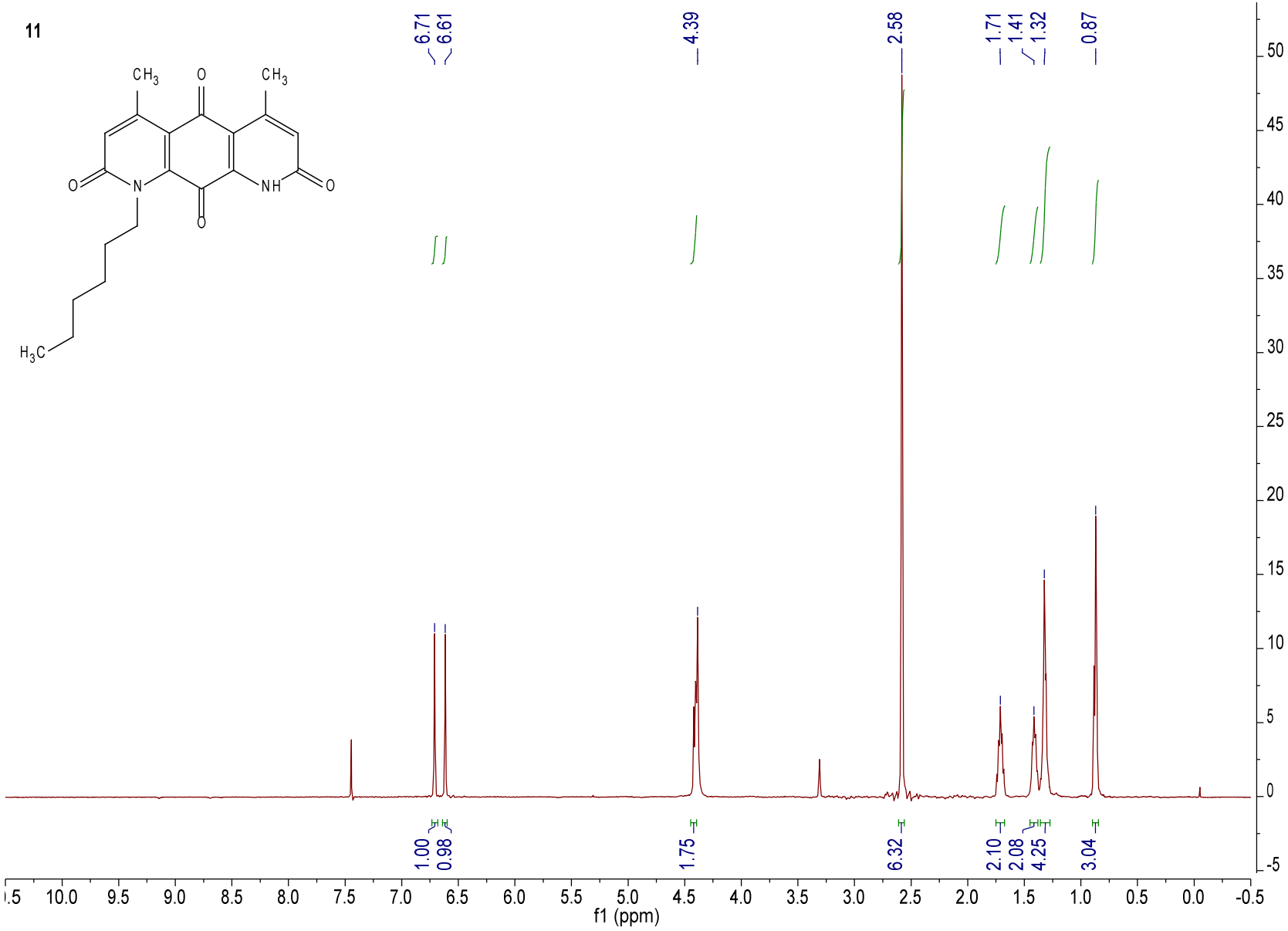

10
181.99
175.57
162.36
162.20
152.19
150.42
139.84
139.06
127.94
127.73
119.98
115.29
47.07
29.36
29.02
23.41
22.61
22.35
14.13
f1 (ppm)

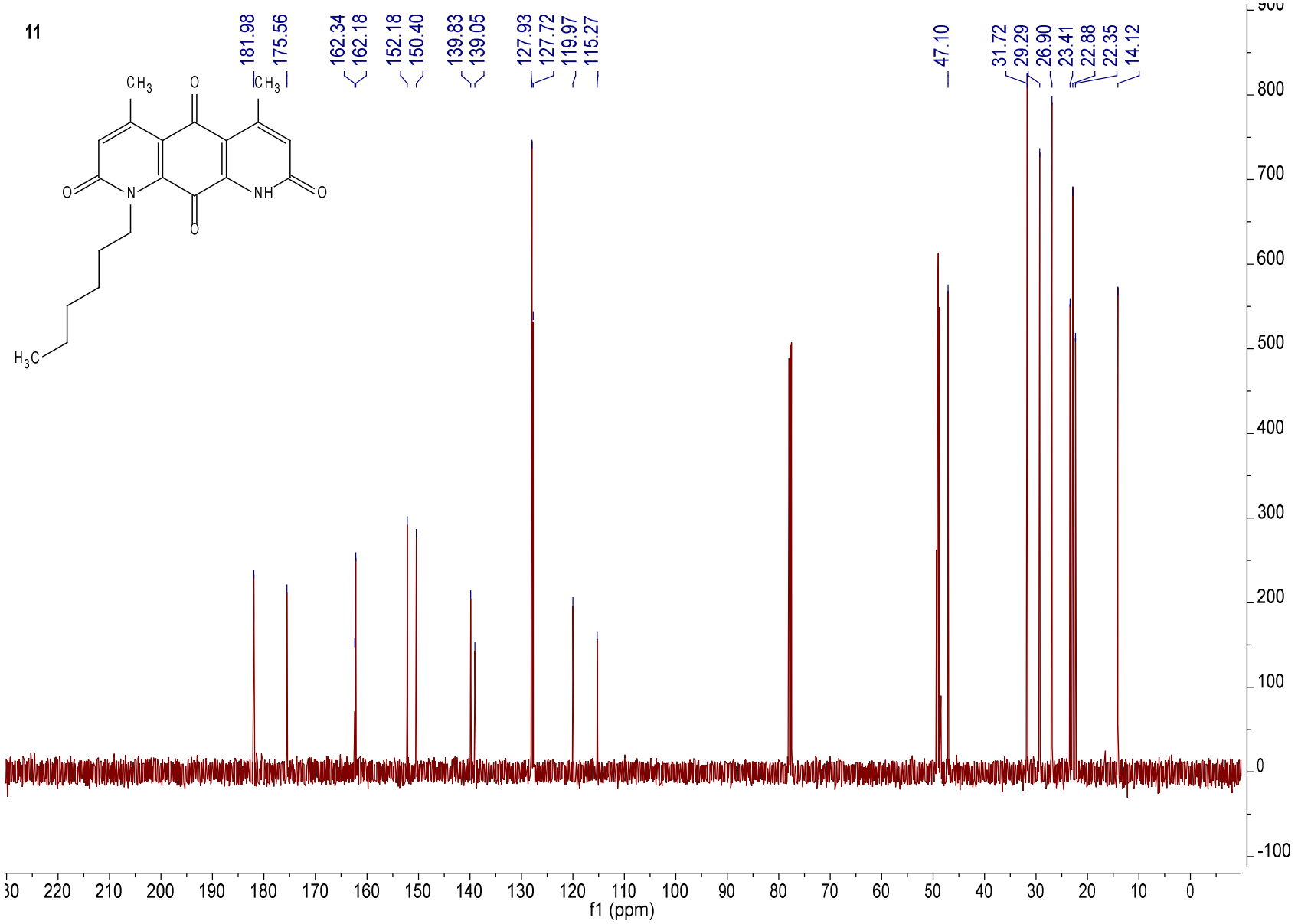

45
O
NH
CH3
H3C
1.89
5.95
3.34
3.33
3.23
3.22
1.98
1.47
1.25
0.84
1.00
2.00
2.86
2.18
6.49
3.21
f1 (ppm)

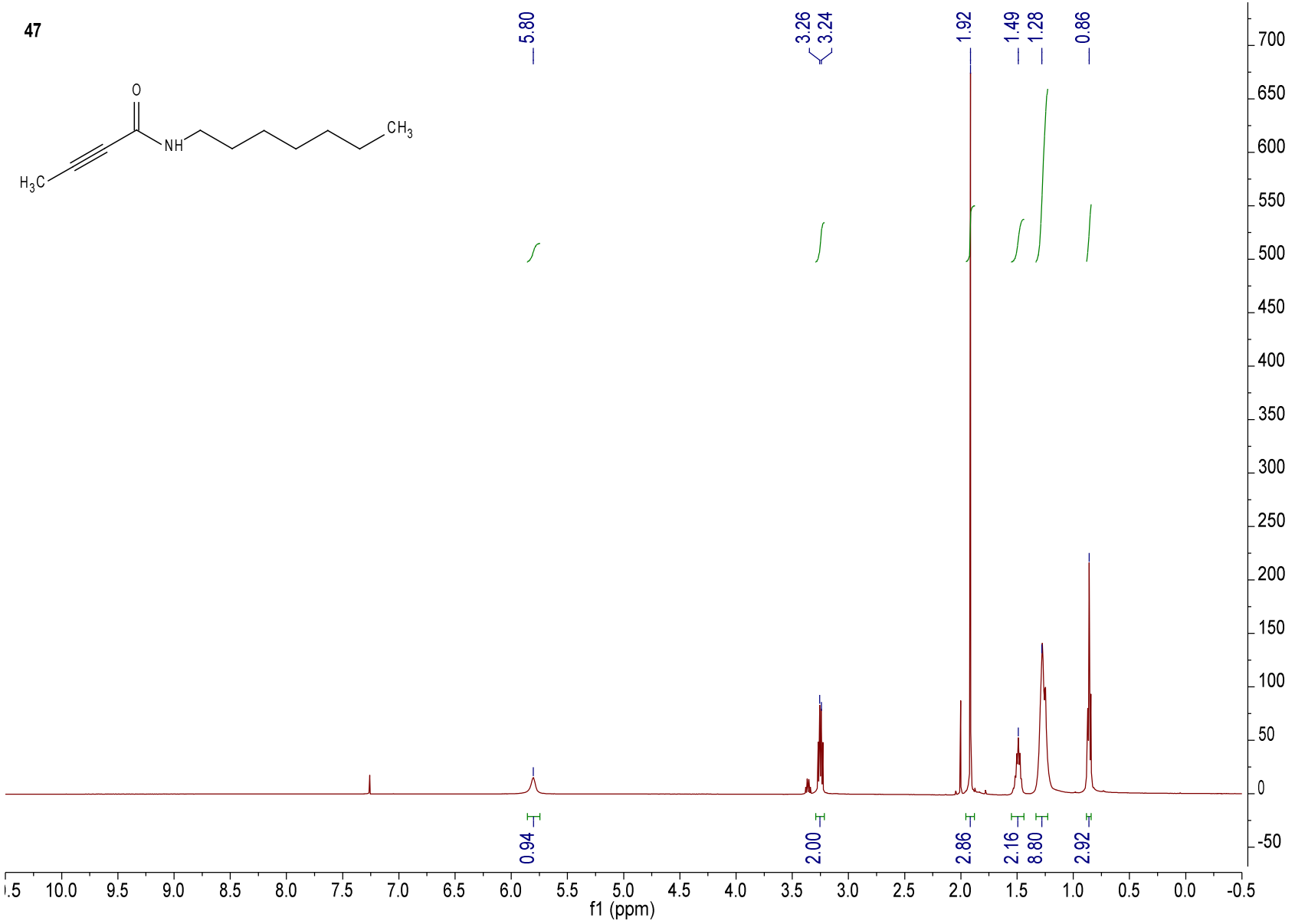

45
O
NH
CH3
H3C
153.58
82.92
75.05
43.37
39.85
31.49
30.56
29.33
26.57
26.22
22.59
14.06
3.69
f1 (ppm)

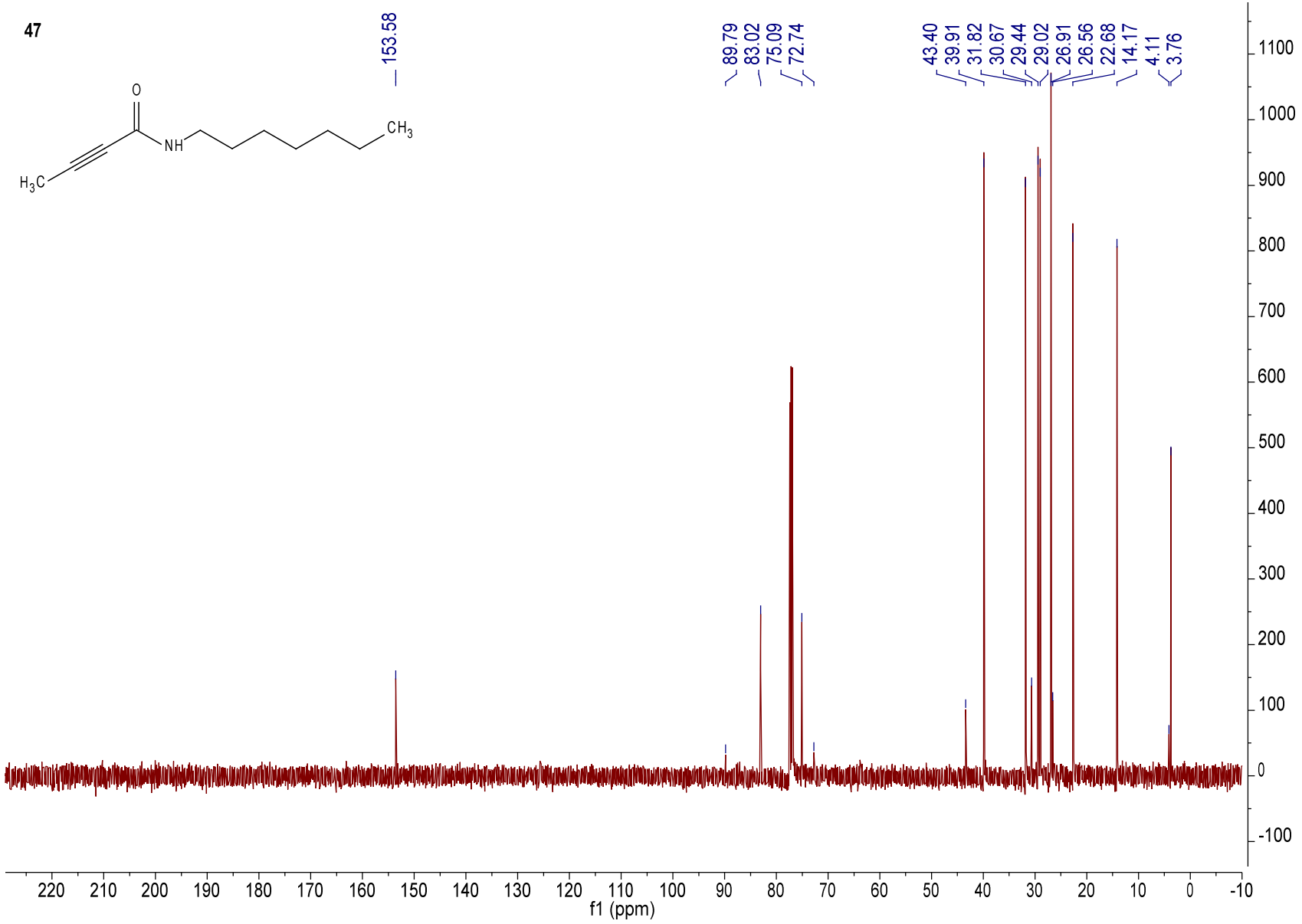

46
O
NH
H_3C
CH_3
2.65
0.88
6.22
3.33
3.31
1.55
1.35
1.29
5.73
0.93
0.89
2.08
3.14
2.11
6.17
3.00
f1 (ppm)

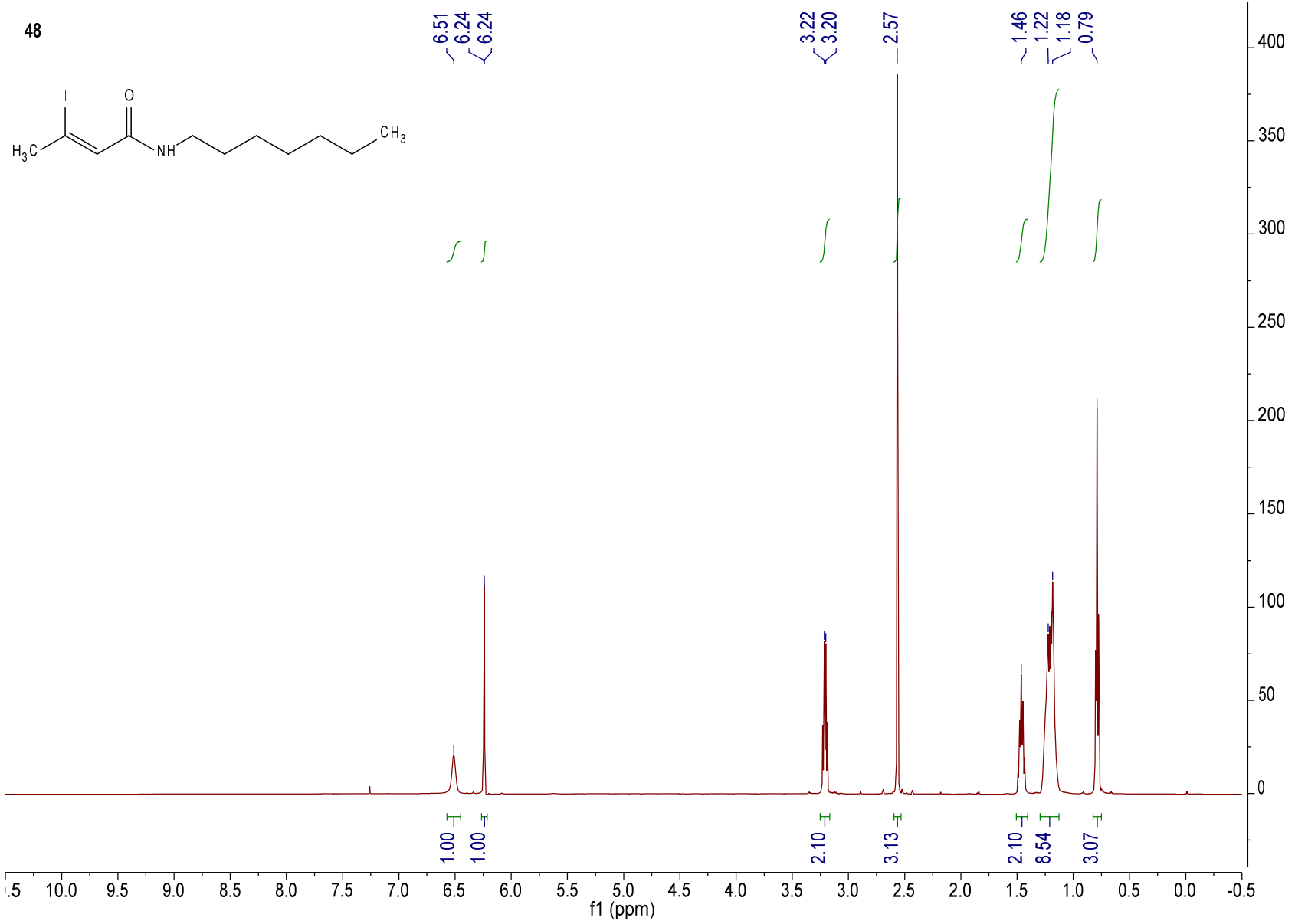

46
I
O
H3C
NH
CH3
164.51
128.65
105.27
39.35
35.58
31.27
29.14
26.49
22.33
13.83
f1 (ppm)

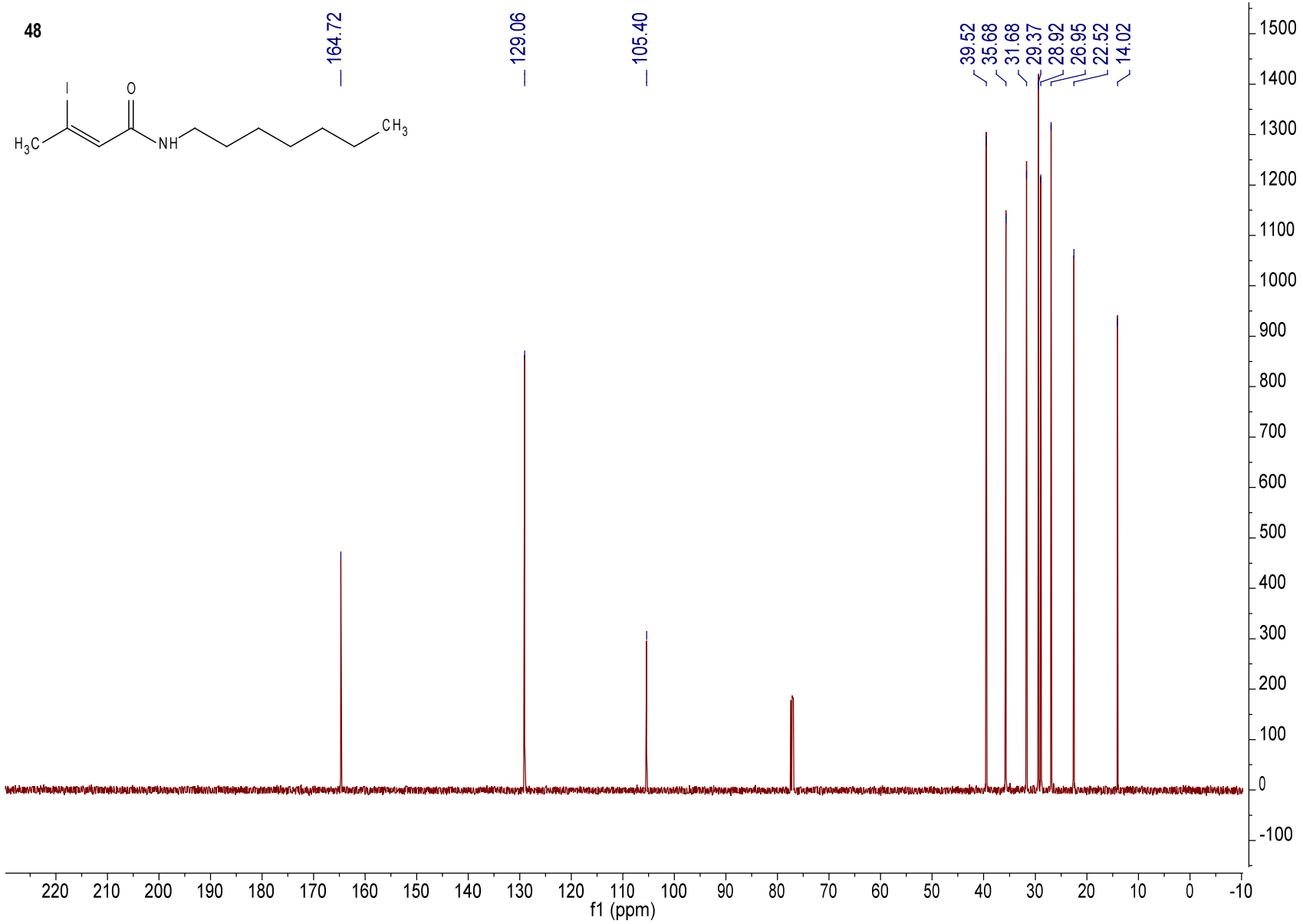

11
CH3
O
CH3
O
N
NH
O
O
H3C
6.71
6.61
4.39
2.58
1.71
1.41
1.32
0.87
1.00
0.98
1.75
6.32
2.10
2.08
4.25
3.04
f1 (ppm)

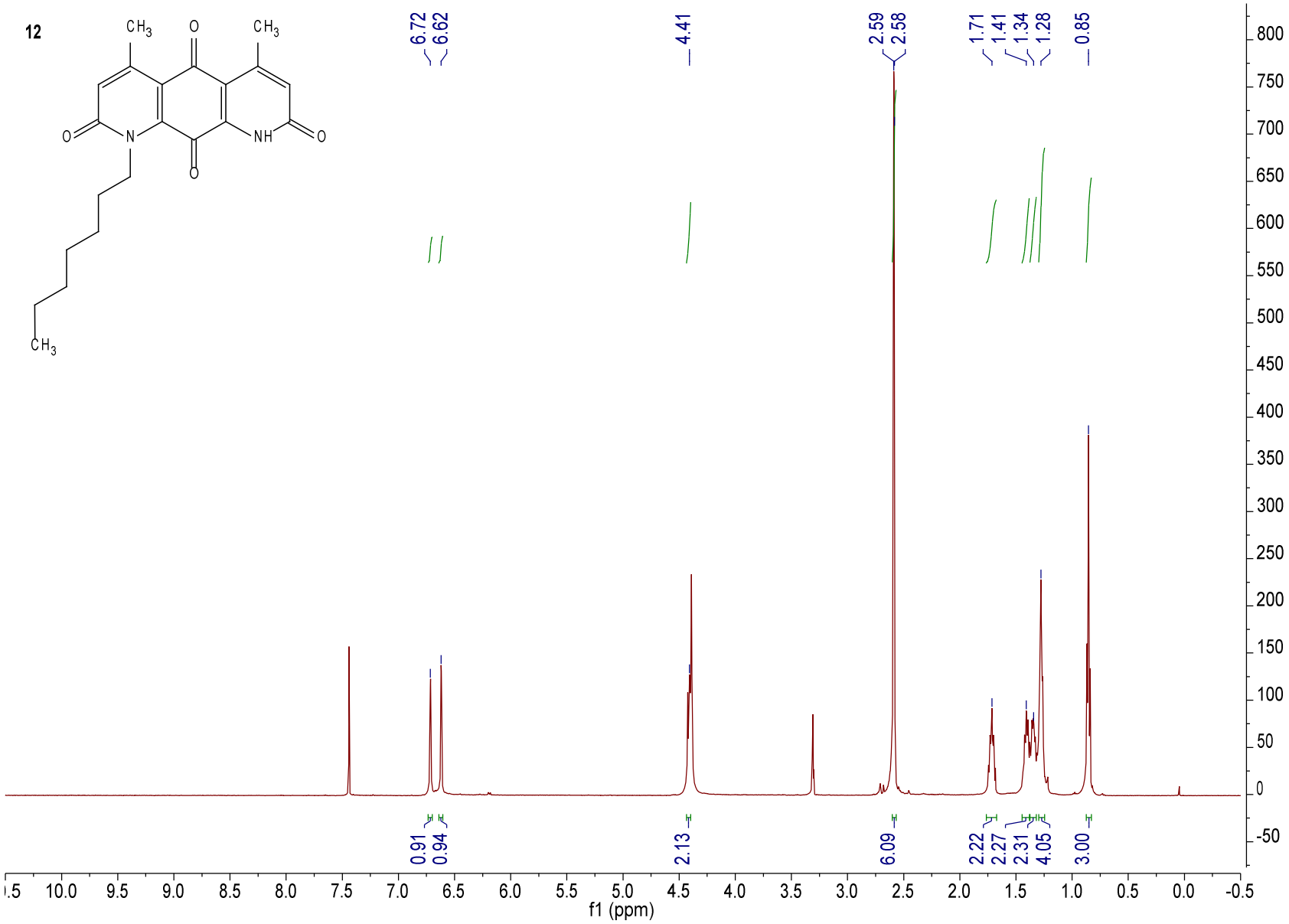

11
181.98
175.56
162.34
162.18
152.18
150.40
139.83
139.05
127.93
127.72
119.97
115.27
47.10
31.72
29.29
26.90
23.41
22.88
22.35
14.12
CH3
O
CH3
O
N
NH
O
O
H3C
f1 (ppm)

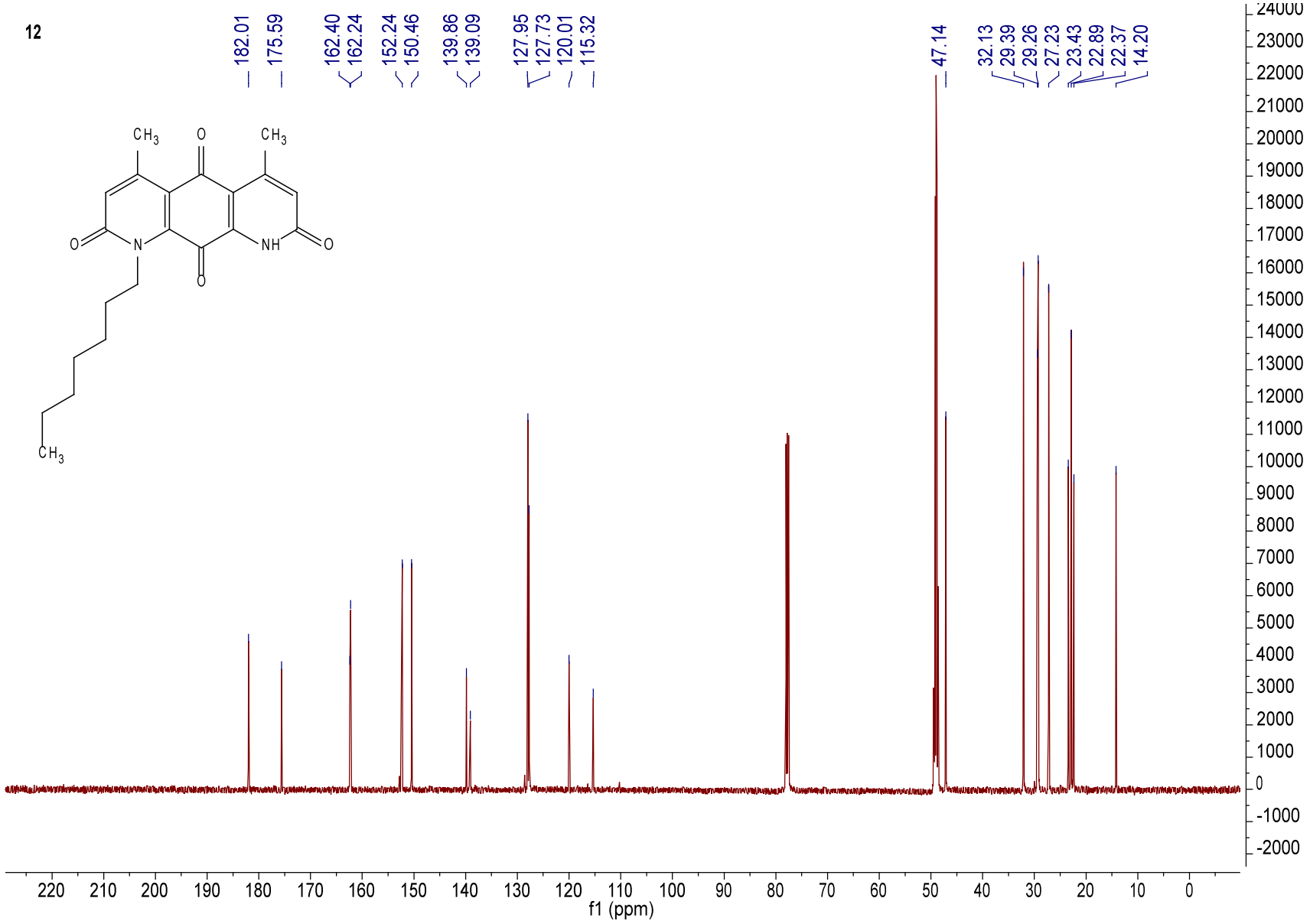

47
O
NH
CH3
H3C
5.80
3.26
3.24
1.92
1.49
1.28
0.86
0.94
2.00
2.86
2.16
8.80
2.92
f1 (ppm)

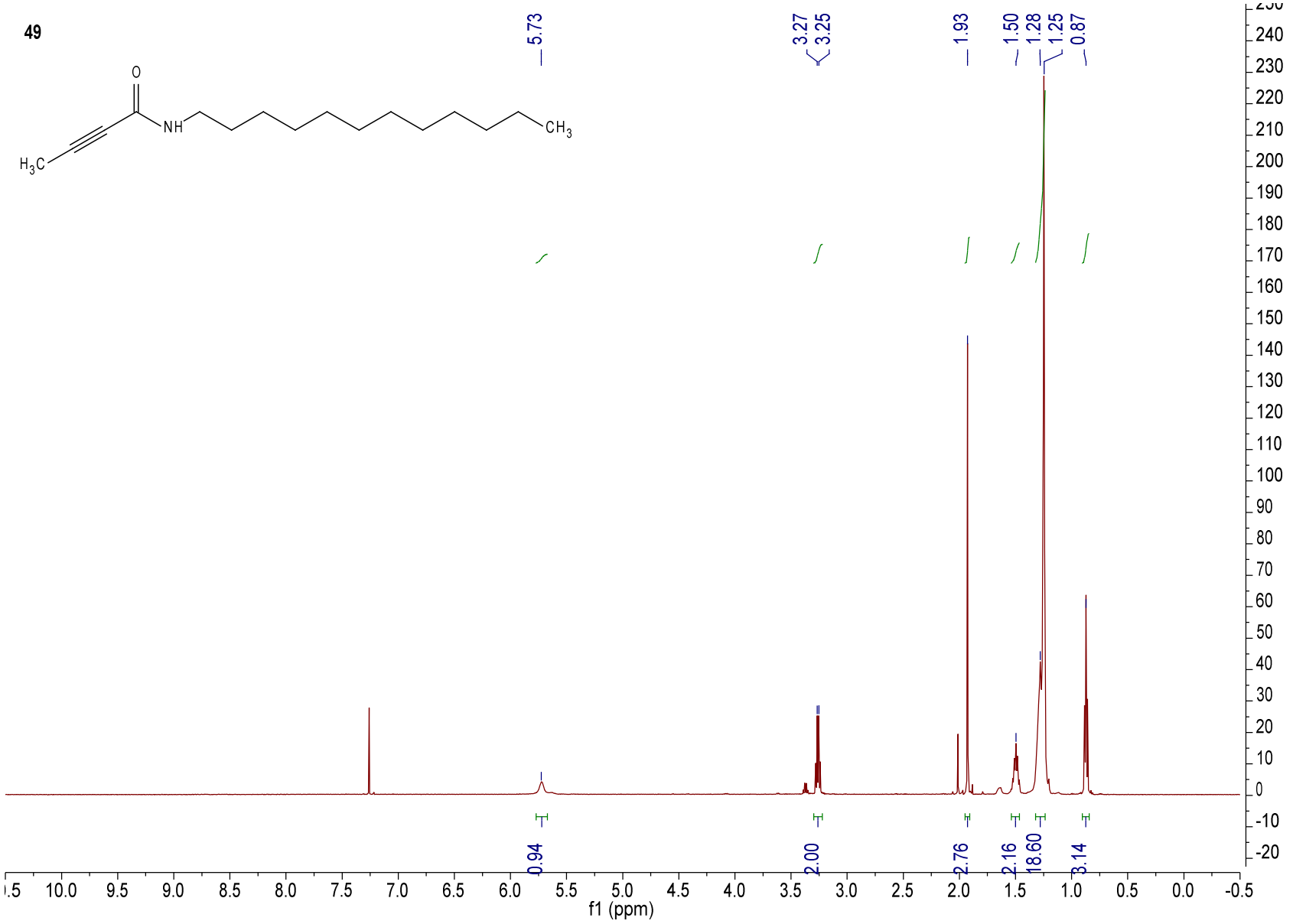

47
153.58
89.79
83.02
75.09
72.74
43.40
39.91
31.82
30.67
29.44
29.02
26.91
26.56
22.68
14.17
4.11
3.76
O
NH
CH3
H3C
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

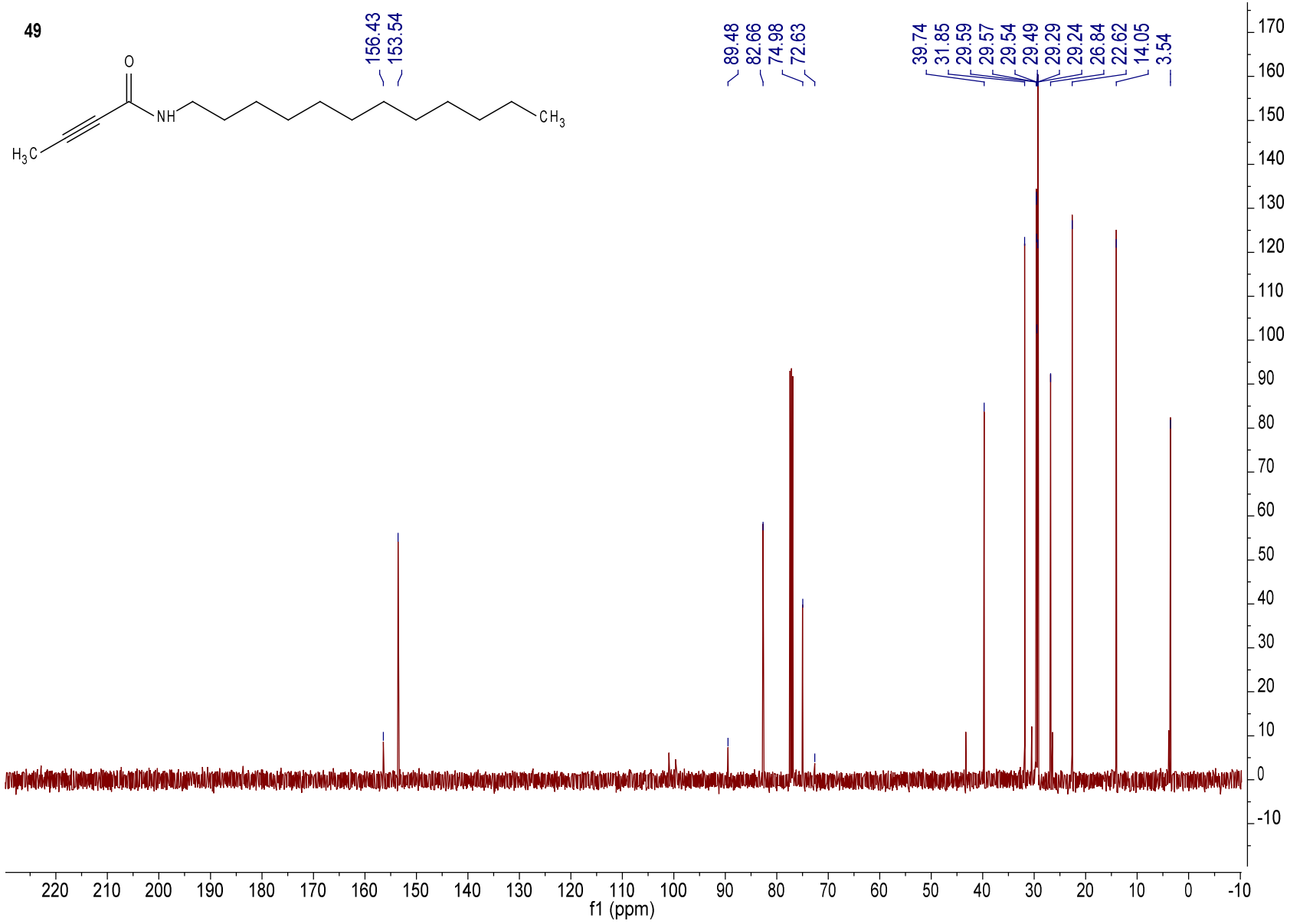

48
O
NH
CH3
H3C
6.51
6.24
6.24
3.22
3.20
2.57
1.46
1.22
1.18
0.79
1.00
1.00
2.10
3.13
2.10
8.54
3.07
f1 (ppm)

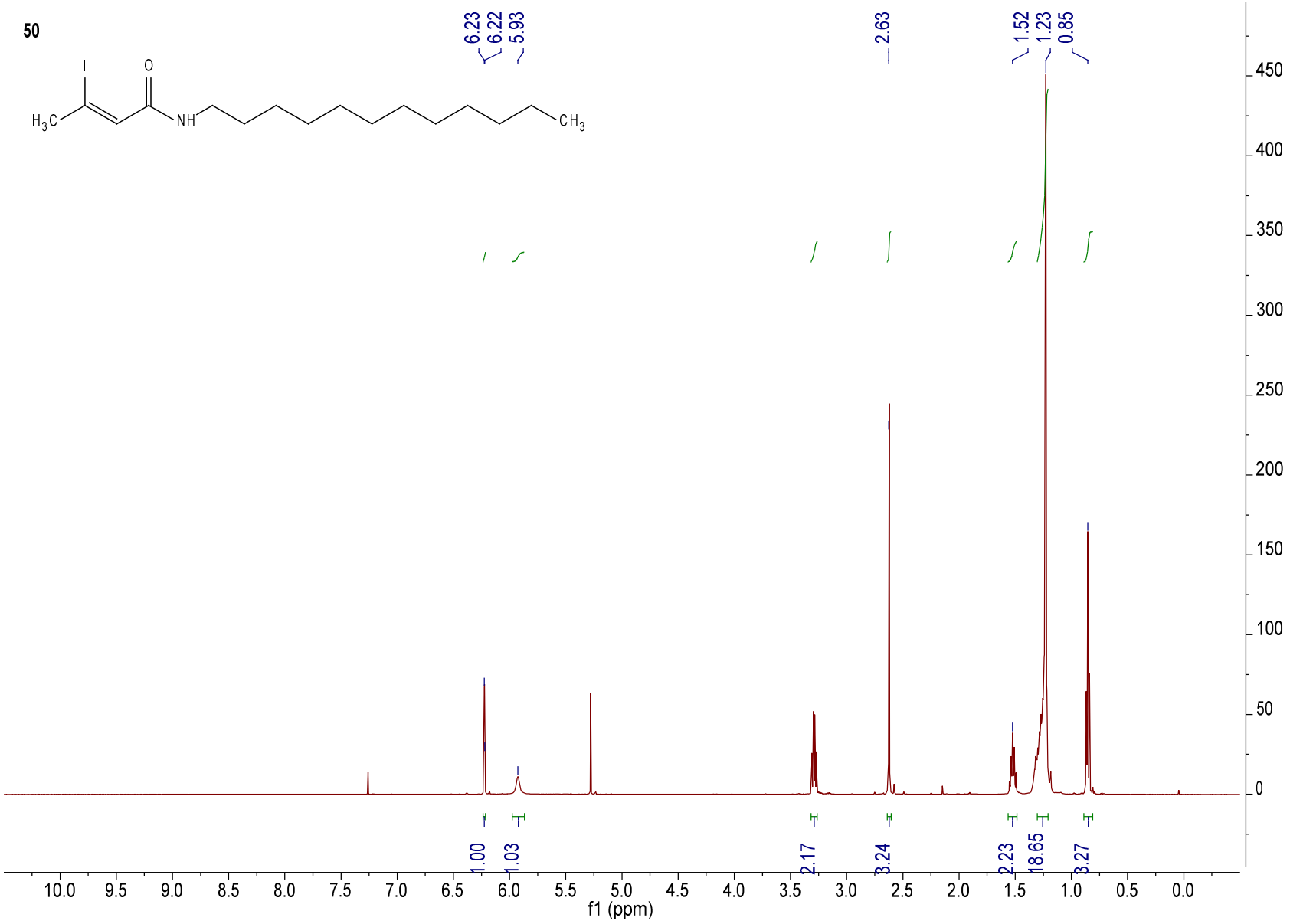

48
164.72
129.06
105.40
39.52
35.68
31.68
29.37
28.92
26.95
22.52
14.02
I
O
H3C
NH
CH3
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

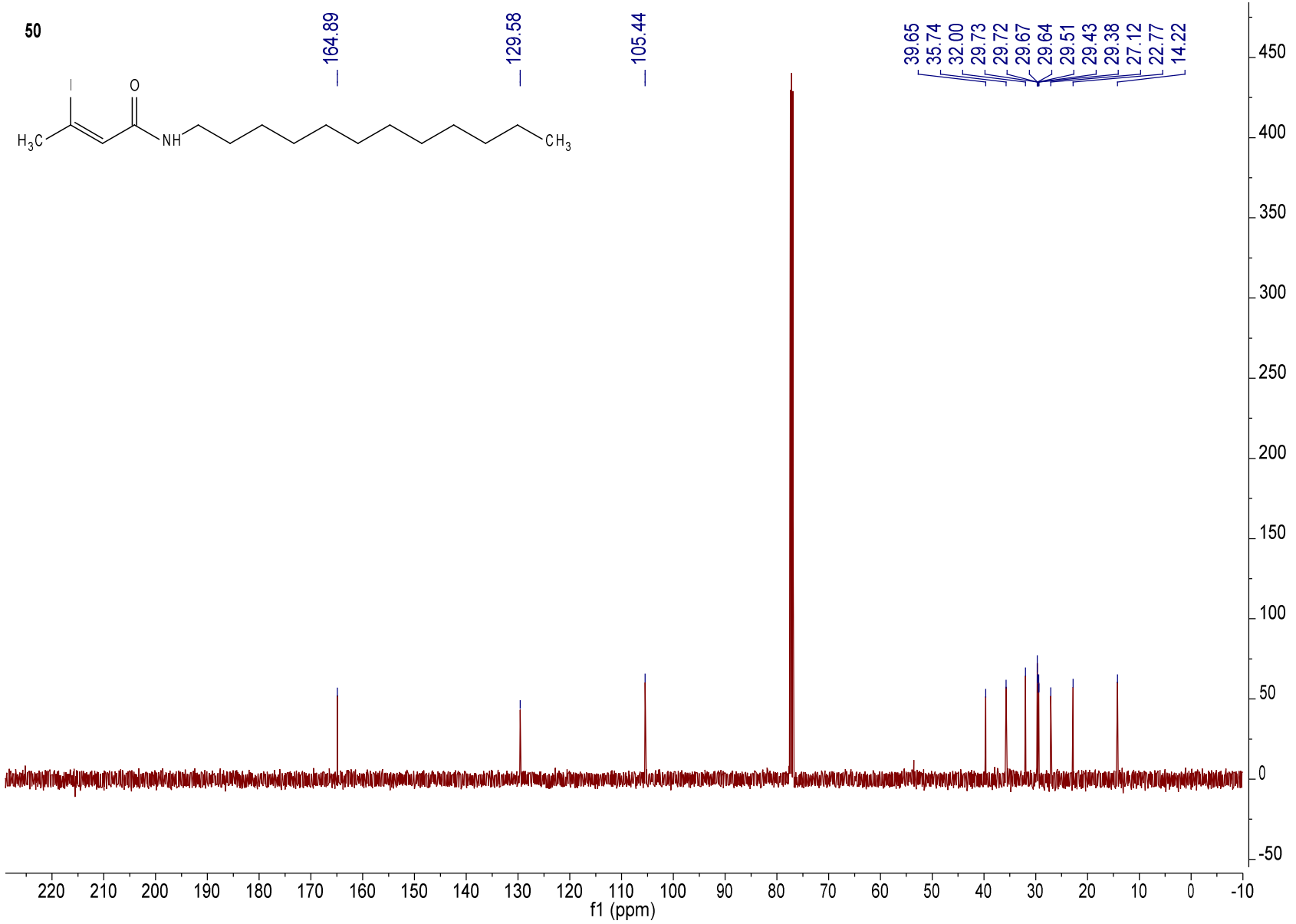

12
CH3
O
CH3
O
N
NH
O
O
CH3
6.72
6.62
4.41
2.59
2.58
1.71
1.41
1.34
1.28
0.85
0.91
0.94
2.13
6.09
2.22
2.27
2.31
4.05
3.00
f1 (ppm)

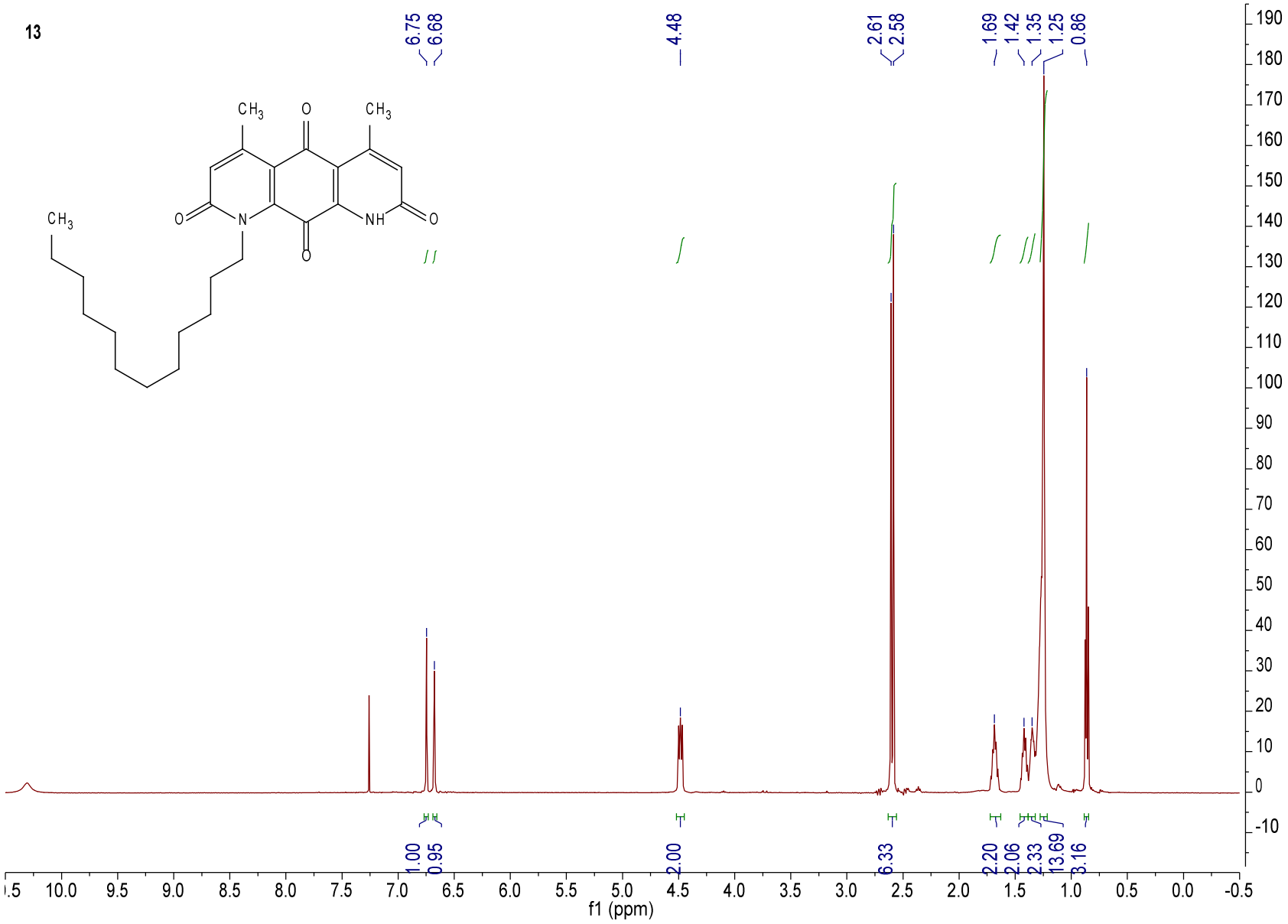

12
182.01
175.59
162.40
162.24
152.24
150.46
139.86
139.09
127.95
127.73
120.01
115.32
47.14
32.13
29.39
29.26
27.23
23.43
22.89
22.37
14.20
CH3
O
CH3
O
N
NH
O
O
CH3
f1 (ppm)

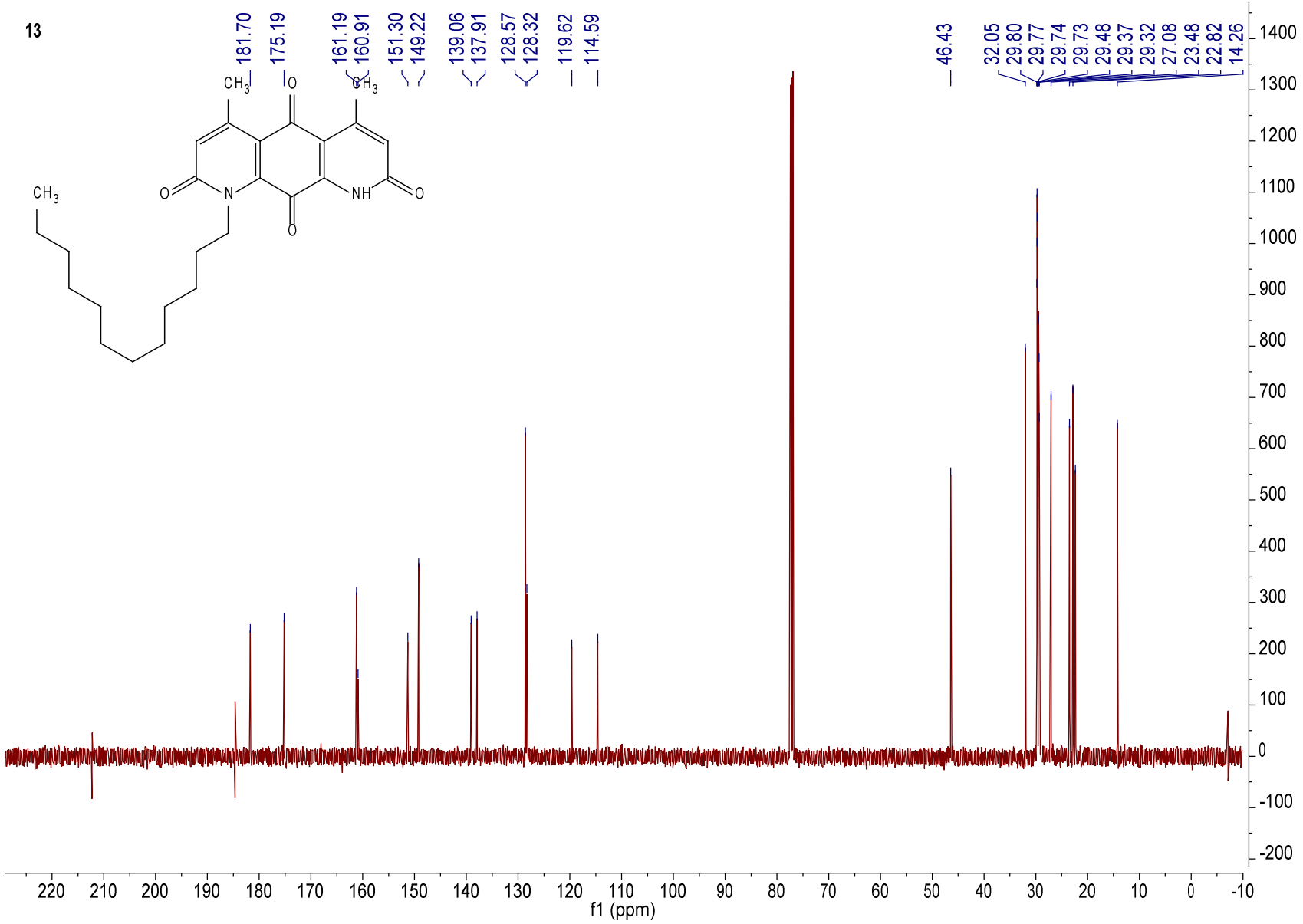

49
O
NH
CH3
H3C
5.73
3.27
3.25
1.93
1.50
1.28
1.25
0.87
0.94
2.00
2.76
2.16
18.60
3.14
f1 (ppm)

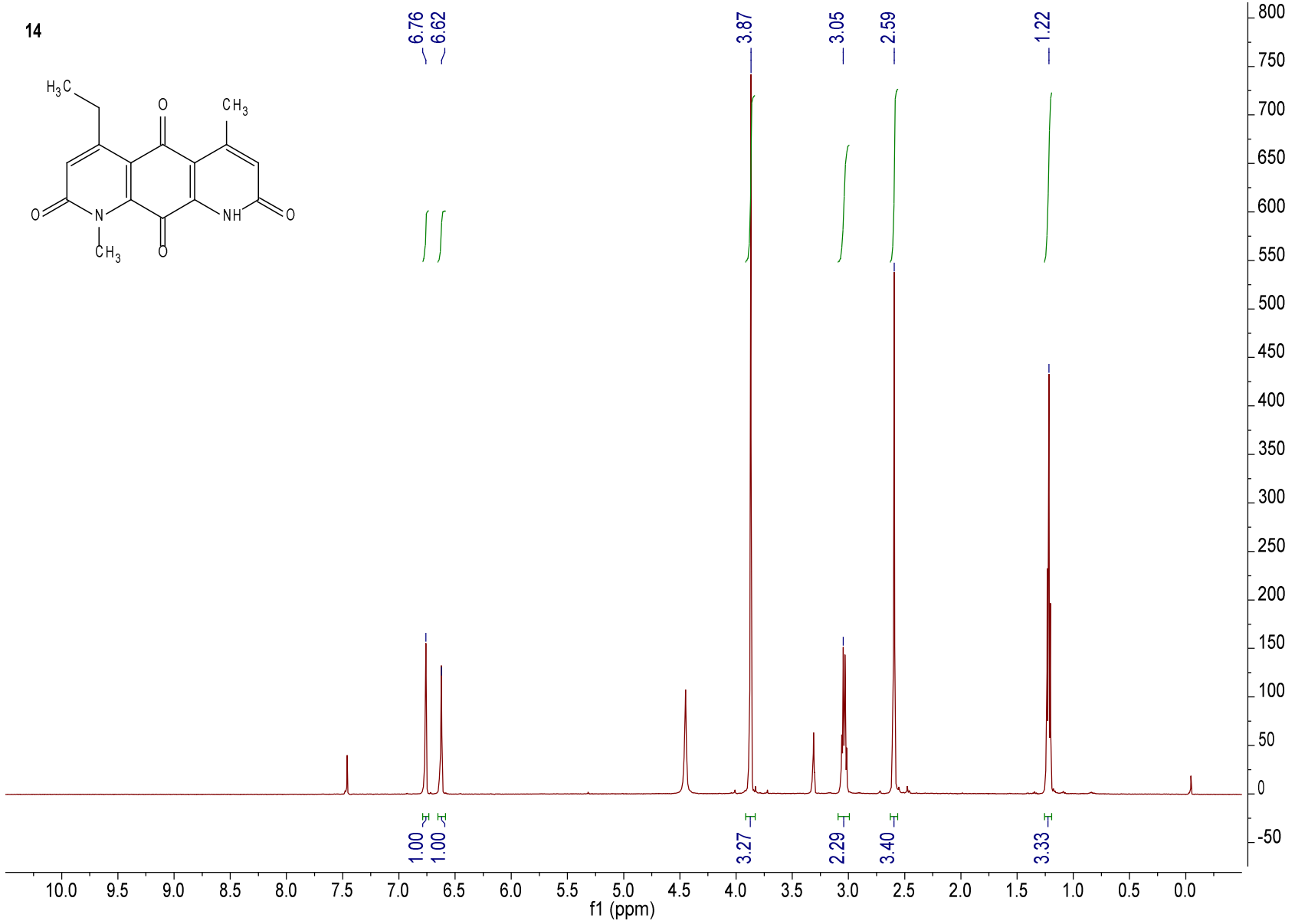

49
O
NH
H_3C
CH_3
156.43
153.54
89.48
82.66
74.98
72.63
39.74
31.85
29.59
29.57
29.54
29.49
29.29
29.24
26.84
22.62
14.05
3.54
f1 (ppm)

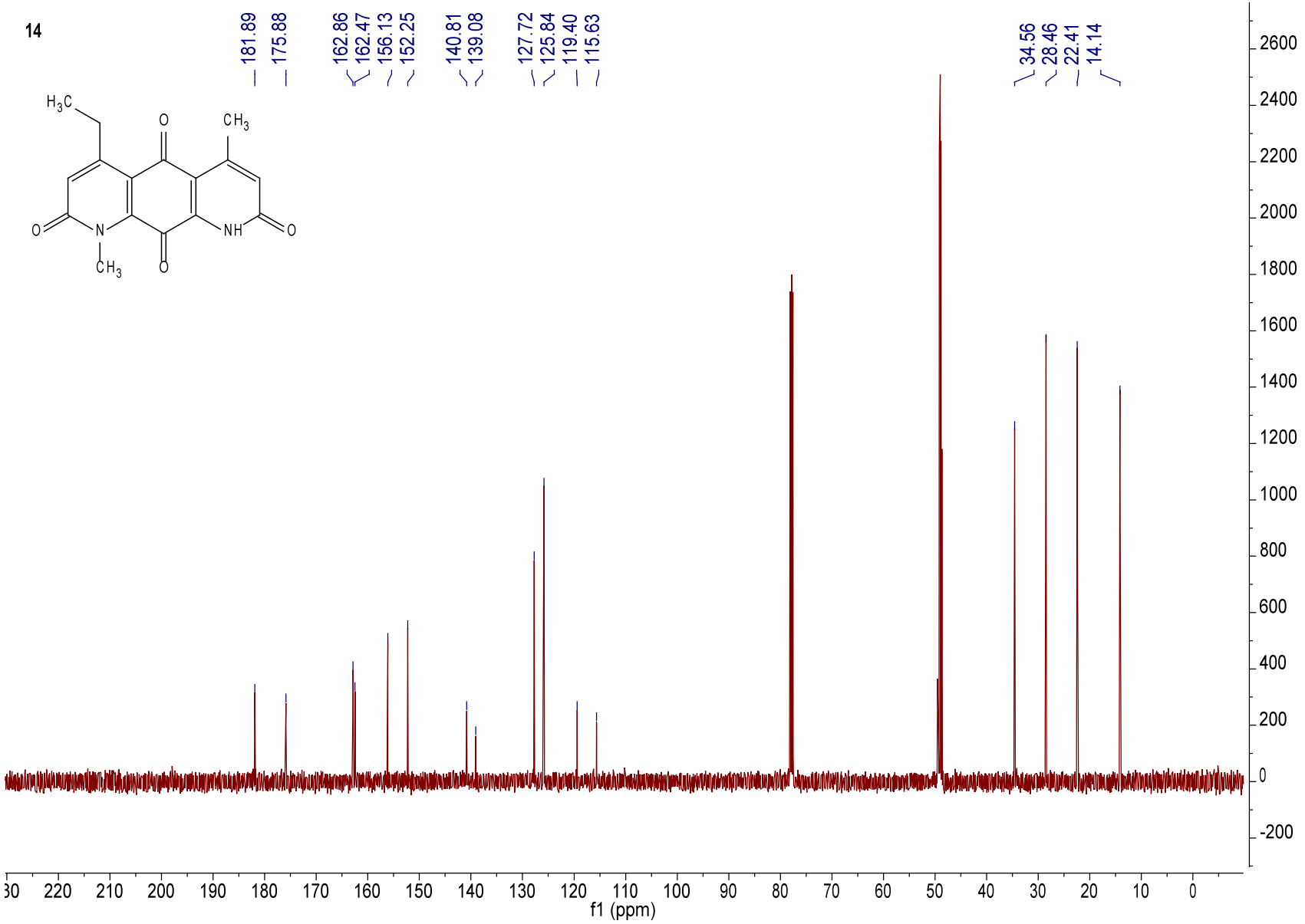

50
6.23
6.22
5.93
2.63
1.52
1.23
0.85
1.00
1.03
2.17
3.24
2.23
18.65
3.27
f1 (ppm)

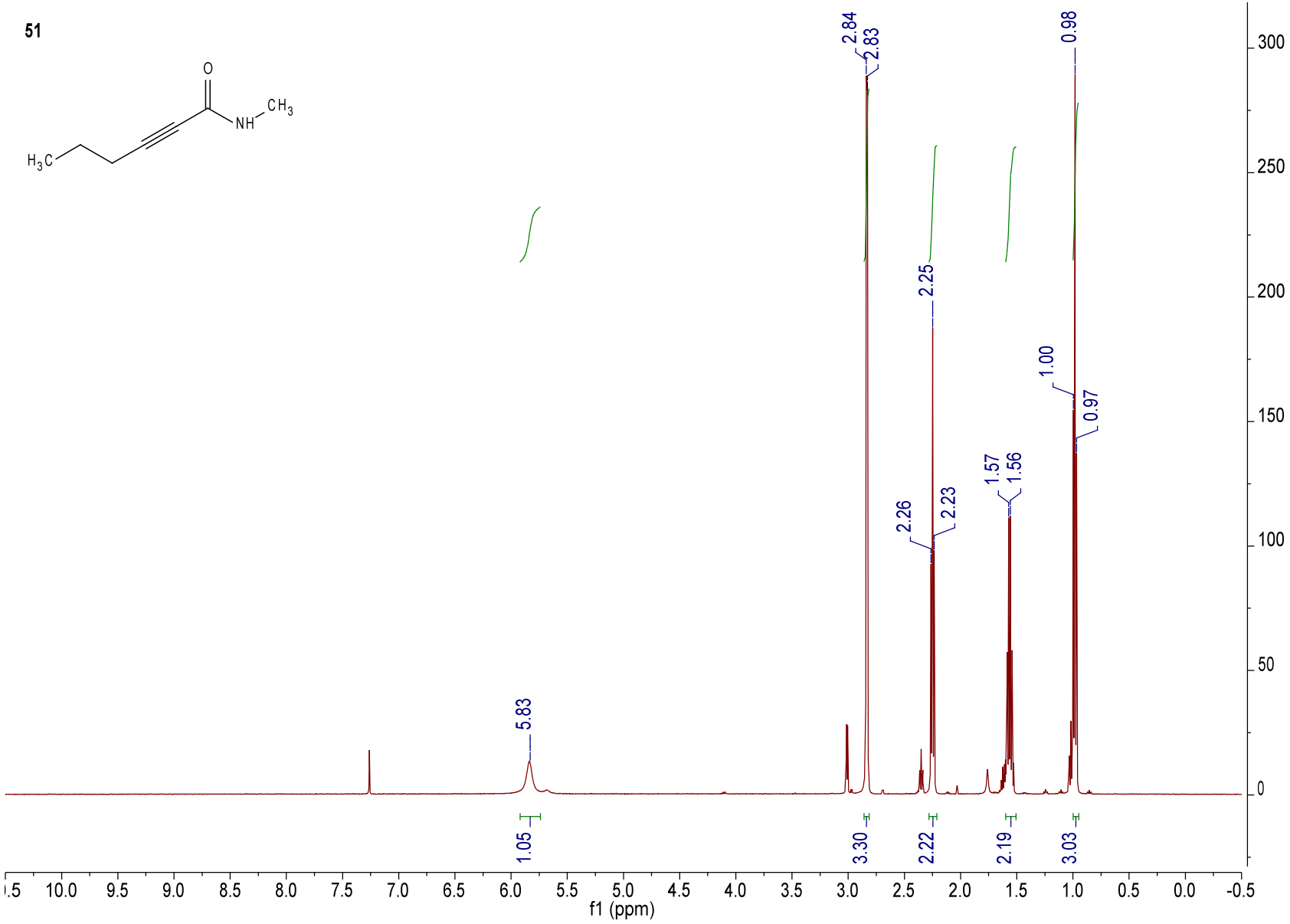

50
164.89
129.58
105.44
39.65
35.74
32.00
29.73
29.72
29.67
29.64
29.51
29.43
29.38
27.12
22.77
14.22
O
NH
H_3C
CH_3
f1 (ppm)

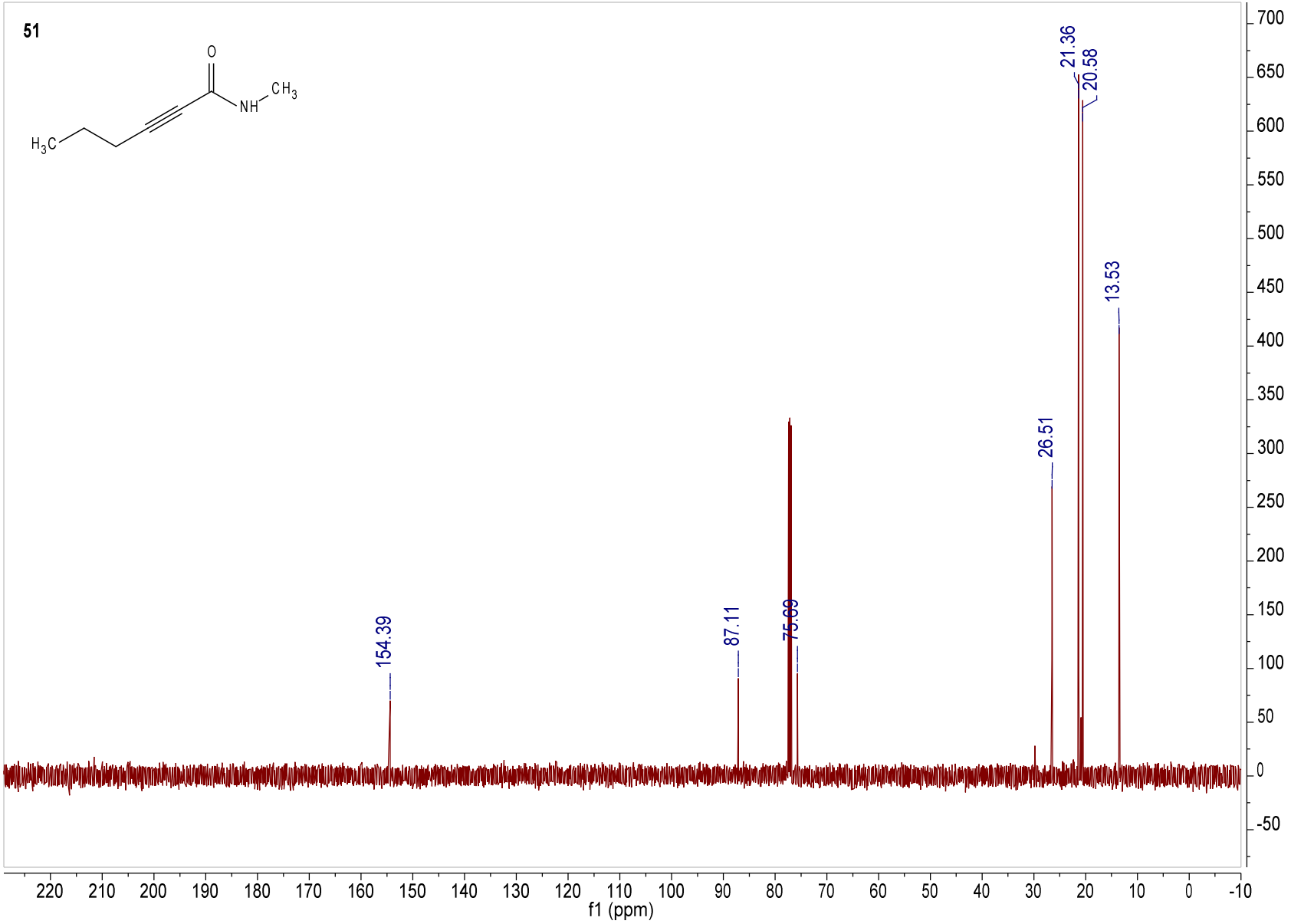

13
6.75
6.68
4.48
2.61
2.58
1.69
1.42
1.35
1.25
0.86
1.00
0.95
2.00
6.33
2.20
2.06
2.33
13.69
3.16
f1 (ppm)

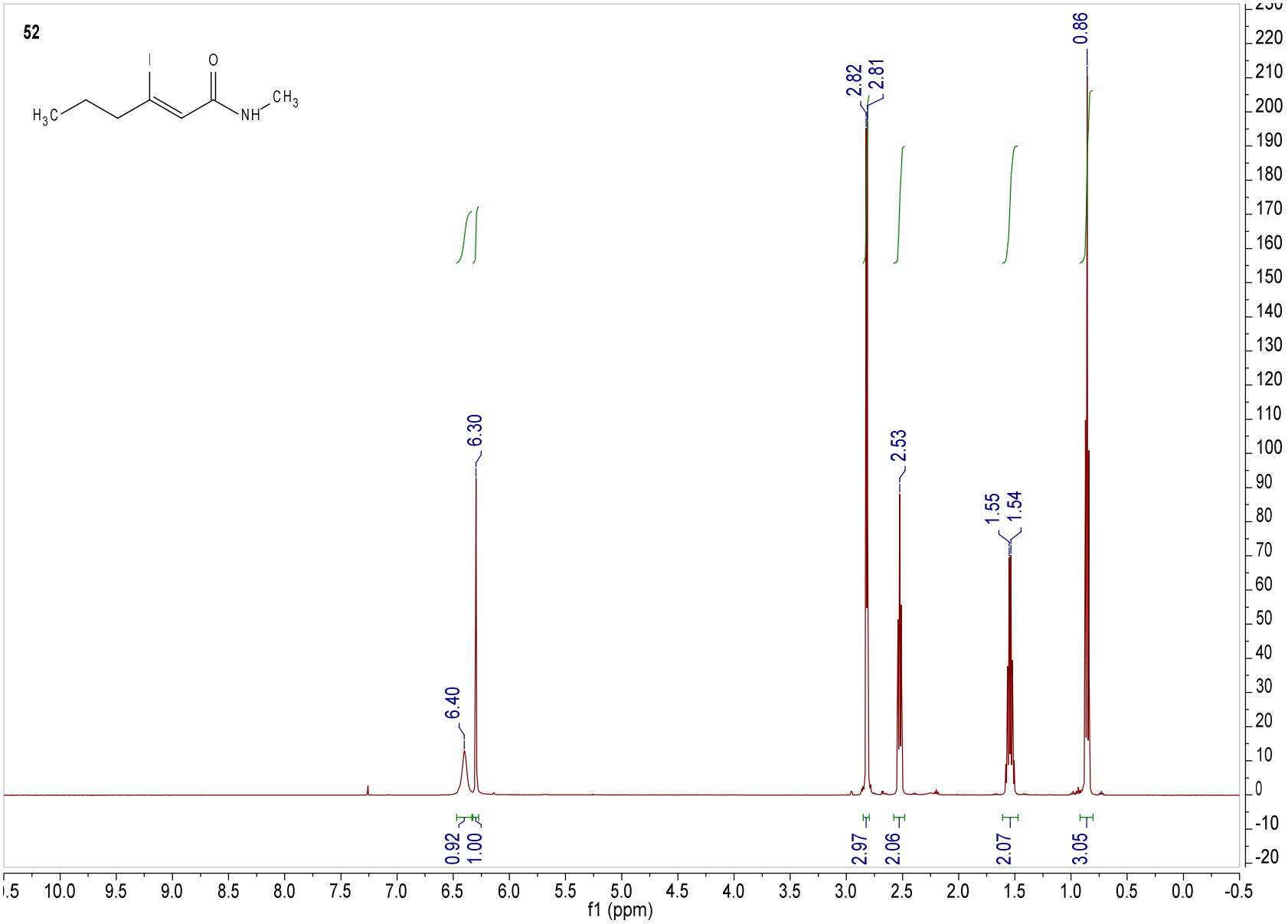

13
181.70
175.19
161.19
160.91
151.30
149.22
139.06
137.91
128.57
128.32
119.62
114.59
46.43
32.05
29.80
29.77
29.74
29.73
29.48
29.37
29.32
27.08
23.48
22.82
14.26
CH3
O
CH3
CH3
O
N
NH
O
O
f1 (ppm)

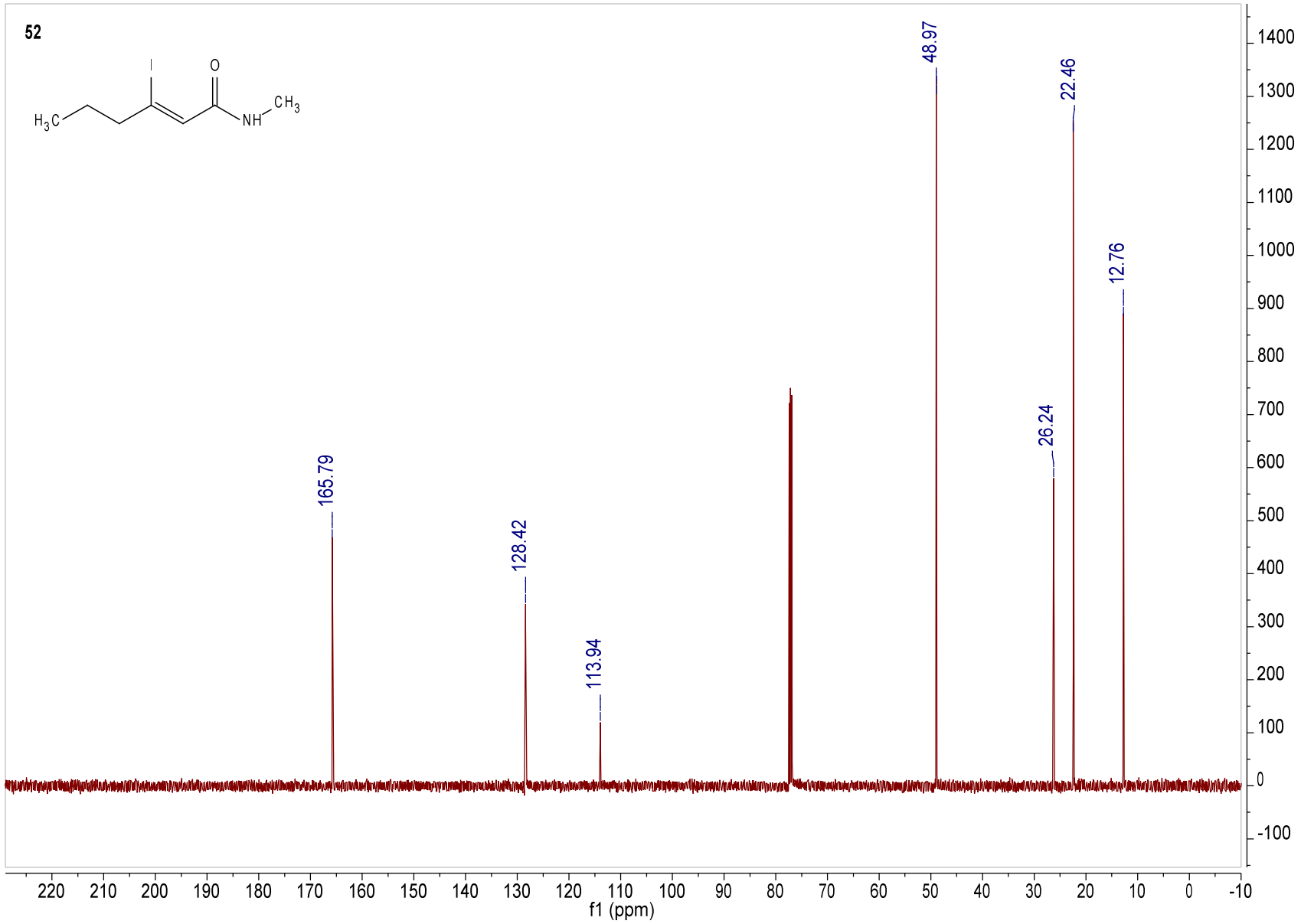

14
6.76
6.62
3.87
3.05
2.59
1.22
1.00
1.00
3.27
2.29
3.40
3.33
f1 (ppm)

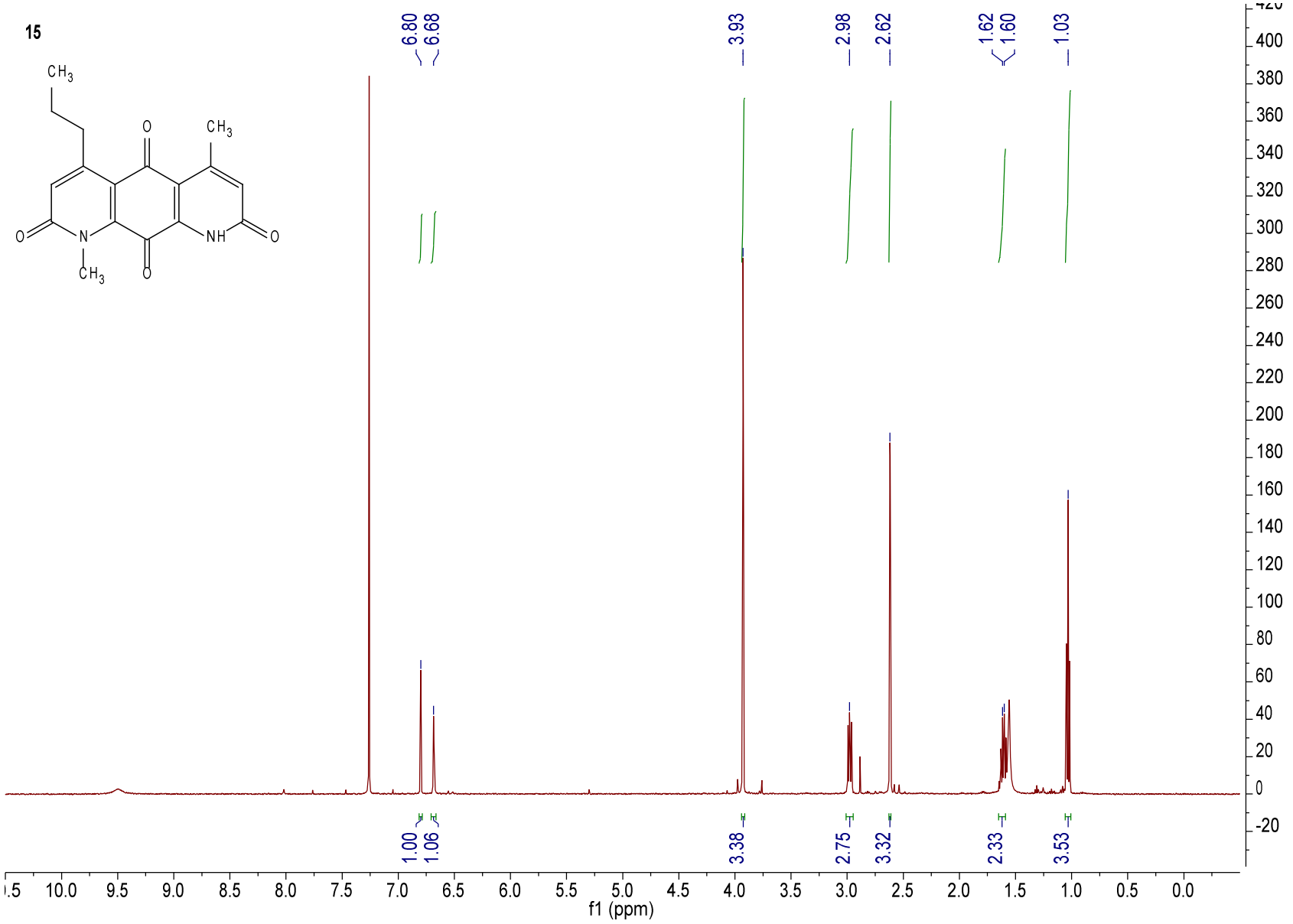

14
181.89
175.88
162.86
162.47
156.13
152.25
140.81
139.08
127.72
125.84
119.40
115.63
34.56
28.46
22.41
14.14
f1 (ppm)

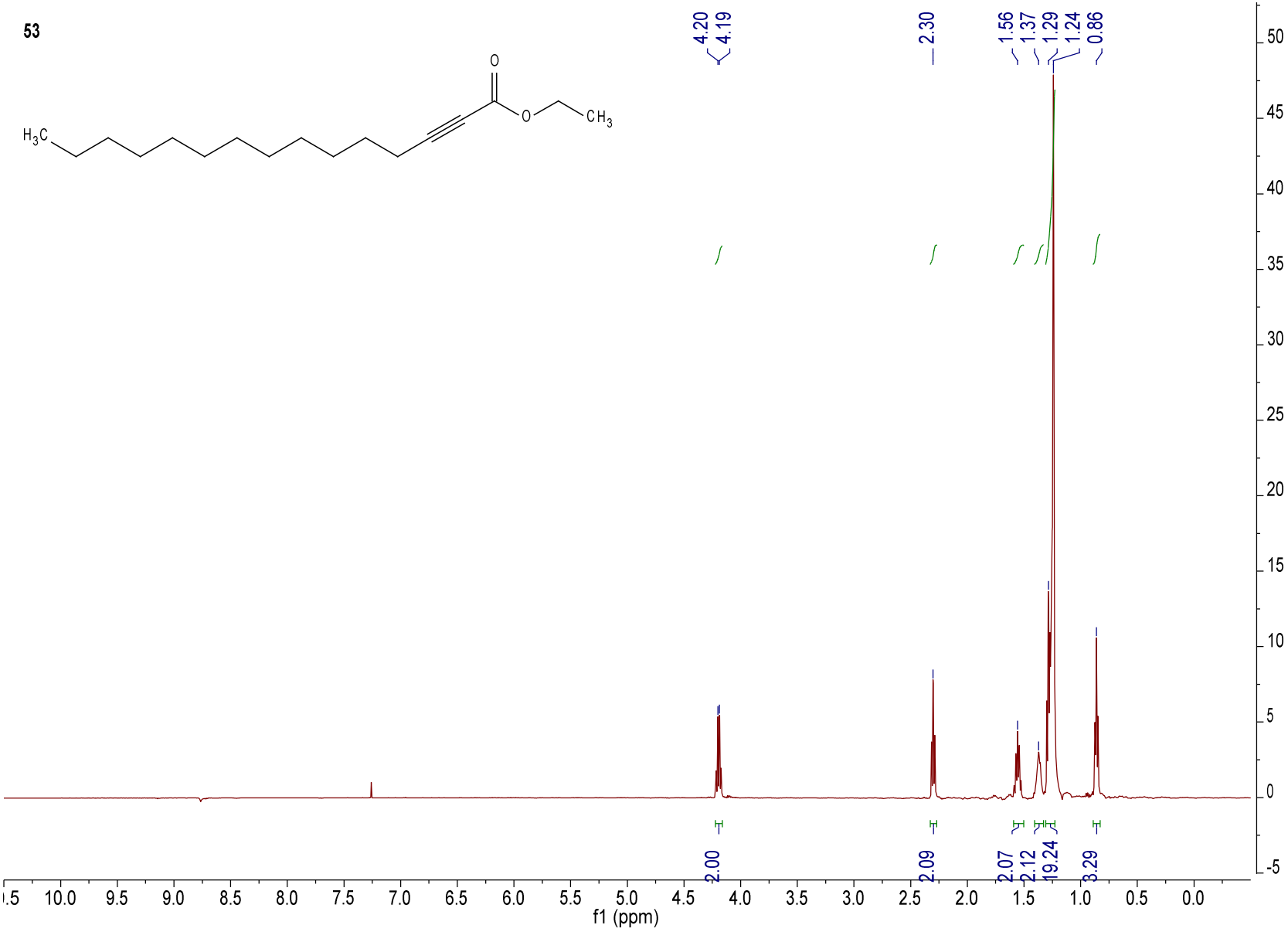

51
O
NH
CH3
H3C
2.84
2.83
0.98
2.25
1.00
0.97
1.57
1.56
2.26
2.23
5.83
1.05
3.30
2.22
2.19
3.03
f1 (ppm)

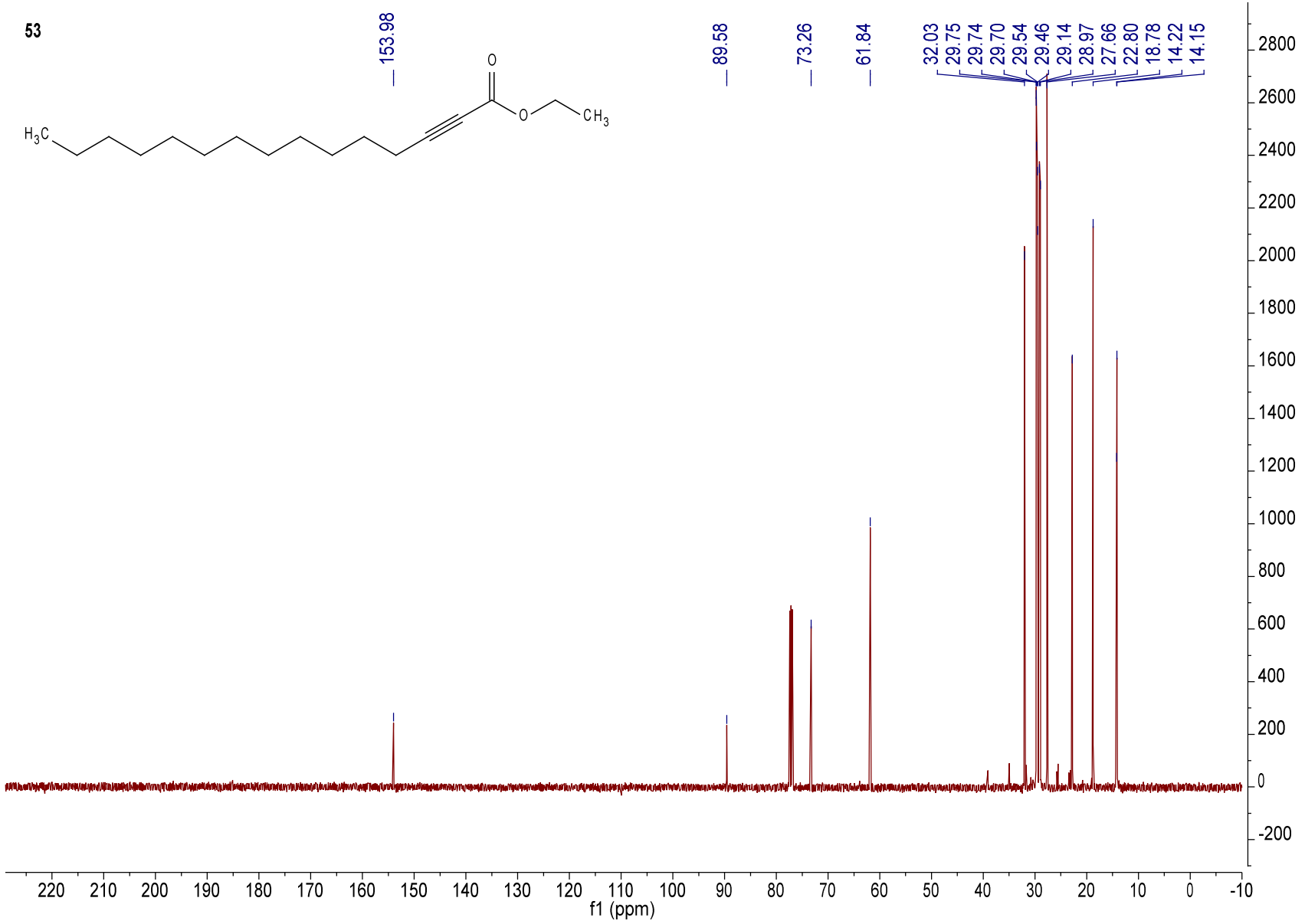

51
O
NH
CH3
H3C
21.36
20.58
13.53
26.51
154.39
87.11
75.69
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

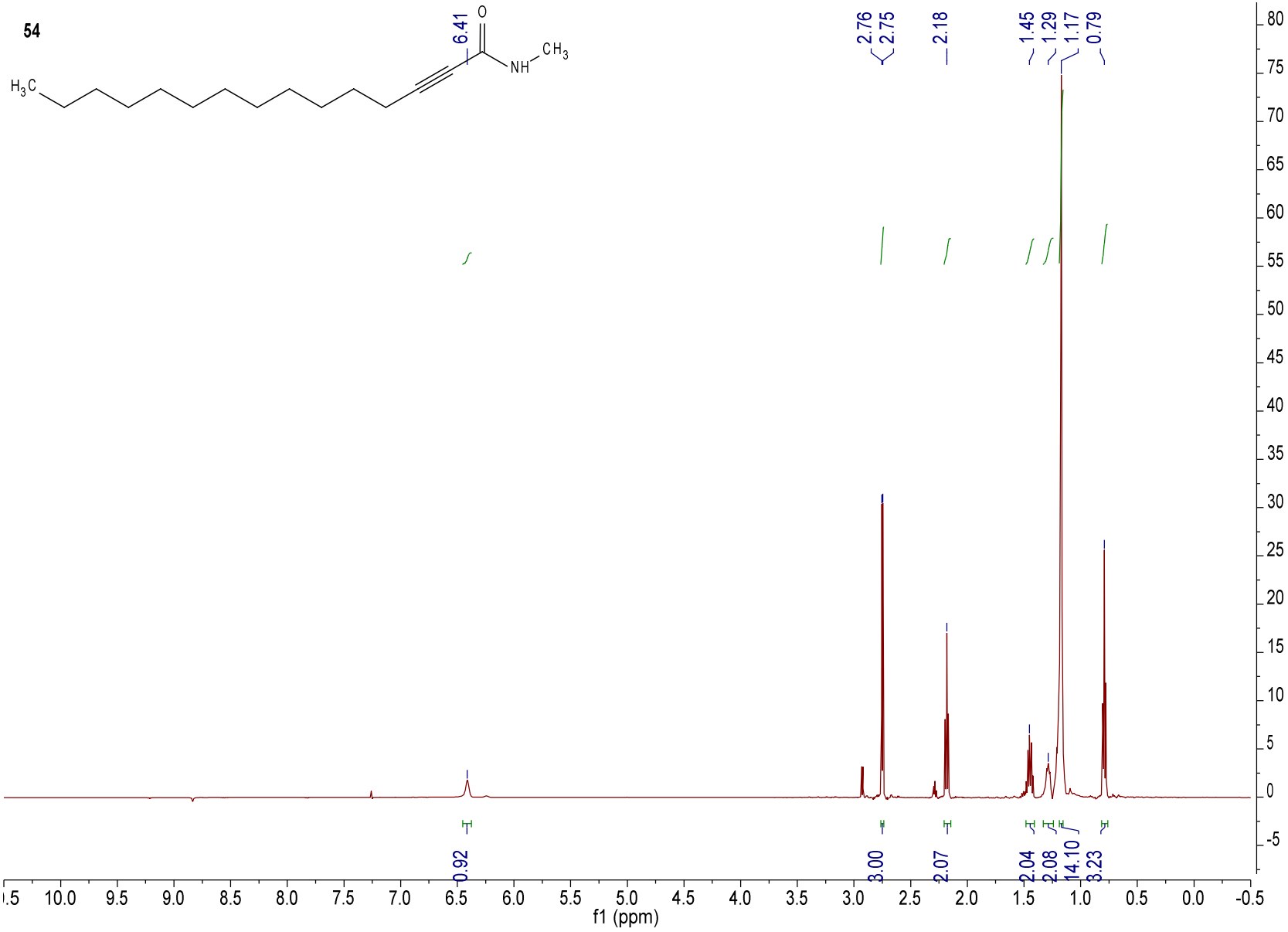

52
I
O
H_3C
NH
CH_3
6.40
6.30
2.82
2.81
2.53
1.55
1.54
0.86
0.92
1.00
2.97
2.06
2.07
3.05
f1 (ppm)

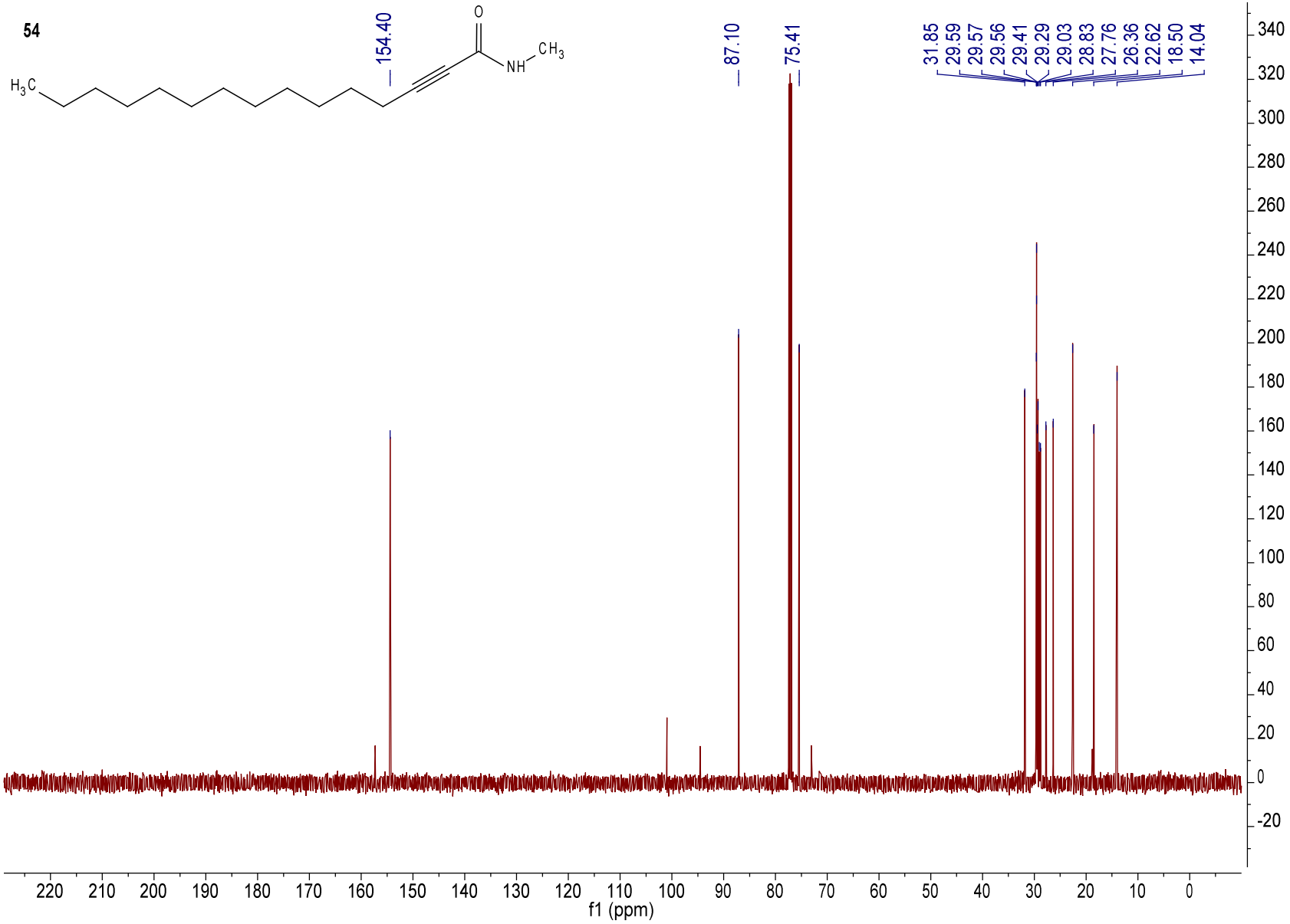

52
H3C
O
NH
CH3
165.79
128.42
113.94
48.97
26.24
22.46
12.76
f1 (ppm)

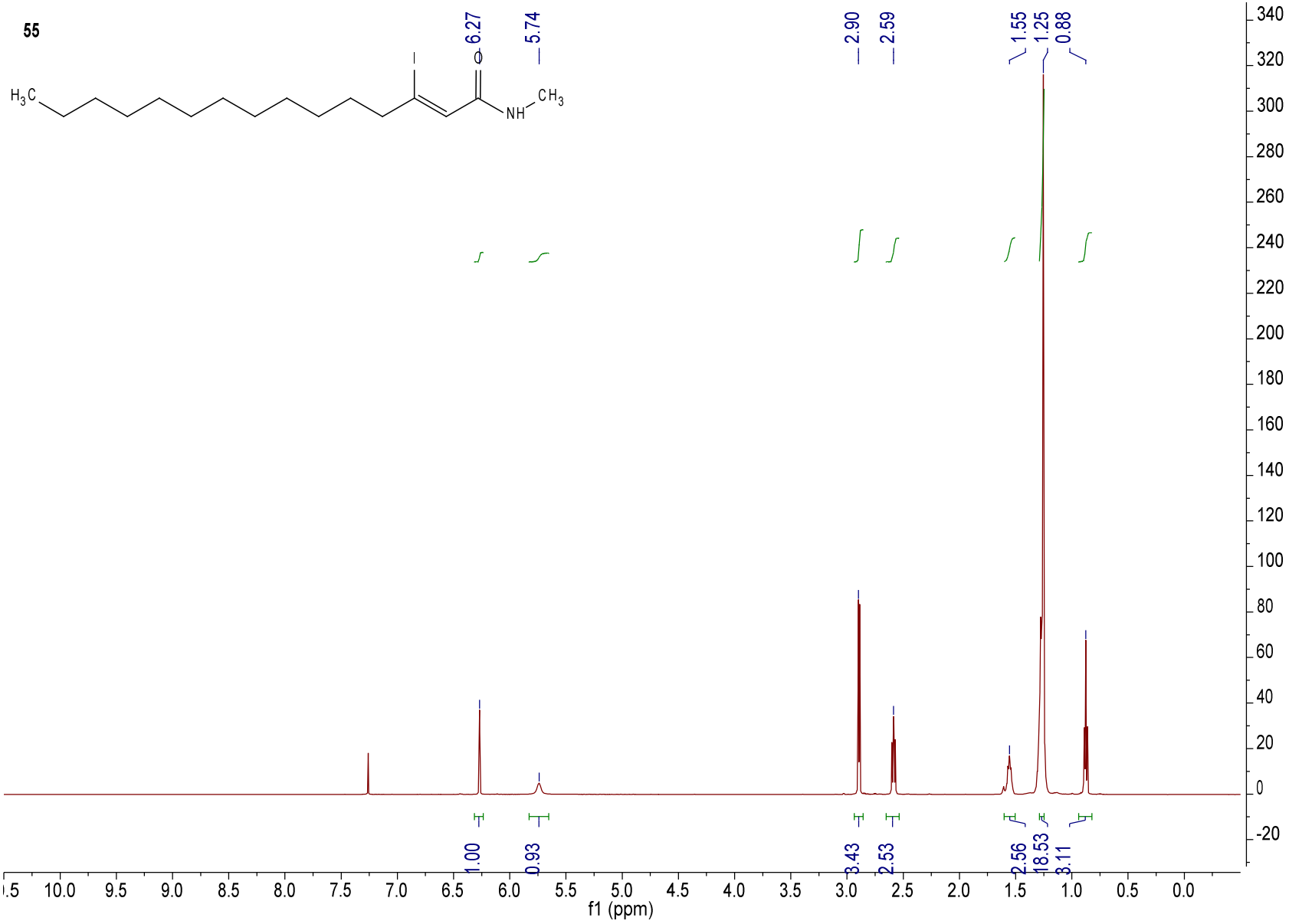

15
6.80
6.68
3.93
2.98
2.62
1.62
1.60
1.03
1.00
1.06
3.38
2.75
3.32
2.33
3.53
f1 (ppm)

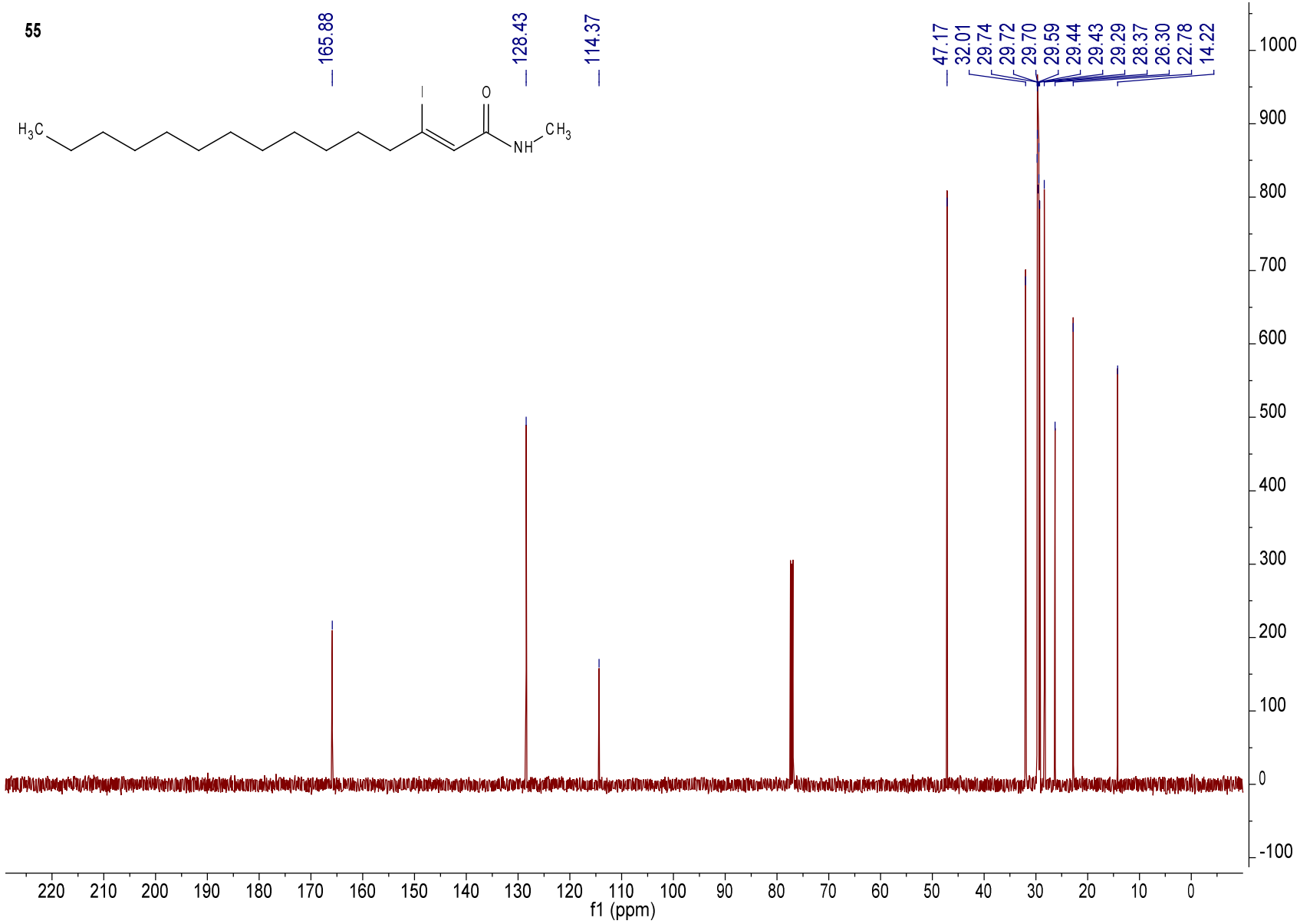

53
H3C
O
O
CH3
4.20
4.19
2.30
1.56
1.37
1.29
1.24
0.86
2.00
2.09
2.07
2.12
19.24
3.29
f1 (ppm)

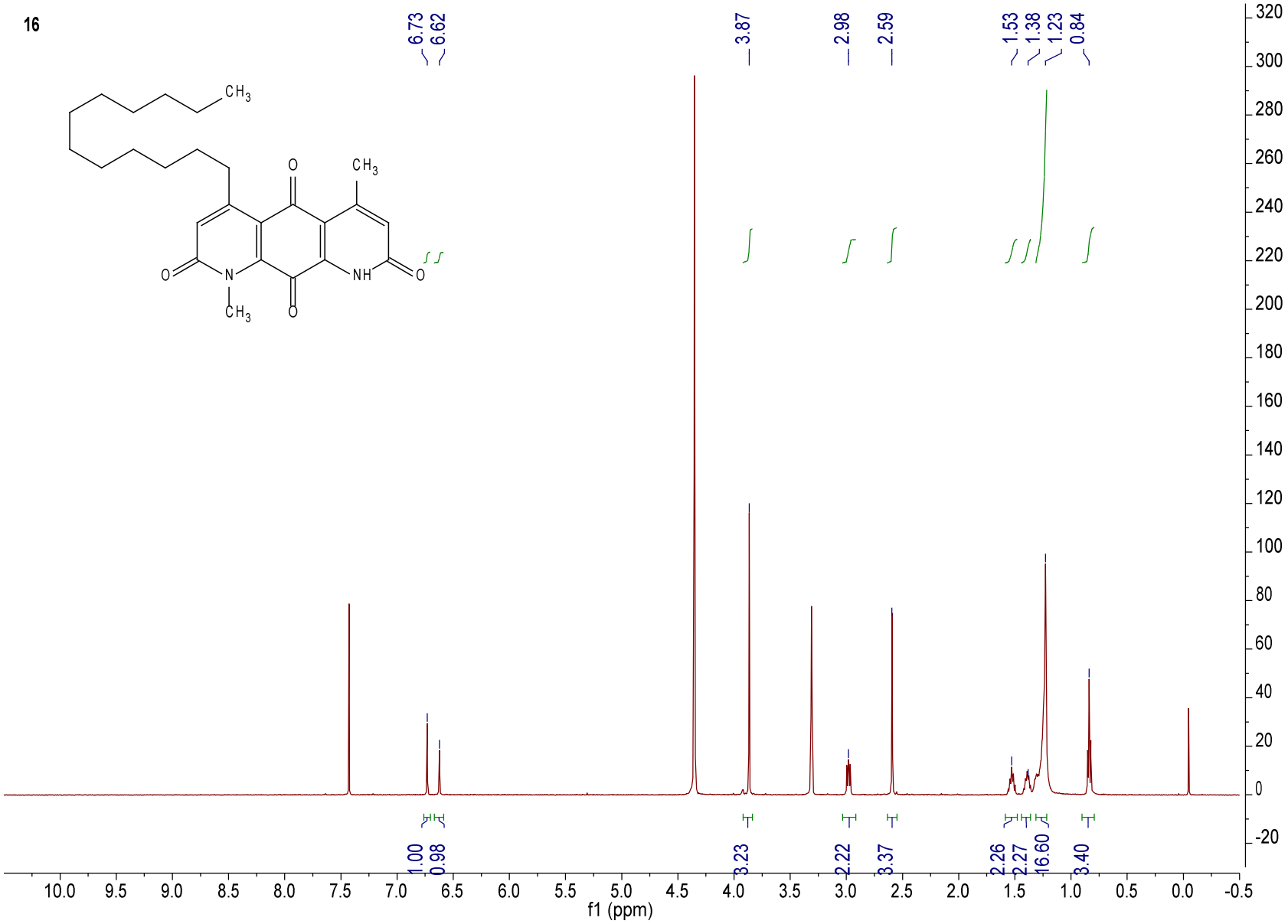

53
153.98
89.58
73.26
61.84
32.03
29.75
29.74
29.70
29.54
29.46
29.14
28.97
27.66
22.80
18.78
14.22
14.15
O
O
H3C
CH3
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

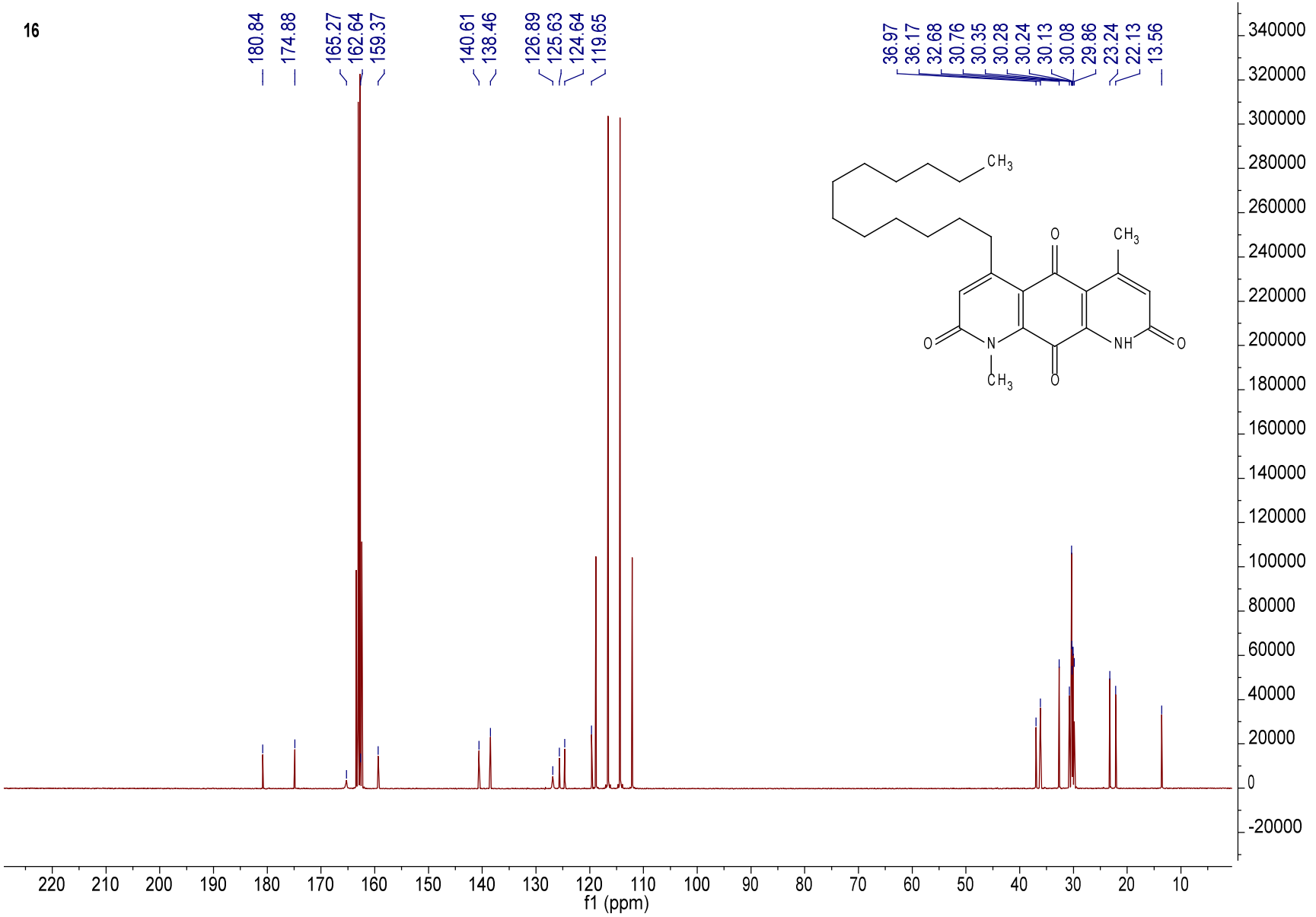

54
6.41
O
NH
CH3
H3C
2.76
2.75
2.18
1.45
1.29
1.17
0.79
0.92
3.00
2.07
2.04
2.08
14.10
3.23
f1 (ppm)

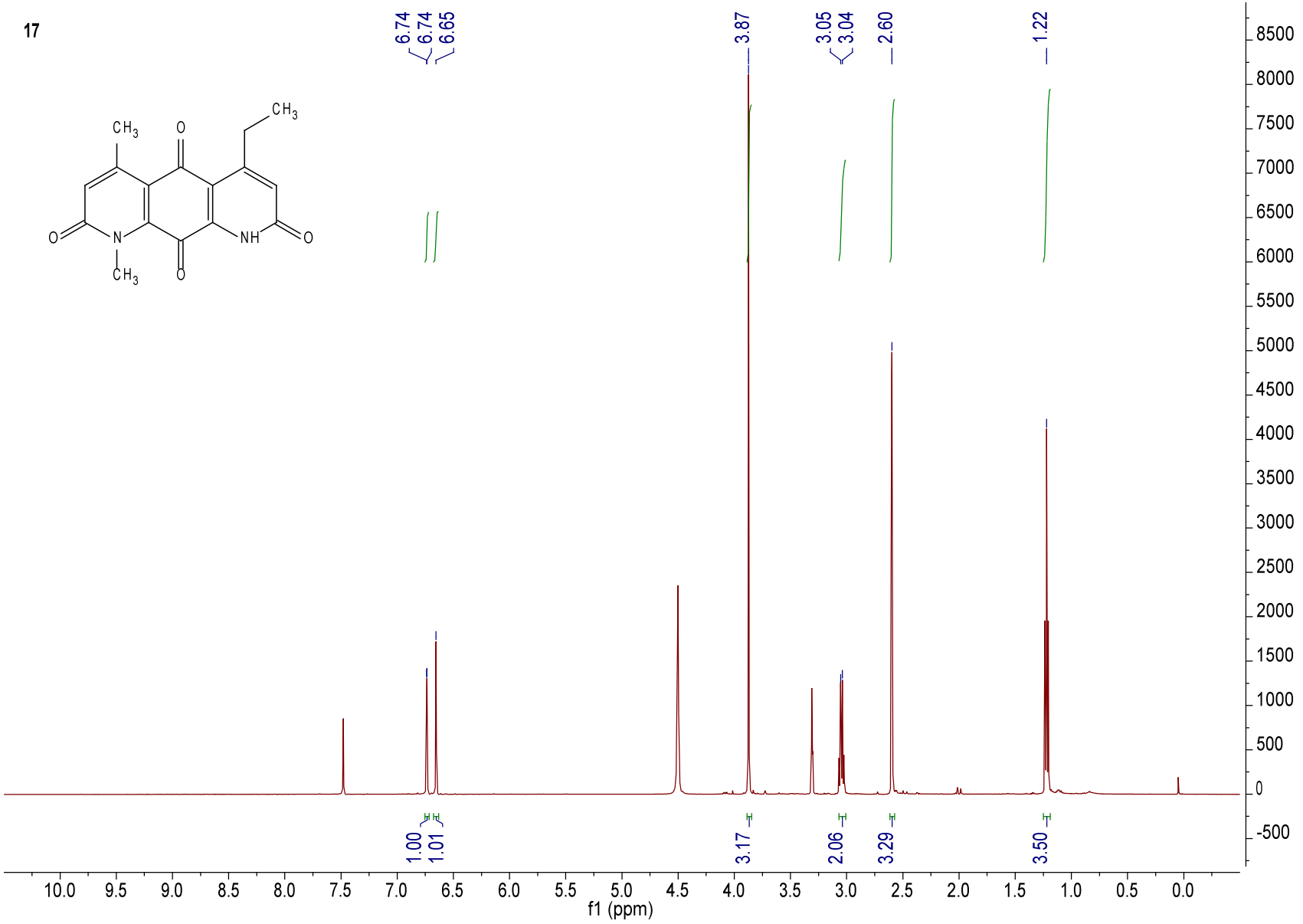

54
154.40
87.10
75.41
31.85
29.59
29.57
29.56
29.41
29.29
29.03
28.83
27.76
26.36
22.62
18.50
14.04
O
NH
CH3
H3C
f1 (ppm)

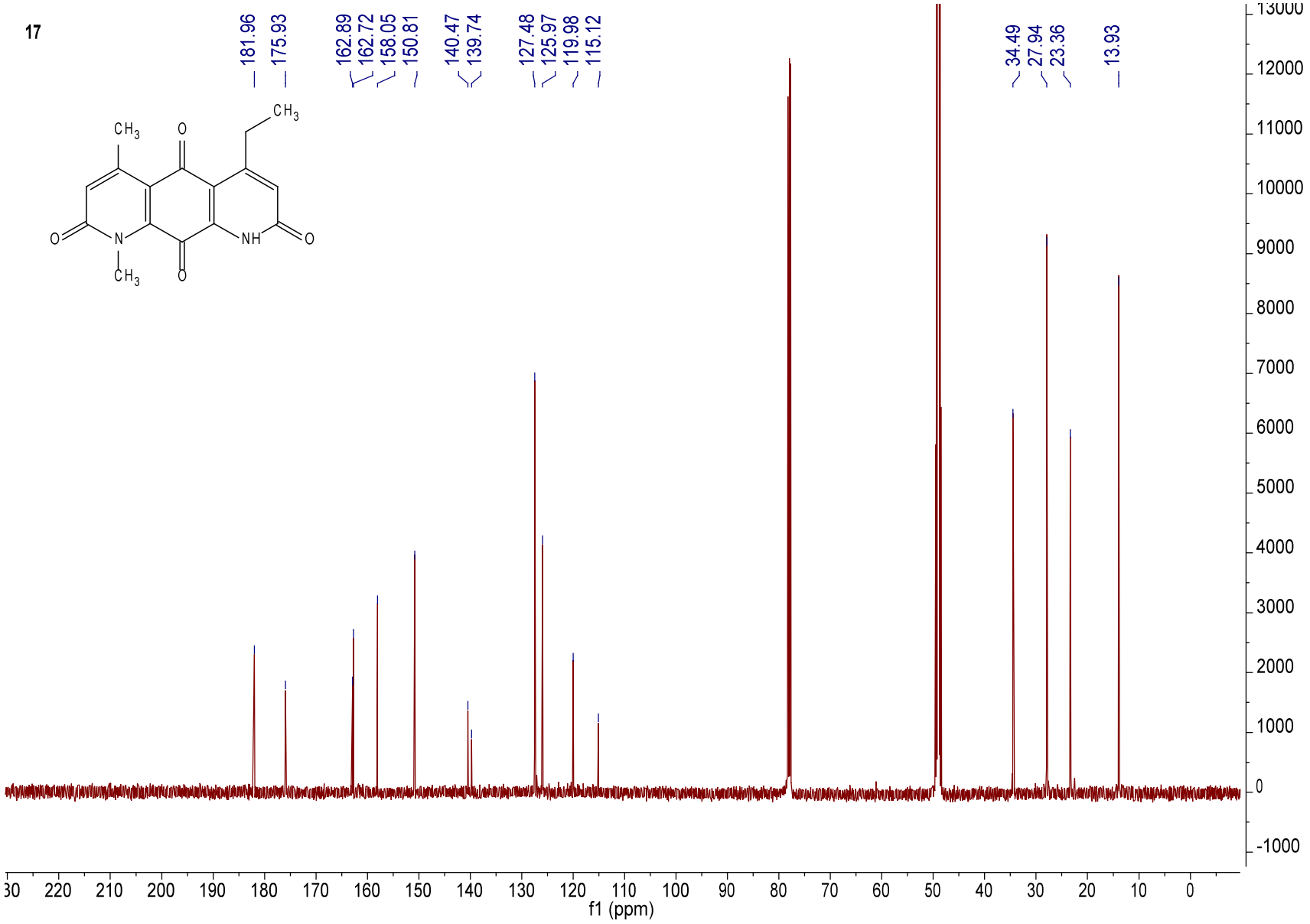

55
6.27
5.74
2.90
2.59
1.55
1.25
0.88
1.00
0.93
3.43
2.53
2.56
18.53
3.11
f1 (ppm)

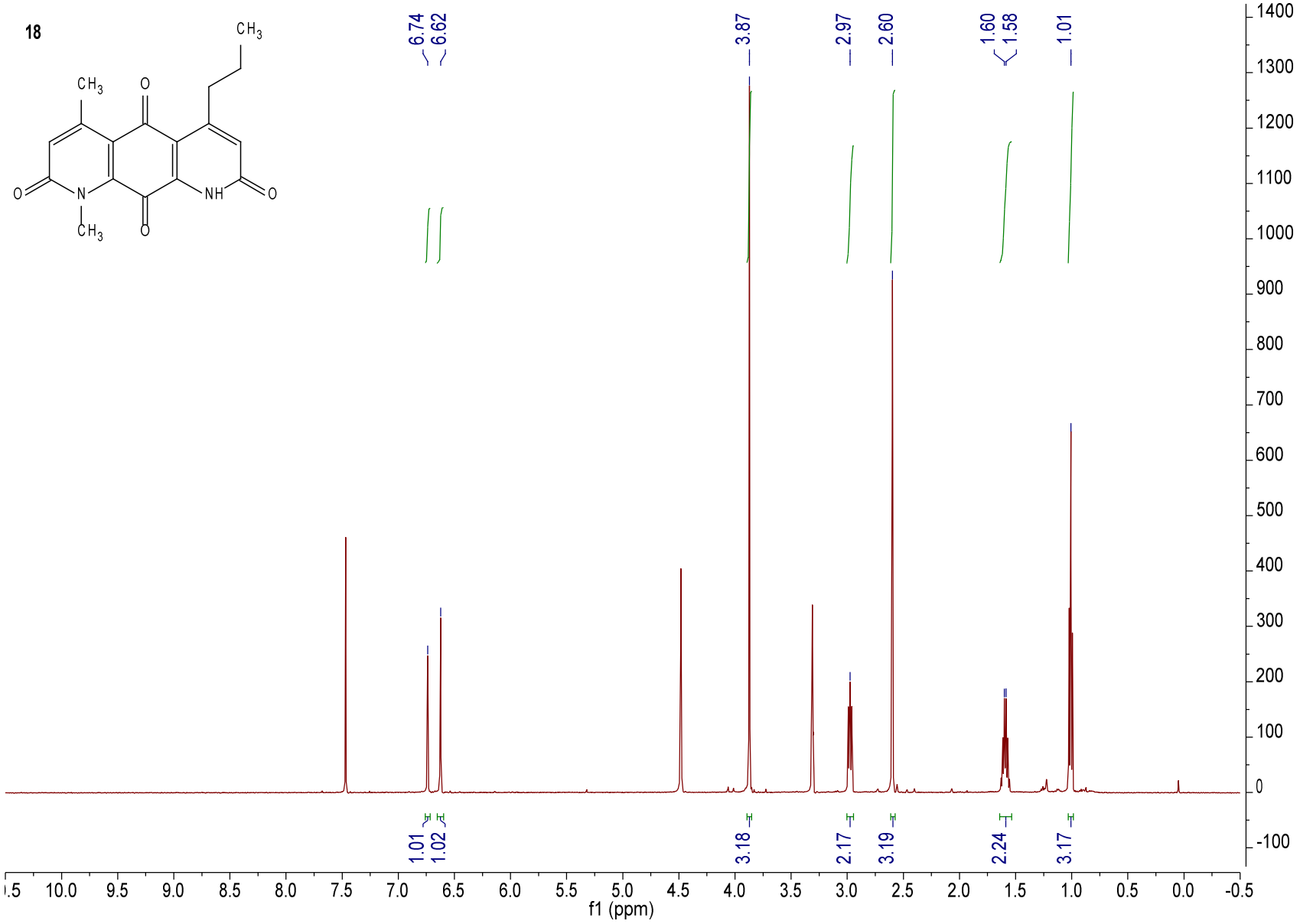

55
165.88
128.43
114.37
47.17
32.01
29.74
29.72
29.70
29.59
29.44
29.43
29.29
28.37
26.30
22.78
14.22
H3C
O
NH
CH3
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

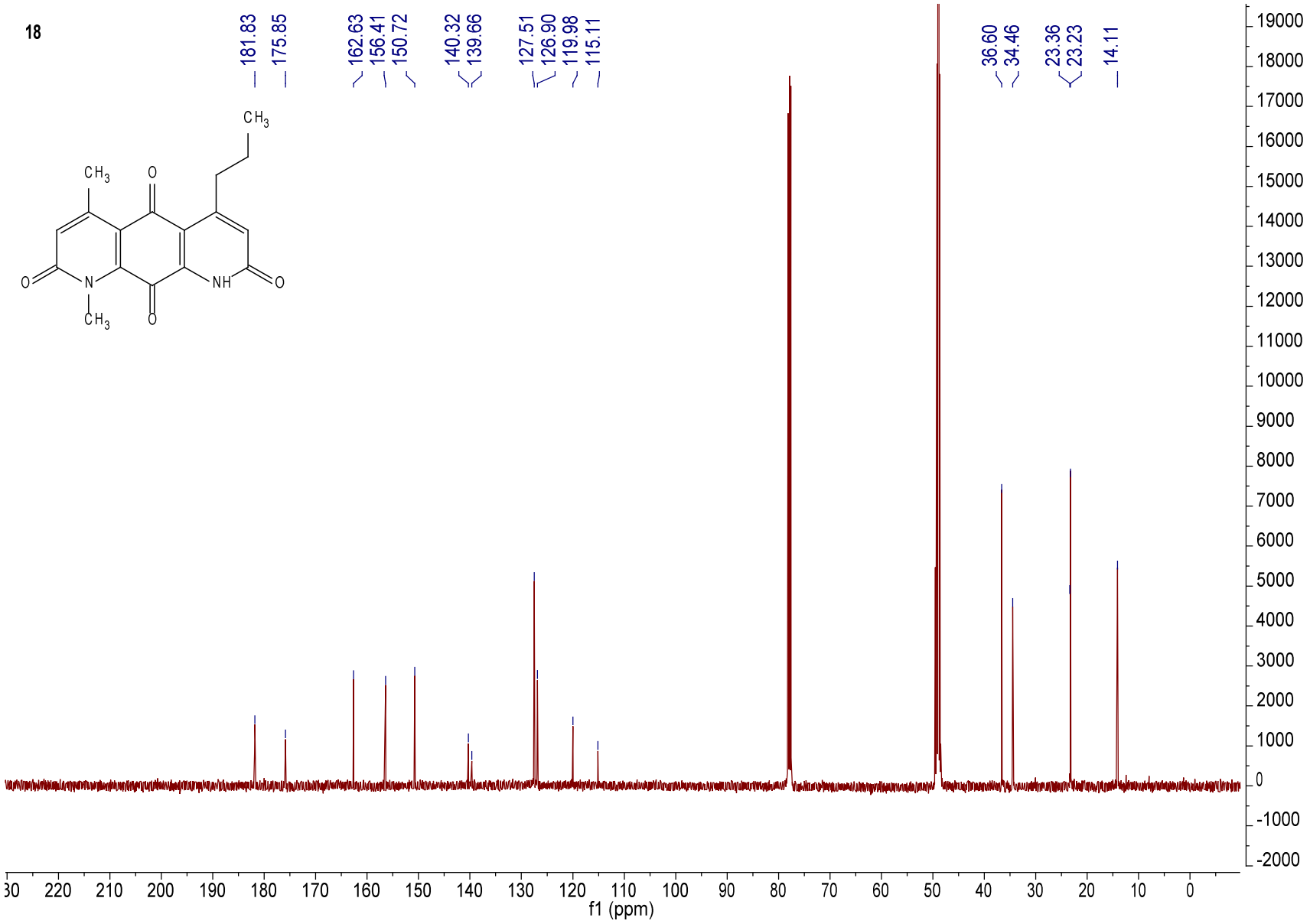

16
6.73
6.62
3.87
2.98
2.59
1.53
1.38
1.23
0.84
1.00
0.98
3.23
2.22
3.37
2.26
2.27
16.60
3.40
f1 (ppm)

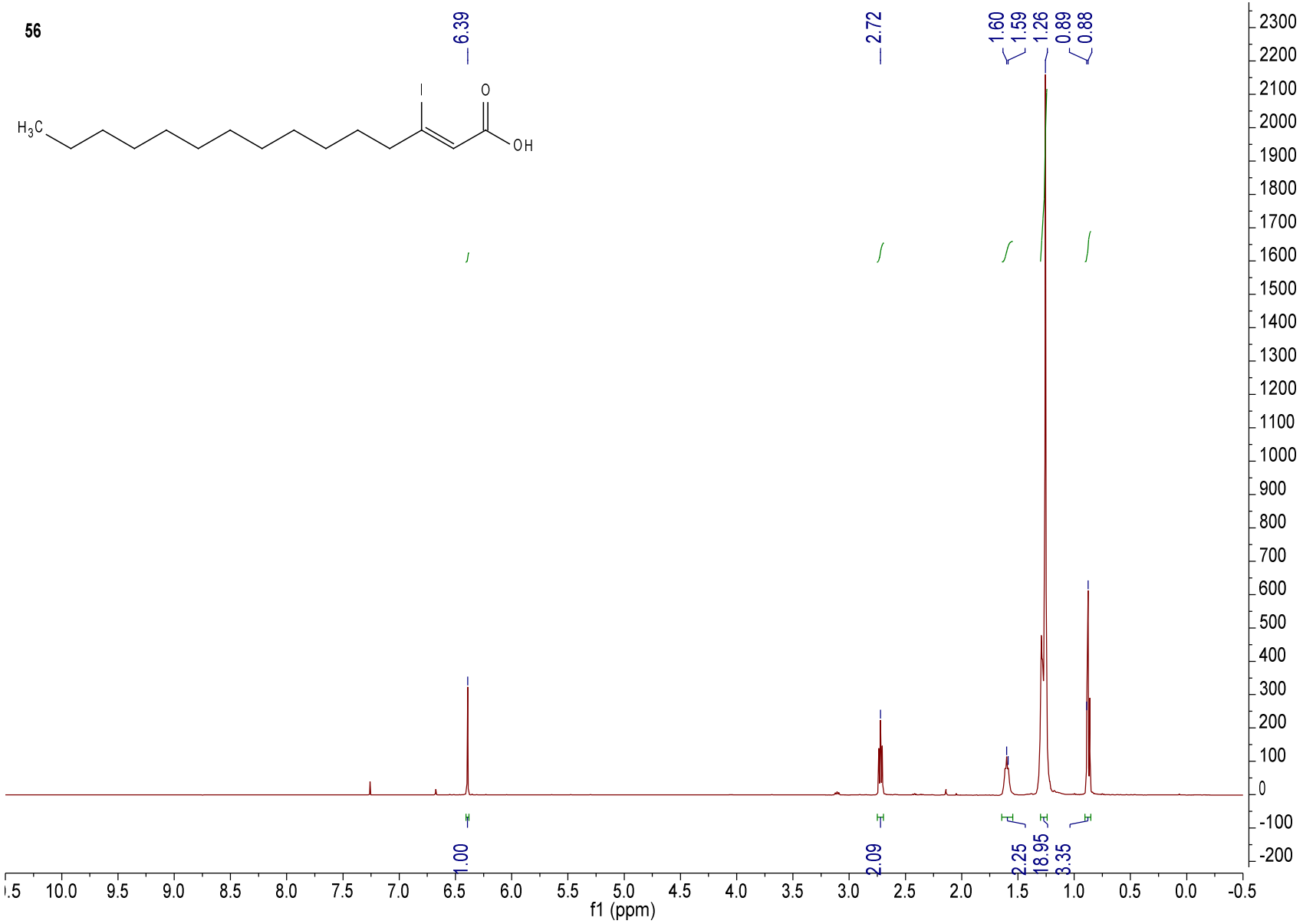

16
180.84
174.88
165.27
162.64
159.37
140.61
138.46
126.89
125.63
124.64
119.65
36.97
36.17
32.68
30.76
30.35
30.28
30.24
30.13
30.08
29.86
23.24
22.13
13.56
CH3
O
CH3
O
N
NH
O
CH3
O
340000
320000
300000
280000
260000
240000
220000
200000
180000
160000
140000
120000
100000
80000
60000
40000
20000
0
-20000
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

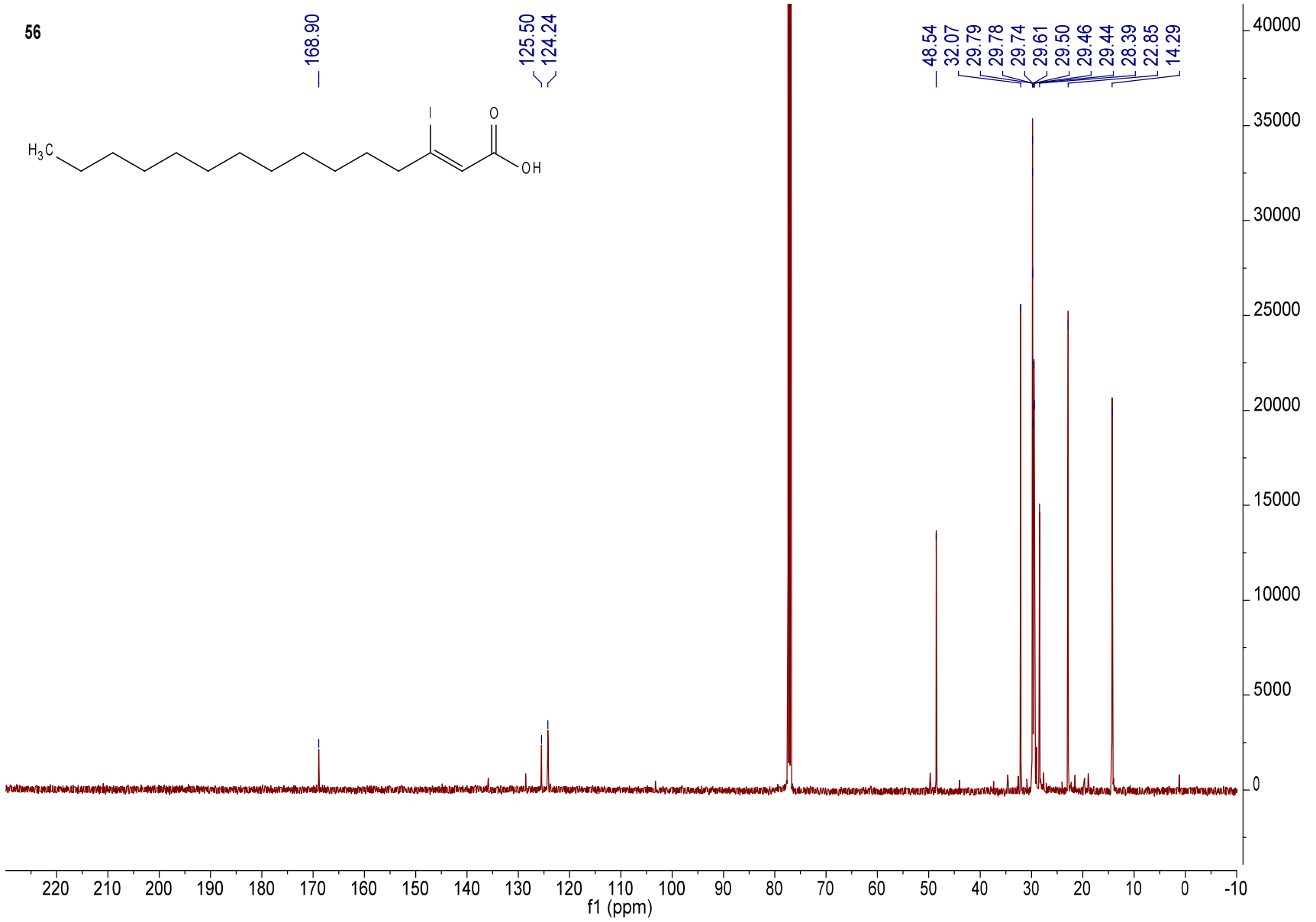

17
6.74
6.74
6.65
3.87
3.05
3.04
2.60
1.22
1.00
1.01
3.17
2.06
3.29
3.50
f1 (ppm)

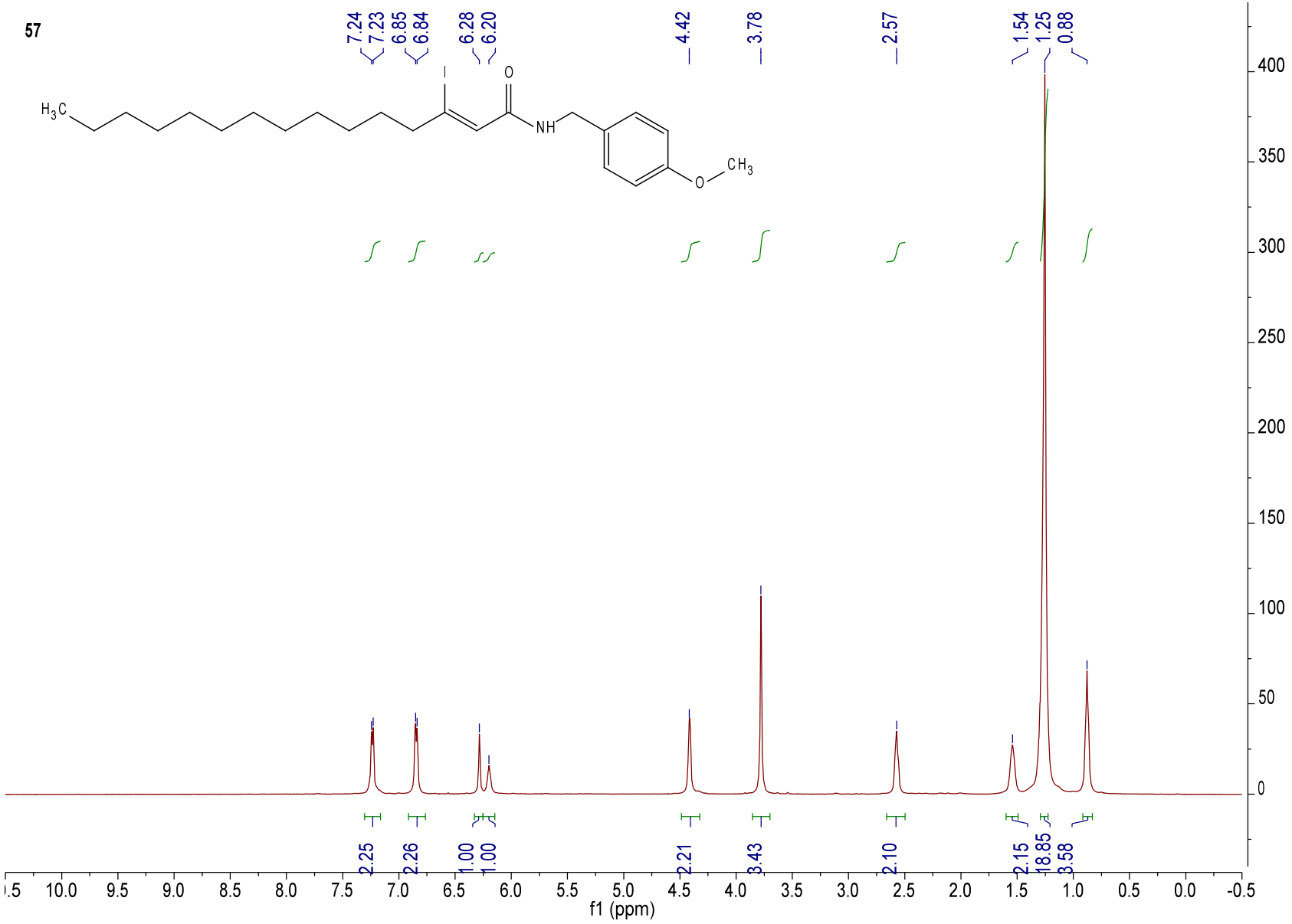

17
181.96
175.93
162.89
162.72
158.05
150.81
140.47
139.74
127.48
125.97
119.98
115.12
34.49
27.94
23.36
13.93
CH3
O
CH3
O
N
NH
O
CH3
O
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

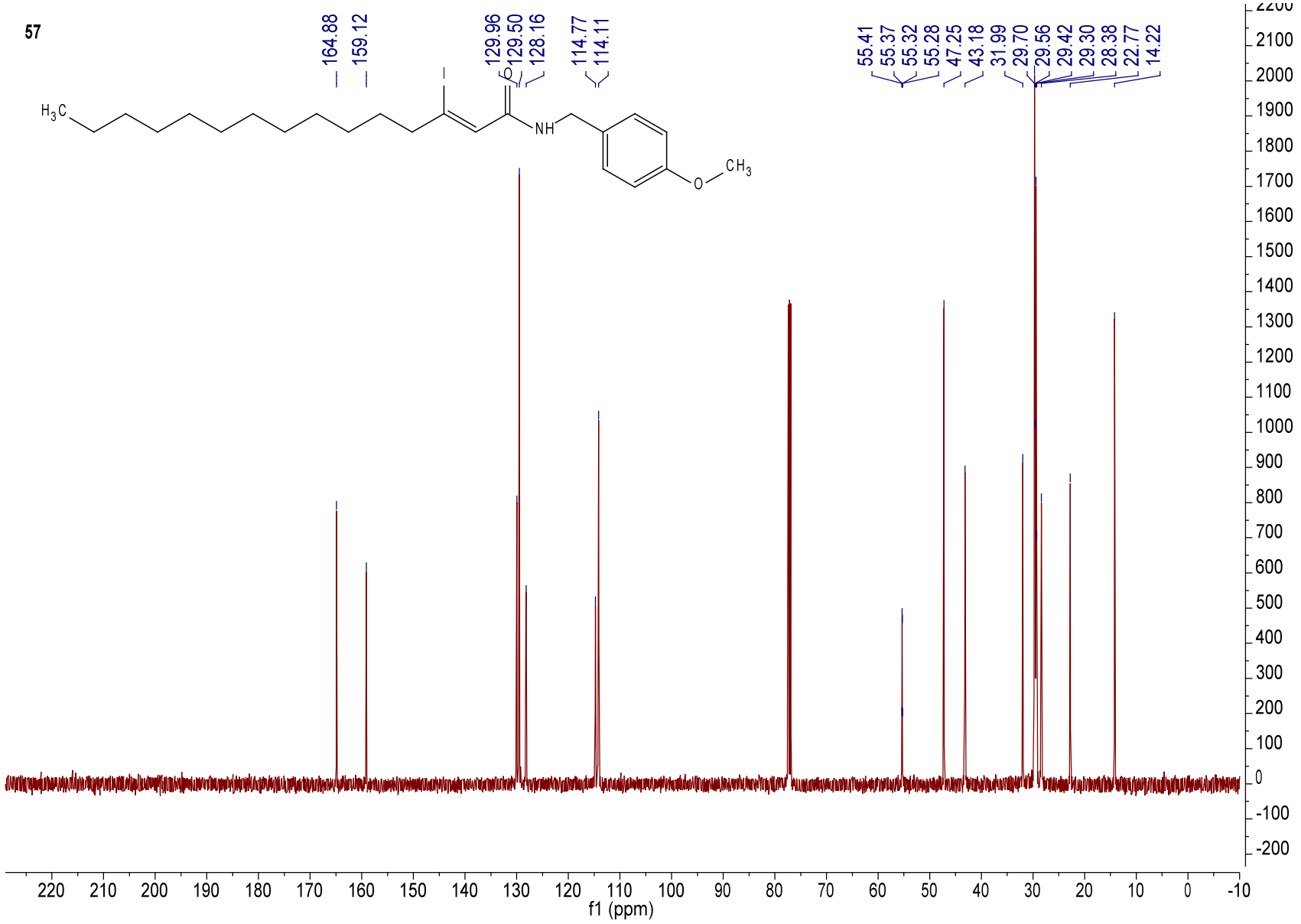

18
CH3
CH3
O
O
N
NH
O
CH3
O
6.74
6.62
3.87
2.97
2.60
1.60
1.58
1.01
1.01
1.02
3.18
2.17
3.19
2.24
3.17
f1 (ppm)

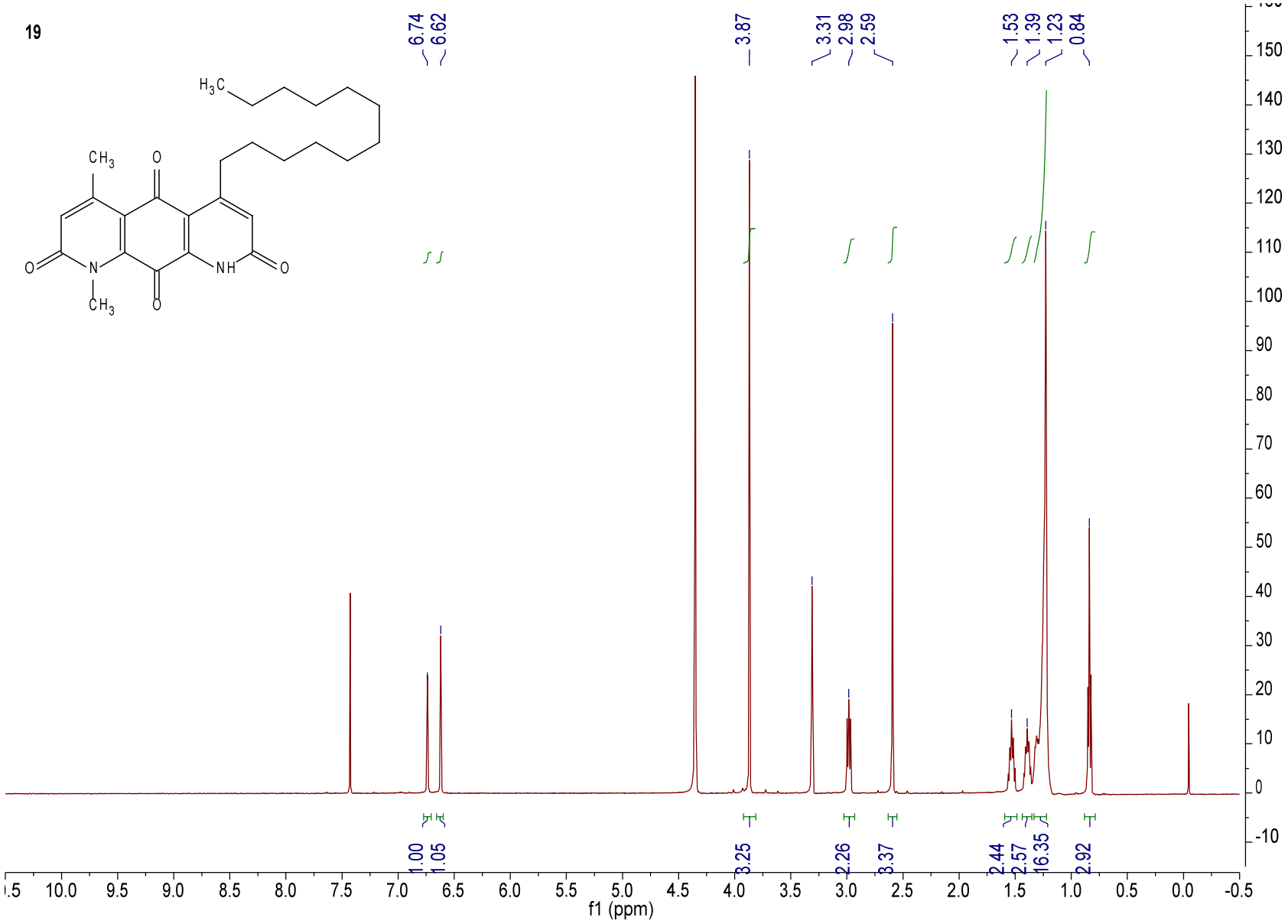

18
181.83
175.85
162.63
156.41
150.72
140.32
139.66
127.51
126.90
119.98
115.11
36.60
34.46
23.36
23.23
14.11
CH3
O
N
NH
f1 (ppm)

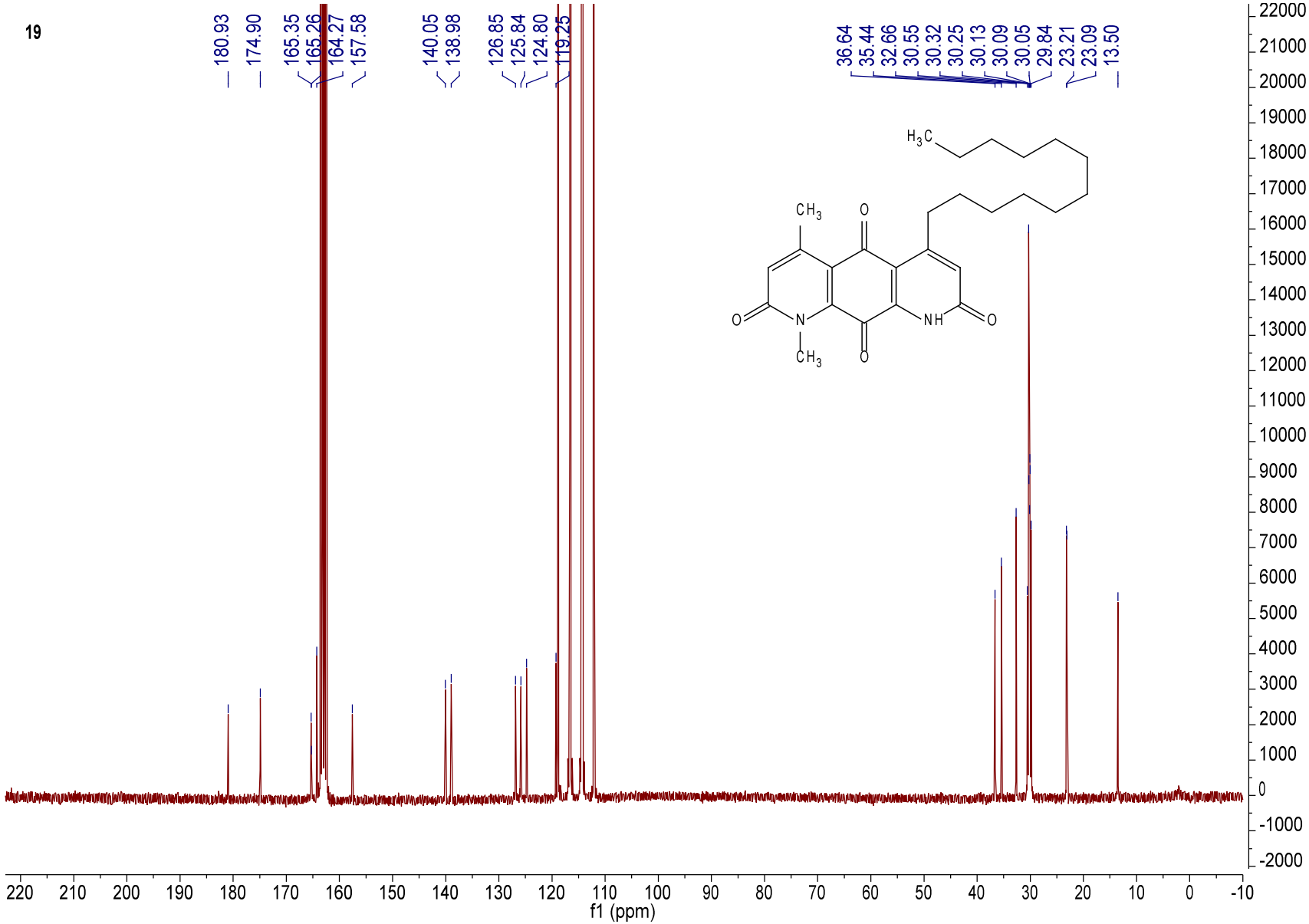

56
6.39
2.72
1.60
1.59
1.26
0.89
0.88
H3C
I
O
OH
1.00
2.09
2.25
18.95
3.35
f1 (ppm)

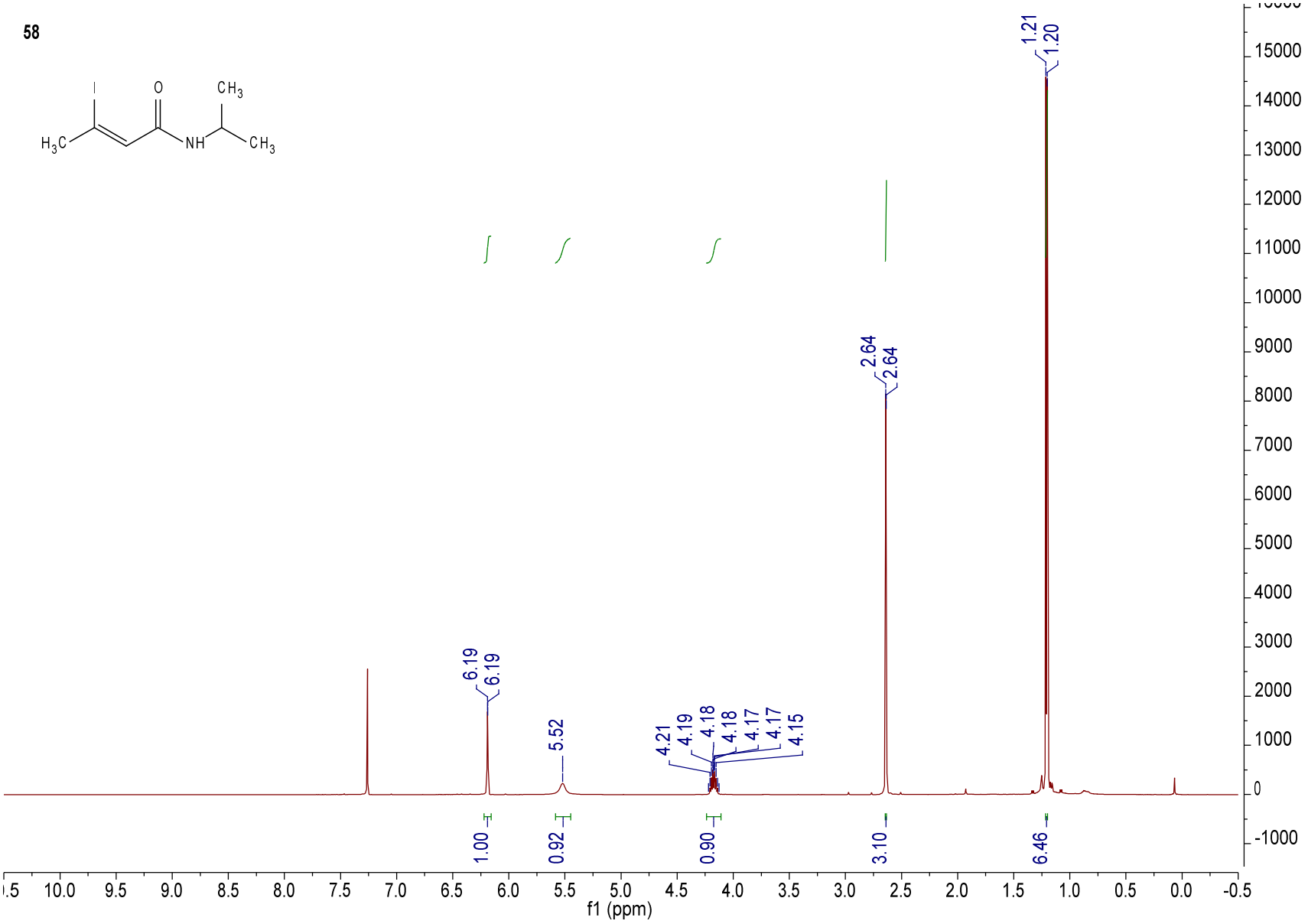

56
168.90
125.50
124.24
48.54
32.07
29.79
29.78
29.74
29.61
29.50
29.46
29.44
28.39
22.85
14.29
H3C
I
O
OH
40000
35000
30000
25000
20000
15000
10000
5000
0
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

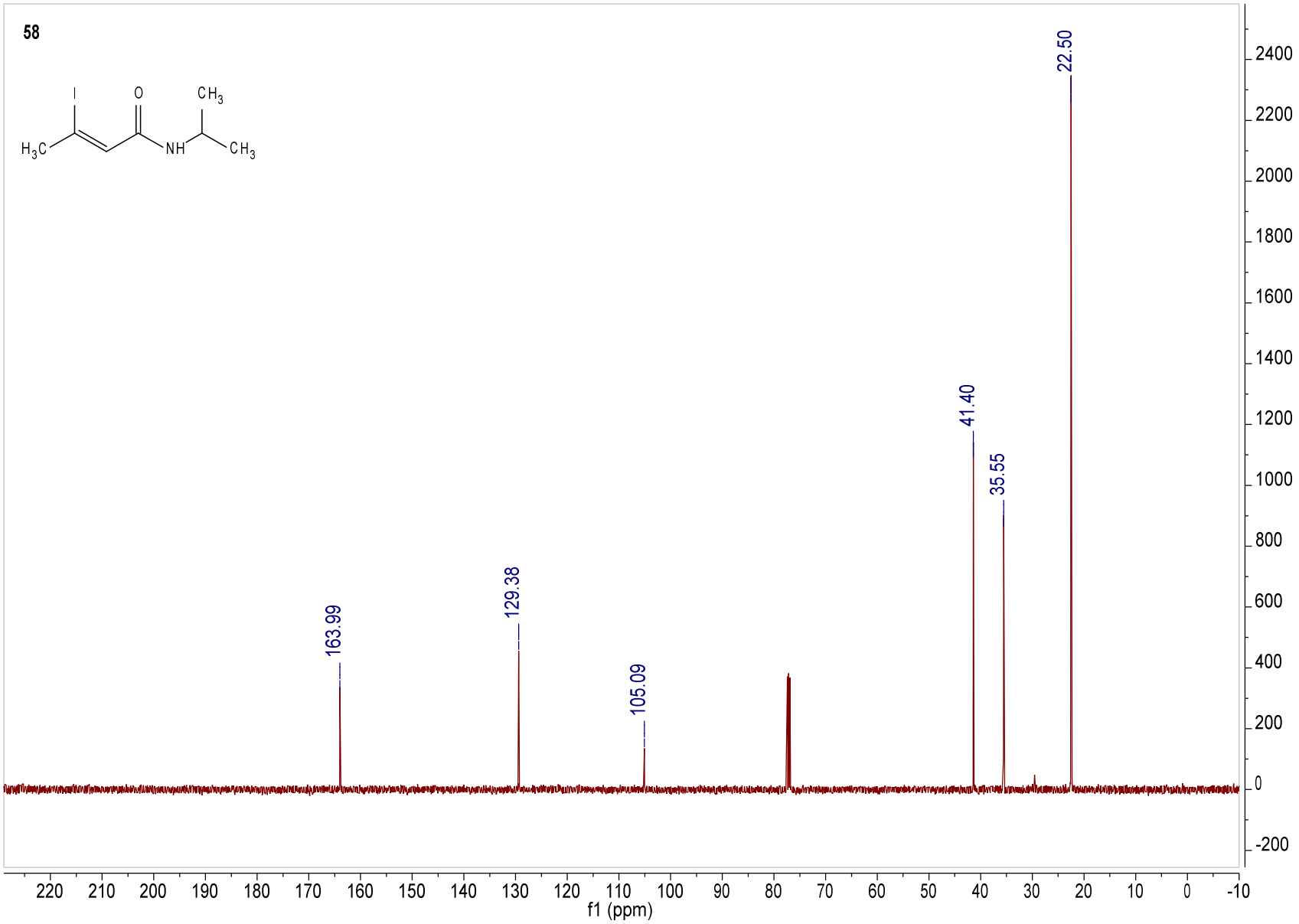

57
7.24
7.23
6.85
6.84
6.28
6.20
4.42
3.78
2.57
1.54
1.25
0.88
H3C
NH
O
CH3
2.25
2.26
1.00
1.00
2.21
3.43
2.10
2.15
18.85
3.58
f1 (ppm)

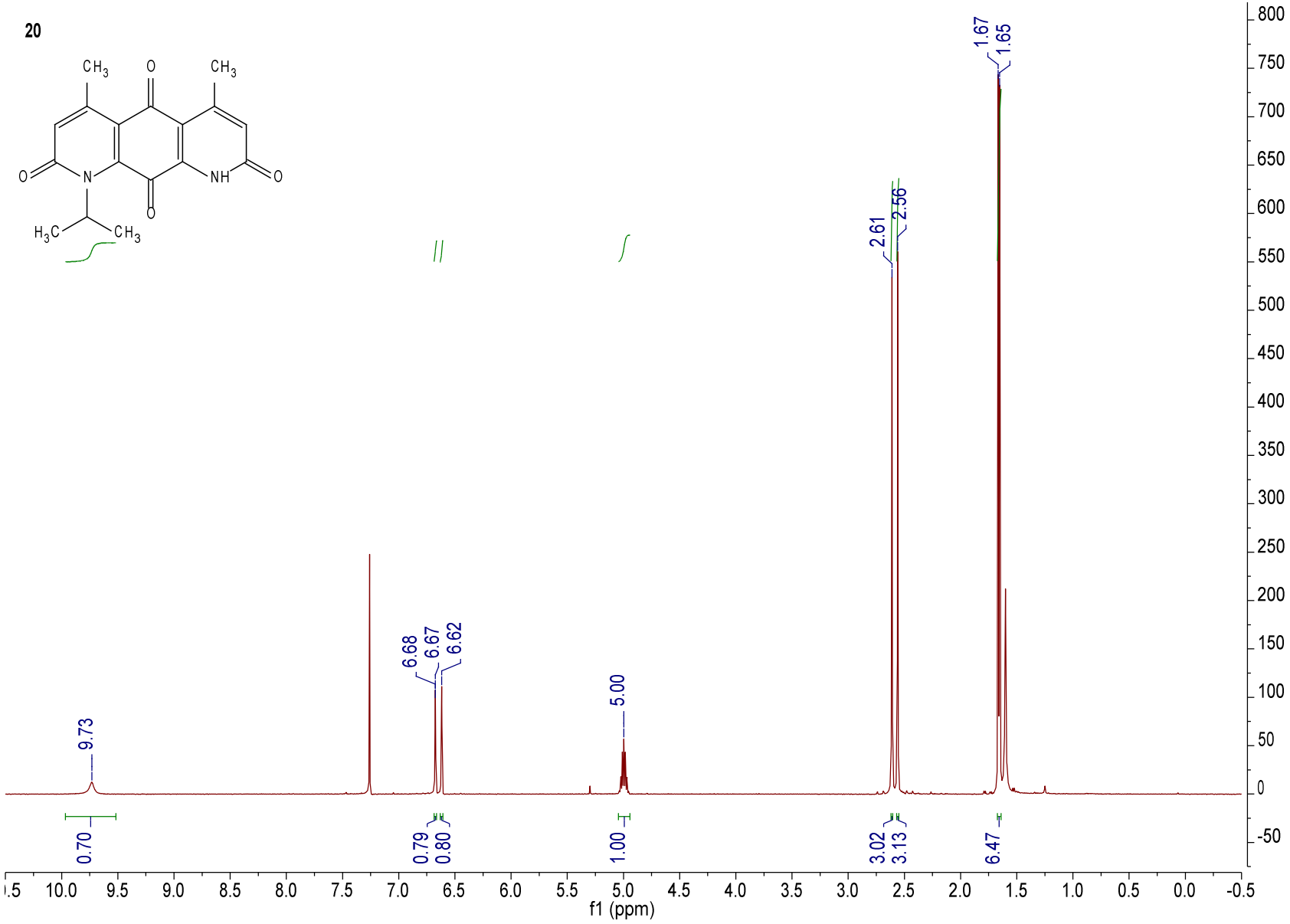

57
164.88
159.12
129.96
129.50
128.16
114.77
114.11
55.41
55.37
55.32
55.28
47.25
43.18
31.99
29.70
29.56
29.42
29.30
28.38
22.77
14.22
H3C
NH
O
CH3
f1 (ppm)

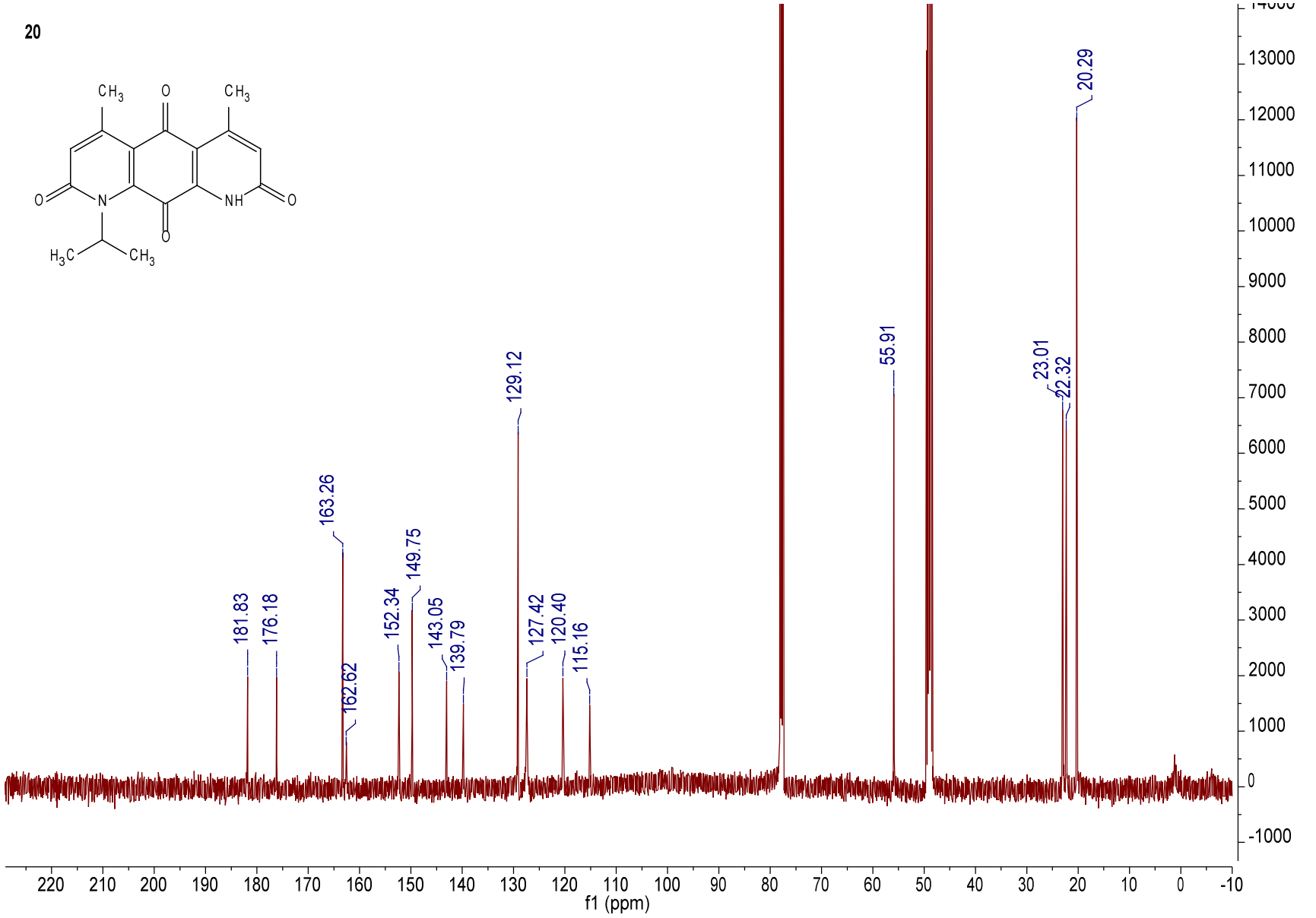

19
6.74
6.62
3.87
3.31
2.98
2.59
1.53
1.39
1.23
0.84
1.00
1.05
3.25
2.26
3.37
2.44
2.57
16.35
2.92
f1 (ppm)

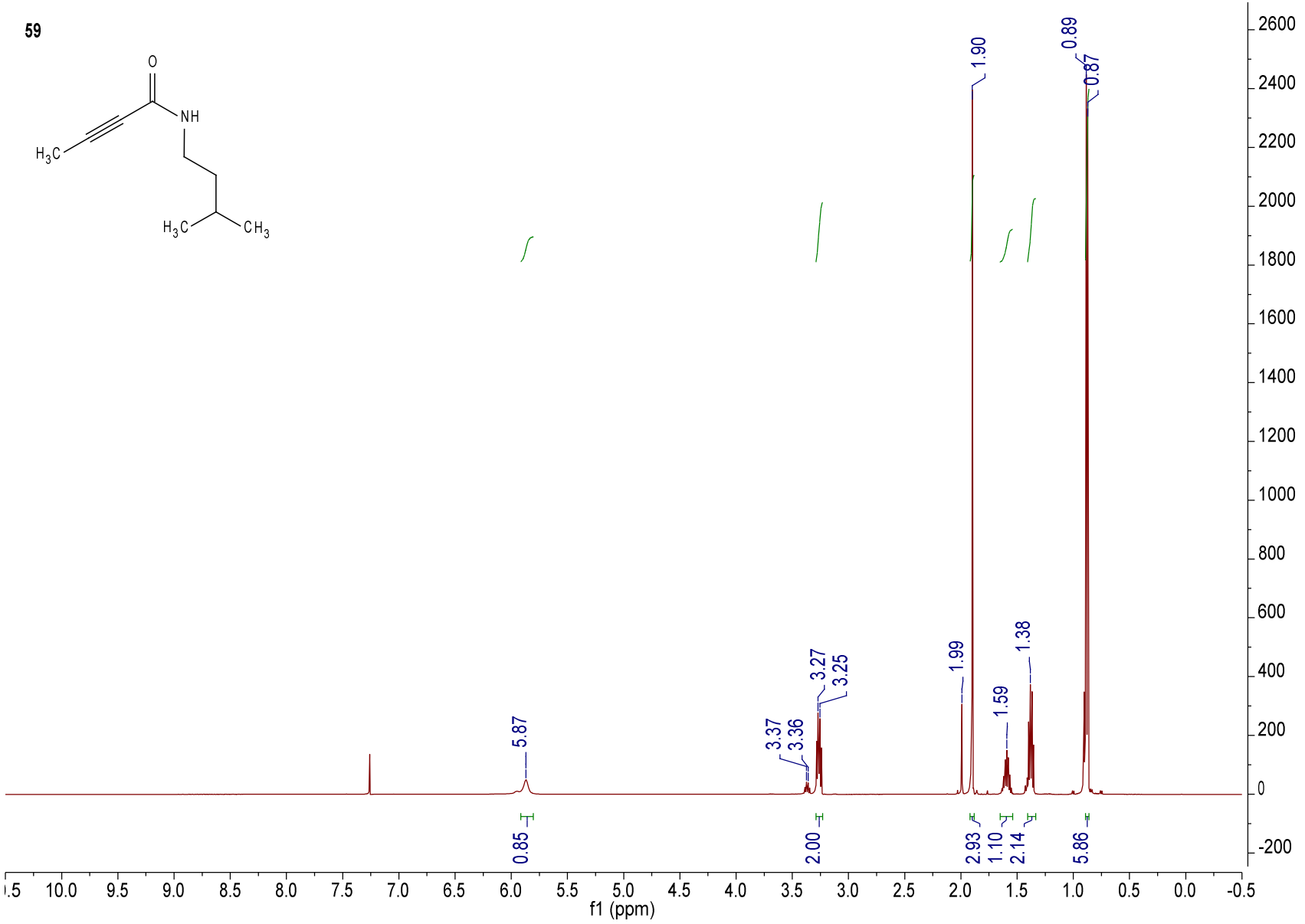

19
180.93
174.90
165.35
165.26
164.27
157.58
140.05
138.98
126.85
125.84
124.80
119.25
36.64
35.44
32.66
30.55
30.32
30.25
30.13
30.09
30.05
29.84
23.21
23.09
13.50
H3C
CH3
O
O
N
NH
O
CH3
O
f1 (ppm)


58
O
CH3
H3C
NH
CH3
1.21
1.20
2.64
2.64
6.19
6.19
5.52
4.21
4.19
4.18
4.18
4.17
4.17
4.15
1.00
0.92
0.90
3.10
6.46
f1 (ppm)

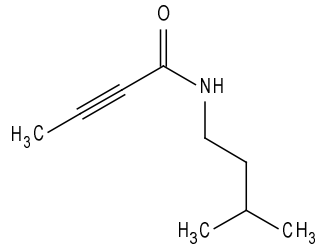

58
I
O
CH3
H3C
NH
CH3
22.50
41.40
35.55
163.99
129.38
105.09
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


20
CH3
O
CH3
O
N
NH
O
O
H3C
CH3
9.73
6.68
6.67
6.62
5.00
2.61
2.56
1.67
1.65
0.70
0.79
0.80
1.00
3.02
3.13
6.47
f1 (ppm)

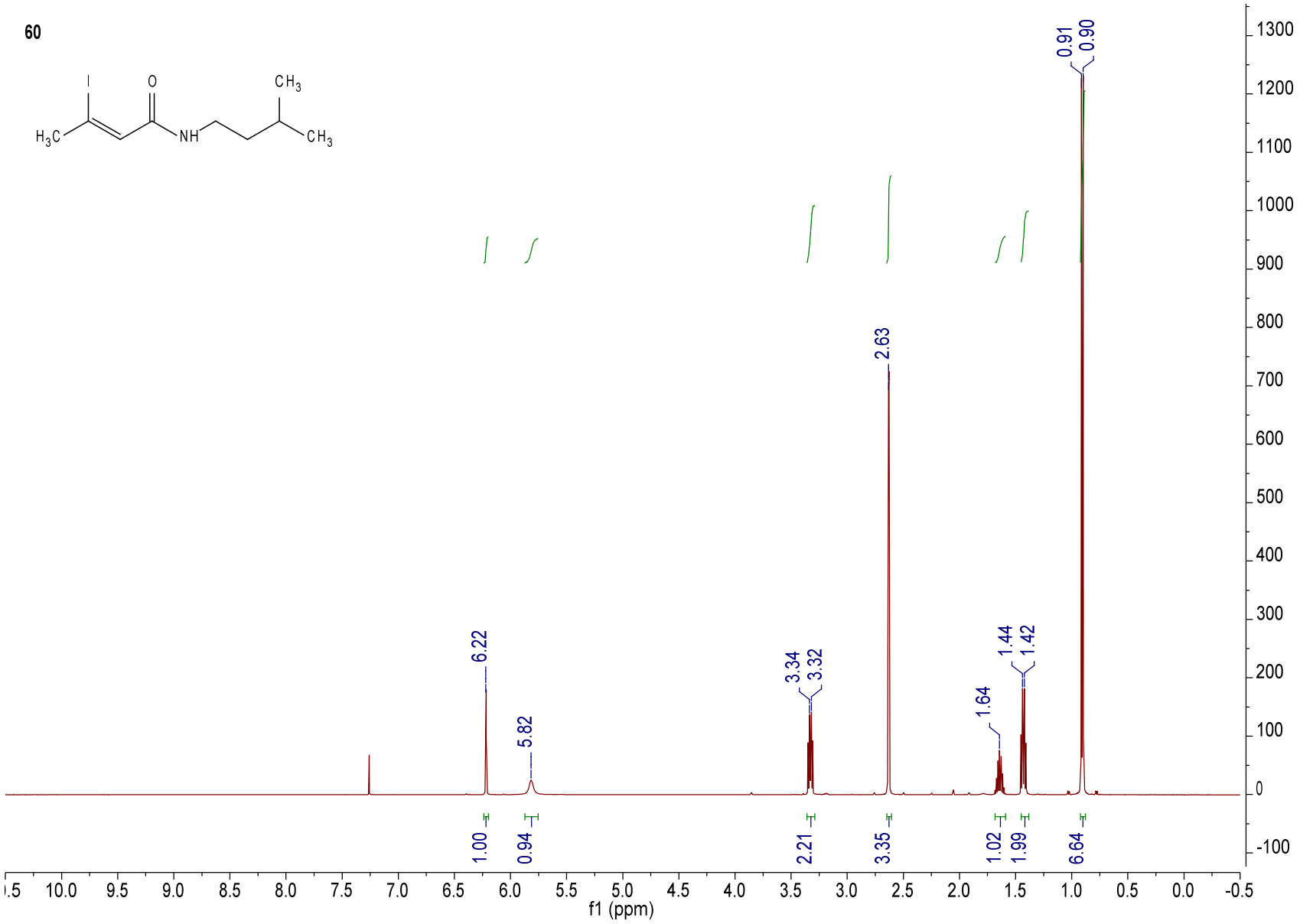

20
CH3
O
CH3
O
N
NH
O
O
H3C
CH3
181.83
176.18
163.26
162.62
152.34
149.75
143.05
139.79
129.12
127.42
120.40
115.16
55.91
23.01
22.32
20.29
f1 (ppm)

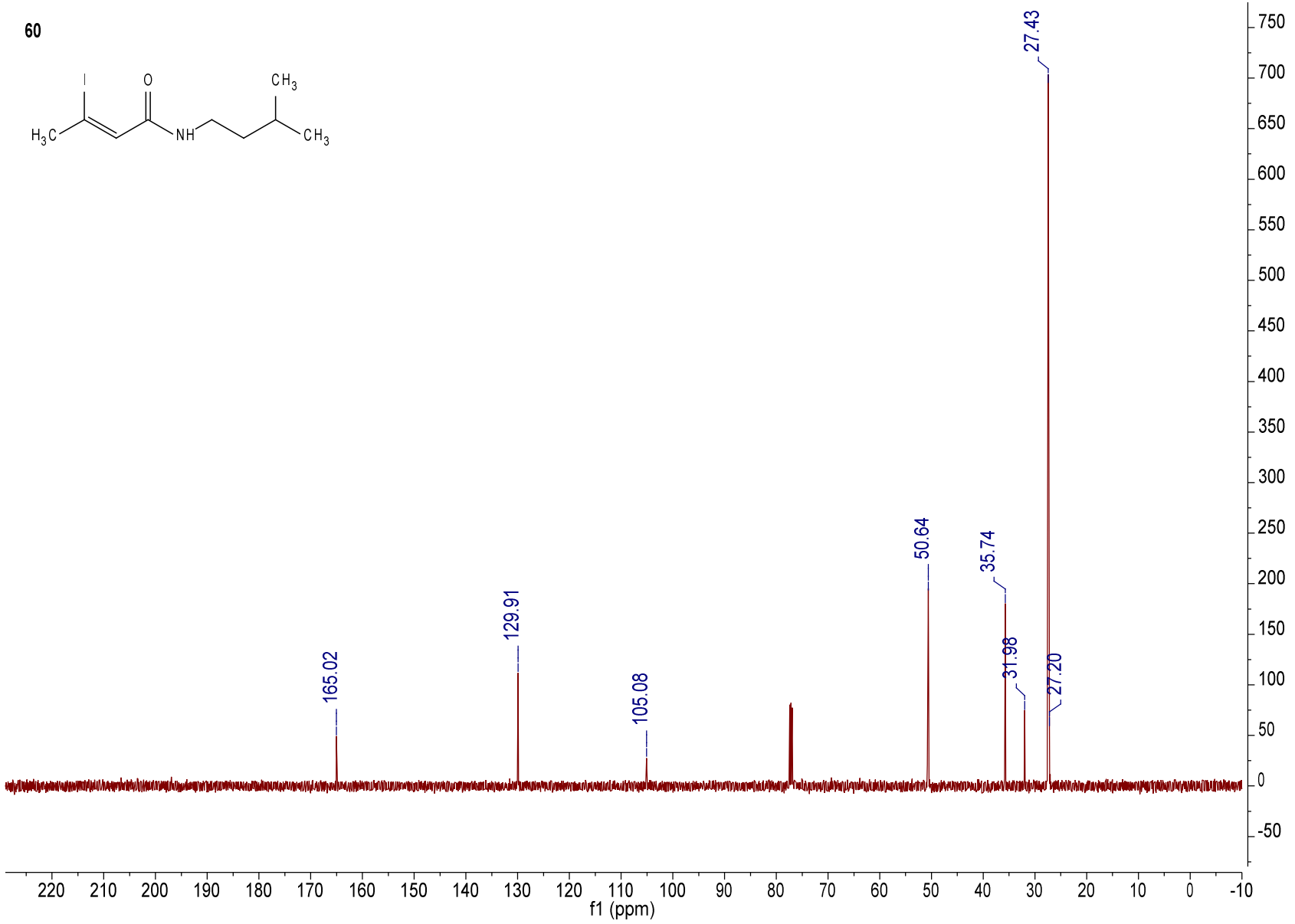

59
O
NH
H3C
H3C
CH3
5.87
3.37
3.36
3.27
3.25
1.99
1.90
1.59
1.38
0.89
0.87
0.85
2.00
2.93
1.10
2.14
5.86
f1 (ppm)

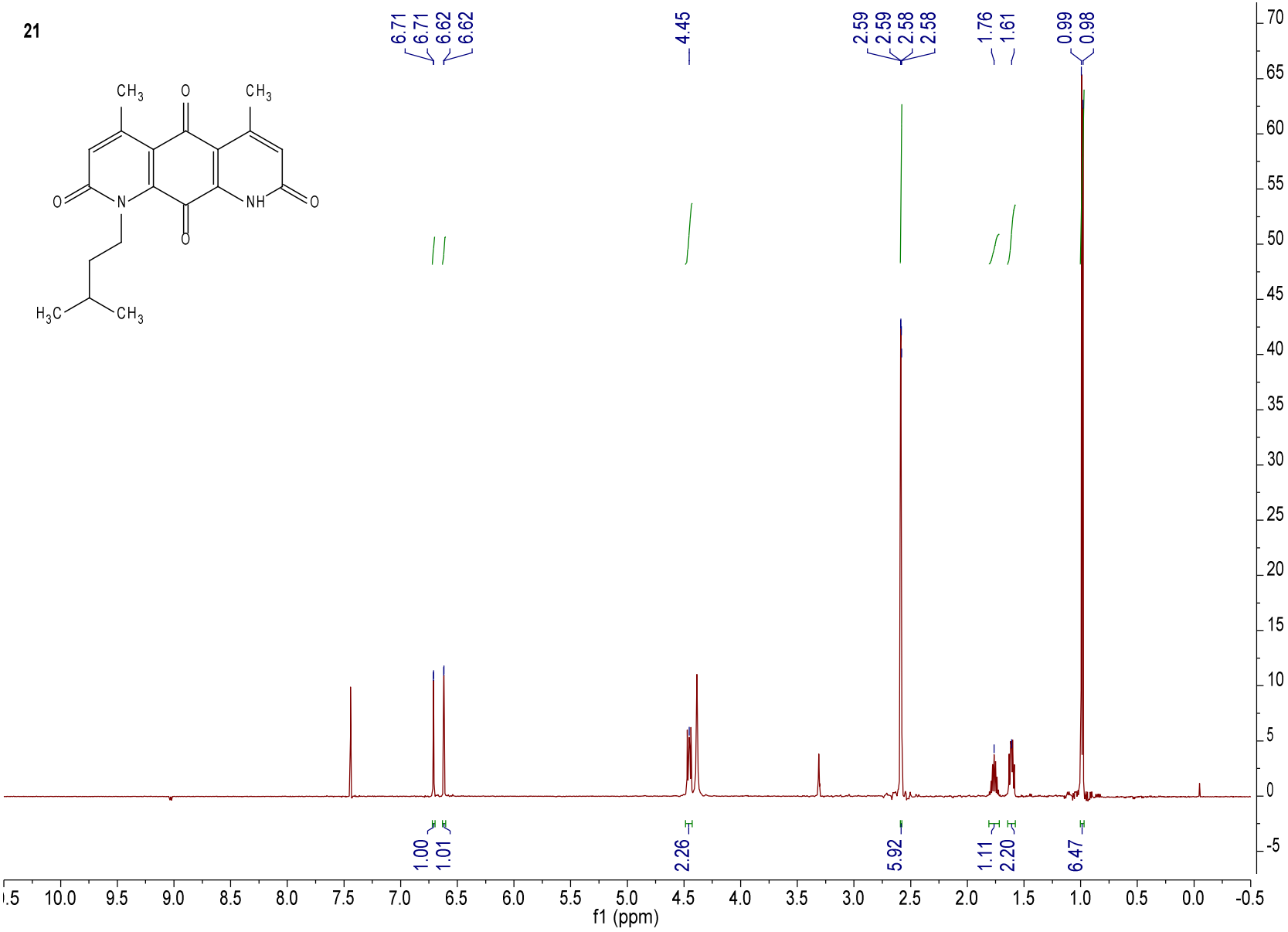
59

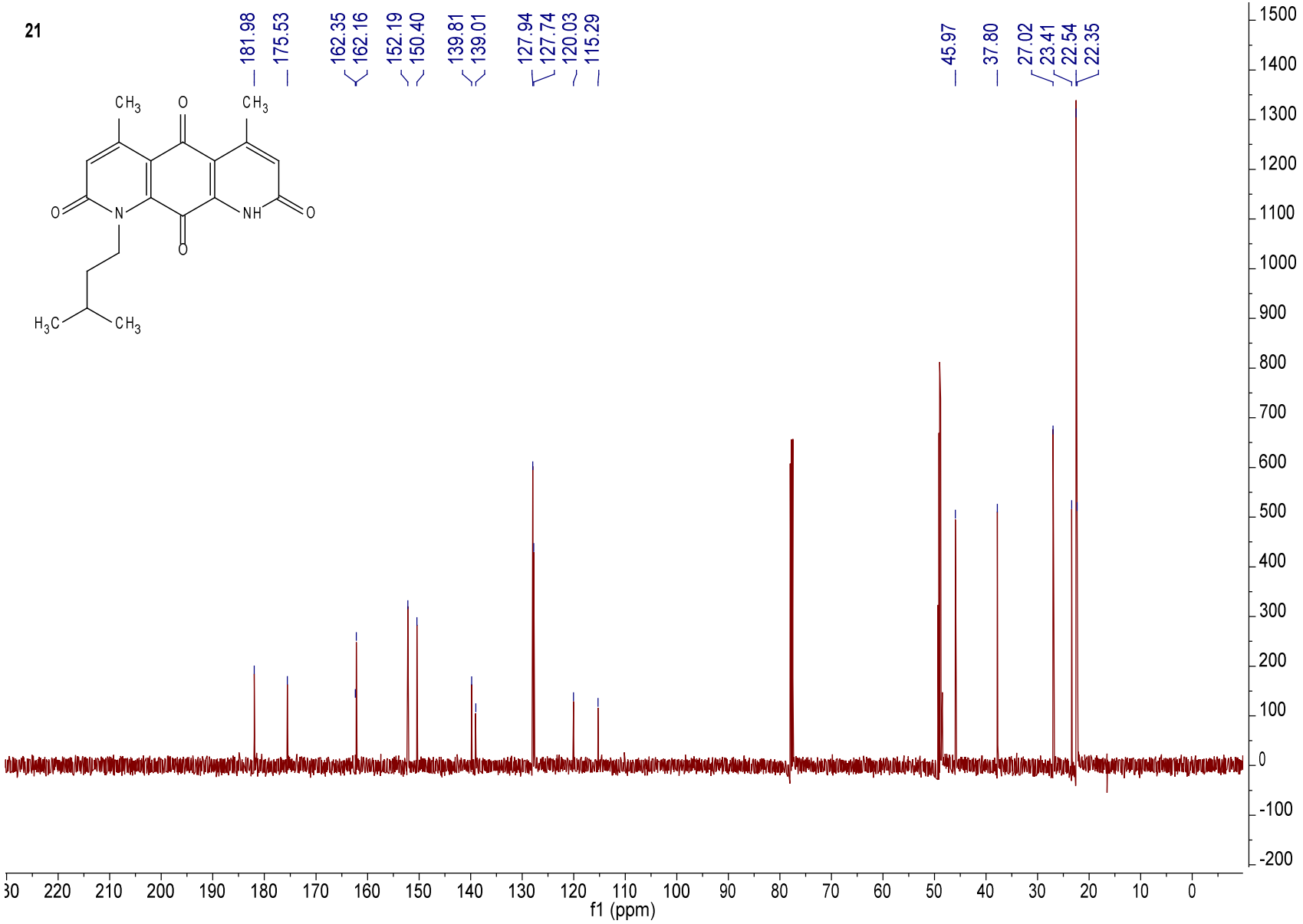

O
NH
H3C
H3C
CH3

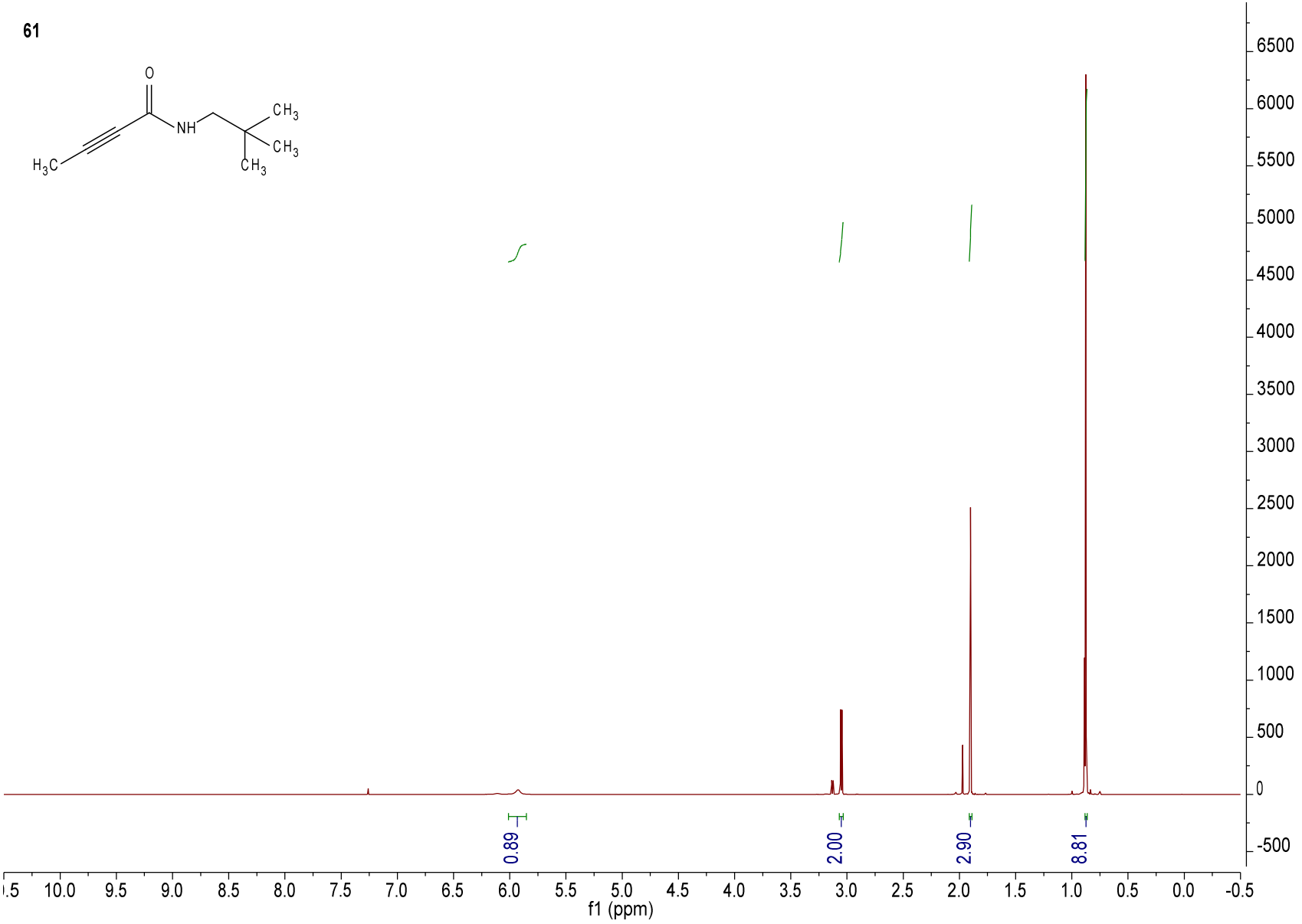
156.19
153.45
89.12
82.24
74.74
72.37
41.28
39.12
37.70
37.63
25.40
25.05
22.02
3.50
3.22
f1 (ppm)

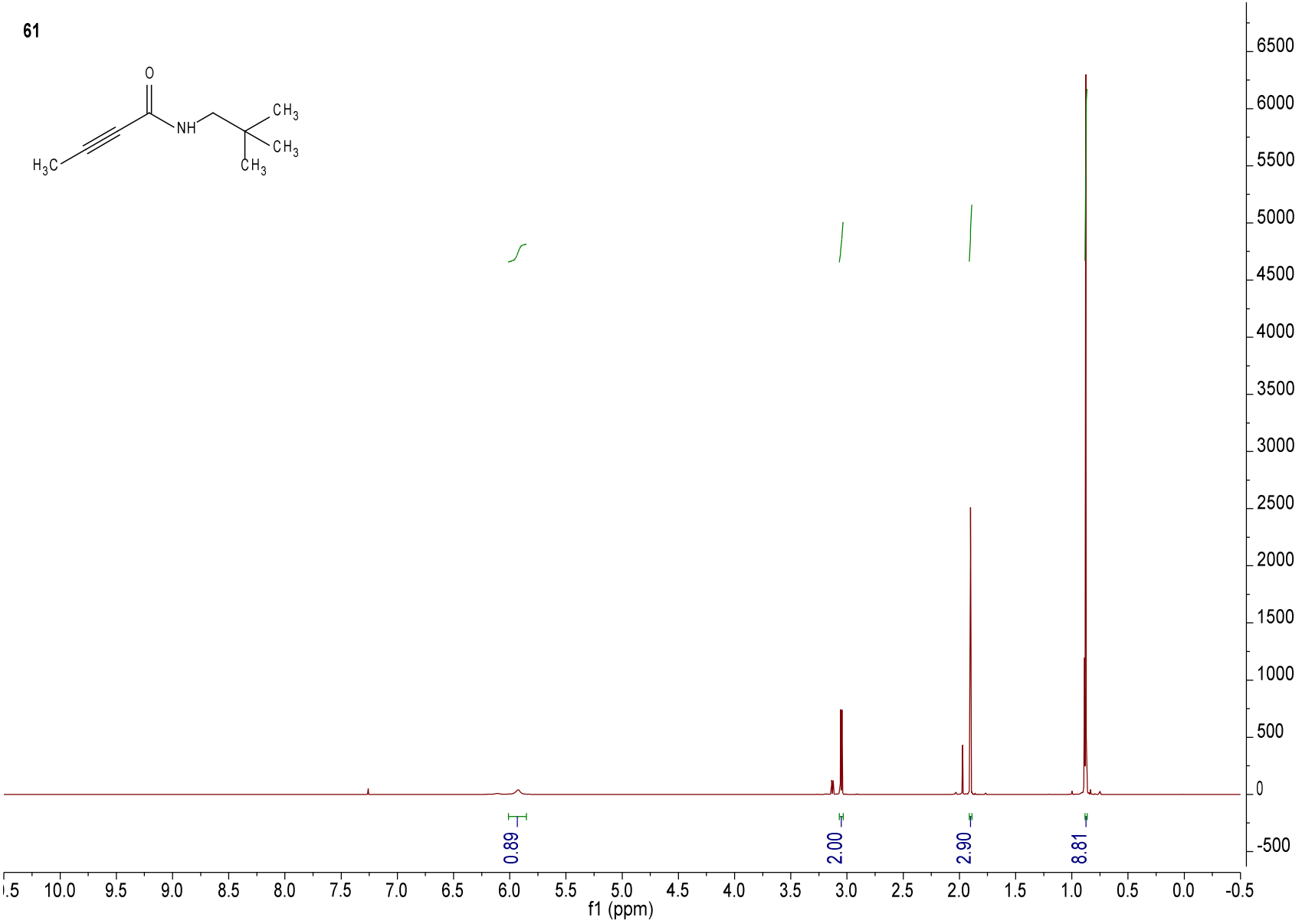

60
I
O
CH3
H3C
NH
CH3
0.91
0.90
2.63
6.22
5.82
3.34
3.32
1.64
1.44
1.42
1.00
0.94
2.21
3.35
1.02
1.99
6.64
f1 (ppm)

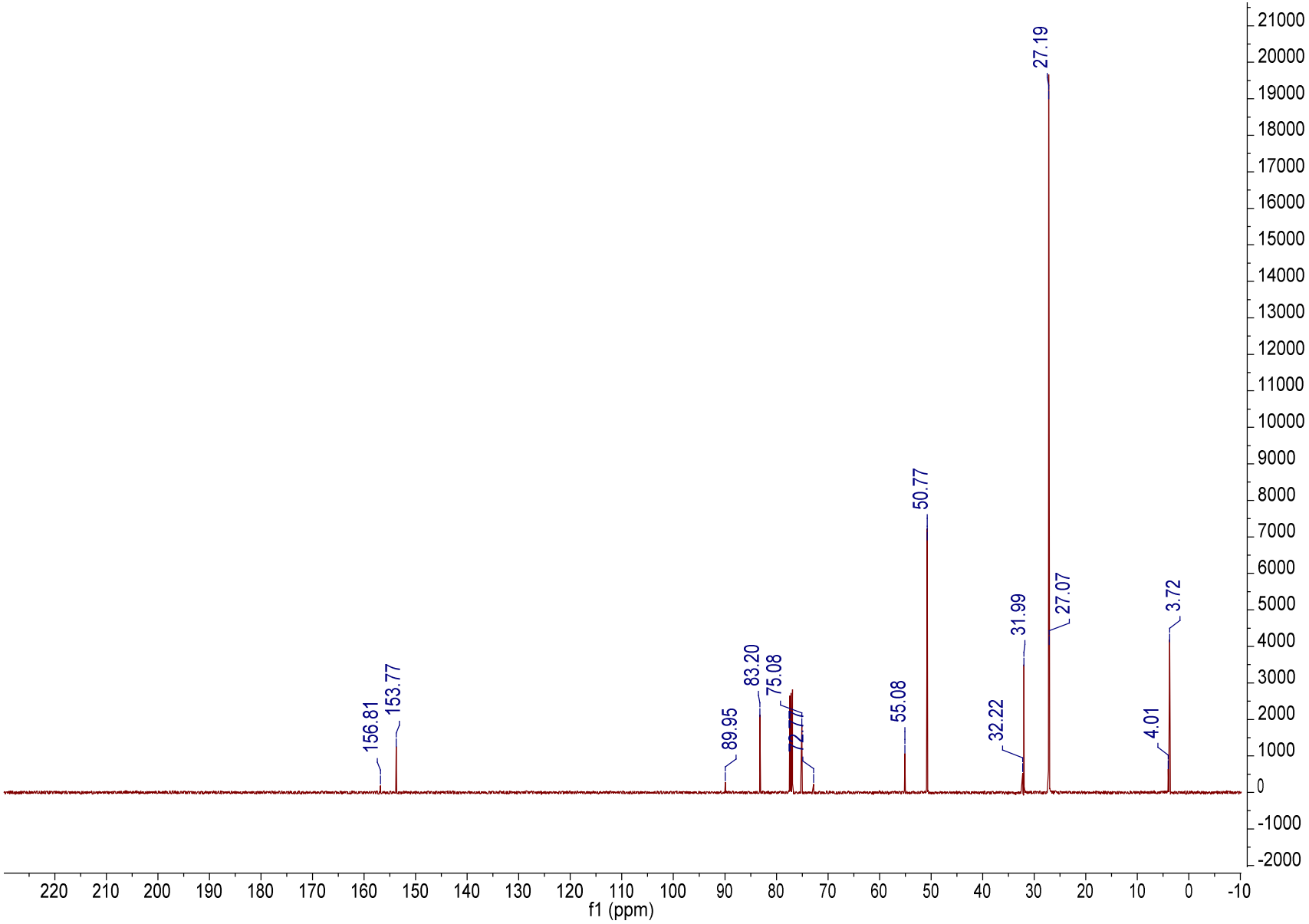

60
O
CH3
H3C
NH
CH3
27.43
50.64
35.74
129.91
165.02
105.08
31.98
27.20
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

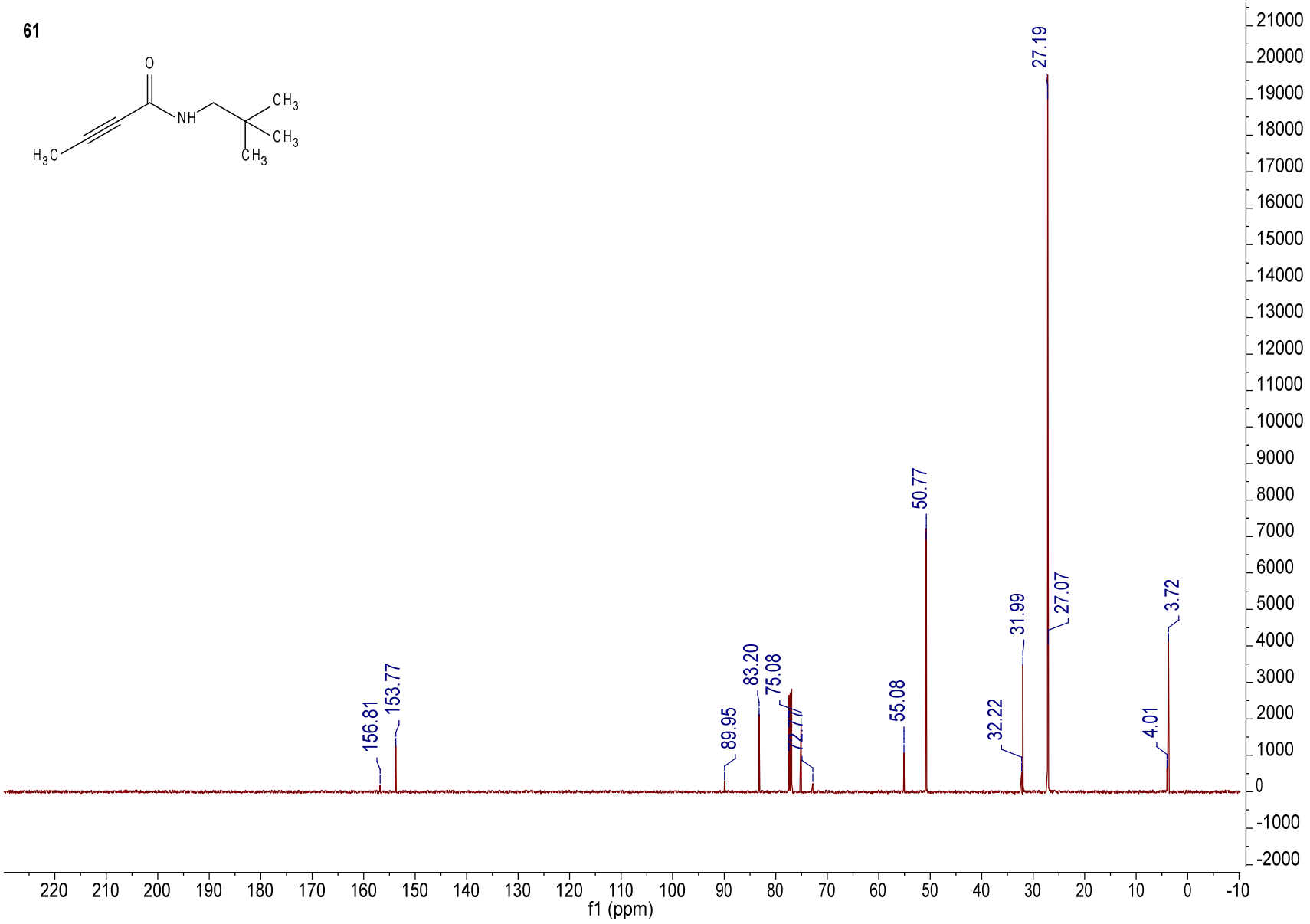

21
6.71
6.71
6.62
6.62
4.45
2.59
2.59
2.58
2.58
1.76
1.61
0.99
0.98
1.00
1.01
2.26
5.92
1.11
2.20
6.47
f1 (ppm)

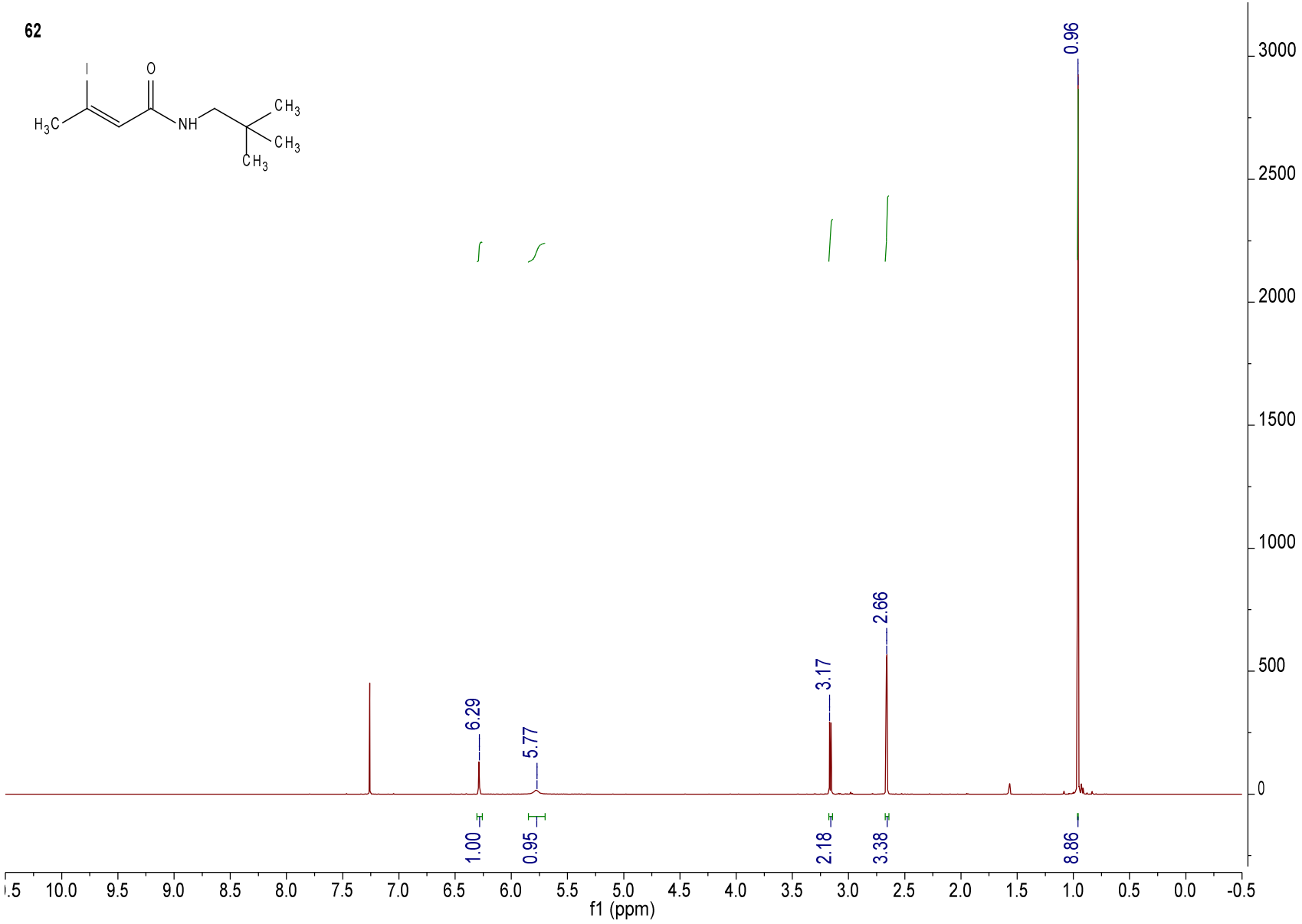

21
181.98
175.53
162.35
162.16
152.19
150.40
139.81
139.01
127.94
127.74
120.03
115.29
45.97
37.80
27.02
23.41
22.54
22.35
f1 (ppm)

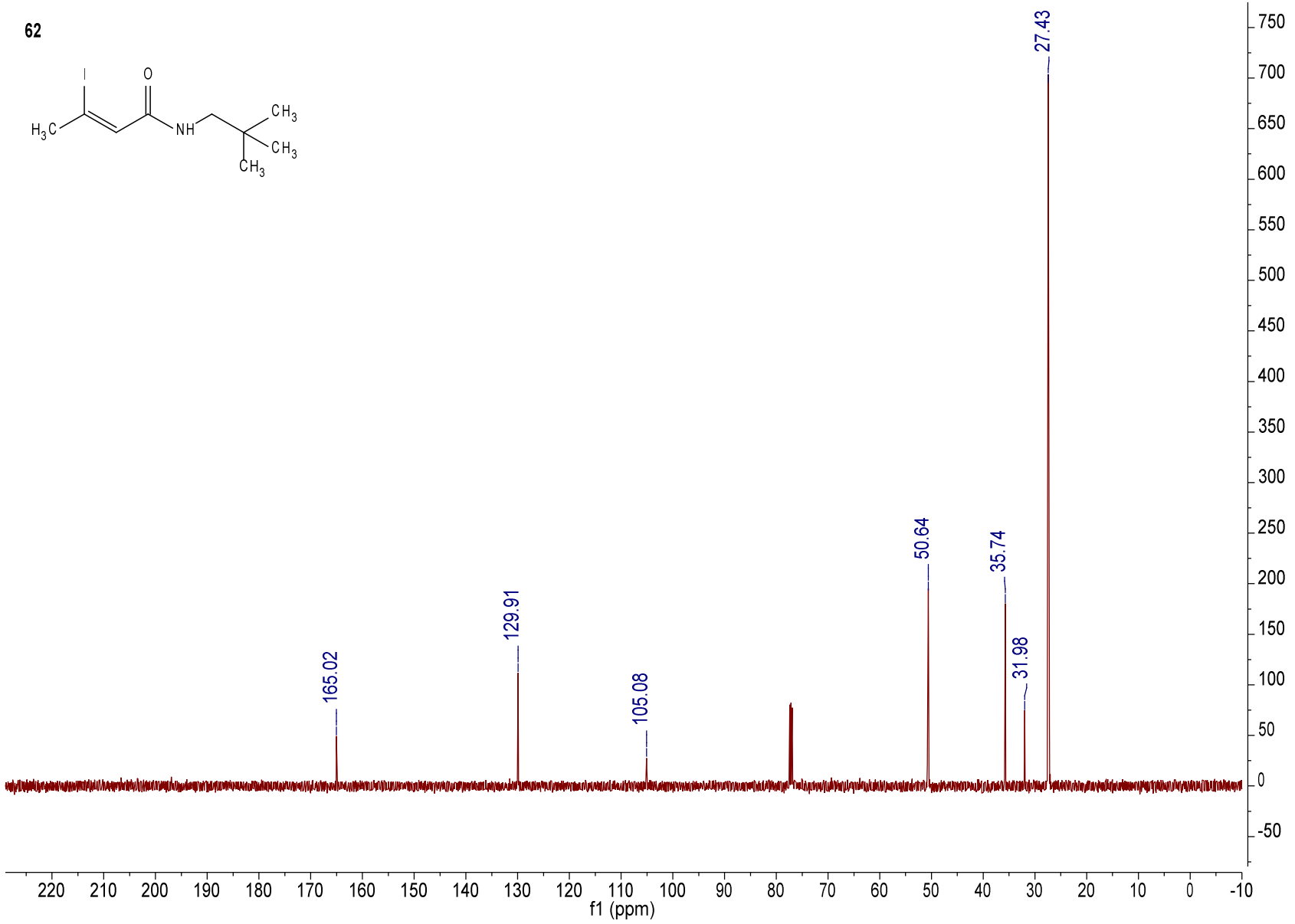

61
O
NH
CH3
CH3
CH3
H3C
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
0.89
2.00
2.90
8.81
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

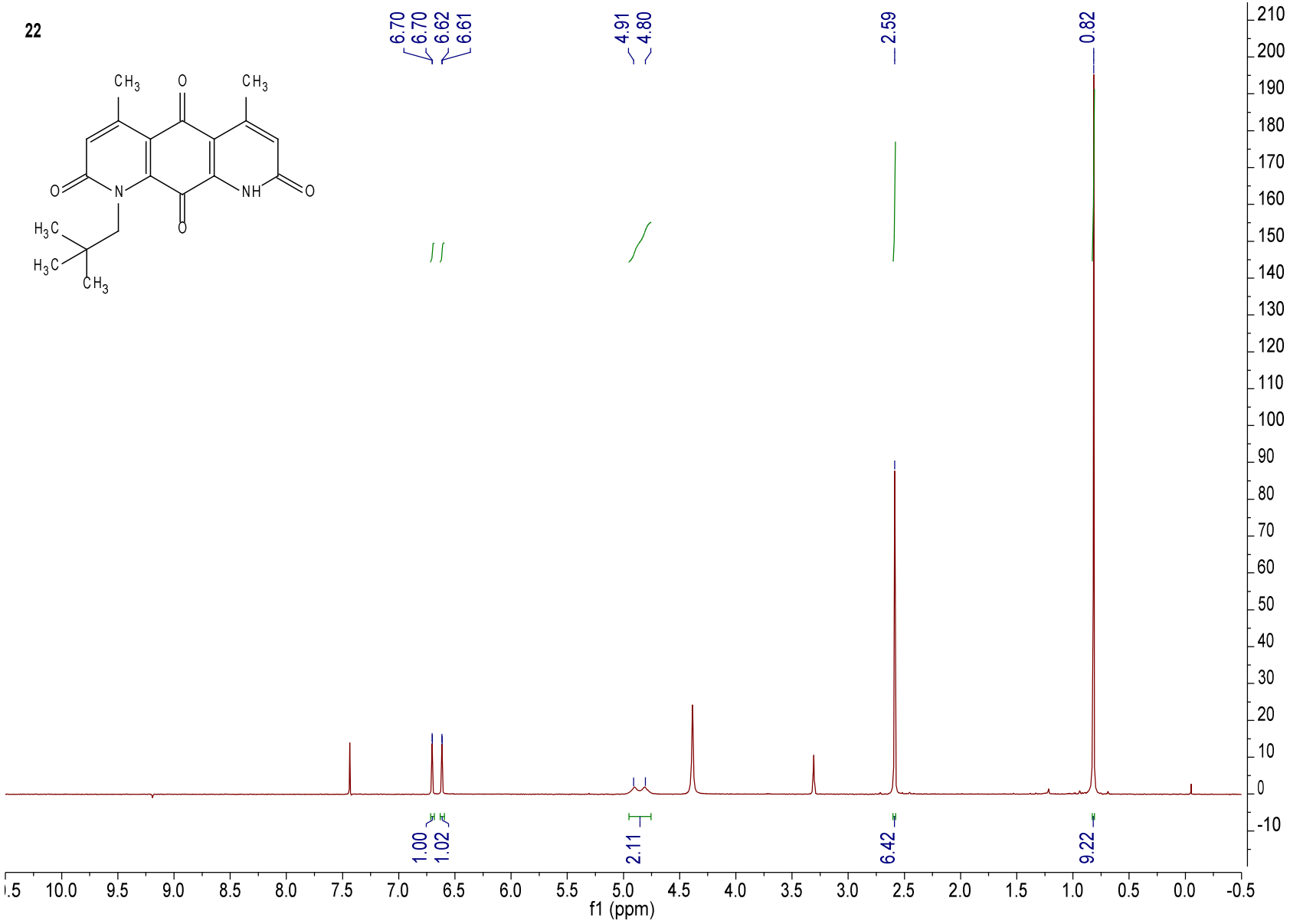

61
O
NH
CH3
CH3
CH3
H3C
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
0.89
2.00
2.90
8.81
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

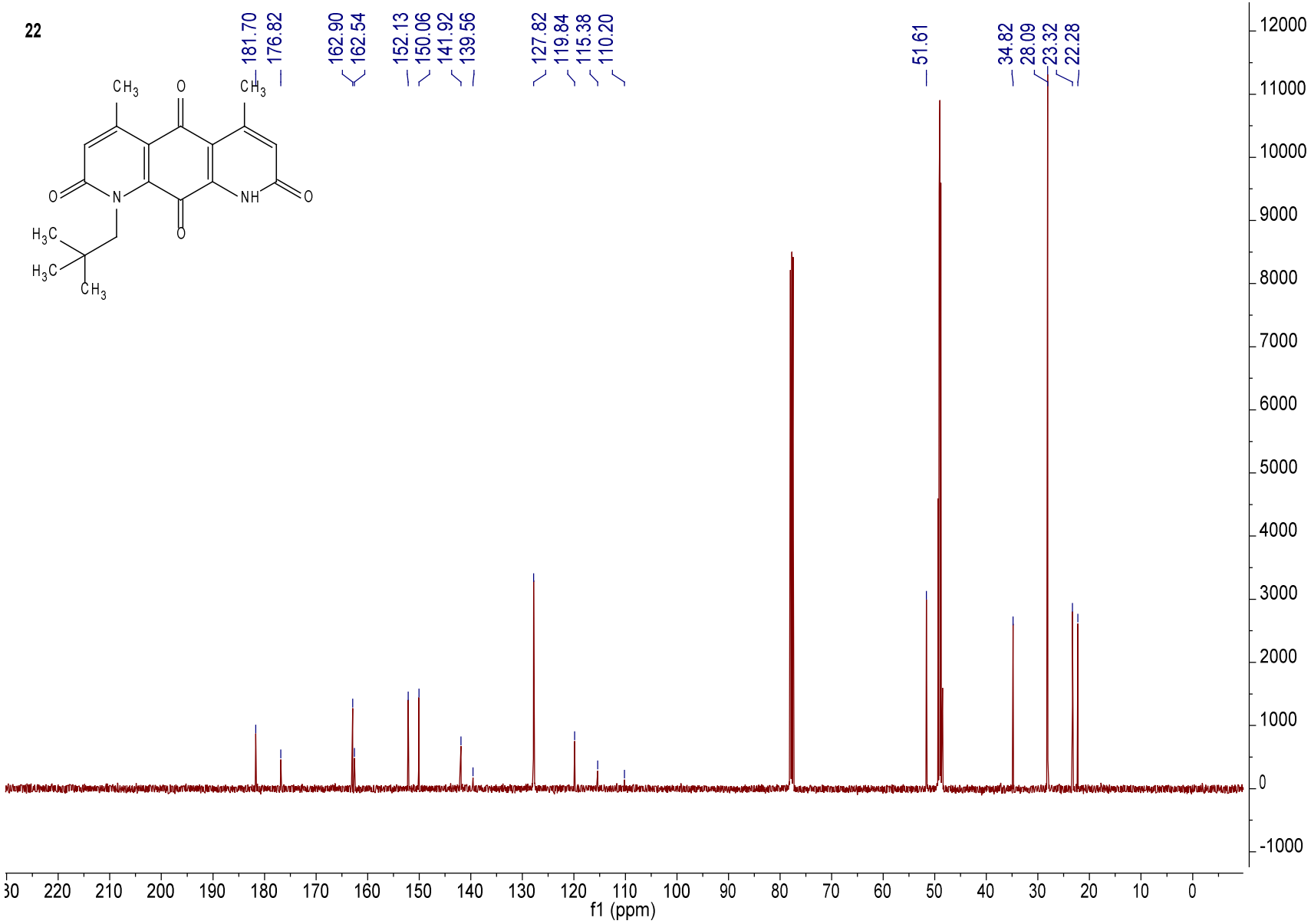

27.19
50.77
27.07
31.99
3.72
83.20
75.08
89.95
55.08
32.22
4.01
156.81
153.77
f1 (ppm)

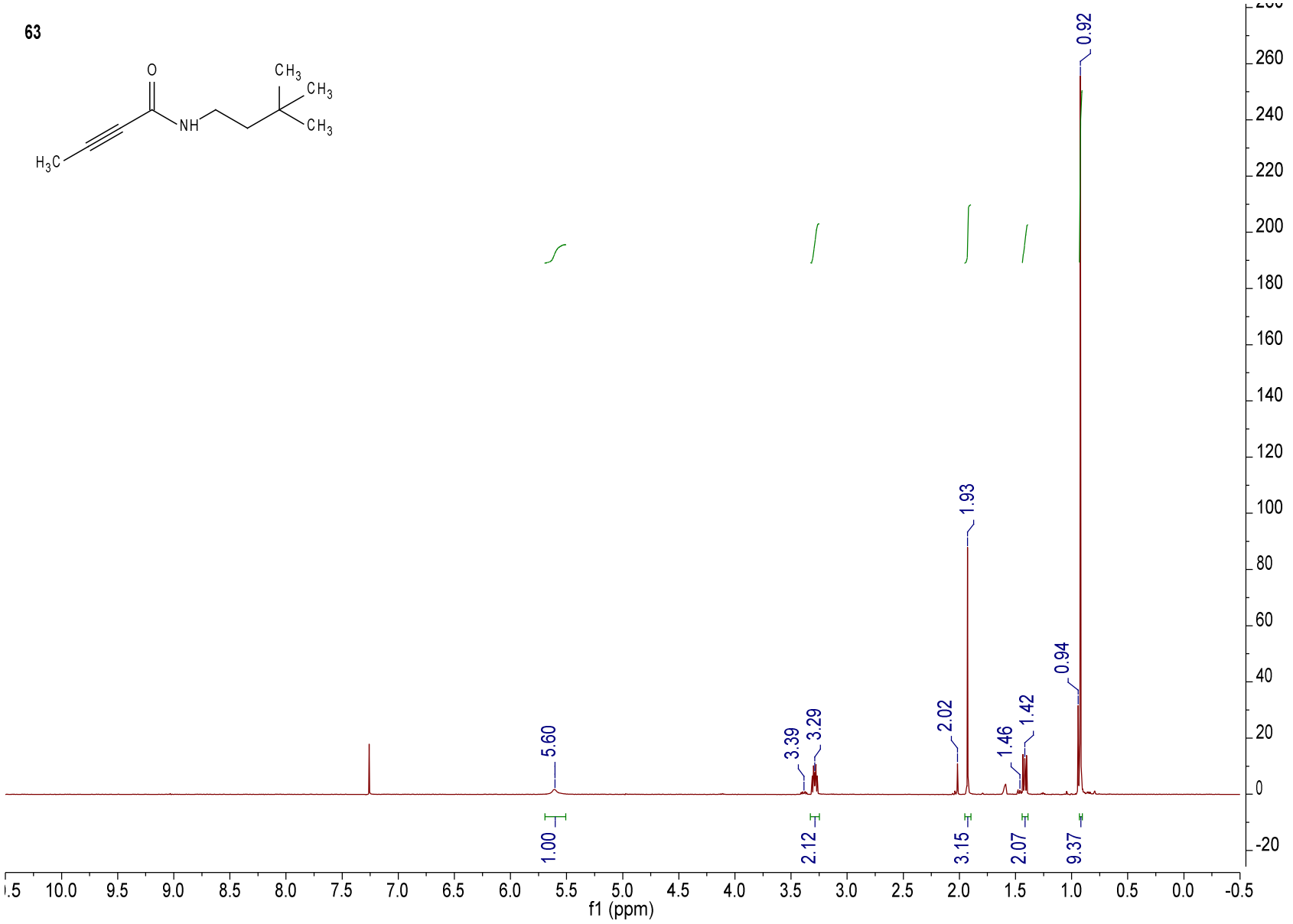

61
O
NH
CH3
CH3
CH3
H3C
27.19
50.77
27.07
31.99
3.72
83.20
75.08
55.08
156.81
153.77
89.95
32.22
4.01
f1 (ppm)


62
I
O
H_3C
NH
CH_3
CH_3
CH_3
0.96
6.29
5.77
3.17
2.66
1.00
0.95
2.18
3.38
8.86
3000
2500
2000
1500
1000
500
0
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

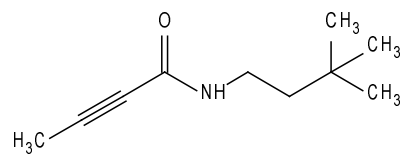

62
I
O
H3C
NH
CH3
CH3
CH3
27.43
50.64
35.74
31.98
129.91
165.02
105.08
750
700
650
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


22
6.70
6.70
6.62
6.61
4.91
4.80
2.59
0.82
1.00
1.02
2.11
6.42
9.22
f1 (ppm)

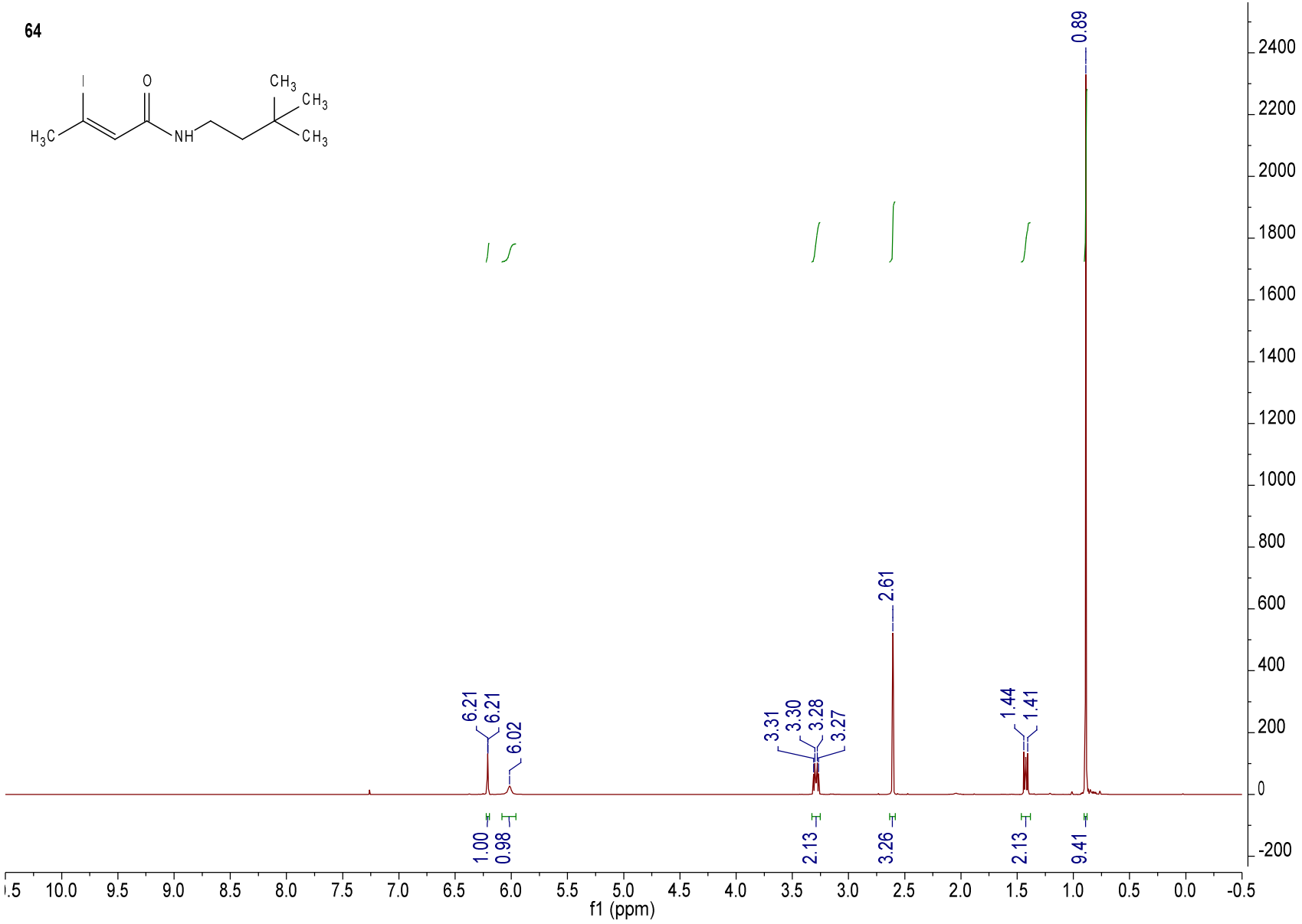

22
181.70
176.82
162.90
162.54
152.13
150.06
141.92
139.56
127.82
119.84
115.38
110.20
51.61
34.82
28.09
23.32
22.28
f1 (ppm)

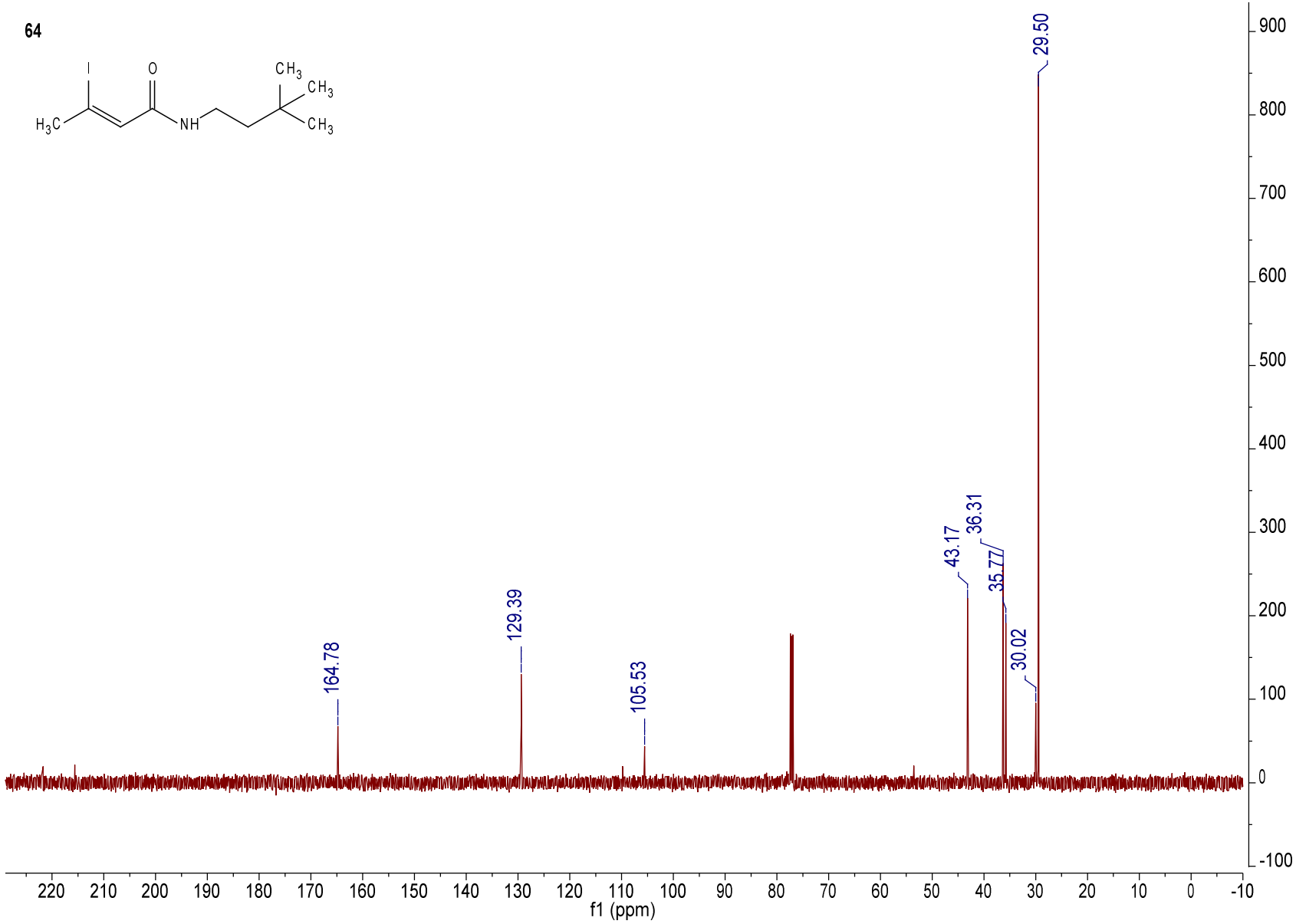

63
O
NH
CH3
CH3
CH3
H3C
0.92
1.93
0.94
2.02
1.42
1.46
3.39
3.29
5.60
1.00
2.12
3.15
2.07
9.37
f1 (ppm)

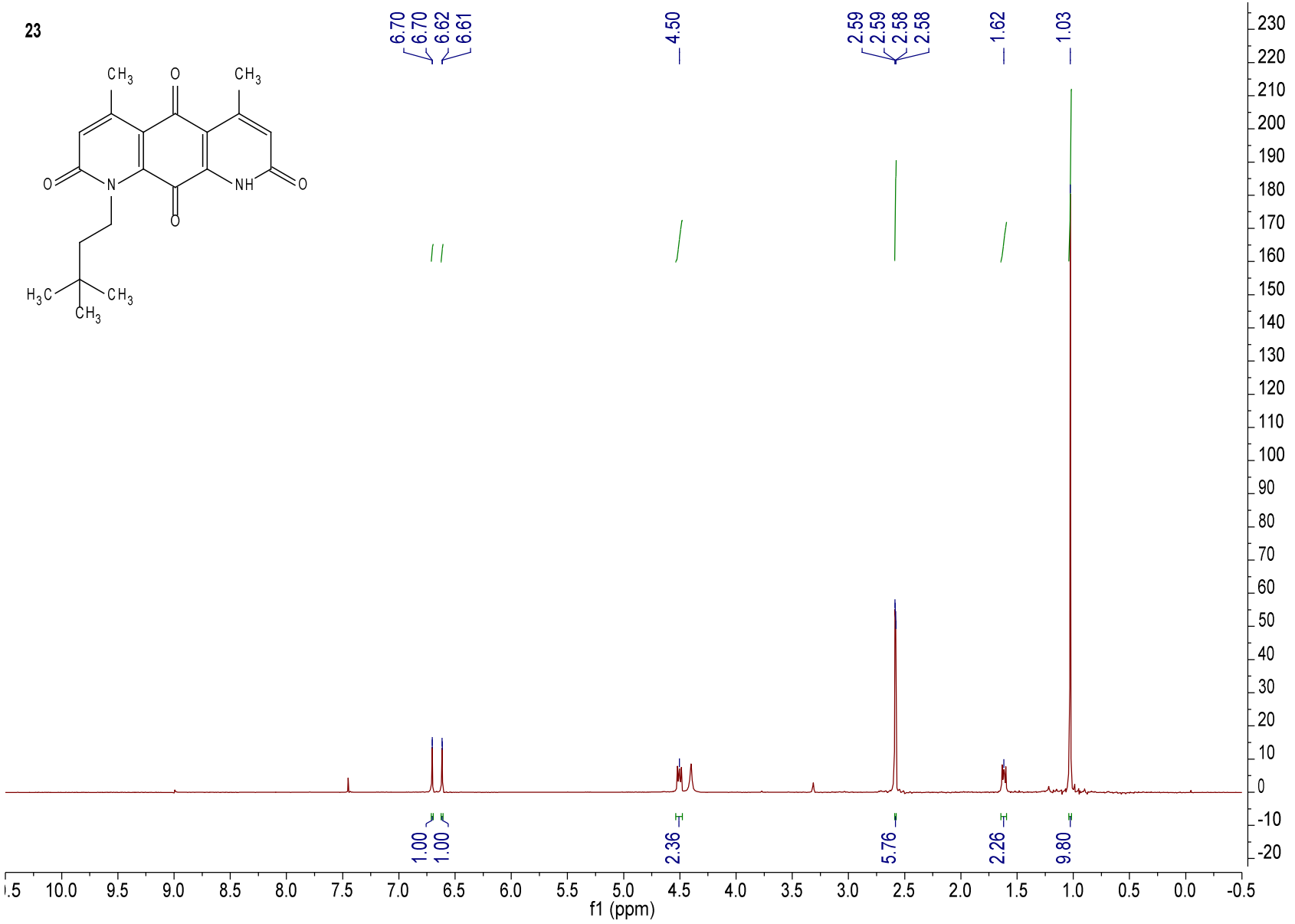
63

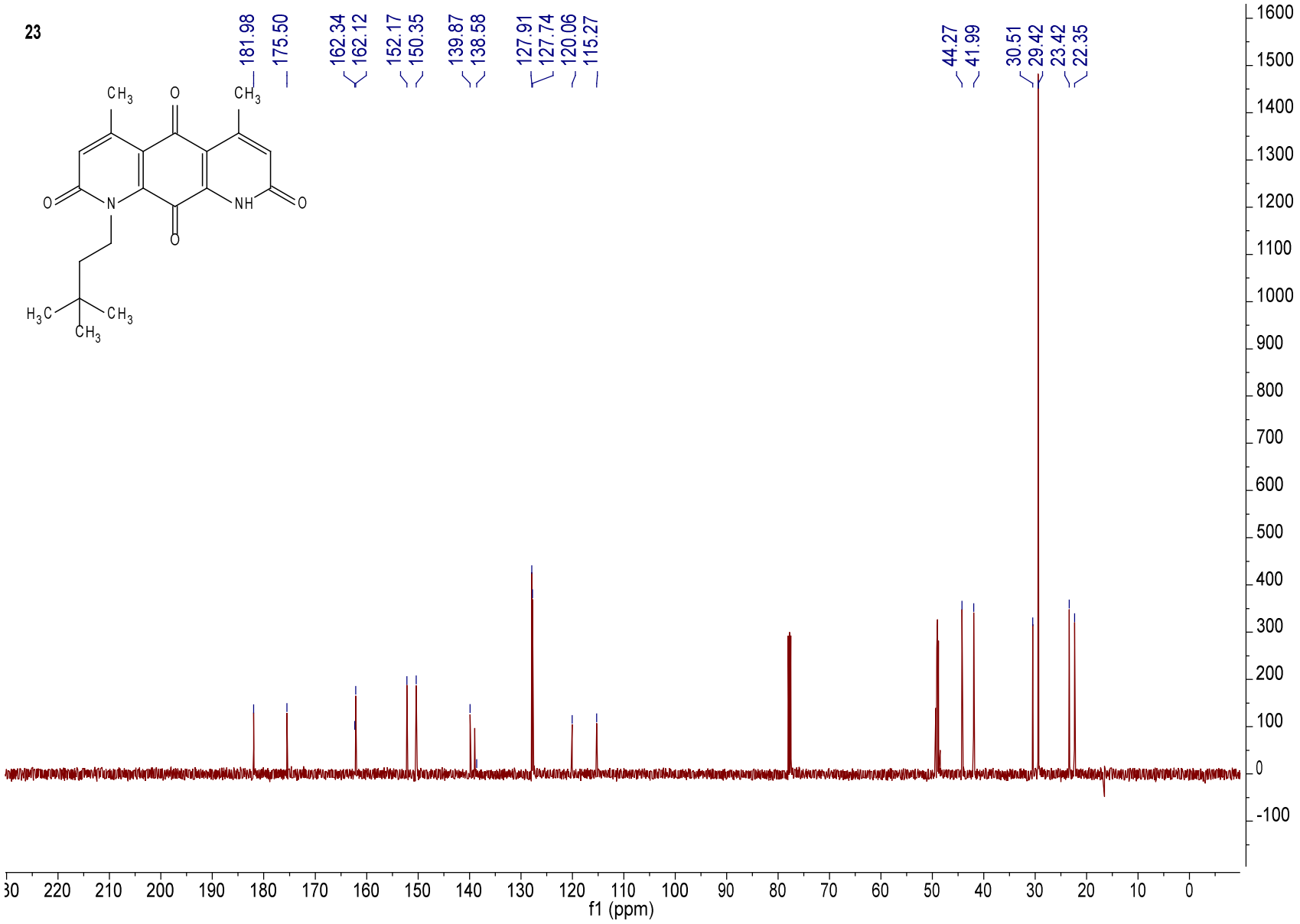

O
CH3
CH3
NH
CH3
H3C

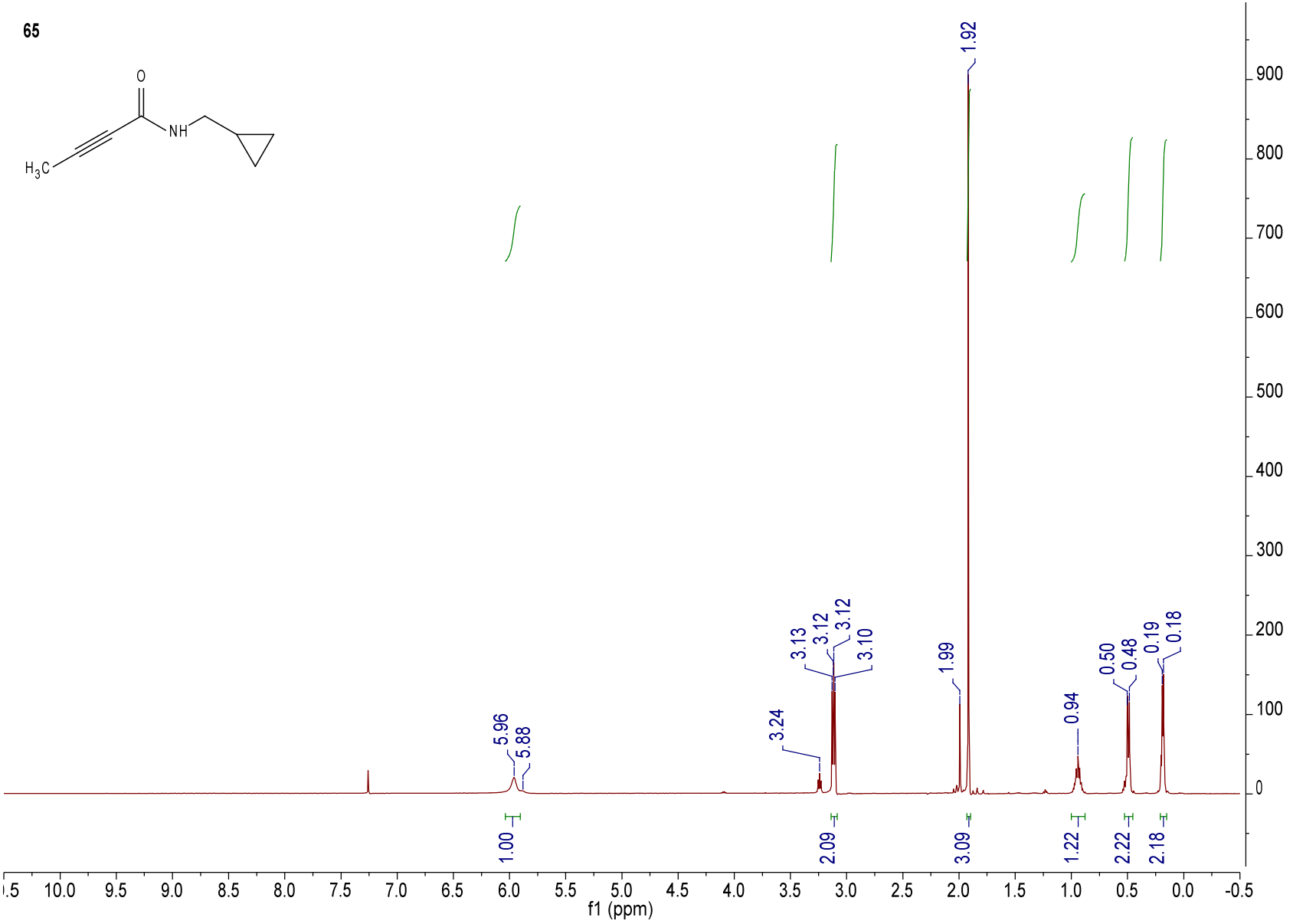
153.56
82.97
75.14
43.10
36.64
30.04
29.49
3.78
400
350
300
250
200
150
100
50
0
-50
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

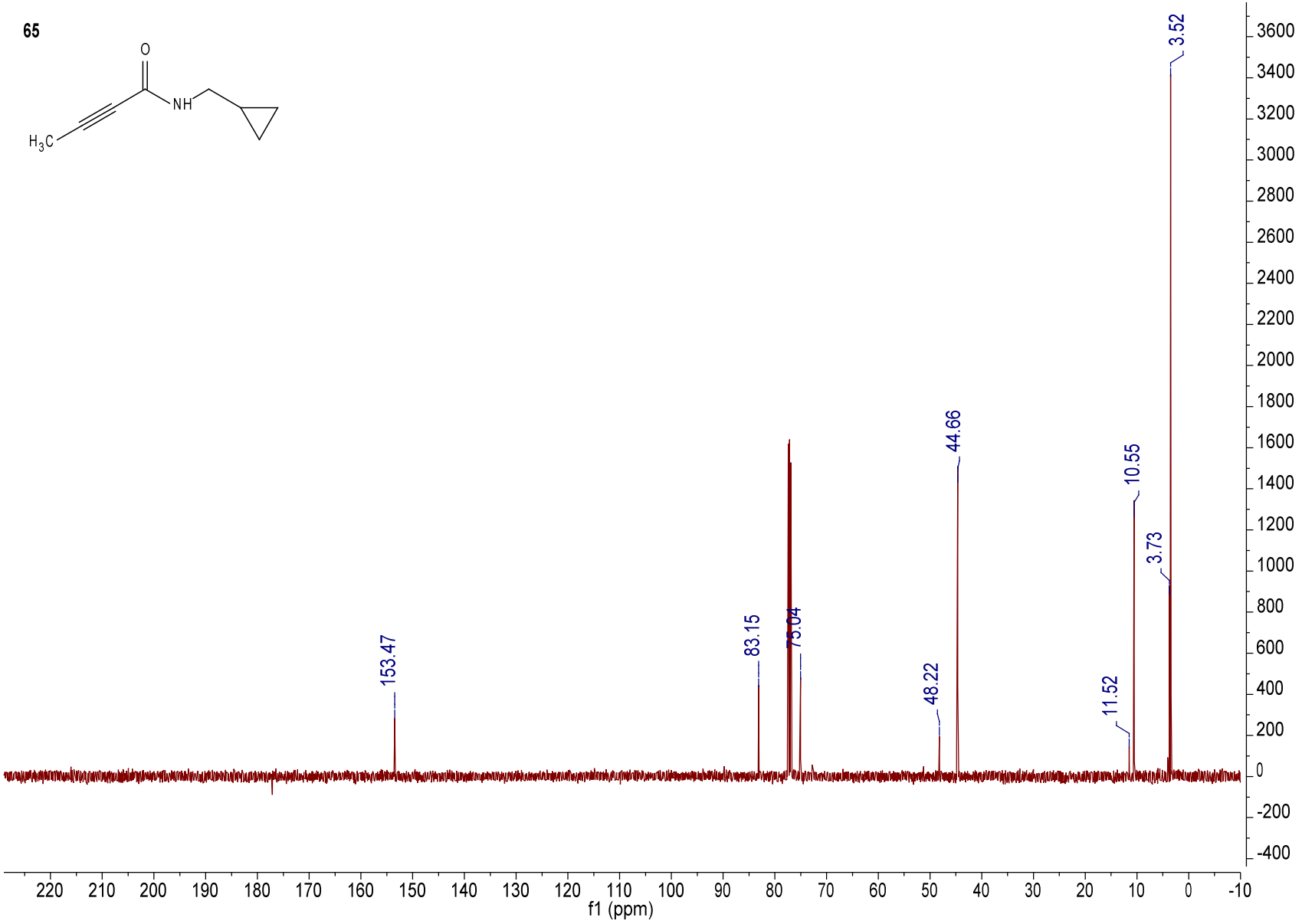

64
O
CH3
CH3
H3C
NH
CH3
6.21
6.21
6.02
3.31
3.30
3.28
3.27
2.61
1.44
1.41
0.89
1.00
0.98
2.13
3.26
2.13
9.41
f1 (ppm)

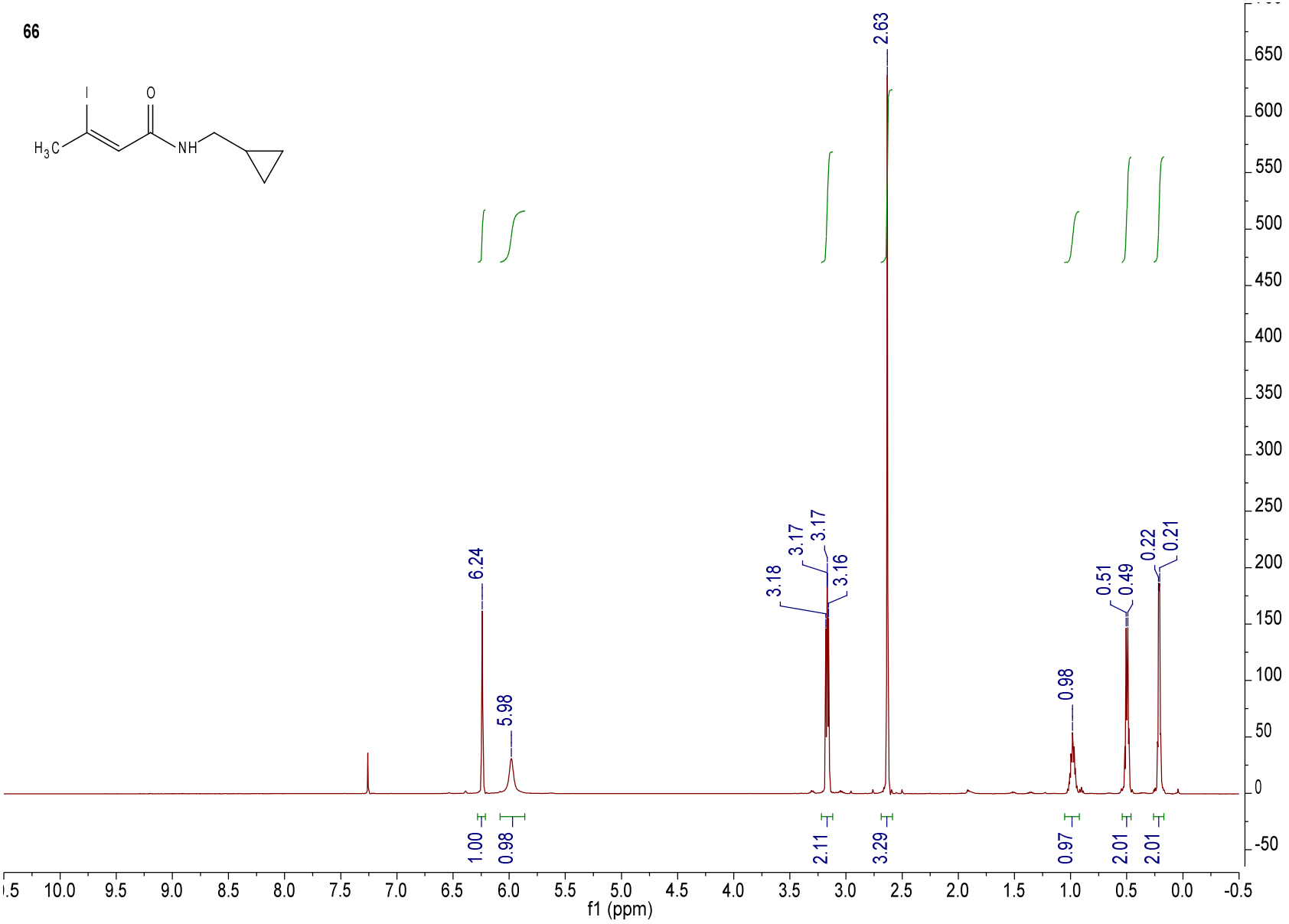

64
I
O
CH3
CH3
H3C
NH
CH3
164.78
129.39
105.53
43.17
36.31
35.77
30.02
29.50
f1 (ppm)

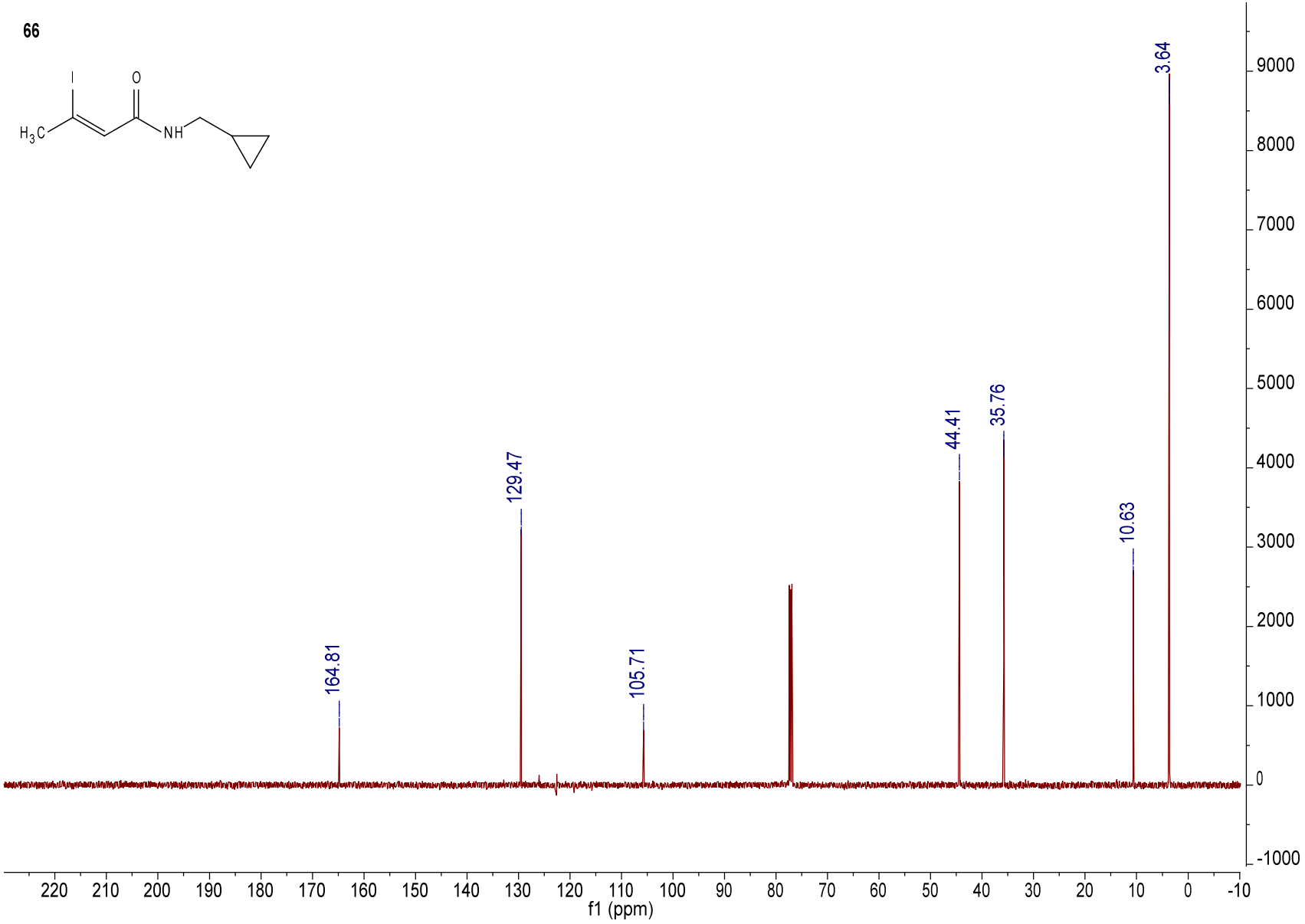

23
6.70
6.70
6.62
6.61
4.50
2.59
2.59
2.58
2.58
1.62
1.03
1.00
1.00
2.36
5.76
2.26
9.80
f1 (ppm)

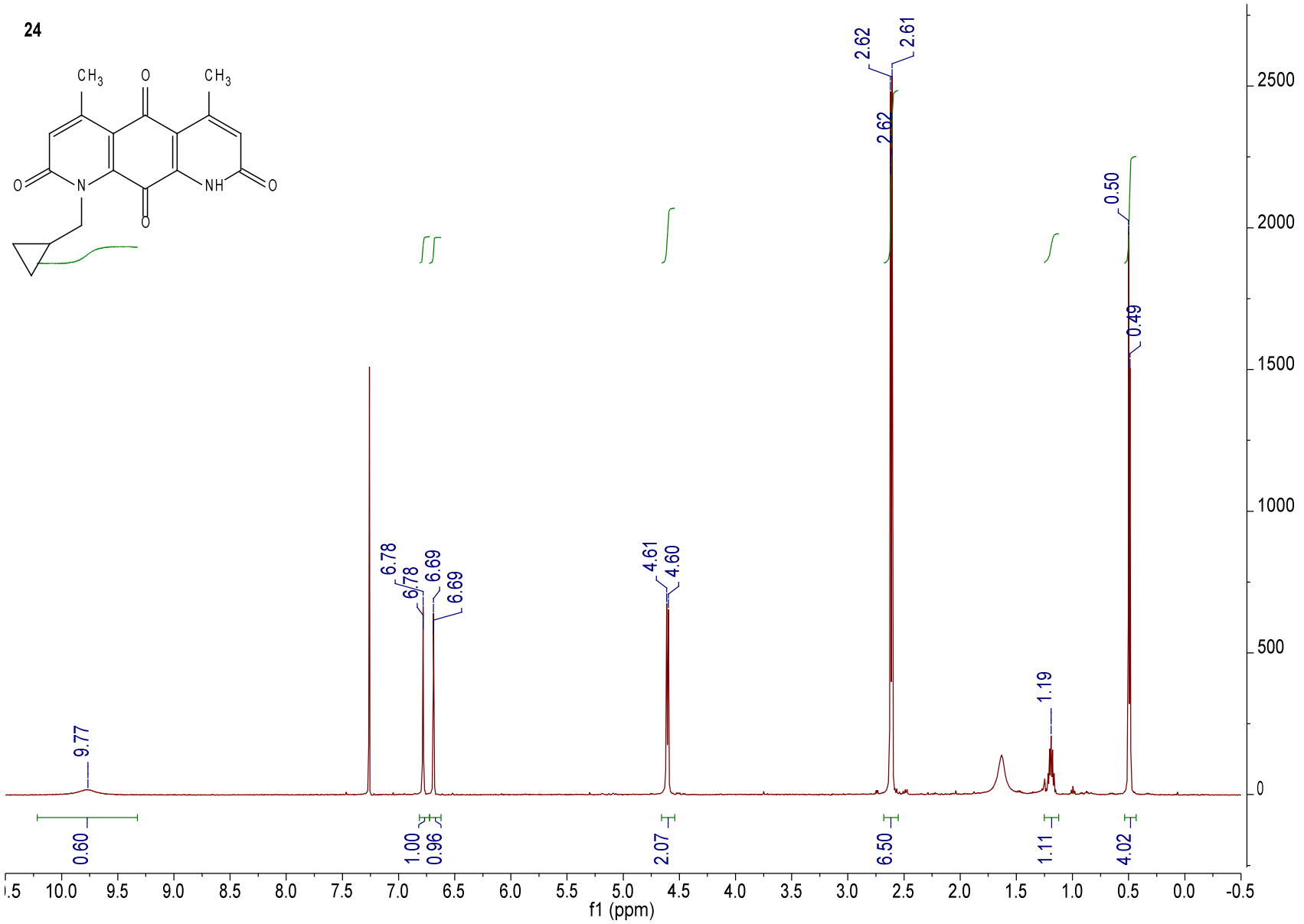

23
181.98
175.50
162.34
162.12
152.17
150.35
139.87
138.58
127.91
127.74
120.06
115.27
44.27
41.99
30.51
29.42
23.42
22.35
f1 (ppm)

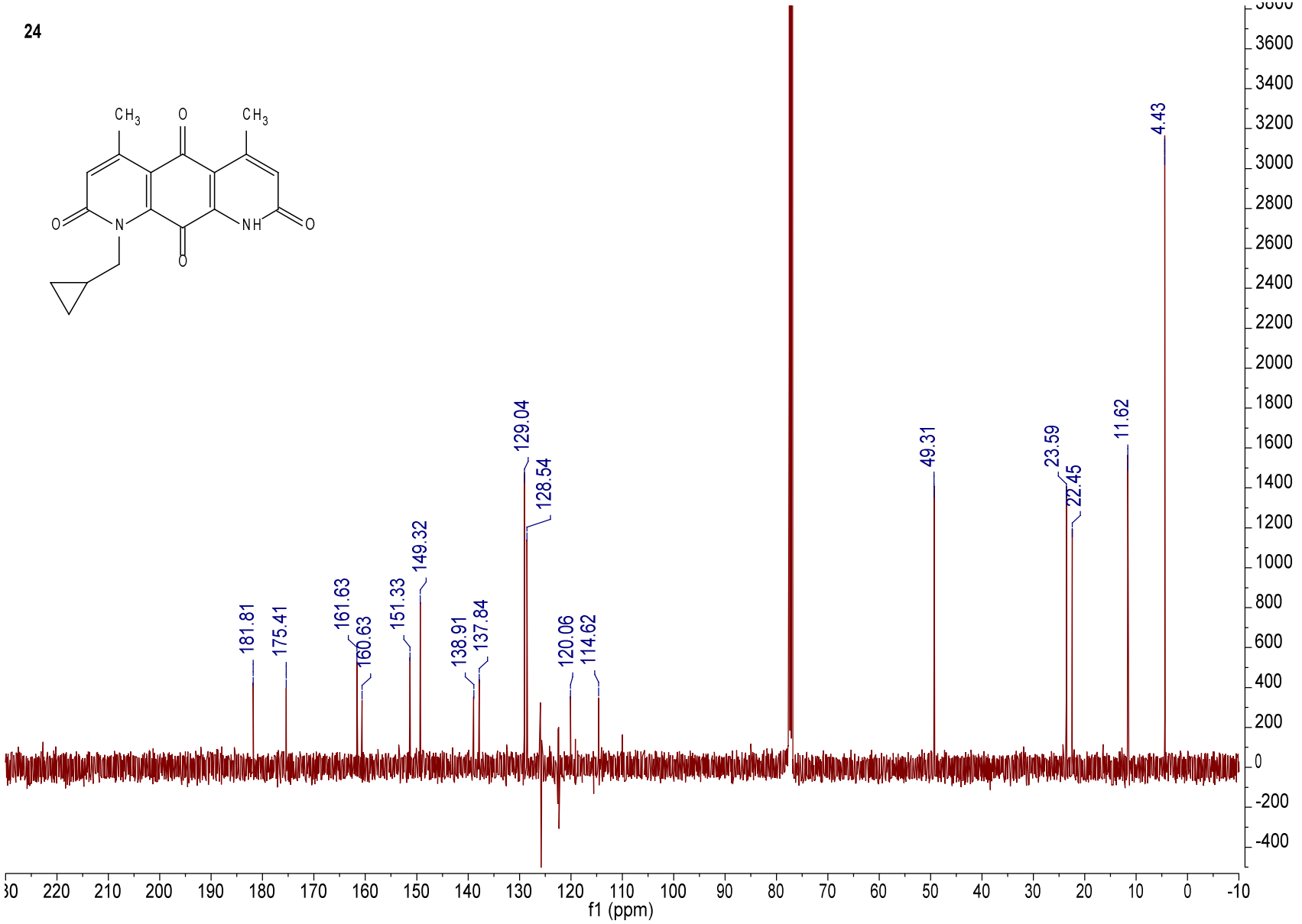

65
O
NH
H_3C
1.92
5.96
5.88
3.24
3.13
3.12
3.12
3.10
1.99
0.94
0.50
0.48
0.19
0.18
1.00
2.09
3.09
1.22
2.22
2.18
f1 (ppm)

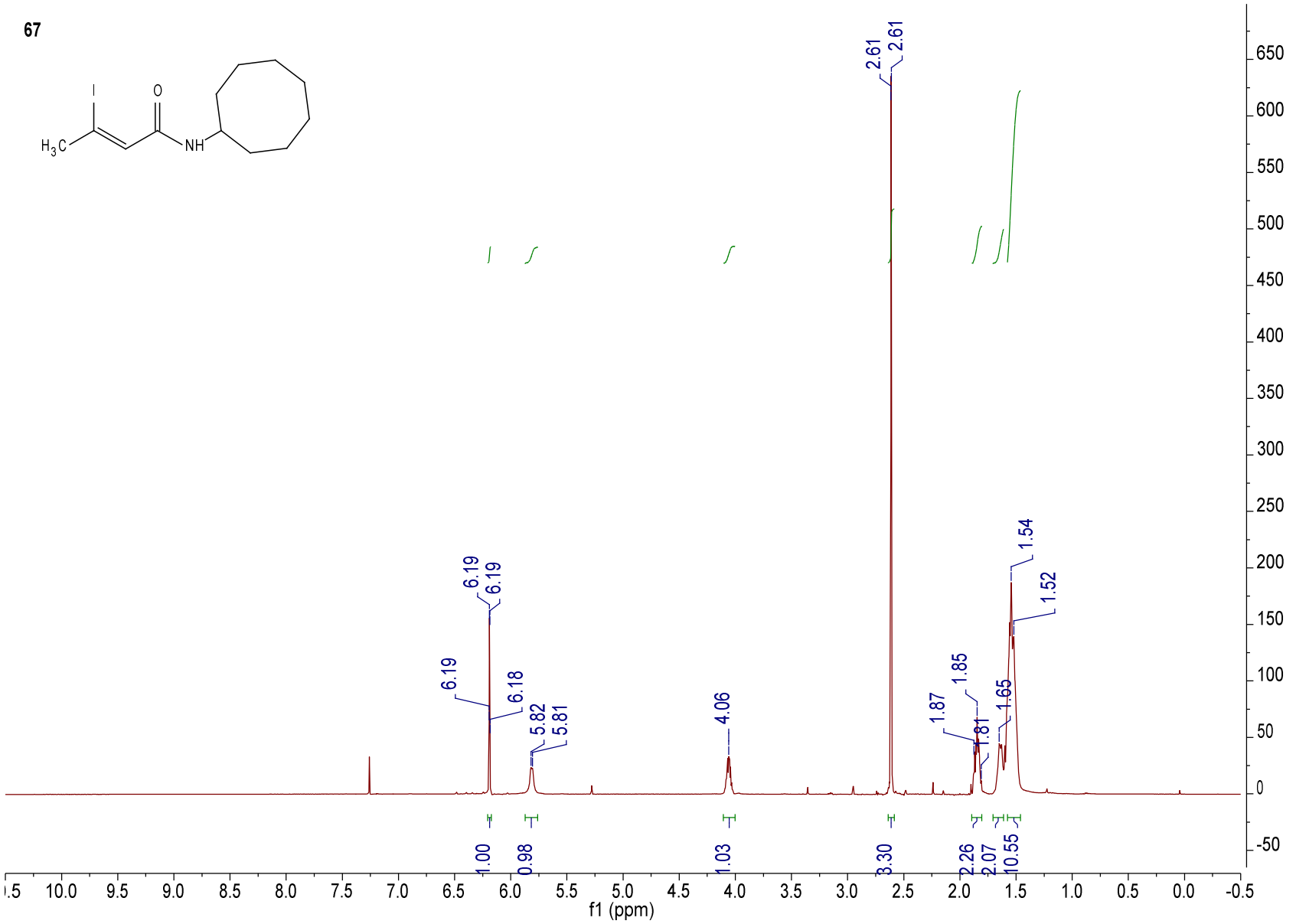

65
O
NH
H3C
153.47
83.15
75.04
48.22
44.66
11.52
10.55
3.73
3.52
f1 (ppm)

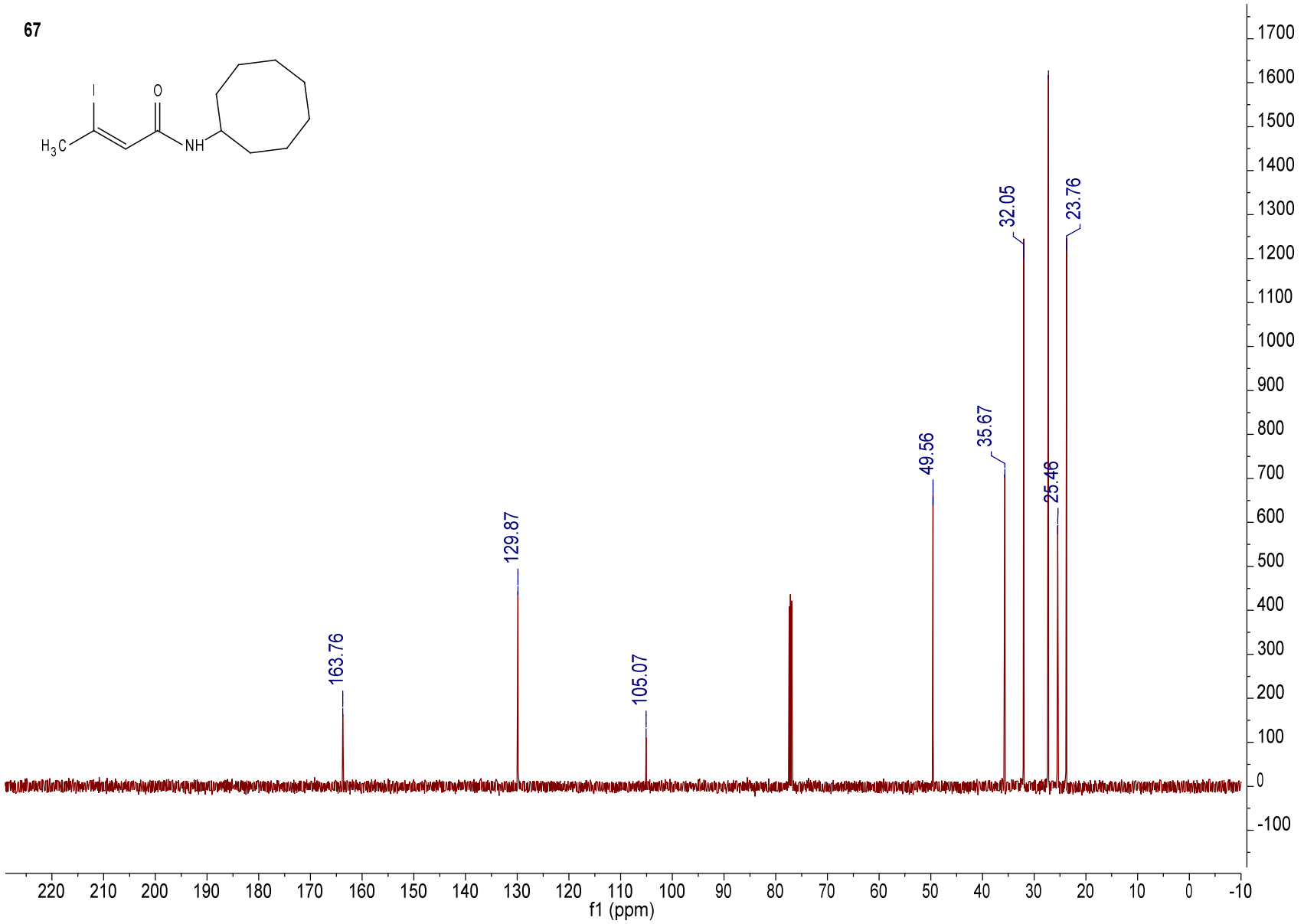

66
I
O
H_3C
NH
6.24
5.98
3.18
3.17
3.17
3.16
2.63
0.98
0.51
0.49
0.22
0.21
1.00
0.98
2.11
3.29
0.97
2.01
2.01
f1 (ppm)

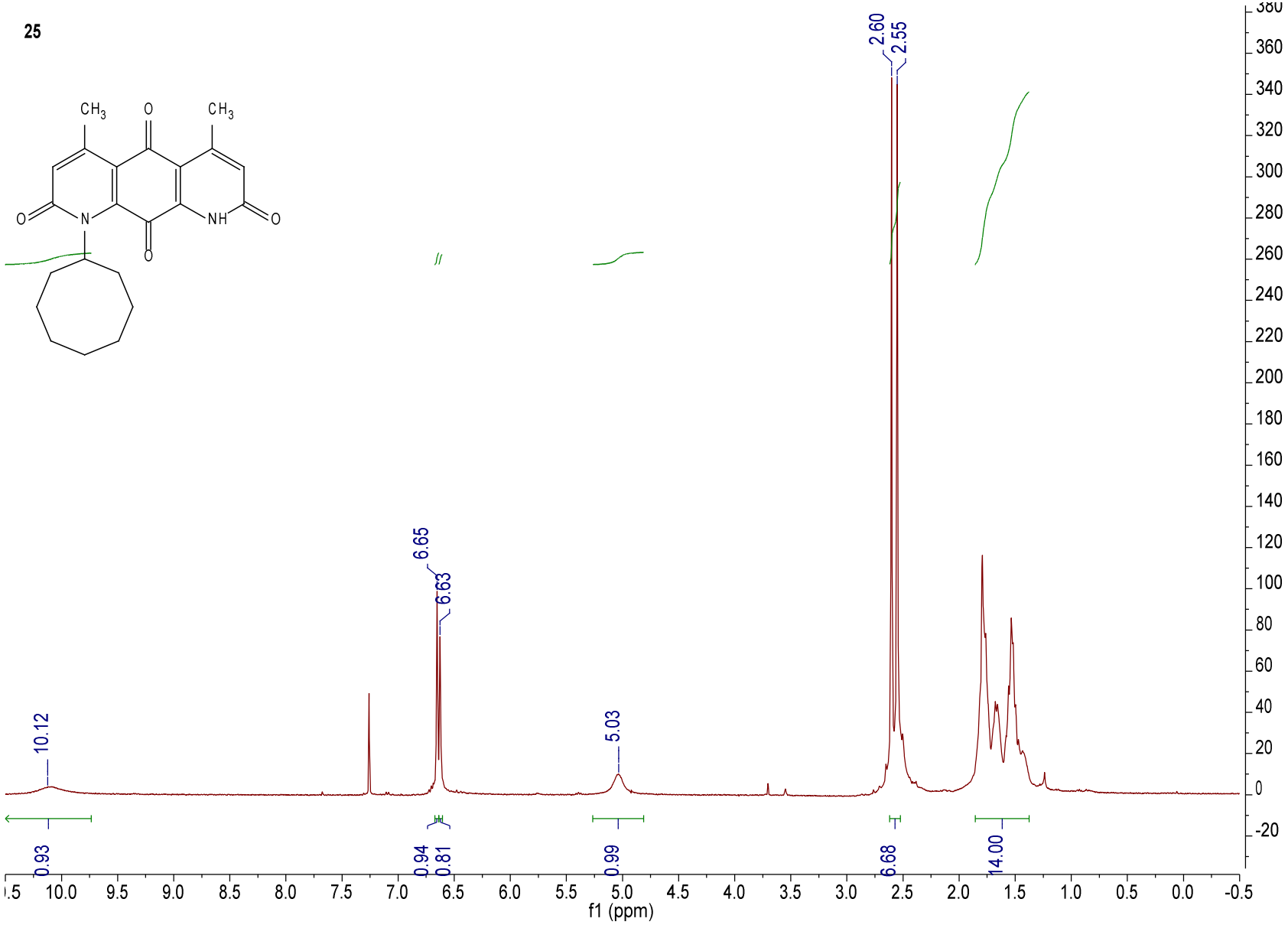

66
I
O
H3C
NH
164.81
129.47
105.71
44.41
35.76
10.63
3.64
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

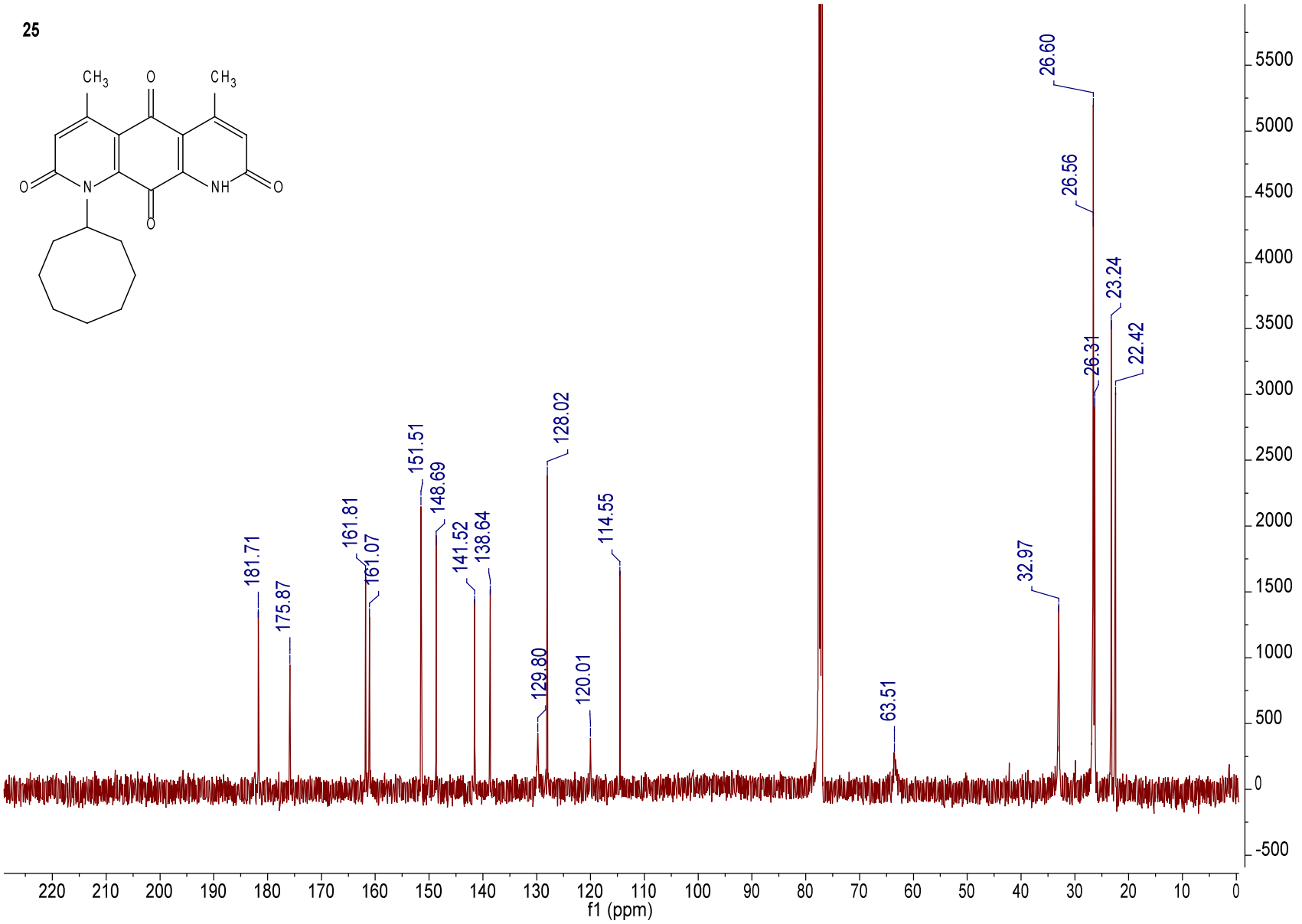

24
CH3
O
CH3
O
N
NH
O
O
2.62
2.61
2.62
0.50
0.49
6.78
6.78
6.69
6.69
4.61
4.60
1.19
9.77
2500
2000
1500
1000
500
0
0.60
1.00
0.96
2.07
6.50
1.11
4.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

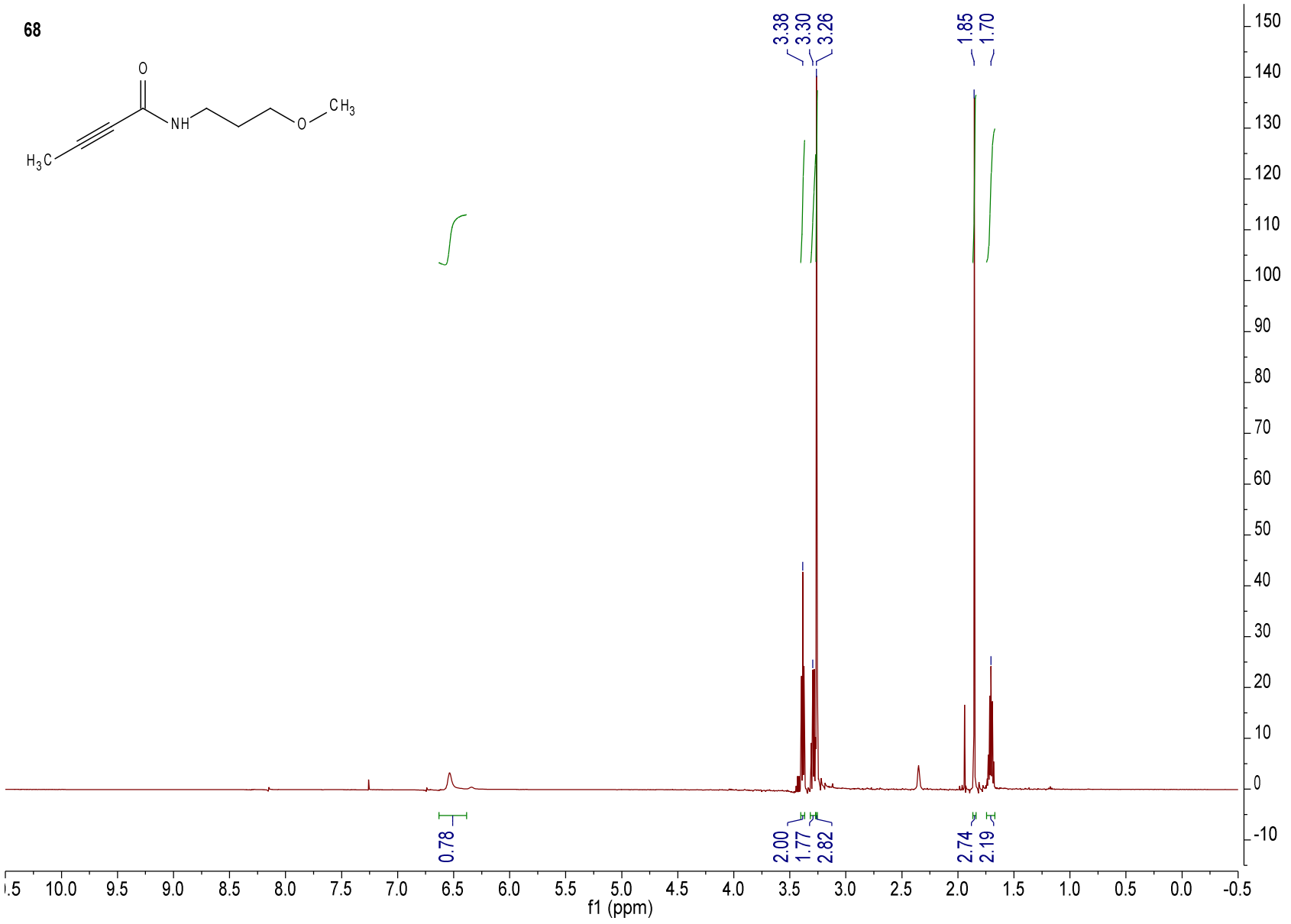

24
CH3
O
CH3
O
N
NH
O
O
181.81
175.41
161.63
160.63
151.33
149.32
138.91
137.84
129.04
128.54
120.06
114.62
49.31
23.59
22.45
11.62
4.43
f1 (ppm)

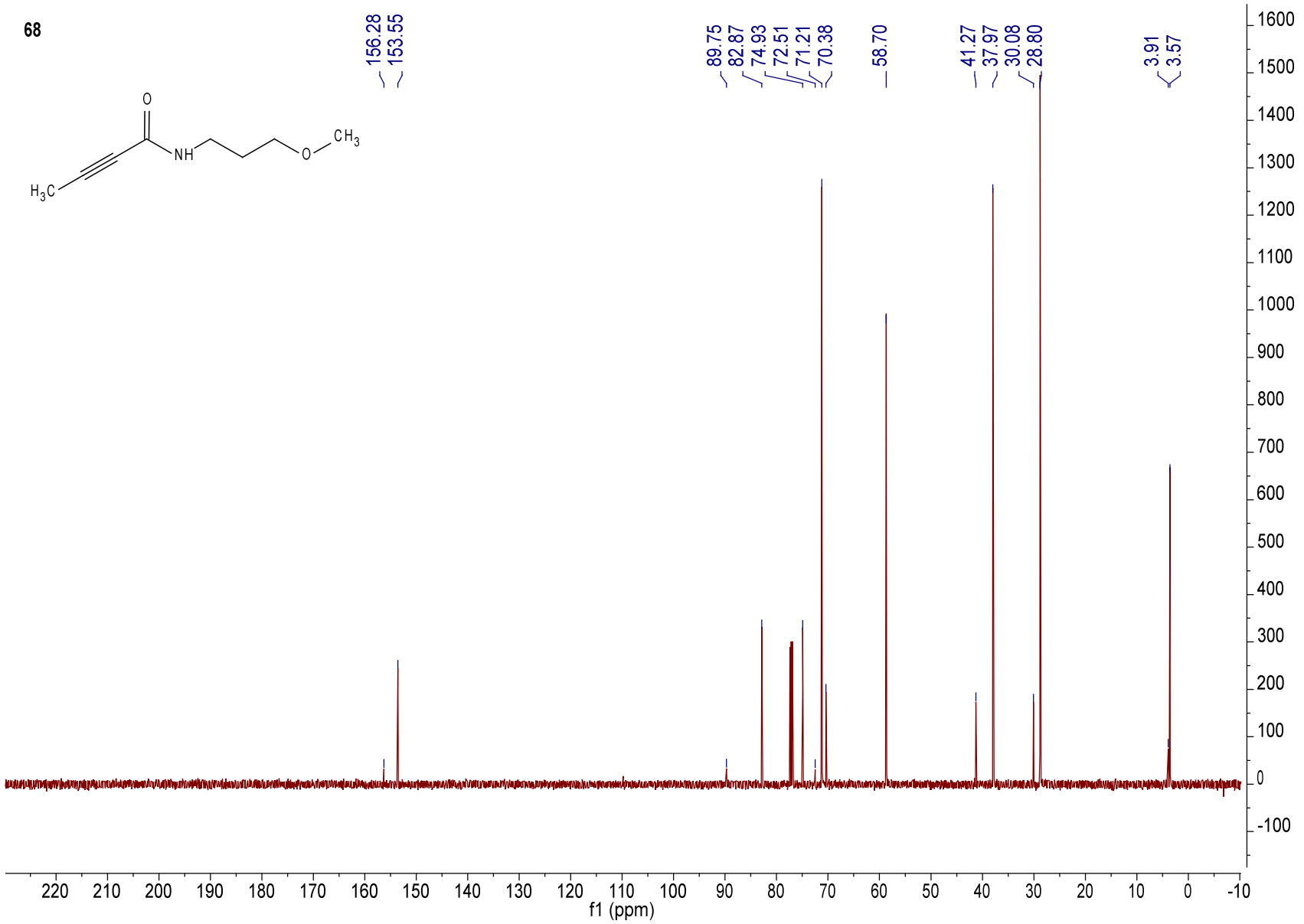

67
I
O
H_3C
NH
2.61
2.61
6.19
6.19
6.19
6.18
5.82
5.81
4.06
1.87
1.85
1.81
1.65
1.54
1.52
1.00
0.98
1.03
3.30
2.26
2.07
10.55
f1 (ppm)

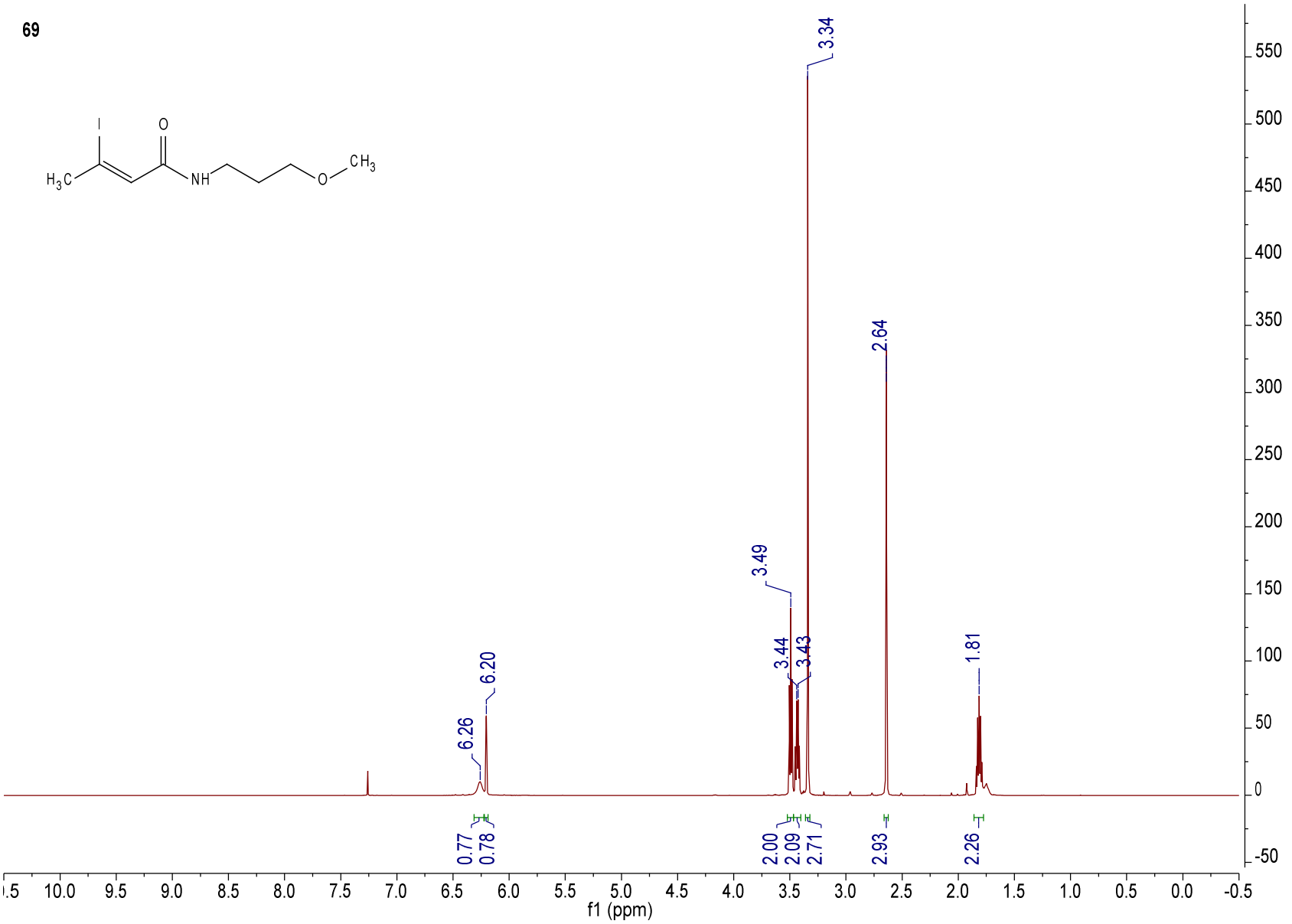

67
I
O
H_3C
NH
163.76
129.87
105.07
49.56
35.67
32.05
25.46
23.76
f1 (ppm)

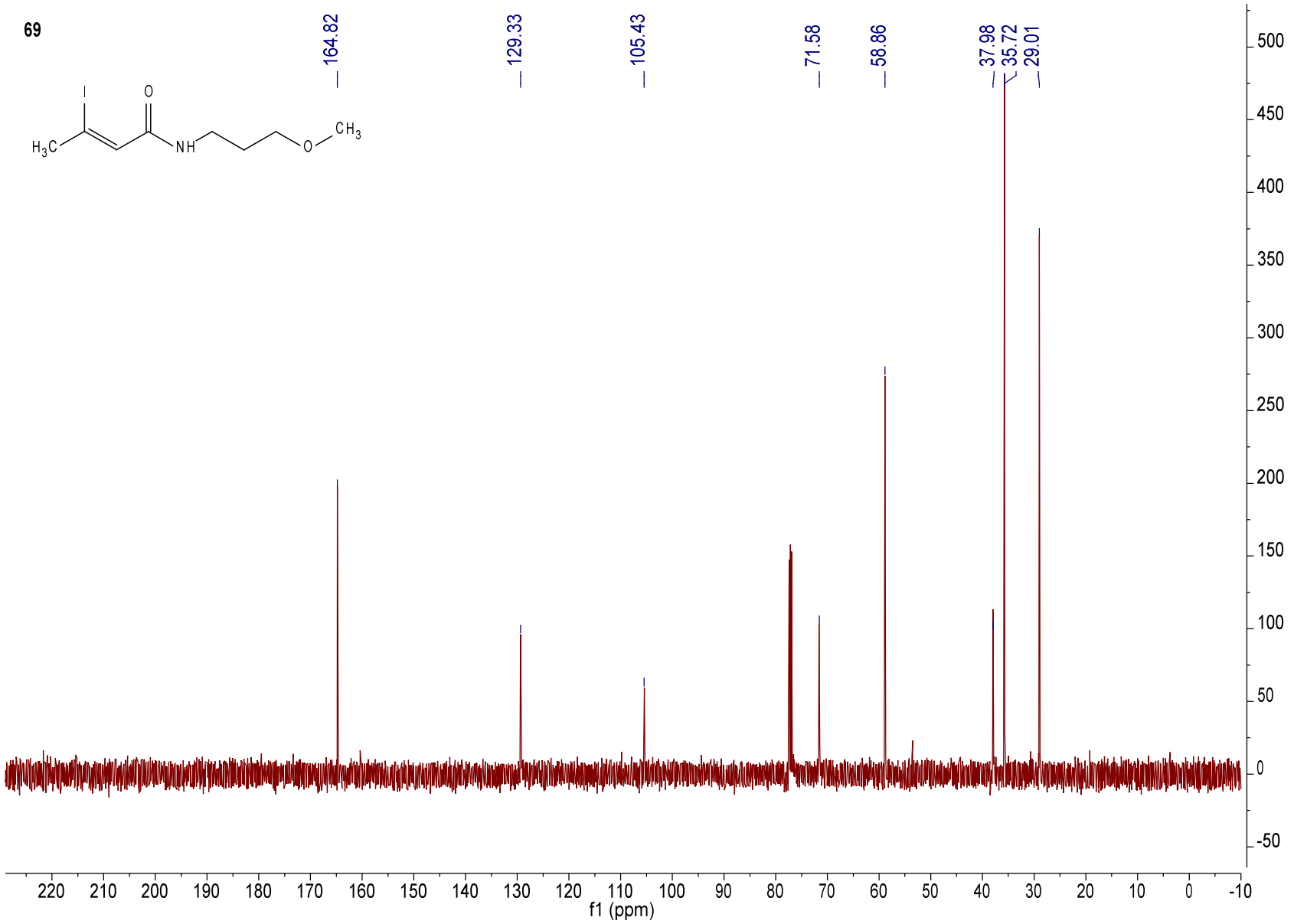

25
CH3
O
CH3
O
N
NH
O
O
2.60
2.55
6.65
6.63
10.12
5.03
0.93
0.94
0.81
0.99
6.68
14.00
f1 (ppm)

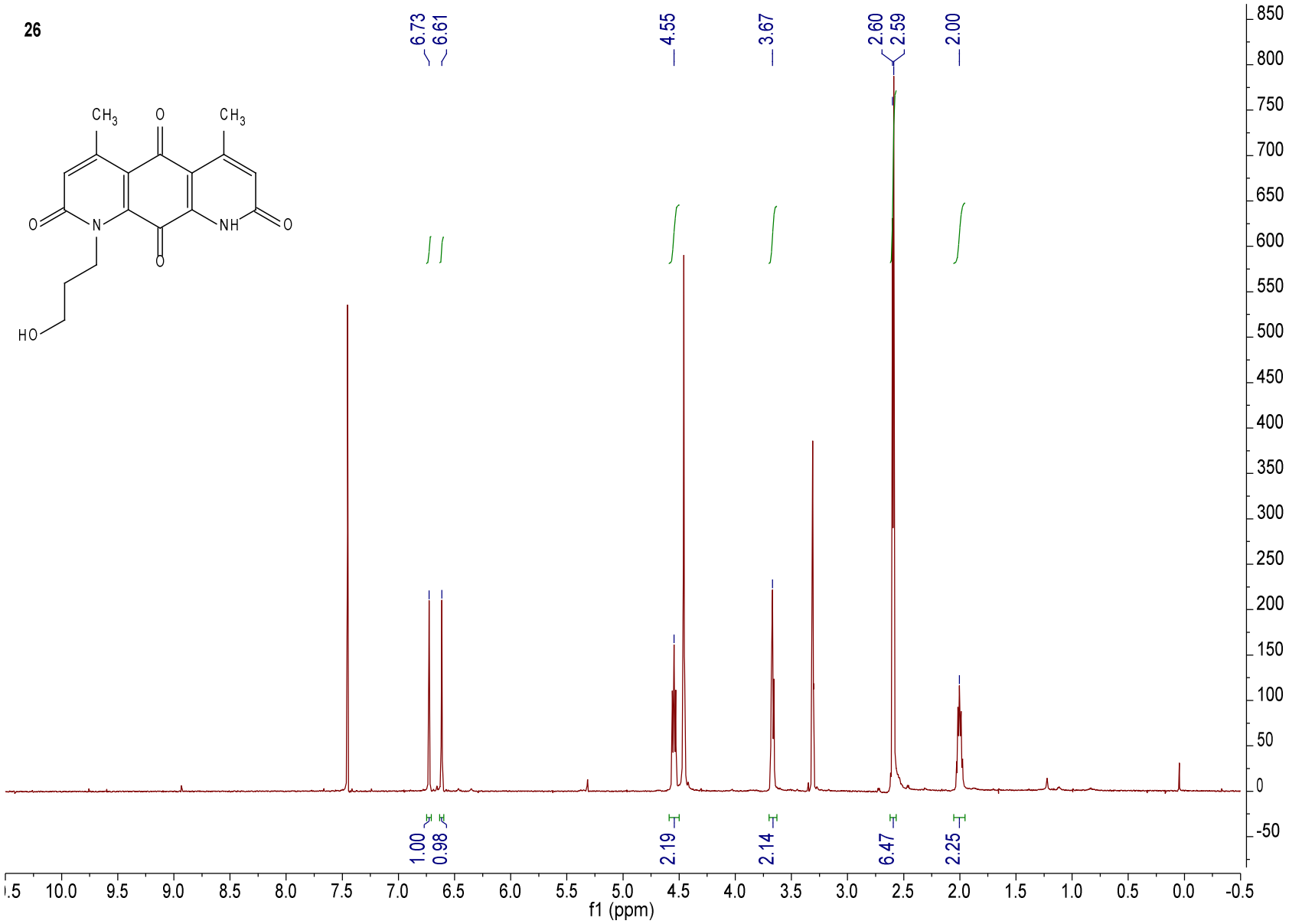

25
CH3
O
CH3
O
N
NH
O
O
181.71
175.87
161.81
161.07
151.51
148.69
141.52
138.64
129.80
128.02
120.01
114.55
63.51
32.97
26.60
26.56
26.31
23.24
22.42
f1 (ppm)

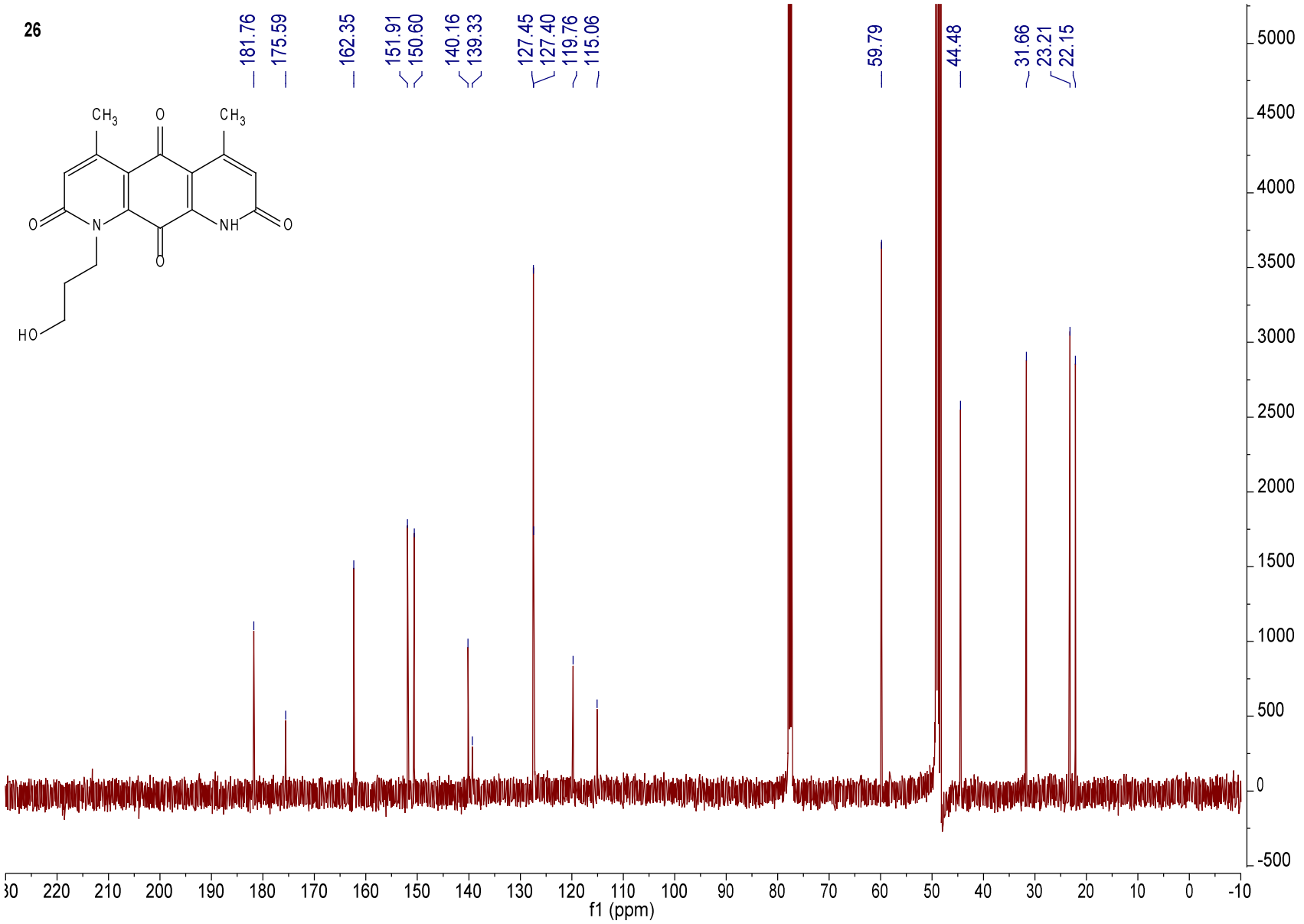

68
O
NH
O
CH3
H3C
3.38
3.30
3.26
1.85
1.70
0.78
2.00
1.77
2.82
2.74
2.19
f1 (ppm)


68
156.28
153.55
89.75
82.87
74.93
72.51
71.21
70.38
58.70
41.27
37.97
30.08
28.80
3.91
3.57
O
NH
O
CH3
H3C
f1 (ppm)


69
I
O
H3C
NH
O
CH3
3.34
2.64
3.49
3.44
3.43
6.20
6.26
1.81
0.77
0.78
2.00
2.09
2.71
2.93
2.26
f1 (ppm)


69
164.82
129.33
105.43
71.58
58.86
37.98
35.72
29.01
f1 (ppm)


26
6.73
6.61
4.55
3.67
2.60
2.59
2.00
CH3
O
CH3
O
N
NH
O
O
HO
1.00
0.98
2.19
2.14
6.47
2.25
f1 (ppm)


26
181.76
175.59
162.35
151.91
150.60
140.16
139.33
127.45
127.40
119.76
115.06
59.79
44.48
31.66
23.21
22.15
CH3
O
CH3
O
N
NH
O
O
HO
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

References

1. Bair, J. S.; Palchaudhuri, R.; Hergenrother, P. J., Chemistry and biology of deoxynyboquinone, a potent inducer of cancer cell death. *J Am Chem Soc* **2010,** *132* (15), 5469-78.