Supplemental material for:

Pt-Catalyzed Cyclization/1,2-Migration for the Synthesis of Indolizines, Pyrrolones, and Indolizinones

Cameron R. Smith, Eric M. Bunnelle, Allison Rhodes, and Richmond Sarpong*

Department of Chemistry, University of California, Berkeley, California 94720

Email: rsarpong@berkeley.edu

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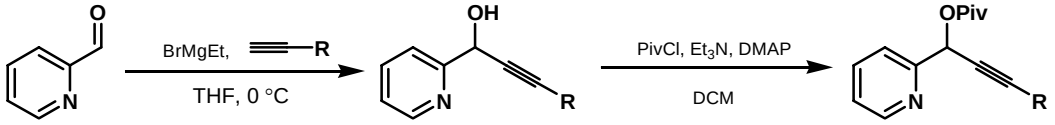
Materials and Methods

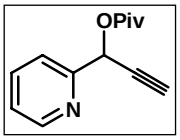
Unless otherwise stated, reactions were performed in flame-dried glassware fitted with rubber septa under a nitrogen atmosphere. Liquid reagents and solvents were transferred via syringe under nitrogen. THF and diethyl ether were distilled over sodium/benzophenone ketyl; dichloromethane, toluene, and benzene, were distilled over calcium hydride. All other solvents were used as received unless otherwise noted. Reagents were purchased from Aldrich, Acros, or Lancaster, and used without purification unless otherwise noted. Platinum catalysts and phosphine ligands were purchased from Strem or Johnson Matthey. Melting points were obtained with a Büchi melting point apparatus. Reaction temperatures above 23 ˚C were controlled by an OptiChem® temperature modulator. Reactions were monitored by thin layer chromatography, performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV irradiation and anisaldehyde stain. Fisher silica gel 240-400 mesh (particle size 0.032-0.063 mm) was used for flash chromatography. ^{1}H and ^{13}C NMR were recorded on Bruker 400 or 500 MHz spectrometers with ^{13}C operating frequencies of 100 and 125 MHz, respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvent signal (δ = 7.26 for ^{1}H NMR and δ = 77.0 for ^{13}C NMR, for $CDCl_3$; and δ = 7.15 ^{1}H NMR and δ = 128.6 for ^{13}C NMR, for C_6D_6). Data for ^{1}H NMR are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogens). Multiplicity is abbreviated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). IR spectra were recorded on a Nicolet MAGNA-IR 850 spectrometer and are reported in frequency of absorption (cm^{-1}). Mass spectral data were obtained from the Mass Spectral Facility at the University of California, Berkeley, with a VG Prospec Micromass spectrometer. Enantiomeric excess was determined by HPLC using a Shimatzu 10A VP series chiral HPLC. Optical rotary data was obtained using a Perkin-Elmer 241 Polarimeter with a 589 nm sodium lamp.

Synthesis of Propargylic Pivalate Substrates



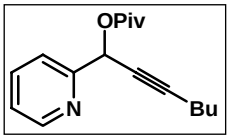
General Procedure: To a stirring solution of the appropriate terminal alkyne (1.2 equiv) in THF (1.0 M) was added ethylmagnesium bromide (1.0 M in THF, 1.1 equiv) at room temperature. The resulting solution was stirred for 30 min. This solution was then added slowly by syringe to a solution of 2-pyridinecarboxaldehyde (1.0 equiv) in THF (0.35 M) at 0 ˚C and stirred for 1 h. The reaction mixture was quenched by addition of satd. aqueous ammonium chloride (40 mL) and extracted twice with EtOAc (20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation to yield the propargylic alcohol, which was used directly without further purification.

To a solution of the crude propargylic alcohol in dichloromethane (0.2 M) at room temperature were added pivaloyl chloride (1.25 equiv), triethylamine (3.0 equiv), and dimethylaminopyridine (5 mol %) and the reaction mixture was stirred for 3 h. The solution was then washed with satd. aqueous ammonium chloride and brine, then dried over $MgSO_4$ and concentrated by rotary evaporation. The crude products were purified by flash chromatography (4:1 hexanes/EtOAc) to yield the desired propargylic pivalates.

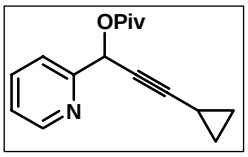


1-(pyridin-2-yl)prop-2-ynyl pivalate (7a): The general procedure was followed with the exception of using commercially available ethynylmagnesium bromide solution (0.5 M in THF) with 1.00 g (9.34 mmol) of 2-pyridinecarboxaldehyde to yield 1.07 g (8.03 mmol, 86%) of the propargylic alcohol, which was carried on to yield 1.46 g (6.75 mmol, 84%) of **7a** as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.63 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.74 (dt, *J* = 7.7, 1.8 Hz, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.28 (ddd, *J* = 7.5, 4.9, 1.0 Hz, 1H), 6.48 (d, *J* = 2.3 Hz, 1H), 2.63 (d, *J* = 2.3 Hz, 1H), 1.25 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.8, 155.8, 149.6, 137.0, 123.5, 121.2, 79.7, 75.3, 66.1, 38.8, 27.0; IR (film) ν_{max} 3265, 2974, 1740,

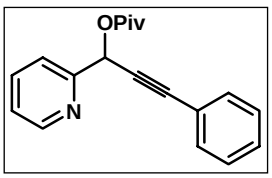
1589, 1479, 1275, 1139, 1033 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{15}NO_2]^+$: *m/z* 217.1103, found 217.1098.



1-(pyridin-2-yl)hept-2-ynyl pivalate (7b): The general procedure was followed using 1.13 g (10.5 mmol) of 2-pyridinecarboxaldehyde and 1.04 g (12.6 mmol) of 1-hexyne to yield 1.98 g (10.5 mmol, 100%) of the crude propargylic alcohol, which was carried on to yield 2.44 g (8.82 mmol, 84%) of **7b** as an orange oil. **^{1}H NMR** (400 MHz, C_6D_6) δ 8.39 (ddd, *J* = 4.77, 1.71, 0.88 Hz, 1H), 7.49 (d, *J* = 7.86 Hz, 1H), 7.06 (dt, *J* = 7.73, 1.81 Hz, 1H), 7.02 (t, *J* = 2.08 Hz, 1H), 6.55 (ddd, *J* = 7.51, 4.79, 1.05 Hz, 1H), 1.95 (dt, *J* = 6.87, 2.07 Hz, 2H), 1.33-1.10 (m, 13H), 0.70 (t, *J* = 7.15 Hz, 3H); **^{13}C NMR** (100 MHz, C_6D_6) δ 176.1, 157.6, 149.4, 136.0, 122.7, 120.8, 87.9, 77.2, 67.2, 38.5, 30.3, 26.9, 21.7, 18.4, 13.3; IR (film) ν_{max} 2960, 2934, 2872, 1737, 1590, 1274, 1138 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{23}NO_2]^+$: *m/z* 273.1729, found 273.1733.

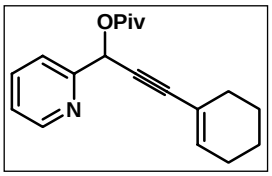


3-cyclopropyl-1-(pyridin-2-yl)prop-2-ynyl pivalate (S1): The general procedure was followed using 0.34 g (3.15 mmol) of 2-pyridinecarboxaldehyde and 0.25 g (3.78 mmol) of cyclopropylacetylene to yield 0.44 g (2.55 mmol, 81%) of the crude propargylic alcohol, which was carried on to yield 0.45 g (1.76 mmol, 69%) of **S1** as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.59 (d, *J* = 4.80 Hz, 1H), 7.71 (dt, *J* = 7.73, 1.70 Hz, 1H), 7.49 (d, *J* = 7.85 Hz, 1H), 7.23 (dd, *J* = 7.46, 4.87 Hz, 1H), 6.43 (d, *J* = 1.79 Hz, 1H), 1.33-1.27 (m, 1H), 1.23 (s, 9H), 0.81-0.66 (m, 4H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.9, 156.9, 149.42, 136.8, 123.1, 121.1, 91.3, 71.3, 66.9, 38.7, 26, 8.4, 8.3, -0.3; IR (film) ν_{max} 2973, 1735, 1590, 1479, 1274, 1140 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{19}NO_2]^+$: *m/z* 257.1416, found 257.1397.

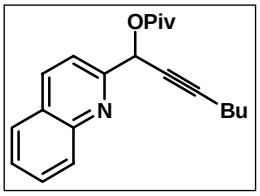


3-phenyl-1-(pyridin-2-yl)prop-2-ynyl pivalate (S2): The general procedure was followed using 0.34 g (3.15 mmol) of 2-pyridinecarboxaldehyde and 0.39 g (3.78 mmol) of phenylacetylene to yield 0.67 g (3.15 mmol, 100%) of the crude propargylic alcohol,

which was carried on to yield 0.79 g (2.71 mmol, 86%) of **S2** as orange crystals. mp 56-58 ˚C; **^{1}H NMR** (500 MHz, C_6D_6) δ 8.37 (dd, *J* = 4.76, 0.81 Hz, 1H), 7.45 (d, *J* = 7.86 Hz, 1H), 7.29 (dd, *J* = 8.05, 1.55 Hz, 2H), 7.17 (s, 1H), 7.01 (dt, *J* = 7.72, 1.80 Hz, 1H), 6.88-6.80 (m, 3H), 6.53 (ddd, *J* = 7.53, 4.79, 0.98 Hz, 1H), 1.15 (s, 9H); **^{13}C NMR** (125 MHz, C_6D_6) δ 176.1, 156.9, 149.4, 136.1, 131.9, 128.4, 128.0, 122.8, 121.0, 87.0, 86.0, 67.1, 38.5, 26.8; IR (film) ν_{max} 2973, 1732, 1590, 1478, 1274, 1137, 1032, 757, 691 cm^{-1}; HRMS (EI) calcd for $[C_{19}H_{19}NO_2]^+$: *m/z* 293.1416, found 293.1414.

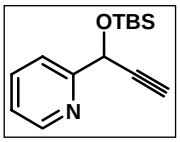


3-cyclohexenyl-1-(pyridin-2-yl)prop-2-ynyl pivalate (S3): The general procedure was followed using 0.56 g (5.26 mmol) of 2-pyridinecarboxaldehyde and 0.67 g (3.78 mmol) of 1-ethynyl-1-cyclohexene to yield 0.67 g (5.05 mmol, 96%) of the crude propargylic alcohol, which was carried on to yield 0.48 g (3.33 mmol, 69%) of **S3** as an orange oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.60 (dd, *J* = 4.80, 0.81 Hz, 1H), 7.72 (dt, *J* = 7.63, 1.52 Hz, 1H), 7.54 (d, *J* = 7.82 Hz, 1H), 7.24 (dd, *J* = 7.50, 4.84 Hz, 1H), 6.59 (s, 1H), 6.18-6.14 (m, 1H), 2.16-2.02 (m, 4H), 1.64-1.51 (m, 4H), 1.24 (s, 9H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 176.9, 156.8, 149.4, 136.9, 136.3, 123.1, 121.2, 119.8, 88.9, 82.3, 67.1, 38.8, 28.9, 27.0, 25.6, 22.1, 21.4; IR (film) ν_{max} 2972, 2933, 2872, 1736, 1590, 1478, 1274, 1138 cm^{-1}; HRMS (EI) calcd for $[C_{19}H_{23}NO_2]^+$: *m/z* 297.1729, found 297.1728.



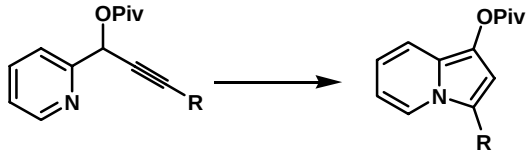
1-(quinolin-2-yl)hept-2-ynyl pivalate (S4): A 0.5 M solution of 1-hexynylmagnesium bromide was generated as per the general procedure and was added slowly to 2-quinolinecarboxaldehyde (0.30 g, 1.91 mmol) in THF (10 mL) at 0 ˚C. The reaction mixture was stirred for 2 h at 0 ˚C, then pivaloyl chloride (0.29 mL, 2.39 mmol) was added and the solution was stirred for an additional 2 h. The reaction mixture was added to satd. ammonium chloride (20 mL) and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, then concentrated by rotary evaporation. The crude product was purified by flash chromatography (4:1 hexanes/EtOAc) to yield 0.39 g (1.18 mmol, 62%) of **S4** as a yellow oil. **^{1}H NMR** (400 MHz, C_6D_6) δ 8.19 (d, *J* = 8.46 Hz, 1H), 7.64 (d, *J* = 8.52 Hz, 1H), 7.61 (d, *J* = 8.63 Hz,

1H), 7.32 (d, *J* = 8.14 Hz, 1H), 7.28 (ddd, *J* = 8.42, 6.93, 1.46 Hz, 1H), 7.17 (t, *J* = 2.14 Hz, 1H), 7.11 (ddd, *J* = 8.10, 6.96, 1.16 Hz, 1H), 1.95 (dt, *J* = 6.85, 2.08 Hz, 2H), 1.28-1.15 (m, 13H), 0.69 (t, *J* = 7.14 Hz, 3H); **^{13}C NMR** (100 MHz, C_6D_6) δ 176.1, 157.4, 147.9, 136.6, 129.9, 129.4, 127.6, 127.3, 126.4, 118.7, 88.6, 77.2, 67.9, 38.6, 30.3, 26.9, 21.7, 18.4, 13.3; IR (film) ν_{max} 2960, 2933, 2872, 1736, 1137 cm^{-1}; HRMS (EI) calcd for $[C_{21}H_{25}NO_2]^+$: *m/z* 323.1885, found 323.1881.



TBS protected 1-(pyridin-2-yl)prop-2-yn-1-ol (S5): 1-(pyridin-2-yl)prop-2-yn-1-ol was synthesized as described for the synthesis of **7**. To a solution of the propargylic alcohol (320 mg, 2.4 mmol) in DMF (15 mL) *tert*-butyldimethylsilyl chloride (0.87 g, 5.76 mmol) and imidazole (0.82 g, 12.0 mmol) were added and the solution was stirred at room temperature for 12 h. The reaction mixture was then added to water (30 mL), extracted with diethyl ether (2 x 20 mL), washed with brine (20 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purifed by flash chromatography (2:1 hexanes/EtOAc) to yield **S5** as a pale brown oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 8.33 (d, *J* = 4.08 Hz, 1H), 7.62 (d, *J* = 7.90 Hz, 1H), 7.05 (dt, *J* = 7.72, 1.75 Hz, 1H), 6.53 (ddd, *J* = 7.43, 4.81, 0.95 Hz, 1H), 5.77 (d, *J* = 2.17 Hz, 1H), 2.09 (d, *J* = 2.25 Hz, 1H), 0.93 (s, 9H), 0.18 (s, 3H), 0.04 (s, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 160.7, 148.7, 136.2, 122.4, 119.9, 84.1, 73.7, 66.9, 25.6, 18.1, -4.9, -5.3; IR (film) ν_{max} 3310, 2930, 2858, 1590, 1471, 1253, 1080, 859, 780, 655 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{21}NOSi]^+$: *m/z* 247.1392, found 247.1391.

Cycloisomerization of Propargylic Pivalates to Indolizines



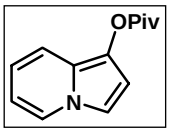
General Procedures:

All reactions were run using new vials and stir bars.

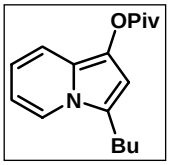
Method A: Platinum (II) chloride (5 mol %) and 2-(di-tert-butylphosphino)biphenyl (10 mol %) were added to a solution of the propargylic pivalate in benzene (0.2 M) and the solution was heated at 70 ˚C in a sealed vial with stirring. Once the reaction was judged

complete by TLC, the mixture was concentrated by rotary evaporation and the residue purified by flash chromatography (4:1 hexanes/EtOAc).

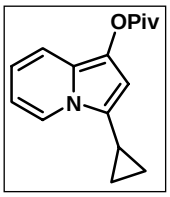
Method B: Indium trichloride (5 mol %) was added to a solution of propargylic pivalate in benzene (0.2 M) and the solution was heated at 70 ˚C in a sealed vial with stirring. Once the reaction was judged complete by TLC the mixture was concentrated by rotary evaporation and the residue purifed by flash chromatography (4:1 hexanes/EtOAc).



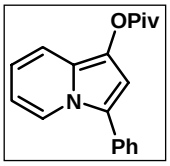
Indolizin-1-yl pivalate (8a): The general procedure was followed using 100 mg (0.46 mmol) of **7a**, with the exception of 2-(dicyclohexylphosphino)biphenyl being used in place of 2-(di-tert-butylphosphino)biphenyl in method A, to yield **8a** as a yellow oil. Method A yielded 79 mg (0.36 mmol, 79%) after 8 h, while method B resulted in no observable reaction. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.18 (d, *J* = 9.08 Hz, 1H), 6.92-6.87 (m, 2H), 6.56 (d, *J* = 2.86 Hz, 1H), 6.23 (ddd, *J* = 9.07, 6.43, 0.85 Hz, 1H), 5.90-5.84 (m, 1H), 1.23 (s, 9H); **^{13}C NMR** (125 MHz, C_6D_6) δ 175.6, 124.4, 122.0, 115.9, 115.5, 109.7, 108.8, 106.6, 38.8, 27.0; IR (film) ν_{max} 2934, 1748, 1428, 1329, 1278, 1123, 733 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{15}NO_2]^+$: *m/z* 217.1103, found 217.1103.



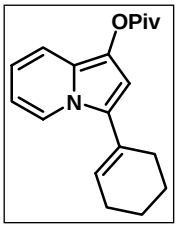
3-butylindolizin-1-yl pivalate (8b): The general procedure was followed using 100 mg (0.366 mmol) of **7b** to yield **8b** as a yellow oil. Method A yielded 95 mg (0.35 mmol, 95%) after 3 h and method B yielded 85 mg (0.31 mmol, 85%) after 4 h. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.30 (d, *J* = 9.01 Hz, 1H), 7.04 (d, *J* = 7.10 Hz, 1H), 6.76 (s, 1H), 6.32 (dd, *J* = 8.99, 6.42 Hz, 1H), 6.06 (t, *J* = 6.76 Hz, 1H), 2.26 (t, *J* = 7.65 Hz, 2H), 1.40-1.32 (m, 2H), 1.27 (s, 9H), 1.18-1.10 (m, 2H), 0.74 (t, *J* = 7.34 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 175.7, 127.1, 121.3, 120.9, 120.7, 116.1, 114.0, 109.6, 105.0, 38.9, 29.0, 27.0, 25.2, 22.4, 13.6; IR (film) ν_{max} 2958, 2931, 2871, 1749, 1278, 1120, 728 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{23}NO_2]^+$: *m/z* 273.1729, found 273.1732.



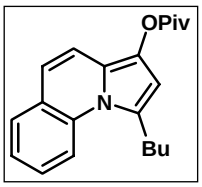
3-cyclopropylindolizin-1-yl pivalate (11): The general procedure was followed using 100 mg (0.389 mmol) of **S1** to yield **11** as a yellow solid. Method A yielded 80 mg (0.31 mmol, 80%) after 20 h and method B yielded 83 mg (0.32 mmol, 83%) after 3 h. mp 67-69 ˚C; **^{1}H NMR** (500 MHz, C_6D_6) δ 7.49 (d, *J* = 7.13 Hz, 1H), 7.28 (d, *J* = 9.03 Hz, 1H), 6.70 (s, 1H), 6.36 (dd, *J* = 9.01, 6.42 Hz, 1H), 6.14-6.09 (m, 1H), 1.30-1.22 (m, 10H), 0.47-0.41 (m, 2H), 0.31-0.27 (m, 2H); **^{13}C NMR** (125 MHz, C_6D_6) δ 175.7, 126.6, 122.4, 121.7, 121.4, 116.0, 114.9, 109.6, 105.0, 38.8, 27.0, 5.9, 5.0; IR (film) ν_{max} 2974, 1749, 1419, 1332, 1278, 1122, 731 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{19}NO_2]^+$: *m/z* 257.1416, found 257.1410.



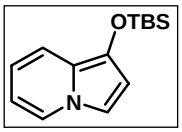
3-phenylindolizin-1-yl pivalate (12): The general procedure was followed using 100 mg (0.341 mmol) of **S2** to yield **12** as a yellow oil. Method A yielded 99 mg (0.34 mmol, 99%) after 3 h and method B yielded 92 mg (0.31 mmol, 92%) after 1 h. **^{1}H NMR** (400 MHz, C_6D_6) δ 7.78 (d, *J* = 7.23 Hz, 1H), 7.31 (d, *J* = 9.02 Hz, 1H), 7.23 (d, *J* = 7.23 Hz, 2H), 7.11 (t, *J* = 7.53 Hz, 2H), 7.07 (s, 1H), 7.04 (t, *J* = 7.34 Hz, 1H), 6.33 (dd, *J* = 8.95, 6.43 Hz, 1H), 5.96 (t, *J* = 6.77 Hz, 1H), 1.30 (s, 9H); **^{13}C NMR** (100 MHz, C_6D_6) δ 175.5, 131.9, 128.7, 128.1, 126.9, 123.1, 121.9, 121.3, 116.3, 115.8, 114.6, 110.5, 107.1, 38.9, 27.0; IR (film) ν_{max} 2973, 1750, 1514, 1476, 1353, 1276, 1124, 733, 699 cm^{-1}; HRMS (EI) calcd for $[C_{19}H_{19}NO_2]^+$: *m/z* 293.1416, found 293.1413.



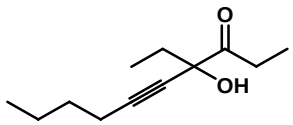
3-cyclohexenylindolizin-1-yl pivalate (13): The general procedure was followed using 100 mg (0.336 mmol) of **S3** to yield **13** as an orange oil. Method A yielded 79 mg (0.27 mmol, 79%) after 24 h and method B yielded 81 mg (0.30 mmol, 81%) after 2 h. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.84 (d, *J* = 7.28 Hz, 1H), 7.27 (d, *J* = 8.99 Hz, 1H), 6.93 (s, 1H), 6.29 (dd, *J* = 8.96, 6.33 Hz, 1H), 6.05-5.99 (m, 1H), 5.78-5.73 (m, 1H), 2.14-2.05 (m, 2H), 1.97-1.88 (m, 2H), 1.51-1.39 (m, 4H), 1.25 (s, 9H); **^{13}C NMR** (125 MHz, C_6D_6) δ 175.5, 128.7, 127.7, 125.4, 123.6, 122.7, 122.5, 116.3, 114.9, 109.9, 105.4, 38.9, 28.7, 27.0, 25.3, 22.8, 22.0; IR (film) ν_{max} 2972, 2931, 1750, 1416, 1278, 1122, 731cm^{-1}; HRMS (EI) calcd for $[C_{19}H_{23}NO_2]^+$: *m/z* 297.1729, found 297.1728.



1-butylpyrrolo[1,2-a]quinolin-3-yl pivalate (14): The general procedure was followed using 100 mg (0.288 mmol) of **S4** to yield **14** as yellow crystals. Method A yielded 88 mg (0.25 mmol, 88%) after 4 h and method B yielded 83 mg (0.24 mmol, 83%) after 2 h. mp 91-92 ˚C; **^{1}H NMR** (500 MHz, C_6D_6) δ 7.91 (d, *J* = 8.52 Hz, 1H), 7.31 (dd, *J* = 7.70, 1.58 Hz, 1H), 7.25 (d, *J* = 9.22 Hz, 1H), 7.09 (ddd, *J* = 8.66, 7.26, 1.65 Hz, 1H), 7.04-6.98 (m, 1H), 6.79 (s, 1H), 6.63 (d, *J* = 9.23 Hz, 1H), 2.81 (t, *J* = 8.52 Hz, 1H), 1.54-1.46 (m, 2H), 1.27 (s, 9H), 1.23-1.15 (m, 2H), 0.75 (t, *J* = 7.37 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 175.6, 135.3, 129.9, 128.4, 128.3, 126.6, 125.9, 122.9, 121.1, 116.9, 116.6, 115.8, 106.4, 38.9, 31.0, 30.4, 27.0, 22.4, 13.7; IR (film) ν_{max} 2959, 2932, 2871, 1750, 1481, 1322, 1134, 785, 751 cm^{-1}; HRMS (EI) calcd for $[C_{21}H_{25}NO_2]^+$: *m/z* 323.1885, found 323.1884.

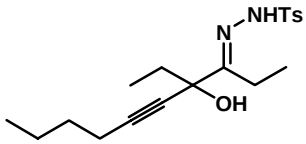


Indolizin-1-yl tert-butyldimethylsilyl ether (15): The general procedure for method A was followed using 100 mg (0.404 mmol) of **S5**, with the exception of 2-(dicyclohexylphosphino)biphenyl being used in place of 2-(di-tert-butylphosphino)biphenyl, to yield **15** as a brown oil. Method A yielded 57 mg (0.23 mmol, 57%) after 16 h. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.34 (d, *J* = 9.05 Hz, 1H), 6.95 (d, *J* = 7.07 Hz, 1H), 6.57 (d, *J* = 2.80 Hz, 1H), 6.34 (d, *J* = 2.82 Hz, 1H), 6.18 (ddd, *J* = 9.05, 6.33, 0.81 Hz, 1H), 5.89-5.85 (m, 1H), 1.02 (s, 9H), 0.13 (s, 6H); **^{13}C NMR** (125 MHz, C_6D_6) δ 127.7, 127.5, 124.2, 116.8, 113.3, 109.5, 107.7, 104.8, 25.6, 18.0, -4.9; IR (film) ν_{max} 2956, 2929, 2857, 1555, 1427, 1331, 1083, 879, 840, 781, 732 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{21}NOSi]^+$: *m/z* 247.1392, found 247.1390.

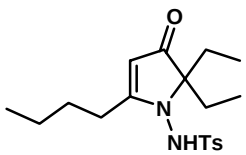


4-ethyl-4-hydroxydec-5-yn-3-one (S6). Following the method of Chisholm[1], a 20 mL Schlenk tube equipped with a stir bar was charged with dicarbonylacetylacetonato rhodium (I) (15 mg, 0.058 mmol, 0.03 equiv) and 2-(di-t-butylphosphino)biphenyl (53 mg, 0.18 mmol, 0.09 equiv). The flask was evacuated and filled with nitrogen before a nitrogen-sparged solution of 1-hexyne (233 µL, 2.00 mmol) and hexane-3,4-dione (723 µL, 6.00 mmol, 3 equiv) in tetrahydrofuran (2.5 mL) was added via syringe. The resulting mixture was

heated to 40 ºC and stirred for 24 h. After cooling to room temperature, 2 g of silica was added to the reaction mixture, and it was concentrated to dryness. The silica-adsorbed product was purified by column chromatography (40 mL silica gel, 8:1 hexanes:ethyl acetate) to yield 256 mg (65%) of a yellow oil. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 4.05 (s, 1H), 2.94 (dq, *J* = 18.0, 7.3 Hz, 1H), 2.54 (dq, *J* = 18.0, 7.3 Hz, 1H), 2.21 (t, *J* = 7.1 Hz, 2H), 1.95 (dq, *J* = 14.9, 7.5 Hz, 1H), 1.74 (dq, *J* = 14.9, 7.5 Hz, 1H), 1.47 (m, 2H), 1.38 (m, 2H), 1.14 (t, *J* = 7.3 Hz, 3H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 209.6, 86.7, 78.9, 75.8, 33.3, 30.4, 29.0, 21.9, 18.4, 13.5, 8.1, 7.7; IR (film) ν_{max} 3466, 2961, 2937, 1719, 1460, 1108 cm^{-1}.



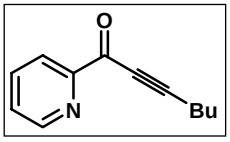
(E)-3-(2-tosylhydrazono)-4-ethyldec-5-yn-4-ol (16): A 25 mL round-bottom flask equipped with a stir bar was charged with **S6** (196 mg, 1.00 mmol), tosyl hydrazide (186 mg, 1.00 mmol, 1.0 equiv) and methanol (10 mL). The reaction solution was stirred for 24 h at room temperature. Silica (1.0 g) was then added to the reaction solution, and it was concentrated to dryness. The silica-adsorbed product was purified by column chromatography (40 mL silica gel, 8:1 hexanes:ethyl acetate) to yield 208 mg (57%) of a colorless oil. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.20 (s, 1H), 7.81 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 4.24-3.96 (m, 1H), 2.41 (s, 3H), 2.38-2.23 (m, 2H), 2.15 (t, *J* = 7.1 Hz, 2H), 1.81 (dq, *J* = 14.7, 7.4 Hz, 1H), 1.54 (dq, *J* = 14.4, 7.2 Hz, 1H), 1.46-1.39 (m, 2H), 1.38-1.28 (m, 2H), 1.10 (t, *J* = 7.7 Hz, 3H), 0.86 (t, *J* = 7.3 Hz, 3H), 0.70 (t, *J* = 7.3 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 160.1, 144.4, 134.6, 129.7, 127.8, 85.6, 79.7, 72.6, 33.9, 30.5, 21.9, 21.5, 20.2, 18.3, 13.5, 9.7, 7.5. HRMS (FAB) calcd for $[C_{19}H_{29}N_2O_3S]^+$: *m/z* 365.1899, found 365.1893.



5-butyl-2,2-diethyl-1-(toluenesulfonamido)-1,2-dihydropyrrol-3-one (19): A 20 mL Schlenk tube equipped with a stir bar was charged with platinum (II) chloride (5 mg, 0.02 mmol, 0.1 equiv). To the tube was added a solution of **16** (73 mg, 0.20 mmol) in toluene (2.0 mL). The Schlenk tube was sealed, and the reaction mixture was heated to 100 ºC for 3 h, then cooled to room temperature. Silica gel (250 mg) was added to the reaction mixture, and

the solvent was removed by rotary evaporation. The adsorbed product was purified by flash chromatography (2:1 hexanes:EtOAc), to yield 52 mg (71%) of a colorless oil. **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.70 (s, 1H), 7.33 (d, *J* = 8. 1 Hz, 2H), 5.19 (s, 1H), 2.44 (s, 3H), 2.43-2.36 (m, 1H), 2.27-2.18 (m, 1H), 1.70-1.52 (m, 2H), 1.52-1.41 (m, 3H), 1.33-1.21 (m, 3H), 0.86 (t, *J* = 7.4 Hz, 3H), 0.61 (t, *J* = 7.2 Hz, 3H), 0.55 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 201.1, 183.0, 144.8, 136.3, 129.8, 127.8, 102.9, 78.1, 28.6, 28.4, 28.2, 27.2, 22.4, 21.6, 13.6, 8.2, 7.8. HRMS (FAB) calcd for $[C_{19}H_{29}N_2O_3S]^+$: *m/z* 365.1899, found 365.1890.

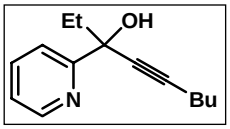
Synthesis of Tertiary Propargylic Alcohol Substrates



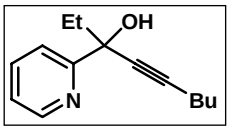
1-(pyridin-2-yl)hept-2-yn-1-one (S7): Ethylmagnesium bromide (15.4 mL, 1.0 M in THF) was added to a solution of 1-hexyne (1.55 g, 18.9 mmol) in THF (20 mL) at room temperature. The reaction mixture was stirred for 30 min then added slowly to 2-pyridinecarboxaldehyde (1.69 g, 15.8 mmol) in THF (40 mL) at 0 ˚C. The reaction mixture was stirred for 2 h at 0 ˚C then quenched by addition of 80 mL of satd. aqueous ammonium chloride and extracted with EtOAc (2 x 30 mL). The combined organic layers were then washed with brine (30 mL), dried over $MgSO_4$, and concentrated by rotary evaporation to give 3.00 g (15.8 mmol, 100% yield) of the crude propargylic alcohol which was carried on without further purification.

To a solution of oxalyl chloride (2.75 mL, 31.5 mmol) in dichloromethane (40 mL) at -78 ˚C, DMSO (4.50 mL, 63.1 mmol) in dichloromethane (10 mL) was added dropwise and the resulting solution was stirred at this temperature for 45 min. The crude alcohol in dichloromethane (10 mL) was then added dropwise. After 45 min, triethylamine (17.5 mL, 126 mmol) was added and the resulting solution was allowed to warm to room temperature. After 4 h the solution was washed with satd. aqueous ammonium chloride (60 mL), brine (40 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purifed by flash chromatography (2:1 hexanes/EtOAc) to give 2.01 g (10.7 mmol, 68%) of **S7** as a black oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.79 (d, *J* = 4.65 Hz, 1H), 8.12 (d, *J* = 7.84 Hz, 1H), 7.85 (dt, *J* = 7.71, 1.66 Hz, 1H), 7.49 (ddd, *J* = 7.53,

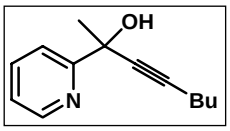
4.74, 1.05 Hz, 1H), 2.54 (t, *J* = 7.19, Hz, 2H), 1.72-1.61 (m, 2H), 1.54-1.45 (m, 2H), 0.94 (t, *J* = 7.35, Hz, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 178.2, 153.2, 149.8, 136.9, 127.3, 123.2, 99.5, 80.5, 29.8, 22.1, 19.3, 13.5.



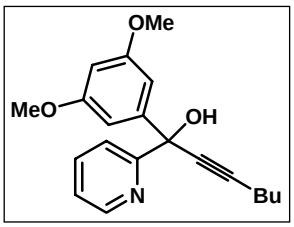
(±)-3-(pyridin-2-yl)non-4-yn-3-ol (20a): Ethylmagnesium bromide (4.49 mL, 1.0 M in THF) was added slowly to a solution of **S7** (700 mg, 3.74 mmol) in THF (20 mL) at 0 ˚C. The reaction mixture was stirred at 0 ˚C for 4 h then quenched by addition of 30 mL of satd. aqueous ammonium chloride. The mixture was then extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purified by flash chromatography (2:1 hexanes/EtOAc) to give 0.43 g (1.98 mmol, 53%) of **20a** as a brown oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 8.10 (d, *J* = 4.85 Hz, 1H), 7.42 (d, *J* = 7.94 Hz, 1H), 7.02 (dt, *J* = 7.51, 1.18 Hz, 1H), 6.49 (dd, *J* = 7.40, 4.92 Hz, 1H), 5.59 (s, 1H), 2.20-2.10 (m, 1H), 2.03-1.94 (m, 3H), 1.32-1.18 (m, 4H), 1.11 (t, *J* = 7.30 Hz, 3H), 0.70 (t, *J* = 7.05 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 162.4, 147.0, 136.3, 121.9, 120.3, 84.3, 83.5, 72.0, 38.2, 30.7, 21.8, 18.3, 13.3, 8.5; IR (film) ν_{max} 3417, 2961, 2934, 2874, 1593, 1467, 1434, 776, 750 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{19}NO]^+$: *m/z* 217.1467, found 217.1462.



(+)-3-(pyridine-2-yl)non-4-yn-3-ol (20a): (±)-20a was resolved using an HPLC system with Rainin SD-1 pumps, Sonntek UV detector and a 2 x 25 cm Chiralpak AD-H column. A solvent system of 4% isopropanol in hexane (0.1% DEA) was used with a flow rate of 15 mL/min. 200 mg of **(±)-20a** yielded 80 mg of **(+)-20a** as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 8.10 (d, *J* = 4.85 Hz, 1H), 7.42 (d, *J* = 7.94 Hz, 1H), 7.02 (dt, *J* = 7.51, 1.18 Hz, 1H), 6.49 (dd, *J* = 7.40, 4.92 Hz, 1H), 5.59 (s, 1H), 2.20-2.10 (m, 1H), 2.03-1.94 (m, 3H), 1.32-1.18 (m, 4H), 1.11 (t, *J* = 7.30 Hz, 3H), 0.70 (t, *J* = 7.05 Hz, 3H); $[\alpha]_D^{23}$ = +17.2˚ (c = 1.0 in $CHCl_3$). Analysis of enantiomers by chiral HPLC (Chiralcel OD column, flow rate 1.0 mL/min, 98:2 hexanes:EtOAc, T_r major 7.43, minor 8.70) determined the ee to be >99.9%.

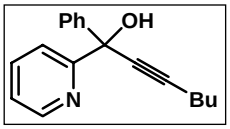


2-(pyridin-2-yl)oct-3-yn-2-ol (20b): Ethylmagnesium bromide (2.94 mL, 1.0 M in THF) was added to a solution of 1-hexyne (0.37 mL, 3.21 mmol) in THF (3 mL) and the reaction mixture was stirred at room temperature for 30 min. The resulting mixture was then added slowly to a solution of 2-acetylpyridine (0.30 mL, 2.67 mmol) in THF (10 mL) at 0 ˚C. The reaction mixture was stirred for 2 h at 0˚C then quenched with 20 mL of satd. aqueous ammonium chloride. The mixture was then extracted with EtOAc (2 x 15 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purified by flash chromatography (2:1 hexanes/EtOAc) to give 227 mg (1.12 mmol, 42%) of **20b** as a pale brown oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 8.11 (d, J = 4.64 Hz, 1H), 7.39 (d, J = 7.95 Hz, 1H), 7.01 (dt, J = 7.78, 1.73 Hz, 1H), 6.49 (ddd, J = 7.41, 4.88, 0.95 Hz, 1H), 5.60 (s, 1H), 1.97 (t, J = 6.90 Hz, 2H), 1.85 (s, 3H), 1.30-1.15 (m, 4H), 0.69 (t, J = 7.18 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 163.3, 147.1, 136.5, 121.9, 119.6, 84.6, 83.6, 68.6, 32.4, 30.6, 21.8, 18.3, 13.3; IR (film) ν_{max} 3385, 2958, 2932, 2872, 1592, 1432, 1194, 1070, 785, 750 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{17}NO]^+$: *m/z* 203.1310, found 203.1307.

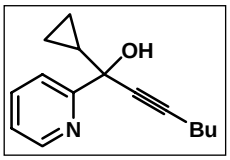


1-(3,5-dimethoxyphenyl)-1-(pyridin-2-yl)hept-2-yn-1-ol (20c): n-Butyllithium (2.5 M in hexane, 0.59 mL, 1.47 mmol) was added slowly to 5-bromo-1,3-dimethoxybenzene (0.32 g, 1.47 mmol) in THF (10 mL) at -78 ˚C. The solution was stirred at this temperature for 45 min, then **S7** (250 mg, 1.34 mmol) in THF (1 mL) was added slowly. The reaction mixture was allowed to warm to room temperature and stirred for 8 h, then quenched with satd. aqueous ammonium chloride. The mixture was then extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purified by flash chromatography (3:1 hexanes/EtOAc) to give 264 mg (0.82 mmol, 61%) of **20c** as a brown oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 8.06 (d, J = 4.86 Hz, 1H), 7.42 (d, J = 8.00 Hz, 1H), 7.29 (d, J = 2.27 Hz, 2H), 6.89 (dt, J = 7.81, 1.69 Hz, 1H), 6.76 (s, 1H), 6.45 (t, J = 2.25 Hz, 1H), 6.42 (ddd, J = 7.37, 4.93, 0.94 Hz, 1H), 3.28 (s, 6H), 1.98 (t, J = 6.76 Hz, 2H), 1.31-1.16 (m, 4H), 0.68 (t, J = 7.13 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 162.4,

161.0, 147.8, 146.5, 136.7, 122.1, 121.3, 105.2, 99.7, 86.7, 83.3, 73.6, 54.5, 30.5, 21.8, 18.4, 13.3; IR (film) ν_{max} 3347, 2957, 2934, 2872, 1595, 1460, 1430, 1204, 1155, 1060, 759, 702 cm^{-1}; HRMS (EI) calcd for $[C_{20}H_{23}NO_3]^+$: *m/z* 325.1678, found 325.1680.

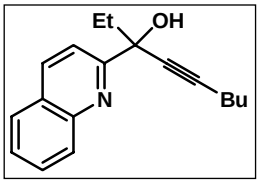


1-phenyl-1-(pyridin-2-yl)hept-2-yn-1-ol (20d): To a stirring solution of 1-hexyne (1.14 mL, 9.96 mmol) in THF (10 mL) ethylmagnesium bromide (9.13 mL, 1.0 M in THF) was added and the reaction mixture was stirred for 30 min. The solution was then added dropwise to a mixture of phenyl-pyridin-2-yl-methanone[2] (1.52 g, 8.30 mmol) in THF (30 mL). The solution was stirred for 30 min, then the reaction mixture was quenched by addition of satd. aqueous ammonium chloride (40 mL). The resulting mixture was extracted with EtOAc (2 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purified by flash chromatography (2:1 hexanes/EtOAc) to yield 1.86 g (85%) of **20d** as a brown oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 8.05 (ddd, *J* = 4.80, 1.42, 0.86 Hz, 1H), 7.92 (dd, *J* = 8.35, 1.14 Hz, 2H), 7.29 (d, *J* = 7.99 Hz, 1H), 7.15 (t, *J* = 8.23 Hz, 2H), 7.01 (t, *J* = 7.37 Hz, 1H), 6.86 (dt, *J* = 7.91, 1.71 Hz, 1H), 6.71 (s, 1H), 6.40 (ddd, *J* = 7.38, 4.90, 0.94 Hz, 1H), 2.00 (t, *J* = 6.95 Hz, 2H), 1.31-1.15 (m, 4H), 0.68 (t, *J* = 7.20 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 162.5, 146.5, 145.4, 136.6, 128.0, 126.7, 126.2, 122.0, 121.4, 86.8, 83.3, 73.5, 30.5, 21.8, 18.4, 13.3; IR (film) ν_{max} 3346, 3059, 2958, 2932, 1592, 1433, 1146, 1036, 778, 700 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{19}NO]^+$: *m/z* 265.1467, found 265.1466.



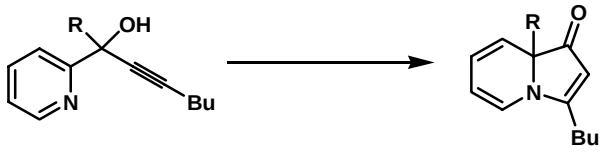
1-cyclopropyl-1-(pyridin-2-yl)hept-2-yn-1-ol (20e): Cyclopropylmagnesium bromide (0.5 M in THF , 3.48 mL, 6.96 mmol) was added slowly to a solution of **S7** (250 mg, 1.34 mmol) in THF (10 mL) at 0 ˚C. The reaction mixture was allowed to warm to room temperature over 9 h, then quenched by addition of satd. aqueous ammonium chloride (20 mL). The mixture was then extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purified by flash chromatography (2:1 hexanes/EtOAc) to give

122 mg (0.55 mmol, 40%) of **20e** as a brown oil. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.50 (ddd, *J* = 4.89, 1.64, 1.01 Hz, 1H), 7.76-7.72 (m, 1H), 7.63 (td, *J* = 7.96, 1.02 Hz, 1H), 7.25 (ddd, *J* = 7.41, 4.93, 1.14 Hz, 1H), 5.59 (s, 1H), 2.21 (dt, *J* = 7.08, 2.34 Hz, 2H), 1.53-1.44 (m, 2H), 1.44-1.33 (m, 2H), 1.27-1.18 (m, 1H), 0.90 (t, *J* = 7.29 Hz, 3H), 0.80-0.69 (m, 2H), 0.57-0.46 (m, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 162.1, 147.0, 137.1, 122.6, 120.6, 85.8, 79.7, 72.5, 30.7, 22.7, 21.9, 18.4, 13.6, 2.7, 1.6; IR (film) ν_{max} 3363, 3009, 2958, 2932, 1592, 1433, 1040, 770 cm^{-1}; HRMS (EI) calcd for $[C_{15}H_{19}NO]^+$: *m/z* 229.1467, found 229.1463.

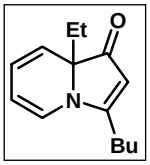


3-(quinolin-2-yl)non-4-yn-3-ol (22): Ethylmagnesium bromide (1.0 M in THF, 1.11 mL, 1.11 mmol) was added slowly to a solution of 1-(quinolin-2-yl)hept-2-yn-1-one (220 mg, 0.93 mmol, synthesized analogously to **S6**) in THF (10 mL) at 0 ˚C. The reaction mixture was stirred for 2 h then quenched by addition of satd. aqueous ammonium chloride (20 mL). The mixture was then extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, and concentrated by rotary evaporation. The crude product was purified by flash chromatography (4:1 hexanes/EtOAc) to give 124 mg (0.46 mmol, 50%) of **22** as a brown oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.88 (d, *J* = 8.44 Hz, 1H), 7.58-7.49 (m, 2H), 7.29 (d, *J* = 8.10 Hz, 1H), 7.24 (ddd, *J* = 8.39, 6.93, 1.43 Hz, 1H), 7.08 (ddd, *J* = 8.09, 6.96, 1.14 Hz, 1H), 6.21 (s, 1H), 2.35-2.21 (m, 1H), 2.08-1.97 (m, 3H), 1.33-1.19 (m, 4H), 1.14 (t, *J* = 7.33 Hz, 3H), 0.71 (t, *J* = 7.18 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 162.1, 145.7, 136.9, 129.5, 128.9, 127.3, 127.2, 126.2, 118.4, 84.5, 83.6, 72.0, 37.8, 30.7, 21.8, 18.4, 13.3, 8.4; IR (film) ν_{max} 3373, 2961, 2933, 2873, 1601, 1505, 1397, 828, 755 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{21}NO]^+$: *m/z* 267.1623, found 267.1617.

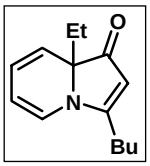
General Procedure for the Synthesis of Indolizinones from Propargylic Alcohols



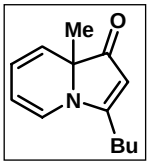
Platinum (II) chloride (5 mol %), 2-(di-tert-butylphosphino)biphenyl (10 mol %), and cesium carbonate (10 mol %) were added to a solution of propargylic alcohol in benzene (0.2 M) and the solution was heated at 100 ˚C in a sealed vial with stirring. Once the reaction was judged complete by TLC the mixture was concentrated by rotary evaporation and the residue purified by flash chromatography (4:1 hexanes/EtOAc).



(±)-3-butyl-8a-ethylindolizin-1(8aH)-one (21a): The general procedure was followed using 50 mg (0.23 mmol) of **(±)-20a** to give 33 mg (0.15 mmol, 66%) of **21a** after 48 h as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 5.95 (d, *J* = 9.28 Hz, 1H), 5.84 (d, *J* = 7.07 Hz, 1H), 5.61 (dd, *J* = 9.26, 5.37 Hz, 1H), 4.99 (t, *J* = 6.21 Hz, 1H), 4.82 (s, 1H), 1.92-1.82 (m, 1H), 1.80-1.64 (m, 3H), 1.16-1.04 (m, 2H), 1.03-0.93 (m, 2H), 0.80 (t, *J* = 7.41 Hz, 3H), 0.65 (t, *J* = 7.29 Hz, 2H); **^{13}C NMR** (125 MHz, C_6D_6) δ 201.0, 175.0, 123.7, 122.2, 121.8, 108.1, 98.3, 70.3, 31.4, 28.4, 26.2, 22.1, 13.3, 6.5; IR (film) ν_{max} 2960, 2932, 2873, 1675, 1534, 1433, 725, 689 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{19}NO]^+$: *m/z* 217.1467, found 217.1467.

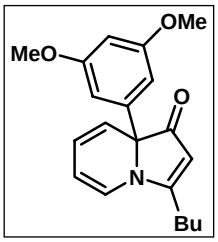


(+)-3-butyl-8a-ethylindolizin-1(8aH)-one (21a): The general procedure was followed using 80 mg (0.37 mmol) of **(+)-20a** to give 32 mg (0.15 mmol, 40%) of **(+)-21a** after 48 h as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 5.95 (d, *J* = 9.28 Hz, 1H), 5.84 (d, *J* = 7.07 Hz, 1H), 5.61 (dd, *J* = 9.26, 5.37 Hz, 1H), 4.99 (t, *J* = 6.21 Hz, 1H), 4.82 (s, 1H), 1.92-1.82 (m, 1H), 1.80-1.64 (m, 3H), 1.16-1.04 (m, 2H), 1.03-0.93 (m, 2H), 0.80 (t, *J* = 7.41 Hz, 3H), 0.65 (t, *J* = 7.29 Hz, 2H); $[\alpha]_D^{23}$ = +1480.8˚ (c = 0.75 in $CHCl_3$).[3] Analysis of enantiomers by chiral HPLC (Chiralcel OD column, flow rate 1.0 mL/min, 98:2 hexanes:EtOAc, T_r minor 10.90, major 20.97) determined the ee to be 97%.

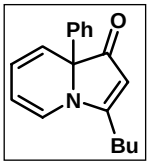


3-butyl-8a-methylindolizin-1(8aH)-one (21b): The general procedure was followed using 50 mg (0.25 mmol) of **20b** to give 20 mg (0.098 mmol, 40%)

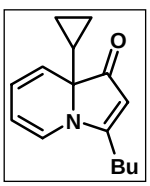
of **21b** after 7 d as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 6.00 (d, *J* = 9.26 Hz, 1H), 5.77 (d, *J* = 7.07 Hz, 1H), 5.57 (dd, *J* = 9.25, 5.36 Hz, 1H), 4.99 (t, *J* = 5.84 Hz, 1H), 4.80 (s, 1H), 1.67-1.62 (m, 2H), 1.30 (s, 3H), 1.09-0.99 (m, 2H), 0.99-0.89 (m, 2H), 0.64 (t, *J* = 7.25 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 201.4, 173.4, 123.7, 121.7, 121.6, 107.6, 96.6, 67.0, 28.1, 26.1, 23.8, 22.1, 13.3; IR (film) ν_{max} 2958, 2931, 2871, 1676, 1532, 1435 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{17}NO]^+$: *m/z* 203.1310, found 203.1314.



3-butyl-8a-(3,5-dimethoxyphenyl)indolizin-1(8aH)-one (21c): The general procedure was followed using 50 mg (0.15 mmol) of **20c** to give 33 mg (0.10 mmol, 66%) of **21c** after 5 d as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 6.88 (d, *J* = 2.19 Hz, 2H), 6.40 (d, *J* = 2.19 Hz, 1H), 6.36 (t, *J* = 2.17 Hz, 1H), 5.99 (d, *J* = 7.07 Hz, 1H), 5.69 (dd, *J* = 9.19, 5.42 Hz, 1H), 5.04-5.01 (m, 1H), 4.76 (s, 1H), 3.31 (s, 6H), 1.85-1.70 (m, 2H), 1.16-1.06 (m, 2H), 1.03-0.92 (m, 2H), 0.65 (t, *J* = 7.31 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 199.4, 175.6, 161.1, 143.2, 122.8, 122.8, 122.5, 108.6, 103.1, 99.2, 97.2, 71.1, 54.5, 28.3, 26.3, 22.1, 13.3; IR (film) ν_{max} 2957, 2872, 1683, 1595, 1536, 1426, 1156, 1063, 725 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{19}NO]^+$: *m/z* 325.1678, found 325.1676.

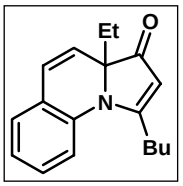


3-butyl-8a-phenylindolizin-1(8aH)-one (21d): The general procedure was followed using 50 mg (0.19 mmol) of **20d**, with the exception that no cesium carbonate was used, to give 35 mg (0.13 mmol, 70%) of **21d** after 48 h as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 7.53 (d, *J* = 7.34 Hz, 2H), 7.16-7.09 (m, 2H), 7.00 (t, *J* = 7.36 Hz, 1H), 6.39 (d, *J* = 9.20 Hz, 1H), 5.95 (d, *J* = 6.99 Hz, 1H), 5.65 (dd, *J* = 9.19, 5.41 Hz, 1H), 4.97 (t, *J* = 6.05 Hz, 1H), 4.74 (s, 1H), 1.85-1.67 (m, 2H), 1.15-1.04 (m, 2H), 1.02-0.92 (m, 2H), 0.65 (t, *J* = 7.29 Hz, 3H); **^{13}C NMR** (125 MHz, C_6D_6) δ 199.5, 175.5, 140.9, 128.2, 127.7, 124.6, 123.0, 122.7, 122.5, 108.7, 97.2, 71.0, 28.2, 26.3, 22.1, 13.3; IR (film) ν_{max} 2957, 2871, 1682, 1567, 1533, 1430, 699 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{19}NO]^+$: *m/z* 265.1467, found 265.1465.



3-butyl-8a-cyclopropylindolizin-1(8aH)-one (21e): The general procedure was followed using 50 mg (0.26 mmol) of **20e** to give 22 mg (0.12 mmol,

44%) of **21e** after 6 d as a yellow oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 5.91 (d, *J* = 9.35 Hz, 1H), 5.82 (d, *J* = 7.09 Hz, 1H), 5.64 (dd, *J* = 9.34, 5.41 Hz, 1H), 4.93 (t, *J* = 6.25 Hz, 1H), 4.78 (s, 1H), 1.72-1.65 (m, 2H), 1.22-1.14 (m, 1H), 1.12-1.02 (m, 2H), 1.01-0.92 (m, 2H), 0.71-0.62 (m, 4H), 0.62-0.54 (m, 1H), 0.31-0.17 (m, 2H); **^{13}C NMR** (125 MHz, C_6D_6) δ 200.9, 174.9, 122.9, 122.7, 121.0, 107.8, 97.4, 68.7, 28.3, 26.2, 22.1, 19.1, 13.3, 0.4, -0.7; IR (film) ν_{max} 2958, 2932, 2872, 1678, 1534, 1431, 724 cm^{-1}; HRMS (EI) calcd for $[C_{15}H_{19}NO]^+$: *m/z* 229.1467, found 229.1467.



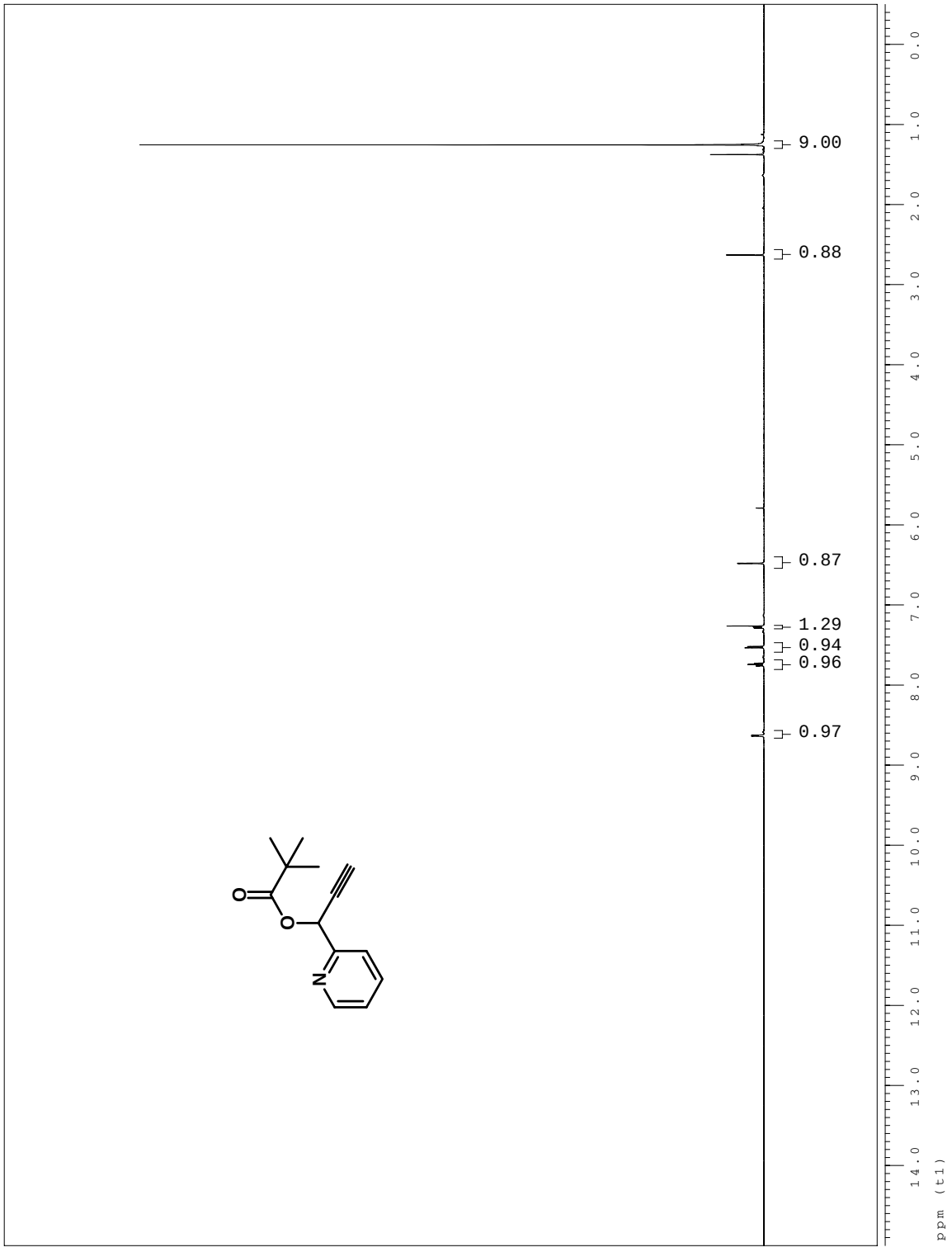
1-butyl-3a-ethylpyrrolo[1,2-a]quinolin-3(3aH)-one (23): The general procedure was followed using 50 mg (0.19 mmol) of **22** to give 13 mg (0.049 mmol, 26%) of **23** after 7 d as an orange oil. **^{1}H NMR** (500 MHz, C_6D_6) δ 6.86 (dt, *J* = 7.63, 1.67 Hz, 1H), 6.81-6.68 (m, 3H), 6.18 (d, *J* = 9.40 Hz, 1H), 5.99 (d, *J* = 9.39 Hz, 1H), 2.17-2.07 (m, 1H), 2.02-1.93 (m, 2H), 1.63-1.54 (m, 1H), 1.22-1.11 (m, 1H), 1.10-1.00 (m, 1H), 0.98-0.88 (m, 2H), 0.77 (t, *J* = 7.37 Hz, 3H), 0.60 (t, *J* = 7.32 Hz, 3H); **NMR** (125 MHz, C_6D_6) δ 198.3, 177.8, 134.9, 131.5, 129.7, 127.5, 127.4, 124.5, 124.4, 122.2, 99.0, 72.5, 29.6, 29.0, 28.2, 22.1, 13.3, 6.9; IR (film) ν_{max} 2962, 2932, 2873, 1675, 1537, 1485, 1414, 781, 755 cm^{-1}; HRMS (EI) calcd for $[C_{15}H_{19}NO]^+$: *m/z* 267.1623, found 267.1618.

References

(1) Dhondi, P.K.; Chisholm, J.D. *Org. Lett.* **2006**, 8, 67-69.

(2) Gros, P.; Fort, Y.; Caubere, P. *J. Chem. Soc. Perkin Trans. 1* **1997**, 3597-3600.

(3) High specific rotation values have previously been observed for similar compounds. See: Allin S.M.; James S.L.; Martin, W.P.; Smith, T.D.; Elsegood, M.J. *J. Chem. Soc. Perkin Trans. 1* **2001**, 3029-3036.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3.0
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5.0
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7.0
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9.0
10.0
11.0
12.0
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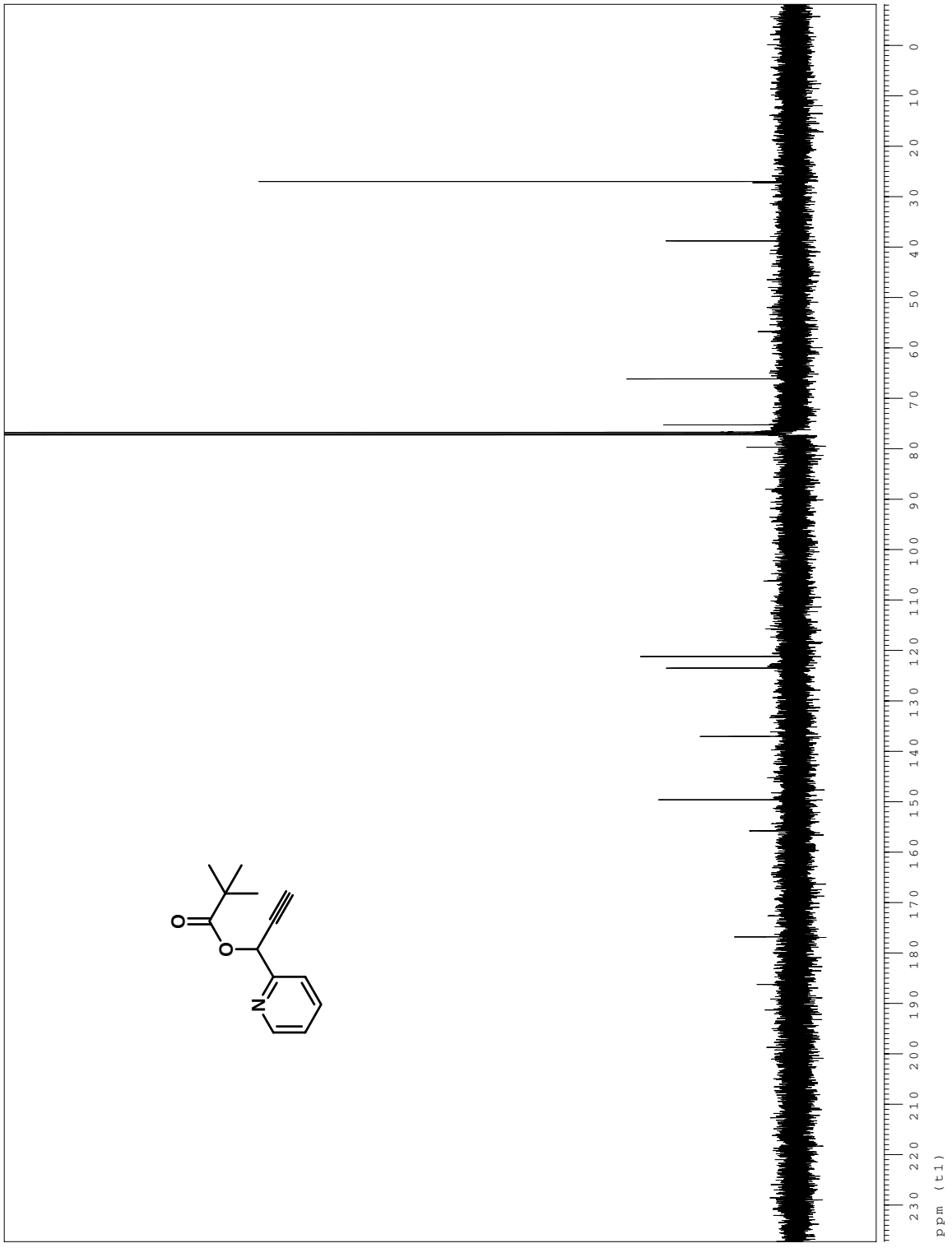
14.0
ppm (t1)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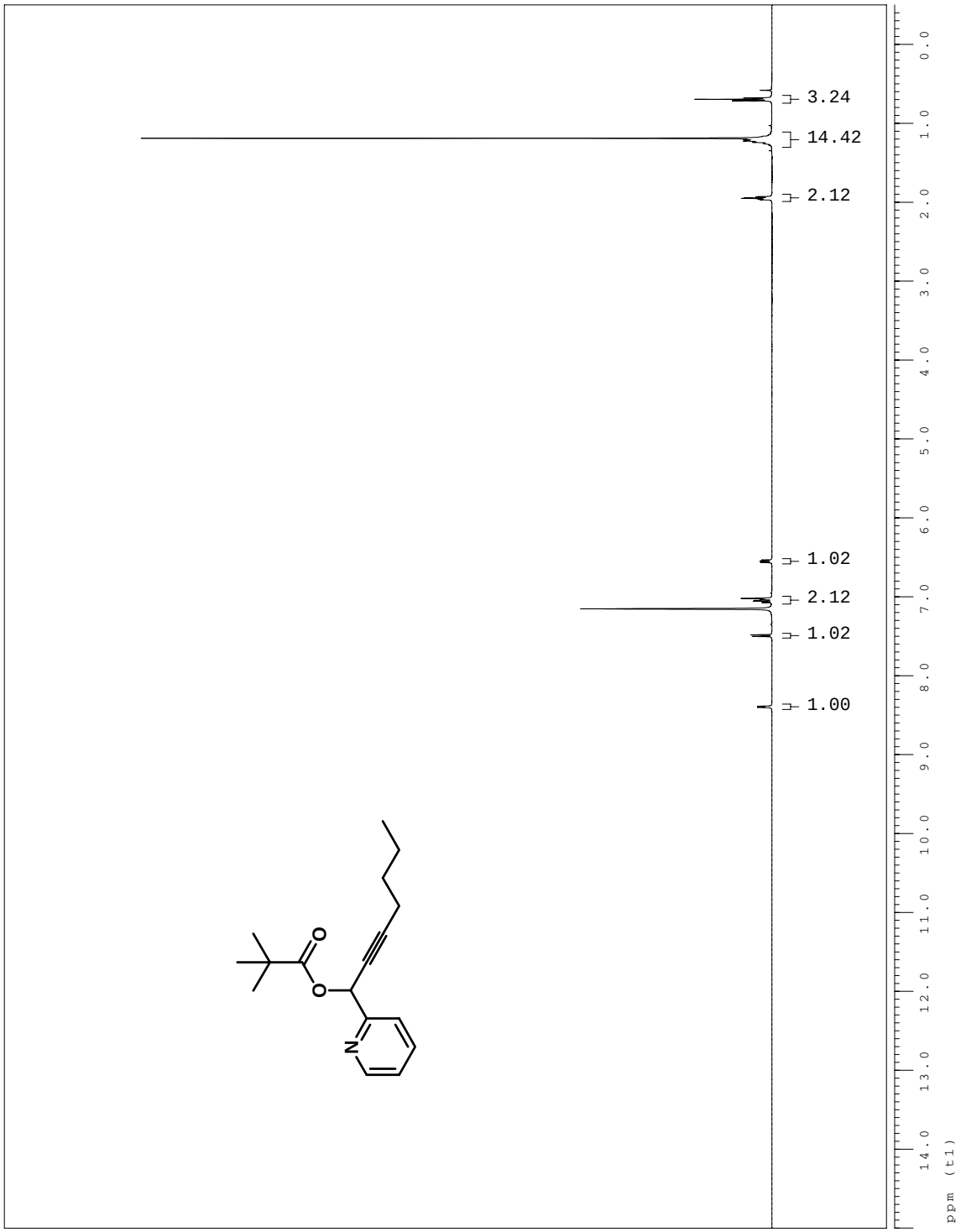
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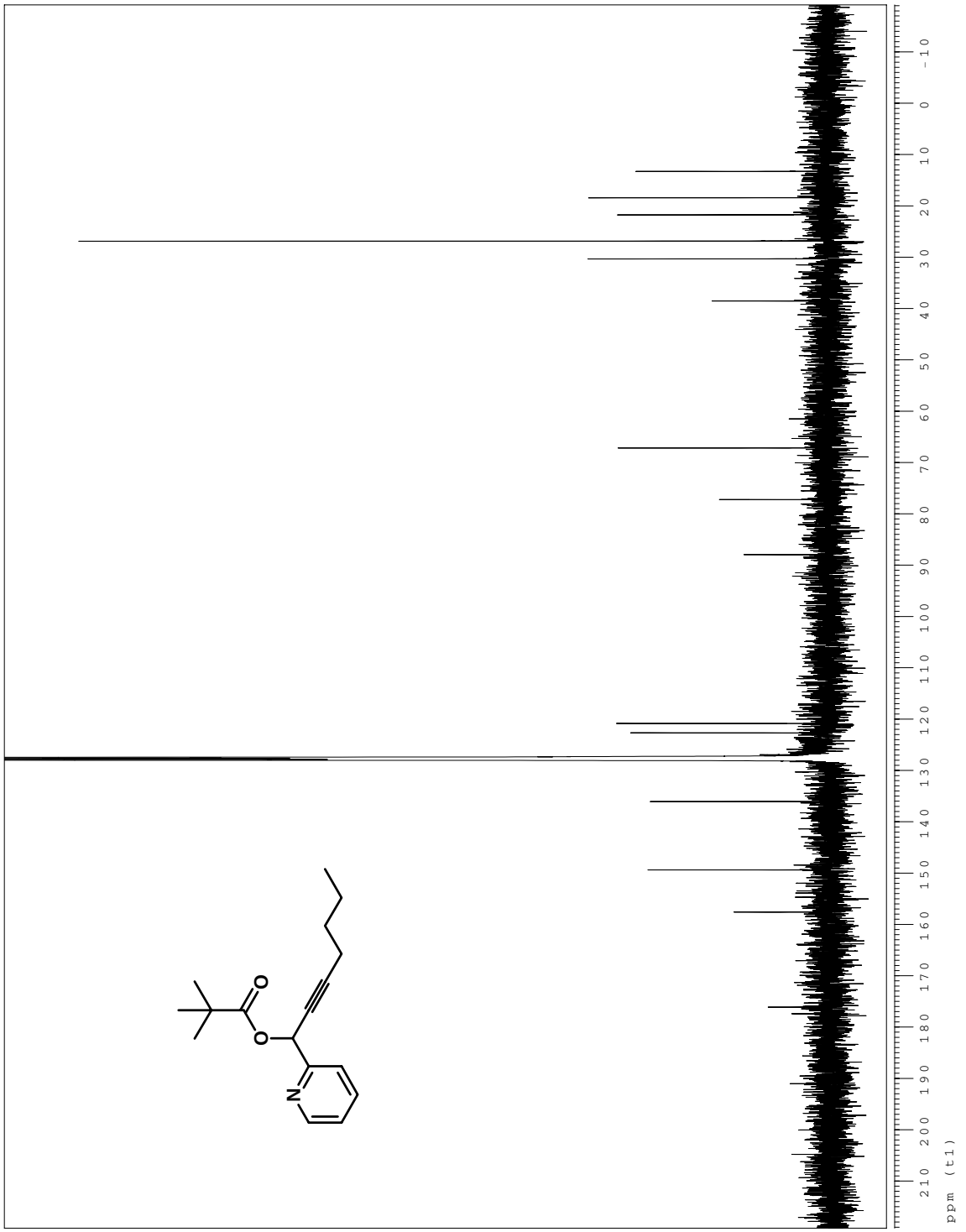
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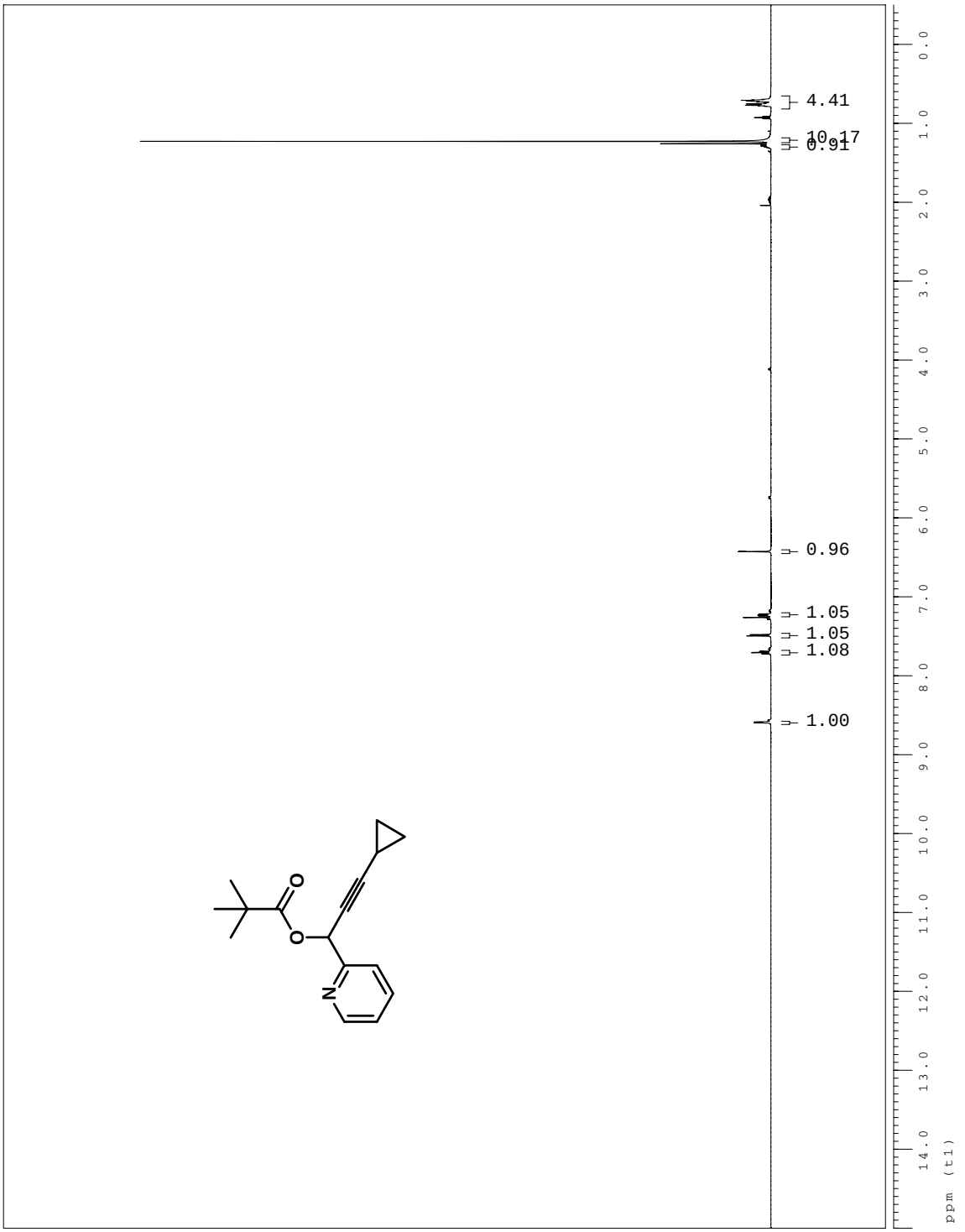
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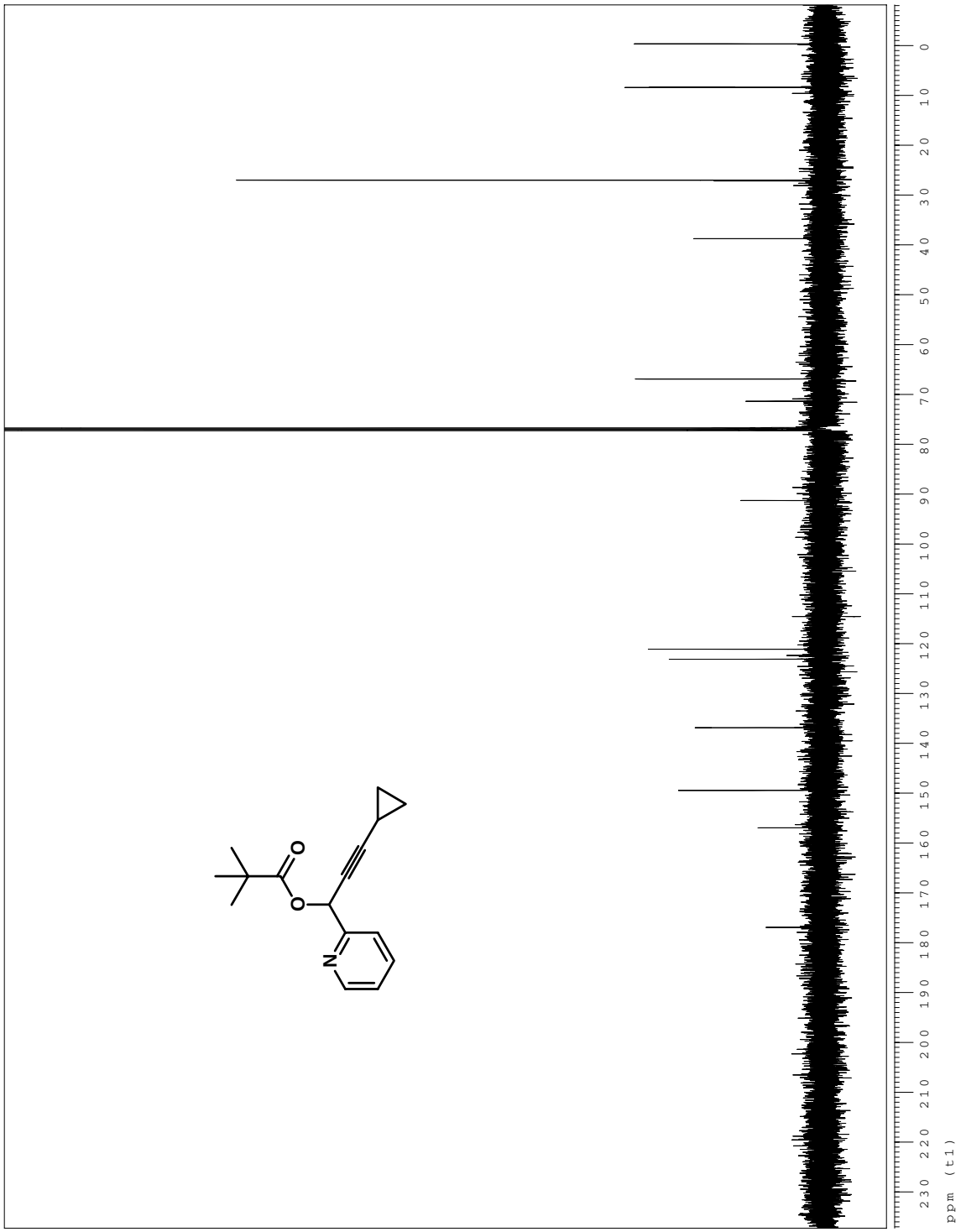
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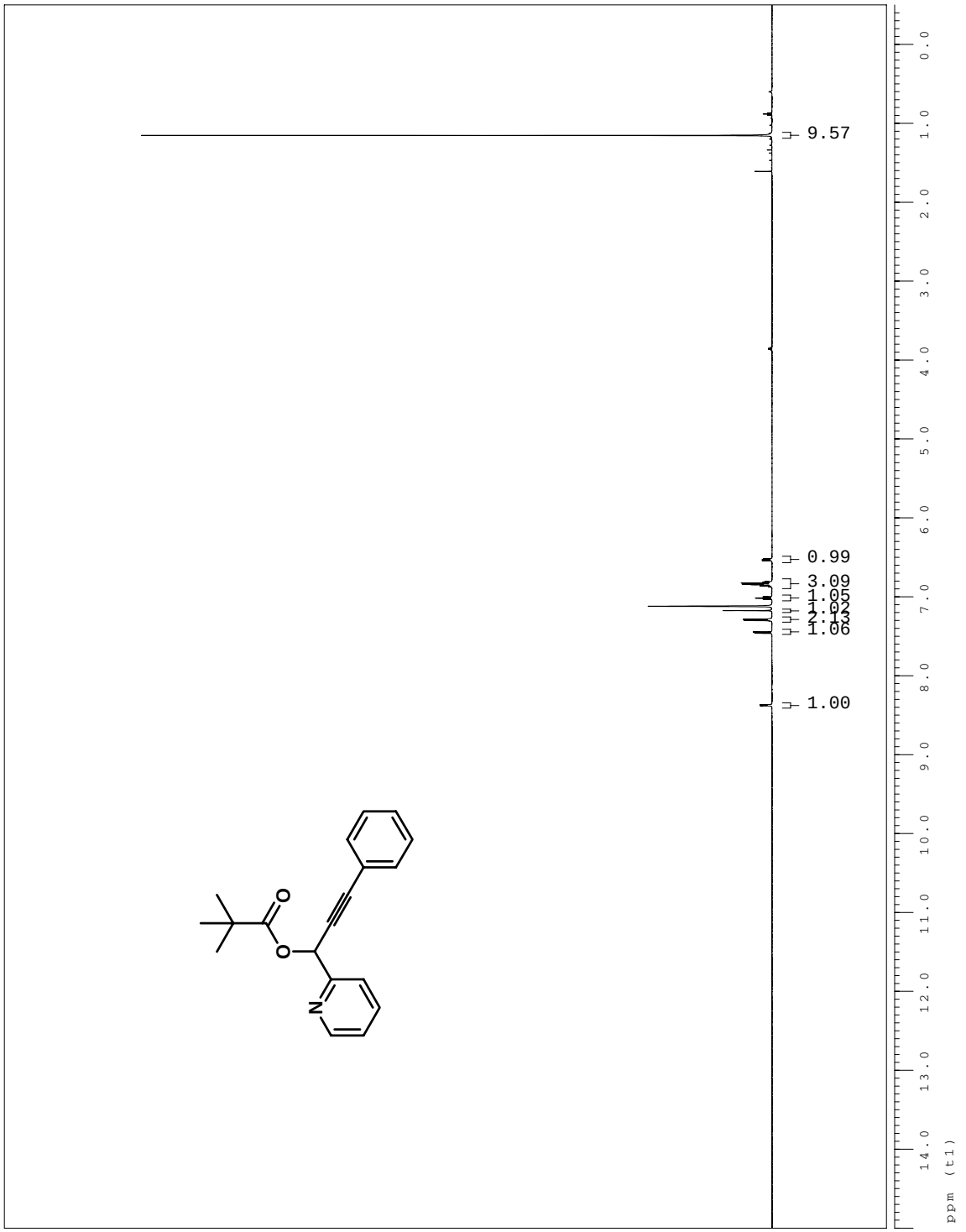
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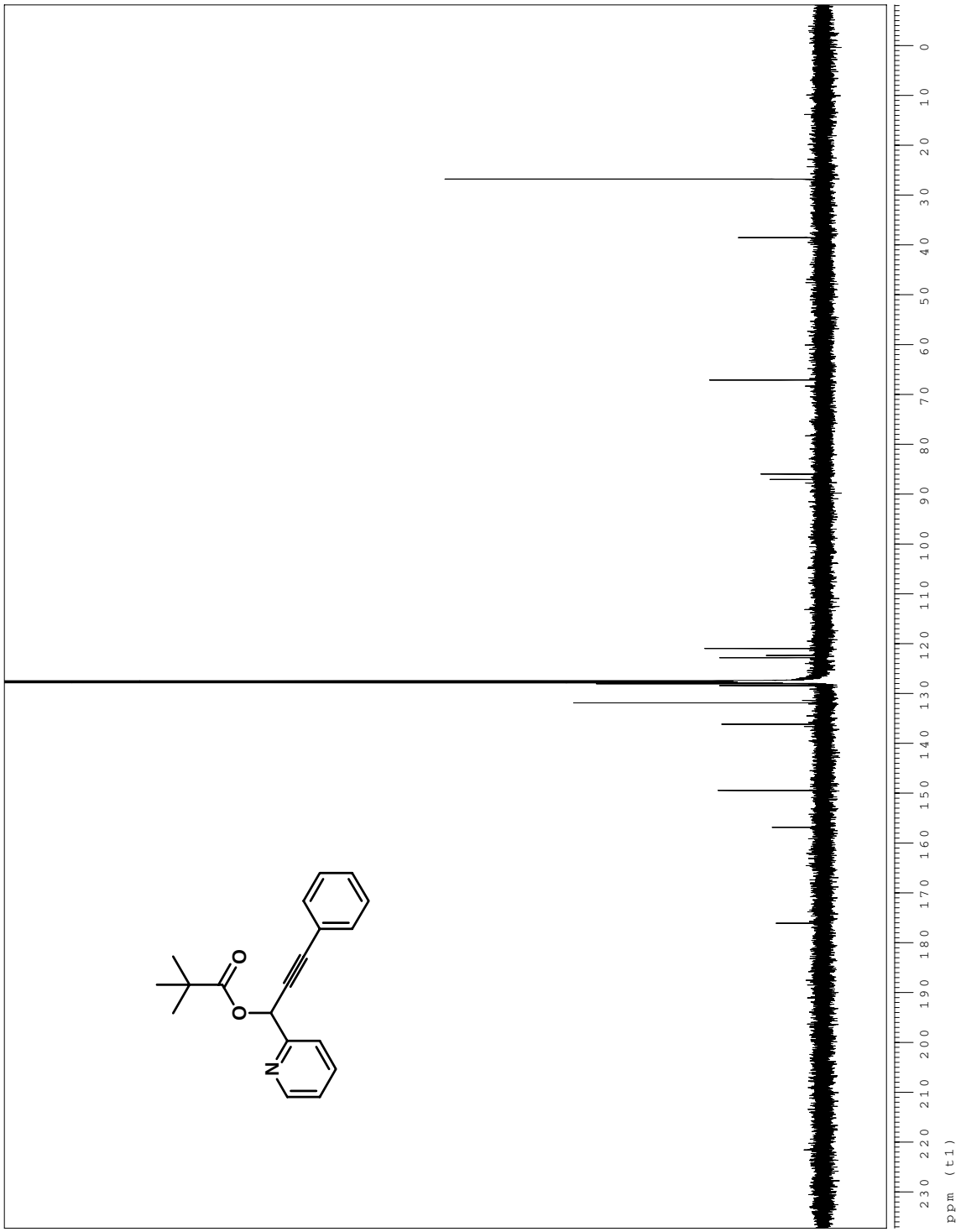
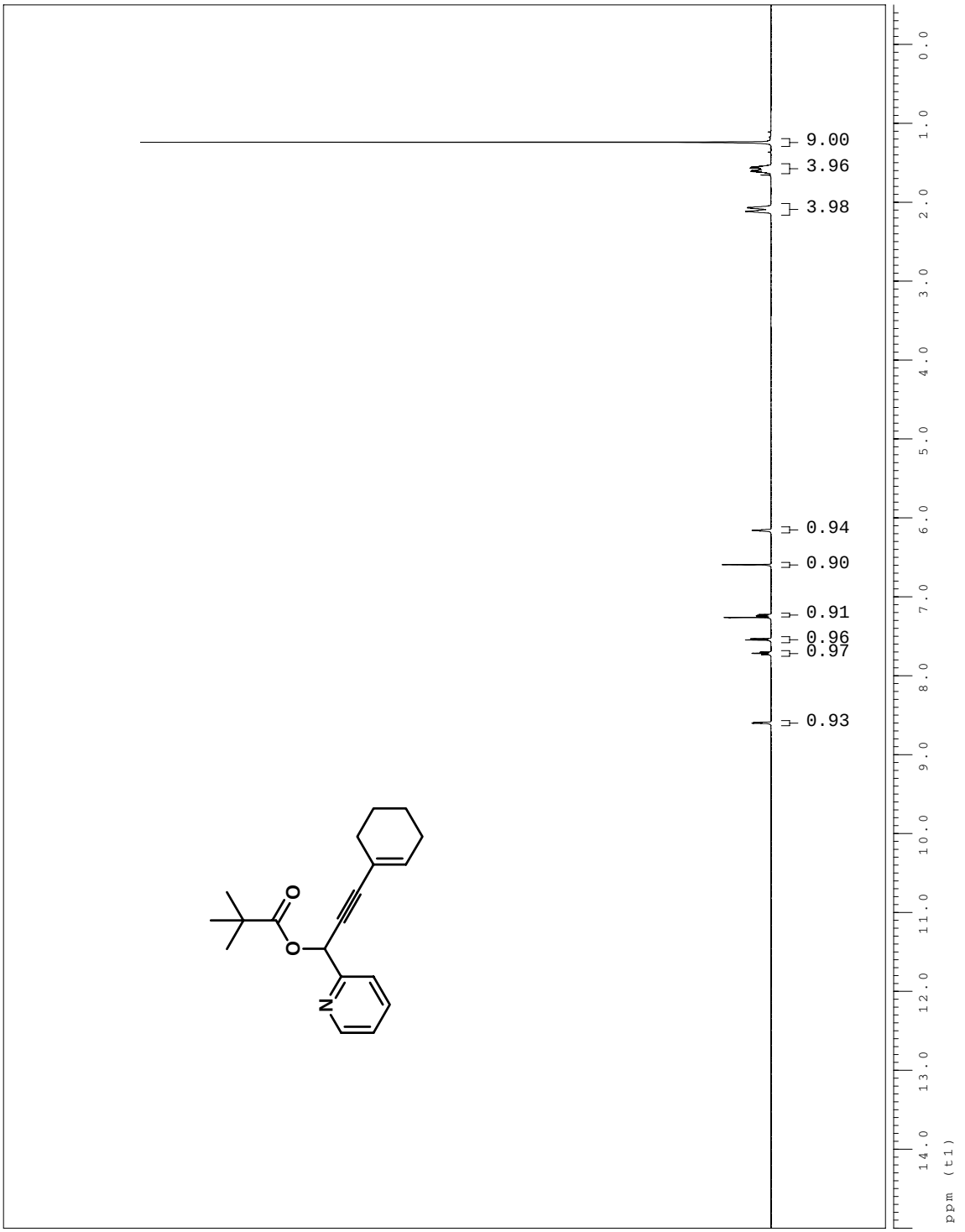
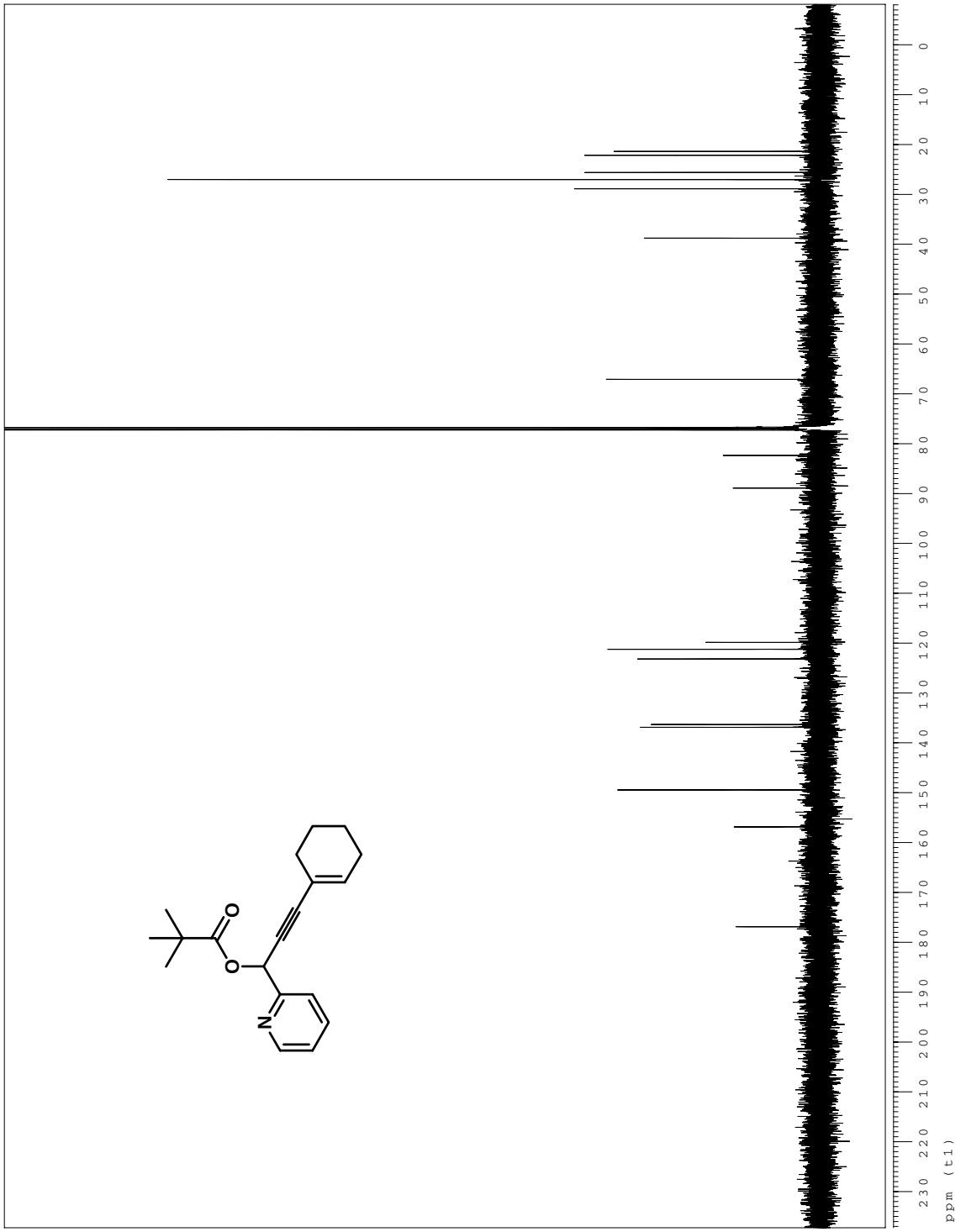
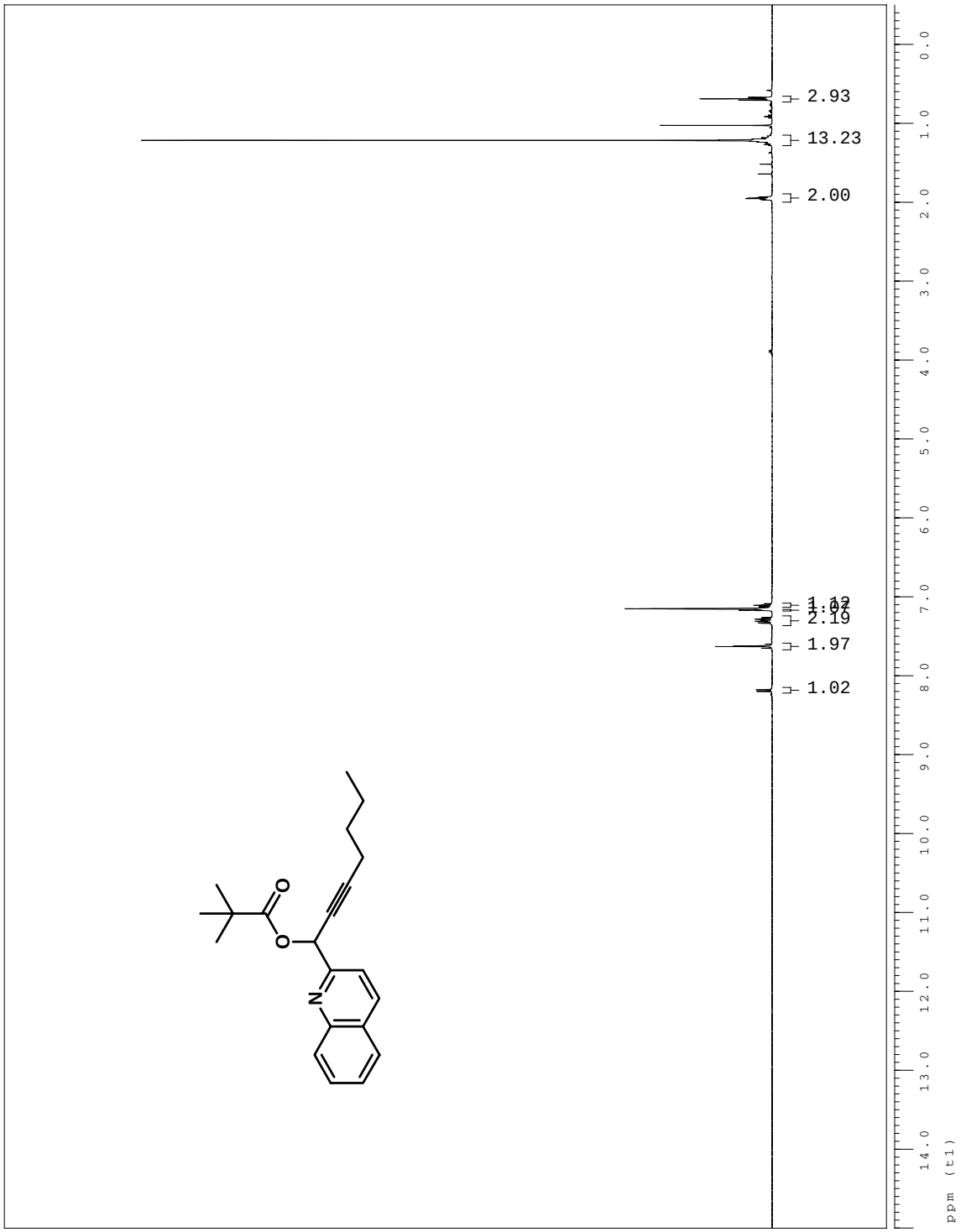
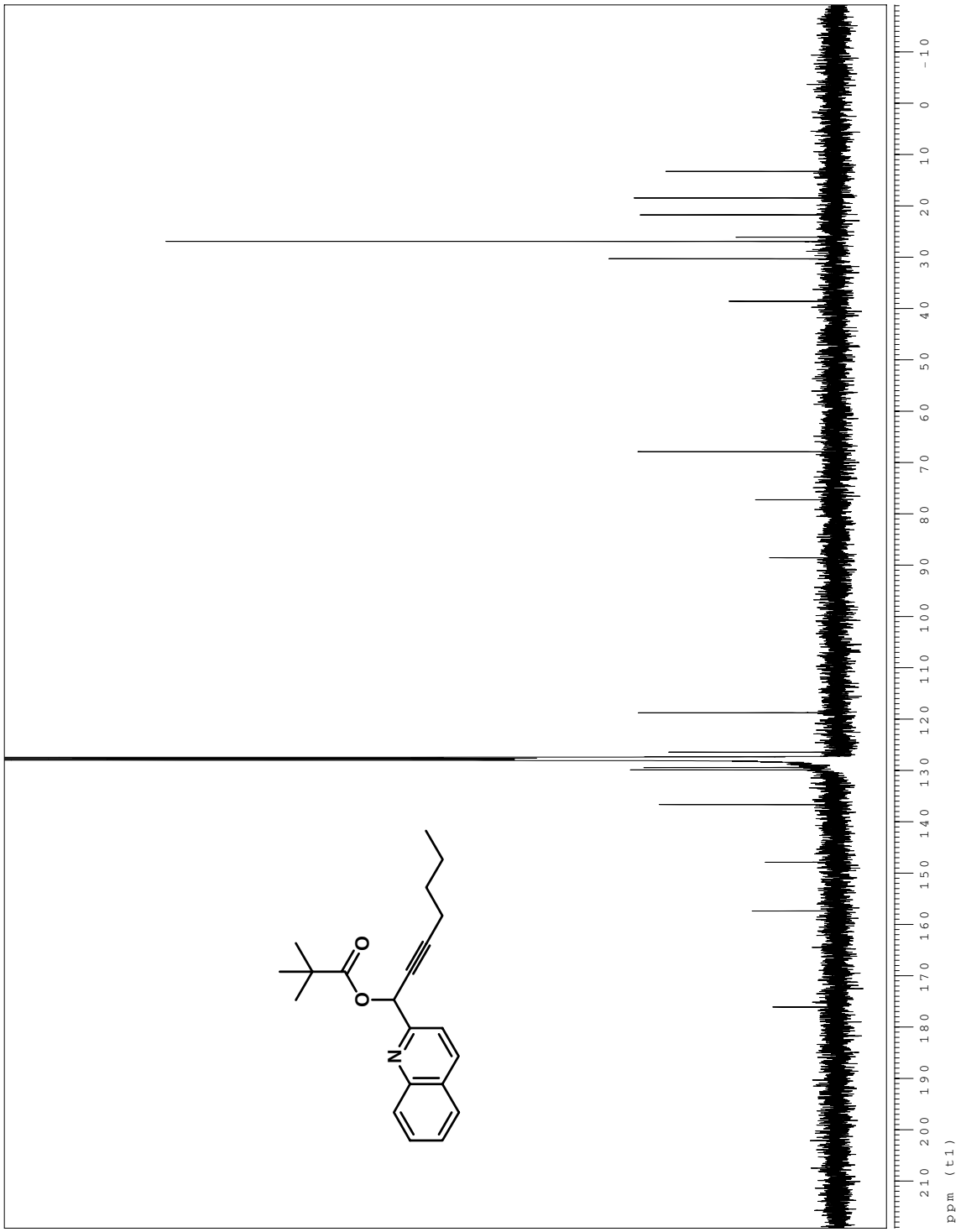
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

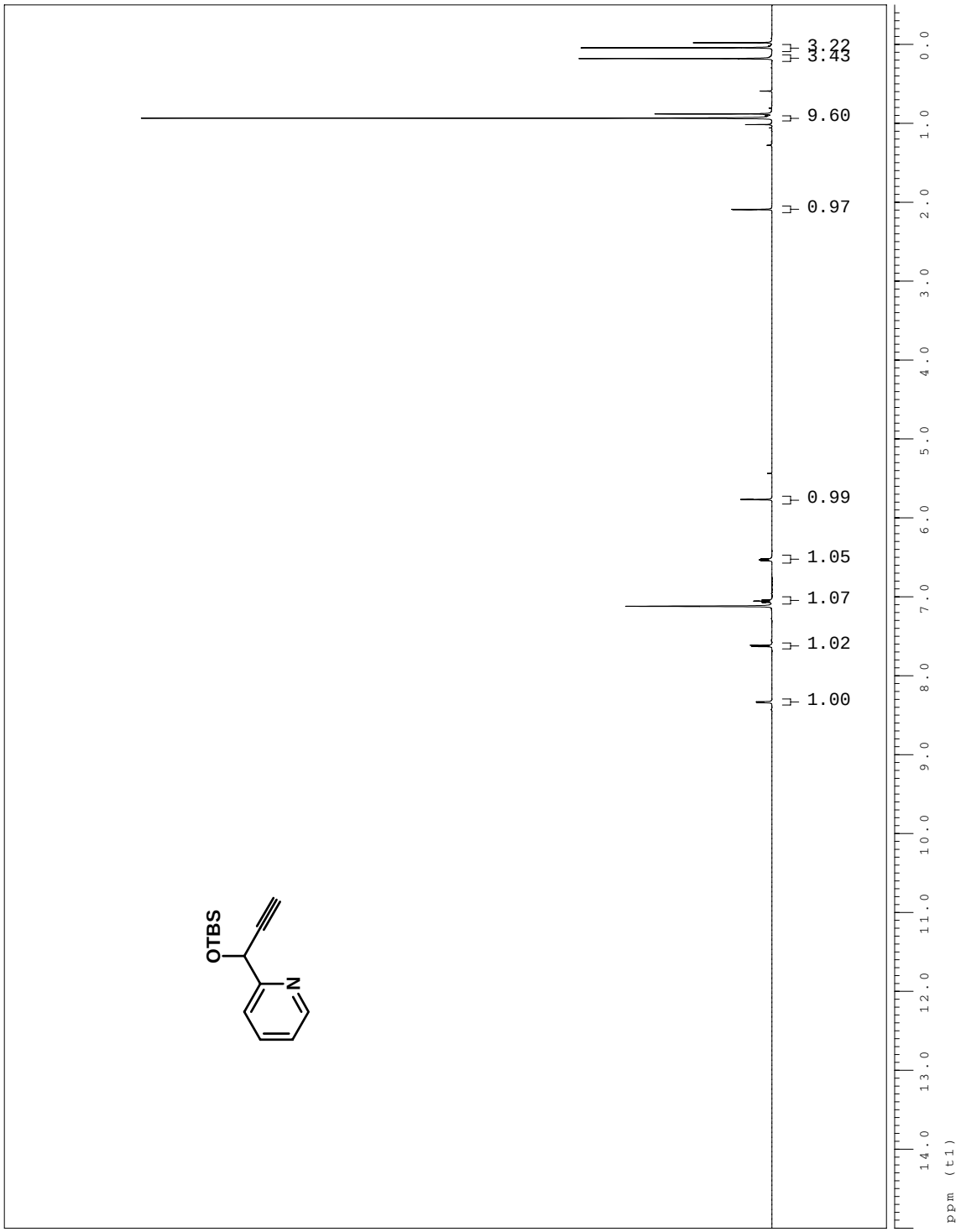

O
O
N
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

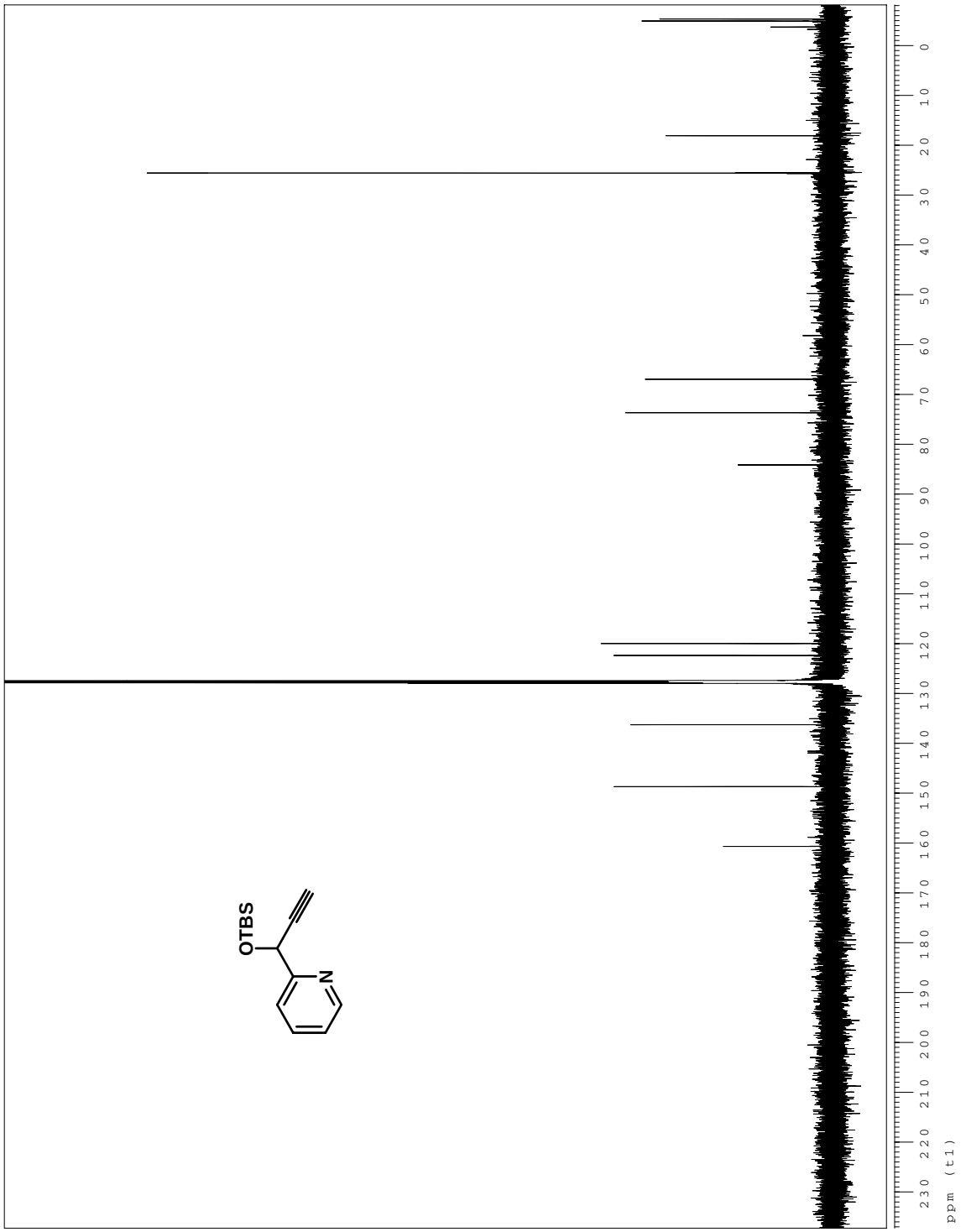

9.00
3.96
3.98
0.94
0.90
0.91
0.96
0.97
0.93
O
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

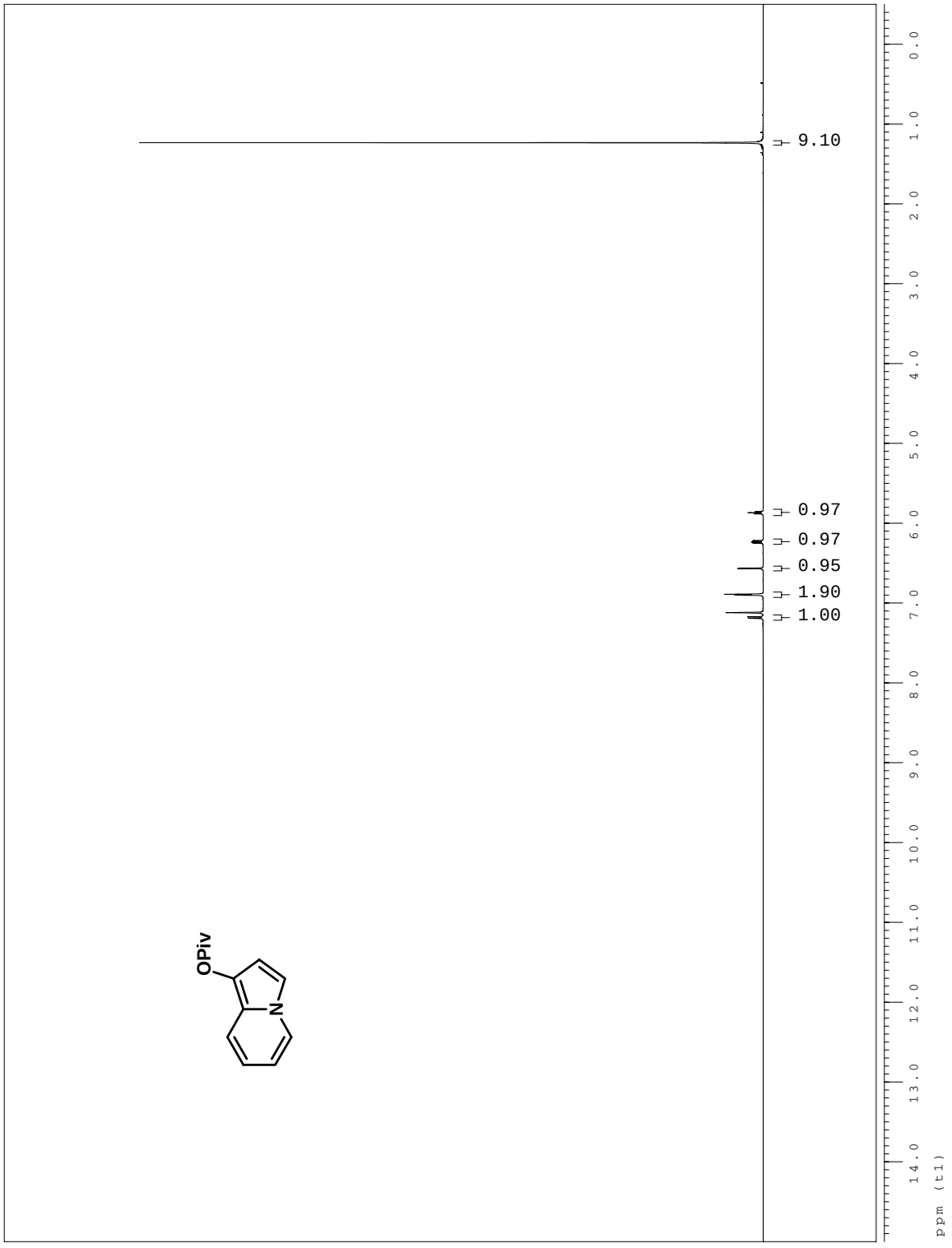

O
O
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

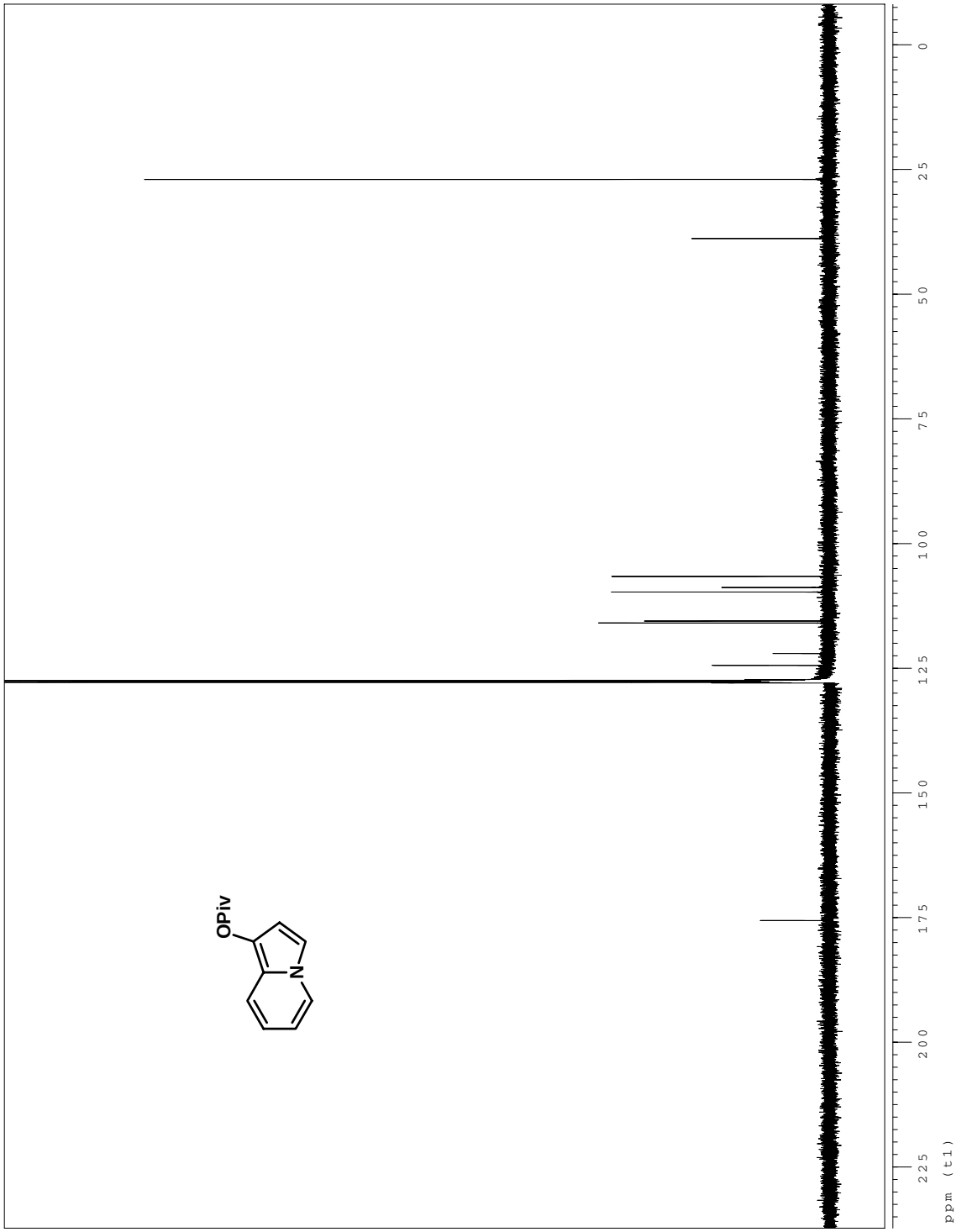

2.93
13.23
2.00
1.12
1.07
2.19
1.97
1.02
O
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

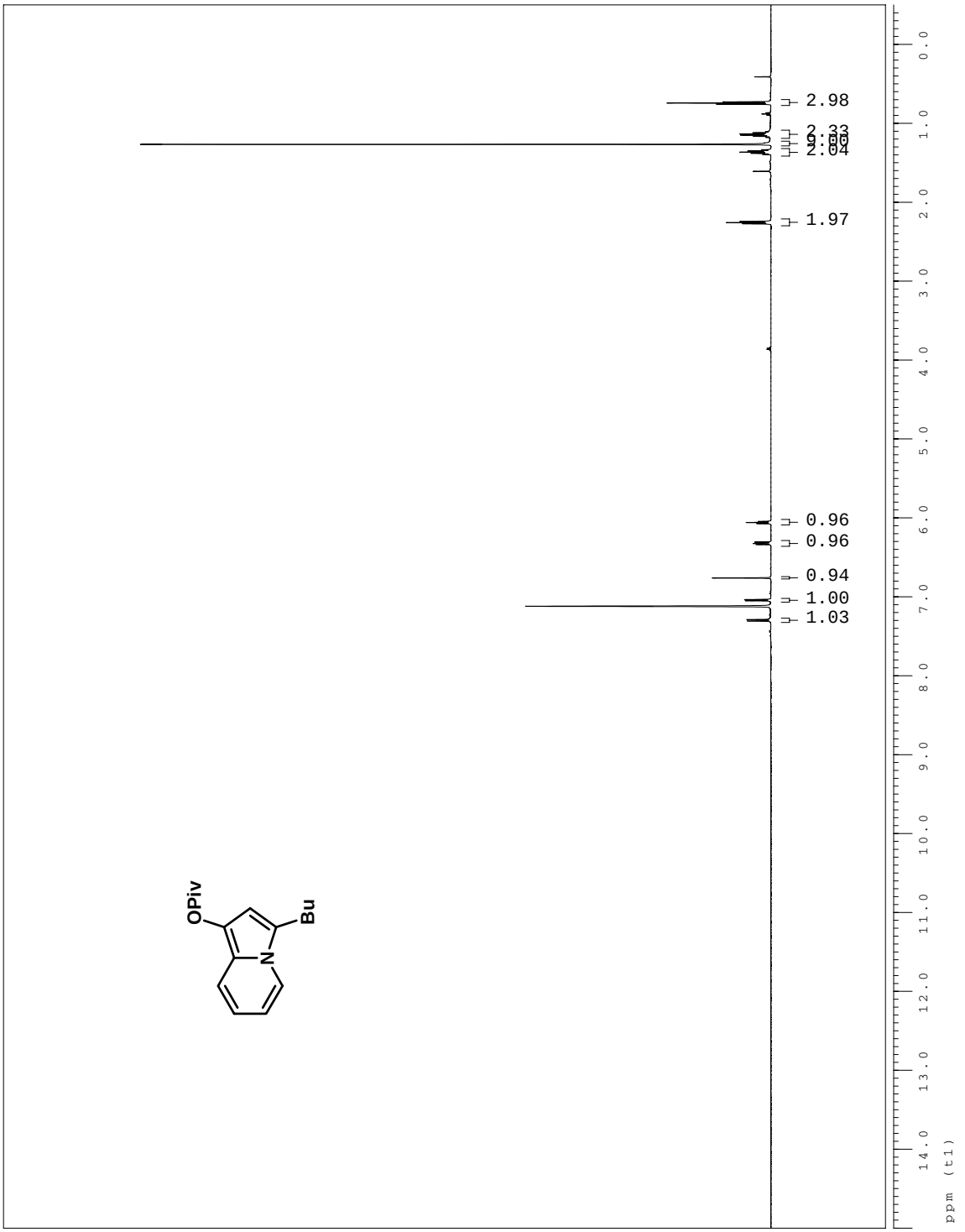

O
O
N
ppm (t1)

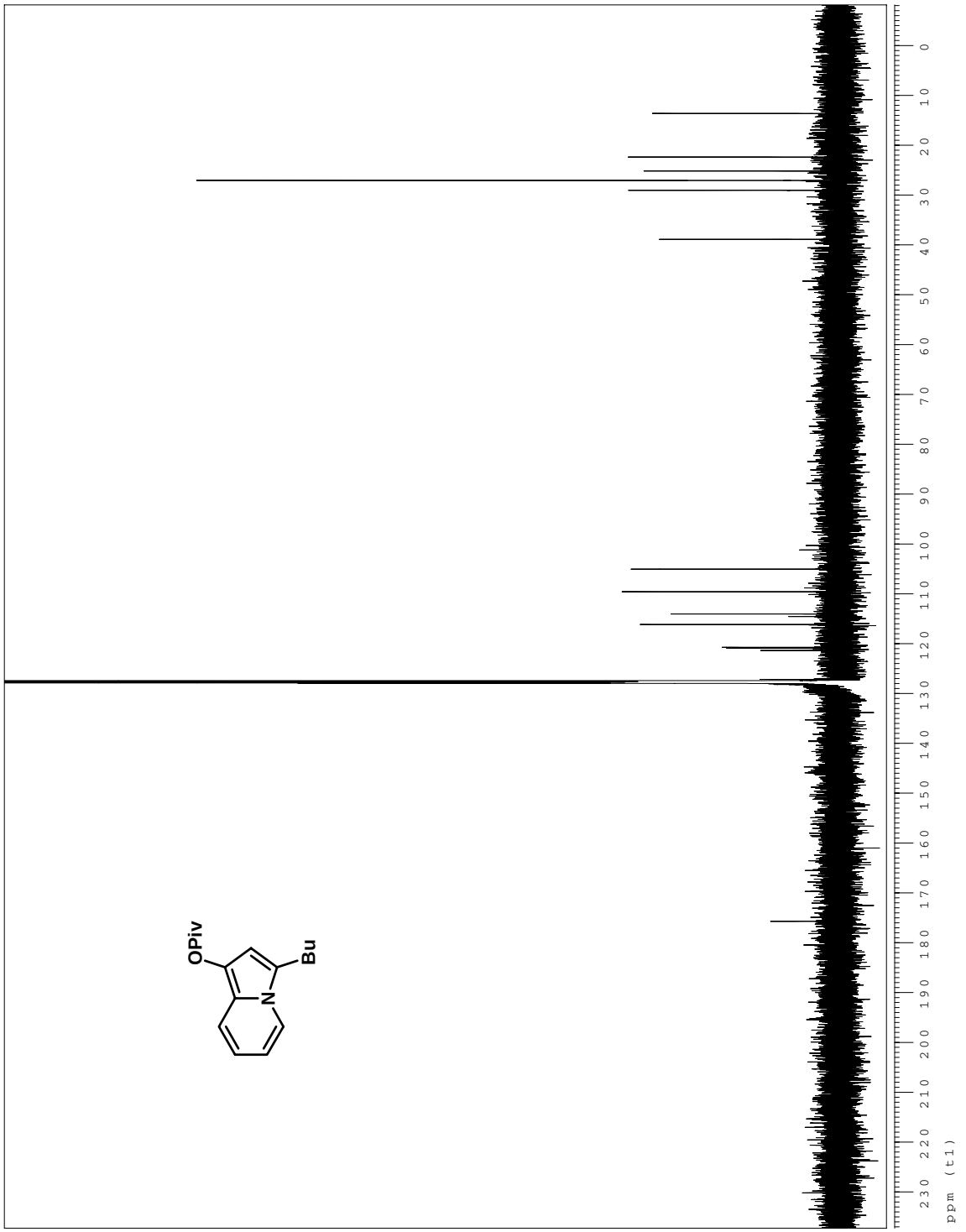

3.22
3.43
9.60
0.97
0.99
1.05
1.07
1.02
1.00
OTBS
N
ppm (t1)

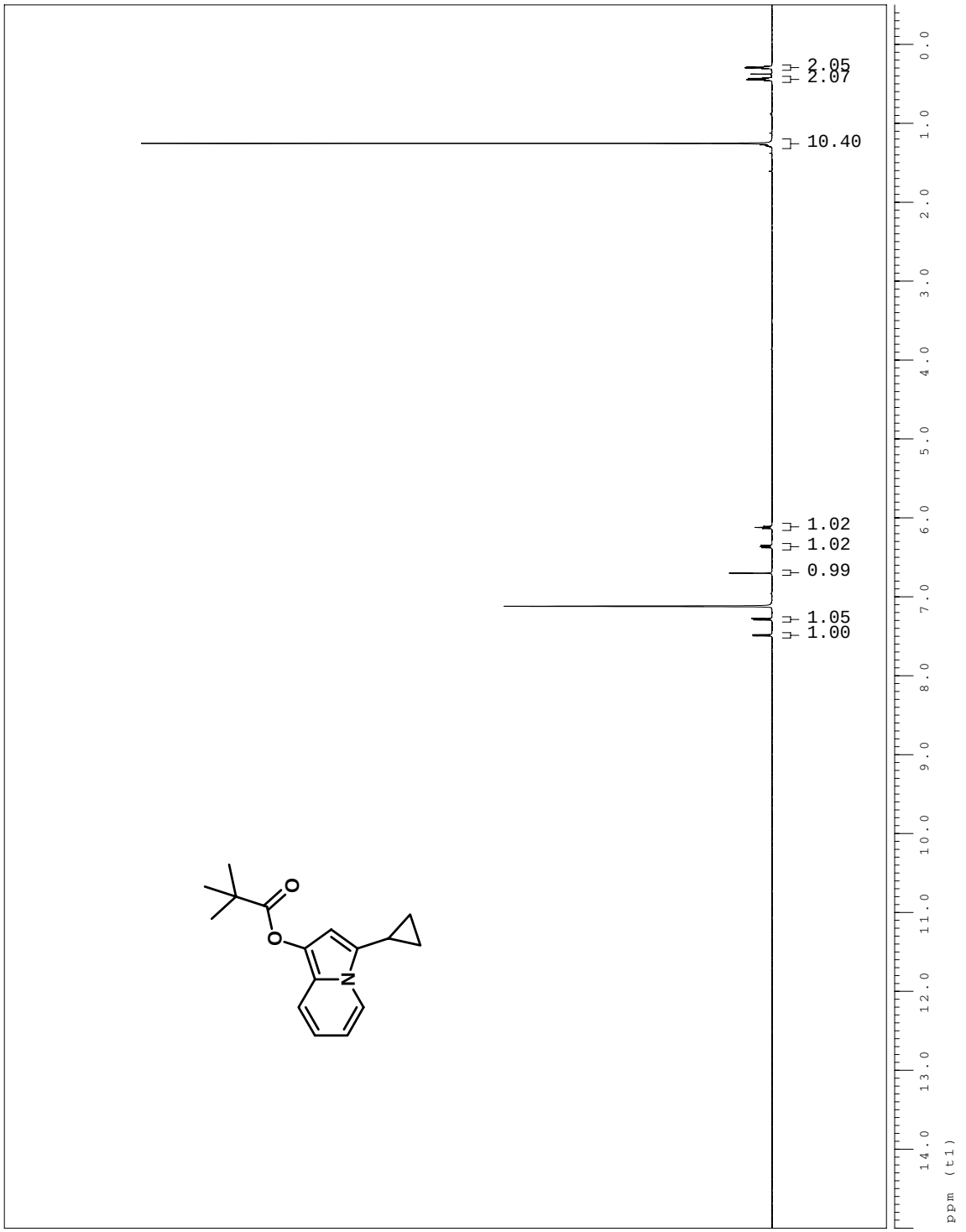

OTBS
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

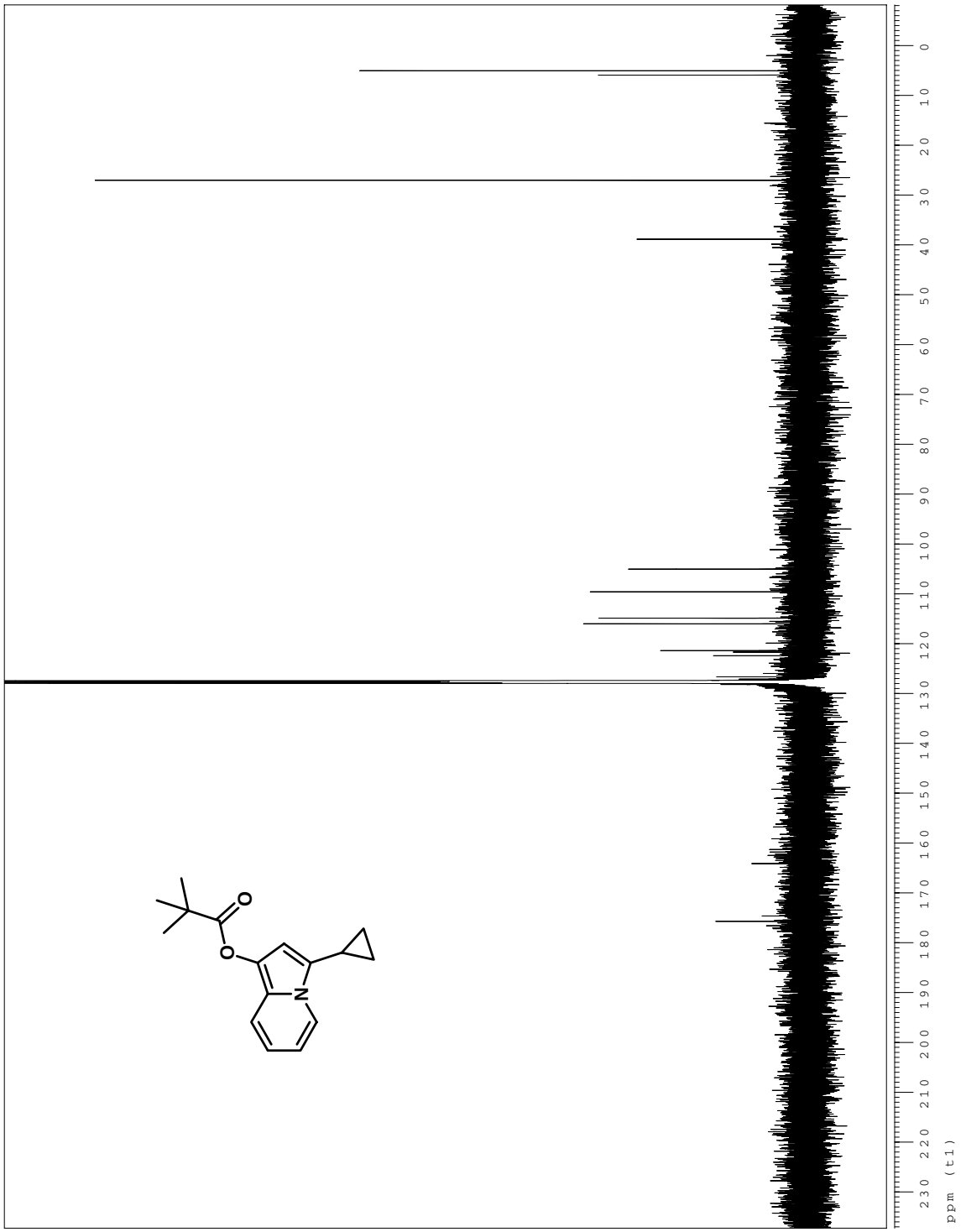

9.10
0.97
0.97
0.95
1.90
1.00
OPiv
N
14.0 13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
ppm (t1)

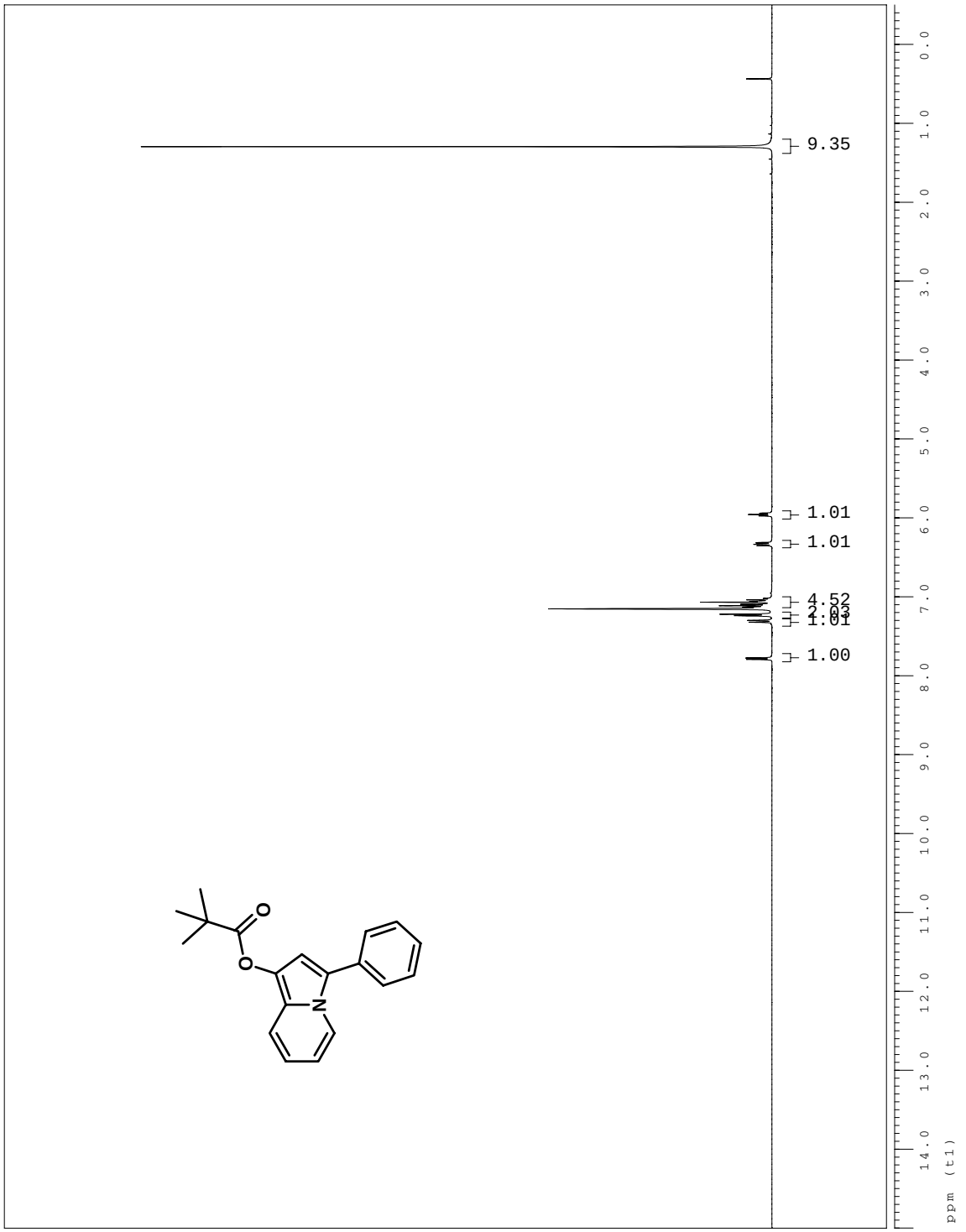

OPiv
N
0
25
50
75
100
125
150
175
200
225
ppm (t1)

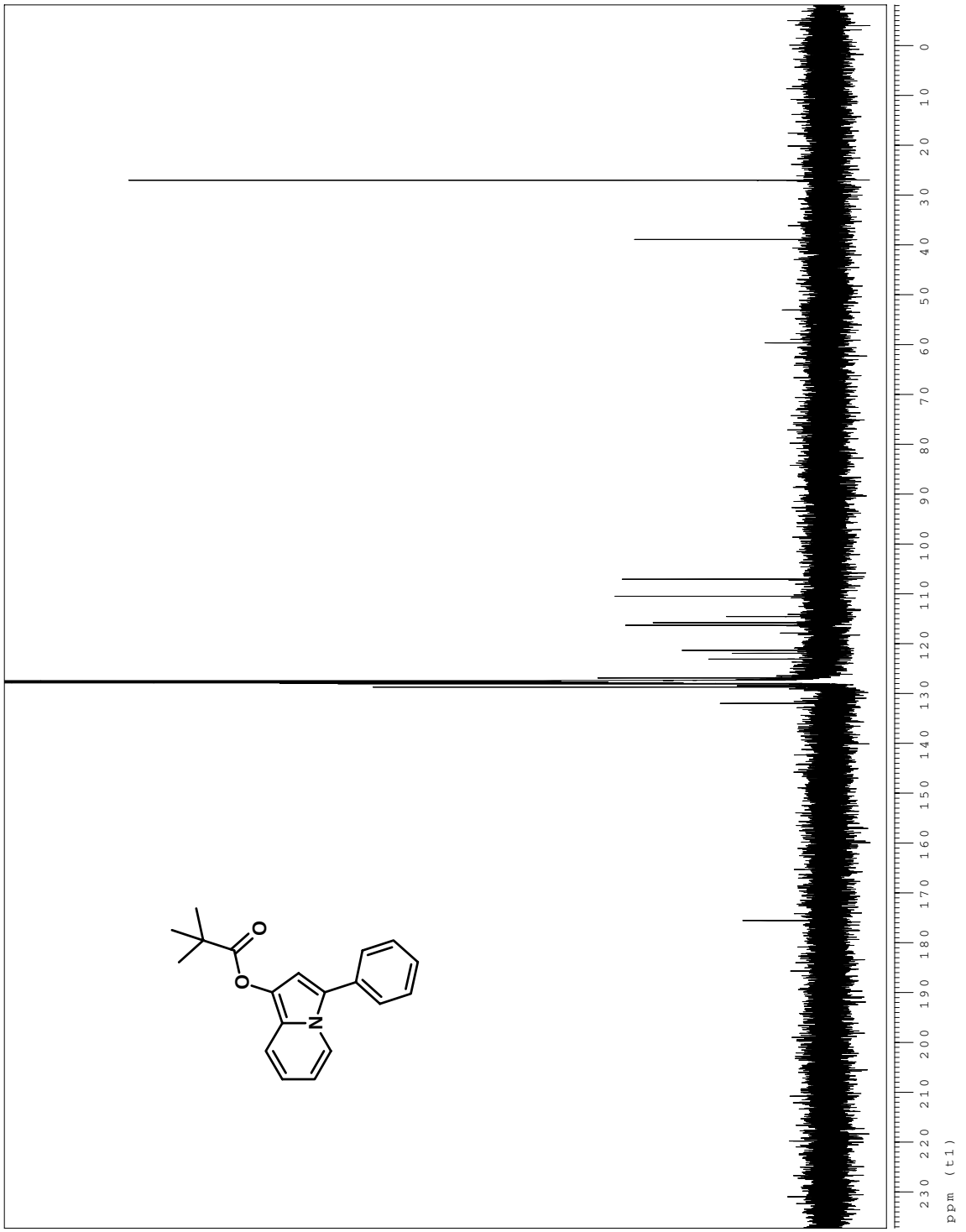

2.98
2.33
3.00
2.04
1.97
0.96
0.96
0.94
1.00
1.03
OPiv
Bu
N
ppm (t1)

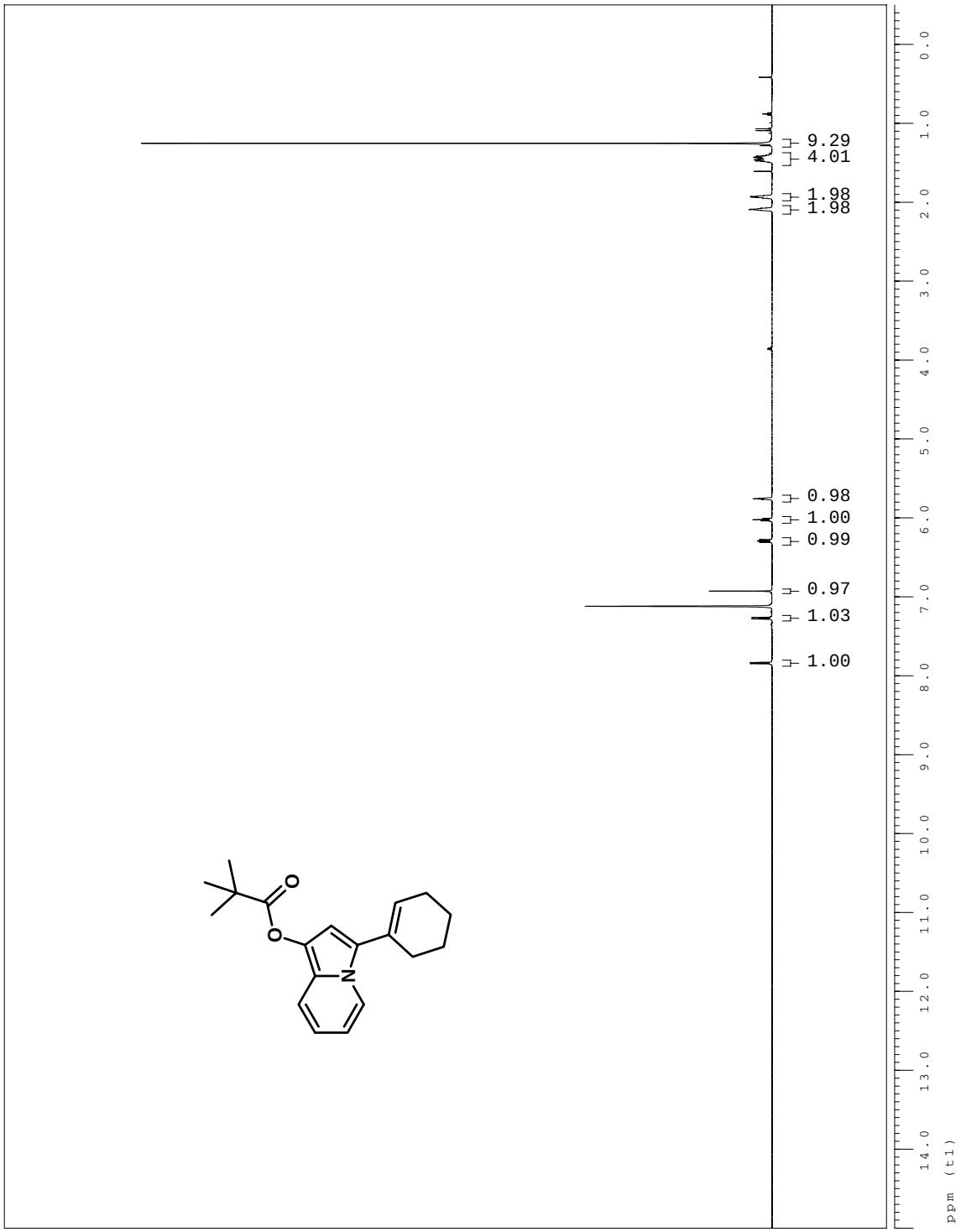

OPiv
Bu
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

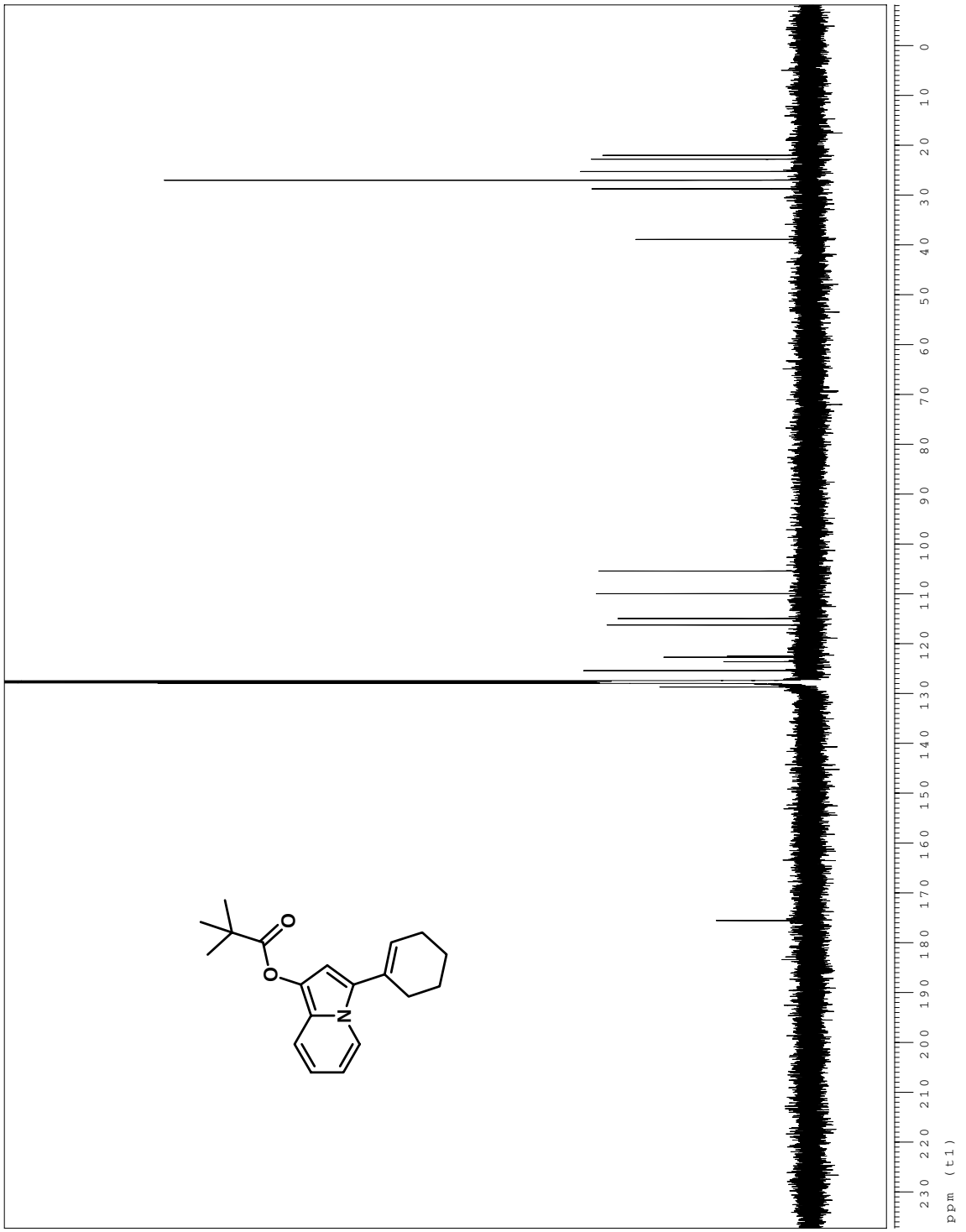

2.05
2.07
10.40
1.02
1.02
0.99
1.05
1.00
O
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

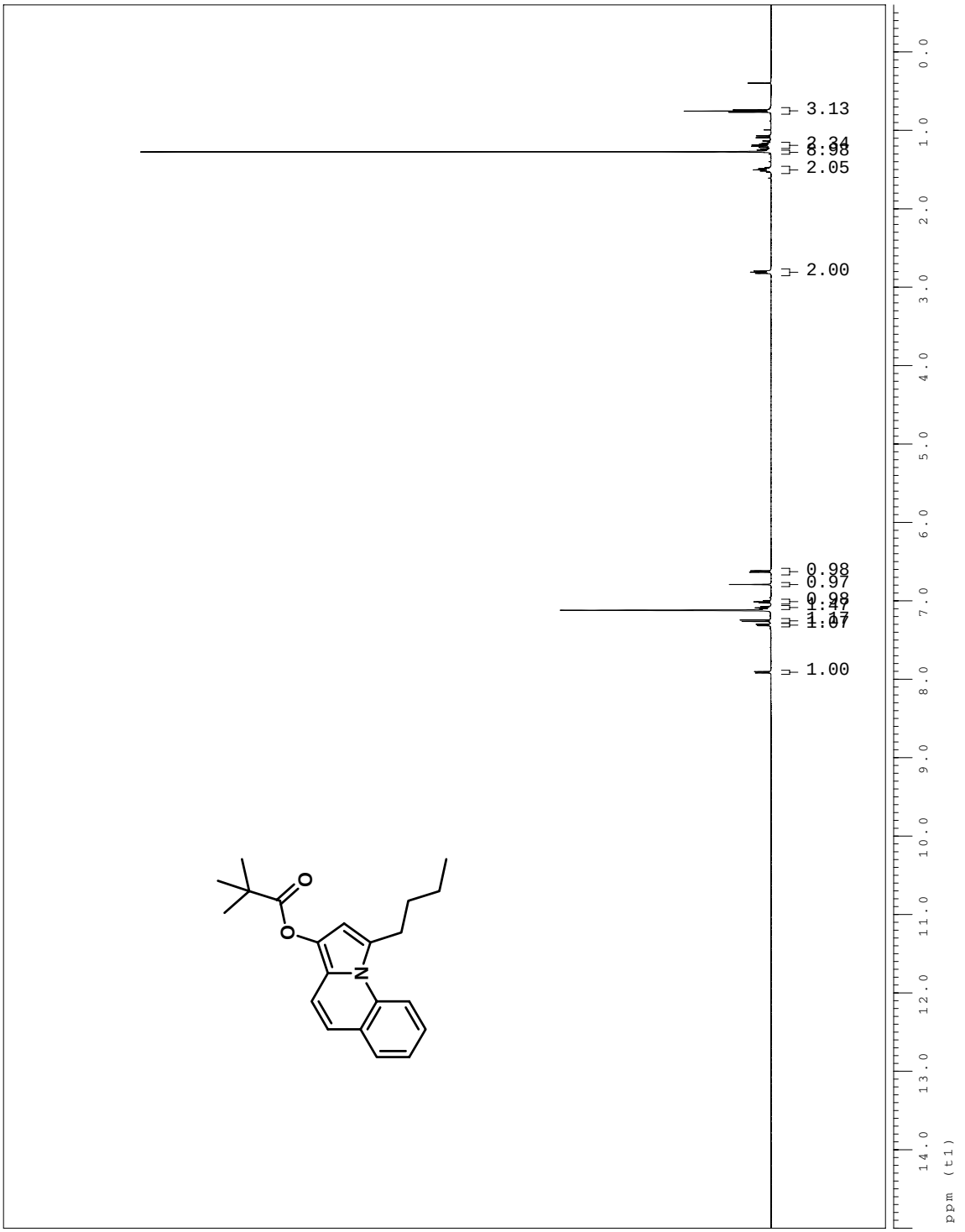

O
O
N
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

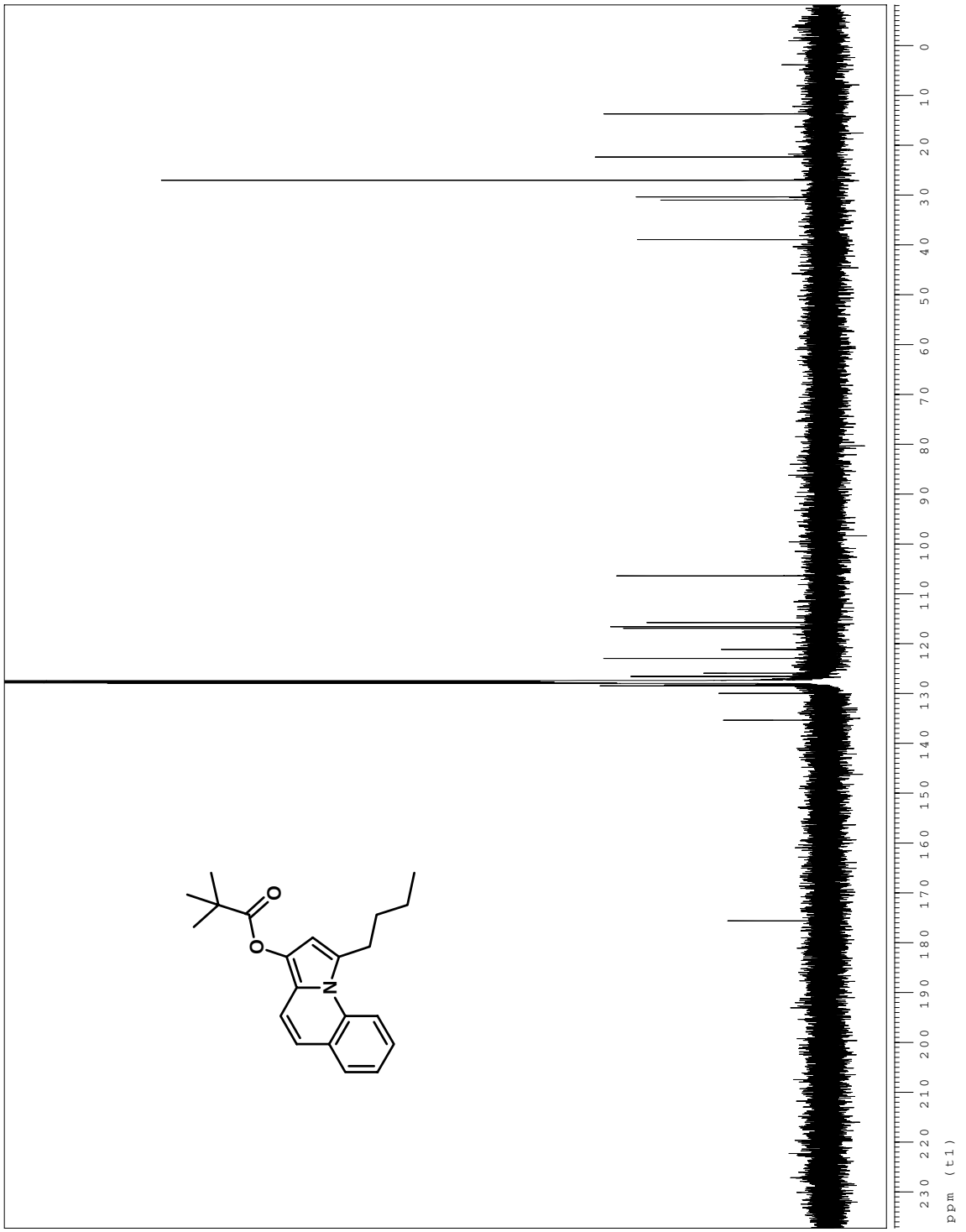

9.35
1.01
1.01
4.52
2.03
1.01
1.00
O
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

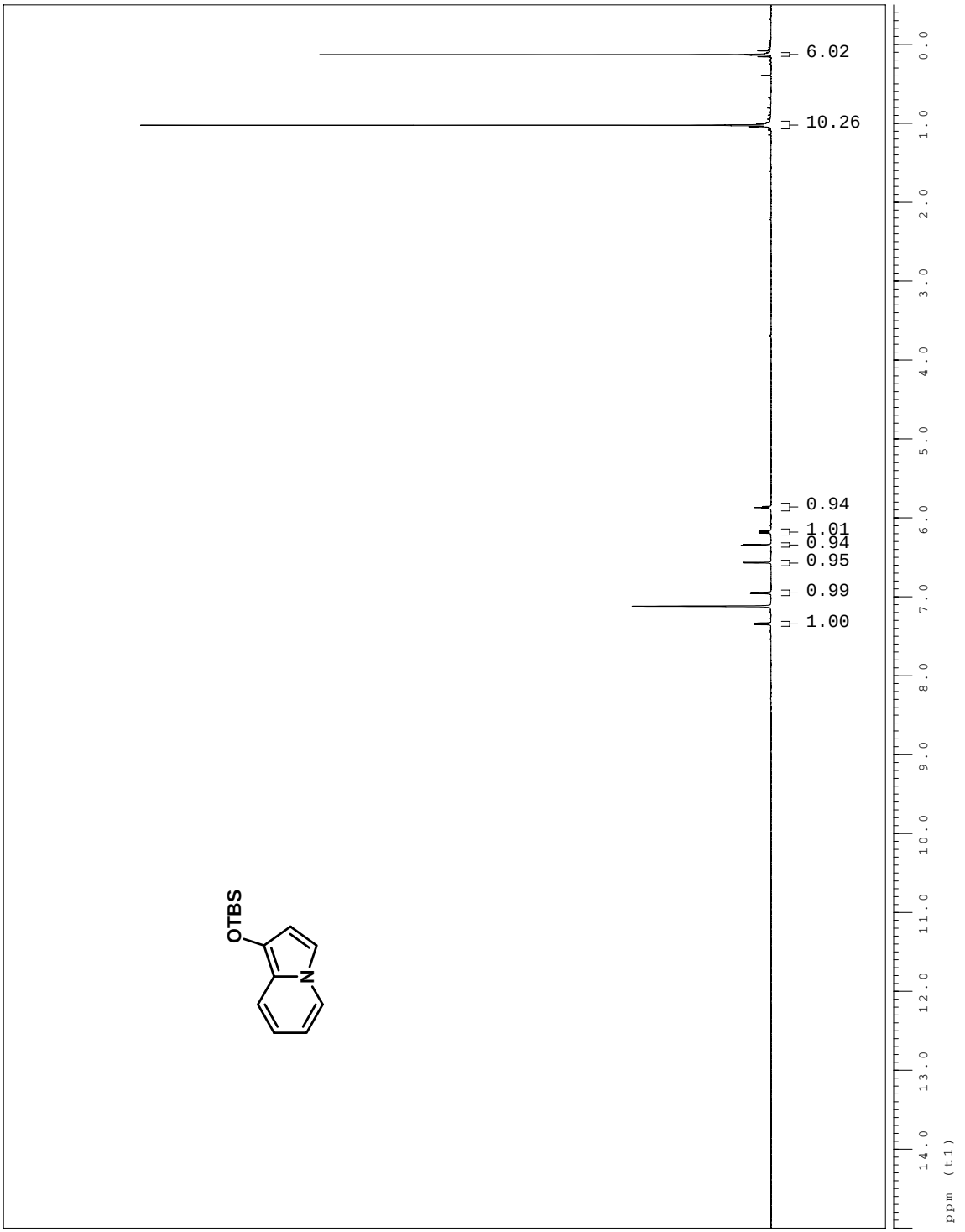

O
O
N
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (t1)

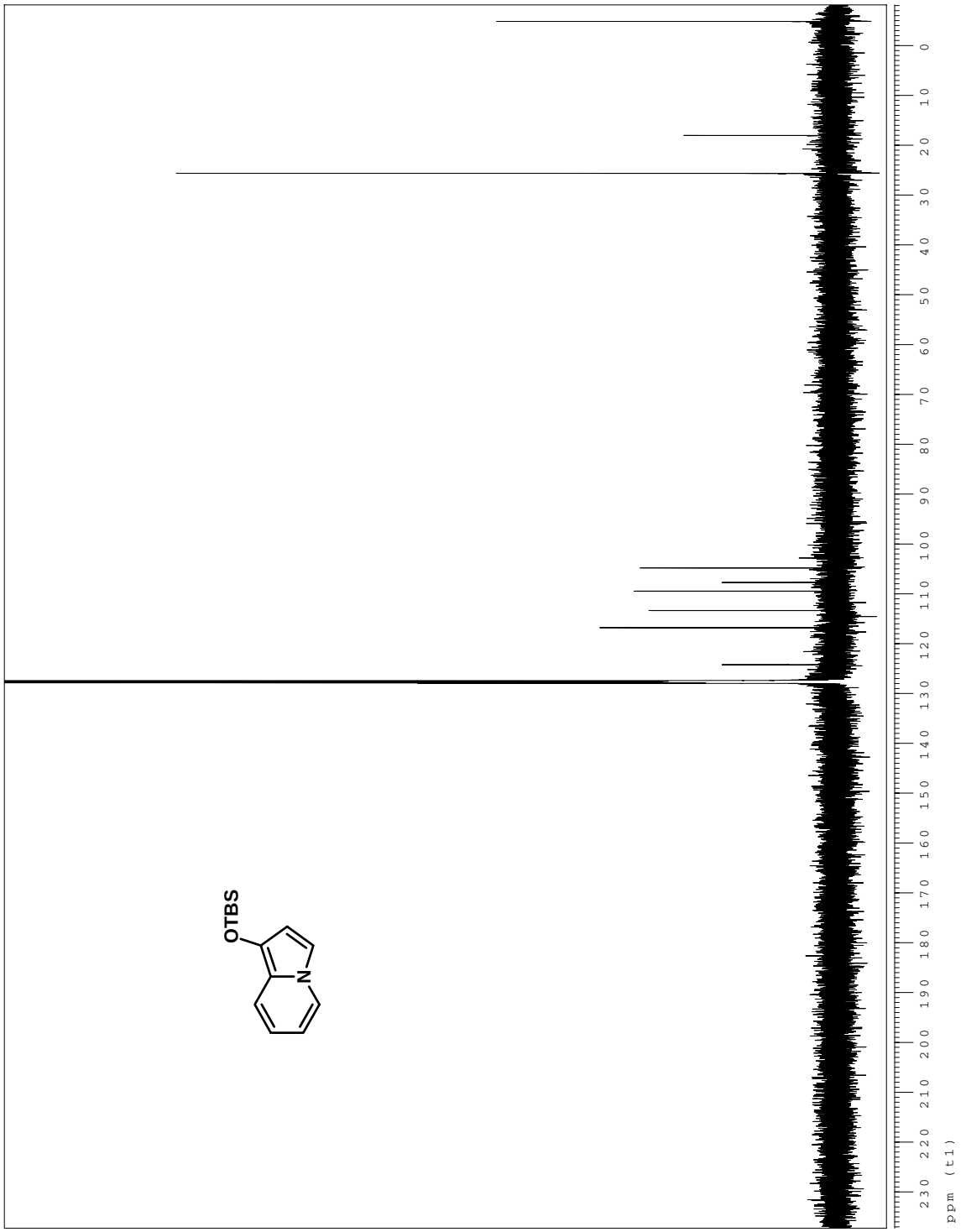

9.29
4.01
1.98
1.98
0.98
1.00
0.99
0.97
1.03
1.00
O
O
N
ppm (t1)

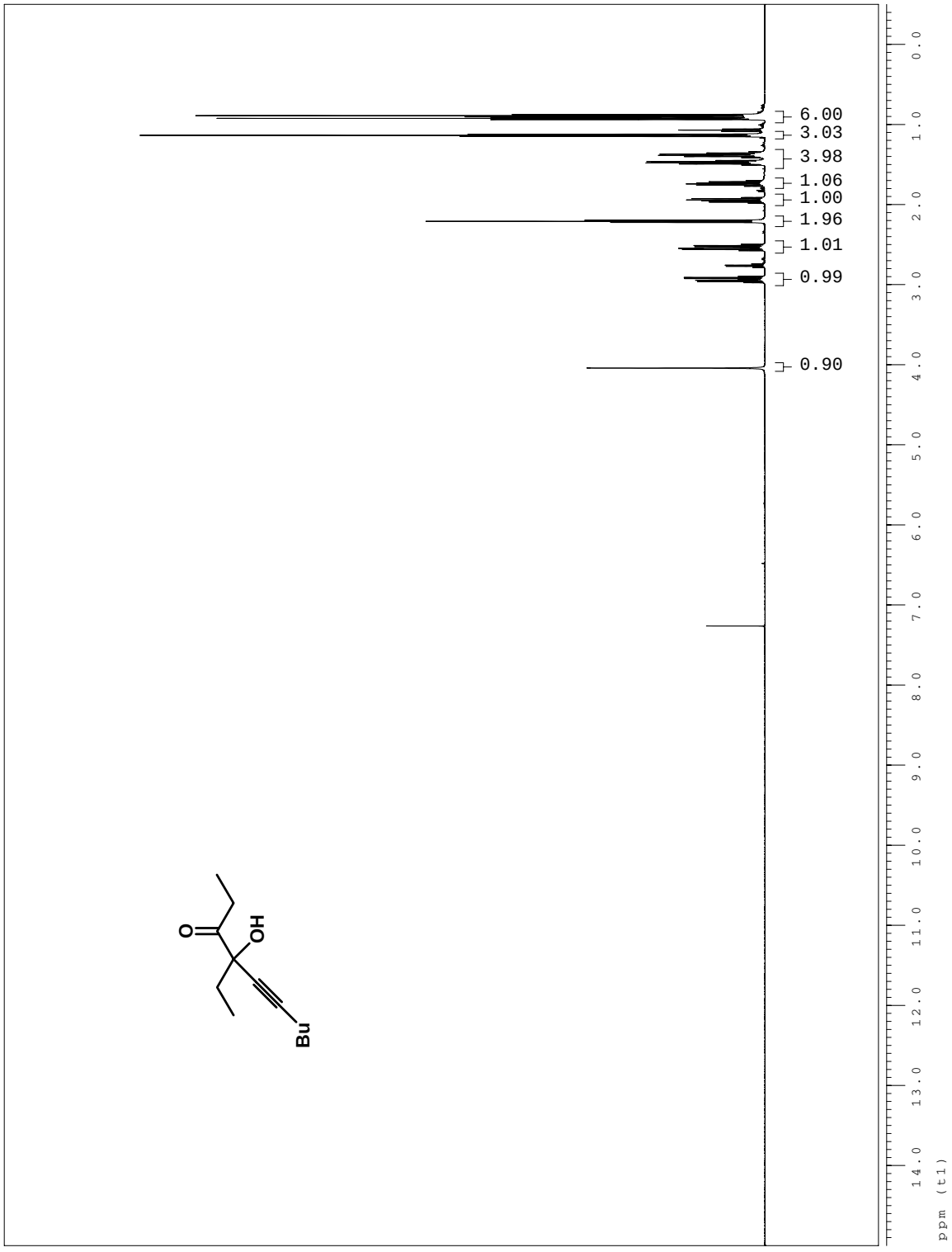

O
O
N
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

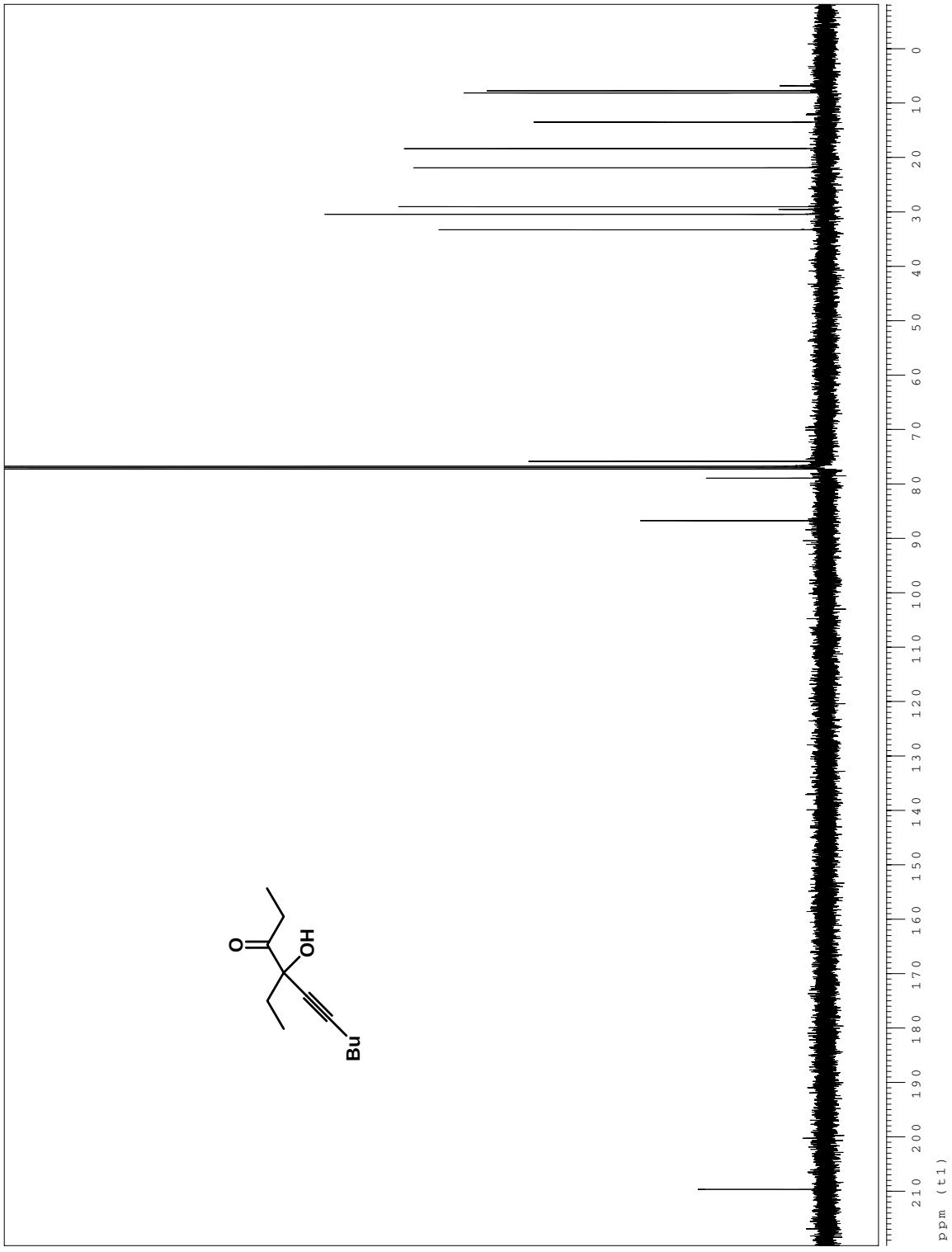

3.13
2.34
8.98
2.05
2.00
0.98
0.97
0.98
1.17
1.07
1.00
O
O
N
ppm (t1)

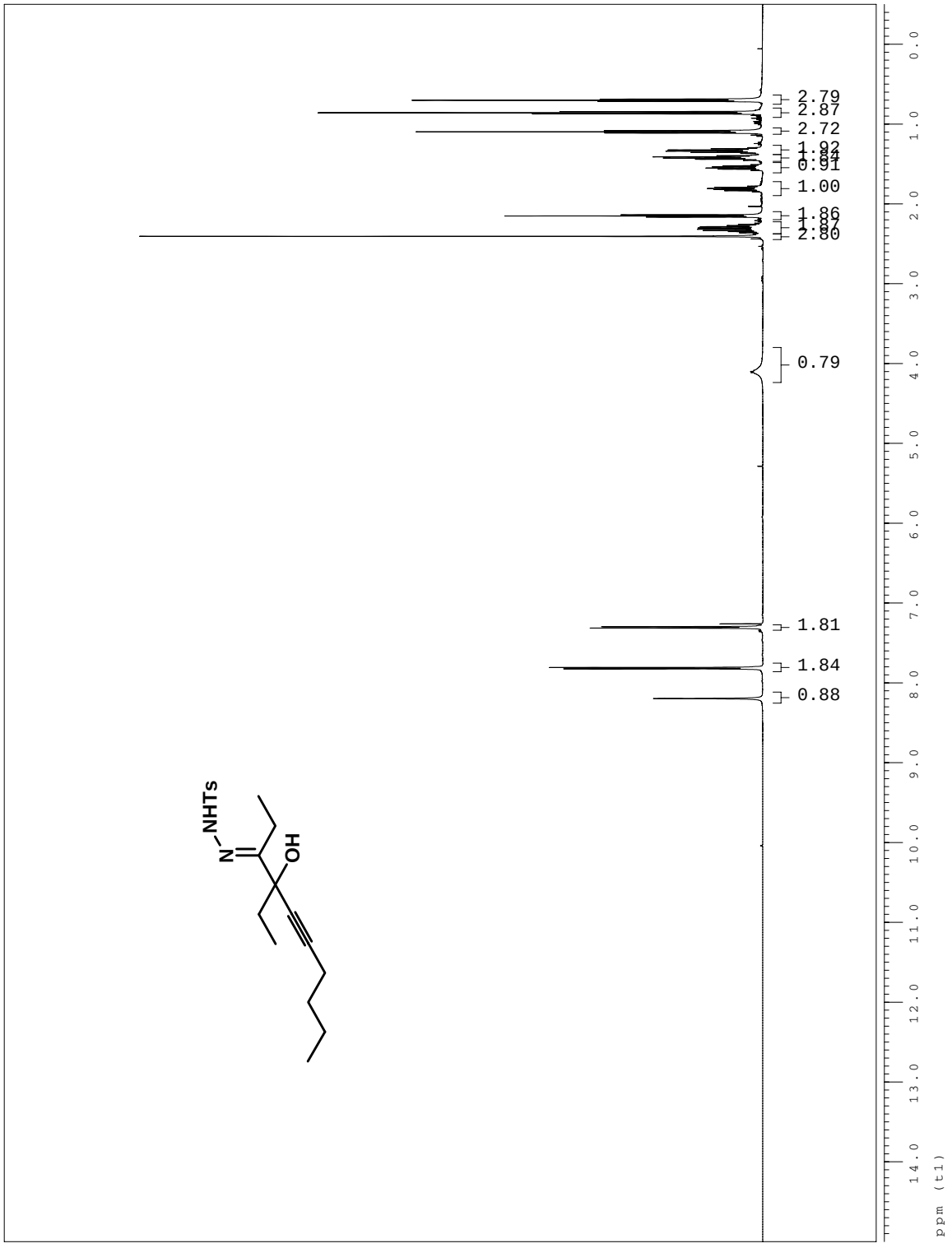

O
O
N
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

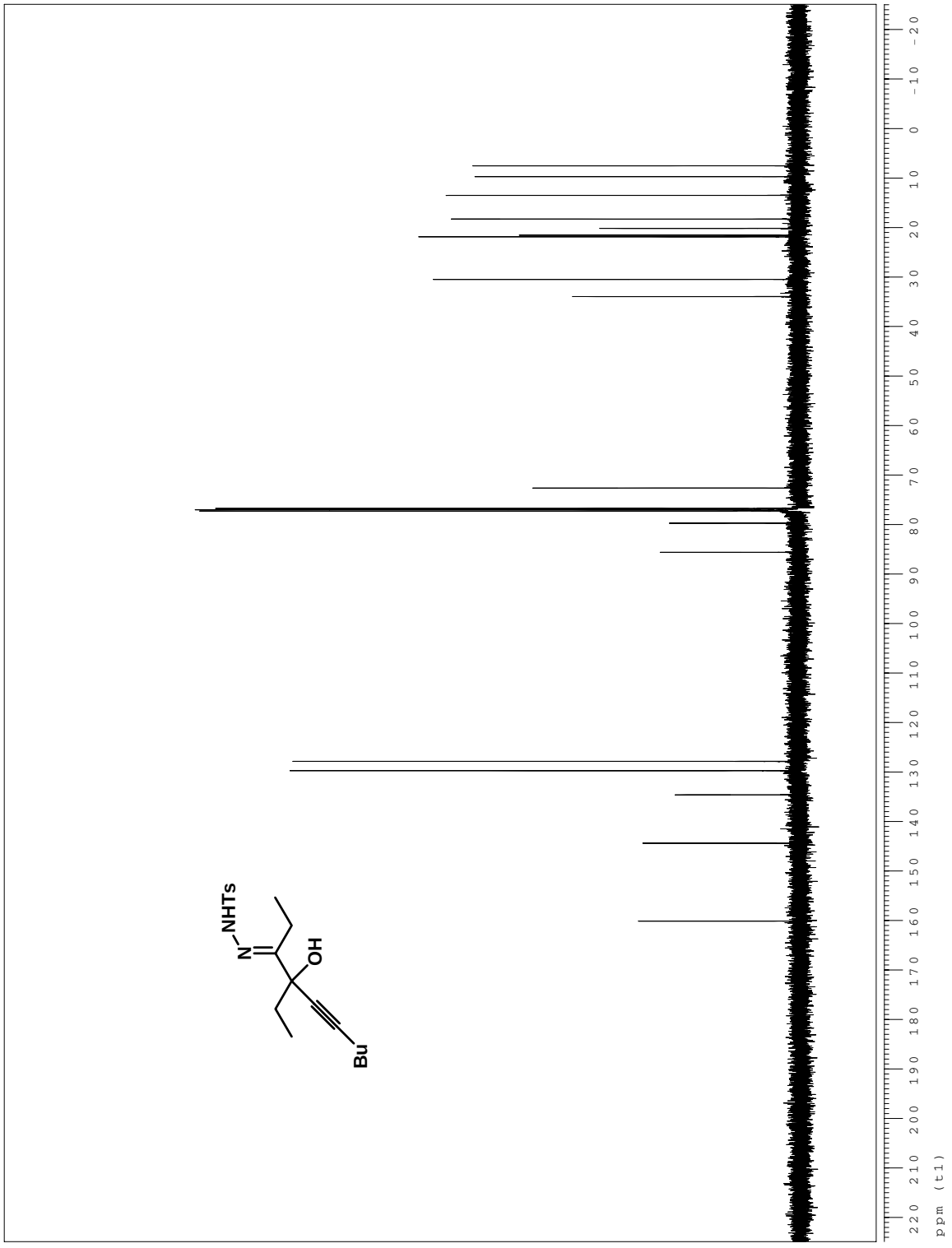

6.02
10.26
0.94
1.01
0.94
0.95
0.99
1.00
OTBS
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

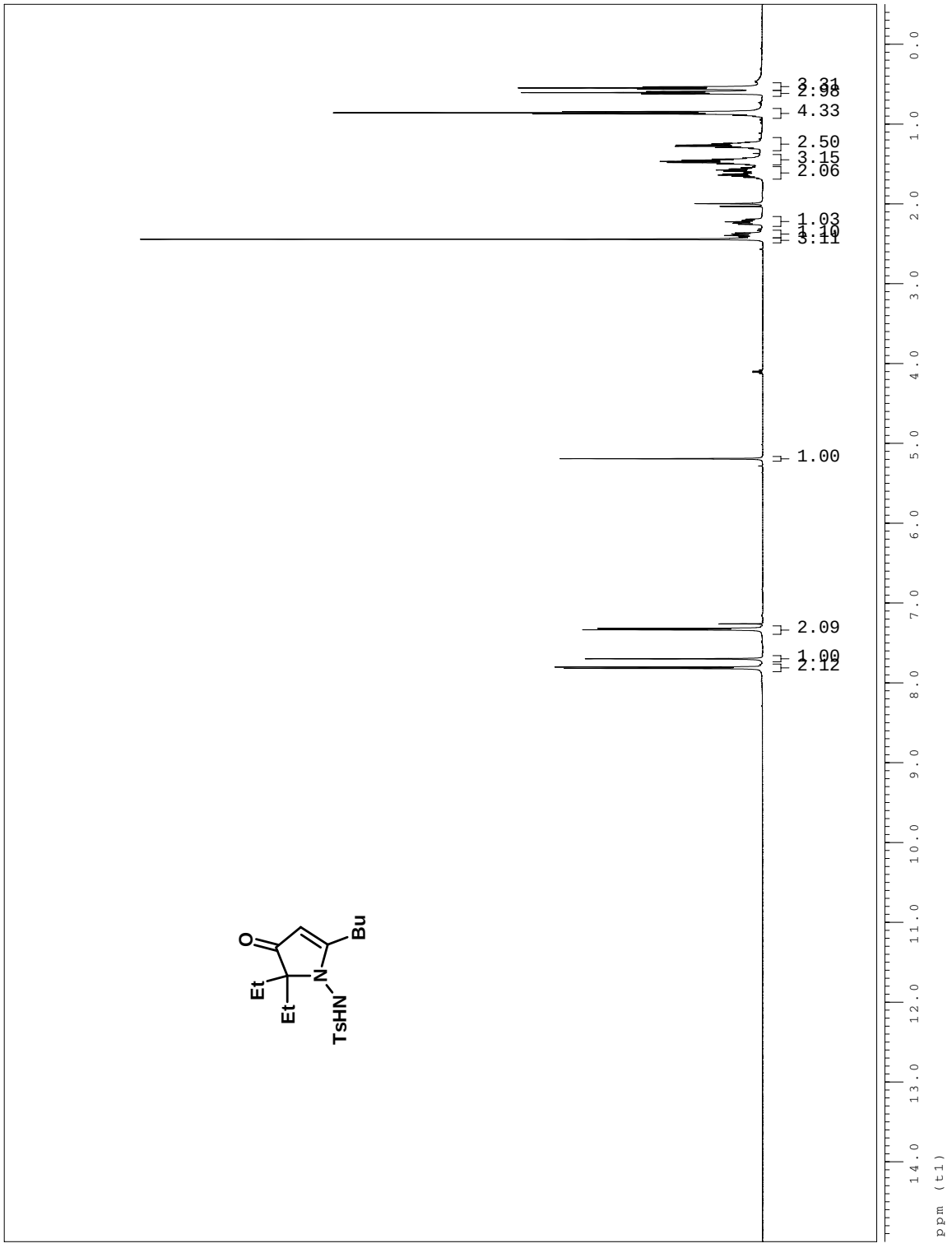

OTBS
N
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm (t1)

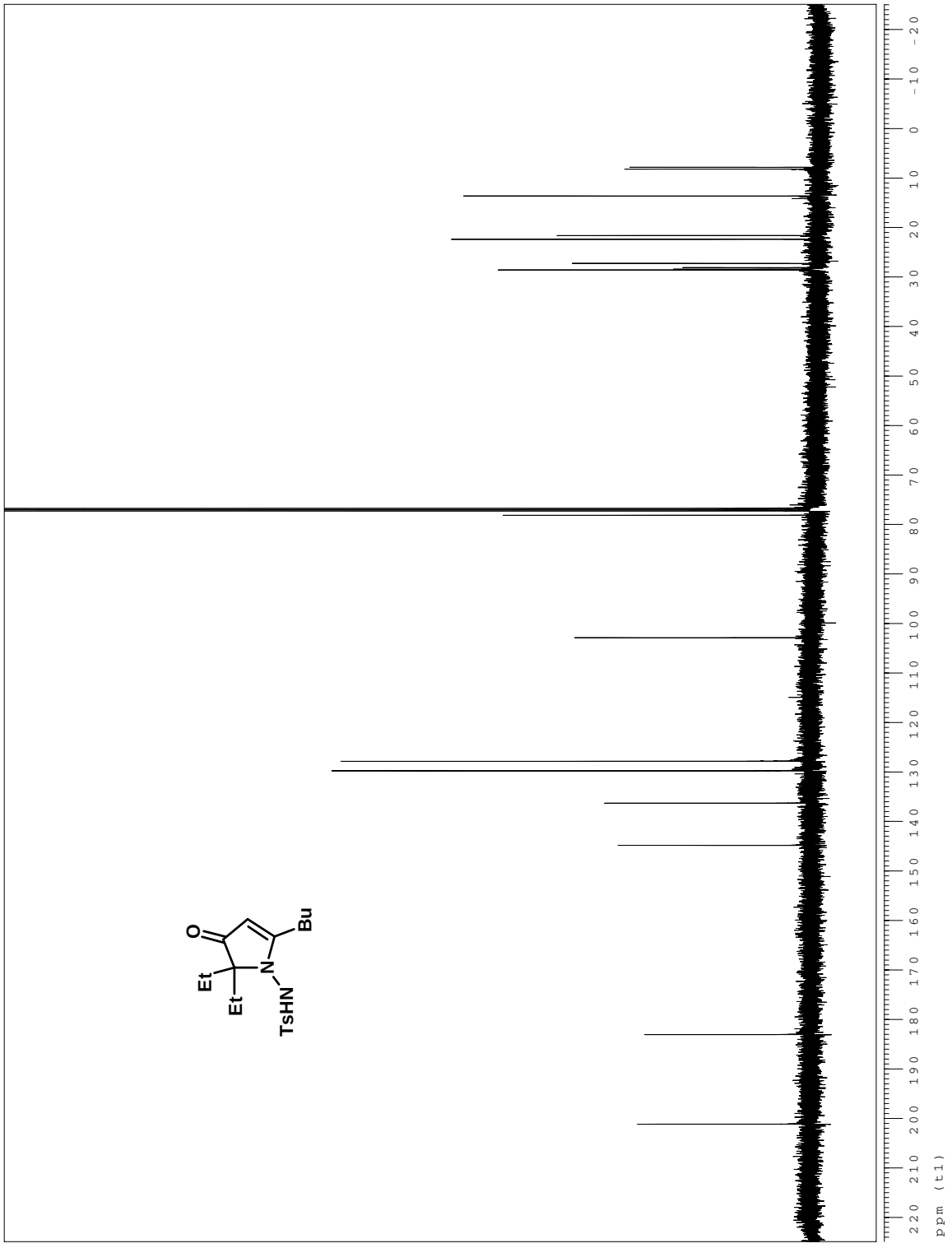

6.00
3.03
3.98
1.06
1.00
1.96
1.01
0.99
0.90
O
OH
Bu
ppm (t1)

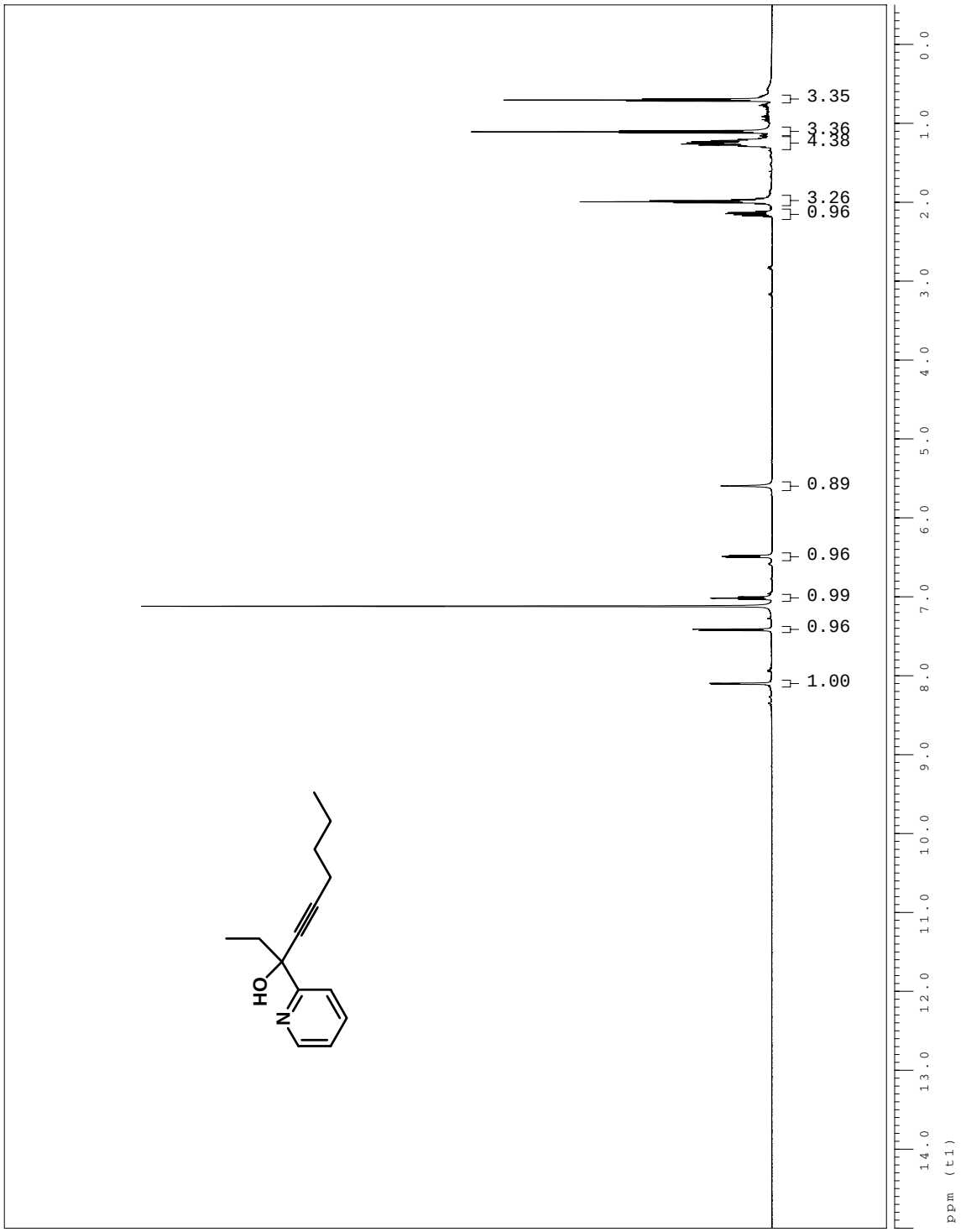

O
OH
Bu
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
ppm (t1)

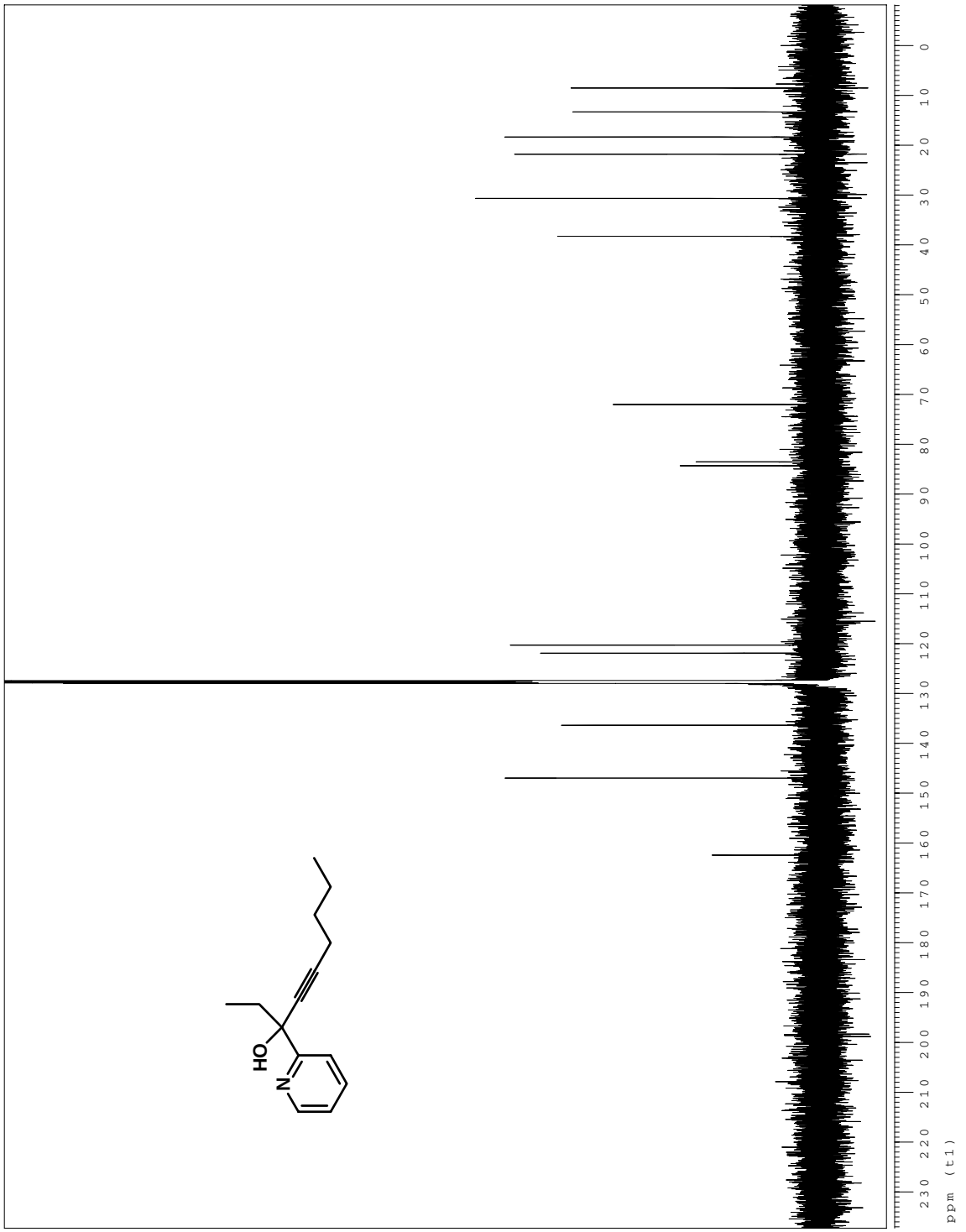

2.79
2.87
2.72
1.92
1.84
0.91
1.00
1.86
1.87
2.80
0.79
1.81
1.84
0.88
NHTs
N
OH
14.0
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

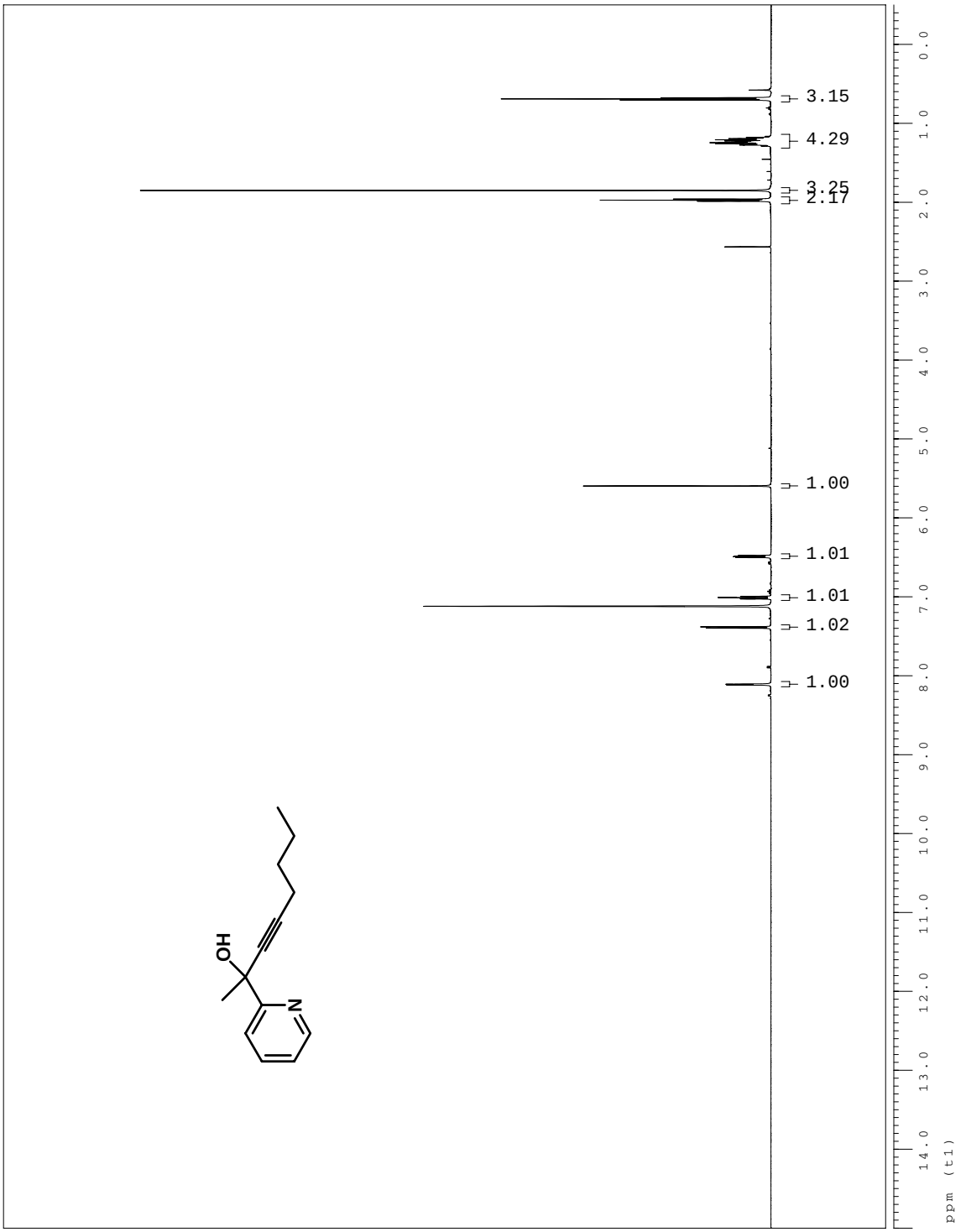

NHTs
N
OH
Bu
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
ppm (t1)

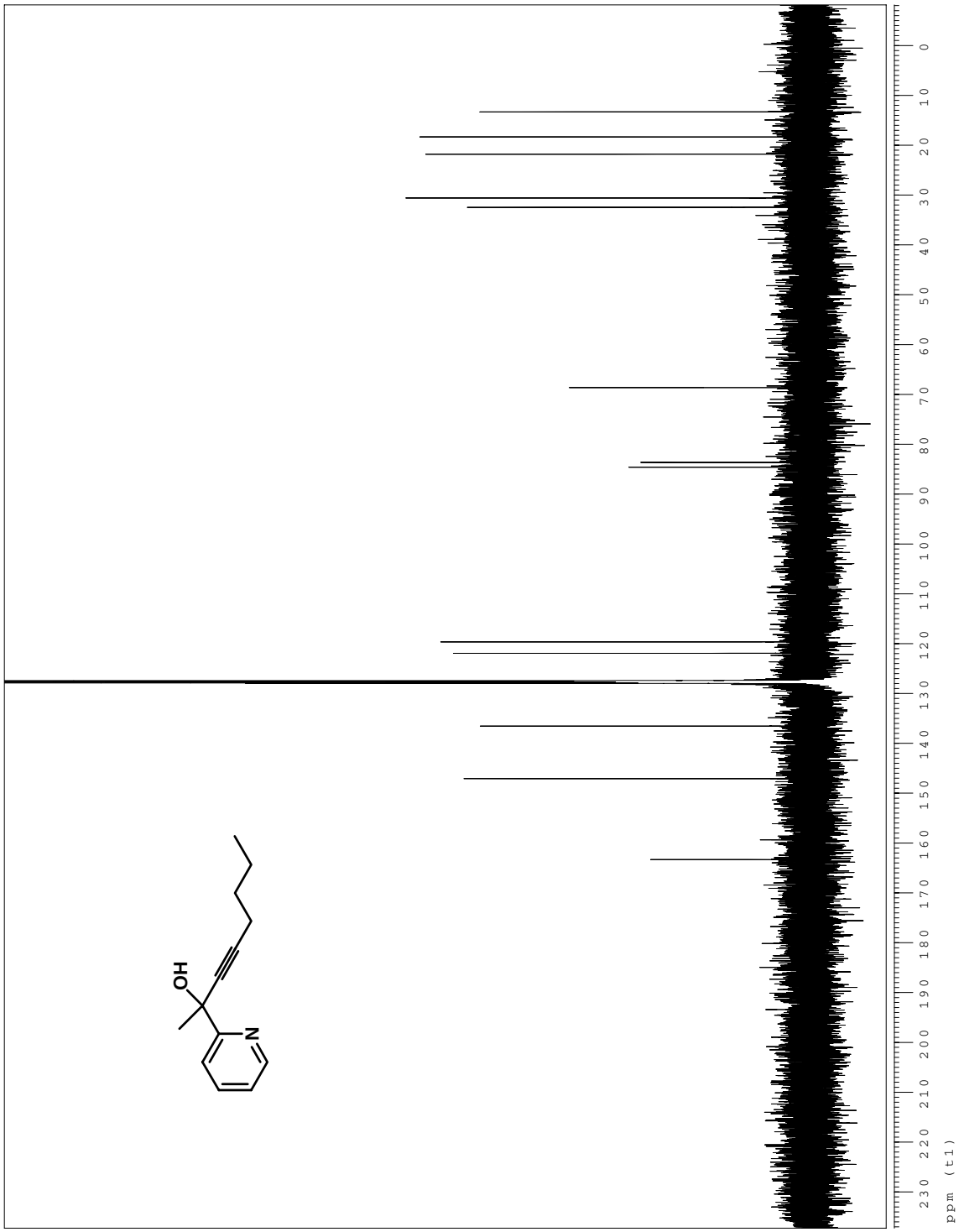

3.31
2.98
4.33
2.50
3.15
2.06
1.03
1.10
3.11
1.00
2.09
1.00
2.12
O
Bu
Et
Et
N
TsHN
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

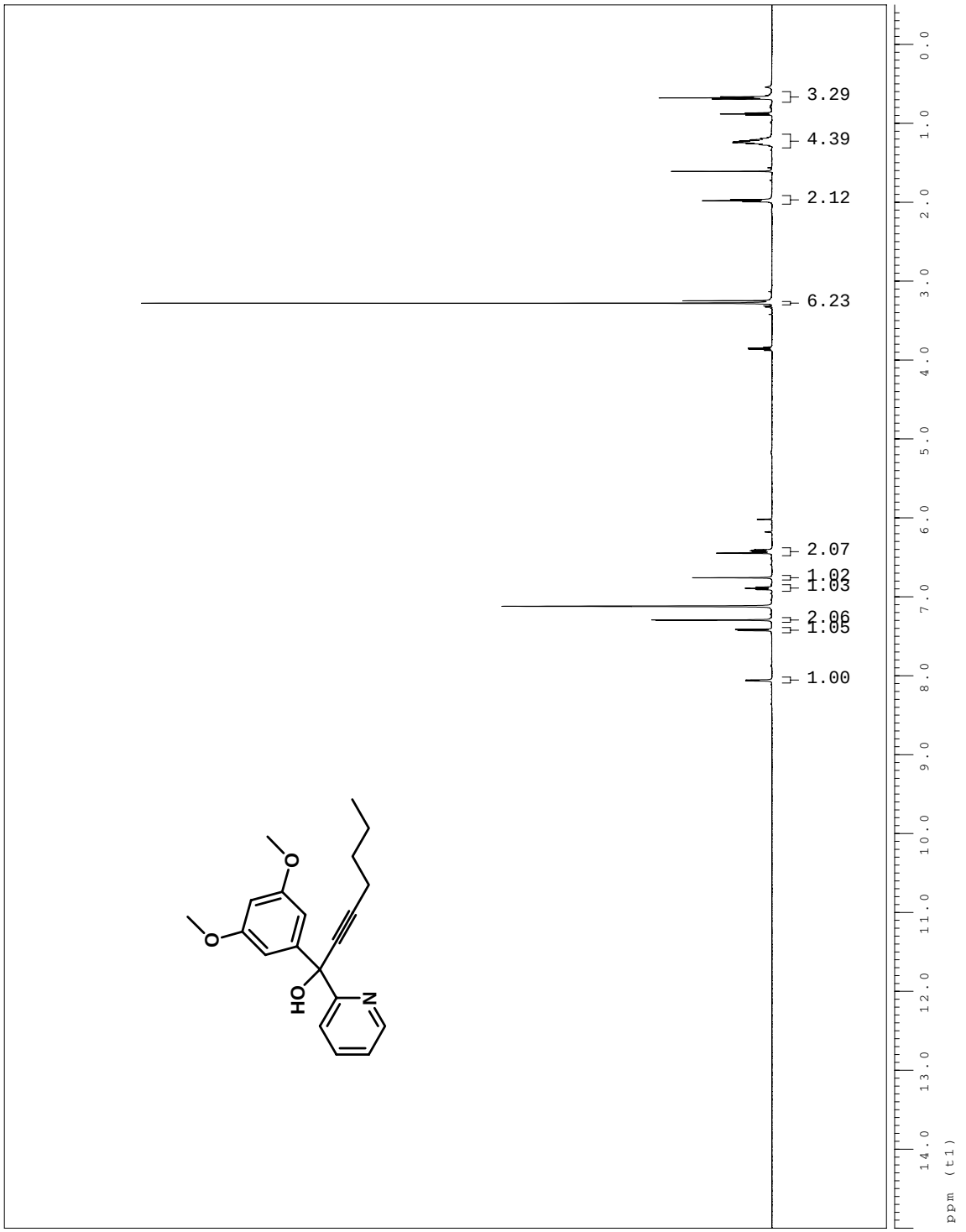

O
Bu
Et
N
Et
TsHN
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
ppm (t1)

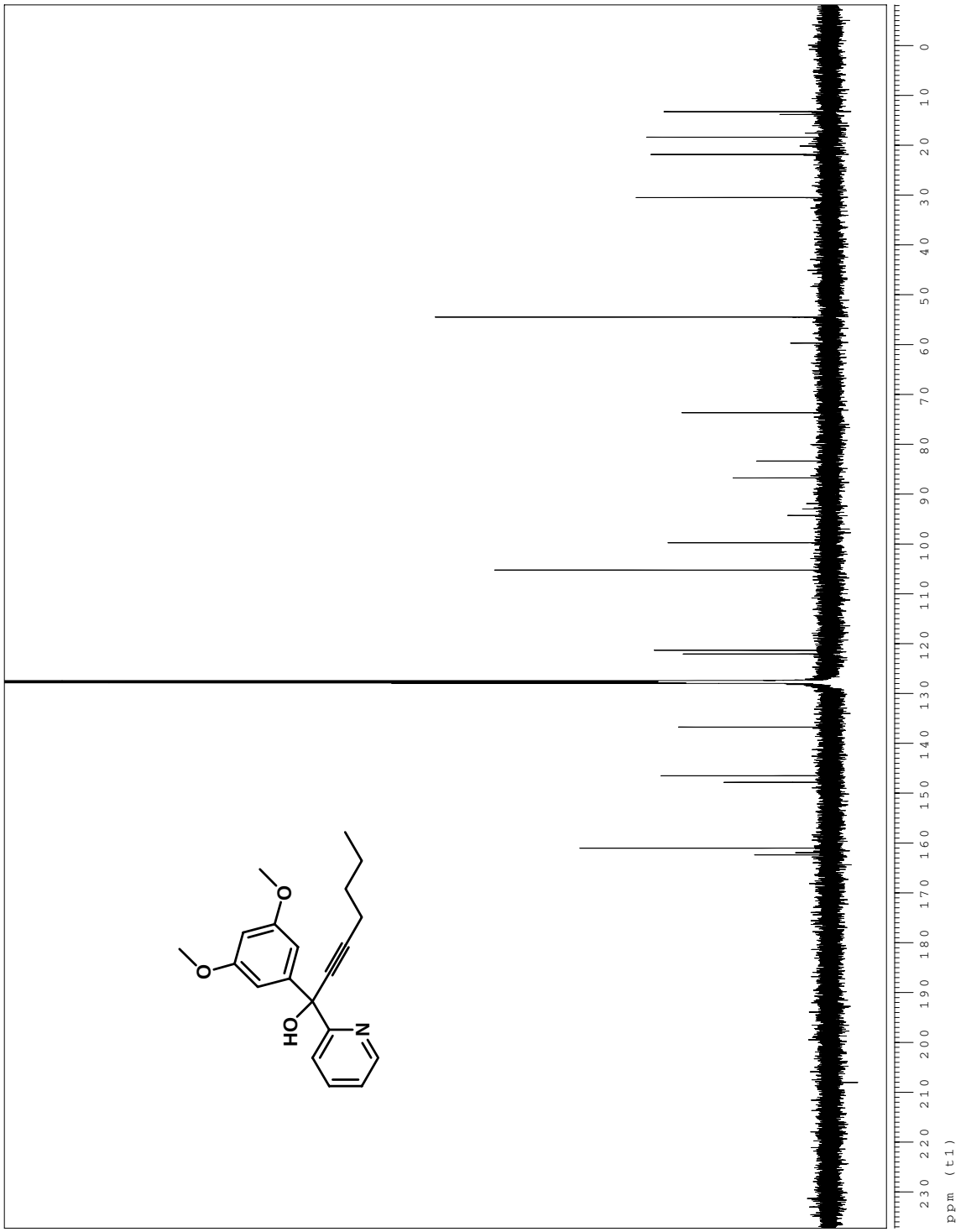

3.35
3.36
4.38
3.26
0.96
0.89
0.96
0.99
0.96
1.00
HO
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

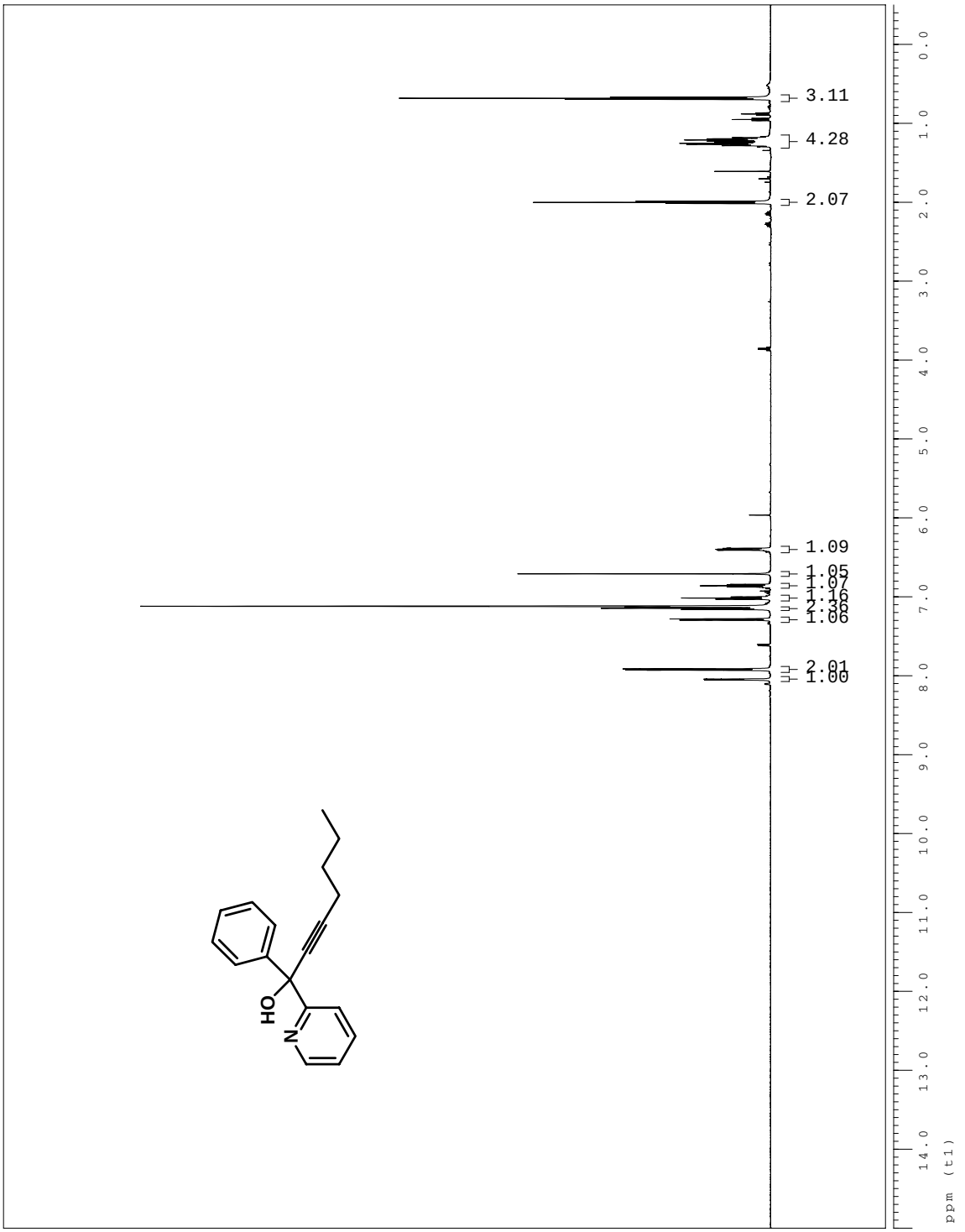

HO
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

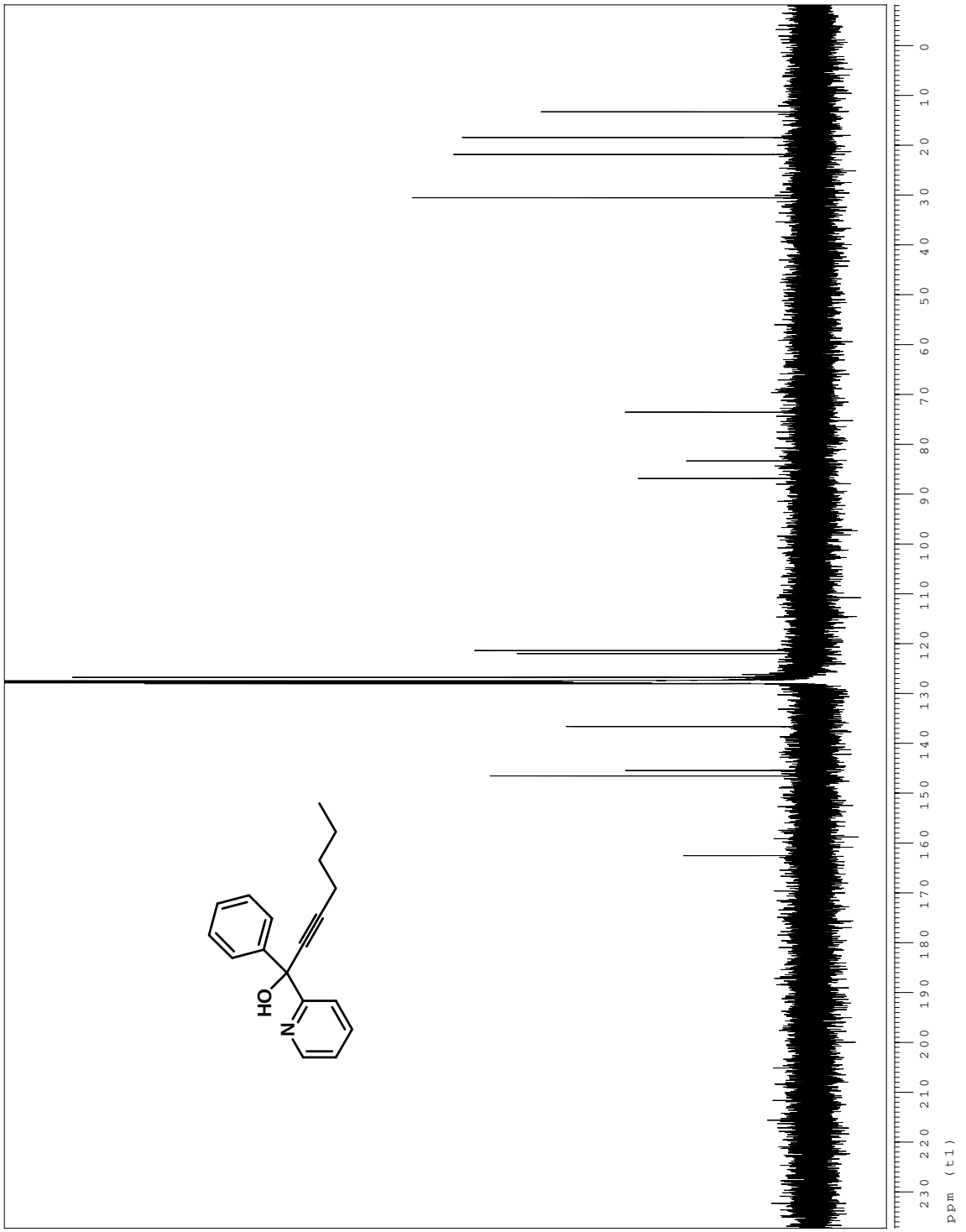

3.15
4.29
3.25
2.17
1.00
1.01
1.01
1.02
1.00
OH
N
ppm (t1)

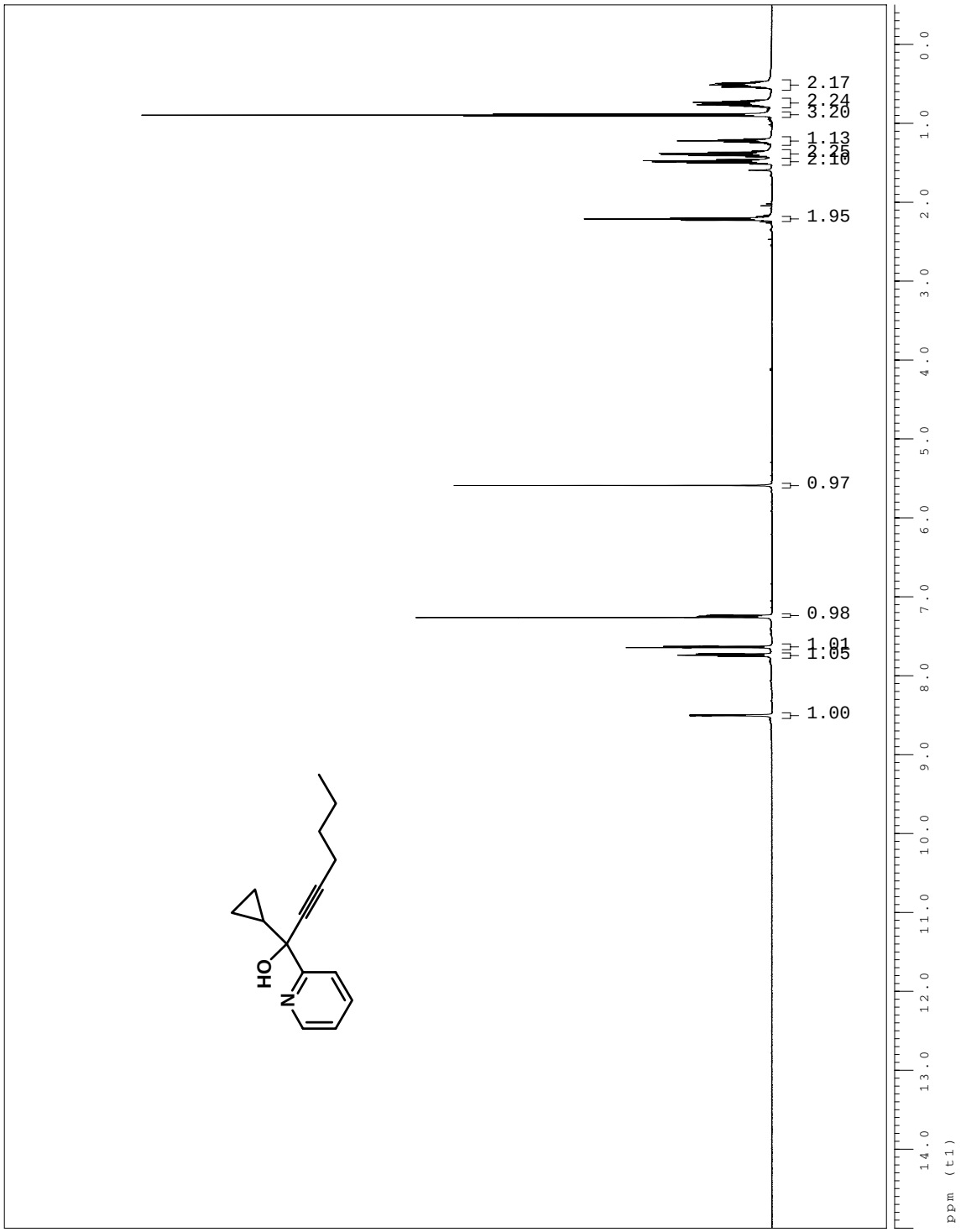

OH
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

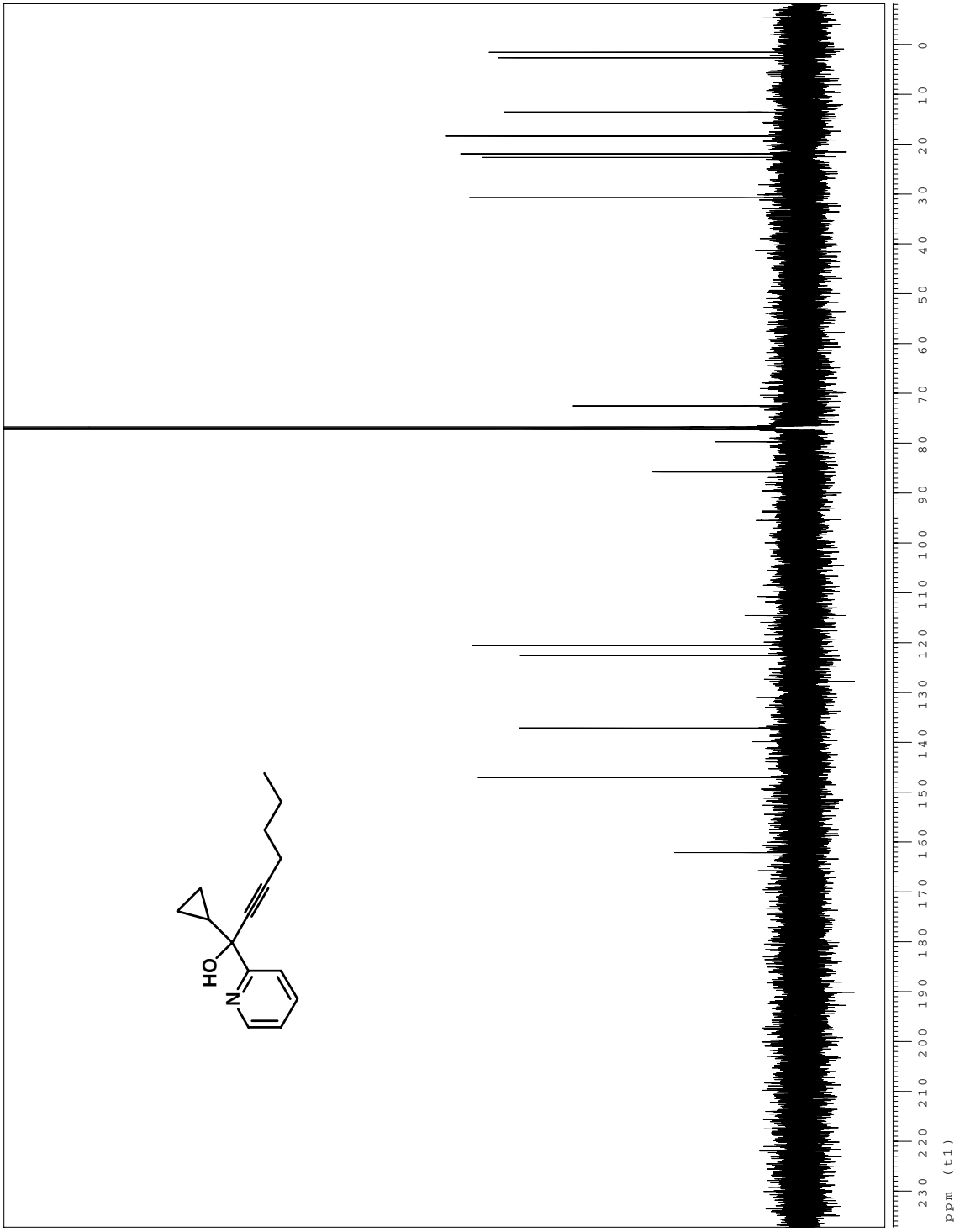

3.29
4.39
2.12
6.23
2.07
1.02
1.03
2.06
1.05
1.00
HO
N
O
O
ppm (t1)

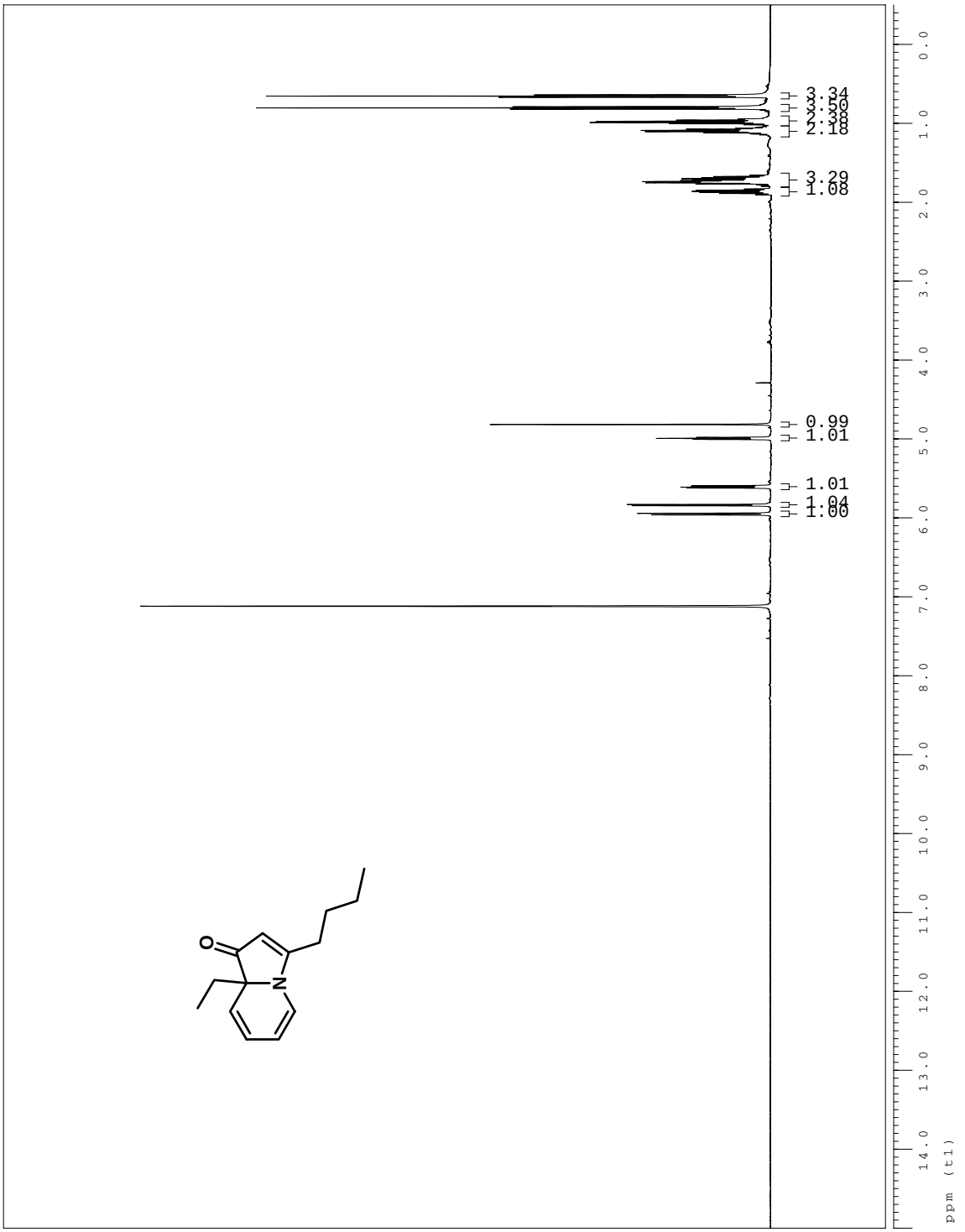

O
O
HO
N
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

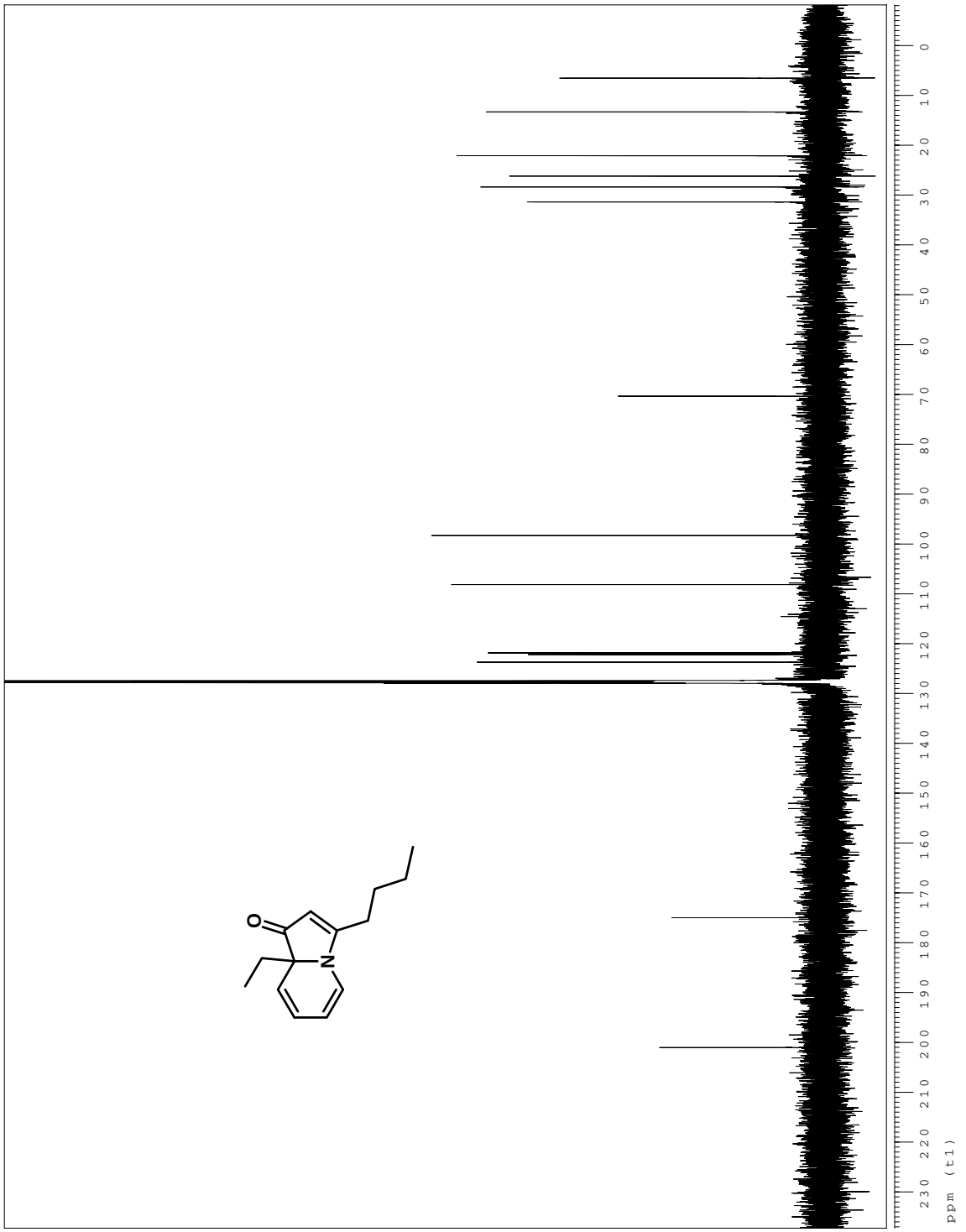

3.11
4.28
2.07
1.09
1.05
1.07
1.16
2.38
1.06
2.01
1.00
HO
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

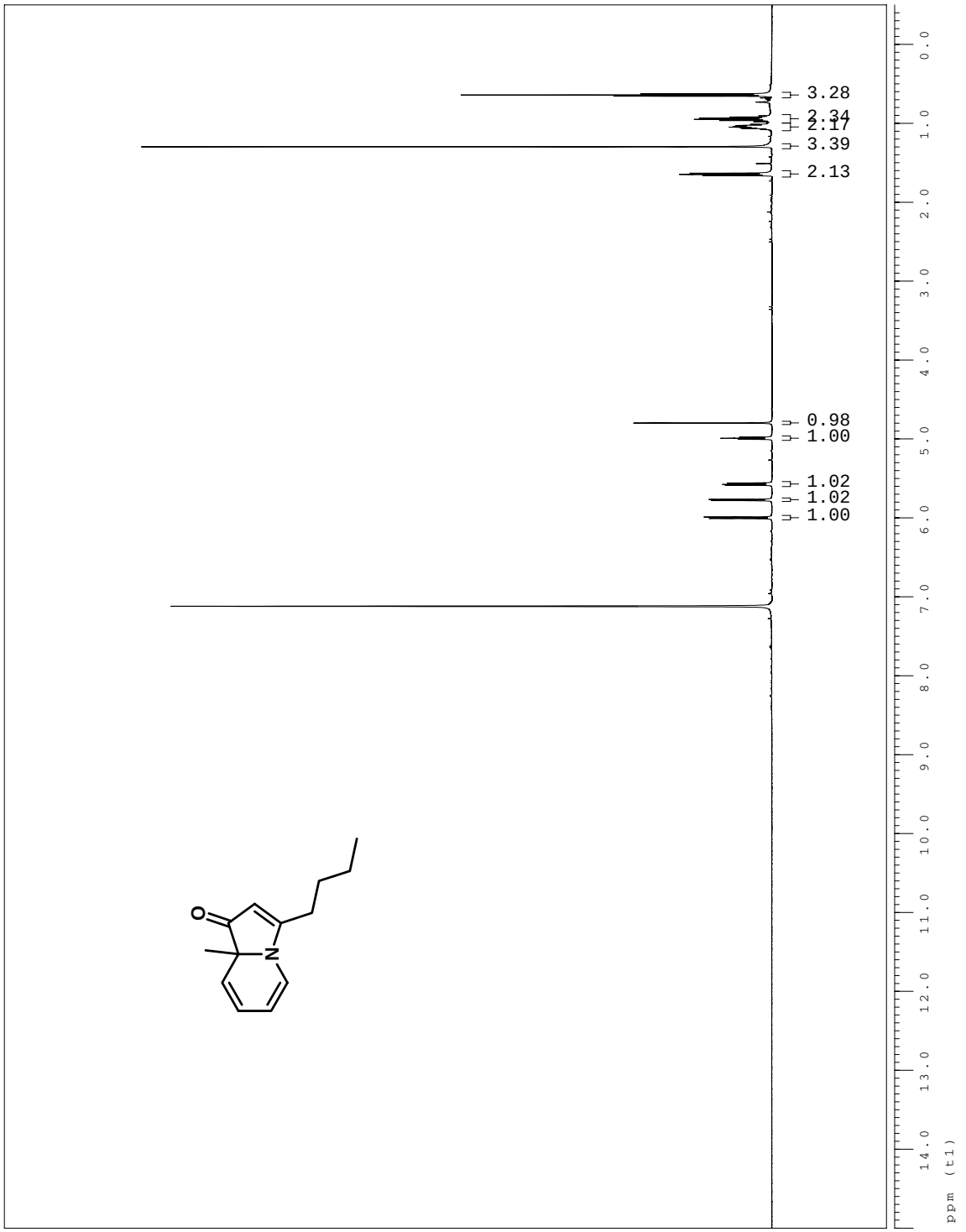

HO
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

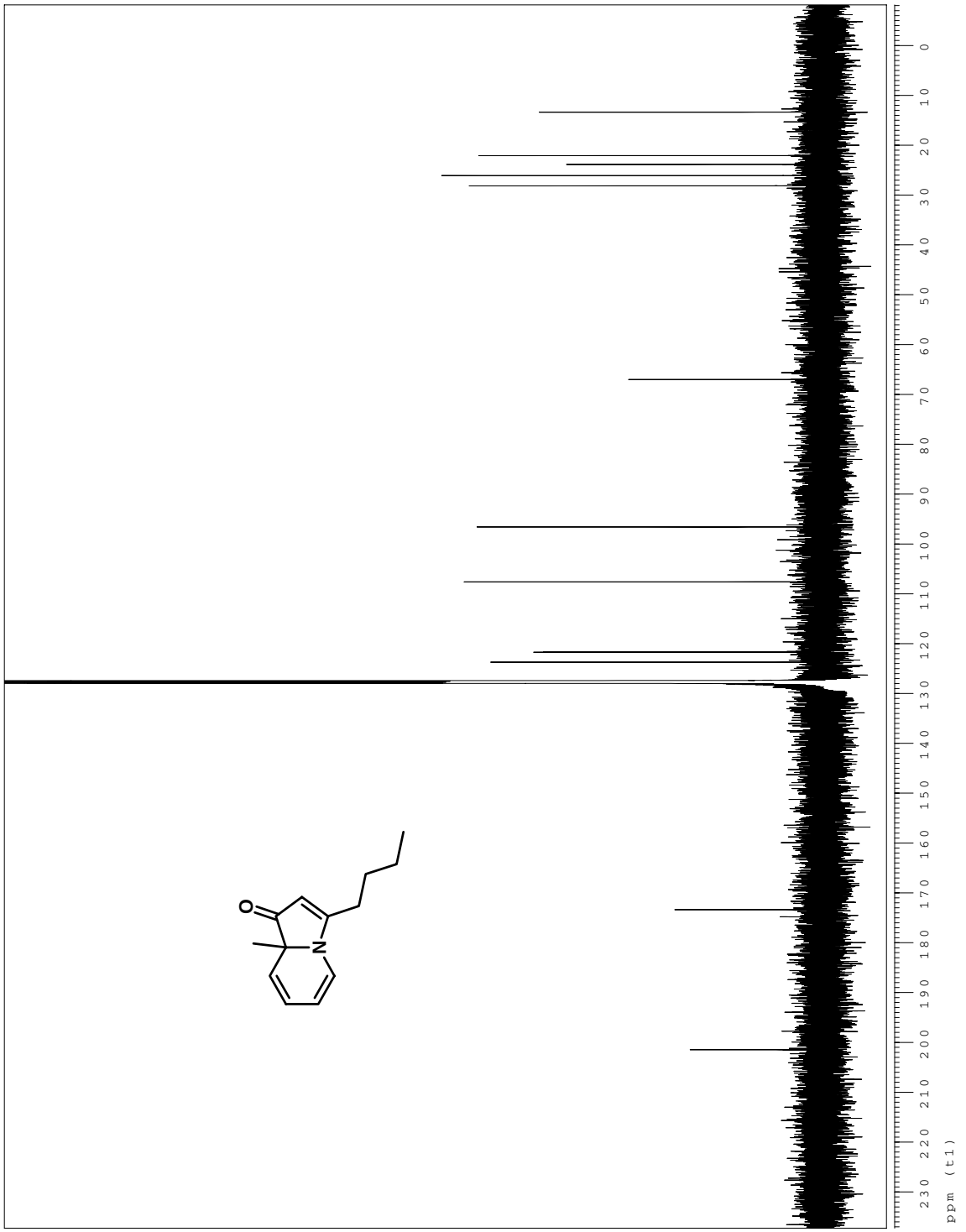

2.17
2.24
3.20
1.13
2.25
2.10
1.95
0.97
0.98
1.01
1.05
1.00
HO
N
ppm (t1)

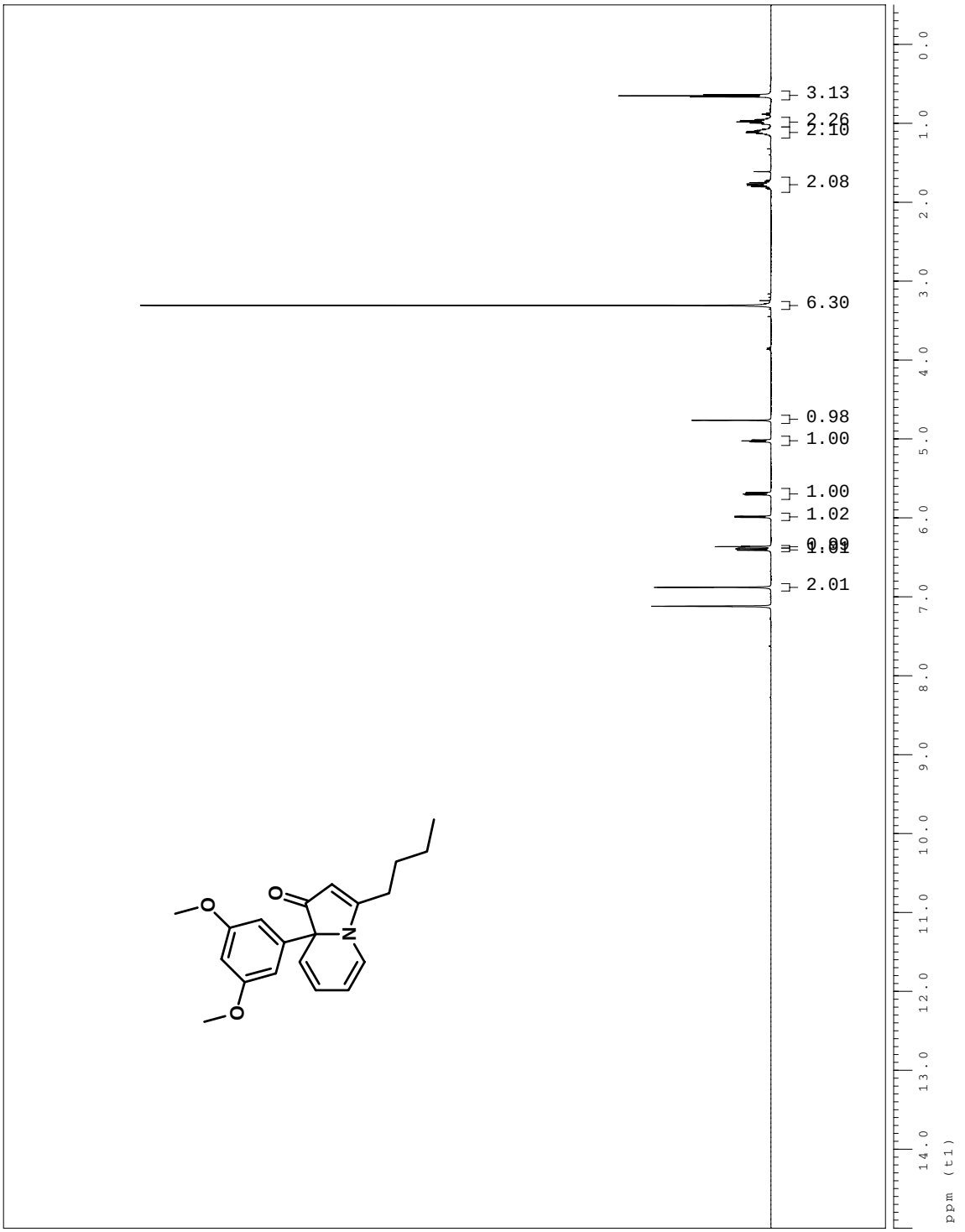

HO
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

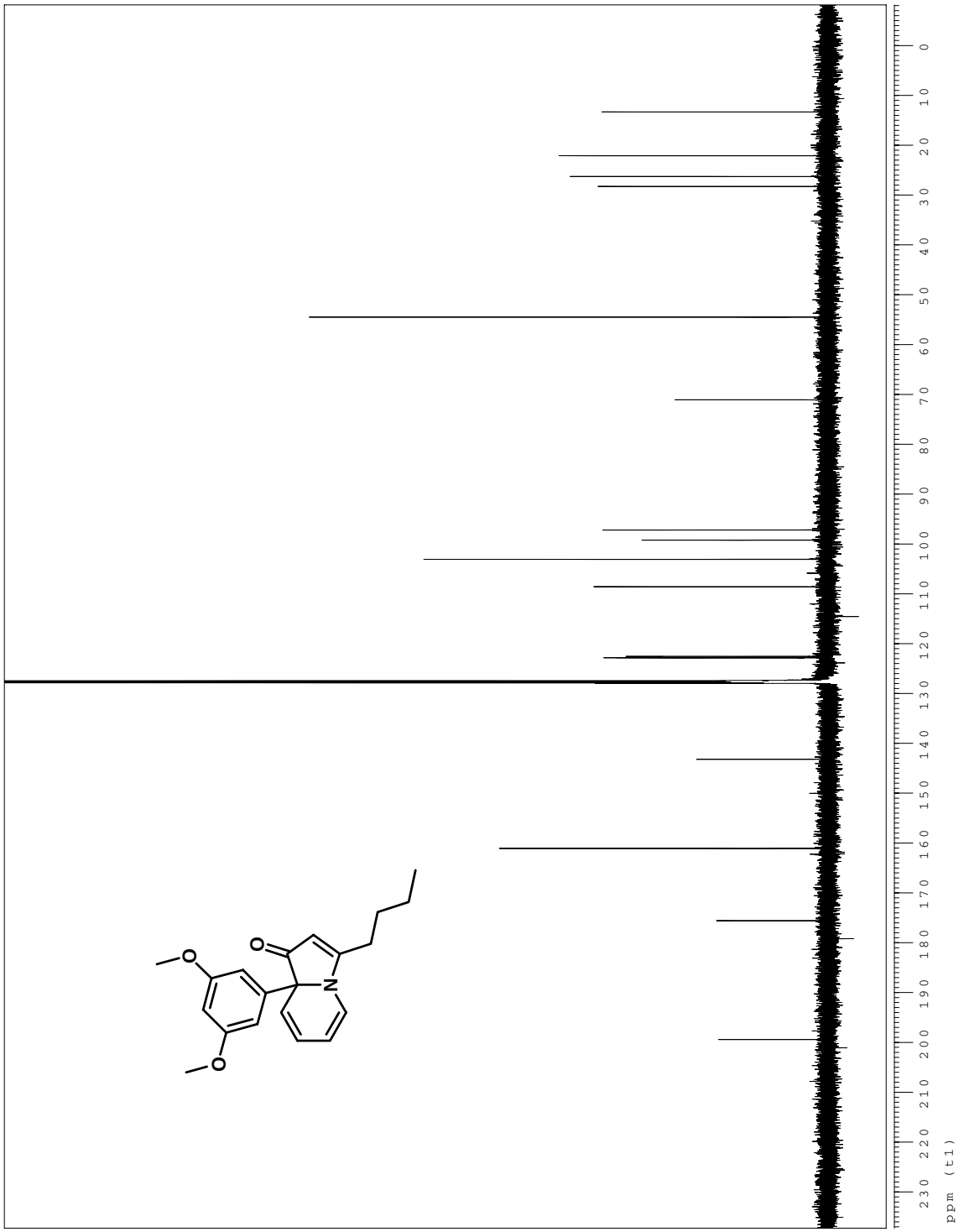

3.34
3.50
2.38
2.18
3.29
1.08
0.99
1.01
1.01
1.04
1.00
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

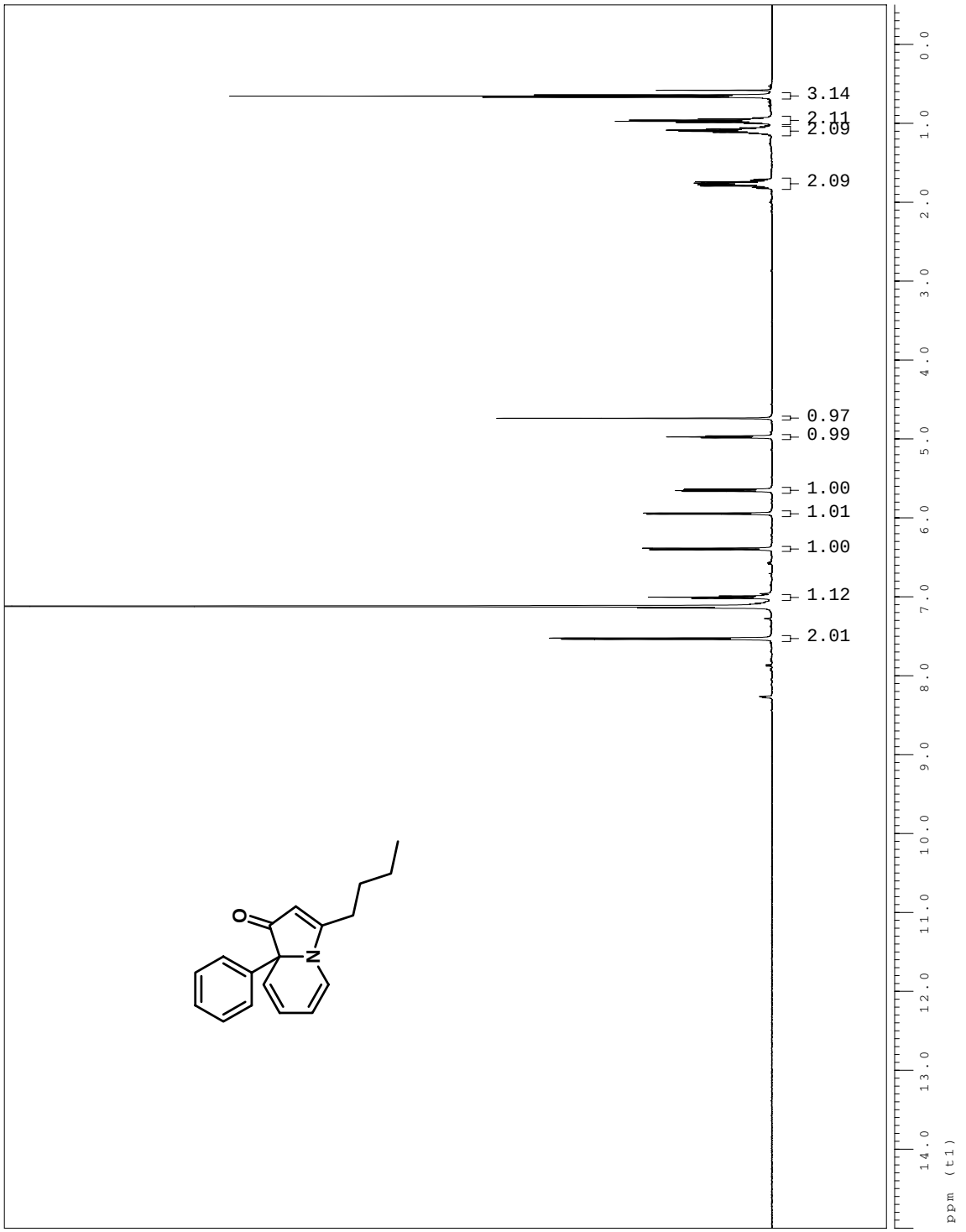

O
N
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

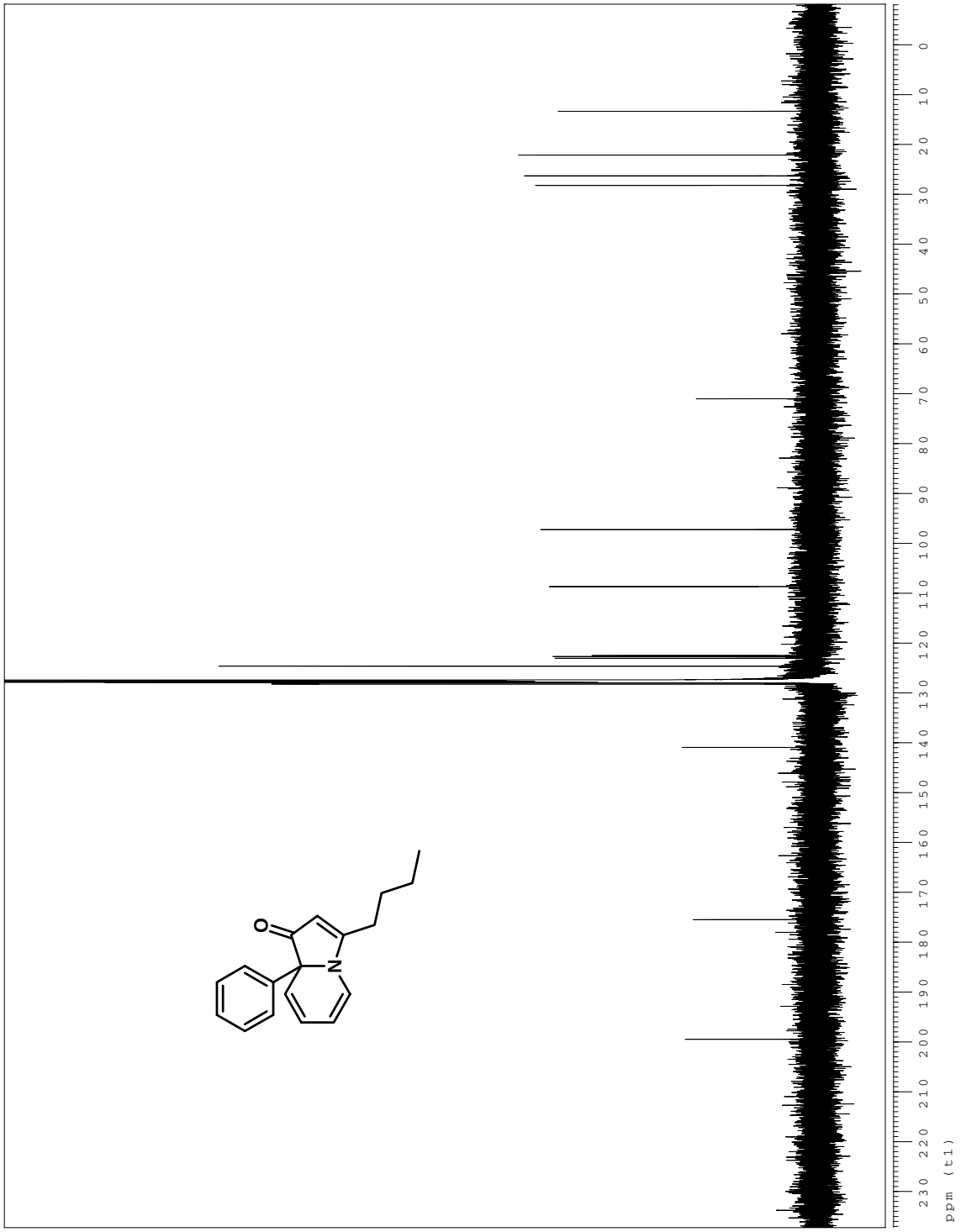

3.28
2.34
2.17
3.39
2.13
0.98
1.00
1.02
1.02
1.00
O
N
ppm (t1)

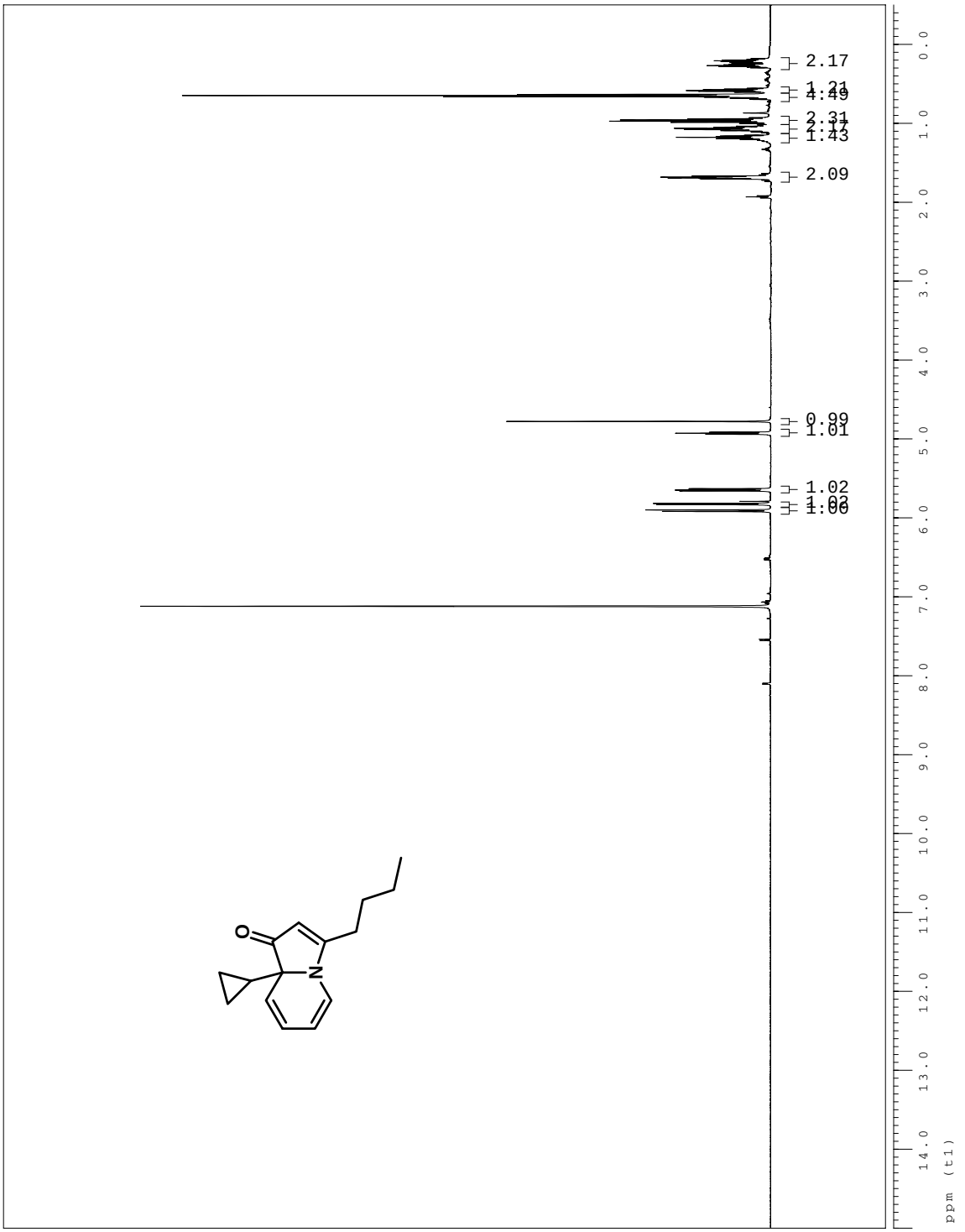

O
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

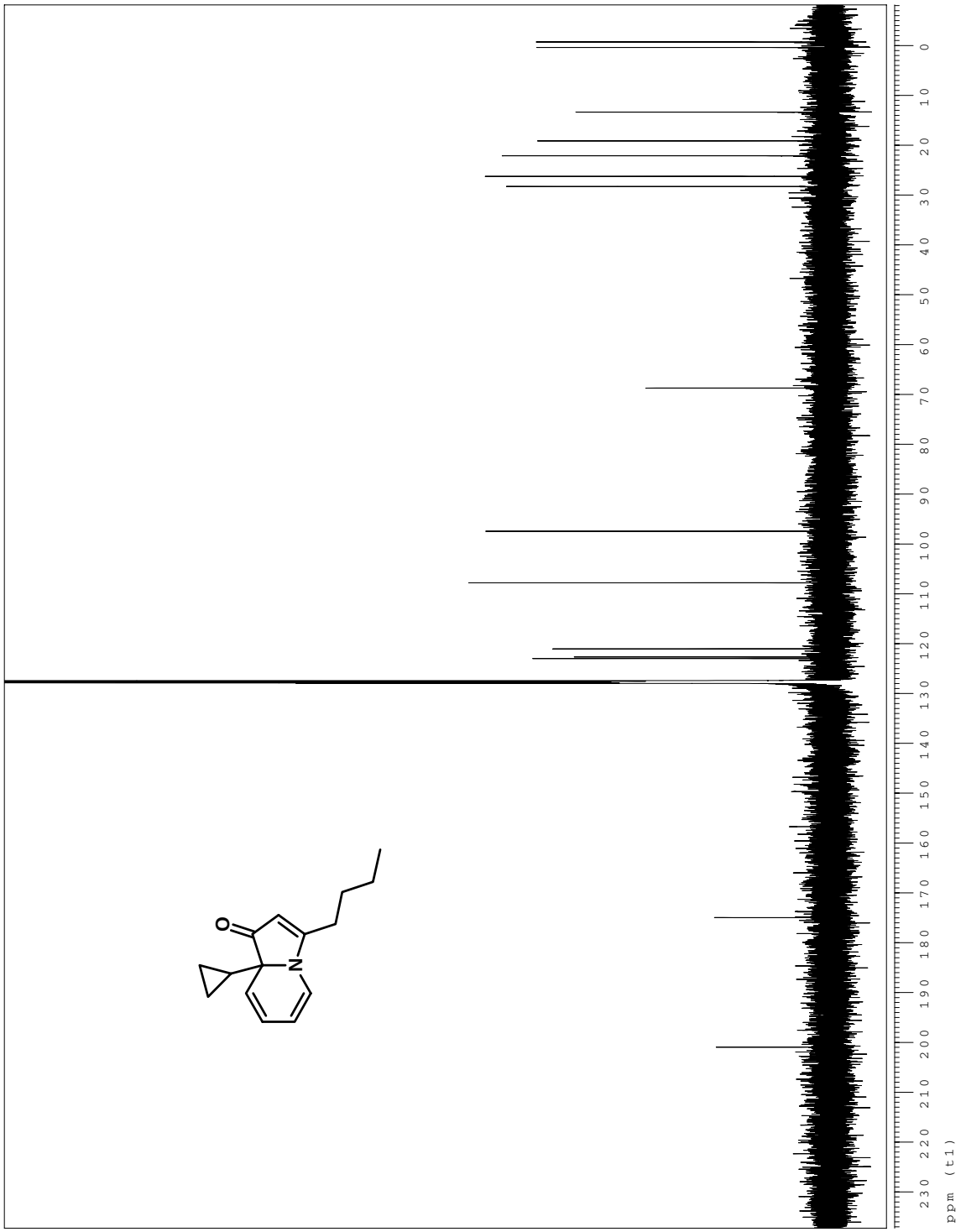

3.13
2.26
2.10
2.08
6.30
0.98
1.00
1.00
1.02
2.01
O
O
O
N
ppm (t1)

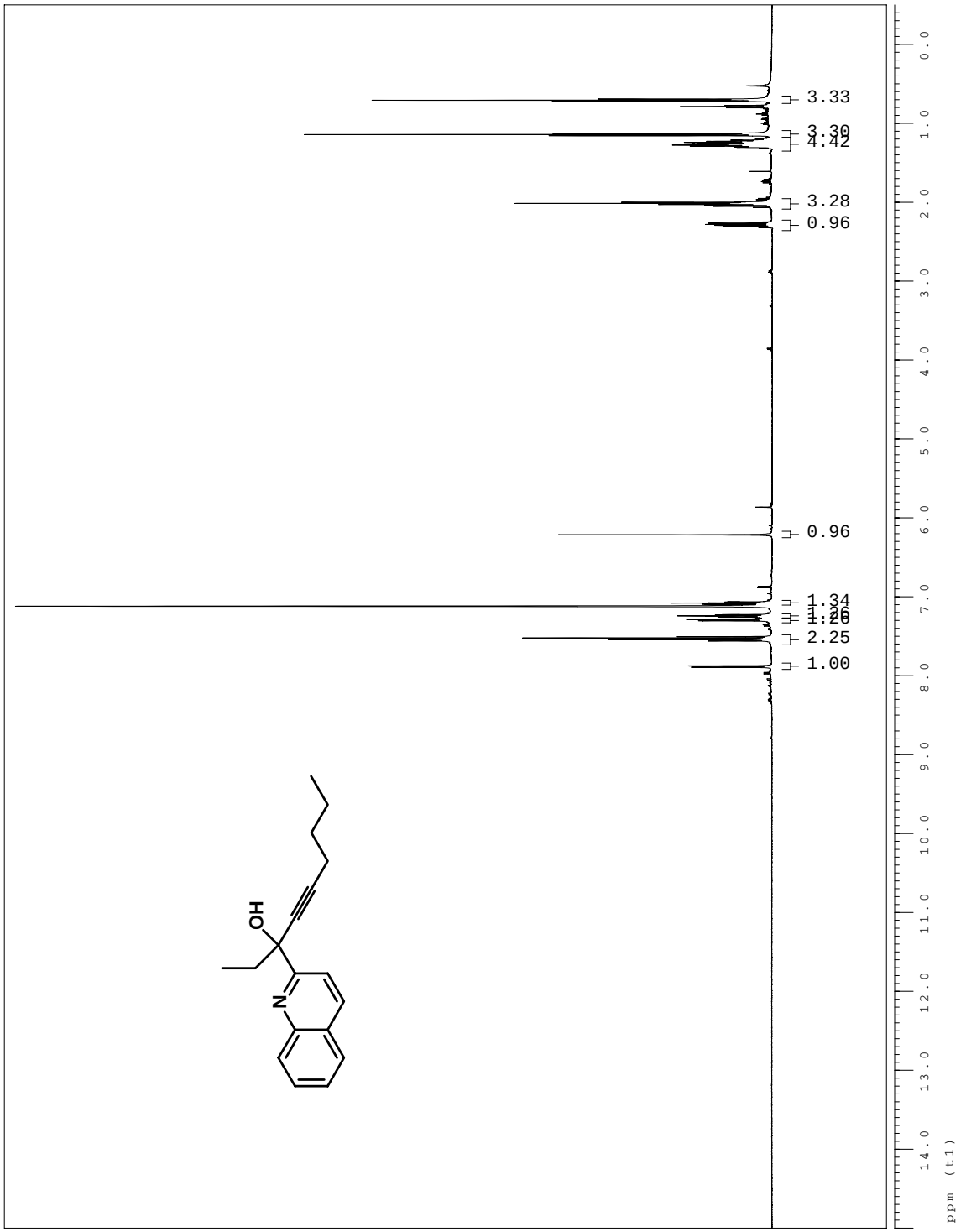

O
N
O
O
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230
ppm (t1)

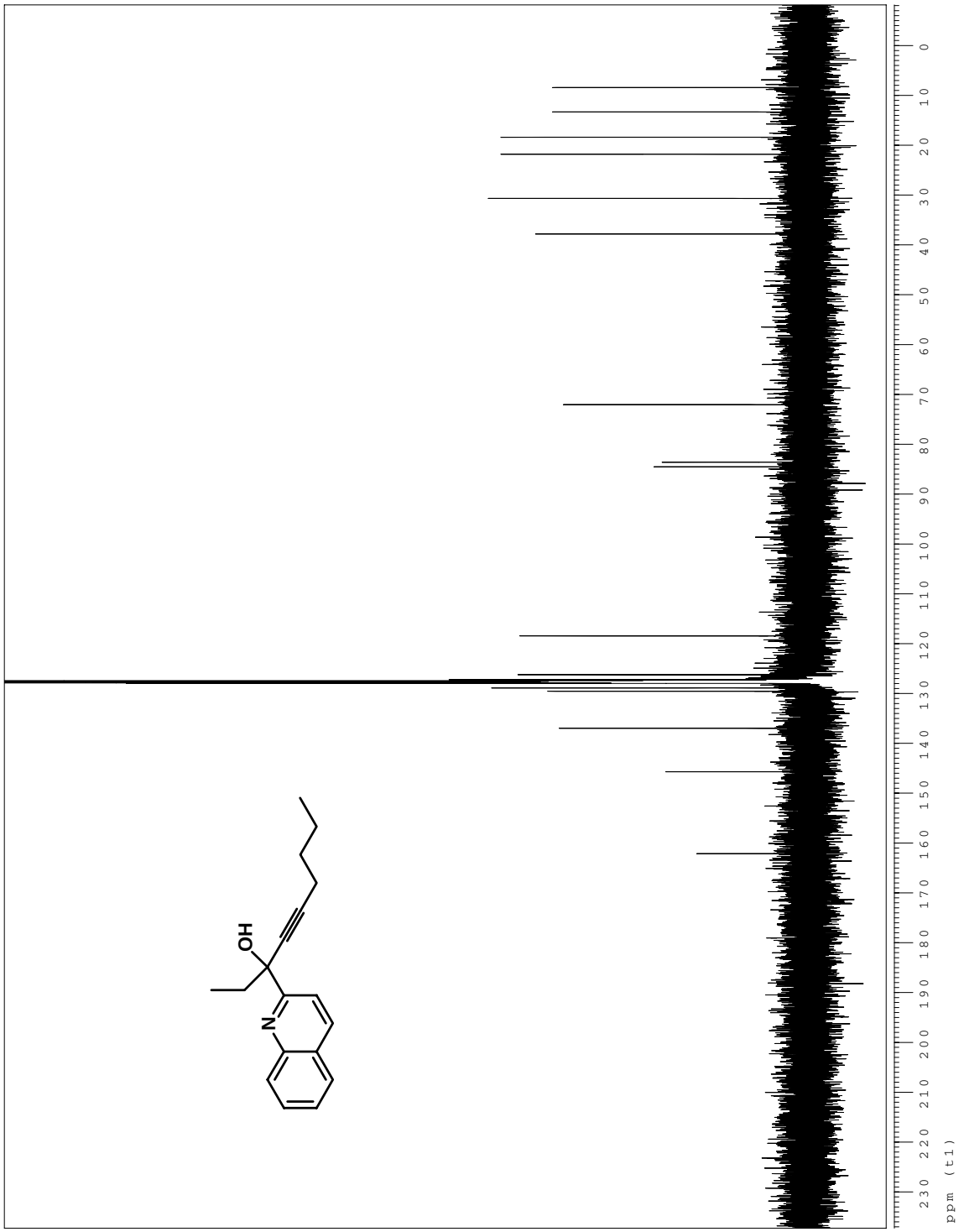

3.14
2.11
2.09
2.09
0.97
0.99
1.00
1.01
1.00
1.12
2.01
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)


O
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)


2.17
1.21
4.49
2.31
2.17
1.43
2.09
0.99
1.01
1.02
1.02
1.00
O
N
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
ppm (t1)

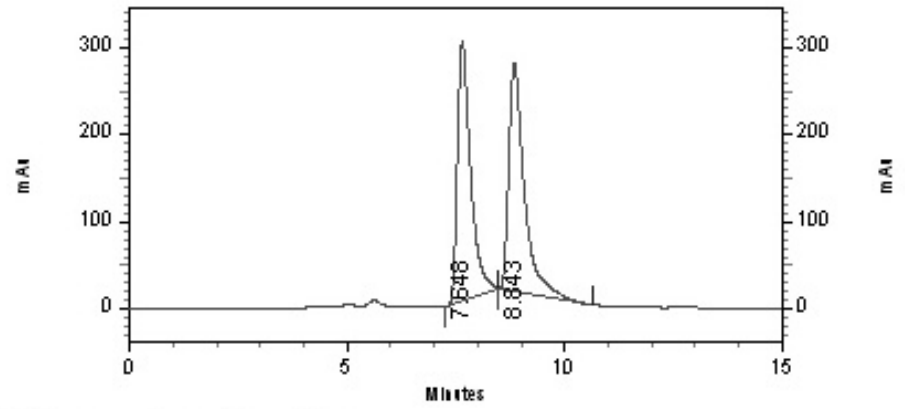

O
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)


3.33
3.30
4.42
3.28
0.96
0.96
1.34
1.26
1.20
2.25
1.00
OH
N
ppm (t1)


OH
N
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210
220
230
ppm (t1)

HPLC Data for the Determination of Enantiomeric Excess

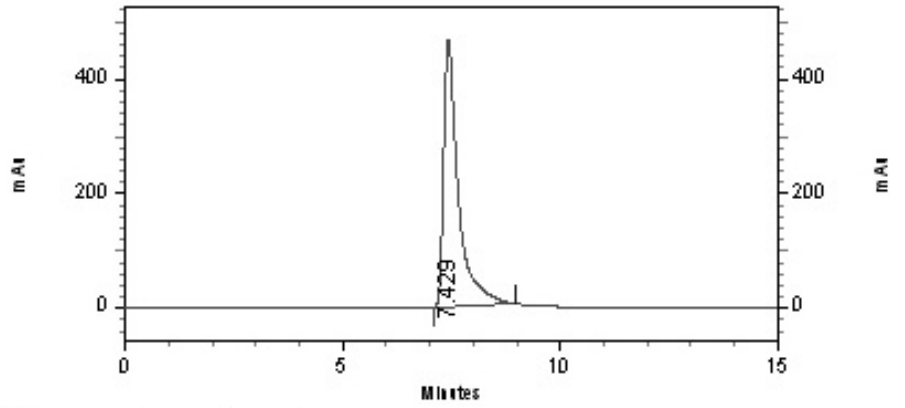
Propargylic Alcohol **(±)-20a**:



2: 254 nm, 4 nm Results

Retention Time	Area	Area Percent
7.648	6312693	49.030
8.843	6562449	50.970

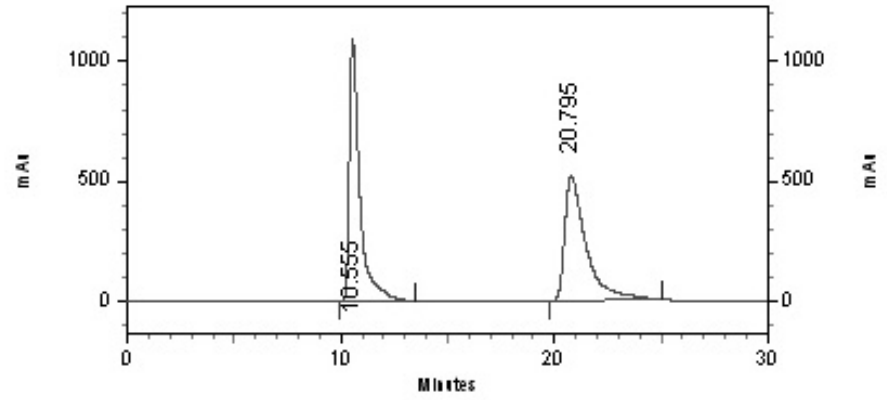
Propargylic Alcohol **(+)-20a**:



2: 254 nm, 4 nm Results

Retention Time	Area	Area Percent
7.429	10969330	100.000

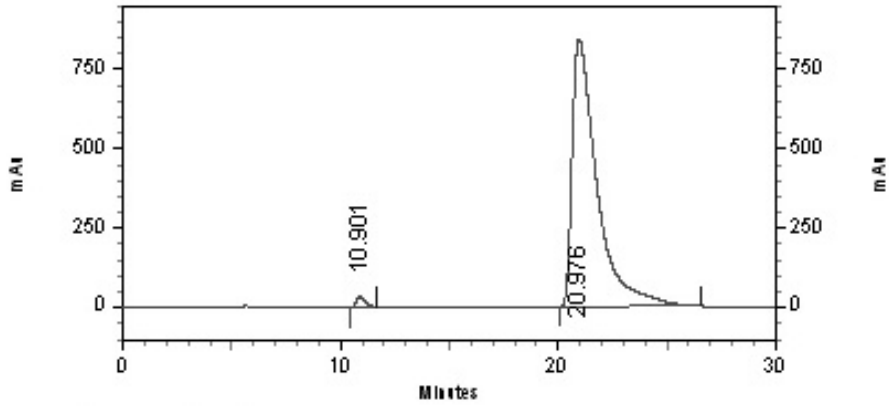
Indolizinone **(±)-21a**:



2: 254 nm, 4 nm Results

Retention Time	Area	Area Percent
10.555	37345948	50.627
20.795	36420666	49.373

Indolizinone **(+)-21a**:



2: 254 nm, 4 nm Results

Retention Time	Area	Area Percent
10.901	930664	1.364
20.976	67311378	98.636