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Supporting Information

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Intermolecular Cope-Type Hydroamination of Alkenes and Alkynes

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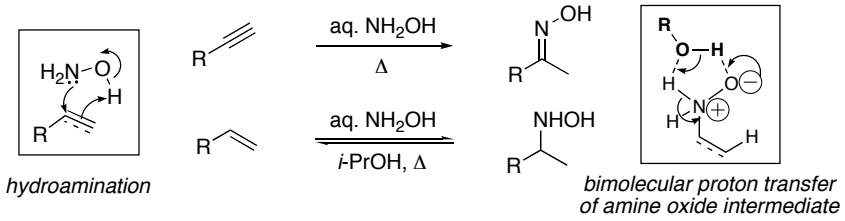


CAUTION: Hydroxylamine free base – 50% wt aqueous solution (HAFB).[1] As many other chemical products HAFB does not cause any problems if handled with care. For example, it is currently produced by BASF (>7000 ton/year) and used for a variety of industrial applications. However, HAFB can decompose spontaneously with the liberation of large volumes of gas if not handled properly. Violent decomposition of hydroxylamine can be caused by:

- metal (especially iron) and metal ion impurities
- oxidizing and reducing agents and bases
- high temperatures above 75 °C
- high concentrations of hydroxylamine, for example due to evaporation

Pure, free hydroxylamine (a solid) is known to decompose at room temperature. Heating ca. 80% wt solutions of NH_2OH has led to fatal accidents at plants in Allentown, PA, USA and Ojima, Gunma, Japan, most likely caused by the presence of trace amounts of iron impurities and issues with reactor design. 50% wt solutions have a better stability profile and are commercially available.[2] In Japan, hydroxylamine solutions are not designated as a dangerous material under the fire protection law if the concentration is 15% or less.[3]

Suggested experimental conditions. *Under our reaction conditions, the hydroxylamine content of the solution being heated is in the 5-10% wt range*. Hydroxylamine concentration should not be increased. **The use of a blast shield to perform the experiments is and should be a standard operating procedure.** During the course of our studies (>200 experiments), we have performed reactions near or at the gram scale and have observed only minimal gas evolution (ie. a bit of pressure was released when we opened our sealed tubes to air, at room temperature, at the end of the reaction). No incidents occurred. However, appropriate safety measures should be taken before scaling up. In addition, process safety literature suggests using old aqueous hydroxylamine solutions and stainless steel vessels should be avoided.

[†] To whom correspondence on DFT calculations should be addressed.

1. See the BASF website for more information.

2. L. O. Cisneros, W. J. Rogers, M. S. Mannan, *J. Haz. Mat.* **2001**, *A82*, 13.

3. For an evaluation of the safety profile of 20 to 85% wt NH_2OH aqueous solutions, see: Y. Iwata, H. Koseki, *Process Safety Progress* **2002**, *21*, 136.

TABLE OF CONTENTS

General Information. Purification of reaction products was carried out by flash column chromatography using Silicycle silica gel (40-63 μm). Analytical thin layer chromatography (TLC) was performed on aluminum sheets pre-coated with silica gel 60 F_{254} (E. Merck), cut to size. Visualization was accomplished with UV light followed by dipping in a potassium permanganate solution and heating. Microwave reactions were run in a CEM Discover LabMate microwave.

^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AVANCE 300 MHz and 75 MHz spectrometers respectively at ambient temperature. Spectral data was reported in ppm using solvent as the reference ($CDCl_3$ at 7.26 ppm, C_6D_6 at 7.15 ppm or DMSO-d_6 at 2.50 ppm for ^{1}H NMR and $CDCl_3$ at 77.0 ppm, C_6D_6 at 128.02 ppm or DMSO-d_6 at 39.43 for ^{13}C NMR). ^{1}H NMR data was reported as: multiplicity (ap = apparent, br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant(s) in Hz. High resolution mass spectroscopy (HRMS) was performed at the Ottawa-Carleton Mass Spectrometry Centre. Infrared (IR) spectra were obtained with neat thin films on a sodium chloride disk and were recorded on a Bomem Michelson 100 Fourier transform infrared spectrometer (FTIR). Melting points were determined using a Gallenkamp melting point apparatus and were uncorrected.

Materials. Unless otherwise noted, all commercially available reagents and solvents were used directly from the bottle without further purification.

Control experiments. Various control experiments have been performed on this reactivity, notably to address the likelihood of Ritter-type reactivity involving carbocationic reaction intermediates. For example, experiments featuring the use of 0.5 equiv. of TFA[4] under otherwise identical reaction conditions for the hydroamination of octyne and norbornene were performed and led to: 1) similar conversion to the oxime for the reaction with 1-octyne; 2) Lower conversion (ca. 20%) with norbornene and appearance of other byproducts that appear to be the endo mono and bis-hydroamination products. In addition, the addition excess (3 equiv. relative to phenylacetylene; 2.5 equiv. of NH_2OH relative to phenylacetylene) pyridine or Hunig's base (*i*-Pr_2NEt) leads to similar conversions to the oxime products.

4. Other acids were surveyed and more details will be reported in a full account of this work. The use of stronger acids, such as TfOH, generally led to reduced or comparable reactivity when used in catalytic quantities (20 mol%).

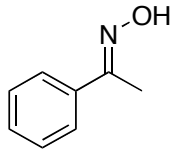
Experimental - Alkynes

General Procedure A (Table 1). In a sealed tube equipped with a magnetic stirbar was added dioxane (1.6 mL, 1.0 M), the alkyne (1.57 mmol, 1.0 equiv.) and a 50 wt. % aqueous hydroxylamine solution (259 mg, 240 μL, 3.92 mmol, 2.5 equiv.). The tube was sealed and heated at 113˚C for 16-18h. After cooling to room temperature, the reaction mixture was diluted with a saturated aqueous $NaHCO_3$ solution and extracted with ether or EtOAc (3x). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give a residue. The crude was then purified by flash chromatography on silica gel with gradients of EtOAc/hexanes as eluent to yield the oxime products.

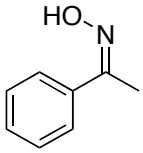
General Procedure B (Table 1). In a sealed tube equipped with a magnetic stirbar was added dioxane (1.6 mL, 2.0 M), the alkyne (3.13 mmol, 1.0 equiv.) and a 50 wt. % aqueous hydroxylamine solution (517 mg, 480 μL, 7.83 mmol, 2.5 equiv.). The tube was sealed and heated at 140˚C for 38-40h. After cooling to room temperature, the reaction mixture was worked up and purified as described in General Procedure A.

General Procedure C (Table 1). In a pressure vessel equipped with a magnetic stirbar was added *i*-PrOH (1.6 mL, 1.0 M), the alkyne (1.60 mmol, 1.0 equiv.) and a 50 wt. % aqueous hydroxylamine solution (528 mg, 490 μL, 8.00 mmol, 5.0 equiv.). The solution was degassed at 0˚C (for volatility issues) by bubbling argon for 10 minutes. The pressure vessel was capped and microwaved at 140 ˚C for 10h. After cooling to room temperature, the reaction mixture was worked up and purified as described in General Procedure A.

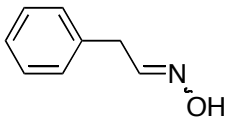
Characterization.



major (Markovnikov) *E*-isomer



(Markovnikov) *Z*-isomer



minor (anti-Markovnikov)

Acetophenone oxime (Table 1, Entry 1, major Markovnikov *E*-isomer). Isolated 180 mg (85% yield) as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.50 (20% EtOAc/hexanes); ^{1}H NMR (C_6D_6, 300 MHz) δ 10.80 (br s, 1H), 7.57-7.51 (m, 2H), 7.12-7.06 (m, 3H), 2.09 (s, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 156.1 (C_4), 136.9 (C_4), 129.3 (CH), 128.7 (CH), 126.4 (CH), 12.4 (CH_3). Spectral data in $CDCl_3$ was found to be in good agreement with those in the literature.[5]

Acetophenone oxime (Markovnikov *Z*-isomer). Isolated 5 mg (2% yield) as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.24 (20% EtOAc/hexanes); ^{1}H NMR (C_6D_6, 300 MHz) δ 7.44-7.40 (m, 2H), 7.15-7.00 (m, 3H), 1.94 (s, 3H); ^{13}C NMR (C_6D_6, 75 MHz) δ 153.7 (C_4), 134.6 (C_4), 21.3 (CH_3) + expecting three other peaks between 129.1 and 126.6 (under the benzene-d_6 solvent peak). This *Z*-isomer readily isomerized to the other more stable major Markovnikov *E*-isomer seen both by TLC and NMR.[6]

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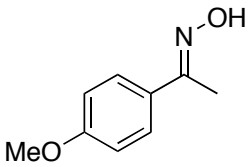
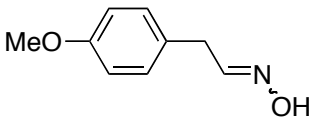
5. J. R. Hwu, W. N. Tseng, H. V. Patel, F. F. Wong, D. Horng, B. R. Liaw, L. C. Lin, *J. Org. Chem.* **1999**, *64*, 2211.
6. G. J. Karabatsos, R. A. Taller, *Tetrahedron* **1968**, *24*, 3347.

2-Phenylacetaldehyde oxime (Table 1, Entry 1, minor anti-Markovnikov). Isolated 10 mg (5% yield)[7] as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.26 (20% EtOAc/hexanes). Spectral data was found to be in good agreement with those in the literature.[8]

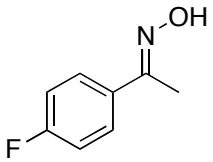
Hereafter, the complete characterization was done for the major Markovnikov product[9] and for the most stable anti-Markovnikov stereoisomer, unless otherwise stated. ^{1}H NMR of a mixture of anti-Markovnikov stereoisomers was also reported.



1-(4-Methoxyphenyl)ethanone oxime (Table 1, Entry 2, major). Isolated 214 mg (83% yield)[9] as white crystals after column chromatography (10-30% EtOAc/hexanes). TLC R_f 0.29 (20% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.22 (br s, 1H), 7.61 (d, 2H, J = 8.9 Hz), 6.93 (d, 2H, J = 8.9 Hz), 3.82 (s, 3H), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.3 (C_4), 155.3 (C_4), 128.8 (C_4), 127.3 (CH), 113.7 (CH), 55.1 (CH_3), 12.2 (CH_3); IR (film): 3235, 3123, 3007, 2966, 2937, 2839, 1652, 1608, 1515, 1462, 1368, 1310, 1297, 1254, 1181, 1025, 925, 836 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO_2[M]^+$: 165.0790; found: 165.0791. Spectral ^{1}H NMR data was found to be in good agreement with those in the literature.[10]



2-(4-Methoxyphenyl)acetaldehyde oxime (Table 1, Entry 2, minor). Isolated 9 mg (3% yield)[7] as white crystals after column chromatography (10-30% EtOAc/hexanes). TLC R_f 0.20 (20% EtOAc/hexanes). Spectral data was found to be in good agreement with those in the literature.[11]



1-(4-Fluorophenyl)ethanone oxime (Table 1, Entry 3, major). Isolated 161 mg (67% yield)[9] as white powder after column chromatography (10-30% EtOAc/hexanes). TLC R_f 0.52 (20% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.18 (br s, 1H), 7.61 (dd, 2H, J = 8.9 and 5.4 Hz), 7.08 (t, 2H, J = 8.7 Hz), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 163.4 (d, C_4, J = 249 Hz), 155.2 (C_4), 132.5 (d, C_4, J = 3 Hz), 127.9 (d, CH, J = 8 Hz), 115.4 (d, CH, J = 22 Hz), 12.4 (CH_3); IR (film): 3294, 3224, 3096, 2933, 1652, 1603, 1513, 1234, 1158, 1009, 929, 834, 827, 756 cm^{-1}; HRMS (EI): Exact mass calcd for

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7. The mixture of *E*- and *Z*-stereoisomers readily equilibrated at room temperature in solution. Upon standing solvent free for one week, the most stable stereoisomer was obtained and confirmed by NMR.

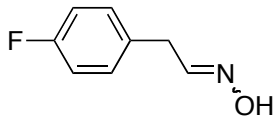
8. R. S. Varma, M. Varma, G. W. Kabalka, *Synth. Comm.* **1985**, *15*, 1325.

9. The characterization for the other Markovnikov stereoisomer was not reported but the yield was given as the combined *E*- and *Z*-stereoisomers of the Markovnikov product.

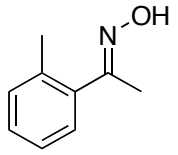
10. E. Brown, M. Moudachirou, *Tetrahedron* **1994**, *50*, 10309.

11. M. Bartra, P. Romea, F. Urpf, J. Vilarrasa, *Tetrahedron* **1990**, *46*, 587.

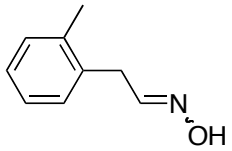
$C_8H_8FNO[M]^+$: 153.0590; found: 153.0585. Mp (recrystallized from 30% Et_2O/hexanes) 75.6-76.2˚C. The melting point was found to be in good agreement with that of the literature (74-76˚C).[12]



2-(4-Fluorophenyl)acetaldehyde oxime (Table 1, Entry 3, minor). Isolated 12 mg (5% yield)[7] as white crystals after column chromatography (10-30% EtOAc/hexanes). TLC R_f 0.29 (20% EtOAc/hexanes); ^{1}H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 9.05 (br s, 2H, isomers 1 and 2), 7.52 (t, 1H, J = 6.3 Hz, isomer 1), 7.24-6.96 (m, 8H, isomers 1 and 2), 6.88 (t, 1H, J = 5.4 Hz, isomer 2), 3.72 (d, 2H, J = 5.4 Hz, isomer 2), 3.52 (d, 2H, J = 6.3 Hz, isomer 1);
Characterization of most stable isomer 2: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.69 (br s, 1H), 7.20 (dd, 2H, J = 8.8 and 5.3 Hz), 7.01 (t, 2H, J = 8.7 Hz), 6.88 (t, 1H, J = 5.4 Hz), 3.72 (d, 2H, J = 5.4 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.7 (d, C_4, J = 243 Hz), 150.6 (CH), 132.2 (d, C_4, J = 3 Hz), 130.2 (d, CH, J = 8 Hz), 115.6 (d, CH, J = 21 Hz), 30.8 (CH_2); IR (film): 3200, 3085, 3038, 2865, 1659, 1600, 1512, 1416, 1225, 927, 831, 818 cm^{-1}; HRMS (EI): Exact mass calcd for $C_8H_8FNO[M]^+$: 153.0590; found: 153.0590.



1-*o*-Tolylethanone oxime (Table 1, Entry 4, major). Isolated 106 mg (45% yield)[9] as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.38 (20% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.89 (br s, 1H), 7.32-7.19 (m, 4H), 2.39 (s, 3H), 2.24 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.8 (C_4), 137.3 (C_4), 135.6 (C_4), 130.6 (CH), 128.5 (CH), 128.1 (CH), 125.7 (CH), 20.0 (CH_3), 15.9 (CH_3); IR (film): 3236 , 3066, 3024, 2959, 2923, 2872, 1644, 1602, 1491, 1457, 1435, 1364, 1305, 1272, 1009, 918, 759, 723, 649 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO[M]^+$: 149.0841; found: 149.0850. Spectral ^{13}C NMR data was found to be in good agreement with those in the literature.[13] Mp (recrystallized from 40% Et_2O/hexanes) 65.4-67.4˚C. The melting point was found to be in good agreement with that of the literature (64.5-65.5˚C).[14]



2-*o*-Tolylacetaldehyde oxime (Table 1, Entry 4, minor). Isolated 25 mg (11% yield)[7] as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.28 (20% EtOAc/hexanes); ^{1}H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 8.49 (br s, 1H), 7.92 (s, 1H), 7.52 (t, 1H, J = 6.1 Hz, isomer 1), 7.20-7.15 (m, 8H, isomers 1 and 2), 6.80 (t, 1H, J = 5.2 Hz, isomer 2), 3.73 (d, 2H, J = 5.2 Hz, isomer 2), 3.54 (d, 2H, J = 6.1 Hz, isomer 1), 2.33 (s, 3H), 2.31 (s, 3H);
Characterization of most stable isomer 2: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.55 (br s, 1H), 7.20-7.17 (ap s, 4H), 6.80 (t, 1H, J = 5.2 Hz), 3.73 (d, 2H, J = 5.22 Hz), 2.31 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.6 (CH), 136.6 (C_4), 135.0 (C_4), 130.4 (CH), 129.5 (CH), 127.0 (CH), 126.3 (CH), 29.7 (CH_2), 19.5 (CH_3);

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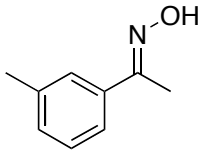
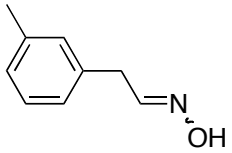
12. R. E. Lyle, H. J. Troscianiec, *J. Org. Chem.* **1955**, *20*, 1757.
13. R. R. Fraser, R. Capoor, *Can. J. Chem.* **1983**, *61*, 2616.
14. D. E. Pearson, W. E. Cole, *J. Org. Chem.* **1955**, *20*, 488.

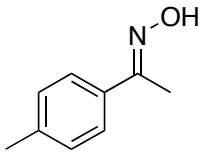
IR (film): 3313, 3200, 3081, 3035, 2918, 2868, 1663, 1493, 1438, 1323, 1044, 924, 766, 746, 720 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO[M]^+$: 149.0841; found: 149.0846.



1-*m*-Tolylethanone oxime (Table 1, Entry 5, major). Isolated 175 mg (75% yield)[9] as light beige crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.56 (20% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.91 (br s, 1H), 7.47 (d, 1H, J = 0.6 Hz), 7.46 (d, 1H, J = 7.5 Hz), 7.31 (td, 1H, J = 7.6 and 0.9 Hz), 7.23 (d, 1H, J = 7.7 Hz), 2.41 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.1 (C_4), 138.1 (C_4), 136.4 (C_4), 130.0 (CH), 128.4 (CH), 126.7 (CH), 123.2 (CH), 21.4 (CH_3), 12.5 (CH_3); IR (film): 3305, 3253, 3043, 2921, 2861, 1633, 1604, 1583, 1490, 1451, 1368, 1307, 1200, 1086, 1009, 941, 908, 855, 785, 745, 697, 656 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO[M]^+$: 149.0841; found: 149.0833. Mp (recrystallized from 30% Et_2O/hexanes) 59.1-61.0˚C. The melting point was found to be in good agreement with those in the literature (57˚C).[15]



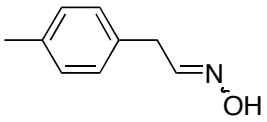
2-*m*-Tolylacetaldehyde oxime (Table 1, Entry 5, minor). Isolated 6 mg (2% yield)[7] as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.39 (20% EtOAc/hexanes); ^1H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 8.49 (br s, 1H), 7.97 (br s, 1H), 7.54 (t, 1H, J = 6.3 Hz, isomer 1), 7.25-7.20 (m, 2H), 7.08-7.01 (m, 6H), 6.90 (t, 1H, J = 5.3 Hz, isomer 2), 3.72 (d, 2H, J = 5.3 Hz, isomer 2), 3.51 (d, 2H, J = 6.3 Hz, isomer 1), 2.35 (s, 6H, isomers 1 and 2);
Characterization of most stable isomer 2: ^1H NMR ($CDCl_3$, 300 MHz) δ 8.24 (br s, 1H), 7.22 (td, 1H, J = 7.2 and 1.2 Hz), 7.07 (d, 1H, J = 8.5 Hz), 7.05 (s, 1H), 7.04 (d, 1H, J = 8.4 Hz), 6.90 (t, 1H, J = 5.3 Hz), 3.71 (d, 2H, J = 5.3 Hz), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.1 (CH), 138.4 (C_4), 136.5 (C_4), 129.5 (CH), 128.6 (CH), 127.4 (CH), 125.8 (CH), 31.5 (CH_2), 21.4 (CH_3); IR (film): 3210, 3089, 3035, 2913, 2872, 1663, 1609, 1488, 1435, 1419, 1320, 1059, 975, 933, 917, 892, 823, 786, 697, 685 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO[M]^+$: 149.0841; found: 149.0836.



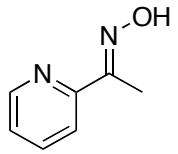
1-*p*-Tolylethanone oxime (Table 1, Entry 6, major). Isolated 97 mg (65% yield)[9] as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.58 (20% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 10.04 (br s, 1H), 7.56 (d, 2H, J = 8.3 Hz), 7.23 (d, 2H, J = 8.0 Hz), 2.40 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 155.8 (C_4), 139.2 (C_4), 133.6 (C_4), 129.2 (CH), 125.9 (CH), 21.2 (CH_3), 12.3 (CH_3); IR (film): 3302, 3237, 3104, 3028, 2923, 1648, 1606, 1514, 1450, 1409, 1365, 1312, 1303, 1184, 1126, 1085, 1006, 925, 817, 765, 749 cm^{-1}; HRMS (EI): Exact mass calcd for

15. T. Posner, G. Schreiber, *Chem. Ber*. **1924**, *57*, 1127.

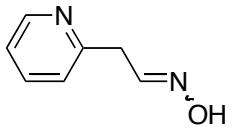
$C_9H_{11}NO[M]^+$: 149.0841; found: 149.0843. Mp (recrystallized from 40% Et_2O/hexanes) 90.1-91.2˚C. The melting point was found to be in good agreement with those in the literature (88-89˚C).[16]



2-*p*-Tolylacetaldehyde oxime (Table 1, Entry 6, minor). Isolated 4 mg (3% yield)[7] as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.26 (20% EtOAc/hexanes); ^{1}H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 7.70 (br s, 1H), 7.48 (t, 1H, J = 6.3 Hz, isomer 1), 7.26 (br s, 1H), 7.12-7.05 (m, 8H), 6.84 (t, 1H, J = 5.0 Hz, isomer 2), 3.66 (d, 2H, J = 5.3 Hz, isomer 2), 3.45 (d, 2H, J = 6.3 Hz, isomer 2), 2.30 (s, 3H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 151.0 (CH), 136.5 (C_4), 136.3 (C_4), 133.6 (C_4), 133.0 (C_4), 129.4 (CH), 129.4 (CH), 128.7 (CH), 128.6 (CH), 35.5 (CH_2), 31.1 (CH_2), 21.0 (CH_3); IR (film): 3208, 3077, 3035, 3024, 2921, 2856, 1657, 1516, 1427, 1410, 1325, 1056, 946, 930, 854, 813, 669 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO[M]^+$: 149.0841; found: 149.0867. Spectral ^{1}H NMR data was found to be in good agreement with those in the literature.[17]



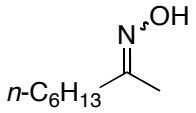
2-Acetylpyridyloxime (Table 1, Entry 7, major). Isolated 155 mg (73% yield)[9] as light beige glass-like crystals after column chromatography (40-60% EtOAc/hexanes). TLC R_f 0.59 (60% EtOAc/hexanes). Spectral data were found to be in good agreement with those in the literature[18] (except coupling constants were as follows) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.67 (br s, 1H), 8.63 (ddd, 1H, J = 4.9, 1.8 and 1.0 Hz), 7.84 (dt, 1H, J = 8.0 and 1.0 Hz), 7.69 (ap td, 1H, J = 8.0 and 1.8 Hz), 7.28 (ddd, 1H, J = 7.4, 4.9 and 1.5 Hz), 2.40 (s, 3H). Mp (recrystallized from 75% Et_2O/hexanes) 122.5-124.0˚C. The melting point was found to be in good agreement with those in the literature (120˚C).[19]



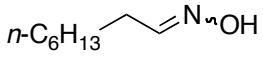
2-(Pyridin-2-yl)acetaldehyde oxime (Table 1, Entry 7, minor). Isolated 32 mg (15% yield)[7] as light beige crystals after column chromatography (40-60% EtOAc/hexanes). TLC R_f 0.15 (60% EtOAc/hexanes); ^{1}H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 10.22 (br s, 1H), 9.79 (br s, 1H), 8.55 (dd, 2H, J = 4.9 and 0.7 Hz), 7.65 (dd, 2H, J = 13.9 and 6.1 Hz), 7.64 (t, 1H, J = 8.6 Hz), 7.28-7.21 (m, 2H), 7.17 (ddd, 2H, J = 7.5, 5.0 and 0.7 Hz), 7.07 (t, 1H, J = 5.3 Hz, isomer 2), 3.95 (d, 2H, J = 5.3 Hz, isomer 2), 3.76 (d, 2H, J = 6.3 Hz, isomer 1);
Characterization of most stable isomer 2: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 10.40 (br s, 1H), 8.55 (d, 1H, J = 4.3 Hz), 7.64 (td, 1H, J = 7.7 and 1.7 Hz), 7.25 (d, 1H, J = 7.8 Hz), 7.17 (dd, 1H, J = 7.1 and 5.3 Hz), 7.07 (t, 1H, J = 5.3 Hz), 3.95 (d, 2H, J = 5.3 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.9 (C_4), 149.2 (CH), 148.4 (CH), 137.1 (CH), 123.6 (CH), 121.8 (CH), 33.9 (CH_2); IR (film): 3175, 3070, 3028, 2855, 2785,

16. O. L. Brady, J. N. E. Day, *J. Chem. Soc.* **1934**, 114.
17. S. H. Lee, Y. J. Park, C. M. Yoon, *Org. Biomol. Chem.* **2003**, *1*, 1099.
18. V. Sharma, R. K. Sharma, R. Bohra, R. Ratnani, V. K. Jain, J. E. Drake, M. B. Hursthouse, M. E. Light, *J. Organomet. Chem.* **2002**, *651*, 98.
19. C. Engler, P. Rosumoff, *Chem. Ber.* **1891**, *24*, 2527.

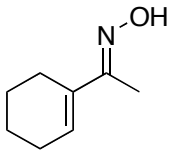
1678, 1652, 1597, 1570, 1480, 1438, 981, 907, 764 cm^{-1}; HRMS (EI): Exact mass calcd for $C_7H_8N_2O[M]^+$: 136.0637; found: 136.0635.



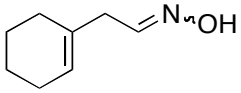
Octan-2-one oxime (Table 1, Entry 8, major). Isolated 279 mg (62% yield) as colorless oil after column chromatography (10-20% EtOAc/hexanes).
Characterization of stereoisomer 1: TLC R_f 0.49 (20% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.12 (br s, 1H), 2.17 (t, 2H, J = 7.4-7.9 Hz), 1.87 (s, 3H), 1.51-1.44 (m, 2H), 1.33-1.23 (m, 6H), 0.88 (t, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 158.5 (C_4), 35.6 (CH_2), 31.3 (CH_2), 28.6 (CH_2), 26.0 (CH_2), 22.3 (CH_2), 13.8 (CH_3), 13.1 (CH_3); IR (film): 3256, 2956, 2929, 2861, 1667, 1462, 1363, 1108, 945 cm^{-1}; HRMS (EI): Exact mass calcd for $C_8H_{17}NO[M]^+$: 143.1310; found: 143.1333.
Characterization of stereoisomer 2: TLC R_f 0.39 (20% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 9.12 (br s, 1H), 2.36 (t, 2H, J = 7.6-8.1 Hz), 1.85 (s, 3H), 1.54-1.44 (m, 2H), 1.38-1.21 (m, 6H), 0.88 (t, 3H, J = 6.7 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.1 (C_4), 31.6 (CH_2), 29.4 (CH_2), 28.6 (CH_2), 25.4 (CH_2), 22.5 (CH_2), 19.8 (CH_3), 14.1 (CH_3).



Octanal oxime (Table 1, Entry 8, minor). Estimated 3 mg (2% conversion) by NMR analysis of the octa-2-one oxime (Table 1, Entry 8, major) ^1H NMR spectral data. ^1H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 7.39 (t, 1H, J = 6.2 H, isomer 1), 6.69 (t, 1H, J = 5.4 Hz, isomer 2), + aliphatic region.



Methyl 1-cyclohexenyl ketoxime (Table 1, Entry 9, major). Isolated 47 mg (22% yield) as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.63 (20% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 300 MHz) δ 10.02 (br s, 1H), 6.20 (tt, 1H, J = 4.1 and 1.4 Hz), 2.27 (td, 2H, J = 5.8 and 1.5 Hz), 2.21-2.15 (m, 2H), 2.02 (s, 3H), 1.70-1.56 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 156.7 (C_4), 134.3 (C_4), 130.1 (CH), 25.9 (CH_2), 24.3 (CH_2), 22.3 (CH_2), 22.0 (CH_2), 9.7 (CH_3); IR (film): 3275, 3226, 3123, 2922, 2861, 2835, 1640, 1432, 1008, 961, 925, 904, 849, 762 cm^{-1}; HRMS (EI): Exact mass calcd for $C_8H_{13}NO[M]^+$: 139.0997; found: 139.0995. Spectral ^1H NMR data was found to be in good agreement with those in the literature.[20]



2-cyclohexenylacetaldehyde oxime (Table 1, Entry 9, minor). Isolated 11 mg (3% yield) as colorless oil after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.48 and 0.41 (20% EtOAc/hexanes); ^1H NMR mixture of stereoisomers ($CDCl_3$, 300 MHz) δ 7.39 (t, 1H, J = 6.4 Hz, isomer 1), 6.74 (t, 1H, J = 5.4 Hz, isomer 2), 5.52-5.49 (m, 2H, isomer 1 and 2), 3.03 (d, 2H, J = 4.8 Hz, isomer 2), 2.80 (d, 2H, J

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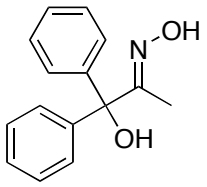
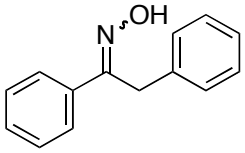
20. K. P. Park, C. Shiue, L. B. Clapp, *J. Org. Chem.* **1970**, *35*, 2065.

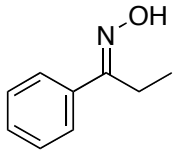
= 5.9 Hz, isomer 1), 2.04-1.87 (m, 8H, isomer 1 and 2), 1.69-1.50 (m, 8H, isomer 1 and 2); ^{13}C NMR mixture of stereoisomers ($CDCl_3$, 75 MHz) δ 150.9 (CH), 150.7 (CH), 132.9 (C_4), 132.6 (C_4), 124.3 (CH), 123.9 (CH), 37.9 (CH_2), 33.5 (CH_2), 28.7 (CH_2), 28.5 (CH_2), 25.2 (CH_2), 22.8 (CH_2), 22.7 (CH_2), 22.1 (CH_2), 22.1 (CH_2); IR (film): 3251, 2927, 2861, 1739, 1656, 1437, 981, 918 cm^{-1}; HRMS (EI): Exact mass calcd for $C_8H_{13}NO[M]^+$: 139.0997; found: 139.0991.



1-Hydroxy-1,1-diphenylpropan-2-one oxime (Table 1, Entry 10, major). Isolated 237 mg (63% yield) as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.22 (20% EtOAc/hexanes); ^{1}H NMR (DMSO-d_6, 300 MHz) δ 10.90 (s, 1H), 7.31-7.30 (m, 8H), 7.28-7.18 (m, 2H), 6.41 (s, 1H), 1.81 (s, 3H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ 159.6 (C_4), 145.1 (C_4), 127.4 (CH), 127.3 (CH), 126.5 (CH), 80.9 (C_4), 12.0 (CH_3); IR (film): 3332, 1659, 1602, 1488, 1443, 1374, 1051, 1013, 968, 880, 758, 728, 694 cm^{-1}; HRMS (EI): Exact mass calcd for $C_{15}H_{14}NO^+[M\text{-}OH]^+$: 224.1070; found: 224.1053. Spectral ^{1}H NMR data in $CDCl_3$ was found to be in good agreement with those in the literature.[21] Mp (recrystallized from 70% EtOAc/PhMe) 162.8-165.5˚C. The melting point was found to be in good agreement with those in the literature (159-160˚C).[22]



1,2-Diphenylethanone oxime (Table 1, Entry 11). Isolated 473 mg (71% yield) as white crystals after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.53 and 0.32 (20% EtOAc/hexanes). Spectral data for the major stereoisomer was found to be in good agreement with those in the literature,[23] however, two other (CH) carbon peaks were seen around δ 128.5.



Propiophenone oxime (Table 1, Entry 12, minor). Isolated 13 mg (3% yield) as colorless oil after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.48 (20% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.15 (br s, 1H), 7.65-7.59 (m, 2H), 7.41-7.36 (m, 3H), 2.83 (q, 2H, J = 7.6 Hz), 1.18 (t, 3H, J = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.8 (C_4), 135.5 (C_4), 129.2 (CH), 128.5 (CH), 126.2 (CH), 19.6 (CH_2), 10.9 (CH_3); IR (film): 3298, 3248, 3062, 2978, 2937, 2880, 1629, 1576, 1462, 1302, 1036, 968, 915, 767, 694 cm^{-1}; HRMS (EI): Exact mass calcd for $C_9H_{11}NO[M]^+$: 149.0841; found: 149.0837.

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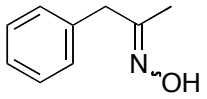
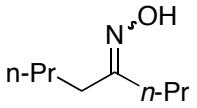
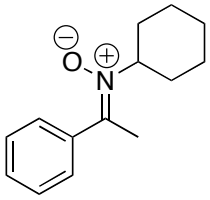
21. R. Bartnik, Y. Diab, A. Laurent, *Tetrahedron* **1977**, *33*, 1279.
22. T. I. Temnikova, *Zh. Obshch. Khim.* **1945**, *15*, 514.
23. T. Ohwada, A. Itai, T. Ohta, K. Shudo, *J. Am. Chem. Soc.* **1987**, *109*, 7036.



1-Phenylpropan-2-one oxime (Table 1, Entry 12, major). Isolated 144 mg (31% yield) as light yellow oil as mixture of stereoisomers after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.29 (20% EtOAc/hexanes). Spectral data was found to be in good agreement with those in the literature. [5]



Octan-4-one oxime (Table 1, Entry 13). Isolated 32 mg (7% yield) as light yellow oil as mixture of stereoisomers after column chromatography (10-20% EtOAc/hexanes). TLC R_f 0.39 (20% EtOAc:hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.99 (s, 1H), 2.36-2.29 (m, 2H), 2.20-2.12 (m, 2H), 1.61-1.41 (m, 4H), 1.40-1.25 (m, 2H), 0.98-0.88 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.8 (C_4), 161.8 (C_4), 36.1 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 28.4 (CH_2), 27.8 (CH_2), 27.3 (CH_2), 23.0 (CH_2), 22.4 (CH_2), 19.6 (CH_2), 19.1 (CH_2), 14.4 (CH_3), 13.9 (CH_3), 13.8 (CH_3), 13.8 (CH_3); IR (film): 3242, 3104, 2960, 2932, 2873, 1657, 1464, 1379, 1113, 963 cm^{-1}; HRMS (EI): Exact mass calcd for $C_8H_{17}NO[M]^+$: 143.1310; found: 143.1302.



(*E*)-*N*-(1-Phenylethylidene)cyclohexanamine-*N*-oxide (Equation 1). A 3 mL screwcap vial was charged with a stir bar, *N*-cyclohexylhydroxylamine[24] (0.050 g, 0.43 mmol), *n*-propanol (0.5 mL) and phenylacetylene (0.22 g, 2.1 mmol). The vial was capped with a septum and purged with argon and an outlet for 2 minutes while stirring. The septum was removed and the vial was then quickly sealed with a screw cap whose joints were sealed with Teflon tape and heated while stirring in an oil bath at 110°C for 14 hrs. The tube was cooled to ambient temperature, concentrated under reduced pressure and purified by silica gel chromatography (2% MeOH/CH_2Cl_2) to give the titled compound (0.049 g, 52%) as a clear, colorless oil. TLC R_f 0.33 (5% MeOH/CH_2Cl_2); ^{1}H NMR (C_6D_6, 300 MHz) 7.05-6.87 (m, 5H), 4.11 (tt, J = 11.4, 11.4, 3.7, 3.7 Hz, 1H), 2.39 (s, 3H), 1.75 (ap d, J = 12.1 Hz, 2H), 1.53-1.15 (m, 4H), 1.08-0.66 (m, 4H); ^{13}C NMR (C_6D_6, 75 MHz) 137.7, 129.0, 128.5, 127.9, 127.7, 67.2, 30.8, 25.2, 24.9, 20.8; IR (film): 3418, 2932, 2855, 1680, 1556, 1210 cm^{-1}; HRMS (EI): exact mass calcd for $C_{14}H_{19}NO$ $[M]^+$: 217.1467. Found: 217.1460.

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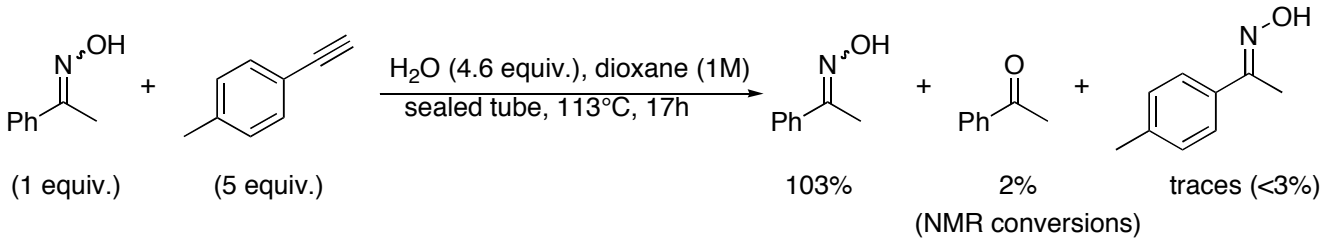
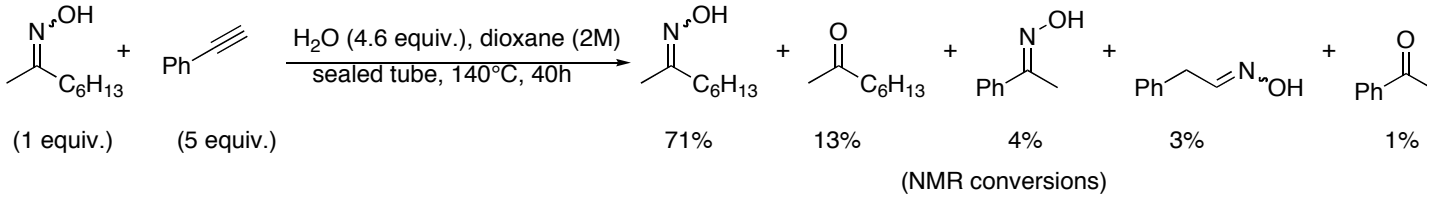
24. R. F. Borch, M. D. Bernstein, H. D. Durst, *J. Am. Chem. Soc.* **1971**, *93*, 2897.

Reversibility Studies. Little reversibility is observed suggesting that under these conditions, the reactions are not under thermodynamic control:

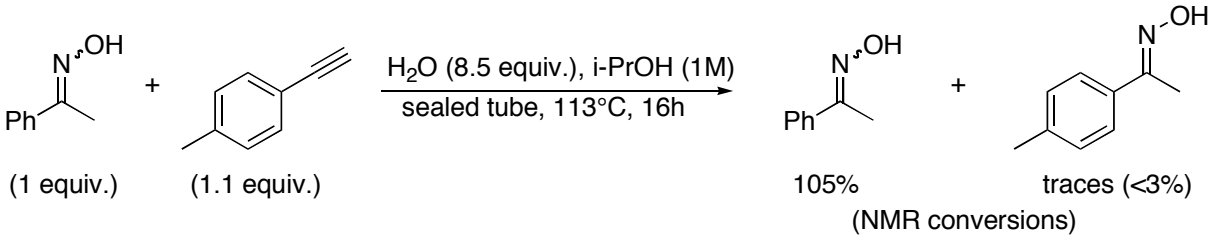


Acetophenone oxime and *p*-tolylacetylene in dioxane (reversibility for General Procedure A). In a sealed tube equipped with a magnetic stirbar was added acetophenone oxime (100 mg, 0.74 mmol, 1.0 equiv.), dioxane (0.7 mL, 1.0 M), *p*-tolylacetylene (430 mg, 3.70 mmol, 5.0 equiv.) and water[25] (61 mg, 61 μL, 3.38 mmol, 4.6 equiv.). The tube was sealed and heated at 113˚C for 17h. After cooling to room temperature, the reaction mixture was worked up as described in General Procedure A. To this crude was added styrene (38 mg, 42 μL, 0.37 mmol, 0.5 equiv.) as an internal standard for NMR conversions. ^{1}H NMR spectra in $CDCl_3$ was recorded, and the % conversion was calculated based on the ratio of the styrene (0.5H) doublet at ~5.3 ppm to the resonance corresponding to the product's protons. The method was estimated to have an error of approximately ±5%. The conversions obtained were estimated at 103% of acetophenone oxime (starting material) and traces (<3%) of 1-*p*-tolylethanone oxime (Markovnikov). Acetophenone was possibly observed as well (1%).



Octa-2-one oxime and phenylacetylene in dioxane (reversibility for General Procedure B). In a sealed tube equipped with a magnetic stirbar was added octa-2-one oxime (139 mg, 0.97 mmol, 1.0 equiv.), dioxane (0.5 mL, 2.0 M), phenylacetylene (494 mg, 531 μL, 4.84 mmol, 5.0 equiv.) and water[25] (80 mg, 80 μL, 4.44 mmol, 4.6 equiv.). The tube was sealed and heated at 140˚C for 40h. After cooling to room temperature, the reaction mixture was worked up as described in General Procedure A. To this crude was added styrene (25 mg, 28 μL, 0.24 mmol, 0.25 equiv.) as an internal standard for NMR conversions. ^{1}H NMR spectra in $CDCl_3$ was recorded, and the % conversion was calculated based on the ratio of the styrene (0.25H) doublet at ~5.3 ppm to the resonance corresponding to the product's protons. The method was estimated to have an error of approximately ±5%. The conversions obtained were estimated at 71% of octa-2-one oxime (starting material), 4% of acetophenone oxime (Markovnikov) and 3% of 2-phenylacetaldehyde oxime (anti-Markovnikov). 13% of octa-2-one and 1% of acetophenone were possibly observed as well.

25. Water was added in order to keep a similar solvent mixture as when hydroxylamine 50 wt. % solution in water was used.



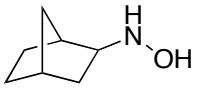
Acetophenone oxime and *p*-Tolylacetylene in *i*-Propanol (reversibility in *i*-PrOH solvent). In a sealed tube equipped with a magnetic stirbar was added acetophenone oxime (108 mg, 0.80 mmol, 1.0 equiv.), *i*-PrOH (0.8 mL, 1.0 M), *p*-tolylacetylene (102 mg, 0.88 mmol, 1.1 equiv.) and water[25] (123 mg, 123 μL, 6.83 mmol, 8.5 equiv.). The tube was sealed and heated at 113˚C for 16h. After cooling to room temperature, the reaction mixture was worked up as described in General Procedure A. To this crude was added styrene (21 mg, 23 μL, 0.20 mmol, 0.25 equiv.) as an internal standard for NMR conversions. ^{1}H NMR spectra in $CDCl_3$ was recorded, and the % conversion was calculated based on the ratio of the styrene (0.25H) doublet at ~5.3 ppm to the resonance corresponding to the product's protons. The method was estimated to have an error of approximately ±5%. The conversions obtained were estimated at 105% of acetophenone oxime (starting material) and traces (<3%) of 1-*p*-tolylethanone oxime (Markovnikov).

Procedure for Solvent Scan (Table 2). A 3 mL sealed tube was charged with a stir bar, an aqueous solution of hydroxylamine (50 wt% in water, 0.99 g, 15 mmol), solvent (1.5 mL), and norbornene (0.14 g, 1.5 mmol). The tube was then sealed with a screw cap and heated while stirring in an oil bath at 95°C for 14 hrs. The tube was cooled to ambient temperature and concentrated under reduced pressure. Styrene (0.16 g, 1.5 mmol) was then added as an internal standard. The biphasic mixture was taken up in $CDCl_3$, and the organic phase was transferred to an NMR tube. ^{1}H NMR spectra of these solutions were recorded, and the conversion calculated based on the relative integration of the resonance corresponding to one of the product's protons (1H) at 2.96 ppm compared to the integration of the resonance corresponding to a styrene proton at 6.69 ppm (1H).

General Procedure A for the Addition of Hydroxylamine to Alkenes (Table 3). A 48mL sealed tube was charged with a stir bar, an aqueous solution of hydroxylamine (50 wt% in water, 1.32 g, 20.0 mmol), isopropanol (4.0 mL), and alkene (10.0 mmol). The tube was capped with a septum and purged with argon and outlet for 10 minutes while stirring. The septum was removed and the tube was then quickly sealed with a Teflon screw cap and heated while stirring in an oil bath at 95-140°C for 18-72 hrs. The tube was cooled to ambient temperature, and the reactions were then monitored by thin layer chromatography (40% EtOAc/hexanes). For substrates where additional reaction time was deemed necessary, the tube was again purged with argon before exposure to heat. The crude reaction mixture was concentrated under reduced pressure and purified by silica gel chromatography (typically 10% EtOAc/hexanes → 50% EtOAc/hexanes) to give the corresponding *N*-alkyl- and *N,N*-dialkylhydroxylamines.

General Procedure B for the Addition of Hydroxylamine to Alkenes (Table 3). Reactions were carried out similarly to procedure A, except 10 equivalents of hydroxylamine were employed, and the amount of isopropanol was also increased such that the concentration of hydroxylamine remained the same as in Procedure A.

Table 3, entry 1. Synthesized according to general procedure A (95°C, 24 hrs). Isolated 0.39 g (31%) of *N*-hydroxybicyclo[2.2.1]heptan-2-amine and 0.76 g (69%, yield reported relative to alkene) of *N*-(bicyclo[2.2.1]heptan-2-yl)-*N*-hydroxybicyclo[2.2.1]heptan-2-amine after column chromatography (10% EtOAc/hexanes → 50% EtOAc/hexanes).



***exo-N*-Hydroxybicyclo[2.2.1]heptan-2-amine (table 3, entry 1).** Isolated 0.39 g (31%) as square white crystals. The stereochemistry was assigned by cleavage of the N-O bond under reductive conditions (Zn, HOAc) and comparison with the ^{1}H NMR of the corresponding known *exo*-amine.[26] TLC R_f 0.26 (40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) 6.41 (br s, 2H), 2.96 (dd, J = 7.7 and 3.7 Hz, 1H), 2.32 (d, J = 3.7 Hz, 1H), 2.17 (t, J = 4.1 Hz, 1H), 1.54-1.37 (m, 3H), 1.36-1.30 (m, 1H), 1.16-1.02 (m,3H), 1.01-0.92 (m, 1H); ^{13}C NMR (100 MHz) 65.1, 38.9, 35.36, 35.34, 34.5, 28.5, 26.5; IR (film): 3252, 3160, 2961, 2869, 1495, 1449, 1350, 1087, 996, 860 cm^{-1}; HRMS (EI): Exact mass calcd for $C_7H_{13}NO$ $[M]^+$: 127.0997. Found: 127.1001.

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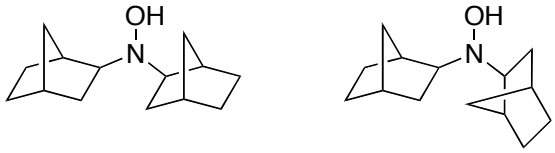
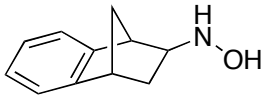
26. G. W. Kabalka, K. A. R. Sastry, G. W. McCollum, H. Yoshioka, *J. Org. Chem.* **1981**, *46*, 4296.

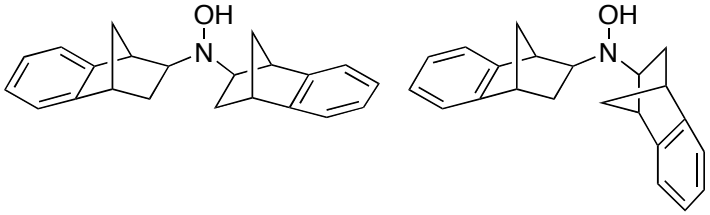


***N*-(Bicyclo[2.2.1]heptan-2-yl)-*N*-hydroxybicyclo[2.2.1]heptan-2-amine (Table 3, entry 1).** Isolated 0.76 g (69%) as a clear, colourless oil (mixture of diastereoisomers). TLC R_f 0.57 (25% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) **major**: 5.21 (br s, 1H), 2.71 (dd, J = 6.6 and 5.3 Hz, 2H), 2.38 (s, 2H), 2.23 (s, 2H), 1.83-1.22 (m, 10H), 1.20-0.97 (m, 6H) **minor**: 5.21 (br s, 1H), 2.78 (dd, J = 7.3 and 5.5 Hz, 2H), 2.38 (s, 2H), 2.23 (s, 2H), 1.83-1.22 (m, 10H), 1.20-0.97 (m, 6H); ^{13}C NMR (DMSO-*d*6, 300 MHz, 100°C)[27] **major**: 66.0, 38.6, 34.89, 34.7, 34.1, 27.69, 27.18 **minor**: 66.0, 37.8, 34.93, 34.85, 34.1, 27.64, 27.24 ; IR (film): 3382, 2950, 2869, 1452, 1313, 998, 733 cm^{-1}; HRMS (EI): Exact mass calcd for $C_{14}H_{23}NO$ $[M]^+$: 221.1780. Found: 221.1757.

Table 3, entry 2. Synthesized according to general procedure A (95°C, 24 hrs) starting with 7.0 mmol (0.18 g) of corresponding alkene. All other reagents and solvents scaled down accordingly. Isolated 0.48 g (39%) of *N*-hydroxy-*N*-(1,3,4-trihydro-1,4-methano-2-naphthalenyl)amine and 0.66 g (59%, yield reported relative to alkene) of *N*-hydroxy-*N,N*-di(1,3,4-trihydro-1,4-methano-2-naphthalenyl)amine after column chromatography (10% EtOAc/hexanes → 50% EtOAc/hexanes).



***exo*-*N*-Hydroxy-*N*-(1,3,4-trihydro-1,4-methano-2-naphthalenyl)amine (Table 3, entry 2).** Isolated 0.48 g (39%) as white crystals. The stereochemistry was assigned by cleavage of the N-O bond under reductive conditions (Zn, HOAc) and comparison with the ^{13}C NMR of the known *exo*-amine.[28] TLC R_f 0.26 (40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.31-7.22 (m, 1H), 7.18 (td, J = 7.7 and 3.8 Hz, 1H), 7.15-7.07 (m, 2H), 6.38 (br s, 2H), 3.54 (s, 1H), 3.34 (d, J = 2.2 Hz, 1H), 3.21 (dd, J = 7.7 and 3.6 Hz, 1H), 1.95-1.84 (m, 2H), 1.64 (ddd, J = 12.2, 7.7 and 1.8 Hz, 1H), 1.41 (td, J = 12.3 and 3.8 Hz, 1H); ^{13}C NMR (75 MHz) 148.9, 145.6, 125.9, 125.7, 121.6, 120.7, 64.0, 46.5, 45.5, 42.7, 33.3; IR (film): 3257, 3144, 2979, 2933, 2870, 2328, 1465, 1046, 879, 743 cm^{-1}; HRMS (EI): Exact mass calcd for $C_{11}H_{13}N_1O_1$ $[M]^+$: 175.0997. Found: 175.1003.



***N*-Hydroxy-*N,N*-di(1,3,4-trihydro-1,4-methano-2-naphthalenyl)amine (Table 3, entry 2).** Isolated 0.66 g (59%) as a white gum (mixture of diastereoisomers). TLC R_f 0.76 (40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) **major**: 7.45-7.15 (m, 8H), 5.46 (br s, 1H), 3.68 (s, 2H), 3.48 (s, 2H), 3.11 (dd, J = 6.8 and 4.2 Hz, 2H), 2.39 (t, J = 8.9 Hz, 4H), 1.93-1.85 (m, 4H), 1.51 (ddd, J = 11.3, 7.7 and 1.8 Hz, 2H) **minor**: 7.45-7.15 (m, 8H), 5.46 (br s, 1H), 3.68 (s, 2H), 3.48 (s, 2H), 3.23 (dd, J = 7.2 and 4.6 Hz, 2H), 2.39 (t, J = 8.9 Hz, 4H), 2.15-1.97 (m, 2H), 1.74 (ddd, J = 10.6, 7.9 and 1.6 Hz, 2H); ^{13}C NMR (100

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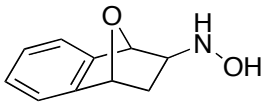
27. Broad peaks were observed in the ^{13}C NMR spectrum if recorded at 22 °C in $CDCl_3$. The compound was therefore dissolved in DMSO-d_6, and spectra were recorded at 100 °C, producing sharp singlets.

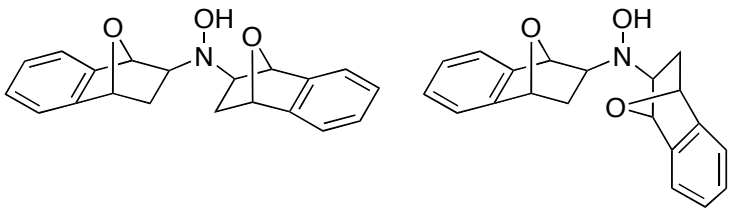
28. P. K. Burn, P. A. Crooks, *Org. Magn. Resonance* **1978**, *11*, 370.

MHz)[29] **major**: 149.09, 147.2, 125.7, 125.4, 121.0, 120.7, 66.8, 47.7 (br), 46.6, 45.8 (br), 43.33 **minor**: 149.1, 147.3, 125.6, 125.4, 120.9, 120.7, 66.8, 47.7 (br), 46.8, 45.8 (br), 43.28 ; IR (film): 3218, 2971, 2943, 2871, 2244, 1627, 1468, 1459, 909, 755, 731, 647 cm^{-1}; HRMS (EI): Exact mass calcd for $C_{22}H_{23}NO$ $[M]^+$: 317.1780. Found: 317.1790.

Table 3, entry 3. Synthesized according to general procedure A (95°C, 24 hrs) starting with 2.5 mmol (0.36 g) of corresponding alkene. All other reagents and solvents scaled down accordingly. Isolated 0.276 g (62%) of *N*-hydroxy-*N*-(1,3,4-trihydro-1,4-oxide-2-naphthalenyl)amine and 0.086 g (21%, yield reported relative to alkene) of *N*-hydroxy-*N,N*-di(1,3,4-trihydro-1,4-oxide-2-naphthalenyl)amine after column chromatography (20% EtOAc/hexanes → 100% EtOAc).



***exo*-*N*-Hydroxy-*N*-(1,3,4-trihydro-1,4-oxide-2-naphthalenyl)amine[30] (Table 3, entry 3).** Isolated 0.276 g (62%). TLC R_f 0.21 (60% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.33-7.27 (m, 1H), 7.23-7.12 (m, 3H), 6.03 (br s, 1H), 5.52 (s, 1H), 5.34 (d, J = 4.8 Hz, 1H), 3.32 (dd, J = 7.5 and 2.7 Hz, 1H), 1.73 (dd, J = 12.4 and 7.5 Hz, 1H), 1.49 (ddd, J = 12.4, 4.8, and 2.7 Hz, 1H); ^{13}C NMR (75 MHz) 146.3, 142.6, 127.0, 126.8, 120.2, 118.8, 80.2, 78.2, 63.6, 32.7; IR (film): 3261, 2999, 2929, 2850, 1453, 843 cm^{-1}; HRMS (EI): $C_{10}H_{11}N_1O_2$ $[M]^+$ not found, exact mass calcd for $C_{10}H_{10}NO$ $[M\text{-}OH]^+$: 160.0762. Found: 160.0780



***N*-Hydroxy-*N,N*-di(1,3,4-trihydro-1,4-oxide-2-naphthalenyl)amine (Table 3, entry 3).**
Isolated 0.086 g (21%) as a mixture of diastereoisomers. **Major.** TLC R_f 0.57 (60% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.36-7.28 (m, 2H), 7.24-7.11 (m, 6H), 5.89 (br s, 1H), 5.61 (s, 2H), 5.43 (d, J = 4.7 Hz, 2H), 3.08 (dd, J = 6.6 and 3.0 Hz, 2H), 2.21-2.06 (m, 2H), 1.44 (dd, J = 11.5 and 7.6 Hz, 2H); ^{13}C NMR (75 MHz) 146.2, 143.9, 126.9, 126.7, 119.7, 119.1, 82.5, 79.1, 66.0, 31.1 (br); IR (film): 3387, 3050, 3003, 2956, 1766, 1453 cm^{-1}; **minor.** Isolated 0.049 g (12%) after column chromatography (20% EtOAc/hexanes → 100% EtOAc). TLC R_f 0.43 (60% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) 7.31-7.14 (m, 8H), 5.61 (s, 2H), 5.47 (d, J = 3.9 Hz, 2H), 3.34-3.25 (m, 2H), 2.24-2.10 (m, 2H), 1.78 (dd, J = 10.9 and 7.8 Hz, 2H); ^{13}C NMR (75 MHz) 146.4, 143.8, 127.0, 126.8, 119.5, 119.2, 80.5, 79.0, 66.7, 32.3; IR (film): 3382, 3051, 3003, 2952, 1764, 1460 cm^{-1}; HRMS (EI): $C_{20}H_{19}NO_3$ $[M]^+$ not found, exact mass calcd for $C_{10}H_{10}N_1O$ $[M\text{-}OH]^+$: 304.1338. Found: 304.1326.

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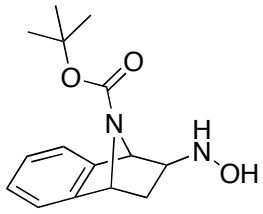
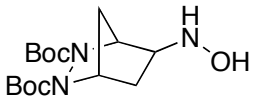
29. Broad peaks were observed in the ^{13}C NMR spectrum when recorded at 22 °C in $CDCl_3$. The compound was therefore dissolved in DMSO-d_6, and spectra were recorded at 100 °C, however rapid decomposition occurred under these conditions.

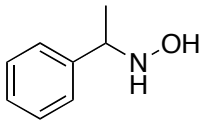
30. The *exo* stereochemistry of the product was assigned by analogy with entries 1 and 2.



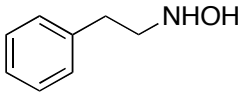
***exo*-*N*-Hydroxy-*N*-(1,3,4-trihydro-1,4-(*tert*-butylcarbamato)-2-naphthalenyl)amine[30] (Table 3, entry 4).** Synthesized according to general procedure A (95°C, 18 hrs) starting with 0.72 mmol (0.18 g) of corresponding alkene. All other reagents and solvents scaled down accordingly. Isolated 0.095 g (48%) after column chromatography ($CHCl_3$ → 5% MeOH/$CHCl_3$). TLC R_f 0.28 (5% MeOH/$CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.32-7.28 (m, 1H), 7.22-7.19 (m, 1H), 7.14-7.11 (m, 2H), 5.30 (s, 1H), 5.05 (d, J = 3.6 Hz, 1H), 3.26 (dd, J = 7.5 and 3.2 Hz, 1H), 1.62 (dd, J = 12.3 and 7.5 Hz, 1H), 1.52 (ddd, J = 12.4, 4.4, 3.5 Hz, 1H), 1.36 (s, 9H); ^{13}C NMR (100 MHz) 155.6, 146.4, 142.7, 142.7, 127.0, 126.8, 121.1, 119.8, 80.6, 64.3, 63.5, 60.7, 33.1, 28.4; IR (film): 3354, 2978, 2932, 2187, 1694, 1681, 1392 cm^{-1}; HRMS (EI): $C_{15}H_{20}N_2O_3$ $[M]^+$ not found, exact mass calcd for $C_{10}H_{11}N_2O$ $[M\text{-Boc}]^+$: 175.0871. Found: 175.0872.



***exo*-Di-*tert*-butyl 5-(hydroxyamino)-2,3-diaza-bicyclo[2.2.1]heptane-2,3-dicarboxylate[30] (Table 3, entry 5).** Synthesized according to general procedure A (95°C, 48 hrs) starting with 2.3 mmol (0.67 g) of corresponding alkene. All other reagents and solvents scaled down accordingly. Isolated 0.41 g (55%) after column chromatography (40% EtOAc/hexanes). TLC R_f 0.34 (40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) 6.03 (br s, 2H), 4.63-4.21 (m, 2H), 3.46-3.26 (m, 1H), 2.08-1.64 (m, 2H), 1.58-1.47 (m, 1H), 1.37 (s, 18 H), 1.18-1.05 (m, 1H); ^{13}C NMR (100 MHz) 158.6, 81.5, 61.9, 61.3, 59.1, 33.9, 32.0, 28.0; IR (film): 3402 (s), 2980, 2934, 2250, 1694, 1455 cm^{-1}; HRMS (EI): exact mass calcd for $C_{15}H_{27}N_3O_5$ $[M]^+$: 329.1951. Found: 329.1962.



***N*-Hydroxy-1-phenylethanamine (Table 3, entry 6).** Synthesized according to general procedure A (140°C, 72 hrs). Isolated 0.16 g (12%) as a white powder after column chromatography (10% EtOAc/hexanes → 50% EtOAc/hexanes). TLC R_f 0.52 (5% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.37-7.23 (m, 5H), 4.08 (q, J = 6.7 Hz, 1H), 1.37 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz) 142.2, 128.5, 127.6, 127.2, 61.7, 19.3. Spectral data were found to be in good agreement with those in the literature.[31]



***N*-Hydroxy-2-phenylethanamine (Table 3, entry 6).** Synthesized according to general procedure A (140°C, 72 hrs). Isolated 0.014 g (1.0%) as thin white crystals after column chromatography (10% EtOAc/hexanes → 50% EtOAc/hexanes). TLC R_f 0.42 (5% MeOH/CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.35-7.18 (m, 5H), 4.62 (br s, 2H), 3.20 (t, J = 7.0 Hz, 2H), 2.89 (t, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz)

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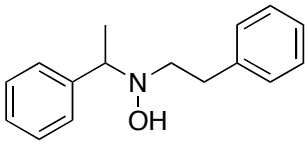
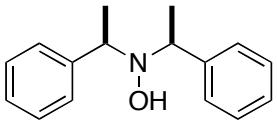
31. Z.-Y. Chang, R. M. Coates, *J. Org. Chem.* **1990**, *55*, 3464.

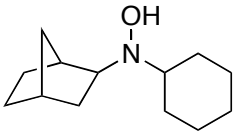
139.0, 128.8, 128.6, 126.3, 54.7, 33.0; Spectral data were found to be in good agreement with those in the literature.[32]



***N*-Hydroxy-*N*-phenethyl-1-phenylethanamine (table 3, entry 6).** Synthesized according to general procedure A (140°C, 72 hrs). Isolated 0.19 g (16%) as a clear, colourless oil after column chromatography (10% EtOAc/hexanes → 50% EtOAc/hexanes). TLC R_f 0.53 (40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.32-7.29 (m, 4H), 7.27-7.21 (m, 3H), 7.19-7.10 (m, 3H), 3.82 (q, J = 6.6 Hz, 1H), 3.00-2.77 (m, 4H), 1.46 (d, J = 6.7 Hz, 3H); ^{13}C NMR (100 MHz) 142.4, 140.1, 128.8, 128.5, 128.3, 127.9, 127.4, 126.0, 67.7, 58.6, 33.8, 19.7; IR (film): 3262, 3027, 2973, 2933, 2866, 1744, 1602, 1494, 1453, 1369, 1073, 1029, 752, 699 cm^{-1}; HRMS (EI): Exact mass calcd for $C_{16}H_{19}NO$ $[M]^+$: 241.1467. Found: 241.1445.



***meso* *N*-Hydroxy-1-phenyl-*N*-(1-phenylethyl)ethanamine (table 3, entry 6).** Synthesized according to general procedure A (140°C, 72 hrs). Isolated 0.12 g (10%) as a clear, colourless oil after column chromatography (10% EtOAc/hexanes → 50% EtOAc/hexanes). TLC R_f 0.61 (40% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) 7.43-7.24 (m, 10H), 3.93 (q, J = 6.6 Hz, 2H), 1.45 (d, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz) 143.3, 128.3, 127.9, 127.1, 62.1, 17.3; Spectral data were found to be in good agreement with those in the literature.[31]



***N*-Cyclohexyl-*N*-hydroxybicyclo[2.2.1]heptan-2-amine (Equation 2).** A 15 mL sealed tube was charged with a stir bar, *N*-cyclohexylhydroxylamine[24] (0.10 g, 0.87 mmol), *n*-propanol (1.4 mL), sodium cyanoborohydride (0.055 g, 0.87 mmol) and norbornene (0.16 g, 1.7 mmol). The tube was capped with a septum and purged with argon and an outlet for 5 minutes while stirring. The septum was removed and the tube was then quickly sealed with a Teflon screw cap and heated while stirring in an oil bath at 110°C for 21 hrs. The tube was cooled to ambient temperature, concentrated under reduced pressure and purified by silica gel chromatography (10% EtOAc/hexanes) to give the titled compound (0.15 g, 83%) as a white gum. When the reaction was performed in the absence of sodium cyanoborohydride the yield was slightly reduced (0.12 g, 67%). TLC R_f 0.35 (10% EtOAc/hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) 4.54 (br s, 1H), 2.85 (t, J = 5.8, 5.8 Hz, 1H), 2.63 (tt, J = 11.3, 11.3, 3.1, 3.1 Hz, 1H), 2.35 (s, 1H), 2.23 (s, 1H), 1.79 (ap d, J = 9.3 Hz, 4H), 1.69-0.98 (m, 14H); ^{13}C NMR ($CDCl_3$, 75 MHz) 65.7, 61.1, 39.5, 36.0, 35.9, 35.2, 28.3, 27.6, 26.0, 25.8, 25.6; IR (film): 3432, 2910, 2851, 1451 cm^{-1}; HRMS (EI): exact mass calcd for $C_{13}H_{23}NO$ $[M]^+$: 209.1780. Found: 209.1797.

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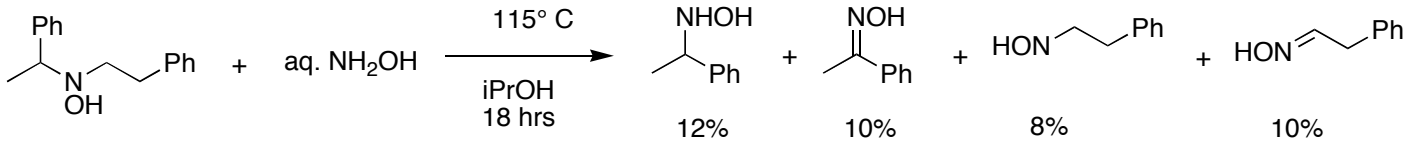
32. R. J. Rahalm, Jr; R. E. Maleczka, Jr, *Org. Lett.* **2005**, *7*, 5087.

Reversibility Experiments



Procedure for Cope Elimination of *N*-hydroxy-*N*-phenethyl-1-phenylethanamine. A 2mL sealed tube was charged with a stir bar, an aqueous solution of hydroxylamine (50 wt% in water, 0.11 g, 1.7 mmol), *i*PrOH (0.40mL) and *N*-hydroxy-*N*-phenethyl-1-phenylethanamine (0.040 g, 0.17 mmol). The tube was capped with a septum and purged with argon and outlet for 10 minutes while stirring. The septum was removed and the tube was then quickly sealed with a screw cap. The tube was heated in an oil bath at 115°C for 18 hrs. The tube was cooled to ambient temperature, the solvent was evaporated and the residue taken up in $CDCl_3$. ^1H NMR analysis revealed that a fraction of the starting *N*-hydroxy-*N*-phenethyl-1-phenylethanamine had been converted to Cope elimination products *N*-hydroxy-1-phenylethanamine (12%), *N*-hydroxy-2-phenylethanamine (8%) as well as the oxidation byproducts acetophenone oxime (10%) and 2-phenylacetaldehyde oxime (10%). The remainder was unreacted starting material. The oxidative byproducts were also observed in the forward reaction. Several attempts to remove O_2 from the reaction vessel slowed but did not suppress the oxidative process. Monosubstituted hydroxylamines are known to undergo anaerobic solvent-induced oxidation.[33]

33. S. Horiyama, K. Suwa, M. Yamaki, H. Kataoka, T. Katagi, M. Takayama, T. Takeuchi, *Chem. Pharm. Bull.* **2002**, *50*, 996.

Computational Details

Density functional theory (DFT) calculations have been performed using the *Gaussian 03* program.[34] Optimized molecular geometries were calculated using the B3LYP[35] exchange-correlation functional.

The triple-zeta TZVP[36] basis set and tight SCF convergence criteria were used for calculations. Wave function stability calculations were performed to confirm that the calculated wave functions corresponded to the ground state. Harmonic frequency calculations were performed to ensure that the stationary points were true energy minima or transition states (TSs) and to calculate free energies of the species. Reaction coordinate[37] scans were performed to verify that the calculated TSs connects the correct minima for a given reaction step. The unscaled vibrational frequencies were used for calculating Gibbs free energies of the species (at 298K and 1 atm). The basis set superposition errors (BSSE) were evaluated using the Boys-Bernardi counterpoise method.[38] However, because all calculated corrections were sufficiently low (less than 0.6 kcal/mol) for the basis set employed, the corrections were not included in the calculation of the energies of the species.

To probe the solvent effects, solvation free energies of the reactants and products for the hydroamination reaction (NH_2OH) with C_7H_{10} in four solvents (benzene, $CHCl_3$, DMSO and methanol) were calculated using the polarizable continuum model (PCM)[39] with the united atom topological radii (UAHF). In addition, solvation free energies of all species for the hydroamination reaction (NH_2OH) with C_2H_4 and C_7H_{10} in methanol were calculated to probe the solvent effect for reaction barriers. The calculated solvation free energies were used to calculate the free energies of the species in solution. The results of these calculations summarized in Table S1. The only species that are affected significantly by solvation are the R-$NH_2^+O^-$ intermediates, which become more stable in polar solvents due to the significant ionic character of the -$NH_2^+O^-$. The free energies of the TSs and the overall reactions show much less variation between the gas phase values and those in the most polar solvent employed (methanol).

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34. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Lyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03, Revision C.01*, Gaussian, Inc.: 2003.

35. A. D. Becke, *J. Chem. Phys.* **1993**, *98*, 5648.

36. A. Schafer, C. Huber, R. Ahlrichs, *J. Chem. Phys.* **1994**, *100*, 5829-5835.

37. (a) C. Gonzalez, H. B. Schlegel, *J. Chem. Phys.* **1989**, *90*, 2154. (b) C. Gonzalez, H. B. Schlegel, *J. Phys. Chem.* **1990**, *94*, 5523.

38. S. F. Boys, F. Bernardi, *Mol. Phys.* **1970**, *19*, 553.

39. M. Cossi, G. Scalmani, N. Rega, V. Barone, *J. Chem. Phys.* **2002**, *117*, 43

Table S1. Free energies (kcal/mol) of the reaction species for hydroamination reactions (NH_2OH) with alkenes and alkynes (evaluated at 298K and 1 atm). The energies are relative to the free reactants.

	Alkenes				**Alkynes**		
Species	**C_2H_4**	**C_7H_{10}**	**C_8H_8 AM**	**C_8H_8 M**	**C_2H_2**	**C_8H_6 AM**	**C_8H_6 M**
RC [a]	5.1 (9.6)[b]	5.8 (11.1)[b]	5.9	5.9	4.5	5.6	5.6
Hydroamination TS	33.2 (32.0)[b]	32.0[c] (34.3)[b]	38.4	33.4	28.5	33.2	30.1
R-$NH_2^+O^-$	13.9 (4.9)[b]	13.1 (8.4)[b]	19.5	18.7	2.9	6.9	8.7
Intramolecular H^+ transfer TS	38.3 (36.0)[b]	37.7 (38.9)[b]	44.0	44.2	23.6	28.9	30.1
bimolecular H^+ transfer TS [d]	20.9 (14.4)[b]	20.1[e] (18.1)[b]	26.5 [e]	25.7 [e]	7.9	11.9 [e]	13.7 [e]
R-NHOH	-6.4 (-6.6)[b]	-7.0 [f] (-3.0)[b]	0.3	-0.5	-24.2	-18.5	-17.2
C=N-OH					-39.2	-28.2	-33.4

a) Reactants complex; b) free energies of the species in methanol; c) for the reactions with NH(Me)OH and $N(Me)_2OH$, the TS free energies are 30.7 and 32.5 kcal/mol, respectively; d) the transition state for proton transfer between R-$NH_2^+O^-$ and *i*-PrOH; e) the energy of the transition state was evaluated using the calculated activation free energy for the proton transfer for the C_2H_5-NH_2O…*i*-PrOH complex (to form C_2H_5-NHOH…*i*-PrOH) for alkenes and the C_2H_3-NH_2O…*i*-PrOH complex (to form C_2H_3-NHOH…*i*-PrOH) for alkynes (7.0 kcal/mol and 5.0 kcal/mol in vacuum, respectively and 9.7 kcal/mol and 7.5 kcal/mol in methanol). These activation energies show little variability to the nature of the proton shuttle. For example, the activation free energy for the proton transfer for the C_2H_5-NH_2O…HOH and C_2H_3-NH_2O…HOH complexes in vacuum are 7.3 kcal/mol and 5.3 kcal/mol, respectively. The energies of the other hydroamination reaction species (minima and TSs) were also evaluated in the presence of H-bound *i*-PrOH. However, this produced only a minor energy change for the hydroamination reaction steps in Figure 1 (except in the proton transfer step); f) -6.2 kcal/mol in C_6H_6, -5.2 kcal/mol in $CHCl_3$ and -4.6 kcal/mol in DMSO.

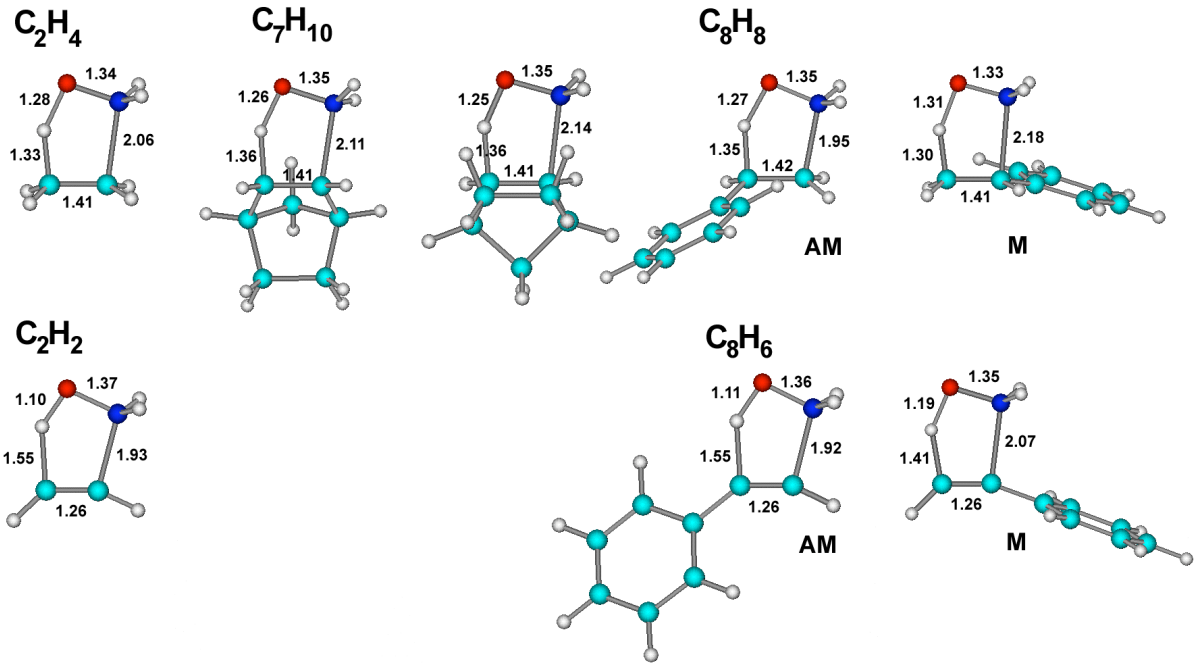


Figure S1. Transition state structures for hydroamination of alkenes and alkynes at the B3LYP/TZVP level of theory; M= Markovnikov product, AM=anti-Markovnikov product. The internuclear distances (Å) are shown only for relevant chemical bonds.

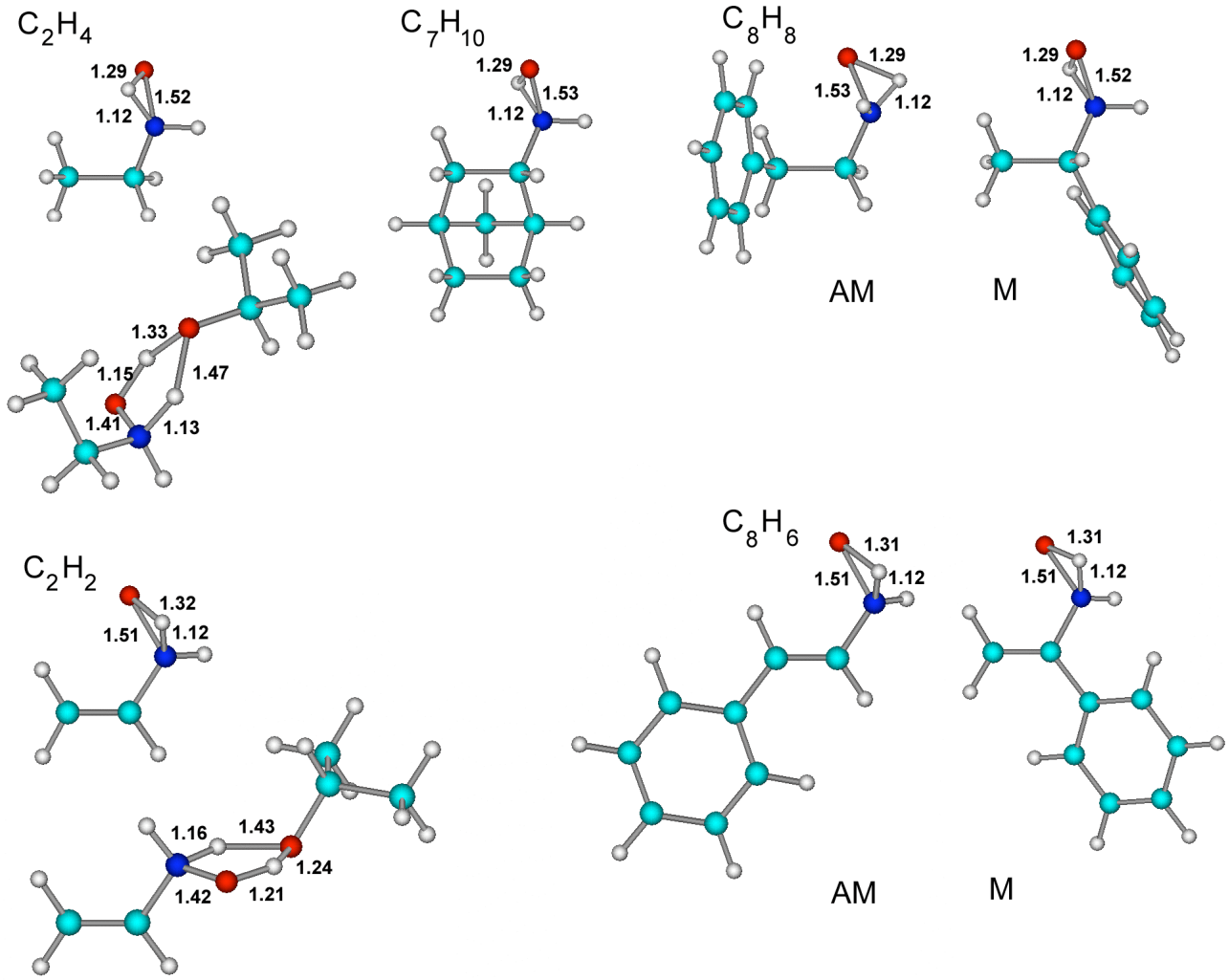


Figure S2. Transition state structures for intramolecular and bimolecular proton transfer in the hydroamination reactions of alkenes and alkynes at the B3LYP/TZVP level of theory; M= Markovnikov product, AM=anti-Markovnikov product. The internuclear distances (Å) are shown only for relevant chemical bonds. The TS structures for bimolecular proton transfer are shown for reactions R-$NH_2^+O^-$ with *i*-PrOH.

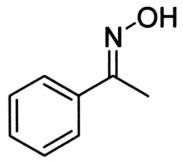
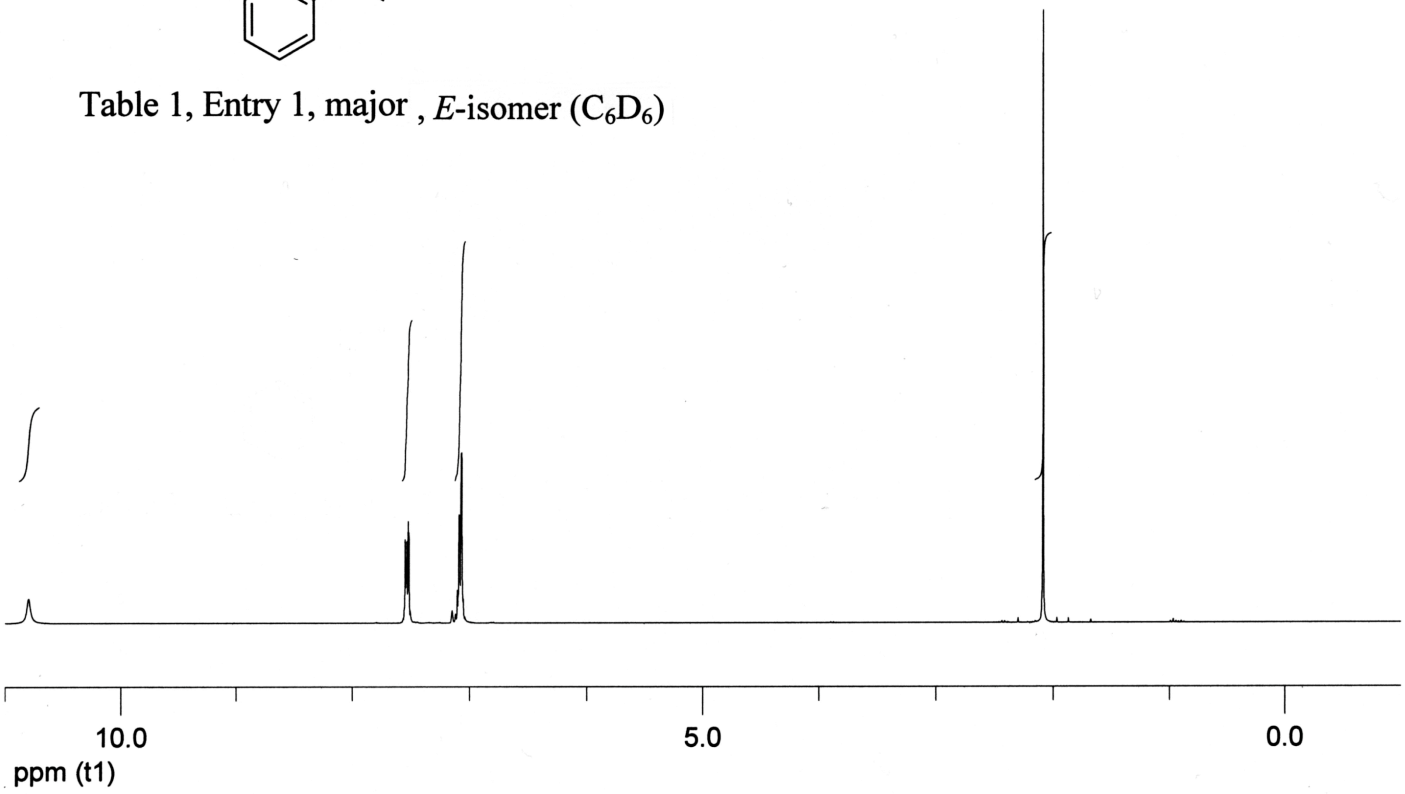
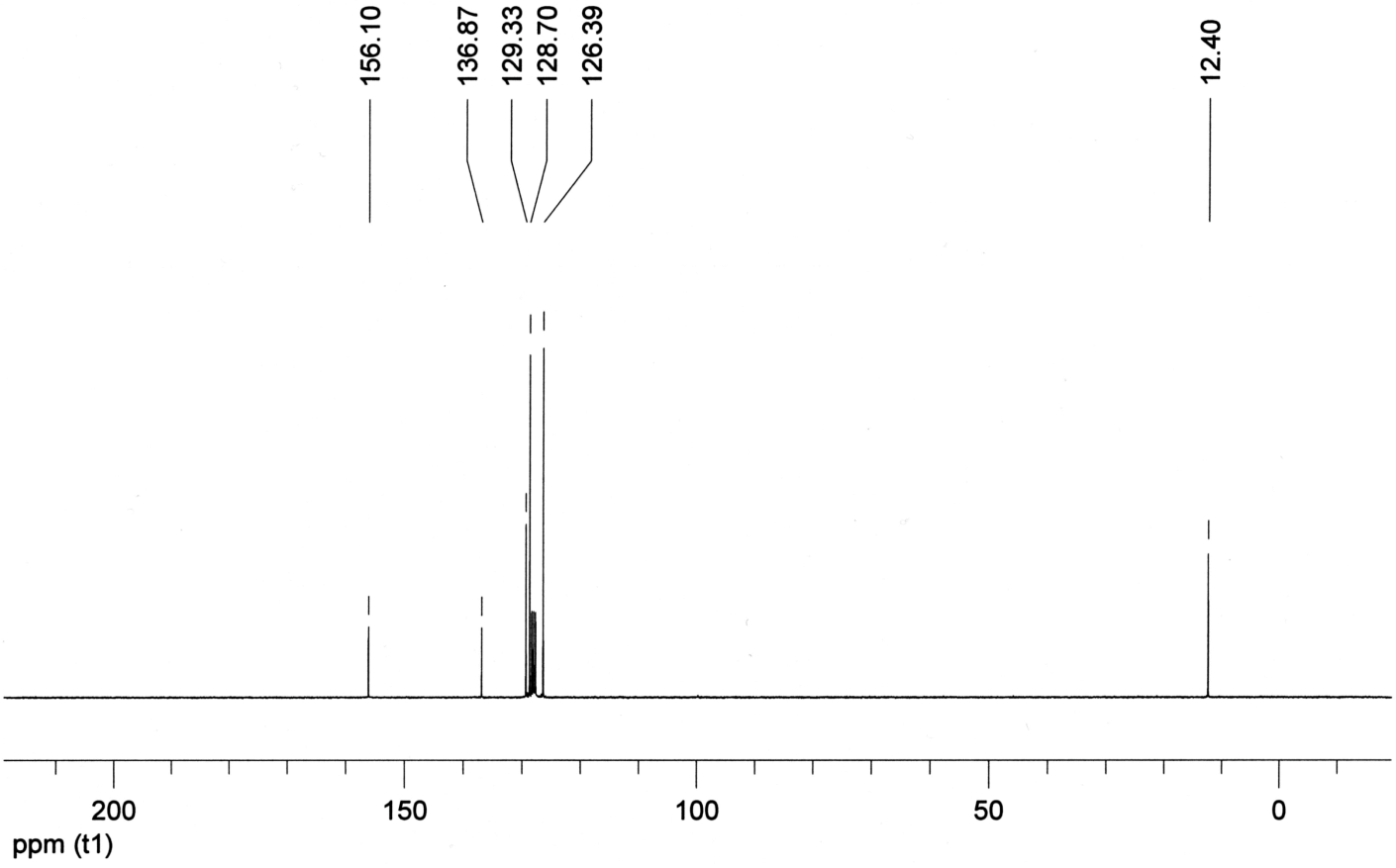
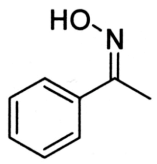


Table 1, Entry 1, major , *E*-isomer (C_6D_6)







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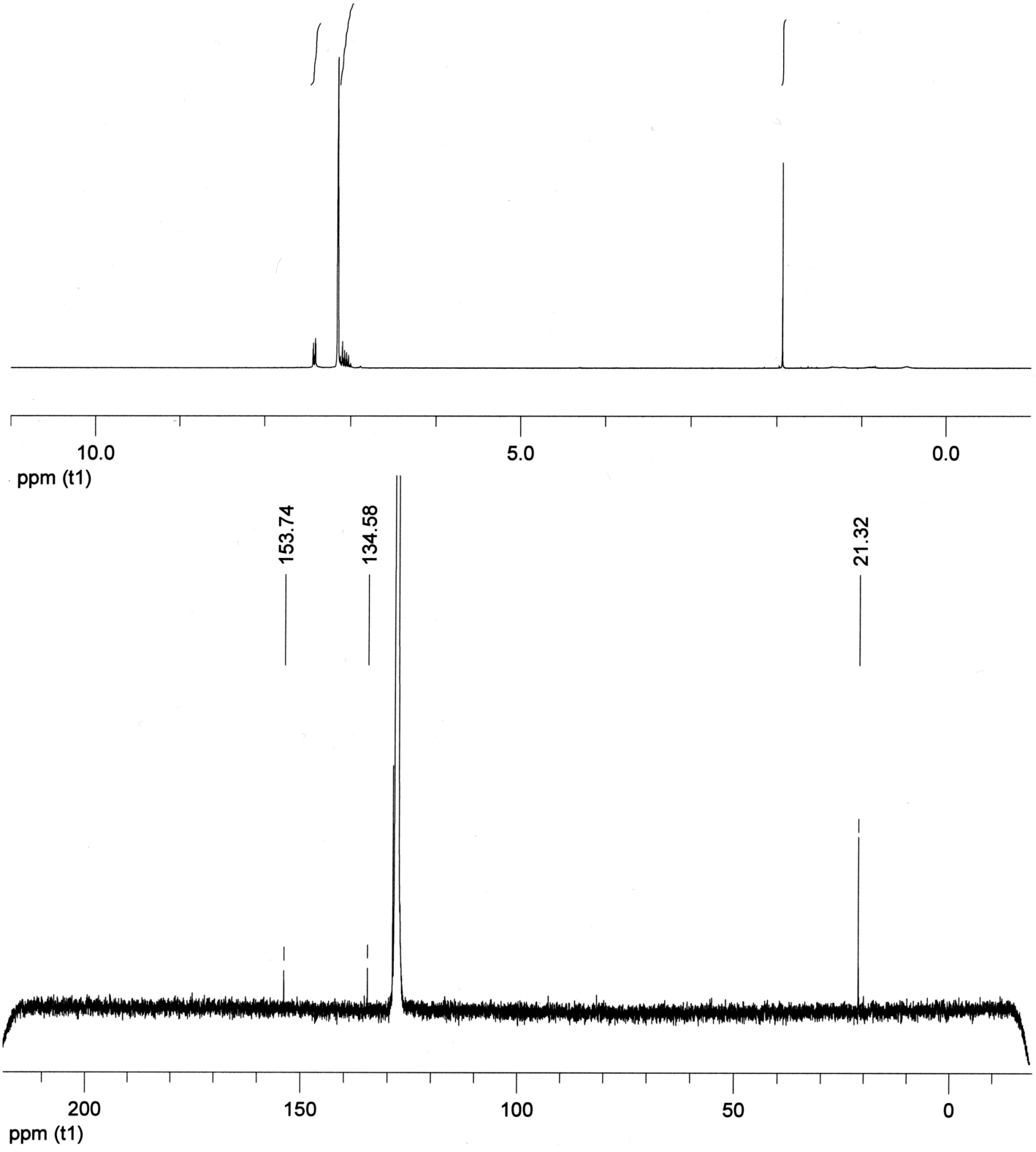

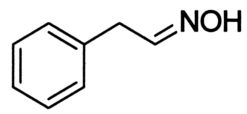

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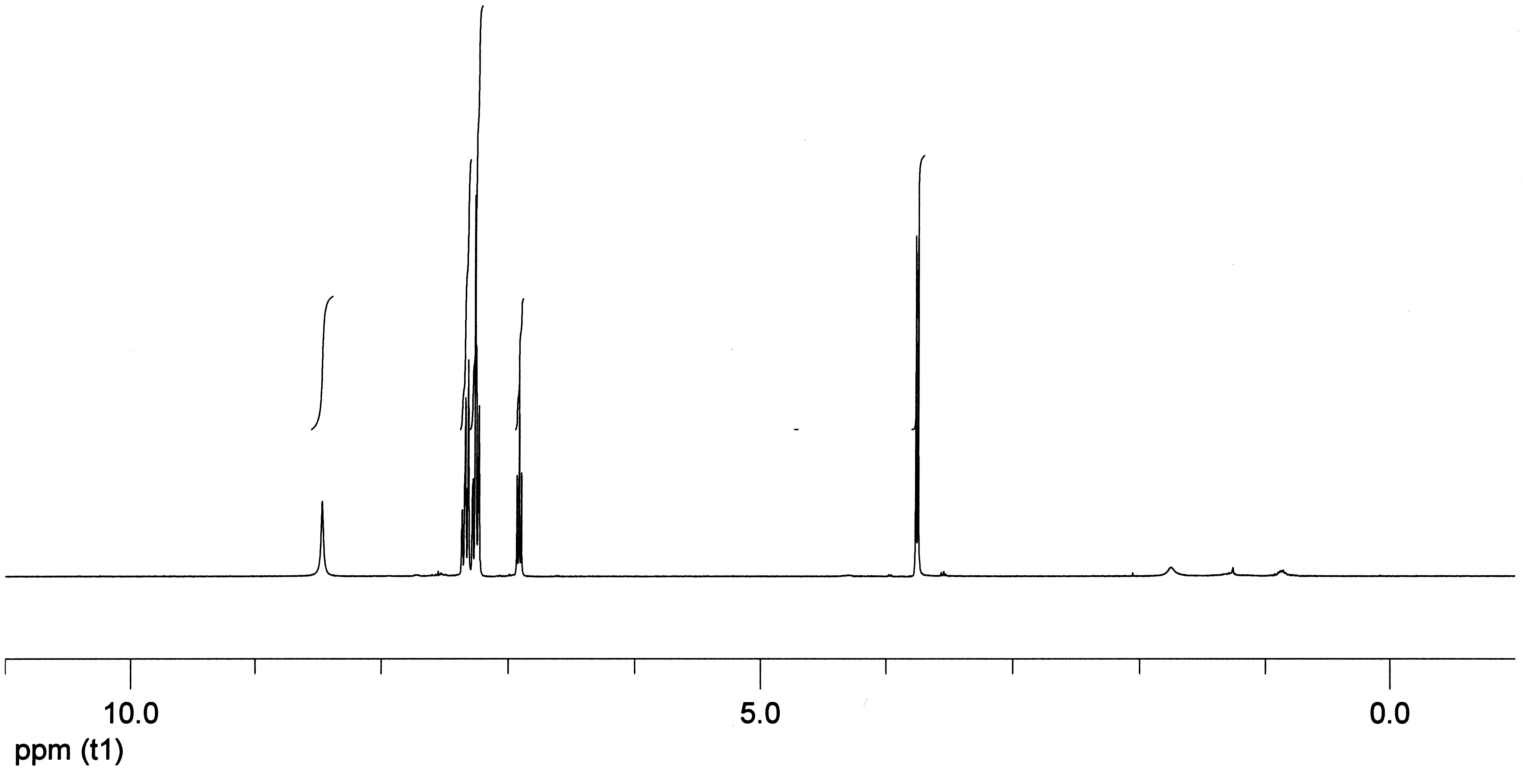

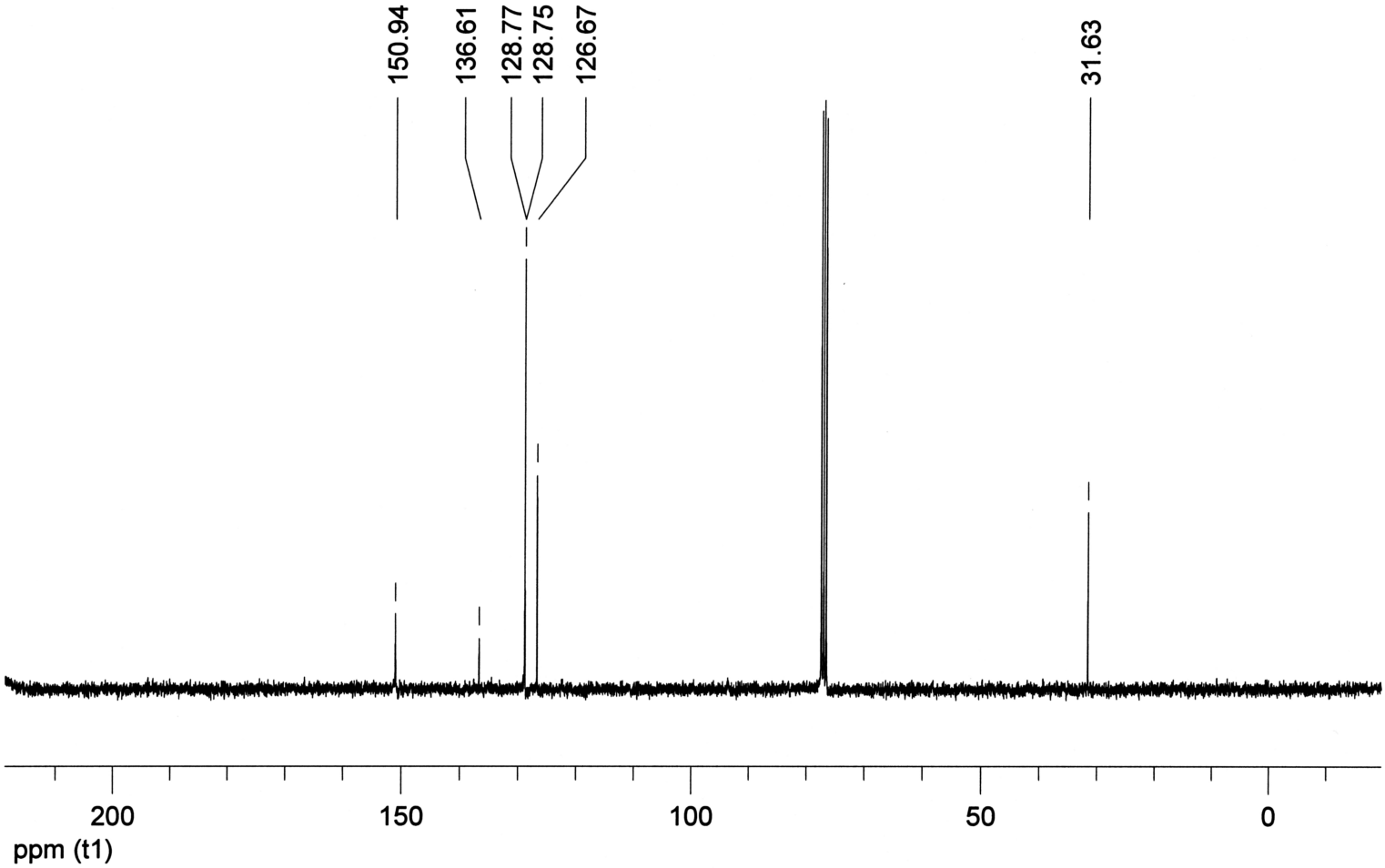

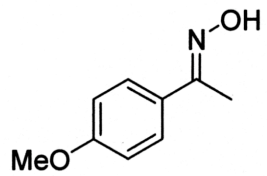

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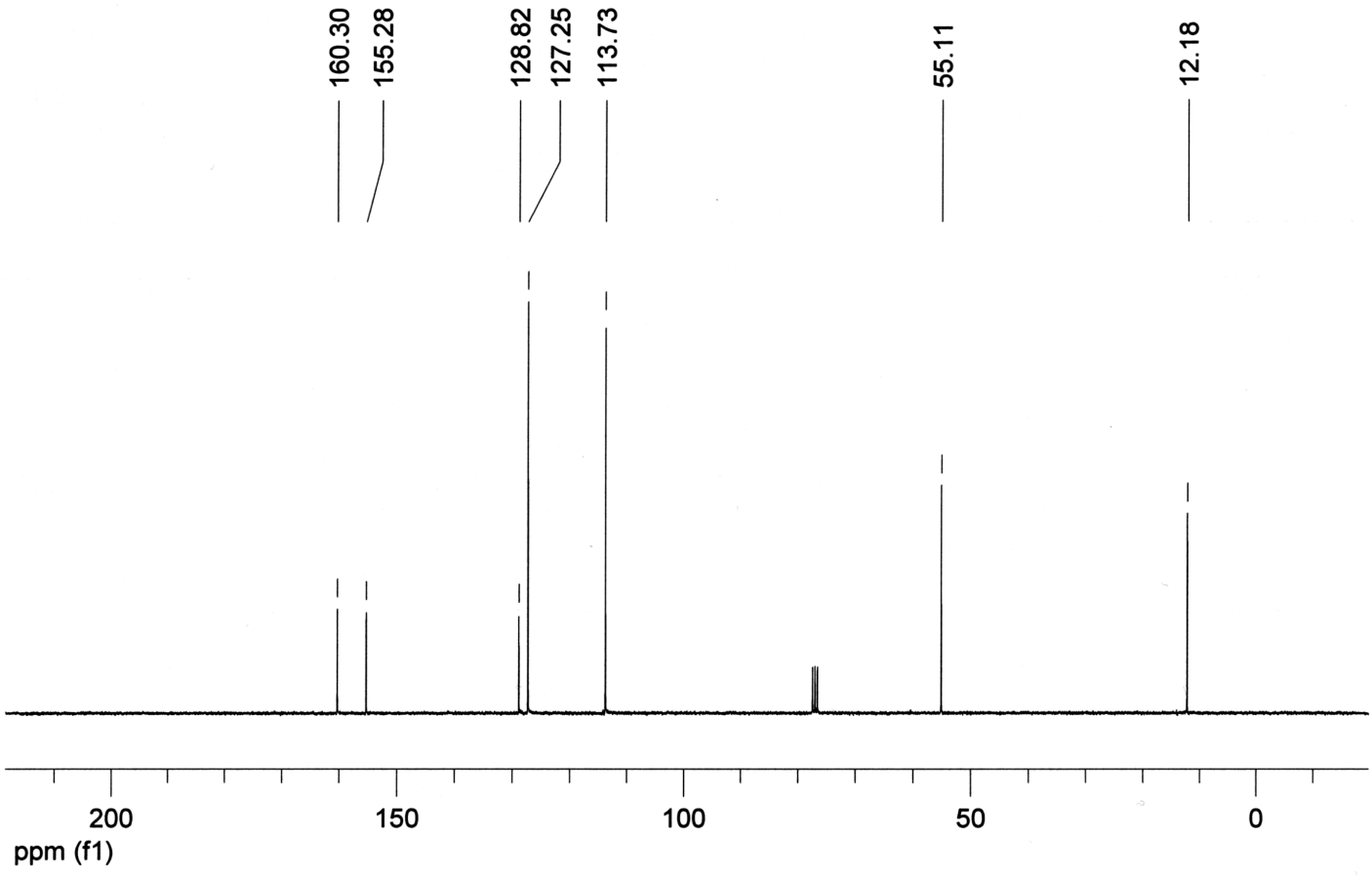

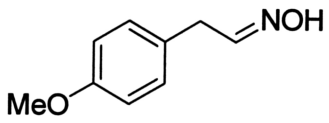

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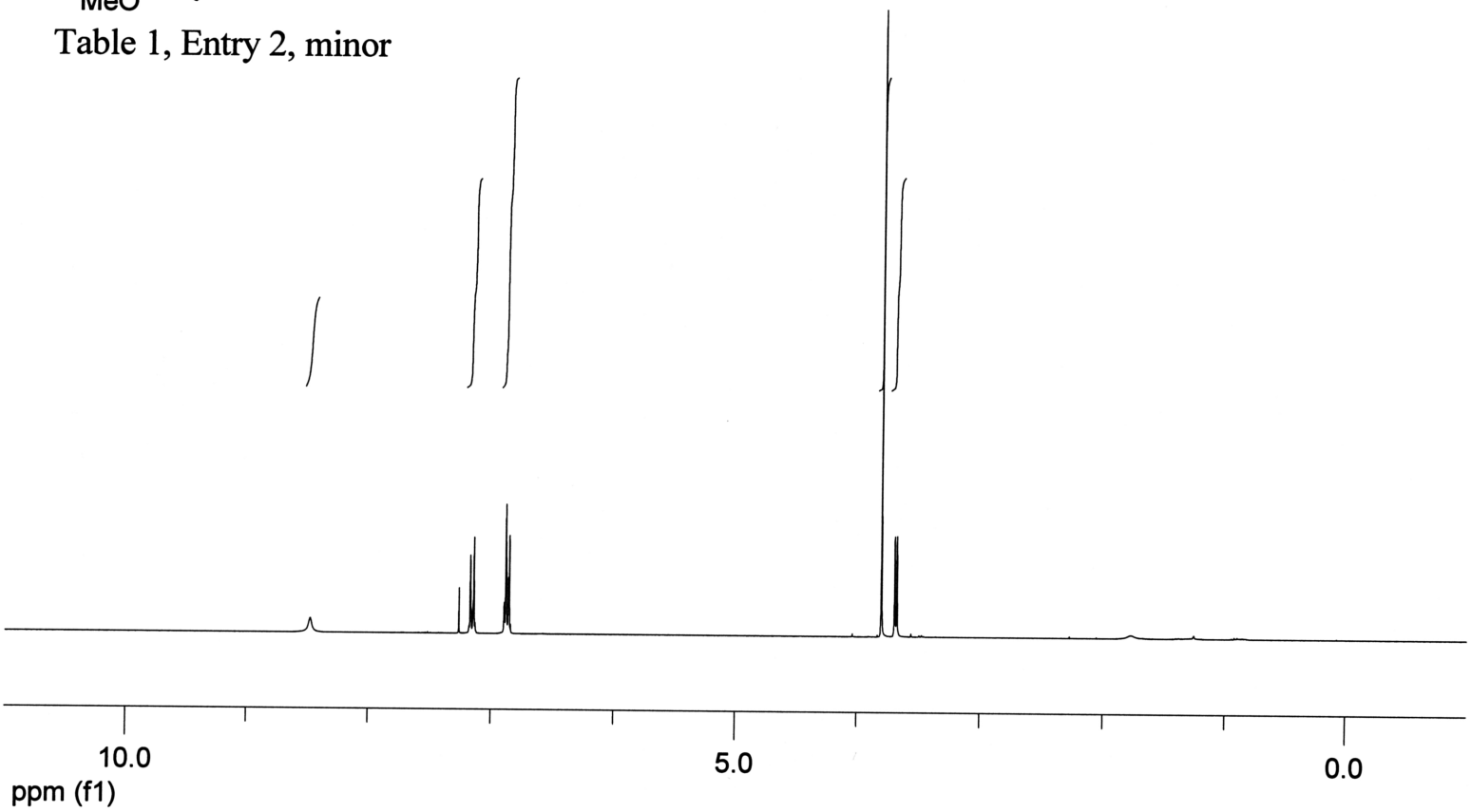

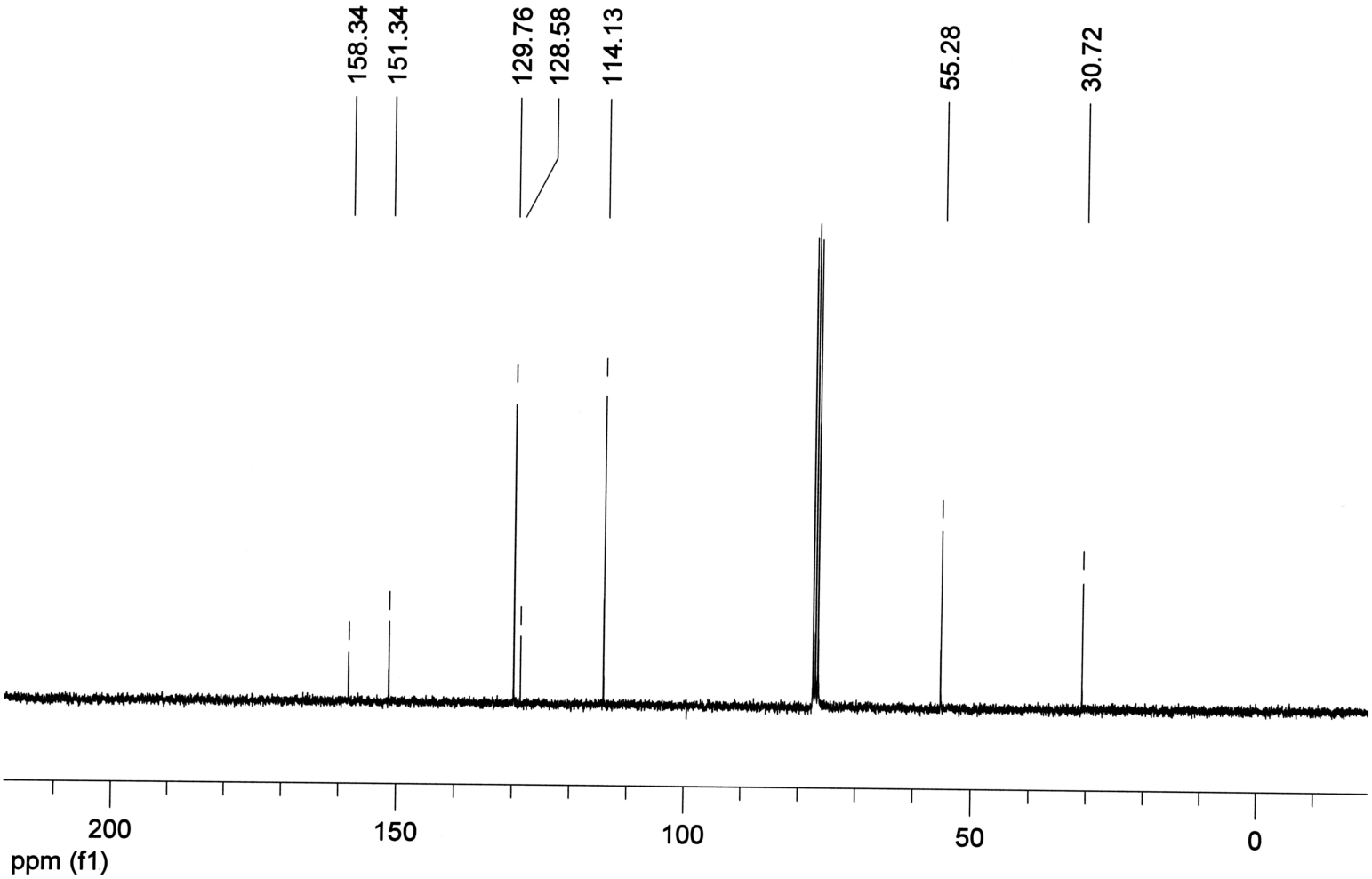

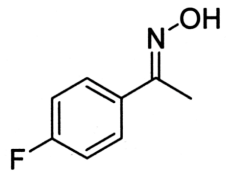

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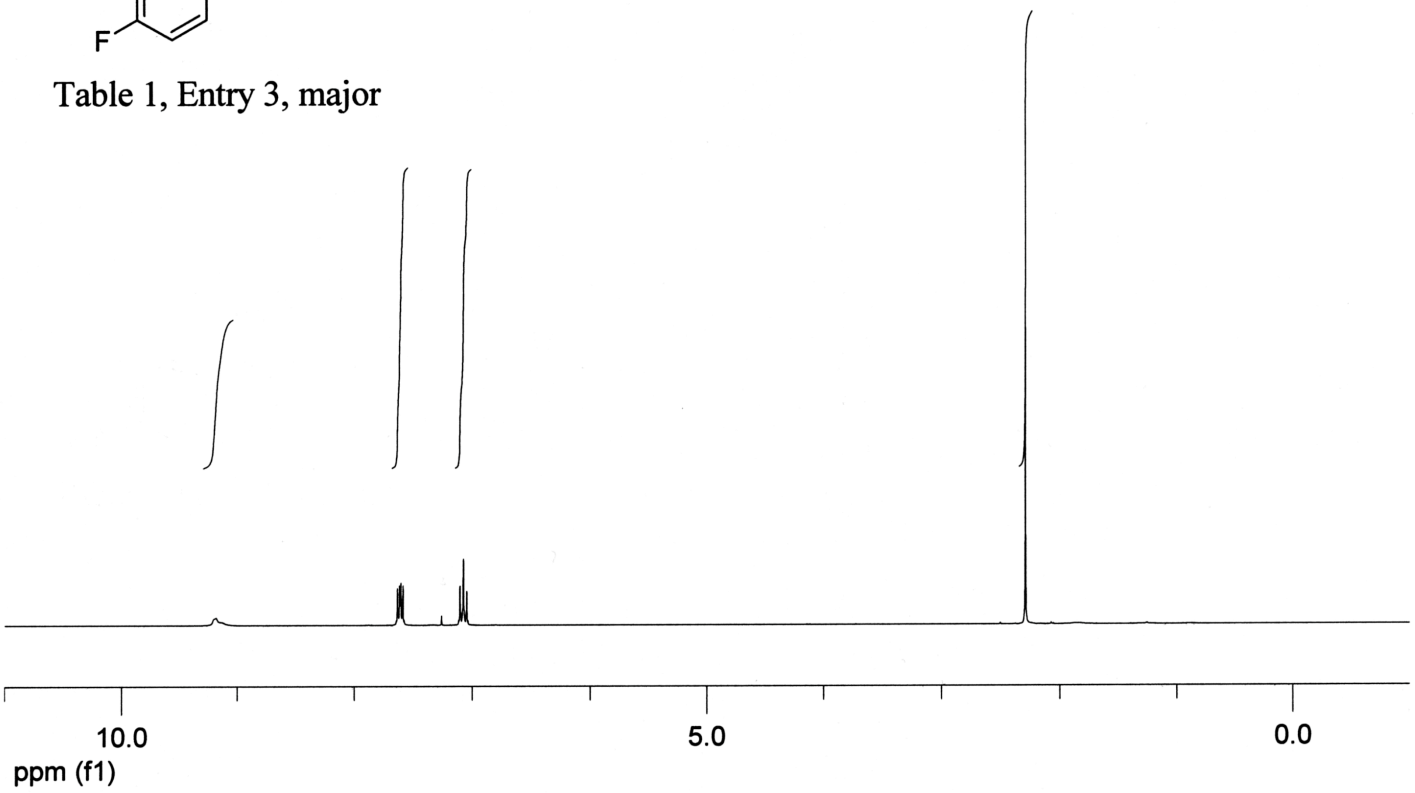

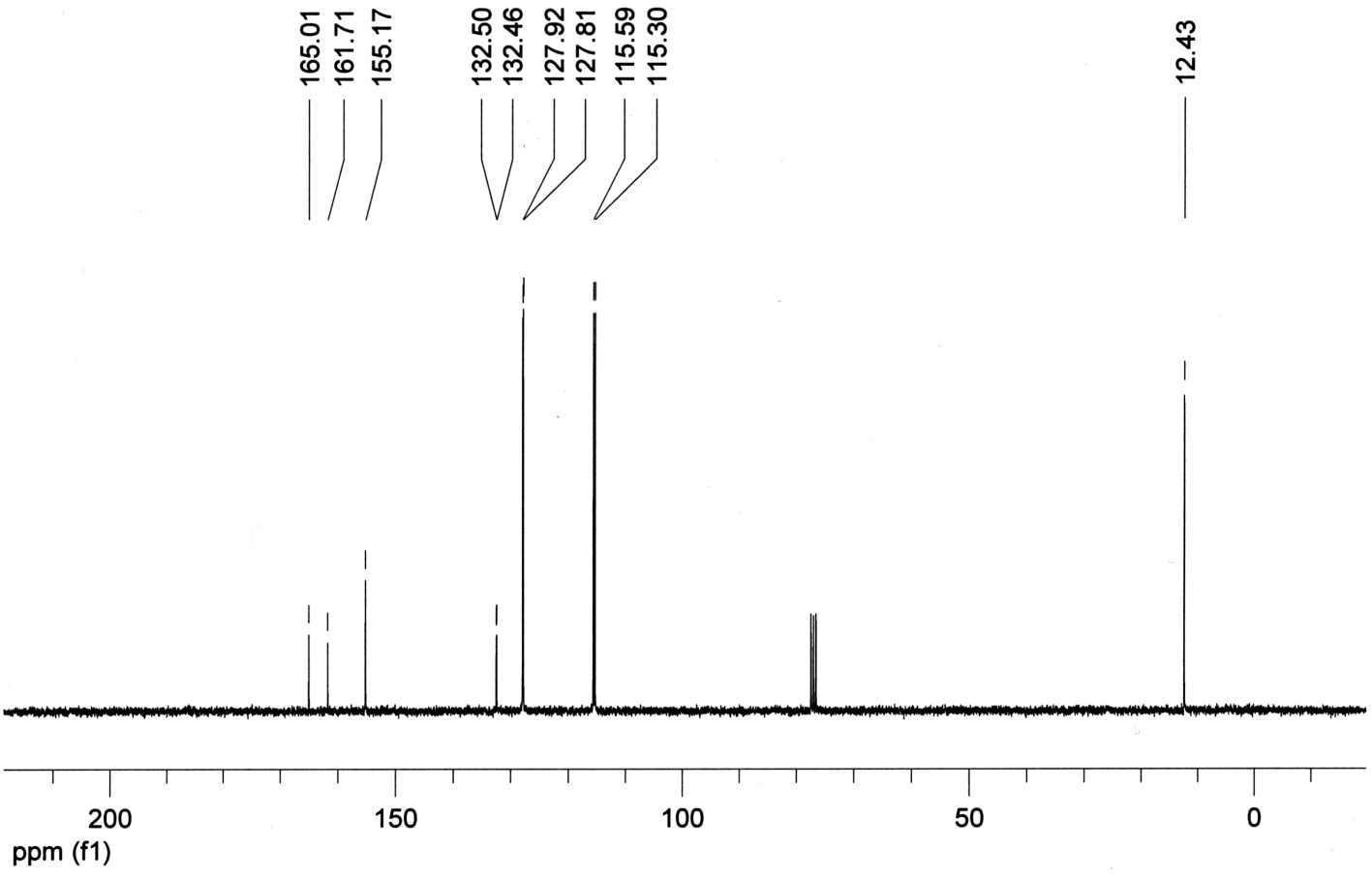

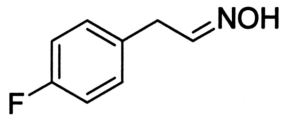

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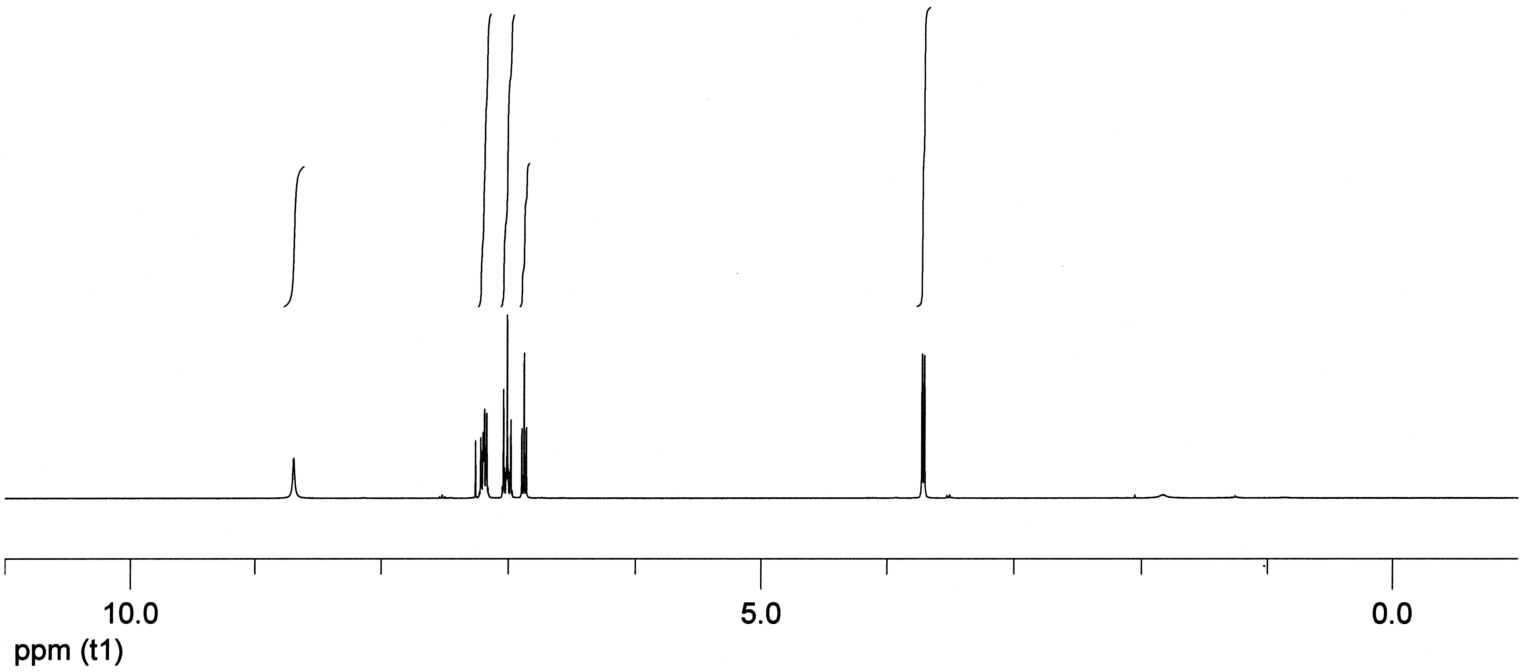

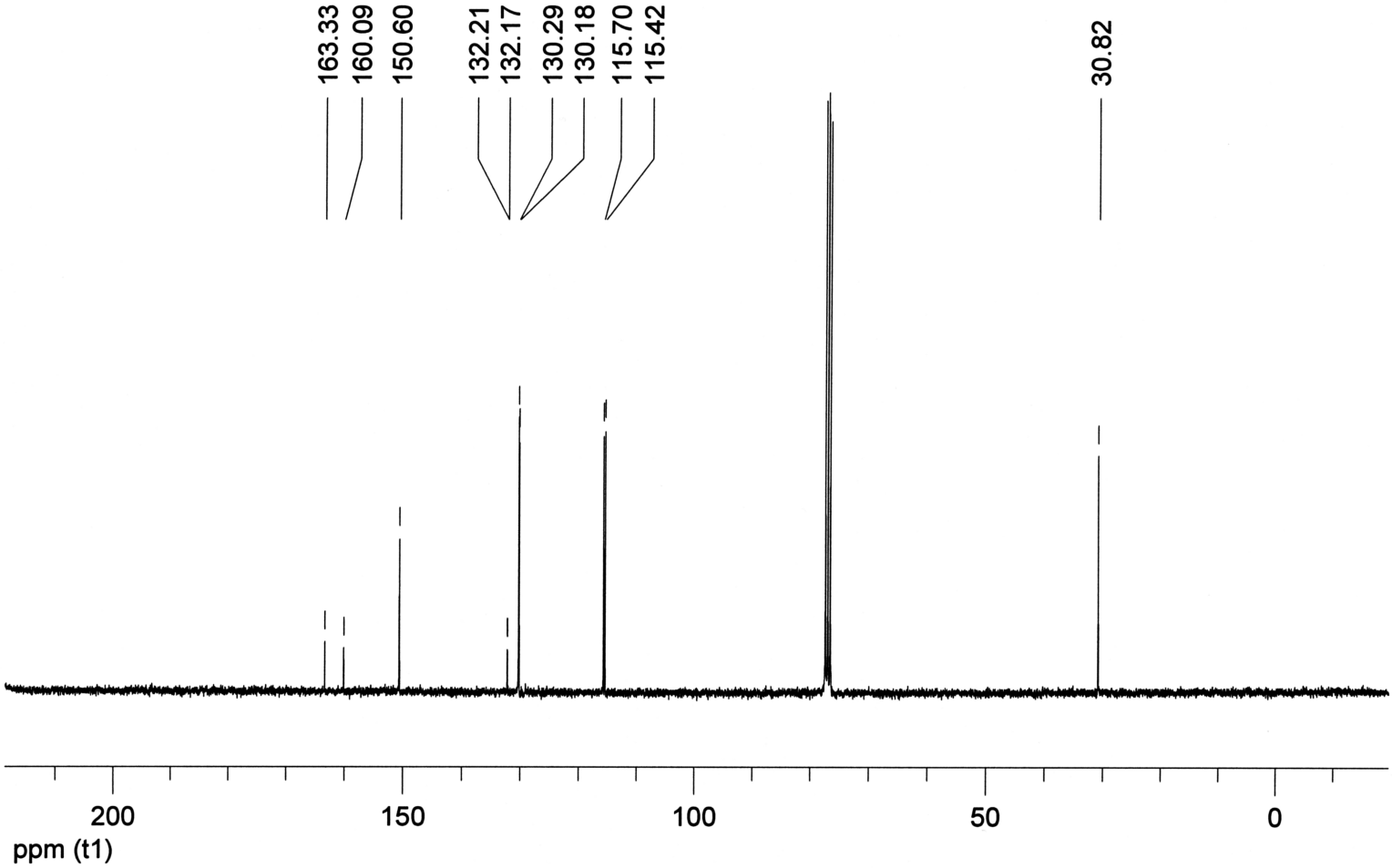

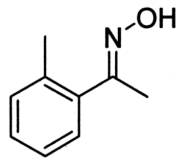

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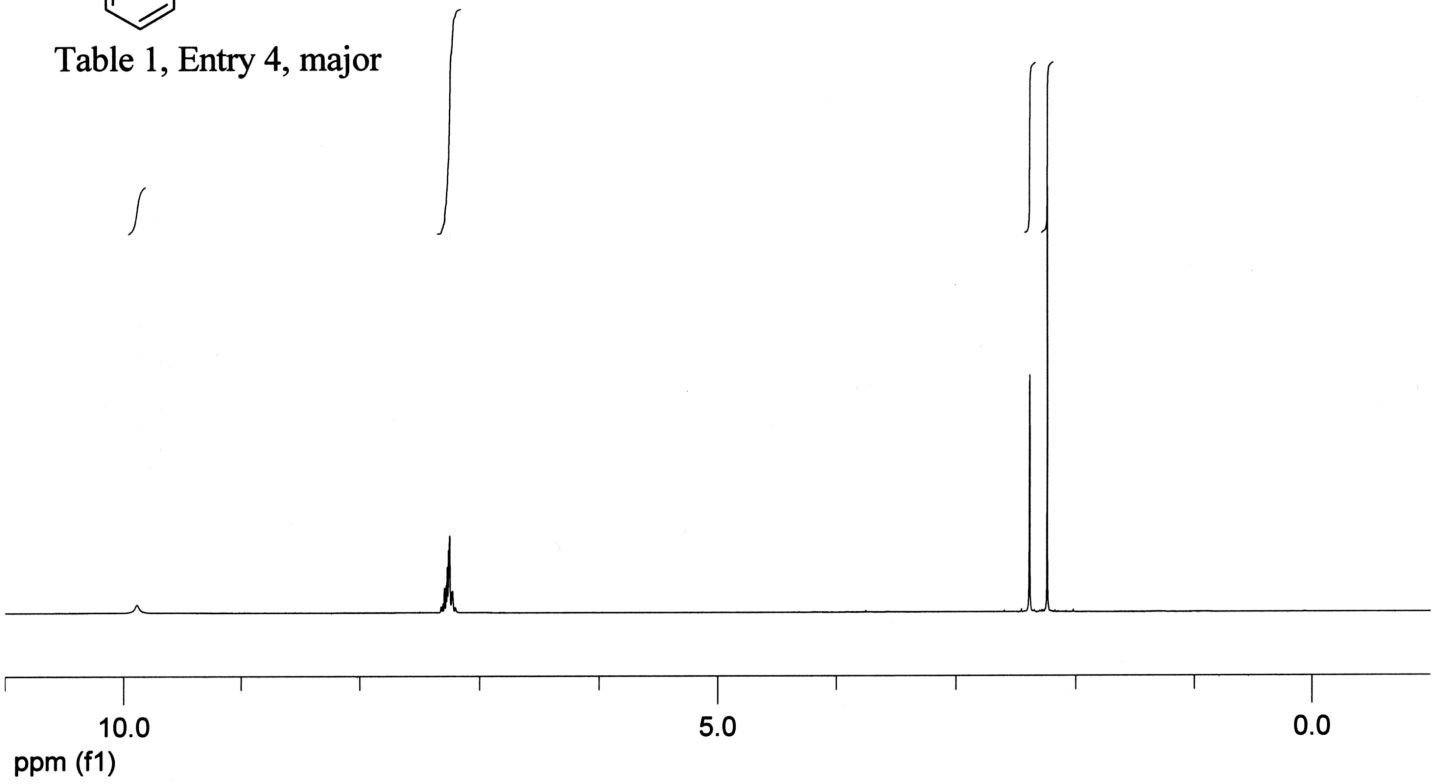

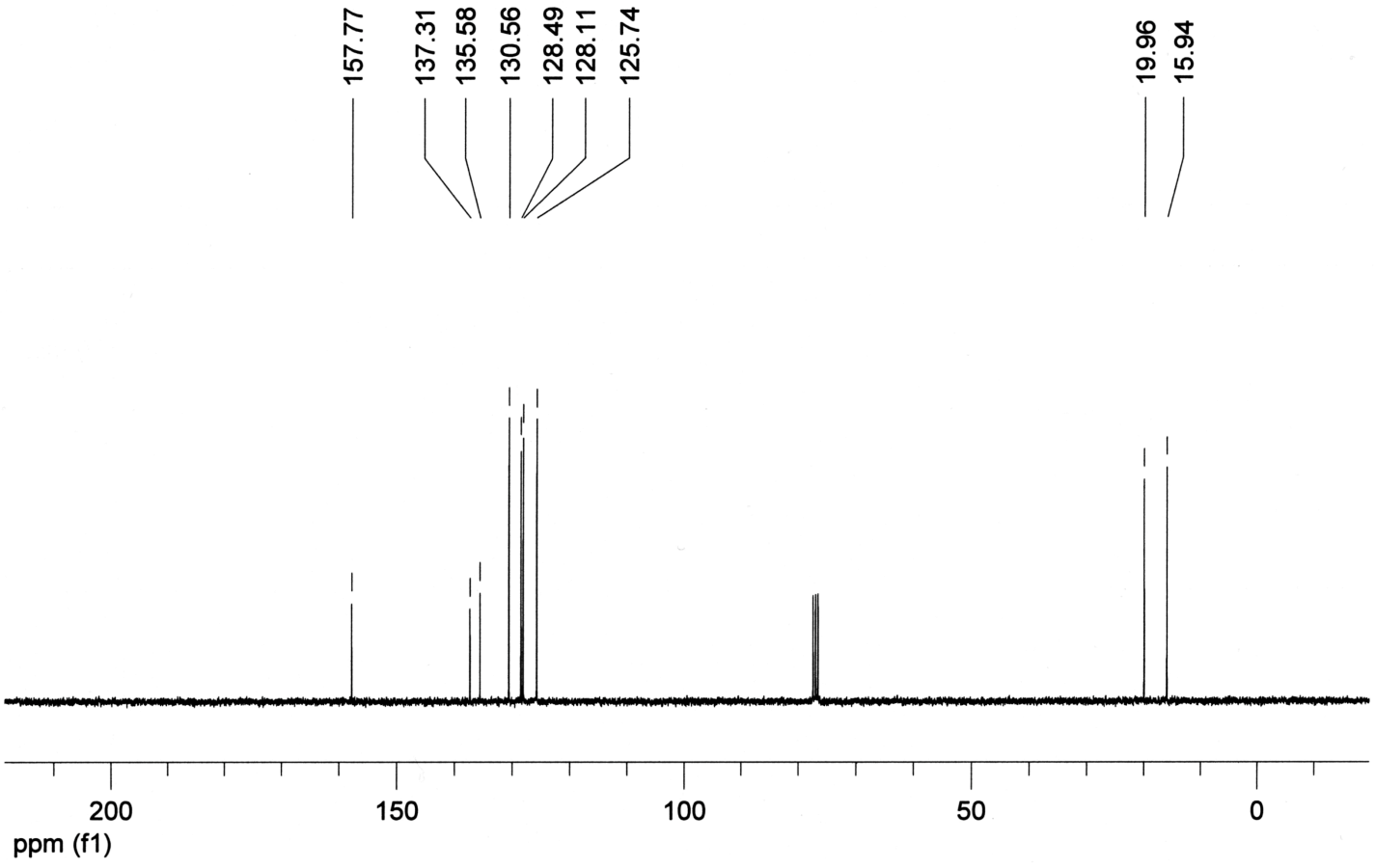

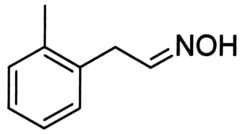

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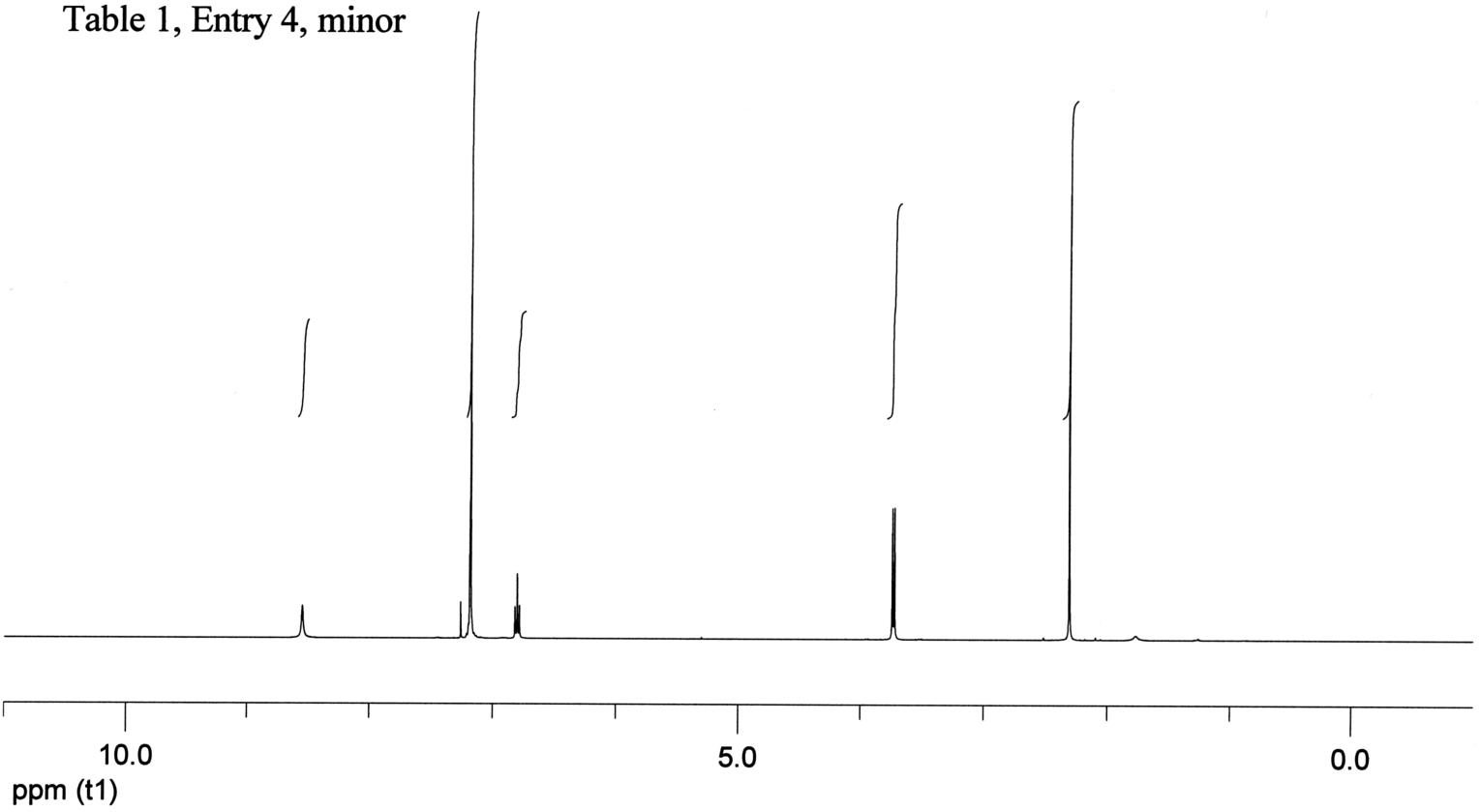

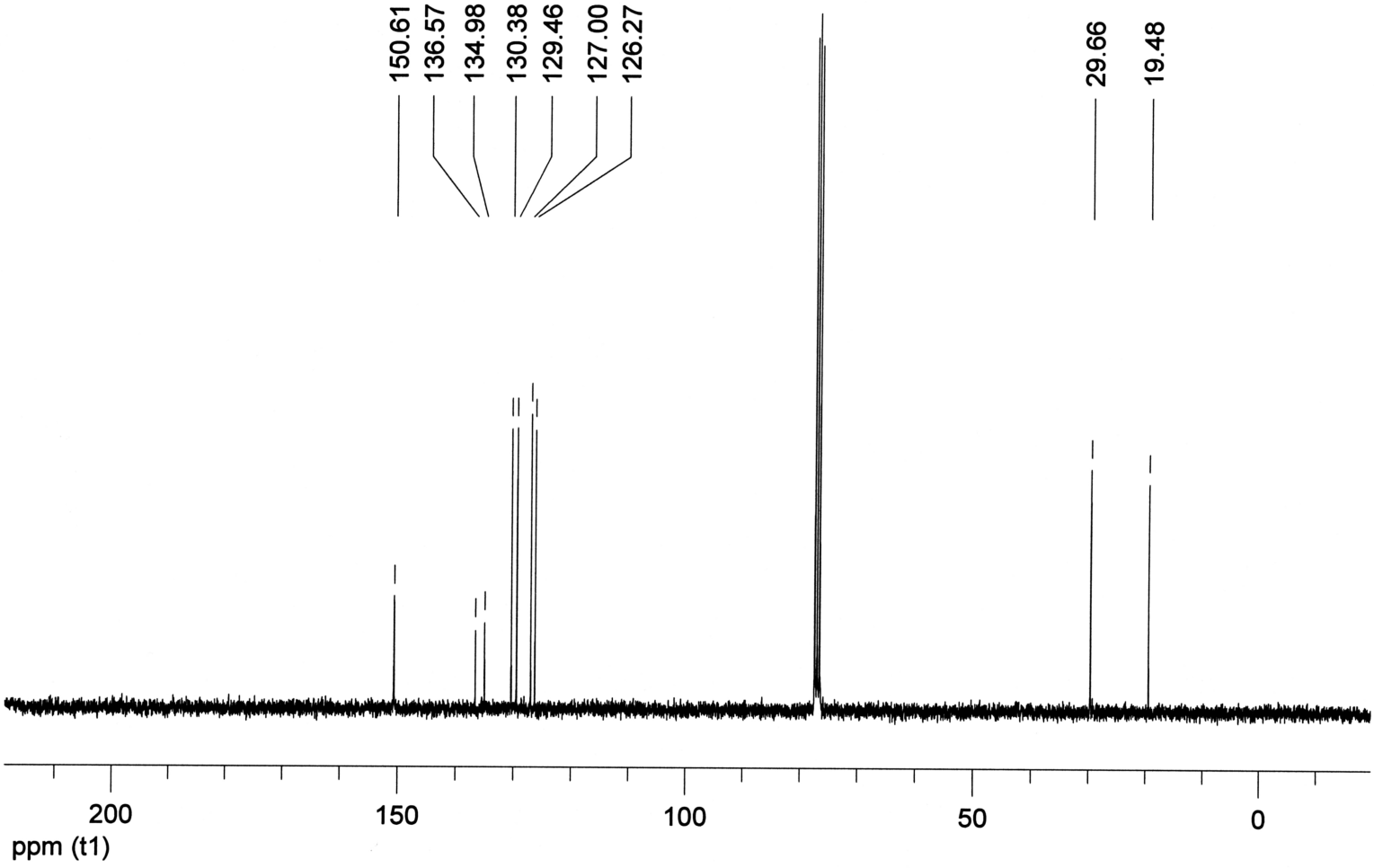

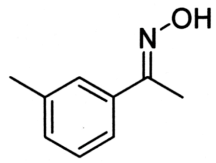

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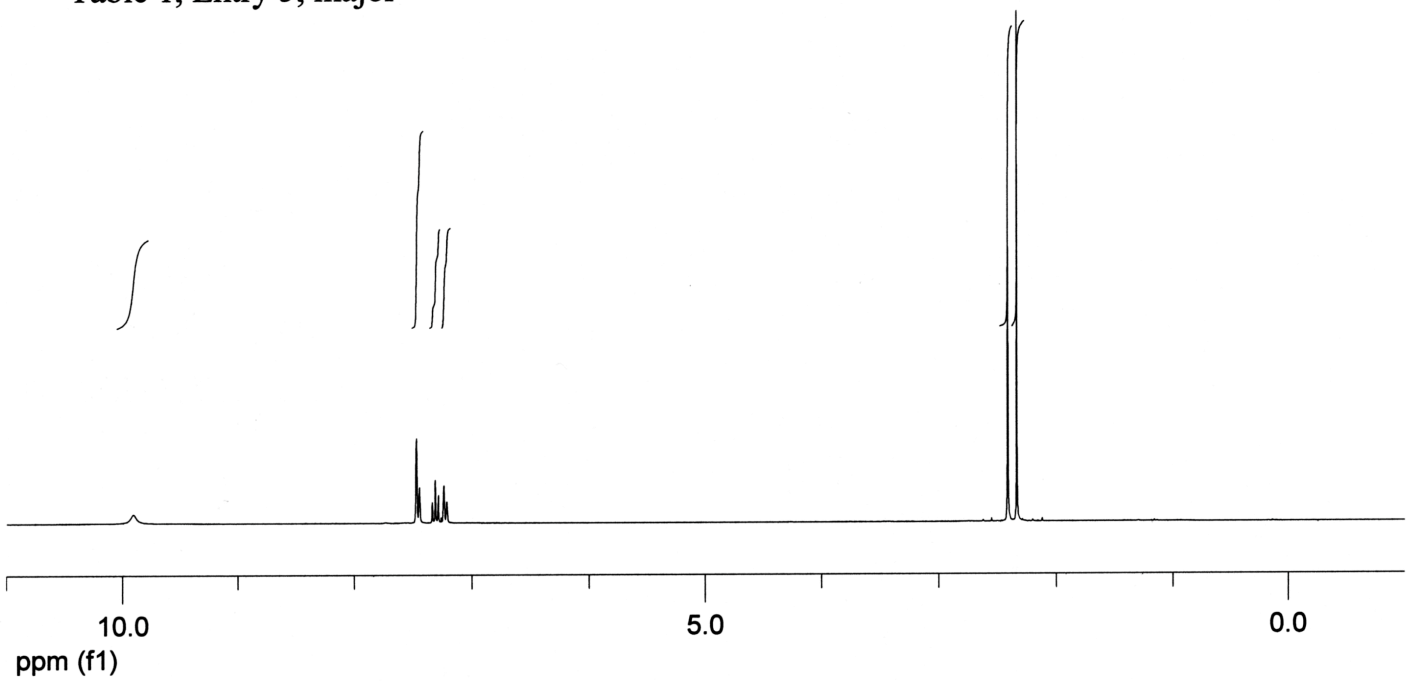

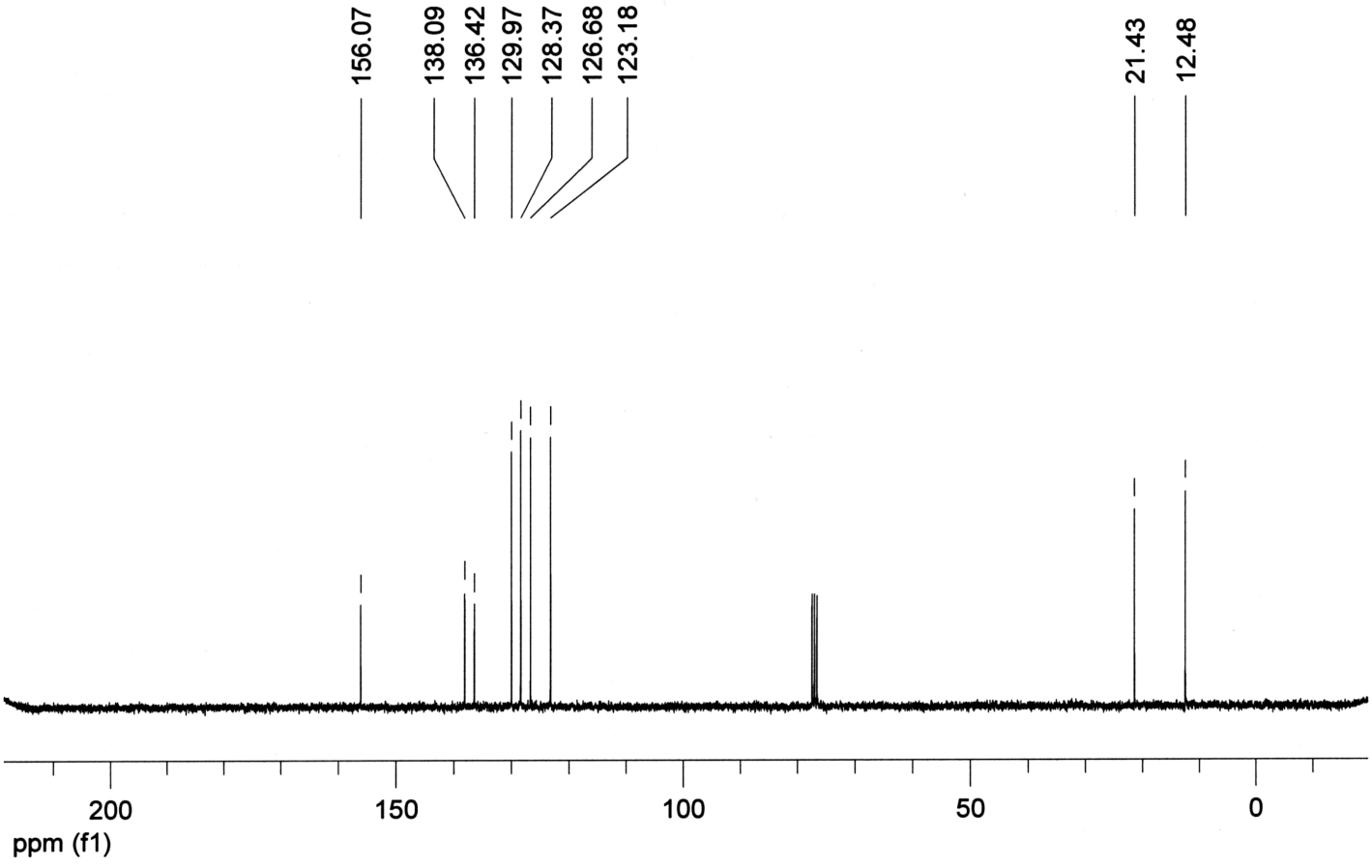

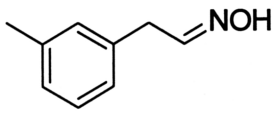

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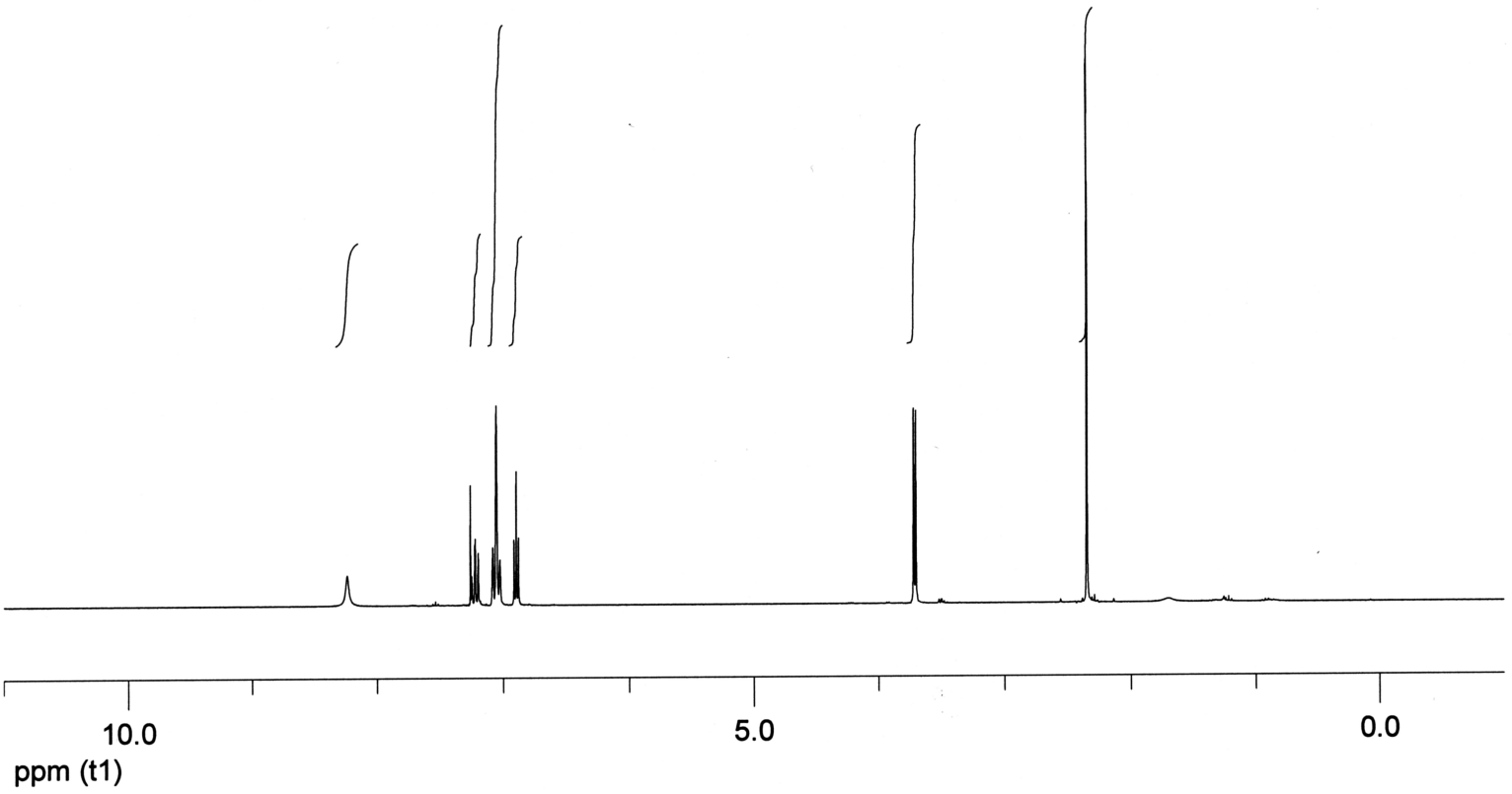
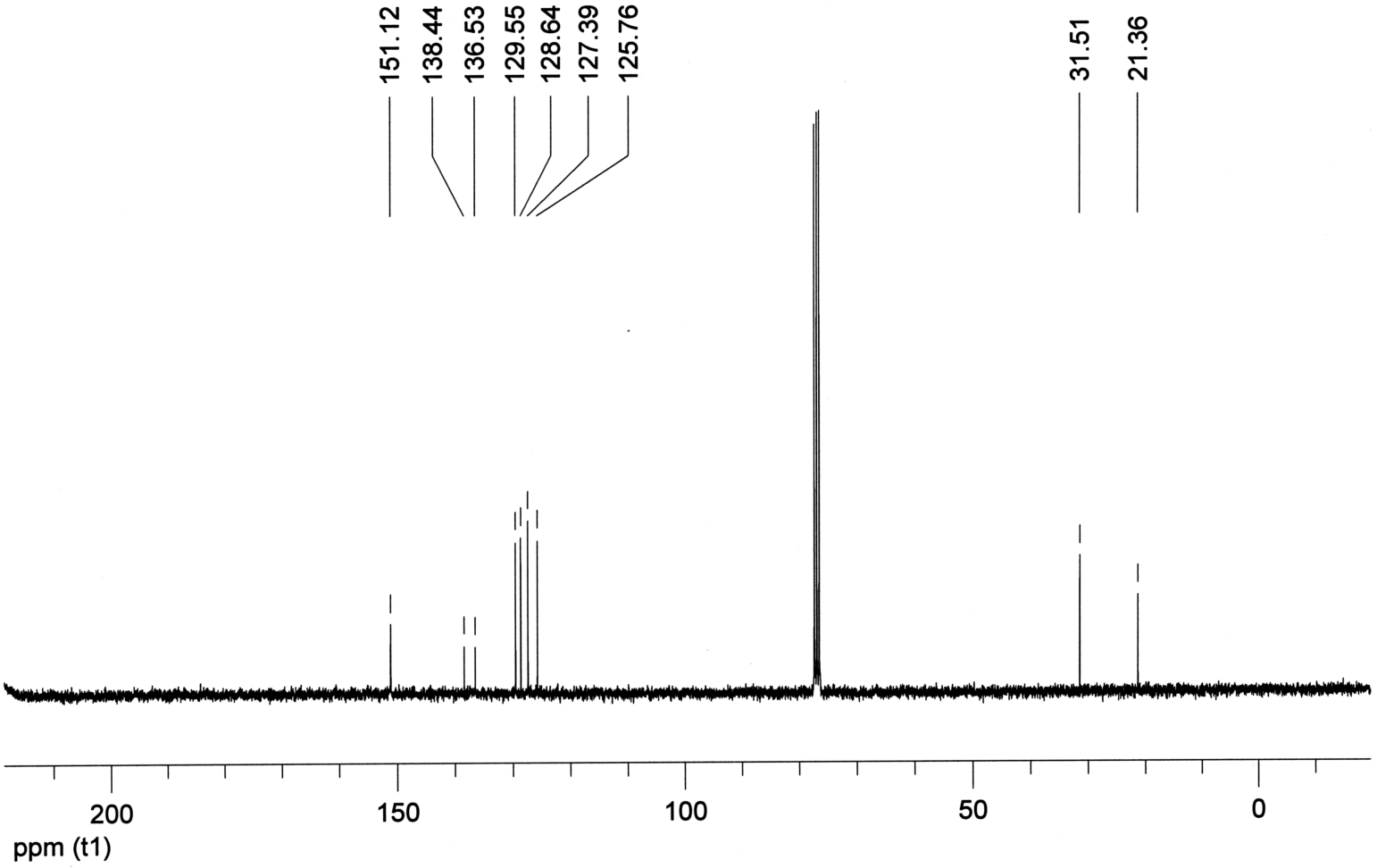




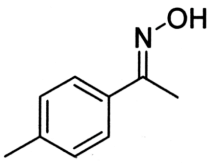
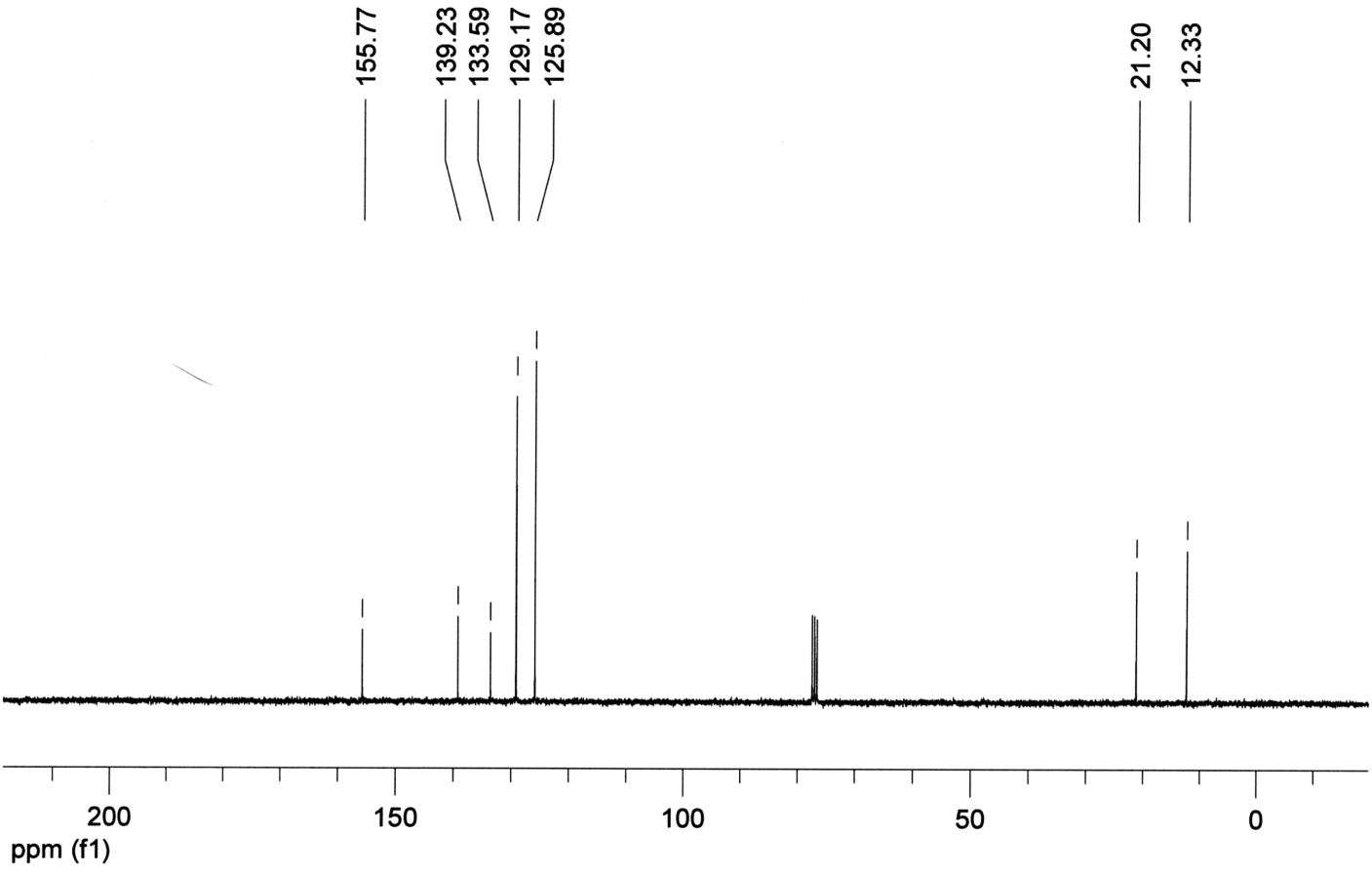
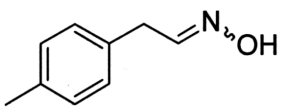


Table 1, Entry 6, major





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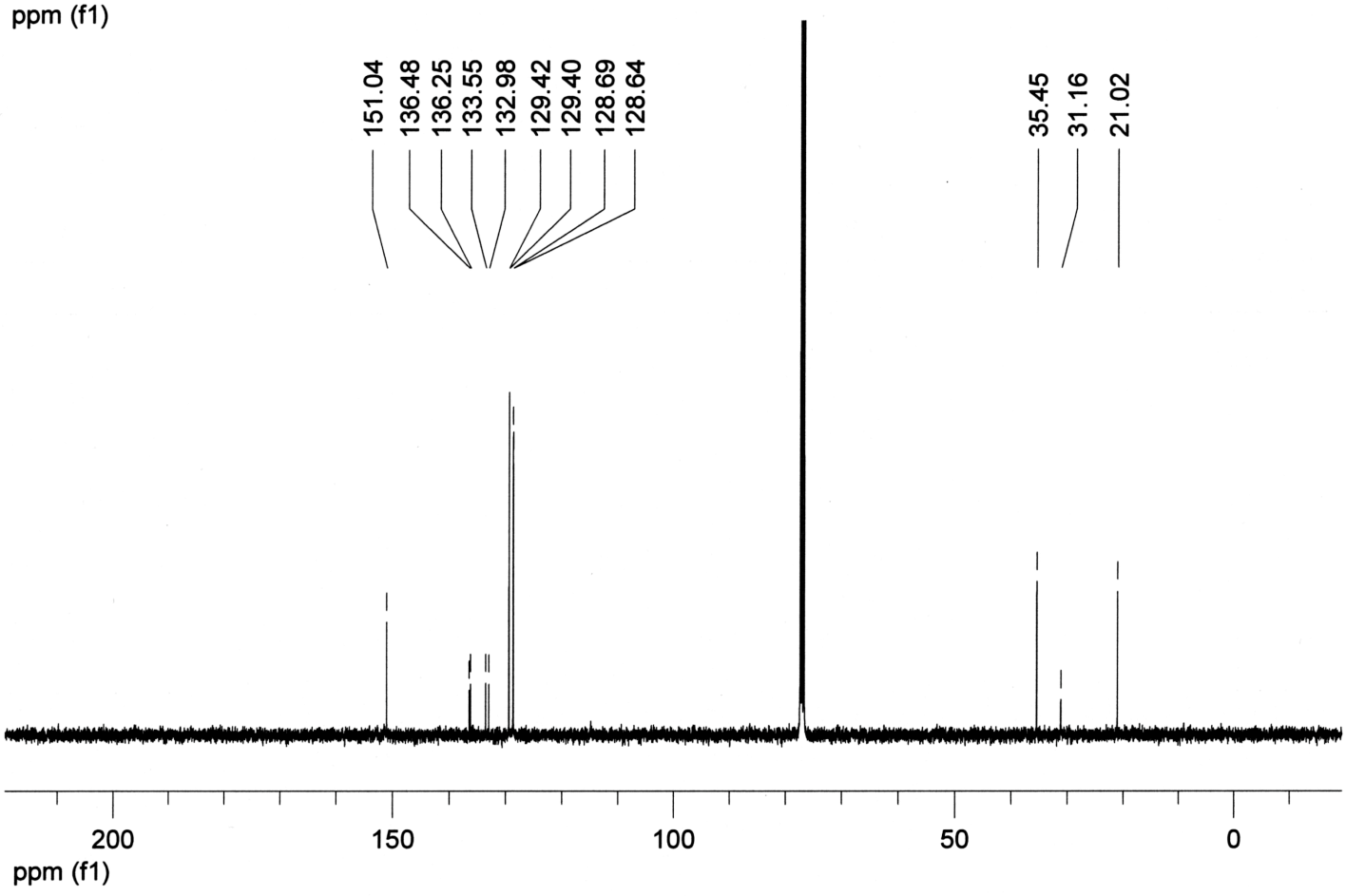

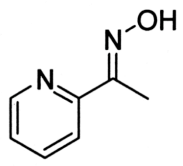

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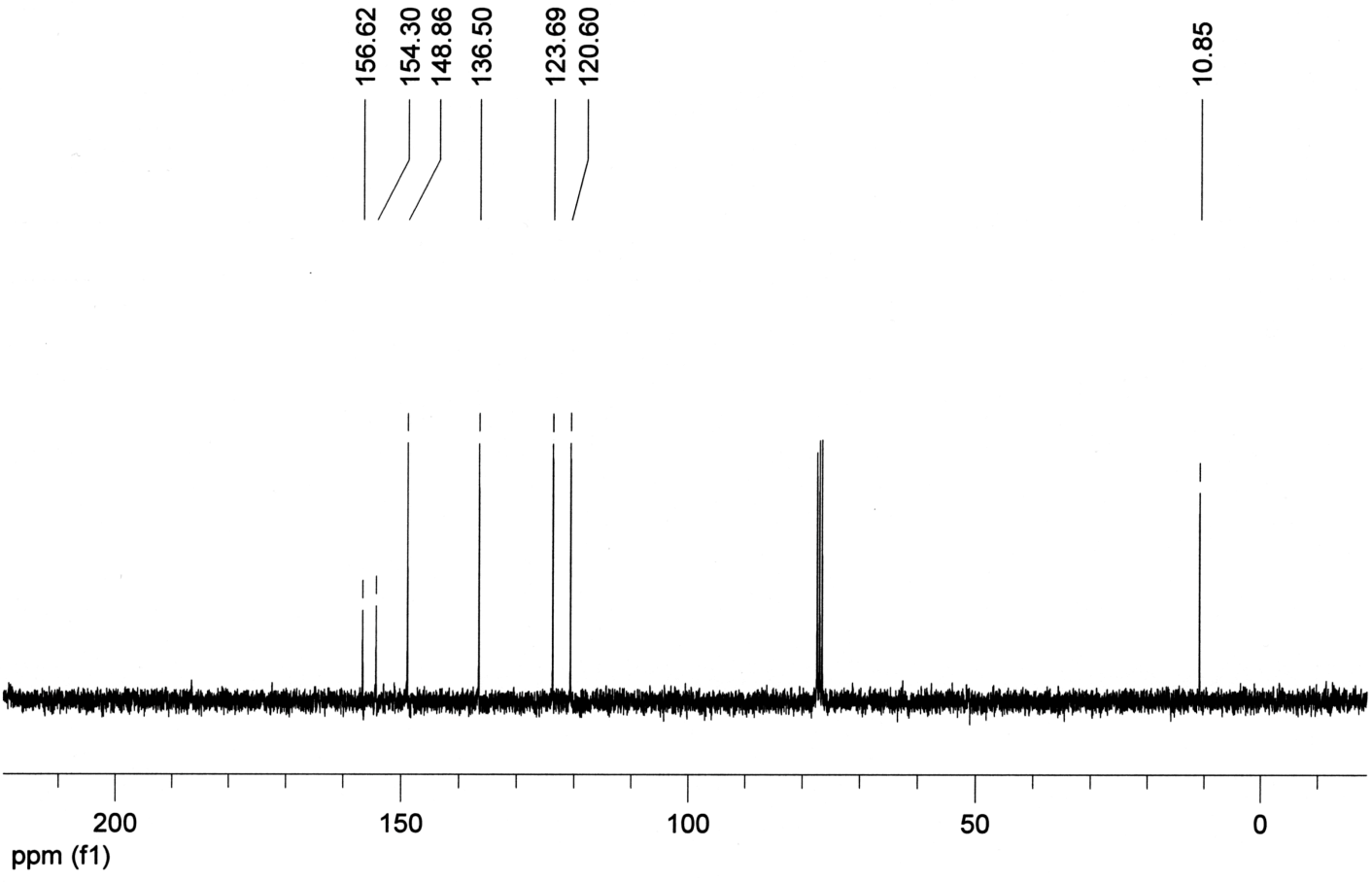

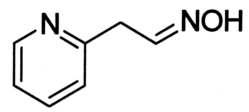

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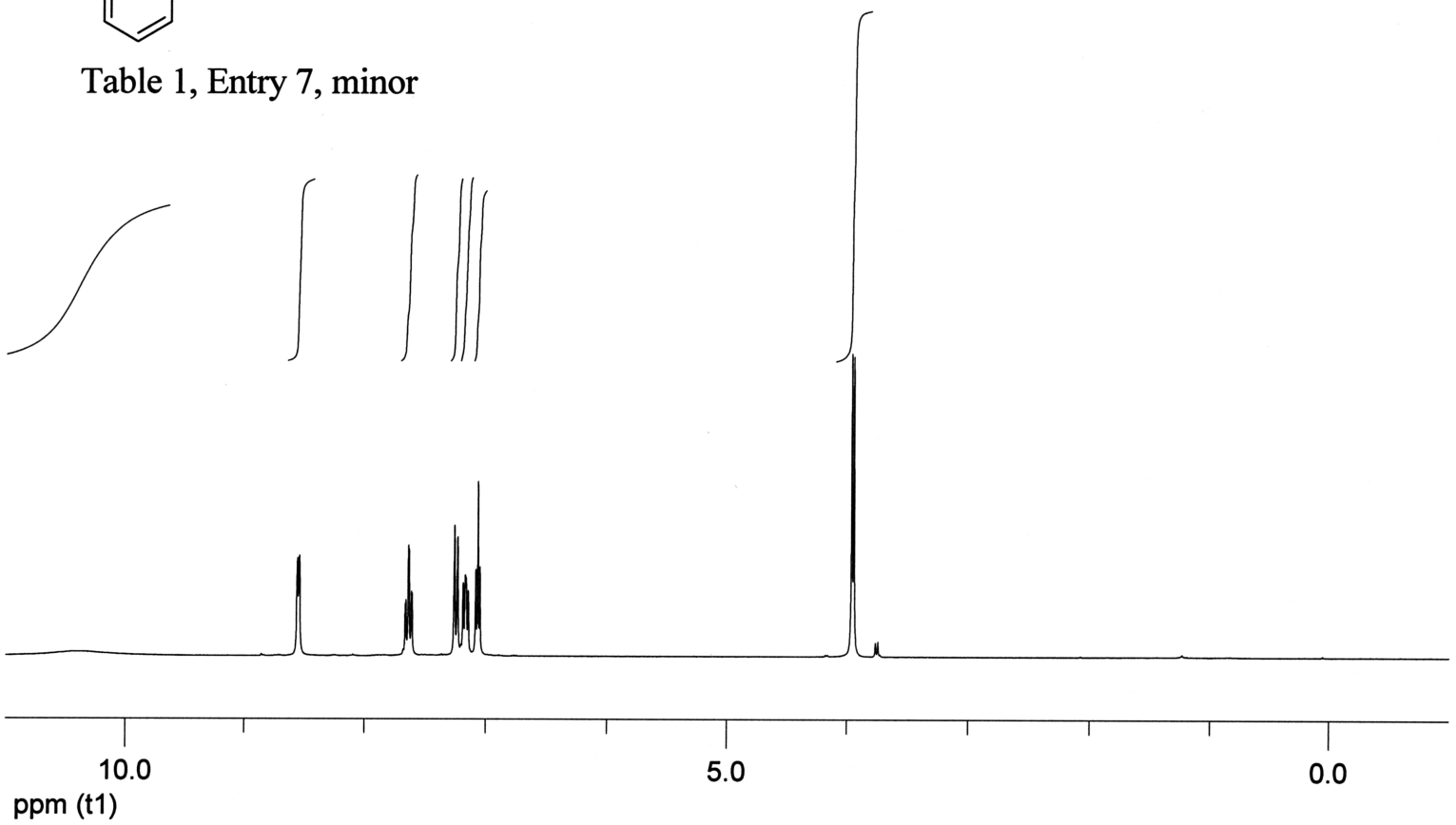

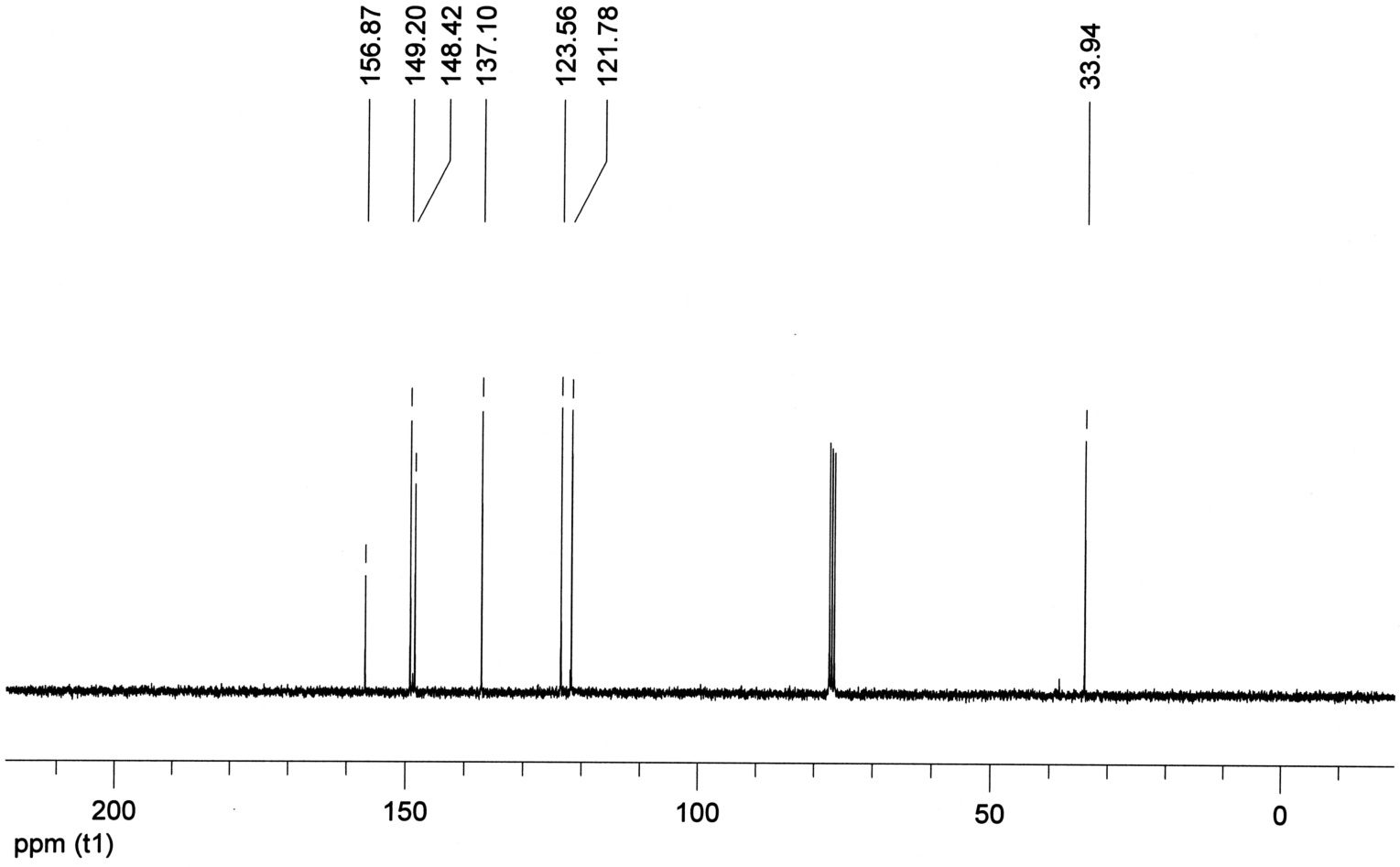

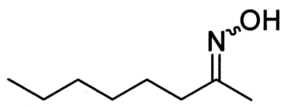

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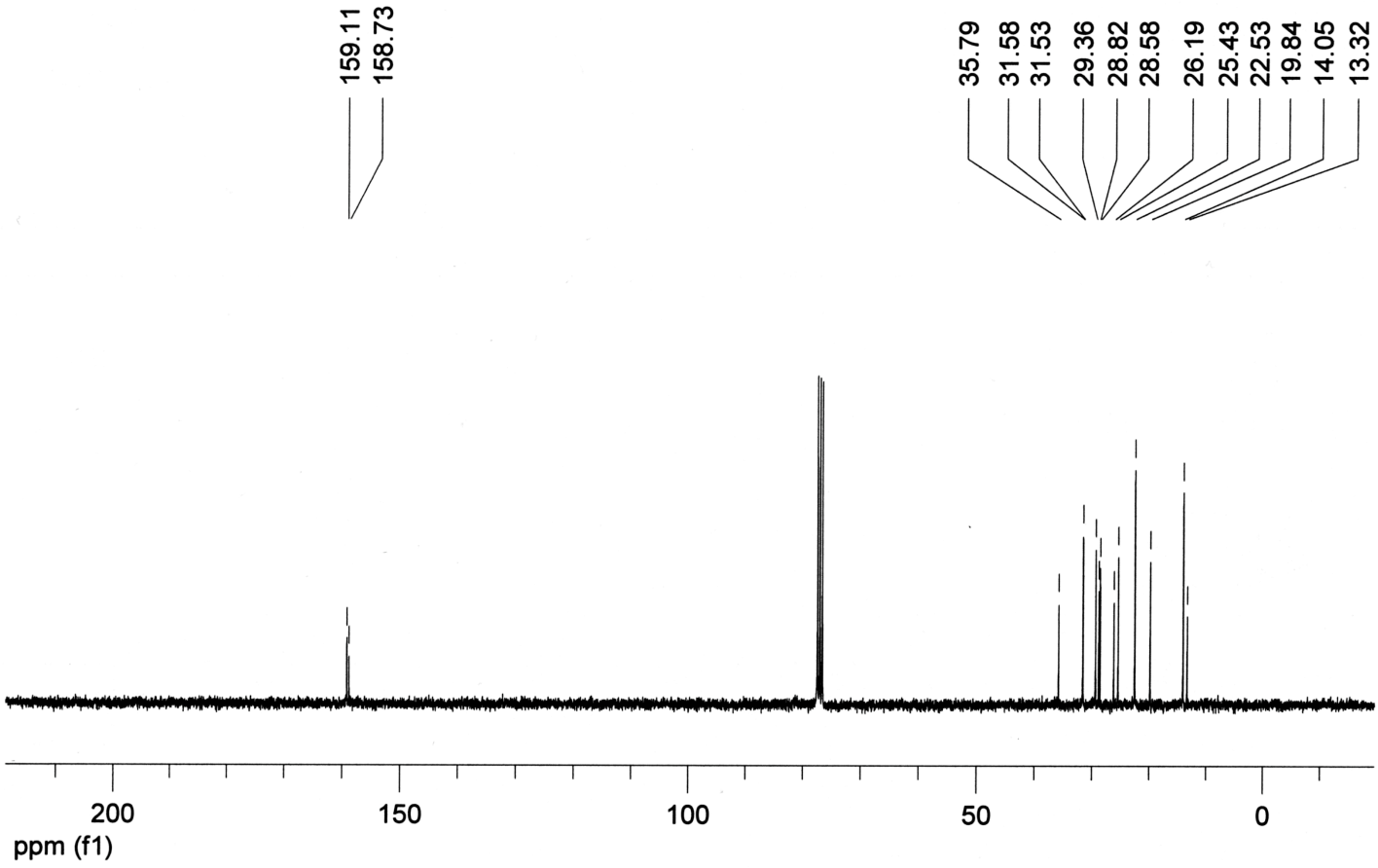

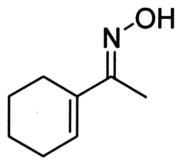

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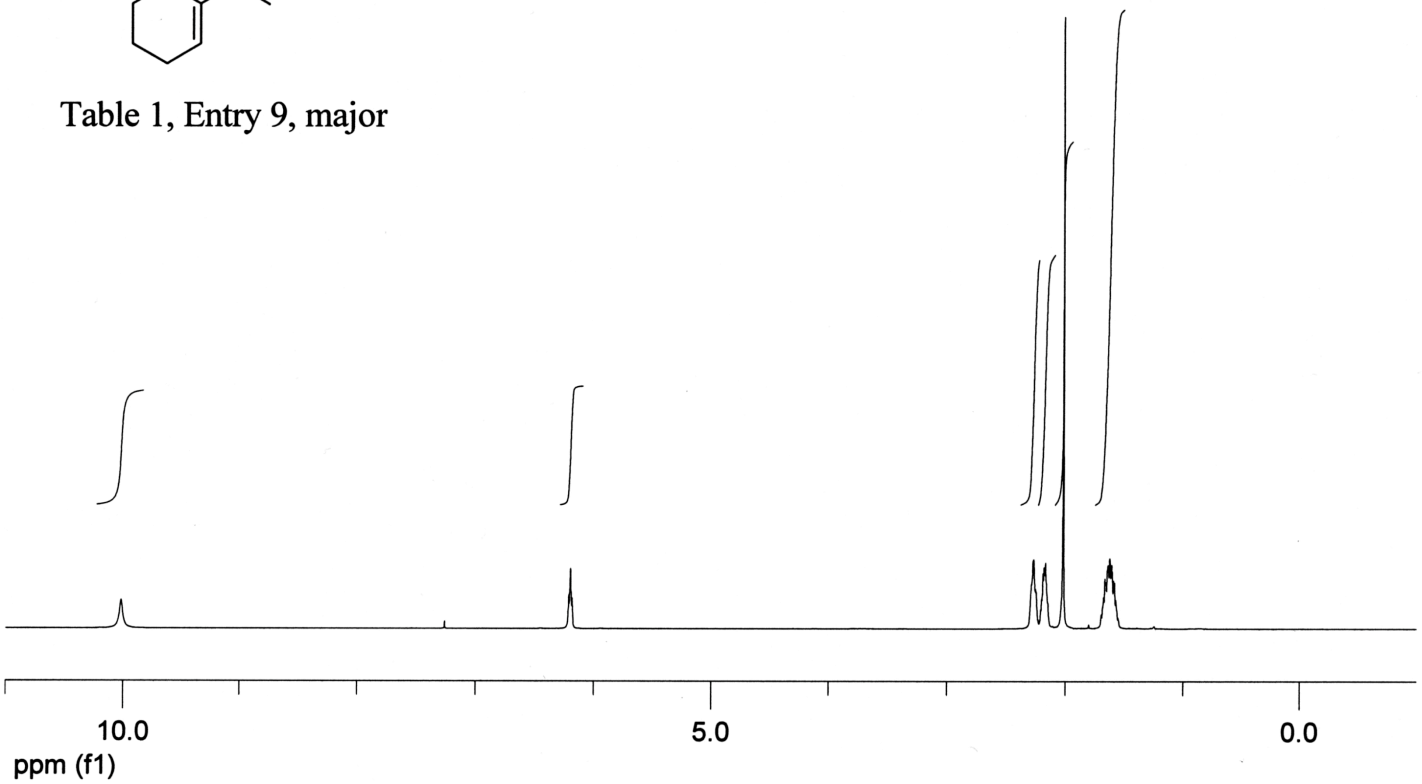

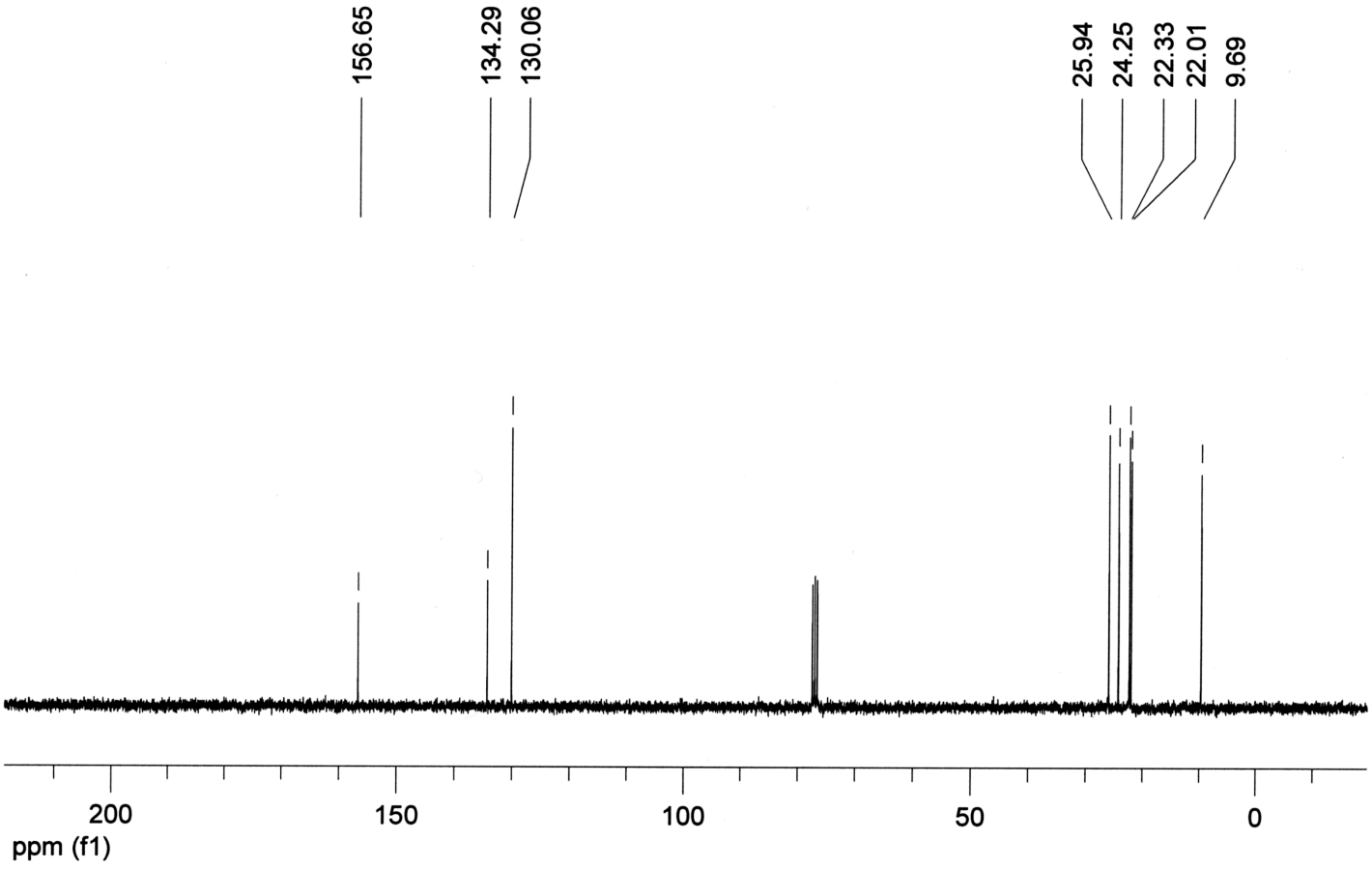

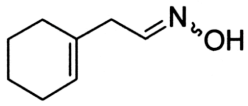

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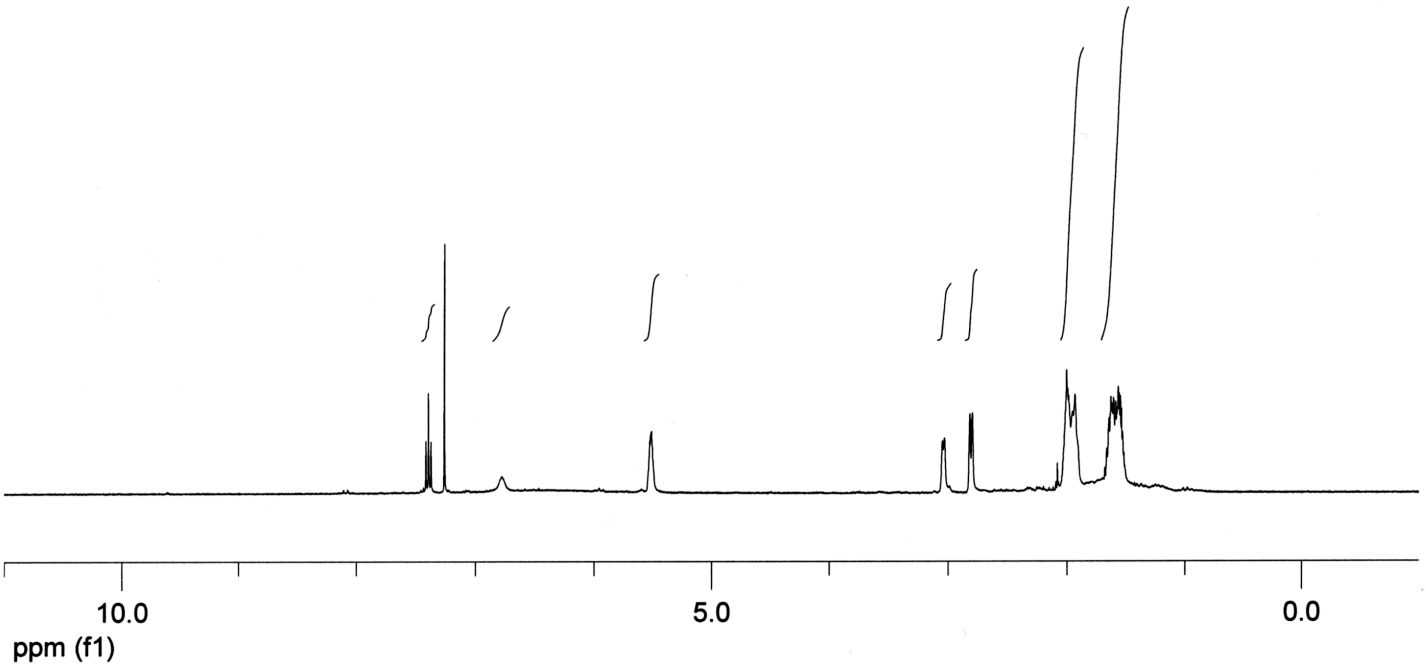

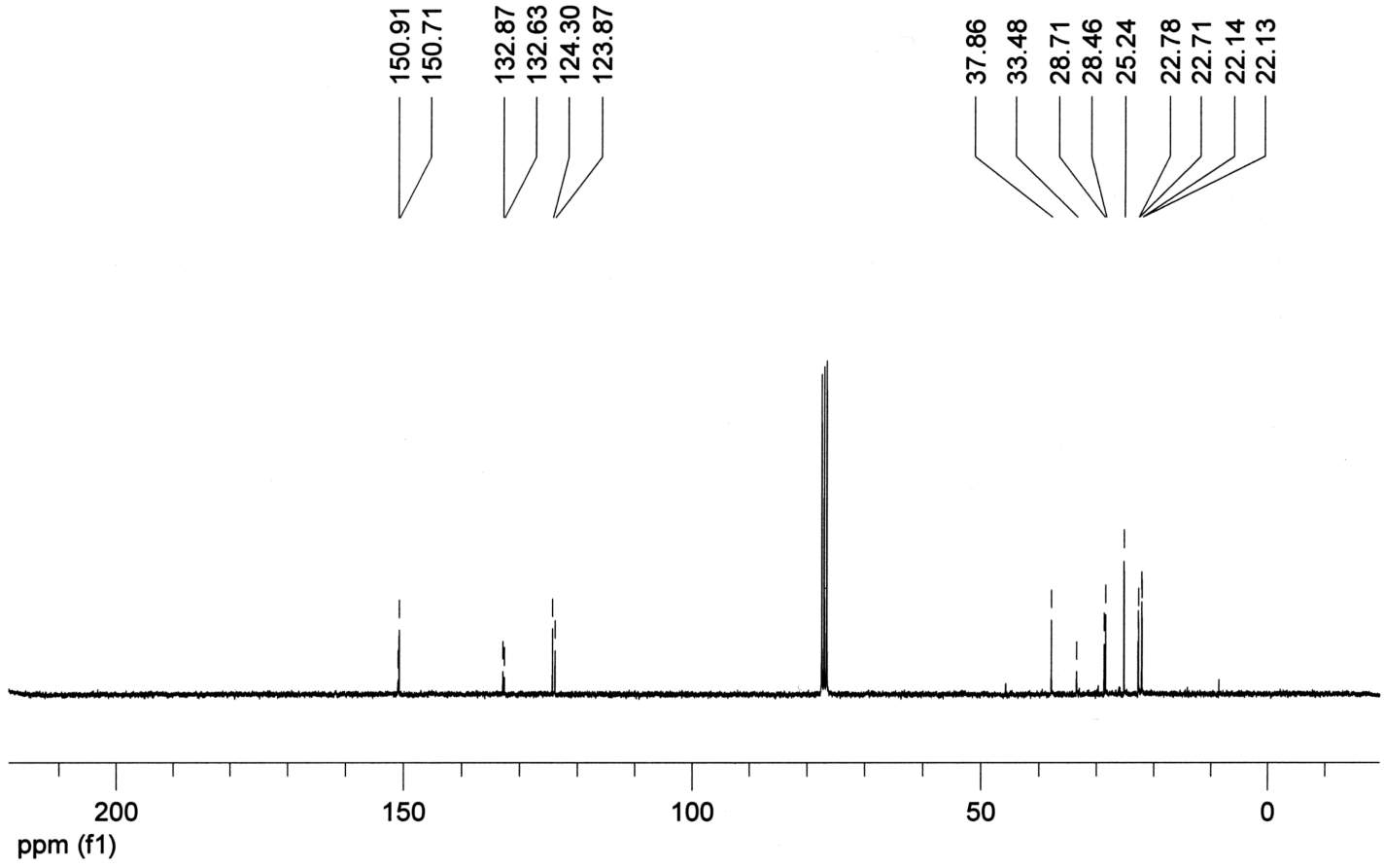

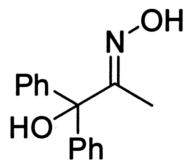

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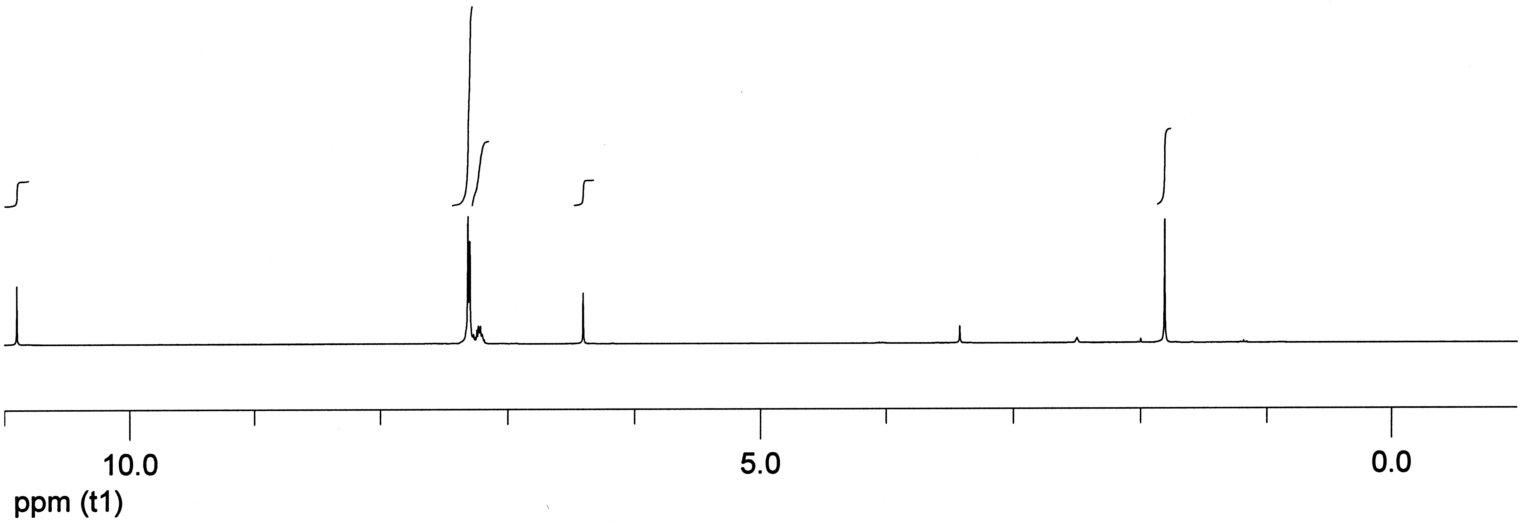
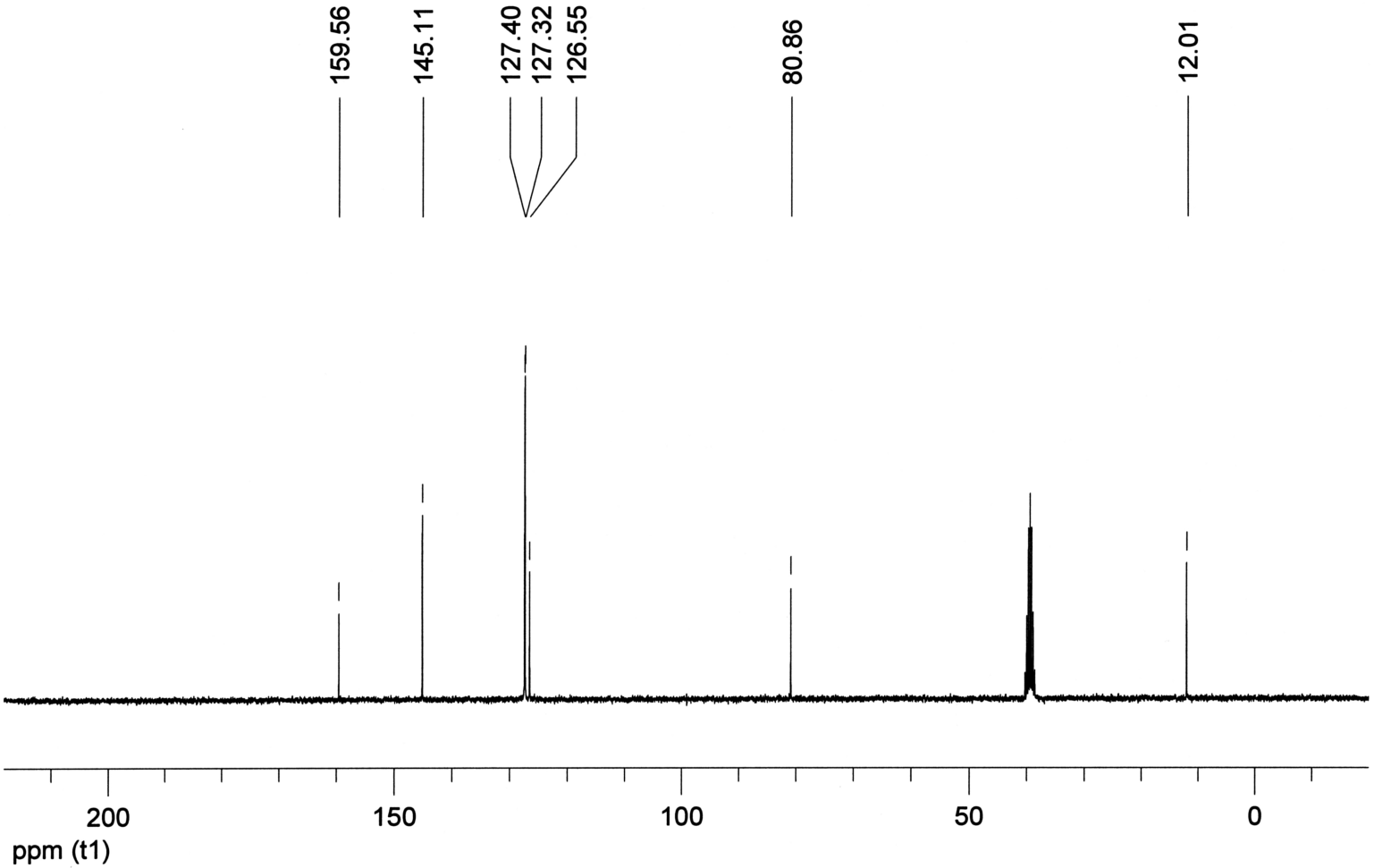




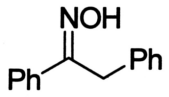
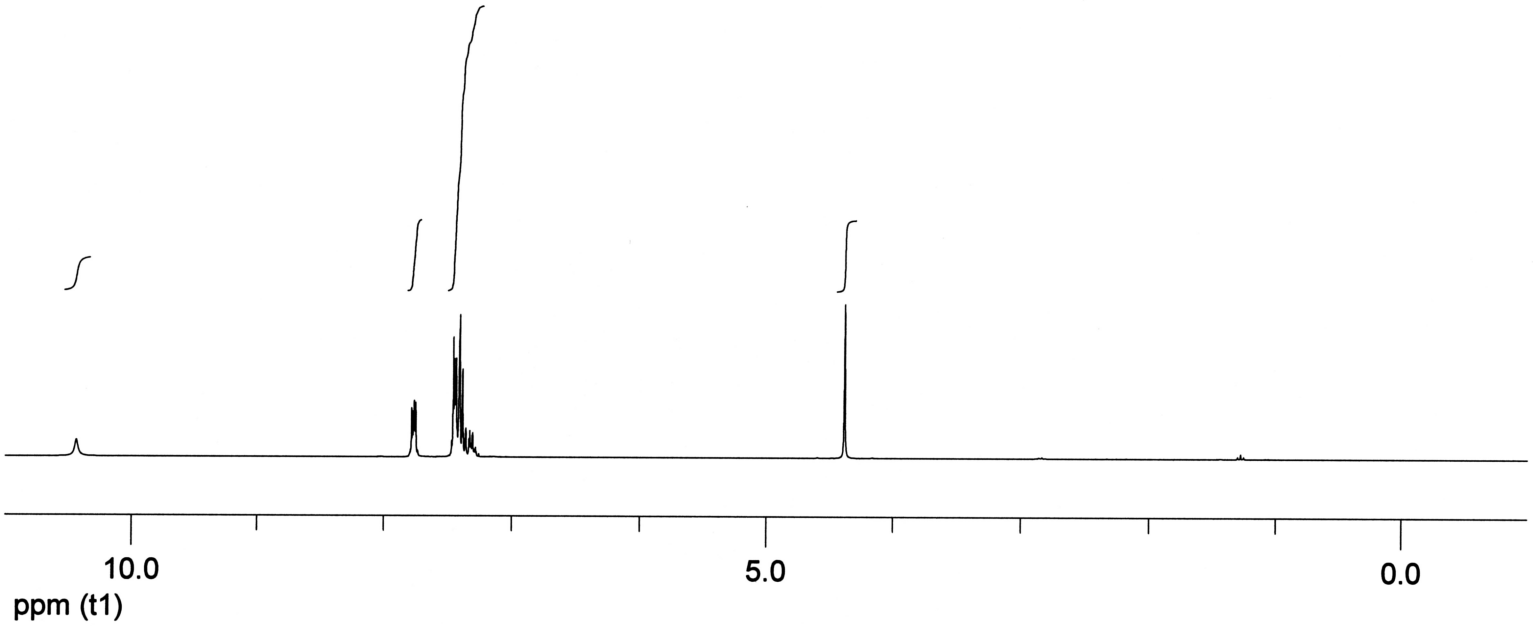
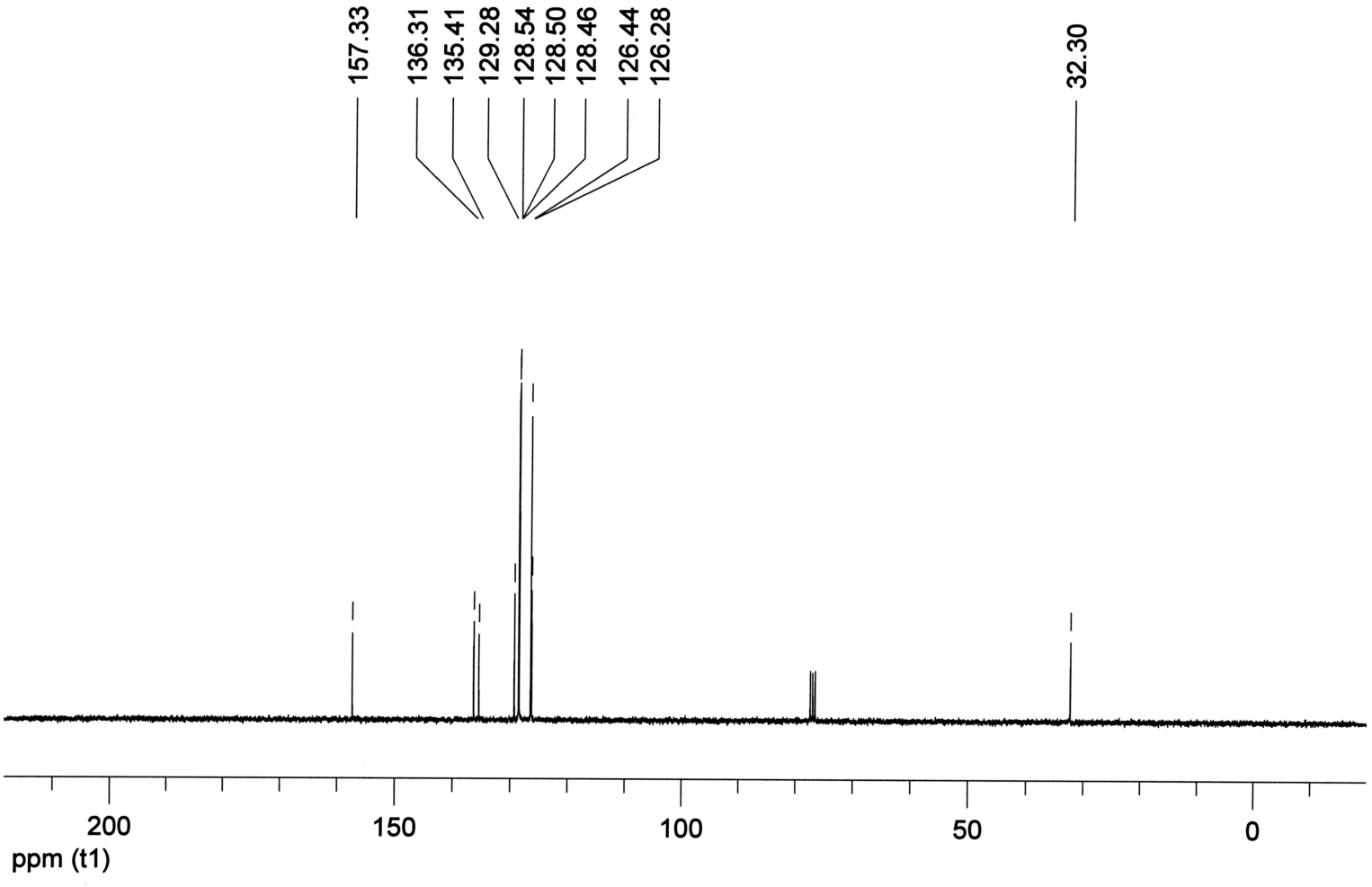


Table 1, Entry 11





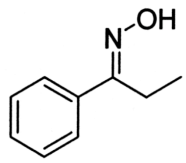
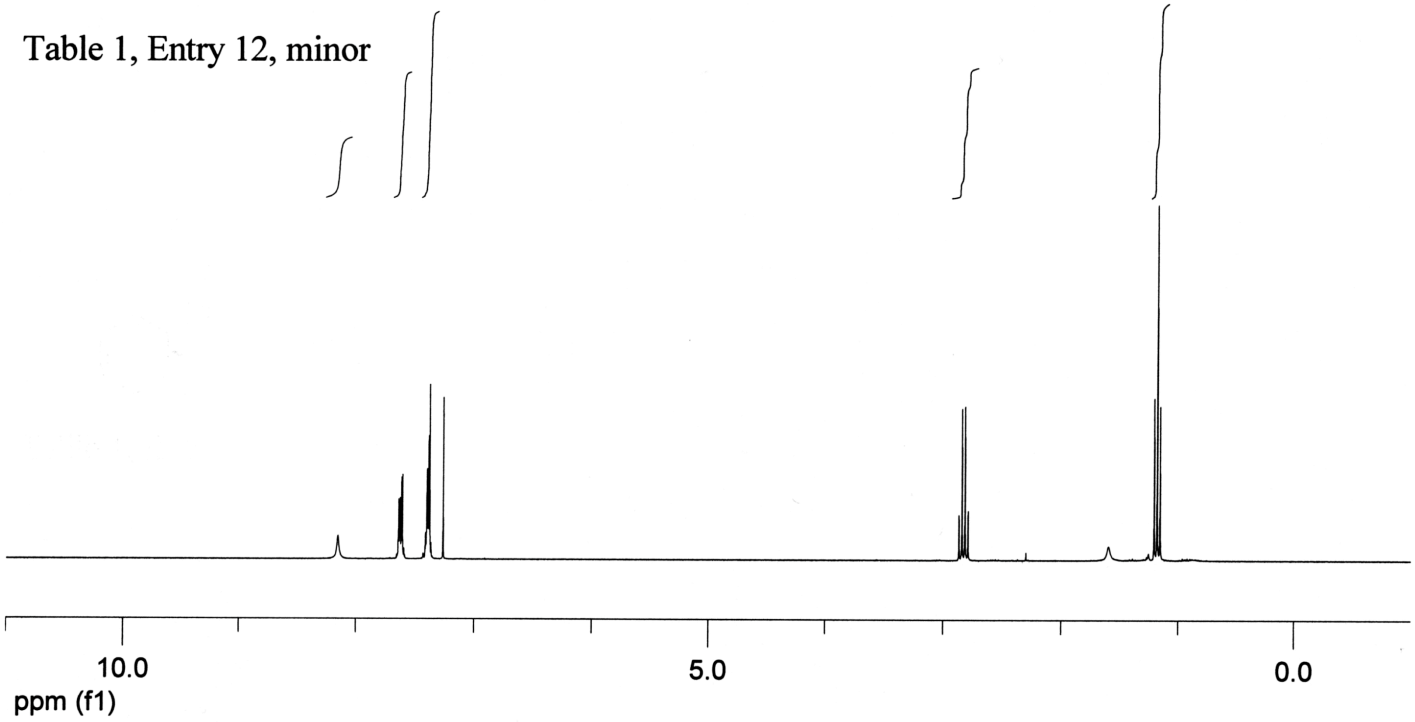
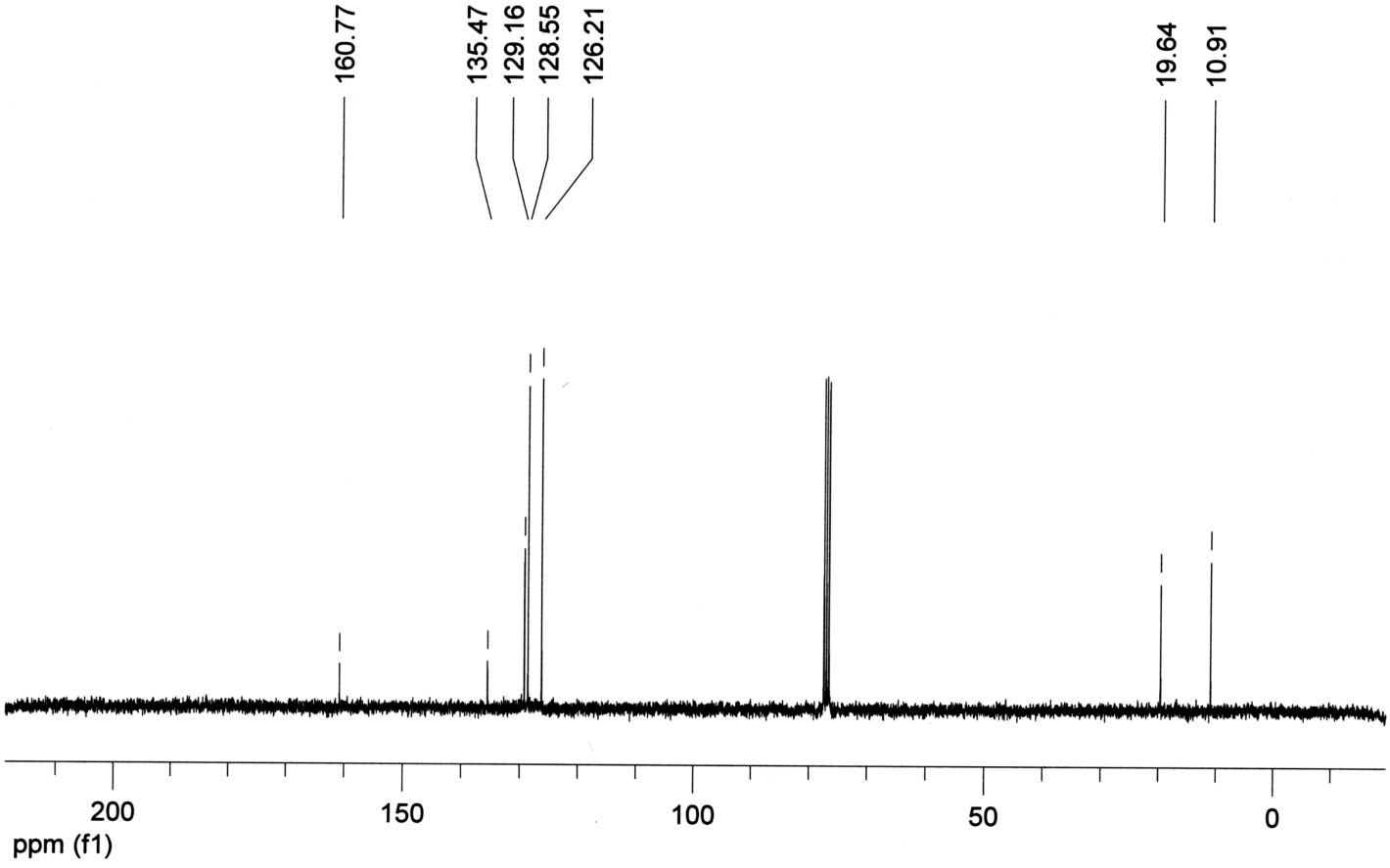
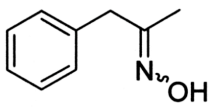


Table 1, Entry 12, minor







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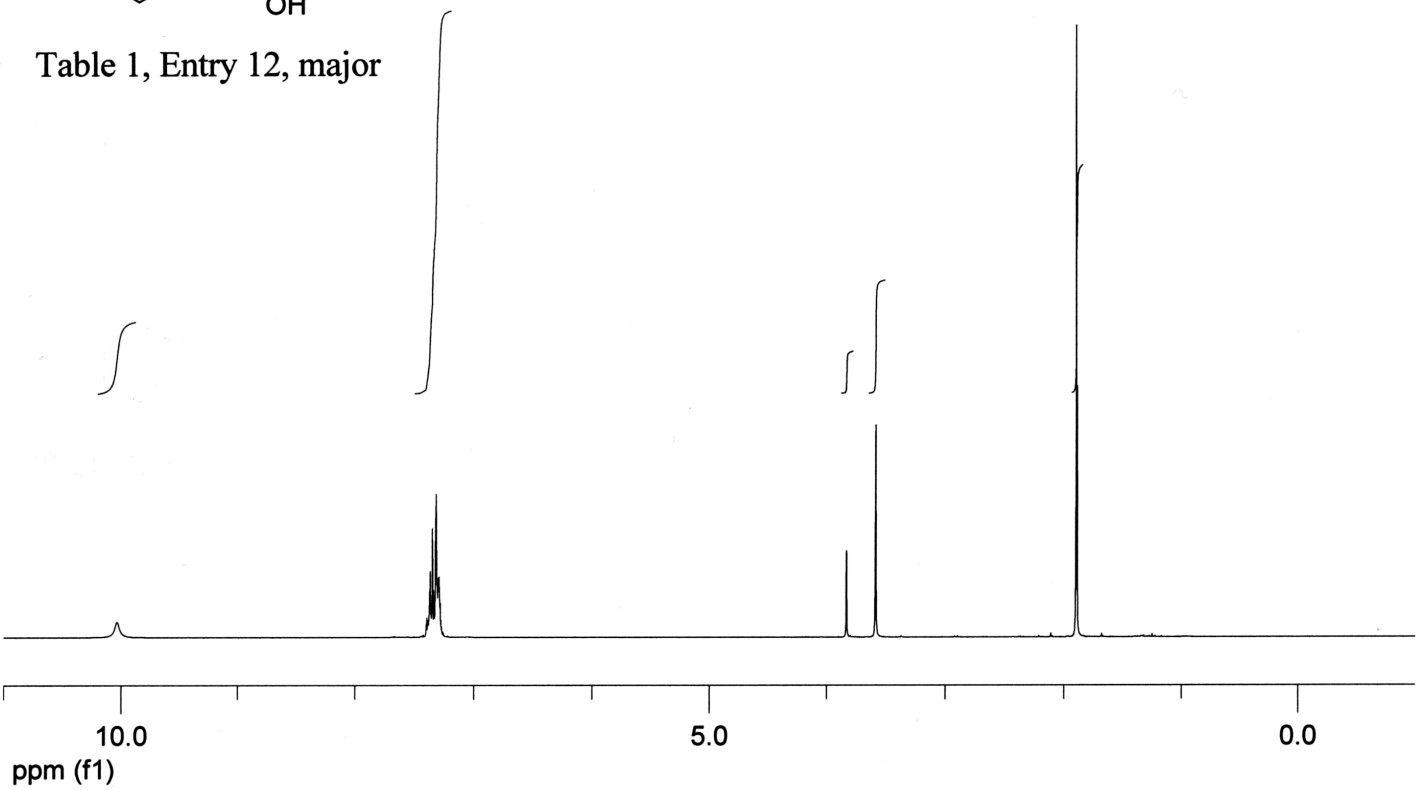

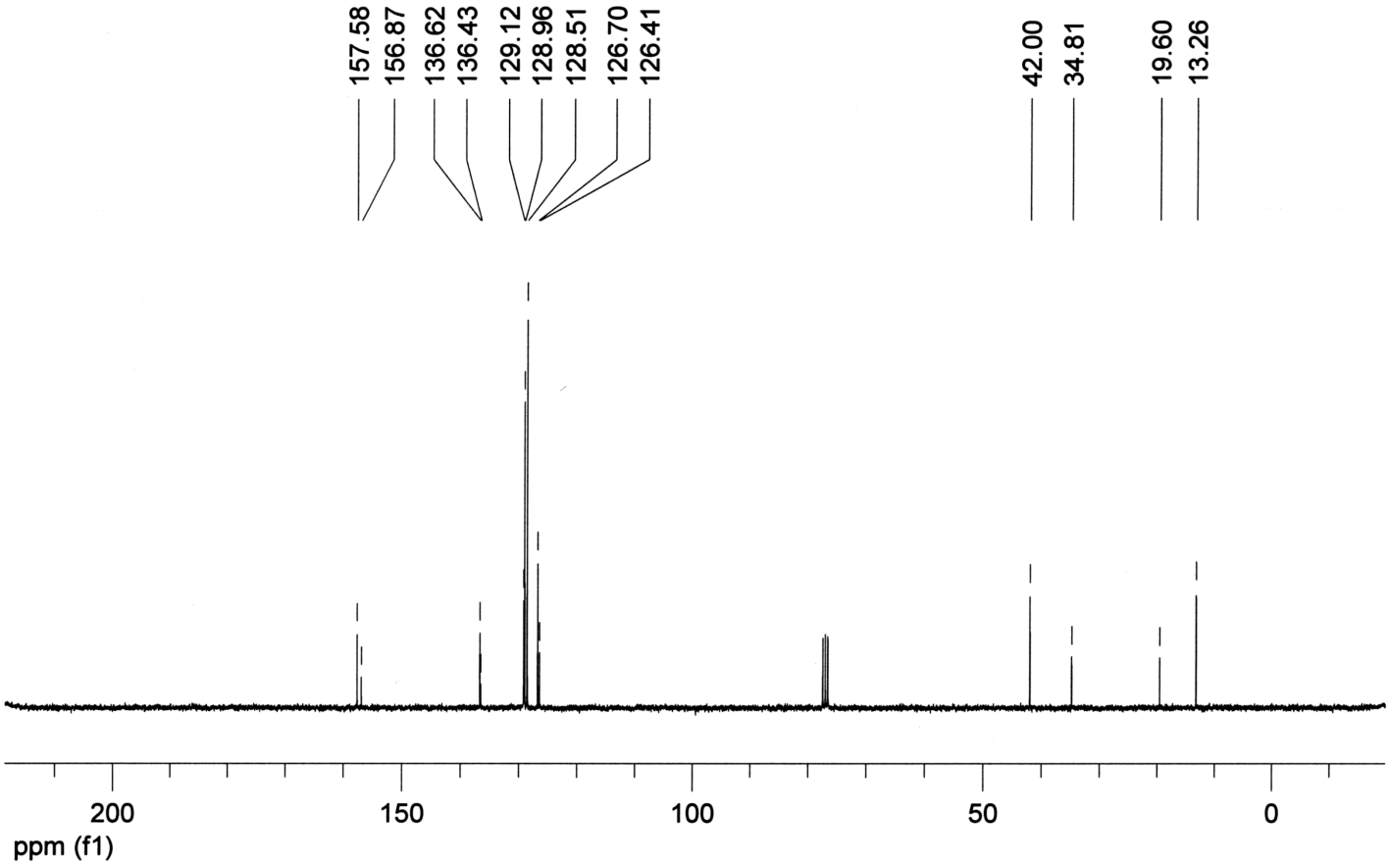

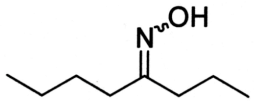

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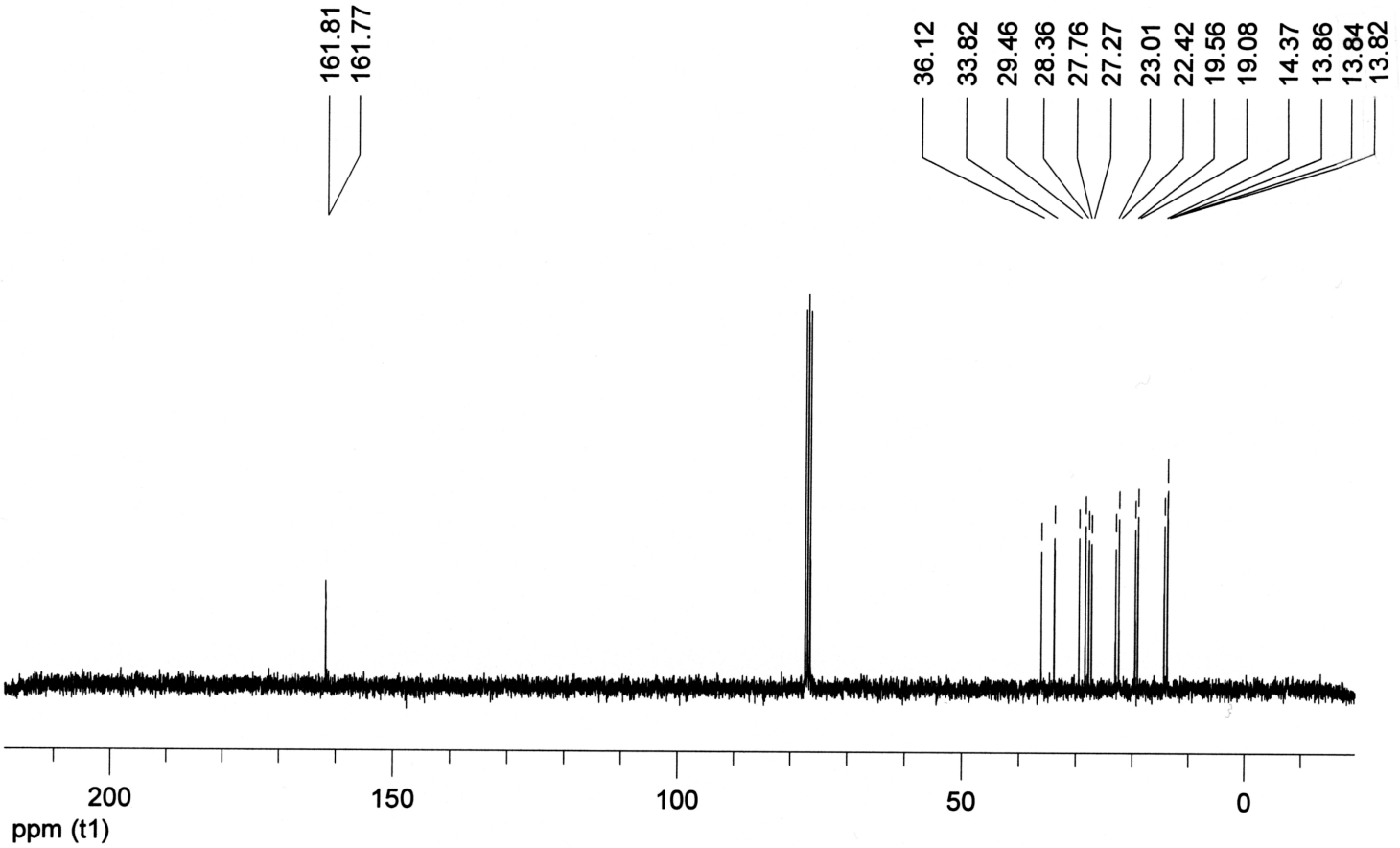


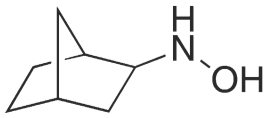
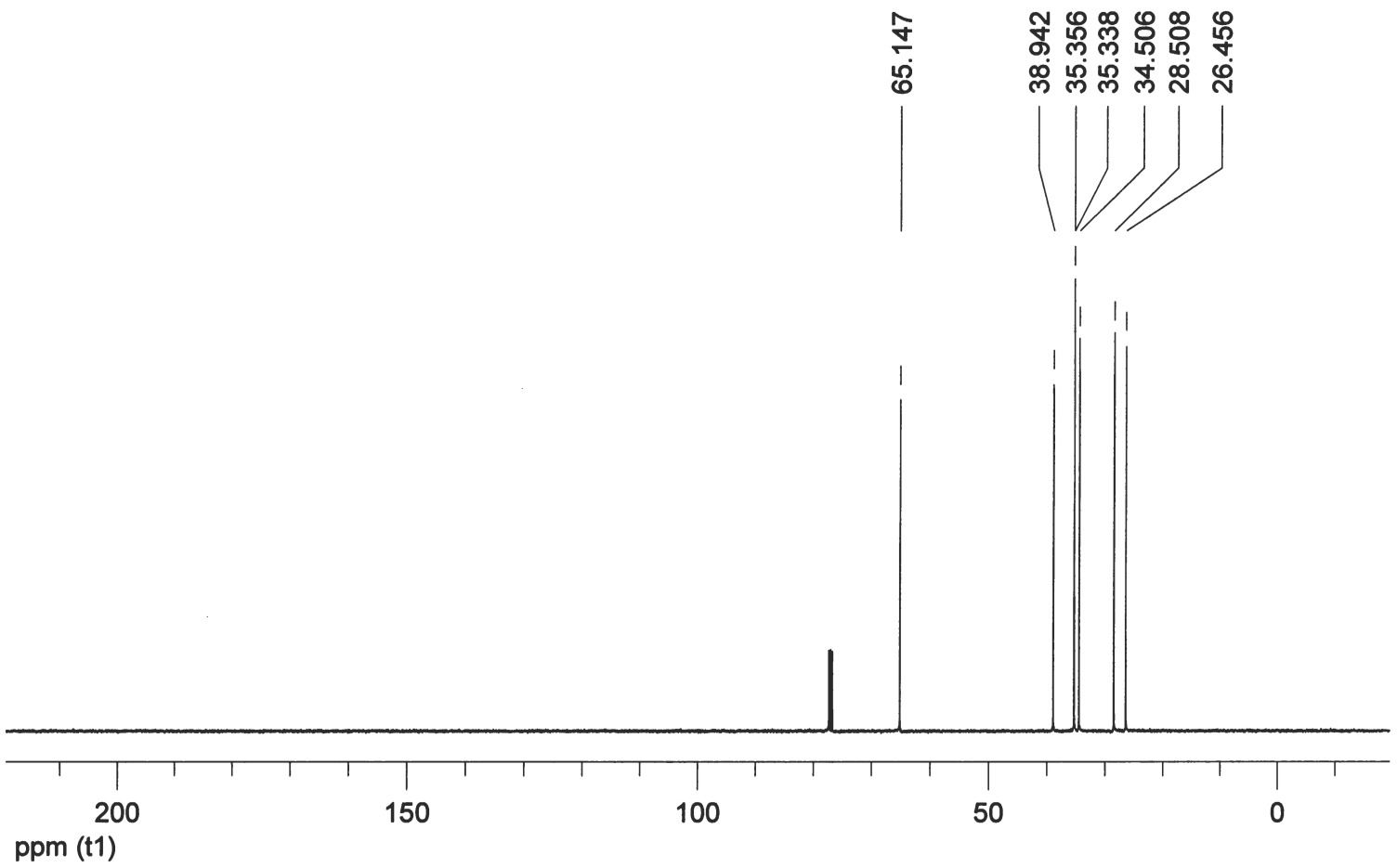
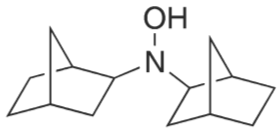


Table 3, Entry 1





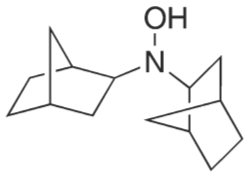
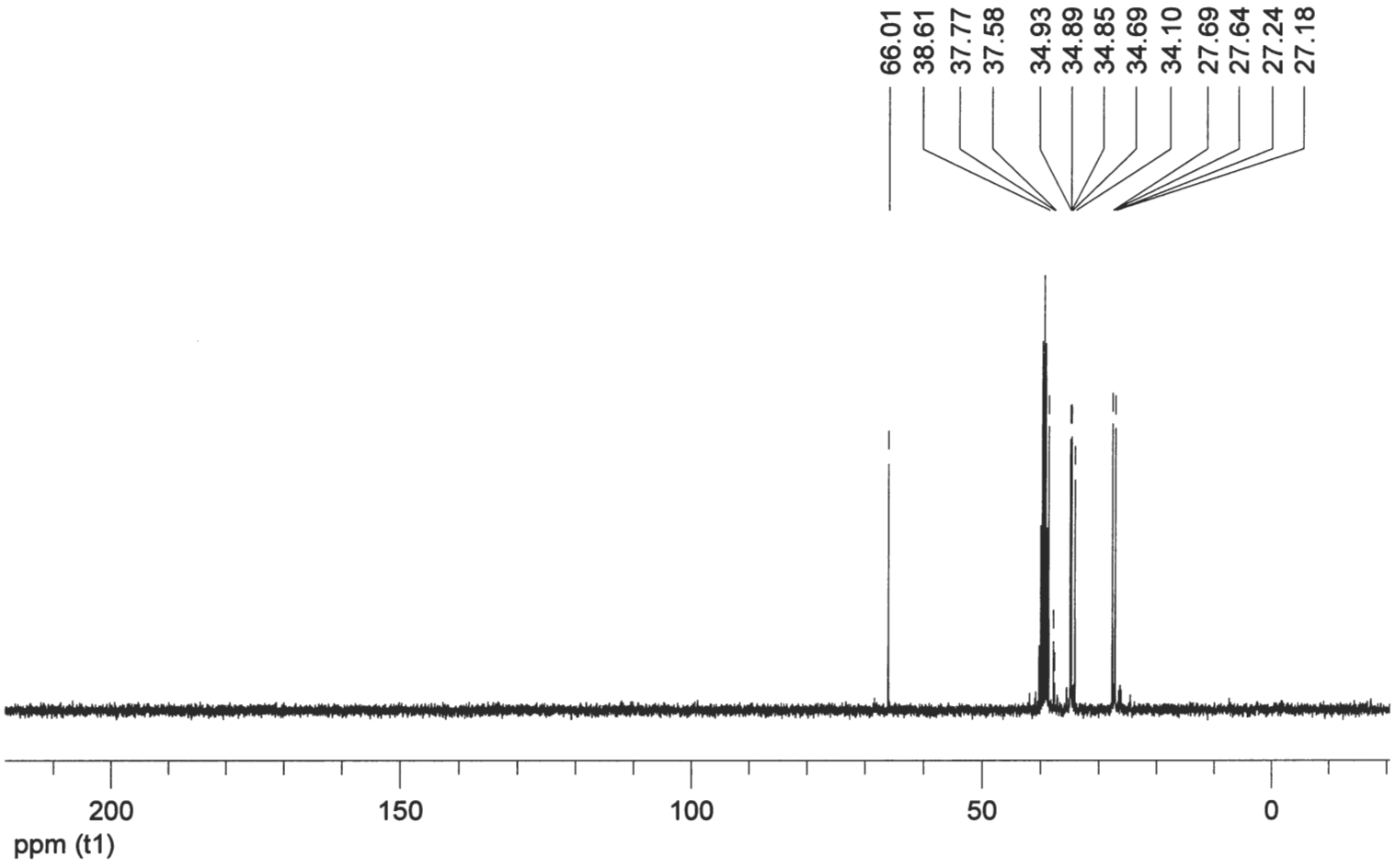
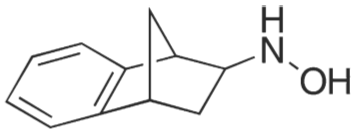


Table 3, Entry 1





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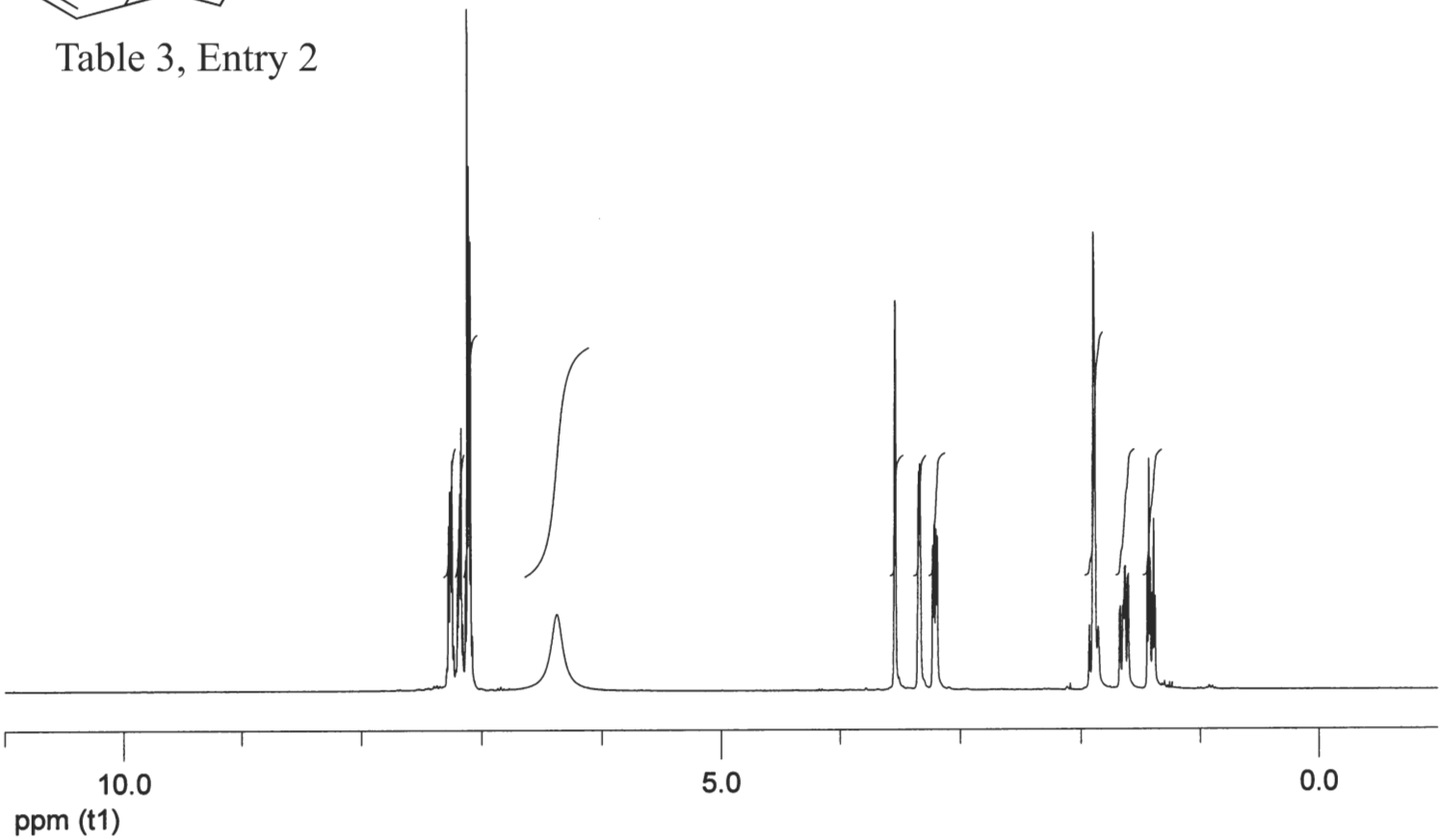

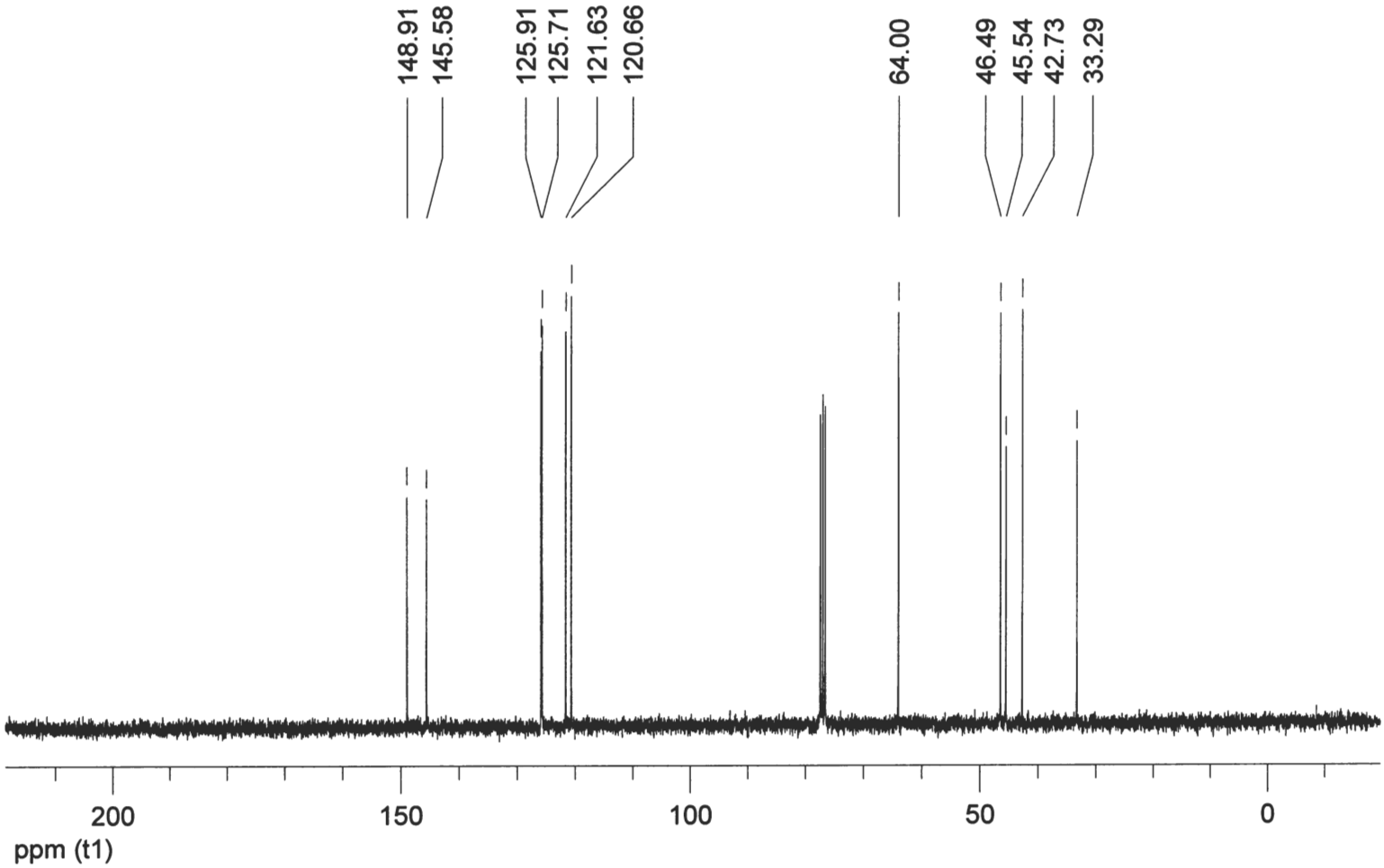

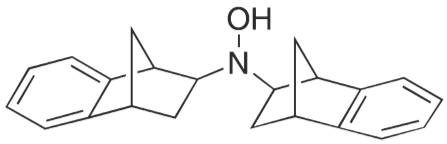

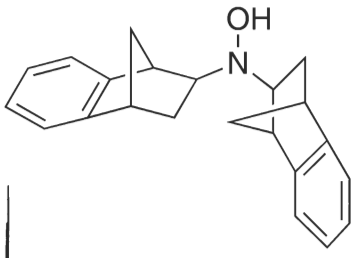

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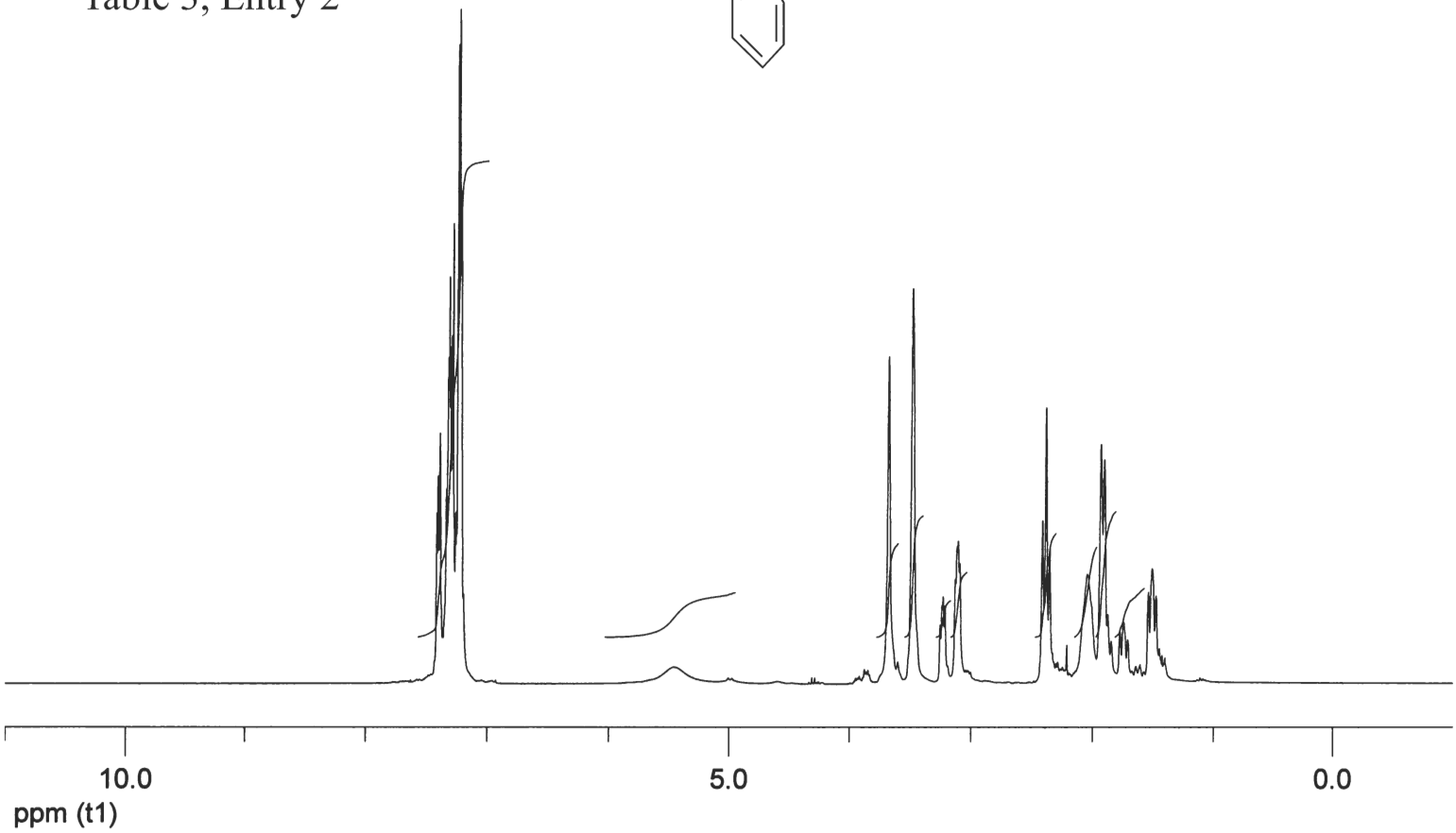

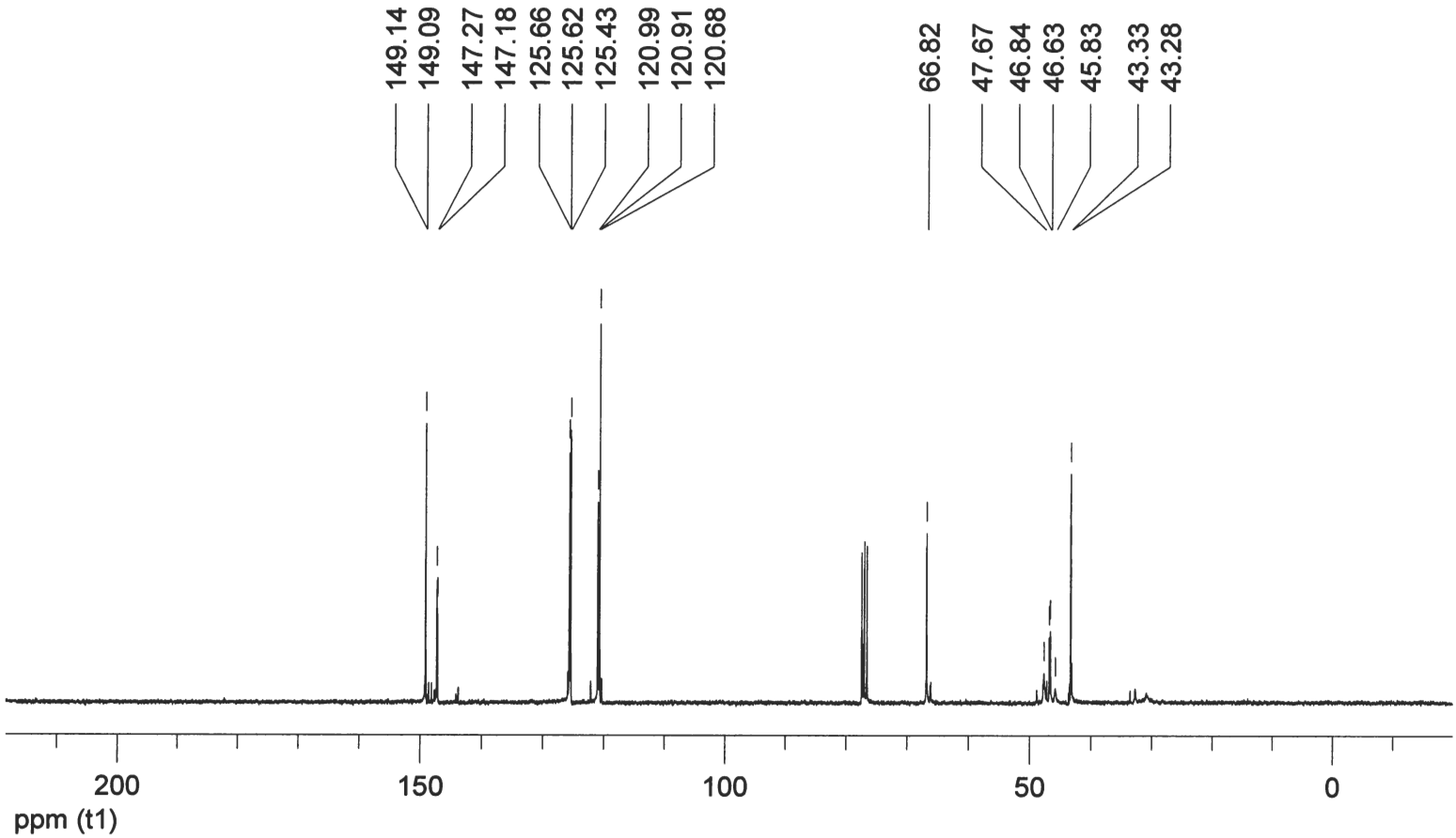

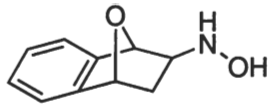

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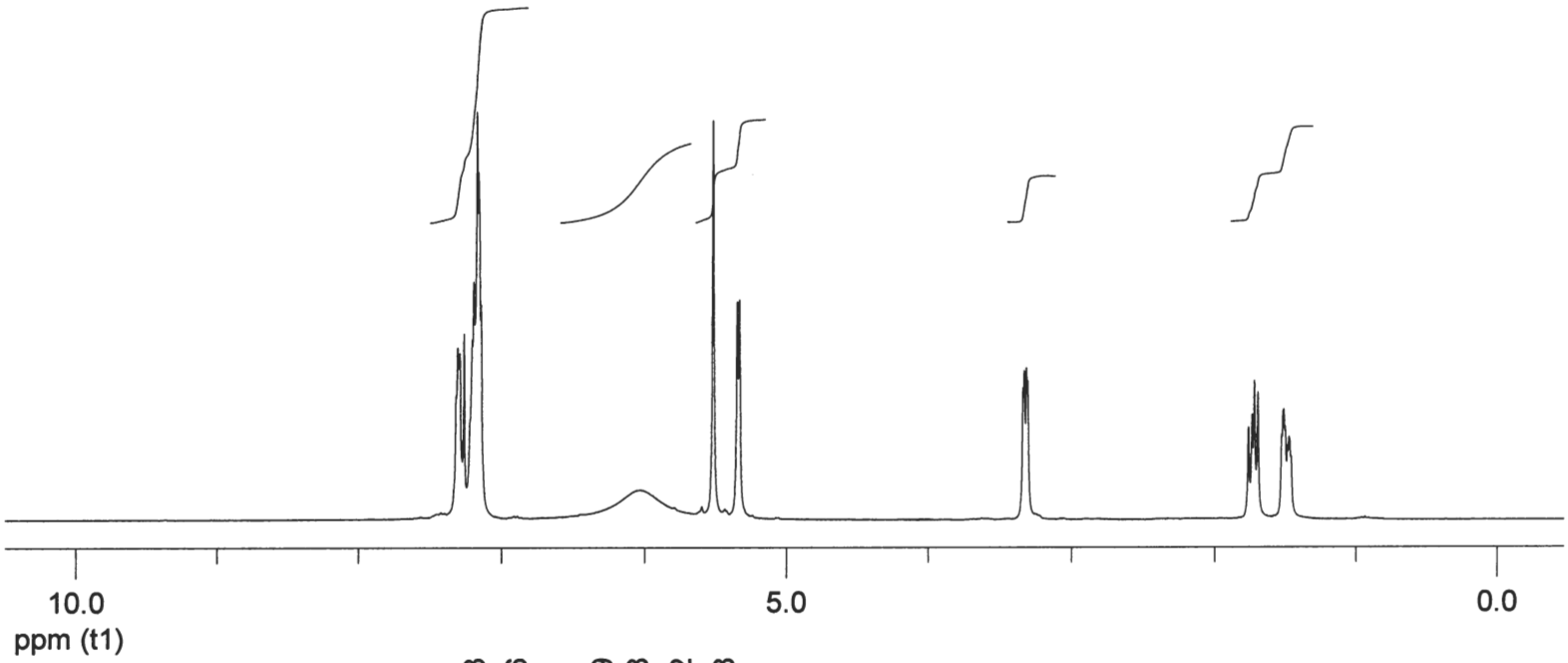

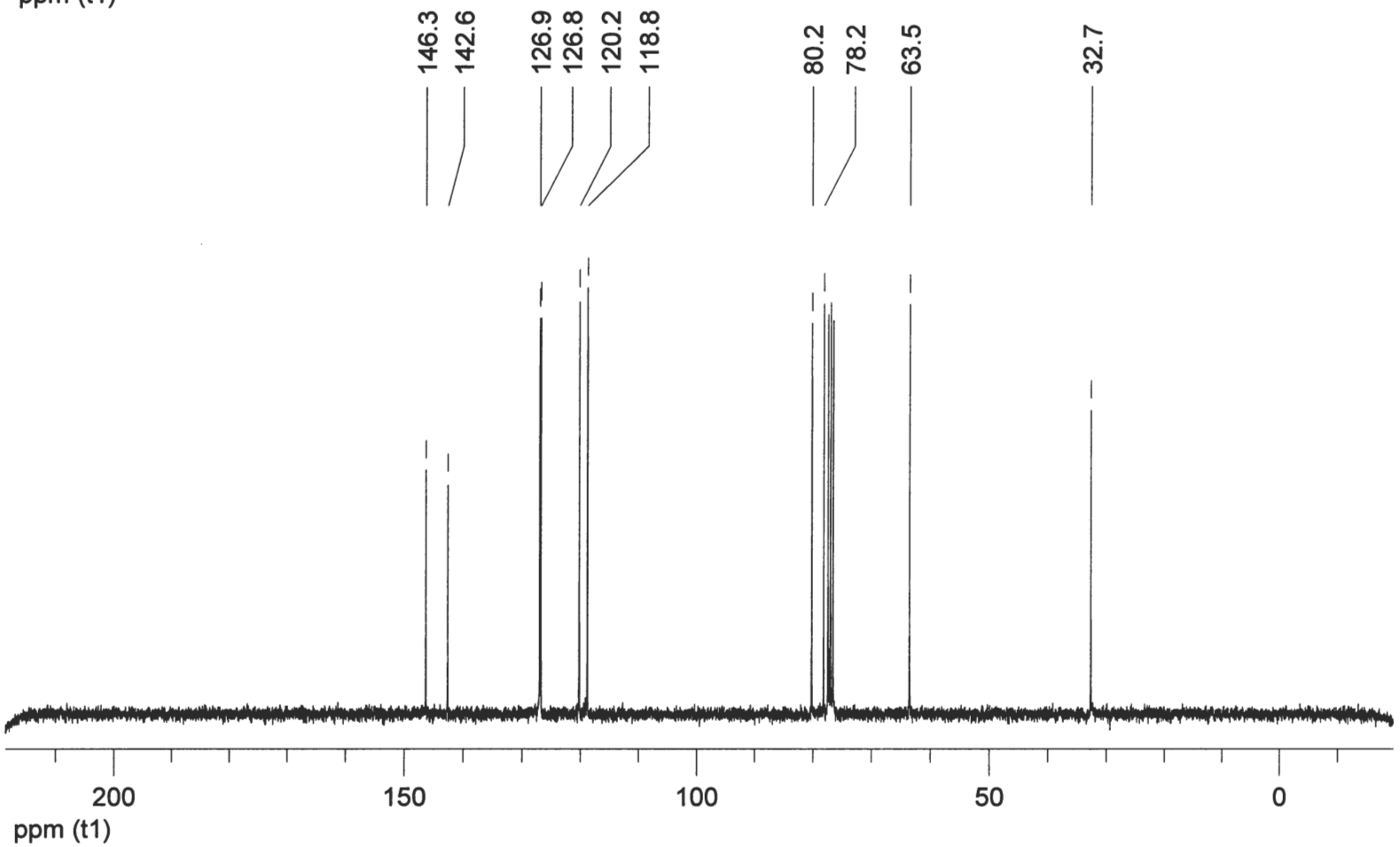

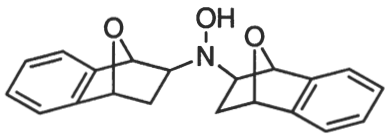

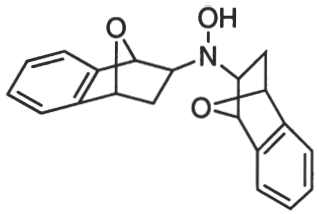

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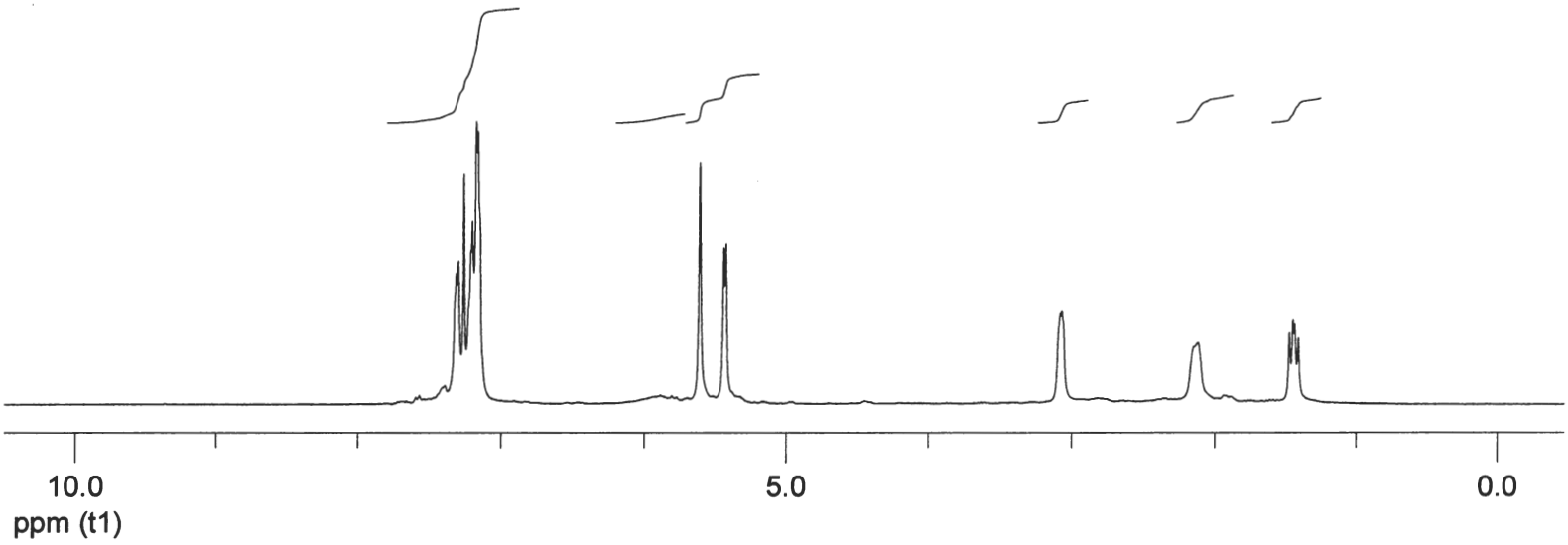

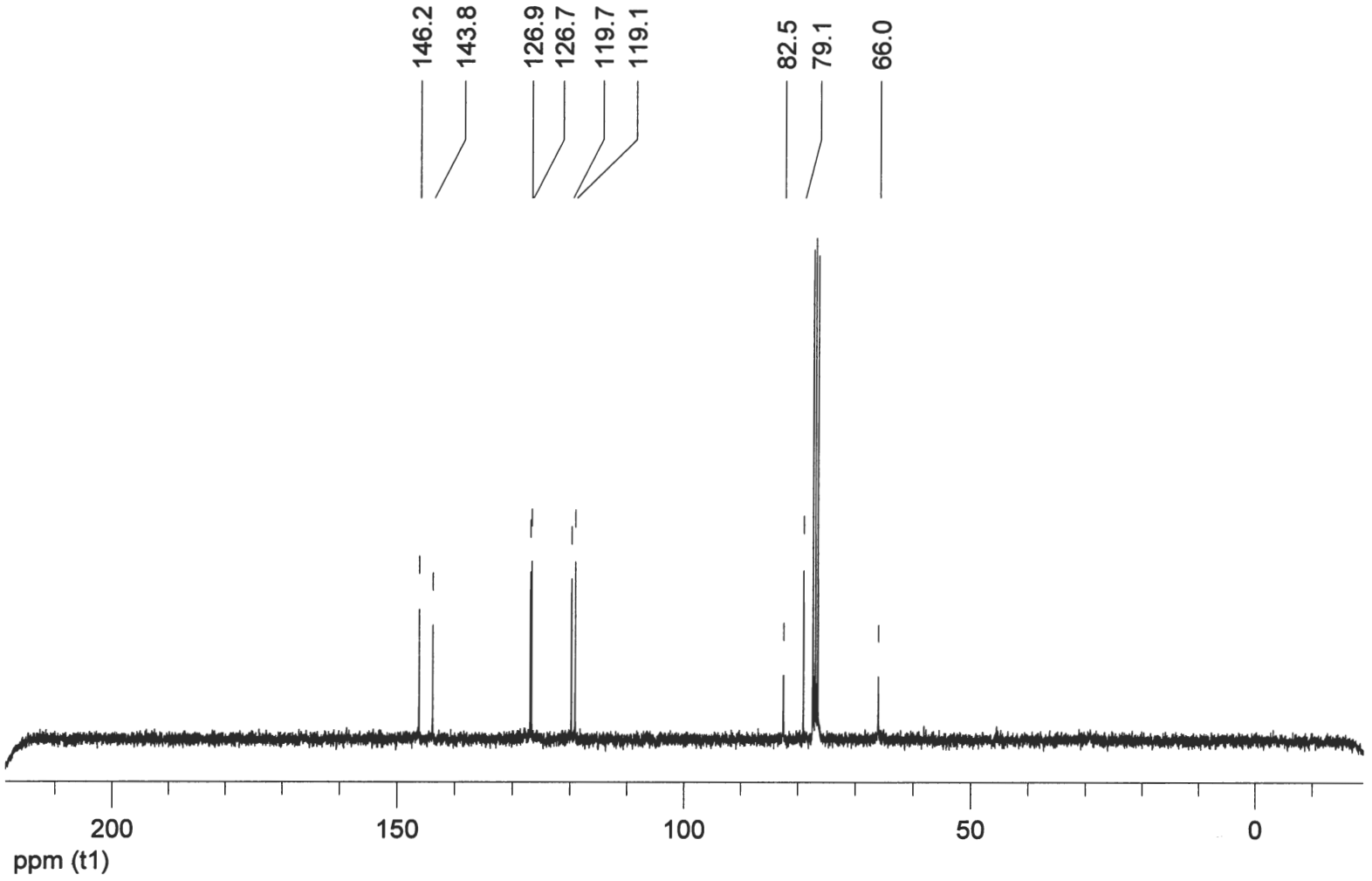

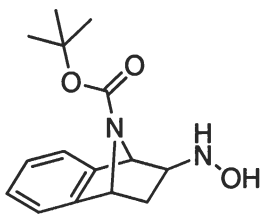

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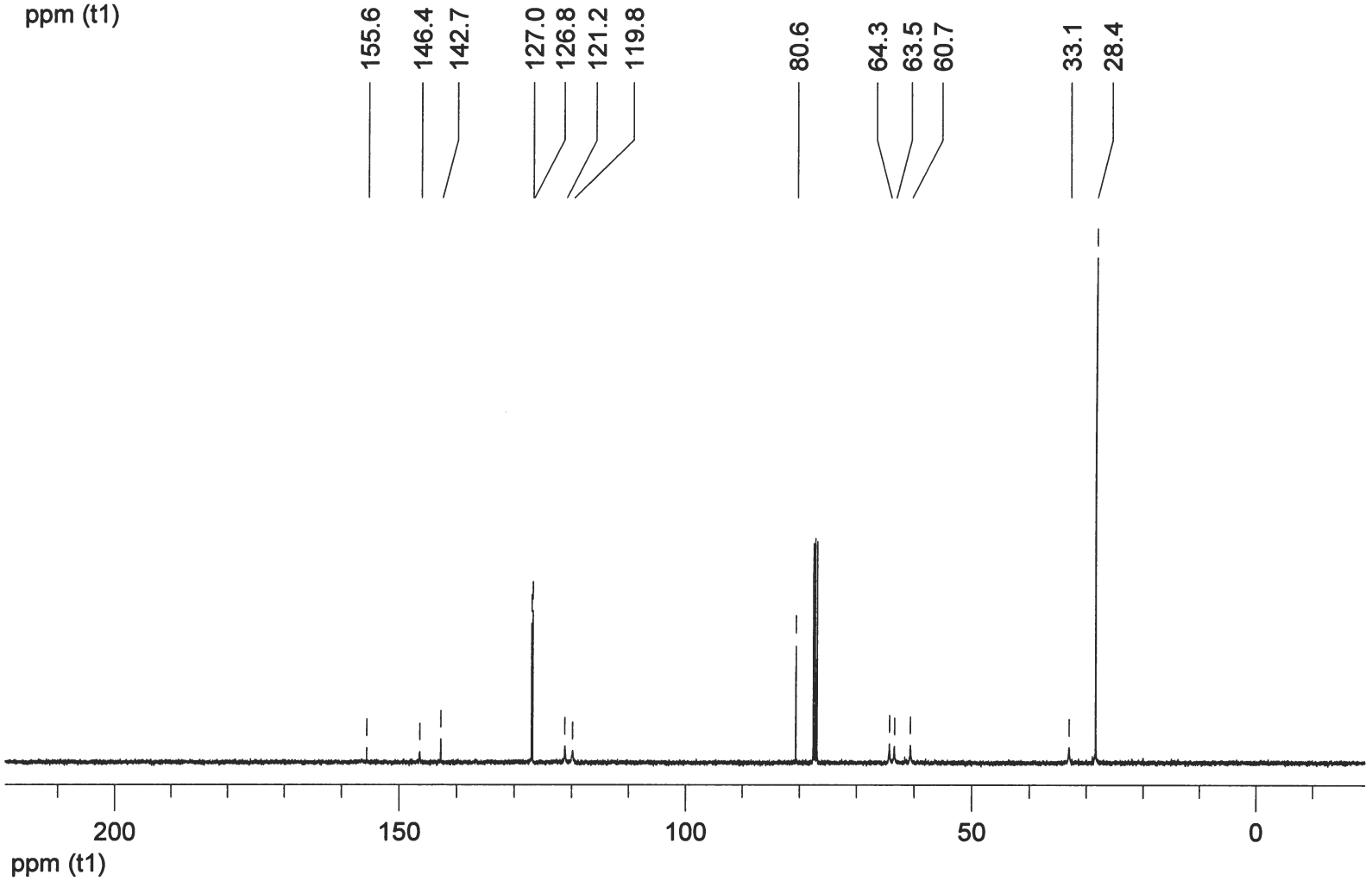

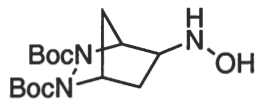

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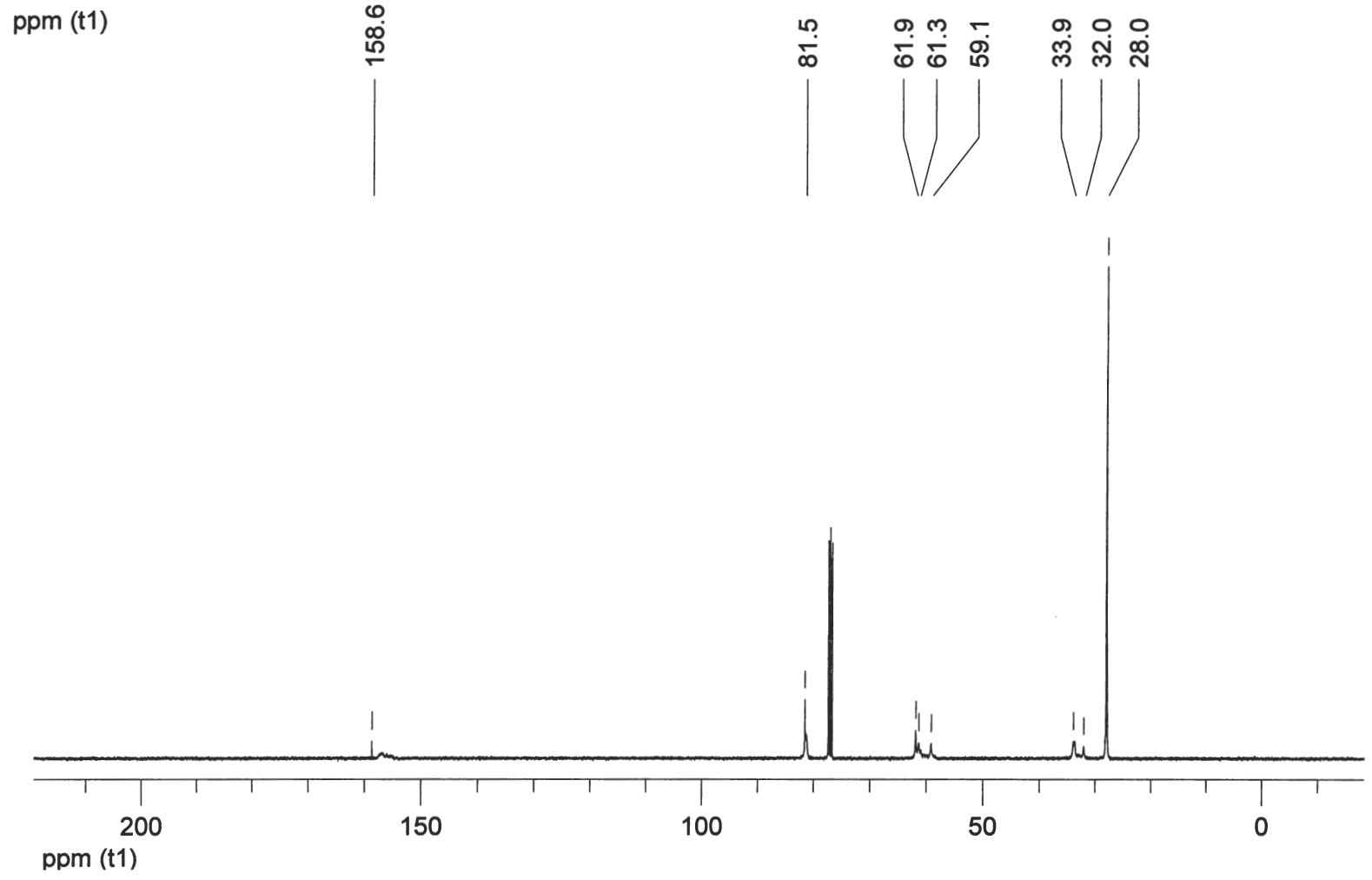


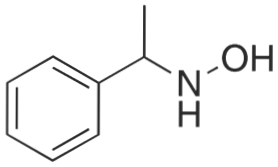
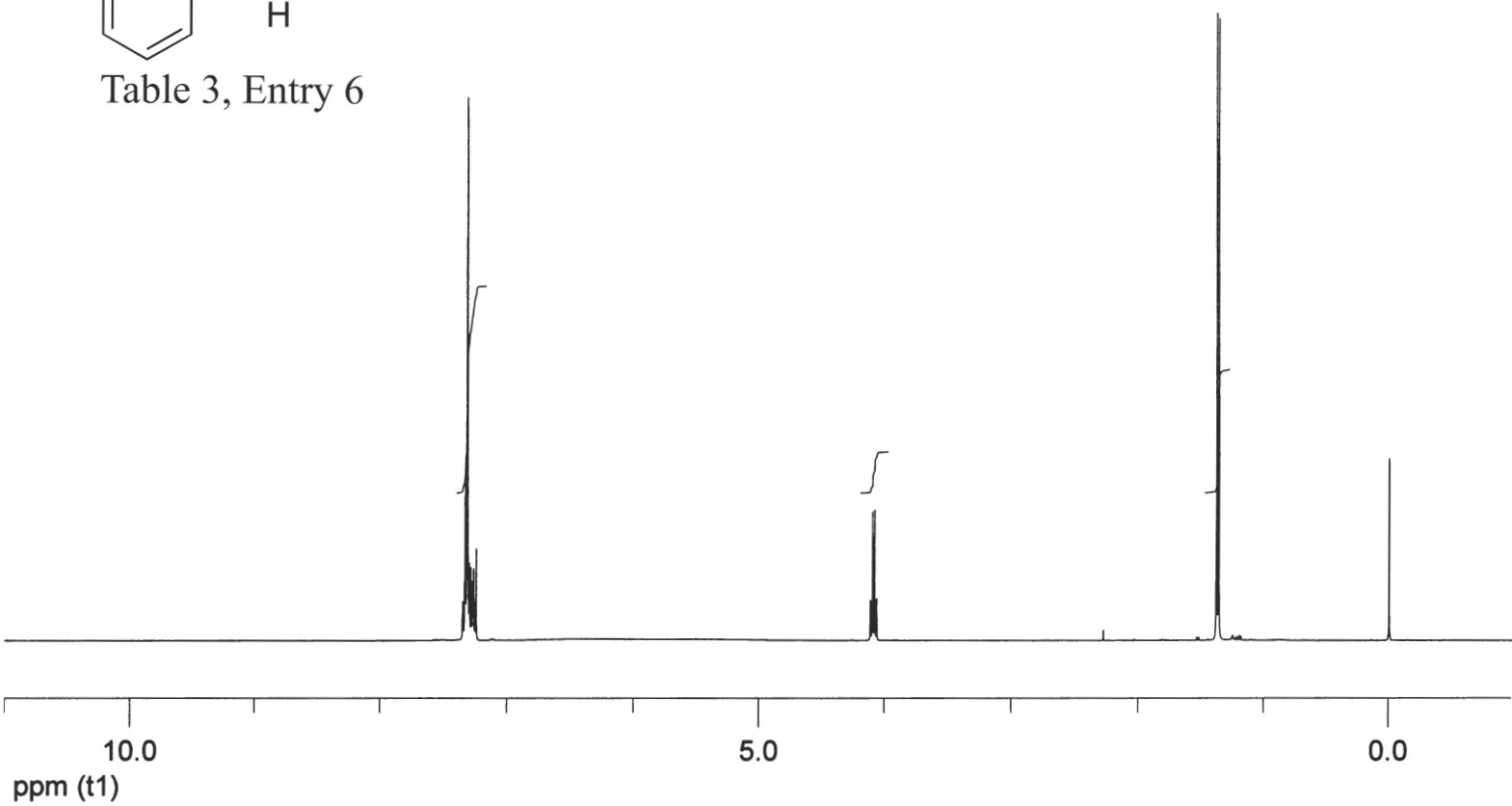
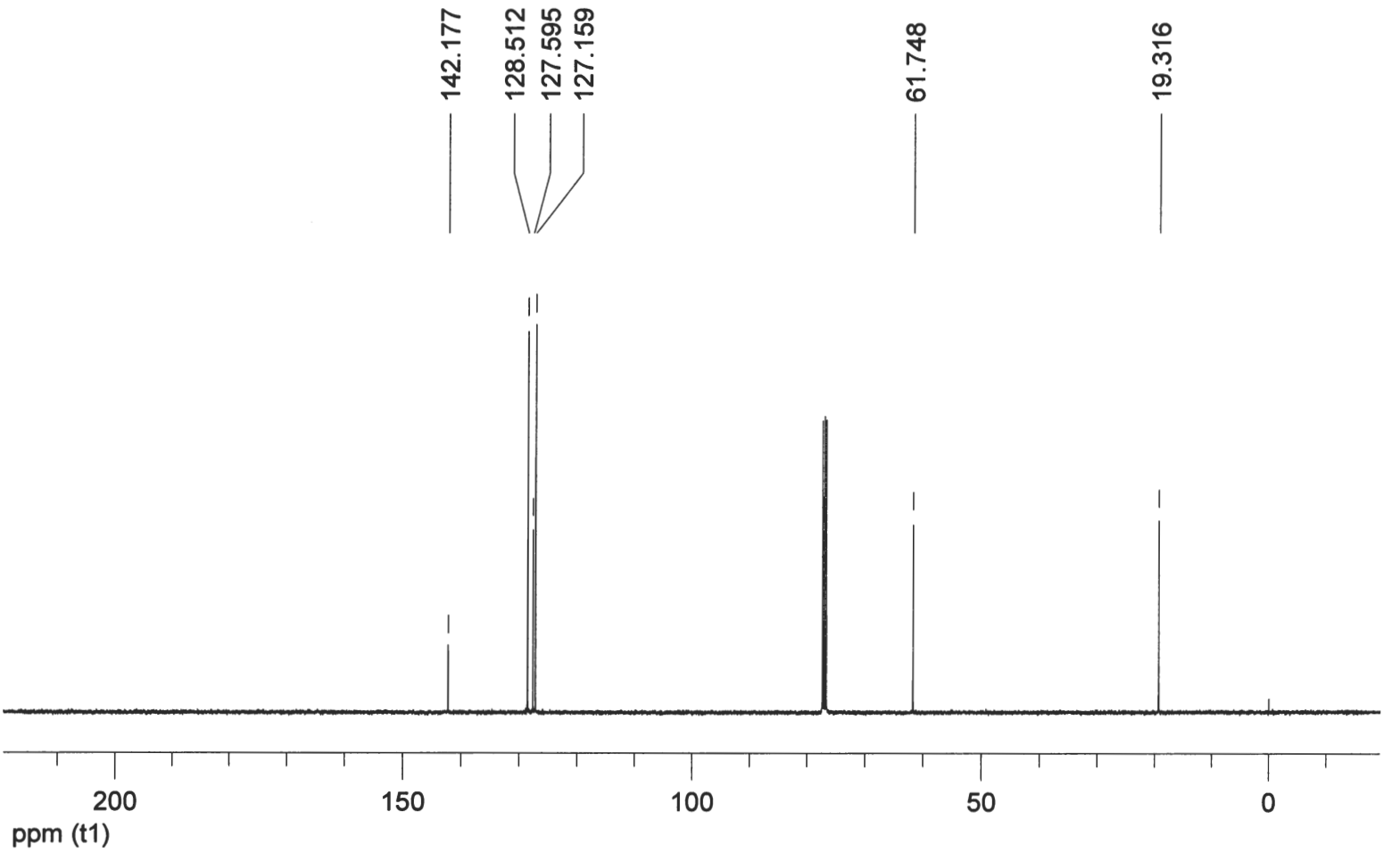


Table 3, Entry 6





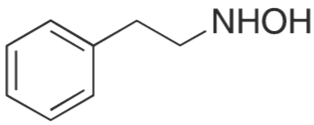
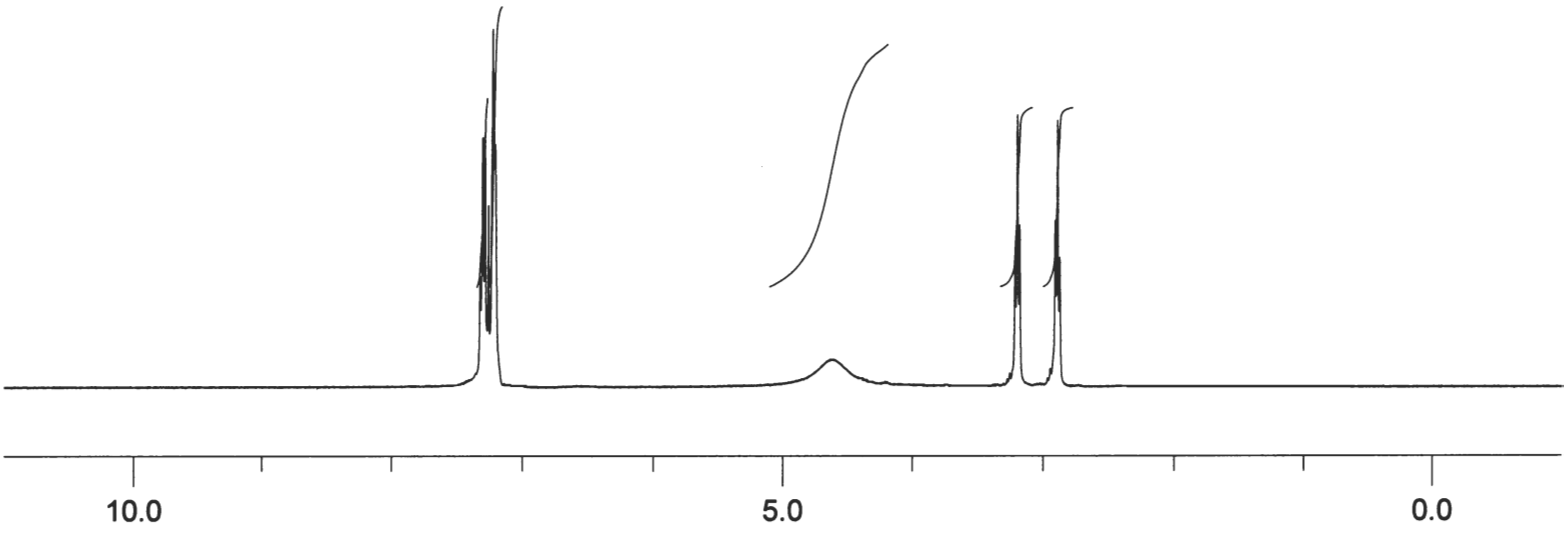
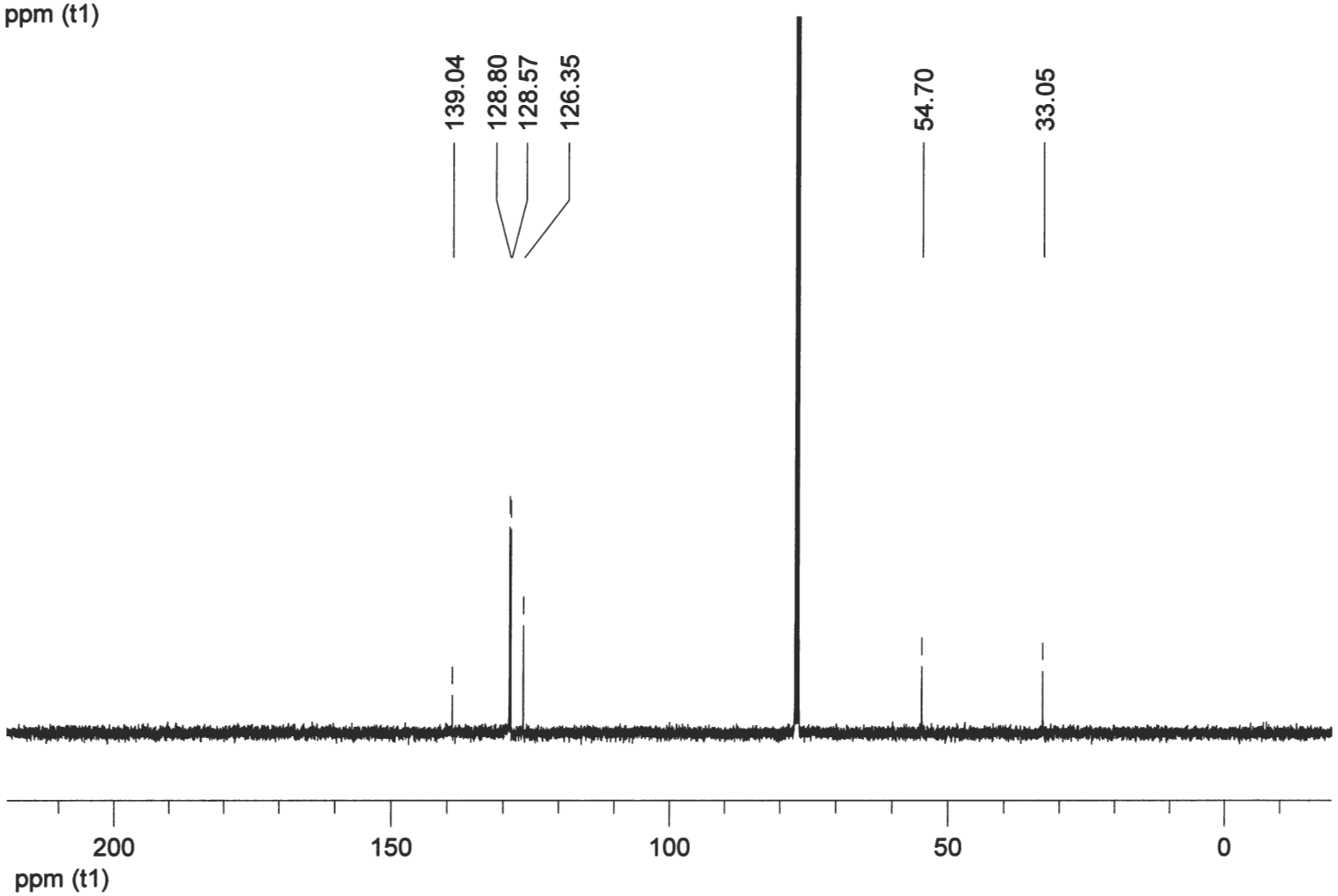
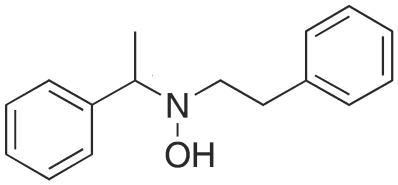


Table 3, Entry 6







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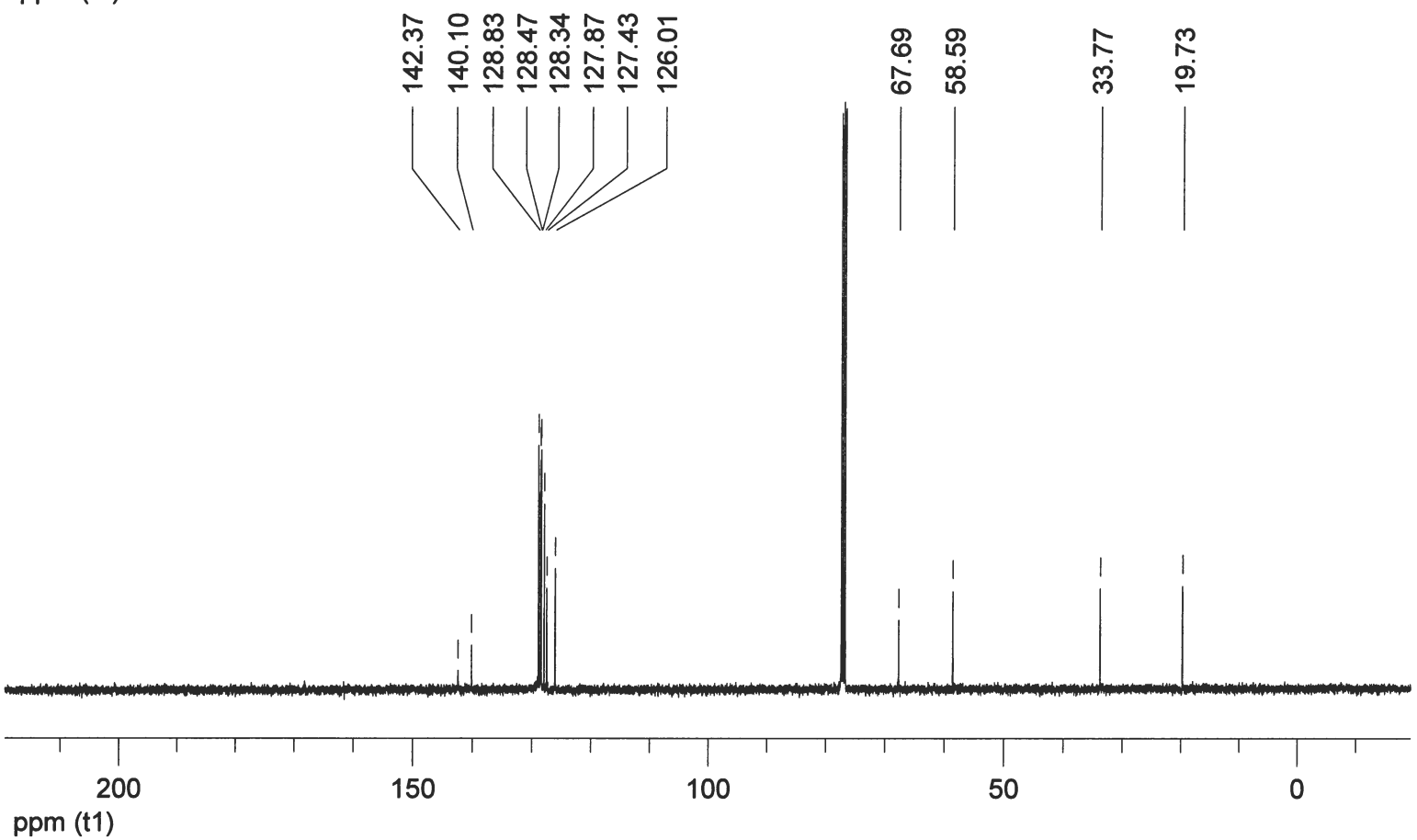


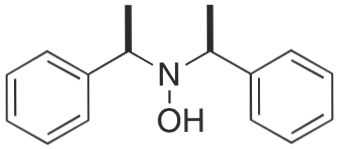
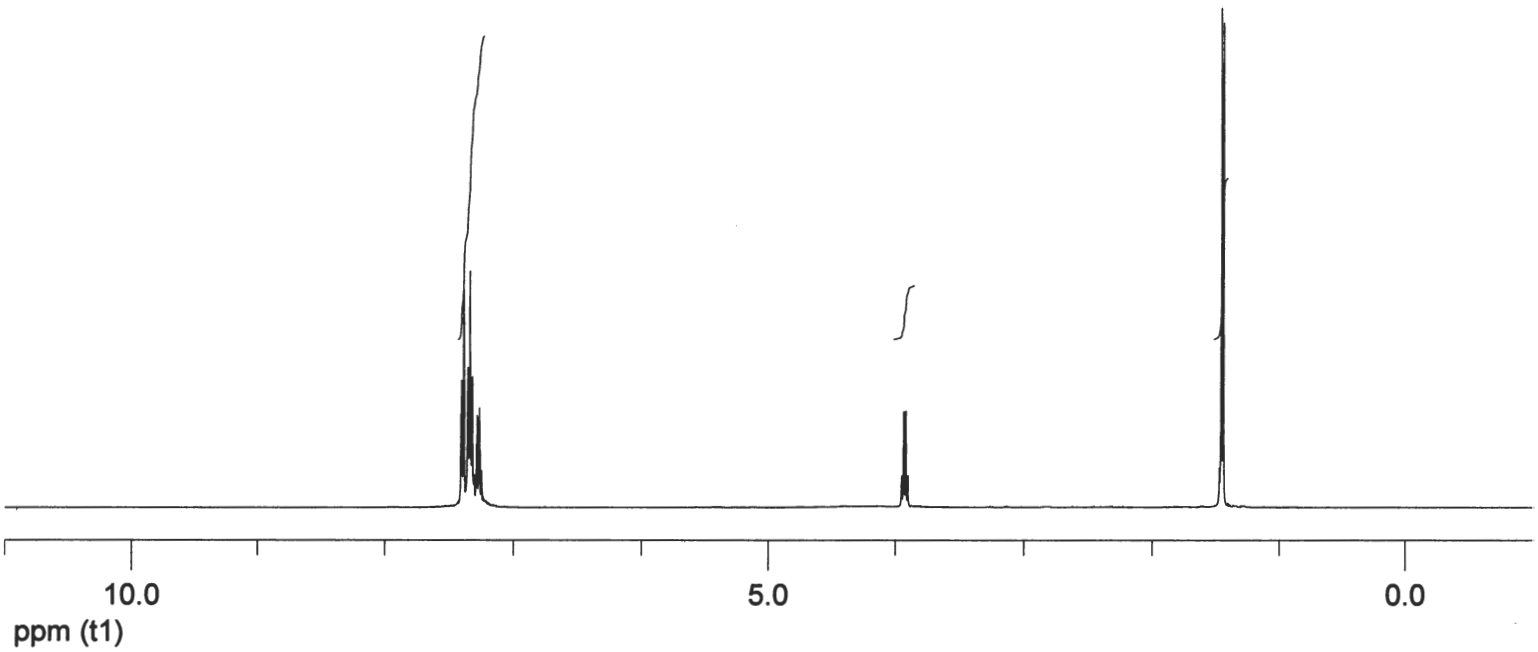
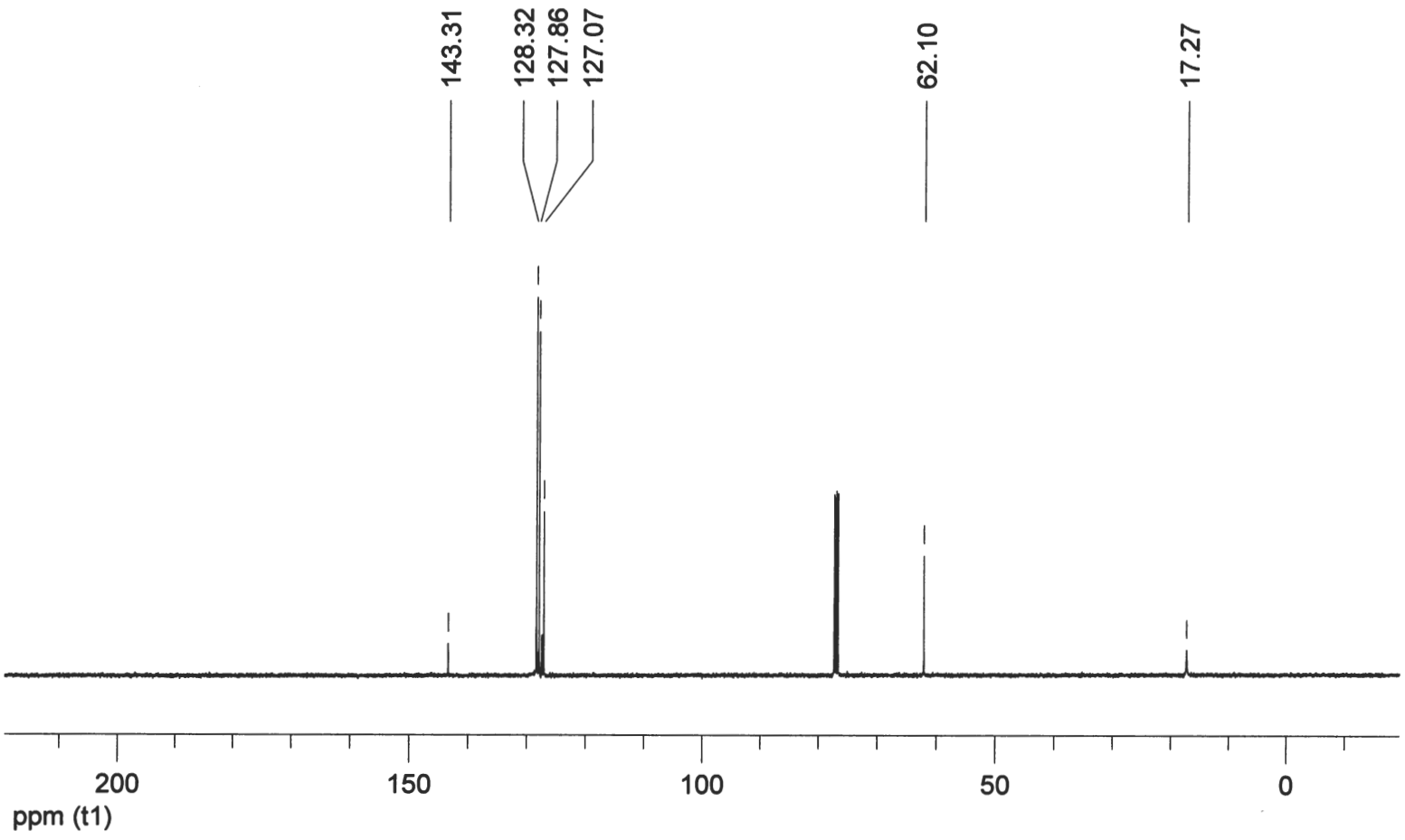
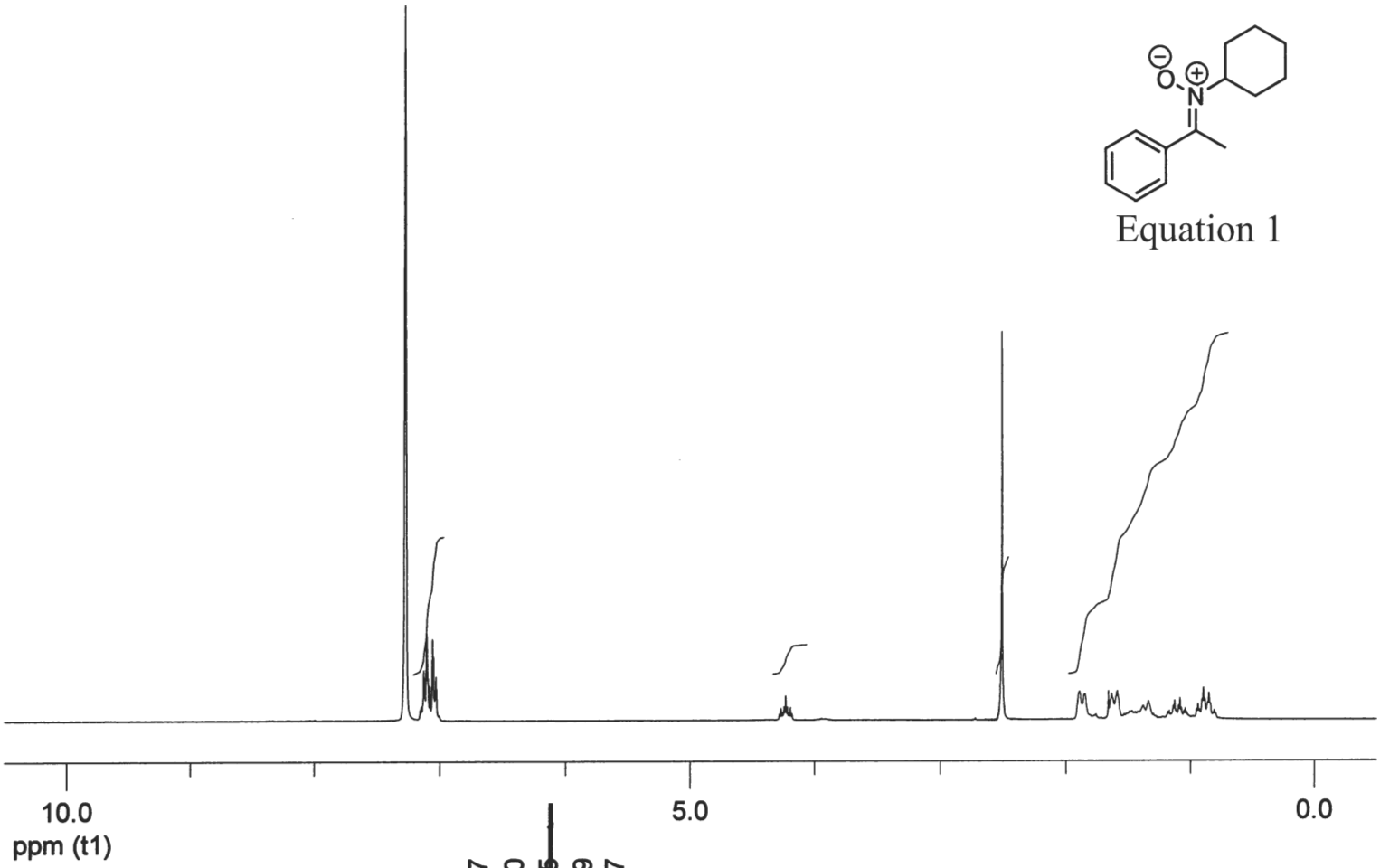


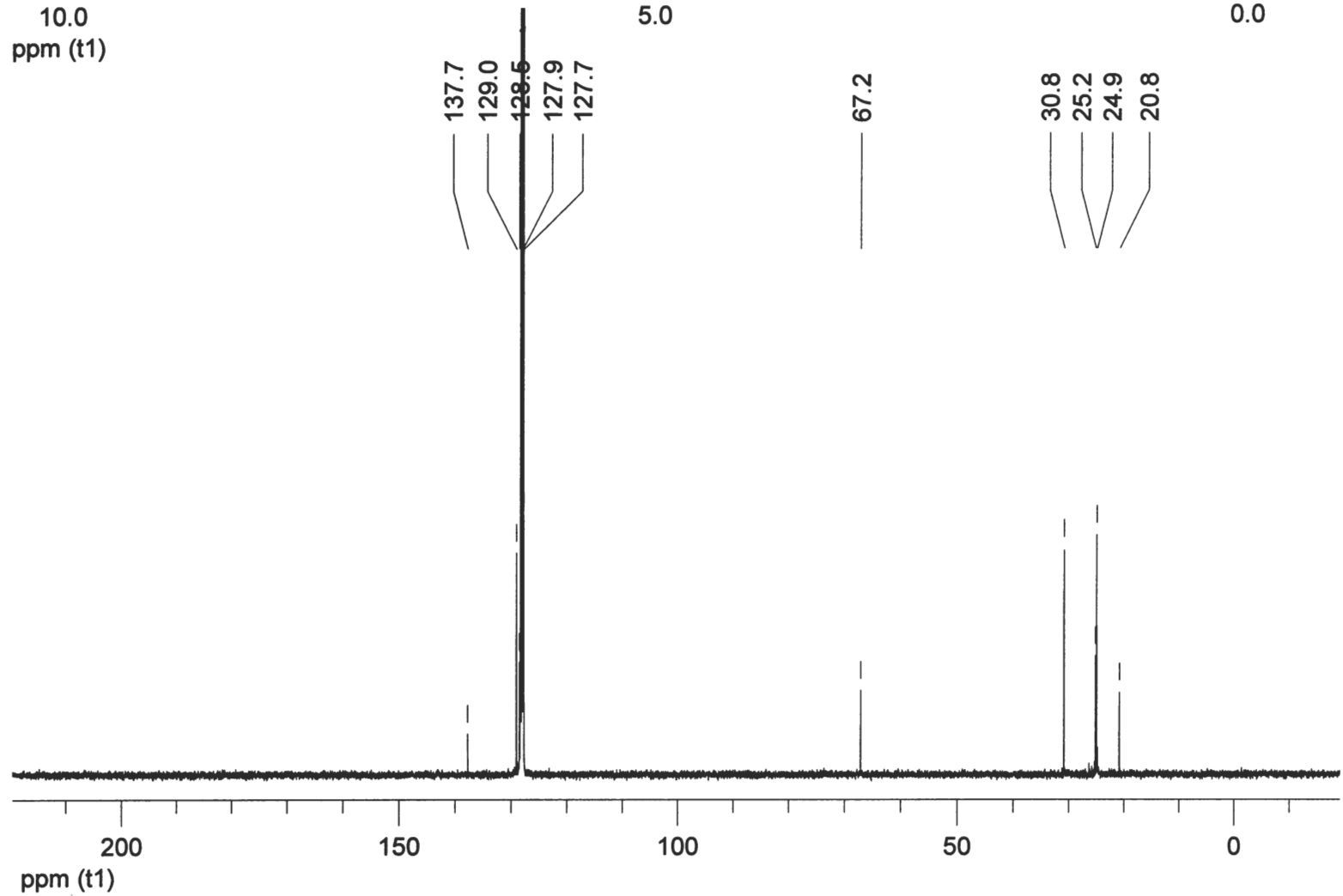
Table 3, Entry 6

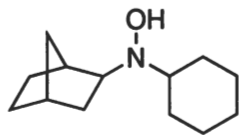





10.0
ppm (t1)
5.0
0.0

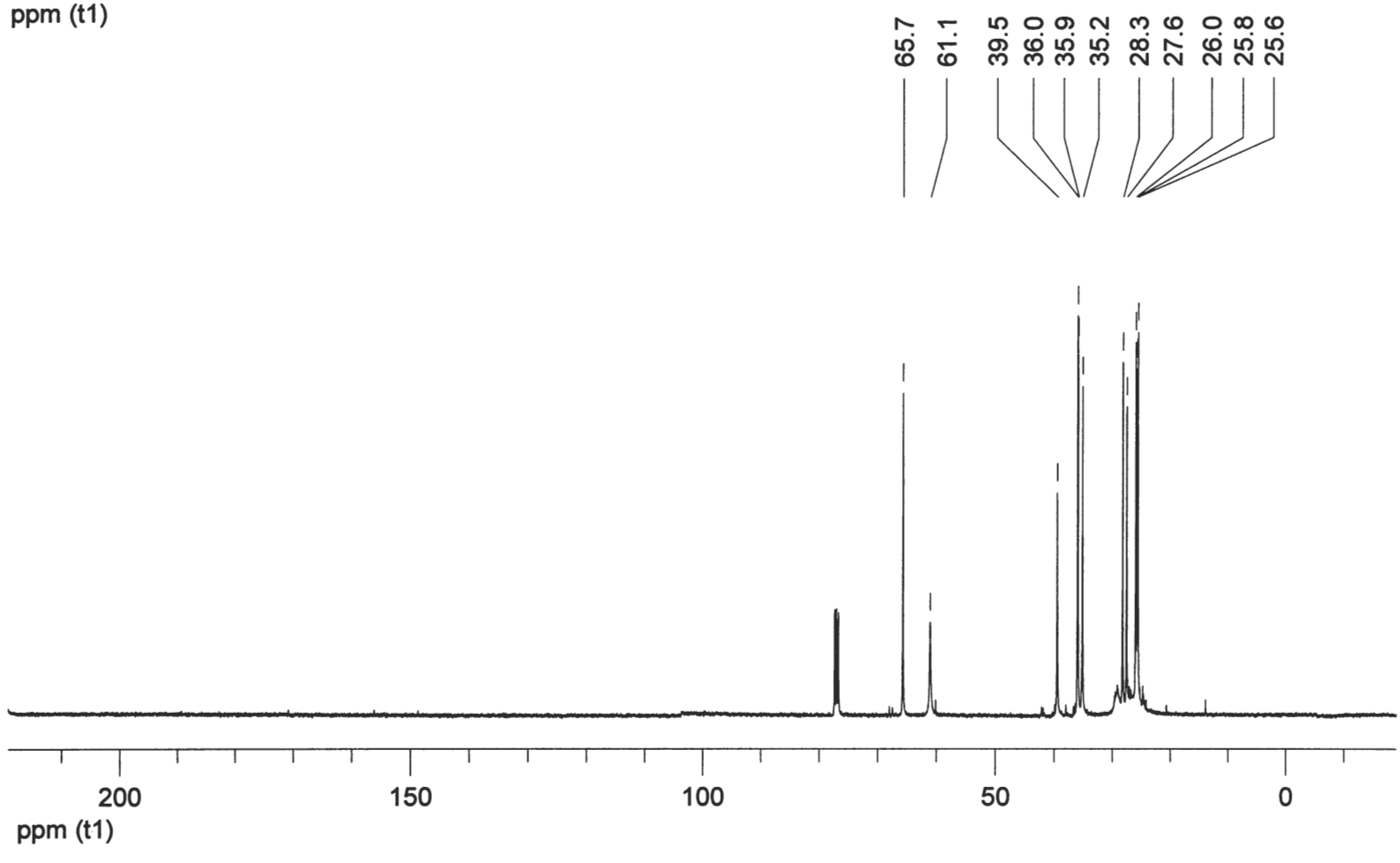
Equation 1


137.7
129.0
128.5
127.9
127.7
67.2
30.8
25.2
24.9
20.8
200
150
100
50
0
ppm (t1)


OH
N

Equation 2

10.0
5.0
0.0
ppm (t1)


65.7
61.1
39.5
36.0
35.9
35.2
28.3
27.6
26.0
25.8
25.6
200
150
100
50
0
ppm (t1)