Combined Oxypalladation/C−H Functionalization: Palladium(II)-catalyzed Intramolecular Oxidative Oxyarylation of Hydroxyalkenes

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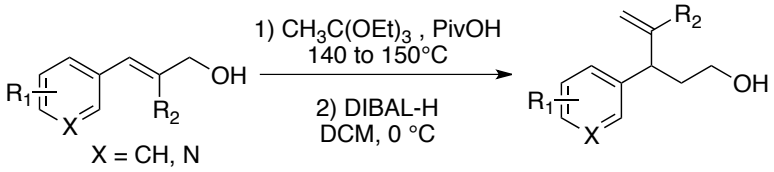
SUPPORTING INFORMATION

General Considerations. All reactions were carried out with dry solvents under anhydrous conditions, unless otherwise noted. Dry toluene was obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. $Pd(OAc)_2$ was purchased from Strem and used as received. Ethyl nicotinate and K_2CO_3 (*ReagentPlus*®, 99%) was purchased from Aldrich and used as received (It is important *not* to grind K_2CO_3). Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. *trans*-Cinnamic alcohol derivatives were prepared either from corresponding commercially available cinnamaldehyde derivatives via sodium borohydride reduction[1] or commercially available benzaldehyde derivatives following a two-step protocol involving a Wittig reaction and a DIBAL-H reduction described by Malkov and co-workers[2]. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. All yields of the palladium-catalyzed oxyarylation reactions stated are the average of at least two experiments. Reactions were monitored by GC and thin-layer chromatography (TLC) carried out on 0.25 mm E. Merck silica gel plates (60F-254) using UV light as a visualizing agent and phosphomolybdic acid in ethanol or $KMnO_4$ solution and heat as developing agents. Flash silica gel chromatography was performed using Silicycle SiliaFlashP60 (230-400 mesh) silica gel. NMR spectra were recorded on a Bruker AMX 400 spectrometer and were calibrated using residual solvent as an internal reference ($CDCl_3$: 7.26 ppm for ^{1}H NMR and 77.16 ppm for ^{13}C NMR). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad, at = apparent triplet, ad = apparent doublet. IR spectra were recorded on a Perkin-Elmer 2000 FTIR spectrometer using KBr plates (thin film). Melting points (m.p.) were obtained on a Mel-Temp capillary melting point apparatus. Gas chromatographic analyses were performed on an Agilent 6890 gas chromatograph. Elemental analyses were performed by Atlantic Microlabs Inc., Norcross, GA.

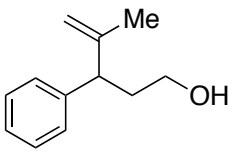
Synthesis and Characterization of the α-Aryl-γ-hydroxyalkene Substrates



General Procedure: Substrate Preparation

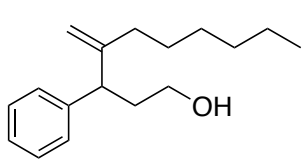
An oven dried round bottom flask equipped with a short path distillation head and a recovery flask was charged with a Teflon-coated magnetic stir bar, the *trans*-cinnamic alcohol derivative (1.0 equiv.), pivalic acid (0.1 equiv.) and triethyl orthoacetate (10 equiv.) The reaction mixture was stirred at 140 °C until no more ethanol was collected and then heated to 150 °C to collect excess orthoacetate. This procedure was repeated until the starting material was found to be completely consumed as judged by TLC analysis (usually two cycles). The residue was cooled to room temperature and diluted with ether and aqueous saturated sodium chloride solution. The aqueous layer was separated and extracted with ether, and the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo* to afford the crude β-aryl-γ,δ-unsaturated ester which was used in the next step without further purification.

An oven dried round bottom flask charged with a Teflon-coated magnetic stir bar and the previously obtained β-aryl-γ,δ-unsaturated ester (1.0 equiv.) was briefly evacuated and backfilled with argon three times. Anhydrous DCM was added under argon to give a 0.5 M solution of the ester. DIBAL-H (1.0 M in hexanes, 2.2 equiv.) was added to the reaction mixture dropwisely at 0 °C under argon and the resulting mixture was stirred at 0 °C for 2 h until the starting material was found to be completely consumed as judged by TLC analysis. Saturated aqueous solution of Rochelle's salt (1 mL/mmol DIBAL-H used) was carefully added to the mixture at 0 °C and stirred vigorously for 1 h. The aqueous layer was separated and extracted with CH_2Cl_2, and the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (EtOAc/hexane) afforded the desired α-aryl-γ-hydroxyalkene.

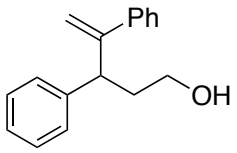


4-methyl-3-phenylpent-4-en-1-ol (Table 2, entry 1) Known compound.[3] Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-methylcinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.19 (m, 5 H), 4.95 (s, 1 H), 4.86 (m, 1 H), 3.65-3.54 (m, 2 H), 3.42 (dd, *J* =7.8 Hz, 7.8 Hz, 1 H), 2.18-2.09 (m, 1 H), 2.02-1.95 (m, 1 H), 1.59 (s, 3 H), 1.47 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 143.1, 128.5, 127.9, 126.5, 110.6, 61.4, 49.1, 35.8, 21.1; IR (film) ν_{max} 3335, 3082, 3026, 2941, 1645, 1600, 1492, 1451, 1374, 1045, 892 cm^{-1}; Anal. Calcd. For $C_{12}H_{16}O$: C,

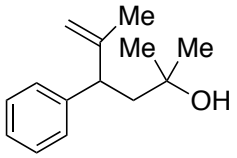
81.77; H, 9.15. Found: C, 81.62; H, 8.99.



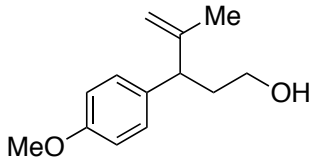
4-methylene-3-phenyldecan-1-ol (Table 2, entry 2) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-*n*-hexylcinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.27 (m, 2 H), 7.22-7.18 (m, 2 H), 4.99 (s, 1 H), 4.90 (m, 1 H), 3.62-3.51 (m, 2 H), 3.41 (dd, *J* =7.8 Hz, 7.5 Hz, 1 H). 2.18-2.09 (m, 1 H), 2.00-1.80 (m, 3 H), 1.37-1.19 (m, 9 H), 0.85 (at, *J* =7.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 143.4, 128.5, 128.1, 126.5, 108.9, 61.4, 47.9, 36.8, 35.1, 31.8, 29.2, 27.9, 22.7, 14.2; IR (film) ν_{max} 3326, 2926, 2856, 1642, 1600, 1492, 1453, 1041, 894 cm^{-1}; Anal. Calcd. For $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.64; H, 10.58.



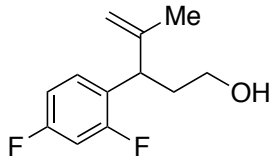
3,4-diphenylpent-4-en-1-ol (Table 2, entry 3) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-phenylcinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.18 (m, 10 H). 5.41 (s, 1 H), 5.21 (s, 1 H), 4.04 (m, 1 H), 3.69-3.56 (m, 2 H), 2.25-2.17 (m, 1 H), 2.09-2.00 (m, 1 H), 1.39 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 142.8, 142.4, 128.6, 128.3, 128.2, 127.4, 126.9, 126.6, 113.5, 61.2, 46.6, 37.9; IR (film) ν_{max} 3338, 3082, 2940, 2881, 1653, 1624, 1492, 1452, 1027, 903 cm^{-1}; Anal. Calcd. For $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.68; H, 7.59.



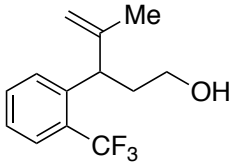
2,5-dimethyl-4-phenylhex-5-en-2-ol (Table 2, entry 4) Following the first step of the general procedure, crude ethyl 4-methyl-3-phenylpent-4-enoate (2.5 g, 11 mmol) was obtained, which was then dissolved in anhydrous ether (20 mL) and treated with 3.0 equiv. of methyl magnesiumbromide solution (3 M in ether) under argon at 0 °C. The mixture was stirred at the same temperature for 2 h and quenched with 30 mL saturated aqueous ammonium chloride solution. The aqueous layer was separated and extracted with ether (3×30 mL), and the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash column chromatography (EtOAc/hexane) afforded the title compound as a sticky colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.19 (m, 5 H). 5.02 (s, 1 H), 4,84 (m, 1 H), 3.59 (at, *J* =7.0 Hz, 7.0 Hz, 1 H), 2.19 (dd, *J* =14.2 Hz, 7.2 Hz, 1 H), 2.01 (dd, *J* =14.2 Hz, 6.8 Hz, 1 H), 1.67 (br, 1 H), 1.65 (s, 3 H), 1.22 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.7, 144.0, 128.5, 128.0, 126.5, 110.8, 71.4, 48.9, 45.6, 30.3, 29.6, 20.7; IR (film) ν_{max} 3405, 2969, 2935, 1644, 1493, 1451, 1374, 1136, 891 cm^{-1}; Anal. Calcd. For $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.11; H, 9.75.



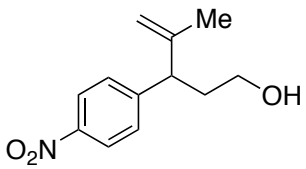
3-(4-methoxyphenyl)-4-methylpent-4-en-1-ol (Table 2 entry 5) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-(4-methoxyphenyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (d, *J* =8.7 Hz, 2 H), 6.84 (d, *J* =8.7 Hz, 2 H). 4.92 (s, 1 H), 4.83 (m, 1 H), 3.79 (s, 3 H), 3.65-3.54 (m, 2 H), 3.36 (dd, *J* =7.6 Hz, 7.6 Hz, 1 H), 2.15-2.04 (m, 1 H), 1.98-1.90 (m, 1 H), 1.58 (s, 3 H), 1.45 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.3, 148.3, 135.1, 128.8, 113.9, 110.3, 61.5, 55.4, 48.3, 36.0, 21.1; IR (film) ν_{max} 3374, 2939, 1644, 1609, 1510, 1248, 1178, 1036 cm^{-1}; Anal. Calcd. For $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.63; H, 8.90.



3-(2,4-difluorophenyl)-4-methylpent-4-en-1-ol (Table 2, entry 6) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-(2,4-difluorophenyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (td, J_F =8.5 Hz, 6.5 Hz, 1 H), 6.84-6.73 (m, 2 H). 4.92 (s, 1 H), 4.89 (s, 1 H), 3.72 (dd, *J* =7.8 Hz, 7.8 Hz, 1 H), 3.56-3.53 (m, 2 H), 2.17-2.08 (m, 1 H), 2.01 (br, 1 H), 1.92-1.84 (m, 1 H), 1.60 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) [complexity observed due to C-F splitting] δ 162.6 (dd, J_F = 245 Hz, 12 Hz), 160.1 (dd, J_F = 246 Hz, 12 Hz), 146.2, 129.4 (dd, J_F = 9 Hz, 6 Hz), 125.8 (dd, J_F = 15 Hz, 4 Hz), 111.3 (dd, J_F = 21 Hz, 4 Hz), 111.4, 103.7 (dd, J_F = 27 Hz, 25 Hz), 60.9, 40.4 (d, J_F = 1 Hz), 35.6, 21.4; IR (film) ν_{max} 3335, 2943, 1647, 1616, 1501, 1283, 1945, 966, 897, 849 cm^{-1}; Anal. Calcd. For $C_{12}H_{14}F_2O$: C, 67.91; H, 6.65. Found: C, 67.63; H, 6.78.

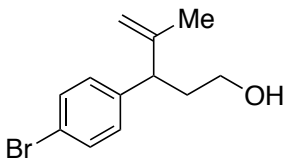


4-methyl-3-(2-(trifluoromethyl)phenyl)pent-4-en-1-ol (Table 2, entry 7) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-(2-trifluoromethyl-phenyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* =7.9 Hz, 1 H), 7.51-7.42 (m, 2 H), 7.30 (dd, *J* =7.6, 7.3 Hz, 1 H), 4.96(s, 2 H), 3.76 (dd, *J* =7.4 Hz, 7.3 Hz, 1 H), 3.64 (m, 1 H), 3.51 (m, 1 H), 2.21 (m, 1 H), 1.93 (m, 1 H), 1.61 (s, 3 H), 1.43 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) [complexity observed due to C-F splitting] δ 146.9, 142.7 (d, J_F = 2 Hz), 132.1, 128.8, 128.8 (q, J_F = 29 Hz), 126.5, 125.9 (q, J_F = 6 Hz), 124.7 (q, J_F = 272 Hz), 111.0, 61.33, 43.3 (d, J_F = 2 Hz), 38.0, 22.7; IR (film) νmax 3331, 2948, 2885, 1646, 1607, 1454, 1312, 1122, 1035, 898 cm^{-1}; Anal. Calcd. For $C_{13}H_{15}F_3O$: C, 63.93; H, 6.19. Found: C, 63.67; H, 6.28.

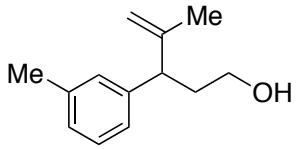


4-methyl-3-(4-nitrophenyl)pent-4-en-1-ol (Table 2, entry 8) Following a slightly modified general procedure in which anhydrous ether was used as the solvent in the DIBAL-H reduction step instead of DCM, the title compound was

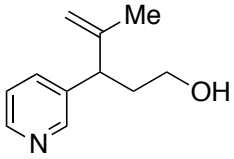
obtained as a sticky yellow oil from *trans*-α-(4-nitrophenyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.8 Hz, 2 H), 7.39 (dd, *J* = 8.7 Hz, 2 H), 4.98 (s, 1 H), 4.87 (m, 1 H), 3.61-3.44 (m, 3 H), 2.18-2.09 (m, 1 H), 1.95-1.84 (m, 1 H), 1.55 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.1, 146.8, 146.2, 128.8, 123.7, 112.1, 60.6, 48.7, 35.5, 21.1; IR (film) ν_{max} 3374, 2941, 2883, 1646, 1604, 1518, 1346, 1045, 898 cm^{-1}; Anal. Calcd. For $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83. Found: C, 65.27; H, 7.02.



3-(4-bromophenyl)-4-methylpent-4-en-1-ol (Table 2, entry 9) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-(4-bromophenyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, *J* =8.4 Hz, 2 H), 7.09 (d, *J* =8.4 Hz, 2 H), 4.92 (s, 1 H), 4.86 (m, 1 H), 3.58-3.50 (m, 2 H), 3.37 (dd, *J* =7.7 Hz, 7.7 Hz, 1 H), 2.13-2.03 (m, 1 H), 1.94-1.87 (m, 1 H), 1.85 (br, 1 H), 1.56 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 142.1, 131.5, 129.7, 120.2, 111.1, 60.89, 48.31, 35.6, 21.0; IR (film) ν_{max} 3346, 2940, 2881, 1645, 1487, 1072, 1010, 1044, 895, 818 cm^{-1}; Anal. Calcd. For $C_{12}H_{15}BrO$: C, 56.49; H, 5.93. Found: C, 56.23; H, 6.03.



4-methyl-3-(*m*-tolyl)pent-4-en-1-ol (Table 2, entry 10) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-(*m*-tolyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.16 (m, 1 H), 7.03-7.01 (m, 3 H). 4.94 (s, 1 H), 4.85 (s, 1 H), 3.65-3.54 (m, 2 H), 3.37 (dd, *J* =7.8 Hz, 7.8 Hz, 1 H), 2.33 (s, 3 H), 2.17-2.08 (m, 1 H), 2.01-1.92 (m, 1 H), 1.59 (s, 3 H), 1.43 (br, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.1, 143.0, 138.1, 128.7, 128.4, 127.3, 125.0, 110.5, 61.5, 49.1, 35.9, 21.6, 21.2; IR (film) ν_{max} 3347, 2941, 1645, 1606, 1447, 1373, 1045, 891 cm^{-1}; Anal. Calcd. For $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.91; H, 9.71.



4-methyl-3-(pyridin-3-yl)pent-4-en-1-ol (Table 2, entry 11) Following the general procedure, the title compound was obtained as a sticky colorless oil from *trans*-α-(pyridine-3-yl)cinnamic alcohol.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* =2.0 Hz, 1 H), 8.38 (dd, *J* =4.8 Hz, 1.6 Hz, 1 H), 7.52 (ddd, *J* =7.9 Hz, 1.9 Hz, 1.9 Hz, 1 H), 7.20 (dd, *J* =7.9 Hz, 4.8 Hz, 1 H), 4.93 (s, 1 H), 4.87 (m, 1 H), 3.61-3.44 (m, 3 H), 2.18-2.09 (m, 1 H), 1.95-1.84 (m, 1 H), 1.55 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.6, 147.6, 146.6, 138.8, 135.5, 123.6, 111.6, 60.17, 46.2, 35.5, 21.1; IR (film) ν_{max} 3314, 2938, 1646, 1424, 1052, 1028, 896 cm^{-1}

General Procedure and Characterization for the Pd(II)-Catalyzed Oxyarylation of α-aryl-γ-hydroxyalkenes

General Procedure A: Reaction Optimization (Table 1, entry 1-3)

An oven-dried 10 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (1.1 mg, 0.05 equiv.), potassium carbonate (6.9 mg, 0.5 equiv.), and oxidant (y equiv.). The tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of three times). 4-methyl-3-phenylpent-4-en-1-ol (17.6 mg, 1.0 equiv.) was added to the tube followed by anhydrous toluene (1.0 mL) via syringe. The sealed tube was placed in a pre-heated 100 °C oil bath. After stirring at the same temperature for 19 h the mixture was allowed to cool to room temperature. Ether (1 mL), methanol (50 μL), dodecane (9.0 mg) and sodium borohydride (1.9 mg, 0.5 equiv.) was then added to the crude mixture and the resulting mixture was stirred for a further 5 min before filtered through a plug of silica gel and analyzed by GC.

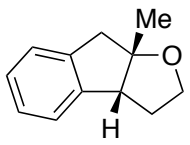
General Procedure B: Reaction Optimization (Table 1, entry 4-12)

An oven-dried 10 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (1.1 mg, 0.05 equiv.), potassium carbonate (6.9 mg, 0.5 equiv.), and ligand (x mol%, for solid ligands, entry 6-10). The tube was then briefly evacuated and backfilled with oxygen (this sequence was repeated a total of three times). Ligand (x mol%, for liquid ligands, entry 5 and 10-12) and 4-methyl-3-phenylpent-4-en-1-ol (17.6 mg, 0.10 mmol, 1.0 equiv.) was added to the tube followed by anhydrous toluene (1.0 mL) via syringe. The sealed tube was placed in a pre-heated 100 °C oil bath. After stirring at the same temperature for 19 h the mixture was allowed to cool to room temperature. Ether (1 mL), methanol (50 μL), dodecane (9.0 mg) and sodium borohydride (1.9 mg, 0.5 equiv.) was then added to the crude mixture and the resulting mixture was stirred for a further 5 min before filtered through a plug of silica gel and analyzed by GC.

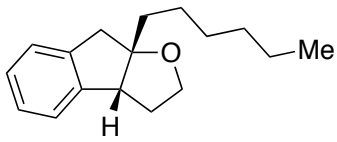
General Procedure C: Substrate Scope (Table 2)

An oven-dried 50 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (5.6 mg, 0.05 equiv.), potassium carbonate (34.5 mg, 0.5 equiv.). The tube was then briefly evacuated and backfilled with oxygen (this sequence was repeated a total of four times). Ethyl nicotinate (4.5 mg, 0.06 equiv.) and α-aryl-γ-hydroxyalkene (0.50 mmol, 1.0 equiv.) was added to the tube followed by anhydrous toluene (5.0 mL) via syringe. The sealed tube was placed in a pre-heated 100 °C oil bath. After stirring at the same temperature for 19 h the mixture was allowed to cool to room temperature. Ether (5 mL), methanol (0.25 mL), and sodium borohydride (9.5 mg, 0.5

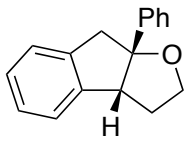
equiv.) were then added and the resulting mixture was stirred for a further 5 min at room temperature. The mixture was then filtered through a plug of silica gel and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (EtOAc/hexane).



***cis*-8a-methyl-3,3a,8,8a-tetrahydro-2H-indeno[2,1-b]furan (3a)** Following general procedure C, the title compound was synthesized from 4-methyl-3-phenylpent-4-en-1-ol (88 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford **3a** (72.7 mg, 84 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.21 (m, 4 H), 3.96 (ddd, *J* =8.1 Hz, 8.1 Hz, 5.2 Hz, 1 H), 3.60 (ddd, *J* =9.2 Hz, 8.6 Hz, 6.3 Hz, 1 H), 3.49 (d, *J* =8.1 Hz, 1 H), 3.26 (d, *J* =17.2 Hz, 1 H), 3.10 (d, *J* =17.2 Hz, 1 H), 2.45-2.35 (m, 1 H), 2.11-2.06 (m, 1 H), 1.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 142.3, 127.1, 126.9, 124.7, 124.4, 90.6, 67.3, 55.3, 46.3, 33.4, 25.7; IR (film) ν_{max} 2962, 2925, 2855, 1480, 1457, 1373, 1079, 1039, 743 cm^{-1}; Anal. Calcd. For $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.58; H, 8.20.

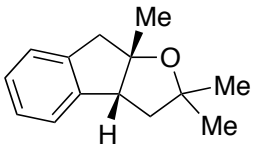


***cis*-8a-*n*-hexyl-3,3a,8,8a-tetrahydro-2H-indeno[2,1-b]furan (3b)** Following general procedure C, the title compound was synthesized from 4-methylene-3-phenyldecan-1-ol (123 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 12:1) to afford **3b** (71.8 mg, 59 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.18 (m, 4 H), 3.94 (ddd, *J* =8.1 Hz, 8.1 Hz, 2.4 Hz, 1 H), 3.55 (ddd, *J* =9.3 Hz, 9.0 Hz, 6.0 Hz, 1 H), 3.52 (d, *J* =7.5 Hz, 1 H), 3.16 (d, *J* =17.4 Hz, 1 H), 3.11 (d, *J* =17.4 Hz, 1 H), 2.38-2.28 (m, 1 H), 2.06-2.01 (m, 1 H), 1.77-1.71 (m, 2 H), 1.50-1.33 (m, 8 H), 0.93-0.90 (m, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 142.5, 127.1, 127.0, 124.7, 124.5, 93.5, 67.2, 54.0, 44.7, 39.5, 33.9, 32.0, 30.0, 24.8, 22.8, 14.2; IR (film) ν_{max} 2929, 2857, 1481, 1458, 1092, 1047, 743 cm^{-1}; Anal. Calcd. For $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.56; H, 10.07.

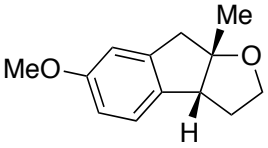


***cis*-8a-phenyl-3,3a,8,8a-tetrahydro-2H-indeno[2,1-b]furan (3c)** Following general procedure C, the title compound was synthesized from 3,4-diphenylpent-4-en-1-ol (119 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 10:1) to afford **3c** (86.5 mg, 74 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.52 (m, 2 H), 7.42-7.38 (m, 2 H), 7.32-7.26 (m, 5 H), 4.08 (ddd, *J* =8.2 Hz, 8.2 Hz, 3.9 Hz, 1 H), 4.00 (d, *J* =7.8 Hz, 1 H), 3.83 (ddd, *J* =8.1 Hz, 8.0 Hz, 7.5 Hz, 1 H), 3.54 (d, *J* =17.3 Hz, 1 H), 3.47 (d, *J* =17.3 Hz, 1 H), 2.38-2.29 (m, 1 H), 2.22-2.17 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 144.6, 142.0, 128.3, 127.4, 127.2, 126.8, 125.1, 124.8, 124.4, 94.4, 68.0, 57.8, 49.0, 32.6; IR (film) ν_{max} 3022, 2940, 2870,

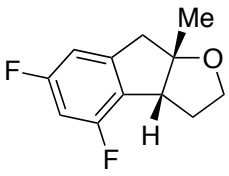
1480, 1446, 1294, 1046 cm^{-1}; Anal. Calcd. For $C_{17}H_{16}O$: C, 86.40; H, 6.82. Found: C, 86.41; H, 6.81.



***cis*-2,2,8a-trimethyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3d)** Following general procedure C, the title compound was synthesized from 2,5-dimethyl-4-phenylhex-5-en-2-ol (102 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 12:1) to afford **3d** (75.2 mg, 74 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.18 (m, 4 H), 3.53 (dd, *J* =8.3 Hz, 3.2 Hz, 1 H), 3.22 (d, *J* =16.8 Hz, 1 H), 3.01 (d, *J* =16.8 Hz, 1 H), 2.31 (dd, *J* =12.6 Hz, 8.3 Hz, 1 H), 2.09 (dd, *J* =12.6 Hz, 3.2 Hz, 1 H), 1.50 (s, 3H), 1.33 (s, 3H), 0.86 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 142.0, 127.0, 126.8, 125.1, 124.3, 91.9, 82.7, 56.7, 47.4, 45.2, 31.1, 29.8, 27.4; IR (film) ν_{max} 2967, 2929, 1481, 1458, 1372, 1156, 1068, 985, 744 cm^{-1}; Anal. Calcd. For $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.92; H, 9.16.

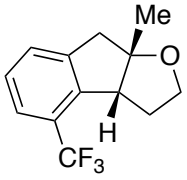


***cis*-6-methoxy-8a-methyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3e)** Following general procedure C, the title compound was synthesized from 3-(4-methoxyphenyl)-4-methylpent-4-en-1-ol (103 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford **3e** (81.2 mg, 80 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, *J* = 8.3 Hz, 1 H), 6.77 (dd, *J* =8.3 Hz, 2.4 Hz, 1 H), 6.72 (s, 1 H), 3.93 (ddd, *J* = 8.1 Hz, 8.1 Hz, 3.0 Hz, 1 H), 3.78 (s, 1 H), 3.57 (ddd, *J* = 9.0 Hz, 9.0 Hz, 6.1 Hz, 1 H), 3.39 (d, *J* =7.9 Hz, 1 H), 3.18 (d, *J* =17.2 Hz, 1 H), 3.04 (d, *J* =17.2 Hz, 1 H), 2.37-2.28 (m, 1 H), 2.03-1.96 (m, 1 H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 143.8, 137.0, 125.0, 113.3, 109.6, 91.2, 67.4, 55.4, 54.5, 46.5, 33.6, 25.8; IR (film) ν_{max} 2962, 2833, 1610, 1586, 1493, 1260, 1038, 807 cm^{-1}; Anal. Calcd. For $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.32; H, 7.93.

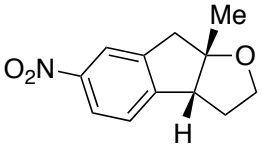


***cis*-4,6-difluoro-8a-methyl-3,3a,8,8a-tetrahydro-2H-indeno[2,1-b]furan (3f)** Following general procedure C, the title compound was synthesized from 3-(2,4- difluorophenyl)-4-methylpent-4-en-1-ol (106 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford **3f** (69.2 mg, 67 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (d, J_F = 8.2 Hz, 1 H), 6.61 (t, J_F =9.4 Hz, 1 H), 3.94 (ddd, *J* =8.2 Hz, 8.1 Hz, 3.4 Hz, 1 H), 3.61 (ddd, *J* =9.0 Hz, 8.8 Hz, 6.2 Hz, 1 H), 3.50 (d, *J* =8.2 Hz, 1 H), 3.20 (d, *J* =17.6 Hz, 1 H), 3.04 (d, *J* =17.6 Hz, 1 H), 2.36-2.26 (m, 1 H), 2.15-2.09 (m, 1 H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) [complexity observed due to C-F splitting] δ 162.8 (dd, J_F = 245 Hz, 11 Hz), 159.2 (dd, J_F = 248 Hz, 13 Hz), 146.5 (dd, J_F = 10 Hz, 7 Hz), 126.5 (dd, J_F = 16 Hz, 3 Hz), 107.6 (dd, J_F = 22 Hz, 4 Hz), 102.6 (dd, J_F = 25 Hz, 26 Hz), 91.0, 67.5, 52.2 (d, J_F

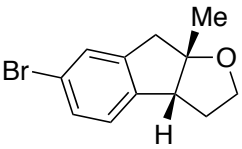
= 2 Hz), 46.8 (d, J_F = 2 Hz), 32.1, 25.7; IR (film) ν_{max} 2968, 2867, 1729, 1628, 1600, 1484, 1440, 1110, 1040, 844 cm^{-1}; Anal. Calcd. For $C_{12}H_{12}F_2O$: C, 68.56; H, 5.75. Found: C, 68.60; H, 5.79.



***cis*-8a-methyl-4-(trifluoromethyl)-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3g)** Following general procedure C, the title compound was synthesized from 4-methyl-3-(2-(trifluoromethyl) phenyl)pent-4-en-1-ol (122 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford **3g** (104.8 mg, 87 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* =7.4 Hz, 1 H), 7.33-7.26 (m, 2 H), 3.92 (ddd, *J* =8.9 Hz, 7.0 Hz, 5.7 Hz, 1 H), 3.75 (ddd, *J* =8.9 Hz, 7.1 Hz, 6.8 Hz, 1 H), 3.66 (m, 1 H), 3.26 (d, *J* =17.5 Hz, 1 H), 3.00 (d, *J* =17.5 Hz, 1 H), 2.50-2.41 (m, 1 H), 2.01-1.94 (m, 1 H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) [complexity observed due to C-F splitting] δ 143.9, 142.5 (d, J_F = 2 Hz), 128.5, 127.5, 127.0 (q, J_F = 31 Hz), 124.6 (q, J_F = 272 Hz), 124.5, (q, J_F = 5 Hz), 90.6, 67.4, 55.3, 45.6, 34.8, (d, J_F = 2 Hz), 26.2; IR (film) ν_{max} 2968, 2860, 1729, 1695, 1596, 1456, 1324, 1167, 1121, 1042, 907, 787 cm^{-1}; Anal. Calcd. For $C_{13}H_{13}F_3O$: C, 64.46; H, 5.41. Found: C, 64.41; H, 5.43.

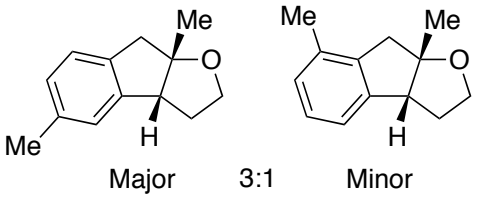


***cis*-6-nitro-8a-methyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3h)** Following general procedure C, the title compound was synthesized from 4-methyl-3-(4-nitrophenyl)pent-4-en-1-ol (111 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 3:1) to afford **3h** (76.7 mg, 70 %) as a sticky orange oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* =8.3 Hz, 2.1 Hz, 1 H), 8.01 (s, 1 H), 7.30 (d, *J* =8.3 Hz, 1 H), 3.95 (ddd, *J* =8.3 Hz, 8.2 Hz, 3.5 Hz, 1 H), 3.56 (ddd, *J* =8.9 Hz, 8.8 Hz, 6.4 Hz, 1 H), 3.50 (d, *J* =7.8 Hz, 1 H), 3.28 (d, *J* =17.5 Hz, 1 H), 3.11 (d, *J* =17.5 Hz, 1 H), 2.49-2.30 (m, 1 H), 2.09-2.06 (m, 1 H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.9, 147.8, 144.2, 125.1, 122.8, 120.0, 91.0, 67.3, 55.2, 45.8, 33.1, 25.3; IR (film) ν_{max} 2967, 2867, 1589, 1523, 1346, 1077, 1037, 814 cm^{-1}; Anal. Calcd. For $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98. Found: C, 65.99; H, 6.02.

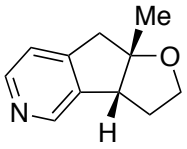


***cis*-6-bromo-8a-methyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3i)** Following a slightly modified general procedure C, the title compound was synthesized using palladium acetate(5.6 mg, 0.05 equiv.), ethyl nicotinate(23 mg, 0.3 equiv.), copper(II) chloride(3.4 mg, 0.05 equiv.), potassium carbonate(34.5 mg, 0.5 equiv.) and 3-(4-bromophenyl)-4-methylpent-4-en-1-ol (127 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford **3i** (62.6 mg, 50 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.29 (m, 2 H),

7.03 (d, *J* =7.9 Hz, 1 H), 3.92 (ddd, *J* =8.4 Hz, 8.0 Hz, 3.1 Hz, 1 H), 3.55 (ddd, *J* =9.0 Hz, 8.9 Hz, 6.2 Hz, 1 H), 3.38 (d, *J* =8.2 Hz, 1 H), 3.18 (d, *J* =17.4 Hz, 1 H), 3.03 (d, *J* =17.5 Hz, 1 H), 2.40-2.31 (m, 1 H), 2.03-1.98 (m, 1 H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 144.1, 130.1, 127.9, 126.0, 120.9, 90.9, 67.4, 54.9, 46.1, 33.3, 25.6; IR (film) ν_{max} 2964, 2864, 1739, 1595, 1473, 1374, 1202, 1080, 1037, 867 cm^{-1}; Anal. Calcd. For $C_{12}H_{13}BrO$: C, 56.94; H, 5.18. Found: C, 56.76; H, 5.02.



***cis*-5,8a-dimethyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3j) and *cis*-7,8a-dimethyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3j')** Following general procedure C, the title compounds was synthesized from 4-methyl-3-(*m*-tolyl)pent-4-en-1-ol (95.1 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford an inseparable 3:1 mixture of **3j** and **3j'** (65.1 mg, 69 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.01 (m, 3 H), 3.94 (ddd, *J* =8.2 Hz, 7.9 Hz, 3.0 Hz, 1 H), 3.59 (ddd, *J* =9.0 Hz, 8.8 Hz, 2.5 Hz, 1 H), 3.48 (**3j'**, d, *J* =8.8 Hz) and 3.43 (**3j**, d, *J* =8.2 Hz), 1 H, 3.18 (**3j**, d, *J* =17.0 Hz) and 3.16 (**3j'**, d, *J* =17.3 Hz), 1 H, 3.03 (**3j**, d, *J* =17.0 Hz) and 2.98 (**3j'**, d, *J* =17.3 Hz), 1 H, 2.38-2.34 (m, 1 H), 2.35 (**3j**, s) and 2.25 (**3j'**, s), 3 H, 2.07-2.03 (m, 1 H), 1.51 (**3j'**, s) and 1.49 (**3j**, s), 3 H; ^{13}C NMR (100 MHz, $CDCl_3$) **3j**: δ 145.2, 139.3, 136.5, 128.0, 125.1, 124.5, 91.0 , 67.3, 55.3, 46.0, 33.5, 25.8, 21.4; **3j'**: δ 144.8, 134.1, 127.9, 127.3, 121.8, 90.3, 67.3, 55.6, 453, 33.6, 25.9, 19.2; IR (film) ν_{max} 2964, 2925, 1493, 1447, 1373, 1080, 1039, 799 cm^{-1}; Anal. Calcd. For $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 83.08; H, 8.66.



***cis*-8a-methyl-3,3a,8,8a-tetrahydro-2*H*-furo[2',3':4,5]cyclopenta[1,2-*c*]pyridine (3k)** Following general procedure C, the title compound was synthesized from 4-methyl-3-(pyridin-3-yl)pent-4-en-1-ol (88 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc:triethylamine = 1:9:0.5) to afford **3l** (63.1 mg, 73 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1 H), 8.36 (d, *J* =5.0 Hz, 1 H), 7.07 (d, *J* =4.8 Hz, 1 H), 3.91 (ddd, *J* =8.2 Hz, 8.2 Hz, 3.1 Hz, 1 H), 3.52 (ddd, *J* =9.0 Hz, 8.8 Hz, 6.4 Hz, 1 H), 3.47 (d, *J* =8.8 Hz, 1 H), 3.17 (d, *J* =18.0 Hz, 1 H), 3.00 (d, *J* =17.9 Hz, 1 H), 2.42-2.33 (m, 1 H), 2.07-2.02 (m, 1 H), 1.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 148.1, 146.4, 141.1, 120.1, 90.6, 67.4, 53.3, 46.0, 33.1, 25.3; IR (film) ν_{max} 3398, 2966, 2867, 1600, 1569, 1485, 1419, 1210, 1081, 1033, 805 cm^{-1}

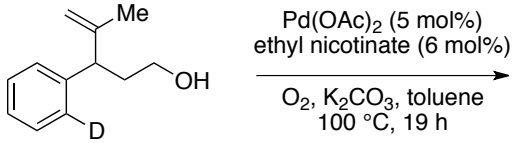
Determination of the Kinetic Isotope Effect (Figure 1)

Intramolecular Case:

Synthesis of 4-methyl-3-(2-deuteriophenyl)pent-4-en-1-ol

Following the general procedure for the synthesis of α-aryl-γ-hydroxyalkene substrates, the title compound was obtained as a sticky colorless oil from 2-deuteriobenzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.19 (m, 4 H), 4.95 (s, 1 H), 4.87 (m, 1 H), 3.64-3.54 (m, 2 H), 3.42 (dd, *J* =7.7 Hz, 7.6 Hz, 1 H), 2.18-2.09 (m, 1 H), 2.02-1.93 (m, 1 H), 1.59 (s, 3 H), 1.59 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 143.0, 128.5, 128.4, 127.9, 127.6 (t, *J* = 24 Hz), 126.5, 110.6, 61.4, 49.1, 35.8, 21.1; IR (film) ν_{max} 3346, 3046, 2941, 1645, 1472, 1442, 1374, 1049, 893 cm^{-1}; D>95% as judged by ^{1}H NMR and GC-MS.

Determination of intramolecular KIE



2-*d*-2a **2-*d*-3a** **3a**

2-*d*-3a:3a	
1st	1.94
2nd	2.03
3rd	2.23
4th	1.94
Ave	2.0±0.1

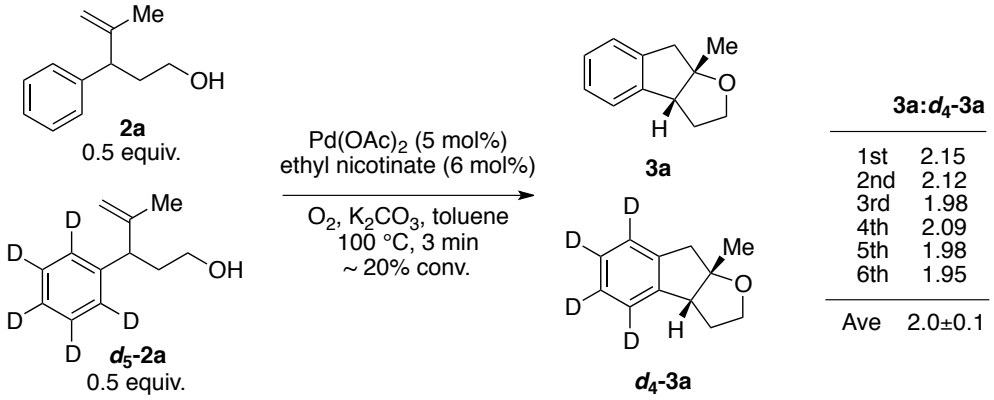
An oven-dried 10 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (1.1 mg, 0.05 equiv.), potassium carbonate (6.9 mg, 0.5 equiv.), The tube was then briefly evacuate and backfilled with oxygen (this sequence was repeated a total three times). Ethyl nicotinate (0.9 mg, 0.06 equiv.) and 4-methyl-3-(2-deuteriophenyl)pent-4-en-1-ol (17.7 mg, 0.10 mmol, 1.0 equiv.) was added to the tube followed by anhydrous toluene (1.0 mL) via syringe. The sealed tube was placed in a pre-heated 100 °C oil bath. After stirring at the same temperature for 19 h the mixture was allowed to cool to room temperature. Ether (1 mL), methanol (50 μL), dodecane (9.0 mg) and sodium borohydride (1.9 mg, 0.5 equiv.) was then added to the crude mixture and the resulting mixture was stirred for a further 5 min before filtered through a plug of silica gel and analyzed by GC-MS. The product ratio was determined by comparing the average abundance of the [M], [M+1] and [M+2] peaks (assuming **3a** and **2-*d*-3a** have similar ionization pattern). This experiment was repeated 4 times and the average ratio of **2-*d*-3a** to **3a** was determined to be 2.0±0.1.

Intermolecular Case:

Synthesis of 4-methyl-3-(*d*$_5$-phenyl)pent-4-en-1-ol

Following the general procedure for the synthesis of α-aryl-γ-hydroxyalkene substrates, the title compound was obtained as a sticky colorless oil from 2,3,4,5,6-*d*$_5$-benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.96 (s, 1 H), 4.87 (m, 1 H), 3.58 (m, 2 H), 3.42 (dd, *J* =7.8 Hz, 7.6 Hz, 1 H), 2.18-2.09 (m, 1 H), 2.02-1.93 (m, 1 H), 1.70 (br, 1 H), 1.59 (s, 3

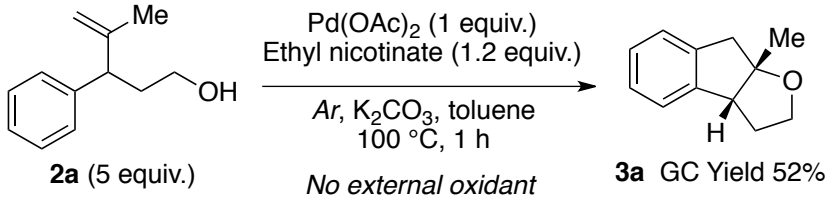
H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.9, 142.9, 127.9 (t, J = 24 Hz), 127.5 (t, J = 24 Hz), 126.0 (t, J = 24 Hz), 110.6, 61.3, 49.0, 35.8, 21.1; IR (film) ν_{max} 3345, 3082, 2939, 1645, 1568, 1436, 1374, 1038, 892 cm^{-1}; D>95% as judged by ^{1}H NMR and GC-MS.



Determination of intermolecular KIE

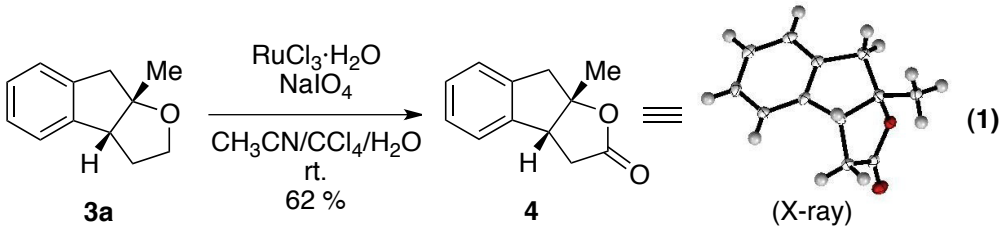
An oven-dried 50 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (5.6 mg, 0.05 equiv.), potassium carbonate (34.5 mg, 0.5 equiv.), The tube was then briefly evacuate and backfilled with oxygen (this sequence was repeated a total of four times). Ethyl nicotinate (4.5 mg, 0.06 equiv.), 4-methyl-3-phenylpent-4-en-1-ol (44.1 mg, 0.25 mmol, 0.50 equiv.), 4-methyl-3-(pentadeuteriophenyl)pent-4-en-1-ol (45.3 mg, 0.25 mmol, 0.50 equiv.) was added to the tube followed by anhydrous toluene (5.0 mL) via syringe. The sealed tube was placed in a pre-heated 100 °C oil bath. After stirring at the same temperature for 3 min the crude mixture was cooled to room temperature and diluted by ether (3 mL). The crude material was filtered through a plug of silica gel and analyzed by ^{1}H NMR and GC-MS. The reaction went to ~20% conversion as judged by ^{1}H NMR. The product ratio was determined by comparing the average abundance of the [M] and [M+4] peaks (assuming **3a** and ***d*$_4$-3a** have similar ionization pattern). This experiment was repeated 6 times and the average ratio of **3a** to ***d*$_4$-3a** was determined to be 2.0±0.1.

Oxyarylation in the Absence of External Oxidant (Scheme 2)



An oven-dried 25 mL re-sealable screw-cap test tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (22.4 mg, 0.1 mmol, 1.0 equiv.), potassium carbonate (34.5 mg, 2.5 equiv.). The tube was then briefly evacuated and backfilled with argon four times. Ethyl nicotinate (18.7 mg, 1.2 equiv.) and **2a** (0.50 mmol, 5.0 equiv.) was added to the tube followed by 5.0 mL anhydrous toluene via syringe. The sealed tube was placed in a pre-heated 100 °C oil bath. After stirring at the same temperature for 1 h the mixture was allowed to cool to room temperature. Ether (5 mL), methanol (0.25 mL), and sodium borohydride (9.5 mg, 0.5 equiv.) were then added and the resulting mixture was stirred for a further 5 min at room temperature. The resulting mixture was filtered through a plug of silica gel and analyzed by GC. The GC Yield based on palladium was determined to be 52%.

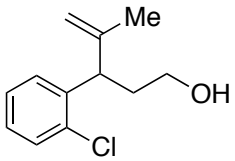
Derivatization of the Oxyarylation Adduct (eq. 1)



***cis*-8a-methyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan-2-one (4)** To a 50 mL round-bottom flask equipped with a Teflon-coated magnetic stir bar was added **3a** (44 mg, 0.25 mmol, 1.0 equiv.), sodium meta-periodate (270 mg, 5 equiv.), acetonitrile (3 mL), carbon tetrachloride (3 mL) and water (4 mL). To the resulting mixture was carefully added ruthenium(III) chloride monohydrate (26 mg, 0.5 equiv.). The mixture was stirred at room temperature for 24 h and diluted by ethyl acetate (20 mL) and saturated aqueous sodium chloride solution (10 mL). The aqueous layer was separated and extracted with ethyl acetate (3×10 mL), and the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (EtOAc/hexane = 1:4) and lactone **4** (29 mg, 62 %) was obtained as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.16 (m, 4 H), 3.67 (d, J =8.9 Hz, 1 H), 3.42 (d, J =17.4 Hz, 1 H), 3.17 (d, J =17.4 Hz, 1 H), 3.09 (dd, J =17.8 Hz, 8.9 Hz, 1 H), 2.73 (dd, J =17.8 Hz, 0.9 Hz, 1 H), 1.66 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 142.7, 140.3, 128.3, 127.7, 125.2, 124.8, 93.9, 50.6, 44.9, 35.5, 24.6; IR (film) ν_{max} 2972, 2929, 1772, 1483, 1459, 1419, 1254, 1170, 1066, 945 cm^{-1}. Anal. Calcd. For $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.40; H, 6.50. M.p. 89-90 °C .The relative stereochemistry was assigned by single crystal X-ray diffraction. (see cif file attached at the end of SI)

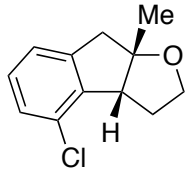
Divergent Pd(II)-catalysis and Pd(0)-catalysis (Scheme 3)

Synthesis and Characterization of Substrate 2l:



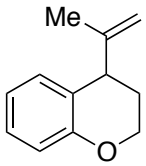
3-(2-chlorophenyl)-4-methylpent-4-en-1-ol (2l) Following the general procedure described in the substrate preparation section, the title compound was obtained as a sticky colorless oil from *trans*-α-(2-chlorophenyl)cinnamic alcohol. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* =7.8 Hz, 1.1 Hz, 1 H), 7.26-7.21 (m, 2 H), 7.16-7.12 (m, 1 H), 4.95 (s, 1 H), 4.93 (m, 1 H), 3.98 (dd, *J* =7.6 Hz, 7.6 Hz, 1 H), 3.58 (m, 2 H), 2.21-2.13 (m, 1 H), 1.95-1.87 (m, 1 H), 1.62 (br, 1 H), 1.61 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.6, 140.6, 134.7, 129.6, 128.4, 127.7, 127.2, 111.3, 61.1, 44.1, 36.5, 21.9; IR (film) ν_{max} 3335, 2942, 2879, 1646, 1473, 1440, 1035, 895 cm^{-1}; Anal. Calcd. For $C_{12}H_{15}ClO$: C, 68.40; H, 7.18. Found: C, 68.28; H, 7.19.

Synthesis of 3l: Oxidative Oxyarylation:



***cis*-4-chloro-8a-methyl-3,3a,8,8a-tetrahydro-2*H*-indeno[2,1-*b*]furan (3l)** Following general procedure C used for table 2, the title compound was synthesized from 3-(2-chlorophenyl)-4-methylpent-4-en-1-ol (**2l**) (105 mg, 0.50 mmol, 1.0 equiv.). The product was purified by silica gel flash column chromatography (hexane:EtOAc = 8:1) to afford **3i** (81.2 mg, 78 %) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18-7.10 (m, 2 H), 7.04 (d, *J* =7.3 Hz, 1 H), 3.92 (ddd, *J* =8.6 Hz, 8.0 Hz, 4.3 Hz, 1 H), 3.65 (ddd, *J* =8.6 Hz, 6.4 Hz, 1 H), 3.52 (dd, *J* =9.0 Hz, 3.2 Hz, 1 H), 3.26 (d, *J* =17.5 Hz, 1 H), 3.06 (d, *J* =17.5 Hz, 1 H), 2.44-2.35 (m, 1 H), 2.19-2.12 (m, 1 H), 1.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.3, 142.5, 131.1, 128.7, 127.2, 123.1, 89.8, 67.2, 55.5, 46.9, 32.7, 26.1; IR (film) νmax 2968, 2859, 1559, 1454, 1374, 1128, 1078, 1038 cm^{-1}; Anal. Calcd. For $C_{12}H_{13}ClO$: C, 69.07; H, 6.28. Found: C, 69.37; H, 6.45.

Synthesis of 5: C–O Coupling



4-(prop-1-en-2-yl)chroman (5) An oven-dried 25 mL re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (1.1 mg, 0.02 equiv.), 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos) (4.8 mg, 0.04 equiv.), potassium carbonate (86 mg, 2.5 equiv.). The tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of four times). **2l** (52.5 mg, 0.25 mmol, 1.0 equiv.) was added to the tube followed by anhydrous toluene (2.0 mL) via syringe. The sealed tube was placed in a pre-heated 90 °C oil bath. After stirring at the same temperature for 20 h the mixture was allowed to cool to room temperature. The mixture was then diluted with 2 mL ether and washed with 2 mL saturated aqueous sodium chloride solution. The aqueous layer was separated and extracted with ether (3×2 mL), and the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. The

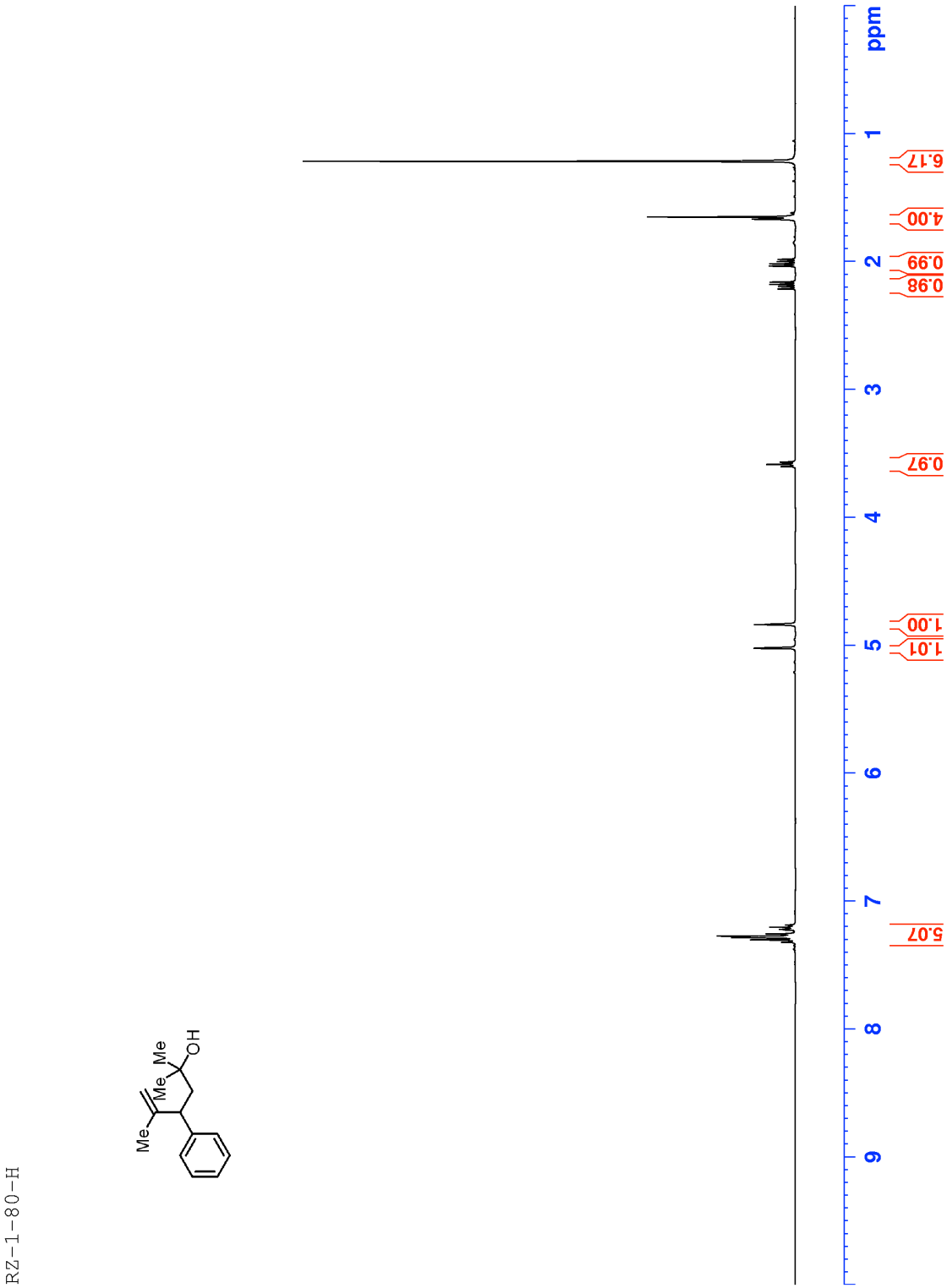
residue was purified by silica gel flash column chromatography (EtOAc/hexane = 1:12) to afford **5** as a colorless oil (38.4 mg, 88%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14-7.09 (m, 1 H), 7.05 (d, *J* =7.5 Hz, 1 H), 6.87-6.81 (m, 1 H), 5.01 (m, 1 H), 4.72 (m, 1 H), 4.24 (m, 1 H), 4.14 (m, 1 H), 3.58 (dd, *J* =6.7 Hz, 6.7 Hz, 1 H), 2.03 (m, 2 H), 1.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 147.5, 130.0, 127.8, 123.7, 120.3, 116.8, 115.0, 64.2, 43.0, 27.0, 19.7; IR (film) ν_{max} 3073, 2953, 2873, 1643, 1606, 1581, 1487, 1451, 1308, 1268, 1247, 1220, 1115, 1065, 901 cm^{-1}; Anal. Calcd. For $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.80; H, 8.31.

Synthesis of 3a: non-oxidative Oxyarylation:

An oven-dried 25 mL re-sealable test tube equipped with a Teflon-coated magnetic stir bar was charged with palladium acetate (1.1 mg, 0.02 equiv.), 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl (XPhos) (4.8 mg, 0.04 equiv.), sodium *tert*-butoxide (60 mg, 2.5 equiv.). The tube was then briefly evacuated and backfilled with argon (this sequence was repeated a total of four times). **2l** (52.5 mg, 0.25 mmol, 1.0 equiv.) was added to the tube followed by anhydrous toluene (2.0 mL) via syringe. The sealed tube was placed in a pre-heated 90 °C oil bath. After stirring at the same temperature for 8 h the mixture was allowed to cool to room temperature. Ether (2 mL), methanol (0.1 mL), and sodium borohydride (4.8 mg, 0.5 equiv.) were then added and the resulting mixture was stirred for a further 5 min at room temperature. The aqueous layer was separated and extracted with ether (3×2 mL), and the combined organic layers were dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (EtOAc/hexane = 1:8) to afford **3a** as a colorless oil (21.6 mg, 50%).

Experimental References

1. R. Correia, P. DeShong, *J. Org. Chem.* **2001,** *66,* 7159.
2. A. V. Malkov, L. Czemerys, D. A. Malyshev, *J. Org. Chem.*, **2009**, *74*, 3350
3. H. Ito, T. Nagahara, K. Ishihara, S. Saito, H. Yamamoto, *Angew. Chem. Int. Ed*. **2004**, *43*, 994.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7
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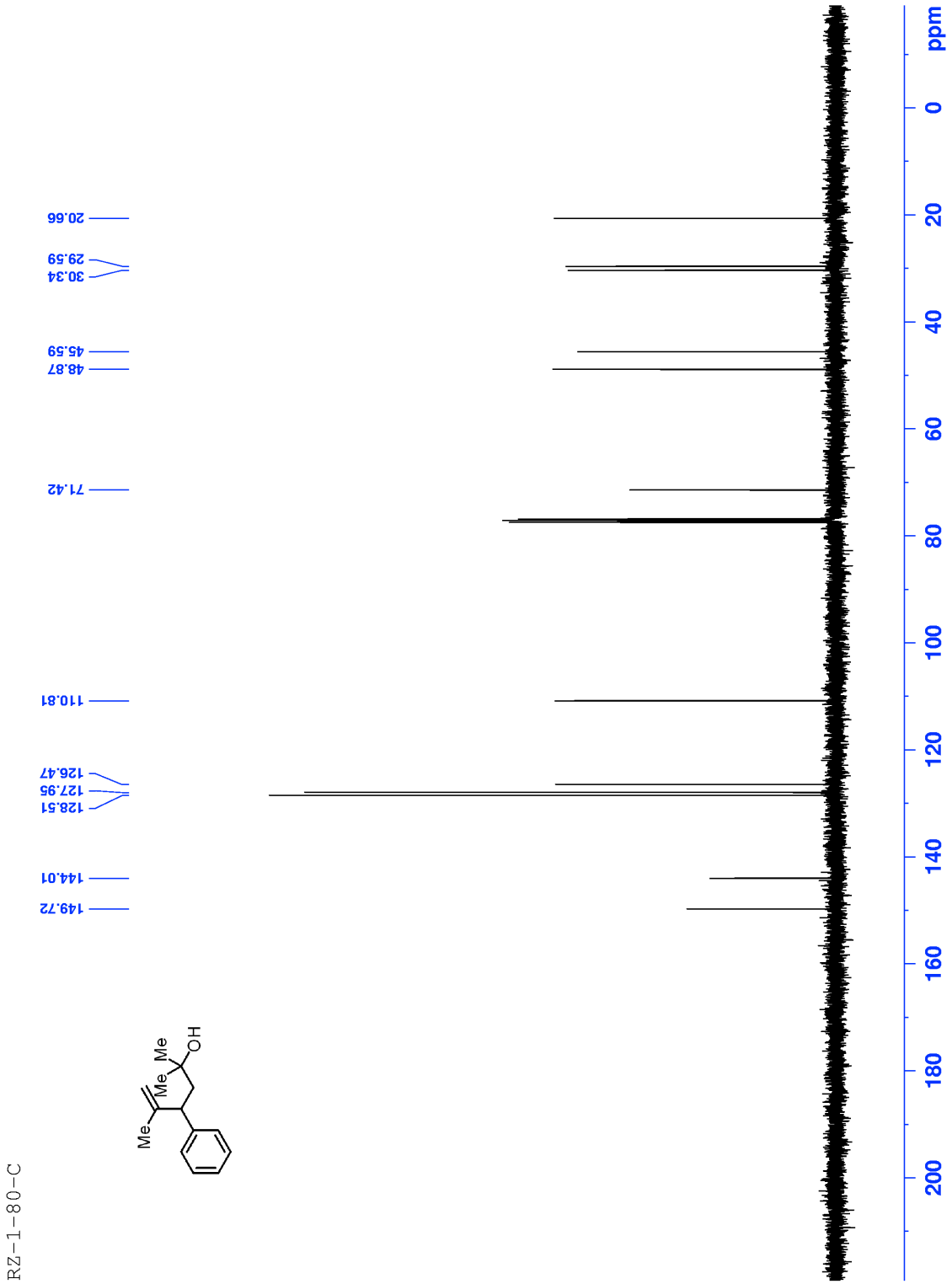
1.01
5.07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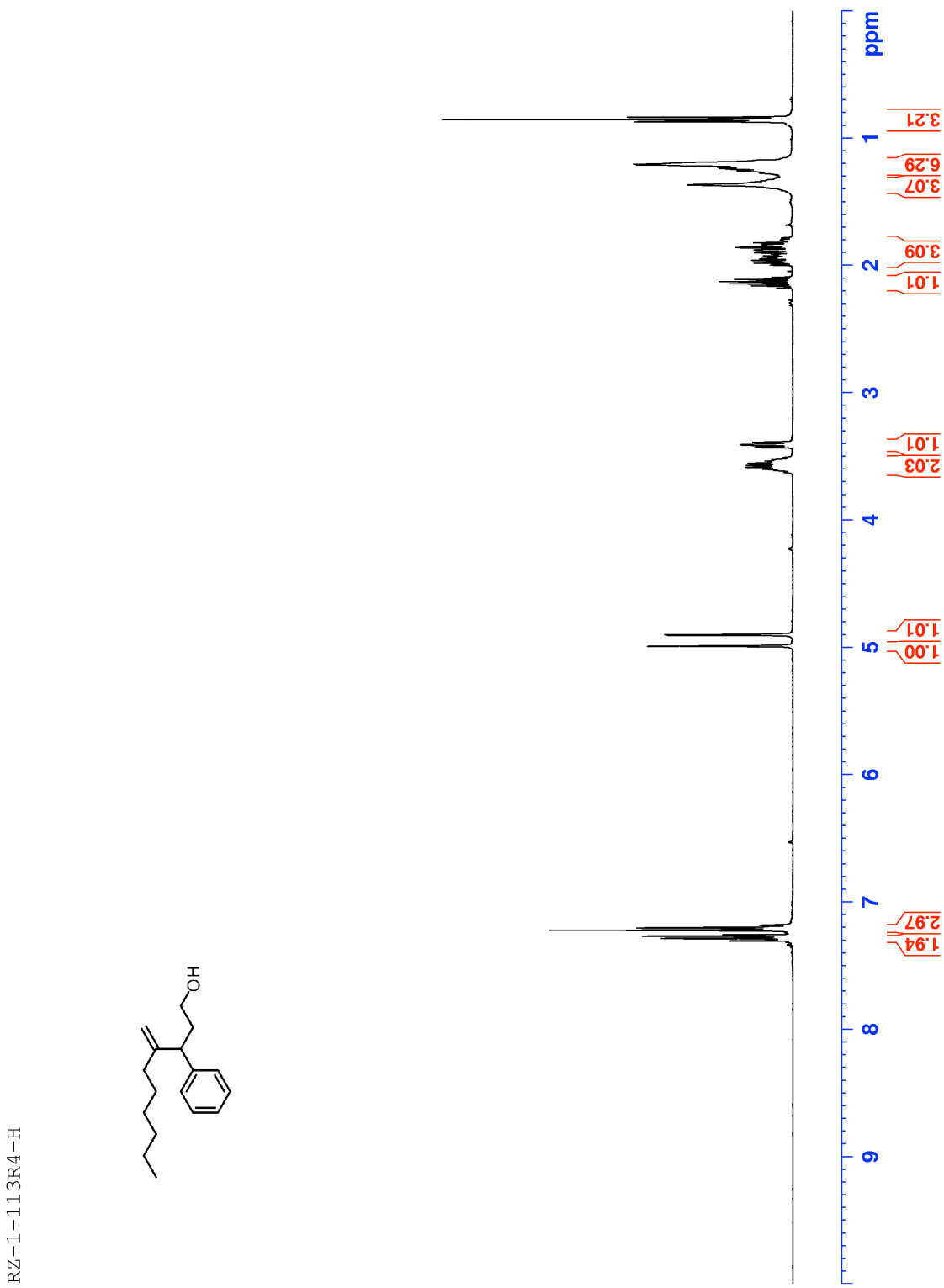
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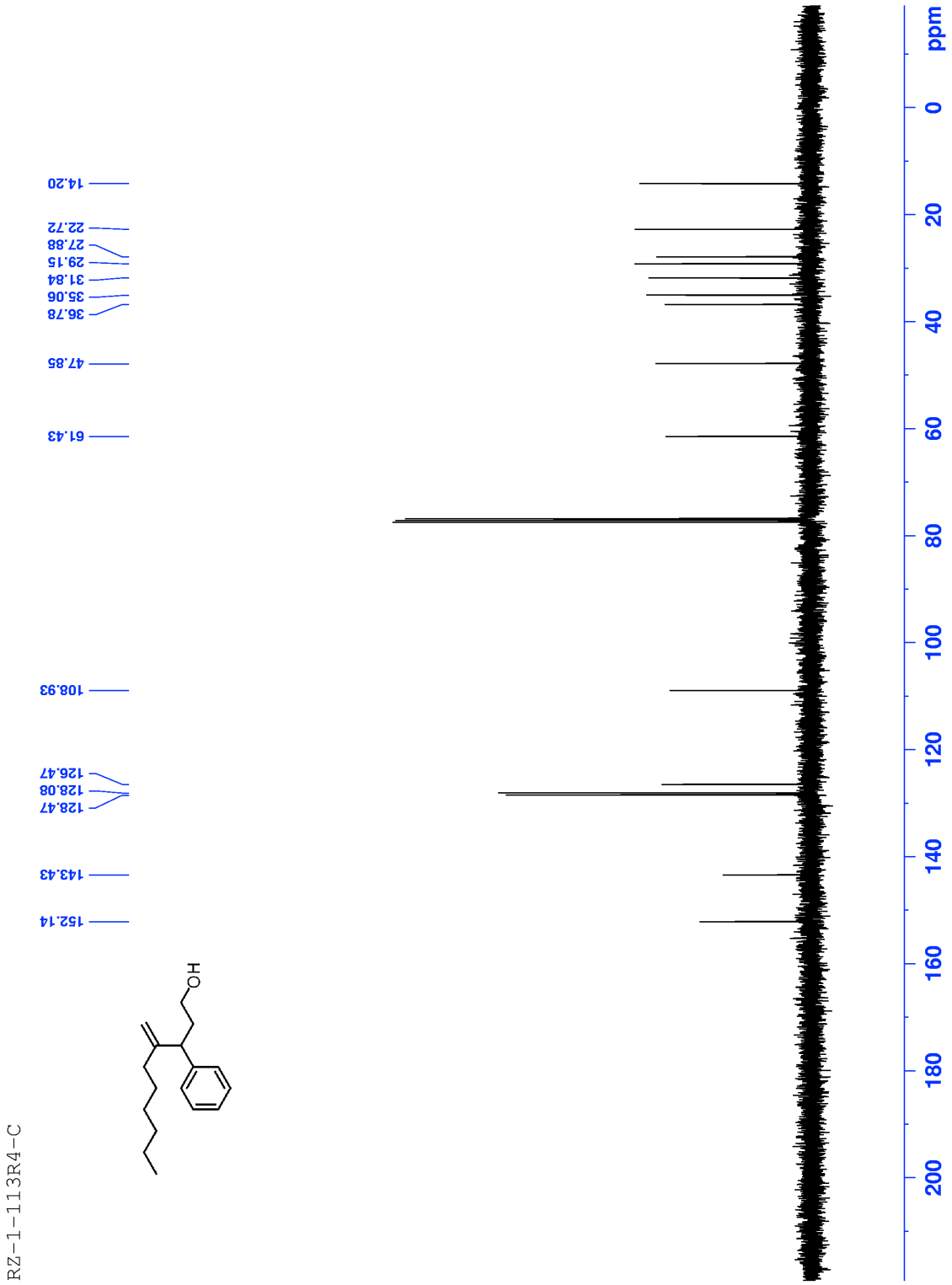
2.97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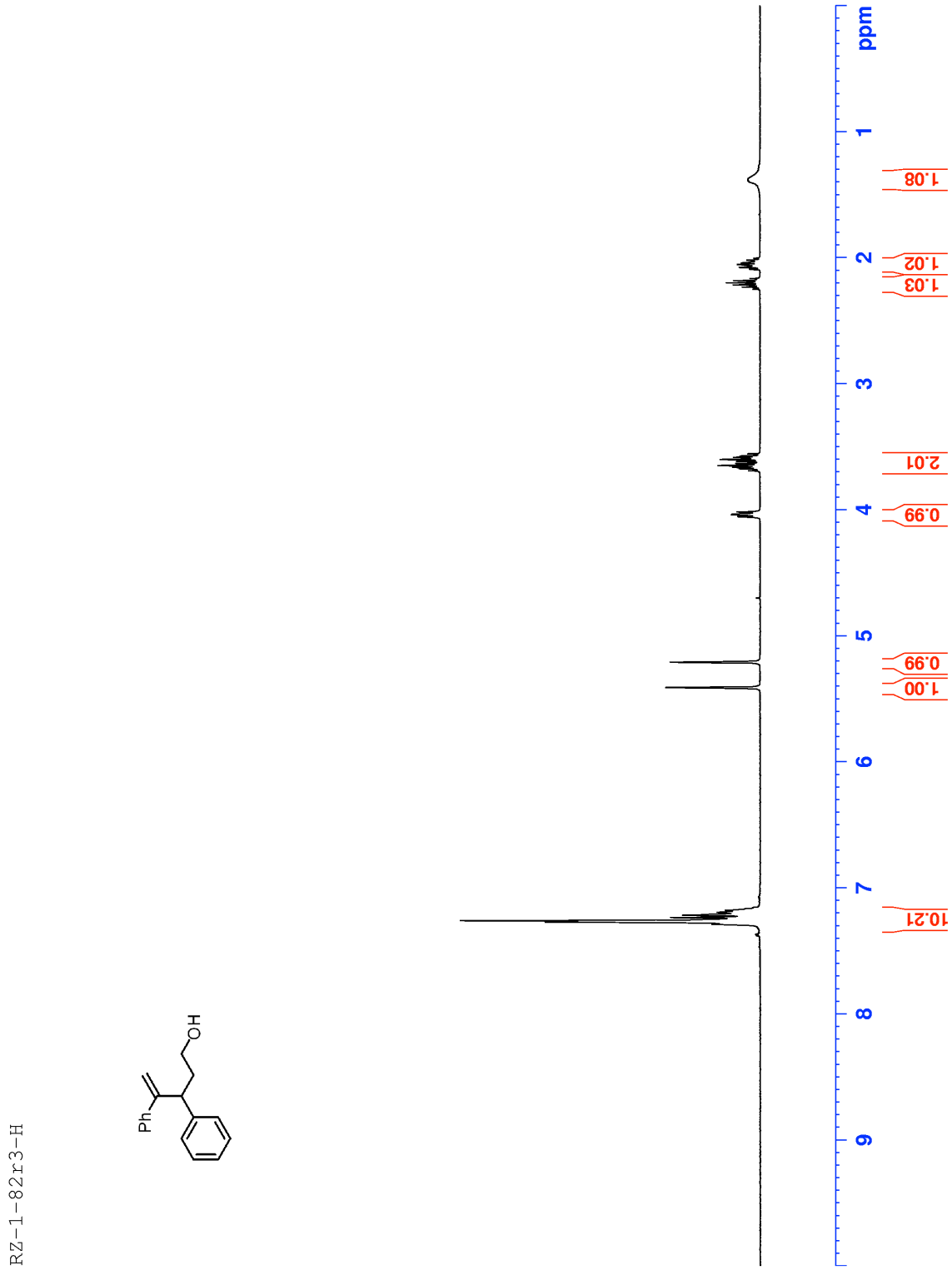
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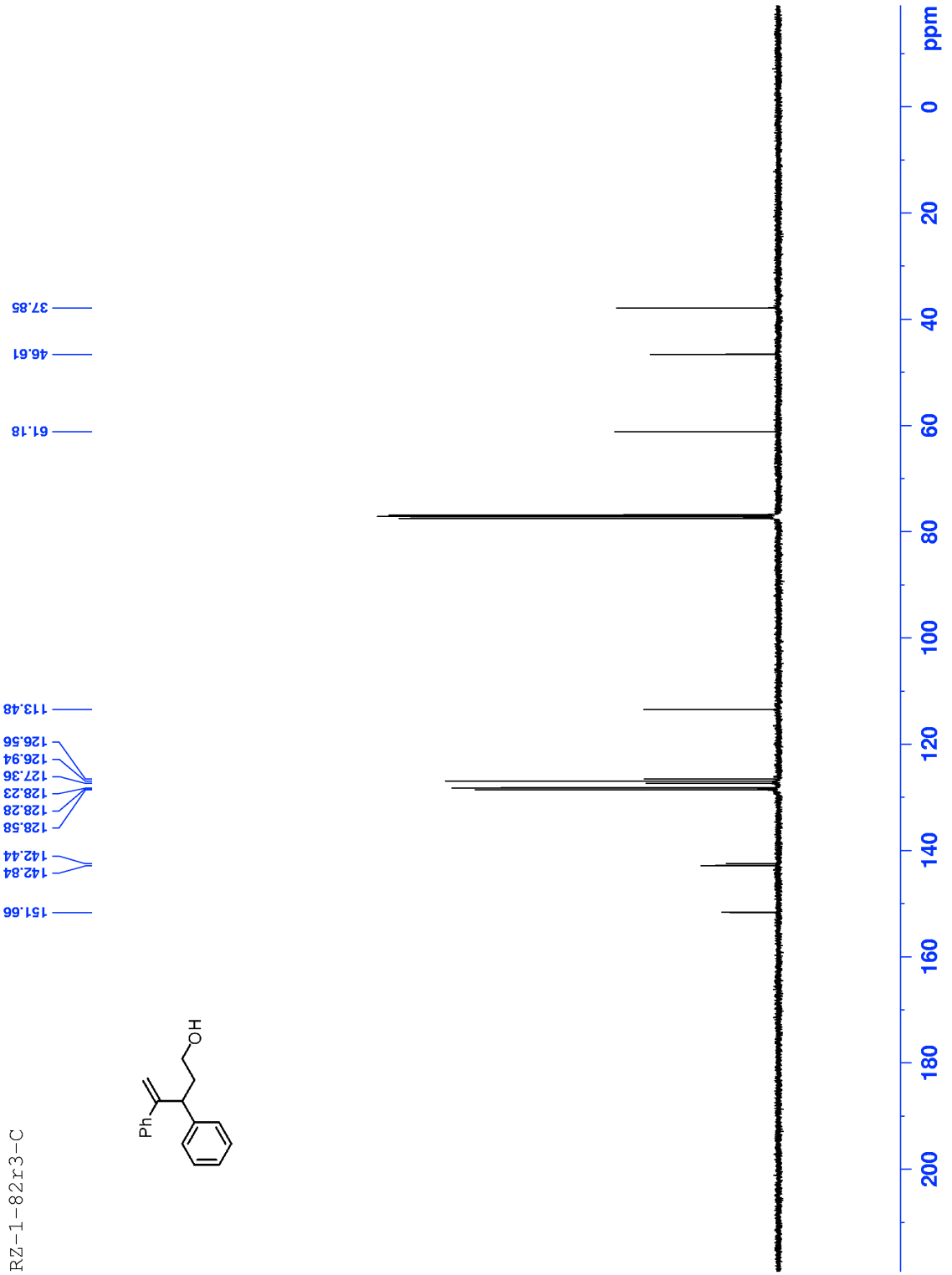
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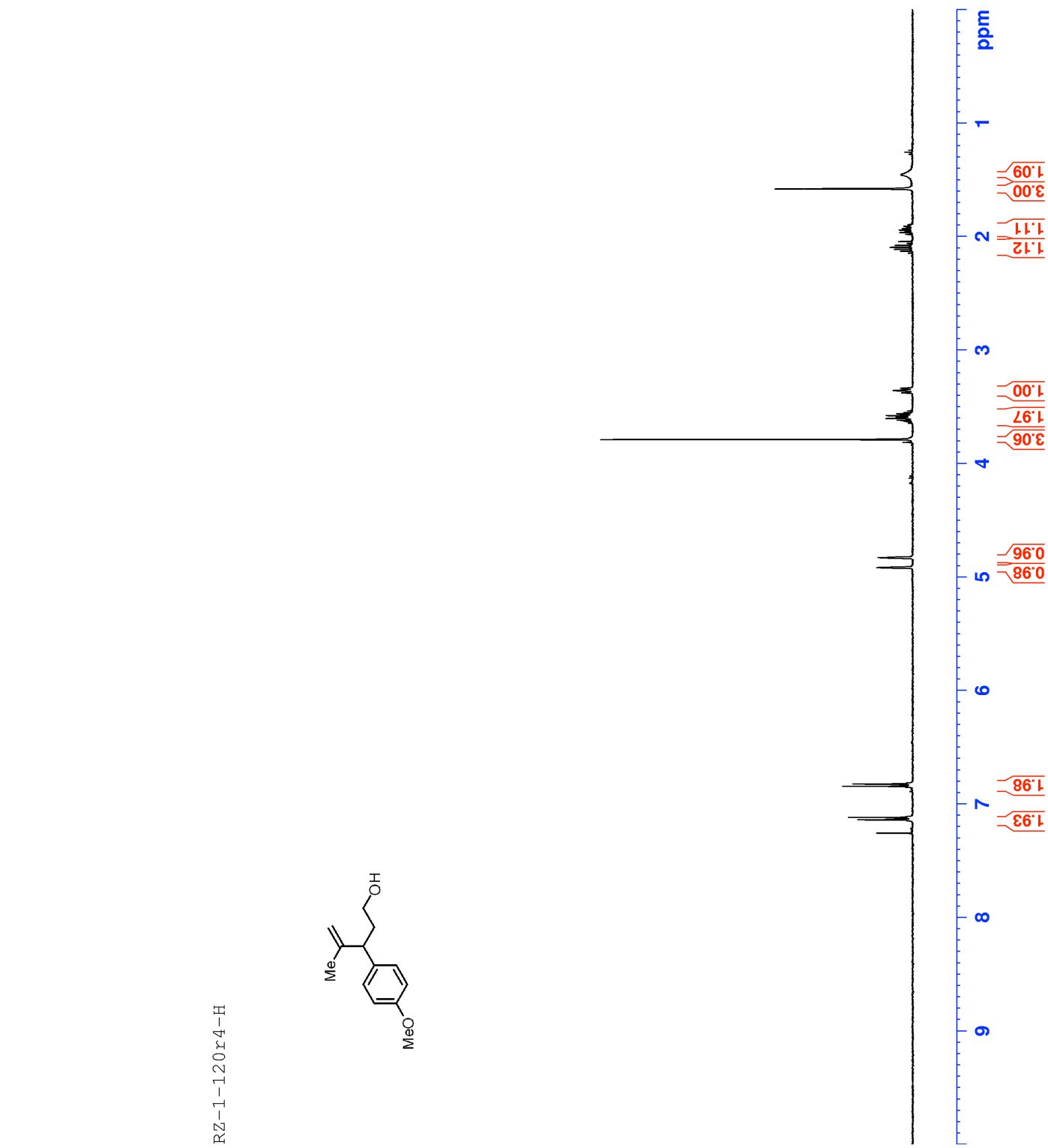
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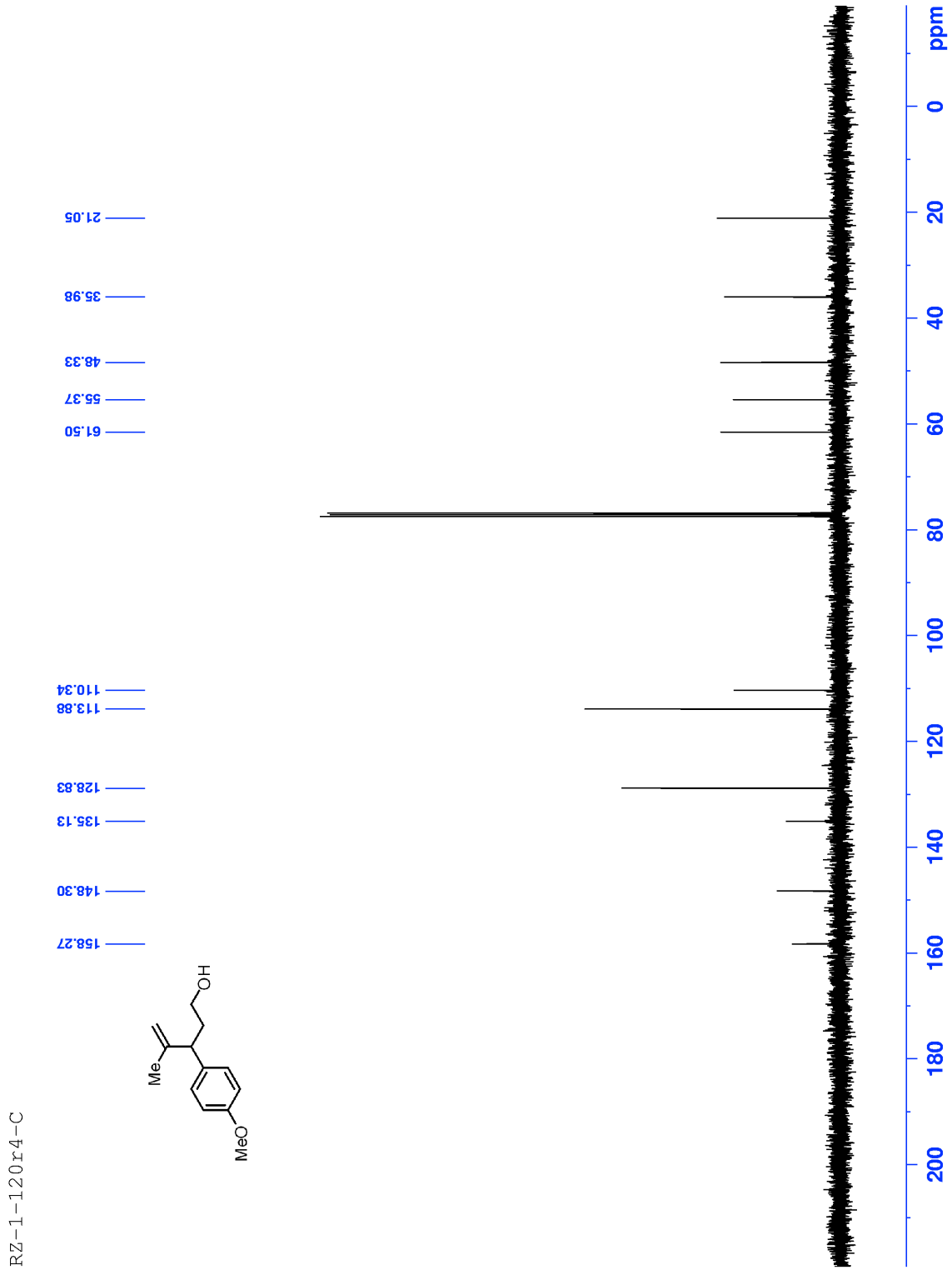
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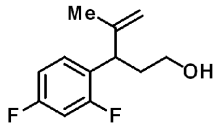

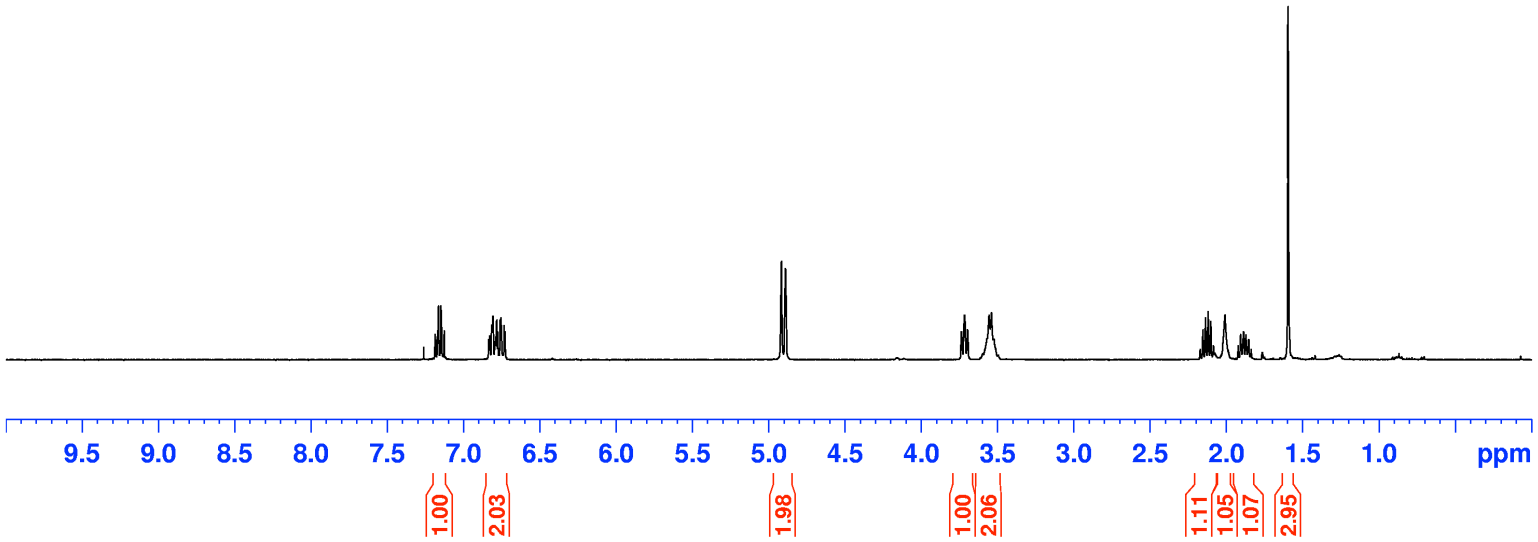

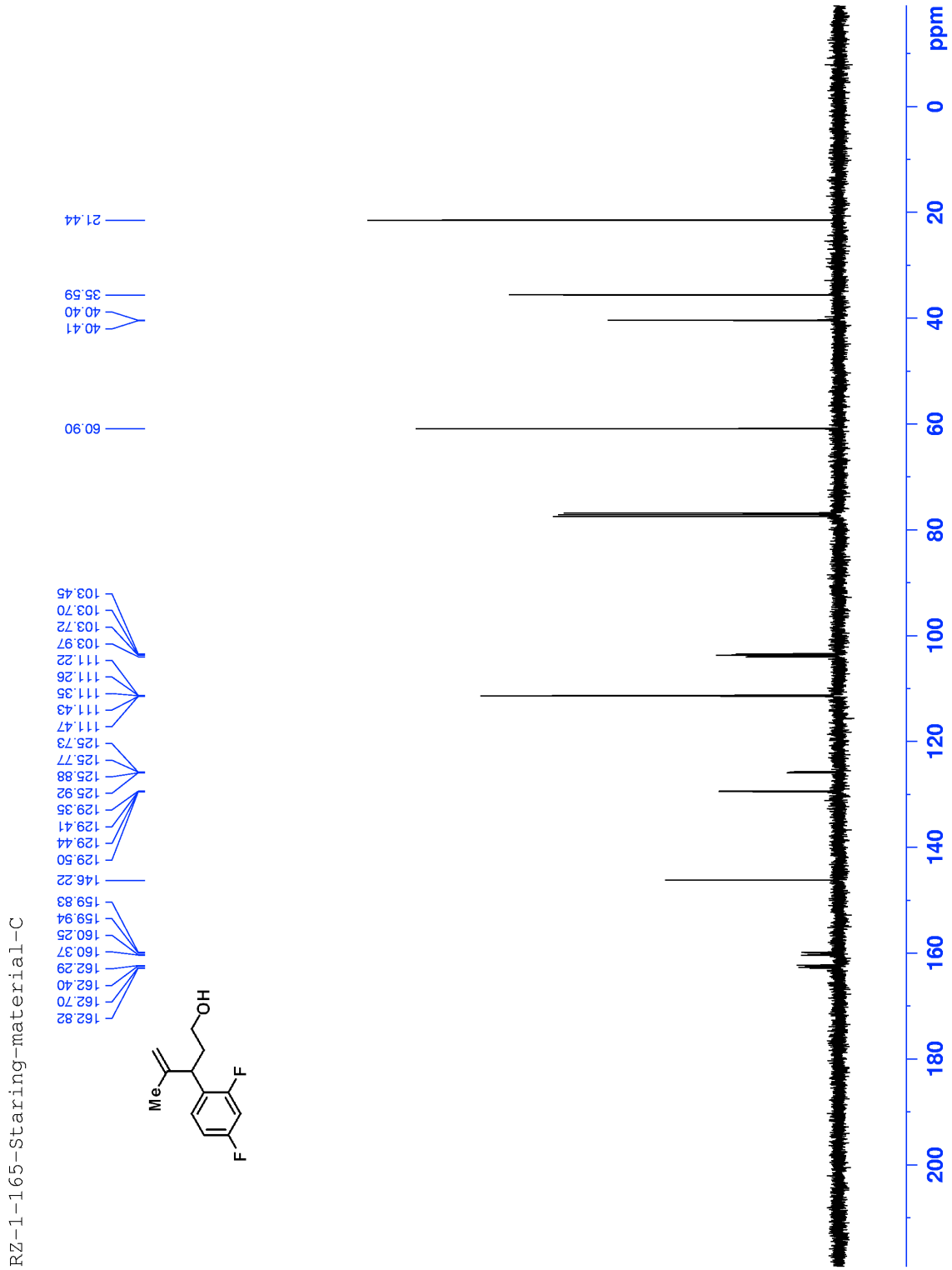
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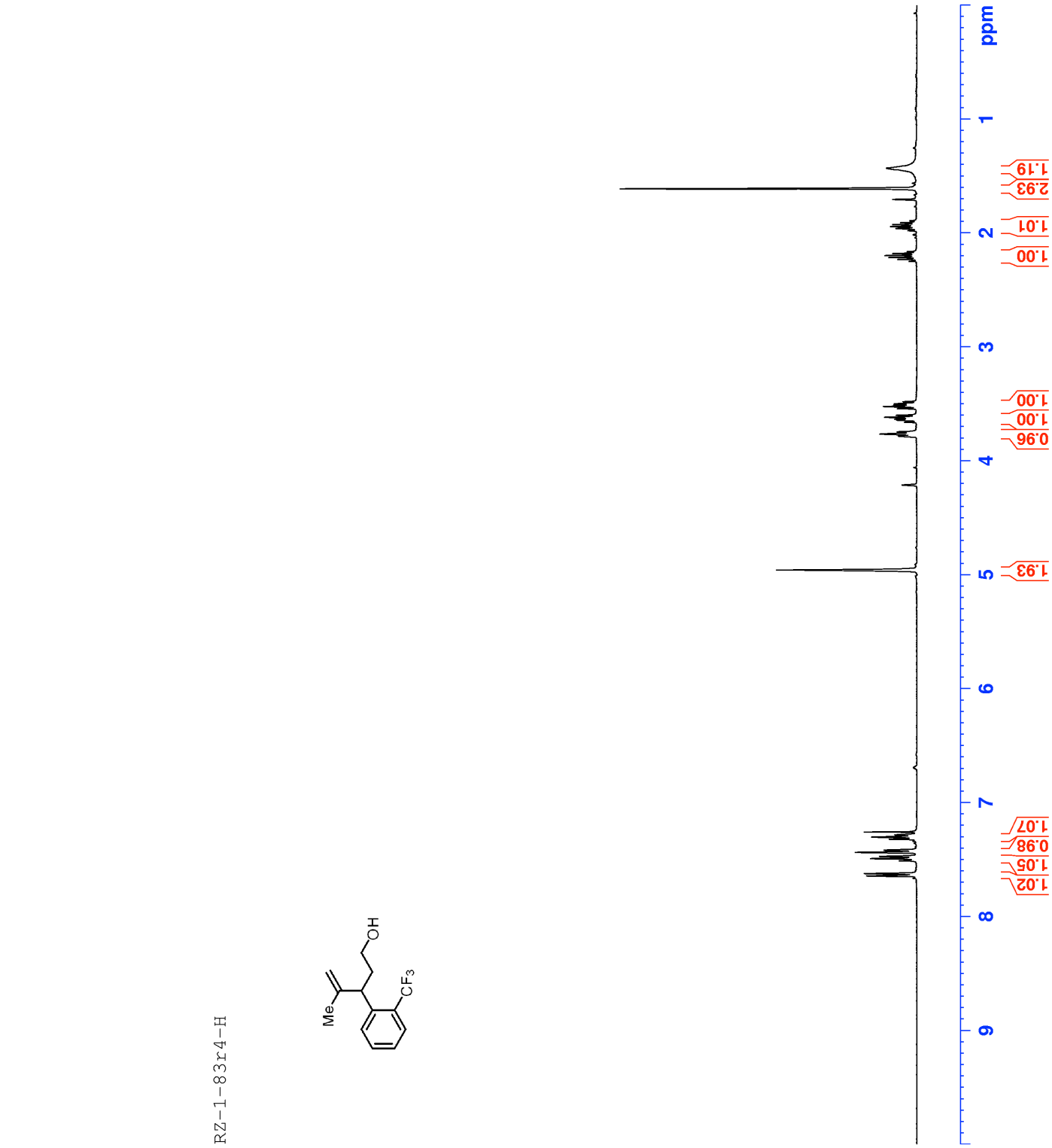
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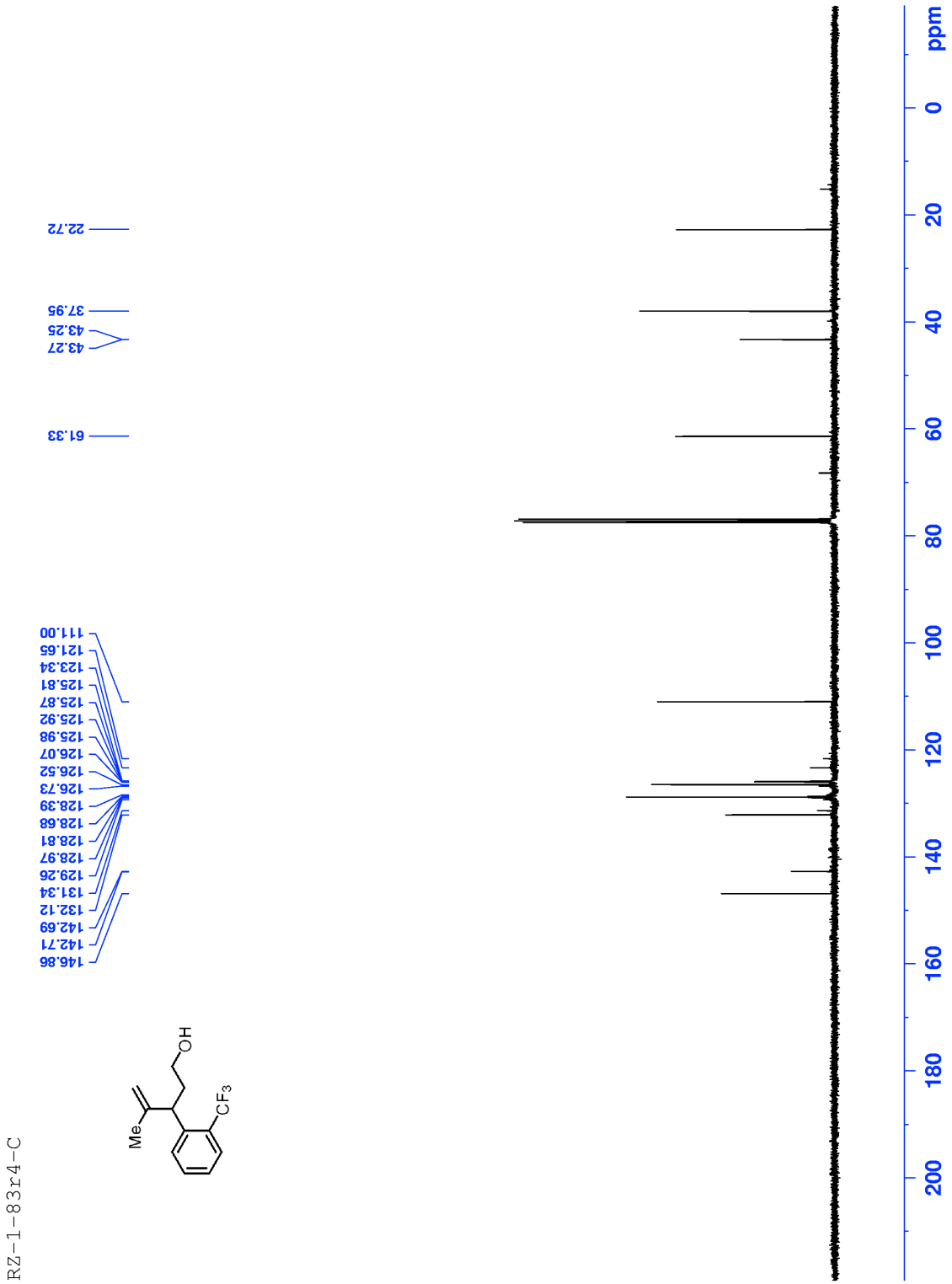
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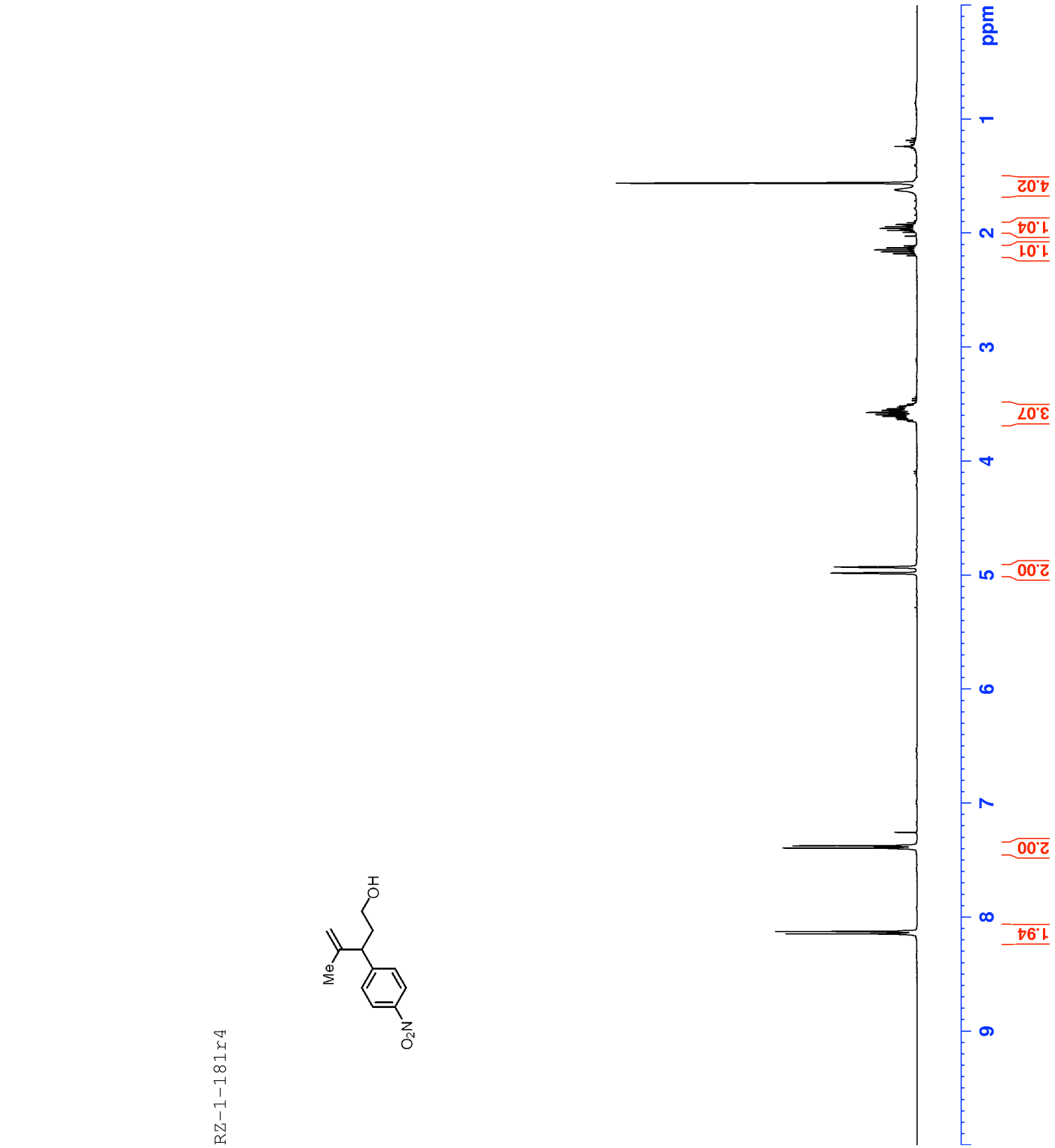
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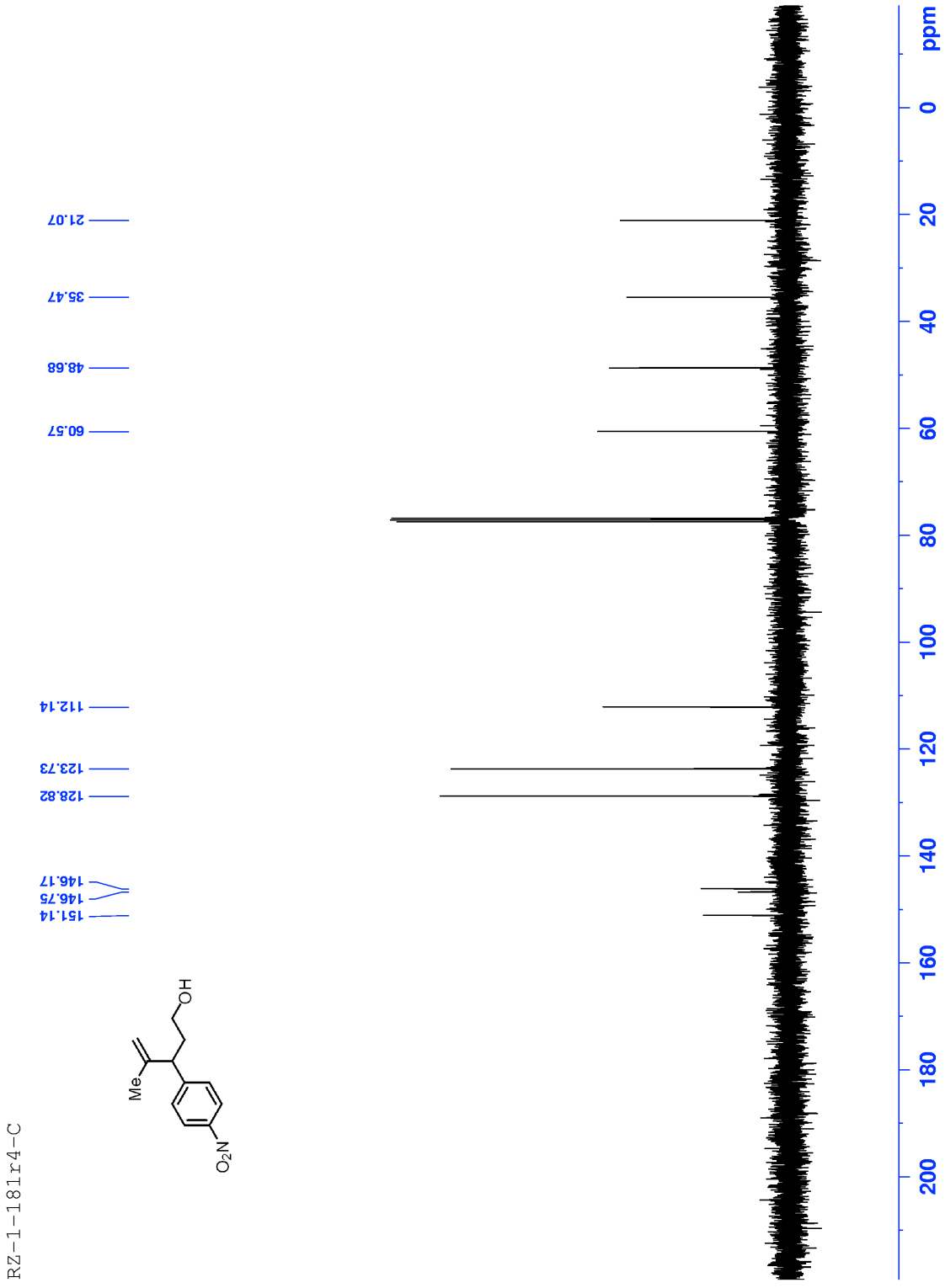
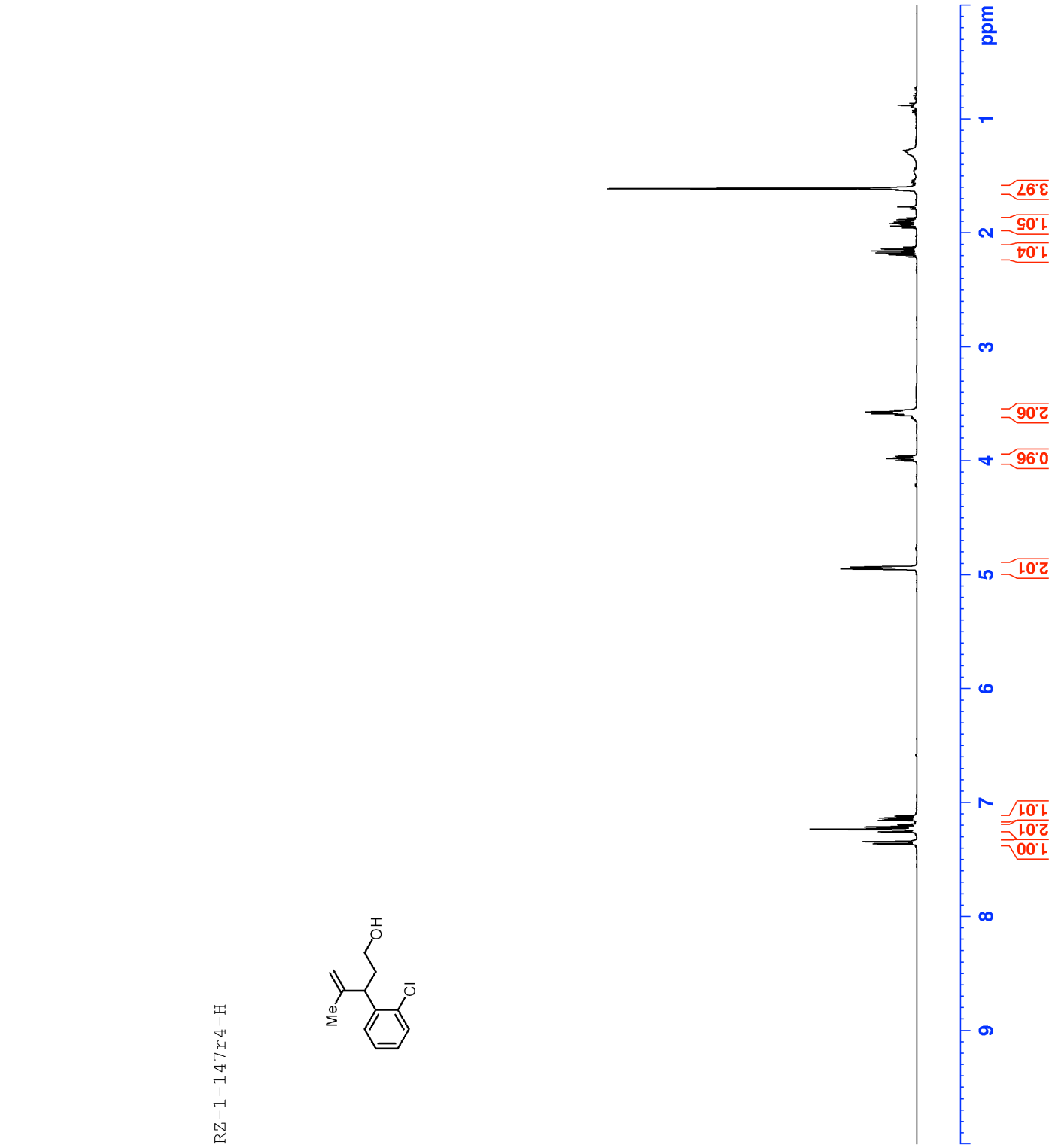
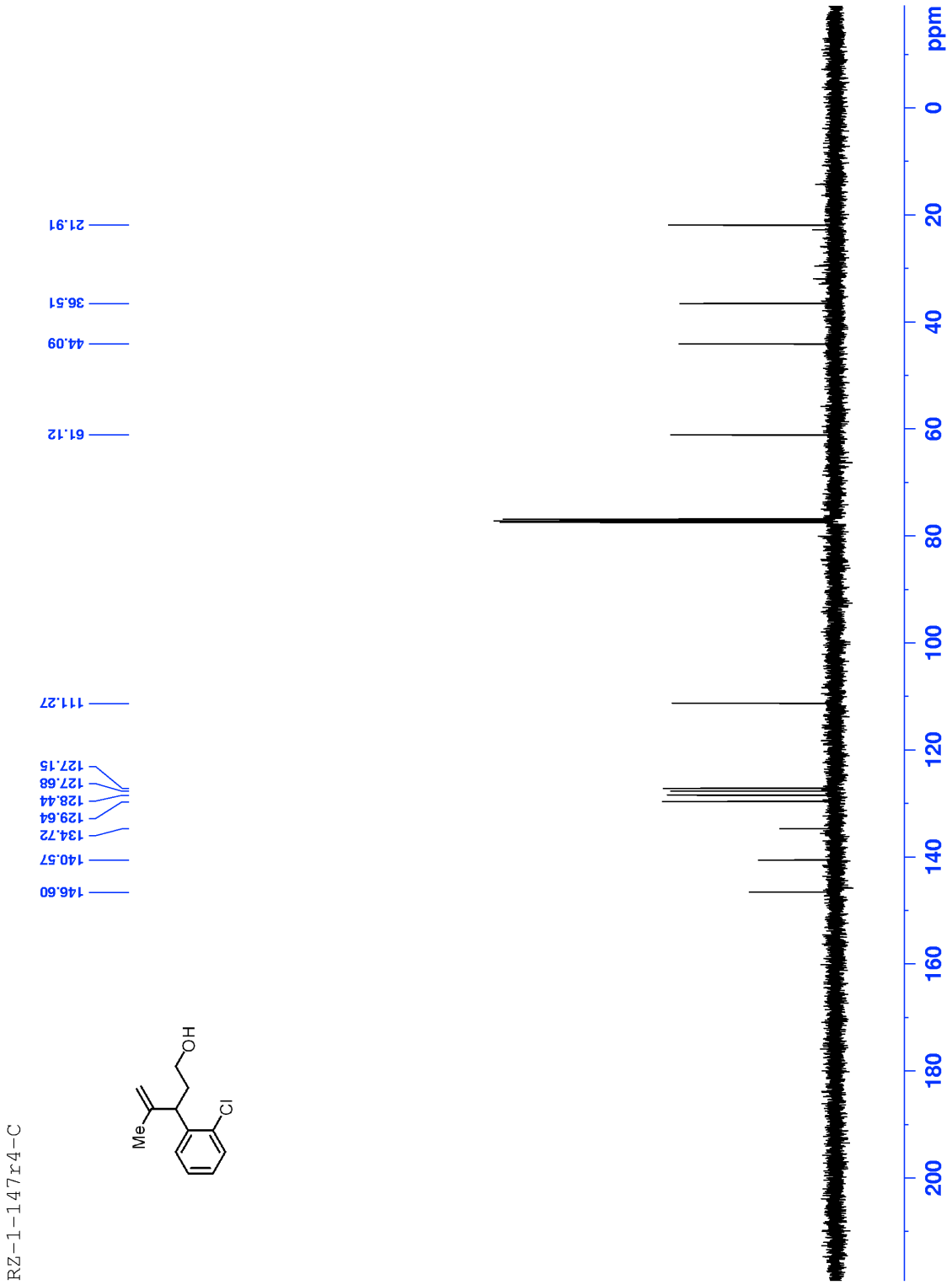
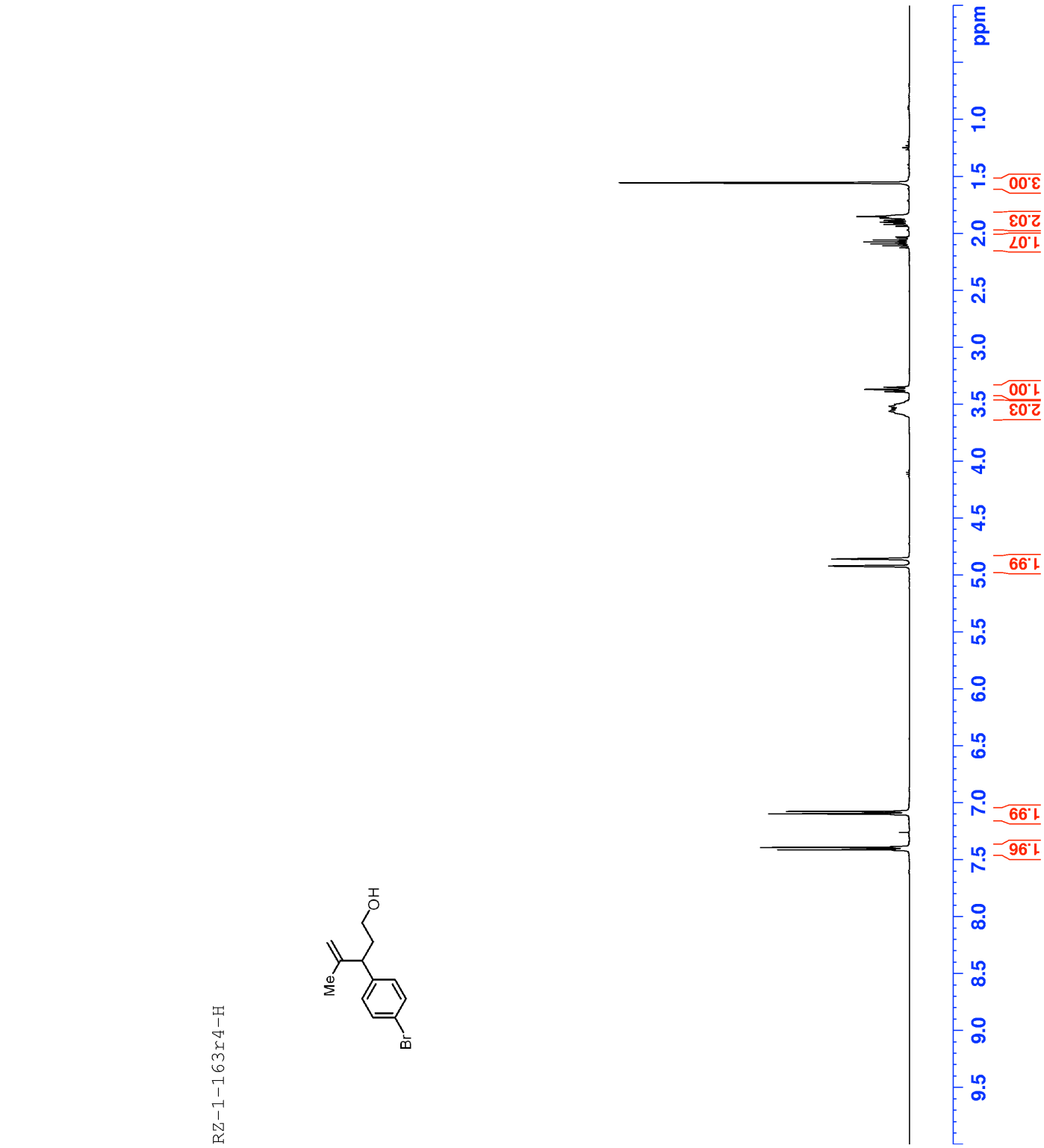
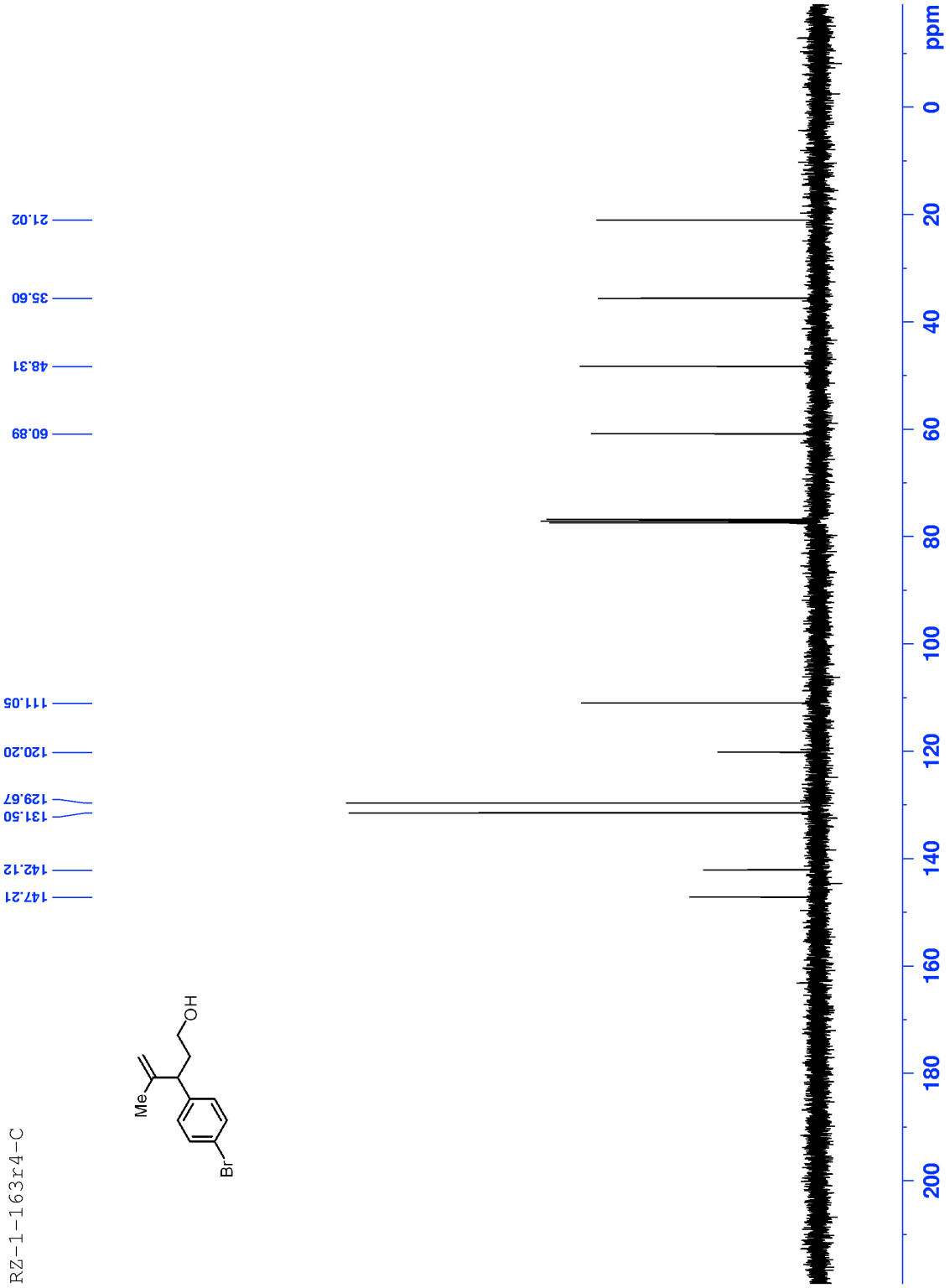
7
8
9
4.02
1.04
1.01
3.07
2.00
2.00
1.94

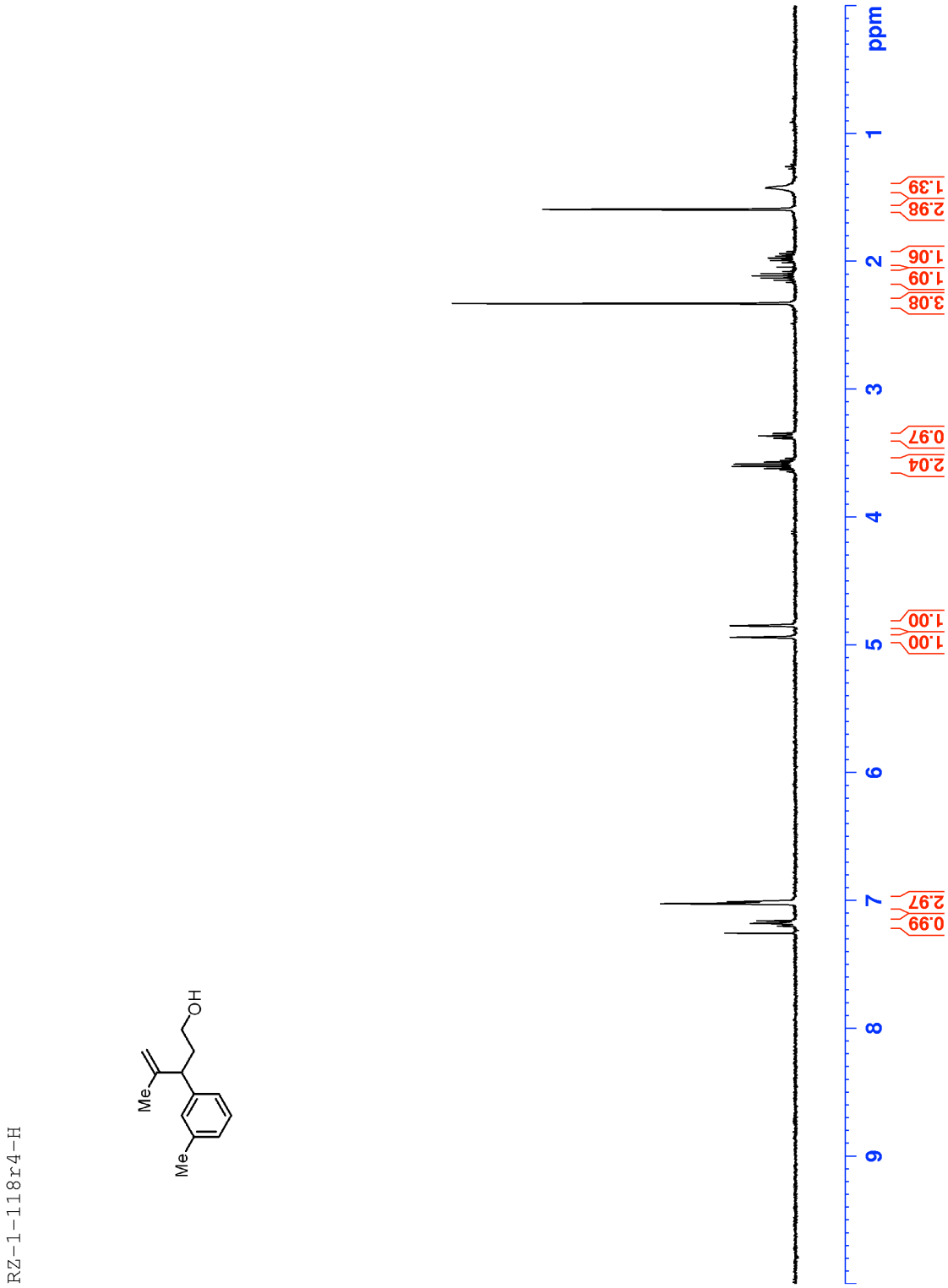

RZ-1-181r4-C
Me
OH
O2N
151.14
146.75
146.17
128.82
123.73
112.14
60.57
48.68
35.47
21.07
ppm
0
20
40
60
80
100
120
140
160
180
200

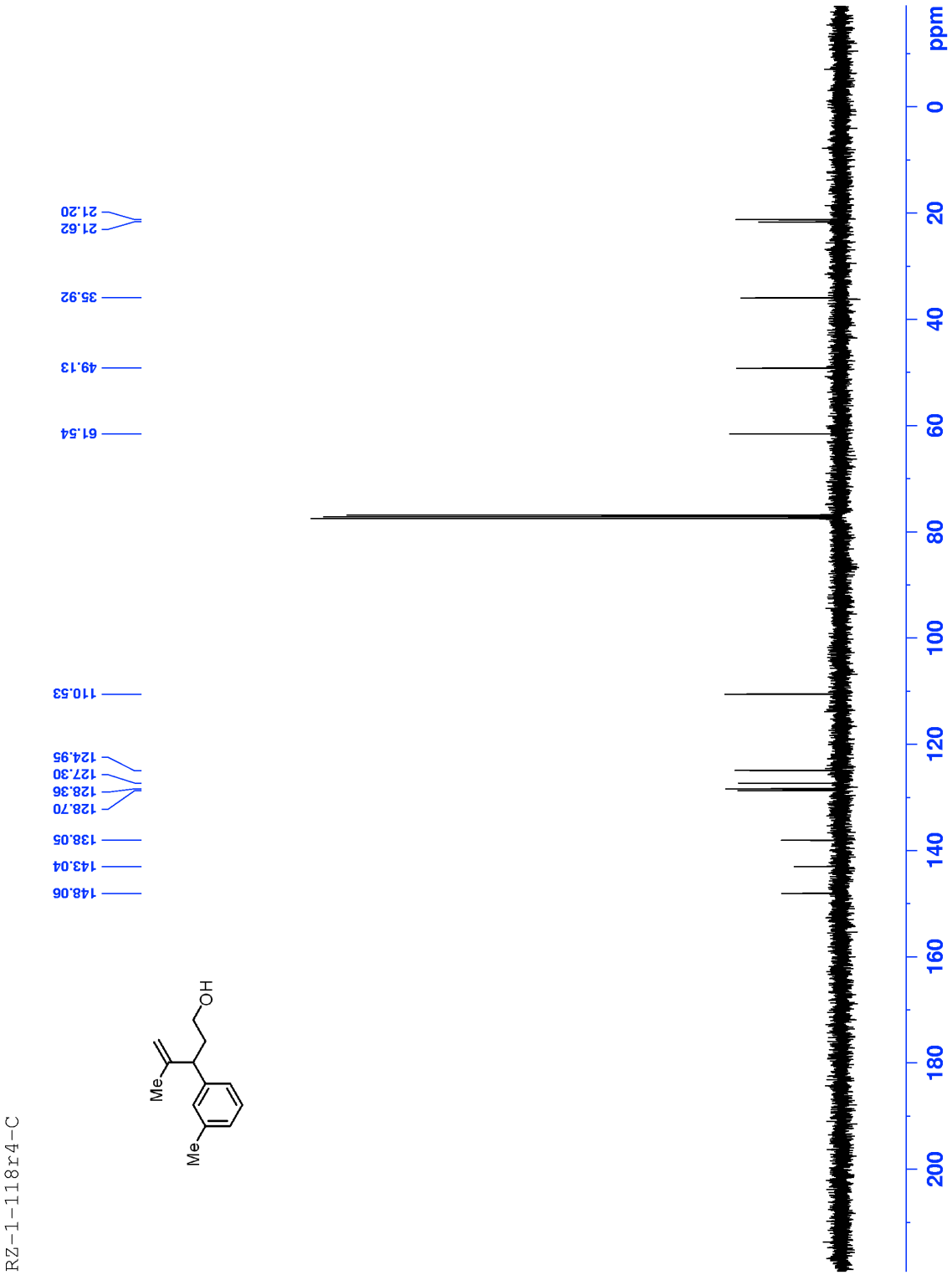

RZ-1-147r4-H
Me
OH
Cl
ppm
1
2
3
4
5
6
7
8
9
3.97
1.05
1.04
2.06
0.96
2.01
1.00
2.01
1.01

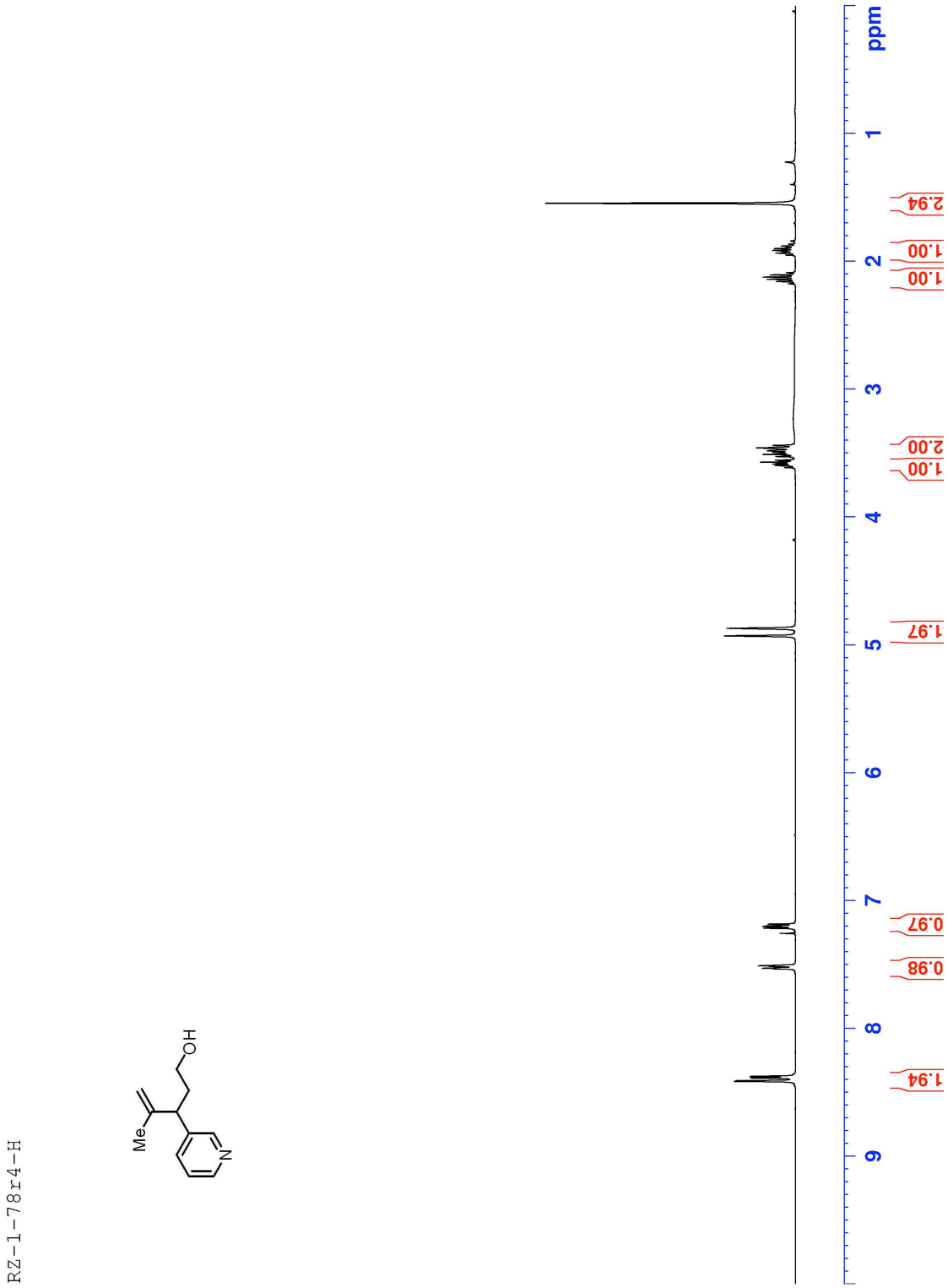

RZ-1-147r4-C
Me
OH
Cl
21.91
36.51
44.09
61.12
111.27
127.15
127.68
128.44
129.64
134.72
140.57
146.60
ppm
0
20
40
60
80
100
120
140
160
180
200

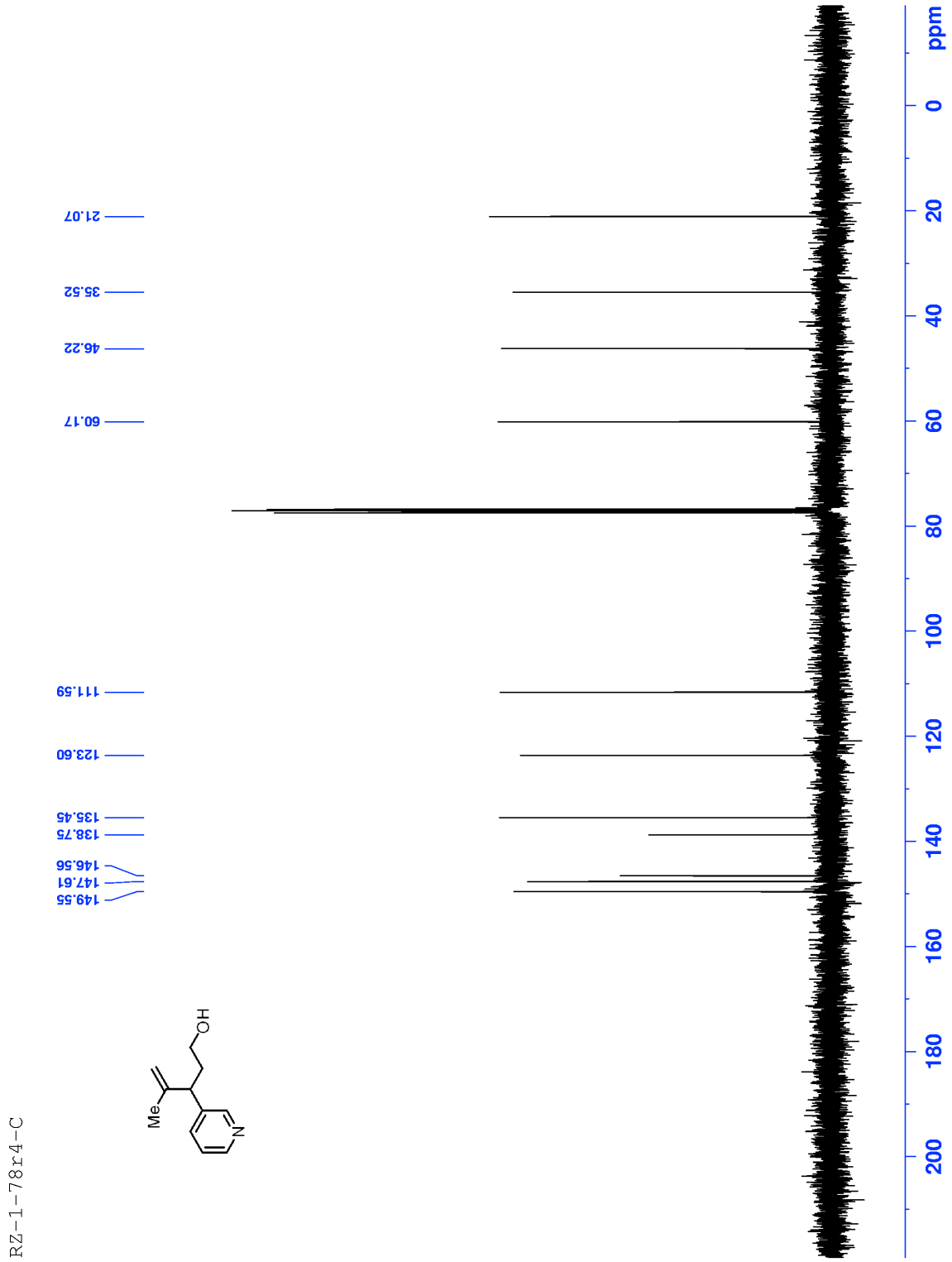

RZ-1-163r4-H
Me
OH
Br
ppm
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
3.00
2.03
1.07
2.03
1.00
1.99
1.99
1.96

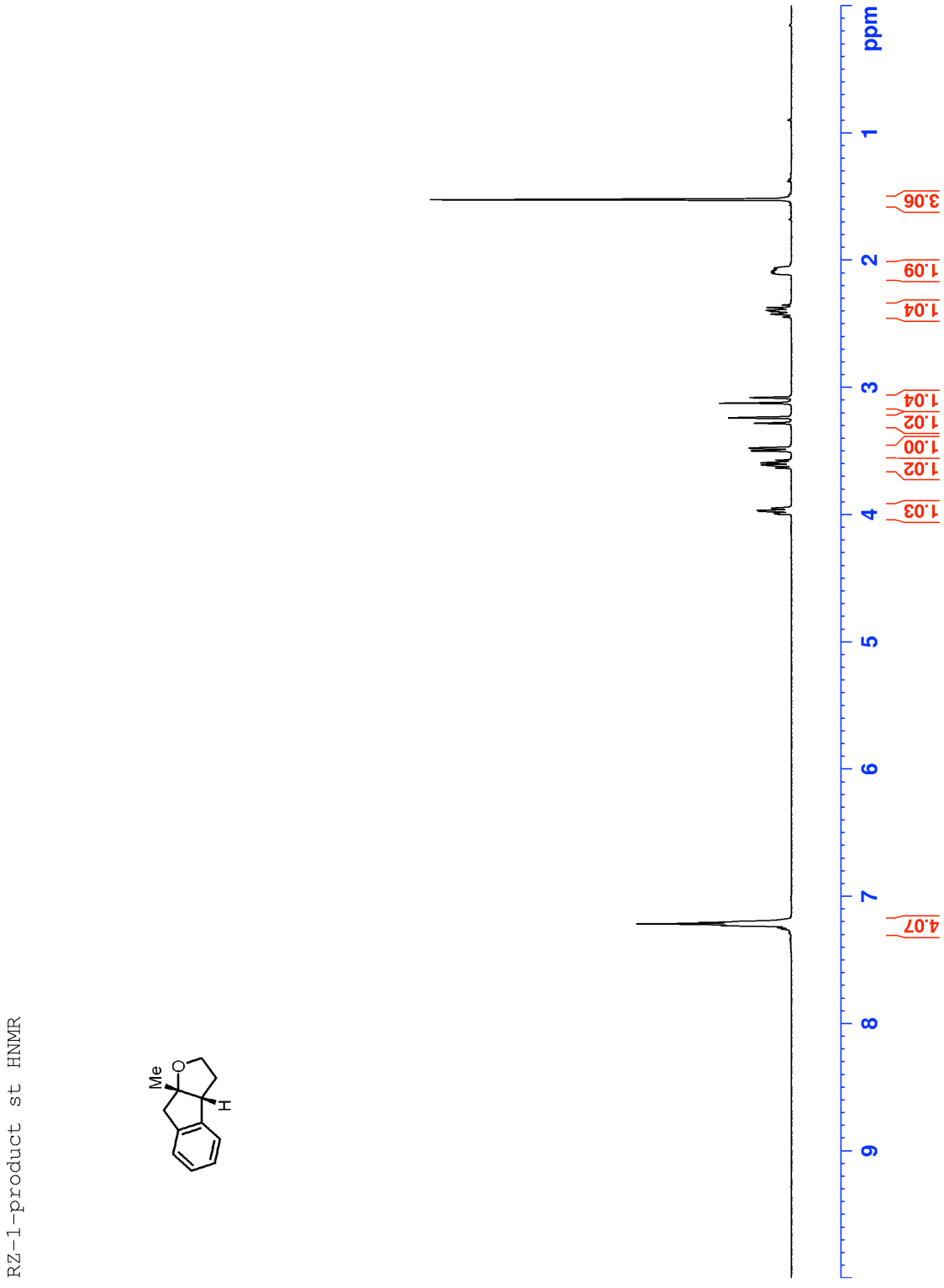

RZ-1-163r4-C
Me
OH
Br
21.02
35.60
48.31
60.89
111.05
120.20
129.67
131.50
142.12
147.21
ppm
0
20
40
60
80
100
120
140
160
180
200

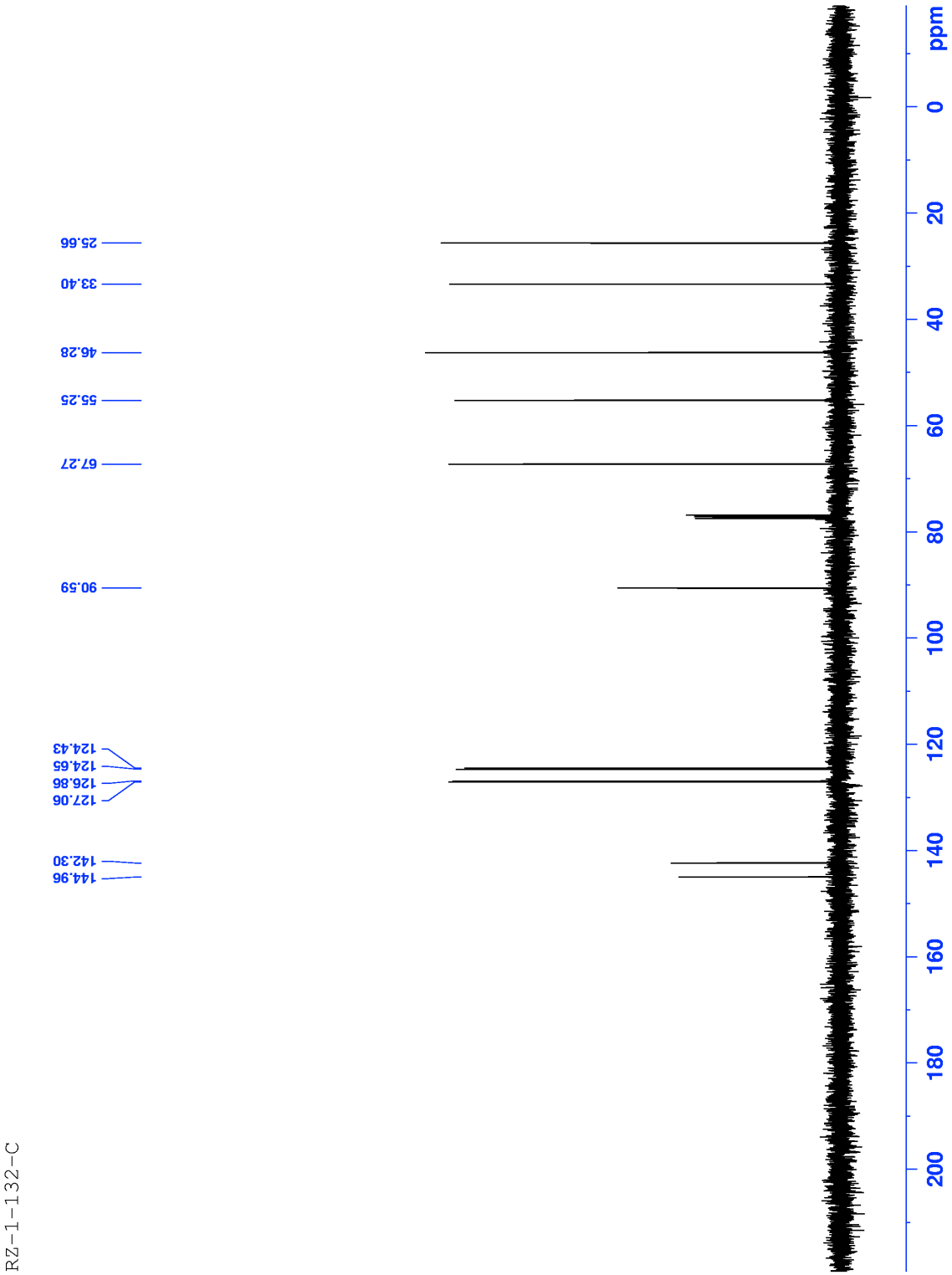

RZ-1-118r4-H
Me
Me
OH
ppm
1
2
3
4
5
6
7
8
9
1.39
2.98
1.06
1.09
3.08
0.97
2.04
1.00
1.00
0.99
2.97

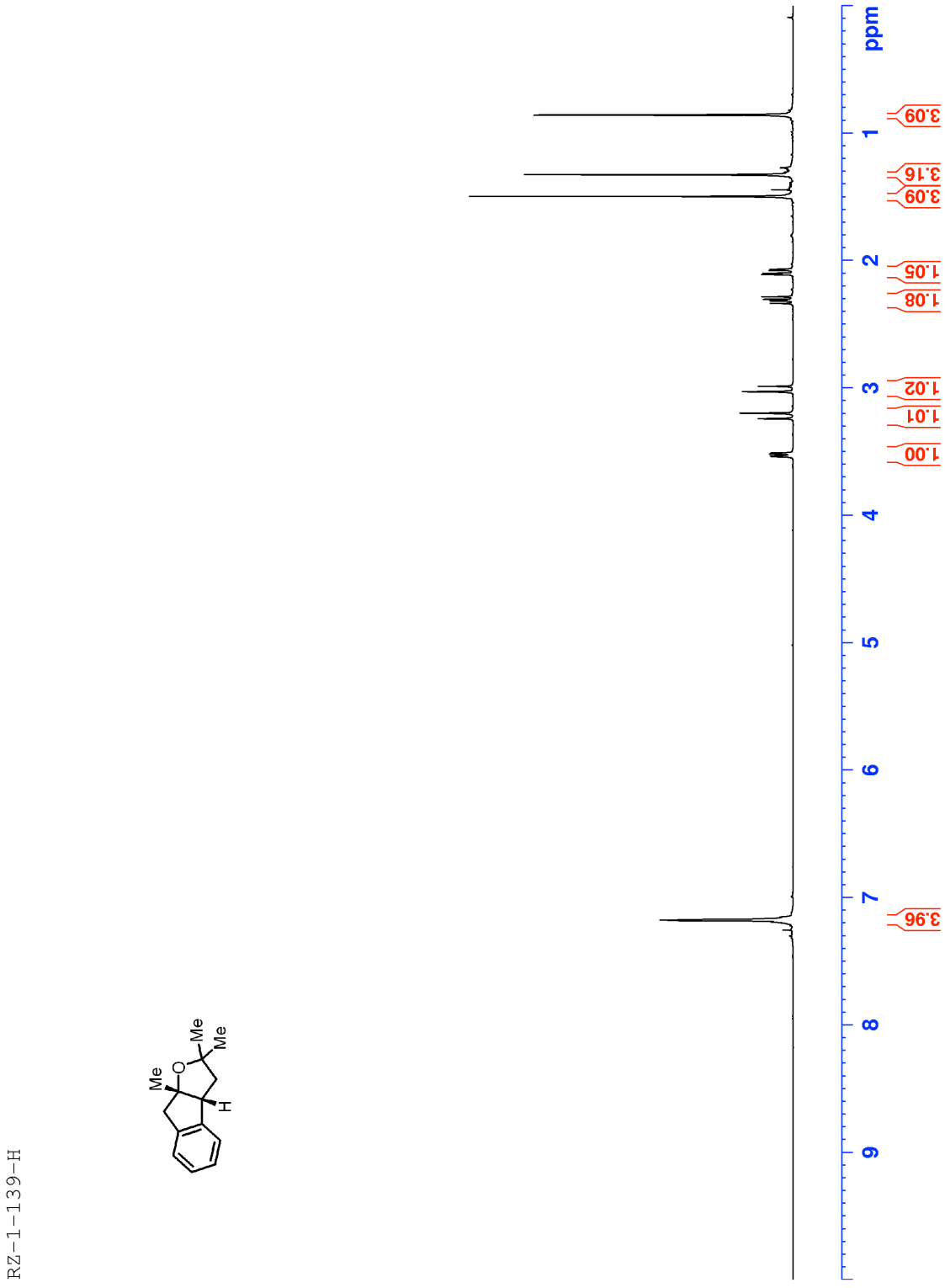

RZ-1-118r4-C
Me
Me
OH
148.06
143.04
138.05
128.70
128.36
127.30
124.95
110.53
61.54
49.13
35.92
21.62
21.20
ppm
0
20
40
60
80
100
120
140
160
180
200

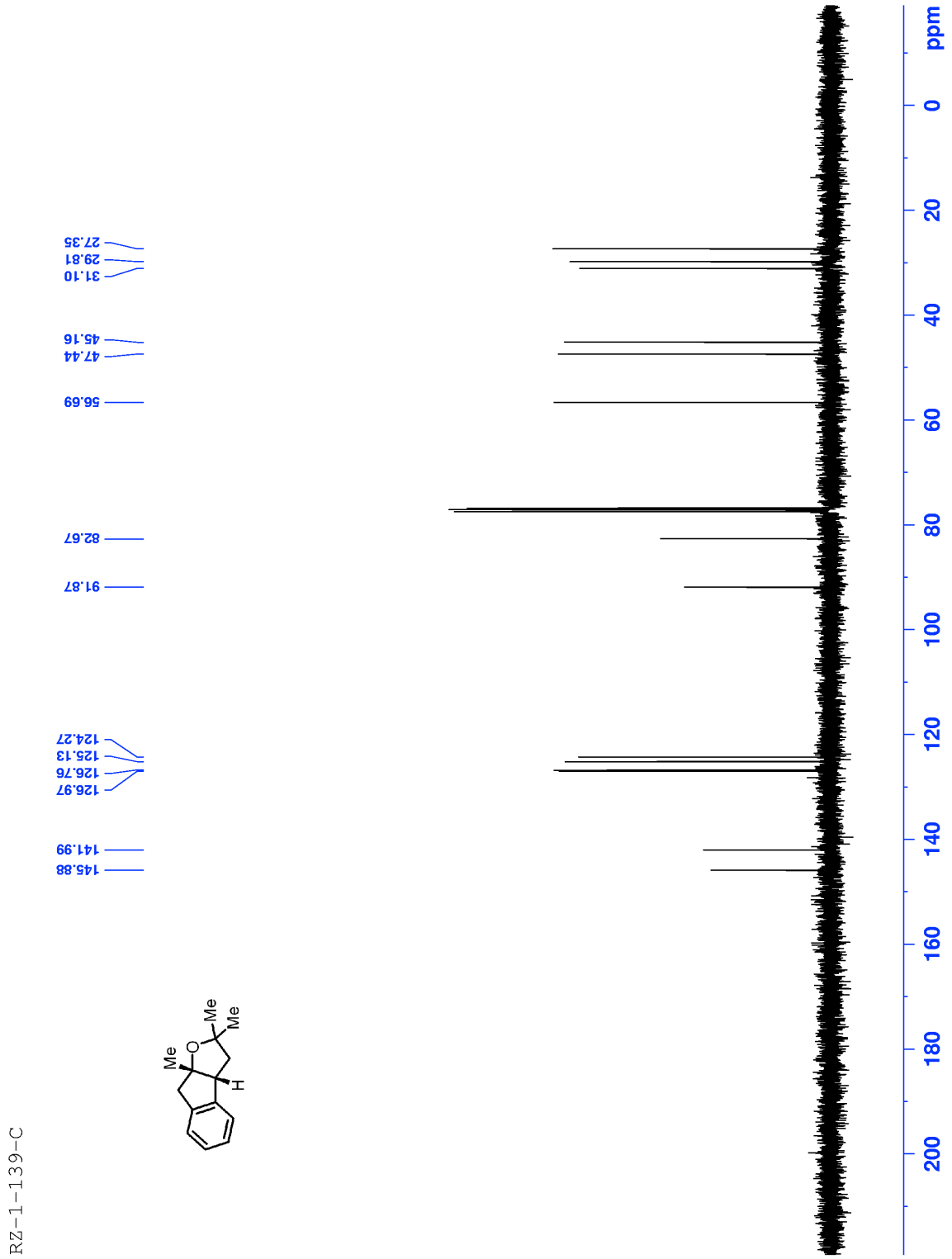

RZ-1-78r4-H
Me
OH
N
ppm
1
2
3
4
5
6
7
8
9
2.94
1.00
1.00
2.00
1.00
1.97
0.97
0.98
1.94

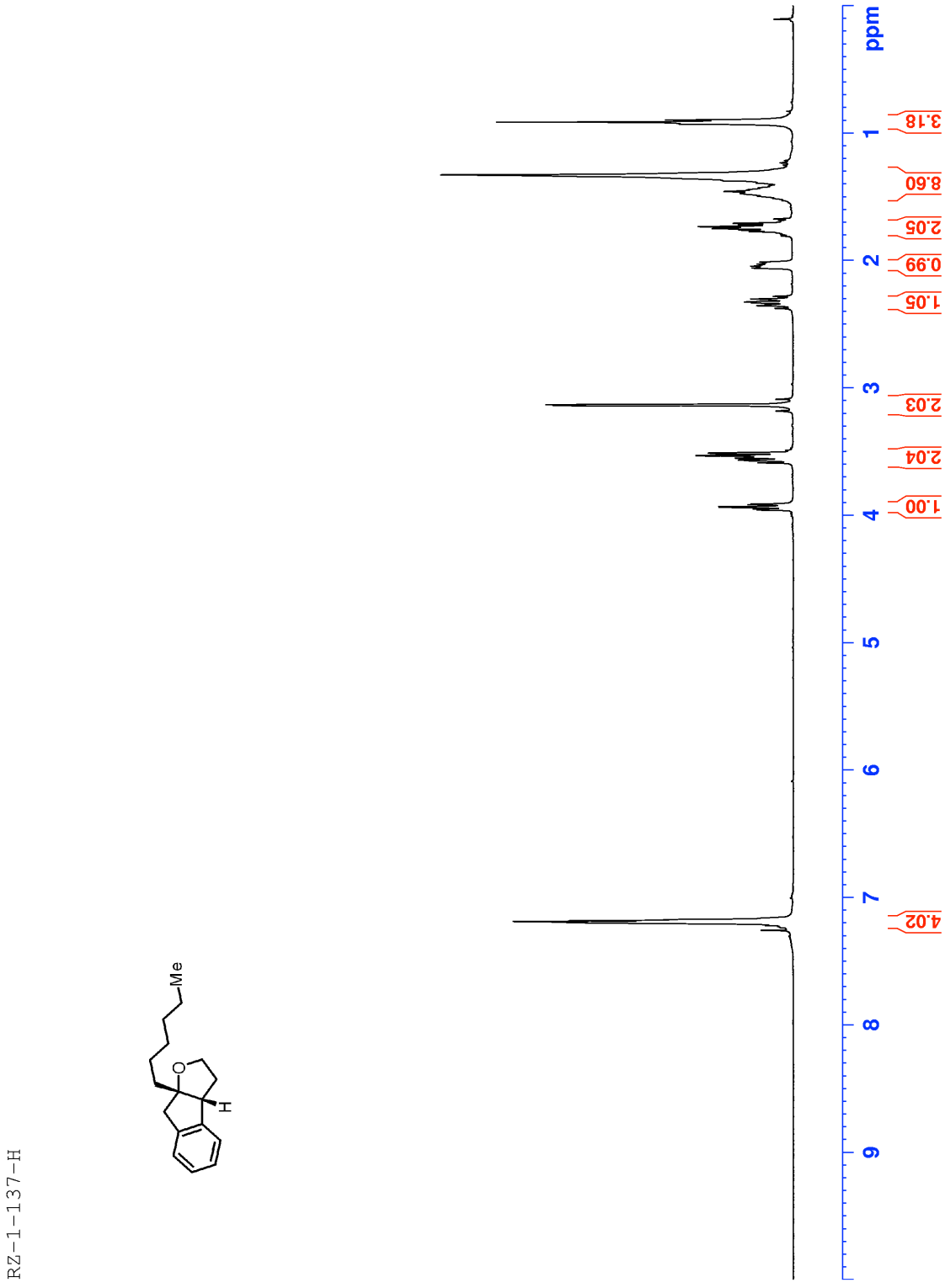

RZ-1-78r4-C
Me
OH
N
21.07
35.52
46.22
60.17
111.59
123.60
135.45
138.75
146.56
147.61
149.55
ppm
0
20
40
60
80
100
120
140
160
180
200

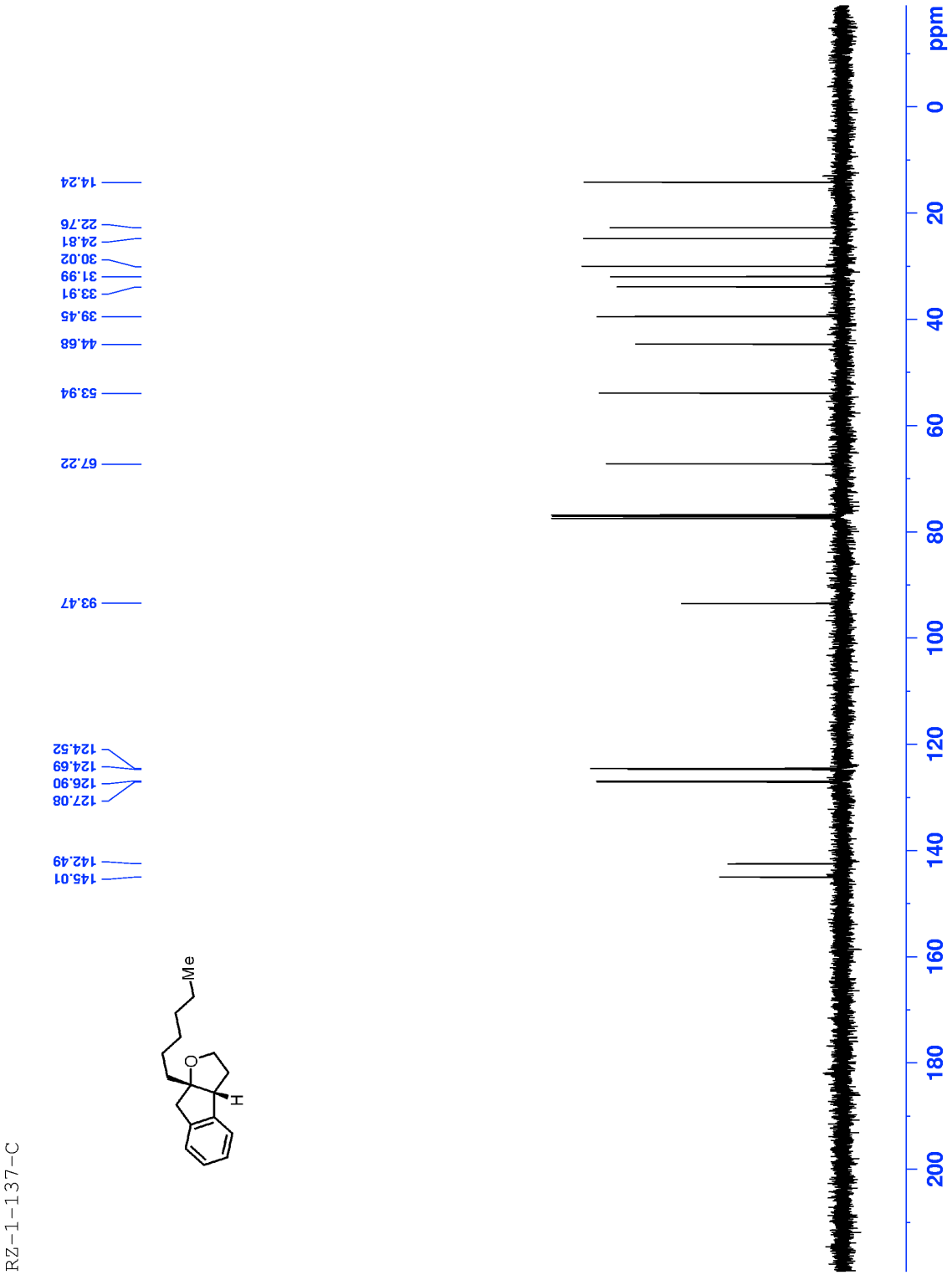

RZ-1-product st HNMR
Me
H
O
ppm
1
2
3
4
5
6
7
8
9
3.06
1.09
1.04
1.04
1.02
1.00
1.02
1.03
4.07

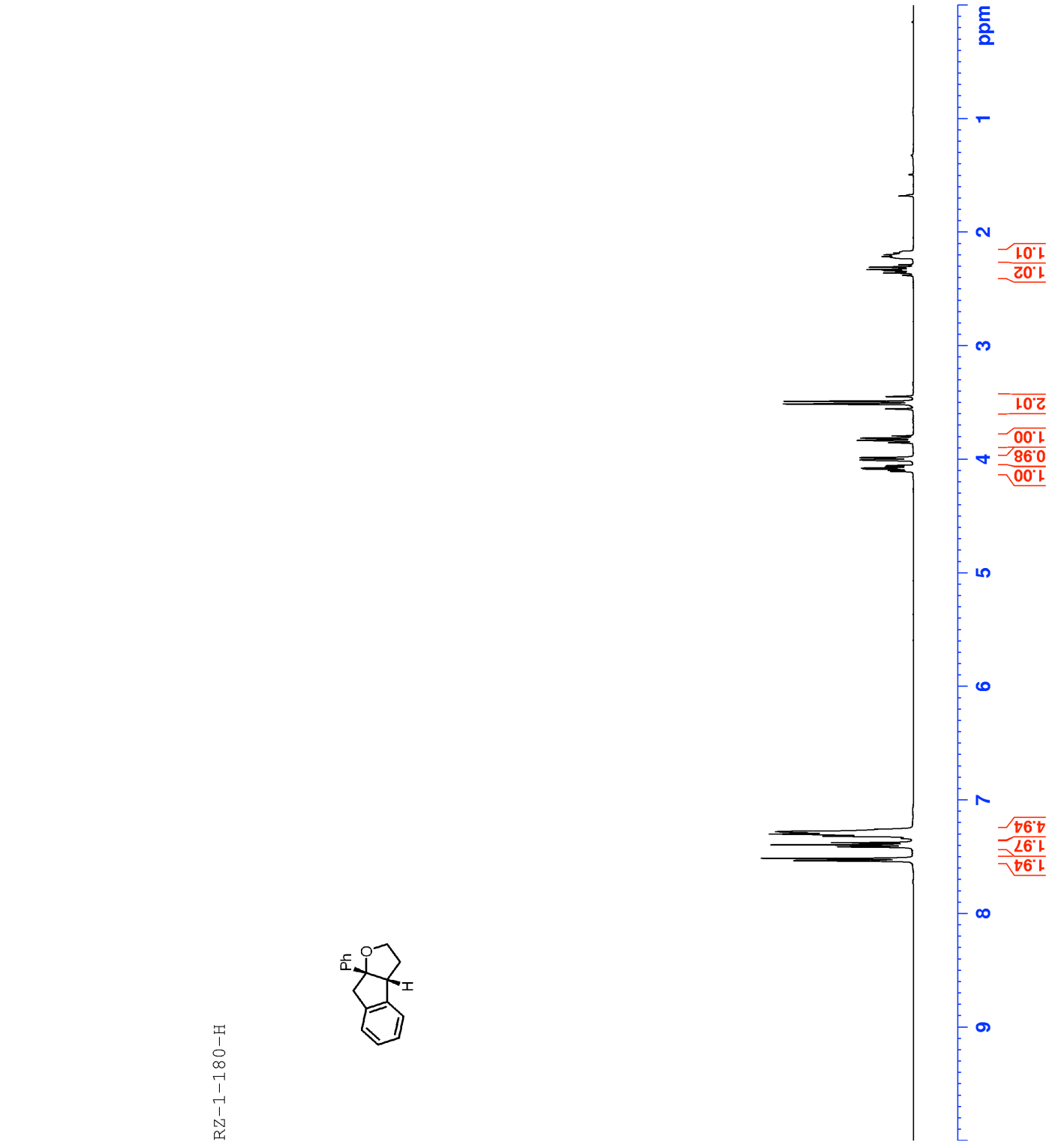

RZ-1-132-C
25.66
33.40
46.28
55.25
67.27
90.59
124.43
124.65
126.86
127.06
142.30
144.96
ppm
0
20
40
60
80
100
120
140
160
180
200

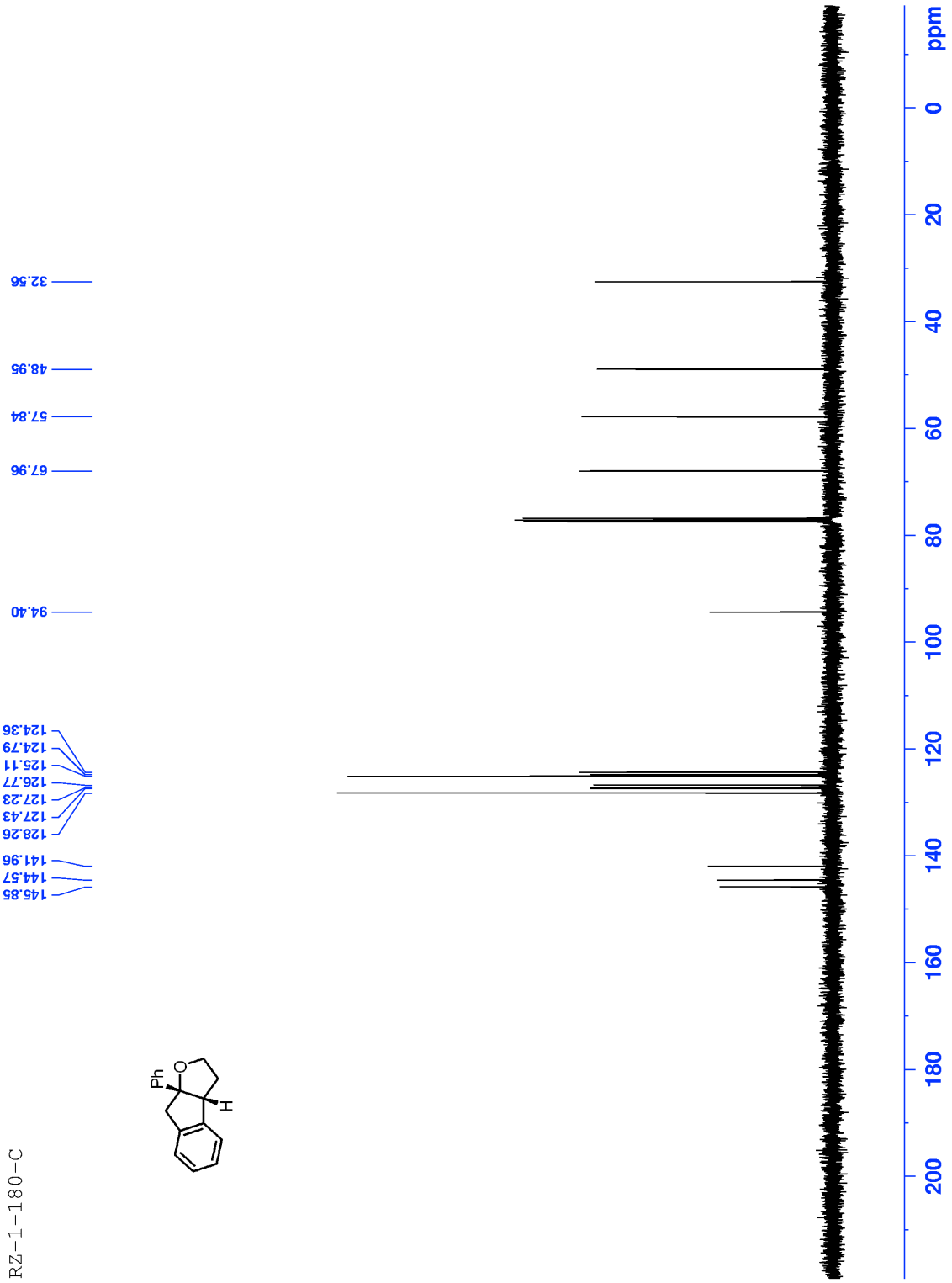

RZ-1-139-H
Me
Me
Me
O
H
ppm
1
2
3
4
5
6
7
8
9
3.09
3.16
3.09
1.05
1.08
1.02
1.01
1.00
3.96

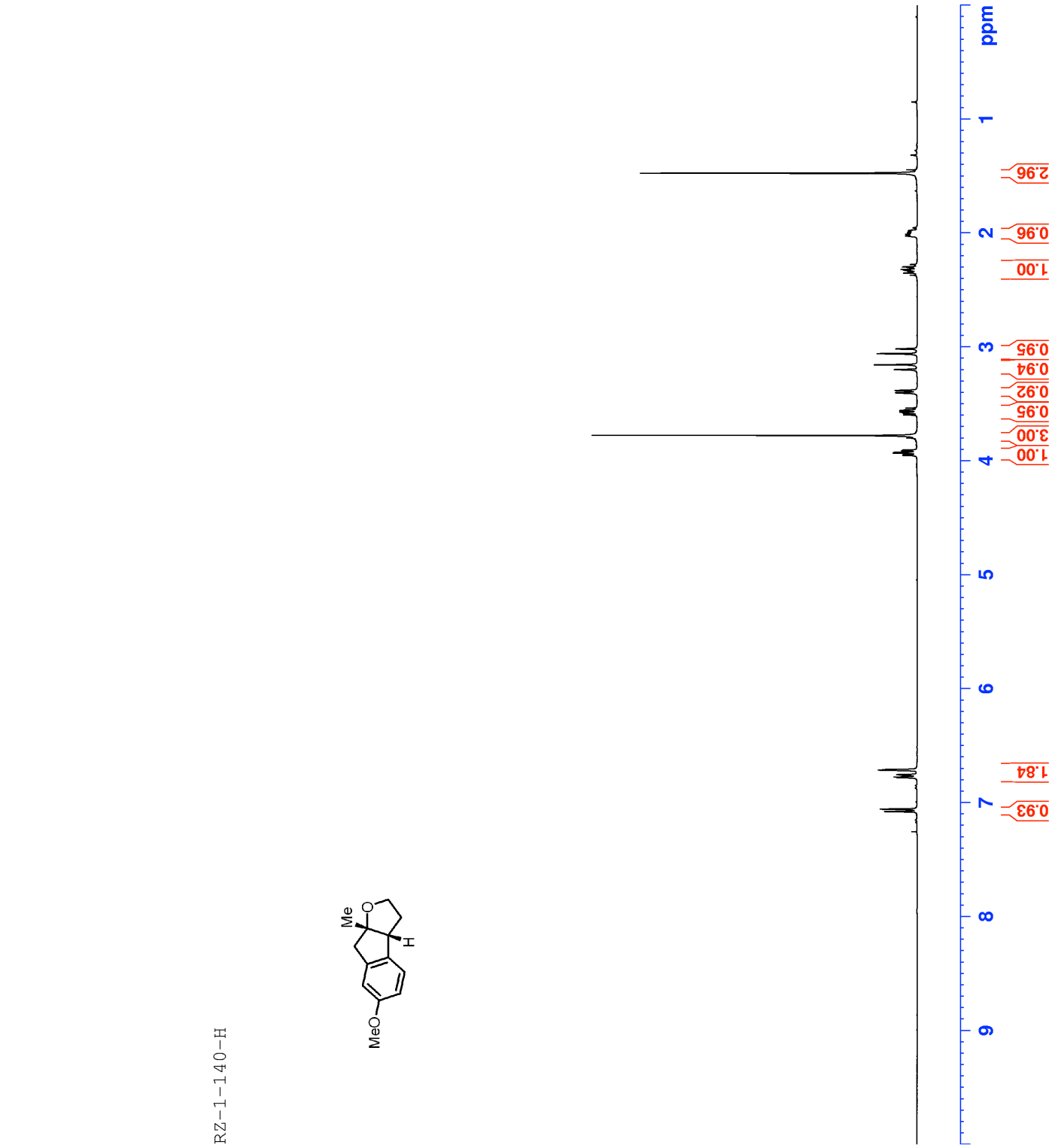

RZ-1-139-C
Me
Me
Me
O
H
27.35
29.81
31.10
45.16
47.44
56.69
82.67
91.87
124.27
125.13
126.76
126.97
141.99
145.88
ppm
0
20
40
60
80
100
120
140
160
180
200

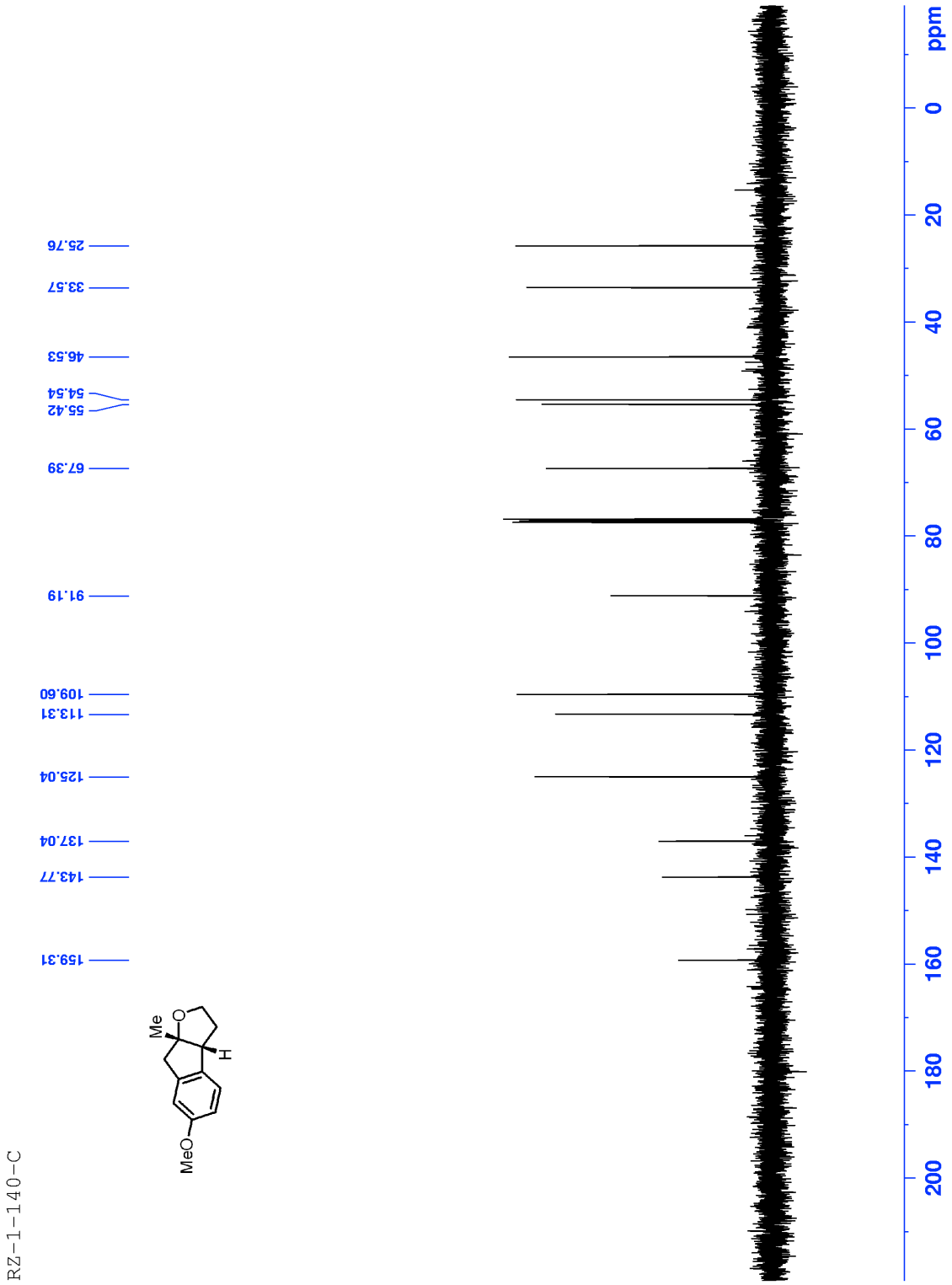

RZ-1-137-H
Me
H
O
ppm
1
2
3
4
5
6
7
8
9
3.18
8.60
2.05
0.99
1.05
2.03
2.04
1.00
4.02

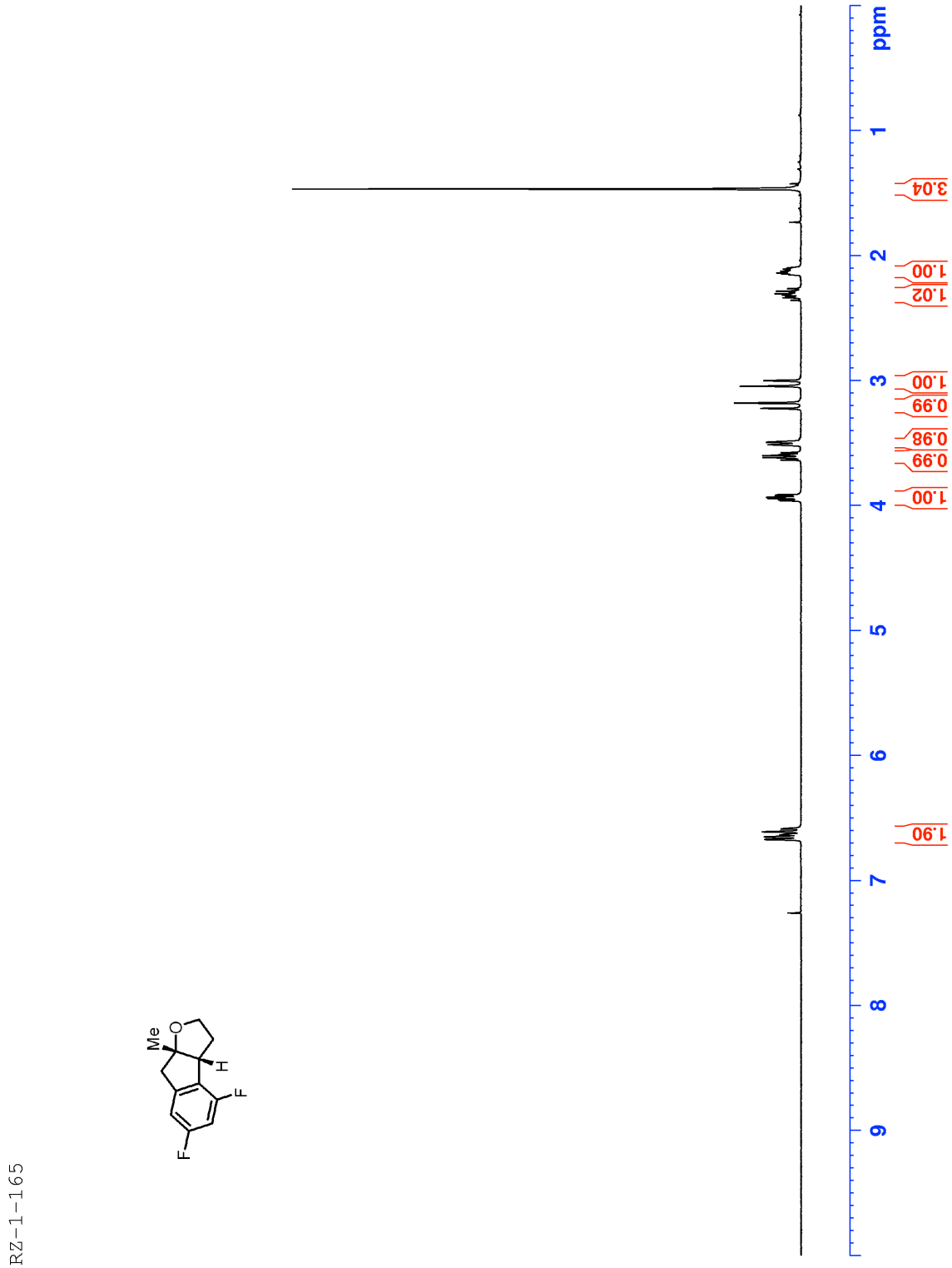

RZ-1-137-C
Me
O
H
14.24
22.76
24.81
30.02
31.99
33.91
39.45
44.68
53.94
67.22
93.47
124.52
124.69
126.90
127.08
142.49
145.01
ppm
0
20
40
60
80
100
120
140
160
180
200

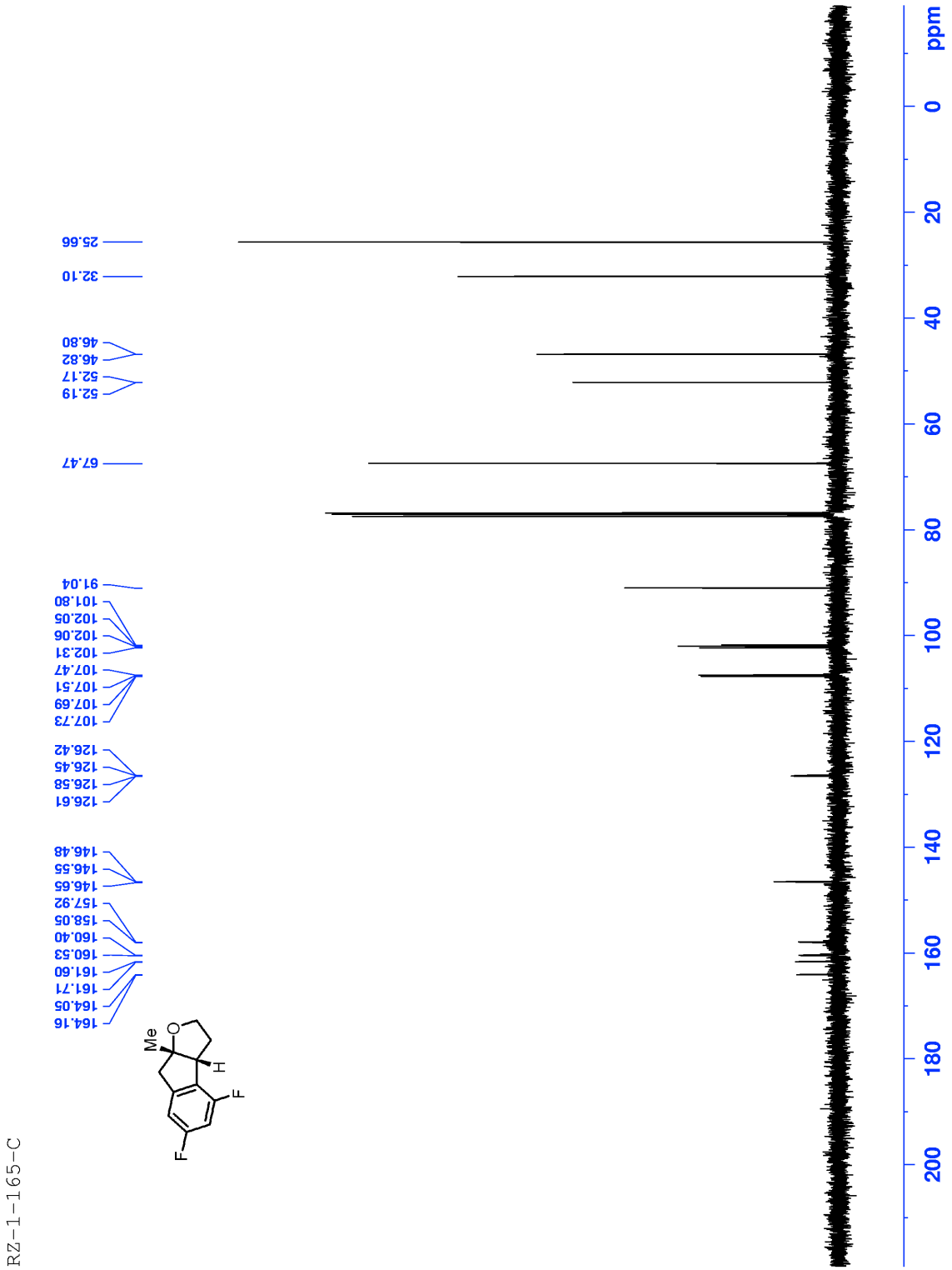

RZ-1-180-H
Ph
O
H
ppm
1
2
3
4
5
6
7
8
9
1.01
1.02
2.01
1.00
0.98
1.00
1.94
1.97
4.94

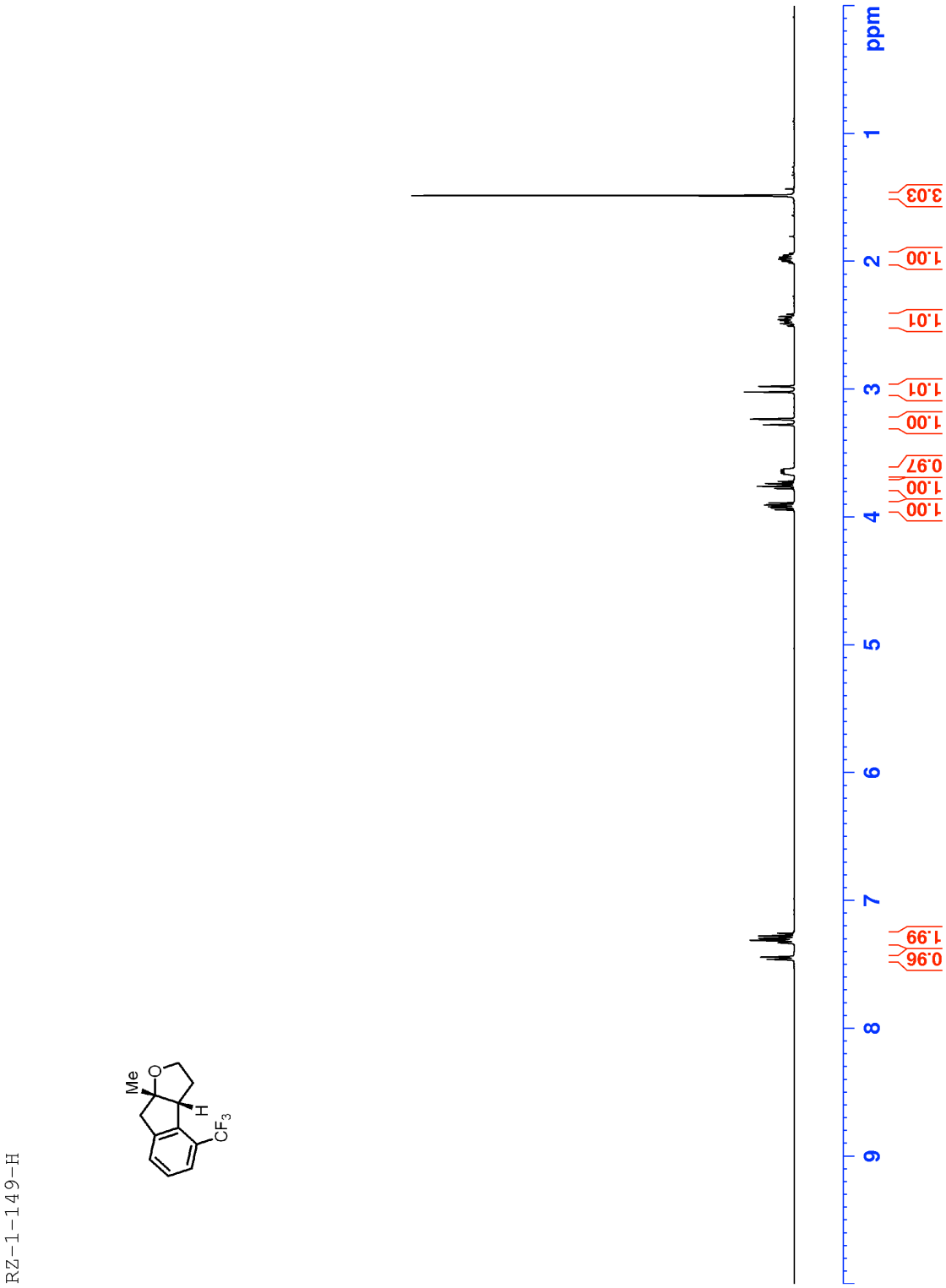

RZ-1-180-C
Ph
O
H
32.56
48.95
57.84
67.96
94.40
124.36
124.79
125.11
126.77
127.23
127.43
128.26
141.96
144.57
145.85
ppm
0
20
40
60
80
100
120
140
160
180
200

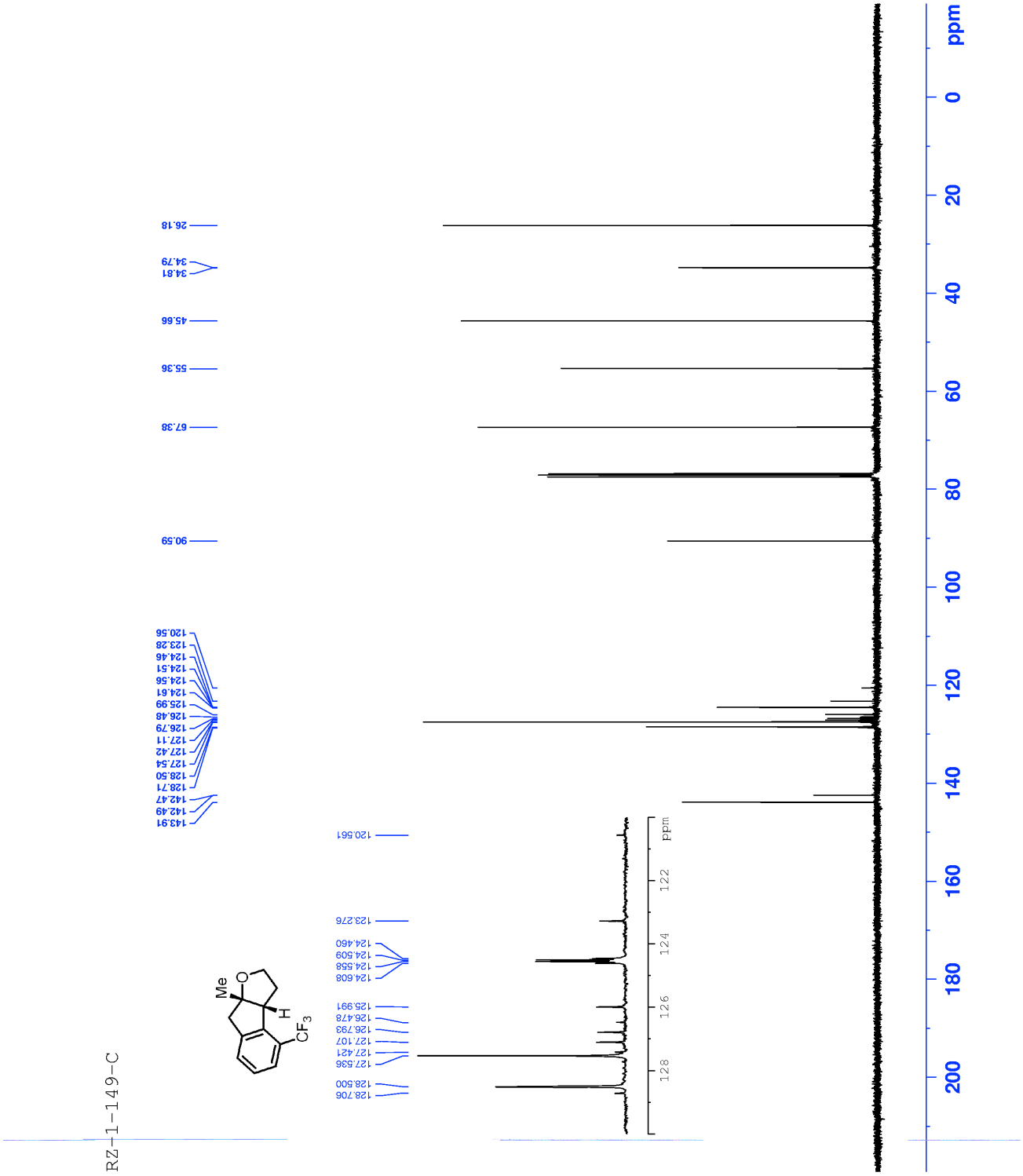

RZ-1-140-H
Me
O
H
MeO
ppm
1
2
3
4
5
6
7
8
9
2.96
0.96
1.00
0.95
0.94
0.92
0.95
3.00
1.00
1.84
0.93

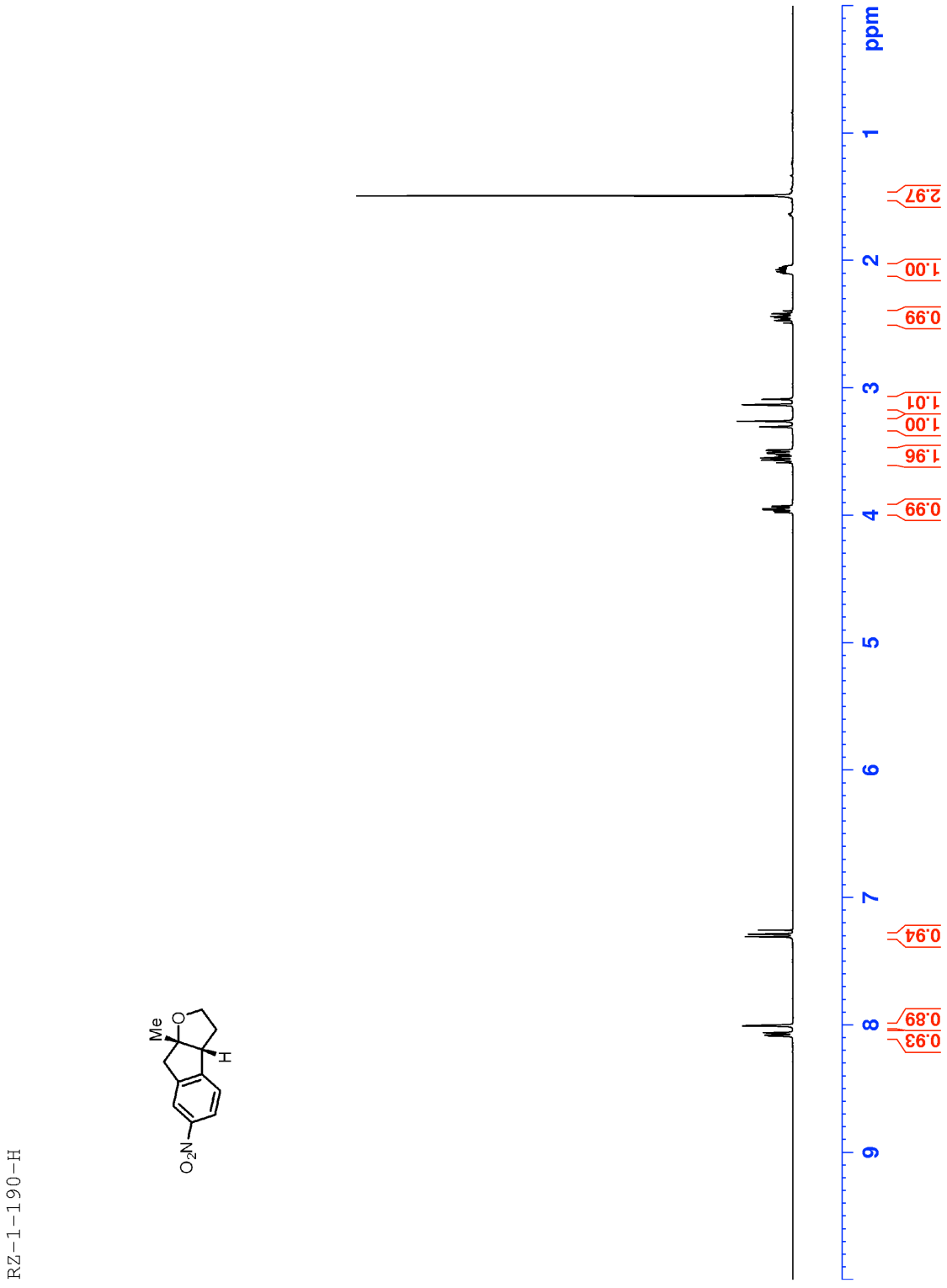

RZ-1-140-C
Me
O
H
MeO
159.31
143.77
137.04
125.04
113.31
109.60
91.19
67.39
55.42
54.54
46.53
33.57
25.76
ppm
0
20
40
60
80
100
120
140
160
180
200

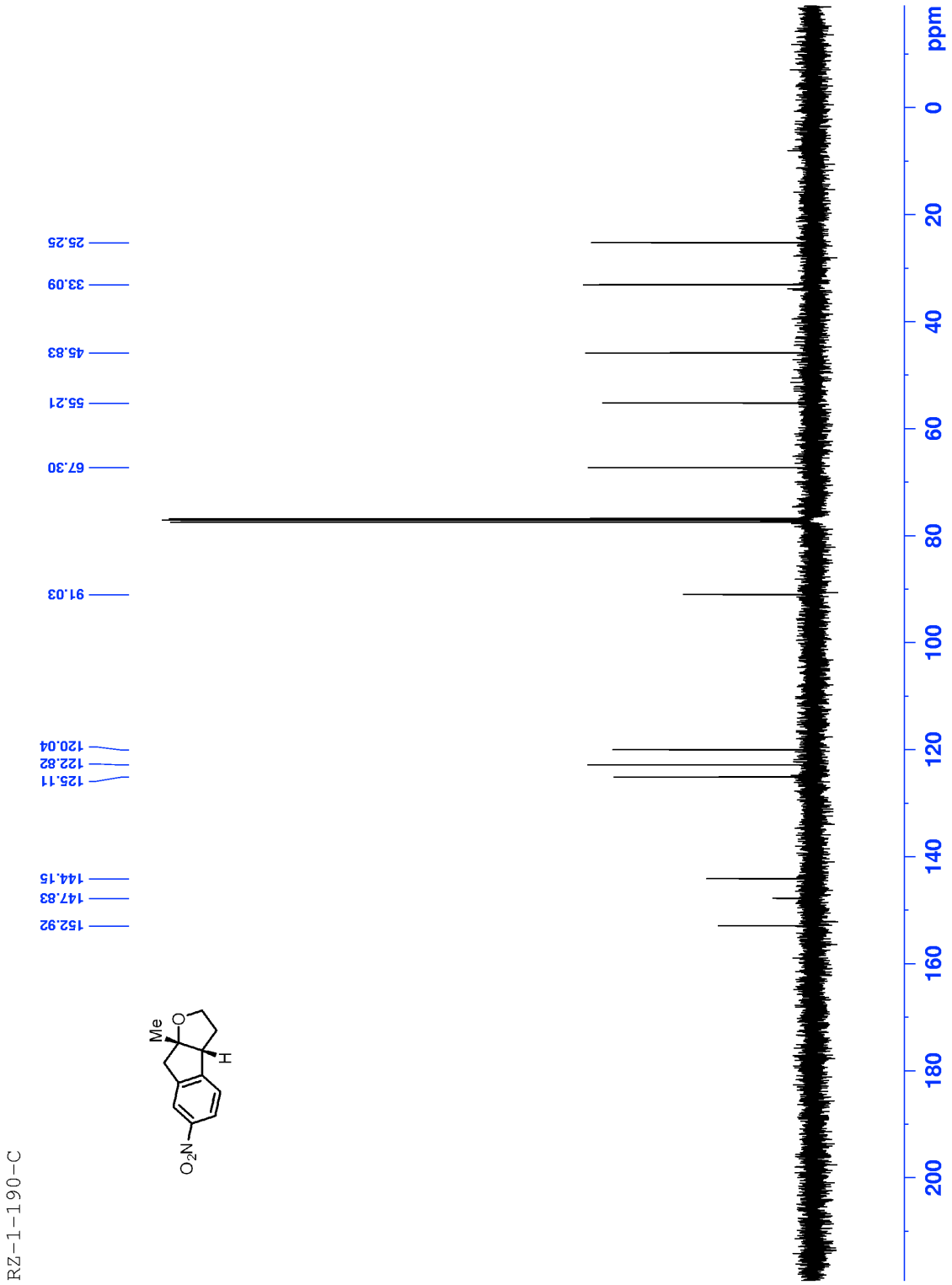

RZ-1-165
Me
O
H
F
F
ppm
1
2
3
4
5
6
7
8
9
3.04
1.00
1.02
1.00
0.99
0.98
0.99
1.00
1.90

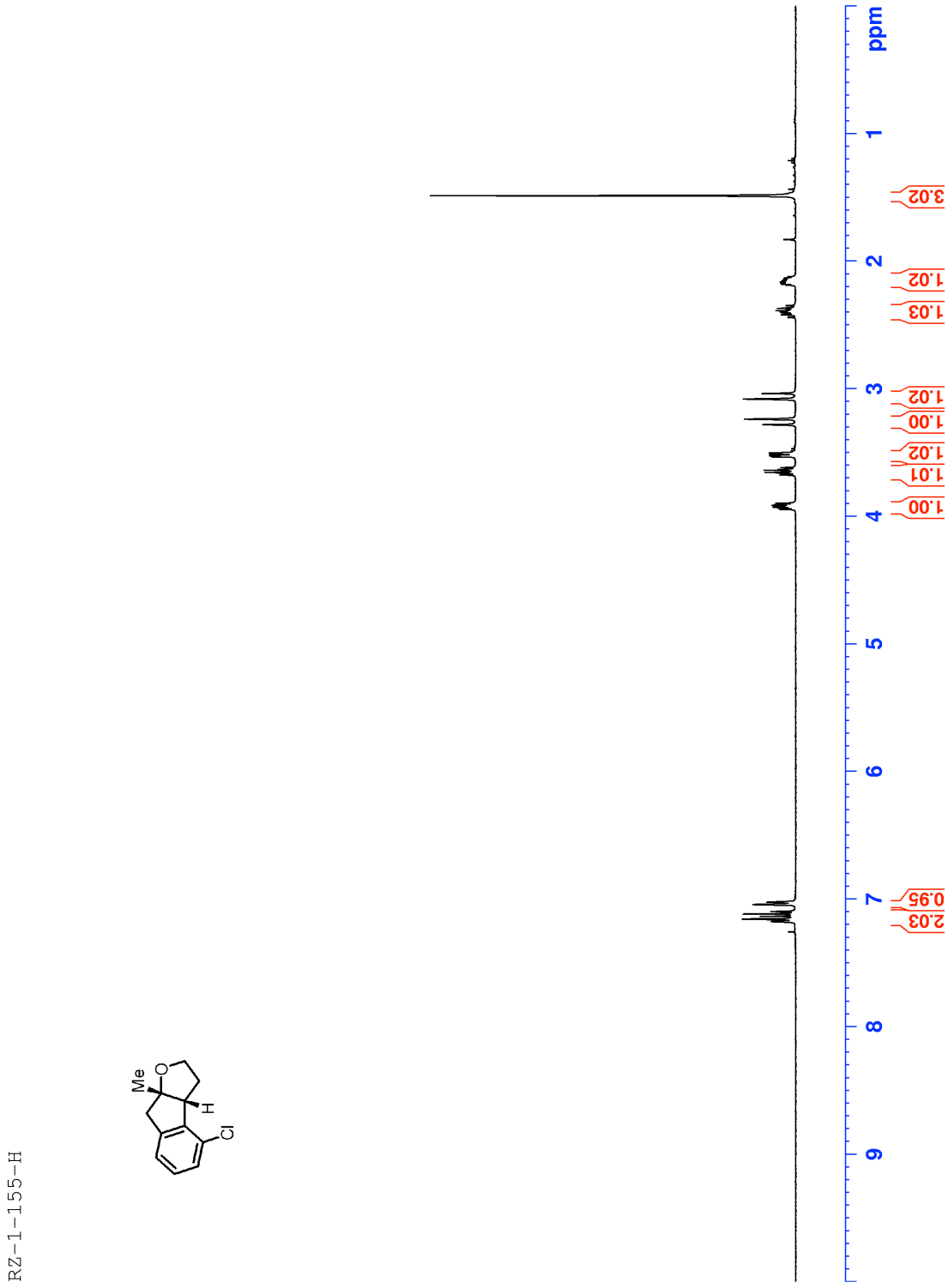

RZ-1-165-C
Me
O
H
F
F
25.66
32.10
46.80
46.82
52.17
52.19
67.47
91.04
101.80
102.05
102.06
102.31
107.47
107.51
107.69
107.73
126.42
126.45
126.58
126.61
146.48
146.55
146.65
157.92
158.05
160.40
160.53
161.60
161.71
164.05
164.16
ppm
0
20
40
60
80
100
120
140
160
180
200

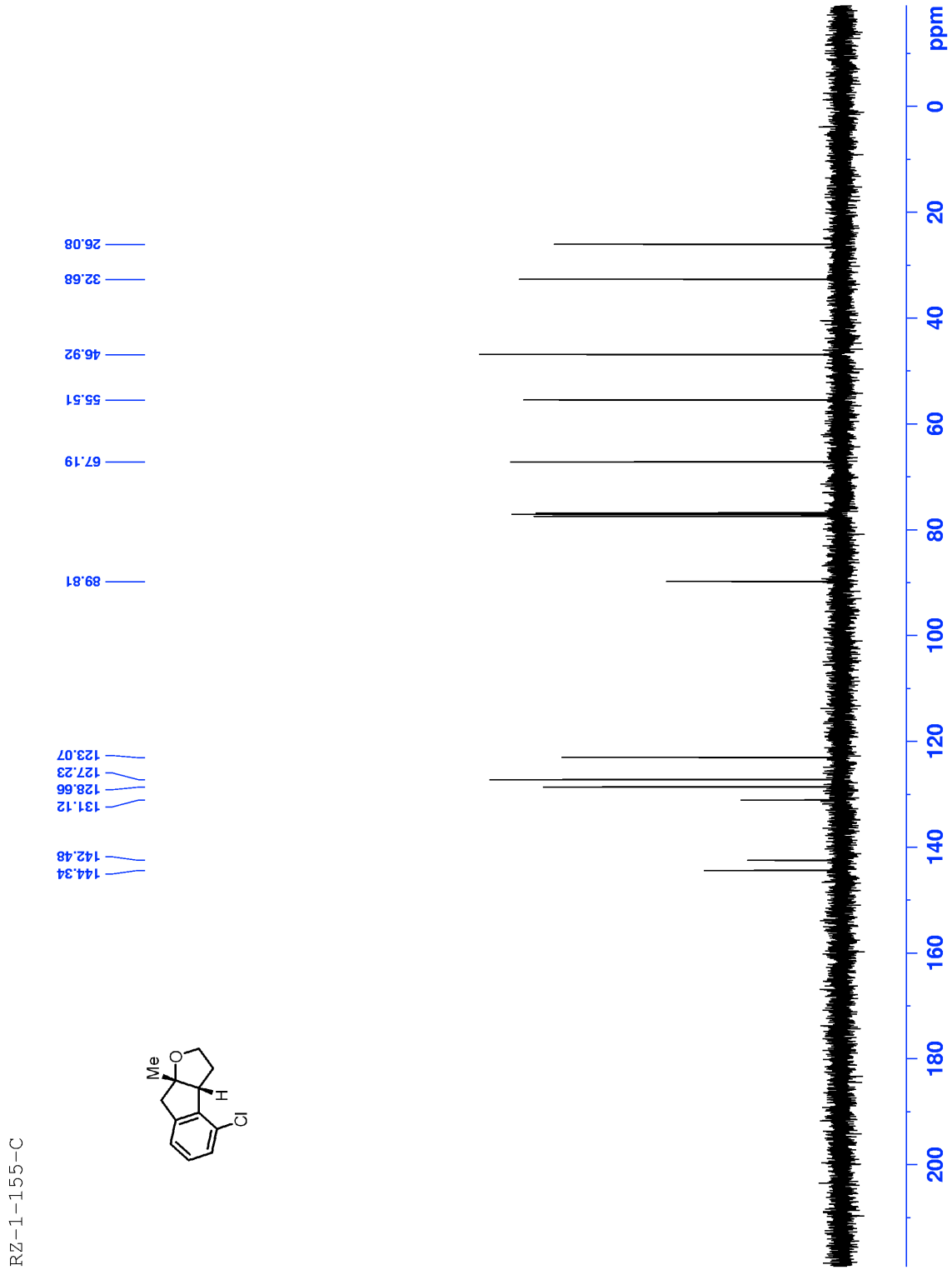

RZ-1-149-H
Me
O
H
CF3
ppm
1
2
3
4
5
6
7
8
9
3.03
1.00
1.01
1.01
1.00
0.97
1.00
1.00
0.96
1.99

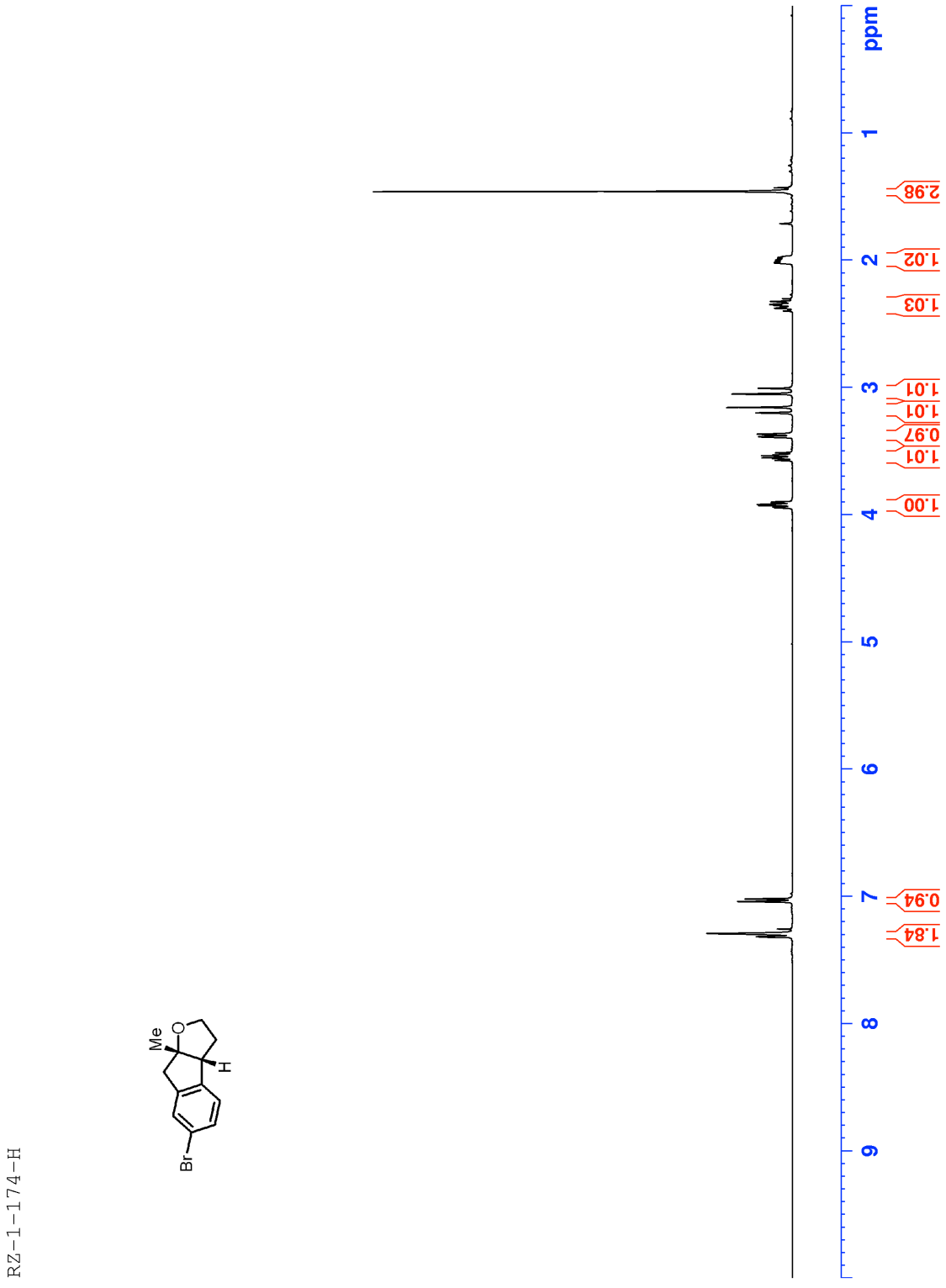

RZ-1-149-C
Me
O
H
CF3
26.18
34.81
34.79
45.66
55.36
67.38
90.59
120.56
123.28
124.46
124.51
124.56
124.61
125.99
126.48
126.79
127.11
127.42
127.54
128.50
128.71
142.47
142.49
143.91
120.561
123.276
124.460
124.509
124.558
124.608
125.991
126.478
126.793
127.107
127.421
127.536
128.500
128.706
ppm
122
124
126
128
ppm
0
20
40
60
80
100
120
140
160
180
200

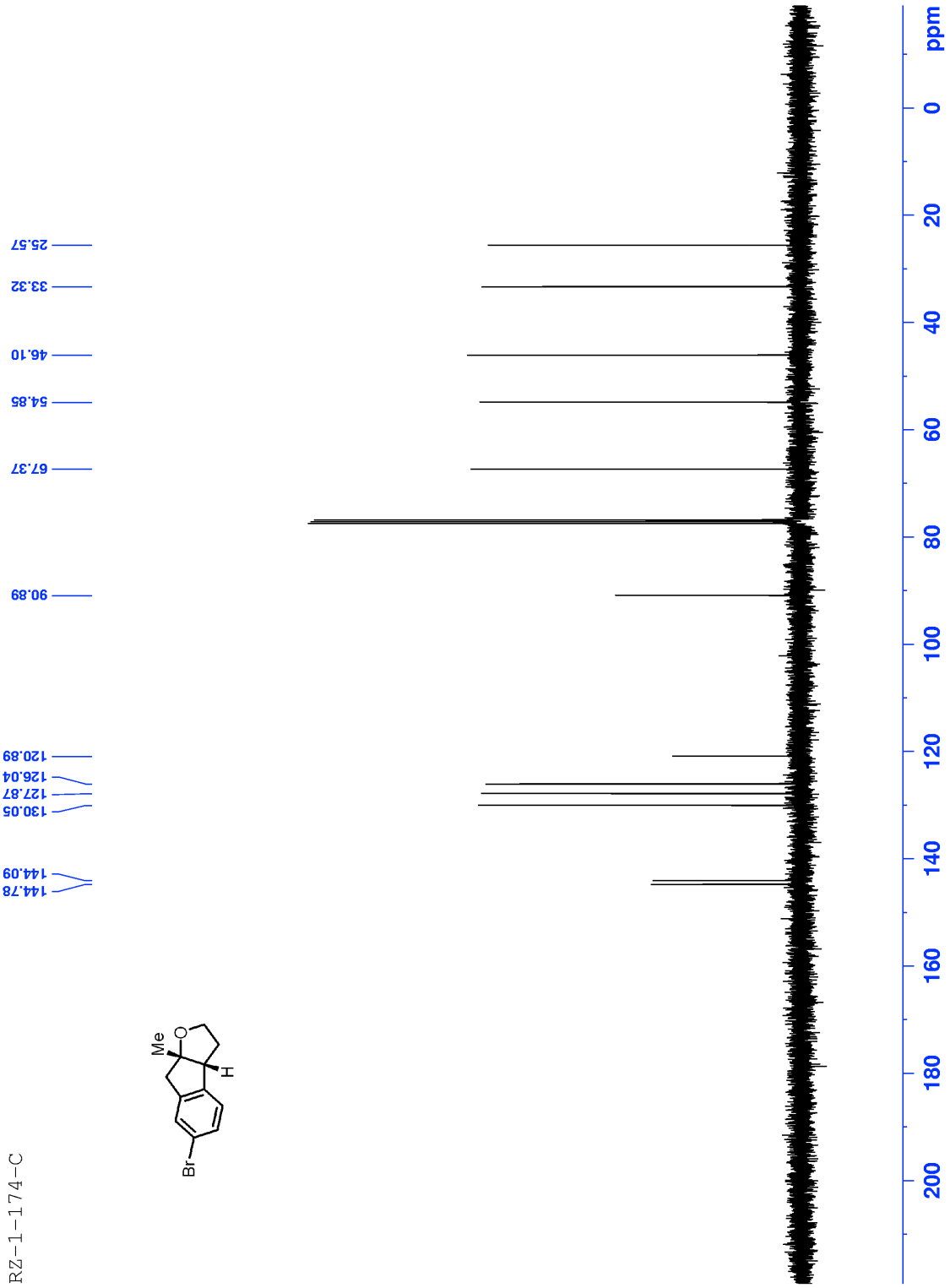

RZ-1-190-H
Me
O
H
O2N
ppm
1
2
3
4
5
6
7
8
9
2.97
1.00
0.99
1.01
1.00
1.96
0.99
0.94
0.93
0.89


RZ-1-190-C
Me
O
H
O2N
25.25
33.09
45.83
55.21
67.30
91.03
120.04
122.82
125.11
144.15
147.83
152.92
ppm
0
20
40
60
80
100
120
140
160
180
200

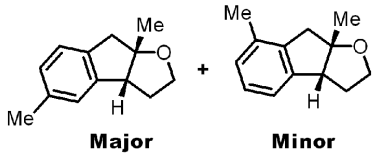

RZ-1-155-H
Me
O
H
Cl
ppm
1
2
3
4
5
6
7
8
9
3.02
1.02
1.03
1.02
1.00
1.02
1.01
1.00
2.03
0.95

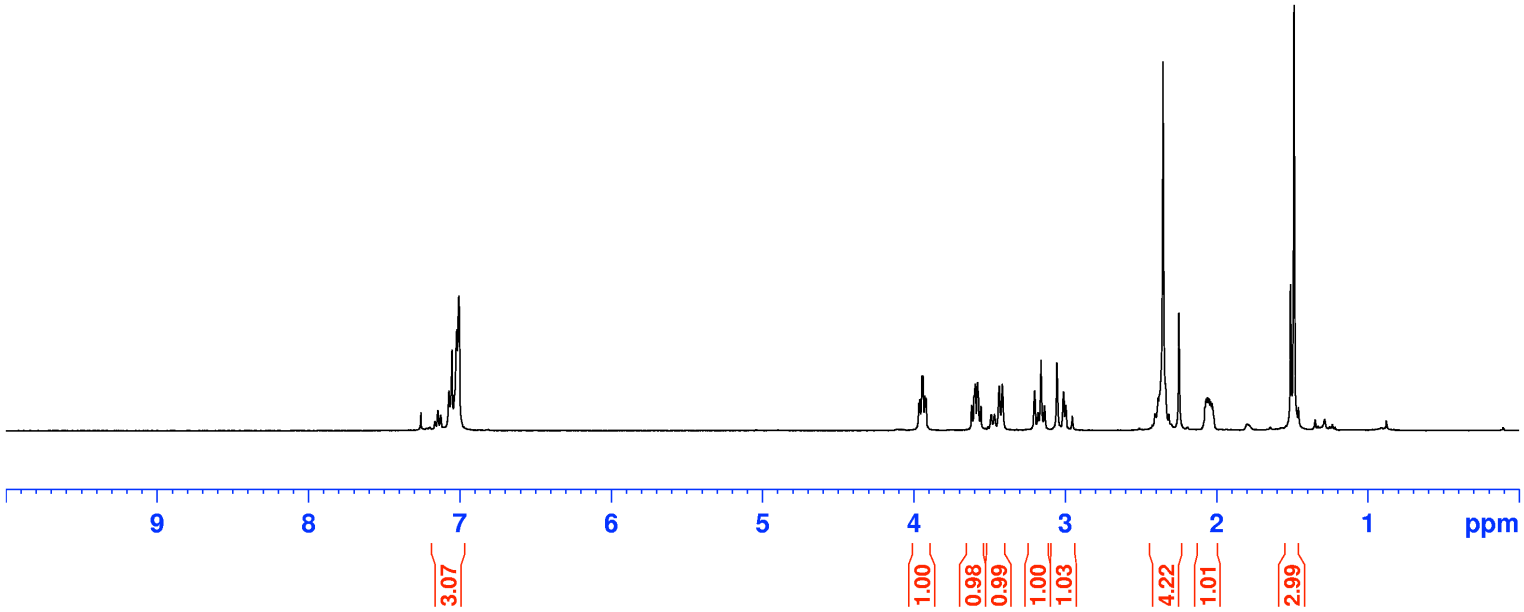

RZ-1-155-C
Me
O
H
Cl
26.08
32.68
46.92
55.51
67.19
89.81
123.07
127.23
128.66
131.12
142.48
144.34
ppm
0
20
40
60
80
100
120
140
160
180
200

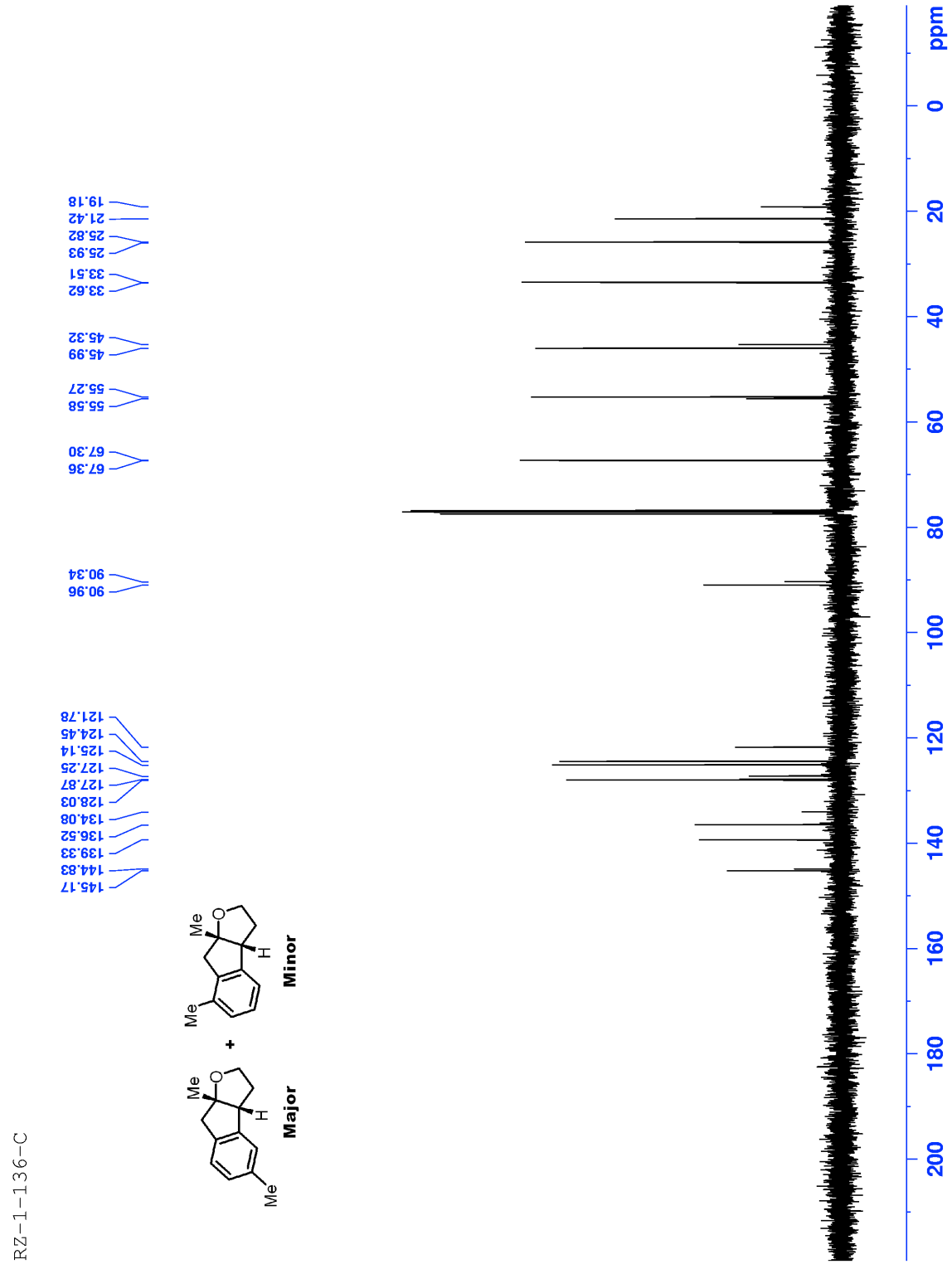

RZ-1-174-H
Me
O
H
Br
ppm
1
2
3
4
5
6
7
8
9
2.98
1.02
1.03
1.01
1.01
0.97
1.01
1.00
0.94
1.84

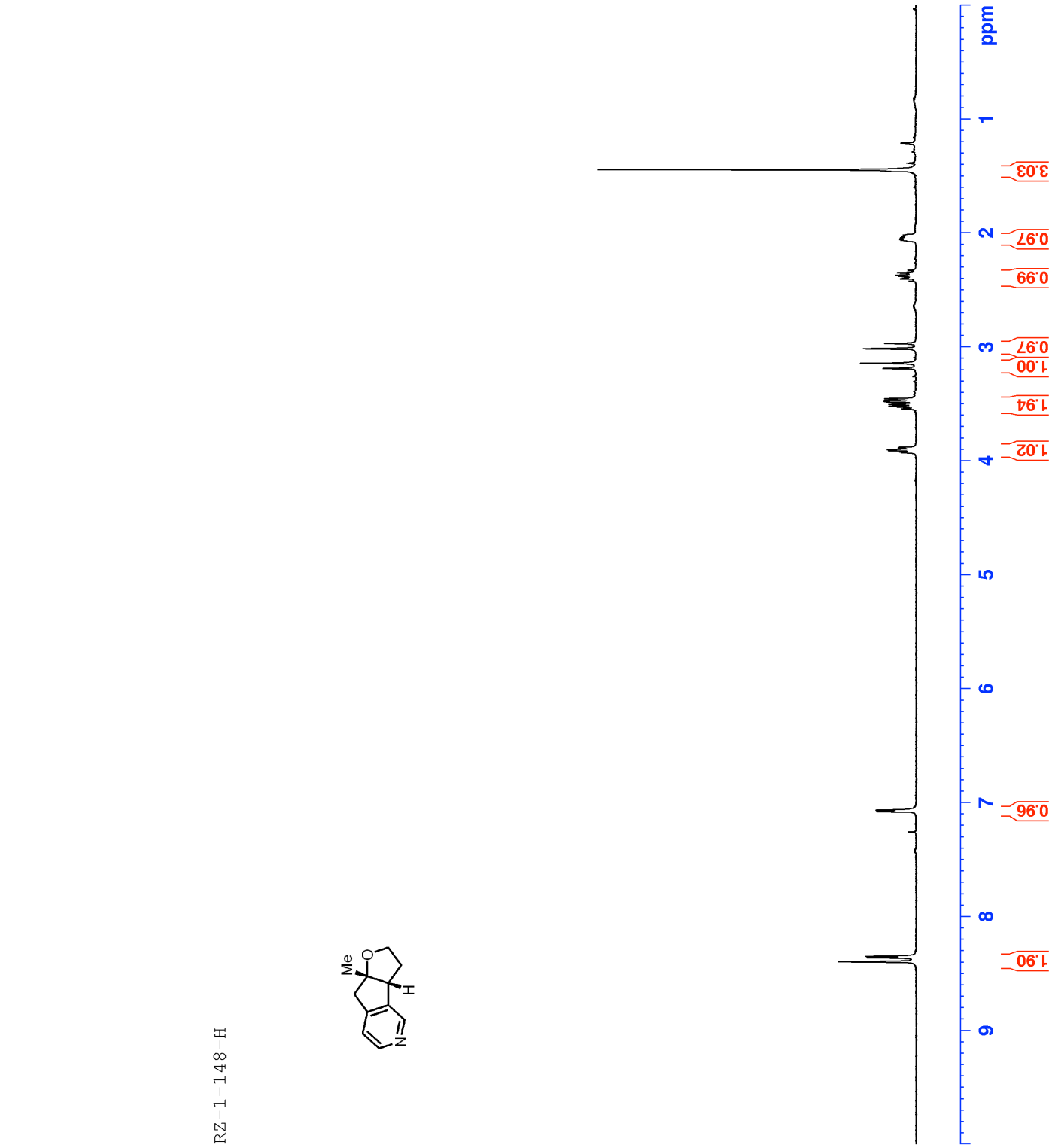

RZ-1-174-C
Me
O
H
Br
25.57
33.32
46.10
54.85
67.37
90.89
120.89
126.04
127.87
130.05
144.09
144.78
ppm
0
20
40
60
80
100
120
140
160
180
200

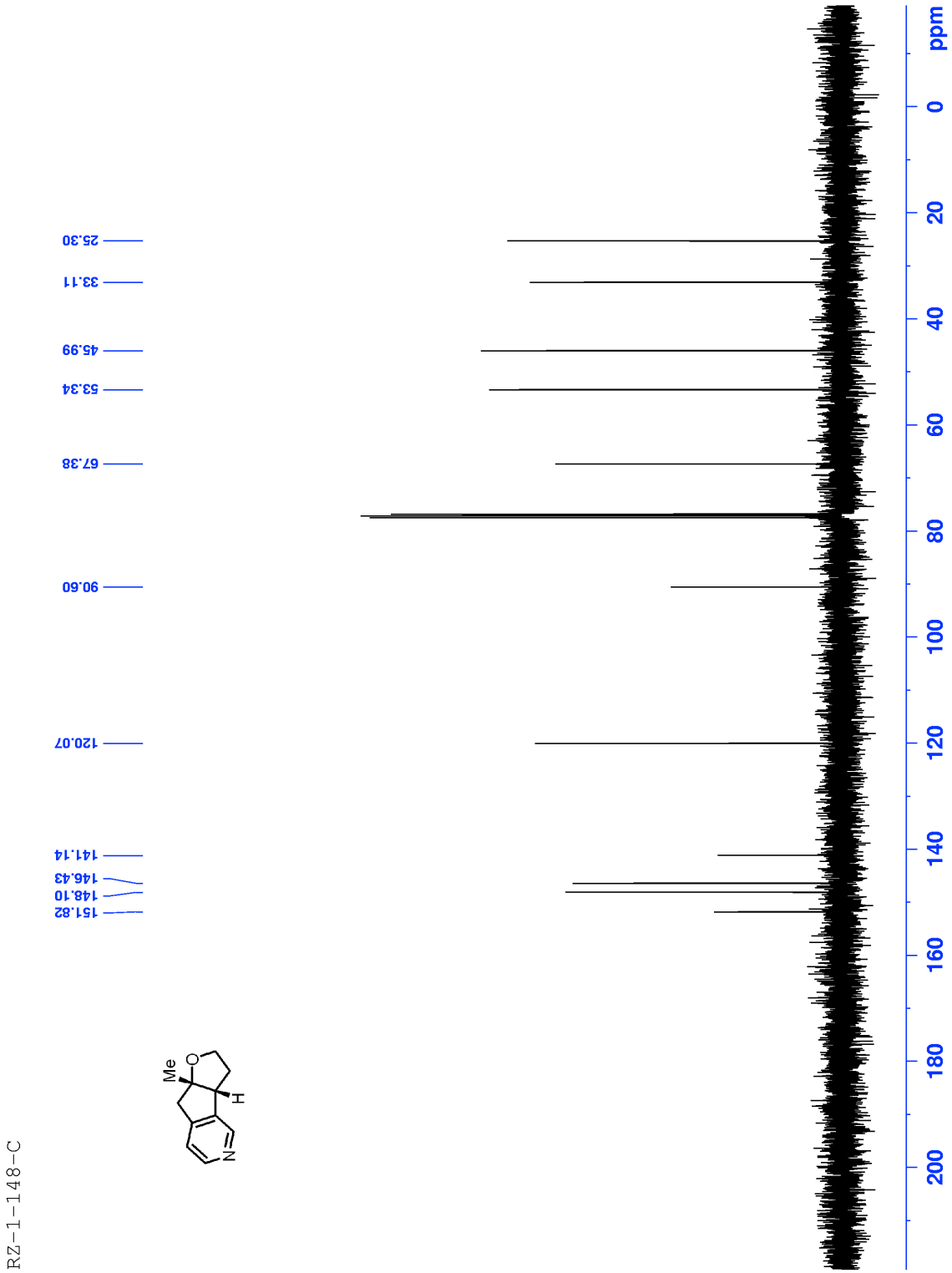
RZ-1-136-H

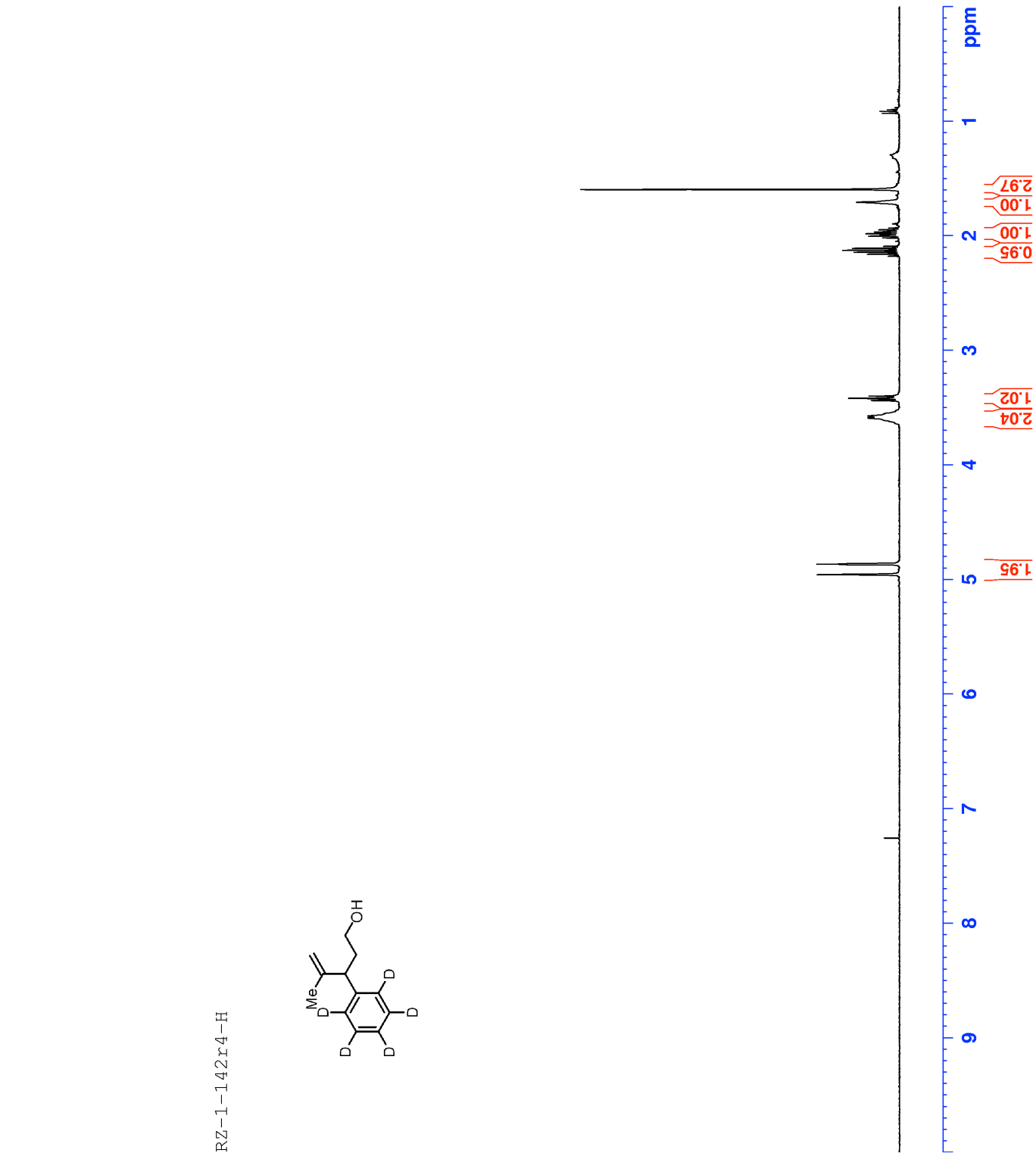

Me
O
H
Me
Major
+
Me
Me
O
H
Minor

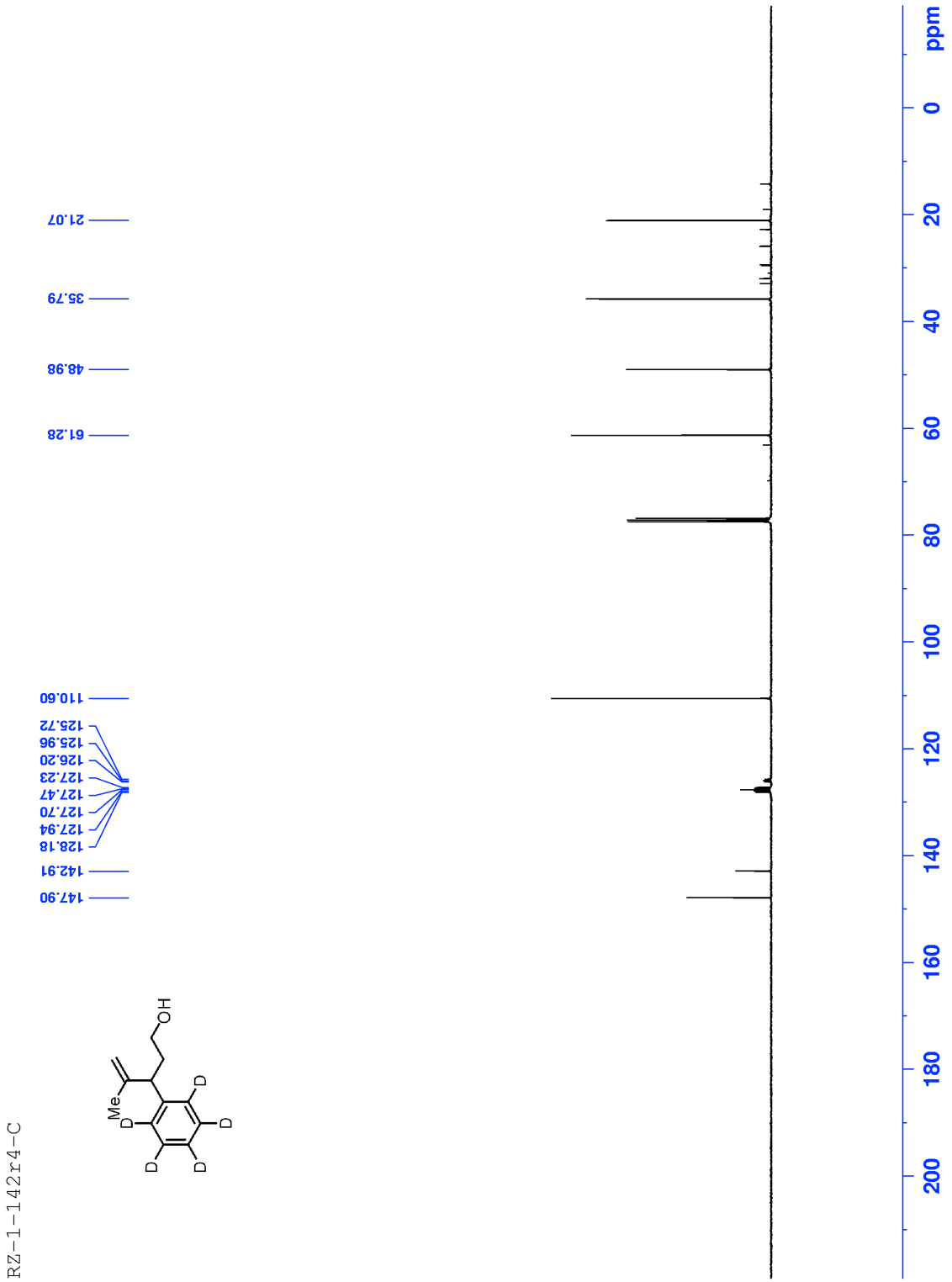

9
8
7
6
5
4
3
2
1
ppm
3.07
1.00
0.98
0.99
1.00
1.03
4.22
1.01
2.99

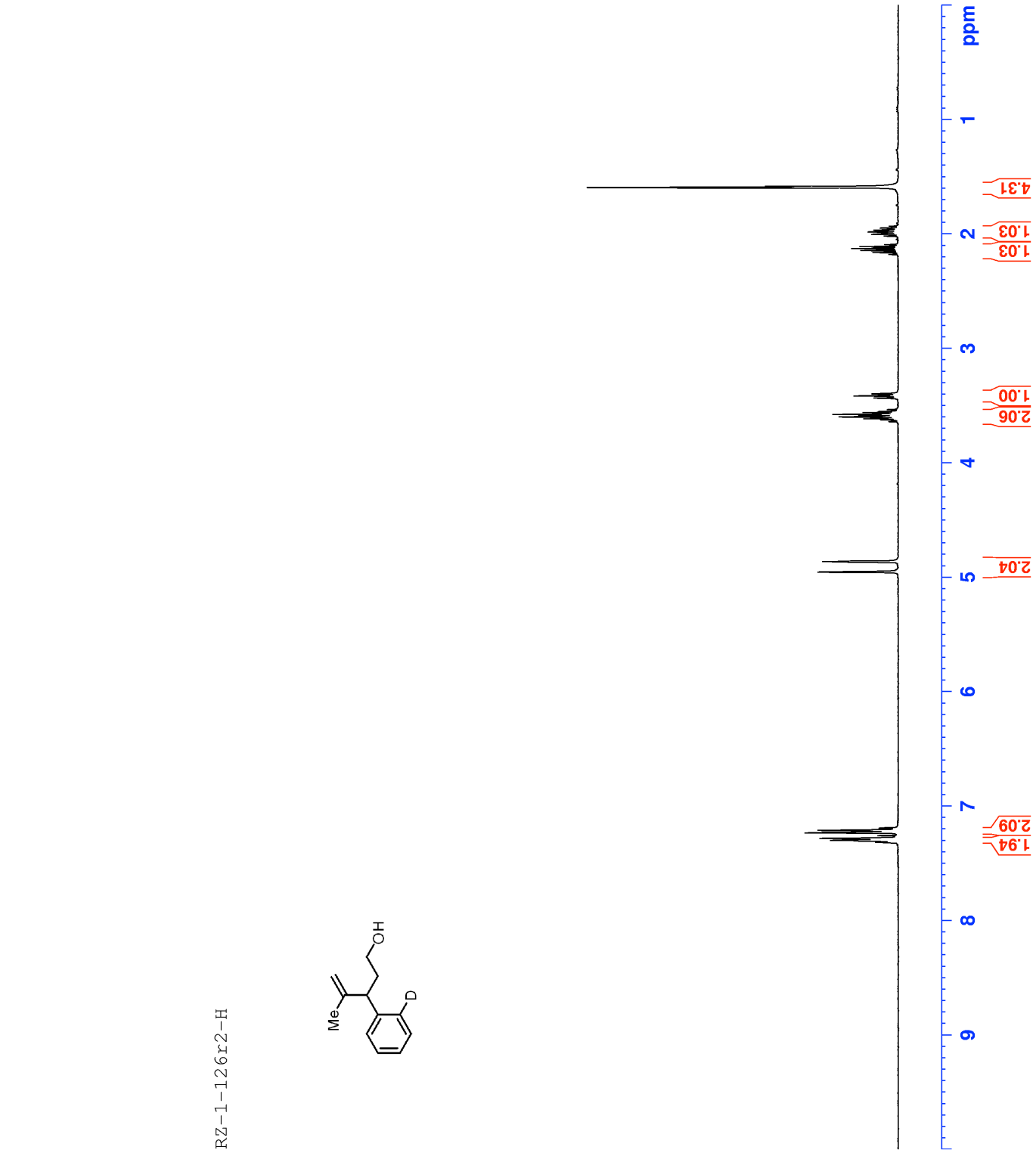

RZ-1-136-C
Me
O
H
Me
Minor
+
Me
O
H
Me
Major
145.17
144.83
139.33
136.52
134.08
128.03
127.87
127.25
125.14
124.45
121.78
90.96
90.34
67.36
67.30
55.58
55.27
45.99
45.32
33.62
33.51
25.93
25.82
21.42
19.18
ppm
200
180
160
140
120
100
80
60
40
20
0

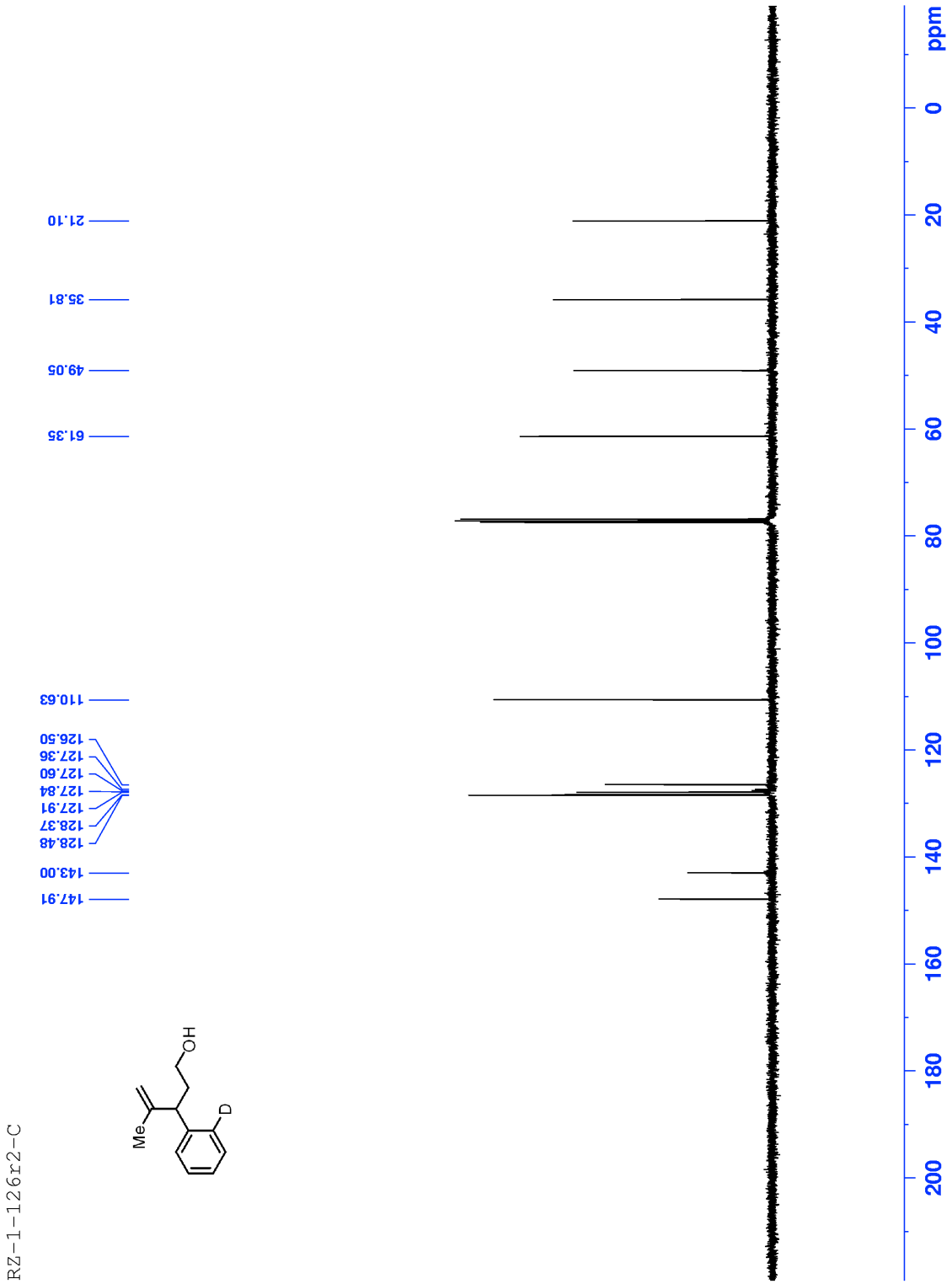

RZ-1-148-H
Me
O
H
N
ppm
1
2
3
4
5
6
7
8
9
3.03
0.97
0.99
0.97
1.00
1.94
1.02
0.96
1.90

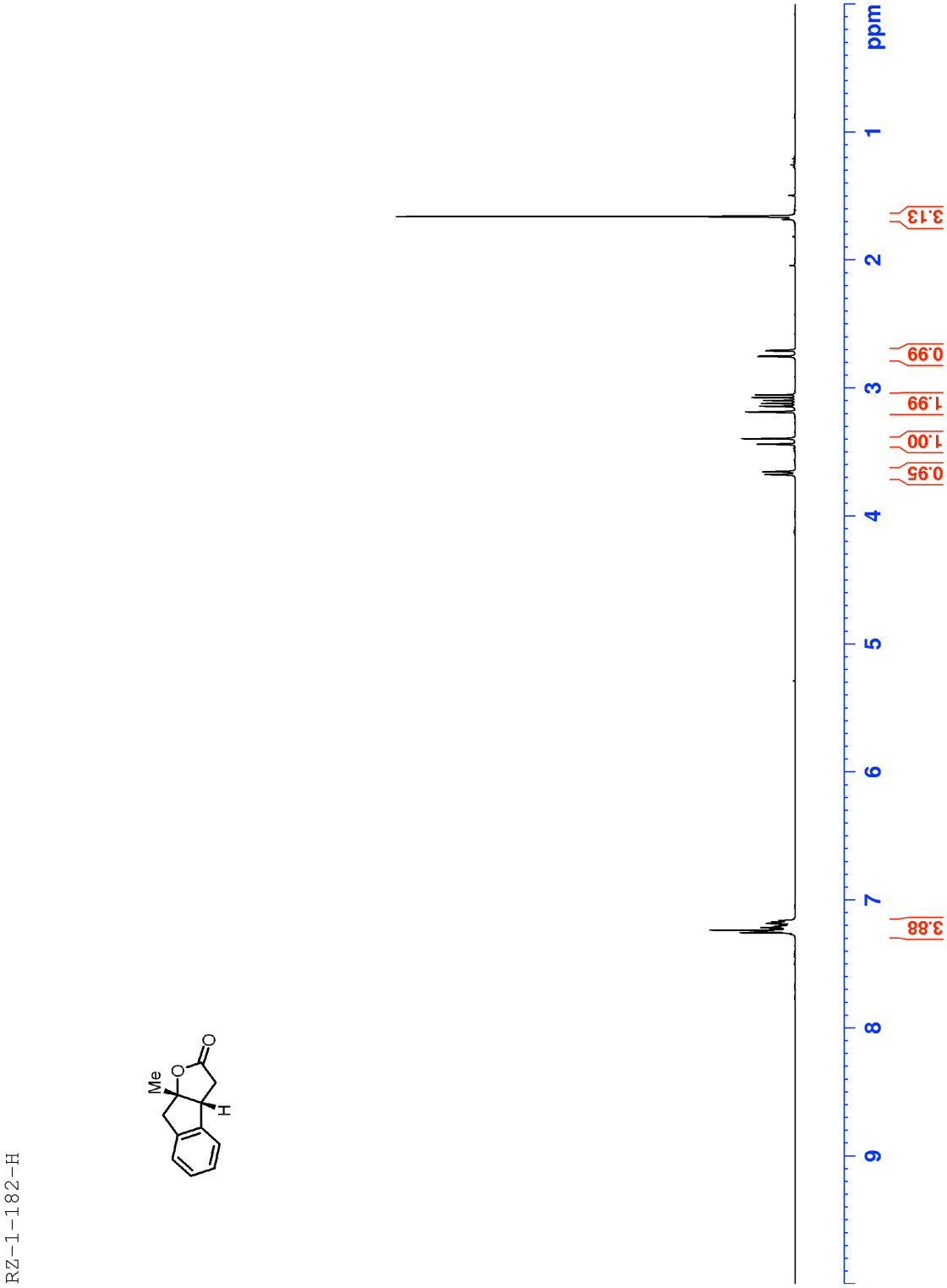

RZ-1-148-C
Me
O
H
N
151.82
148.10
146.43
141.14
120.07
90.60
67.38
53.34
45.99
33.11
25.30
ppm
0
20
40
60
80
100
120
140
160
180
200

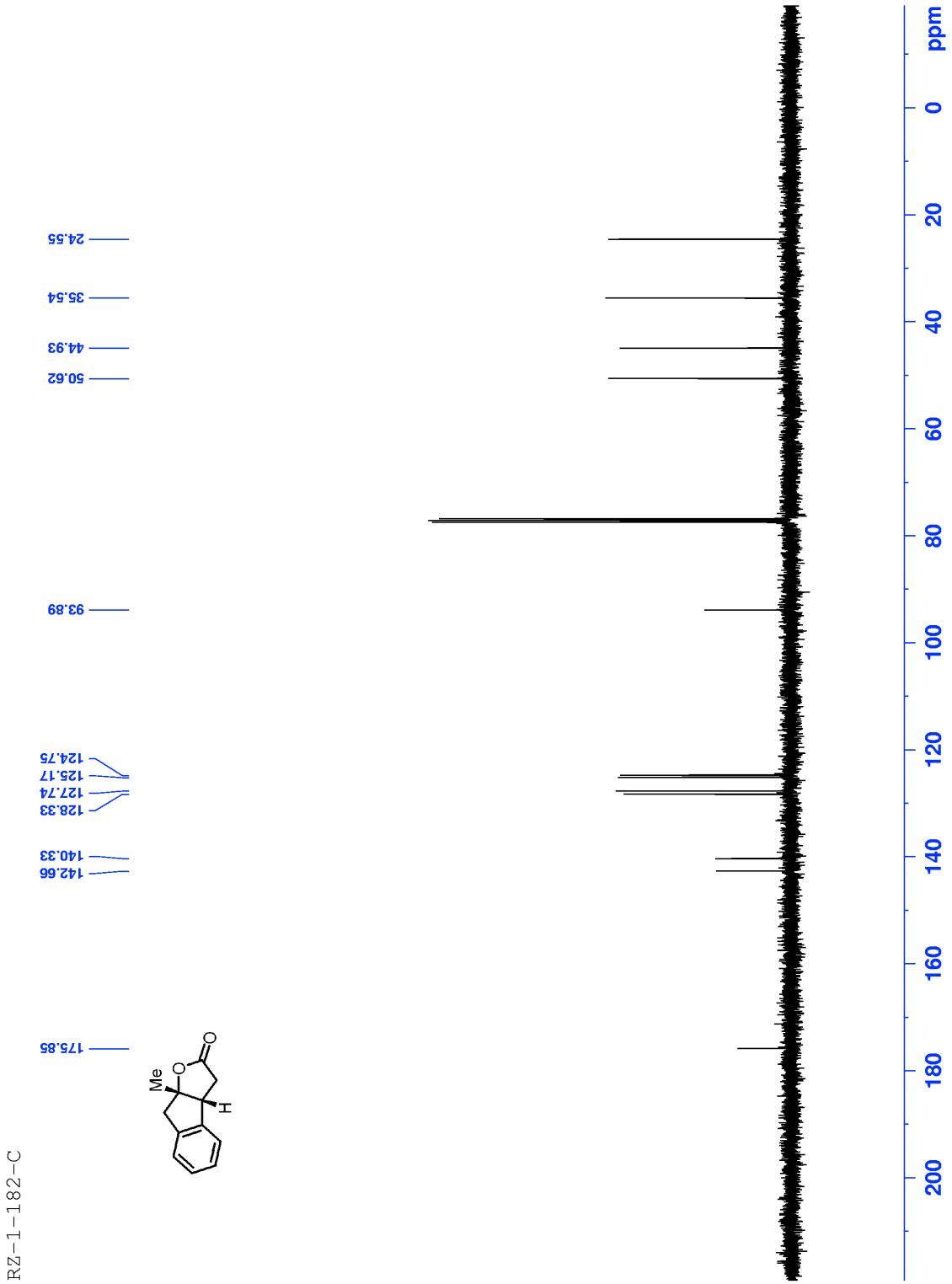

RZ-1-142r4-H
OH
Me
D
D
D
D
D
ppm
1
2
3
4
5
6
7
8
9
2.97
1.00
0.95
1.00
2.04
1.02
1.95

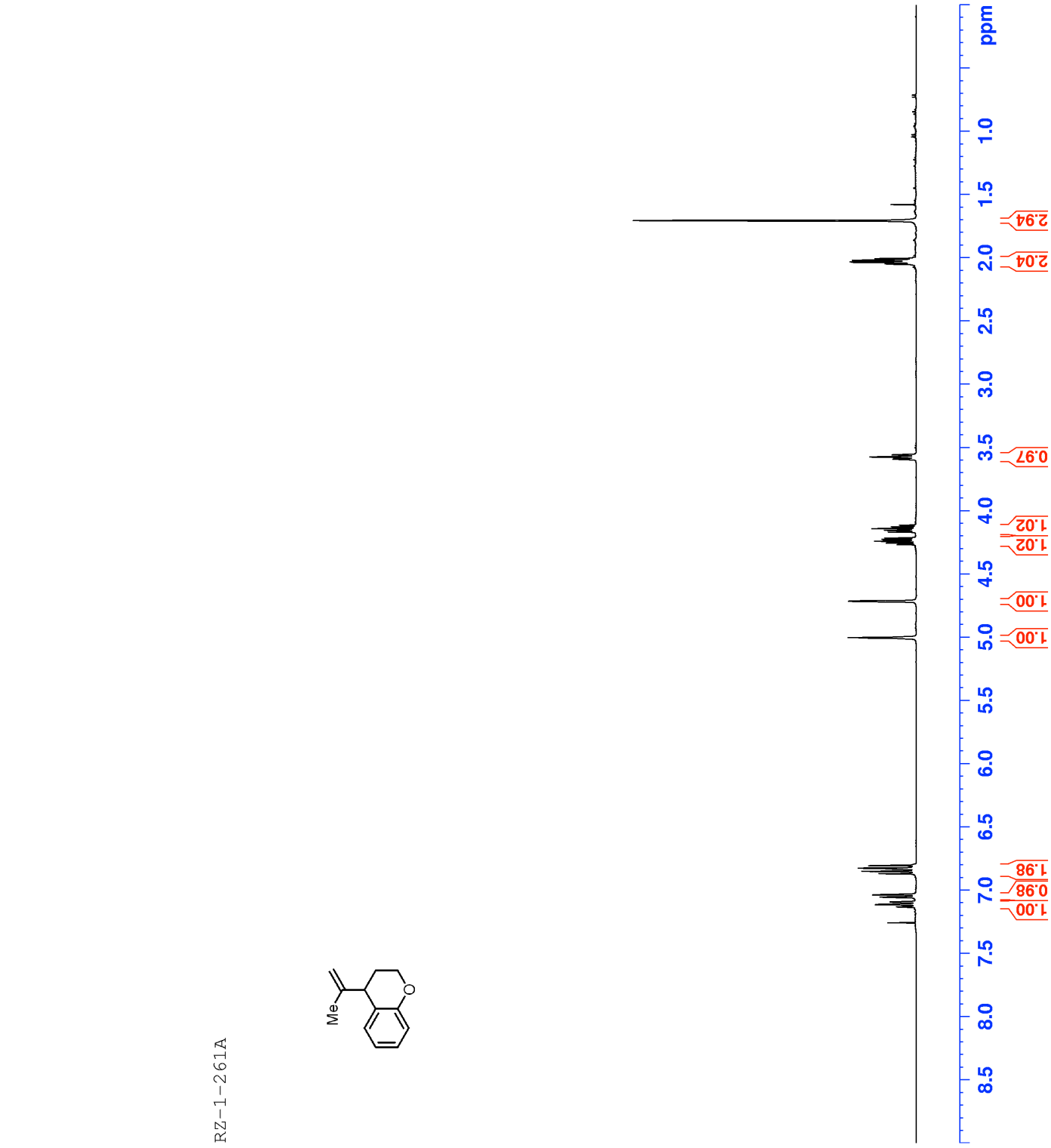

RZ-1-142r4-C
OH
Me
D
D
D
D
D
147.90
142.91
128.18
127.94
127.70
127.47
127.23
126.20
125.96
125.72
110.60
61.28
48.98
35.79
21.07
ppm
0
20
40
60
80
100
120
140
160
180
200

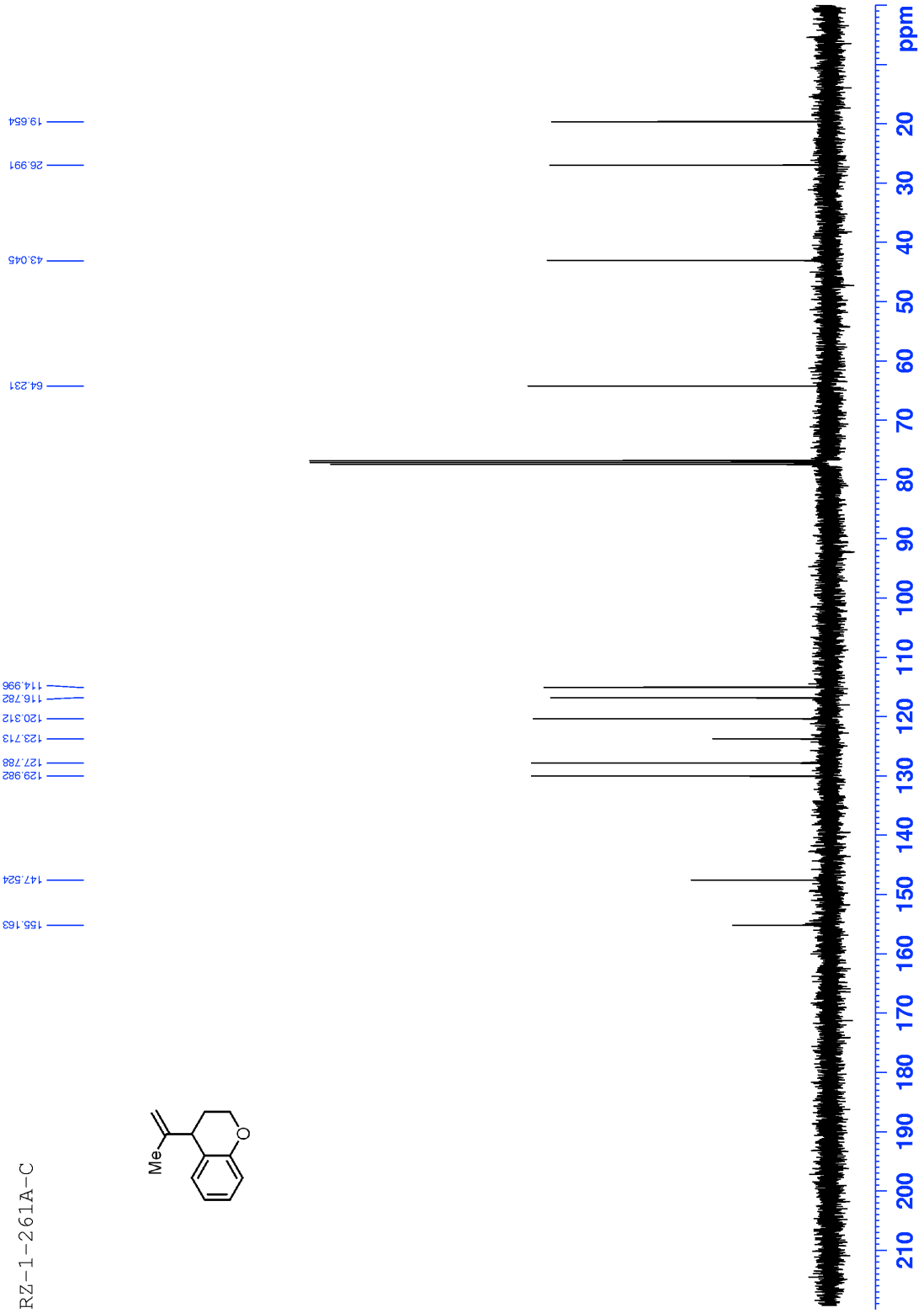

RZ-1-126r2-H
Me
OH
D
ppm
1
2
3
4
5
6
7
8
9
4.31
1.03
1.03
2.06
1.00
2.04
1.94
2.09


RZ-1-126r2-C
Me
OH
D
147.91
143.00
128.48
127.91
127.84
127.60
127.36
126.50
110.63
61.35
49.05
35.81
21.10
ppm
0
20
40
60
80
100
120
140
160
180
200


RZ-1-182-H
Me
O
H
ppm
1
2
3
4
5
6
7
8
9
3.13
0.99
1.99
1.00
0.95
3.88


RZ-1-182-C
175.85
142.66
140.33
128.33
127.74
125.17
124.75
93.89
50.62
44.93
35.54
24.55
Me
H
O
O
ppm
0
20
40
60
80
100
120
140
160
180
200


RZ-1-261A
Me
O
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1.00
0.98
1.98
1.00
1.00
1.02
1.02
0.97
2.04
2.94


RZ-1-261A-C
Me
O
19.654
26.991
43.045
64.231
114.996
116.782
120.312
123.713
127.788
129.982
147.524
155.163
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
200
210