SUPPLEMENTARY MATERIAL

Silver(I)-Catalyzed Addition of Zirconocenes to Epoxy Esters: A New Entry to 1,4-Dicarbonyl Compounds and Pyridazinones

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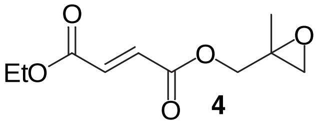
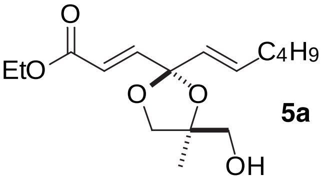
Experimental parts. ^{1}H and ^{13}C NMR spectra for all new compounds.

General: All reactions were performed in flame-dried or oven-dried glassware under a dry nitrogen atmosphere. THF and ether were distilled over Na/benzophenone, while CH_2CH_2 was distilled over CaH_2. Hexane, EtOAc and TMSCl were distilled prior to use. All other reagents and solvents were used as received unless otherwise noted. Analytical thin layer chromatography was performed on pre-coated silica gel 60 F-254 plates available from Merck. Flash chromatography was performed using silica gel 60 (230-400 mesh) available from Baker. NMR spectra were recorded in $CDCl_3$ (or unless otherwise noted) at either 300 MHz (^{1}H NMR) or 75 MHz (^{13}C NMR) using Bruker Avance 300 with XWIN-NMR software. Chemical shifts (δ) are expressed relative to tetramethylsilane. IR spectra were obtained on a Nicolet Avatar 360 FT-IR, optical rotations were measured on a Perkin-Elmer 241 polarimeter, and mass spectra were obtained on a VG-70-70 HF.



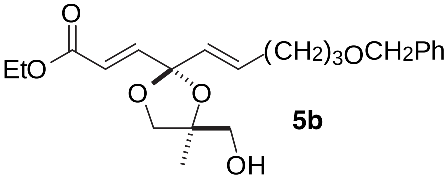
4

But-2-enedioic acid ethyl ester 2-methyl-oxiranylmethyl ester (4). A solution of monoethyl fumarate (7.50 g, 52.0 mmol) in 100 mL of CH_2Cl_2 was cooled to 0 °C and 600 mg (4.91 mmol) of DMAP was added followed by 2-methyl-2-propen-1-ol (5.00 mL, 59.4 mmol) and DCC (12.0 g, 58.2 mmol). After 1 h the reaction mixture was warmed to room temperature and stirred for another 11 h. Filtration of the byproducts, concentration, and chromatography on SiO_2 (hexane/EtOAc, 20:1) yielded 9.51 g (92%) of the diester which was redissolved in 100 mL of CH_2Cl_2. At 0 °C, mCPBA (16.57 g; 48.0 mmol assuming 50% purity) was added portionwise. After 3 h the cooling bath was removed and stirring was continued for 9 h. The suspension was treated with 1.5 M $Na_2S_2O_5$, stirred for 90 min, and the organic layer was washed with 2 N NaOH. The solution was dried (Na_2SO_4), filtered, and concentrated to give 10.05 g (90% based on monoethyl fumarate) of oily **4**: IR (neat) 2985, 2941, 1722, 1390, 1376, 1303, 1264, 1228, 1157, 1033, 984 cm^{-1}; ^{1}H NMR δ 6.93 (s, 2 H), 4.41 (d, 1 H, J = 12.0 Hz), 4.30 (q, 2 H, J = 7.1 Hz), 4.12 (d, 1 H, J = 12.0 Hz), 2.84 (d, 1 H, J = 4.7 Hz), 2.74 (d, 1 H, J = 4.7 Hz), 1.45 (s, 3 H), 1.36 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 164.6, 164.4, 134.3, 132.8, 67.9, 61.3, 54.5, 51.7, 18.3, 14.0; MS (EI) *m/z* (rel intensity) 169 (M$^+$, 0.3), 155 (0.3), 145 (1), 141 (2), 138 (2), 127 (100), 99 (6), 82 (5), 71 (7), 55 (12); HRMS (EI) *m/z* calculated for $C_{10}H_{14}O_5$ 169.0501, found 169.0504.



5a

General procedure A for alkenylzirconocene addition to 4 (5a-d). (2*SR*,4*SR*)-3-[(2-Hex-1-(*E*)-enyl)-4-hydroxymethyl-4-methyl-[1,3]dioxolan-2-yl)]-acrylic acid ethyl ester (5a). A solution of 110 mg (1.34 mmol) of 1-hexyne in 7 mL of CH_2Cl_2 was treated portionwise with 366 mg (1.43 mmol) of Cp_2ZrHCl[1] and stirred for 20 min. At 0 °C, the epoxy-ester **4** (212 mg, 0.991 mmol) was added via syringe followed by $P(OPh)_3$ (22 mg, 0.071 mmol, 0.05 eq.) and 20 wt% $AgClO_4$/Celite (74 mg, 0.072 mmol Ag(I), 0.05 eq.). After stirring at room temperature overnight, the mixture was diluted with 5 mL of CH_2Cl_2, filtered through a plug of SiO_2, washed twice with 10% HCl and then twice with saturated $NaHCO_3$. The organic layer was dried ($MgSO_4$), filtered, and concentrated. Chromatography on SiO_2 (hexane/EtOAc, 4:1) provided recovered epoxy-ester **4** (17 mg; 8%) and 215 mg (73%) of oily **5a** as a single diastereomer: IR (neat) 3491, 2958, 2931, 2874, 1723, 1664, 1466, 1392, 1369, 1302, 1268, 1176, 1123, 1039, 978 cm^{-1}; ^{1}H NMR δ 6.81 (d, 1 H, J = 15.5 Hz), 6.10 (d, 1 H, J = 15.7 Hz), 5.87 (dt, 1 H, J = 15.6 Hz), 5.49 (d, 1 H, J = 15.7 Hz), 4.19 (q, 2 H, J = 7.1 Hz), 4.01 (d, 1 H, J = 8.4 Hz), 3.62 (d, 1 H, J = 8.4 Hz), 3.47-3.56 (m, 2 H), 2.25-2.15 (br, 1H), 2.03 (q, 2 H, J = 6.7 Hz), 1.22-1.37 (m, 10 H), 0.86 (t, 3 H, J = 7.0 Hz); ^{13}C NMR δ 166.4, 146.5, 134.7, 128.5, 121.5, 107.0, 82.7, 71.7, 67.3, 60.8, 31.8, 30.9, 22.3, 21.4, 14.3, 14.0; MS (EI) *m/z* (rel intensity) 298 (M$^+$, 2), 267 (57), 253 (20), 225 (100), 215 (20), 199 (45), 193 (25), 137 (62), 130 (55), 111 (43), 71 (44), 55 (52); HRMS (EI) *m/z* calculated for $C_{16}H_{26}O_5$ 298.1780, found 298.1769.



5b

(2*SR*,4*SR*)-3-[2-(5-Benzyloxy-pent-1-(*E*)-enyl))-4-hydroxymethyl-4-methyl-[1,3]dioxolan-2-yl)]-acrylic acid ethyl ester (5b). According to general procedure A, 587 mg (2.74 mmol) of epoxy ester **4** and 530 mg (3.04 mmol) of *O*-benzyl-1-pentynol provided recovered **4** (70 mg, 12%) and 736 mg (69%) of oily **5b** as a single diastereomer: IR (neat) 3473, 2979, 2935, 2871, 1720, 1661, 1454, 1367, 1301, 1268, 1175, 1099, 1039, 978 cm^{-1}; ^{1}H NMR δ 7.35-7.25 (m, 5 H), 6.83 (d, 1 H, J = 15.7 Hz), 6.13 (d, 1 H. J = 15.5 Hz), 5.92 (dt, 1 H, J = 15.7,

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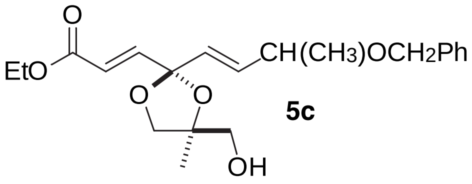
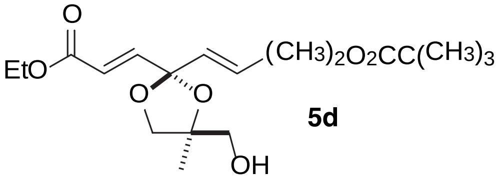
[1] Buchwald, S. L.; La Maire, S. J.; Nielson, R. B.; Watson, B. T.; King, S. M. *Tetrahedron Lett.* **1987**, *28*, 3895.

6.7 Hz), 5.53 (d, 1 H, *J* = 15.6 Hz), 4.49 (s, 2 H), 4.22 (q, 2 H, *J* = 7.1 Hz), 4.02 (d, 1 H, *J* = 8.4 Hz), 3.64 (d, 1 H, *J* = 8.3 Hz), 3.5-3.4 (m, 4 H), 2.17 (dt, 2 H, *J* = 7.1, 6.6 Hz), 2.1-2.0 (m, 1H), 1.75-1.66 (m, 2 H), 1.34-1.24 (m, 6 H); ^{13}C NMR δ 166.4, 146.4, 138.6, 133.8, 129.1, 128.5, 127.8, 127.7, 121.6, 106.9, 82.8, 73.0, 71.7, 69.6, 67.2, 60.8, 28.9, 21.5, 14.3; MS (EI) *m/z* (rel intensity) 390 (M^+, 0.1), 359 (0.5), 345 (2), 317 (14), 291 (6), 130 (14), 91 (100), 84 (34), 71 (22); HRMS (EI) *m/z* calculated for $C_{22}H_{30}O_6$ 390.2042, found 390.2046.



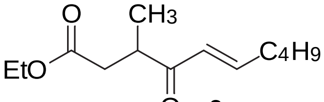
5c

(2*SR*,4*SR*)-3-[2-(3-Benzyloxy-but-1-(*E*)-enyl)-4-hydroxymethyl-4-methyl-[1,3]dioxolan-2-yl)]-acrylic acid ethyl ester (5c). According to general procedure A with an additional 3 mol% Ag(I) added after 4 h, 225 mg (1.05 mmol) of **4** and 200 mg (1.25 mmol) of *O*-benzyl-3-butyn-2-ol gave 95 mg (42%) of recovered **4** and 122 mg (31%) of oily **5c** as a ca. 10:1 mixture of diastereomers. Major diastereomer: IR (neat) 3432, 2977, 2917, 2871, 2849, 1722, 1659, 1651, 1454, 1369, 1303, 1274, 1177, 1112, 1038 cm^{-1}; ^{1}H NMR δ 7.33-7.25 (m, 5 H), 6.85 (d, 1 H, *J* = 15.7 Hz), 6.16 (d, 1 H. *J* = 15.6 Hz), 5.92 (dd, 1 H, *J* = 15.7, 6.7 Hz), 5.72 (d, 1 H, *J* = 15.9 Hz), 4.54 (d, 1 H, *J* = 11.8 Hz), 4.39 (d, 1 H, *J* = 11.9 Hz), 4.23 (q, 2 H, *J* = 7.1 Hz), 4.04 (d, 1 H, *J* = 8.3 Hz), 3.99 (m, 1 H, *J* = 6.5 Hz), 3.67 (d, 1 H, *J* = 8.3 Hz), 3.55, 3.49 (AB, 2H, *J* = 11.3 Hz), 2.0-1.9 (bm, 1H), 1.35-1.27 (m, 9 H); ^{13}C NMR δ 166.3, 145.9, 138.5, 135.2, 130.0, 128.5, 127.8, 121.9, 106.7, 83.0, 74.7, 71.7, 70.4, 67.1, 60.9, 21.5, 21.4, 14.3; MS (EI) *m/z* (rel intensity) 376 (M^+, 0.2), 361 (0.6), 347 (0.3), 331 (8), 303 (15), 285 (29), 270 (16), 241 (30), 215 (25), 189 (17), 182 (17), 153 (17), 127 (24), 91 (100); HRMS (EI) *m/z* calculated for $C_{19}H_{23}O_5$ [$M-OCH_2CH_3$] 331.1545, found 331.1543.



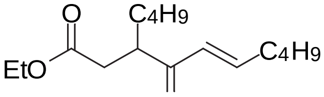
5d

(2*SR*,4*SR*)-3-{2-[4-(2,2-Dimethyl-propionyloxy)-but-1-(*E*)-enyl]-4-hydroxymethyl-4-methyl-[1,3]dioxolan-2-yl)-acrylic acid ethyl ester (5d). According to general procedure A, 190 mg (0.888 mmol) of **4** and 125 mg (0.811 mmol) of *O*-pivaloyl-3-butynol provided 198 mg (66%) of oily **5d** as a single diastereomer: IR (neat) 3435, 2978, 2930, 2875, 1726, 1660, 1481, 1368, 1302, 1161, 1039 cm^{-1}; ^{1}H NMR δ 6.81 (d, 1 H, *J* = 15.5 Hz), 6.12 (d, 1 H. *J* = 15.6 Hz), 5.89 (dt, 1 H, *J* = 15.7, 6.8 Hz), 5.61 (d, 1 H, *J* = 15.6 Hz), 4.21 (q, 2 H, *J* = 7.1 Hz), 4.12 (t, 2 H, *J* = 6.3 Hz), 4.03 (d, 1 H, *J* = 8.4 Hz), 3.65 (d, 1 H, *J* = 8.3 Hz), 3.54, 3.48 (AB, 2H, *J* = 11.3 Hz), 2.39 (dt, 2 H, *J* = 6.5, 5.5 Hz), 2.0-1.8 (bm, 1 H), 1.32-1.27 (m, 6 H), 1.17 (s, 9 H); ^{13}C NMR δ 178.6, 166.3, 146.2, 131.2, 129.6, 121.7, 106.7, 82.9, 71.7, 67.3, 62.9, 60.8, 38.9, 31.6, 27.3, 21.5, 14.3; MS (EI) *m/z* (rel intensity) 370 (M^{+}, 1), 324 (6), 296 (16), 236 (46), 194 (35), 180 (16), 168 (27), 129 (24), 106 (55), 81 (33), 71 (29), 57 (100); HRMS (EI) *m/z* calculated for $C_{19}H_{30}O_7$ 370.1992, found 370.2005.



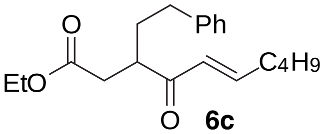
6a

General procedure B for the conjugate addition to dialkenyl acetals (6a-c, 6e-f). 3-Methyl-4-oxo-dec-5-enoic acid ethyl ester (6a). A suspension of CuBr•SMe$_2$ (1.13 g, 5.50 mmol) in 20 mL of THF at -78 °C was treated with 7.9 mL (11.1 mmol) of a 1.4 M solution of MeLi in ether. The reaction mixture was warmed to -20 °C and stirred until colorless. At -78 °C, 0.70 mL (5.52 mmol) of TMSCl was added followed by a precooled solution of **5a** (549 mg, 1.84 mmol) in 2 mL of THF. Over a 30 min period the temperature was raised to -25 °C and the solution was stirred at that temperature for another 20 min before being quenched by dropwise addition of 4 mL of 10% HCl. The mixture was diluted with EtOAc, and washed with 10% HCl and saturated NaHCO$_3$. The organic layer was concentrated, dissolved in 20 mL of acetone/H$_2$O (9:1), and treated with TsOH (70 mg, 0.37 mmol). The reaction mixture was heated at reflux for 6 h, concentrated to 5 mL, poured into saturated NaHCO$_3$ solution, and extracted with EtOAc. The combined organic layers were dried (MgSO$_4$), filtered and concentrated. Chromatography on SiO$_2$ (hexane/EtOAc, 20:1) gave 398 mg (96%) of oily **6a**: IR (neat) 2967, 2931, 2872, 1735, 1695, 1673, 1630, 1184 cm^{-1}; ^{1}H NMR δ 6.89 (dt, 1 H, *J* = 15.7, 7.1 Hz), 6.13 (dt, 1 H, *J* = 15.6, 1.4 Hz), 4.06 (q, 2 H, *J* = 7.1 Hz), 3.28-3.12 (m, 1 H), 2.74 (dd, 1 H, *J* = 16.6, 8.3 Hz), 2.30-2.15 (m, 3 H), 1.45-1.20 (m, 4 H), 1.20 (t, 3 H, *J* = 7.1 Hz), 1.10 (d, 3 H, *J* = 7.2 Hz), 0.89 (t, 3 H, *J* = 7.1 Hz); ^{13}C NMR δ 201.9, 172.3, 148.1, 128.5, 60.4, 39.7, 37.0, 32.2, 30.2, 22.3, 17.1, 14.1, 13.8; MS (EI) *m/z* (rel intensity) 226 (M^{+}, 8), 199 (5), 181 (20), 165 (3), 143 (14), 125 (15), 111 (100), 95 (12), 84 (12), 68 (15), 55 (67); HRMS (EI) *m/z* calculated for $C_{13}H_{22}O_3$ 226.1569, found 226.1562.



6b

3-Butyl-4-oxo-dec-5-enoic acid ethyl ester (6b). According to general procedure B, 500 mg (1.68 mmol) of acetal **5a** and Bu_2CuLi (4.8 eq.) provided 401 mg (89%) of ketoester **6b** as an oil: IR (neat) 2958, 2930, 2872, 2861, 1736, 1695, 1670, 1628, 1178 cm^{-1}; ^{1}H NMR δ 6.89 (dt, 1 H, J = 15.7, 7.0 Hz), 6.16 (dt, 1 H, J = 15.7, 1.5 Hz), 4.06 (q, 2 H, J = 7.1 Hz), 3.25-3.15 (m, 1 H), 2.74 (dd, 1 H, J = 16.7, 9.3 Hz), 2.34 (dd, 1 H, J = 16.7, 4.9 Hz), 2.25-2.15 (m, 2 H), 1.65-1.50 (m, 1 H), 1.46-1.17 (m, 13 H), 0.89 (t, 3 H, J = 7.2 Hz), 0.84 (t, 3 H, J = 7.1 Hz); ^{13}C NMR δ 202.0, 172.4, 147.8, 129.4, 60.4, 44.7, 35.4, 32.1, 31.6, 30.1, 29.0, 22.6, 22.2, 14.1, 13.8; MS (EI) *m/z* (rel intensity) 268 (M$^+$, 8), 223 (41), 212 (43), 185 (5), 166 (5), 139 (5), 111 (100), 84 (14), 69 (13), 68 (12); HRMS (EI) *m/z* calculated for $C_{16}H_{28}O_3$ 268.2038, found 268.2037.



6c

4-Oxo-3-phenethyl-dec-5-enoic acid ethyl ester (6c). According to general procedure B, 170 mg (0.570 mmol) of acetal **5a** and $(PhCH_2CH_2)_2CuLi$[2] (4.9 eq.) gave 165 mg (92%) of oily **6c**: IR (neat) 2957, 2930, 2861, 1735, 1694, 1668, 1627, 1455, 1372, 1182, 1113 cm^{-1}; ^{1}H NMR δ 7.30-7.13 (m, 5 H), 6.84 (dt, 1 H, J = 15.7, 6.8 Hz), 4.09 (q, 2 H, J = 7.1 Hz), 3.27-3.24 (m, 1 H), 2.82 (dd, 1 H, J = 16.5, 9.2 Hz), 2.59 (t, 2 H, J = 8.0 Hz), 2.43 (dd, 1 H, J = 16.5, 5.0 Hz), 2.25-2.18 (m, 2 H), 2.0-1.9 (m, 1 H), 1.8-1.7 (m, 1 H), 1.5-1.3 (m, 4 H), 1.23 (t, 3 H, J = 7.1 Hz), 0.89 (t, 3 H, J = 7.3 Hz); ^{13}C NMR δ 201.9, 172.4, 148.6, 141.3, 129.5, 128.6, 128.5, 126.2, 60.7, 44.2, 35.6, 33.7, 33.2, 32.4, 30.3, 22.4, 14.3, 14.0; MS (EI) *m/z* (rel intensity) 316 (M$^+$, 3), 271 (20), 212 (100), 187 (40), 166 (34), 139 (50), 117 (24), 111 (52), 91 (97), 55 (95); HRMS (EI) *m/z* calculated for $C_{20}H_{28}O_3$ 316.2038, found 316.2025.

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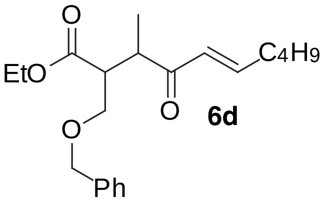
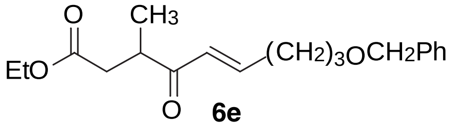
[2] Preparation of $PhCH_2CH_2Li$: Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.* **1990**, *55*, 5404.



6d

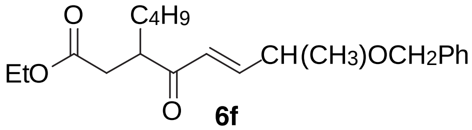
General procedure C for bisfunctionalization of dialkenyl acetals (6d, 6g). 2-Benzyloxymethyl-3-methyl-4-oxo-dec-5-enoic acid ethyl ester (6d). A suspension of CuBr•SMe$_2$ (648 mg, 3.15 mmol) in 3 mL of THF was treated at -78 °C with 4.50 mL (6.30 mmol) of a 1.4 M solution of MeLi in ether. The reaction mixture was slowly warmed to -20 °C, stirred 30 min and then recooled to -78 °C. Subsequently, TMSCl (1.00 mL, 7.88 mmol) was added followed by a solution of acetal **5a** (180 mg, 0.604 mmol) in 1 mL of THF. The temperature was raised to -30 °C and the reaction mixture was stirred for 2 h before quenching with saturated NH$_4$Cl. The mixture was diluted with 5 mL of ether and the organic layer washed with 10% HCl and 2 N NaOH, dried (MgSO$_4$), filtered, and concentrated. The residue was dissolved in 3 mL of CH$_2$Cl$_2$ and treated with imidazole (100 mg, 1.47 mmol) and TBSCl (140 mg, 0.933 mmol). After stirring for 10 h, the mixture was washed with 10% HCl and saturated NaHCO$_3$, dried (MgSO$_4$), filtered, concentrated and chromatographed on SiO$_2$ (hexane/EtOAc, 9:1) to provide 230 mg (89%) of the intermediate protected acetal: ^{1}H NMR δ 5.76 (dt, 1 H, J = 15.5, 7.0 Hz), 5.37 (dd, 1 H, J = 15.7, 1.4 Hz), 4.13 (q, 2 H, J = 7.1 Hz), 3.88-3.84 (m, 1 H), 3.64-3.43 (m, 3 H), 2.63 (dd, 1 H, J = 15.2, 4.5 Hz), 2.3-2.2 (m, 1 H), 2.1-1.95 (m, 3 H), 1.4-1.2 (m, 10 H), 0.97-83 (m, 15 H), 0.03 (m, 6 H).

A solution of this acetal (65 mg, 0.152 mmol) in 1 mL of THF was treated at -78 °C with 2.0 M LDA in heptane/THF/ethylbenzene (0.100 mL, 0.200 mmol), warmed slowly (30 min) to -30 °C, and recooled to -78 °C. After addition of PhCH$_2$OCH$_2$Cl (30 μL, 0.216 mmol), the cooling bath was removed and after 3 h the solution was diluted with 3 mL of ether and washed with 10% HCl and saturated NaHCO$_3$ solution. The mixture was concentrated and redissolved in 5 mL of acetone/water (4:1). TsOH was added (3 mg, 0.016 mmol) and the mixture was heated at reflux for 6 h, diluted with ether, washed with 10% HCl and saturated NaHCO$_3$ solution, and dried (MgSO$_4$). Filtration, concentration and chromatography on SiO$_2$ (hexane/EtOAc, 20:1) provided 40 mg (76%) of **6d** as an oil: IR (neat) 2959, 2931, 2873, 1734, 1694, 1669, 1627, 1455, 1374, 1181, 1106 cm^{-1}; ^{1}H NMR δ 7.33-7.24 (m, 5 H), 6.89 (dt, 1 H, J = 15.9, 6.9 Hz), 6.20-6.09 (m, 1 H), 4.5-4.4 (m, 2 H), 4.2-4.1 (m, 2 H), 3.8-3.5 (m, 2 H), 3.15-3.05 (m, 2 H), 2.19 (dt, 2 H, J = 7.2 Hz), 1.45-1.15 (m, 7 H), 1.15-1.05 (m, 3 H), 0.90 (t, 3 H, J = 6.7 Hz); ^{13}C NMR δ 201.4, 173.1, 148.6, 148.0, 138.1, 129.0, 128.9, 128.3, 127.5, 73.2, 73.0, 69.5, 67.9, 60.7, 48.4, 47.5, 42.4, 41.4, 32.3, 30.2, 22.3, 15.4, 14.6, 14.3, 13.9; MS (EI) *m/z* (rel intensity) 346 (M$^+$, 2), 301 (5), 239 (6), 225 (4), 207 (9), 183 (5), 140 (50), 111 (55), 91 (100), 55 (35); HRMS (EI) *m/z* calculated for C$_{21}$H$_{30}$O$_4$ 346.2144, found 346.2146.



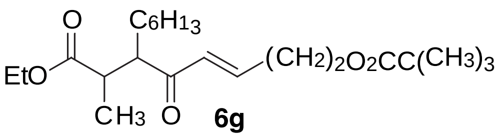
6e

9-Benzyloxy-3-methyl-4-oxo-non-5-enoic acid ethyl ester (6e). According to general procedure B, 144 mg (0.369 mmol) of acetal **5b** and Me_2CuLi (4.9 eq.) provided 114 mg (97%) of **6e** as an oil: IR (neat) 2977, 2934, 2857, 1734, 1695, 1670, 1628, 1455, 1268, 1185, 1103, 1029 cm^{-1}; ^1H NMR δ 6.93 (dt, 1 H, *J* = 15.7, 6.9 Hz), 6.18 (d, 1 H, *J* = 15.7 Hz), 4.50 (s, 2 H), 4.10 (q, 2 H, *J* = 7.1 Hz), 3.50 (t, 2 H, *J* = 6.3 Hz), 3.28-3.18 (m, 1 H), 2.78 (dd, 1 H, *J* = 16.6, 8.3 Hz), 2.38-2.27 (m, 3 H), 1.84-1.75 (m, 1 H), 1.23 (t, 3 H, *J* = 7.1 Hz), 3.12 (d, 3 H, *J* = 7.2 Hz); ^{13}C NMR δ 202.1, 172.5, 147.5, 138.5, 128.8, 128.5, 127.8, 73.1, 69.4, 60.6, 39.9, 37.1, 29.4, 28.3, 17.3, 14.3; MS (EI) *m/z* (rel intensity) 318 (M^+, 7), 273 (4), 247 (1), 227 (3), 203 (5), 160 (15), 143 (20), 138 (18), 91 (100); HRMS (EI) *m/z* calculated for $C_{19}H_{26}O_4$ 318.1831, found 318.1798.



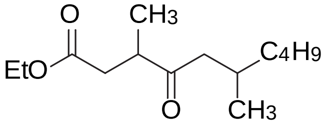
6f

7-Benzyloxy-3-butyl-4-oxo-oct-5-enoic acid ethyl ester (6f). According to general procedure B, 100 mg (0.266 mmol) of acetal **5c** with Bu_2CuLi (4.7 eq.) yielded 76 mg (82%) of **6f** as an oil: IR (neat) 2958, 2931, 2861, 1734, 1697, 1673, 1633, 1455, 1372, 1346, 1180, 1099 cm^{-1}; ^1H NMR (333 K) δ 7.35-7.27 (m, 5 H), 6.81 (dd, 1 H, *J* = 15.9, 5.9 Hz), 6.37 (dt, 1 H, *J* = 15.9, 0.9 Hz), 4.61-4.47 (m, 2 H), 4.17-4.07 (m, 3 H), 3.25-3.15 (m, 1 H), 2.76 (dd, 1 H, *J* = 16.4, 8.4 Hz), 2.38 (dd, 1 H, *J* = 16.5, 5.4 Hz), 1.7-1.6 (m, 1 H), 1.5-1.4 (m, 1 H), 1.4-1.2 (m, 10 H), 0.90 (t, 3 H, *J* = 6.7 Hz); ^{13}C NMR δ 202.2, 172.6, 147.6, 138.2, 128.6, 128.4, 127.8, 74.3, 70.9, 60.7, 45.5, 45.3, 35.4, 32.0, 31.6, 29.8, 29.2, 23.1, 22.8, 20.9, 14.3, 14.0; MS (EI) *m/z* (rel intensity) 301 ($[M\text{-}OEt]^+$, 2), 273 (0.5), 240 (15), 194 (12), 171 (5), 111 (5), 91 (100), 82 (17), 69 (16); HRMS (EI) *m/z* calculated for $C_{19}H_{25}O_3$ [M-OEt] 301.1804, found 301.1803.



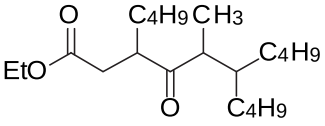
6g

8-(2,2-Dimethyl-propionyloxy)-3-hexyl-2-methyl-4-oxo-oct-5-enoic acid ethyl ester (6g). According to general procedure C, 550 mg (1.48 mmol) of acetal **5d** and $(C_6H_{13})_2CuLi$ (5.1 eq.) provided 615 mg (73%) of the TBS-protected acetal: ^1H NMR δ 5.85-5.73 (m, 1 H), 5.53-5.46 (m, 1 H), 4.15-3.94 (m, 4 H), 3.94-3.80 (m, 1 H), 3.63-3.41 (m, 3 H), 2.47-2.34 (m, 3 H), 2.22-2.07 (m, 2 H), 1.6-1.5 (m, 2 H), 1.29-1.20 (m, 23 H), 0.89-0.85 (m, 12 H), 0.06-0.01 (m, 6 H). This acetal (215 mg, 0.377 mmol) with 0.250 mL (0.500 mmol) of 2.0M LDA in heptane/THF/ethylbenzene and 0.200 mL (3.22 mmol) of MeI provided 111 mg (77%) of the desired oily enone **6g**: IR (neat) 2959, 2930, 2859, 1732, 1694, 1668, 1632, 1463, 1378, 1284, 1149 cm^{-1}; ^1H NMR δ 6.9-6.75 (m, 1 H), 6.23 (d, 1 H, *J* = 15.8 Hz), 4.20-4.00 (m, 4 H), 3.1-2.9 (m, 1 H), 2.8-2.6 (m, 1 H), 2.55 (br, 2 H), 1.65-1.55 (m, 1 H), 1.5-1.3 (m, 1 H), 1.22-1.11 (m, 20 H), 1.03 (d, 3 H, *J* = 6.9 Hz), 0.82 (br, 3 H); ^{13}C NMR δ 202.1, 178.4, 175.7, 175.5, 143.3, 142.4, 132.5, 131.6, 62.3, 62.2, 60.6, 51.8, 51.3, 42.1, 40.2, 38.8, 32.0, 31.9, 31.6, 31.2, 29.6, 29.4, 28.1, 27.2, 26.5, 22.6, 16.0, 14.3, 14.1; MS (EI) *m/z* (rel intensity) 382 (M$^+$, 3), 280 (4), 235 (21), 196 (34), 179 (15), 123 (16), 102 (20), 99 (95), 81 (65), 57 (100); HRMS (EI) *m/z* calculated for $C_{22}H_{38}O_5$ 382.2719, found 382.2739.



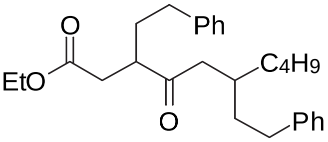
7a

General procedure D for conjugate addition to enones (7a-g). 3,6-Dimethyl-4-oxo-decanoic acid ethyl ester (7a). A suspension of 720 mg (3.51 mmol) of CuBr•SMe$_2$ in 10 mL of THF was treated at -78 °C with 5.00 mL (7.00 mmol) of a 1.4 M solution of MeLi in ether. The suspension was warmed to -20 °C and stirred for 20 min before recooling to -78 °C. A solution of enone **6a** (267 mg, 1.18 mmol) in 1 mL of THF was added dropwise and the temperature was raised to -30 °C. After 30 min, the reaction mixture was quenched with 10% HCl, diluted with 15 mL of EtOAc and washed with 2 N NaOH. Drying (MgSO$_4$), filtration and concentration yielded 276 mg (97%) of the desired oily **7a**. GC-MS analysis indicated a 1:1 mixture of diastereostereomers: IR (neat) 2959, 2929, 2874, 2859, 1736, 1714, 1460, 1409, 1393, 1377, 1341, 1272, 1187, 1148, 1100, 1030 cm^{-1}; ^1H NMR δ 4.09 (q, 2 H, *J* = 7.1 Hz), 3.0-2.8 (m, 1 H), 2.75 (dq, 1 H, *J* = 8.8, 1.7 Hz), 2.53-2.21 (m, 3 H), 2.15-1.85 (m, 1 H), 1.25-1.15 (m, 9 H), 1.08 (dd, 3 H, *J* = 7.1, 1.5 Hz), 0.87-0.82 (m, 6 H); ^{13}C NMR δ 212.8, 172.5, 60.6, 48.8, 42.6, 42.3, 37.1, 36.7, 29.3, 28.8, 22.9, 19.9, 16.7, 14.3, 14.2; MS (EI) *m/z* (rel intensity) 242 (M^+, 4), 197 (30), 158 (77), 143 (16), 139 (19), 127 (95), 112 (60), 69 (21), 57 (100); HRMS (EI) *m/z* calculated for $C_{14}H_{26}O_3$ 242.1882, found 242.1881.



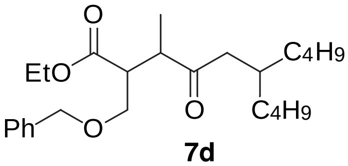
7b

3,6-Dibutyl-5-methyl-4-oxo-decanoic acid ethyl ester (7b). According to general procedure D, 36.0 mg (0.134 mmol) of **6b** and Bu_2CuLi (3.0 eq.) gave 35.9 mg (79%) of oily **7b** as a mixture of diastereomers upon quenching at –78 °C with 0.10 mL of MeI (12 eq.) and stirring at room for 11 h: IR (neat) 2956, 2927, 2861, 1736, 1711, 1460, 1375, 1259, 1178, 1099, 1031 cm^{-1}; ^1H NMR δ 4.10 (q, 2 H, *J* = 7.1 Hz), 3.1-3.0 and 3.0-2.9 (2m, 1 H), 2.80-2.30 (m, 3 H), 1.8-1.7 (m, 1 H), 1.7-1.55 (m, 2 H), 1.40-1.10 (m, 19 H), 1.00 (d, 3 H, *J* = 6.9 Hz), 0.95-0.87 (m, 9 H); ^{13}C NMR δ 216.1, 172.7, 60.6, 48.0, 47.6, 47.4, 46.1, 38.3, 35.7, 35.2, 33.6, 32.9, 31.1, 30.7, 29.7, 29.3, 29.2, 29.0, 28.9, 23.3, 23.1, 22.8, 14.2, 14.0; MS (EI) *m/z* (rel intensity) 341 ($[M+1]^+$, 3), 295 (10), 281 (6), 269 (5), 237 (7), 214 (35), 185 (100), 158 (95), 155 (55), 144 (38), 111 (35); HRMS (EI) *m/z* calculated for $C_{21}H_{40}O_3$ 340.2977, found 340.2991.



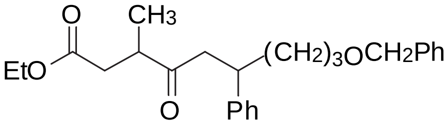
7c

4-Oxo-3,6-diphenethyl-decanoic acid ethyl ester (7c). According to general procedure D, 20 mg (0.0632 mmol) of **6c** and $(PhCH_2CH_2)_2CuLi^2$ (5.5 eq.) provided 24 mg (90%) of **7c** as an oil: ^1H NMR δ 7.32-7.12 (m, 10 H), 4.14-4.06 (m, 2 H), 3.1-2.9 (m, 1 H), 2.8-2.4 (m, 7 H), 2.1-1.8 (m, 2 H), 1.7-1.5 (m, 4 H), 1.3-1.2 (m, 9 H), 0.9-0.8 (m, 3 H).



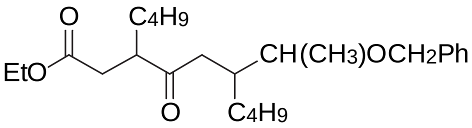
7d

2-Benzyloxymethyl-6-butyl-3-methyl-4-oxo-decanoic acid ethyl ester (7d). According to general procedure D, 40 mg (0.115 mmol) of **6d** and Bu_2CuLi (2.1 eq.) gave 45 mg (97%) of the desired oil: ^1H NMR δ 7.36-7.27 (m, 5 H), 4.48 (s, 2 H), 4.17 (q, 2 H, *J* = 7.1 Hz), 3.67-3.62 (m, 1 H), 3.55-3.50 (m, 1 H), 3.15-3.05 (m, 1 H), 2.90-2.80 (m, 1 H), 2.5-2.3 (m, 2 H), 1.95-1.85 (m, 1 H), 1.3-1.15 (m, 15 H), 1.08 (d, 3 H, *J* = 7.0 Hz), 0.88 (2t, 6 H, *J* = 7.0 Hz).



7e

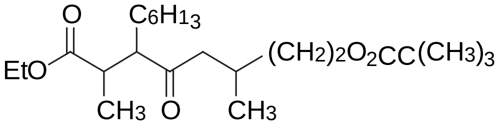
9-Benzyloxy-3-methyl-4-oxo-6-phenyl-nonanoic acid ethyl ester (7e). According to general procedure D, 114 mg (0.358 mmol) of **6e**, Ph_2CuLi (3.4 eq.) and TMSCl (0.20 mL) gave 129 mg (91%) of the phenyl adduct **7e** upon treatment with aqueous TBAF (190 mg, 0.728 mmol): IR (neat) 3028, 2934, 2856, 1732, 1715, 1495, 1456, 1454, 1371, 1190, 1102, 1029 cm^{-1}; ^1H NMR δ 7.36-7.16 (m, 10 H), 4.44 (d, 2 H, *J* = 2.0 Hz), 4.14-4.02 (m, 2 H), 3.43-3.39 (m, 2 H), 3.25-3.15 (m, 1 H), 2.90-2.64 (m, 4 H), 2.22 (dd, 1 H, *J* = 16.7, 5.5 Hz), 1.75-1.40 (m, 4 H), 1.24 and 1.19 (2t, 3 H, *J* = 7.1 Hz), 1.09 (d, 1 H, *J* = 7.1 Hz), 0.86 (d, 1 H, *J* = 7.1 Hz); ^{13}C NMR δ 211.5, 172.4, 172.2, 144.7, 144.6, 138.7, 128.6, 128.5, 127.7, 127.6, 126.4, 72.9, 70.3, 60.6, 48.9, 48.6, 42.6, 40.6, 40.5, 37.0, 36.9, 32.8, 27.8, 16.6, 16.1, 14.3; MS (EI) *m/z* (rel intensity) 396 (M^+, 3), 351 (1), 287 (5), 259 (2), 247 (6), 221 (1), 201 (4), 147 (50), 115 (20), 91 (100); HRMS (EI) *m/z* calculated for $C_{25}H_{32}O_4$ 396.2301, found 396.2290.



7f

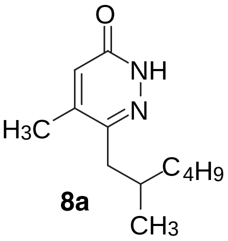
6-(1-Benzyloxyethyl)-3-butyl-4-oxo-decanoic acid ethyl ester (7f). According to general protocol D, 36 mg (0.104 mmol) of **6f** with Bu_2CuLi (5.4 eq.) gave 38 mg (90%) of oily **7f**: IR (neat) 2958, 2931, 2860, 1735, 1714, 1633, 1455, 1374, 1182, 1070 cm^{-1}; ^1H NMR δ 7.34-

7.21 (m, 5 H), 4.59-4.41 (m, 2 H), 4.1-4.0 (m, 2 H), 3.6-3.5 (m, 1 H), 3.0-2.9 (m, 1 H), 2.7-2.3 (m, 4 H), 2.15-2.05 (m, 1 H), 1.6-1.1 (m, 19 H), 0.88-0.82 (m, 6 H); ^{13}C NMR 212.8, 172.6, 139.2, 128.9, 128.4, 127.8, 127.5, 75.9, 75.8, 70.7, 60.6, 47.7, 47.5, 43.1, 41.0, 38.2, 38.1, 35.5, 35.3, 31.2, 30.4, 29.5, 29.2, 23.1, 22.8, 16.7, 14.3, 14.2, 14.0; MS (EI) *m/z* (rel intensity) 404 (M^+, 0.5), 359 (5), 295 (6), 269 (10), 223 (15), 200 (20), 185 (40), 144 (17), 111 (13), 91 (100); HRMS (EI) *m/z m/z* calculated for $C_{25}H_{40}O_4$ 404.2927, found 404.2926.



7g

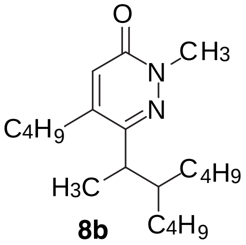
3-[5-(2,2-Dimethyl-propionyloxy)-3-methyl-pentanoyl]-2-methyl-nonanoic acid ethyl ester (7g). According to general procedure D, 36 mg (0.094 mmol) of **6g** and Me_2CuLi (2.2 eq.) provided 37 mg (99%) of oily **7g**: ^{1}H NMR δ 4.17-4.02 (m, 4 H), 2.78-2.69 (m, 2 H), 2.5-2.3 (m, 2 H), 2.2-2.1 (m, 1 H), 1.7-1.6 (m, 1 H), 1.5-1.4 (m, 1 H), 1.3-1.1 (m, 22 H), 1.15-1.05 (m, 3 H), 0.96-0.92 (m, 3 H), 0.86 (t, 3 H, J = 6.8 Hz).



8a

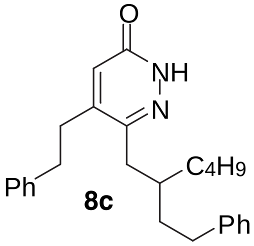
General procedure E for the cyclization and oxidation of ketoesters (7a-g) to pyridazinones (8a-h). 5-Methyl-6-(2-methyl-hexyl)-2*H*-pyridazin-3-one (8a). A solution of the ketoester **7a** (147 mg, 0.607 mmol) in 5 mL of absolute EtOH was treated with 0.35 mL (6.1 mmol) of AcOH and 0.20 mL (6.4 mmol) of NH_2NH_2, and stirred for 15 h. After addition of 20 mL of EtOAc, the solution was washed with 10% HCl and 2 N NaOH, and dried ($MgSO_4$). Filtration and concentration yielded the dihydropyridazinone: ^{1}H NMR δ 8.30 (br, 1 H), 2.60-1.95 (m, 5 H), 1.85-1.75 (m, 1 H), 1.35-1.25 (m, 6 H), 1.15 (2d, 3 H, J = 7.0 Hz), 0.97-0.88 (m, 6 H).

The dihydropyridazinone intermediate was dissolved in 5 mL of MeCN and treated with 165 mg (1.23 mmol) of $CuCl_2$. After heating at reflux for 1 h and cooling to room temperature, the mixture was diluted with EtOAc and washed with 10% HCl followed by 2 N NaOH (3 x 15 mL). Drying ($MgSO_4$), filtration and concentration yielded an oil which was chromatographed on SiO_2 (hexane/EtOAc, 2:1) to give 116 mg (92%) of solid **8a**: Mp 109.2-110.6 °C; IR (CCl_4) 2956, 2928, 2891, 2871, 2856, 1667, 778, 751 cm^{-1}; ^{1}H NMR δ 12.32 (s, 1 H), 6.72 (s, 1 H), 2.58 (dd, 1 H, *J* = 14.4, 5.8 Hz), 2.34 (dd, 1 H, *J* = 14.3, 8.4 Hz), 2.20 (s, 3 H), 1.95-1.80 (m, 1 H), 1.35-1.15 (m, 6 H), 0.90-0.85 (m, 6 H); ^{13}C NMR δ 162.4, 148.6, 144.8, 128.0, 39.5, 36.7, 31.9, 29.3, 22.9, 19.5, 19.3, 14.1; MS (EI) *m/z* (rel intensity) 208 (M$^+$, 15), 165 (10), 151 (12), 124 (100), 110 (9), 66 (7), 55 (8); HRMS (EI) *m/z* calculated for $C_{12}H_{20}N_2O$ 208.1576, found 208.1576.



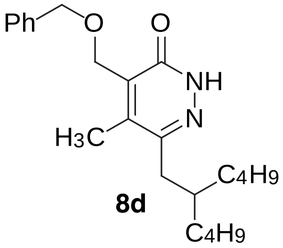
8b

5-Butyl-6-(2-butyl-1-methyl-hexyl)-2-methyl-2*H*-pyridazin-3-one (8b). According to general procedure E, cyclization of **7b** (20 mg, 0.059 mmol) with 0.100 mL of MeNHNH$_2$ in refluxing EtOH (2 d) followed by oxidation gave 14 mg (75%) of oily **8b**: IR (neat) 2958, 2924, 2857, 1668 cm^{-1}; ^{1}H NMR δ 6.66 (s, 1 H), 3.74 (s, 3 H), 2.50-2.40 (m, 3 H), 1.8-1.7 (m, 1 H), 1.6-1.5 (m, 2 H), 1.5-1.35 (m, 2 H), 1.3-1.1 (m, 12 H), 1.14 (d, 3 H, *J* = 6.9 Hz), 0.97 (t, 3 H, *J* = 7.3 Hz), 0.92-0.88 (m, 6 H); ^{13}C NMR δ 160.8, 151.3, 147.2, 126.5, 41.4, 39.6, 36.6, 36.5, 33.1, 30.8, 30.7, 30.5, 28.8, 23.0, 22.3, 14.1, 13.8; MS (EI) *m/z* (rel intensity) 320 (M$^+$, 9), 306 (6), 263 (10), 249 (7), 194 (100), 180 (39), 165 (54), 152 (46), 138 (24); HRMS (EI) *m/z* calculated for $C_{20}H_{36}N_2O$ 320.2828, found 320.2830.



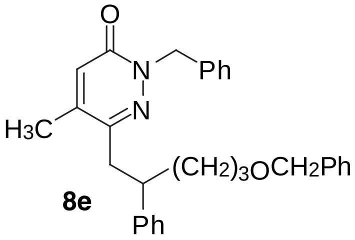
8c

5-Phenethyl-6-(2-phenethyl-hexyl)-2*H*-pyridazin-3-one (8c). According to general procedure E, 20 mg (0.047 mmol) of **7c** and 0.100 mL of hydrazine gave 15 mg (82%) of solid **8c**: Mp 69.1-72.4 °C; IR (neat) 2951, 2925, 2854, 1665, 1599, 1495, 1453, 1157, 1116, 1073 cm^{-1}; ^{1}H NMR δ 11.07 (br, 1 H), 7.35-7.11 (m, 10 H), 6.70 (s, 1 H), 2.90-2.85 (m, 2 H), 2.75-2.70 (m, 2 H), 2.65-2.50 (m, 4 H), 1.9-1.8 (m, 1 H), 1.62 (dt, 2 H, *J* = 7.8, 6.2 Hz), 1.4-1.25 (m, 6 H), 0.9-0.85 (m, 3 H); ^{13}C NMR δ 161.2, 148.3, 142.4, 139.8, 128.8, 128.4, 126.8, 125.8, 36.5, 36.0, 35.2, 34.6, 33.6, 33.3, 32.9, 29.8, 28.8, 23.1, 14.2; MS (EI) *m/z* (rel intensity) 388 (M$^+$, 8), 297 (8), 214 (16), 170 (6), 91 (100), 77 (6), 65 (13); HRMS (EI) *m/z* calculated for $C_{26}H_{32}N_2O$ 388.2515, found 388.2523.



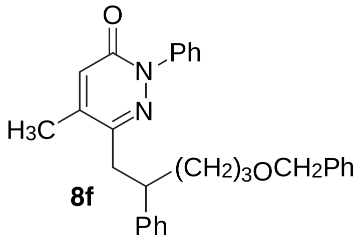
8d

4-Benzyloxymethyl-6-(2-butyl-hexyl)-5-methyl-2*H*-pyridazin-3-one (8d). According to general procedure E, ketoester **7d** (20 mg, 0.049 mmol) and 0.100 mL of hydrazine provided 12 mg (66%) of solid **8d**: Mp 86.3-88.4 °C; IR (neat) 2953, 2926, 2856, 1731, 1653, 1599, 1544, 1454, 1380, 1285, 1267, 1196, 1071 cm^{-1}; ^1H NMR δ 10.40 (br, 1 H), 7.37-7.30 (m, 5 H), 4.63 (s, 3 H), 4.60 (s, 3 H), 2.49 (d, 2 H, *J* = 7.0 Hz), 2.25 (s, 3 H), 1.75-1.65 (m, 1 H), 1.29-1.26 (m, 12 H), 0.91-0.87 (m, 6 H); ^{13}C NMR δ 161.4, 149.4, 144.2, 138.0, 128.6, 128.2, 128.0, 73.4, 62.4, 37.7, 36.3, 33.2, 28.8, 23.2, 15.6, 14.3; MS (EI) *m/z* (rel intensity) 264 ($[M-C_7H_6O]^+$, 100), 207 (10), 169 (8), 138 (48), 91 (39), 81 (26), 69 (59), 58 (65); HRMS (EI) calculated for $C_{16}H_{28}N_2O$ ($M-C_7H_6O$) 264.2202, found 264.2195; MS (CI) 371 (M^+, 38), 264 (100).



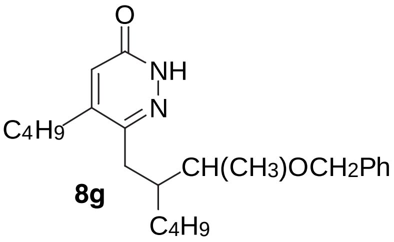
8e

6-(5-Benzyloxy-2-phenyl-pentyl)-5-methyl-2-benzyl-2*H*-pyridazin-3-one (8e). According to general procedure E, 64 mg (0.16 mmol) of **7e** and 315 mg (1.62 mmol) of $BnNHNH_2$•2HCl was cyclized in refluxing EtOH for 13 h, and provided upon oxidation 46 mg (0.10 mmol, 64%) of **8e**: IR (neat) 2921, 2853, 1666, 1598, 1495, 1454, 1204, 1166, cm^{-1}; ^1H NMR δ 7.34-7.17 (m, 8 H), 7.05 (d, 2 H, *J* = 6.5 Hz), 6.95 (s, 1 H), 5.26, 5.23 (AB, 2 H, *J* = 11 Hz), 4.44 (s, 2 H), 3.38 (t, 2 H, *J* = 6.4 Hz), 3.1-3.0 (m, 1 H), 2.91-2.85 (m, 2 H), 2.05 (s, 3 H), 1.85-1.70 (m, 2 H), 1.55-1.45 (m, 2 H); ^{13}C NMR δ 160.5, 149.1, 144.9, 143.7, 138.6, 135.7, 128.9, 128.7, 128.5, 128.1, 127.7, 127.3, 126.7, 73.0, 70.3, 55.8, 44.1, 39.3, 32.6, 27.8, 18.8; MS (EI) *m/z* (rel intensity) 452 (M^+, 29), 361 (43), 346 (15), 290 (15), 214 (30), 147 (100), 115 (8), 71 (42); HRMS (EI) *m/z* calculated for $C_{30}H_{32}N_2O_2$ 452.2464, found 452.2478.



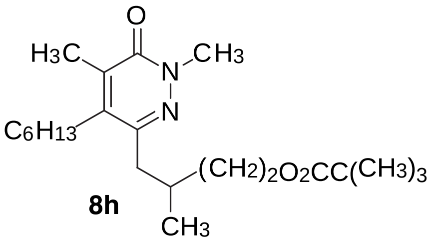
8f

6-(5-Benyloxy-2-phenyl-pentyl)-5-methyl-2-phenyl-2*H*-pyridazin-3-one (8f). According to general procedure E, 60 mg (0.15 mmol) of **7e** and 0.200 mL of $PhNHNH_2$ was cyclized in refluxing EtOH for 11 h, and provided upon oxidation 48 mg (0.10 mmol, 72%) of oily **8f**: IR (neat) 3061, 3028, 2929, 2856, 1671, 1610, 1493, 1453, 1313, 1167, 1131, 1029 cm^{-1}; ^1H NMR δ 7.40-7.25 (m, 8 H), 7.14 (d, 2 H, *J* = 6.8 Hz), 6.74 (s, 1 H), 4.45 (s, 2 H), 3.48-3.38 (m, 2 H), 3.1-2.8 (m, 3 H), 2.11 (s, 3 H), 1.95-1.75 (m, 2 H), 1.60-1.50 (m, 2 H); ^{13}C NMR δ 159.9, 147.2, 143.9, 143.1, 141.6, 138.6, 129.2, 128.7, 128.5, 128.0, 127.7, 126.7, 125.5, 73.0, 70.3, 44.5, 39.6, 32.7, 27.9, 18.7; MS (EI) *m/z* (rel intensity) 438 (M^+, 15), 347 (17), 200 (32), 147 (20), 105 (11), 91 (100), 77 (38), 65 (10); HRMS (EI) *m/z* calculated for $C_{29}H_{30}N_2O_2$ 438.2307, found 438.2299.



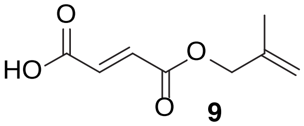
8g

6-[2-(1-Benzyloxyethyl)-hexyl]-5-butyl-2*H*-pyridazin-3-one (8g). According to general procedure E, 80 mg (0.20 mmol) of **7f** and 0.200 mL of hydrazine provided 59 mg (81%) of oily **8g**: IR (neat) 2956, 2929, 2870, 2861, 1666, 1597, 1463, 1455, 1378, 1110 cm^{-1}; ^1H NMR δ 12.06 (br, 1 H), 7.35-7.24 (m, 5 H), 6.68 (s, 1 H), 4.61-4.37 (m, 2 H), 3.68-3.54 (m, 1 H), 2.90-2.65 (m, 1 H), 2.67-2.30 (m, 3 H), 2.2-2.0 (m, 1 H), 1.58-1.45 (m, 2 H), 1.45-1.15 (m, 13 H), 0.97-0.84 (m, 6 H); ^{13}C NMR (125 MHz) δ 162.3, 149.6, 149.3, 148.6, 148.3, 139.0, 128.3, 127.7, 127.5, 127.4, 75.5, 75.4, 70.6, 70.5, 41.6, 40.9, 32.0, 31.5, 31.4, 31.3, 30.3, 29.9, 29.5, 29.4, 23.1, 23.0, 22.4, 16.2, 14.9, 14.1, 13.9; MS (EI) *m/z* (rel intensity) 370 (M^+, 6), 279 (75), 235 (60), 166 (43), 124 (32), 99 (62), 91 (100), 70 (23), 56 (80); HRMS (EI) *m/z* calculated for $C_{23}H_{34}N_2O_2$ 370.2620, found 370.2623.



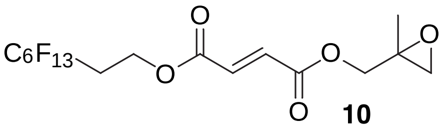
8h

2,2-Dimethyl-propionic acid 4-(4-hexyl-1,5-dimethyl-6-oxo-1,6-dihydro-pyridazin-3-yl)-3-methyl-butyl ester (8h). According to general procedure E, 10 mg (0.025 mmol) of **7g** and 0.100 mL of $MeNHNH_2$ in refluxing EtOH (6 h), providing upon oxidation 7.0 mg (74%) of **8h**: IR (neat) 2959, 2928, 2873, 2855, 1729, 1646, 1596, 1481, 1462, 1285, 1158 cm^{-1}; ^{1}H NMR δ 4.16-4.12 (m, 2 H), 3.75 (s, 3 H), 2.62-2.37 (m, 4 H), 2.18 (s, 3 H), 2.10-2.00 (m, 2 H), 1.80-1.70 (m, 2 H), 1.60-1.50 (m, 2 H), 1.40-1.10 (m, 14 H), 0.97 (d, 3 H, J = 6.6 Hz), 0.95-0.88 (m, 3 H); ^{13}C NMR δ 178.6, 161.2, 145.9, 142.4, 135.8, 120.6, 62.5, 40.3, 39.6, 38.8, 35.4, 31.5, 29.7, 29.6, 29.1, 29.0, 27.3, 22.6, 19.6, 14.1, 12.6; MS (EI) *m/z* (rel intensity) 378 (M$^+$, 37), 363 (30), 293 (45), 277 (35), 261 (20), 249 (42), 222 (18), 207 (69), 152 (30), 97 (24), 83 (28), 69 (46), 57 (100); HRMS (EI) *m/z* calculated for $C_{22}H_{38}N_2O_3$ 378.2882, found 378.2884.



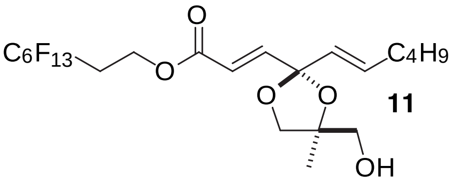
9

But-2-enedioic acid mono-(2-methyl-allyl) ester (9). A solution of fumaryl chloride (2.50 mL, 0.0232 mol) and 2-methyl-2-propen-1-ol (2.00 mL, 0.0238 mol) in 50 mL of dry THF at –78 °C was treated dropwise with NEt_3 (3.00 mL, 0.0215 mol) and stirred for 3 h. After dropwise addition of 1 mL of water and 3.00 mL of NEt_3, the temperature was slowly raised to –30 °C over 8 h. The mixture was poured into excess EtOAc and washed with 10% HCl, dried ($MgSO_4$), filtered and concentrated to provide a yellow solid that upon recrystallization from ether/hexane yielded 2.21 g (56%) of fumarate **9**: Mp 60.2-60.4 °C; IR (KBr) 3426, 3083, 1717, 1682, 1426, 1401, 1293, 1271, 1234, 1171, 1002, 911, 648, 577 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 13.21 (s, 1 H), 6.70 (s, 2 H), 4.95 (s, 1 H), 4.91 (s, 1 H), 4.57 (s, 2 H), 1.69 (s, 3 H); ^{13}C NMR (MeOH-d_4) δ 166.3, 164.7, 139.8, 134.2, 132.8, 112.3, 68.0, 18.2; MS (EI) *m/z* (rel intensity) 170 (M$^+$, 0.2), 152 (0.6), 99 (100), 81 (24), 72 (74), 55 (31); HRMS (EI) *m/z* calculated for $C_8H_8O_3$ (M – H_2O) 152.0473, found 152.0470.



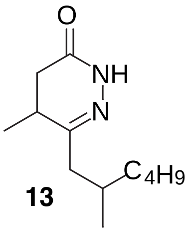
10

But-2-enedioic acid 2-methyl-oxiranylmethyl ester 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl ester (10). A solution of fumaric acid **9** (740 mg, 4.35 mmol) and *1H,1H,2H,2H*-perfluorooctanol (1.00 mL, 4.53 mmol) in 10 mL of CH_2Cl_2 at 0 °C was treated with DCC (1.10 g, 5.34 mmol) followed by DMAP (28 mg, 0.23 mmol). The reaction mixture was stirred at room temperature for 8 h, filtered, washed with 10% HCl, 2 N NaOH, and finally dried ($MgSO_4$). The suspension was filtered, concentrated, and redissolved in 10 mL of CH_2Cl_2. At 0 °C, mCPBA (2.95 g, 8.58 mmol for a 50% purity) was added and the mixture was stirred overnight at 5 °C, quenched with saturated $Na_2S_2O_3$, stirred for 30 min, and washed with 2 N NaOH. Drying ($MgSO_4$), filtration, and concentration followed by chromatography on SiO_2 (EtOAc/hexane, 1:9) provided 1.92 g (83%) of oily **10**: ^{1}H NMR δ 6.91, 6.90 (AB, 2 H, *J* = 16.1 Hz), 4.52 (t, 2 H, *J* = 6.4 Hz), 4.39 (d, 1 H, *J* = 12.0 Hz), 4.09 (d, 2 H, *J* = 12.0 Hz), 2.80 (d, 1 H, *J* = 4.6 Hz), 2.71 (d, 1 H, *J* = 4.6 Hz), 2.54 (tt, 2 H, *J* = 18.2, 6.4 Hz) 1.42 (s, 3 H); MS (EI) *m/z* (rel intensity) 445 ($[M-C_4H_7O_2]^+$, 100), 169 (5), 99 (23), 71 (26); HRMS (EI) *m/z* calculated for $C_{12}H_6O_3F_{13}$ 445.0109, found 445.0103.



11

(2*S*,4*S*),(2*R*,4*R*)-3-[(2-Hex-1-(*E*)-enyl)-4-hydroxymethyl-4-methyl-[1,3]dioxolan-2-yl)]-acrylic acid 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-octyl ester (11). According to general procedure A with 10% $(PhO)_3P$ and an additional 5 mol% Ag(I) added after 5 h, 135 mg (0.254 mmol) of **10** and 0.050 mL (0.435 mmol) of hexyne of provided 72 mg (46%) of oily **11** as a ca. 2:1 mixture of diastereomers. Major isomer: ^{1}H NMR δ 6.88 (d, 1 H, *J* = 15.4 Hz), 6.14 (d, 1 H, *J* = 15.3 Hz), 5.90 (dt, 1 H, *J* = 15.7, 6.7 Hz), 5.52 (d, 1 H, *J* = 15.4 Hz), 4.48 (t, 2 H, *J* = 6.5 Hz), 4.05 (d, 1 H, *J* = 8.4 Hz), 3.66 (d, 1 H, *J* = 8.4 Hz), 3.48-3.59 (m, 2 H), 2.54 (tt, 2H, *J* = 18.4, 6.3 Hz), 2.07 (dt, 2 H, *J* = 6.9, 6.8 Hz), 1.40-1.20 (m, 10 H), 0.87 (t, 3 H, *J* = 6.9 Hz); MS (EI) *m/z* (rel intensity) 616 (M^+, 4), 585 (84), 533 (33), 445 (42), 264 (27), 253 (39), 225 (100), 199 (59), 130 (96), 111 (50), 71 (65), 57 (50); HRMS (EI) *m/z* calculated for $C_{22}H_{25}O_5F_{13}$ 616.1494, found 616.1465.



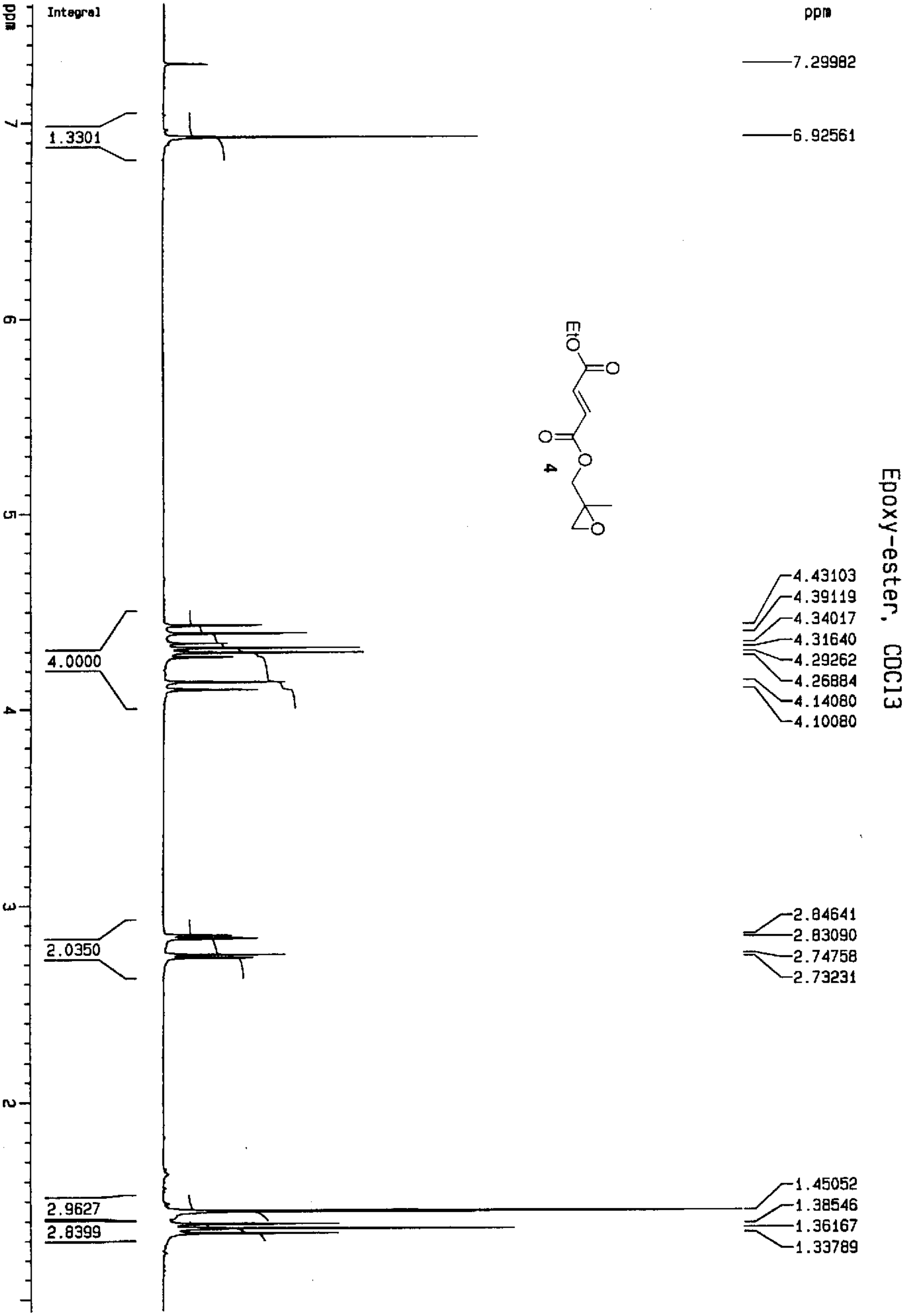
13

5-Methyl-6-(2-methyl-hexyl)-4,5-dihydro-2H-pyridazin-3-one (13). A suspension of CuBr•SMe$_2$ (100 mg, 0.486 mmol) in 2 mL of THF at –30 °C was treated with 0.700 mL of a 1.4 M (0.98 mmol) MeLi/ether solution and warmed slowly to 0 °C. After turning homogeneous, the solution was cooled to –78 °C and TMSCl (0.100 mL, 0.789 mmol) was added followed by a solution of the acetal **11** (61 mg, 0.099 mmol) in 1 mL of THF. The yellow solution was warmed to –30 °C over 1 h, then stirred for an additional 1 h before quenching with 1 mL of saturated NaHCO$_3$ and filtering through a pad of SiO$_2$. The mixture was concentrated, poured into 2 mL of MeOH and 1 mL of water, and extracted five times with excess FC-72. The combined FC-72 layers were dried (MgSO$_4$), filtered and concentrated *in vacuo* to give 57 mg of crude acetal.

A solution of this acetal in 3 mL of acetone/water (10:1) was treated with TsOH (4.1 mg, 0.0216 mmol) and heated at reflux for 9 h. The reaction mixture was treated with 1 mL of saturated NaHCO$_3$ solution, filtered through a pad of SiO$_2$, and concentrated. The oily residue was dissolved in MeOH/water and extracted 5 times with excess FC-72. The combined fluorous layers were dried (MgSO$_4$), and concentrated *in vacuo*. Dilution of the MeOH/water layer with water and extraction with EtOAc indicated no desired compound remained. The crude enone was dissolved in 1 mL of THF for the next step.

A suspension of CuBr•SMe$_2$ (44 mg, 0.214 mmol) in 1 mL of THF was treated at –30 °C with 1.4 M MeLi/ether (0.300 mL, 0.420 mmol), warmed to 0 °C and stirred until homogeneous. Upon recooling to –78 °C, the enone solution was added and the mixture was stirred for 4 h, quenched with water, filtered through a plug of SiO$_2$, concentrated and dissolved in MeOH/water. After FC-72 extraction (5 times), drying (MgSO$_4$) and removal of the fluorous solvent *in vacuo* provided 42 mg (76%) of the fluorous keto-ester. This material was slightly impure by TLC analysis. A sample was chromatographed on SiO$_2$ (EtOAc/hexane, 1:20) to give pure **12**: IR (neat) 2960, 2930, 1744, 1714, 1659, 1642, 1240, 1204, 1145, 1081 cm^{-1}; ^{1}H NMR δ 4.37 (t, 2 H, J = 6.6 Hz), 3.05-2.95 (m, 1 H), 2.96-2.75 (m, 1 H), 2.55-2.25 (m, 5 H), 2.1-2.0 (m, 1 H), 1.3-1.1 (m, 6 H), 1.14 (2d, 3 H, J = 7.1 Hz), 0.91-0.86 (m, 6 H); ^{13}C NMR (125 MHz) δ 212.5, 172.1, 118.4-108.4 (m), 56.4, 48.6, 42.6, 42.2, 36.7, 36.6, 36.5, 30.7, 30.5, 30.3, 29.3, 29.2, 28.8, 22.9, 19.9, 16.7, 16.6, 14.1; MS (EI) *m/z* (rel intensity) 560 (M$^+$, 6), 541 (3), 503 (11), 476 (68), 461 (28), 391 (36), 197 (70), 139 (31), 127 (97), 112 (62), 69 (39), 57 (100); HRMS (EI) *m/z* calculated for $C_{20}H_{25}O_3F_{13}$ 560.1596, found 560.1610.

A solution of the crude keto-ester **12** (18 mg, 0.032 mmol) in 1 mL of absolute EtOH was stirred for 23 h in the presence of hydrazine (0.10 mL) and AcOH (0.17 mL). The mixture was poured into 3 mL of EtOAc, washed with 10% HCl, 2 N NaOH, and brine, dried ($MgSO_4$) and filtered. The solution was concentrated to an oily residue and suspended in MeCN, then washed five times with excess FC-72. The MeCN layer was concentrated to give the desired dihydropyridazinone **13** (5.8 mg, 66%) in 98.7% purity (GC-MS): ^{1}H NMR δ 8.21 (s, 1 H), 2.6-1.9 (m, 5 H), 1.85-1.75 (m, 1 H), 1.35-1.25 (m, 6 H), 1.16 (2d, 3 H, J = 7.3 Hz), 0.97-0.89 (m, 6 H); MS (EI) *m/z* (rel intensity) 210 (M^+, 12), 195 (2), 167 (4), 153 (11), 126 (100), 111 (6), 91 (6), 69 (12), 55 (10); HRMS (EI) *m/z* calculated for $C_{12}H_{22}N_2O$ 210.1732, found 210.1726.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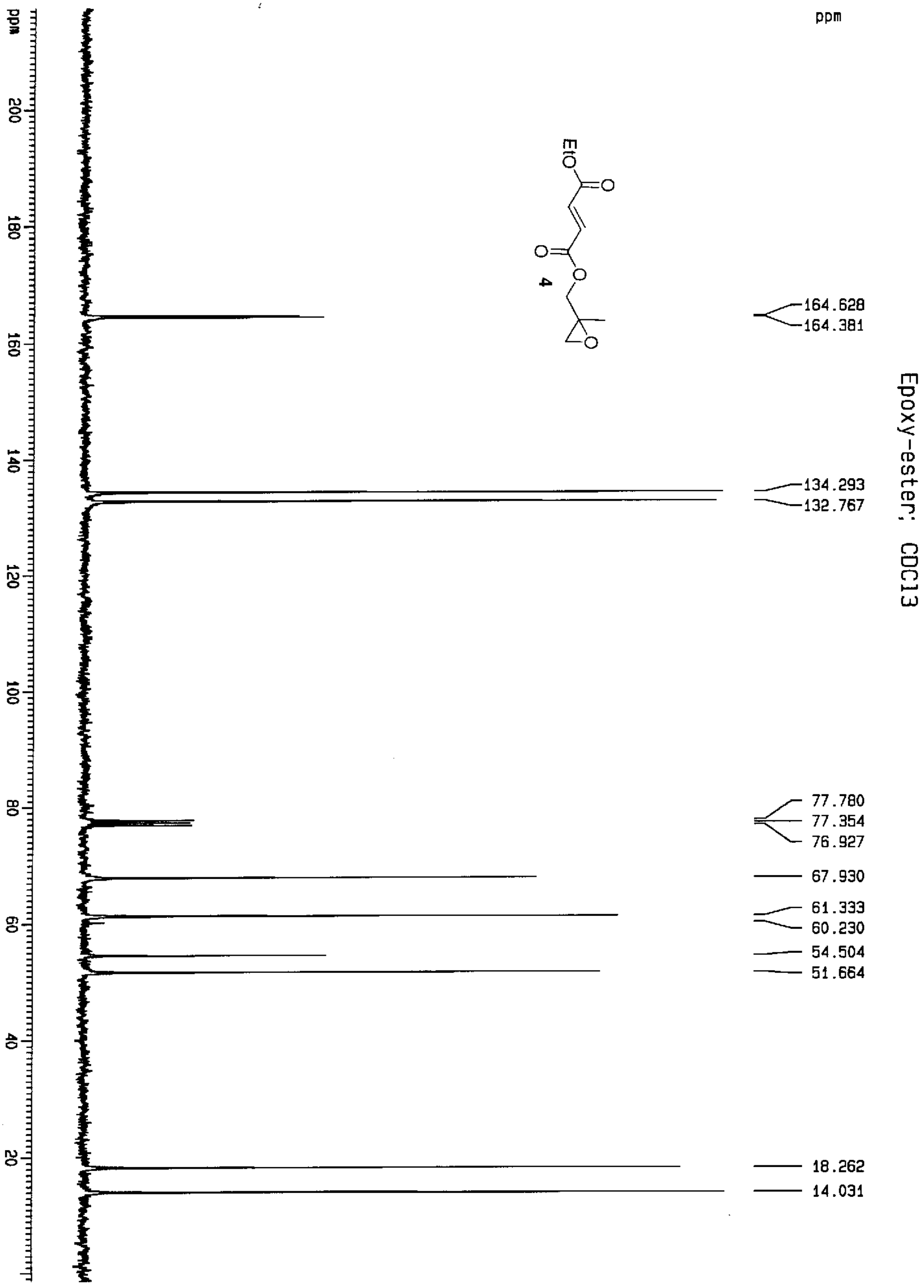
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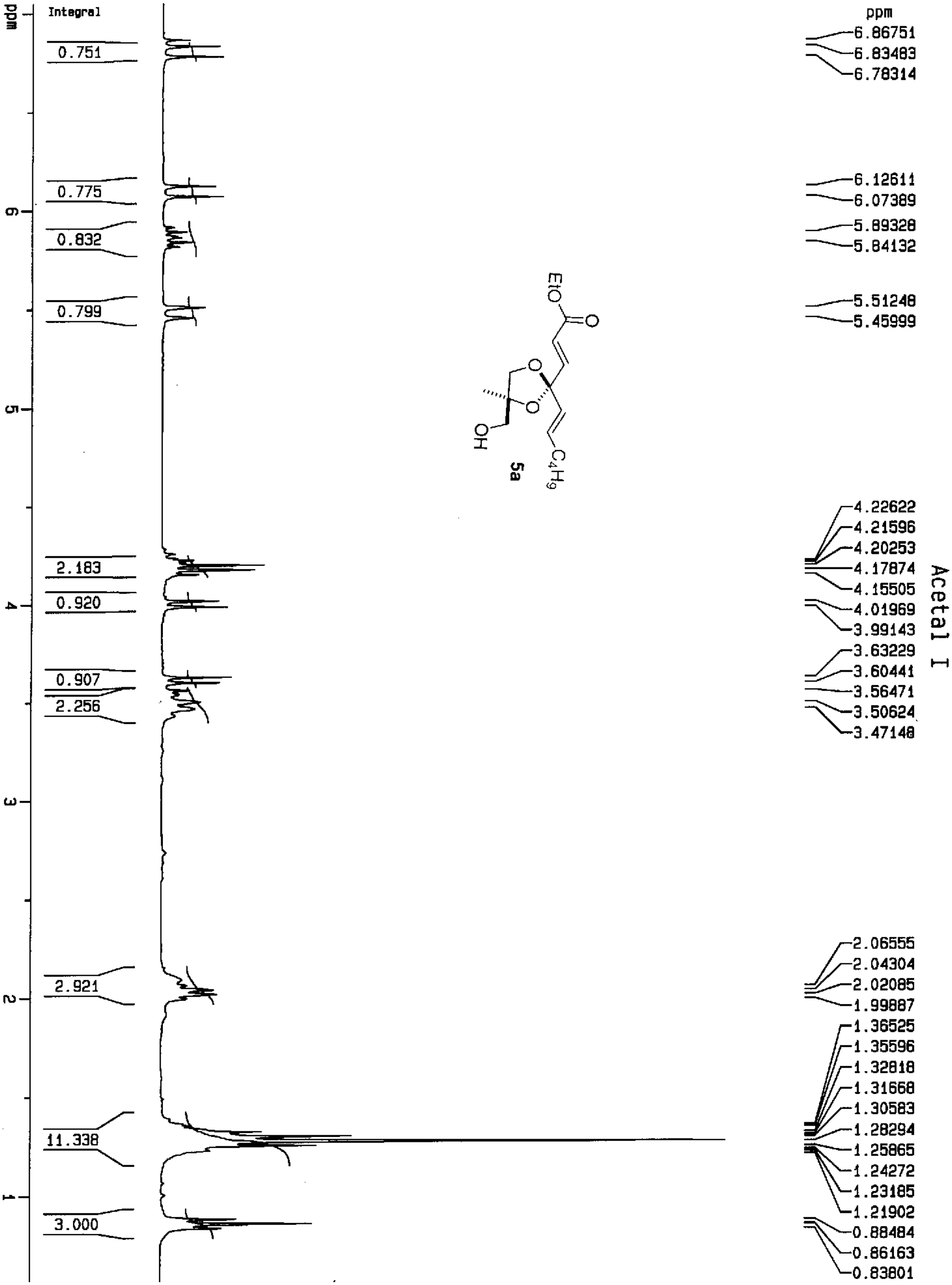
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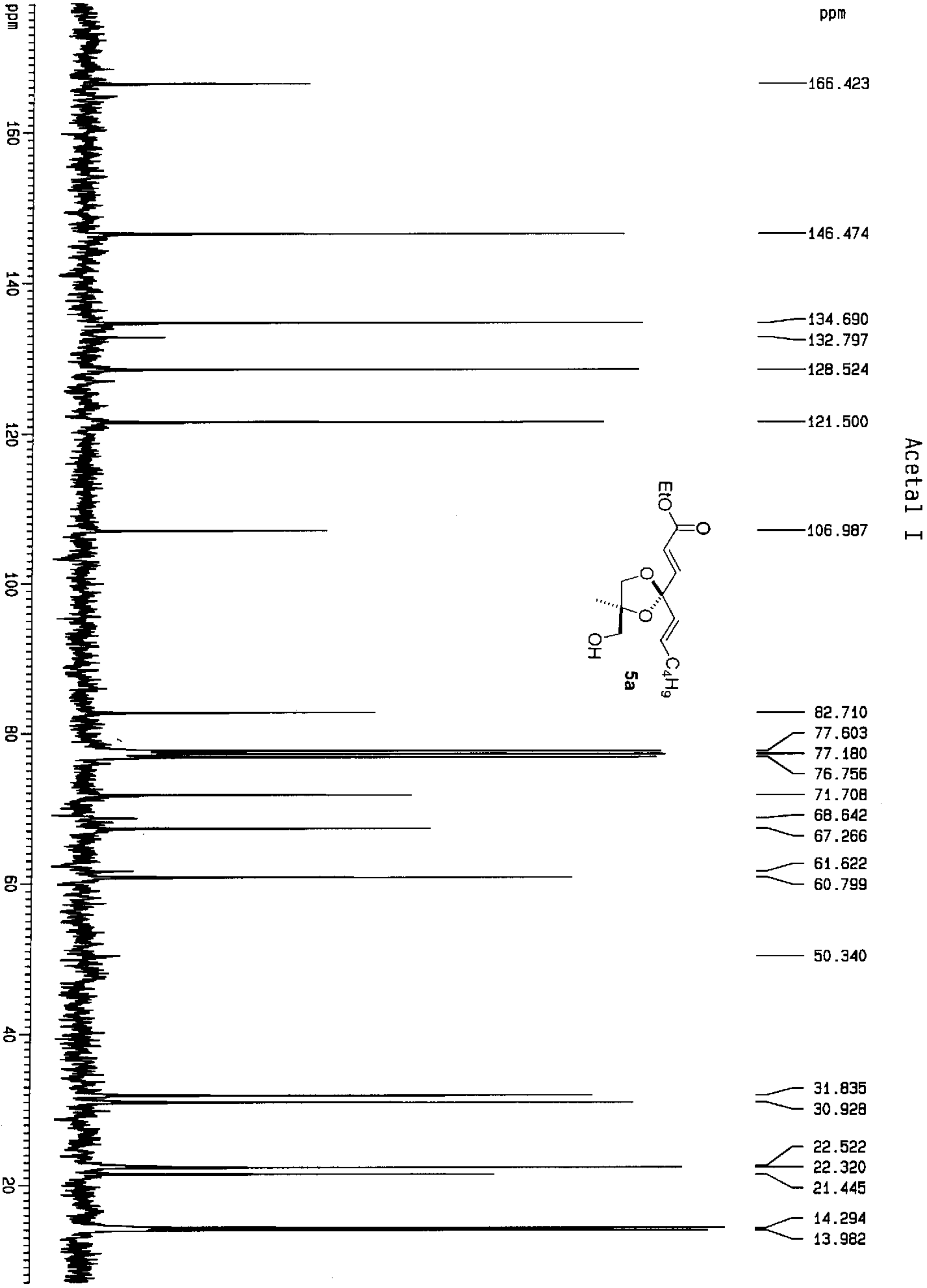
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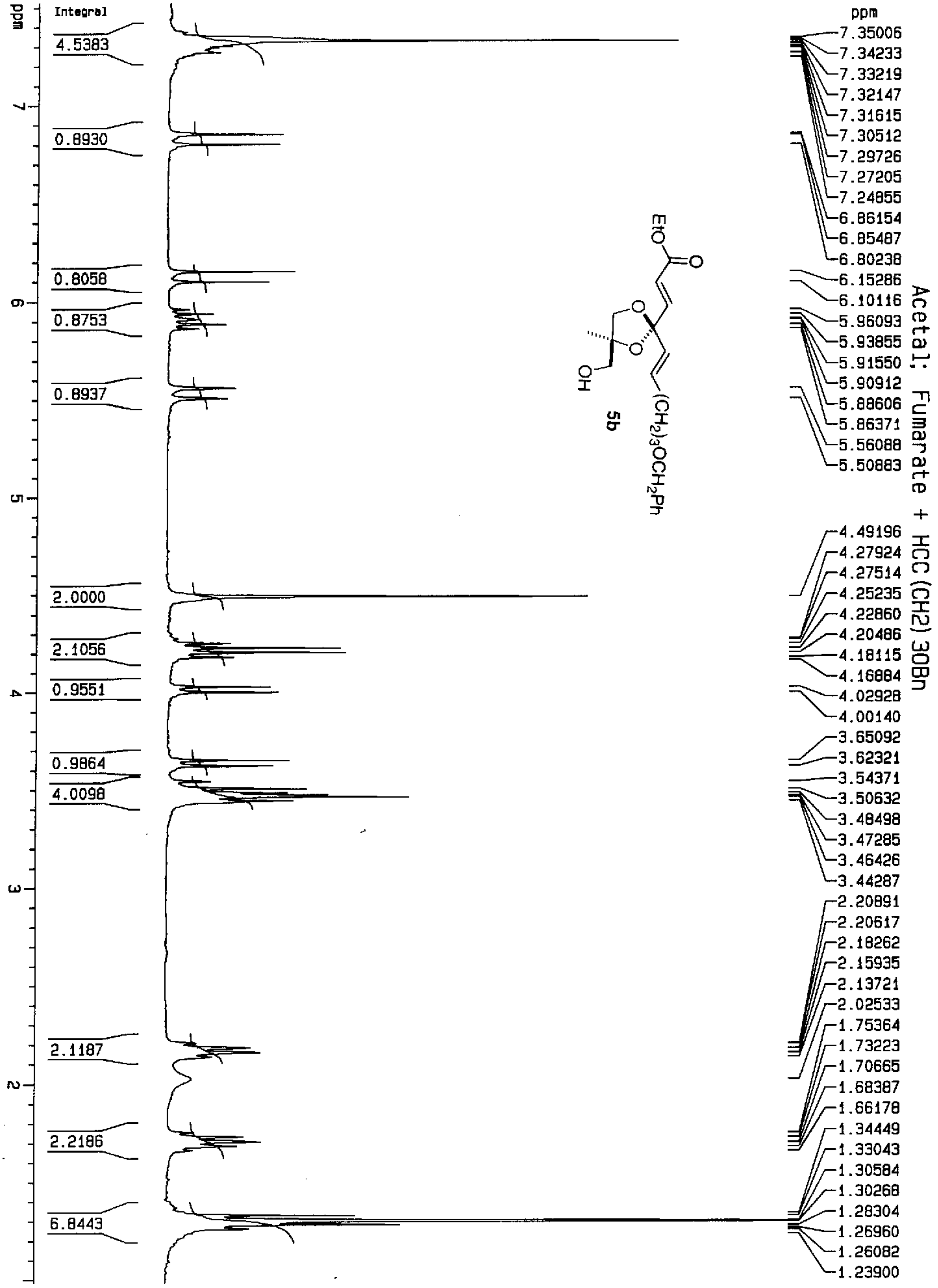
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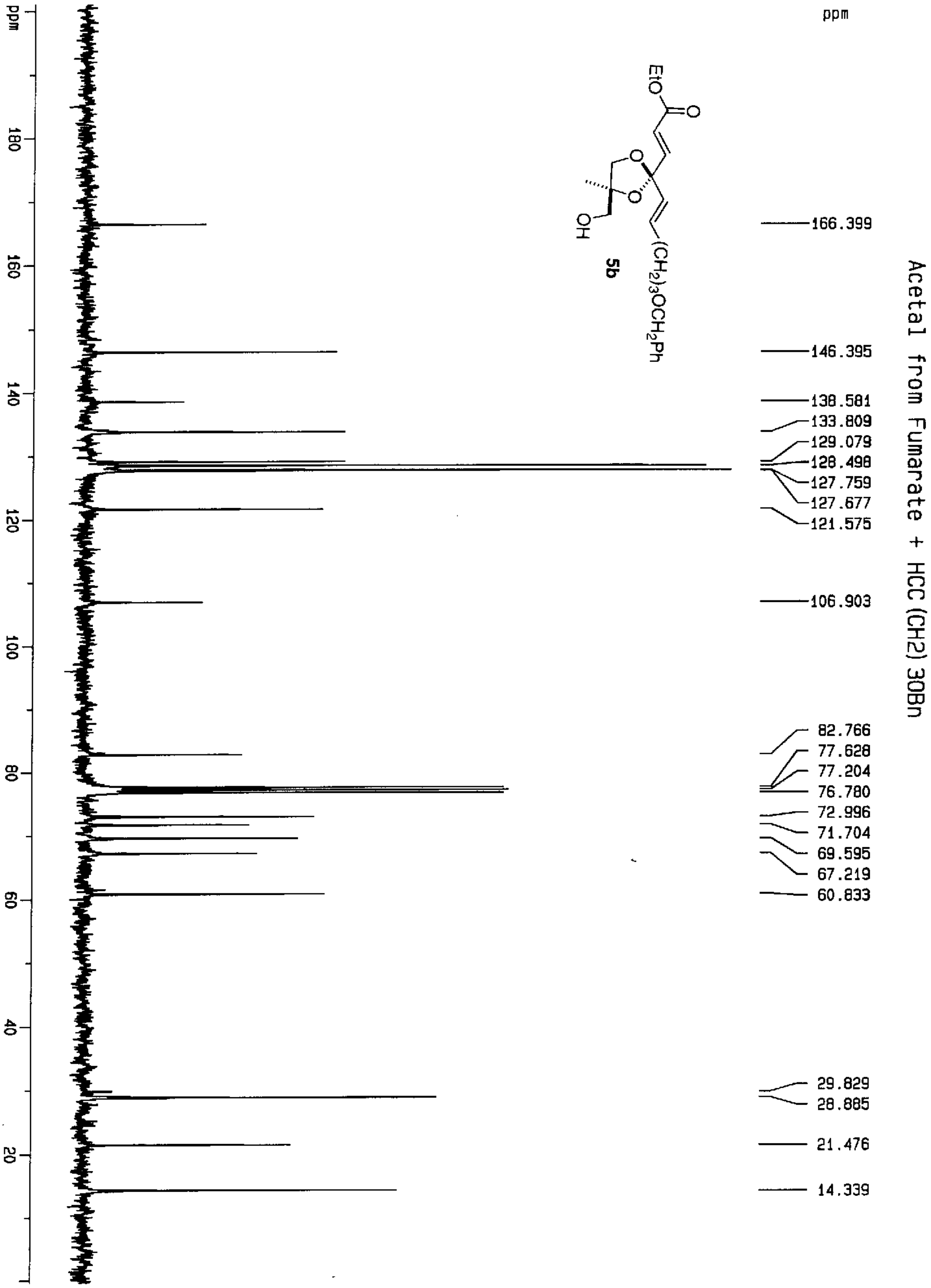
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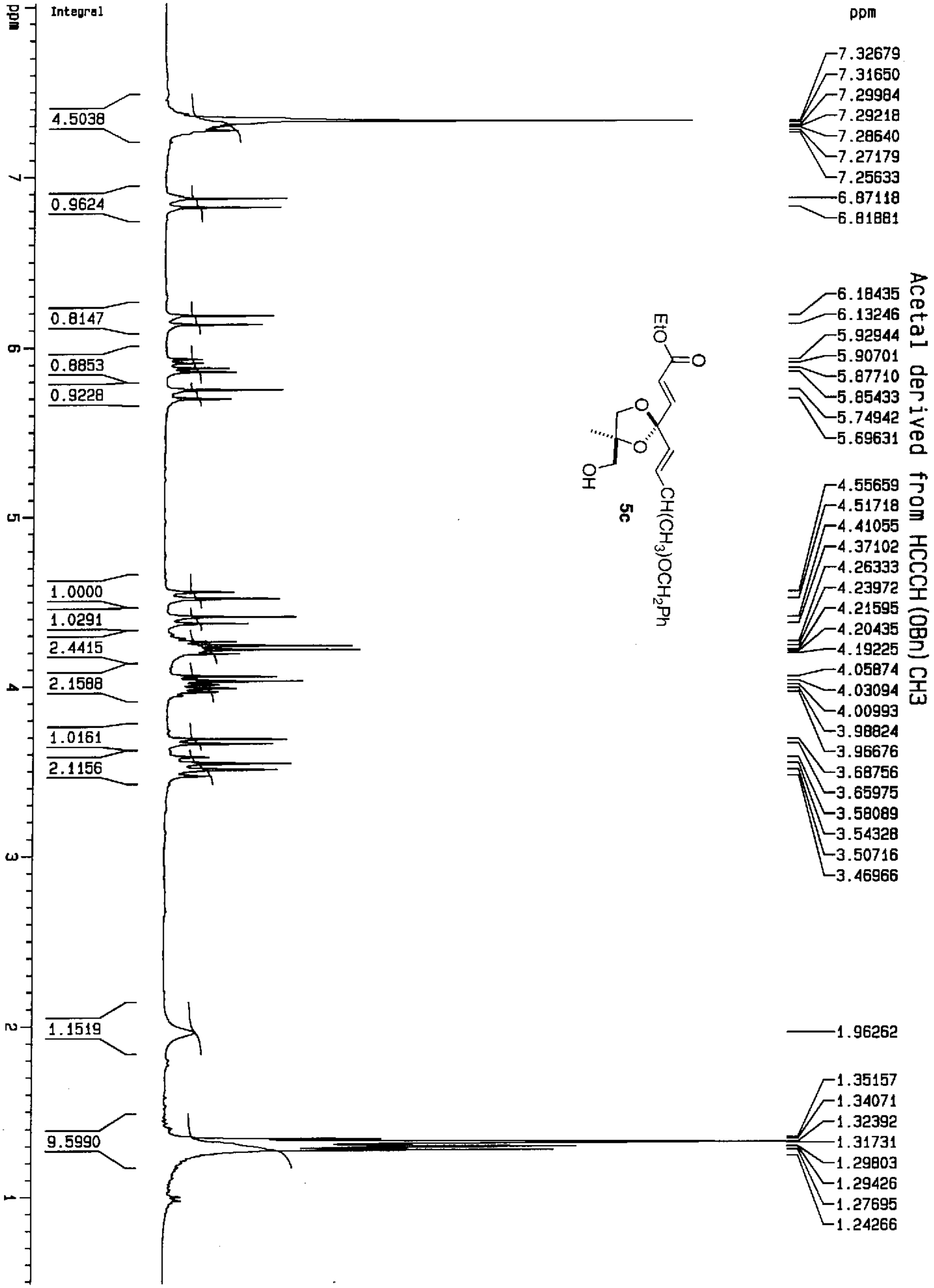
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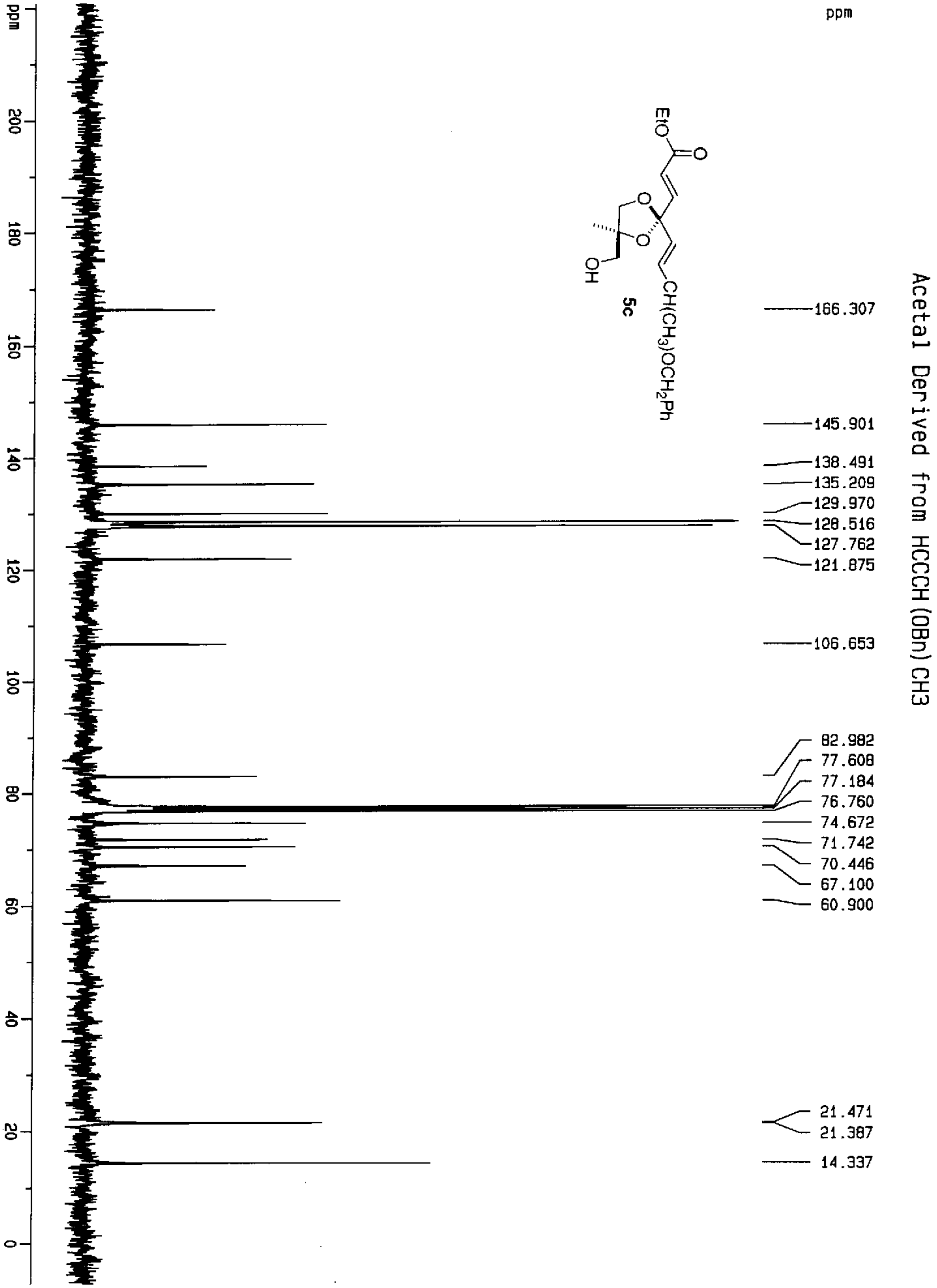
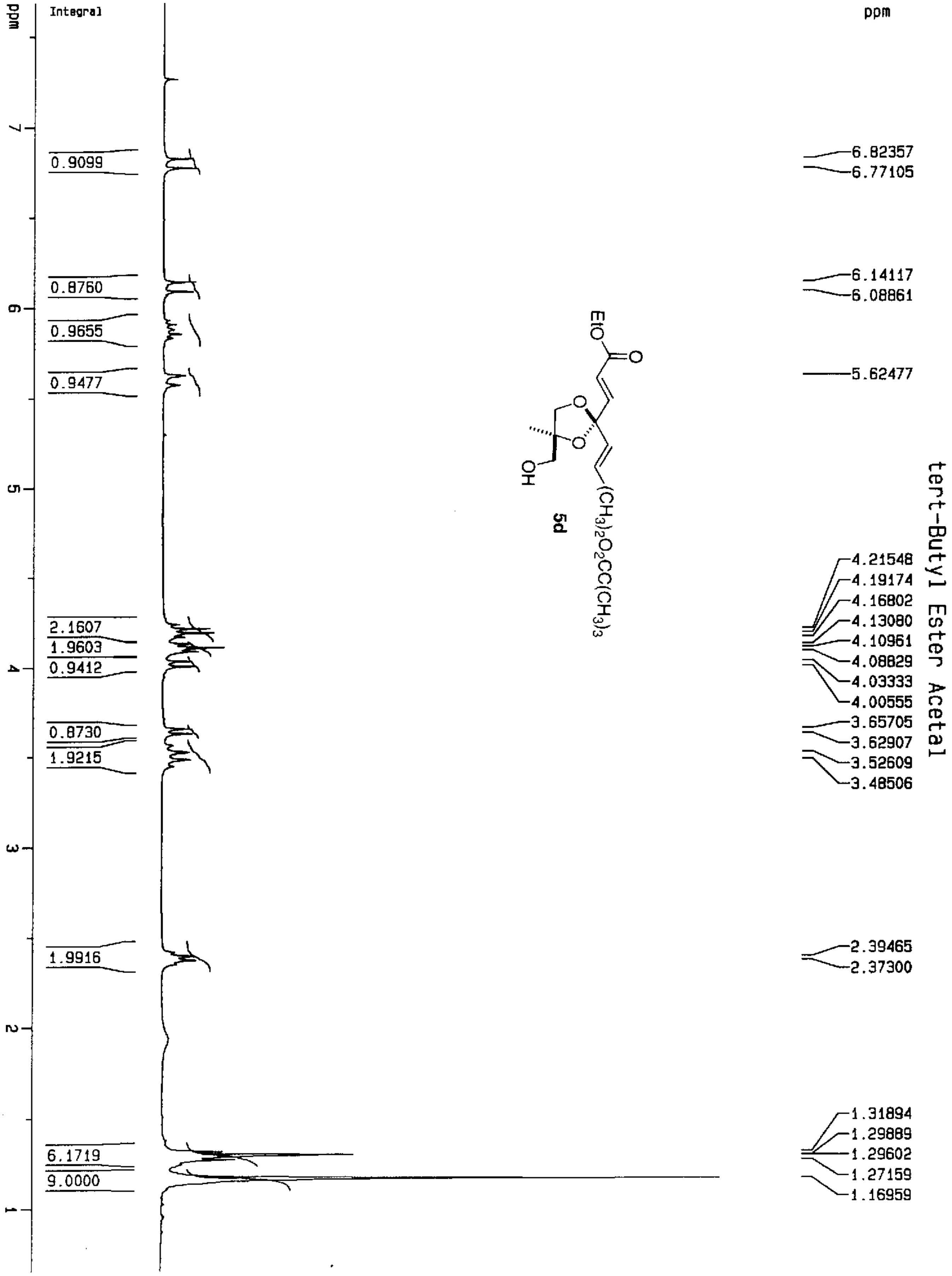
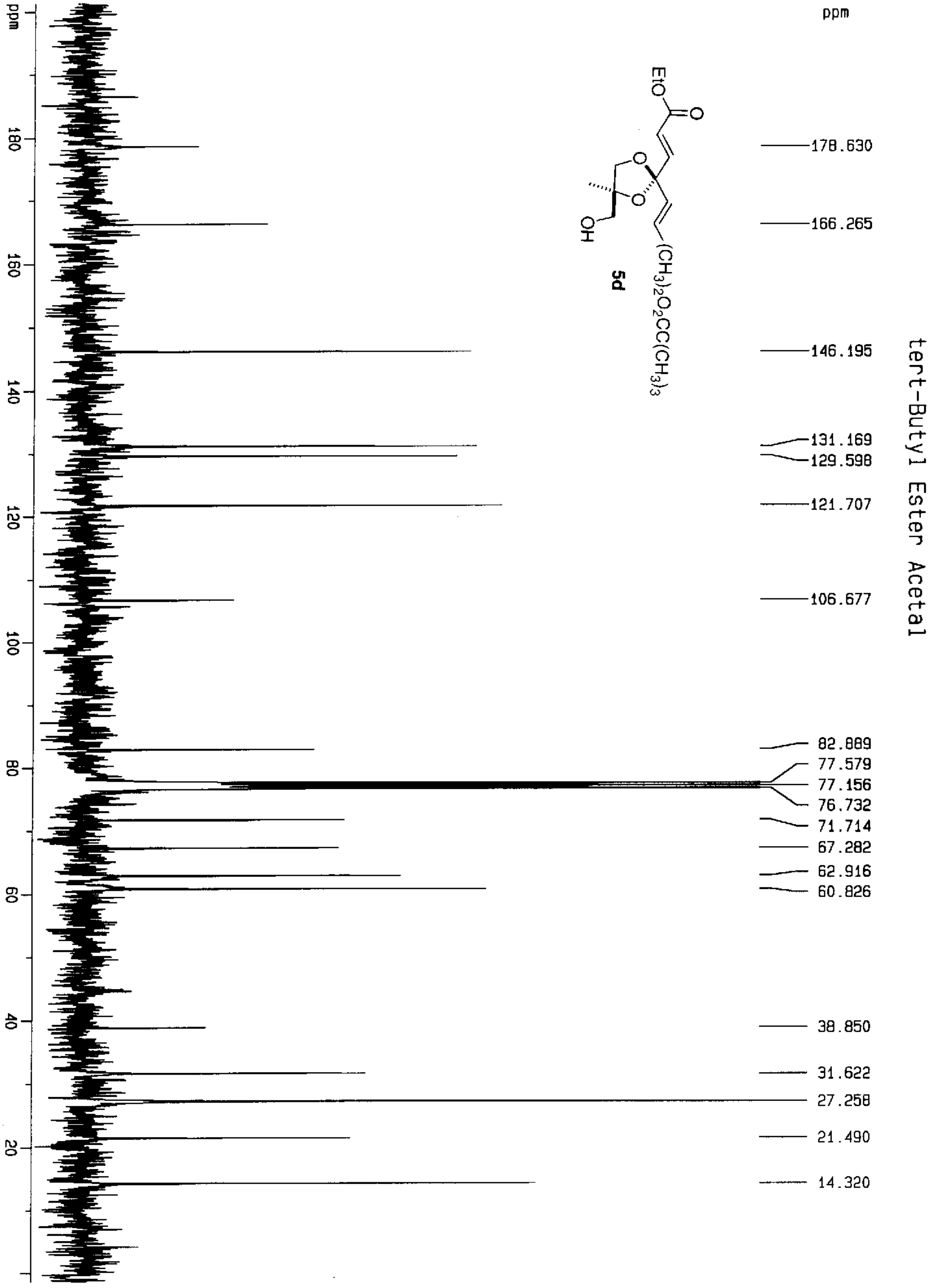
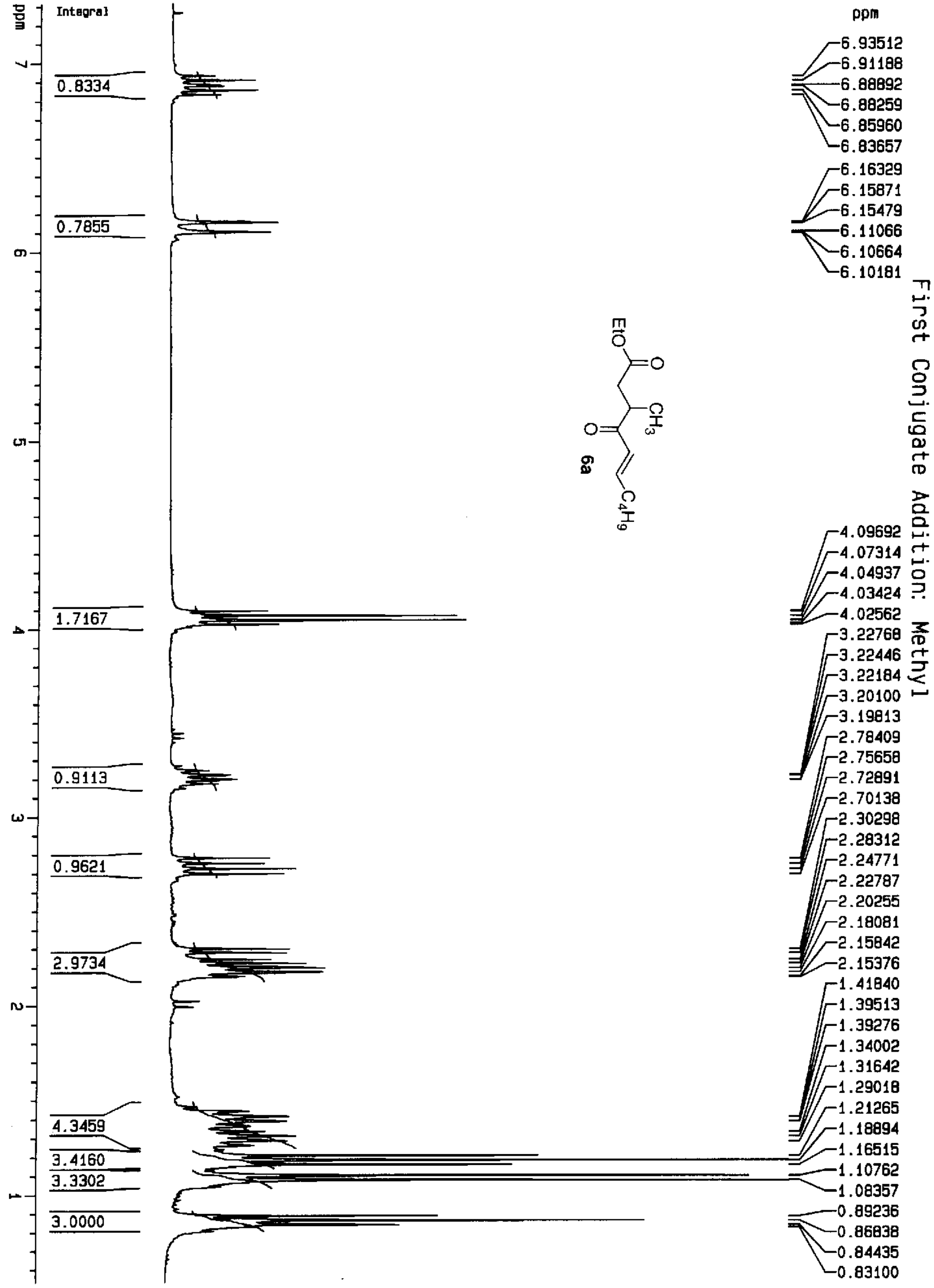
4.37102
4.26333
4.23972
4.21595
4.20435
4.19225
4.05874
4.03094
4.00993
3.98824
3.96676
3.68756
3.65975
3.58089
3.54328
3.50716
3.46966
1.96262
1.35157
1.34071
1.32392
1.31731
1.29803
1.29426
1.27695
1.24266

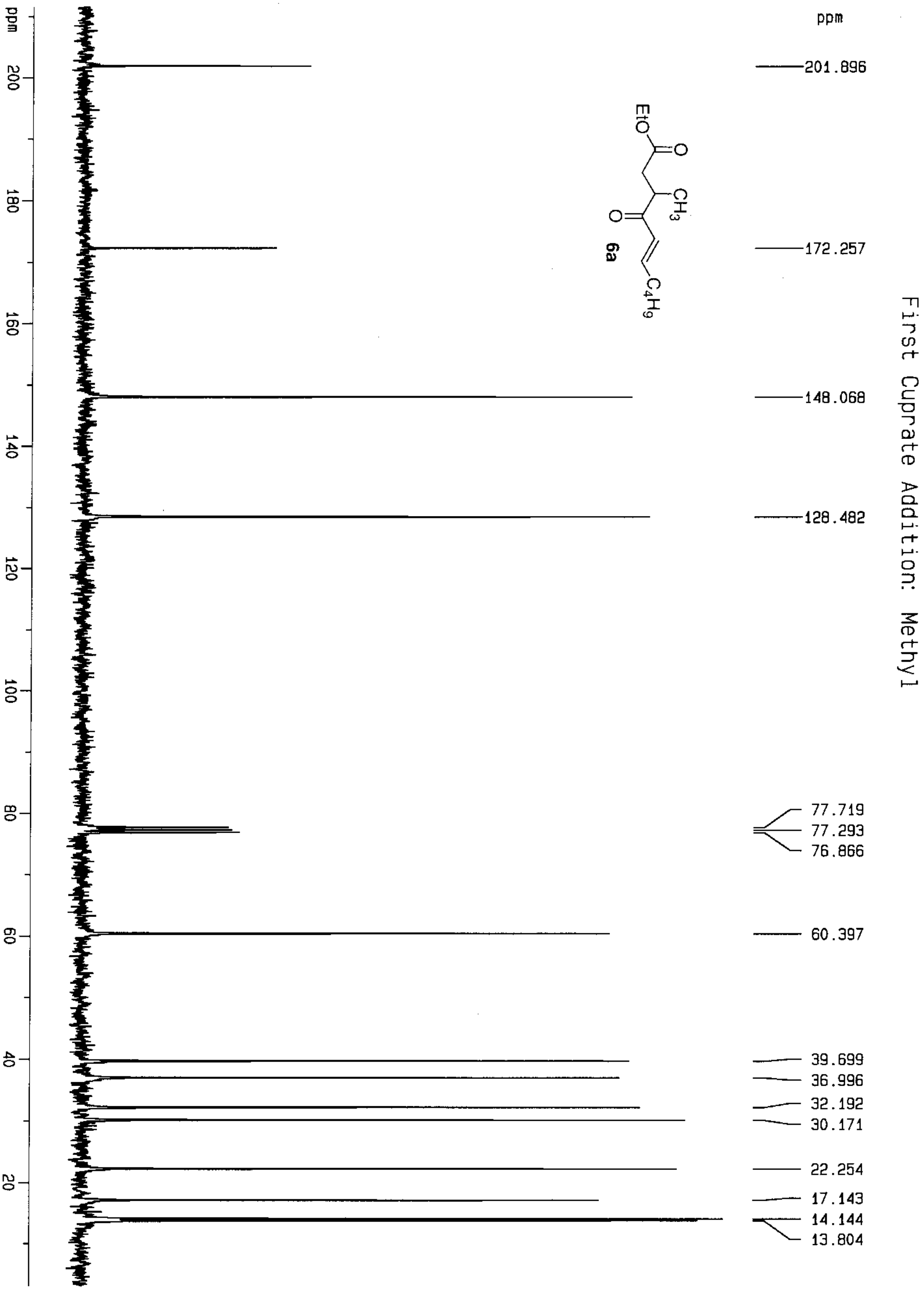

Acetal Derived from HCCCH(OBn)CH3
EtO
O
CH(CH3)OCH2Ph
OH
5c
ppm
166.307
145.901
138.491
135.209
129.970
128.516
127.762
121.875
106.653
82.982
77.608
77.184
76.760
74.672
71.742
70.446
67.100
60.900
21.471
21.387
14.337
ppm
200
180
160
140
120
100
80
60
40
20
0

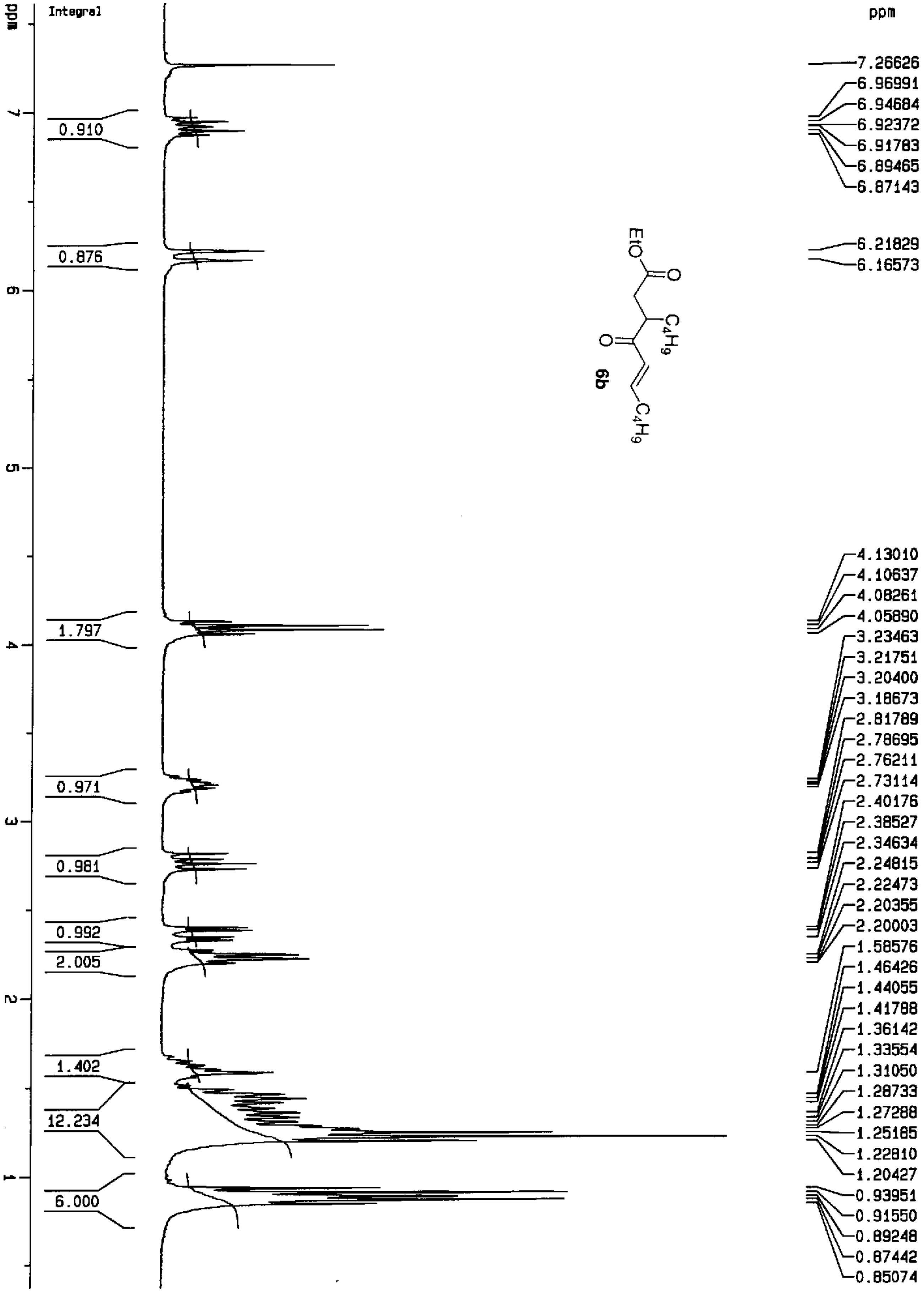

5d

tert-Butyl Ester Acetal
ppm
Integral
7
6
5
4
3
2
1
0.9099
0.8760
0.9655
0.9477
2.1607
1.9603
0.9412
0.8730
1.9215
1.9916
6.1719
9.0000
6.82357
6.77105
6.14117
6.08861
5.62477
4.21548
4.19174
4.16802
4.13080
4.10961
4.08829
4.03333
4.00555
3.65705
3.62907
3.52609
3.48506
2.39465
2.37300
1.31894
1.29889
1.29602
1.27159
1.16959
EtO
O
OH
$(CH_3)_2O_2CC(CH_3)_3$

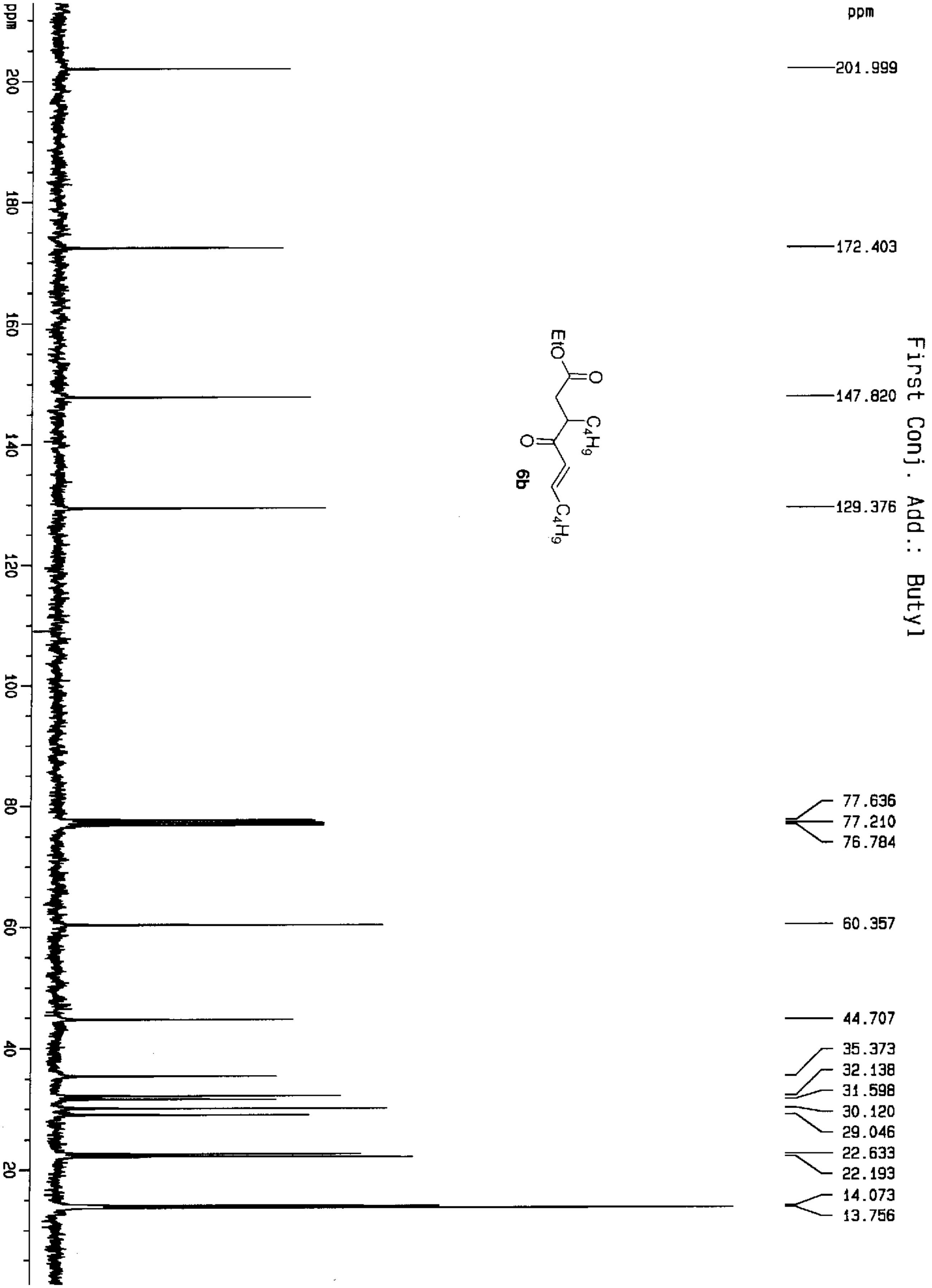

tert-Butyl Ester Acetal
EtO
O
O
O
OH
$(CH_3)_2O_2CC(CH_3)_3$
5d
ppm
178.630
166.265
146.195
131.169
129.598
121.707
106.677
82.889
77.579
77.156
76.732
71.714
67.282
62.916
60.826
38.850
31.622
27.258
21.490
14.320
ppm
180
160
140
120
100
80
60
40
20

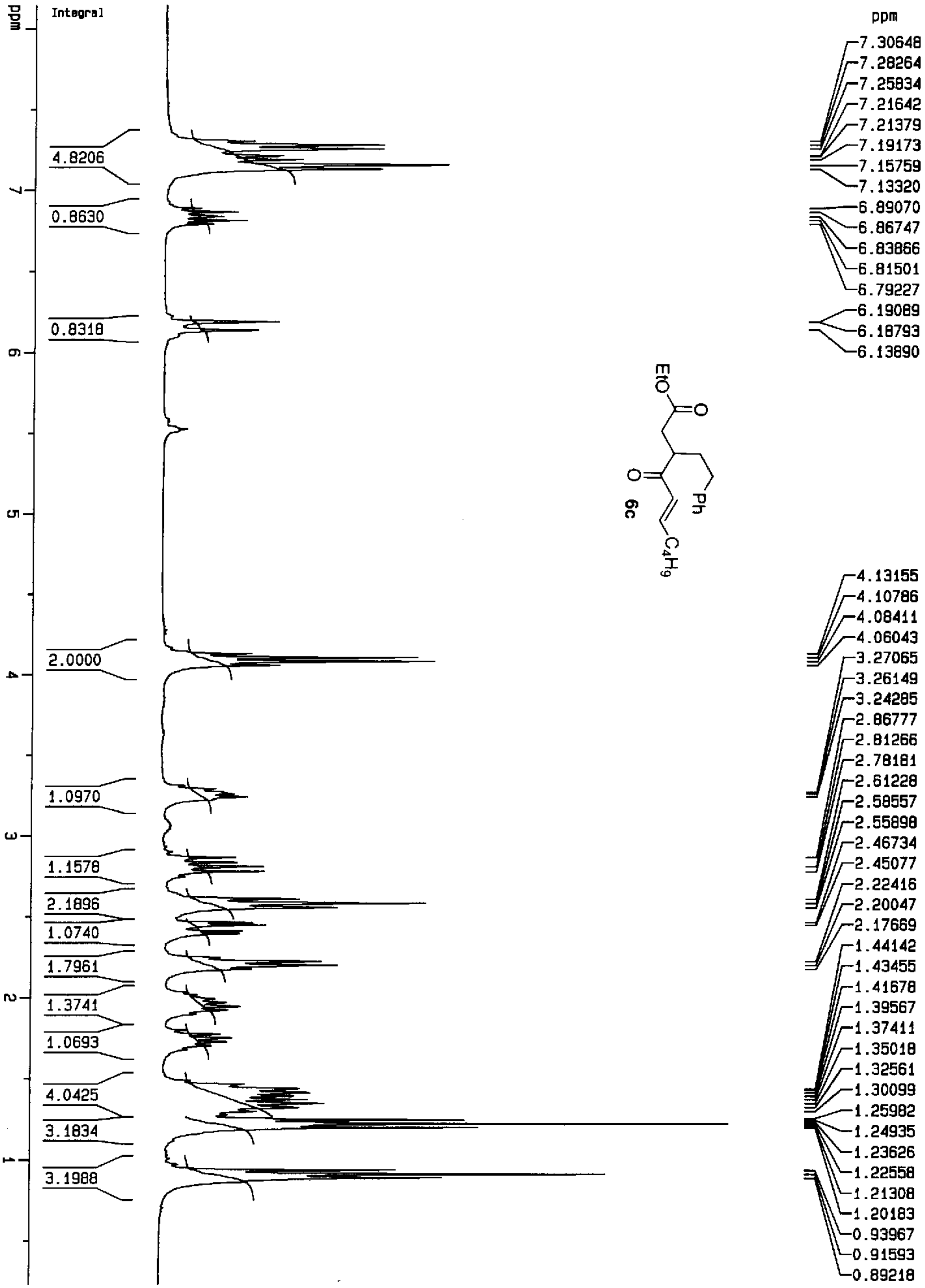

First Conjugate Addition: Methyl
ppm
Integral
0.8334
0.7855
1.7167
0.9113
0.9621
2.9734
4.3459
3.4160
3.3302
3.0000
7
6
5
4
3
2
1
6.93512
6.91188
6.88892
6.88259
6.85960
6.83657
6.16329
6.15871
6.15479
6.11066
6.10664
6.10181
4.09692
4.07314
4.04937
4.03424
4.02562
3.22768
3.22446
3.22184
3.20100
3.19813
2.78409
2.75658
2.72891
2.70138
2.30298
2.28312
2.24771
2.22787
2.20255
2.18081
2.15842
2.15376
1.41840
1.39513
1.39276
1.34002
1.31642
1.29018
1.21265
1.18894
1.16515
1.10762
1.08357
0.89236
0.86838
0.84435
0.83100
EtO
O
CH3
O
C4H9
6a


First Cuprate Addition: Methyl
6a
EtO
O
CH3
O
C4H9
ppm
200
180
160
140
120
100
80
60
40
20
ppm
201.896
172.257
148.068
128.482
77.719
77.293
76.866
60.397
39.699
36.996
32.192
30.171
22.254
17.143
14.144
13.804

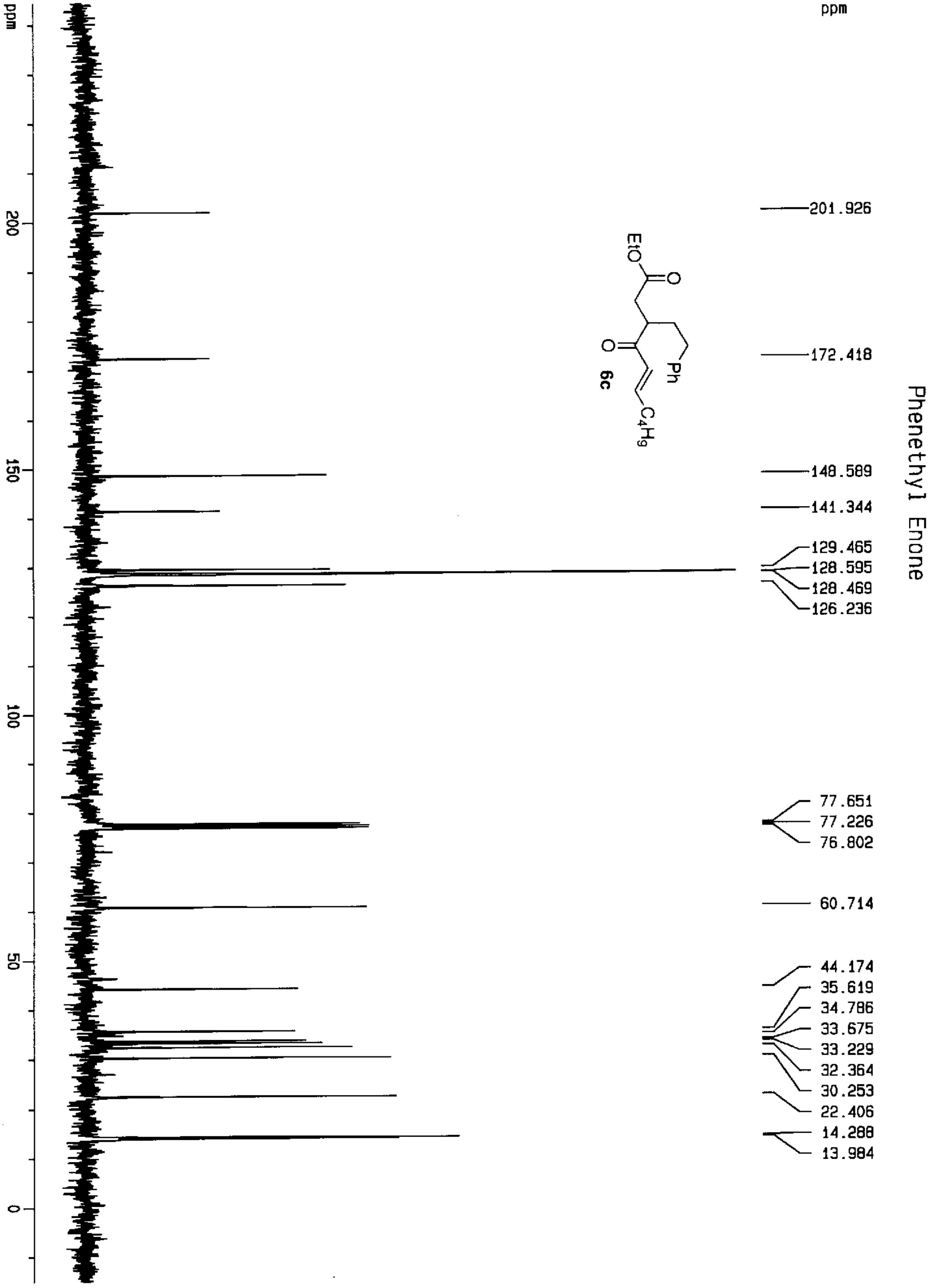

ppm
Integral
7
6
5
4
3
2
1
0.910
0.876
1.797
0.971
0.981
0.992
2.005
1.402
12.234
6.000
ppm
7.26626
6.96991
6.94684
6.92372
6.91783
6.89465
6.87143
6.21829
6.16573
4.13010
4.10637
4.08261
4.05890
3.23463
3.21751
3.20400
3.18673
2.81789
2.78695
2.76211
2.73114
2.40176
2.38527
2.34634
2.24815
2.22473
2.20355
2.20003
1.58576
1.46426
1.44055
1.41788
1.36142
1.33554
1.31050
1.28733
1.27288
1.25165
1.22810
1.20427
0.93951
0.91550
0.89248
0.87442
0.85074
EtO
O
C4H9
O
C4H9

6b


First Conj. Add.: Butyl
ppm
201.999
172.403
147.820
129.376
77.636
77.210
76.784
60.357
44.707
35.373
32.138
31.598
30.120
29.046
22.633
22.193
14.073
13.756
ppm
200
180
160
140
120
100
80
60
40
20
EtO
O
C_4H_9
O
C_4H_9
6b

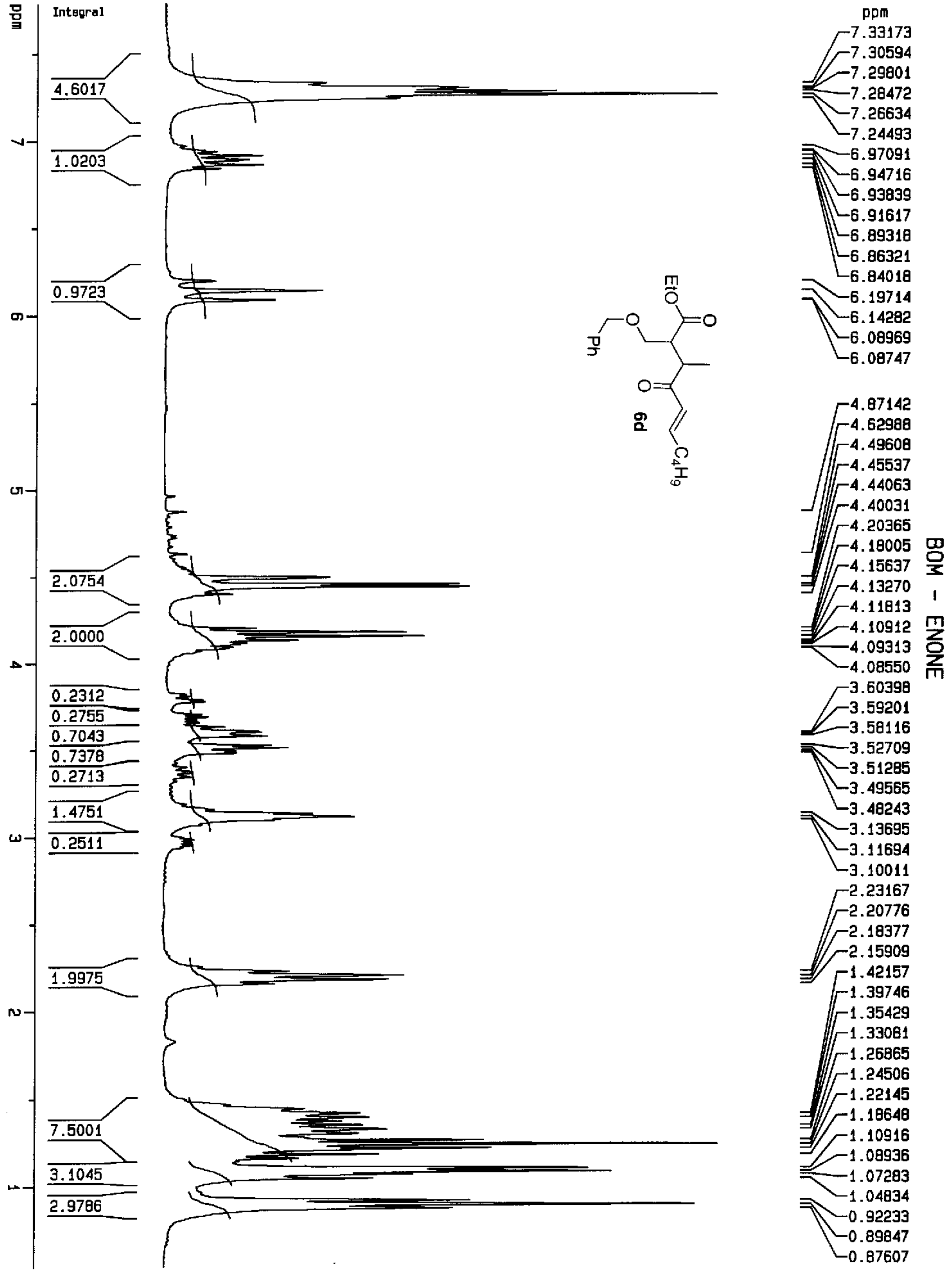


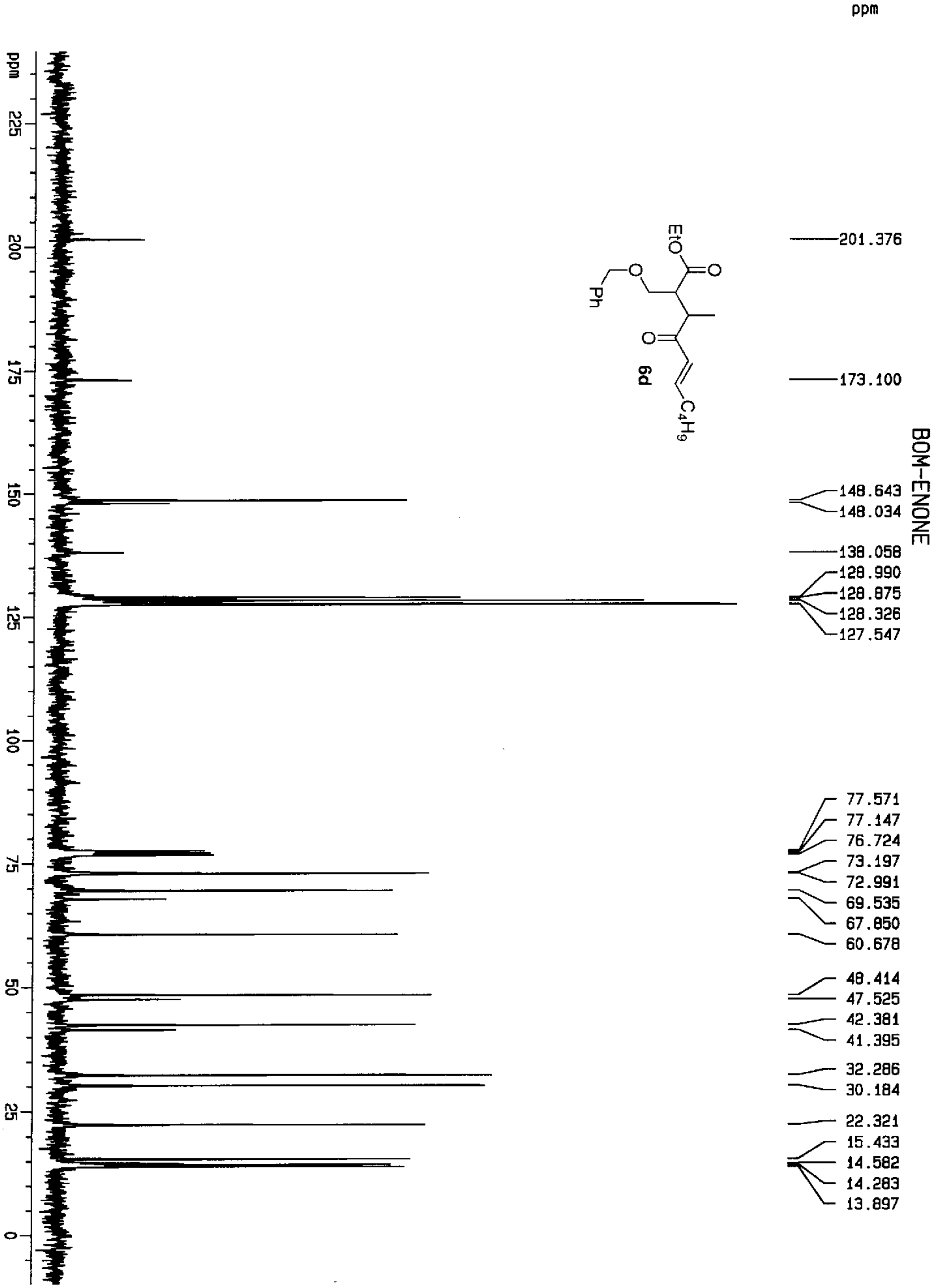
Phenethyl Enone

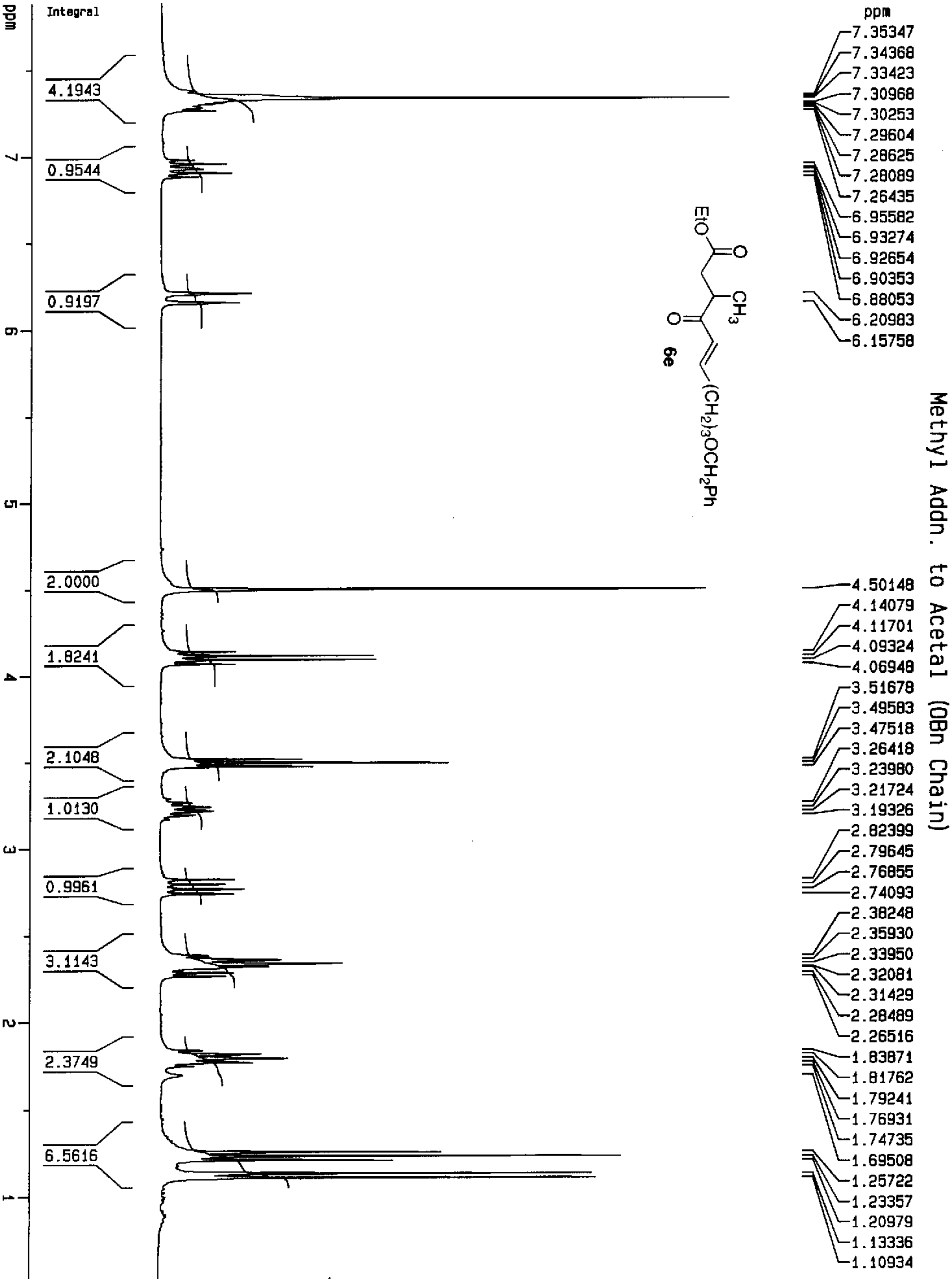


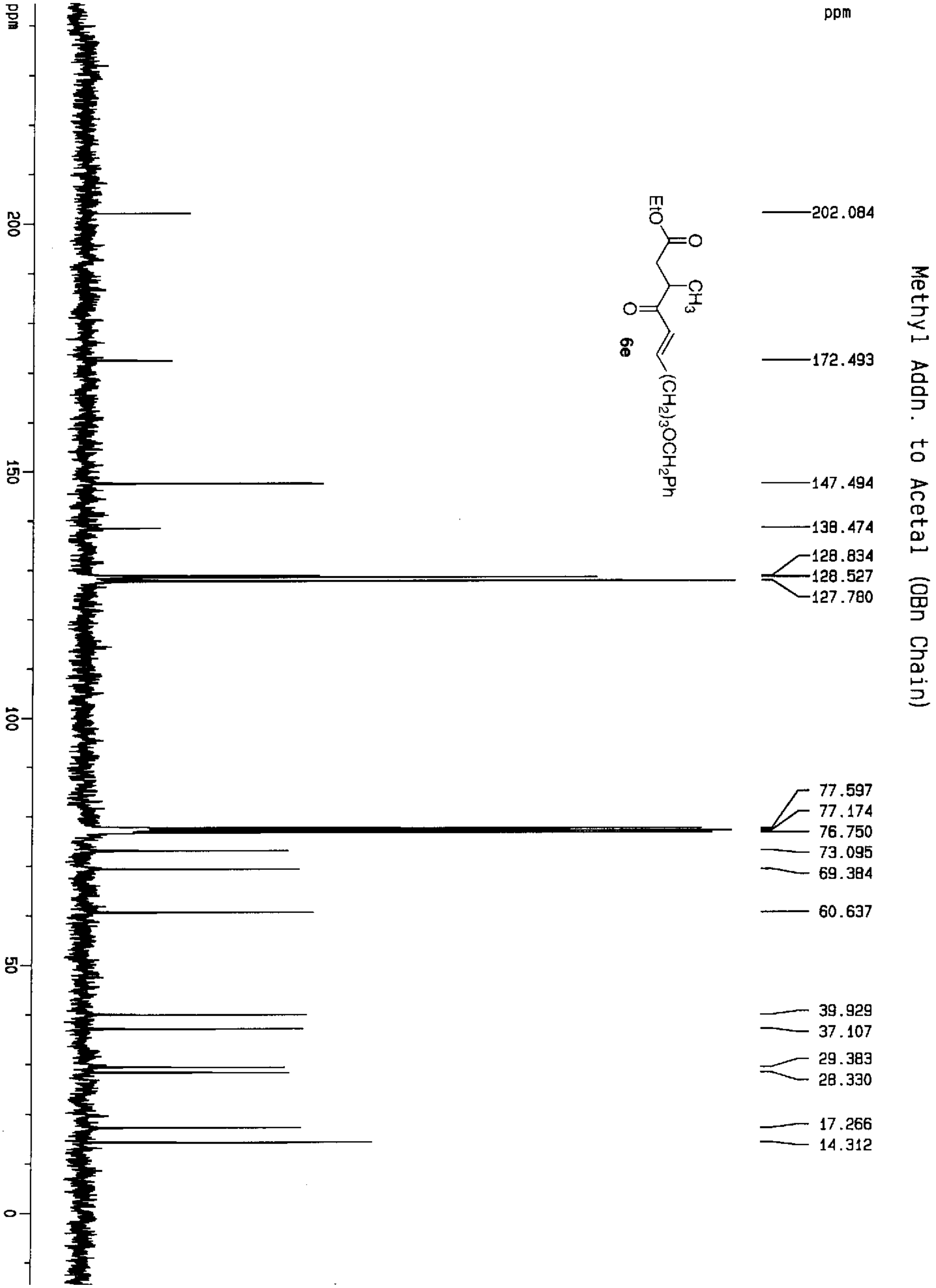
6c

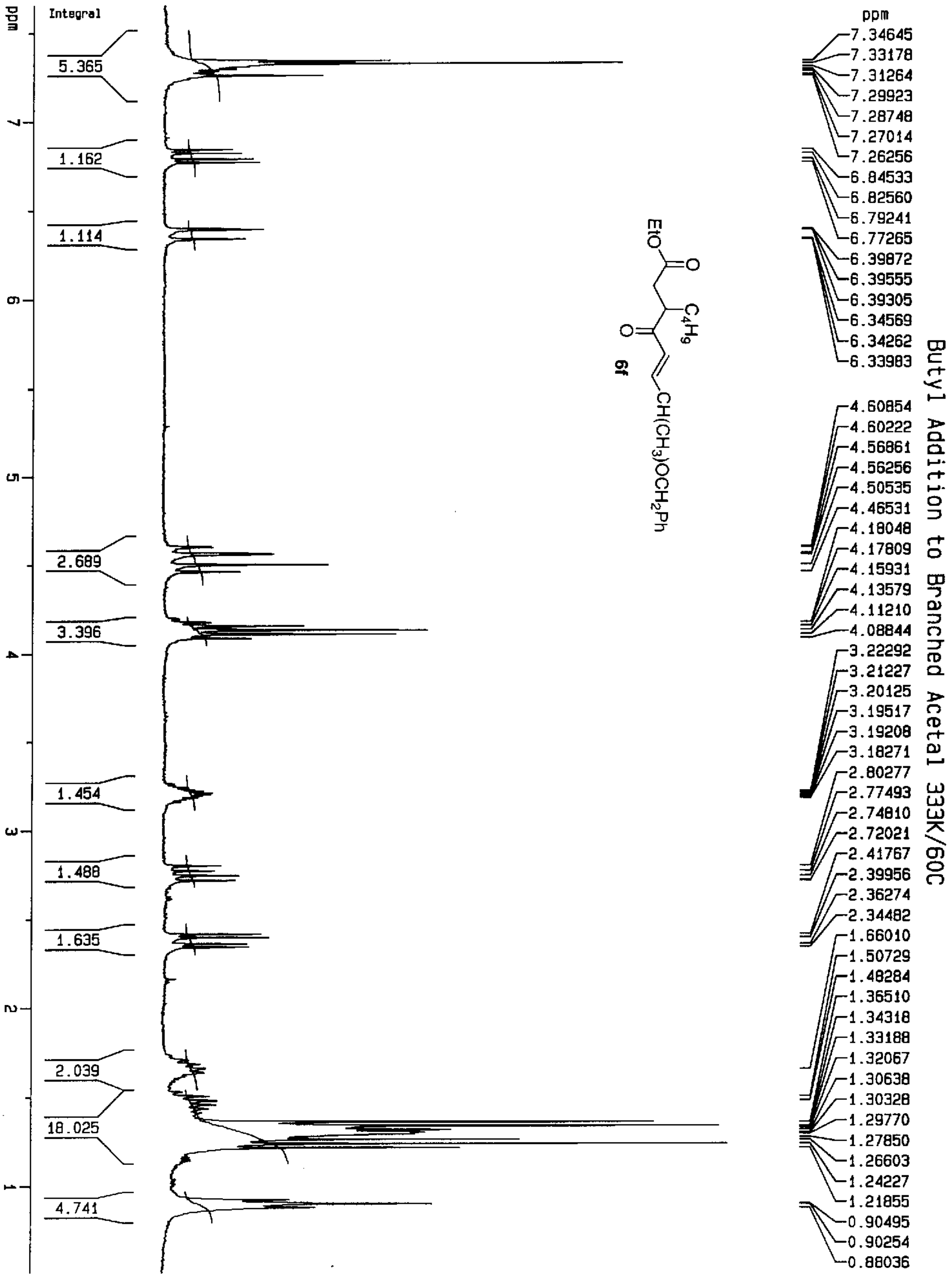
Phenethyl Enone
ppm
201.926
172.418
148.589
141.344
129.465
128.595
128.469
126.236
77.651
77.226
76.802
60.714
44.174
35.619
34.786
33.675
33.229
32.364
30.253
22.406
14.288
13.984
200
150
100
50
0
ppm
EtO
O
O
Ph
C_4H_9

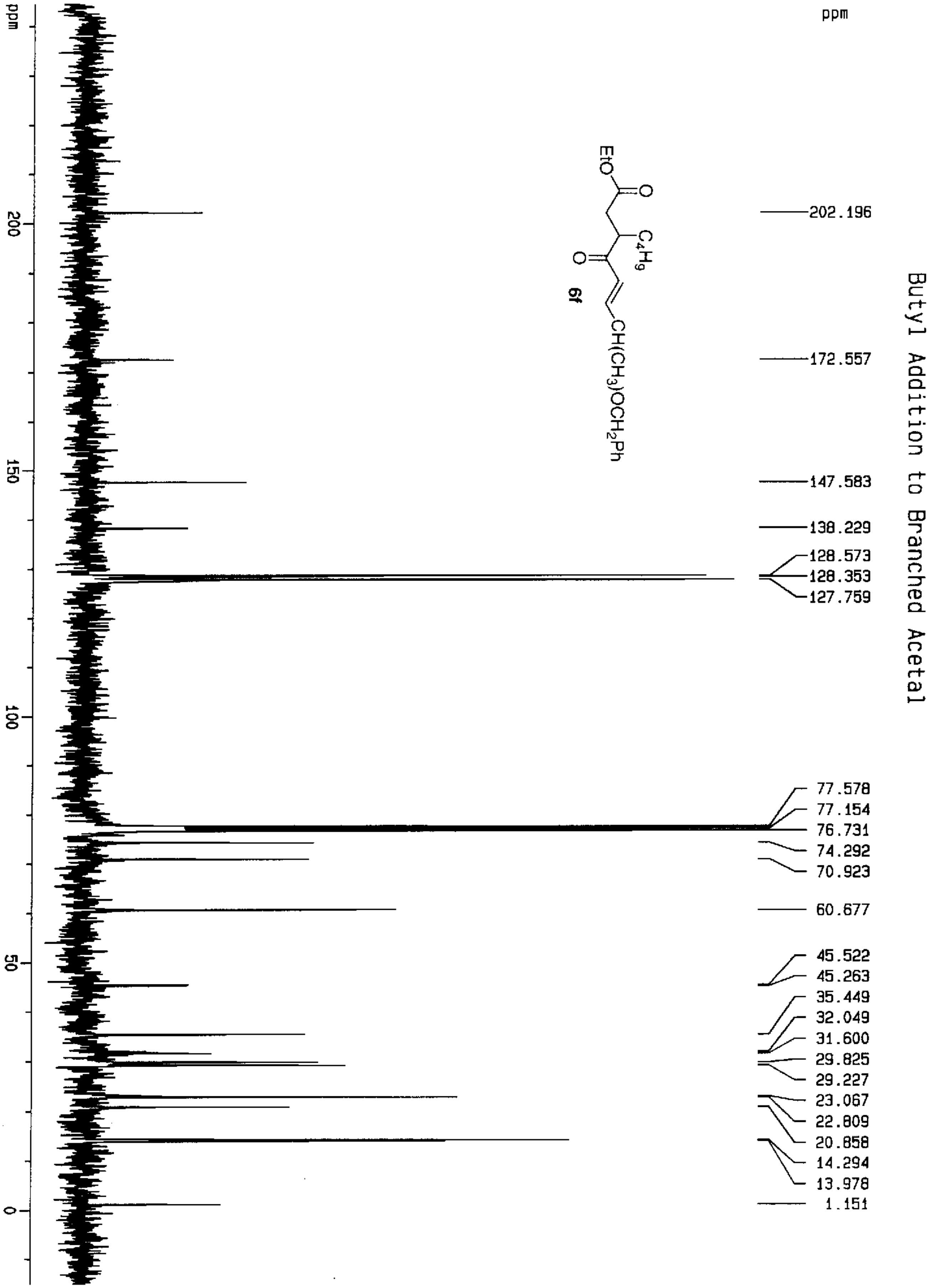

ppm
Integral
7
6
5
4
3
2
1
4.6017
1.0203
0.9723
2.0754
2.0000
0.2312
0.2755
0.7043
0.7378
0.2713
1.4751
0.2511
1.9975
7.5001
3.1045
2.9786
EtO
O
O
Ph
O
6d
C4H9
ppm
7.33173
7.30594
7.29801
7.28472
7.26634
7.24493
6.97091
6.94716
6.93839
6.91617
6.89318
6.86321
6.84018
6.19714
6.14282
6.08969
6.08747
4.87142
4.62988
4.49608
4.45537
4.44063
4.40031
4.20365
4.18005
4.15637
4.13270
4.11813
4.10912
4.09313
4.08550
3.60398
3.59201
3.58116
3.52709
3.51285
3.49565
3.48243
3.13695
3.11694
3.10011
2.23167
2.20776
2.18377
2.15909
1.42157
1.39746
1.35429
1.33081
1.26865
1.24506
1.22145
1.18648
1.10916
1.08936
1.07283
1.04834
0.92233
0.89847
0.87607
BOM - ENONE

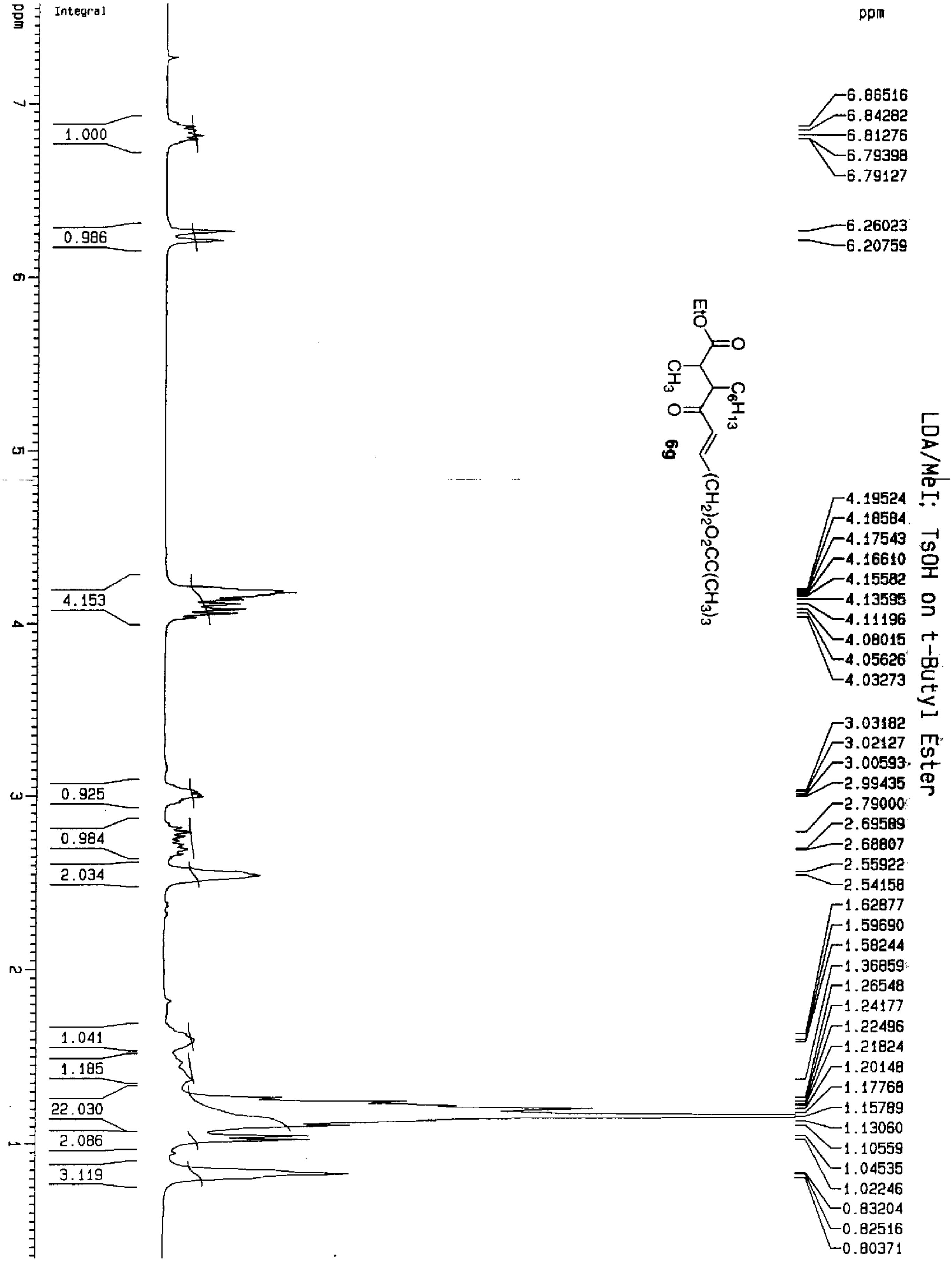

BOM-ENONE
ppm
201.376
173.100
148.643
148.034
138.058
128.990
128.875
128.326
127.547
77.571
77.147
76.724
73.197
72.991
69.535
67.850
60.678
48.414
47.525
42.381
41.395
32.286
30.184
22.321
15.433
14.582
14.283
13.897
EtO
O
O
Ph
C_4H_9
6d
ppm
225
200
175
150
125
100
75
50
25
0

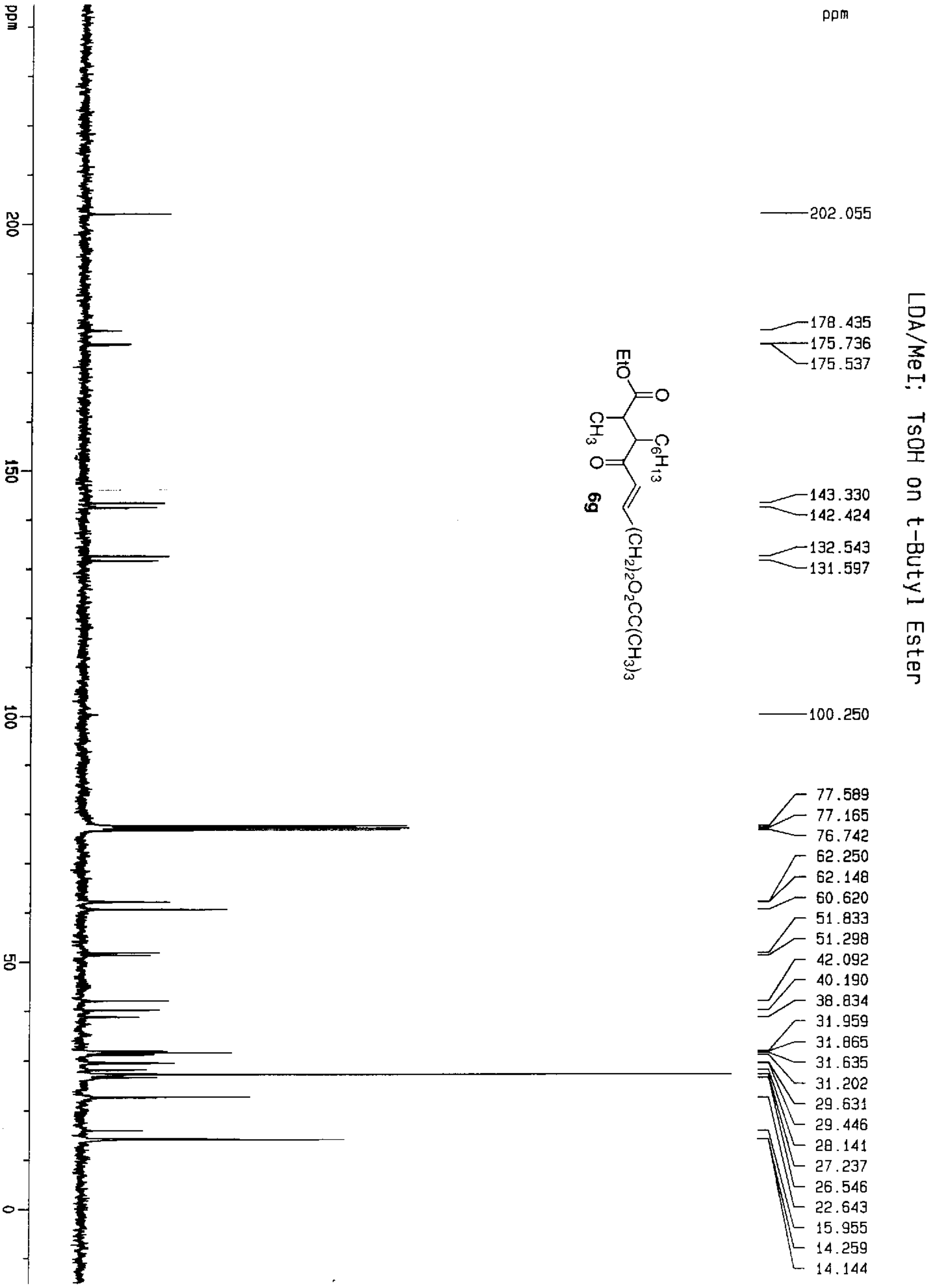

Methyl Addn. to Acetal (OBn Chain)
EtO
O
CH3
O
(CH2)3OCH2Ph
6e
ppm
Integral
4.1943
0.9544
0.9197
2.0000
1.8241
2.1048
1.0130
0.9961
3.1143
2.3749
6.5616
7
6
5
4
3
2
1
ppm
7.35347
7.34368
7.33423
7.30968
7.30253
7.29604
7.28625
7.28089
7.26435
6.95582
6.93274
6.92654
6.90353
6.88053
6.20983
6.15758
4.50148
4.14079
4.11701
4.09324
4.06948
3.51678
3.49583
3.47518
3.26418
3.23980
3.21724
3.19326
2.82399
2.79645
2.76855
2.74093
2.38248
2.35930
2.33950
2.32081
2.31429
2.28489
2.26516
1.83871
1.81762
1.79241
1.76931
1.74735
1.69508
1.25722
1.23357
1.20979
1.13336
1.10934


Methyl Addn. to Acetal (OBn Chain)
ppm
202.084
172.493
147.494
138.474
128.834
128.527
127.780
77.597
77.174
76.750
73.095
69.384
60.637
39.929
37.107
29.383
28.330
17.266
14.312
ppm
200
150
100
50
0
EtO
O
CH3
O
(CH2)3OCH2Ph
6e


Butyl Addition to Branched Acetal 333K/60C
6f
EtO
O
C4H9
O
CH(CH3)OCH2Ph
ppm
Integral
5.365
1.162
1.114
2.689
3.396
1.454
1.488
1.635
2.039
18.025
4.741
7
6
5
4
3
2
1
ppm
7.34645
7.33178
7.31264
7.29923
7.28748
7.27014
7.26256
6.84533
6.82560
6.79241
6.77265
6.39872
6.39555
6.39305
6.34569
6.34262
6.33983
4.60854
4.60222
4.56861
4.56256
4.50535
4.46531
4.18048
4.17809
4.15931
4.13579
4.11210
4.08844
3.22292
3.21227
3.20125
3.19517
3.19208
3.18271
2.80277
2.77493
2.74810
2.72021
2.41767
2.39956
2.36274
2.34482
1.66010
1.50729
1.48284
1.36510
1.34318
1.33188
1.32067
1.30638
1.30328
1.29770
1.27850
1.26603
1.24227
1.21855
0.90495
0.90254
0.88036

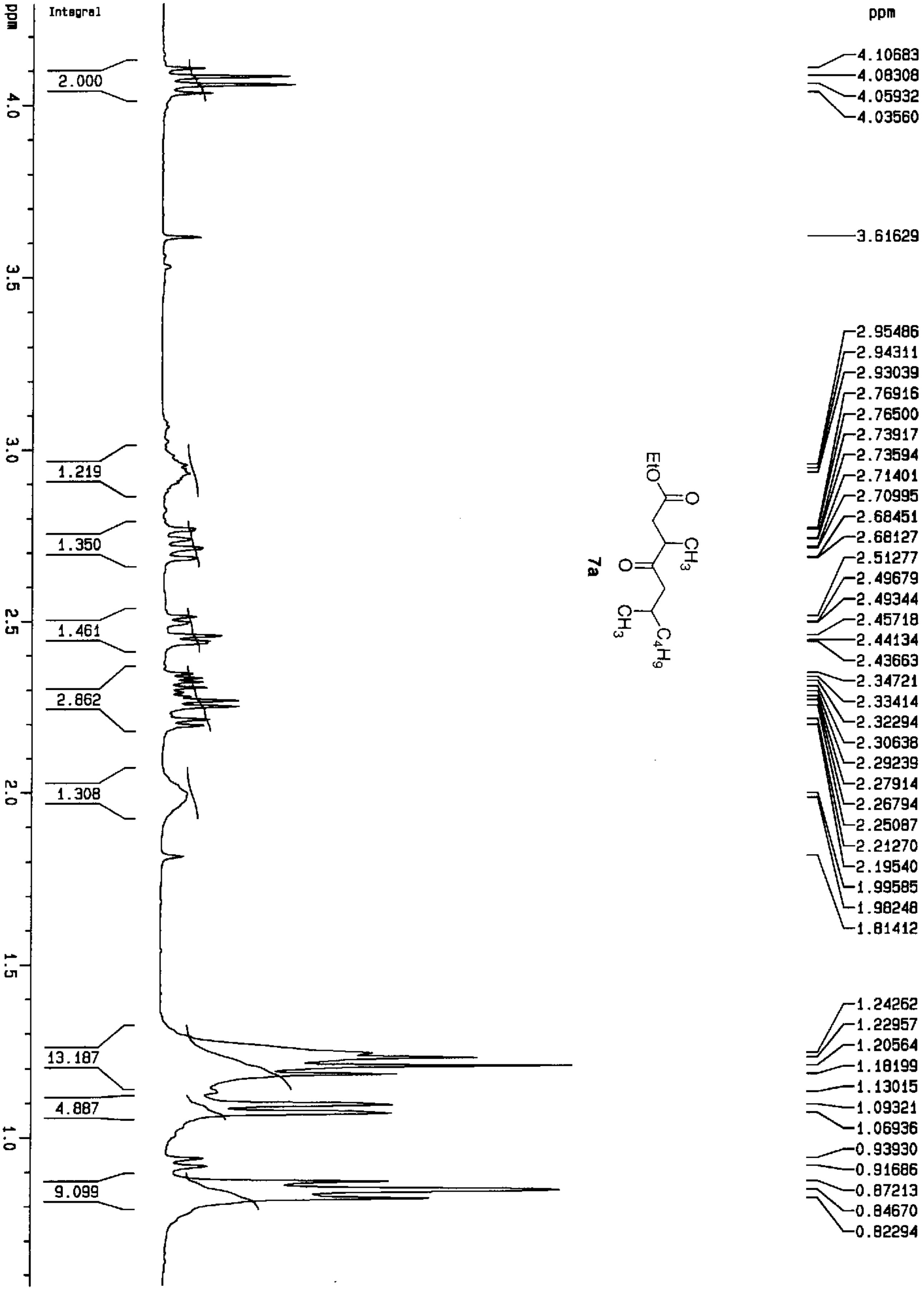

Butyl Addition to Branched Acetal
ppm
EtO
O
O
C_4H_9
$CH(CH_3)OCH_2Ph$
6f
202.196
172.557
147.583
138.229
128.573
128.353
127.759
77.578
77.154
76.731
74.292
70.923
60.677
45.522
45.263
35.449
32.049
31.600
29.825
29.227
23.067
22.809
20.858
14.294
13.978
1.151
ppm
200
150
100
50
0


LDA/MeI; TsOH on t-Butyl Ester
EtO
O
CH3
C6H13
O
(CH2)2O2CC(CH3)3
6g
ppm
Integral
7
6
5
4
3
2
1
1.000
0.986
4.153
0.925
0.984
2.034
1.041
1.185
22.030
2.086
3.119
ppm
6.86516
6.84282
6.81276
6.79398
6.79127
6.26023
6.20759
4.19524
4.18584
4.17543
4.16610
4.15582
4.13595
4.11196
4.08015
4.05626
4.03273
3.03182
3.02127
3.00593
2.99435
2.79000
2.69589
2.68807
2.55922
2.54158
1.62877
1.59690
1.58244
1.36859
1.26548
1.24177
1.22496
1.21824
1.20148
1.17768
1.15789
1.13060
1.10559
1.04535
1.02246
0.83204
0.82516
0.80371



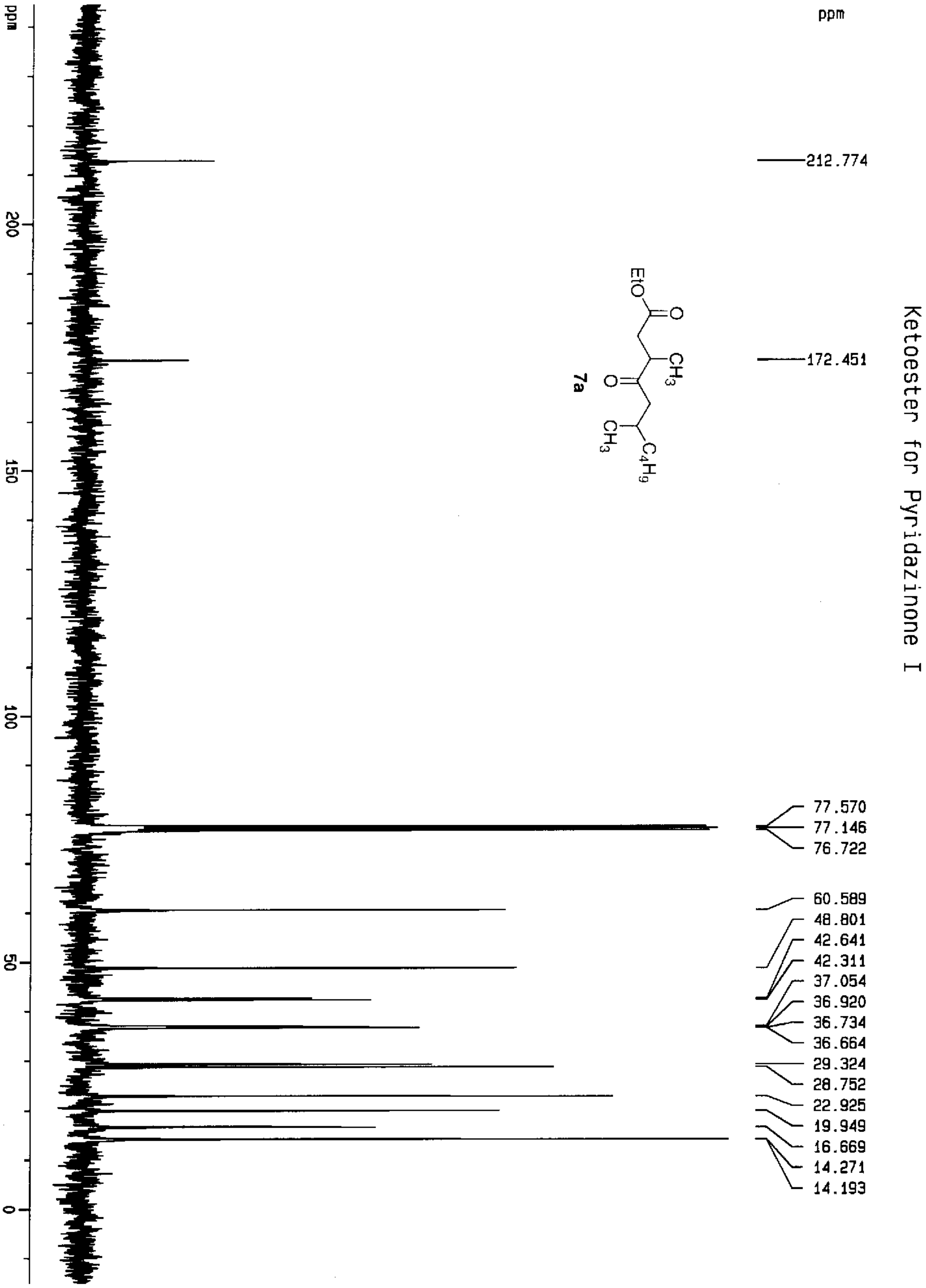
6g

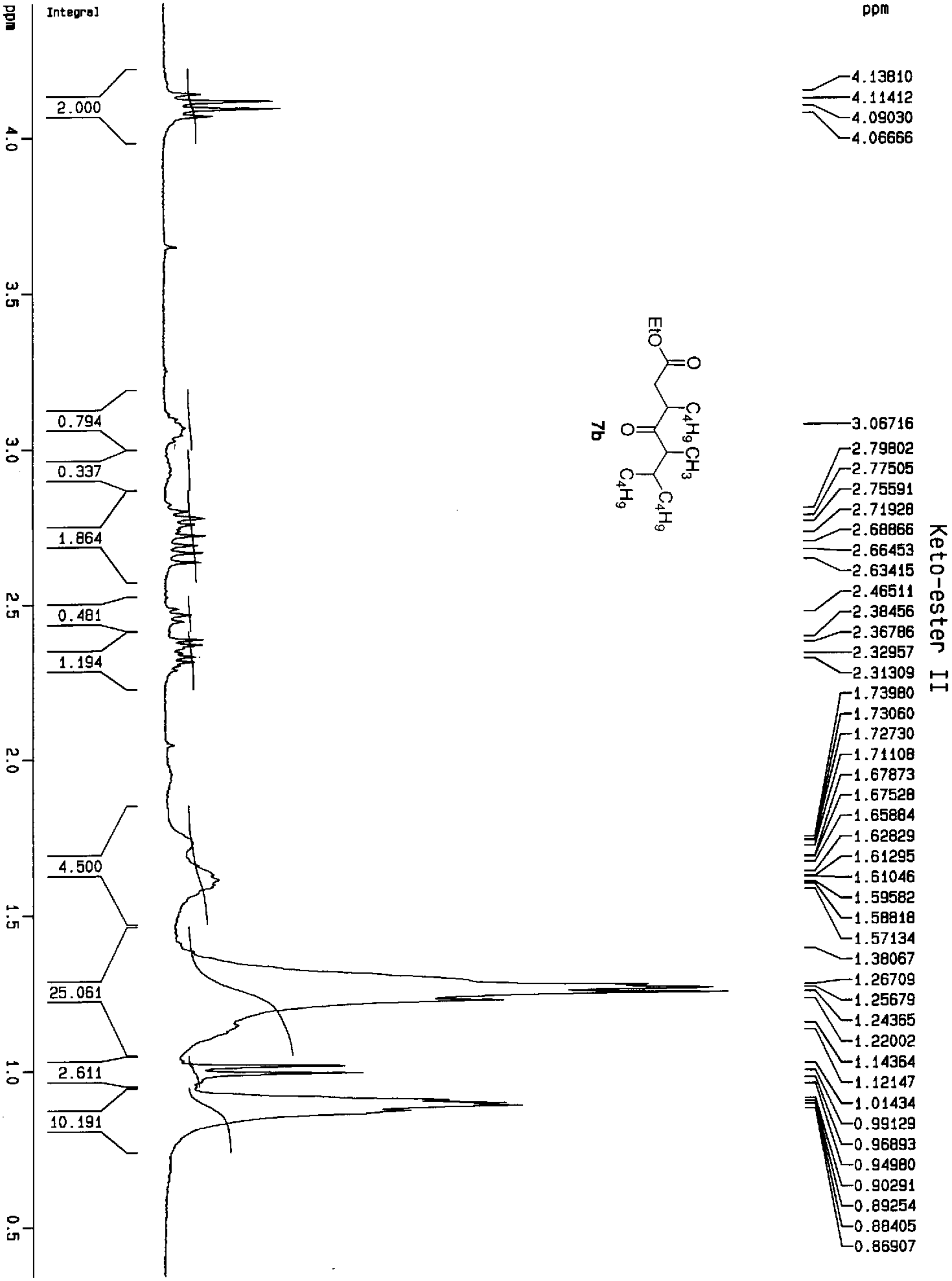
LDA/MeI; TsOH on t-Butyl Ester

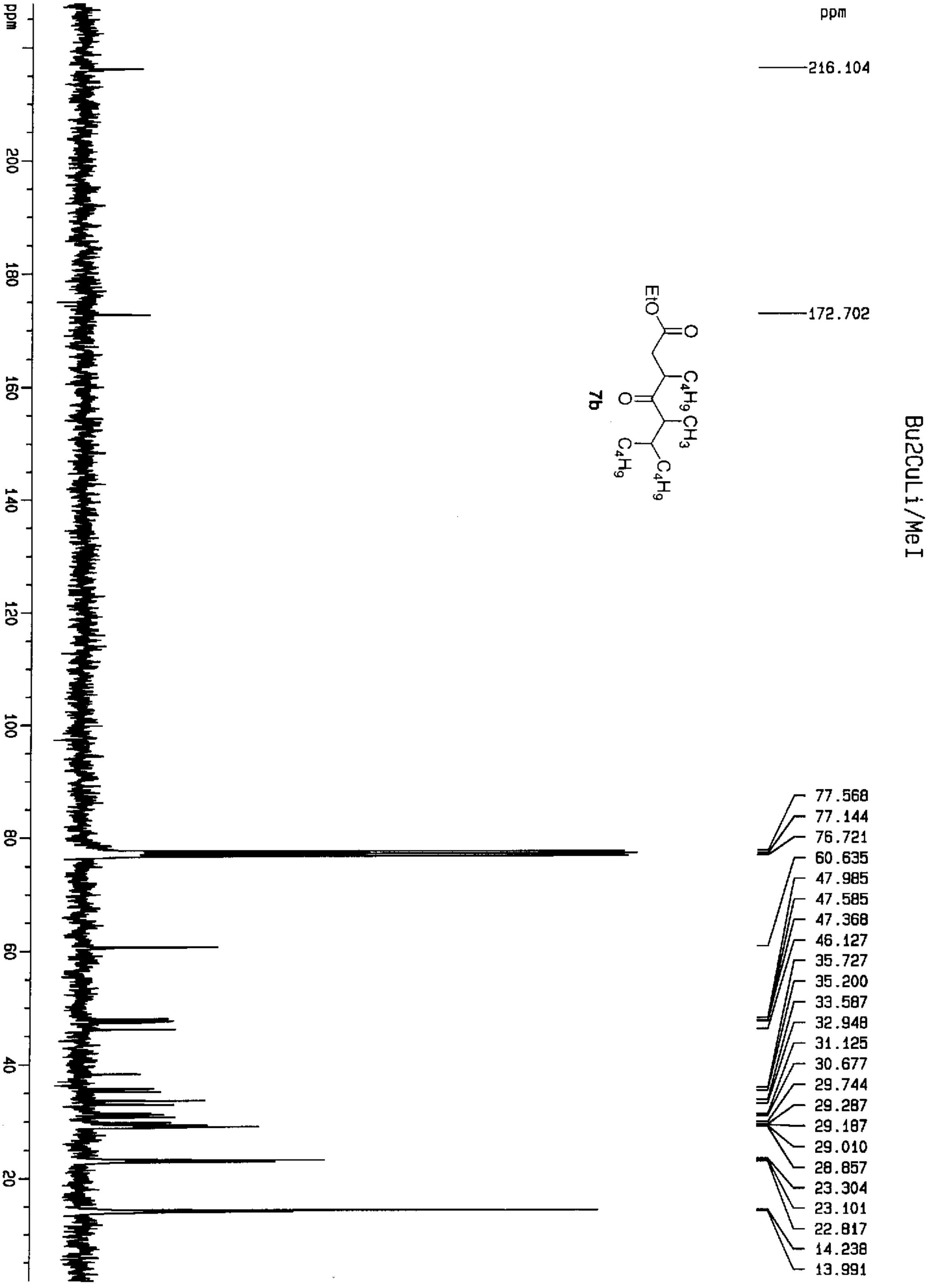


7a

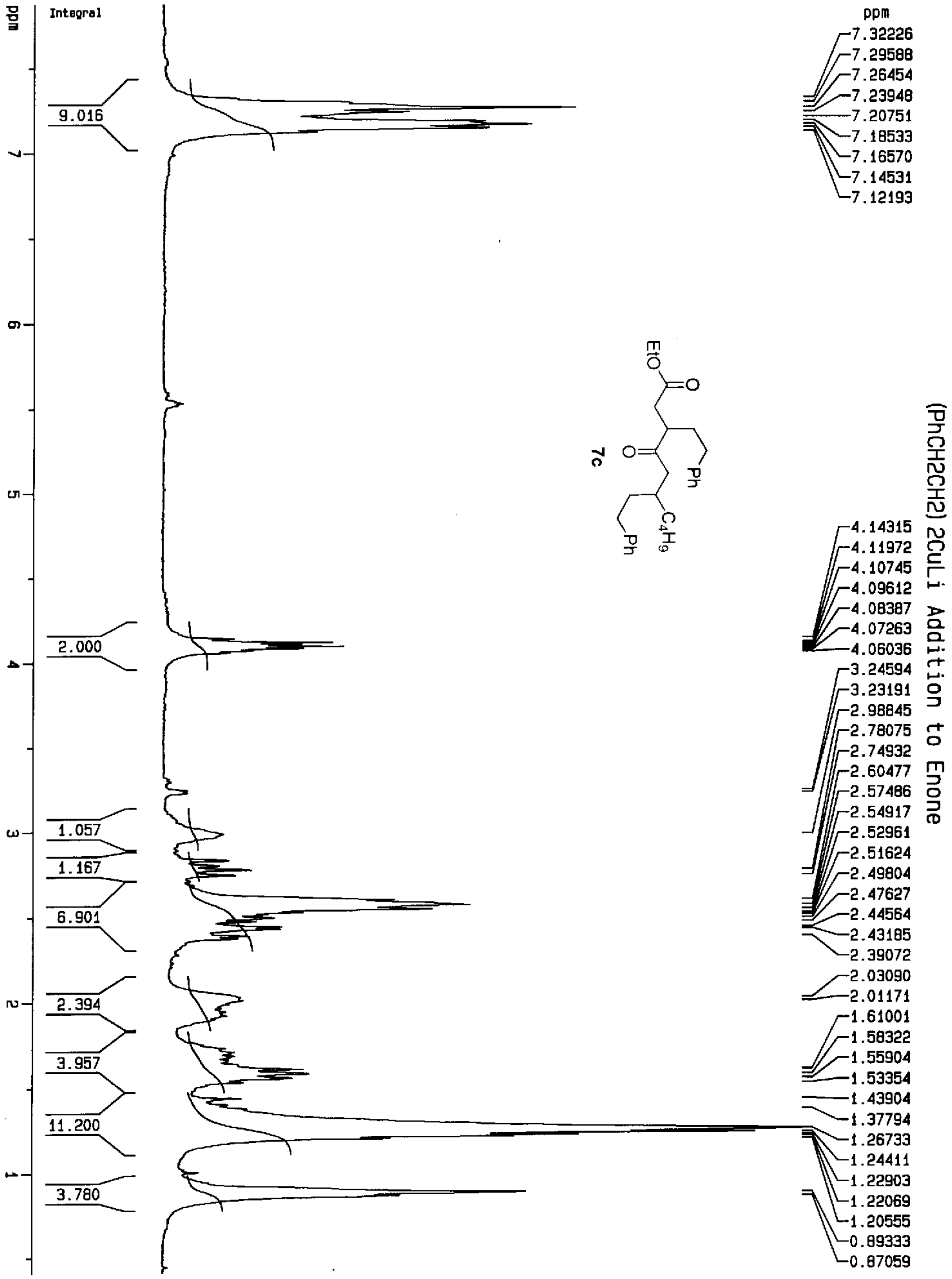
Second Conjugate Addition: Methyl

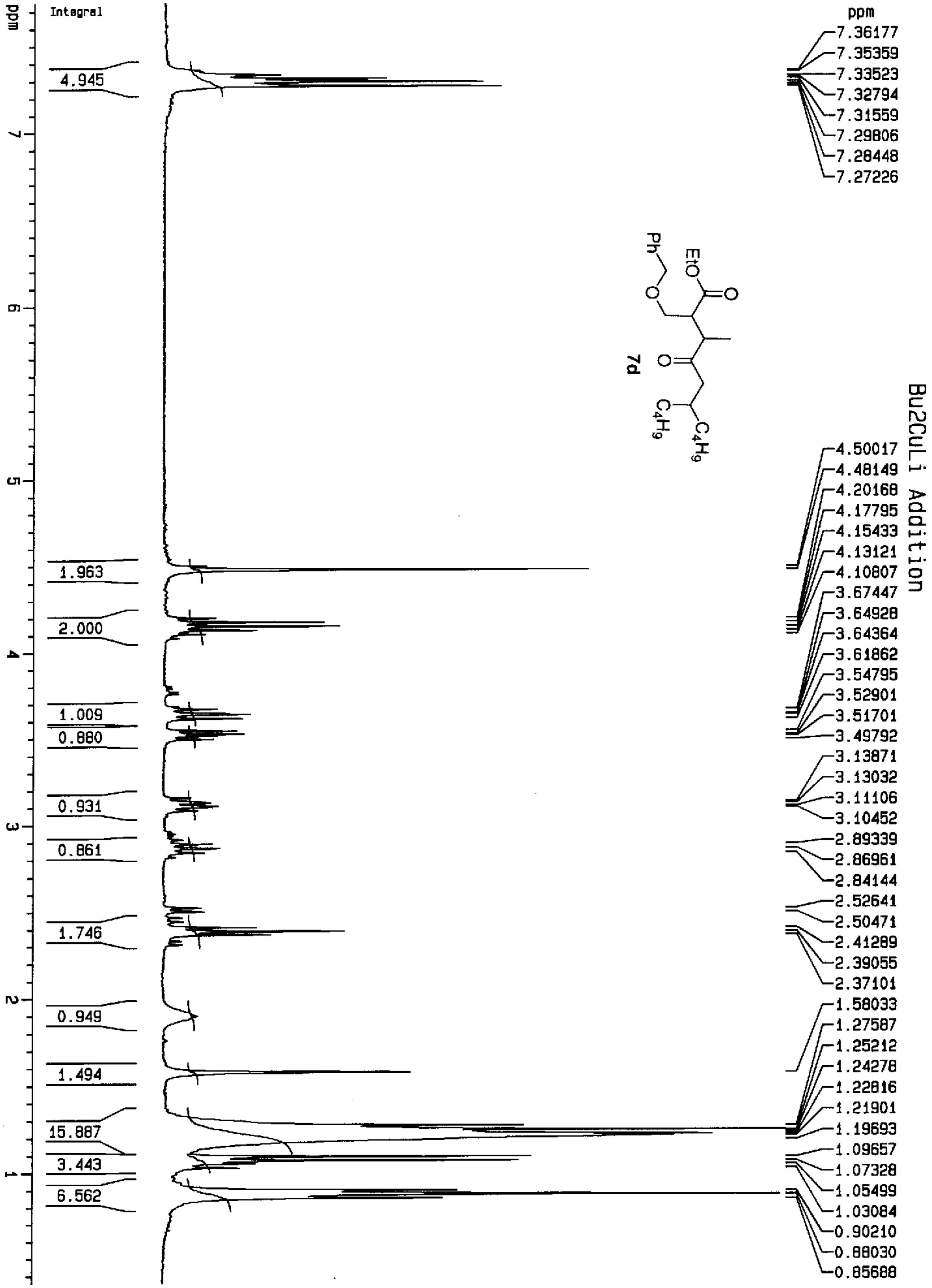

Ketoester for Pyridazinone I

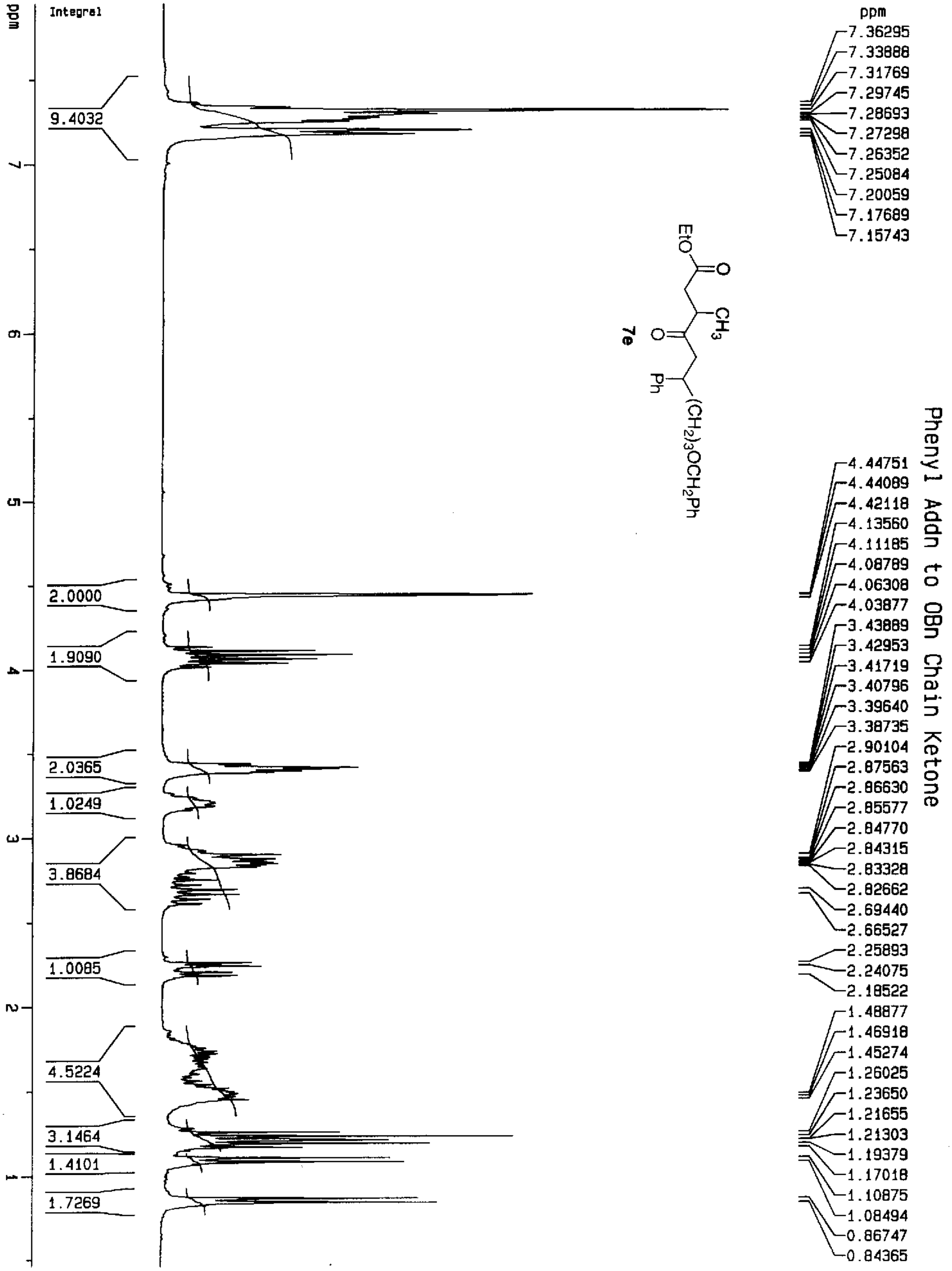

ppm
Integral
2.000
0.794
0.337
1.864
0.481
1.194
4.500
25.061
2.611
10.191
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.13810
4.11412
4.09030
4.06666
3.06716
2.79802
2.77505
2.75591
2.71928
2.68866
2.66453
2.63415
2.46511
2.38456
2.36786
2.32957
2.31309
1.73980
1.73060
1.72730
1.71108
1.67873
1.67528
1.65884
1.62829
1.61295
1.61046
1.59582
1.58818
1.57134
1.38067
1.26709
1.25679
1.24365
1.22002
1.14364
1.12147
1.01434
0.99129
0.96893
0.94980
0.90291
0.89254
0.88405
0.86907
Keto-ester II
EtO
O
O
C_4H_9
CH_3
C_4H_9
C_4H_9
7b


ppm
200
180
160
140
120
100
80
60
40
20
ppm
216.104
172.702
77.568
77.144
76.721
60.635
47.985
47.585
47.368
46.127
35.727
35.200
33.587
32.948
31.125
30.677
29.744
29.287
29.187
29.010
28.857
23.304
23.101
22.817
14.238
13.991
EtO
O
O
C_4H_9
CH_3
C_4H_9
C_4H_9
Bu2CuLi/MeI

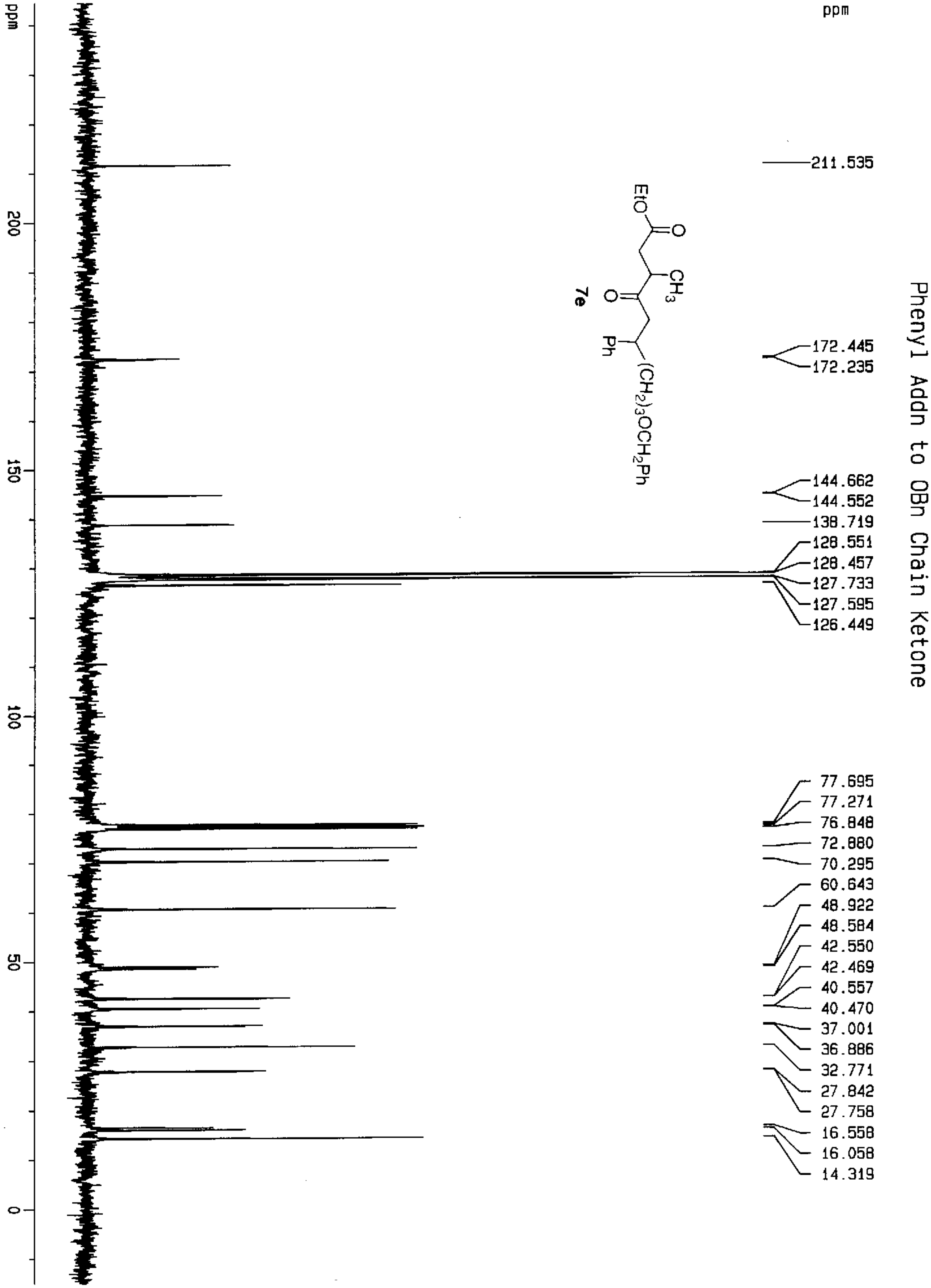
7b

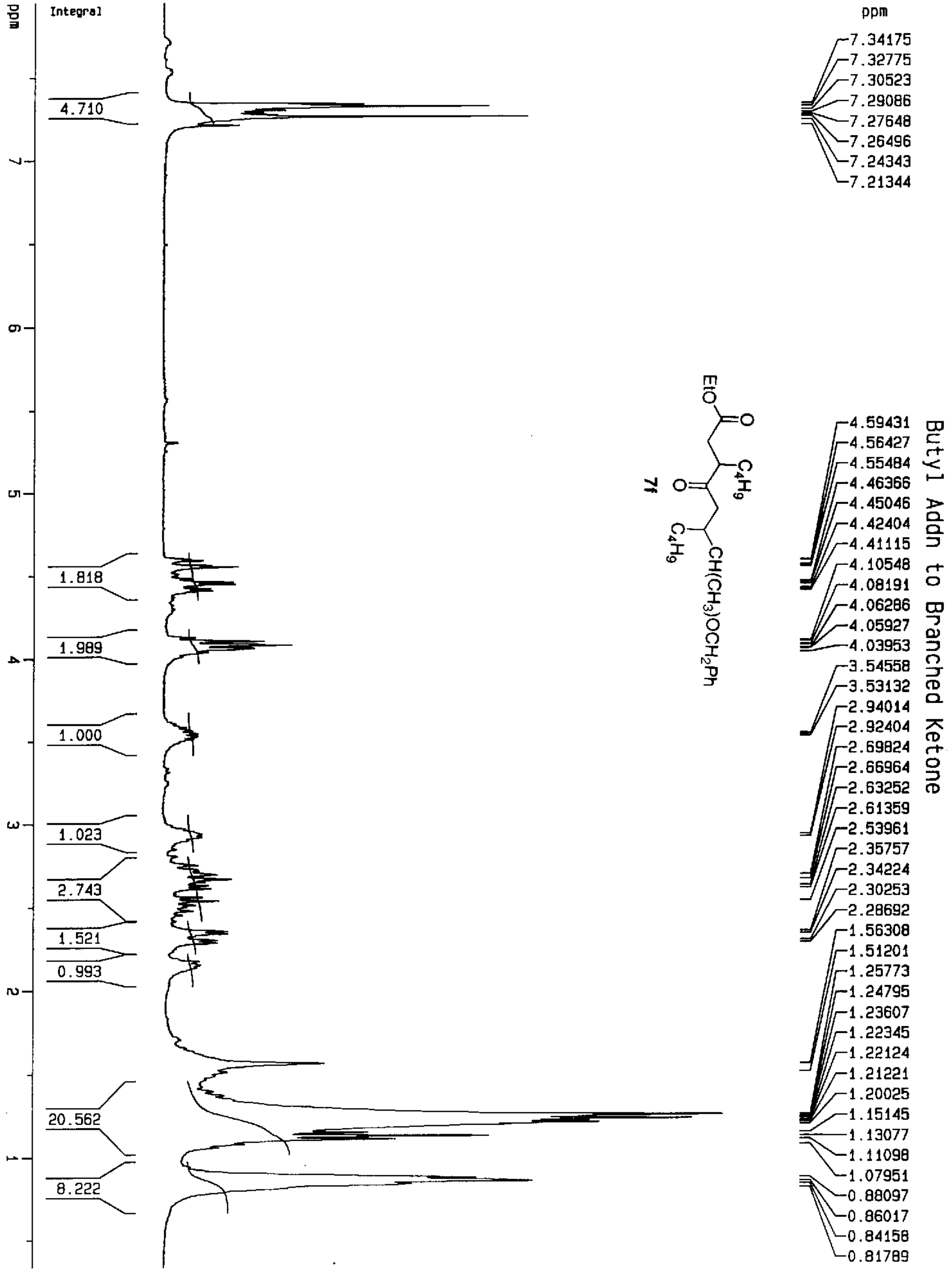

(PhCH2CH2) 2CuLi Addition to Enone
7c
EtO
O
O
Ph
C4H9
Ph
ppm
Integral
9.016
2.000
1.057
1.167
6.901
2.394
3.957
11.200
3.780
7
6
5
4
3
2
1
ppm
7.32226
7.29588
7.26454
7.23948
7.20751
7.18533
7.16570
7.14531
7.12193
4.14315
4.11972
4.10745
4.09612
4.08387
4.07263
4.06036
3.24594
3.23191
2.98845
2.78075
2.74932
2.60477
2.57486
2.54917
2.52961
2.51624
2.49804
2.47627
2.44564
2.43185
2.39072
2.03090
2.01171
1.61001
1.58322
1.55904
1.53354
1.43904
1.37794
1.26733
1.24411
1.22903
1.22069
1.20555
0.89333
0.87059

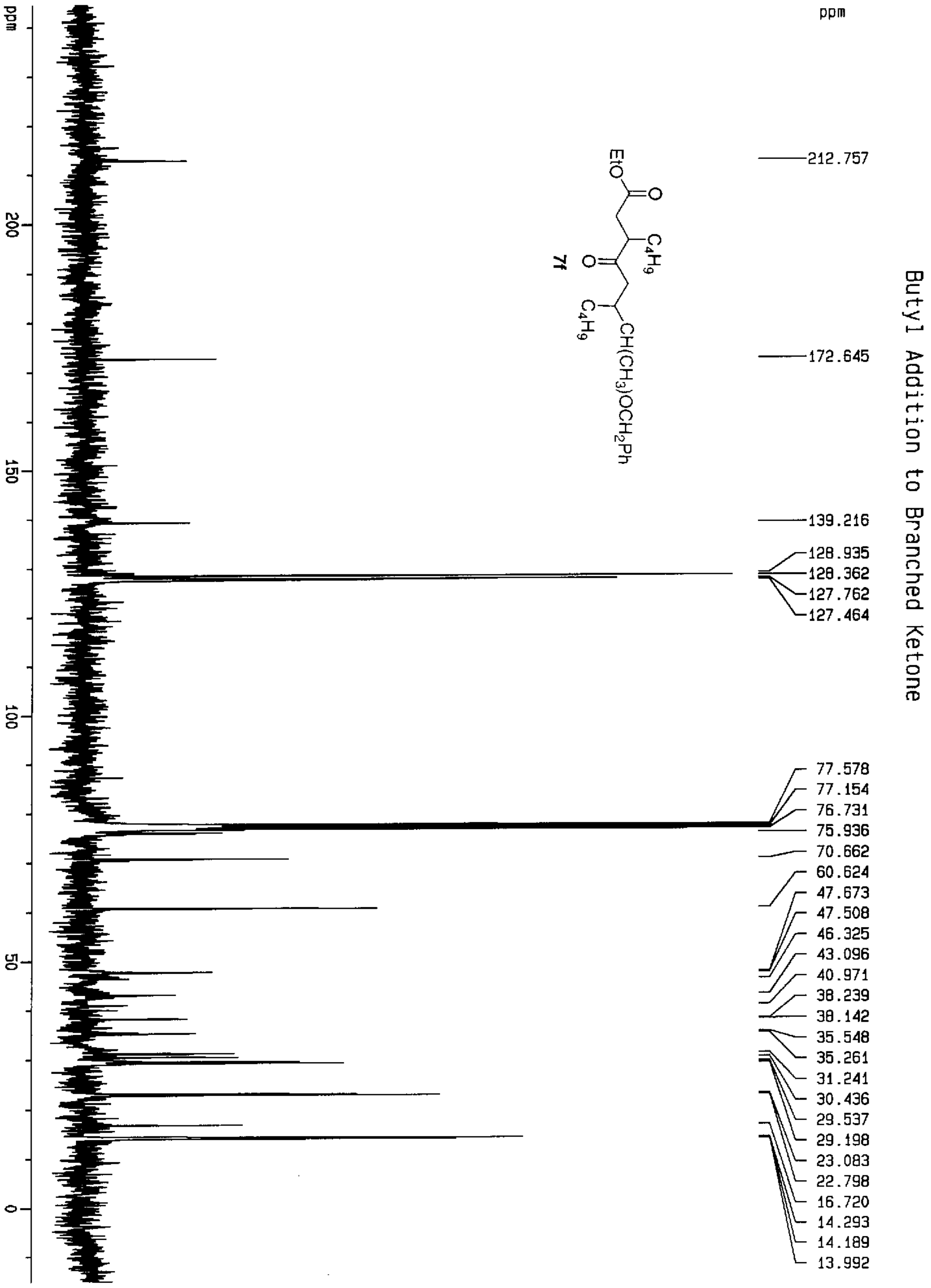

ppm
Integral
7
6
5
4
3
2
1
4.945
1.963
2.000
1.009
0.880
0.931
0.861
1.746
0.949
1.494
15.887
3.443
6.562
ppm
7.36177
7.35359
7.33523
7.32794
7.31559
7.29806
7.28448
7.27226
4.50017
4.48149
4.20168
4.17795
4.15433
4.13121
4.10807
3.67447
3.64928
3.64364
3.61862
3.54795
3.52901
3.51701
3.49792
3.13871
3.13032
3.11106
3.10452
2.89339
2.86961
2.84144
2.52641
2.50471
2.41289
2.39055
2.37101
1.58033
1.27587
1.25212
1.24278
1.22816
1.21901
1.19693
1.09657
1.07328
1.05499
1.03084
0.90210
0.88030
0.85688
Ph
O
EtO
O
O
C_4H_9
C_4H_9
7d
Bu2CuLi Addition

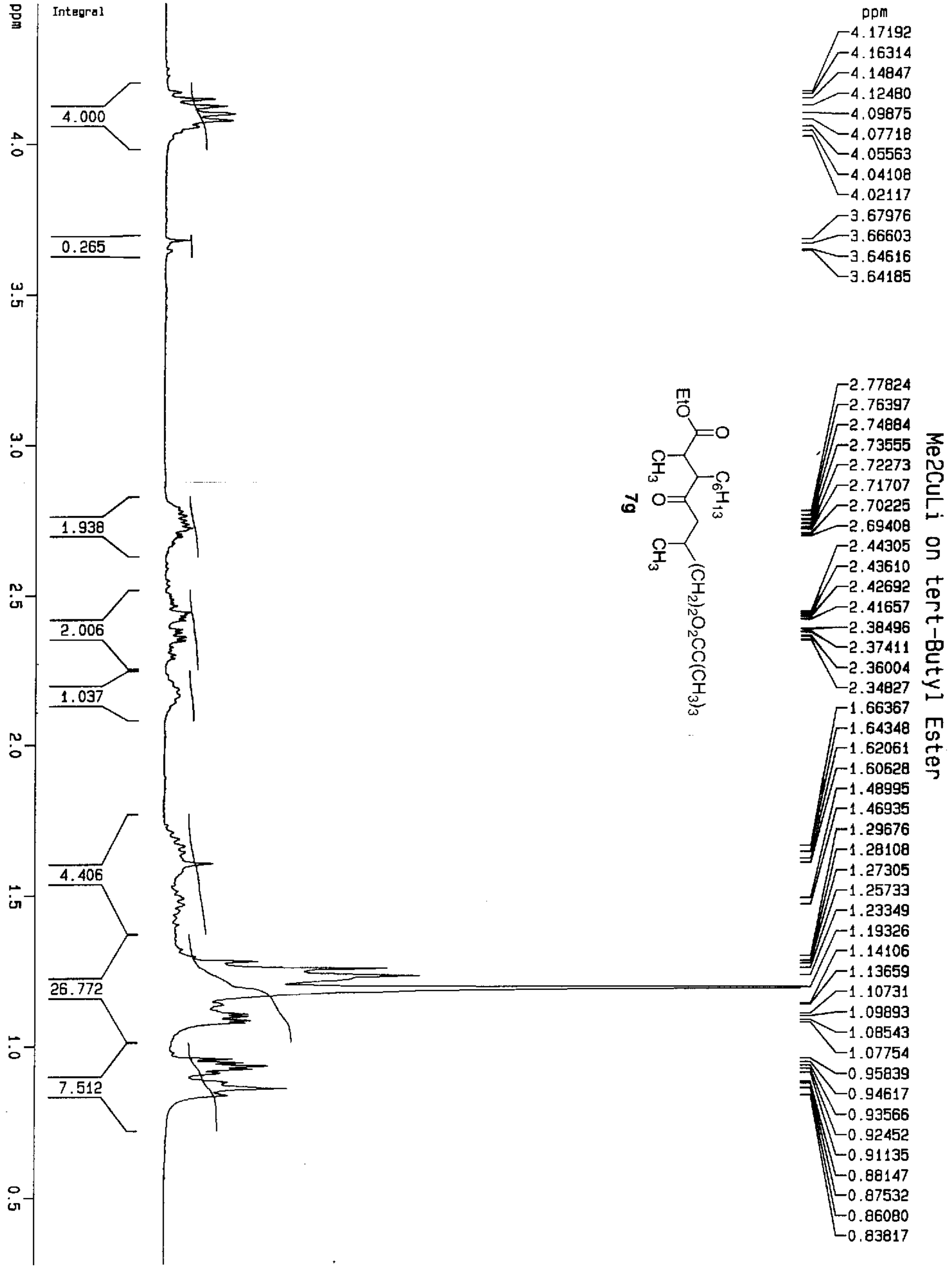


Phenyl Addn to OBn Chain Ketone


Phenyl Addn to OBn Chain Ketone
ppm
211.535
172.445
172.235
144.662
144.552
138.719
128.551
128.457
127.733
127.595
126.449
77.695
77.271
76.848
72.880
70.295
60.643
48.922
48.584
42.550
42.469
40.557
40.470
37.001
36.886
32.771
27.842
27.758
16.558
16.058
14.319
EtO
O
CH3
O
Ph
(CH2)3OCH2Ph
7e
ppm
200
150
100
50
0

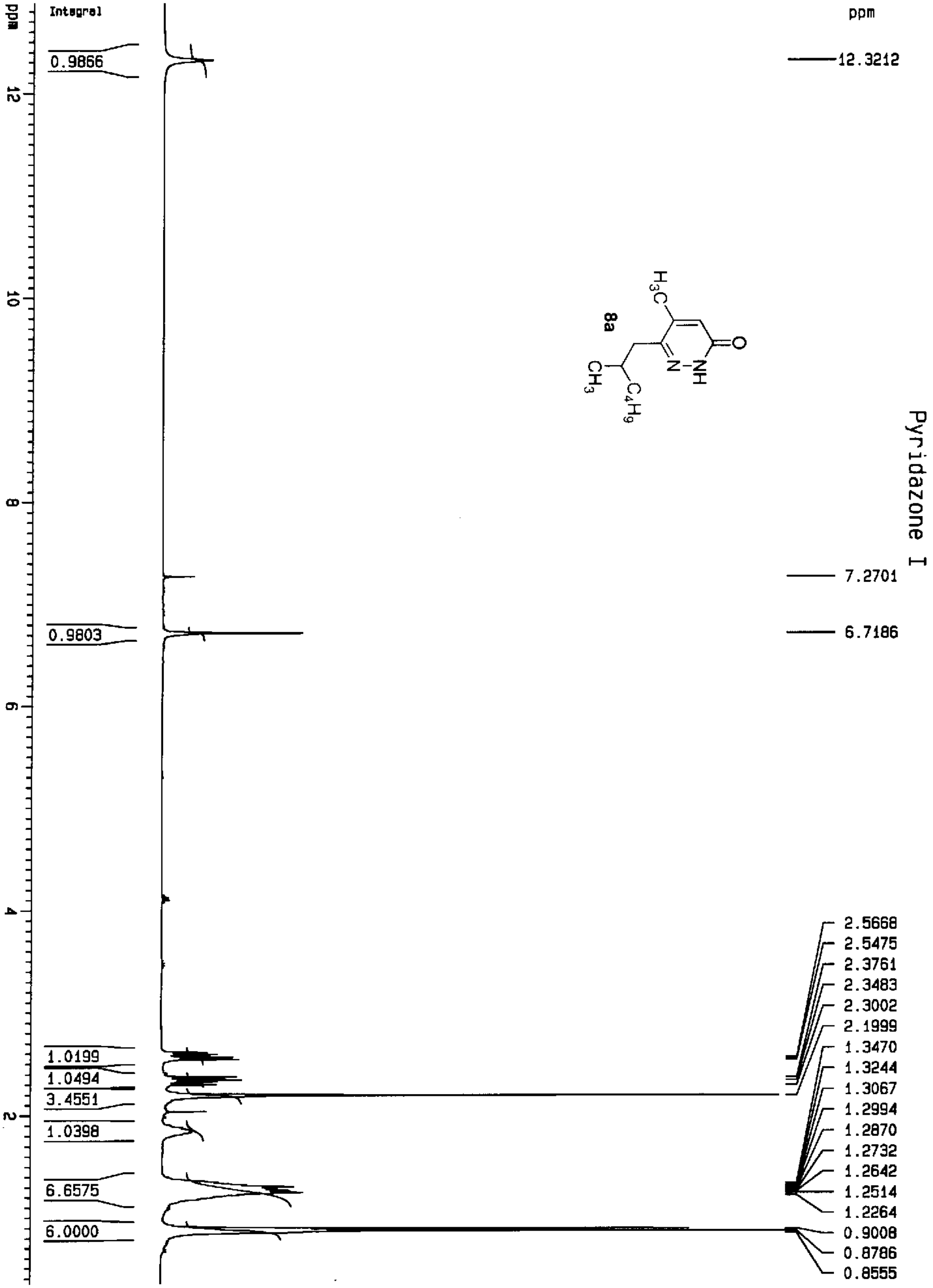

Butyl Addn to Branched Ketone
EtO
O
C$_4$H$_9$
O
C$_4$H$_9$
CH(CH$_3$)OCH$_2$Ph
7f
ppm
Integral
4.710
1.818
1.989
1.000
1.023
2.743
1.521
0.993
20.562
8.222
7
6
5
4
3
2
1
ppm
7.34175
7.32775
7.30523
7.29086
7.27648
7.26496
7.24343
7.21344
4.59431
4.56427
4.55484
4.46366
4.45046
4.42404
4.41115
4.10548
4.08191
4.06286
4.05927
4.03953
3.54558
3.53132
2.94014
2.92404
2.69824
2.66964
2.63252
2.61359
2.53961
2.35757
2.34224
2.30253
2.28692
1.56308
1.51201
1.25773
1.24795
1.23607
1.22345
1.22124
1.21221
1.20025
1.15145
1.13077
1.11098
1.07951
0.88097
0.86017
0.84158
0.81789

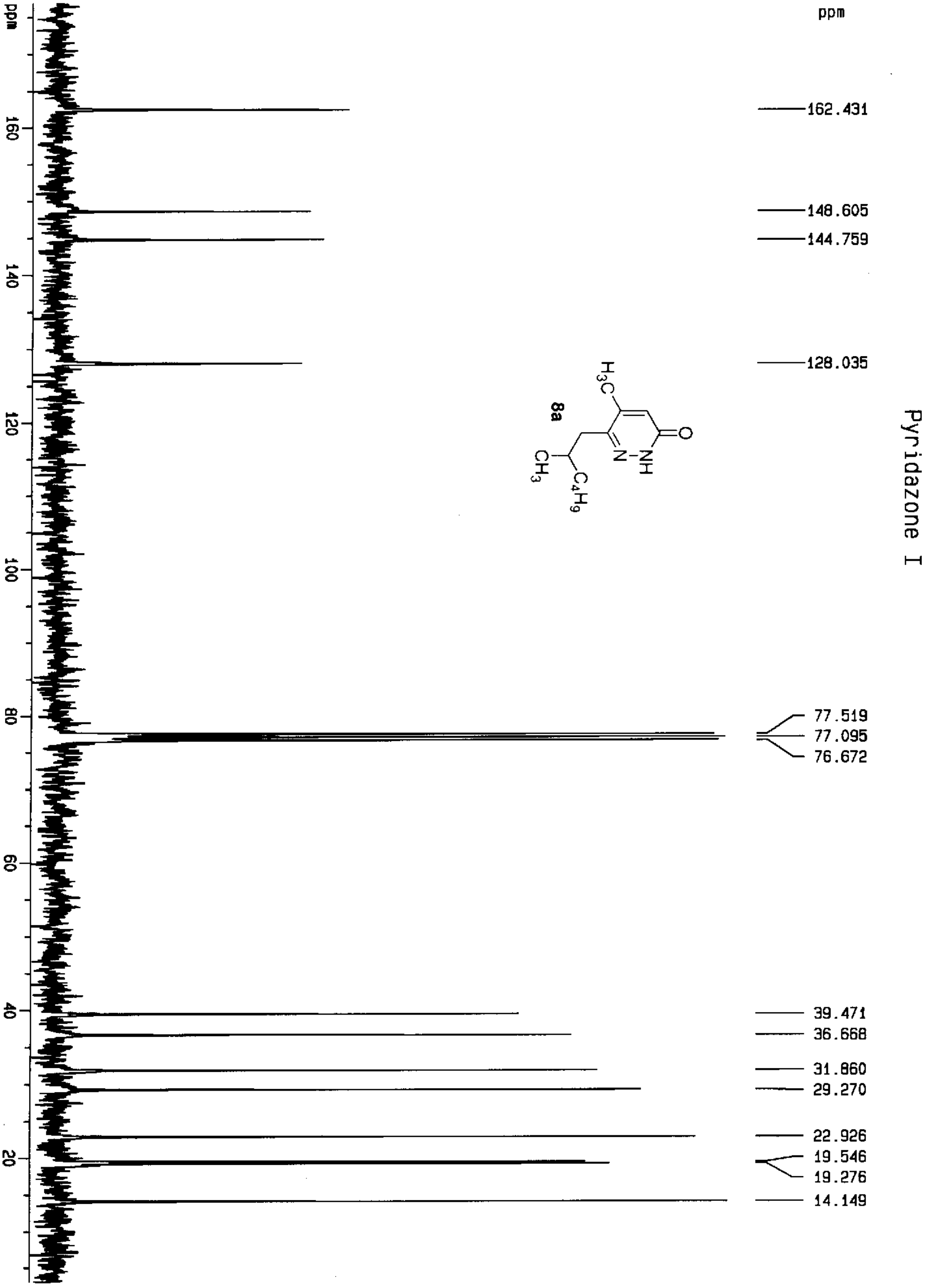

Butyl Addition to Branched Ketone
71
EtO
O
C4H9
O
C4H9
CH(CH3)OCH2Ph
ppm
212.757
172.645
139.216
128.935
128.362
127.762
127.464
77.578
77.154
76.731
75.936
70.662
60.624
47.673
47.508
46.325
43.096
40.971
38.239
38.142
35.548
35.261
31.241
30.436
29.537
29.198
23.083
22.798
16.720
14.293
14.189
13.992
ppm
200
150
100
50
0

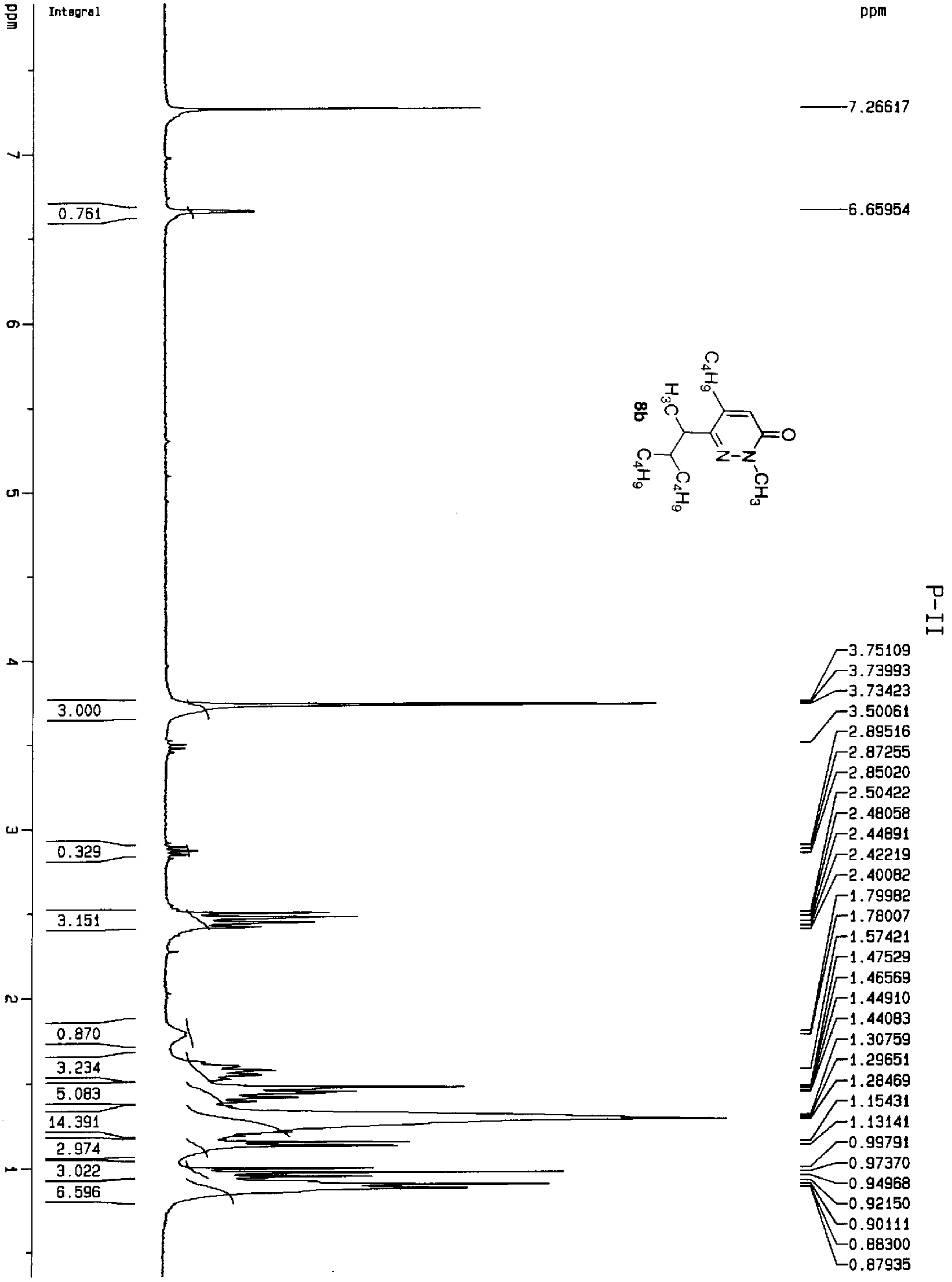


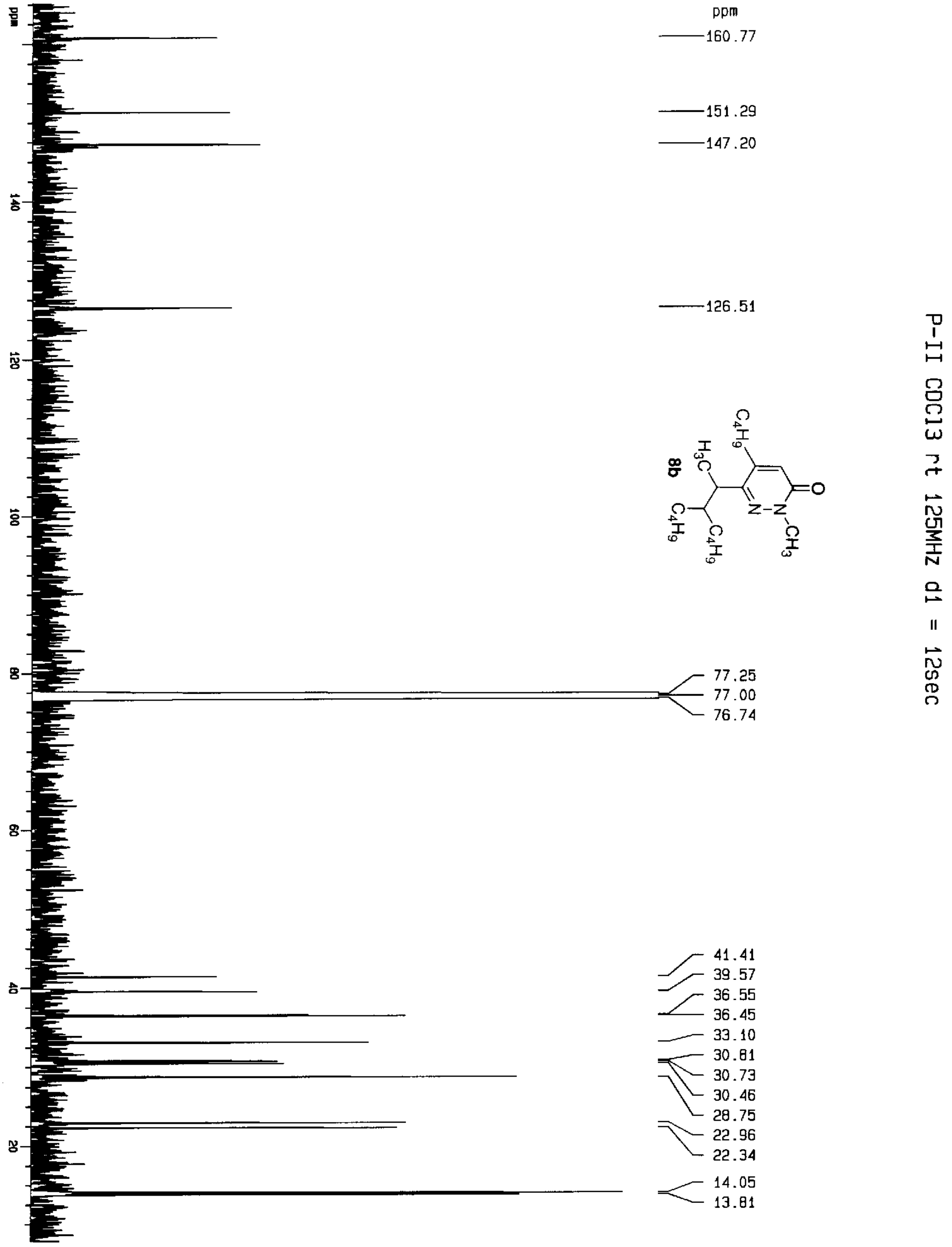
7g

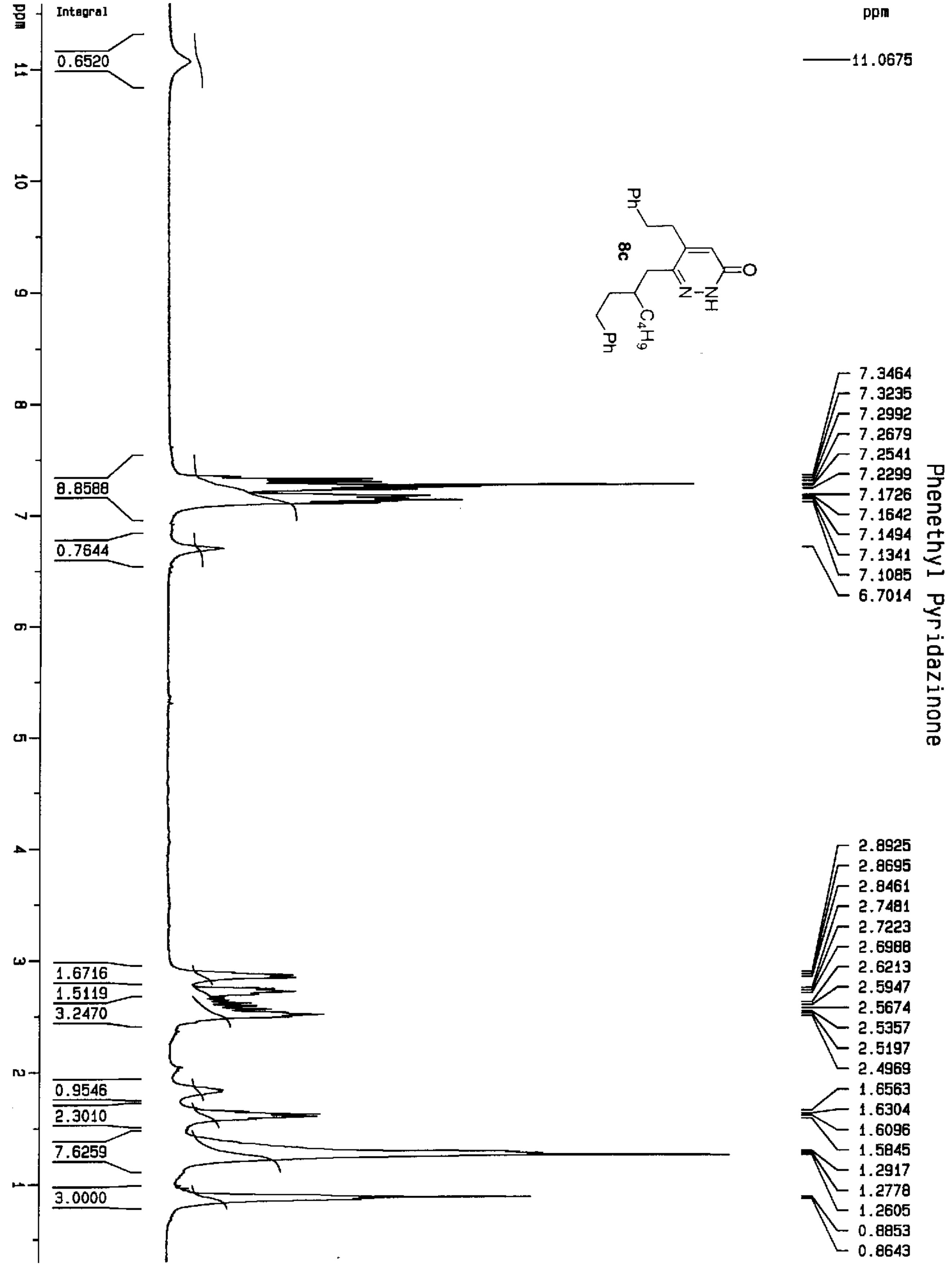
Me2CuLi on tert-Butyl Ester


ppm
Integral
0.9866
0.9803
1.0199
1.0494
3.4551
1.0398
6.6575
6.0000
12
10
8
6
4
2
ppm
12.3212
7.2701
6.7186
2.5668
2.5475
2.3761
2.3483
2.3002
2.1999
1.3470
1.3244
1.3067
1.2994
1.2870
1.2732
1.2642
1.2514
1.2264
0.9008
0.8786
0.8555
Pyridazone I
8a
H_3C
O
NH
N
C_4H_9
CH_3

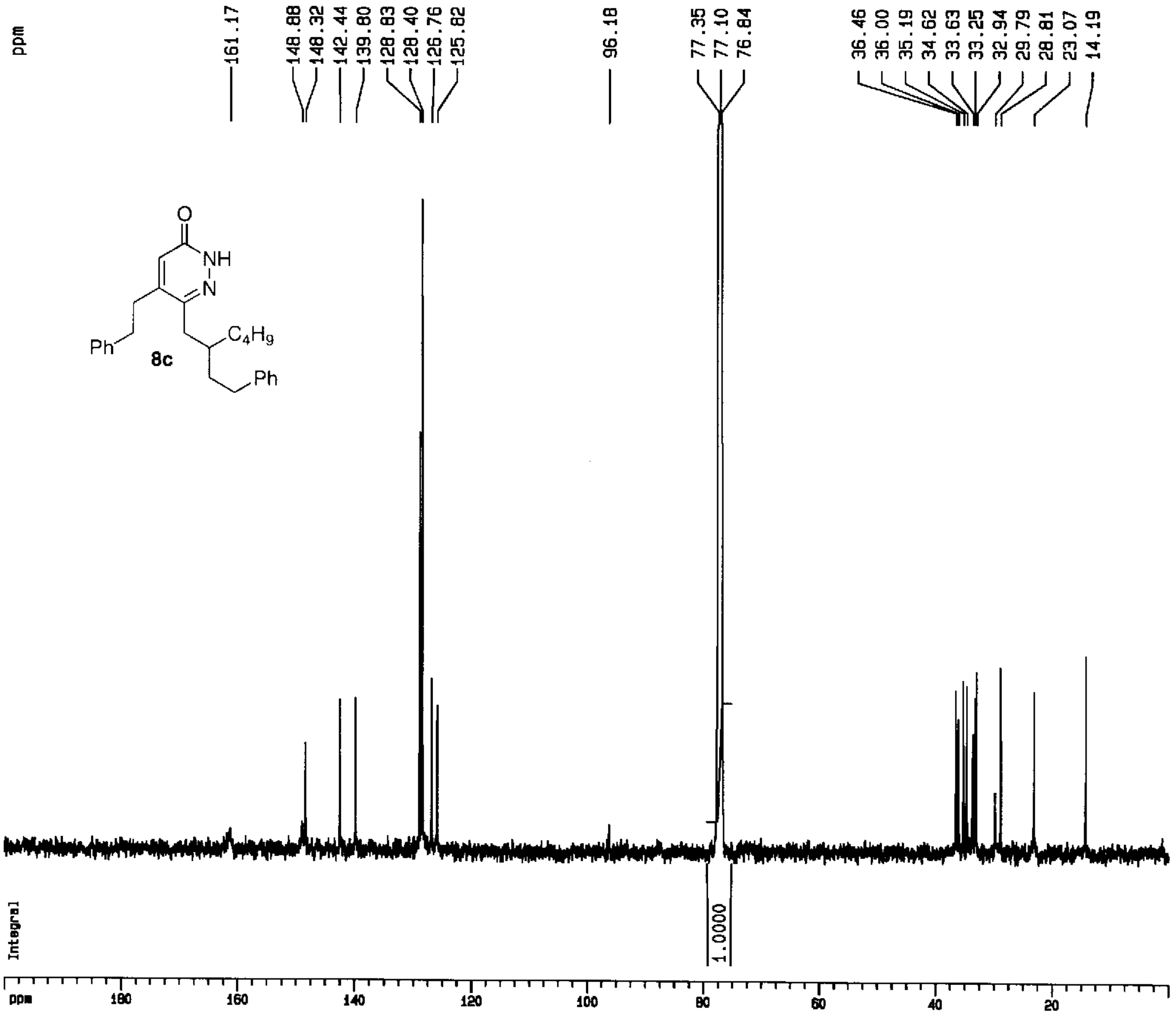

Pyridazone I
8a
H$_3$C
O
NH
N
C$_4$H$_9$
CH$_3$
ppm
162.431
148.605
144.759
128.035
77.519
77.095
76.672
39.471
36.668
31.860
29.270
22.926
19.546
19.276
14.149
ppm
160
140
120
100
80
60
40
20


ppm
Integral
7
6
5
4
3
2
1
0.761
3.000
0.329
3.151
0.870
3.234
5.083
14.391
2.974
3.022
6.596
ppm
7.26617
6.65954
3.75109
3.73993
3.73423
3.50061
2.89516
2.87255
2.85020
2.50422
2.48058
2.44891
2.42219
2.40082
1.79982
1.78007
1.57421
1.47529
1.46569
1.44910
1.44083
1.30759
1.29651
1.28469
1.15431
1.13141
0.99791
0.97370
0.94968
0.92150
0.90111
0.88300
0.87935
C4H9
H3C
O
N
N
CH3
C4H9
C4H9
8b
P-II


P-II CDCl3 rt 125MHz d1 = 12sec
8b
C4H9
H3C
C4H9
C4H9
O
N
N
CH3
ppm
160.77
151.29
147.20
126.51
77.25
77.00
76.74
41.41
39.57
36.55
36.45
33.10
30.81
30.73
30.46
28.75
22.96
22.34
14.05
13.81
ppm
140
120
100
80
60
40
20


Phenethyl Pyridazinone
8c
Ph
O
NH
N
C4H9
Ph
ppm
Integral
0.6520
8.8588
0.7644
1.6716
1.5119
3.2470
0.9546
2.3010
7.6259
3.0000
ppm
11.0675
7.3464
7.3235
7.2992
7.2679
7.2541
7.2299
7.1726
7.1642
7.1494
7.1341
7.1085
6.7014
2.8925
2.8695
2.8461
2.7481
2.7223
2.6988
2.6213
2.5947
2.5674
2.5357
2.5197
2.4969
1.6563
1.6304
1.6096
1.5845
1.2917
1.2778
1.2605
0.8853
0.8643
11
10
9
8
7
6
5
4
3
2
1

JOEY P-8 cdcl3 rt 125MHz 13C 1H decp delay 24sec 5/15/99



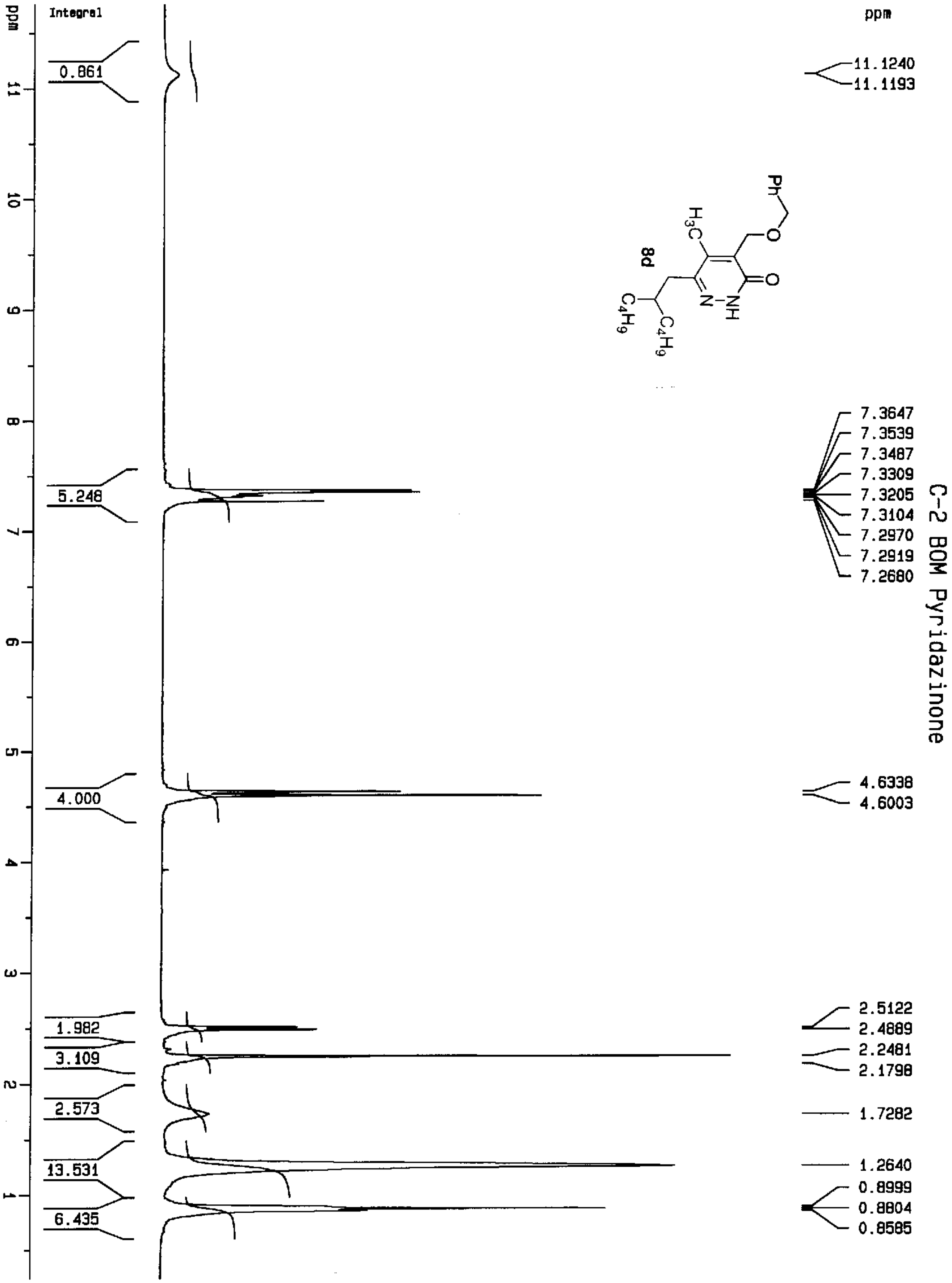
8c

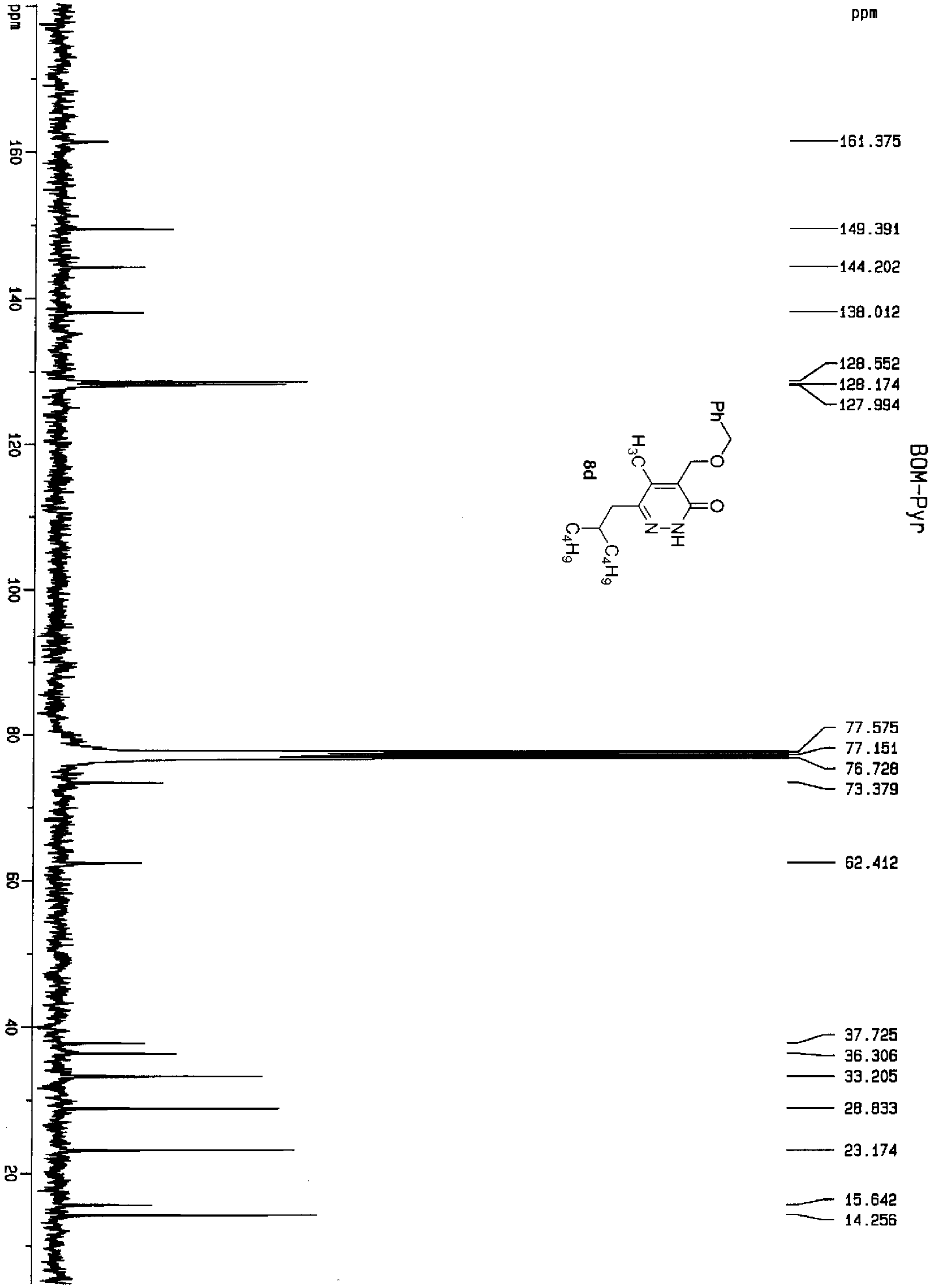
```
Current Data Parameters
NAME             joey-p8
EXPNO                  2
PROCNO                 1

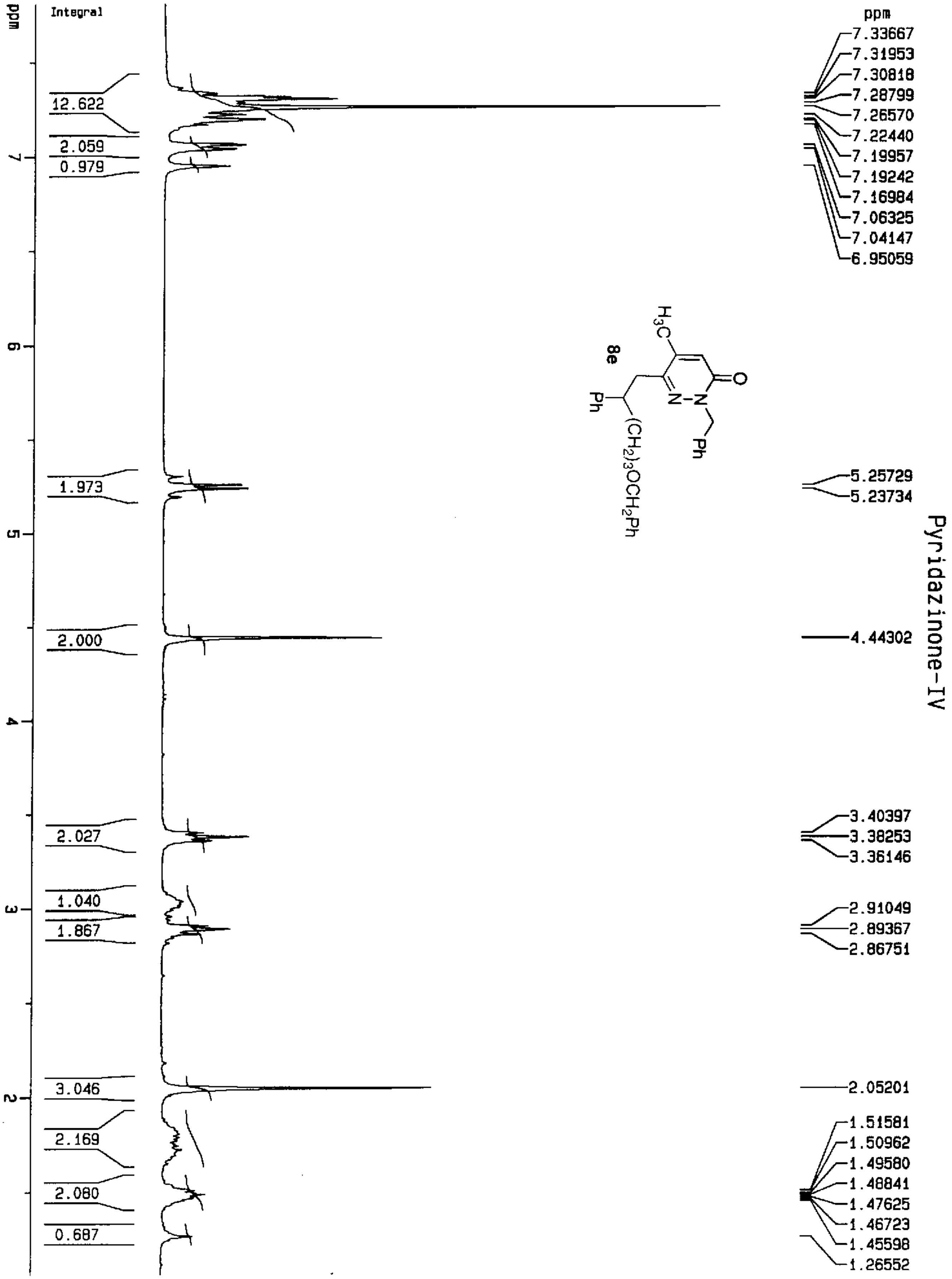
F2 - Acquisition Parameters
Date_             990515
Time                9.41
INSTRUM            spect
PROBHD     5 mm TXI 13C
PULPROG         c13wonoe
TD                 32768
SOLVENT            CDC13
NS                  3693
DS                     0
SWH           32679.738 Hz
FIDRES         0.997306 Hz
AQ            0.5014004 sec
RG                 32768
DW                15.300 usec
DE                  6.00 usec
TE                 290.0 K
D3            0.00100000 sec
PL12               12.00 dB
D1           24.00000000 sec
CPDPRG2          waltz16
PCPD2             100.00 usec
SFO2         500.1325006 MHz
NUC2                  1H
PL2               120.00 dB
P1                 13.00 usec
DE                  6.00 usec
SFO1         125.7722011 MHz
NUC1                 13C
PL1                -6.00 dB

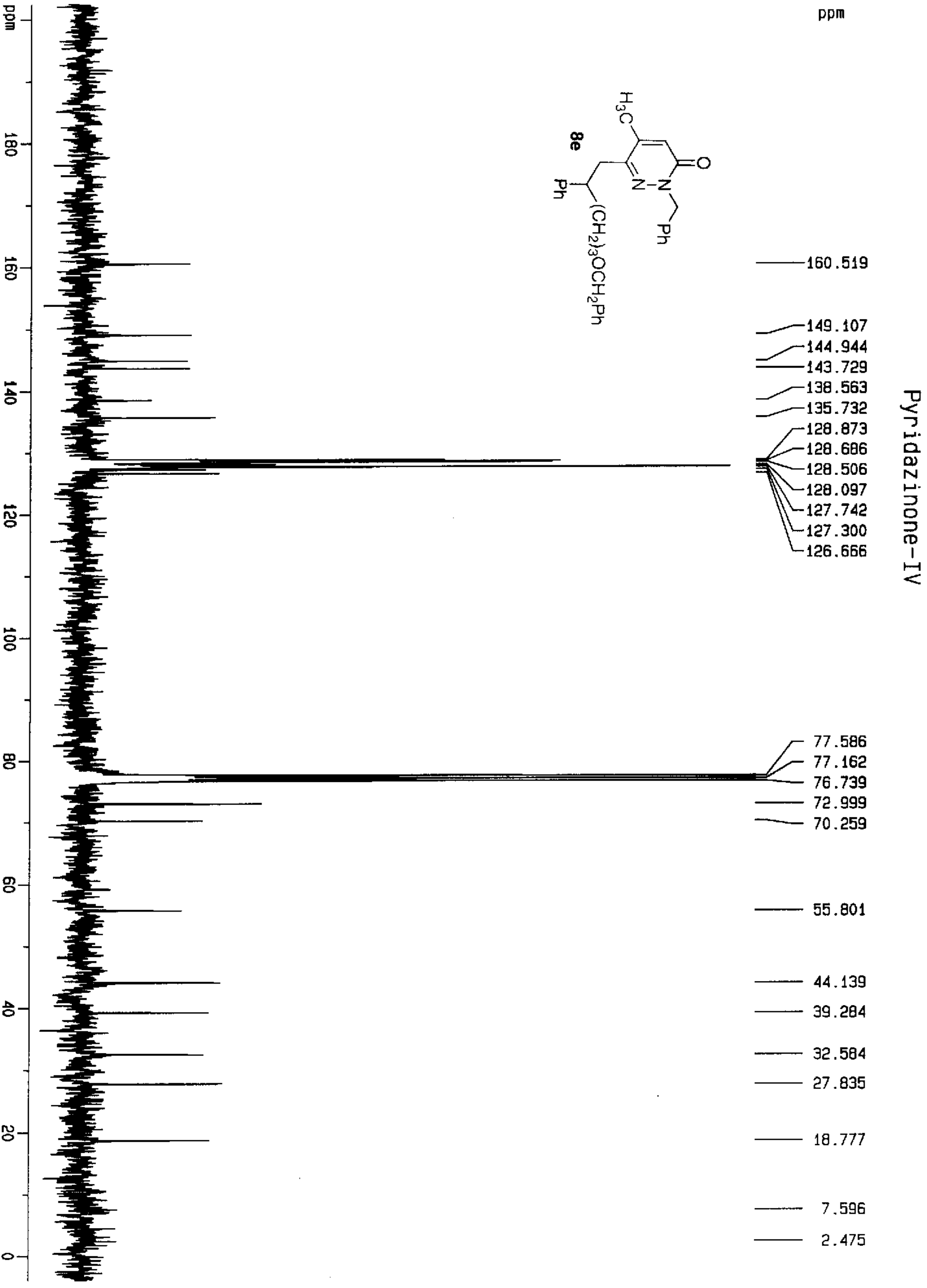
F2 - Processing parameters
SI                  8192
SF           125.7577832 MHz
WDW                   EM
SSB                    0
LB                  4.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                 20.00 cm
F1P              200.000 ppm
F1              25151.56 Hz
F2P                0.000 ppm
F2                  0.00 Hz
PPMCM           10.00000 ppm/cm
HZCM          1257.57788 Hz/cm
```


C-2 BOM Pyridazinone
8d
Ph
O
O
NH
N
H_3C
C_4H_9
C_4H_9
ppm
Integral
0.861
5.248
4.000
1.982
3.109
2.573
13.531
6.435
ppm
11.1240
11.1193
7.3647
7.3539
7.3487
7.3309
7.3205
7.3104
7.2970
7.2919
7.2680
4.6338
4.6003
2.5122
2.4889
2.2481
2.1798
1.7282
1.2640
0.8999
0.8804
0.8585
11
10
9
8
7
6
5
4
3
2
1

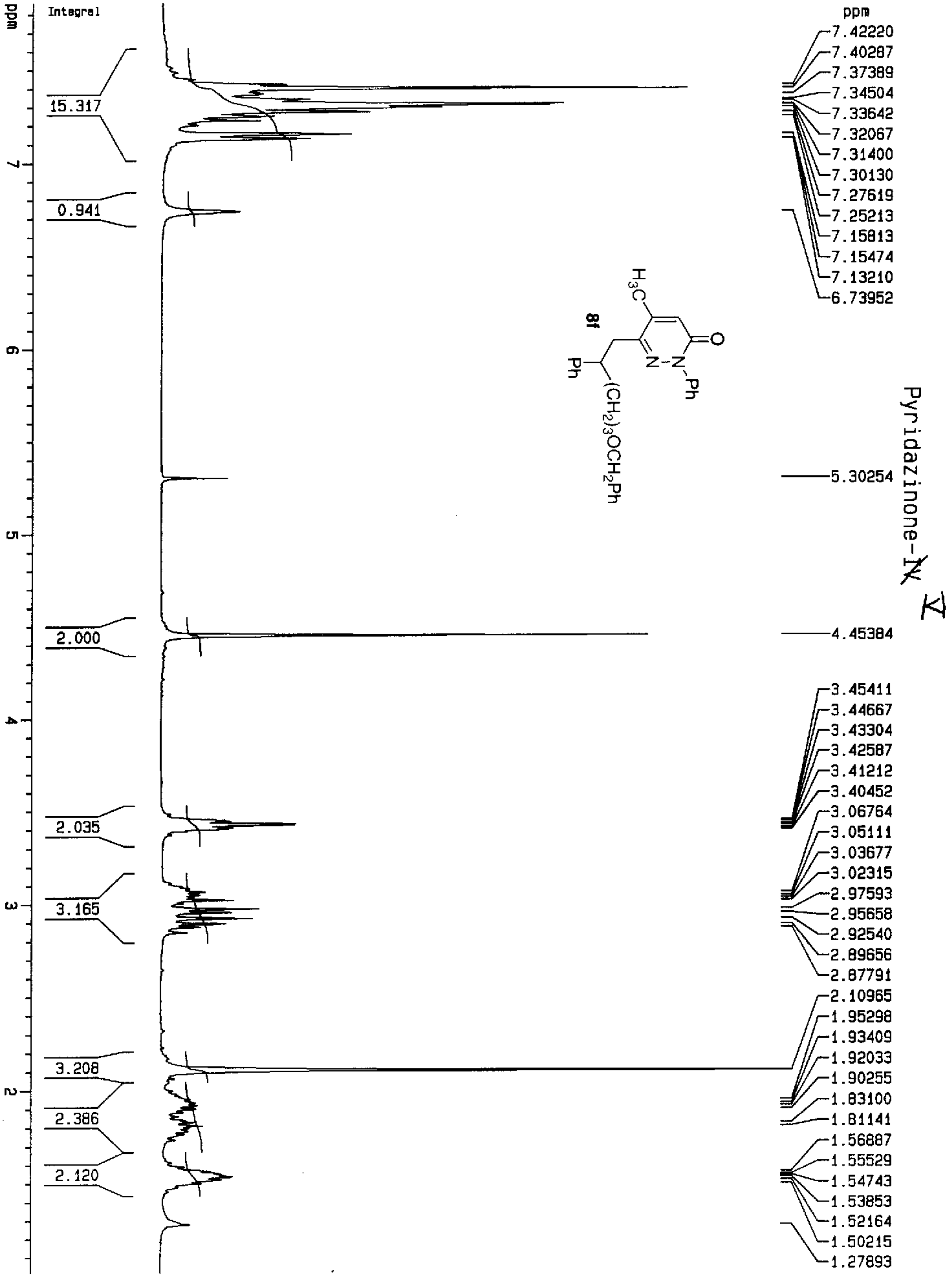

BOM-Pyr
8d
Ph
O
O
NH
N
H3C
C4H9
C4H9
ppm
161.375
149.391
144.202
138.012
128.552
128.174
127.994
77.575
77.151
76.728
73.379
62.412
37.725
36.306
33.205
28.833
23.174
15.642
14.256
ppm
160
140
120
100
80
60
40
20

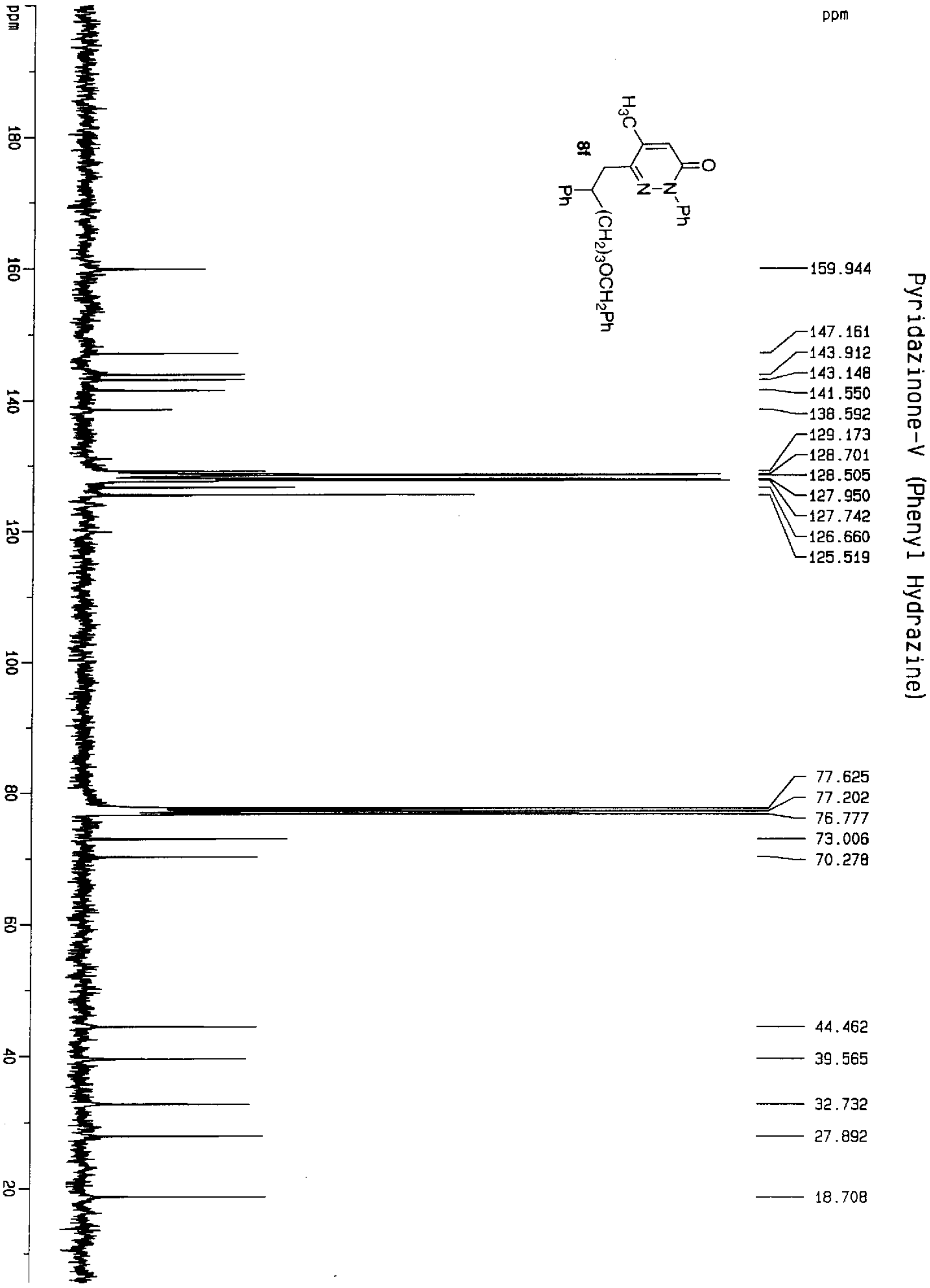

Pyridazinone-IV
8e
H_3C
O
N
N
Ph
Ph
$(CH_2)_3OCH_2Ph$
ppm
Integral
12.622
2.059
0.979
1.973
2.000
2.027
1.040
1.867
3.046
2.169
2.080
0.687
7
6
5
4
3
2
ppm
7.33667
7.31953
7.30818
7.28799
7.26570
7.22440
7.19957
7.19242
7.16984
7.06325
7.04147
6.95059
5.25729
5.23734
4.44302
3.40397
3.38253
3.36146
2.91049
2.89367
2.86751
2.05201
1.51581
1.50962
1.49580
1.48841
1.47625
1.46723
1.45598
1.26552

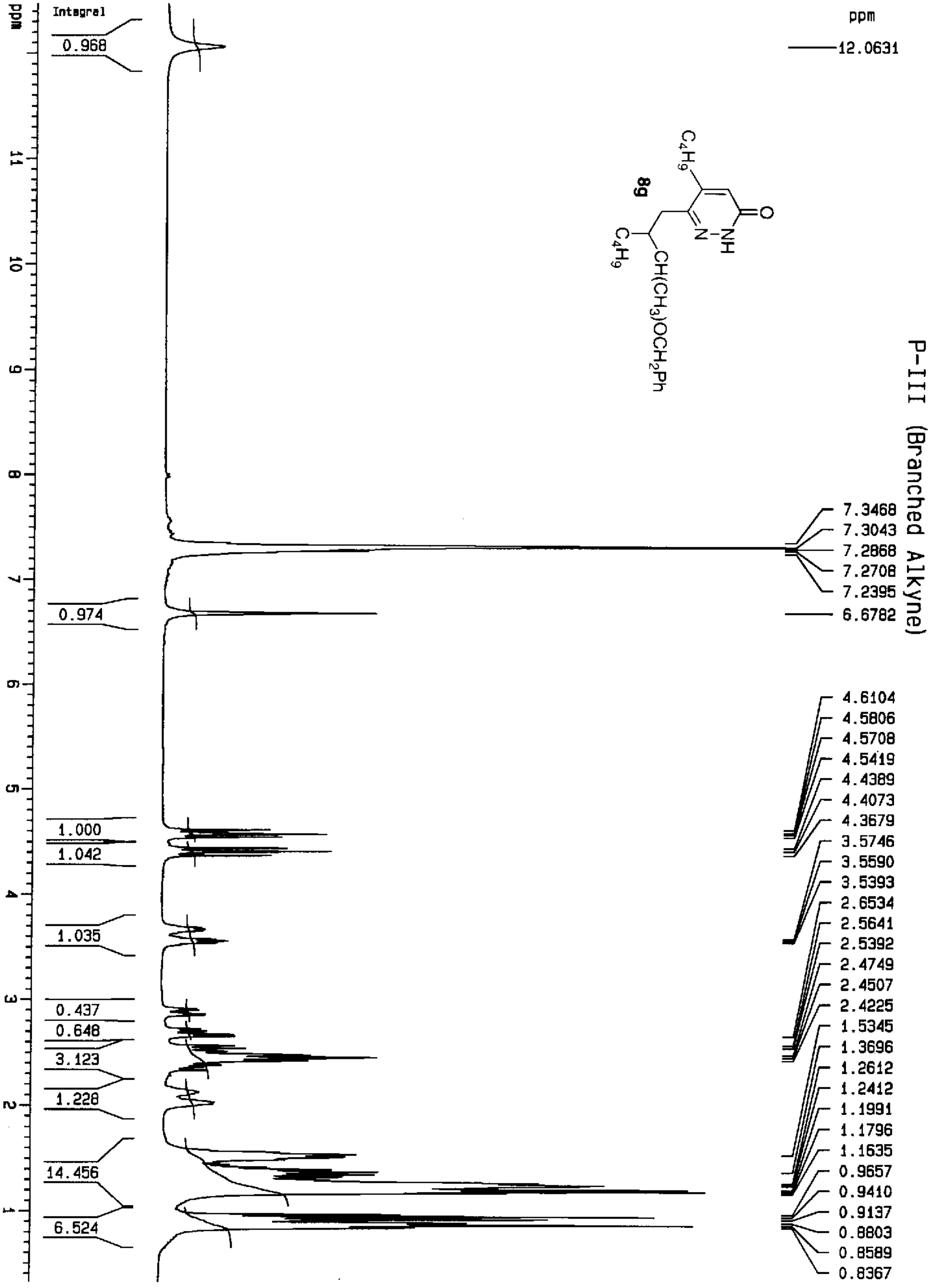


8e

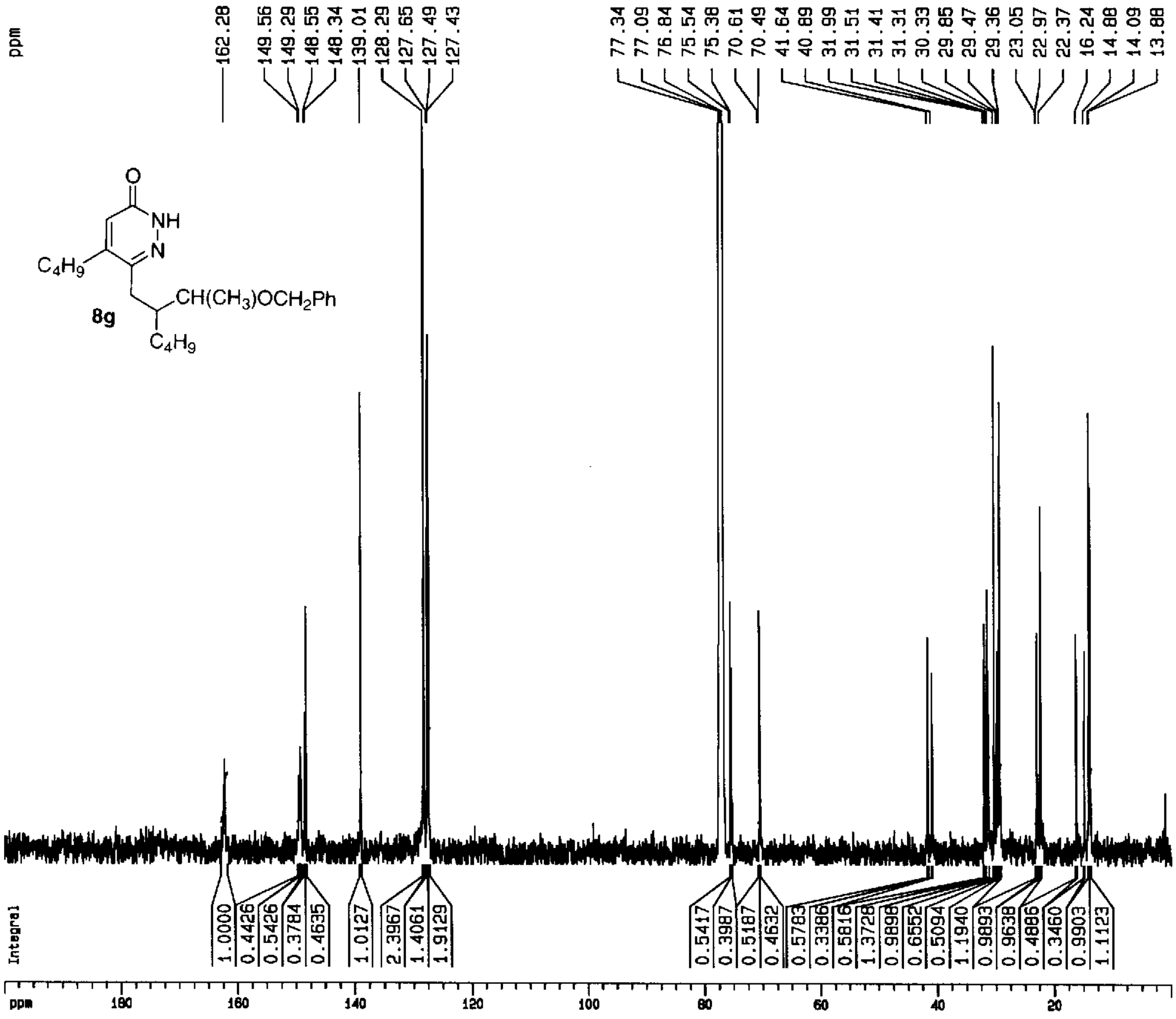
Pyridazinone-IV
ppm
H3C
O
N–N
Ph
Ph
(CH2)3OCH2Ph
160.519
149.107
144.944
143.729
138.563
135.732
128.873
128.686
128.506
128.097
127.742
127.300
126.666
77.586
77.162
76.739
72.999
70.259
55.801
44.139
39.284
32.584
27.835
18.777
7.596
2.475
ppm
180
160
140
120
100
80
60
40
20
0


ppm
Integral
15.317
0.941
2.000
2.035
3.165
3.208
2.386
2.120
7
6
5
4
3
2
ppm
7.42220
7.40287
7.37389
7.34504
7.33642
7.32067
7.31400
7.30130
7.27619
7.25213
7.15813
7.15474
7.13210
6.73952
5.30254
4.45384
3.45411
3.44667
3.43304
3.42587
3.41212
3.40452
3.06764
3.05111
3.03677
3.02315
2.97593
2.95658
2.92540
2.89656
2.87791
2.10965
1.95298
1.93409
1.92033
1.90255
1.83100
1.81141
1.56887
1.55529
1.54743
1.53853
1.52164
1.50215
1.27893
H_3C
8f
O
N
N
Ph
Ph
$(CH_2)_3OCH_2Ph$
Pyridazinone-~~IV~~ V


Pyridazinone-V (Phenyl Hydrazine)
8f
ppm
159.944
147.161
143.912
143.148
141.550
138.592
129.173
128.701
128.505
127.950
127.742
126.660
125.519
77.625
77.202
76.777
73.006
70.278
44.462
39.565
32.732
27.892
18.708
ppm
180
160
140
120
100
80
60
40
20


P-III (Branched Alkyne)
8g
C_4H_9
O
NH
N
CH(CH$_3$)OCH$_2$Ph
C_4H_9
ppm
Integral
0.968
0.974
1.000
1.042
1.035
0.437
0.648
3.123
1.228
14.456
6.524
11
10
9
8
7
6
5
4
3
2
1
ppm
12.0631
7.3468
7.3043
7.2868
7.2708
7.2395
6.6782
4.6104
4.5806
4.5708
4.5419
4.4389
4.4073
4.3679
3.5746
3.5590
3.5393
2.6534
2.5641
2.5392
2.4749
2.4507
2.4225
1.5345
1.3696
1.2612
1.2412
1.1991
1.1796
1.1635
0.9657
0.9410
0.9137
0.8803
0.8589
0.8367

P-III cdcl3 rt 125MHz 13C 1H decp delay 24sec 4/13/99



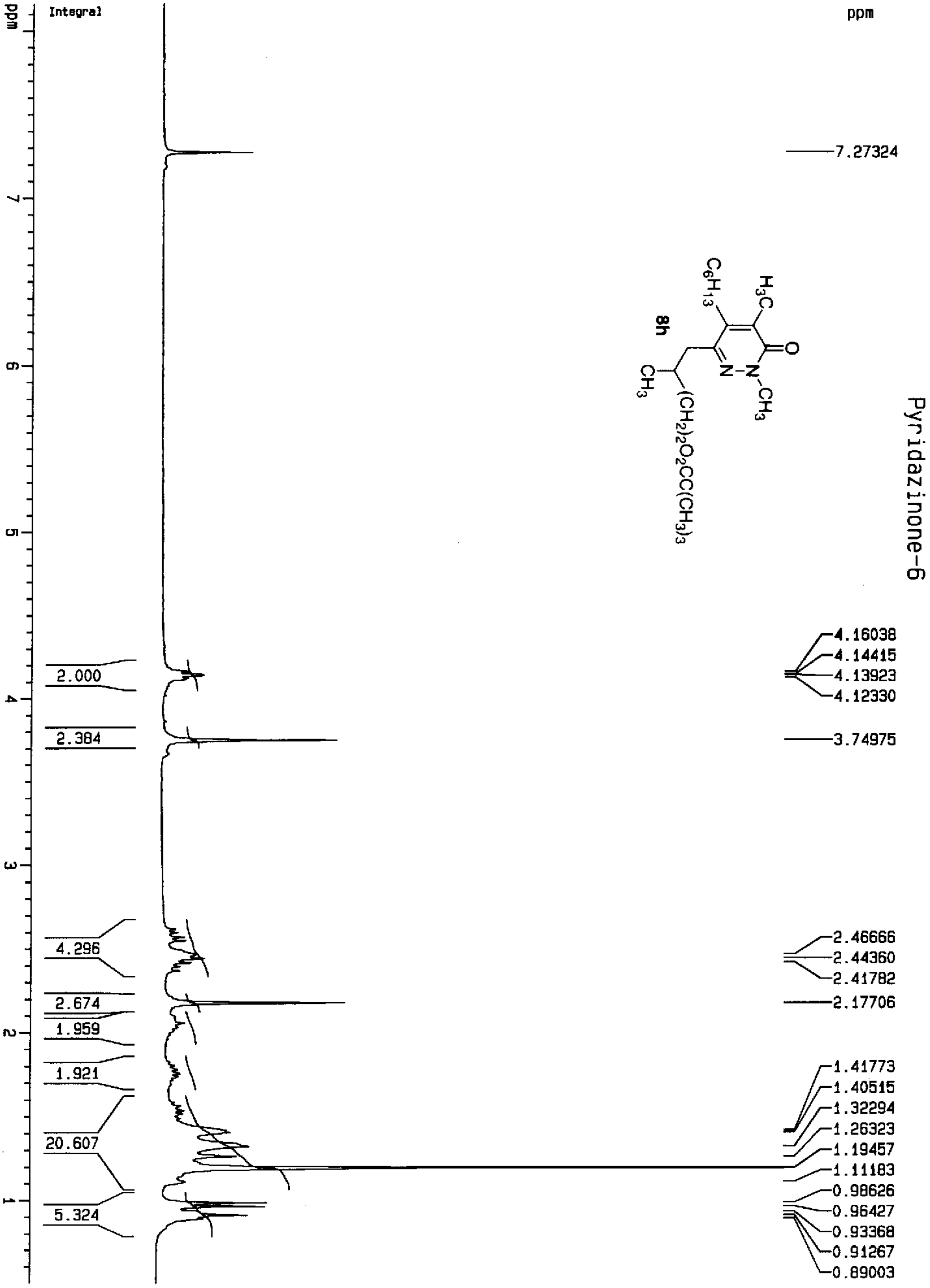
8g

```
Current Data Parameters
NAME              p-iii
EXPNO                 2
PROCNO                1

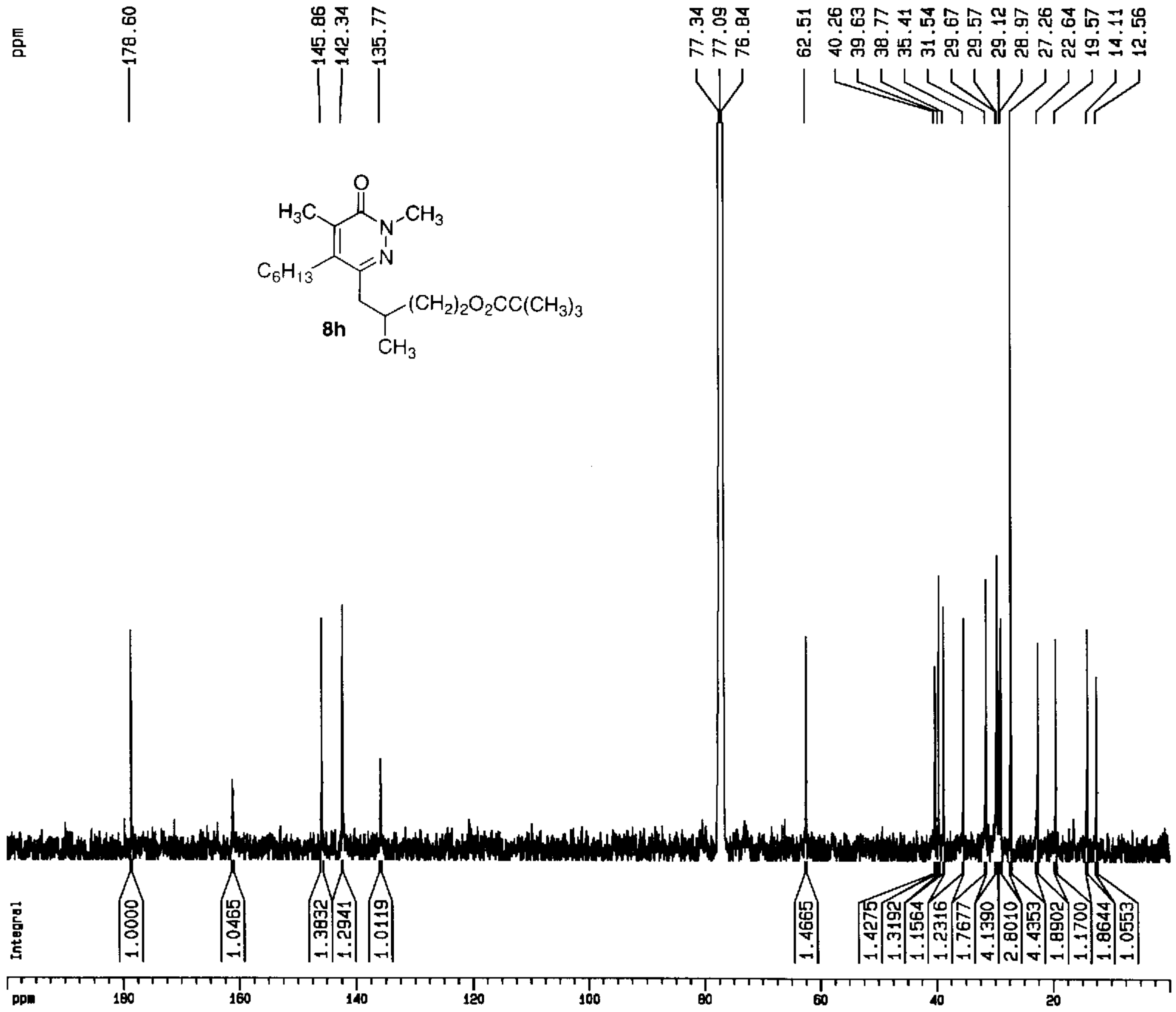
F2 - Acquisition Parameters
Date_            990413
Time               9.37
INSTRUM           spect
PROBHD     5 mm TXI 13C
PULPROG        c13wonoe
TD                32768
SOLVENT           CDC13
NS                  844
DS                    0
SWH          32679.738 Hz
FIDRES        0.997306 Hz
AQ           0.5014004 sec
RG             18390.4
DW              15.300 usec
DE                6.00 usec
TE               290.0 K
D3          0.00100000 sec
PL12             12.00 dB
D1         24.00000000 sec
CPDPRG2         waltz16
PCPD2           100.00 usec
SFO2       500.1325006 MHz
NUC2                 1H
PL2             120.00 dB
P1               11.00 usec
DE                6.00 usec
SFO1       125.7722011 MHz
NUC1                13C
PL1              -6.00 dB

F2 - Processing parameters
SI                 8192
SF         125.7577872 MHz
WDW                  EM
SSB                   0
LB                 4.00 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                20.00 cm
F1P             200.000 ppm
F1             25151.56 Hz
F2P               0.000 ppm
F2                 0.00 Hz
PPMCM          10.00000 ppm/cm
HZCM         1257.57788 Hz/cm
```


Pyridazinone-6
8h
H3C
C6H13
O
N
N
CH3
CH3
(CH2)2O2CC(CH3)3
ppm
Integral
ppm
7
6
5
4
3
2
1
2.000
2.384
4.296
2.674
1.959
1.921
20.607
5.324
7.27324
4.16038
4.14415
4.13923
4.12330
3.74975
2.46666
2.44360
2.41782
2.17706
1.41773
1.40515
1.32294
1.26323
1.19457
1.11183
0.98626
0.96427
0.93368
0.91267
0.89003

Joey 1314 cdcl3 rt 125MHz 13C 1H decp delay 12sec 4/7/99

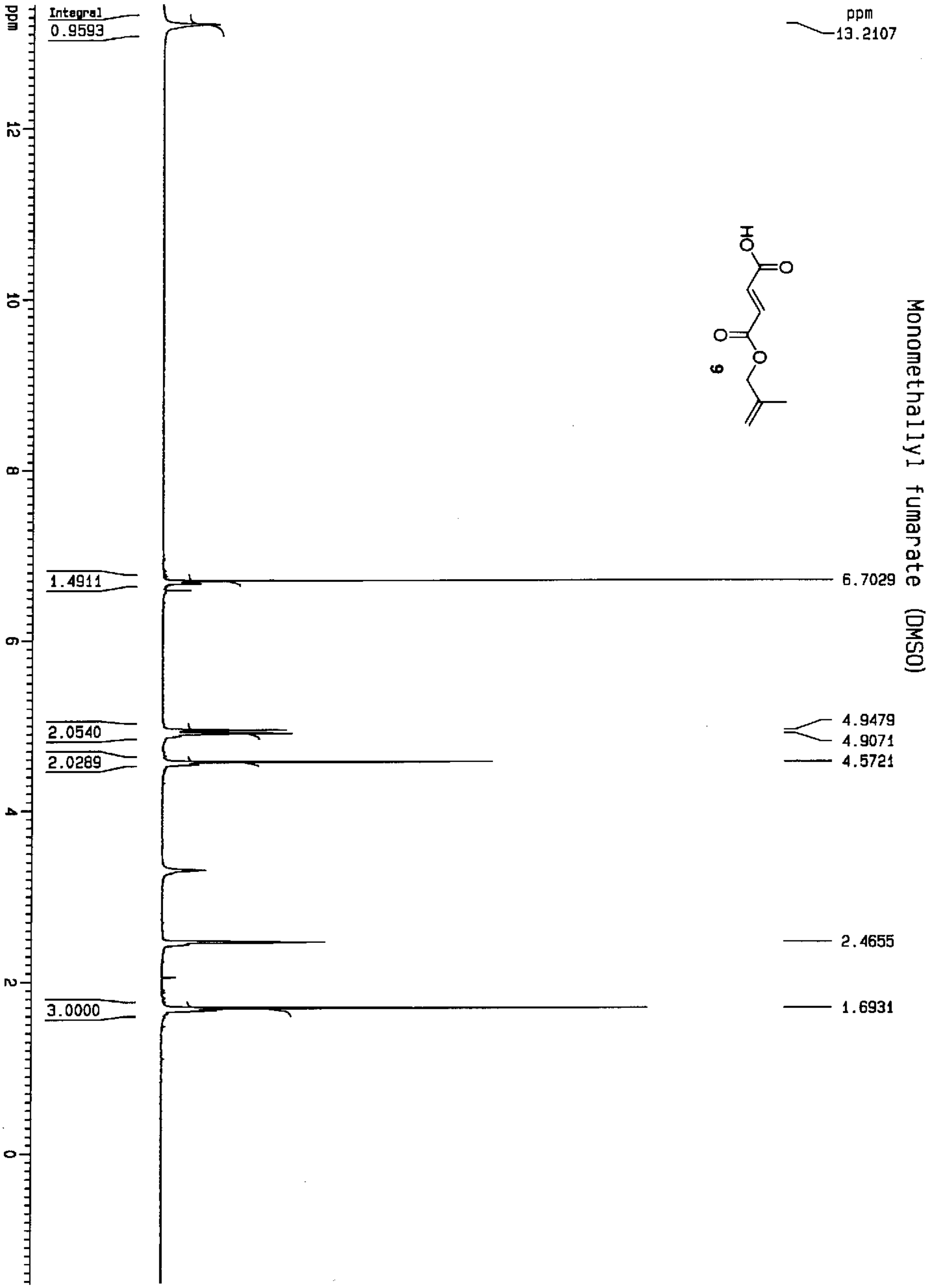


```
Current Data Parameters
NAME              joey
EXPNO                2
PROCNO               1

F2 - Acquisition Parameters
Date_           990406
Time             13.39
INSTRUM          spect
PROBHD    5 mm TXI 13C
PULPROG       c13wonoe
TD               32768
SOLVENT          CDCl3
NS                5906
DS                   4
SWH          32679.738 Hz
FIDRES        0.997306 Hz
AQ           0.5014004 sec
RG               32768
DW              15.300 usec
DE                6.00 usec
TE               290.0 K
D3          0.00100000 sec
PL12             12.00 dB
D1         12.00000000 sec
CPDPRG2        waltz16
PCPD2           100.00 usec
SFO2       500.1325006 MHz
NUC2                1H
PL2             120.00 dB
P1               11.00 usec
DE                6.00 usec
SFO1       125.7722011 MHz
NUC1               13C
PL1              -6.00 dB

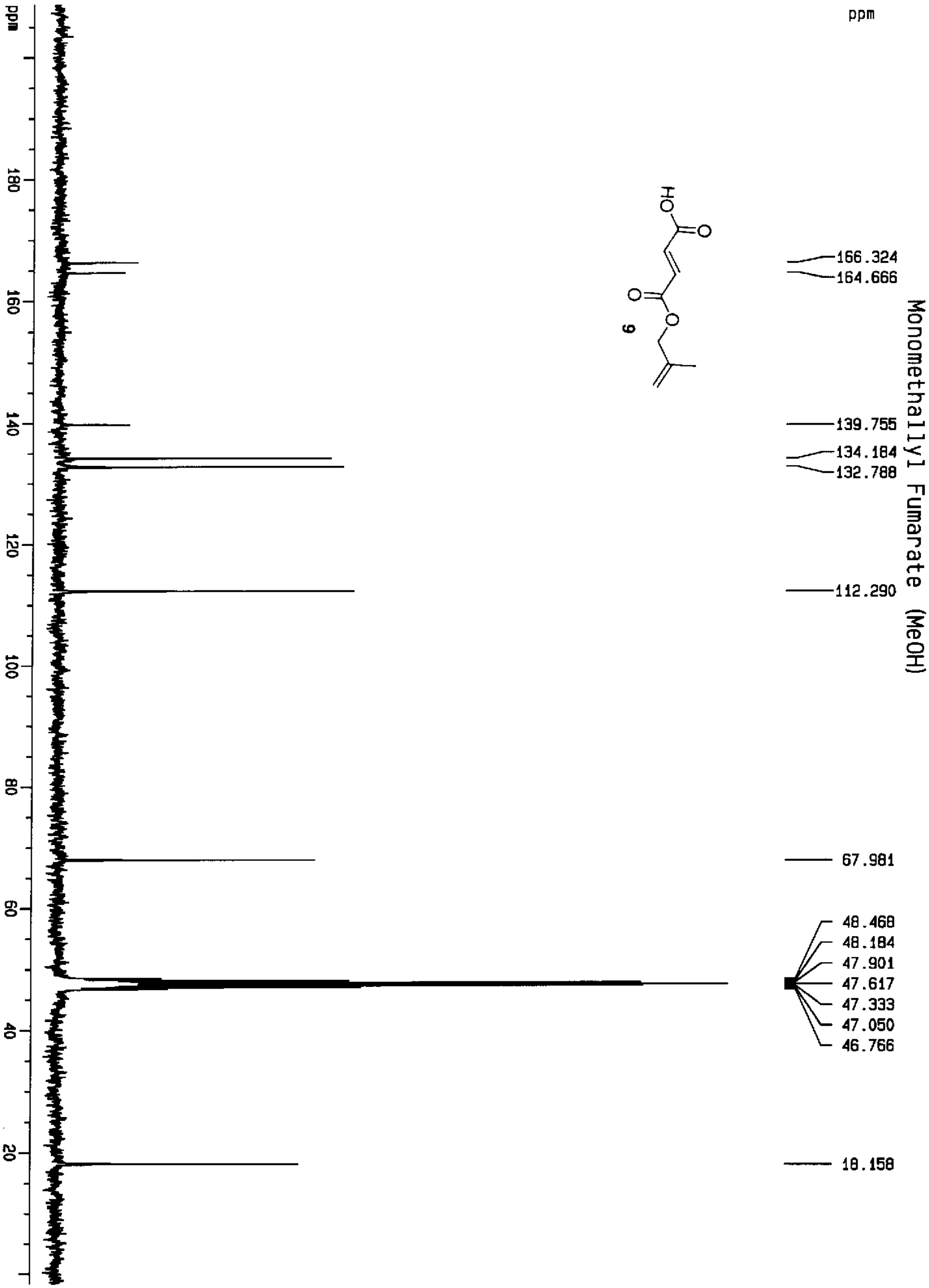
F2 - Processing parameters
SI                8192
SF         125.7577832 MHz
WDW                 EM
SSB                  0
LB                4.00 Hz
GB                   0
PC                1.00

1D NMR plot parameters
CX               20.00 cm
F1P            200.000 ppm
F1            25151.56 Hz
F2P              0.000 ppm
F2                0.00 Hz
PPMCM         10.00000 ppm/cm
HZCM        1257.57788 Hz/cm
```

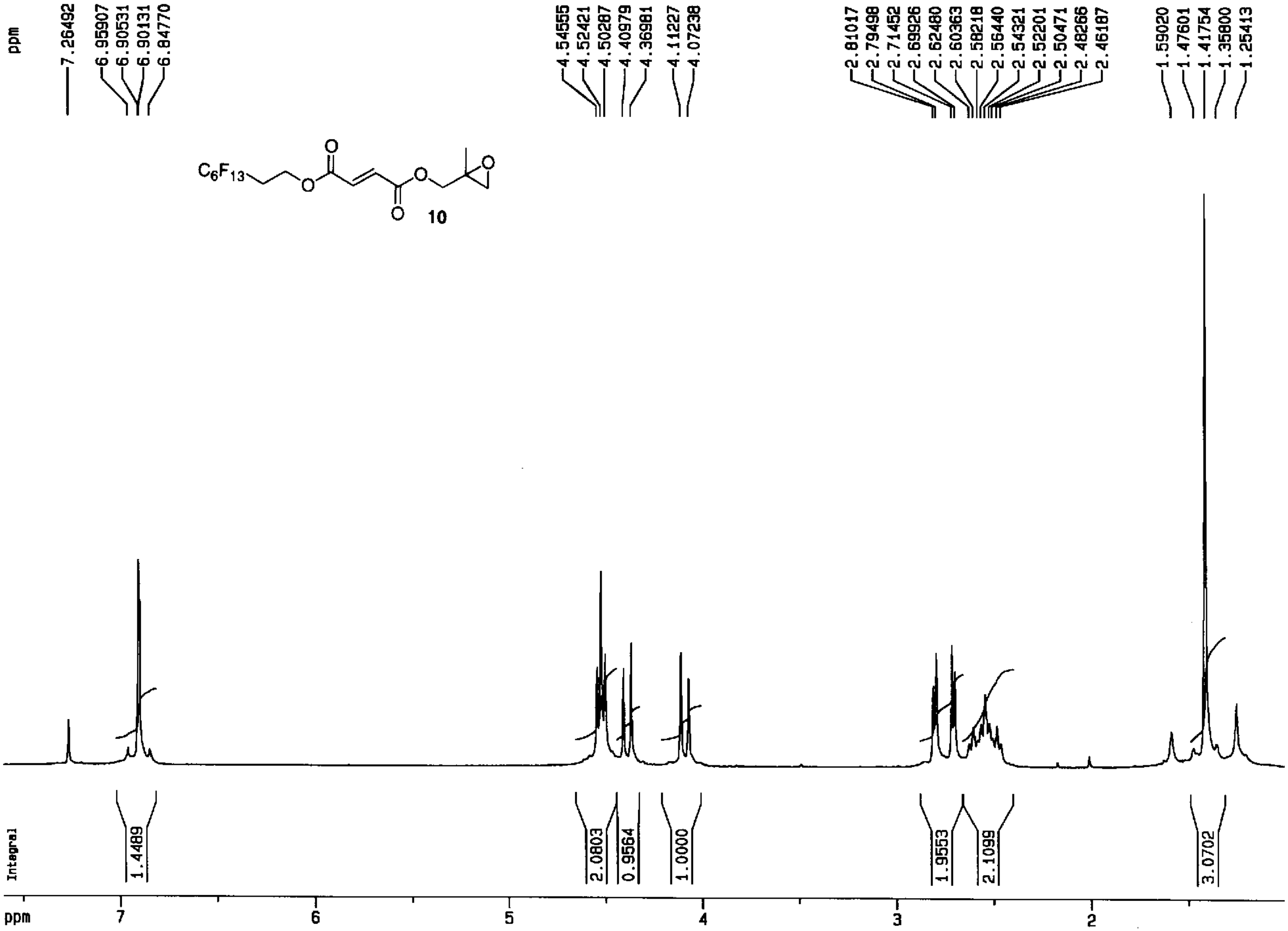


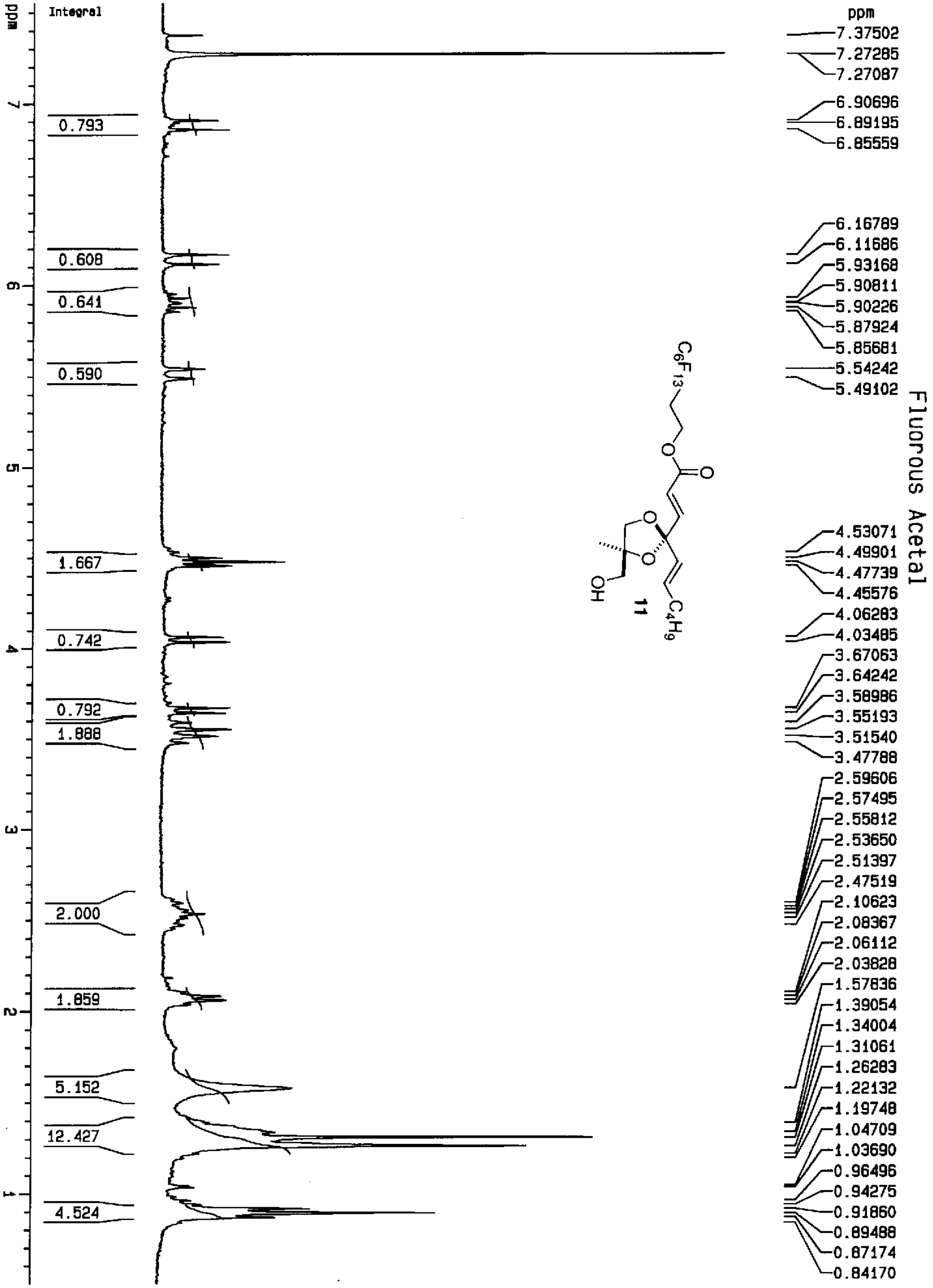
9

Monomethallyl fumarate (DMSO)

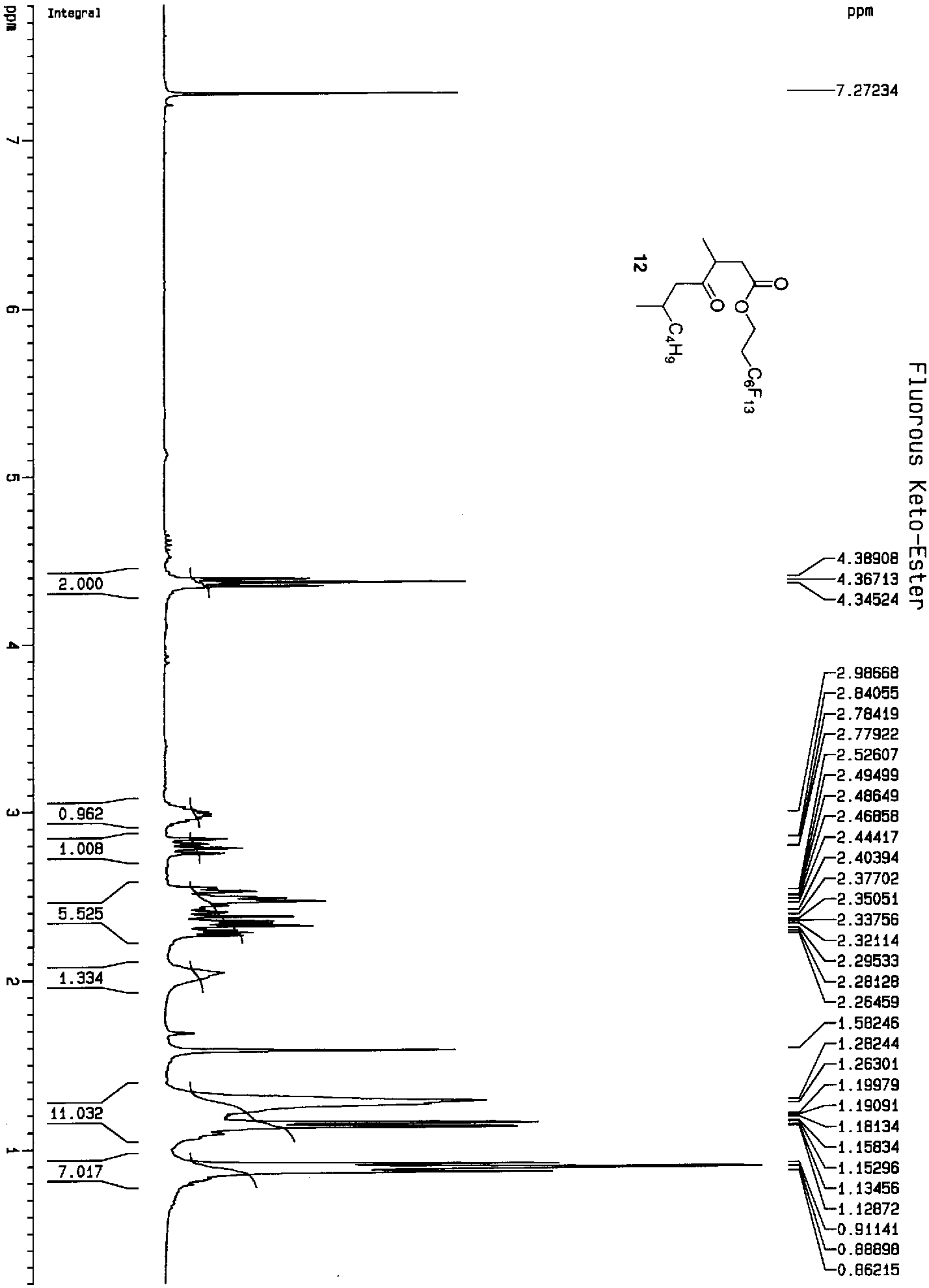

Monomethallyl Fumarate (MeOH)
HO
O
O
O
9
ppm
166.324
164.666
139.755
134.184
132.788
112.290
67.981
48.468
48.184
47.901
47.617
47.333
47.050
46.766
18.158
ppm
180
160
140
120
100
80
60
40
20

1H, 1H, 2H, 2H-Perfluorooctyl Methallyl Fumarate (CDCl3)

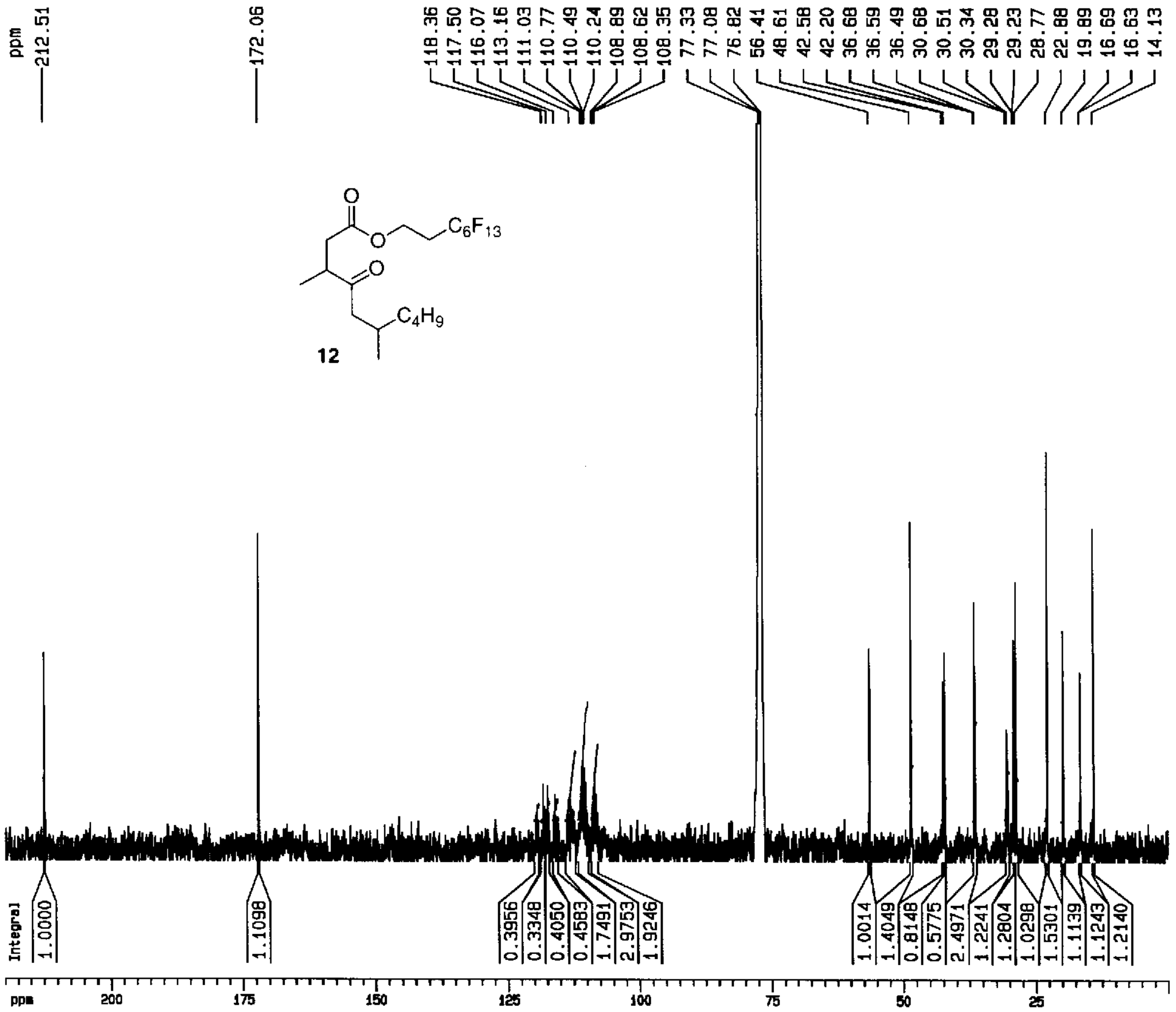



ppm
Integral
0.793
0.608
0.641
0.590
1.667
0.742
0.792
1.888
2.000
1.859
5.152
12.427
4.524
7
6
5
4
3
2
1
ppm
7.37502
7.27285
7.27087
6.90696
6.89195
6.85559
6.16789
6.11686
5.93168
5.90811
5.90226
5.87924
5.85681
5.54242
5.49102
4.53071
4.49901
4.47739
4.45576
4.06283
4.03485
3.67063
3.64242
3.58986
3.55193
3.51540
3.47788
2.59606
2.57495
2.55812
2.53650
2.51397
2.47519
2.10623
2.08367
2.06112
2.03828
1.57636
1.39054
1.34004
1.31061
1.26283
1.22132
1.19748
1.04709
1.03690
0.96496
0.94275
0.91860
0.89488
0.87174
0.84170
Fluorous Acetal
C_6F_{13}
O
O
O
O
OH
C_4H_9

11


Fluorous Keto-Ester

Joey Fluorous Keto Ester cdcl3 rt 125MHz 13C 1H decp delay 12sec 5/22/99



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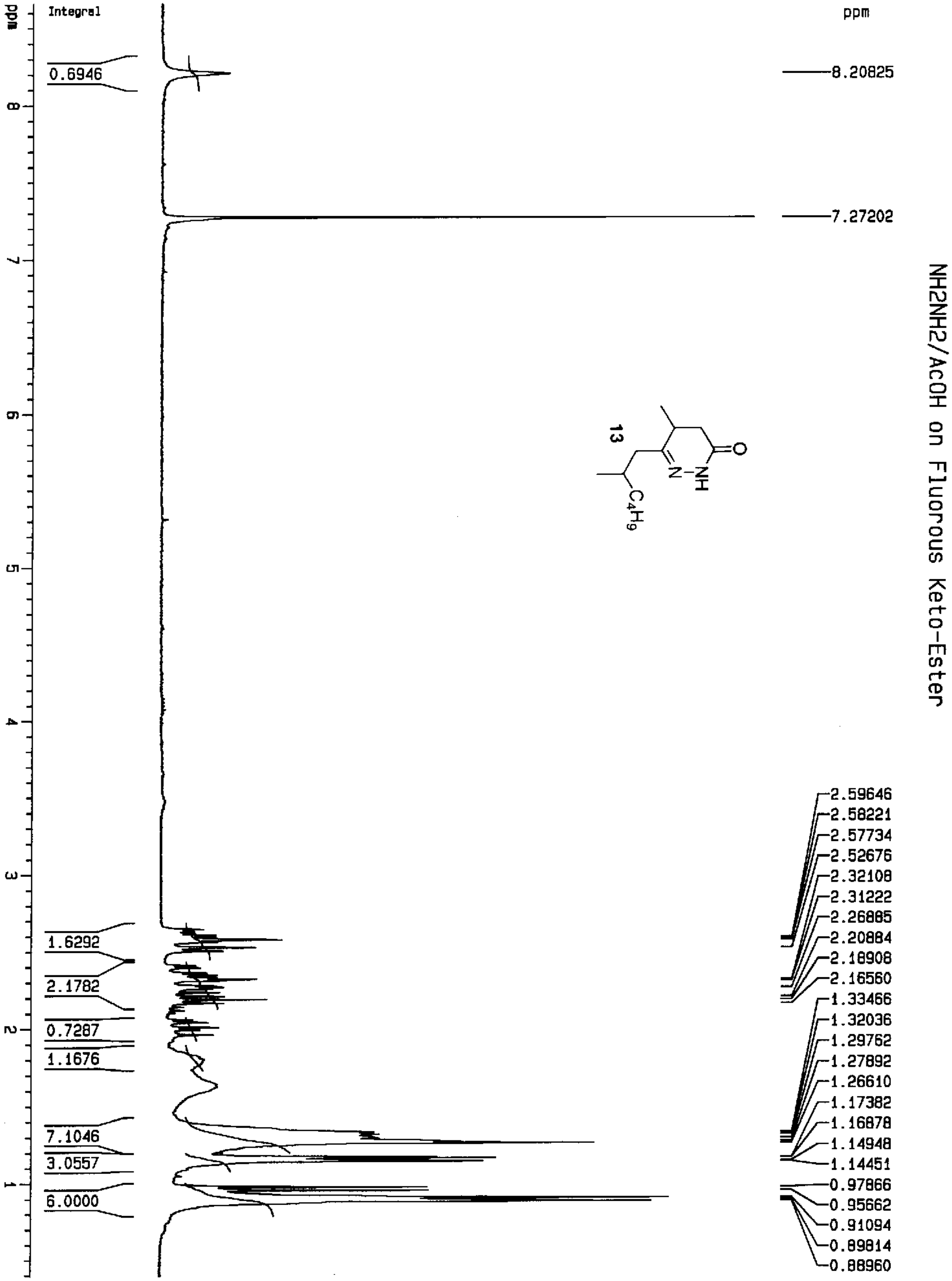
Current Data Parameters
NAME              joey-ke
EXPNO                   2
PROCNO                  1

F2 - Acquisition Parameters
Date_              990521
Time                16.09
INSTRUM             spect
PROBHD     5 mm TXI 13C
PULPROG          c13wonoe
TD                  32768
SOLVENT             CDC13
NS                   5021
DS                      4
SWH           32679.738 Hz
FIDRES         0.997306 Hz
AQ            0.5014004 sec
RG                  32768
DW               15.300 usec
DE                 6.00 usec
TE                290.0 K
D3           0.00100000 sec
PL12              12.00 dB
D1          12.00000000 sec
CPDPRG2           waltz16
PCPD2            100.00 usec
SFO2        500.1325006 MHz
NUC2                   1H
PL2              120.00 dB
P1                11.00 usec
DE                 6.00 usec
SFO1        125.7722011 MHz
NUC1                  13C
PL1               -6.00 dB

F2 - Processing parameters
SI                   8192
SF          125.7577832 MHz
WDW                    EM
SSB                     0
LB                 4.00 Hz
GB                      0
PC                   1.00

1D NMR plot parameters
CX                20.00 cm
F1P             220.000 ppm
F1             27666.71 Hz
F2P               0.000 ppm
F2                 0.00 Hz
PPMCM          11.00000 ppm/cm
HZCM         1383.33557 Hz/cm
```


NH2NH2/AcOH on Fluorous Keto-Ester
13
O
NH
N
C_4H_9
Integral
0.6946
1.6292
2.1782
0.7287
1.1676
7.1046
3.0557
6.0000
ppm
8
7
6
5
4
3
2
1
8.20825
7.27202
2.59646
2.58221
2.57734
2.52676
2.32108
2.31222
2.26885
2.20884
2.18908
2.16560
1.33466
1.32036
1.29762
1.27892
1.26610
1.17382
1.16878
1.14948
1.14451
0.97866
0.95662
0.91094
0.89814
0.88960