

Supporting information for:

Asymmetric Synthesis of Four Isomers of 2-C-Trifluoro methylerythritol

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1. General Experimental Methods

¹H NMR, ¹⁹F NMR and ¹³C NMR spectra were recorded at 25 °C. Chemical shifts (δ) are quoted in ppm and referenced to internal TMS (δ 0) for ¹H NMR, and CDCl₃ (δ 77.0) or MeOH-d₄ (δ 49.0) for ¹³C NMR; coupling constants (J) are quoted in Hz; data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; Flash chromatography was performed on silica gel (300-400 mesh). All reactions were conducted in oven-dried glassware under inert atmosphere of nitrogen with anhydrous solvents. The solvents and reagents were purified and dried according to standard procedures.

2. Chemical data of (12a Mosher's ester), 12b, 12c, 12d, 12e, 12f, 12g, 12i, 13b, 13c, 13d.

(R)-12a-3-Mosher's ester. Oil, in 67% yield. ¹H NMR (CDCl₃) δ 1.16 (t, 3H, J = 7.2 Hz), 3.51 (d, 3H, J = 1.2 Hz), 3.71 (d, 1H, J = 9.9 Hz), 3.83 (d, 1H, J = 9.9 Hz), 4.01~4.10 (m, 2H), 4.44~4.53 (m, 3H), 5.47 (s, 1H) 7.25~7.56 (m, 10H); ¹³C NMR (CDCl₃) δ 13.7 (s), 29.7 (s), 55.4 (s), 62.8 (s), 67.2 (s), 70.9 (s), 74.2 (s), 75.4 (q, J = 27.5 Hz), 84.8 (q, J = 29.4 Hz), 123.1 (q, J = 288.7 Hz), 123.7 (q, J = 286.2 Hz), 127.4 (s), 127.9 (s), 128.2 (s), 128.4 (s), 128.5 (s), 129.4 (s), 131.4 (s), 136.7 (s), 165.4 (s), 166.5 (s); ¹⁹F NMR (CDCl₃) δ -71.9 (s), -78.0 (s); IR (thin film) ν_{max} 3512, 3069, 1760, 1454, 1187, 1108 cm⁻¹; MS (ESI): *m/z* 539.2 (M+H⁺). HRMS (M+Na⁺) Anal. Calc'd for C₂₄H₂₄O₇F₆Na 561.1319; Found: 561.1318. [α]_D²⁰ +9.1 (c 1.5, CDCl₃).

(S)-12a-3-Mosher's ester. Oil, in 39% yield. ¹H NMR (CDCl₃) δ 1.17 (t, 3H, J = 7.2 Hz), 3.61 (d, 3H, J = 1.2 Hz), 3.67 (d, 1H, J = 9.9 Hz), 3.85 (d, 1H, J = 9.9 Hz), 4.00~4.20 (m, 2H), 4.38 (s, 1H), 4.46 (d, 1H, J = 11.7 Hz), 4.52 (d, 1H, J = 10.8 Hz), 5.47 (s, 1H), 7.25~7.44 (m, 8H), 7.58~7.60 (m, 2H); ¹³C NMR (CDCl₃) δ 13.7 (s), 29.7 (s), 55.6 (s), 62.8 (s), 67.2 (s), 70.8 (s), 74.2 (s), 75.5 (q, J = 26.7 Hz), 84.6 (q, J = 27.7 Hz), 123.1 (q, J = 287.2 Hz), 123.6 (q, J = 284.8 Hz), 127.4 (s), 127.9 (s), 128.2 (s), 128.4 (s), 128.5 (s), 128.8 (s), 131.7 (s), 136.7 (s), 165.3 (s), 167.2 (s); ¹⁹F NMR (CDCl₃) δ -72.0 (s), -78.3 (s); IR (thin film) ν_{max} 3505, 3068, 2987, 1759, 1454, 1187, 1108 cm⁻¹; MS (ESI): *m/z* 539.2

(M+H⁺). HRMS (M+Na⁺) Anal. Calc'd for C₂₄H₂₄O₇F₆Na 561.1319; Found: 561.1318. [α]²⁰_D -17.9 (c 1.2, CDCl₃).

(2S, 3S)-2-Benzoxymethyl-1,1,1-trifluoro-2,3-dihydroxy-butyric acid ethyl ester (12b).

Compound **12b** was purified on silica gel (PE: EtOAc = 5:1, *R_f* = 0.4) in 77% yield as solid. mp: 35.5–36 °C. ¹H NMR (CDCl₃) δ 1.30 (t, 3H, *J* = 7.2 Hz), 3.29 (br, 1H), 3.80 (d, 1H, *J* = 10.2 Hz), 3.84 (d, 1H, *J* = 10.2 Hz), 4.00 (br, 1H), 4.20~4.33 (m, 2H), 4.51 (s, 1H), 4.62 (s, 1H), 7.30~7.40 (m, 5H). ¹³C NMR (CDCl₃) δ 13.9 (s), 62.8 (s), 68.2 (q, *J* = 2.3 Hz), 70.4 (s), 74.2 (s) 76.4 (q, *J* = 26.2 Hz), 124.5 (q, *J* = 285.2 Hz), 127.8 (s), 128.1 (s), 128.5 (s), 137.1 (s), 171.4 (s). ¹⁹F NMR (CDCl₃) δ -76.2 (t, *J* = 7.1 Hz); IR (thin film) ν_{max} 3476, 2897, 1738, 1277, 1188, 1110 cm⁻¹; MS (EI): *m/z* 322 (M⁺, 0.8). Anal. Calc'd for C₁₄H₁₇O₅F₃: C, 52.17%; H, 5.28%. Found: C, 52.14%; H, 5.31%. [α]²⁰_D +4.6 (c 0.84, CHCl₃). *t_r* (2S, 3S) = 17.14 min *t_r* (2R,3R) = 20.10 min, (Chiraldak OJ, column No. OJ00CE-HI043, λ = 254 nm, Hex: *i*-PrOH = 90:10, 0.7 mL/min).

1-(Benzoxy)-2-(trifluoromethyl)butane-2,3,4-triol (12c). Oil, in 81% yield. ¹H NMR (CDCl₃) δ 2.29 (s), 3.07 (s), 3.61~3.79 (m, 5H), 4.01 (s), 4.19 (s), 4.55 (s, 2H), 7.28~7.38 (m, 5H); ¹³C NMR (CDCl₃) δ 61.9 (s), 68.1 (s), 71.4 (s), 74.1 (s) 76.5 (q, *J* = 26.3 Hz), 125.0 (q, *J* = 285.1 Hz), 127.8 (s), 128.2 (s), 128.6 (s), 136.7 (s); ¹⁹F NMR (CDCl₃) δ -76.5 (s); IR (thin film) ν_{max} 3420, 2936, 1456, 1182, 1151, 1095 cm⁻¹; MS (ESI): *m/z* 298.1 (M+NH₄⁺). HRMS (M+Na⁺) Anal. Calc'd for C₁₂H₁₅O₄F₃Na 303.0820 Found: 303.0822. [α]²⁰_D +4.3 (c 0.55, CHCl₃)

2-((Benzoxy)methyl)-1,1,1-trifluoro-2,3-dihydroxybutyl benzoate (12d). Oil, in 81% yield. ¹H NMR (CDCl₃) δ 3.14 (d, 1H, *J* = 5.4 Hz), 3.76 (d, 1H, *J* = 10.2 Hz), 3.87 (d, 1H, *J* = 10.2 Hz), 3.92(s, 1H), 4.27~4.32 (br, 1H), 4.42~4.49 (m, 1H), 4.58~4.63 (m, 3H), 7.29~7.38 (m, 5H), 7.42 (t, 2H, *J* = 7.5 Hz), 7.56 (t, 1H, *J* = 7.5 Hz), 8.01 (d 2H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃) δ 64.8 (s), 68.2 (s), 70.8 (s), 74.2 (s), 75.3 (q, *J* = 26.5 Hz), 124.7 (q, *J* = 285.0 Hz), 127.8 (s), 128.2 (s), 128.5 (s), 128.6 (s), 129.6 (s), 129.7 (s), 133.3 (s), 136.7 (s), 166.9 (s); ¹⁹F NMR (CDCl₃) δ -76.2 (s); IR (thin film) ν_{max} 3456,

3399, 2905, 1704, 1291, 1191 cm^{-1} ; MS (EI): m/z 384 (M^+ , 0.2). Anal. Calc'd for $C_{19}H_{19}O_5F_3$: C, 59.38%; H, 4.98%. Found: C, 59.42%; H, 5.08%.

2-(Trifluoromethyl)-1,2,3-trihydroxybutyl benzoate (12e). Solid, in 76% yield. mp: 139-140 $^{\circ}\text{C}$. ^1H NMR (CDCl_3) δ 3.84 (d, 1H, J = 11.7 Hz), 4.00 (d, 2H, J = 11.7 Hz), 4.38~4.50 (m, 2H), 4.69~4.73 (m, 1H), 7.51 (t, 2H, J = 7.5 Hz), 7.64 (t, 1H, J = 7.5 Hz), 8.08 (d, 2H, J = 7.5 Hz); ^{13}C NMR (CDCl_3) δ 61.1 (s), 65.7 (s), 70.0 (s), 75.7 (q, J = 24.37 Hz), 126.1 (q, J = 284.9 Hz), 128.4 (s), 129.5 (s), 130.4 (s), 133.0 (s); ^{19}F NMR (CDCl_3) δ -75.2 (s); IR (thin film) ν_{max} 3376, 2966, 1703, 1293, 1176 cm^{-1} ; MS (EI): m/z 165 ($M-\text{C}_3\text{H}_4\text{F}_3\text{O}_2^+$, 72.2). Anal. Calc'd for $C_{12}H_{13}F_3O_5$: C, 48.99%; H, 4.45%. Found: C, 48.63%; H, 4.56%.

Benzoic acid 2-(tert-butyl-diphenyl-silanyloxymethyl)-1,1,1-trifluoro-2,3-dihydroxy-butyl ester (12f). Oil, in 81% yield. ^1H NMR (CDCl_3) δ 1.10 (s, 9H), 2.94 (br, 1H), 3.76 (s, 1H), 3.97 (q, 2H, J = 11.4 Hz), 4.31~4.33 (br, 1H), 4.47~4.67 (m, 2H), 7.40~7.49 (m, 8H), 7.54~7.60 (m, 1H), 7.66~7.70 (m, 4H), 8.00~8.03 (m, 2H); ^{13}C NMR (CDCl_3) δ 19.3 (s), 26.8 (s), 62.3 (s), 65.4 (s), 70.0 (s), 75.5 (q, J = 26.1 Hz), 125.3 (q, J = 259.4 Hz), 128.1 (s), 128.5 (s), 129.6 (s), 130.2 (s), 131.9 (s), 132.0 (s), 133.3 (s), 135.6 (s); ^{19}F NMR (CDCl_3) δ -76.3 (s); IR (thin film) ν_{max} 3482, 2869, 1724, 1707, 1278, 1180, 1114 cm^{-1} ; MS (ESI): m/z 532.4 ($M+\text{H}^+$). HRMS.($M+\text{Na}^+$) Anal. Calc'd for $C_{28}H_{31}F_3O_5\text{SiNa}$: 555.1780. Found: 555.1785.

Benzoic acid -1,1,1-trifluoro-2,3-dihydroxy-2-trityloxymethyl butyl ester (12g). White solid, in 83% yield. mp: 108.5-110 $^{\circ}\text{C}$. ^1H NMR (CDCl_3) δ 2.72 (d, 1H, J = 4.8 Hz), 3.46~3.67 (m, 2H), 4.26~4.48 (m, 2H), 7.19~7.57 (m, 13H), 7.95~7.98 (m, 2H). ^{13}C NMR (CDCl_3) δ 61.6 (s), 65.3 (s), 70.3 (s), 75.6 (q, J = 28.1 Hz), 88.1 (s), 125.2 (q, J = 286.3 Hz), 127.6 (s), 128.0 (s), 128.2 (s), 128.5 (s), 128.6 (s), 129.7 (s), 130.9 (s), 142.9 (s), 166.9 (s); ^{19}F NMR (CDCl_3) δ -75.5 (s); IR (thin film) ν_{max} 3349, 3061, 2846, 1701, 1601, 1450, 1179, 1063 cm^{-1} ; MS (ESI): m/z 559.2 ($M+\text{Na}^+$). HRMS.($M+\text{Na}^+$) Anal. Calc'd for $C_{31}H_{27}O_5F_3\text{Na}$: 559.1706. Found: 559.1702.

(2S, 3R)-2-Benzylloxymethyl-1,1,1-trifluoro-2,3-dihydroxy-butyric acid ethyl ester (12h). Oil, in 81% yield. ^1H NMR (CDCl_3) δ 1.31 (t, 3H, $J = 7.2$ Hz), 3.26 (d, 1H, $J = 7.2$ Hz), 3.75 (d, 1H, $J = 10.2$ Hz), 3.92 (d, 1H, $J = 10.2$ Hz), 3.94 (s, 1H), 4.25~4.34 (m, 2H), 4.51 (d, 1H, $J = 6.9$ Hz), 4.64 (s, 2H) 7.31~7.40 (m, 5H); ^{13}C NMR (CDCl_3) δ 13.9 (s), 62.9 (s), 68.1 (s), 70.4 (s), 74.2 (s), 76.4 (q, $J = 31.8$ Hz), 126.5 (q, $J = 283.6$ Hz), 127.8 (s), 128.1 (s), 128.5 (s), 137.0 (s), 171.5 (s); ^{19}F NMR (CDCl_3) δ -76.5 (s); IR (thin film) ν_{max} 3489, 3428, 2901, 1740, 1251, 1098 cm^{-1} ; MS (ESI): m/z 323.0 ($\text{M}+\text{H}^+$). HRMS. ($\text{M}+\text{Na}^+$) Anal. Calc'd for $\text{C}_{14}\text{H}_{17}\text{O}_5\text{F}_3\text{Na}$: 345.0925, Found: 345.0920. $[\alpha]^{20}_{\text{D}} -21.3$ (c 0.75, CHCl_3). (82% ee). t_r (2R, 3S) = 20.50 min t_r (2S, 3R) = 21.44 min, (Chiralpak AS, column No. AS00CE-JG019, $\lambda = 214$ nm, Hex: *i*-PrOH = 90:10, 0.7 mL/min).

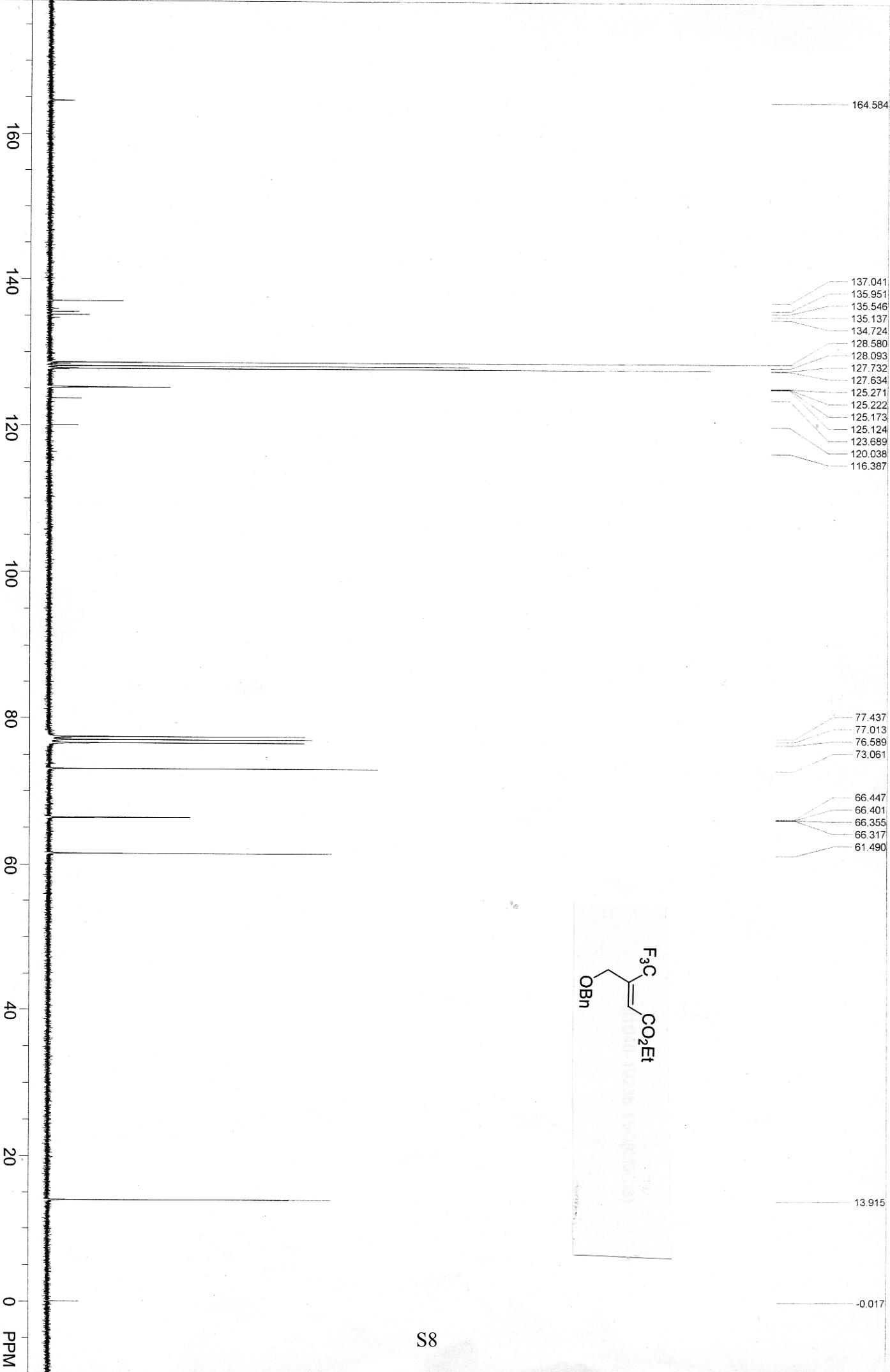
(2R, 3R)-2-Benzylloxymethyl-1,1,1-trifluoro-2,3-dihydroxy-butyric acid ethyl ester (12i). Oil, in 79% yield. ^1H NMR (CDCl_3) δ 1.21 (t, 3H, $J = 7.5$ Hz), 3.35 (d, 1H, $J = 6.6$ Hz), 3.72 (d, 1H, $J = 9.9$ Hz), 3.89 (d, 1H, $J = 10.2$ Hz), 4.08 (s, 1H), 4.07~4.20 (m, 2H), 4.48 (d, 1H, $J = 6.6$ Hz), 4.53 (d, 1H, $J = 11.7$ Hz), 4.60 (d, 1H, $J = 11.1$ Hz), 7.31~7.39 (m, 5H); ^{13}C NMR (CDCl_3) δ 13.8 (s), 62.9 (s), 67.2 (s), 69.2 (s), 74.2 (s), 76.3 (q, $J = 26.4$ Hz), 124.3 (q, $J = 284.8$ Hz), 128.1 (s), 128.2 (s), 128.5 (s), 136.9 (s), 171.6 (s); ^{19}F NMR (CDCl_3) δ -77.4 (s); IR (thin film) ν_{max} 3474, 2941, 1737, 1278, 1188, 1154 cm^{-1} ; MS (ESI): m/z 323.2. ($\text{M}+\text{H}^+$). HRMS. ($\text{M}+\text{Na}^+$) Anal. Calc'd for $\text{C}_{14}\text{H}_{17}\text{O}_5\text{F}_3\text{Na}$: 345.0925. Found: 345.0920. $[\alpha]^{20}_{\text{D}} -3.5$ (c 0.90, CHCl_3) (50% ee). t_r (2S, 3S) = 31.14 min t_r (2R, 3R) = 36.64 min, (Chiralpak AS, column No. AS00CE-JG019, $\lambda = 220$ nm, Hex: *i*-PrOH = 95:5, 0.7 mL/min).

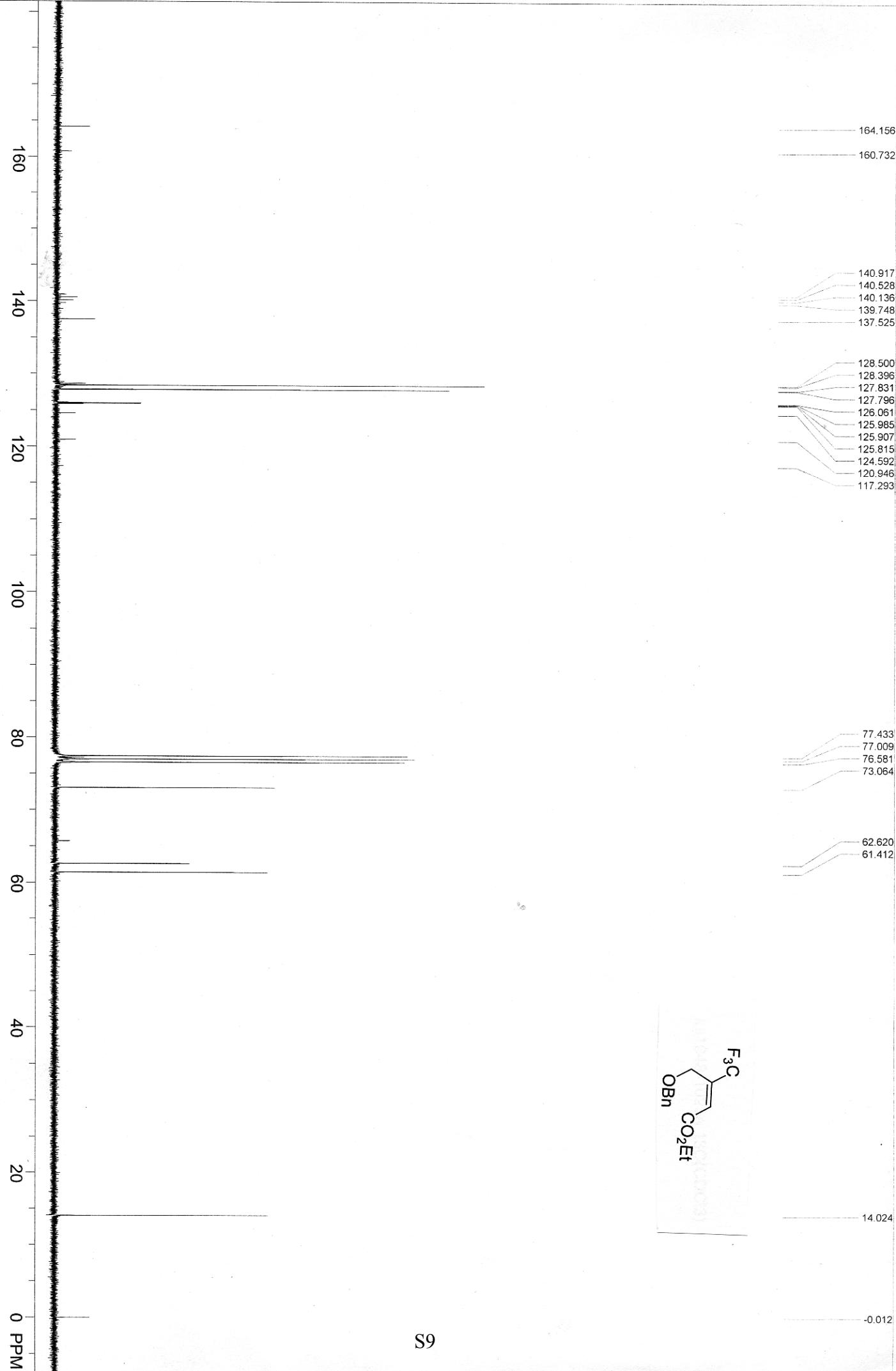
(2S, 3R)-2-C-Trifluoromethylerythritol (13b). Oil, in 92% yield. ^1H NMR (MeOH-d_4) δ 3.60~3.73 (m, 2H), 3.82~3.89 (m, 2H), 3.95~3.98 (m, 1H); ^{13}C NMR (MeOH-d_4) δ 61.0 (s), 61.9 (s), 71.9 (s), 75.9 (q, $J = 24.8$ Hz), 125.9 (q, $J = 286.9$ Hz); ^{19}F NMR (MeOH-d_4) δ -76.5 (s); IR (thin film) ν_{max} 3401, 2960, 1639, 1181, 1099, 1054 cm^{-1} ; MS (ESI): m/z 208.1 ($\text{M}+\text{NH}_4^+$). HRMS ($\text{M}+\text{Na}^+$) Anal. Calc'd for $\text{C}_5\text{H}_9\text{O}_4\text{F}_3\text{Na}$: 213.0352. Found: 213.0345. $[\alpha]^{20}_{\text{D}} +6.3$ (c 1.2, MeOH).

(2S, 3S)-2-C-Trifluoromethylerythritol (13c). Oil, in 94% yield. ^1H NMR (MeOH-d_4) δ 3.74~3.84 (m, 4H), 3.92~3.94 (m, 1H); ^{13}C NMR (MeOH-d_4) δ 60.3 (s), 62.1 (s), 70.9 (s), 76.1 (q, $J =$

24.3 Hz), 126.2 (q, J = 285.8 Hz); ^{19}F NMR (MeOH-d₄) δ -77.6 (s); IR (thin film) ν_{max} 3450, 2956, 1419, 1238, 1185, 1043 cm⁻¹; MS (ESI): m/z 191.1 (M+H⁺). HRMS (M+Na⁺) Anal. Calc'd for C₅H₉O₄F₃Na: 213.0352. Found: 213.0345. $[\alpha]^{20}_{\text{D}} -10.2$ (*c* 0.55, MeOH).

(2*R*, 3*S*)-2-C-Trifluoromethylerythritol (13d). Oil, in 89% yield. ^1H NMR (MeOH-d₄) δ 3.61~3.73 (m, 2H), 3.83~3.88 (m, 2H), 3.95~3.98 (m, 1H); ^{13}C NMR (MeOH-d₄) δ 60.9 (s), 61.8 (s), 71.8 (s), 75.9 (q, J = 24.8 Hz), 125.9 (q, J = 285.4 Hz); ^{19}F NMR (MeOH-d₄) δ -76.5 (s); IR (thin film) ν_{max} 3379, 2959, 1418, 1179, 1137, 1110, 1028 cm⁻¹; MS (ESI): m/z 208.1 (M+NH₄⁺). HRMS (M+Na⁺) Anal. Calc'd for C₅H₉O₄F₃Na: 213.0352. Found: 213.0345. $[\alpha]^{20}_{\text{D}} -1.3$ (*c* 1.0, MeOH).

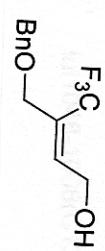




S9

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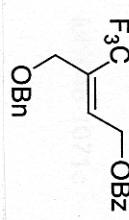
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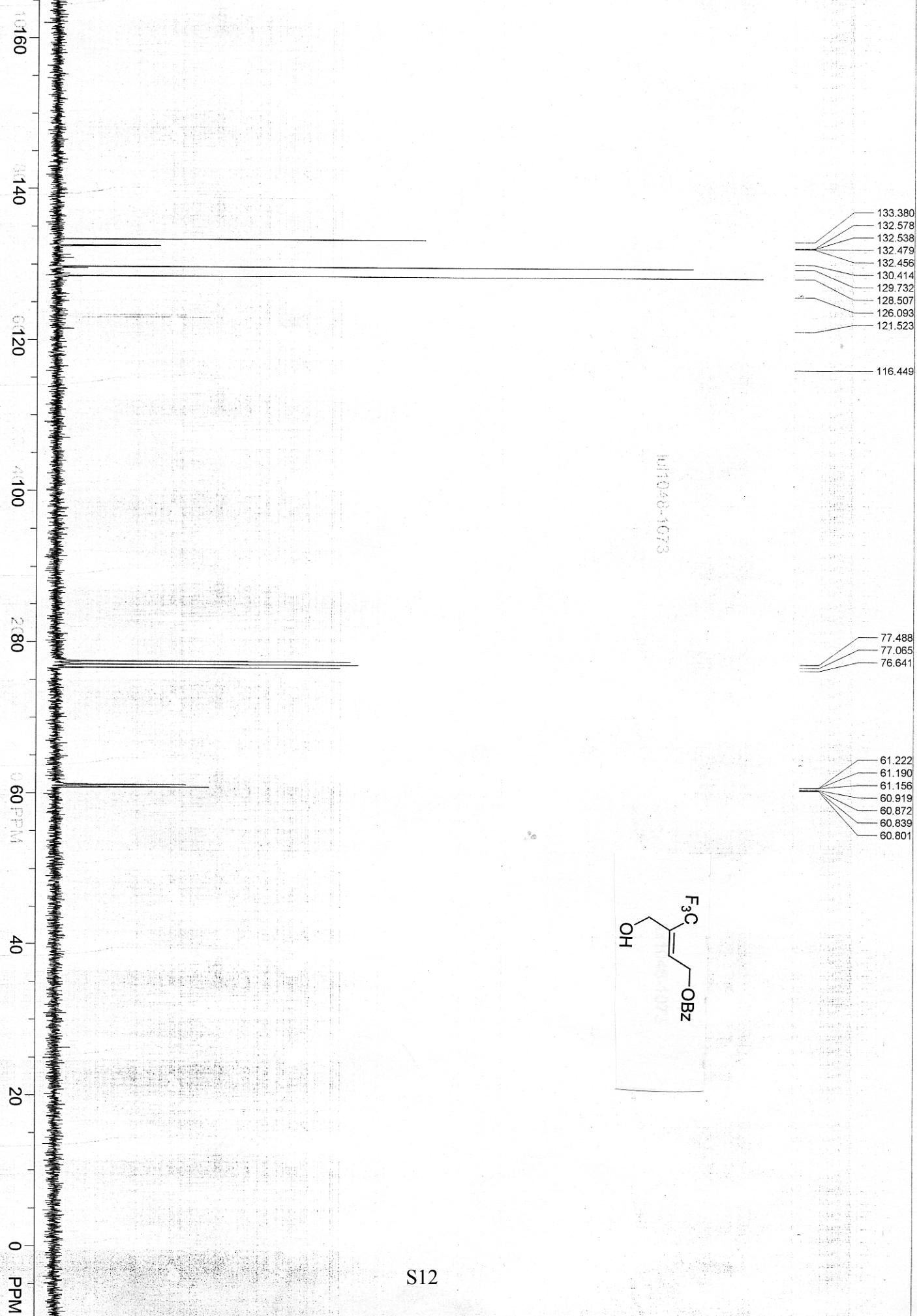


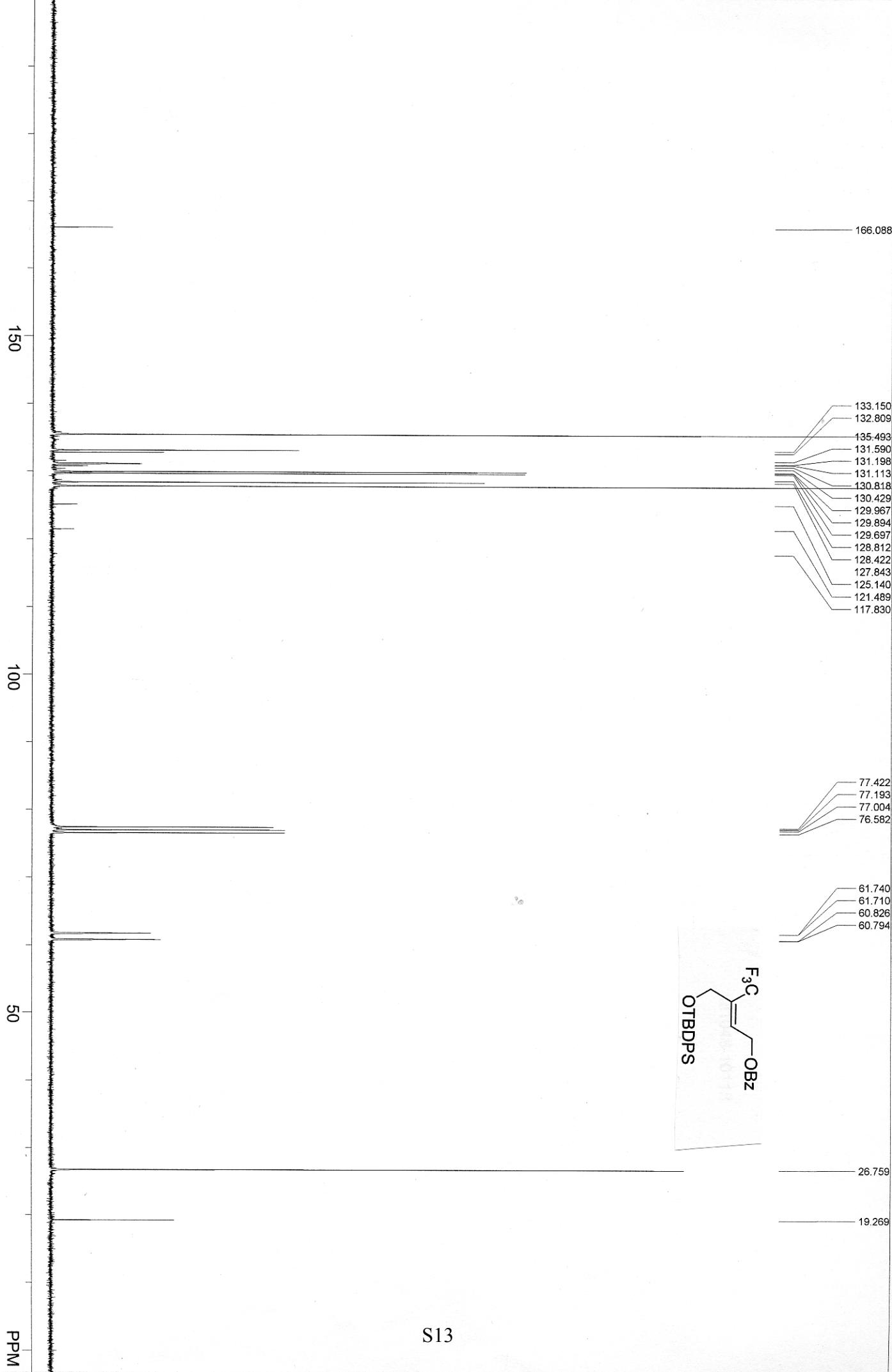
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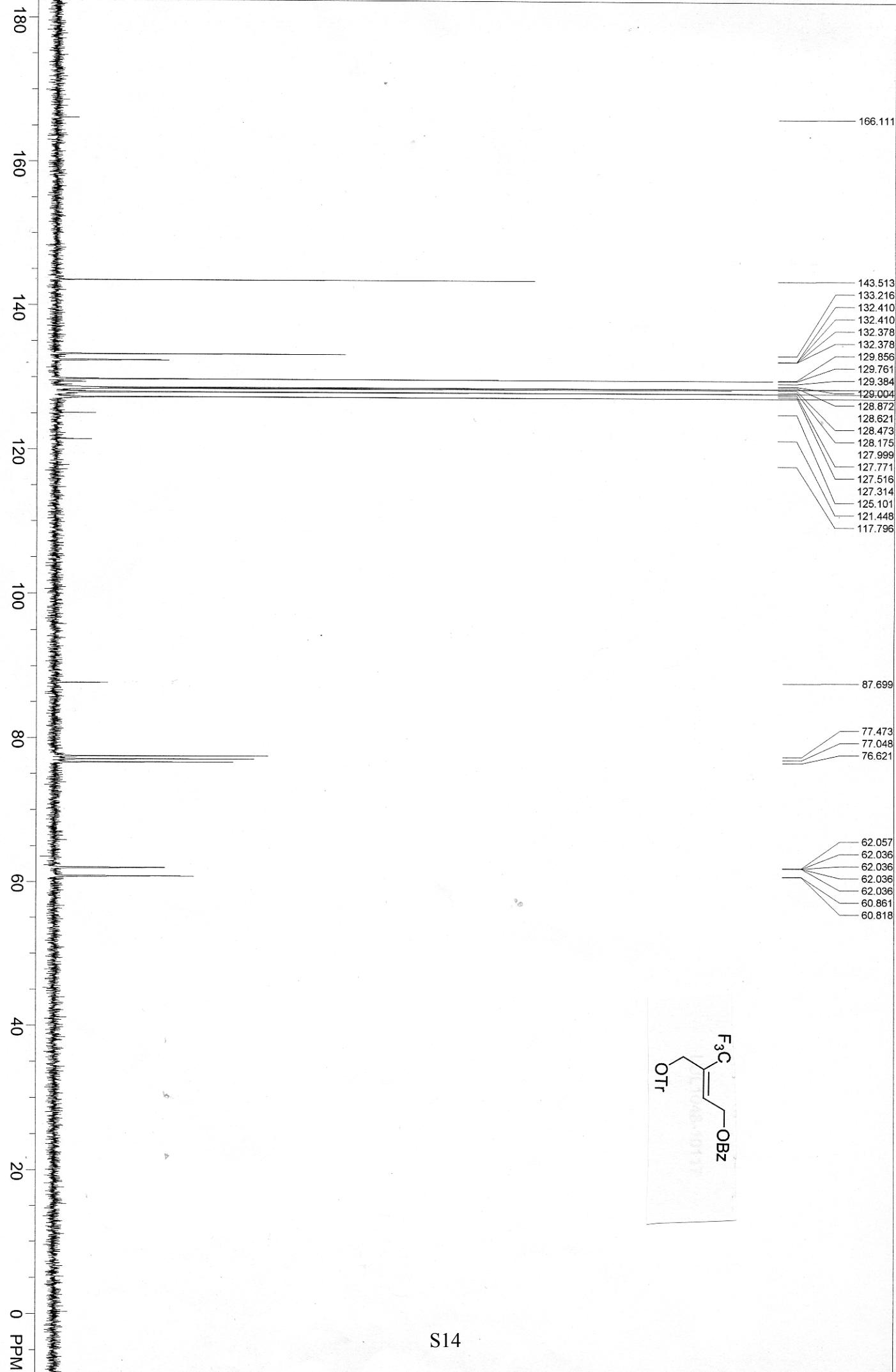
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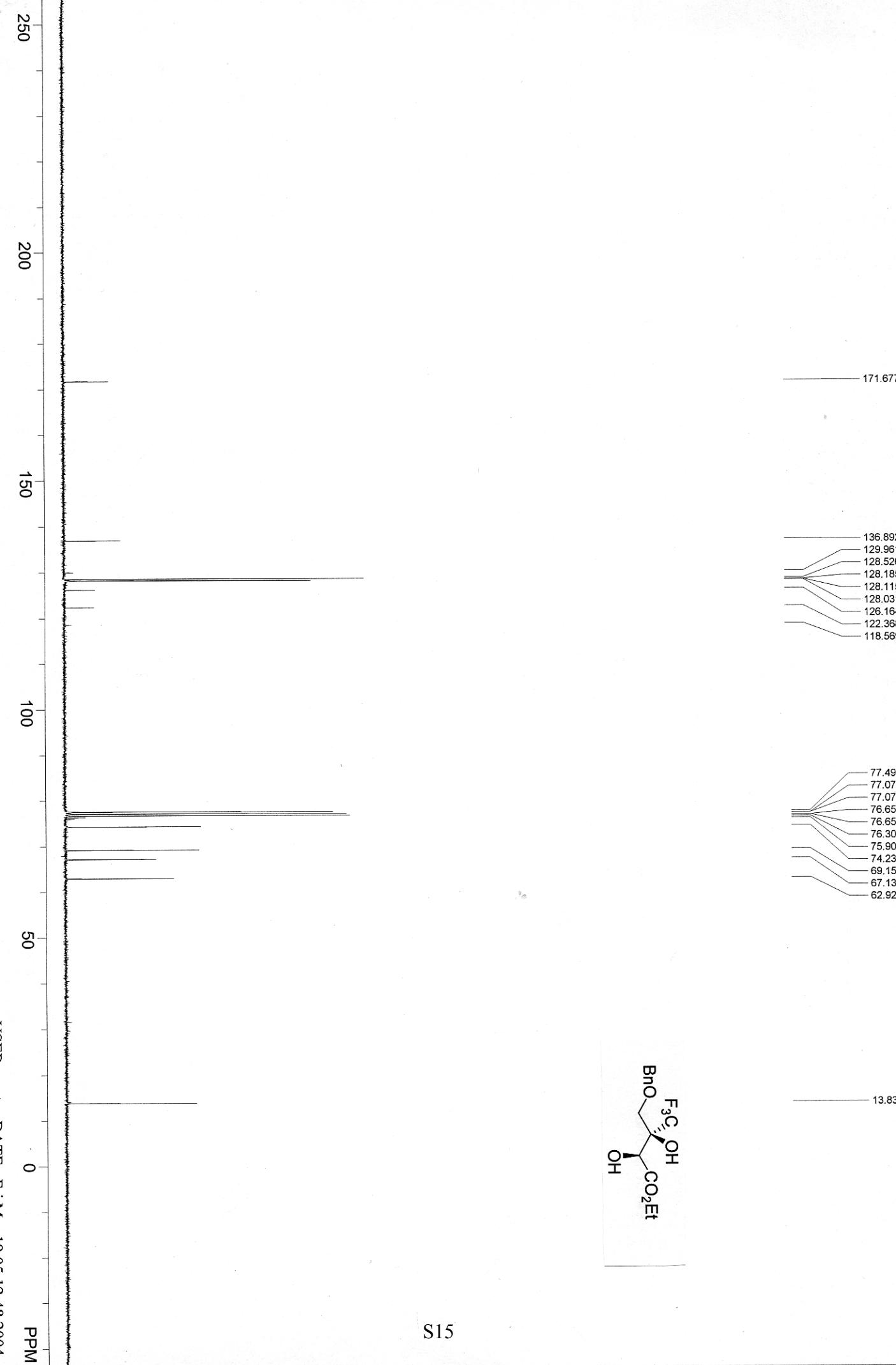
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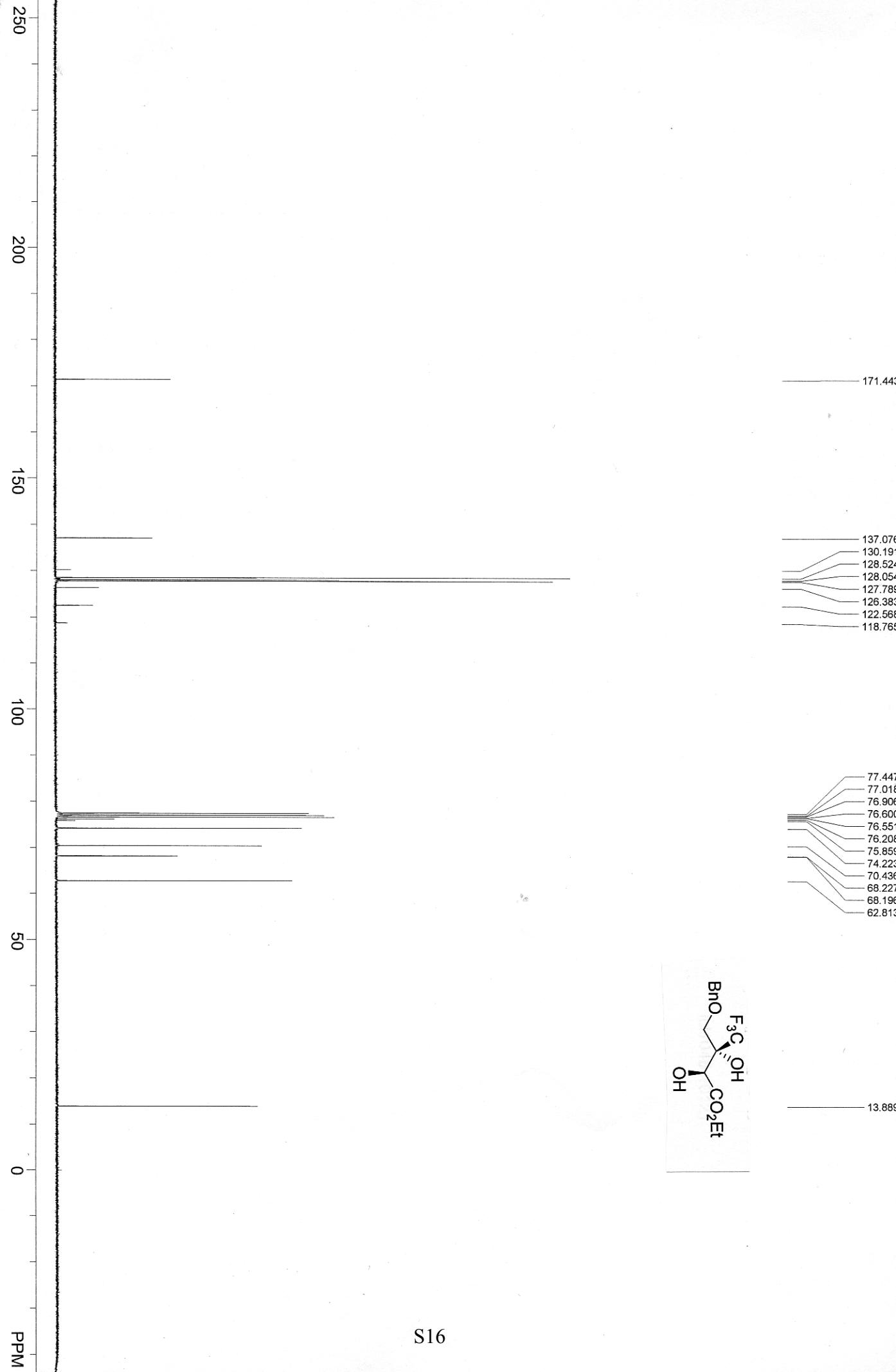


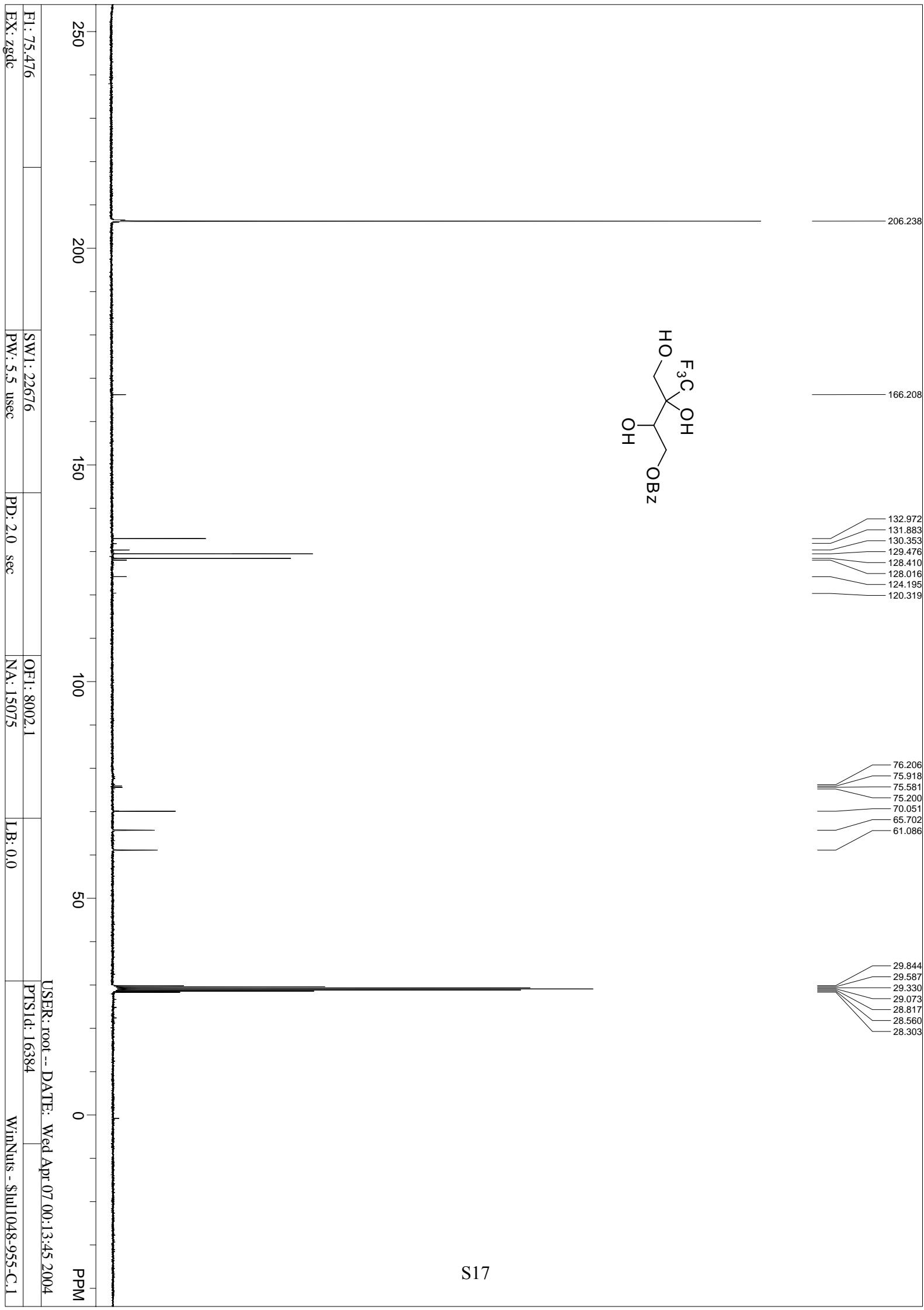


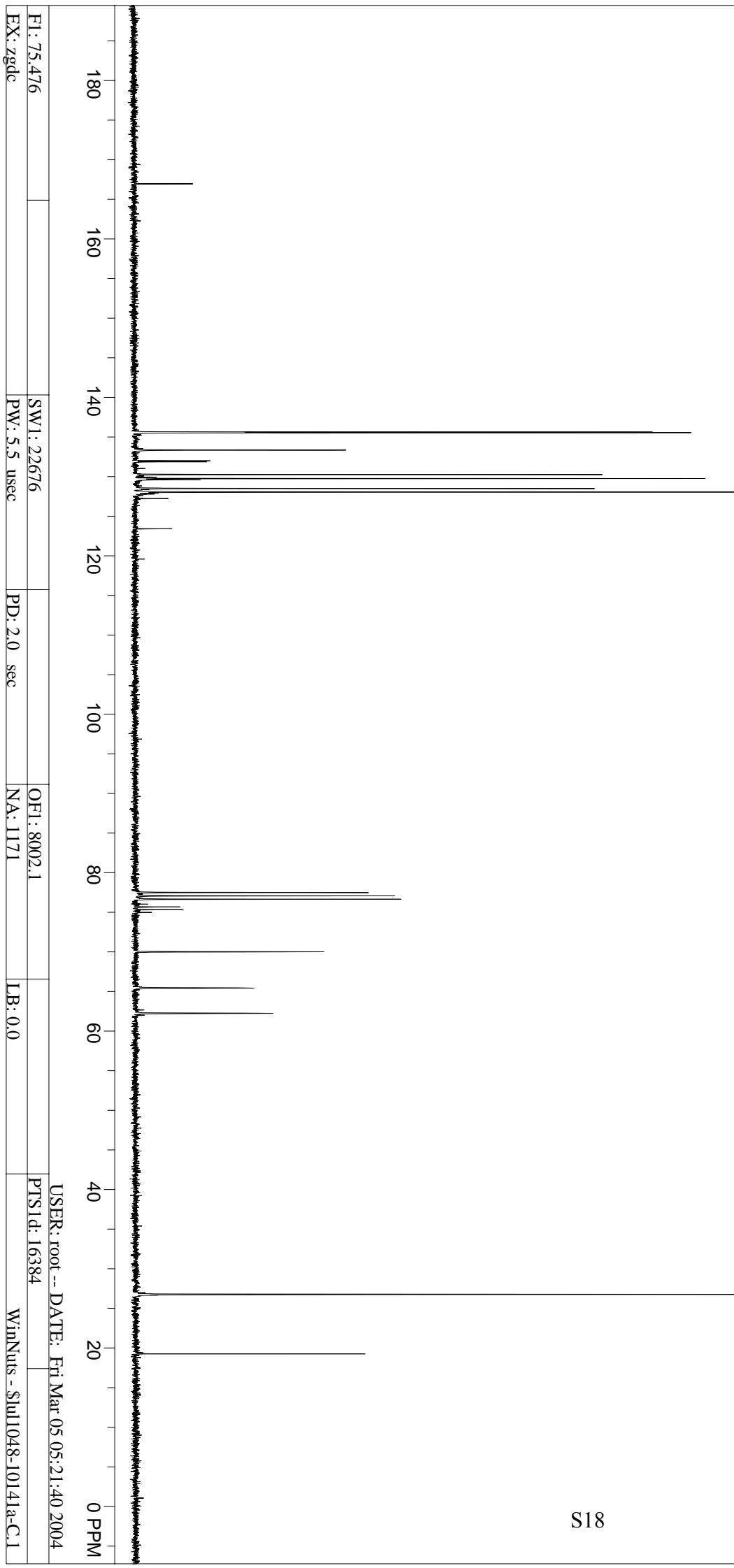
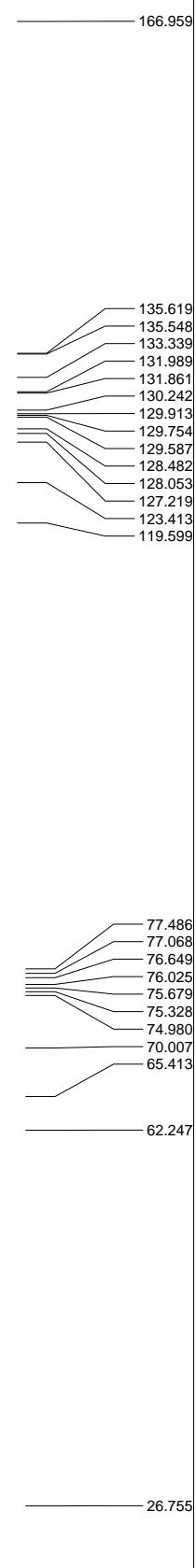
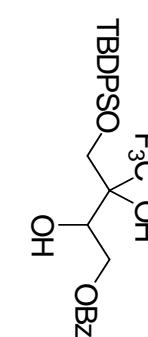


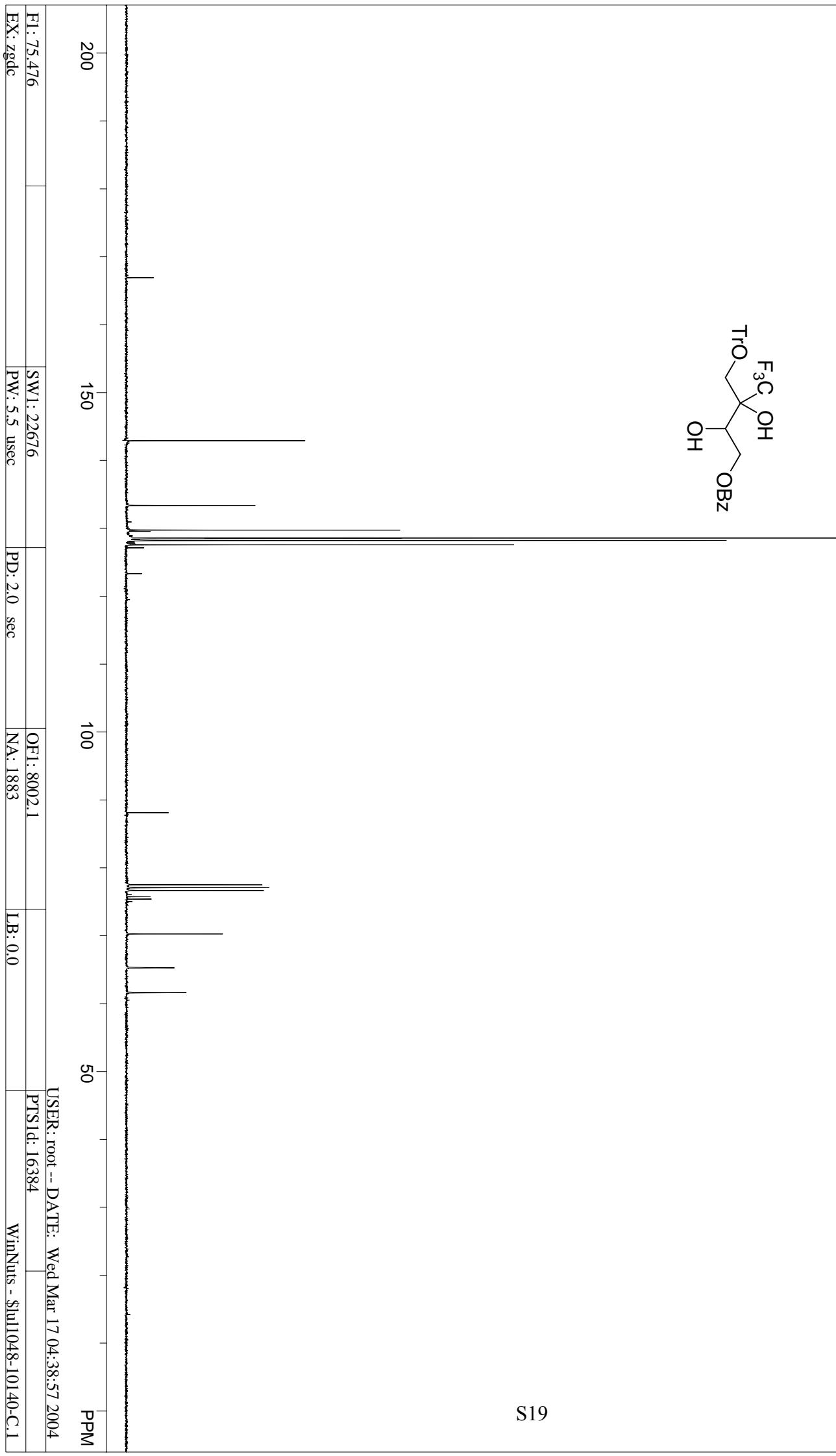
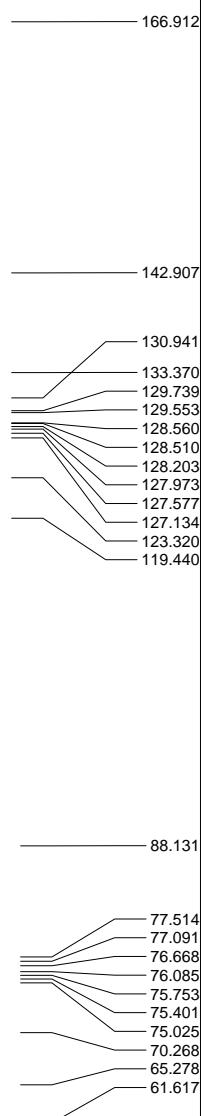
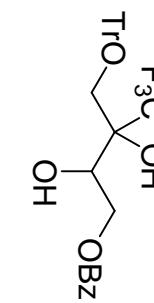


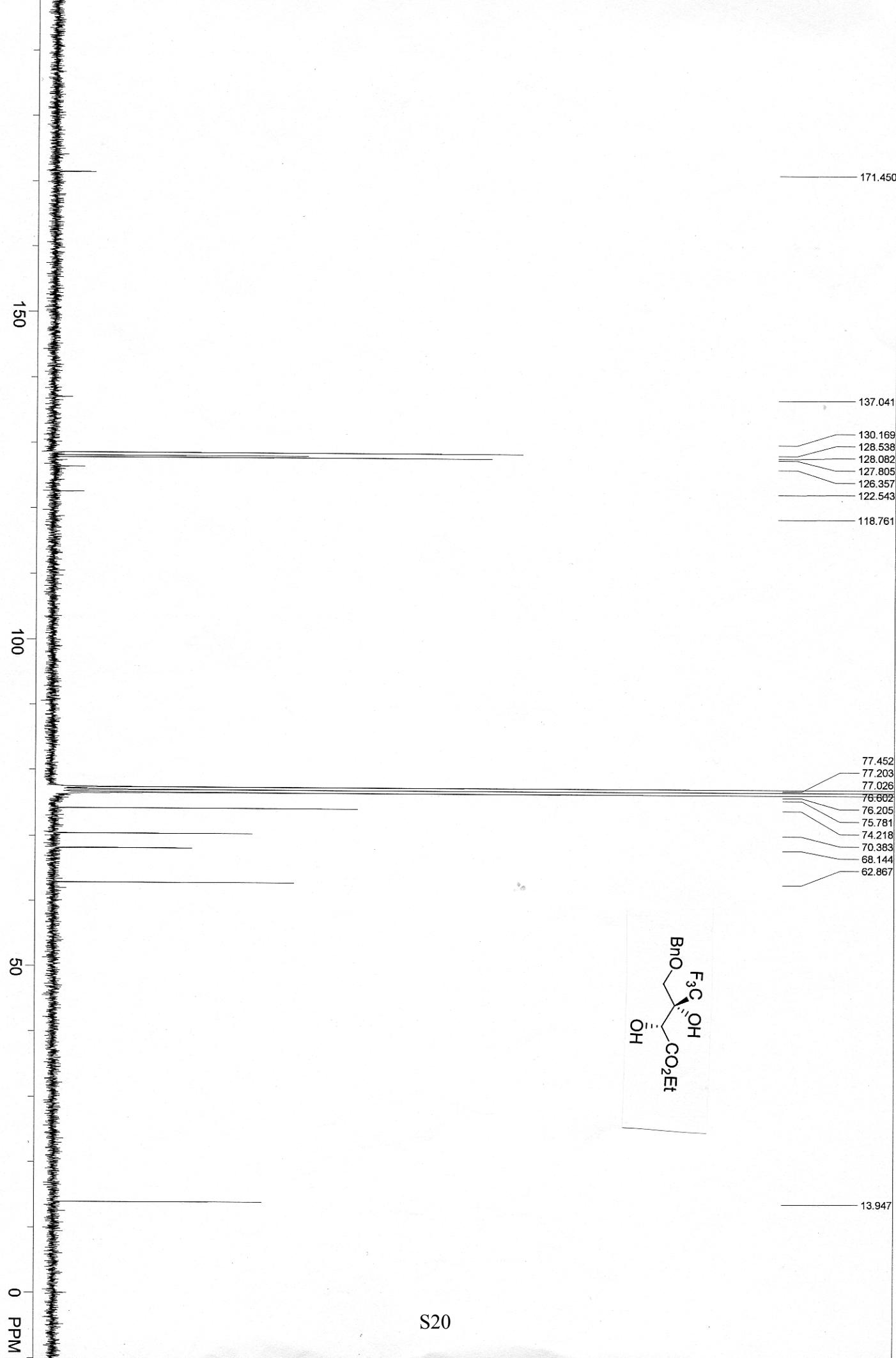


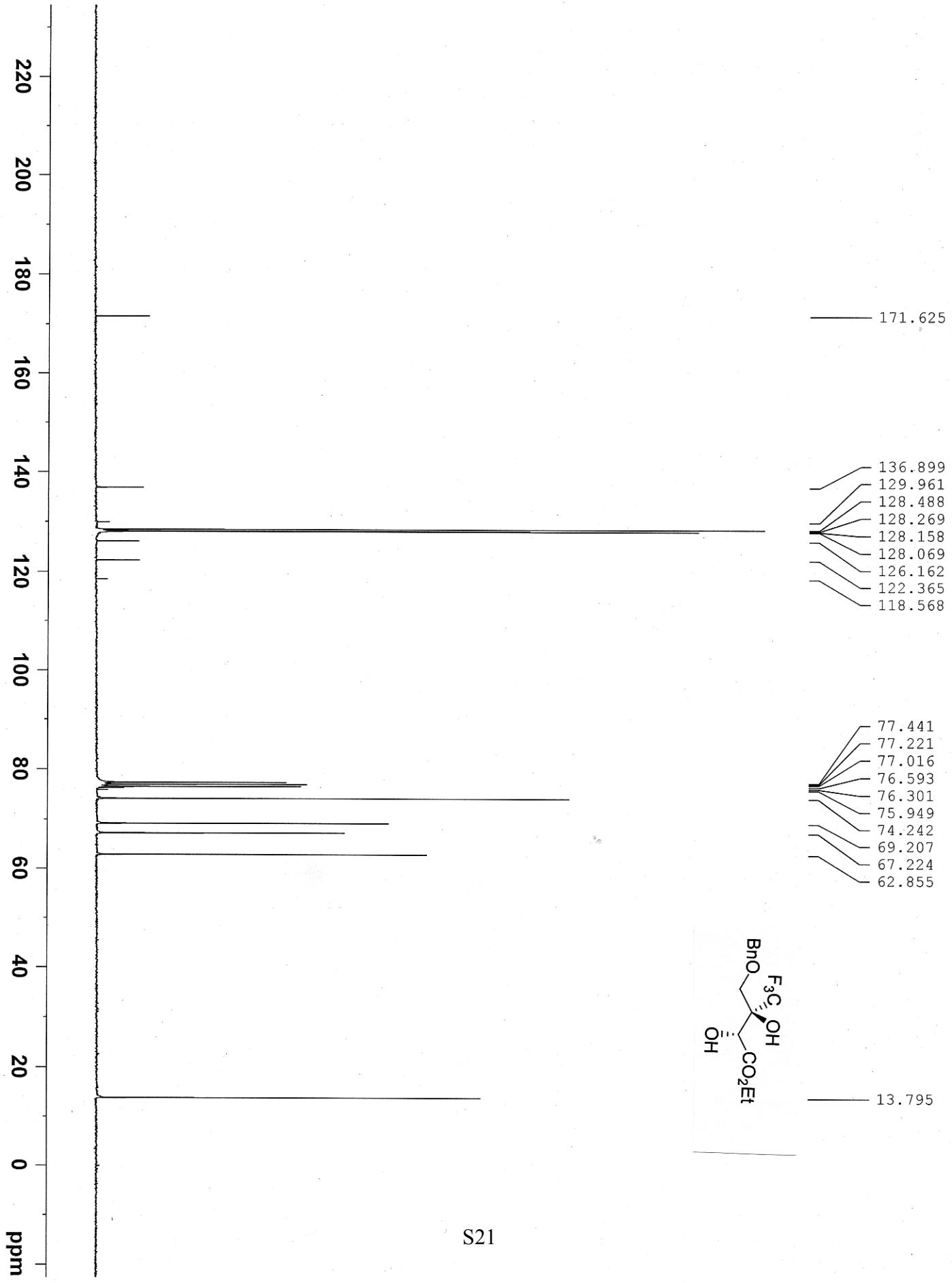


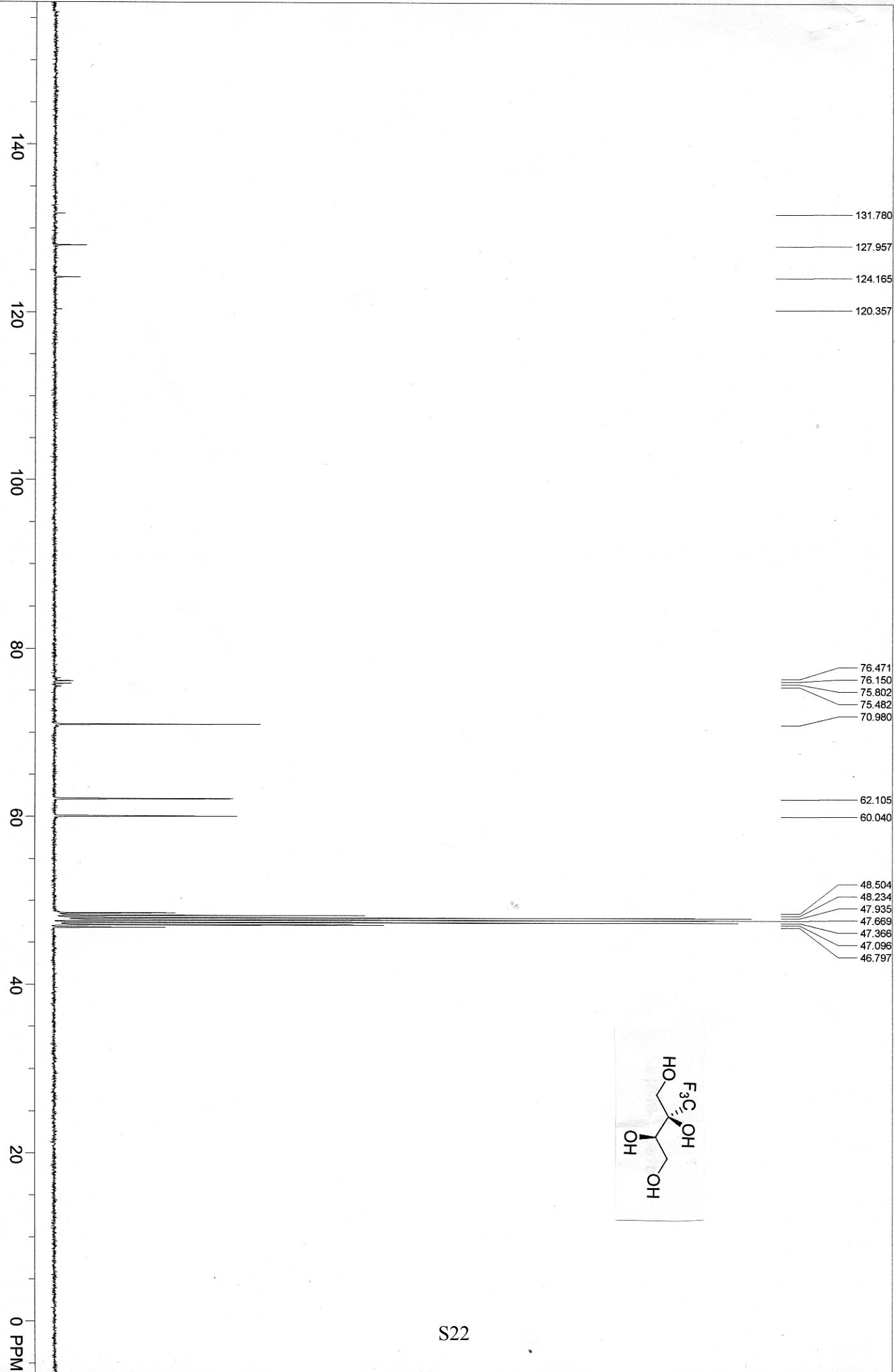


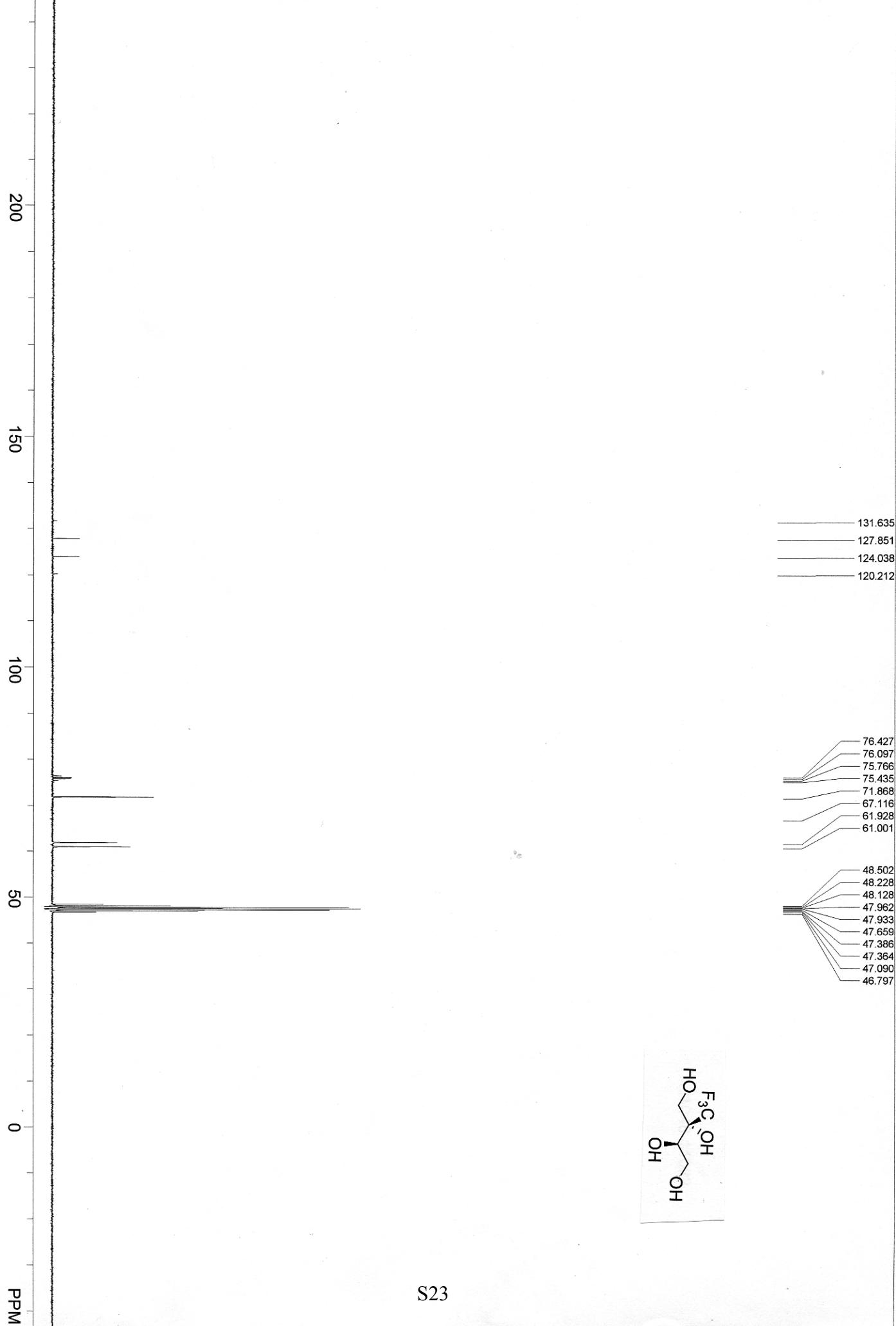


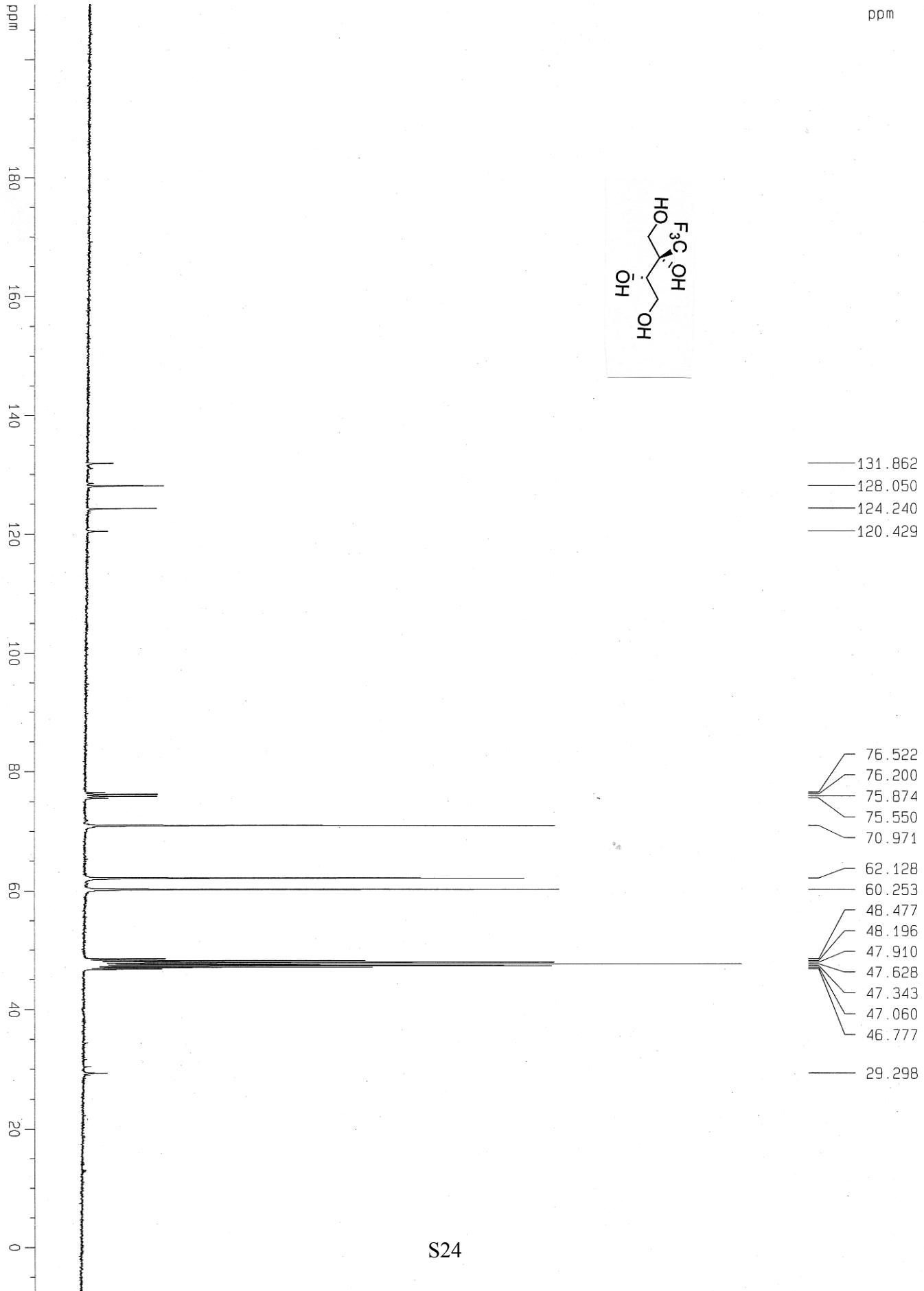


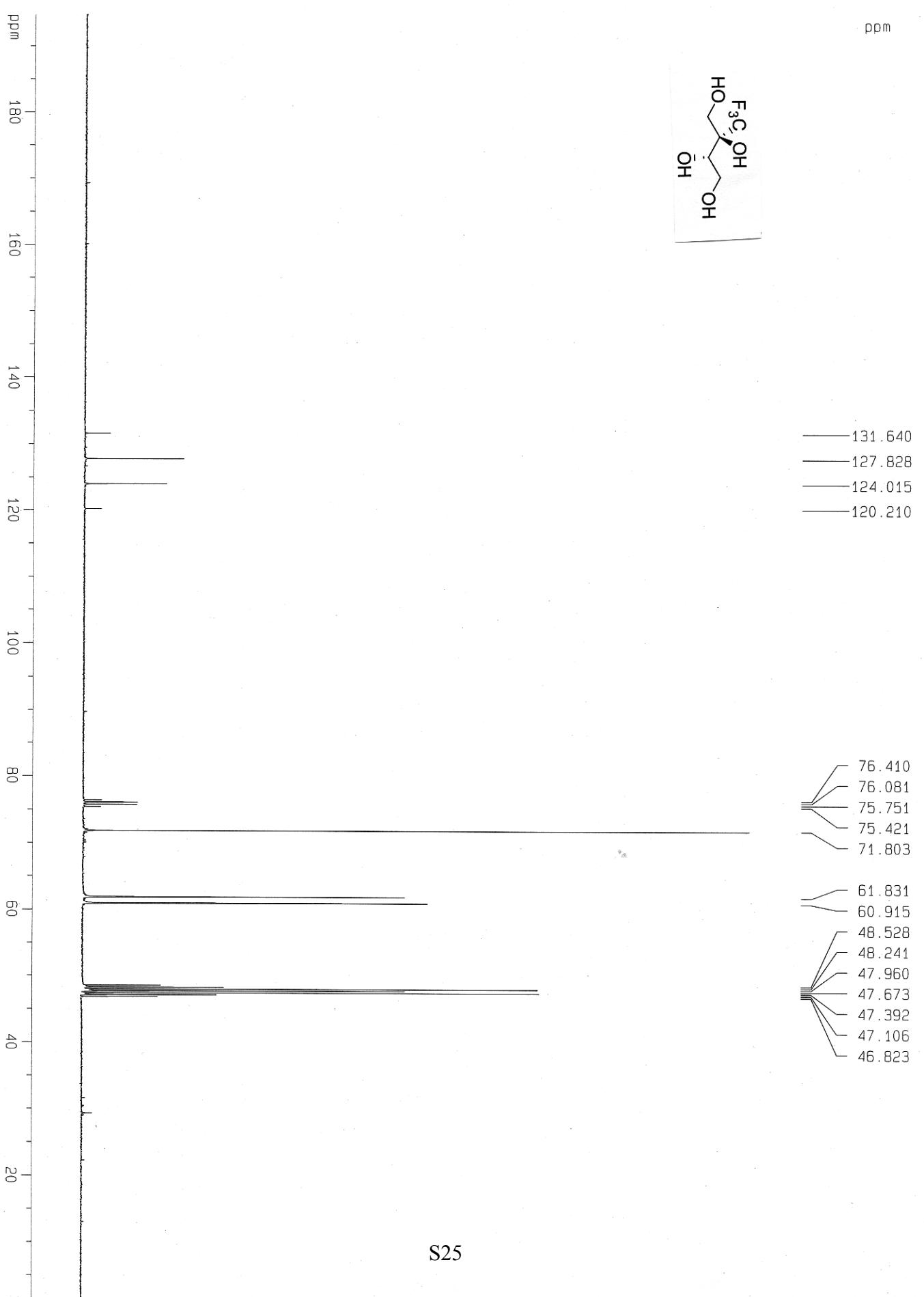


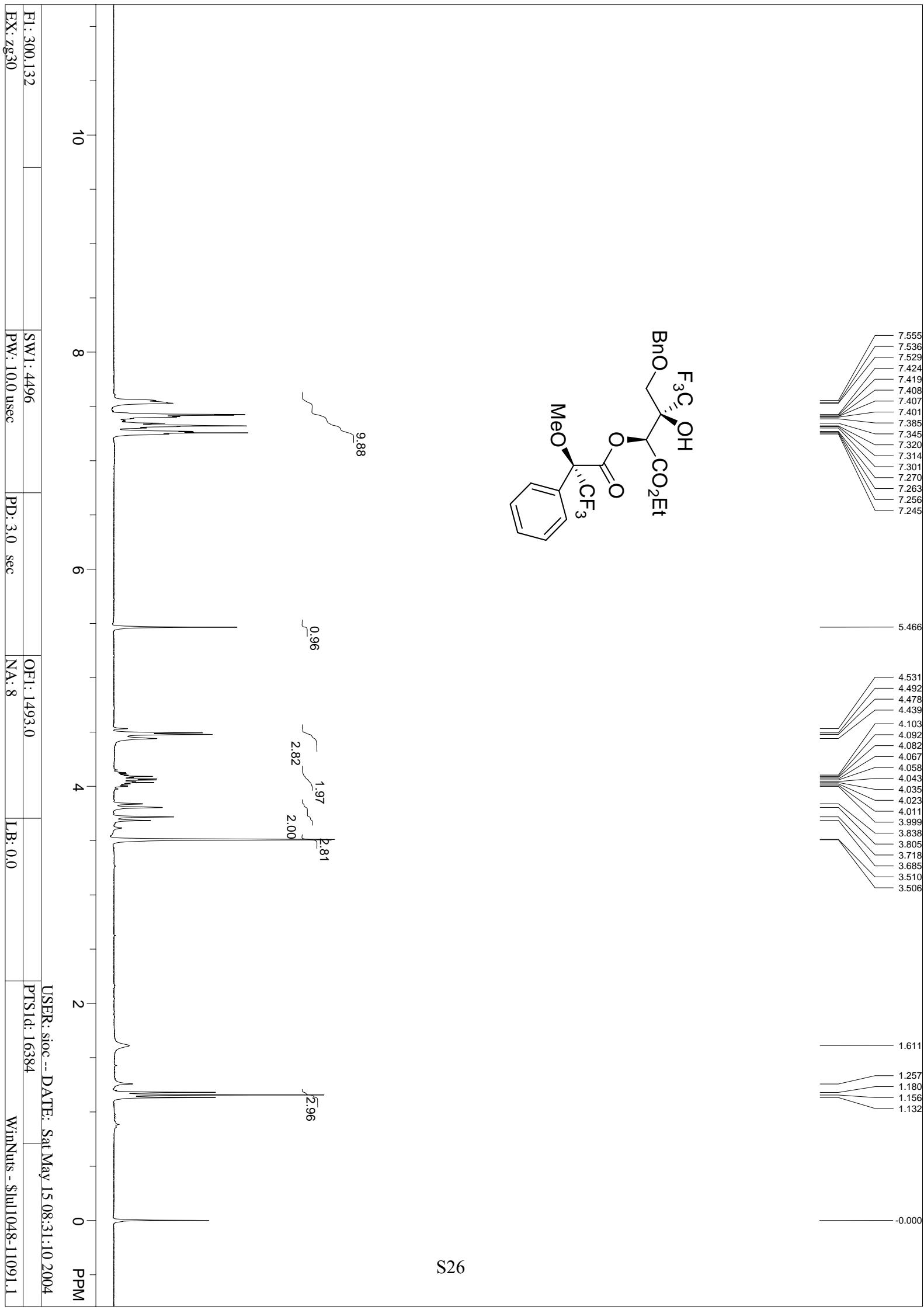












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