# Supporting Information

**Stereochemical modification of geminal dialkyl substituents on pantothenamides alters antimicrobial activity**

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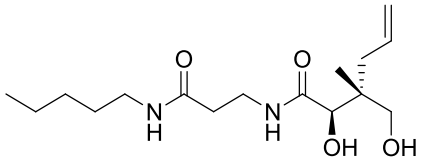
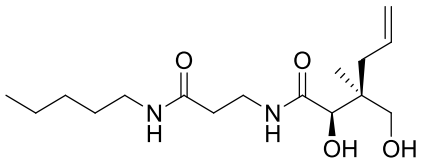
**General Methods**

All reagents were purchased from Sigma-Aldrich Canada Ltd. (Oakville, ON, Canada), Alfa Aesar (Ward Hill, MA, USA) Chem Impex (Wood Dale, IL, USA). Reagents were used without further purification unless otherwise stated. Dry solvents were obtained from an Innovative Tech Pure Solve MD-7 solvent purification system. Anhydrous chemical reactions were performed under nitrogen or argon using standard dry techniques for experimental setup. TLC analysis (F-254) was performed with 60 Å silica-coated plates from Silicycle (Quebec, QC, Canada). Flash chromatography of compounds was performed using a CombiFlash Rf system (Gold columns) from Teledyne Isco (Lincoln, NE, USA) or a Biotage Isolera Spektra One (BioZip columns) system from Biotage (Charlotte, NC, USA). $^{1}$H and $^{13}$C NMR spectra were measured on either of Varian 300, 400 or 500 MHz instruments with the signal of residual protons in the solvent as internal standard. The chemical shifts (δ) are reported in parts per million (ppm). The following abbreviations are used to describe NMR coupling patterns: bs, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublet; dt, doublet of triplet; tt, triplet of triplet; qd, quartet of doublet. The coupling constants, *J*, are reported in Hertz (Hz). HRMS spectra were acquired at the McGill University Mass Spectral Facility by ESI on an EXACTIVE instrument in orbitrap mode.

**Chemistry**

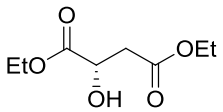



**(2*R*,3*R*)-2-Hydroxy-3-(hydroxymethyl)-3-methyl-N-(3-oxo-3-(pentylamino)propyl)hex-5-enamide (1).** This known diastereomer was synthesized according to a previously described protocol.[1]




**(2*R*,3*S*)-2-Hydroxy-3-(hydroxymethyl)-3-methyl-*N*-(3-oxo-3-(pentylamino)propyl)hex-5-enamide (2).** Compound **12** (14 mg, 32 μmol) was deprotected by stirring in acetic acid (90% aq.) for 4 h. Following freezing and lyophilization, the final product was purified by silica gel

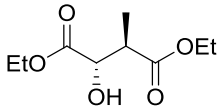
chromatography as a clear oily residue. Yield: 5.7 mg, 57%. $R_f$ = 0.24 (10% MeOH/DCM). $t_R$ = 21.6 min (Method A), 7.7 min (Method B). $^1$H NMR (500 MHz, $CDCl_3$) δ 7.51 (bs, 1H), 6.04 (bs, 1H), 5.16–5.04 (m, 2H), 4.11 (bs, 1H), 4.08 (s, 1H), 3.69 (s, 1H), 3.61–3.48 (m, 3H), 3.43 (d, *J* = 11.5, 1H), 3.20 (dd, *J* = 13.1, 7.1, 2H), 2.42 (t, *J* = 6.0, 2H), 2.33 (dd, *J* = 13.7, 7.7, 1H), 2.15 (dd, *J* = 13.6, 7.4, 1H), 1.99 (s, 1H), 1.53–1.43 (m, 2H), 1.36–1.20 (m, 5H), 0.88 (t, *J* = 6.9, 3H), 0.84 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$) δ 173.6, 171.3, 134.5, 118.2, 76.5, 68.2, 42.4, 39.7, 39.3, 35.7, 35.3, 29.1, 29.0, 22.3, 17.2, 13.9; HRMS for $C_{16}H_{30}N_2O_4$ $[M+Na]^+$ calcd. 337.2104, found 337.2085.



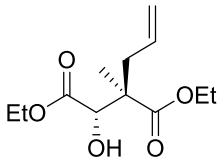

**(*S*)-Diethyl 2-hydroxysuccinate (3).** L-(-)-Malic acid (12 g, 89.5 mmol) was dissolved in anhydrous ethanol (50 ml). Thionyl chloride (3.3 ml, 44.8 mmol) was added and the reaction was stirred at room temperature for 16 h. The reaction mixture was diluted in diethyl ether (200 ml) and washed with saturated sodium bicarbonate (2 × 80 ml) and brine (1 × 80 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated to yield the crude product, which was purified by silica gel chromatography to afford the product as a clear liquid. Yield: 12.1 g, 71%. $R_f$ = 0.41 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.44 (dd, *J* = 10.1, 5.0, 1H), 4.21 (q, *J* = 7.2, 2H), 4.12 (q, *J* = 7.1, 2H), 3.36 (d, *J* = 5.1, 1H), 2.85–2.68 (m, 2H), 1.23 (dt, *J* = 10.3, 7.1, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.3, 170.5, 67.3, 61.9, 60.9, 38.7, 14.0. HRMS for $C_8H_{14}O_5$ $[M+Na]^+$ calcd. 213.0739, found 213.0731.

**General alkylation protocol[1] (used to generate compounds 4, 5a-f).** THF (40 ml per 5 mmol sample) was added to an oven-dried flask purged with nitrogen, and cooled to 0°C. To form the lithium diisopropylamine (LDA) reagent, diisopropylamine (DIPA, 2.4 eq) and butyl lithium (BuLi, 2.2 eq) were added to the reaction flask and stirred for 15 min in an ice bath. The reaction mixture was cooled to -78°C prior to the addition of compound **3** (1 eq), or its monoalkylated derivative **4** (1eq), dissolved in THF (4 ml). The reaction was allowed to warm to -40°C over 1 h, and re-cooled to -78°C before addition of the alkyl halide (2.7 eq). The mixture was stirred for 16 h and allowed to warm to room temperature, after which it was cooled to -78°C and quenched with saturated ammonium chloride (15 ml). The product was extracted in ethyl acetate (3 × 30

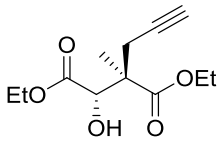
ml), and the combined organic layers were washed with brine and dried over anhydrous sodium sulfate. The desired product was purified by flash chromatography.



**(2*S*,3*R*)-Diethyl 2-hydroxy-3-methylsuccinate (4).** The previously established general alkylation protocol[1] was used to synthesize the novel diastereomer (**4**) from L-malic ester (**3**) (3.1 g, 16 mmol) as a yellow oily liquid. Yield: 2.4 g, 73%. $R_f$ = 0.47 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.23–3.99 (m, 5H), 3.27 (bs, 1H), 2.92 (qd, $J$ = 7.2, 3.7, 1H), 1.25–1.11 (m, 9H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.1, 172.7, 72.3, 61.7, 60.7, 43.1, 14.0, 13.9, 12.7; HRMS for $C_9H_{16}O_5$ $[M+Na]^+$ calcd. 227.0896, found 227.0885.

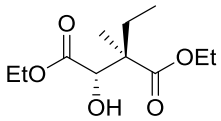


**(2*R*,3*S*)-Diethyl 2-allyl-3-hydroxy-2-methylsuccinate (5a).** Prepared from **4** (1.1 g, 5.4 mmol) and allyl bromide (1.2 ml, 15 mmol) using the general alkylation protocol. The product was obtained as a yellow oily liquid. Yield: 0.77 g, 58%. $R_f$ = 0.58 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 5.83–5.67 (m, 1H), 5.16–5.05 (m, 2H), 4.30–4.08 (m, 5H), 3.37 (d, $J$ = 7.7, 1H), 2.53 (dd, $J$ = 13.7, 7.0, 1H), 2.33 (dd, $J$ = 13.7, 7.8, 1H), 1.30 (t, $J$ = 7.2, 3H), 1.27 (t, $J$ = 7.2, 3H), 1.18 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.20, 172.7, 133.0, 118.8, 75.2, 61.7, 60.9, 49.8, 39.4, 17.8, 14.1, 14.1; HRMS for $C_{12}H_{20}O_5$ $[M+Na]^+$ calcd. 267.1209, found 267.1199.

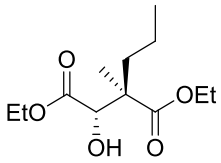


**(2*R*,3*S*)-Diethyl 3-hydroxy-2-methyl-2-(prop-2-yn-1-yl)succinate (5b).** Prepared from **4** (1.6 g, 7.8 mmol) and propargyl bromide (1.36 ml (80% solution in toluene), 12.2 mmol) using the general alkylation protocol. The product was obtained as an orange/red oily liquid. Yield: 0.57 g, 30%. $R_f$ = 0.68 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.16 (s, 1H), 4.14–3.95

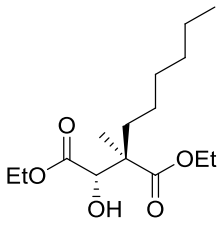
(m, 4H), 3.34 (bs, 1H), 2.46 (d, $J$ = 2.6, 2H), 1.93 (t, $J$ = 2.6, 1H), 1.21 (s, 3H), 1.16 (t, $J$ = 7.1, 3H), 1.11 (t, $J$ = 7.1, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.1, 172.4, 79.9, 74.2, 71.1, 61.8, 61.1, 49.5, 24.8, 18.5, 13.9, 13.8; HRMS for $C_{12}H_{18}O_5$ $[M+H]^+$ calcd. 243.1232, found 243.1221.



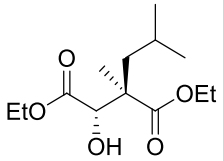

**(2*R*,3*S*)-Diethyl 2-ethyl-3-hydroxy-2-methylsuccinate (5c).** Prepared from **4** (1.0 g, 5.1 mmol) and ethyl iodide (1.1 ml, 14 mmol) using the general alkylation protocol. The product was obtained as a yellow oily liquid. Yield: 0.89 g, 75%. $R_f$ = 0.28 (50% $Et_2O$/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.26–4.13 (m, 5H), 3.38 (d, $J$ = 8.0, 1H), 1.90–1.72 (m, 1H), 1.67–1.50 (m, 1H), 1.28 (t, $J$ = 7.1, 3H), 1.26 (t, $J$ = 7.1, 3H), 1.12 (s, 3H), 0.86 (t, $J$ = 7.5 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 174.7, 172.9, 75.6, 61.7, 60.9, 50.4, 28.2, 16.7, 14.1, 14.1, 8.7; HRMS for $C_{11}H_{20}O_5$ $[M+Na]^+$ calcd. 255.1209, found 255.1211.




**(2*R*,3*S*)-Diethyl 3-hydroxy-2-methyl-2-propylsuccinate (5d).** Prepared from **4** (1.4 g, 7.0 mmol) and 1-iodopropane (1.2 ml, 19 mmol) using the general alkylation protocol. The product was obtained as a yellow oily liquid. Yield: 1.0 g, 60%. $R_f$ = 0.59 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.26–4.06 (m, 5H), 3.40 (d, $J$ = 7.8, 1H), 1.78–1.62 (m, 1H), 1.52–1.40 (m, 1H), 1.37–1.12 (m, 8H), 1.10 (s, 3H), 0.86 (t, $J$ = 7.2, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 174.9, 172.8, 75.8, 61.7, 60.9, 50.0, 37.7, 17.6, 17.3, 14.5, 14.1, 14.1; HRMS for $C_{12}H_{22}O_5$ $[M+Na]^+$ calcd. 269.1365, found 269.1363.

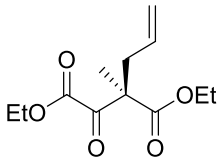


**(2*R*,3*S*)-Diethyl 2-hexyl-3-hydroxy-2-methylsuccinate (5e).** Prepared from **4** (2.0 g, 10 mmol) and 1-iodohexane (4.0 ml, 27 mmol) using the general alkylation protocol. The product was obtained as a yellow oily liquid. Yield: 1.1 g, 38%. $R_f$ = 0.68 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.30–4.09 (m, 5H), 3.38 (d, *J* = 7.9, 1H), 1.82–1.67 (m, 1H), 1.59–1.43 (m, 1H), 1.32–1.20 (m, 14H), 1.13 (s, 3H), 0.85 (t, *J* = 6.6, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 174.8, 172.8, 75.7, 61.6, 60.8, 50.0, 35.4, 31.6, 29.7, 24.1, 22.5, 17.2, 14.1, 14.1, 14.0; HRMS for $C_{15}H_{28}O_5$ $[M+Na]^+$ calcd. 311.1835, found 311.1815.

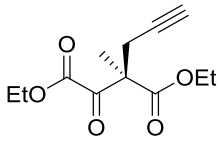



**(2*R*,3*S*)-Diethyl 3-hydroxy-2-isobutyl-2-methylsuccinate (5f).** Prepared from **4** (0.71 g, 2.8 mmol) and 2-methyl-1-iodopropane (0.87 ml, 7.6 mmol) using the general alkylation protocol. The product was obtained as a yellow oil. Yield: 0.73 g, 81%. $R_f$ = 0.68 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.30–4.08 (m, 5H), 3.41 (d, *J* = 8.4, 1H), 1.79 (dd, *J* = 13.7, 7.0, 1H), 1.74–1.57 (m, 1H), 1.47 (dd, *J* = 13.7, 5.0, 1H), 1.27 (t, *J* = 7.1, 3H), 1.26 (t, *J* = 7.1, 3H), 1.13 (s, 3H), 0.90 (d, *J* = 6.6, 3H), 0.82 (d, *J* = 6.5, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 175.0, 172.5, 76.5, 61.5, 60.8, 49.7, 43.8, 24.7, 24.5, 23.0, 16.8, 14.0, 13.9; HRMS for $C_{13}H_{24}O_5$ $[M+Na]^+$ calcd. 283.1522, found 283.1509.

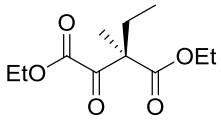
**General protocol for Swern oxidation (used to generate compounds 6a-f).** DCM was cooled to -78°C in an oven-dried flask purged with nitrogen. Oxalyl chloride (2.0 M in DCM, 2 eq) and dimethylsulfoxide (DMSO, 4 eq) were added, and the resulting gases were vented. The reaction was stirred for 30 min before adding a solution of the alcohol in DCM (1 eq in 5 ml) and reacting for 1 h at -78°C. Triethylamine (6 eq) was added and the reaction was stirred for 16 h while warming to room temperature. Upon reaction completion, the mixture was washed with dilute hydrochloric acid (20 ml, 10% aq) followed by saturated sodium bicarbonate (30 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated to yield the crude ketone. The product was purified by silica gel chromatography.



**(*R*)-Diethyl 2-allyl-2-methyl-3-oxosuccinate (6a).** Prepared from **5a** (0.61 g, 2.5 mmol) using the general Swern oxidation protocol described above. The product was obtained as a light yellow oil. Yield: 0.51 g, 84%. $R_f$ = 0.39 (10% EtOAc/hexanes). $^1$H NMR (500 MHz, $CDCl_3$) δ 5.61–5.50 (m, 1H), 5.04–4.95 (m, 2H), 4.23 (q, *J* = 7.1, 2H), 4.09 (q, *J* = 7.2, 2H), 2.64–2.53 (m, 2H), 1.34 (s, 3H), 1.27 (t, *J* = 7.1, 3H), 1.14 (t, *J* = 7.1, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 191.1, 171.3, 160.1, 131.7, 119.3, 62.5, 61.3, 56.1, 39.3, 19.2, 13.9, 13.8; HRMS for $C_{12}H_{18}O_5$ $[M+Na]^+$ calcd. 265.1056, found 265.1054.

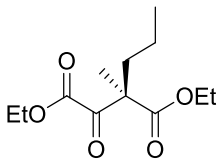


**(*R*)-Diethyl 2-methyl-3-oxo-2-(prop-2-yn-1-yl)succinate (6b).** Prepared from **5b** (0.55 g, 2.3 mmol) using the general Swern oxidation protocol described above. The product was obtained as an orange oil. Yield: 0.34 g, 62%. $R_f$ = 0.24 (10% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.26 (q, *J* = 7.1, 2H), 4.13 (q, *J* = 7.1, 2H), 2.96–2.87 (m, 1H), 2.75–2.66 (m, 1H), 2.00 (t, *J* = 2.7, 1H), 1.47 (s, 3H), 1.29 (t, *J* = 7.1, 3H), 1.16 (t, *J* = 7.1, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 189.2, 170.4, 159.5, 78.1, 72.4, 62.7, 61.8, 55.5, 25.0, 19.1, 13.8, 13.8; HRMS for $C_{12}H_{16}O_5$ $[M+Na]^+$ calcd. 241.1076, found 241.1063.

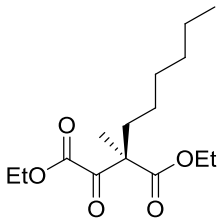


**(*R*)-Diethyl 2-ethyl-2-methyl-3-oxosuccinate (6c).** Prepared from **5c** (1.9 g, 8.2 mmol) using the general Swern oxidation protocol described above. The product was obtained as a yellow oil. Yield: 1.58 g, 84%. $R_f$ = 0.54 (25% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.18 (q, *J* = 7.1 Hz, 1H), 4.05 (q, *J* = 7.1 Hz, 1H), 1.83 (q, *J* = 7.6 Hz, 2H), 1.29 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.10 (t, *J* = 7.1 Hz, 3H), 0.71 (t, *J* = 7.6 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 191.8,

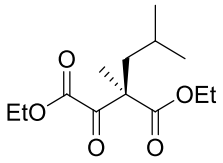
171.7, 160.3, 62.3, 61.1, 56.5, 27.8, 18.8, 13.8, 13.8, 8.2; HRMS for $C_{11}H_{18}O_5$ $[M+Na]^+$ calcd. 253.1052, found 253.1052.




**(*R*)-Diethyl 2-methyl-3-oxo-2-propylsuccinate (6d).** Prepared from **5d** (1.5 g, 6.1 mmol) using the general Swern oxidation protocol described above. The product was obtained as a yellow oil. Yield: 1.3 g, 88%. $R_f$ = 0.37 (10% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.28 (q, $J$ = 7.1, 2H), 4.15 (q, $J$ = 7.1, 2H), 1.86 (t, $J$ = 9.0, 2H), 1.41 (s, 3H), 1.33 (t, $J$ = 7.1, 3H), 1.20 (t, $J$ = 7.1, 3H), 1.28–1.06 (m, 2H), 0.89 (t, $J$ = 7.2, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 192.0, 172.0, 160.4, 62.4, 61.3, 56.4, 37.1, 19.5, 17.3, 14.3, 13.9, 13.9; HRMS for $C_{12}H_{20}O_5$ $[M+Na]^+$ calcd. 267.1209, found 267.1202.

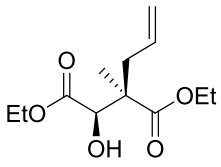



**(*R*)-Diethyl 2-hexyl-2-methyl-3-oxosuccinate (6e).** Prepared from **5e** (0.56 g, 1.9 mmol) using the general Swern oxidation protocol described above. The product was obtained as a yellow oil. Yield: 0.41 g, 74%. $R_f$ = 0.47 (25% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.19 (q, $J$ = 7.1, 2H), 4.06 (q, $J$ = 7.1, 2H), 1.78 (t, $J$ = 9.0, 2H), 1.31 (s, 3H), 1.24 (t, $J$ = 7.1, 3H), 1.11 (t, $J$ = 7.1, 3H), 1.20–0.93 (m, 8H), 0.74 (t, $J$ = 6.5, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 191.8, 171.8, 160.4, 62.3, 61.1, 56.2, 34.8, 31.3, 29.3, 23.7, 22.3, 19.3, 13.8, 13.8, 13.8; HRMS for $C_{15}H_{26}O_5$ $[M+Na]^+$ calcd. 309.1678, found 309.1662.



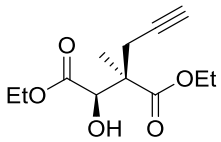
**(*R*)-Diethyl 2-isobutyl-2-methyl-3-oxosuccinate (6f).** Prepared from **5f** (0.56 g, 2.2 mmol) using the general Swern oxidation protocol described above. The product was obtained as a yellow oil. Yield: 0.45 g, 81%. $R_f$ = 0.48 (25% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.22 (q, *J* = 7.1, 2H), 4.07 (q, *J* = 7.1, 2H), 1.85 (dd, *J* = 14.4, 6.2, 1H), 1.77 (dd, *J* = 14.4, 6.2, 1H), 1.59–1.44 (m, 1H), 1.36 (s, 3H), 1.26 (t, *J* = 7.1, 3H), 1.13 (t, *J* = 7.1, 3H), 0.79 (d, *J* = 6.6, 3H), 0.74 (d, *J* = 6.6, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 192.3, 172.1, 160.5, 62.3, 61.2, 56.1, 43.5, 24.1, 23.9, 23.9, 20.2, 13.8, 13.8; HRMS for $C_{13}H_{22}O_5$ $[M+H]^+$ calcd. 259.1545, found 259.1532.

**General protocol for the enantioselective reduction using Baker's Yeast (used to generate compounds 7a-f).** Compounds **7a-f** were synthesized from compounds **6a-f** by reduction with Baker's yeast. Distilled water (60 ml) was added to a 1 L Erlenmeyer flask, followed by Baker's yeast (20 g) and methyl vinyl ketone (290 µl). The mixture was stirred at 50°C for 30 min, upon which the ketone (250 mg) was added and allowed to react for a full 24 h at 30°C with gentle stirring. To work up the Baker's yeast reaction, ethyl acetate (400 ml) and HyFlo Celite (50 g) were added, and the mixture was stirred for 30 min at room temperature. The mixture was filtered through and additional layer of HyFlo Celite (1 cm thickness) using a Buchner funnel. During this process, the surface of the Celite layer was gently scratched with a spatula to prevent clogging. The filtrate was collected and the layers were separated. The aqueous layer was washed with ethyl acetate (2 × 50 ml) and the combined organic layers were washed with brine (100 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The product was purified twice using silica gel chromatography: 10% EtOAc/hexanes followed by 10% EtOAc/DCM.

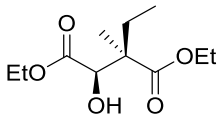



**(2*R*,3*R*)-Diethyl 2-allyl-3-hydroxy-2-methylsuccinate (7a).** Prepared from **6a** (1.3 g, 5.4 mmol) using the Baker's yeast reduction protocol described above. The product was obtained as a yellow oily liquid. Yield: 0.89 g, 68%. First purification $R_f$ = 0.11 (10% EtOAc/hexanes), and second purification $R_f$ = 0.61 (5% EtOAc/DCM). $t_R$ = 26.3 min (Method A), 13.3 min (Method

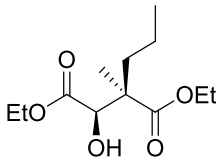
B). $^1$H NMR (300 MHz, $CDCl_3$) δ 5.74–5.56 (m, 1H), 5.10–4.98 (m, 2H), 4.40 (s, 1H), 4.28–3.99 (m, 4H), 3.16 (bs, 1H), 2.50 (dd, $J$ = 13.7, 7.1, 1H), 2.34 (dd, $J$ = 13.7, 7.7, 1H), 1.22 (t, $J$ = 7.1, 3H), 1.21 (t, $J$ = 7.1, 3H), 1.00 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 173.8, 173.2, 133.1, 118.6, 74.5, 62.0, 60.6, 50.3, 40.8, 15.1, 14.1, 14.0; HRMS for $C_{12}H_{20}O_5$ $[M+Na]^+$ calcd. 267.1209, found 267.1212.



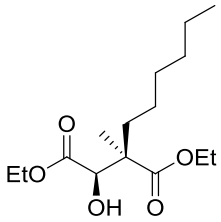

**(2*R*,3*R*)-Diethyl 3-hydroxy-2-methyl-2-(prop-2-yn-1-yl)succinate (7b).** Prepared from **6b** (0.34 g, 1.4 mmol) using the Baker's yeast reduction protocol described above. The product was obtained as a yellow oil. Yield: 0.22 g, 65%. First purification $R_f$ = 0.16 (10% EtOAc/hexanes), and second purification $R_f$ = 0.67 (5% EtOAc/DCM). $t_R$ = 24.6 min (Method A), 11.0 min (Method B). $^1$H NMR (500 MHz, $CDCl_3$) δ 4.43 (s, 1H), 4.29–4.15 (m, 4H), 3.15 (bs, 1H), 2.72–2.56 (m, 2H), 2.01 (t, $J$ = 2.7, 1H), 1.28 (t, $J$ = 7.2, 3H), 1.28 (t, $J$ = 7.2, 3H), 1.23 (s, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 173.0, 172.8, 79.9, 73.9, 71.1, 62.3, 61.1, 49.9, 26.2, 16.0, 14.1, 14.0; HRMS for $C_{12}H_{18}O_5$ $[M+H]^+$ calcd. 243.1232, found 243.1220.



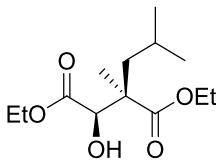

**(2*R*,3*R*)-Diethyl 2-ethyl-3-hydroxy-2-methylsuccinate (7c).** Prepared from **6c** (1.0 g, 4.5 mmol) using the Baker's yeast reduction protocol described above. The product was obtained as a yellow oil. Yield: 0.39 g, 37%. First purification $R_f$ = 0.10 (10% EtOAc/hexanes), and second purification $R_f$ = 0.44 (10% EtOAc/DCM). $t_R$ = 25.3 min (Method A), 12.1 min (Method B). $^1$H NMR (500 MHz, $CDCl_3$) δ 4.44 (s, 1H), 4.28–4.08 (m, 4H), 3.06 (bs, 1H), 1.88–1.76 (m, 1H), 1.72–1.63 (m, 1H), 1.27 (t, $J$ = 7.1, 3H), 1.25 (t, $J$ = 7.1, 3H), 1.02 (s, 3H), 0.85 (t, $J$ = 7.5, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.3, 173.6, 74.7, 62.1, 60.5, 50.6, 29.4, 14.6, 14.1, 14.0, 8.7; HRMS for $C_{11}H_{20}O_5$ $[M+H]^+$ calcd. 233.1389, found 233.1384.



**(2*R*,3*R*)-Diethyl 3-hydroxy-2-methyl-2-propylsuccinate (7d).** Prepared from **6d** (1.1 g, 4.6 mmol) using the Baker's yeast reduction protocol described above. The product was obtained as a yellow oil. Yield: 0.35 g, 31%. First purification $R_f$ = 0.12 (10% EtOAc/hexanes), and second purification $R_f$ = 0.35 (10% EtOAc/DCM). $t_R$ = 27.5 min (Method A), 14.7 min (Method B). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.42 (s, 1H), 4.27–4.08 (m, 4H), 3.03 (bs, 1H), 1.77 – 1.53 (m, 2H), 1.39–1.04 (m, 2H), 1.24 (t, *J* = 7.1, 3H), 1.23 (t, *J* = 7.1, 3H), 1.01 (s, 3H), 0.87 (t, *J* = 7.2, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 174.4, 173.5, 74.9, 62.0, 60.5, 50.3, 38.8, 17.6, 15.1, 14.5, 14.1, 14.0; HRMS for $C_{12}H_{22}O_5$ $[M+Na]^+$ calcd. 269.1365, found 269.1353.

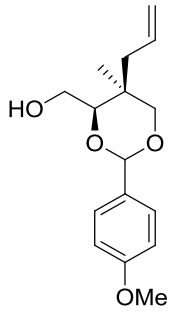


**(2*R*,3*R*)-Diethyl 2-hexyl-3-hydroxy-2-methylsuccinate (7e).** Prepared from **6e** (0.25 g, 0.9 mmol) using the Baker's yeast reduction protocol described above. The product was obtained as a yellow oil. Yield: 52 mg, 21%. First purification $R_f$ = 0.11 (10% EtOAc/hexanes), and second purification $R_f$ = 0.26 (10% EtOAc/DCM). $t_R$ = 24.5 min (Method B), 12.1 min (Method C). $^1$H NMR (500 MHz, $CDCl_3$) δ 4.44 (s, 1H), 4.28–4.11 (m, 4H), 3.04 (bs, 1H), 1.80–1.72 (m, 1H), 1.67–1.59 (m, 1H), 1.32–1.21 (m, 14H), 1.04 (s, 3H), 0.87 (t, *J* = 6.9, 3H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 174.4, 173.6, 74.9, 62.1, 60.5, 50.3, 36.5, 31.6, 29.6, 24.1, 22.5, 15.1, 14.1, 14.0; HRMS for $C_{15}H_{28}O_5$ $[M+H]^+$ calcd. 289.2015, found 289.2001.



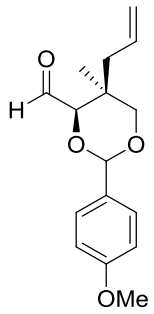
**(2*R*,3*R*)-Diethyl 3-hydroxy-2-isobutyl-2-methylsuccinate (7f).** Prepared from **6f** (0.25 g, 1.0 mmol) using the Baker's yeast reduction protocol described above. The product was obtained as

a yellow oil. Yield: 66 mg, 26%. First purification $R_f$ = 0.10 (10% EtOAc/hexanes), and second purification $R_f$ = 0.29 (10% EtOAc/DCM). $t_R$ = 29.4 min (Method A), 17.4 min (Method B). $^1$H NMR (300 MHz, $CDCl_3$) δ 4.36 (s, 1H), 4.31–4.07 (m, 4H), 3.05 (bs, 1H), 1.79–1.56 (m, 3H), 1.28 (t, *J* = 7.1, 3H), 1.26 (t, *J* = 7.1, 3H), 1.05 (s, 3H), 0.91 (d, *J* = 6.4, 3H), 0.83 (d, *J* = 6.4, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 174.8, 173.5, 75.5, 62.2, 60.5, 50.2, 44.6, 25.0, 24.5, 23.0, 14.9, 14.0; HRMS for $C_{13}H_{24}O_5$ $[M+H]^+$ calcd. 261.1697, found 261.1694.

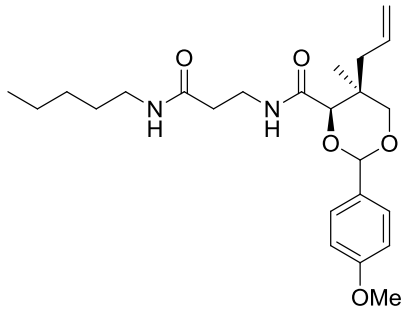



**((4*R*,5*S*)-5-Allyl-2-(4-methoxyphenyl)-5-methyl-1,3-dioxan-4-yl)methanol (8).** Compound **7a** was reduced and protected according to a previously described protocol.[1] THF (6 ml) was added to an oven-dried flask purged with nitrogen, and cooled to 0°C. Lithium aluminum hydride (2 M in THF, 8.2 mmol) was added to the flask, followed by **7a** (0.67 g, 2.8 mmol) dissolved in THF (4 ml). The reaction was stirred at 0°C for 15 min, and was subsequently refluxed at 50°C for 16 h. The remaining $LiAlH_4$ was quenched with saturated ammonium chloride (8 ml) and the product was extracted in ethyl acetate (3 × 30 ml). The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure to yield the crude triol, which was directly protected as a 1,3-para-methoxy phenyl (PMP) acetal. DCM (10 ml) was then added to the flask containing the crude triol. 4-Methoxy benzaldehyde dimethyl acetal (700 µl, 4.1 mmol) was added as well as a catalytic amount of camphor sulfonic acid (64 mg, 0.23 mmol). The reaction was stirred for 2 h at room temperature before quenching with triethylamine (77 µl, 0.55 mmol). The product was purified using silica gel chromatography as a yellow oil. Yield 520 mg, 68%. $R_f$ = 0.29 (30% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.6, 1H), 6.89 (d, *J* = 8.6, 1H), 5.92–5.72 (m, 1H), 5.43 (s, 1H), 5.18–5.06 (m, 2H), 3.89 (d, *J* = 11.4, 1H), 3.75 (s, 3H), 3.68–3.49 (m, 4H), 3.32 (d, *J* = 11.5, 1H), 2.75 (dd, *J* = 13.2, 7.8, 2H), 1.83 (dd, *J* = 13.4, 7.3, 1H), 0.72 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 160.1, 133.9, 130.9, 127.7, 118.5,

113.6, 102.1, 87.0, 74.3, 60.9, 55.2, 35.1, 34.4, 18.3; HRMS for $C_{16}H_{22}O_4$ $[M+H]^+$ calcd. 279.1596, found 279.1592.



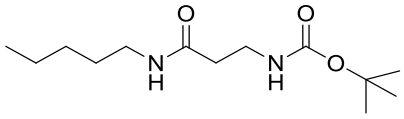

**(4*R*,5*S*)-5-Allyl-2-(4-methoxyphenyl)-5-methyl-1,3-dioxane-4-carbaldehyde (9).** Compound **8** (520 mg, 1.9 mmol) was dissolved in DCM (10 ml), and Dess-Martin periodinane (1.2 g, 2.8 mmol) was added to the mixture. The reaction was stirred at room temperature for 2 h. The mixture was washed using a solution of saturated sodium thiosulfate in saturated sodium bicarbonate (1:1 v/v, 5 ml), after which the organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The desired product was purified using silica gel chromatography as a yellow oil. Yield: 380 mg, 74%. $R_f$ = 0.36 (20% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.49 (d, $J$ = 8.7, 2H), 6.93 (d, $J$ = 8.7, 2H), 5.91–5.71 (m, 1H), 5.50 (s, 1H), 5.27–5.08 (m, 2H), 3.99-3.88 (m, 2H), 3.79 (s, 3H), 3.47 (d, $J$ = 11.6, 1H), 2.81 (dd, $J$ = 13.5, 7.4, 1H), 2.17 (dd, $J$ = 13.4, 7.7, 1H), 0.98 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 201.6, 160.3, 133.4, 130.2, 127.6, 119.3, 113.8, 101.7, 87.9, 74.7, 55.3, 37.3, 35.8, 17.7; HRMS for $C_{16}H_{20}O_4$ $[M+H]^+$ calcd. 277.1440, found 277.1436.




**(4*R*,5*S*)-5-Allyl-2-(4-methoxyphenyl)-5-methyl-*N*-(3-oxo-3-(pentylamino)propyl)-1,3-dioxane-4-carboxamide (11).** The aldehyde (**9**) was first oxidized to the corresponding acid (**10**) via a Pinnick oxidation. Thus, a mixture of sodium chlorite ($NaClO_2$, 100 mg, 1.1 mmol) and

sodium phosphate monobasic ($NaH_2PO_4$, 260 mg, 2.2 mmol) was dissolved in water (1.5 ml). The aldehyde (**9**) (60 mg, 0.22 mmol) was dissolved in acetone/DCM (6 ml, 3:1 v/v) and added to the aqueous solution together with the radical scavenger 2-methyl-2-butene (120 µl, 1.1 mmol). The reaction was stirred at room temperature for 1 h, upon which it was quenched with saturated sodium sulfite (2 ml). The product was extracted in ethyl acetate (2 × 10 ml). The organic layer was dried over anhydrous sodium sulfite and evaporated under reduced pressure to yield the crude acid intermediate (**11**), which was used directly in the following amide coupling.

Compound **12** (85 mg, 0.33 mmol) was deprotected by stirring in TFA/DCM (1 ml, 1:1 v/v) for 30 min. The reaction was concentrated under reduced pressure to afford the crude Boc-deprotected intermediate (**13**). The amine (**13**) was dissolved in THF (3 ml) with EDC (127 mg, 0.66 mmol) and HOBt (59 mg, 0.44 mmol). The acid (**10**) was dissolved in THF (2 ml) and added to the reaction mixture, followed by DIPEA (190 µl, 1.1 mmol). The reaction was stirred at room temperature for 16 h. Upon completion, saturated ammonium chloride (3 ml) was added and the product was extracted in ethyl acetate (2 × 10 ml). After drying the organic layer over anhydrous sodium sulfate and evaporating under reduced pressure, the product was purified by silica gel chromatography to afford a yellow oily residue. Yield: 43 mg, 45%. $R_f$ = 0.35 (80% EtOAc/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.7, 2H), 7.08 (bs, 1H), 6.91 (d, *J* = 8.8, 2H), 5.89 (bs, 1H), 5.84–5.66 (m, 1H), 5.47 (s, 1H), 5.15–5.06 (m, 2H), 4.12 (s, 1H), 3.93 (d, *J* = 11.7, 1H), 3.81 (s, 3H), 3.61–3.42 (m, 3H), 3.18 (dd, *J* = 13.3, 6.8, 2H), 2.67 (dd, *J* = 13.2, 7.9, 1H), 2.39 (t, *J* = 6.2, 2H), 1.91 (dd, *J* = 13.3, 6.9, 1H), 1.45 (dt, *J* = 14.4, 7.4, 2H), 1.35–1.17 (m, 4H), 1.04 (s, 3H), 0.87 (t, *J* = 6.8, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 170.6, 169.3, 160.2, 133.3, 130.0, 127.5, 118.9, 113.7, 101.5, 84.2, 74.2, 55.3, 39.6, 36.1, 35.9, 35.0, 35.0, 29.2, 29.0, 22.3, 18.7, 14.0; HRMS for $C_{24}H_{36}N_2O_5$ $[M+Na]^+$ calcd. 455.2522, found 455.2515.




**tert-Butyl (3-oxo-3-(pentylamino)propyl)carbamate (12).** Compound **12** was generated by dissolving Boc-β-alanine (500 mg, 2.6 mmol), EDC (660 mg, 3.4 mmol), and HOBt (570 mg, 4.2 mmol) in THF (15 ml) under nitrogen. Subsequently, pentylamine (370 µl, 3.2 mmol) and DIPEA (2.5 ml, 14.5 mmol) were added, and the reaction was stirred overnight at room

temperature. Upon completion, saturated ammonium chloride (10 ml) was added and the product was extracted in ethyl acetate (3 × 20 ml). The organic layer was dried over anhydrous sodium sulfate and evaporated under reduced pressure. The product was purified by silica gel chromatography as a white solid (MP = 58-60°C). Yield: 630 mg, 92%. $R_f$ = 0.54 (10% MeOH/DCM). $^1$H NMR (300 MHz, $CDCl_3$) δ 6.19 (bs, 1H), 5.30 (bs, 1H), 3.33 (dd, *J* = 12.2, 6.2, 2H), 3.16 (dd, *J* = 13.0, 7.1, 2H), 2.33 (t, *J* = 6.1, 2H), 1.52–1.31 (m, 11H), 1.29–1.18 (m, 4H), 0.83 (t, *J* = 6.8, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$) δ 171.3, 156.2, 79.2, 39.5, 36.7, 36.2, 29.2, 29.0, 28.3, 22.3, 13.9; HRMS for $C_{13}H_{26}N_2O_3$ $[M+Na]^+$ calcd. 281.1841, found 281.1840.

**Biological Evaluation**

**Antibacterial activity**

A pre-screening using the agar diffusion method was first completed with *Staphylococcus aureus* (ATCC 29213), *Acinetobacter baumannii* (ATCC 19606), *Pseudomonas aeruginosa* (ATCC 27853), *Klebsiella pneumoniae* (ATCC 13883), *Escherichia coli* 0157:H7 (ATCC 43895), *Escherichia coli* (ATCC 25922), *Bacillus subtilis* (ATCC 6051 and ATCC 6633), according to the National Committee of Clinical Laboratory Standards (NCCLS)[2] and previously described in detail.[1] Antibacterial activity of compound **2** was further evaluated against *S. aureus* (ATCC 29213, oxacillin susceptible), *S. aureus* (43300, oxacillin resistant) and *E. coli* (ATCC 25922) using the standard microdilution broth method in 96-well microtiter plates according to the Natural Committee for Clinical Laboratory Standards (NCCLS).[2] Bacteria were grown in trypticase soy media (BD, Mississauga, ON). A bacterial suspension of $10^6$ cfu/ml was aliquoted into each well, and incubated for 18 h at 37 °C in the presence of various concentrations of **2**. No bacterial growth inhibition could be detected at the maximal concentration tested, 512 μM. These results were replicated in four separate experiments. The published antibacterial activity of compound **1** was confirmed with the same method.[1]

**Antiplasmodial activity**

The chloroquine-sensitive 3D7 strain of *Plasmodium falciparum* was maintained *in vitro* as described previously with modifications.[3] The antiplasmodial activity of the compounds was determined using SYBR Safe DNA gel stain,[4] using conditions similar to those described by

Spry *et al.*[5] Experiments were initiated with parasites in the ring stage and with both the hematocrit and parasitemia set to 0.5%. Parasites were incubated in the presence of the compounds for 96 h. The 50% inhibitory concentrations ($IC_{50}$ values) of the test compounds were determined by fitting sigmoidal curves to the data using SigmaPlot (Systat Software).

**Mammalian cell toxicity**

The toxicity of the pantothenamides to mammalian cells *in vitro* (Figure S1) was assessed using human foreskin fibroblasts (HFF cells) and the same SYBR safe-based growth assay used to assess parasite proliferation (see above), with only minor modifications. HFF cells were maintained in Dulbecco's Modified Eagle Medium as described previously.[6] The experiment, however, was carried out in RPMI-1640 in order for the extracellular pantothenate concentration to be comparable between the antiplasmodial and mammalian cell toxicity assays. For this purpose, RPMI-1640 medium was supplemented with bovine calf serum (10 % v/v), penicillin (50 U/ml) streptomycin (50 μg/ml), amphotericin B (0.25 μg/mL), gentamycin (10 μg/mL) and L-glutamine (200 μM) and maintained at 37°C for 40 hours prior to initiating the experiment. The pantothenate concentration in bovine calf serum[7] is not expected to alter the RPMI-1640 pantothenate concentration appreciably. To initiate the experiment, the HFF cells were transferred to the supplemented RPMI-1640 and seeded in 96-well plates at a density of ~50,000 cells/mL. Cyclohexamide (a protein synthesis inhibitor) was included as a control to indicate complete inhibition of HFF cell growth. Plates were incubated at 37°C in a humidified 5% $CO_2$ incubator for 48 h. A sample of the supernatant (150 μL) was then carefully aspirated from each well and discarded. The plates were next stored at -20°C. After thawing, the SYBR safe lysis solution (150 μL) was added to each well and mixed via pipetting to ensure the HFF cells were detached from the plate and lysed. The plates were then processed as described for the antiplasmodial assay.[4]

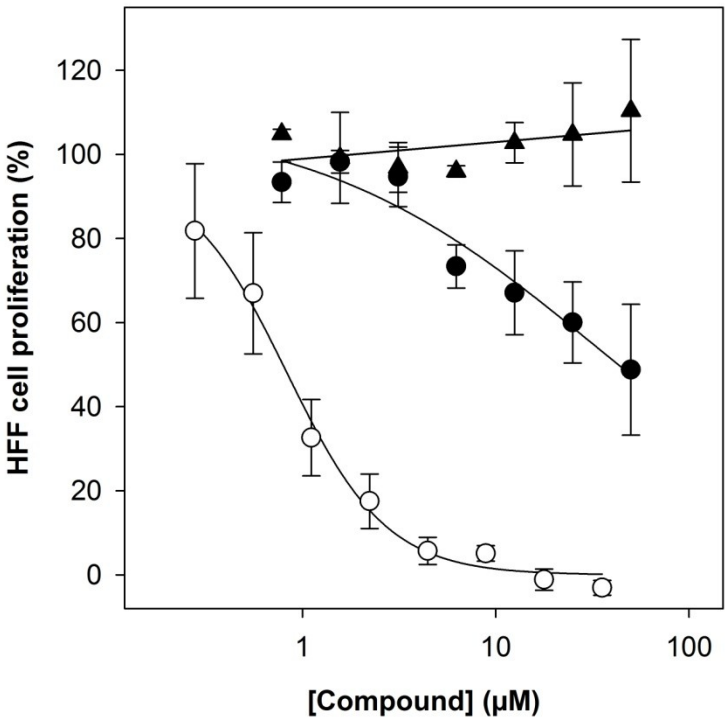
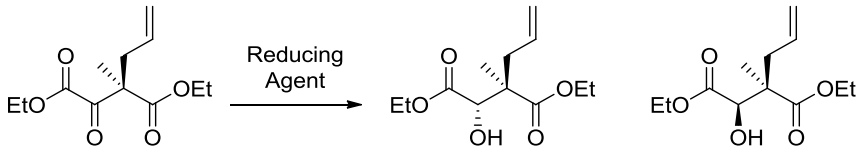



**Figure S1**. Toxicity assay of the *syn*-isomer 2 (dark circles) and the *anti*-isomer 1 (dark triangles), in comparison with the positive control cyclohexamide (open circles), against human foreskin fibroblasts. The experiment was carried out in RPMI-1640 culture medium and the cells were incubated in the presence of the pantothenamides for 48 h before estimation of cell proliferation. Error bars represent SEM from 3 independent experiments (*syn*-isomer and cyclohexamide) or range/2 from two independent experiments (*anti*-isomer). Each experiment was carried out in triplicate.

**Table S1. Ketone reduction**

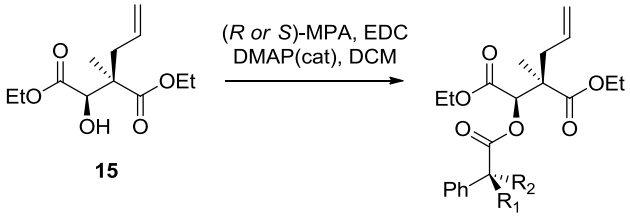



**10** *anti* *syn*

| Entry | Reducing Agent | Amount[a] | dr[b] | Solvent | T (°C) | t (h) |
|---|---|---|---|---|---|---|
| **1** | DIBAL-H | 1 eq | 60:40 | THF | -78 | 16 |
| **2** | $NABH_4$ | 0.4 eq | 74:26 | MeOH | 0 | 16 |
| **3** | $ZnBH_4$ | 1 eq | 70:30 | THF | -78 | 16 |
| **4** | (*R*)-CBS | 0.1 eq | 78:22 | THF | -20 | 16 |
| **5** | (*S*)-CBS | 0.1 eq | 66:34 | THF | -20 | 16 |
| **6** | Baker's Yeast | 80:1 (w/w yeast:ketone) | >99:1 (*syn*) | $H_2O$ | 50<br>30 | 0.5<br>24 |

[a]Amt, amount; Compound **10** (50 mg, 0.2 mmol); [b]Diastereomeric ratio determined by NMR.

**Determination of absolute stereochemistry of the secondary alcohol in compound 15**

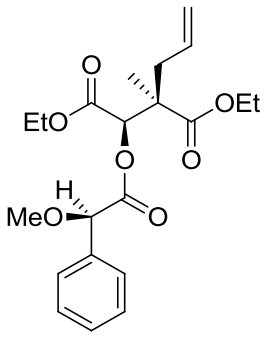



**15**

(*R*)MPA derivative: $R_1$ = H, $R_2$ = OMe
(*S*)MPA derivative: $R_1$ = OMe, $R_2$ = H

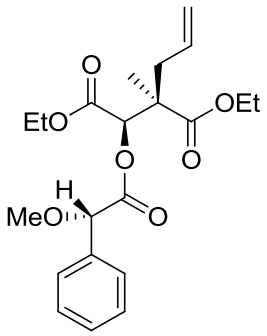
(*R, S*)-MPA-derivatives were synthesized by coupling compound **15** with (*R* or *S*)-methoxy-phenylacetic acid to yield a chiral derivative that was used for NMR analysis of the absolute stereochemistry of the secondary chiral alcohols. Thus compound **15** (25 mg, 0.1 mmol, 1eq) was esterified by adding (*R* or *S*)-MPA (16.6 mg, 0.1 mmol, 1eq), and the coupling agent EDC (23.0 mg, 0.12 mmol, 1.2 eq) with DMAP (1 mg, 0.01 mmol, 0.1 eq). The reaction was stirred in DCM (2 ml) for 16 h at room temperature. The reaction was quenched with saturated ammonium

chloride (2 ml), and extracted with ethyl acetate (3 × 5 ml). The solution was concentrated and the product purified by preparative TLC. Finally the $^1$H NMR of the purified (*R*)-MPA derivative and (*S*)-MPA were measured.




**(*R*)-MPA derivative**

This compound was synthesized by coupling with (*R*)-MPA. $R_f$ 0.72 (50% ethyl acetate/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.51-7.44 (m, 2H), 7.42-7.32 (m, 3H), 5.72-5.54 (m, 1H), 5.46 (s, 1H), 5.00-4.87 (m, 3H), 4.13 (q, *J* = 7.0, 2H), 4.01 (q, *J* = 7.0, 2H), 3.51 (s, 3H), 2.38 (dd, *J* = 7.3, 13.7, 1H), 2.17 (dd, *J* = 7.5, 13.7, 1H), 1.23 (t, *J* = 7.0, 3H), 1.14 (s, 3H), 1.06 (t, *J* = 7.0, 3H).




**(*S*)-MPA derivative**

This compound was synthesized by coupling with (*S*)-MPA. $R_f$ = 0.72 (50% ethyl acetate/hexanes). $^1$H NMR (300 MHz, $CDCl_3$) δ 7.51-7.44 (m, 2H), 7.42-7.32 (m, 3H), 5.57-5.37 (m, 2H), 4.94-4.87 (m, 2H), 4.75-4.64 (d, *J* = 17.4, 1H), 4.16 (m, 2H), 4.07 (q, *J* = 7.3, 2H), 2.09 (dd, *J* = 6.7, 13.9, 1H), 1.70 (dd, *J* = 7.7, 13.9, 1H), 1.21 (t, *J* = 7.3, 6H), 1.04 (s, 3H).

**LC-MS Purity Traces**

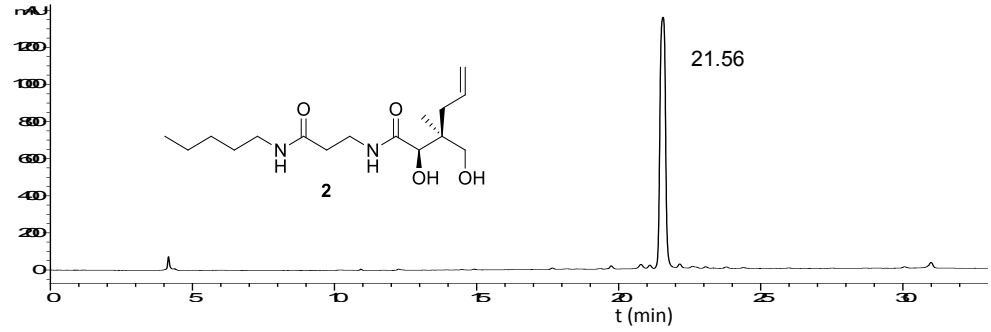
Compound purity was analyzed by reversed-phase HPLC using an Agilent 1100 modular system (Santa Clara, CA, United States), equipped with an autosampler, a quaternary pump system, a photodiode array detector, and a thermostated column compartment. The HPLC was coupled to a 6120 Quadrupole for ESI-MS analysis. Separation was achieved using an analytical 250 × 4.60 mm SYNERGI 4µ Hydro-RP 80A C18 column from Phenomenex (Torrance, CA, USA). Absorbance was monitored at a wavelength of 214 nm. The elution gradients used are described below, at a flow rate of 0.5 ml/min.

| **Method A:** | **t (min)** | **$H_2O$ (%)** | **ACN (%)** |
|---|---|---|---|
| | 0 | 99 | 1 |
| | 30 | 1 | 99 |

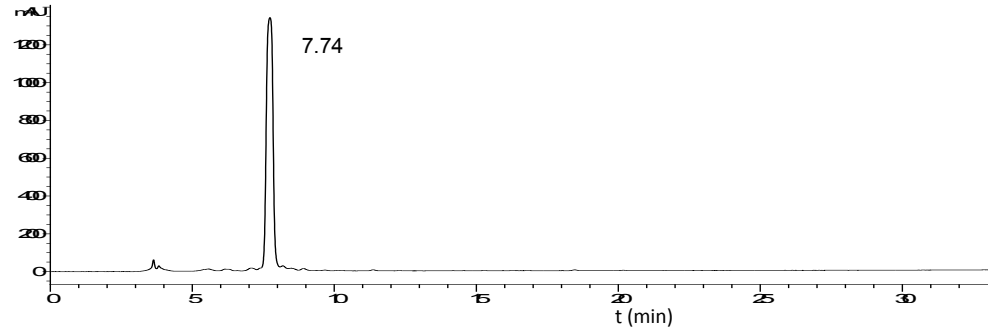
| **Method B:** | **t (min)** | **$H_2O$ (%)** | **ACN (%)** |
|---|---|---|---|
| | 0 | 50 | 50 |
| | 30 | 1 | 99 |

| **Method C:** | **t (min)** | **$H_2O$ (%)** | **ACN (%)** |
|---|---|---|---|
| | 0 | 20 | 80 |
| | 30 | 1 | 99 |

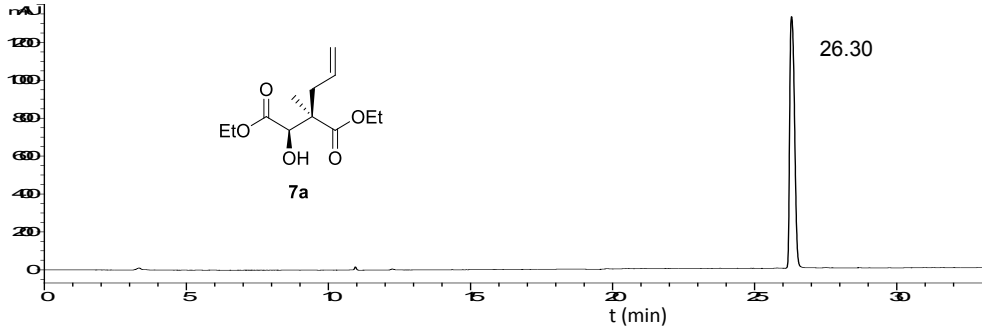
Method A.



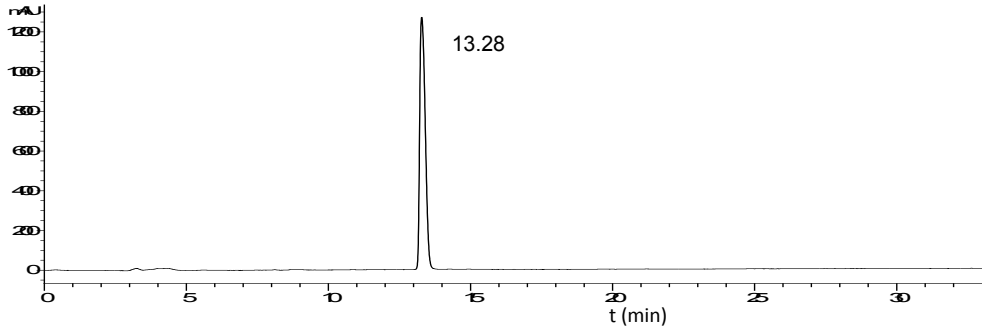

Method B.



Method A.

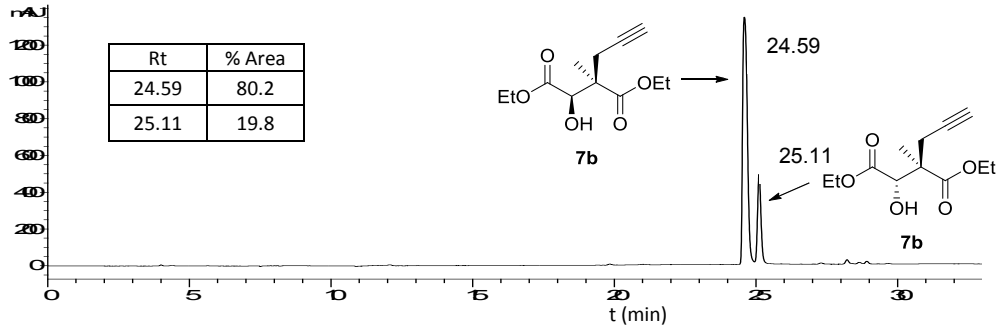



Method B.



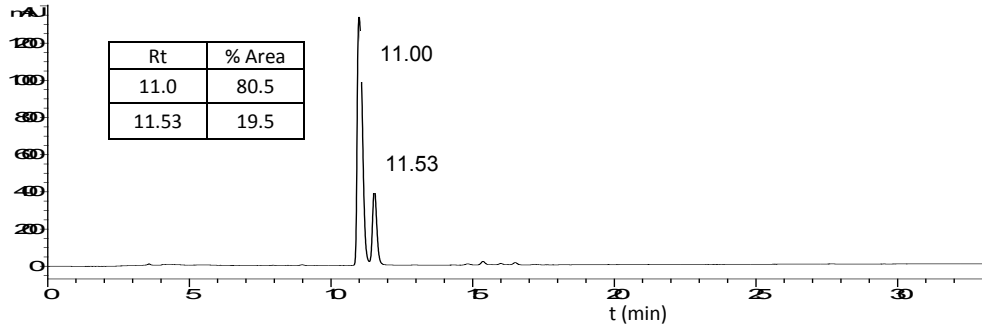

Method A.

| Rt | % Area |
|---|---|
| 24.59 | 80.2 |
| 25.11 | 19.8 |

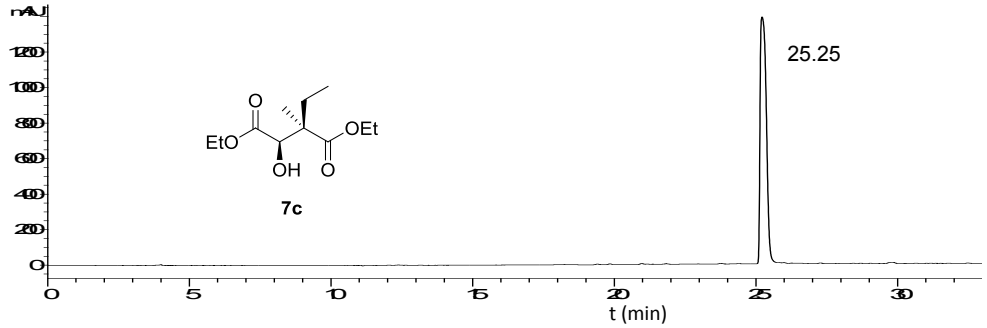



Method B.

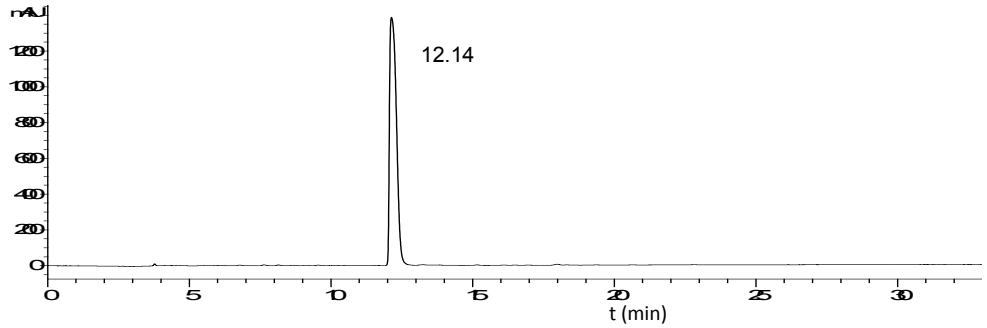
| Rt | % Area |
|---|---|
| 11.0 | 80.5 |
| 11.53 | 19.5 |



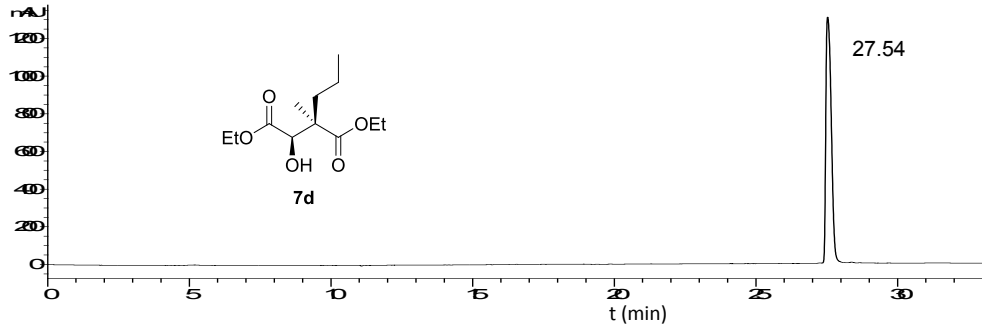
Method A.



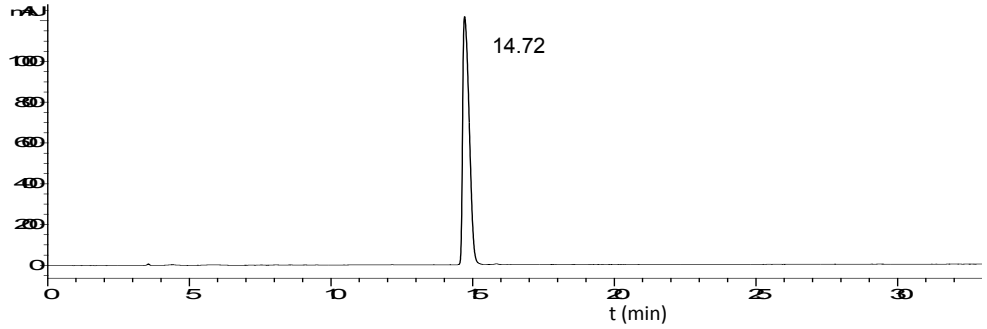

Method B.



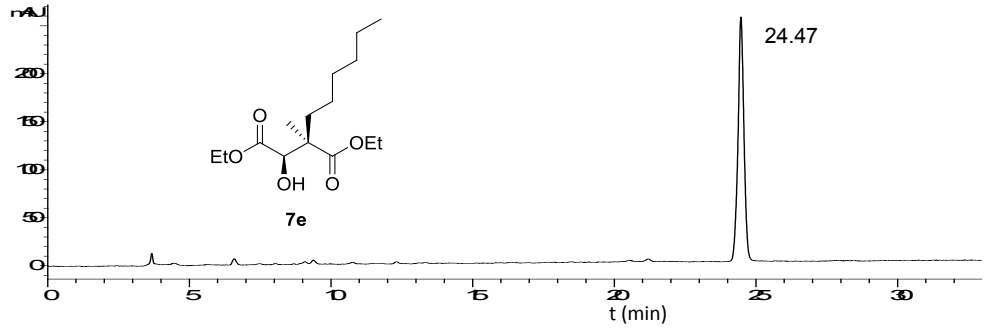

Method A.



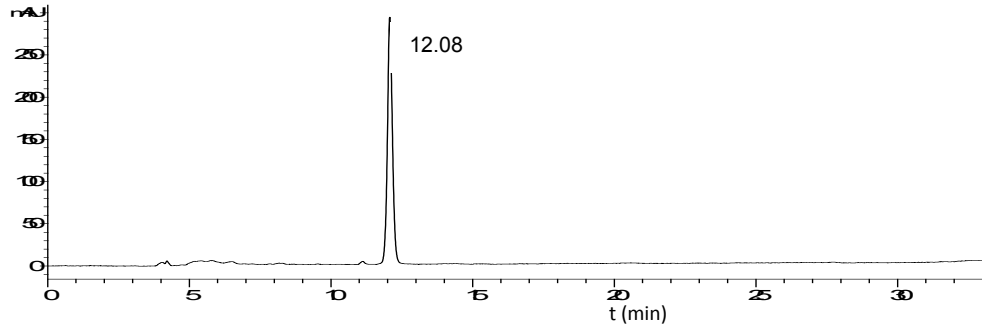

Method B.



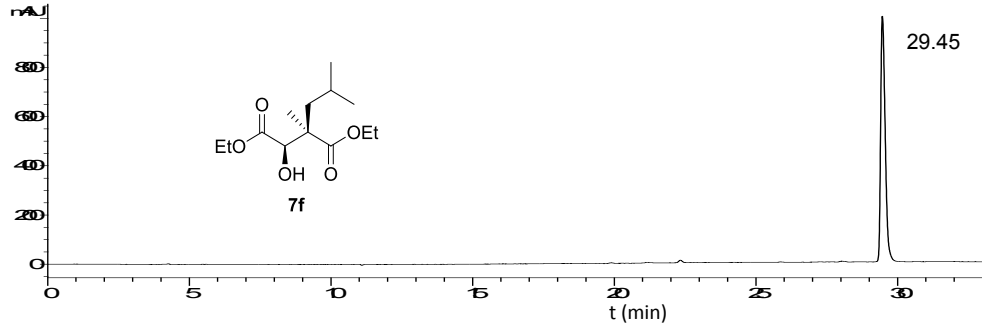
Method B.



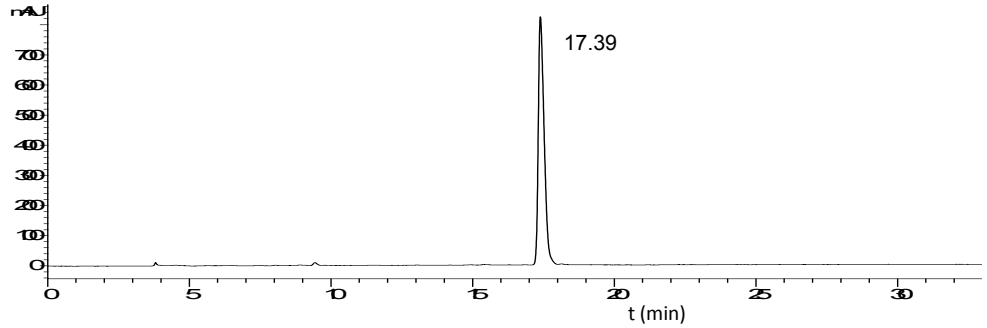

Method C.




Method A.

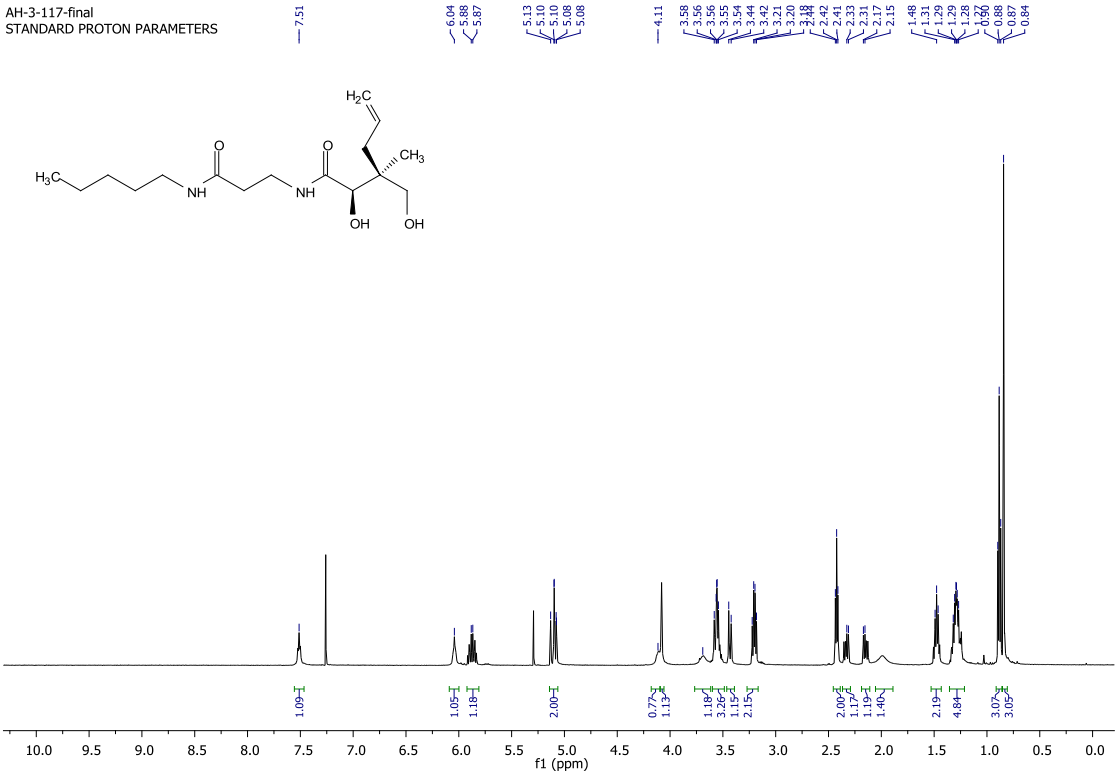


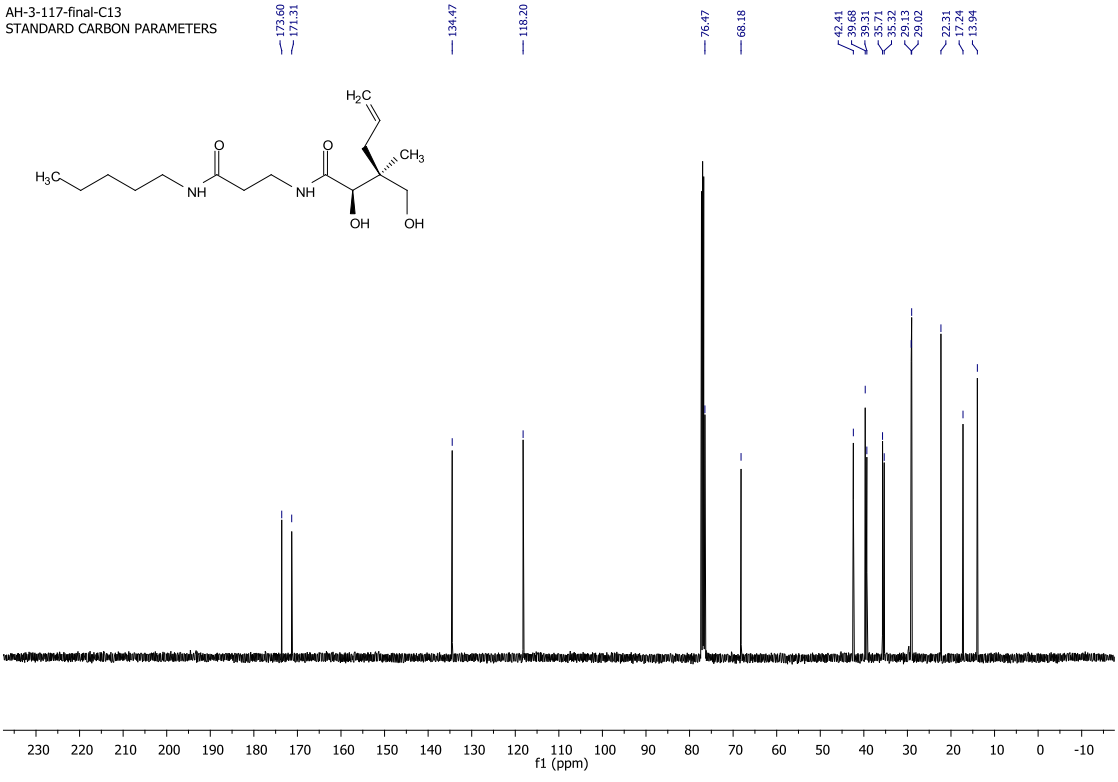

Method B.



# NMR Spectra

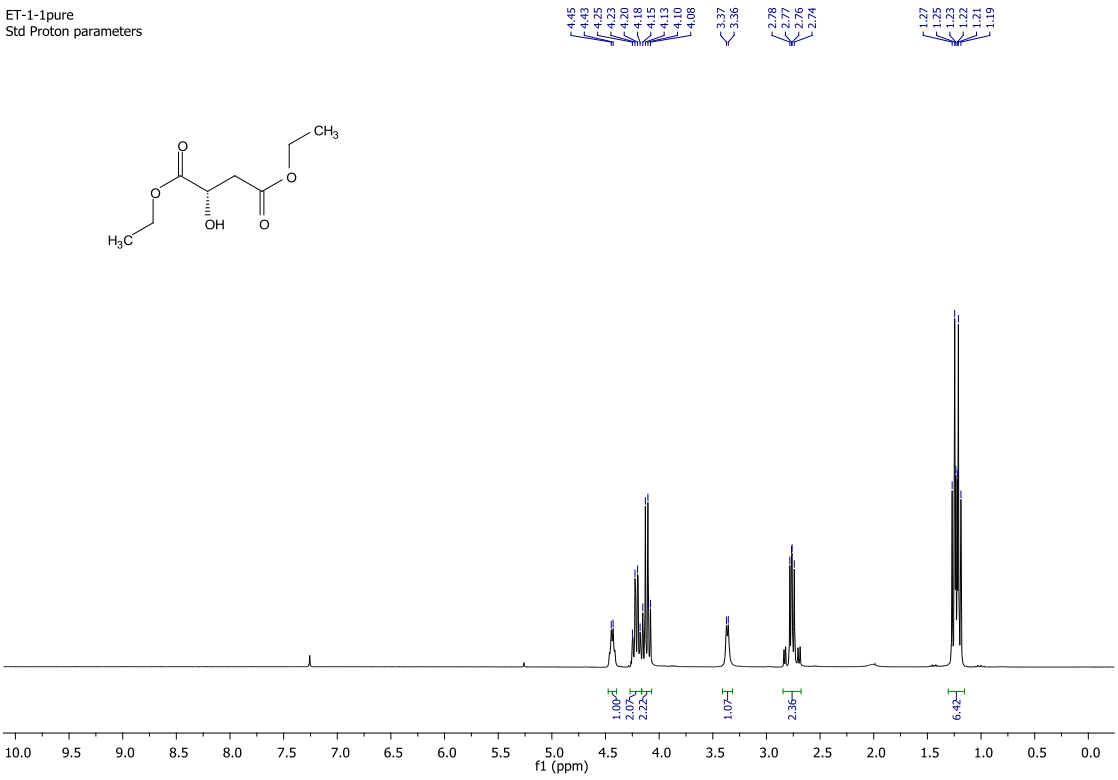
## Compound 2



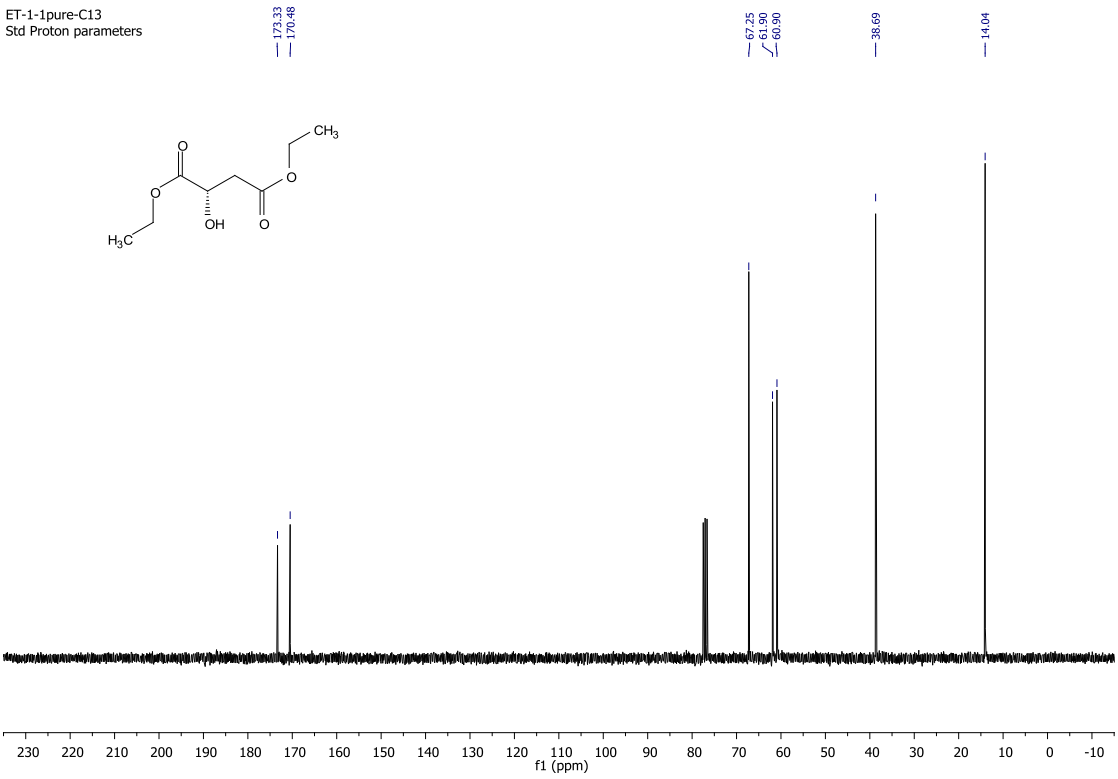



# Compound 3

ET-1-1pure
Std Proton parameters

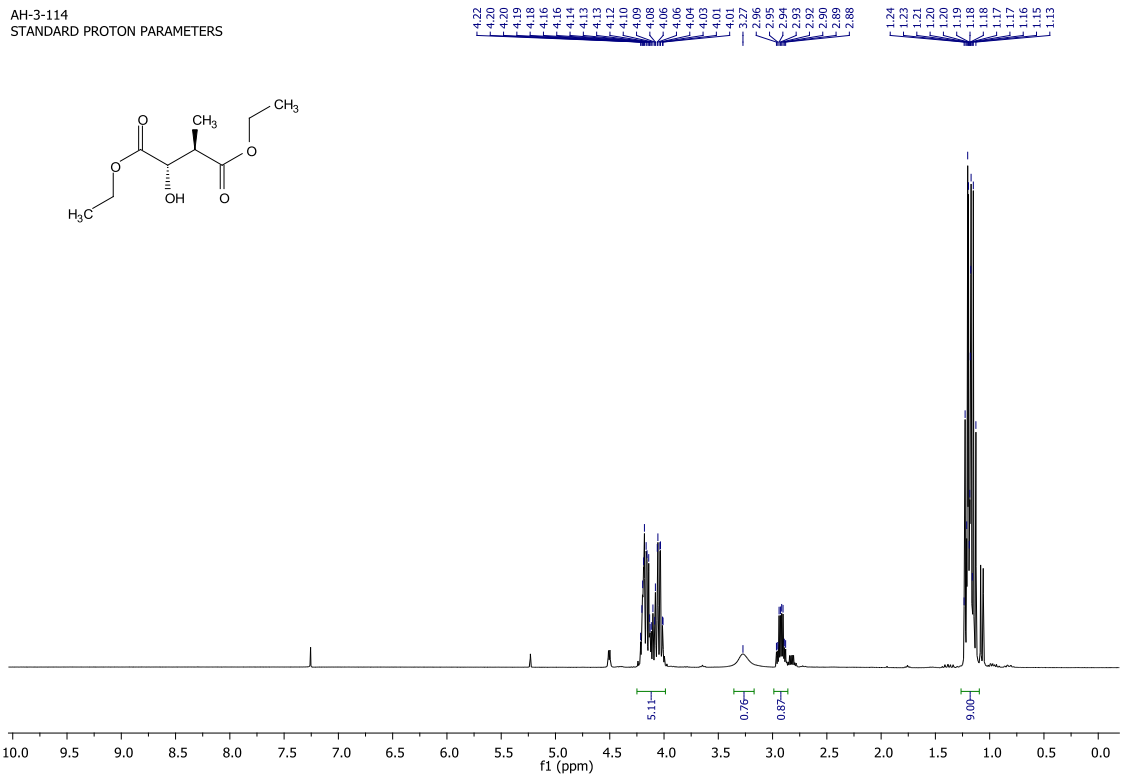



ET-1-1pure-C13
Std Proton parameters

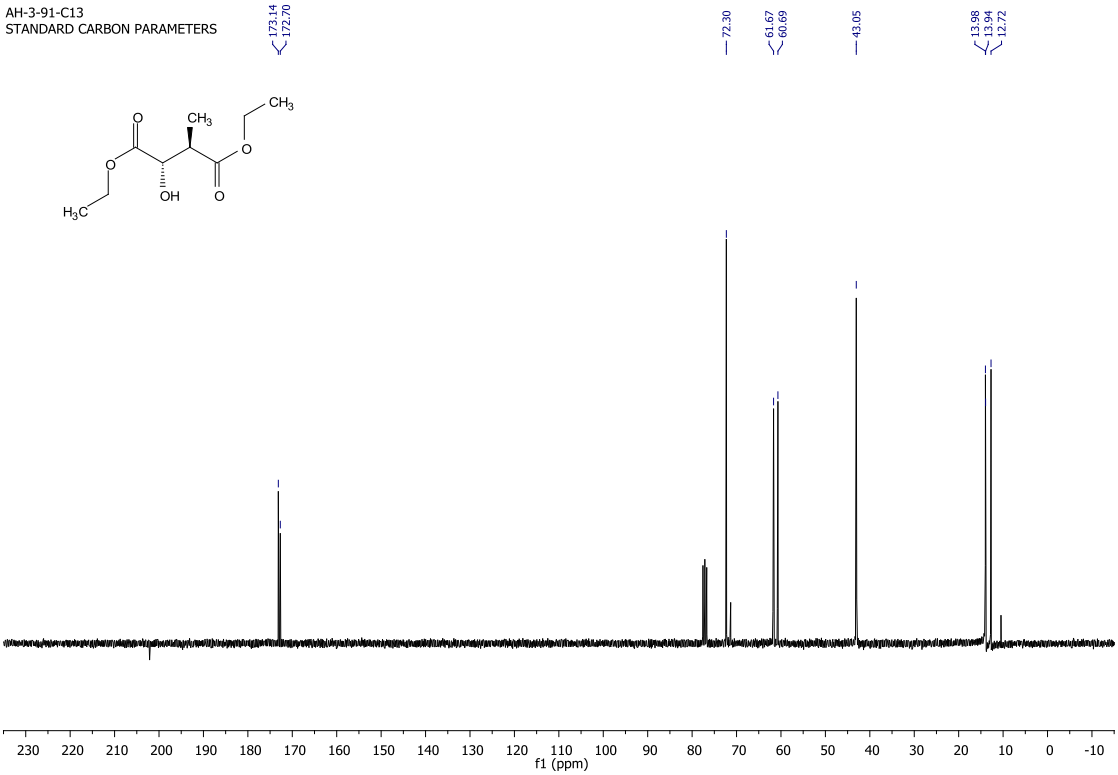


## Compound 4

AH-3-114
STANDARD PROTON PARAMETERS

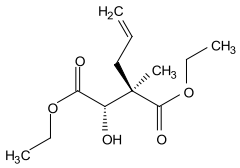



AH-3-91-C13
STANDARD CARBON PARAMETERS



# Compound 5a

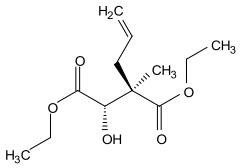
HD-3-14Aproton
Std Proton parameters





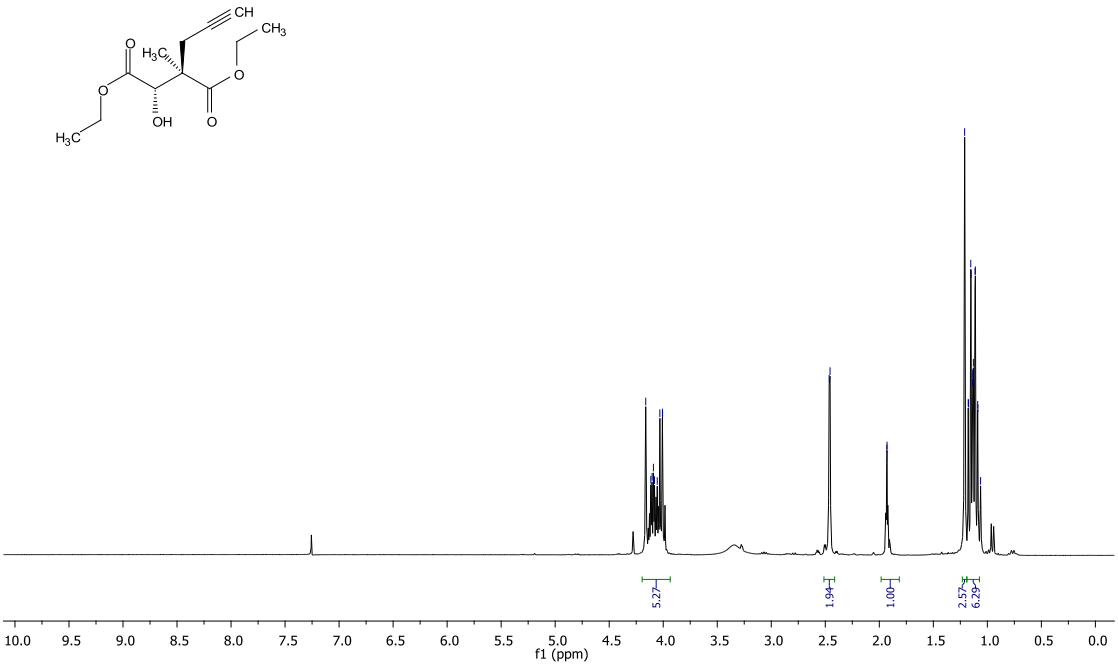


AH-3-95-C13
STANDARD CARBON PARAMETERS

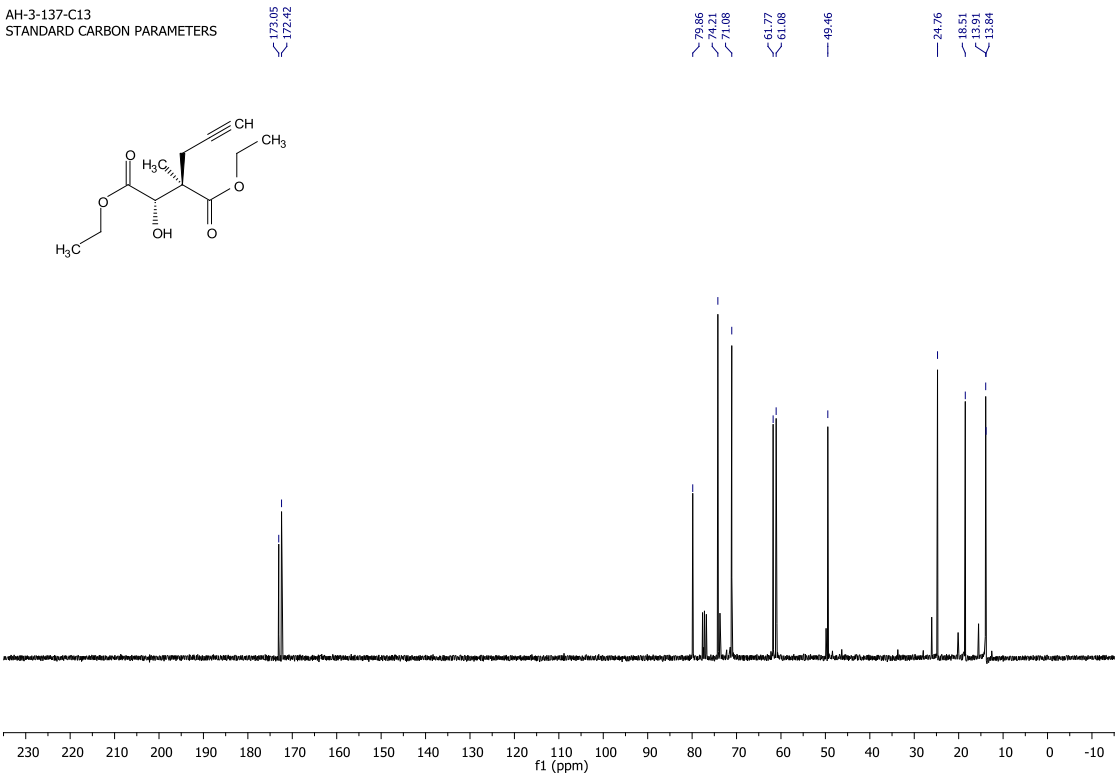


## Compound 5b

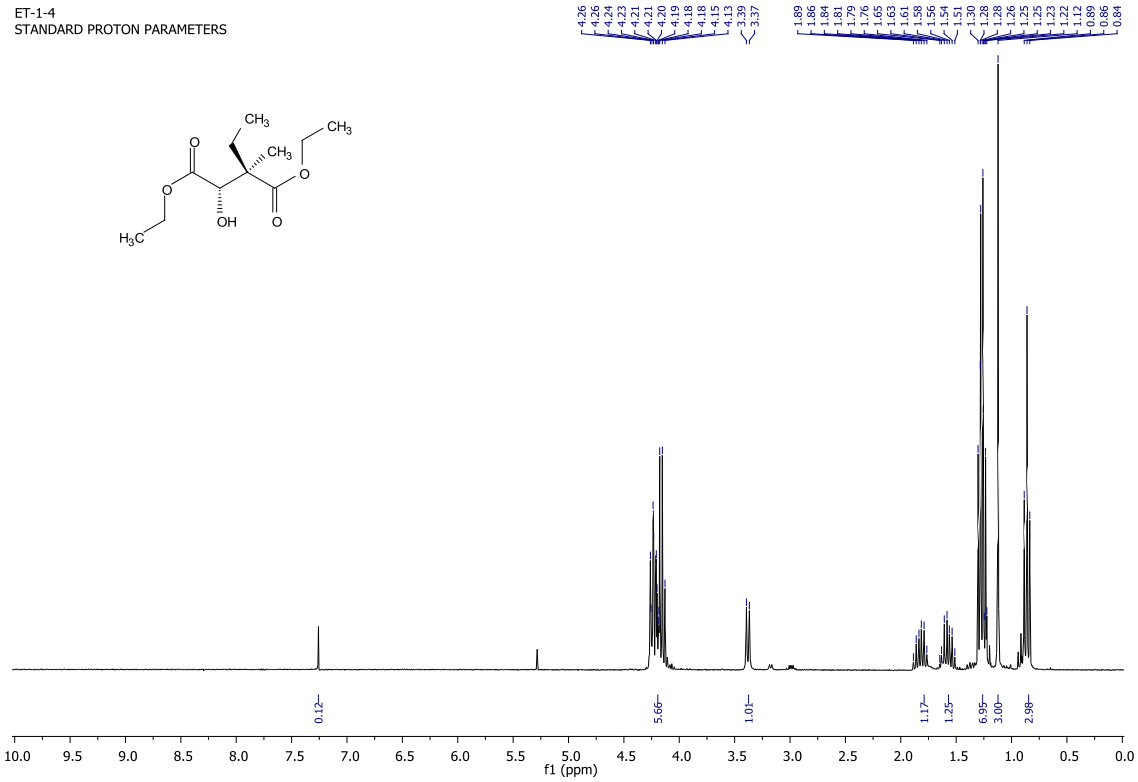
AH-3-137
STANDARD PROTON PARAMETERS

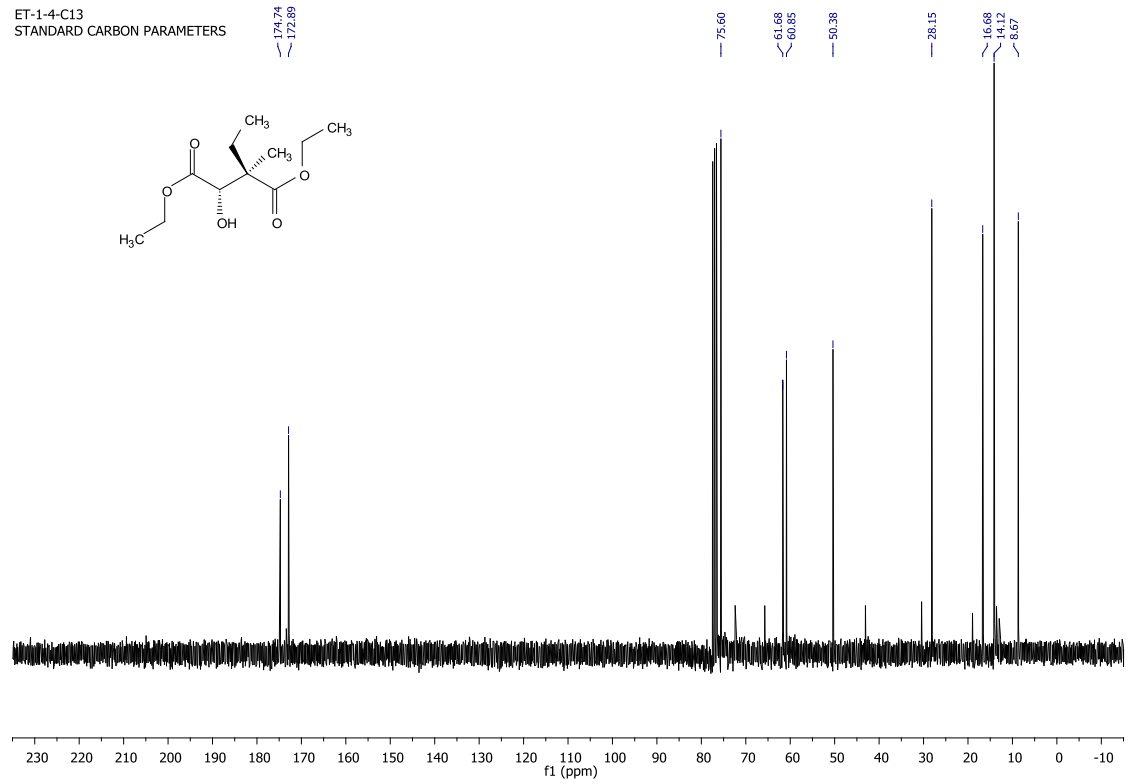



AH-3-137-C13
STANDARD CARBON PARAMETERS



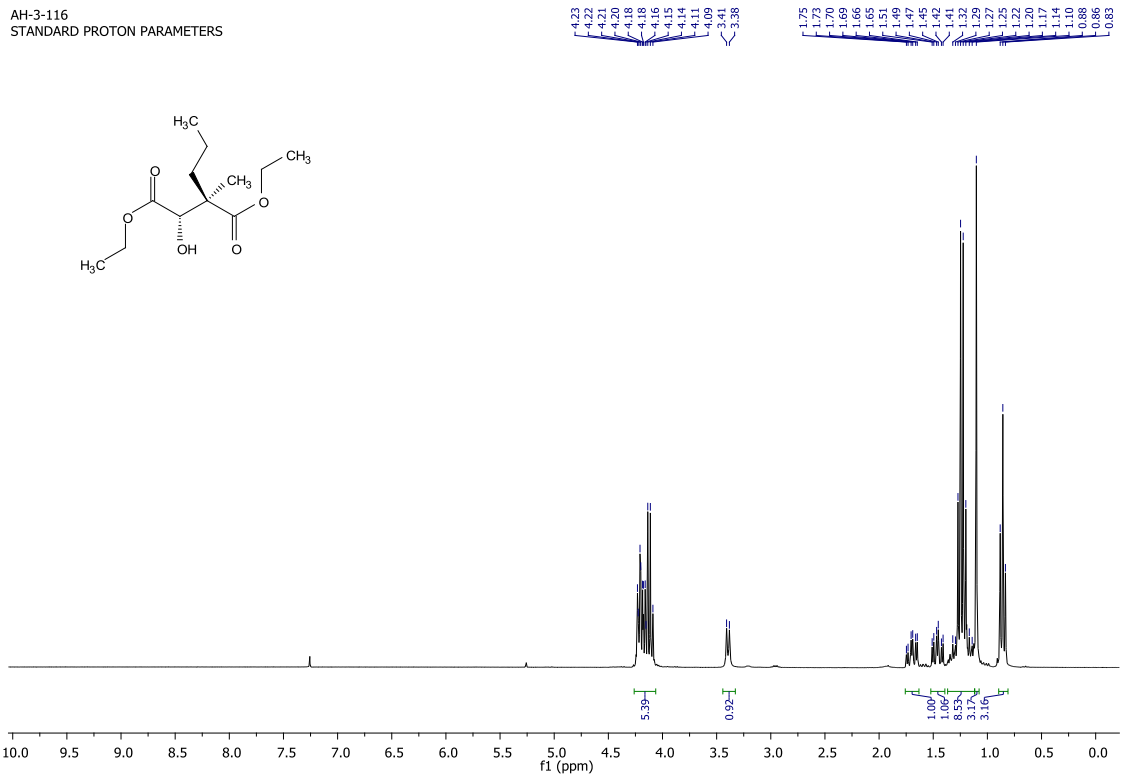
# Compound 5c


ET-1-4
STANDARD PROTON PARAMETERS
4.26 4.26 4.24 4.23 4.21 4.21 4.20 4.19 4.18 4.18 4.15 4.13 3.39 3.37
1.89 1.86 1.84 1.81 1.79 1.76 1.65 1.63 1.61 1.58 1.56 1.54 1.51 1.30 1.28 1.28 1.26 1.25 1.25 1.23 1.22 1.12 0.89 0.86 0.84
CH3
CH3
CH3
O
O
O
O
OH
O
H3C
0.12 5.66 1.01 1.17 1.25 6.95 3.00 2.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

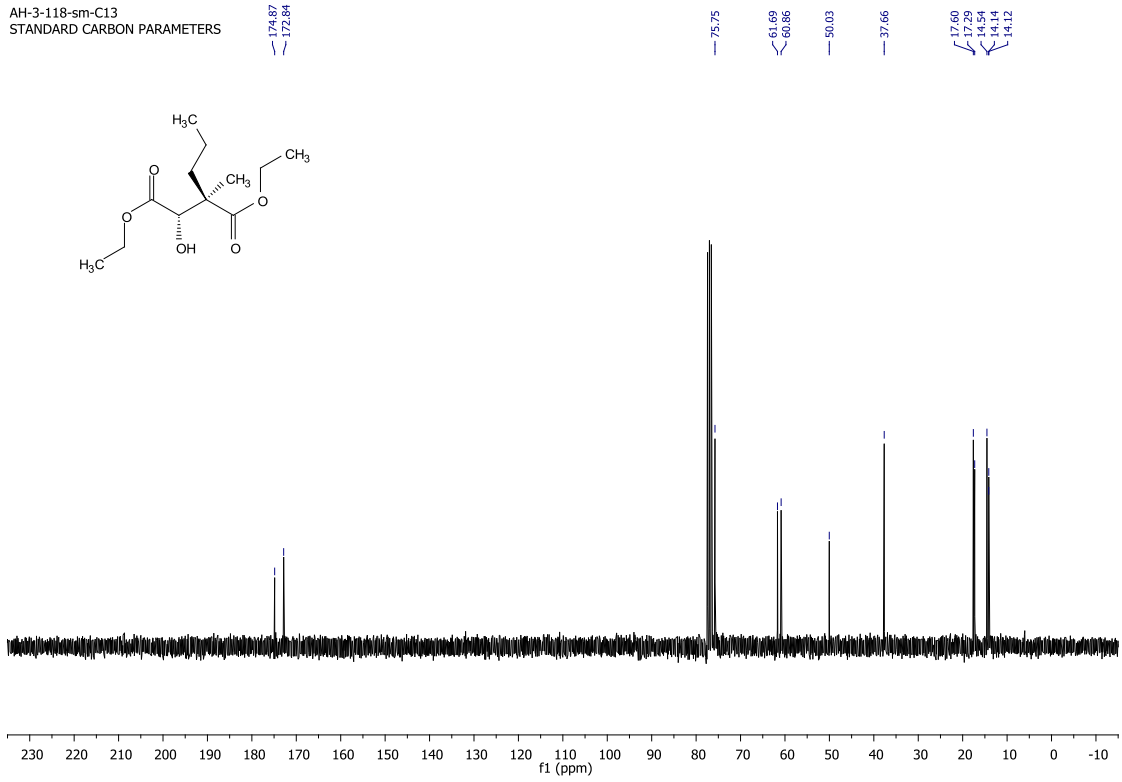

ET-1-4-C13
STANDARD CARBON PARAMETERS
174.74 172.89
75.60 61.68 60.85 50.38 28.15 16.68 14.12 8.67
CH3
CH3
CH3
O
O
O
O
OH
O
H3C
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

# Compound 5d

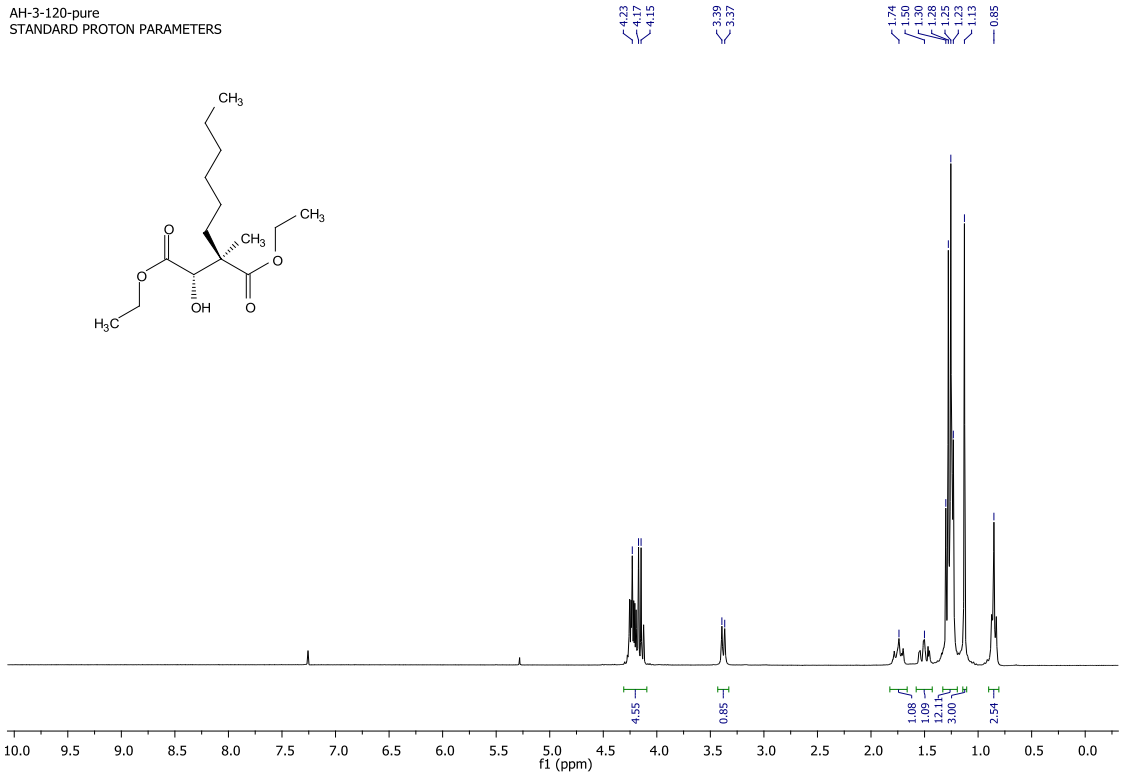
AH-3-116
STANDARD PROTON PARAMETERS

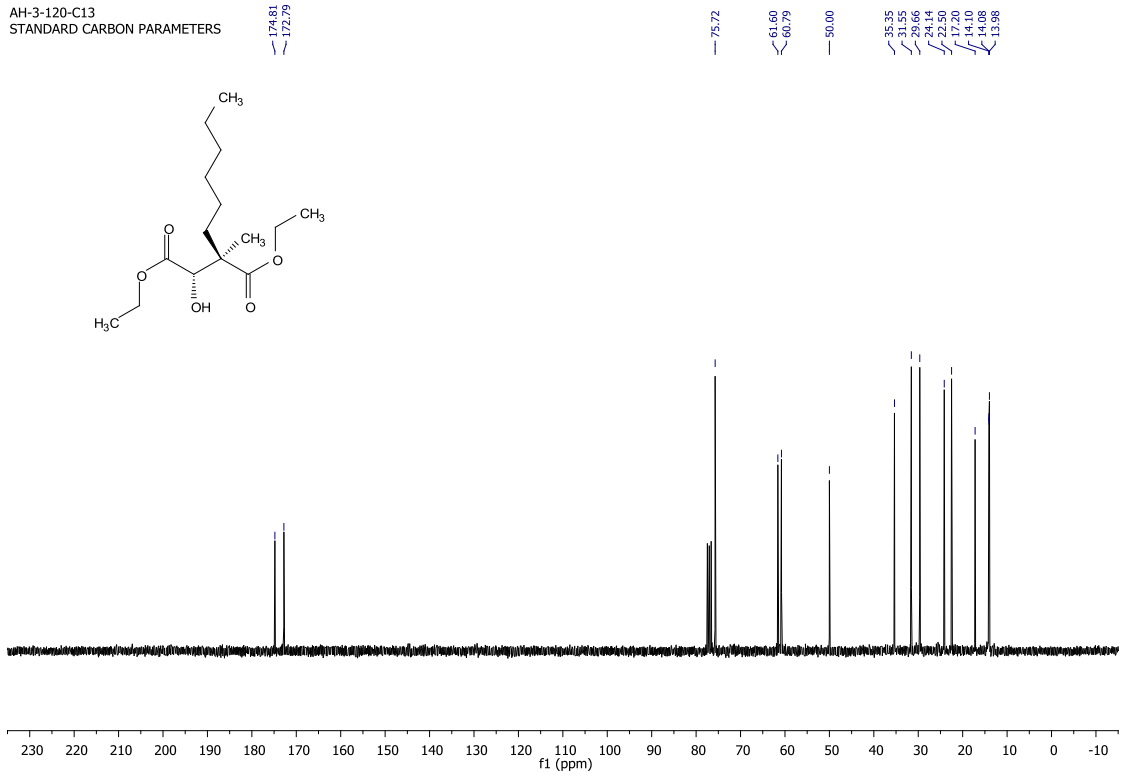



AH-3-118-sm-C13
STANDARD CARBON PARAMETERS



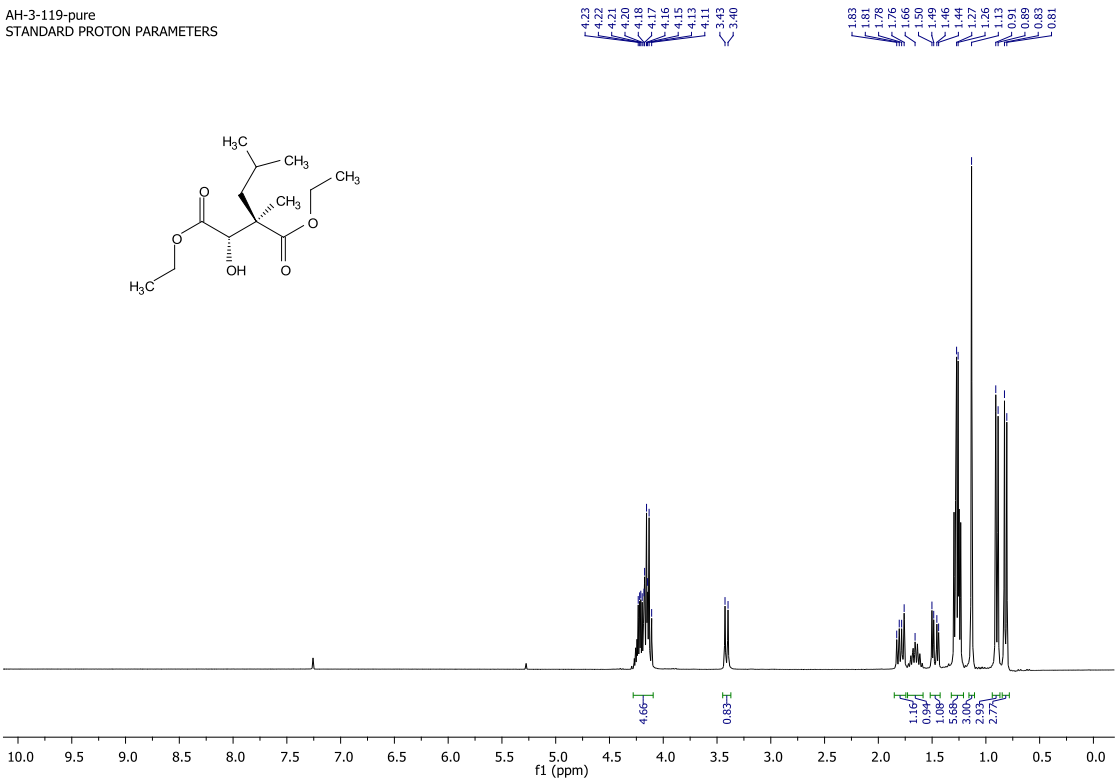
# Compound 5e


AH-3-120-pure
STANDARD PROTON PARAMETERS
4.23
4.17
4.15
3.39
3.37
1.74
1.50
1.30
1.28
1.25
1.23
1.13
0.85
4.55
0.85
1.08
1.09
1.21
3.00
2.54
f1 (ppm)

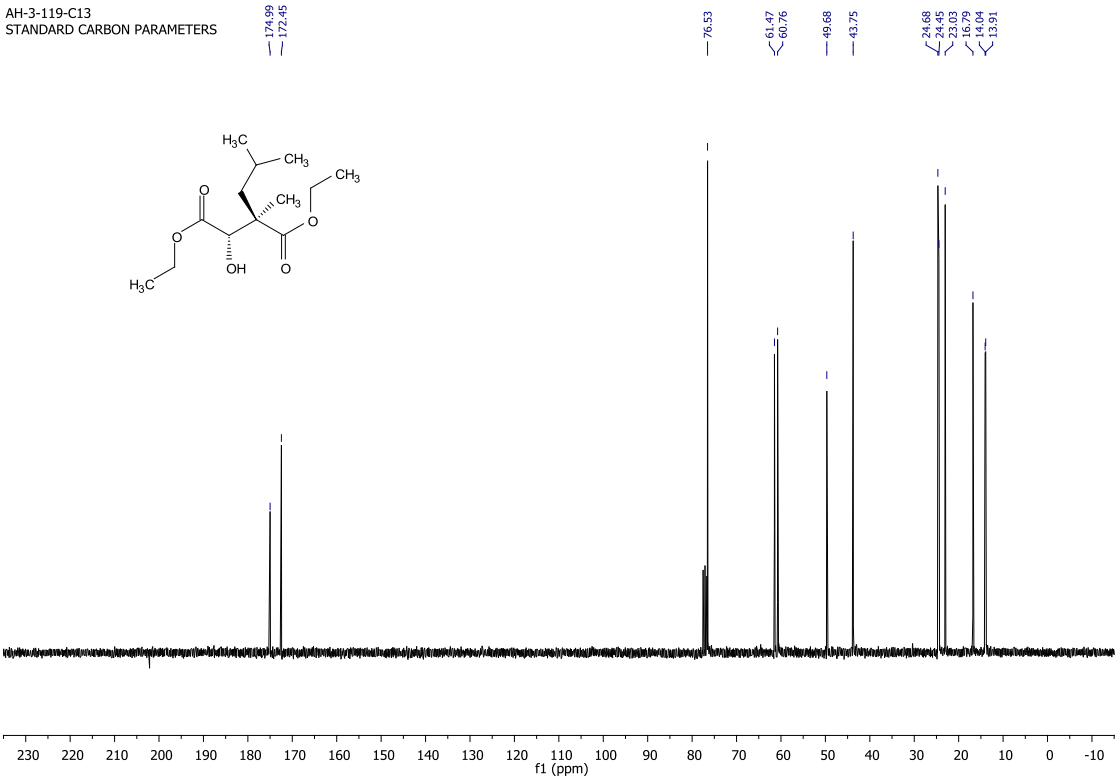

AH-3-120-C13
STANDARD CARBON PARAMETERS
174.81
172.79
75.72
61.60
60.79
50.00
35.35
31.55
29.66
24.14
22.50
17.20
14.10
14.08
13.98
f1 (ppm)

# Compound 5f

AH-3-119-pure
STANDARD PROTON PARAMETERS

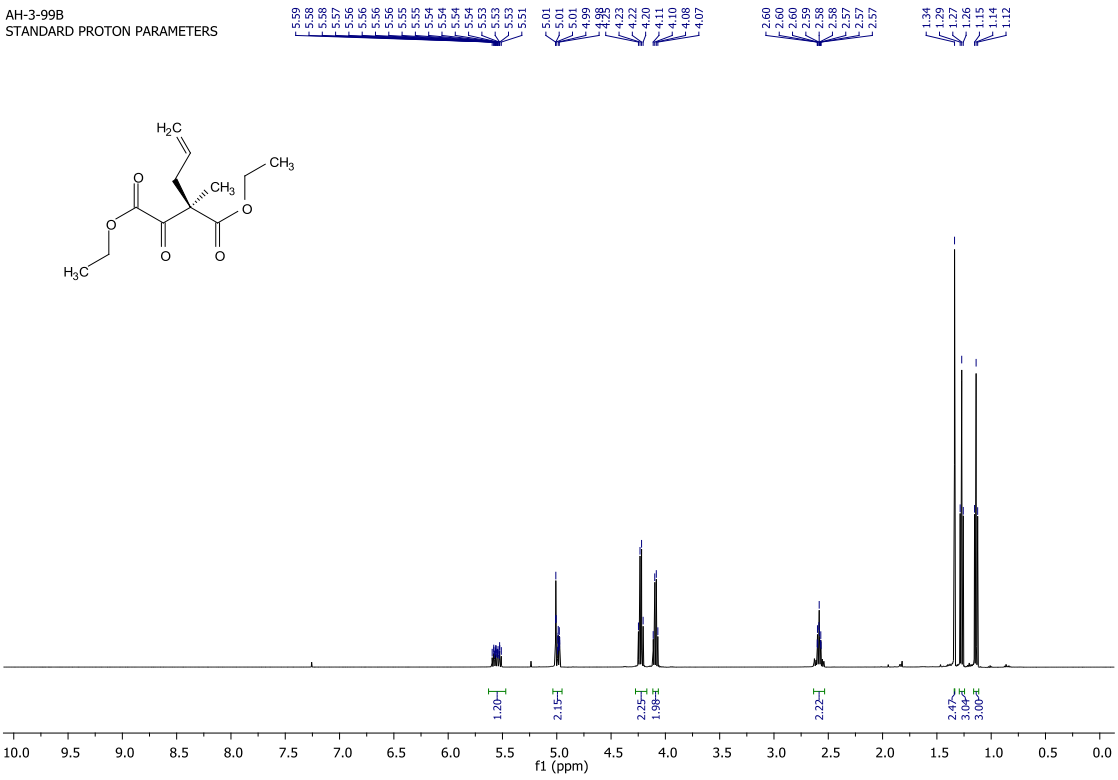



AH-3-119-C13
STANDARD CARBON PARAMETERS

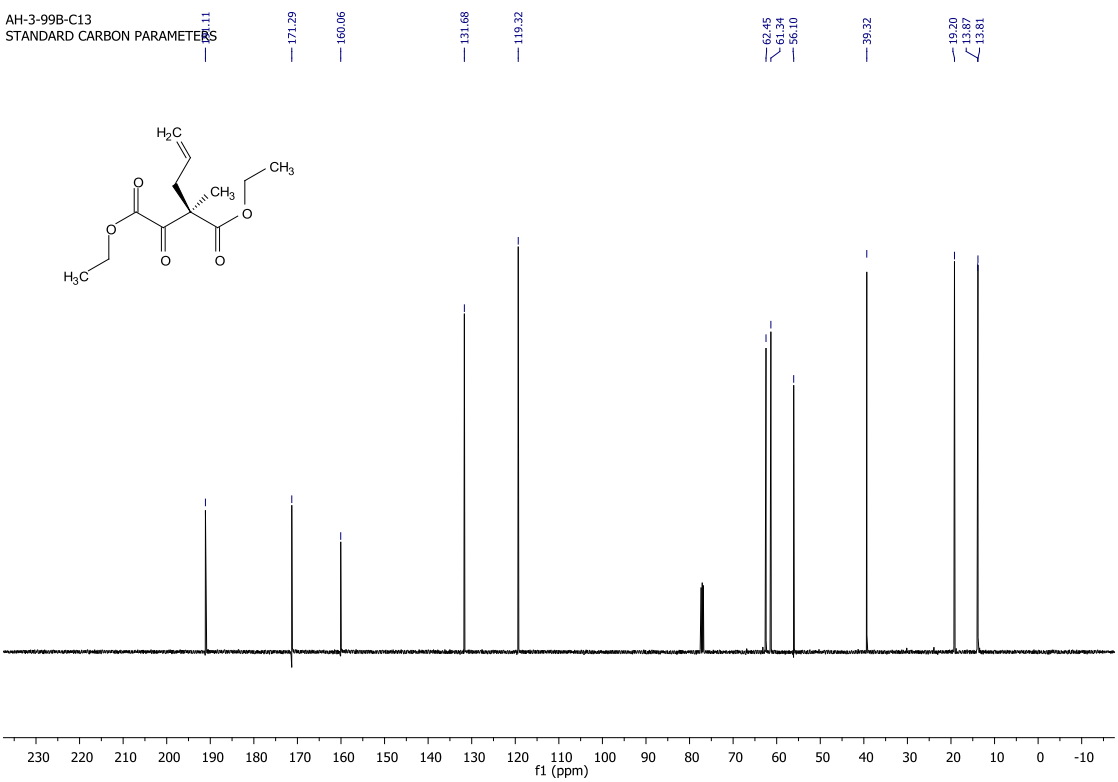


# Compound 6a

AH-3-99B
STANDARD PROTON PARAMETERS

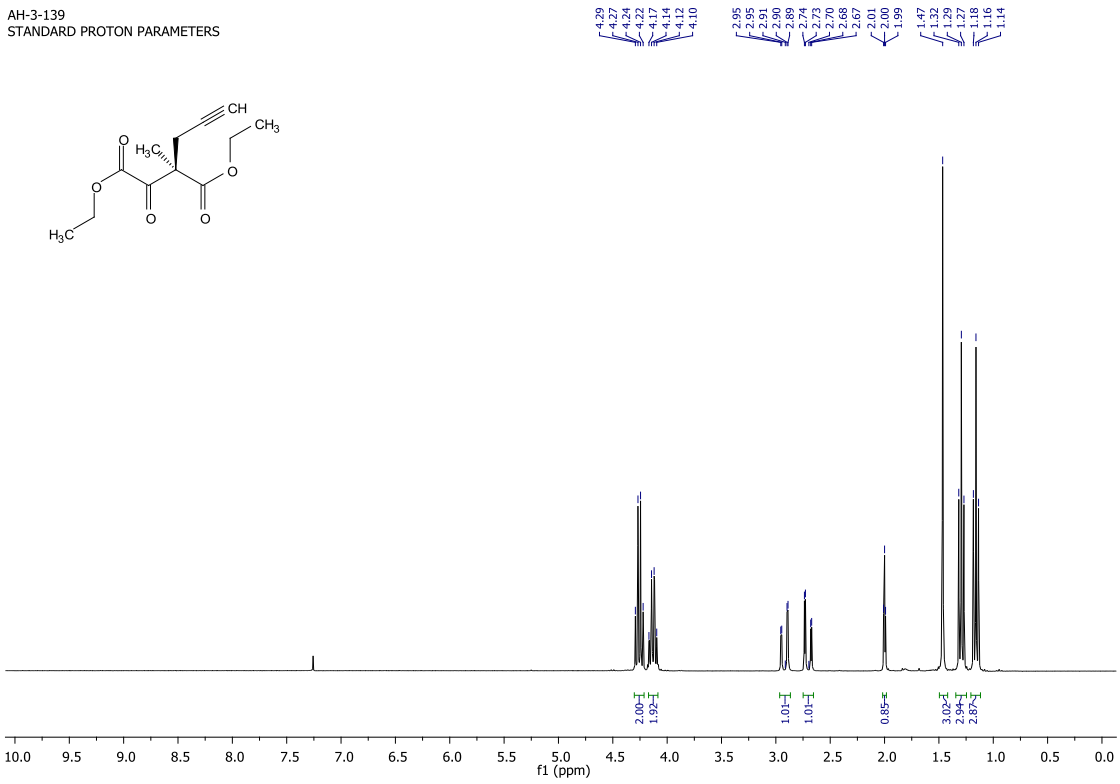



AH-3-99B-C13
STANDARD CARBON PARAMETERS

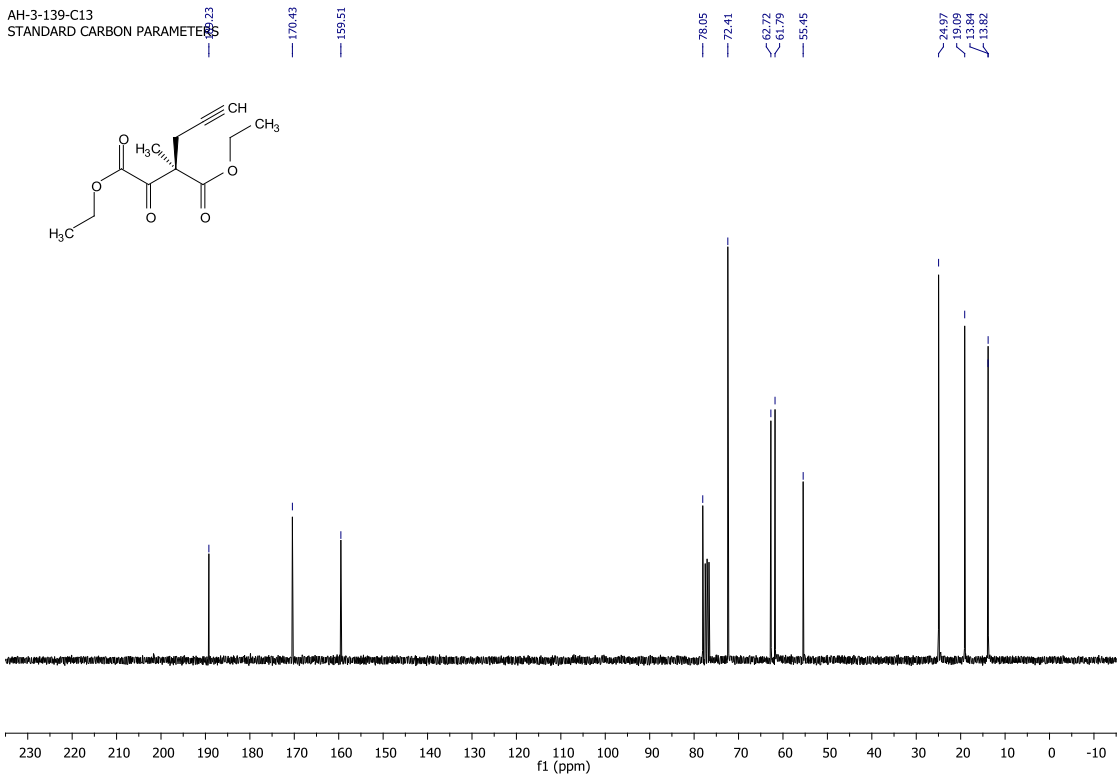


# Compound 6b

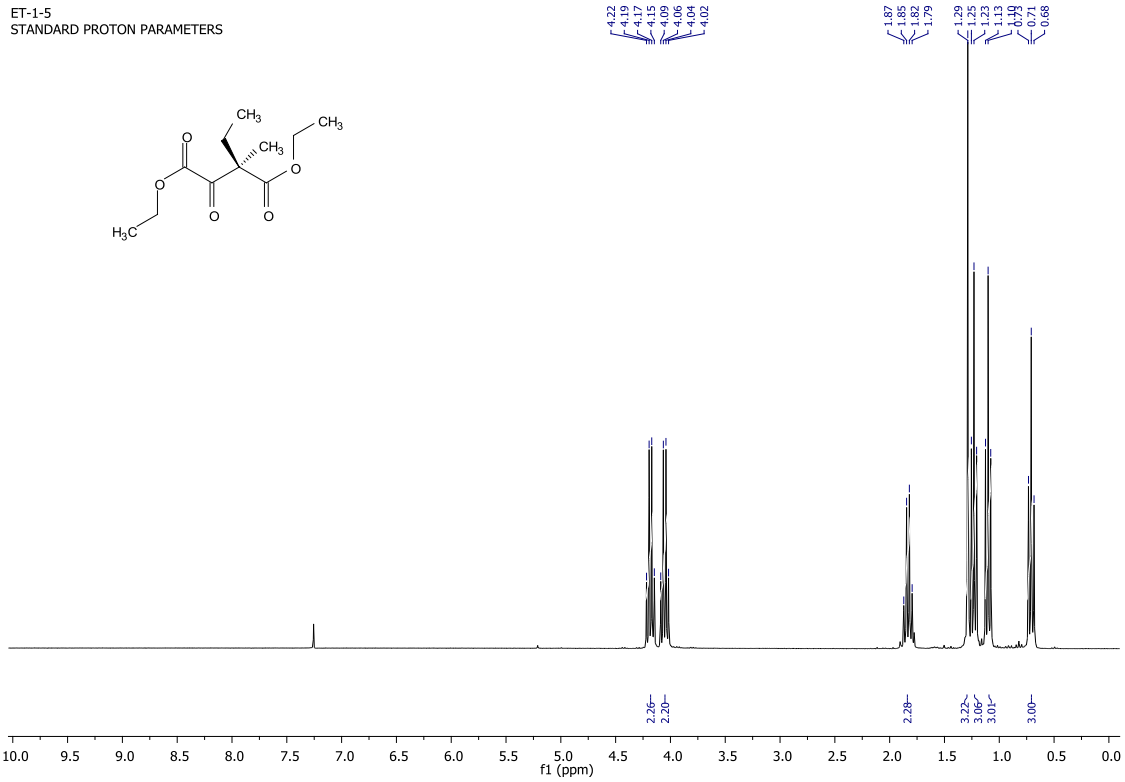
AH-3-139
STANDARD PROTON PARAMETERS

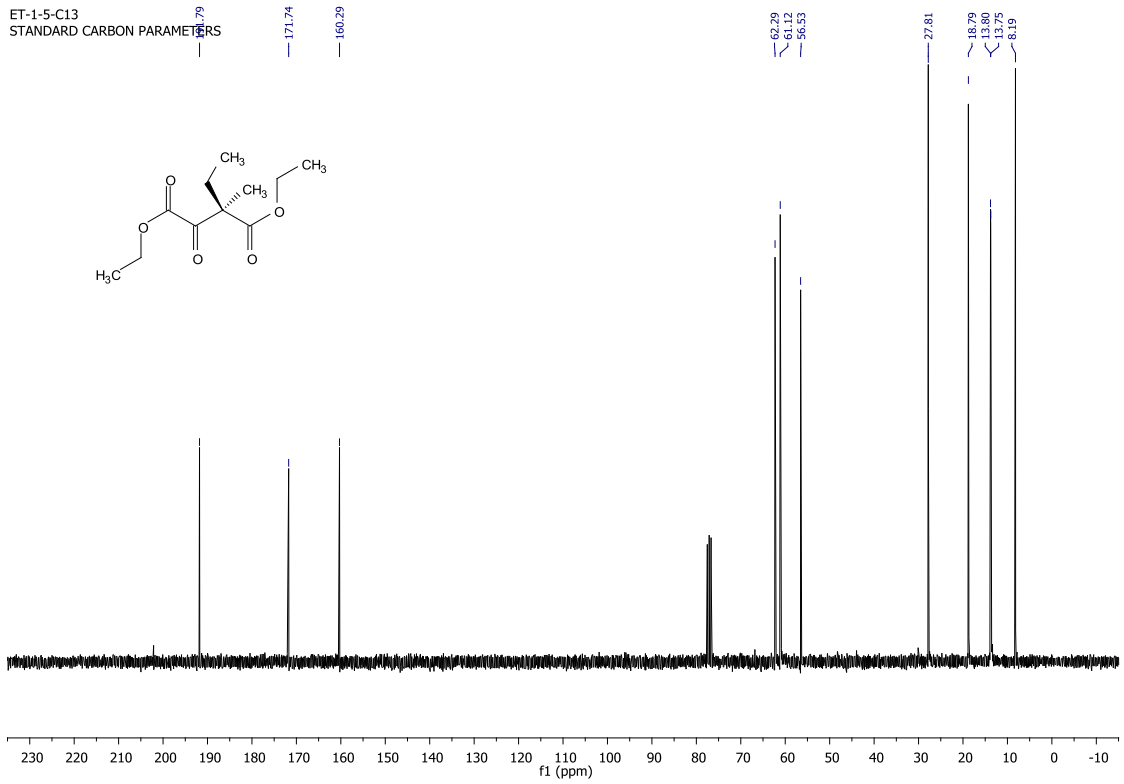



AH-3-139-C13
STANDARD CARBON PARAMETERS



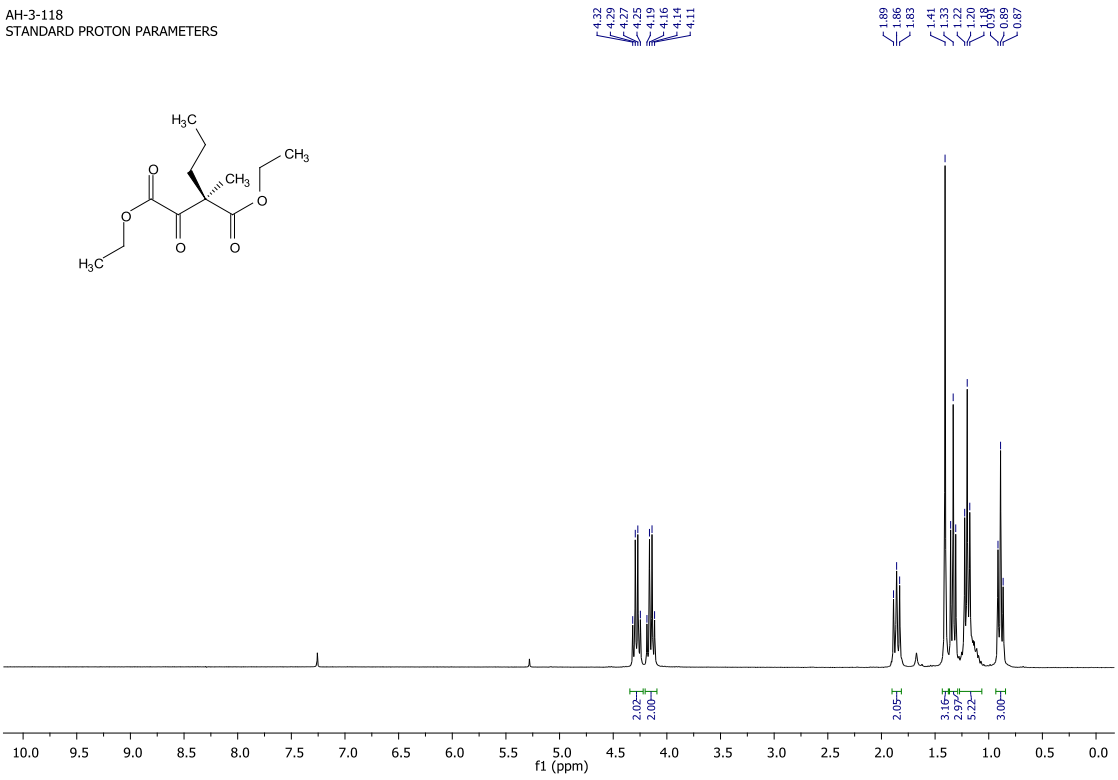
## Compound 6c


ET-1-5
STANDARD PROTON PARAMETERS
4.22
4.19
4.17
4.15
4.09
4.06
4.04
4.02
1.87
1.85
1.82
1.79
1.29
1.25
1.23
1.13
0.73
0.71
0.68
2.26
2.20
2.29
3.22
3.06
3.01
3.00
f1 (ppm)

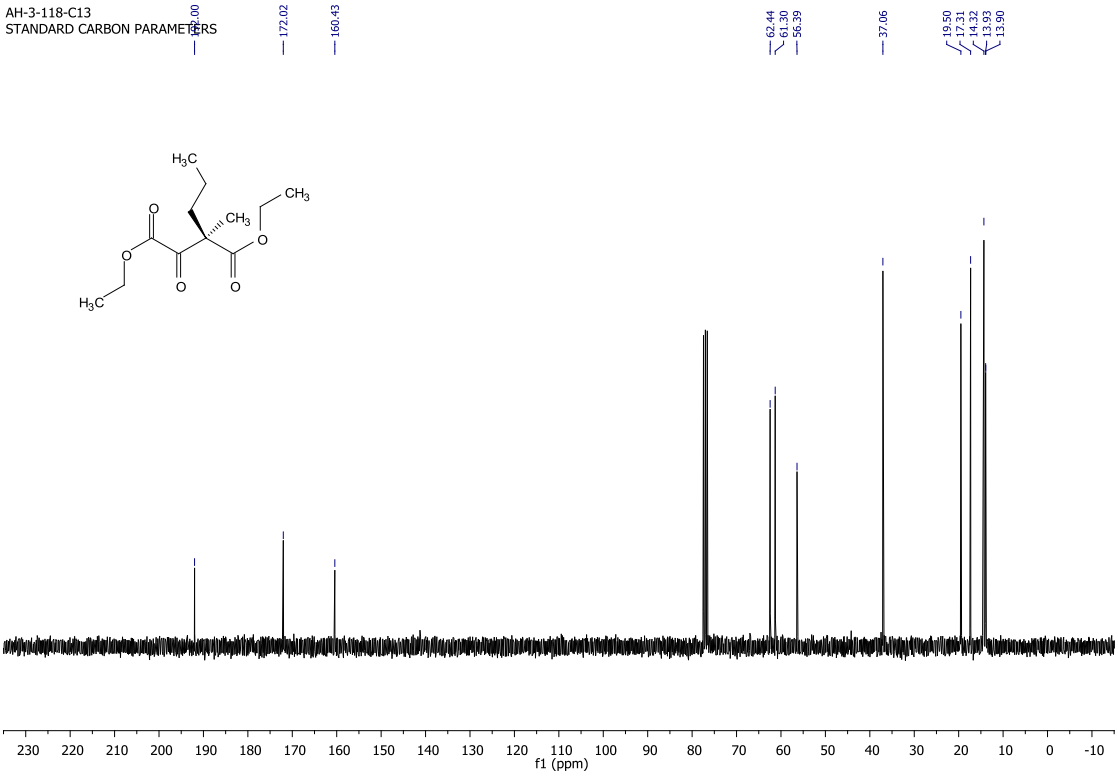

ET-1-5-C13
STANDARD CARBON PARAMETERS
171.74
160.29
62.29
61.12
56.53
27.81
18.79
13.80
13.75
8.19
f1 (ppm)

# Compound 6d

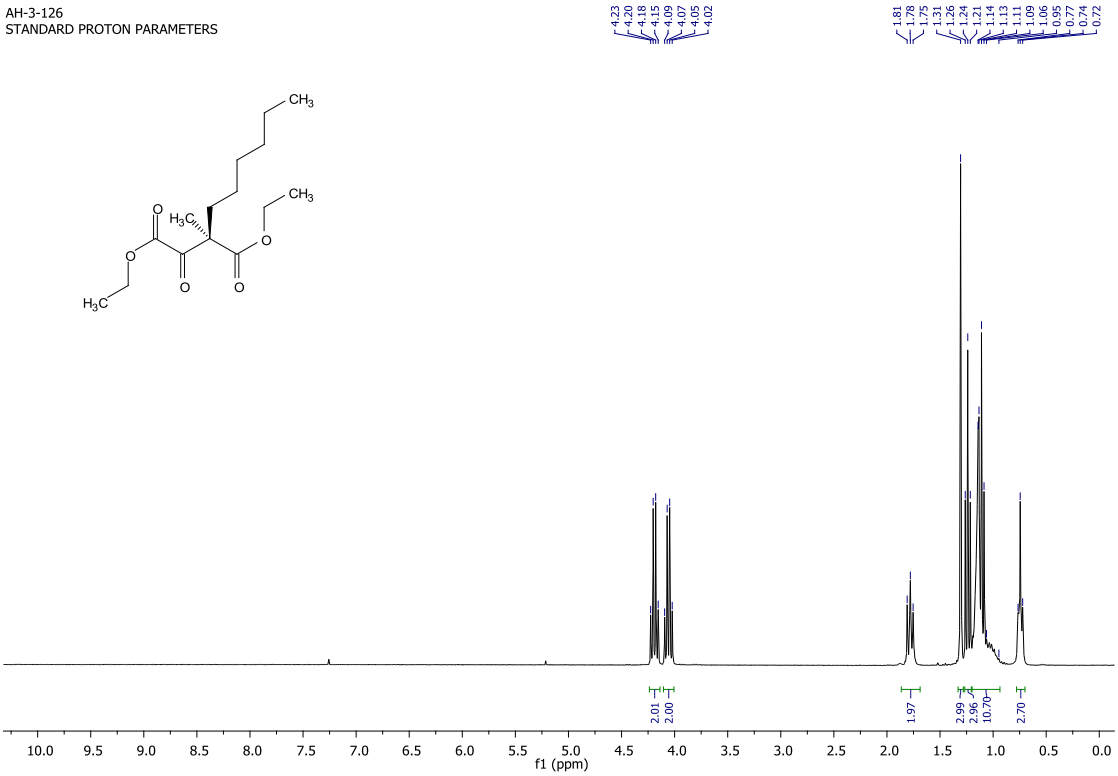
AH-3-118
STANDARD PROTON PARAMETERS

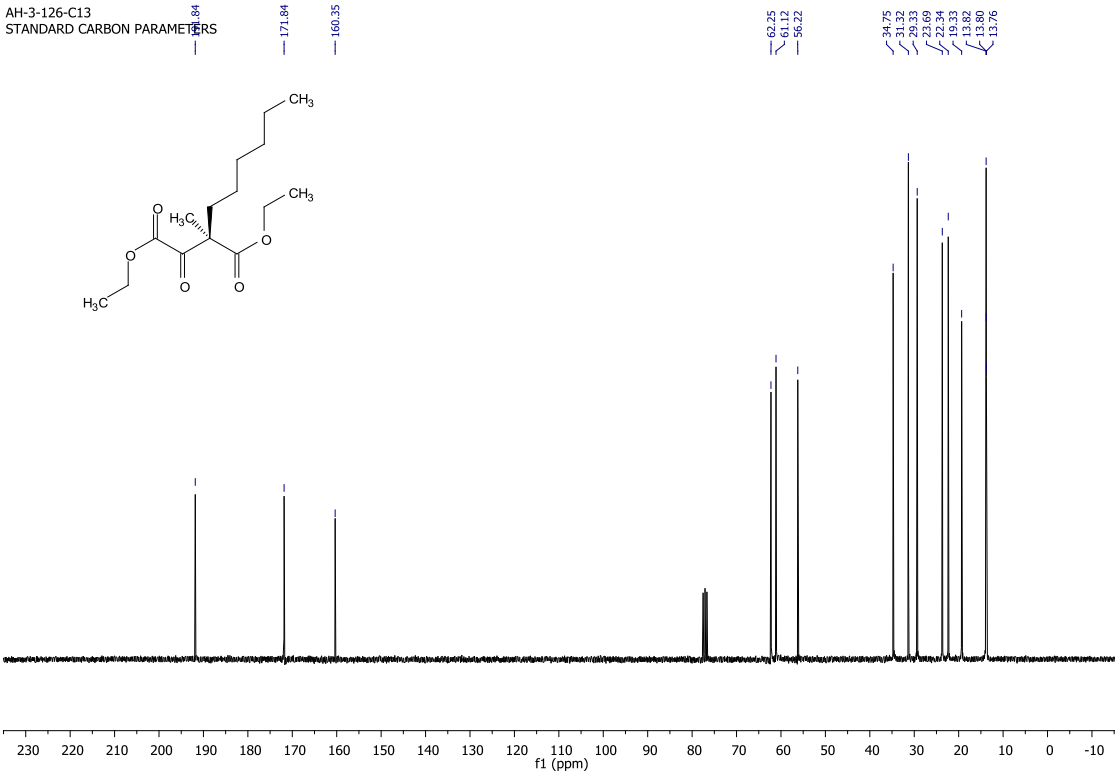



AH-3-118-C13
STANDARD CARBON PARAMETERS

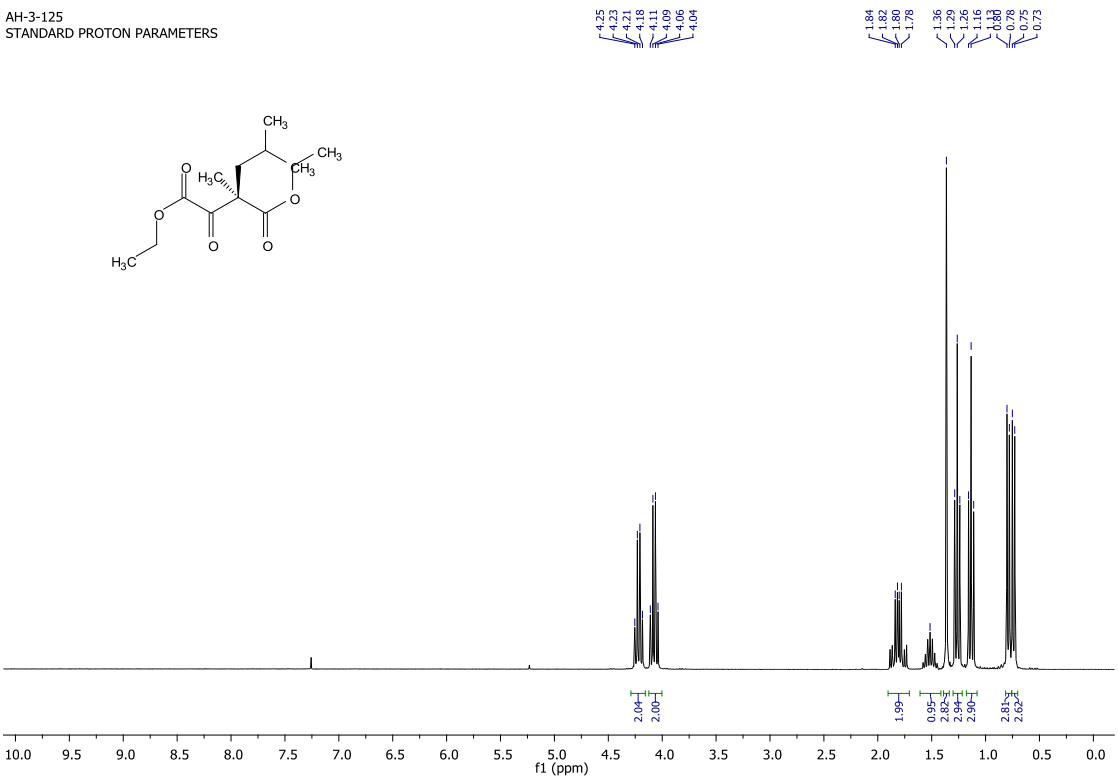


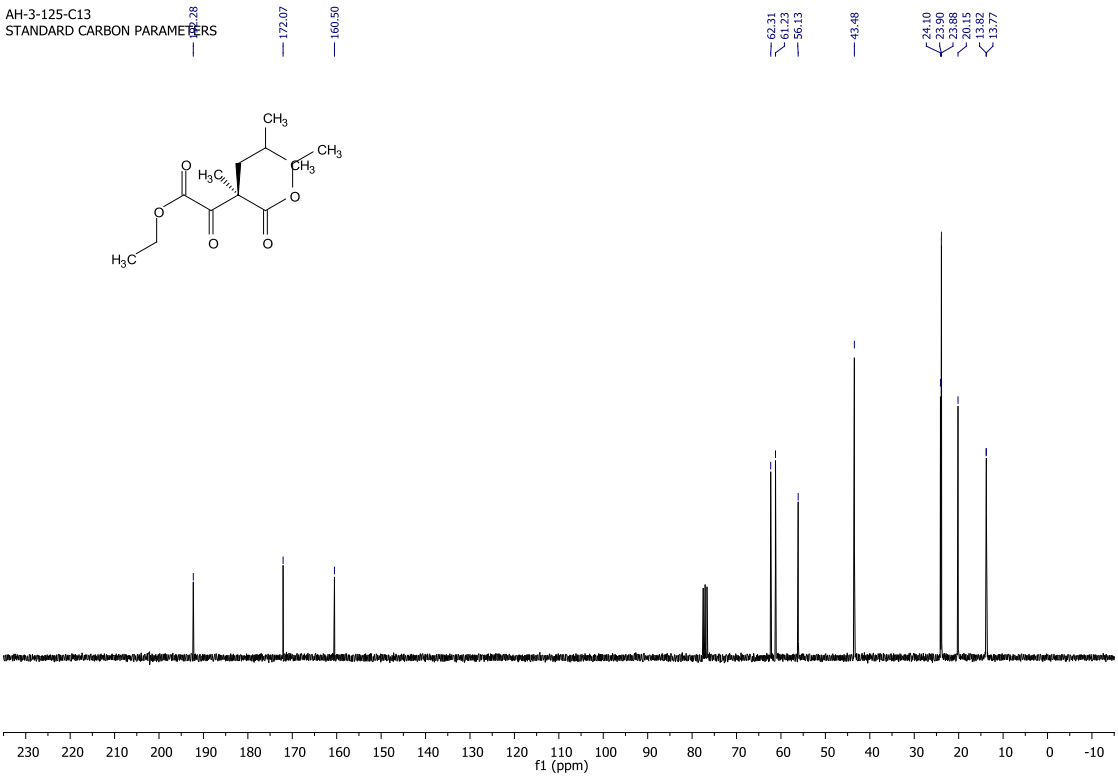
## Compound 6e


AH-3-126
STANDARD PROTON PARAMETERS
4.23
4.20
4.18
4.15
4.09
4.07
4.05
4.02
1.81
1.78
1.75
1.31
1.26
1.24
1.21
1.14
1.13
1.11
1.09
1.06
0.95
0.77
0.74
0.72
CH3
CH3
H3C
O
O
O
O
O
H3C
2.01
2.00
1.97
2.99
2.96
10.70
2.70
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

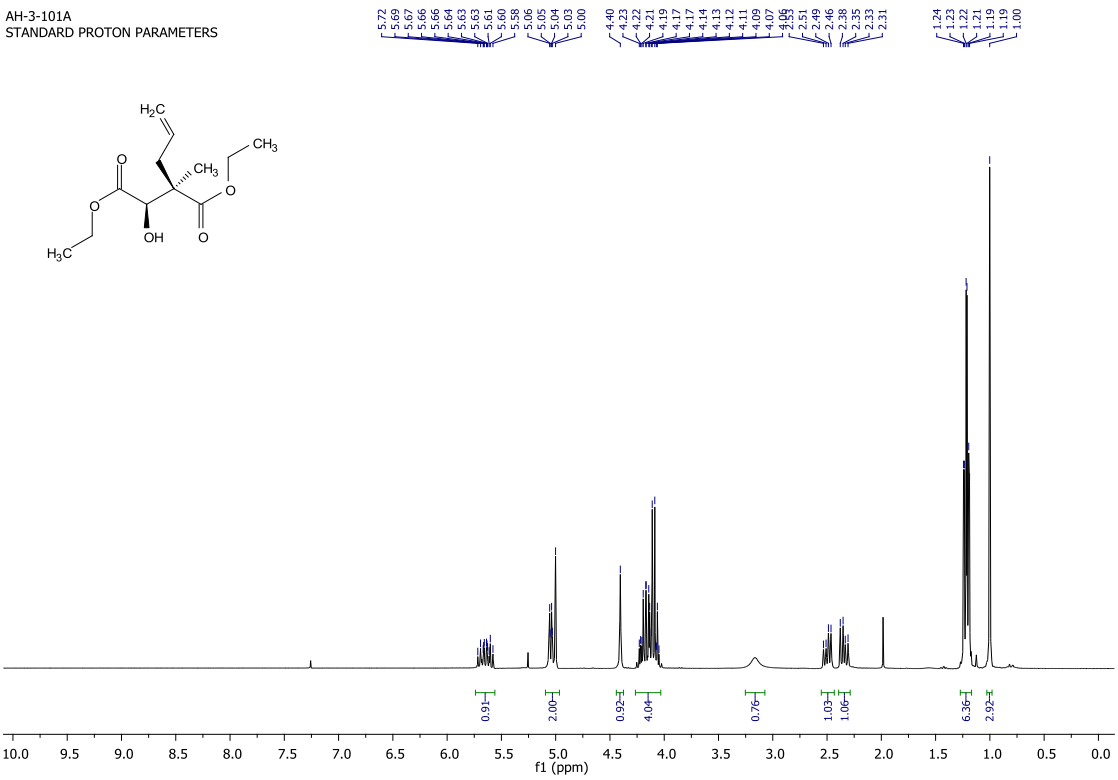

AH-3-126-C13
STANDARD CARBON PARAMETERS
171.84
171.84
160.35
62.25
61.12
56.22
34.75
31.32
29.33
23.69
22.34
19.33
13.82
13.80
13.76
CH3
CH3
H3C
O
O
O
O
O
H3C
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

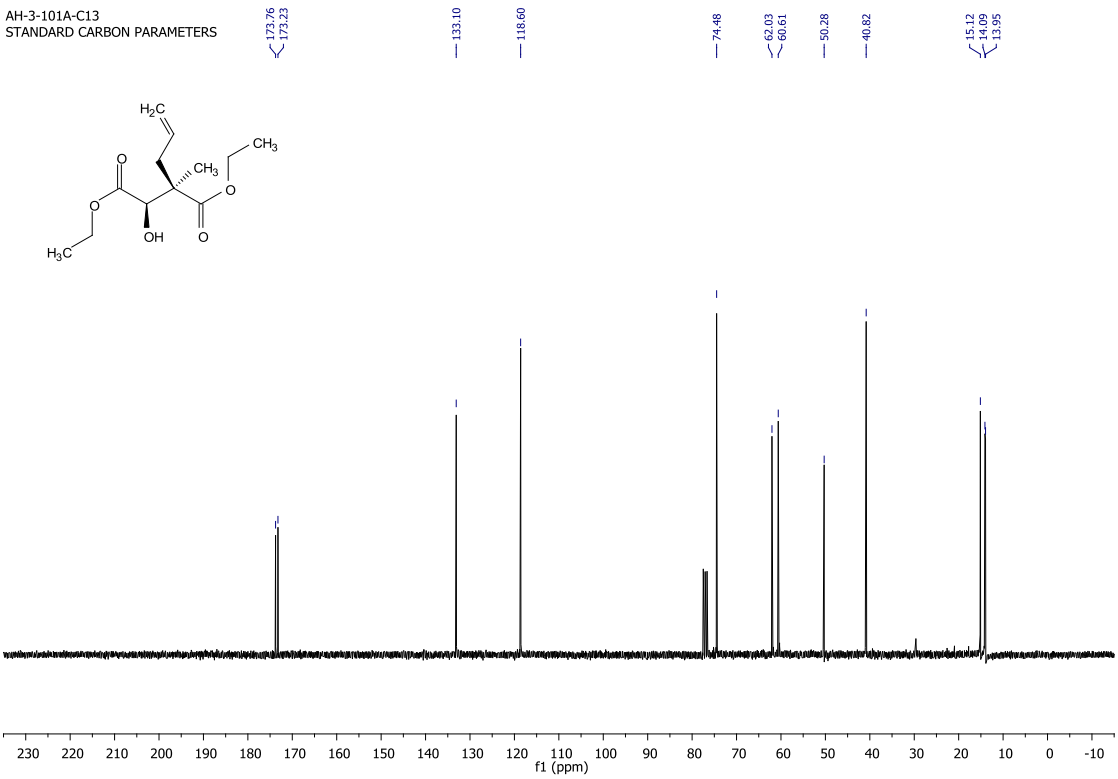
## Compound 6f


AH-3-125
STANDARD PROTON PARAMETERS
4.25
4.23
4.21
4.18
4.11
4.09
4.06
4.04
1.84
1.82
1.80
1.78
1.36
1.29
1.26
1.16
1.13
0.80
0.78
0.75
0.73
2.04
2.00
1.99
0.95
2.82
2.94
2.90
2.81
2.62
f1 (ppm)

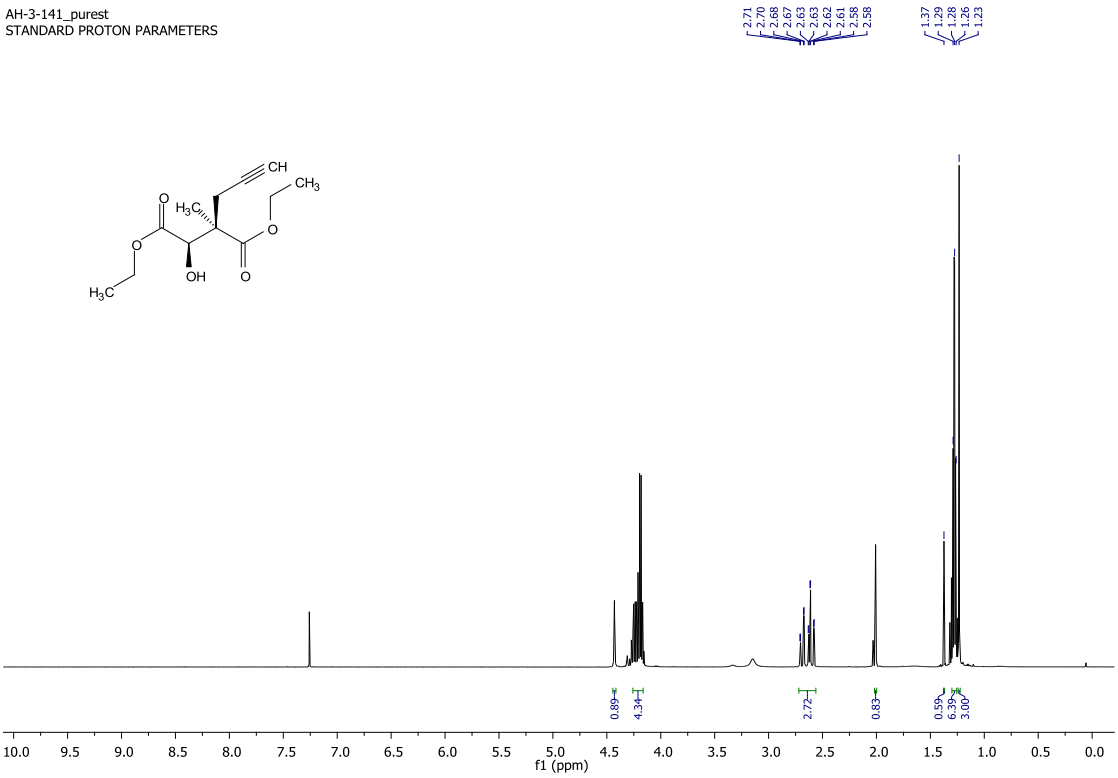

AH-3-125-C13
STANDARD CARBON PARAMETERS
172.07
160.50
62.31
61.23
56.13
43.48
24.10
23.90
23.88
20.15
13.82
13.77
f1 (ppm)

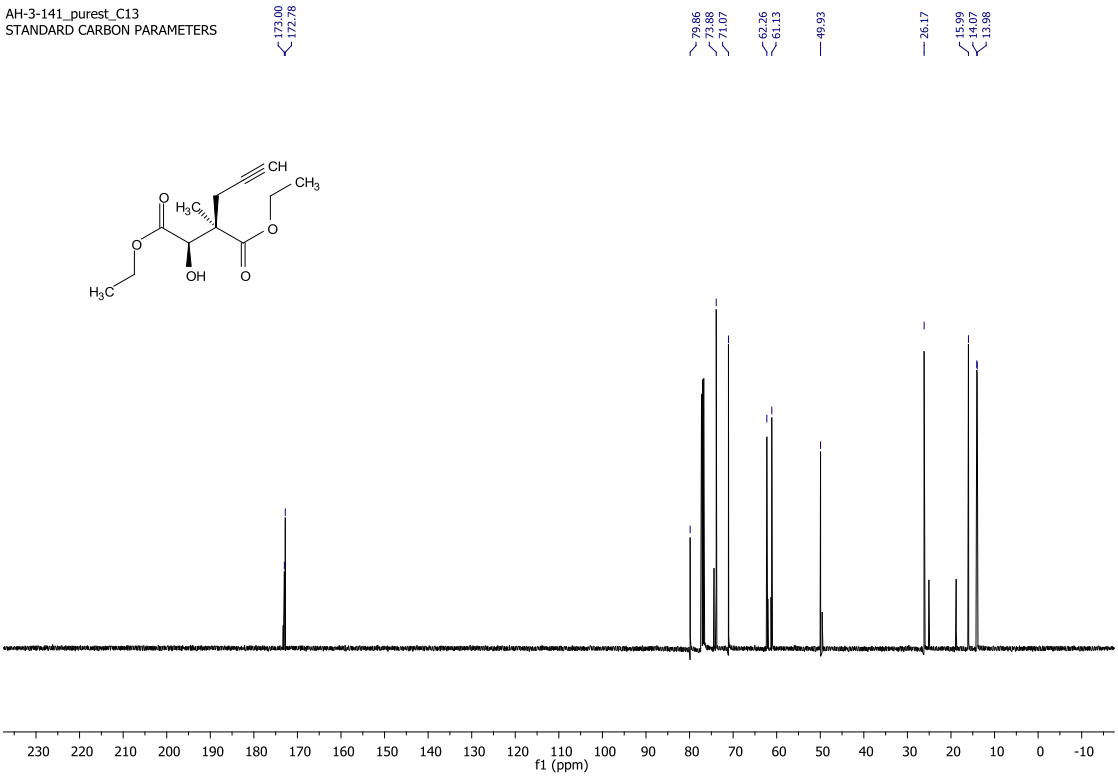
# Compound 7a


AH-3-101A
STANDARD PROTON PARAMETERS
f1 (ppm)

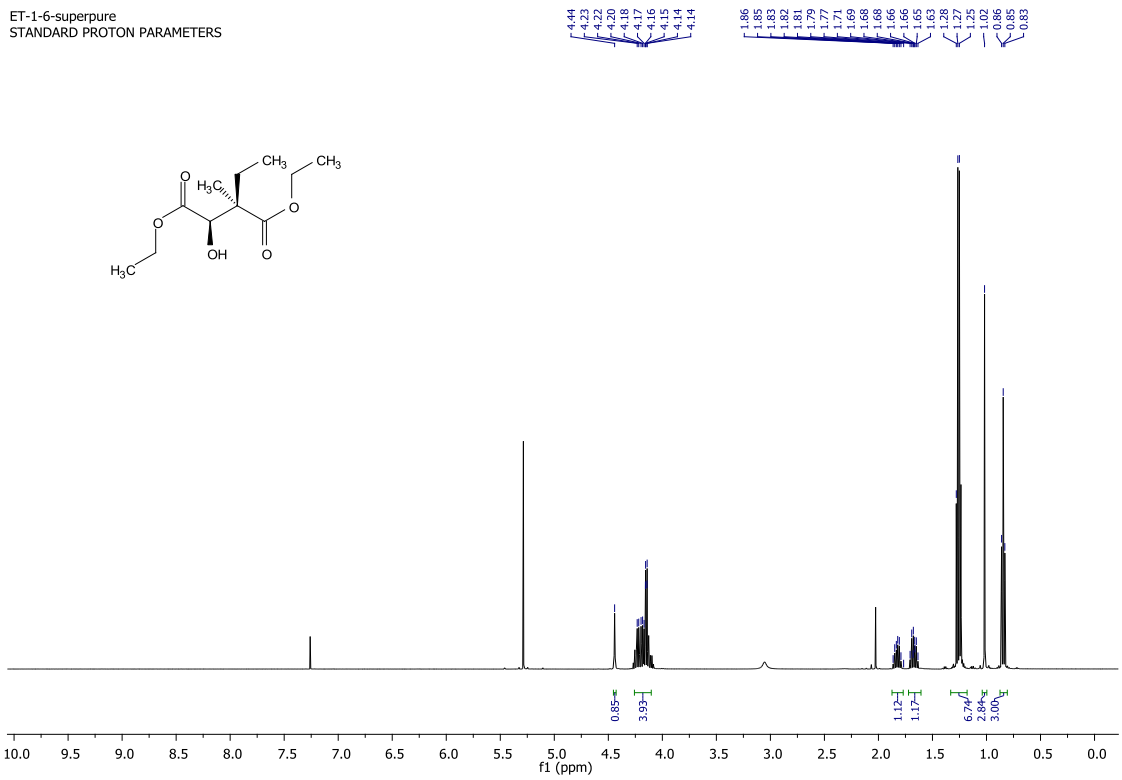

AH-3-101A-C13
STANDARD CARBON PARAMETERS
f1 (ppm)

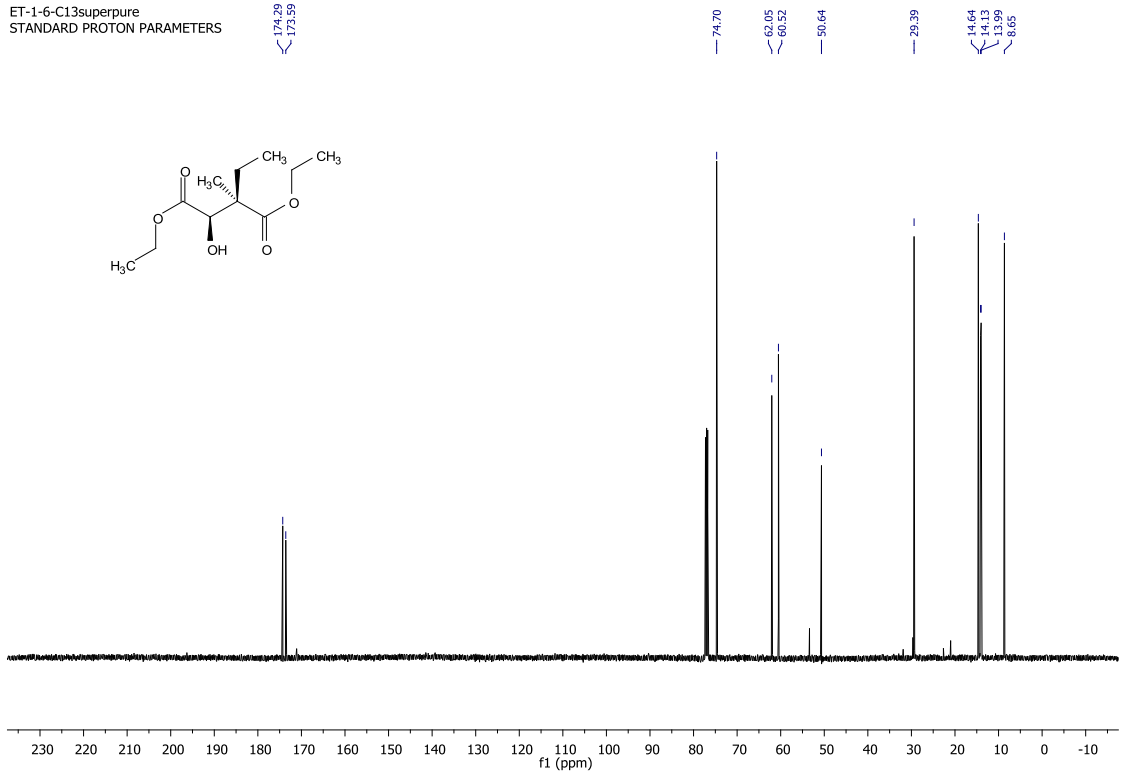
# Compound 7b


AH-3-141_purest
STANDARD PROTON PARAMETERS
2.71
2.70
2.68
2.67
2.63
2.63
2.62
2.61
2.58
2.58
1.37
1.29
1.28
1.26
1.23
CH
CH3
O
H3C
O
O
OH
O
H3C
0.89
4.34
2.72
0.83
0.59
6.39
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


AH-3-141_purest_C13
STANDARD CARBON PARAMETERS
173.00
172.78
79.86
73.88
71.07
62.26
61.13
49.93
26.17
15.99
14.07
13.98
CH
CH3
O
H3C
O
O
OH
O
H3C
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

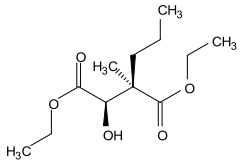
# Compound 7c


ET-1-6-superpure
STANDARD PROTON PARAMETERS
4.44
4.23
4.22
4.20
4.18
4.17
4.16
4.15
4.14
4.14
1.86
1.85
1.83
1.82
1.81
1.79
1.77
1.71
1.69
1.68
1.68
1.66
1.66
1.65
1.63
1.28
1.27
1.25
1.02
0.86
0.85
0.83
CH3
CH3
H3C
O
O
O
OH
O
H3C
0.85
3.93
1.12
1.17
6.74
2.84
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


ET-1-6-C13superpure
STANDARD PROTON PARAMETERS
174.29
173.59
74.70
62.05
60.52
50.64
29.39
14.64
14.13
13.99
8.65
CH3
CH3
H3C
O
O
O
OH
O
H3C
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

# Compound 7d

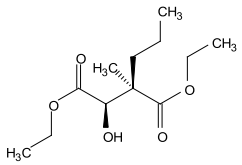
AH-3-140-pure
STANDARD PROTON PARAMETERS



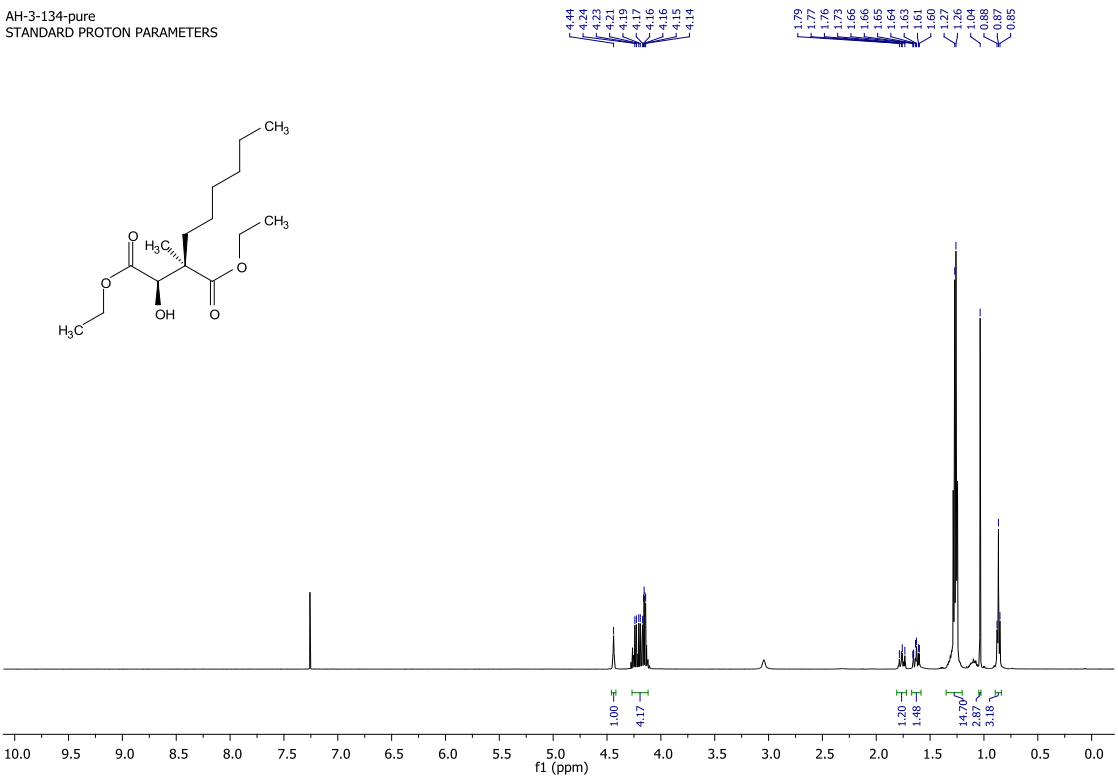


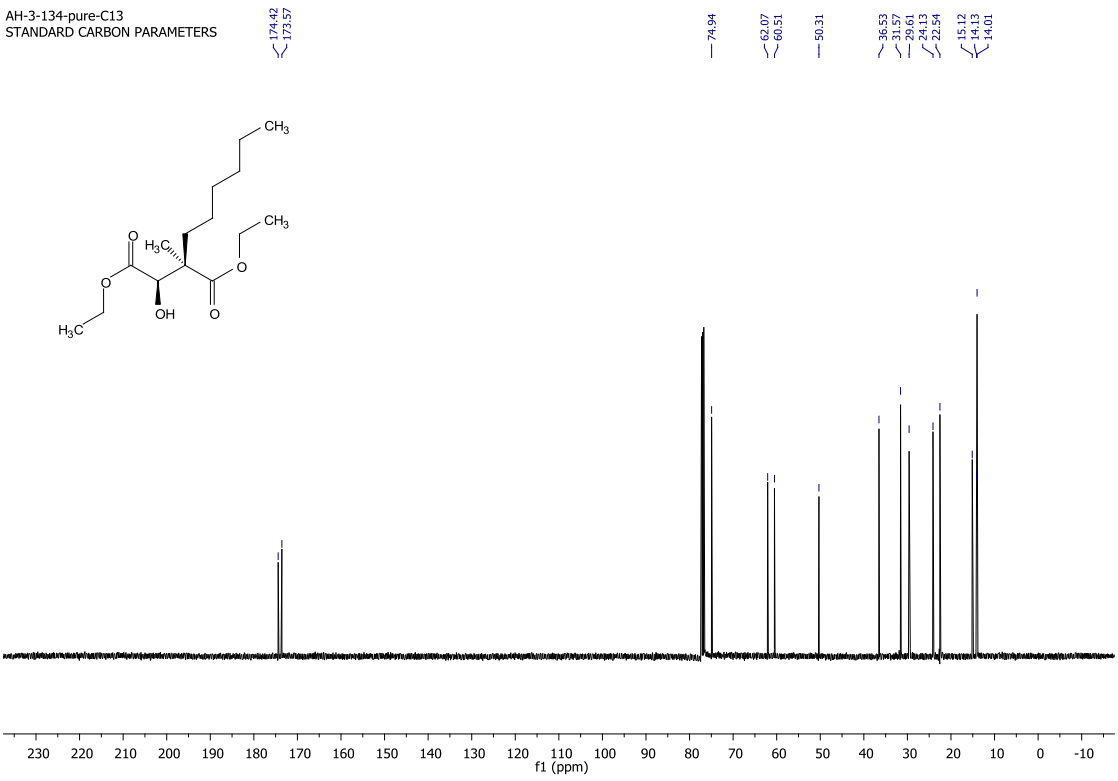


AH-3-140-pure-C13
STANDARD CARBON PARAMETERS

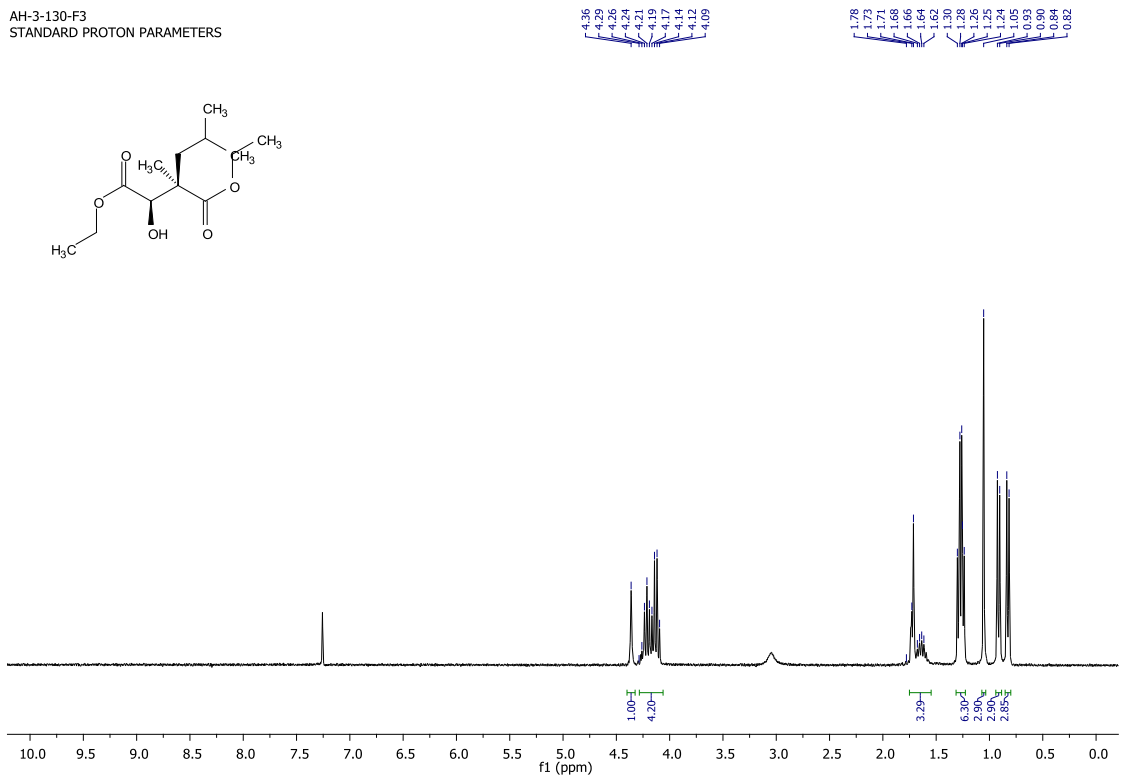


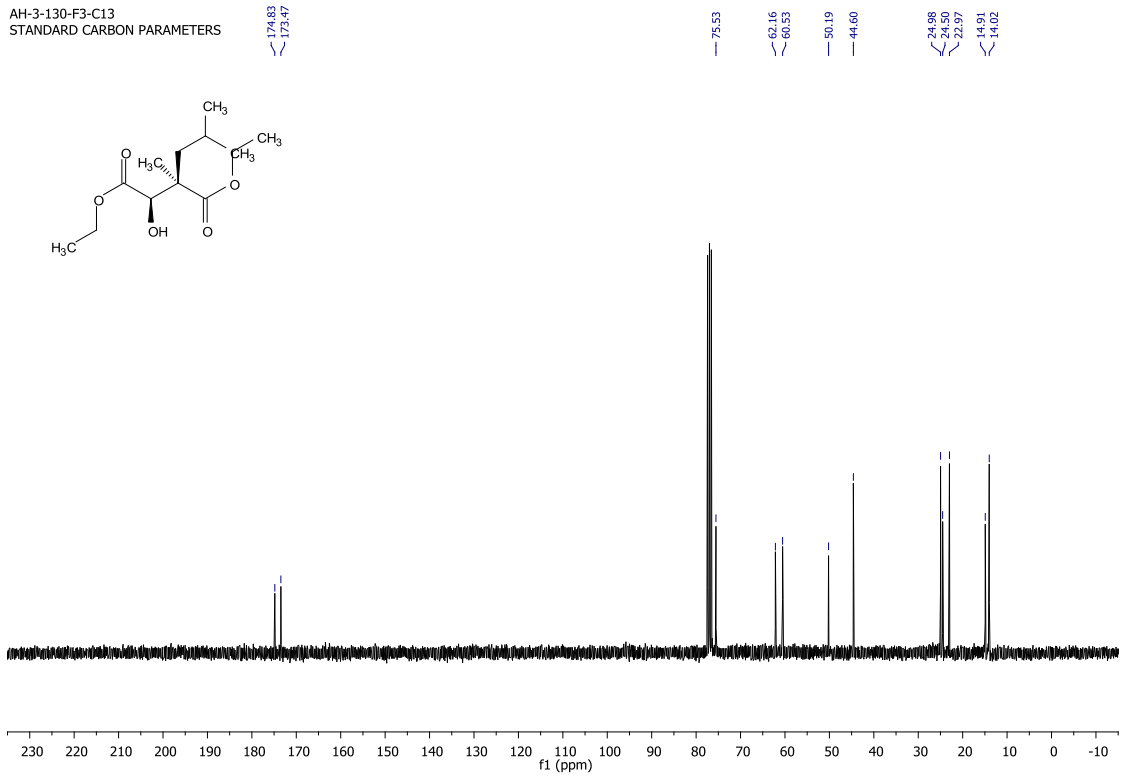
## Compound 7e


AH-3-134-pure
STANDARD PROTON PARAMETERS
4.44
4.24
4.23
4.21
4.19
4.17
4.16
4.16
4.15
4.14
1.79
1.77
1.76
1.73
1.66
1.66
1.65
1.64
1.63
1.61
1.60
1.27
1.26
1.04
0.88
0.87
0.85
CH3
CH3
O
H3C
O
O
OH
O
H3C
1.00
4.17
1.20
1.48
14.70
2.87
3.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

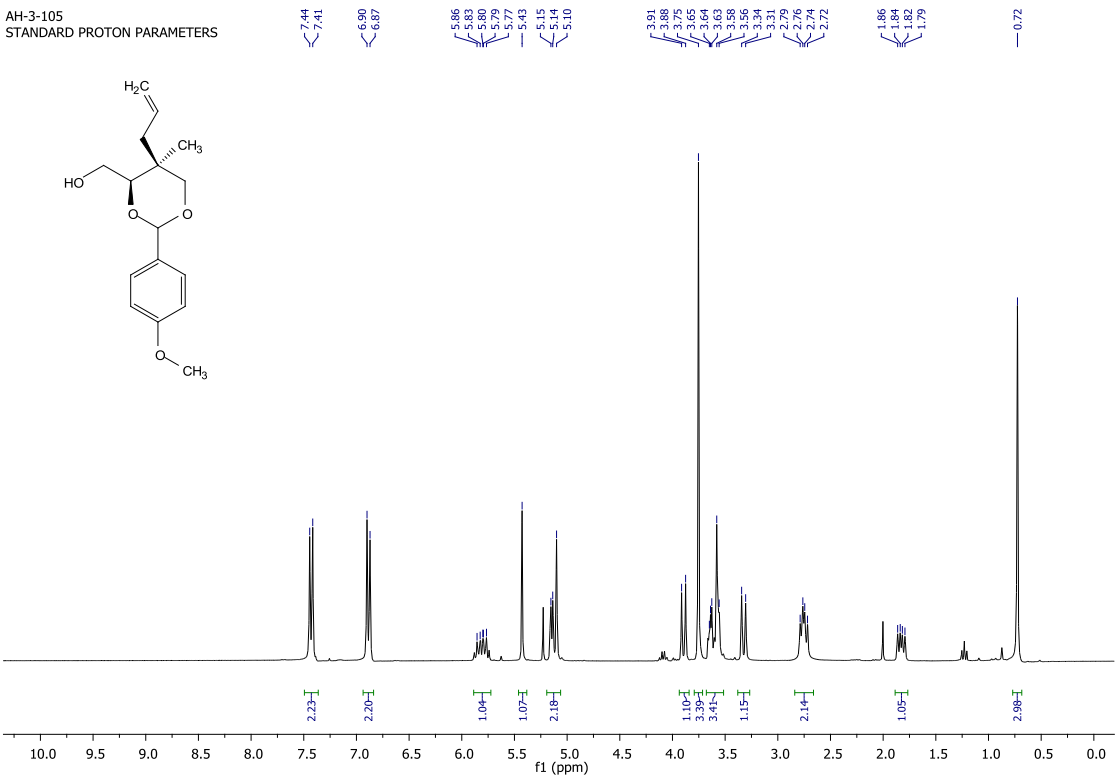

AH-3-134-pure-C13
STANDARD CARBON PARAMETERS
174.42
173.57
74.94
62.07
60.51
50.31
36.53
31.57
29.61
24.13
22.54
15.12
14.13
14.01
CH3
CH3
O
H3C
O
O
OH
O
H3C
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

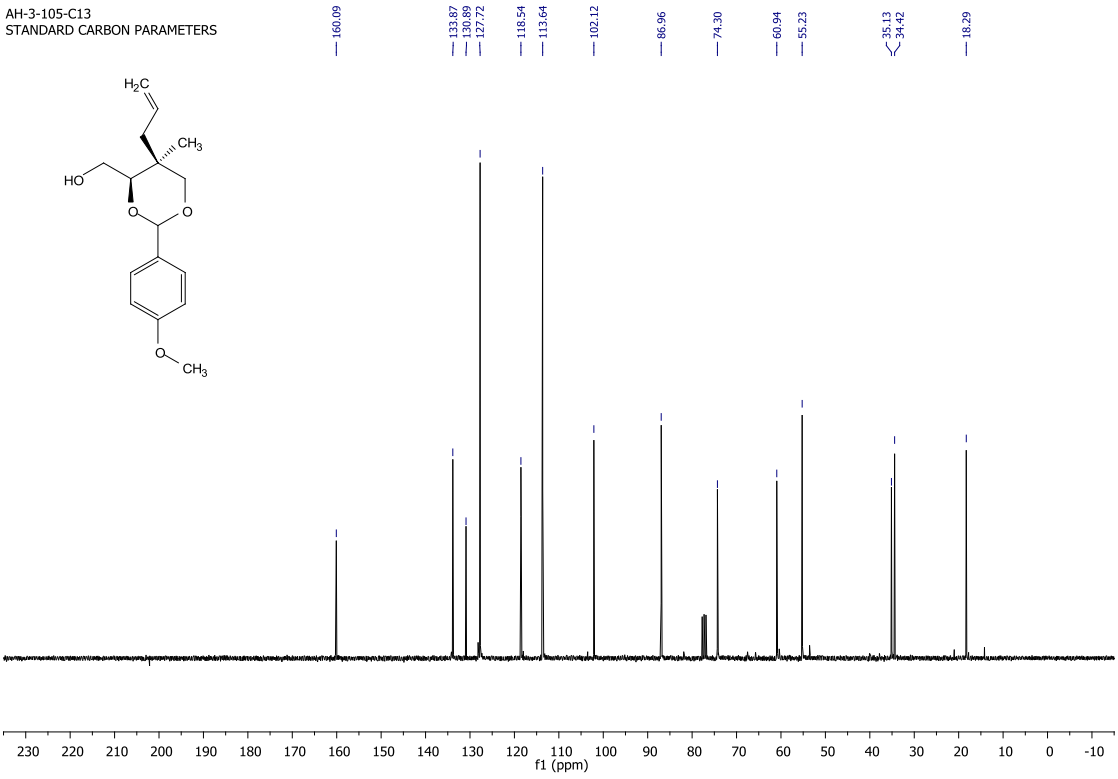
## Compound 7f


AH-3-130-F3
STANDARD PROTON PARAMETERS
4.36
4.29
4.26
4.24
4.21
4.19
4.17
4.14
4.12
4.09
1.78
1.73
1.71
1.68
1.66
1.64
1.62
1.30
1.28
1.26
1.25
1.24
1.05
0.93
0.90
0.84
0.82
1.00
4.20
3.29
6.30
2.90
2.90
2.85
f1 (ppm)

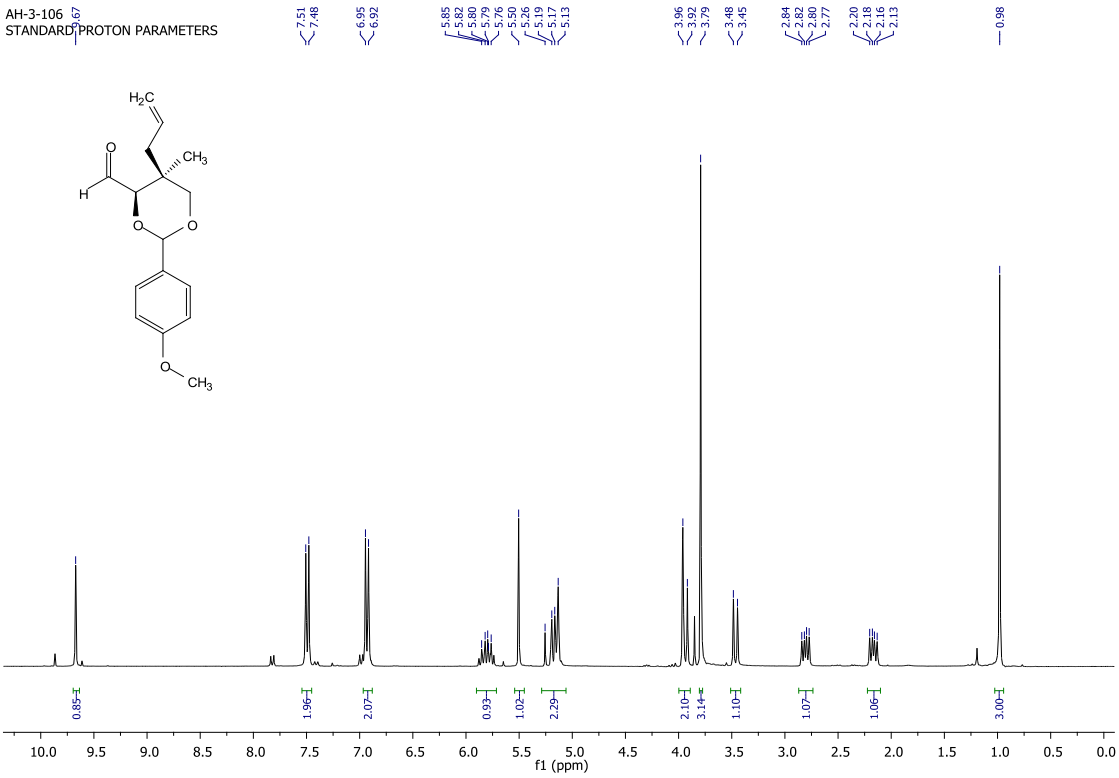

AH-3-130-F3-C13
STANDARD CARBON PARAMETERS
174.83
173.47
75.53
62.16
60.53
50.19
44.60
24.98
24.50
22.97
14.91
14.02
f1 (ppm)

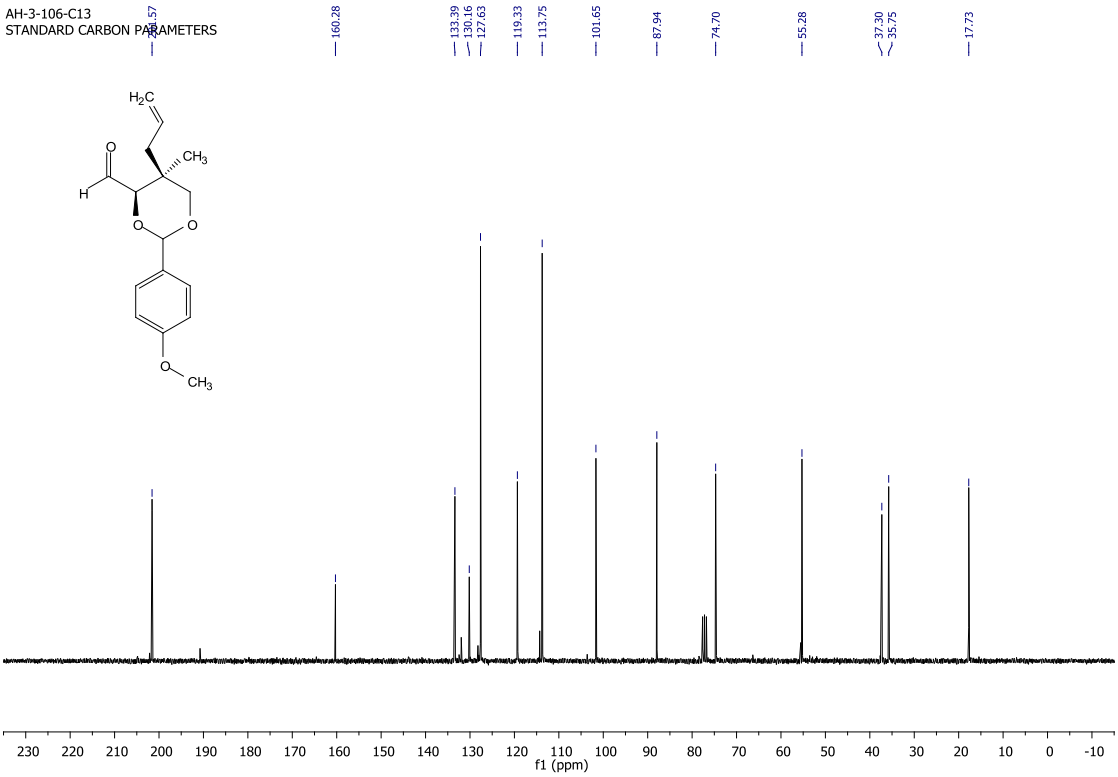
## Compound 8


AH-3-105
STANDARD PROTON PARAMETERS
7.44
7.41
6.90
6.87
5.86
5.83
5.80
5.79
5.77
5.43
5.15
5.14
5.10
3.91
3.88
3.75
3.65
3.64
3.63
3.58
3.56
3.34
3.31
2.79
2.76
2.74
2.72
1.86
1.84
1.82
1.79
0.72
H2C
CH3
HO
O
O
O
CH3
2.23
2.20
1.04
1.07
2.18
1.10
3.39
3.41
1.15
2.14
1.05
2.98
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

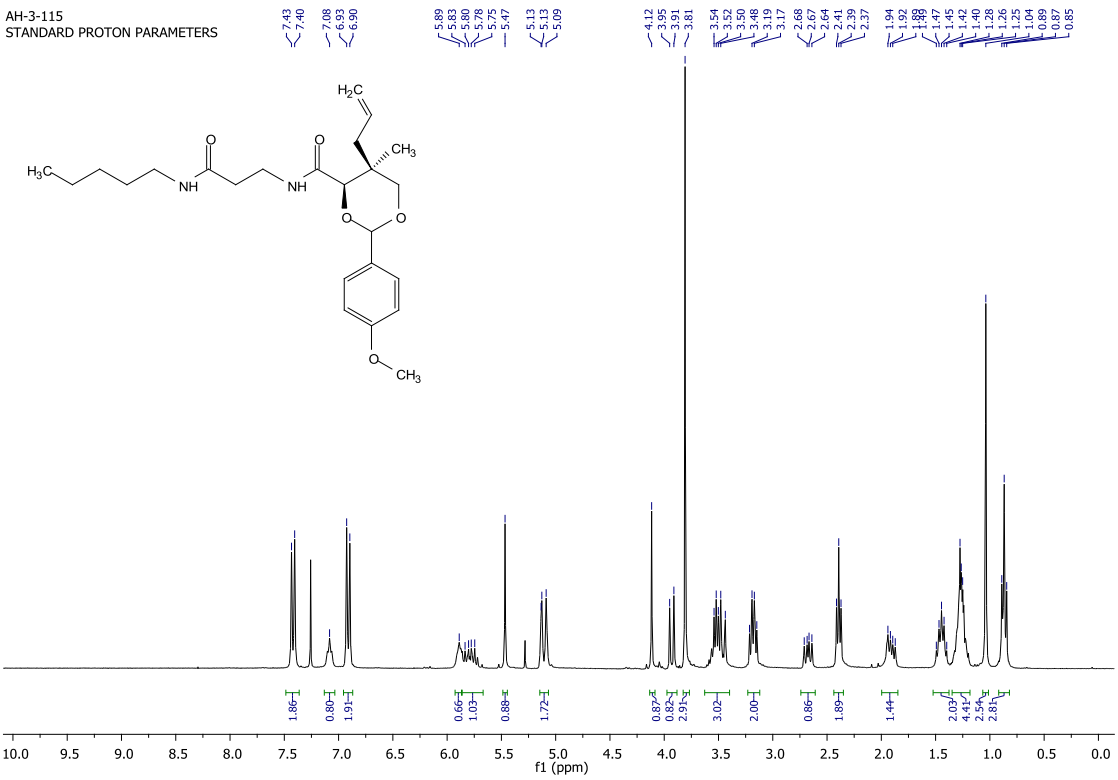

AH-3-105-C13
STANDARD CARBON PARAMETERS
160.09
133.87
130.89
127.72
118.54
113.64
102.12
86.96
74.30
60.94
55.23
35.13
34.42
18.29
H2C
CH3
HO
O
O
O
CH3
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

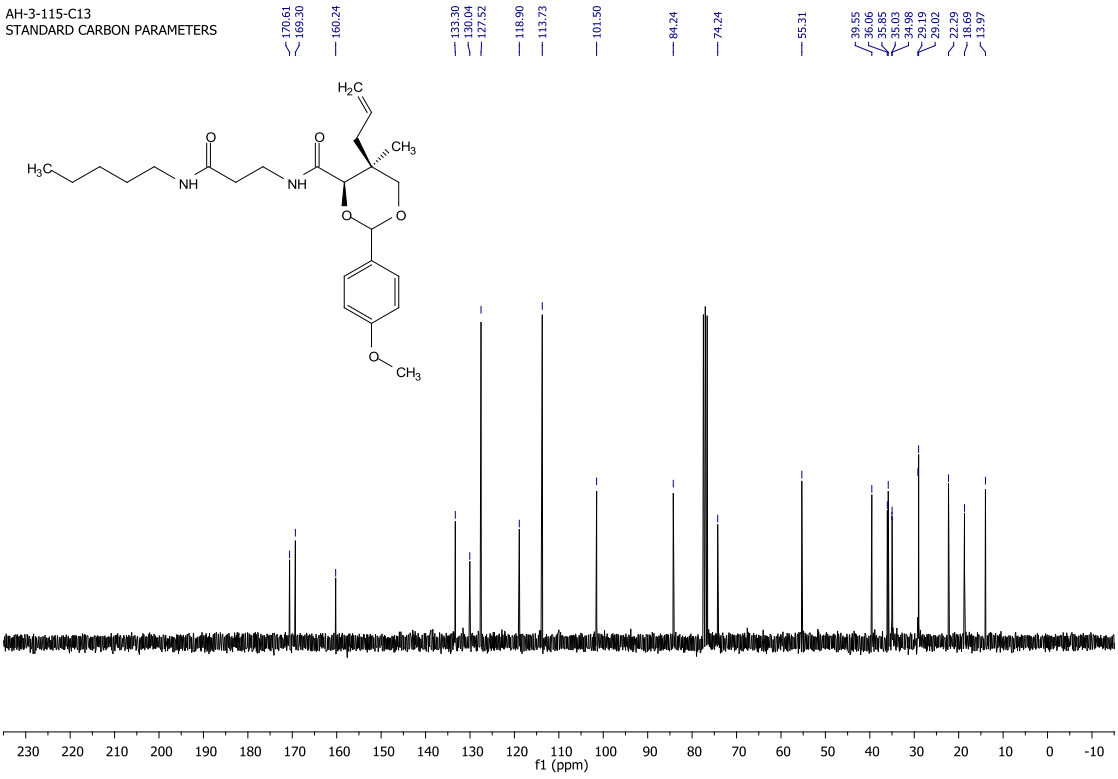
## Compound 9


AH-3-106
STANDARD PROTON PARAMETERS
9.67
7.51
7.48
6.95
6.92
5.85
5.82
5.80
5.79
5.76
5.50
5.26
5.19
5.17
5.13
3.96
3.92
3.79
3.48
3.45
2.84
2.82
2.80
2.77
2.20
2.18
2.16
2.13
0.98
0.85
1.96
2.07
0.93
1.02
2.29
2.10
3.14
1.10
1.07
1.06
3.00
f1 (ppm)

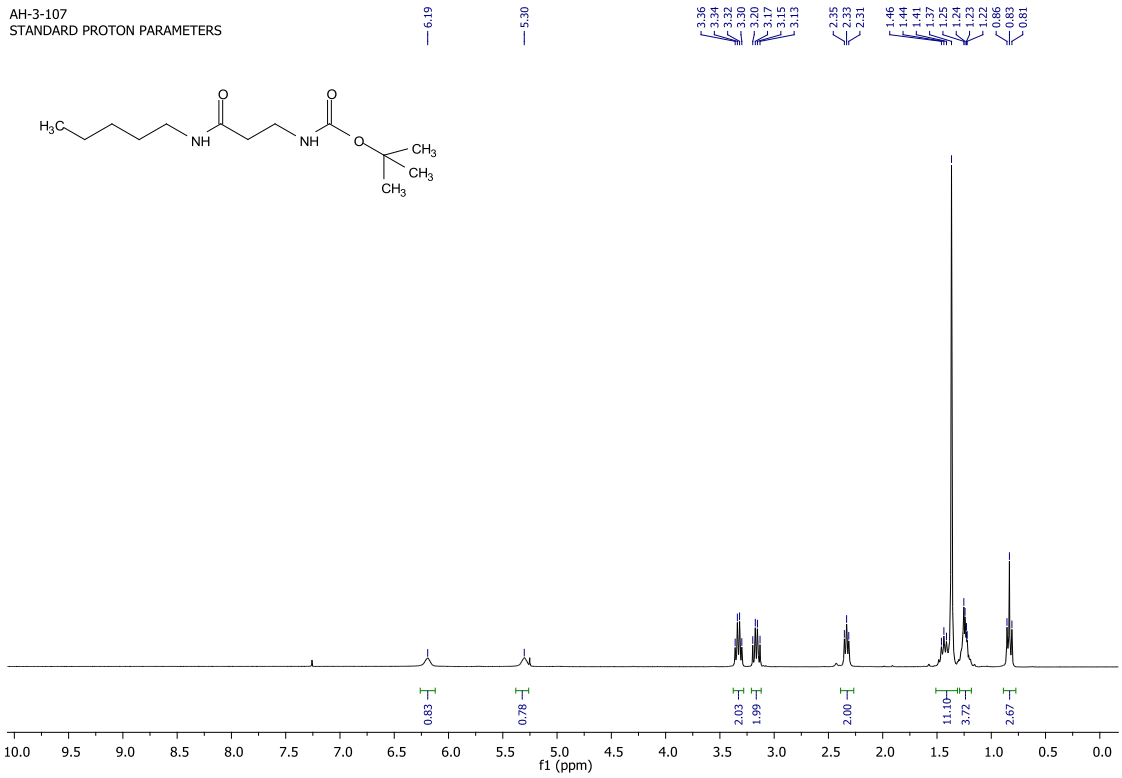

AH-3-106-C13
STANDARD CARBON PARAMETERS
160.28
133.39
130.16
127.63
119.33
113.75
101.65
87.94
74.70
55.28
37.30
35.75
17.73
f1 (ppm)

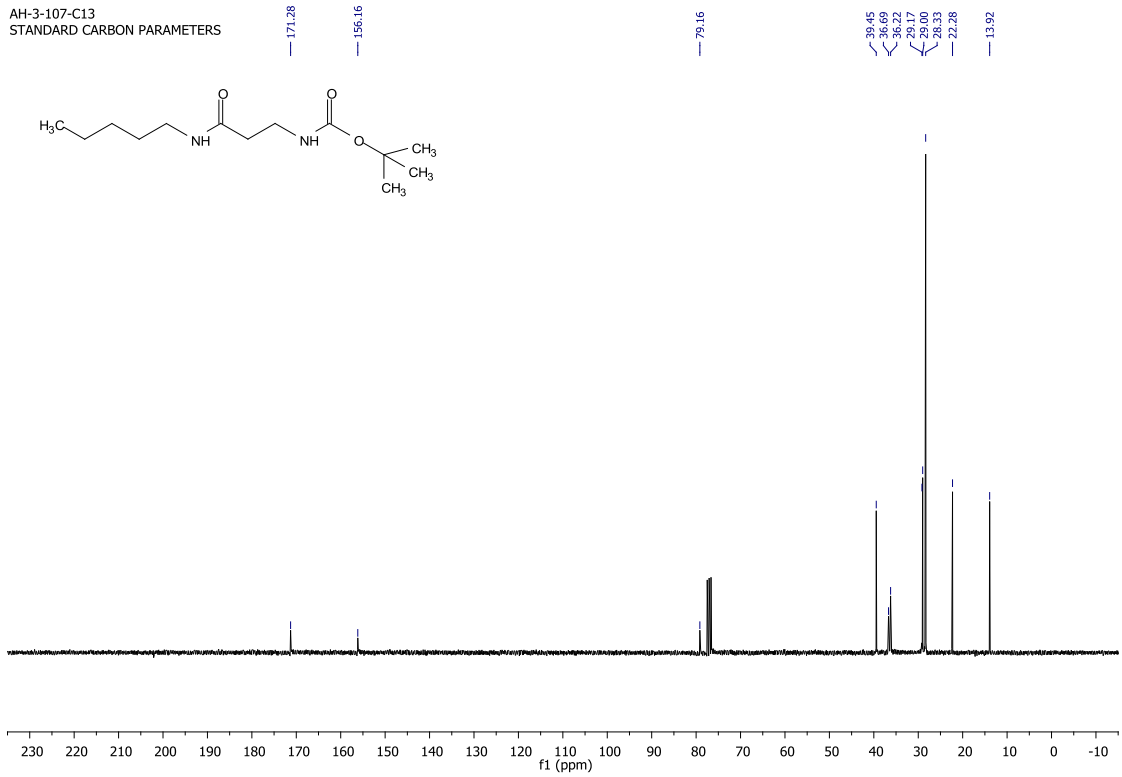
## Compound 11


AH-3-115
STANDARD PROTON PARAMETERS
f1 (ppm)


AH-3-115-C13
STANDARD CARBON PARAMETERS
f1 (ppm)

## Compound 12


AH-3-107
STANDARD PROTON PARAMETERS
6.19
5.30
3.36
3.34
3.32
3.30
3.20
3.17
3.15
3.13
2.35
2.33
2.31
1.46
1.44
1.41
1.37
1.25
1.24
1.23
1.22
0.86
0.83
0.81
0.83
0.78
2.03
1.99
2.00
11.10
3.72
2.67
f1 (ppm)


AH-3-107-C13
STANDARD CARBON PARAMETERS
171.28
156.16
79.16
39.45
36.69
36.22
29.17
29.00
28.33
22.28
13.92
f1 (ppm)

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