Enantioselective β-Protonation by a Cooperative Catalysis Strategy

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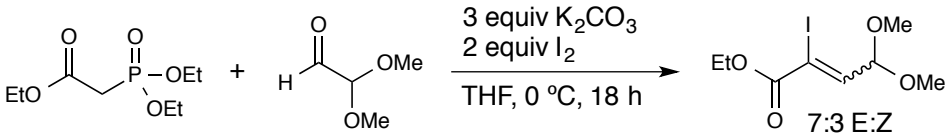
General Information

All reactions were carried out under a nitrogen atmosphere in oven-dried glassware with magnetic stirring. THF, toluene, and DMF were purified by passage through a bed of activated alumina.[1] Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.[2] 1,2-Dichloroethane (DCE) was distilled from CaH_2. Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and ceric ammonium nitrate stain or potassium permangenate stain followed by heating. Infrared spectra were recorded on a Bruker Tensor 37 FT-IR spectrometer. ^{1}H NMR spectra were recorded on AVANCE III 500 MHz w/ direct cryoprobe (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = apparent triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration.) Proton-decoupled ^{13}C NMR spectra were recorded on an AVANCE III 500 MHz w/ direct cryoprobe (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm). ^{19}F NMR spectra were acquired at 26 °C on a 400 MHz Agilent 400MR-DD2 spectrometer equipped with a OneNMR probe and a 7600AS autosampler; this system was funded by NSF CRIF grant CHE-104873. Optical rotations were measured on a Perkin Elmer Model 341 Polarimeter with a sodium lamp. Mass spectra were obtained on a WATERS Acquity-H UPLC-MS with a single quad detector (ESI) or on a Varian 1200 Quadrupole Mass Spectrometer and Micromass Quadro II Spectrometer (ESI).

Triazolium precatalyst **A** is commercially available. Co-catalyst **HBD3** was synthesized according to Taylor, et. al. [3]

General Procedure for the Synthesis of Vinyl Iodide



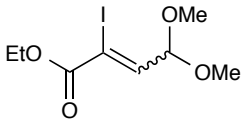
To a mixture of ethyl 2-(diethoxyphosphoryl)acetate (10 g, 44.6 mmol, 1 equiv), K_2CO_3 (18.49 g, 134 mmol, 3 equiv), and iodine (22.64 g, 89 mmol, 2 equiv) in THF (112 ml, 0.4 M) at 0 °C was added 2,2-dimethoxyacetaldehyde (60 wt. % in H_2O, 8.51 g, 49.1 mmol, 1.1 equiv) dropwise over 1 h. The mixture was allowed to warm to 23 °C overnight. Conversion was monitored by ^{1}H NMR ($CDCl_3$, 500 MHz). After complete

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers F. J., *Organometallics* **1996**, *15*, 1518-1520.

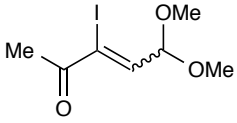
[2] Perrin, D. D.; Armarego, W. L. *Purification of Laboratory Chemicals;* 3rd Ed., Pergamon Press, Oxford. **1988**.

[3] Rostami, A.; Colin, A.; Li, X. Y.; Chudzinski, M. G.; Lough, A. J.; Taylor, M. S. *J. Org. Chem.* **2010**, *75*, 3983-3992.

conversion, the mixture was filtered through Celite and eluted with Et_2O. The organic phase was washed with saturated $Na_2S_2O_3$ solution, water, and brine, and then dried over Na_2SO_4 and concentrated. The crude mixture was purified by flash column chromatography on silica gel (10% EtOAc/hex; TLC 20% EtOAc/hex, UV, $KMnO_4$ or CAM, R_f 0.7) to afford ethyl 2-iodo-4,4-dimethoxybut-2-enoate (12.6 g, 41.9 mmol, 94%) as a clear yellow oil as a 7:3 mixture of Z:E isomers.

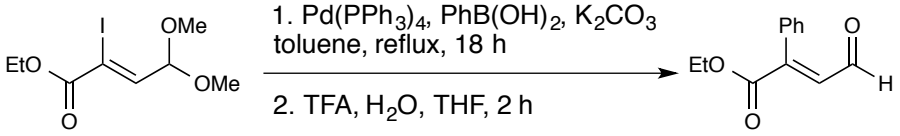


Ethyl 2-iodo-4,4-dimethoxybut-2-enoate: Prepared according to the general procedure using ethyl 2-(diethoxyphosphoryl)acetate (10 g, 44.6 mmol) and purified by flash column chromatography on silica gel (10% EtOAc/hex; TLC 20% EtOAc/hex, UV, $KMnO_4$ or CAM, R_f 0.7) to afford ethyl 2-iodo-4,4-dimethoxybut-2-enoate (12.6 g, 41.9 mmol, 94%) as a clear yellow oil as a 7:3 mixture of Z:E isomers. Analytical data: Z isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, J = 6.2 Hz, 1H), 5.03 (d, J = 6.2 Hz, 1H), 3.42 (s, 6H), 1.33 (t, J = 7.1 Hz, 3H). E isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (d, J = 6.0 Hz, 1H), 5.34 (d, J = 6.0 Hz, 1H), 3.36 (s, 6H), 1.34 (t, J = 5.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 162.6, 148.2, 146.5, 105.8, 100.6, 97.3, 89.3, 63.3, 62.7, 53.8, 53.7, 14.3, 14.1; IR (film) 2982, 2935, 2830, 1717, 1622, 1444, 1366, 1347, 1298, 1237, 1191, 1122, 1089, 1053,1033, 973, 912, 863, 748, 671, 639, 614, 606 cm^{-1}; LRMS (ESI): Mass calcd for $C_7H_{10}IO_3$ $[M\text{-}OMe]^+$: 269; found 269.



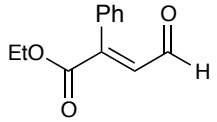
(Z)-3-iodo-5,5-dimethoxypent-3-en-2-one: Prepared according to the general procedure using diethyl (2-oxopropyl)phosphonate (2 g, 10.30 mmol, 1 equiv) and purified by flash column chromatography on silica gel (10% EtOAc/hex; TLC 20% EtOAc/hex, UV, $KMnO_4$, R_f 0.5) to afford 3-iodo-5,5-dimethoxypent-3-en-2-one (1.2 g, 4.32 mmol, 42%) as a clear yellow oil as a >20:1 mixture of Z:E isomers. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.97 (d, J = 6.0 Hz, 1H), 5.12 (d, J = 6.0 Hz, 1H), 3.44 (s, 6H), 2.52 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.6, 146.3, 113.0, 106.6, 54.2, 25.2; IR (film) 2996, 2934, 2831, 1687, 1613, 1442, 1354, 1222, 1190, 1126, 1057, 970 cm^{-1}; LRMS (ESI): Mass calcd for $C_6H_8IO_2$ $[M\text{-}OMe]^+$: 239; found 239.

General Procedure for the Synthesis of Unsaturated Aldehyde

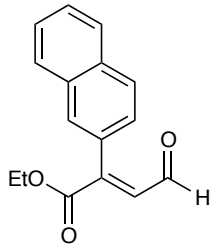


To a stirred suspension of (Z)-ethyl 2-iodo-4,4-dimethoxybut-2-enoate (3 g, 10.00 mmol, 1 equiv), phenylboronic acid (1.828 g, 15.00 mmol, 1.5 equiv), and K_2CO_3 (2.76 g, 19.99 mmol, 2 equiv) in toluene (50.0 ml, 0.2 M) under N_2 was added $Pd(PPh_3)_4$ (0.058 g, 0.050

mmol, 0.005 equiv) and the mixture was heated at reflux for 18 h and monitored by ^{1}H NMR ($CDCl_3$, 500MHz). When complete, the mixture was filtered through Celite and eluted with EtOAc. The filtrate was then washed with saturated $NaHCO_3$ solution and brine. Dried over Na_2SO_4 and concentrated. The oil was then passed through a plug of silica, eluting with 10% EtOAc/hex and concentrated to give ethyl 4,4-dimethoxy-2-phenylbut-2-enoate as a pale yellow oil, which was carried on without further purification. In a round-bottom flask equipped with stir bar and septum, the acetal was dissolved in THF (19.98 ml, 0.5 M) and H_2O (7.20 ml, 400 mmol, 40 equiv) was added. The mixture was cooled to 0 °C, and trifluoroacetic acid (7.70 ml, 100 mmol, 10 equiv) was added dropwise via syringe. The solution was allowed to warm to 23 °C, stirred for 2 h, and monitored by ^{1}H NMR ($CDCl_3$, 500 MHz). Once complete, the solution was diluted with Et_2O and carefully neutralized with saturated $NaHCO_3$ solution. The organic phase was separated, and the aqueous was extracted with Et_2O (2 x 25 mL). The organics were combined and washed with brine. The crude was dried over Na_2SO_4, concentrated, and purified by flash column chromatography (10% EtOAc/hex; TLC 20% EtOAc/hex, UV, CAM or KMnO4, R_f 0.6) to afford (E)-ethyl 4-oxo-2-phenylbut-2-enoate (1.0 g, 4.96 mmol, 50% over 2 steps) as a yellow solid. Note: Several of the enal substrates will solidify upon standing over a period of 2 weeks. This process can be rapidly accelerated by azeotroping the oil with Et_2O, and then placing the oil in a -30 °C freezer for 3-18 h.

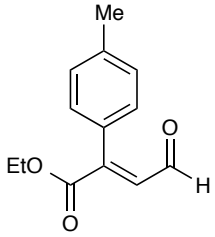


Ethyl (*E*)-4-oxo-2-phenylbut-2-enoate (1): Prepared according to the general procedure using phenylbronic acid (1.8 g, 15.0 mmol, 1.5 equiv) to afford 1.0 g (50% yield over 2 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.66 (d, *J* = 7.8 Hz, 1H), 7.56 – 7.42 (m, 3H), 7.42 – 7.35 (m, 2H), 7.01 (d, *J* = 7.8 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.68, 166.59, 149.66, 134.75, 131.91, 130.60(2C), 129.91, 128.37(2C), 62.40, 14.23; IR (film) 3059, 2983, 2939, 2850, 2757, 1721, 1682, 1608, 1574, 1495, 1466, 1444, 1390, 1369, 1340, 1299, 1175, 1106, 1025, 1000, 865, 782, 712, 696 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{13}O_3$ $[M+H]^+$: 205; found 205.

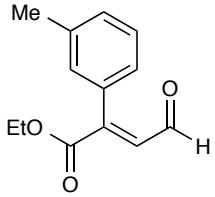


Ethyl (E)-2-(naphthalen-2-yl)-4-oxobut-2-enoate: Prepared according to the general procedure using naphthalen-2-ylboronic acid (1.72 g, 10 mmol, 1.5 equiv) to afford to afford 0.82 g (49% yield over 2 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.67 (d, *J* = 7.7 Hz, 1H), 7.94 – 7.83 (m, 3H), 7.85 – 7.77 (m, 1H), 7.62 – 7.53 (m, 2H), 7.47 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.7,

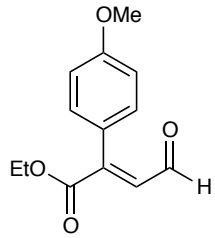
166.7, 149.7, 135.1, 133.7, 132.6, 131.1, 129.5, 128.5, 128.1, 127.9, 127.6, 127.14, 127.07, 62.5, 14.3; IR (film) 3060, 2983, 2932, 2906, 2852, 2749, 1721, 1679, 1600, 1505, 1469, 1446, 1391, 1370, 1325, 1241, 1209, 1185, 1164, 1130, 1102, 1035, 909, 863, 822, 779,732 cm^{-1}; LRMS (ESI): Mass calcd for $C_{16}H_{15}O_3$ $[M+H]^+$: 255; found 255.



Ethyl (*E*)-4-oxo-2-(*p*-tolyl)but-2-enoate: Prepared according to the general procedure using *p*-tolylboronic acid (0.997 g, 7.33 mmol, 1.1 equiv) to afford 0.9 g (62% yield over 2 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.64 (d, J = 7.8 Hz, 1H), 7.25 (m, 4H), 6.94 (d, J = 7.8 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 166.8, 149.7, 140.3, 134.4, 130.7(2C), 129.1(2C), 129.0, 62.3, 21.5, 14.2; IR (film) 3030, 2982, 2940, 2923, 2848, 2755, 1721, 1682, 1612, 1476, 1390, 1338, 1280, 1107, 1094, 1001, 829, 732 cm^{-1}; LRMS (ESI): Mass calcd for $C_{13}H_{15}O_3$ $[M+H]^+$: 219; found 219.

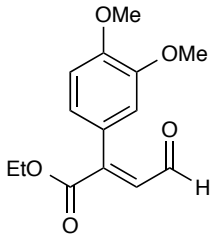


Ethyl (*E*)-4-oxo-2-(*m*-tolyl)but-2-enoate: Prepared according to the general procedure using *m*-tolylboronic acid (1.994 g, 14.66 mmol, 1.1 equiv) to afford 1.1 g (38% yield over 2 steps) of product as a yellow solid. Analytical data: 1H NMR (500 MHz, $CDCl_3$) δ 9.64 (d, J = 7.7 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H), 7.31 – 7.26 (m, 1H), 7.16 (d, J = 8.5 Hz, 2H), 6.96 (d, J = 7.8 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 2.41 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); 13C NMR (126 MHz, $CDCl_3$) δ 193.8, 166.7, 149.9, 138.2, 134.6, 131.8, 131.2, 130.7, 128.3, 127.8, 62.4, 21.5, 14.2; IR (film) 3058, 2982, 2940, 2923, 2849, 2754, 1720, 1687, 1559, 1582, 1389, 1344, 1334, 1238, 1151, 1109, 1037, 999, 861, 797, 724, 683 cm^{-1}; LRMS (ESI): Mass calcd for $C_{13}H_{15}O_3$ $[M+H]^+$: 219; found 219.

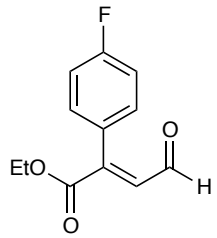


Ethyl (E)-2-(4-methoxyphenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (4-methoxyphenyl)boronic acid (0.608 g, 0.40 mmol, 1.2 equiv) to afford 0.448 g (58% yield over 2 steps) of product as a yellow oil. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.66 (d, J = 7.8 Hz, 1H), 7.31 (d, J = 8.8 Hz, 2H), 6.94 (dd, J

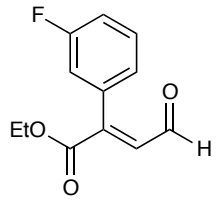
= 18.8, 8.3 Hz, 3H), 4.32 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.7, 193.5, 168.8, 153.6, 135.7, 134.7, 134.1, 129.0(2C), 128.8(2C), 62.1, 52.8, 31.6, 14.1; IR (film) 2982, 2962, 2937, 2900, 2841, 2755, 1719,1675, 1605, 1569, 1512, 1464, 1443, 1389, 1369, 1338, 1294, 1242, 1174, 1107, 1027, 910, 837, 772 cm^{-1}; LRMS (ESI): Mass calcd for $C_{13}H_{15}O_4$ $[M+H]^+$: 235; found 235.



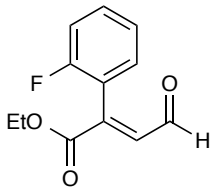
Ethyl (E)-2-(3,4-dimethoxyphenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (3,4-dimethoxyphenyl)boronic acid (1.09 g, 6 mmol, 1.2 equiv) to afford 483 mg (36% yield over 2 steps) of product as a yellow oil. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.66 (d, J = 7.6 Hz, 1H), 6.95 – 6.87 (m, 4H), 4.33 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 166.9, 150.8, 149.2, 148.7, 134.2, 124.6, 124.4, 113.3, 110.6, 62.3, 56.1, 14.3; IR (film) 2985, 2963, 2937, 2906,2840, 1720, 1676, 1600, 1579, 1516, 1464, 1388, 1369, 1350, 1321, 1259, 1144, 1108, 1025, 914, 865, 816, 778, 731, 635 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{17}O_5$ $[M+H]^+$: 265; found 265.



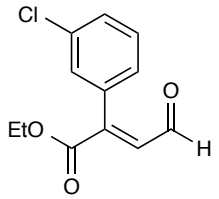
Ethyl (E)-2-(4-fluorophenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (4-fluorophenyl)boronic acid (0.513 g, 3.67 mmol, 1.1 equiv) to afford 0.435 g (59% yield over 2 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.66 (d, J = 7.8 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.22 – 7.11 (m, 2H), 7.02 (d, J = 7.7 Hz, 1H), 4.35 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.2, 166.4, 163.7 (d, $J_{C\text{-}F}$ = 250.9 Hz), 148.3, 135.0(2C), 132.6 (2C, d, $J_{C\text{-}F}$ = 8.4 Hz), 127.9 (d, $J_{C\text{-}F}$ = 3.5 Hz), 115.6 (d, $J_{C\text{-}F}$ = 21.9 Hz), 62.5, 14.2; ^{19}F NMR (376 MHz; $CDCl_3$): δ –110.5 (m); IR (film) 3108, 3075, 2985, 2938, 2917, 2850, 2758, 1723, 1684, 1601, 1508, 1472, 1447, 1394, 1369, 1338, 1301, 1242, 1176, 1163, 1106, 1031, 1015, 981, 866, 843, 772, 738 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{12}O_3F$ $[M+H]^+$: 223; found 223.



Ethyl (E)-2-(3-fluorophenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (3-fluorophenyl)boronic acid (0.466 g, 3.33 mmol, 1.0 equiv) to afford 0.384 g (52% yield over 2 steps) of product as a yellow oil. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.64 (d, J = 7.8 Hz, 1H), 7.42 (m, 1H), 7.22 – 7.07 (m, 3H), 7.00 (d, J = 7.8 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.1, 166.0, 162.4 (d, $J_{C\text{-}F}$ = 248.0 Hz), 148.1 (d, $J_{C\text{-}F}$ = 2.1 Hz), 135.3, 133.8 (d, $J_{C\text{-}F}$ = 8.1 Hz), 130.0 (d, $J_{C\text{-}F}$ = 8.4 Hz), 126.5 (d, $J_{C\text{-}F}$ = 3.1 Hz), 117.5 (d, $J_{C\text{-}F}$ = 22.8 Hz), 117.0 (d, $J_{C\text{-}F}$ = 21.1 Hz), 62.6, 14.2; ^{19}F NMR (376 MHz; $CDCl_3$): δ –112.3 (m); IR (film) 3070, 2984, 2939, 2917, 2850, 2757, 2727, 1722, 1683, 1608, 1582, 1487, 1440, 1391, 1369, 1343, 1300, 1244, 1143, 1104, 1033, 1002, 906, 881, 795, 765, 726, 684 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{12}O_3F$ $[M+H]^+$: 223; found 223.

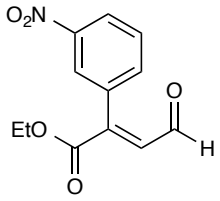


Ethyl (E)-2-(2-fluorophenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (2-fluorophenyl)boronic acid (0.466 g, 3.33 mmol, 1.0 equiv) to afford 0.322 g (44% yield over 2 steps) of product as a yellow oil. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.64 (dd, J = 7.9, 1.5 Hz, 1H), 7.50 – 7.44 (m, 1H), 7.30 – 7.27 (m, 1H), 7.23 (td, J = 7.5, 1.0 Hz, 1H), 7.20 – 7.15 (m, 1H), 7.06 (d, J = 7.9 Hz, 1H), 4.32 (q, J = 7.1 Hz, 2H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.8, 165.7, 161.1, 159.1, 144.1, 136.1, 132.5, 132.5, 124.2, 124.2, 116.2, 116.0, 62.5, 14.2; IR (film) 2983, 2939, 2906, 2849, 1721, 1682, 1488, 1449, 1242, 1220, 1174, 1153, 1111, 1096, 1026, 837, 758, 748, 693 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{12}FO_3$ $[M+H]^+$: 223; found 223.

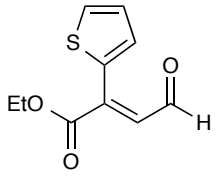


Ethyl (E)-2-(3-chlorophenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (3-chlorophenyl)boronic acid (0.860 g, 5.5 mmol, 1.1 equiv) to afford 0.620 g (52% yield over 2 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 (d, J = 7.8 Hz, 1H), 7.45 (d, J = 8.7 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.23 (d, J = 7.6 Hz, 1H), 7.01 (d, J = 7.8 Hz, 1H), 4.33 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.0, 166.0, 148.0, 135.4, 134.6, 133.6, 130.4, 130.0, 129.7, 128.8, 62.6, 14.2; IR (film) 3067, 2983, 2938, 2906, 2850, 2754,

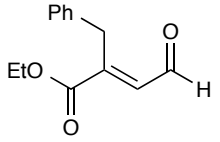
1722, 1681, 1243, 1199, 1178, 1110, 1032 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{12}ClO_3$ $[M+H]^+$: 239; found 239.



Ethyl (E)-2-(3-nitrophenyl)-4-oxobut-2-enoate: Prepared according to the general procedure using (3-nitrophenyl)boronic acid (1.40 g, 8.4 mmol, 1.2 equiv) to afford 1.03 g (60% yield over 2 steps) of product as a yellow solid. Analytical data: ^1H NMR (500 MHz; $CDCl_3$): δ 9.63 (d, J = 7.8 Hz, 1H), 8.34 (dt, J = 7.2, 2.2 Hz, 1H), 8.26 (m, 1H), 7.72-7.60 (m, 2H), 7.11 (d, J = 7.8 Hz, 1H), 4.34 (q, J = 7.1 Hz, 2H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 192.1, 165.5, 148.1, 146.6, 136.4, 136.1, 133.5, 129.6, 125.3, 124.6, 62.9, 14.2; IR (film) 3115, 3086, 2984, 2941, 2907, 2873, 2759, 1772, 1723, 1681, 1524, 1465, 1431, 1303, 1235, 1186, 1127, 1033, 1001, 908, 864, 811, 801, 772, 723, 689, 616 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{11}NO_5$ $[M+H]^+$: 249; found 249.

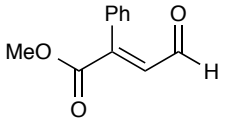


Ethyl (Z)-4-oxo-2-(thiophen-2-yl)but-2-enoate: Prepared according to the general procedure using thiophen-2-ylboronic acid (1.02 g, 8.0 mmol, 1.2 equiv) to afford 0.716 g (51% yield over 2 steps) of product as a yellow solid. Analytical data: ^1H NMR (500 MHz, $CDCl_3$) δ 9.87 (d, J = 7.4 Hz, 1H), 7.63 (dd, J = 5.2, 1.2 Hz, 1H), 7.27 (d, J = 1.3 Hz, 1H), 7.13 (dd, J = 5.2, 3.6 Hz, 1H), 6.95 (d, J = 7.4 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 1.38 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.0, 166.2, 141.6, 133.8, 133.6, 132.7, 131.7, 127.2, 62.7, 14.2; IR (film) 3098, 3083, 3061, 2988, 2942, 2905, 2885, 1710, 1665, 1627, 1581, 1512, 1473, 1423, 1363, 1321, 1250, 1239, 1143, 1110, 1099, 1089, 1056, 1027, 1002, 978, 885, 867, 853, 812, 788, 769, 746, 729, 679, 613 cm^{-1}; LRMS (ESI): Mass calcd for $C_{10}H_{11}SO_3$ $[M+H]^+$: 211; found 211.

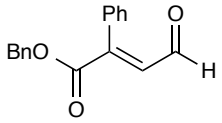


Ethyl (E)-2-benzyl-4-oxobut-2-enoate: To a 100 mL rbf was added ethyl 2-(diethoxyphosphoryl)-3-phenylpropanoate (1.2799 g, 4.07 mmol, 1 equiv), 2,2-dimethoxyacetaldehyde (1.060 g, 6.11 mmol, 60 wt% in H_2O, 1.5 equiv), heptane (10.18 ml, 0.4 molar), and K_2CO_3 (0.844 g, 6.11 mmol, 1.5 equiv). The mixture was stirred and refluxed overnight. Monitored by ^1H NMR. Upon completion, reaction mixture was cooled to 23 °C, diluted with Et_2O. The aqueous was separated and was back extracted.

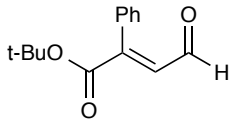
Combined organics was washed with water and then brine. Dried over $MgSO_4$ and concentrated. The crude contained a 6:4 E/Z ratio of products, and was carried on without further purification. The crude acetal was dissolved in acetone (40 mL, 0.1 molar) and water (0.798 mL) was added. Amberlyst 15 (0.50 g, approx. 0.5 equiv by weight) was added and the mixture stirred overnight. Once complete, the Amberlyst was filtered off, and the filtrate concentrated. The crude was diluted with Et_2O, washed with saturated aqueous $NaHCO_3$ solution, and brine, and then dried over $MgSO_4$, filtered, and concentrated. Purification by flash column chromatography (10% EtOAc/hexanes) afforded 0.296 g (33% yield over two steps) of product as yellow oil. Analytical data: ^{1}H 1H NMR (500 MHz, $CDCl_3$) δ 10.26 (d, J = 7.5 Hz, 1H), 7.29 (d, J = 7.1 Hz, 2H), 7.19 (d, J = 7.0 Hz, 3H), 6.90 (d, J = 7.5 Hz, 1H), 4.20 (q, J = 7.1 Hz, 2H), 4.13 (s, 2H), 1.24 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.9, 166.8, 148.0, 137.3, 134.1, 128.9, 128.6, 127.1, 62.1, 32.7, 14.1; IR (film) 3063, 3029, 2982, 2938,2870, 2760, 1716, 1677,1600, 1495, 1453, 1368, 1315, 1294,1248, 1192, 1124, 1095, 1077, 1049, 1029, 1010, 935, 891, 858, 831, 742, 697 cm^{-1}; LRMS (ESI): Mass calcd for $C_{13}H_{15}O_3$ $[M+H]^+$: 219; found 219.



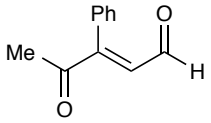
Methyl (E)-4-oxo-2-phenylbut-2-enoate: To a mixture of methyl 2-(diethoxyphosphoryl)acetate (3.15 g, 15 mmol), K_2CO_3 (6.22 g, 45.0 mmol, 3 equiv), and iodine (7.61 g, 30.0 mmol, 2 equiv) in THF (37.5 ml) at 0 °C was added 2,2-dimethoxyacetaldehyde (2.86 g, 16.50 mmol, 60 wt% in H_2O, 1.1 equiv) dropwise. The mixture was allowed to warm to 23 °C overnight and then filtered through Celite and eluted with Et_2O. The filtrate was washed with $Na_2S_2O_3$, then water, and brine. Dried over Na_2SO_4, and concentrated. The crude was passed through a plug of silica, eluting with EtOAc, and carried on without purification. The crude was dissolved in toluene (75 ml), and phenylboronic acid (2.74 g, 22.49 mmol, 1.5 equiv), K_2CO_3 (4.15 g, 30.0 mmol, 2 equiv), and $Pd(Ph_3P)_4$ (0.087 g, 0.075 mmol, 0.5 mol %) were added. The flask was flushed with nitrogen, and then the mixture was heated at reflux for 18 h. After confirming complete conversion by ^{1}H NMR, the mixture was filtered through Celite with a thin pad of silica on top, eluting with EtOAc. The filtrate was then washed with $NaHCO_3$ and brine. Dried over $MgSO_4$, concentrated, and carried on without purification. Finally, the crude was diluted with H_2O (10.80 ml, 599 mmol) and THF (Volume: 30.0 ml), and trifluoroacetic acid (11.54 ml, 150 mmol, 10 equiv) was added dropwise. After stirring for 1 h, the solution was diluted with Et_2O, carefully quenched with sat. aq. $NaHCO_3$ and brine. The crude was dried over Na_2SO_4, filtered, concentrated, and purified by flash column chromatography (10% EtOAc/hexanes) to afford 0.599 g (21% yield over 3 steps) of product as yellow solid. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.63 (d, J = 7.8 Hz, 1H), 7.49 – 7.44 (m, 3H), 7.36 – 7.33 (m, 2H), 6.99 (d, J = 7.8 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.5, 167.1, 149.3, 135.1, 131.9, 130.5, 129.9, 128.4, 53.3; IR (film) 3060, 2958, 2887, 2849, 1719, 1667, 1606, 1595, 1573, 1495, 1445, 1435, 1396, 1352, 1242, 1190, 1167, 1104, 1079, 1036, 1018, 999, 971, 930, 908, 888, 862, 853, 784, 762, 716, 695, 611 cm^{-1}; LRMS (ESI): Mass calcd for $C_{11}H_{11}O_3$ $[M+H]^+$: 191; found 191.



Benzyl (E)-4-oxo-2-phenylbut-2-enoate: Prepared according to similar procedure as methyl (*E*)-4-oxo-2-phenylbut-2-enoate using benzyl 2-(diethoxyphosphoryl)acetate (4.29 g, 15 mmol) to afford 1.89 g (47% yield over 3 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.64 (d, J = 7.8 Hz, 1H), 7.51-7.33 (m, 10H), 7.01 (d, J = 7.7 Hz, 1H), 5.30 (s, 2H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.5, 166.4, 149.3, 135.2, 135.0, 131.7, 130.6, 130.0, 128.8, 128.7, 128.4, 67.9; IR (film) 3066, 3034, 2959, 2848, 2758, 2721, 1718, 1678, 1498, 1260, 1170, 1105, 1010, 715, 696, 627, 618 cm^{-1}; LRMS (ESI): Mass calcd for $C_{17}H_{15}O_3$ $[M+H]^+$: 267; found 267.



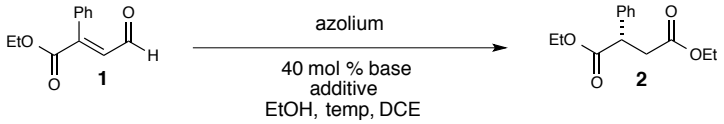
Tert-butyl (E)-4-oxo-2-phenylbut-2-enoate: Prepared according to similar procedure as methyl (*E*)-4-oxo-2-phenylbut-2-enoate using tert-butyl 2-(diethoxyphosphoryl)acetate (2.018 g, 8 mmol) to afford 0.599 g (34% yield over 3 steps) of product as a yellow oil. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (d, J = 7.9 Hz, 1H), 7.43 – 7.41 (m, 2H), 7.32 (dd, J = 7.7, 1.7 Hz, 3H), 6.87 (d, J = 7.9 Hz, 1H), 1.50 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.0, 165.6, 151.2, 134.1, 132.3, 130.6, 129.7, 128.3, 83.2, 28.1; IR (film) 3059, 2978, 2933, 2846, 1713, 1677, 1608, 1456, 1444, 1392, 1368, 1347, 1265, 1252, 1154, 1103, 1078, 1041, 1031, 1001, 985, 888, 847, 814, 787, 773, 741, 717, 703, 969, 619, 605 cm^{-1}; LRMS (ESI): Mass calcd for $C_{16}H_{20}NO_3$ $[M+H+MeCN]^+$: 274; found 274.



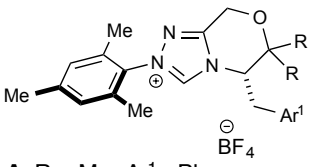
(E)-4-oxo-3-phenylpent-2-enal: Prepared according to the general procedure using (Z)-3-iodo-5,5-dimethoxypent-3-en-2-one (0.500 g, 1.851 mmol) and phenylboronic acid (0.217 g, 2.22 mmol) to afford 0.135 g (42% yield over 2 steps) of product as a yellow solid. Analytical data: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.64 (d, J = 7.6 Hz, 1H), 7.52 – 7.40 (m, 4H), 7.29 – 7.27 (m, 1H), 6.73 (d, J = 7.6 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 199.8, 194.2, 155.5, 132.9, 132.1, 130.2, 129.8, 128.7, 28.1; IR (film) 3045, 3007, 2929, 2881, 1683, 1665, 1632, 1608, 1441, 1421, 1369, 1336, 1319, 1228, 1168, 1111, 1078, 1024, 1017, 999, 985, 930, 898, 856, 776, 738, 707, 698, 663, 638, 614 cm^{-1}; LRMS (ESI): Mass calcd for $C_{11}H_{11}O_2$ $[M+H]^+$: 175; found 175.

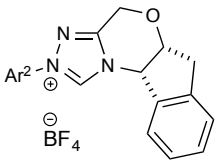
Optimization Table for Enantioselective β-Protonation

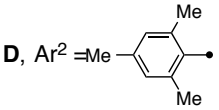
Table 1. Optimization of reaction conditions.

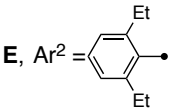


Entry	base	Additive (mol %)	Temp. (ºC)	azolium (mol %)	EtOH (equiv)	Time (h)	Conv. (%)	yield (%)	er
1	*i*-Pr_2NEt	-	23	**A** (10)	10	12	100	80	66:34
2	Et_3N	-	23	**A** (10)	10	10	100	-	64:36
3	TMEDA	-	23	**A** (10)	10	8	100	-	60:40
4	*i*-Pr_2NEt	$Mg(OtBu)_2$ (20)	23	**A** (10)	10	24	50	-	65:35
5	*i*-Pr_2NEt	$Ti(OiPr)_4$ (20)	23	**A** (10)	10	16	100	-	70:30
6	*i*-Pr_2NEt	$Sc(OTf)_3$ (20)	23	**A** (10)	10	18	100	-	64:36
7	*i*-Pr_2NEt	LiCl (20)	23	**A** (10)	10	12	100	-	80:20
8	*i*-Pr_2NEt	**HBD1** (20)	23	**A** (10)	10	16	100	-	82:18
9	*i*-Pr_2NEt	**HBD1** (30)	23	**A** (10)	10	12	100	44	88:12
10	*i*-Pr_2NEt	**HBD1** (40)	23	**A** (10)	10	6	100	33	90:10
11	*i*-Pr_2NEt	**HBD4** (30)	23	**A** (10)	10	14	100	-	86:14
12	*i*-Pr_2NEt	**HBD5** (30)	23	**A** (10)	10	18	100	-	82:18
13	*i*-Pr_2NEt	**HBD6** (30)	23	**A** (10)	10	20	100	-	82:18
14	*i*-Pr_2NEt	**HBD7** (30)	23	**A** (10)	10	4	100	-	64:36
15	*i*-Pr_2NEt	**HBD8** (30)	23	**A** (10)	10	8	100	-	82:18
16	*i*-Pr_2NEt	**HBD9** (30)	23	**A** (10)	10	8	100	-	82:18
17	*i*-Pr_2NEt	**HBD10** (30)	23	**A** (10)	10	14	100	-	86:14
18	*i*-Pr_2NEt	**HBD11** (30)	23	**A** (10)	10	12	100	-	85:15
19	*i*-Pr_2NEt	**HBD1** (30)	0	**A** (10)	10	12	100	41	93:7
20	*i*-Pr_2NEt	**HBD1** (30), **DMAP** (10)	0	**A** (10)	10	10	100	71	92:8
21	*i*-Pr_2NEt	**HBD1** (30), **DMAP** (10)	0	**B** (10)	10	-	-	40	84:16
22	*i*-Pr_2NEt	**HBD1** (30), **DMAP** (10)	0	**C** (10)	10	-	-	17	66:34
23	*i*-Pr_2NEt	**HBD1** (30), **DMAP** (10)	0	**D** (10)	10	-	-	42	73:27
24	*i*-Pr_2NEt	**HBD1** (30), **DMAP** (10)	0	**E** (10)	10	-	-	40	74:26
25	*i*-Pr_2NEt	**HBD2** (30), **DMAP** (10)	0	**A** (10)	10	20	100	84	92:8
26	*i*-Pr_2NEt	**HBD3** (30), **DMAP** (10)	0	**A** (10)	10	24	100	94	91:9
27	*i*-Pr_2NEt	**HBD3** (30)	0	**A** (10)	10	36	100	81	96:4
28	*i*-Pr_2NEt	**HBD3** (30), **DMAP** (5)	0	**A** (10)	10	24	100	85	94:6
29	*i*-Pr_2NEt	**HBD3** (30)	0	**A** (5)	10	120	80	62	96:4
30	*i*-Pr_2NEt	**HBD3** (30), **DMAP** (5)	0	**A** (5)	10	96	100	82	95:5
31	*i*-Pr_2NEt	**HBD3** (30)	0	**A** (10)	7	40	100	79	96:4
32	*i*-Pr_2NEt	**HBD3** (30)	0	**A** (10)	5	52	100	69	95:5
33	*i*-Pr_2NEt	**HBD3** (30)	0	**A** (10)	2	72	100	54	92:8





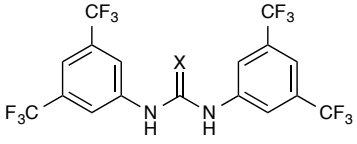




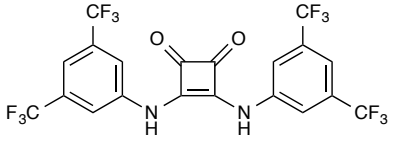
A, R = Me, Ar^1 = Ph;
B, R = Ph, Ar^1 = Ph;
C, R = Ph, Ar^1 = 3-indolyl

D, Ar^2 =

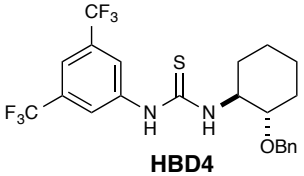
E, Ar^2 =



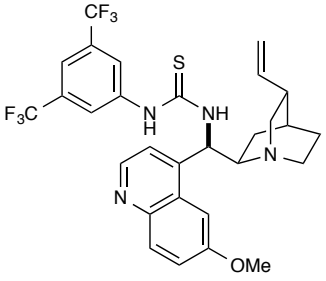
HBD1: X = S
HBD2: X = O



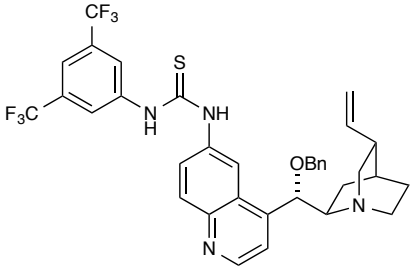
HBD3



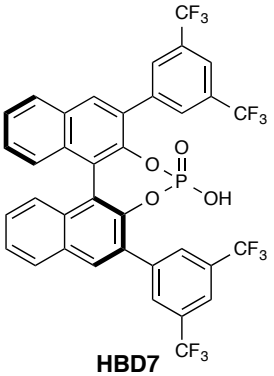
HBD4



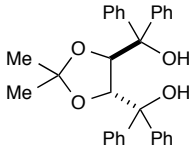
HBD5



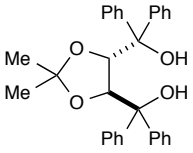
HBD6



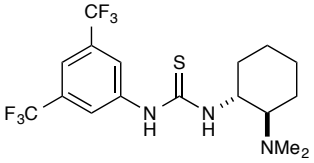
HBD7



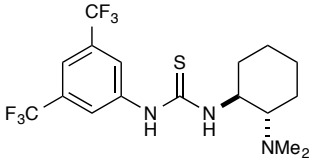
HBD8



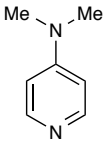
HBD9



HBD10



HBD11



DMAP

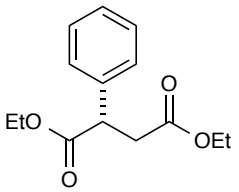
General Procedure A for the Synthesis of Succinic Diester

In a nitrogen filled dry box a screw-capped 2 dram vial equipped with a magnetic stirbar was charged with the corresponding enal **1** (0.200 mmol), triazolium precatalyst **A** (0.1 equiv), and **HBD3** (0.30 equiv). The vial was capped with a septum cap, removed from the drybox and put under positive N_2 pressure. The heterogeneous mixture was then diluted with degassed 1,2-dichloroethane (4.0 mL, 0.05 M) stirred, and cooled to 0 °C in an ice bath. Ethanol (120 μL, 10 equiv), water (1.8 μL, 5 equiv), and Hünig's base (14 μL, 0.4 equiv) were added sequentially via syringe. The reaction mixture was stirred at 0 °C for 36 h under static nitrogen pressure. Upon consumption of the aldehyde, monitored by NMR (all reactions were completed within 48 hours), the reaction mixture was concentrated *in vacuo*. The material was purified by flash chromatography with EtOAc/hexanes to afford the corresponding succinic diester **2**.

The corresponding racemic compounds were prepared by employing a similar protocol, except achiral triazolium precatalyst 2-mesityl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazol-2-ium tetrafluoroborate (10 mol %) was used instead of **A**, and the cocatalysts **HBD3** and **DMAP** were not added.

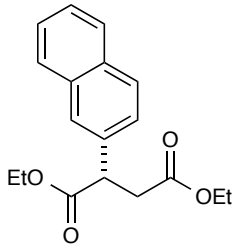
General Procedure B for the Synthesis of Succinic Diester

In a nitrogen filled dry box a screw-capped 2 dram vial equipped with a magnetic stirbar was charged with the corresponding enal **1** (0.200 mmol), triazolium precatalyst **A** (0.1 equiv), and **HBD3** (0.30 equiv). The vial was capped with a septum cap, removed from the drybox and put under positive N_2 pressure. The heterogeneous mixture was then diluted with degassed 1,2-dichloroethane (4.0 mL, 0.05 M) stirred, and cooled to 0 °C in an ice bath. Ethanol (120 μL, 10 equiv), water (1.8 μL, 5 equiv), DMAP (50 μL of 0.2 M solution in 1,2-dichloroethane, 0.05 equiv) and Hünig's base (14 μL, 0.4 equiv) was added sequentially via syringe. The reaction mixture was stirred at 0 °C for 24 h under static nitrogen pressure. Upon consumption of the aldehyde, monitored by ^{1}H NMR (all reactions were completed within 24 hours), the reaction mixture was concentrated *in vacuo*. The material was purified by flash chromatography with EtOAc/hexanes to afford the corresponding succinic diester **2**.

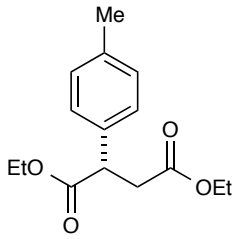


Diethyl (S)-2-phenylsuccinate (2): Prepared according to the general procedure using (*E*)-ethyl 4-oxo-2-phenylbut-2-enoate (0.041 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 41 mg (81% yield) of **2** as a colorless oil. Analytical data for **2**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 5H), 4.26 – 4.01 (m, 5H), 3.18 (dd, J = 16.9, 10.2 Hz, 1H), 2.65 (dd, J = 16.9, 5.3 Hz, 1H), 1.21 (dt, J = 13.0, 7.1 Hz, 6H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 173.1, 171.7, 138.0, 128.9(2C), 127.9(2C), 127.7, 61.3, 60.9, 47.4, 38.0, 14.3, 14.2; IR (film) 3089, 3064, 3032, 2982,

2937, 2907, 2874, 1733, 1603, 1585, 1497, 1464, 1447, 1410, 1393, 1371, 1327, 1296, 1251, 1227, 1157, 1114, 1096, 1029, 856, 773, 731, 698 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{19}O_4$ $[M+H]^+$: 251; found 251; $[a]_D^{23}$ = +85.7 ($CHCl_3$, c = 1.19)[4]; Enantiomeric ratio was measured by chiral phase HPLC (Whelk-O, 0.5% *i*-PrOH/Hexanes, 1.0 mL/min, 230 nm), Rt (major) = 34.0 min, Rt (minor) = 31.7 min; er = 96:4. Following general procedure B affords 42 mg (85% yield) **2**, 94:6 er.



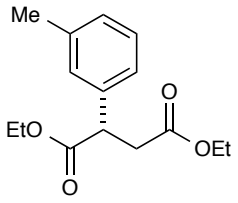
Diethyl (S)-2-(naphthalen-2-yl)succinate (3): Prepared according to the general procedure using (E)-ethyl 2-(naphthalen-2-yl)-4-oxobut-2-enoate (0.051 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 46 mg (76% yield) of **3** as a colorless oil. Analytical data for **3**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.80 (m, 3H), 7.76 – 7.74 (m, 1H), 7.49 – 7.46 (m, 2H), 7.42 (dd, J = 8.5, 1.8 Hz, 1H), 4.30 – 4.03 (m, 5H), 3.29 (dd, J = 16.9, 10.0 Hz, 1H), 2.75 (dd, J = 16.9, 5.4 Hz, 1H), 1.21 (dt, J = 15.6, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.7, 135.4, 133.5, 132.8, 128.7, 128.0, 127.8, 126.8, 126.4, 126.2, 125.8, 61.4, 60.9, 47.5, 38.1, 14.3, 14.2; IR (film) 3058, 2982, 2936, 2907, 1730, 1373, 1330, 1268, 1221, 1155, 1096, 1029, 908, 859, 818, 731, 648 cm^{-1}; LRMS (ESI): Mass calcd for $C_{18}H_{21}O_4$ $[M+H]^+$: 301; found 301; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 0.5% *i*-PrOH/Hexanes, 1.0 mL/min, 230 nm), Rt (major) = 21.9 min, Rt (minor) = 29.0 min; er = 94:6.



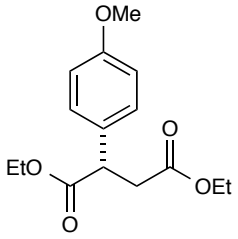
Diethyl (S)-2-(p-tolyl)succinate (4): Prepared according to the general procedure using (E)-ethyl 4-oxo-2-(p-tolyl)but-2-enoate (0.044 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0392 g (74%) of **4** as a colorless oil. Analytical data for **4**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 – 7.10 (m, 4H), 4.23 – 4.06 (m, 4H), 4.02 (dd, J = 10.2, 5.3 Hz, 1H), 3.16 (dd, J = 16.9, 10.2 Hz, 1H), 2.63 (dd, J = 16.9, 5.3 Hz, 1H), 2.32 (s, 3H), 1.21 (dt, J = 14.3, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.7, 135.4, 133.5, 132.8, 128.7, 128.0, 127.8, 126.8, 126.4, 126.2, 125.8, 61.4, 60.9, 47.5, 38.1, 14.3, 14.2; IR (film) 2981, 2926, 1732, 1514, 1445, 1412, 1370, 1336, 1293, 1256, 1227, 1157, 1096, 1031, 856, 823, 791 cm^{-1}; LRMS (ESI): Mass calcd for $C_{15}H_{21}O_4$ $[M+H]^+$: 265; found 265; Enantiomeric ratio was measured by chiral

[4] Y.-C. Chung, D. Janmanchi, H.-L. Wu, *Org. Lett.* **14**, 2766-2769 (2012).

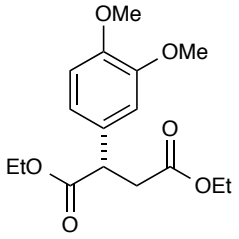
phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 6.96 min, Rt (minor) = 8.59 min; er = 91:9. Following general procedure B afforded 0.0435 g (82% yield) of **4**, 90:10 er.



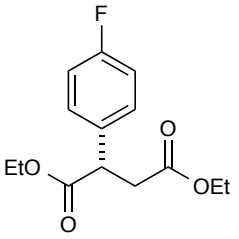
Diethyl (S)-2-(m-tolyl)succinate (5): Prepared according to the general procedure using (E)-ethyl 4-oxo-2-(m-tolyl)but-2-enoate (0.044 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0408 g (77%)of **5** as a colorless oil. Analytical data for **5**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (t, J = 7.5 Hz, 1H), 7.08 (d, J = 8.1 Hz, 3H), 4.23 – 4.05 (m, 4H), 4.02 (dd, J = 10.3, 5.1 Hz, 1H), 3.17 (dd, J = 16.9, 10.3 Hz, 1H), 2.63 (dd, J = 16.9, 5.2 Hz, 1H), 2.33 (s, 3H), 1.21 (dt, J = 11.8, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 171.7, 138.6, 137.9, 128.8, 128.5, 128.4, 124.9, 61.2, 60.8, 47.3, 38.1, 21.5, 14.3, 14.2; IR (film) 3450, 2981, 2934, 2905, 2872, 1742, 1730, 1607, 1590, 1491, 1464, 1445, 1411, 1370, 1335, 1297, 1212, 1096, 1031, 858, 784, 735, 696 cm^{-1}; LRMS (ESI): Mass calcd for $C_{15}H_{21}O_4$ $[M+H]^+$: 265; found 265; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 0.5% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 13.9 min, Rt (minor) = 19.3 min; er = 96:4.



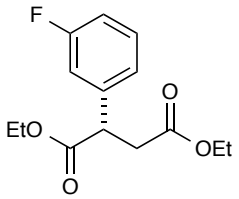
Diethyl (S)-2-(4-methoxyphenyl)succinate (6): Prepared according to the general procedure using (E)-ethyl 2-(4-methoxyphenyl)-4-oxobut-2-enoate (0.047 g, 0.200 mmol) and purified by flash chromatography using 20% EtOAc/hexanes to afford 0.0436 g (78%) of **6** as a colorless oil. Analytical data for **6**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 – 7.18 (m, 2H), 6.87 – 6.83 (m, 2H), 4.12 (dddd, J = 21.1, 14.0, 10.8, 7.1 Hz, 4H), 4.01 (dd, J = 10.0, 5.5 Hz, 1H), 3.79 (s, 3H), 3.15 (dd, J = 16.8, 10.1 Hz, 1H), 2.63 (dd, J = 16.8, 5.5 Hz, 1H), 1.21 (dt, J = 12.9, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.2, 171.6, 159.0, 129.9, 128.8, 114.2, 61.0, 60.7, 55.3, 46.5, 38.0, 14.2, 14.1; IR (film) 2982, 2936, 2908, 2837, 1726, 1611, 1584, 1512, 1464, 1443, 1410, 1393, 1371, 1302, 1248, 1177, 1159, 1112, 1096, 1030, 906, 856, 833, 794, 727, 648 cm^{-1}; LRMS (ESI): Mass calcd for $C_{15}H_{21}O_5$ $[M+H]^+$: 281; found 281; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel IA, 5% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 10.2 min, Rt (minor) = 9.5 min; er = 92:8.



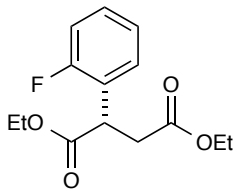
Diethyl (S)-2-(3,4-dimethoxyphenyl)succinate (7): Prepared according to the general procedure using (E)-ethyl 2-(3,4-dimethoxyphenyl)-4-oxobut-2-enoate (0.053 g, 0.200 mmol) and purified by flash chromatography using 20% EtOAc/hexanes to afford 0.0441 g (71%) of **7** as a colorless oil. Analytical data for **7**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.82 (dd, J = 6.8, 2.8 Hz, 3H), 4.21 – 4.08 (m, 4H), 4.00 (dd, J = 10.0, 5.4 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.16 (dd, J = 16.8, 10.1 Hz, 1H), 2.65 (dd, J = 16.8, 5.4 Hz, 1H), 1.22 (dt, J = 11.1, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.3, 171.7, 149.2, 148.6, 130.5, 120.1, 111.4, 110.9, 61.2, 60.9, 56.0, 47.0, 38.2, 31.1, 14.3, 14.2; IR (film) 2981, 2962, 2937, 2908, 2874, 2837, 1731, 1592, 1516, 1465, 1420, 1393, 1371, 1328, 1295, 1261, 1243, 1174, 1152, 1096, 1028, 914, 858, 808, 765, 731, 647 cm^{-1}; LRMS (ESI): Mass calcd for $C_{16}H_{23}O_6$ $[M+H]^+$: 311; found 311; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ADH, 3% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 28.3 min, Rt (minor) = 24.2 min; er = 93:7. Following general procedure B afforded 0.0578 g (93% yield) of **7**, er = 90:10.



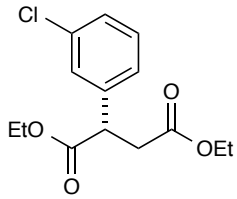
Diethyl (S)-2-(4-fluorophenyl)succinate (8): Prepared according to the general procedure using (E)-ethyl 2-(4-fluorophenyl)-4-oxobut-2-enoate (0.044 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0404 g (75%) of **8** as a colorless oil. Analytical data for **8**: ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.30 – 7.22 (m, 2H), 7.04 – 6.97 (m, 2H), 4.22 – 4.00 (m, 5H), 3.15 (ap dd, J = 16.8, 9.8 Hz, 1H), 2.64 (ap dd, J = 16.9, 5.7 Hz, 1H), 1.22 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 172.8, 171.3, 162.2 (d, $J_{C\text{-}F}$ = 246.1 Hz), 133.6 (d, $J_{C\text{-}F}$ = 3.3 Hz), 129.4 (2C, d, J = 8.1 Hz), 115.7 (2C, d, $J_{C\text{-}F}$ = 21.5 Hz), 61.3, 60.8, 46.5, 37.9, 14.2, 14.1; ^{19}F NMR (376 MHz; $CDCl_3$): δ –114.9 (m); IR (film) 2983, 2939, 2908, 2875, 1734, 1606, 1466, 1447, 1412, 1393, 1372, 1334, 1295, 1226, 1158, 1098, 1030, 841, 811 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{18}O_4F$ $[M+H]^+$: 269; found 269; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel IA, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 16.6 min, Rt (minor) = 12.1 min; er = 93:7.



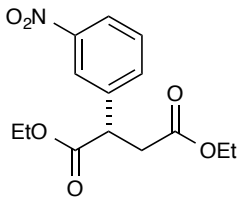
Diethyl (S)-2-(3-fluorophenyl)succinate (9): Prepared according to the general procedure using (E)-ethyl 2-(3-fluorophenyl)-4-oxobut-2-enoate (28 mg, 0.126 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 18.1 mg (54% yield) of **9** as a colorless oil. Analytical data for **9**: ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.32 (ap td, *J* = 8.0, 6.0 Hz, 1H), 7.09 (ap dt, *J* = 7.7, 1.2 Hz, 1H), 7.06 – 6.97 (m, 2H), 4.34 – 3.99 (m, 5H), 3.19 (ap dd, *J* = 16.9, 9.9 Hz, 1H), 2.68 (ap dd, *J* = 16.9, 5.5 Hz, 1H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 172.6, 171.4, 163.0 (d, $J_{C\text{-}F}$ = 246.7 Hz), 140.3 (d, $J_{C\text{-}F}$ = 7.4 Hz), 130.4 (d, $J_{C\text{-}F}$ = 8.3 Hz), 123.6 (d, $J_{C\text{-}F}$ = 2.9 Hz), 115.0 (d, $J_{C\text{-}F}$ = 22.0 Hz), 114.7 (d, $J_{C\text{-}F}$ = 21.0 Hz), 61.5, 61.0, 47.1, 37.8, 37.8, 14.3, 14.2; ^{19}F NMR (376 MHz; $CDCl_3$): δ –112.3 (m); IR (film) 3067, 2983, 2938, 2908, 2875, 1733, 1615, 1591, 1489, 1449, 1411, 1393, 1372, 1336, 1298, 1263, 1240, 1217, 1176, 1160, 1096, 1030, 966, 941, 899, 873, 861, 786, 688 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{18}O_4F$ $[M+H]^+$: 269; found 269; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 8.26 min, Rt (minor) = 18.4 min; er = 93:7. Following general procedure B afforded 0.0234 g (69% yield) of **9**, er = 92:8.



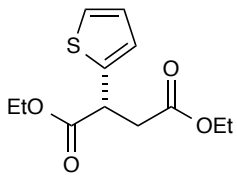
Diethyl (S)-2-(2-fluorophenyl)succinate (10): Prepared according to the general procedure using (E)-ethyl 2-(2-fluorophenyl)-4-oxobut-2-enoate (0.044 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0334 g (62%) of **10** as a colorless oil. Analytical data for **10**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (dd, J = 3.5, 1.8 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.13 – 7.03 (m, 2H), 4.38 (dd, J = 9.5, 5.7 Hz, 1H), 4.20 – 4.10 (m, 4H), 3.17 (dd, J = 16.8, 9.5 Hz, 1H), 2.65 (dd, J = 16.8, 5.7 Hz, 1H), 1.21 (dt, J = 11.7, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.4, 171.5, 161.5, 159.5, 129.4, 129.4, 129.3, 125.5, 125.4, 124.5, 124.5, 116.0, 115.8, 61.5, 60.9, 40.8, 40.8, 37.0, 14.3, 14.2; IR (film) 2983, 2937, 1735, 1493, 1458, 1371, 130, 1301, 1233, 1161, 1096, 1029, 759 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{18}FO_4$ $[M+H]^+$: 269; found 269; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 8.88 min, Rt (minor) = 24.3 min; er = 89:11. Following general procedure B afforded 0.0403 g (75% yield) of **10**, er = 87:13.



Diethyl (S)-2-(3-chlorophenyl)succinate (11): Prepared according to the general procedure using (E)-ethyl 2-(3-chlorophenyl)-4-oxobut-2-enoate (0.048 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0401 g (70%) of **11** as a colorless oil. Analytical data for **11**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (m, 1H), 7.25 (m, 2H), 7.20 – 7.15 (m, 1H), 4.24 – 4.06 (m, 4H), 4.03 (dd, J = 9.9, 5.5 Hz, 1H), 3.16 (dd, J = 16.9, 9.9 Hz, 1H), 2.65 (dd, J = 16.9, 5.5 Hz, 1H), 1.22 (q, J = 7.3 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.5, 171.3, 139.8, 134.7, 130.2, 128.1, 128.0, 126.1, 61.5, 61.0, 47.1, 37.8, 14.3, 14.2; IR (film) 3066, 2982, 2937, 2907, 2873, 1733, 1596, 1574, 1477, 1432, 1410, 1393, 1370, 1334, 1293, 1250, 1229, 1174, 1159, 1095, 1082, 1000, 856, 788, 771, 686 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{18}ClO_4$ $[M+H]^+$: 285; found 285; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 230 nm), Rt (major) = 8.11 min, Rt (minor) = 18.3 min; er = 93:7.

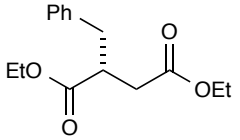


Diethyl (S)-2-(3-nitrophenyl)succinate (12): Prepared according to the general procedure using (E)-ethyl 2-(3-nitrophenyl)-4-oxobut-2-enoate (0.050 g, 0.200 mmol) and purified by flash chromatography using 20% EtOAc/hexanes to afford 0.0339 g (57%) of **12** as a colorless oil. Analytical data for **12**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (t, J = 1.9 Hz, 1H), 8.15 (ddd, J = 8.1, 2.1, 0.9 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H), 7.52 (t, J = 7.9 Hz, 1H), 4.23 – 4.09 (m, 5H), 3.22 (dd, J = 16.9, 9.3 Hz, 1H), 2.73 (dd, J = 16.9, 6.1 Hz, 1H), 1.26 – 1.19 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.9, 171.0, 148.6, 139.9, 134.2, 129.9, 123.1, 122.9, 61.8, 61.2, 47.0, 37.6, 14.3, 14.2; IR (film) 3448, 3090, 2982, 2938, 1733, 1532, 1477, 1465, 1445, 1410, 1394, 1370, 1351, 1301, 1255, 1230, 1176, 1160, 1097, 1028, 736, 681 cm^{-1}; LRMS (ESI): Mass calcd for $C_{14}H_{18}NO_6$ $[M+H]^+$: 296; found 296; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 3% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 25.0 min, Rt (minor) = 12.5 min; ee = 89:11. Following general procedure B afforded 0.0401 g (68% yield) of **12**, er = 83:17.

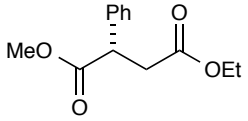


Diethyl (R)-2-(thiophen-2-yl)succinate (13): Prepared according to the general procedure using (Z)-ethyl 4-oxo-2-(thiophen-2-yl)but-2-enoate (0.042 g, 0.200 mmol) and purified by flash chromatography using 10% EtOAc/hexanes to afford 0.0315 g

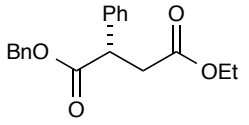
(61%) of **13** as a clear yellow oil. Analytical data for **13**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (dd, J = 4.5, 1.8 Hz, 1H), 6.95 (d, J = 4.7 Hz, 2H), 4.35 (dd, J = 10.0, 5.3 Hz, 1H), 4.25 – 4.09 (m, 4H), 3.21 (dd, J = 16.8, 10.0 Hz, 1H), 2.78 (dd, J = 16.8, 5.3 Hz, 1H), 1.24 (t, J = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 171.2, 139.9, 127.0, 125.6, 125.0, 61.6, 61.0, 42.6, 38.5, 14.3, 14.2; IR (film) 3108, 2982, 2936, 1732, 1465, 1445, 1409, 1393, 1373, 1349, 1329, 1256, 1228, 1174, 1160, 1115, 1096, 1028, 854, 702 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{17}O_4S$ $[M+H]^+$: 257; found 257; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 230 nm), Rt (major) = 14.5 min, Rt (minor) = 34.1 min; er = 95:5. Following general procedure B afforded 0.0411 g (80% yield) of **12**, er = 77:23.



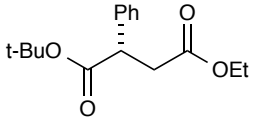
Ethyl (E)-2-benzyl-4-oxobut-2-enoate (14): Prepared according to the general procedure using (E)-ethyl 2-benzyl-4-oxobut-2-enoate (0.044 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 23 mg (44% yield) of **14** as a colorless oil. Analytical data for **14**: ^{1}H 1H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 7.1 Hz, 1H), 7.24 – 7.19 (m, 2H), 7.17 (d, J = 7.0 Hz, 2H), 4.10 (dq, J = 10.8, 7.1 Hz, 4H), 3.13 – 3.07 (m, 1H), 3.04 (dd, J = 13.5, 6.5 Hz, 1H), 2.76 (dd, J = 13.5, 8.2 Hz, 1H), 2.66 (dd, J = 16.7, 9.2 Hz, 1H), 2.39 (dd, J = 16.7, 5.0 Hz, 1H), 1.21 (dt, J = 16.6, 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 172.0, 138.4, 129.2, 128.6, 126.8, 60.8, 60.7, 43.3, 38.0, 35.4, 14.3, 14.2; IR (film) 3028, 2980, 2930, 1728, 1496, 1454, 1446, 1393, 1371, 1348, 1327, 1256, 1176, 1158, 1096, 1076, 1030, 971, 856, 743, 699 cm^{-1}; LRMS (ESI): Mass calcd for $C_{15}H_{21}O_4$ $[M+H]^+$: 265; found 265; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 12.6 min, Rt (minor) = 18.1 min; er = 92:8. Following general procedure B afforded 0.0302 g (57% yield) of **14**, er = 85:15.



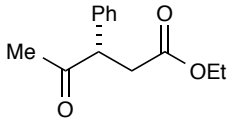
4-ethyl 1-methyl (S)-2-phenylsuccinate (15): Prepared according to the general procedure using (E)-methyl 4-oxo-2-phenylbut-2-enoate (0.038 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0339 g (72%) of **15** as a colorless oil. Analytical data for **15**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 5H), 4.15 – 4.11 (m, 2H), 4.10 – 4.07 (m, 1H), 3.68 (s, 3H), 3.20 (dd, J = 16.9, 10.2 Hz, 1H), 2.66 (dd, J = 16.9, 5.3 Hz, 1H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.6, 171.6, 137.8, 129.0, 127.9, 127.8, 60.9, 52.5, 47.3, 38.1, 14.3; LRMS (ESI): Mass calcd for $C_{13}H_{17}O_4$ $[M+H]^+$: 237; found 237; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel Whelk-O, 0.5% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 36.0 min, Rt (minor) = 10.2 min; er = 90:10.



1-benzyl 4-ethyl (S)-2-phenylsuccinate (16): Prepared according to the general procedure using (E)-benzyl 4-oxo-2-phenylbut-2-enoate (0.053 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0432 g (69%)of **16** as a colorless oil. Analytical data for **16**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29 (q, J = 5.7 Hz, 8H), 7.21 (dd, J = 7.2, 2.0 Hz, 2H), 5.12 (q, J = 12.5 Hz, 2H), 4.15 (dd, J = 10.1, 5.3 Hz, 1H), 4.10 (qd, J = 7.1, 1.8 Hz, 2H), 3.21 (dd, J = 16.9, 10.1 Hz, 1H), 2.69 (dd, J = 16.9, 5.4 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, CDCl3) δ 172.9, 171.6, 137.7, 135.9, 129.0, 128.6, 128.2, 128.0, 127.9, 127.8, 66.9, 60.9, 47.4, 37.9, 14.2; IR (film) 3065, 3033, 2980, 2918,2849, 1732, 1652, 1635, 1602, 1576, 1558, 1540, 1506, 1497, 1472, 1455, 1409, 1373, 1329, 1293, 1279, 1250, 1221, 1153, 1095, 1025, 913, 850, 774, 733, 696, 656, 603 cm^{-1}; LRMS (ESI): Mass calcd for $C_{19}H_{21}O_4$ $[M+H]^+$: 313; found 313; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel Whelk-O, 0.5% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 61.2 min, Rt (minor) = 55.2 min; er = 95:5.

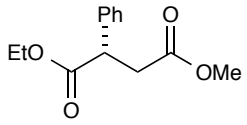


1-(tert-butyl) 4-ethyl (S)-2-phenylsuccinate (17): Prepared according to the general procedure using (E)-tert-butyl 4-oxo-2-phenylbut-2-enoate (0.046 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.046 g (83%) of **17** as a colorless oil. Analytical data for **17**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 5H), 4.12 (q, J = 7.1 Hz, 2H), 3.97 (dd, J = 10.1, 5.4 Hz, 1H), 3.11 (dd, J = 16.7, 10.1 Hz, 1H), 2.61 (dd, J = 16.7, 5.4 Hz, 1H), 1.39 (s, 9H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.1, 171.8, 138.5, 128.8, 127.8, 127.5, 81.2, 60.8, 48.4, 38.1, 28.0, 14.3; IR (film) 2979, 2932, 1724, 1496, 1454, 1409, 1392, 1367, 1349, 1329, 1294, 1248, 1182, 1143, 1096, 1026, 1004, 992, 846, 783, 754, 728, 697 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_{15}O_4$ $[M\text{-}t\text{-}BuO+H_2O]^+$: 223; found 223; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel IA, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 8.26 min, Rt (minor) = 7.57 min; er = 97:3.

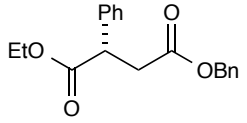


Ethyl (S)-4-oxo-3-phenylpentanoate (18): Prepared according to the general procedure using (E)-4-oxo-3-phenylpent-2-enal (34.8 mg, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 27 mg (62% yield) of **18** as a colorless oil. Analytical data for **18**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 3H), 7.22 – 7.20 (m, 2H), 4.18 (dd, J = 9.8, 5.0 Hz, 1H), 4.10 (tq, J = 7.1, 3.6 Hz, 2H), 3.20 (dd, J = 17.0, 9.8 Hz, 1H), 2.52 (dd, J = 17.0, 5.0 Hz, 1H), 2.12 (s, 3H), 1.22 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 207.0, 172.2, 137.5, 129.3, 128.4, 127.9, 60.8, 55.0, 37.2, 29.1, 14.3; IR (film) 3062, 3029, 2982, 2931, 1734, 1718, 1599, 1494, 1454,

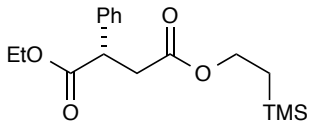
1409, 1394, 1374, 1353, 1322, 1291, 1240, 1189, 1157, 1114, 1096, 1028, 756, 701 cm^{-1}; LRMS (ESI): Mass calcd for $C_{13}H_{17}O_3$ $[M+H]^+$: 221; found 221; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 3% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 10.7 min, Rt (minor) = 8.58 min; er = 83:17.



1-ethyl 4-methyl (S)-2-phenylsuccinate (19): Prepared according to the general procedure using (E)-ethyl 4-oxo-2-phenylbut-2-enoate (0.041 g, 0.200 mmol) and methanol (0.081 mL, 2 mmol) and purified by flash chromatography using 8% Acetone/hexanes to afford 0.0469 g (99%) of **19** as a colorless oil. Analytical data for **19**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 5H), 4.18 – 4.04 (m, 3H), 3.67 (s, 3H), 3.20 (dd, J = 16.9, 10.2 Hz, 1H), 2.66 (dd, J = 16.9, 5.3 Hz, 1H), 1.20 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 172.2, 138.0, 129.0, 127.9, 127.7, 77.4, 61.3, 52.0, 47.4, 37.8, 14.2; IR (film) 3031, 2982, 2953, 1727, 1496, 1454, 1436, 1409, 1365, 1329, 1294, 1250, 1226, 1197, 1154, 1113, 1095, 1072, 1021, 1004, 990, 856, 772, 731, 697 cm^{-1}; LRMS (ESI): Mass calcd for $C_{13}H_{17}O_4$ $[M+H]^+$: 237; found 237; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 15.8 min, Rt (minor) = 28.3 min; er = 91:9.

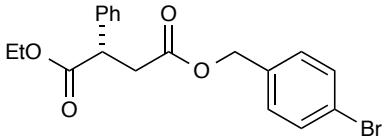


4-benzyl 1-ethyl (S)-2-phenylsuccinate (20): Prepared according to the general procedure using (E)-ethyl 4-oxo-2-phenylbut-2-enoate (0.041 g, 0.200 mmol) and benzyl alcohol (0.208 mL, 2 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0506 g (81%) of **20** as a colorless oil. Analytical data for **20**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 10H), 5.19 – 5.03 (m, 2H), 4.19 – 4.02 (m, 3H), 3.25 (dd, J = 16.9, 10.1 Hz, 1H), 2.73 (dd, J = 16.9, 5.4 Hz, 1H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.0, 171.5, 137.8, 135.8, 129.0, 128.7, 128.4, 128.3, 127.9, 127.7, 66.7, 61.3, 47.4, 38.0, 14.1; IR (film) 3089, 3065, 3033, 2982, 2939, 2905, 1730, 1602, 1497, 1455, 1408, 1384, 1371, 1329, 1294, 1254, 1228, 1156, 1095, 1021, 968, 909, 857, 731, 697, 648 cm^{-1}; LRMS (ESI): Mass calcd for $C_{19}H_{21}O_4$ $[M+H]^+$: 313; found 313; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel Whelk-O, 5% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 23.2 min, Rt (minor) = 20.7 min; er = 93:7.



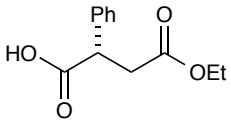
1-ethyl 4-(2-(trimethylsilyl)ethyl) (S)-2-phenylsuccinate (21): Prepared according to the general procedure using (E)-ethyl 4-oxo-2-phenylbut-2-enoate (0.041 g, 0.200 mmol) and 2-(trimethylsilyl)ethanol (0.287 mL, 2 mmol) and purified by flash chromatography using 8% Acetone/hexanes to afford 0.0398 g (62%) of **21** as a colorless oil. Analytical

data for **21**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 5H), 4.20 – 4.11 (m, 4H), 4.06 (dd, J = 10.2, 5.2 Hz, 1H), 3.17 (dd, J = 16.9, 10.2 Hz, 1H), 2.63 (dd, J = 16.9, 5.2 Hz, 1H), 1.20 (t, J = 7.1 Hz, 3H), 0.95 (dd, J = 9.1, 8.0 Hz, 2H), 0.02 (s, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 171.8, 138.1, 128.9, 127.9, 127.7, 63.1, 61.2, 47.4, 38.2, 17.4, 14.2, -1.4; IR (film) 2978, 2954, 2899, 1728, 1454, 1385, 1370, 1343, 1327, 1293, 1248, 1225, 1154, 1113, 1096, 1065, 1038, 1021, 970, 937, 856, 834, 764, 729, 696, 663 cm^{-1}; LRMS (ESI): Mass calcd for $C_{34}H_{52}NaO_8Si_2$ $[2M+Na]^+$: 667; found 667; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ADH, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 11.4 min, Rt (minor) = 8.48 min; er = 91:9.

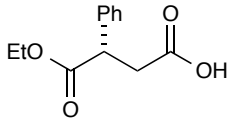


4-(4-bromobenzyl) 1-ethyl (S)-2-phenylsuccinate (22): Prepared according to the general procedure using (E)-ethyl 4-oxo-2-phenylbut-2-enoate (0.041 g, 0.200 mmol) and (4-bromophenyl)methanol (0.374 g, 2 mmol) and purified by flash chromatography using 10% EtOAc/hexanes to afford 0.0554 g (71%) of **22** as a white solid. Analytical data for **22**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 – 7.44 (m, 2H), 7.32 – 7.27 (m, 5H), 7.16 (d, J = 8.4 Hz, 2H), 5.10 – 4.99 (m, 2H), 4.15 – 4.04 (m, 3H), 3.24 (dd, J = 16.9, 10.0 Hz, 1H), 2.72 (dd, J = 16.9, 5.5 Hz, 1H), 1.17 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.9, 171.4, 137.7, 134.8, 131.8, 130.0, 129.0, 127.9, 127.8, 122.4, 65.8, 61.4, 47.4, 38.0, 14.1; IR (film) 3088, 3063, 3031, 2980, 2934, 2849, 1730, 1595, 1489, 1454, 1406, 1370, 1329, 1293, 1252, 1228, 1154, 1095, 1070, 1013, 855, 832, 800 cm^{-1}; LRMS (ESI): Mass calcd for $C_{19}H_{20}BrO_4$ $[M+H]^+$: 393; found 393; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel Whelk-O, 5% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 26.6 min, Rt (minor) = 22.9 min; er = 93:7. After recrystallization from slow evaporation of hexanes, 0.0497 g (64% yield) of **22**, er = 99:1.

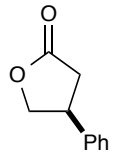
General Procedures for the Synthetic Transformations



(S)-4-ethoxy-4-oxo-2-phenylbutanoic acid (23): In a 20 mL vial with a stir bar was added 1-benzyl 4-ethyl 2-phenylsuccinate (0.544 mmol), 10% palladium/carbon (0.054 mmol), and EtOAc (3.6 mL). The system was purged with H_2 via a hydrogen balloon, and the reaction mixture was stirred overnight under an H_2 atmosphere. The reaction mixture was filtered through a Celite plug, eluting with EtOAc, and concentrated to afford 120 mg (99% yield) of **23** as a white solid. Analytical data for **23**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 5H), 4.24 – 3.96 (m, 3H), 3.17 (dd, J = 17.0, 10.0 Hz, 1H), 2.68 (dd, J = 17.0, 5.3 Hz, 1H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.0, 171.5, 137.1, 129.1, 128.1, 128.0, 61.0, 46.9, 37.6, 14.2; IR (film) 3255, 3032, 2982, 2917, 2849, 1734, 1709, 1602, 1585, 1540, 1497, 1455, 1418, 1395,1374, 1279, 1252, 1164, 1095, 1024, 856, 762, 726, 698, 656 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_5O_4$ $[M+H]^+$: 223; found 223.

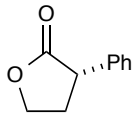


(S)-4-ethoxy-4-oxo-3-phenylbutanoic acid (24): In a 20 mL vial with a stir bar was added 4-benzyl 1-ethyl 2-phenylsuccinate (1.201 mmol), 10% palladium/carbon (0.120 mmol), and EtOAc (8.0 mL). The system was purged with H_2 via a hydrogen balloon, and the reaction mixture was stirred overnight under an H_2 atmosphere. The reaction mixture was filtered through a Celite plug, eluting with EtOAc, and concentrated to afford 265 mg (99% yield) of **24** as a white solid. Analytical data for **24**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 5H), 4.14 (ddd, J = 38.9, 10.8, 7.1 Hz, 2H), 4.04 (dd, J = 10.2, 5.0 Hz, 1H), 3.26 (dd, J = 17.3, 10.2 Hz, 1H), 2.71 (dd, J = 17.3, 5.1 Hz, 1H), 1.19 (t, J = 7.1 Hz, 3H).; ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.8, 137.5, 128.9, 127.7, 61.3, 47.0, 37.4, 14.0; IR (film) 3255, 3032, 2982, 2936, 1731, 1711, 1618, 1585, 1497, 1454, 1402, 1371, 1295, 1263, 1230, 1174, 1020, 699 cm^{-1}; LRMS (ESI): Mass calcd for $C_{12}H_5O_4$ $[M+H]^+$: 223; found 223.

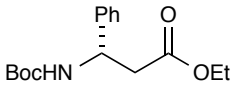


(*R*)-ethyl 2-phenylcyclopent-2-enecarboxylate (25)[5]: In a oven dried 20 mL vial with a stir bar was added 4-ethoxy-4-oxo-2-phenylbutanoic acid (0.225 mmol), and THF (1.5 mL). The solution was cooled to 0 °C and (tetrahydro-1H-furan-1-ium-1-yl)trihydroborate (337 μL, 0.337 mmol) was added dropwise by a syringe. Stirred at 0°C for 15 minutes and then warmed to 23 °C overnight. Cooled to -10 °C and trifluoroborate dietherate (70 μL, 0.567 mmol) was added by syringe. Stirred at 0 to 23 °C overnight. Quenched by the addition of brine and extracted with EtOAc, dried over $MgSO_4$, filtered and concentrated. Purified by flash column chromatography 30% EtOAc/hexanes to afford 32 mg (86% yield) of **25** the product lactone as an oil. Analytical data for **25**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, J = 7.4 Hz, 2H), 7.31 (t, J = 7.4 Hz, 1H), 7.24 (d, J = 7.2 Hz, 2H), 4.75 – 4.62 (m, 1H), 4.33 – 4.25 (m, 1H), 3.80 (p, J = 8.4 Hz, 1H), 2.94 (dd, J = 17.5, 8.7 Hz, 1H), 2.69 (dd, J = 17.5, 9.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.6, 139.5, 129.3, 127.9, 126.8, 74.2, 41.3, 35.9; IR (film) 3032, 2962, 2916, 2849, 2349, 1781, 1603, 1542, 1496, 1473, 1455, 1419, 1376, 1350, 1285, 1225, 1207, 1167, 1041, 1020, 1000, 991, 947, 898, 854, 850, 818, 762, 751, 700, 671, 664, 656, 641 cm^{-1}; LRMS (ESI): Mass calcd for $C_{10}H_{11}O_2$ $[M+H]^+$: 163; found 163; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel IA, 1% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 36.2 min, Rt (minor) = 42.1 min; er = 94:6.

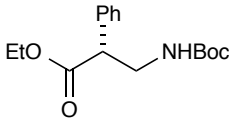
[5] L. Zhou, X. Liu, J. Ji, Y. Zhang, X. Hu, L. Lin, X. Feng, *J. Am. Chem. Soc.* **2012**, ***134***, 17023-17026.



(S)-3-phenyldihydrofuran-2(3H)-one (26)[6]: Prepared analogously to **25**, using **24** (0.225 mmol) to afford 27 mg (74% yield) of **26** as a clear liquid. Analytical data for **26**: ^{1}H 1H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, J = 7.3 Hz, 2H), 7.31 (ddd, J = 8.6, 7.2, 2.5 Hz, 3H), 4.49 (td, J = 8.7, 3.3 Hz, 1H), 4.36 (td, J = 9.2, 6.7 Hz, 1H), 3.87 – 3.78 (m, 1H), 2.78 – 2.67 (m, 1H), 2.51 – 2.40 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 177.5, 136.7, 129.1, 128.0, 127.8, 66.6, 45.6, 31.8; IR (film) 3063, 3030, 2988, 2915, 1766, 1732,1682, 1651, 1602, 1497, 1454, 1372, 1266, 1216, 1148, 1096, 1069, 1022, 995, 952, 918, 805, 751, 697, 667, 662, 626 cm^{-1}; LRMS (ESI): Mass calcd for $C_{10}H_{11}O_2$ $[M+H]^+$: 163; found 163; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel IA, 3% *i*-PrOH/Hexanes, 1.0 mL/min, 210 nm), Rt (major) = 28.2 min, Rt (minor) = 25.5 min; er = 91:9.



Ethyl (S)-3-((tert-butoxycarbonyl)amino)-3-phenylpropanoate (27)[7]: In a oven dried 2 dram vial with a stir bar was added 4-ethoxy-4-oxo-2-phenylbutanoic acid (0.225 mmol), *t*-BuOH (0.5 mL), triethylamine (33 μL, 0.237 mmol), and diphenyl phosphorazidate (51 μL, 0.237 mmol), heated at 85°C for 48 h. Then, the mixture was cooled to 23 °C, diluted with EtOAc (5 mL), washed with saturated $NaHCO_3$ (5 mL), H_2O (5 mL), and brine. The organic layer dried over $MgSO_4$, filtered and concentrated. Purified by flash column chromatography 10% EtOAc/hexanes to afford 47 mg (71% yield) of **27** as a colorless oil. Analytical data for **27**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.31 (dt, J = 14.1, 7.3 Hz, 5H), 5.47 (s, 1H), 5.11 (s, 1H), 4.06 (q, J = 7.1 Hz, 2H), 2.93 – 2.73 (m, 2H), 1.42 (s, 9H), 1.16 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.0, 155.0, 141.1, 128.6, 127.5, 126.2, 79.7, 60.7, 51.2, 41.0, 28.4, 14.1; IR (film) 3360, 3064, 3032, 3979, 3931, 1715, 1496, 1455, 1391, 1366, 1289, 1246, 1166, 1096, 1080, 1044, 1023, 963, 872, 757, 699, 667, 656 cm^{-1}; LRMS (ESI): Mass calcd for $C_{16}H_{24}NO_4$ $[M+H]^+$: 294; found 294; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ADH, 5% *i*-PrOH/Hexanes, 1.0 mL/min, 254 nm), Rt (major) = 18.3 min, Rt (minor) = 15.4 min; er = 94:6.

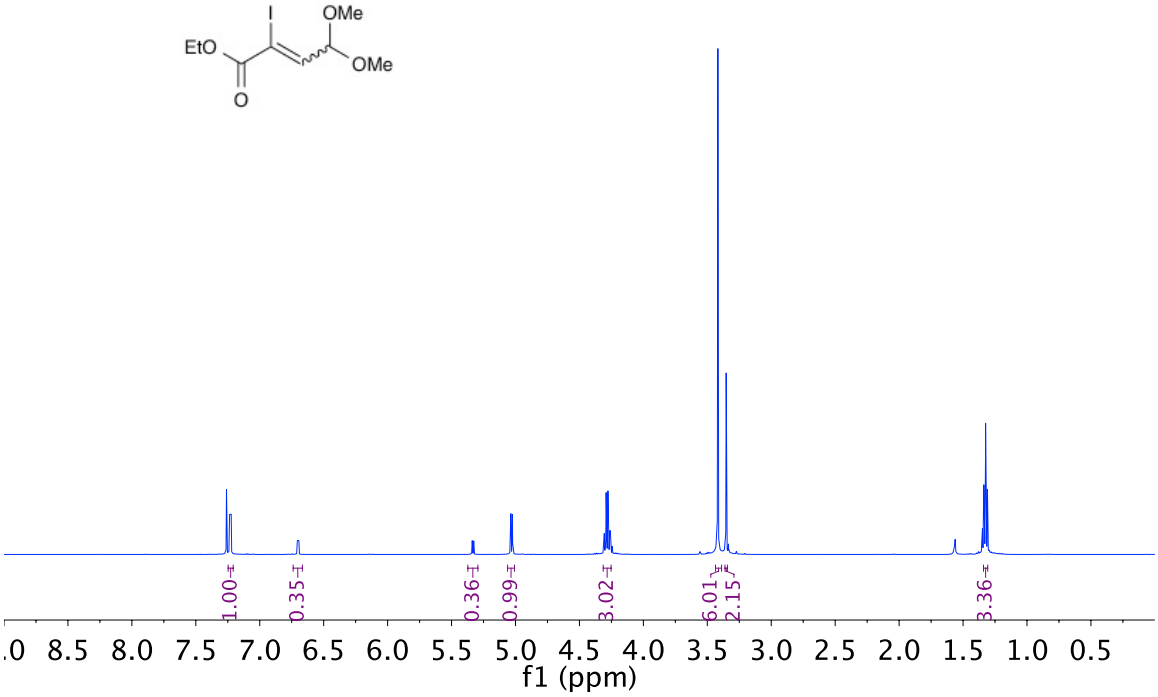


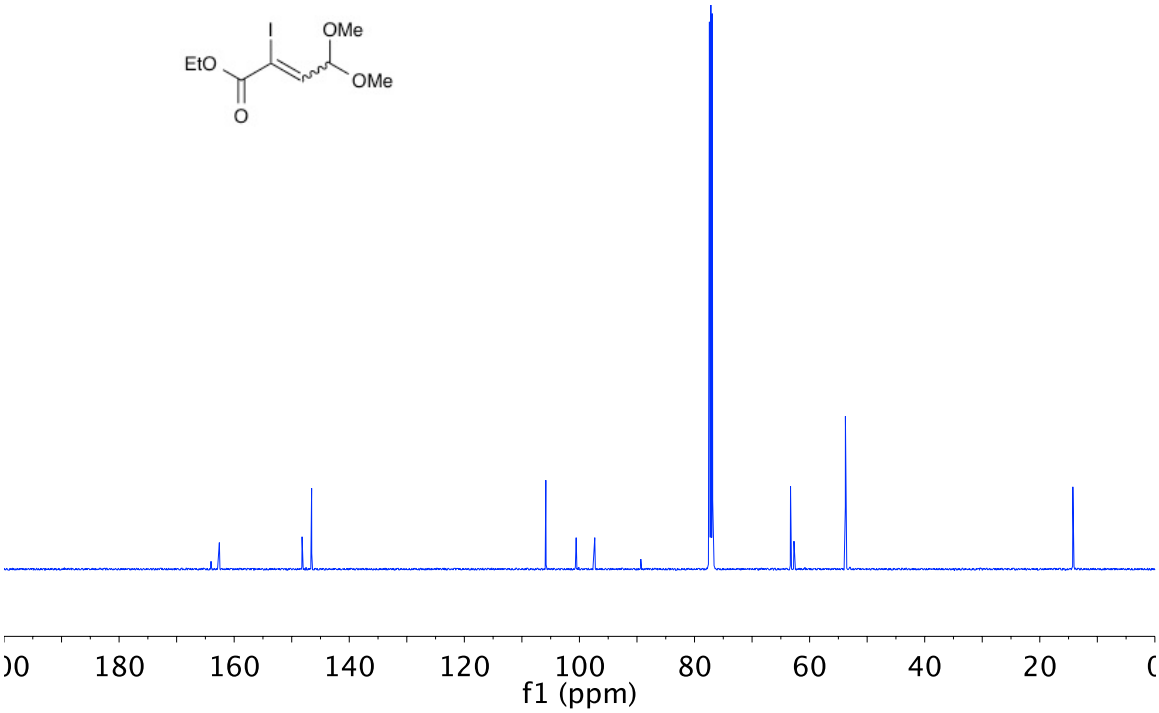
Ethyl (R)-3-((tert-butoxycarbonyl)amino)-2-phenylpropanoate (28): Prepared analogously to **27**, using **24** (65 mg, 0.292 mmol) to afford 61 mg (71% yield) of **28** as a colorless oil. Analytical data for **28**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 5H), 4.86 (s, 1H), 4.27 – 4.06 (m, 2H), 3.92 – 3.81 (m, 1H), 3.64 – 3.55 (m, 1H), 3.55 – 3.44

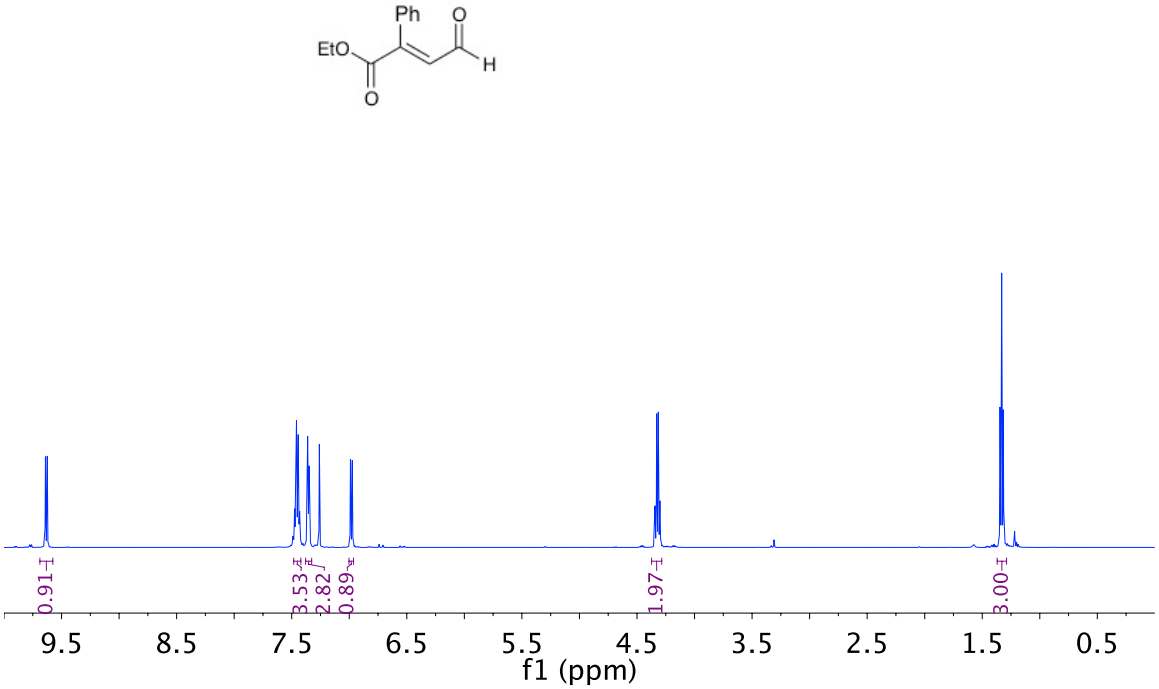
[6] Z. Huang, Z. Chen, L. H. Lim, G. C. P. Quang, H. Hirao, J. Zhou, *Angew. Chem. Int. Ed.* **2013**, *52*, 5807-5812.
[7] G. A. Molander, P. J. Stengel, *Tetrahedron* **1997**, *53*, 8887-8912.

(m, 1H), 1.42 (s, 9H), 1.21 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.1, 155.9, 136.7, 129.0, 128.1, 127.7, 79.6, 61.2, 51.8, 43.6, 28.5, 14.2; IR (film) 3380, 3064, 3031, 2978, 2934, 1718, 1507, 1455, 1392, 1366, 1279, 1250, 1197, 1171, 699 cm^{-1}; LRMS (ESI): Mass calcd for $C_{16}H_{24}NO_4$ $[M+H]^+$: 294; found 294; Enantiomeric ratio was measured by chiral phase HPLC (Chiralcel ODH, 0.5% *i*-PrOH/Hexanes, 0.5 mL/min, 210 nm), Rt (major) = 46.0 min, Rt (minor) = 39.7 min; er = 93:7.

Selected NMR Spectra



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5.5
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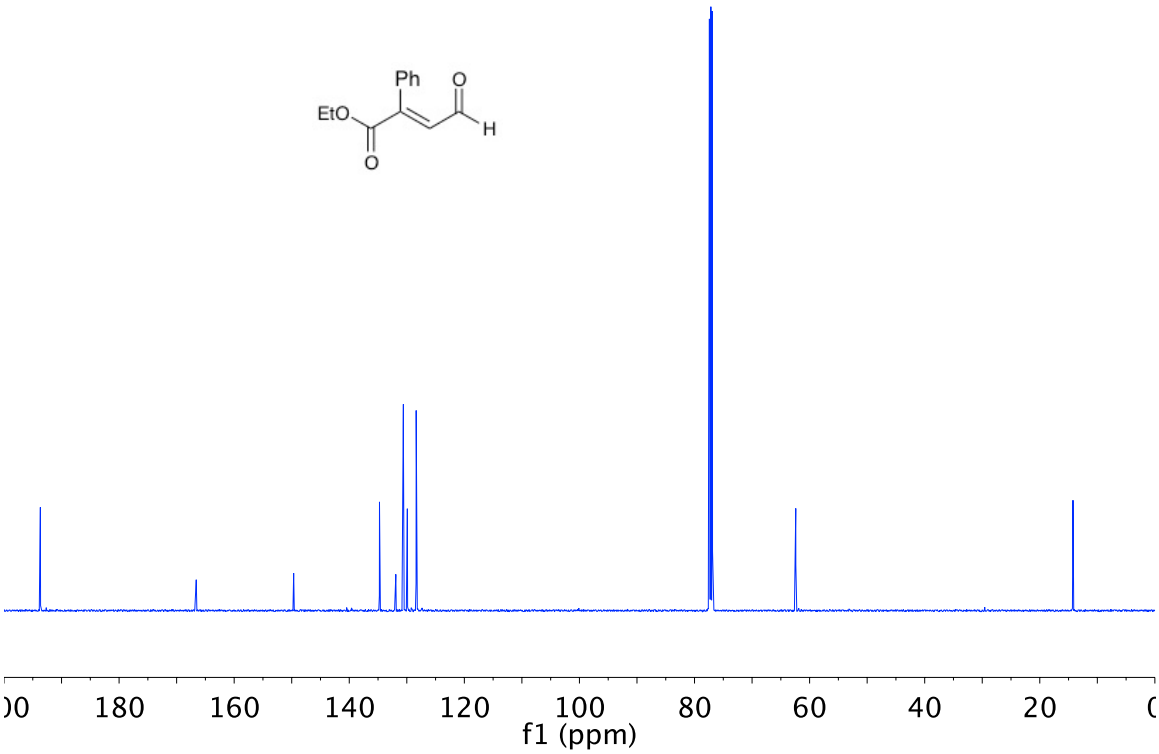
2.5
1.5
0.5
f1 (ppm)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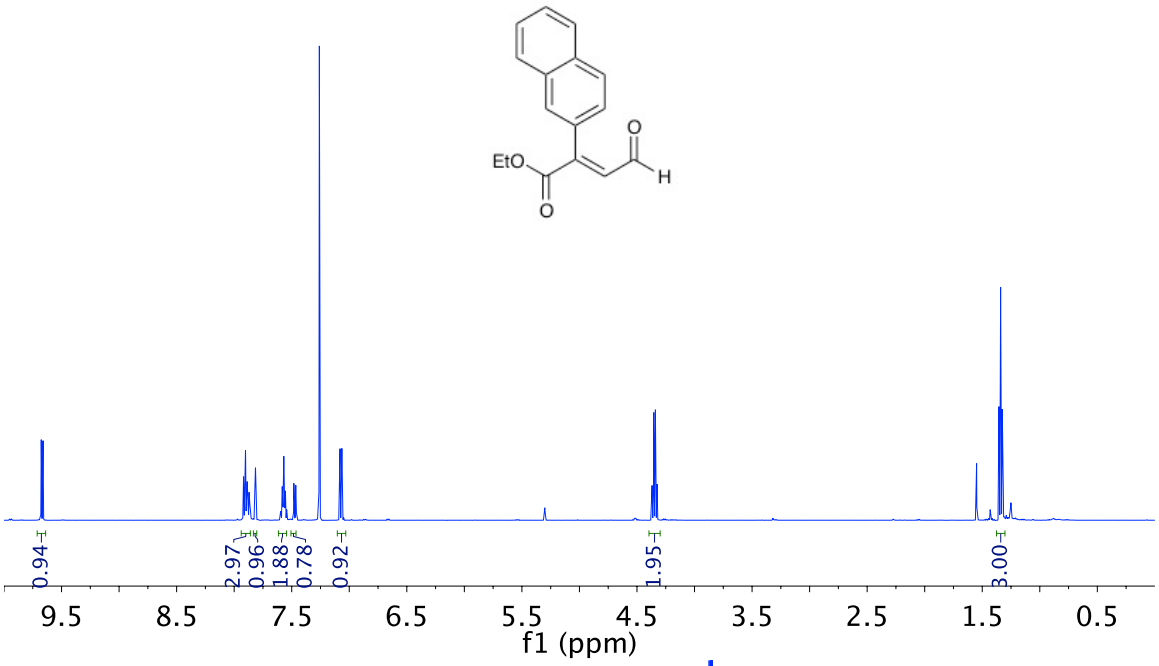
f1 (ppm)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5.5
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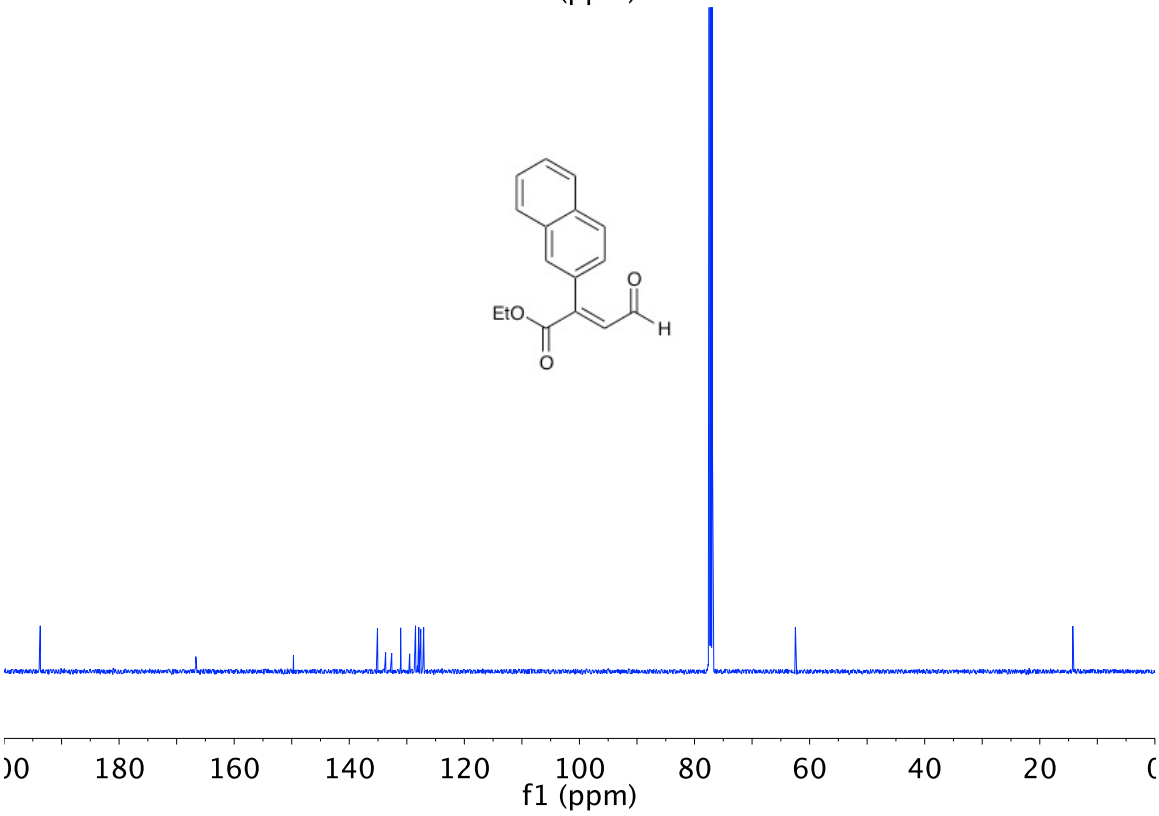
f1 (ppm)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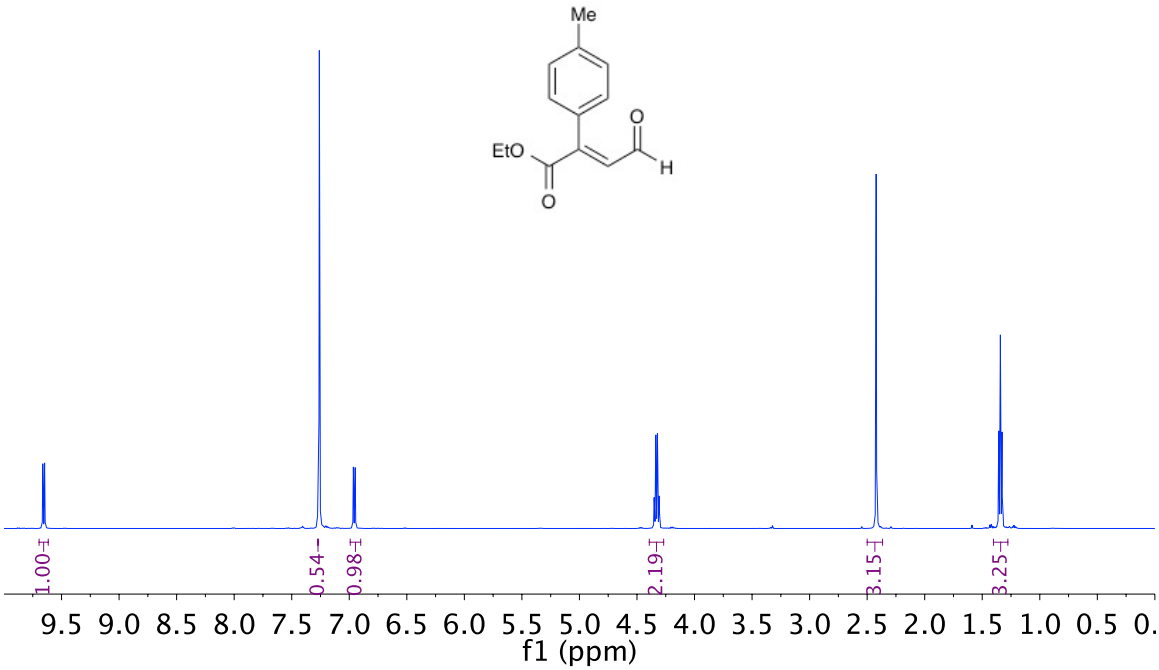
20
f1 (ppm)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3.15
3.25
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
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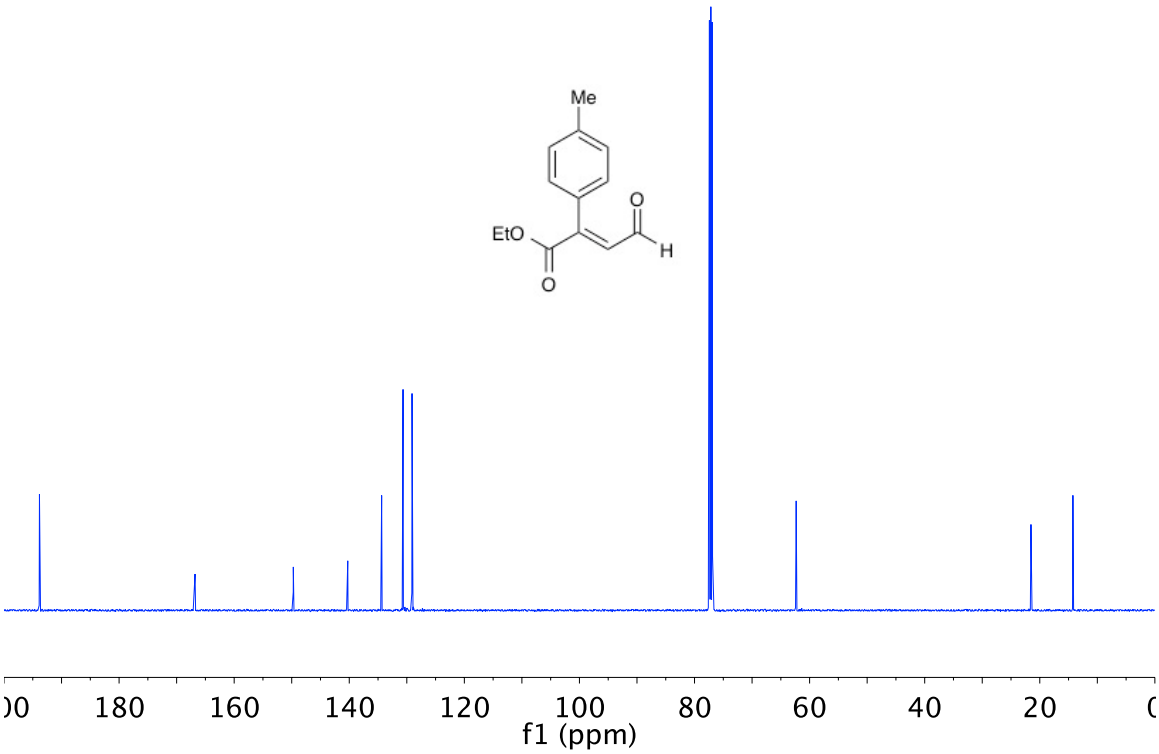
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O
H
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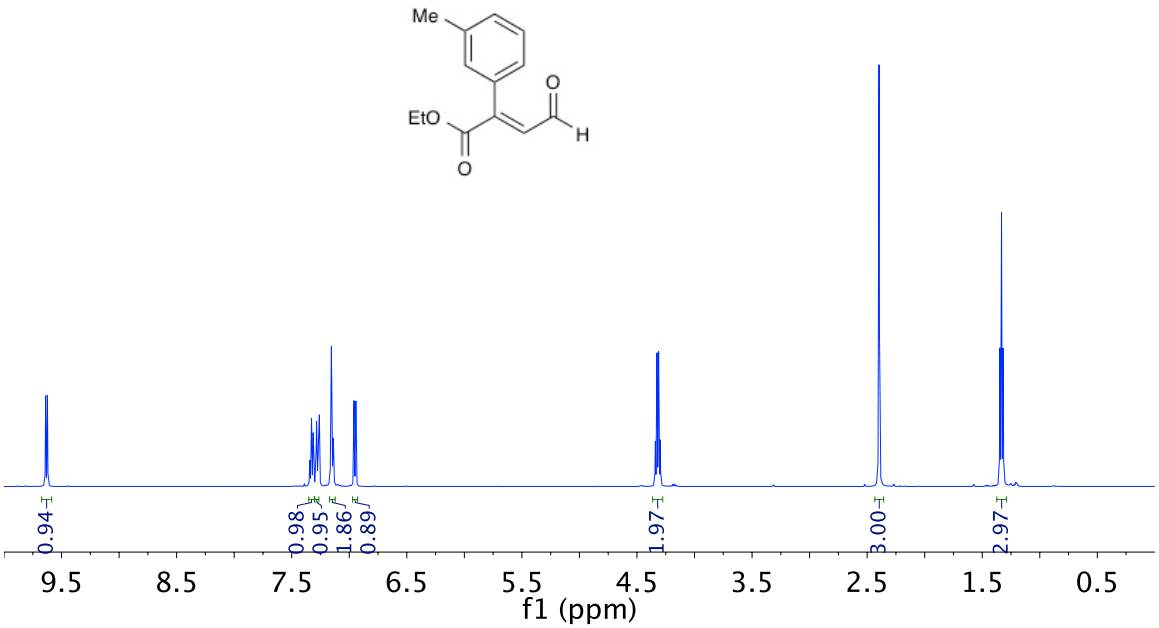
f1 (ppm)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2.5
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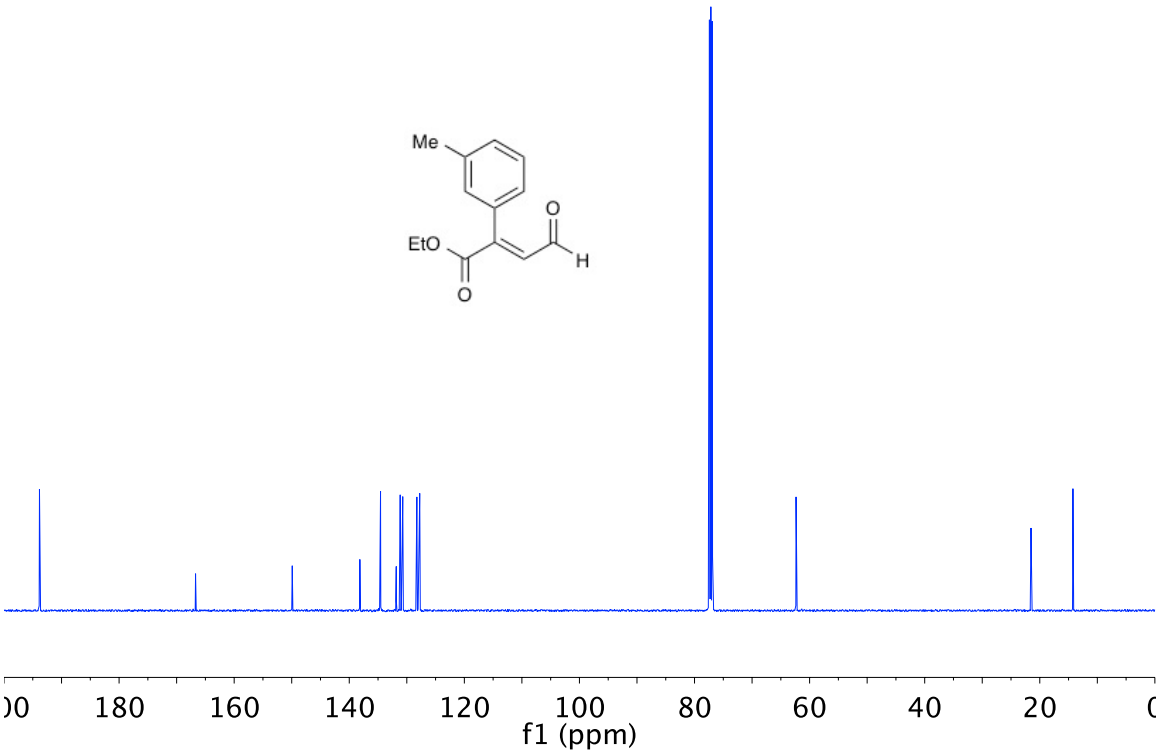
f1 (ppm)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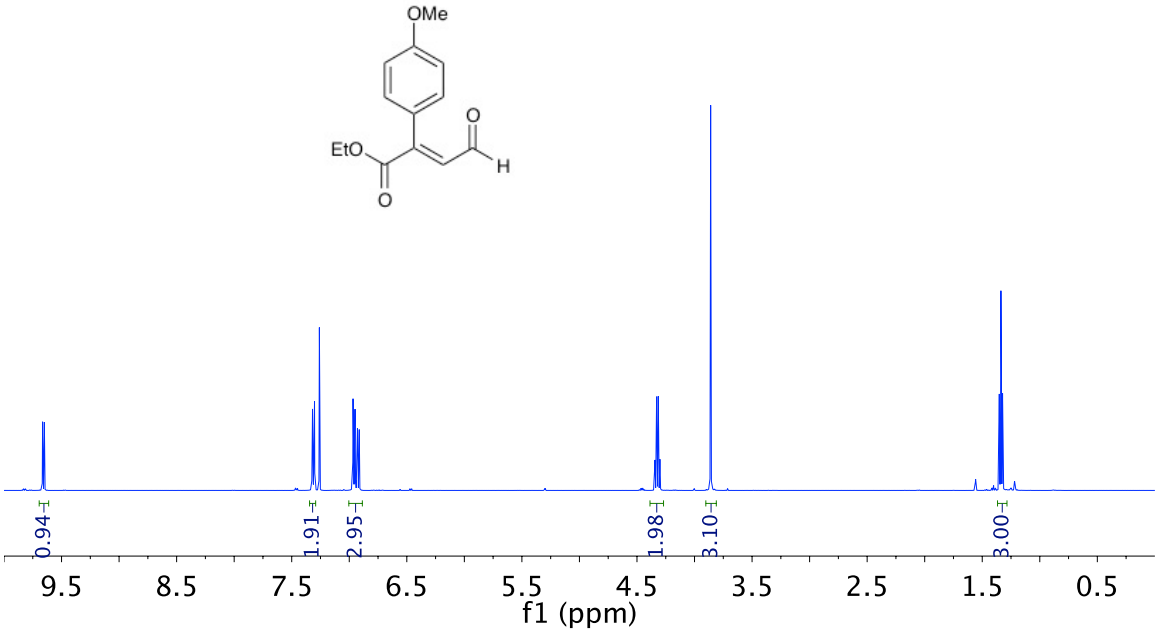
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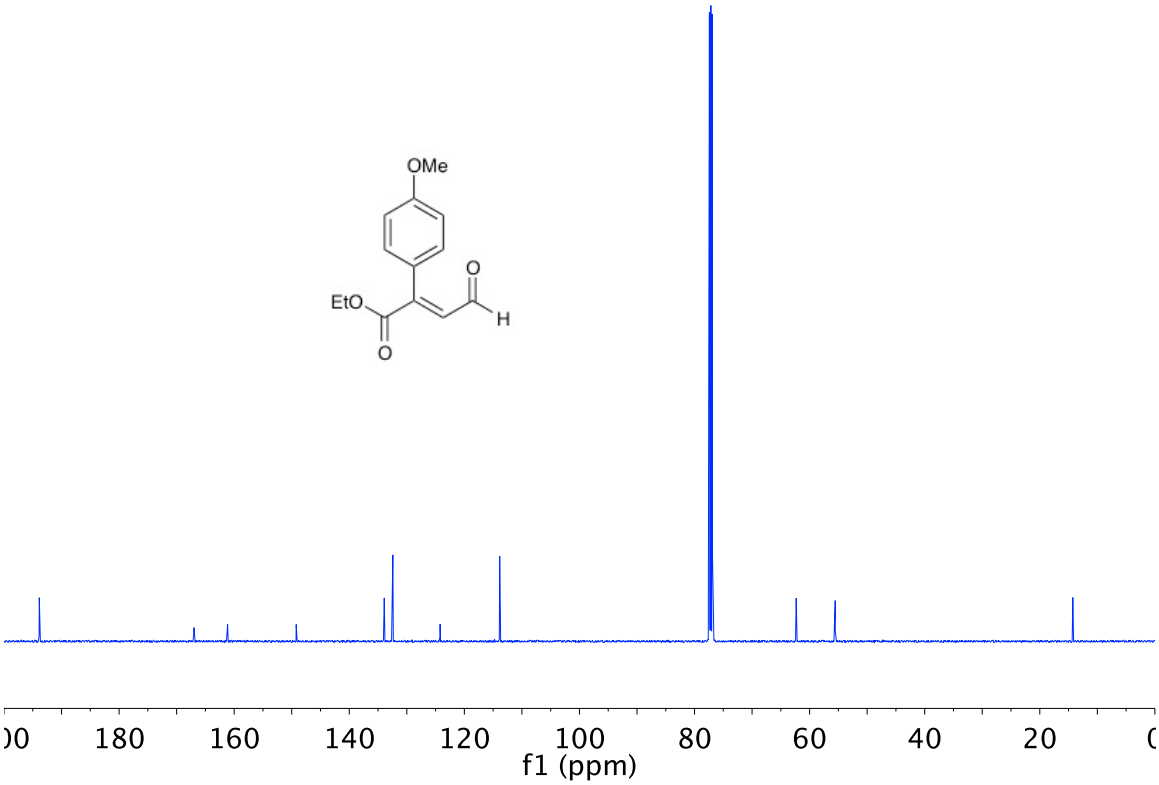
0.5
f1 (ppm)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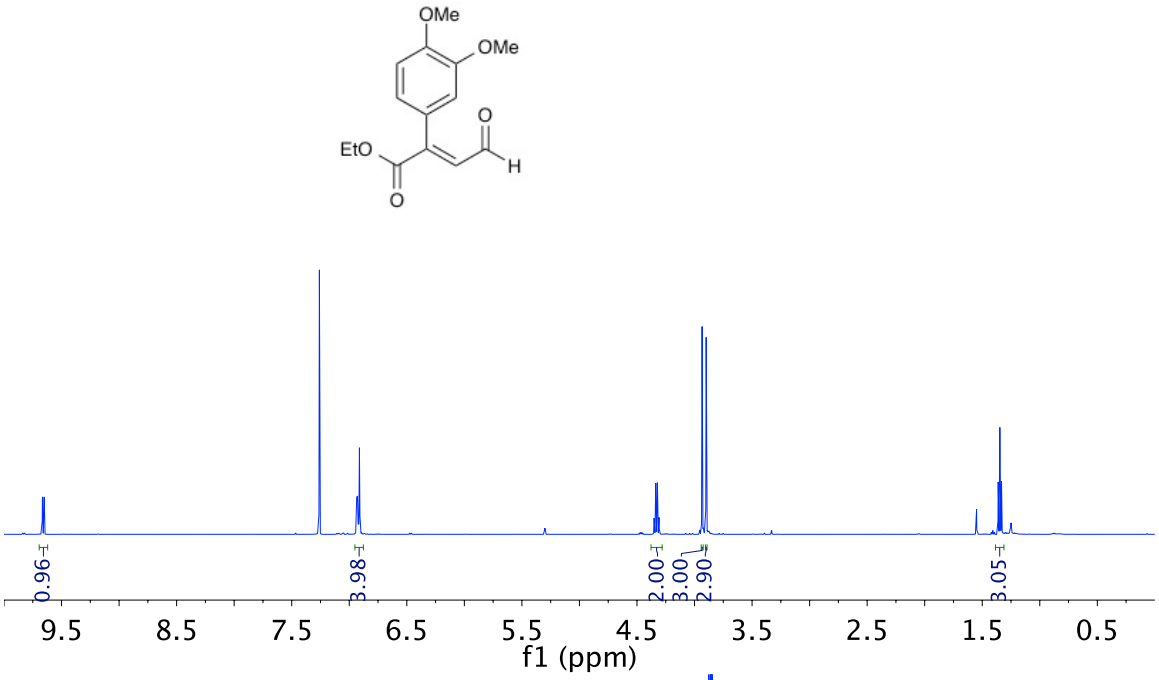
f1 (ppm)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7.5
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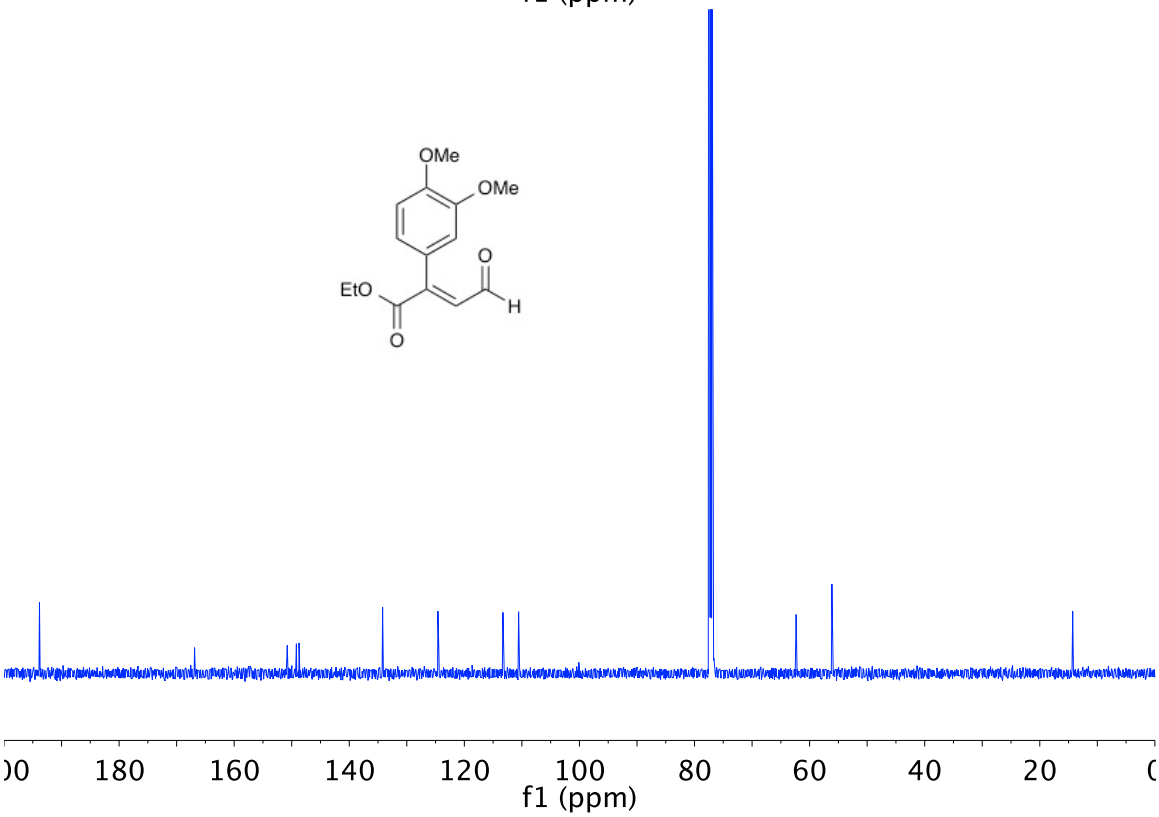
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)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OMe
EtO
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O
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160
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120
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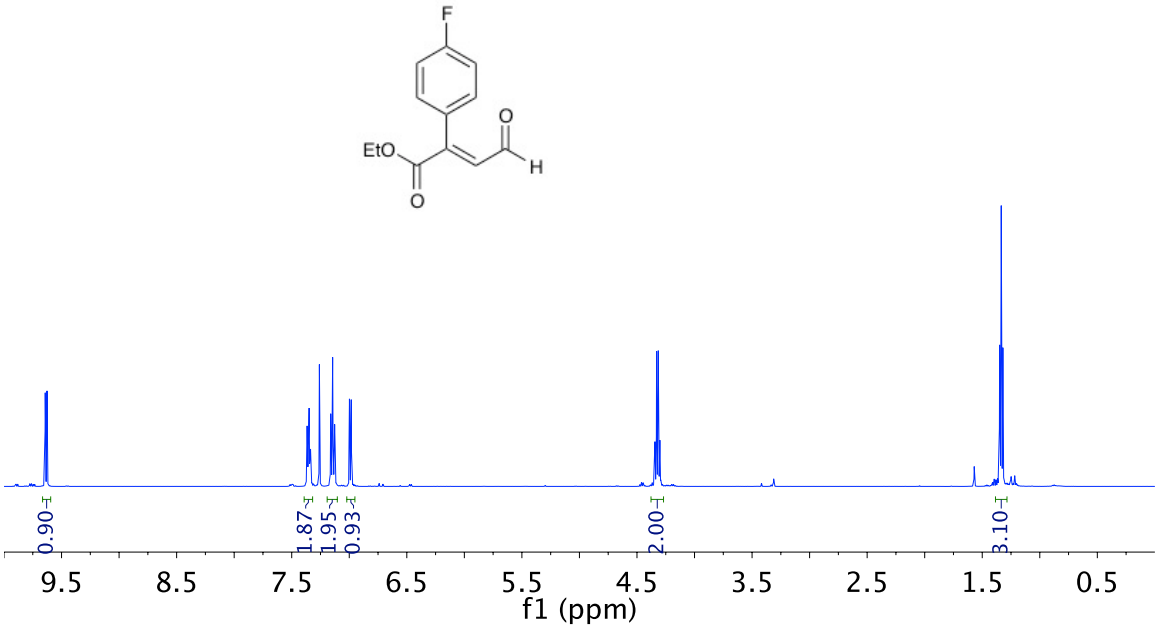
60
40
20
f1 (ppm)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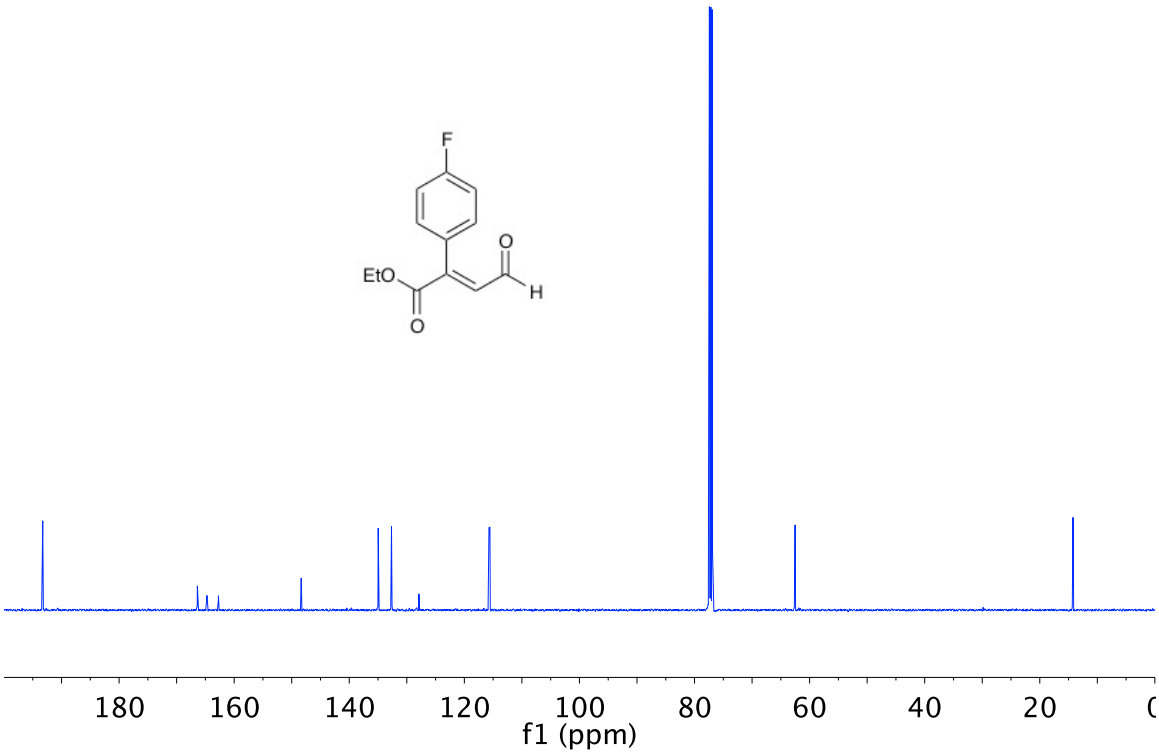
3.5
2.5
1.5
0.5
f1 (ppm)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EtO
H
O
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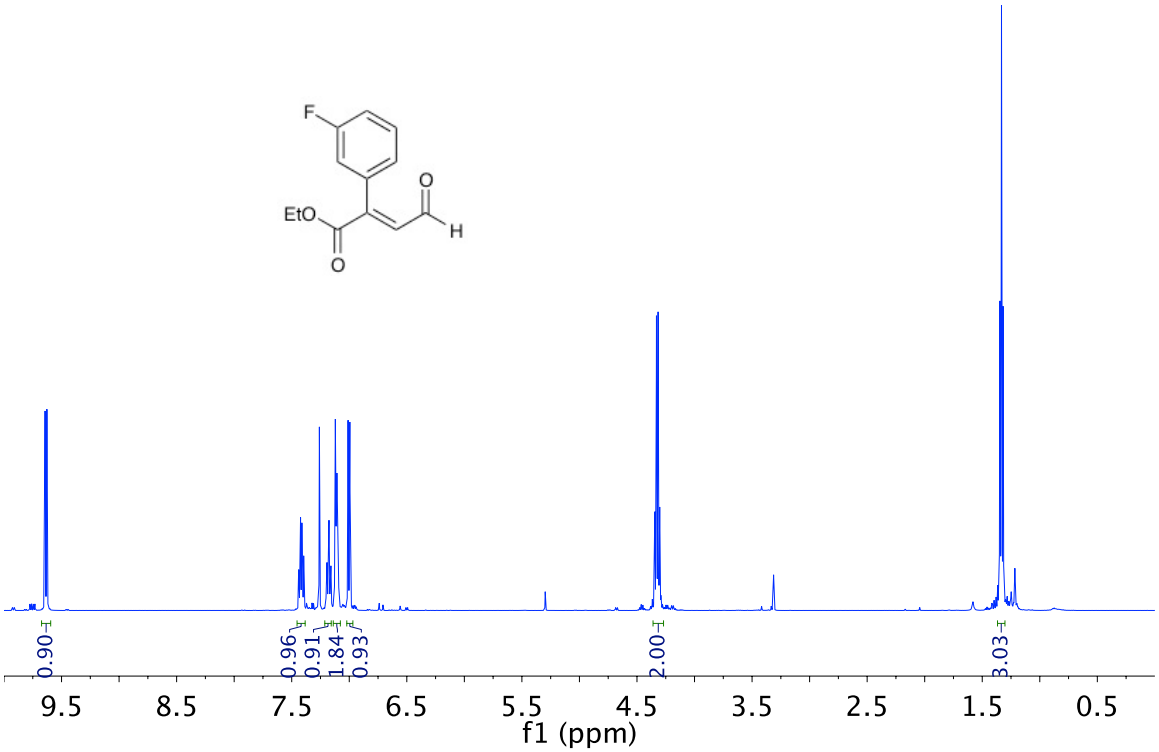
20
f1 (ppm)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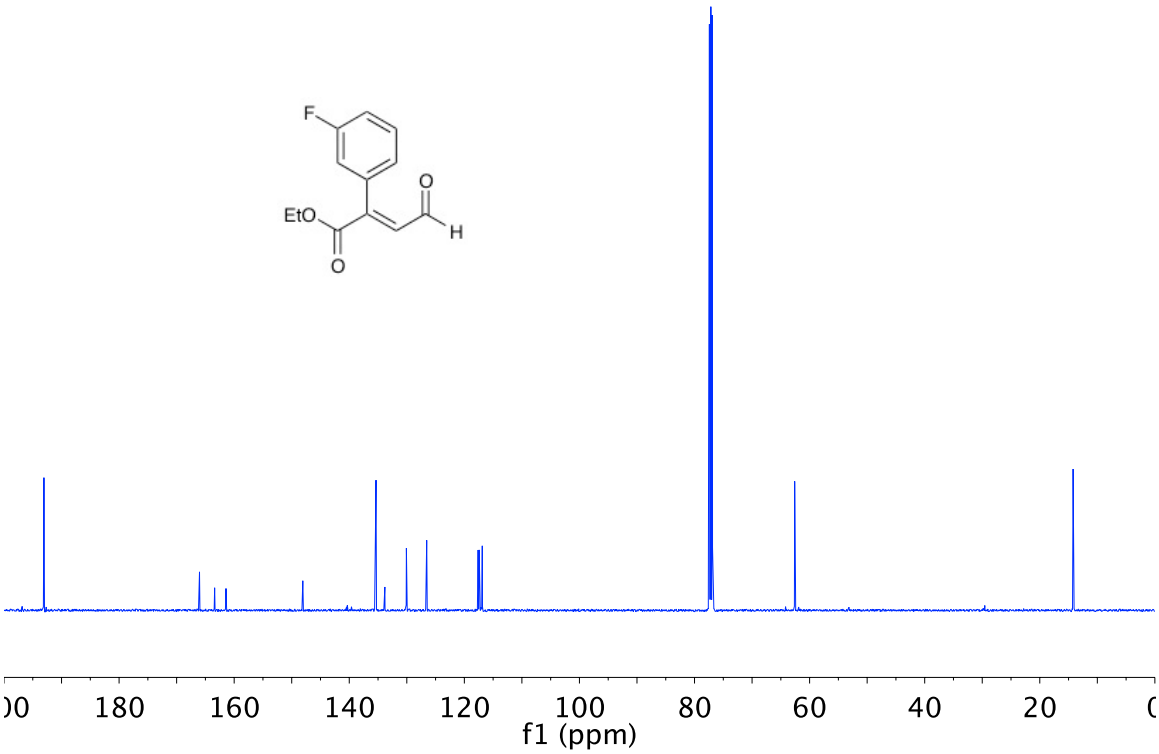
f1 (ppm)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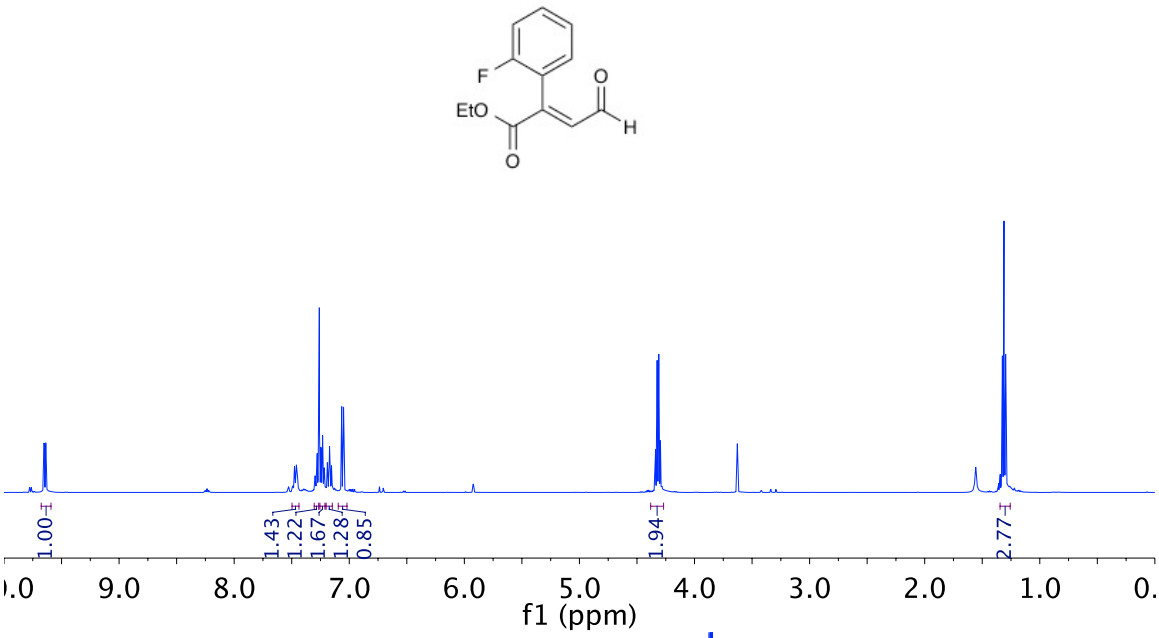
f1 (ppm)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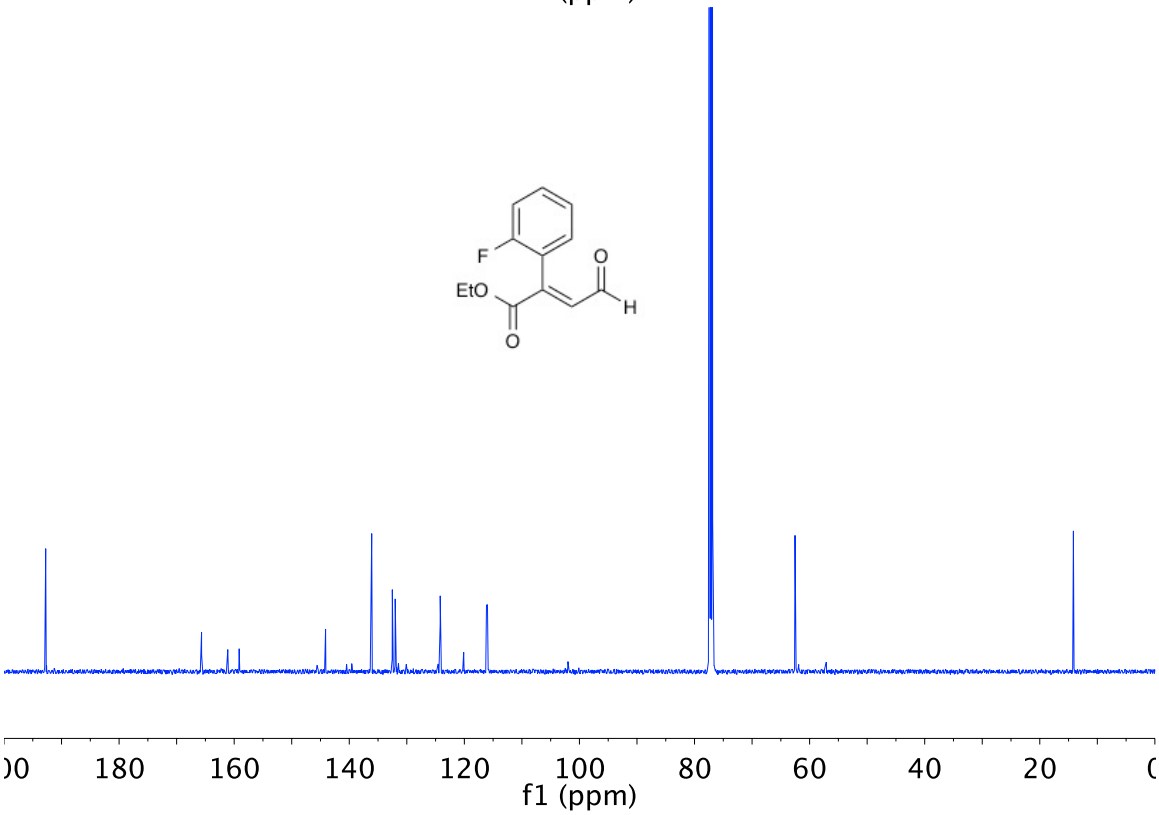
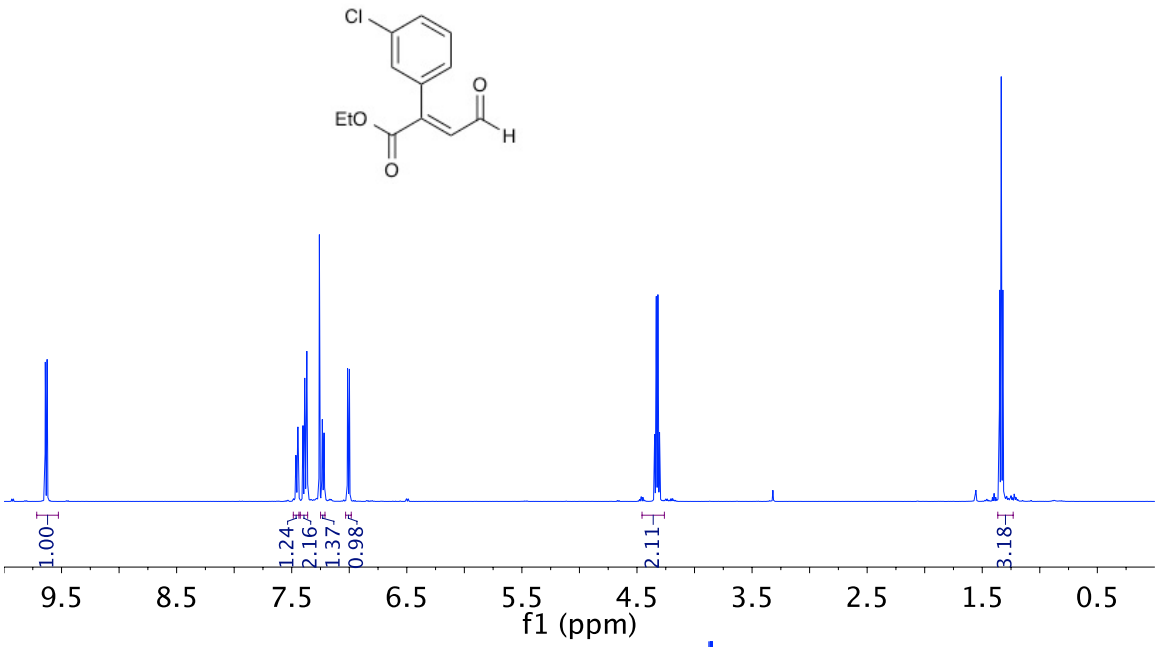
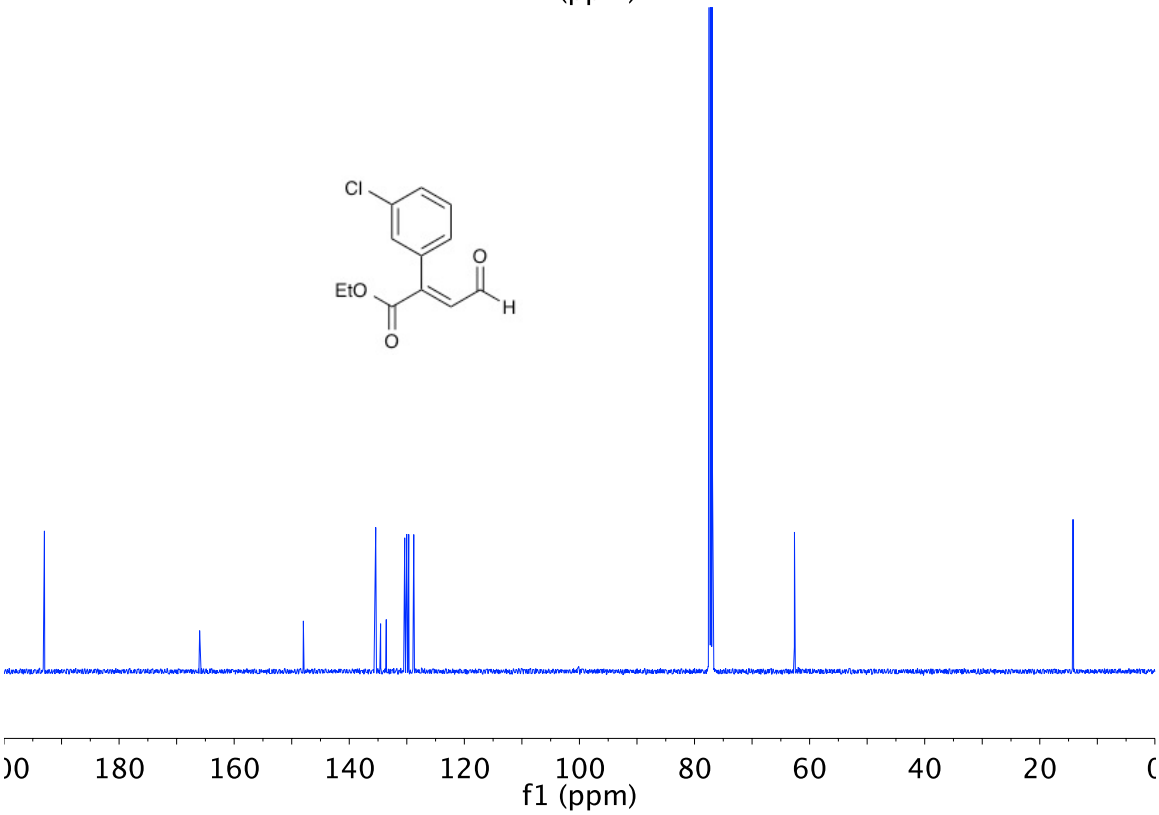
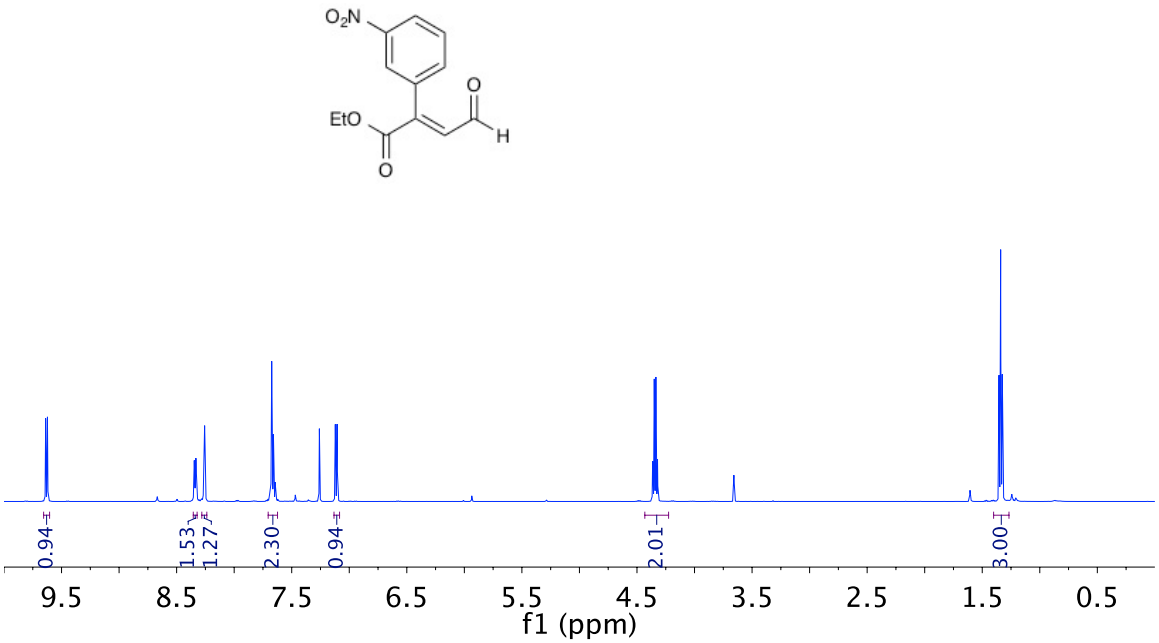
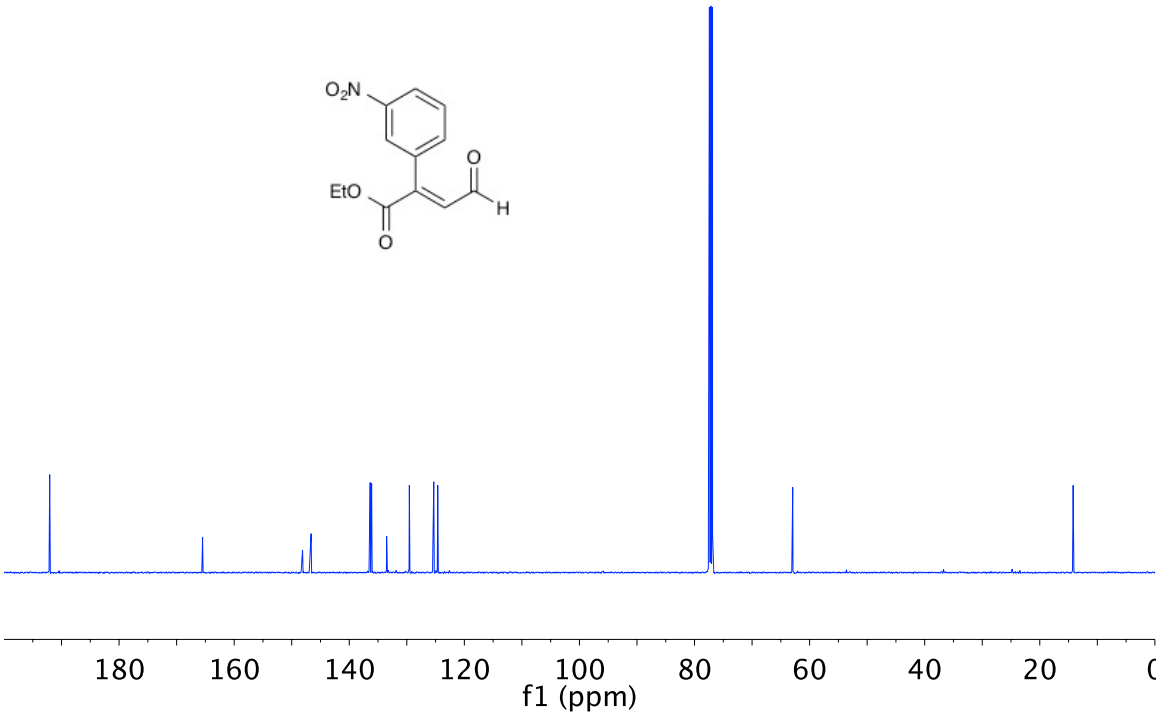
EtO
O
O
H
1.00
1.43
1.22
1.67
1.28
0.85
1.94
2.77
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)

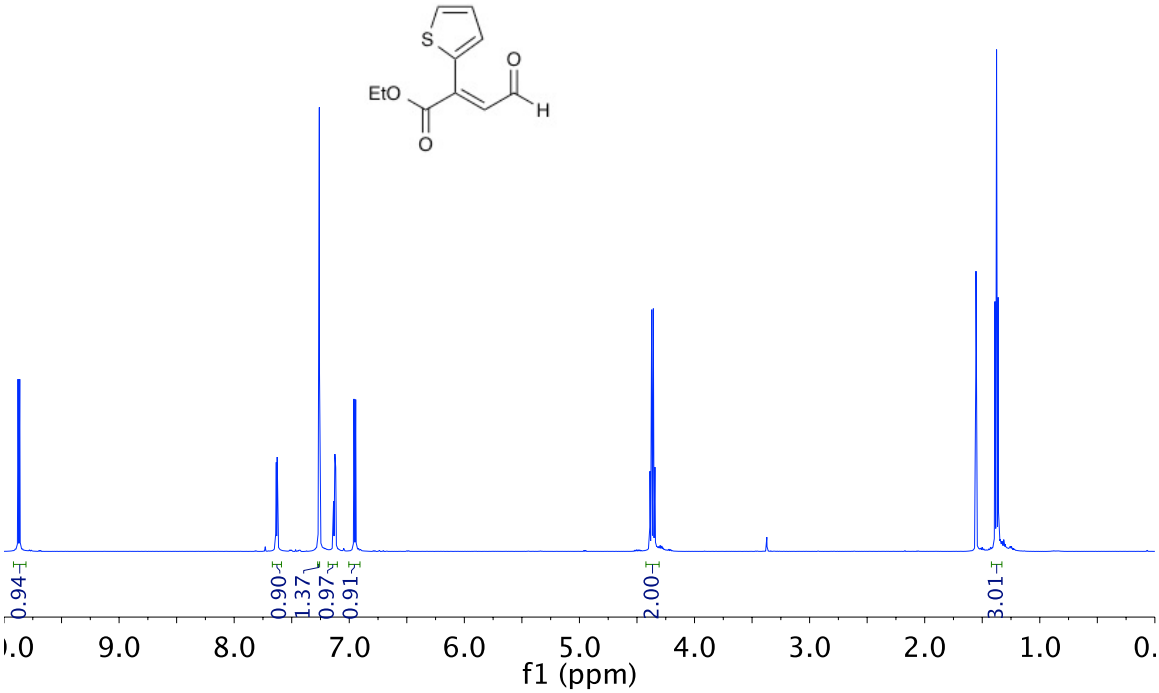

F
EtO
O
O
H
180
160
140
120
100
80
60
40
20
f1 (ppm)

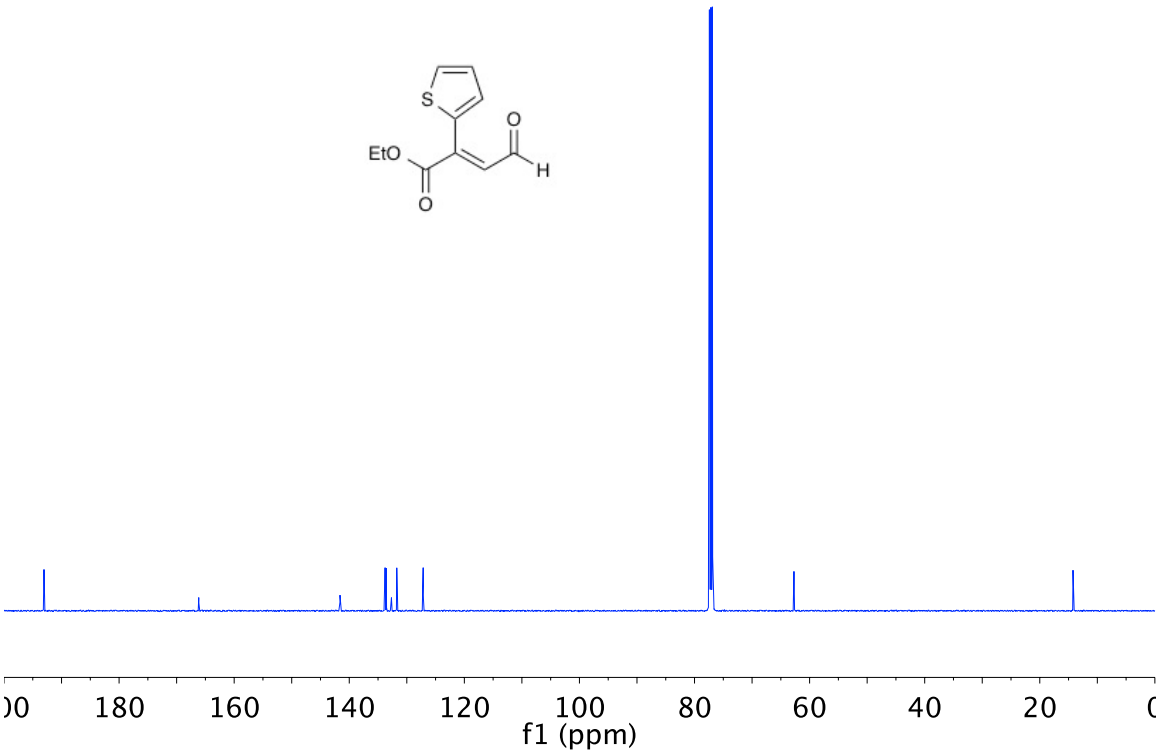

Cl
EtO
O
O
H
1.00
1.24
2.16
1.37
0.98
2.11
3.18
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

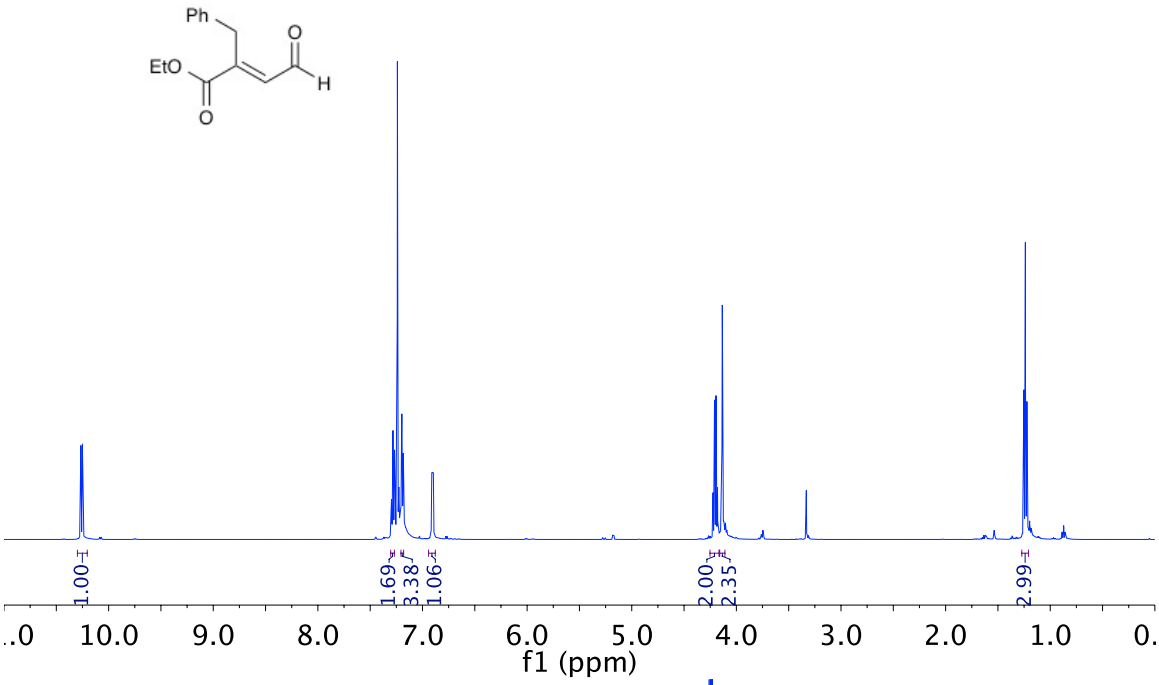

Cl
EtO
O
O
H
180
160
140
120
100
80
60
40
20
f1 (ppm)

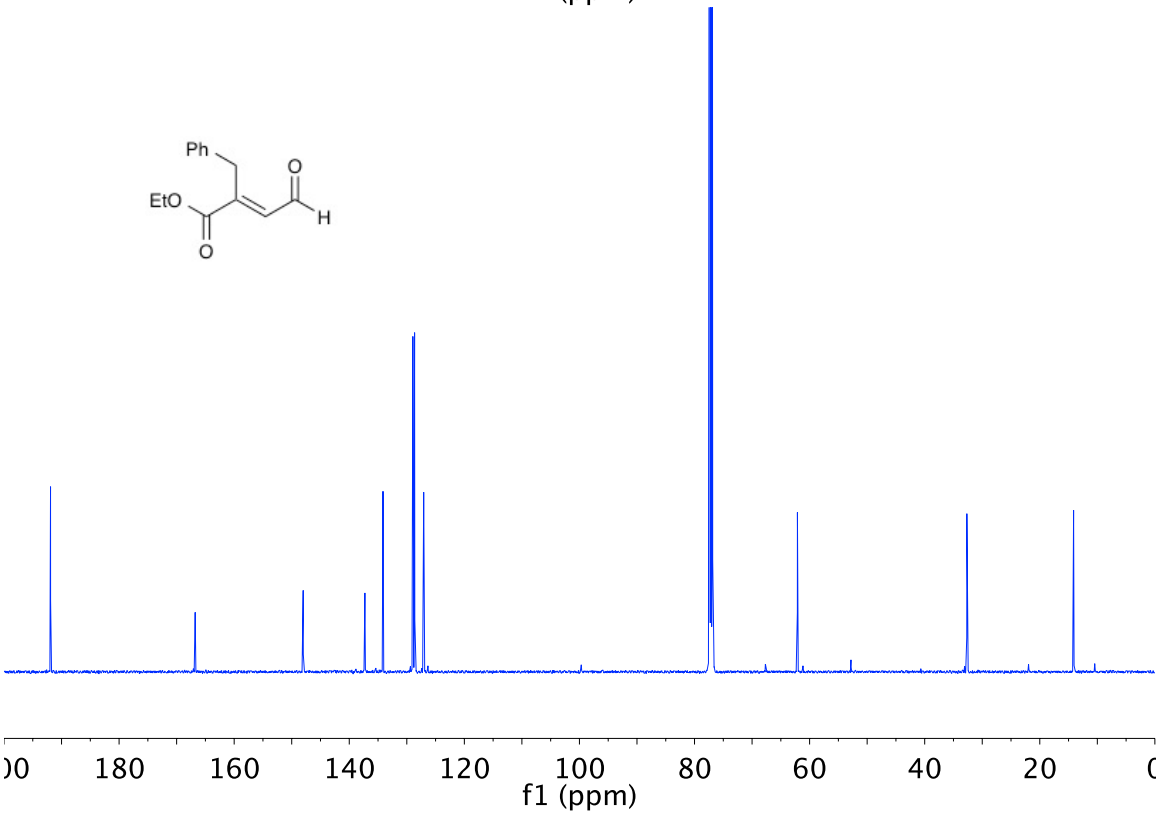

O2N
EtO
O
H
O
0.94
1.53
1.27
2.30
0.94
2.01
3.00
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

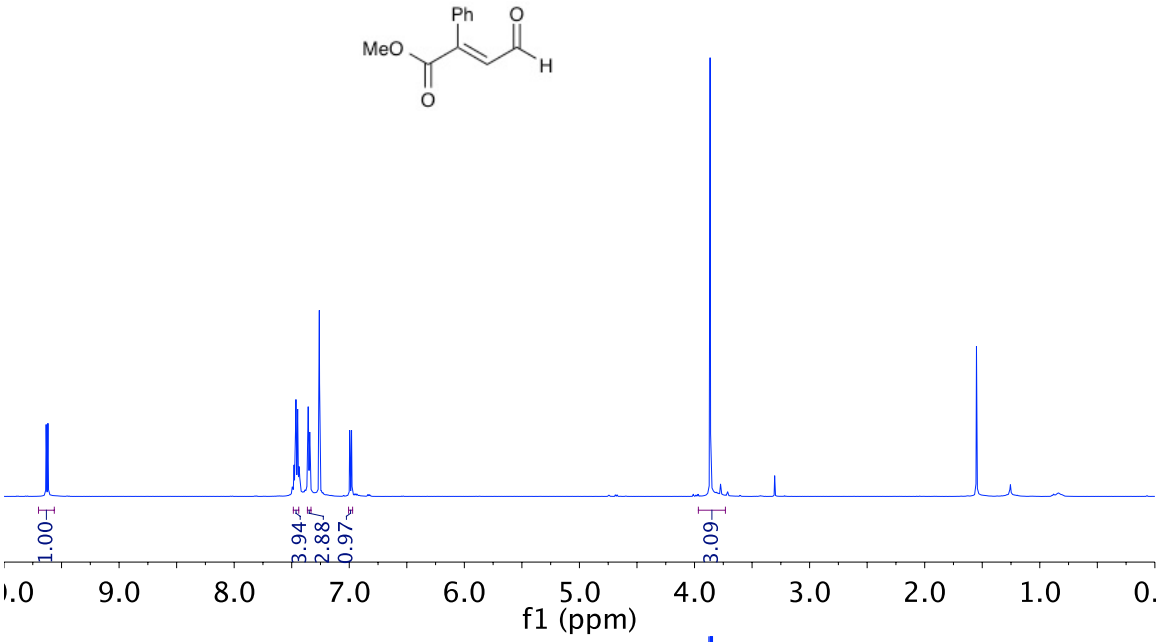

O2N
EtO
O
H
O
180
160
140
120
100
80
60
40
20
f1 (ppm)

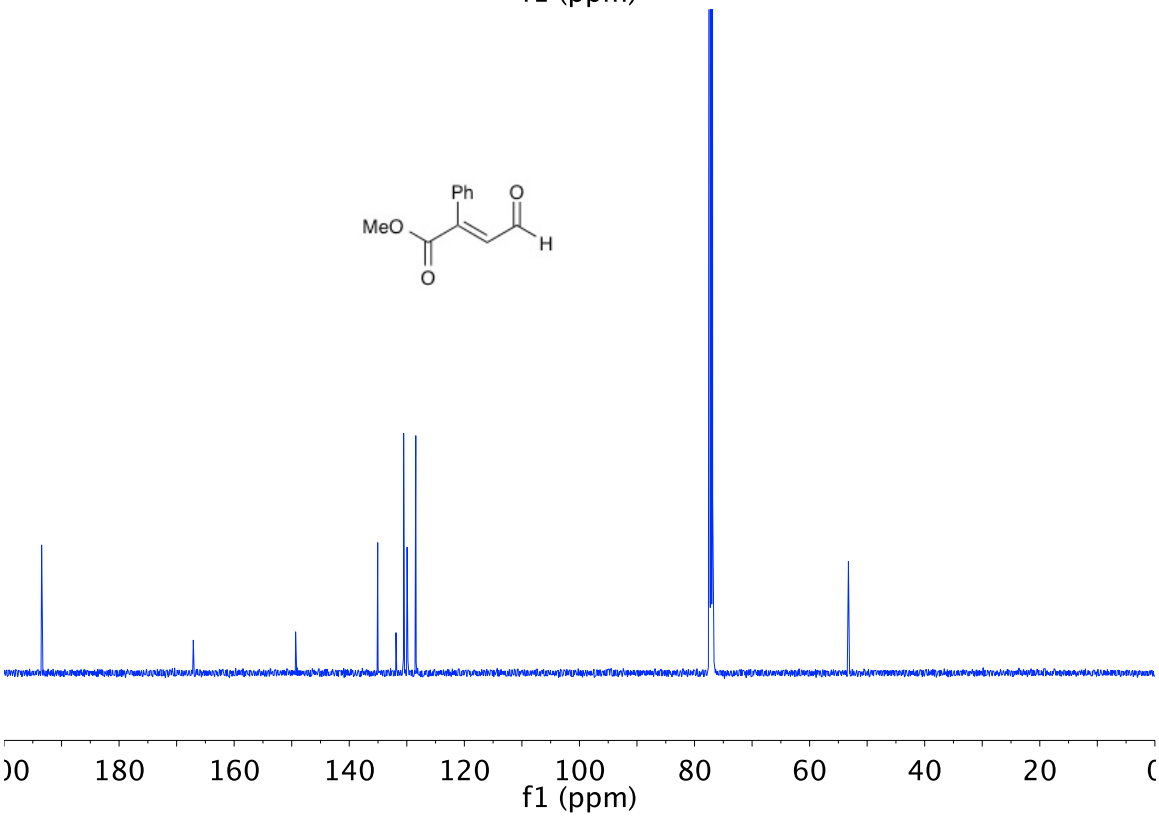

S
O
EtO
H
O
0.94
0.90
1.37
0.97
0.91
2.00
3.01
f1 (ppm)

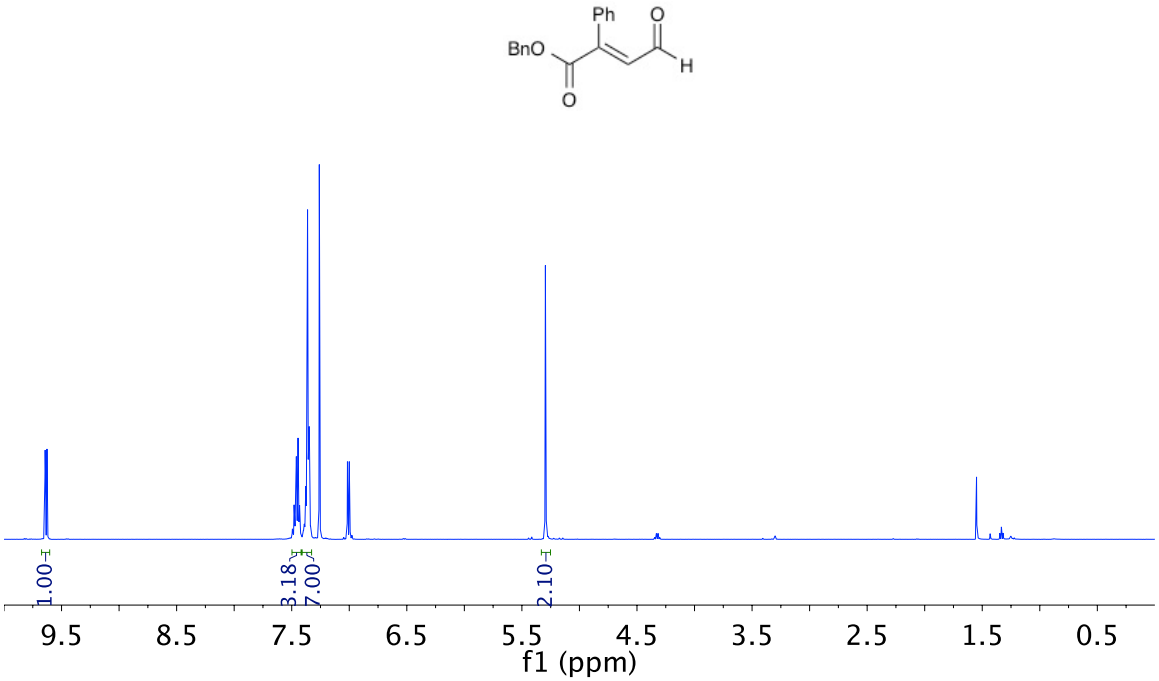

S
O
EtO
H
O
f1 (ppm)

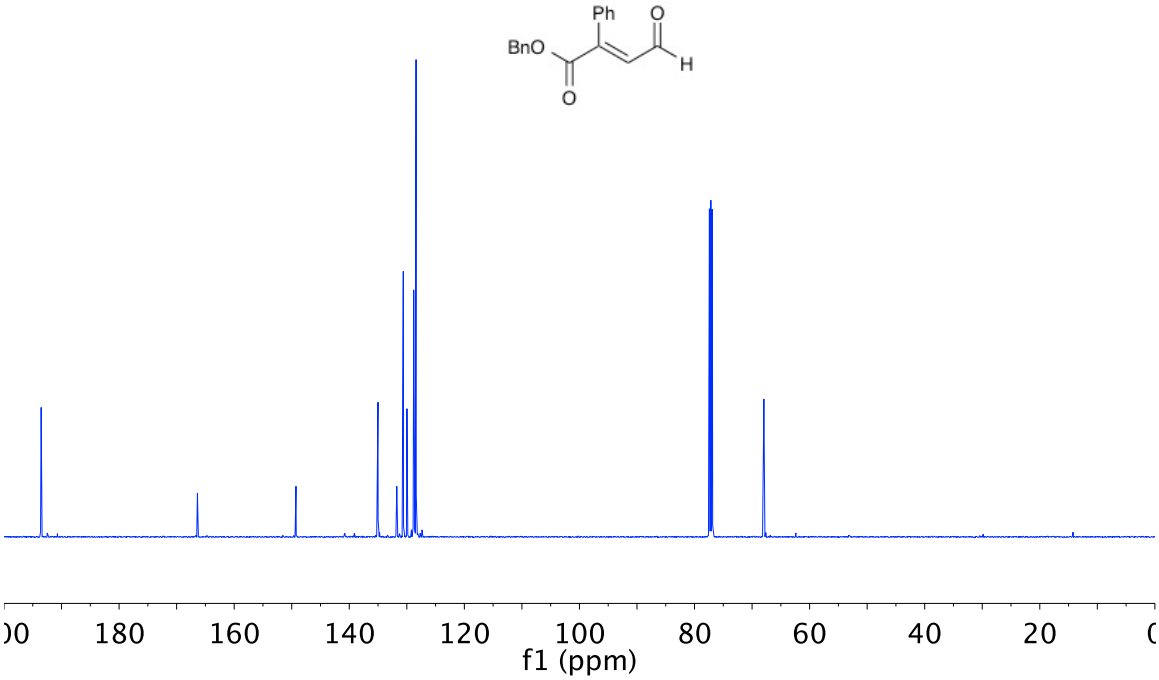

Ph
O
EtO
H
O
1.00
1.69
3.38
1.06
2.00
2.35
2.99
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)

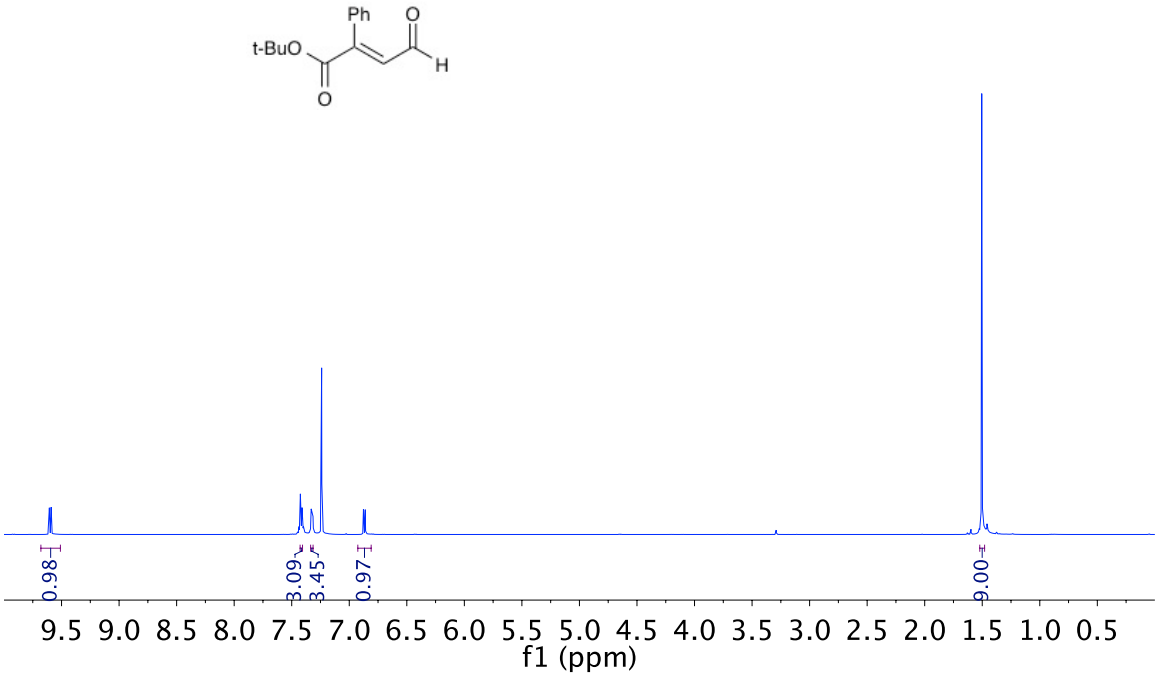

Ph
O
EtO
H
O
180
160
140
120
100
80
60
40
20
f1 (ppm)

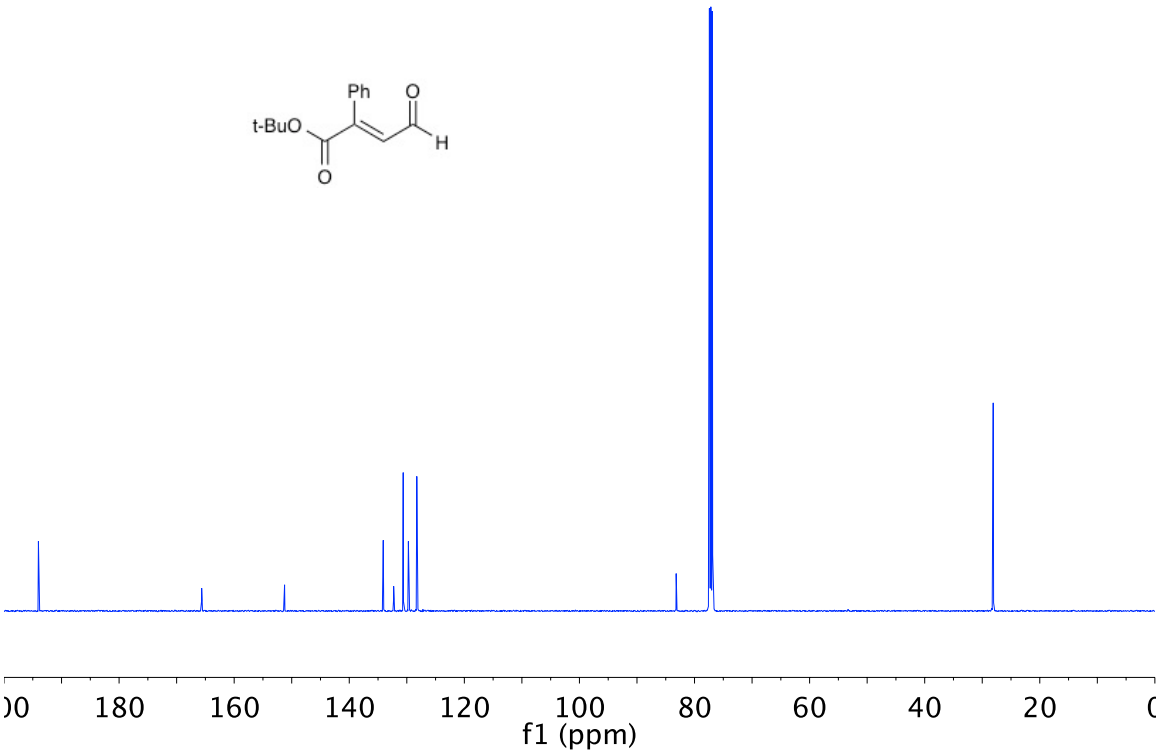

Ph
O
MeO
H
O
1.00
3.94
2.88
0.97
3.09
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
f1 (ppm)

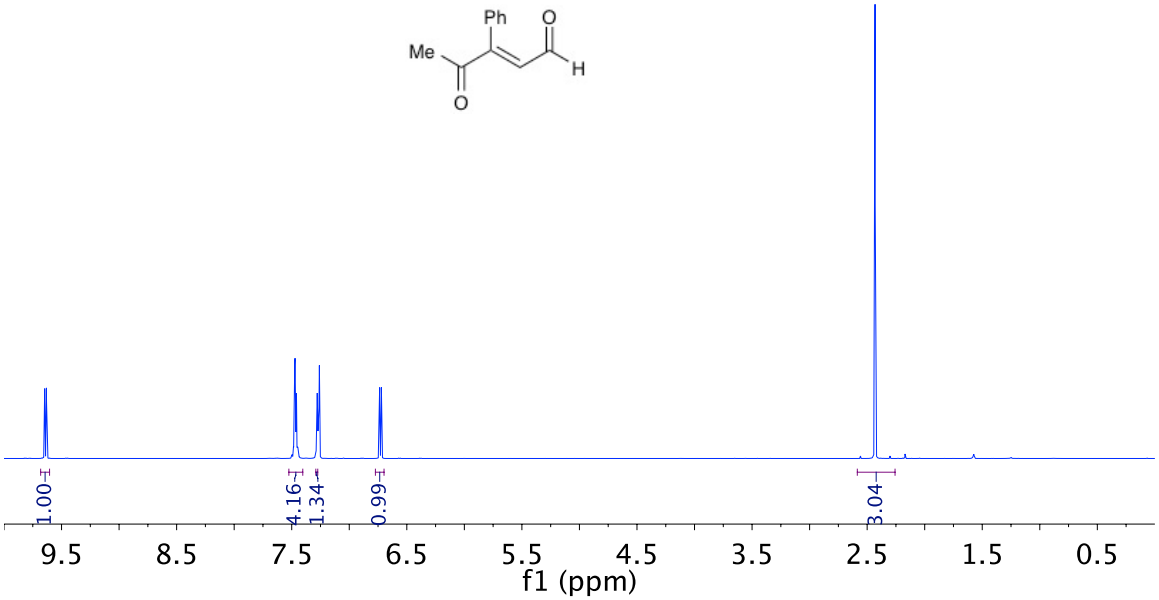

Ph
O
MeO
H
O
180
160
140
120
100
80
60
40
20
f1 (ppm)

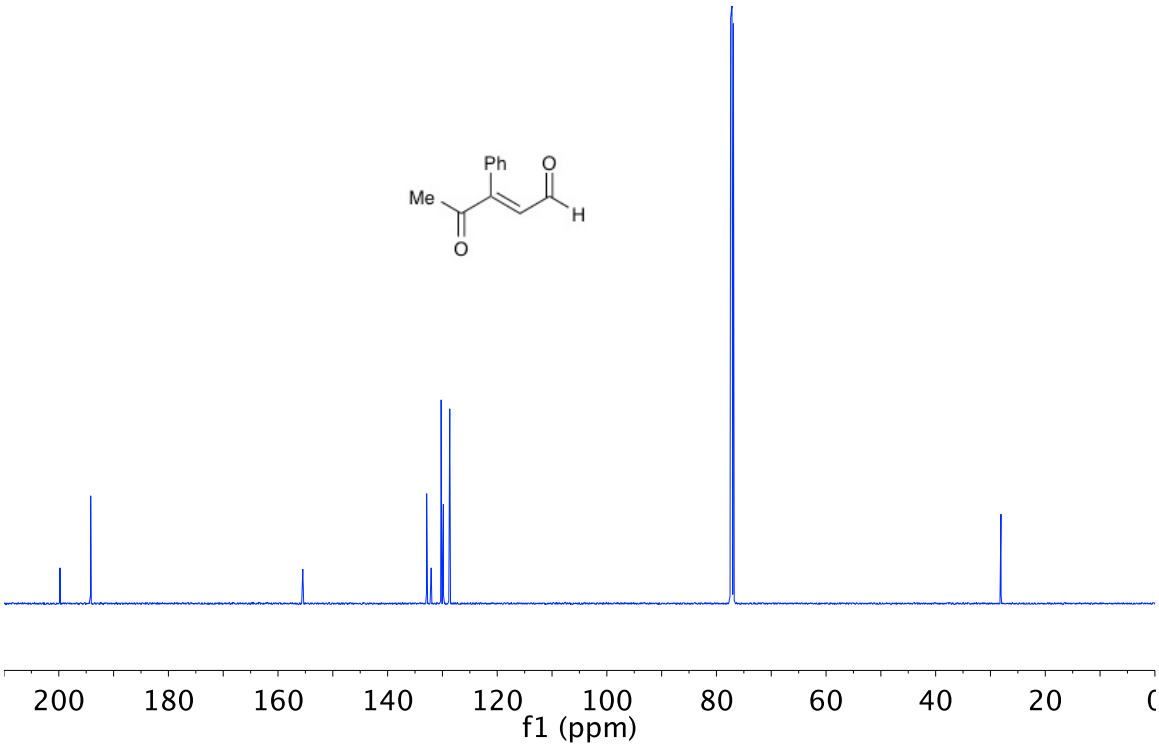

Ph
O
BnO
H
O
1.00
3.18
7.00
2.10
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

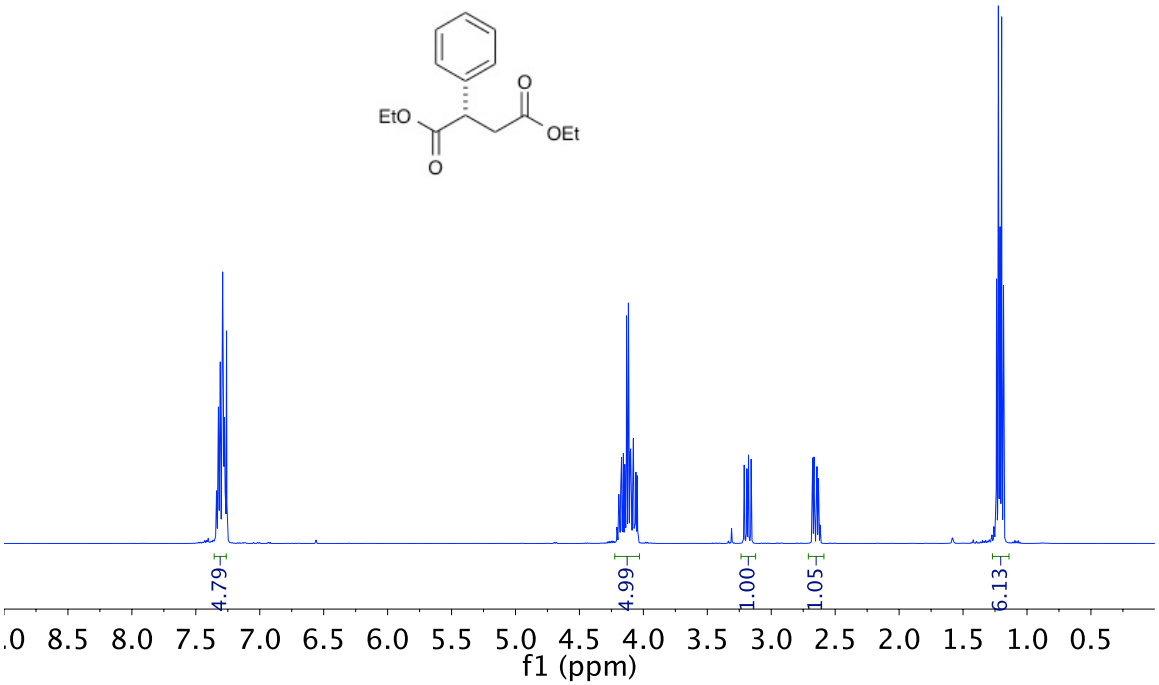

Ph
O
BnO
H
O
180
160
140
120
100
80
60
40
20
f1 (ppm)

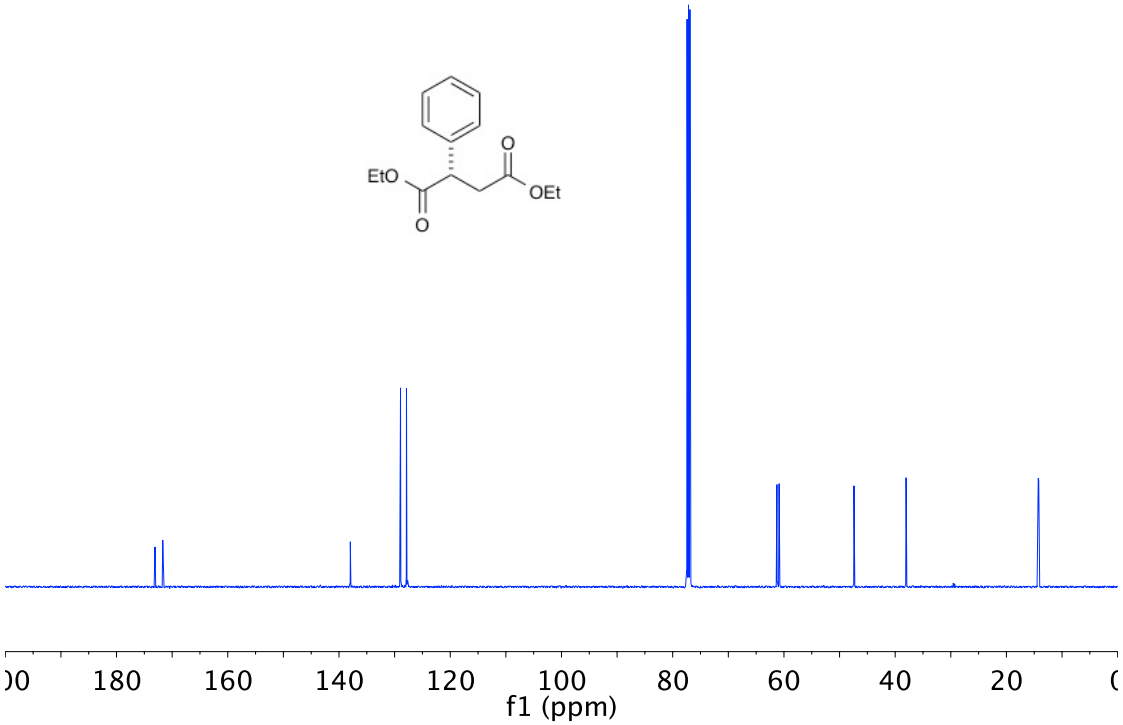

Ph
O
t-BuO
H
O
0.98
3.09
3.45
0.97
9.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

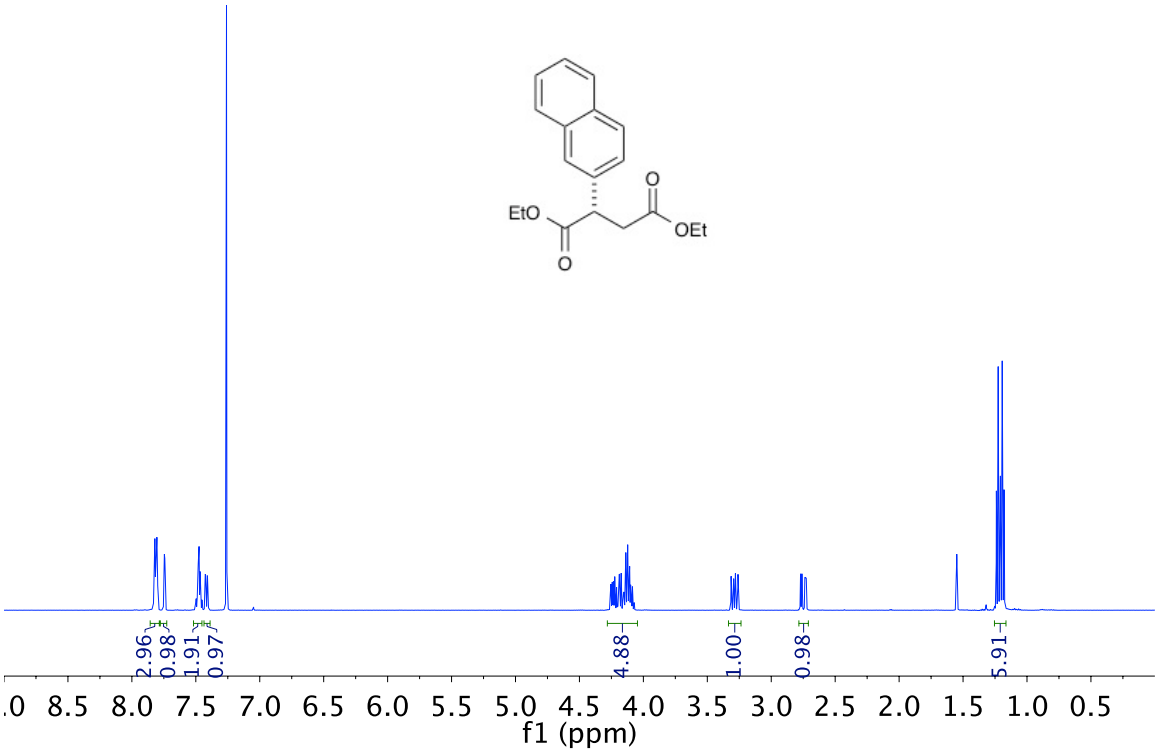

Ph
O
t-BuO
H
O
180 160 140 120 100 80 60 40 20
f1 (ppm)

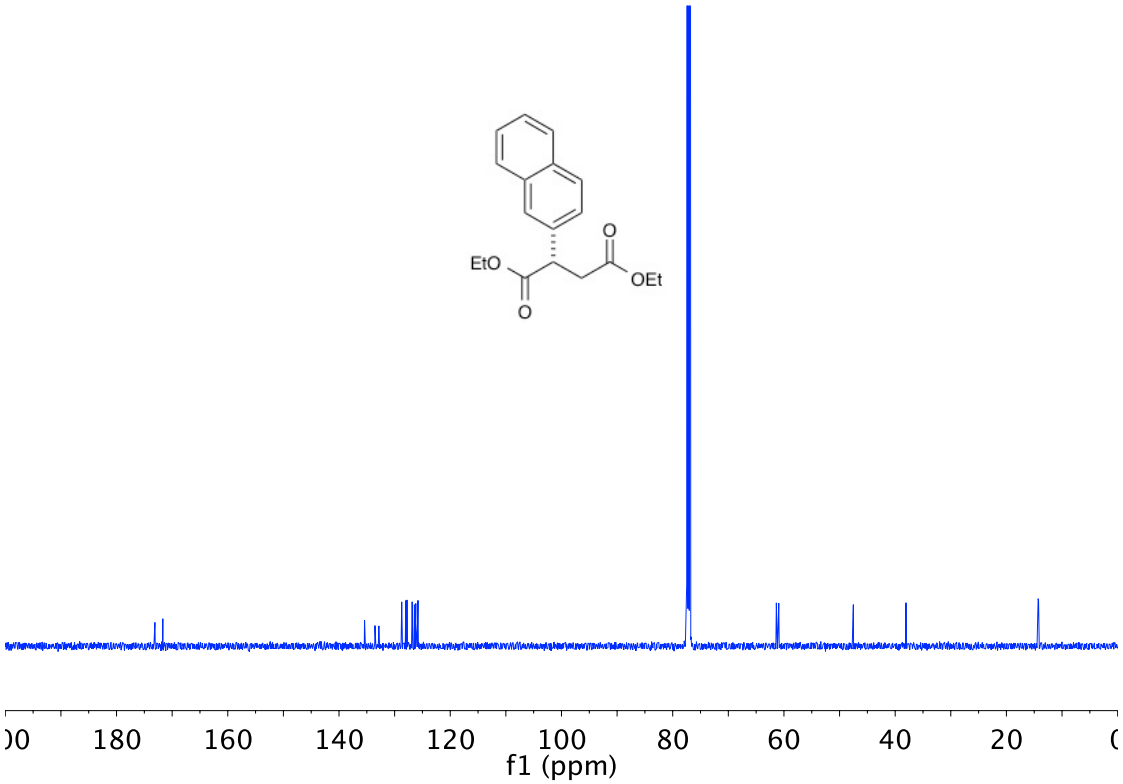

Ph
O
Me
H
O
1.00
4.16
1.34
0.99
3.04
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

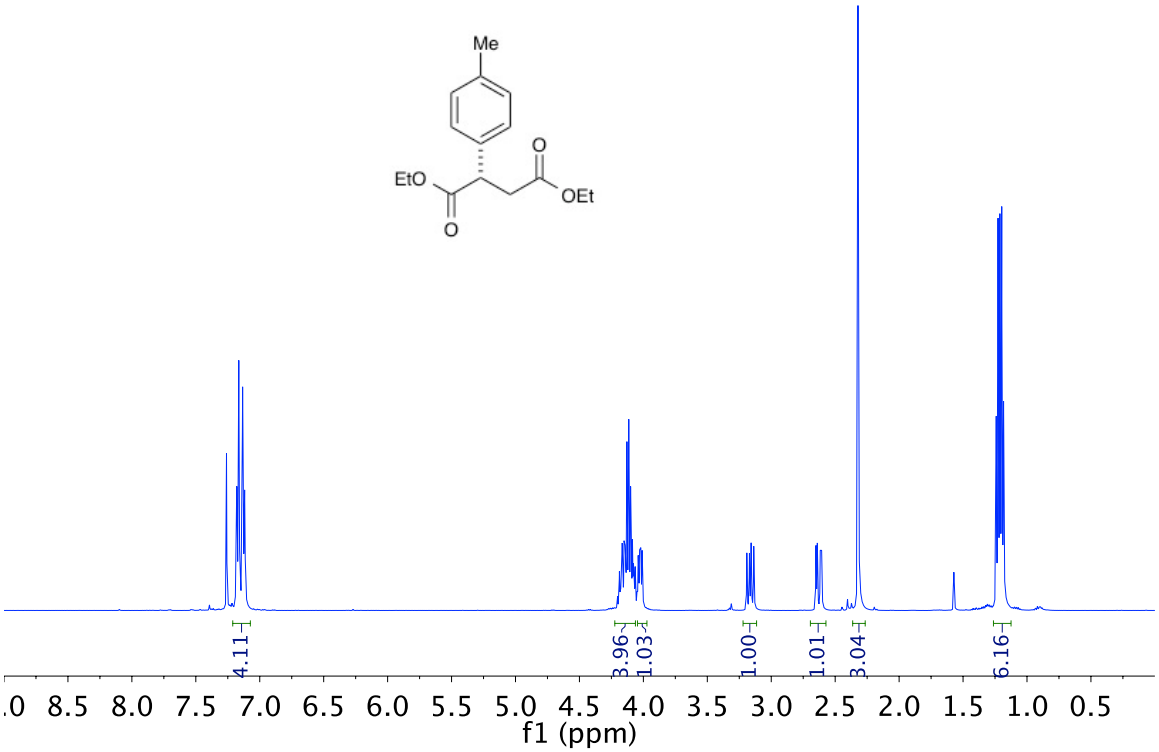

Ph
O
Me
H
O
200
180
160
140
120
100
80
60
40
20
f1 (ppm)

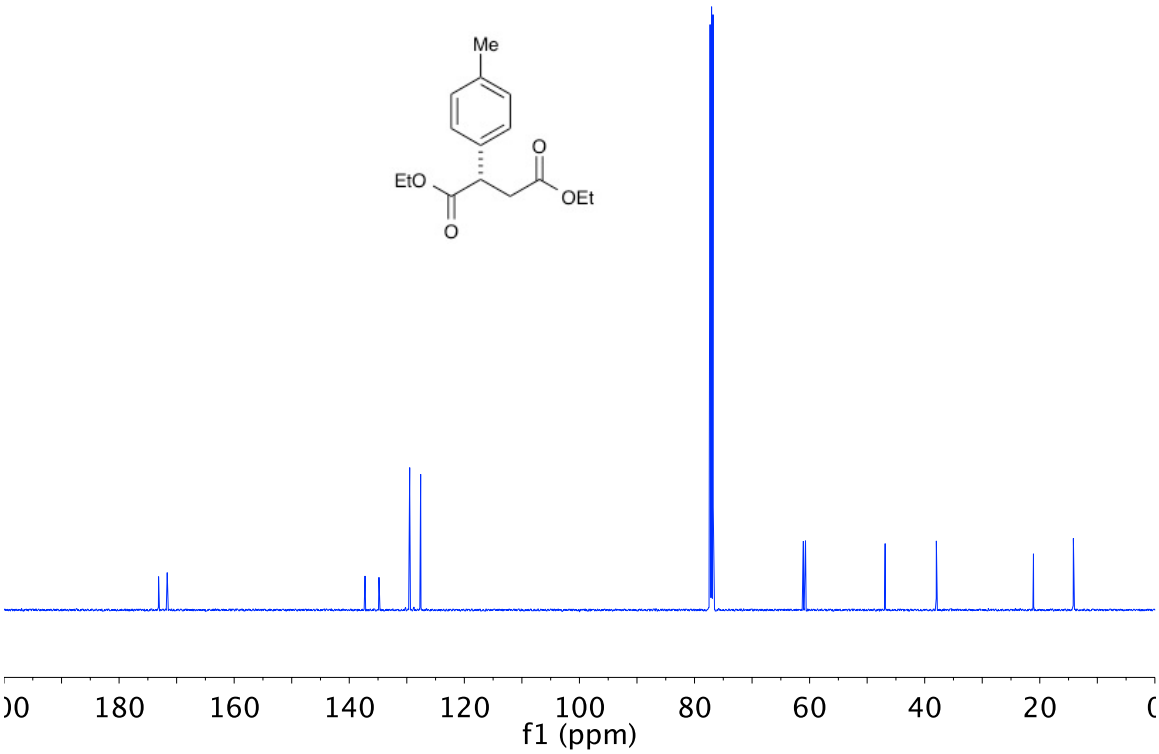

EtO
O
O
OEt
O
4.79
4.99
1.00
1.05
6.13
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

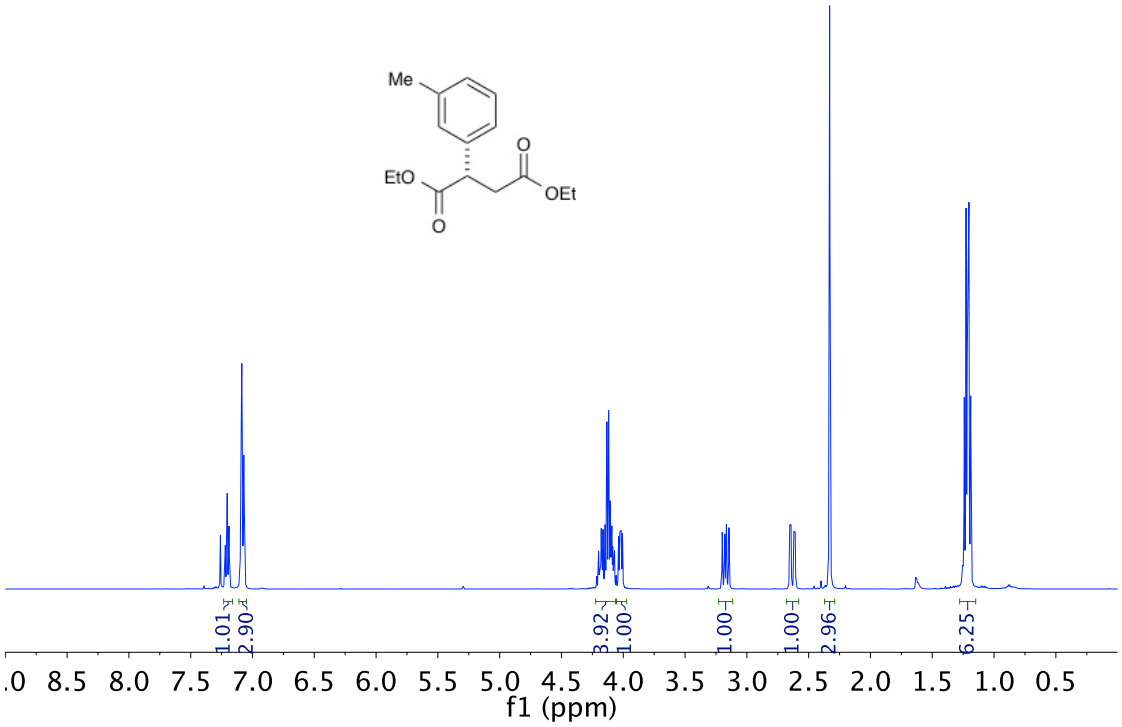

EtO
O
O
OEt
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

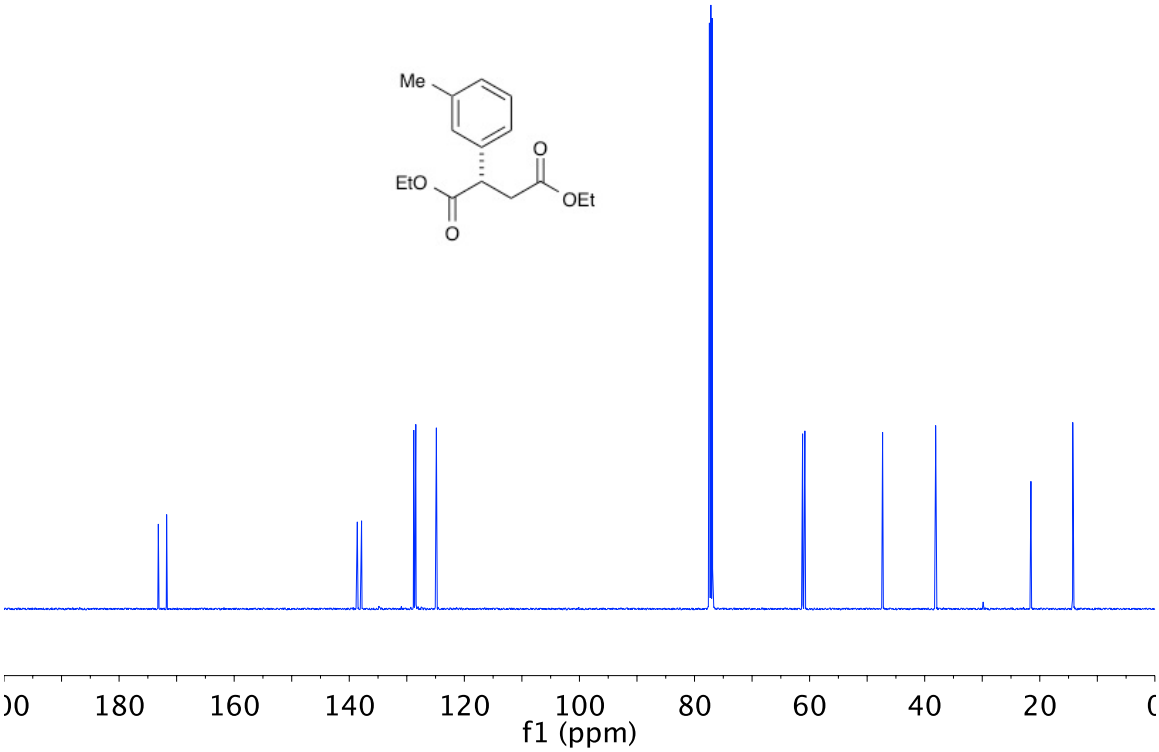

EtO
O
OEt
O
2.96
0.98
1.91
0.97
4.88
1.00
0.98
5.91
f1 (ppm)

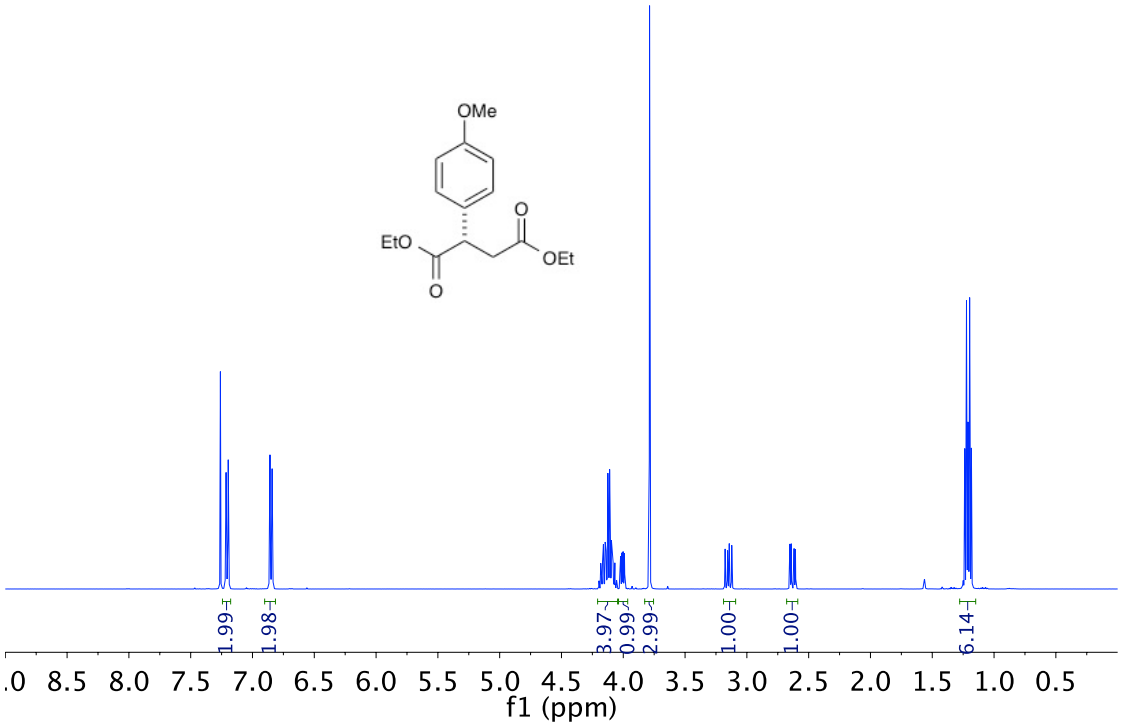

EtO
O
OEt
O
f1 (ppm)

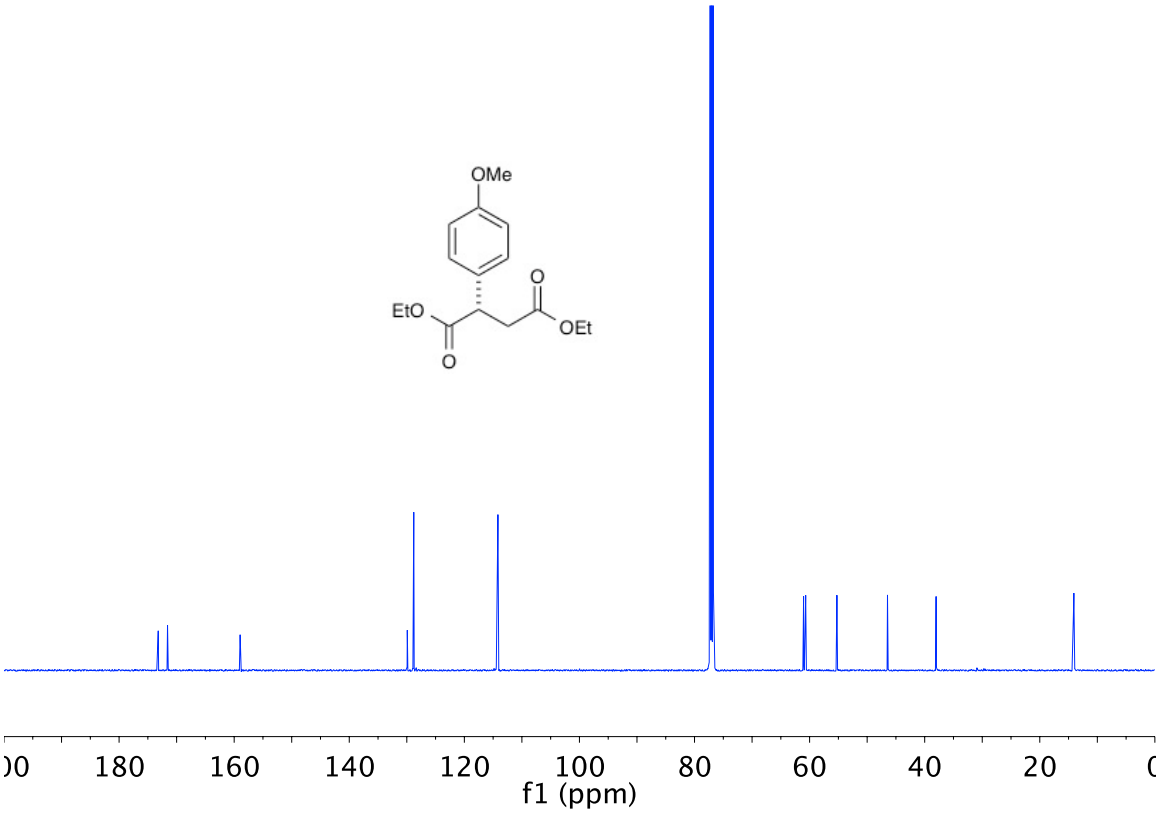

Me
EtO
O
OEt
O
4.11
3.96
1.03
1.00
1.01
3.04
6.16
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

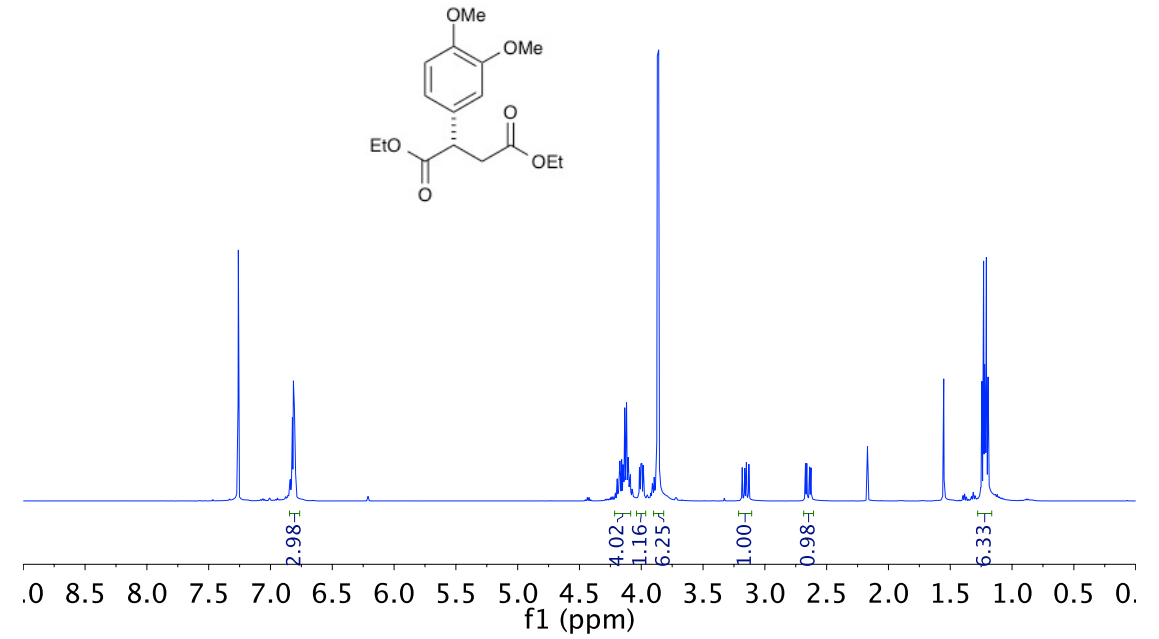

Me
EtO
O
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

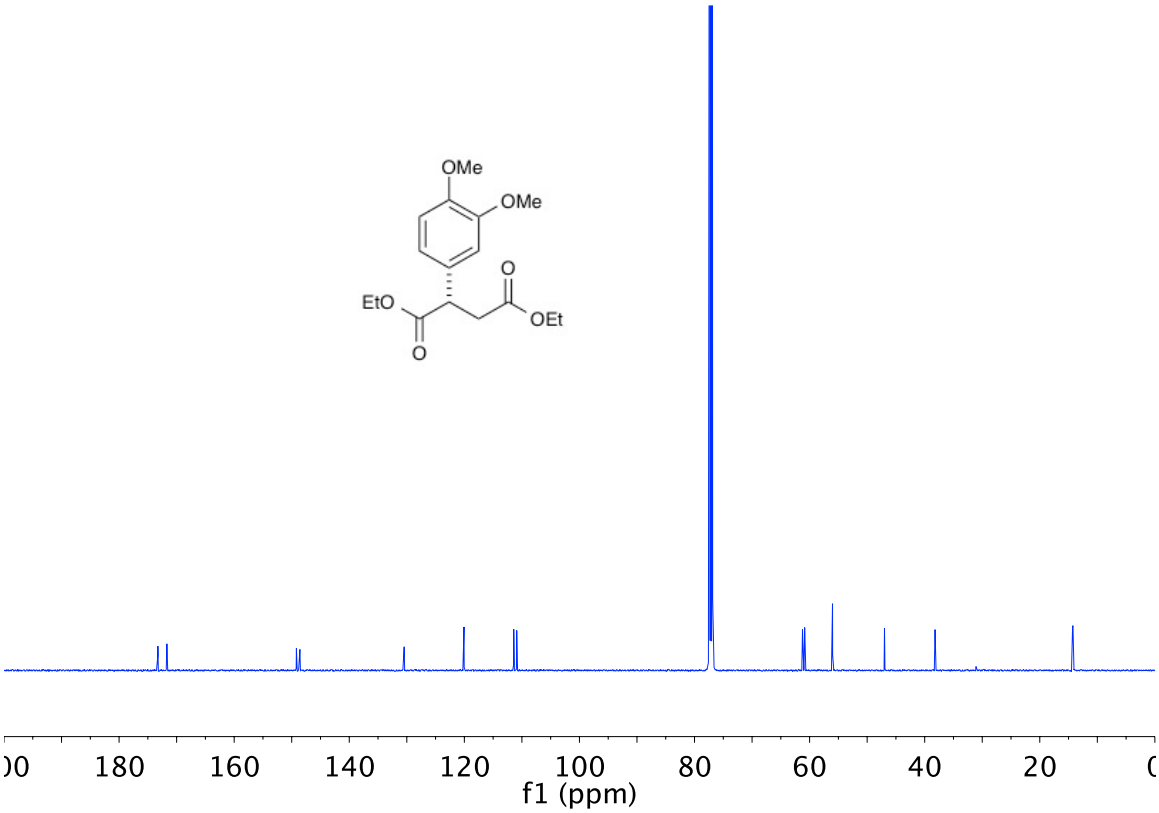

Me
EtO
O
OEt
O
1.01
2.90
3.92
1.00
1.00
1.00
2.96
6.25
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

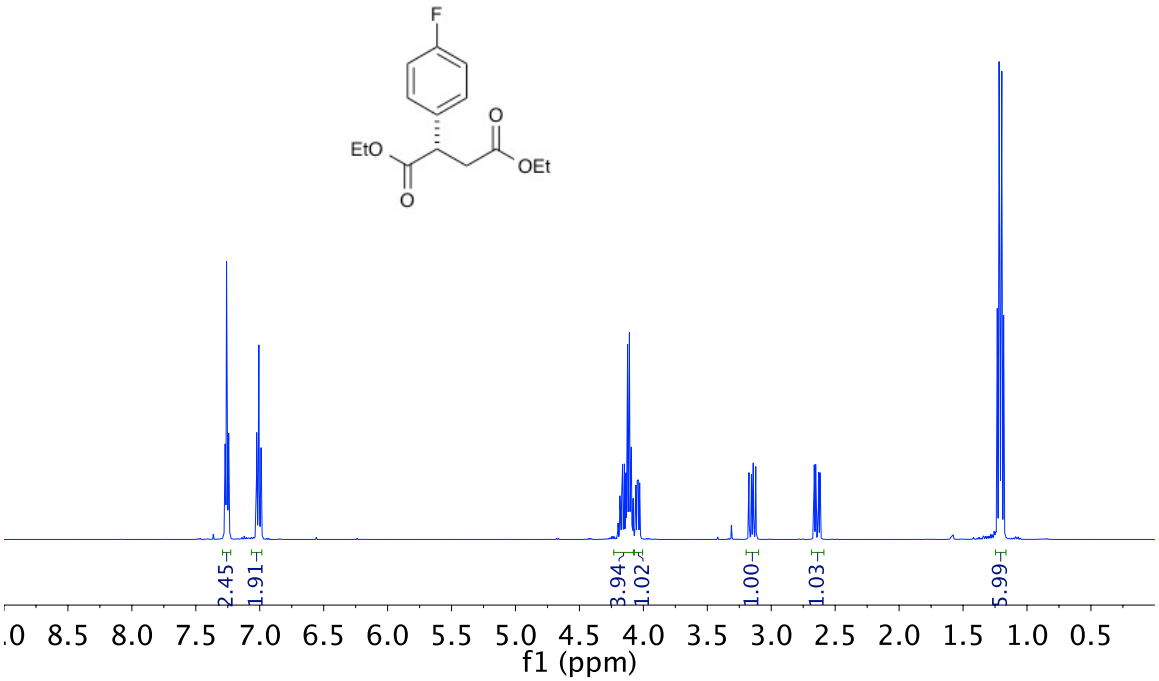

Me
EtO
O
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

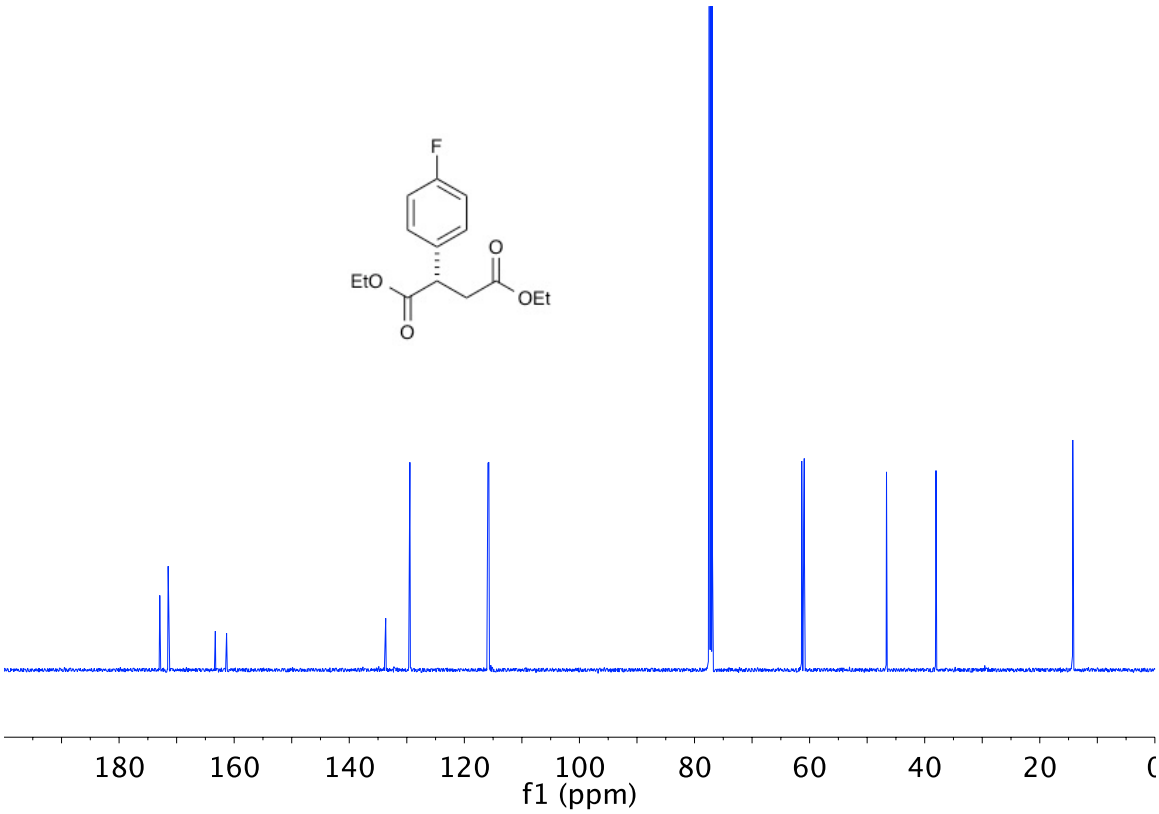

OMe
EtO
O
OEt
O
1.99
1.98
3.97
0.99
2.99
1.00
1.00
6.14
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

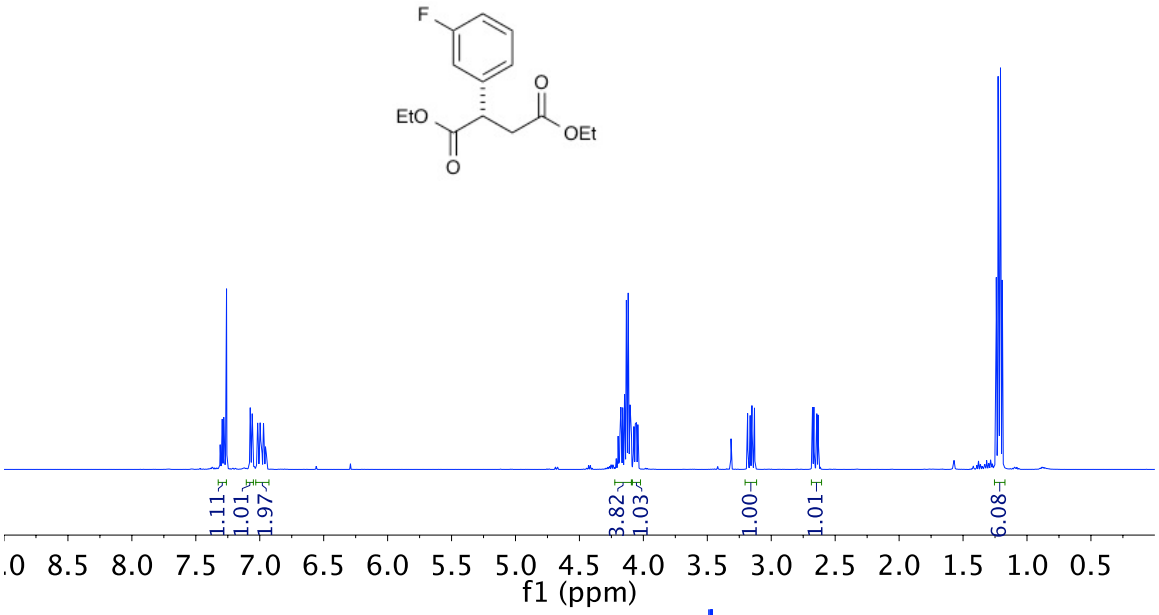

OMe
EtO
O
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

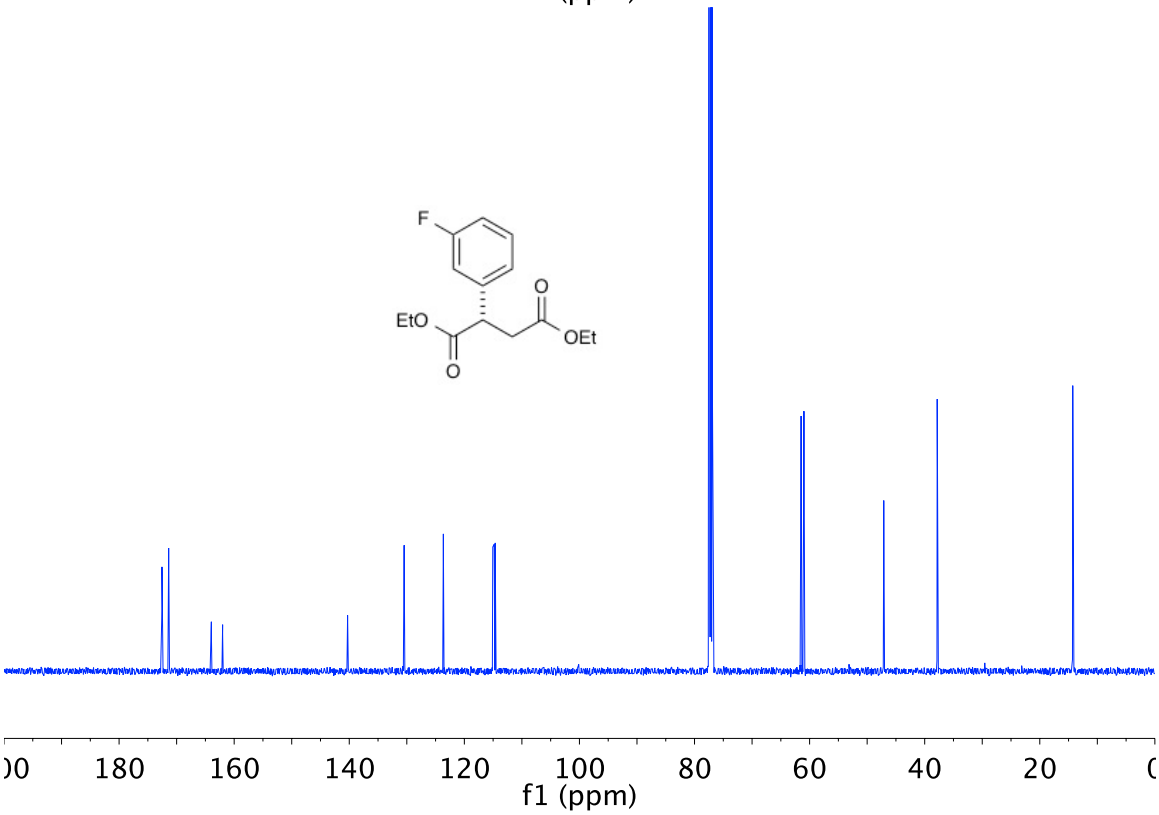

OMe
OMe
EtO
O
OEt
O
2.98
4.02
1.16
6.25
1.00
0.98
6.33
f1 (ppm)

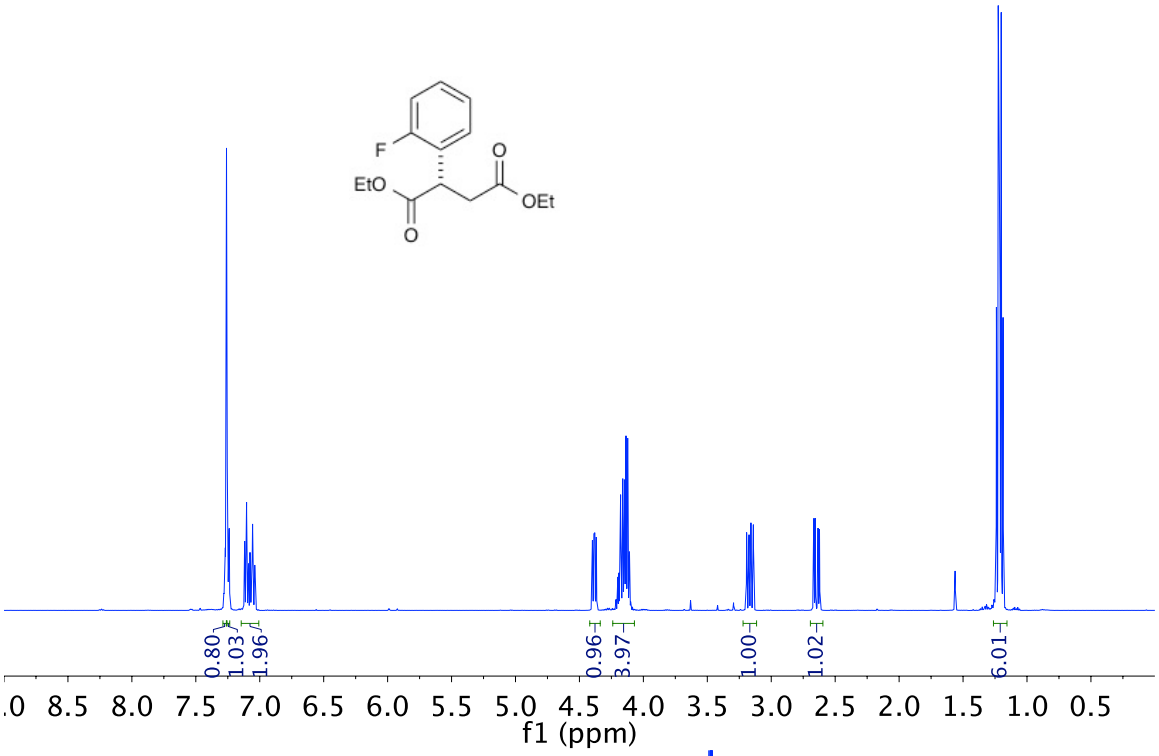

OMe
OMe
EtO
O
OEt
O
f1 (ppm)

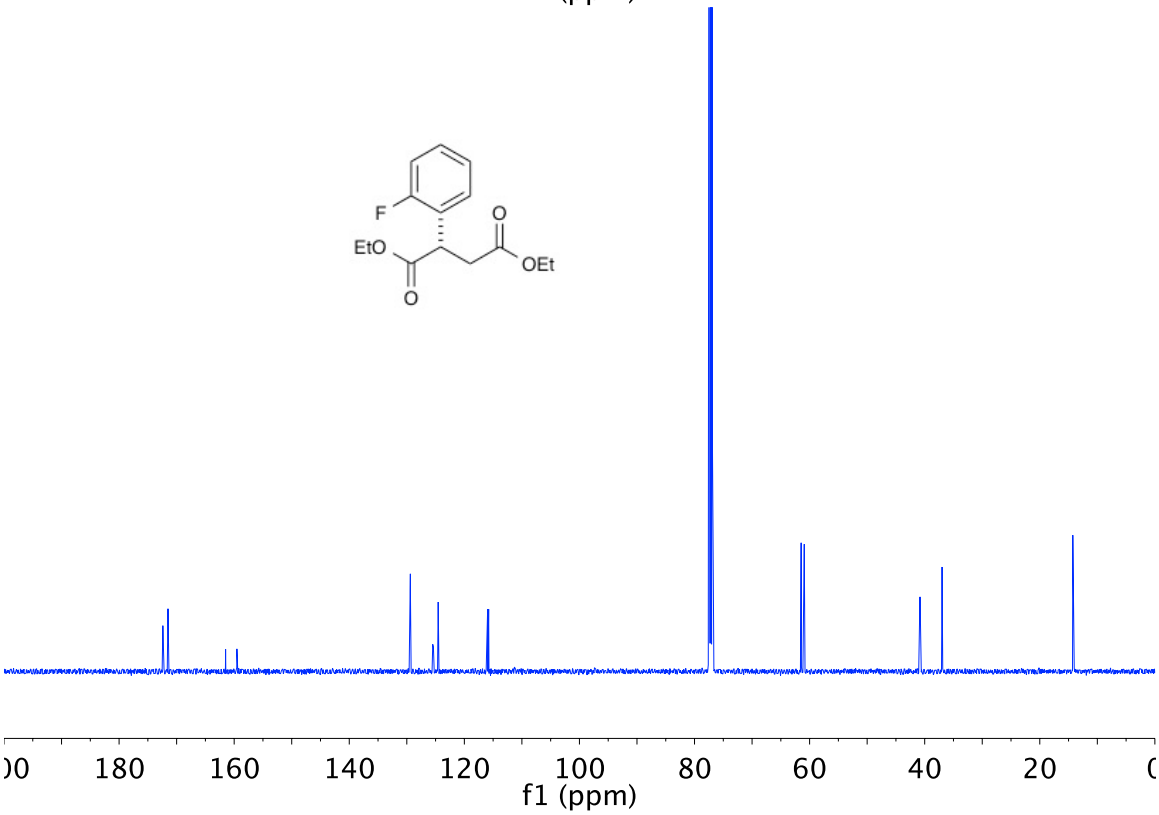

F
EtO
O
O
OEt
2.45
1.91
3.94
1.02
1.00
1.03
5.99
f1 (ppm)

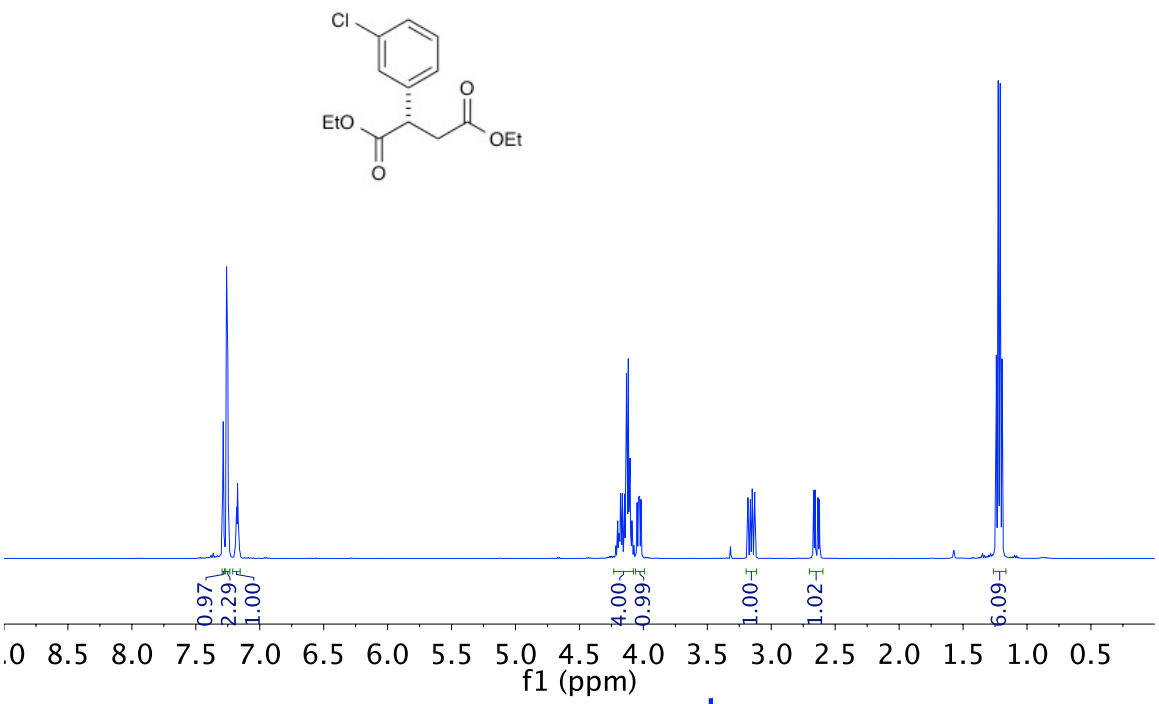

F
EtO
O
O
OEt
f1 (ppm)

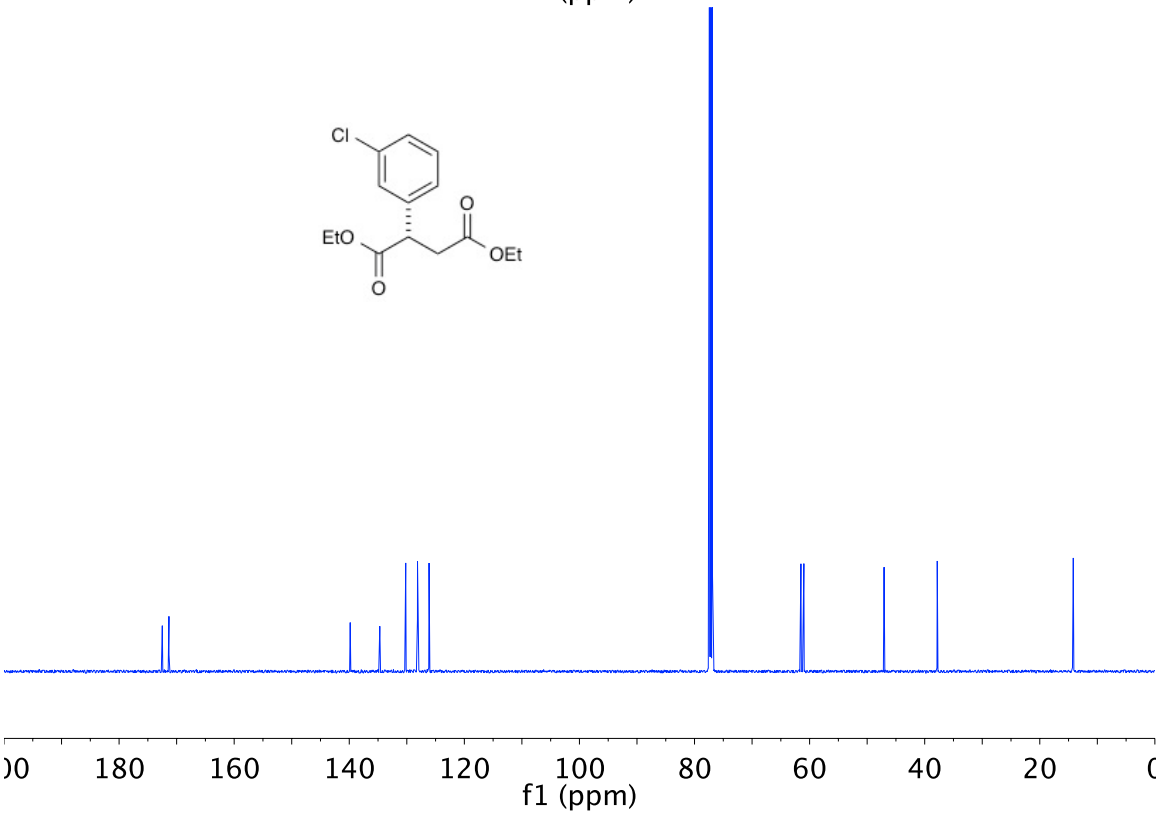

F
EtO
O
OEt
O
1.11
1.01
1.97
3.82
1.03
1.00
1.01
6.08
f1 (ppm)

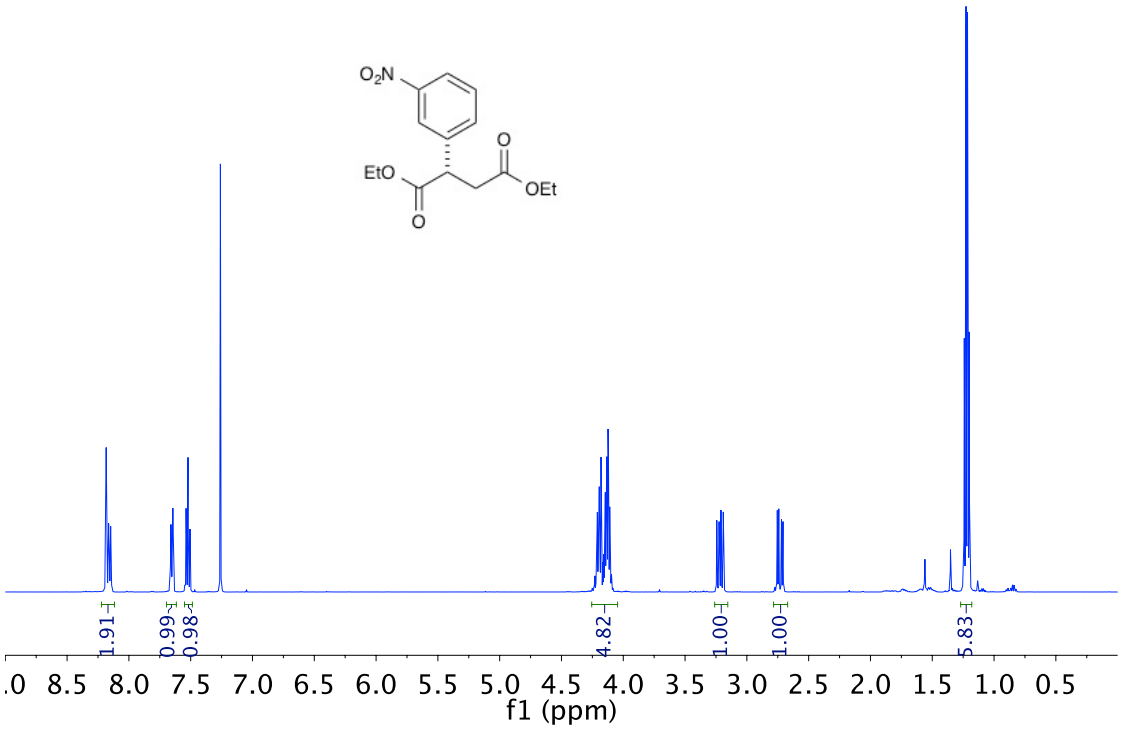

F
EtO
O
OEt
O
f1 (ppm)

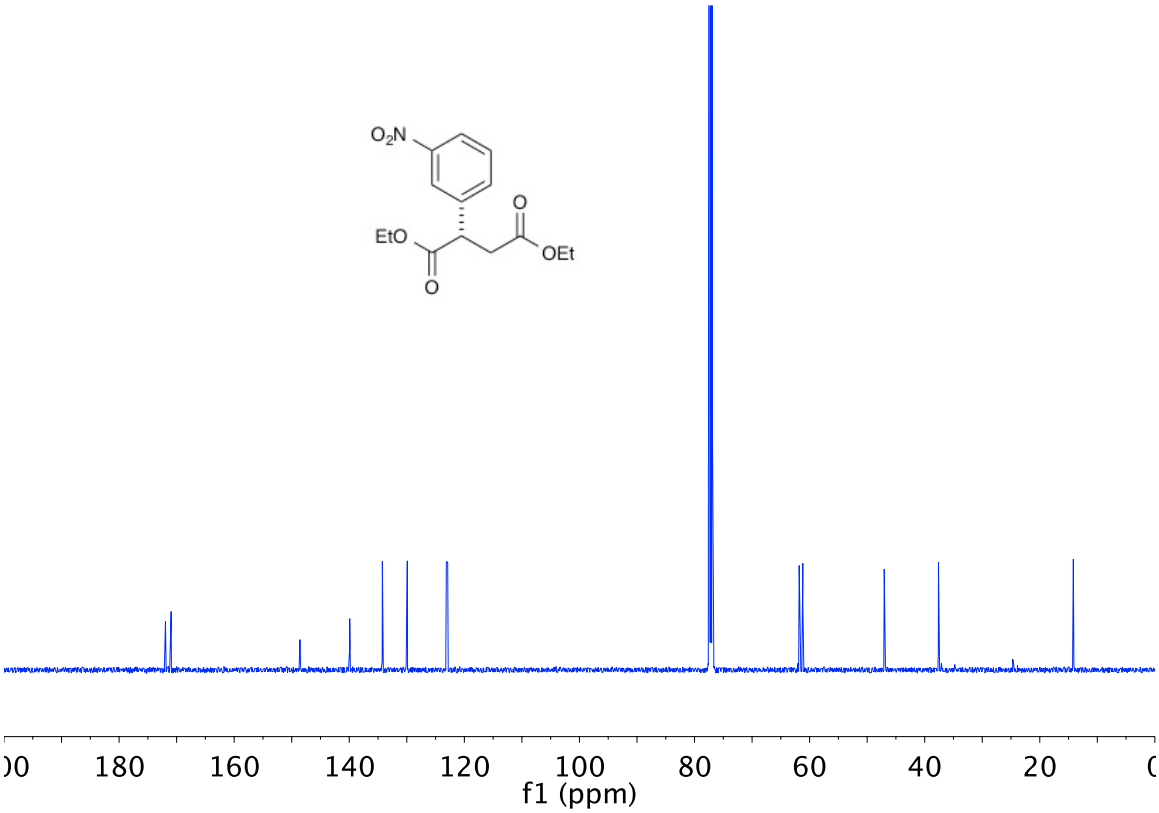

F
O
EtO
OEt
O
0.80
1.03
1.96
0.96
3.97
1.00
1.02
6.01
f1 (ppm)

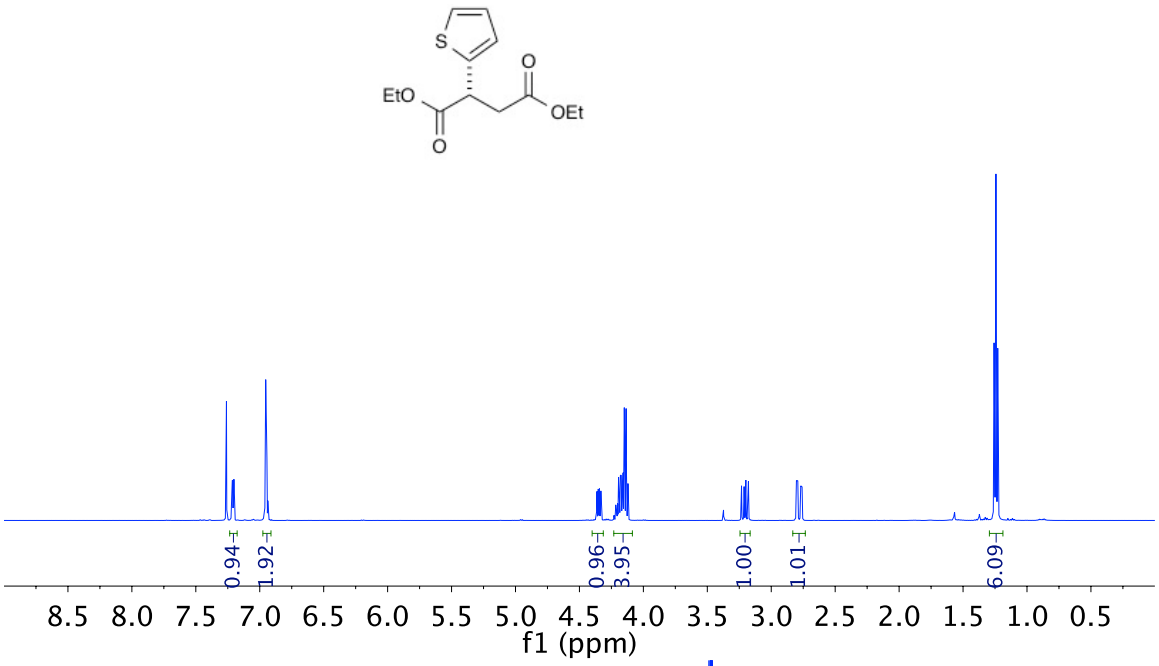

F
O
EtO
OEt
O
f1 (ppm)

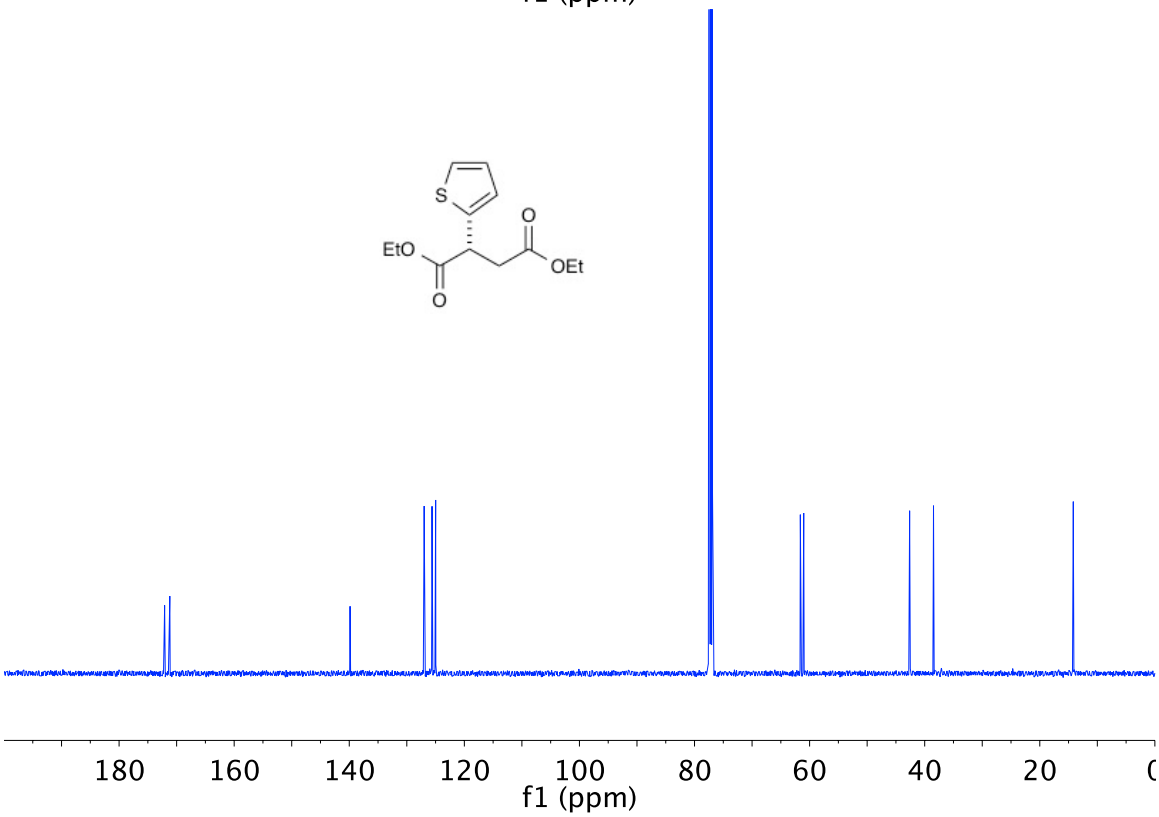

Cl
EtO
O
OEt
O
0.97
2.29
1.00
4.00
0.99
1.00
1.02
6.09
f1 (ppm)

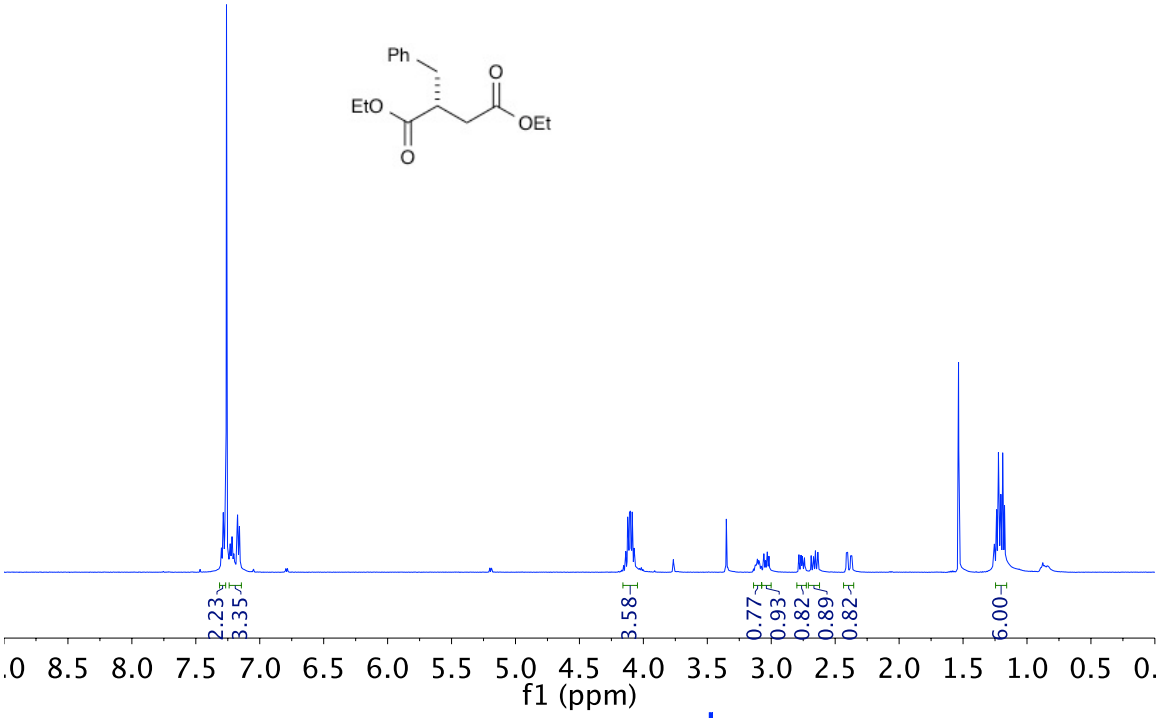

Cl
EtO
O
OEt
O
f1 (ppm)

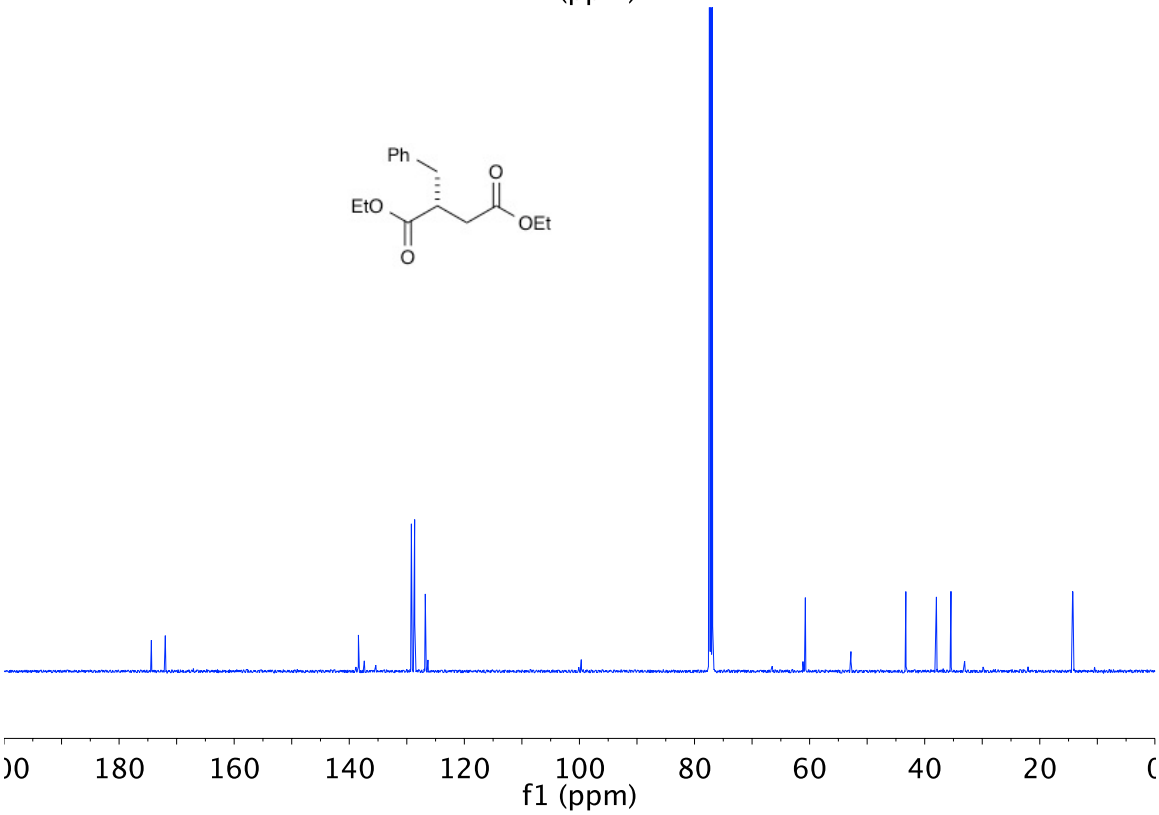

O2N
EtO
O
OEt
O
1.91
0.99
0.98
4.82
1.00
1.00
5.83
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

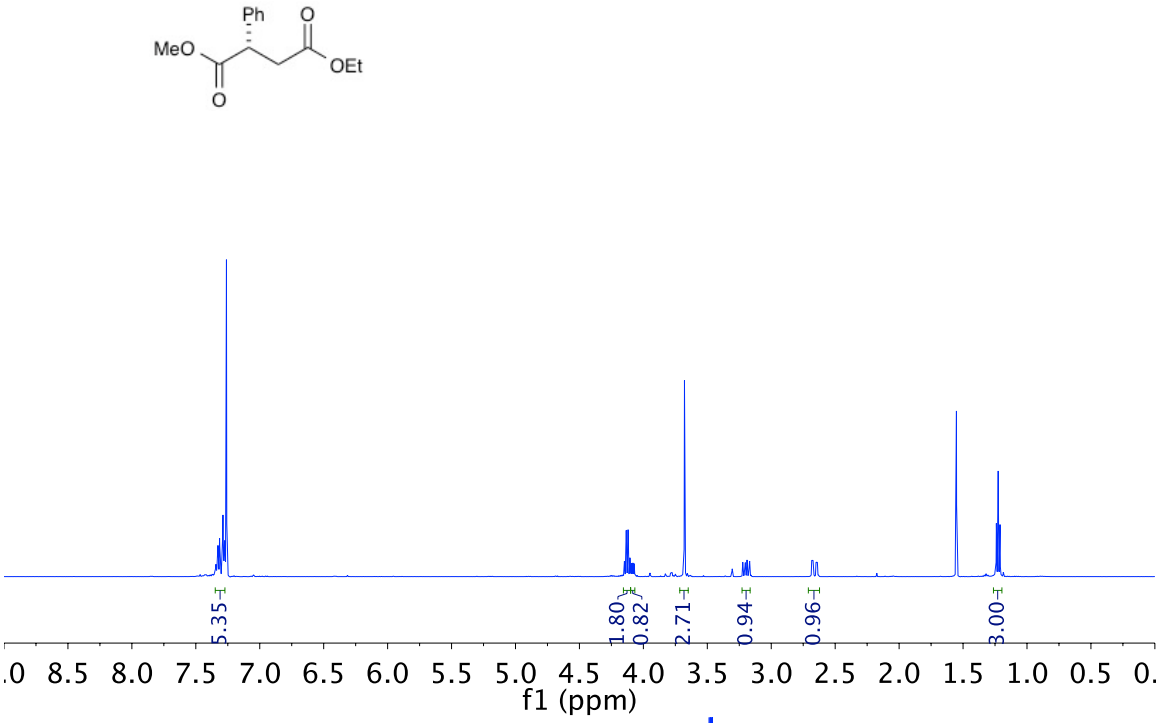

O2N
EtO
O
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

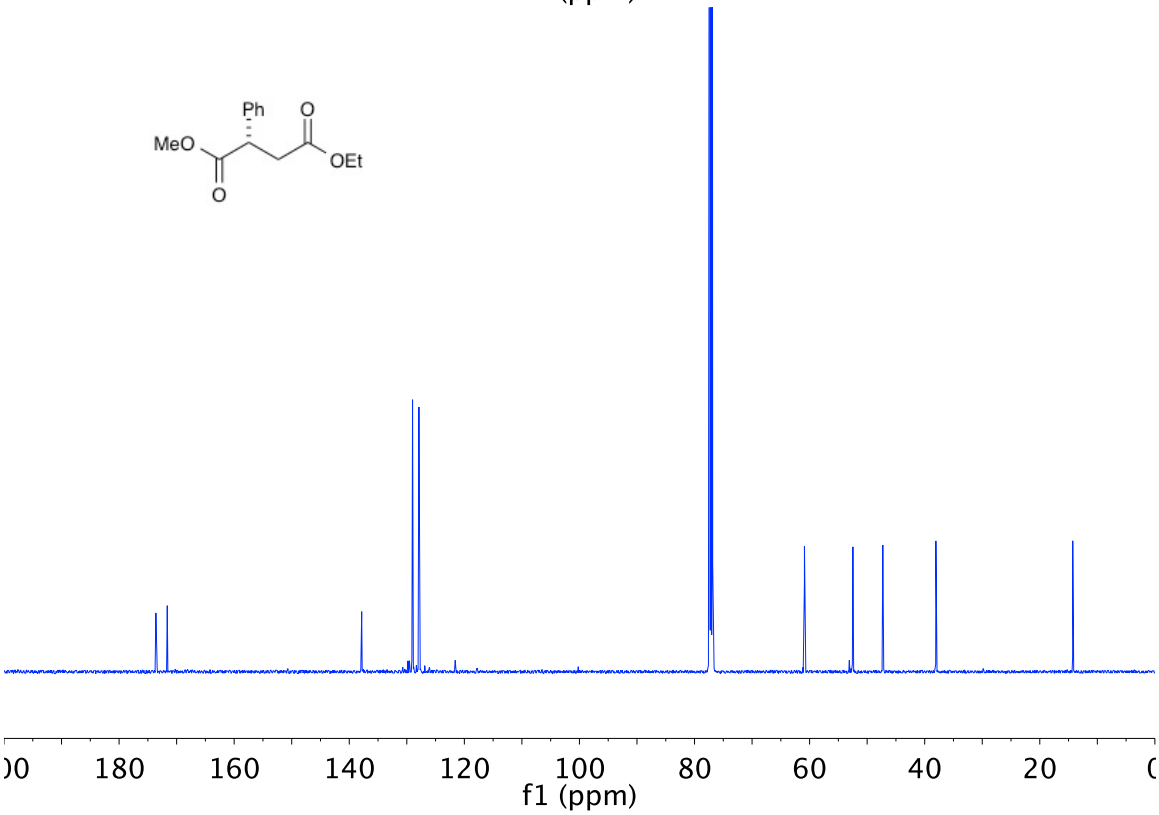

S
O
EtO
OEt
O
0.94
1.92
0.96
3.95
1.00
1.01
6.09
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

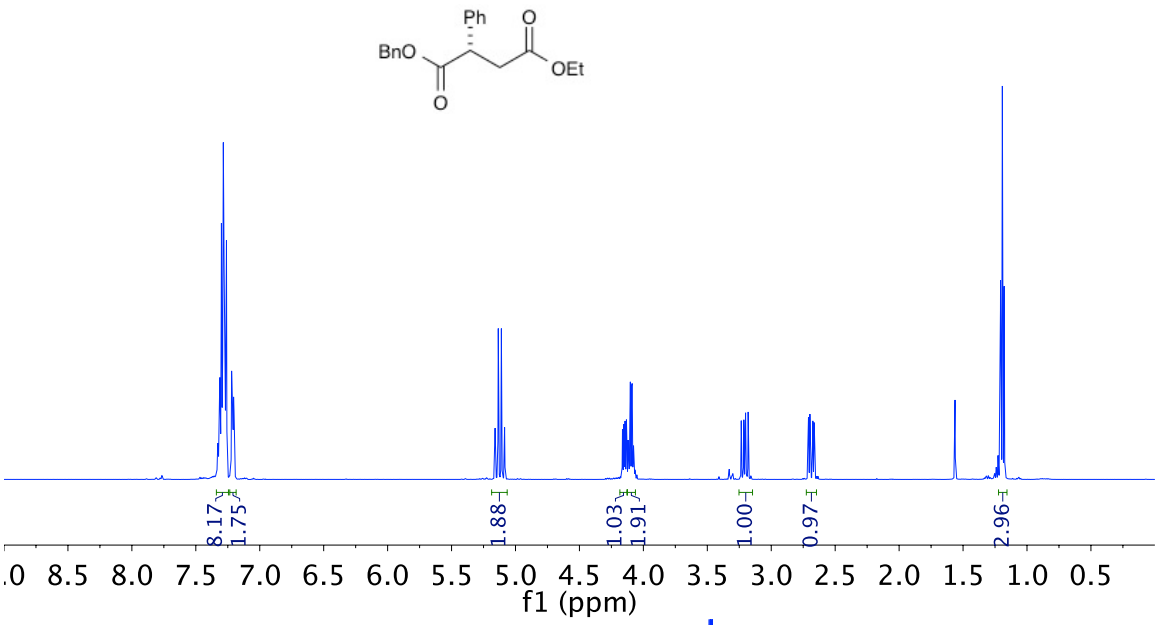

S
O
EtO
OEt
O
180 160 140 120 100 80 60 40 20
f1 (ppm)

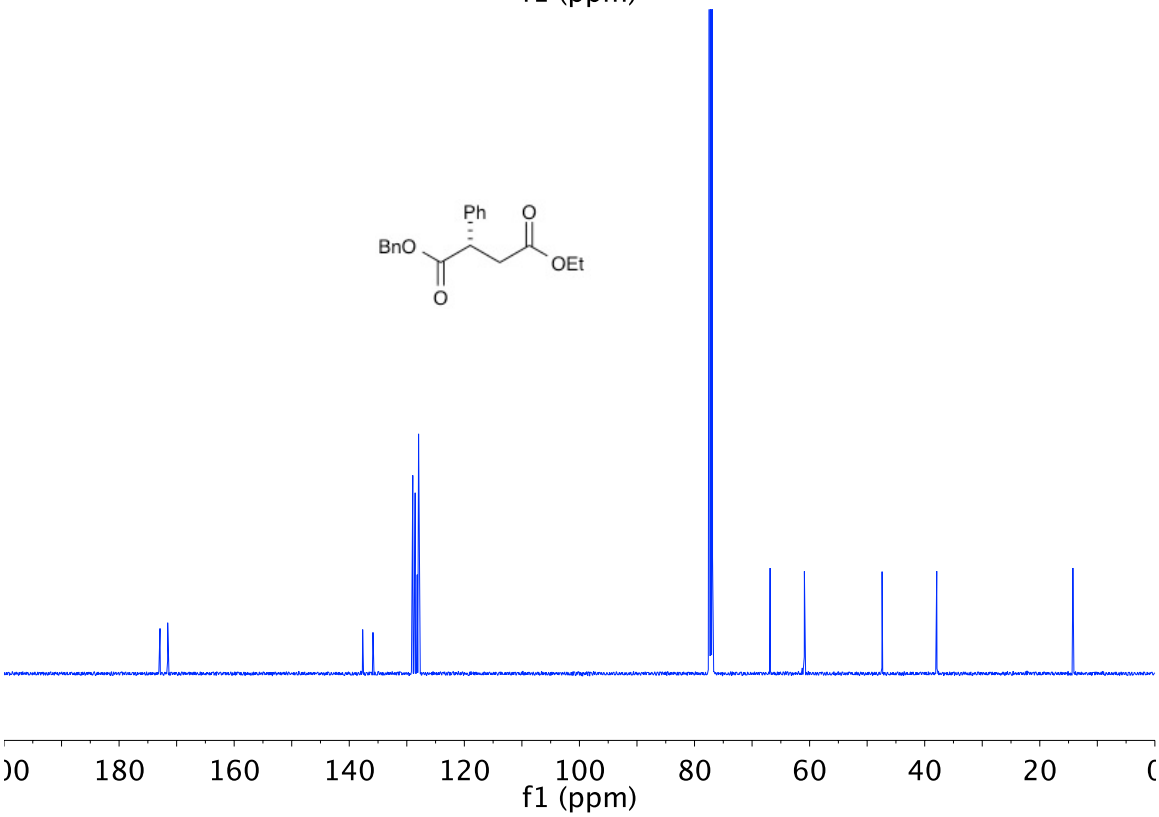

Ph
EtO
O
OEt
O
2.23
3.35
3.58
0.77
0.93
0.82
0.89
0.82
6.00
f1 (ppm)

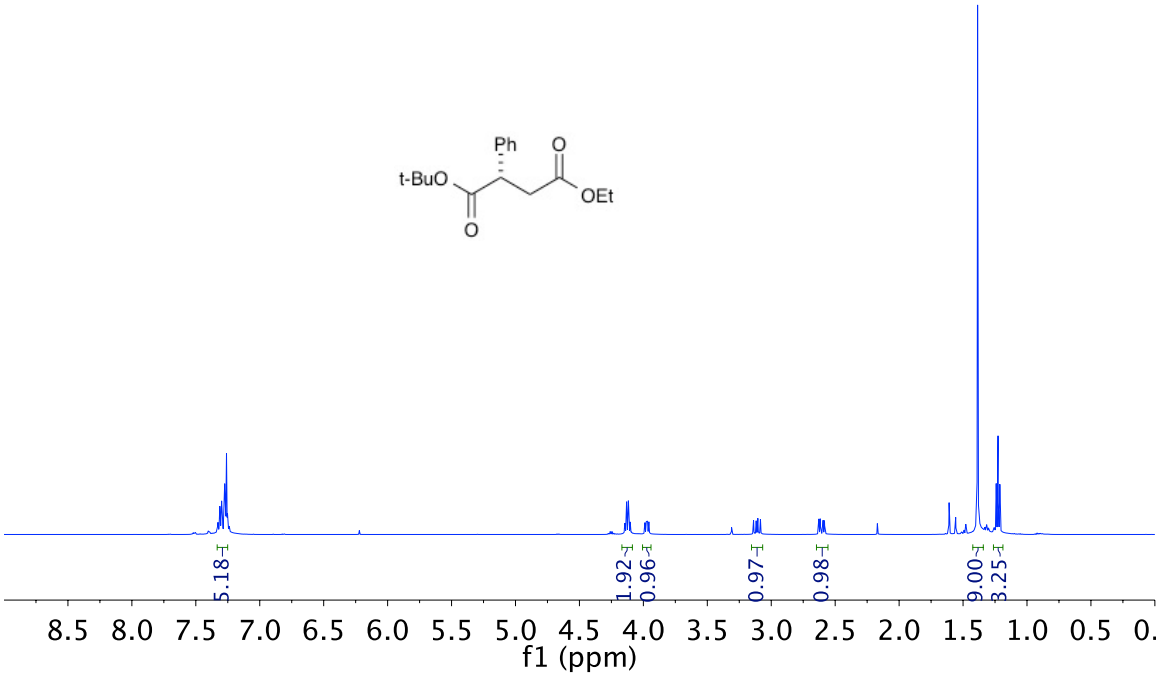

Ph
EtO
O
OEt
O
f1 (ppm)

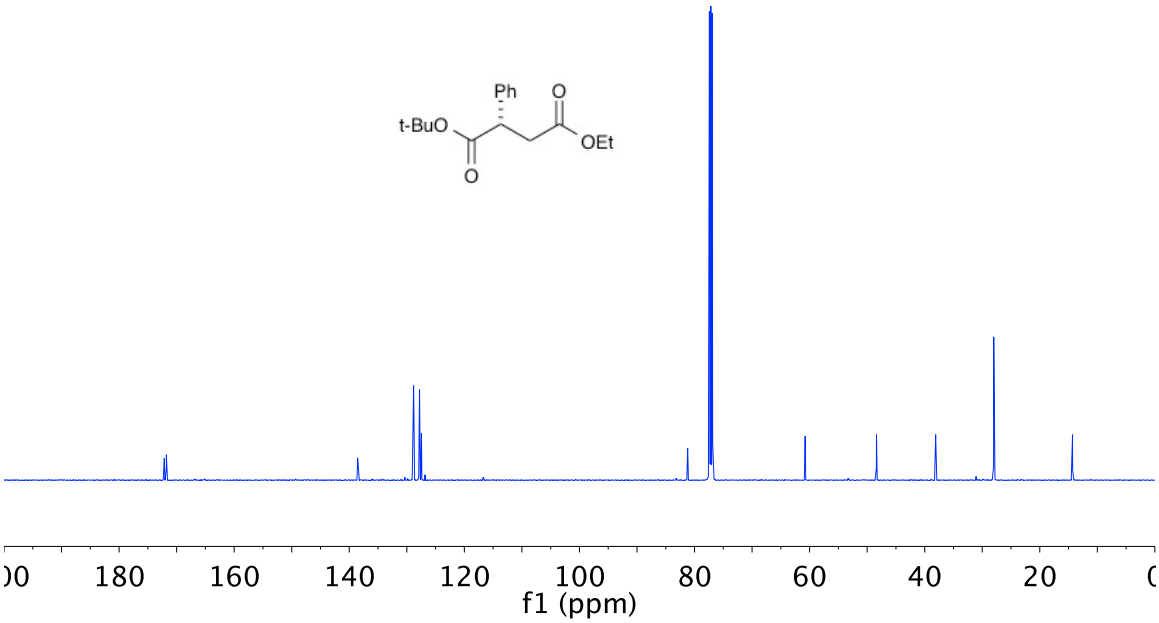

Ph
O
MeO
OEt
O
5.35
1.80
0.82
2.71
0.94
0.96
3.00
f1 (ppm)

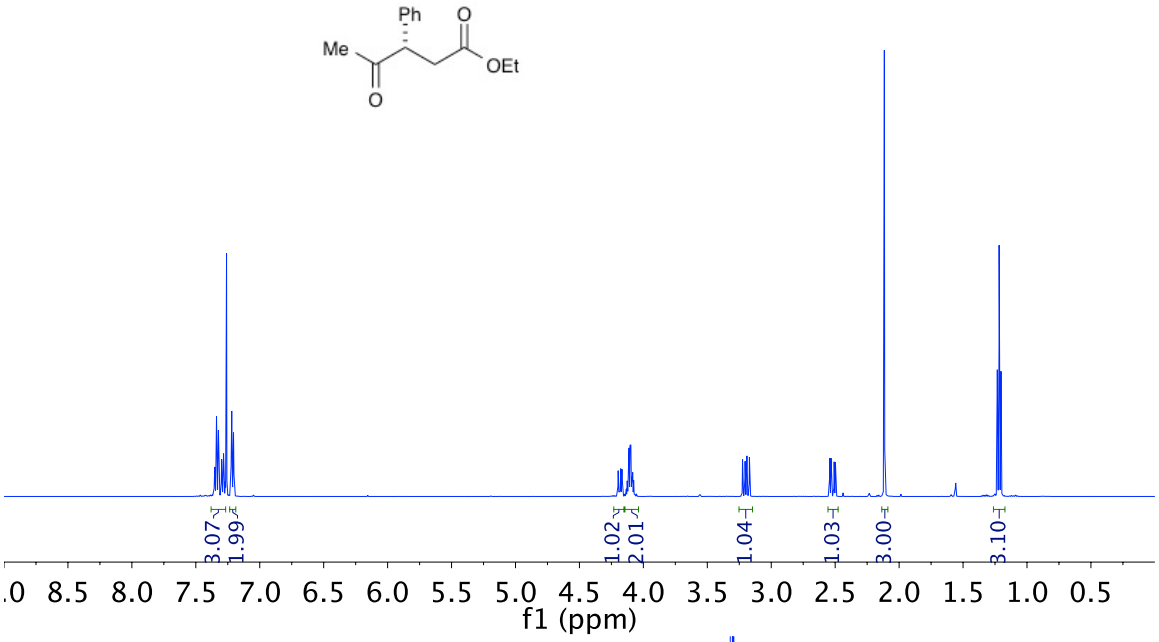

Ph
O
MeO
OEt
O
f1 (ppm)

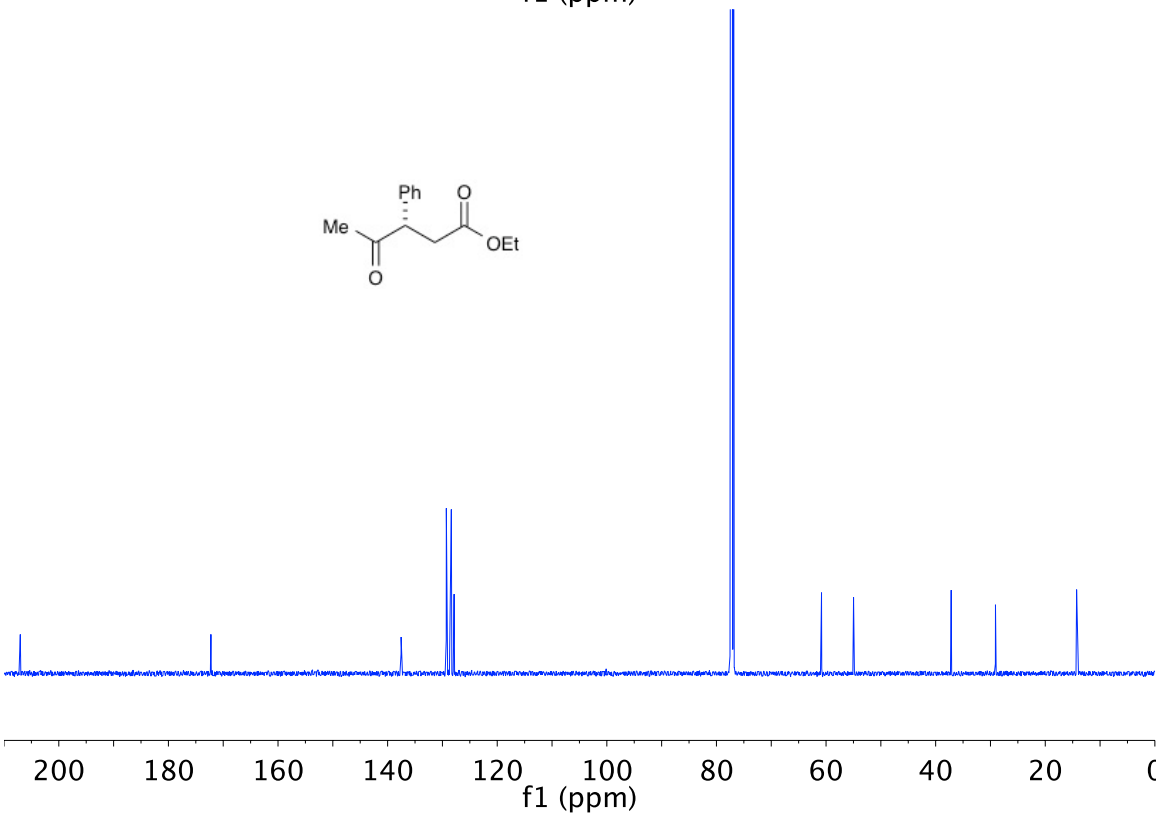

Ph
O
BnO
OEt
O
8.17
1.75
1.88
1.03
1.91
1.00
0.97
2.96
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

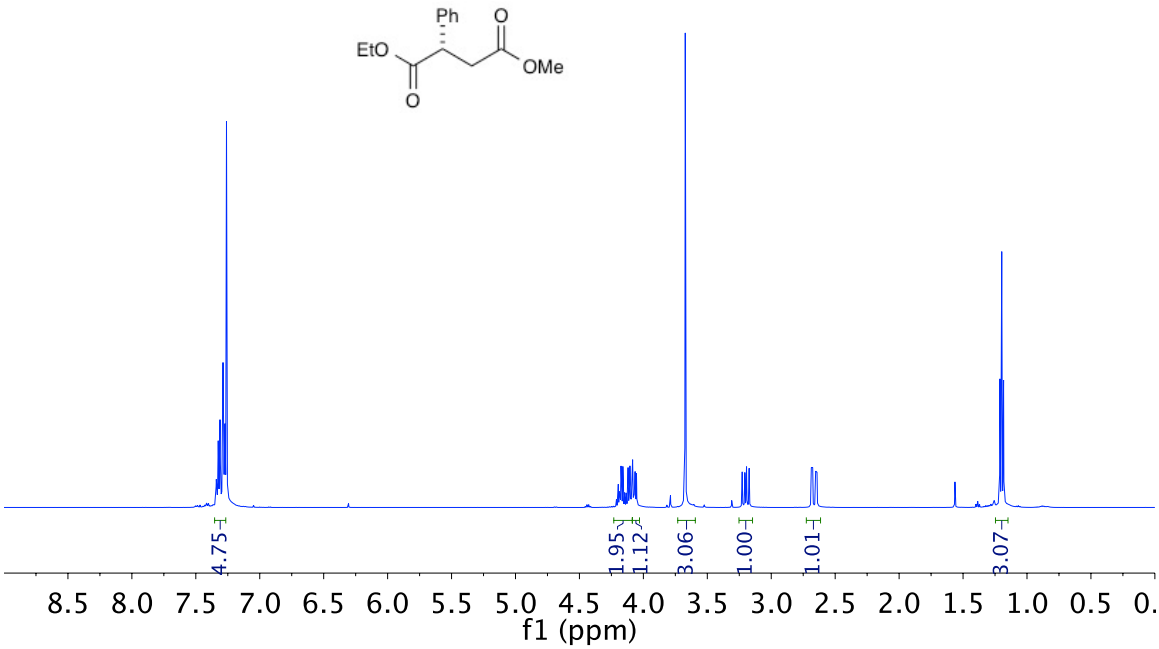

Ph
O
BnO
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

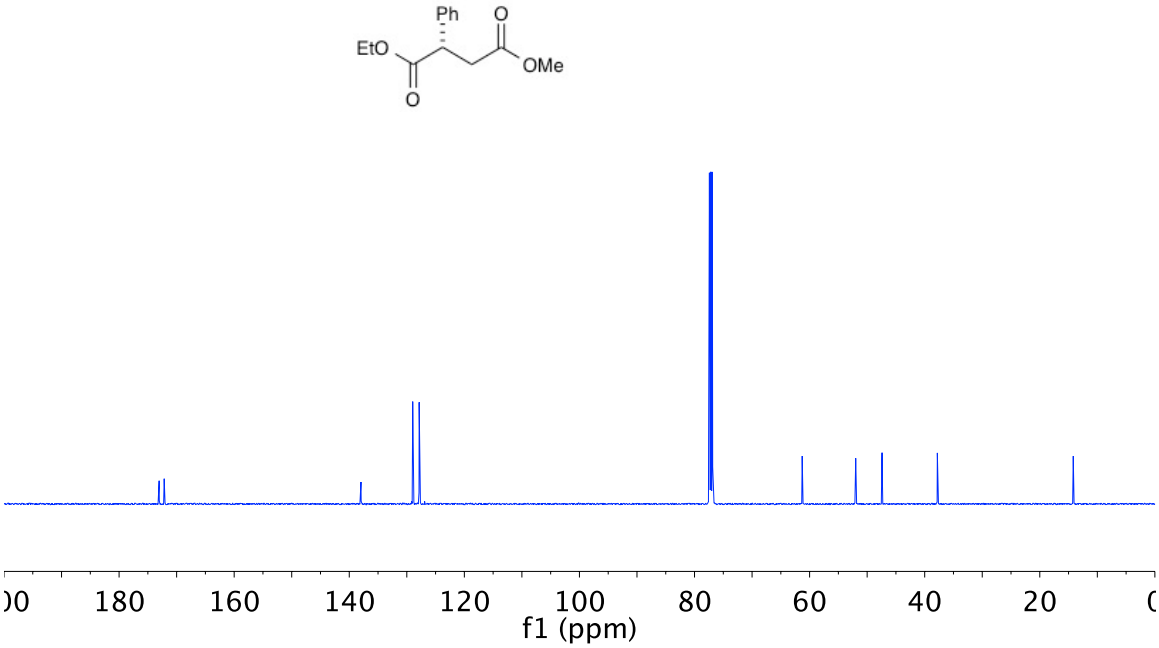

Ph
O
t-BuO
OEt
O
5.18
1.92
0.96
0.97
0.98
9.00
3.25
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

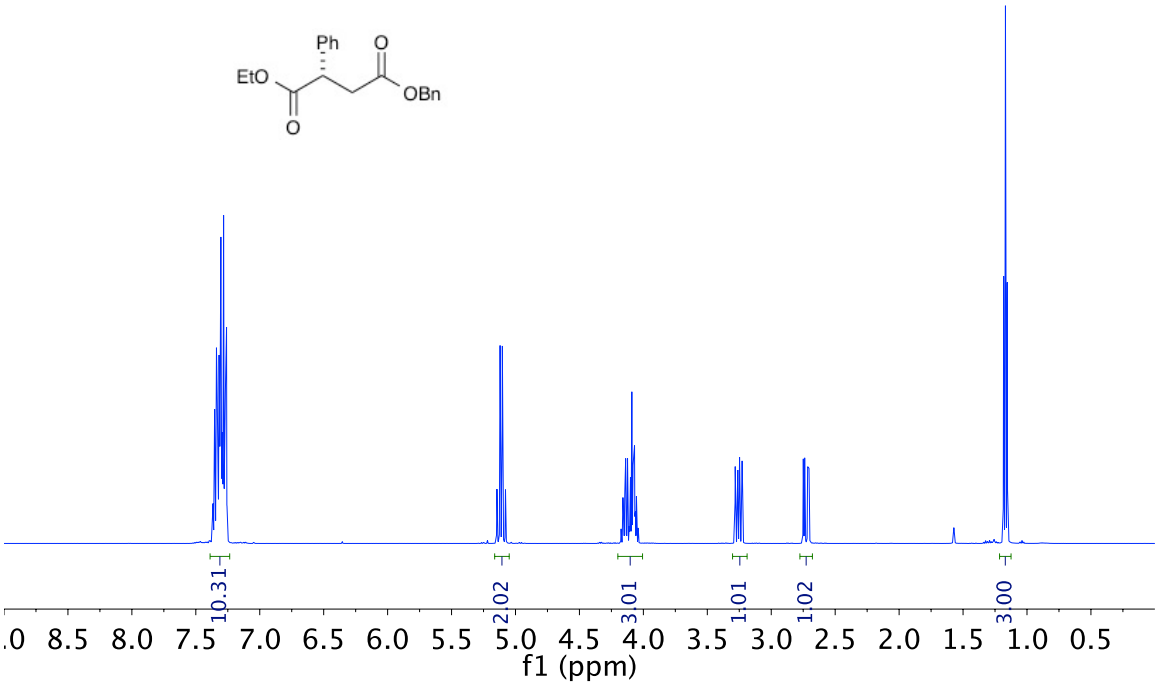

Ph
O
t-BuO
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

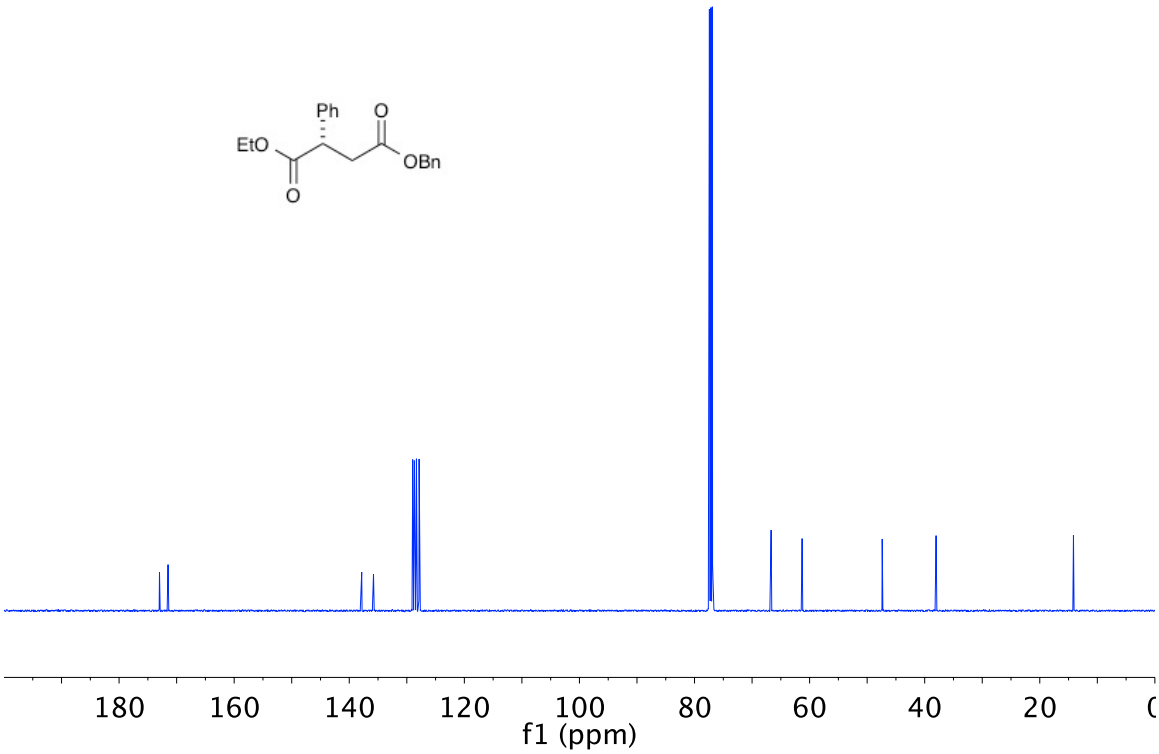

Ph
O
Me
OEt
O
3.07
1.99
1.02
2.01
1.04
1.03
3.00
3.10
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

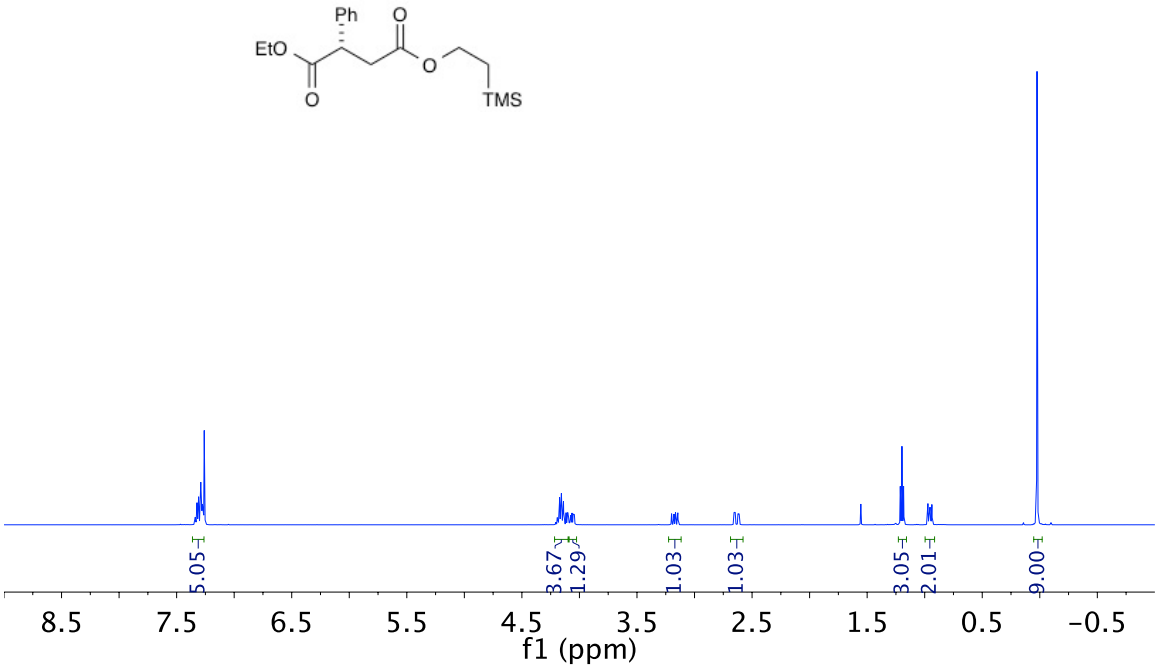

Ph
O
Me
OEt
O
200 180 160 140 120 100 80 60 40 20
f1 (ppm)

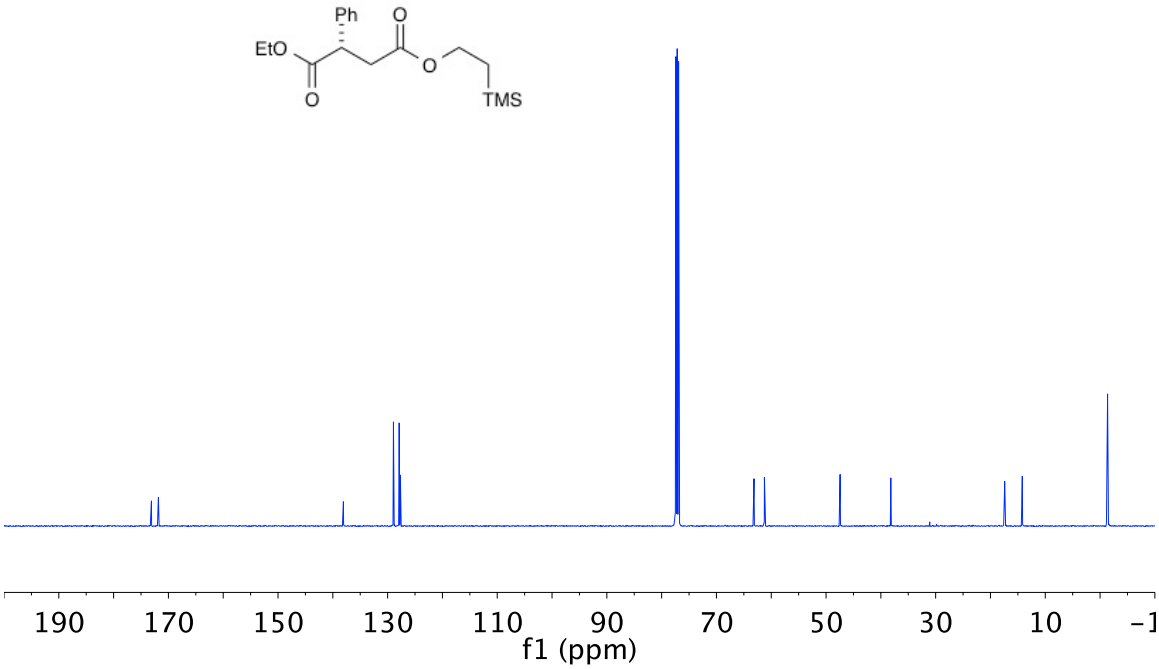

Ph
O
EtO
OMe
O
4.75
1.95
1.12
3.06
1.00
1.01
3.07
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

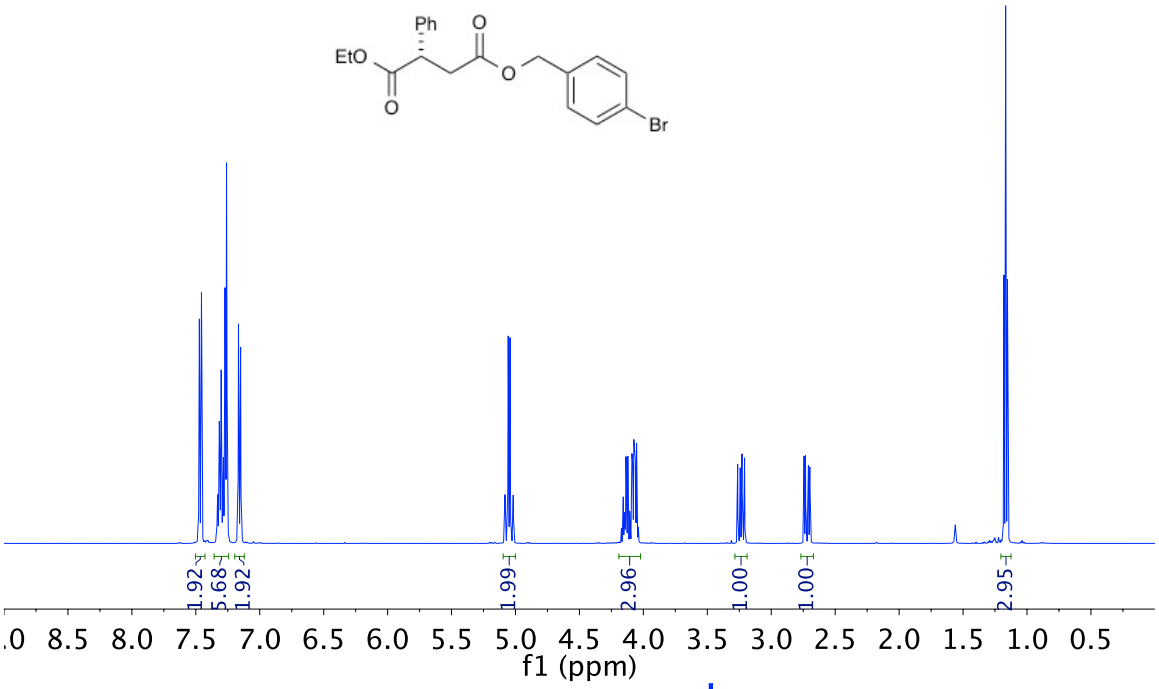

Ph
O
EtO
OMe
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

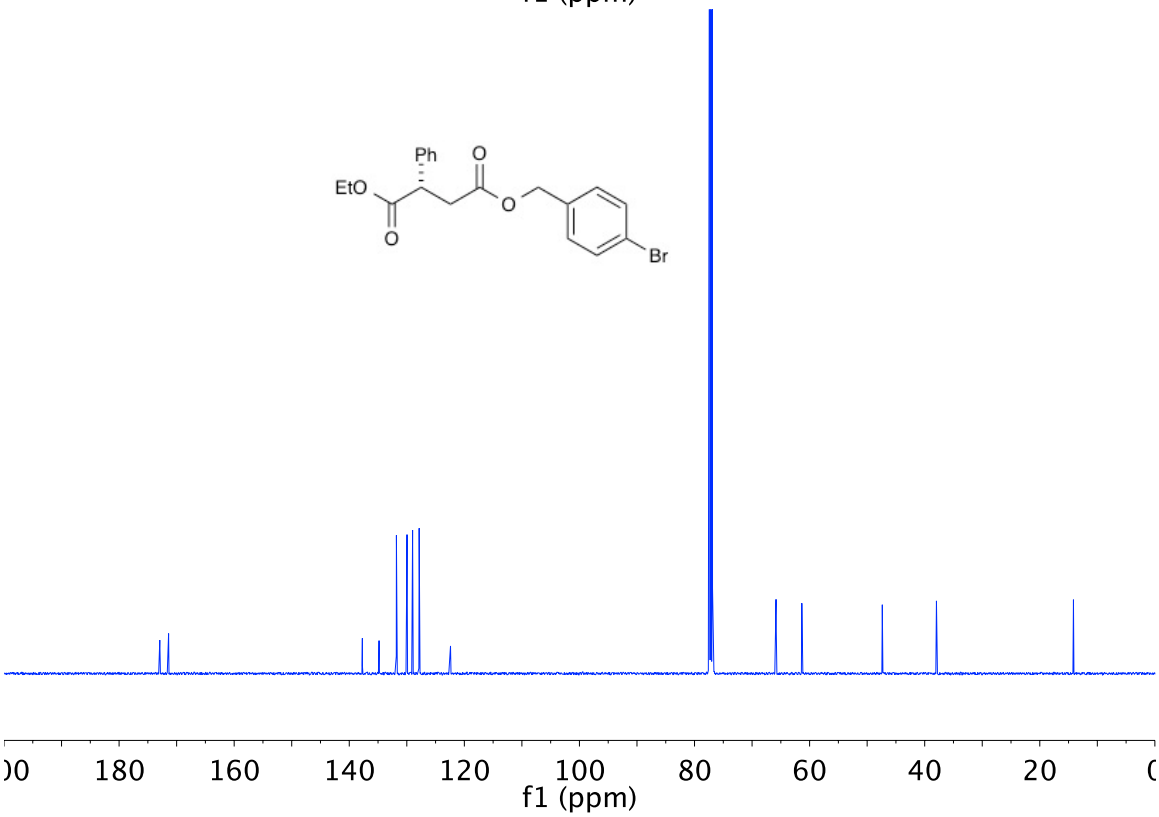

Ph
O
EtO
OBn
O
10.31
2.02
3.01
1.01
1.02
3.00
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

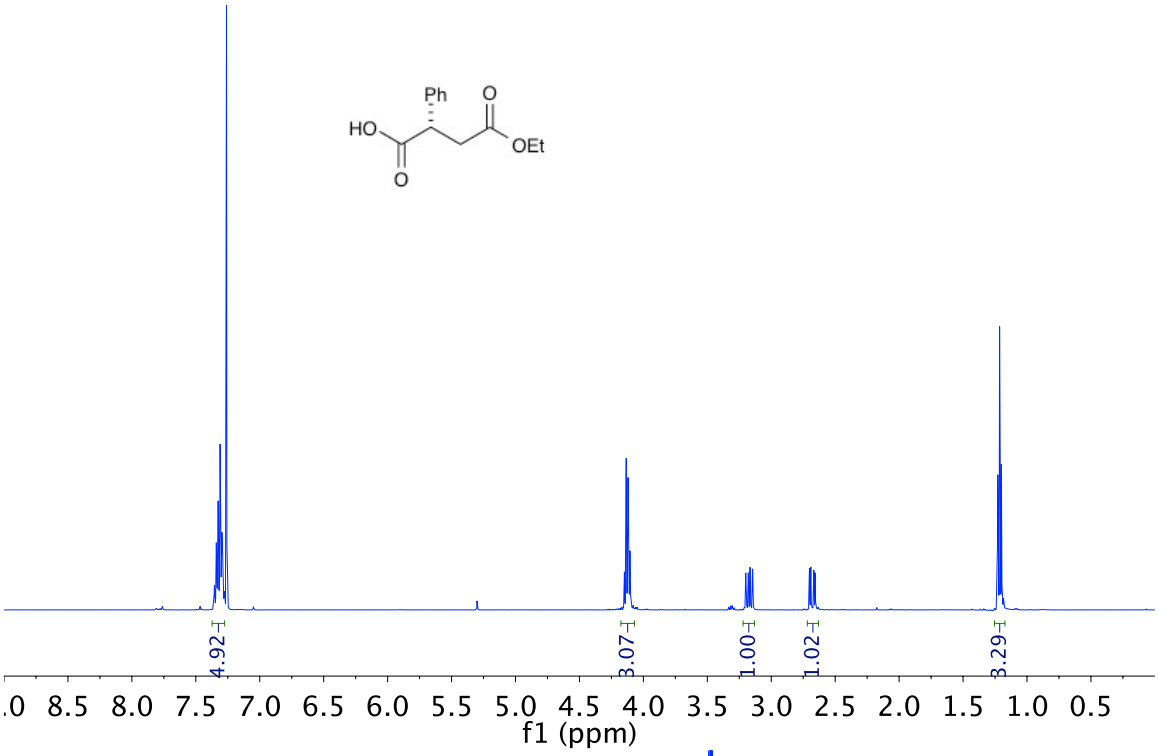

Ph
O
EtO
OBn
O
180 160 140 120 100 80 60 40 20
f1 (ppm)

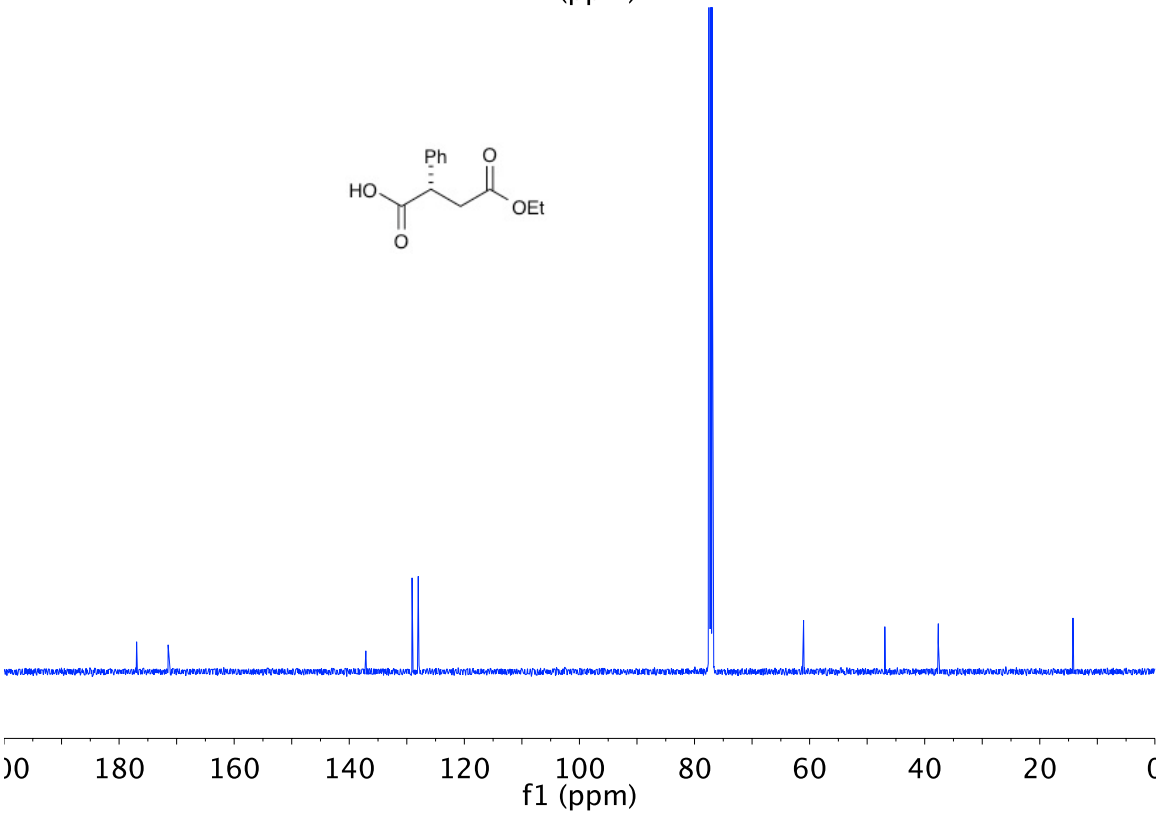

Ph
O
EtO
O
O
TMS
5.05
3.67
1.29
1.03
1.03
3.05
2.01
9.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

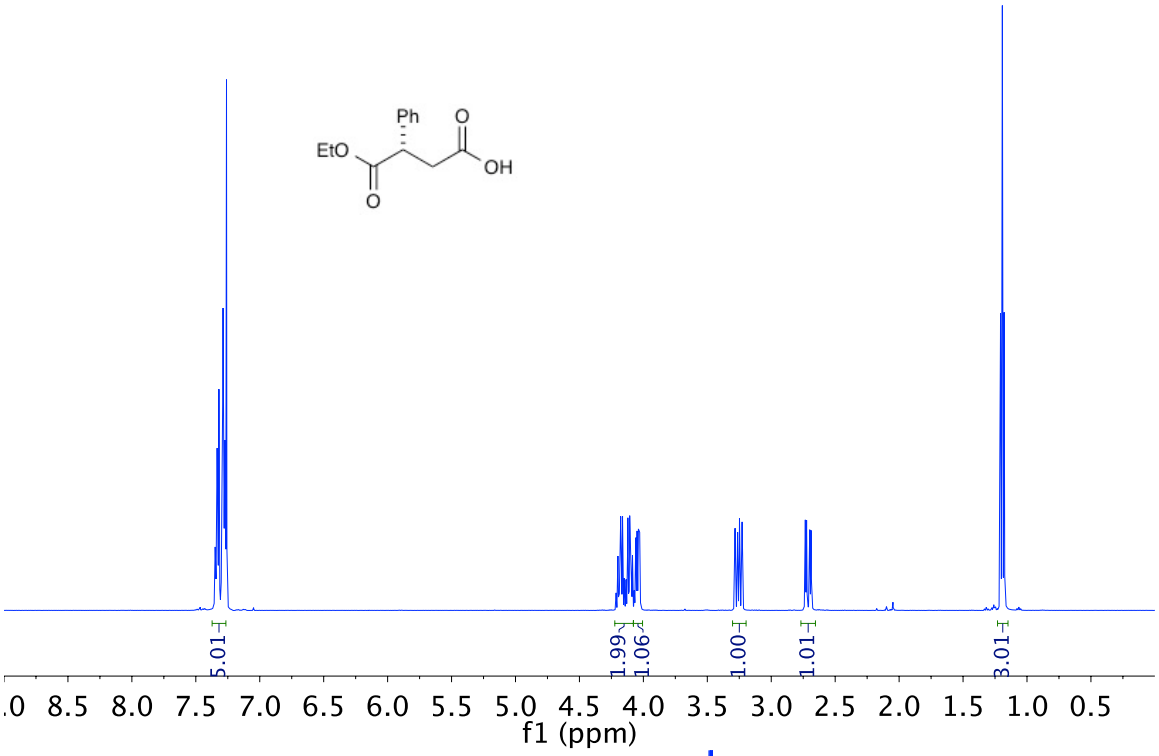

Ph
O
EtO
O
O
TMS
190
170
150
130
110
90
70
50
30
10
-1
f1 (ppm)

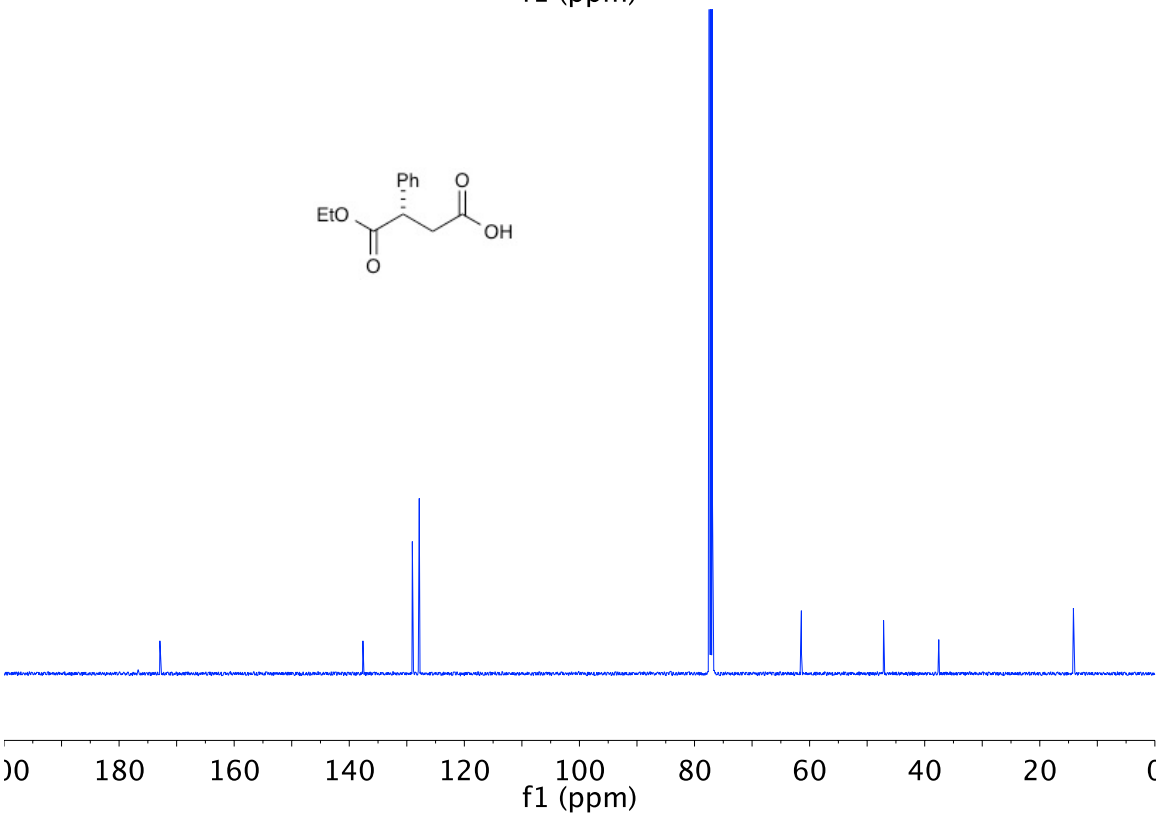

Ph
O
EtO
O
O
Br
1.92
5.68
1.92
1.99
2.96
1.00
1.00
2.95
f1 (ppm)

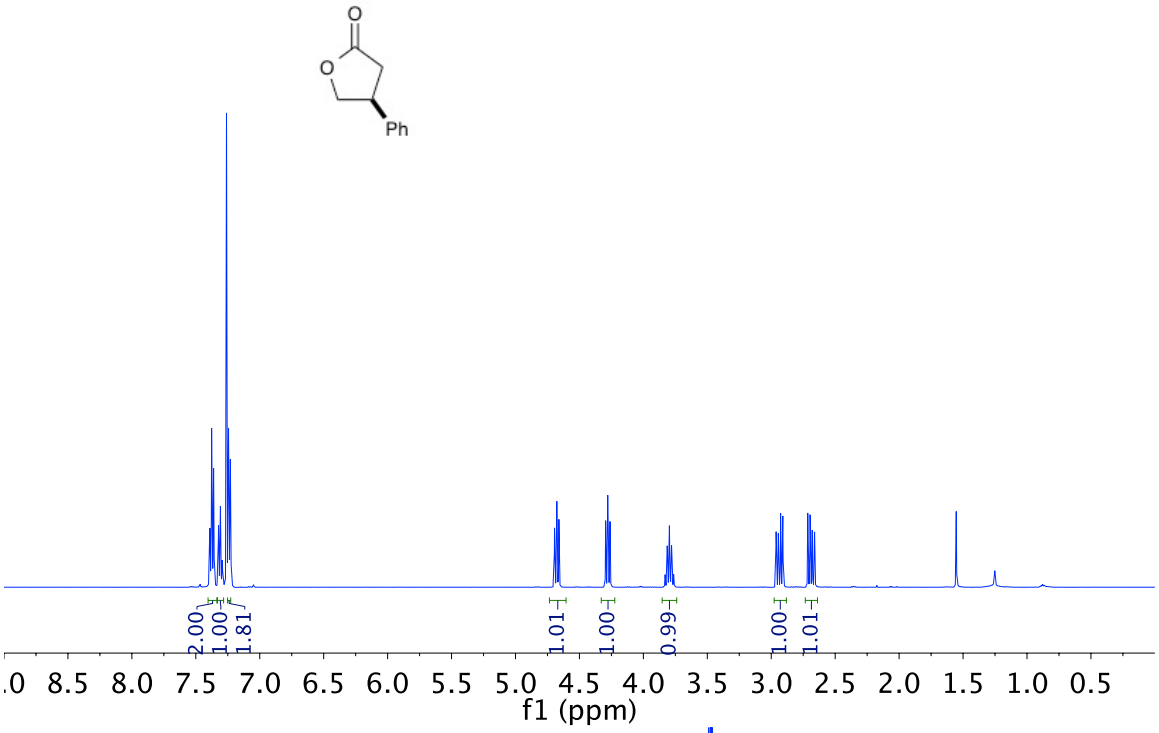

Ph
O
EtO
O
O
Br
f1 (ppm)

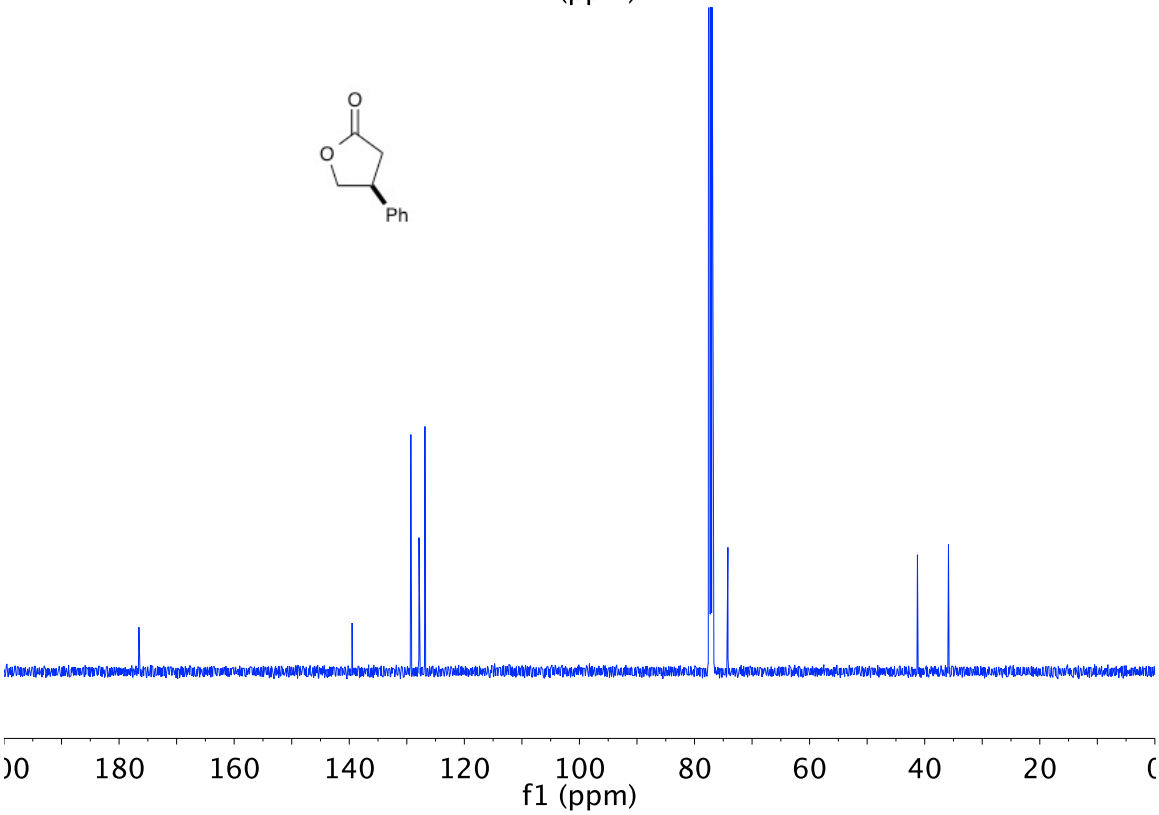

Ph
O
HO
OEt
O
4.92
3.07
1.00
1.02
3.29
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

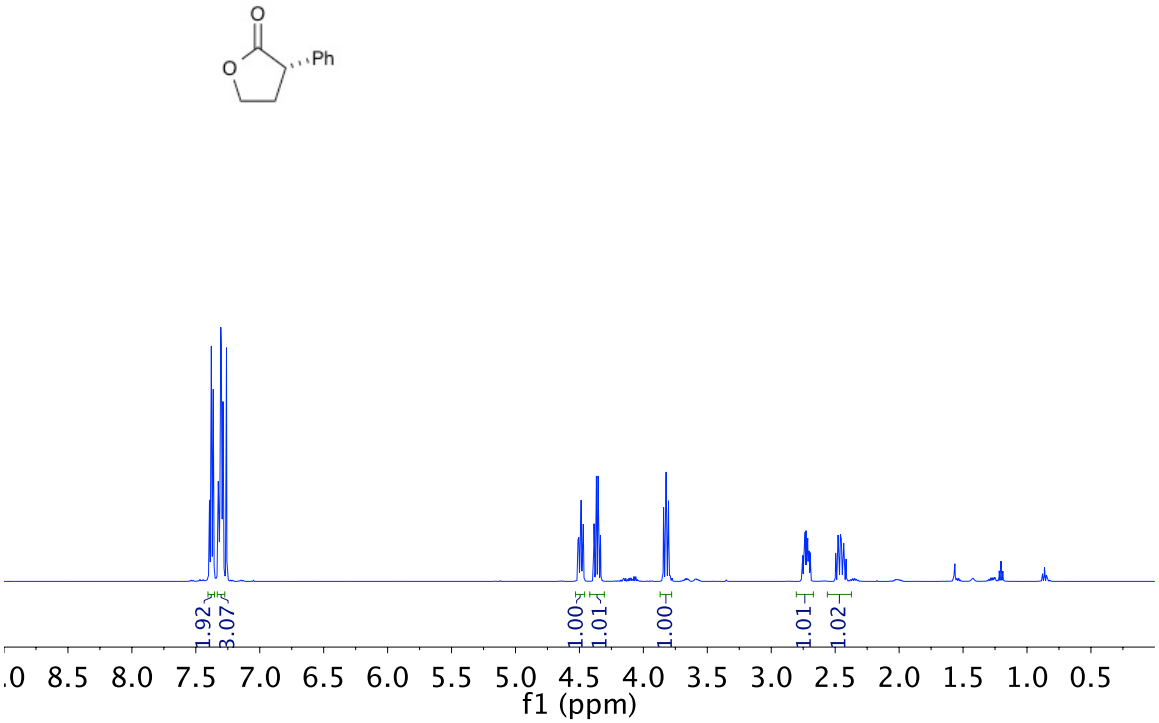

Ph
O
HO
OEt
O
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

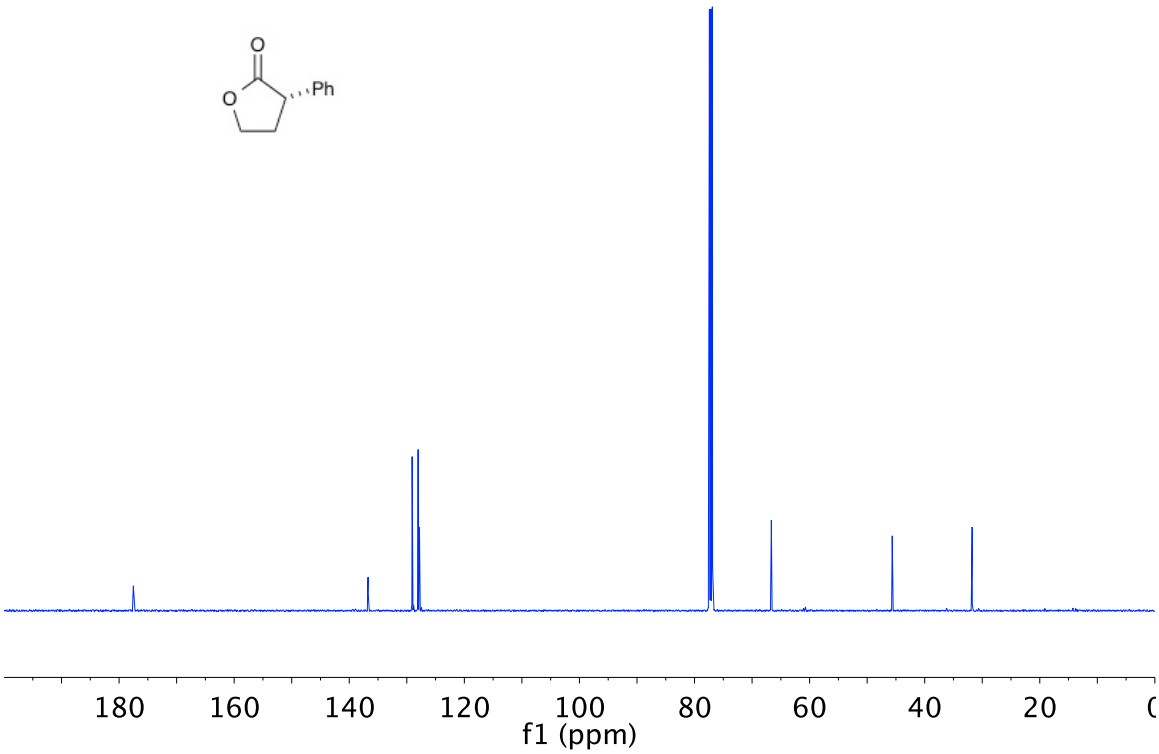

Ph
O
EtO
OH
O
5.01
1.99
1.06
1.00
1.01
3.01
f1 (ppm)

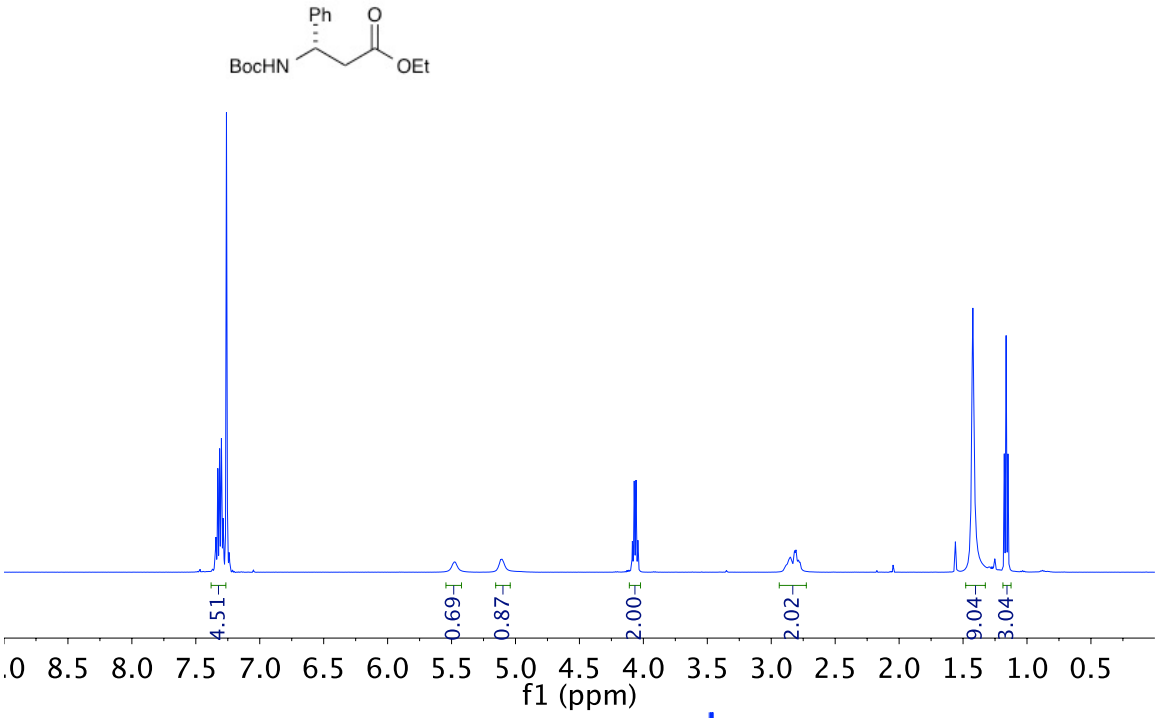

Ph
O
EtO
OH
O
f1 (ppm)

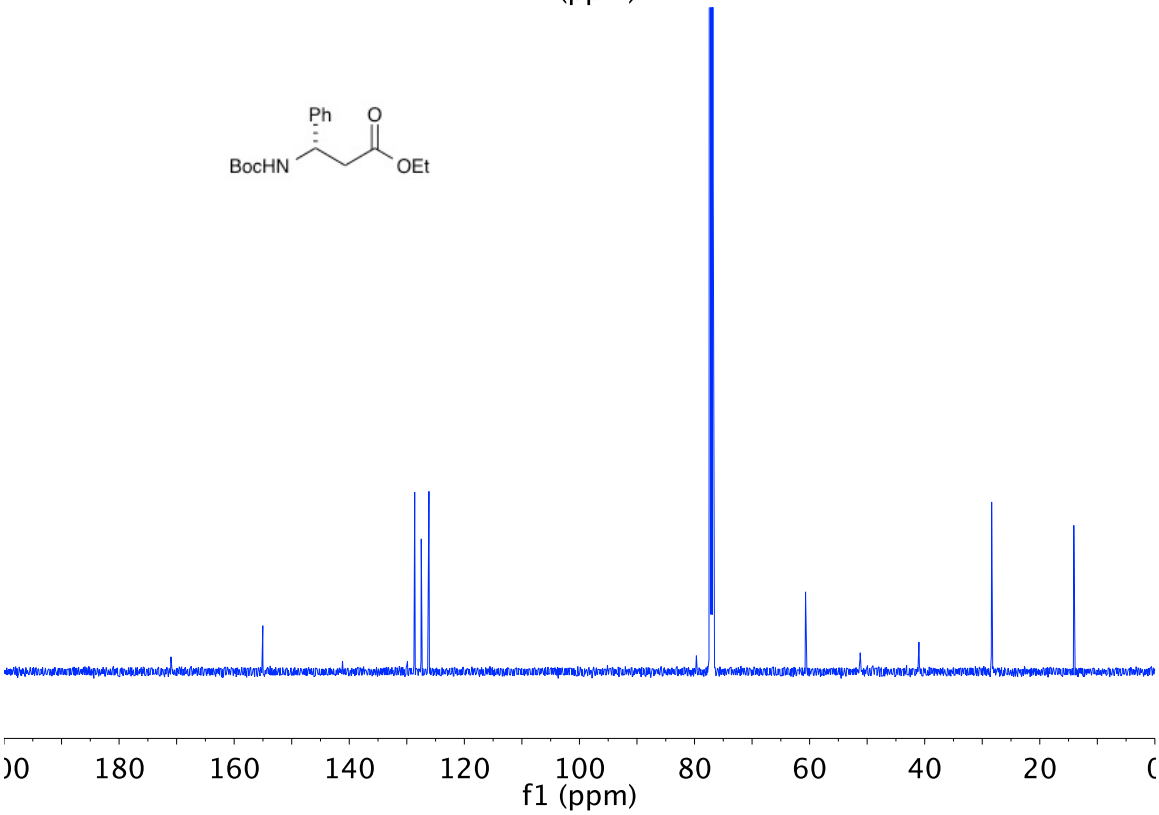

O
O
Ph
2.00
1.00
1.81
1.01
1.00
0.99
1.00
1.01
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

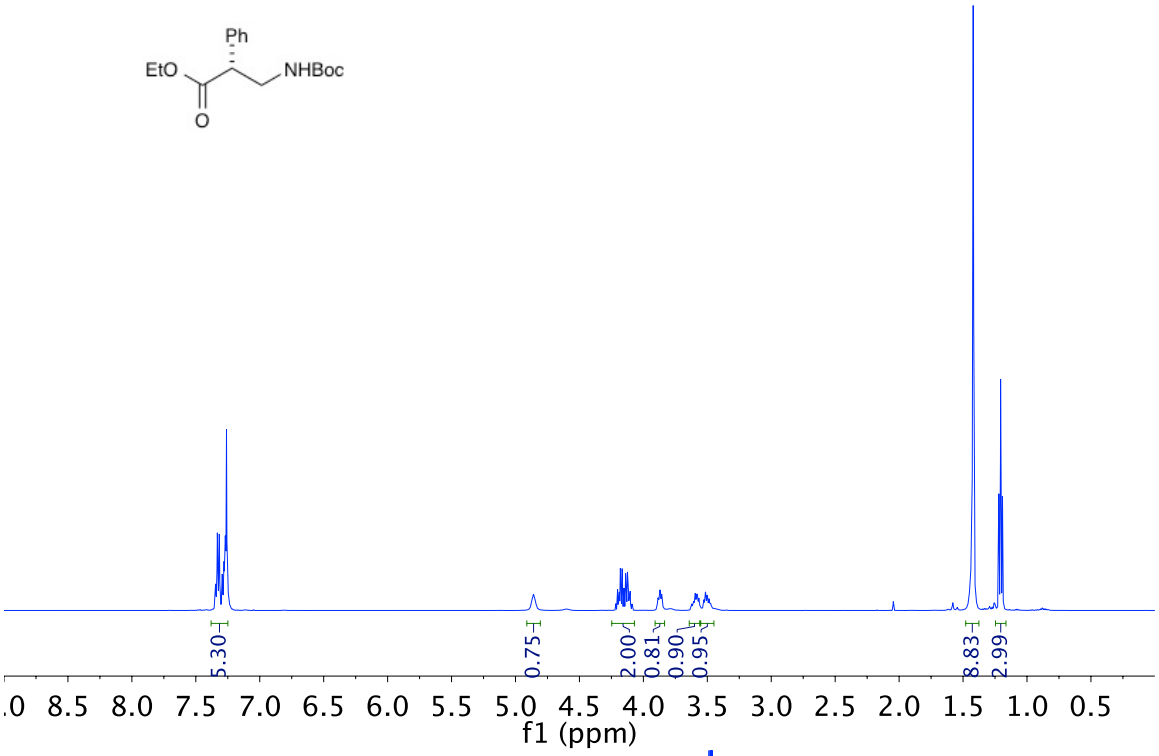

O
O
Ph
)0 180 160 140 120 100 80 60 40 20 (
f1 (ppm)

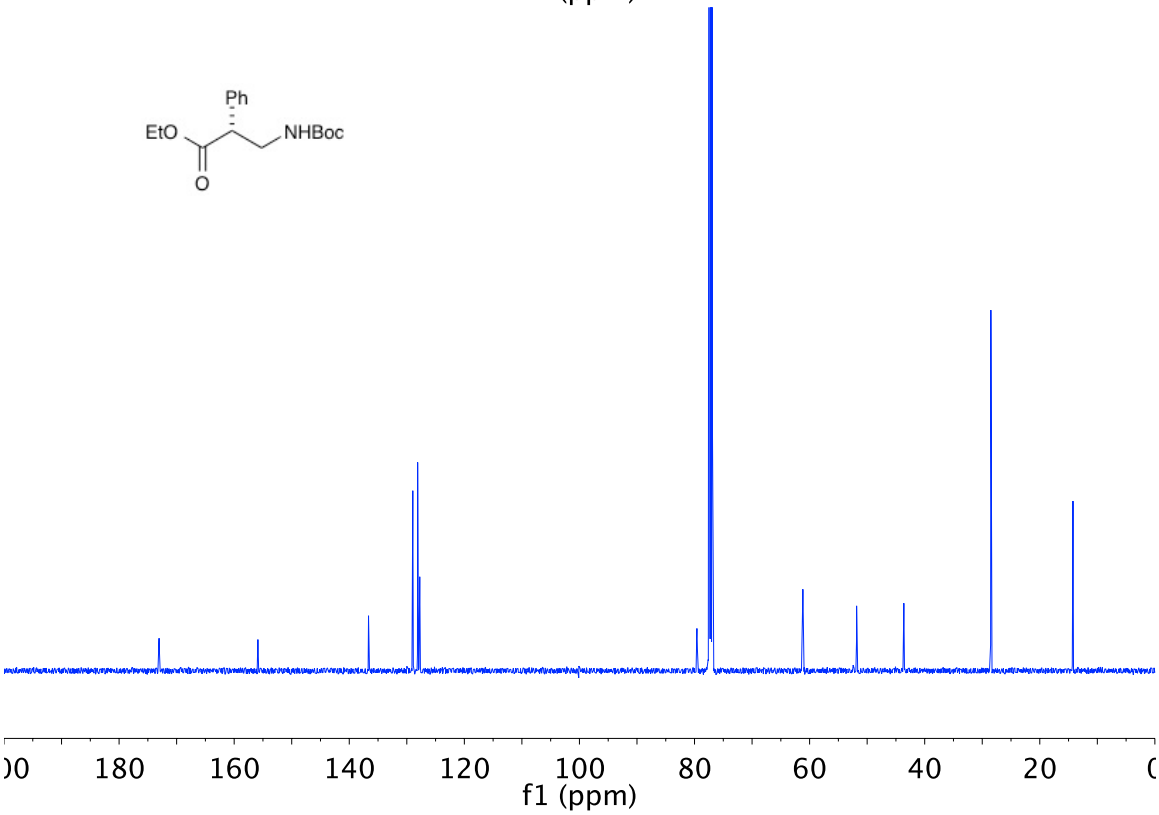

O
O
Ph
1.92
3.07
1.00
1.01
1.00
1.01
1.02
.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


O
O
Ph
180 160 140 120 100 80 60 40 20
f1 (ppm)


Ph
O
BocHN
OEt
4.51
0.69
0.87
2.00
2.02
9.04
3.04
f1 (ppm)


Ph
O
BocHN
OEt
f1 (ppm)


Ph
EtO
NHBoc
O
5.30
0.75
2.00
0.81
0.90
0.95
8.83
2.99
f1 (ppm)

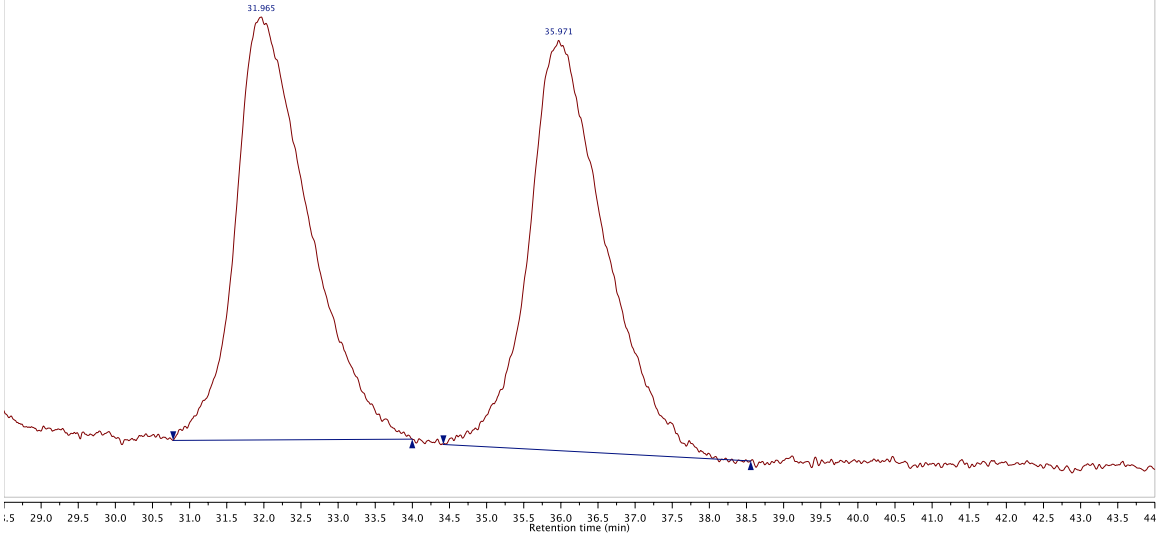

Ph
EtO
NHBoc
O
f1 (ppm)

HPLC Traces of Racemic and Enantioenriched Compounds

Racemic 2

/Users/michael...17-86-PH-RAC.D/ Injection 1 DAD D, Sig=230,16 Ref=360,100 Chromatogram

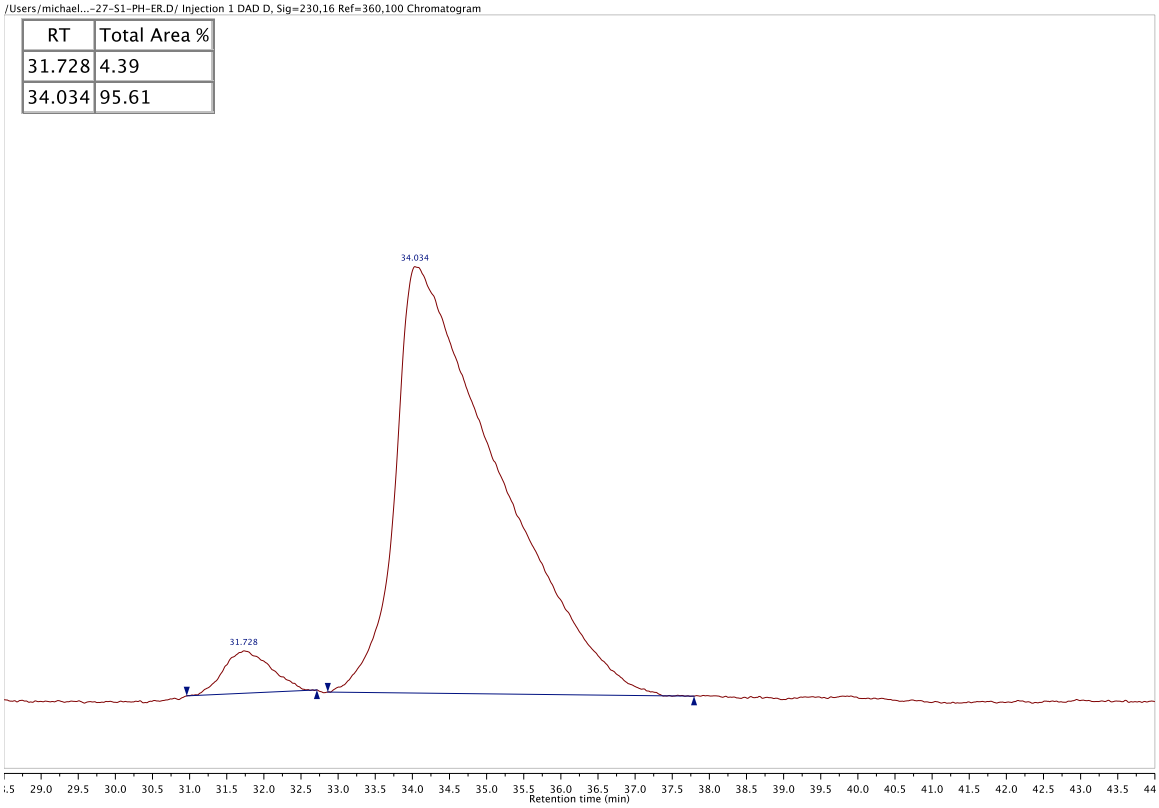
RT	Total Area %
31.965	49.53
35.971	50.47



Enantioenriched 2

/Users/michael...-27-S1-PH-ER.D/ Injection 1 DAD D, Sig=230,16 Ref=360,100 Chromatogram

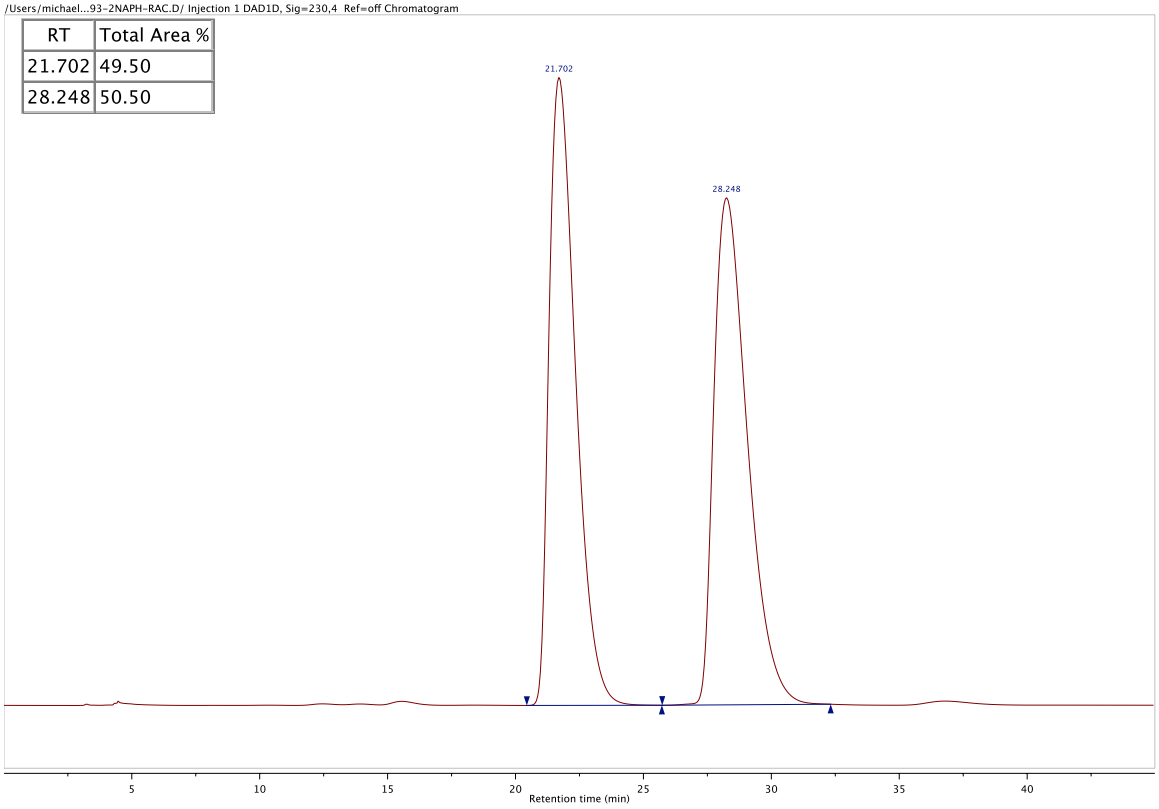
RT	Total Area %
31.728	4.39
34.034	95.61



Racemic 3

/Users/michael...93-2NAPH-RAC.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

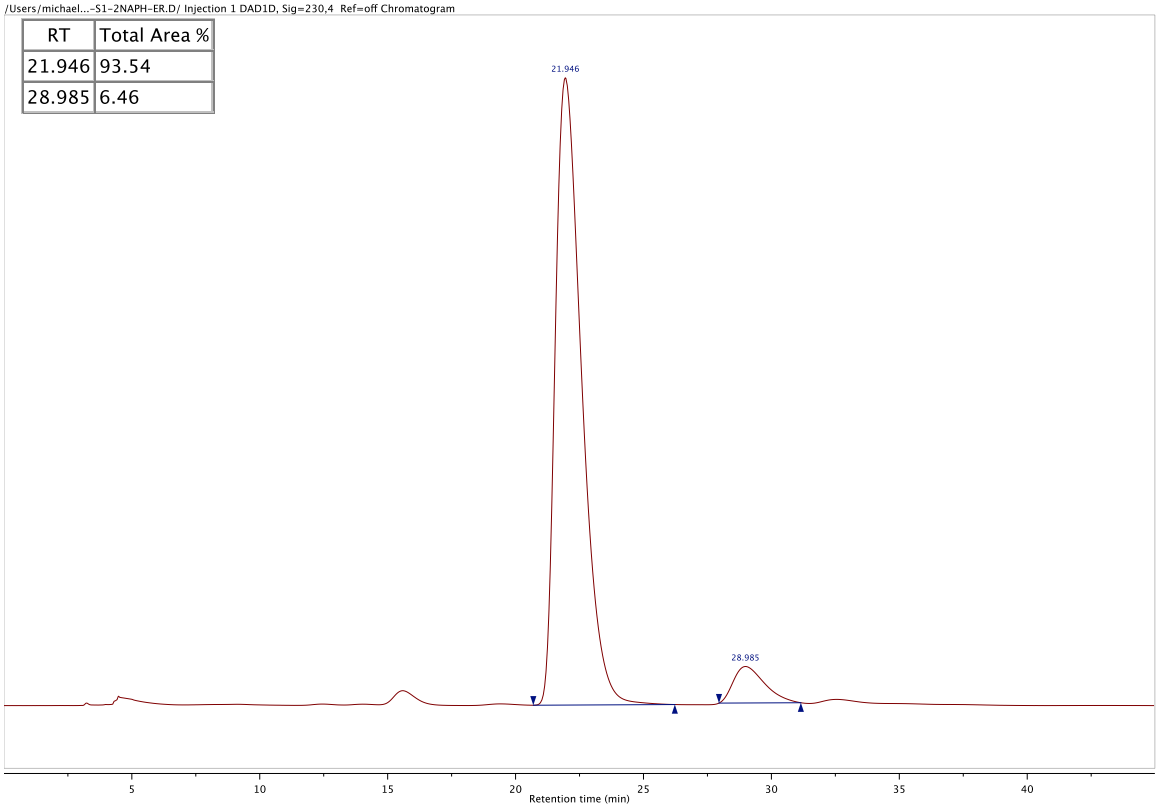
RT	Total Area %
21.702	49.50
28.248	50.50



Enantioenriched 3

/Users/michael...-S1-2NAPH-ER.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

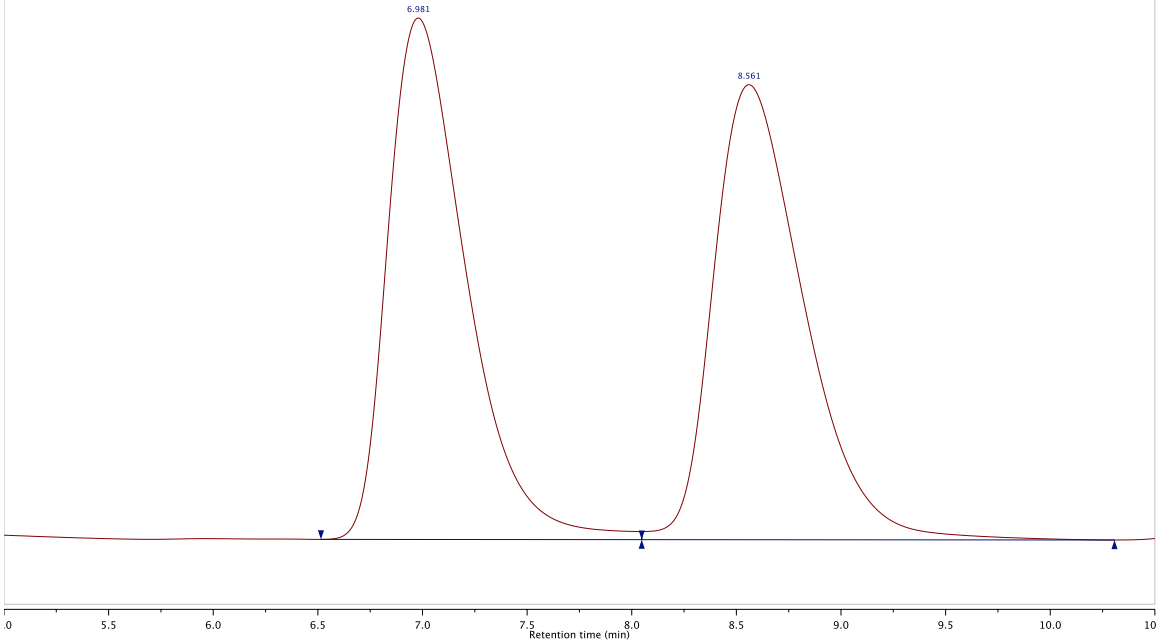
RT	Total Area %
21.946	93.54
28.985	6.46



Racemic 4

/Users/michael...5-28-4ME-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

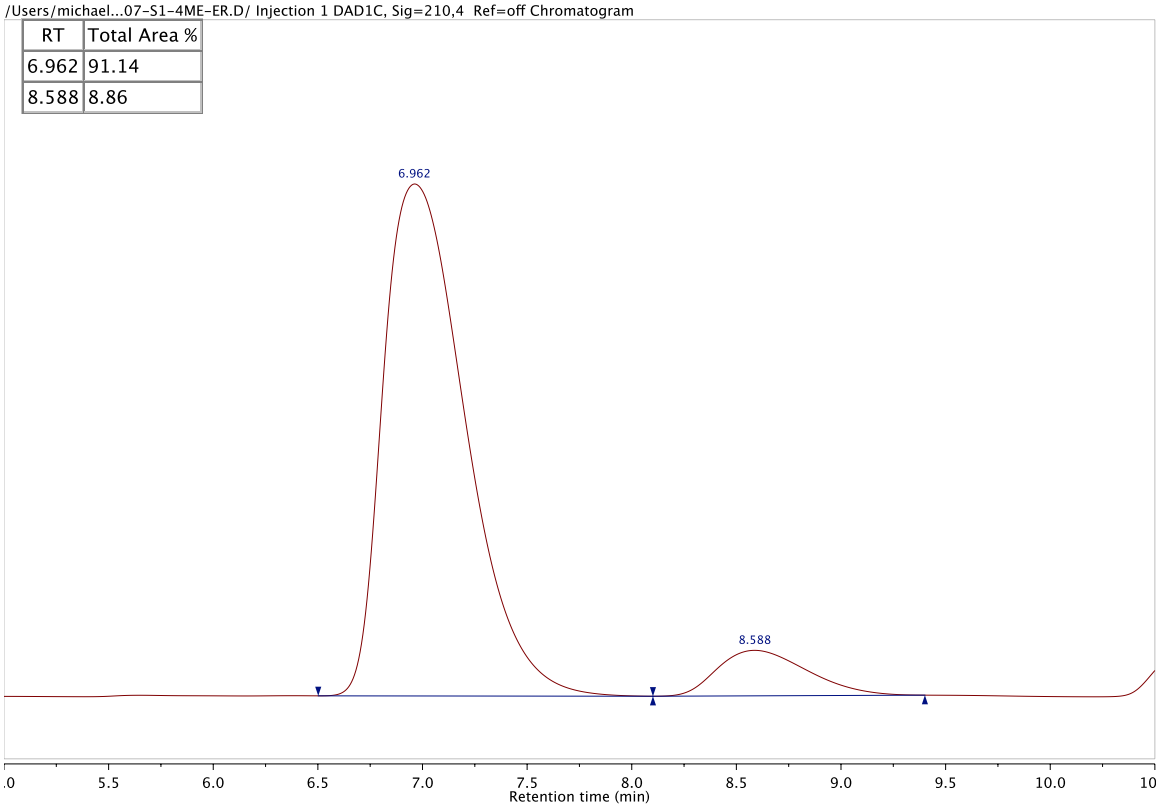
RT	Total Area %
6.981	49.85
8.561	50.15



Enantioenriched 4

/Users/michael...07-S1-4ME-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

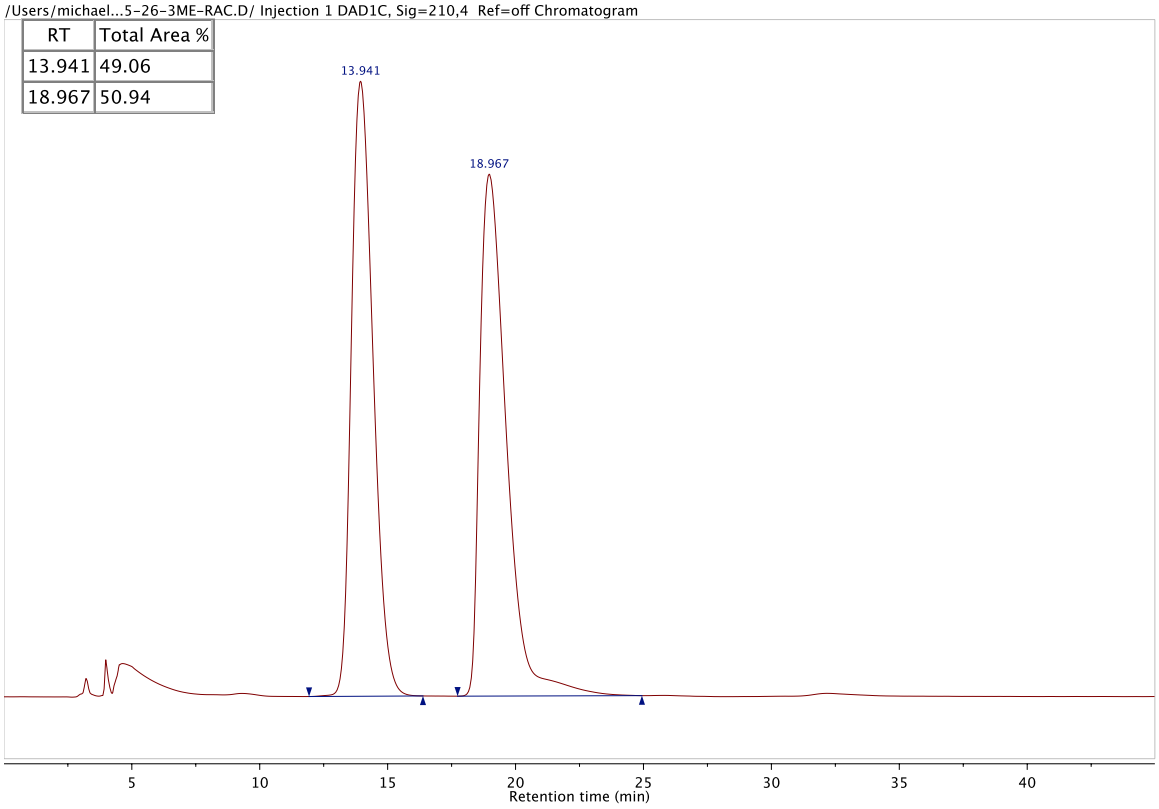
RT	Total Area %
6.962	91.14
8.588	8.86



Racemic 5

/Users/michael...5-26-3ME-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

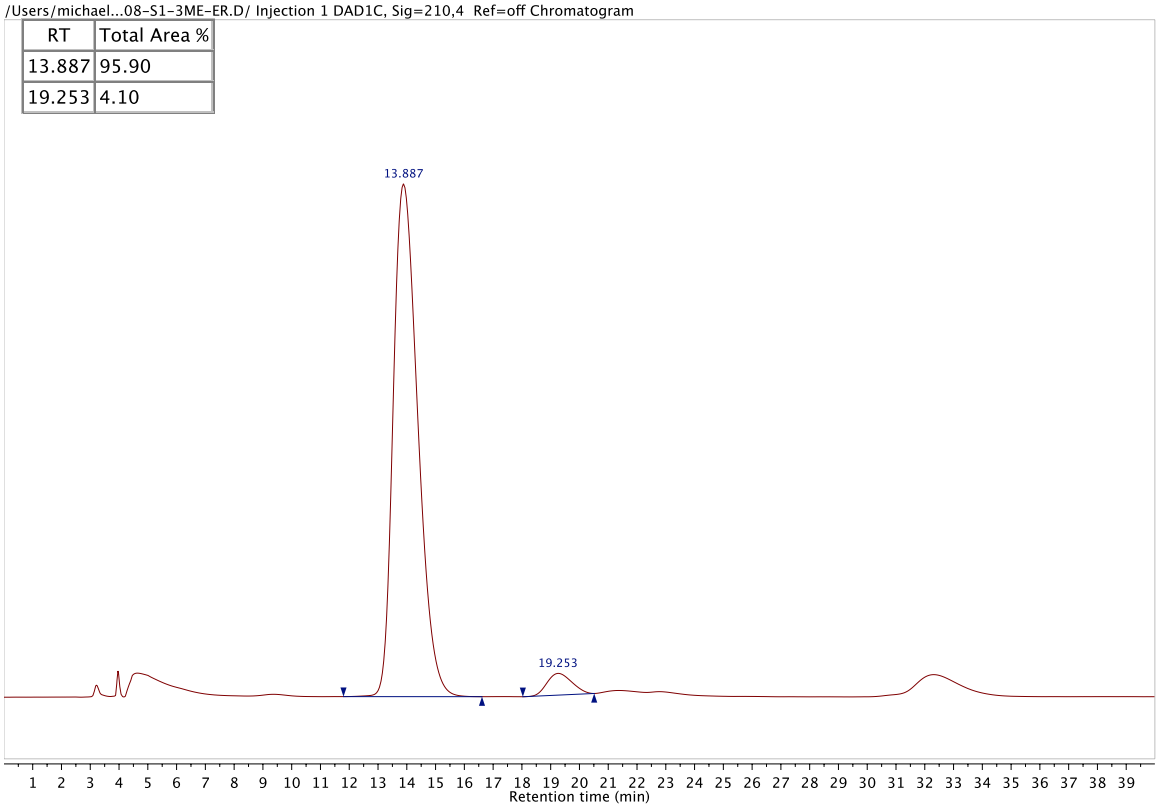
RT	Total Area %
13.941	49.06
18.967	50.94



Enantioenriched 5

/Users/michael...08-S1-3ME-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

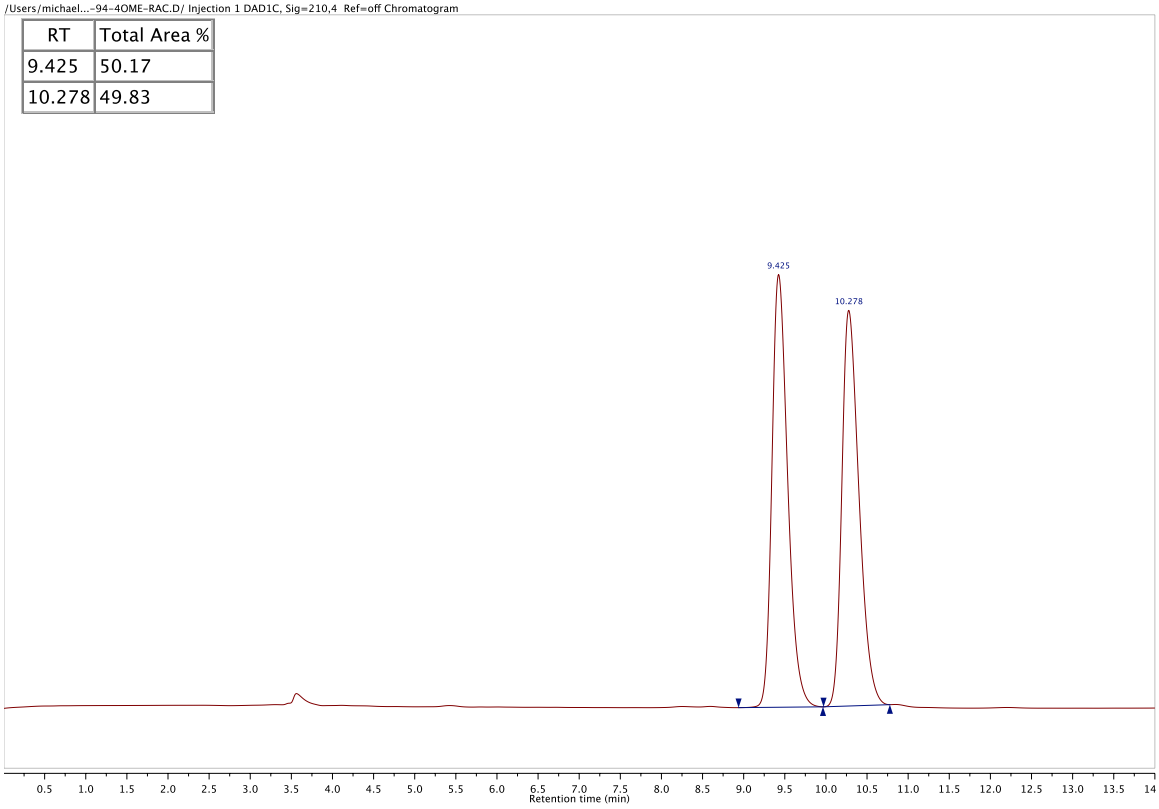
RT	Total Area %
13.887	95.90
19.253	4.10



Racemic 6

/Users/michael...-94-4OME-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

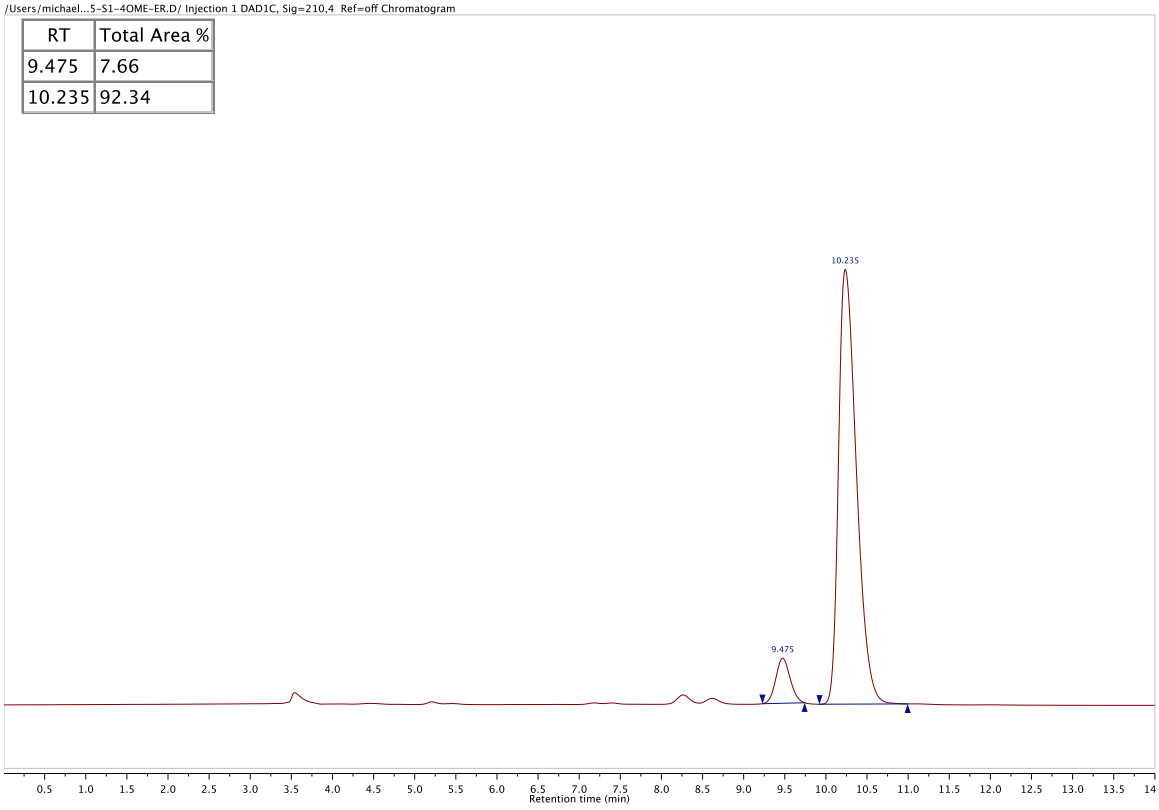
RT	Total Area %
9.425	50.17
10.278	49.83



Enantioenriched 6

/Users/michael...5-S1-4OME-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

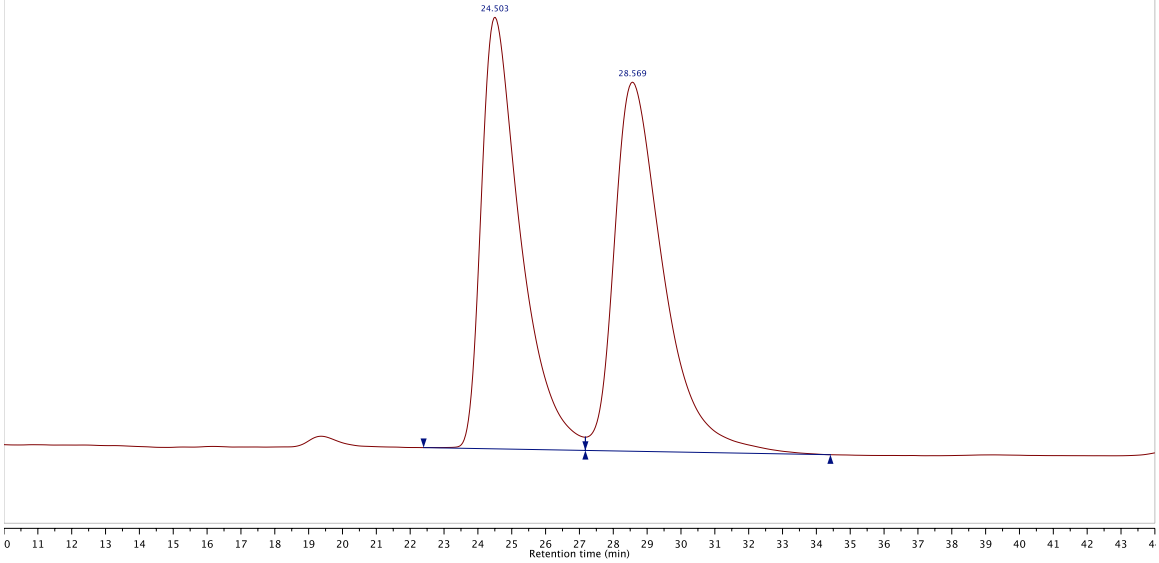
RT	Total Area %
9.475	7.66
10.235	92.34



Racemic 7

/Users/michael...14-34OME-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

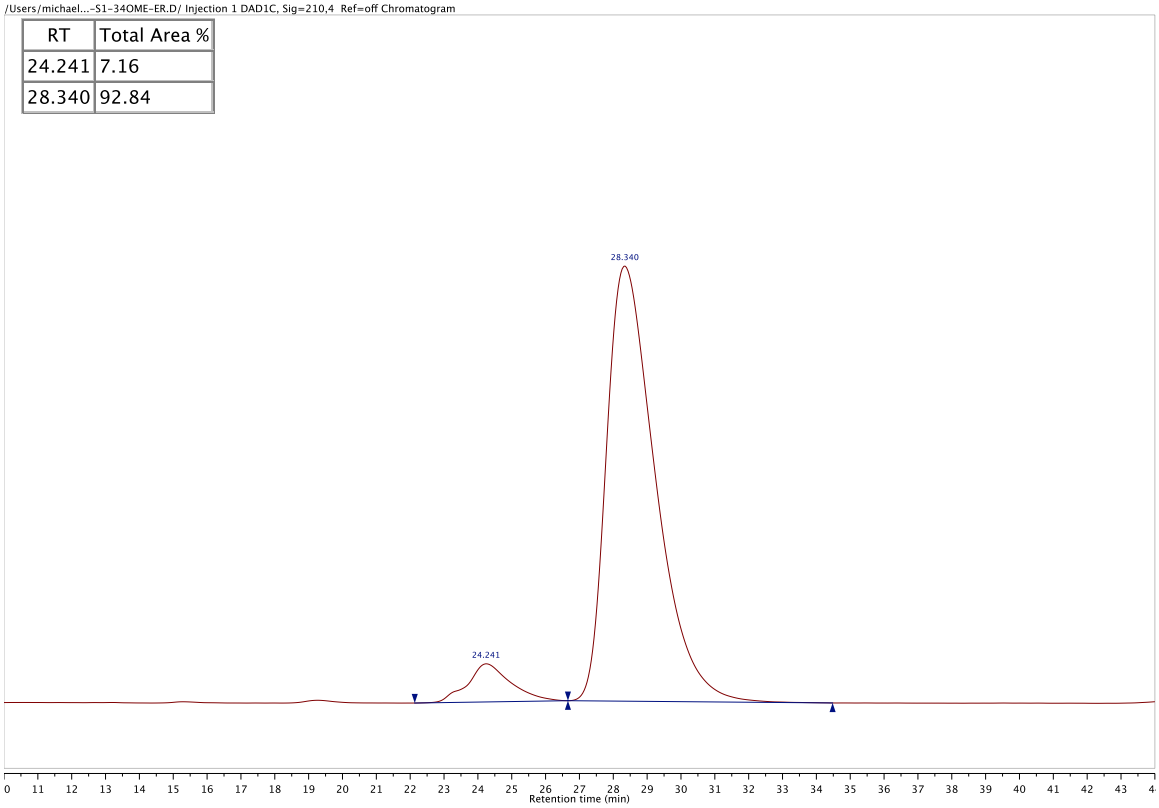
RT	Total Area %
24.503	48.46
28.569	51.54



Enantioenriched 7

/Users/michael...-S1-34OME-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

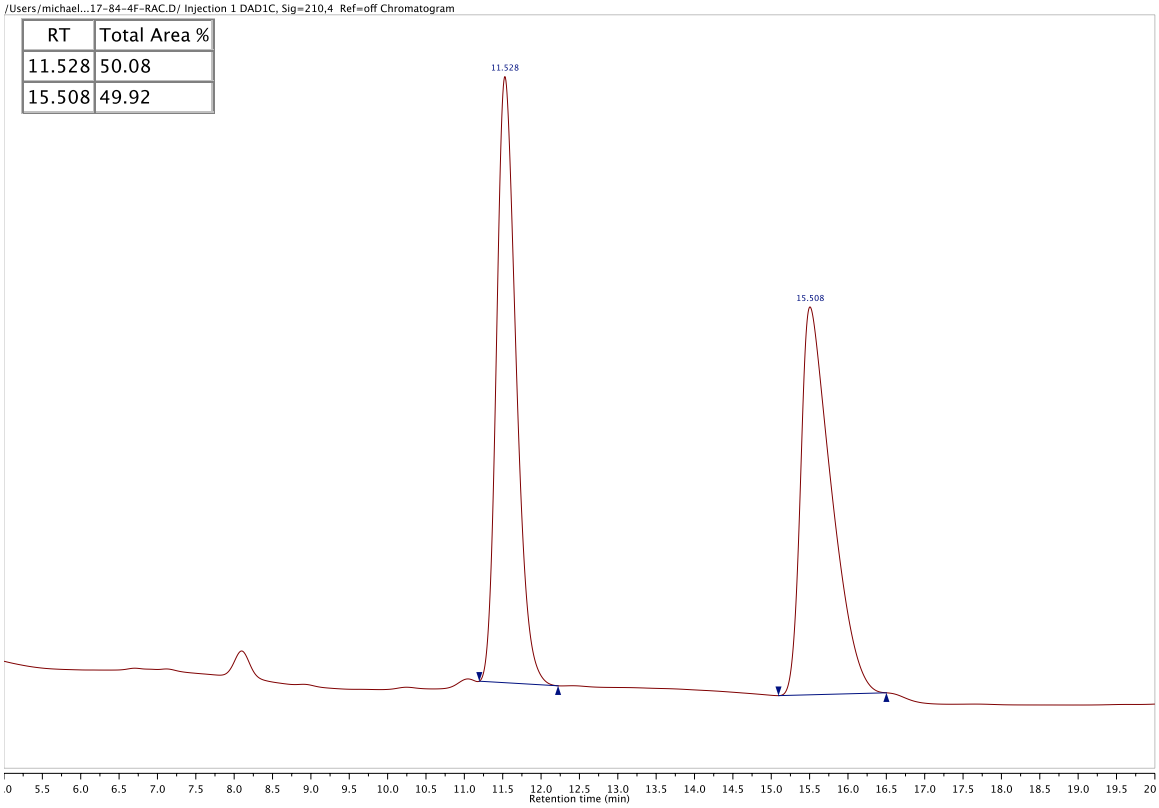
RT	Total Area %
24.241	7.16
28.340	92.84



Racemic 8

/Users/michael...17-84-4F-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

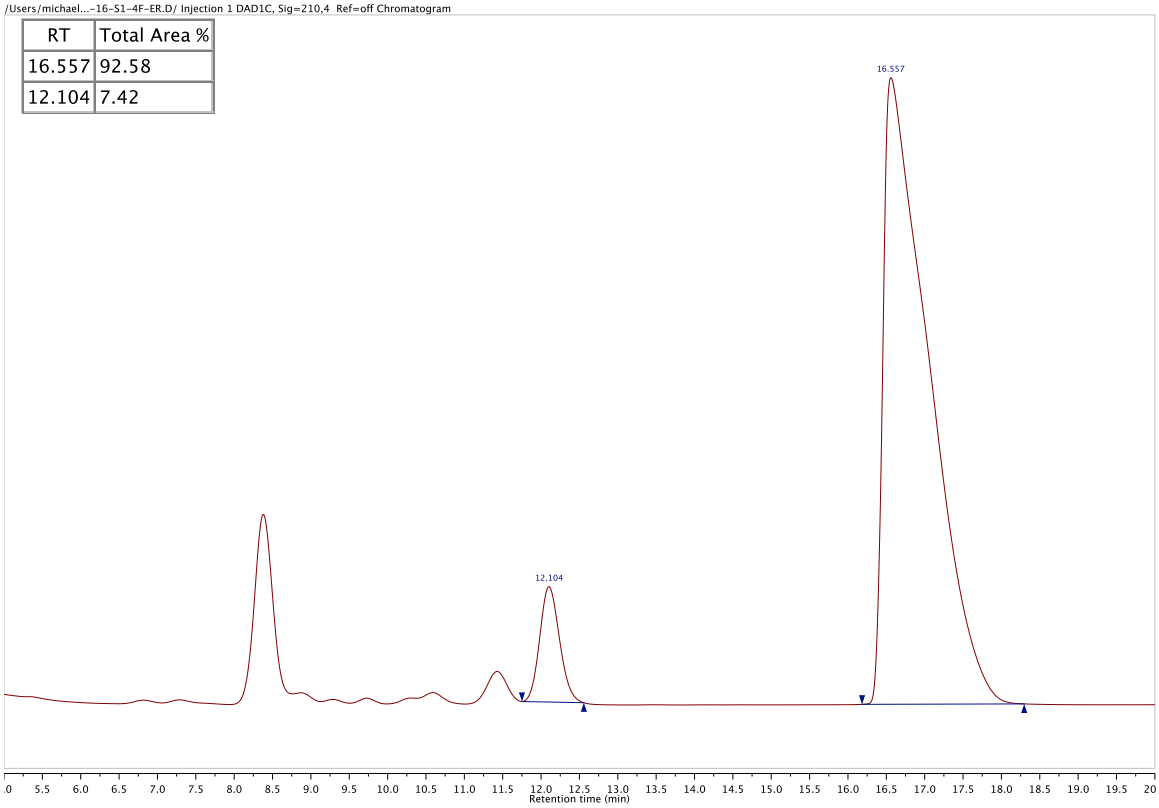
RT	Total Area %
11.528	50.08
15.508	49.92



Enantioenriched 8

/Users/michael...-16-S1-4F-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

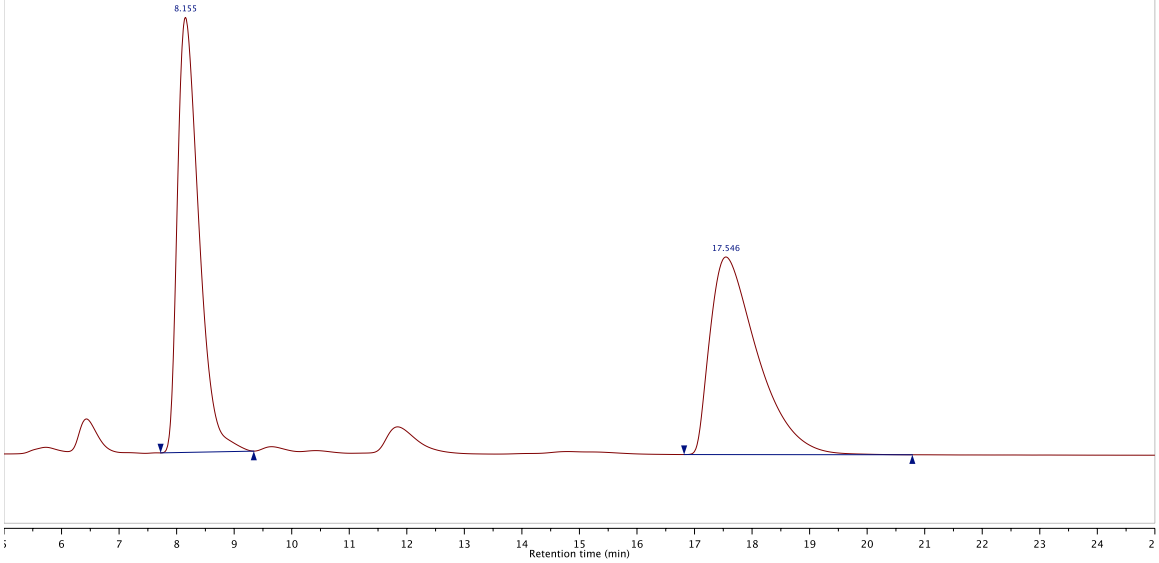
RT	Total Area %
16.557	92.58
12.104	7.42



Racemic 9

/Users/michael...-PLUG-3F-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

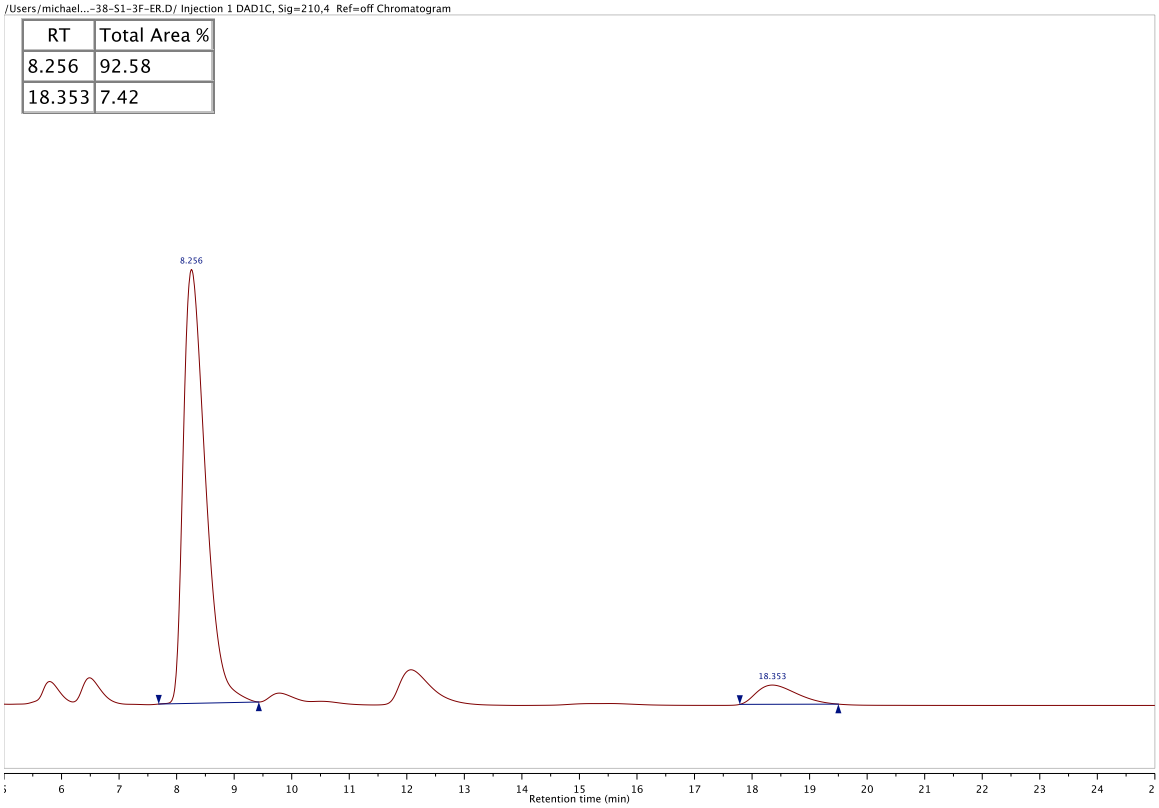
RT	Total Area %
8.155	50.08
17.546	49.92



Enantioenriched 9

/Users/michael...-38-S1-3F-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

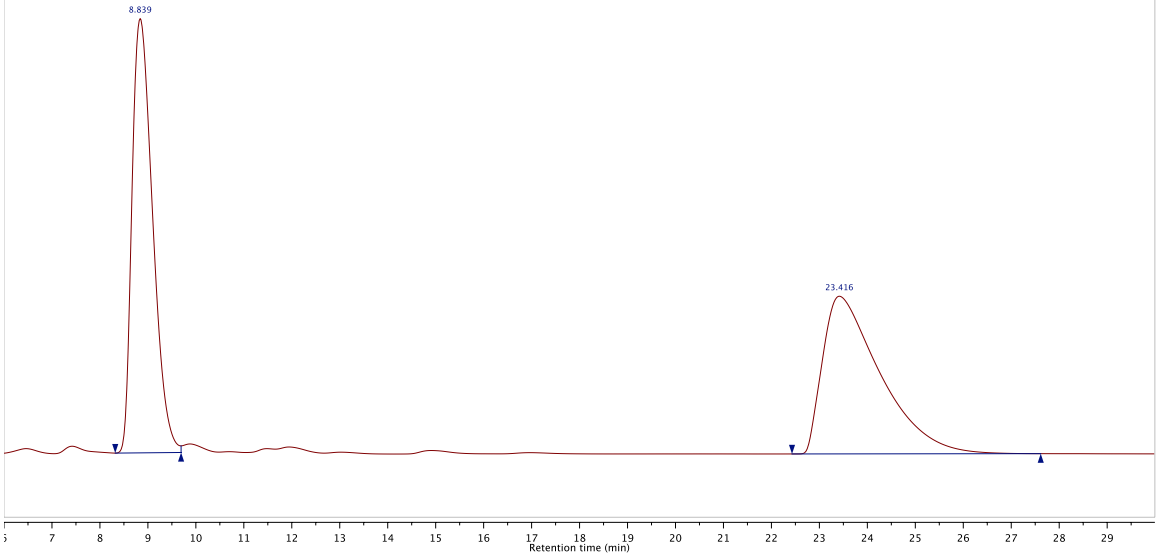
RT	Total Area %
8.256	92.58
18.353	7.42



Racemic 10

/Users/michael...18-44-2F-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

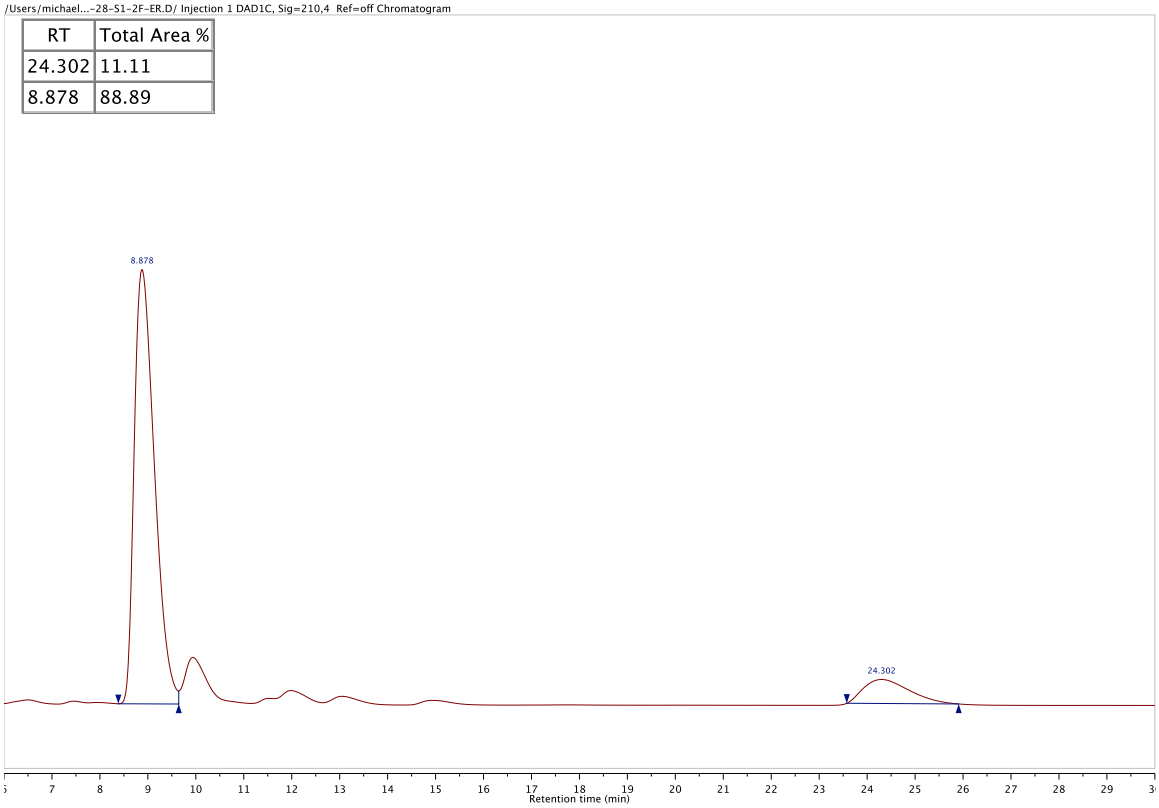
RT	Total Area %
8.839	49.75
23.416	50.25



Enantioenriched 10

/Users/michael...-28-S1-2F-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

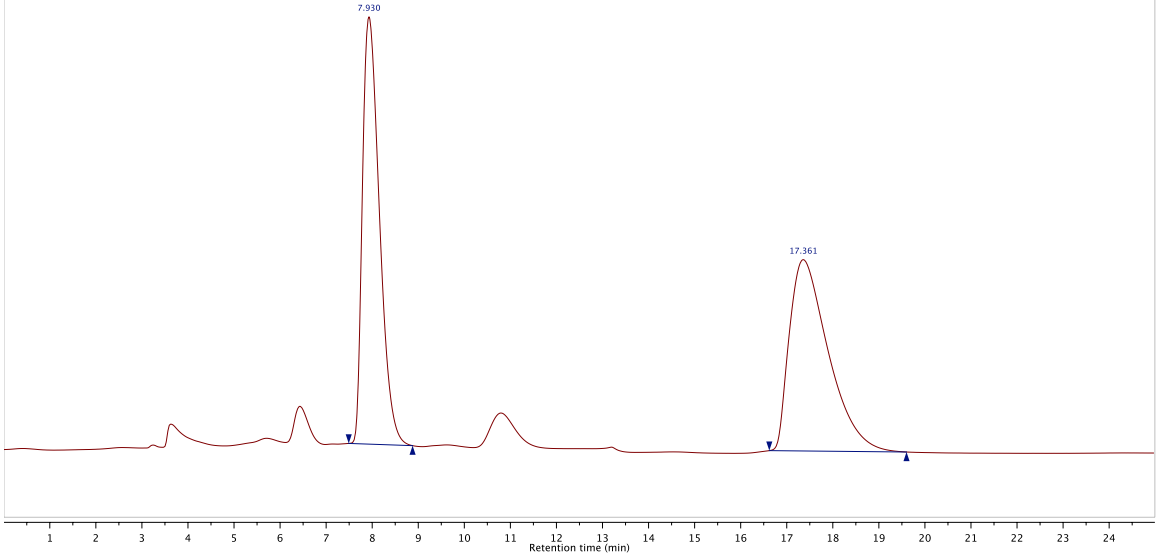
RT	Total Area %
24.302	11.11
8.878	88.89



Racemic 11

/Users/michael...8-23-3CL-RAC.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

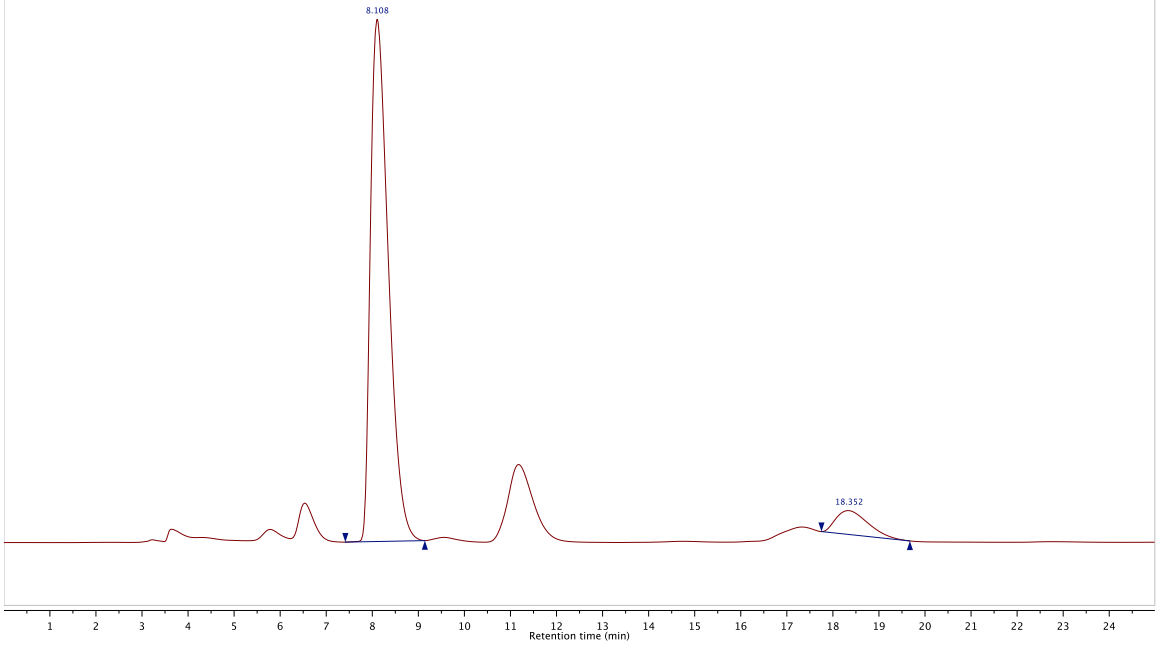
RT	Total Area %
7.930	49.45
17.361	50.55



Enantioenriched 11

/Users/michael...23-10-3CL-ER.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

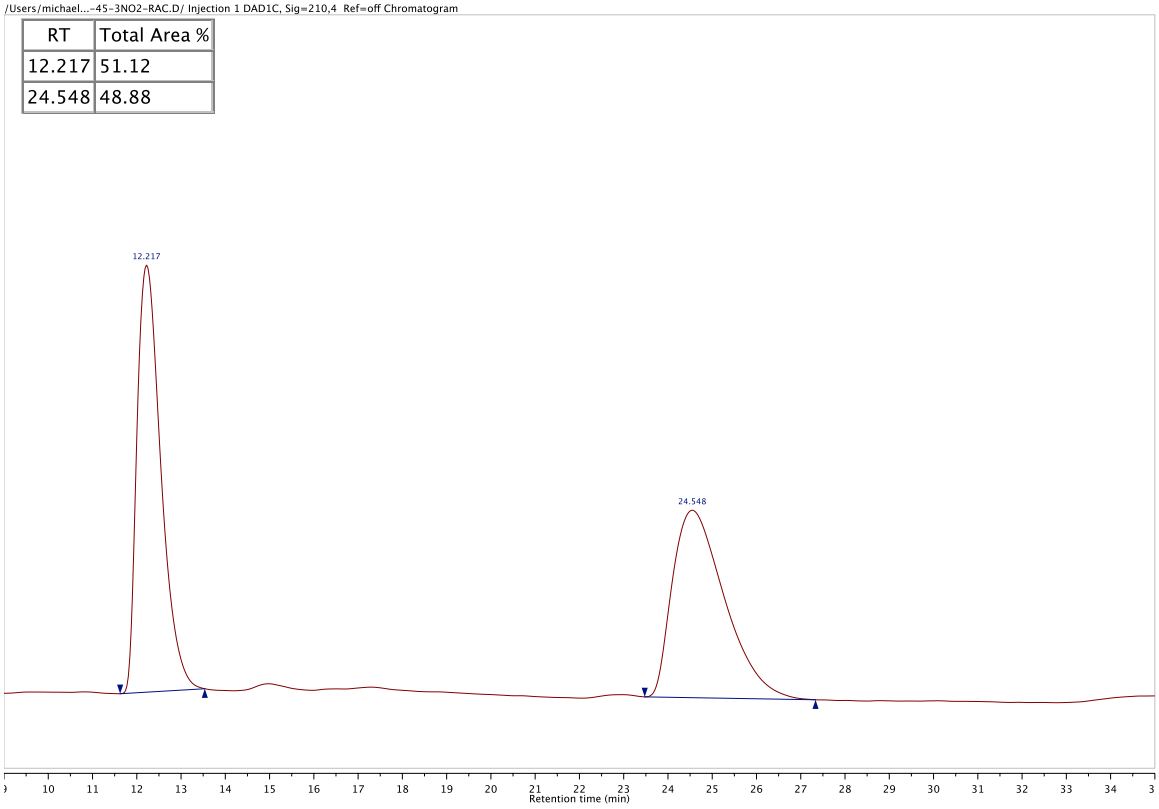
RT	Total Area %
8.108	92.90
18.346	7.10



Racemic 12

/Users/michael...-45-3NO2-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

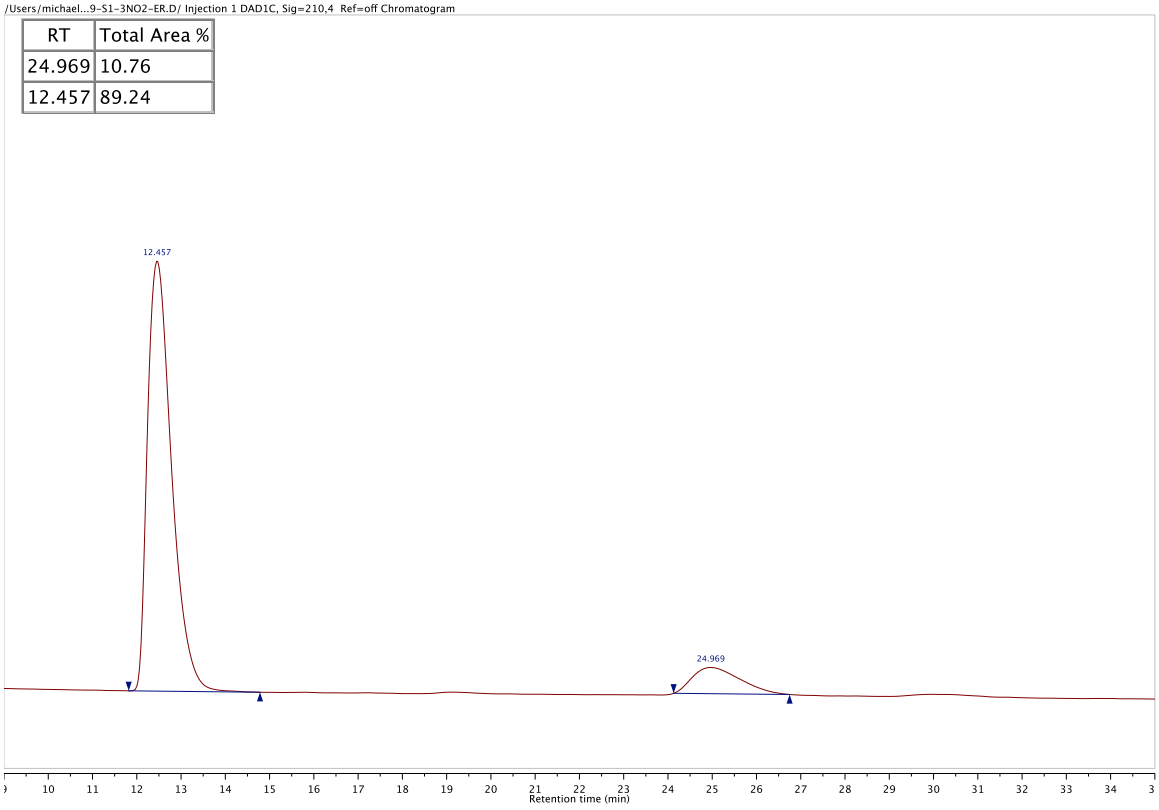
RT	Total Area %
12.217	51.12
24.548	48.88



Enantioenriched 12

/Users/michael...9-S1-3NO2-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

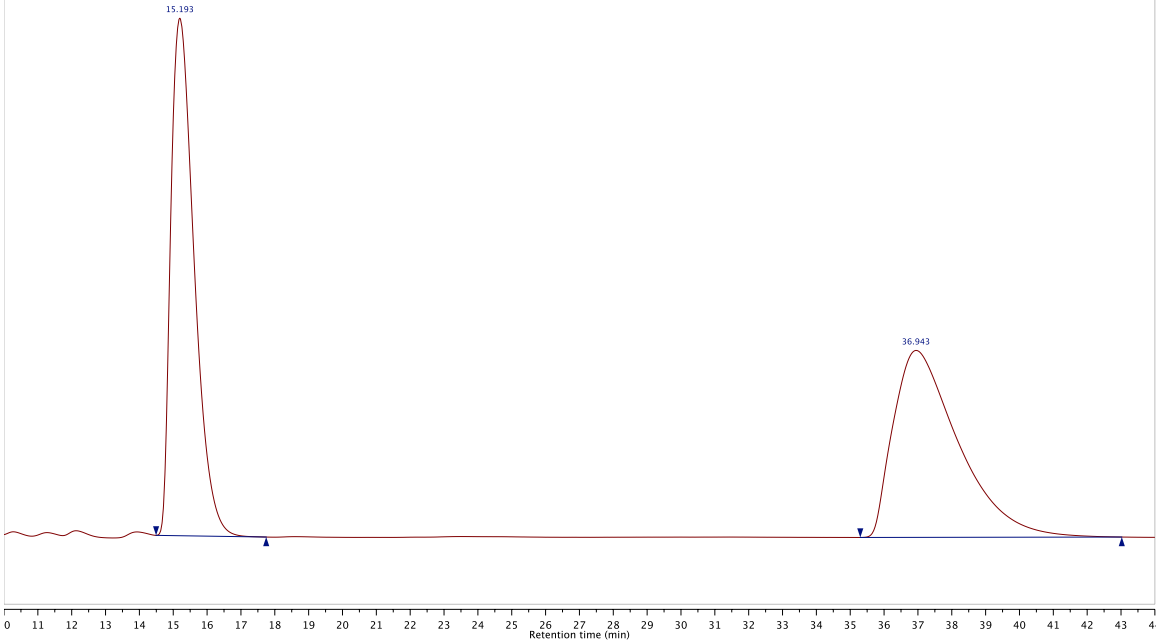
RT	Total Area %
24.969	10.76
12.457	89.24



Racemic 13

/Users/michael...-46-THIO-RAC.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

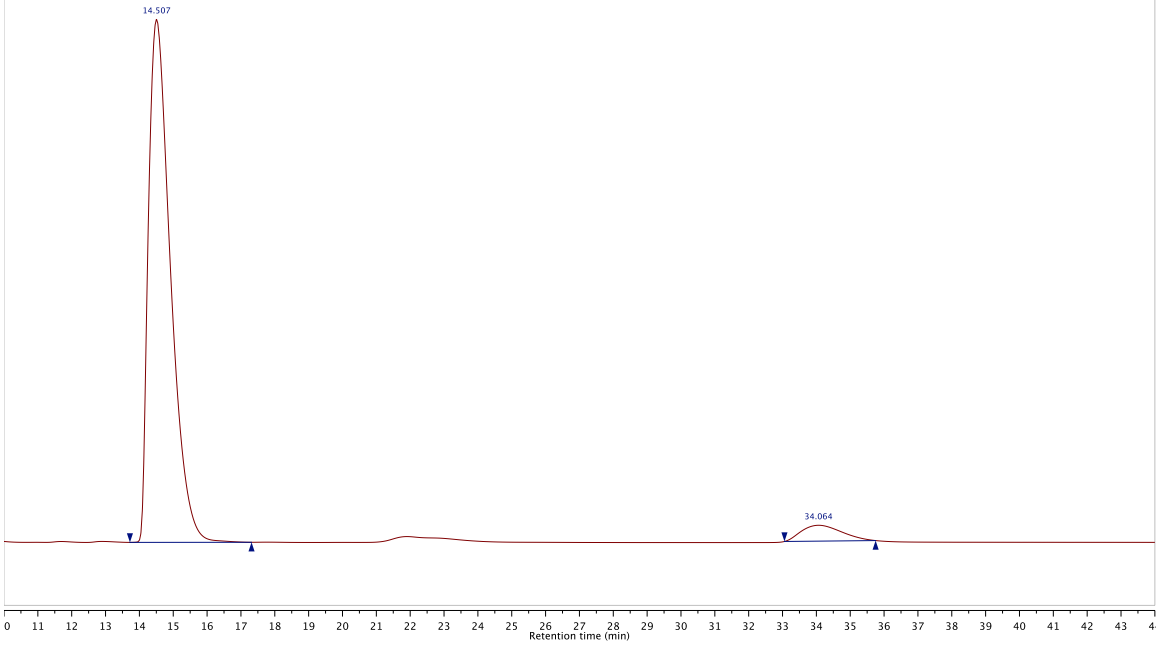
RT	Total Area %
15.193	49.95
36.943	50.05



Enantioenriched 13

/Users/michael...7-S1-THIO-ER.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

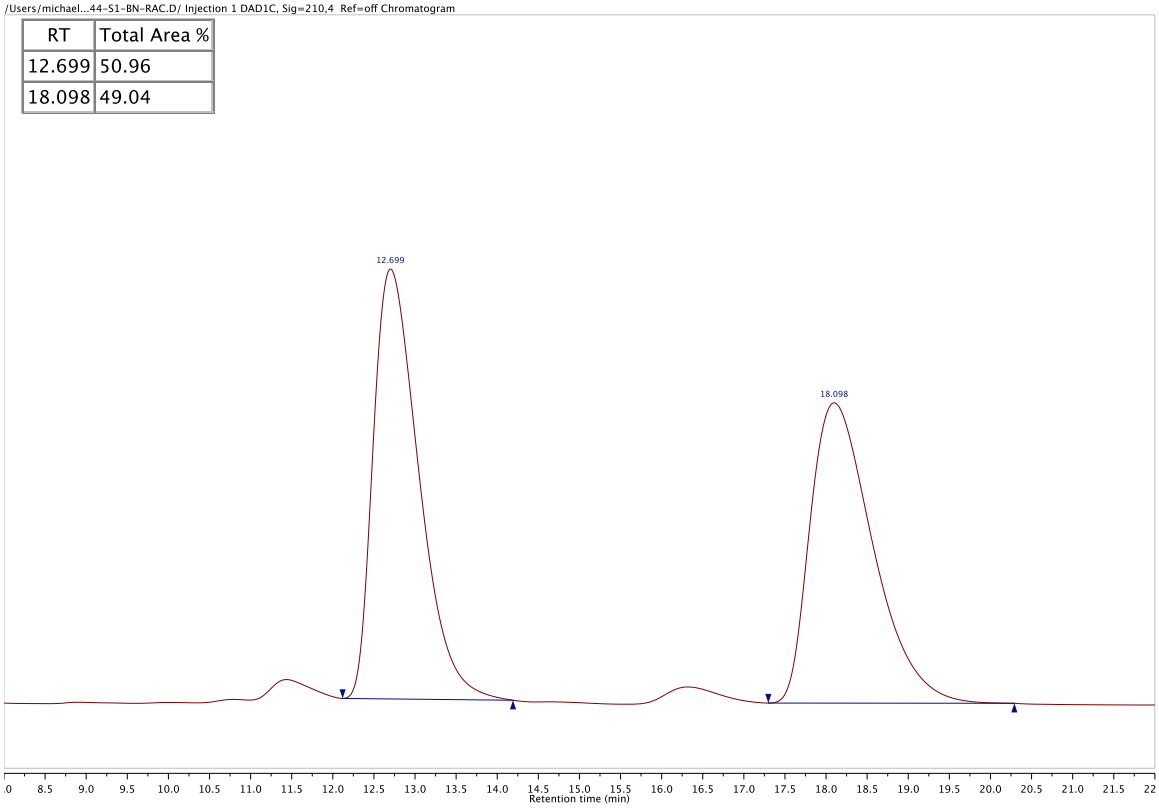
RT	Total Area %
14.507	94.76
34.064	5.24



Racemic 14

/Users/michael...44-S1-BN-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

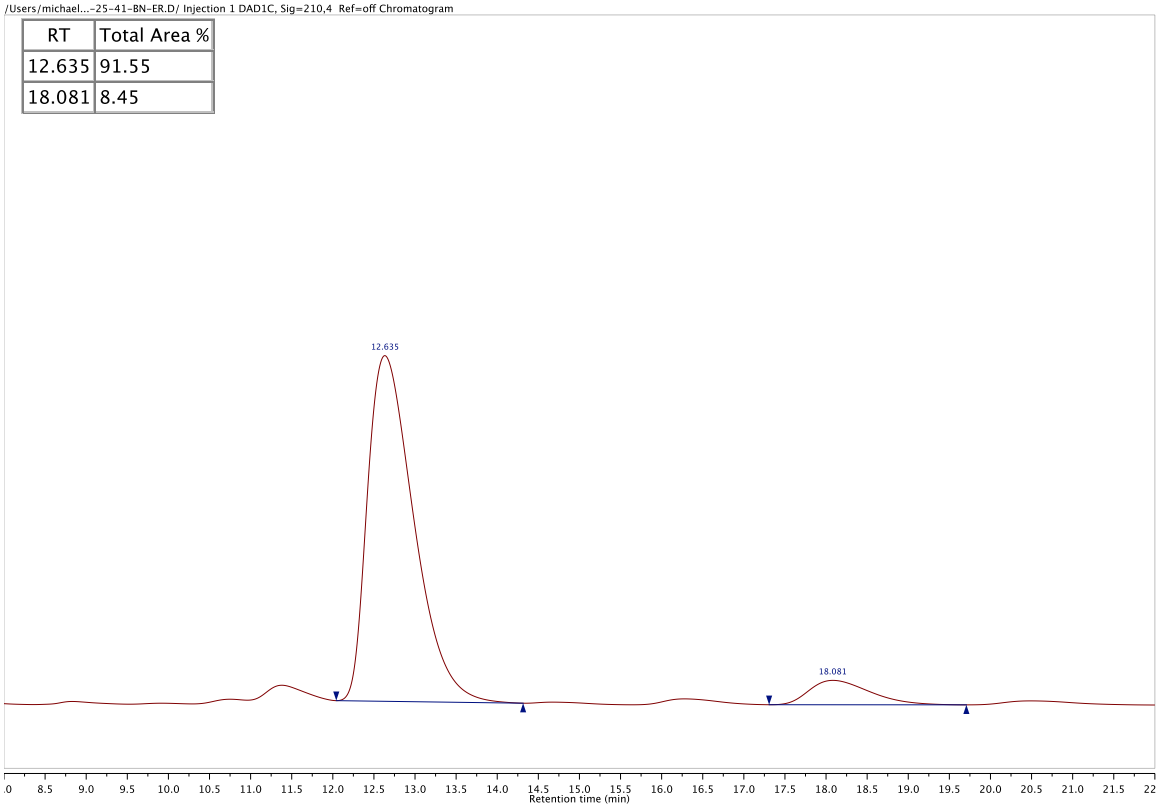
RT	Total Area %
12.699	50.96
18.098	49.04



Enantioenriched 14

/Users/michael...-25-41-BN-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

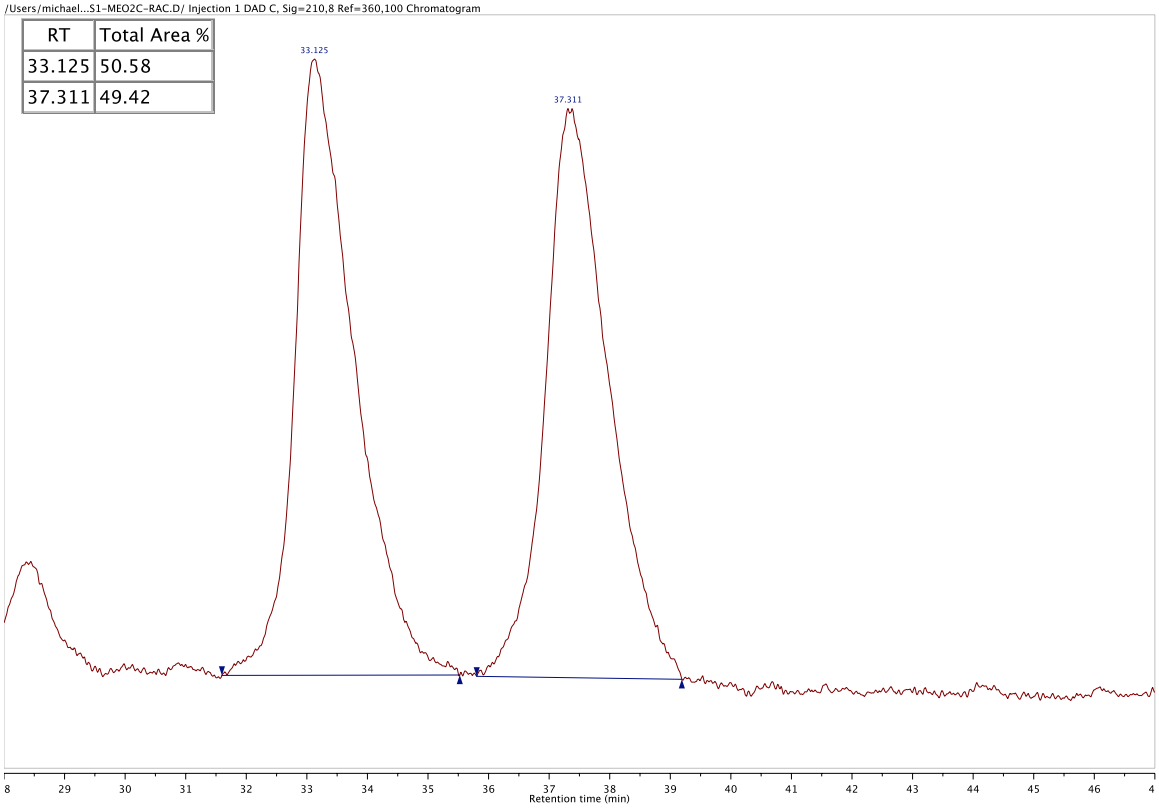
RT	Total Area %
12.635	91.55
18.081	8.45



Racemic 15

/Users/michael...S1-MEO2C-RAC.D/ Injection 1 DAD C, Sig=210,8 Ref=360,100 Chromatogram

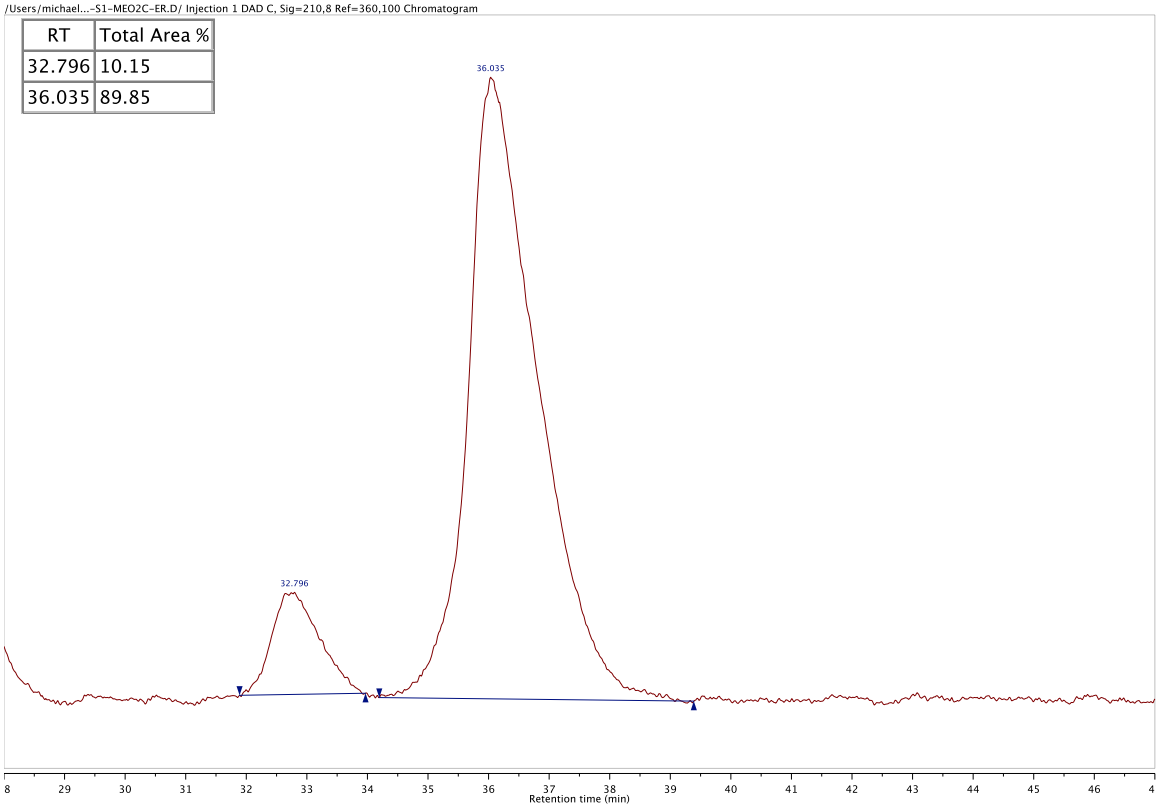
RT	Total Area %
33.125	50.58
37.311	49.42



Enantioenriched 15

/Users/michael...-S1-MEO2C-ER.D/ Injection 1 DAD C, Sig=210,8 Ref=360,100 Chromatogram

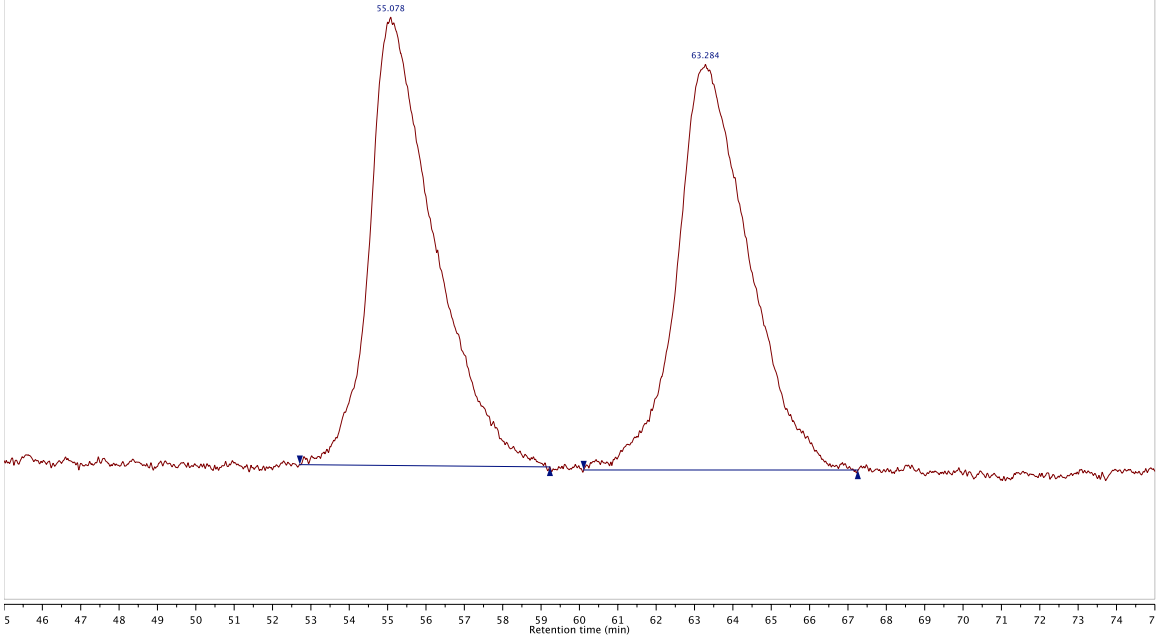
RT	Total Area %
32.796	10.15
36.035	89.85



Racemic 16

/Users/michael...11-BNO2C-RAC.D/ Injection 1 DAD C, Sig=210,8 Ref=360,100 Chromatogram

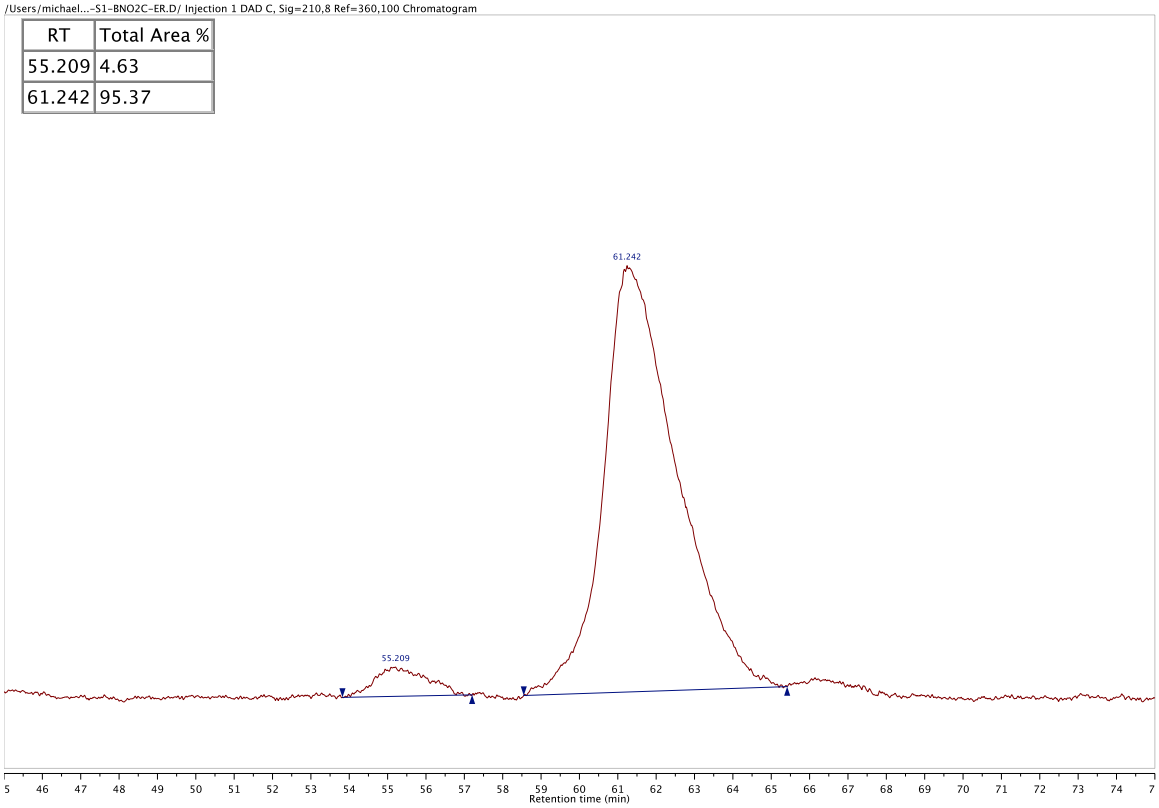
RT	Total Area %
55.078	50.00
63.284	50.00



Enantioenriched 16

/Users/michael...-S1-BNO2C-ER.D/ Injection 1 DAD C, Sig=210,8 Ref=360,100 Chromatogram

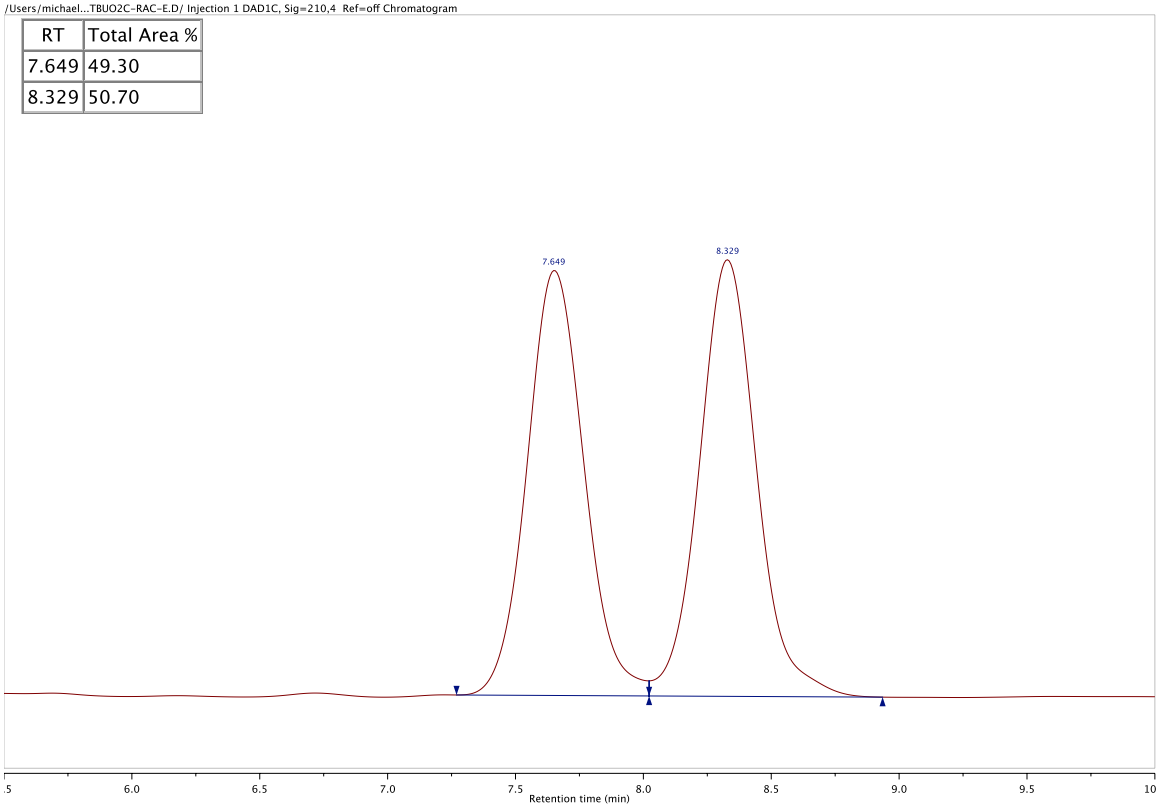
RT	Total Area %
55.209	4.63
61.242	95.37



Racemic 17

/Users/michael...TBUO2C-RAC-E.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

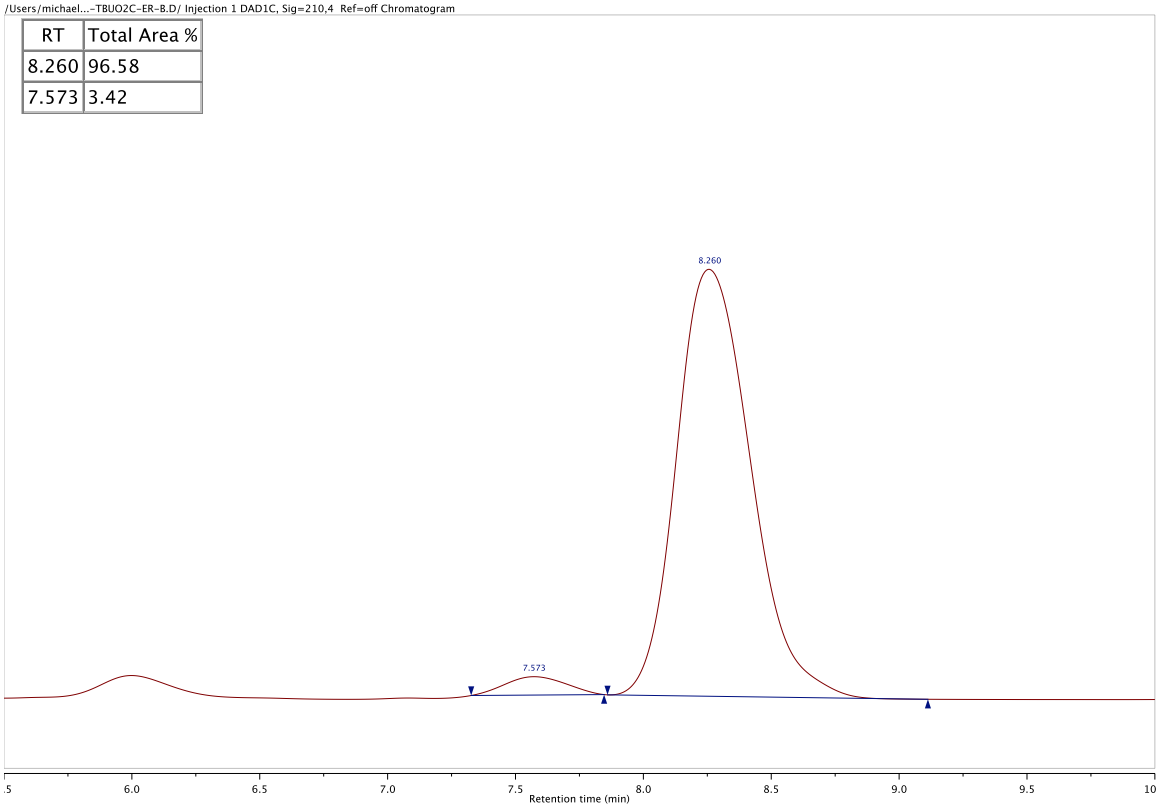
RT	Total Area %
7.649	49.30
8.329	50.70



Enantioenriched 17

/Users/michael...-TBUO2C-ER-B.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

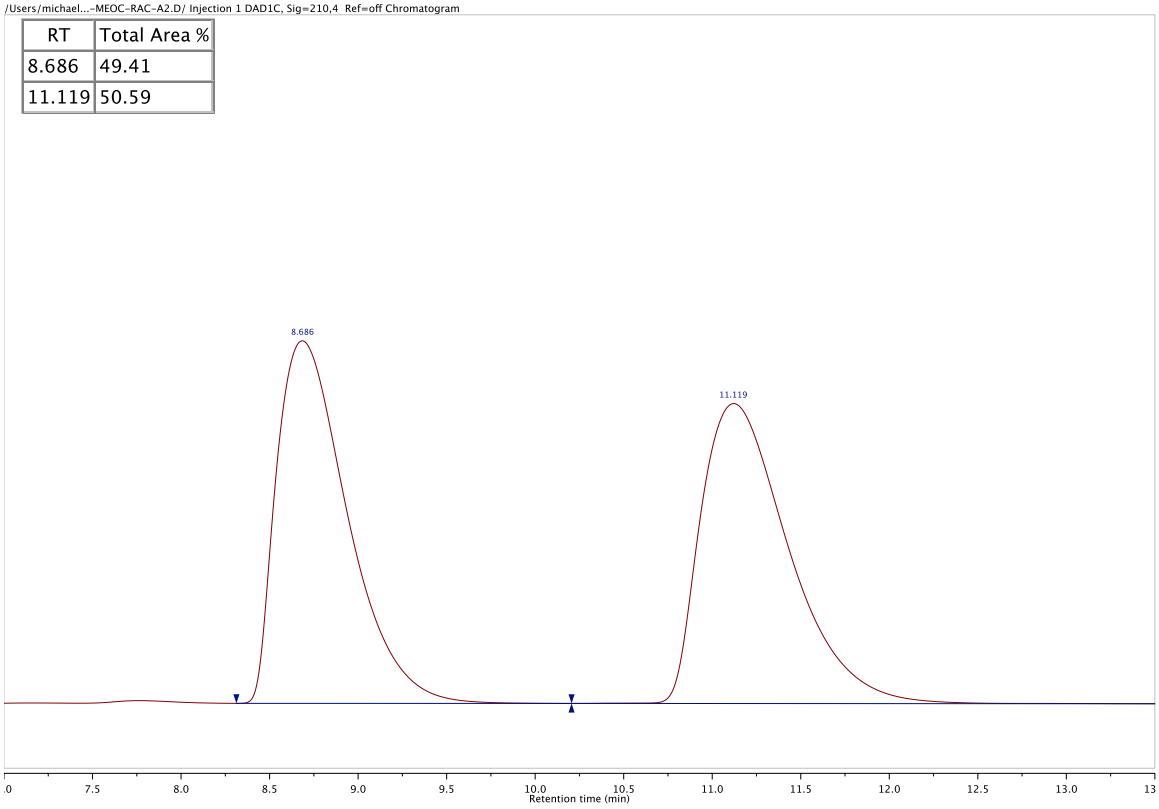
RT	Total Area %
8.260	96.58
7.573	3.42



Racemic 18

/Users/michael...-MEOC-RAC-A2.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

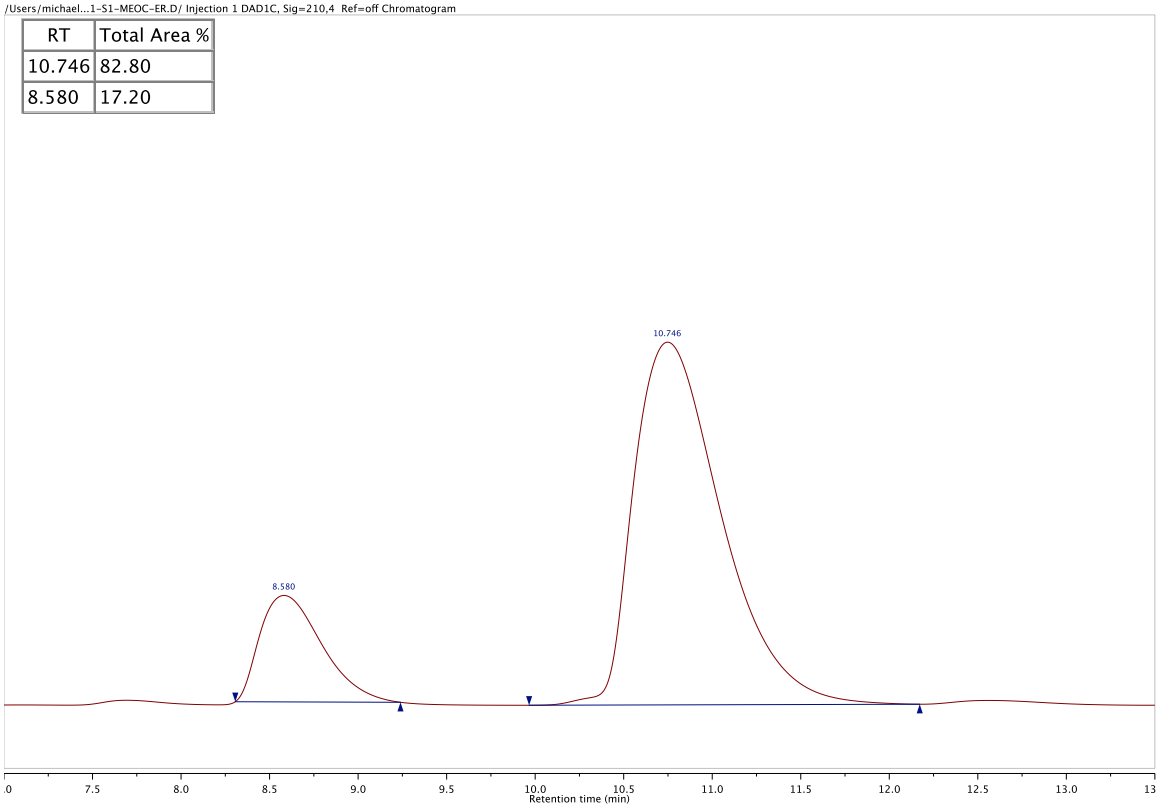
RT	Total Area %
8.686	49.41
11.119	50.59



Enantioenriched 18

/Users/michael...1-S1-MEOC-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

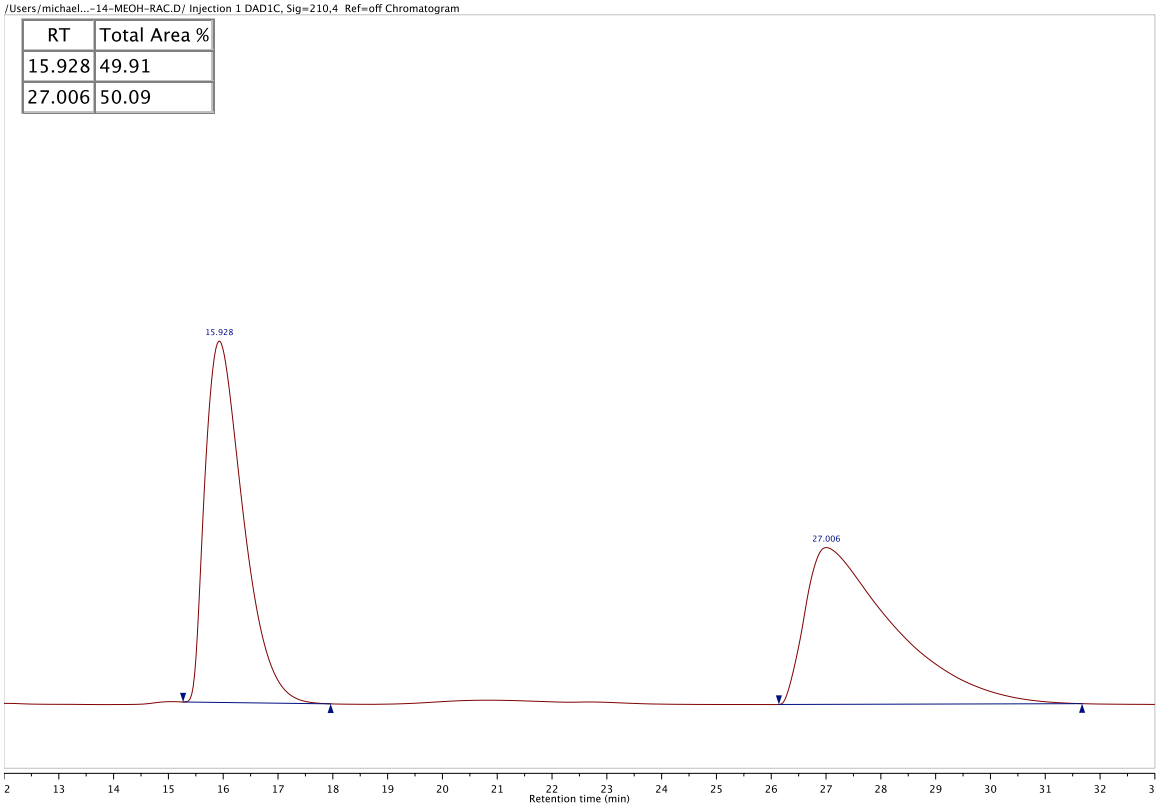
RT	Total Area %
10.746	82.80
8.580	17.20



Racemic 19

/Users/michael...-14-MEOH-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

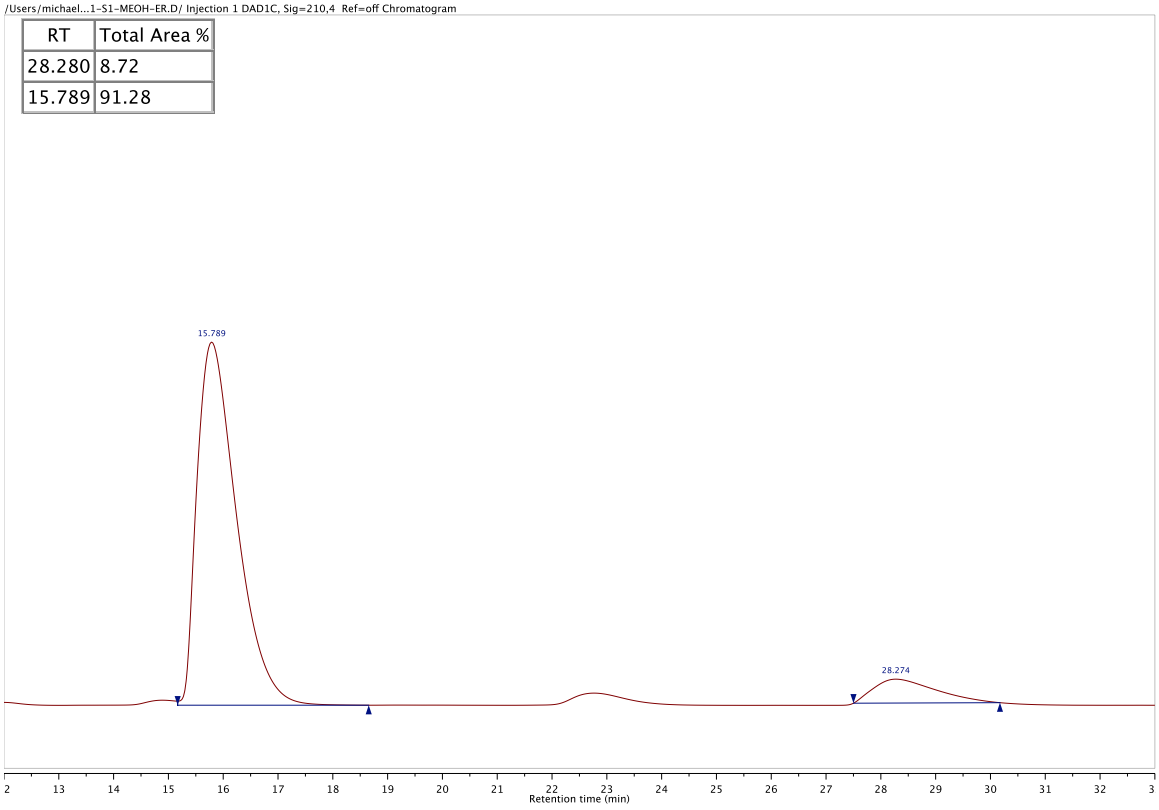
RT	Total Area %
15.928	49.91
27.006	50.09



Enantioenriched 19

/Users/michael...1-S1-MEOH-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

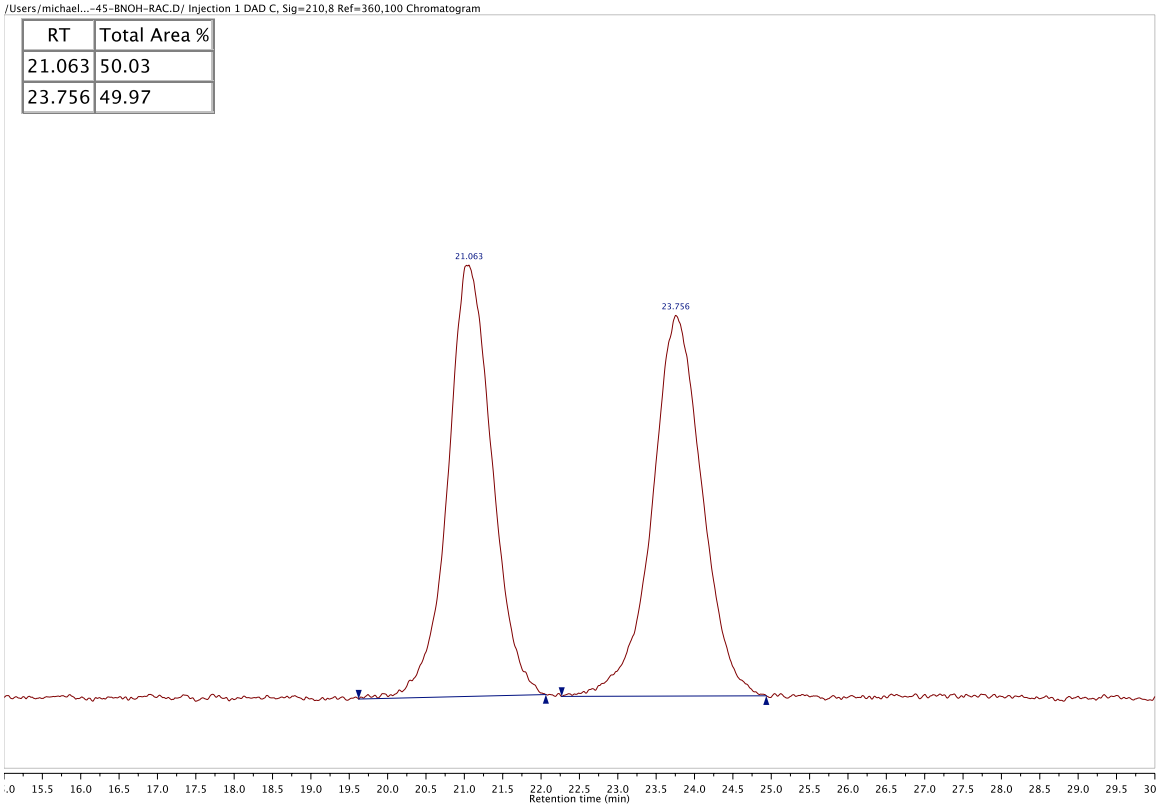
RT	Total Area %
28.280	8.72
15.789	91.28



Racemic 20

/Users/michael...-45-BNOH-RAC.D/ Injection 1 DAD C, Sig=210,8 Ref=360,100 Chromatogram

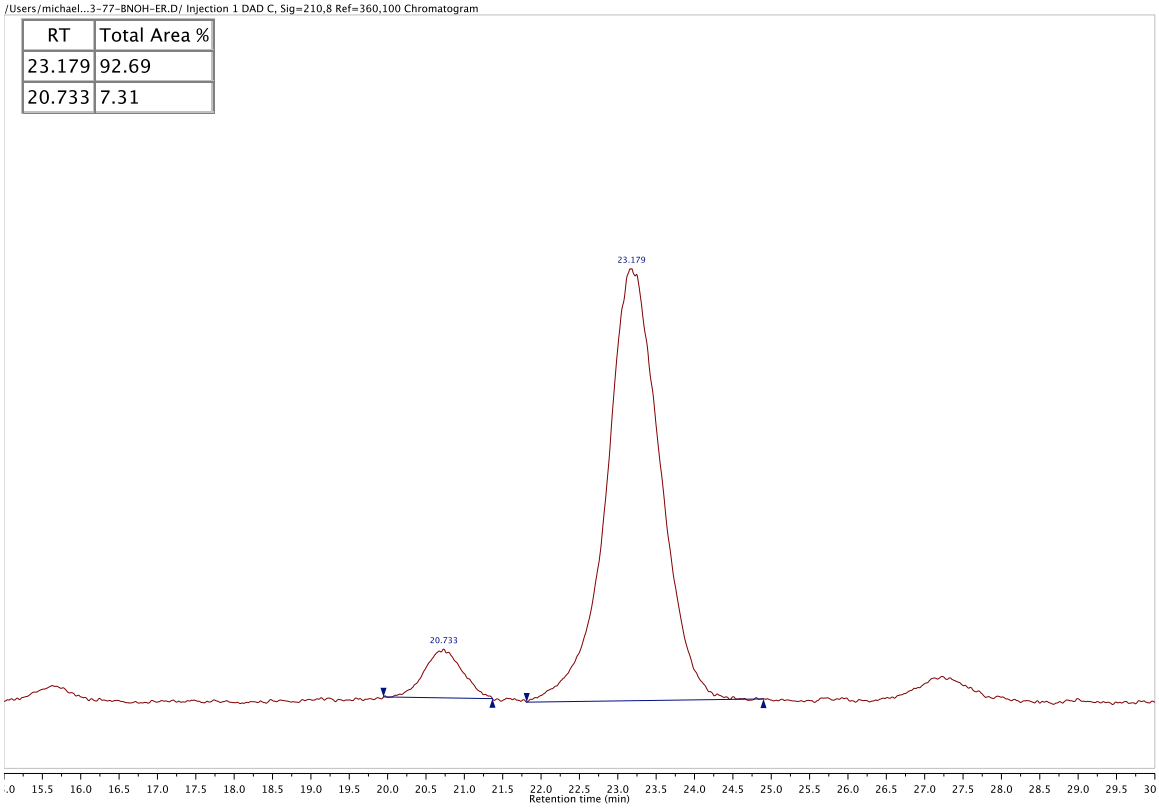
RT	Total Area %
21.063	50.03
23.756	49.97



Enantioenriched 20

/Users/michael...3-77-BNOH-ER.D/ Injection 1 DAD C, Sig=210,8 Ref=360,100 Chromatogram

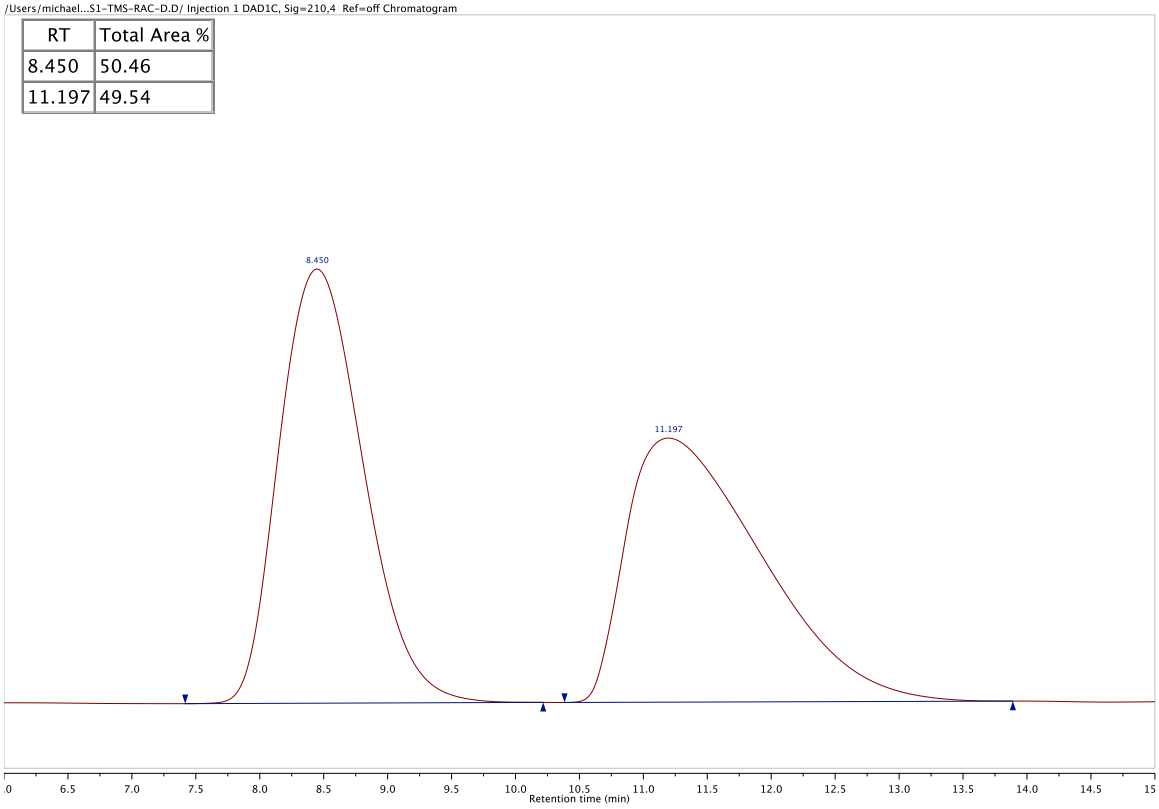
RT	Total Area %
23.179	92.69
20.733	7.31



Racemic 21

/Users/michael...S1-TMS-RAC-D.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

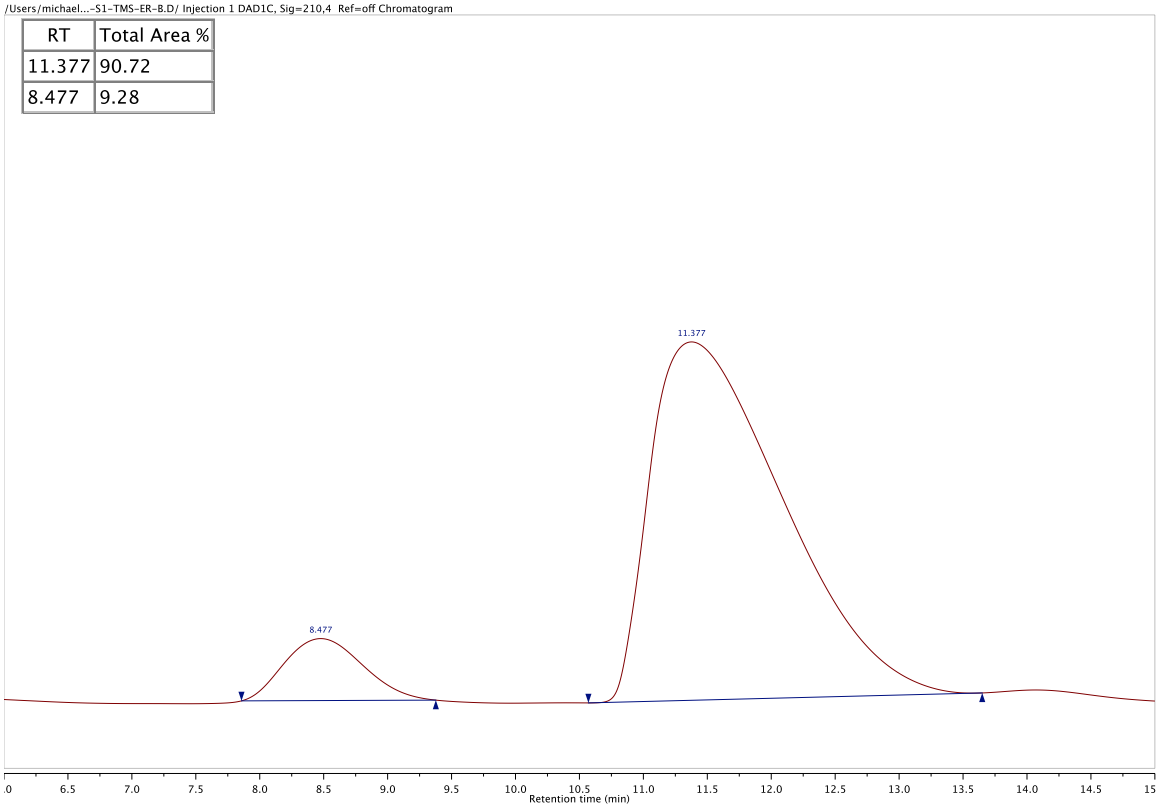
RT	Total Area %
8.450	50.46
11.197	49.54



Enantioenriched 21

/Users/michael...-S1-TMS-ER-B.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

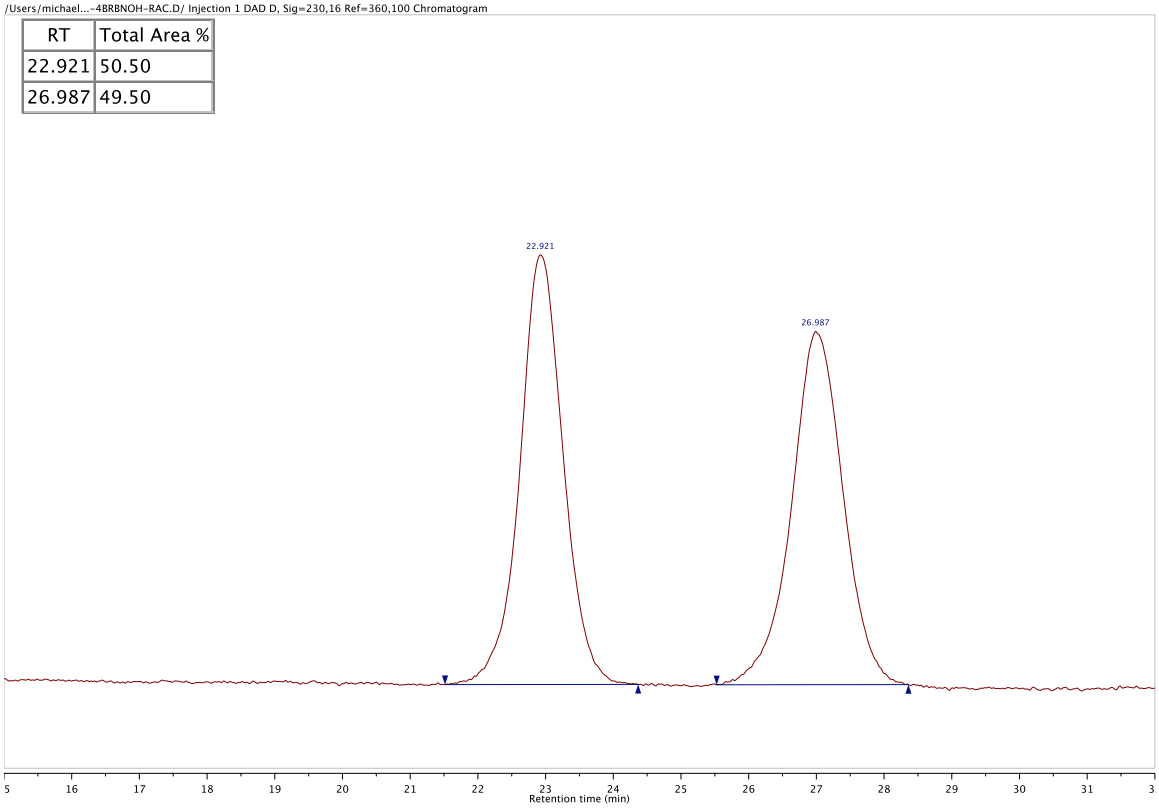
RT	Total Area %
11.377	90.72
8.477	9.28



Racemic 22

/Users/michael...-4BRBNOH-RAC.D/ Injection 1 DAD D, Sig=230,16 Ref=360,100 Chromatogram

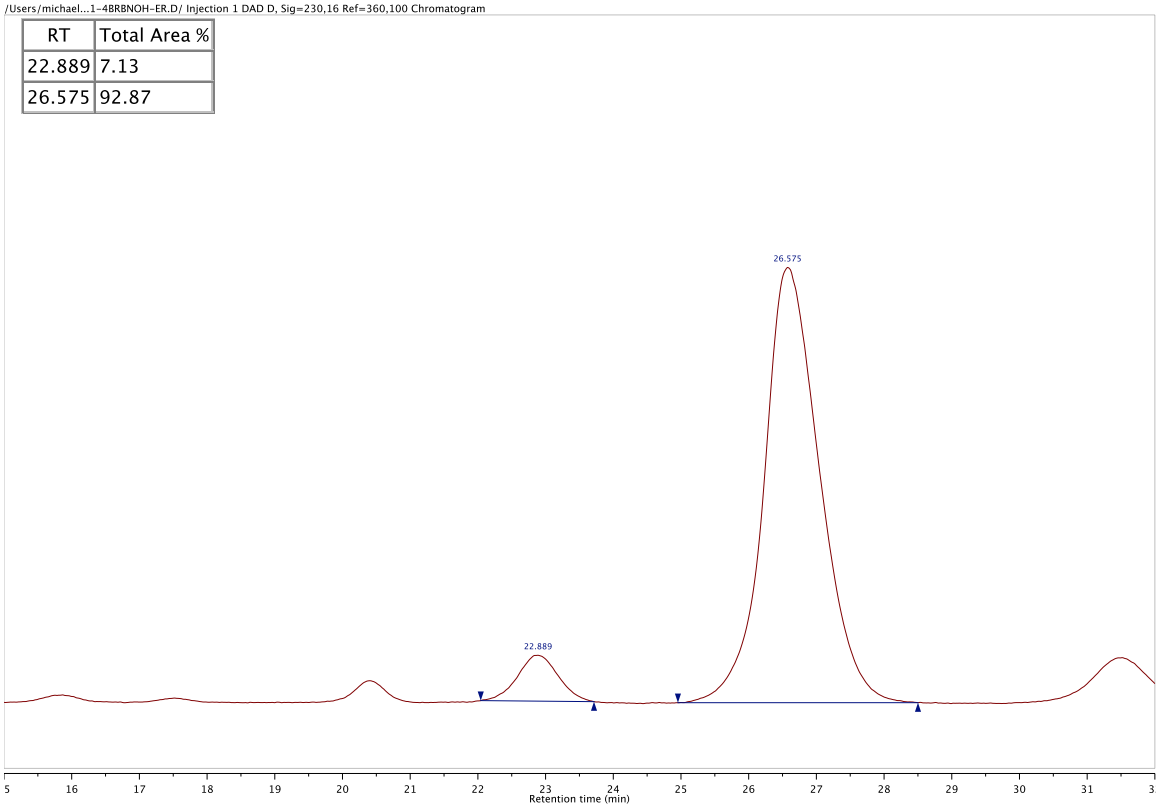
RT	Total Area %
22.921	50.50
26.987	49.50



Enantioenriched 22

/Users/michael...1-4BRBNOH-ER.D/ Injection 1 DAD D, Sig=230,16 Ref=360,100 Chromatogram

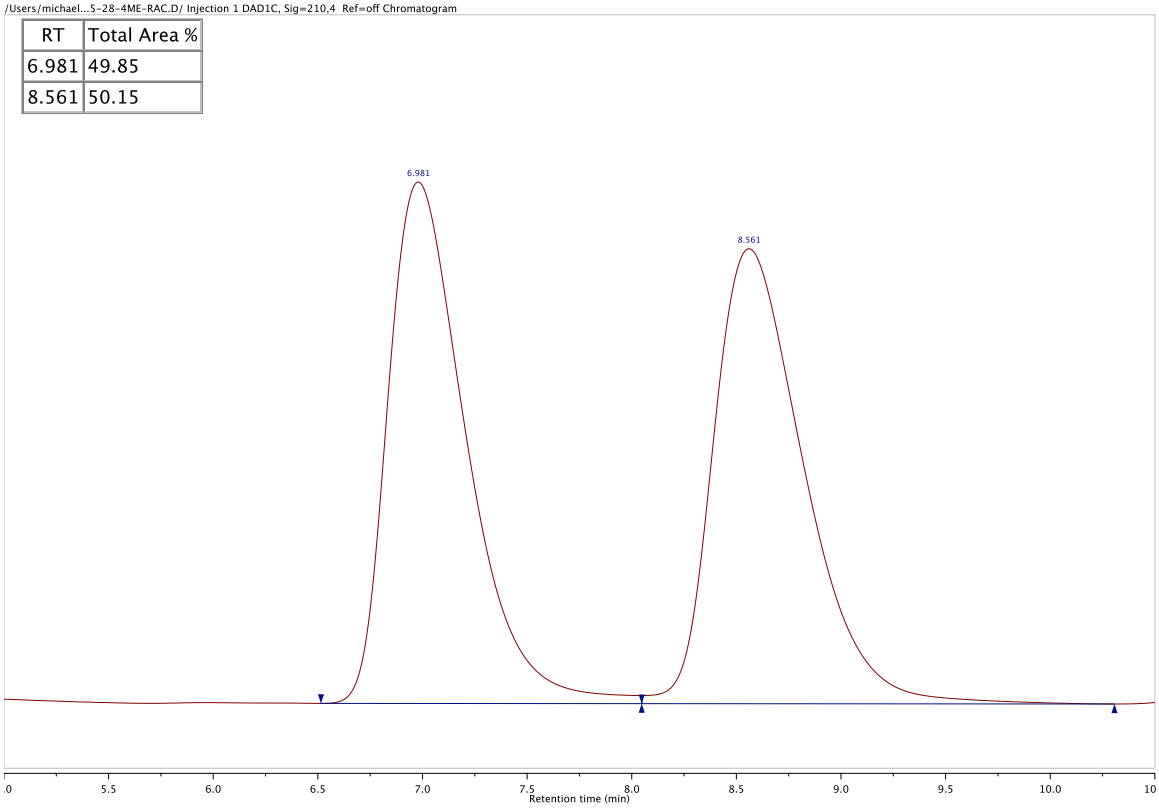
RT	Total Area %
22.889	7.13
26.575	92.87



Racemic 4

/Users/michael...5-28-4ME-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

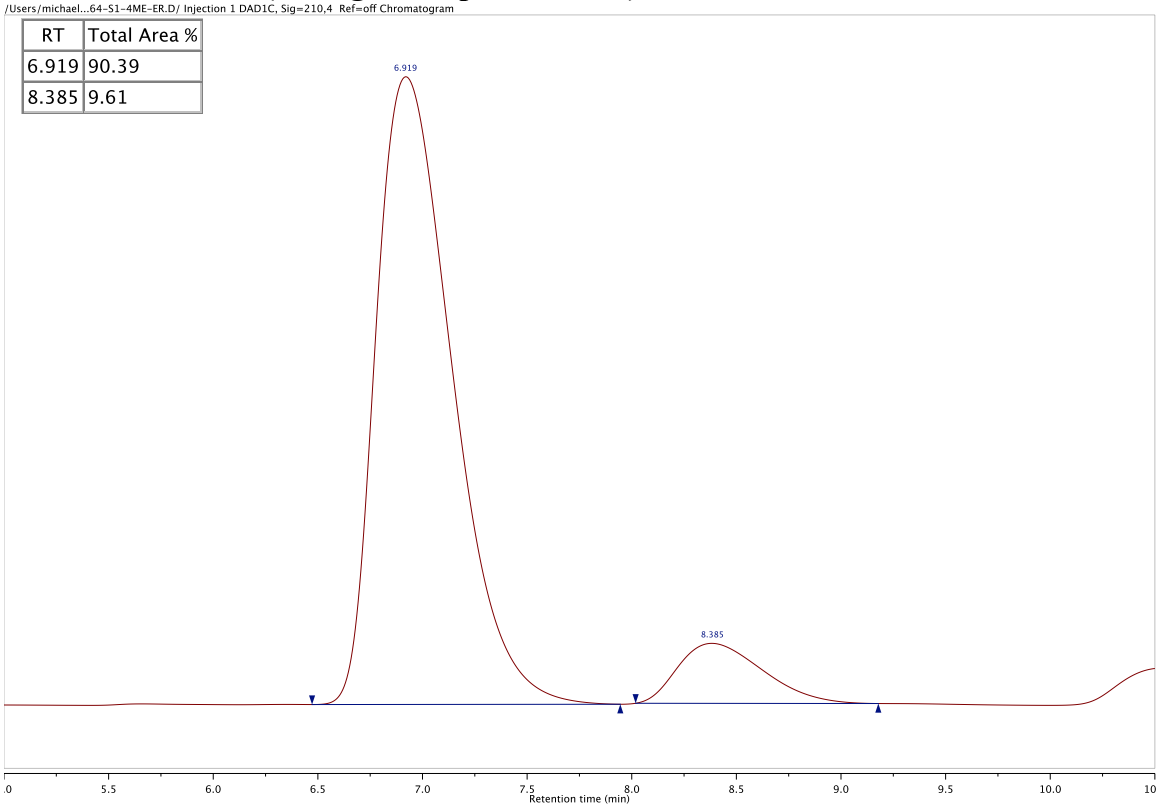
RT	Total Area %
6.981	49.85
8.561	50.15



Enantioenriched 4 (from general procedure B)

/Users/michael...64-S1-4ME-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

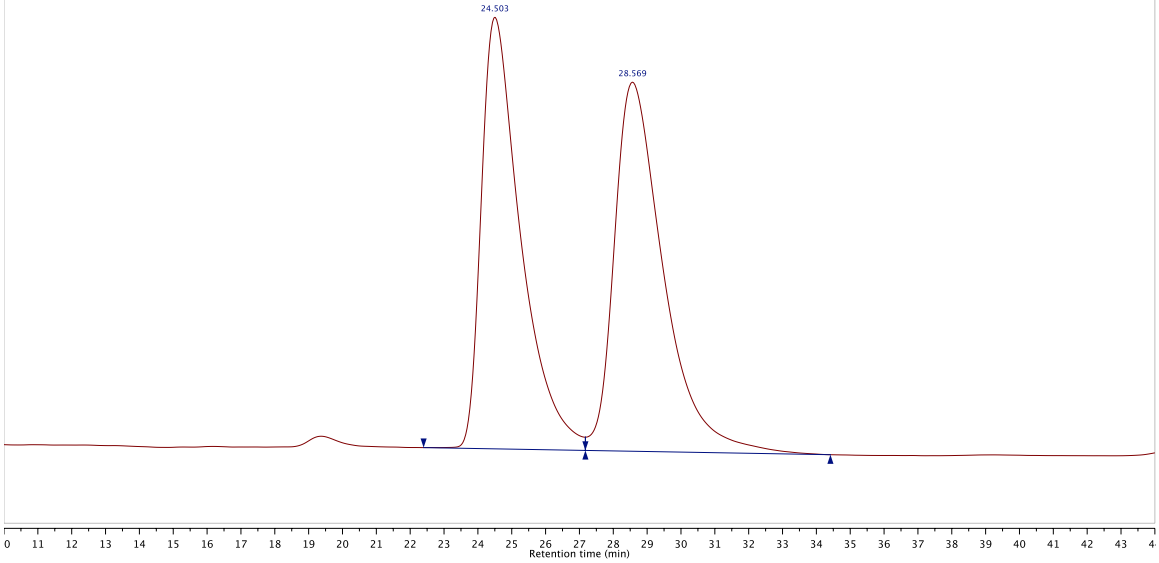
RT	Total Area %
6.919	90.39
8.385	9.61



Racemic 7

/Users/michael...14-34OME-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

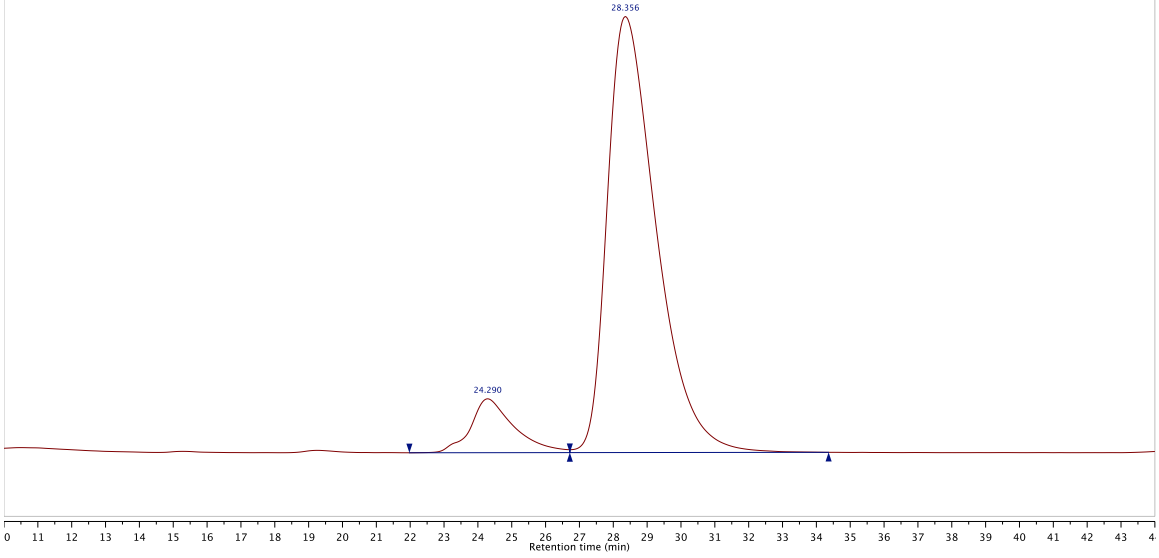
RT	Total Area %
24.503	48.46
28.569	51.54



Enantioenriched 7 (from general procedure B)

/Users/michael...-S1-34OME-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

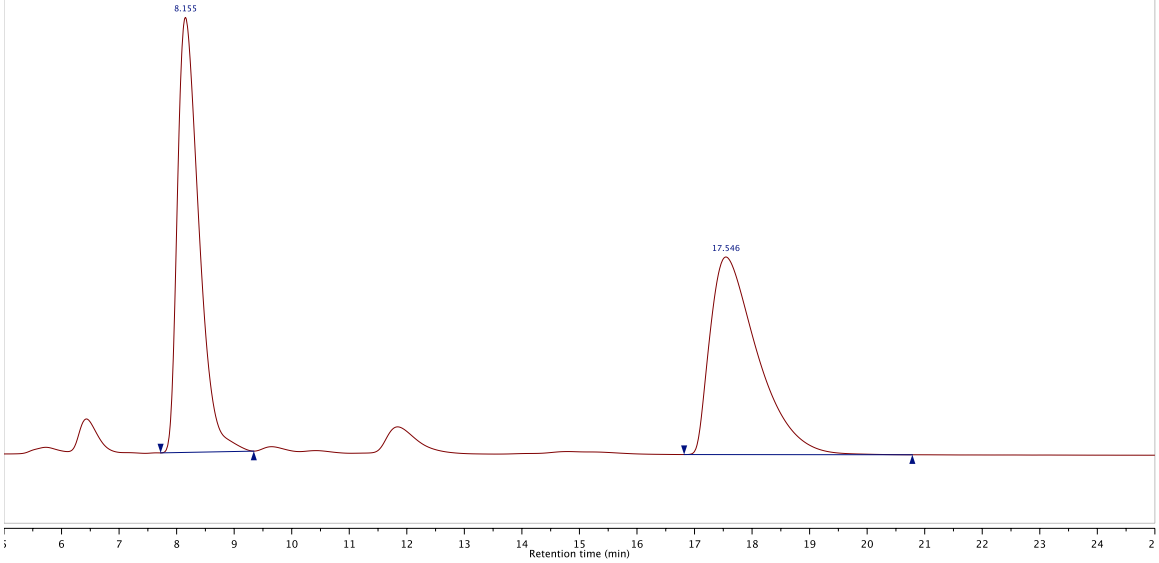
RT	Total Area %
24.290	9.87
28.356	90.13



Racemic 9

/Users/michael...-PLUG-3F-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

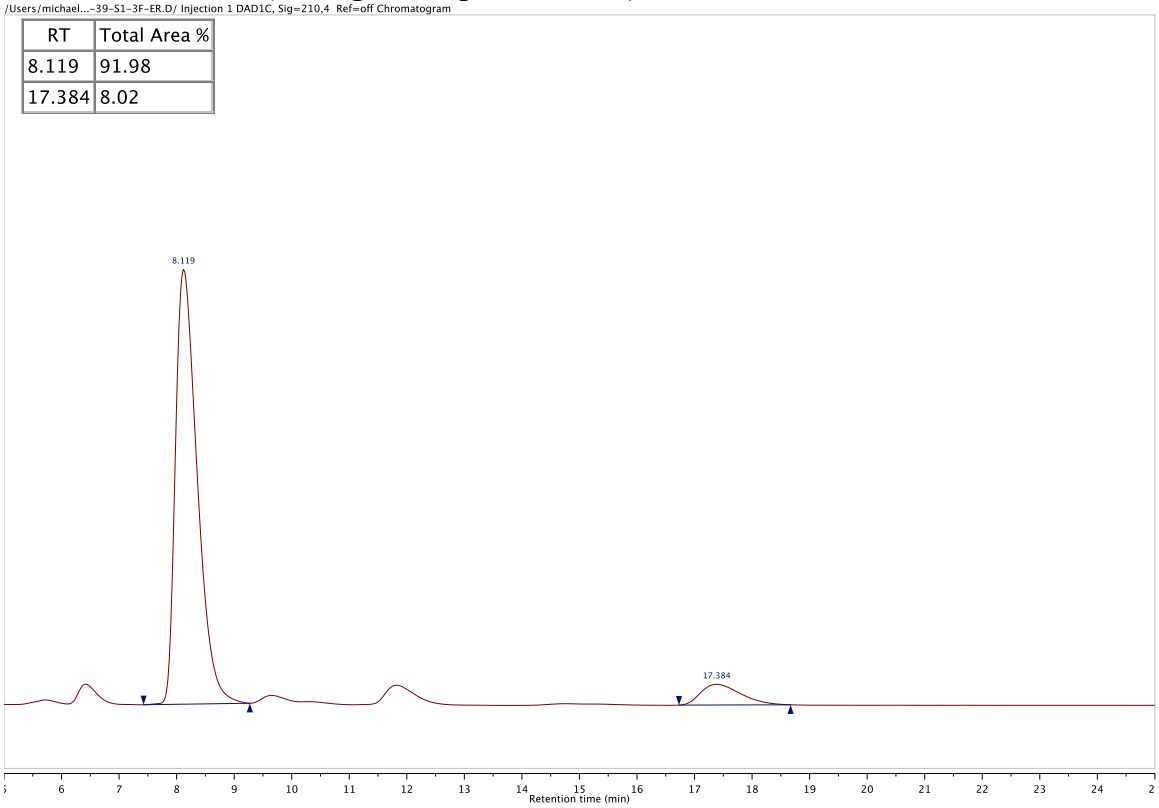
RT	Total Area %
8.155	50.08
17.546	49.92



Enantioenriched 9 (from general procedure B)

/Users/michael...-39-S1-3F-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

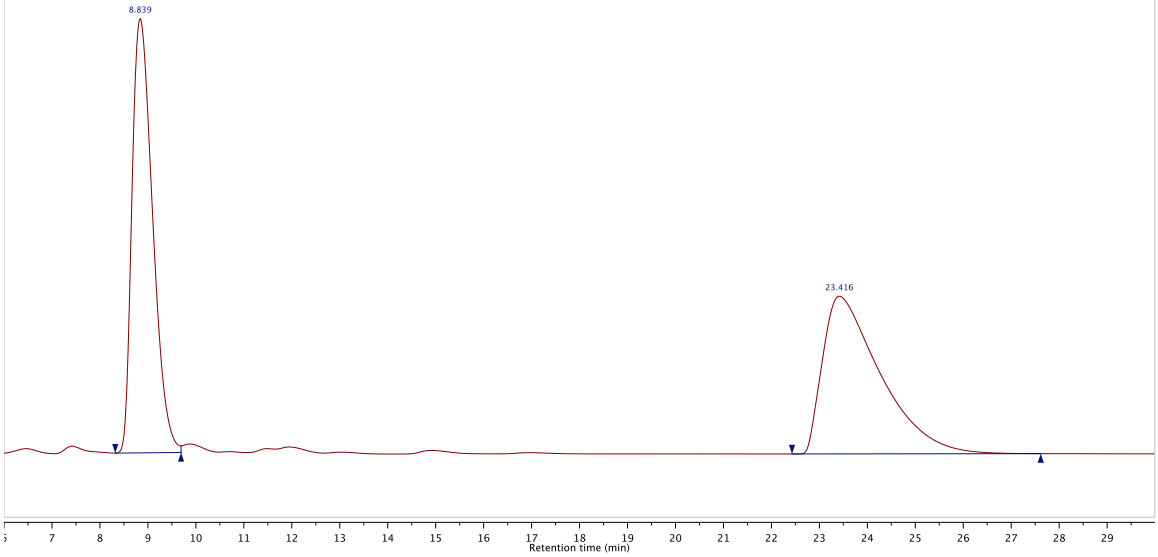
RT	Total Area %
8.119	91.98
17.384	8.02



Racemic 10

/Users/michael...18-44-2F-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

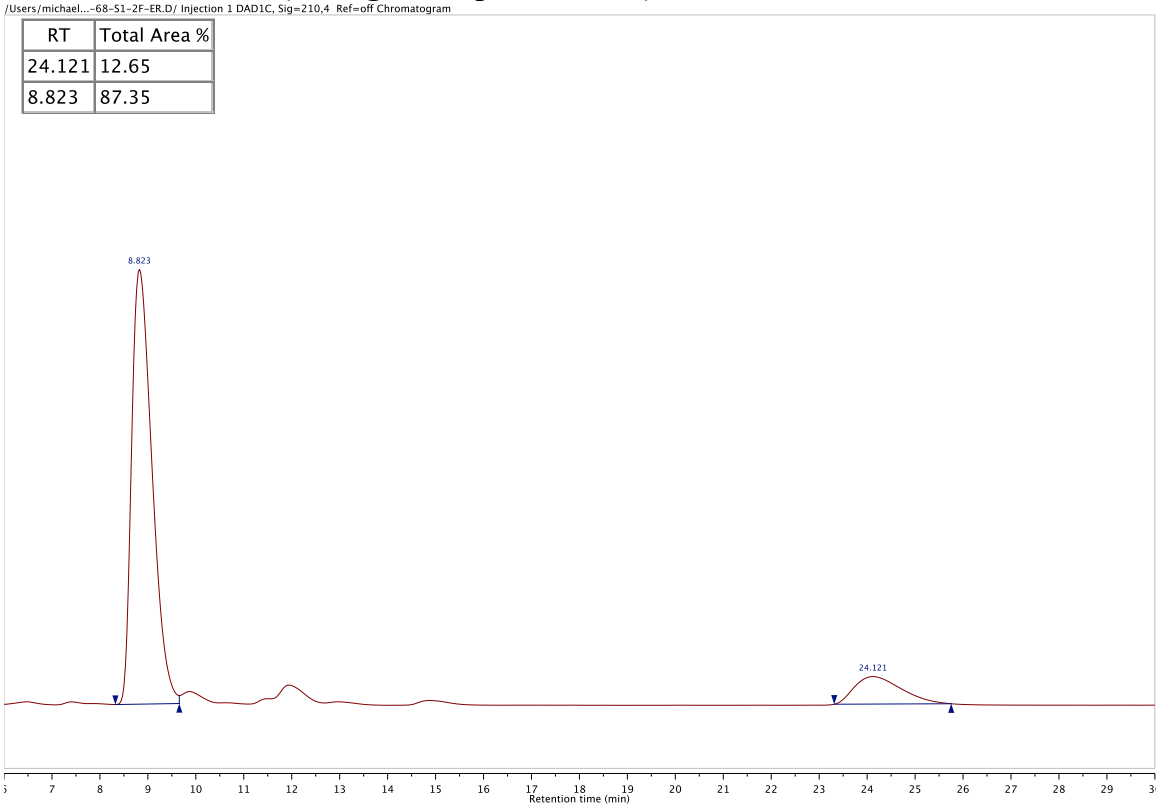
RT	Total Area %
8.839	49.75
23.416	50.25



Enantioenriched 10 (from general procedure B)

/Users/michael...-68-S1-2F-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

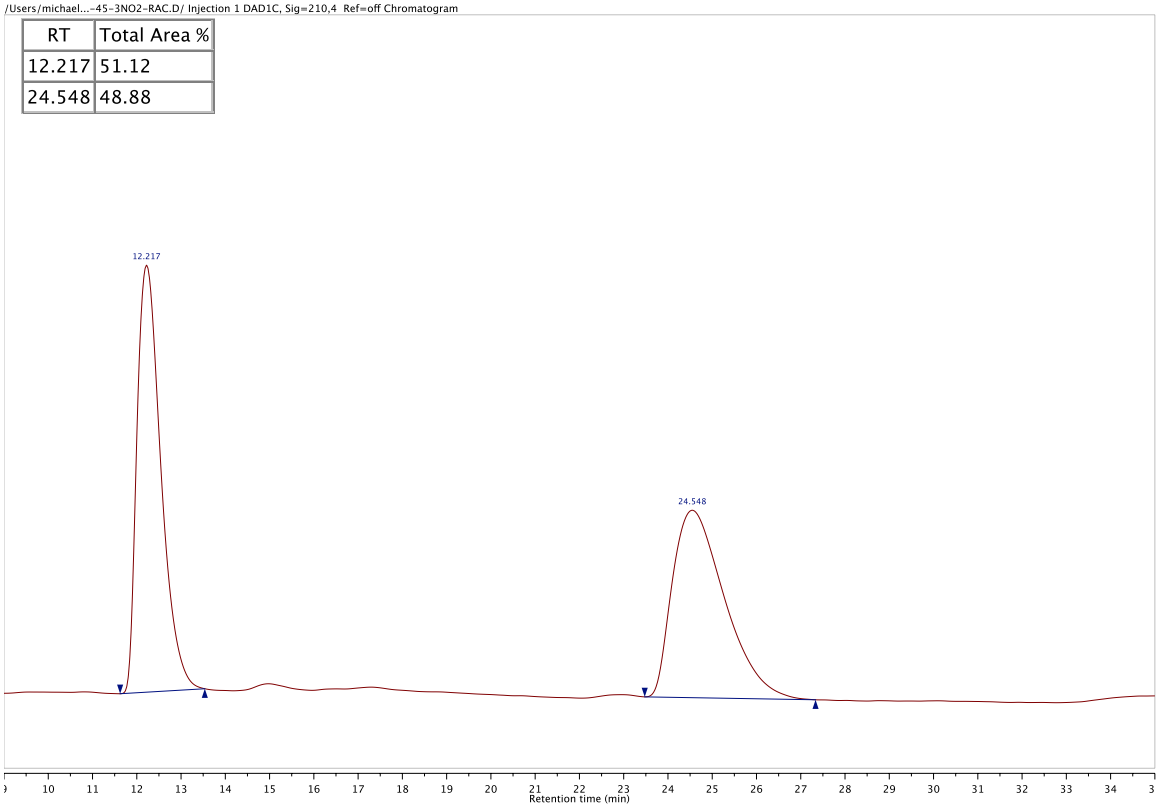
RT	Total Area %
24.121	12.65
8.823	87.35



Racemic 12

/Users/michael...-45-3NO2-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

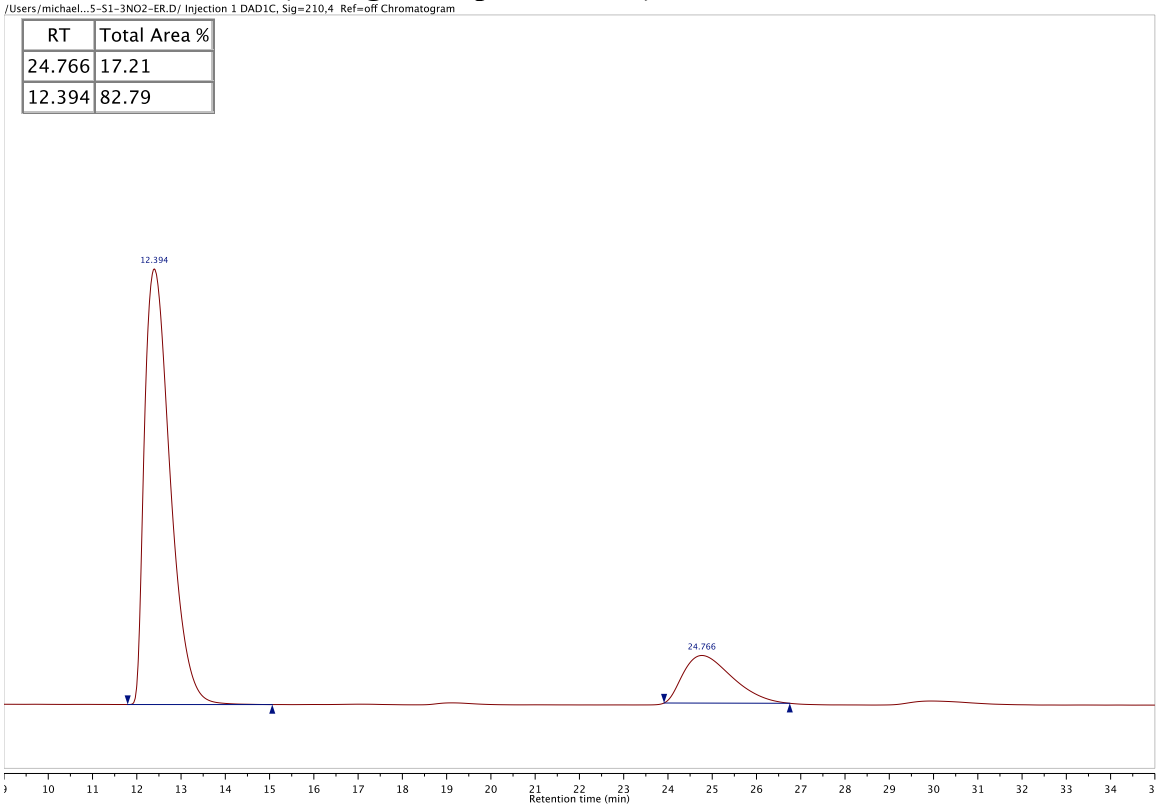
RT	Total Area %
12.217	51.12
24.548	48.88



Enantioenriched 12 (from general procedure B)

/Users/michael...5-S1-3NO2-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

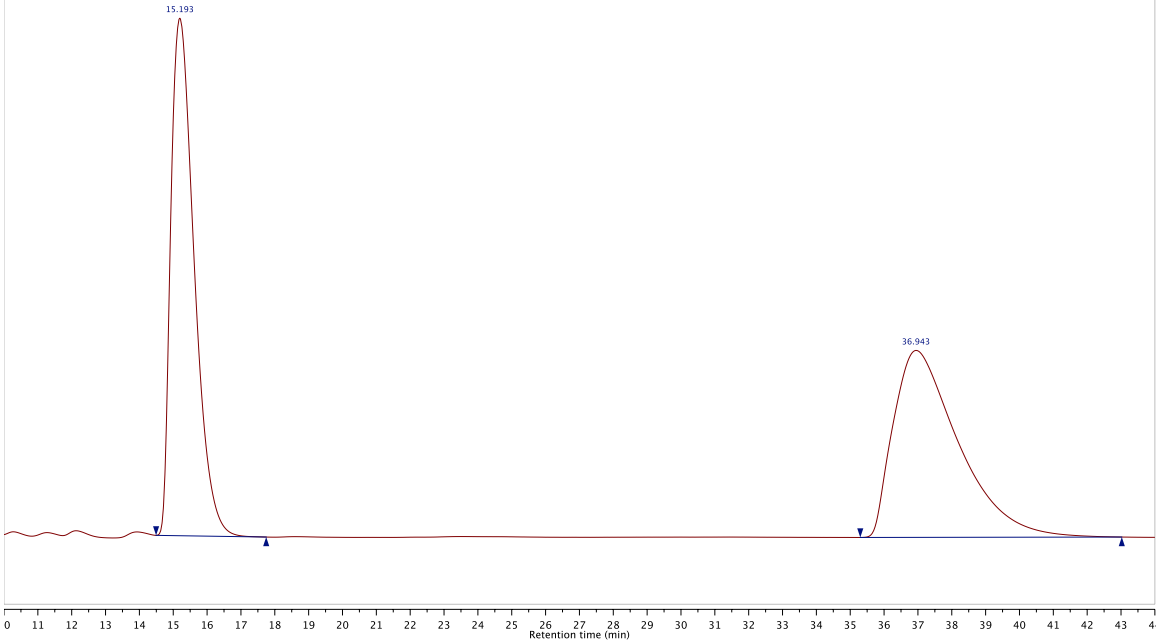
RT	Total Area %
24.766	17.21
12.394	82.79



Racemic 13

/Users/michael...-46-THIO-RAC.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

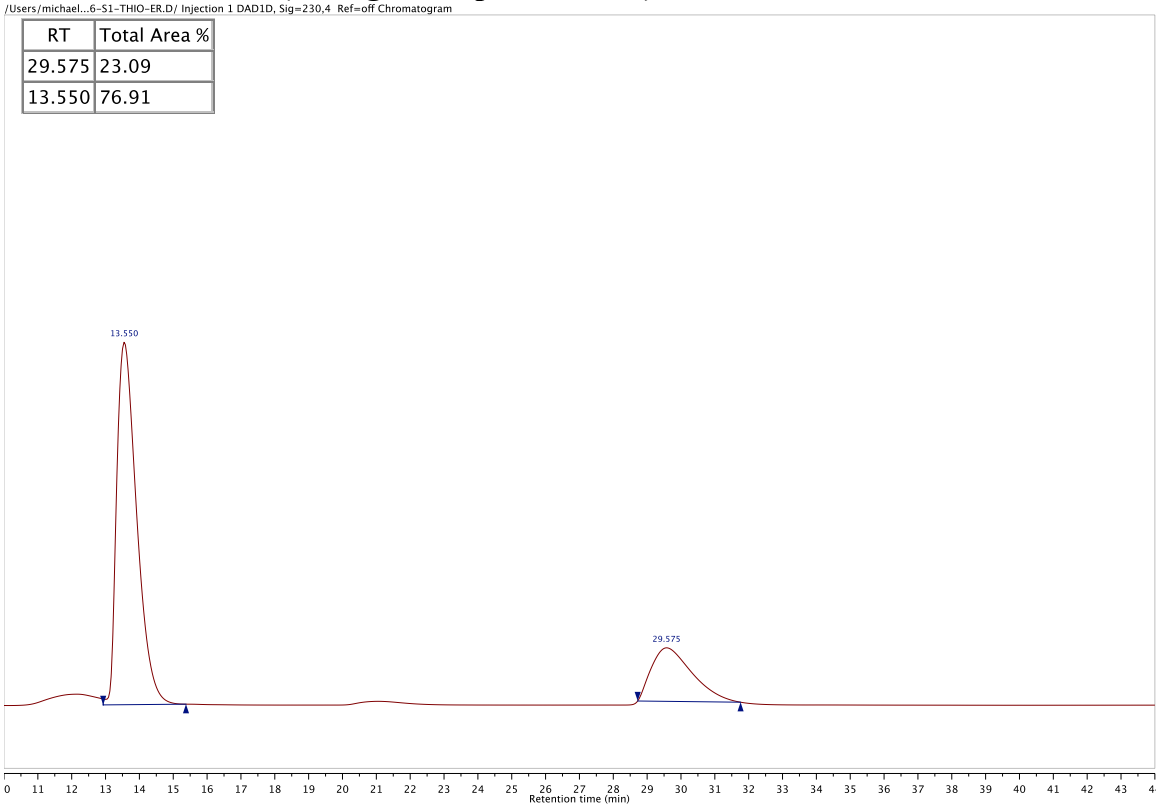
RT	Total Area %
15.193	49.95
36.943	50.05



Enantioenriched 13 (from general procedure B)

/Users/michael...6-S1-THIO-ER.D/ Injection 1 DAD1D, Sig=230,4 Ref=off Chromatogram

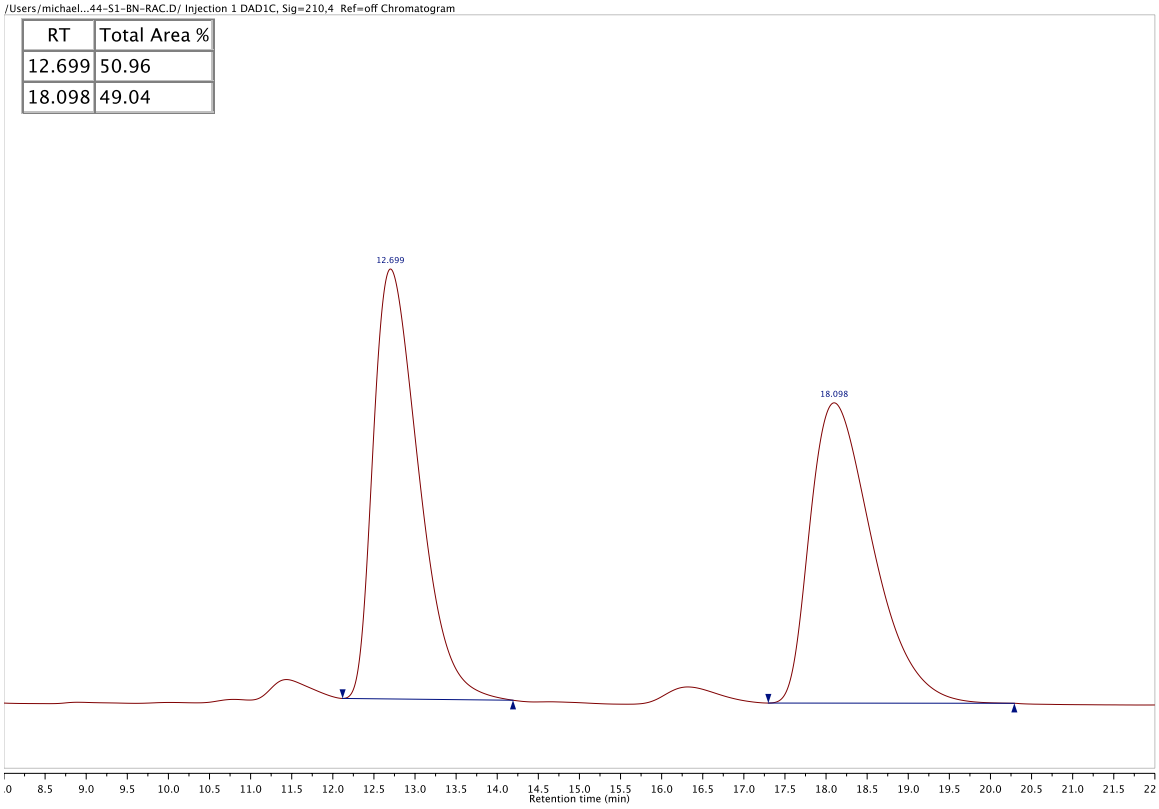
RT	Total Area %
29.575	23.09
13.550	76.91



Racemic 14

/Users/michael...44-S1-BN-RAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

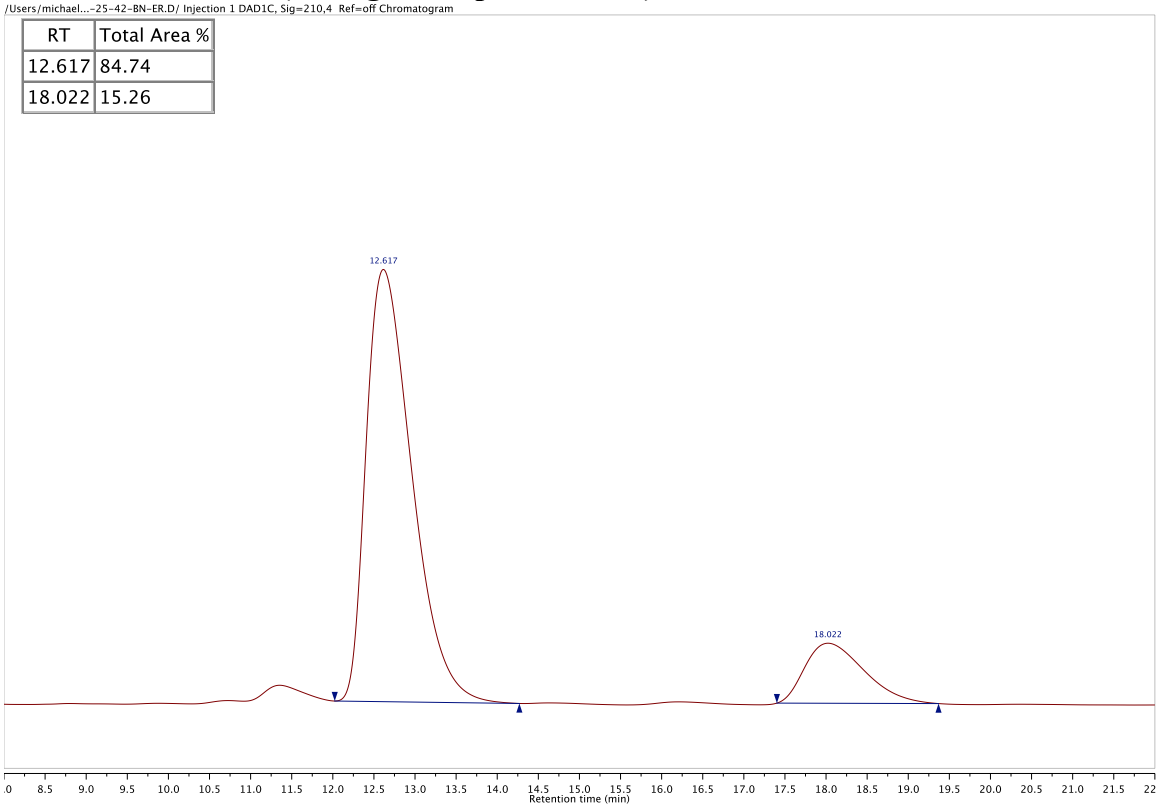
RT	Total Area %
12.699	50.96
18.098	49.04



Enantioenriched 14 (from general procedure B)

/Users/michael...-25-42-BN-ER.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

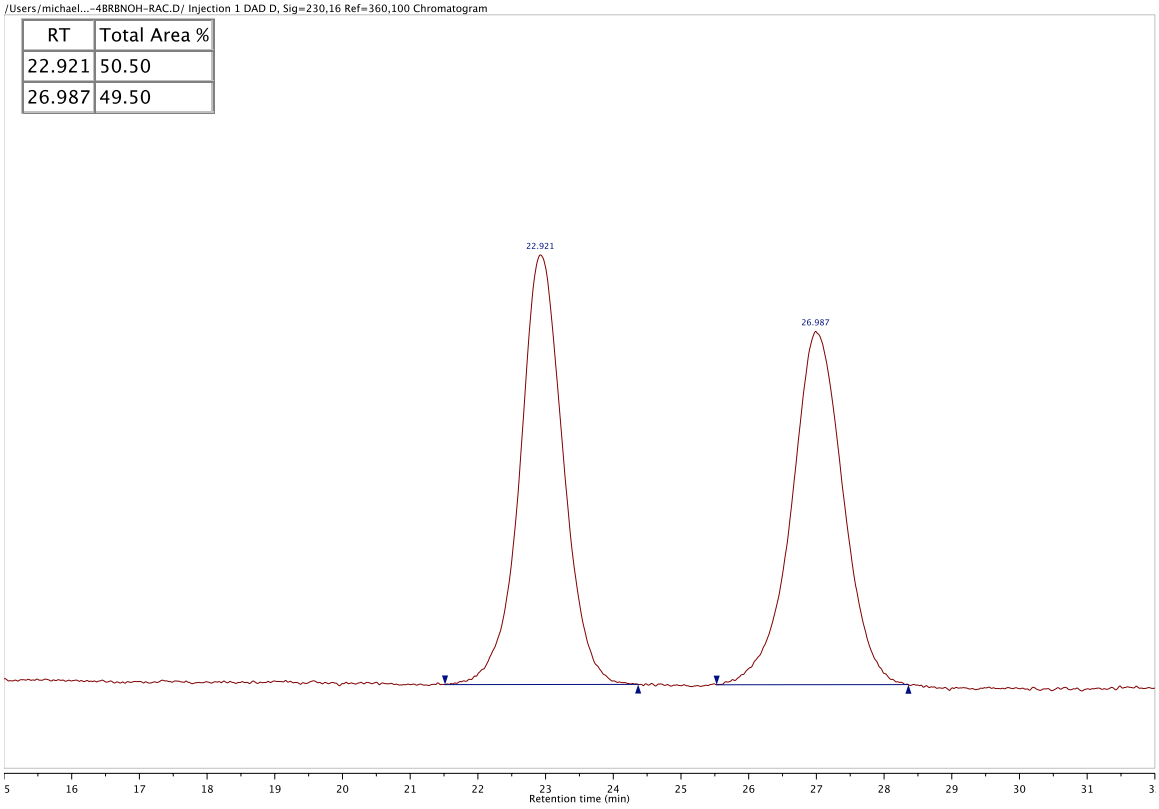
RT	Total Area %
12.617	84.74
18.022	15.26



Racemic 22

/Users/michael...-4BRBNOH-RAC.D/ Injection 1 DAD D, Sig=230,16 Ref=360,100 Chromatogram

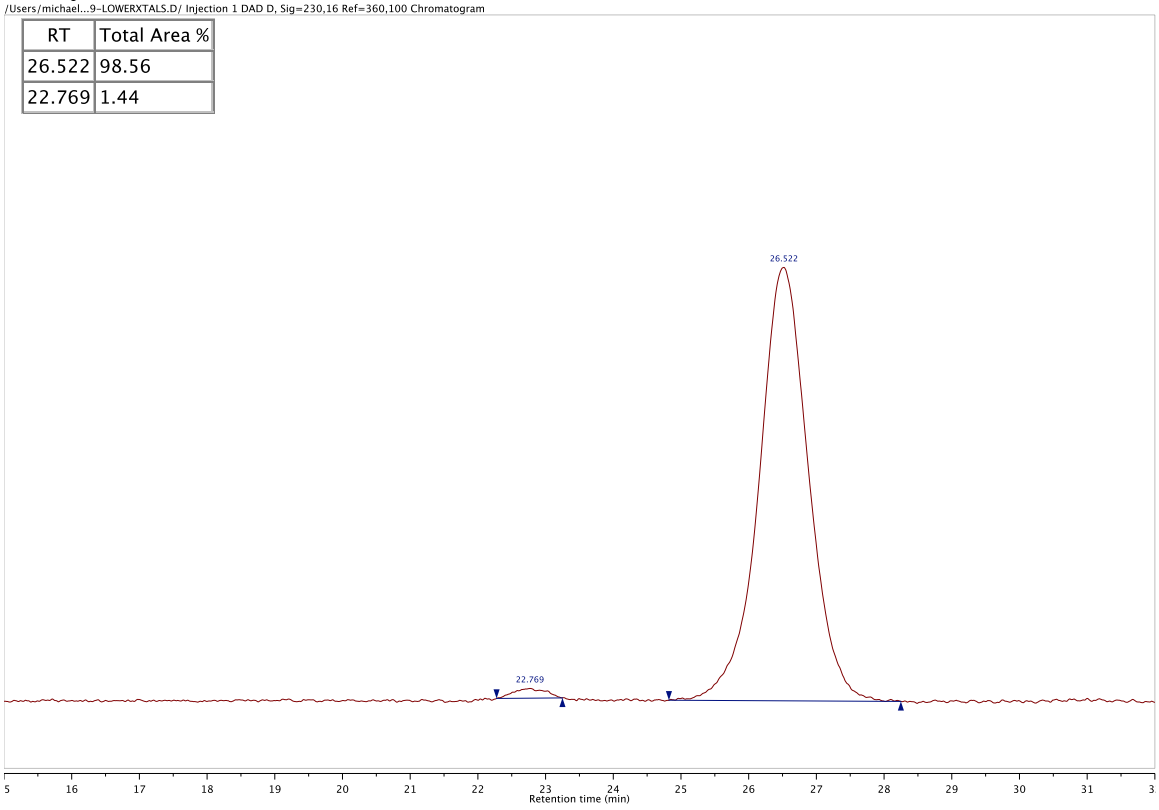
RT	Total Area %
22.921	50.50
26.987	49.50



Recrystallized 22

/Users/michael...9-LOWERXTALS.D/ Injection 1 DAD D, Sig=230,16 Ref=360,100 Chromatogram

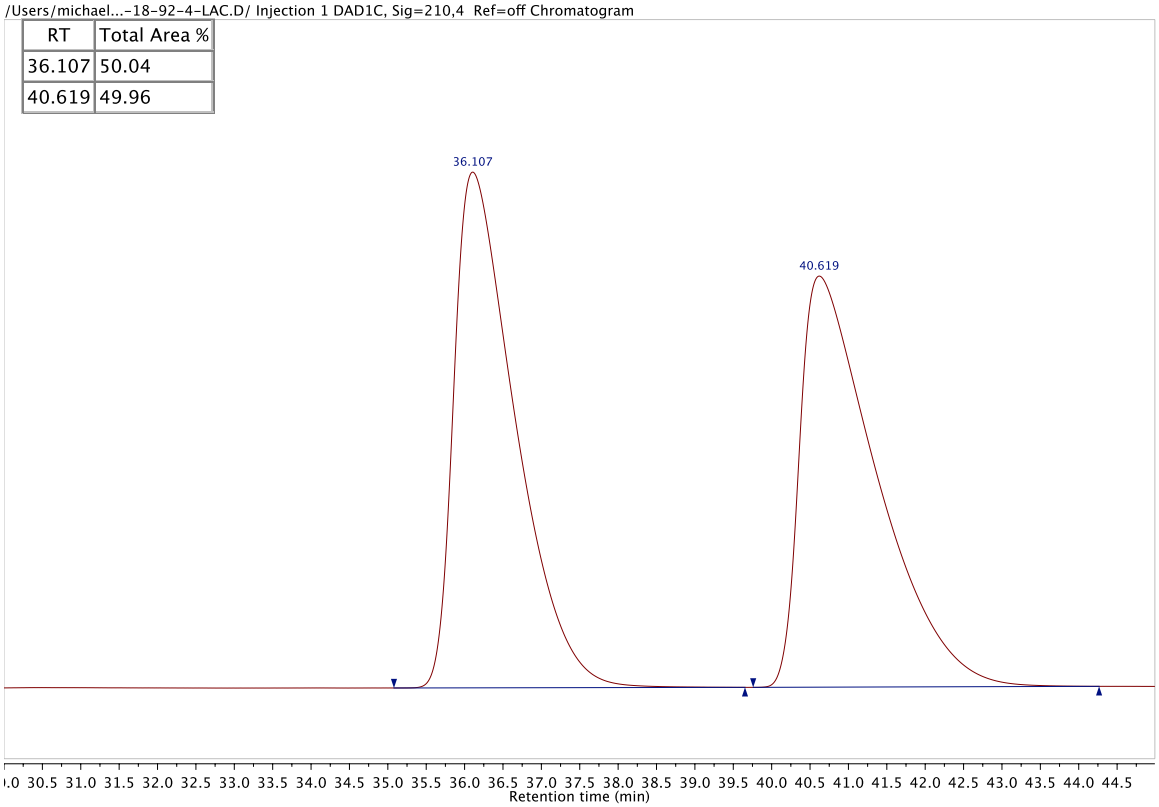
RT	Total Area %
26.522	98.56
22.769	1.44



Racemic 25

/Users/michael...-18-92-4-LAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

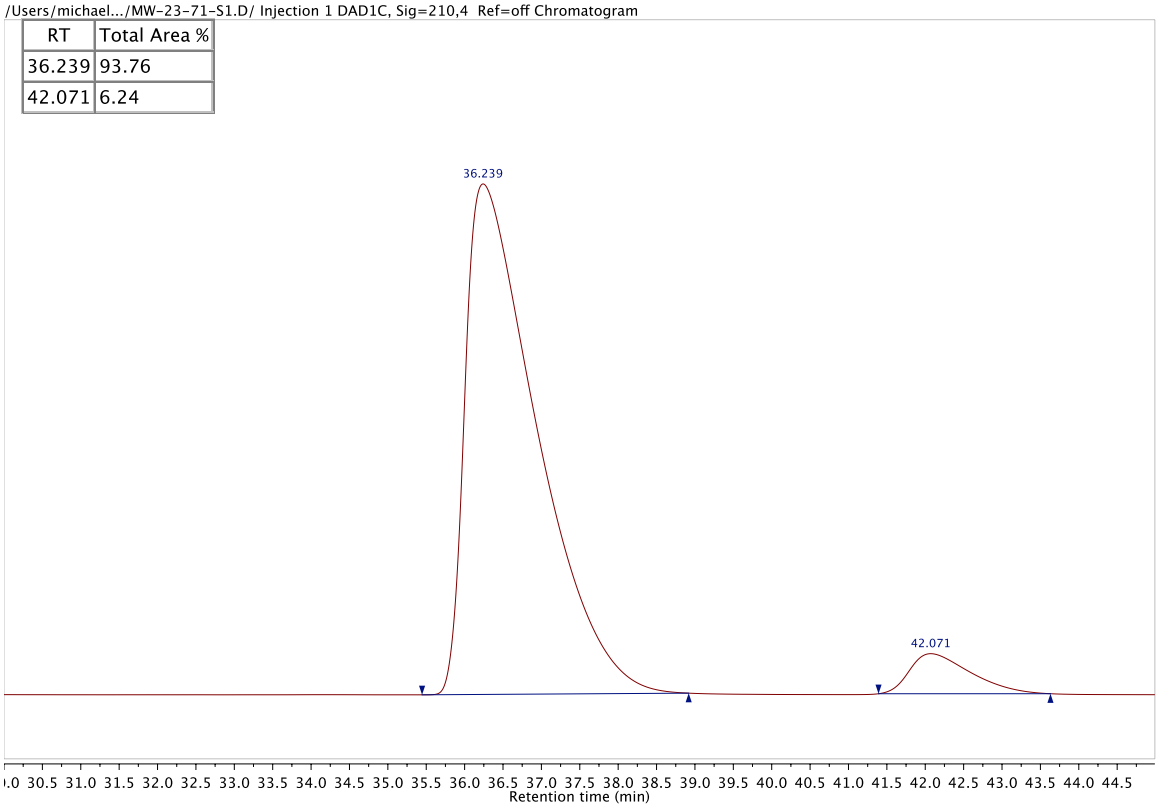
RT	Total Area %
36.107	50.04
40.619	49.96



Enantioenriched 25

/Users/michael.../MW-23-71-S1.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

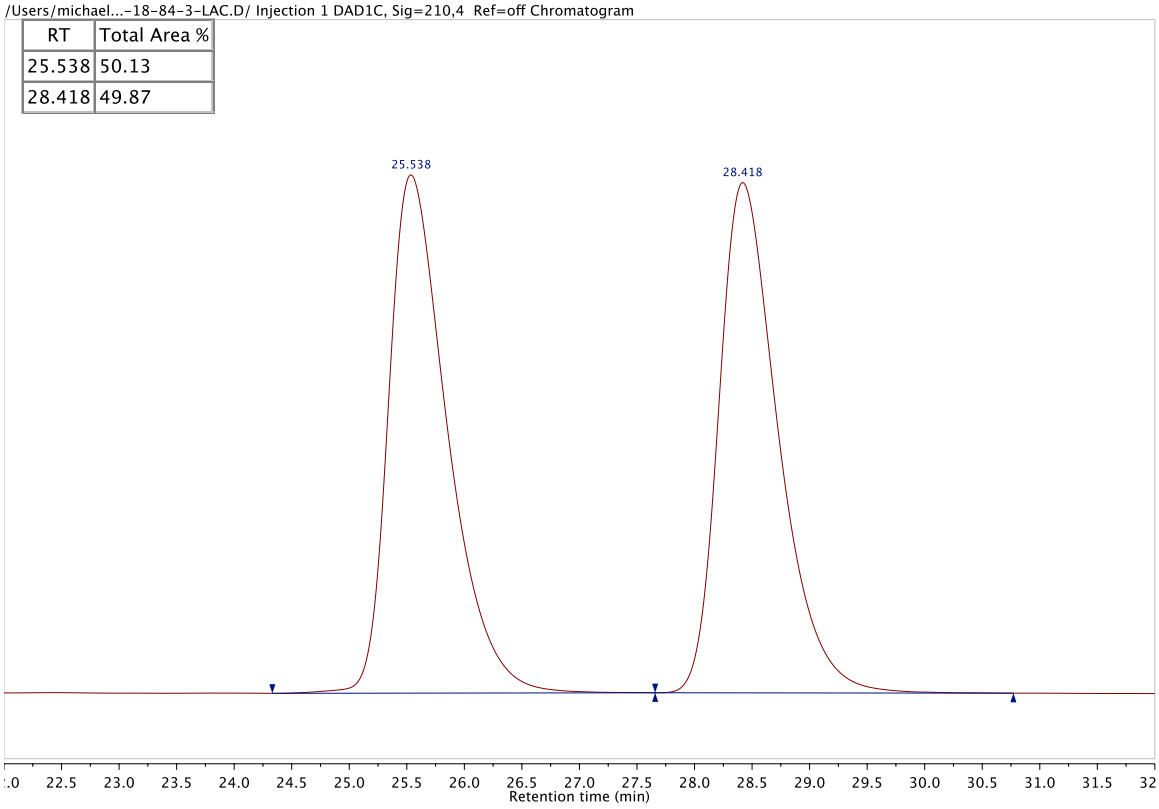
RT	Total Area %
36.239	93.76
42.071	6.24



Racemic 26

/Users/michael...-18-84-3-LAC.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

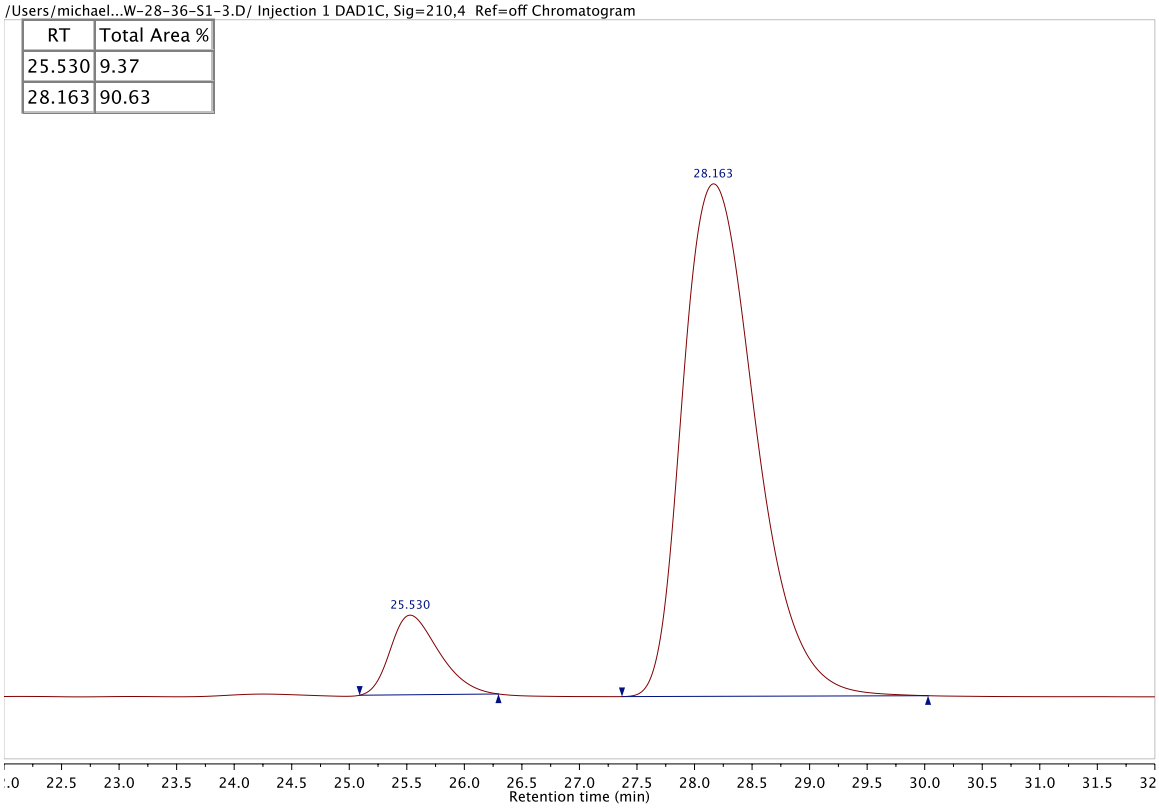
RT	Total Area %
25.538	50.13
28.418	49.87



Enantioenriched 26

/Users/michael...W-28-36-S1-3.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

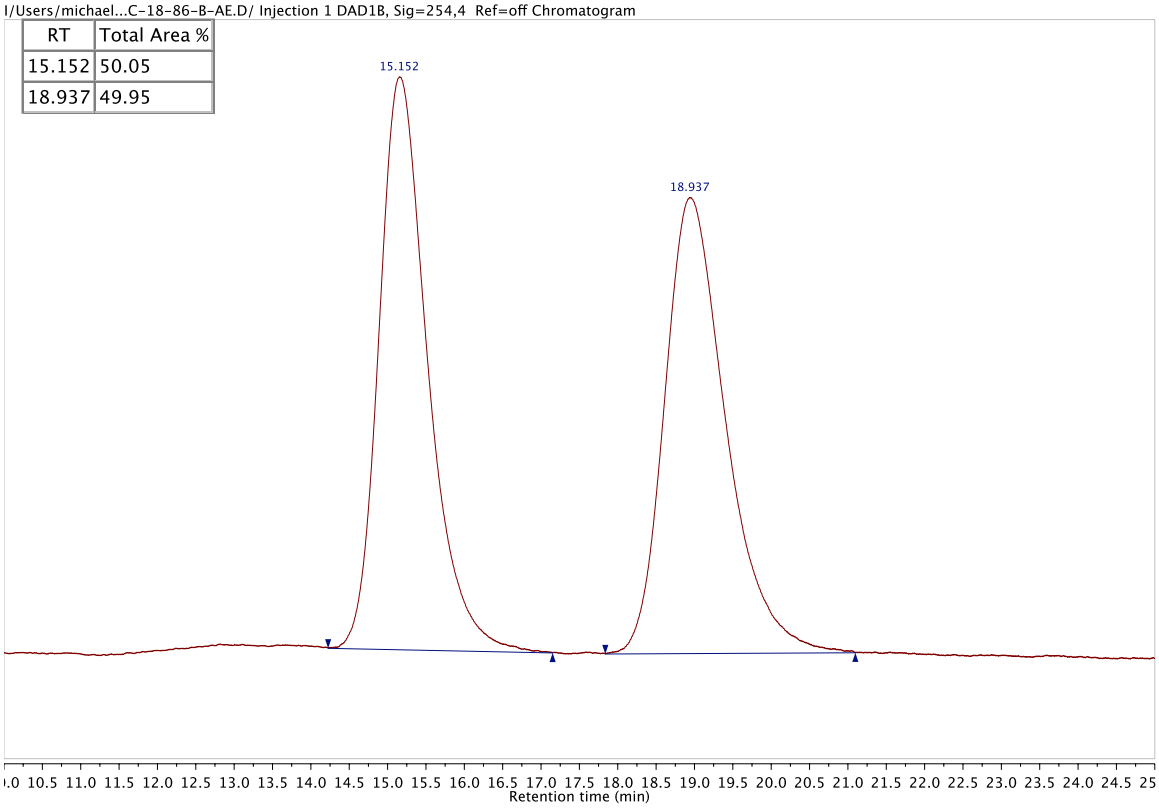
RT	Total Area %
25.530	9.37
28.163	90.63



Racemic 27

I/Users/michael...C-18-86-B-AE.D/ Injection 1 DAD1B, Sig=254,4 Ref=off Chromatogram

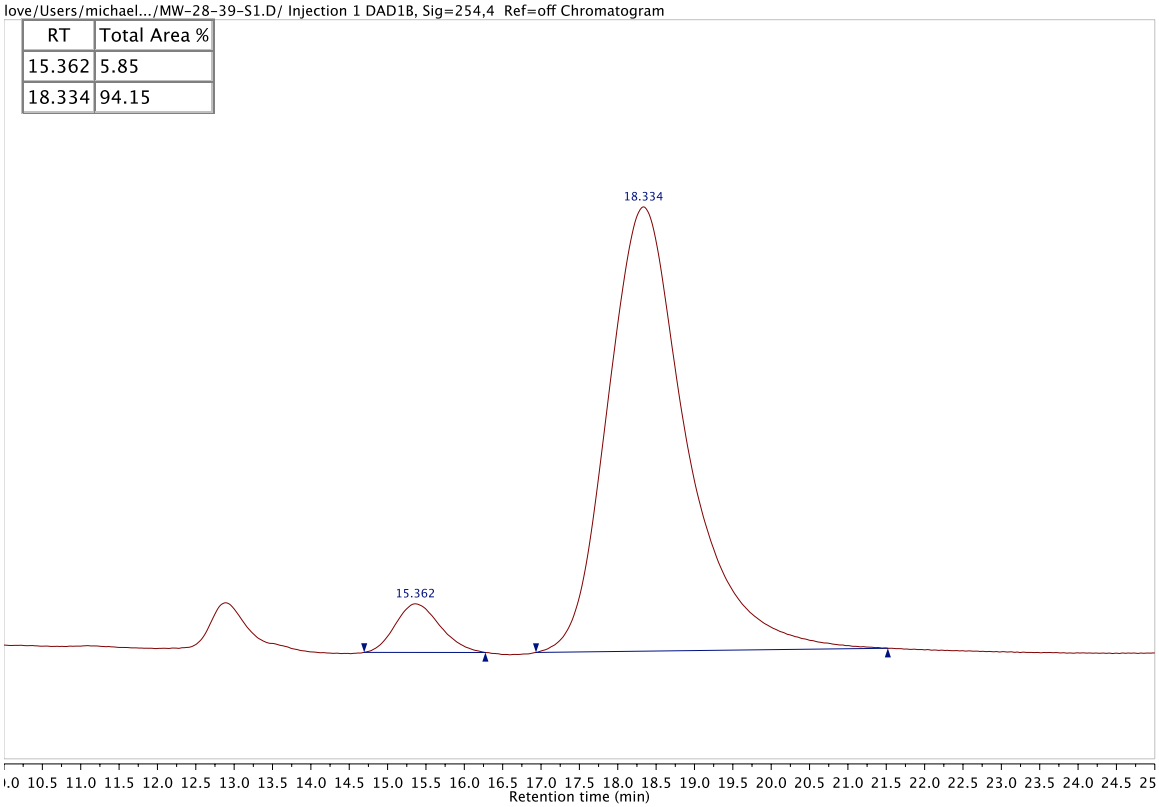
RT	Total Area %
15.152	50.05
18.937	49.95



Enantioenriched 27

love/Users/michael.../MW-28-39-S1.D/ Injection 1 DAD1B, Sig=254,4 Ref=off Chromatogram

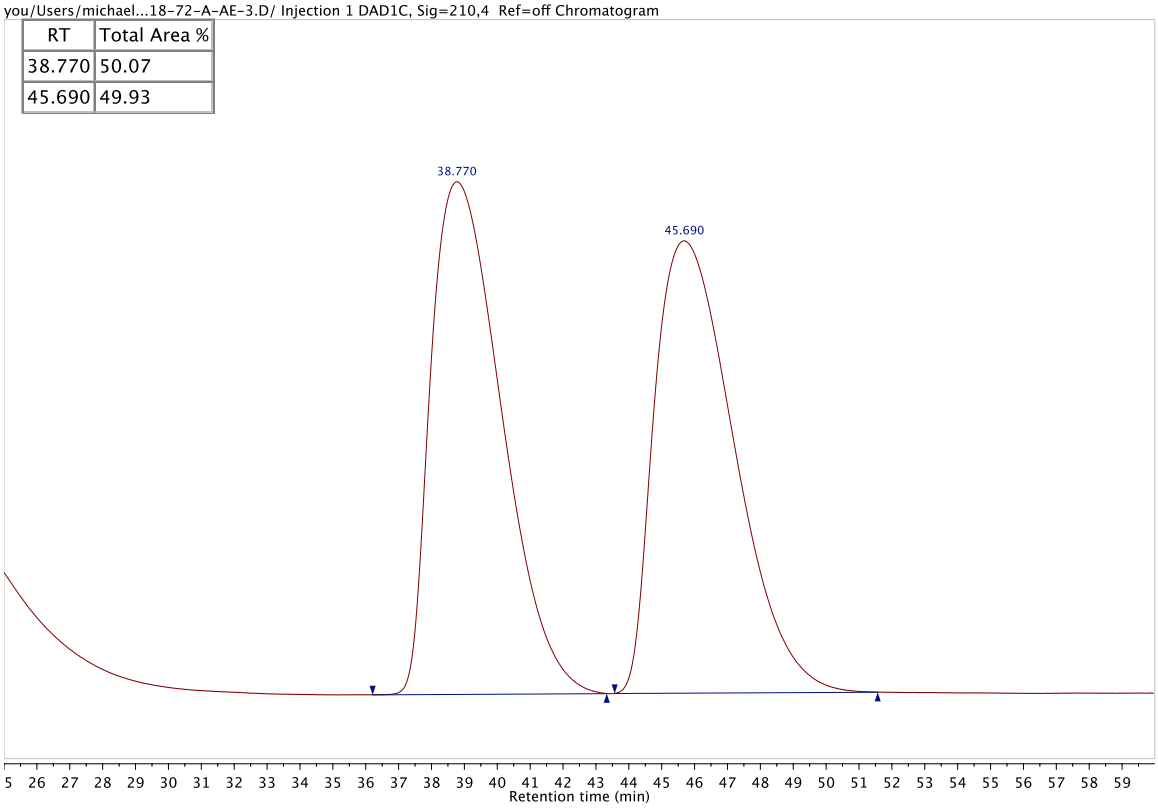
RT	Total Area %
15.362	5.85
18.334	94.15



Racemic 28

you/Users/michael...18-72-A-AE-3.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

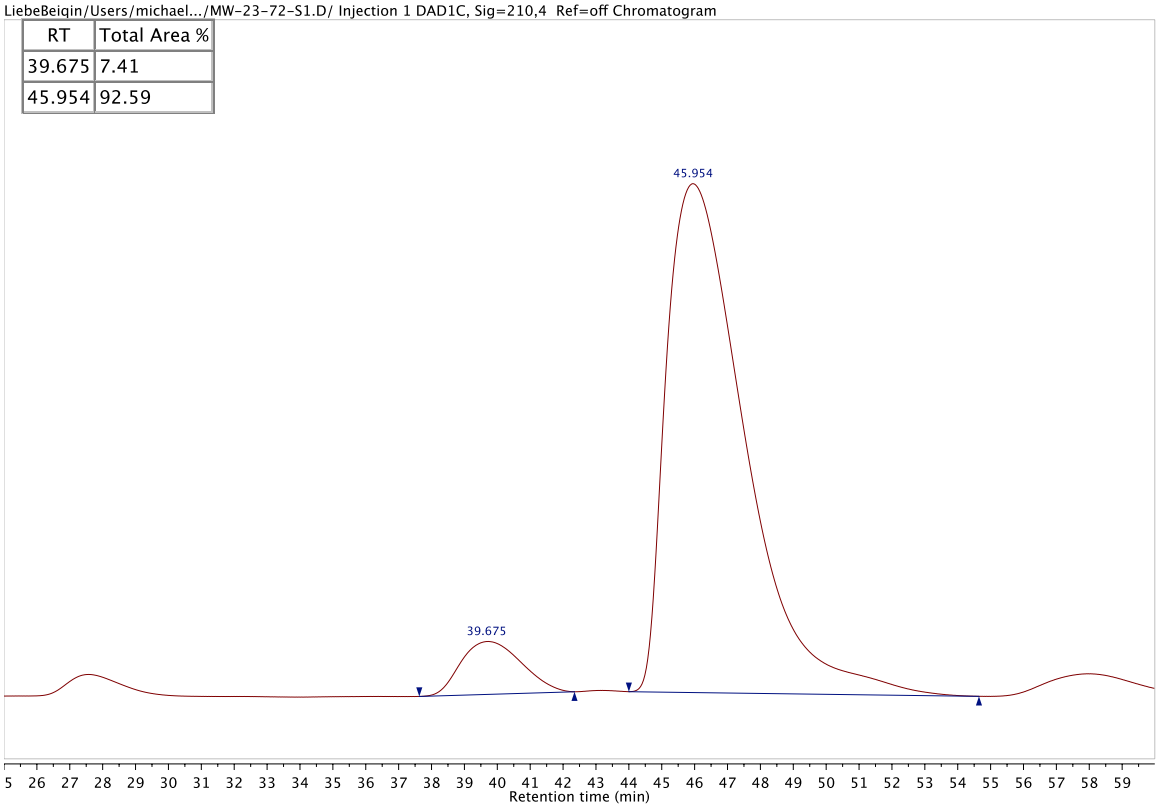
RT	Total Area %
38.770	50.07
45.690	49.93



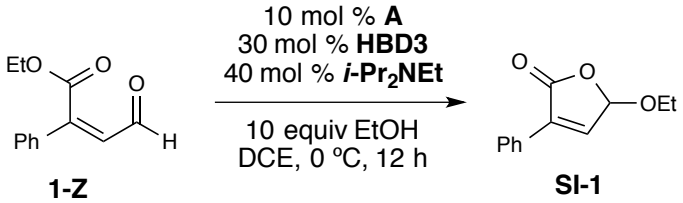
Enantioenriched 28

LiebeBeiqin/Users/michael.../MW-23-72-S1.D/ Injection 1 DAD1C, Sig=210,4 Ref=off Chromatogram

RT	Total Area %
39.675	7.41
45.954	92.59



Control experiment with *Z*-isomer starting material



1-Z **SI-1**

5-ethoxy-3-phenylfuran-2(5H)-one (SI-1): Prepared according to the general procedure using (*Z*)-ethyl 4-oxo-2-phenylbut-2-enoate (0.041 g, 0.200 mmol) and purified by flash chromatography using 8% EtOAc/hexanes to afford 0.0372 mg (91% yield) of **SI-1** as a colorless oil. Analytical data for **SI-1**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (dd, J = 6.6, 3.1 Hz, 2H), 7.42 (dd, J = 5.0, 1.8 Hz, 3H), 7.28 (d, J = 1.3 Hz, 1H), 5.95 (d, J = 1.3 Hz, 1H), 4.05 – 3.93 (m, 1H), 3.87 – 3.75 (m, 1H), 1.32 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.8, 141.5, 135.2, 130.1, 129.0, 128.8, 127.6, 100.8, 66.2, 15.3; LRMS (ESI): Mass calcd for $C_{12}H_{13}O_3$ $[M+H]^+$: 205; found 205.

Procedure for DFT calculations

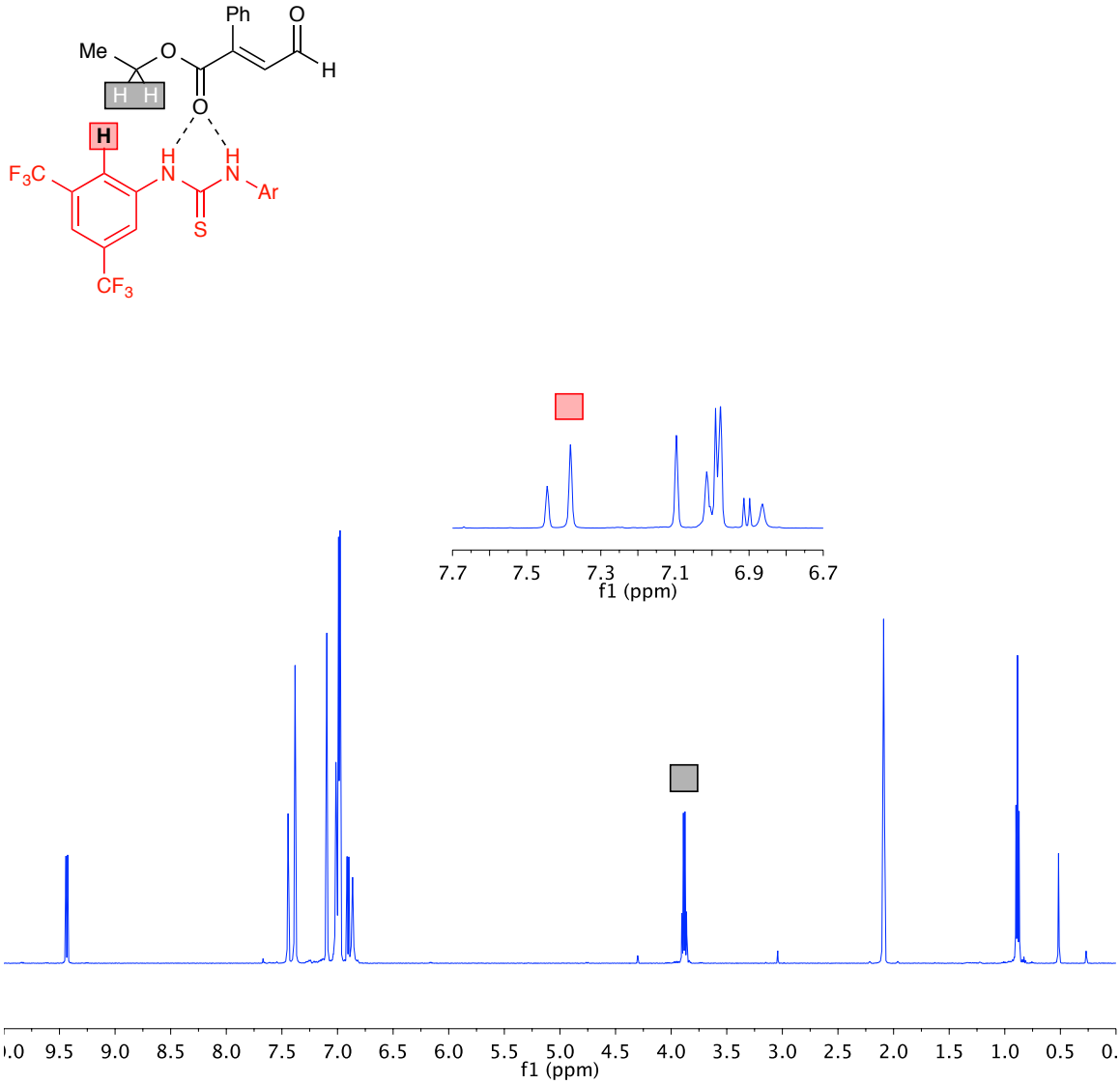
The Density Functional Theory (DFT) calculations were performed on the compounds **NHC_HE1** and **NHC_HE2** using Jaguar 7.8 implemented in the Schrodinger 9.1 suite. For this closed shell system, we used the 6-31G**++ basis set with a hybrid functional of B3LYP. Selecting a fine grid density option and applying a convergence scheme of DIIS the optimization of the compound was performed. The energy optimization was carried out along with the computations of the vibrational frequencies and other thermochemical properties.

Ref: Jaguar, version 7.8, Schrodinger, Inc., New York, 2014

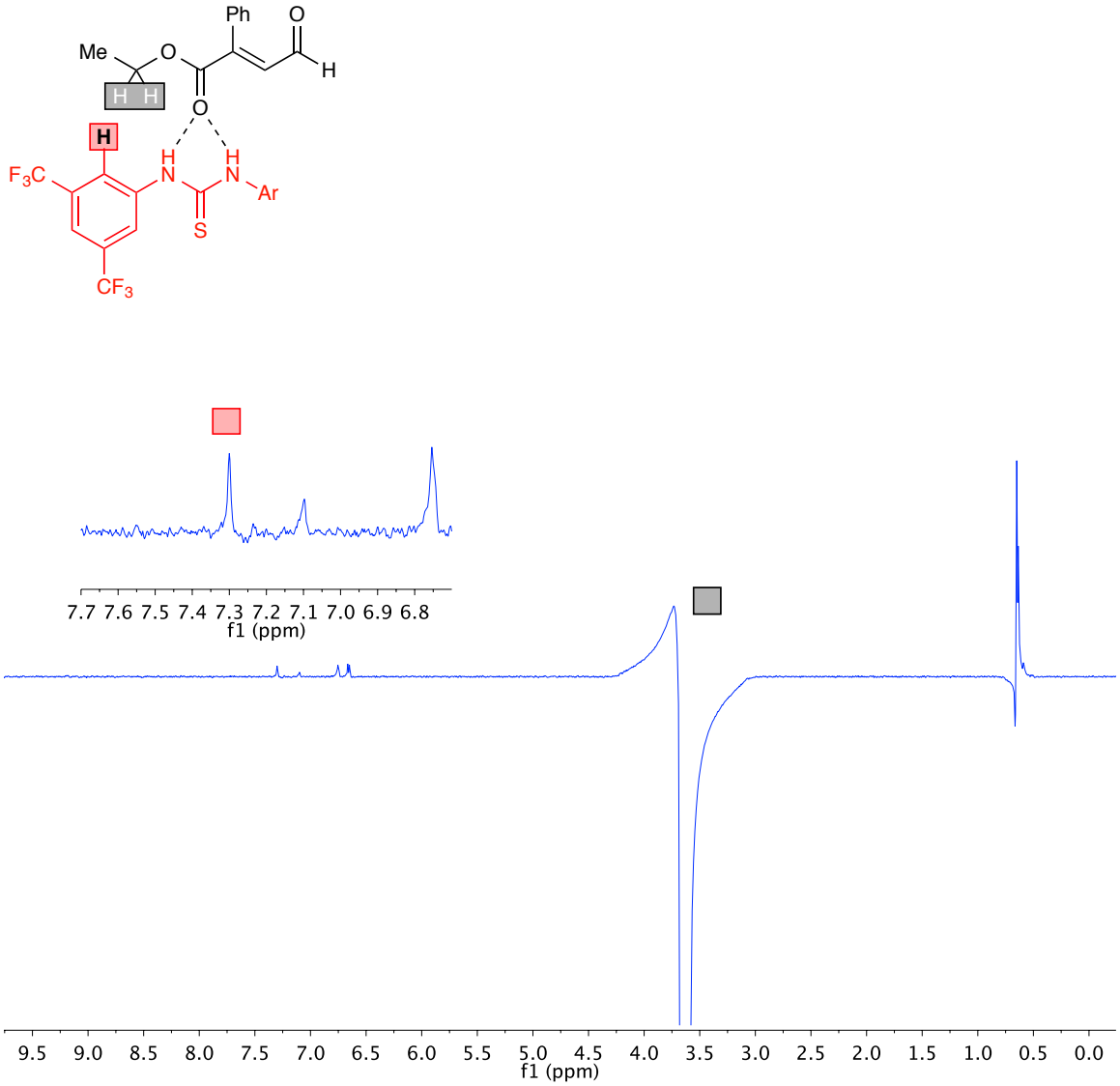
Procedure for 1D NOE experiment

In an NMR tube was combined **1** (2.3 mg), **HBD1** (5 mg), and 0.5 mL toluene-d8. 1D NOESY was acquired with irradiation on 3.88 ppm (delta = 0.1 ppm), with 1024 scans and 800 ms mixing time.

^{1}H NMR (toluene-d8) 1+HBD1

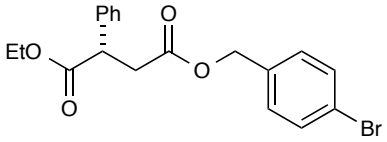


1D NOE (toluene-d8) 1+HBD1



Determination of Absolute Configuration of 22

The absolute configuration of **22** was determined by X-ray diffraction. Recrystallized from hexanes.



X-ray crystal structure of 4-(4-bromobenzyl) 1-ethyl (S)-2-phenylsuccinate (**22**): X-ray diffraction was performed at 99.88 K and raw frame data were processed using SAINT. Molecular structures was solved using direct methods and refined on F2 by full-matrix least-square techniques. The GOF = 1.071 for 218 variables refined to R1 = 0.0252 for 2803 reflections with I>2α(I). A multi-scan absorption correction was performed and the Flack parameter was -0.0033(10). Further information can be found in the CIF file. This crystal structure was deposited in the Cambridge Crystallographic Data Centre and assigned as 1037055.