Highly Enantioselective, Intermolecular Hydroamination of Allenyl Esters Catalyzed by Bifunctional Phosphinothioureas

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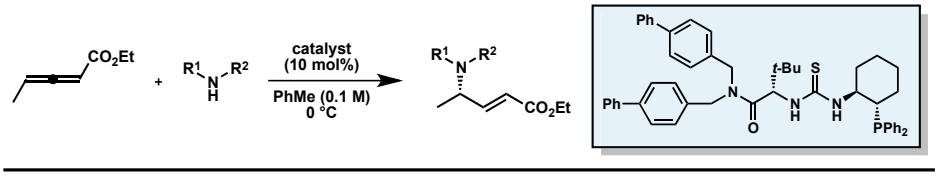
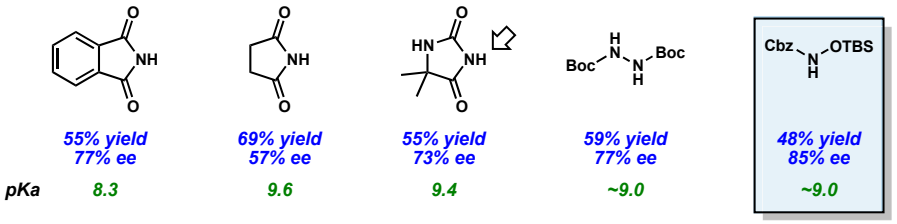
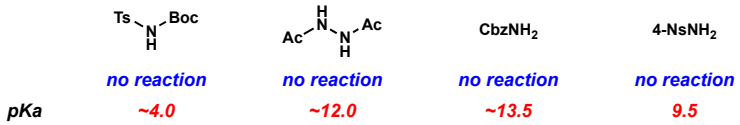
1. Supporting data for optimization studies

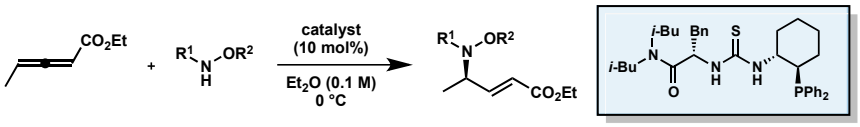
1.1 Table S-1: Nitrogen nucleophile survey

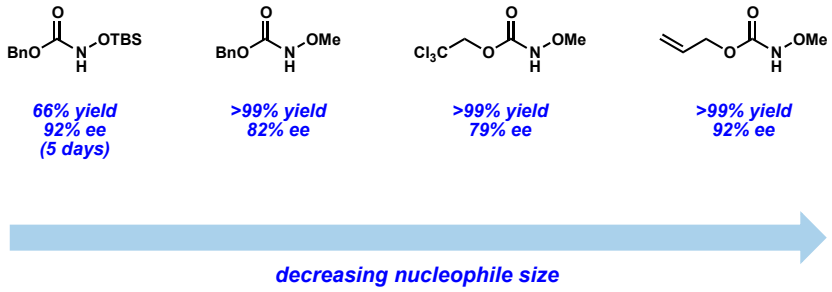




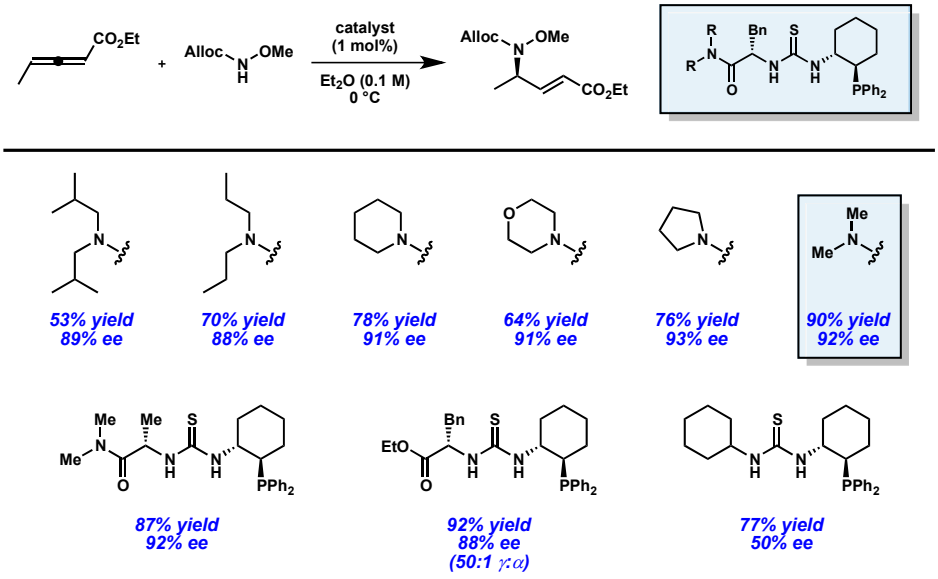


1.2 Table S-2: Carbamate nucleophile optimization

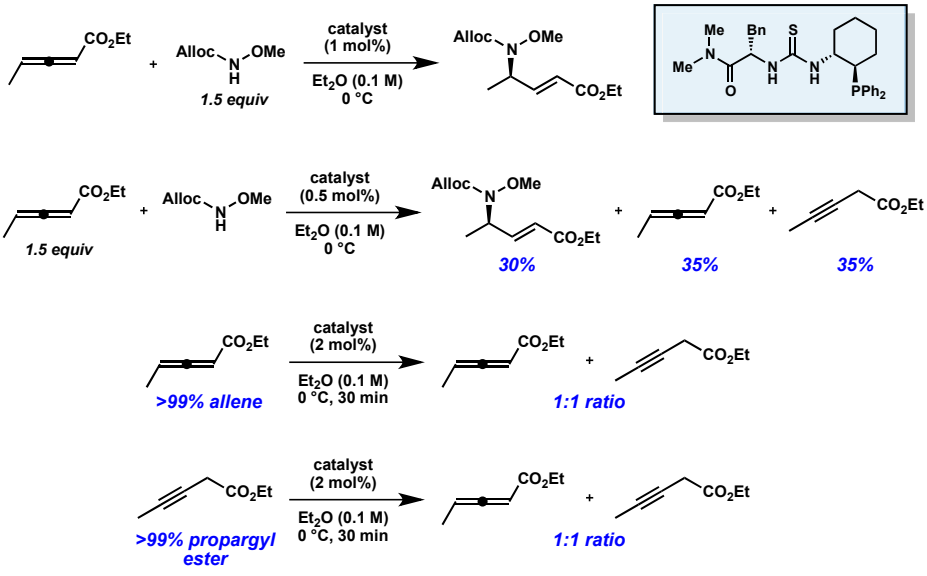




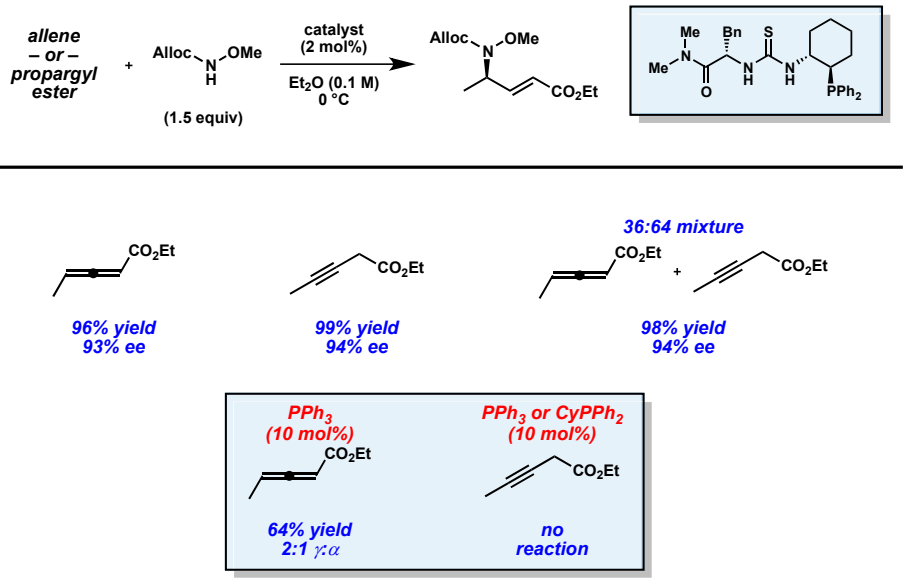
1.3 Table S-3: Catalyst fine-tuning optimization



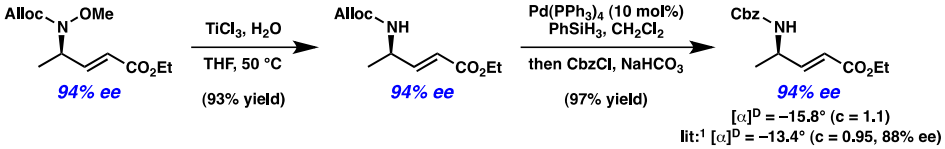
1.4 Scheme S-1: Phosphinothiourea-catalyzed equilibration of propargyl and allenyl esters



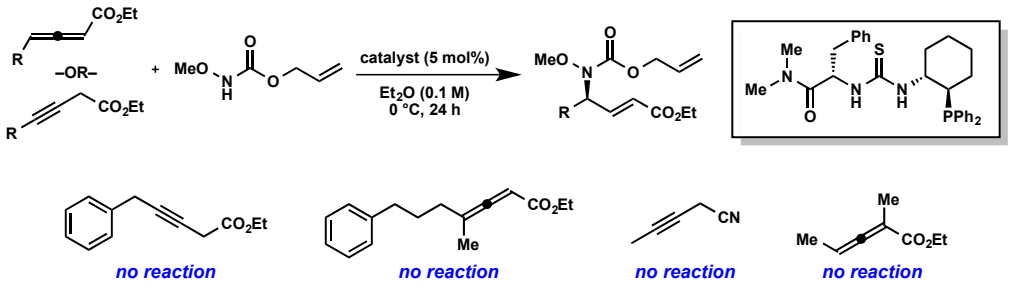
1.5 Table S-4: Comparison of polyfunctional and monofunctional phosphine catalysis



1.6 Scheme S-2: Deprotection and absolute stereochemistry assignment [1]



1.7 Scheme S-3: Examples of failed substrates



2. Experimental Procedures

2.1 General Information

All reaction vessels were evacuated and backfilled with nitrogen three times before use unless otherwise noted. Solvents and solutions were transferred by syringes or cannulae using standard inert atmosphere techniques.

^{1}H, ^{13}C, and ^{31}P NMR spectra were obtained using an Inova-600, Inova-500 or Mercury 400 spectrometer. ^{1}H NMR spectra were referenced to residual $CHCl_3$ peak (7.26 ppm) using $CDCl_3$ as solvent. ^{13}C NMR spectra were referenced to solvent carbons (77.23 ppm for $CDCl_3$). When ^{13}C signals are coupled to ^{31}P, no specific couplings were assigned. ^{31}P NMR spectra were referenced to the external H_3PO_4 signal.

Infrared spectra were obtained using thin films of products. Only absorption frequencies higher than 1000 cm^{-1} are reported. Optical rotations were measured using a 2.0 mL cell with a 1.0 dm path length. High Resolution Mass Spectrometry (HRMS) data were obtained at the Harvard University mass spectrometry facility. Chiral SFC analysis was performed using superfluid CO_2/MeOH as the eluent. Chiral HPLC analysis was performed using hexanes/isopropanol as the eluent.

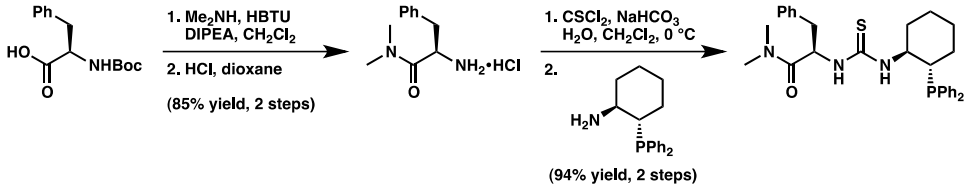
Analytical TLC was performed using EM Separations pre-coated silica gel 0.2 mm layer UV 254 fluorescent sheets. Column chromatography was carried out as flash chromatography on EM Science silica gel 60 (230–400 mesh) using the indicated eluent. Unless otherwise specified, extracts were dried over $MgSO_4$ and volatile solvents were removed with a rotary evaporator at reduced pressure (~40 mmHg).

Carbamate **2a** was prepared using MacMillan's method.[2] Carbamate **2b** was prepared us Kikugawa's method.[3] Carbamate **2c** was prepared according to the literature method followed by vacuum distillation purification.[4] Allenyl ester **1** was prepared (>99% purity, 87% yield) following a published procedure from propionyl chloride, ethyl (triphenylphosphoranylidene)acetate, and Et_3N.[5] Propargyl ester **6** (>99% purity) was prepared using a DCC/DMAP coupling of pent-3-ynoic acid[6] and EtOH at 0 °C. Additional propargyl ester substrates in Table 2 were prepared according to Fu's CuI-catalyzed reaction of terminal alkynes and ethyl diazoacetate in CH_3CN at room temperature.[7] The method provided the corresponding propargyl ester containing 2–10% of the corresponding allenyl ester, which was used without removal of the allenyl esters.

Racemic samples for Table 2, entries 2, 7, 10 were prepared by PPh_3-catalyzed addition of **2b** or **2c** to corresponding allene substrate. The sample contains certain amount of the α-addition adduct (after chromatographic separation) in the SFC trace. For the remaining entries in Table 2, SFC or HPLC traces corresponding to the pure product samples from anti-poles of the catalyst performed using slightly different catalyst loadings.

2.2 Catalyst preparation

(*R*)-2-(3-((*1S,2S*)-2-(diphenylphosphino)cyclohexyl)thioureido)-*N,N*-dimethyl-3-phenylpropanamide (**3e**)



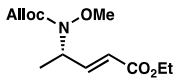
To a suspension of Boc-D-Phe-OH (0.795 g, 3.0 mmol) and HBTU (1.25 g, 3.3 mmol) in CH_2Cl_2 (15 mL) was sequentially added DIPEA (1.05 mL, 6 mmol) and dimethylamine (2 mL, 2 M in THF). The mixture was stirred at room temperature for 3 hours and the residue following removal of solvent was purified by silica gel column chromatography (50% EtOAc in hexanes) to yield the product as a gum-like compound. The gum was dissolved in an HCl in dioxane solution (7.5 mL, 4 M) and stirred at room temperature for 3 hours. Excess HCl and dioxane was removed under reduced pressure and the residue was triturated with Et_2O (~10 mL), filtered, washed with Et_2O (3 × 5 mL) and dried under vacuum to give the product as a white solid (0.585 g, 85% yield, 2 steps).

To a vigorously stirring mixture of the amine hydrochloride salt (0.114 g, 0.5 mmol) in a biphasic mixture of CH_2Cl_2 (5 mL) and $NaHCO_3$ (10 mL) at 0 °C was added $CSCl_2$ (0.042 mL, 0.55 mmol). (Caution: Highly toxic and stench!) The mixture was stirred at this temperature for 15 minutes and warmed to room temperature, where it was stirred for an additional 10 minutes. The biphasic solution was partitioned and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product (120.6 mg), which was used in next step without further purification.

To a solution of the crude isothiocyanate in CH_2Cl_2 (2.5 mL) was added (*S,S)-trans*-hexaneaminophosphine (145.6 mg, 0.514 mmol) under a N_2 atmosphere. The resulting solution was stirred at room temperature for 18 hours and then concentrated under vacuum. The residue was purified by silica gel flash chromatography (33% EtOAc in hexanes) to afford catalyst **3e** as a foamy white solid (0.250 g, 94% yield): $[\alpha]^D = 25.0°$ (c = 0.8, $CHCl_3$); IR (thin film): 3311, 3053, 2928, 1735, 1628, 1532, 1433, 1239, 1092 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.53–7.50 (4H, m), 7.34–7.25 (12H, m), 6.86 (1H, br), 5.79 (1H, br), 4.33 (1H, br), 3.28 (1H, dd, *J* = 12.6, 4.4 Hz), 2.92 (1H, dd, *J* = 12.3, 10.5 Hz), 2.80 (3H, s), 2.60 (3H, s), 2.44 (1H, td, J^t = 9.5 Hz J^d = 2.9 Hz), 2.37 (1H, br), 1.86–1.73 (4H, m), 1.45–1.36 (2H, m), 1.31–1.26 (1H, m), 1.16–1.11 (1H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.4, 172.2, 136.9, 136.8, 136.7, 135.94, 135.8, 134.7, 134.6, 133.1, 133.0, 129.7, 129.1, 128.6, 128.53, 128.49, 128.44, 128.38, 128.3, 127.1, 55.5, 54.7, 54.6, 41.0, 40.9, 40.4, 37.4, 35.8, 33.4, 27.4, 25.4, 24.4; ^{31}P NMR (162 MHz, $CDCl_3$) δ –8.3; HRMS (TOF-ESI) calc'd for $C_{30}H_{37}N_3OPS$ $[M+H]^+$ 518.2390, found 518.2401.

2.3 Phosphinothiourea-Catalyzed Hydroamination

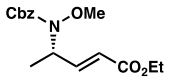
(*S, E*)-Ethyl 4-((allyloxycarbonyl)(methoxy)amino)pent-2-enoate (Table 2, entry 1)



General procedure for phosphinothiourea-catalyzed hydroamination of propargyl esters: An oven-dried 2-dram vial was charged with catalyst **3e** (2.1 mg, 2 mol%) and capped with a Teflon septum. After three cycles of evacuation and backfilling with nitrogen, dry Et_2O (2 mL) was added to the vial via syringe. Upon cooling the catalyst solution to 0 ºC, carbamate **2c** (26.2 mg, 0.2 mmol) and propargyl ester **6** (38 mg, 0.3 mmol) were added sequentially. The sealed vial was maintained with stirring at 0 ºC (ice bath) for 20 hours until TLC analysis showed complete consumption of the carbamate starting material. Upon completion, the solvent was removed under reduced pressure and the crude residue was purified by silica gel column chromatography (20% EtOAc in hexanes) to give the product (**4c**) as a colorless oil (51.4 mg, 99% yield). A larger scale reaction (16 mmol) afforded the product in 97% yield and 94% ee. The enantiomeric excess was determined to be 94% by chiral SFC ((*S,S*)-Whelk-O, 3% methanol in CO_2, 3

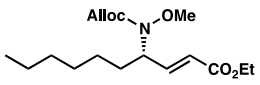
mL/min, 30 °C, 210 nm. t_R(minor): 3.48 min, t_R(major): 3.87 min). $[\alpha]^D = -30.1°$ (c = 1.0, $CHCl_3$); IR (thin film): 2982, 2941, 1713, 1658, 1448, 1369, 1268, 1182, 1062, 1034 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.95 (1H, dd, J = 15.8, 5.9 Hz), 5.94 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.92 (1H, dd, J = 15.9, 1.5 Hz), 5.34 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.25 (1H, dq, J^d = 10.4 Hz, J^q = 1.3 Hz), 4.78 (1H, qdd, J^q = 6.9 Hz, J^d = 6.0, 1.6 Hz), 4.70–4.64 (2H, m), 4.19 (2H, q, J = 7.1 Hz), 3.74 (3H, s), 1.39 (3H, d, J = 6.7 Hz), 1.28 (3H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 157.4, 146.1, 132.3, 122.7, 118.6, 67.1, 64.8, 60.7, 56.2, 16.5, 14.4; HRMS (TOF-ESI) calc'd for $C_{12}H_{19}NO_5Na$ $[M+Na]^+$ 280.1155, found: 280.1155.

(*S, E*)- ethyl 4-((benzyloxycarbonyl)(methoxy)amino)pent-2-enoate (Table 2, entry 2)



The general procedure was followed using carbamate **2b** (71.5 mg, 0.394 mmol), propargyl ester **6** (75.6 mg, 0.6 mmol), and catalyst **3e** (6.2 mg, 3 mol%) in Et_2O (4 mL). After stirring at 0 °C for 15 hours, the product (**4b**) was obtained as a colorless oil (111.1 mg, 92% yield). The enantiomeric excess was determined to be 92% by chiral SFC ((*S*,*S*)-Whelk-O, 5% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 4.93 min, t_R(major): 5.59 min). $[\alpha]^D = -26.9°$ (c = 0.9, $CHCl_3$); IR (thin film): 2981, 2940, 1713, 1658, 1455, 1389, 1268, 1182, 1063, 1033 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.30 (5H, m), 6.95 (1H, dd, J = 15.8, 6.0 Hz), 5.91 (1H, dd, J = 15.8, 1.6 Hz), 5.22 (1H, AB, J = 12.1 Hz), 5.20 (1H, AB, J = 12.1 Hz), 4.78 (1H, qdd, J^q = 6.9 Hz, J^d = 6.0, 1.6 Hz), 4.19 (2H, q, J = 7.1 Hz), 3.73 (3H, s), 1.38 (3H, d, J = 6.9 Hz), 1.28 (3H, t, J = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 157.5, 146.0, 136.0, 128.8, 128.5, 128.3, 122.6, 68.1, 64.8, 60.7, 56.3, 16.4, 14.4; HRMS (TOF-ESI) calc'd for $C_{16}H_{21}NO_5Na$ $[M+Na]^+$ 330.1312; found: 330.1312.

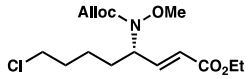
(*S, E*)- ethyl 4-((allyloxycarbonyl)(methoxy)amino)dec-2-enoate (Table 2, entry 3)



The general procedure was followed using carbamate **2c** (26.6 mg, 0.203 mmol),

propargyl ester (58.9 mg, 0.3 mmol), and catalyst **3e** (3.1 mg, 3 mol%) in Et_2O (2 mL). After maintaining the reaction with stirring at 0 °C for 22 hours, the product was obtained as a colorless oil (62.6 mg, 94% yield). The enantiomeric excess was determined to be 96% by chiral SFC ((*S*,*S*)-Whelk-O, 2% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 6.14 min, t_R(major): 6.56 min). $[\alpha]^D = -15.9°$ (c = 0.9, $CHCl_3$); IR (thin film): 2932, 1716, 1716, 1461, 1369, 1305, 1264, 1179, 1035 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.92 (1H, dd, J = 15.8, 7.0 Hz), 5.95 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.94 (1H, dd, J = 16.0, 1.0 Hz), 5.34 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.25 (1H, dq, J^d = 10.4 Hz, J^q = 1.2 Hz), 4.69–4.64 (2H, m), 4.56 (1H, tdd, J^t = 7.7 Hz, J^d = 6.7, 1.0 Hz), 4.19 (2H, q, J = 7.1 Hz), 3.75 (3H, s), 3.53 (2H, t, J = 6.9 Hz), 1.83 (1H, dddd, J = 13.5, 9.1, 8.2, 5.3 Hz), 1.66 (1H, dddd, J = 13.5, 9.4, 7.0, 5.3 Hz), 1.37–1.27 (11H, m), 0.88 (3H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 157.5, 145.1, 132.3, 123.2, 118.5, 67.0, 64.5, 61.0, 60.7, 31.8, 31.1, 29.2, 26.3, 22.8, 14.4, 14.2; HRMS (TOF-ESI) calc'd for $C_{17}H_{29}NO_5Na$ $[M+Na]^+$ 350.1938; found: 350.1939.

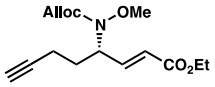
(*S, E*)- ethyl 4-((allyloxycarbonyl)(methoxy)amino)-8-chlorooct-2-enoate (Table 2, entry 4)



The general procedure was followed using carbamate **2c** (26.6 mg, 0.203 mmol), propargyl ester (60.8 mg, 0.3 mmol), and catalyst **3e** (3.1 mg, 3 mol%) in Et_2O (2 mL). After maintaining the reaction with stirring at 0 °C for 22 hours, the product was obtained as a colorless oil (64.1 mg, 95% yield). The enantiomeric excess was determined to be 96% by chiral SFC ((*S*,*S*)-Whelk-O, 2% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 7.39 min, t_R(major): 8.15 min). $[\alpha]^D = -16.7°$ (c = 1.0, $CHCl_3$); IR (thin film): 2939, 1714, 1667, 1267, 1182, 1093, 1038 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.92 (1H, dd, J = 15.8, 7.0 Hz), 5.95 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.95 (1H, dd, J = 15.8, 1.2 Hz), 5.35 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.26 (1H, dq, J^d = 10.4 Hz, J^q = 1.2 Hz), 4.70–4.64 (2H, m), 4.58 (1H, tdd, J^t = 7.7 Hz, J^d = 6.6, 1.0 Hz), 4.19 (2H, q, J = 7.1 Hz), 3.75 (3H, s), 3.53 (2H, t, J = 6.9 Hz), 1.90–1.75 (3H, m), 1.72–1.66 (1H, m), 1.55–1.45 (2H, m), 1.29 (3H, t, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 157.5,

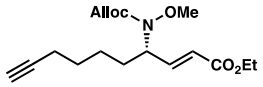
144.5, 132.2, 123.5, 118.6, 67.0, 64.5, 60.7, 60.7, 44.7, 32.3, 30.3, 23.6, 14.4; HRMS (TOF-ESI) calc'd for $C_{15}H_{24}ClNO_5Na$ $[M+Na]^+$ 356.1235; found: 356.1238.

(*S,E*)- ethyl 4-((allyloxycarbonyl)(methoxy)amino)oct-2-en-7-ynoate (Table 2, entry 5)



The general procedure was followed using carbamate **2c** (39.3 mg, 0.30 mmol), propargyl ester (73.9 mg, 0.45 mmol), and catalyst **3e** (3.1 mg, 2 mol%) in Et_2O (3 mL). After maintaining the reaction with stirring at 0 °C for 12 hours, the product was obtained as a colorless oil (74.8 mg, 85% yield). The enantiomeric excess was determined to be 96% by chiral SFC ((*S*,*S*)-Whelk-O, 2% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 5.11 min, t_R(major): 5.77 min). $[\alpha]^D = -4.4°$ (c = 1.0, $CHCl_3$); IR (thin film): 3292, 2940, 2119, 1714, 1369, 1267, 1161, 1092, 1030 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.91 (1H, dd, J = 15.8, 7.3 Hz), 5.99 (1H, dd, J = 15.8, 1.2 Hz), 5.94 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.35 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.26 (1H, dq, J^d = 10.4 Hz, J^q = 1.3 Hz), 4.75 (1H, dtd, J^t = 7.0 Hz, J^d = 8.2, 1.2 Hz), 4.70–4.64 (2H, m), 4.19 (2H, q, J = 7.1 Hz), 3.76 (3H, s), 2.36–2.23 (2H, m), 2.09 (1H, ddt, J^d = 13.8, 8.5 Hz, J^t = 7.0 Hz), 2.01 (1H, ddt, J = 2.6 Hz), 1.91 (1H, dtd, J^d = 13.8, 6.5 Hz, J^t = 7.3 Hz), 1.29 (3H, t, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1, 157.4, 143.8, 132.1, 123.9, 118.6, 82.8, 69.8, 67.1, 64.5, 60.7, 60.0, 29.9, 15.6, 14.4; HRMS (TOF-ESI) calc'd for $C_{15}H_{21}NO_5Na$ $[M+Na]^+$ 318.1312; found: 318.1315.

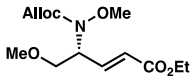
(*S, E*)-ethyl 4-((allyloxycarbonyl)(methoxy)amino)dec-2-en-9-ynoate (Table 2, entry 6)



The general procedure was followed using carbamate **2c** (39.0 mg, 0.298 mmol), propargyl ester (86.5 mg, 0.45 mmol), and catalyst **3e** (4.7 mg, 3 mol%) in Et_2O (3 mL). After maintaining the reaction with stirring at 0 °C for 36 hours, the product was obtained as a colorless oil (92.0 mg, 96% yield). The enantiomeric excess was determined to be

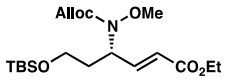
95% by chiral SFC ((*S*,*S*)-Whelk-O, 2% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 6.73 min, t_R(major): 7.31 min). $[\alpha]^D = -16.2°$ (c = 0.8, $CHCl_3$); IR (thin film): 3293, 2940, 2117, 1713, 1657, 1369, 1265, 1183 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.92 (1H, dd, *J* = 16.0, 7.2 Hz), 5.95 (1H, dd, *J* = 16.1, 1.2 Hz), 5.95 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.35 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.26 (1H, dq, J^d = 10.4 Hz, J^q = 1.3 Hz), 4.70–4.64 (2H, m), 4.58 (1H, dt, J^d = 8.0 Hz, J^t = 7.0 Hz), 4.19 (2H, q, *J* = 7.1 Hz), 3.75 (3H, s), 2.20 (2H, td, J^t = 7.0 Hz, J^d = 2.6 Hz), 1.94 (1H, t, *J* = 2.6 Hz), 1.85 (1H, dddd, *J* = 13.8, 10.0, 8.5, 5.6 Hz), 1.69 (1H, ddt, J^d = 13.8, 10.0 Hz, J^t = 6.2 Hz), 1.61–1.43 (4H, m), 1.29 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2, 157.5, 144.7, 132.2, 123.4, 118.6, 84.2, 68.8, 67.0, 64.5, 60.8, 60.7, 30.5, 28.2, 25.4, 18.4, 14.4; HRMS (TOF-ESI) calc'd for $C_{17}H_{25}NO_5Na$ $[M+Na]^+$ 346.1625; found: 346.1628.

(*S, E*)- ethyl 4-((allyloxycarbonyl)(methoxy)amino)-5-methoxypent-2-enoate (Table 2, entry 7)



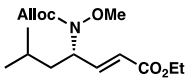
The general procedure was followed using carbamate **2c** (39.2 mg, 0.30 mmol), propargyl ester (70.3 mg, 0.45 mmol), and catalyst **3e** (7.8 mg, 5 mol%) in Et_2O (3 mL). After maintaining the reaction with stirring at 0 °C for 36 hours, the product was obtained as a colorless oil (62.6 mg, 94% yield). The enantiomeric excess was determined to be 92% by chiral SFC ((*S*,*S*)-Whelk-O, 1.5% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 12.17 min, t_R(major): 13.11 min). $[\alpha]^D = -10.7°$ (c = 1.0, $CHCl_3$); IR (thin film): 2983, 2937, 1715, 1659, 1448, 1369, 1309, 1266, 1180, 1033 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.87 (1H, dd, *J* = 16.1, 6.4 Hz), 6.01 (1H, dd, *J* = 16.1, 1.5 Hz), 5.94 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.35 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.25 (1H, dq, J^d = 10.4 Hz, J^q = 1.2 Hz), 4.89 (1H, dddd, *J* = 8.8, 6.4, 5.6, 1.5 Hz), 4.70–4.64 (2H, m), 4.19 (2H, q, *J* = 7.1 Hz), 3.77 (3H, s), 3.74 (1H, dd, *J* = 10.0, 8.8 Hz), 3.49 (1H, dd, *J* = 10.0, 5.6 Hz), 3.38 (3H, s), 1.28 (3H, t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0, 157.6, 141.7, 132.2, 124.5, 118.5, 70.7, 67.1, 64.3, 60.8, 60.0, 59.1, 14.4; HRMS (TOF-ESI) calc'd for $C_{13}H_{21}NO_6Na$ $[M+Na]^+$ 310.1261; found: 310.1261.

(*S, E*)- ethyl 4-((allyloxycarbonyl)(methoxy)amino)-6-(tert-butyldimethylsilyloxy)hex-2-enoate (Table 2, entry 8)



The general procedure was followed using carbamate **2c** (26.1 mg, 0.20 mmol), propargyl ester (81.1 mg, 0.30 mmol), and catalyst **3e** (5.2 mg, 5 mol%) in Et_2O (2 mL). After maintaining the reaction with stirring at 0 °C for 13 hours, the product was obtained as a colorless oil (63.0 mg, 79% yield). The enantiomeric excess was determined to be 97% by chiral SFC ((*S*,*S*)-Whelk-O, 2% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 6.01 min, t_R(major): 6.89 min). $[\alpha]^D = -2.9°$ (c = 0.9, $CHCl_3$); IR (thin film): 2931, 1719, 1369, 1256, 1166, 1095 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.93 (1H, dd, J = 16.0, 7.2 Hz), 5.95 (1H, dd, J = 15.8, 1.5 Hz), 5.93 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.34 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.25 (1H, dq, J^d = 10.4 Hz, J^q = 1.3 Hz), 4.82 (1H, tdd, J^t = 7.7 Hz, J^d = 6.6, 1.3 Hz), 4.69–4.62 (2H, m), 4.19 (2H, q, J = 7.1 Hz), 3.75 (3H, s), 3.70 (1H, ddd, J = 10.4, 7.0, 5.1 Hz), 3.63 (1H, ddd, J = 10.4, 7.0, 5.0 Hz), 2.06 (1H, dddd, J = 13.8, 7.9, 6.4, 5.3 Hz), 1.88 (1H, dddd, J = 13.8, 7.0, 6.7, 5.3 Hz), 1.28 (3H, t, J = 7.2 Hz), 0.89 (9H, s), 0.04 (6H, s); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 157.4, 144.7, 132.3, 123.4, 118.5, 67.0, 64.3, 60.7, 59.4, 58.1, 34.2, 26.1, 18.4, 14.4, –5.23, –5.24; HRMS (TOF-ESI) calc'd for $C_{19}H_{35}NO_6SiNa$ $[M+Na]^+$ 424.2126; found: 424.2129.

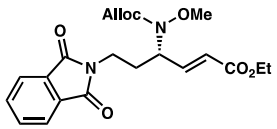
(*S, E*)-ethyl 4-((allyloxycarbonyl)(methoxy)amino)-6-methylhept-2-enoate (Table 2, entry 9)



The general procedure was followed using carbamate **2c** (13.2 mg, 0.101 mmol), propargyl ester (25.2 mg, 0.15 mmol), and catalyst **3e** (5.2 mg, 10 mol%) in Et_2O (1 mL). After maintaining the reaction with stirring at 0 °C for 21 hours, the product was obtained

as a colorless oil (26.3 mg, 87% yield). The enantiomeric excess was determined to be 98% by chiral HPLC (ChiralCel OD-H, 5% IPA in hexanes, 1 mL/min, 23 °C, 210 nm. t_R(major): 5.52 min, t_R(minor): 6.57 min). $[\alpha]^D = -22.0°$ (c = 0.8, $CHCl_3$); IR (thin film): 2960, 2872, 1720, 1654, 1466, 1387, 1369, 1306, 1267, 1180, 1134, 1083, 1038 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.91 (1H, dd, J = 15.8, 7.0 Hz), 5.94 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.94 (1H, dd, J = 16.0, 1.0 Hz), 5.34 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.25 (1H, dq, J^d = 10.4 Hz, J^q = 1.2 Hz), 4.69–4.63 (3H, m), 4.18 (2H, q, J = 7.1 Hz), 3.74 (3H, s), 1.74 (1H, ddd, J = 13.7, 8.4, 6.4 Hz), 1.64 (1H, nonet, J = 6.6 Hz), 1.50 (1H, dt, J^d = 13.7 Hz, J^t = 7.1 Hz), 1.28 (3H, t, J = 7.0 Hz), 0.94 (3H, d, J = 6.7 Hz), 0.93 (3H, d, J = 6.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.3, 157.5, 145.2, 132.3, 123.2, 118.5, 67.0, 64.5, 60.7, 59.2, 34.0, 24.8, 22.7, 22.6, 14.4; HRMS (TOF-ESI) calc'd for $C_{15}H_{25}NO_5Na$ $[M+Na]^+$ 322.1625; found: 322.1627.

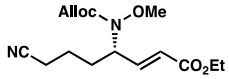
(*S,E*)-ethyl 4-((allyloxycarbonyl)(methoxy)amino)-6-(1,3-dioxoisoindolin-2-yl)hex-2-enoate (Table 2, entry 10)



An oven-dried 2-dram vial was charged with catalyst **3e** (7.8 mg, 7.5 mol%) and solid propargyl ester (85.6 mg, 0.3 mmol) and capped with a Teflon septum. After three cycles of evacuation and backfilling with nitrogen, dry CH_2Cl_2 (2 mL) was added to the vial via syringe. The resulting solution was cooled to 0 ºC and carbamate **2c** (26.1 mg, 0.2 mmol) was added. The sealed vial was maintained with stirring at 0 ºC (ice bath) for 48 hours until TLC analysis showed complete consumption of the carbamate starting material. Following removal of the solvent under reduced pressure, the crude residue was purified by silica gel column chromatography (20%→25% EtOAc in hexanes) to give the product as a colorless oil (72.5 mg, 87% yield). The enantiomeric excess was determined to be 96% by chiral SFC (ChiralPak AD-H, 5% methanol in CO_2, 3 mL/min, 30 °C, 215 nm. t_R(major): 3.81 min, t_R(major): 4.75 min). $[\alpha]^D = -5.5°$ (c = 0.8, $CHCl_3$); IR (thin film): 2940, 2255, 1773, 1707, 1656, 1438, 1370, 1306, 1265, 1184, 1072, 1037 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.86–7.83 (2H, m), 7.74–7.71 (2H, m), 6.90 (1H, dd, J = 15.8, 7.0

Hz), 6.01 (1H, dd, J = 15.8, 1.2 Hz), 5.92 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.33 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.24 (1H, dq, J^d = 10.4 Hz, J^q = 1.3 Hz), 4.69–4.42 (3H, m), 4.17 (2H, q, J = 7.1 Hz), 3.85 (3H, s), 3.84–3.76 (2H, m), 2.20 (1H, dddd, J = 13.8, 8.8, 8.5, 6.4 Hz), 1.88 (1H, dddd, J = 13.8, 8.5, 6.7, 6.2 Hz), 1.27 (3H, t, J = 7.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3, 166.0, 157.6, 143.4, 134.2, 132.2, 132.1, 124.0, 123.4, 118.6, 67.2, 64.6, 60.7, 58.9, 35.4, 29.9, 14.3; HRMS (TOF-ESI) calc'd for $C_{21}H_{24}N_2O_7Na$ $[M+Na]^+$ 439.1476; found: 439.1474.

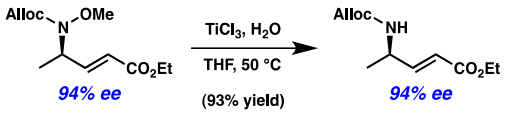
(*S, E*)-ethyl 4-((allyloxycarbonyl)(methoxy)amino)-7-cyanohept-2-enoate (Table 2, entry 11)



The general procedure was followed using carbamate **2c** (39.7 mg, 0.30 mmol), propargyl ester (80.6 mg, 0.45 mmol), and catalyst **3e** (7.8 mg, 5 mol%) in Et_2O (3 mL). After maintaining the reaction with stirring at 0 °C for 44 hours, the product was obtained as a colorless oil (84.5 mg, 79% yield). The enantiomeric excess was determined to be 99% by chiral SFC ((*S*,*S*)-Whelk-O, 5% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 5.25 min, t_R(major): 5.76 min). $[\alpha]^D$ = –18.3° (c = 0.8, $CHCl_3$); IR (thin film): 2940, 2250, 1714, 1658, 1446, 1370, 1309, 1270, 1189, 1094, 1038 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.91 (1H, dd, J = 15.8, 6.4 Hz), 5.98 (1H, dd, J = 16.1, 1.0 Hz), 5.95 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.6 Hz), 5.36 (1H, dq, J^d = 17.2 Hz, J^q = 1.5 Hz), 5.28 (1H, dq, J^d = 10.4 Hz, J^q = 1.3 Hz), 4.70–4.65 (2H, m), 4.62 (1H, q, J = 7.2 Hz), 4.20 (2H, q, J = 7.1 Hz), 3.76 (3H, s), 2.40 (2H, t, J = 6.9 Hz), 2.06–2.00 (1H, m), 1.85–1.67 (3H, m), 1.29 (3H, t, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.9, 157.4, 143.7, 132.0, 124.0, 119.2, 118.8, 67.2, 64.6, 60.8, 59.9, 29.9, 22.3, 17.1, 14.3; HRMS (TOF-ESI) calc'd for $C_{15}H_{22}N_2O_5Na$ $[M+Na]^+$ 333.1421; found: 333.1421.

2.4 *N*-Methoxy Cleavage:

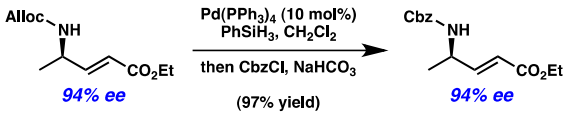
(*S, E*)- Ethyl 4-(allyloxycarbonylamino)pent-2-enoate



To a suspension of $TiCl_3$ in THF (5 mL) was added a solution of *N*-methoxycarbamate **4c** (1.15 g, 4.47 mmol) and H_2O (0.241 mL, 13.4 mmol) in THF (10 mL) via cannula. Another portion of THF (7 mL) was used to rinse the flask containing carbamate **4c** into the $TiCl_3$ flask. The reaction mixture was heated to 50 °C and maintained at that temperature for 5 hours before cooling to room temperature. The reaction was quenched by pouring it into a stirring saturated $NaHCO_3$ solution (100 mL). After maintaining with stirring at room temperature for 30 minutes, Celite (5 g) was added and the mixture was filtered through a Celite pad. The black filter cake was washed with Et_2O thoroughly and the filtrate was extracted with Et_2O (3 × 50 mL). The combined organic extracts were dried over $MgSO_4$ and purified by silica gel column chromatography (20% EtOAc in hexanes) to give the product as a colorless oil (0.945 g, 93% yield). The enantiomeric excess was determined to be 94% by chiral SFC (ChiralPak AS-H, 2% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 2.17 min, t_R(major): 2.91 min). $[\alpha]^D = -32.5°$ (c = 1.0, $CHCl_3$); IR (thin film): 3331, 2979, 2924, 1696, 1658, 1524, 1453, 1369, 1307, 1237, 1180, 1044 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.87 (1H, dd, J = 15.8, 5.0 Hz), 5.91 (1H, dd, J = 15.8, 1.2 Hz), 5.91 (1H, ddt, J^d = 17.2, 10.4 Hz, J^t = 5.9 Hz), 5.30 (1H, d, J = 17.3 Hz), 5.22 (1H, dq, J^d = 10.3 Hz, J^q = 1.2 Hz), 4.74 (1H, br), 4.59–4.54 (2H, m), 4.46 (1H, br), 4.19 (2H, q, J = 7.1 Hz), 1.30 (3H, d, J = 6.4 Hz), 1.28 (3H, t, J = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 155.5, 148.9, 132.9, 120.7, 118.1, 66.0, 60.7, 47.7, 20.5, 14.4; HRMS (TOF-ESI) calc'd for $C_{11}H_{17}NO_4Na$ $[M+Na]^+$ 250.1050; found: 250.1046.

2.5 *N*-Alloc Cleavage and Absolute Stereochemistry Determination

(*S, E*)- Ethyl 4-(benzyloxycarbonylamino)pent-2-enoate



To a solution of the carbamate (162.7 mg, 0.716 mmol) and $PhSiH_3$ (0.44 mL, 3.58 mmol) in CH_2Cl_2 (4 mL) was added $Pd(PPh_3)_4$ (0.072 mmol, 84 mg). After maintaining the resulting reaction with stirring for 10 minutes, the mixture was diluted with CH_2Cl_2 (6 mL) and 1:1 $NaHCO_3/Na_2CO_3$ buffer (1 M, 3 mL, 3 mmol) and cooled to 0 ºC. CbzCl (121 μL, 0.86 mmol) was added and the mixture was stirred at 0 °C for another 1 hour and then at room temperature for 0.5 hours. The reaction mixture was then extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic extracts were dried over $MgSO_4$. The product was further purified using silica gel column chromatography to give the carbamate product as a colorless oil (192.5 mg, 97% yield). The enantiomeric excess was determined to be 94% by chiral SFC (ChiralCel OD-H, 5% methanol in CO_2, 3 mL/min, 30 °C, 210 nm. t_R(minor): 5.04 min, t_R(major): 5.76 min). $[\alpha]^D = -15.8$ ° (c = 1.0, $CHCl_3$) for 94% ee sample (Lit: $[\alpha]^D = -13.4$ ° (c = 0.95, $CHCl_3$) for an 88% ee sample of *S* configuration product[1]); IR (thin film): 3296, 2979, 1716, 1684, 1656, 1537, 1455, 1290, 1252, 1161, 1077, 1025 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.30 (5H, m), 6.87 (1H, dd, *J* = 15.8, 5.0 Hz), 5.91 (1H, d, *J* = 15.3 Hz), 5.12 (1H, AB, *J* = 12.1 Hz), 5.08 (1H, AB, *J* = 12.1 Hz), 4.78 (1H, br), 4.47 (1H, br), 4.19 (2H, q, *J* = 7.2 Hz), 1.29 (3H, d, *J* = 7.1 Hz), 1.28 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 155.6, 148.9, 136.5, 128.8, 128.4, 128.4, 120.7, 67.2, 60.7, 47.8, 20.5, 14.4.

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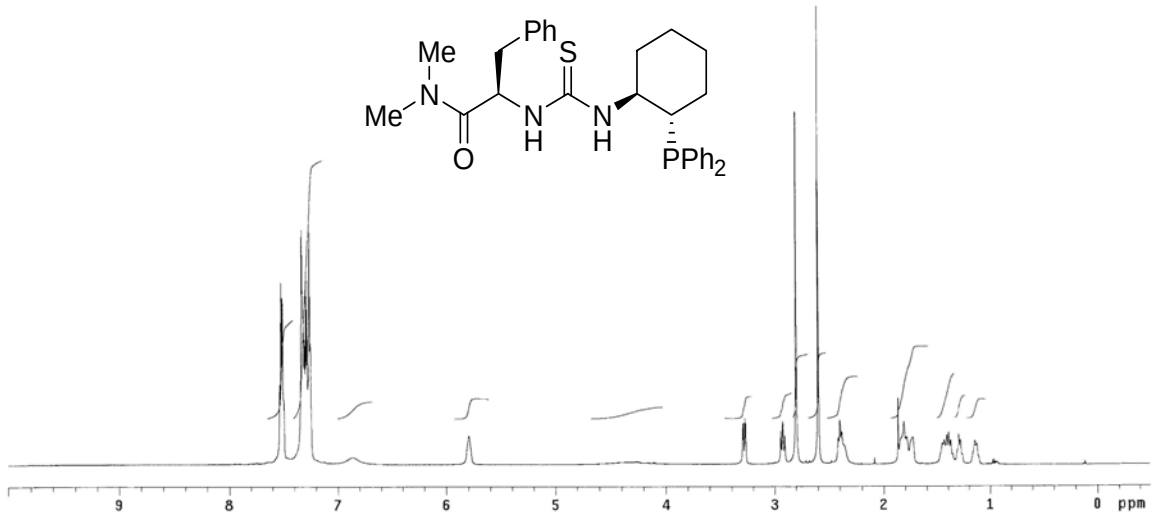
[1] Tsubaki, K.; Kusumoto, T.; Hayashi, N.; Tanima, D.; Fuji, K.; Kawabata, T. *Tetrahedron Asymm.* **2005,** *16*, 739.
[2] Chen, Y. K.; Yoshida, M.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2006**, *128*, 9328.
[3] Kawase, M.; Kitamura, T.; Kikugawa, Y. *J. Org. Chem.* **1989**, *54*, 3394.
[4] Griffith, B. R.; Krepel, C.; Fu, X.; Blanchard, S.; Ahmed, A.; Edmiston, C. E.; Thorson, J. S. *J. Am. Chem. Soc.* **2007**, *129*, 8150.
[5] Lang, R. W.; Hansen, H.-J. *Org. Synth.* **1984**, *62*, 202; *Org. Synth. Coll. Vol.* **1990**, *7*, 232.
[6] Obata, R.; Sunazuka, T.; Li, Z.; Tian, Z.; Harigaya, Y.; Tabata, N.; Tomoda, H.; Omura, S. *J. Antibiot.* **1996**, *49*, 1133.
[7] Suárez, A.; Fu, G. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 3580.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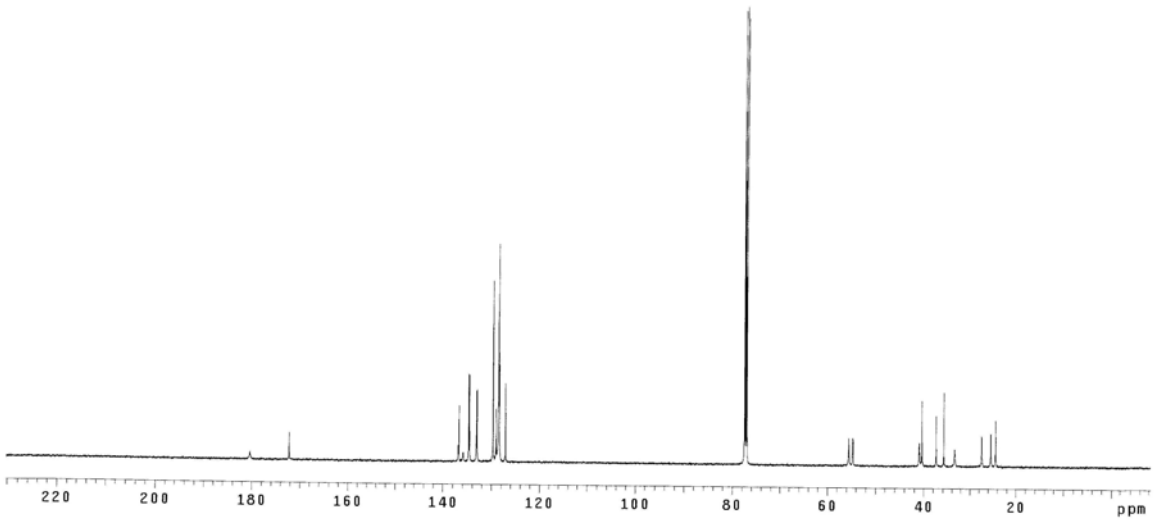
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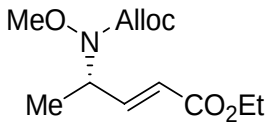
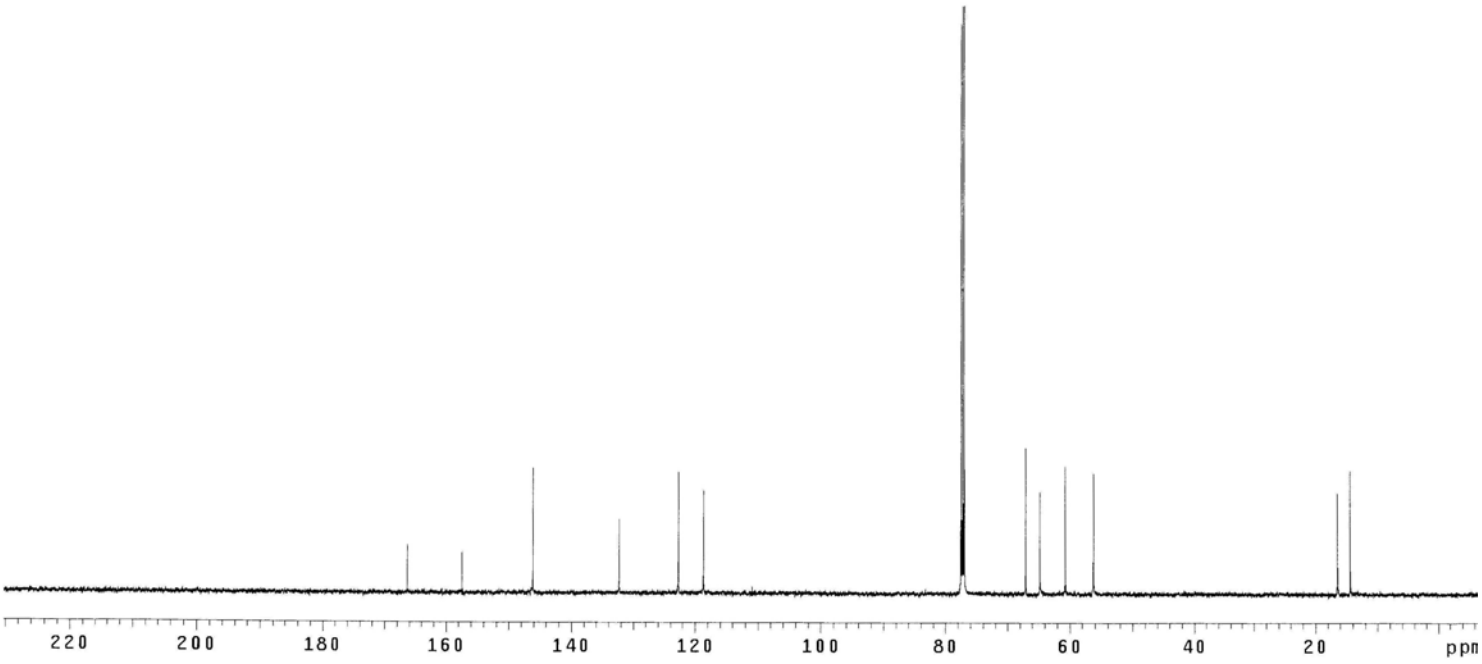
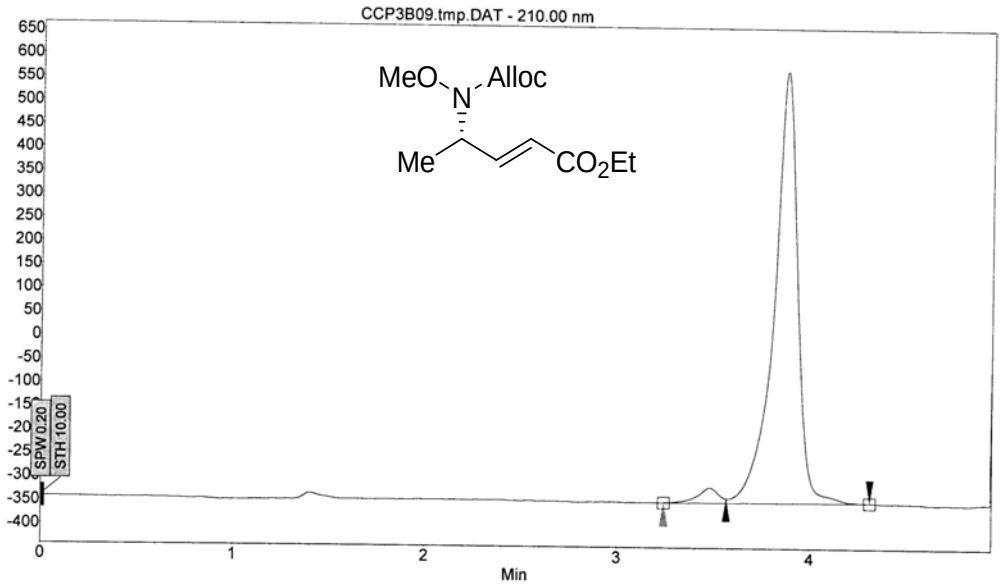


(Table 2, entry 1)





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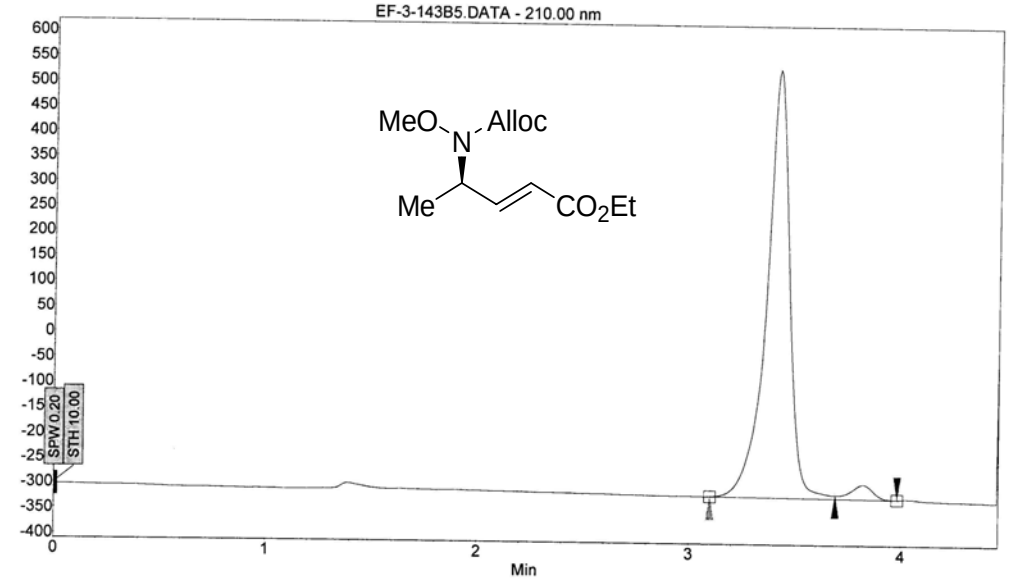
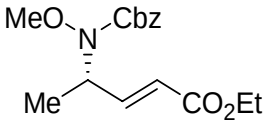
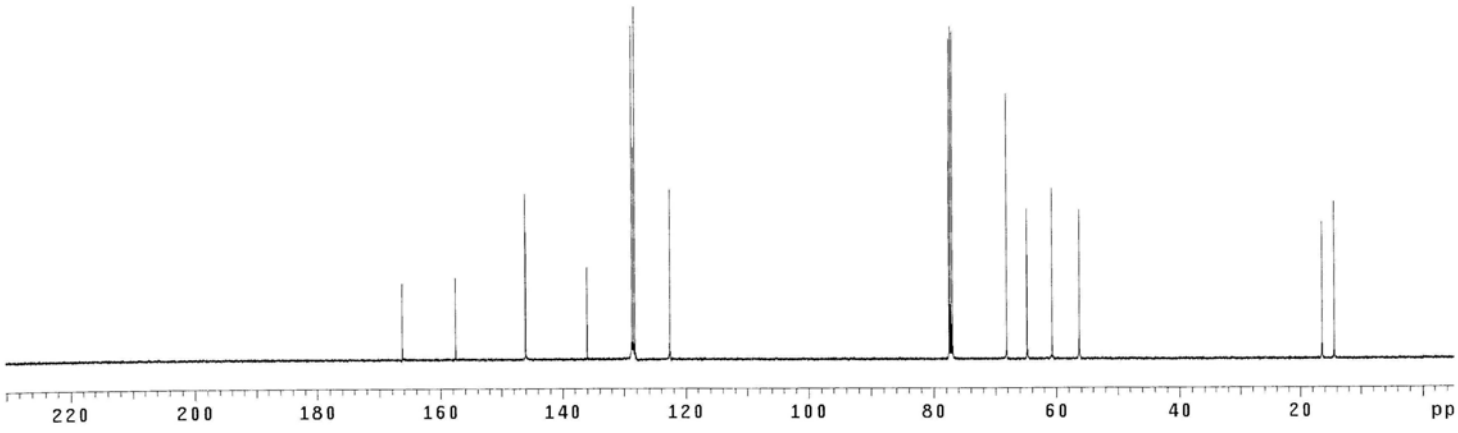
2	UNKNOWN	3.57	3.87	4.31	0.00	96.98	919.3	130.2	96.985
Total						100.00	951.3	134.2	100.000

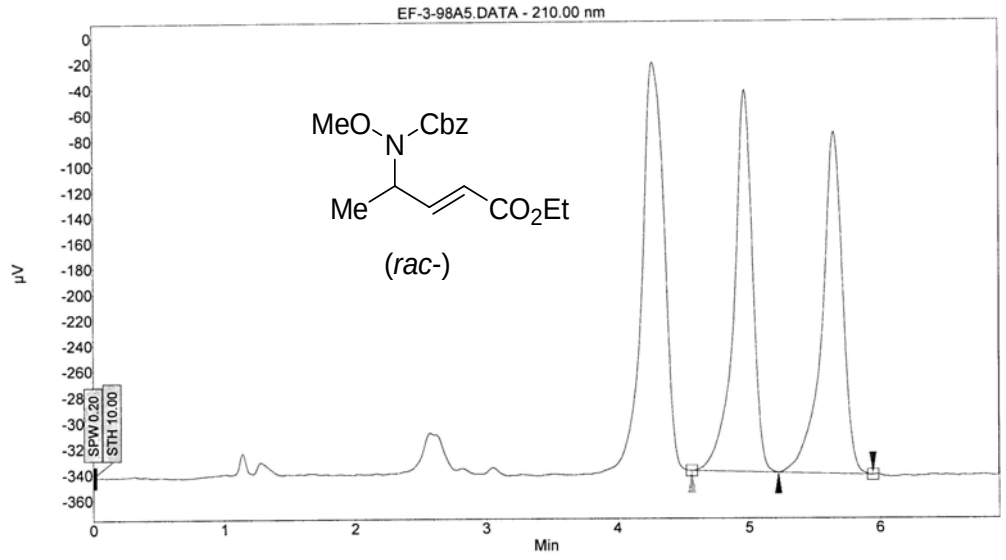


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.10	3.41	3.69	0.00	96.73	852.9	106.4	96.731
2	UNKNOWN	3.69	3.82	3.98	0.00	3.27	28.8	3.6	3.269
Total						100.00	881.7	109.9	100.000

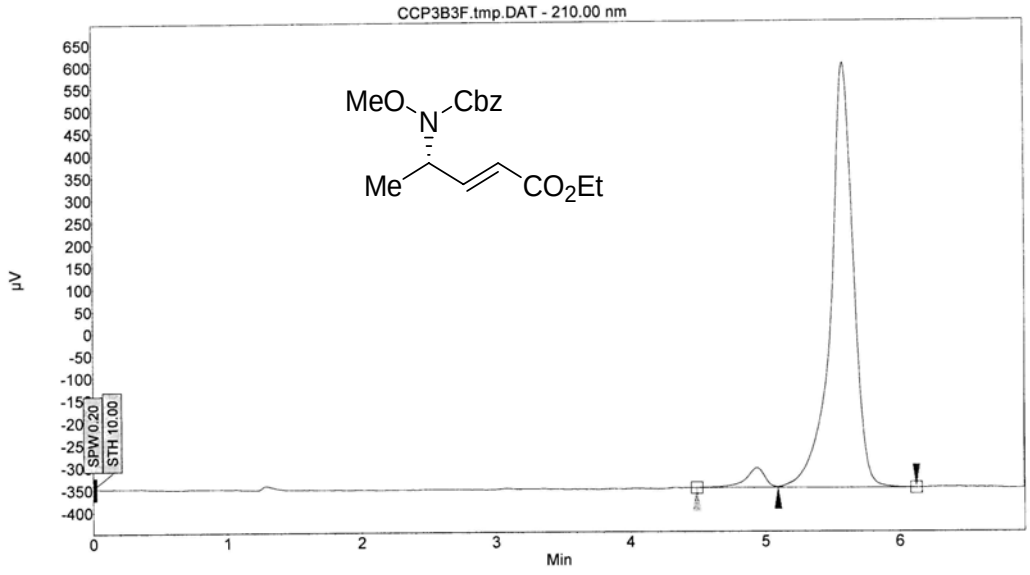


(Table 2, entry 2)

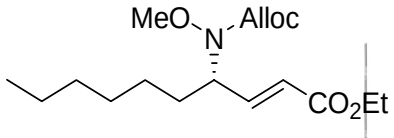




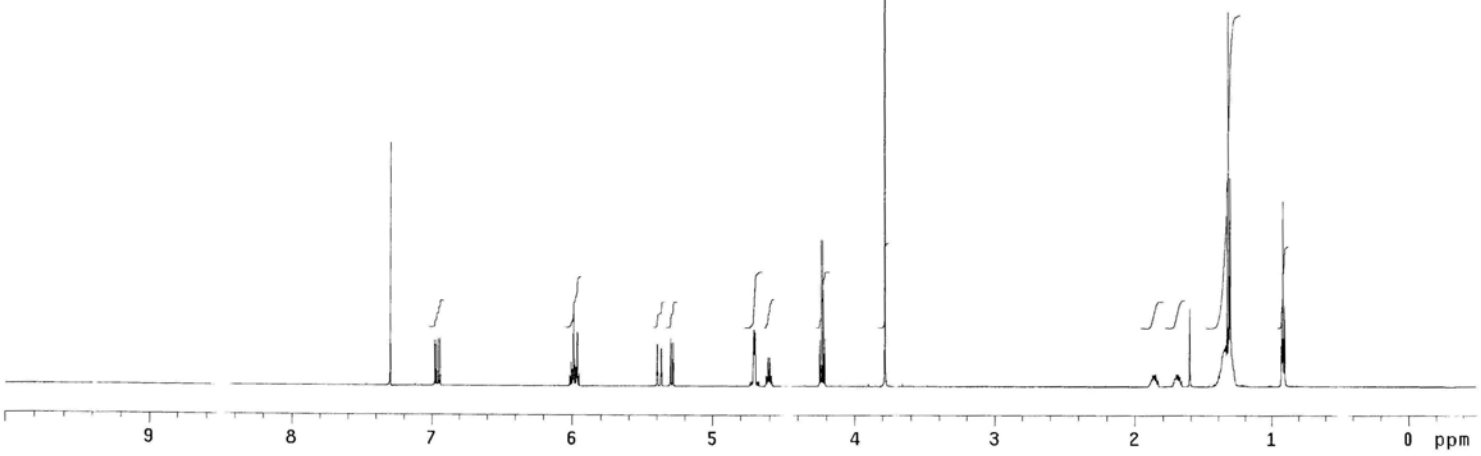
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.56	4.97	5.22	0.00	49.99	296.9	48.4	49.989
2	UNKNOWN	5.22	5.65	5.95	0.00	50.01	265.7	48.5	50.011
Total						100.00	562.6	96.9	100.000

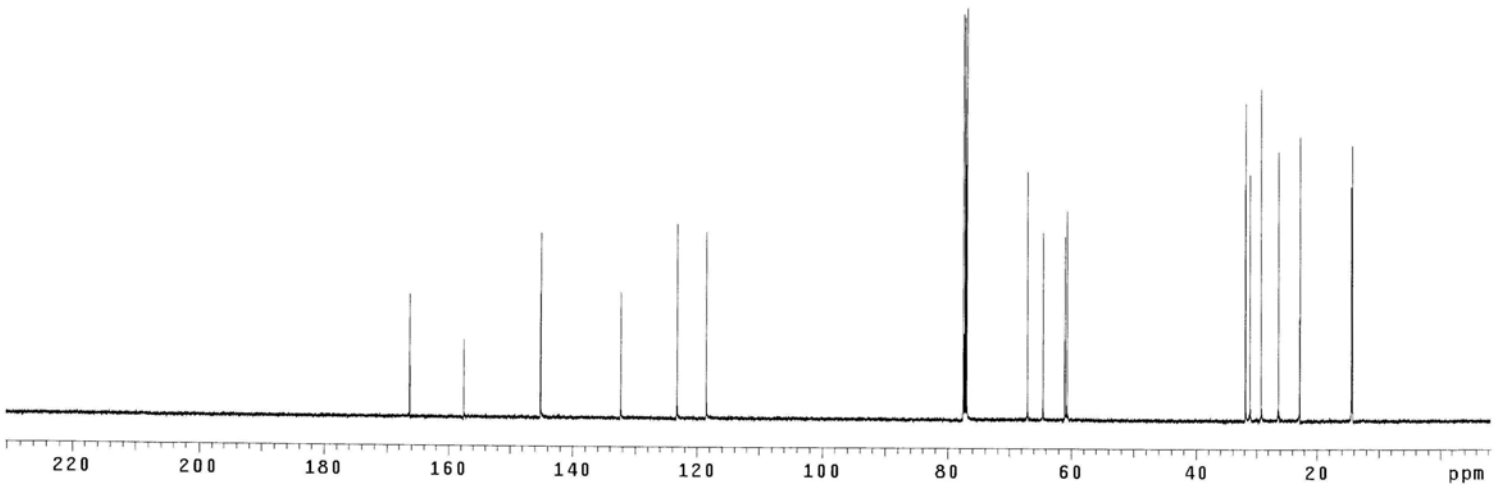


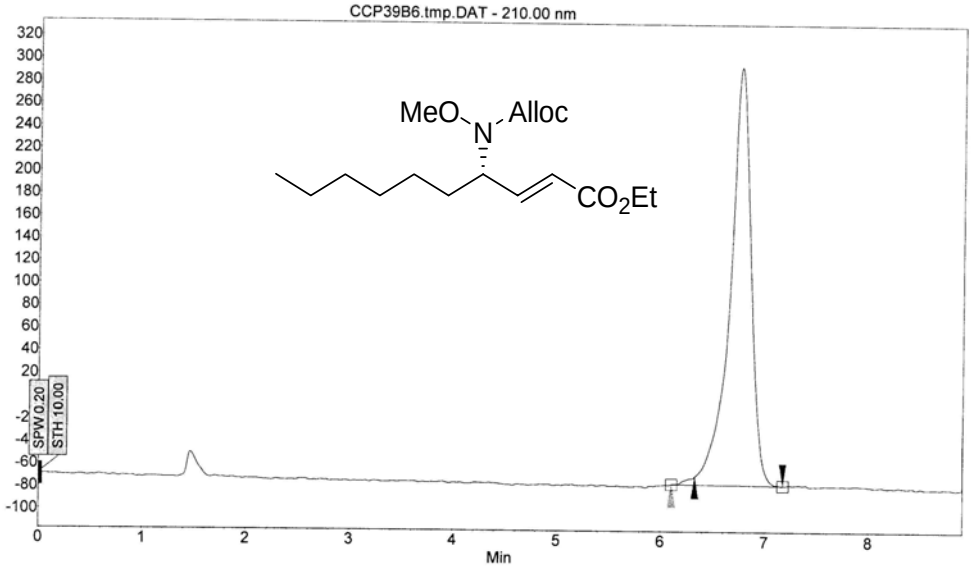
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	4.49	4.93	5.09	0.00	3.78	43.3	7.3	3.784
2	UNKNOWN	5.09	5.59	6.12	0.00	96.22	951.0	184.5	96.216
Total						100.00	994.3	191.7	100.000



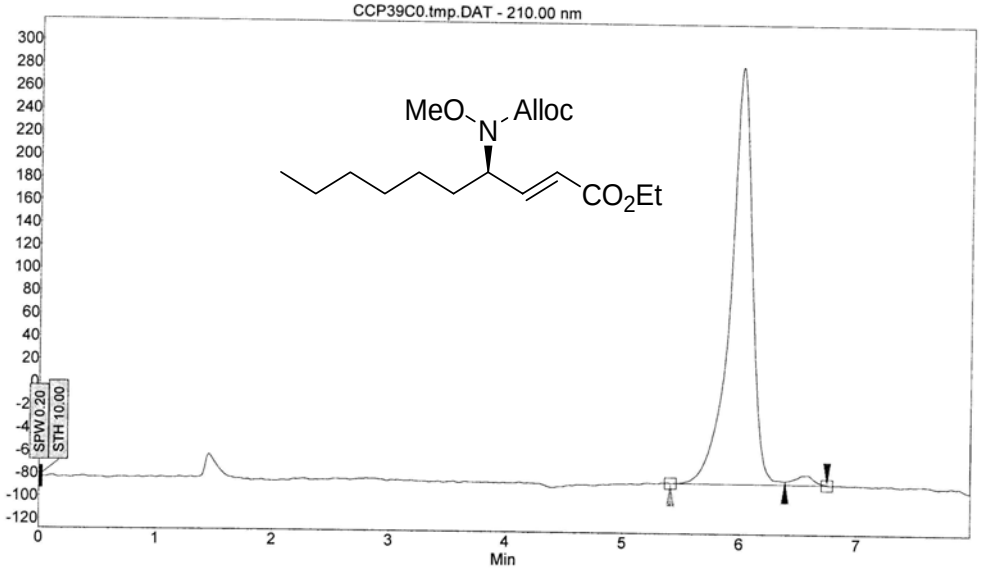
(Table 2, entry 3)



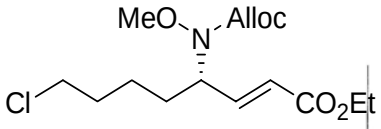




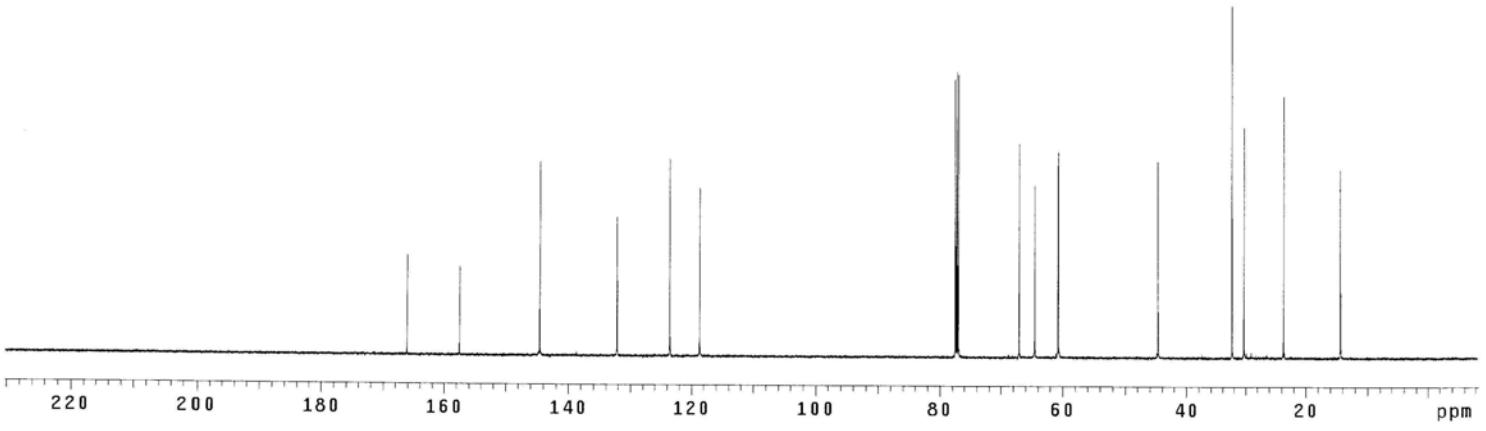
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.10	6.33	6.33	0.00	0.79	7.3	0.7	0.794
2	UNKNOWN	6.33	6.75	7.17	0.00	99.21	371.9	87.0	99.206
Total						100.00	379.2	87.7	100.000

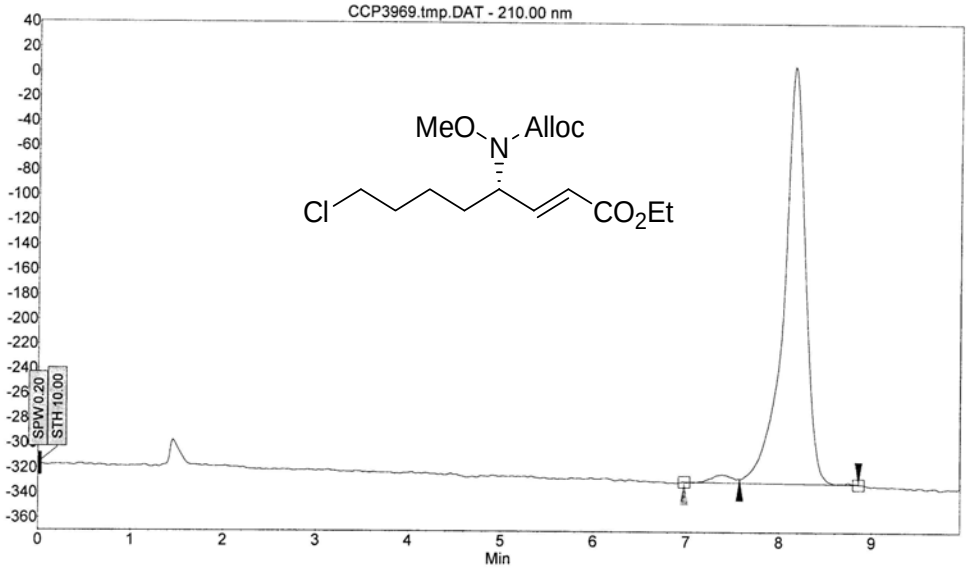


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.41	6.01	6.39	0.00	97.88	365.5	78.8	97.883
2	UNKNOWN	6.39	6.58	6.75	0.00	2.12	8.5	1.7	2.117
Total						100.00	374.0	80.5	100.000



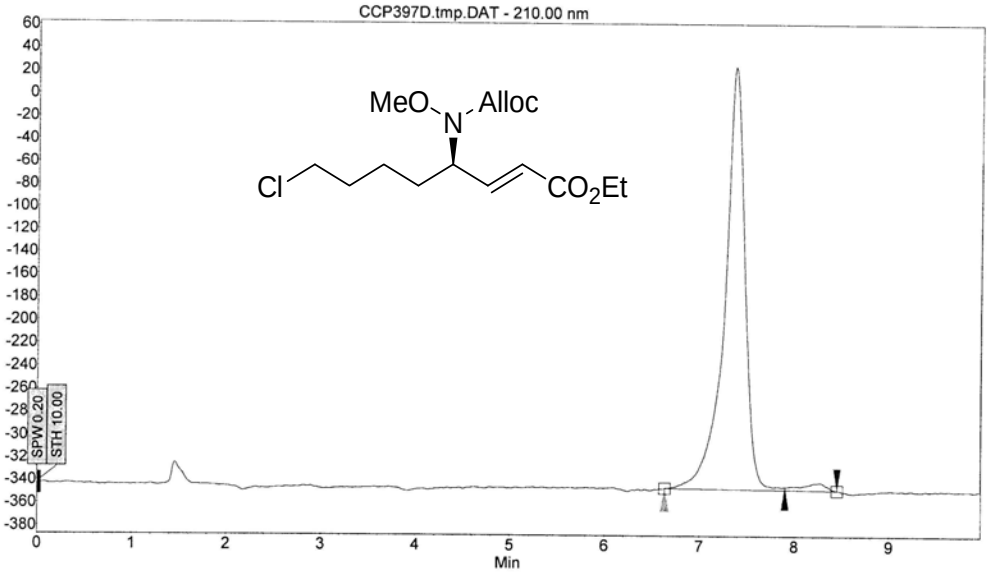
(Table 2, entry 4)





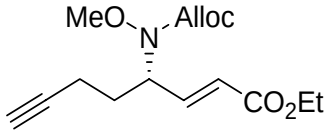
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.98	7.39	7.57	0.00	1.83	6.5	1.7	1.825
2	UNKNOWN	7.57	8.15	8.86	0.00	98.17	336.8	91.4	98.175
Total						100.00	343.3	93.1	100.000

96%

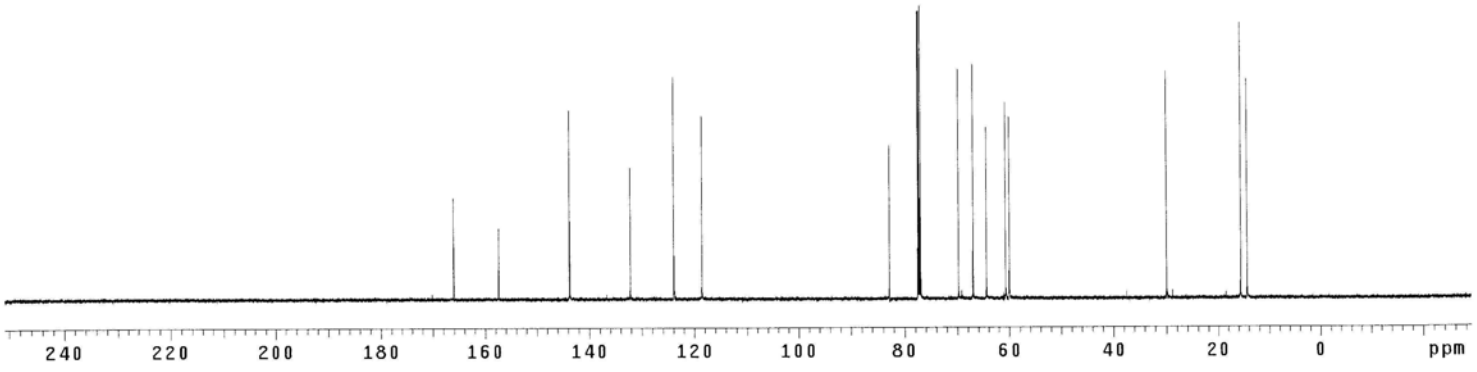


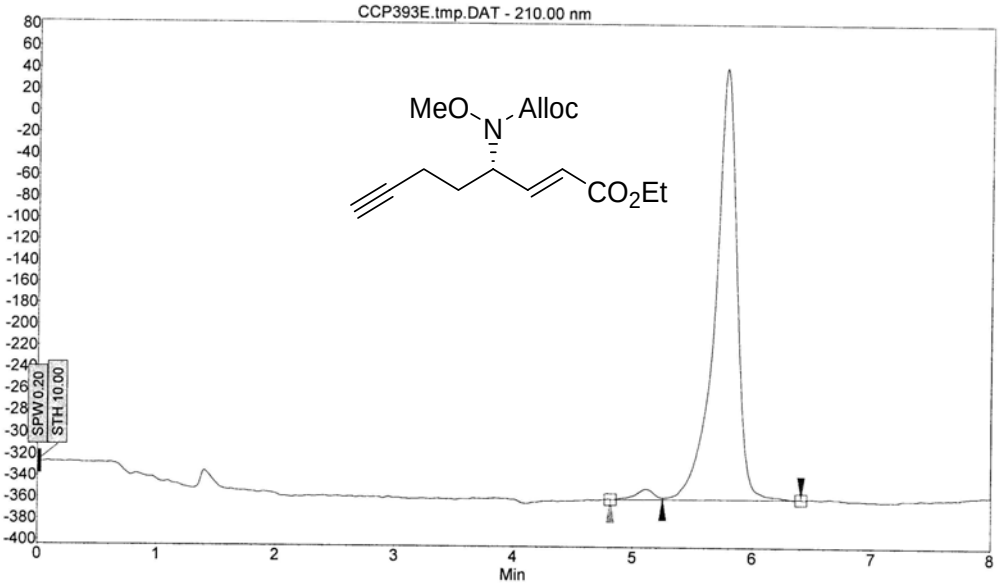
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.63	7.36	7.90	0.00	97.77	371.1	91.7	97.773
2	UNKNOWN	7.90	8.27	8.45	0.00	2.23	6.6	2.1	2.227
Total						100.00	377.8	93.8	100.000

97%



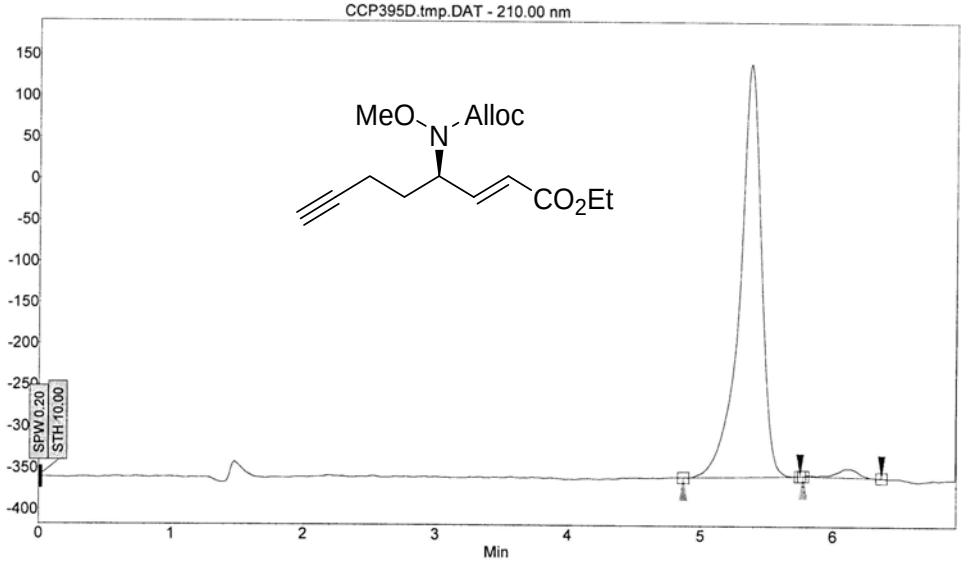
(Table 2, entry 5)





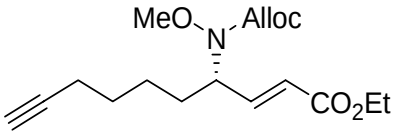
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.81	5.11	5.25	0.00	1.99	9.6	1.7	1.989
2	UNKNOWN	5.25	5.77	6.41	0.00	98.01	401.7	85.4	98.011
Total						100.00	411.3	87.1	100.000

96 i.e.

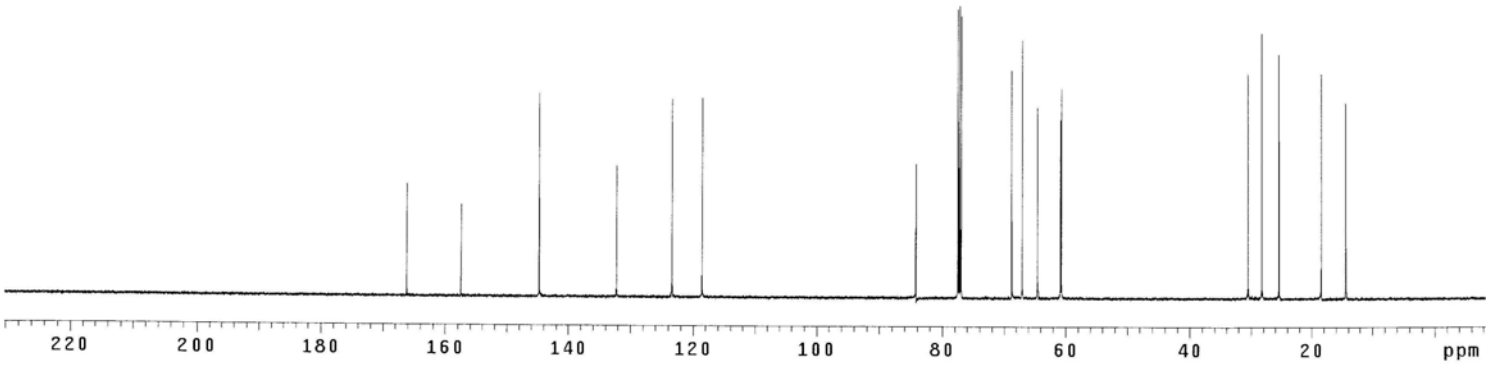


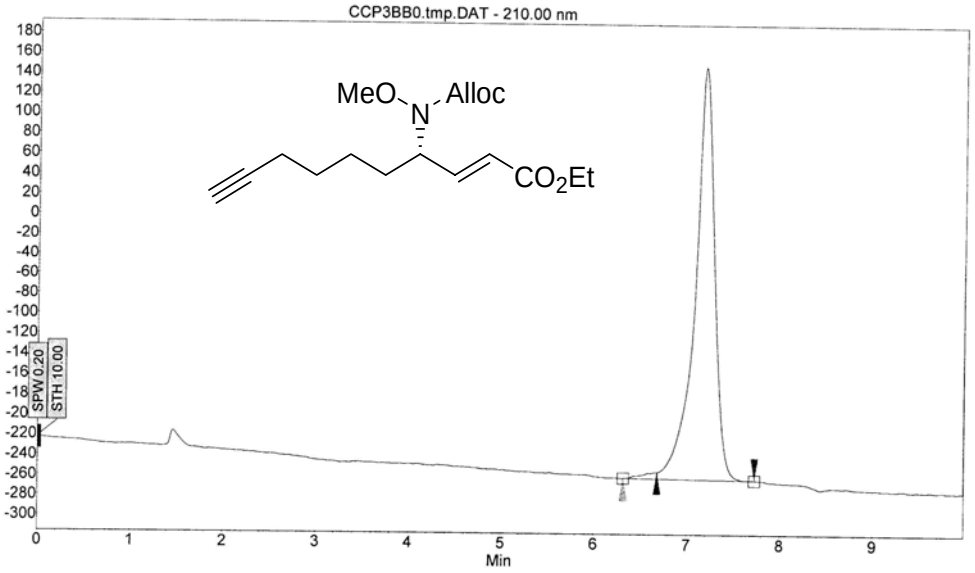
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.87	5.37	5.75	0.00	97.81	498.4	94.1	97.809
2	UNKNOWN	5.77	6.10	6.37	0.00	2.19	10.3	2.1	2.191
Total						100.00	508.7	96.2	100.000

96 %

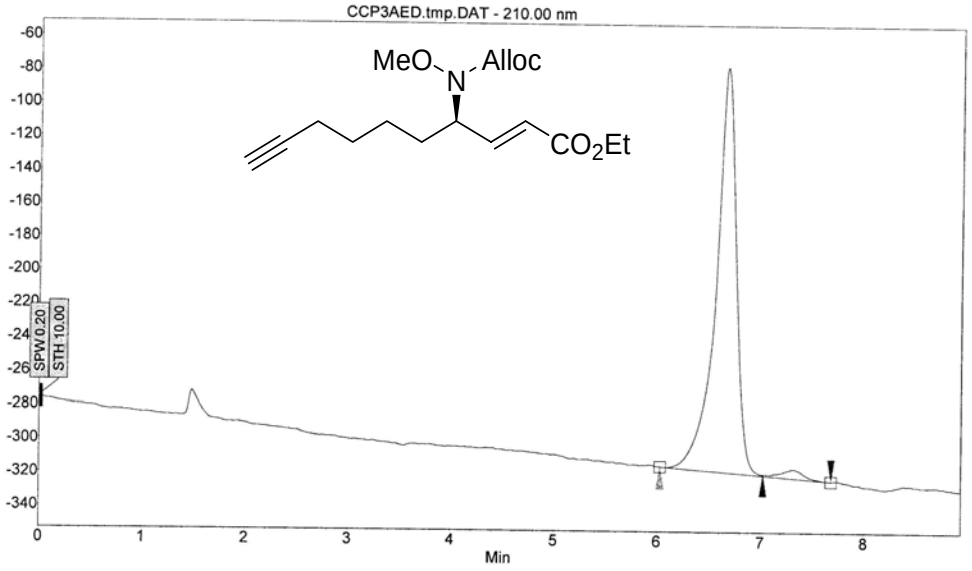


(Table 2, entry 6)

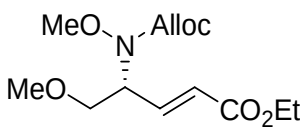




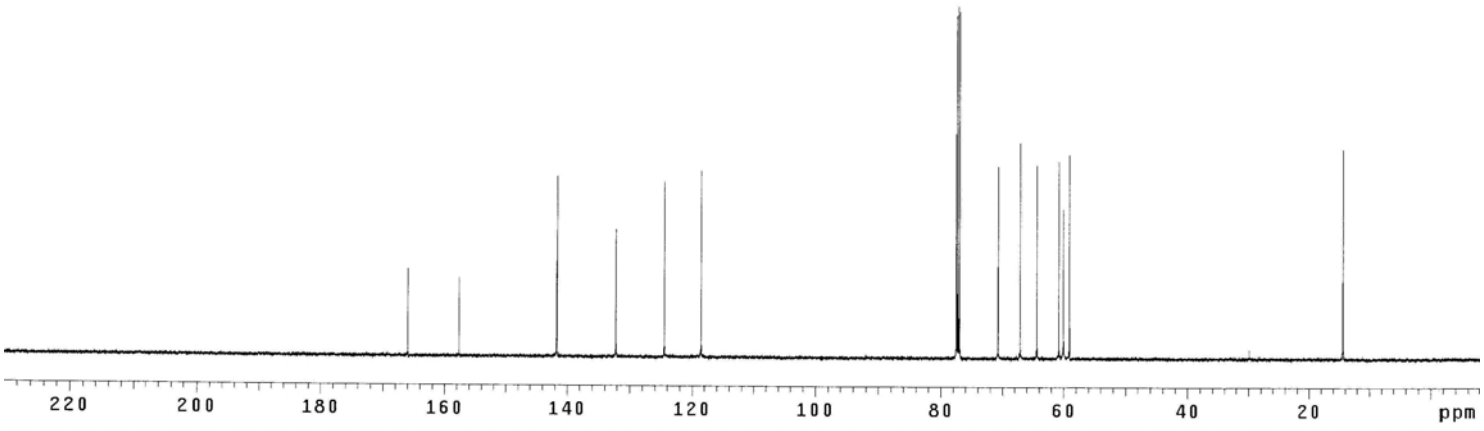
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.32	6.68	6.68	0.00	1.26	6.6	1.3	1.258
2	UNKNOWN	6.68	7.17	7.73	0.00	98.74	410.9	99.7	98.742
Total						100.00	417.5	101.0	100.000

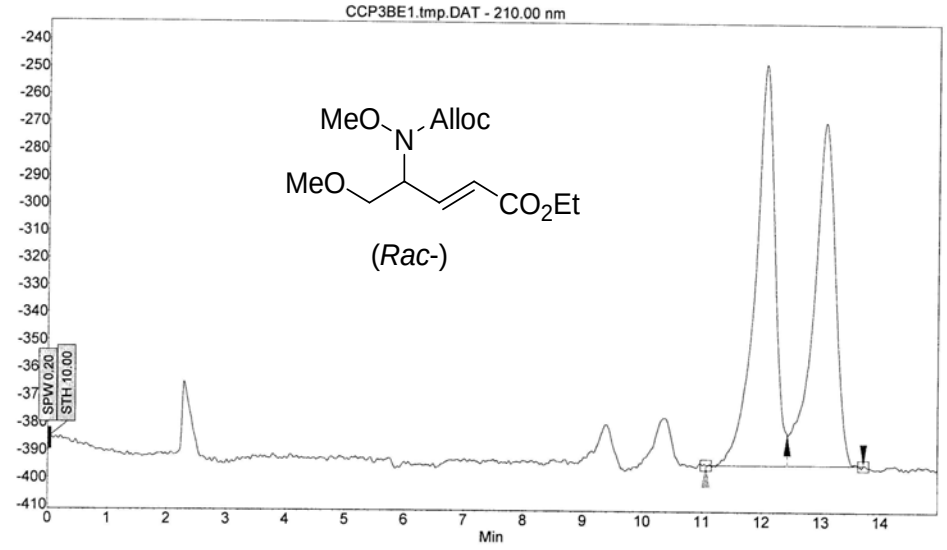


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.02	6.66	7.02	0.00	97.50	241.2	54.8	97.496
2	UNKNOWN	7.02	7.32	7.68	0.00	2.50	5.6	1.4	2.504
Total						100.00	246.7	56.2	100.000

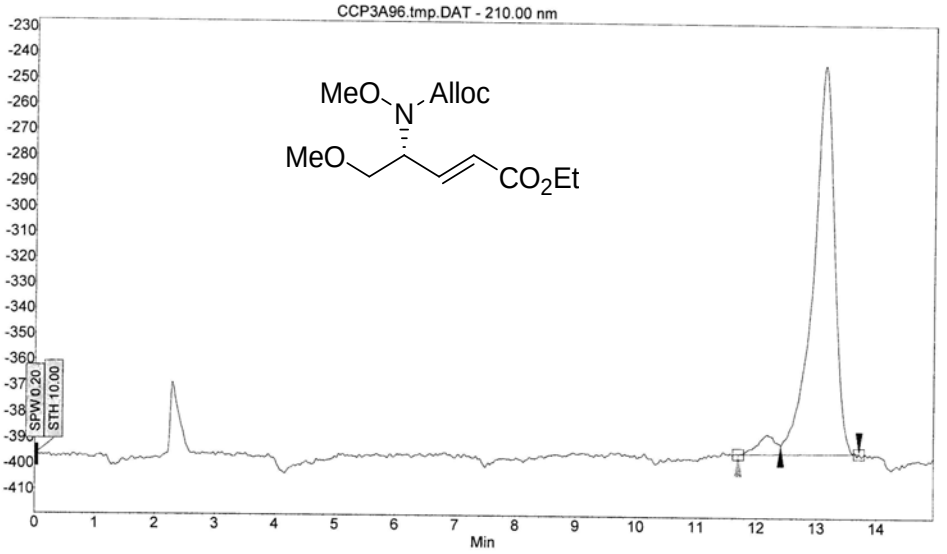


(Table 2, entry 7)

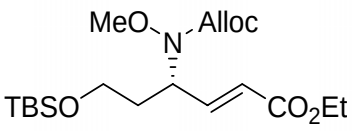




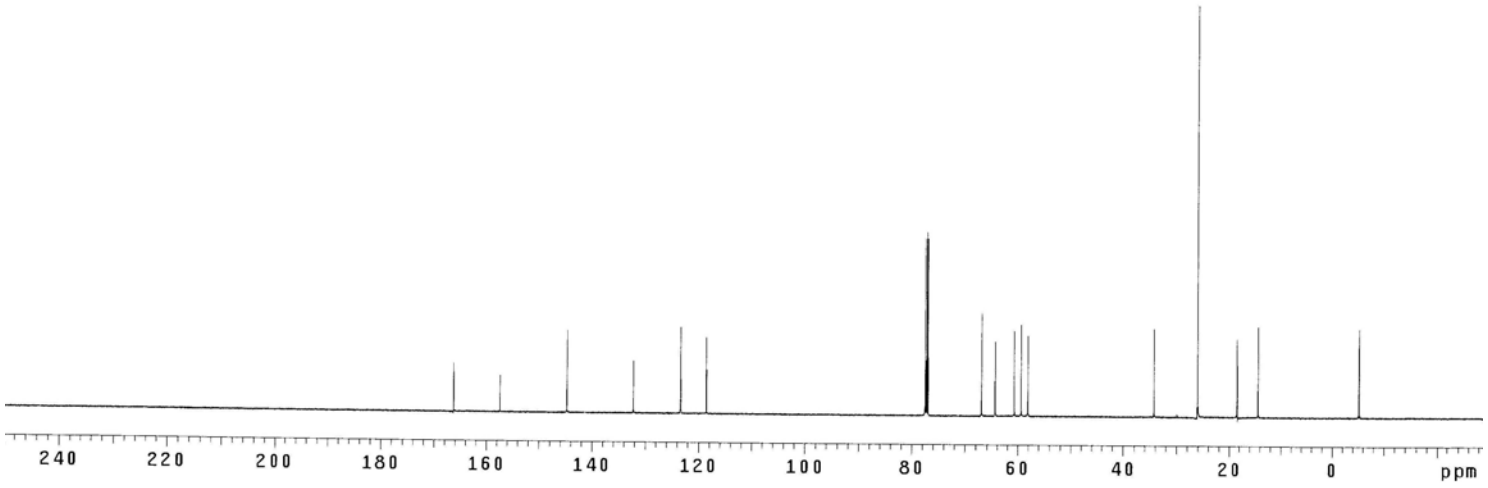
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.06	12.05	12.43	0.00	51.42	146.2	56.3	51.421
2	UNKNOWN	12.43	13.05	13.71	0.00	48.58	125.0	53.2	48.579
Total						100.00	271.2	109.4	100.000

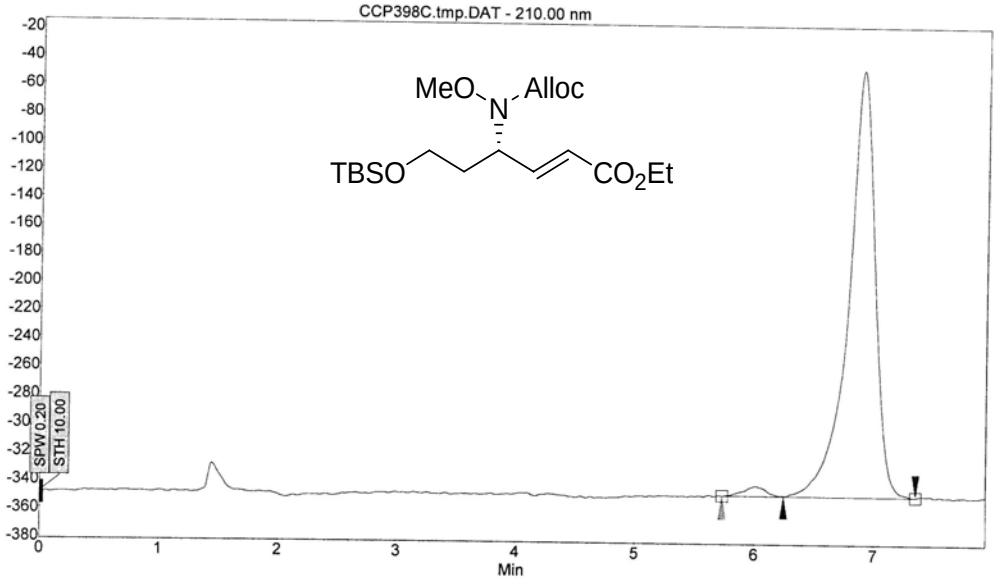


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.70	12.17	12.40	0.00	4.19	7.6	2.7	4.186
2	UNKNOWN	12.40	13.11	13.71	0.00	95.81	151.4	61.6	95.814
Total						100.00	159.0	64.3	100.000

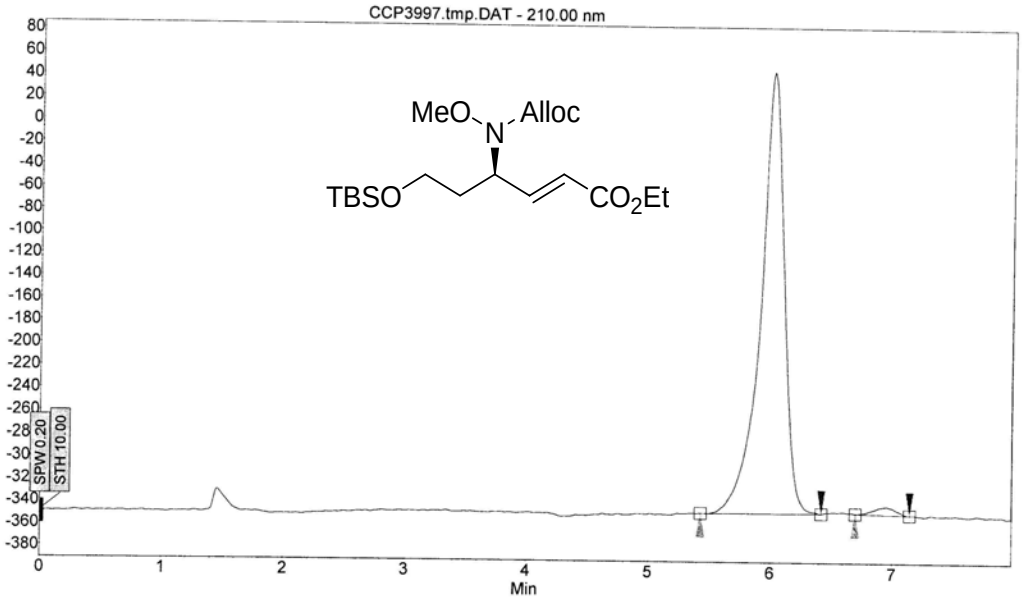


(Table 2, entry 8)

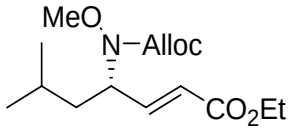




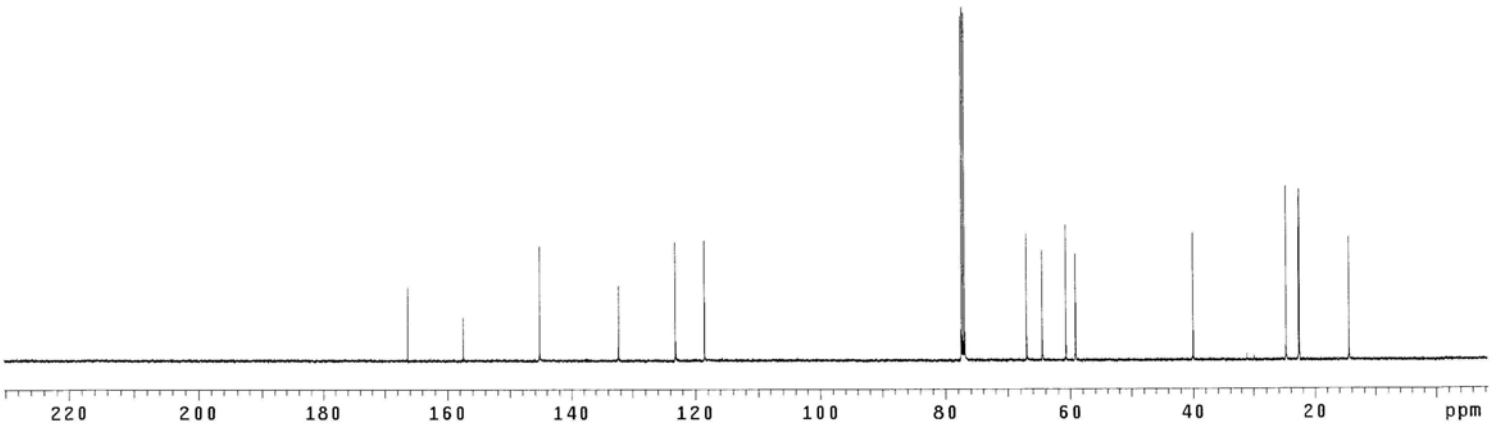
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.73	6.01	6.24	0.00	1.97	7.1	1.6	1.973
2	UNKNOWN	6.24	6.89	7.35	0.00	98.03	302.5	78.1	98.027
Total						100.00	309.6	79.7	100.000

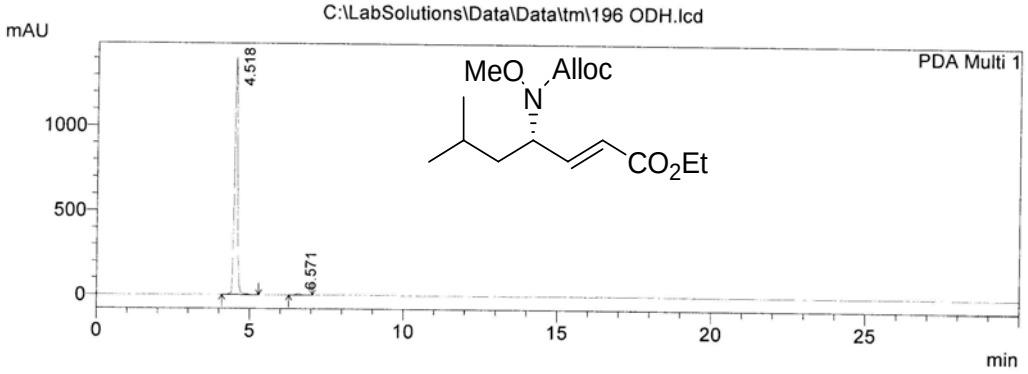


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.43	6.00	6.42	0.00	98.32	393.3	87.5	98.317
2	UNKNOWN	6.70	6.95	7.14	0.00	1.68	7.2	1.5	1.683
Total						100.00	400.5	89.0	100.000



(Table 2, entry 9)

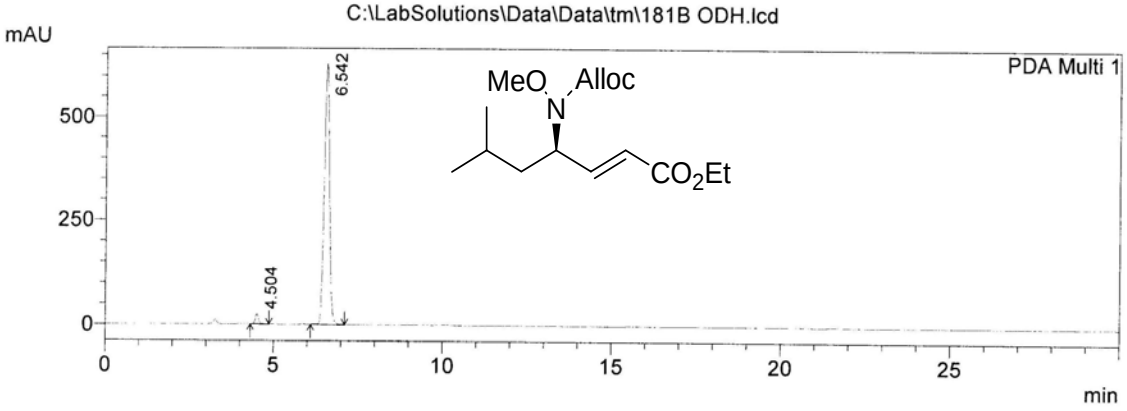




PeakTable

PDA Ch2 254nm 4nm

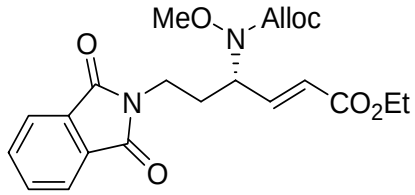
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.518	280280	40993	98.971	99.464
2	6.565	2913	221	1.029	0.536
Total		283193	41214	100.000	100.000



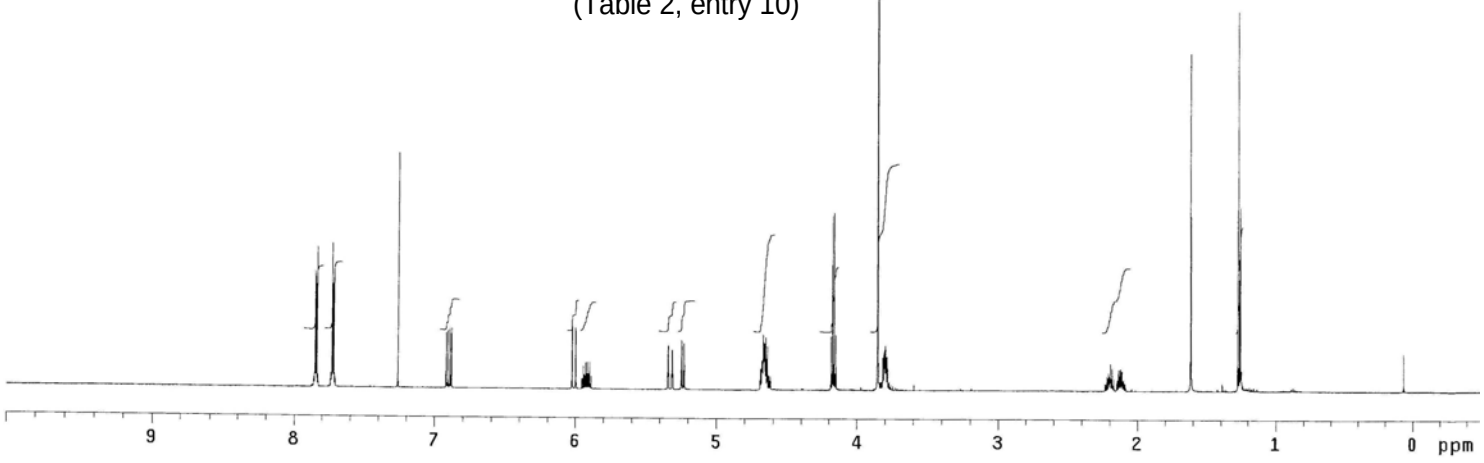
PeakTable

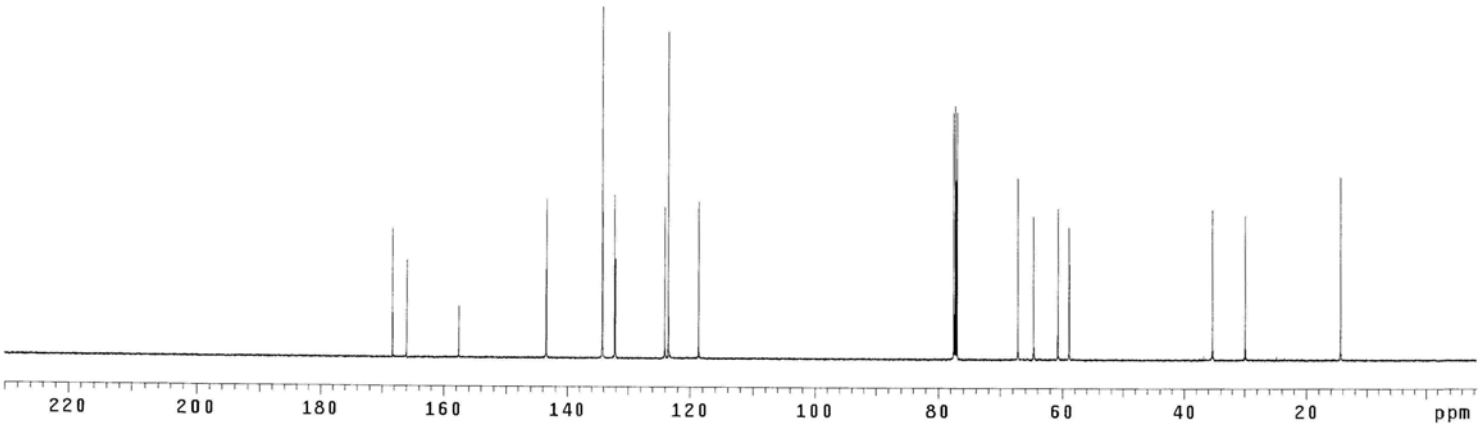
PDA Ch2 254nm 4nm

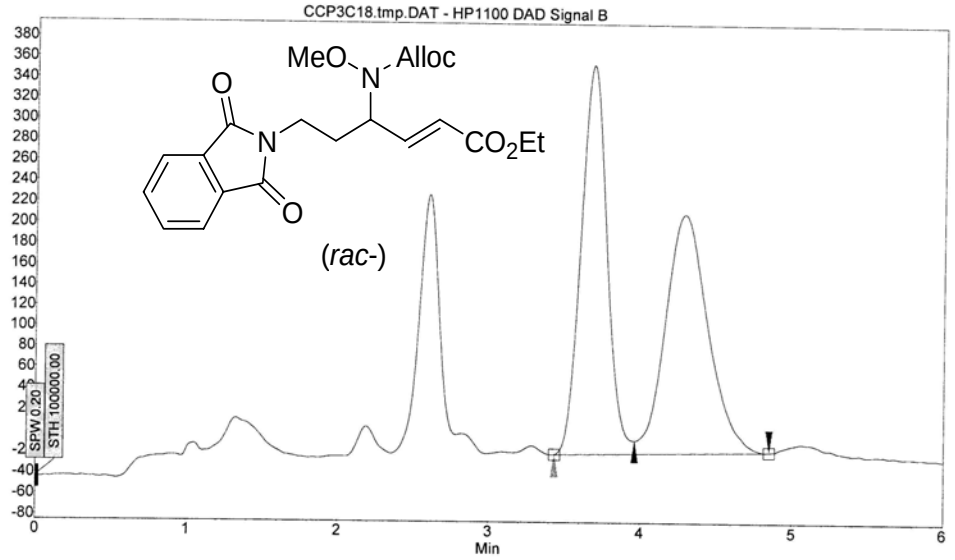
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.501	3560	567	1.888	3.192
2	6.542	185034	17189	98.112	96.808
Total		188594	17756	100.000	100.000



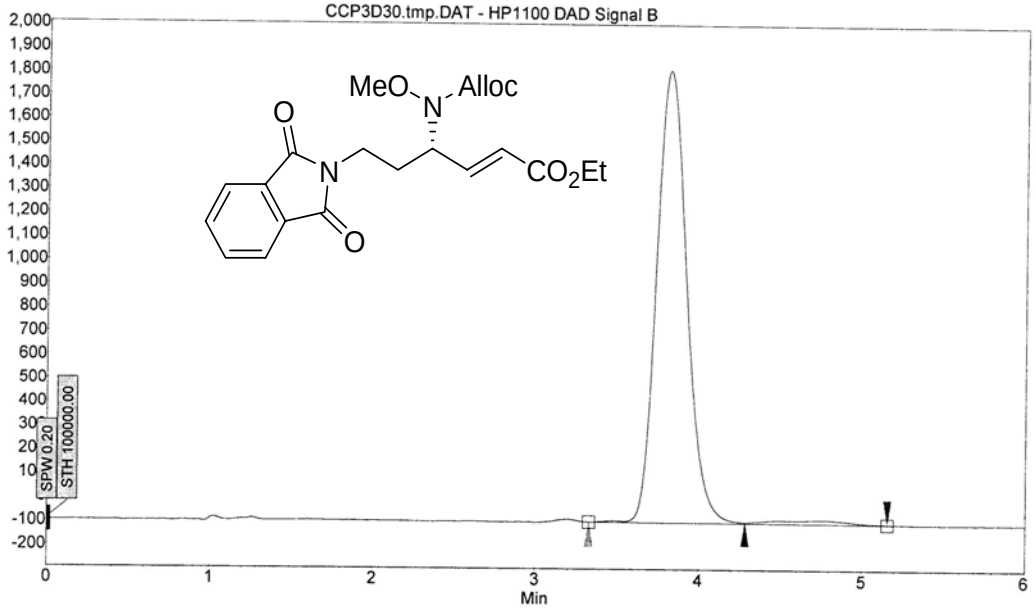
(Table 2, entry 10)



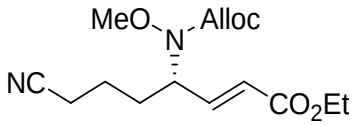




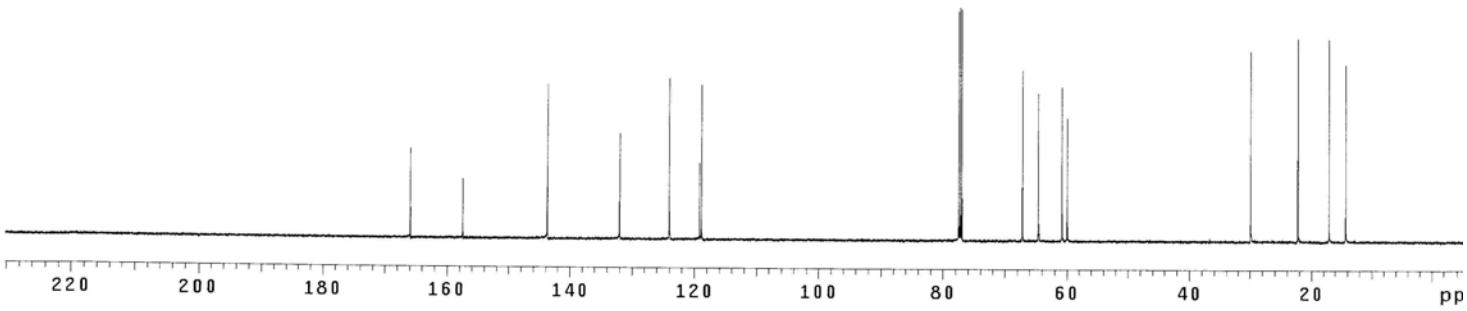
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.43	3.68	3.96	0.00	49.92	374.9	74.2	49.921
2	UNKNOWN	3.96	4.29	4.85	0.00	50.08	229.3	74.4	50.079
Total						100.00	604.2	148.6	100.000

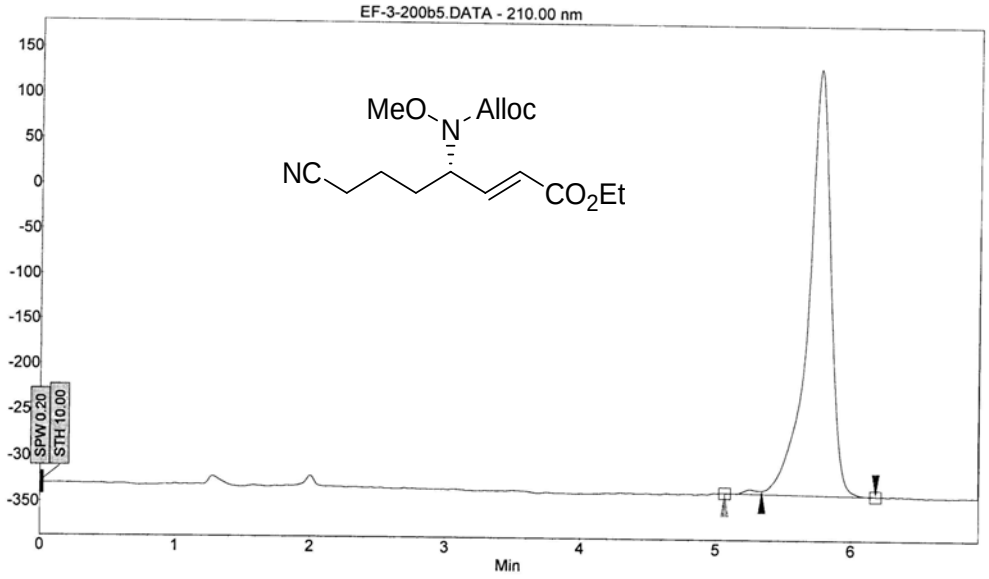


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.33	3.81	4.29	0.00	97.84	1913.1	407.3	97.837
2	UNKNOWN	4.29	4.75	5.16	0.00	2.16	17.0	9.0	2.163
Total						100.00	1930.1	416.3	100.000

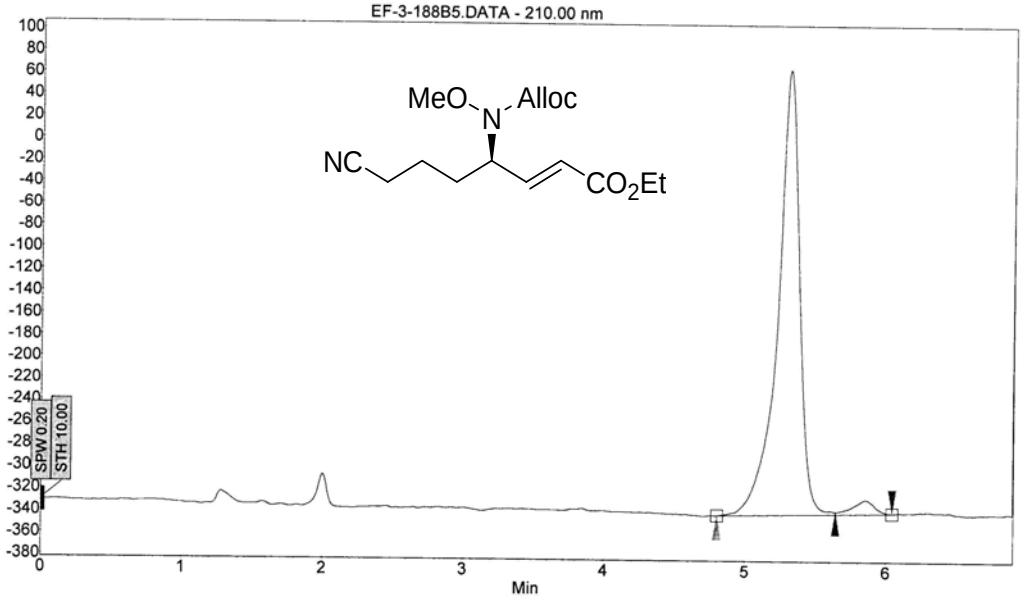


(Table 2, entry 11)

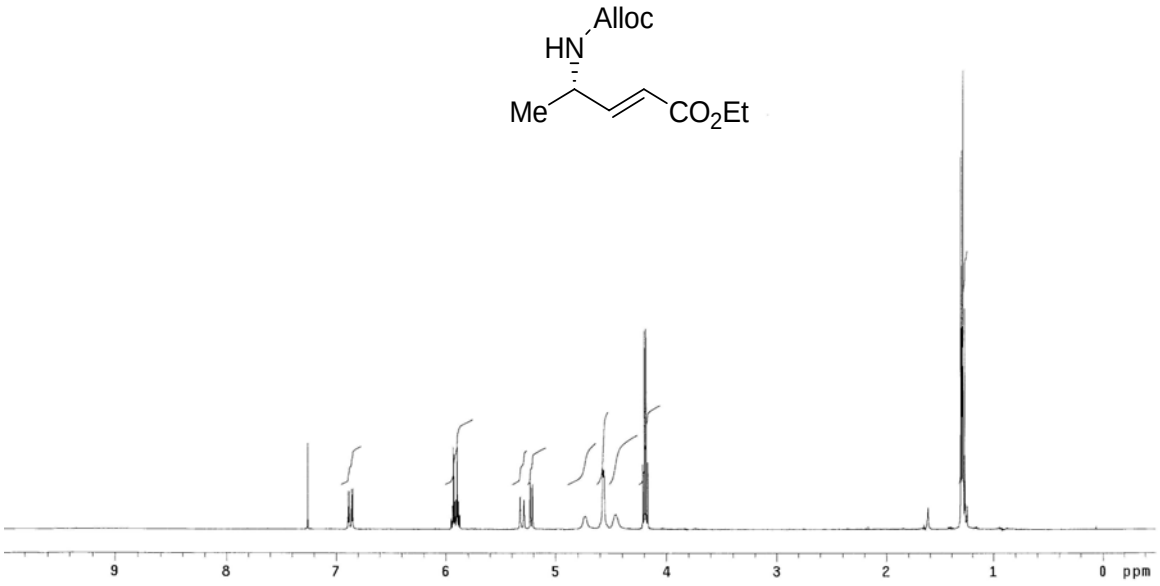


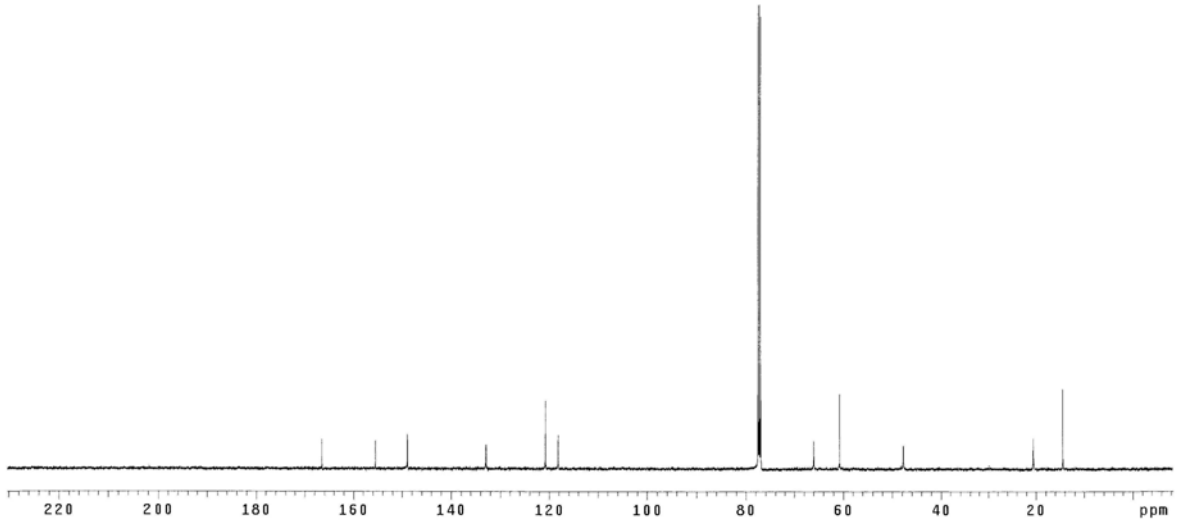


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.07	5.25	5.34	0.00	0.64	5.0	0.6	0.640
2	UNKNOWN	5.34	5.76	6.18	0.00	99.36	470.1	89.8	99.360
Total						100.00	475.1	90.3	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.80	5.30	5.64	0.00	96.87	406.3	72.3	96.870
2	UNKNOWN	5.64	5.85	6.04	0.00	3.13	12.6	2.3	3.130
Total						100.00	418.9	74.6	100.000


Alloc
HN
Me
CO2Et
9
8
7
6
5
4
3
2
1
0 ppm


220
200
180
160
140
120
100
80
60
40
20
ppm