Supporting Information

Enantioselective a-Allylation of Aryl Acetic Acid Esters via C1-Ammonium Enolate Nucleophiles: Identification of a Broadly Effective Palladium Catalyst for Electron-Deficient Electrophiles.

Luke Hutchings-Goetz,[#] Chao Yang[#] and Thomas. N. Snaddon[*]
Department of Chemistry, Indiana University, 800 E. Kirkwood Ave., Bloomington, Indiana 47405, United States.

Corresponding Author: tsnaddon@indiana.edu

General Information

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Unless otherwise noted, all reactions have been carried out with distilled and degassed solvents under an atmosphere of dry N_2 in flame or oven dried glassware with standard vacuum-line techniques. All reactions were carried out in Teflon screw cap reaction vials with magnetic stirring unless otherwise indicated. Dichloromethane, tetrahydrofuran, dioxane, and acetonitrile were purified under a positive pressure of dry argon by passage through two columns of activated alumina. Toluene was purified under a positive pressure of dry argon by passage through columns of activated alumina and Q5 (Grubbs apparatus). Tert-butyl methyl ether, cyclopentyl methyl ether, dimethoxy ethane, and 2-methyl tetrahydrofuran were dried and purified following the guidelines of Perrin and Armarego.[1] All workup and purification procedures were carried out with reagent grade solvents (purchased from Sigma-Aldrich) in air. Standard column chromatography techniques using ZEOprep 60/40-63 μm silica gel were used for purification. Liquids and solutions were transferred via syringe or cannula. Pd_2dba_3 obtained from Strem Chemical and used without further purification. All the starting pentafluorophenyl esters were obtained from group's inventory and verified pure.

^1H and ^{13}C NMR spectra were recorded at room temperature on Varian Inova-instrumentation: Varian I400 (^1H NMR at 400MHz and ^{13}C NMR at 100 MHz), Varian VXR400 (^1H NMR at 400 MHz and ^{13}C NMR at 100 MHz), and Varian I500 (^1H NMR at 500 MHz and ^{13}C NMR at 125 MHz) using deuterium lock. Data for ^1H NMR spectra are quoted relative to chloroform as an internal standard (7.26 ppm or 2.1 ppm) and data for ^{13}C NMR spectra are quoted relative to chloroform or as an internal standard (77.23 ppm or 128.39 ppm) and are reported in terms of chemical shift (δ ppm). Carbon signals of aryl pentafluorophenyl esters in ^{13}C NMR not observed due to fluorine splitting. Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). Infrared spectra (IR) were obtained on the Bruker TENSOR II FTIR Spectrometer and recorded in wavenumbers (cm^{-1}). Melting points were obtained on a Thomas Hoover capillary melting point apparatus without correction. High Resolution Mass (HRMS) analysis was obtained using Electron Impact Ionization (EI), Chemical Ionization (CI), Electrospray (ESI) and Atmospheric Pressure Chemical Ionization (APCI) and reported as m/z (relative intensity) for the $[M]^+$, $[M+H]^+$ or $[M+Na]^+$ molecular ion. Chiral HPLC analyses were performed on an Agilent 1200 Series system.

Experimental Section

Catalysts

(*R*)-(+)-Benzotetramisole, [(+)-BTM, CAS: 885051-07-0] and **(*S*)-(–)-Benzotetramisole** [(–)-BTM, CAS: 950194-37-3] were prepared from (R)-(–)-2-phenylglycinol or (S)-(+)-2-phenylglycinol, respectively, by the procedure of Smith and co-workers.[2]

Pd_2dba_3 [CAS: 51364-51-3] was obtained from Strem Chemical and used without further purification.

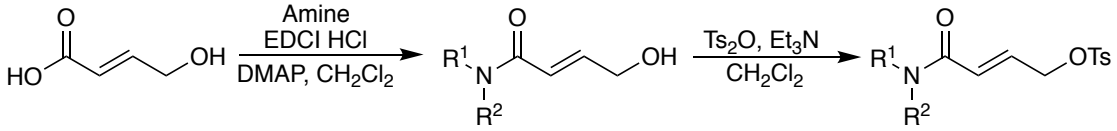
Pd Xantphos G3 was prepared by the procedure of Buchwald and co-workers.[3]

P(2-thienyl)$_3$ [CAS: 24171-89-9] was obtained from Alfa Aesar and used without further purification.

Tris[tri(2-thienyl)phosphine]palladium was prepared following the procedure of Bo and co-workers.[4]

Preparation of Allyl Tosylates

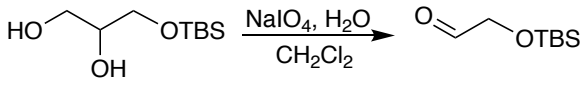
General Procedure A for preparation of amide substituted allylic tosylates:



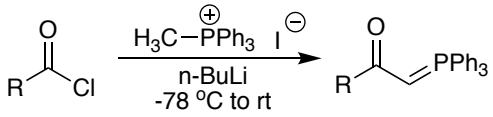
A 100 mL round bottom flask was charged with (*E*)-4-hydroxybut-2-enoic acid (510 mg, 5.0 mmol, 1.0 equiv.) the specified amine (5.5 mmol, 1.1 equiv.) and CH_2Cl_2 (50 mL). The resulting suspension was cooled to 0 °C, and *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide HCl (1.05 g, 5.5 mmol, 1.1 equiv.) followed by 4-dimethylaminopyridine (61 mg, 0.5 mmol, 0.1 equiv.) was added. The reaction was vigorously stirred and allowed to warm to room temperature over 16 hr. The reaction mixture was washed with 1 M HCl (2 × 20 mL), and brine (20 mL). The organic layer was dried with $MgSO_4$, concentrated under reduced pressure, and then used without further purification.

A 100 mL round bottom flask was charged with the crude residue, *p*-toluenesulfonic anhydride (1.8 g, 5.5 mmol, 1.1 equiv.), and CH_2Cl_2 (50 mL). The resulting solution was cooled to 0 °C in an ice bath, and triethylamine (557 mg, 0.767 mL, 5.5 mmol, 1.1 equiv.) was added dropwise over 5 min. The reaction was stirred and allowed to warm to room temperature over 2 hours. The reaction mixture was concentrated under reduced pressure, and purified immediately by column chromatography (silica gel, specified eluent).

General Procedure B for the preparation of ketone substituted allylic alcohols:

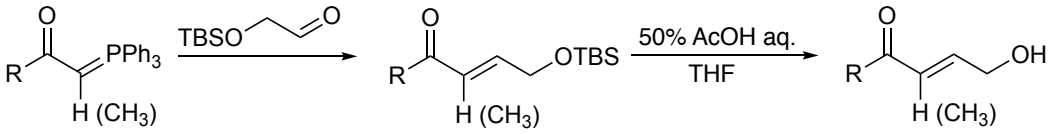


2-((tert-Butyldimethylsilyl)oxy)acetaldehyde: *Using a modification of the procedure of Casey and co-workers*.[12] Add the solution of monoprotected glycerol (8.3 g, 40 mmol) in DCM (60 mL) to a vigorously stirred solution of $NaIO_4$ (12.83 g, 60 mmol) in water (60 mL). The reaction was monitored by ^1H NMR until disappearance of the starting material (generally 2 hours). The organic layer was separated and washed with brine and dried over $MgSO_4$, concentrated under reduced pressure to give colorless oil (6.9 g, 40 mmol, 99% yield). No further purification was needed.



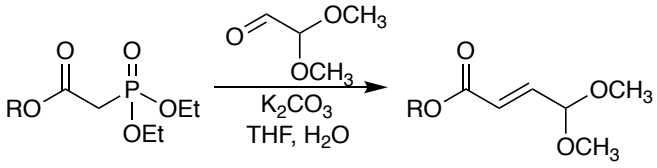
Preparation of α-Triphenyl phosphonium ylide: *Using a modification of the procedure of Atherton and co-workers*.[13] To a vigorously stirred suspension of methyl triphenylphosphonium iodide (16.2 g, 40

mmol) in 200 mL THF under N_2 at −78 °C was added nBuLi (2.5 M in hexane, 19.2 mL, 48 mmol) via syringe pump over 30 min. Acyl chloride (20 mmol) in 20 mL THF was added at the same temperature over 15 min. Then the reaction was allowed to warm to room temperature and stirred overnight. Upon completion, THF was remove under reduced pressure. The dark residue was dissolved in EtOAc and washed with water and brine, dried over $MgSO_4$ and concentrated to give crude ylide products. These ylide compounds should be stored in the freezer or used right away.

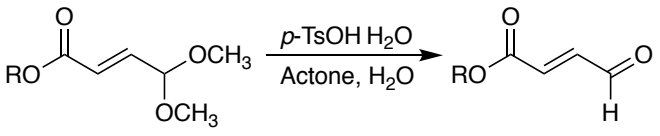


Preparation of Allylic Alcohol: *Using a modification of the procedure of Atherton and co-workers and of Casey and co-workers*.[12,13] The 2-((tert-Butyldimethylsilyl)oxy)acetaldehyde (20 mmol) and the appropriate ketone substituted α-triphenyl phosphonium ylide (21 mmol, 1.05 equiv.) were mixed in THF (100 mL) under N_2 and stirred at 70 °C overnight. The reaction was concentrated and filtered through a short path silica gel column [Petroleum ether: EtOAc, 95:5]. The fractions were collected and concentrated. The crude product in 20 ml THF was transferred to a stirred solution of 50% AcOH (60 mL). The deprotection of TBS usually takes 2-6 hours. The reaction was diluted with 100 ml water and basified with $NaHCO_3$ until pH = 8. The aqueous solution was extracted with EtOAc (100 mL × 3) and the combined organic phase was dried over $MgSO_4$, concentrated to give a colorless oil following purification by column chromatography (silica gel, specified eluent).

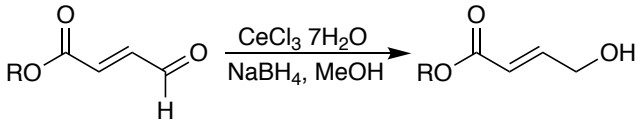
General Procedure C for the preparation of ester substituted allylic alcohols:



Preparation of α,β-unsaturated dimethoxyacetal: *Using a modification of the procedure of Vasudevan and co-workers*.[5] To a solution of R substituted diethylphosphonoacetate (10 mL, 50 mmol, 1.0 equiv.) and dimethoxyacetaldehyde (60% aqueous solution, 7.5 mL, 55 mmol, 1.1 equiv.) in 100 mL THF/H_2O (0.4 M, 7:1, v/v) was added K_2CO_3 (8.3 g, 55 mmol, 1.1 equiv.). The resulting mixture was stirred at room temperature for 4 hours. Upon completion, the reaction was poured into Et_2O (3 mL/mmol) and extracted. The organic layer was separated and washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude mixture can be used in the next step without any purification.

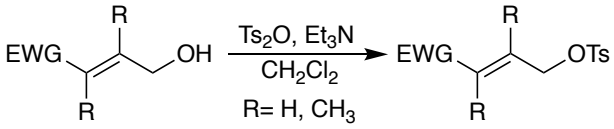


Preparation of α,β-unsaturated aldehyde: *Using a modification of the procedure of Sakai and co-workers*.[6] To a solution of α,β-unsaturated dimethoxyacetal (30 mmol) in 100mL acetone/water (0.3M, 1:1, v/v) was added *p*-toluenesulfonic acid (0.1 eq.). The reaction solution was stirred at 50°C for 2 hours. Once full consumption of the starting material was indicated by ^{1}H NMR, acetone was evaporated under reduced pressure. To the crude mixture was added sat. $NaHCO_3$ (50 mL) and extracted with Et_2O (50 mL × 3). The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was found pure by ^{1}H NMR and can be used for the next step without further purification.

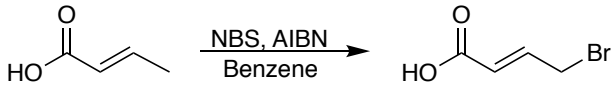


Preparation of α,β-unsaturated alcohol: To a solution of α,β-unsaturated aldehyde (10 mmol) and $CeCl_3$•$7H_2O$ (10 mmol, 3.8 g) in 100 mL methanol was added $NaBH_4$ (10 mmol, 0.4 g) slowly at 0°C and stirred for 30 min. The reaction was quenched by adding 1M HCl at 0 °C until effervescence ceased. Methanol was evaporated and the aqueous solution was extracted with EtOAc (50 mL × 3). The combined organic layer was washed with sat. $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated. The crude product was purified by column chromatography (silica gel, specified eluent).

General Procedure D for tosylation of allylic alcohols:

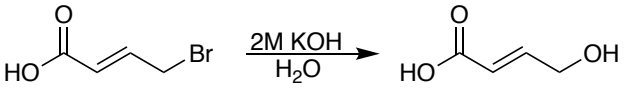


To a stirred solution of specified allylic alcohol (5.0 mmol, 1.0 equiv.) and *p*-toluenesulfonic anhydride (1.8 g, 5.5 mmol, 1.1 equiv.) in CH_2Cl_2 (50 mL) was added triethylamine (557 mg, 0.767 mL, 5.5 mmol, 1.1 equiv.) dropwise over 5 min. The reaction was stirred and allowed to warm to room temperature over 2 hours. The reaction mixture was concentrated under reduced pressure, and purified immediately by column chromatography (silica gel, specified eluent).



(*E*)-4-Bromobut-2-enoic acid (S1): *Using a modification of the procedure of Dixon and co-workers*.[17] A 500 mL round bottom flask was charged with crotonic acid (10.0 g, 116 mmol, 1.0 equiv.), *N*-bromosuccinaimide, (21.4 g, 120 mmol, 1.03 equiv.), Azobisisobutyronitrile (330 mg, 2.01 mmol, 0.016 equiv.), and benzene (100 mL). The resulting suspension was refluxed at 85 °C for 2 hours, cooled to 6 °C, and filtered through celite. The celite was washed with 50 mL of cold toluene, and the combined filtrates were concentrated under reduced pressure. The residue was extracted with refluxing hexanes

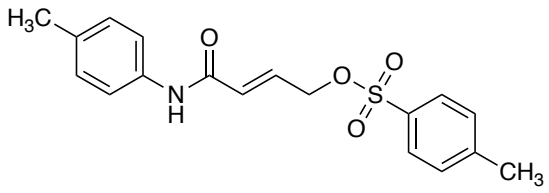
(100 mL × 4). The combined extracts were concentrated and recrystallized from hexane to give the title compound as a white colorless solid (8.14 g, 49.3 mmol, 43%).



(*E*)-4-Hydroxybut-2-enoic acid (S2): *Using a modification of the procedure of Charlier and co-workers*.[19] In a 500 mL round bottom flask (*E*)-4-bromobut-2-enoic acid (8.0 g, 48.5 mmol, 1.0 equiv.) was dissolved in water (80 mL) and cooled to 0 °C. Aqueous KOH (2 M, 162 mL) was added dropwise to the stirring reaction mixture. The solution was refluxed at 120 °C for 1.5 hours, then concentrated under reduced pressure. The residue was purified by column chromatography [SiO_2, EtOAc-MeOH, 97:3] to give the title compound (3.03 g, 29.7 mmol, 61%.).

^{1}H NMR (400 MHz, CD_3OD): δ 6.99 (dt, *J* = 15.7, 3.9 Hz, 1H), 6.01 (dt, *J* = 15.6, 2.2 Hz, 1H), 4.22 (dd, *J* = 3.9, 2.2 Hz, 2H).
Spectroscopic data was consistent with literature report.[19]

(***E*)-4-Oxo-4-(*p*-tolylamino)but-2-en-1-yl 4-methylbenzenesulfonate (S3):** Prepared according to General Procedure A. The *title compound* was obtained (1.02 g, 2.95 mmol, 59%) as white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 60:40].



M.p. (Et_2O, plates) = 104–106 °C.

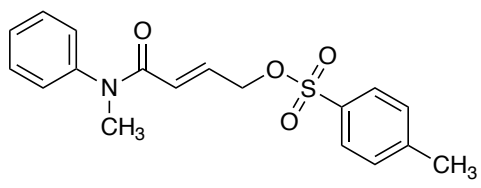
IR (neat): 3346, 3017, 2970, 2953, 2931, 2836, 1740, 1679, 1643, 1598, 1525, 1351, 1172, 921, 815, 587, 550 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 9.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.33 (s, 1H), 6.92 – 6.81 (m, 3H), 6.23 (dt, *J* = 15.2, 2.0 Hz, 1H), 4.73 (dd, *J* = 4.4, 1.9 Hz, 2H), 3.81 (s, 3H), 2.47 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 162.2, 156.7, 145.3, 135.6, 132.6, 130.7, 130.1, 128.0, 125.7, 121.7, 114.2, 68.1, 55.5, 21.7.

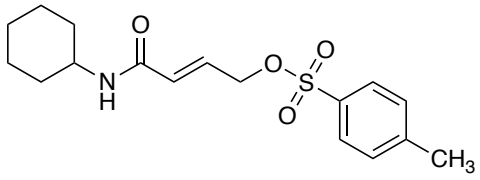
HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{18}H_{20}NO_4S$: 346.1113 Found: 346.1100.

(*E*)-4-(Methyl(phenyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S4): Prepared according to General Procedure A using *N*-methyl aniline. The *title compound* was obtained (484 mg, 1.4 mmol, 28%) as a clear colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20].



Unable to obtain characterization compound degrades quickly upon isolation. Used immediately after chromatography.

(*E*)-4-(Cyclohexylamino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S5): Prepared according to General Procedure A using cyclohexylamine. The *title compound* was obtained (709 mg, 2.1 mmol, 42%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 60:40].



M.p. (Et_2O, plates) = 98–101 °C.

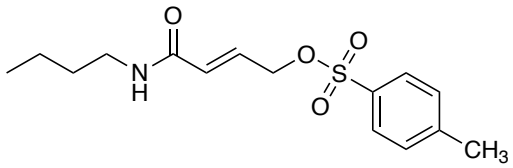
IR (neat): 3277, 3082, 2932, 2923, 2853, 1674, 1557, 1348, 932, 814, 765, 659, 529 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.1 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.67 (dt, *J* = 15.2, 4.4 Hz, 1H), 6.03 – 5.95 (m, 1H), 5.34 (s, 1H), 4.64 (dd, *J* = 4.4, 1.9 Hz, 2H), 3.85 – 3.74 (m, 1H), 2.44 (s, 3H), 1.95 – 1.86 (m, 2H), 1.75 – 1.64 (m, 2H), 1.64 – 1.53 (m, 2H), 1.35 (m, 2H), 1.12 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.4, 145.2, 134.2, 132.6, 130.0, 127.9, 126.0, 68.1, 48.4, 33.0, 25.4, 24.8, 21.6.

HRMS (Cl): *m/z* calcd for $[M+Na]^+$ $C_{17}H_{23}NO_4NaS$: 360.1245 Found: 360.1257.

(*E*)-4-(Butylamino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S6): Prepared according to General Procedure A using *n*-butyl amine. The *title compound* was obtained (810 mg, 2.6 mmol, 51%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 60:40].



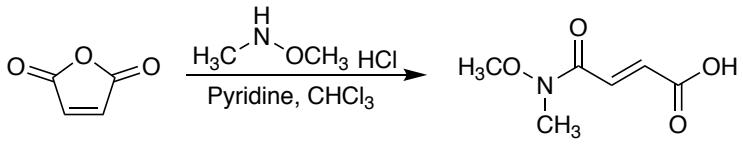
M.p. (Et_2O, plates) = 92–93 °C.

IR (neat): 3276, 3081, 2958, 2931, 2872, 1678, 1630, 1598, 1547, 1446, 1357, 1173, 1096, 920, 813, 730, 662, 552 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 7.9 Hz, 2H), 6.69 (dt, *J* = 15.2, 4.4 Hz, 1H), 6.01 (dt, *J* = 15.2, 2.0 Hz, 1H), 5.45 (s, 1H), 4.64 (dd, *J* = 4.5, 1.9 Hz, 2H), 3.29 (td, *J* = 7.1, 5.8 Hz, 2H), 2.44 (s, 3H), 1.53 – 1.44 (m, 2H), 1.38 – 1.28 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).

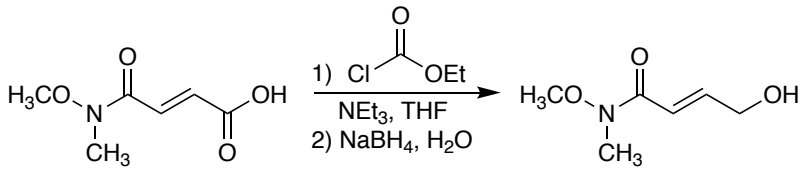
^{13}C NMR (126 MHz, $CDCl_3$): δ 164.3, 145.2, 134.4, 132.7, 130.0, 127.9, 125.7, 68.1, 39.4, 31.5, 21.7, 20.0, 13.7.

HRMS (Cl): *m/z* calcd for $[M+H]^+$ $C_{15}H_{22}NO_4S$: 312.1264 Found: 312.1264.



(*E*)-4-(Methoxy(methyl)amino)-4-oxobut-2-enoic acid (S7): *Using a modification of the procedure of Udodong and co-workers*.[20] A 500 mL round bottom flask was charged with maleic anhydride (10 g, 102 mmol, 1.0 equiv.), *N*,*O*-dimethylhydroxylamine HCl (10.9 g, 112 mmol, 1.1 equiv.), and $CHCl_3$ (150 mL). The resulting solution was cooled to 0 °C, and pyridine (181 mL, 224 mmol, 2.2 equiv.) was added slowly over 10 min. The reaction was warmed to room temperature and stirred for 24 hours. The residue was concentrated under reduced pressure, diluted with brine (30 mL), water (30 mL), and then extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed with (45 mL) of brine, dried with $MgSO_4$, and concentrated under reduced pressure to afford a solid residue. The *title compound* was obtained (7.62 g, 47.9 mmol, 57%) as a white solid following recrystallization in diethyl ether.

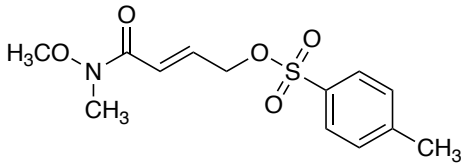
^{1}H NMR (400 MHz, $CDCl_3$): δ 11.40 (s, 1H), 7.50 (d, *J* = 15.6 Hz, 1H), 6.88 (d, *J* = 15.6 Hz, 1H), 3.73 (s, 3H), 3.28 (s, 3H).



(*E*)-4-Hydroxy-*N*-methoxy-*N*-methylbut-2-enamide (S8): In a 250 mL round bottom flask (*E*)-4-(Methoxy(methyl)amino)-4-oxobut-2-enoic acid (1.59 g, 10 mmol, 1.0 equiv.) was dissolved into THF (25 mL), and cooled to 0 °C. Triethylamine (1.01 g, 0.89 mL, 11 mmol, 1.1 equiv.) followed by ethyl chloroformate (1.09 g, 0.96 mL, 11 mmol, 1.1 equiv.) was added dropwise over 15 min to the stirring reaction mixture. The resulting slurry was vigorously stirred for 1 hour. The cold reaction mixture was filtered, and the filter cake was washed with THF (25 mL). The combined filtrates were added dropwise over 30 min to a vigorously stirring solution of $NaBH_4$ (946 mg, 25 mmol, 2.5 equiv.) in water (15 mL). The reaction was stirred for an additional 45 min. The reaction was quenched with aqueous HCl (1 M, 10 mL), extracted with ethyl acetate (3 × 75 mL), dried with $MgSO_4$, concentrated under reduced pressure. The *title compound* was obtained (685 mg, 4.7 mmol, 47%) as a colorless clear oil following purification by column chromatography [SiO_2, CH_2Cl_2–Acetone, 70:30].

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (dt, *J* = 15.5, 3.9 Hz, 1H), 6.58 (dt, *J* = 15.5, 2.2 Hz, 1H), 4.26 (dd, *J* = 4.0, 2.1 Hz, 2H), 3.62 (s, 3H), 3.16 (s, 3H).
Spectroscopic data was consistent with literature report.[20]

(*E*)-4-(Methoxy(methyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S9): Prepared according to General Procedure A. The *title compound* was obtained (1.11 g, 3.7 mmol, 74.00 %) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 70:30].



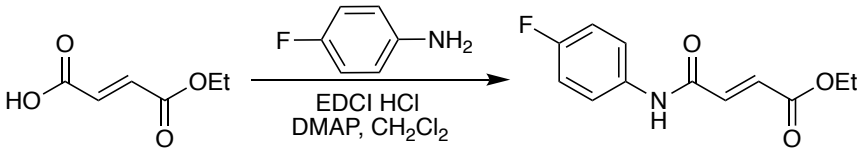
M.p. (Et_2O, plates) = 56–57 °C.

IR (neat): 3024, 2970, 2926, 1738, 1367, 1217, 668, 459 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.36 – 7.30 (m, 2H), 6.78 (dt, *J* = 15.4, 4.6 Hz, 1H), 6.62 (d, *J* = 15.6 Hz, 1H), 4.69 (dd, *J* = 4.6, 1.8 Hz, 2H), 3.66 (s, 3H), 3.21 (s, 3H), 2.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.1, 137.0, 132.7, 129.94, 127.9, 121.0, 68.3, 61.9, 21.6.

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{13}H_{18}NO_5S$: 300.0900 Found: 300.0895.



Ethyl (*E*)-4-((4-fluorophenyl)amino)-4-oxobut-2-enoate (S10): A 250 mL round bottom flask was charged with (*E*)-4-ethoxy-4-oxobut-2-enoic acid (6.0 g, 41.63 mmol, 1.0 equiv.), 4-fluoroaniline (6.48 g, 5.52 mL, 58.28 mmol, 1.4 equiv.), and CH_2Cl_2 (100 mL). The resulting suspension was cooled to 0 °C in an ice bath, and *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide HCl (10.37 g, 54.11 mmol, 1.3 equiv.) followed by 4-dimethylaminopyridine (508 mg, 4.16 mmol, 0.1 equiv.) was added. The suspension was vigorously stirred and warmed to room temperature over 16 hours. The reaction was washed with 1 M HCl (2 × 50 mL), and brine (2 × 50 mL). The organic layer was dried with $MgSO_4$, concentrated under reduced pressure. The *title compound* was obtained (7.22 g, 28.7 mmol, 69%) as a pale yellow solid following recrystallization in diethyl ether.

M.p. (Et_2O, needles) = 151–153 °C.

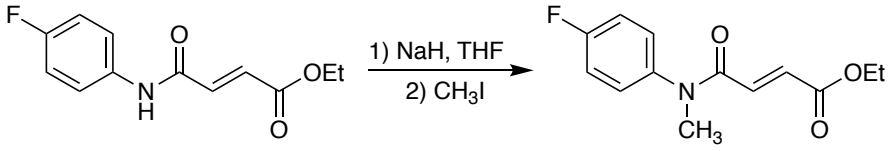
IR (neat): 3302, 3076, 2990, 2945, 2905, 1717, 1670, 1644, 1547, 1506, 1295, 1203, 982, 835, 691, 543, 518, 465 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ 7.64 (dd, *J* = 9.1, 4.8 Hz, 2H), 7.15 (d, *J* = 15.4 Hz, 1H), 7.05 (t, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 15.4 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, CD_3OD): δ 165.3, 162.4, 159.5 (d, *J* = 242.9 Hz), 136.5, 134.3, 130.2, 121.6 (d, *J* = 7.9 Hz), 115.0 (d, *J* = 22.8 Hz), 60.9, 13.0.

^{19}F NMR (376 MHz, CD_3OD): δ -119.55 (tt, *J* = 8.7, 4.8 Hz).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{12}H_{13}FNO_3$: 238.0874 Found: 238.0869.



Ethyl (*E*)-4-((4-fluorophenyl)(methyl)amino)-4-oxobut-2-enoate (S11): A flame dried 210 mL resealable pressure tube was charged with 60% sodium hydride in mineral oil (927 mg, 23.2 mmol, 1.1 equiv.). The tube was purged and back filled three times with nitrogen, filled with anhydrous THF (50 mL), and cooled to 0 °C. The resulting suspension was vigorously stirred while a solution of ethyl (*E*)-4-((4-fluorophenyl)amino)-4-oxobut-2-enoate (5.0 g, 21.1 mmol, 1.0 equiv.) in THF (50 mL) was added dropwise over 20 min. Once gas expulsion had ceased (45 min), the suspension was warmed to room temperature, methyl iodide was added (3.29 g, 1.44 mL, 23.2 mmol, 1.1 equiv.), and the tube was hermetically sealed. The suspension was heated at 80 °C for 16 hours while being vigorously stirred. The mixture was cooled to room temperature, and slowly quenched with saturated aqueous NH_4Cl (40 mL). The solution was extracted with diethyl ether (3 × 100 mL), dried with $MgSO_4$, and concentrated under reduced pressure. The *title compound* was obtained (5.30 g, 10.3 mmol, 49%) as a clear oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20].

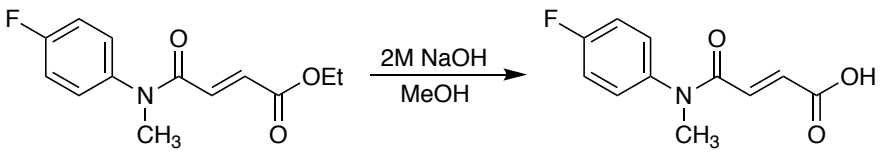
IR (neat): 3069, 2982, 2940, 2906, 1719, 1660, 1637, 1506, 1370, 1295, 1223, 1174, 1122, 1095, 1025, 973, 844, 728, 597, 566 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 – 7.02 (m, 4H), 6.79 (d, *J* = 15.2 Hz, 1H), 6.76 (d, *J* = 15.2 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.29 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.4, 163.9, 161.8 (d, *J* = 248.6 Hz), 138.6 (d, *J* = 3.3 Hz), 133.7, 131.2, 128.8 (d, *J* = 8.8 Hz), 116.8 (d, *J* = 23.0 Hz), 61.0, 37.7, 14.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -112.84 (td, *J* = 8.0, 3.9 Hz).

HRMS (CI): *m/z* calcd for $[M+Na]^+$ $C_{13}H_{14}NF_5O_3Na$: 274.0850 Found: 274.0846.



(*E*)-4-((4-Fluorophenyl)(methyl)amino)-4-oxobut-2-enoic acid (S12): A 250 mL round bottom flask was charged with ethyl (*E*)-4-((4-fluorophenyl)(methyl)amino)-4-oxobut-2-enoate (2.45 g, 9.75 mmol, 1.0 equiv.), methanol (50 mL), and aqueous sodium hydroxide (2 M, 15 mL). The resulting solution was stirred for 2 hours, acidified to pH of 2 with HCl (1 M), and extracted with ethyl acetate (3 × 100 mL). The organic layer was dried with $MgSO_4$ and concentrated under reduced pressure. The *title compound* was obtained (1.81 g, 8.1 mmol, 83%) as a pale yellow solid following recrystallization in diethyl ether.

M.p. (Et_2O, needles) = 149–151 °C.

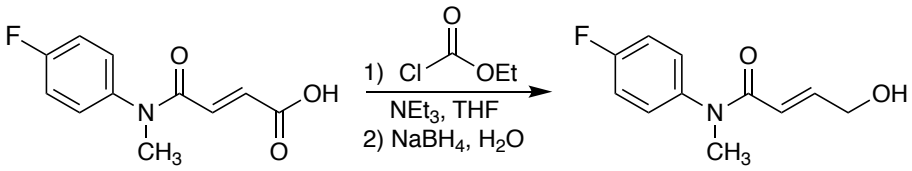
IR (neat): 3459, 3080, 2944, 2235, 2083, 1704, 1659, 1614, 1505, 1438, 1391, 1351, 1307, 1221, 1049, 988, 923, 849, 627, 596, 567 cm^{-1}.

^1H NMR (400 MHz, CD_3OD): δ 7.35 – 7.28 (m, 2H), 7.20 (t, *J* = 8.5 Hz, 2H), 6.76 (d, *J* = 15.2 Hz, 1H), 6.66 (d, *J* = 15.3 Hz, 1H), 3.32 (s, 3H).

^{13}C NMR (101 MHz, CD_3OD): δ 166.7, 164.6, 162.1 (d, *J* = 247.2 Hz), 138.6, 133.7, 131.1, 129.0 (d, *J* = 8.8 Hz), 116.4 (d, *J* = 23.1 Hz), 36.7.

^{19}F NMR (376 MHz, CD_3OD): δ -114.89 (tt, *J* = 8.7, 5.0 Hz).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{11}H_{11}FO_3N$: 224.0717 Found: 224.0712.



(*E*)-*N*-(4-Fluorophenyl)-4-hydroxy-*N*-methylbut-2-enamide (S13): In a 250 mL round bottom flask (*E*)-4-((4-Fluorophenyl)(methyl)amino)-4-oxobut-2-enoic acid (2.23 g, 10 mmol, 1.0 equiv.) was dissolved into THF (25 mL), and cooled to 0 °C. Triethylamine (1.01 g, 0.89 mL, 11 mmol, 1.1 equiv.) followed by ethyl chloroformate (1.09 g, 0.96 mL, 11 mmol, 1.1 equiv.) was added dropwise over 15 min to the stirring reaction mixture. The resulting slurry was vigorously stirred for 1 hour. The cold reaction mixture was filtered, and the filter cake was washed with THF (25 mL). The combined filtrates were added dropwise over 30 min to a vigorously stirring solution of $NaBH_4$ (946 mg, 25 mmol, 2.5 equiv.) in water (15 mL). The reaction was stirred for an additional 45 min. The reaction was quenched with aqueous HCl (1 M, 10 mL), extracted with ethyl acetate (3 × 75 mL), dried with $MgSO_4$, concentrated under reduced pressure. The *title compound* was obtained (1.53 g, 7.3 mmol, 73%) as a colorless clear oil following purification by column chromatography [SiO_2, CH_2Cl_2: Acetone, 70:30].

IR (neat): 3374, 3071, 3053, 2913, 2860, 1662, 1619, 1381, 1222, 1096, 908, 843, 725, 562 cm^{-1}.

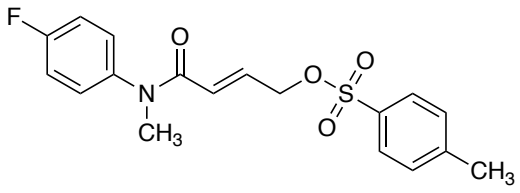
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.02 – 6.97 (m, 4H), 6.91 (t, *J* = 8.5 Hz, 1H), 6.73 (dt, *J* = 15.2, 4.1 Hz, 1H), 5.81 (d, *J* = 15.2 Hz, 1H), 3.97 (dd, *J* = 4.2, 2.1 Hz, 2H), 3.10 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 166.1, 161.4 (d, *J* = 247.5 Hz), 145.1, 139.2 (d, *J* = 3.2 Hz), 128.9 (d, *J* = 8.6 Hz), 119.2, 116.4 (d, *J* = 22.8 Hz), 61.4, 37.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -113.72 (t, *J* = 7.0 Hz).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{11}H_{13}NF_5O_2$: 210.0925 Found: 210.0921.

(*E*)-4-((4-Fluorophenyl)(methyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S14): Prepared according to General Procedure D. The *title compound* was obtained (636 mg, 1.8 mmol, 35%) as a white solid following purification by column chromatography [SiO_2, Petroleum–EtOAc, 80:20].



M.p. (Et_2O, needles) = 96–98 °C.

IR (neat): 3052, 2927, 1669, 1598, 1508, 1358, 1175, 914, 814, 726, 552 cm^{-1}.

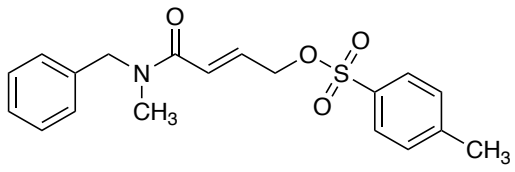
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.10 – 7.03 (m, 4H), 6.72 (dt, *J* = 15.2, 5.0 Hz, 1H), 5.90 (d, *J* = 15.2 Hz, 1H), 4.53 (dd, *J* = 5.1, 1.9 Hz, 2H), 3.26 (s, 3H), 2.40 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.5, 161.7 (d, *J* = 248.0 Hz), 159.4, 145.1, 139.0 (d, *J* = 3.9 Hz), 135.8, 132.7, 129.9, 128.9 (d, *J* = 9.8 Hz), 127.8, 123.6, 116.6 (d, *J* = 23.0 Hz), 68.1, 37.6, 21.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -113.16 (p, *J* = 6.6 Hz).

HRMS (CI): *m/z* calcd for $[M+Na]^+$ $C_{18}H_{18}FNNaO_4S$: 386.0838 Found: 386.0838.

(*E*)-4-(Benzyl(methyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S15): Prepared according to General Procedure A using *N*-methyl benzyl amine. The *title compound* was obtained (1.29 g, 3.6 mmol, 72%) as a clear colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20].



IR (neat): 3062, 3030, 2925, 1667, 1619, 1451, 1402, 1355, 1173, 1095, 927, 814, 662, 552 cm^{-1}.

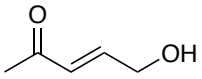
^{1}H NMR (400 MHz, $CDCl_3$): [Note: At this temperature, two rotamers (A: Major; B: Minor) in 55:45 ratio are visible.] δ 1.92 [A] 7.77 (d, *J* = 8.3 Hz, 2H), 1.59 [B] 7.70 (d, *J* = 8.4 Hz, 2H), 9.65 [A+B] 7.36 – 7.22 (m, 10H), 2.11 [A] 7.21 – 7.17 (m, 2H), 1.64 [B] 7.13 – 7.09 (m, 2H), 1.80 [A+B] 6.76 (ddt, *J* = 15.1, 7.3, 4.6 Hz,

2H), 2.00 [A+B] 6.50 (ddt, *J* = 20.3, 15.1, 1.9 Hz, 2H), 2.23 [A] 4.68 (dd, *J* = 4.5, 1.9 Hz, 2H), 1.99 [B] 4.63 (dd, *J* = 4.7, 1.9 Hz, 2H), 2.18 [A] 4.59 (s, 2H), 1.83 [B] 4.50 (s, 2H), 6.05 [A+B] 2.93 (m, 6H), 6.04 [A+B] 2.40 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.7, 165.2, 145.2, 145.1, 136.9, 136.3, 136.3, 132.7, 132.6, 130.0, 129.9, 128.9, 128.6, 128.0, 127.9, 127.8, 127.8, 127.4, 126.5, 122.7, 122.6, 68.5, 68.4, 53.4, 51.1, 34.9, 34.1, 21.6.

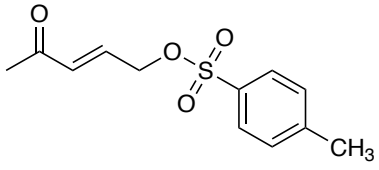
HRMS (CI): *m/z* calcd for $[M]^+$ $C_{19}H_{21}O_4NS$: 359.1186 Found: 359.1197.

(*E*)-5-Hydroxypent-3-en-2-one (S16): Prepared according to General Procedure B from methyl ketone triphenylphosphonium ylide. The title compound was obtained (0.9 g, 9.0 mmol, 45% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 6.87 (dt, *J* = 16.0, 4.1 Hz, 1H), 6.34 (dt, *J* = 16.0, 2.0 Hz, 1H), 4.38 (dd, *J* = 4.1, 2.1 Hz, 2H), 2.28 (s, 3H), 2.19 – 2.03 (s, 1H).
Spectroscopic data was consistent with literature report.[15]

(*E*)-4-Oxopent-2-en-1-yl 4-methylbenzenesulfonate (S17): Prepared according to General Procedure D. The title compound was obtained (0.77 g, 3 mmol, 60%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



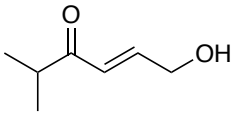
IR (neat): 2926, 1702, 1680, 1639, 1597, 1495, 1445, 1356, 1306, 1253, 1189, 1173, 1096, 1058, 1004, 941, 904, 852, 815, 778, 754, 664, 612, 551, 512 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.30 (m, 2H), 6.59 (dt, *J* = 16.0, 4.8 Hz, 1H), 6.23 (dt, *J* = 16.0, 1.8 Hz, 1H), 4.67 (dd, *J* = 4.8, 1.8 Hz, 2H), 2.42 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 197.1, 145.3, 137.0, 132.6, 131.7, 129.99, 127.9, 67.8, 27.6, 21.6.

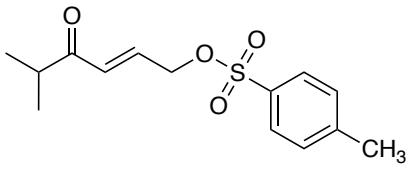
HRMS (APCI): m/z calcd for $[M+NH_4]^+$ $C_{12}H_{18}O_4NS$: 272.0951. Found: 272.0947.

(*E*)-6-Hydroxy-2-methylhex-4-en-3-one (S18): Prepared according to General Procedure B from isopropyl ketone triphenylphosphonium ylide. The title compound was obtained (0.89 g, 7 mmol, 35% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (dt, *J* = 15.7, 4.0 Hz, 1H), 6.06 (dt, *J* = 15.7, 2.1 Hz, 1H), 5.09 – 5.03(m, 1H), 4.33 (dd, *J* = 4.0, 2.1 Hz, 2H), 1.94 (s, 1H), 1.26 (d, *J* = 6.3 Hz, 6H).
Spectroscopic data was consistent with literature report.[17]

(*E*)-5-methyl-4-oxohex-2-en-1-yl 4-methylbenzenesulfonate (S19): Prepared according to General Procedure D. The title compound was obtained (0.66 g, 2.4 mmol, 47%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



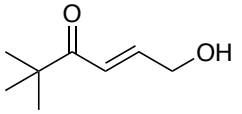
IR (neat): 2970, 2932, 2874, 1699, 1676, 1638, 1598, 1466, 1447, 1358, 1206, 1174, 1095, 1077, 1038, 944, 930, 814, 790, 766, 662, 576, 552, 535 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.41 – 7.31 (m, 2H), 6.68 (dt, *J* = 15.6, 4.6 Hz, 1H), 6.39 (dt, *J* = 15.7, 1.9 Hz, 1H), 4.69 (dd, *J* = 4.6, 1.9 Hz, 2H), 2.76 – 2.69 (m, 1H), 2.45 (s, 3H), 1.08 (d, *J* = 6.9 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.4, 145.2, 136.1, 132.6, 130.0, 128.9, 127.9, 68.2, 39.4, 27.1, 21.6, 18.0.

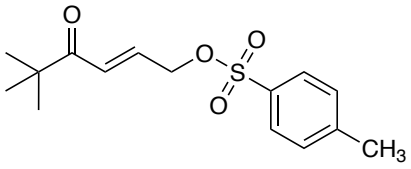
HRMS (CI): m/z calcd for $[M+H]^+$ $C_{14}H_{19}O_4S$: 283.1004. Found: 283.0999.

(*E*)-6-Hydroxy-2,2-dimethylhex-4-en-3-one (S20): Prepared according to General Procedure B from *t*-butyl ketone triphenylphosphonium ylide. The title compound was obtained (0.78 g, 5.5 mmol, 28% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^1H NMR (400 MHz, $CDCl_3$): δ 7.00 (dt, *J* = 15.3, 3.8 Hz, 1H), 6.80 (dt, *J* = 15.3, 2.1 Hz, 1H), 4.38 (dd, *J* = 3.8, 2.1 Hz, 2H), 1.78 (s, 1H), 1.17 (s, 9H).
Spectroscopic data was consistent with literature report.[17]

(*E*)-5,5-dimethyl-4-oxohex-2-en-1-yl 4-methylbenzenesulfonate (S21): Prepared according to General Procedure D. The title compound was obtained (1.2 g, 4.1 mmol, 82%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



M.p. (Et_2O, needles) = 42–43 °C.

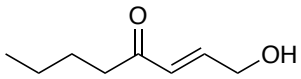
IR (neat): 2969, 2933, 2871, 1695, 1636, 1598, 1477, 1363, 1314, 1283, 1190, 1176, 1089, 1050, 1010, 963, 924, 866, 816, 786, 765, 665, 574, 554 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 6.73 – 6.67 (m, 2H), 4.70 (d, *J* = 3.2 Hz, 1H), 2.44 (s, 3H), 1.11 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 203.1, 145.2, 136.6, 132.7, 130.0, 127.9, 125.3, 77.3, 77.0, 76.7, 68.4, 43.1, 25.8, 21.6.

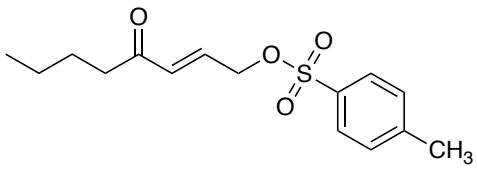
HRMS (CI): m/z calcd for $[M+H]^+$ $C_{15}H_{21}O_4S$: 297.1161. Found: 297.1142.

(*E*)-1-Hydroxyoct-2-en-4-one (S22): Prepared according to General Procedure B from *n*-butyl ketone triphenylphosphonium ylide. The title compound was obtained (1 g, 7.5 mmol, 38% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (dt, *J* = 15.9, 4.0 Hz, 1H), 6.37 (dt, *J* = 15.9, 2.1 Hz, 1H), 4.37 (dd, *J* = 4.0, 2.1 Hz, 2H), 2.55 (t, *J* = 7.4 Hz, 2H), 1.99 (br s, 1H), 1.63 – 1.56 (m, 2H), 1.38 – 1.28 (m, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).
Spectroscopic data was consistent with literature report.[16]

(*E*)-4-oxooct-2-en-1-yl 4-methylbenzenesulfonate (S23): Prepared according to General Procedure D. The title compound was obtained (0.6 g, 1.9 mmol, 38%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



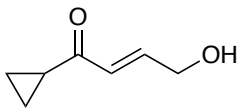
IR (neat): 2958, 2931, 2872, 1700, 1677, 1640, 1598, 1450, 1402, 1360, 1189, 1174, 1096, 1042, 943, 814, 763, 663, 552 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 7.7 Hz, 2H), 6.64 (dt, *J* = 15.9, 4.8 Hz, 1H), 6.29 (dt, *J* = 15.9, 1.8 Hz, 1H), 4.69 (dd, *J* = 4.8, 1.9 Hz, 2H), 2.50 (t, *J* = 7.4 Hz, 2H), 2.45 (s, 3H), 1.59 – 1.53 (m, 2H), 1.37 – 1.26 (m, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 199.4, 145.3, 135.9, 132.7, 130.8, 130.0, 128.0, 68.1, 40.8, 25.9, 22.3, 21.7, 13.8.

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{15}H_{21}O_4S$: 297.1161. Found: 297.1155.

(*E*)-1-Cyclopropyl-4-hydroxybut-2-en-1-one (S24): Prepared according to General Procedure B from cyclopropyl ketone triphenylphosphonium ylide. The title compound was obtained (0.8 g, 6.4 mmol, 32% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



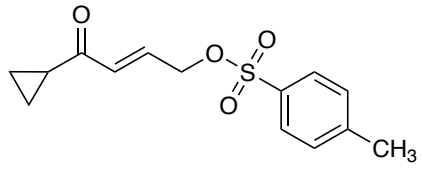
IR (neat): 3419, 3011, 2892, 2848, 1681, 1652, 1629, 1472, 1442, 1394, 1266, 1208, 1187, 1118, 1102, 1090, 1025, 1010, 961, 934, 905, 889 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.94 (dt, *J* = 15.9, 4.0 Hz, 1H), 6.49 (dt, *J* = 15.8, 2.1 Hz, 1H), 4.38 (t, *J* = 2.9 Hz, 2H), 2.16 – 2.11 (m, 1H), 2.07 (s, 1H), 1.11 – 1.08 (m, 2H), 0.95 – 0.91 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 200.2, 144.2, 128.2, 62.1, 19.4, 11.3.

HRMS (CI): *m/*z calcd for $[M+H]^+$ $C_7H_{11}O_2$: 127.0754. Found 127.0756, D 1.6 ppm.

(*E*)-4-cyclopropyl-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S25): Prepared according to General Procedure D. The title compound was obtained (0.5 g, 1.7 mmol, 33%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



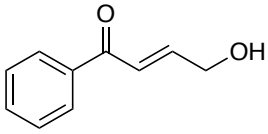
IR (neat): 3010, 1687, 1668, 1637, 1598, 1444, 1392, 1361, 1190, 1176, 1095, 1052, 1020, 943, 908, 815, 681, 662, 554 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 6.69 (dt, *J* = 15.7, 4.7 Hz, 1H), 6.42 (dt, *J* = 15.8, 1.8 Hz, 1H), 4.71 (dd, *J* = 4.8, 1.8 Hz, 2H), 2.45 (s, 3H), 2.09 – 2.02 (m, 1H), 1.12 – 1.05 (m, 2H), 0.97 – 0.92 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 199.0, 145.2, 135.6, 132.7, 130.9, 129.9, 127.9, 68.1, 21.6, 19.7, 11.6.

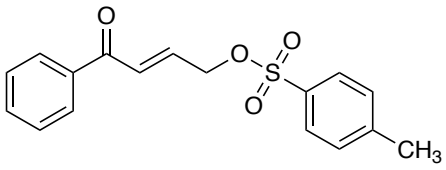
HRMS (APCI): m/z calcd for $[M+H]^+$ $C_{14}H_{17}O_4S$: 281.0842. Found: 281.0837.

(*E*)-4-Hydroxy-1-phenylbut-2-en-1-one (S26): Prepared according to General Procedure B from phenyl ketone triphenylphosphonium ylide. The title compound was obtained (1.6 g, 9.8 mmol, 49% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 70:30].



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.37 (m, 2H), 7.27 – 7.21 (m, 2H), 7.14 – 7.11 (m, 2H), 6.33 (dt, *J* = 15.7, 2.2 Hz, 1H), 4.44 – 4.42 (m, 2H), 1.79 (s, 1H).
Spectroscopic data was consistent with literature report.[11]

(*E*)-4-oxo-4-phenylbut-2-en-1-yl 4-methylbenzenesulfonate (S27): Prepared according to General Procedure D. The title compound was obtained (1.2 g, 3.8 mmol, 76%) as white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



M.p. (Et_2O, needles) = 42–43 °C.

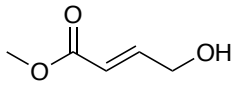
IR (neat): 1677, 1631, 1597, 1579, 1448, 1361, 1284, 1212, 1190, 1176, 1097, 1061, 1020, 960, 924, 815, 759, 692, 666, 554 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.92 – 7.89 (m, 2H), 7.83 (d, *J* = 8.3 Hz, 2H), 7.61 – 7.56 (m, 1H), 7.47 (dd, *J* = 8.3, 7.1 Hz, 2H), 7.38 – 7.34 (m, 2H), 7.12 (dt, *J* = 15.5, 1.9 Hz, 1H), 6.86 (dt, *J* = 15.4, 4.4 Hz, 1H), 4.80 (dd, *J* = 4.4, 1.9 Hz, 2H), 2.43 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 189.3, 145.3, 138.3, 133.3, 130.1, 128.7, 128.7, 128.0, 126.6, 68.39, 21.7.

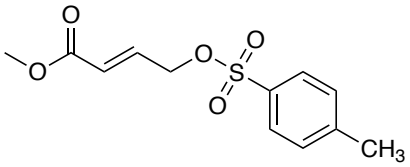
HRMS (CI): m/z calcd for $[M+H]^+$ $C_{17}H_{17}O_4S$: 317.0848. Found: 317.0852.

Methyl (*E*)-4-hydroxybut-2-enoate (S28): Prepared according to General Procedure C from methyl diethylphosphonoacetate. The title compound was obtained (0.75 g, 6.5 mmol, 65%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (dt, J = 15.56, 3.97 Hz, 1H), 6.15–6.08 (m, 1H), 4.38–4.33 (m, 2H), 3.74 (s, 3H).
Spectroscopic data was consistent with literature report.[7]

Methyl *(E)*-4-(tosyloxy)but-2-enoate (S29): Prepared according to General Procedure D. The title compound was obtained (0.9 g, 3.3 mmol, 65%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



M.p. (Et_2O, needles) = 43–45 °C.

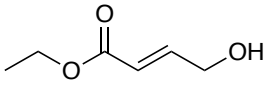
IR (neat): 2953, 1725, 1438, 1361, 1311, 1279, 1251, 1190, 1175, 963, 932, 816, 664, 554 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.78 (dt, *J* = 15.7, 4.7 Hz, 1H), 6.02 (dt, *J* = 15.7, 1.9 Hz, 1H), 4.65 (dd, *J* = 4.7, 1.9 Hz, 2H), 3.70 (s, 3H), 2.42 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.7, 145.3, 138.8, 132.6, 129.9, 127.9, 123.1, 67.6, 51.8, 21.6.

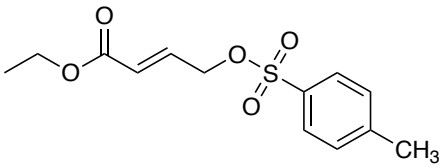
HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{12}H_{14}O_5SNa$: 293.0460. Found: 293.0460.

Ethyl (*E*)-4-hydroxybut-2-enoate (S32): Prepared according to General Procedure C from ethyl diethylphosphonoacetate. The title compound was obtained (0.9 g, 7 mmol, 70%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01 (dt, *J* = 15.7, 4.0 Hz, 1H), 6.08 (dt, *J* = 15.7, 2.1 Hz, 1H), 4.35–4.32 (m, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.64 (t, *J* = 5.9 Hz, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).
Spectroscopic data was consistent with literature report.[8]

Ethyl (*E*)-4-(tosyloxy)but-2-enoate (S33): Prepared according to General Procedure D. The title compound was obtained (0.88 g, 3.1 mmol, 62%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].



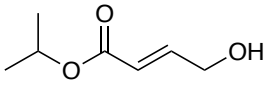
IR (neat): 2982, 2937, 1718, 1667, 1598, 1446, 1361, 1275, 1173, 1096, 1034, 956, 928, 813, 661, 552 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.76 (m, 2H), 7.40 – 7.32 (m, 2H), 6.79 (dt, *J* = 15.7, 4.8 Hz, 1H), 6.04 (dt, *J* = 15.7, 1.9 Hz, 1H), 4.67 (dd, *J* = 4.7, 1.9 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 165.2, 145.2, 138.4, 132.6, 129.9, 127.9, 123.6, 77.3, 77.0, 76.7, 67.6, 60.7, 21.6, 14.1.

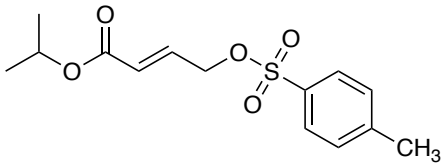
HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{13}H_{16}O_5SNa$: 307.0616. Found: 307.0612.

Isopropyl (*E*)-4-hydroxybut-2-enoate (S34): Prepared according to General Procedure C from isopropyl diethylphosphonoacetate. The title compound was obtained (1.2 g, 8.3 mmol, 83%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^1H NMR (400 MHz, $CDCl_3$): δ 6.98 (dt, *J* = 15.7, 4.0 Hz, 1H), 6.04 (dt, *J* = 15.7, 2.1 Hz, 1H), 5.07–5.01 (m, 1H), 4.31 (dd, *J* = 4.0, 2.1 Hz, 2H), 1.92 (s, 1H), 1.24 (d, *J* = 6.3 Hz, 6H).
Spectroscopic data was consistent with literature report.[9]

Isopropyl (*E*)-4-(tosyloxy)but-2-enoate (S35): Prepared according to General Procedure D. The title compound was obtained (0.5 g, 1.8 mmol, 35%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 95:5].



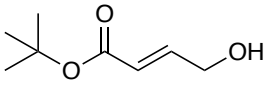
IR (neat): 2983, 2939, 1718, 1667, 1598, 1365, 1306, 1279, 1190, 1177, 1108, 1056, 953, 934, 816, 664, 538 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.81 – 7.79 (m, 2H), 7.37 – 7.35 (m, 2H), 6.75 (dt, *J* = 15.7, 4.8 Hz, 1H), 5.99 (dt, *J* = 15.7, 1.9 Hz, 1H), 5.09 – 4.99 (m, 1H), 4.65 (dd, *J* = 4.8, 1.9 Hz, 2H), 2.43 (s, 3H), 1.22 (d, *J* = 6.3 Hz, 7H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.8, 145.2, 138.1, 132.7, 129.9, 127.9, 124.2, 68.2, 67.7, 21.8, 21.6.

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{14}H_{19}O_5S$: 299.0953. Found: 299.0948.

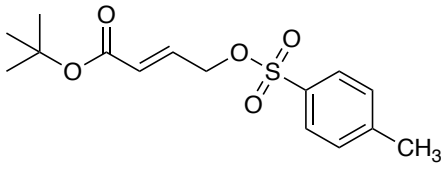
***t*-Butyl (*E*)-4-hydroxybut-2-enoate (S36):** Prepared according to General Procedure C from *t*-butyl



diethylphosphonoacetate. The title compound was obtained (1.2 g, 7.3 mmol, 73%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.90 (dt, *J* = 15.7, 4.2 Hz, 1H), 5.99 (dt, *J* = 15.7, 2.1 Hz, 1H), 4.36 – 4.27 (m, 2H), 1.46 (s, 9H).
Spectroscopic data was consistent with literature report.[10]

***t*-Butyl (*E*)-4-(tosyloxy)but-2-enoate (S37):** Prepared according to General Procedure D. The title compound was obtained (0.7 g, 2.3 mmol, 45%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 95:5].



M.p. (Et_2O, needles) = 45–46 °C.

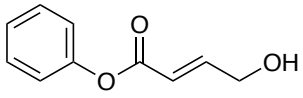
IR (neat): 2979, 2933, 1713, 1666, 1598, 1455, 1364, 1313, 1292, 1250, 1189, 1174, 1152, 1096, 1055, 1017, 930, 845, 814, 761, 688, 661, 591, 577, 553 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.41 – 7.30 (m, 2H), 6.66 (dt, *J* = 15.7, 4.9 Hz, 1H), 5.94 (dt, *J* = 15.7, 1.9 Hz, 1H), 4.63 (dd, *J* = 4.9, 1.9 Hz, 2H), 2.43 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 164.5, 145.2, 137.2, 132.7, 129.9, 127.9, 125.5, 81.00, 67.8, 27.9, 21.6.

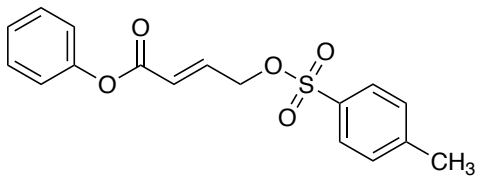
HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{15}H_{20}O_5SNa$: 335.0929. Found: 335.0927.

Phenyl (*E*)-4-hydroxybut-2-enoate (S38): Prepared according to General Procedure C from phenyl diethylphosphonoacetate. The title compound was obtained (0.87 g, 4.9 mmol, 49%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 – 7.37 (t, *J* = 7.9 Hz, 2H), 7.27 – 7.21 (m, 2H), 7.14 – 7.11 (m, 2H), 6.33 (d, *J* = 15.7 Hz, 1H), 4.44 – 4.22 (m, 2H), 1.80 (t, *J* = 5.8 Hz, 1H).
Spectroscopic data was consistent with literature report.[11]

Phenyl (*E*)-4-(tosyloxy)but-2-enoate (S39): Prepared according to General Procedure D. The title compound was obtained (0.88 g, 2.7 mmol, 53%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 95:5].



M.p. (Et_2O, needles) = 44–45 °C.

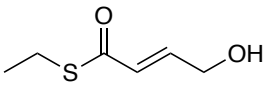
IR (neat): 3067, 1738, 1666, 1596, 1492, 1362, 1304, 1246, 1191, 1176, 1165, 1151, 1097, 1056, 956, 934, 815, 776, 689, 664, 598, 554, 500 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.3 Hz, 2H), 7.39 – 7.33 (m, 4H), 7.26 – 7.18 (m, 1H), 7.10 – 7.05 (m, 1H), 6.98 (dt, *J* = 15.7, 4.5 Hz, 1H), 6.24 (dt, *J* = 15.7, 2.0 Hz, 1H), 4.74 (dd, *J* = 4.5, 2.0 Hz, 2H), 2.44 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 163.7, 150.4, 145.4, 140.7, 132.6, 130.0, 129.4, 127.9, 125.9, 122.6, 121.4, 67.5, 21.7.

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{17}H_{16}O_5SNa$: 355.0616. Found: 355.0611.

S-Ethyl (*E*)-4-hydroxybut-2-enethioate (S40): Prepared according to General Procedure C from S-ethyl diethylphosphonoacetate. The title compound was obtained (0.87 g, 6.0 mmol, 30% over 2 steps) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



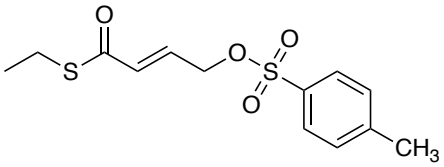
IR (neat): 3397, 2970, 2931, 2873, 1658, 1626, 1449, 1413, 1374, 1258, 1151, 1095, 1053, 1031, 952, 904, 834, 809, 607, 490 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.93 (dt, *J* = 15.6, 3.9 Hz, 1H), 6.38 (dt, *J* = 15.6, 2.1 Hz, 1H), 4.35 (ddd, *J* = 5.9, 3.9, 2.1 Hz, 2H), 2.95 (q, *J* = 7.4 Hz, 2H), 1.99 (t, *J* = 5.6 Hz, 1H), 1.27 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 190.1, 142.5, 127.0, 61.7, 23.2, 14.7.

HRMS (CI): *m/*z calcd for $[M+H]^+$ $C_6H_{11}O_2S$: 147.0474. Found 147.0474.

S-Ethyl (*E*)-4-(tosyloxy)but-2-enethioate (S41): Prepared according to General Procedure D. The title compound was obtained (0.88 g, 3.0 mmol, 59%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 90:10].

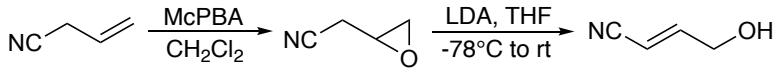


IR (neat): 2970, 2931, 2874, 1669, 1639, 1597, 1449, 1359, 1263, 1189, 1174, 1095, 1071, 1052, 1026, 955, 922, 811, 786, 665, 552 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H), 6.68 (dt, *J* = 15.5, 4.6 Hz, 1H), 6.27 (dt, *J* = 15.5, 1.9 Hz, 1H), 4.67 (dd, *J* = 4.6, 1.9 Hz, 2H), 2.94 (q, *J* = 7.4 Hz, 2H), 2.45 (s, 3H), 1.27 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 189.0, 145.3, 133.9, 132.6, 130.0, 129.7, 127.9, 67.6, 23.4, 21.6, 14.6.

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{13}H_{17}O_4S$: 301.0568. Found: 301.0563.



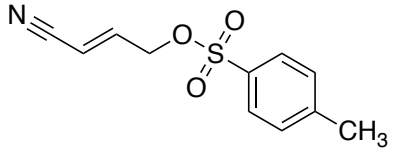
(*E*)-4-Hydroxybut-2-enenitrile (S42): *Using a modification of the procedure of Steward and co-workers*.[22] A 250 mL round bottom flask was charged with 3-alkenenitrile (5.52 g, 80 mmol, 1.0 equiv.), *meta*-chloroperoxybenzoic acid (27.6 g, 120 mmol, 1.5 equiv.), and dichloromethane (80 mL). The resulting solution was stirred at room temperature for 5 days. The reaction was filtered through a celite pad. The filtrate was washed saturated aq. Na_2SO_4 (40 mL), sodium bicarbonate (6 X 30 mL), and brine (50 mL). The organic layer was dried with Mg_2SO_4, concentrated, and purified via column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20] to give a clear oil. Used without further purification.

While under nitrogen, a flame dried 100 mL round bottom flask was charged with diisopropylamine (2.44 g, 3.38 mL, 24.08 mmol, 2.0 equiv), and anhydrous tetrahydrofuran (24 mL). The resulting solution was cooled to -78°C, n-butyllithium (2.5 M, 9.63 mL, 24.08 mmol, 2.0 equiv.) was added over a 10 min period. A solution of 2-(oxiran-2-yl)acetonitrile (1.0 g, 12.04 mmol, 1.0 equiv) in anhydrous tetrahydrofuran (12 mL), was added slowly over 15 min. After 20 min of stirring at -78°C the reaction was quenched with acetic acid (2.89 g, 2.75 mL, 48.16 mmol, 4.0 equiv.), and diluted with ethyl acetate (110 mL). The mixture was warmed to room temperature and filtered through a celite pad, the filtrated was concentrated, and purified via column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 50:50] to give the *title compound* (920 mg, 11.08 mmol, 92 %) as a clear colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.81 (dt, *J* = 16.2, 3.4 Hz, 1H), 5.67 (dt, *J* = 16.3, 2.4 Hz, 1H), 4.26 (dd, *J* = 3.5, 2.4 Hz, 2H), 4.05 (s, 1H).

Spectroscopic data was consistent with literature report.[22]

(***E*)-3-Cyanoallyl 4-methylbenzenesulfonate (S43):** Prepared according to General Procedure D. The title compound was obtained (1.06 g, 4.45 mmol, 89%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 95:5].

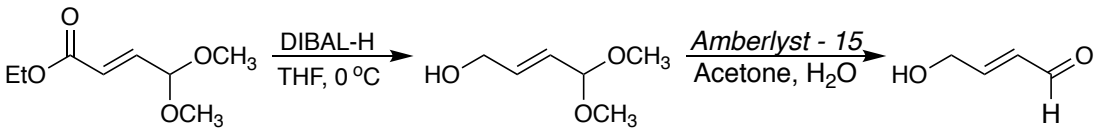


IR (neat): 3067, 2928, 2229, 1597, 1359, 1173, 1095, 1055, 928, 813, 664, 549 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.3 Hz, 2H), 6.59 (dt, *J* = 16.3, 4.3 Hz, 1H), 5.62 (dt, *J* = 16.3, 2.2 Hz, 1H), 4.65 (dd, *J* = 4.4, 2.2 Hz, 2H), 2.45 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 145.74, 145.28, 132.22, 130.18, 127.94, 115.99, 102.28, 67.03, 21.69.

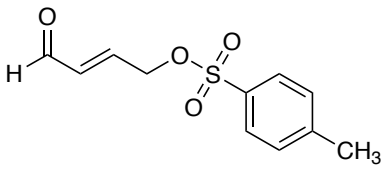
HRMS (ESI): m/z calcd for $[M+H]^+$ $C_{11}H_{12}O_3S$: 238.0532. Found: 238.0534.



Preparation of (*E*)-4-Hydroxybut-2-enal (S44): *Using a modification of the procedure of Liao and co-workers*.[14] To a solution of Ethyl (*E*)-4,4-dimethoxybut-2-enoate (20 mmol, 3.48 g) in 22 mL dry THF was added DIBAL-H solution (1.0 M in THF, 44 mL, 2.2 equiv) at 0°C via syringe pump over 30 min. The reaction was stirred for 1 more hour and poured slowly to an ice-cold 200 mL 10% potassium sodium tartrate solution. Stir vigorously until no gel-like solid existed. The aqueous solution was extracted with EtOAc 3 times (50 mL × 3) and the combined organic phase was dried over $MgSO_4$ then concentrated to give a colorless oil. The crude oil was transferred to a mixed solvent (0.4 M) acetone/water (10:1, v/v) followed by addition of 600 mg Amberlyst−15 resin. The reaction was stirred for 30 min and then the resin was removed by filtration. The acetone was evaporated. The concentrated aqueous solution was extracted with EtOAc 3 times (50 mL × 3) and the combined organic phase was dried over Mg_2SO_4, concentrated to give a bright yellow oil. Purified by column chromatography [SiO_2, Petroleum Ether: EtOAc, 70:30] to give the product (0.843 g, 9.8 mmol, 49% over 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, *J* = 7.9 Hz, 1H), 6.92 (dt, *J* = 15.7, 3.8 Hz, 1H), 6.40 (ddt, *J* = 15.8, 7.9, 2.1 Hz, 1H), 4.47 (d, *J* = 5.2 Hz, 2H), 1.96 (s, 1H).
Spectroscopic data was consistent with literature report.[14]

(*E*)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S45): Prepared according to General Procedure D. The title compound was obtained (1 g, 4 mmol, 81%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 9:1].



M.p. (Et_2O, needles) = 55–56 °C.

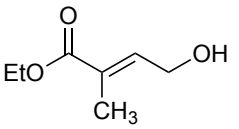
IR (neat): 2830, 2363, 2331, 1693, 1598, 1361, 1190, 1176, 1096, 1055, 965, 941, 838, 816, 765, 751, 669, 615, 553 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.50 (d, *J* = 7.6 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 2H), 6.66 (dt, *J* = 15.8, 4.5 Hz, 1H), 6.24 (ddt, *J* = 15.8, 7.6, 1.8 Hz, 1H), 4.77 (dd, *J* = 4.6, 1.8 Hz, 2H), 2.43 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 192.1, 146.4, 145.5, 132.9, 132.4, 130.1, 127.9, 67.3, 21.6.

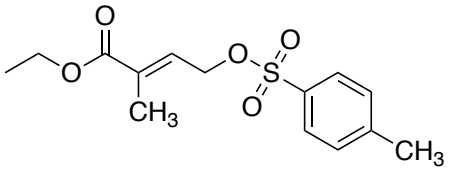
HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{11}H_{12}O_4SNa$: 263.0354. Found: 263.0355.

Ethyl (*E*)-4-hydroxy-2-methylbut-2-enoate (S46): Prepared according to General Procedure C. The title compound was obtained as a colorless oil (2.22 g, 15.4 mmol, 77%) over 2 steps following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 80:20].



^{1}H NMR (400 MHz, $CDCl_3$): δ 6.77 (tq, *J* = 6.0, 1.4 Hz, 1H), 4.29 (dq, *J* = 6.1, 1.2 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.63 (s, 1H), 1.78 (q, *J* = 1.2 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 3H).
Spectroscopic data was consistent with literature report.[21]

Ethyl (*E*)-2-methyl-4-(tosyloxy)but-2-enoate (S47): Prepared according to General Procedure D. The title compound was obtained (1.25 g, 4.2 mmol, 84%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 95:5].

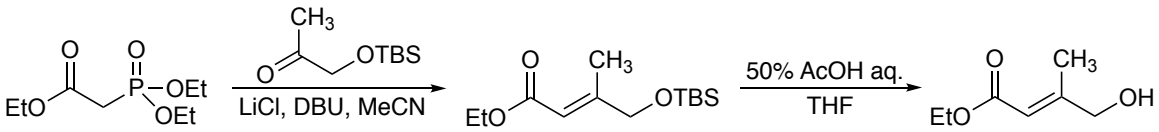


IR (neat): 3031, 2980, 1664, 1460, 1310, 1191, 933, 590 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 2H), 6.61 (tq, *J* = 6.5, 1.5 Hz, 1H), 4.70 (dd, *J* = 6.4, 1.2 Hz, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.43 (s, 3H), 1.77 (q, *J* = 1.2 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H).

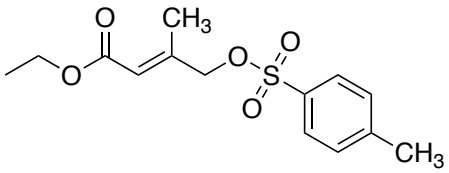
^{13}C NMR (101 MHz, $CDCl_3$): δ 166.6, 145.1, 132.9, 132.5, 131.8, 129.9, 127.9, 66.05, 61.0, 21.6, 14.1, 12.8.

HRMS (CI): m/z calcd for $[M+Na]^+$ $C_{14}H_{18}O_5NaS$: 321.0767. Found: 321.0768.



Ethyl (*E*)-4-hydroxy-3-methylbut-2-enoate: A 250 mL round bottom flask was charged with lithium chloride (5.64 g, 133 mmol, 1.2 equiv.), and was flame dried while under vacuum. While under nitrogen, acetonitrile (110 mL), diethylphosphonoacetate (29.8 g, 26.4 mL, 133 mmol, 1.2 equiv.), 2-((tert-Butyldimethylsilyl)oxy)acetaldehyde (20.9 g, 111 mmol, 1.0 equiv.), and 1,8-diazabicyclo[5.4.0]undec-7-ene (16.9 g, 16.6 mL, 111 mmol, 1.0 equiv.) was added to the round bottom flask. The resulting solution was stirred for 24 hours at room temperature then concentrated under reduced pressure, dissolved in to ethyl acetate (100 mL), washed with 1 M hydrochloric acid (3 X 50 mL). The organic layer was dried over magnesium sulfate, dry loaded onto silica, and run through a silica plug [Petroleum Ether: Ethyl Acetate 80:20]. The clear oil residue was dissolved into tetrahydrofuran (120 mL), cooled to 0 °C, and was added to a solution of 50% acetic acid and stirred for 12 hours. The reaction was diluted with 100 ml water, and basified with $NaHCO_3$ until pH = 8. The aqueous solution was extracted with EtOAc (100 mL × 3) and the combined organic phase was dried over $MgSO_4$, concentrated to give a colorless oil, which was used without any further purification.

Ethyl (*E*)-3-methyl-4-(tosyloxy)but-2-enoate (S48): Prepared according to General Procedure D. The title compound was obtained (1.03 g, 3.45 mmol, 69%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: Ethyl Acetate 95:5].



IR (neat): 3029, 2979, 2965, 1666, 1460, 1311, 943, 591 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* =

8.1 Hz, 2H), 5.86 (d, *J* = 1.5 Hz, 1H), 4.46 (d, *J* = 1.5 Hz, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.45 (s, 3H), 2.04 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).

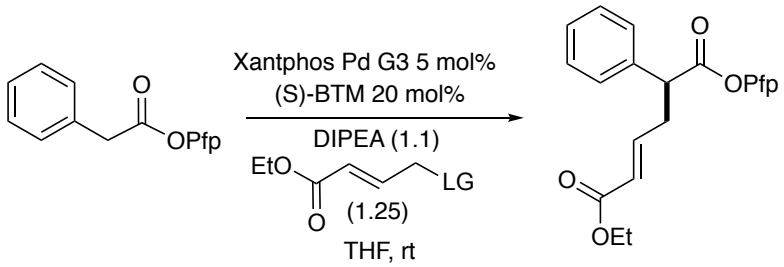
^{13}C NMR (101 MHz, $CDCl_3$): δ 165.8, 148.7, 145.2, 132.7, 129.9, 127.9, 117.8, 72.5, 60.1, 21.6, 15.4, 14.2.

HRMS (ESI): m/z calcd for $[M+H]^+$ $C_{15}H_{20}O_5S$: 299.0948. Found: 299.0949.

General Procedure for Optimization

An oven dried 1 dram vial was charged with a stir bar, the Pd catalyst, ligand and phenyl acetic acid pentafluorophenyl ester (30 mg, 0.1 mmol, 1 equiv). The vial was then sealed with a PTFE lined cap and purged with nitrogen (× 3) before the addition of solvent (0.8 mL, 0.1 M). *i*Pr_2NEt was then added *via* a microsyringe. (+)-BTM (0.1 mL, 0.2 M, 0.02 mmol, 20 mol%) and the corresponding electrophile (0.1 mL, 1.25 M, 0.125 mmol, 1.25 equiv) as a solution in the appropriate solvent. The reaction was then allowed to stir at rt for a further 24 h before being quenched with petroleum ether (4 mL). The resulting solution was then passed through a plug of acidic alumina, washing the vial and alumina plug with Et_2O (2 × 4 mL). The solution was then concentrated under vacuum before adding durene (0.1 mL, 0.25 M, 0.025 mmol, 0.25 equiv) as a solution in $CDCl_3$. The reaction mixture was then diluted with $CDCl_3$ and analyzed by ^{1}H NMR.

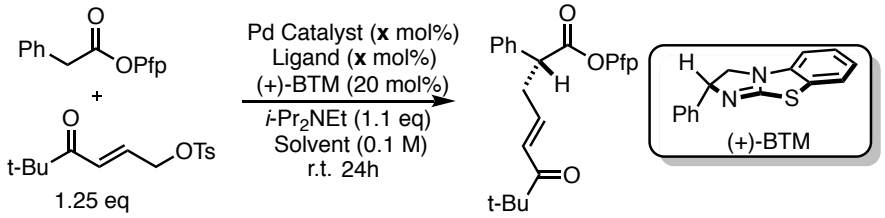
Leaving Group



Entry	LG	%Yield[b]	%ee[c]
1	OAc	0	—
2	OPiv	0	—
3	$OP(O)(OEt)_2$	60	41
4	OBoc	33	39
5[a]	OBoc	54	63
6	**OTs**	**74**	**91**

a. No addition of DIPEA
b. Yields determined by ^{1}H NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene).
c. Determined by chiral HPLC analysis.

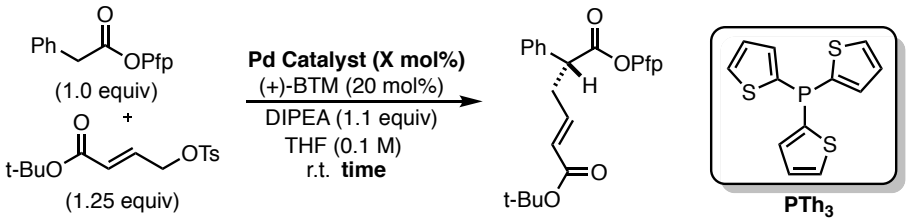
Ligand Screen (Ketone)



Entry	Catalyst (mol%)	Ligand (mol%)	[Pd]/L	Solvent	Yield[%][b]	ee[%][c]	Pfp%
1	Xantphos G3 (5)	–	–	THF	45	–	35
2	Pd_2dba_3 (5)	Xantphos (10)	1:1	THF	41	–	30
3	Pd_2dba_3 (5)	DPEphos (10)	1:1	THF	0	–	50
4	Pd_2dba_3 (5)	dppe (10)	1:1	THF	0	–	50
5	Pd_2dba_3 (5)	dppf (10)	1:1	THF	36	–	45
6	Pd_2dba_3 (5)	P(4-anisole)$_3$ (20)	1:2	THF	0	–	50
7	Pd_2dba_3 (5)	P(2-furyl)$_3$ (20)	1:2	THF	50	–	30
8	Pd_2dba_3 (5)	PPh_3 (20)	1:2	THF	70	30	23
9	Pd_2dba_3 (5)	P(2-thienyl)$_3$ (20)	1:2	THF	70	71	20
10	Pd_2dba_3 (2.5)	P(2-thienyl)$_3$ (10)	1:2	THF	70	85	15
11[d]	**Pd_2dba_3 (2.5)**	**P(2-thienyl)$_3$ (10)**	1:2	**THF**	**80**	**85**	**12**
12	**Pd_2(4-OMe-dba)$_3$ (2.5)**	**P(2-thienyl)$_3$ (20)**	**1:4**	**THF**	**68**	**85**	**13**

a. Reaction conditions: Pd and ligand were stirred in THF for 30 min followed by addition of Pfp ester (0.1 mmol), *i*Pr_2NEt (0.11 mmol), (+)-BTM (20 mol%), tosylate (0.125 mmol) sequentially. The resulting mixture was stirred at room temperature for 24h.
b. Yields determined by ^{1}H NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene).
c. Determined by chiral HPLC analysis.
d. The reaction was run for 48h.

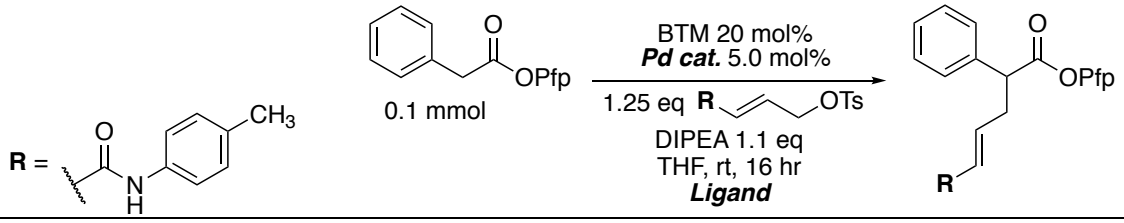
Stoichiometry Screen



Entry	Catalyst (mol%)	Time (h)	Yield[%][b]	ee[%][c]	Pfp%
1	$Pd(PTh_3)_3$ (5)	16	80	81	8
2	$Pd(PTh_3)_3$ (10)	16	55	74	30
3	$Pd(PTh_3)_3$ (5)	2	77	93	13
4	$Pd(PTh_3)_3$ (5)	6	75	90	15
5	$Pd(PTh_3)_3$ (5)	12	81	87	13
6[d]	**$Pd(PTh_3)_3$ (5)**	**2**	**87**	**93**	**20**
7	Pd_2dba_3(2.5) /PTh_3 (10)	2	10	—	70
8	Xantphos Pd G3 (5)	2	20	—	60

a. Reaction conditions: $Pd(PTh_3)_3$ was stirred in THF for 5 min followed by an addition of Pfp ester (0.1 mmol), iPr$_2$NEt (0.11 mmol), (+)-BTM (20 mol%), tosylate (0.125 mmol) sequentially. The resulting mixture was stirred at room temperature.
b. Yields determined by ^{1}H NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene).
c. Determined by chiral HPLC analysis.
d. **Tosylate (0.1 mmol), Pfp ester (0.125 mmol) were used.**

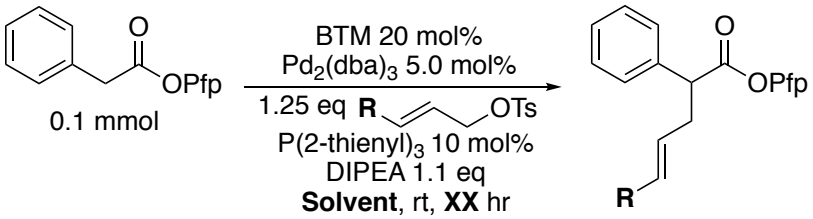
Ligand Screen (Amides)



Entry	***Pd cat.***	***Ligand*** (mol%)	(*E*) Yield [%][a]	(*Z*) Yield [%][a]	(*E*) *ee* [%][b]	(*Z*) *ee* [%][b]
1	XantphosPd G3	—	27	13	93	92
2	$Pd_2(dba)_3$	Xantphos (10 mol%)	40	16	90	91
3	$Pd_2(dba)_3$	DPEphos (10 mol%)	30	10	92	91
4	$Pd_2(dba)_3$	dppf (10 mol%)	25	12	90	89
5	$Pd_2(dba)_3$	dppe (10 mol%)	17	9	92	90
6	$Pd_2(dba)_3$	PPh_3 (20 mol%)	42	8	90	91
7	$Pd_2(dba)_3$	PCy_3 (20 mol%)	—	—	—	—
8	$Pd_2(dba)_3$	P(*o*-tol)$_3$ (20 mol%)	—	—	—	—
9	$Pd_2(dba)_3$	P(*p*-anisole)$_3$ (20 mol%)	20	8	88	89
10	$Pd_2(dba)_3$	P(2-furyl)$_3$ (20 mol%)	15	0	85	—
11	$Pd_2(dba)_3$	P(2-thienyl)$_3$ (20 mol%)	40	3	93	—
12[c]	$Pd_2(dba)_3$	PPh_3 (20 mol%)	52	9	87	87
13[c]	$Pd_2(dba)_3$	P(2-furyl)$_3$ (20 mol%)	20	0	88	—
14[c]	$Pd_2(dba)_3$	P(2-thienyl)$_3$ (20 mol%)	51	3	92	—
15[d]	$Pd_2(dba)_3$	—	42	7	93	—
16[d]	$Pd(PPh_3)_4$	—	30	15	82	85
17[cd]	$Pd(PPh_3)_4$	—	37	17	81	80

[a]Yields dertminded by 1H-NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene).
[b]Determined by Chiral HPLC analysis in comparison with the racemate.
[c]Run for 48 hr.
[d]10 mol% palladium source.

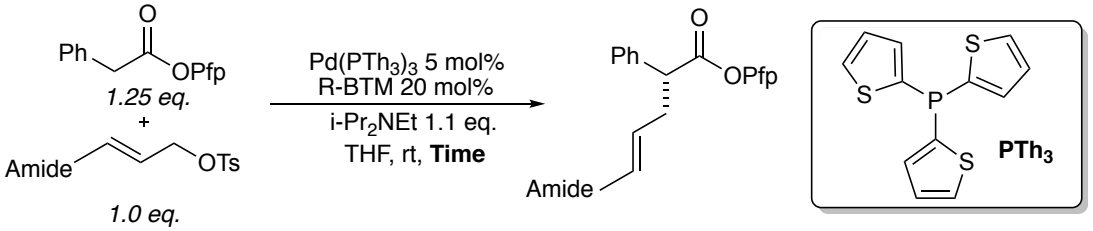
Solvent Screen

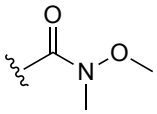
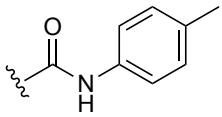
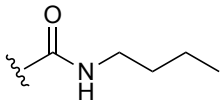
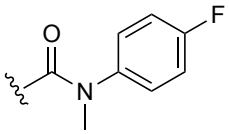
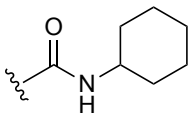


Entry	***Solvent***	***Time***	(*E*) Yield [%][a]	(*Z*) Yield [%][a]	(*E*) *ee* [%][b]	(*Z*) *ee* [%][b]
1	THF	24 hr	69	6	91	—
2	Dioxane	24 hr	56	10	84	85
3	Toluene	24 hr	34	10	84	—
4	CH_2Cl_2	24 hr	20	5	75	—
5	CH_3CN	24 hr	5	—	—	—
6	Et_2O	24 hr	—	—	—	—
7	THF	48 hr	85	10	88	87
8	Dioxane	48 hr	78	12	82	83

[a]Yields dertminded by 1H-NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene).
[b]Determined by Chiral HPLC analysis in comparison with the racemate.

Time Study



Entry	Amide	Time (h)	%Yield (*E*)[b]	ee (%)[c]
1		1	45	95
		2	53	95
		6	69	95
		19	73	94
2		1	20	91
		2	26	90
		6	33	90
		19	42	90
3		1	50	89
		2	56	88
		6	63	88
		19	68	85
4[d]		1	52 (49)	73 (82)
		2	63 (64)	73 (81)
		6	68 (67)	73 (81)
		19	79 (78)	69 (79)
5[d]		1	43 (40)	89 (89)
		2	51 (49)	87 (87)
		6	68 (67)	81 (84)
		19	75 (73)	61 (79)

a. Reaction conditions: $Pd(PTh_3)_3$ was stirred in THF followed by addition of Pfp ester (0.1 mmol), *i*Pr_2NEt (0.11 mmol), (+)-BTM (20 mol%), tosylate (0.125 mmol) sequentially. The resulting mixture was stirred at room temperature.

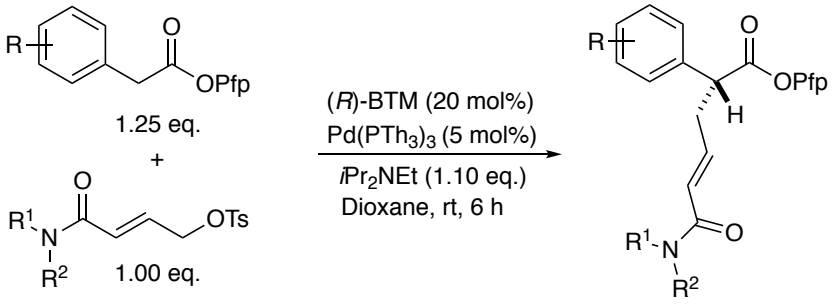
b. Yields determined by ^1H NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene). E/Z ratio was calculated by ^1H NMR.

c. Determined by chiral HPLC.

d. Results in the brackets was obtained when using 1,4-dioxane as the solvent.

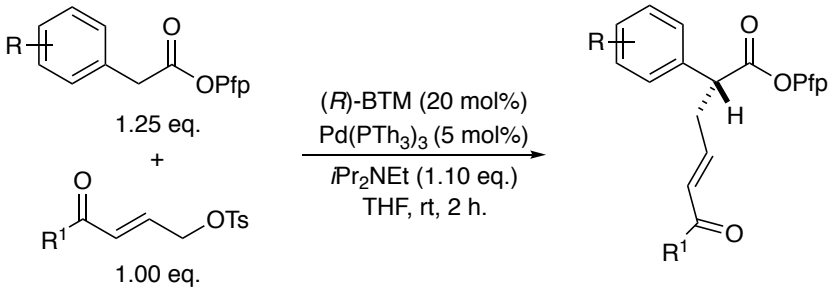
Preparation of product esters

General Procedure F for allylation with amide substituted electrophiles



Tris(tri-2-thienylphosphine)palladium(0) (4.47 mg, 0.005 mmol, 5 mol%), the specified tosylate (0.1 mmol, 1.0 equiv.), the specified pentafluorophenyl ester (0.125 mmol, 1.25 equiv.), (+)-benzotetramisole (5.1 mg, 20 mol%), and a magnetic stir bar was charged to a 4 mL vial with Teflon septa insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous 1,4-dioxane (0.9 mL) and *i*Pr_2NEt (19 µL, 0.11 mmol, 1.1 equiv.), were added sequentially via syringe. The reaction was stirred at room temperature for 6 hours. The reaction was diluted with diethyl ether (complete vial volume) and stirred for 5 min. The reaction was filtered through acidic Al_2O_3 (the vial and Al_2O_3 were washed with 3 × diethyl ether). The combined filtrates were concentrated and the residue was purified by column chromatography [SiO_2, specified eluent].

General Procedure G for allylation with ketone and ester substituted electrophiles

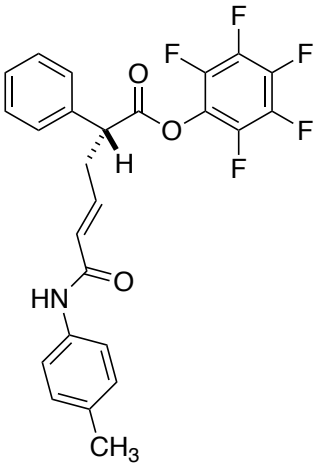


Tris(tri-2-thienylphosphine)palladium(0) (4.47 mg, 0.005 mmol, 5 mol%) and a magnetic stir bar was charged to a 4 mL vial with Teflon septa insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous THF (0.5 mL), the specified pentafluorophenyl ester (1.25 M in THF, 100 µL, 0.125 mmol, 1.25 equiv.), and *i*Pr_2NEt (19 µL, 0.11 mmol, 1.1 equiv.), (+)-benzotetramisole (0.4 M in THF, 50 µL, 20 mol%), the specified tosylate (0.4 M in THF, 250 µL, 0.1 mmol, 1.0 equiv.) were added sequentially via syringe, and the reaction was stirred at room temperature for 2 hours. The reaction was quenched with pentane (complete vial volume) and stirred for 5 min. The reaction was filtered through

acidic Al_2O_3 (the vial and Al_2O_3 were washed with 3 × diethyl ether). The combined filtrates were concentrated and the residue was purified by column chromatography [SiO_2, specified eluent].

Products from Scheme 2

Pentafluorophenyl (*E*)-6-oxo-2-phenyl-6-(*p*-tolylamino)hex-4-enoate (2): Prepared according to General Procedure F. The *title compound* was obtained (28 mg, 0.059 mmol, 59%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 60:40]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with racemate.



M.p. (Et_2O, needles) = 141–144 °C.

$[\alpha]_D^{23}$ -33.3° (c = 1.00, $CHCl_3$).

IR (neat): 3326, 3033, 2970, 5953, 2923, 2360, 2342, 1771, 1670, 1516, 1364, 1217, 1105, 979, 815, 696, 515 cm^{-1}.

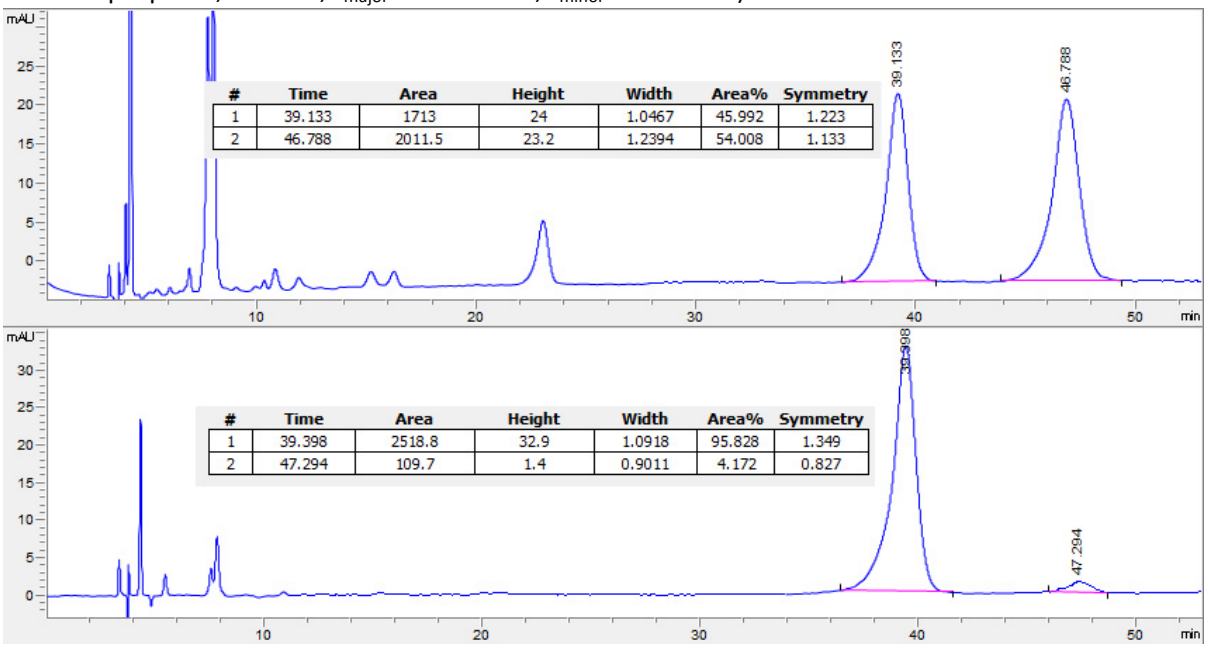
^1H NMR (400 MHz, $CDCl_3$): δ 7.38 – 7.21 (m, 7H), 7.18 (s, 1H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.82 (dt, *J* = 14.7, 7.2 Hz, 1H), 5.91 (d, *J* = 15.0 Hz, 1H), 3.99 (t, *J* = 7.5 Hz, 1H), 3.01 (dt, *J* = 15.4, 7.8 Hz, 1H), 2.72 (dt, *J* = 15.4, 7.8 Hz, 1H), 2.23 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.2, 163.0, 140.6, 136.1, 135.2, 134.2, 129.5, 129.2, 128.3, 127.8, 126.9, 120.0, 50.0, 35.6, 20.9.

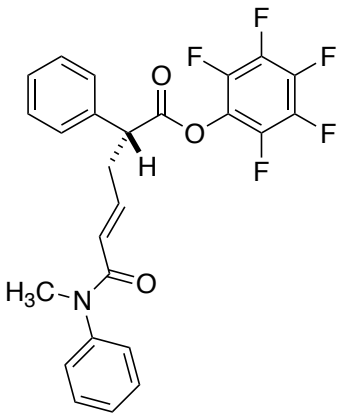
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.30 – -152.49 (m), -157.62 (t, *J* = 21.7 Hz), -162.12 (td, *J* = 22.5, 5.0 Hz).

HRMS (CI): *m/z* calcd for $[M]^+$ $C_{25}H_{18}F_5NO_3$: 475.1201 Found: 475.1184.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 1.00 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 39.40 min, t_{minor} = 47.3 min).



Pentafluorophenyl (*E*)-6-(methyl(phenyl)amino)-6-oxo-2-phenylhex-4-enoate (3): Prepared according to General Procedure F. The *title compound* was obtained (34 mg, 0.071 mmol, 71%) as a pale yellow oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20]. The enantiomeric ratio (91:9) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -56.6° (c = 1.00, $CHCl_3$).

IR (neat): 3065, 3033, 2934, 2362, 1781, 1666, 1633, 1595, 1520, 1471, 1378, 1113, 995, 700 cm^{-1}

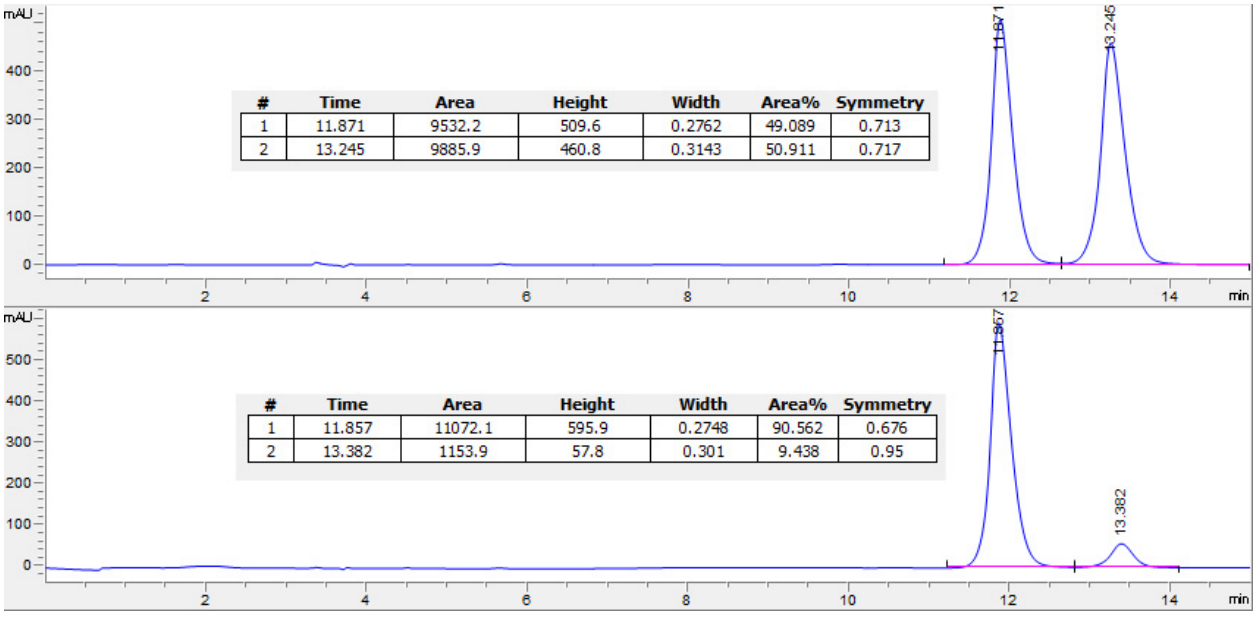
^1H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.23 (m, 8H), 7.06 – 6.99 (m, 2H), 6.84 – 6.74 (m, 1H), 5.76 (d, *J* = 15.1 Hz, 1H), 3.94 (t, *J* = 7.7 Hz, 1H), 3.29 (d, *J* = 1.7 Hz, 3H), 2.91 (dt, *J* = 14.8, 7.3 Hz, 1H), 2.65 (dt, *J* = 15.0, 7.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.0, 165.3, 143.3, 140.1, 136.1, 129.5, 129.0, 128.1, 127.9, 127.4, 127.2, 124.4, 49.9, 37.4, 35.5.

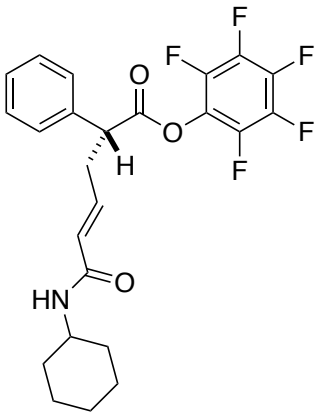
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.31 (d, *J* = 17.9 Hz), -157.84 (t, *J* = 21.6 Hz), -162.32 (td, *J* = 22.5, 4.9 Hz).

HRMS (CI): *m/z* calcd for $[M+Na]^+$ $C_{25}H_{18}F_5NO_3Na$: 498.1083 Found: 498.1105.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 1.00 mL/min, 95:5 hexane:isopropanol, 210 nm, t_{major} = 11.86 min, t_{minor} = 13.38 min).



Pentafluorophenyl (*E*)-6-(cyclohexylamino)-6-oxo-2-phenylhex-4-enoate (4): Prepared according to General Procedure F. The *title compound* was obtained (31 mg, 0.066 mmol, 66%) as a pale yellow oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 60:40]. The enantiomeric ratio (94:6) was determined by chiral HPLC in comparison with racemate.



M.p. (Et_2O, plates) = 108–109 °C.

$[\alpha]_D^{23}$ -71.3° (c = 1.00, $CHCl_3$).

IR (neat): 3342, 3016, 2970, 2936, 2855, 2360, 1778, 1738, 1631, 1518, 1367, 1228, 1108, 1006, 979, 693, 507 cm^{-1}

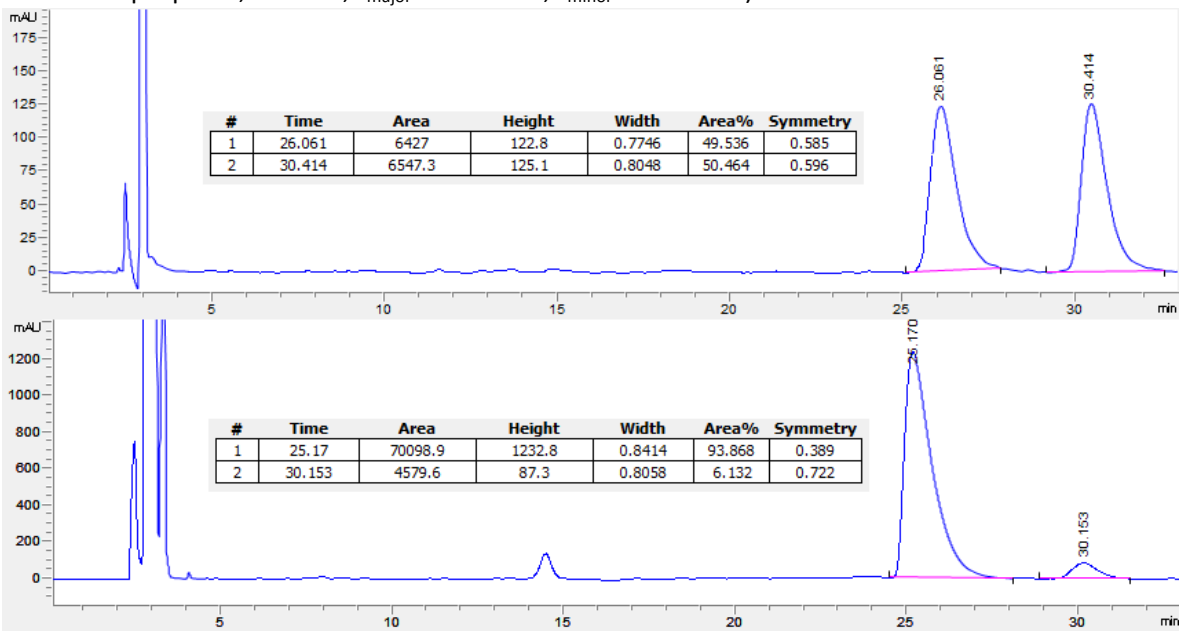
^1H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.28 (m, 5H), 6.75 (dt, *J* = 14.7, 7.1 Hz, 1H), 5.79 (d, *J* = 15.2 Hz, 1H), 5.22 (s, 1H), 4.04 (dd, *J* = 8.6, 6.6 Hz, 1H), 3.87 – 3.75 (m, 1H), 3.03 (dt, *J* = 15.5, 8.3 Hz, 1H), 2.77 – 2.67 (m, 1H), 1.90 (m, 2H), 1.74 – 1.64 (m, 2H), 1.60 (m, 1H), 1.40 – 1.31 (m, 2H), 1.25 – 1.07 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.2, 164.0, 138.8, 136.2, 129.1, 128.2, 127.8, 126.8, 50.1, 48.5, 35.5, 33.1, 25.5, 24.8.

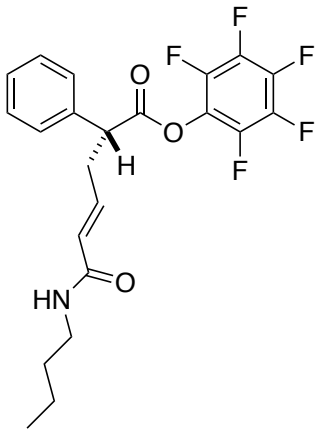
^{19}F NMR (376 MHz, $CDCl_3$ δ -152.21 – -152.43 (m), -157.70 (t, *J* = 21.7 Hz), -162.01 – -162.48 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{24}H_{23}NF_5O_3$: 468.1602 Found: 468.1598.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.25 mL/min, 95:5 hexane:isopropanol, 210 nm, t_{major} = 25.2 min, t_{minor} = 30.2 min).



Pentafluorophenyl (*E*)-6-(butylamino)-6-oxo-2-phenylhex-4-enoate (5): Prepared according to General Procedure F. The *title compound* was obtained (29 mg, 0.065 mmol, 65%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 70:30]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with racemate.



M.p. (Et_2O, needles) = 84–86 °C.

$[\alpha]_D^{23}$ -60.7° (c = 1.00, $CHCl_3$).

IR (neat): 3331, 2963, 2938, 2867, 1773, 1666, 1629, 1518, 1106, 1041, 978, 695, 512 cm^{-1}

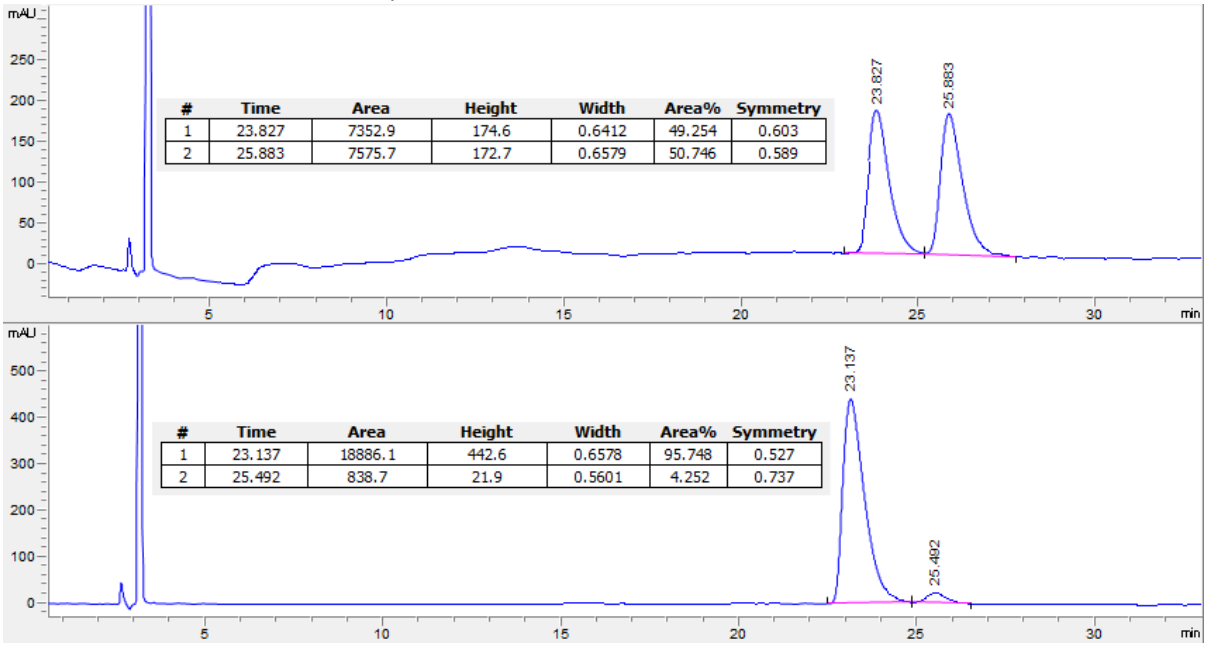
^1H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.29 (m, 5H), 6.76 (ddd, *J* = 15.2, 7.6, 6.6 Hz, 1H), 5.81 (dd, *J* = 15.2, 1.5 Hz, 1H), 5.38 (s, 1H), 4.04 (dd, *J* = 8.4, 6.7 Hz, 1H), 3.29 (tdd, *J* = 7.0, 5.8, 3.2 Hz, 2H), 3.10 – 2.98 (m, 1H), 2.73 (dtd, *J* = 14.9, 6.7, 1.6 Hz, 1H), 1.48 (m, 2H), 1.39 – 1.27 (m, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.2, 165.1, 139.0, 136.2, 129.1, 128.3, 127.8, 126.6, 50.1, 39.3, 35.5, 31.7, 20.0, 13.7.

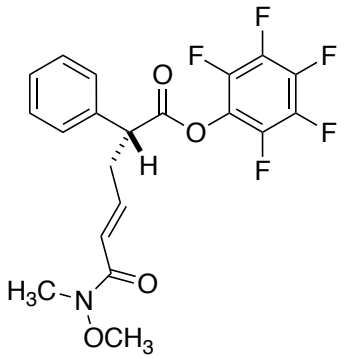
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.29 – -152.44 (m), -157.69 (t, *J* = 21.7 Hz), -162.22 (dd, *J* = 21.8, 17.3 Hz).

HRMS (CI): *m/z* calcd for $[M+Na]^+$ $C_{22}H_{20}F_5NO_3Na$: 464.1245 Found: 464.1261.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.25 mL/min, 95:5 hexane:isopropanol, 210 nm, t_{major} = 23.14 min, t_{minor} = 25.49 min).



Pentafluorophenyl (*E*)-6-(methoxy(methyl)amino)-6-oxo-2-phenylhex-4-enoate (6): Prepared according to General Procedure F. The *title compound* was obtained (30 mg, 0.070 mmol, 70%) as a clear oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 85:15]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -17.8° (c = 1.00, $CHCl_3$).

IR (neat): 3033, 2968, 2940, 1779, 1665, 1633, 1518, 1456, 1417, 1383, 1097, 731, 698 cm^{-1}.

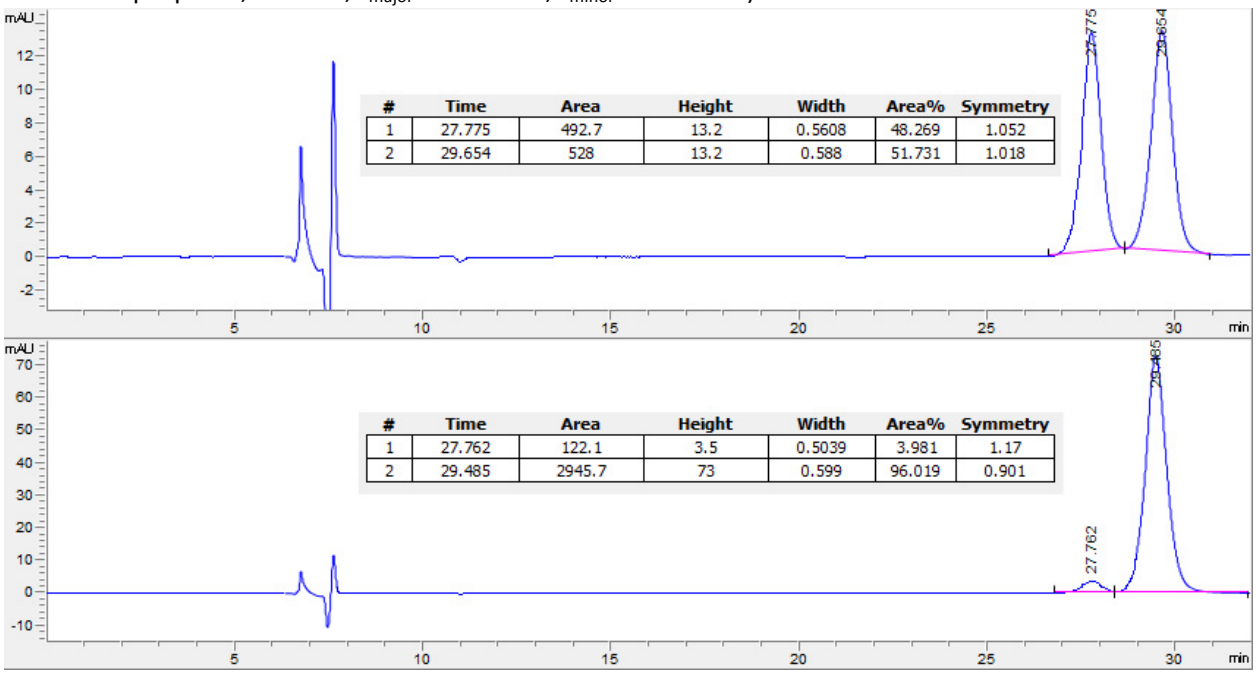
^1H NMR (500 MHz, $CDCl_3$): δ 7.43 – 7.32 (m, 5H), 6.91 (dt, *J* = 15.3, 7.1 Hz, 1H), 6.48 (d, *J* = 15.4 Hz, 1H), 4.11 (t, *J* = 7.6 Hz, 1H), 3.62 (s, 3H), 3.24 (s, 3H), 3.15 (dtd, *J* = 15.0, 7.6, 1.4 Hz, 1H), 2.86 (dtd, *J* = 14.7, 7.2, 1.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.1, 166.0, 141.8, 136.2, 129.1, 128.2, 127.9, 121.8, 61.6, 50.0, 35.8, 32.2.

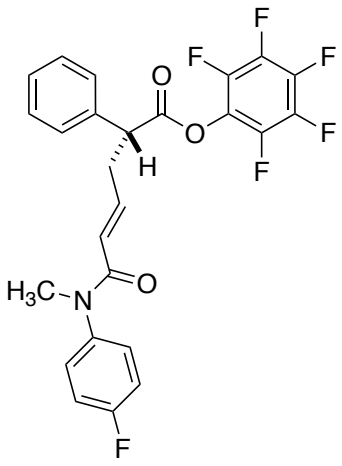
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.29 – -152.42 (m), -157.77 (t, *J* = 21.7 Hz), -162.18 – -162.38 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{20}H_{17}F_5NO_4$: 430.1062 Found: 430.1078.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 0.50 mL/min, 95:5 hexane:isopropanol, 210 nm, t_{major} = 29.5 min, t_{minor} = 27.8 min).



Pentafluorophenyl (*E*)-6-((4-fluorophenyl)(methyl)amino)-6-oxo-2-phenylhex-4-enoate (7): Prepared according to General Procedure F. The *title compound* was obtained (34 mg, 0.068 mmol, 68%) as a pale yellow oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20]. The enantiomeric ratio (92:8) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -38.1° (c = 1.00, $CHCl_3$).

IR (neat): 3065, 2923, 1780, 1666, 1632, 1519, 1374, 1223, 1112, 994 cm^{-1}.

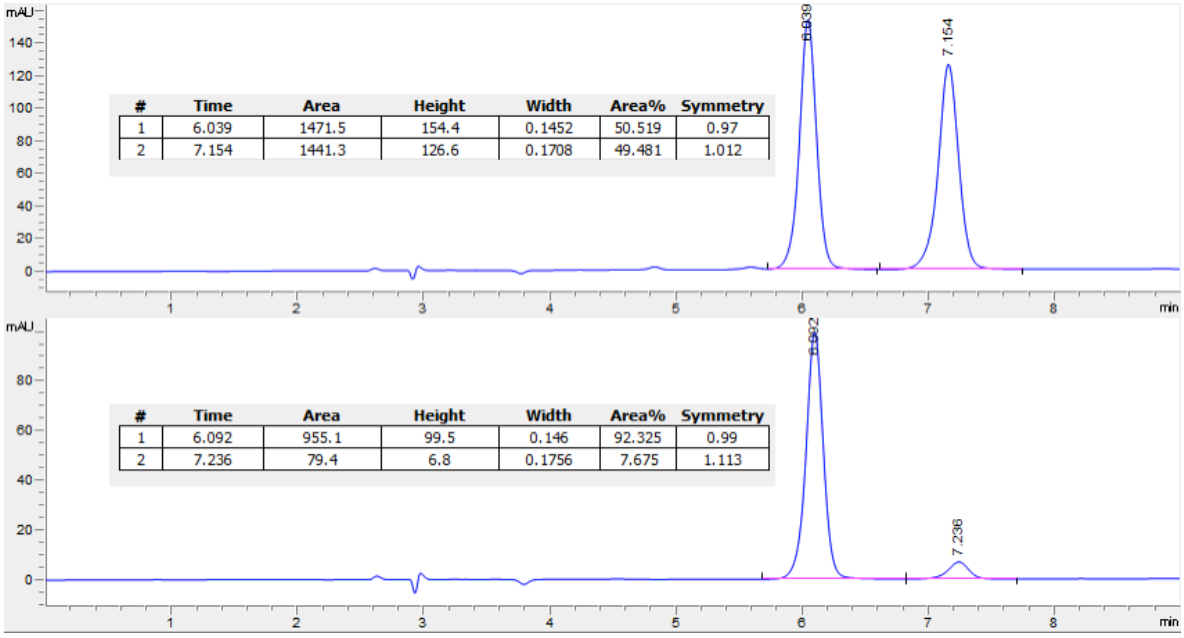
^1H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.29 (m, 5H), 7.26 (s, 1H), 7.08 – 6.95 (m, 4H), 6.80 (dt, *J* = 14.8, 7.2 Hz, 1H), 5.70 (d, *J* = 15.1 Hz, 1H), 3.94 (t, *J* = 7.5 Hz, 1H), 3.26 (s, 3H), 2.92 (dt, *J* = 14.8, 7.4 Hz, 1H), 2.66 (dt, *J* = 14.5, 7.4 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.0, 165.3, 161.5 (d, *J* = 247.4 Hz), 140.5, 139.4 (d, *J* = 3.1 Hz), 136.1, 129.1, 128.9 (d, *J* = 8.7 Hz), 128.1, 127.9, 124.2, 116.5 (d, *J* = 22.7 Hz), 49.9, 37.5, 35.6.

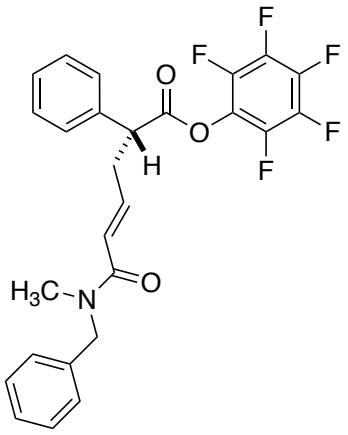
^{19}F NMR (376 MHz, $CDCl_3$): δ -113.75, -152.29 – -152.46 (m), -157.75 (t, *J* = 21.7 Hz), -162.17 – -162.40 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{25}H_{18}NF_6O_3$: 494.1191 Found: 494.1183.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 1.25 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 6.09 min, t_{minor} = 7.24 min).



Pentafluorophenyl (*E*)-6-(benzyl(methyl)amino)-6-oxo-2-phenylhex-4-enoate (8): Prepared according to General Procedure F. The *title compound* was obtained (39 mg, 0.080 mmol, 80%) as a colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -66.0° (c = 1.00, $CHCl_3$).

IR (neat): 3064, 3032, 2926, 1779, 1661, 1620, 1519, 1495, 1454, 1401, 993, 735, 698 cm^{-1}.

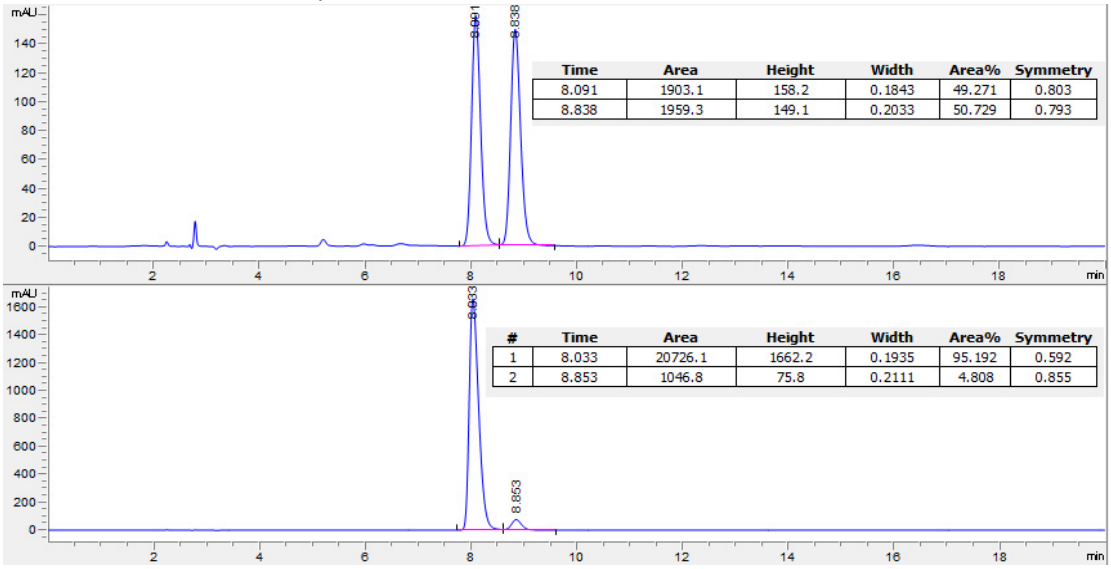
^1H NMR (500 MHz, $CDCl_3$): [Note: At this temperature, two rotamers (A ; B) in 51:49 ratio are visible.] δ [A+B] 7.46 – 7.09 (m, 20H), [A+B] 6.89 (ddt, *J* = 21.7, 14.7, 7.2 Hz, 2H), [A] 6.38 (d, *J* = 15.1 Hz, 1H), [B] 6.31 (d, *J* = 15.1 Hz, 1H), [A] 4.65 (q, *J* = 14.7 Hz, 2H), [B] 4.54 – 4.43 (m, 2H), [A] 4.12 (t, *J* = 7.6 Hz, 1H), [B] 4.05 (t, *J* = 7.6 Hz, 1H), [A] 3.15 (dt, *J* = 15.3, 7.8 Hz, 1H), [B] 3.10 – 3.04 (m, 1H), [A] 2.98 (s, 3H), [B] 2.92 (s, 3H), [A+B] 2.82 (ddt, *J* = 21.2, 14.3, 6.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.2, 169.1, 166.6, 166.0, 141.0, 140.8, 137.2, 136.6, 136.3, 136.2, 129.1, 129.0, 128.9, 128.6, 128.3, 128.2, 128.0, 127.9, 127.6, 127.4, 126.4, 123.6, 123.5, 53.3, 51.1, 50.1, 50.1, 36.0, 35.8, 34.8, 34.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.23 – -152.54 (m), -157.76 (dt, *J* = 28.6, 21.5 Hz), -162.25 (ddd, *J* = 23.3, 18.0, 13.2 Hz).

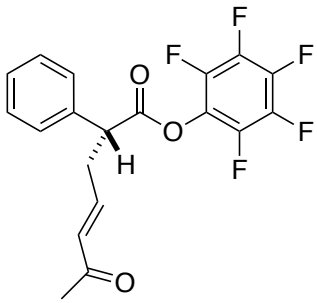
HRMS (CI): *m/z* calcd for $[M]^+$ $C_{26}H_{19}NF_5O_3$: 489.1351 Found: 489.1358.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.00 mL/min, 95:5 hexane:isopropanol, 210 nm, t_{major} = 8.03 min, t_{minor} = 8.85 min).



Products from Scheme 5

Pentafluorophenyl (*E*)-6-oxo-2-phenylhept-4-enoate (13): Prepared according to General Procedure G. The title compound was obtained (25 mg, 0.065 mmol, 65%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 76–77 °C.

$[\alpha]_D^{23}$ –49.7 (*c* = 1.00, $CHCl_3$).

IR (neat): 1779, 1702, 1677, 1631, 1517, 1360, 1254, 1106, 1087, 992, 746, 699 cm^{-1}.

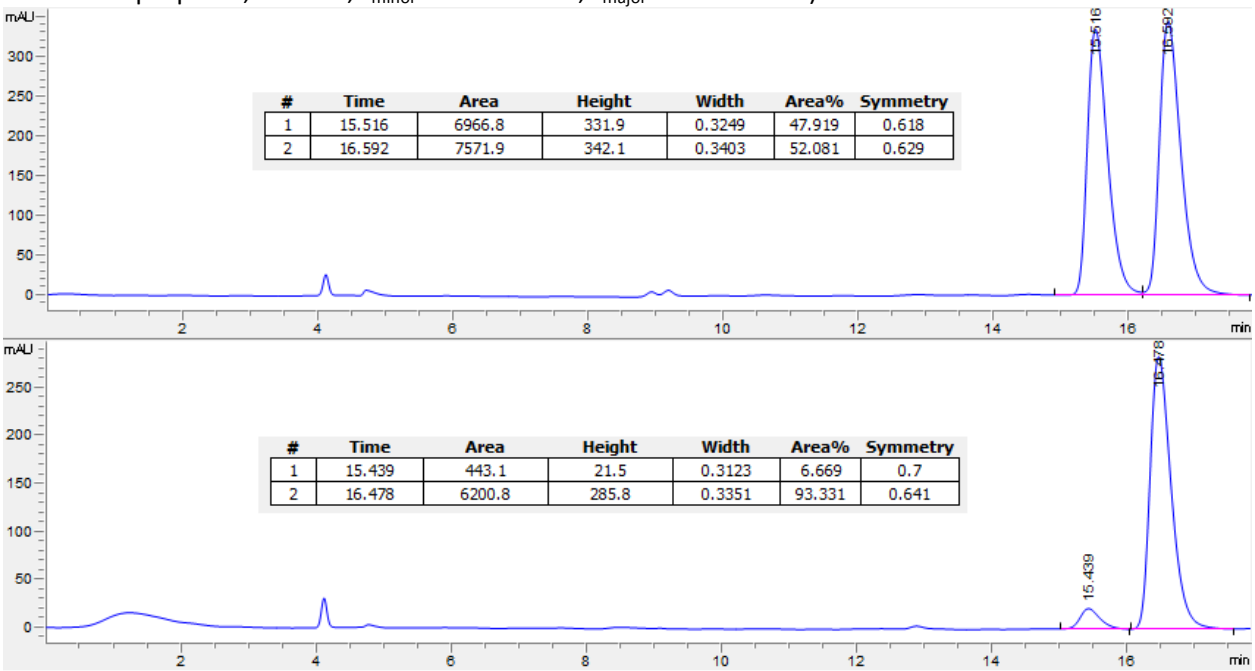
^1H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.30 (m, 5H), 6.72 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.16 (dt, *J* = 15.9, 1.5 Hz, 1H), 4.09 (dd, *J* = 8.5, 6.8 Hz, 1H), 3.14 – 3.04 (m, 1H), 2.85 – 2.77 (m, 1H), 2.22 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 169.0, 142.3, 135.9, 133.4, 129.2, 128.4, 127.7, 50.0, 35.8, 27.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.45 – -152.72 (m), -157.49 (t, *J* = 21.6 Hz), -162.01 – -162.12 (m).

HRMS (EI): m/z calcd for $[M]^+$ $C_{19}H_{13}O_3F_5$: 384.0779. Found: 384.0786.

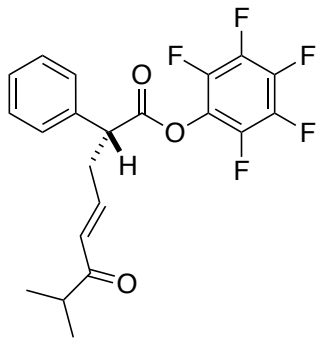
HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 15.439 min, t_{major} = 16.478 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	15.516	6966.8	331.9	0.3249	47.919	0.618
2	16.592	7571.9	342.1	0.3403	52.081	0.629

#	Time	Area	Height	Width	Area%	Symmetry
1	15.439	443.1	21.5	0.3123	6.669	0.7
2	16.478	6200.8	285.8	0.3351	93.331	0.641

Pentafluorophenyl (*E*)-7-methyl-6-oxo-2-phenyloct-4-enoate (14): Prepared according to General Procedure G. The title compound was obtained (28 mg, 0.067 mmol, 67%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (94:6) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 59–60 °C.

$[\alpha]_D^{23}$ –53.9 (*c* = 1.00, $CHCl_3$).

IR (neat): 1781, 1698, 1674, 1631, 1519, 1469, 1457, 1355, 1145, 1110, 1090, 1026, 995, 748, 699 cm^{-1}.

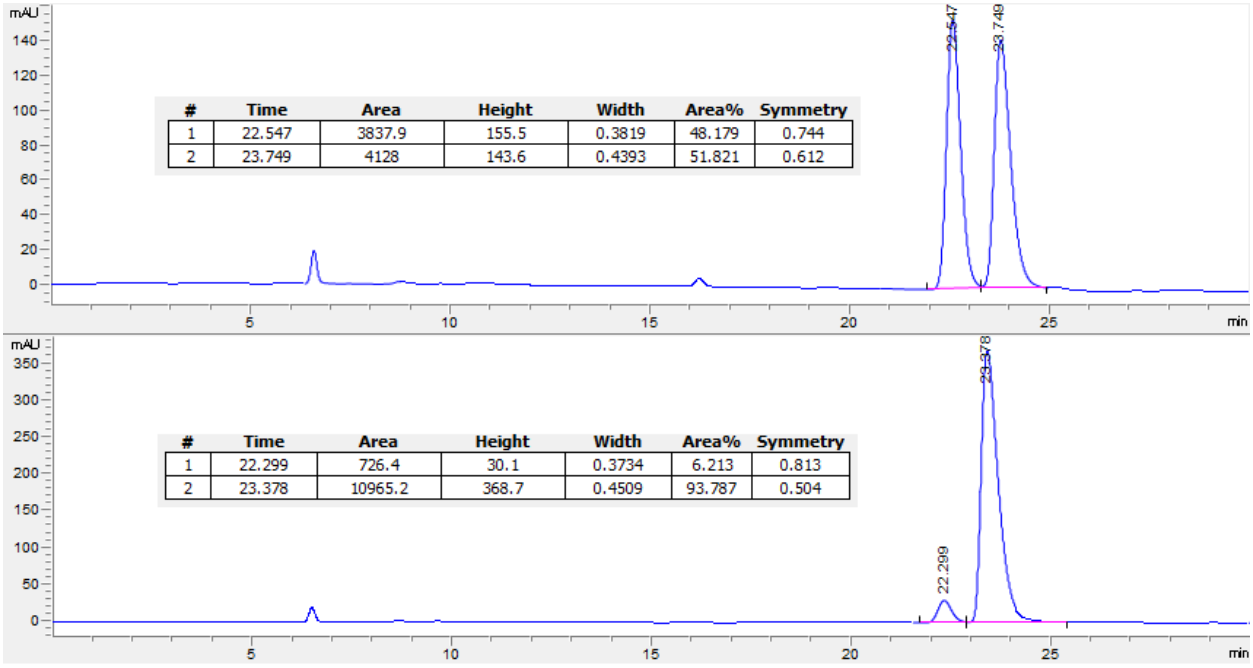
^1H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.29 (m, 5H), 6.78 (dt, *J* = 15.7, 7.1 Hz, 1H), 6.23 (dt, *J* = 15.7, 1.5 Hz, 1H), 4.08 (dd, *J* = 8.3, 6.9 Hz, 1H), 3.13 – 3.05 (m, 1H), 2.88 – 2.68 (m, 2H), 1.07 (dd, *J* = 6.9, 2.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 203.2, 169.0, 141.1, 136.0, 130.7, 129.1, 128.3, 127.8, 50.0, 38.8, 35.8, 18.2, 18.1.

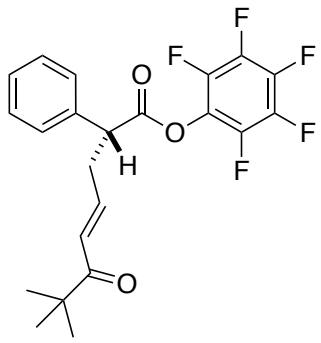
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.14 – -152.81 (m), -157.61 (t, *J* = 21.7 Hz), -161.78 – -162.50 (m).

HRMS (EI): m/z calcd for $[M]^+$ $C_{21}H_{17}O_3F_4$: 412.1060. Found: 412.1048.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 22.299 min, t_{major} = 23.378 min).



Pentafluorophenyl (*E*)-7,7-dimethyl-6-oxo-2-phenyloct-4-enoate (15): Prepared according to General Procedure G. The title compound was obtained (29 mg, 0.067 mmol, 67%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 78–80 °C.

$[\alpha]_D^{23}$ –55.7 (*c* = 1.00, $CHCl_3$).

IR (neat): 2980, 2969, 2930, 2339, 1769, 1687, 1629, 1515, 1469, 1361, 1275, 1257, 1115, 1090, 1024, 992, 747, 696 cm^{-1}.

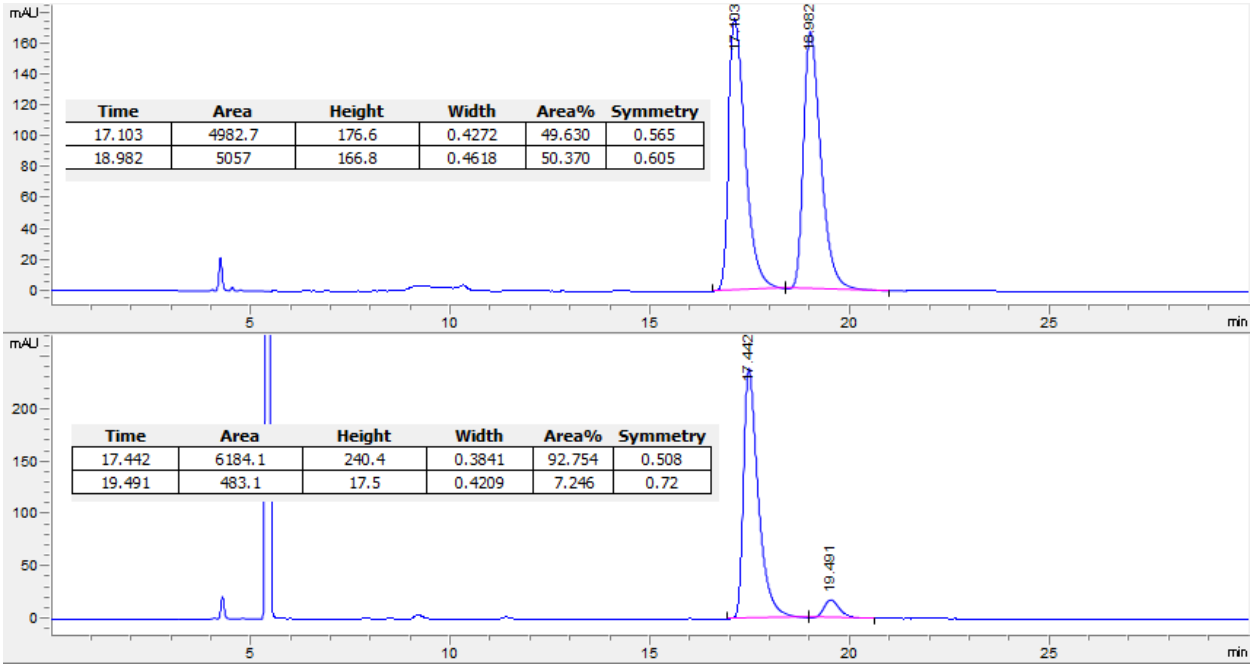
^1H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.29 (m, 5H), 6.84 (dt, *J* = 14.7, 7.1 Hz, 1H), 6.58 – 6.47 (m, 1H), 4.07 (t, *J* = 7.6 Hz, 1H), 3.13 – 3.06 (m, 1H), 2.88 – 2.72 (m, 1H), 1.10 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 203.7, 169.0, 141.3, 136.1, 129.1, 128.2, 127.8, 127.0, 49.9, 42.7, 35.8, 25.9.

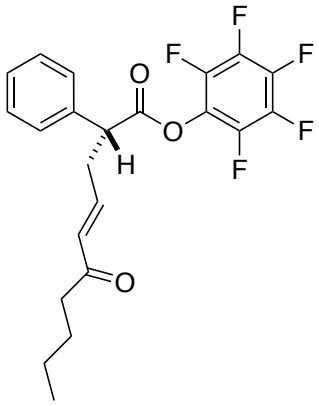
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.20 – -152.61 (m), -157.71 (t, *J* = 21.6 Hz), -162.20 – -162.31 (m)

HRMS (EI): m/z calcd for $[M]^+$ $C_{22}H_{19}O_3F_5$: 426.1249. Found: 426.1250.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.75 mL/min, 150:1 Hexane:Isopropanol, 210 nm, t_{minor} = 19.491 min, t_{major} = 17.442 min).



Pentafluorophenyl (*E*)-6-oxo-2-phenyldec-4-enoate (16): Prepared according to General Procedure G. The title compound was obtained (28 mg, 0.065 mmol, 65%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 50–52 °C.

$[\alpha]_D^{23}$ –54.5 (*c* = 1.00, $CHCl_3$).

IR (neat): 2960, 2932, 2873, 2363, 2158, 2030, 1780, 1698, 1672, 1634, 1518, 1469, 1456, 1097, 1038, 1027, 992, 698 cm^{-1}.

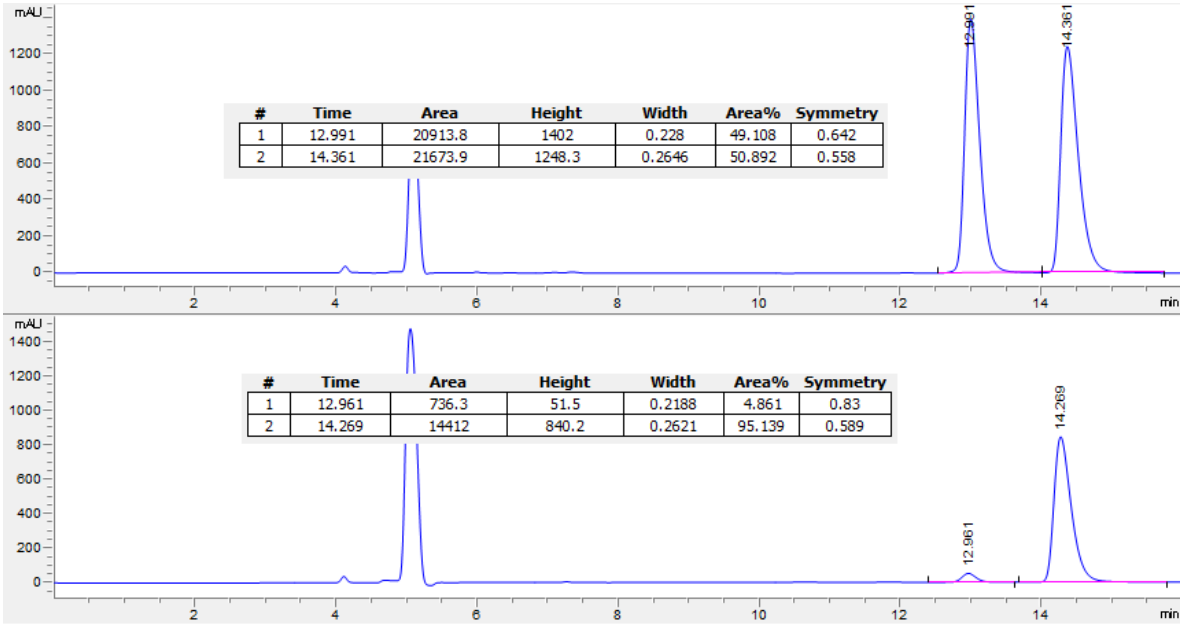
^1H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.28 (m, 5H), 6.73 (dt, *J* = 15.9, 7.0 Hz, 1H), 6.17 (dt, *J* = 15.8, 1.4 Hz, 1H), 4.08 (dd, *J* = 8.4, 6.9 Hz, 1H), 3.16 – 3.00 (m, 1H), 2.83 – 2.76 (m, 1H), 2.49 (t, *J* = 7.4 Hz, 2H), 1.55 (q, *J* = 7.5 Hz, 2H), 1.30 (dt, *J* = 14.7, 7.5 Hz, 2H), 0.90 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2, 169.0, 141.0, 136.0, 132.5, 129.2, 128.3, 127.7, 50.0, 40.1, 35.8, 26.2, 22.3, 13.8.

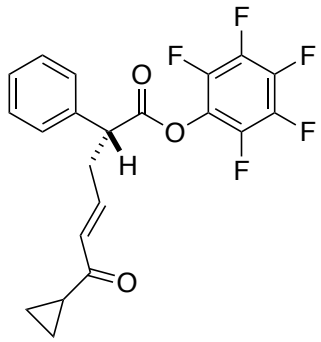
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.23 – -152.80 (m), -157.56 (t, *J* = 21.7 Hz), -162.07 – -162.18 (m).

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{22}H_{19}O_3F_5Na$: 449.1152. Found: 449.1173, D 4.7 ppm.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 12.961min, t_{major} = 14.269 min).



Pentafluorophenyl (*E*)-6-cyclopropyl-6-oxo-2-phenylhex-4-enoate (17): Prepared according to General Procedure G. The title compound was obtained (28 mg, 0.068 mmol, 68%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (94:6) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 85–86 °C.

$[\alpha]_D^{23}$ –50.2 (*c* = 1.00, $CHCl_3$).

IR (neat): 1780, 1686, 1665, 1629, 1519, 1390, 1206, 1100, 995, 699 cm^{-1}

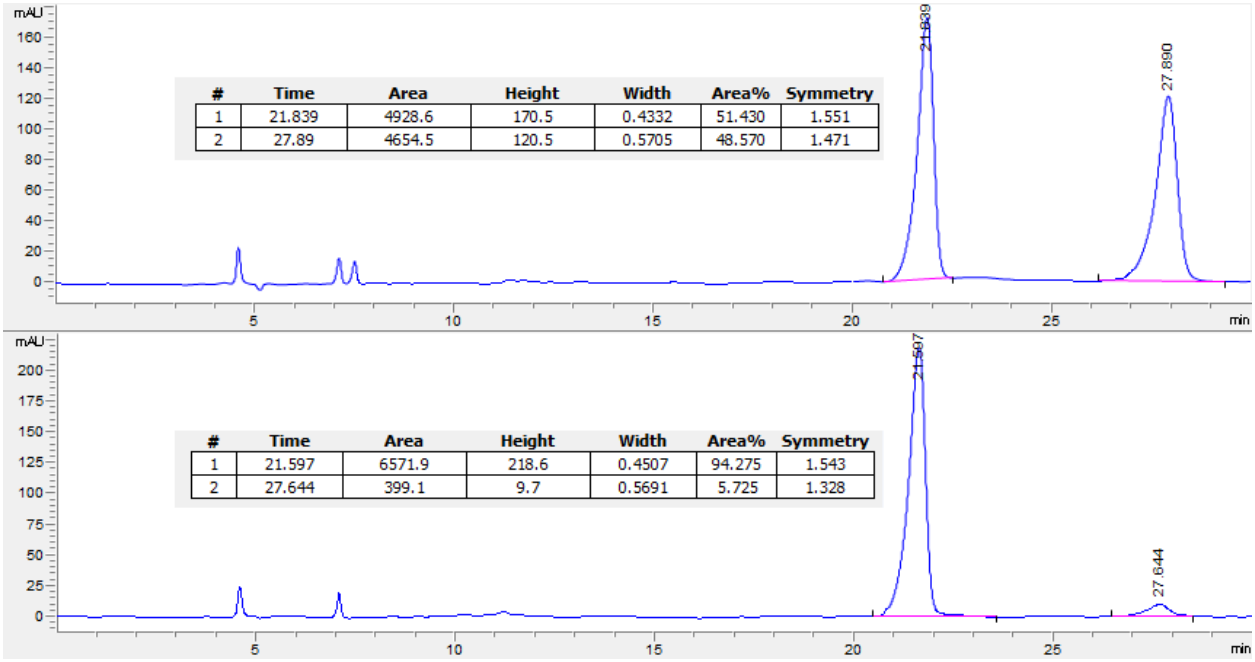
^1H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.29 (m, 5H), 6.81 (dt, *J* = 15.8, 7.0 Hz, 1H), 6.31 (dt, *J* = 15.7, 1.5 Hz, 1H), 4.10 (dd, *J* = 8.4, 6.8 Hz, 1H), 3.15 – 3.07 (m, 1H), 2.86 – 2.78 (m, 1H), 2.09 – 2.03 (m, 1H), 1.12 – 1.02 (m, 2H), 0.96 – 0.85 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 199.6, 169.0, 140.7, 136.0, 132.6, 129.2, 128.3, 127.8, 50.0, 35.8, 19.0, 11.2, 11.1.

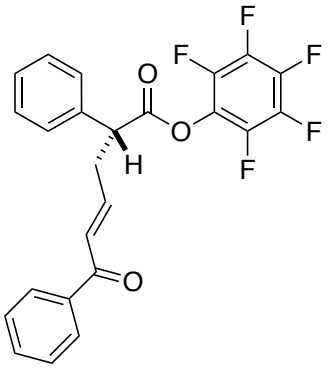
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.26 – -152.67 (m), -157.62 (t, *J* = 21.7 Hz), -161.96 – -162.36 (m).

HRMS (APCI): m/z calcd for $[M+H]^+$ $C_{21}H_{16}O_3F_5$: 411.1014. Found: 411.1017.

HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 27.644 min, t_{major} = 21.597 min).



Pentafluorophenyl (*E*)-6-oxo-2,6-diphenylhex-4-enoate (18): Prepared according to General Procedure G. The title compound was obtained (33 mg, 0.073 mmol, 73%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 102–103 °C.

$[\alpha]_D^{23}$ –64.1 (*c* = 1.00, $CHCl_3$).

IR (neat): 2364, 2334, 2176, 2158, 1779, 1672, 1624, 1519, 1498, 1448, 1283, 1261, 1227, 1111, 1086, 1002, 696 cm^{-1}.

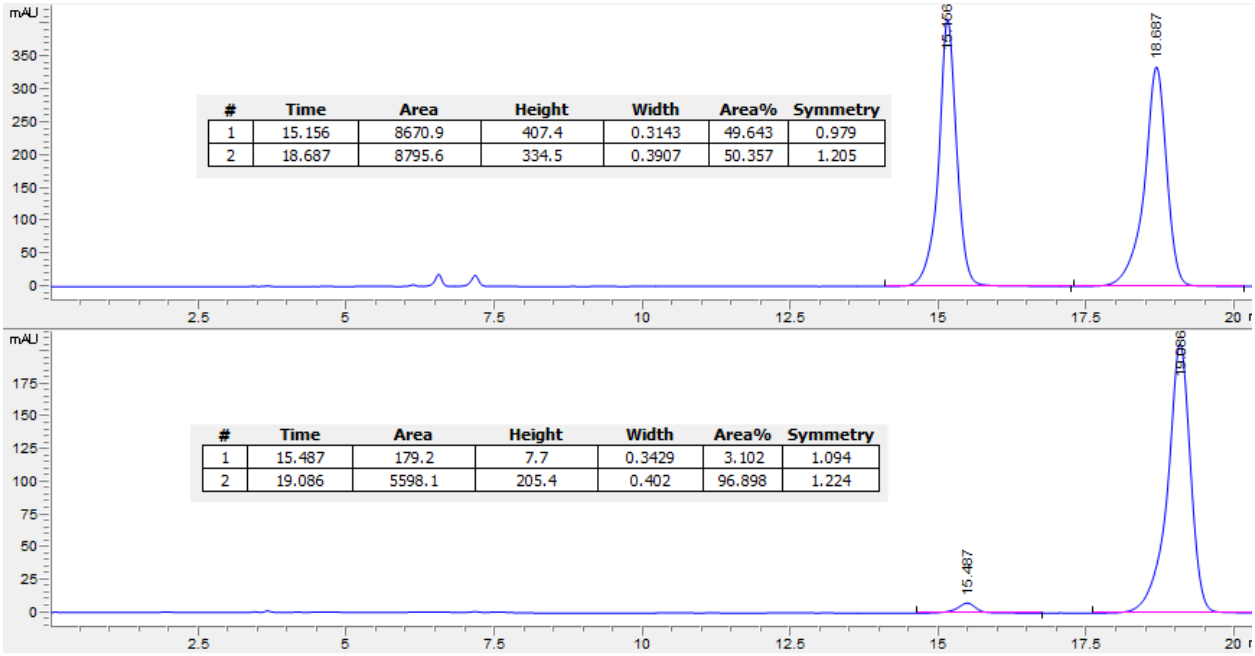
^1H NMR (400 MHz, $CDCl_3$): δ 7.91 – 7.30 (m, 9H), 6.99 – 6.90 (m, 1H), 4.15 (t, *J* = 7.6 Hz, 1H), 3.27 – 3.13 (m, 1H), 2.98 – 2.84 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2, 169.0, 143.5, 137.4, 136.0, 132.9, 129.2, 128.6, 128.5, 128.3, 127.8, 50.0, 36.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -151.63 – -153.05 (m), -157.62 (t, *J* = 21.7 Hz), -161.43 – -162.77 (m).

HRMS (EI): m/z calcd for $[M]^+$ $C_{24}H_{15}O_3F_5$: 446.0936. Found: 446.0937.

HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 1.00 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 15.487 min, t_{major} = 19.086 min).

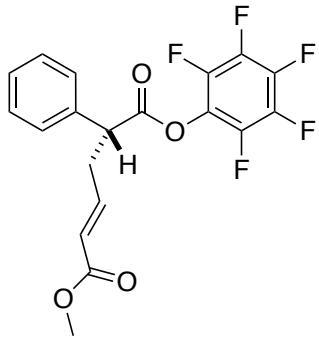


#	Time	Area	Height	Width	Area%	Symmetry
1	15.156	8670.9	407.4	0.3143	49.643	0.979
2	18.687	8795.6	334.5	0.3907	50.357	1.205

#	Time	Area	Height	Width	Area%	Symmetry
1	15.487	179.2	7.7	0.3429	3.102	1.094
2	19.086	5598.1	205.4	0.402	96.898	1.224

Products from Scheme 6

1-Methyl 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (19): Prepared according to General Procedure G. The title compound was obtained (33 mg, 0.083 mmol, 83%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 66–67 °C.

$[\alpha]_D^{23}$ –56.4 (*c* = 1.00, $CHCl_3$).

IR (neat): 2954, 1779, 1723, 1660, 1517, 1437, 1276, 1211, 1107, 992, 748, 699 cm^{-1}.

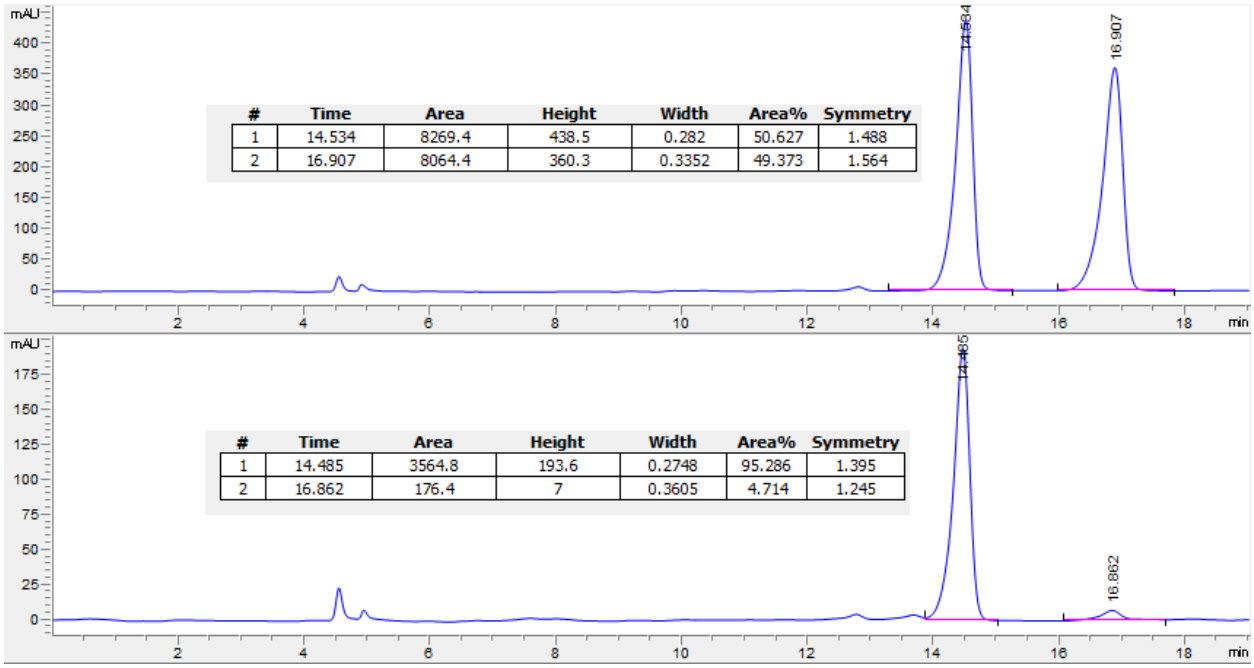
^1H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.28 (m, 5H), 6.87 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.89 (dt, *J* = 15.7, 1.5 Hz, 1H), 4.04 (t, *J* = 7.6 Hz, 1H), 3.70 (s, 3H), 3.14 – 2.99 (m, 1H), 2.85 – 2.71 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 166.3, 143.8, 135.9, 129.1, 128.3, 127.8, 123.8, 51.6, 49.8, 35.5.

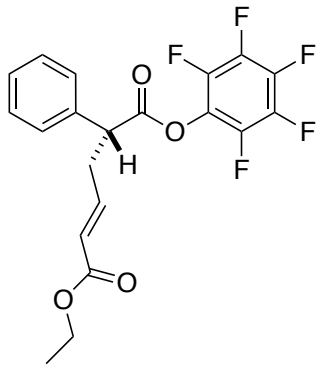
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.31 – -152.56 (m), -157.68 (t, *J* = 21.6 Hz), -162.05 – -162.38 (m).

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{19}H_{13}O_4F_5Na$: 423.0632. Found: 423.0629.

HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 16.862 min, t_{major} = 14.485 min).



1-Ethyl 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (20): Prepared according to General Procedure G. The title compound was obtained (36 mg, 0.087 mmol, 87%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 49–50 °C.

$[\alpha]_D^{23}$ –55.1 (*c* = 1.00, $CHCl_3$).

IR (neat): 2920, 2853, 1779, 1720, 1656, 1518, 1369, 1265, 1162, 1100, 991, 774, 698 cm^{-1}.

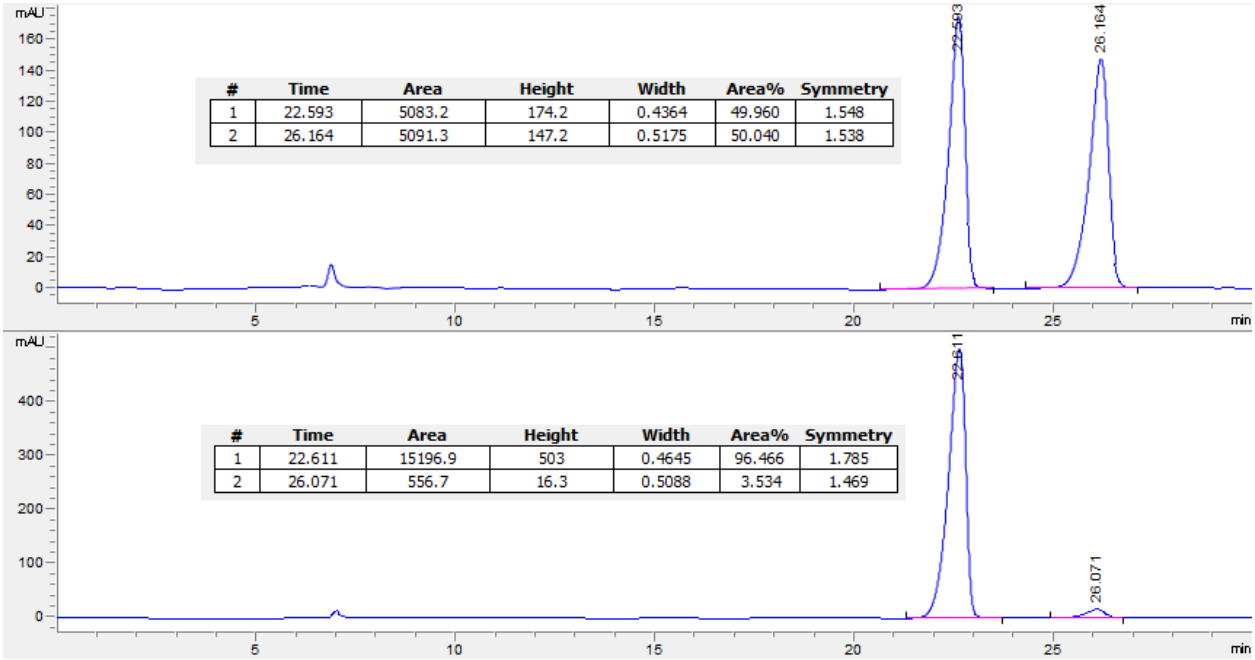
^1H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.29 (m, 5H), 6.89 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.91 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.07 (dd, *J* = 8.3, 6.9 Hz, 1H), 3.12 – 3.04 (m, 1H), 2.83 – 2.75 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 165.9, 143.4, 136.0, 129.1, 128.3, 127.8, 124.3, 60.4, 50.0, 35.5, 14.2.

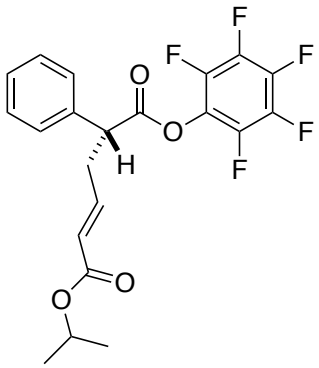
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.24 – -152.55 (m), -157.69 (t, *J* = 21.6 Hz), -162.08 – -162.39 (m).

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{20}H_{15}O_4F_5Na$: 437.0788. Found: 437.0775.

HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 0.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 26.071 min, t_{major} = 22.611 min).



1-Isopropyl 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (21): Prepared according to General Procedure G. The title compound was obtained (38 mg, 0.089 mmol, 89%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 59–60 °C.

$[\alpha]_D^{23}$ –53.8 (*c* = 1.00, $CHCl_3$).

IR (neat): 2982, 2360, 2342, 1781, 1716, 1655, 1519, 1359, 1310, 1276, 1107, 994, 740, 699 cm^{-1}.

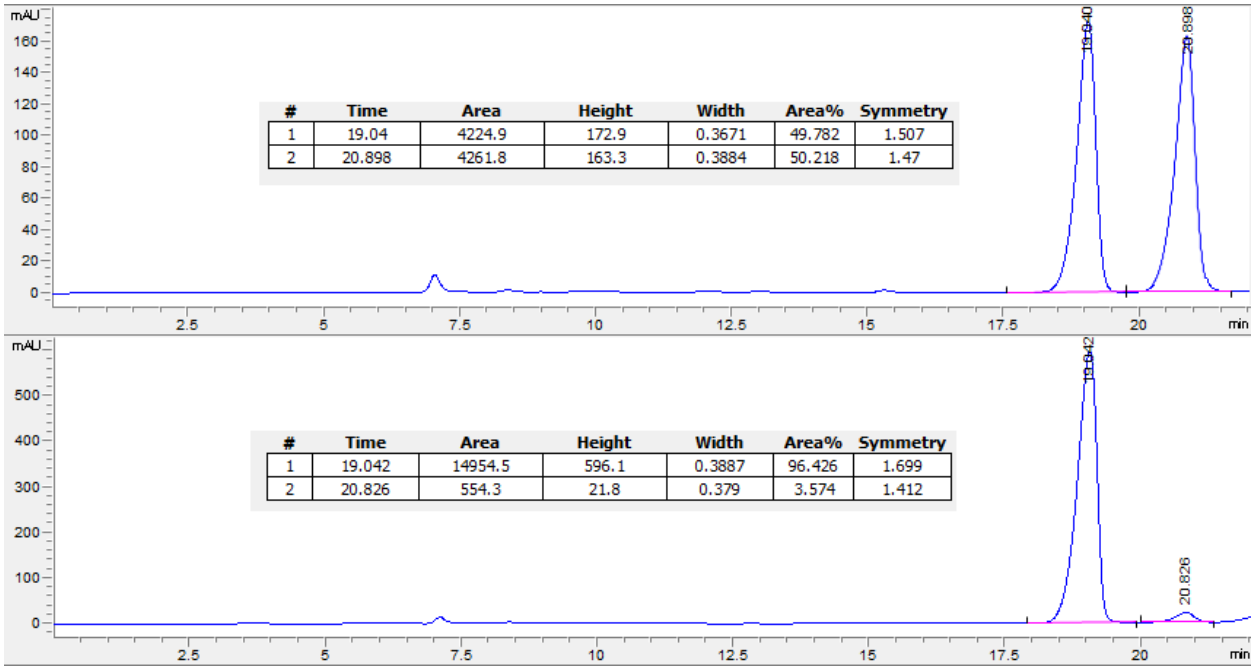
^1H NMR (400 MHz, $CDCl_3$): δ 7.42 – 7.29 (m, 5H), 6.85 (dt, *J* = 15.7, 7.1 Hz, 1H), 5.88 (dt, *J* = 15.6, 1.5 Hz, 1H), 5.06 – 5.00 (m, 1H), 4.05 (dd, *J* = 8.5, 6.7 Hz, 1H), 3.10 – 3.02 (m, 1H), 2.79 – 2.72 (m, 1H), 1.23 (dd, *J* = 6.2, 1.6 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 165.4, 143.1, 136.0, 129.1, 128.3, 127.7, 124.7, 67.7, 49.9, 35.6, 21.8.

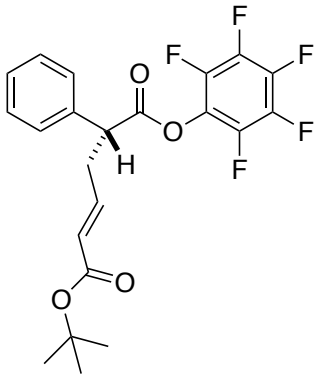
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.26 – -152.51 (m), -157.70 (t, *J* = 21.6 Hz), -162.26 (dd, *J* = 21.8, 17.2 Hz).

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{21}H_{17}O_4F_5Na$: 451.0945. Found: 451.0945.

HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 20.826 min, t_{major} = 19.042 min).



1-(tert-Butyl) 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (22): Prepared according to General Procedure G. The title compound was obtained (38 mg, 0.086 mmol, 86%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 84–85 °C.

$[\alpha]_D^{23}$ –51.3 (*c* = 1.00, $CHCl_3$).

IR (neat): 1782, 1715, 1655, 1519, 1368, 1152, 1109, 1004, 996, 698 cm^{-1}.

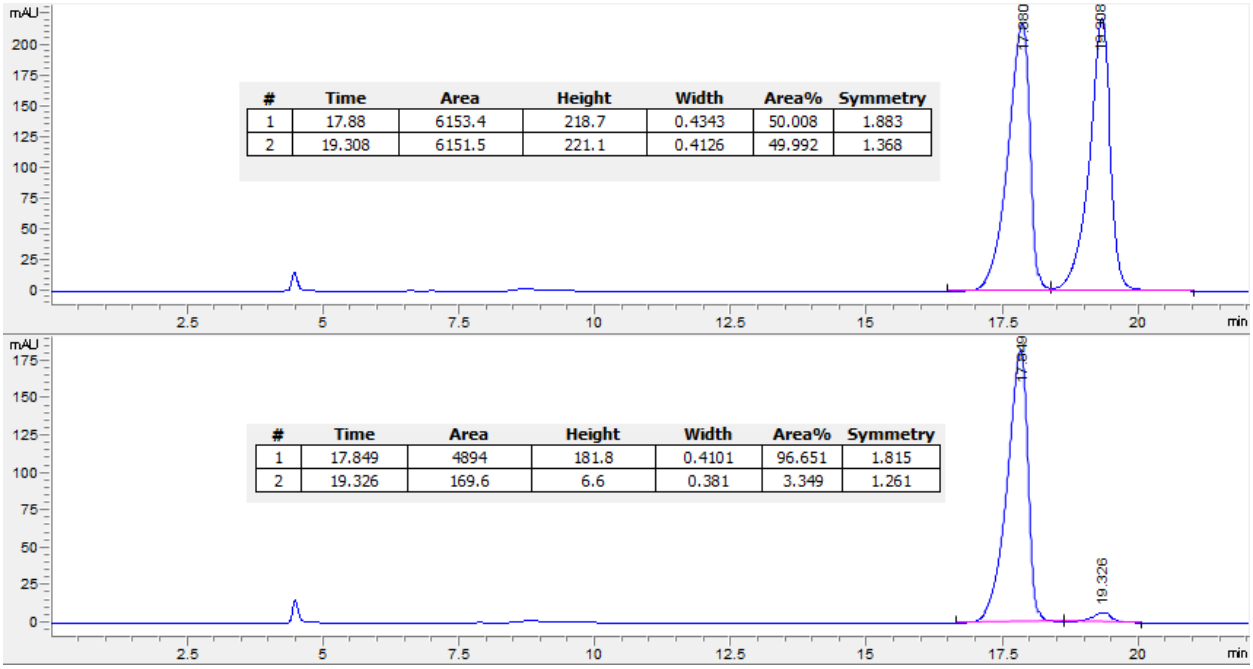
^1H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.21 (m, 5H), 6.72 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.78 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.99 (dd, *J* = 8.6, 6.6 Hz, 1H), 3.02 – 2.94 (m, 1H), 2.71 – 2.64 (m, 1H), 1.40 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 165.2, 142.1, 136.1, 129.1, 128.3, 127.7, 126.0, 80.4, 50.0, 35.5, 28.0.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.22 – -152.50 (m), -157.75 (t, *J* = 21.6 Hz), -162.24 – -162.35 (m).

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{22}H_{19}O_4F_5Na$: 465.1101. Found: 465.1097.

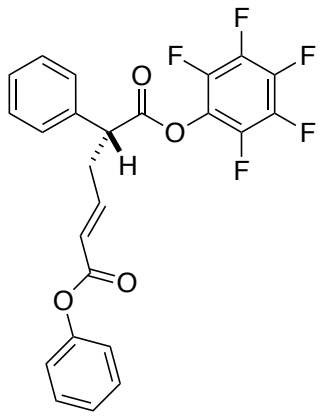
HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 0.75 mL/min, 200:1 Hexane:Isopropanol, 210 nm, t_{minor} = 19.326 min, t_{major} = 17.849 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	17.88	6153.4	218.7	0.4343	50.008	1.883
2	19.308	6151.5	221.1	0.4126	49.992	1.368

#	Time	Area	Height	Width	Area%	Symmetry
1	17.849	4894	181.8	0.4101	96.651	1.815
2	19.326	169.6	6.6	0.381	3.349	1.261

6-(Pentafluorophenyl) 1-phenyl (*E*)-5-phenylhex-2-enedioate (23): Prepared according to General Procedure G. The title compound was obtained (37 mg, 0.08 mmol, 80%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 103–104 °C.

$[\alpha]_D^{23}$ –60.6 (*c* = 0.5, $CHCl_3$).

IR (neat): 2359, 2342, 2332, 2179, 2162, 2023, 1975, 1781, 1740, 1654, 1520, 1493, 1198, 1143, 1110, 1004 cm^{-1}.

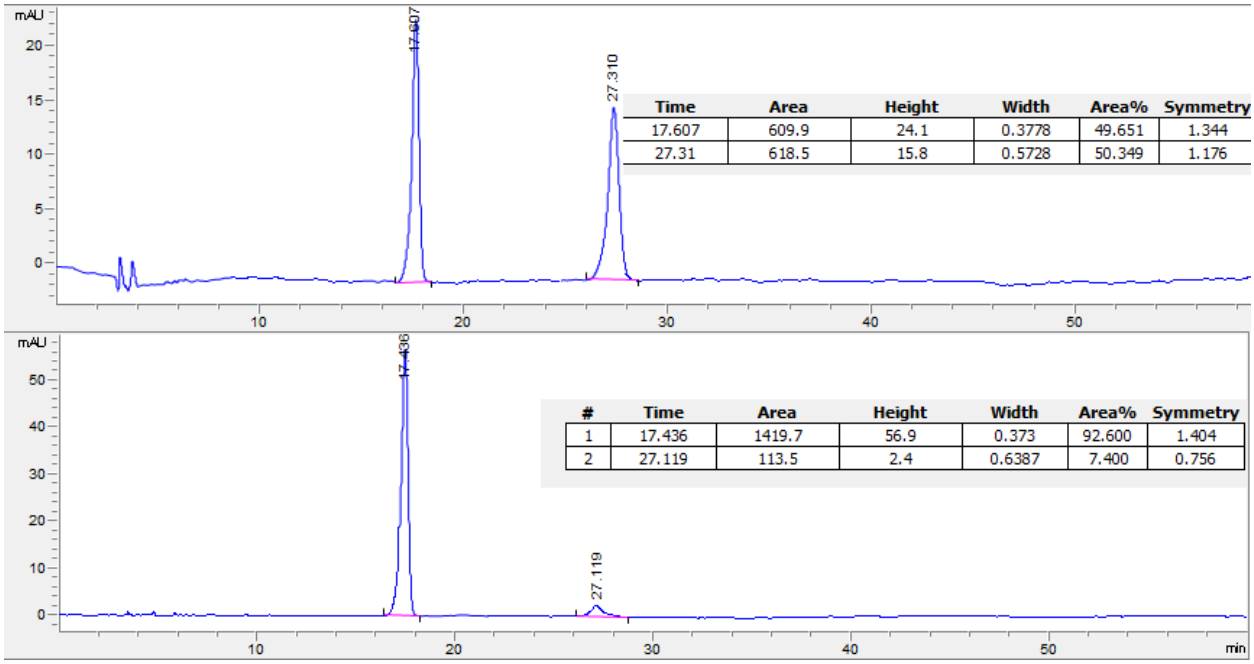
^1H NMR (400 MHz, $CDCl_3$): δ 7.47 – 7.33 (m, 5H), 7.25 – 7.21 (m, 1H), 7.15 – 7.04 (m, 2H), 6.13 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.14 (dd, *J* = 8.3, 6.9 Hz, 1H), 3.24 – 3.09 (m, 1H), 2.92 – 2.84 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 164.2, 150.6, 145.7, 135.9, 129.4, 129.2, 129.1, 128.4, 127.8, 125.8, 123.5, 121.5, 49.8, 35.7.

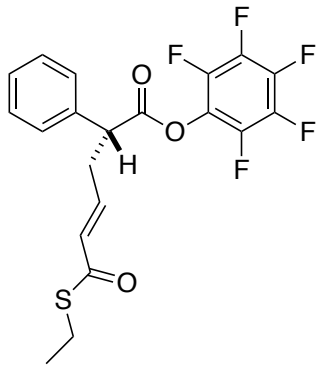
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.29 – -152.51 (m), -157.55 (t, *J* = 21.6 Hz), -162.06 – -162.17 (m).

HRMS (ESI): m/z calcd for $[M+Na]^+$ $C_{24}H_{15}O_4F_5Na$: 485.0788. Found: 485.0776.

HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 27.119 min, t_{major} = 17.436 min).



Pentafluorophenyl (*E*)-6-(ethylthio)-6-oxo-2-phenylhex-4-enoate (24): Prepared according to General Procedure G. The title compound was obtained (32 mg, 0.075 mmol, 75%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 87–88 °C.

$[\alpha]_D^{23}$ –53.9 (*c* = 1.00, $CHCl_3$).

IR (neat): 2972, 1780, 1670, 1634, 1517, 1455, 1355, 1265, 1143, 1106, 1087, 1025, 993, 820, 746, 699 cm^{-1}.

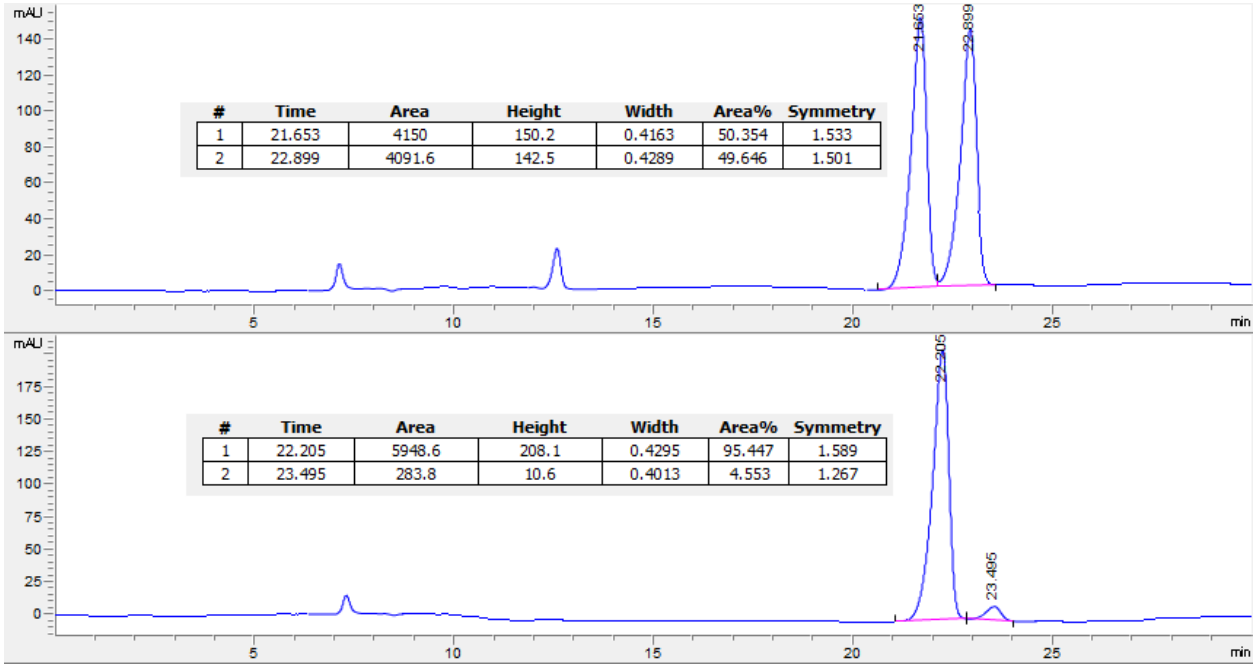
^1H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.30 (m, 5H), 6.79 (dt, *J* = 15.5, 7.1 Hz, 1H), 6.17 (dt, *J* = 15.5, 1.5 Hz, 1H), 4.07 (dd, *J* = 8.1, 7.0 Hz, 1H), 3.11 – 3.03 (m, 1H), 2.94 (q, *J* = 7.4 Hz, 2H), 2.82 – 2.74 (m, 1H), 1.27 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6, 168.9, 139.1, 135.9, 131.1, 129.2, 128.3, 127.7, 49.8, 35.5, 23.2, 14.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.20 – -152.55 (m), -157.68 (t, *J* = 21.6 Hz), -162.15 – -162.26 (m).

HRMS (APCI): m/z calcd for $[M+H]^+$ $C_{20}H_{16}O_3F_5S$: 431.0738. Found: 431.0735.

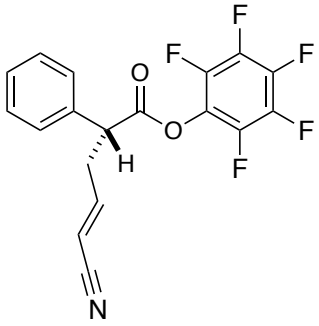
HPLC analysis using a chiral column (Chiralpak IB 5µ column, 22 °C, 0.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 23.495 min, t_{major} = 22.205 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	21.653	4150	150.2	0.4163	50.354	1.533
2	22.899	4091.6	142.5	0.4289	49.646	1.501

#	Time	Area	Height	Width	Area%	Symmetry
1	22.205	5948.6	208.1	0.4295	95.447	1.589
2	23.495	283.8	10.6	0.4013	4.553	1.267

Pentafluorophenyl (*E*)-5-cyano-2-phenylpent-4-enoate (25): Prepared according to General Procedure G at 0 °C. The title compound was obtained (29 mg, 0.079 mmol, 79%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 90:10]. The enantiomeric ratio (88:12) was determined by chiral HPLC in comparison with the racemate.



M.p. (diethyl ether, plates) = 83°C.

$[\alpha]_D^{23}$ –27.8 (*c* = 1.00, $CHCl_3$).

IR (neat): 3070, 2934, 2231, 1777, 1725, 1659, 1513, 1365, 1271, 1160 cm^{-1}.

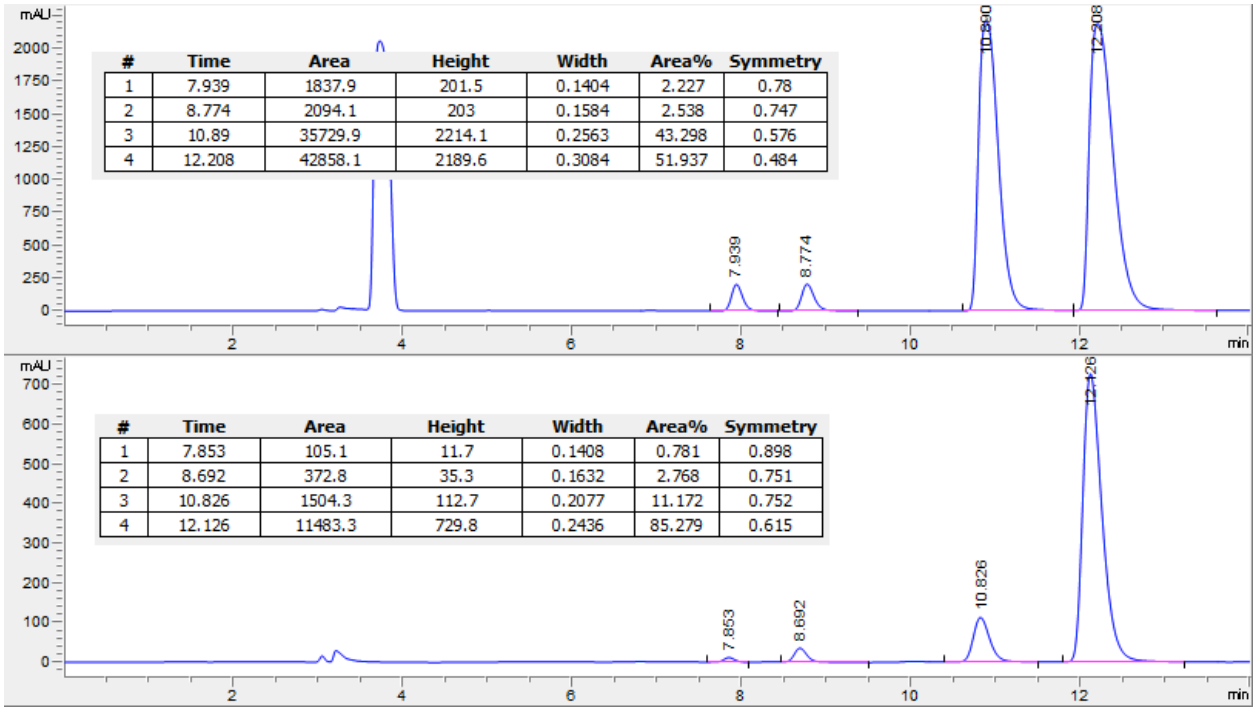
^1H NMR (400 MHz, $CDCl_3$): δ 7.46 – 7.30 (m, 5H), 6.62 (dt, *J* = 16.3, 7.3 Hz, 1H), 5.42 (dt, *J* = 16.3, 1.5 Hz, 1H), 4.05 (t, *J* = 7.6 Hz, 1H), 3.07 (dtd, *J* = 15.1, 7.6, 1.5 Hz, 1H), 2.83 (dtd, *J* = 14.7, 7.2, 1.7 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 150.5, 135.4, 129.5, 128.8, 127.9, 116.8, 103.3, 49.7, 36.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.12 – -152.97 (m), -157.28 (t, *J* = 21.6 Hz), -161.65 – -162.23 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{18}H_{11}F_5O_2N$: 368.0704 Found: 368.0705.

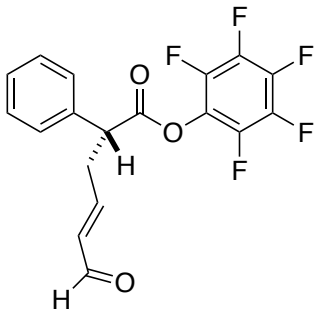
HPLC analysis using a chiral column (Chiralpak IA 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 10.826 min, t_{major} = 12.126 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	7.939	1837.9	201.5	0.1404	2.227	0.78
2	8.774	2094.1	203	0.1584	2.538	0.747
3	10.89	35729.9	2214.1	0.2563	43.298	0.576
4	12.208	42858.1	2189.6	0.3084	51.937	0.484

#	Time	Area	Height	Width	Area%	Symmetry
1	7.853	105.1	11.7	0.1408	0.781	0.898
2	8.692	372.8	35.3	0.1632	2.768	0.751
3	10.826	1504.3	112.7	0.2077	11.172	0.752
4	12.126	11483.3	729.8	0.2436	85.279	0.615

Pentafluorophenyl (*E*)-6-oxo-2-phenylhex-4-enoate (26): Prepared according to General Procedure G. The title compound was obtained (19 mg, 0.05 mmol, 50%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 49–50 °C.

$[\alpha]_D^{23}$ –83.3 (*c* = 1.00, $CHCl_3$).

IR (neat): 2362, 2341, 2160, 1976, 1779, 1690, 1517, 1130, 1100, 1037, 1027, 992, 741, 698, 546 cm^{-1}.

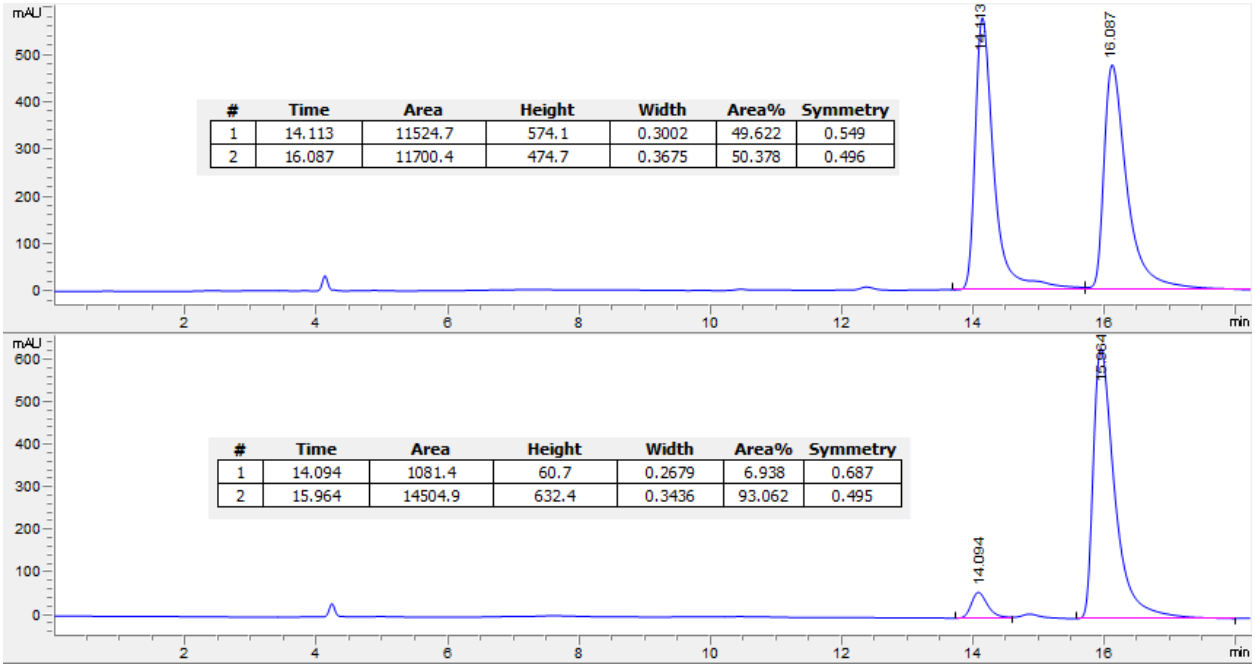
^1H NMR (400 MHz, $CDCl_3$): δ 9.49 (d, *J* = 7.7 Hz, 1H), 7.48 – 7.31 (m, 5H), 6.75 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.19 (ddt, *J* = 15.7, 7.7, 1.4 Hz, 1H), 4.13 (t, *J* = 7.6 Hz, 1H), 3.24 – 3.16 (m, 1H), 2.98 – 2.91 (m, 1H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 193.2, 168.8, 152.2, 135.6, 135.1, 129.3, 128.5, 127.7, 49.7, 35.8.

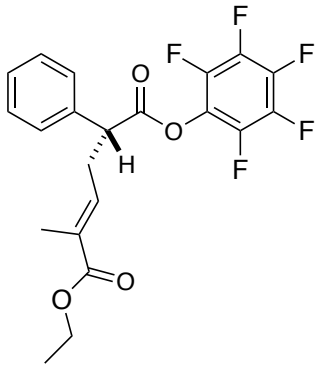
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.43 – -152.66 (m), -157.39 (t, *J* = 21.7 Hz), -161.83 – -162.17 (m).

HRMS (EI): m/z calcd for $[M]^+$ $C_{18}H_{11}O_3F_5$: 370.0623. Found: 370.0620.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 14.094 min, t_{major} = 15.964 min).



1-Ethyl 6-(pentafluorophenyl) (*E*)-2-methyl-5-phenylhex-2-enedioate (27): Prepared according to General Procedure G. The title compound was obtained (30 mg, 0.070 mmol, 70%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 97:3]. The enantiomeric ratio (90:10) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane, needles) = 62–63 °C.

$[\alpha]_D^{23}$ –35.7 (*c* = 1.00, $CHCl_3$).

IR (neat): 3033 2921, 1782, 1723, 1660, 1515, 1370, 1158, 1095, 998 cm^{-1}.

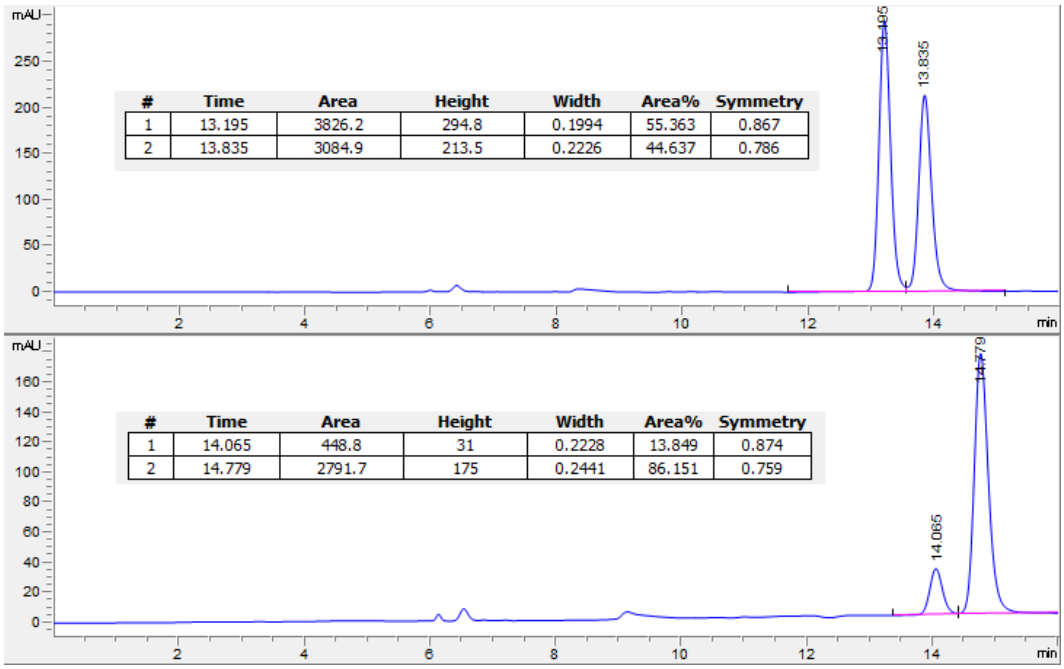
^1H NMR (400 MHz, $CDCl_3$): δ 7.37 (m, 5H), 6.71 (ddt, *J* = 7.6, 6.1, 1.6 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.05 (dd, *J* = 8.3, 7.1 Hz, 1H), 3.06 (dt, *J* = 15.5, 7.9 Hz, 1H), 2.82 – 2.71 (m, 1H), 1.82 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): 169.3, 167.6, 136.4, 136.3, 130.7, 129.1, 128.2, 127.8, 60.6, 50.1, 32.5, 14.1, 12.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.28 – -152.66 (m), -157.76 (t, *J* = 21.7 Hz), -162.04 – -162.53 (m).

HRMS (CI): *m/z* calcd for $[M+Na]^+$ $C_{21}H_{18}F_5O_4Na$: 451.0939 Found: 451.0938.

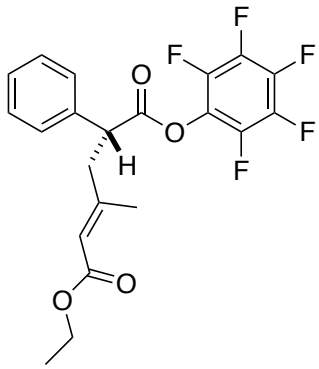
HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.50 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 14.065 min, t_{major} = 14.779 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	13.195	3826.2	294.8	0.1994	55.363	0.867
2	13.835	3084.9	213.5	0.2226	44.637	0.786

#	Time	Area	Height	Width	Area%	Symmetry
1	14.065	448.8	31	0.2228	13.849	0.874
2	14.779	2791.7	175	0.2441	86.151	0.759

1-Ethyl 6-(pentafluorophenyl) (*E*)-3-methyl-5-phenylhex-2-enedioate (28): Prepared according to General Procedure G. The *title compound* was obtained (33 mg, 0.076 mmol, 76%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 97:3]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with racemate.



M.p. (pentane, needles) = 77–78 °C.

$[\alpha]_D^{23}$ -39.4° (c = 1.00, $CHCl_3$).

IR (neat): 3028 2920, 2854, 1780, 1721, 1661, 1515, 1370, 1265, 1158, 1098, 994 cm^{-1}.

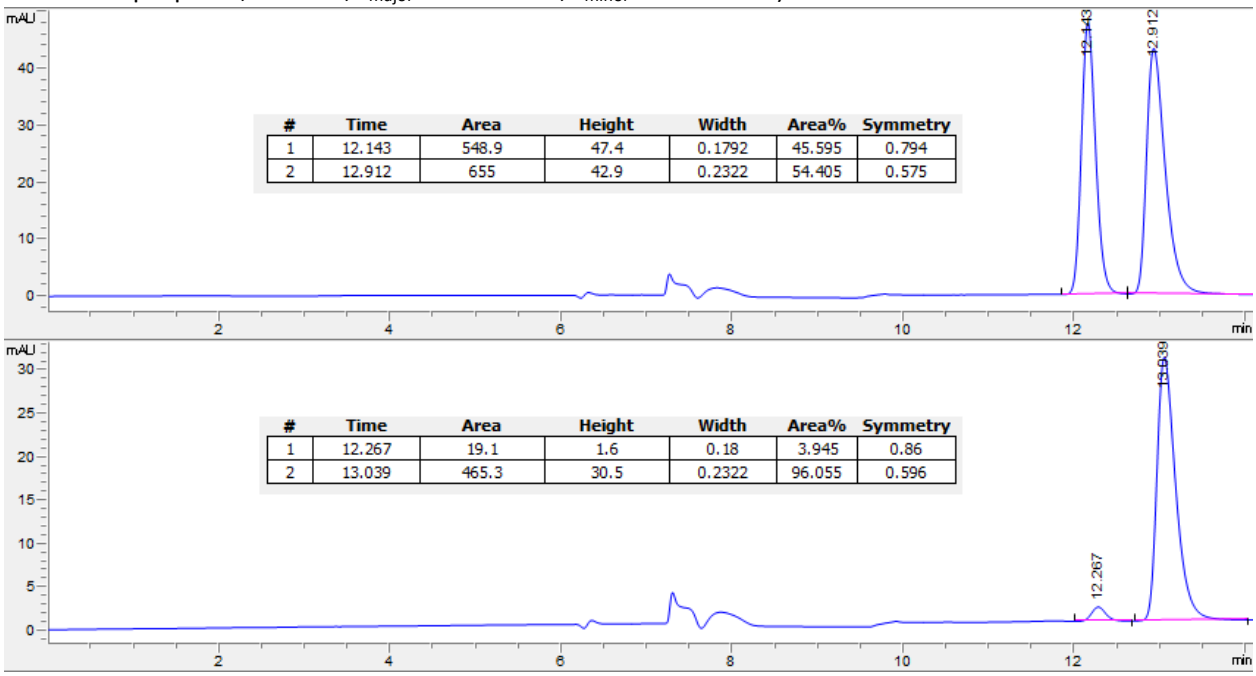
^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (m, 5H), 5.70 (s, 1H), 4.20 – 4.08 (m, 3H), 3.04 (dd, *J* = 14.6, 8.9 Hz, 1H), 2.66 (dd, *J* = 14.6, 6.5 Hz, 1H), 2.19 (s, 2H), 1.25 (td, *J* = 7.1, 1.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.1, 166.2, 154.3, 136.2, 129.1, 128.2, 127.7, 118.3, 59.7, 49.1, 43.9, 18.7, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.23 – -152.64 (m), -157.75 (t, *J* = 21.7 Hz), -162.14 – -162.47 (m).

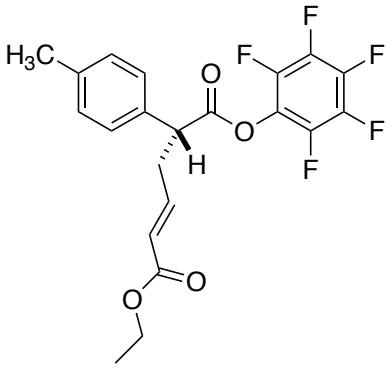
HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{21}H_{18}F_5O_4$: 429.1120 Found: 429.1123.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.50 mL/min, 99:1 hexane:isopropanol, 210 nm, t_{major} = 13.04 min, t_{minor} = 12.27 min).



Products from Scheme 7

1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(p-tolyl)hex-2-enedioate (29): Prepared according to General Procedure G. The title compound was obtained (30 mg, 0.07 mmol, 70%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 50–51 °C.

$[\alpha]_D^{23}$ –46.6 (*c* = 1.00, $CHCl_3$).

IR (neat): 1781, 1720, 1656, 1519, 1470, 1447, 1369, 1312, 1268, 1205, 1186, 1159, 1107, 1040, 995 cm^{-1}.

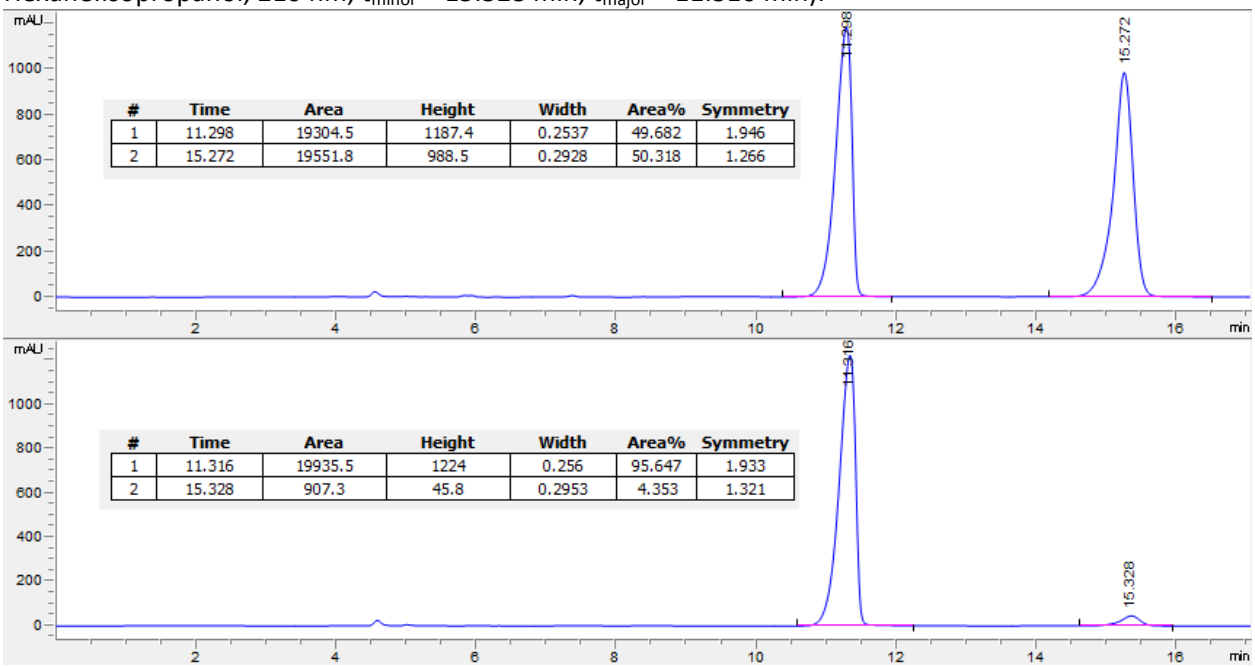
^1H NMR (400 MHz, $CDCl_3$): δ 7.24 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.88 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.91 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.03 (dd, *J* = 8.2, 7.0 Hz, 1H), 3.10 – 3.02 (m, 1H), 2.80 – 2.73 (m, 1H), 2.36 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.1, 165.9, 143.6, 138.1, 132.9, 129.8, 127.6, 124.2, 60.4, 49.5, 35.6, 21.1, 14.2.

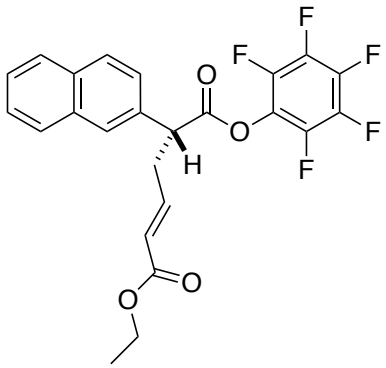
^{19}F NMR (376 MHz, $CDCl_3$): δ -151.75 – -152.85 (m), -157.80 (t, *J* = 21.7 Hz), -161.53 – -163.61 (m).

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{21}H_{18}O_4F_5$: 429.1120. Found: 429.1116.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 15.328 min, t_{major} = 11.316 min).



1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(naphthalen-2-yl)hex-2-enedioate (30): Prepared according to General Procedure G. The title compound was obtained (32 mg, 0.069 mmol, 69%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 74–75 °C

$[\alpha]_D^{23}$ –63.5 (*c* = 1.00, $CHCl_3$).

IR (neat): 1781, 1719, 1656, 1601, 1519, 1470, 1445, 1369, 1311, 1270, 1213, 1175, 1149, 1108, 1041, 995 cm^{-1}.

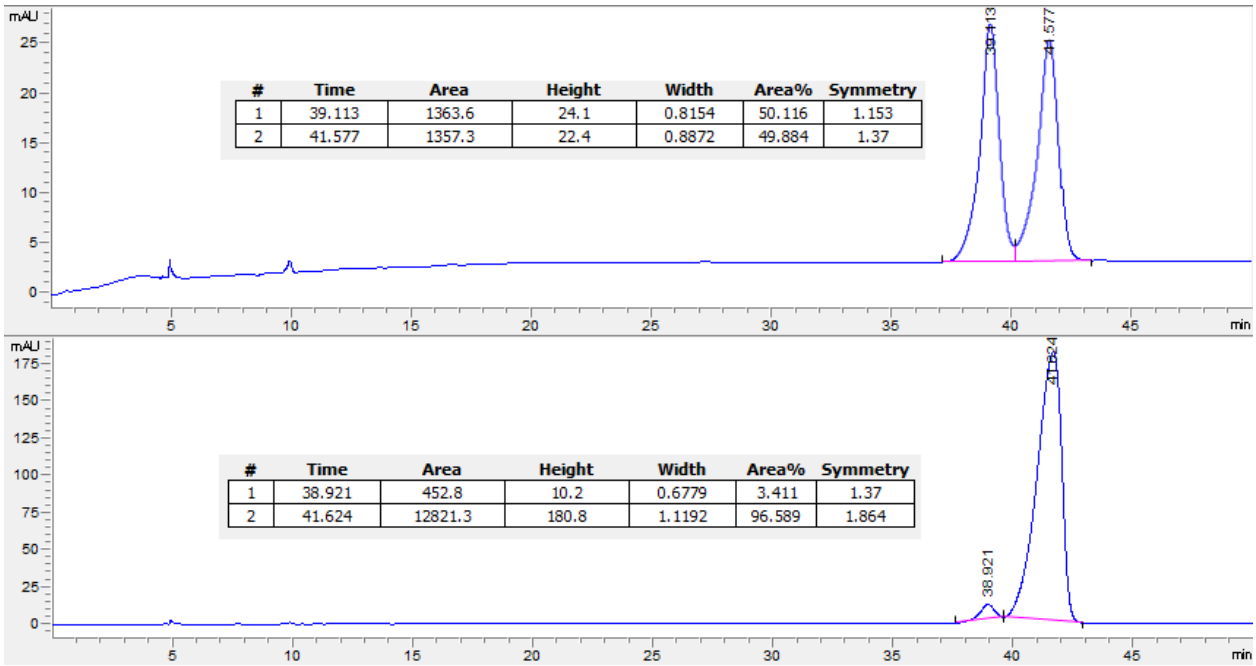
^1H NMR (400 MHz, $CDCl_3$): δ 7.95 – 7.78 (m, 4H), 7.59 – 7.39 (m, 3H), 6.93 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.95 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.25 (dd, *J* = 8.1, 7.0 Hz, 1H), 4.21 – 4.14 (m, 2H), 3.22 – 3.14 (m, 1H), 2.93 – 2.86 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.0, 165.9, 143.4, 133.4, 133.3, 132.9, 129.1, 127.9, 127.7, 127.2, 126.6, 126.5, 125.1, 124.3, 60.4, 50.0, 35.6, 14.1.

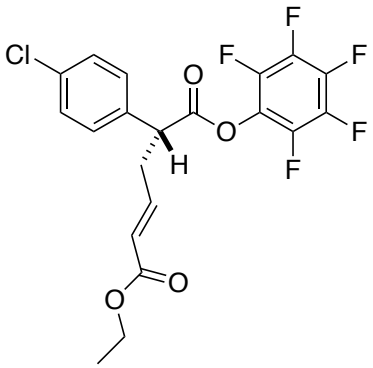
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.03 – -152.53 (m), -157.63 (t, *J* = 21.7 Hz), -161.83 – -162.62 (m).

HRMS (CI): m/z calcd for $[M]^+$ $C_{24}H_{17}O_4F_5$: 464.1042. Found: 464.1027.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 38.921min, t_{major} = 41.624 min).



1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(4-chlorophenyl)hex-2-enedioate (31): Prepared according to General Procedure G. The reaction was run at 0 °C for 30 min. The title compound was obtained (38 mg, 0.085 mmol, 85%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 63–64 °C.

$[\alpha]_D^{23}$ –62.7 (*c* = 1.00, $CHCl_3$).

IR (neat): 2984, 1782, 1719, 1657, 1519, 1494, 1392, 1314, 1271, 1207, 1191, 1160, 1093, 1040, 995 cm^{-1}.

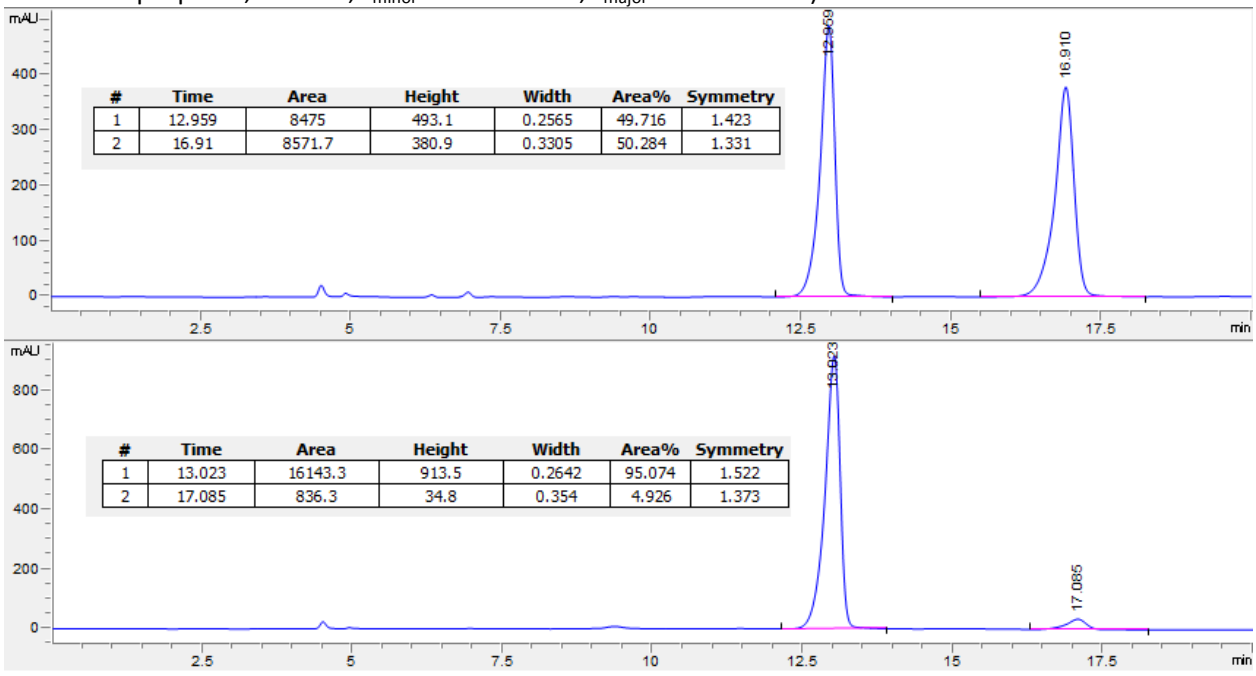
^1H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 6.85 (dt, *J* = 15.6, 7.1 Hz, 1H), 5.90 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.05 (t, *J* = 7.6 Hz, 1H), 3.12 – 3.00 (m, 1H), 2.80 – 2.73 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 165.8, 142.8, 134.4, 134.4, 129.4, 129.1, 124.6, 60.5, 49.2, 35.4, 14.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.16 – -152.75 (m), -157.36 (t, *J* = 21.7 Hz), -161.55 – -162.30 (m).

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{20}H_{15}O_4ClF_5$: 449.0583. Found: 449.0574.

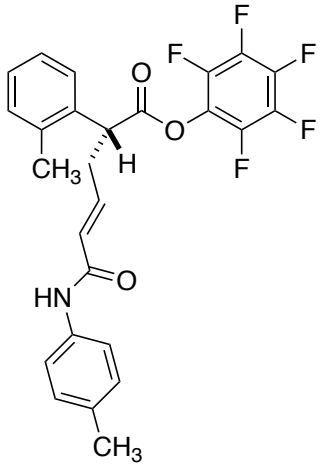
HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 17.085 min, t_{major} = 13.023 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	12.959	8475	493.1	0.2565	49.716	1.423
2	16.91	8571.7	380.9	0.3305	50.284	1.331

#	Time	Area	Height	Width	Area%	Symmetry
1	13.023	16143.3	913.5	0.2642	95.074	1.522
2	17.085	836.3	34.8	0.354	4.926	1.373

Pentafluorophenyl (*E*)-6-oxo-2-(*o*-tolyl)-6-(*p*-tolylamino)hex-4-enoate (32): Prepared according to General Procedure F. The *title compound* was obtained (26 mg, 0.054 mmol, 54%) as a pale yellow oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -33.3° (c = 1.00, $CHCl_3$).

IR (neat): 3317, 3030, 2922, 2859, 1774, 1669, 1636, 1596, 1517, 1340, 1019, 978, 508 cm^{-1}.

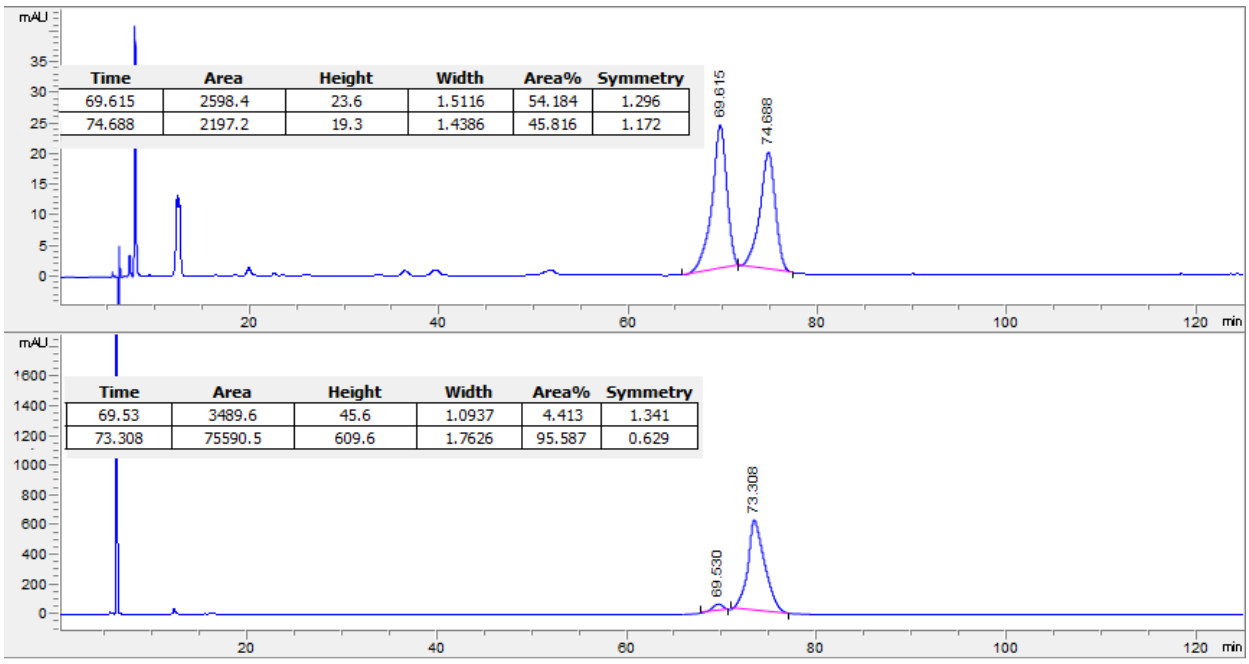
^1H NMR (500 MHz, $CDCl_3$): δ 7.45 (d, *J* = 7.9 Hz, 2H), 7.35 – 7.31 (m, 1H), 7.28 – 7.25 (m, 3H), 7.17 – 7.11 (m, 3H), 6.93 (dt, *J* = 14.8, 7.2 Hz, 1H), 6.01 (dd, *J* = 15.1, 1.5 Hz, 1H), 4.37 (dd, *J* = 8.2, 6.6 Hz, 1H), 3.13 (dt, *J* = 15.4, 7.9 Hz, 1H), 2.77 (dtd, *J* = 14.8, 6.7, 1.5 Hz, 1H), 2.47 (s, 3H), 2.34 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.5, 163.0, 140.8, 136.1, 134.7, 131.1, 129.5, 128.1, 126.9, 126.8, 126.6, 120.0, 45.7, 35.2, 20.9, 19.8.

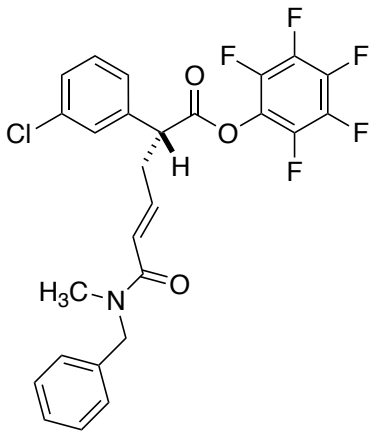
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.17 – -152.51 (m), -157.69 (t, *J* = 21.6 Hz), -161.75 – -162.54 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{26}H_{21}F_5NO_3$: 490.1447 Found: 490.1440.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 0.85 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 73.31 min, t_{minor} = 69.53 min).



Pentafluorophenyl (*E*)-6-(benzyl(methyl)amino)-2-(3-chlorophenyl)-6-oxohex-4-enoate (33): Prepared according to General Procedure F. The *title compound* was obtained (43 mg, 0.083 mmol, 83%) as a clear colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20]. The enantiomeric ratio (92:8) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -45.8° (c = 1.00, $CHCl_3$).

IR (neat): 3030, 2943, 1775, 1669, 1623, 1514, 1483, 795, 691 cm^{-1}.

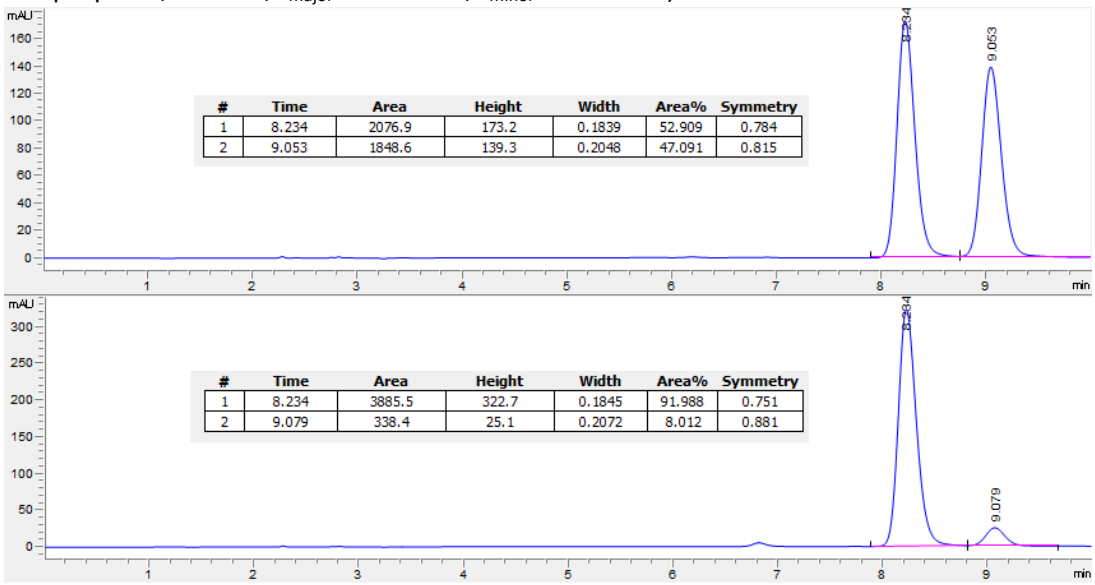
^1H NMR (500 MHz, $CDCl_3$): [Note: At this temperature, two rotamers in 50:50 ratio are visible.] δ 7.43 – 7.20 (m, 16H), 7.13 (d, *J* = 7.4 Hz, 2H), 6.87 (ddt, *J* = 22.0, 14.7, 7.2 Hz, 2H), 6.40 (d, *J* = 15.1 Hz, 1H), 6.32 (d, *J* = 15.0 Hz, 1H), 4.69 (d, *J* = 14.6 Hz, 1H), 4.63 (d, *J* = 14.6 Hz, 1H), 4.53 (d, *J* = 16.8 Hz, 1H), 4.48 (d, *J* = 16.8 Hz, 1H), 4.09 (t, *J* = 7.6 Hz, 1H), 4.02 (t, *J* = 7.6 Hz, 1H), 3.14 (dt, *J* = 15.4, 7.9 Hz, 1H), 3.10 – 3.03 (m, 1H), 2.99 (s, 3H), 2.93 (s, 3H), 2.86 – 2.76 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 168.7, 168.6, 166.4, 165.9, 140.5, 140.3, 138.1, 138.0, 137.1, 136.5, 135.0, 134.9, 130.4, 130.3, 128.9, 128.62, 128.56, 128.5, 128.2, 128.0, 127.7, 127.4, 126.3, 126.2, 123.9, 123.8, 53.3, 51.1, 49.72, 49.66, 35.9, 35.7, 34.8, 34.1.

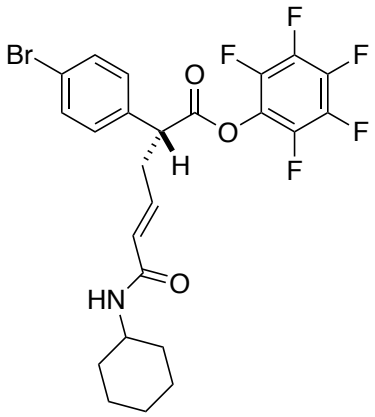
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.18 – -152.71 (m), -157.41 (dt, *J* = 28.0, 21.7 Hz), -162.01 (tdd, *J* = 22.8, 13.2, 5.5 Hz).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{26}H_{20}ClF_5NO_3$: 524.1046 Found: 524.1047.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.25 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 9.11 min, t_{minor} = 8.75 min).



Pentafluorophenyl (*E*)-2-(4-bromophenyl)-6-(cyclohexylamino)-6-oxohex-4-enoate (34): Prepared according to General Procedure F. The *title compound* was obtained (44 mg, 0.081 mmol, 81%) as a pale yellow oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 60:40]. The enantiomeric ratio (90:10) was determined by chiral HPLC in comparison with racemate.



M.p. (Et_2O, plates) = 198–199 °C.

$[\alpha]_D^{23}$ -64.5° (c = 1.00, $CHCl_3$).

IR (neat): 3035, 2947, 1774, 1670, 1620, 1511, 1486, 791, 690 cm^{-1}.

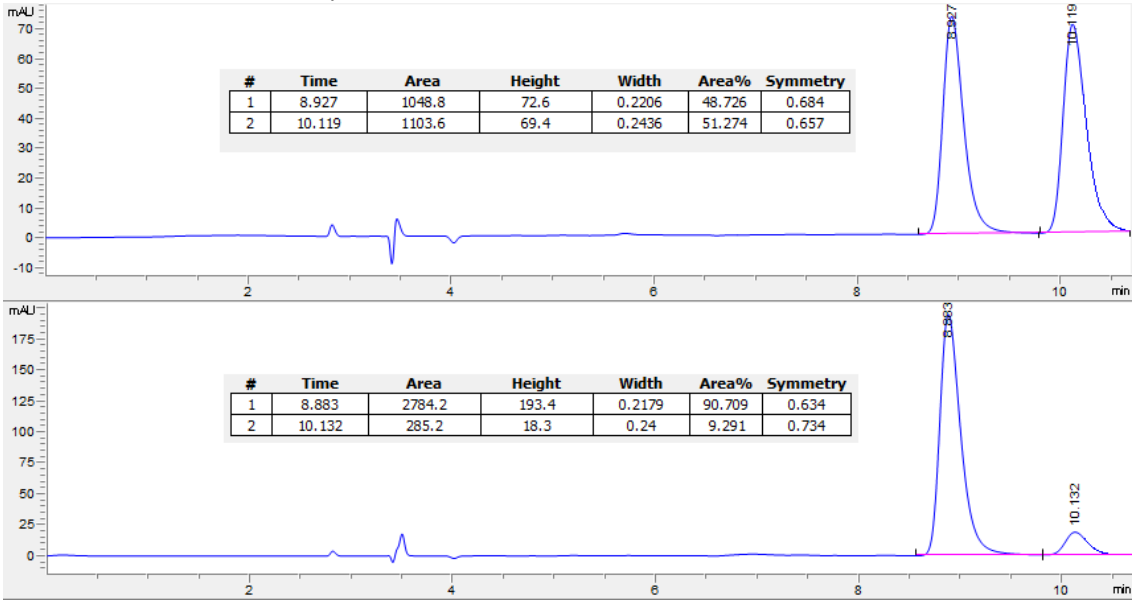
^1H NMR (400 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.72 (dt, *J* = 14.7, 7.2 Hz, 1H), 5.78 (d, *J* = 15.1 Hz, 1H), 5.27 (d, *J* = 8.2 Hz, 1H), 4.00 (t, *J* = 7.5 Hz, 1H), 3.80 (tdt, *J* = 11.0, 8.1, 4.0 Hz, 1H), 3.00 (dt, *J* = 15.4, 7.9 Hz, 1H), 2.69 (ddd, *J* = 14.8, 7.6, 6.1 Hz, 1H), 1.96 – 1.85 (m, 2H), 1.68 (dt, *J* = 13.2, 4.0 Hz, 2H), 1.62 – 1.55 (m, 1H), 1.42 – 1.28 (m, 2H), 1.12 (pd, *J* = 12.2, 6.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.8, 163.9, 138.3, 135.1, 132.3, 129.5, 127.1, 122.4, 49.5, 48.2, 35.4, 33.1, 25.5, 24.8.

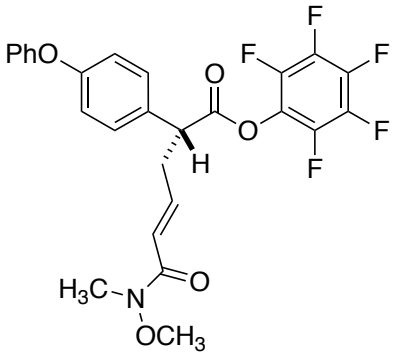
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.28 – -152.53 (m), -157.37 (t, *J* = 21.7 Hz), -161.91 – -162.09 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{24}H_{22}BrF_5NO_3$: 548.0677 Found: 548.0678.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.00 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 9.11 min, t_{minor} = 8.75 min).



Pentafluorophenyl (*E*)-6-(methoxy(methyl)amino)-6-oxo-2-(4-phenoxyphenyl)hex-4-enoate (35):



Prepared according to General Procedure F. The *title compound* was obtained (39 mg, 0.075 mmol, 75%) as a clear colorless oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 70:30]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with racemate.

$[\alpha]_D^{23}$ -58.2° (c = 1.00, $CHCl_3$).

IR (neat): 3067, 2971, 2931, 1773, 1660, 1518, 1487, 1236, 1058, 985, 789, 694, 518 cm^{-1}.

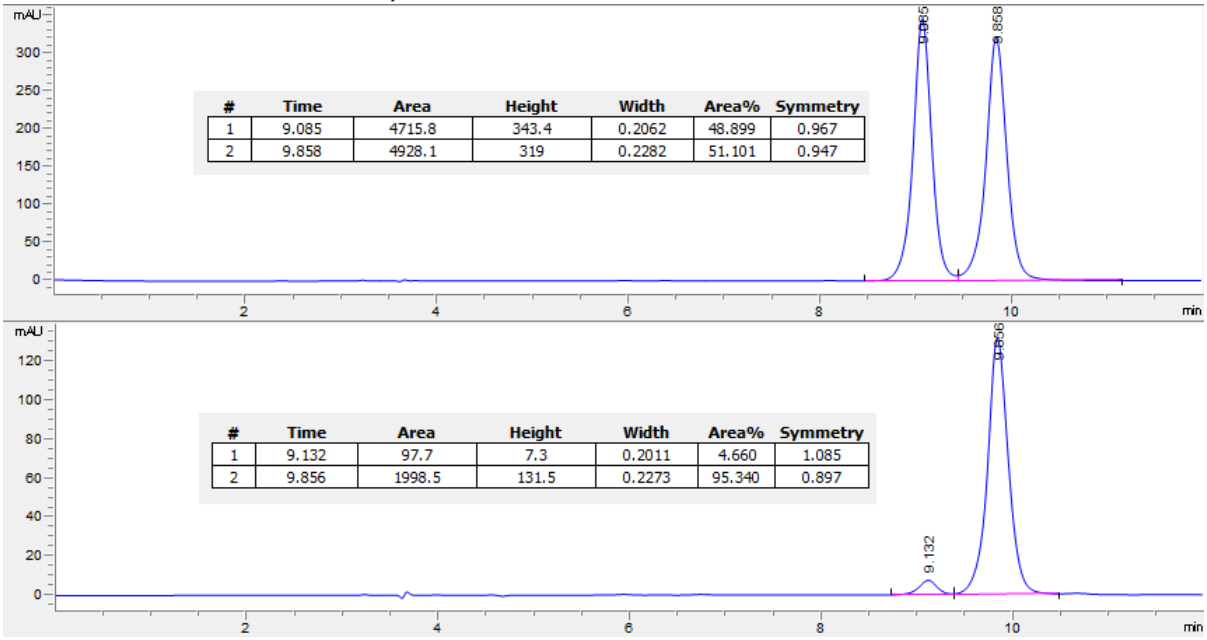
^1H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.27 (m, 4H), 7.11 (td, *J* = 7.3, 1.2 Hz, 1H), 7.04 – 6.95 (m, 4H), 6.88 (dt, *J* = 15.4, 7.1 Hz, 1H), 6.47 (d, *J* = 15.4 Hz, 1H), 4.05 (t, *J* = 7.6 Hz, 1H), 3.62 (s, 3H), 3.21 (s, 3H), 3.10 (dtd, *J* = 15.0, 7.6, 1.4 Hz, 1H), 2.82 (dtd, *J* = 14.7, 7.4, 1.6 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 169.1, 166.0, 157.5, 156.6, 141.8, 130.6, 129.8, 129.3, 123.6, 121.8, 119.2, 119.0, 61.6, 49.3, 35.8.

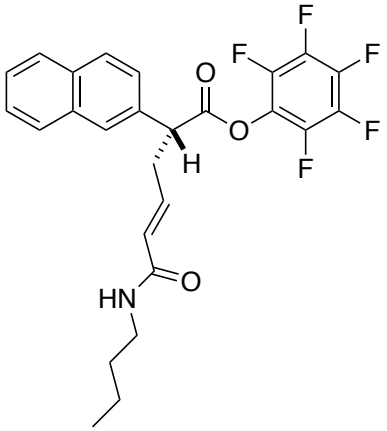
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.20 – -152.60 (m), -157.73 (t, *J* = 21.7 Hz), -161.58 – -162.80 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{26}H_{21}F_5NO_5$: 522.1334 Found: 522.1338.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 1.00 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 9.13 min, t_{minor} = 9.86 min).



Pentafluorophenyl (*E*)-6-(butylamino)-2-(naphthalen-2-yl)-6-oxohex-4-enoate (36): Prepared according to General Procedure F. The *title compound* was obtained (34 mg, 0.049 mmol, 69%) as a white solid following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 70:30]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with racemate.



M.p. (Et_2O, Plates) = 81–83 °C.

$[\alpha]_D^{23}$ -54.1° (c = 1.00, $CHCl_3$).

IR (neat): 3303, 3065, 2960, 2930, 2873, 1774, 1670, 1631, 1518, 1103, 981, 816, 478 cm^{-1}.

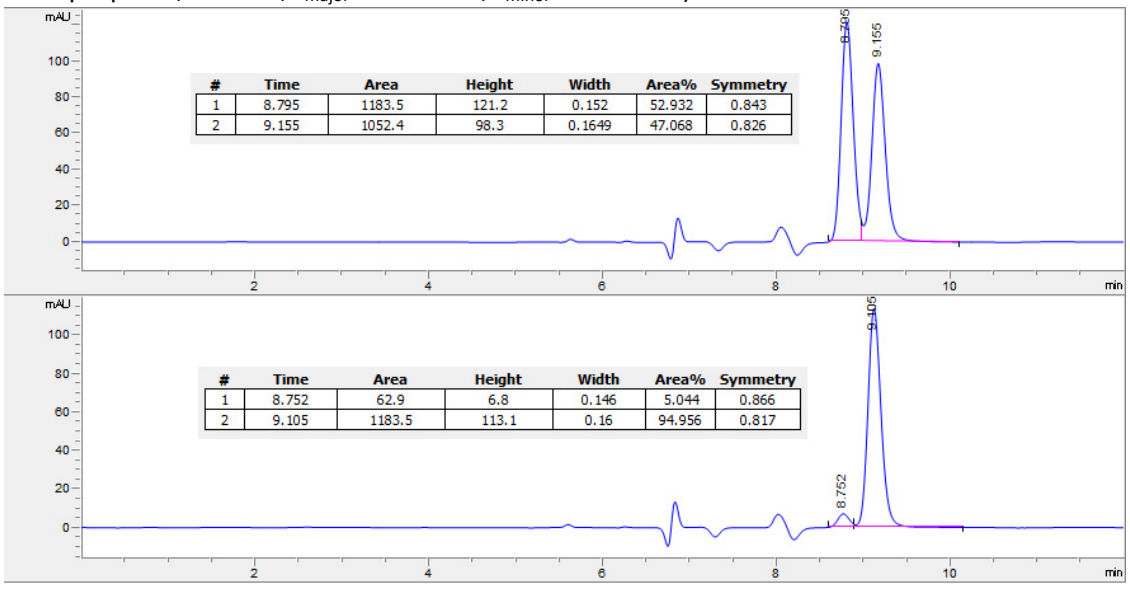
^1H NMR (400 MHz, $CDCl_3$): δ 7.88 – 7.78 (m, 4H), 7.53 – 7.41 (m, 3H), 6.80 (ddd, *J* = 15.1, 8.0, 6.2 Hz, 1H), 5.83 (d, *J* = 15.8 Hz, 1H), 5.42 (d, *J* = 6.0 Hz, 1H), 4.21 (t, *J* = 7.5 Hz, 1H), 3.27 (ddd, *J* = 10.9, 8.4, 5.9 Hz, 2H), 3.13 (dt, *J* = 15.1, 7.8 Hz, 1H), 2.88 – 2.78 (m, 1H), 1.46 (p, *J* = 7.3 Hz, 2H), 1.36 – 1.27 (m, 2H), 0.89 (td, *J* = 7.3, 1.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 169.2, 165.0, 138.9, 133.5, 133.4, 132.9, 129.0, 127.9, 127.7, 127.1, 126.7, 126.6, 126.4, 125.1, 50.2, 39.3, 35.5, 31.6, 20.0, 13.7.

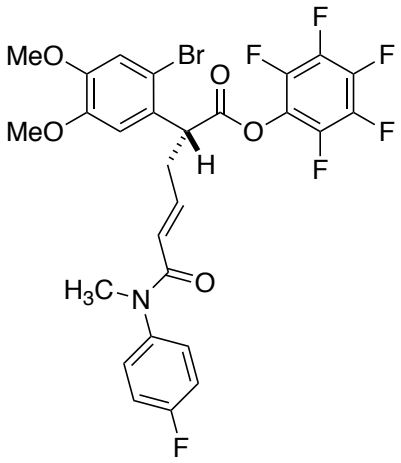
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.13 – -152.47 (m), -157.65 (t, *J* = 21.7 Hz), -162.18 (td, *J* = 22.3, 5.0 Hz).

HRMS (CI): *m/z* calcd for $[M]^+$ $C_{26}H_{22}F_5NO_3$: 491.1514 Found: 491.1501. *m/z* calcd for $[M+H]^+$ $C_{26}H_{23}F_5NO_3$: 492.1593 Found: 492.1578.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.50 mL/min, 67:33 hexane:isopropanol, 210 nm, t_{major} = 9.11 min, t_{minor} = 8.75 min).



Pentafluorophenyl (*E*)-2-(2-bromo-4,5-dimethoxyphenyl)-6-((4-fluorophenyl)(methyl)amino)-6-oxohex-4-enoate (37): Prepared according to General Procedure D. The *title compound* was obtained (46 mg, 0.072 mmol, 72%) as a yellow oil following purification by column chromatography [SiO_2, Petroleum Ether: EtOAc, 80:20]. The enantiomeric ratio (90:10) was determined by chiral HPLC in comparison with racemate.



$[\alpha]_D^{23}$ -30.1° (c = 1.00, $CHCl_3$).

IR (neat): 2960, 2937, 2847, 1779, 1665, 1631, 1509, 1378, 1214, 1164, 994, 911, 843, 728, 564 cm^{-1}.

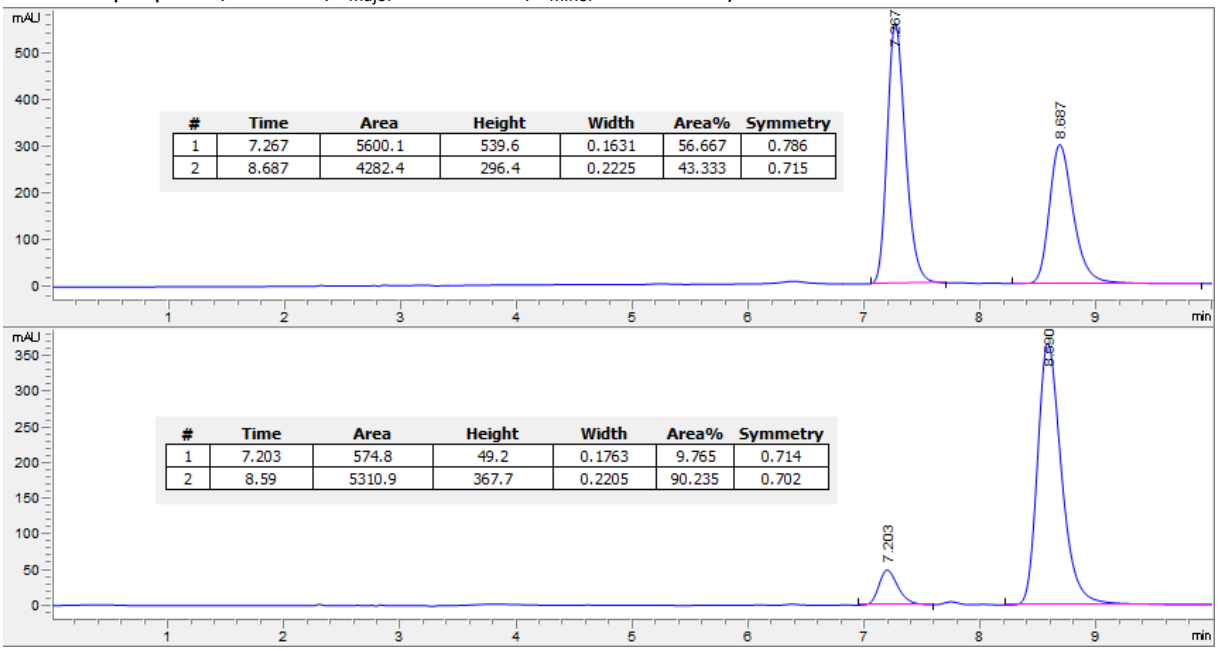
^1H NMR (400 MHz, $CDCl_3$): δ 7.10 – 6.93 (m, 5H), 6.82 (dt, *J* = 14.7, 7.1 Hz, 1H), 6.68 (s, 1H), 5.69 (d, *J* = 15.1 Hz, 1H), 4.51 (t, *J* = 7.3 Hz, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.26 (s, 3H), 2.84 (dt, *J* = 14.7, 7.3 Hz, 1H), 2.61 (dt, *J* = 14.8, 7.2 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 168.8, 165.3, 161.5 (d, *J* = 246.9 Hz), 159.4, 149.2, 148.9, 140.0, 139.4 (d, *J* = 3.0 Hz), 128.9 (d, *J* = 8.6 Hz), 127.5, 124.3, 116.4 (d, *J* = 22.7 Hz), 115.6, 114.8, 110.4, 56.1, 56.0, 48.3, 37.4, 35.0.

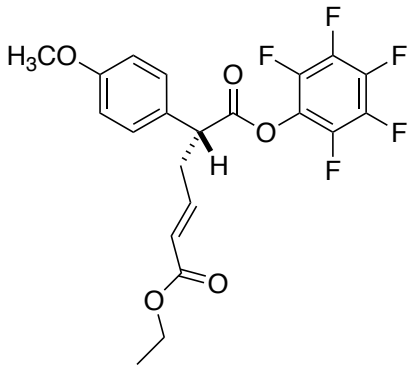
^{19}F NMR (376 MHz, $CDCl_3$): δ -113.70 (p, *J* = 6.4 Hz), -152.23 – -152.45 (m), -157.51 (t, *J* = 21.7 Hz), -161.89 – -162.34 (m).

HRMS (CI): *m/z* calcd for $[M+H]^+$ $C_{27}H_{21}BrF_6NO_5$: 632.0502 Found: 632.0480.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.25 mL/min, 85:15 hexane:isopropanol, 210 nm, t_{major} = 8.59 min, t_{minor} = 7.20 min).



1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(4-methoxyphenyl)hex-2-enedioate (38): Prepared according to General Procedure G. The title compound was obtained (29 mg, 0.065 mmol, 65%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 94–95 °C

$[\alpha]_D^{23}$ –69.8 (*c* = 1.00, $CHCl_3$).

IR (neat): 1781, 1720, 1656, 1612, 1519, 1468, 1445, 1369, 1305, 1255, 1181, 1160, 1111, 1036, 996 cm^{-1}.

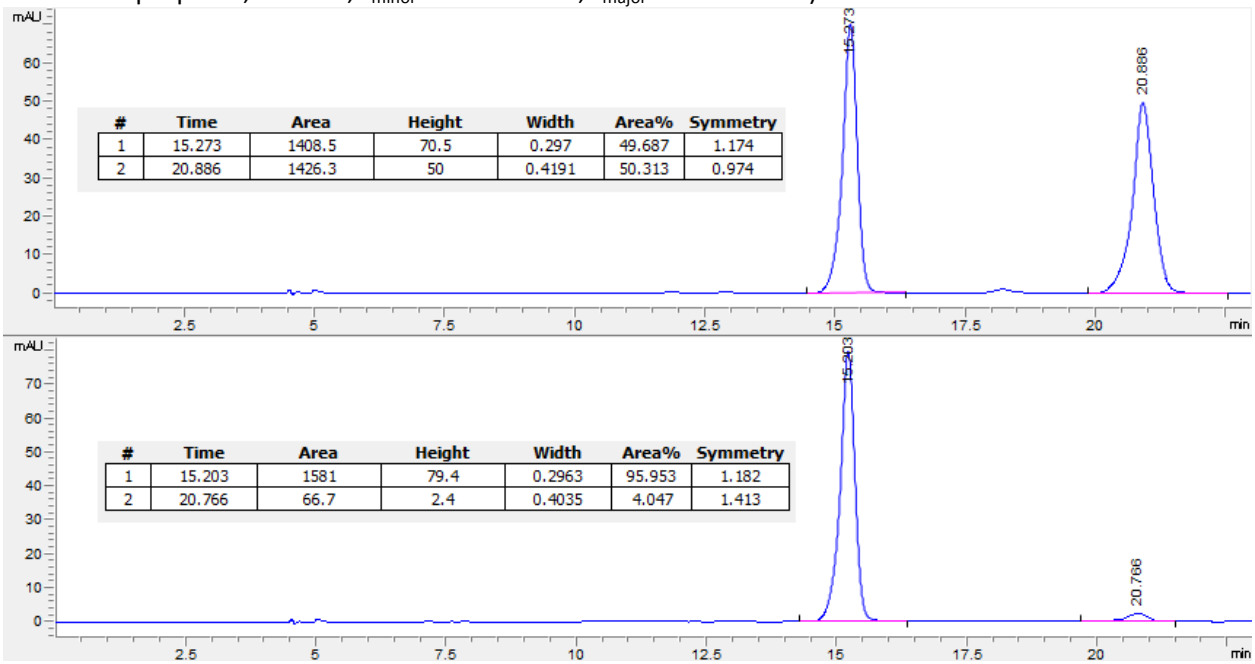
^1H NMR (400 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.8 Hz, 2H), 6.99 – 6.77 (m, 3H), 5.91 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 4.01 (t, *J* = 7.6 Hz, 1H), 3.13 – 2.97 (m, 1H), 2.80 – 2.72 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 165.9, 159.5, 143.6, 128.9, 127.9, 124.2, 114.5, 60.4, 55.3, 49.1, 35.6, 14.2.

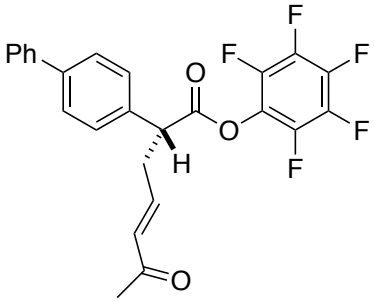
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.12 – -152.70 (m), -157.79 (t, *J* = 21.7 Hz), -161.96 – -162.62 (m).

HRMS (CI): m/z calcd for $[M]^+$ $C_{21}H_{17}O_5F_5$: 444.0991. Found: 444.0979.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 20.765 min, t_{major} = 15.202 min).



Pentafluorophenyl (*E*)-2-([1,1'-biphenyl]-4-yl)-6-oxohept-4-enoate (39): Prepared according to General Procedure G. The title compound was obtained (35 mg, 0.075 mmol, 75%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (91:9) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 103–104 °C.

$[\alpha]_D^{23}$ –92.2 (*c* = 1.00, $CHCl_3$).

IR (neat): 1781, 1700, 1678, 1632, 1520, 1488, 1361, 1254, 1107, 996, 760, 699 cm^{-1}.

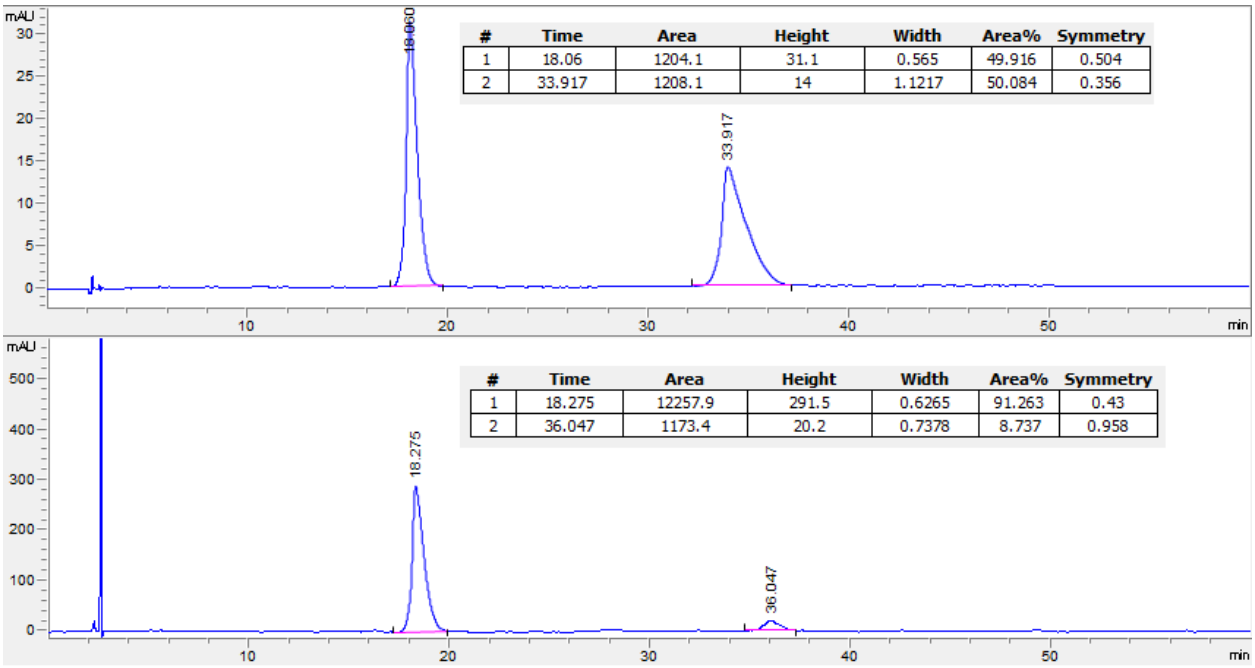
^1H NMR (400 MHz, $CDCl_3$): δ 7.69 – 7.55 (m, 4H), 7.50 – 7.41 (m, 4H), 7.40 – 7.33 (m, 1H), 6.76 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.20 (dt, *J* = 16.0, 1.5 Hz, 1H), 4.14 (dd, *J* = 8.5, 6.8 Hz, 1H), 3.17 – 3.09 (m, 1H), 2.89 – 2.82 (m, 1H), 2.24 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 169.0, 142.2, 141.3, 140.2, 134.8, 133.5, 128.8, 128.1, 127.8, 127.6, 127.0, 49.7, 35.8, 27.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.22 – -152.68 (m), -157.44 (t, *J* = 21.7 Hz), -161.57 – -162.41 (m).

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{25}H_{18}O_3F_5$: 461.1171. Found: 461.1149.

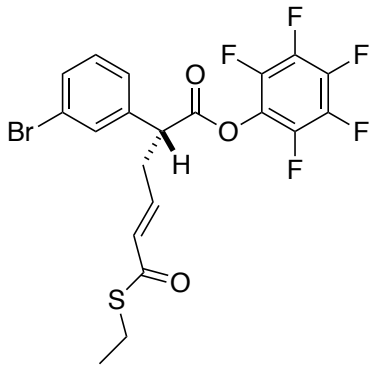
HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 1.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 36.047 min, t_{major} = 18.275 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	18.06	1204.1	31.1	0.565	49.916	0.504
2	33.917	1208.1	14	1.1217	50.084	0.356

#	Time	Area	Height	Width	Area%	Symmetry
1	18.275	12257.9	291.5	0.6265	91.263	0.43
2	36.047	1173.4	20.2	0.7378	8.737	0.958

Pentafluorophenyl (*E*)-2-(3-bromophenyl)-6-(ethylthio)-6-oxohex-4-enoate (40): Prepared according to General Procedure G. The title compound was obtained (38 mg, 0.075 mmol, 75%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 68–70 °C

$[\alpha]_D^{23}$ –98.5 (*c* = 1.00, $CHCl_3$).

IR (neat): 1782, 1669, 1633, 1571, 1518, 1475, 1430, 1144, 1109, 1095, 994, 820 cm^{-1}.

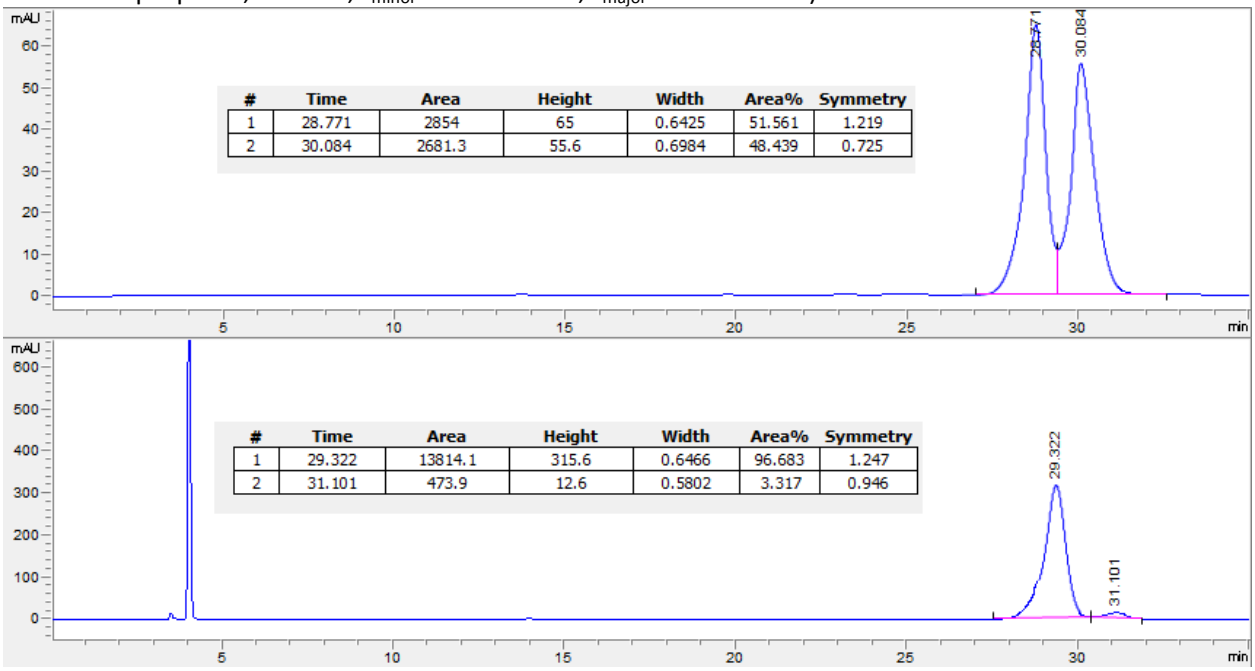
^1H NMR (400 MHz, $CDCl_3$): δ 7.55 – 7.45 (m, 2H), 7.33 – 7.24 (m, 2H), 6.76 (dt, *J* = 14.7, 7.1 Hz, 1H), 6.17 (dd, *J* = 15.5, 1.5 Hz, 1H), 4.03 (t, *J* = 7.6 Hz, 1H), 3.05 (dt, *J* = 15.4, 7.8 Hz, 1H), 2.98 – 2.90 (m, 2H), 2.82 – 2.70 (m, 1H), 1.27 (t, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5, 168.4, 138.4, 138.0, 131.6, 131.4, 130.9, 130.7, 126.4, 123.1, 49.4, 35.3, 23.2, 14.6.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.00 – -152.69 (m), -157.30 (t, *J* = 21.7), -161.85 – -162.01 (m).

HRMS (APCI): m/z calcd for $[M+H]^+$ $C_{20}H_{15}O_3BrF_5S$: 508.9840. Found: 508.9843.

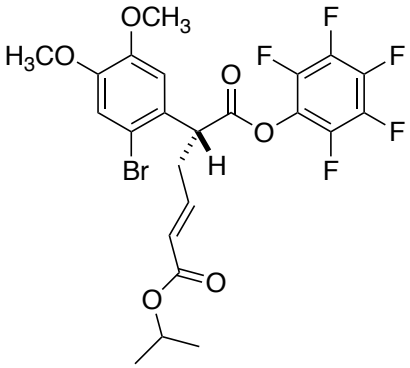
HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 1.00 mL/min, 200:1 Hexane:Isopropanol, 210 nm, t_{minor} = 31.101 min, t_{major} = 29.322 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	28.771	2854	65	0.6425	51.561	1.219
2	30.084	2681.3	55.6	0.6984	48.439	0.725

#	Time	Area	Height	Width	Area%	Symmetry
1	29.322	13814.1	315.6	0.6466	96.683	1.247
2	31.101	473.9	12.6	0.5802	3.317	0.946

1-Isopropyl 6-(pentafluorophenyl) (*E*)-5-(2-bromo-4,5-dimethoxyphenyl)hex-2-enedioate (41): Prepared according to General Procedure G. The title compound was obtained (28 mg, 0.05 mmol, 50%) as a colorless oil following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (90:10) was determined by chiral HPLC in comparison with the racemate.



$[\alpha]_D^{23}$ –21.1 (*c* = 1.00, $CHCl_3$).

IR (neat): 2979, 2958, 2922, 2851, 1780, 1715, 1656, 1602, 1518, 1466, 1441, 1377, 1355, 1309, 1263, 1217, 1167, 1107, 1029, 992, 909, 858, 829, 797, 734 cm^{-1}.

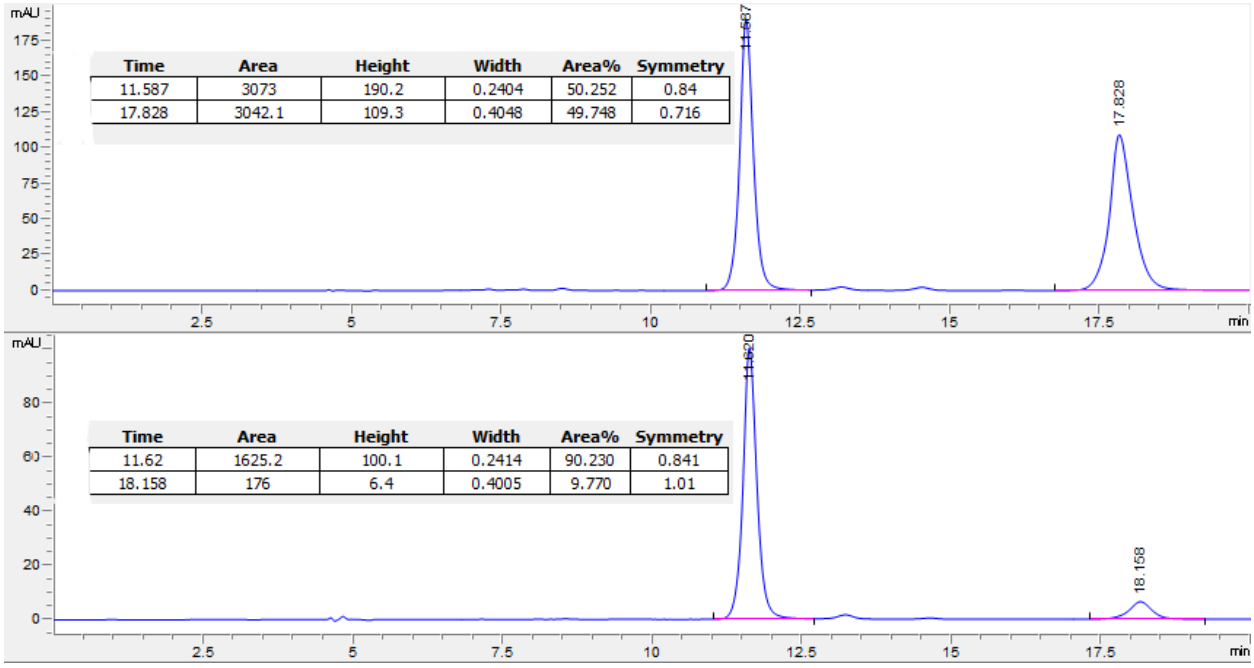
^1H NMR (400 MHz, $CDCl_3$): δ 7.07 (s, 1H), 6.90 (dt, *J* = 15.6, 7.1 Hz, 1H), 6.81 (s, 1H), 5.88 (dt, *J* = 15.6, 1.5 Hz, 1H), 5.05 (m, 1H), 4.61 (dd, *J* = 8.3, 6.3 Hz, 1H), 3.86 (d, *J* = 10.0 Hz, 6H), 3.00 – 2.92 (m, 1H), 2.76 – 2.69 (m, 1H), 1.25 (d, *J* = 6.3 Hz, 7H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 165.4, 149.3, 149.0, 142.8, 127.5, 124.9, 115.7, 114.6, 110.4, 67.7, 56.2, 56.0, 48.4, 35.1, 29.7, 21.8.

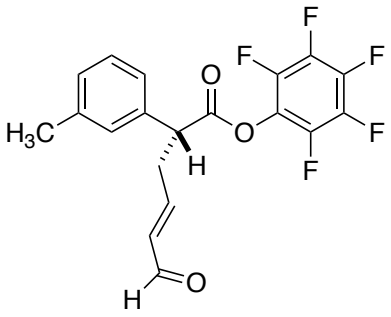
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.10 – -152.53 (m), -157.45 (t, *J* = 21.6 Hz), -161.85 – -162.28 (m).

HRMS (APCI): m/z calcd for $[M+H]^+$ $C_{23}H_{21}O_6BrF_5$: 567.0436. Found: 567.0438.

HPLC analysis using a chiral column (Chiralpak IB 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 18.157 min, t_{major} = 11.620 min).



Pentafluorophenyl (*E*)-6-oxo-2-(m-tolyl)hex-4-enoate (42): Prepared according to General Procedure G. The title compound was obtained (21 mg, 0.055 mmol, 55%) as a colorless oil following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (90:10) was determined by chiral HPLC in comparison with the racemate.



$[\alpha]_D^{23}$ –33.5 (*c* = 1.00, $CHCl_3$).

IR (neat): 1781, 1695, 1520, 1131, 1107, 1039, 1104 cm^{-1}.

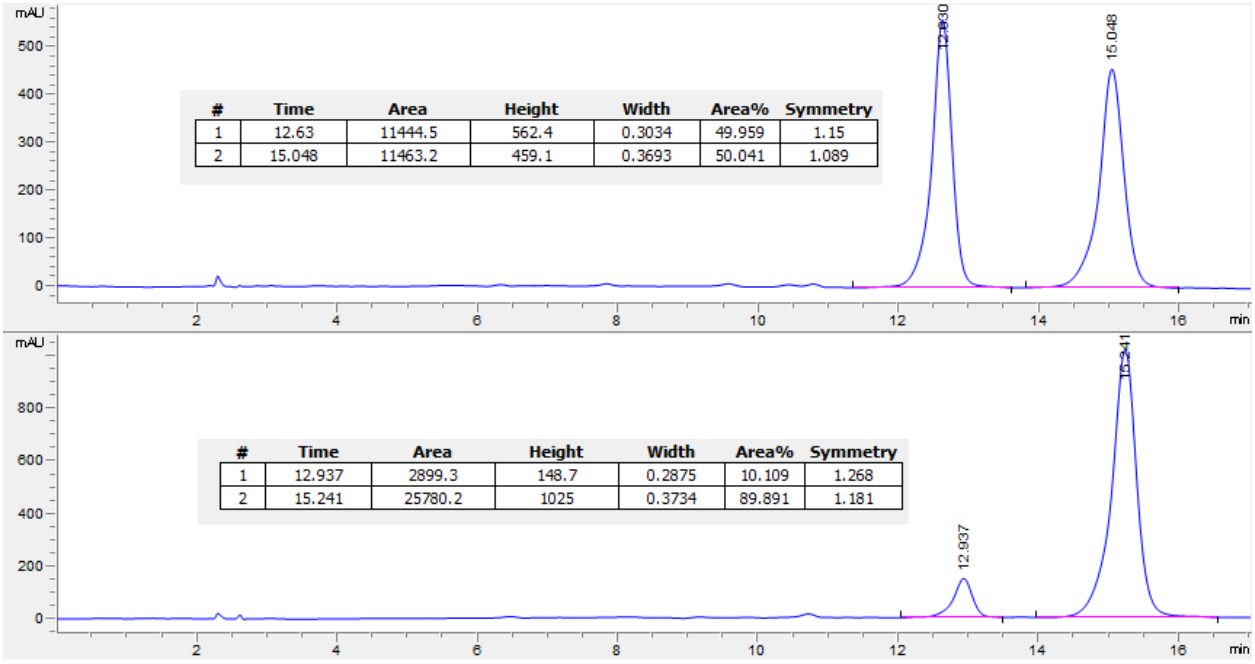
^1H NMR (400 MHz, $CDCl_3$): δ 9.49 (d, *J* = 7.7 Hz, 1H), 7.30 (dd, *J* = 8.5, 7.2 Hz, 1H), 7.20 – 7.12 (m, 3H), 6.75 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.19 (ddt, *J* = 15.7, 7.8, 1.5 Hz, 1H), 4.08 (t, *J* = 7.6 Hz, 1H), 3.19 (dddd, *J* = 15.3, 8.3, 7.1, 1.4 Hz, 1H), 2.93 (dtd, *J* = 15.3, 6.9, 1.5 Hz, 1H), 2.38 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 168.9, 152.4, 139.1, 135.5, 135.0, 129.2, 129.1, 128.4, 124.7, 49.6, 35.9, 21.4.

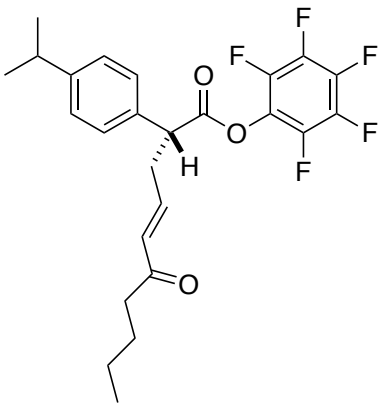
^{19}F NMR (376 MHz, $CDCl_3$): δ -152.16 – -152.87 (m), -157.46 (t, *J* = 21.7 Hz), -161.67 – -162.51 (m).

HRMS (CI): m/z calcd for $[M+H]^+$ $C_{19}H_{14}O_3F_5$: 385.0858. Found: 385.0844.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 1.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 12.937 min, t_{major} = 15.241 min).



Pentafluorophenyl (*E*)-2-(4-isopropylphenyl)-6-oxodec-4-enoate (43): Prepared according to General Procedure G. The title compound was obtained (36 mg, 0.076 mmol, 76%) as a white solid following purification by column chromatography [SiO_2, Pentane: Diethyl Ether 10:1]. The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with the racemate.



M.p. (pentane–diethyl ether, 200:1; needles) = 54–55 °C

$[\alpha]_D^{23}$ –50.5 (*c* = 1.00, $CHCl_3$).

IR (neat): 2962, 2933, 2874, 1782, 1699, 1677, 1634, 1520, 1468, 1099, 1002 cm^{-1}.

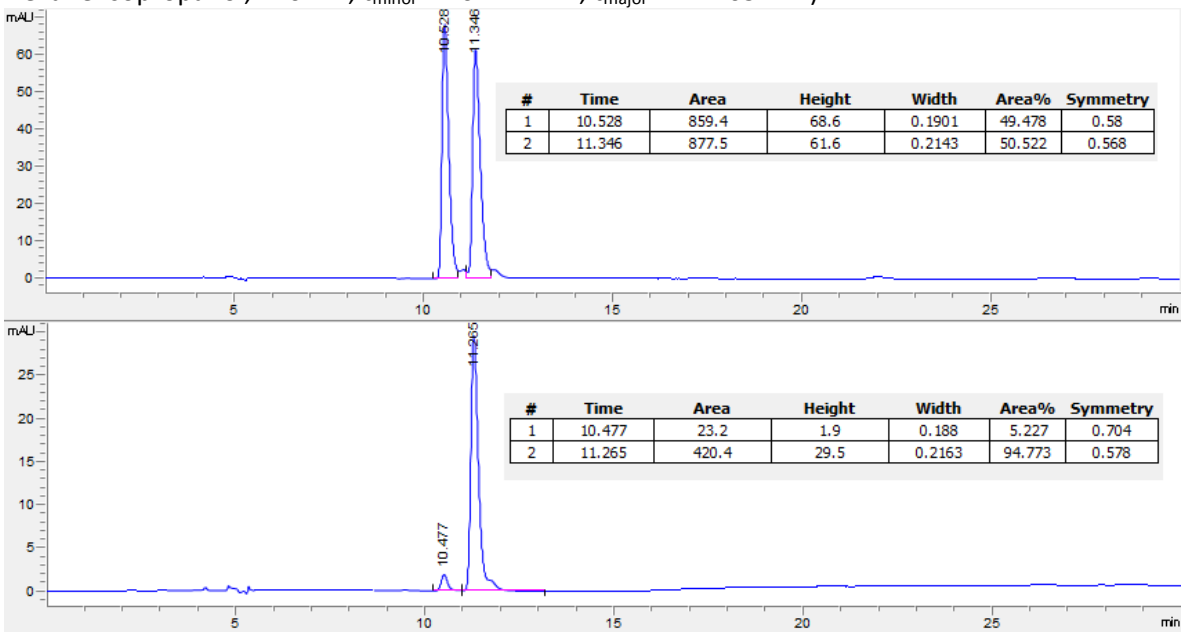
^1H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.15 (m, 4H), 6.72 (dt, *J* = 15.8, 7.0 Hz, 1H), 6.16 (dd, *J* = 15.9, 1.4 Hz, 1H), 4.03 (dd, *J* = 8.5, 6.7 Hz, 1H), 3.10 – 2.99 (m, 1H), 2.90 (p, *J* = 6.9 Hz, 1H), 2.75 (dtd, *J* = 14.9, 6.7, 1.5 Hz, 1H), 2.47 (t, *J* = 7.5 Hz, 2H), 1.58 – 1.50 (m, 2H), 1.34 – 1.22 (m, 8H), 0.88 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 200.2, 169.1, 149.0, 141.3, 133.2, 132.4, 127.6, 127.2, 49.6, 40.1, 35.9, 33.7, 26.2, 23.8, 22.3, 13.8.

^{19}F NMR (376 MHz, $CDCl_3$): δ -152.07 – -152.68 (m), -157.72 (t, *J* = 21.7 Hz), -161.77 – -162.61 (m).

HRMS (APCI): m/z calcd for $[M+H]^+$ $C_{25}H_{26}O_3F_5$: 469.1800. Found: 469.1797.

HPLC analysis using a chiral column (Chiralpak IA 3µ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, t_{minor} = 10.477 min, t_{major} = 11.265 min).

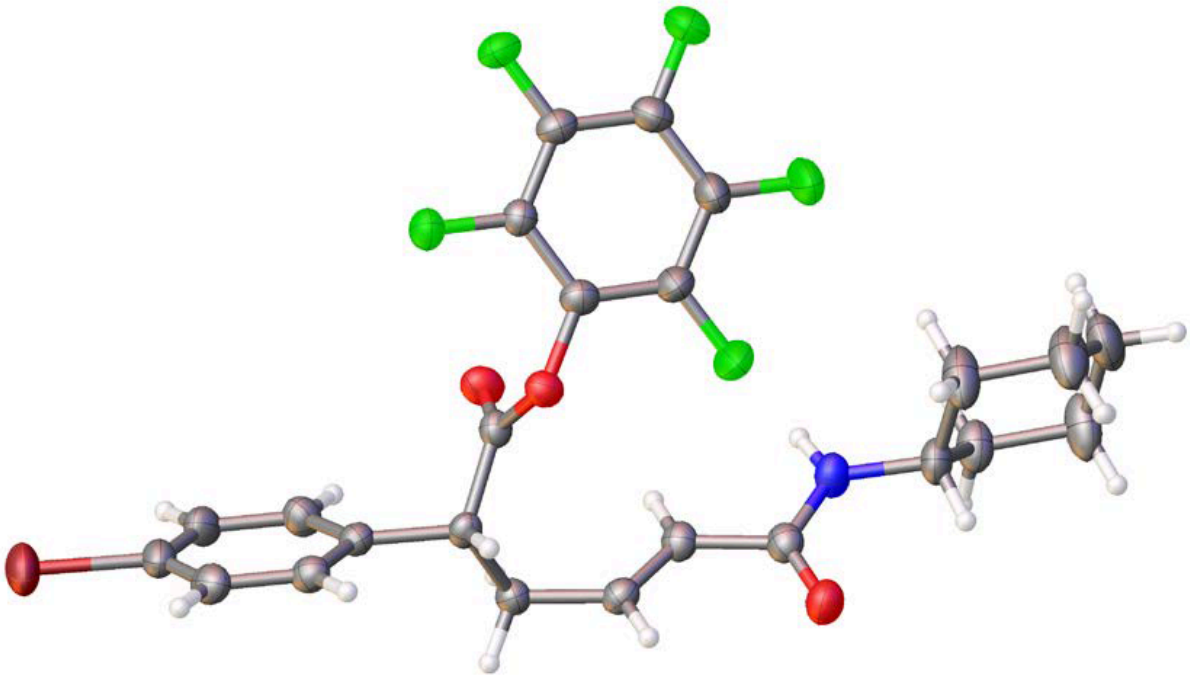


Confirmation of absolute stereochemistry via X-ray analysis of 34.

X-Ray

Single crystals of sufficient quality were obtained by slow diffusion of pentane into a saturated solution of **34** in THF. Single crystal analysis confirmed the absolute stereochemistry as (*R*)- and is derived from (*R*)-BTM. Thus, we have assigned all stereochemistry in analogy to this.

This structure has been deposited at the Cambridge Crystallographic Data Center and can be found under the deposition number: CCDC 1865226.



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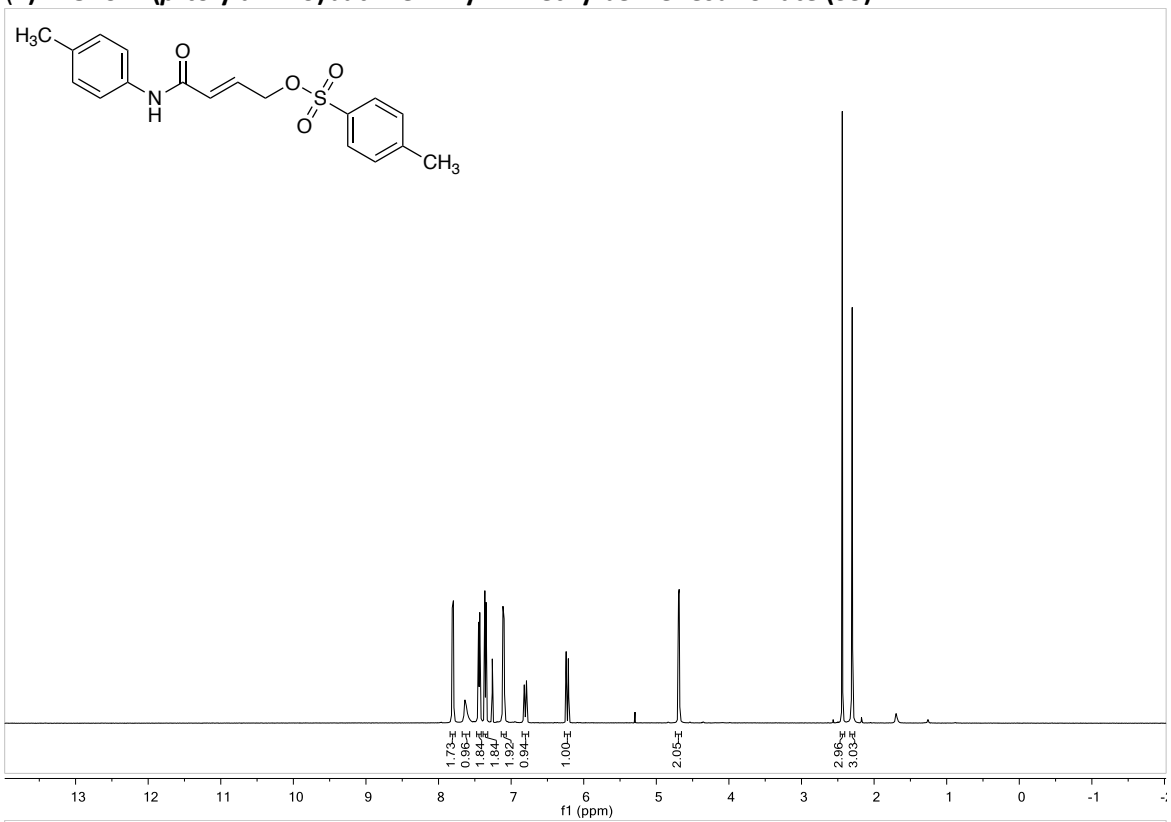
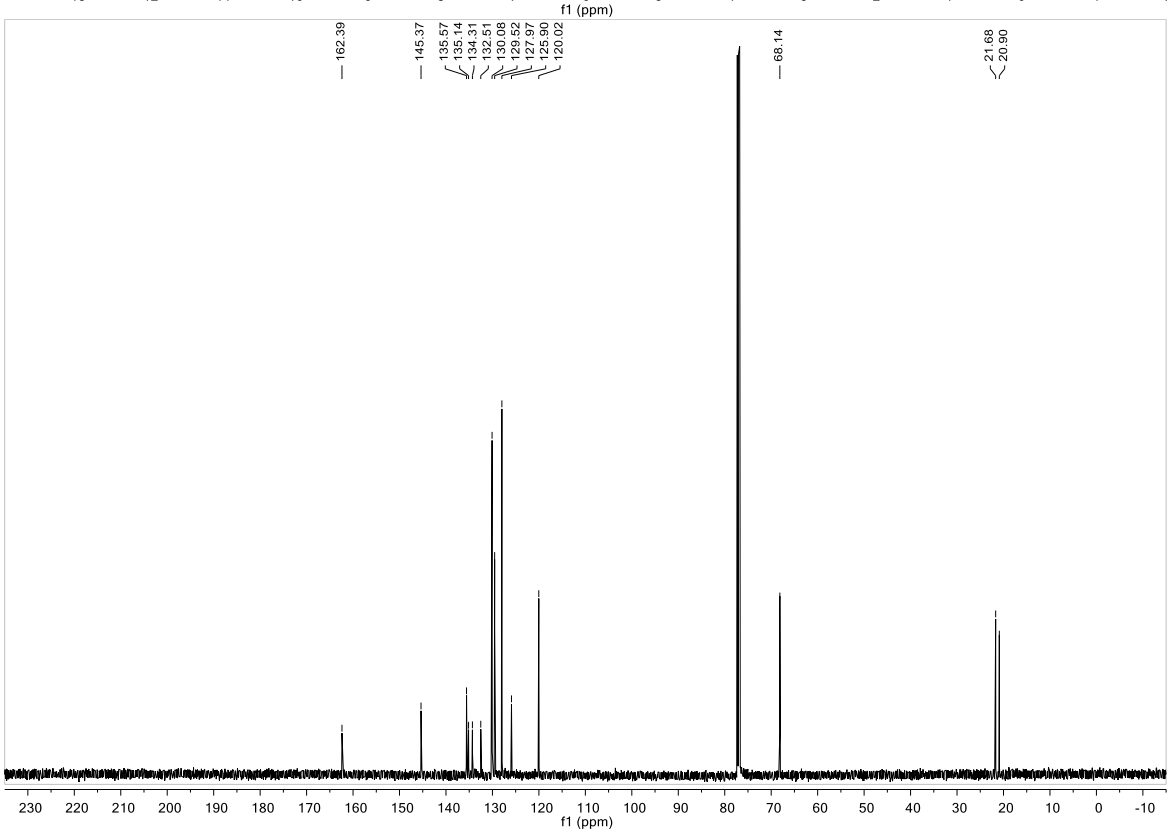
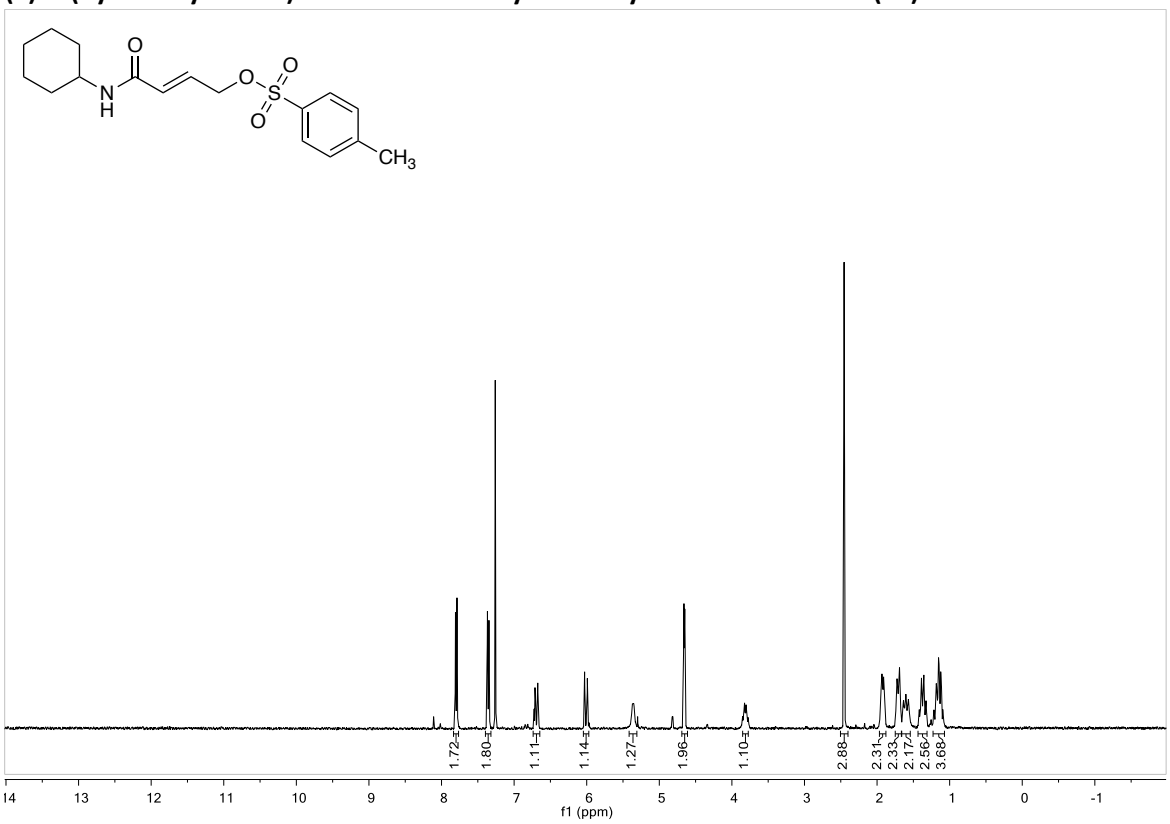
NMR Spectra

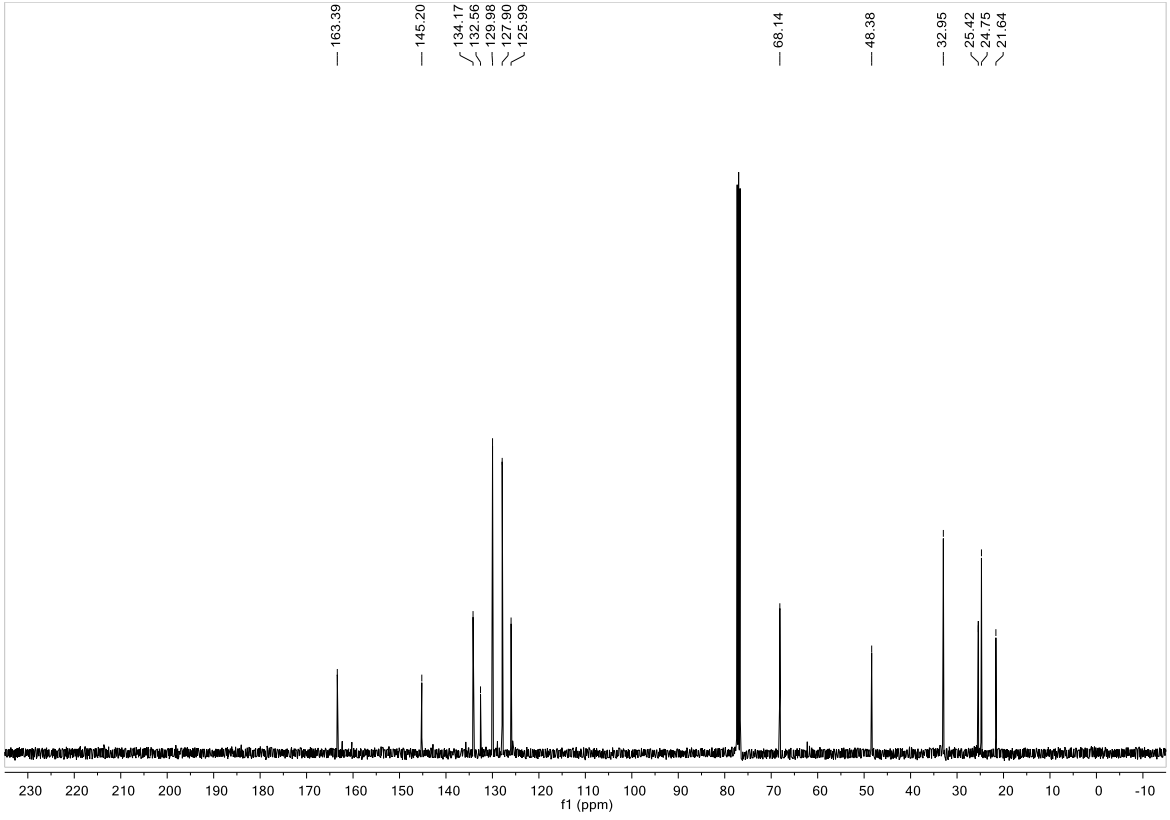
(*E*)-4-Oxo-4-(*p*-tolylamino)but-2-en-1-yl 4-methylbenzenesulfonate (S3)



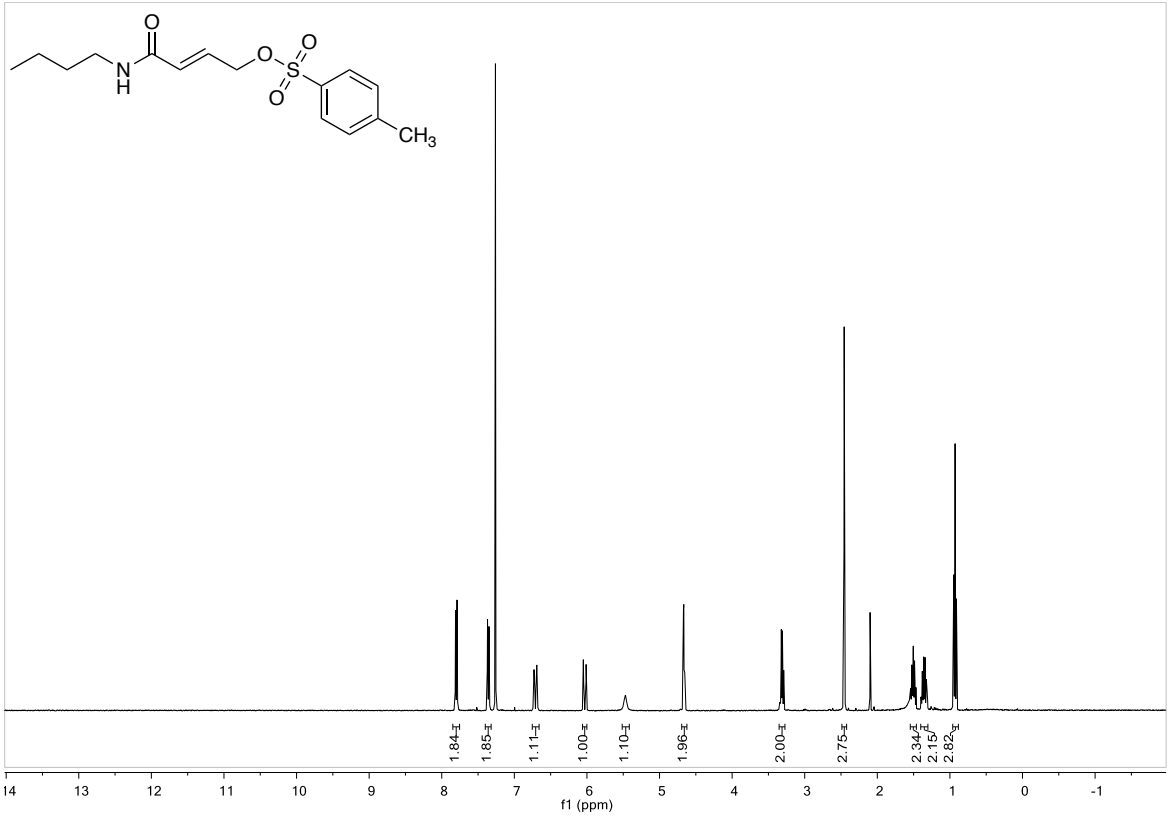


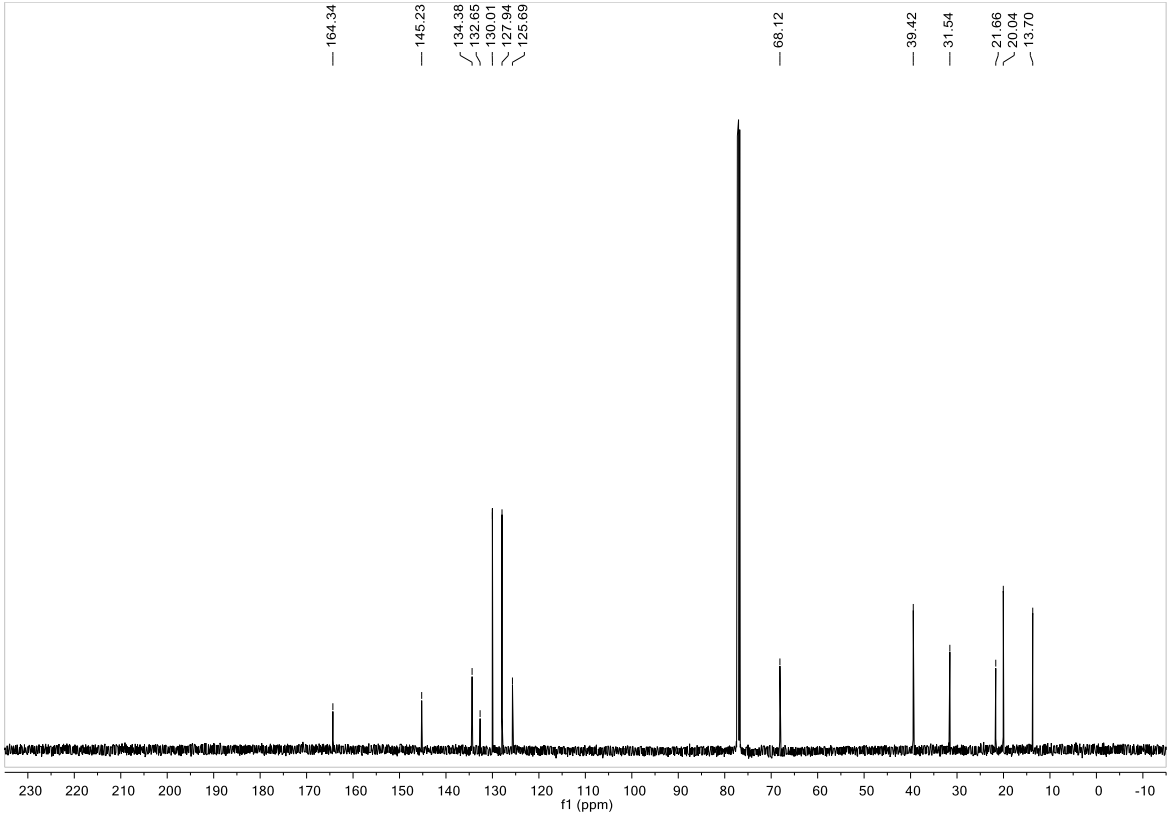
(*E*)-4-(Cyclohexylamino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S5)



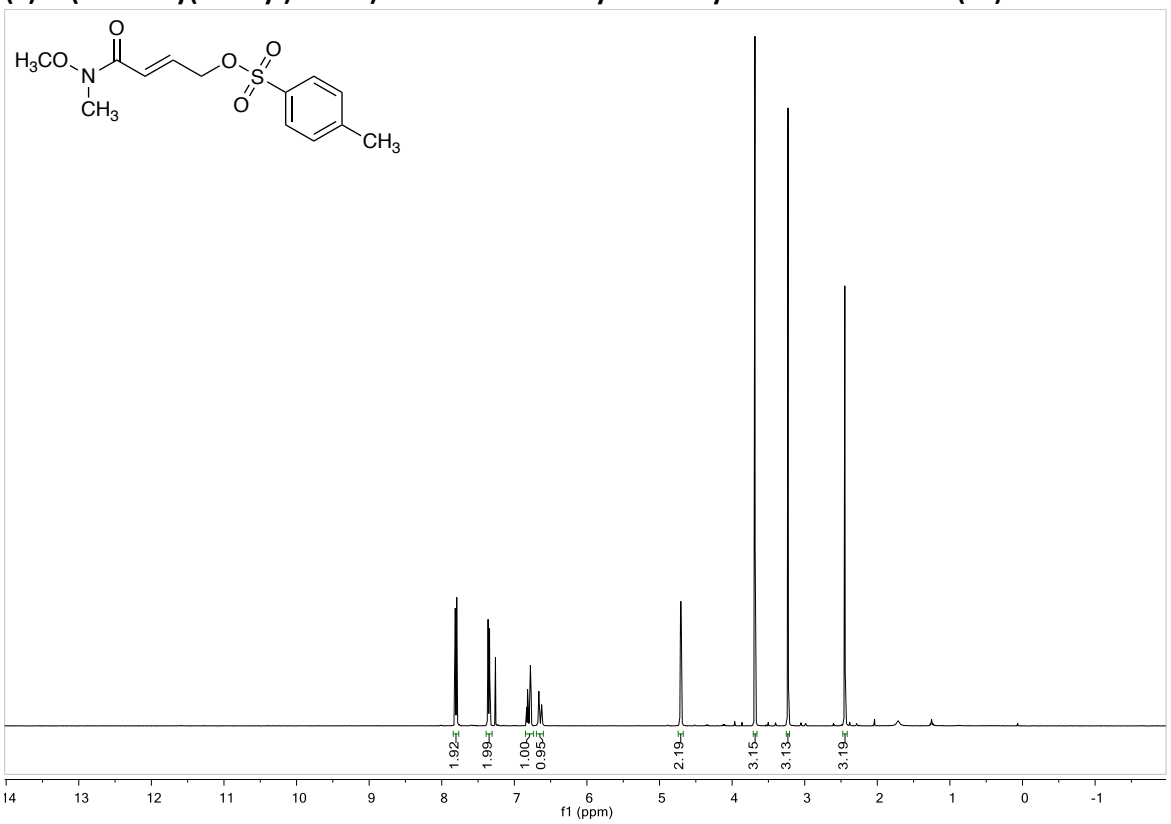


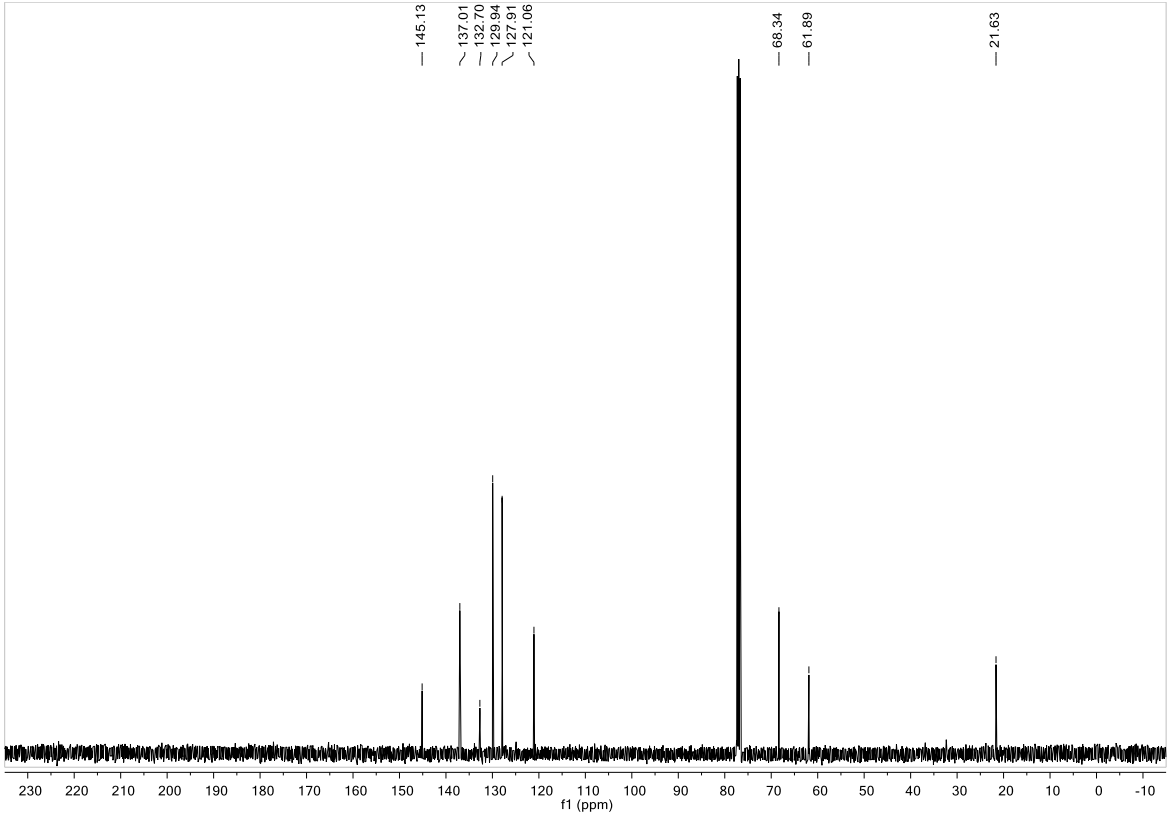
(*E*)-4-(Butylamino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S6)



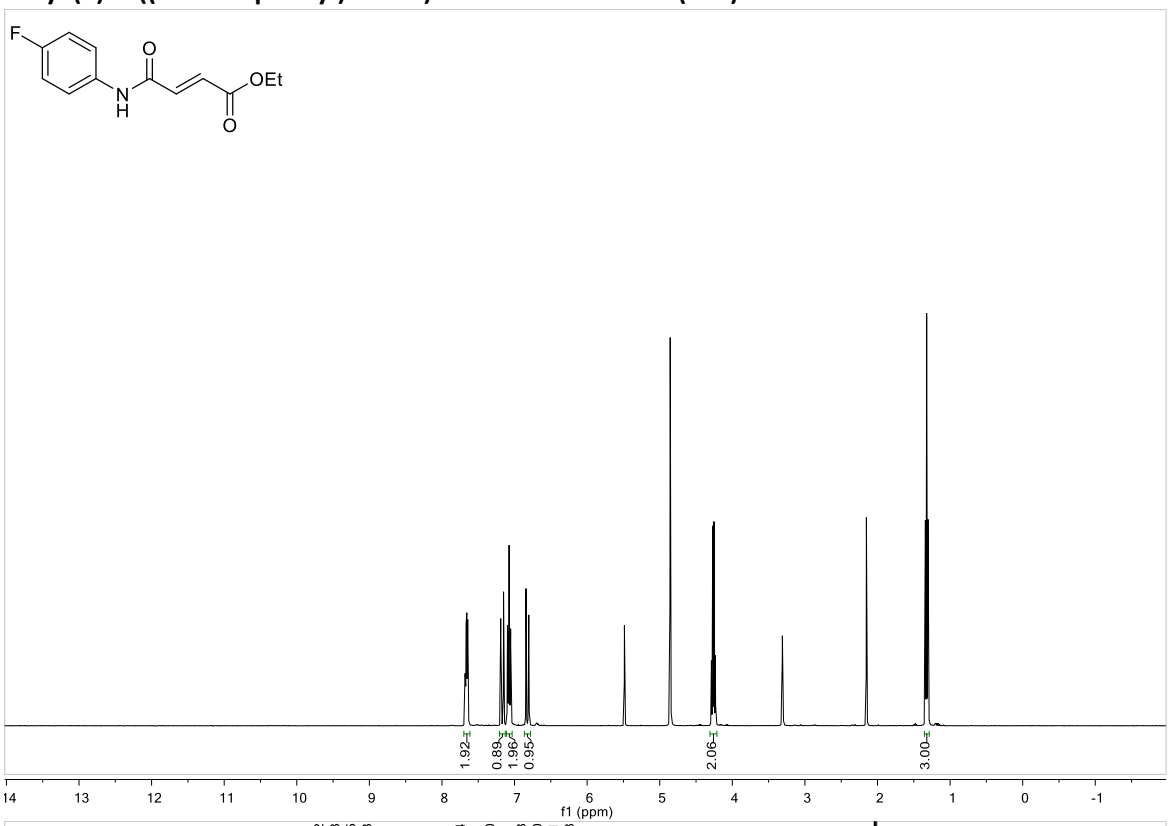


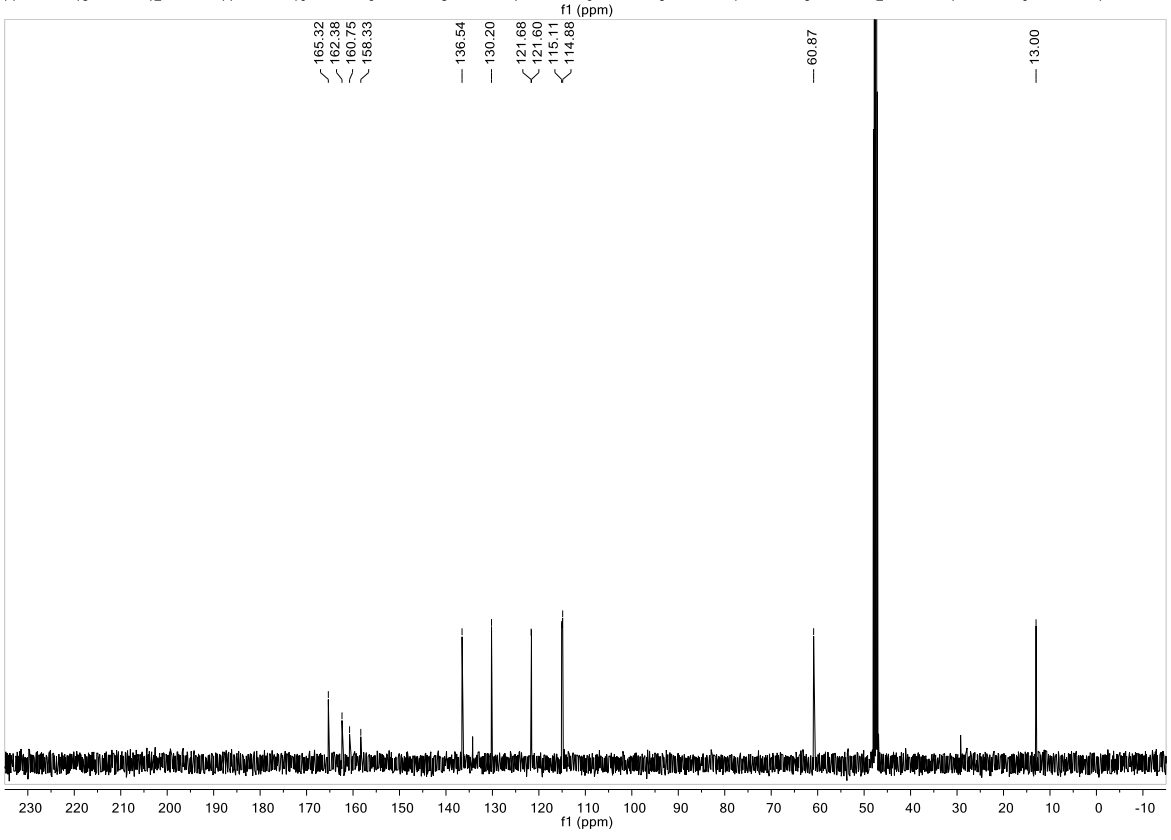
(*E*)-4-(Methoxy(methyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S9)



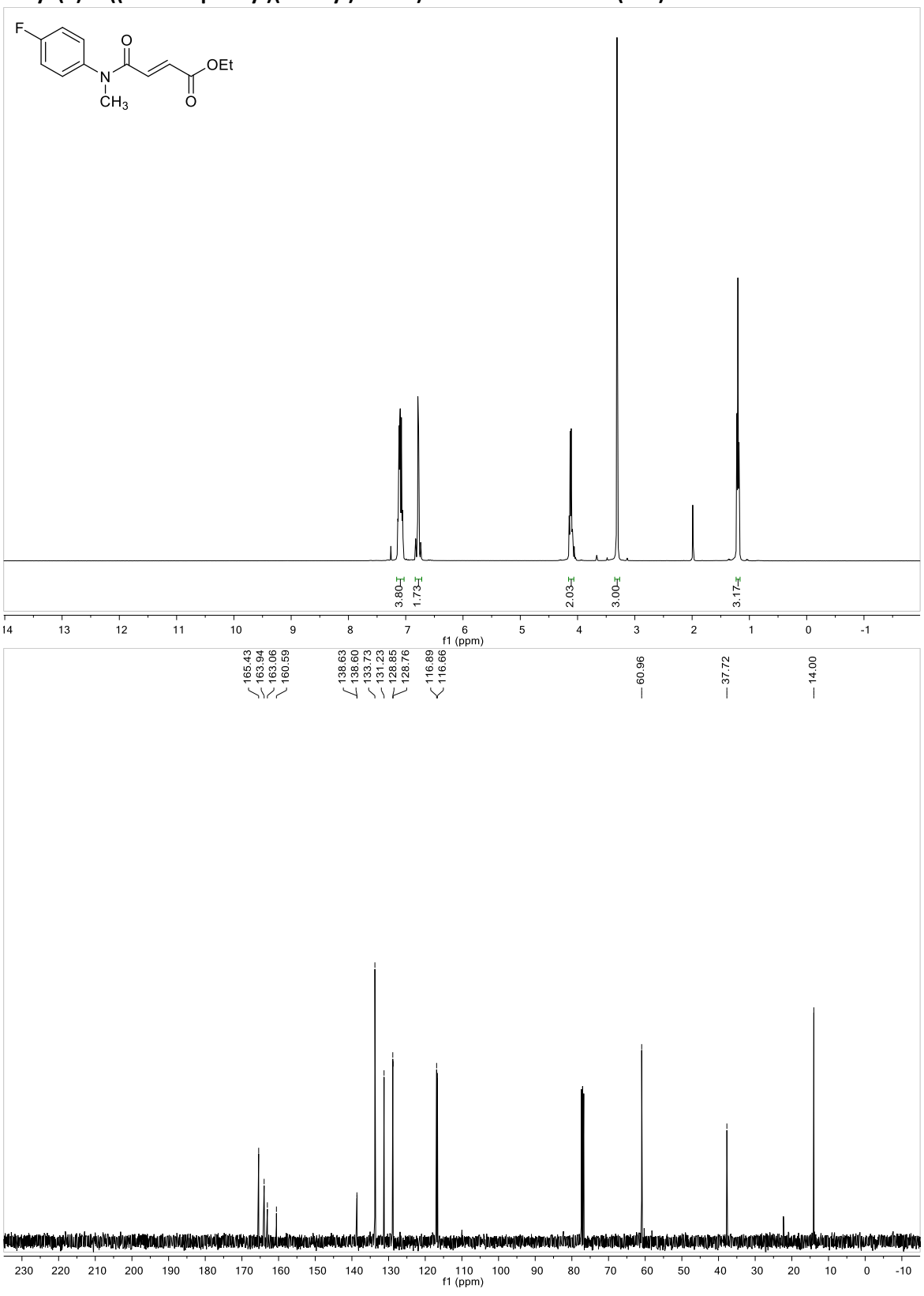


Ethyl (*E*)-4-((4-fluorophenyl)amino)-4-oxobut-2-enoate (S10)

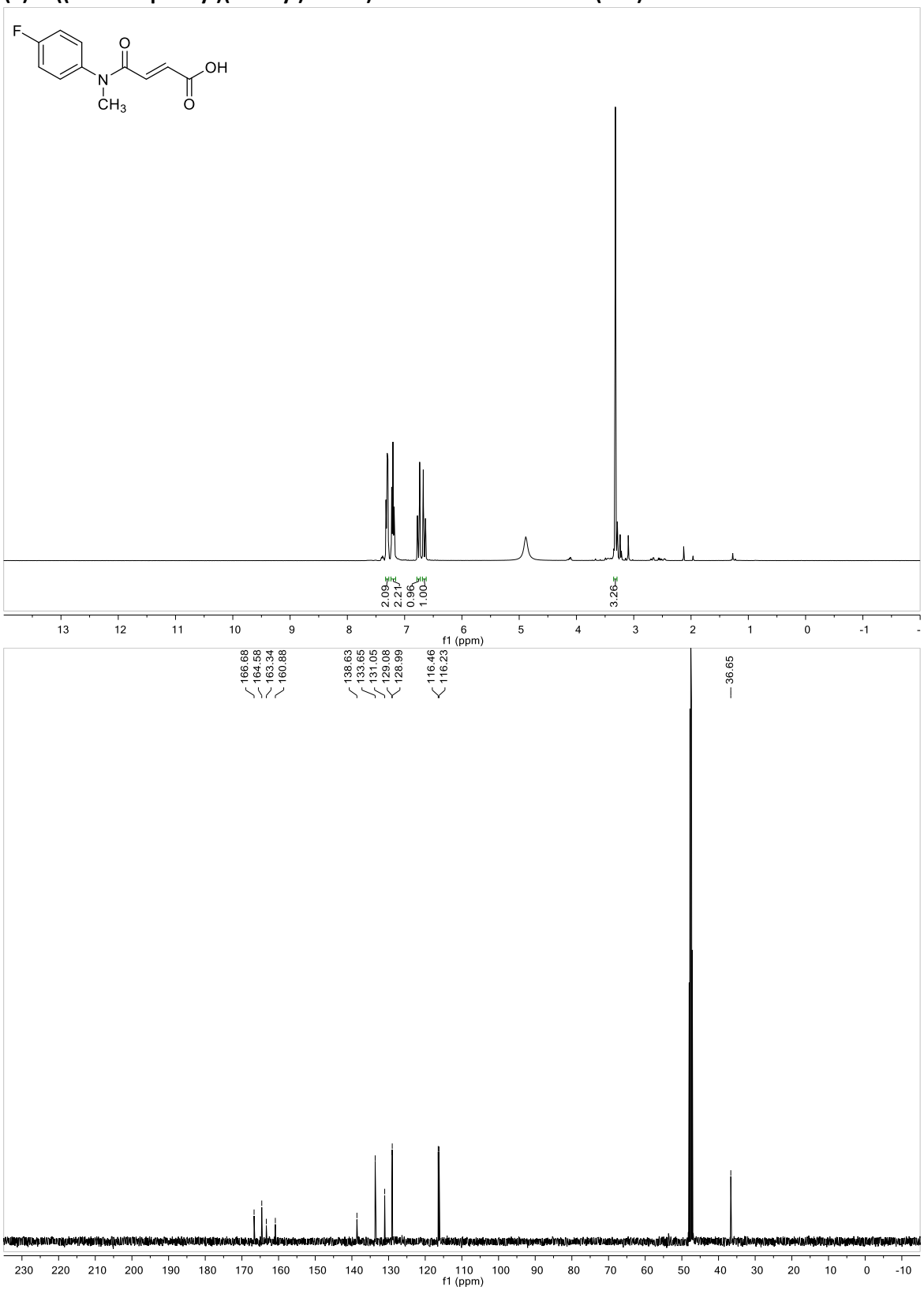




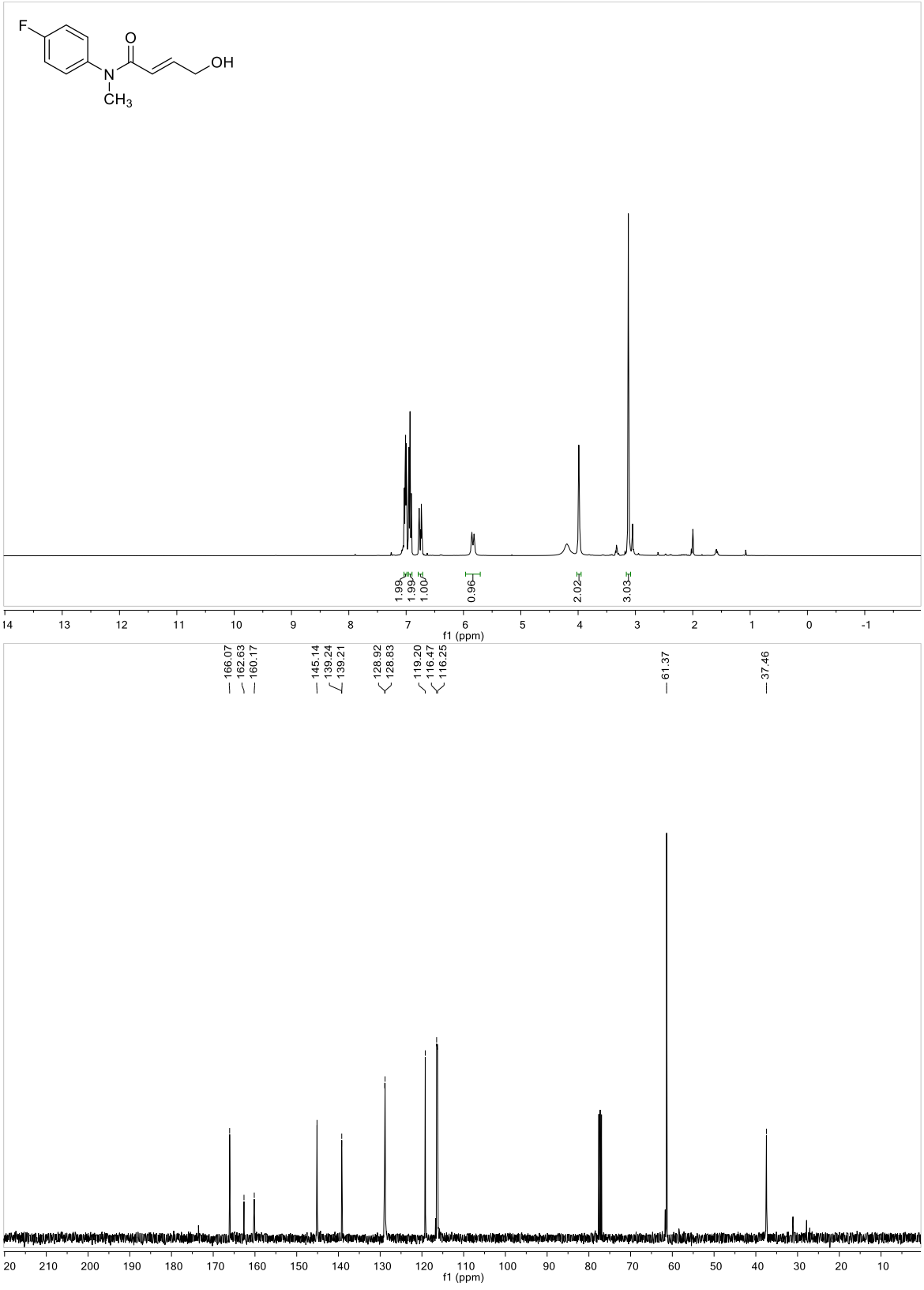
Ethyl (*E*)-4-((4-fluorophenyl)(methyl)amino)-4-oxobut-2-enoate (S11)



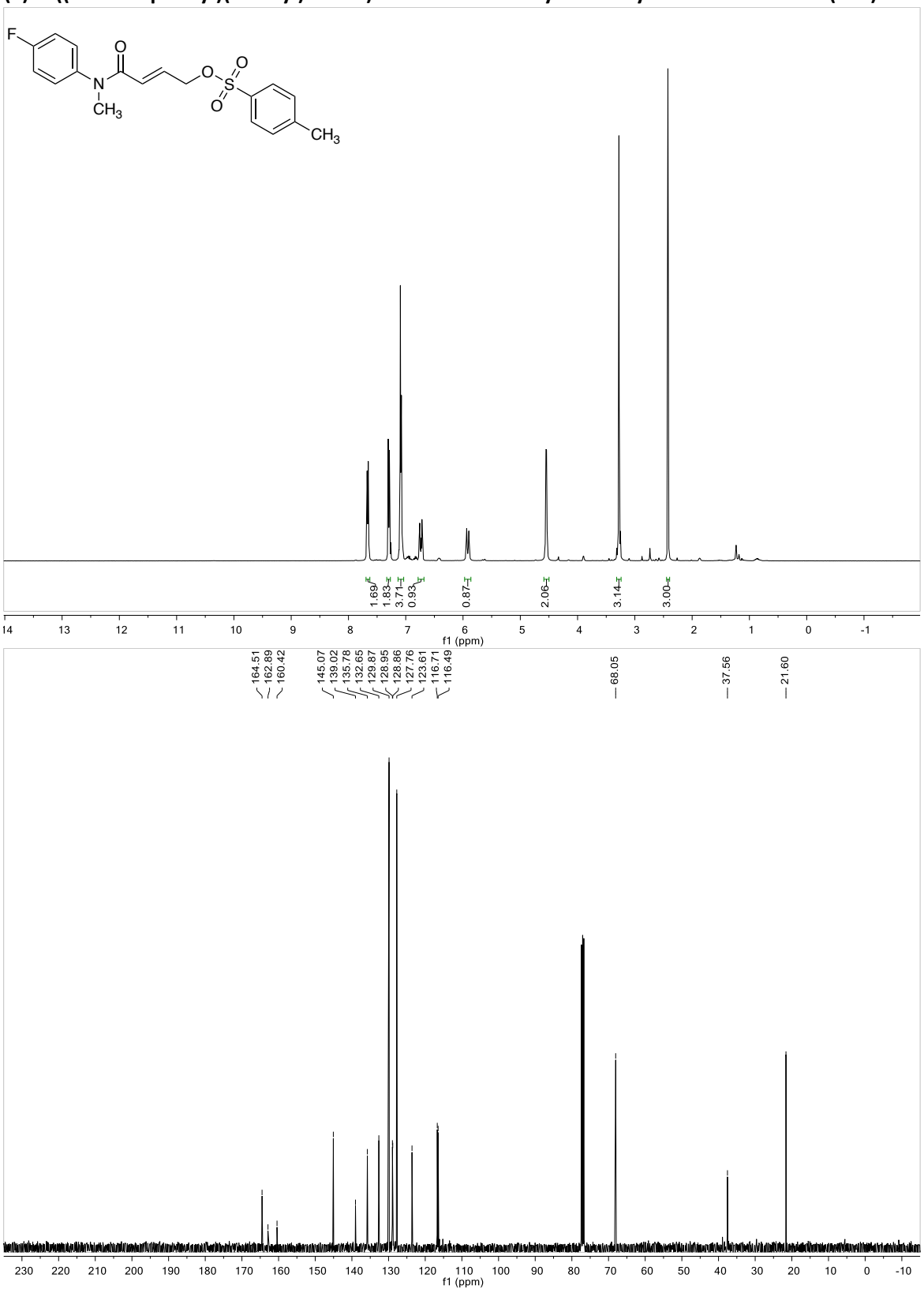
(*E*)-4-((4-Fluorophenyl)(methyl)amino)-4-oxobut-2-enoic acid (S12)



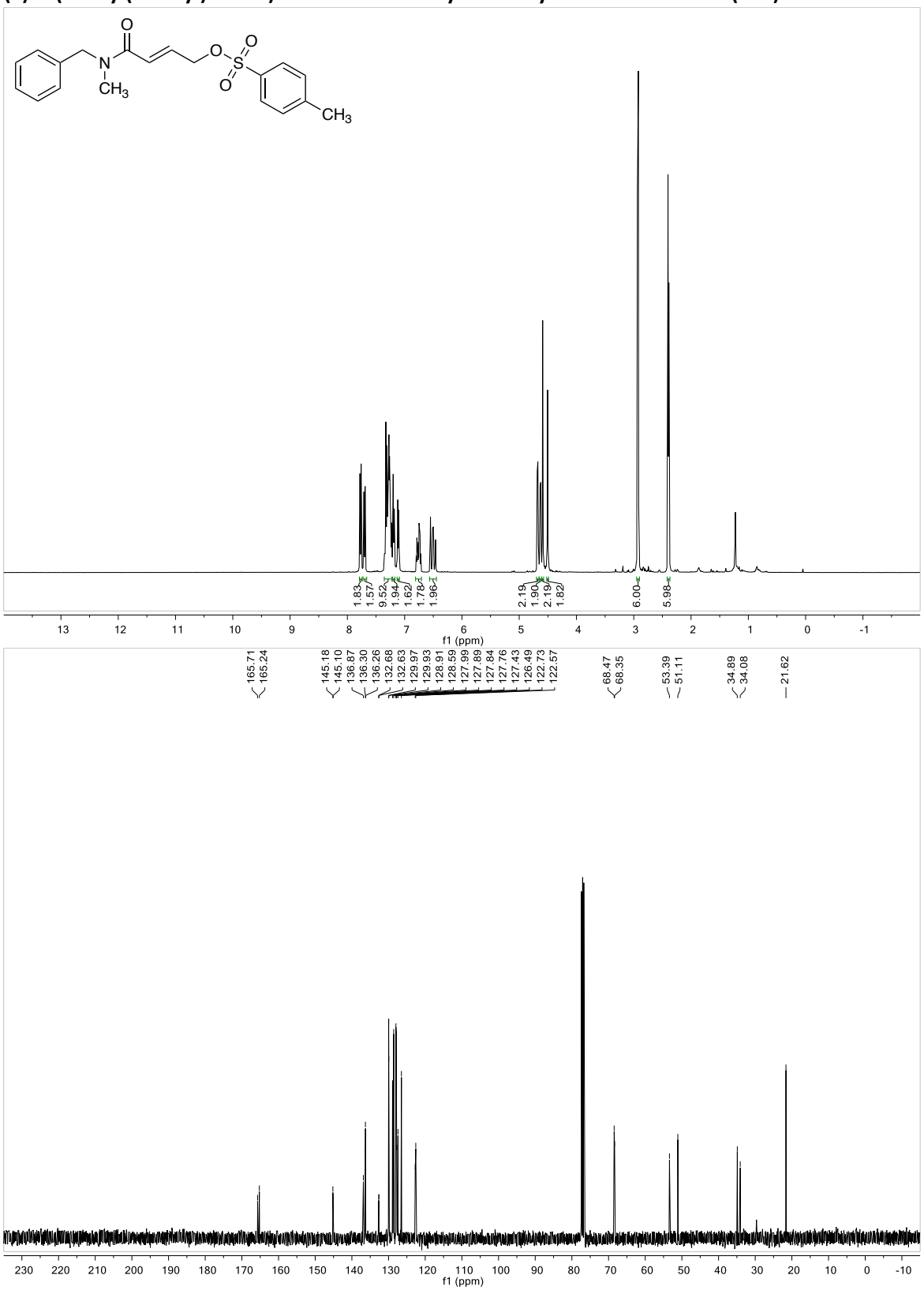
(*E*)-*N*-(4-Fluorophenyl)-4-hydroxy-*N*-methylbut-2-enamide (S13)



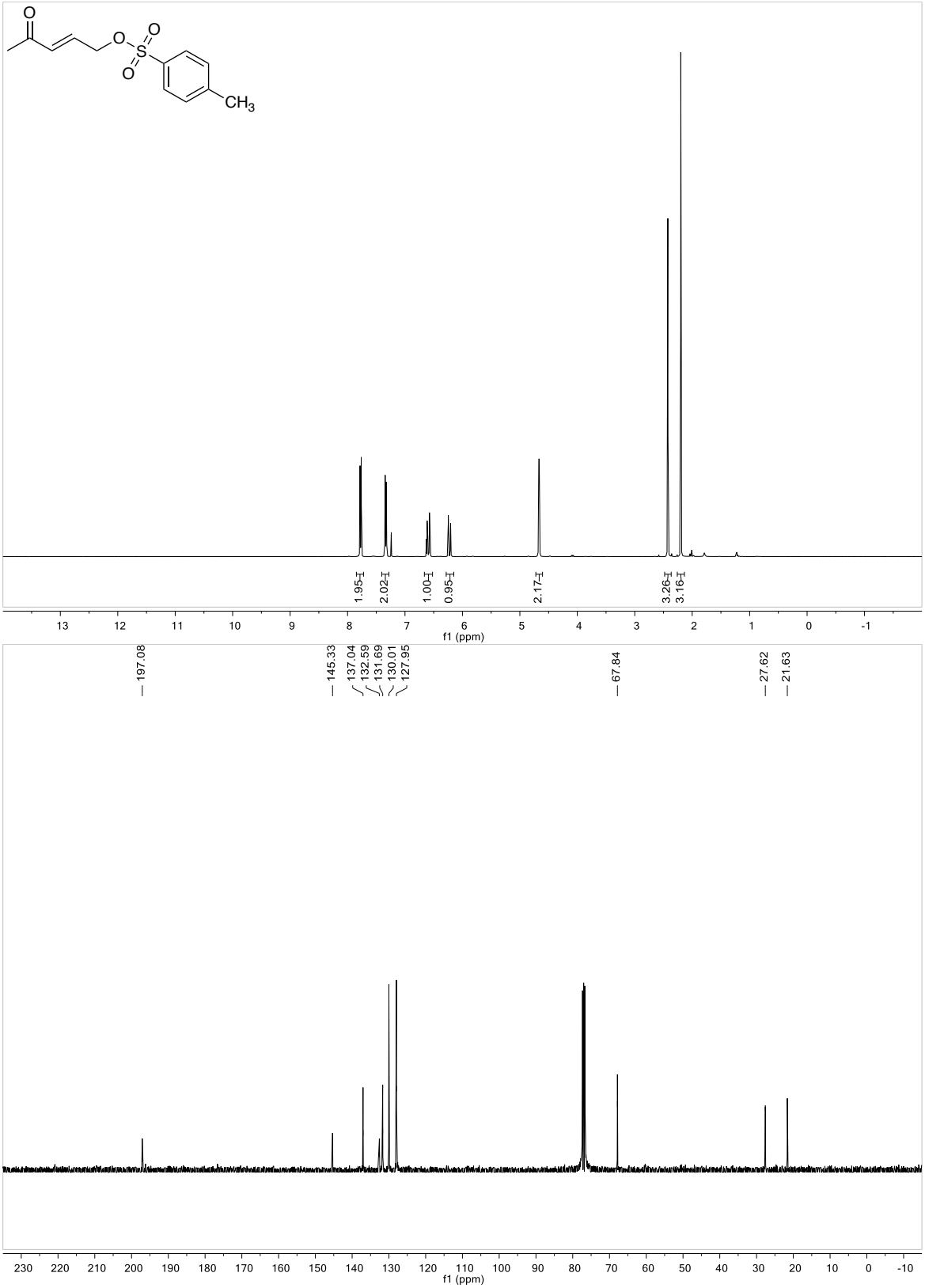
(*E*)-4-((4-Fluorophenyl)(methyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S14)



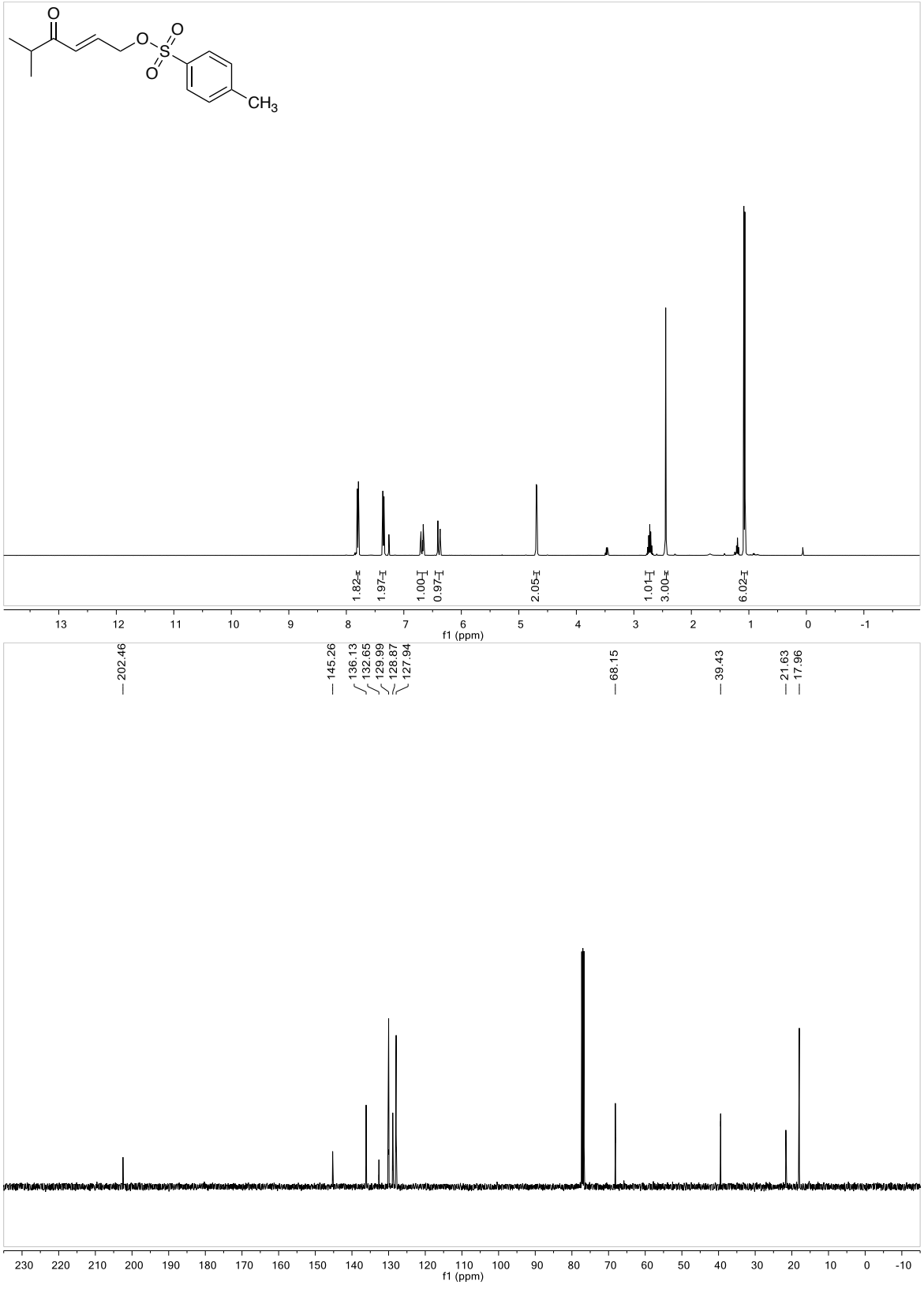
(*E*)-4-(Benzyl(methyl)amino)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S15)



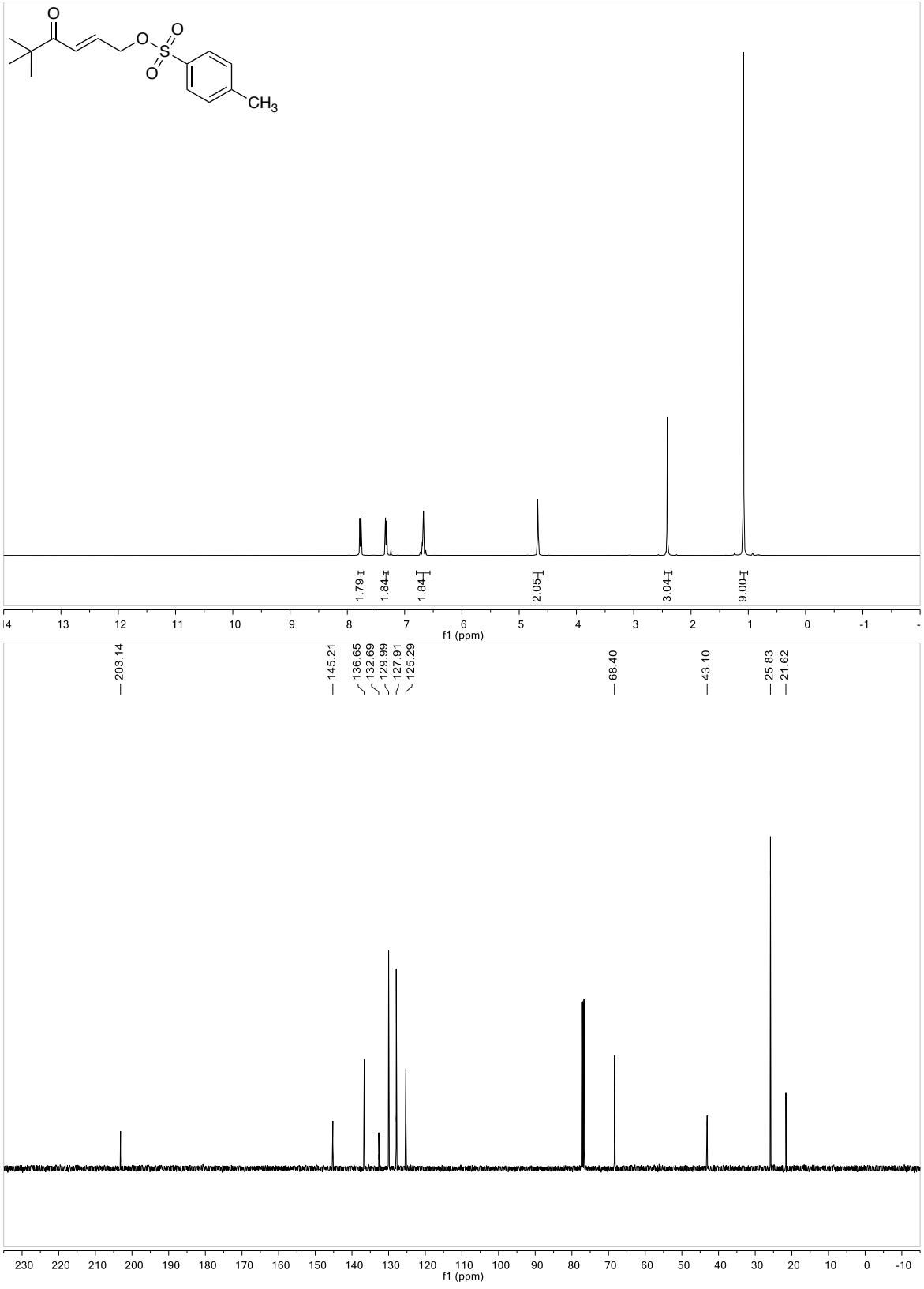
(*E*)-4-Oxopent-2-en-1-yl 4-methylbenzenesulfonate (S17)



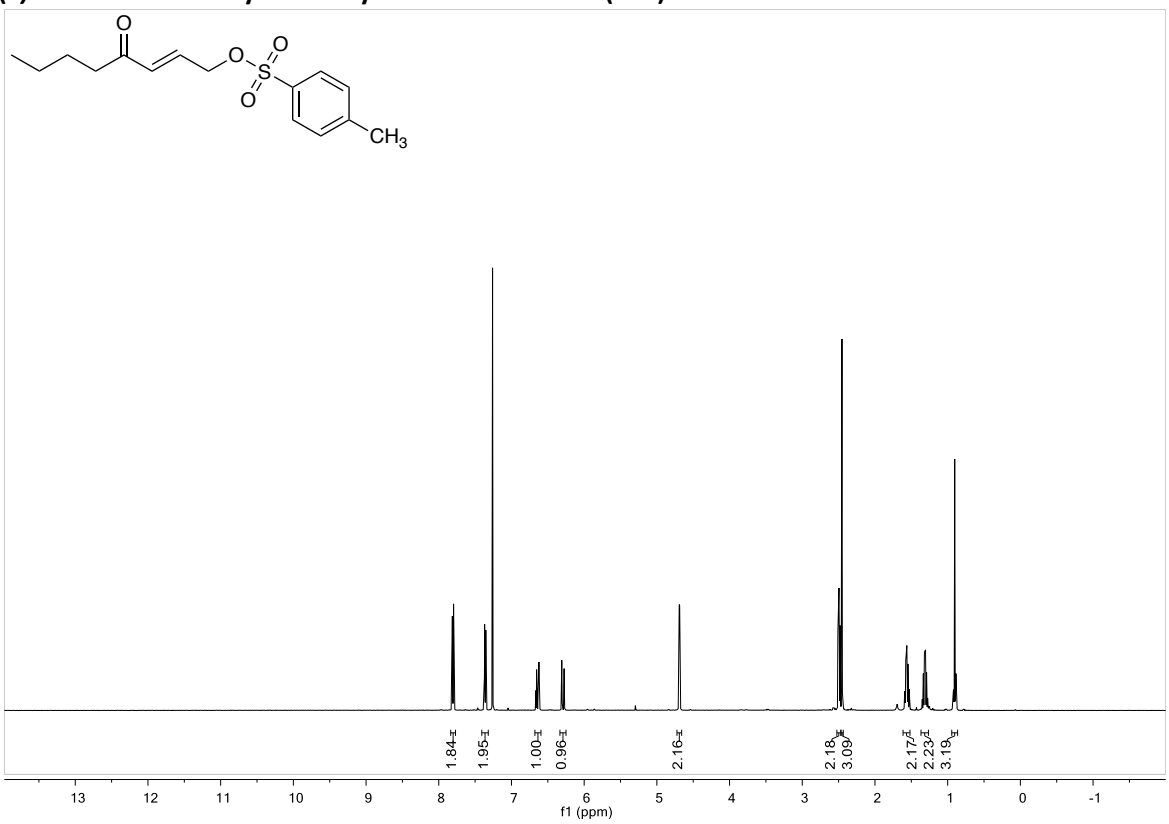
(*E*)-5-methyl-4-oxohex-2-en-1-yl 4-methylbenzenesulfonate (S19)

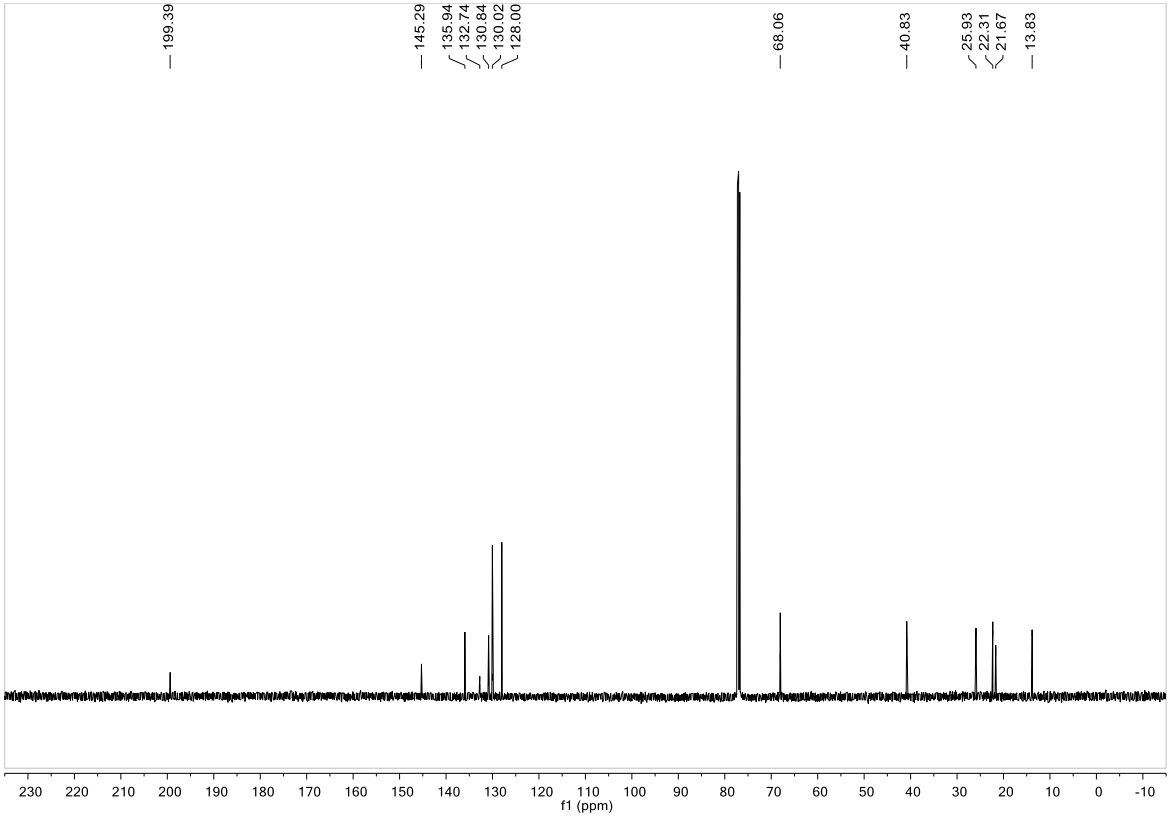


(*E*)-5,5-dimethyl-4-oxohex-2-en-1-yl 4-methylbenzenesulfonate (S21)

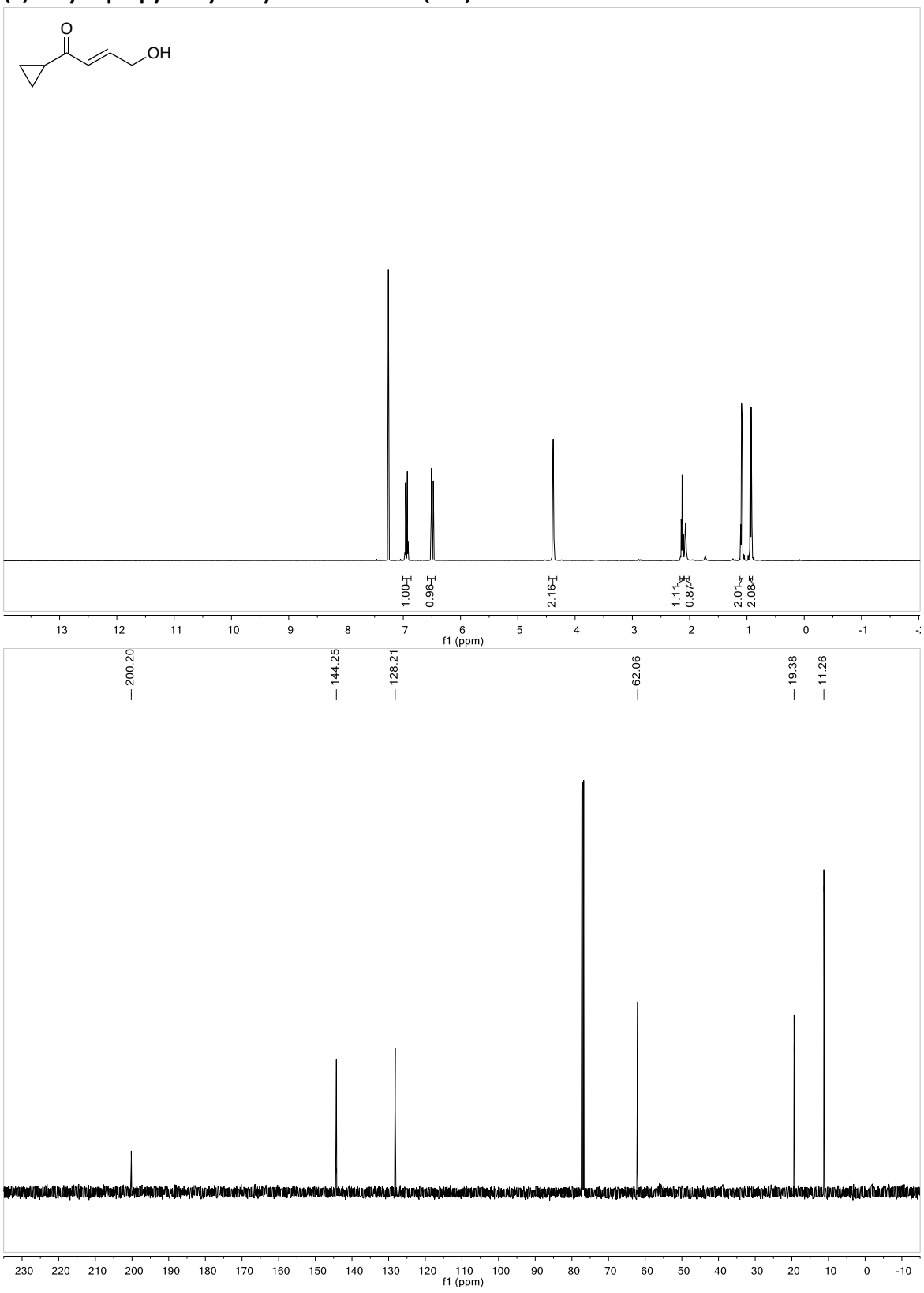


(*E*)-4-oxooct-2-en-1-yl 4-methylbenzenesulfonate (S23)

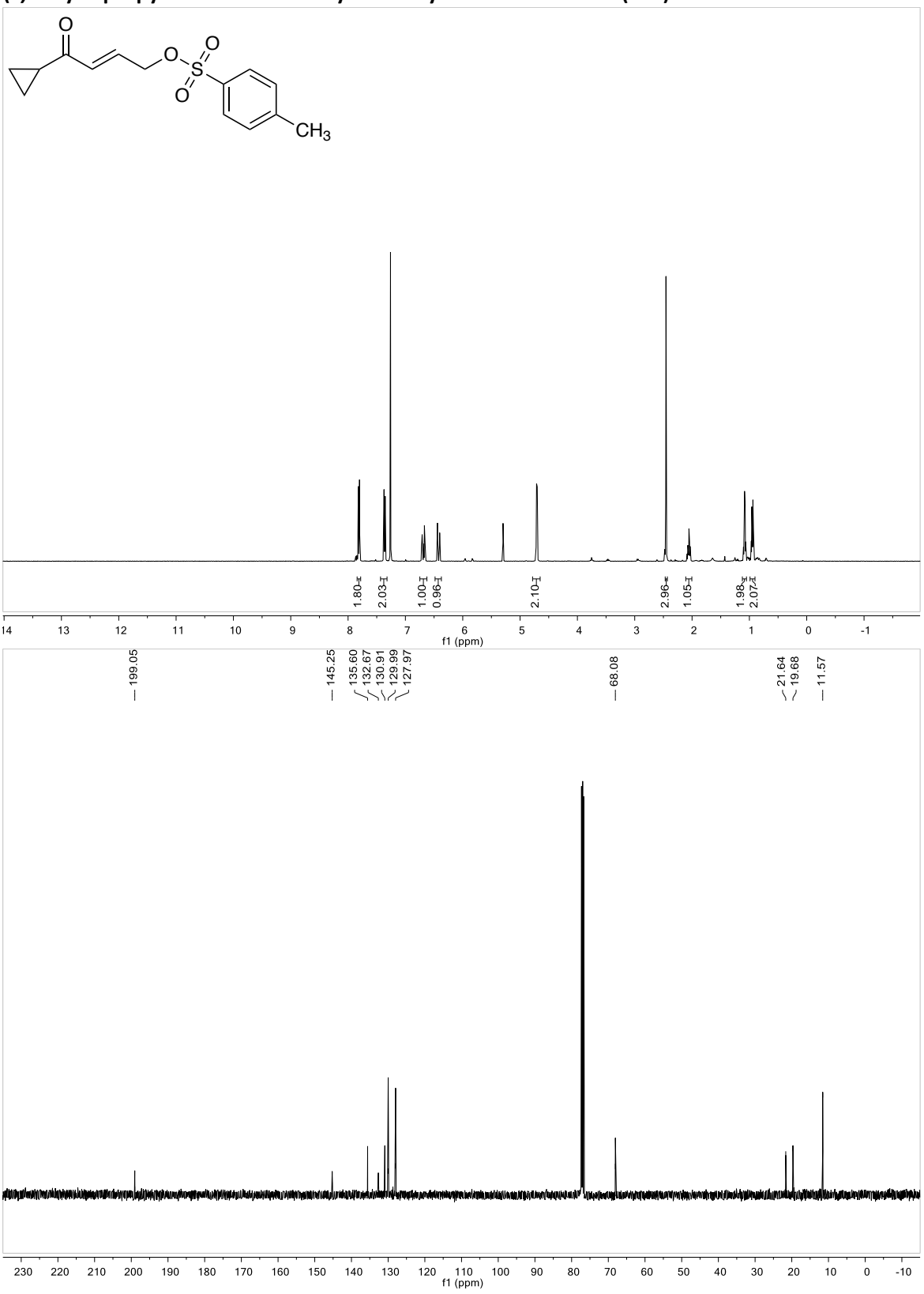




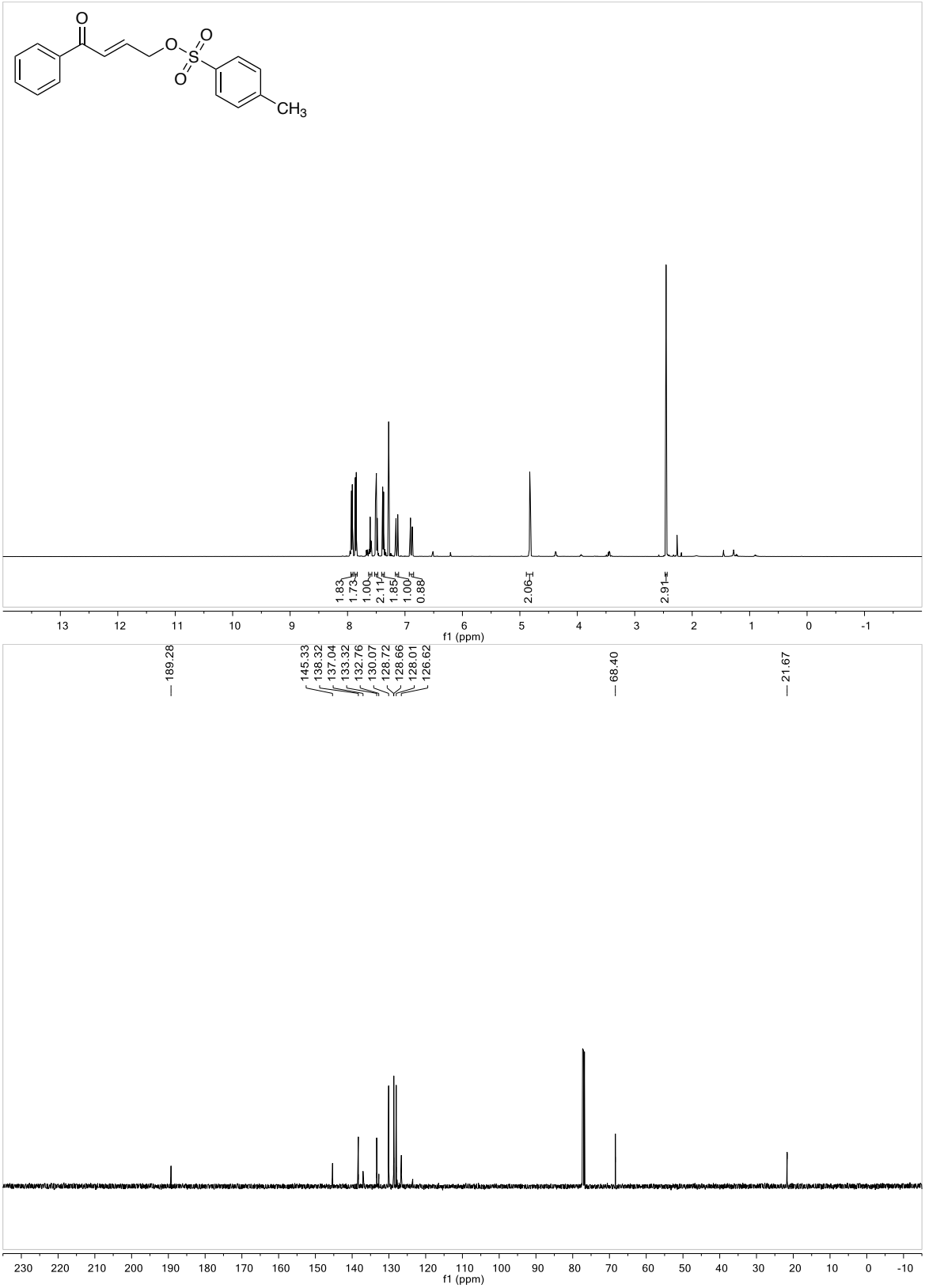
(*E*)-1-Cyclopropyl-4-hydroxybut-2-en-1-one (S24)



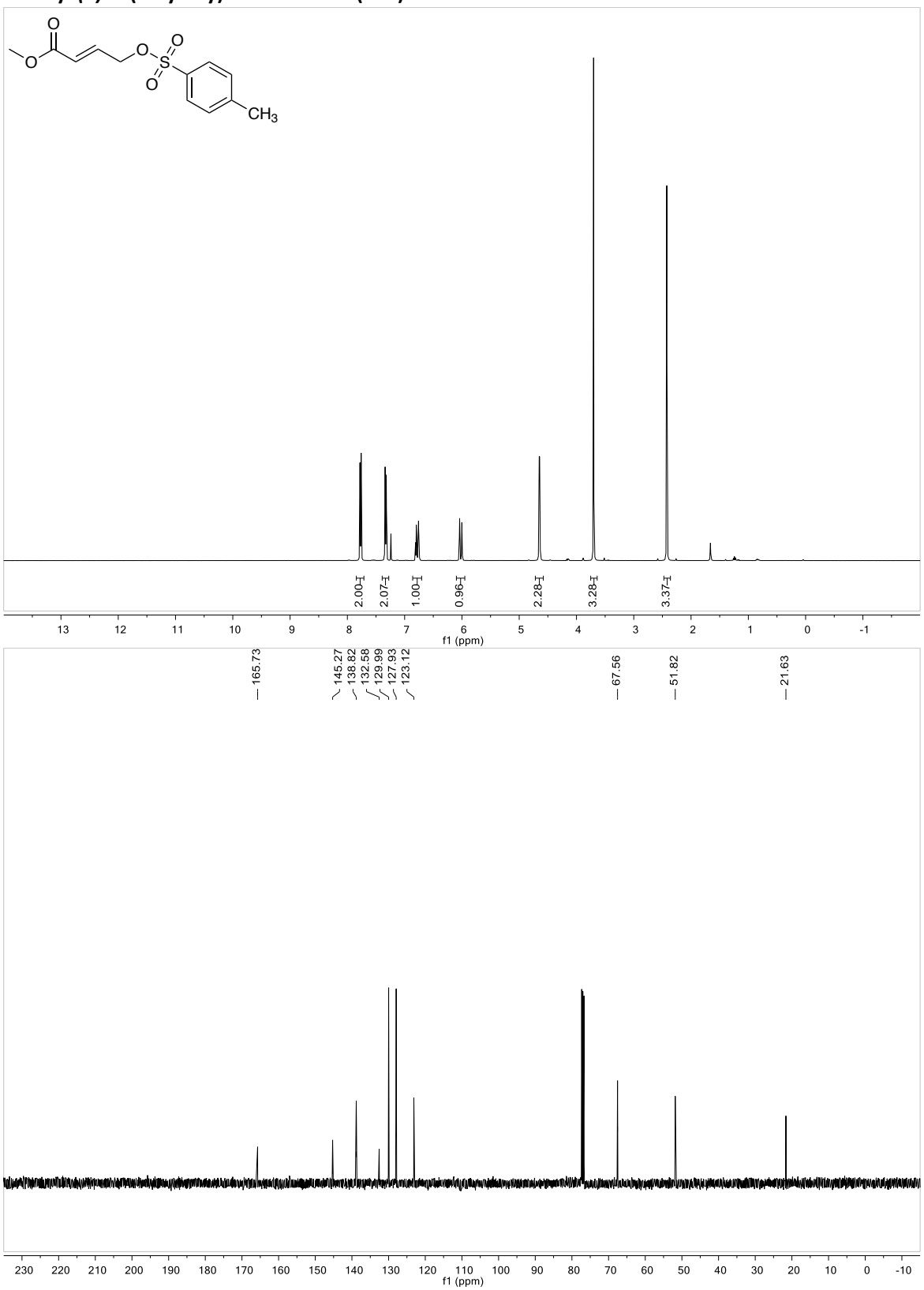
(*E*)-4-cyclopropyl-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S25)



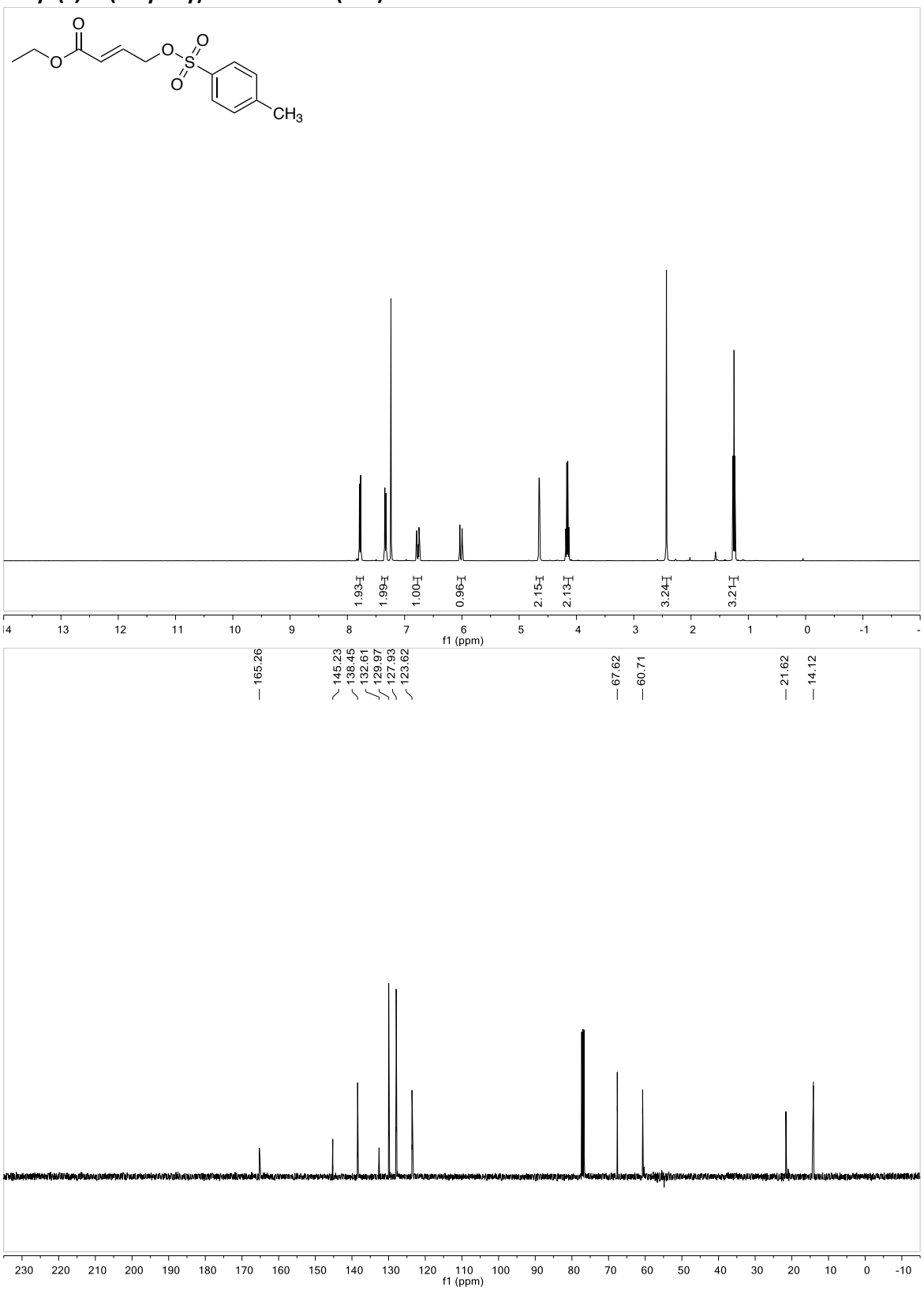
(*E*)-4-oxo-4-phenylbut-2-en-1-yl 4-methylbenzenesulfonate (S27)



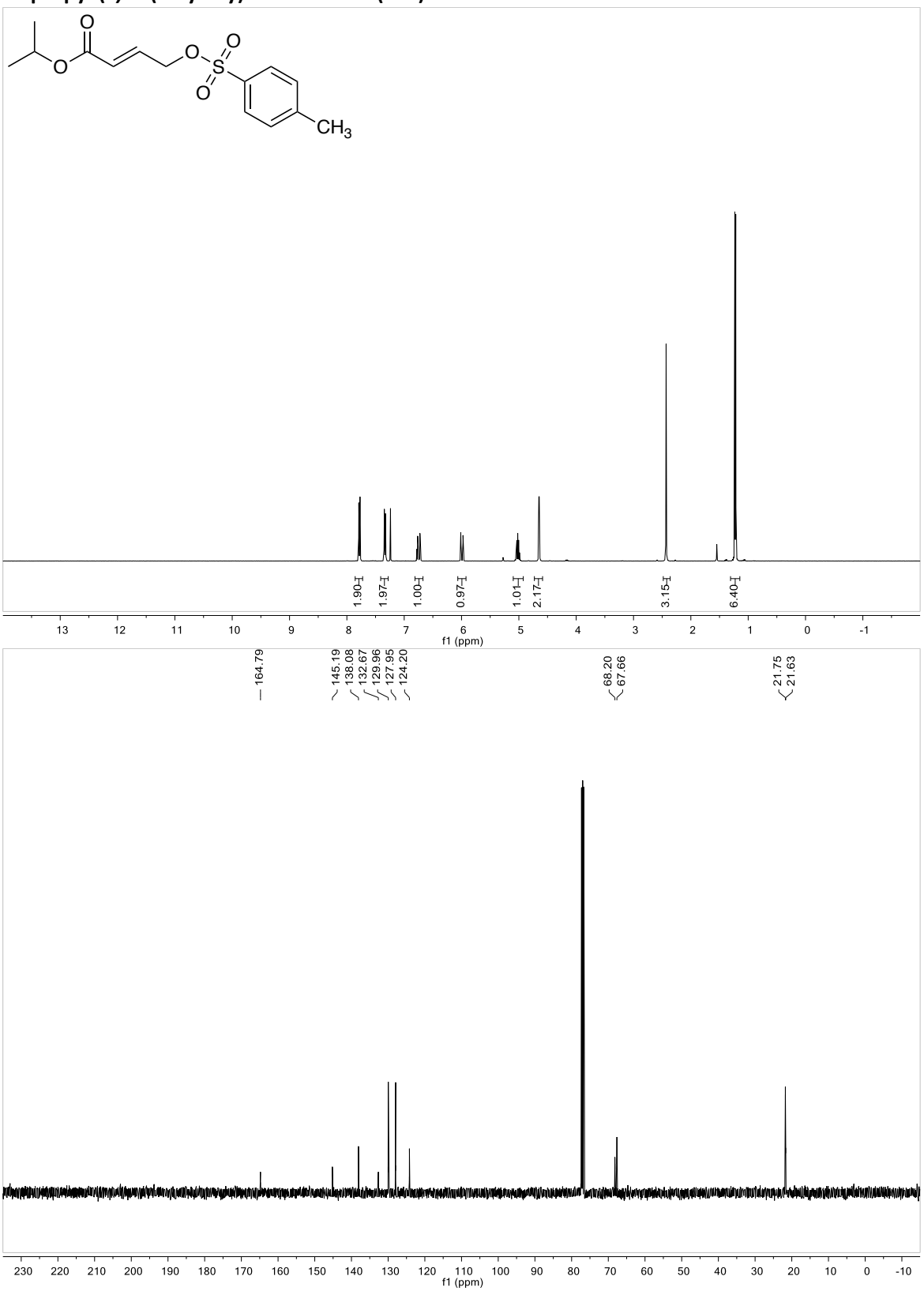
Methyl *(E)*-4-(tosyloxy)but-2-enoate (S29)



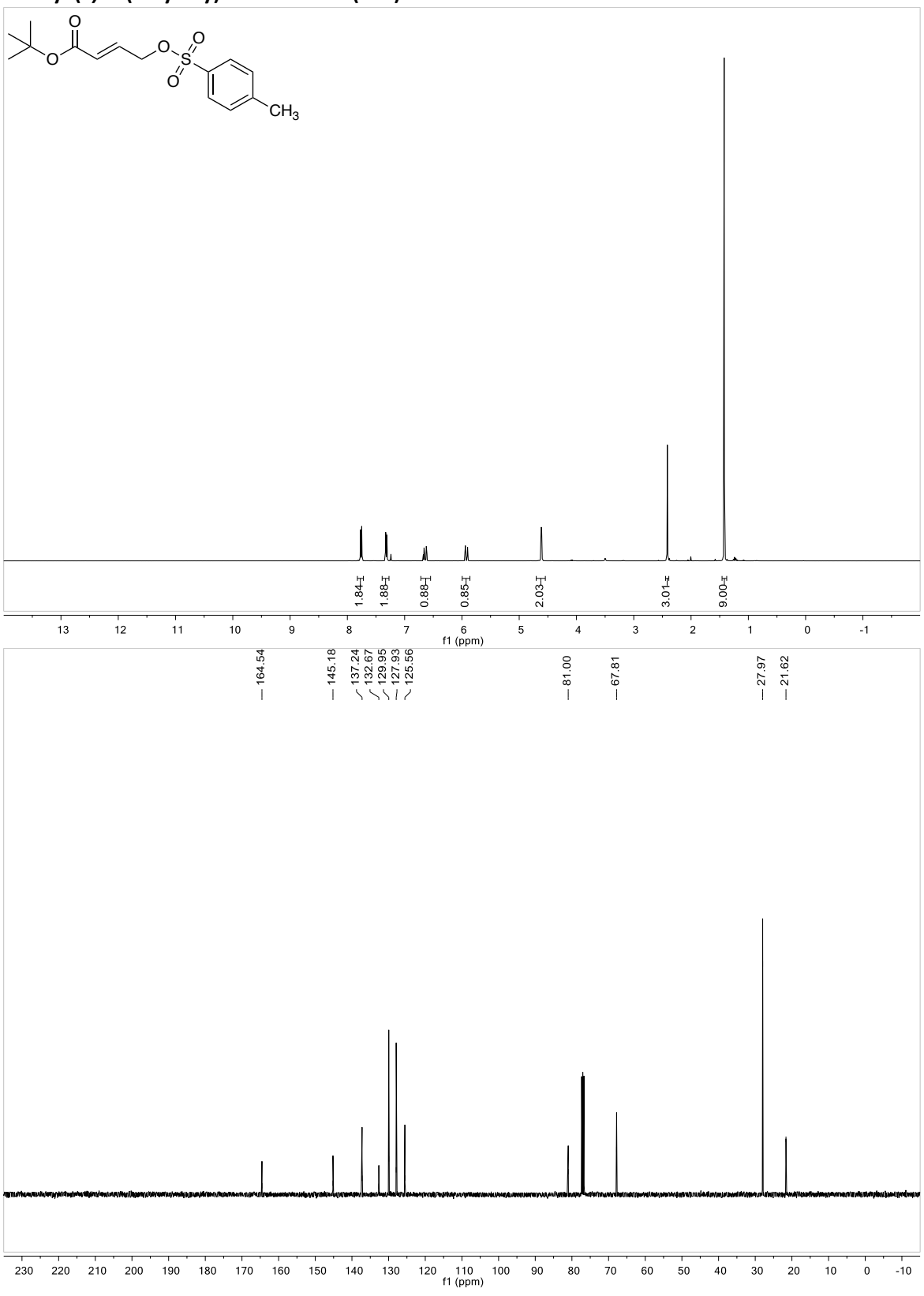
Ethyl (*E*)-4-(tosyloxy)but-2-enoate (S33)



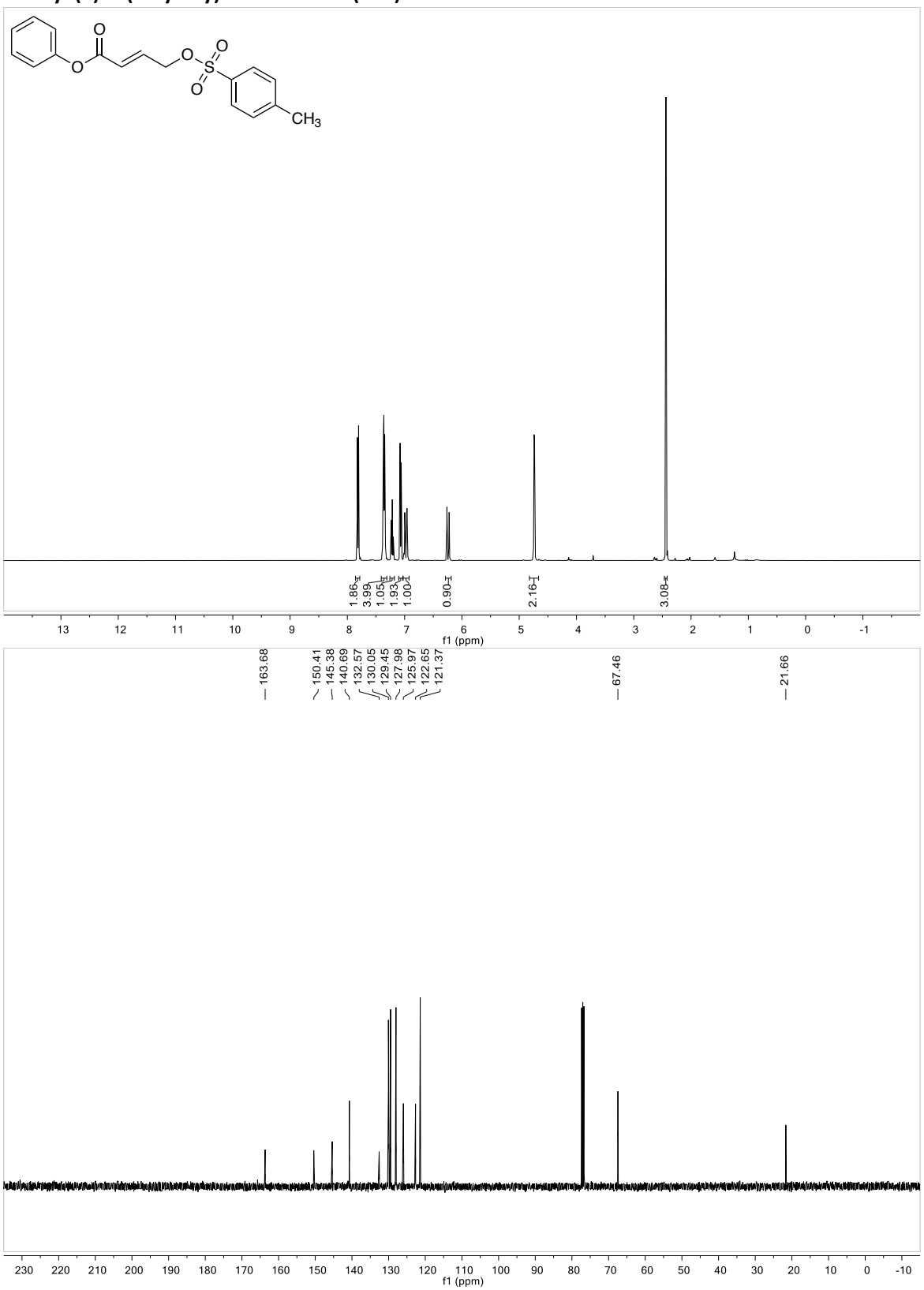
Isopropyl (*E*)-4-(tosyloxy)but-2-enoate (S35)



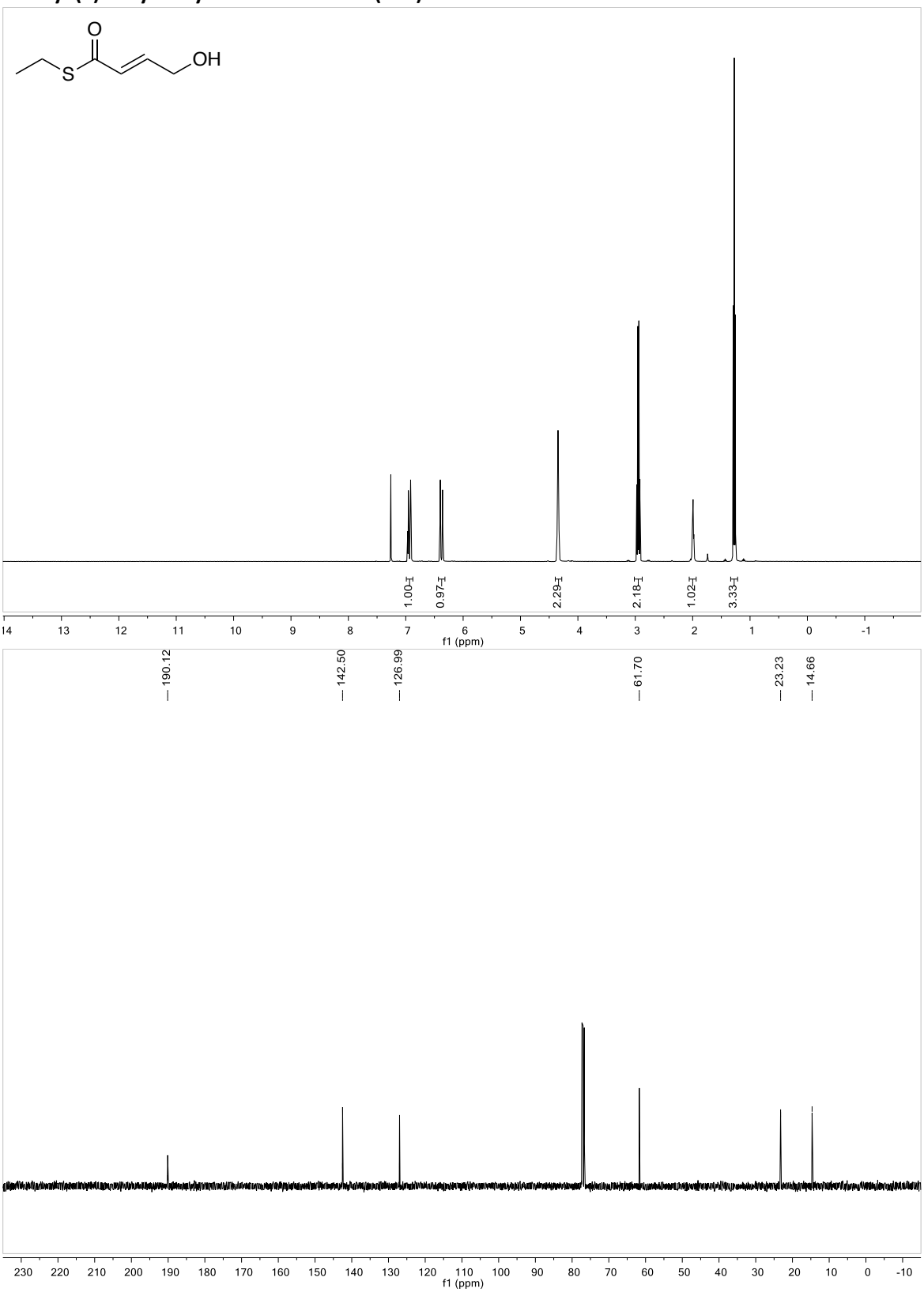
***t*-Butyl (*E*)-4-(tosyloxy)but-2-enoate (S37)**



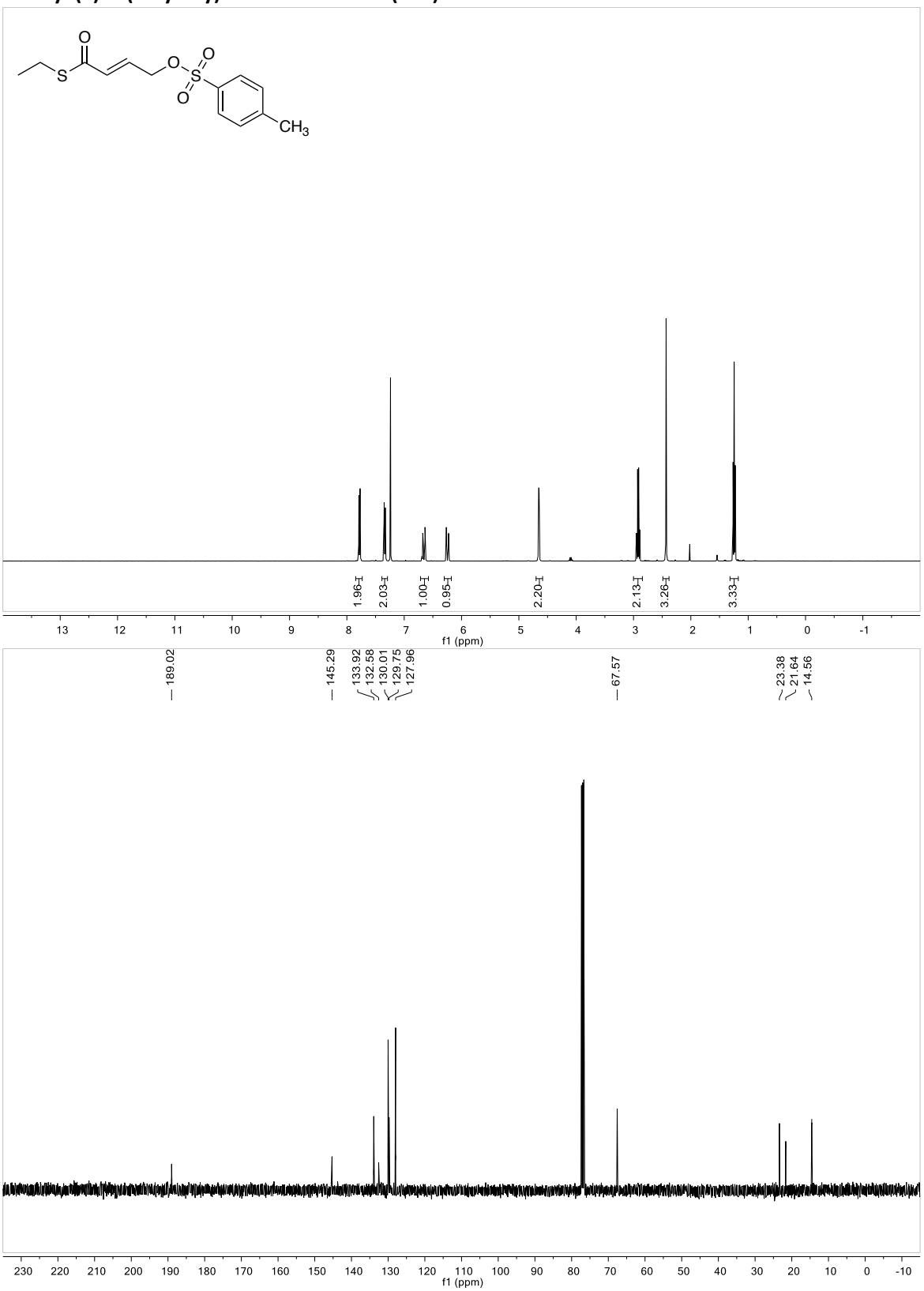
Phenyl (*E*)-4-(tosyloxy)but-2-enoate (S39)



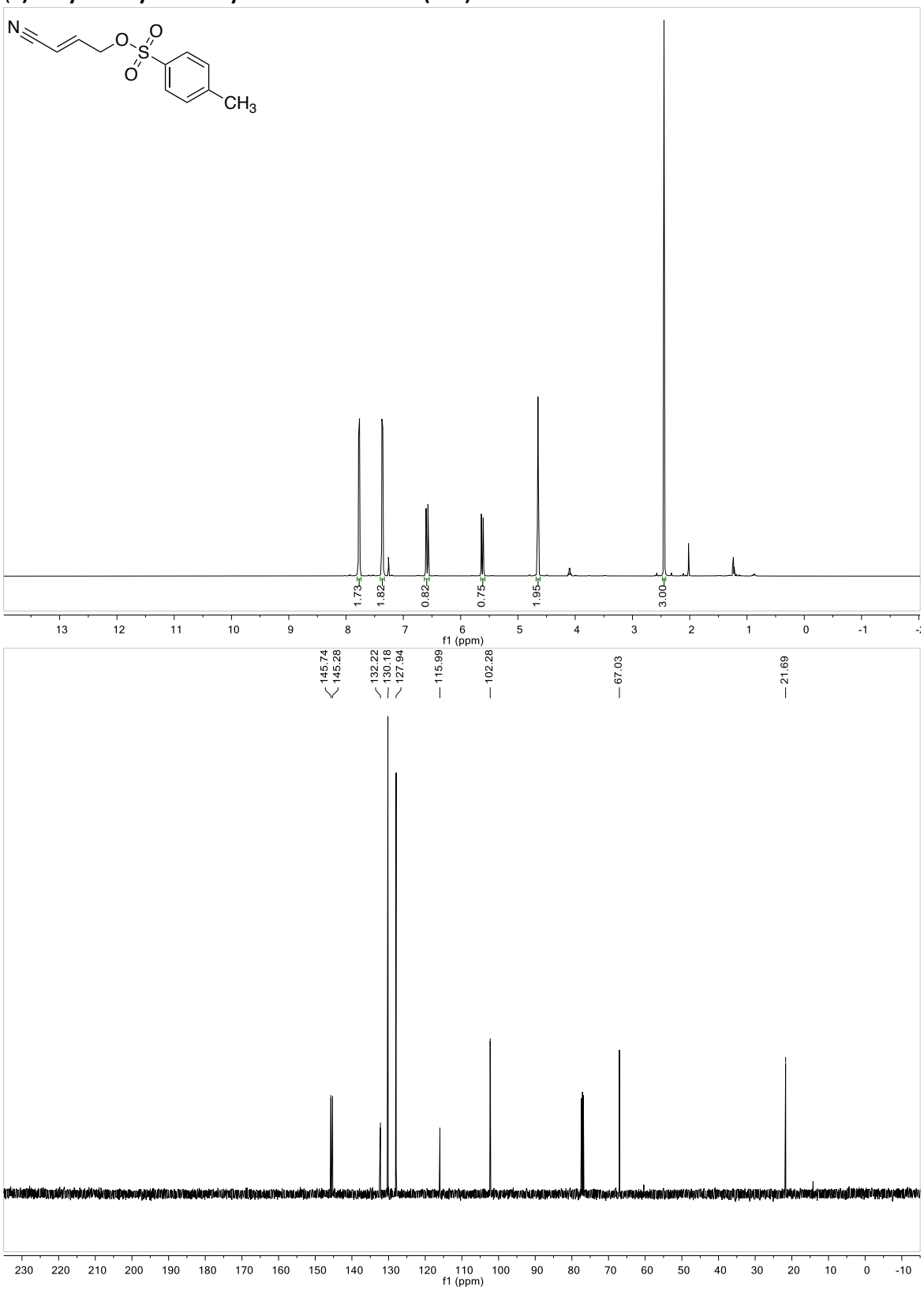
S-Ethyl (*E*)-4-hydroxybut-2-enethioate (S40)



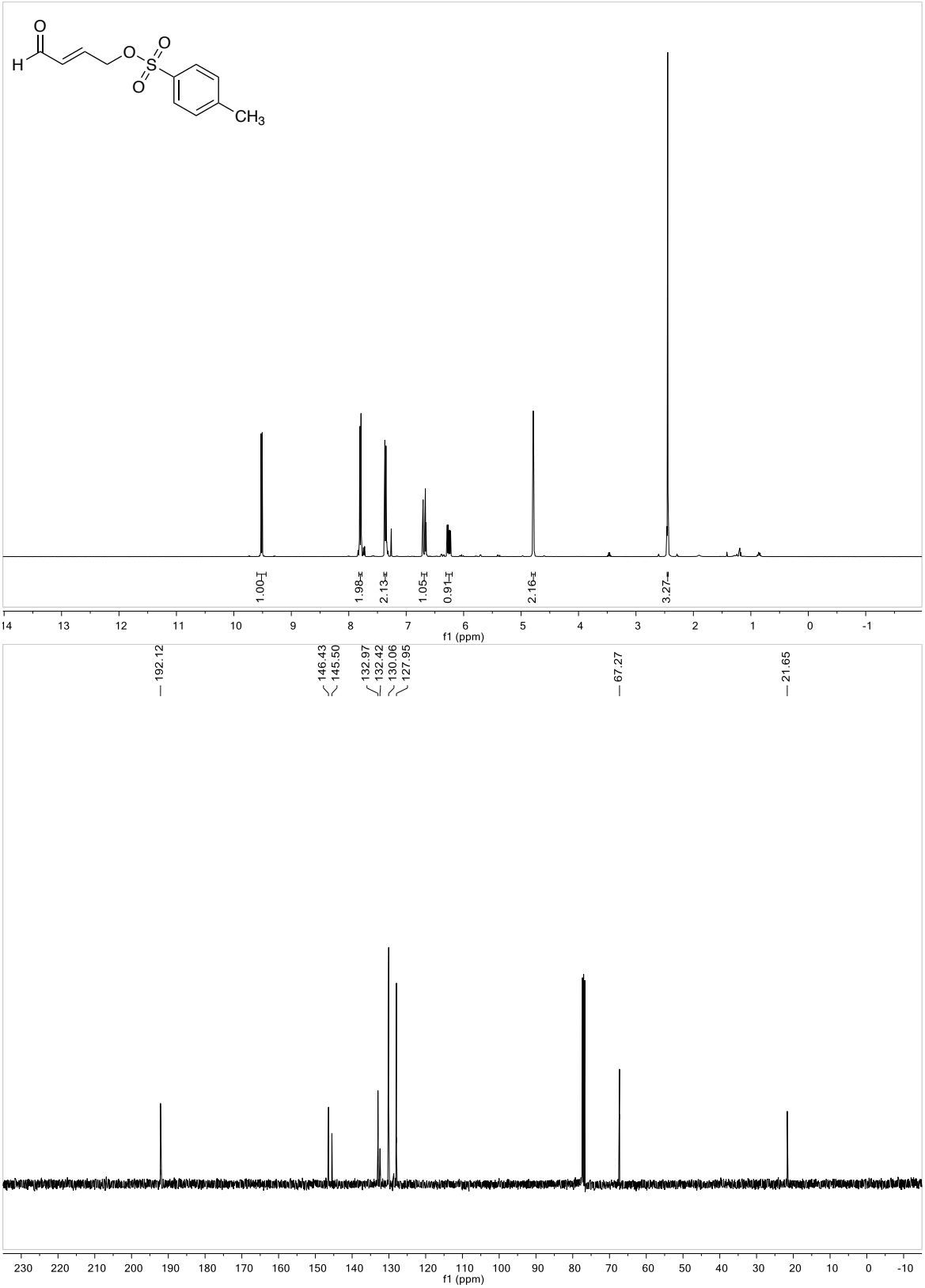
S-Ethyl (*E*)-4-(tosyloxy)but-2-enethioate (S41)



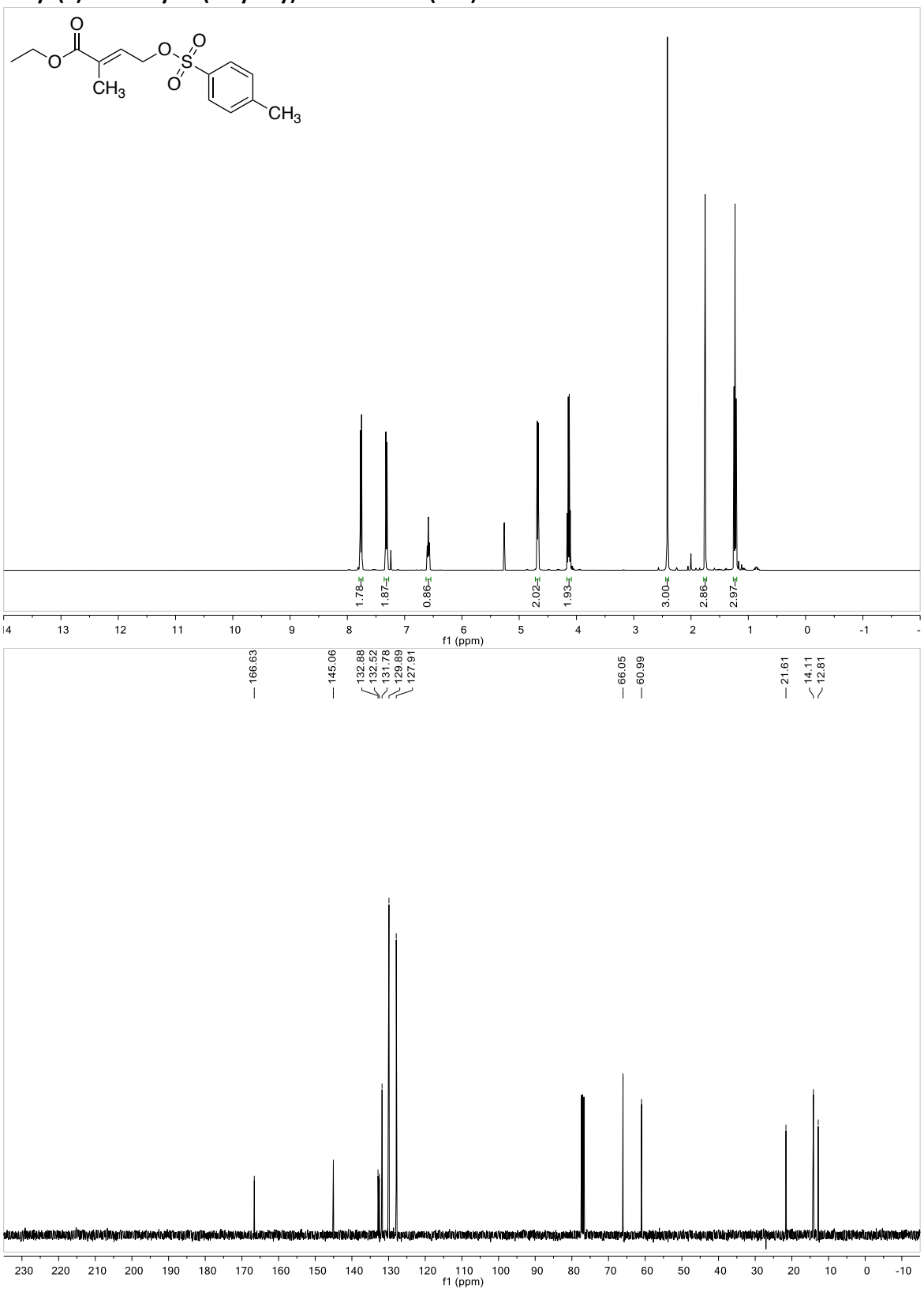
(*E*)-3-Cyanoallyl 4-methylbenzenesulfonate (S43)



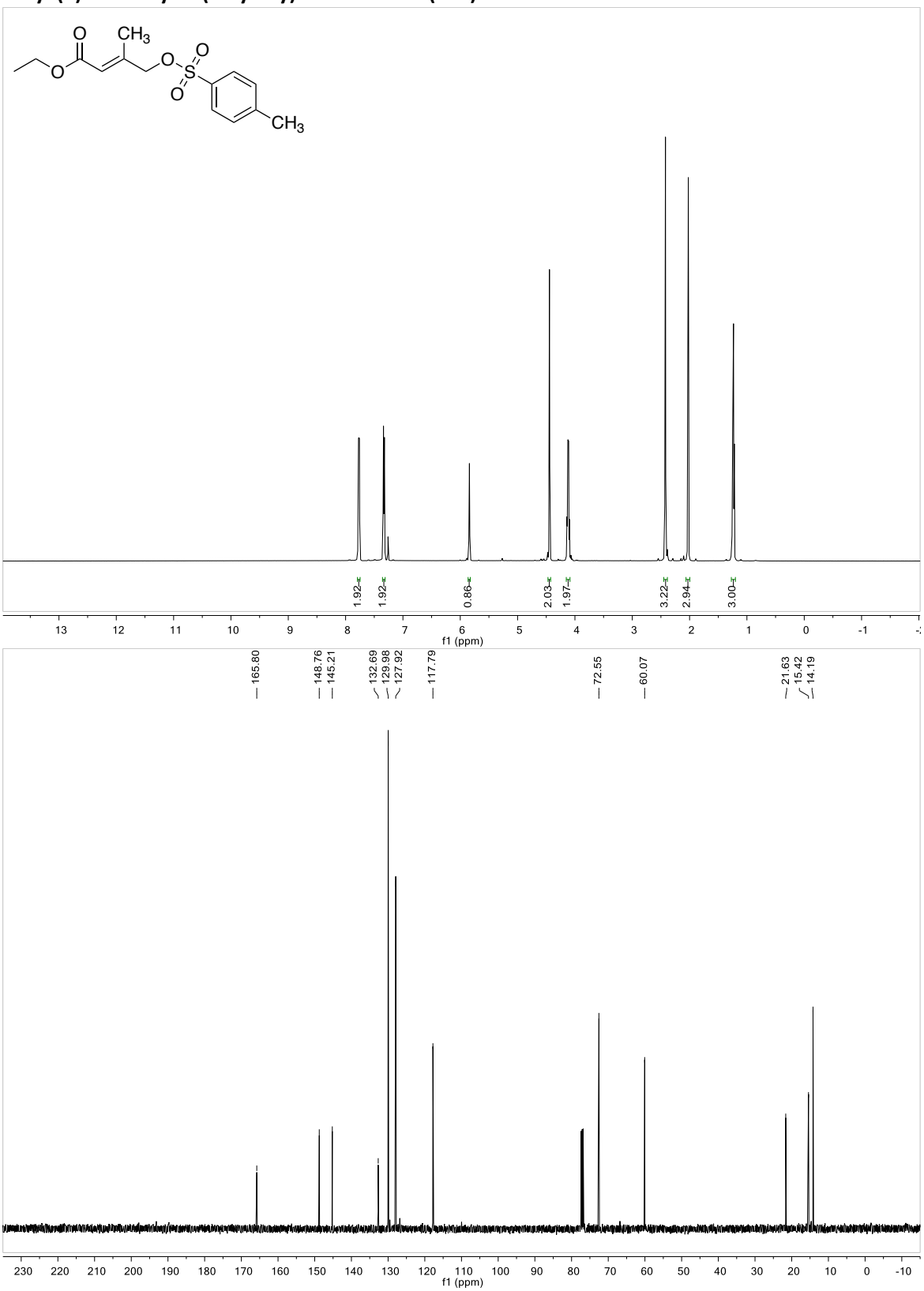
(*E*)-4-oxobut-2-en-1-yl 4-methylbenzenesulfonate (S45)



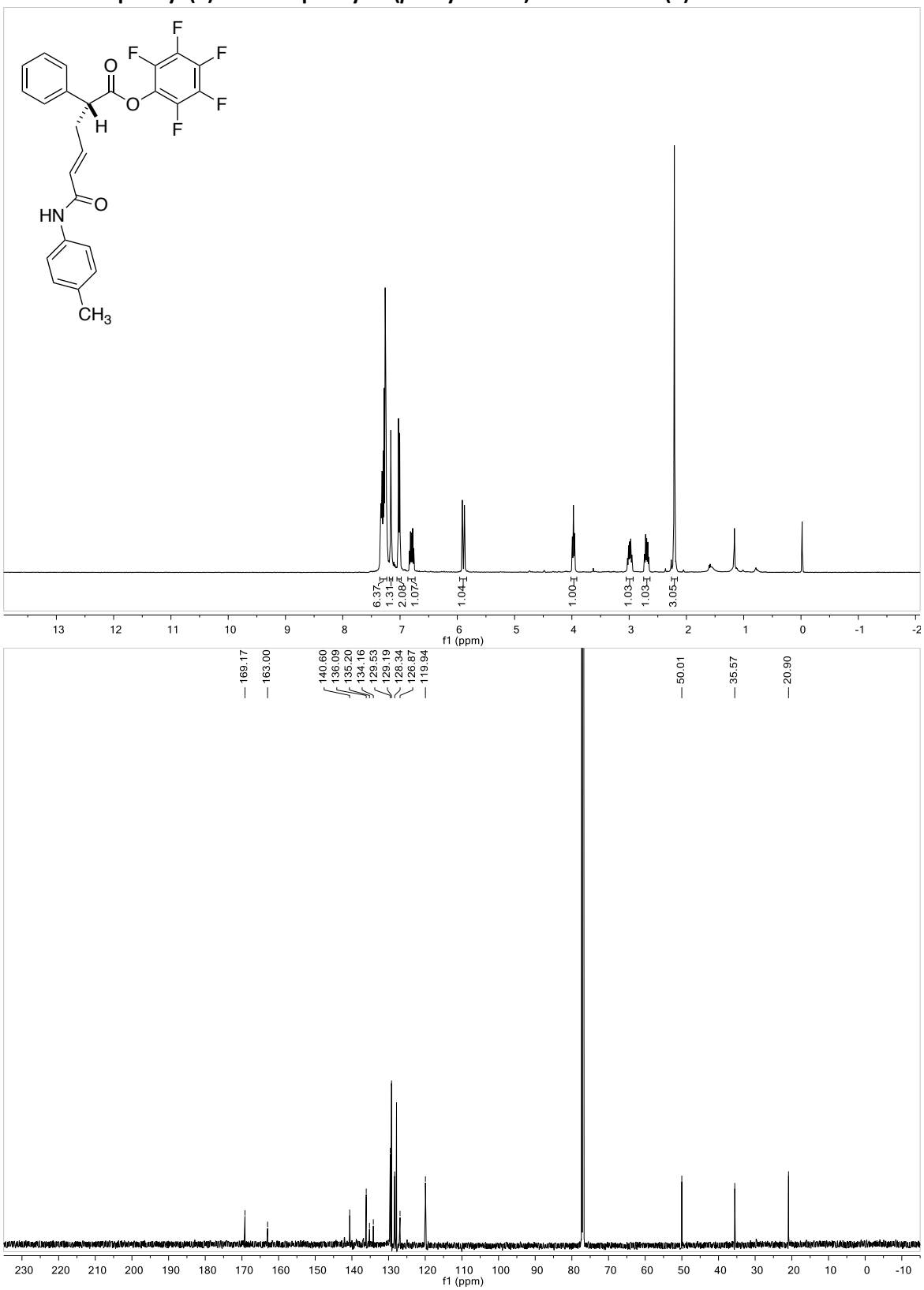
Ethyl (*E*)-2-methyl-4-(tosyloxy)but-2-enoate (S47)



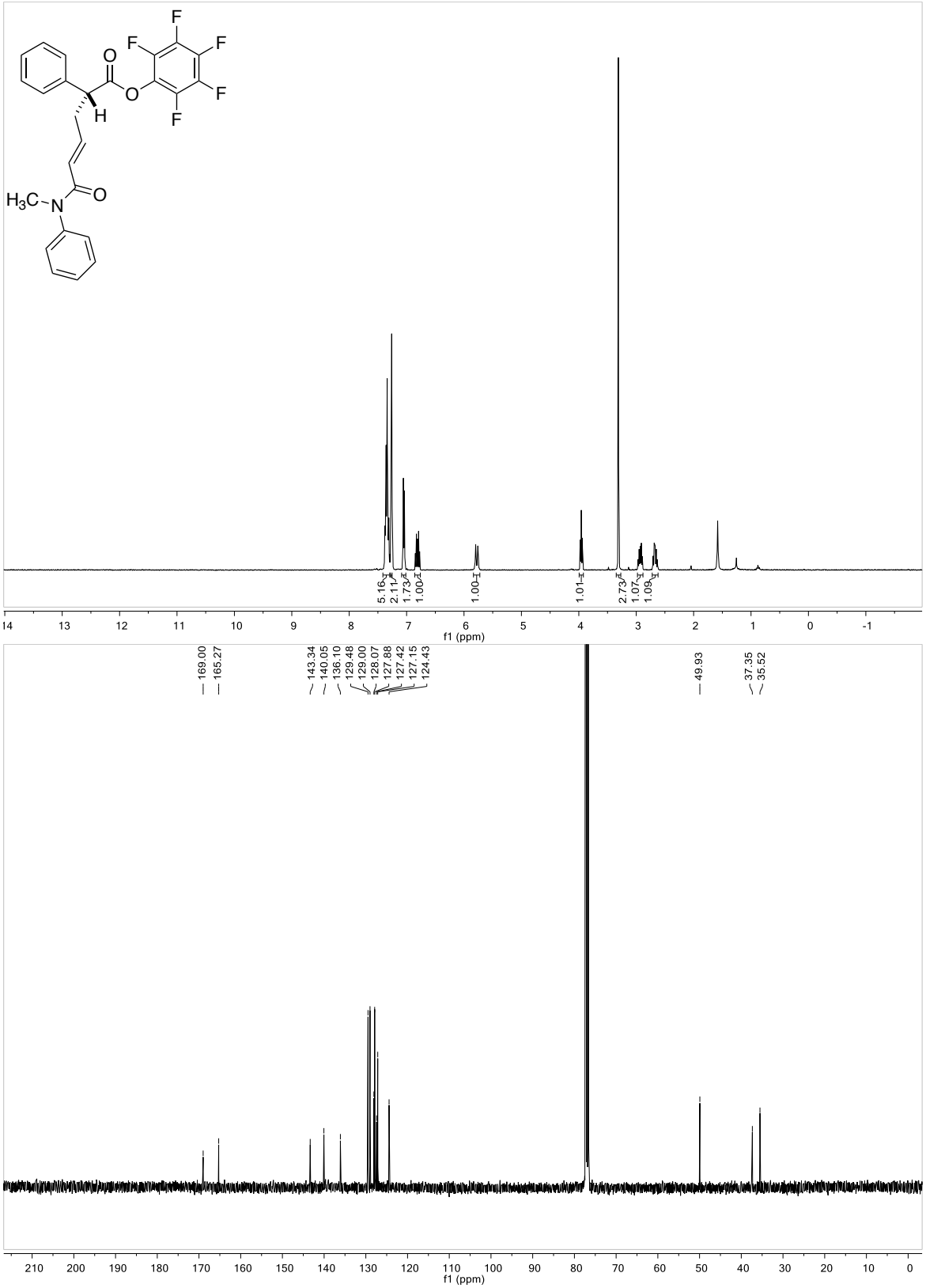
Ethyl (*E*)-3-methyl-4-(tosyloxy)but-2-enoate (S48)



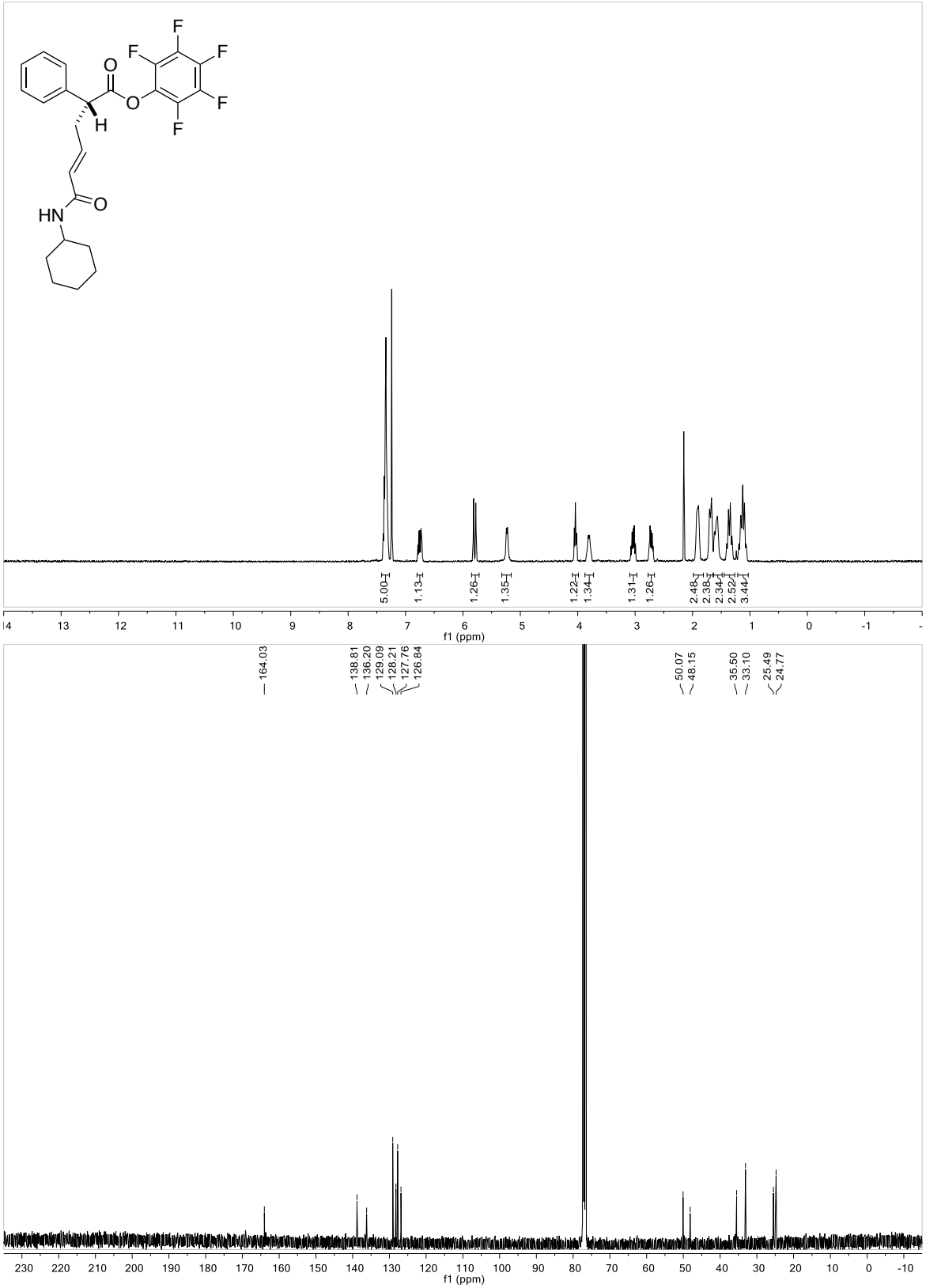
Pentafluorophenyl (*E*)-6-oxo-2-phenyl-6-(*p*-tolylamino)hex-4-enoate (2)



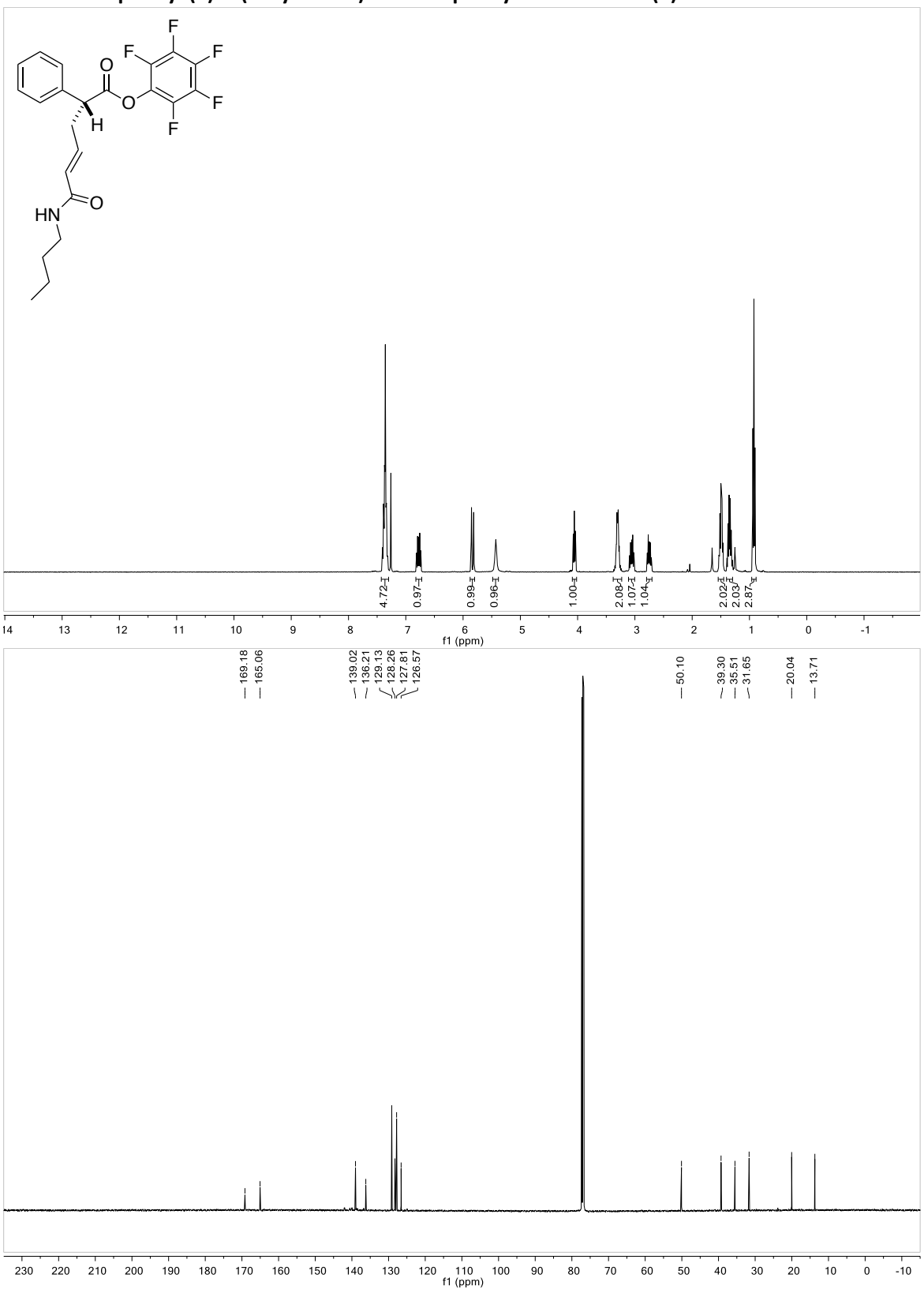
Pentafluorophenyl (*E*)-6-(methyl(phenyl)amino)-6-oxo-2-phenylhex-4-enoate (3)



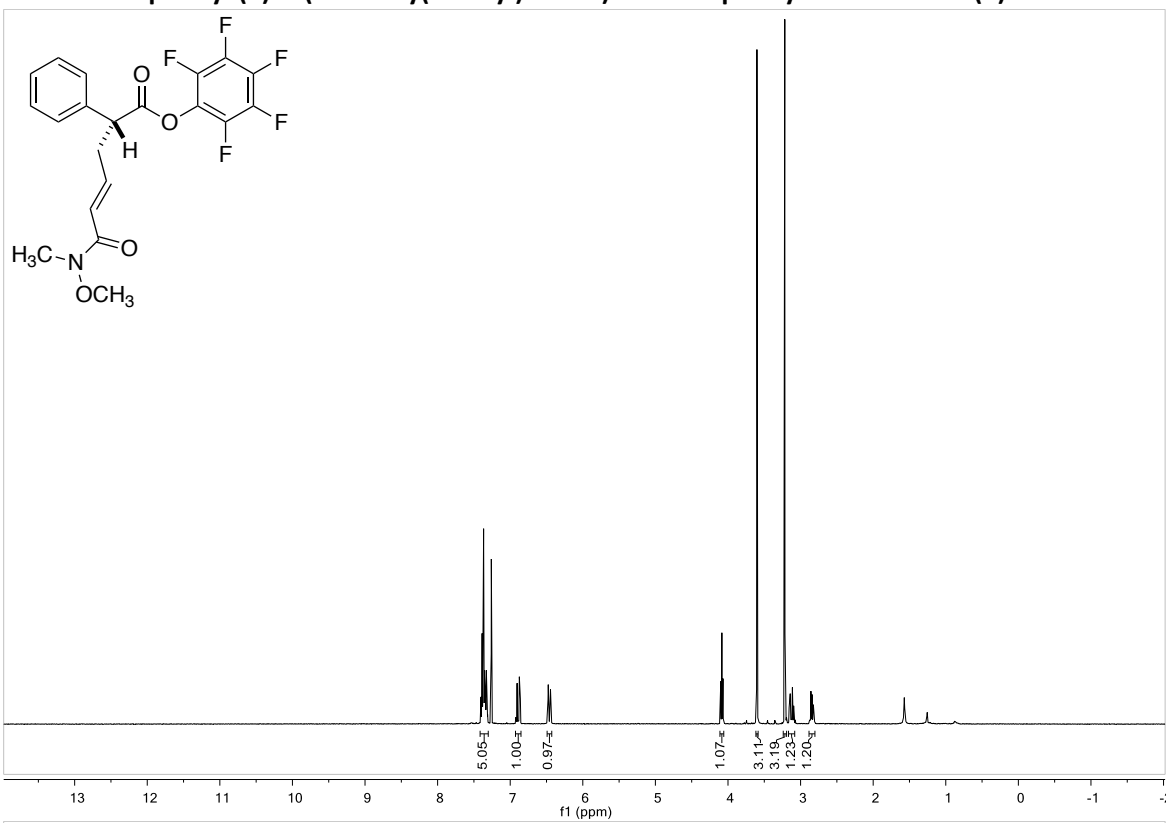
Pentafluorophenyl (*E*)-6-(cyclohexylamino)-6-oxo-2-phenylhex-4-enoate (4)

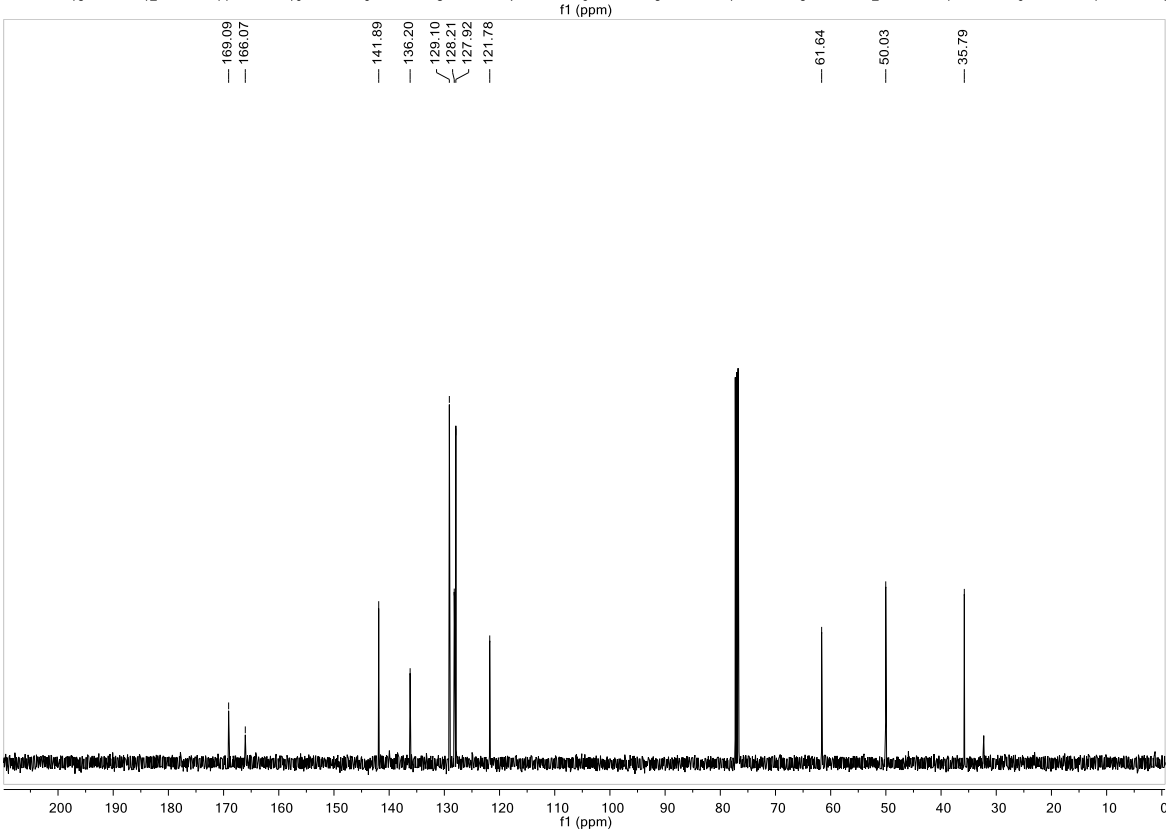


Pentafluorophenyl (*E*)-6-(butylamino)-6-oxo-2-phenylhex-4-enoate (5)

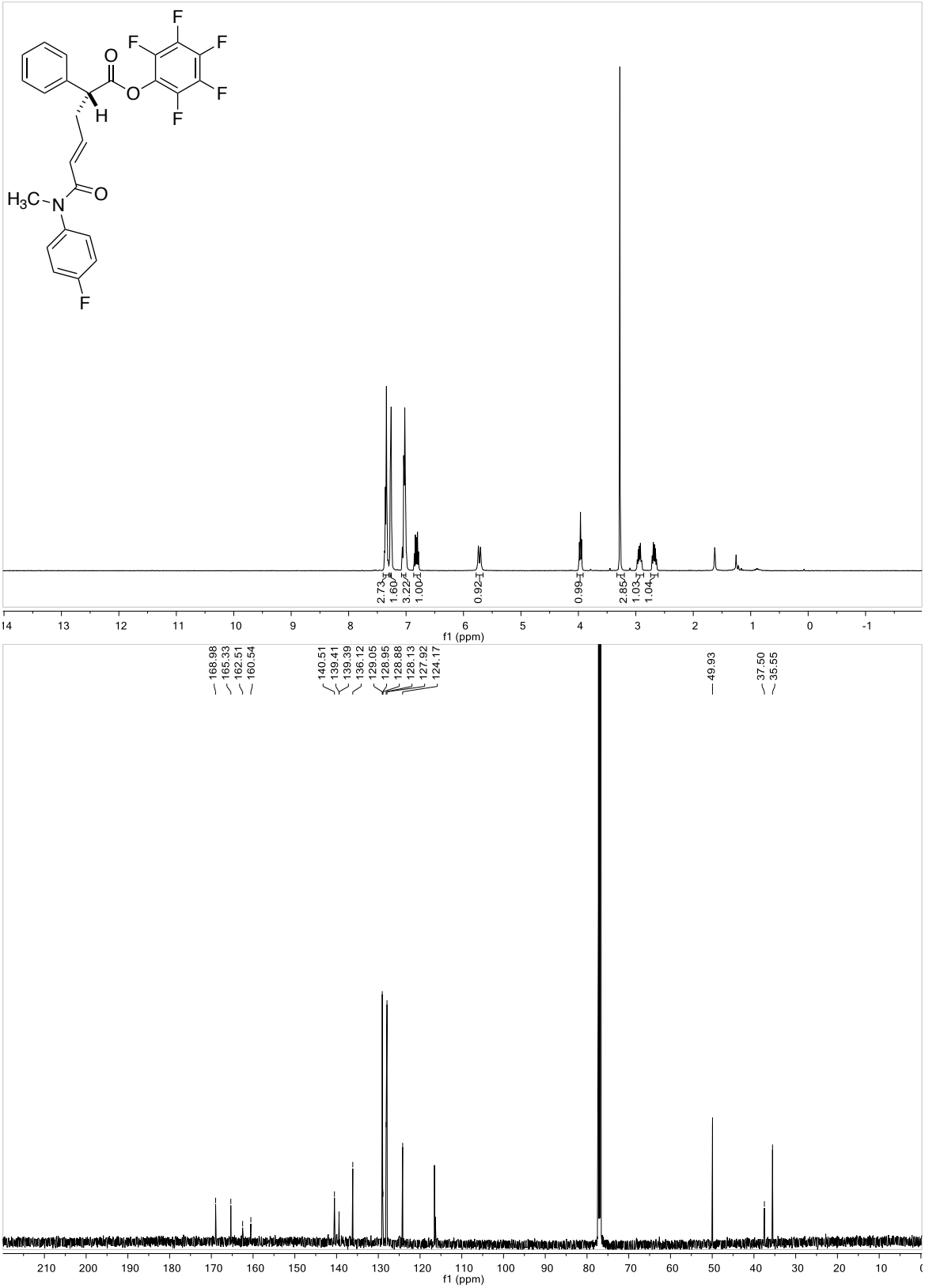


Pentafluorophenyl (*E*)-6-(methoxy(methyl)amino)-6-oxo-2-phenylhex-4-enoate (6)

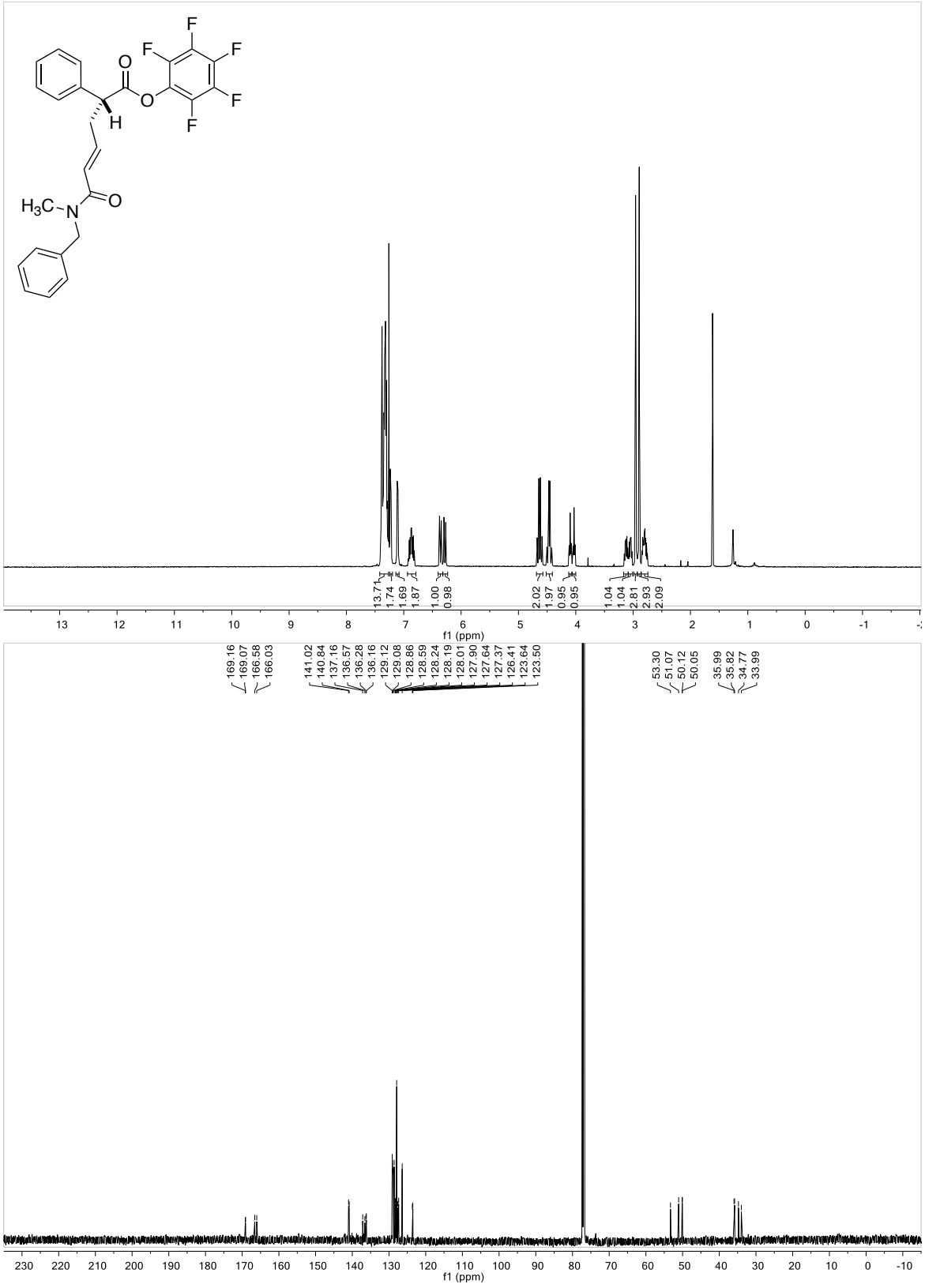




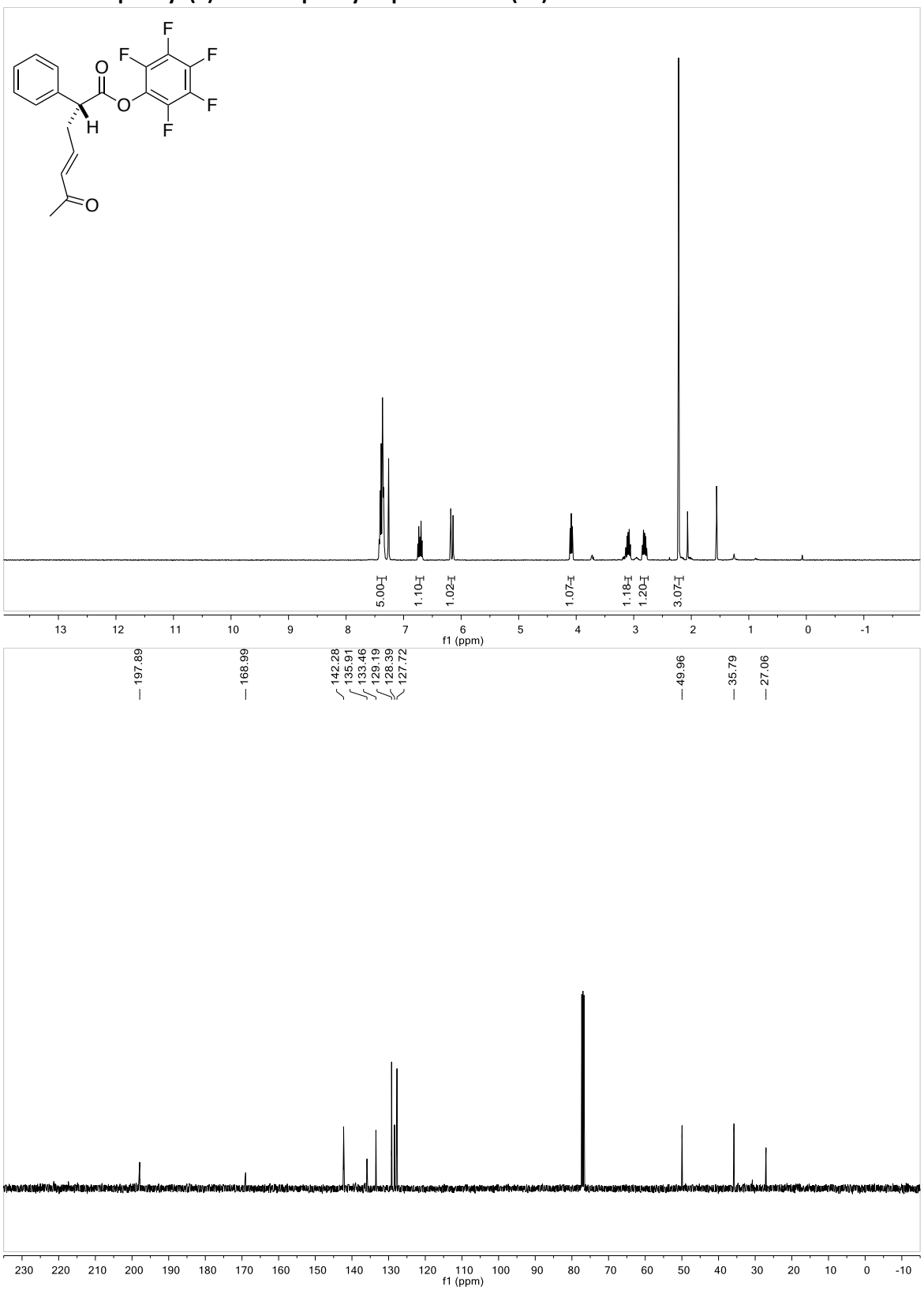
Pentafluorophenyl (*E*)-6-((4-fluorophenyl)(methyl)amino)-6-oxo-2-phenylhex-4-enoate (7)



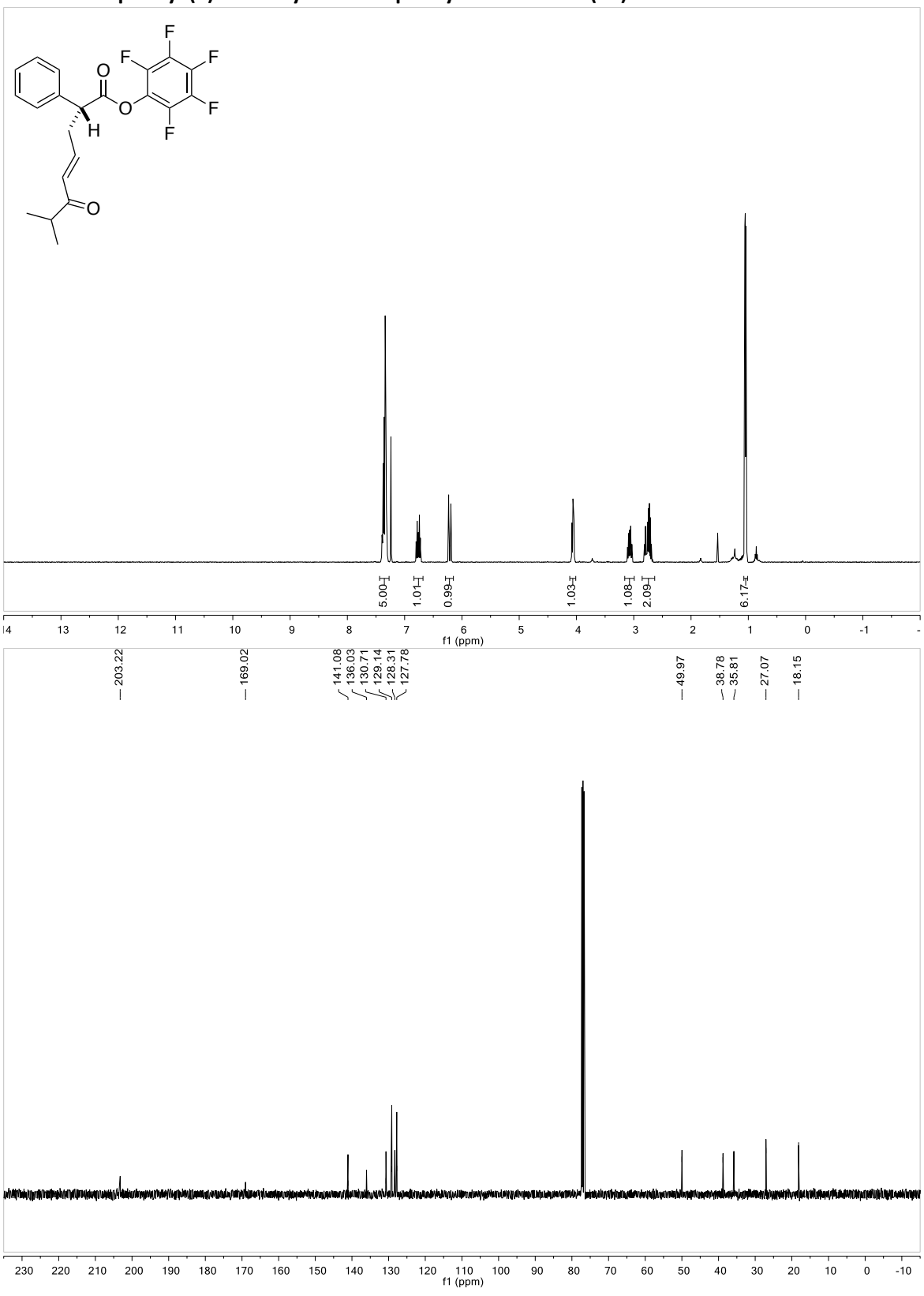
Pentafluorophenyl (*E*)-6-(benzyl(methyl)amino)-6-oxo-2-phenylhex-4-enoate (8)



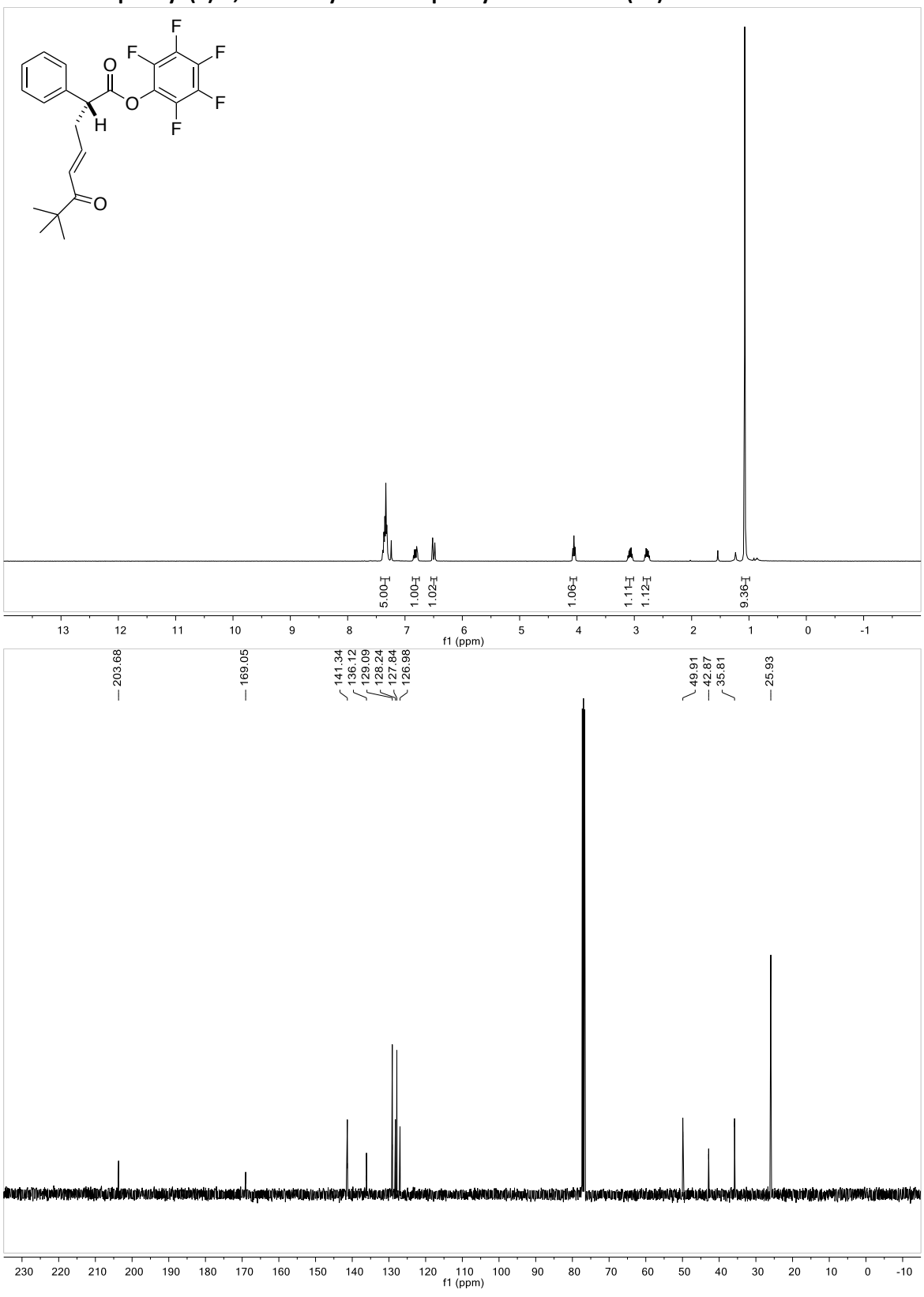
Pentafluorophenyl (*E*)-6-oxo-2-phenylhept-4-enoate (13)



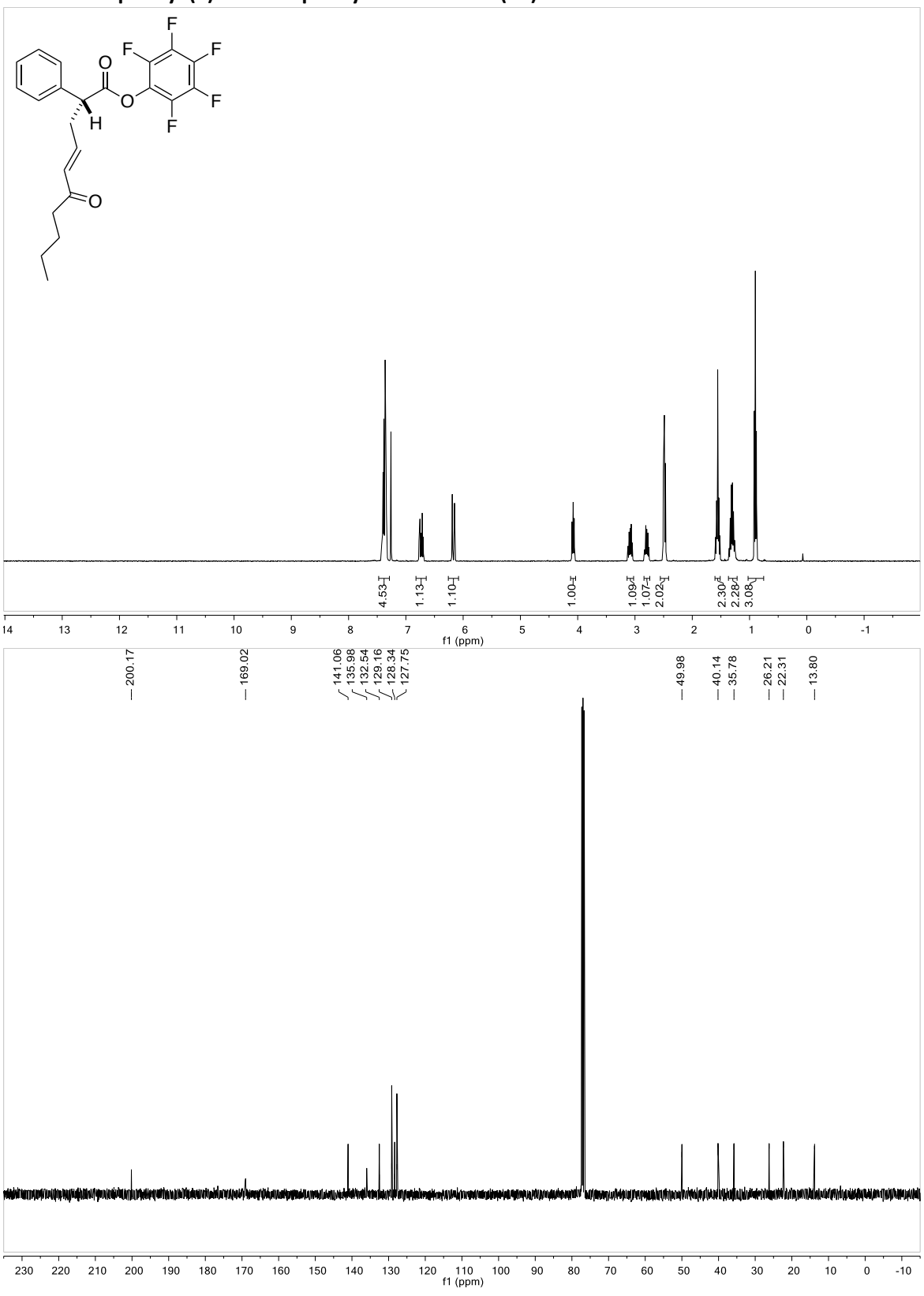
Pentafluorophenyl (*E*)-7-methyl-6-oxo-2-phenyloct-4-enoate (14)



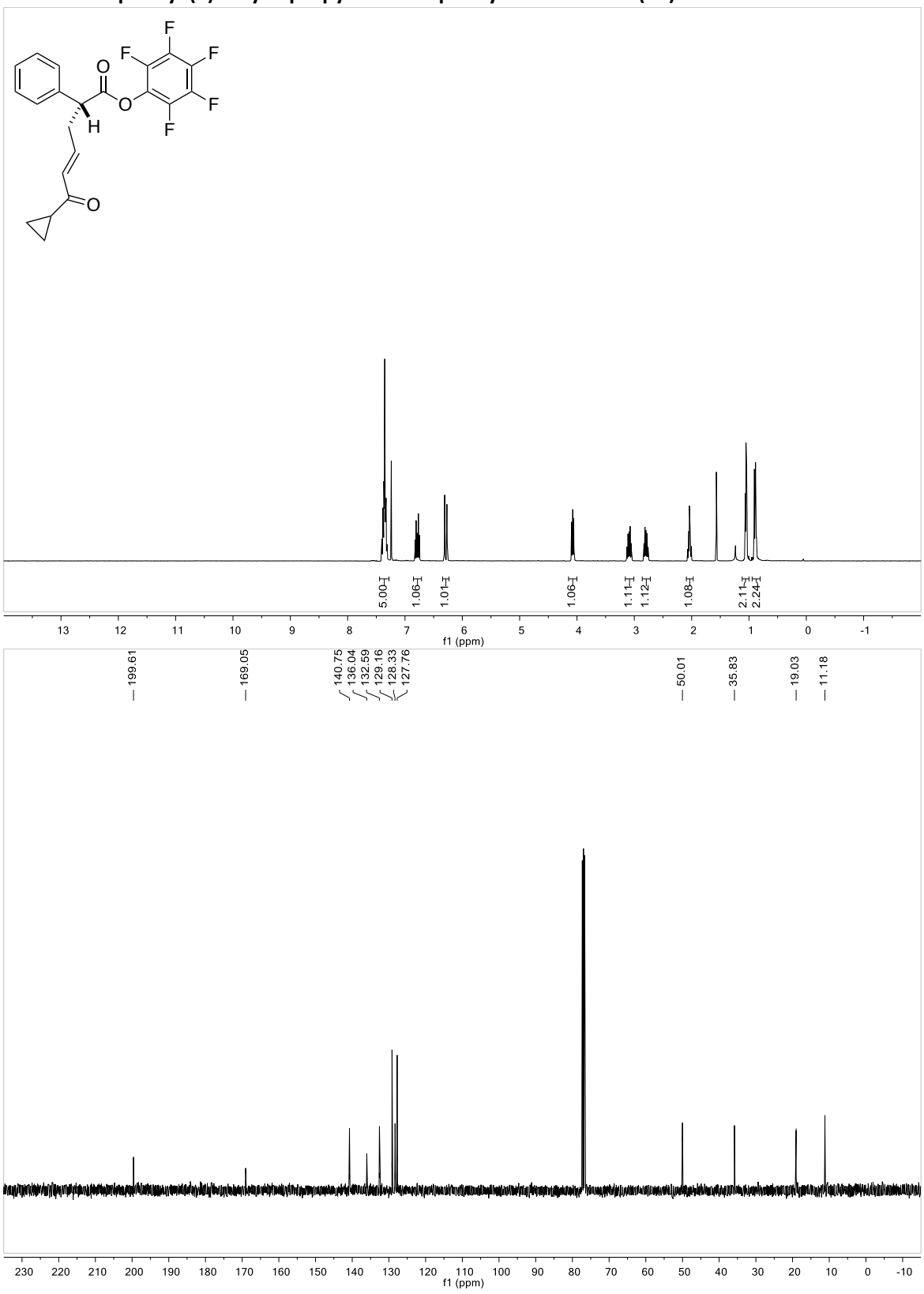
Pentafluorophenyl (*E*)-7,7-dimethyl-6-oxo-2-phenyloct-4-enoate (15)



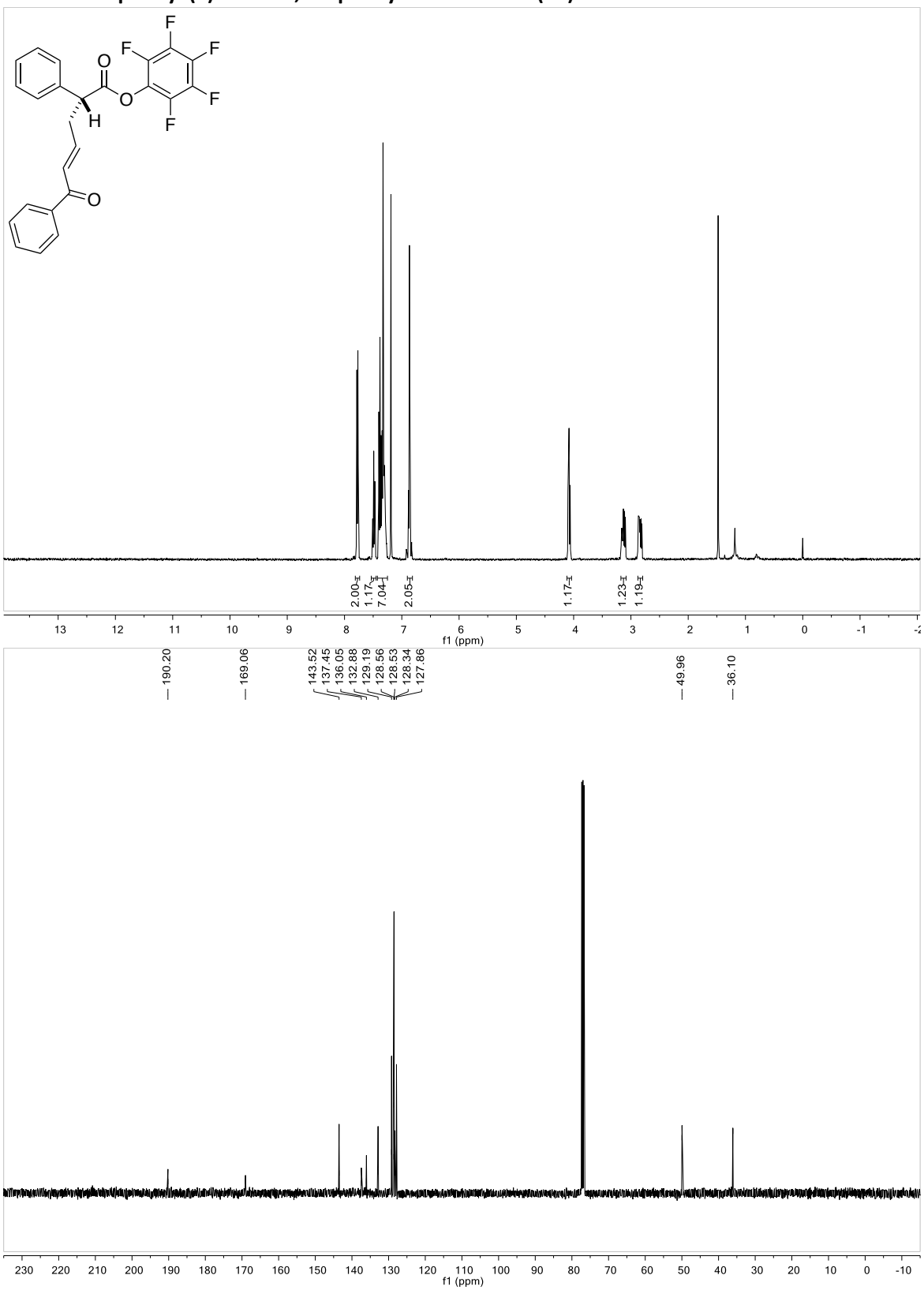
Pentafluorophenyl (*E*)-6-oxo-2-phenyldec-4-enoate (16)



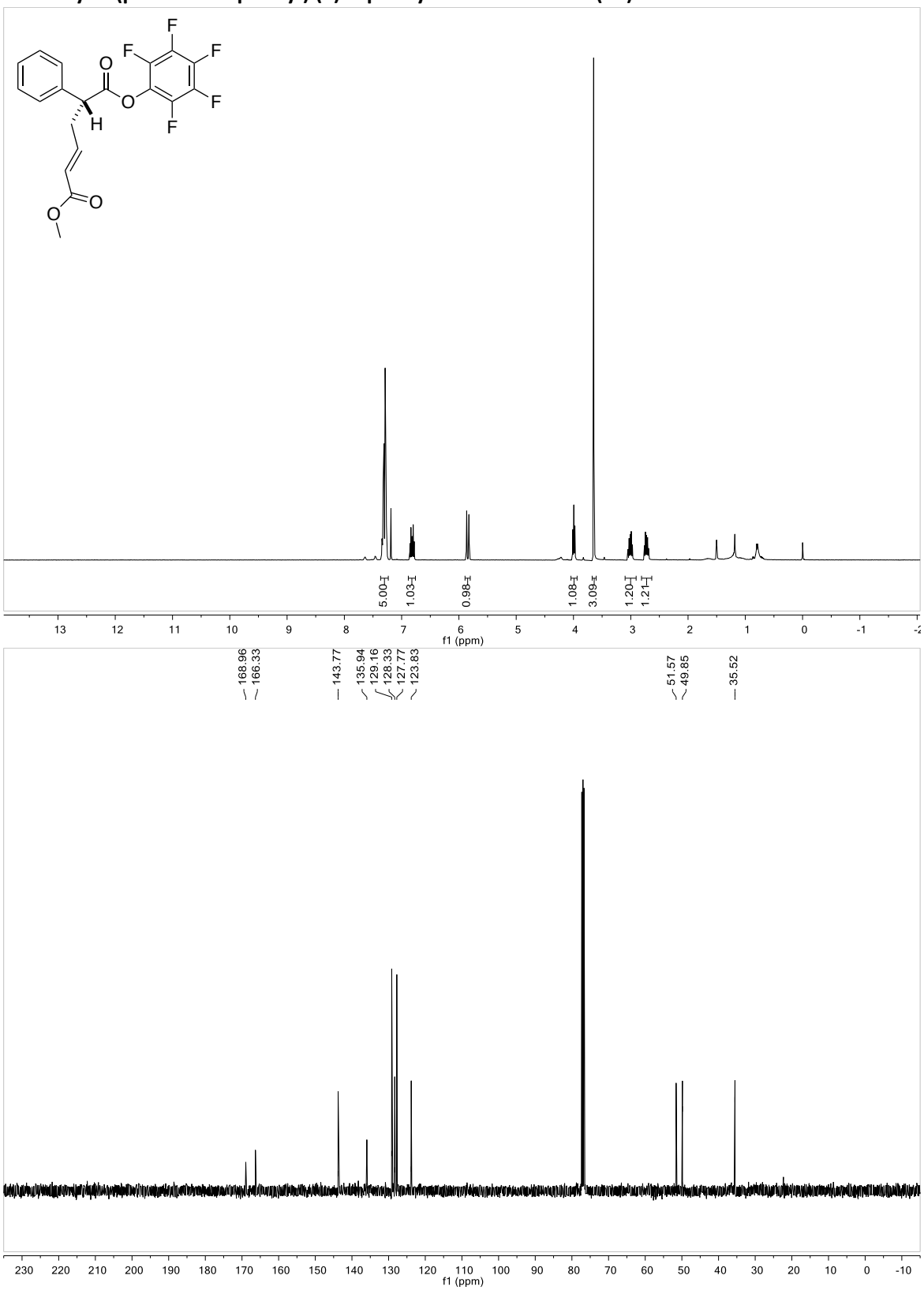
Pentafluorophenyl (*E*)-6-cyclopropyl-6-oxo-2-phenylhex-4-enoate (17)



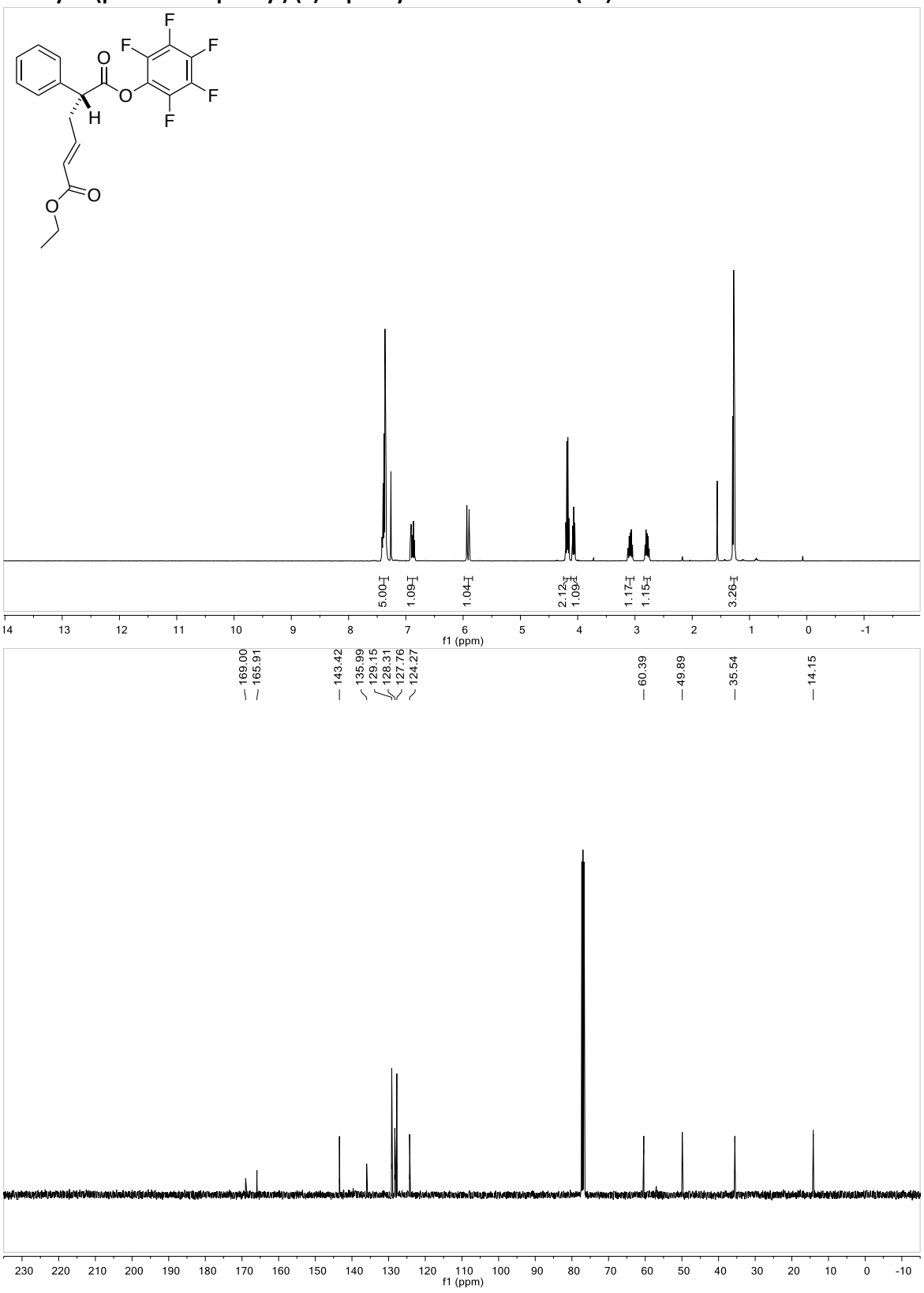
Pentafluorophenyl (*E*)-6-oxo-2,6-diphenylhex-4-enoate (18)



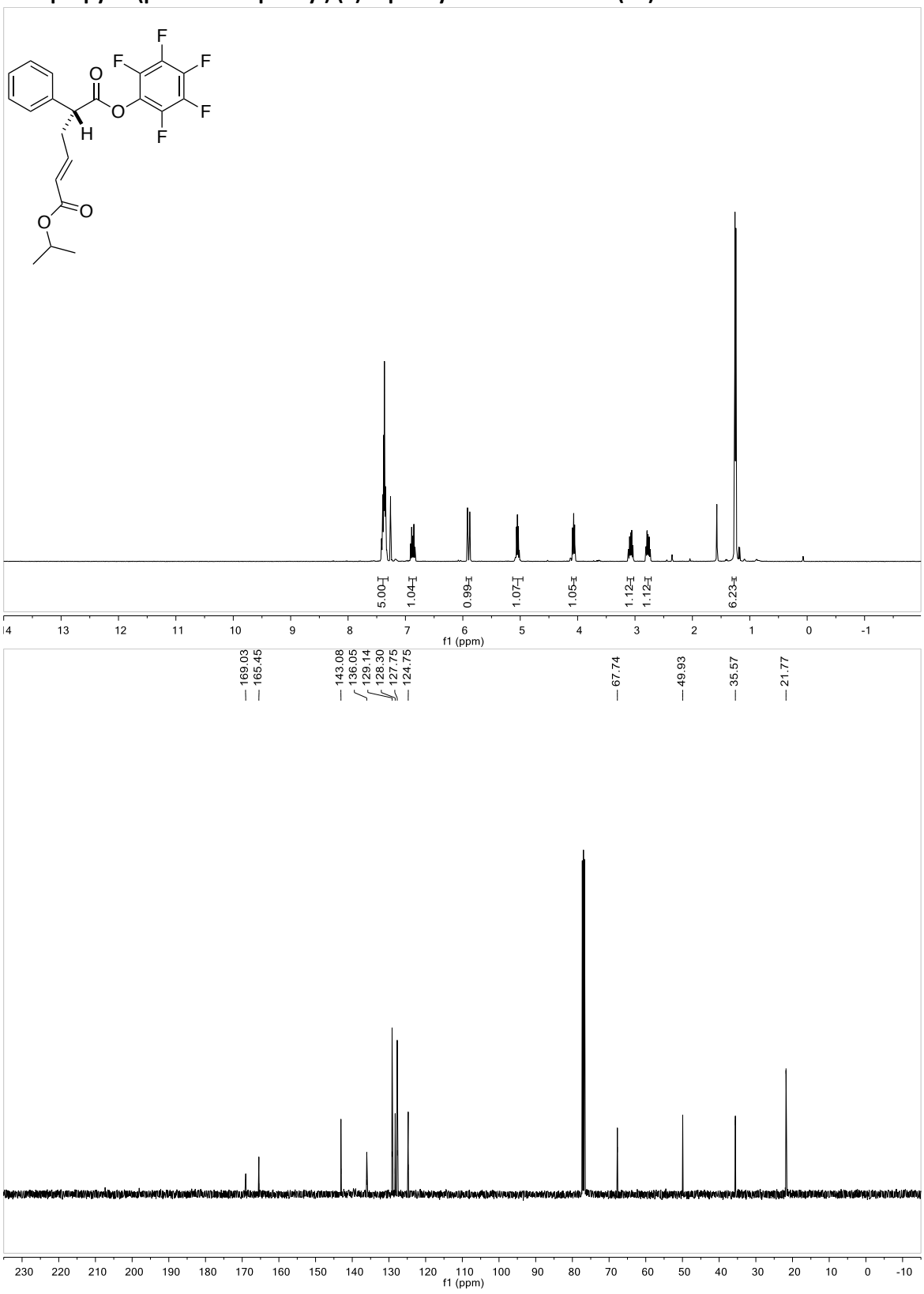
1-Methyl 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (19)



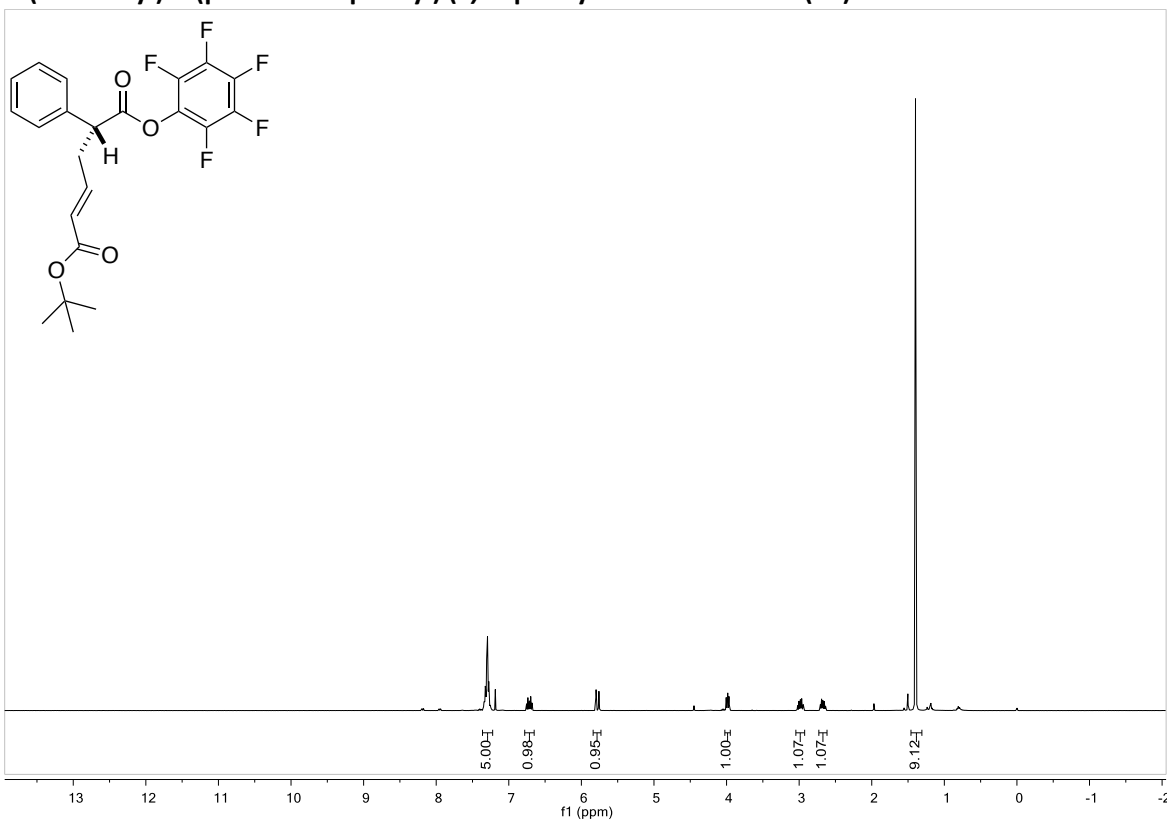
1-Ethyl 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (20)

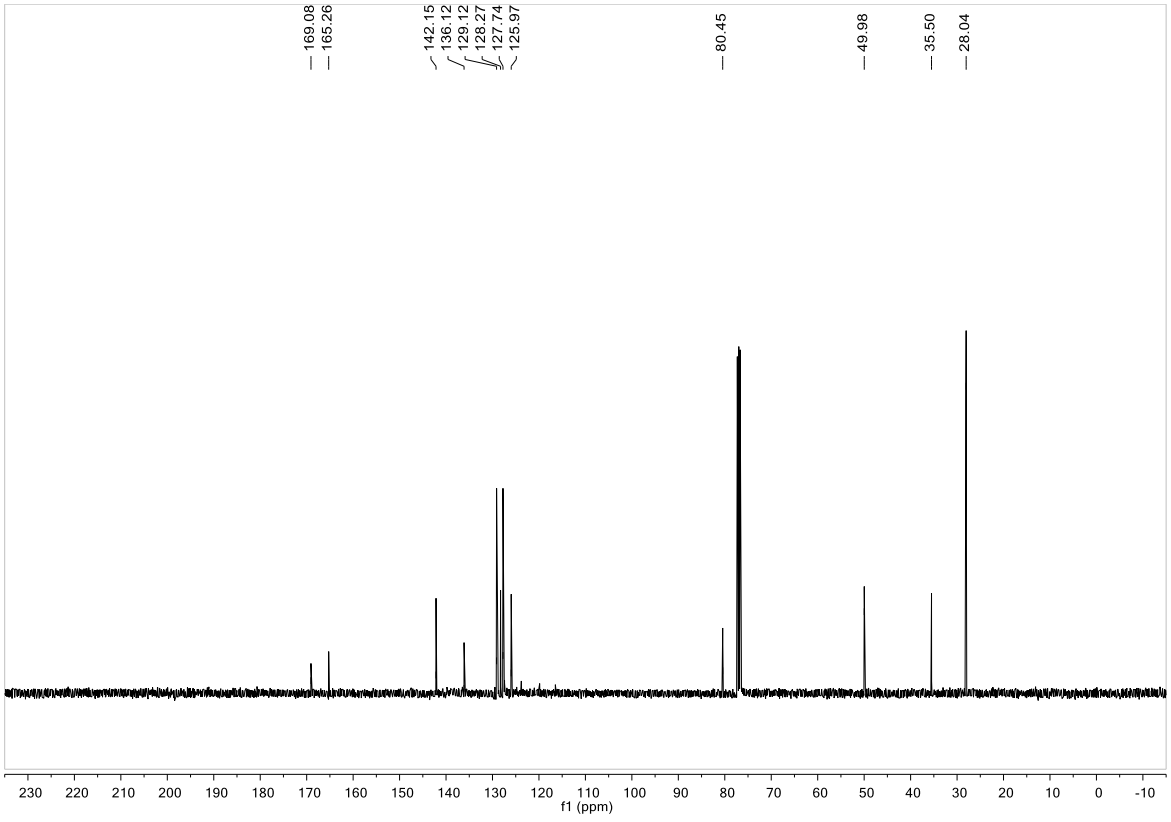


1-Isopropyl 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (21)

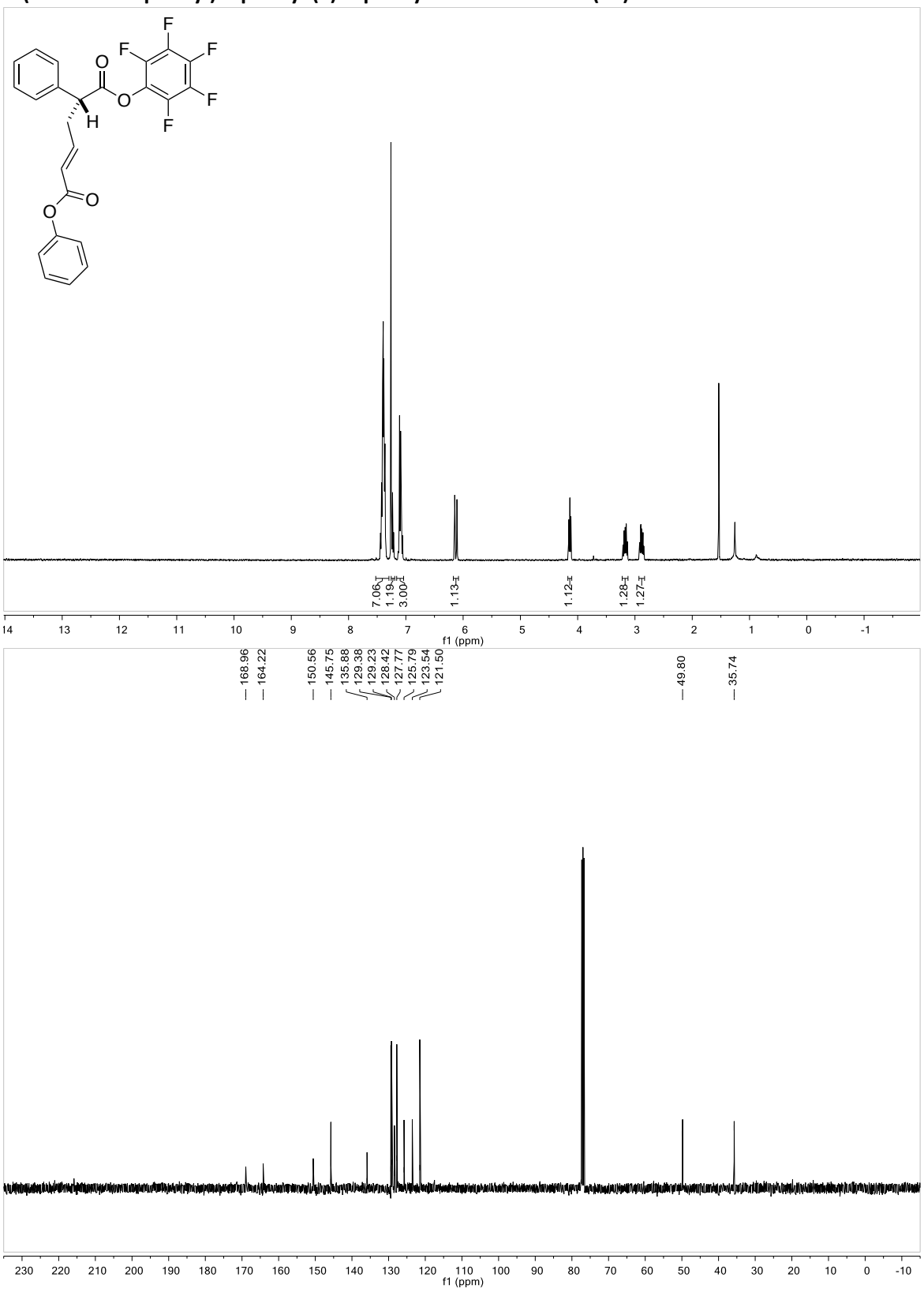


1-(tert-Butyl) 6-(pentafluorophenyl) (*E*)-5-phenylhex-2-enedioate (22)

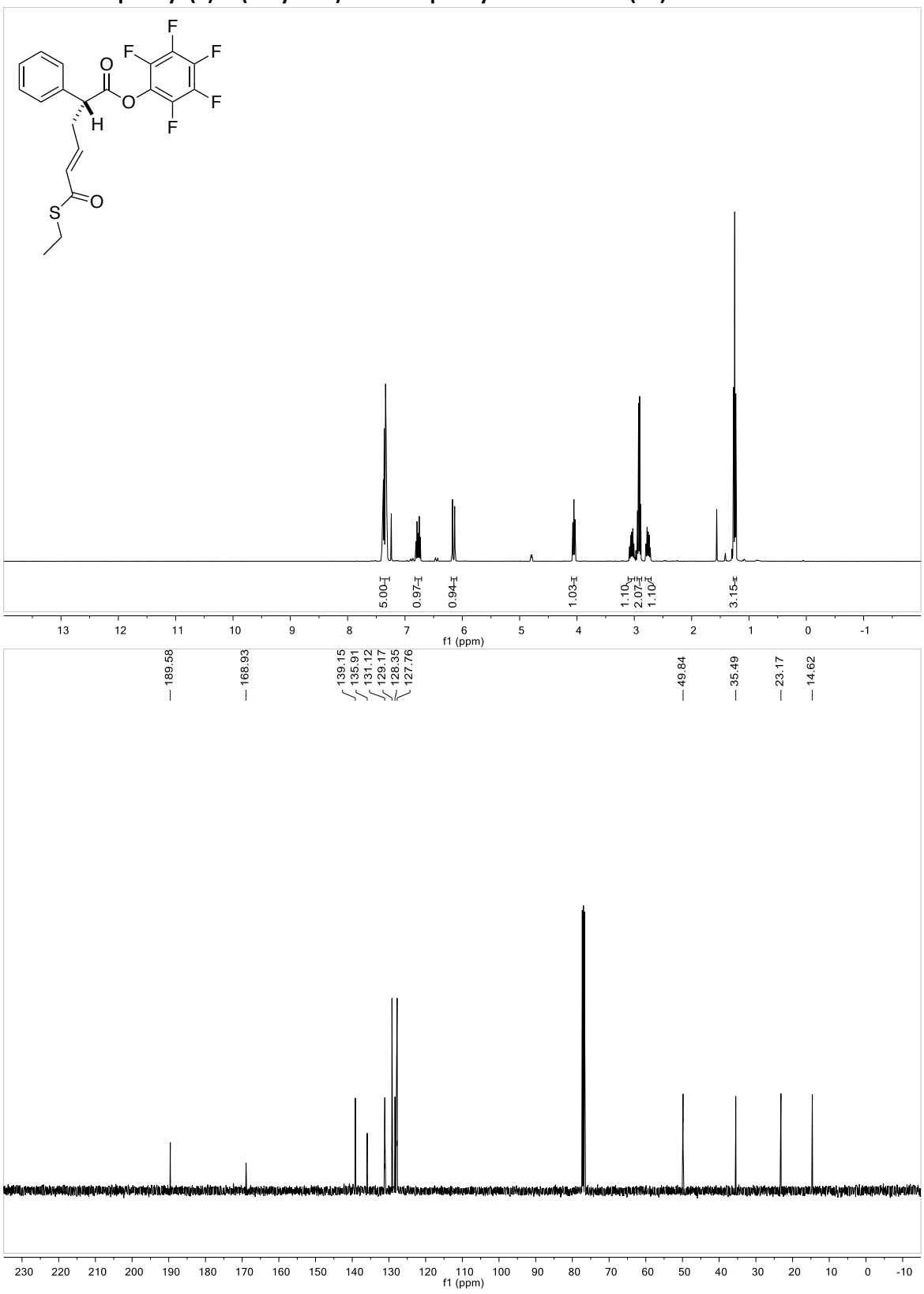




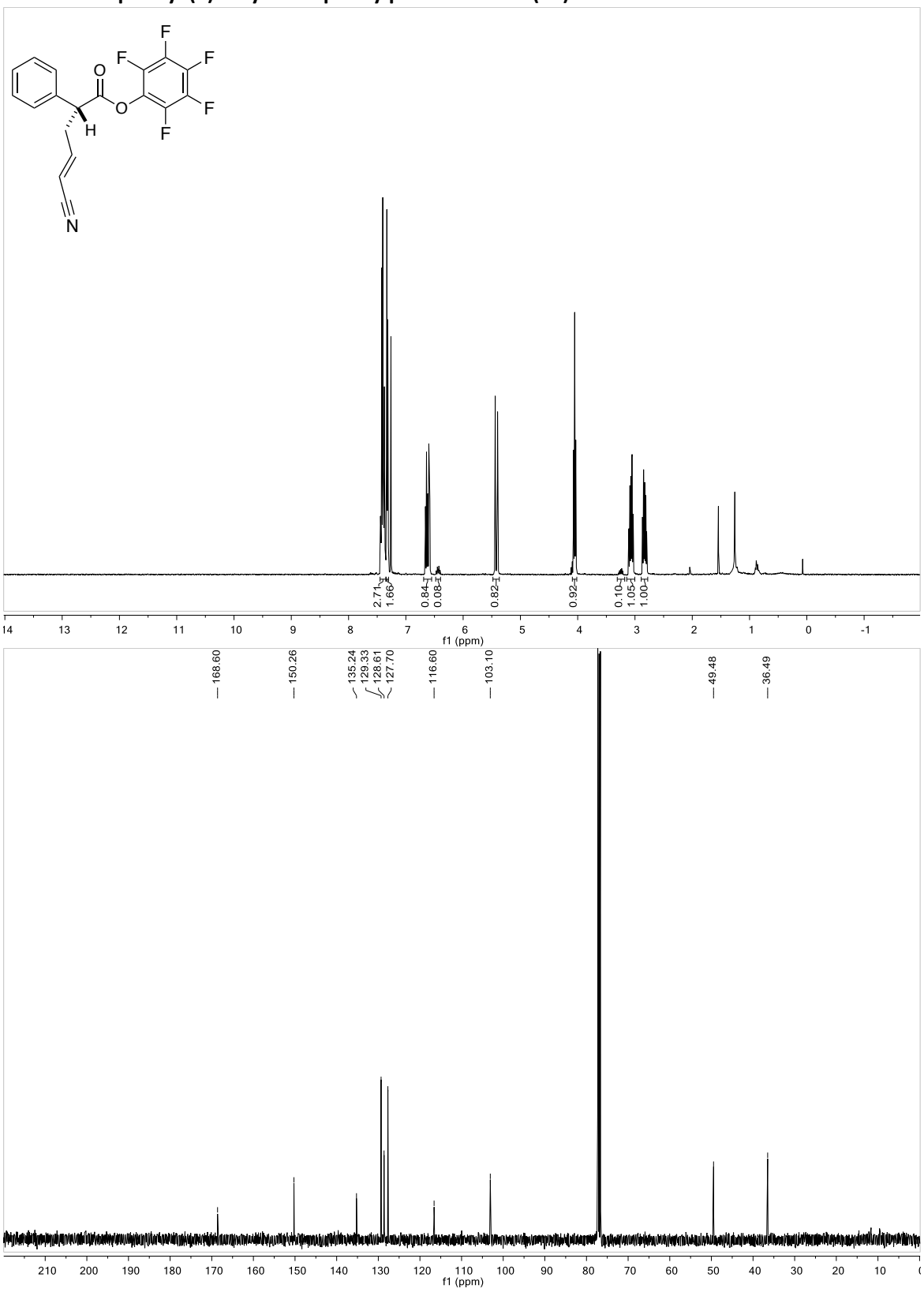
6-(Pentafluorophenyl) 1-phenyl (*E*)-5-phenylhex-2-enedioate (23)



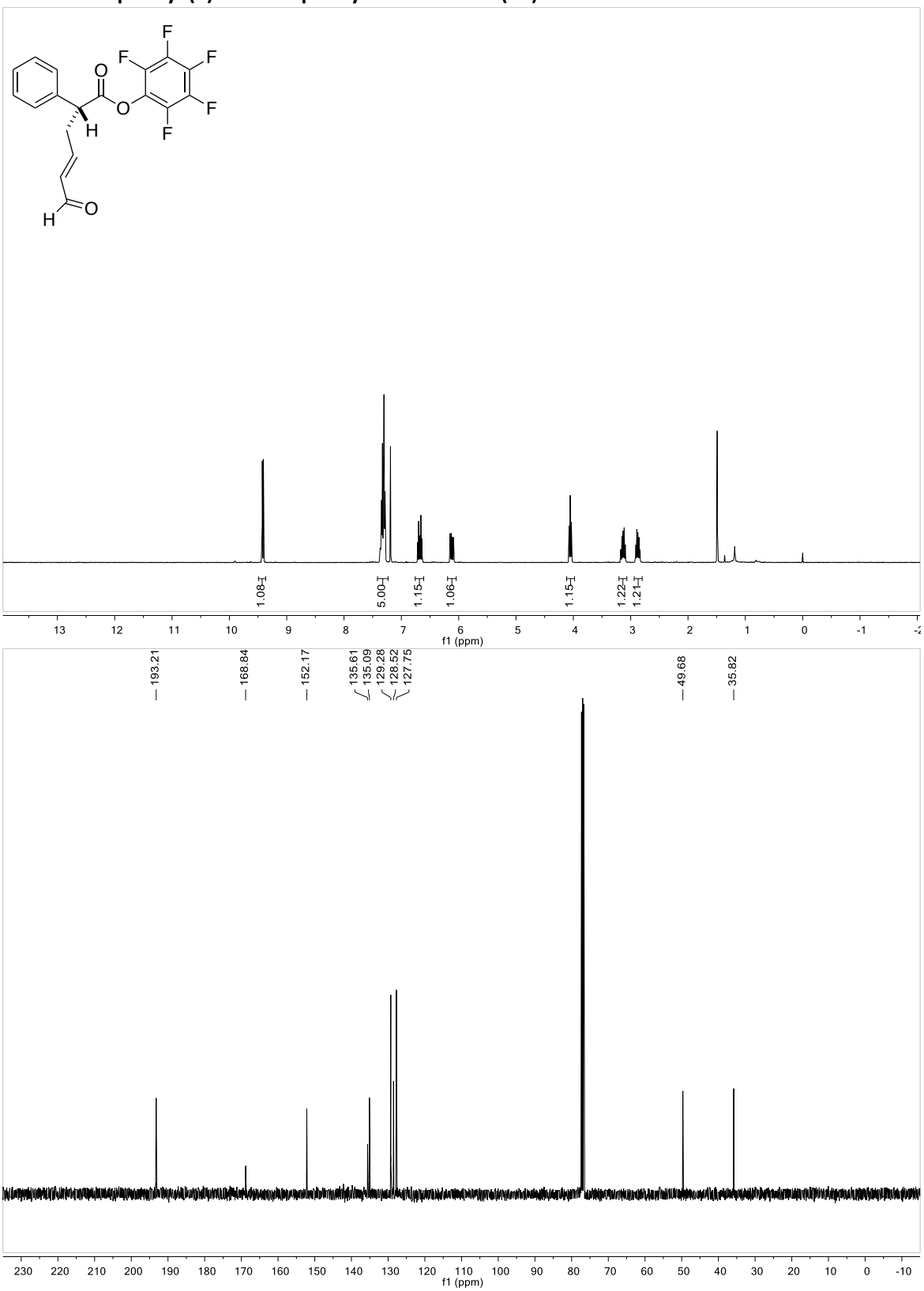
Pentafluorophenyl (*E*)-6-(ethylthio)-6-oxo-2-phenylhex-4-enoate (24)



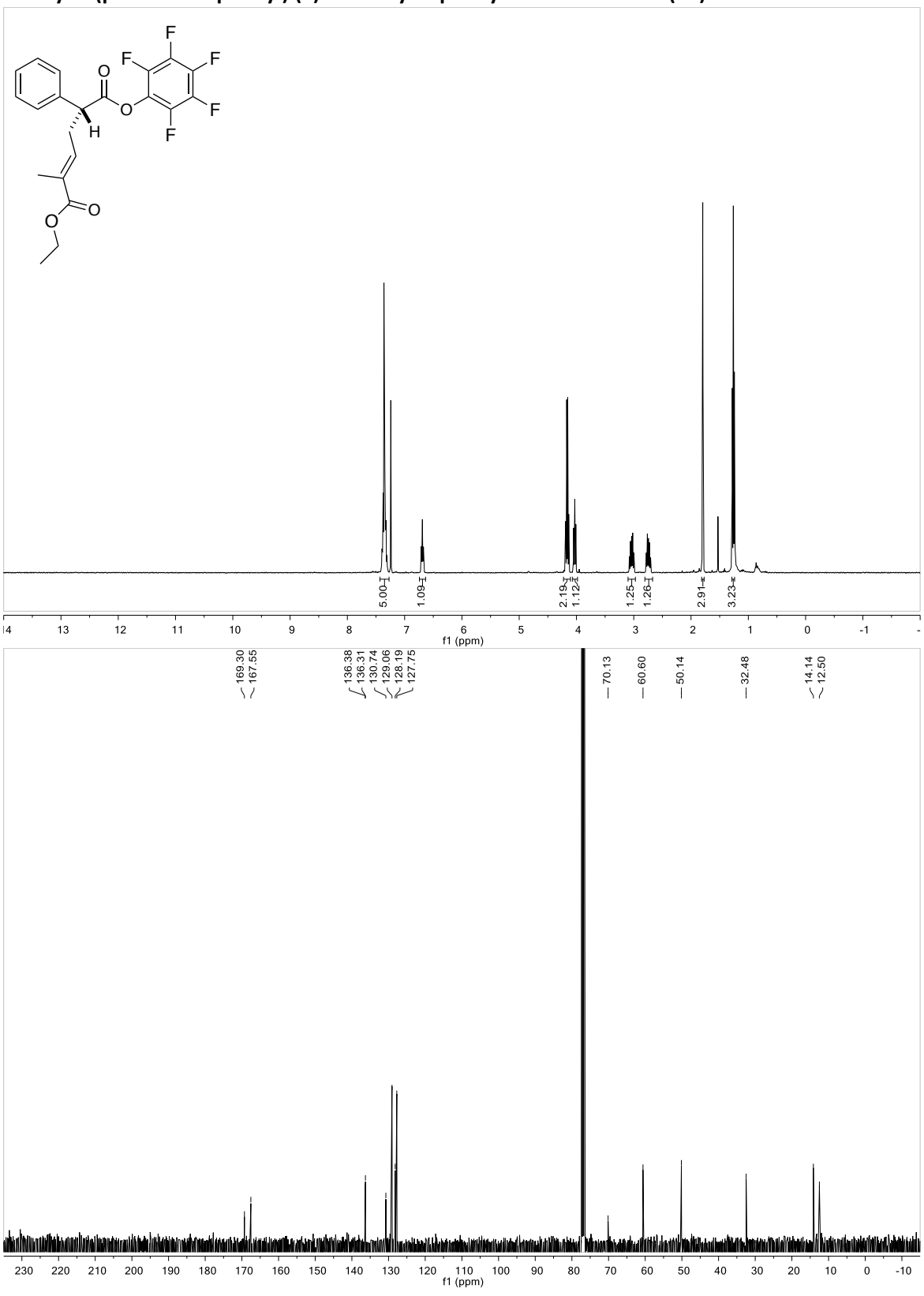
Pentafluorophenyl (*E*)-5-cyano-2-phenylpent-4-enoate (25)



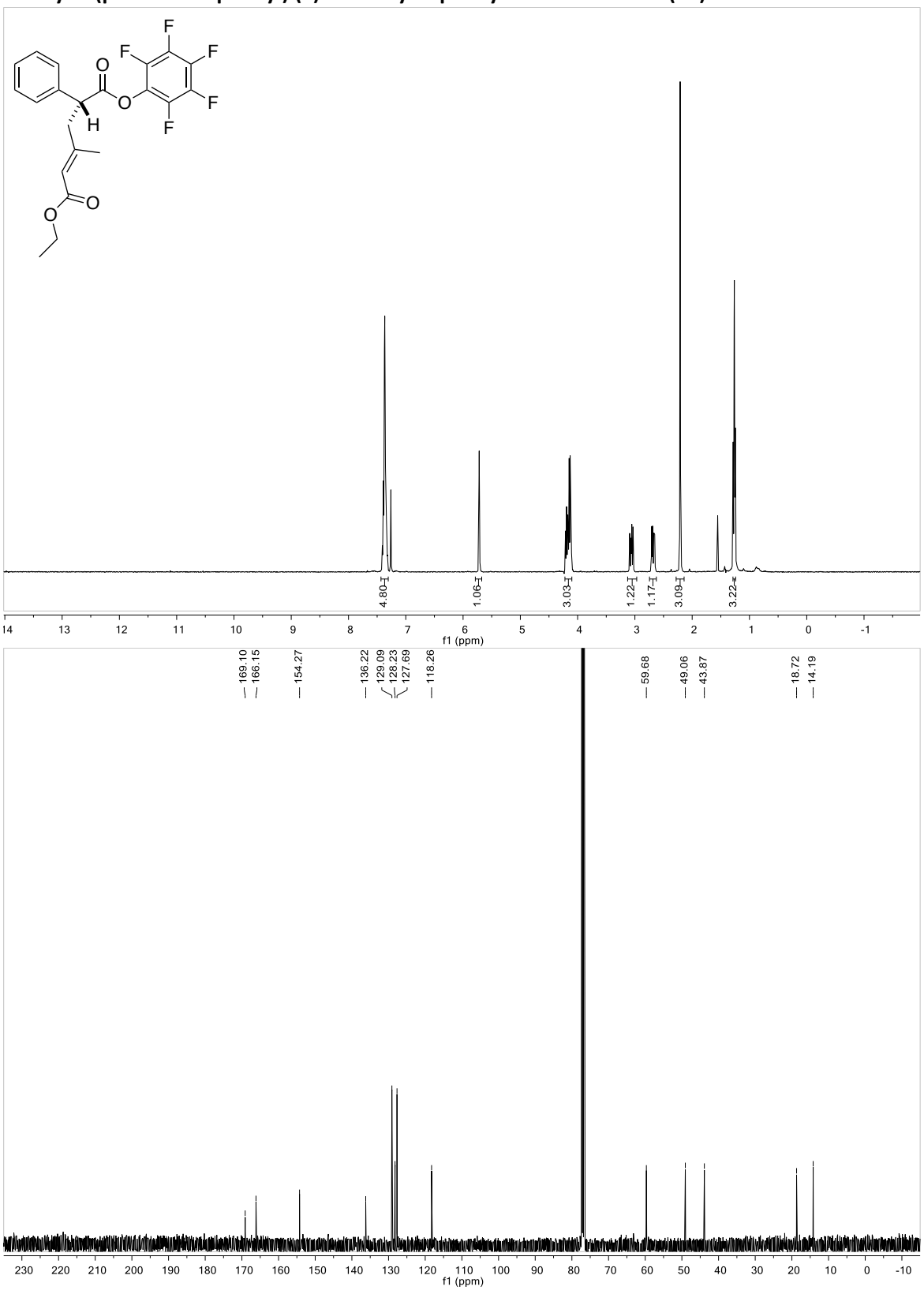
Pentafluorophenyl (*E*)-6-oxo-2-phenylhex-4-enoate (26)



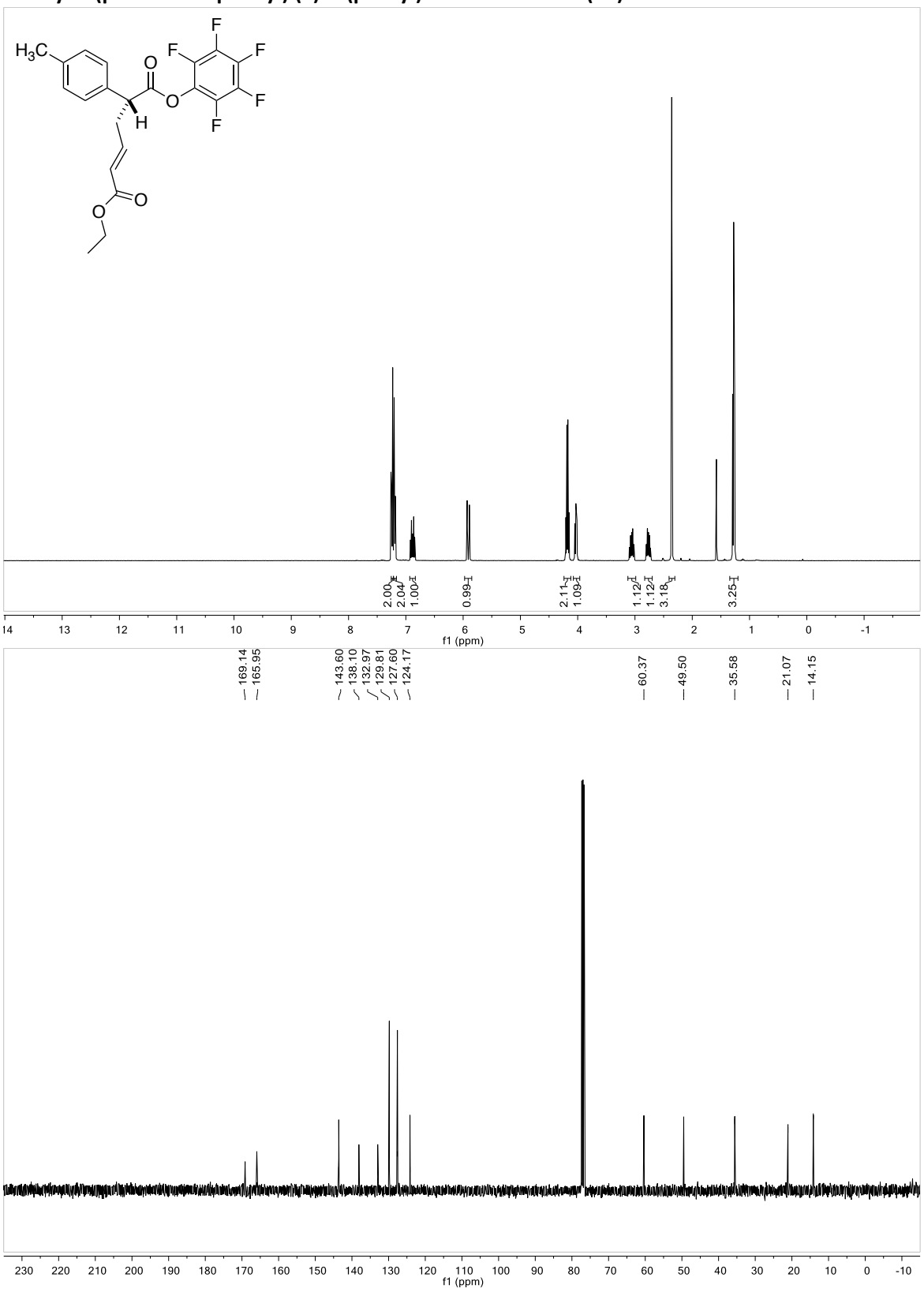
1-Ethyl 6-(pentafluorophenyl) (*E*)-2-methyl-5-phenylhex-2-enedioate (27)



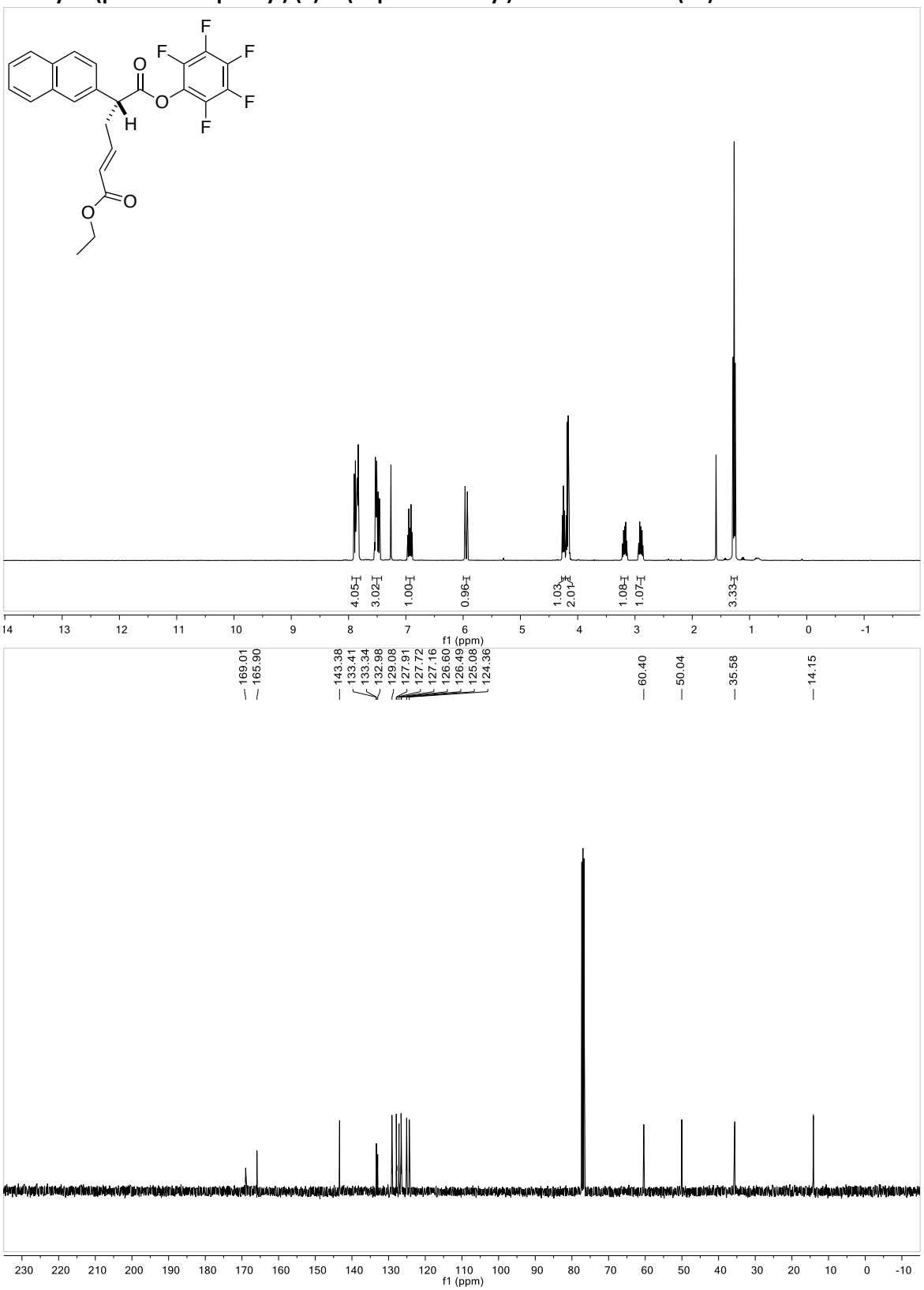
1-Ethyl 6-(pentafluorophenyl) (*E*)-3-methyl-5-phenylhex-2-enedioate (28)



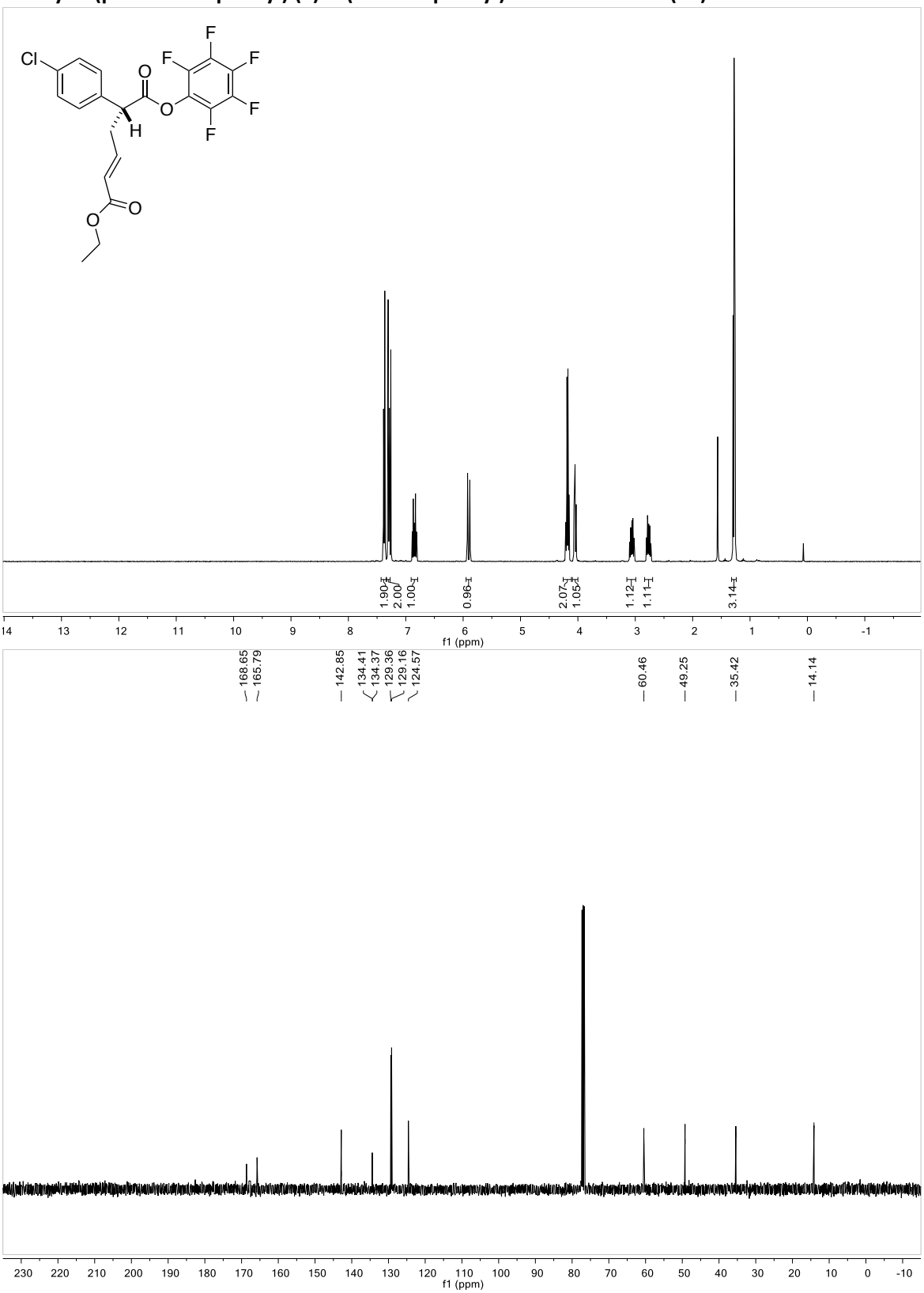
1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(p-tolyl)hex-2-enedioate (29)



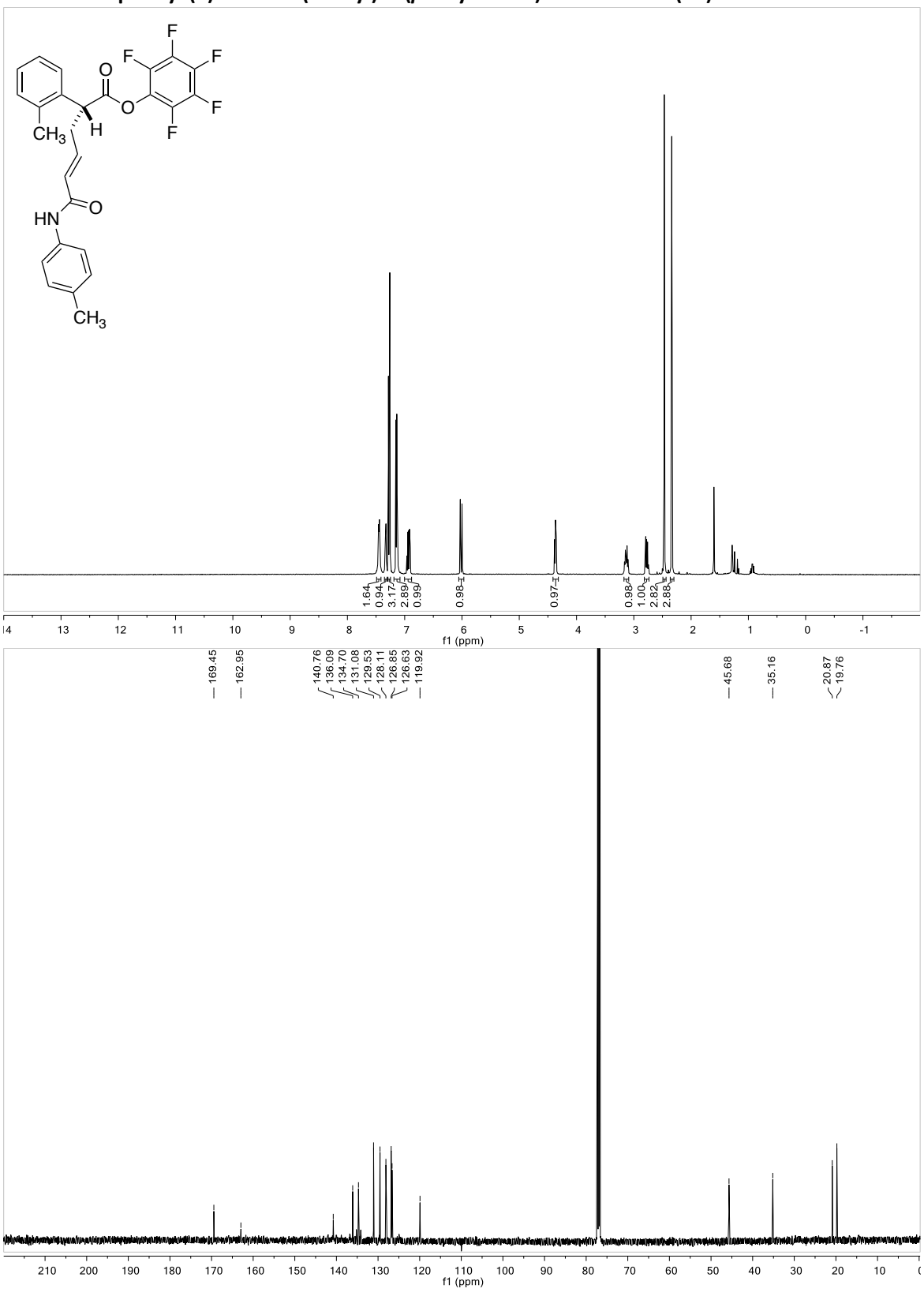
1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(naphthalen-2-yl)hex-2-enedioate (30)



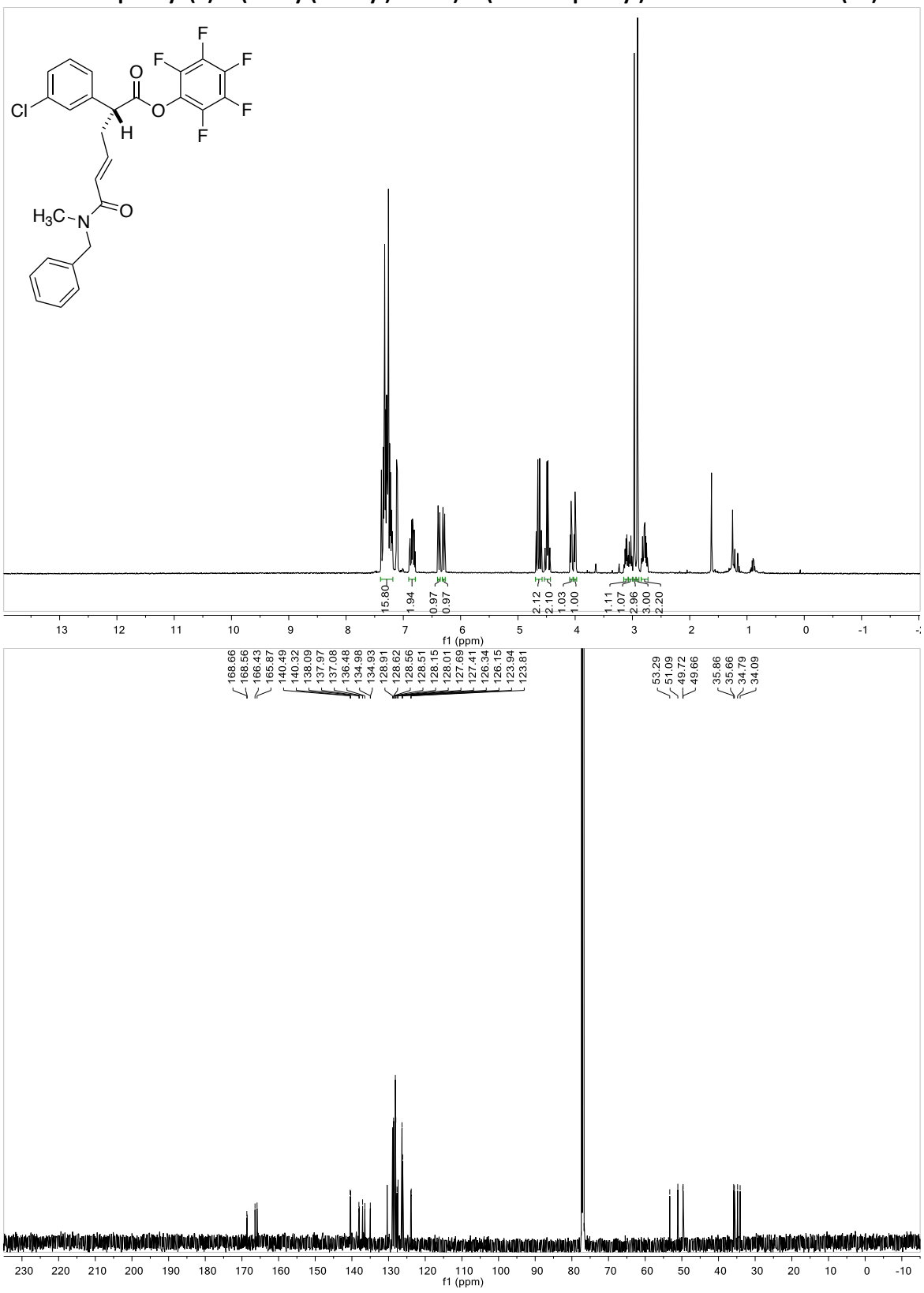
1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(4-chlorophenyl)hex-2-enedioate (31)



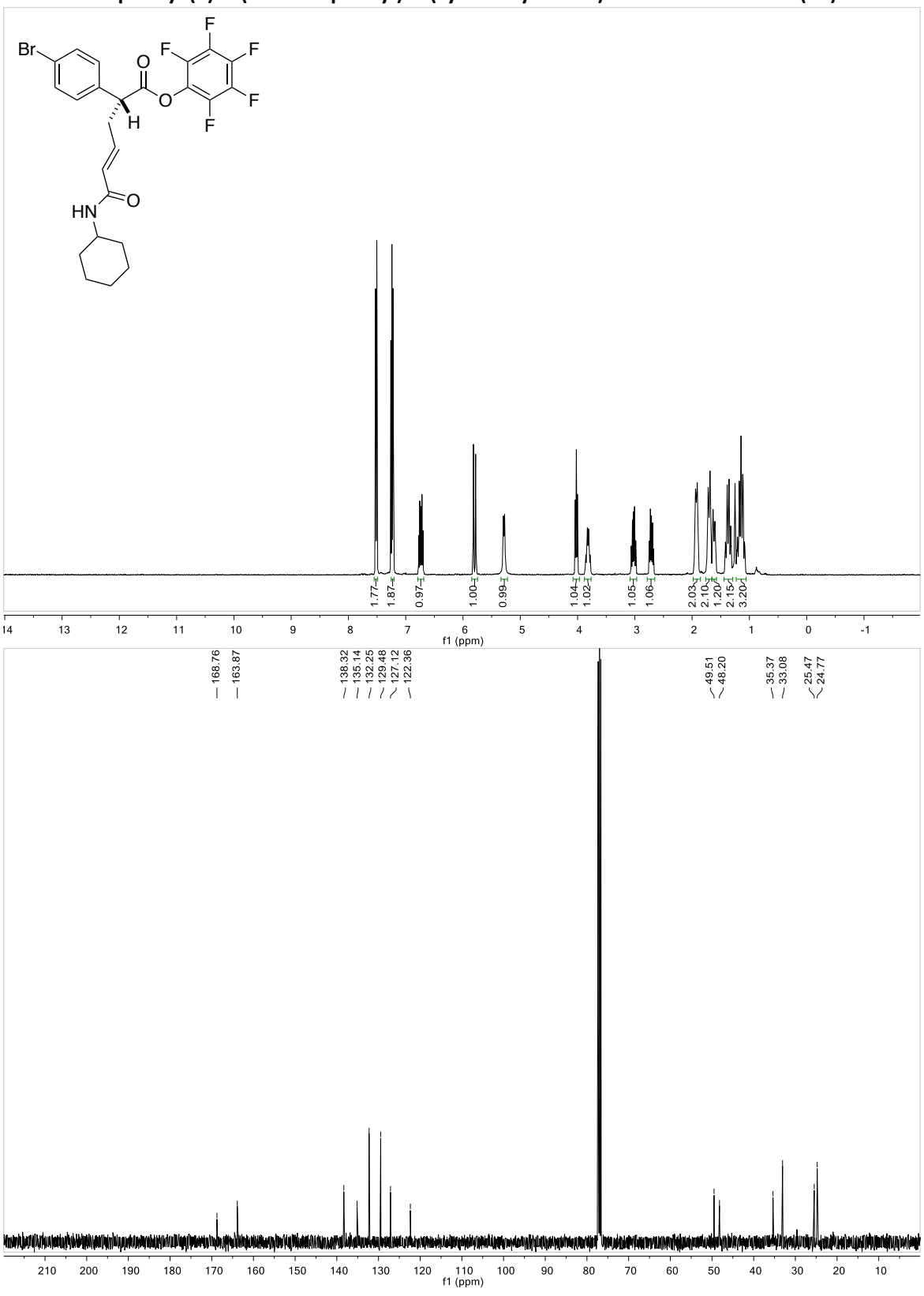
Pentafluorophenyl (*E*)-6-oxo-2-(*o*-tolyl)-6-(*p*-tolylamino)hex-4-enoate (32)



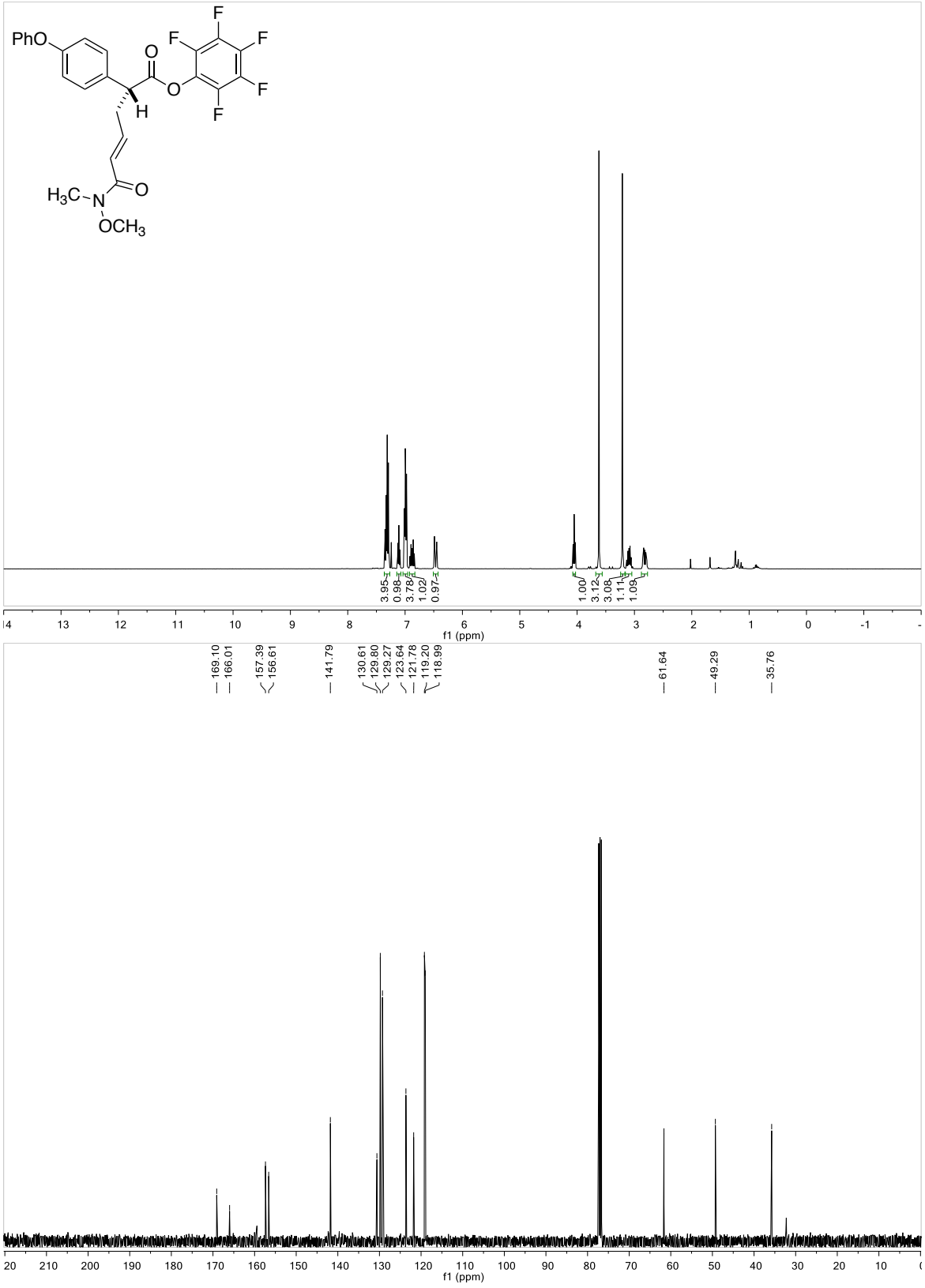
Pentafluorophenyl (*E*)-6-(benzyl(methyl)amino)-2-(3-chlorophenyl)-6-oxohex-4-enoate (33)



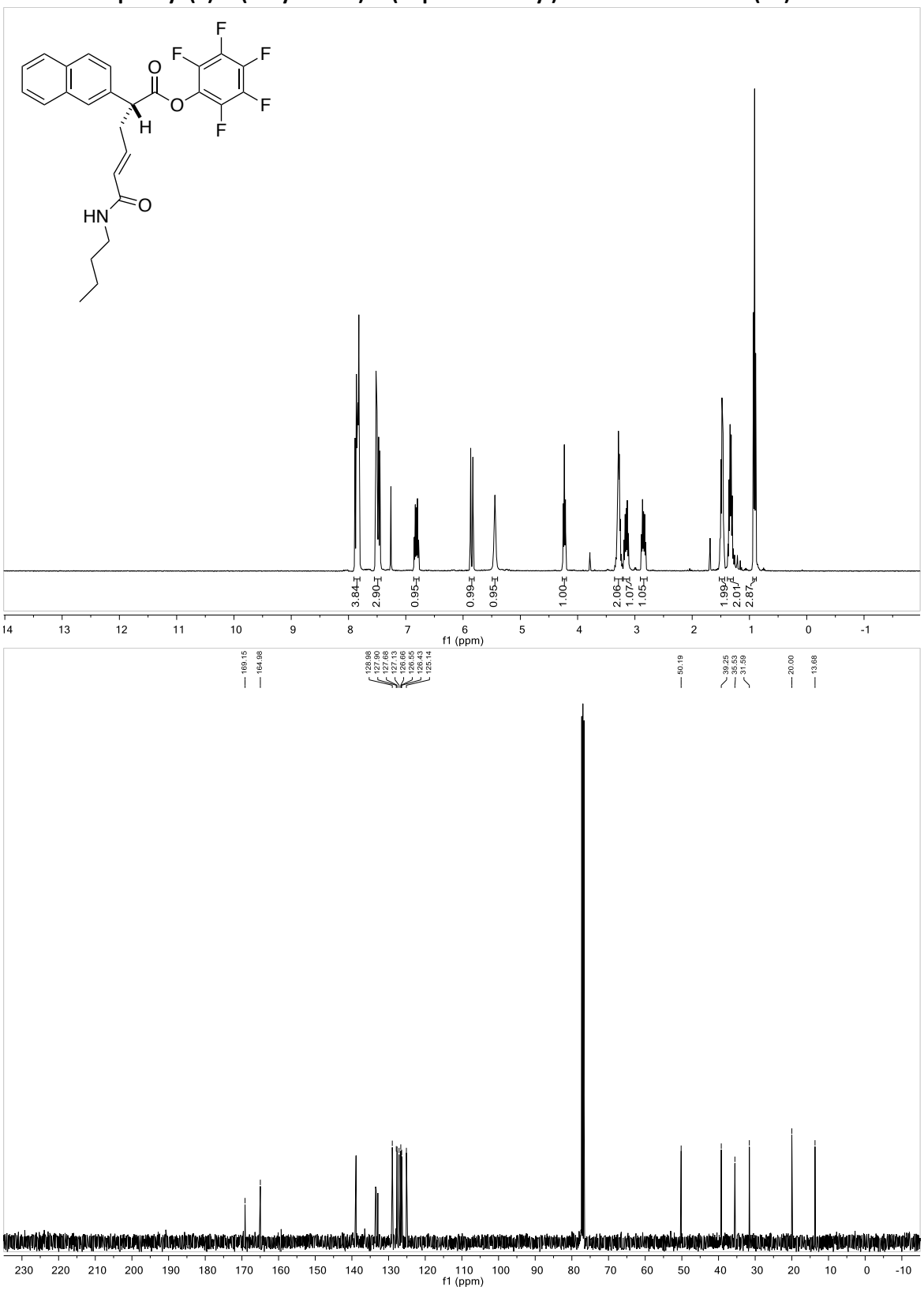
Pentafluorophenyl (*E*)-2-(4-bromophenyl)-6-(cyclohexylamino)-6-oxohex-4-enoate (34)



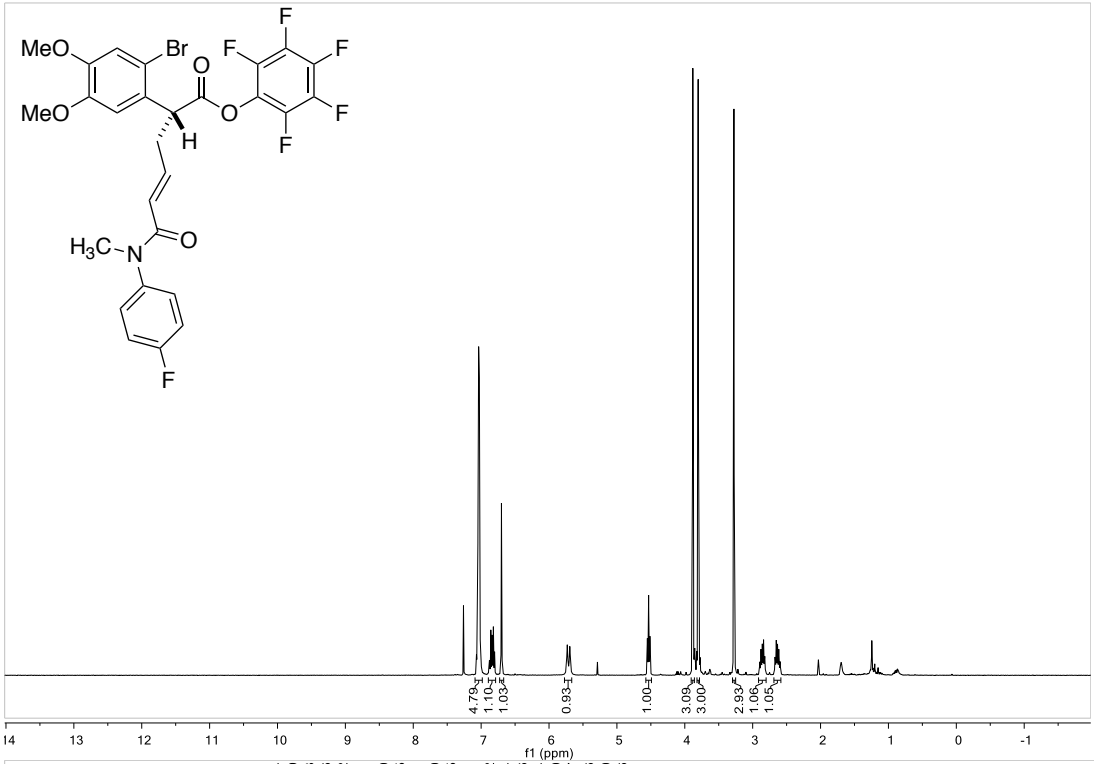
Pentafluorophenyl (*E*)-6-(methoxy(methyl)amino)-6-oxo-2-(4-phenoxyphenyl)hex-4-enoate (35)

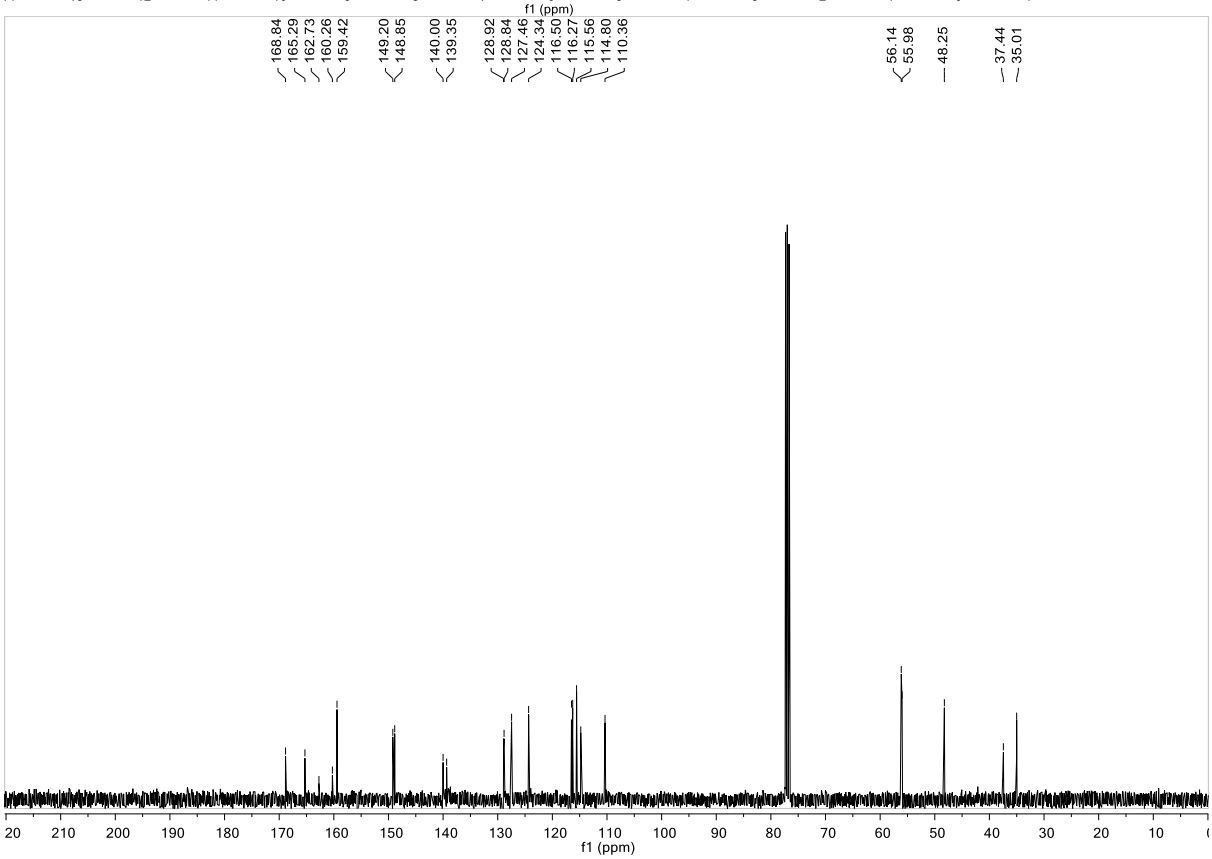


Pentafluorophenyl (*E*)-6-(butylamino)-2-(naphthalen-2-yl)-6-oxohex-4-enoate (36)

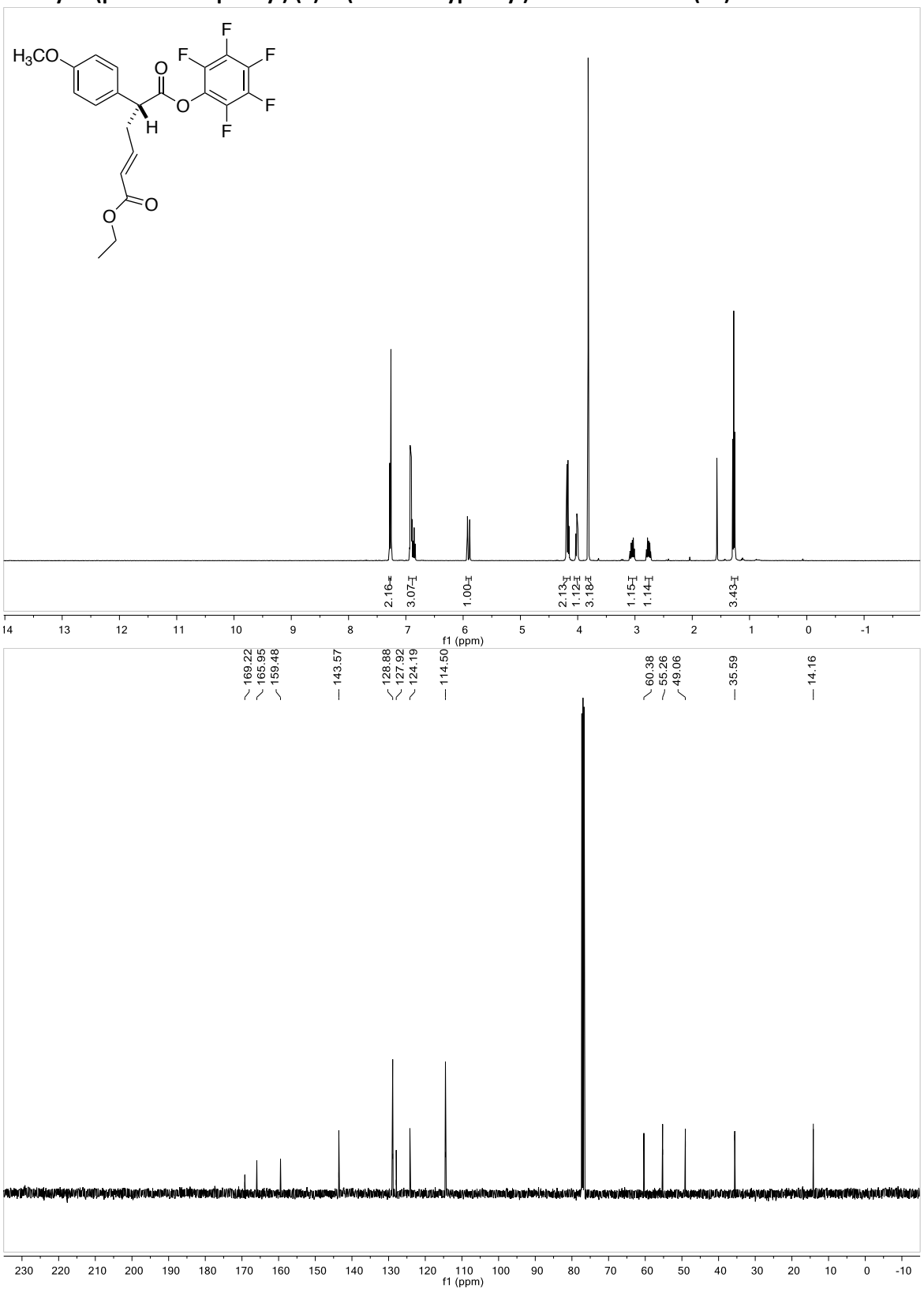


Pentafluorophenyl (*E*)-2-(2-bromo-4,5-dimethoxyphenyl)-6-((4-fluorophenyl)(methyl)amino)-6-oxohex-4-enoate (37)

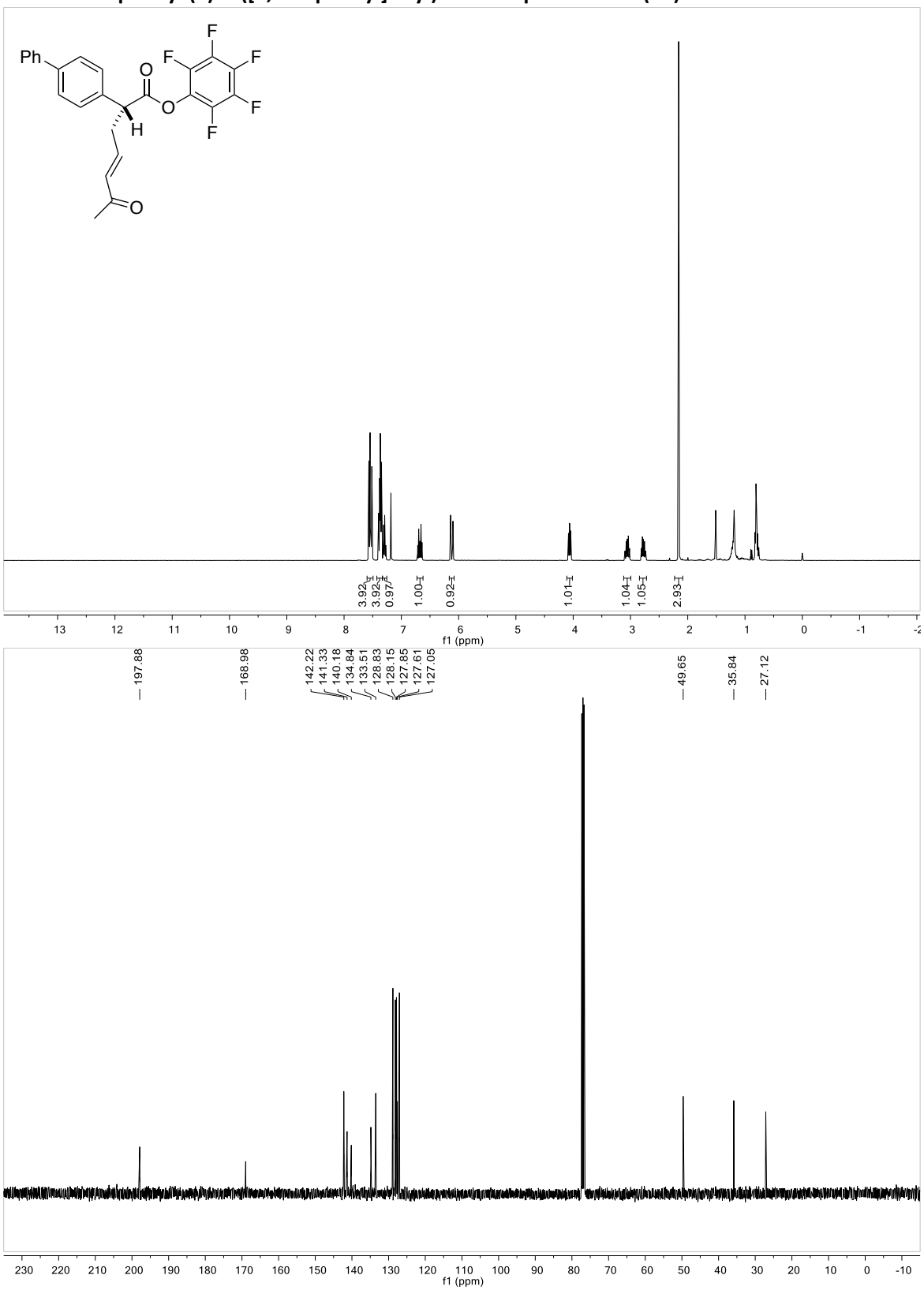




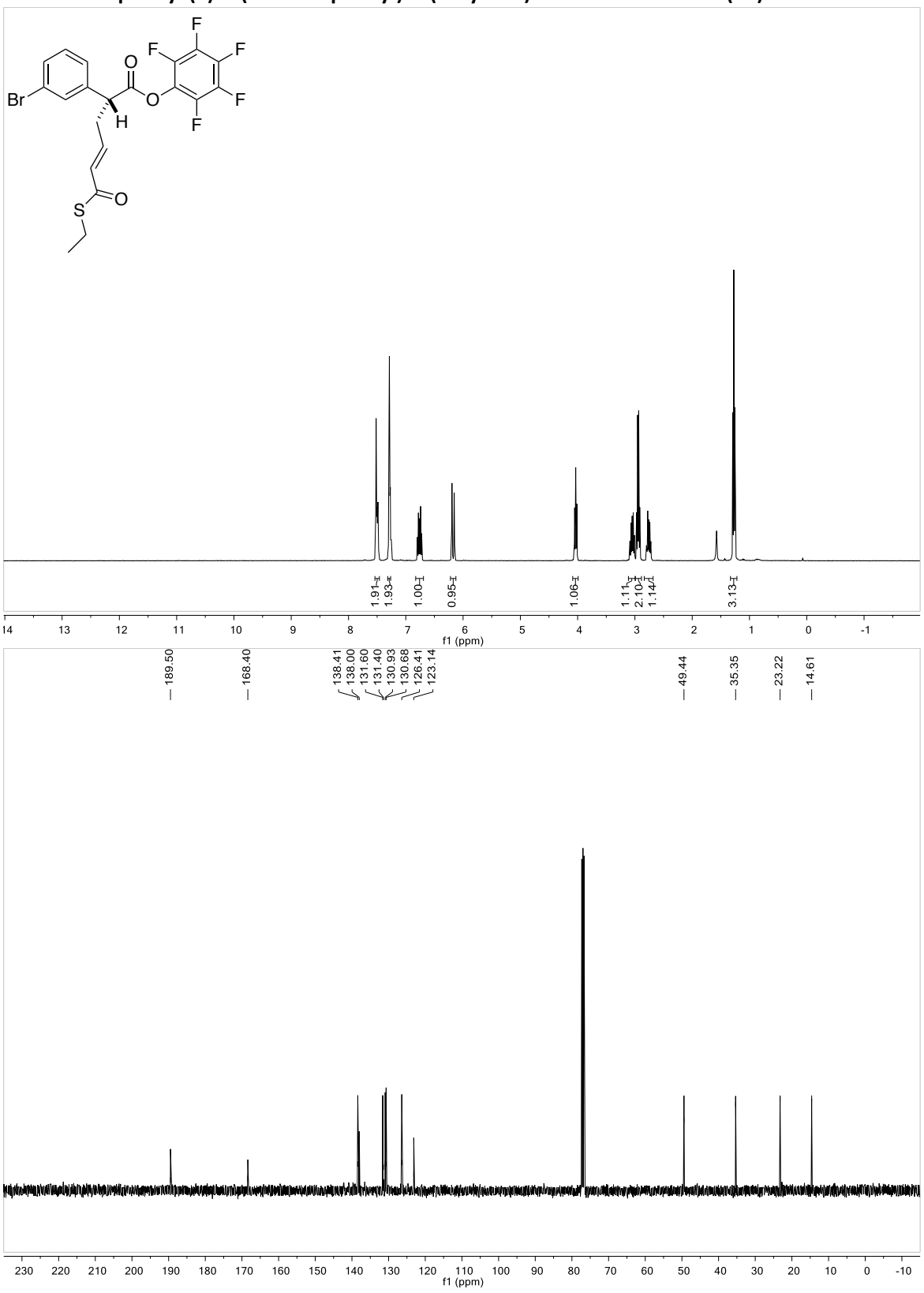
1-Ethyl 6-(pentafluorophenyl) (*E*)-5-(4-methoxyphenyl)hex-2-enedioate (38)



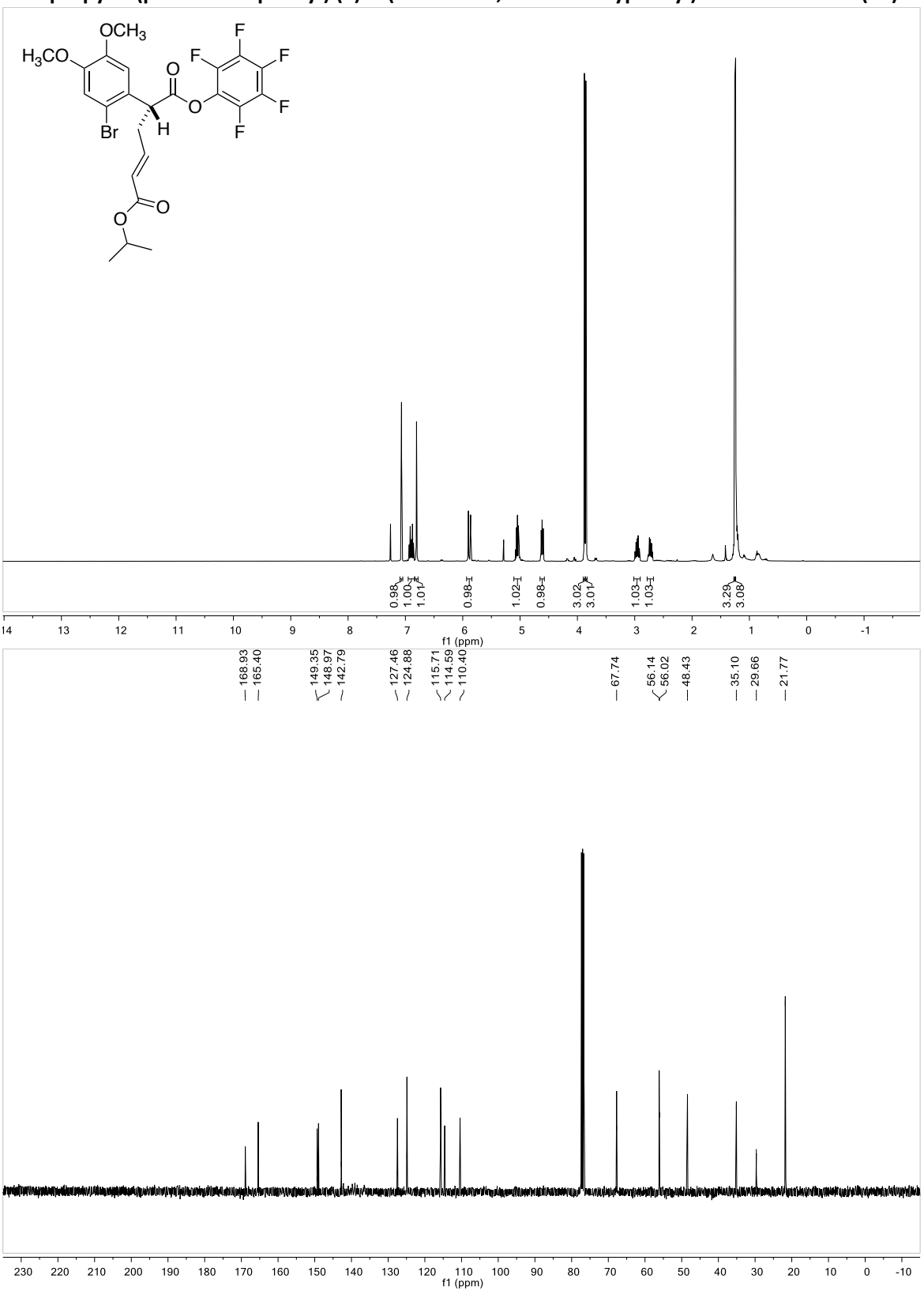
Pentafluorophenyl (*E*)-2-([1,1'-biphenyl]-4-yl)-6-oxohept-4-enoate (39)



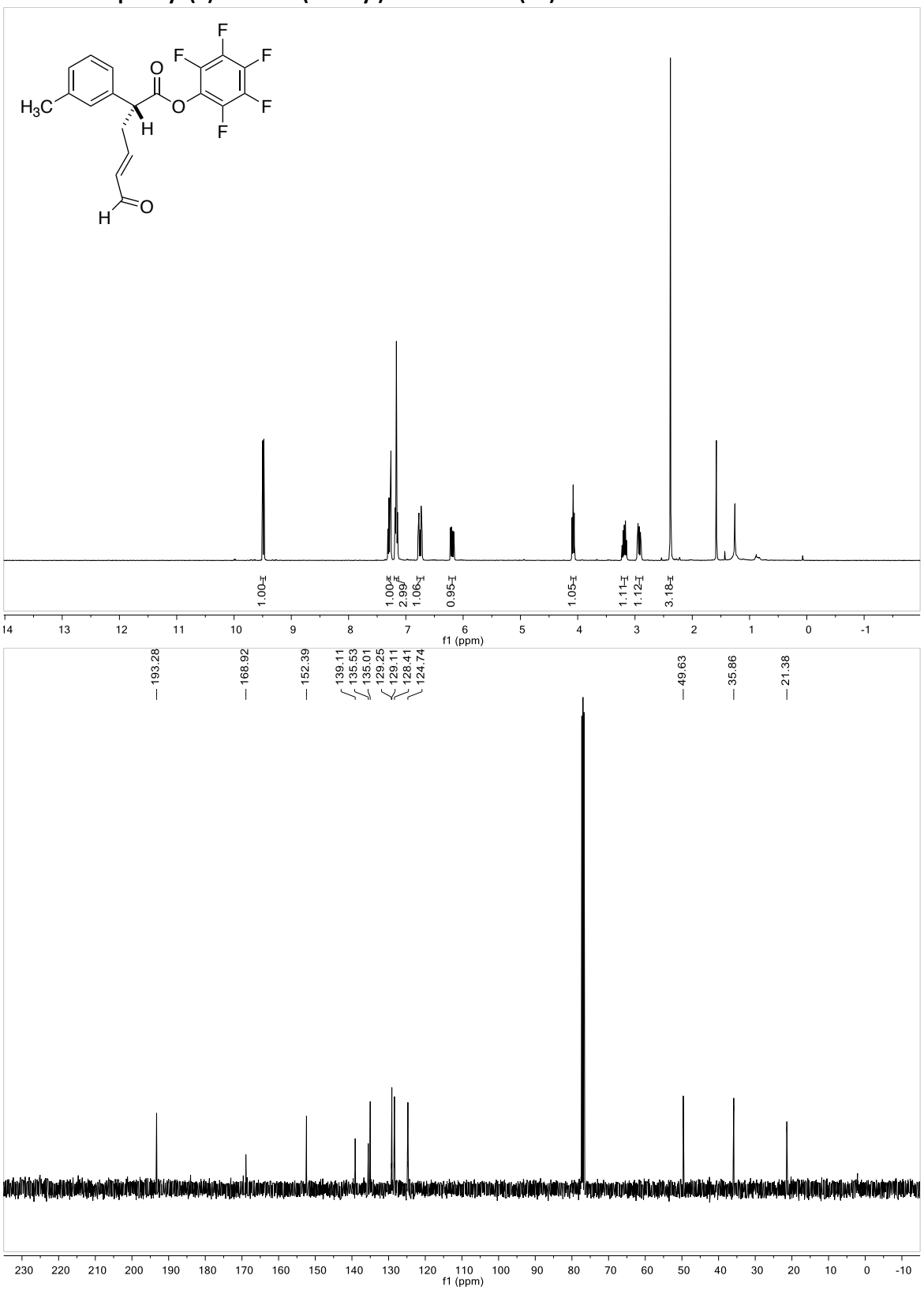
Pentafluorophenyl (*E*)-2-(3-bromophenyl)-6-(ethylthio)-6-oxohex-4-enoate (40)



1-Isopropyl 6-(pentafluorophenyl) (*E*)-5-(2-bromo-4,5-dimethoxyphenyl)hex-2-enedioate (41)



Pentafluorophenyl (*E*)-6-oxo-2-(m-tolyl)hex-4-enoate (42)



Pentafluorophenyl (*E*)-2-(4-isopropylphenyl)-6-oxodec-4-enoate (43)