δ-Unsaturated γ-Amino Acids: Enantiodivergent Synthesis and Cell Imaging Studies

Dnyaneshwar Kand,[a] Dinesh Pratapsinh Chauhan,[a] Tanmoy Saha,[a] Mayurika Lahiri,[b] and Pinaki Talukdar*[a]

[a] Department of Chemistry, Dmitri Mendeleev Block, Indian Institute of Science Education and Research Pune, India. Fax: +91 20 2589 9790; Tel: +91 20 2590 8001

E-mail: ptalukdar@iiserpune.ac.in

[b] Department of Biology, Indian Institute of Science Education and Research Pune, India. Fax: +91 20 2589 9790; Tel: +91 20 2590 8001

Supporting Information

I. General Methods.

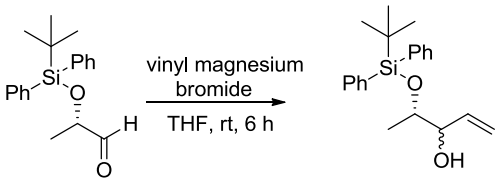
All the chemicals were purchased from commercial sources and used as received unless stated otherwise. Solvents: petroleum ether and ethyl acetate (EtOAc) were distilled prior to thin layer and column chromatography. THF and *m*-xylene were pre-dried over Na wire. Then each of the solvents was refluxed over Na (1% w/v) and benzophenone (0.2% w/v) under an inert atmosphere until the blue color of the benzophenone ketyl radical anion persists. Methylene chloride (DCM) was pre-dried over calcium hydride and then distilled. *N*, *N*-Dimethylformamide (DMF) was pre-dried over calcium hydride and then distilled under vacuum. Column chromatography was performed on silica gel (100–200 mesh). TLC was carried out with silica gel 60-F_{254} plates. All air and water sensitive reactions were performed under nitrogen atmosphere. Crystal structures were recorded on a single crystal X-Ray diffractometer. HPLC for determining diastereomeric excess was performed on a High Performance Liquid Chromatography (HPLC) instrument using a reverse phase column.

II. Physical Measurements

The ^{1}H and ^{13}C NMR spectra were recorded on 400 MHz (or 100 MHz for ^{13}C) spectrometers using either residual solvent signals as an internal reference or from internal tetramethylsilane on the δ scale ($CDCl_3$ δ_H 7.24 ppm, δ_C 77.0 ppm, CD_3OD δ_H 3.31 ppm, δ_C 49.0 ppm). The chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. The following abbreviations are used: m (multiplet), s (singlet), br s (broad singlet), d (doublet), t (triplet) dd (doublet of doublet). High-resolution mass spectra were obtained from ESI-TOF MS spectrometer. (FT-IR) spectra were obtained using FT-IR spectrophotometer as KBr disc and reported in cm^{-1}. All melting points were measured in open glass capillary and values are uncorrected. The fluorescence images were taken on a confocal fluorescence microscope.

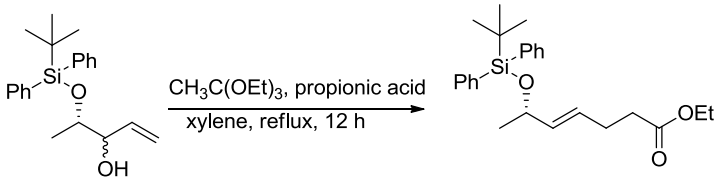
III. Experimental Procedures:

Synthesis of (4*S*)-4-((tert-butyldiphenylsilyl) oxy) pent-1-en-3-ol [$C_{21}H_{28}O_2Si$] (5):



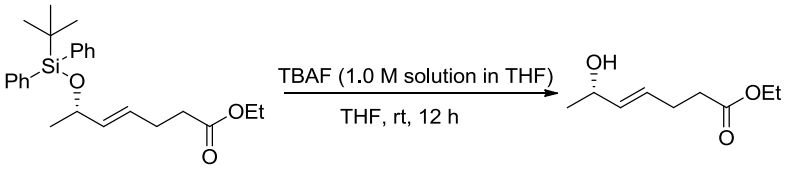
A 250 mL round bottom flask containing a solution of aldehyde **4** (8.0 g, 25.6 mmol) in THF (80 mL) was cooled to 0 °C in an ice bath. To this solution was added dropwise the vinyl magnesium bromide (31.0 mL, 1.0 M in THF, 30.7 mmol) at 0 °C. After stirring for 6 h at room temperature, the reaction mixture was evaporated under reduced pressure. The residue was partitioned between EtOAc and H_2O. The organic layer was dried over Na_2SO_4 and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (20:1) to afford the diastereomeric mixture of allylic alcohol **5** (7.4 g, 85%) as colorless oil. IR (Neat): ν_{max}/cm^{-1} 3744, 2933, 2891, 2859, 1466, 1426, 1383, 1103; ^{1}H NMR (400 MHz, $CDCl_3$): Major isomer: 7.64 – 7.70 (m, 4H), 7.36 – 7.45 (m, 6H), 5.70 – 5.83 (m, 1H), 5.12 – 5.22 (m, 1H), 4.05 – 4.06 (m, 1H), 3.86 – 3.93 (m, 1H), 3.77 (q, *J* = 6.4 Hz, 1H), 2.34 (d, *J* = 3.7 Hz, 1H), 1.07 (s, 9H), 0.98 (s, 3H); minor isomer: 7.64 – 7.70 (m, 4H), 7.36 – 7.45 (m, 6H), 5.70 – 5.83 (m, 1H), 5.28 – 5.34 (m, 1H), 5.12 – 5.22 (m, 2H), 2.57 (d, *J* = 4.6 Hz, 1H), 1.05 (s, 9H), 0.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$):137.53, 136.4, 136.0, 135.9, 134.0, 133.4, 130.0, 129.9, 127.9, 127.7, 127.6, 116.9, 116.6, 73.0, 72.5, 27.1, 19.6, 19.5, 19.4, 17.1; HRMS (ESI): Calc. for $C_{21}H_{28}NaO_2Si$ $[M+Na]^+$: 363.1756; Found: 363.1758.

Synthesis of (*S*, *E*)-ethyl 6-((tert-butyldiphenylsilyl) oxy) hept-4-enoate [$C_{25}H_{34}O_3Si$] (6-*E*):



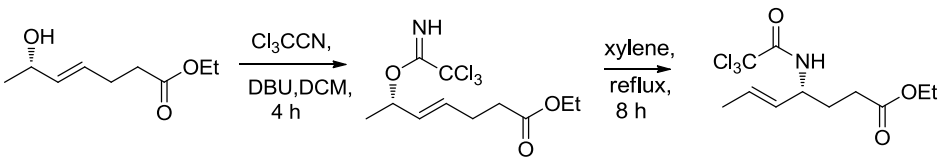
To a 50 mL round bottom flask containing a solution of allylic alcohol **5** (900 mg, 2.64 mmol) in *m*-xylene (15 mL) were added triethyl orthoacetate (4.9 mL, 26.4 mmol) and propionic acid (25 µL, 0.3 mmol) at room temperature. After stirring at 140 ^{o}C for 12 h, the reaction mixture was evaporated under reduced pressure. The crude product was chromatographed on silica gel with petroleum ether/ethyl acetate (96:4) to give ester **6-*E*** (1.3 g, 87%) as colorless oil. IR (Neat): ν_{max}/cm^{-1}: 3398, 1732, 1728; ^{1}H NMR (400 MHz, $CDCl_3$): 7.63 – 7.68 (m, 4H), 7.32 – 7.43 (m, 6H), 5.46 (ddd, *J* = 1.1, 6.0, 15.3 Hz, 1H), 5.32 – 5.38 (m, 1H), 4.23 (quintet, *J* = 6.2, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 2.16 – 2.31 (m, 4H), 2.13 (t, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H), 1.04 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.2, 136.0, 135.9, 135.5, 134.7, 134.4, 129.6, 129.5, 127.5, 127.4, 127.3, 70.2, 60.4, 34.0, 27.4, 27.1, 24.5, 19.3, 17.7; $[\alpha]^{24}_{D}$ = - 8.2 (*c* = 1.0, $CHCl_3$); HRMS (ESI): Calc. for $C_{25}H_{34}NaO_3Si$ $[M+Na]^+$: 433.2175; Found: 433.2129.

Synthesis of (*S*, *E*)-ethyl 6-hydroxyhept-4-enoate [$C_9H_{16}O_3$] (7-*E*):



To a 500 mL round bottom flask containing THF (200 mL) were added ester **6-*E*** (22.0 g, 53.6 mmol) and Tetrabutylammonium fluoride ($Bu_4N^+F^-$) (64.0 mL, 1.0 M in THF, 64 mmol). The solution was stirred at room temperature for 12 h and evaporated under reduced pressure. The thick oil was poured into H_2O. The product was extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (from 10:1 to 2:1) to afford allylic alcohol **7-*E*** (7.5 g, 81 %). IR (Neat): ν_{max}/cm^{-1} 3441, 2976, 1726, 1449, 1372, 1342, 1249, 1166, 1140, 1099, 1059; ^{1}H NMR (400 MHz, $CDCl_3$): 5.63 – 5.49 (m, 2H), 4.22 (quintet, *J* = 6.1 Hz, 1H), 4.12 – 4.06 (m, 2H), 2.37 – 2.30 (m, 4H), 1.88 (br s, 1H), 1.25 – 1.19 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.1, 135.5, 128.4, 68.6, 60.4, 33.9, 27.4, 23.4, 14.3; $[\alpha]^{24}_{D}$ = + 3.92 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_9H_{16}NNaO_3$ $[M+Na]^+$: 195.0917; Found: 195.0973.

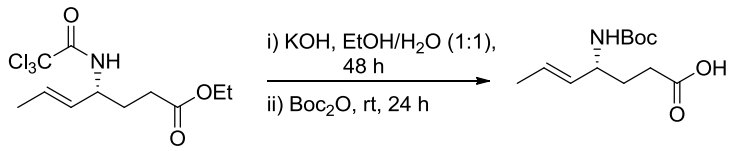
Synthesis of (*R*, *E*)-ethyl 4-(2, 2, 2-trichloroacetamido) hept-5-enoate [$C_{11}H_{16}Cl_3NO_3$] (8-*R*):



A 50 mL round bottom flask containing a solution of allylic alcohol **7-*E*** (500 mg, 2.9 mmol) in DCM (10 mL) was cooled to 0°C in an ice bath. To the solution were added DBU (260 µL,

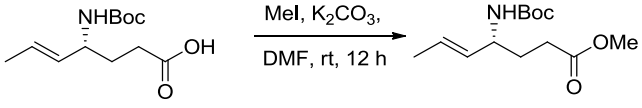
1.74 mmol) and Cl_3CN (349 µL, 3.48 mmol) over period of 15 min. After stirring at 0°C for 1 h, the reaction mixture was warmed to room temperature and stirred for 3 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with 5% Aqueous HCl solution (2 mL). The organic layer was evaporated under reduced pressure to give crude trichloroacetimidate intermediate, which was used for the next step without any purification. The crude imidate was dissolved in dry *m*-xylene (20 mL). The mixture was heated at reflux temperature for 8 h. After cooling to rt, the mixture was evaporated in vacuo. The residue was chromatographed on silica gel with petroleum ether/EtOAc (9:1) to give trichloroacetamide **8-*R*** (555 mg, 60% over 2 steps) as yellow oil. IR (Neat): ν_{max}/cm^{-1} 3333, 2980, 1697, 1514, 1446, 1375, 1338, 1173, 1099, 1068, 1028; ^1H NMR (400 MHz, $CDCl_3$): 6.96 (d, J = 3.1 Hz, 1H), 5.74 – 5.65 (m, 1H), 5.39 – 5.34 (m, 1H), 4.34 (quintet, J = 5.8 Hz, 1H), 4.12 (q, J = 7.1 Hz, 2H), 2.46 – 2.30 (m, 2H), 1.94 (q, J = 7.1 Hz, 2H), 1.74 – 1.68 (m, 3H), 1.27 – 1.21 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.5, 161.2, 128.6 (2C), 92.7, 60.8, 53.2, 30.6, 29.1, 17.8, 14.1; $[\alpha]^{24}_D$ = + 6.4 (c = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{11}H_{16}Cl_3NNaO_3$ $[M+Na]^+$: 338.0093; Found: 338.0120.

Synthesis of (*R*, *E*)-4-((tert-butoxycarbonyl) amino) hept-5-enoic acid [$C_{12}H_{21}NO_4$] (9-*R*):



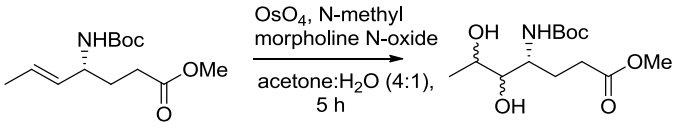
To a 100 mL round bottom flask containing a solution of trichloroacetamide **8-*R*** (2.0 g, 17.0 mmol) in ethanol: H_2O (1:1) (40 mL) was added KOH (2.0 g, 17.0 mmol) and heated at 100°C for 48 h. Then reaction mixture was allowed to cool at room temperature. Then BOC anhydride (2.0 g, 17.0 mmol) was added to the reaction mixture and stirred at room temperature for 24 h. After completion of the reaction, the reaction mixture was evaporated under reduced pressure to remove ethanol and acidified with 6 N HCl. The aqueous solution was extracted with ethyl acetate. The combined extracts were washed with brine, dried over Na_2SO_4, and concentrated to afford an acid **9-*R*** (1.3 g, 83%) as off white solid. M.p. = 88 – 89 °C; IR (Neat): ν_{max}/cm^{-1} 3362, 2983, 1711, 1682, 1515, 1445, 1411, 1392, 1369, 1307, 1289, 1238, 1168, 1049; ^1H NMR (400 MHz, $CDCl_3$): 5.57 – 5.63 (m, 1H), 5.28 – 5.34 (m, 1H), 4.50 (br s, 1H), 4.05 (br s, 1H), 2.37 (t, J = 7.4 Hz, 2H), 1.74 – 1.85 (m, 2H), 1.65 – 1.67 (m, 3H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 178.6, 155.6, 130.9, 126.9, 79.6, 51.9, 30.8, 30.4, 28.4 (3C), 17.7; $[\alpha]^{24}_D$ = + 10.4 (c = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{12}H_{21}NNaO_4$ $[M+Na]^+$: 266.1368; Found: 266.1363.

Synthesis of (*R*, *E*)-methyl 4-((tert-butoxycarbonyl) amino) hept-5-enoate [$C_{13}H_{23}NO_4$] (10-*R*):



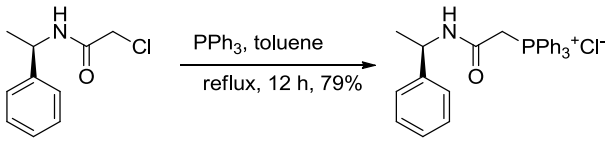
To a 25 mL round bottom flask containing a solution of the acid **9-*R*** (600 mg, 2.47 mmol) in DMF (5 mL) were added K_2CO_3 (340 mg, 2.47 mmol) and MeI (0.62 mL, 9.88 mmol). The resulting solution was stirred at room temperature for 12 h and poured into H_2O. The product was extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (from 10:1 to 2:1) to afford ester **10-*R*** (580 mg, 92 %) as yellow oil. IR (KBr): ν_{max}/cm^{-1} 3366, 2986, 1706, 1678, 1519, 1449, 1390, 1281, 1161; ^{1}H NMR (400 MHz, $CDCl_3$): 5.64 – 5.55 (m, 1H), 5.32 (dd, *J* = 7.5, 3.2 Hz, 1H), 4.49 (br s, 1H), 4.03 (br s, 1H), 3.68 – 3.65 (m, 3H), 2.34 (t, *J* = 7.5 Hz, 2H), 1.83 – 1.78 (m, 2H), 1.67 (d, *J* = 6.5 Hz, 3H), 1.44 – 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 174.0, 155.4, 131.1, 126.7, 79.3, 52.0, 51.7, 30.7, 30.5, 28.4 (3C), 17.7; $[\alpha]^{24}_D$ = + 3.0 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{13}H_{23}NNaO_4$ $[M+Na]^+$: 280.1525; Found: 280.1533.

Synthesis of (4*R*)-methyl 4-((tert-butoxycarbonyl) amin o)-5,6-dihydroxyheptanoate [$C_{13}H_{25}NO_6$] (11-*R*):



A 50 mL round bottom flask containing a solution of olefin **10-*R*** (100 mg, 0.31 mmol) in acetone: H_2O (4:1) (5 mL) was cooled to 0°C in an ice bath. To the solution were added NMO (50% aq. solution, 128 µL, 0.47 mmol), OsO_4 (1 mg) were added and the reaction mixture was stirred at room temperature for 5 h. Reaction mixture was evaporated to remove acetone and then diluted with H_2O (4.0 mL). The product was extracted with EtOAc (2 x 10 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (from 3:7) to afford diol **11-*R*** (112 mg, > 99 %). IR (Neat): ν_{max}/cm^{-1} 3362, 2978, 1714, 1682, 1520, 1454, 1418, 1392, 1366, 1247, 1164, 1050,1019; ^{1}H NMR (400 MHz, $CDCl_3$): 4.79 – 4.89 (m, 2H), 3.84 – 4.01 (m, 2H), 3.68 – 3.69 (m, 6H), 3.41 – 3.50 (m, 2H), 3.03 (t, *J* = 4.6 Hz, 1H), 2.35 – 2.49 (m, 5H), 2.19 – 2.78 (m, 1H), 1.85 – 1.92 (m, 2H), 1.65 – 1.73 (m, 7H), 1.42 – 1.43 (m, 19H), 1.22 – 1.25 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$):174.5, 157.3, 156.3, 85.1, 80.4, 79.6, 69.7, 66.2, 52.9, 51.9, 51.0, 31.0, 30.7, 28.4, 26.1, 19.2, 19.0; HRMS (ESI): Calc. for $C_{13}H_{25}NNaO_6$ $[M+Na]^+$: 314.1580; Found: 314.1581.

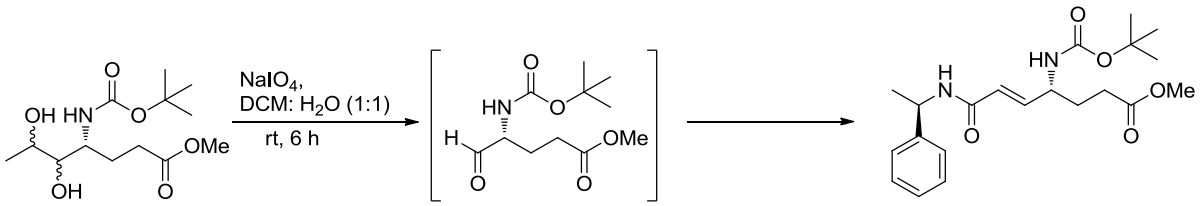
Synthesis of (*R*)-2-(chlorotriphenylphosphoranyl)-N-(1-phenylethyl) acetamide [$C_{28}H_{27}ClNOP$] (13a):



To a 50 mL round bottom flask containing a solution of (*R*)-2-chloro-*N*-(1-phenylethyl) acetamide (1.0 g, 5.08 mmol) in Toluene (20 mL) was added PPh_3 (1.6 g, 6.09 mmol). The

reaction mixture was refluxed for 12 h. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel ($CHCl_3$ /MeOH 9:1) to afford the corresponding Wittig salt **13a** (1.7 g, 79 %) as white solid M.p. = 213 – 214 ^oC; IR (Neat): ν_{max}/cm^{-1} 3183, 2993, 2819, 2755, 1660, 1563, 1538, 1485, 1438, 1327, 1104; ^1H NMR (400 MHz, CD_3OD): 7.63 – 7.84 (m, 15H), 7.15 – 7.31 (m, 5H), 4.85 (s, 3H), 4.80 (q, *J* = 6.8 Hz, 1H), 1.32 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD): 162.1, 142.9, 134.9, 133.8, 133.7, 130.0, 129.9, 128.3, 127.0, 125.9, 119.1, 118.2, 49.7, 47.0, 20.9; HRMS (ESI): Calc. for $C_{28}H_{27}NOPPh_3^+$ $[M- Cl]^+$: 424.1825; Found: 424.1831.

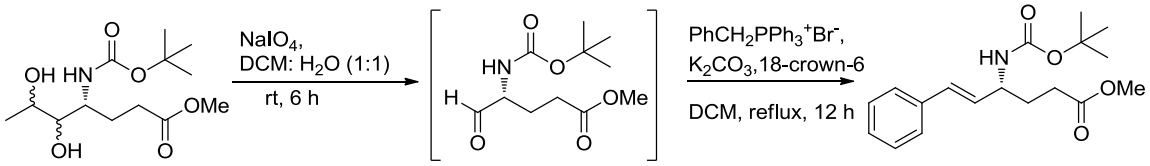
Synthesis of (*R*, *E*)-methyl 4-((tert-butoxycarbonyl)amino)-7-oxo-7-(((R)-1-phenylethyl)amino)hept-5-enoate [$C_{21}H_{30}N_2O_5$] (14a-*R*):



A 50 mL round bottom flask containing a solution of diol **11-*R*** (350 mg, 1.20 mmol) in DCM: H_2O (4:1) (30 mL) was cooled to 0°C in an ice bath. To the reaction mixture $NaIO_4$ (390 mg, 1.80 mmol) was added and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (8 mL) was added wittig salt **13a** (610 mg, 1.44 mmol) and the reaction mixture was refluxed for 6 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14a-*R*** (380 mg, 82 %) as white solid. M.p. = 160 – 161 ^oC; IR (Neat): ν_{max}/cm^{-1} 3344, 2982, 1734, 1679, 1633, 1523, 1448, 1368, 1302, 1255, 1166, 1047, 1016; ^1H NMR (400 MHz, $CDCl_3$): 7.33 (s, 5H), 6.68 (dd, *J* = 15.0, 7.0, Hz, 1H), 5.89 (dd, *J* =15.0, 1.1 Hz, 1H), 5.80 (br s, 1H), 5.19 (quintet, *J* = 7.2 Hz, 1H), 4.64 (br s, 1H), 4.27 (br s, 1H), 3.66 (s, 3H), 2.38 (t, *J* = 7.4 Hz, 2H), 1.81 – 1.95 (m, 2H), 1.53 (d, *J* = 6.9 Hz, 3H),1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.6, 164.3, 155.3, 143.3, 143.0, 128.8, 127.5, 126.4, 124.1, 79.9, 51.9, 51.2, 48.9, 30.5, 29.6, 28.5 (3C), 21.7; HRMS (ESI): Calc. for $C_{21}H_{30}N_2NaO_5$ $[M+Na]^+$: 413.2052; Found: 413.2056; HPLC: CHIRALPAK IC column (2-Propanol:*n*-Hexane = 10:90, flow rate 1.0 mL/min, λ = 250 nm). Retention time (min): 26.81(minor) and 29.05 (major), *de* = 94%. (Fig. S5).

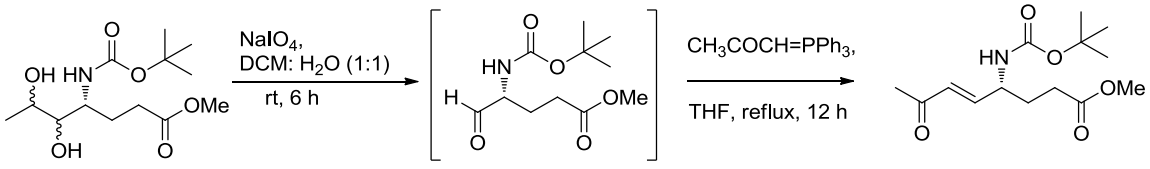
Synthesis of (*R*)-methyl 4-((tert-butoxycarbonyl) amino)-6-phenylhex-5-enoate [$C_{18}H_{25}NO_4$] (14b-*R*):



A 25 mL round bottom flask containing a solution of diol **11-*R*** (200 mg, 0.69 mmol) in DCM: H_2O (8 mL) was cooled to 0°C in an ice bath. To the reaction mixture $NaIO_4$ (220 mg, 1.03 mmol) was added and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (10 mL) were added phosphonium salt of $[PhCH_2PPh_3]^+Br^-$ **13b** (300 mg, 0.69 mmol), potassium carbonate (100 mg, 0.76 mmol) and 18-crown-6 (33 mg, 0.12 mmol) and the reaction mixture was refluxed for 12 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14b-*R*** (170 mg, 80 %) as white solid. M.p. = 86 – 87 ^oC; IR (Neat): ν_{max}/cm^{-1} 3334, 2973, 1679, 1522, 1420, 1351, 1149; ^1H NMR (400 MHz, $CDCl_3$): 7.21 – 7.35 (m, 5H), 6.52 (d, *J* = 15.8 Hz, 1H), 6.07 (dd, *J* = 15.9, 6.2 Hz, 1H), 4.61 (br s, 1H), 4.29 (br s, 1H), 3.65 (s, 3H), 2.42 (t, *J* = 14.9 Hz, 2H), 1.91 – 1.98 (m, 2H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.9, 155.4, 136.6, 130.7, 129.6, 128.8, 127.8, 126.5, 79.6, 51.8, 30.8, 30.5, 28.5 (3C); $[\alpha]^{24}_D$ = + 16.2 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{21}H_{16}NNaO$ $[M+Na]^+$: 342.1681; Found: 342.1681.

Synthesis of (*R*, *E*)-methyl 4-((tert-butoxycarbonyl) amino)-7-oxooct-5-enoate [$C_{14}H_{23}NO_5$] (18a*R*):

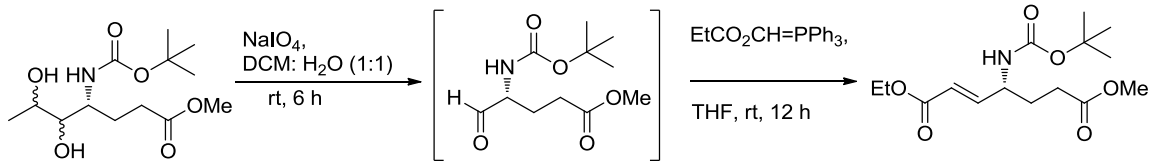


A 25 mL round bottom flask containing a solution of diol **11-*R*** (150 mg, 0.51 mmol) in DCM: H_2O (6 mL) was cooled to 0°C in an ice bath. To the reaction mixture $NaIO_4$ (170 mg, 0.76 mmol) was added and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in THF (8 mL) was added methylcarbonylmethylenephosphorane ($CH_3COCHPPh_3$) **13c** (160 mg, 0.51 mmol) and the reaction mixture was refluxed for 12 h in nitrogen atmosphere. The resulting solution

was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 8:2) to afford the corresponding unsaturated compound **14c-*R*** (130 mg, 83 %) as pink colored oil. IR (Neat): ν_{max}/cm^{-1} 3744, 2977, 1680, 1515, 1444, 1363, 1247, 1161, 1051, 1022; ^{1}H NMR (400 MHz, $CDCl_3$): 6.66 (d, *J* = 15.7 Hz, 1H), 6.17 (d, *J* = 15.7 Hz, 1H), 4.66 (br s, 1H), 4.33 (br s, 1H), 3.67 (s, 3H), 2.42 – 2.39 (m, 2H), 2.25 (s, 3H), 1.97 (br s, 1H), 1.82 (br s, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 198.3, 173.5, 155.2, 146.5, 130.0, 80.1, 52.0, 51.2, 30.5, 29.4, 28.4 (3C), 27.5; $[\alpha]^{24}_D$ = + 12.32 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{21}H_{16}NNaO$ $[M+Na]^+$: 308.1474; Found: 308.1475.

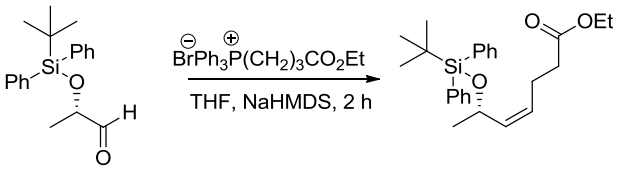
Synthesis of (*R*, *E*)-1-ethyl 7-methyl 4-((tert-butoxycarbonyl) amino) hept-2-enedioate [$C_{15}H_{25}NO_6$] (14d-*R*):



A 25 mL round bottom flask containing a solution of diol **11-*R*** (200 mg, 0.69 mmol) in DCM: H_2O (8 mL) was cooled to 0°C in an ice bath. To the reaction mixture $NaIO_4$ (220 mg, 1.03 mmol) was added and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

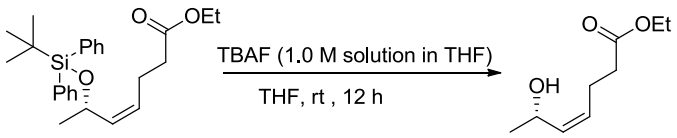
To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (8 mL) was added ethoxycarbonylmethylenephosphorane ($EtO_2CCHPPh_3$) **13d** (280 mg, 0.82 mmol) and the reaction mixture was refluxed for 12 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14d-*R*** (140 mg, 87%). IR (Neat): ν_{max}/cm^{-1} 2978, 1706, 1658, 1515, 1446, 1367, 1247, 1160, 1092, 1037; ^{1}H NMR (400 MHz, $CDCl_3$): 6.82 (dd, *J* = 12.5, 4.2 Hz, 1H), 5.94 (dd, *J* = 12.5, 1.1 Hz, 1H), 4.60 (br s, 1H), 4.33 (br s, 1H), 4.18 (q, *J* = 5.7 Hz, 2H), 3.68 (s, 3H), 2.40 (t, *J* = 5.9 Hz, 2H), 1.98 – 1.95 (m, 1H), 1.84 – 1.79 (m, 1H), 1.44 (s, 9H), 1.28 (t, *J* = 5.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.5, 166.2, 155.2, 147.5, 121.4, 80.0, 60.6, 51.9, 51.1, 30.5, 29.5, 28.4 (3C), 14.3; $[\alpha]^{24}_D$ = + 7.8 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{15}H_{25}NNaO_6$ $[M+Na]^+$: 338.1580; Found: 338.1578.

Synthesis of (*S*, *Z*)-ethyl 6-((tert-butyldiphenylsilyl) oxy) hept-4-enoate [$C_{25}H_{34}O_3Si$] (6-*Z*):[S1]



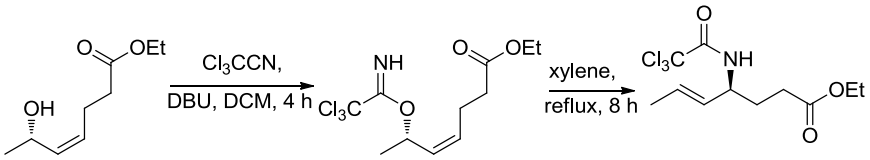
A 250 mL round bottom flask containing the solution of phosphonium salt of $[EtCO_2(CH_2)_3PPh_3]^+Br^-$ (24.2 g, 52.8 mmol) in THF (80 mL) was cooled to 0°C in an ice bath. To the solution was added $NaN(TMS)_2$ (52.8 mL, 1.0 M in THF, 52.8 mmol) dropwise at 0°C. After 0.5 h stirring at ice-bath temperature, the mixture was cooled to -78°C and a solution of aldehyde **6** (11.0 g, 35.2 mmol) in THF (25 mL) was added slowly. After the addition, the mixture was stirred at -78 °C for 2 h and then allowed to warm to ambient temperature, stirred for 2 h and poured into saturated NH_4Cl. The product was extracted with EtOAc (2 x 500 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was subjected to chromatography on silica gel with petroleum ether / EtOAc (20:1) to afford olefin **6-Z** (23.4 g, 81%) as colorless oil. Obtained data was matched with the literature data.

Synthesis of (*S*, *Z*)-ethyl 6-hydroxyhept-4-enoate [$C_9H_{16}O_3$] (7-*Z*):[S2]



To a 500 mL round bottom flask containing THF (200 mL) were added olefin **6-*Z*** (22.0 g, 53.6 mmol) and Tetrabutylammonium fluoride ($Bu_4N^+F^-$) (64 mL, 1.0 M in THF, 64 mmol). The solution was stirred at room temperature for 12 h and evaporated under reduced pressure. The thick oil was poured into H_2O. The product was extracted with EtOAc (2 x 500 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (from 10:1 to 2:1) to afford allyl alcohol **7-*Z*** (7.9 g, 86%) as colorless oil. Obtained data was matched with the literature data.

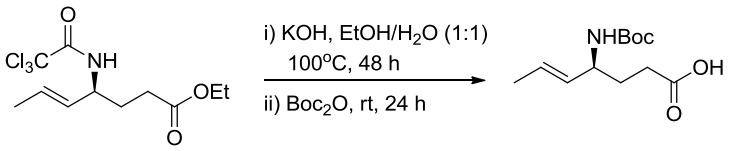
Synthesis of (*S*, *E*)-ethyl 4-(2, 2, 2-trichloroacetamido) hept-5-enoate [$C_{11}H_{16}Cl_3NO_3$] (8-*S*):



A 50 mL round bottom flask containing a solution of allyl alcohol **7-*Z*** (500 mg, 2.9 mmol) in DCM (10 mL) was cooled to 0°C in an ice bath. To the reaction mixture were added DBU (260 µL, 1.74 mmol) and Cl_3CN (349 µL, 3.48 mmol) over period of 15 min. After stirring at 0°C for 1 h, the reaction mixture was warmed to room temperature and stirred for 3 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL) and washed with 5% Aqueous HCl solution (2 mL). The organic layer was evaporated under reduced pressure to give crude trichloroacetimidate **2**, which was used for the next step without any purification. The crude imidate was dissolved in dry *m*-xylene (20 mL). The mixture was heated at reflux temperature for 8 h. After cooling to rt, the mixture was evaporated in vacuo. The residue was chromatographed on silica gel with petroleum ether/EtOAc (9:1) to give trichloroacetamide

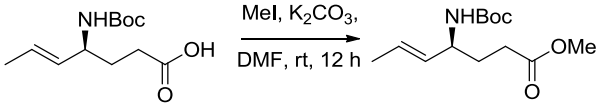
8-*S* (597 mg, 65% over 2 steps) as yellow oil. IR (Neat): ν_{max}/cm^{-1} 3333, 2980, 1697, 1514, 1447, 1375, 1338, 1247, 1173, 1099, 1066, 1028; ^1H NMR (400 MHz, $CDCl_3$): 6.95 (d, *J* = 2.2 Hz, 1H), 5.72 – 5.65 (m, 1H), 5.39 – 5.32 (m, 1H), 4.34 (quintet, *J* = 7.1 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 2.44 – 2.30 (m, 2H), 1.96 – 1.91 (m, 2H), 1.70 (d, *J* = 6.5 Hz, 3H), 1.23 (t, *J* = 4.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.5, 161.2, 128.6 (2C), 92.7, 60.8, 53.2, 30.6, 29.1, 17.7, 14.1; $[\alpha]^{24}_D$ = - 6.0 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{11}H_{16}Cl_3NNaO_3$ $[M+Na]^+$: 338.0093; Found: 338.0120.

Synthesis of (*S*, *E*)-4-((tert-butoxycarbonyl) amino) hept-5-enoic acid [$C_{12}H_{21}NO_4$] (9-*S*):



To a 50 mL round bottom flask containing a solution of trichloroacetamide **8-*S*** (300 mg, 0.95 mmol) in ethanol: H_2O (1:1) (10 mL) was added KOH (636 mg, 11.37 mmol) and heated at 100 ^oC for 48 h. The reaction mixture was allowed to cool at room temperature. Then BOC anhydride (248 mg, 1.14 mmol) was added to the reaction mixture and stirred at room temperature for 24 h. After completion of the reaction, the reaction mixture was evaporated under reduced pressure to remove ethanol and acidified with 6 N HCl. The aqueous solution was extracted with ethyl acetate. The combined extract was washed with brine, dried over Na_2SO_4, and concentrated to afford acid **9-*S*** (212 mg, 92 %) as off white solid. M.p. = 89 – 90 ^oC; IR (KBr): ν_{max}/cm^{-1} 3366, 2978, 1713, 1672, 1511, 1444, 1392, 1286, 1168; ^1H NMR (400 MHz, DMSO-d_6): 11.96 (s, 1 H), 5.37 – 5.43 (m, 1H), 5.23 – 5.27 (m, 1H), 3.9 (br s, 1H), 2.09 – 2.12 (m, 2H), 1.52 – 1.56 (m, 5H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 178.5, 155.5, 130.9, 126.9, 79.6, 52.0, 30.8, 30.4, 28.4, 17.7; $[\alpha]^{24}_D$ = - 10.1 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{12}H_{21}NNaO_4$ $[M+Na]^+$: 266.1368; Found: 266.1364.

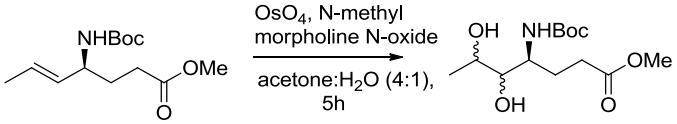
Synthesis of (*S*, *E*)-methyl 4-((tert-butoxycarbonyl) amino) hept-5-enoate [$C_{13}H_{23}NO_4$] (10-*S*):



To a 50 mL round bottom flask containing a solution of the acid **9-*S*** (600 mg, 2.47 mmol) in DMF (5 mL) were added K_2CO_3 (340 mg, 2.47 mmol) and MeI (0.62 mL, 9.88 mmol). The solution was stirred at room temperature for 12 h and poured into H_2O. The product was extracted with EtOAc (2 x 15 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (from 10:1 to 2:1) to afford ester **10-*S*** (610 mg, 97 %) as colorless oil. IR (Neat): ν_{max}/cm^{-1} 3360, 2974, 1694, 1513, 1445, 1365, 1243, 1163, 1048, 1021; ^1H NMR (400 MHz, $CDCl_3$): 5.64 – 5.55 (m, 1H), 5.32 (ddd, *J* = 15.3, 6.4, 1.5 Hz, 1H), 4.48 (br s, 1H), 4.03 (br s, 1H), 3.66 (s, 1H), 2.34 (t, *J* = 7.6 Hz, 2H), 1.84 – 1.76 (m, 2H), 1.67 – 1.65 (m, 3H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.9, 155.4, 131.1,

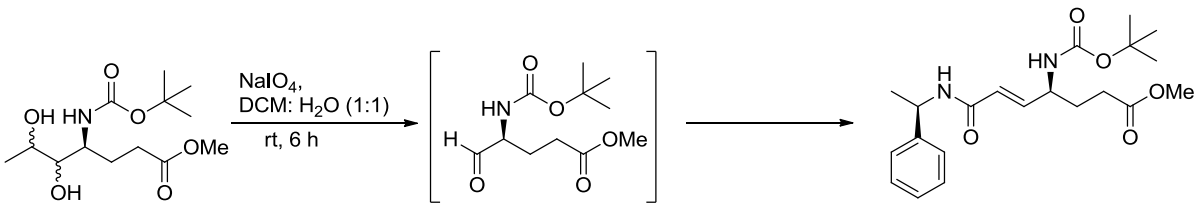
126.7, 79.4, 52.1, 51.7, 30.8, 30.5, 28.4 (3C), 17.8; $[\alpha]^{24}_{D}$ = - 2.8 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{13}H_{23}NNaO_4$ $[M+Na]^+$: 280.1525; Found: 280.1525.

Synthesis of (4*S*)-methyl 4-((tert-butoxycarbonyl) amino)-5, 6-dihydroxyheptanoate [$C_{13}H_{25}NO_6$] (11-*S*):



A 50 mL round bottom flask containing a solution of olefin **10-*S*** (100 mg, 0.31 mmol) in acetone: H2O (4:1) (5 mL) was cooled to 0°C in an ice bath. To the solution were added NMO (50% aq. Solution, 128 µL, 0.47 mmol), OsO_4 (1 mg) and the reaction mixture was stirred at room temperature for 5 h. Reaction mixture was evaporated to remove acetone and then diluted with H_2O. The product was extracted with EtOAc (2 x 10 mL). The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated to afford a residual oil, which was chromatographed on silica gel with petroleum ether / EtOAc (from 3:7) to afford diastereomeric mixture of diol **11-*S*** (110 mg, 95 %). IR (KBr): ν_{max}/cm^{-1} 3360, 2981, 1713, 1683, 1514, 1446, 1390, 1366, 1287, 1167, 1050; ^{1}H NMR (400 MHz, $CDCl_3$): 5.34 – 5.35 (m, 2H), 4.75 – 4.85 (m, 2H), 4.61 (d, *J* = 8.2 Hz, 1H), 3.90 – 3.97 (m, 6H), 3.82 – 3.84 (m, 4H), 3.66 – 3.69 (m, 12H), 3.47 (s, 6H), 3.23 – 3.25 (m, 2H), 3.00 – 3.02 (m, 1H), 2.56 – 2.74 (m, 7H), 2.37 – 2.46 (m, 10H), 2.13 – 2.20 (m, 2H), 1.81 – 1.88 (m, 8H), 1.40 – 1.44 (m, 48H), 1.20 – 1.33 (m, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): 176.8, 174.5, 157.3, 156.3, 85.1, 80.4, 79.6, 68.7, 66.3, 52.8, 51.9, 50.9, 30.9, 30.7, 28.4, 25.9, 25.5, 19.9, 19.0, 18.9; HRMS (ESI): Calc. for $C_{13}H_{25}NNaO_6$ $[M+Na]^+$: 314.1580; Found: 314.1580.

Synthesis of (*S*, *E*)-methyl 4-((tert-butoxycarbonyl)amino)-7-oxo-7-(((*R*)-1-phenylethyl)amino)hept-5-enoate [$C_{21}H_{30}N_2O_5$] (14a-*S*):

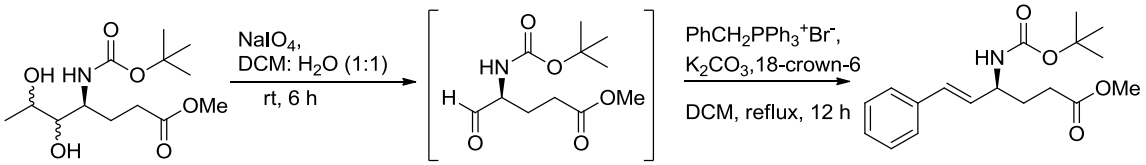


A 50 mL round bottom flask containing a solution of diol **11-*S*** (300 mg, 1.03 mmol) in DCM: H_2O (4:1) (15 mL) was cooled to 0°C in an ice bath. To the solution was added $NaIO_4$ (340 mg, 1.59 mmol) and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (8 mL) was added wittig salt **13a** (520 mg, 1.24 mmol) and the reaction mixture was refluxed for 6 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14a-*S*** (320 mg, 80 %) as off white solid.

M.p. = 154 – 156 ^{o}C; IR (Neat): ν_{max}/cm^{-1} 3342, 3322, 2981, 1731, 1679, 1520, 1441, 1367, 1296; ^{1}H NMR (400 MHz, $CDCl_3$): 7.30 (s, 5H), 6.68 (dd, *J* = 15.1, 5.9 Hz, 1H), 5.87 (d, *J* = 15.1 Hz, 1H), 5.76 (br s, 1H), 5.17 (quintet, *J* = 7.4 Hz, 1H), 4.59 (br s, 1H), 4.27 (br s, 1H), 3.65 (s, 3H), 2.37 (t, *J* = 7.2 Hz, 2H), 1.85 – 1.96 (m, 2H), 1.52 (d, *J* = 6.8 Hz, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.6, 164.3, 155.3, 143.4, 143.0, 128.8, 127.5, 126.3, 123.9, 79.9, 51.9, 51.2, 48.9, 30.5, 29.7, 28.4 (3C), 21.7; HRMS (ESI): Calc. for $C_{21}H_{30}N_2NaO_5$ $[M+Na]^+$: 413.2052; Found: 413.2044; HPLC: CHIRALPAK IC column (2-Propanol: *n*-Hexane = 10:90, flow rate 1.0 mL/min, λ = 250 nm). Retention time (min): 26.79 (major), de 100%. (Fig. S6).

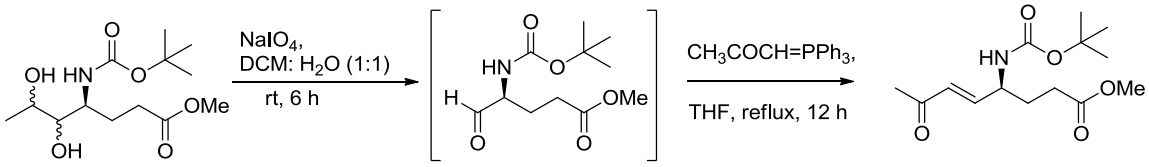
Synthesis of (*S*)-methyl 4-((tert-butoxycarbonyl) amino)-6-phenylhex-5-enoate [$C_{18}H_{25}NO_4$] (14b-*S*):



A 25 mL round bottom flask containing a solution of diol **11-*S*** (300 mg, 1.03 mmol) in DCM: H_2O (4:1) (10 mL) was cooled to 0°C in an ice bath. To the solution was added $NaIO_4$ (340 mg, 1.59 mmol) and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (10 mL) was added phosphonium salt of $[PhCH_2PPh_3]^+Br^-$ **13b** (450 mg, 1.03 mmol), potassium carbonate (160 mg, 1.13 mmol) and 18-crown-6 (49 mg, 0.18 mmol) and the reaction mixture was refluxed for 12 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14b-*S*** (270 mg, 82 %) as white solid. M.p. = 86 – 87^{o}C; IR (Neat): ν_{max}/cm^{-1} 3332, 2971, 1684, 1513, 1417, 1358, 1251, 1155; ^{1}H NMR (400 MHz, $CDCl_3$): 7.21 – 7.36 (m, 5H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.07 (dd, *J* = 15.9, 6.4 Hz, 1H), 4.60 (br s, 1H), 4.29 (br s, 1H), 3.66 (s, 3H), 2.42 (t, *J* = 14.9 Hz, 2H), 1.88 – 1.99 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.9, 155.4, 136.6, 130.7, 129.6, 128.6, 127.8, 126.5, 79.6, 51.8, 30.8, 30.1, 28.5; $[\alpha]^{24}_{D}$ = - 18.2 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{18}H_{26}NNaO_4$ $[M+Na]^+$: 342.1681; Found: 342.1682.

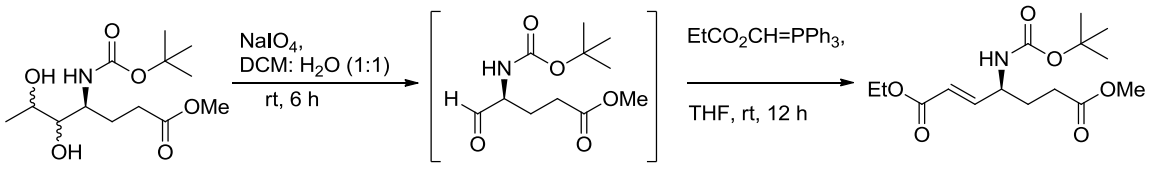
Synthesis of (*S*, *E*)-methyl 4-((tert-butoxycarbonyl) amino)-7-oxooct-5-enoate [$C_{14}H_{23}NO_5$] (14c-*S*):



A 25 mL round bottom flask containing a solution of diol **11-*S*** (400 mg, 1.37 mmol) in DCM: H_2O (6 mL) was cooled to 0°C in an ice bath. To the solution was added $NaIO_4$ (440 mg, 2.06 mmol) and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in THF (10 mL) was added methylcarbonylmethylenephosphorane ($CH_3COCHPPh_3$) **13c** (430 mg, 1.37 mmol) and the reaction mixture was refluxed for 3 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 8:2) to afford the corresponding unsaturated compound **14c-*S*** (330 mg, 84 %) as colorless oil. IR (Neat): ν_{max}/cm^{-1} 3744, 2977, 1680, 1515, 1444, 1363, 1247, 1161, 1051, 1022; ^1H NMR (400 MHz, $CDCl_3$): 6.69 (dd, *J* = 16.0, 5.0 Hz, 1H), 6.19 (d, *J* = 16.0 Hz, 1H), 4.67 (br s, 1H), 4.35 (br s, 1H), 3.69 (s, 3H), 2.43 (t, *J* = 7.3 Hz 2H), 2.27 (s, 3H), 1.97 – 2.02 (m, 1H), 1.81-1.86 (m, 1H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 198.3, 173.5, 155.3, 146.5, 129.9, 80.0, 51.9, 51.2, 30.5, 29.3, 28.4 (3C), 27.5; $[\alpha]^{24}_D$ = - 12.40 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{21}H_{16}NNaO$ $[M+Na]^+$: 308.1474; Found: 308.1471.

Synthesis of (*S*, *E*)-1-ethyl 7-methyl 4-((tert-butoxycarbonyl) amino) hept-2-enedioate [$C_{15}H_{25}NO_6$] (14d-*S*):

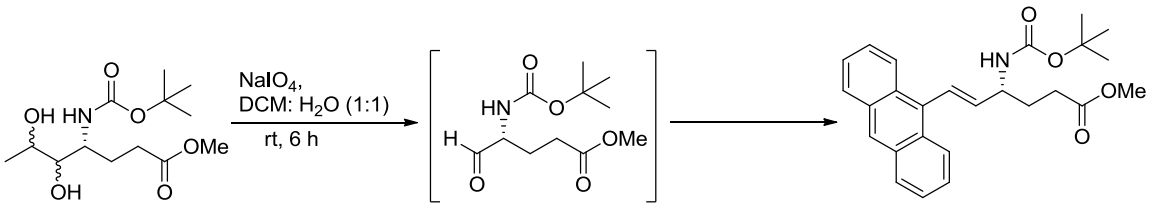


A 25 mL round bottom flask containing a solution of diol **11-*S*** (300 mg, 1.03 mmol) in DCM: H_2O (4:1) (10 mL) was cooled to 0°C in an ice bath. To the solution was added $NaIO_4$ (340 mg, 1.59 mmol) and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (8 mL) was added ethoxycarbonylmethylenephosphorane ($EtO_2CCHPPh_3$) **13d** (430 mg, 1.24 mmol) and the reaction mixture was refluxed for 12 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14d-*S*** (270 mg, 82 %) as colorless oil. IR (Neat): ν_{max}/cm^{-1} 2978, 1706, 1658, 1515, 1446, 1367, 1247, 1160, 1092, 1037; ^1H NMR (400 MHz, $CDCl_3$): 6.82 (dd, *J* = 12.5, 4.2 Hz, 1H), 5.93 (d, *J* = 12.5 Hz, 1H), 4.61 (br s, 1H), 4.33 (br s, 1H), 4.19 (q, *J* = 5.7 Hz, 2H), 3.67 (s, 3H), 2.40 (t, *J* = 5.9 Hz, 2H), 1.98 – 1.94 (m, 1H), 1.83 – 1.80 (m, 1H), 1.43 (s, 9H), 1.28 (t, *J* = 5.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.5, 166.2, 155.2, 147.5, 121.4, 80.0, 60.6,

51.9, 51.1, 30.5, 29.5, 28.4 (3C), 14.3; $[\alpha]^{24}_{D}$ = - 7.2 (*c* = 0.50, $CHCl_3$); HRMS (ESI): Calc. for $C_{15}H_{25}NNaO_6$ $[M+Na]^+$: 338.1580; Found: 338.1580.

Synthesis of (R, E)-methyl 6-(anthracen-9-yl)-4-((tert-butoxycarbonyl)amino)hex-5-enoate [$C_{26}H_{29}NO_4$] (14e-*R*):



A 50 mL round bottom flask containing a solution of diol **11-*R*** (350 mg, 1.20 mmol) in DCM: H_2O (4:1) (30 mL) was cooled to 0°C in an ice bath. To the solution was added $NaIO_4$ (390 mg, 1.80 mmol) and the reaction mixture was stirred at room temperature for 6 h. The resulting solution was partitioned between DCM and H_2O. The organic layer was separated, dried over Na_2SO_4 and concentrated to afford an aldehyde which was used for next reaction without any purification.

To a 25 mL round bottom flask containing a solution of crude aldehyde in DCM (8 mL) was added wittig salt **13e** (790 mg, 1.44 mmol) and the reaction mixture was refluxed for 6 h in nitrogen atmosphere. The resulting solution was allowed to cool to room temperature, concentrated in vacuo and chromatographed on silica gel (petroleum ether /ethyl acetate 9:1) to afford the corresponding unsaturated compound **14e-*R*** (350 mg, 69 %) as yellow solid. M.p. = 114 – 115 ^oC; IR (Neat): ν_{max}/cm^{-1} 3344, 2982, 1734, 1679, 1633, 1523, 1448, 1368, 1302, 1255, 1166, 1047, 1016; ^1H NMR (400 MHz, $CDCl_3$): 8.36 (s, 1H), 8.15 – 1.30 (m, 2H), 7.90 – 8.04 (m, 2H), 7.37 – 7.52 (m, 4H), 7.28 (d, *J* = 16.2 Hz, 1H), 5.87 (dd, *J* = 16.2, 6.4 Hz, 1H), 4.79 (s, 1H), 4.53 (s, 1H), 3.71(s, 3H), 2.58 (t, *J* = 7.4 Hz, 2H), 1.97 – 2.23 (m, 2H), 1.51 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 173.9, 155.5, 138.2, 131.4, 129.5, 128.7, 127.0, 126.4, 126.0, 125.5, 125.2, 79.8, 53.0, 52.0, 31.0, 30.3, 28.5 (3C); HRMS (ESI): Calc. for $C_{26}H_{29}NNaO_4$ $[M+Na]^+$: 442.1994; Found: 442.1987.

IV. Photohysical Properties of 14e-*R*.

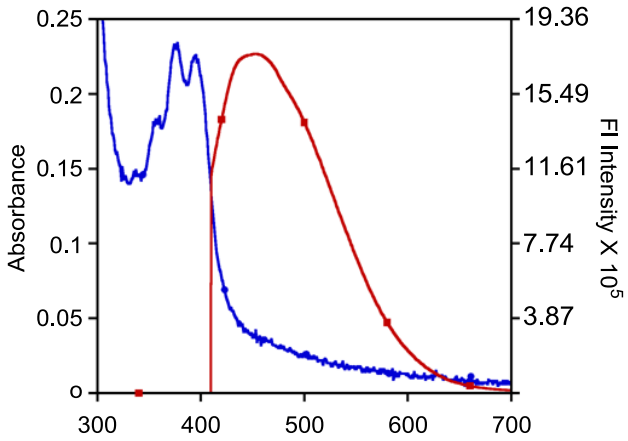


Fig. S1 Normalized UV-vis absorption and fluorescent emission spectra **14e-*R***.

V. Crystal structures.

Crystal structure of compound 14a-*S* (CCDC 922311): $C_{21}H_{30}N_2O_5$; Compound **14a-*S*** was crystallized from slow evaporation of methanol/water at room temperature. A colorless needle shaped crystal with approximate dimensions 0.185 x 0.161 x 0.058 mm gave an Orthorhombic with space group *P21/n*; *a* = 19.851(4) *b* = 20.966(5) *c* = 5.1137(11) Å, α = 90° β = 90° γ = 90°; *V* = 2128.3(8) Å^3; *T* = 296 (2) K; *Z* = 4; ρ_{calc} = 1.219 Mgm^{-3}; $2\theta_{max}$ = 54.76°; *MoKαλ* = 0.71073 Å. Fine-focus sealed tube source with graphite monochromator. *R* = 0.0361 (for 4159 reflection $I>2\sigma(I)$), *wR* = 0.0820 which was refined against |*F2*| and S = 0.935 for 258 parameters and 4839 unique reflections. The structure was obtained by direct methods using SHELXS-97.[S3] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were fixed geometrically in the idealized position and refined in the final cycle of refinement as riding over atoms to which they are bonded. μ = 0.087 mm^{-1}.

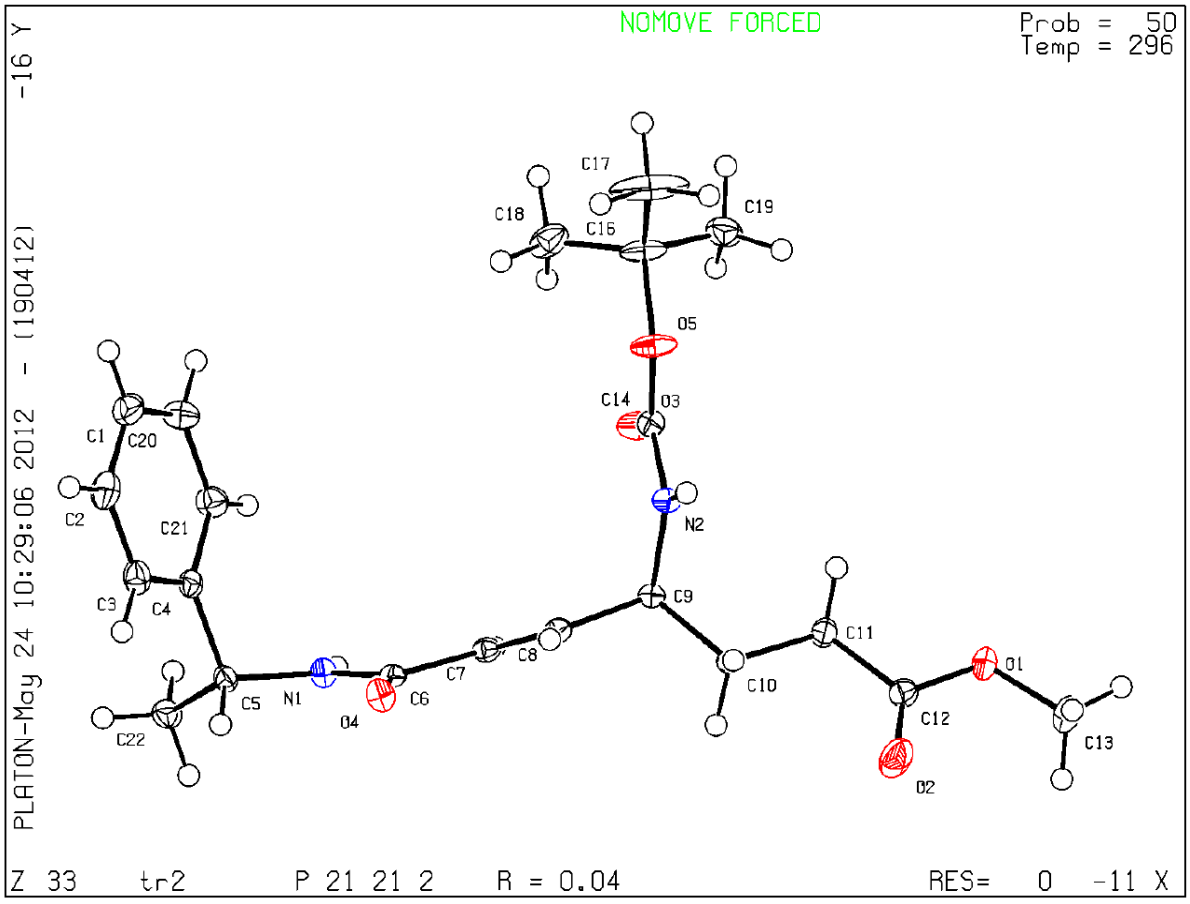


Fig. S2 ORTEP diagram of **14a-*S***.

Crystal structure of compound 14a-*R* (CCDC 922310): $C_{21}H_{30}N_2O_5$; Compound **14a-*R*** was crystallized from slow evaporation of methanol/water at room temperature. A colorless needle shaped crystal with approximate dimensions 0.224 x 0.148 x 0.022 mm gave an Monoclinic with space group *P21*; a = 5.155(3) b = 36.609(18) c = 11.688(6) Å, α = 90° β = 102.638(9)° γ = 90°; V = 2152(2) Å^3; T = 200 K; Z = 4; ρ_{calc} = 1.205 Mgm^{-3}; $2\theta_{max}$ = 52.86°; *MoKαλ* = 0.71073 Å. Fine-focus sealed tube source with graphite monochromator. R = 0.0632 (for 4811 reflection $I>2\sigma(I)$), wR = 0.1503 which was refined against |*F2*| and S = 0.999 for 516 parameters and 8384 unique reflections. The structure was obtained by direct methods using SHELXS-97.[S3] All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were fixed geometrically in the idealized position and refined in the final cycle of refinement as riding over the atoms to which they are bonded. μ = 0.086 mm^{-1}.

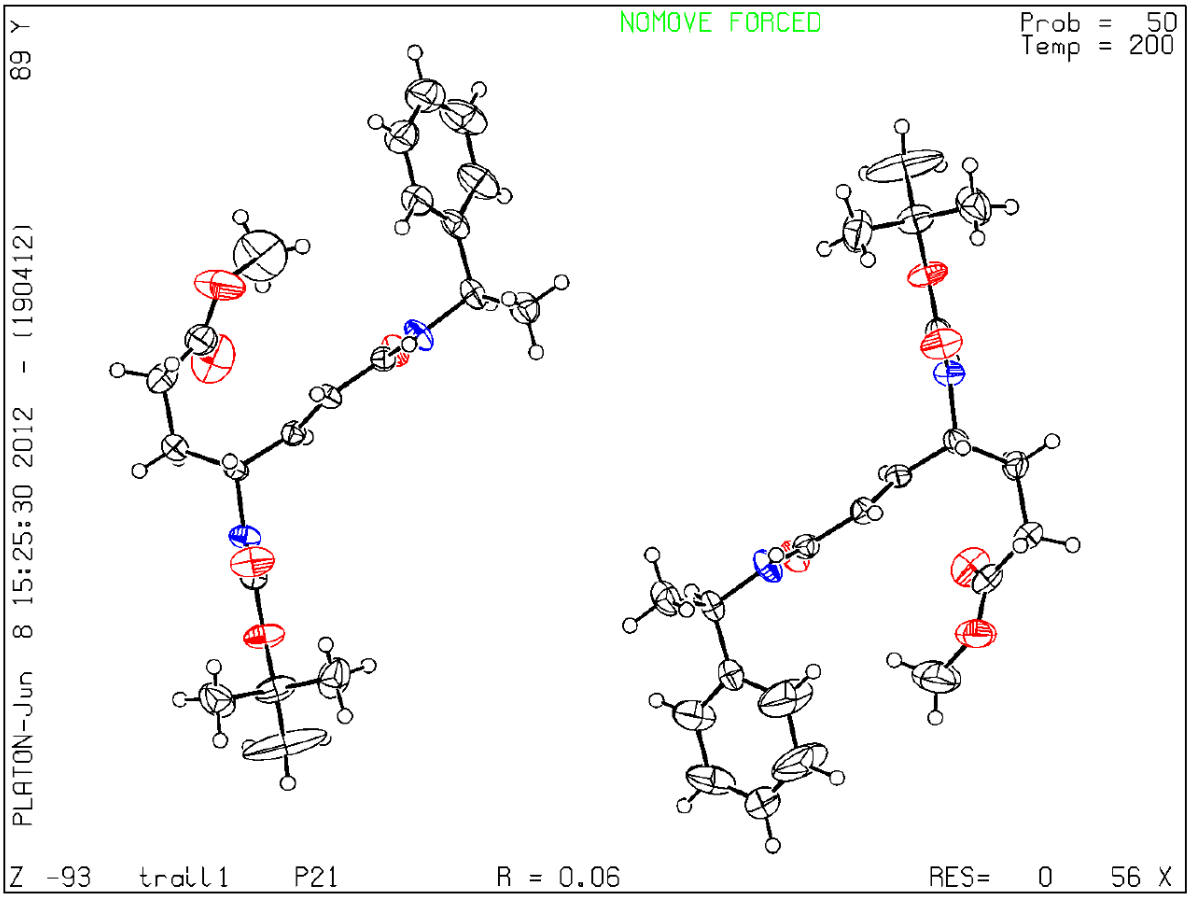


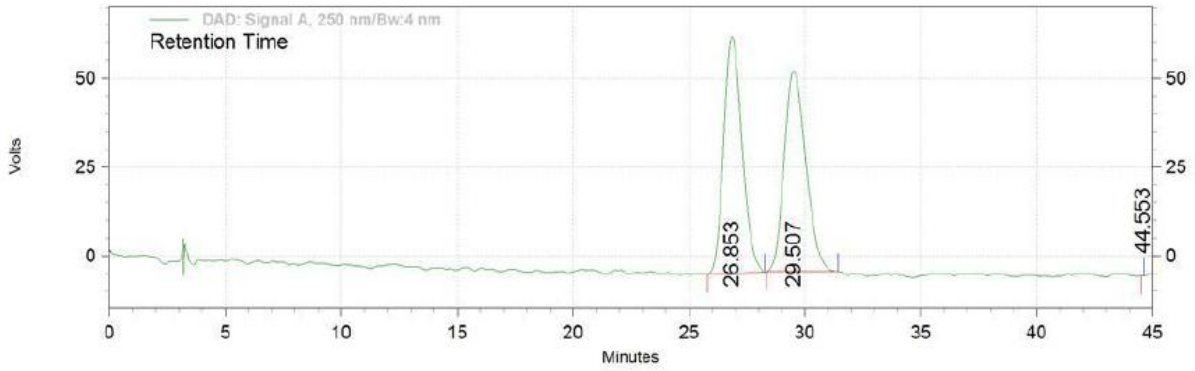
Fig. S3 ORTEP diagram of **14a-*R***.

VI. HPLC Data.

Chiral HPLC of mixture of 14a-*R* and 14a-*S*:

Area % Report

Data File: C:\EZChrom Elite\Enterprise\Projects\Default\Data\Kavita\DK chiral 14.dat
Method: C:\EZChrom Elite\Enterprise\Projects\Default\Method\PT\DK\Chiral_10%IPA hexane.met
Acquired: 5/28/2012 10:57:39 PM
Printed: 5/29/2012 9:40:35 AM



DAD: Signal A,
250 nm/Bw:4 nm
Results

Retention Time	Area	Area %	Height	Height %
26.853	7698448	50.19	140041	54.10
29.507	7640147	49.81	118694	45.86
44.553	358	0.00	100	0.04
Totals	15338953	100.00	258835	100.00

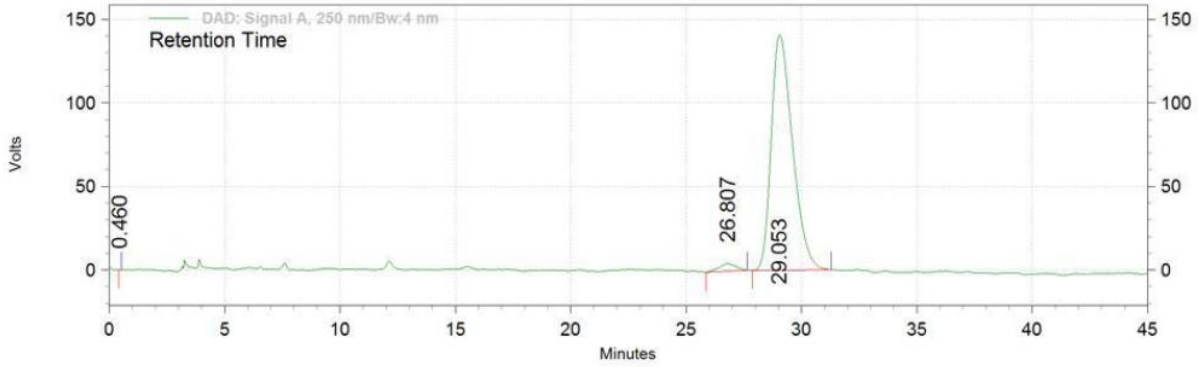
Fig. S4 Chiral HPLC of diastereomeric mixture of **14a-*R*** and **14a-*S*.**

Column: CHIRALPAK IC (0.46 cm × 25 cm)
Flow: 1.0 mL/min
Method: Isocratic
10 % Isopropanol
90 % *n*-hexane
Wavelength: 250 nm.
Racemic sample: *tR* [**14a-*S***] = 26.85 min, *tR* [**14a-*R***] = 29.51 min.

Chiral HPLC of mixture of 14a-*R*:

Area % Report

Data File: C:\EZChrom Elite\Enterprise\Projects\Default\Data\Kavita\DK 04-60R2.dat
Method: C:\EZChrom Elite\Enterprise\Projects\Default\Method\PT\DK\Chiral_10%IPA hexane.met
Acquired: 5/29/2012 2:47:05 AM
Printed: 5/29/2012 10:18:25 AM



DAD: Signal A,
250 nm/Bw:4 nm
Results

Retention Time	Area	Area %	Height	Height %
0.460	110	0.00	42	0.01
26.807	477599	2.46	9614	3.15
29.053	18964853	97.54	295577	96.84
Totals	19442562	100.00	305233	100.00

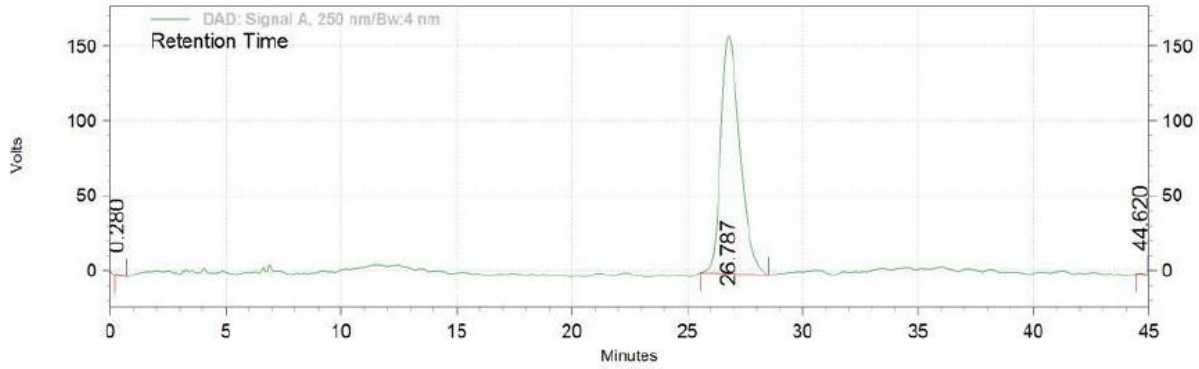
Fig. S5 Chiral HPLC of **14a-*R***.

Column: CHIRALPAK IC (0.46 cm × 25 cm)
Flow: 1.0 mL/min
Method: Isocratic
10 % Isopropanol
90 % *n*-hexane
Wavelength: 250 nm.
tR [**14a-*S***] = 26.81 min, *tR* [**14a-*R***] = 29.05 min.

Chiral HPLC of compounds 14a-*S*:

Area % Report

Data File: C:\EZChrom Elite\Enterprise\Projects\Default\Data\Kavita\DK 04-58R5.dat
Method: C:\EZChrom Elite\Enterprise\Projects\Default\Method\PT\DK\Chiral_10%IPA hexane.met
Acquired: 5/29/2012 7:23:54 AM
Printed: 5/29/2012 10:06:42 AM



DAD: Signal A,
250 nm/Bw:4 nm
Results

Retention Time	Area	Area %	Height	Height %
0.280	23025	0.12	833	0.25
26.787	19051483	99.77	333101	99.34
44.620	21272	0.11	1386	0.41
Totals	19095780	100.00	335320	100.00

Fig. S6 Chiral HPLC of **14a-*S***.

Column: CHIRALPAK IC (0.46 cm × 25 cm)
Flow: 1.0 mL/min
Method: Isocratic
10 % Isopropanol
90 % *n*-hexane
Wavelength: 250 nm.
tR [**14a-*S***] = 26.79 min.

VII. NMR Data.

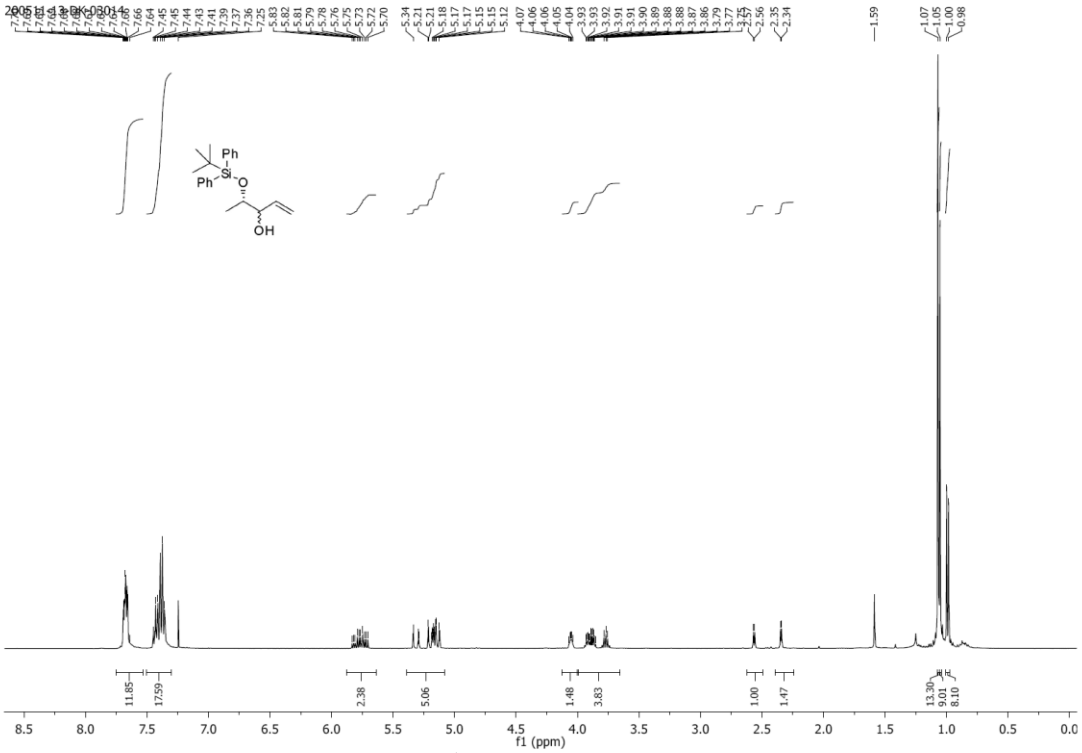


Fig. S7 ^{1}H NMR spectra of **5** in $CDCl_3$.

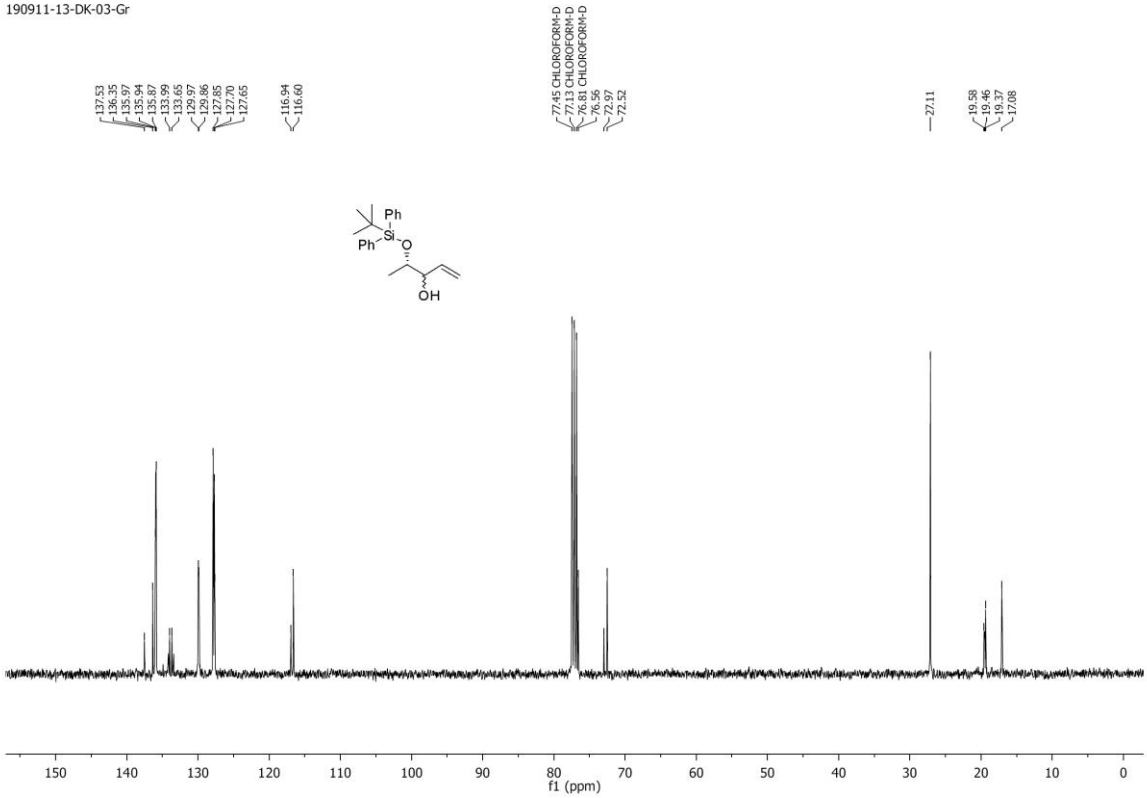


Fig. S8 ^{13}C NMR spectra of **5** in $CDCl_3$.

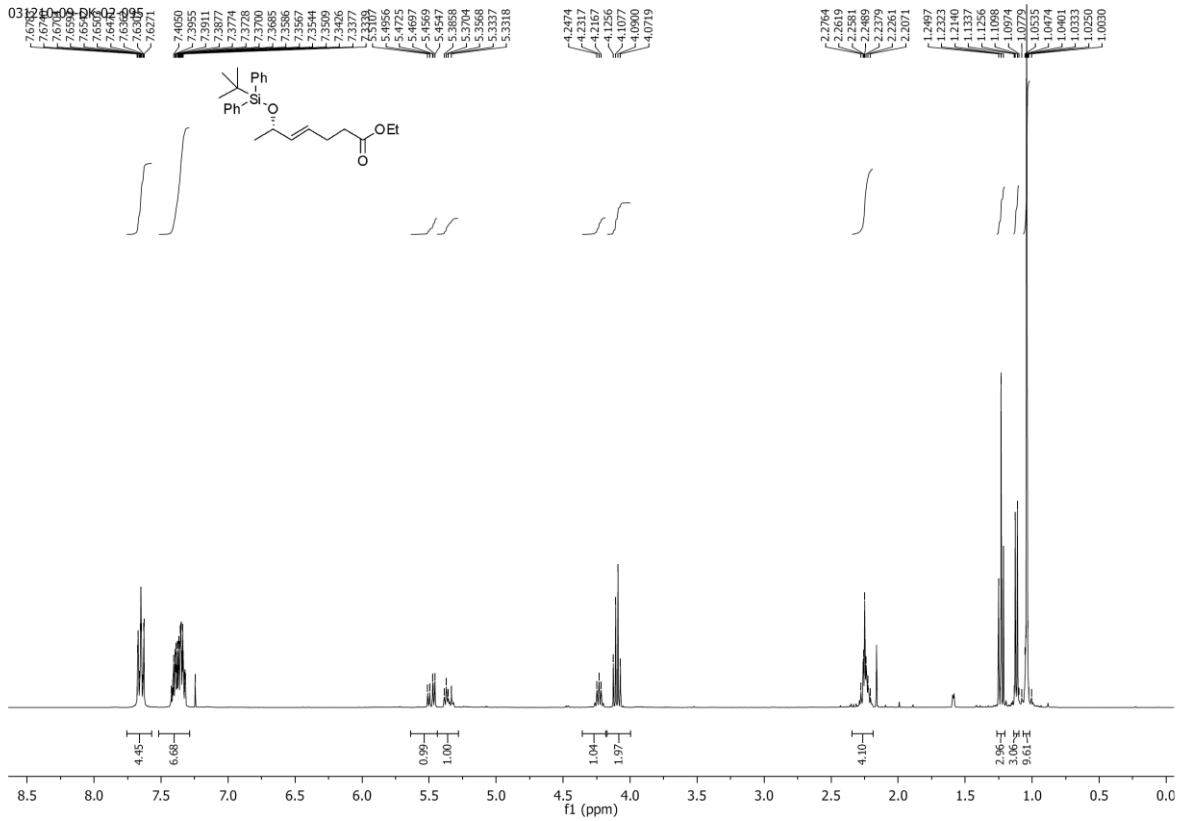


Fig. S9 ^{1}H NMR spectra of **6-*E*** in $CDCl_3$.

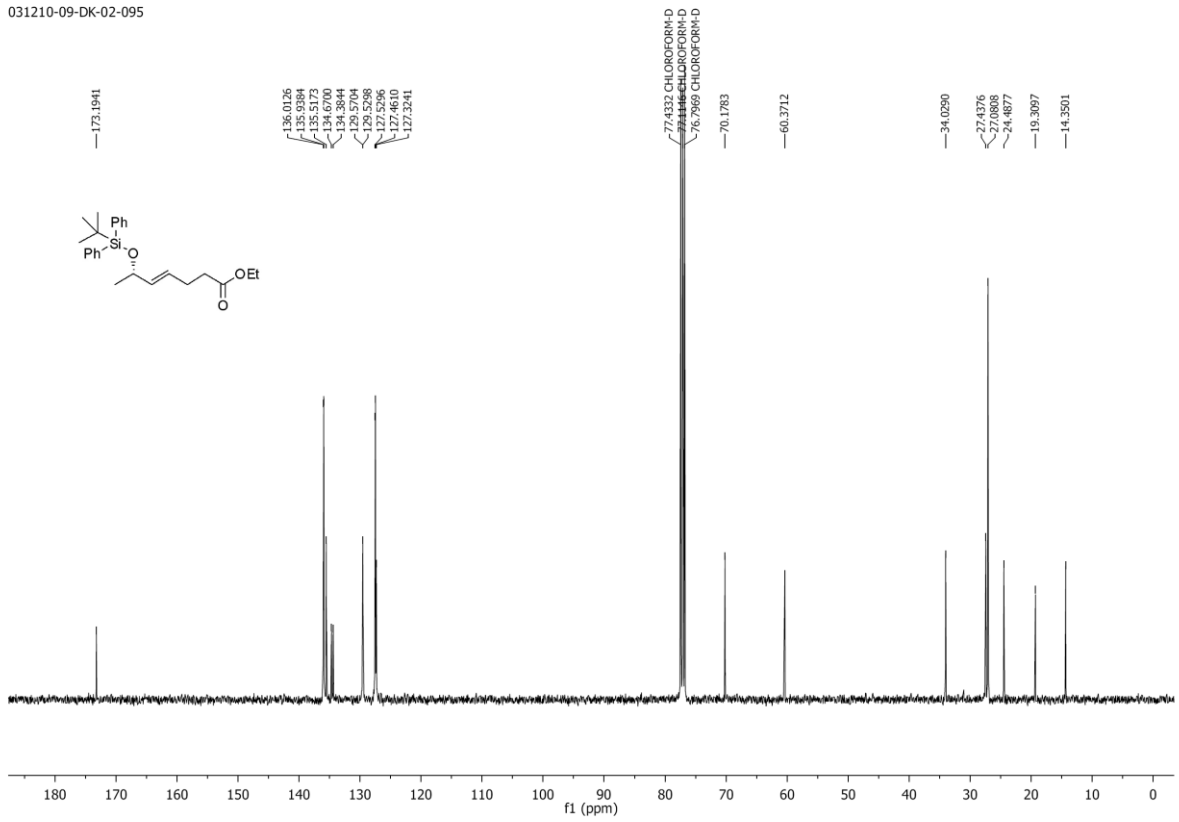


Fig. S10 ^{13}C NMR spectra of **6-*E*** in $CDCl_3$.

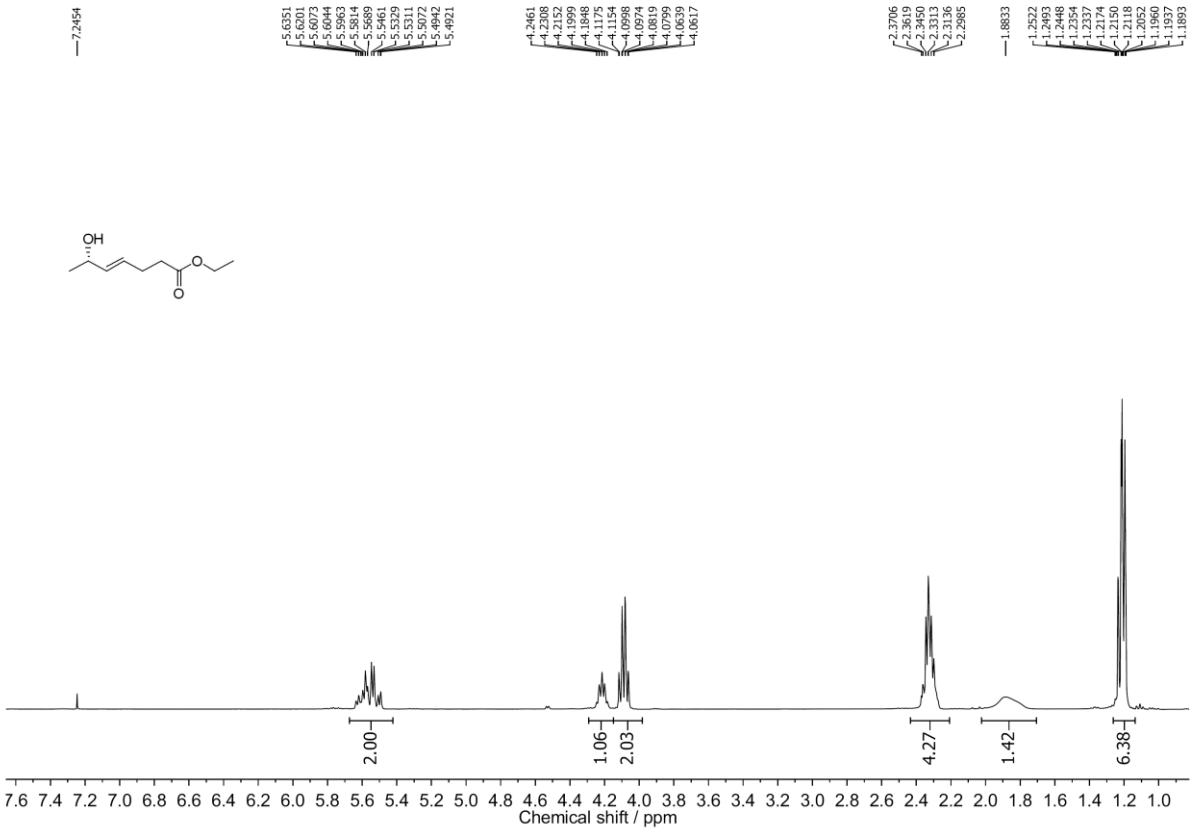


Fig. S11 ^{1}H NMR spectra of **7-*E*** in $CDCl_3$.

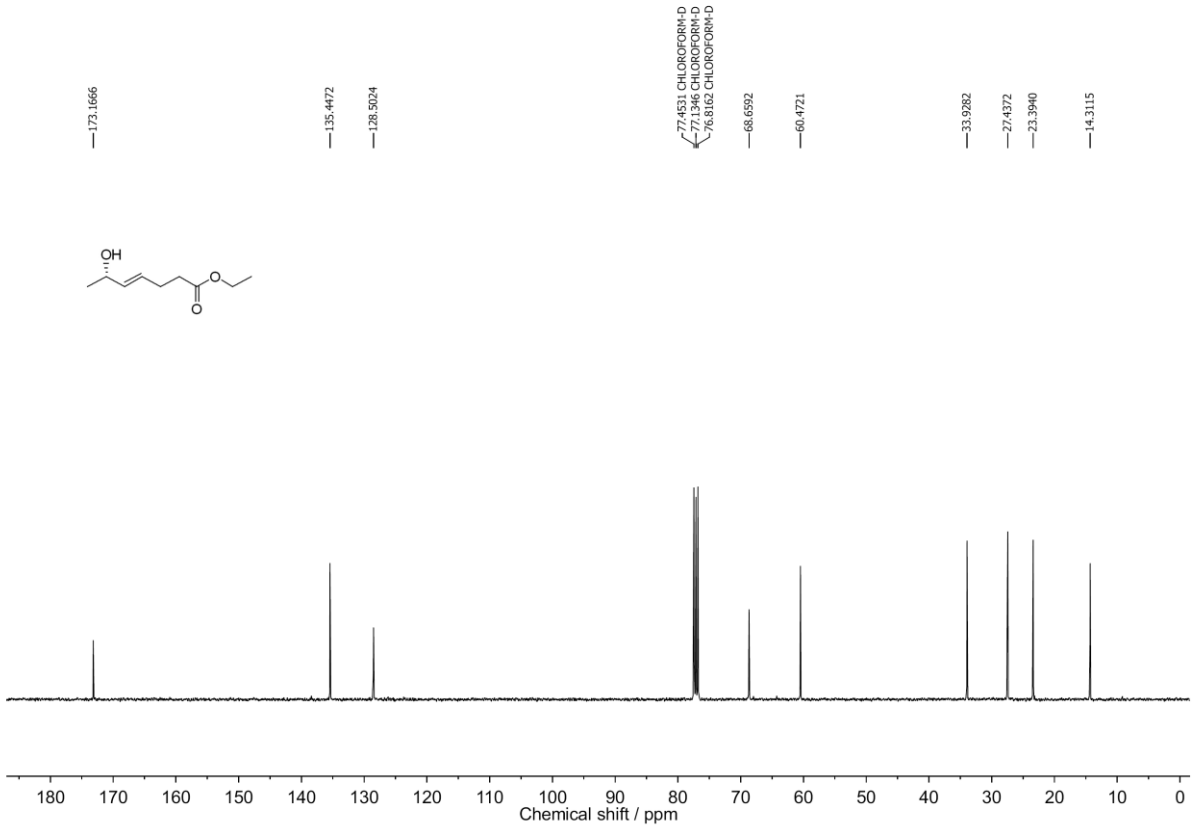


Fig. S12 ^{13}C NMR spectra of **7-*E*** in $CDCl_3$.

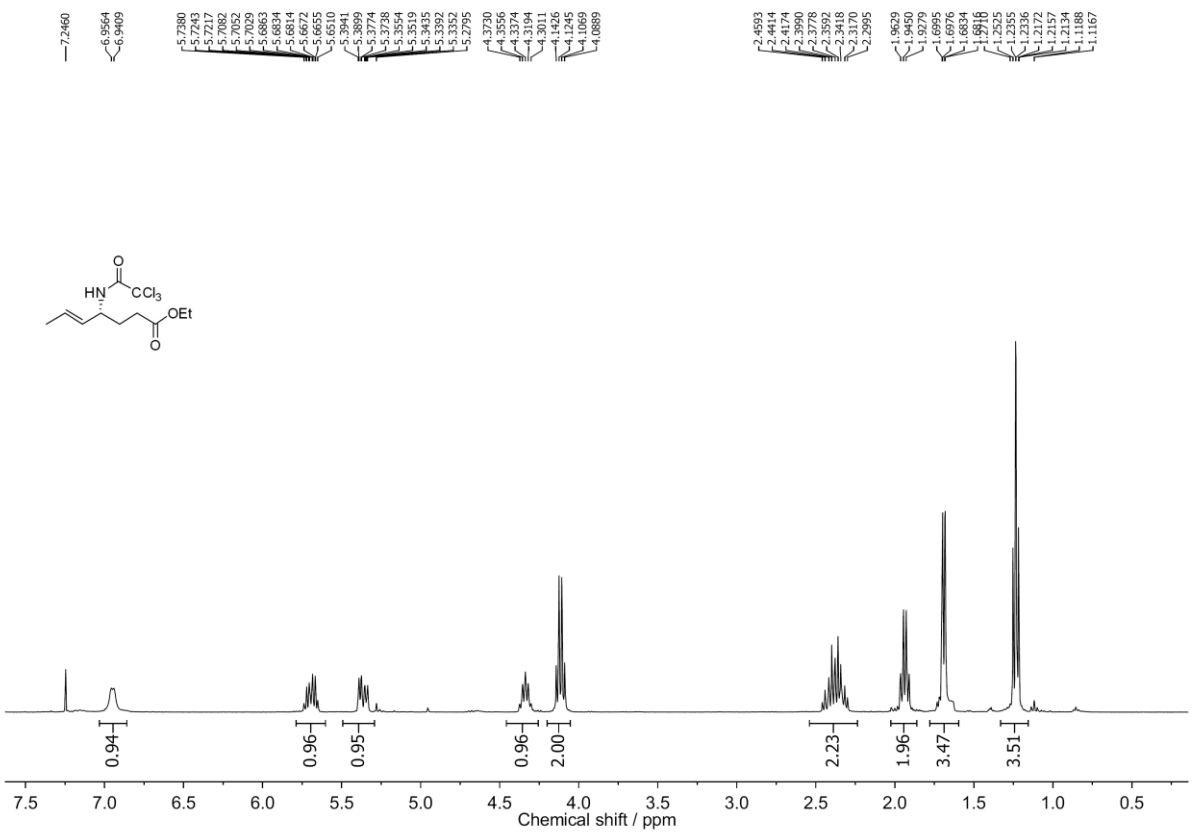


Fig. S13 ^{1}H NMR spectra of **8-*R*** in $CDCl_3$.

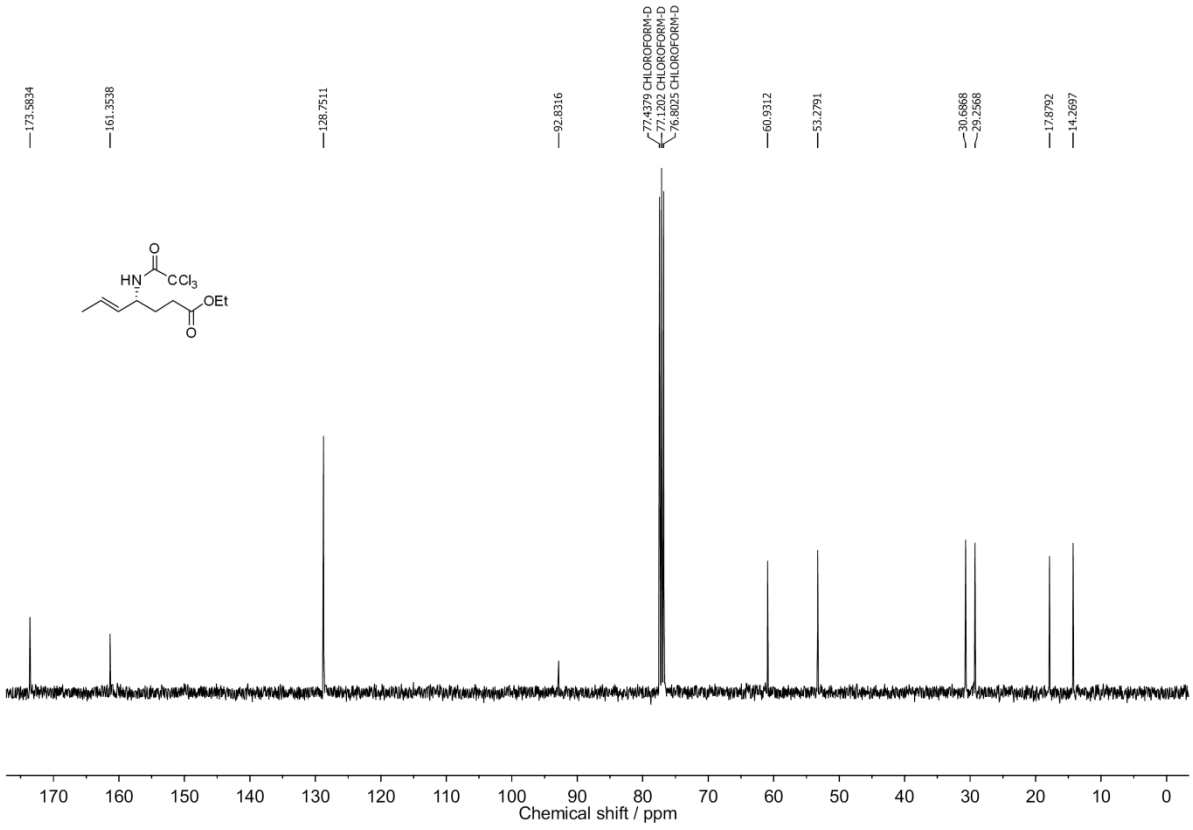


Fig. S14 ^{13}C NMR spectra of **8-*R*** in $CDCl_3$.

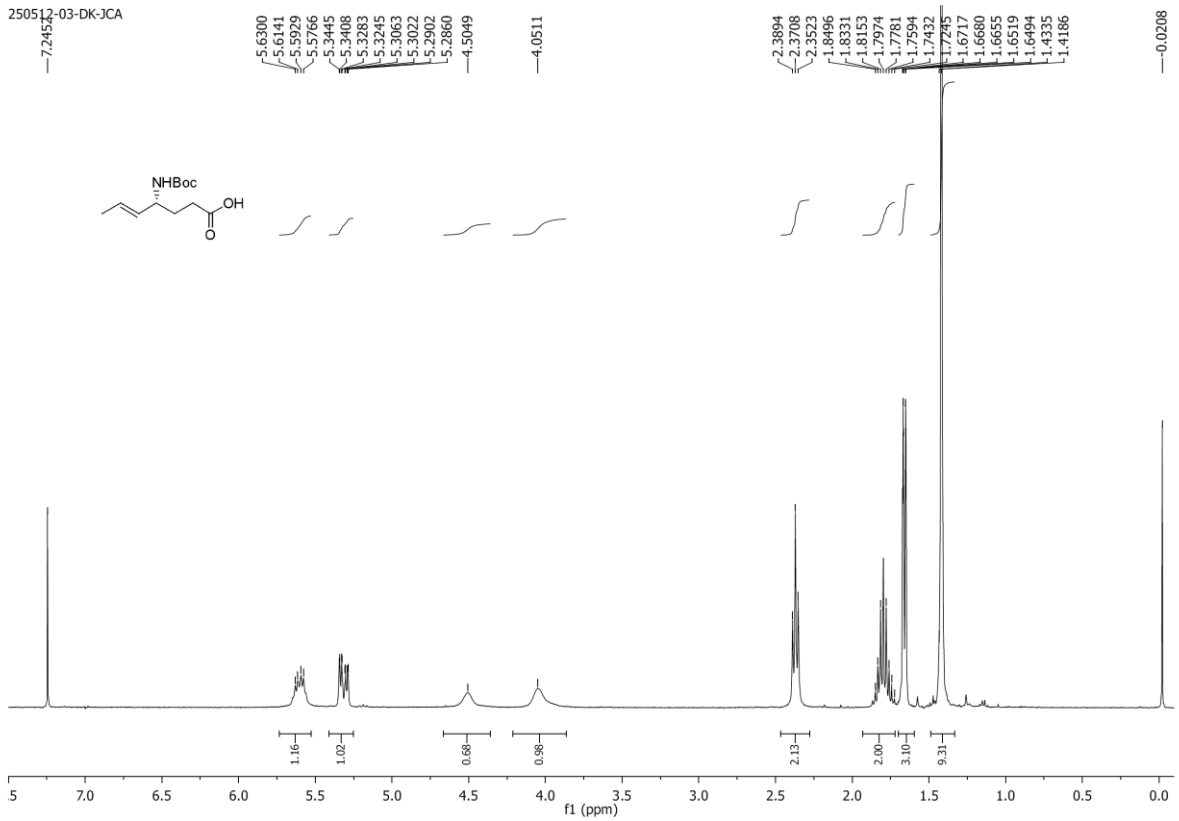


Fig. S15 ^{1}H NMR spectra of **9-*R*** in $CDCl_3$.

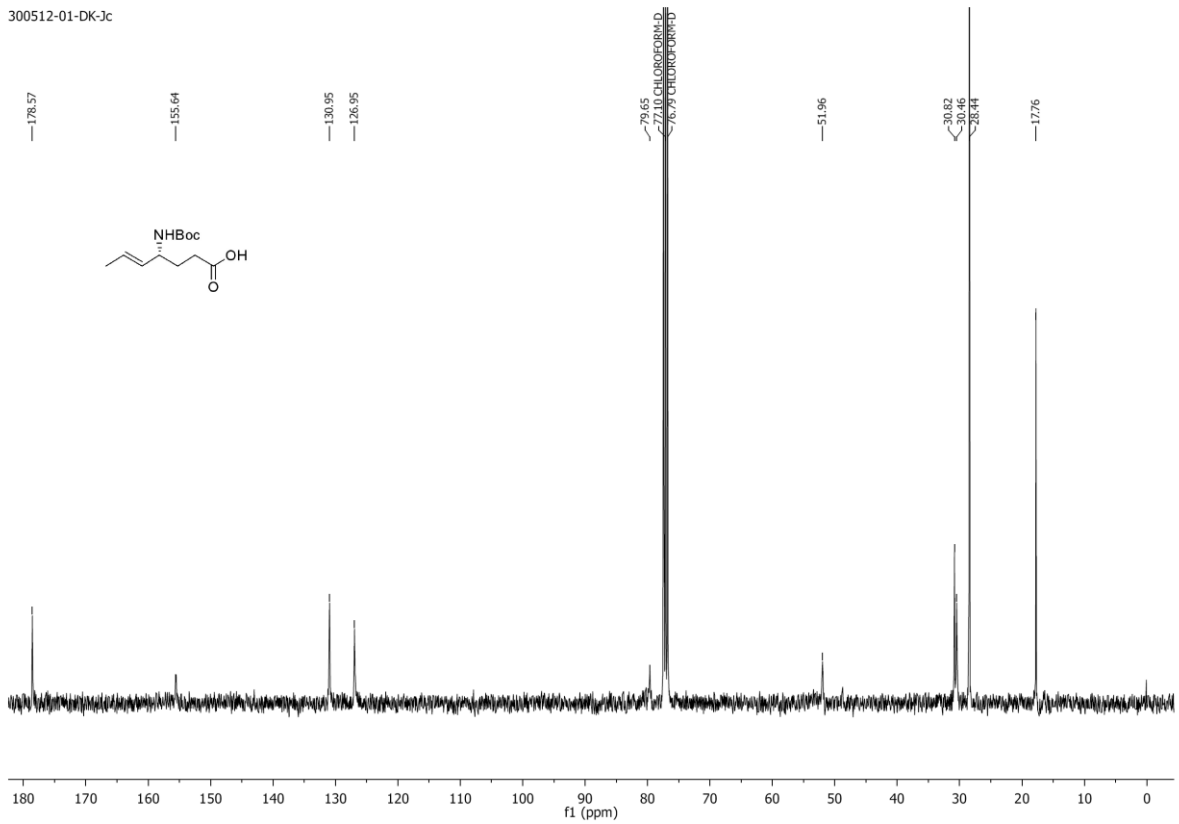


Fig. S16 ^{13}C NMR spectra of **9-*R*** in $CDCl_3$.

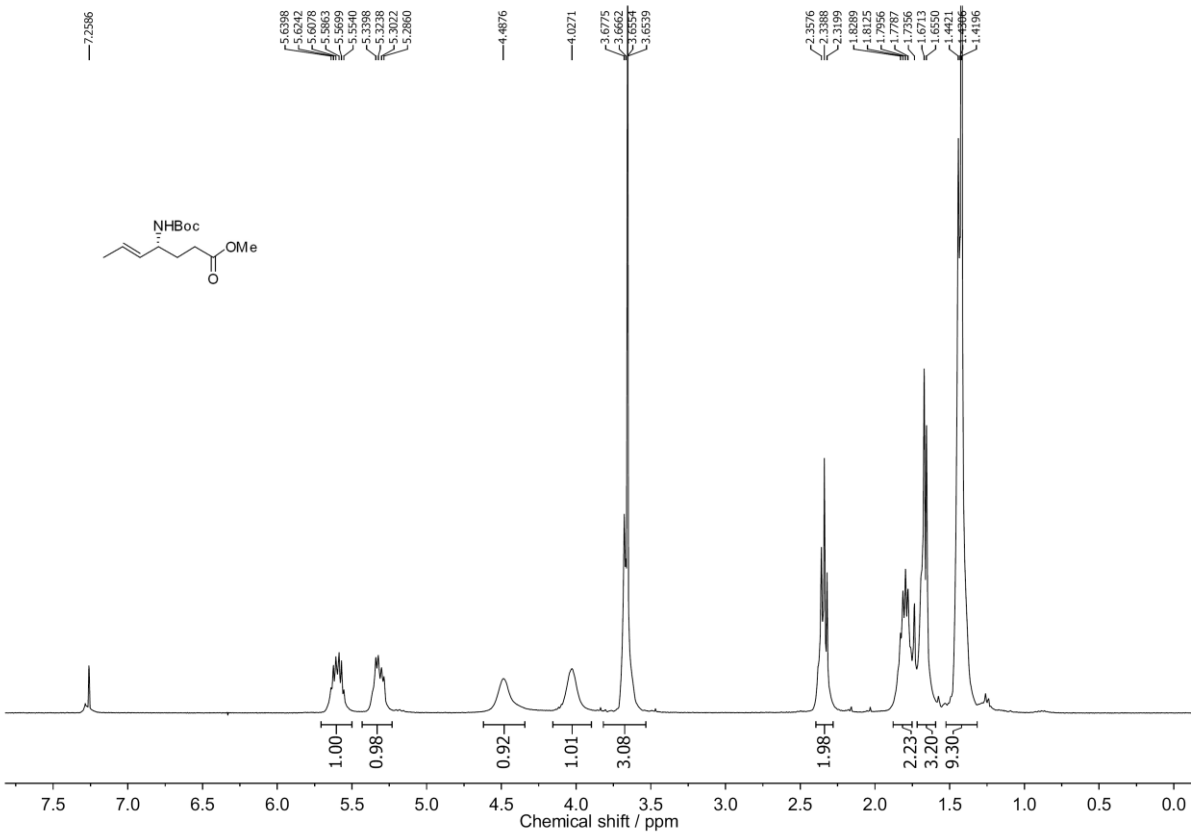


Fig. S17 ^{1}H NMR spectra of **10-*R*** in $CDCl_3$.

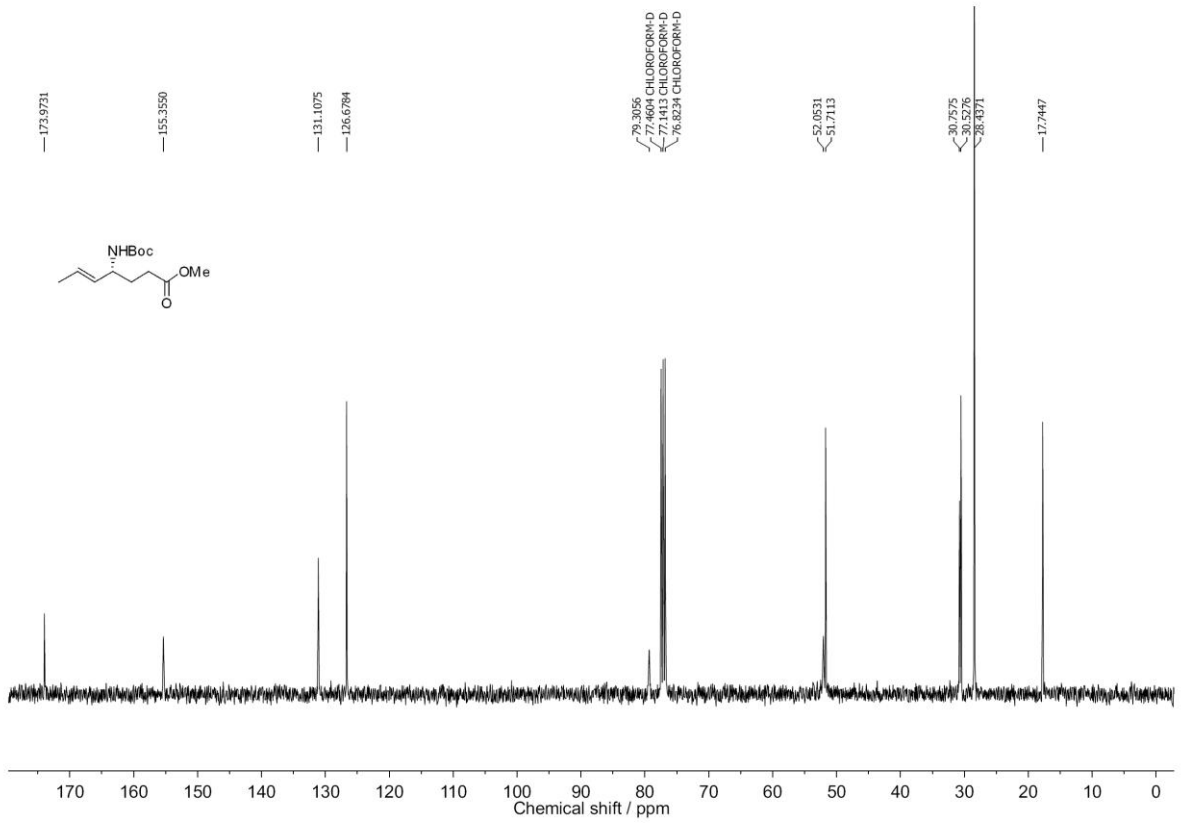


Fig. S18 ^{13}C NMR spectra of **10-*R*** in $CDCl_3$.

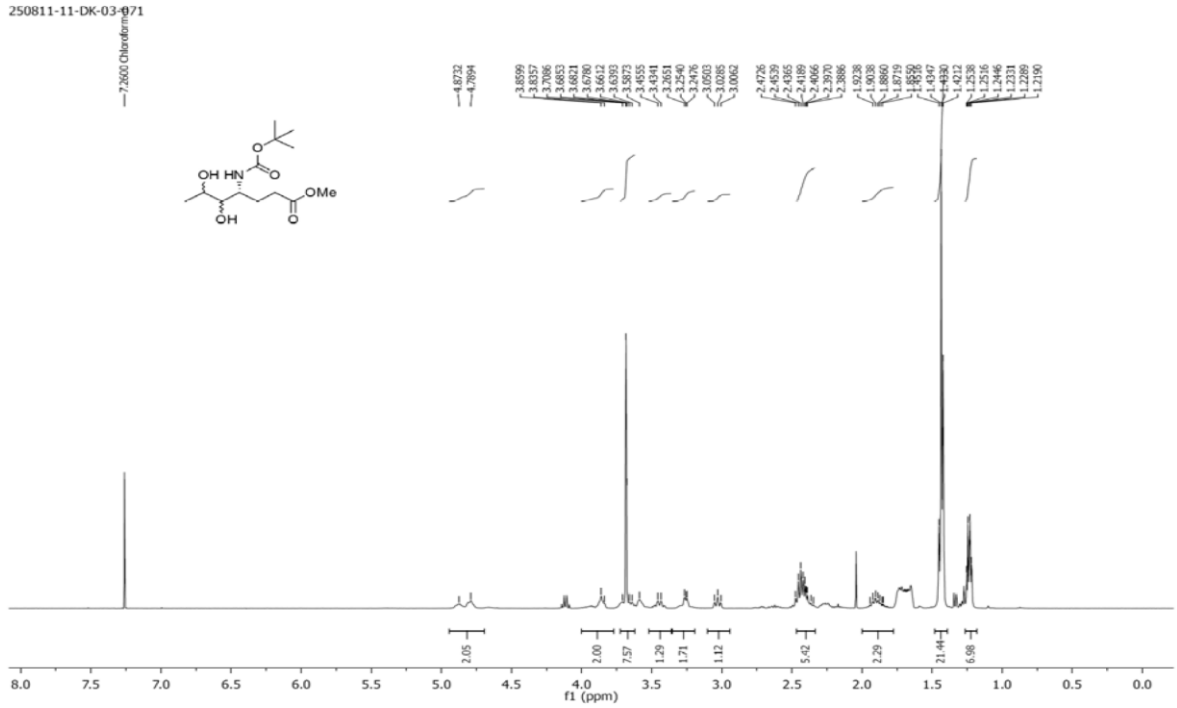


Fig. S19 ^{1}H NMR spectra of **11-*R*** in $CDCl_3$.

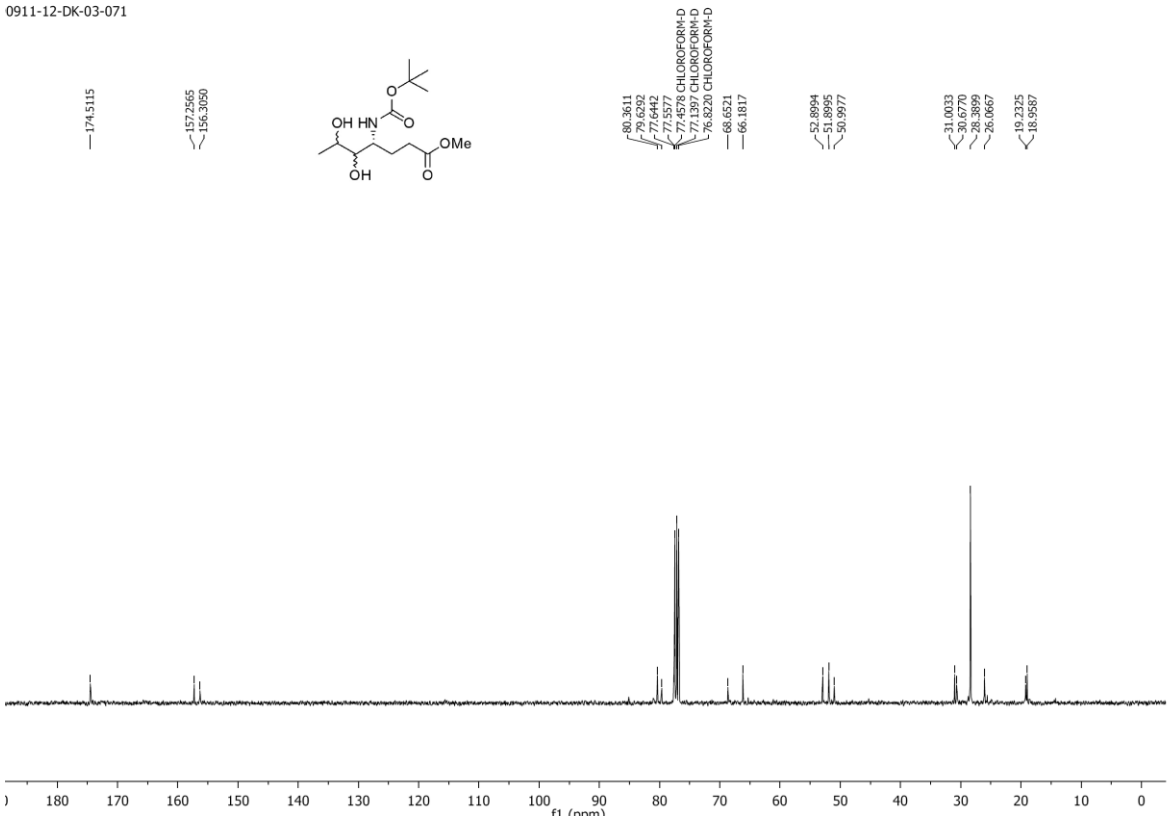


Fig. S20 ^{13}C NMR spectra of **11-*R*** in $CDCl_3$.

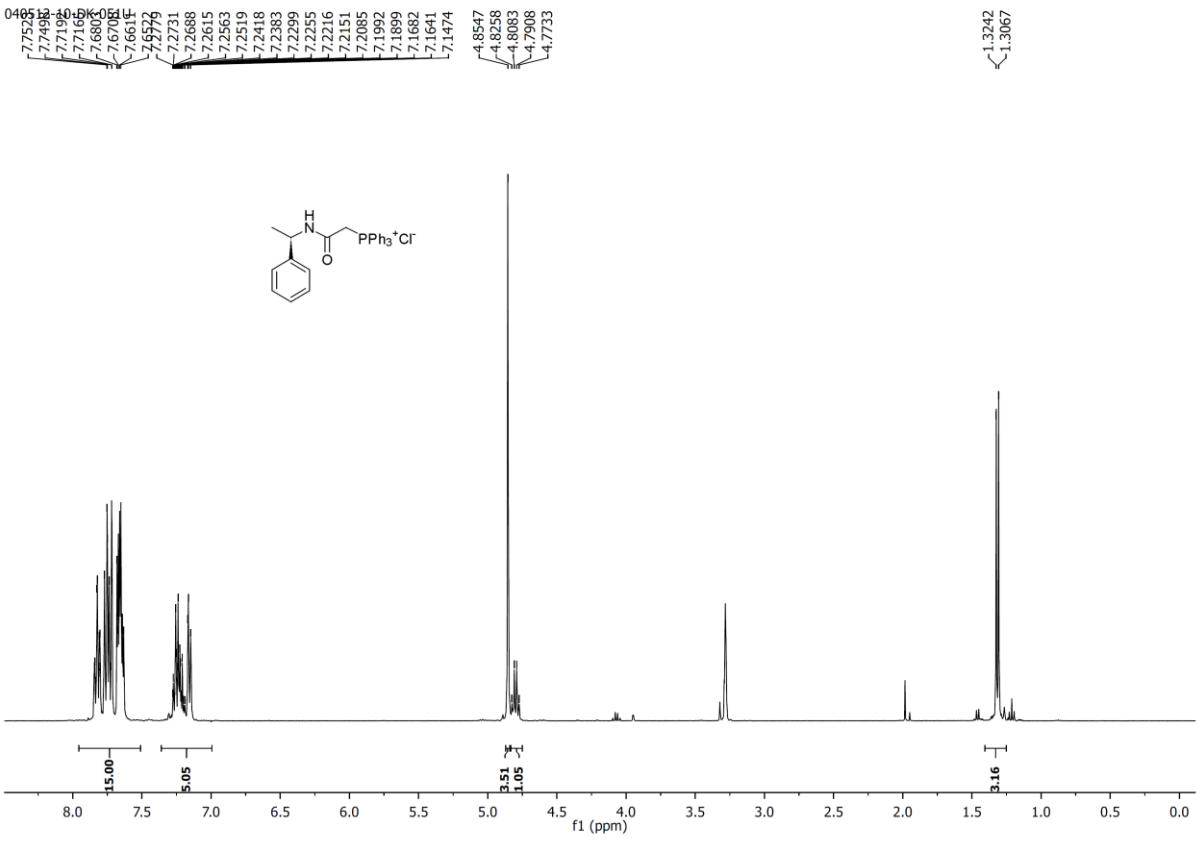


Fig. S21 ^{1}H NMR spectra of **13a** in CD_3OD.

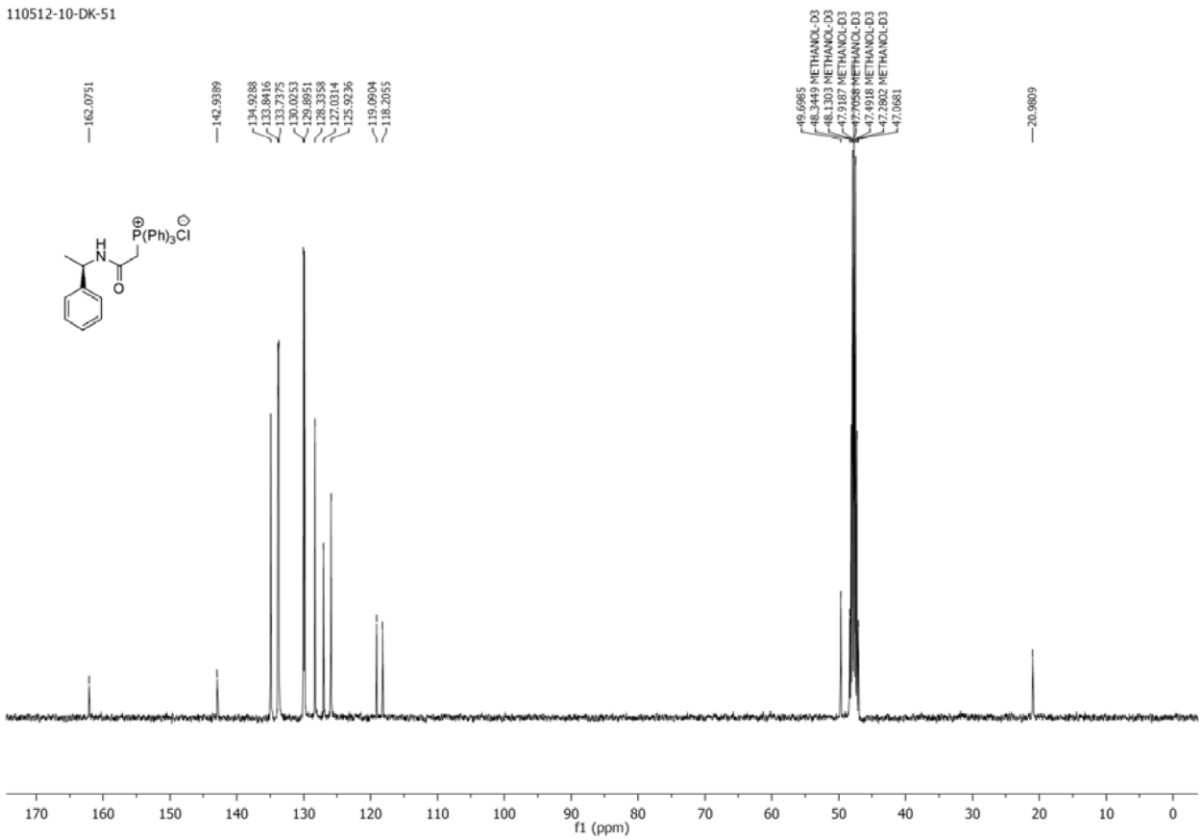


Fig. S22 ^{13}C NMR spectra of **7 13a** in CD_3OD.

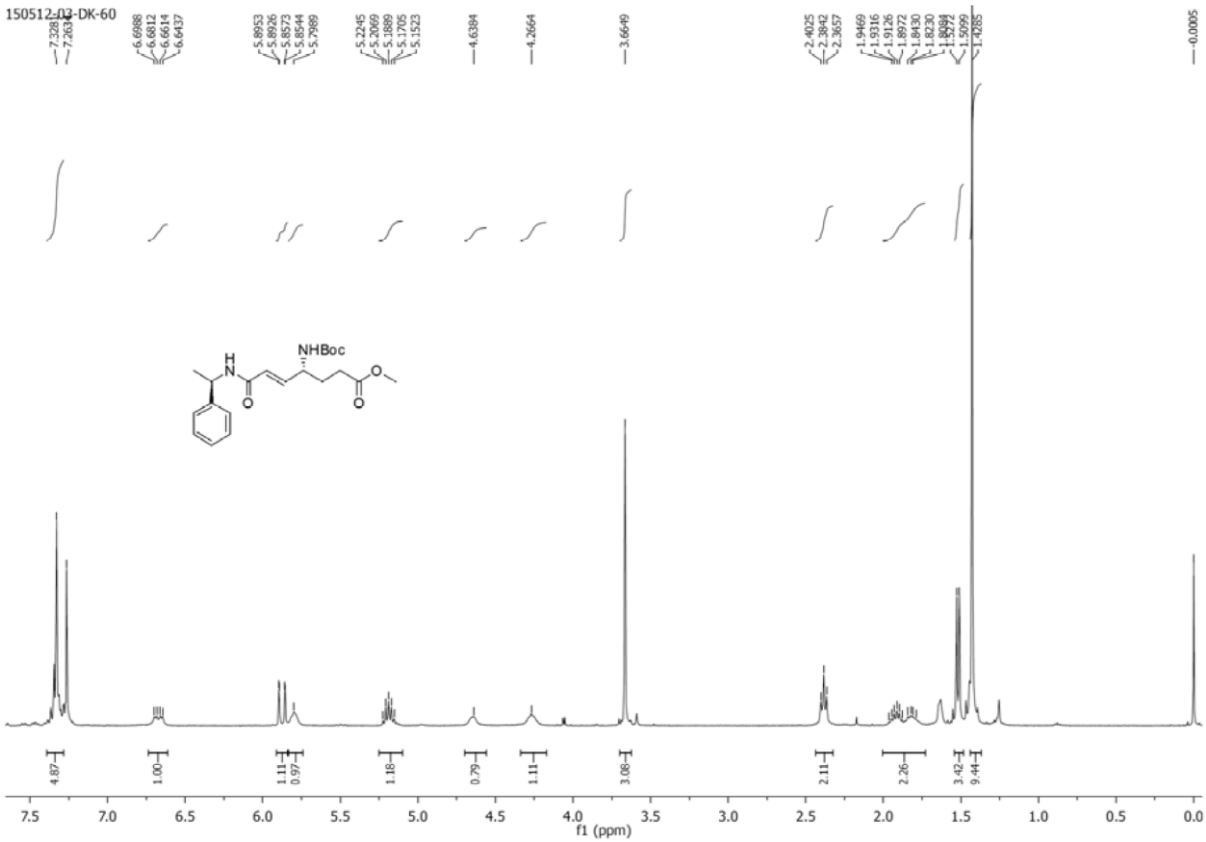


Fig. S23 ^{1}H NMR spectra of **14a-*R*** in $CDCl_3$.

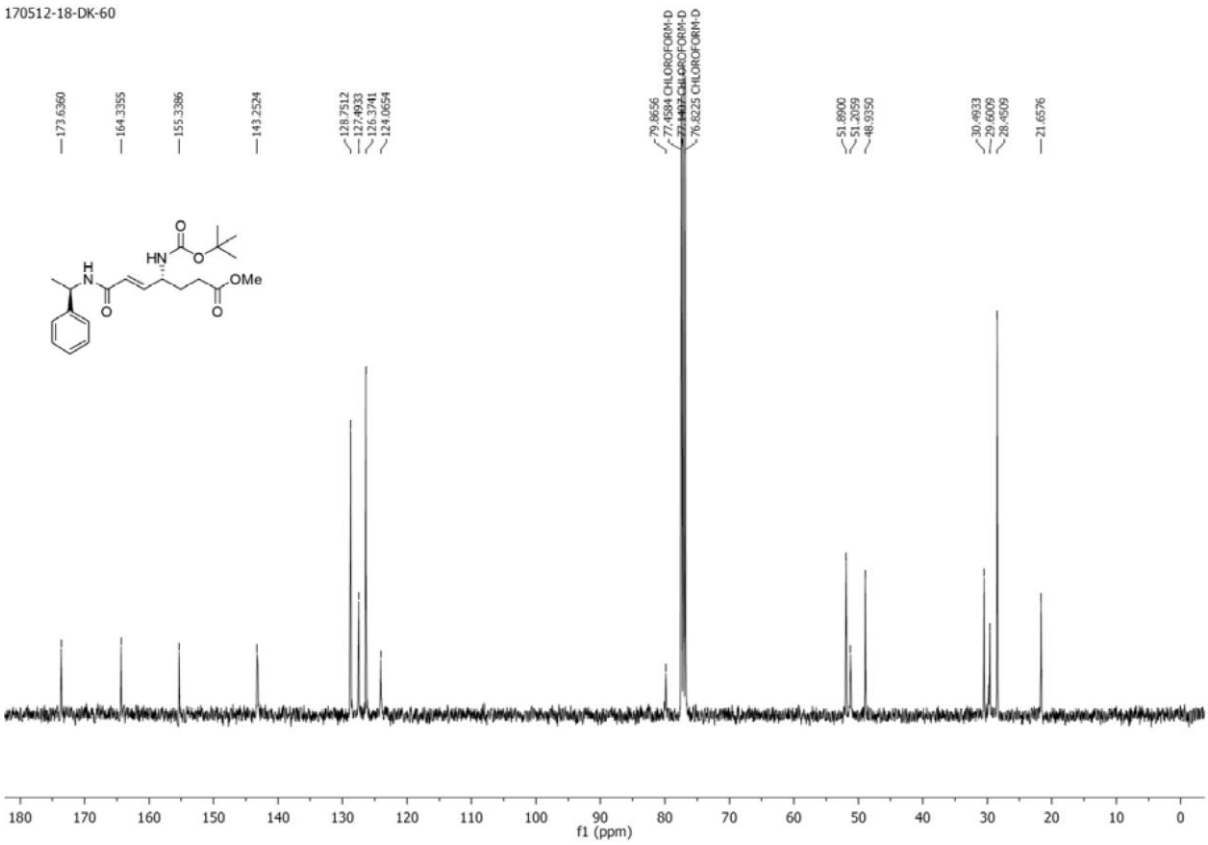


Fig. S24 ^{13}C NMR spectra of **14a-*R*** in $CDCl_3$.

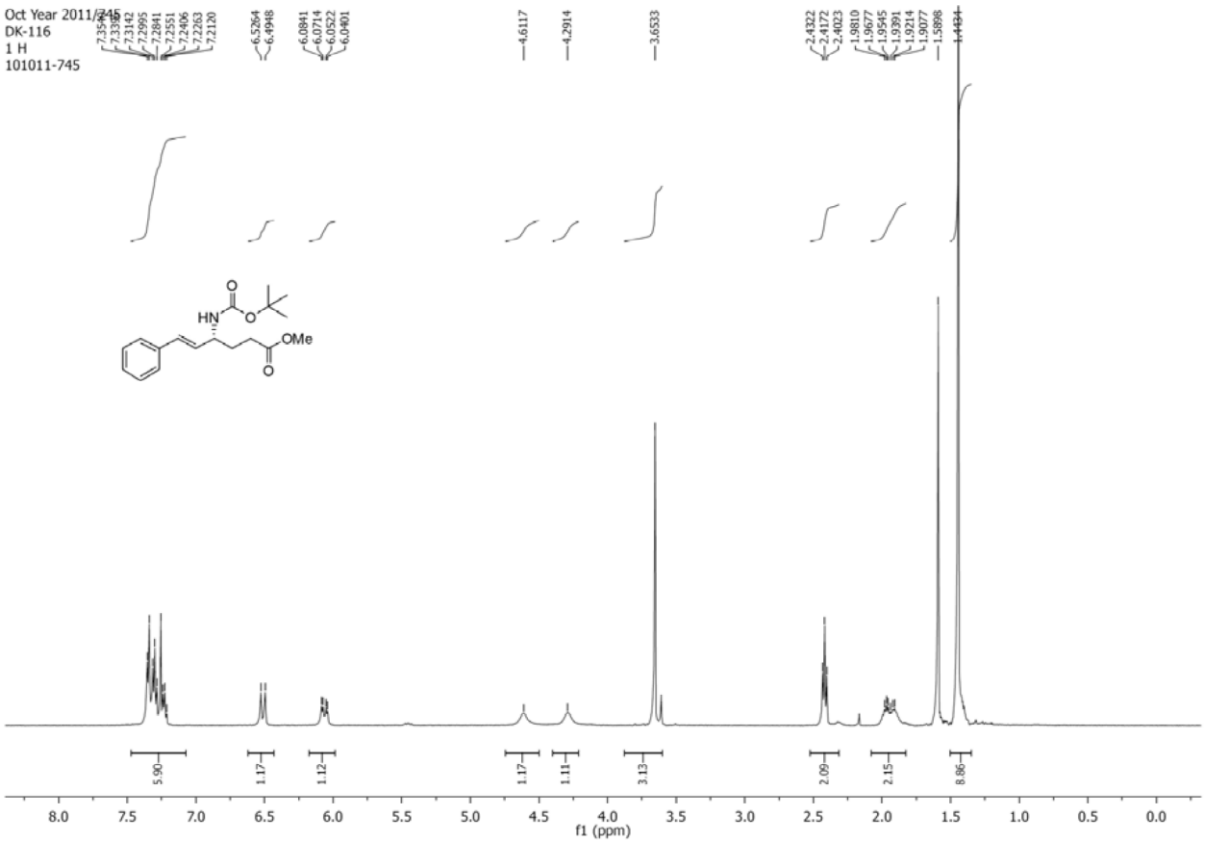


Fig. S25 ^{1}H NMR spectra of **14b-*R*** in $CDCl_3$.

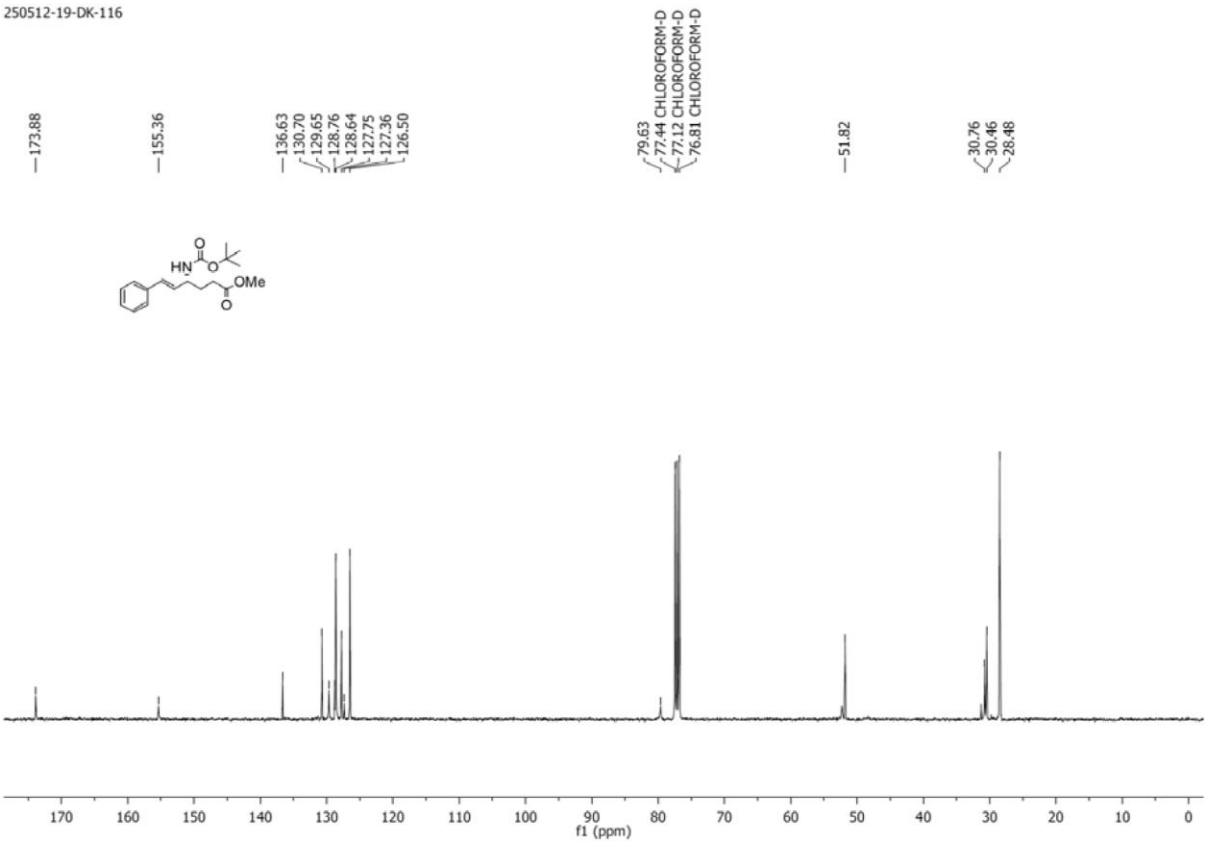


Fig. S26 ^{13}C NMR spectra of **14b-*R*** in $CDCl_3$.

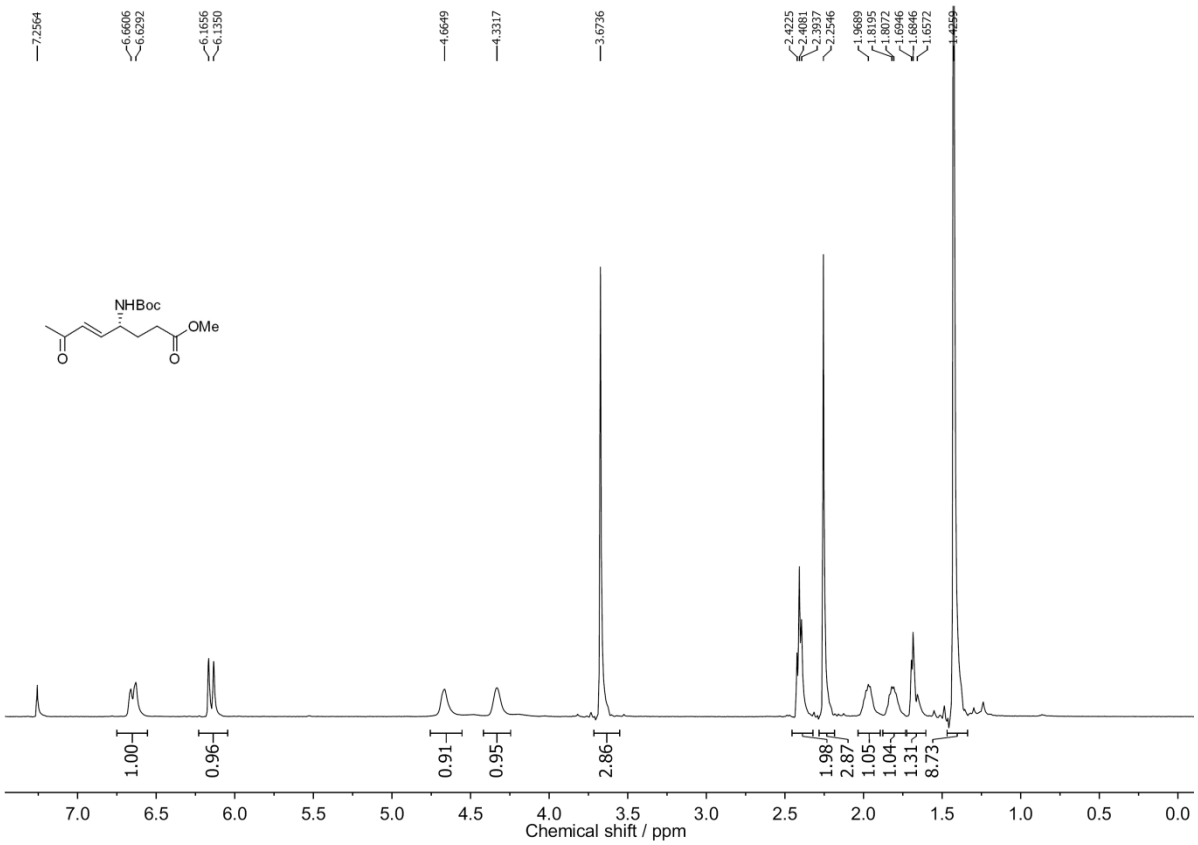


Fig. S27 ^{1}H NMR spectra of **14c-*R*** in $CDCl_3$.

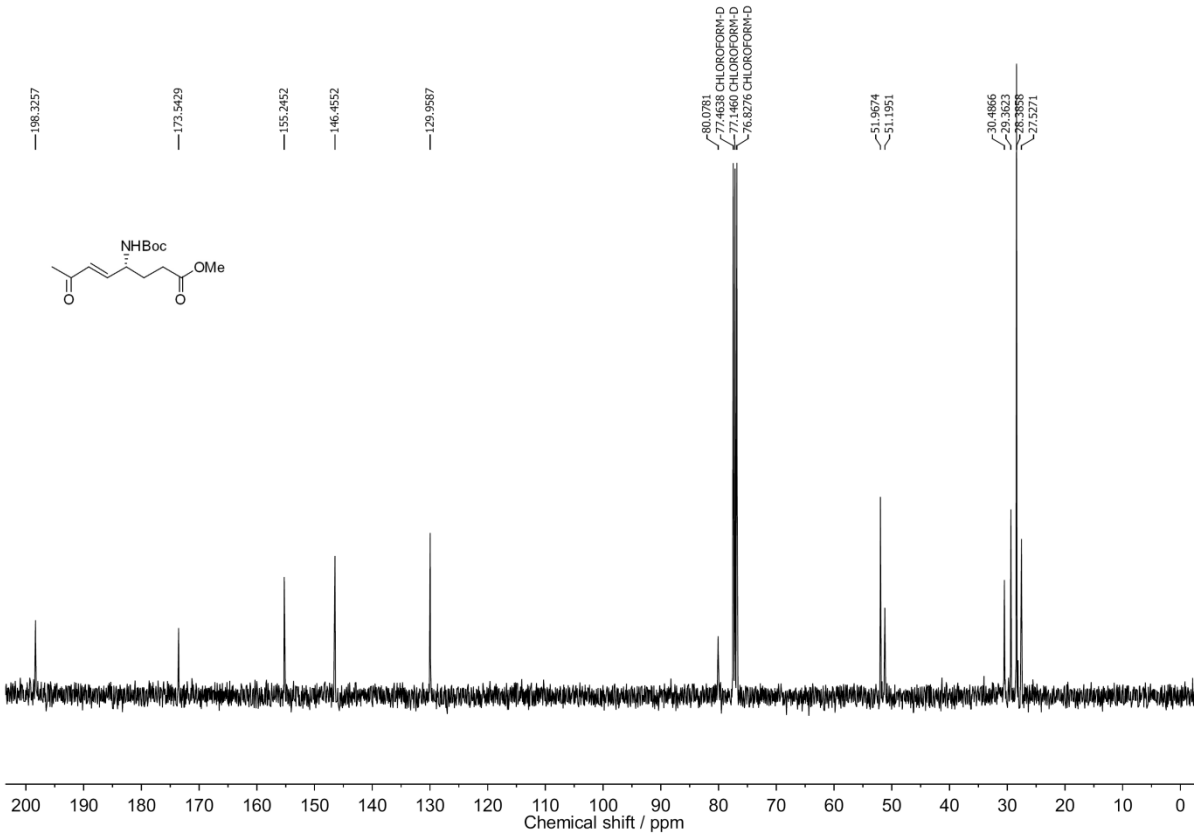


Fig. S28 ^{13}C NMR spectra of **14c-*R*** in $CDCl_3$.

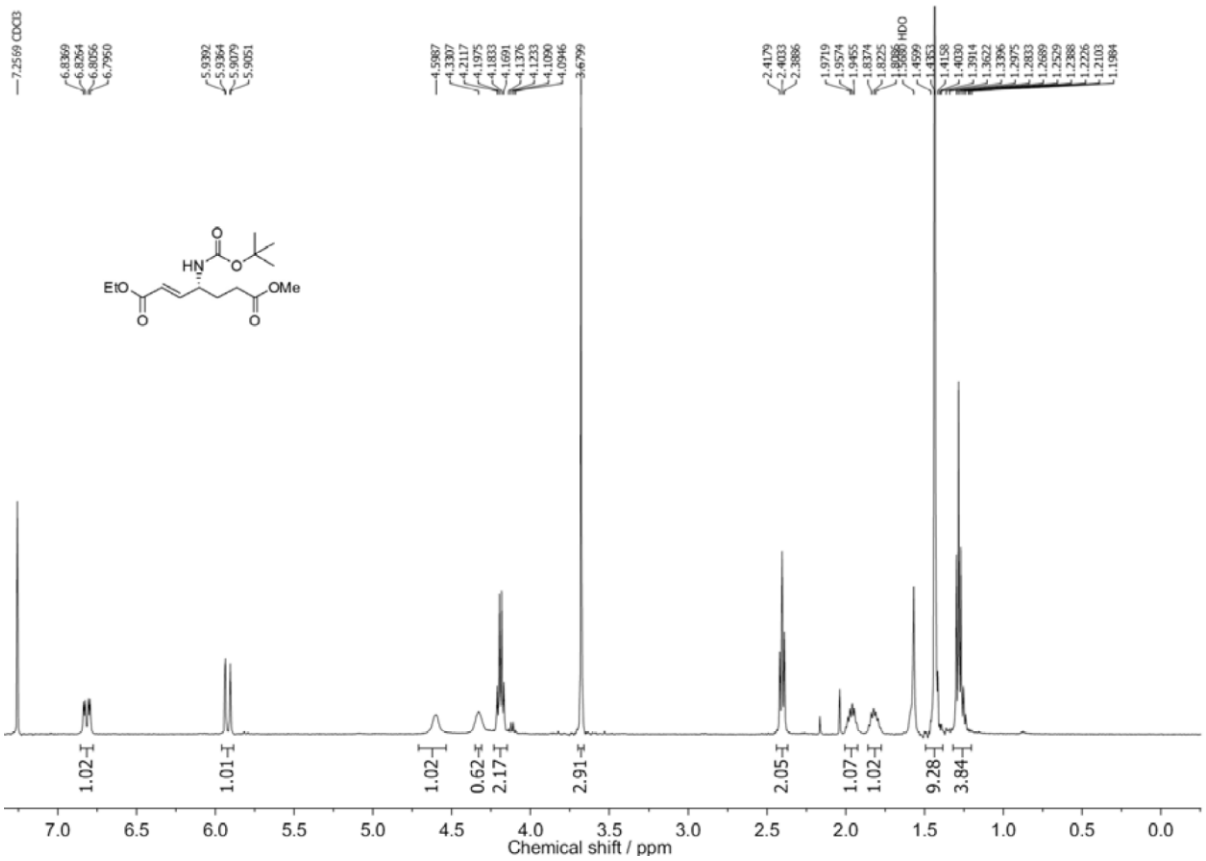


Fig. S29 ^{1}H NMR spectra of **14d-*R*** in $CDCl_3$.

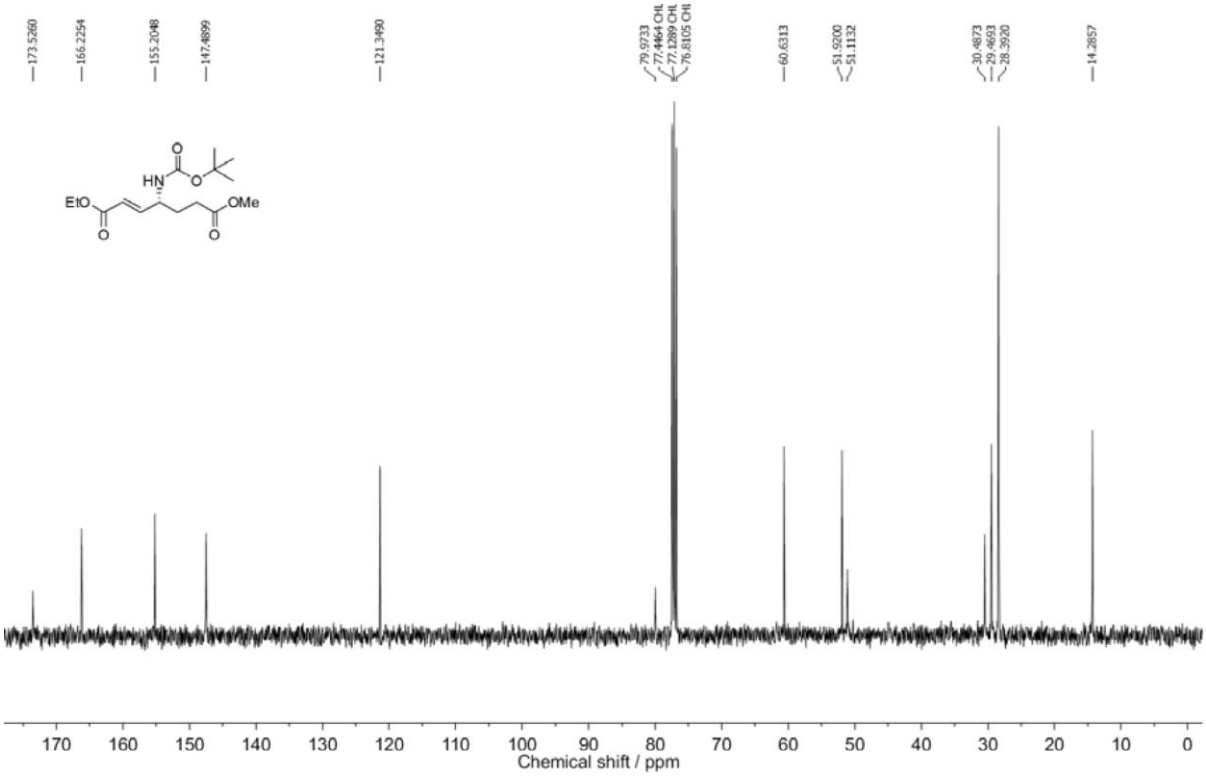


Fig. S30 ^{13}C NMR spectra of **14d-*R*** in $CDCl_3$.

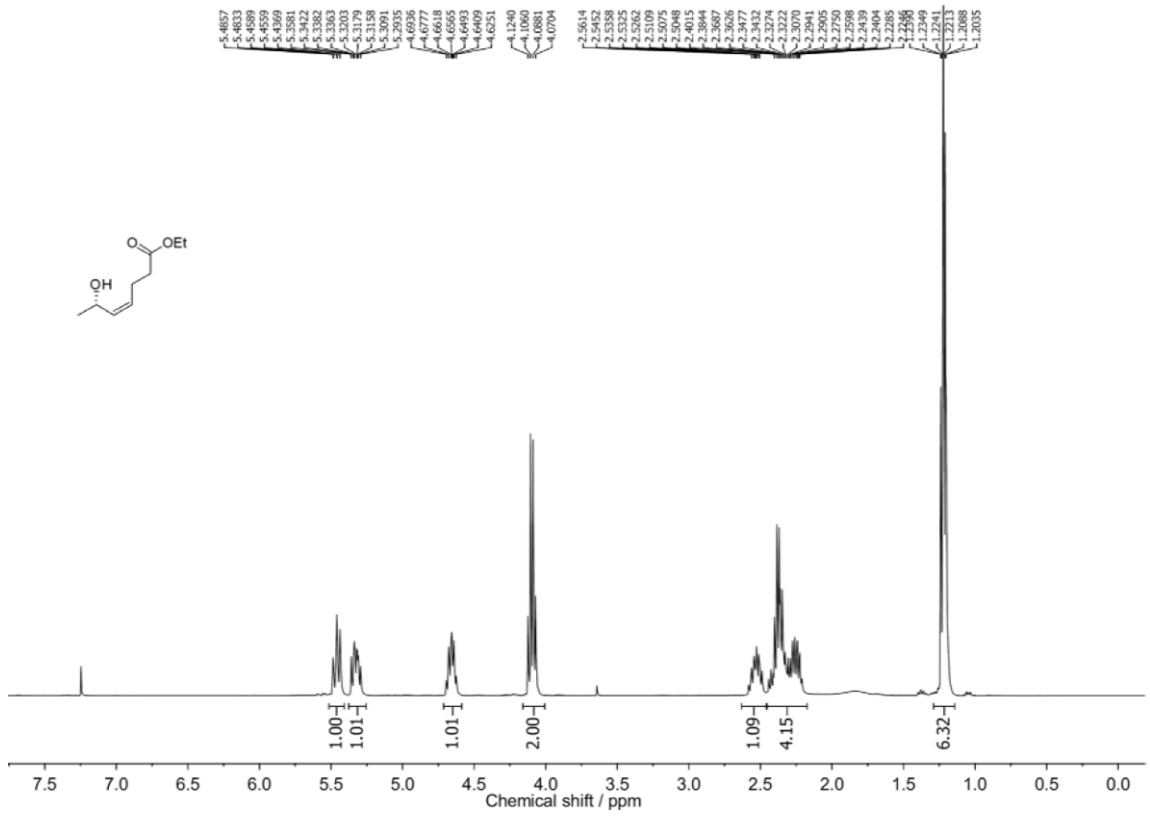


Fig. S31. ^{1}H NMR spectra of **7-*Z*** in $CDCl_3$.

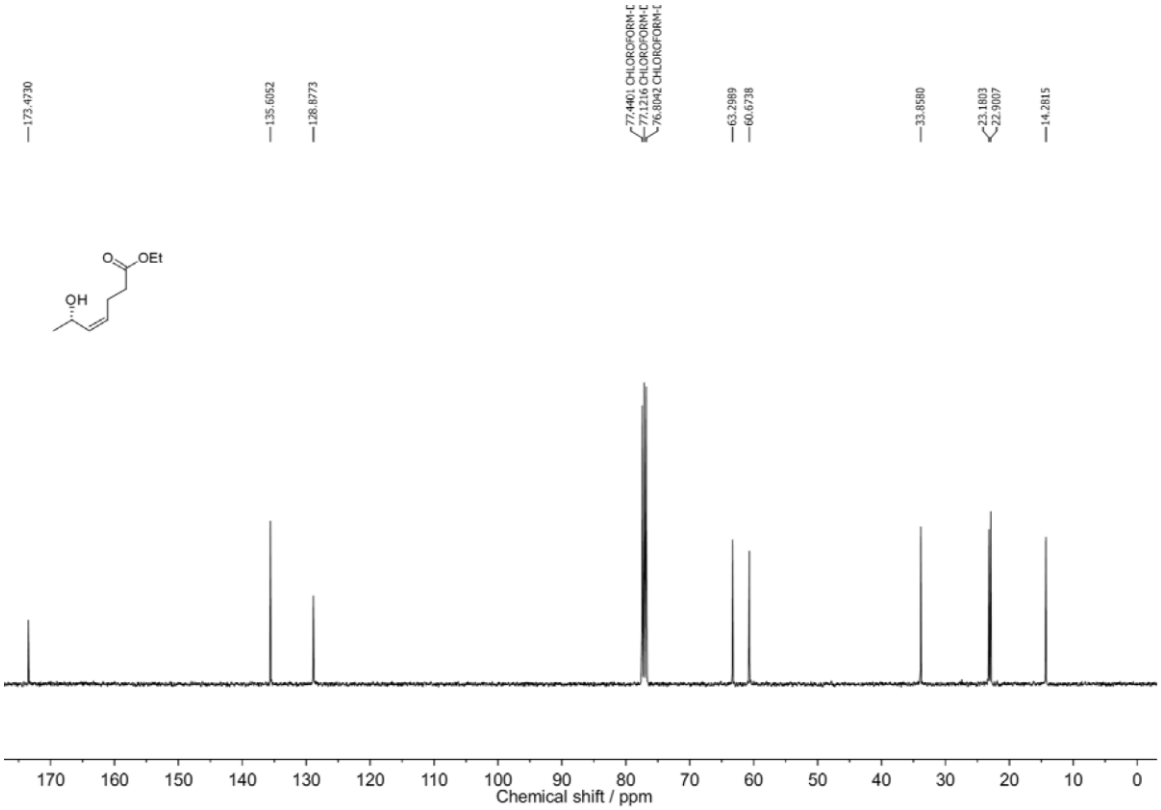


Fig. S32 ^{13}C NMR spectra of **7-*Z*** in $CDCl_3$.

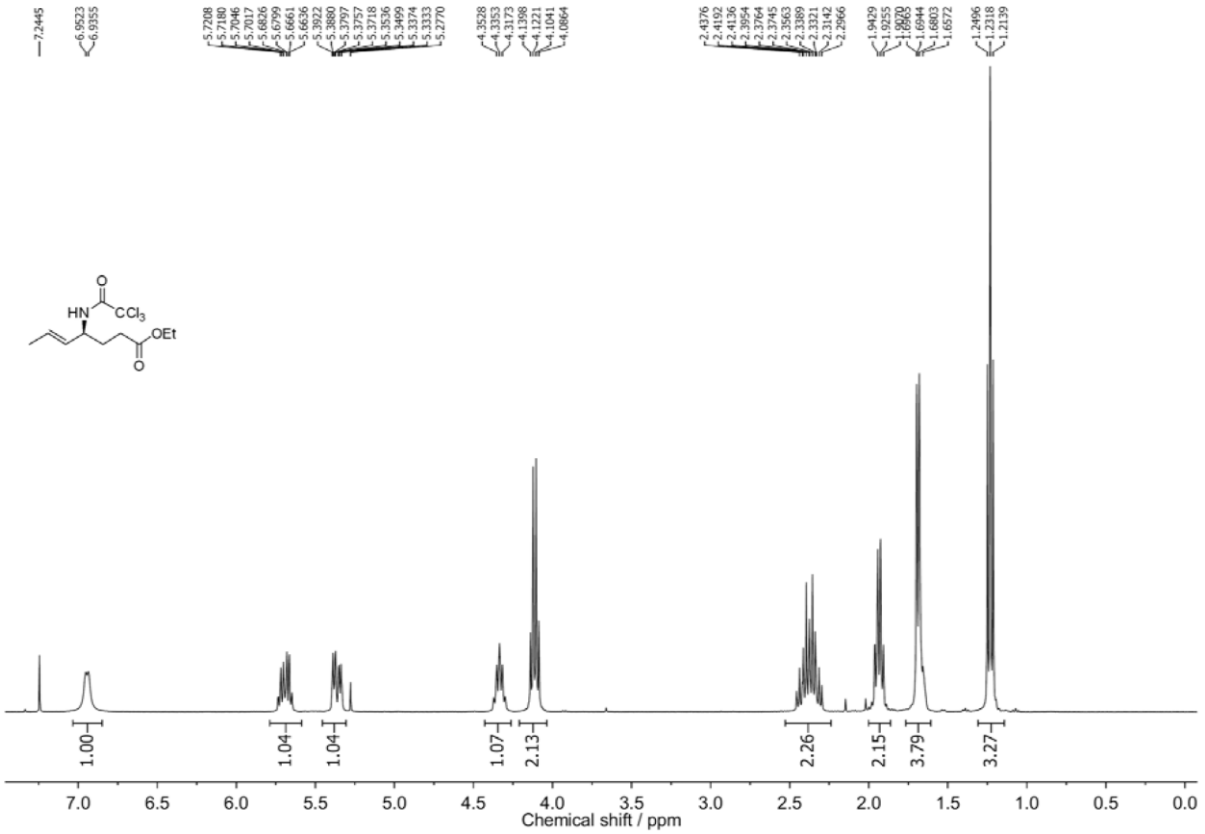


Fig. S33 ^{1}H NMR spectra of **8-*S*** in $CDCl_3$.

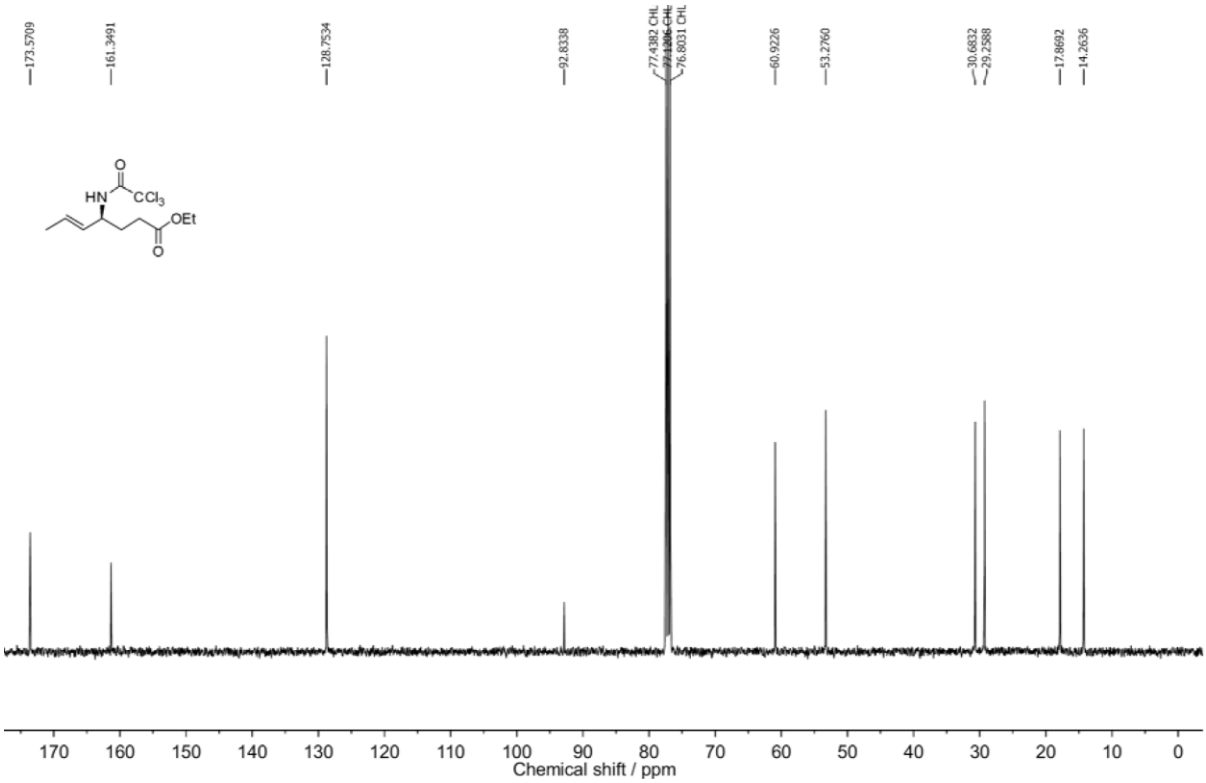


Fig. S34 ^{13}C NMR spectra of **8-*S*** in $CDCl_3$.

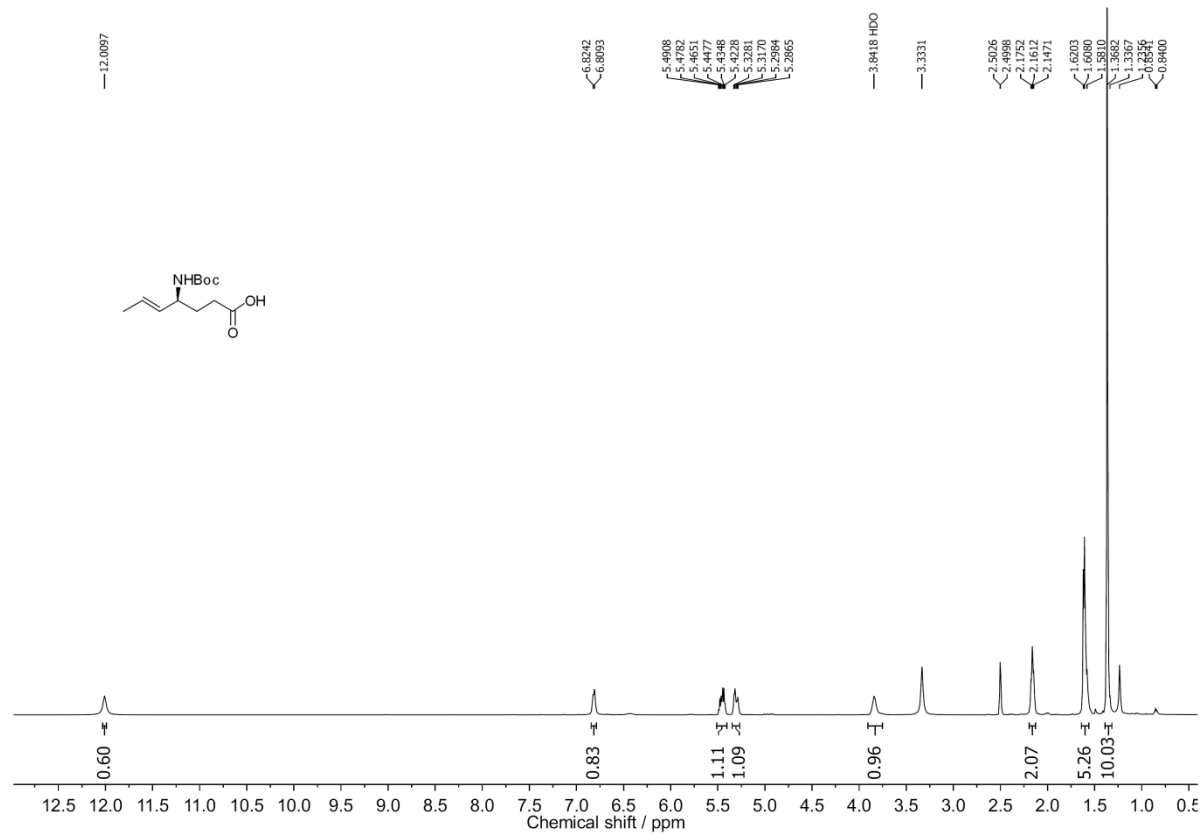


Fig. S35 ^{1}H NMR spectra of **9-*S*** in DMSO-d_6.

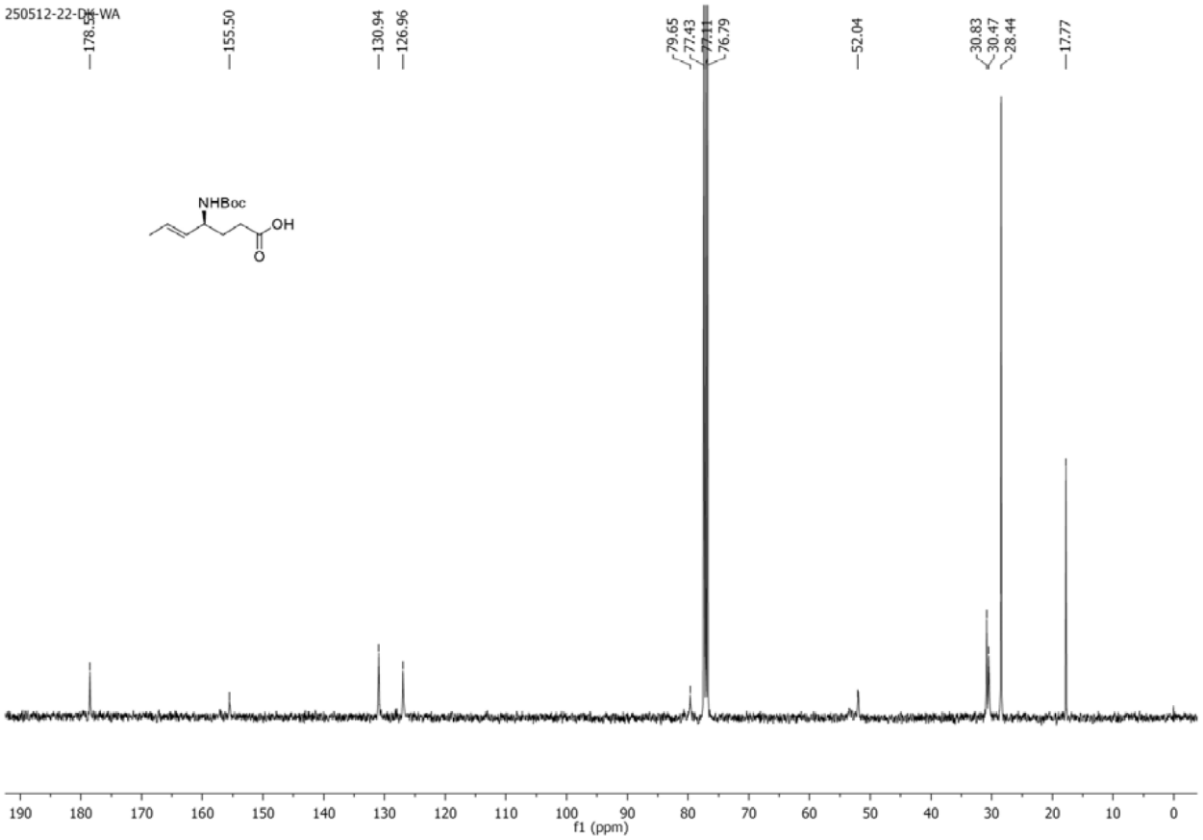


Fig. S36 ^{13}C NMR spectra of **9-*S*** in $CDCl_3$.

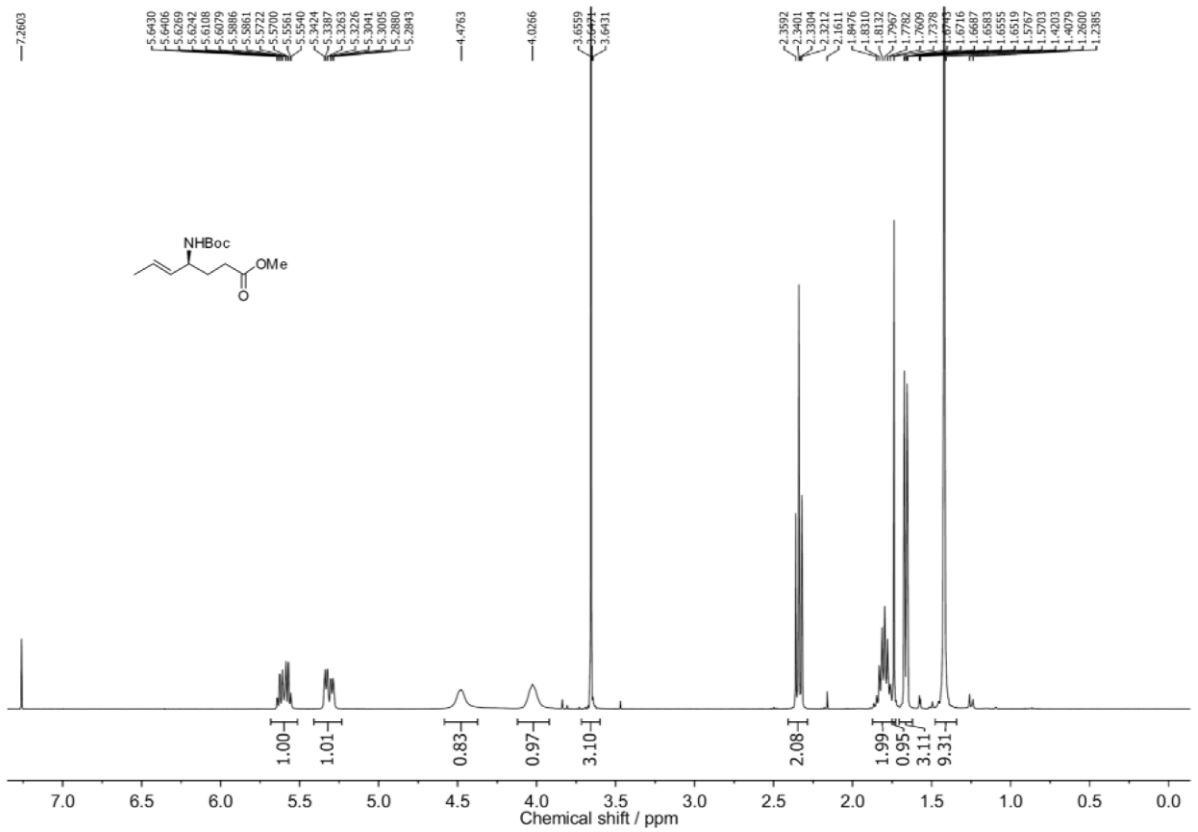


Fig. S37 ^{1}H NMR spectra of **10-*S*** in $CDCl_3$.

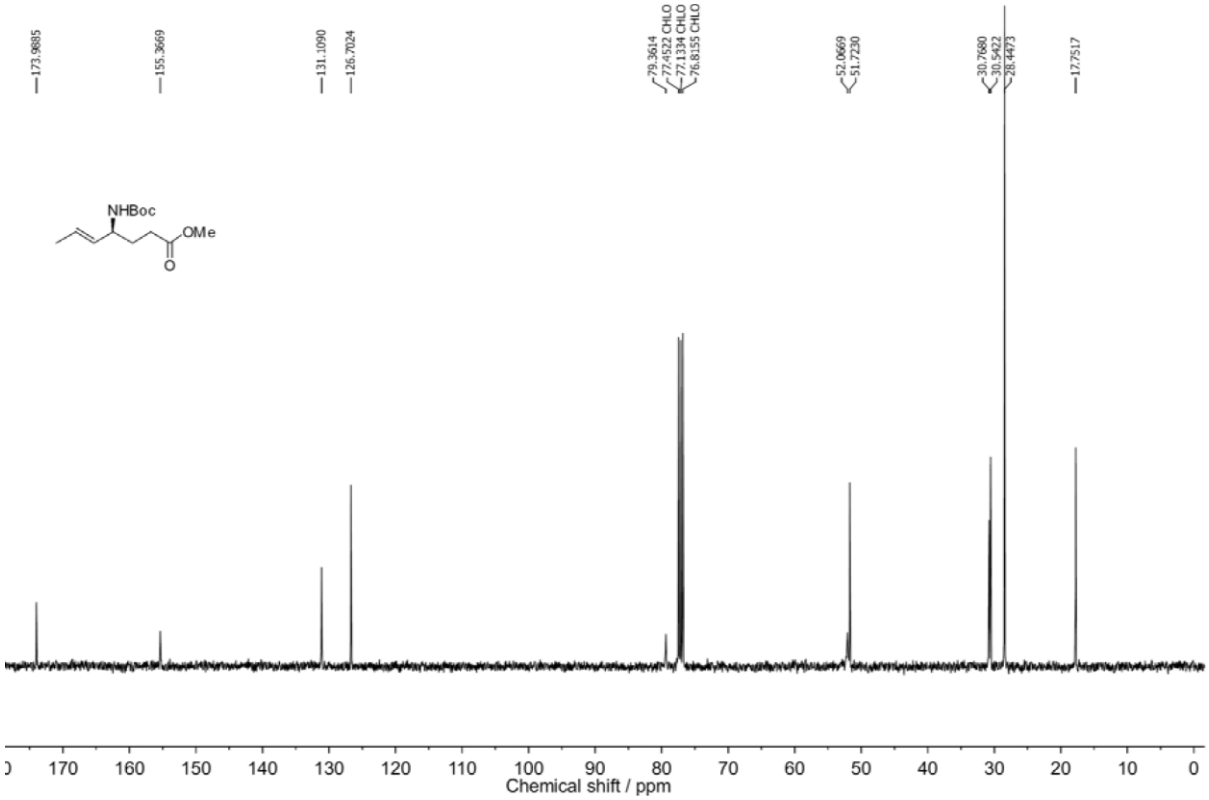


Fig. S38 ^{13}C NMR spectra of **10-*S*** in $CDCl_3$.

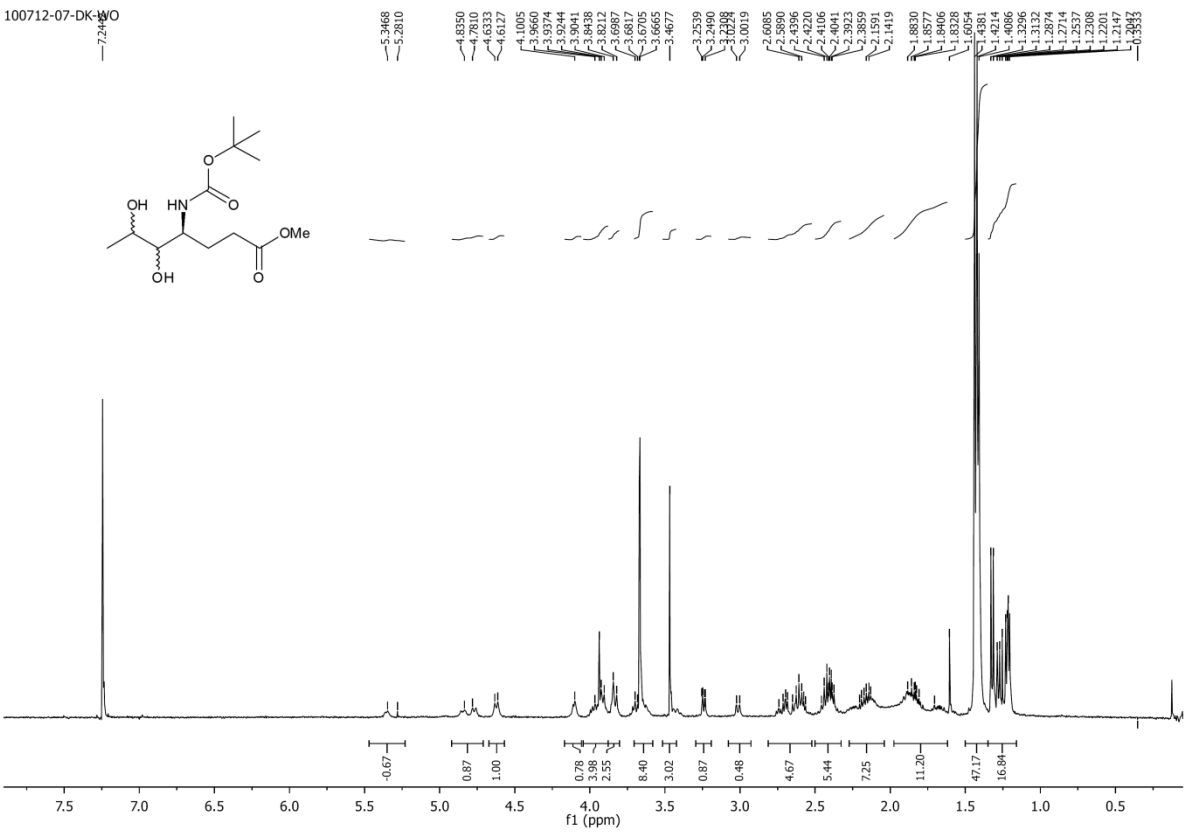


Fig. S39 ^{1}H NMR spectra of **11-*S*** in $CDCl_3$.

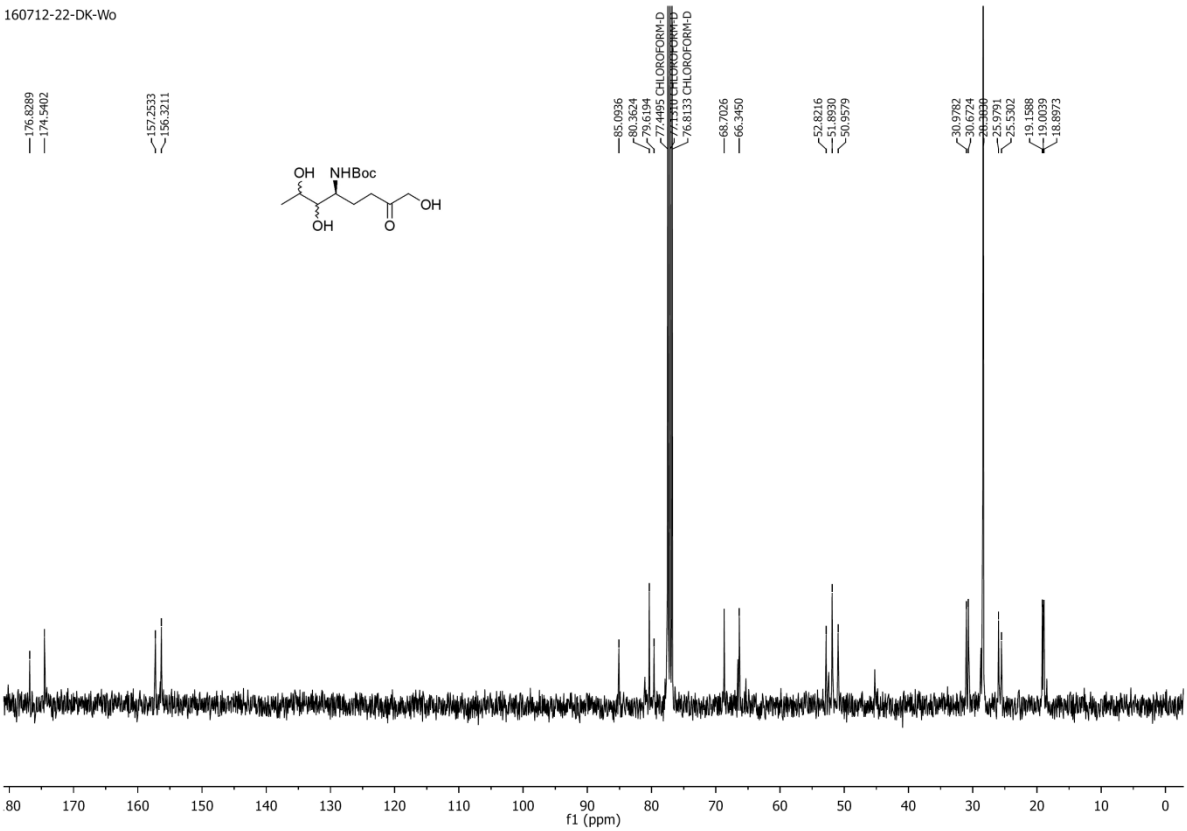


Fig. S40 ^{13}C NMR spectra of **11-*S*** in $CDCl_3$.

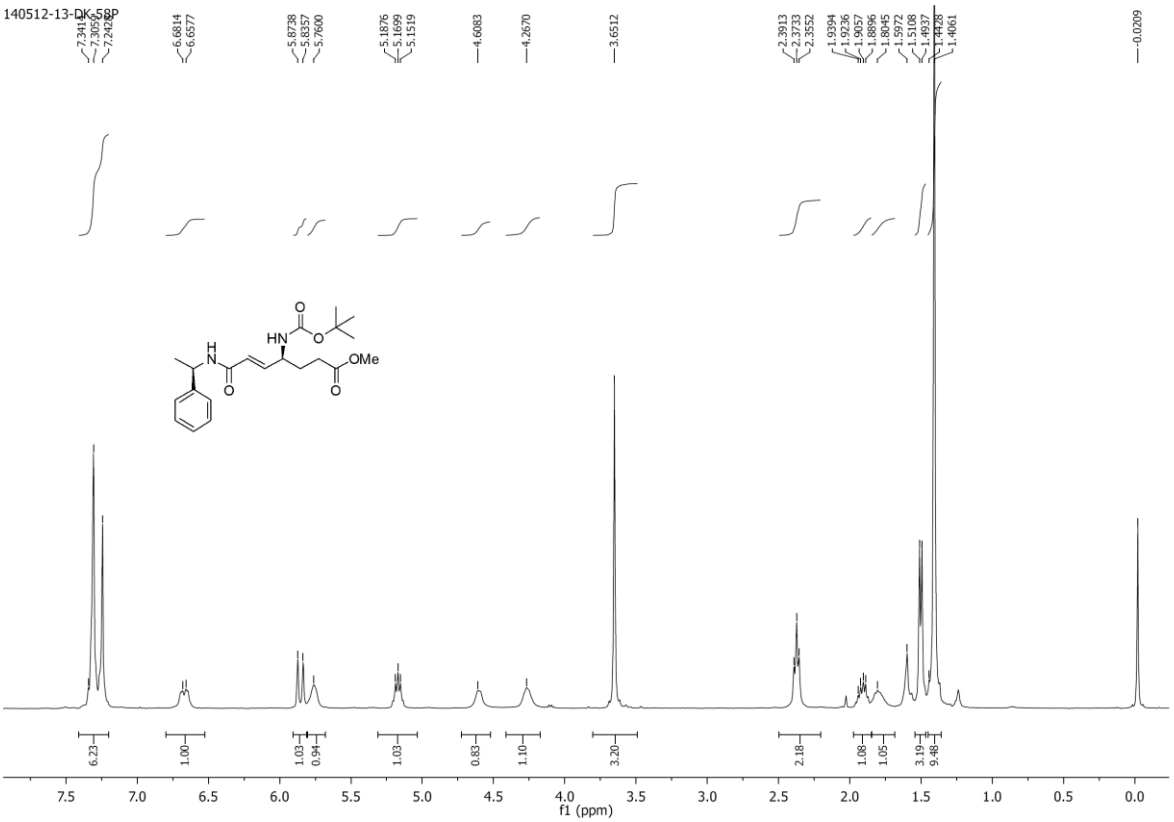


Fig. S41 ^{1}H NMR spectra of **14a-*S*** in $CDCl_3$.

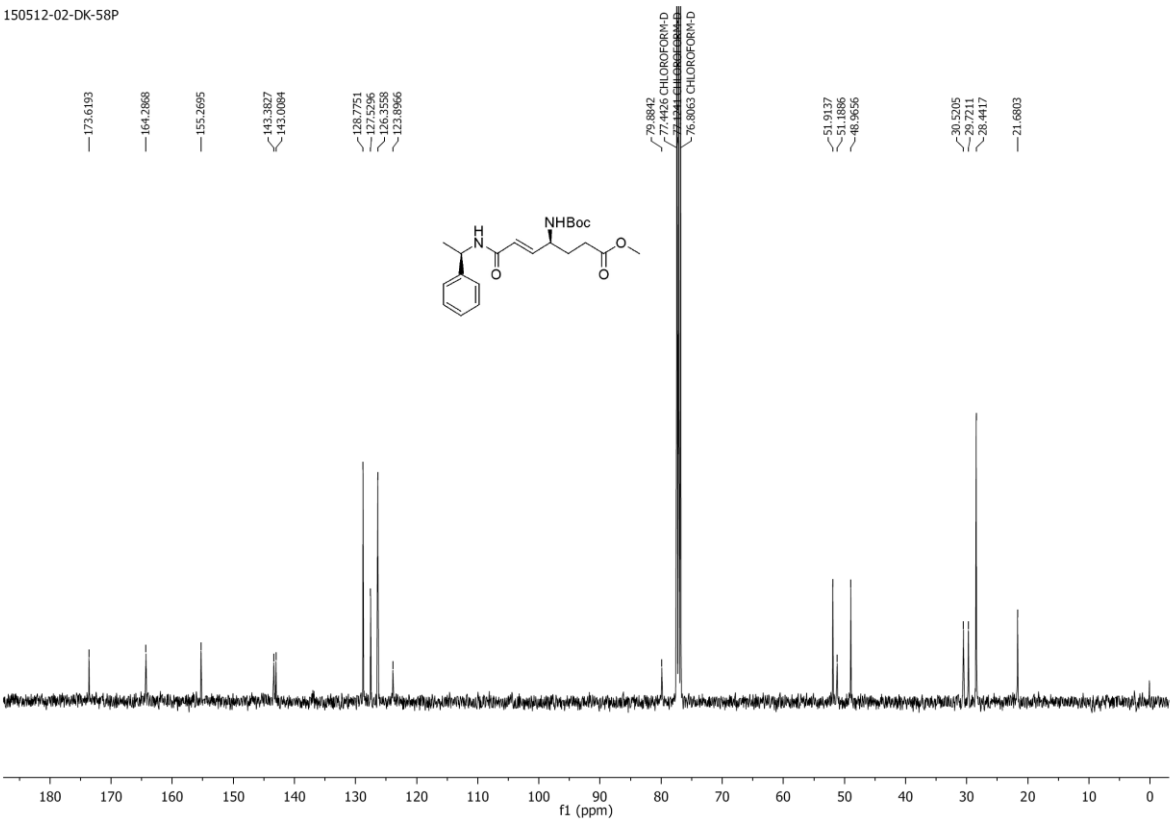


Fig. S42 ^{13}C NMR spectra of **14a-*S*** in $CDCl_3$.

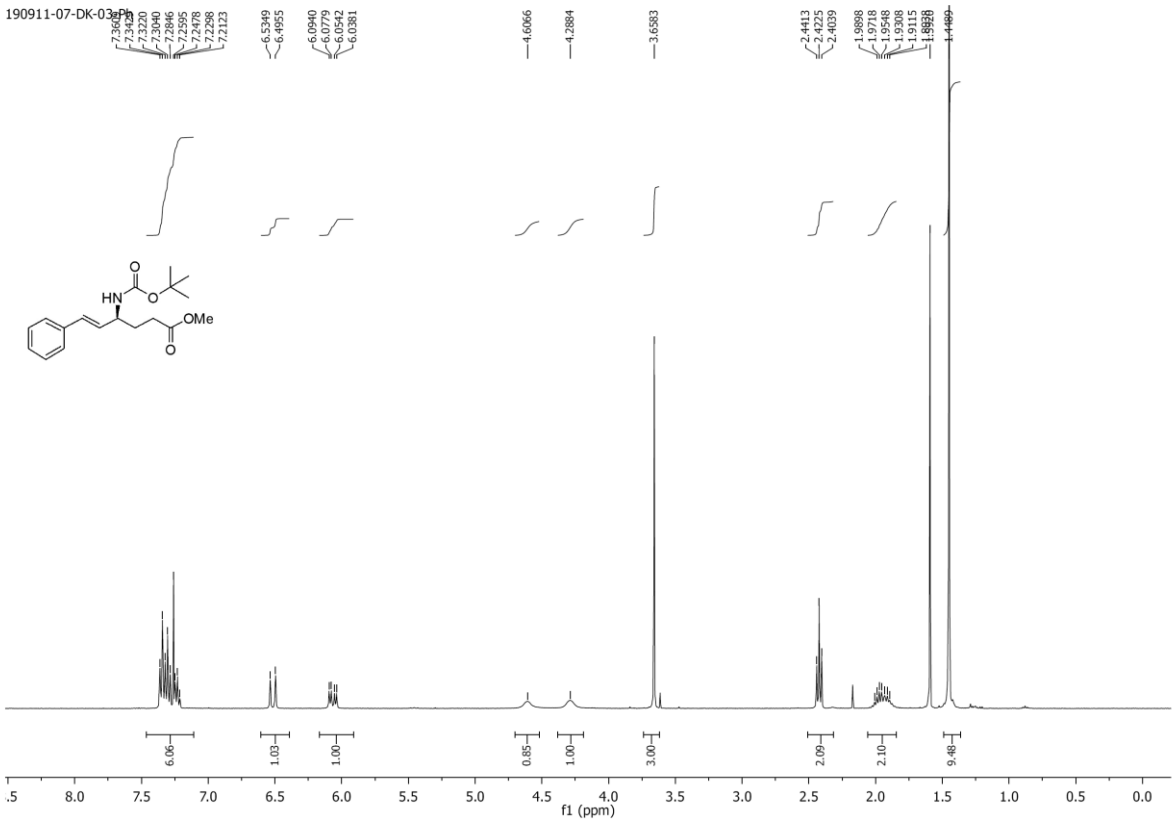


Fig. S43 ^{1}H NMR spectra of **14b-*S*** in $CDCl_3$.

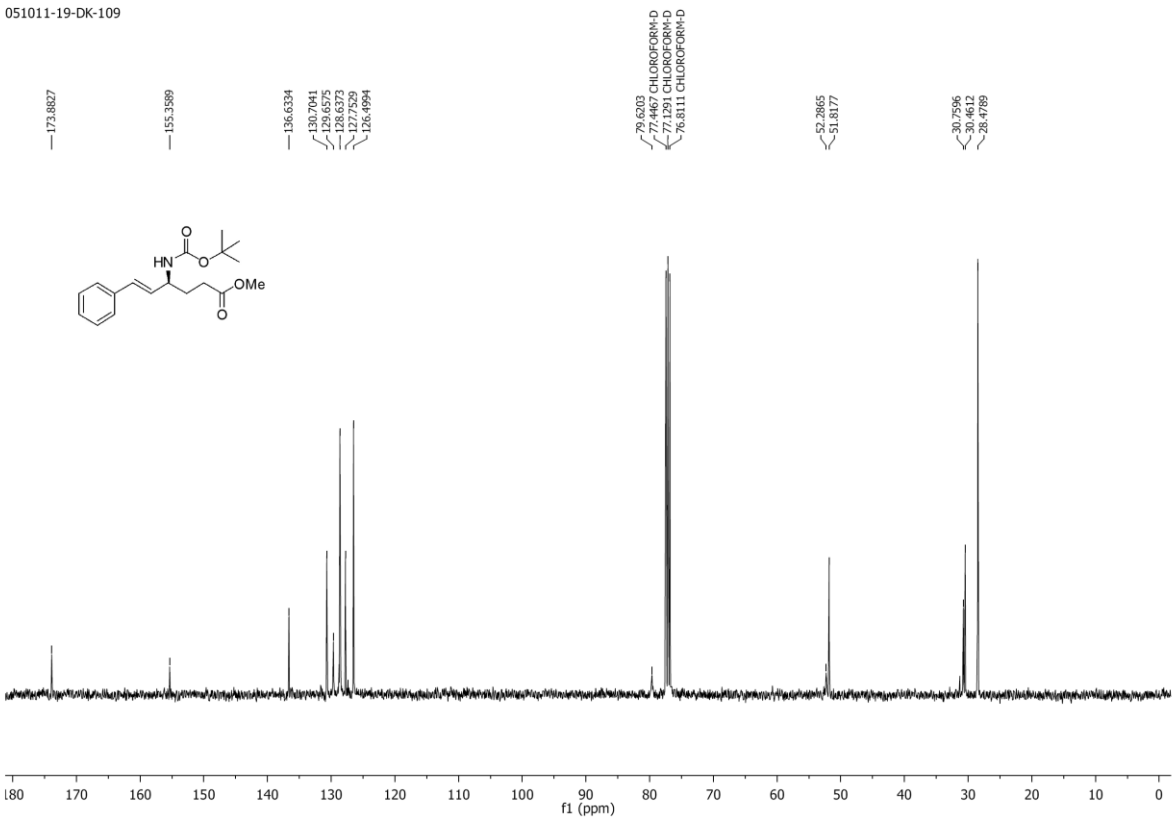


Fig. S44 ^{13}C NMR spectra of **14b-*S*** in $CDCl_3$.

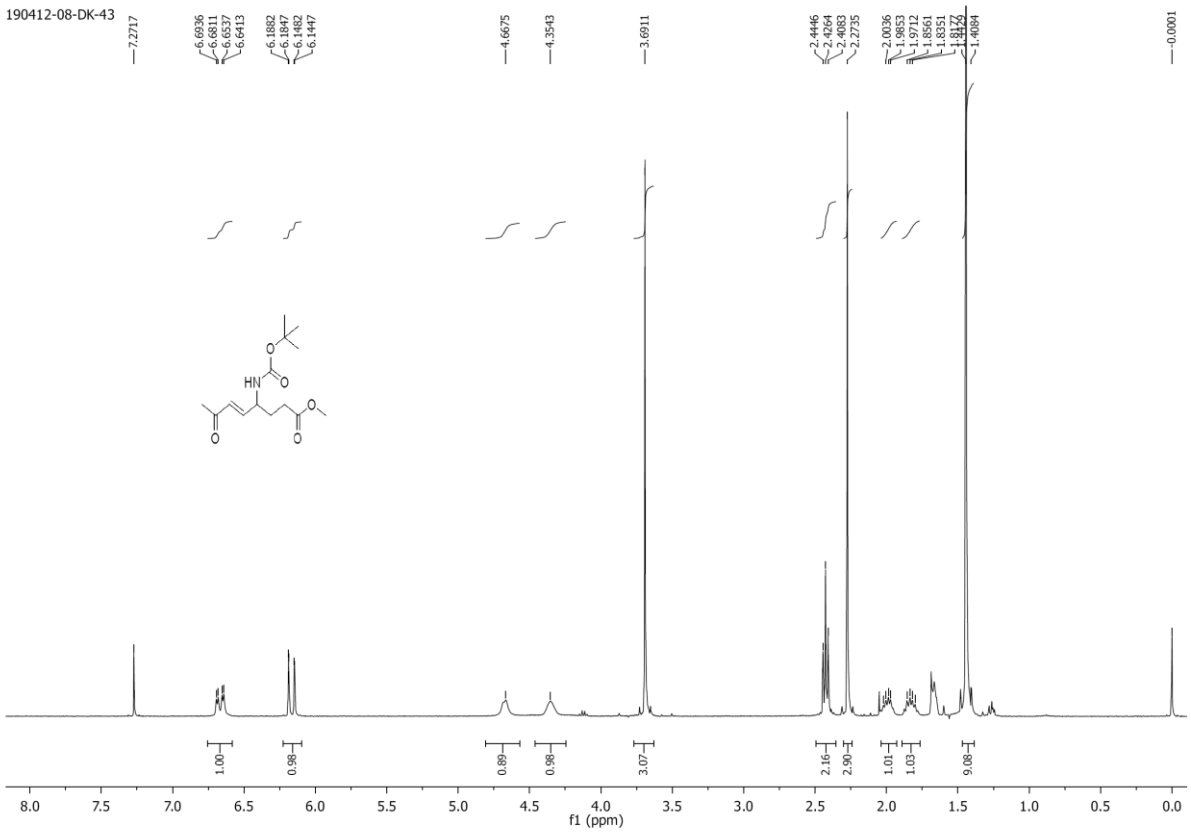


Fig. S45 ^{1}H NMR spectra of **14c-*S*** in $CDCl_3$.

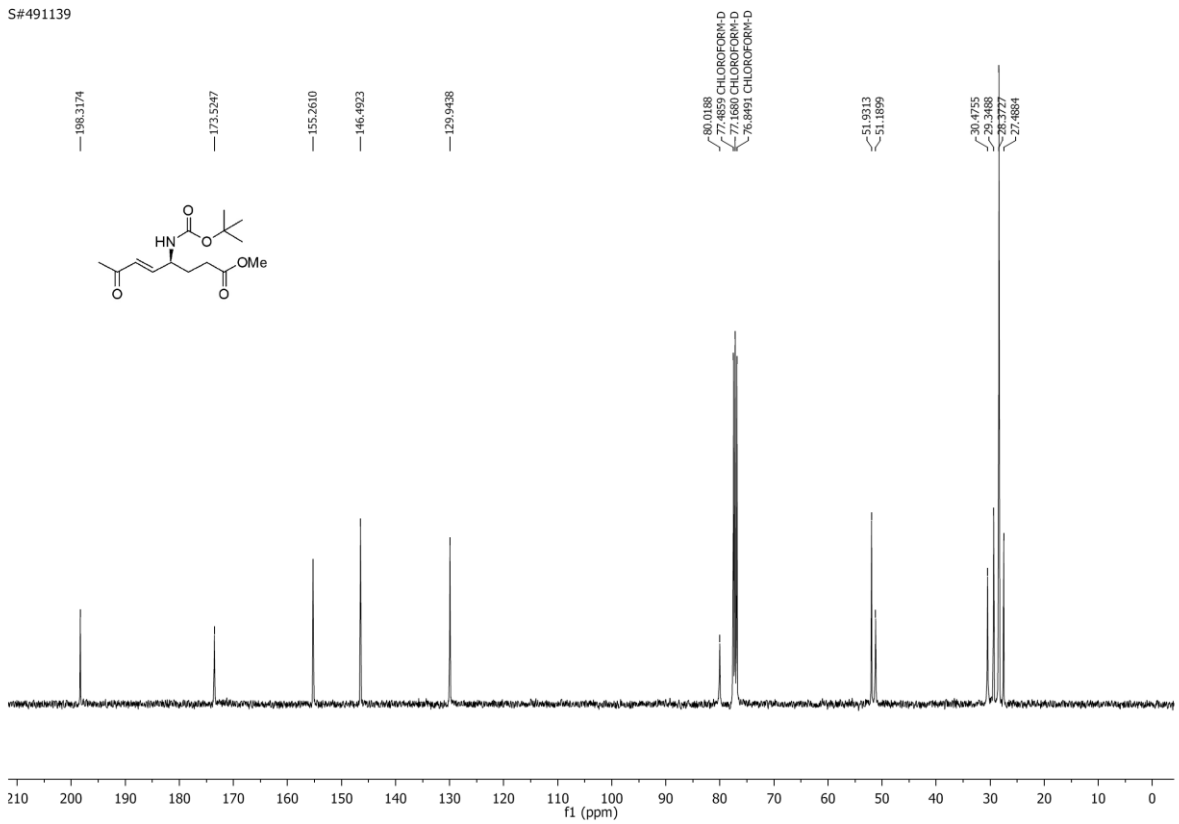


Fig. S46 ^{13}C NMR spectra of **14c-*S*** in $CDCl_3$.

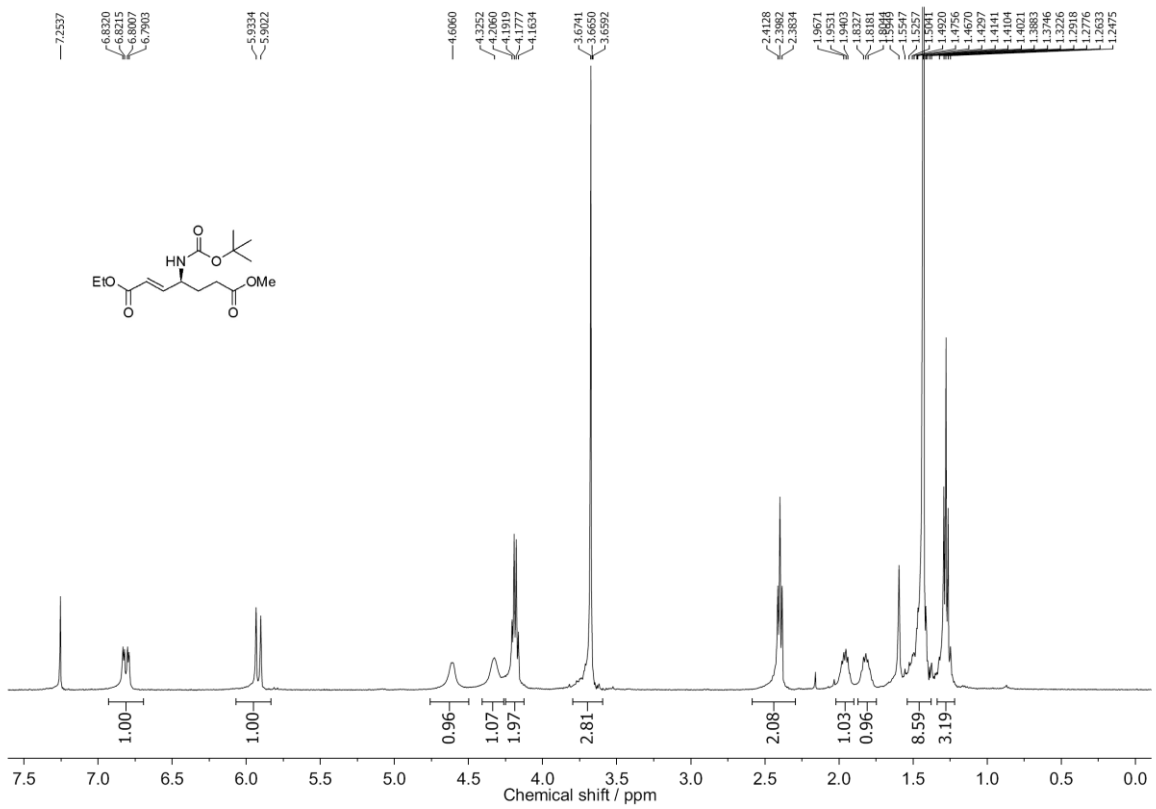


Fig. S47 ^{1}H NMR spectra of **14d-*S*** in $CDCl_3$.

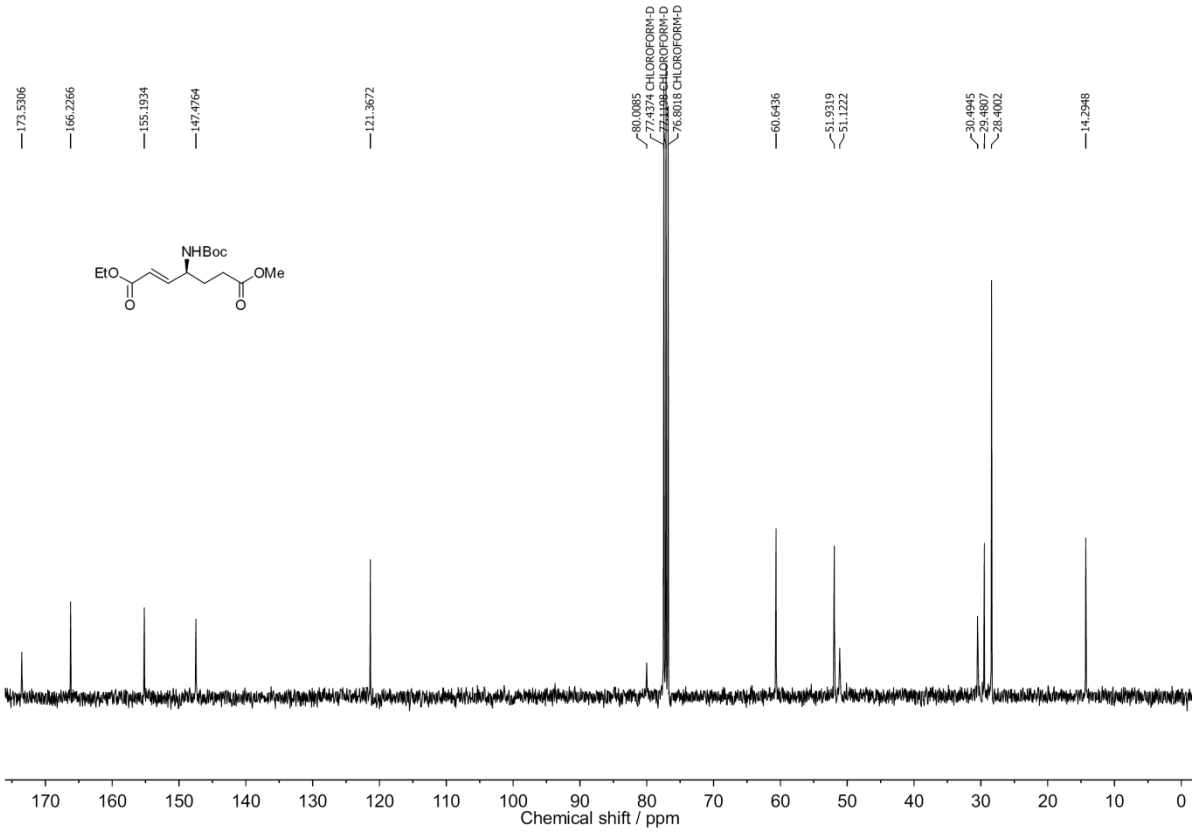


Fig. S48 ^{13}C NMR spectra of **14d-*S*** in $CDCl_3$.

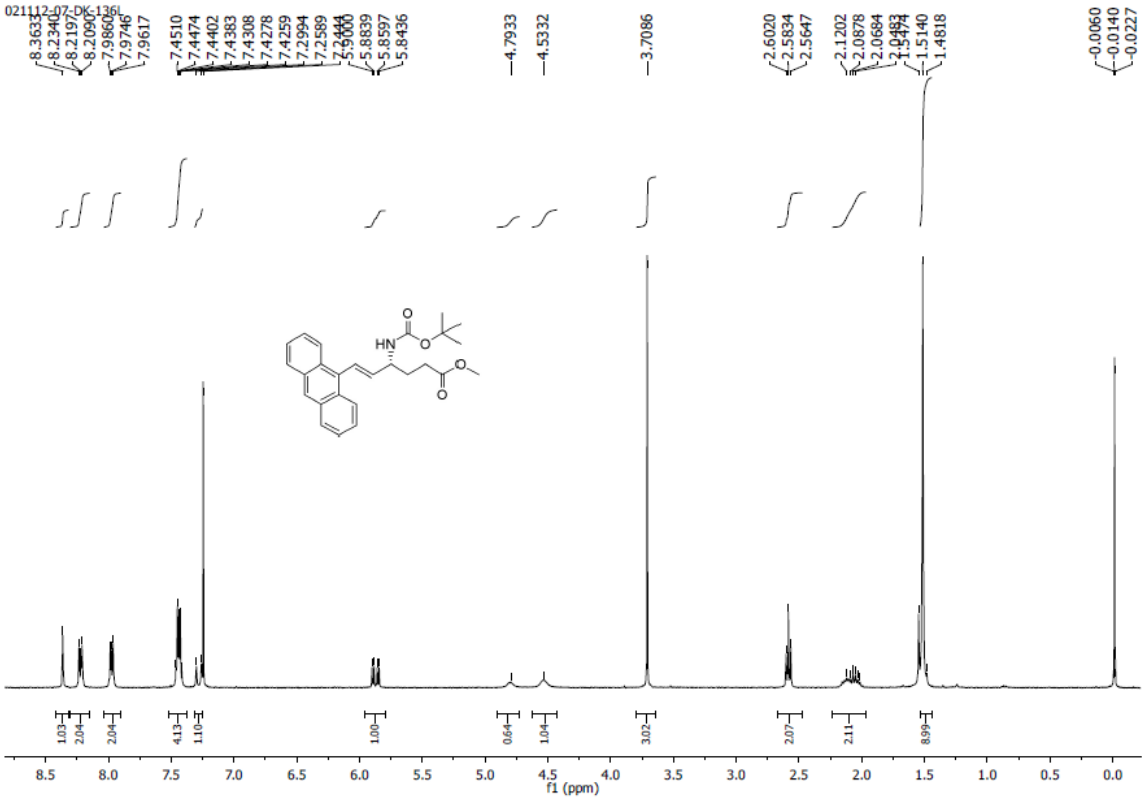


Fig. S49 ^{1}H NMR spectra of **14e-*R*** in $CDCl_3$.

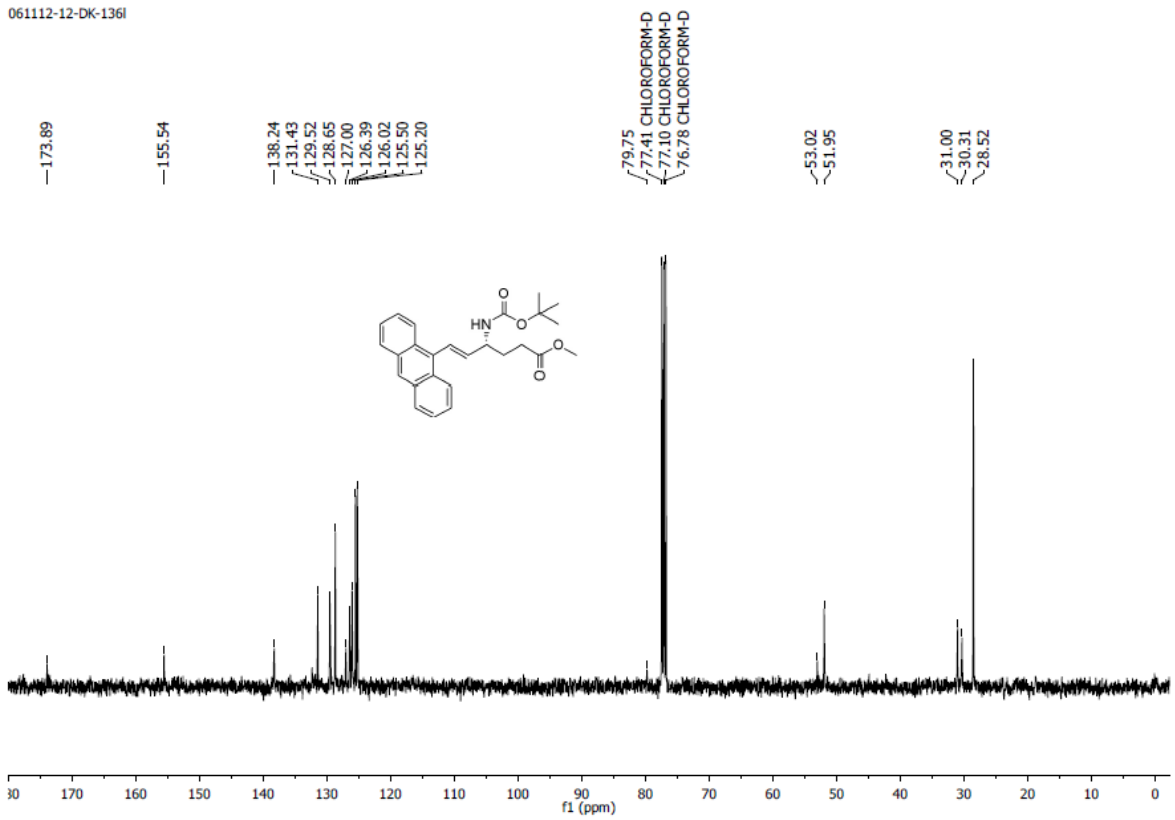


Fig. S50 ^{13}C NMR spectra of **14e-*R*** in $CDCl_3$.

VIII. References.

S1. Bratt, K.; Garavelas, A.; Perlmutter, P.; Westman, G. *J. Org. Chem.* **1996**, *61*, 2109.
S2. Nishikimi, Y.; Iimori, T.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1989**, *54*, 3354.
S3. SHELXS-97: (a) Sheldrick, G. M. *Acta Crystallogr., Sect. A: Found. Crystallogr.*, **1990**, *46*, 467. (b) Sheldrick, G. M. *SHELXL-97*, *Universität Göttingen (Germany)*, **1997**.