

# Highly Stereoselective *Anti*-S<sub>N</sub>2'-Substitutions of (*Z*)-Allylic Pentafluorobenzoates with Polyfunctionalized Zinc-Copper Reagents

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## Supporting Information

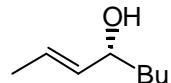
### General Considerations:

All NMR spectra were run in CDCl<sub>3</sub> and referenced to the solvent peak (CDCl<sub>3</sub>: <sup>13</sup>C NMR,  $\delta$  77.0; <sup>1</sup>H NMR,  $\delta$  7.26). The oil pump vacuum was 2.1 mbar. The concentrations of diorganozinc reagent solutions, where stated, were determined by reaction with iodine and back titration with aqueous sodium thiosulfate.

### Experimental:

#### Preparation of (1*R*, 2*E*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-*E*-4)

##### a) (2*E*, 4*R*)-2-Octen-4-ol<sup>1</sup>



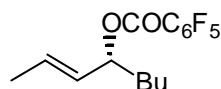
*n*-BuLi (1.6 M in hexane; 42 mL, 67 mmol) was added dropwise over 50 min to a stirred solution at -78 °C under an argon atmosphere of crotonaldehyde (5 mL, 60 mmol) in THF (100 mL) and the mixture was allowed to warm slowly to -30 °C over 4.5 h. Water was added to quench the reaction, followed by acidification with 1 M HCl, and the mixture was stirred. The phases were then separated and the aqueous phase was extracted once with Et<sub>2</sub>O. The combined organic layers were washed with saturated, aqueous NaHCO<sub>3</sub> solution, then with brine, and dried (MgSO<sub>4</sub>). Evaporation of the solvents *in vacuo* provided a yellow liquid, which was distilled under vacuum (ca. 10 mbar; 65 °C) yielding the racemic alcohol (6.55 g, 85 %) as a colourless liquid. The racemic allylic alcohol was kinetically resolved<sup>1</sup> as follows. (*E*)-2-Octen-4-ol (1.01 g, 7.9 mmol), (+)-dicyclo-dodecyltartrate (DCDT) (570 mg, 1.2 mmol) and *n*-decane (0.3 mL) were stirred with freshly activated, powdered 4 Å molecular sieves in dry CH<sub>2</sub>Cl<sub>2</sub> (25 mL) at rt under an argon atmosphere for 20 min. The mixture was then cooled to -20 °C and treated with titanium isopropoxide (0.23 mL, 0.8 mmol), then stirred 1.25 h at this temperature. An aliquot was taken as a sample for GC-analysis. The mixture was then treated with a solution of *t*-BuOOH (5-6 M in nonane; 1.0 mL) in dry CH<sub>2</sub>Cl<sub>2</sub> (5 mL) which had been stirred at rt with powdered 4 Å molecular sieves for 1 h. The reaction mixture was stirred at -20 °C for 3 h (monitored by GC to > 50 % conversion), then quenched with 15 mL of an aqueous FeSO<sub>4</sub>-citric acid solution (prepared from 33 g of FeSO<sub>4</sub>·7H<sub>2</sub>O and 11 g of citric acid in 100 mL of water). The resulting mixture was stirred vigorously at rt for 0.5 h, then was extracted twice with CH<sub>2</sub>Cl<sub>2</sub> and the combined extracts were washed with brine and dried (MgSO<sub>4</sub>). Distillation *in vacuo*

(10 mbar, 65 °C) to separate the product from DCDT resulted in ca. 200 mg (1.6 mmol, 20 %) of (2*E*, 4*R*)-2-octen-4-ol.

GC (50 °C; column: TFA  $\gamma$ -cyclodextrin, 30 m, 0.25 mm):  $t_R$ /min = 23.0 (*R*), 24.7 (*S*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.84-0.93 (m, 3H), 1.16-1.71 (m, 6H), 1.68 (dm,  $J$  = 6.3 Hz, 3H), 3.97-4.08 (m, 1H), 5.47 (ddq,  $J$  = 15.0, 6.9, 1.5 Hz, 1H), 5.64 (dqd,  $J$  = 15.0, 6.3, 0.9 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 14.0, 17.6, 22.6, 27.6, 37.0, 73.1, 126.7, 134.4.  $\nu_{max}/cm^{-1}$  (film): 3350 (br), 1670.

**b) (1*R*, 2*E*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-*E*-4)**



Pentafluorobenzoyl chloride (0.22 mL, 1.5 mmol, 1.2 equiv.) was added under argon to a stirred mixture at 0 °C of (2*E*, 4*R*)-2-octen-4-ol (166 mg, 1.3 mmol), pyridine (0.15 mL, 1.9 mmol, 1.5 equiv.) and DMAP (9 mg, 0.07 mmol, 0.05 equiv.) in CH<sub>2</sub>Cl<sub>2</sub> (3 mL). The resulting mixture was stirred at 0 °C for 50 min, then 1M HCl was added and the mixture was extracted twice with Et<sub>2</sub>O. The combined extracts were washed with saturated, aqueous NaHCO<sub>3</sub> solution, then with brine, and dried (MgSO<sub>4</sub>). Evaporation of the solvents followed by column chromatographical purification (SiO<sub>2</sub>; 1 % Et<sub>2</sub>O/pentane) gave the ester *E*-4 (350 mg, 1.1 mmol, 85 %) in 94 % ee.

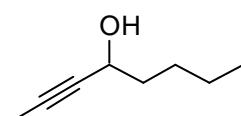
$[\alpha]_D$  = -8.5 (c = 4.75, CHCl<sub>3</sub>)

HPLC (Chiralcel OD-H; 1 % *i*-PrOH, 0.6 mL/min):  $t_R$ /min = 13.1 (*S*), 14.5 (*R*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.87-0.96 (m, 3H), 1.24-1.44 (m, 4H), 1.60-1.88 (m, 2H), 1.73 (dd,  $J$  = 6.8, 1.6 Hz, 3H), 5.42-5.55 (m, 2H), 5.85 (dq,  $J$  = 14.2, 6.8 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 150 MHz): 13.9, 17.7, 22.4, 27.2, 34.1, 78.5, 109.4, 128.6, 130.8, 137.7 (dm,  $J$  | 254 |, 2 x CF), 142.9 (dm,  $J$  | 259 |, CF), 145.2 (dm,  $J$  | 253 |, 2 x CF), 158.4.  $\delta_F$  (CDCl<sub>3</sub>, 376 MHz): -159.7 to -159.5 (m, 2F), -148.5 (tt,  $J$  | 21 |, | 4 |, 1F), -137.7 to -137.5 (m, 2F).  $\nu_{max}/cm^{-1}$  (film): 1740, 1680, 1650, 1520, 1500.  $m/z$ : 322.1014 (M<sup>+</sup>). C<sub>15</sub>H<sub>15</sub>O<sub>2</sub>F<sub>5</sub> requires M<sup>+</sup>, 322.0992).

**Preparation of (1*R*, 2*Z*)-1-butyl-2-butyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-*Z*-4)**

**a) 2-Octyn-4-ol<sup>2</sup>**

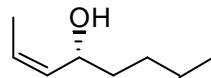


*n*-BuLi (1.6 M in hexanes; 55 mL, 88 mmol) was added dropwise over 1 h to a solution of 1-bromopropene (mixture of *Z* and *E* isomers; 5 mL, 58 mmol) in THF (36 mL) at -78 °C under argon and the resulting mixture was stirred for 2 h at -78 °C. Valeraldehyde (4 mL, 38 mmol) was then added dropwise as a solution in THF (20 mL) over 1 h, and the reaction mixture was allowed to warm to rt overnight (15 h). Saturated aqueous ammonium chloride was added to quench the reaction mixture, followed by enough water to dissolve the salts formed. The phases were separated, the aqueous phase was extracted with ether (100 mL) and the combined organic phases were washed with brine and dried over MgSO<sub>4</sub>. Evaporation of the solvents and distillation *in vacuo* afforded 2-octyn-4-ol (3.67 g, 77 %) as a colourless liquid.

GC (80 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm):  $t_R$ /min 32.8 (*S*), 34.8 (*R*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.86-0.95 (m, 3H), 1.25-1.47 (m, 4H), 1.58-1.72 (m, 2H), 1.77 (d,  $J$  = 5.4 Hz, 1H), 1.84 (d,  $J$  = 1.8, 3H), 4.24-4.36 (m, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 3.5, 14.0, 22.4, 27.3, 37.9, 62.7, 80.5, 80.8.  $\nu_{max}/cm^{-1}$  (film): 3350 (br), 2220.

b) (2Z,4R)-2-Octen-4-ol<sup>1, 3</sup>



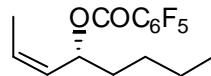
Palladium on barium sulfate (5 % Pd; 50 mg) and freshly distilled quinoline (1 mL, 8.5 mmol) were added to a solution at rt under an argon atmosphere of 2-octyn-4-ol (1.26 g, 10 mmol) in dry methanol (200 mL). The flask was then evacuated and flushed with hydrogen several times, and the reaction mixture was stirred under a hydrogen atmosphere for 1.5 h. The mixture was then filtered and the solvent was evaporated *in vacuo*. Filtration of the reaction mixture and evaporation of the solvents were repeated several times. Column chromatographical purification (SiO<sub>2</sub>; 25 % Et<sub>2</sub>O/pentane) of the residue afforded the racemic allylic alcohol (1.08 g, 8.4 mmol, 84 %) as a mixture of (Z)- and (E)-isomers (ca. 94:6). A mixture of the racemic alcohol (2.28 g, 17.8 mmol), L-(+)-dicyclododecyl tartrate (1.29 g, 2.67 mmol), *n*-decane (0.7 mL) and activated molecular sieves 4Å (509 mg) in dry CH<sub>2</sub>Cl<sub>2</sub> (63 mL) was stirred at rt under an argon atmosphere for 45 min, then cooled to -20 °C. Titanium isopropoxide (0.53 mL, 1.8 mmol) was added and the mixture was stirred 1.5 h at -20 °C. An aliquot was taken for GC-analysis, then a solution of *t*-BuOOH (5-6 M in nonane; 2.25 mL) in dry CH<sub>2</sub>Cl<sub>2</sub> (13 mL) which had been stirred for 1.25 h with activated molecular sieves 4Å (250 mg) was added dropwise. The reaction mixture was stirred at -20 °C for 64 h, then was quenched with aqueous FeSO<sub>4</sub>-citric acid (100 mL; containing 33 g FeSO<sub>4</sub>·7H<sub>2</sub>O and 11 g citric acid) and stirred 1 h at rt. The phases were separated, the aqueous phase was extracted twice with Et<sub>2</sub>O and the combined organic phases were washed first with water, then with brine, and dried (MgSO<sub>4</sub>). The solvents were evaporated *in vacuo*, the residue was distilled (bp.: 89 °C/11 Torr), and the distillate was purified by column chromatography (SiO<sub>2</sub>) affording (2Z,4R)-2-octen-4-ol (530 mg) as a colourless liquid.

$[\alpha]_D = +25.2$  (c = 1.15, CHCl<sub>3</sub>)

GC (50 °C; column: TFA  $\gamma$ -cyclodextrin, 30.0 m x 0.25 mm):  $t_R$ /min = 26.8 (*R*), 31.3 (*S*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.85-0.95 (m, 3H), 1.16-1.71 (m, 6H), 1.67 (dd,  $J$  = 6.9, 1.8 Hz, 3H), 4.40-4.52 (m, 1H), 5.39 (ddq,  $J$  = 11.1, 8.6, 1.8 Hz, 1H), 5.56 (dqd,  $J$  = 11.1, 6.9, 0.9 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 13.2, 14.0, 22.6, 27.4, 37.1, 67.3, 126.1, 133.6.  $\nu_{max}/cm^{-1}$  (film): 3350 (br), 1660.

c) (1*R*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-Z-4)



Pentafluorobenzoyl chloride (0.8 mL, 5.6 mmol) was added drop-wise to a mixture stirred at -35 °C under an argon atmosphere of (2*Z*,4*R*)-2-octen-4-ol (500 mg, 3.9 mmol), dry pyridine (0.51 mL, 6.3 mmol) and DMAP (47 mg, 0.38 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (35 mL) and the resulting mixture was allowed to warm to 0°C over 4h. Water was added to quench the reaction mixture and the phases were separated. The aqueous phase was extracted twice with Et<sub>2</sub>O, the combined extracts were washed with saturated, aqueous NaHCO<sub>3</sub>, then brine, and dried (MgSO<sub>4</sub>). Following evaporation of the solvents *in vacuo*, the residue was dissolved in pentane and washed repeatedly with saturated, aqueous NaHCO<sub>3</sub> until the organic layer was clear. Pentane was evaporated *in vacuo* and impurities were removed under vacuum (oil pump; several days) to give the pentafluorobenzoate ester ((*R*)-Z-4) (1.04 g, 83 %) as a colourless liquid.

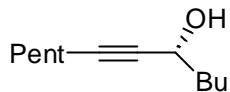
$[\alpha]_D = -58.3$  (c = 1.2, CHCl<sub>3</sub>).

Found, C, 55.8 %; H, 4.8 %. C<sub>15</sub>H<sub>15</sub>F<sub>5</sub>O<sub>2</sub> requires C, 55.9 %; H, 4.7 %.  $\delta_H$  (CDCl<sub>3</sub>, 400 MHz): 0.87-0.96 (m, 3H), 1.25-1.45 (m, 4H), 1.57-1.87 (m, 2H), 1.79 (dd,  $J$  6.8, 1.7 Hz, 3H), 5.41 (ddq,  $J$  = 10.8, 9.2, 1.7 Hz, 1H), 5.73 (dq,  $J$  = 10.8, 6.8 Hz, 1H), 5.82 (dt,  $J$  = 9.2, 6.8 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>,

150 MHz): 13.5, 13.9, 22.4, 27.0, 34.2, 73.5, 108.9 (m), 128.0, 129.6, 140.3 (dm,  $J$  |253|, 2xCF), 142.9 (dm,  $J$  |257|, CF), 145.1 (dm,  $J$  |259|, 2xCF), 158.4.  $\delta_F$  (CDCl<sub>3</sub>, 376 MHz): -159.4 to -159.7 (m, 2F), -148.4 (tt,  $J$  |21|, |4|, 1F), -137.8 to -137.5 (m, 2F).  $\nu_{max}/cm^{-1}$  (film): 1740, 1650, 1520, 1510.  $m/z$  (EI<sup>+</sup>): 323.1104 ([M+H]<sup>+</sup>). C<sub>15</sub>H<sub>15</sub>O<sub>2</sub>F<sub>5</sub> requires [M+H]<sup>+</sup>, 323.1070).

**Preparation of (1*R*, 2*Z*)-1-butyl-2-octenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-Z-6)**

a) (5*R*)-6-Dodecyne-5-ol<sup>4</sup>

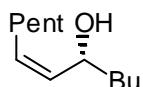


6-Dodecyne-5-one (30 mmol), prepared by AlCl<sub>3</sub>-catalyzed coupling of 1-heptynyl(trimethyl)silane with pentanoyl chloride in CH<sub>2</sub>Cl<sub>2</sub> at 0°C,<sup>5</sup> was added to a 0.5 M solution of *R*-Alpine-Borane (Aldrich, 84 mL, 1.4 equiv.) in THF under argon at rt and stirred for 5d. The reaction mixture was then cooled down to 0 °C, and acetaldehyde (0.8 mL) was added. After stirring for 30 min, pinene was evaporated in vacuo (oil pump, 6 h). Ethyl acetate (20 mL) and ethanolamine (2.5 mL) were added, the formed precipitate was removed by filtration and the remaining crude was distilled in an oil pump vacuo resulting in ca. 70 % yield of (5*R*)-6-dodecyne-5-ol in 90 % ee.

GC (90 °C (3 min), 0.3 °C/min, 140 °C (20 min); column: Chiraldex B-PH, 30.0 m x 0.25 mm):  $t_R$ /min = 86.6 (*R*), 87.4 (*S*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 4.28-4.38 (m, 1H), 2.14-2.23 (m, 2H), 1.76-1.87 (m, 1H), 1.59-1.74 (m, 2H), 1.22-1.56 (m, 10H), 0.82-0.96 (m, 6H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 85.5, 81.3, 62.7, 37.9, 31.0, 28.3, 27.4, 22.4, 22.1, 18.6, 14.0, 13.9.  $\nu_{max}/cm^{-1}$  (film): 3369 (br), 2957 (s), 2957 (s), 2931 (s), 2861 (s), 2231 (s), 1468-1298 (m), 1037 (m). MS (EI): 181 ([M-H]<sup>+</sup>, 1), 153 (5), 139 (9), 125 (100), 107 (28), 91 (25), 81 (96), 107 (28), 91 (25), 81 (96), 67 (27), 55 (91), 41 (69).  $m/z$  (EI<sup>+</sup>): 181.1593 (M<sup>+</sup>). C<sub>12</sub>H<sub>22</sub>O requires M<sup>+</sup>, 181.1587).

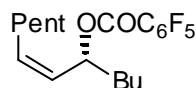
b) (5*R*, 6*Z*)-Dodec-6-en-5-ol<sup>6</sup>



(5*R*)-6-Dodecyne-5-ol (1.823 g, 10 mmol, 1.0 equiv.) was added dropwise at 0 °C to a 2.0 M solution of *i*-BuMgBr (11.5 mL, 2.3 equiv.) in Et<sub>2</sub>O and Cp<sub>2</sub>TiCl<sub>2</sub> (249 mg, 1.0 mmol, 0.1 equiv.), prepared at 0 °C under argon, and the reaction mixture was stirred overnight at rt. Column chromatographical purification (pentane/Et<sub>2</sub>O = 9/1 + 1 vol.-% Et<sub>3</sub>N) resulted in ca. 90 % yield of (5*R*, 6*Z*)-6-dodecene-5-ol as a colorless liquid.

Found, C, 77.81 %; H, 13.41 %. C<sub>12</sub>H<sub>24</sub>O requires C, 78.20 %; H, 13.12 %.  $\delta_H$  (CDCl<sub>3</sub>, 600 MHz): 5.28-5.50 (m, 1H), 5.34-5.44 (m, 1H), 4.35-4.42 (m, 2H), 1.99-2.11 (m, 2H), 1.71 (s, 1H), 1.53-1.61 (m, 1H), 1.21-1.43 (m, 12H), 0.82-0.92 (m, 6H).  $\delta_C$  (125 MHz): 132.7, 132.1, 67.6, 37.2, 31.4, 29.3, 27.6, 27.5, 22.6, 22.4, 14.0, 13.9.  $\nu_{max}/cm^{-1}$  (film): 3338 (s), 3958 (s), 2929 (s), 2859 (s), 1657 (w), 1467 (m), 1379 (w), 1007 (m), 730 (m). MS (EI): 184 (M<sup>+</sup>), 166 (2), 155 (4), 142 (8), 127 (66), 113 (42), 109 (97), 95 (12), 81 (13), 71 (15), 67 (41), 57 (100), 55 (20), 41 (33).  $m/z$  (EI<sup>+</sup>): 184.1829 (M<sup>+</sup>). C<sub>12</sub>H<sub>24</sub>O requires M<sup>+</sup>, 184.1827).

c) (1*R*, 2*Z*)-1-butyl-2-octenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-Z-6)



(5*R*, 6*Z*)-6-Dodecene-5-ol (1.84 g, 10 mmol) was added to a solution of dry  $\text{CH}_2\text{Cl}_2$  (100 ml) and  $\text{Et}_3\text{N}$  (2.1 mL, 1.5 equiv.). The mixture was cooled to 0 °C, and pentafluorobenzoyl chloride (1.7 mL, 12 mmol, 1.2 equiv.) was added dropwise. After stirring overnight at rt, the reaction mixture was quenched with a saturated aqueous solution of  $\text{NH}_4\text{Cl}$  (100 ml) at 0 °C. The layers were separated, and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  (3 x 100 mL). The combined organic layers were dried with  $\text{MgSO}_4$ , and after filtration, evaporation and column chromatographical purification (pentane/ $\text{Et}_2\text{O}$  = 98/2 + 1 vol-%  $\text{Et}_3\text{N}$ ) (*R*)-Z-6 resulted in 80 – 90 % yield.

Found, C, 60.11 %; H, 6.20 %.  $\text{C}_{19}\text{H}_{23}\text{F}_5\text{O}_2$  requires C, 60.31 %; H, 6.13 %.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 300 MHz): 5.82 (dt,  $J$  = 9.4, 6.8 Hz, 1H), 5.64 (dt,  $J$  = 10.5, 7.7 Hz, 1H), 5.35-5.42 (m, 2H), 2.08-2.32 (m, 2H), 1.72-1.88 (m, 1H), 1.55-1.70 (m, 1H), 1.22-1.47 (m, 10H), 0.85-0.95 (m, 6H).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 125 MHz): 158.3, 145.2 (d,  $J_{\text{C-F}}$  = 257.1 Hz), 142.9 (d,  $^1J_{\text{C-F}}$  = 258.2 Hz), 137.7 (d,  $J_{\text{C-F}}$  = 253.2 Hz), 135.6, 126.9, 109.0, 73.7, 34.3, 31.4, 29.1, 27.9, 27.1, 22.5, 22.4, 13.9, 13.9.  $\nu_{\text{max}}$ /cm<sup>-1</sup> (film): 3018 (w), 2961 (m), 2933 (m), 2862 (m), 1739 (s), 1652 (m), 1524 (s), 1504 (s), 1468 (w), 1424 (w), 1342 (m), 1330 (m), 1230 (s), 1104 (w), 1000(s), 937 (m), 766 (w). MS (EI): 378 ( $\text{M}^+$ , 0), 321 (1), 307 (1), 211 (4), 196 (6), 194 (100), 183 (3), 168 (8), 166 (7), 148 (1), 137 (1), 124 (2), 123 (2), 118 (1), 117 (2), 111 (1), 110 (4), 109 (5).  $m/z$  (EI<sup>+</sup>): 378.1648 ( $\text{M}^+$ ).  $\text{C}_{19}\text{H}_{23}\text{F}_5\text{O}_2$  requires  $\text{M}^+$ , 378.1618.

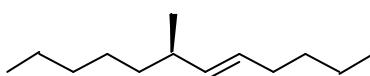
**TP1: Typical procedure for the copper(I)-mediated addition of dialkylzinc reagents to pentafluorobenzoates**

The dialkylzinc reagent (1.2 mmol) was added dropwise to a solution stirred at – 30 °C under an argon atmosphere of  $\text{CuCN}\cdot 2\text{LiCl}$  (1 M solution in THF; 0.6 mL, 0.6 mmol) in NMP (sufficient to give an overall ratio of THF:NMP = 2:1). The resulting mixture was stirred 0.5 h at – 30 °C, then the pentafluorobenzoate ester (0.5 mmol) was added dropwise as a solution in THF (0.8 mL) and the reaction mixture was allowed to warm to – 10 °C over 1.5 h. The reaction mixture was stirred at – 10 °C until the conversion was complete, then water (2 mL) was added, followed by 25 % aqueous ammonia solution (20 mL), and the reaction mixture was stirred at rt until the copper salts had dissolved. Brine was added, and the mixture was extracted with  $\text{Et}_2\text{O}$  (2 x 25 mL). The combined extracts were washed with brine and dried ( $\text{MgSO}_4$ ). Evaporation of the solvents and purification by column chromatography afforded the desired alkene.

**TP2: Typical procedure for the ozonolytic cleavage of alkenes with *in situ* oxidation to carboxylic acids using Jones reagent.**

Ozone was bubbled through a solution of the alkene in acetone (10 mL) at – 78 °C until the solution turned blue (3 - 10 min), then nitrogen was bubbled through until it became colourless again. The cooling bath was replaced with an ice bath and Jones reagent (2.67 M in Cr(VI); 26.7 g  $\text{CrO}_3$ , 23 ml conc.  $\text{H}_2\text{SO}_4$ , diluted with water to 100 ml) was added dropwise until the orange colour persisted. The mixture was stirred 15 min at 0 °C, then *i*-PrOH was added until the mixture turned green. It was stirred 15 min at 0 °C, then 1h at rt, then was filtered and the precipitate rinsed with  $\text{Et}_2\text{O}$ . The solvents were evaporated and the residue was dissolved in  $\text{Et}_2\text{O}$  and washed with water, then brine, and dried ( $\text{MgSO}_4$ ). The solvents were evaporated *in vacuo* and the residue was purified by column chromatography, followed by evaporation under vacuum of any remaining byproduct, to give the desired carboxylic acid.

**(5*E*, 7*R*)-7-Methyl-5-dodecene ((*R*)-E-5)**

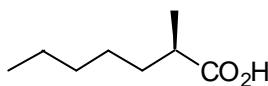


According to TP1, *(R)-E-5* was prepared from *(1R, 2Z)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((R)-Z-4)* (160 mg, 0.5 mmol, 95 % *ee*) and dipentylzinc (5.1 M in THF; 0.24 mL, 1.2 mmol) in the presence of NMP (0.7 mL) as co-solvent. The reaction mixture was stirred at –10 °C for 1 h. Column chromatographical purification (SiO<sub>2</sub>; pentane) of the crude product mixture afforded *(5E, 7R)-7-methyl-5-dodecene ((R)-E-5)* (88 mg, 97 %) as a colourless liquid.

$[\alpha]_D = -16.5$  (c = 1.2, CHCl<sub>3</sub>).

$\delta_H$  (CDCl<sub>3</sub>, 400 MHz): 0.85-0.92 (m, 6H), 0.94 (d, *J* = 6.8 Hz, 3H), 1.16-1.40 (m, 12H), 1.93-2.08 (m, 3H), 5.24 (ddm, *J* = 15.2, 7.2 Hz, 1H), 5.34 (dt, *J* = 15.2, 6.3 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 100 MHz): 13.9, 14.1, 20.9, 22.2, 22.7, 27.0, 31.9, 32.0, 31.2, 36.7, 37.2, 128.4, 136.5.  $\nu_{max}/cm^{-1}$  (film): 2930, 2960, 2860, 1450. *m/z* (EI<sup>+</sup>): 182.2037 (M<sup>+</sup>. C<sub>13</sub>H<sub>26</sub> requires M<sup>+</sup>, 182.2035).

Determination of configuration and *ee* by transformation of *(5E, 7R)-7-methyl-5-dodecene ((R)-E-5)* to *(2R)-2-methylheptanoic acid*<sup>7</sup>:



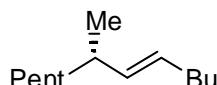
According to TP2 *(5E, 7R)-7-methyl-5-dodecene ((R)-E-5)* (62 mg, 0.34 mmol) was transformed to *(2R)-2-methylheptanoic acid* by ozonolytic cleavage. Column chromatographical purification (ca. 15 % Et<sub>2</sub>O/pentane) provided *(2R)-2-methylheptanoic acid* (27 mg, 55 %, 93 % *ee*) as a colourless oil.

$[\alpha]_D = -15.6$  (c = 0.55, EtOH).

GC (130 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t<sub>R</sub>*/min 15.8 (*S*), 16.3 (*R*).

Found, C, 66.2 %; H, 11.1 %. C<sub>8</sub>H<sub>16</sub> requires C, 66.6 %; H, 11.2 %.  $\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.84-0.93 (m, 3H), 1.18 (d, *J* = 7.2 Hz, 3H), 1.20-1.50 (m, 7H), 1.62-1.75 (m, 1H), 2.46 (qt, *J* = 7.2, 6.9 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 14.0, 16.8, 22.5, 26.8, 31.7, 33.5, 39.3, 183.0.  $\nu_{max}/cm^{-1}$  (film): 3600-2200, 1710.

### (5E, 7S)-7-Methyl-dodecene ((S)-E-5)



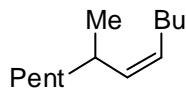
Dimethylzinc (4 M solution in THF, 0.5 mL, 2.0 equiv.) was added dropwise to a solution stirred at –30 °C under argon of CuCN·2LiCl (1 M solution in THF, 1.2 mL, 1.2 equiv.) in NMP (1.2 mL). After stirring for 0.5 h at –30 °C, a solution of 375 mg (1.00 mmol, 1.0 equiv.) of *(1R, 2Z)-1-butyl-2-octenyl 2,3,4,5,6-pentafluorobenzoate ((R)-Z-6)* in THF (1.4 mL) was added dropwise at –30 °C resulting in an overall ratio of THF/NMP of 2.3/1. The reaction mixture was allowed to warm to –10 °C over 1.5 h. After stirring for 30 h at –10 °C, the reaction mixture was quenched with a saturated aqueous solution of NH<sub>4</sub>Cl (10 mL). To remove the copper salts, the resulting mixture was stirred with 100 mL of saturated aqueous NH<sub>4</sub>Cl containing 2 mL of NH<sub>3</sub> (25 %). Extraction with Et<sub>2</sub>O (3 x 100 mL), drying of the combined organic phases, evaporation of the solvents and column chromatography (SiO<sub>2</sub>, pentane) resulted in 164 mg (90 %) of *(5E, 7S)-7-methyldodecene ((S)-E-5)* in 89 % *ee* (determined by transformation to *(2S)-2-methylheptanoic acid*, see experimental details given for *(R)-E-5*).

$[\alpha]_D = +18.5$  (c = 0.65, EtOH)

Found, C, 85.33 %; H, 14.34 %. C<sub>13</sub>H<sub>26</sub> requires C, 85.63 %; H, 14.37 %.  $\delta_H$  (CDCl<sub>3</sub>, 600 MHz): 5.34 (td, *J* = 15.1, 6.6 Hz, 1H), 5.25 (dd, *J* = 15.2, 7.9 Hz, 1H), 2.00-2.08 (m, 1H), 1.95-2.01 (m, 2H), 1.18-1.37 (m, 12H), 0.95 (d, *J* = 6.6 Hz, 3H), 0.86-0.92 (m, 6H).  $\delta_C$  (CDCl<sub>3</sub>, 125 MHz): 136.5,

128.4, 37.2, 36.7, 32.3, 32.0, 31.9, 27.0, 22.7, 22.2, 20.9, 14.1, 13.9.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 2958 (s), 2926 (s), 2873 (s), 2857 (s), 1459 (m), 1378 (w), 968 (m). MS (EI): 182 ( $M^+$ , 3), 126 (2), 111 (18), 97 (7), 83 (19), 69 (100), 55 (90), 41 (63).  $m/z$  (EI $^+$ ): 182.2044 ( $M^+$ ).  $C_{13}H_{26}$  requires  $M^+$ , 182.2035.

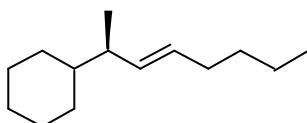
**(5Z)-7-Methyl-5-dodecen (Z-5)<sup>3,8</sup>**



7-Methyl-5-dodecene, prepared by Zn/Cu-mediated coupling of 2-iodoheptane with 1-bromohexyne (-50 °C, THF), was *cis*-selectively reduced by hydrogenation under Lindlar conditions (Pd/BaSO<sub>4</sub>, quinoline, MeOH, rt).<sup>3</sup> When the conversion was complete (2 h, GC-analysis), the catalyst was removed by filtration, the solvent was removed by evaporation, and the resulting crude was purified by column chromatography to obtain (Z-5) as a colorless oil in 95 % yield, including 5 % of the *trans*-isomer (5E)-7-methyl-5-dodecen (E-5).

Found, C, 85.29 %; H, 14.85 %.  $C_{13}H_{26}$  requires C, 85.63 %; H, 14.37 %.  $\delta_H$  (CDCl<sub>3</sub>, 600 MHz): 5.27-5.32 (m, 1H), 5.12 (t,  $J$  = 10.3 Hz, 1H), 2.38-2.48 (m, 1H), 2.10-2.20 (m, 2H), 1.22-1.41 (m, 12H), 0.87-0.94 (m, 9H).  $\delta_C$  (CDCl<sub>3</sub>, 125 MHz): 136.5, 128.3, 37.6, 32.2, 32.1, 31.7, 27.2, 27.2, 22.7, 22.4, 21.4, 14.1, 14.0.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 2999 (m), 2958 (s), 2926 (s), 2873 (s), 2857 (s), 1458 (m), 1378 (w), 728 (w). MS (EI) 183 (4), 182 ( $M^+$ , 21), 126 (20), 111 (100).  $m/z$  (EI $^+$ ): 182.2024 ( $M^+$ ).  $C_{13}H_{26}$  requires  $M^+$ , 182.2035.

**[(1*R*, 2*E*)-1-Methyl-2-heptenyl]cyclohexane ((*R*)-*E*-7)**

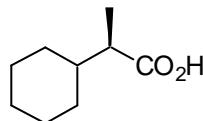


Dicyclohexylzinc was prepared as follows. Diethylborane<sup>9</sup> (7.3 M in dimethyl sulfide; 0.41 mL, 3.0 mmol) was added dropwise to cyclohexene (0.3 mL, 3.0 mmol) at rt under argon, and the resulting mixture was stirred at rt for 15 h, then cooled to 0 °C. Diethylzinc (0.6 mL, 5.9 mmol) was added dropwise and the reaction mixture was stirred at 0 °C for 3 h. The solvent and excess reagents were removed under reduced pressure (oil pump; 0 °C to rt). The residue was dissolved in THF to give a 1.4 M solution. According to TP1 (1*R*, 2*Z*)-1-butyl-2-but enyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-Z-4) (161 mg, 0.5 mmol, 98 % *ee*) was reacted with dicyclohexylzinc (1.4 M in THF; 0.86 mL, 1.2 mmol) in the presence of NMP (1.1 mL) as co-solvent. The reaction mixture was stirred at -10 °C for 11 h. Column chromatographical purification (SiO<sub>2</sub>; pentane) of the crude product mixture afforded the alkene (*R*)-*E*-7 (77 mg, 79 %) as a colourless liquid.

$[\alpha]_D = -20.8$  (c = 0.95, CHCl<sub>3</sub>).

Found, C, 86.4 %; H, 13.0 %.  $C_{14}H_{26}$  requires C, 86.5 %; H, 13.5 %.  $\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.80-1.39 (m, 16H), 0.92 (d,  $J$  = 6.9 Hz, 3H), 1.57-1.77 (m, 5H), 1.81-2.03 (m, 3H), 5.21-5.37 (m, 2H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 13.9, 17.8, 22.2, 26.7 (2C), 26.8, 30.3, 30.4, 31.9, 32.3, 42.4, 43.2, 129.1, 134.9.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 2850, 1450.  $m/z$  (EI $^+$ ): 194.2011 ( $M^+$ ).  $C_{14}H_{26}$  requires  $M^+$ , 194.2035.

Determination of configuration and *ee* by transformation of [(1*R*, 2*E*)-1-methyl-2-heptenyl]cyclohexane ((*R*)-*E*-7) to (2*R*)-2-cyclohexylpropanoic acid:



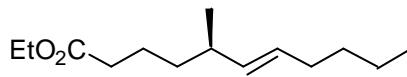
According to TP2 [(1*R*, 2*E*)-1-methyl-2-heptenyl]cyclohexane ((*R*)-**7**) (51 mg, 0.26 mmol) was converted to (2*R*)-2-cyclohexylpropanoic acid by ozonolytic cleavage. Column chromatographical purification (SiO<sub>2</sub>; 15 % Et<sub>2</sub>O/pentane) provided (2*R*)-2-cyclohexylpropanoic acid (29 mg, 71 %, 95 % *ee*) as a colourless oil.

$[\alpha]_D = -16.7$  (c = 0.55, CHCl<sub>3</sub>).

GC (140 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t*<sub>R</sub>/min = 34.4 (*S*), 35.7 (*R*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.87-1.36 (m, 5H), 1.13 (d, *J* = 7.2 Hz, 3H), 1.51-1.80 (m, 6H), 2.22-2.34 (m, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz) 13.9, 26.2, 26.3 (2C), 29.4, 31.1, 40.5, 45.2, 128.3.  $\nu_{max}/cm^{-1}$  (film) 3600-2350, 1700. *m/z* (EI<sup>+</sup>): 157.1264 ([M+H]<sup>+</sup>. C<sub>9</sub>H<sub>16</sub>O<sub>2</sub> requires [M+H]<sup>+</sup>, 157.1229).

### Ethyl(5*R*, 6*E*)-5-methyl-6-undecenoate ((*R*)-**8**)

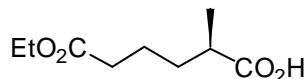


(*R*)-**8** was prepared according to TP1, from (1*R*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-**4**) (160 mg, 0.5 mmol, 98 % *ee*) and di(3-carbethoxypropyl)zinc<sup>8, 10</sup> (1.35 M in THF; 0.89 mL, 1.2 mmol) in the presence of NMP (1.1 mL) as co-solvent. The reaction mixture was stirred at -10 °C for 11 h. Column chromatographical purification (SiO<sub>2</sub>; 0.5 %, then 1 % Et<sub>2</sub>O/pentane) of the crude product mixture afforded ethyl-(5*R*, 6*E*)-5-methyl-6-undecenoate ((*R*)-**8**) (77 mg, 68 % *ee*) as a colourless liquid.

$[\alpha]_D = -16.3$  (c = 1.15, CHCl<sub>3</sub>).

Found, C, 74.0 %; H, 11.9 %. C<sub>14</sub>H<sub>26</sub>O<sub>2</sub> requires C, 74.3 %; H, 11.6 %.  $\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.84-0.92 (m, 3H), 0.95 (d, *J* = 6.6 Hz, 3H), 1.17-1.39 (m, 6H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.50-1.70 (m, 2H), 1.91-2.14 (m, 3H), 2.26 (t, *J* = 7.5 Hz, 2H), 4.12 (q, *J* = 7.2 Hz, 2H), 5.22 (dd, *J* = 15.3, 7.5 Hz, 1H), 5.36 (dt, *J* = 15.3, 6.5 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 13.9, 14.2, 20.9, 22.2, 22.8, 31.8, 32.2, 34.4, 36.5, 60.1, 129.0, 135.7, 173.8.  $\nu_{max}/cm^{-1}$  (film): 1740. *m/z* (EI<sup>+</sup>): 226.1925 (M<sup>+</sup>. C<sub>14</sub>H<sub>26</sub>O<sub>2</sub> requires M<sup>+</sup>, 226.1933).

Determination of configuration and *ee* by transformation of ethyl (5*R*, 6*E*)-5-methyl-6-undecenoate ((*R*)-**8**) to (2*R*)-6-ethoxy-2-methyl-6-oxohexanoic acid:



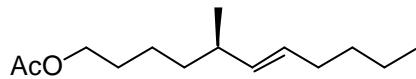
According to TP2 ethyl(5*R*, 6*E*)-5-methyl-6-undecenoate ((*R*)-**8**) (48 mg, 0.21 mmol) was converted to (2*R*)-6-ethoxy-2-methyl-6-oxohexanoic acid. Column chromatographical purification (SiO<sub>2</sub>; 20 %, then 50 % Et<sub>2</sub>O/pentane), followed by evaporation of the pentanoic acid byproduct under vacuum provided (2*R*)-6-ethoxy-2-methyl-6-oxohexanoic acid (10 mg, 25 %, 95 % *ee*) as a yellowish oil.

$[\alpha]_D = -8.8$  (c = 0.5, CHCl<sub>3</sub>).

GC (150 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t*<sub>R</sub>/min 56.6 (*S*), 58.9 (*R*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 1.20 (d, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.42-1.54 (m, 1H), 1.60-1.79 (m, 3H), 2.26-2.36 (m, 2H), 2.42-2.55 (m, 1H), 4.13 (q, *J* = 7.1 Hz, 2H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 14.2, 16.8, 22.5, 32.8, 34.1, 39.0, 60.3, 173.4, 182.1.  $\nu_{max}/cm^{-1}$  (film): 3690-2260, 1740, 1710. *m/z* (EI<sup>+</sup>) 189.1122 ([M+H]<sup>+</sup>. C<sub>9</sub>H<sub>16</sub>O<sub>4</sub> requires [M+H]<sup>+</sup>, 189.1127).

**(5*R*, 6*E*)-5-Methyl-6-undecenyl acetate ((*R*)-**E-9**)**

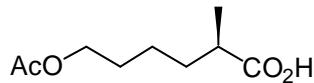


According to TP1, **E-9** was prepared from (1*R*, 2*Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate (**Z-4**) (162 mg, 0.5 mmol, 98 % *ee*) and di(4-acetoxybutyl)zinc<sup>8, 10</sup> (1.43 M in THF; 0.84 mL, 1.2 mmol) in the presence of NMP (1.1 mL) as cosolvent. The reaction mixture was stirred at -10 °C for 6 h. Column chromatographical purification (SiO<sub>2</sub>; 0.5 % Et<sub>2</sub>O / pentane, then 1 % Et<sub>2</sub>O / pentane) of the crude product mixture afforded the alkene (5*R*, 6*E*)-5-methyl-6-undecenyl acetate (**E-9**) (80 mg, 71 %) as a colourless liquid.

$[\alpha]_D = -15.4$  (c = 1.25, CHCl<sub>3</sub>).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.84-0.92 (m, 3H), 0.95 (d, *J* = 6.9 Hz, 3H), 1.20-1.40 (m, 8H), 1.52-1.66 (m, 2H), 1.92-2.10 (m, 3H), 2.04 (s, 3H), 4.04 (t, *J* = 6.8 Hz, 2H), 5.22 (dd, *J* = 15.0, 7.5 Hz, 1H), 5.35 (dt, *J* = 15.0, 6.3 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 13.9, 20.9, 21.0, 22.1, 23.6, 28.7, 31.8, 32.2, 36.6, 36.7, 64.6, 128.8, 136.0, 171.2.  $\nu_{max}/cm^{-1}$  (film): 1740. *m/z* (EI<sup>+</sup>): 227.1972 ([M+H]<sup>+</sup>. C<sub>14</sub>H<sub>26</sub>O<sub>2</sub> requires [M+H]<sup>+</sup>, 127.2011).

Determination of configuration and *ee* by conversion of (5*R*, 6*E*)-5-methyl-6-undecenyl acetate ((*R*)-**E-9**) to (2*R*)-6-(acetoxy)-2-methylhexanoic acid:



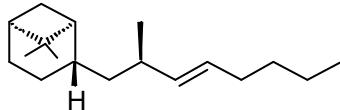
According to TP2 (5*R*, 6*E*)-5-methyl-6-undecenyl acetate ((*R*)-**E-9**) (55 mg, 0.24 mmol) was converted to (2*R*)-6-(acetoxy)-2-methylhexanoic acid by ozonolytic cleavage. Column chromatographical purification (20 %, then 50 % Et<sub>2</sub>O/pentane, then neat Et<sub>2</sub>O), followed by evaporation of the pentanoic acid byproduct under vacuum (oil pump) provided (2*R*)-6-(acetoxy)-2-methylhexanoic acid (23 mg, 56 %, 95 % *ee*) as a yellow oil.

$[\alpha]_D = -12.0$  (c = 1.15, CHCl<sub>3</sub>).

GC (150 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t<sub>R</sub>*/min = 67.7 (*S*), 70.6 (*R*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 1.19 (d, *J* = 6.9 Hz, 3H), 1.34-1.53 (m, 3H), 1.59-1.78 (m, 3H), 2.04 (s, 3H), 2.17 (s, 1H), 2.42-2.53 (m, 1H), 4.06 (t, *J* = 6.6 Hz, 2H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 16.8, 21.0, 23.6, 28.4, 33.0, 39.1, 64.2, 171.2, 181.9.  $\nu_{max}/cm^{-1}$  (film): 3660-2340, 1740, 1710.

**(1*S*, 2*S*, 5*S*)-6,6-Dimethyl-2-[(2*R*, 3*E*)-2-methyl-3-octenyl]bicyclo[3.1.1]heptane (*E*-**10**)**



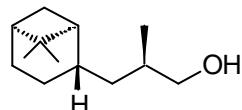
Dimyrtanylzinc was prepared as follows. Diethylborane (7.3 M solution in dimethyl sulfide; 1.4 mL, 10.2 mmol) was added dropwise to (1*S*)-(-)- $\beta$ -pinene (1.6 mL, 10.2 mmol) stirred at 0 °C under an argon atmosphere and the resulting solution was allowed to warm to rt overnight. The solvent was removed under vacuum (oil pump; 0 °C, then rt, then 35 °C). The residue was cooled to 0 °C, diethylzinc (0.65 mL, 6.3 mmol) was added dropwise, and the mixture was stirred at 0 °C under argon for a further 0.5 h, then under vacuum (oil pump; 0 °C, then rt, 1.5 h). Hexane (1 mL) was

added to the residue, the mixture was cooled to 0 °C and diethylzinc (0.6 mL, 5.9 mmol) was again added dropwise. The reaction mixture was stirred at 0 °C under argon for 1 h, then under vacuum (oil pump; 0 °C, then rt, then 40 °C, 2.5 h). THF (3 mL) was added to the black residue at rt, to give a solution of dimyrtanylzinc (1.2 M). According to TP1 (*1R, 2Z*)-1-butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-**4**) (161 mg, 0.5 mmol, 98 % *ee*) was reacted with dimyrtanylzinc (1.2 M in THF; 1 mL, 1.2 mmol) in the presence of NMP (1.2 mL) as cosolvent. The reaction mixture was stirred at –10 °C for 20 h. Column chromatographical purification (SiO<sub>2</sub>; pentane) of the crude product mixture afforded the alkene (*1S, 2S, 5S*)-6,6-dimethyl-2-[*(2R, 3E)*-2-methyl-3-octenyl]bicyclo[3.1.1]heptane (*E*-**10**) (99 mg, 80 %) as a colourless liquid.

$[\alpha]_D = -41.4$  (c = 1.3, CHCl<sub>3</sub>).

Found, C, 86.8 %; H, 12.7 %. C<sub>18</sub>H<sub>32</sub> requires C, 87.0 %; H, 13.0 %.  $\delta_H$  (CDCl<sub>3</sub>, 600 MHz): 0.87 (d, *J* = 9.5 Hz, 1H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.93 (d, *J* = 6.7 Hz, 3H), 1.01 (s, 3H), 1.18 (s, 3H), 1.21–1.46 (m, 7H), 1.75–2.06 (m, 8H), 2.06–2.15 (m, 1H), 2.28–2.35 (m, 1H), 5.18 (dd, *J* = 15.2, 8.1 Hz, 1H), 5.34 (dt, *J* = 15.2, 6.7 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 150 MHz): 13.9, 21.9, 22.1, 22.3, 23.4, 26.6, 28.3, 31.9, 32.2, 33.9, 34.9, 38.7 (2C), 41.6, 45.7, 47.3, 128.7, 136.3.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 2920, 1470. *m/z* (EI<sup>+</sup>): 248.2494 (M<sup>+</sup>). C<sub>18</sub>H<sub>32</sub> requires M<sup>+</sup>, 248.2504).

Determination of configuration and *ee* by transformation of (*1S, 2S, 5S*)-6,6-dimethyl-2-[*(2R, 3E)*-2-methyl-3-octenyl]bi-cyclo[3.1.1]heptane (*E*-**10**) to (*2R*)-3-[*(1S, 2S, 5S*)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]-2-methyl-1-propanol



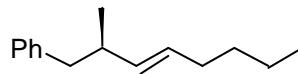
Ozone was bubbled through a solution of the alkene (*E*-**10**) (60 mg, 0.24 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at –78 °C until the solution turned blue (5 min), then nitrogen was bubbled through until it became colourless again. The cooling bath was replaced with an ice bath and a 1:1 EtOH:H<sub>2</sub>O mixture (1.6 mL) was added dropwise, followed by NaBH<sub>4</sub> (38 mg, 1.0 mmol) in three portions. The reaction mixture was allowed to warm to rt overnight, then was poured into 1M HCl (15 mL). The resulting mixture was extracted twice with Et<sub>2</sub>O and the combined extracts were washed with brine and dried (MgSO<sub>4</sub>). The solvents were evaporated *in vacuo* and the residue was purified by column chromatography (SiO<sub>2</sub>; 15 % Et<sub>2</sub>O/pentane) to give (*2R*)-3-[*(1S, 2S, 5S*)-6,6-dimethylbicyclo[3.1.1]hept-2-yl]-2-methyl-1-propanol (32 mg, 68 %, 92 % *ee*) as a colourless oil.

$[\alpha]_D = -19.4$  (c = 1.45, CHCl<sub>3</sub>).

GC (150 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t<sub>R</sub>*/min 15.7 (*2R*), 16.2 (*2S*).

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.87 (d, *J* = 9.6 Hz, 1H), 0.90 (d, *J* = 6.6 Hz, 3H), 1.00 (s, 3H), 1.08–1.22 (m, 1H), 1.17 (s, 3H), 1.35–2.16 (m, 9H), 2.25–2.37 (m, 1H), 3.37 (dd, *J* = 10.5, 6.6 Hz, 1H), 3.51 (dd, *J* = 10.5, 5.4 Hz, 1H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 17.1, 23.2, 23.3, 26.5, 28.2, 33.6, 33.7, 38.5, 38.7, 41.1, 41.5, 45.8, 68.4.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 3340 (br). *m/z* (EI<sup>+</sup>): 196.1791 (M<sup>+</sup>). C<sub>13</sub>H<sub>24</sub>O requires M<sup>+</sup>, 196.1827).

### [*2R, 3E*]-2-Methyl-3-octenylbenzene ((*R*)-**11**)



CuCN·2LiCl (1 M solution in THF; 0.6 mL, 0.6 mmol) was added dropwise to a mixture stirred at –30 °C under an argon atmosphere of dibenzylzinc<sup>11</sup> (1 M in toluene, 1.2 mL, 1.2 mmol) and THF (1 mL). NMP (1.2 mL) was added and the mixture was stirred at –30 °C for 0.5 h, then (*1R, 2Z*)-1-

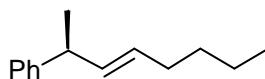
butyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-**4**) (160 mg, 0.5 mmol) was added as a solution in THF (1 mL) and the cooling bath was allowed to warm to  $-10\text{ }^{\circ}\text{C}$  over 45 min. The reaction mixture was stirred at  $-10\text{ }^{\circ}\text{C}$  for a further 16 h, then was quenched with water (2 mL) and stirred with 25 % aqueous ammonia (20 mL) until the copper salts had dissolved. Brine was then added and the mixture was extracted with  $\text{Et}_2\text{O}$  (2 x 25 mL). The combined extracts were washed with brine and dried ( $\text{MgSO}_4$ ), the solvents were evaporated *in vacuo* and the residue was purified by column chromatography ( $\text{SiO}_2$ ; pentane) to provide the alkene [(2*R*, 3*E*)-2-methyl-3-octenyl]benzene ((*R*)-**11**) (84 mg, 83 %, 95 % *ee*) as a colourless liquid.

$[\alpha]_D = 40.4$  ( $c = 1.05$ ,  $\text{CHCl}_3$ )

GC (60  $^{\circ}\text{C}$ ; column: TFA  $\gamma$ -Cyclodextrin, 30.0 m x 0.25 mm):  $t_R/\text{min}$  160.1 (*R*), 164.4 (*S*).

Found, C, 88.9 %; H, 10.9 %.  $\text{C}_{15}\text{H}_{22}$  requires C, 89.0 %; H, 11.0 %.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 300 MHz): 0.83-0.92 (m, 3H), 0.96 (d,  $J = 6.6$  Hz, 3H), 1.16-1.35 (m, 4H), 1.90-2.01 (m, 2H), 2.31-2.45 (m, 1H), 3.76 (dd,  $J = 13.3$  Hz, 7.7 Hz, 1H), 3.98 (dd,  $J = 13.3$ , 6.9 Hz, 1H), 5.25-5.41 (m, 2H), 7.10-7.21 (m, 3H), 7.22-7.31 (m, 2H).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 75 MHz): 13.9, 20.1, 22.1, 31.7, 32.2, 38.4, 43.8, 125.6, 128.0, 128.9 (2C), 129.3, 135.4, 141.0.  $m/z$  ( $\text{EI}^+$ ): 202.1745 ( $\text{M}^+$ ).  $\text{C}_{15}\text{H}_{22}$  requires  $\text{M}^+$ , 202.1721).

### [(1*S*, 2*E*)-1-Methyl-2-heptenyl]benzene ((*S*)-**12**)



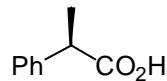
**E-12**

*t*-BuLi (1.4 M in pentane; 3.5 mL, 4.9 mmol) was added dropwise to a solution stirred at  $-78\text{ }^{\circ}\text{C}$  under argon of iodobenzene (0.3 mL, 2.66 mmol) in THF (5 mL). The resulting yellow mixture was stirred at  $-78\text{ }^{\circ}\text{C}$  for a further 0.5 h, becoming heterogeneous, then at  $-30\text{ }^{\circ}\text{C}$  for 10 min, during which time it again became homogeneous. A solution of  $\text{ZnBr}_2$  (1.5 M in THF; 0.8 mL, 1.2 mmol) was then added dropwise and the resulting colourless mixture was stirred at  $-30\text{ }^{\circ}\text{C}$  for a further 0.5 h. Evaporation of the solvent *in vacuo* (oil pump;  $-30\text{ }^{\circ}\text{C}$  to rt, 1 h), left the zinc reagent as a white solid, which was then dissolved in THF (2 mL) and the solution cooled to  $-30\text{ }^{\circ}\text{C}$ .  $\text{CuCN}2\text{LiCl}$  (1 M solution in THF; 0.6 mL, 0.6 mmol, 1.2 equiv.) was added dropwise, the resulting mixture was stirred at  $-30\text{ }^{\circ}\text{C}$  for a further 0.5 h, then the pentafluorobenzoate ester (*R*)-**4** (160 mg, 0.5 mmol, 95 % *ee* in this case) was added as a solution in THF (0.8 mL) and the reaction mixture was allowed to warm slowly to  $-10\text{ }^{\circ}\text{C}$  over 1.25 h. It was stirred a further 3 h at  $-10\text{ }^{\circ}\text{C}$ , then water (2 mL) was added to quench the reaction and 25 % aqueous ammonia solution (20 mL) was added to dissolve the copper salts. The mixture was stirred at rt for 60 h, then extracted with  $\text{Et}_2\text{O}$  (2 x 25 mL) and the combined extracts were washed with brine and dried ( $\text{MgSO}_4$ ). Following evaporation of the solvents *in vacuo* and column chromatographical purification ( $\text{SiO}_2$ ; pentane) afforded the alkene (*S*)-**12** (70 mg, 74 %) as a colourless liquid.

$[\alpha]_D = +10.6$  ( $c=1.15$ ,  $\text{CHCl}_3$ ).

Found, C, 89.2 %; H, 10.8 %. ( $\text{C}_{14}\text{H}_{20}$  requires C, 89.3 %; H, 10.7 %).  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 300 MHz): 0.83-0.95 (m, 3H), 1.22-1.42 (m, 4H), 1.32 (d,  $J = 7.2$  Hz, 3H), 1.94-2.07 (m, 2H), 3.40 (qd,  $J = 7.2$ , 6.8 Hz, 1H), 5.44 (dtm,  $J = 15.6$ , 6.6 Hz, 1H), 5.58 (ddm,  $J = 15.6$ , 6.8 Hz, 1H), 7.12-7.34 (m, 5H).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 75 MHz): 13.9, 21.5, 22.2, 31.7, 32.2, 42.2, 125.8, 127.1 (2C), 128.3 (2C), 129.2, 134.8, 146.5.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 1940, 1870, 1800, 1670, 1600.  $m/z$  ( $\text{EI}^+$ ): 188.1571 ( $\text{M}^+$ ).  $\text{C}_{14}\text{H}_{20}$  requires  $\text{M}^+$ , 188.1565).

Determination of configuration and *ee* by conversion of [(1*S*, 2*E*)-1-methyl-2-heptenyl]benzene ((*S*)-**12**) to (2*R*)-2-phenylpropanoic acid



According to TP2, *(S)-E-12* (34 mg, 0.18 mmol) was converted to *(2R)-2-phenylpropanoic acid* by ozonolytic cleavage. Column chromatographical purification (10 % Et<sub>2</sub>O/pentane, then neat Et<sub>2</sub>O), followed by evaporation of the pentanoic acid byproduct *in vacuo*, provided the carboxylic acid (17 mg, 63 %, 93 % *ee*) as a yellowish oil.

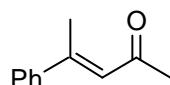
$[\alpha]_D = -64.4$  (c=0.45, CHCl<sub>3</sub>) (Lit.<sup>12</sup>  $[\alpha]_D = -72$  (c = 1.6, CHCl<sub>3</sub>)).

GC (150 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm):  $t_R$ /min 39.1 (*S*), 40.2 (*R*).

$\delta_H$  (CDCl<sub>3</sub>, 400 MHz): 1.52 (d,  $J = 7.0$  Hz, 3H), 3.74 (q,  $J = 7.0$  Hz, 1H), 7.24-7.40 (m, 5H).  $\delta_C$  (CDCl<sub>3</sub>, 100 MHz): 18.1, 45.3, 127.4, 127.6 (2C), 128.7 (2C), 139.8, 180.3.  $\nu_{max}/cm^{-1}$  (film): 3690-2210, 1950, 1710, 1600, 1590.

### Preparation of *(1R, 2E)-1-methyl-3-phenyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((R)-E-13)*

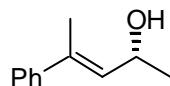
#### a) *(3E)-4-Phenyl-3-penten-2-one*<sup>13</sup>



A solution of bromobenzene (7.9 mL, 75 mmol) in dry THF (30 mL) was added dropwise over 40 min to a stirred suspension of magnesium (1.81 g, 74 mmol) in dry THF (20 mL), heating the mixture to reflux. The resulting dark grey solution was stirred 40 min at rt, then a solution of acetylacetone (2.5 mL, 24 mmol) in THF (25 mL) was added dropwise over 20 min and the resulting mixture was stirred at rt for 22 h. It was then poured into ice-cold, saturated aqueous NH<sub>4</sub>Cl (100 mL) with stirring. The phases were separated, the aqueous phase was extracted twice with Et<sub>2</sub>O and the combined organic phases were washed with brine and dried (MgSO<sub>4</sub>). The solvents were evaporated to leave a yellow oil, and the crude keto-alcohol thus obtained was taken up in methanol (10 mL) and refluxed for 2 h. The resulting red mixture was allowed to cool to rt, then was filtered, washed with Et<sub>2</sub>O and the solvents evaporated *in vacuo*. Distillation of the residue (0.9 Torr, 75 °C) provided the product, contaminated with an impurity, that was removed under oil pump vacuum, to give the  $\alpha,\beta$ -unsaturated ketone (2.08 g, 54 %) as a pale yellow liquid.

$\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 2.30 (s, 3H), 2.54 (d,  $J = 1.5$  Hz, 3H), 6.49-6.53 (m, 1H), 7.30-7.43 (m, 3H), 7.44-7.52 (m, 2H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 18.3, 32.2, 124.5, 126.5 (2C), 128.5 (2C), 129.1, 142.5, 153.9, 198.9.  $\nu_{max}/cm^{-1}$  (film): 1960, 1890, 1680, 1600, 1570.

#### b) *(2R, 3E)-4-Phenyl-3-penten-2-ol*<sup>13</sup>



Sodium borohydride (247 mg, 6.5 mmol) was added to a stirred solution of *(3E)-4-phenyl-3-penten-2-one* (995 mg, 6.2 mmol) in methanol (8 mL) at 0 °C and the resulting mixture was stirred a further 1.25 h at this temperature. Acetic acid (1.2 mL) was then added dropwise and the mixture was stirred a further 10 min at 0 °C. The solvents were evaporated *in vacuo* and the residue was filtered and washed with Et<sub>2</sub>O. Following evaporation of the solvents *in vacuo* and column chromatographical purification of the residue (SiO<sub>2</sub>; 10 %, then 15 %, then 20 % Et<sub>2</sub>O/pentane), the white solid (764 mg, 76 %) thus obtained was recrystallised from hexane to yield *(3E)-4-phenyl-3-penten-2-ol* (413 mg, 41 %) as white crystals. The racemic allylic alcohol was kinetically resolved<sup>1</sup> (16 h

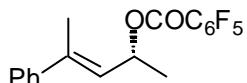
reaction time; for details see preparation of (*2E, 4R*)-2-octen-4-ol ((*R*)-**4**, section a) to obtain (*2R, 3E*)-4-phenyl-3-penten-2-ol in 98 % *ee* (see chiral GC in appendix).

$[\alpha]_D = +30.6$  ( $c = 1.9$ , EtOH).

GC (120 °C; column: Chiraldex B-PH, 30 m x 0.25 mm):  $t_R$ /min 54.6 (*R*), 58.6 (*S*).

Found, C, 81.3 %; H, 8.7 %.  $C_{11}H_{14}$  requires C, 81.4 %; H, 8.7 %. m.p. 60.5-61.5 °C (Lit.<sup>14</sup> 63-64 °C).  $\delta_H$  ( $CDCl_3$ , 300 MHz): 1.35 (d,  $J = 6.1$  Hz, 3H), 1.65-1.70 (m, 1H), 2.11 (d,  $J = 1.2$  Hz, 3H), 4.76 (dq,  $J = 8.4$ , 6.1 Hz, 1H), 5.81 (dq,  $J = 8.4$ , 1.2 Hz, 1H), 7.22-7.44 (m, 5H).  $\delta_C$  ( $CDCl_3$ , 75 MHz): 16.1, 23.5, 65.2, 125.8, 127.2, 128.3, 131.9, 136.2, 142.9.  $\nu_{max}/cm^{-1}$  (KBr disc): 3290 (br), 1950, 1890, 1760, 1640, 1600, 1580.

c) (*1R, 2E*)-1-Methyl-3-phenyl-2-butenyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-**13**)

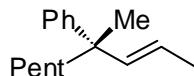


Pentafluorobenzoyl chloride (0.31 mL, 2.15 mmol) was added dropwise to a mixture stirred at -60 °C under an argon atmosphere of (*1R, 2E*)-4-phenyl-3-penten-2-ol (250 mg, 1.54 mmol), dry pyridine (0.2 mL, 2.47 mmol) and DMAP (19 mg, 0.16 mmol) in dry  $CH_2Cl_2$  (13 mL). The resulting mixture was allowed to warm to -20 °C over 2.5 h, then was stirred at 0 °C for 40 min, then at rt for 1 h. The reaction mixture was quenched by water and was extracted twice with  $Et_2O$ . The combined extracts were washed with saturated aqueous  $NaHCO_3$ , then brine, and dried ( $MgSO_4$ ). Following evaporation of the solvents *in vacuo*, the residue was taken up in pentane and washed twice with saturated aqueous  $NaHCO_3$ , then with brine, and dried ( $MgSO_4$ ). The pentane was evaporated *in vacuo* and impurities were removed under an oil pump vacuum to give the pentafluorobenzoate ester ((*R*)-**13**) (545 mg, 99 %) as a pale yellow oil.

HPLC (column: Chiralcel OD-H, 0.46 cm x 25 cm; heptane:*i*-PrOH = 99:1, 0.2 mL/min):  $t_R$ /min 38.9 (*S*), 46.8 (*R*).

Found, C, 60.38 %; H, 3.42 %.  $C_{18}H_{13}F_5O_2$  requires C, 60.68 %; H, 3.68 %.  $\delta_H$  ( $CDCl_3$ , 600 MHz): 1.53 (d,  $J = 6.0$  Hz, 3H), 2.20 (d,  $J = 1.2$  Hz, 3H), 5.79 (dm,  $J = 8.7$  Hz, 1H), 6.05 (dq,  $J = 8.7$ , 6.0 Hz, 1H), 7.26-7.36 (m, 3H), 7.39-7.43 (m, 2H).  $\delta_C$  ( $CDCl_3$ , 150 MHz): 16.5, 20.7, 71.6, 108.9 (m), 125.9 (2C), 126.0, 127.7, 128.3 (2), 137.6 (dm,  $J \parallel 253 \parallel$ , 2xCF), 139.7, 142.4, 143.0 (dm,  $J \parallel 258 \parallel$ , CF), 145.2 (dm,  $J \parallel 251 \parallel$ , 2xCF), 158.4.  $\delta_F$  ( $CDCl_3$ , 376 MHz) -159.6 to -159.4 (m, 2F), -148.2 (tt,  $J \parallel 21 \parallel$ , 4F), -137.7 to -137.5 (m, 2F).  $\nu_{max}/cm^{-1}$  (film): 1740, 1650, 1600, 1580, 1520, 1500.

[(*1S, 2E*)-1-Methyl-1-pentyl-2-butenyl]benzene ((*S*)-**14**)

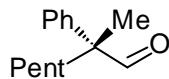


Dipentylzinc (4.8 M; 72  $\mu$ L, 0.34 mmol) was added dropwise to a stirred solution of  $CuCN \cdot 2LiCl$  (1 M in THF; 0.186 mL, 0.19 mmol) in THF (1 mL) at -30 °C under an argon atmosphere, and the resulting mixture was stirred at -30 °C for 35 min. The pentafluorobenzoate ((*R*)-**13**) (51 mg, 0.14 mmol) was then added as a solution in THF (1 mL) and the mixture was allowed to warm to -10 °C over 1.25 h. It was stirred at -10 °C for 15 h, then water was added to quench the reaction mixture. It was extracted twice with  $Et_2O$  and the combined extracts were washed with brine and dried ( $MgSO_4$ ). Evaporation of the solvents *in vacuo* and purification by column chromatography ( $SiO_2$ ; pentane) afforded the alkene ((*S*)-**14**) (25 mg, 84 %) as a colourless liquid.

$\delta_H$  ( $CDCl_3$ , 300 MHz): 0.76-0.85 (m, 3H), 0.96-1.34 (m, 6H), 1.30 (s, 3H), 1.56-1.77 (m, 2H), 1.68 (dd,  $J = 6.3$ , 1.8 Hz, 3H), 5.38 (dq,  $J = 15.3$ , 6.3 Hz, 1H), 5.61 (dq,  $J = 15.3$ , 1.8 Hz, 1H), 7.09-7.16 (m, 1H), 7.20-7.30 (m, 4H).  $\delta_C$  ( $CDCl_3$ , 75 MHz) 14.1, 18.2, 22.6, 24.2, 25.6, 32.6, 41.8, 43.5, 121.7,

125.4, 126.6, 127.9, 140.2, 148.6.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 1940, 1600.  $m/z$  (EI $^+$ ): 216.1863 ( $M^+$ .  $C_{16}\text{H}_{24}$  requires  $M^+$ , 216.1878).

Determination of the enantiomeric excess by transformation of the alkene (*S*)-**14** to (2*R*)-2-methyl-2-phenylheptanal (*R*-**15**):

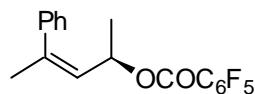


Ozone was bubbled through a solution of the alkene (50 mg, 0.23 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) at -78 °C until the solution turned blue (4 min), then nitrogen was bubbled through until it became colourless again. Triphenylphosphine (80 mg, 0.31 mmol) was added in one portion and the mixture was stirred and allowed to warm slowly to rt overnight under a nitrogen atmosphere. It was then diluted with  $\text{Et}_2\text{O}$  and washed with water, then brine, and dried ( $\text{MgSO}_4$ ). The solvents were evaporated *in vacuo* and the residue was purified by column chromatography ( $\text{SiO}_2$ ; 2 %  $\text{Et}_2\text{O}$ /pentane) to give 2-methyl-2-phenylheptanal (38 mg, 81 %) as a liquid in 94 % *ee* (see chiral GC in appendix).

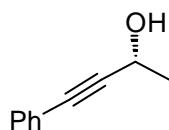
GC (100 °C; column: TFA  $\gamma$ -Cyclodextrin, 30.0 m x 0.25 mm):  $t_R/\text{min} = 45.1$  (*S*), 48.0 (*R*).

$\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 300 MHz): 0.80-0.88 (m, 3H), 1.00-1.34 (m, 6H), 1.43 (s, 3H), 1.76-1.98 (m, 2H), 7.21-7.41 (m, 5H), 9.50 (s, 1H).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 75 MHz): 14.0, 18.9, 22.4, 23.6, 32.4, 35.9, 54.0, 127.1, 128.8, 140.2, 202.6.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 1950, 1730, 1600, 1580, 1500.  $m/z$  (EI $^+$ ): 205.1596 ( $[\text{M}+\text{H}]^+$ .  $C_{14}\text{H}_{20}\text{O}$  requires  $[\text{M}+\text{H}]^+$ , 205.1592).

### Preparation of (1*R*, 2*Z*)-1-methyl-3-phenyl-2-butenyl 2,3,4,5,6-pentafluorobenzoic acid ester ((*R*)-**13**)



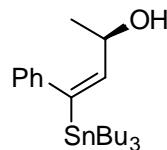
#### a) (3*R*)-4-Phenyl-3-butyn-2-ol



A dry and argon-fused 100-ml Schlenk-flask was charged with copper(I) iodide (0.6 g, 3.0 mmol) and *bis*(triphenylphosphine)palladium(II) chloride (0.1 g, 0.2 mmol). The flask was flushed several times with argon. The solids were dissolved in 40 mL pyrrolidine and iodobenzene (6.3 g, 31.0 mmol) was added. The mixture was cooled to 0 °C and (2*R*)-3-butyn-2-ol (2.1 g, 30.0 mmol) was added dropwise to the stirred solution. The ice bath was removed and the reaction mixture was stirred at rt for 5 h. During this time the mixture changed colour from yellow to black. The conversion was followed by GC-analysis. The reaction mixture was quenched by addition of sat.  $\text{NH}_4\text{Cl}$  solution. The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  and the organic phase was concentrated *in vacuo*. The residue was purified by flash chromatography ( $\text{CH}_2\text{Cl}_2$ ), yielding the product as a yellow oil (4.4 g, 100 %).

Found, C, 82.1 %; H, 6.8 %.  $C_{10}\text{H}_{10}\text{O}$  requires C, 82.2 %; H, 6.9 %.  $\delta_{\text{H}}$  ( $\text{CDCl}_3$ , 300 MHz): 1.56 (d,  $J = 6.6$  Hz, 3 H), 2.15 (d,  $J = 4.9$  Hz, 1 H), 4.76 (quint.,  $J = 6.6$  Hz, 1 H), 7.28-7.33 (m, 3 H), 7.40-7.44 (m, 2 H).  $\delta_{\text{C}}$  ( $\text{CDCl}_3$ , 75 MHz): 24.3, 58.8, 84.0, 90.9, 122.6, 128.2, 128.3, 131.6.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 3338 (br), 2982 (m), 1598 (w), 1490 (s), 1444 (m), 1330 (m), 1106 (s), 1073 (m), 1038 (m), 933 (m), 852 (w), 756 (s), 691 (s).  $m/z$  (EI $^+$ , 70 eV): 146 (25), 145 (44), 131 (100), 103 (58), 77 (29); identification by MS-library comparison.

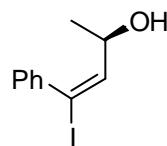
**b) (2*R*, 3*E*)-4-Phenyl-4-(tributylstannylyl) 3-buten-2-ol**



(3*R*)-4-Phenyl-3-buten-2-ol (4.4 g, 30.0 mmol) and *bis*(tri-phenylphosphine)palladium(II) chloride (0.2 g, 0.3 mmol) was dissolved in 30.0 ml THF in a dry and argon-flushed 100 mL Schlenk-flask. After dropwise addition of tri-*n*-butyltin hydride (9.6 g, 33.0 mmol) at 0 °C the mixture was stirred at rt for 1 h. The conversion was followed by GC-analysis. THF was removed under vacuum and the residue was purified by flash chromatographical purification (pentane:EtOAc = 94:6), yielding the product as a yellow oil (11.6 g, 88 %).

Found, C, 60.4 %; H, 8.4 %. C<sub>10</sub>H<sub>10</sub>O requires C, 60.4 %; H, 8.8 %. δ<sub>H</sub> (CDCl<sub>3</sub>, 300 MHz): 0.86-0.93 (m, 15 H), 1.23-1.33 (m, 9-10 H), 1.44-1.46 (m, 6 H), 4.38 (m, 1 H), 5.82 (d, *J* = 8.5 Hz, 1 H), 6.80-7.00 (m, 2 H), 7.10-7.20 (m, 1 H), 7.25-7.33 (m, 2 H). δ<sub>C</sub> (CDCl<sub>3</sub>, 75 MHz): 9.9, 13.6, 23.5, 27.2, 28.9, 65.1, 125.1, 126.4, 128.1, 144.3, 144.7, 147.0. ν<sub>max</sub>/cm<sup>-1</sup> (film): 3338 (br), 2957 (s), 2926 (s), 2872 (m), 2853 (m), 1489 (w), 1464 (m), 1376 (w), 1128 (w), 1054 (m), 762 (w), 702 (m). *m/z* (EI<sup>+</sup>): 437.1847 ([M-H]<sup>+</sup>. C<sub>22</sub>H<sub>37</sub>OSn requires [M-H]<sup>+</sup>, 437.1866).

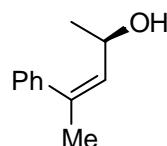
**c) (2*R*, 3*E*)-4-iodo-4-phenyl-3-buten-2-ol**



(2*R*, 3*E*) 4-Phenyl-4-(tributylstannylyl) 3-buten-2-ol (7.4 g, 17.0 mmol) was dissolved in 20 mL CH<sub>2</sub>Cl<sub>2</sub>. At 0 °C, under light exclusion, iodine (5.2 g, 20.0 mmol) was added in one portion and the mixture was stirred at room temperature for 30 min. The reaction mixture was followed by TLC-analysis (pentane:Et<sub>2</sub>O = 7:3). Then 20 mL of an aqueous sat. KF solution was added and the mixture was stirred for another 30 min. The mixture was filtered through Celite and the residue was washed with further 200 mL of CH<sub>2</sub>Cl<sub>2</sub>. The filtrate was washed with sat. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> and dried with sat. NaCl. CH<sub>2</sub>Cl<sub>2</sub> was removed under vacuum at 30 °C and the residue was purified by flash chromatography (CH<sub>2</sub>Cl<sub>2</sub>), yielding the product as a yellow oil (4.6 g, 99 %).

Found, C, 43.9 %; H, 4.2 %; I, 46.3%. C<sub>10</sub>H<sub>11</sub>IO requires C, 43.8 %; H, 4.1 %; I, 46.3%. δ<sub>H</sub> (CDCl<sub>3</sub>, 300 MHz): 1.19 (d, *J* = 6.2 Hz, 3 H), 1.50 (d, *J* = 4.0 Hz, 1 H), 4.12-4.19 (m, 1 H), 6.44 (d, *J* = 8.9 Hz, 1 H), 7.18-7.28 (m, 5 H). δ<sub>C</sub> (CDCl<sub>3</sub>, 75 MHz): 22.9, 66.7, 88.8, 98.2, 128.3, 128.5, 141.3, 146.1. ν<sub>max</sub>/cm<sup>-1</sup> (KBr-disk): 3271 (br), 3056 (w), 2974 (w), 2924 (w), 1632 (w), 1488 (w), 1440 (m), 1372 (m), 1307 (w), 1174 (w), 1130 (s), 1064 (s), 938 (m), 868 (m), 766 (s), 701 (s). *m/z* (EI<sup>+</sup>, 70 eV): 274 (1), 259 (2), 241 (1), 147 (71), 128 (8), 103 (100), 91 (2), 77 (15). *m/z* (EI<sup>+</sup>): 273.9868 ([M]<sup>+</sup>. C<sub>10</sub>H<sub>11</sub>IO requires [M]<sup>+</sup>, 273.9855).

**d) (2*R*, 3*Z*)-4-Phenyl-3-penten-2-ol**

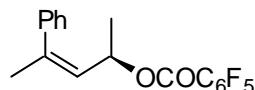


MeLi (3.8 mL, 6.0 mmol) was added dropwise to a well stirred solution of ZnCl<sub>2</sub> (4.4 mL, 6.6 mmol) in THF at - 30 °C. The mixture was warmed up slowly to room temperature and stirred for another hour. Bis-(tri-phenylphosphine)palladium(II) chloride (70 mg, 0.1 mmol) was added in a dry and argon-flushed 50 mL Schlenk-flask, and dissolved in THF (1 mL). To this solution was added at rt (2*R*, 3*E*)-4-iodo-4-phenyl 3-buten-2-ol (560 mg, 2.0 mmol) in THF (3 mL). The mixture was stirred for 30 min at rt and then the MeZnCl solution was added dropwise at 0 °C. The reaction mixture was stirred at rt for 3h and followed by GC-analysis. The reaction mixture was quenched by addition of sat. NH<sub>4</sub>Cl solution, the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> and the organic phase was concentrated in vacuum. The residue was purified by flash chromatography (CH<sub>2</sub>Cl<sub>2</sub>), yielding the product as a yellow oil (340 mg, 100 %, 98 % *ee* (see chiral GC in appendix)).

GC (120 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t<sub>R</sub>*/min 22.1 (*R*), 23.4 (*S*).

Found, C, 81.3 %; H, 8.4 %. C<sub>11</sub>H<sub>14</sub>O requires C, 81.4 %; H, 8.7 %.  $\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 1.16 (d, *J* = 6.2 Hz, 3 H), 1.41 (s, 1 H), 1.97 (d, *J* = 1.7 Hz, 3 H), 4.16-4.25 (m, 1 H), 5.41-5.42 (dq, *J* = 9.4 Hz, *J* = 1.8 Hz, 1 H), 7.08-7.13 (m, 2 H), 7.15-7.30 (m, 3 H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 23.7, 25.5, 65.3, 127.0, 127.7, 128.1, 131.2, 138.5, 141.2.  $\nu_{max}/cm^{-1}$  (film): 3339 (br), 3080 (w), 3057 (w), 3024 (w), 2969 (s), 2926 (m), 2914 (m), 1601 (w), 1494 (m), 1444 (m), 1435 (m), 1373 (m), 1261 (w), 1144 (w), 1100 (m) 1060 (s), 1010 (m), 934 (m), 864 (m), 799 (w), 766 (s), 702 (s). *m/z* (EI<sup>+</sup>, 70 eV): 162 (10), 147 (100), 145 (9), 129 (41), 128 (20), 115 (18), 105 (50), 91 (34), 77 (17). *m/z* (EI<sup>+</sup>): 162.1028 ([M]<sup>+</sup>. C<sub>11</sub>H<sub>14</sub>O requires [M]<sup>+</sup>, 162.1045).

**e) (1*R*, 2*Z*)-1-Methyl-3-phenyl-2-butenyl 2,3,4,5,6-pentafluorobenzoic acid ester ((*R*)-Z-13)**

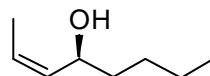


(2*R*, 3*Z*) 4-Phenyl 3-penten-2-ol (560 mg, 3.5 mmol), 0.5 mL pyridine and DMAP (45 mg, 0.4 mmol) was dissolved in a dry and argon-flushed 25 mL Schlenk-flask in CH<sub>2</sub>Cl<sub>2</sub> (20 mL). The mixture was cooled to - 60 °C and pentafluorobenzoyl chloride (1.1 g, 4.8 mmol) was added dropwise. The mixture was warmed up slowly to - 20 °C and stirred for 2.5 h, than for 1h at 0 °C. The reaction conversion was followed by TLC-analysis (CH<sub>2</sub>Cl<sub>2</sub>). The reaction was quenched by addition of water. The aqueous phase was extracted with Et<sub>2</sub>O and the organic phase was washed two times with sat. NaHCO<sub>3</sub> solution. The organic phase was concentrated in vacuum and the residue was taken up in pentane. The organic phase was washed two times with sat. NaHCO<sub>3</sub> solution dried with sat. NaCl. The organic phase was concentrated in vacuum to yield the product as a yellow oil (1.1 g, 89 %).

Found, C, 60.8 %; H, 3.6 %. C<sub>18</sub>H<sub>13</sub>F<sub>5</sub>O<sub>2</sub> requires C, 60.7 %; H, 3.7 %.  $\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 1.40 (d, *J* = 6.2 Hz, 3 H), 2.08 (d, *J* = 5.3 Hz, 3 H), 5.52-5.57 (m, 1 H), 7.19-7.22 (m, 2 H), 7.30-7.40 (m, 3 H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 21.0, 25.8, 72.7, 125.6, 127.3, 127.3, 128.4, 140.7, 142.1.  $\nu_{max}/cm^{-1}$  (film): 2978 (w), 1739 (s), 1653 (m), 1524 (s), 1499 (s), 1422 (w), 1377 (w), 1340 (s), 1324 (m), 1234 (s), 1156 (w), 1102 (w), 1033 (m), 997 (s) 943 (m), 859 (m), 767 (m), 702 (m).

**Preparation of (1*S*, 2*Z*)-1-butyl-2-butenyl-2,3,4,5,6-pentafluorobenzoate ((*S*)-Z-4)**

**a) (2*Z*, 4*S*)-2-Octen-4-ol**

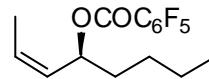


Titanium isopropoxide (0.55 mL, 1.9 mmol) was added to a mixture stirred at - 20 °C, under an argon atmosphere, of racemic (2*Z*)-octen-4-ol (see experimental of (*R*)-Z-4 for preparation of

racemic alcohol, 2.36 g, 18.4 mmol), D-(-)-dicyclododecyl tartrate<sup>1</sup> (1.34 g, 2.8 mmol), *n*-tetradecane (0.7 mL) and freshly activated molecular sieves in dry CH<sub>2</sub>Cl<sub>2</sub> (64 mL). The resulting mixture was stirred for 15 h at -20 °C (reaction monitored by GC MS to >50 % conversion), quenched with an aqueous FeSO<sub>4</sub>-citric acid solution and vigorously stirred for 4 h at rt. The phases were separated, the aqueous phase was extracted twice with CH<sub>2</sub>Cl<sub>2</sub> and the combined organic phases were washed with brine and dried (MgSO<sub>4</sub>). The solvents were evaporated *in vacuo*, the residue was distilled (ca. 10 mbar; oil bath 100 °C), and the distillate was purified by column chromatography (SiO<sub>2</sub>; 5 %, then 10 % Et<sub>2</sub>O/pentane) to afford the *S*-allylic alcohol (1.00 g, 42 %, 98 % *ee*). This material was then resubjected to a second Sharpless kinetic resolution, following the above procedure, and reacted this time for 4 h at -20 °C with D-(-)-dicyclododecyl tartrate (568 mg, 1.2 mmol), titanium isopropoxide (0.23 mL, 0.8 mmol) and *t*-BuOOH (5-6 M in nonane; 1.19 mL) in the presence of *n*-tetradecane (0.3 mL) and freshly activated molecular sieves. Work-up and distillation and column chromatography (SiO<sub>2</sub>; 5 %, then 10 % Et<sub>2</sub>O/pentane) provided the *S*-allylic alcohol (186 mg, 8 %, 99.3 % *ee* (see chiral GC in appendix; containing 0.5 % of (2*E*, 4*S*)-2-octen-4-ol, giving an “real” *ee* for the purpose of the allylation reaction of 98.6 %). The *ee* and *Z*-*E* ratio were determined by chiral GC.

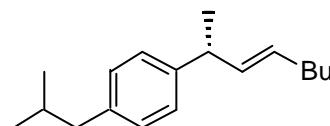
GC (50 °C; column: TFA  $\gamma$ -cyclodextrin, 30.0 m x 0.25 mm): *t*<sub>R</sub>/min = 26.8 (*R*), 31.3 (*S*).  
[ $\alpha$ ]<sub>D</sub> = -23.1 (c = 1.15, CHCl<sub>3</sub>).

b) **(1*S*, 2*Z*)-1-Butyl-2-butenyl-2,3,4,5,6-pentafluorobenzoate ((*S*)-Z-4)**



Pentafluorobenzoyl chloride (2.46 mL, 17.1 mmol) was added dropwise to a mixture stirred at -30 °C under an argon atmosphere of (2*Z*, 4*S*)-2-octen-4-ol (1.54 g, 12.0 mmol), dry pyridine (1.57 mL, 19.4 mmol) and DMAP (145 mg, 1.2 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (100 mL) and the resulting mixture was allowed to warm to -8 °C over 2 h. Water was added to quench the reaction and the phases were separated. The aqueous phase was extracted twice with Et<sub>2</sub>O and the combined extracts were washed with saturated, aqueous NaHCO<sub>3</sub>, then brine, and dried (MgSO<sub>4</sub>). Following evaporation of the solvents *in vacuo*, the residue was dissolved in pentane and washed with saturated, aqueous NaHCO<sub>3</sub> (until the organic layer was clear), then with brine, and dried (MgSO<sub>4</sub>). The pentane was evaporated *in vacuo* and impurities were removed under vacuum to give the pentafluorobenzoate ester (*S*)-Z-4 (3.27 g, 84 %) as a colourless liquid. [ $\alpha$ ]<sub>D</sub> = +58.9 (c = 1.05, CHCl<sub>3</sub>).

**1-Isobutyl-4-[(1*R*, 2*E*)-1-methyl-2-heptenyl]benzene (18)**



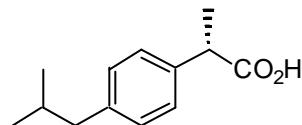
*t*-BuLi (1.6 M in pentane; 3.13 mL, 5.00 mmol) was added dropwise to a stirred solution of 4-isobutyliodobenzene (0.684 g, 2.63 mmol) in dry THF (12 mL) at -78 °C under an argon atmosphere. The resulting solution was stirred at -78 °C for a further 30 min, then at -30 °C for 20 min. A solution of ZnBr<sub>2</sub> (1.5 M in THF; 0.8 mL, 1.25 mmol) was added dropwise and the resulting mixture was stirred at -30 °C under argon for a further 20 min, then the solvents were evaporated *in vacuo* using an oil pump (-30 °C, then rt; 10 min), to leave a oily residue. This was redissolved in THF (3 mL) and cooled to -30 °C, whereupon a solution of CuCN·2LiCl (1 M in THF; 0.62 mL, 0.62 mmol) was added dropwise. The mixture was stirred a further 30 min, then the

pentafluorobenzoate ester (*S*)-**4** (161 mg, 0.50 mmol) was added dropwise as a solution in THF (0.8 mL) and the reaction mixture was allowed to warm to  $-10$  °C over 2 h, then was stirred at this temperature for a further 18 h. Saturated aqueous NH<sub>4</sub>Cl (20 mL) was added to quench the reaction and the mixture was stirred with 25 % aqueous ammonia (1 mL) until the copper salts had dissolved. The mixture was then extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 20 mL), the combined extracts were washed with brine and the brine layer was reextracted with CH<sub>2</sub>Cl<sub>2</sub> (20 mL). The combined organic layers were dried (MgSO<sub>4</sub>), the solvents were evaporated *in vacuo* and the residue was subjected to column chromatography (SiO<sub>2</sub>; pentane), followed by further purification under an oil pump vacuum, to provide **18** (111 mg, 91 %) as a colourless liquid.

$[\alpha]_D = -12.0$  (c = 1.2, CHCl<sub>3</sub>).

Found, C, 88.4 %; H, 11.6 %. C<sub>18</sub>H<sub>28</sub> requires C, 88.5 %; H, 11.6 %.  $\delta_H$  (CDCl<sub>3</sub>, 400 MHz): 0.87-0.92 (m, 3H), 0.91 (d,  $J = 6.8$  Hz, 6H), 1.21-1.40 (m, 4H), 1.33 (d,  $J = 6.8$  Hz, 3H), 1.85 (non,  $J = 6.8$  Hz, 1H), 1.98-2.06 (m, 2H), 2.45 (d,  $J = 6.8$  Hz, 2H), 3.94 (q,  $J = 6.8$  Hz, 1H), 5.44 (dtm,  $J = 15.2$ , 6.6 Hz, 1H), 5.59 (ddt,  $J = 15.2$ , 6.8, 1.2 Hz, 1H), 7.05-7.14 (m, 4H).  $\delta_C$  (CDCl<sub>3</sub>, 100 MHz): 13.9, 21.6, 22.2, 22.4, 30.2, 31.8, 32.2, 41.9, 45.1, 126.8, 129.0, 135.1, 139.1, 143.8.  $\nu_{\text{max}}/\text{cm}^{-1}$  (film): 1510. *m/z* (EI<sup>+</sup>): 244.2200 (M<sup>+</sup>). C<sub>18</sub>H<sub>28</sub> requires M<sup>+</sup>, 244.2191).

### (*S*)-(+)-Ibuprofen (**16**)



(*S*)-(+)-Ibuprofen was prepared according to TP2 and starting from **18** (86 mg, 0.35 mmol). After addition of Jones reagent at  $-78$  °C the mixture was stirred while warming up to rt. Excess of isopropanol was added and the solvents were removed *in vacuo*. The residue was partitioned in Et<sub>2</sub>O:water = 4:1 and the layers separated. The organic layer was washed with HCl 1 M. The carboxylic acids extracted with NaOH 1 M; the aqueous layer cooled to 0 °C and reacidified with HCl 6M. The carboxylic acids were extracted with Et<sub>2</sub>O. The organic layer was dried (Na<sub>2</sub>SO<sub>4</sub>) and the solvent was removed. Evaporation of the pentanoic acid by-product *in vacuo* (oil pump), provided (+)-ibuprofen (58 mg, 80 %, 97.2 % *ee*, see chiral GC in appendix) as a colourless oil (white solid in the case of the racemate!). The enantiomeric excess was determined by chiral GC (160 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm): *t<sub>R</sub>*/min 97.2 (*S*), 104.4 (*R*).

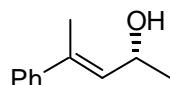
$[\alpha]_D = +54.5$  (c = 1.1, CHCl<sub>3</sub>).

M.p. (racemate): 69-71 °C (Lit.<sup>15</sup> 76-77 °C).  $\delta_H$  (CDCl<sub>3</sub>, 300 MHz): 0.90 (d,  $J = 6.6$  Hz, 6H), 1.50 (d,  $J = 6.9$  Hz, 3H), 1.75-1.95 (m, 1H), 2.45 (d,  $J = 6.9$ , 2H), 3.71 (q,  $J = 6.9$  Hz, 1H), 7.06-7.14 (m, 2H), 7.18-7.26 (m, 2H).  $\delta_C$  (CDCl<sub>3</sub>, 75 MHz): 18.1, 22.4, 30.2, 45.0, 45.1, 127.3, 129.4, 137.0, 140.9, 180.6.  $\nu_{\text{max}}/\text{cm}^{-1}$  (KBr disk): 3660-2300, 1720, 1510.

### Appendix I: Determination of enantiomeric excess by chiral GC.

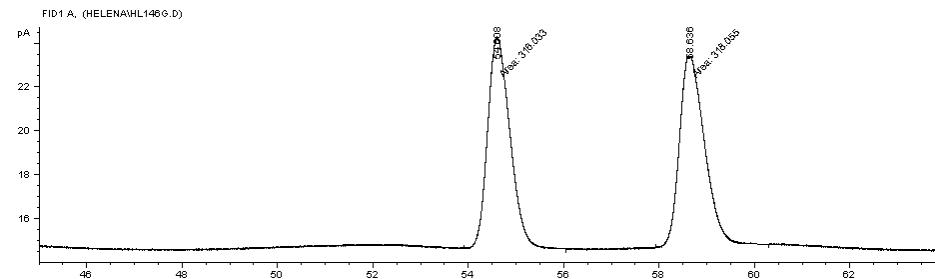
#### (*2R, 3E*)-4-Phenyl-3-penten-2-ol

(determination of the *ee* of (*1R, 2E*)-1-methyl-3-phenyl-2-but enyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-*E*-**13**))

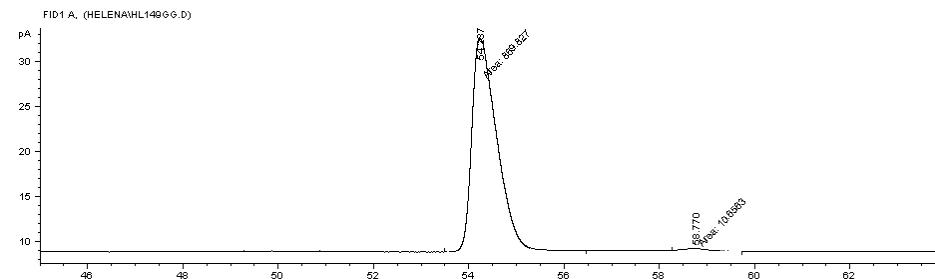
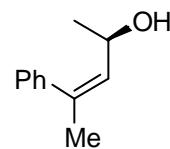


GC (120 °C; column: Chiraldex B-PH, 30 m x 0.25 mm): *t<sub>R</sub>*/min 54.6 (*R*), 58.6 (*S*); 98 % *ee*.

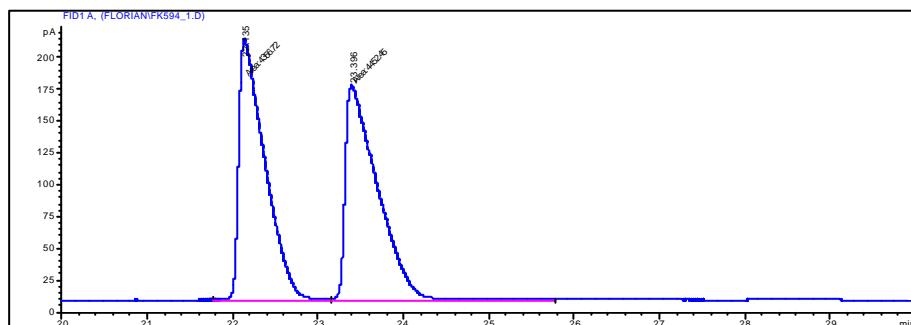
a) racemic



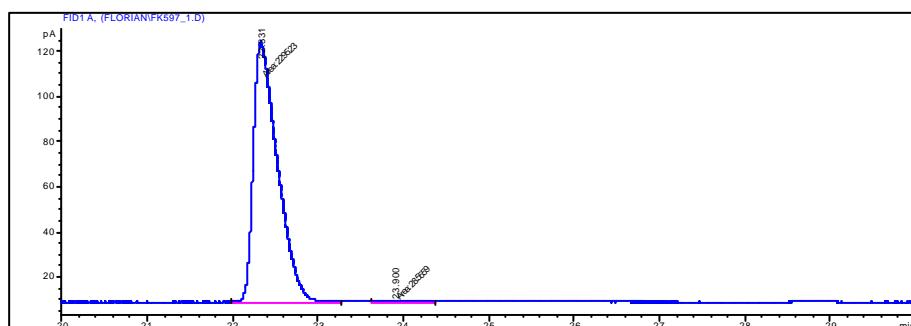
b) chiral

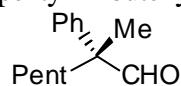
**(2R, 3Z) 4-Phenyl 3-penten-2-ol**(determination of the *ee* of (1*R*, 2*Z*)-1-methyl-3-phenyl-2-but enyl 2,3,4,5,6-pentafluorobenzoate ((*R*)-Z-13))GC (120 °C; column: Chiraldex B-PH, 30.0 m x 0.25 mm):  $t_R$ /min 22.1 (R), 23.4 (S); 98 % *ee*.

a) racemic



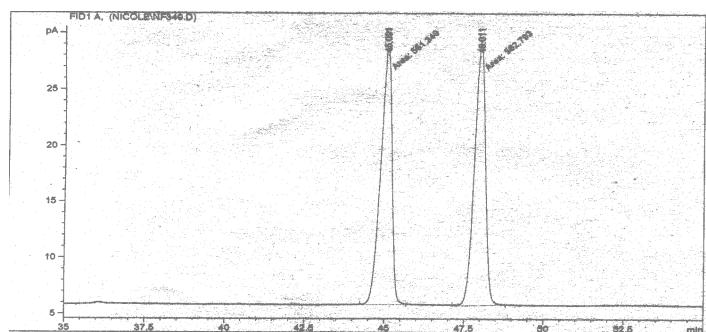
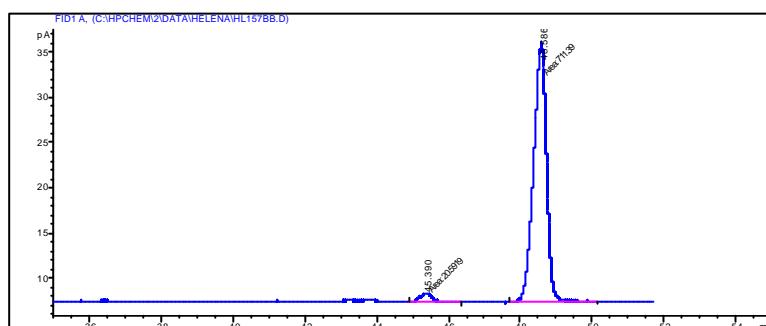
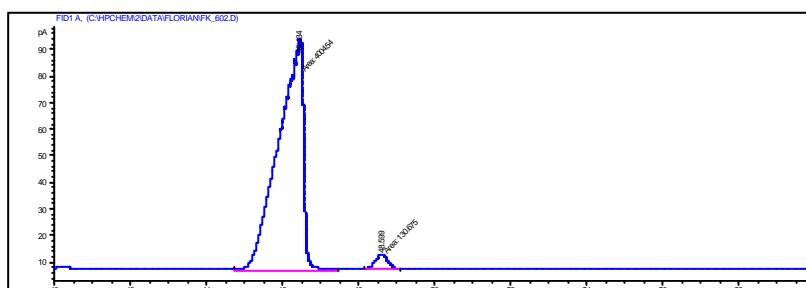
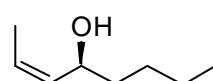
b) chiral



**(2*R*)-2-Methyl-2-phenylheptanal ((*R*)-15 and (*S*)-15)**(determination of the *ee* of [(2*E*)-1-methyl-1-pentyl-2-butenyl]benzene, (*S*)-*E*-14) and (*R*)-*E*-14)

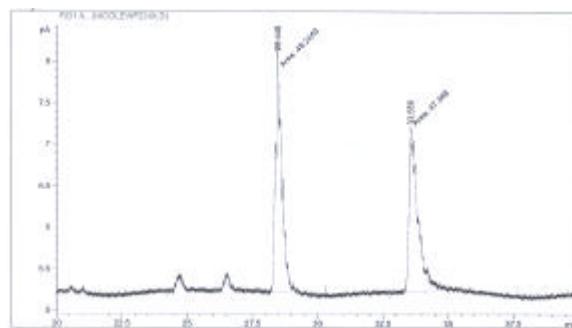
chiral GC (100 °C; column: TFA  $\gamma$ -cyclodextrin, 30 m x 0.25 mm):  $t_R$ /min: 45.4 (*S*), 48.6 (*R*); 94 % *ee*.

a) racemic

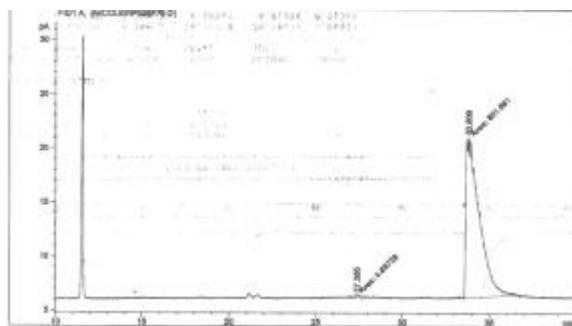
b) (*R*)-15c) (*S*)-15**(2*Z*, 4*S*)-2-Octen-4-ol**

GC (50 °C; column: TFA  $\gamma$ -cyclodextrin, 30.0 m x 0.25 mm):  $t_R$ /min = 26.8 (*R*), 31.3 (*S*).

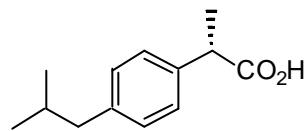
a) racemic



b) chiral

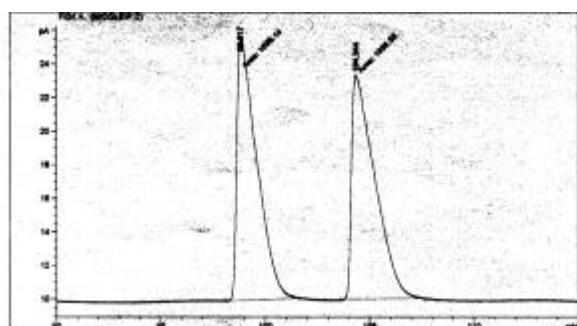


**(S)-(+)-Ibuprofen (16)**

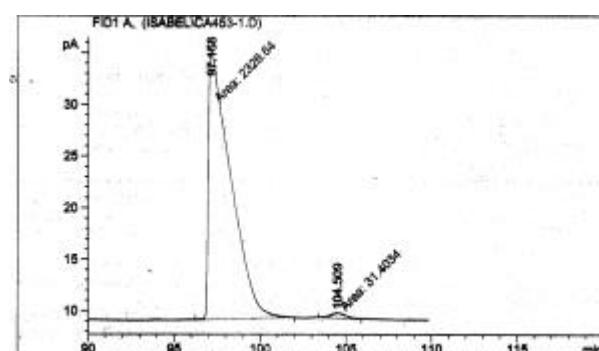


chiral GC (160 °C; Chiraldex B-PH, 30 m, 0.25 mm):  $t_R$ /min 97.2 (S), 104.4 (R); 97.2 % ee.

a) racemic

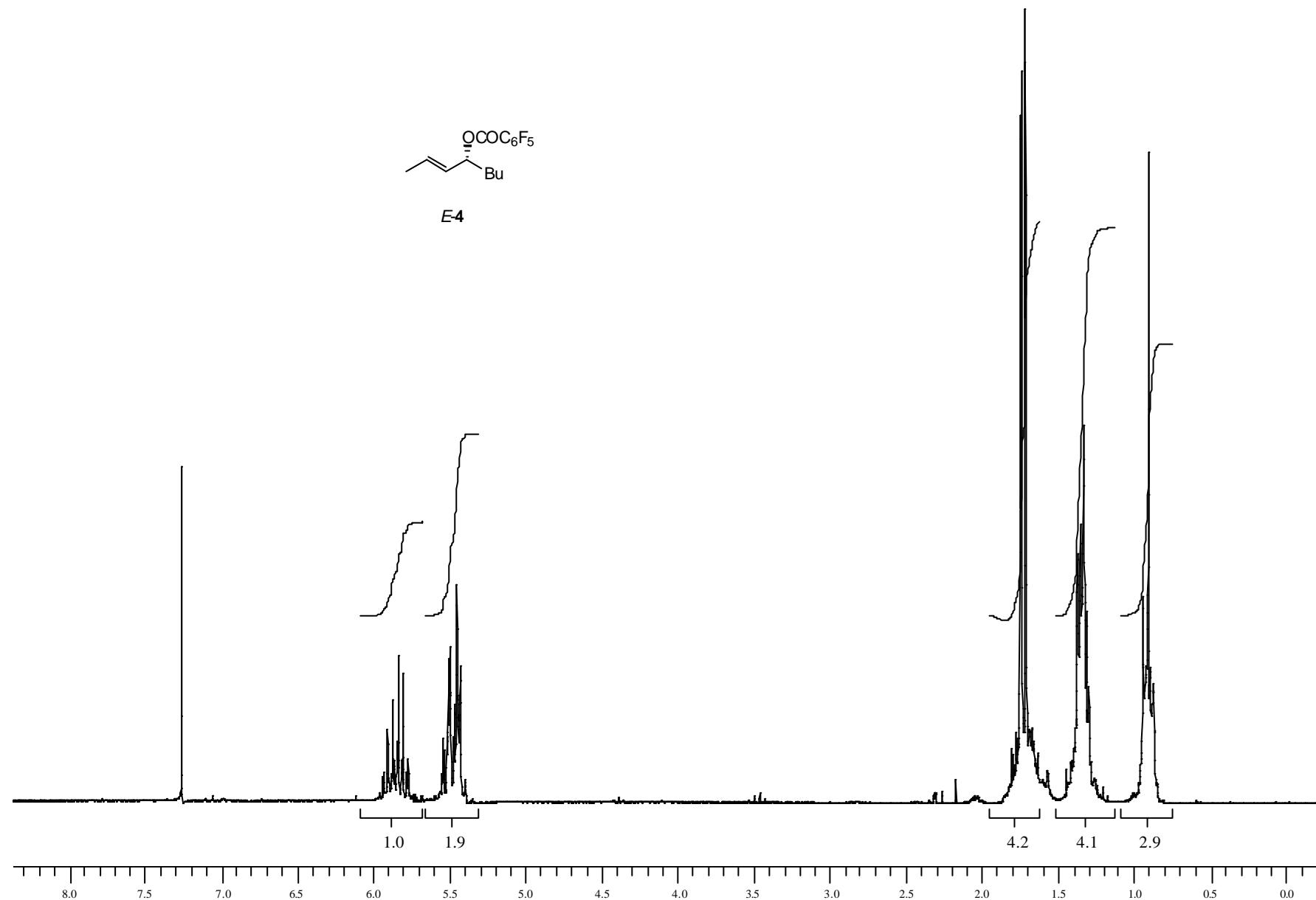


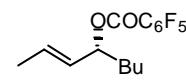
b) chiral



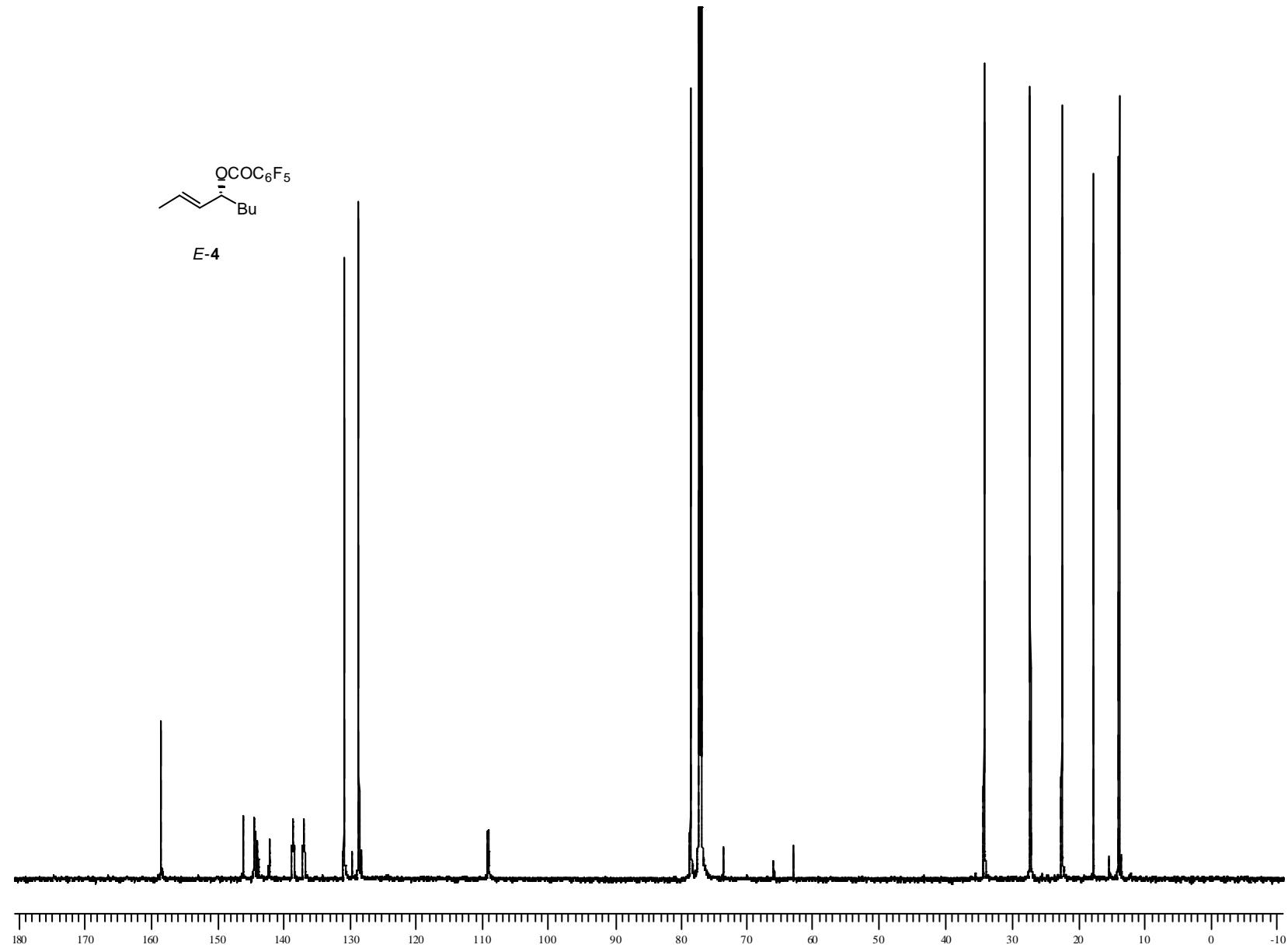
## References and notes

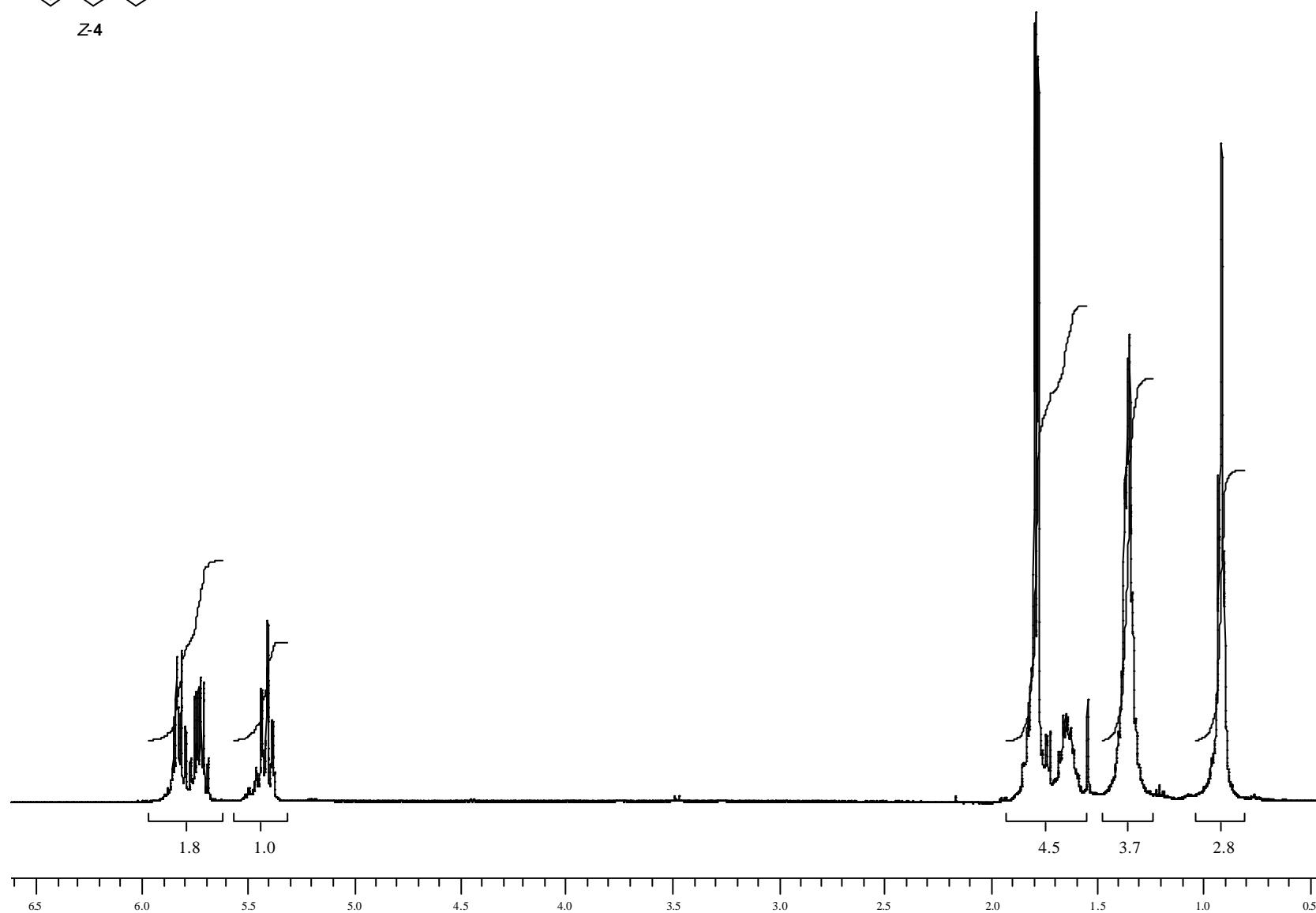
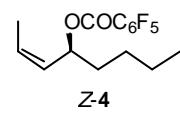
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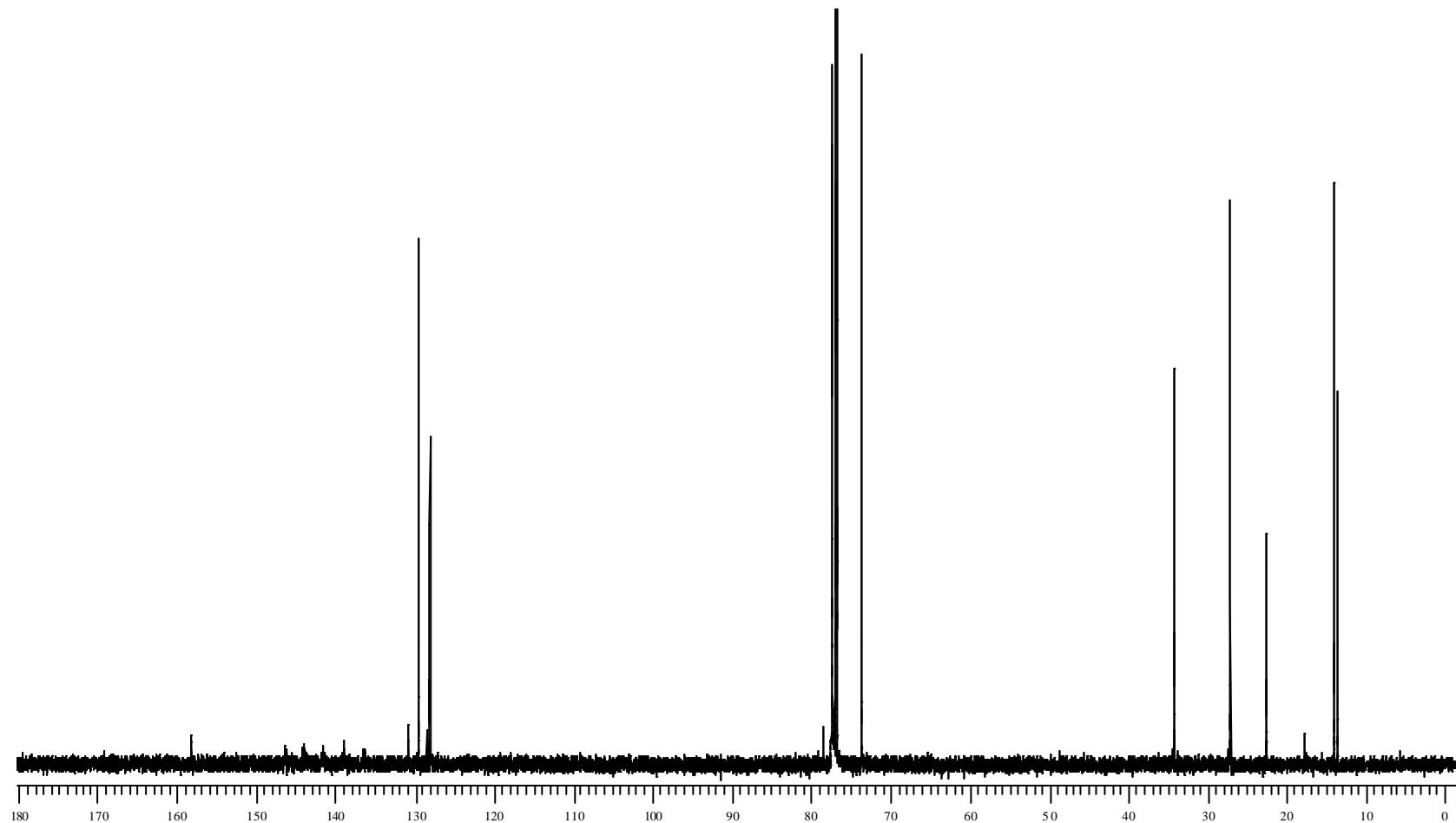
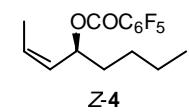


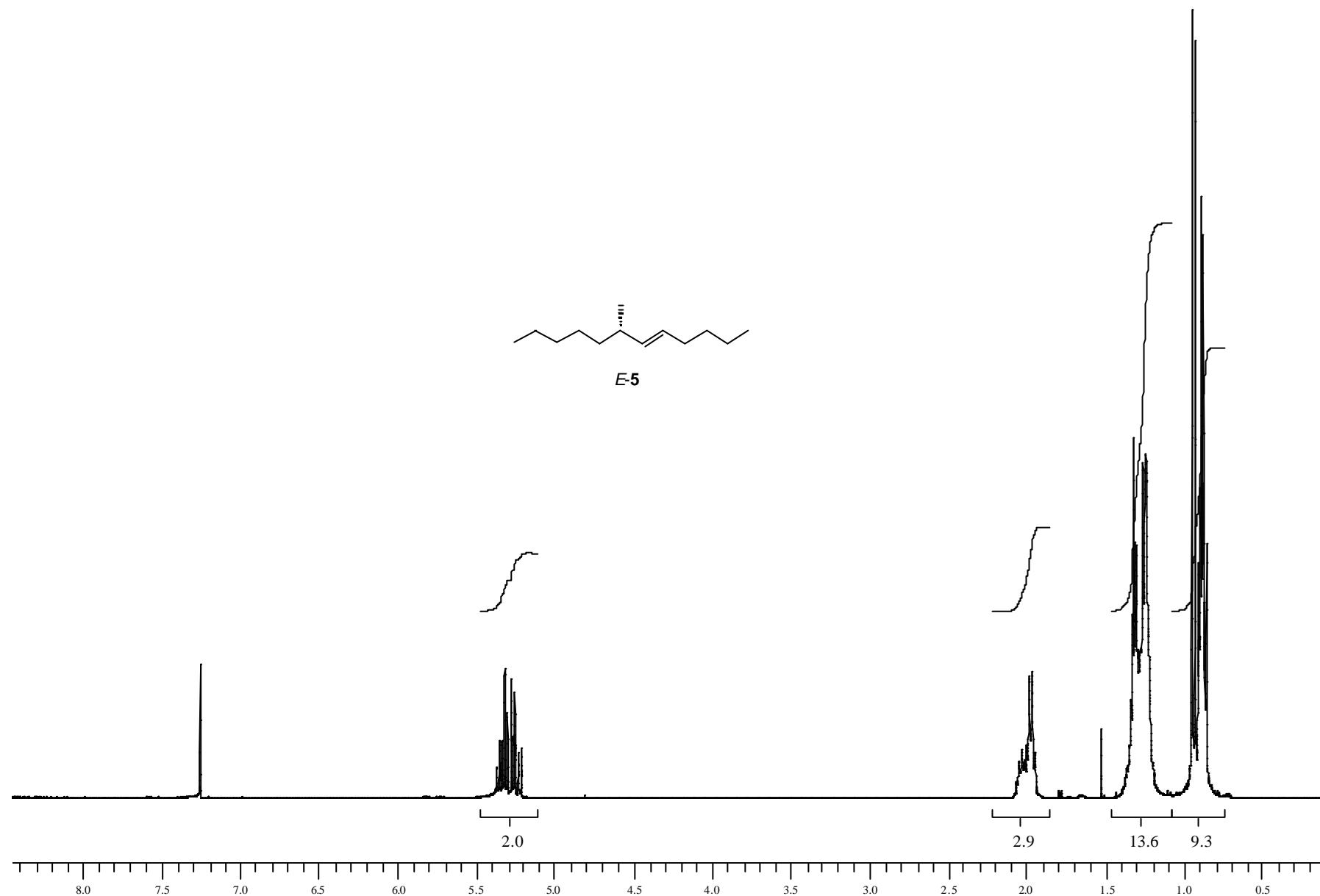


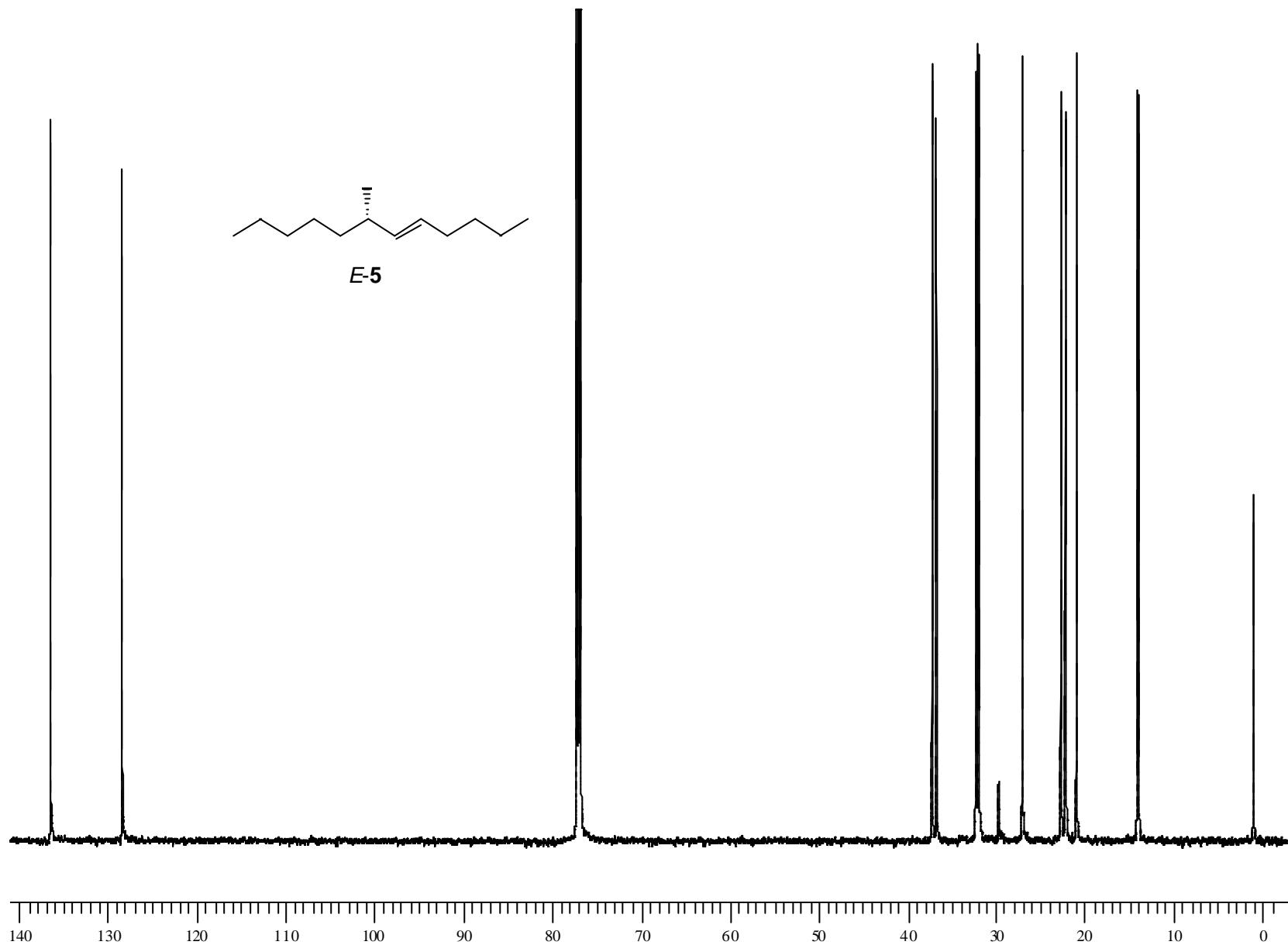
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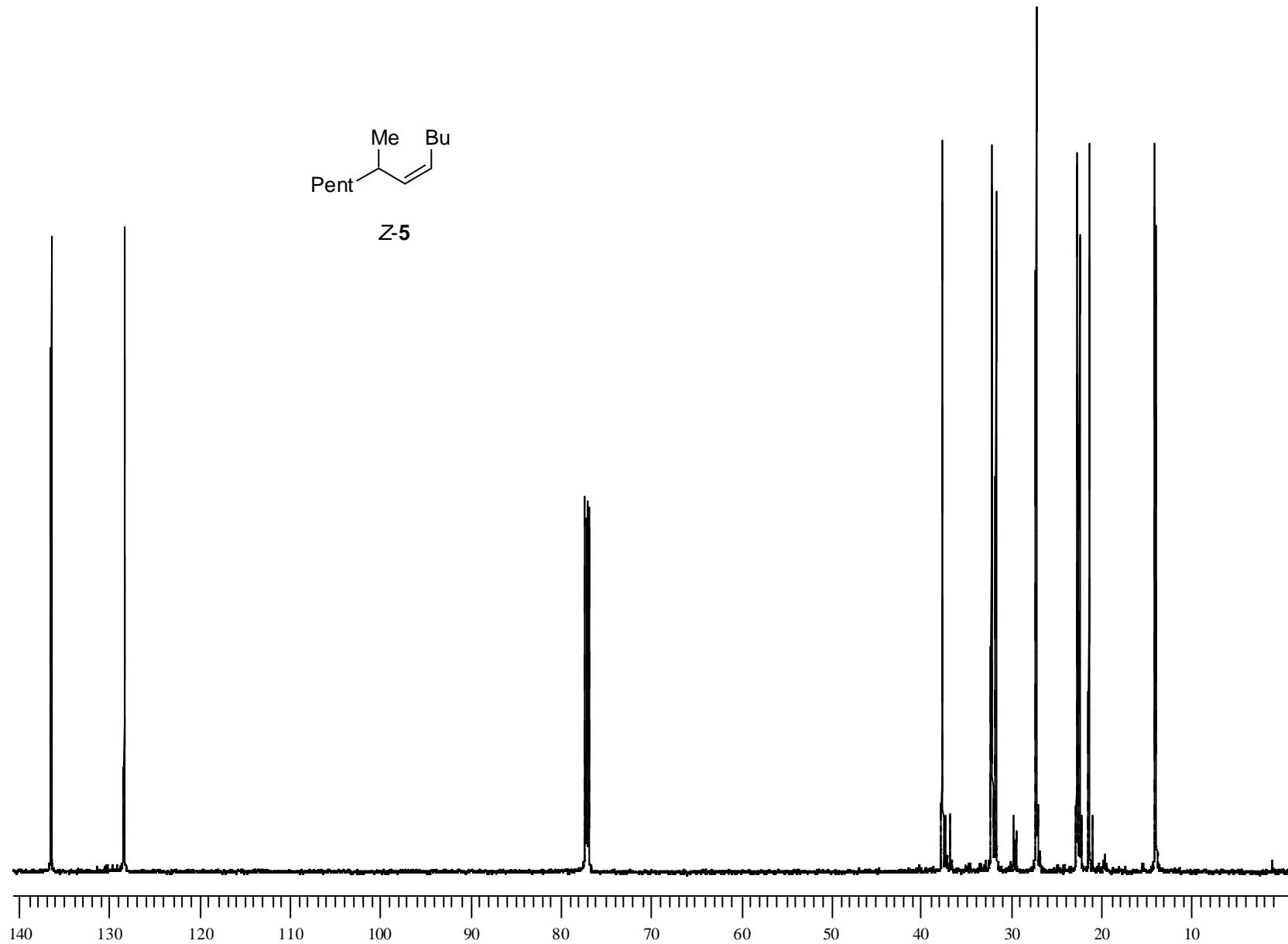


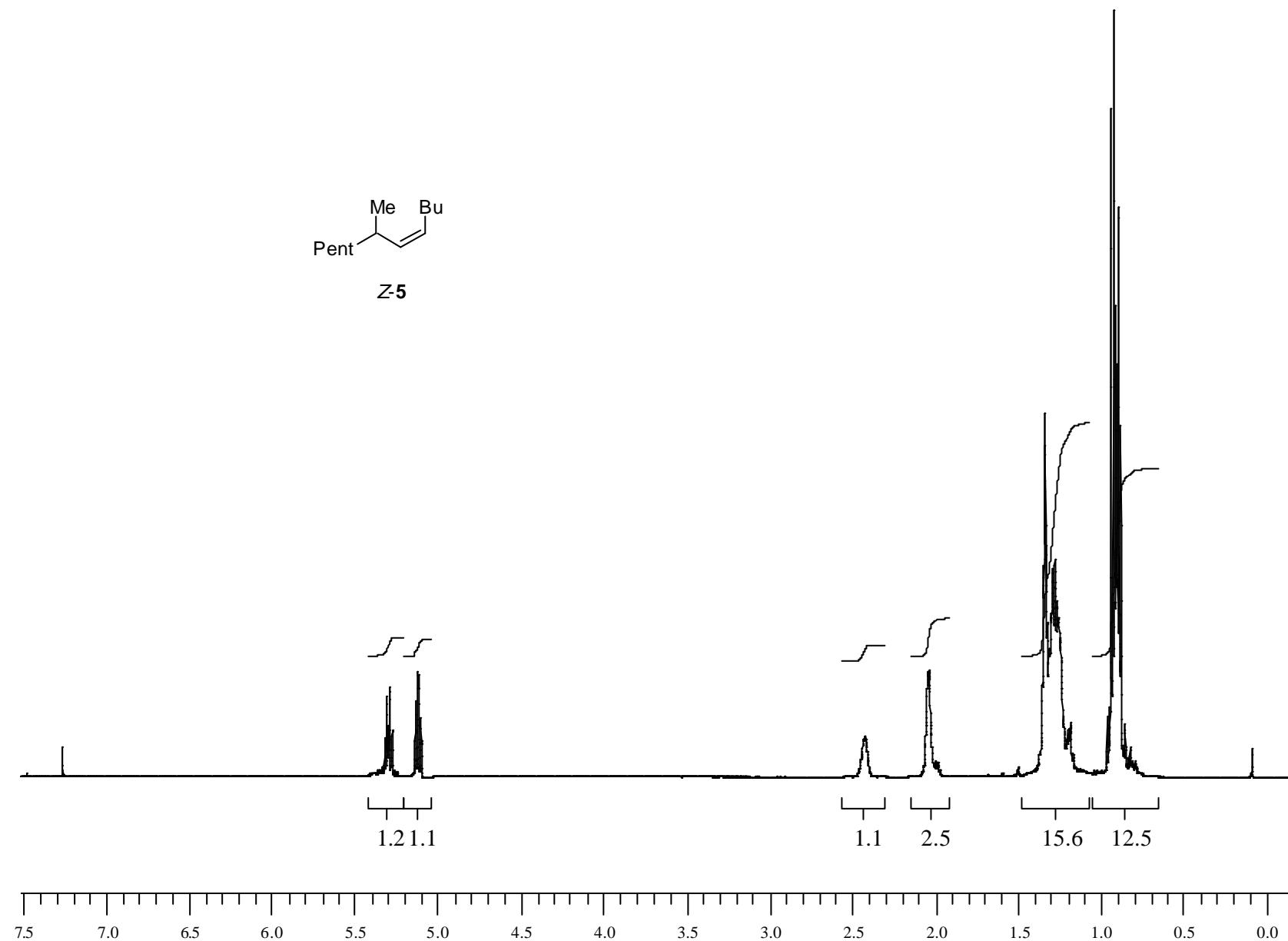


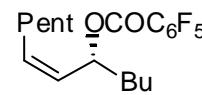




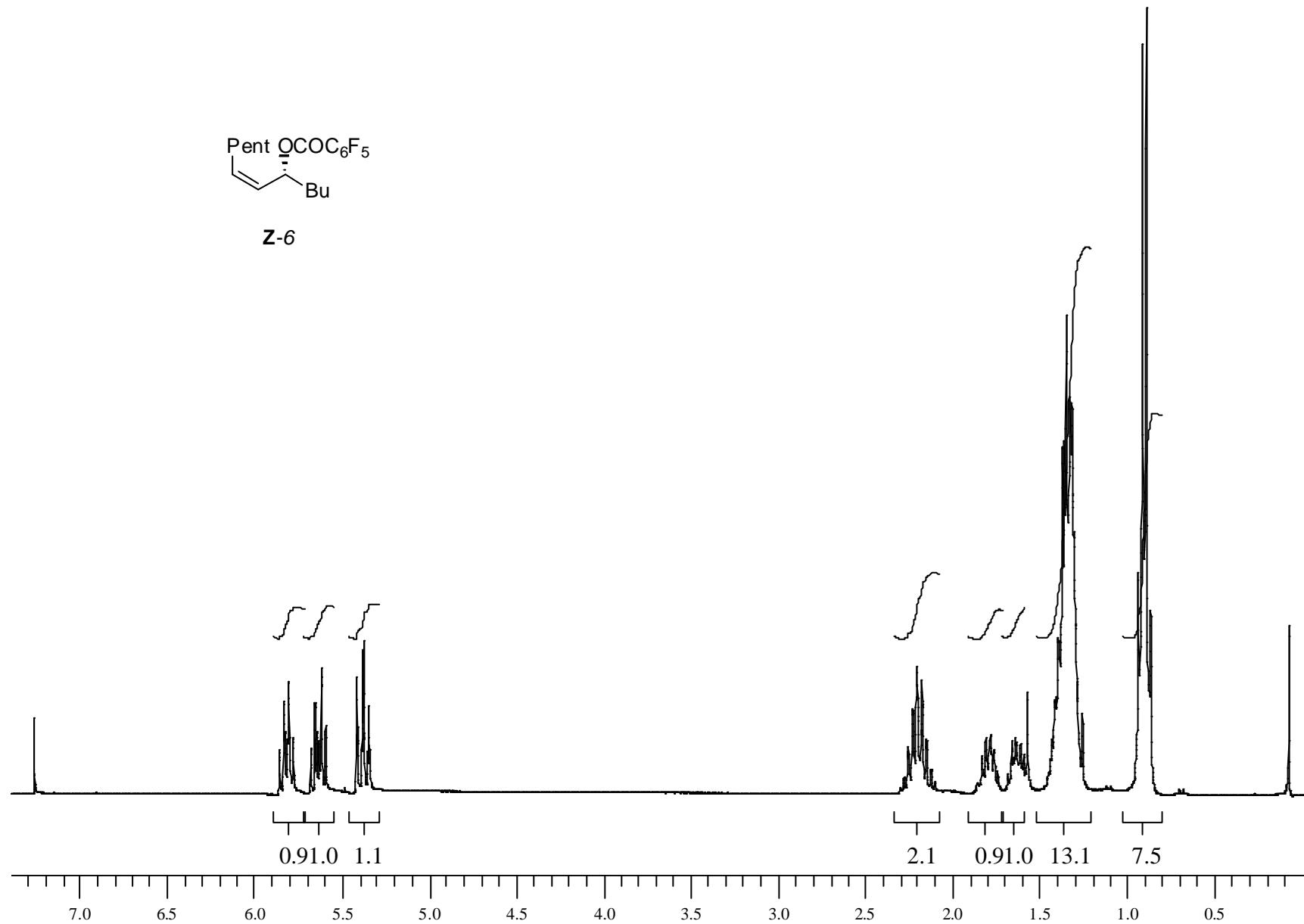


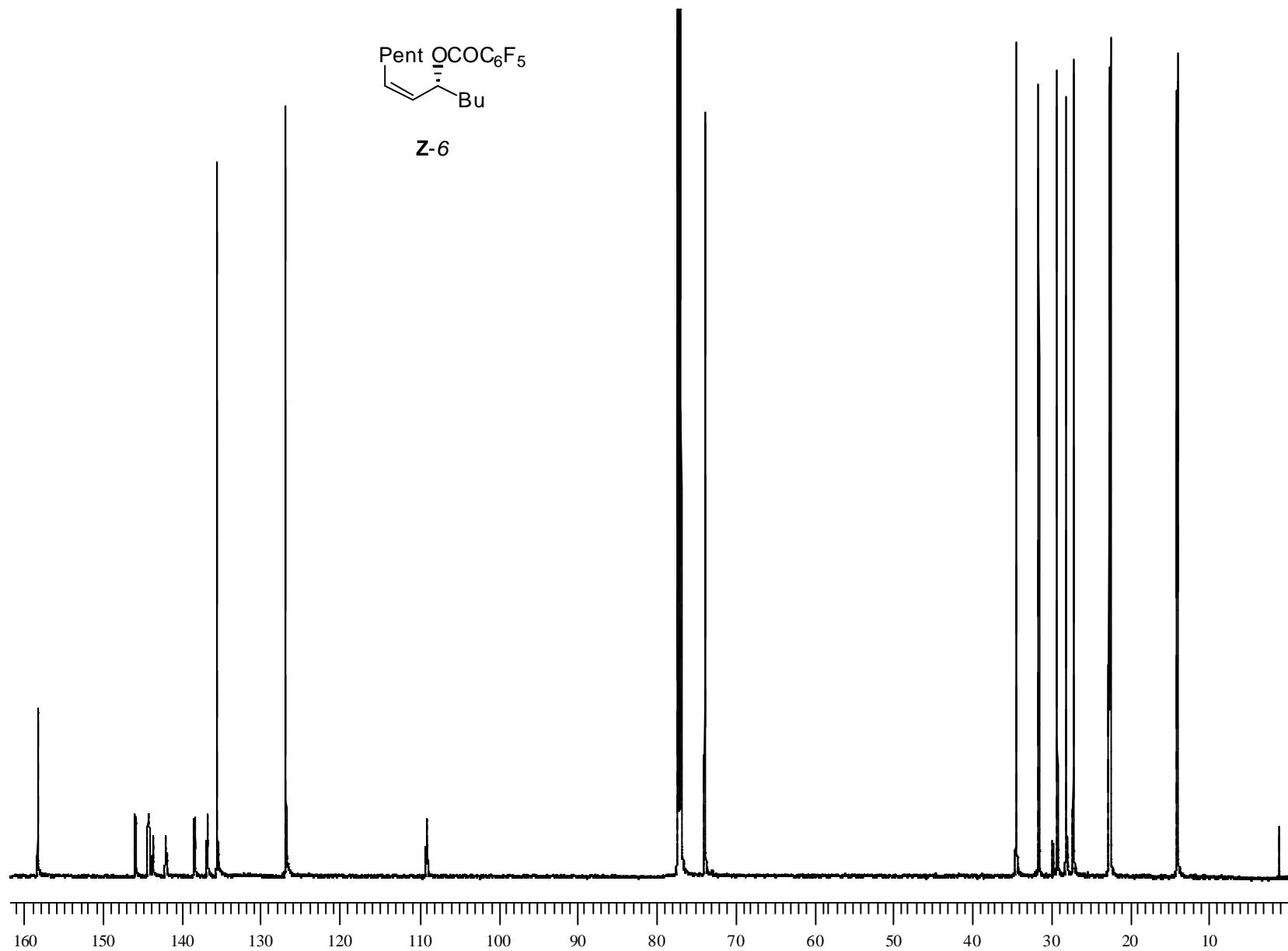


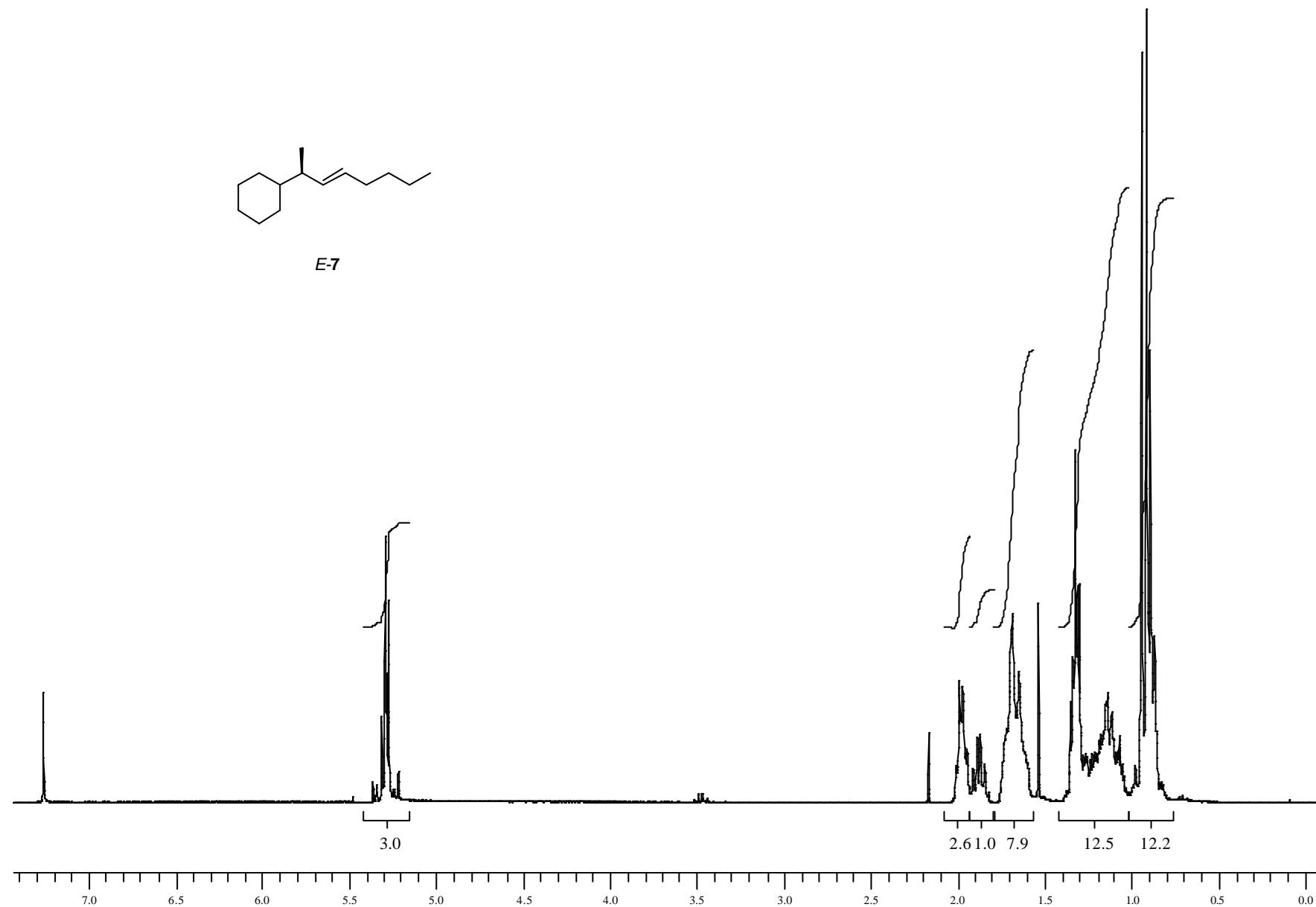


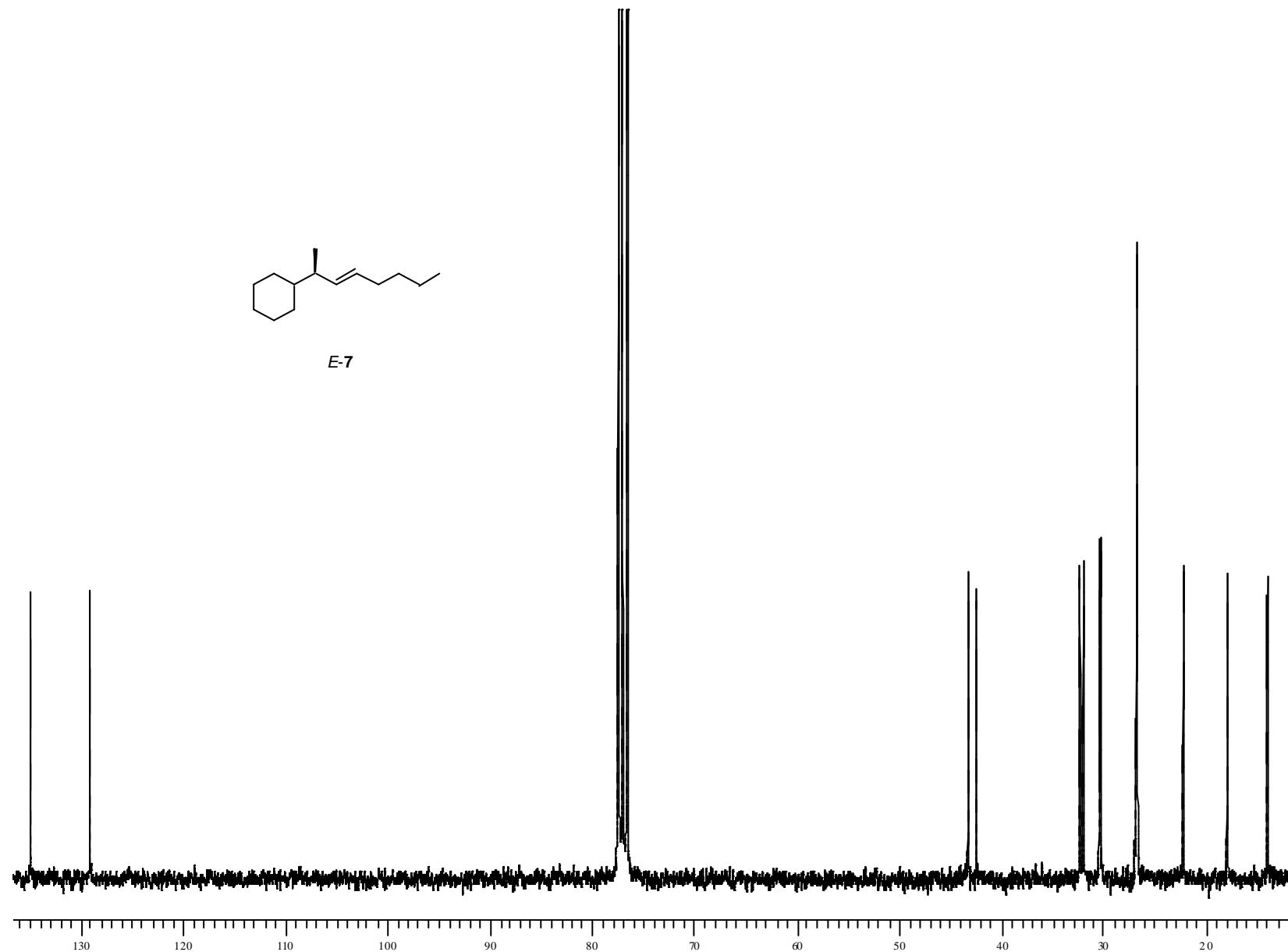


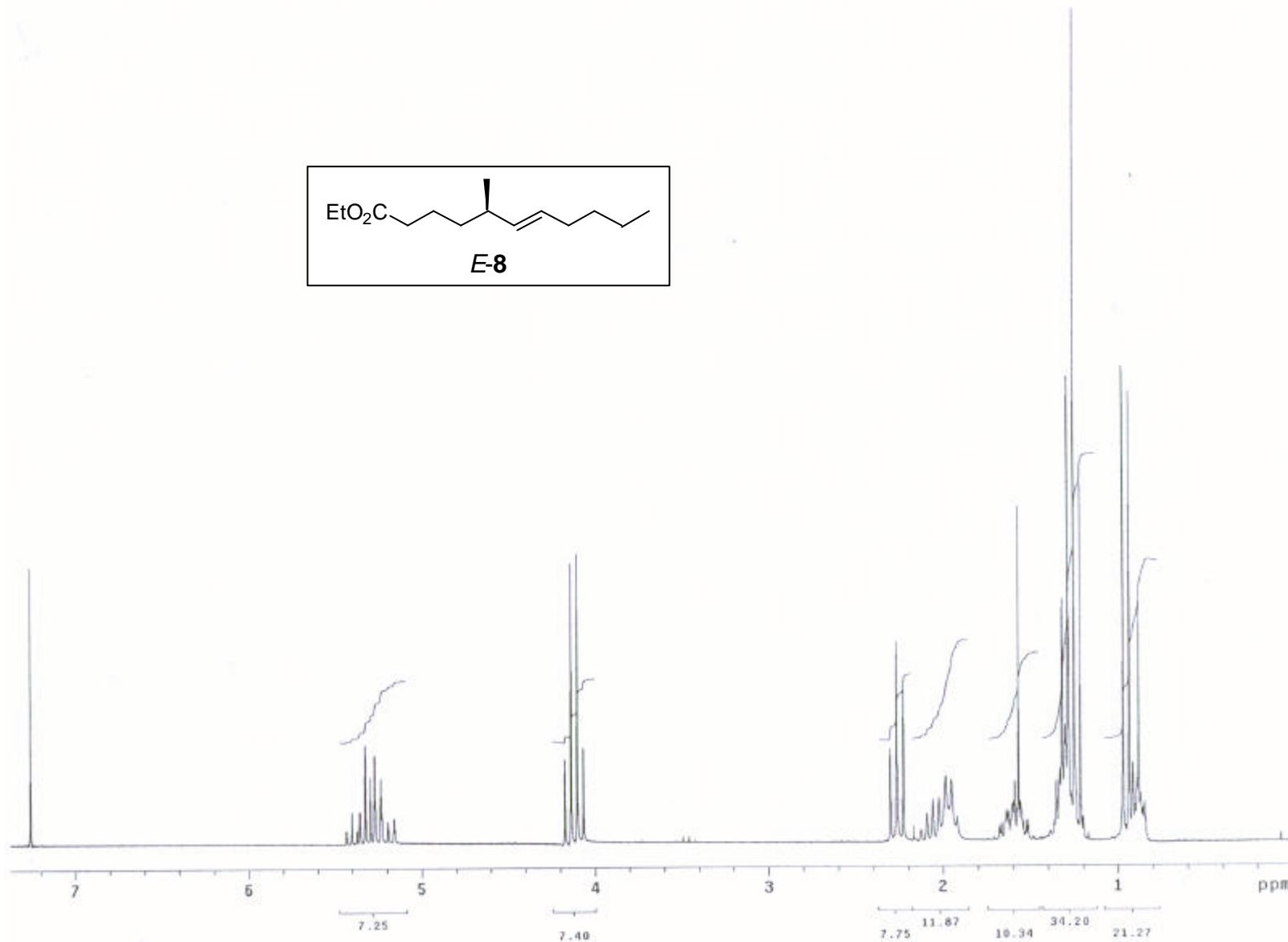
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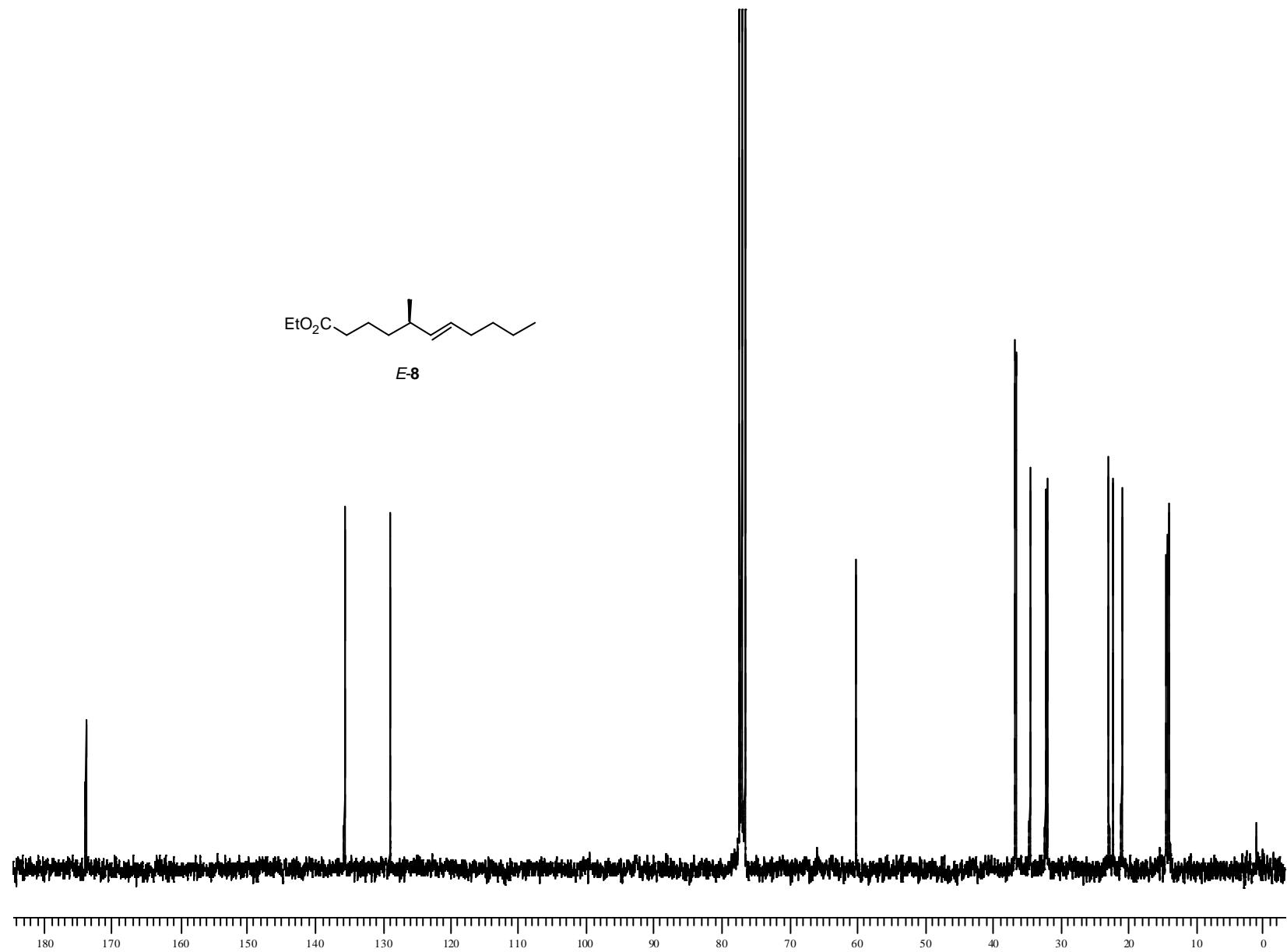


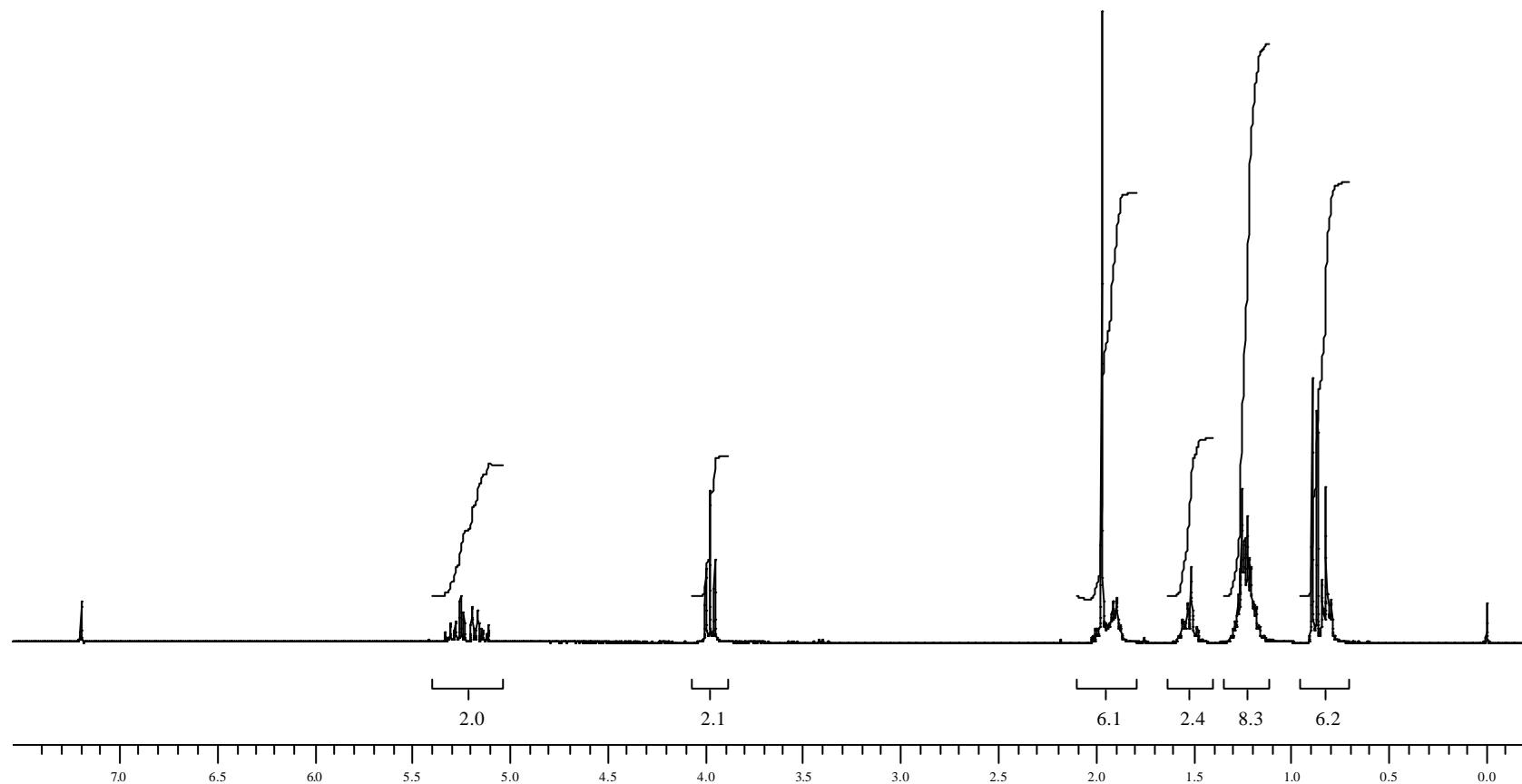
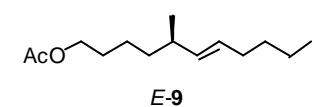


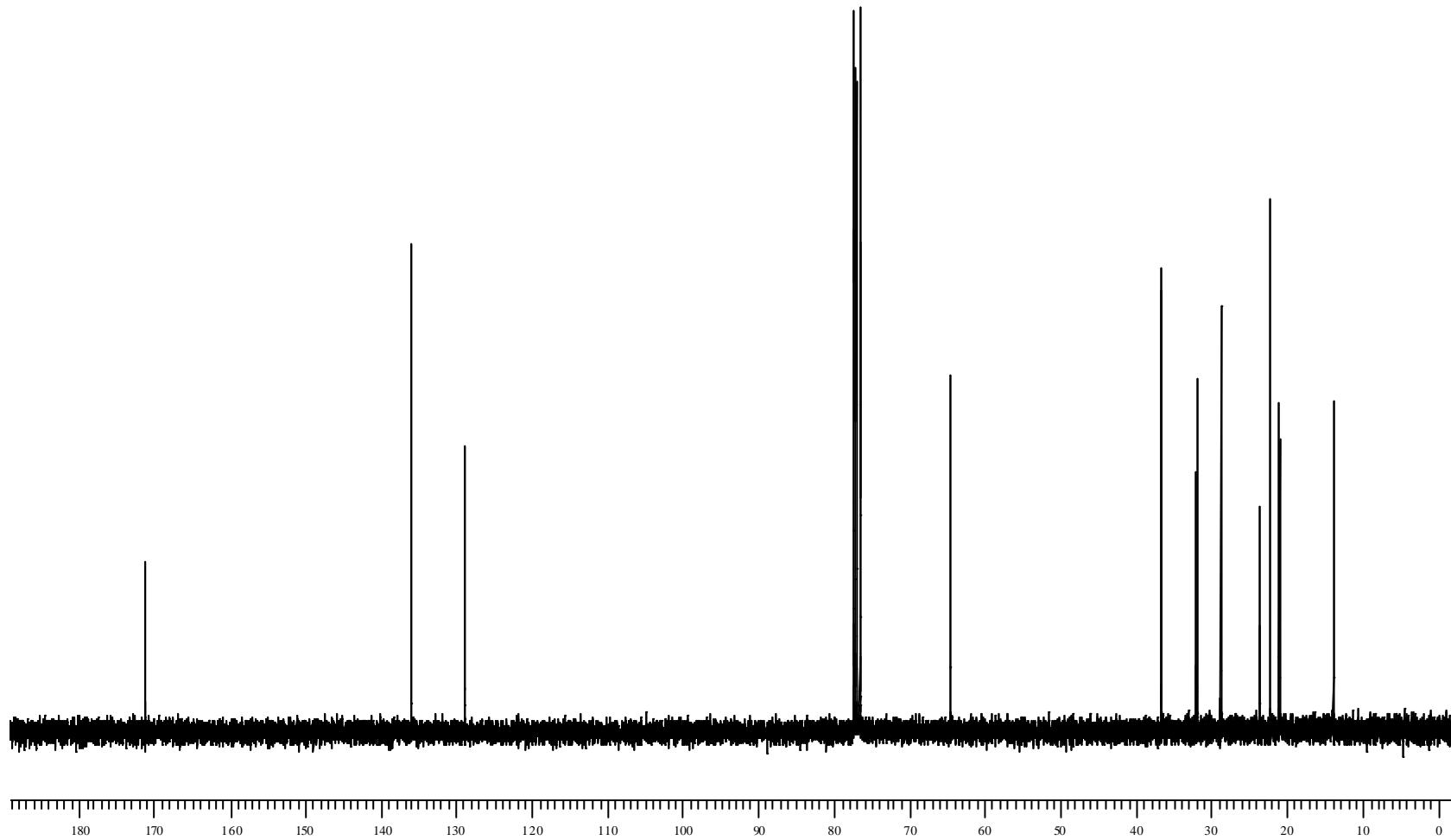
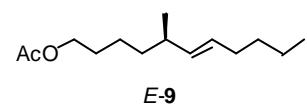


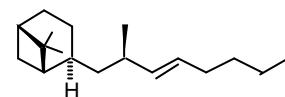




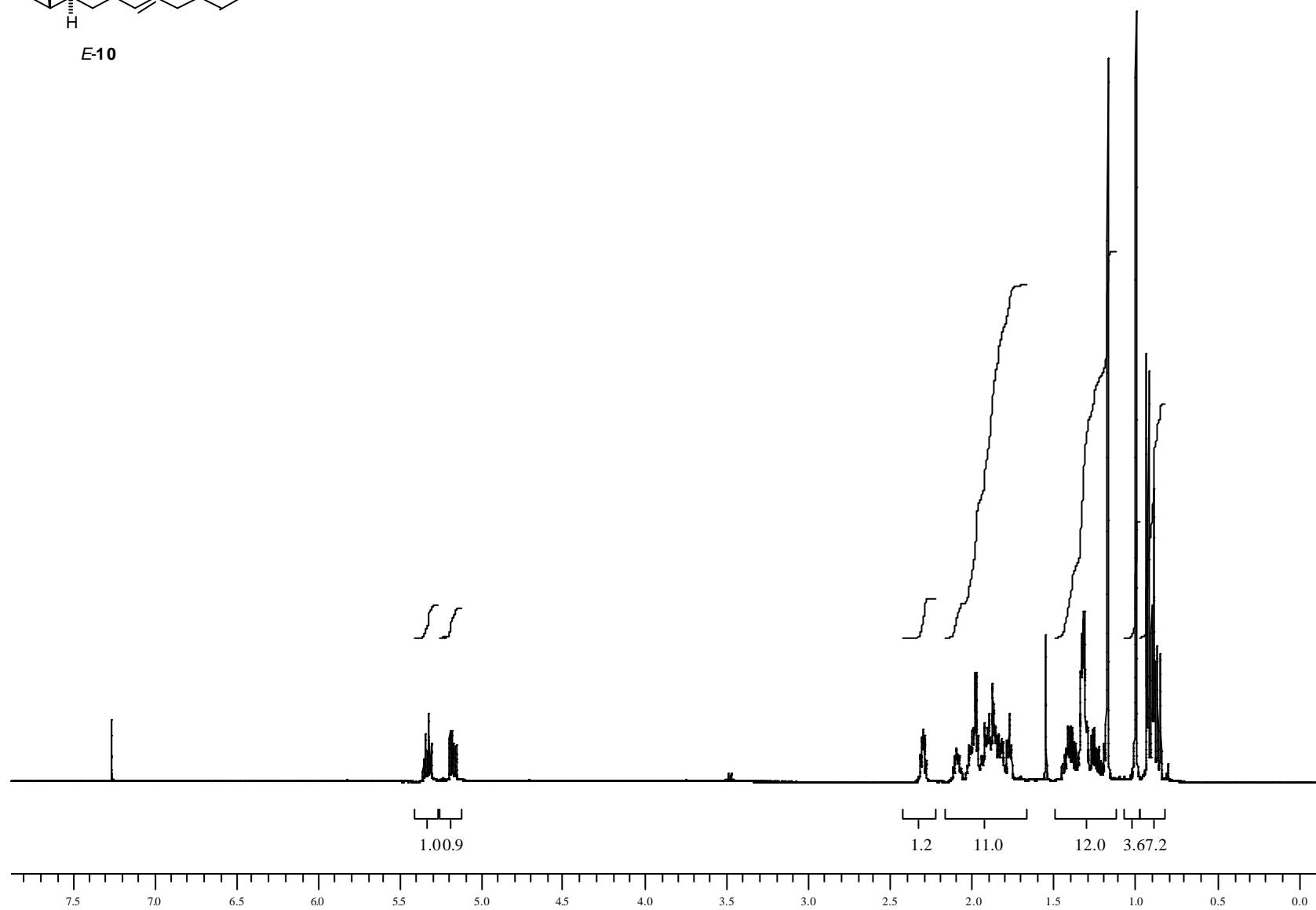


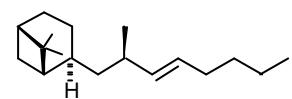




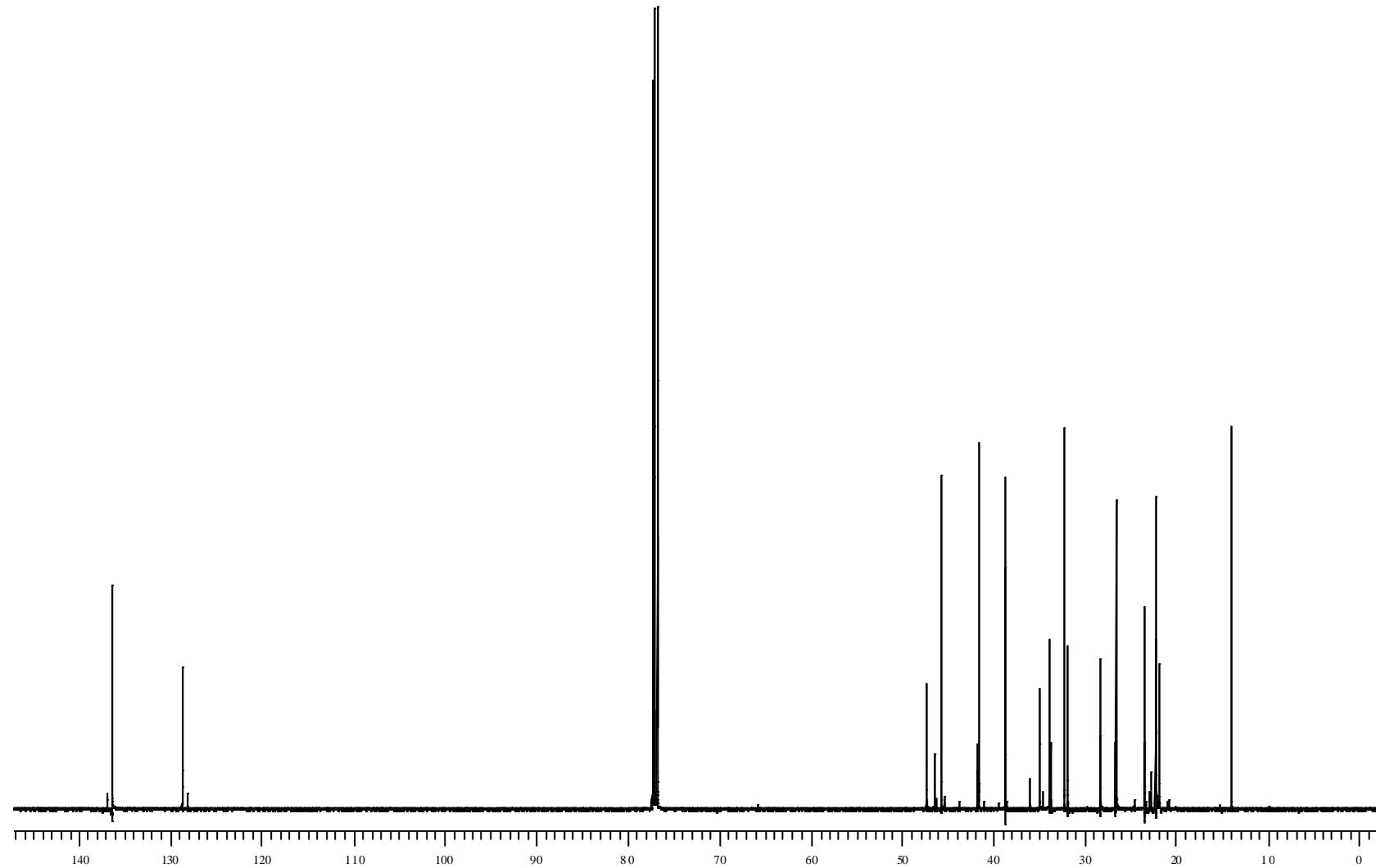


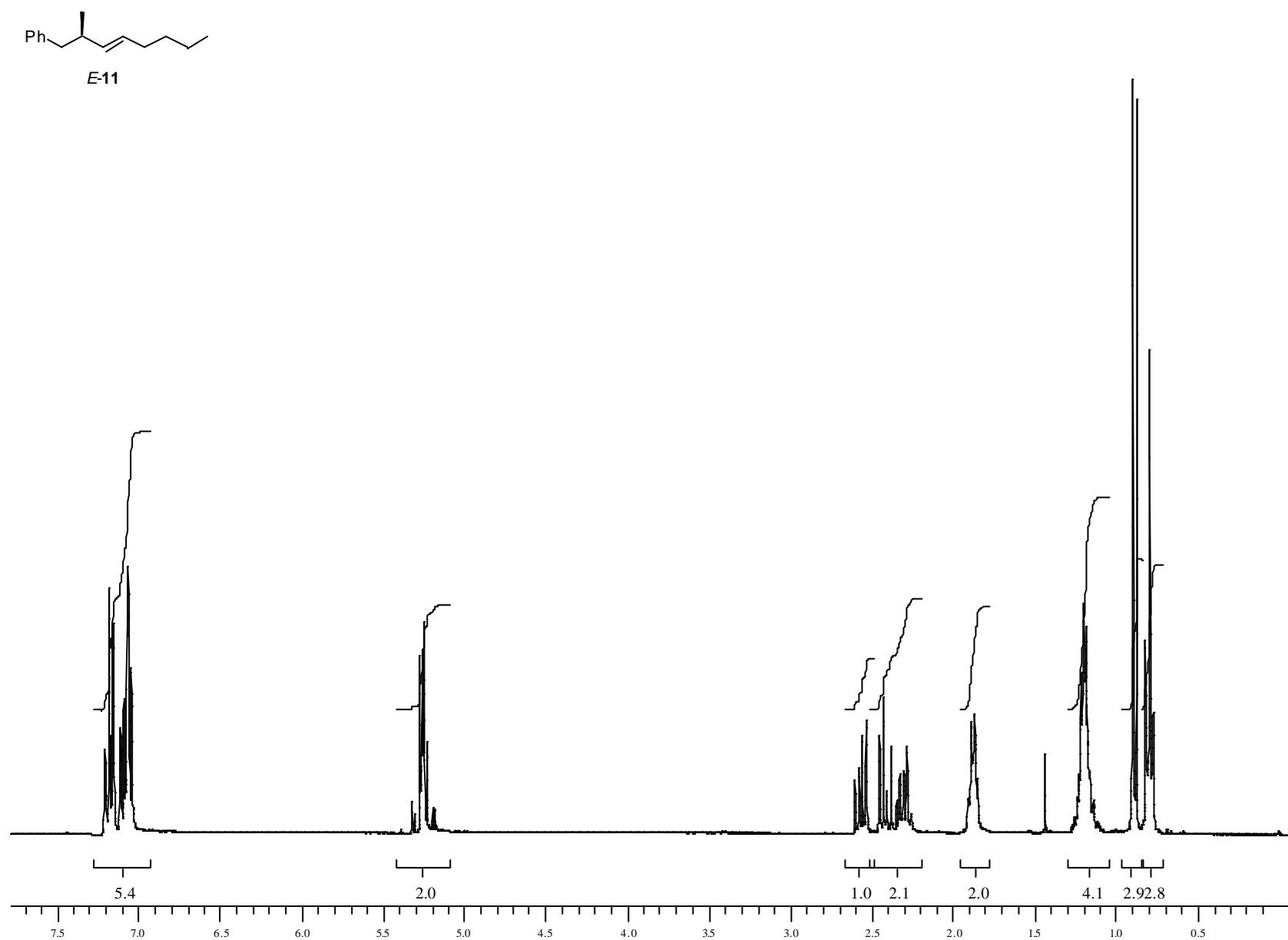
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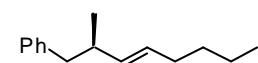




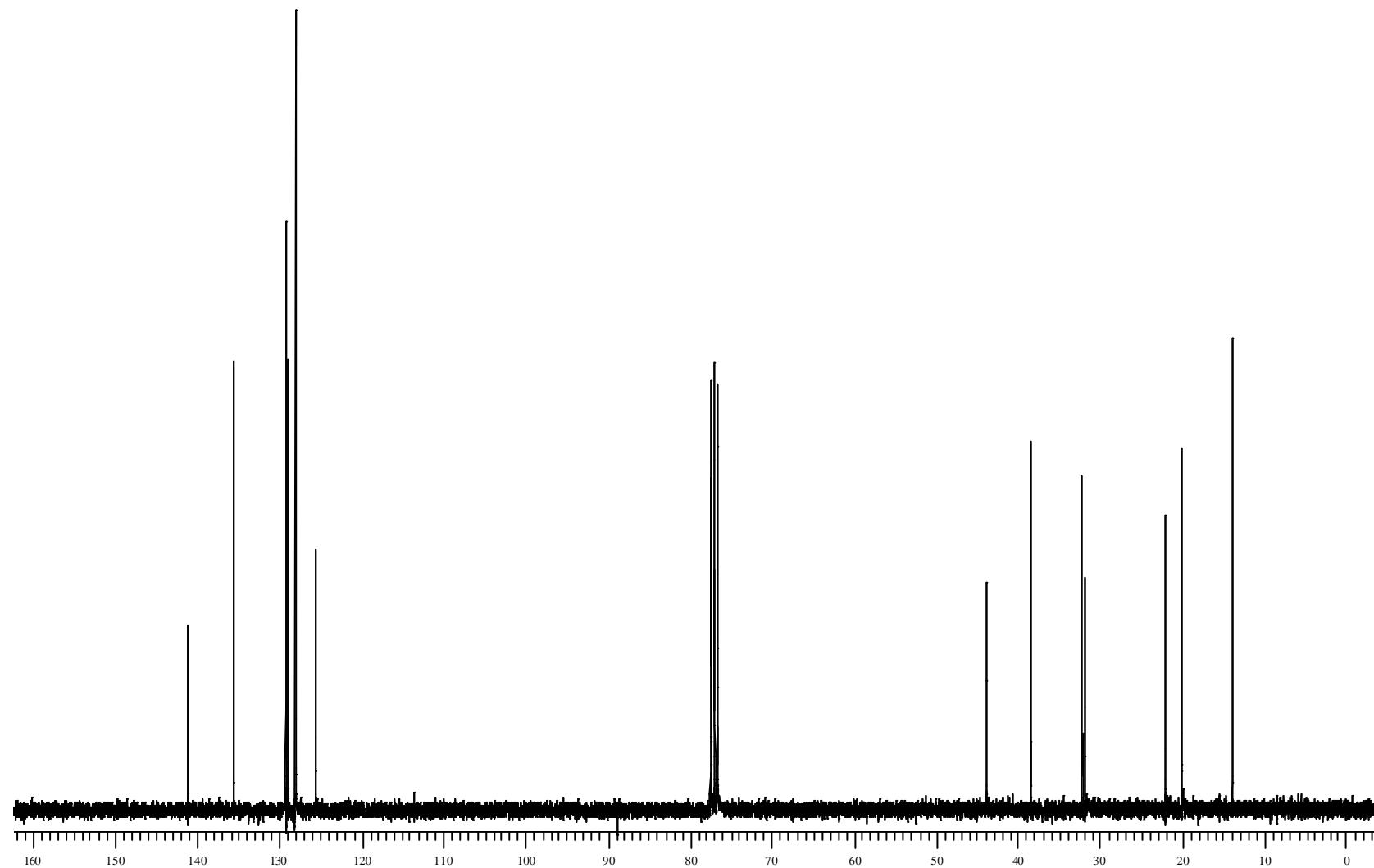
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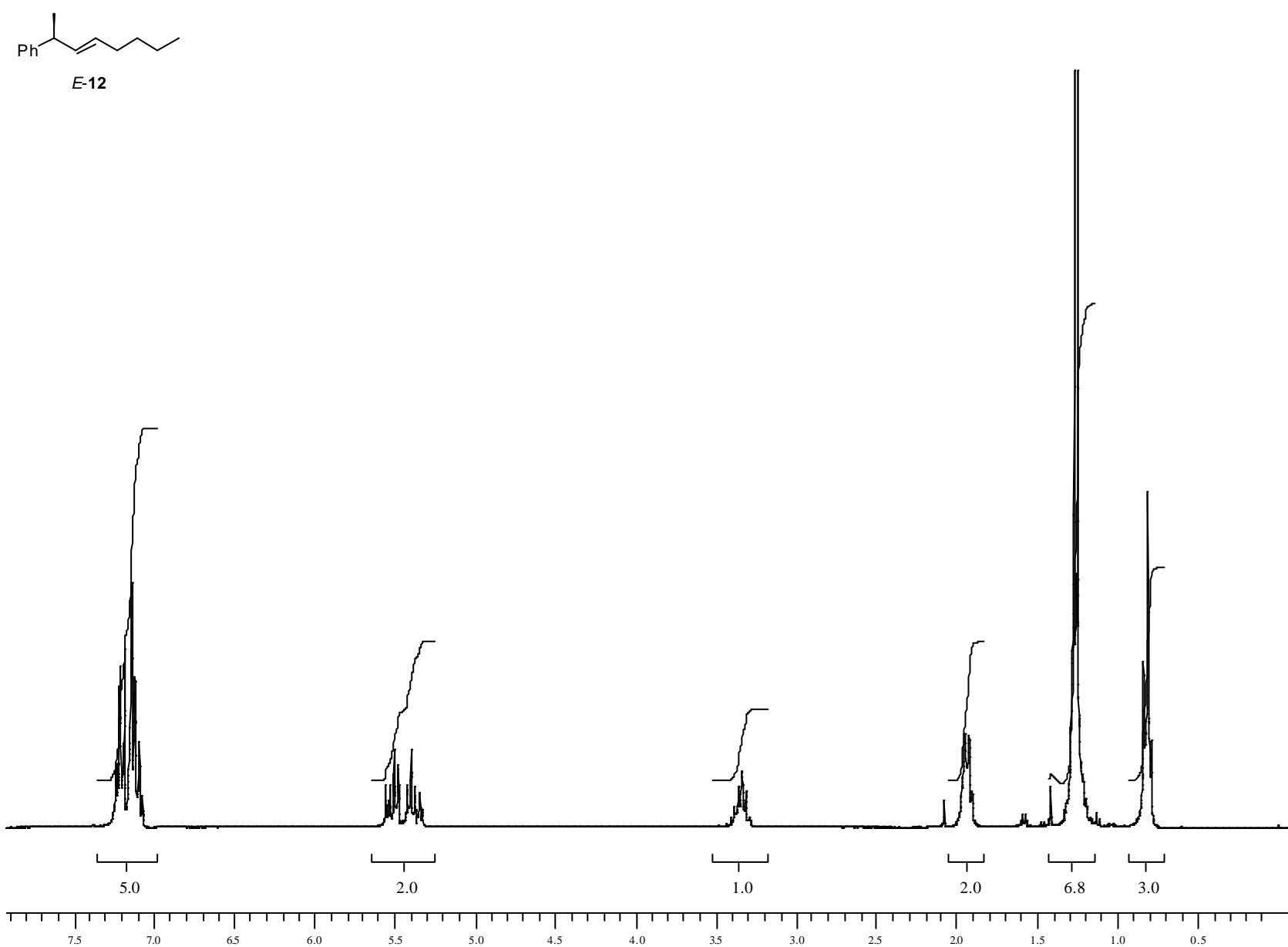


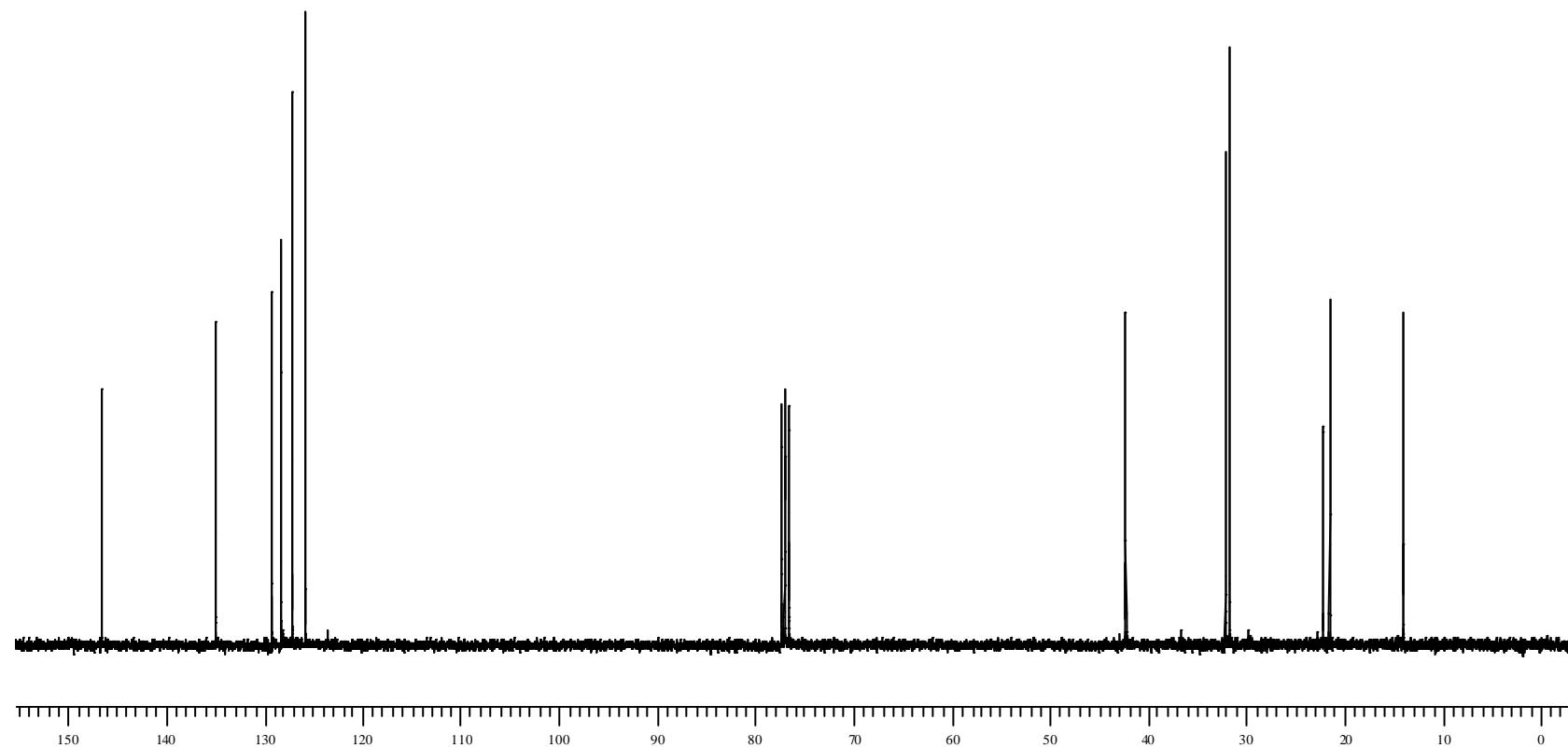
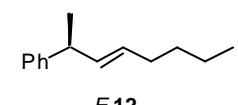


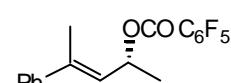


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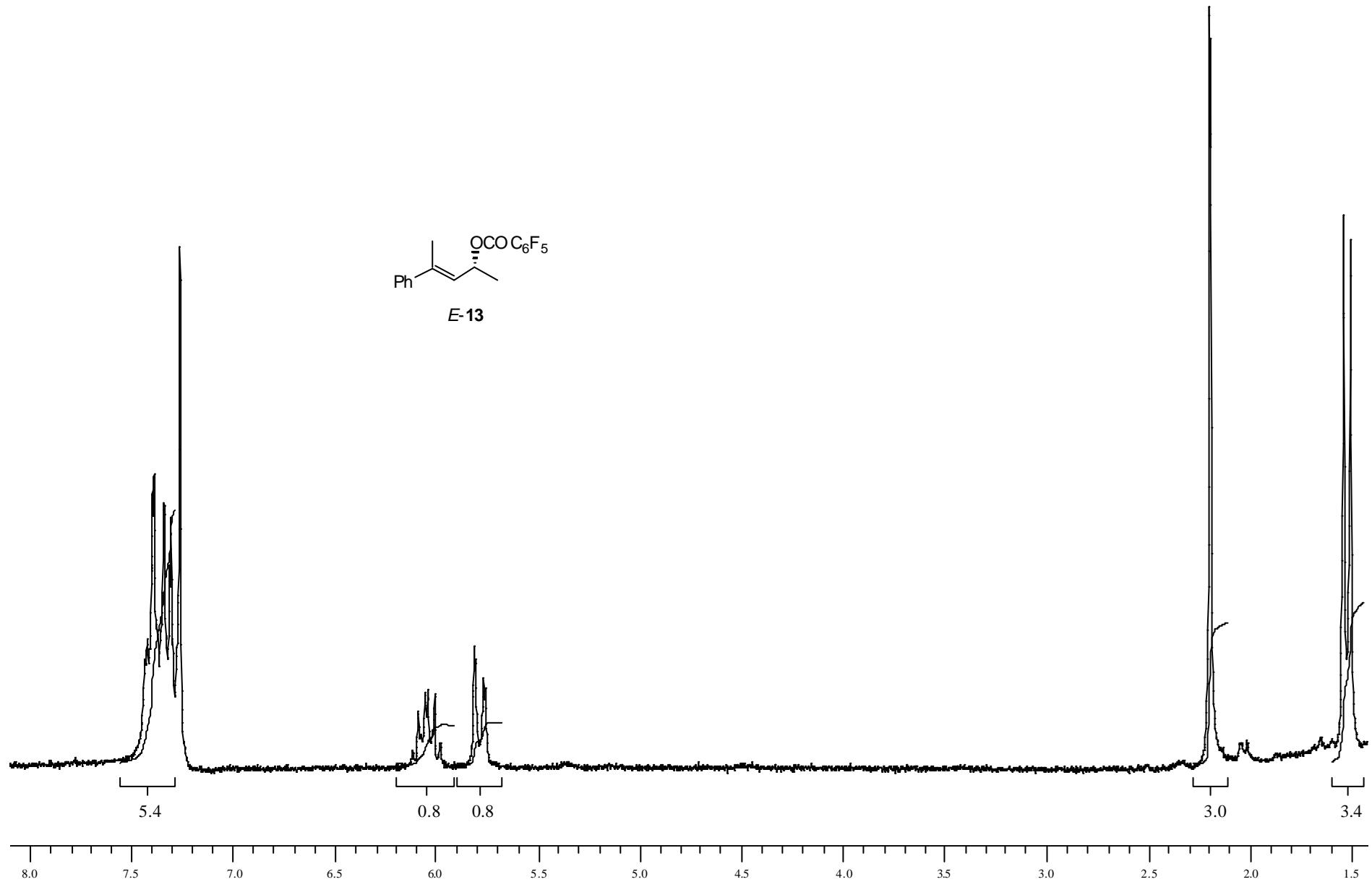


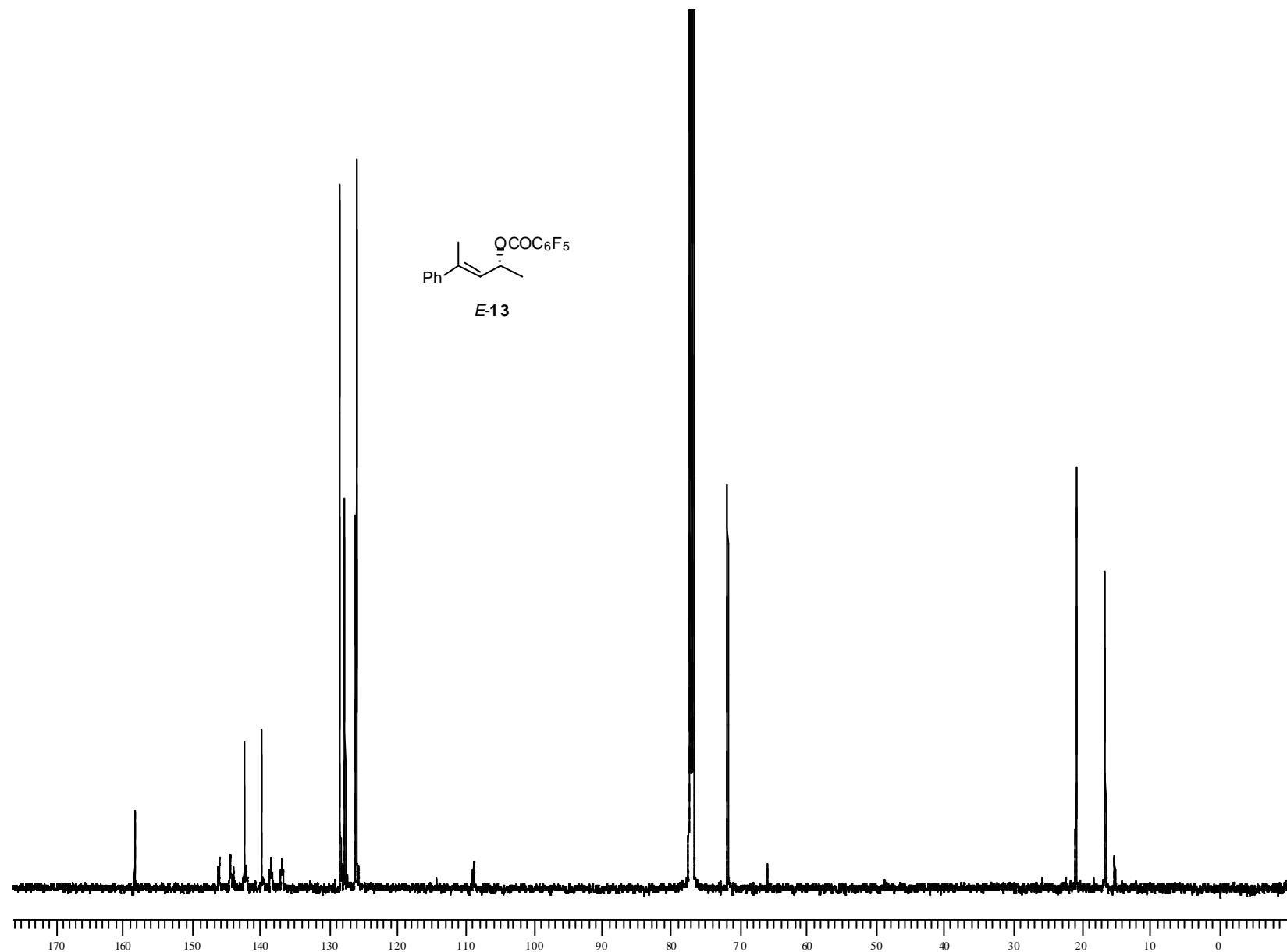


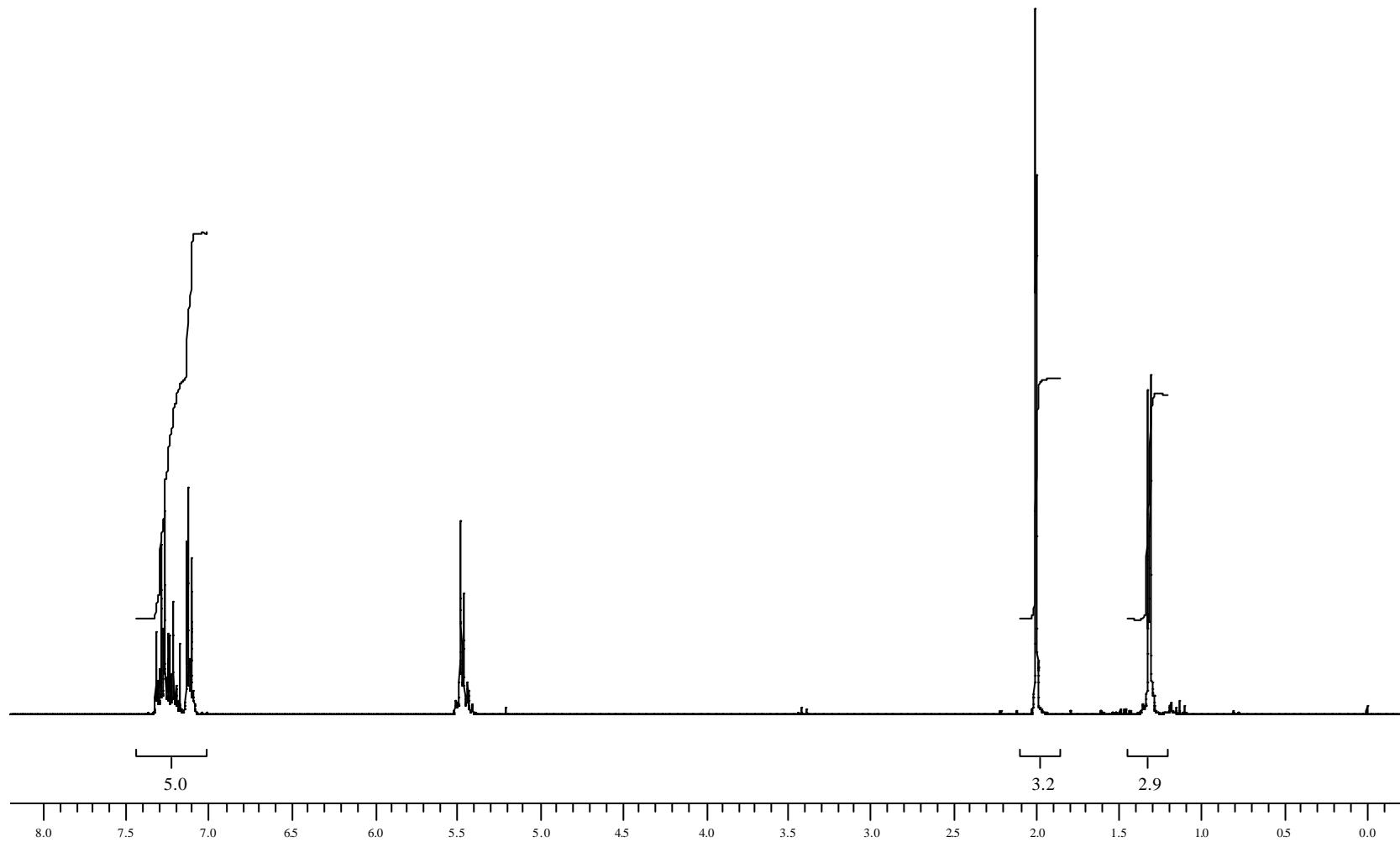
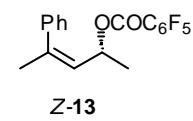


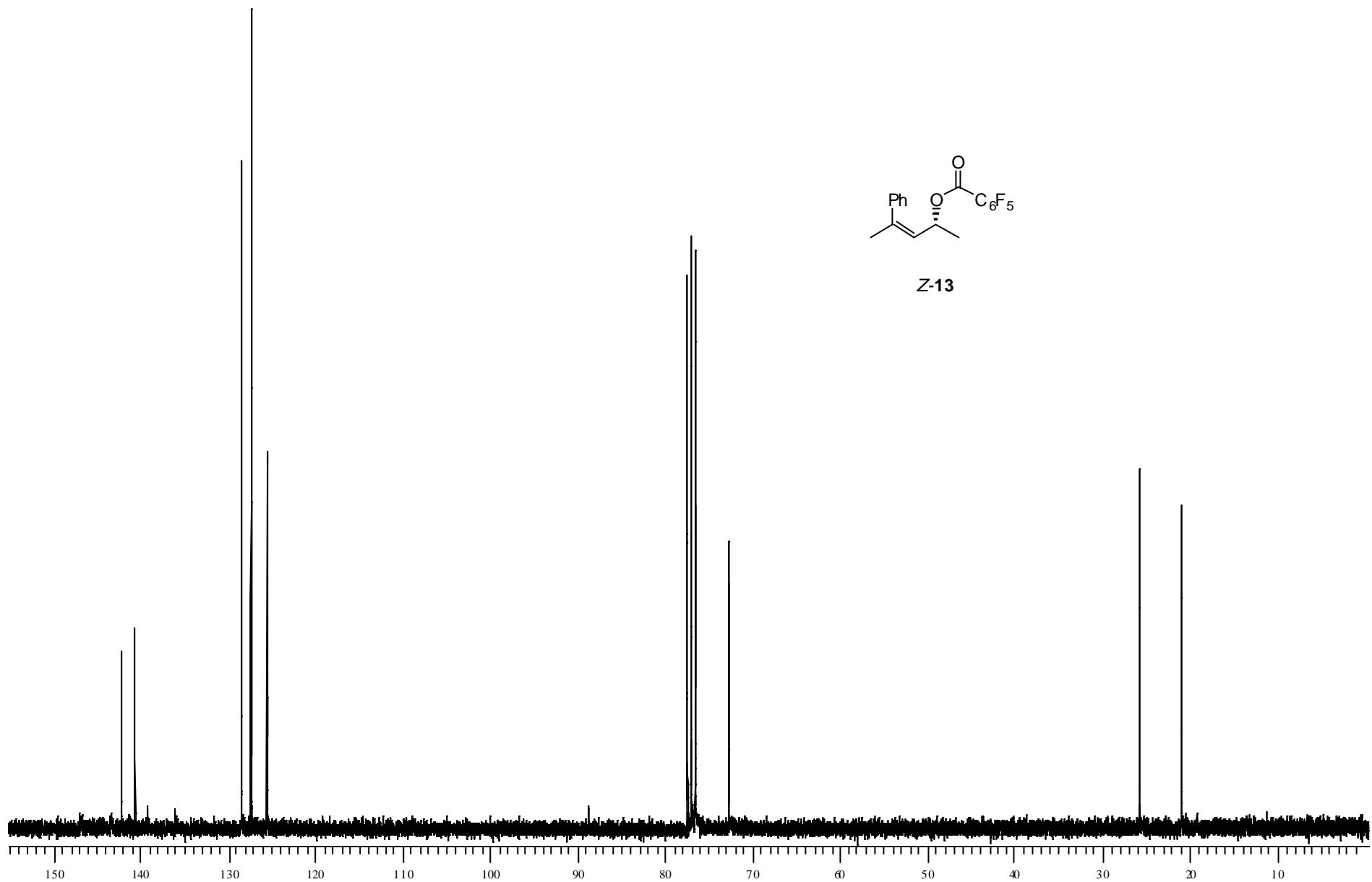


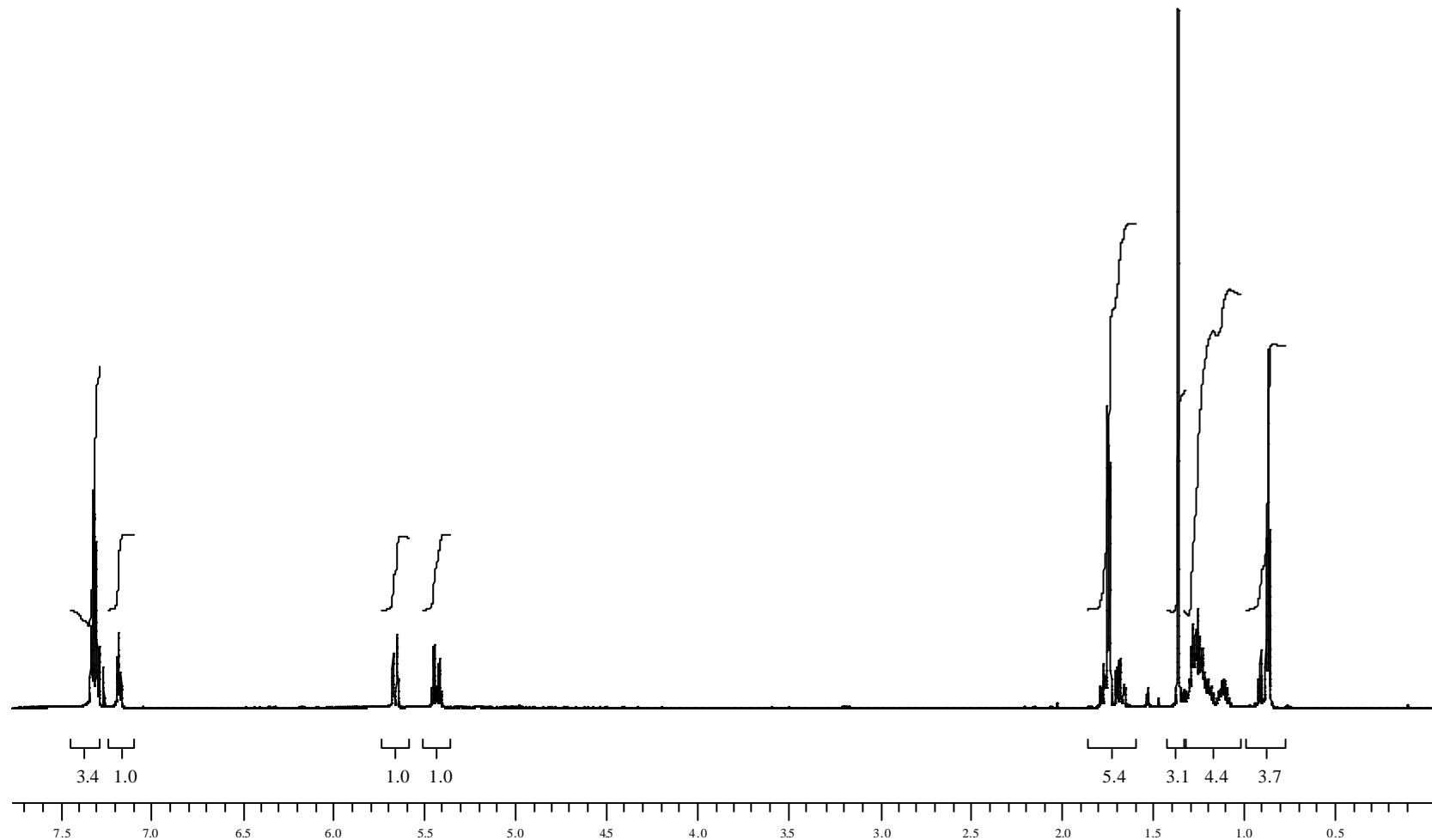
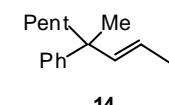
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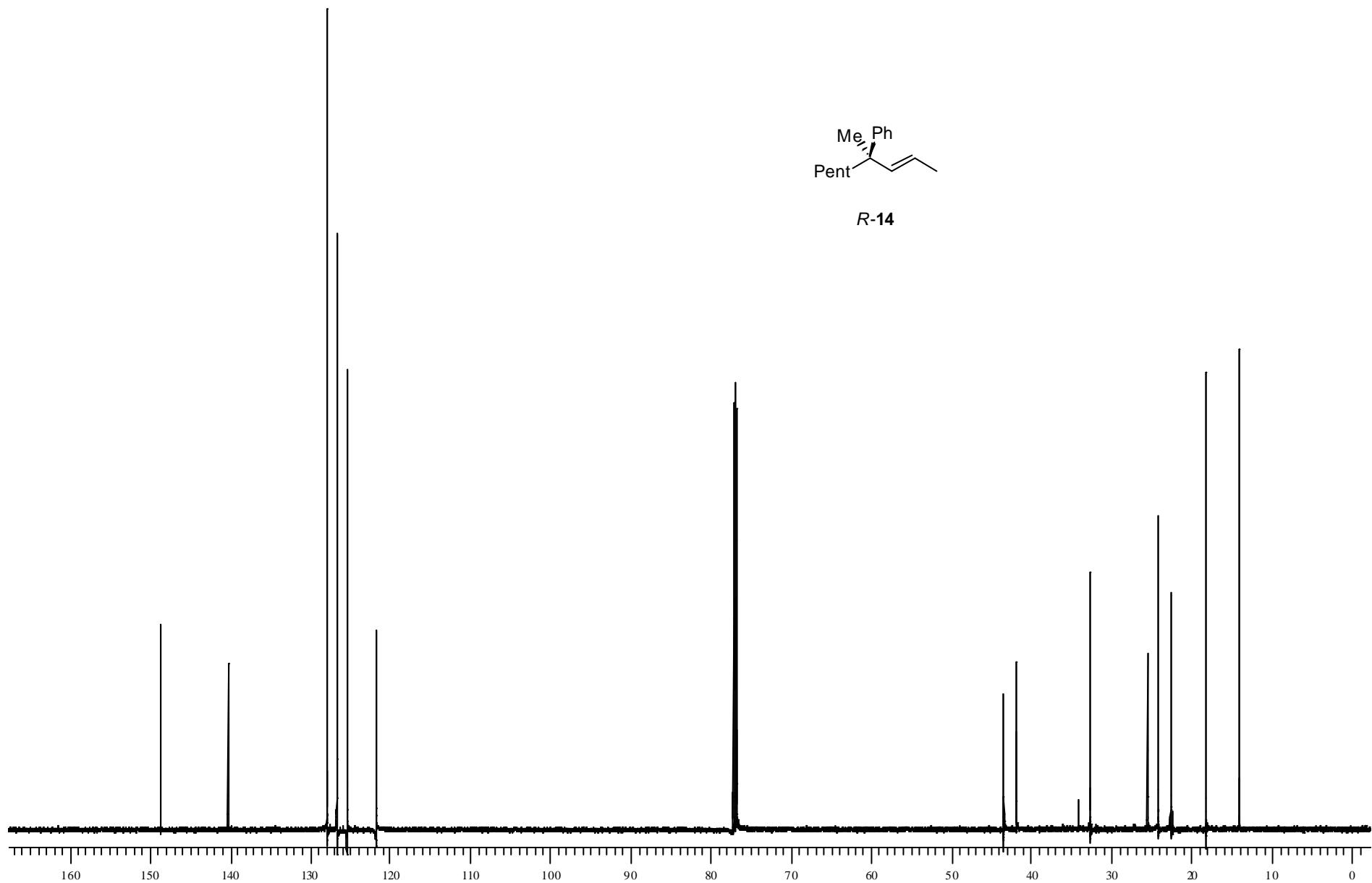


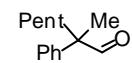










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