Supporting Information

First Enantioselective Total Synthesis of (+)-(*R*)-Pinnatolide Using an Asymmetric Domino Allylation Reaction

Lutz F. Tietze,*[,†] Thomas Wolfram[†], Julian J. Holstein[‡], Birger Dittrich[‡]

[†]*Institute of Organic and Biomolecular Chemistry, Georg-August-University, Tammannstr. 2, D-37077 Göttingen, Germany, and* [‡]*Institute of Inorganic Chemistry, Georg-August-University, Tammannstr. 4, D-37077 Göttingen, Germany*

Content:

1. General Experimental Procedures

All reactions were carried in pre-dried round bottom flasks. All solvents were reagent grade and stored over molecular sieves. If it was not mentioned otherwise the commercially available reagents were used without further purification and the mentioned concentrations refer to solutions in water. Degasing was subsequently done by freezing the solvent or respectively the solution and evaporation for a number of times. Due to the necessary reaction temperature short-term cooling was performed either with an ice / water or with a dry ice / acetone bath. Long-term cooling was performed by using the cryostat EK 90 from the *Haake* company. All reactions were magnetically stirred and monitored by thin layer chromatography (TLC) on silica plates Si 60 F_{254} from the *Merck* company. Flash chromatography was performed under increased pressure (p = 0.2–0.4 bar) with silica gel 60 (mesh: 0.032–0.063 mm) from the *Merck* company. For high performance liquid chromatography (HPLC) the samples were membrane-filtered (0.2 µm) and the used solvents were HPLC grade. Both used columns Chiralpak® IA (250×4.6 mm, 5 µm) and Chiralpak® IB (250×4.6 mm, 5 µm) were from *Daicel Chemical Industries Ltd.*. Yields refer to isolated and purified compounds, unless otherwise stated.

2. Compound Characterization Data

NMR: For the NMR spectroscopy several devices with a magnetic field range corresponding to 300 MHz up to 600 MHz from the *Varian* company were used. By default ^{1}H NMR spectra were recorded on a 300 MHz spectrometer and ^{13}C NMR spectra either on a 500 MHz or on a 600 MHz device. Chemical shifts were reported relative to the standard (Me_4Si). Standard-free samples were locked on the used solvents like e.g. chloroform (^{1}H: δ 7.26 ppm, ^{13}C: δ 77.0 ppm). For characterization of the NMR signals the following abbreviations were used: s (singlet), d (doublet), t (triplet), m (multiplet), m_c (centered multiplet) and br (broadened signals).

IR: The recording of the IR spectra was carried out either on a spectrometer Vector 22 from the *Bruker* company or on an ATR-device FT/IR-4100 from the *Jasco* company. To characterize the IR signals the following abbreviations were used: s (strong), m (medium), w (weak) and br (broadened signals).

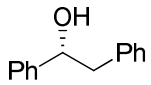
UV/Vis: UV spectra were recorded on an UV spectrometer V-630 from the *Jasco* company. By default acetonitrile (λ ≥ 190) was used as solvent.

ORP/CD: Optical rotation powers were measured on a P-2000 polarimeter. Solvent and sample concentration were stated in each case. The recording of the CD spectra were carried out in acetonitrile as standard solvent and recorded on a J-680 spectropolarimeter. Both spectroscopic devices were products from the *Jasco* company.

MS: For recording the EI and EI-HRMS spectra a spectrometer AccuTOF from the *Jeol* company were used. ESI spectra were recorded either on an ion trap device LCQ from the *Finnigan* company or on a spectrometer mircoTOF from the *Bruker* company. The recording of the ESI-HRMS spectra was carried out either on an ion cyclotron resonance device (FTICR) APEX IV from the *Bruker* company or on the mircoTOF spectrometer. For the recording of ESI or ESI-HRMS spectra methanol was used as solvent and the presented signals correspond to the positive ion mode, unless otherwise mentioned. Signals were stated as mass-to-charge ratio (m/z) and its relative intensities in comparison to the basic peak (I = 100).

3. Synthesis of the (+)-(*R*)-Phenylbenzyl Auxiliary (4)

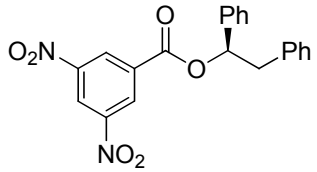
(–)-(*R*)-1,2-diphenylethanol (14)



A: To a solution of diphenyl-L-prolinol (265 mg, 1.0 mmol) in toluene (30 mL) was added $BH_3{\cdot}SMe_2$ (12 mL of an 1 M sol. in CH_2Cl_2, 12 mmol) at ambient temperature. To the resulting mixture benzylphenylketone (2.0 g, 10 mmol) was added dropwise as 1 M sol. in THF at 45 °C over a period of 1.5 h. Afterwards the reaction mixture was stirred for another 30 min and then quenched by addition of MeOH (2 mL). The solution was washed with sat. NH_4Cl-sol. (20 mL), the aqueous layer was extracted with CH_2Cl_2 (3×50 mL), the combined organic layers were washed with sat. NaCl-sol. (20 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure yielded the crude alcohol (*R*)-**14** (2.1 g, 10 mmol, quant., 84% *ee*) as colorless solid.

B: To a solution of the dinitrobenzoate (*R*)-**15** (2.9 g, 7.4 mmol) in CH_2Cl_2 / MeOH / H_2O 30:10:1 (8.2 mL) was added $LiOH{\cdot}H_2O$ (0.8 g, 19 mmol) and the reaction mixture was stirred at ambient temperature for 1 h. The solution was diluted with CH_2Cl_2 (20 mL), washed with sat. $NaHCO_3$-sol. (2×10 mL) as well as sat. NaCl-sol. (5 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure and purification of the residue by flash chromatography on silica gel (petroleum ether / EtOAc 20:1) yielded the alcohol (*R*)-**14** (1.5 g, 7.4 mmol, quant.) as colorless solid. m.p. 66 °C with >99% ee. $[\alpha]_D^{20} = -50.3°$ (*c* 1, EtOH). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.99 ppm (d, *J* = 2.7 Hz, 1 H), 3.00 (dd, *J* = 13.5, 8.2 Hz, 1 H), 3.07 (dd, *J* = 13.5, 5.1 Hz, 1 H), 4.92 (m_c, 1 H), 7.18–7.40 (m, 10 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 46.1 ppm, 75.3, 125.9 (2×), 126.6, 127.6, 128.4 (2×), 128.5 (2×), 129.5 (2×), 138.0, 143.8. IR: $\tilde{\nu}$ 3294 cm^{-1} (s, br), 3026 (w), 2860 (w), 1495 (m), 1453 (m), 1316 (m), 1273 (m), 1071 (m), 1039 (s), 1026 (s), 778 (m), 760 (s), 742 (s). UV: λ_{max} (lg ε) 253 nm (2.5516), 258 (2.6105), 264 (2.5050). MS (EI): *m*/*z* (%) 77 (24), 91 (29), 92 (100), 107 (74), 180 (23), 198 (3). HRMS: 198.1040, calc'd for $[C_{14}H_{14}O]^{+\cdot}$: 198.1045. HPLC (Chiralpak® IA, hexane / MTBE / *i*-PrOH 75:24.5:0.5, 0.8 mL/min, 210 nm, 1 mg/mL, 8 µL): t_R = 10.3 min (*R*), 12.2 (*S*) (not observed using purified **15** in method B).

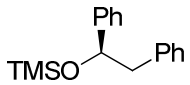
(+)-(*R*)-1,2-diphenylethyl 3,5-dinitrobenzoate (15)



To a solution of the crude alcohol (*R*)-**14** (2.1 g, 10 mmol, 84% *ee*), 3,5-dinitrobenzoyl chloride (3.0 g, 13 mmol) and DMAP (210 mg, 1.0 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (2.4 mL, 17 mmol) dropwise at 0 °C. The reaction mixture was stirred for 3 h at ambient temperature. The solution was diluted with CH_2Cl_2 (100 mL) and washed with sat. $NaHCO_3$-sol. (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2×30 mL) and the combined organic layers were washed with sat. NaCl-sol. (10 mL) and dried over Na_2SO_4. During the removal of the solvent under reduced pressure the crude product was instantly adsorbed on silica gel (3.8 g). Purification by flash chromatography (petroleum ether / CH_2Cl_2 2:1→1:2) yielded the dinitrobenzoate (*R*)-**15** (3.8 g, 9.5 mmol, 95%, 84% *ee*) as colorless solid. Recrystallization from EtOAc / heptane afforded (*R*)-**15** (2.9 g, 7.4 mmol, 82%) as an almost single stereoisomer (>99% *ee*). m.p. 107 °C. $[\alpha]_D^{20} = +21.0°$ (*c* 0.1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.00 ppm (dd, *J* = 14.0, 5.7 Hz, 1 H), 3.40 (dd, *J* = 14.0, 8.4 Hz, 1 H), 6.22 (dd, *J* = 8.4, 5.7 Hz, 1 H), 7.15–7.42 (m, 10 H), 9.07 (d, *J* = 2.1 Hz, 2 H), 9.18 (t, *J* = 2.1 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 42.8 ppm, 75.3, 122.3, 126.7 (2×), 127.0, 128.5 (2×), 128.7 (2×), 129.3 (2×), 129.3 (2×), 129.4 (2×), 134.0, 136.3, 138.7, 148.6, 161.6. IR: $\tilde{\nu}$ 3087 cm^{-1} (w), 1729 (s), 1628 (m), 1543 (s), 1455 (m), 1341 (s), 1272 (s), 1164 (s), 1074 (m), 947 (s).

UV: λ_{max} (lg ε) 208 nm (4.5501). MS (ESI, CH_3CN): *m/z* (%) 410.1 (20), 415.1 (17), 431.0 (10), 807.2 (100). HRMS: 415.0895, calc'd for $[C_{21}H_{16}N_2O_6+Na]^+$: 415.0901.

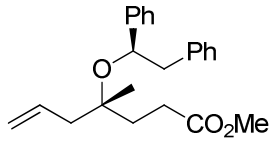
(+)-(*R*)-(1,2-diphenylethoxy)trimethylsilane (4)



To a solution of the alcohol (*R*)-**14** (1.5 g, 7.4 mmol) and Et_3N (5.7 mL, 39.0 mmol) in CH_2Cl_2 (80 mL) was added TMSOTf (3.0 mL, 16.5 mmol) dropwise at 0 °C and stirred for 2 h at ambient temperature. The reaction was quenched by addition of sat. $NaHCO_3$-sol. (40 mL). The aqueous layer was extracted with CH_2Cl_2 (2×30 mL). The combined organic layers were washed with sat. NaCl-sol. (10 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure and purification of the residue by flash chromatography on silica gel (petroleum ether / MTBE 80:1) yielded the (*R*)-phenylbenzyl auxiliary (**4**) (1.9 g, 6.9 mmol, 93%) as colorless oil. $[\alpha]_D^{20}$ = +27.0° (*c* 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ –0.16 ppm (s, 9 H), 2.89 (d, *J* = 6.5 Hz, 2 H), 4.74 (t, *J* = 6.5 Hz, 1 H), 7.09–7.31 (m, 10 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ –0.3 ppm (3×), 47.5, 76.4, 125.8 (2×), 126.1, 127.0, 127.9 (2×), 128.0 (2×), 129.8 (2×), 139.0, 144.9. IR: $\tilde{\nu}$ 3028 cm^{-1} (w), 2954 (w), 1495 (m), 1453 (m), 1250 (s), 1088 (s), 1066 (s), 942 (m), 835 (s). UV: λ_{max} (lg ε) 252 nm (2.5678), 258.0 (2.6450), 264.0 (2.5313). MS (EI): *m/z* (%) 73.1 (91), 179.2 (100), 269.3 (2). HRMS: 293.1334, calc'd for $[C_{17}H_{22}OSi+Na]^+$: 293.1332.

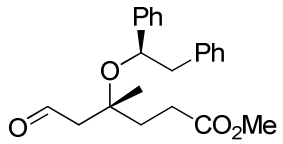
4. Synthesis of (+)-(*R*)-Pinnatolide (1)

(+)-(*R*,*R*)-methyl 4-(1,2-diphenylethoxy)-4-methylhept-6-enoate (6)



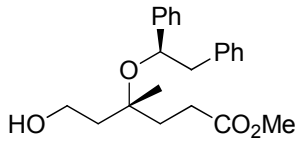
To a solution of methyl levulinate (**2**) (390 mg, 3.0 mmol) under an argon atmosphere was added at –78 °C TfOH (60 µL, 0.3 mmol), allyltrimethylsilane (**3**) (410 mg, 3.6 mmol) and the (*R*)-phenylbenzyl auxiliary (**4**) (810 mg, 3.0 mmol) in CH_2Cl_2 (1.5 mL). The reaction mixture was stirred for 14 h and then quenched by addition of Et_3N (0.1 mL) at this temperature. After evaporation of the solvent under reduced pressure the residue was purified by flash chromatography on silica gel (petroleum ether / MTBE 50:1→20:1) to afford the diastereomeric mixture of the homoallylic ether (*R*,*R*)-**6** (960 mg, 2.7 mmol, 91%, *dr:* 94:6) as colorless oil. $[\alpha]_D^{20}$ = +29.9° (*c* 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): *major diastereomer:* δ 0.82 ppm (s, 3 H), 1.66 (ddd, *J* = 14.2, 9.6, 6.3 Hz, 1 H), 1.74 (ddd, *J* = 14.2, 9.3, 6.6 Hz, 1 H), 1.94 (dd br, *J* = 13.9, 7.4 Hz, 1 H), 2.07 (dd br, *J* = 13.9, 7.2 Hz, 1 H), 2.23 (ddd, *J* = 16.1, 9.3, 6.3 Hz, 1 H), 2.30 (ddd, *J* = 16.1, 9.6, 6.6 Hz, 1 H), 2.83 (dd, *J* = 13.2, 5.4 Hz, 1 H), 2.95 (dd, *J* = 13.2, 7.8 Hz, 1 H), 3.63 (s, 3 H), 4.62 (dd, *J* = 7.8, 5.4 Hz, 1 H), 4.91–5.00 (m, 2 H), 5.58 (ddt, *J* = 16.7, 10.4, 7.3 Hz, 1 H), 7.07–7.31 (m, 10 H). ^{13}C NMR (126 MHz, $CDCl_3$): *major diastereomer:* δ 23.6 ppm, 28.5, 34.2, 43.2, 46.9, 51.4, 75.7, 77.1, 117.4, 126.0, 126.2 (2×), 126.8, 127.8 (2×), 127.9 (2×), 129.8 (2×), 134.1, 138.6, 145.2, 174.3. IR: $\tilde{\nu}$ 3028 cm^{-1} (m), 1739 (s), 1639 (w), 1603 (m), 1495 (s), 1454 (s), 1379 (m), 1308 (m), 1172 (s), 1057 (s), 916 (m). UV: λ_{max} (lg ε) 253.0 nm (2.5510), 258.5 (2.6314), 264.0 (2.5107). MS (ESI): *m/z* (%) 370.2 (22), 375.2 (100). HRMS: 375.1934, calc'd for $[C_{23}H_{28}O_3+Na]^+$: 375.1931.

(+)-(*R*,*R*)-methyl 4-(1,2-diphenylethoxy)-4-methyl-6-oxohexanoate (7)



Under an argon atmosphere ozone was passed at –78 °C through a solution of the diastereomeric mixture of the homoallylic ether (*R*,*R*)-**6** (880 mg, 2.5 mmol, *dr:* 94:6) in CH_2Cl_2/MeOH 10:1 (55 mL) until the solution was colored slightly blue (ca. 15 min). Afterwards argon was passed through until the solution was decolorized. Then triphenylphosphine (860 mg, 3.3 mmol) was added to the solution at –78 °C and the reaction mixture was allowed to warm up to ambient temperature over a period of 14 h. After removal of the solvents under reduced pressure the crude mixture was purified by rapid flash chromatography on silica gel (petroleum ether / MTBE 20:1→3:1) to yield the diastereomeric mixture of aldehyde (*R*,*R*)-**7** (870 mg, 2.45 mmol, 98%, *dr:* 94:6) as colorless oil. $[\alpha]_D^{20} = +22.7°$ (*c* 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): *major diastereomer:* δ 0.89 ppm (s, 3 H), 1.69 (ddd, *J* = 14.3, 9.4, 6.3 Hz, 1 H), 1.77 (ddd, *J* = 14.3, 9.0, 6.6 Hz, 1 H), 2.08 (dd, *J* = 15.1, 2.9 Hz, 1 H), 2.16 (m_c, 2 H), 2.25 (dd, *J* = 15.1, 2.9 Hz, 1 H), 2.81 (dd, *J* = 13.4, 5.1 Hz, 1 H), 2.88 (dd, *J* = 13.4, 8.3 Hz, 1 H), 3.57 (s, 3 H), 4.58 (dd, *J* = 8.3, 5.1 Hz, 1 H), 7.08–7.30 (m, 10 H), 9.36 (t, *J* = 2.9 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): *major diastereomer:* δ 24.0 ppm, 28.4, 34.9, 46.6, 51.5, 51.9, 76.3, 76.5, 126.1 (2×), 126.3, 127.2, 128.0 (2×), 128.2 (2×), 129.7 (2×), 138.4, 144.5, 173.5, 201.6. IR: $\tilde{\nu}$ 3028 cm^{-1} (w), 2947 (m), 2842 (w), 1731 (s), 1718 (s), 1496 (m), 1453 (m), 1436 (m), 1381 (m), 1307 (m), 1170 (s), 1112 (s), 1053 (s). UV: λ_{max} (lg ε) 253 nm (2.6991), 259 (2.7369). MS (ESI): *m/z* (%) 377.2 (32), 409.2 (100) $[M+MeOH+Na]^+$, 795.4 (2). HRMS: 377.1732, calc'd for $[C_{22}H_{26}O_4+Na]^+$: 377.1723.

(+)-(*R*,*R*)-methyl 4-(1,2-diphenylethoxy)-6-hydroxy-4-methylhexanoate (10)

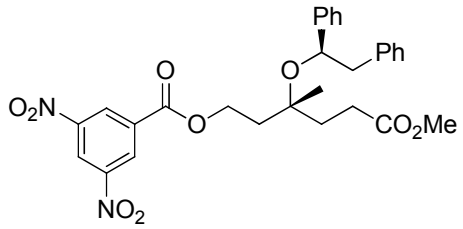


A: To a solution of the crude mixture of (*R*,*R*)-**7** (2.5 mmol obtained from **6**) in MeOH (20 mL) $NaBH_4$ (110 mg, 2.9 mmol) was added in portions at 0 °C. After gas formation has ceased the cooling bath was removed and the reaction mixture was stirred for 30 min at ambient temperature. The reaction was quenched by addition of NH_4Cl (100 mg) and the solution was concentrated under reduced pressure. Afterwards water (10 mL) was added and the resulting mixture was extracted with MTBE (3×15 mL). The combined organic layers were washed with sat. NaCl-sol. (5 mL) and dried over Na_2SO_4. After removal of the solvents purification of the residue by flash chromatography on silica gel (petroleum ether / MTBE 4:5) afforded a diastereomeric mixture of the alcohol (*R*,*R*)-**10** (870 mg, 2.45 mmol, 98%, *dr:* 94:6) as colorless solid.

B: To a solution of the dinitrobenzoate (*R*,*R*)-**11** (1.4 g, 2.5 mmol) in CH_2Cl_2/MeOH 1:1 (100 mL) was added $LiOH{\cdot}H_2O$ (10 mg, 0.24 mmol) at ambient temperature. The reaction mixture was stirred for 1 h and the reaction was quenched by addition of half-sat. NH_4Cl-sol. (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (3×15 mL). The combined organic layers were washed with sat. NaCl-sol. (5 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel (CH_2Cl_2 / MeOH 99:1) to afforded the alcohol (*R*,*R*)-**10** (0.9 g, 2.5 mmol, quant.) as colorless solid. m.p. 62 °C (*dr:* >99:1). $[\alpha]_D^{23} = +6.9°$ (*c* 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.83 ppm (s, 3 H), 1.41 (dt, *J* = 14.3, 5.6 Hz, 1 H), 1.58–1.72 (m, 3 H), 1.96 (ddd, *J* = 16.3, 9.2, 6.4 Hz, 1 H), 2.10 (ddd, *J* = 16.3, 9.0, 7.6 Hz, 1 H), 2.54 (m br, 1 H), 2.83 (dd, *J* = 13.3, 5.5 Hz, 1 H), 2.90 (dd, *J* = 13.3, 7.9 Hz, 1 H), 3.51 (s, 3 H), 3.46–3.67 (2×m, 2 H), 4.60 (dd, *J* = 7.9, 5.5 Hz, 1 H), 7.05–7.28 (2×m, 10 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.0 ppm, 28.6, 34.1, 40.7, 46.8, 51.4, 59.0, 76.1, 78.8, 126.3 (3×), 127.1, 128.0 (2×), 128.2 (2×), 129.8 (2×), 138.3, 144.5, 173.9. IR: $\tilde{\nu}$ 3269 cm^{-1} (m), 2926 (w), 1725 (s), 1450 (m), 1432 (m), 1284 (s), 1246 (m), 1143 (s), 1102 (s),

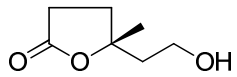
1047 (s), 1024 (s). UV: λ_{max} (lg ε) 253 nm (2.6899), 259 (2.7345). MS (ESI): *m/z* (%) 357.2 (6), 379.2 (100), 735.4 (10). HRMS: 379.1879, calc'd for $[C_{22}H_{28}O_4+Na]^+$: 379.1880.

(+)-(*R*,*R*)-3-(1,2-diphenylethoxy)-6-methoxy-3-methyl-6-oxohexyl 3,5-dinitrobenzoate (11)



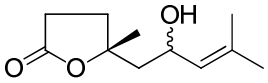
To a solution of the diastereomeric mixture of alcohol (*R*,*R*)-**10** (1.2 g, 3.3 mmol, *dr:* 94:6), 3,5-dinitrobenzoyl chloride (1.0 g, 4.3 mmol) and DMAP (40 mg, 0.33 mmol) in CH_2Cl_2 (60 mL) under an argon atmosphere was added dropwise at 0 ° Et_3N (0.81 mL, 5.7 mmol). The reaction mixture was stirred for 2 h at ambient temperature and afterwards the reaction was quenched by addition of sat. NH_4Cl-sol. (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3×20 mL). Silica gel (7 g) was added to the combined organic layers and the solvent was removed under reduced pressure. Purification of the residue by flash chromatography on silica gel ($CHCl_3$ / EtOH 99:1) yielded the dinitrobenzoate (*R*,*R*)-**11** (1.7 g, 3.0 mmol, 91%, *dr:* 94:6) as colorless solid. Recrystallization from EtOAc / heptane afforded (*R*,*R*)-**11** (1.4 g, 2.5 mmol, 82%) as a single stereoisomer (*dr:* >99:1). m.p. 136.5 °C. $[\alpha]_D^{24}$ = +35.1° (*c* 1, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 ppm (s, 3 H), 1.60–1.81 (m, 4 H), 2.15 (ddd, *J* = 16.2, 9.7, 6.0 Hz, 1 H), 2.25 (ddd, *J* = 16.2, 10.1, 6.3 Hz, 1 H), 2.84 (dd, *J* = 13.5, 5.0 Hz, 1 H), 2.91 (dd, *J* = 13.5, 8.4 Hz, 1 H), 3.58 (s, 3 H), 4.13 (ddd, *J* = 10.8, 8.9, 6.2 Hz, 1 H), 4.26 (ddd, *J* = 10.8, 9.0, 6.0 Hz, 1 H), 4.60 (dd, *J* = 8.4, 5.0 Hz, 1 H), 7.09–7.34 (m, 10 H), 9.06 (d, *J* = 2.2 Hz, 2 H), 9.20 (t, *J* = 2.2 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 23.6 ppm, 28.5, 34.5, 36.9, 46.8, 51.5, 63.3, 76.1, 76.2, 122.2, 126.2 (3×), 127.2, 128.1 (2×), 128.3 (2×), 129.3, 129.8 (2×), 134.0, 138.8, 145.0, 148.6, 162.3, 173.8. IR: $\tilde{\nu}$ 3103 cm^{-1} (w), 2923 (m), 1734 (s), 1719 (s), 1630 (m), 1546 (s), 1454 (m), 1341 (s), 1281 (s), 1170 (s), 1148 (s), 1057 (s). UV: λ_{max} (lg ε) 209 nm (4.5529). MS (ESI): *m/z* (%) 573.2 (100), 1123.4 (31). HRMS: 573.1845, calc'd for $[C_{29}H_{30}N_2O_9+Na]^+$: 573.1844.

(–)-(*R*)-5-(2-hydroxyethyl)-5-methyldihydrofuran-2-one (9)



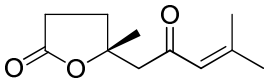
Under an argon atmosphere a mixture of a degased solution of alcohol (*R*,*R*)-**10** (400 mg, 1.1 mmol) and 10 w% palladium on charcoal (120 mg, 0.11 mmol) in THF/MeOH 2:1 (12 mL) was prepared. The atmosphere was exchanged to hydrogen and the mixture was stirred for at least 3 h at 45 °C. After full conversion (TLC) the suspension was filtered through a pad of celite and the residue was washed with CH_2Cl_2 (3×15 mL). The solvents were removed under reduced pressure (*caution:* p > 150 mbar) and the residue was purified by flash chromatography on silica gel (CH_2Cl_2 / MeOH 98:2) to afford the γ-lactone **9** (160 mg, 1.1 mmol, quant.) as colorless oil. $[\alpha]_D^{23}$ = –3.7° (*c* 1, $CHCl_3$) [Lit.[1]: $[\alpha]_D$ = –5.67° (*c* 1.53, CH_2Cl_2)]. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 ppm (s, 3 H), 1.85 (dt, *J* = 15.3, 6.6 Hz, 1 H), 1.90 (t, *J* = 15.3, 6.5 Hz, 1 H), 1.95 (ddd, *J* = 12.9, 8.5, 7.5 Hz, 1 H), 2.16 (dt, *J* = 12.9, 8.6 Hz, 1 H), 2.50–2.57 (m, 2 H), 2.74 (s br, 1 H), 3.66 (dd, *J* = 11.0, 6.5 Hz, 1 H), 3.73 (dd, *J* = 11.0, 6.6 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.7 ppm, 28.8, 33.4, 42.6, 58.0, 86.1, 176.9. IR: $\tilde{\nu}$ 3406 cm^{-1} (m, br), 2935 (w), 1749 (s), 1384 (m), 1184 (m), 1091 (m), 1054 (m), 933 (s). MS (ESI): *m/z* (%) 167.1 (11), 311.2 (100). HRMS: 167.0679, calc'd for $[C_7H_{12}O_3+Na]^+$: 167.0679.

(–)-(5*R*)-5-(2-hydroxy-4-methylpent-3-en-1-yl)-5-methyldihydrofuran-2-one (13)



Under an argon atmosphere DMP[2] (60 mg, 140 µmol) was added to a solution of alcohol (*R*)-**9** (10 mg, 69 µmol) in CH_2Cl_2 (3 mL) at 0 °C. The reaction mixture was stirred for 20 min at this temperature. Afterwards the suspension was fractionated filtered through a pad of silica gel and the residue was washed with Et_2O (ca. 50 mL). The filtrate was concentrated under reduced pressure (*caution: p* > 600 mbar) and the residue was dissolved in anhydrous THF (2 mL). At –60 °C 2-methyl-1-propenyl magnesium bromide (**12**) (0.17 mL of a 0.5 M sol. in THF, 85 µmol) was added dropwise and the reaction mixture was stirred for 2 h at this temperature. The reaction was quenched by addition of sat. NH_4Cl-sol. (1 mL) and the mixture was extracted with MTBE (3×10 mL). The combined organic layers were washed with sat. NaCl-sol. (5 mL) and dried over Na_2SO_4. Removal of the solvent under reduced pressure (*caution: p* > 100 mbar) and purification of the residue by flash chromatography on silica gel (hexane / MTBE 3:7) afforded the diastereomeric mixture of the allylic alcohol (5*R*)-**13** (5.5 mg, 28 µmol, 40%, *dr:* 1:1.1) as colorless oil. $[\alpha]_D^{23} = -13.5°$ (*c* 0.41, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): *diastereomeric mixture:* δ 1.42 ppm, 1.44 (2×s, 6 H), 1.66, 1.68 (2×s, 12 H), 1.74 (dd, *J* = 14.6, 3.7 Hz, 2 H), 1.88–2.04 (m, 4 H), 2.27 (dt, *J* = 12.9, 8.7 Hz, 2 H), 2.53–2.62 (m, 4 H), 4.51–4.64 (m, 2 H), 5.18 (d, *J* = 8.7 Hz, 2 H).^{13}C NMR (126 MHz, $CDCl_3$): δ 18.1 ppm (2×), [25.6, 26.0], [26.5, 26.9], [28.7,29.0], [33.6, 33.8], [47.3, 47.7], [65.0, 65.4], [85.9, 86.3], [127.7, 127.9], [134.9, 135.0], [176.6, 176.7]. IR: $\tilde{\nu}$ 3430 cm^{-1} (m, br), 2972 (w), 2931 (m), 1753 (s), 1673 (w), 1449 (m), 1380 (m), 1175 (s), 1080 (s), 933 (s). MS (ESI): *m/z* (%) 221.1 (35), 419.3 (100). HRMS: 221.1149, calc'd for $[C_{11}H_{18}O_3+Na]^+$: 221.1148.

(+)-(*R*)-pinnatolide (1)



Under an argon atmosphere DMP[2] (8.5 mg, 20 µmol) was added to a solution of the diastereomeric mixture of allylic alcohol (5*R*)-**13** (2.0 mg, 10.0 µmol, *dr:* 1:1.1) in CH_2Cl_2 (0.5 mL) at 0 °C and the reaction mixture was stirred for 2 h at ambient temperature. Afterwards the suspension was filtered through a pad of silica gel, the residue was washed with Et_2O (2×10 mL) and the solvent was removed under reduced pressure (*caution: p* > 300 mbar). Purification of the residue by flash chromatography on silica gel (pentane / Et_2O 5:3) afforded (+)-(*R*)-pinnatolide (**1**) (1.8 mg, 9.0 µmol, 90%) as colorless oil. $[\alpha]_D^{23} = +10.8°$ (*c* 0.21, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.45 ppm (s, 3 H), 1.87 (m_c, 3 H), 2.12 (m_c, 3 H), 2.11 (ddd, *J* = 13.1, 8.4, 7.4 Hz, 1 H), 2.32 (ddd, *J* = 13.1, 9.4, 8.3 Hz, 1 H), 2.59 (m_c, 2 H), 2.78 (d, *J* = 16.1 Hz, 1 H), 2.83 (d, *J* = 16.1 Hz, 1 H), 6.06 (sep, *J* = 1.3 Hz, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.0 ppm, 26.7, 27.9, 28.9, 32.6, 53.5, 84.8, 124.0, 157.2, 176.4, 196.5. IR: $\tilde{\nu}$ 2931 cm^{-1} (m), 1767 (s), 1686 (s), 1617 (s), 1444 (m), 1378 (m), 1278 (m), 1174 (s), 1102 (m), 1077 (m), 1044 (m), 942 (s). UV: λ_{max} (lg ε) 237 nm (3.2705). MS (ESI): *m/z* (%) 219.1 (100), 415.2 (90). HRMS: 219.0992, calc'd for $[C_{11}H_{16}O_3+Na]^+$: 219.0992. HPLC (Chiralpak® IB, hexane / *i*-PrOH 85:15, 0.6 mL/min, 237 nm, 1 mg/mL, 3 µL): t_R = 14.2 min (*S*) (not observed), 14.7 (*R*).

5. Crystal Structure of Dinitrobenzoate (*R*,*R*)-11

Crystals of dinitrobenzoate (*R*,*R*)-**11** were recrystallized by slow cooling from a refluxed ethyl acetate / heptane solution. X-ray data (XRD) collection of diffraction intensities was performed on a Bruker SMART 6000 area detector diffractometer with CuK_{α} radiation generated from a 5 kW rotating anode. The raw data were integrated with SAINT[3] and an empirical absorption correction with SADABS[4] was applied.

The structure was solved by direct methods (SHELXS-97) and refined against all data by full-matrix least-squares methods on F^2 (SHELXL-97).[5] SHELXLE[6] was used as refinement GUI. All non-hydrogen atoms were refined with anisotropic displacement parameters. All non-hydrogen atoms were refined with anisotropic displacement parameters for which the rigid-bond restraint DELU was used. The SAME command was employed to restrain bond length and angles of the two disordered parts. Hydrogen atoms were constrained using suitable HFIX commands.

Compared to the conventional enantiomorph distinguishing parameter after Flack[7] [x = 0.11(17)], both methods after Parsons[8] [y = -0.02(3)] and Hooft[9,10] [x = -0.01(3)] reduce absolute value as well as standard uncertainty. With this enhanced accuracy both methods provide clear evidence of the absolute configuration of (*R*,*R*)-**11**. (see figure 1 and table 1)

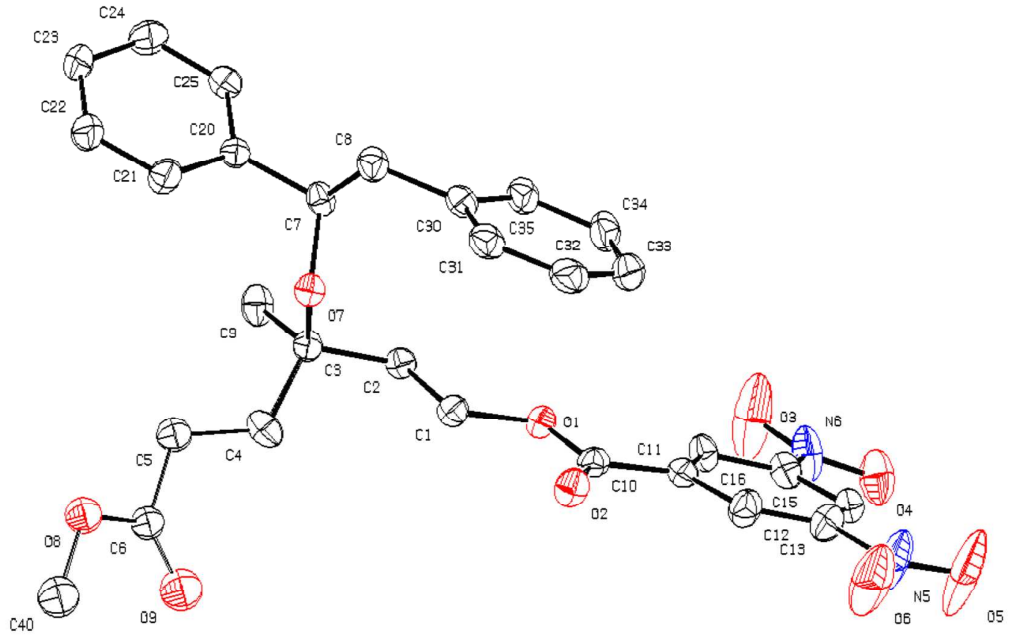


Figure 1 crystal structure of (*R*,*R*)-**11** with anisotropic displacement parameters of 50%. Figure was created with *Platon*.

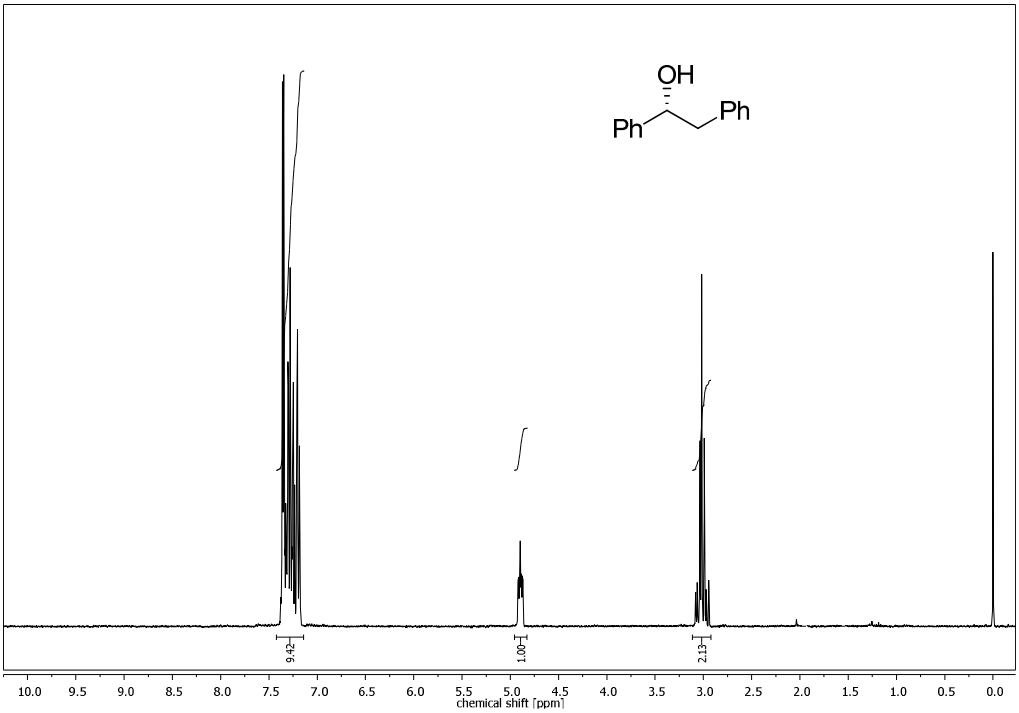
Table 1 Crystal and structure refinement parameters for (*R*,*R*)-**11**.

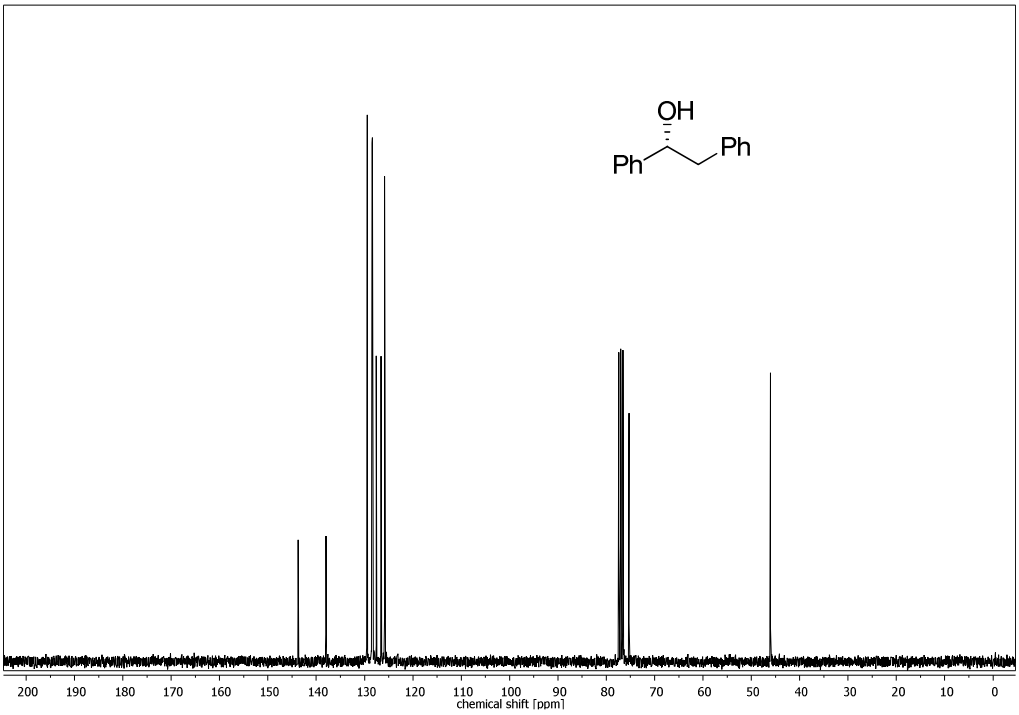
Parameters	
Empirical formula	$C_{29}H_{30}N_2O_9$
Formula weight	550.55
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	a = 6.8209(2) Å
	b = 27.0063(8) Å
	c = 7.7986(2) Å
	β = 111.561(1)°
Volume, Z	1336.04(7) Å^3, 2
Density (calcd)	1.369 g/cm^3
Absorption coefficient	0.855 mm^{-1}
F (000)	580
Crystal size	0.18 x 0.09 x 0.07 mm
θ range for data collection	3.3 to 73.7°
Limiting indices	$-8 \le h \le 8$, $-33 \le k \le 33$, $-9 \le l \le 7$
Reflections collected	42964
Independent reflections	5177 (R_{int} = 0.034)
Completeness to θ	97.7% (θ = 73.7°)
Refinement method	full - matrix least - squares on F^2
Data/ restraints/ parameters	5177 / 112 / 404
Goodness - of - fit on F^2	1.14
Final R indices [$I > 2\sigma(I)$]	$R1$ = 0.0364, $wR2$ = 0.0993
R indices (all data)	$R1$ = 0.0377, $wR2$ = 0.1076
Flack x	0.11(17)
Parsons x	-0.02(3)
Hooft y	-0.01(3)
Largest diff. peak and hole	0.35 and -0.29 eÅ^{-3}

CCDC 890179 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

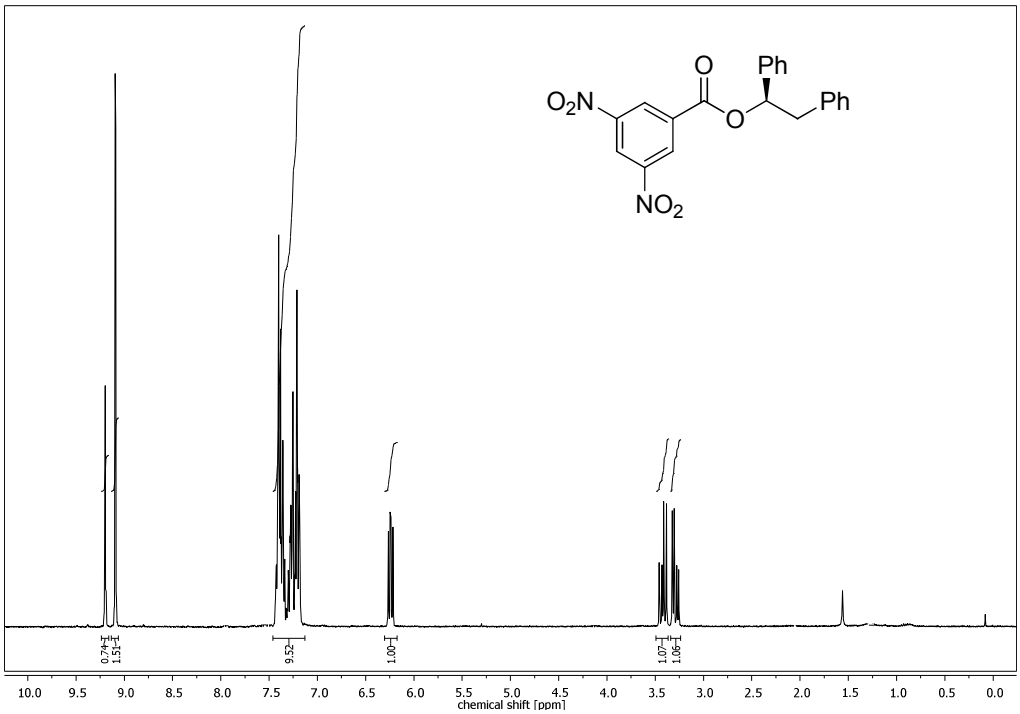
6. ^{1}H NMR and ^{13}C NMR Spectra

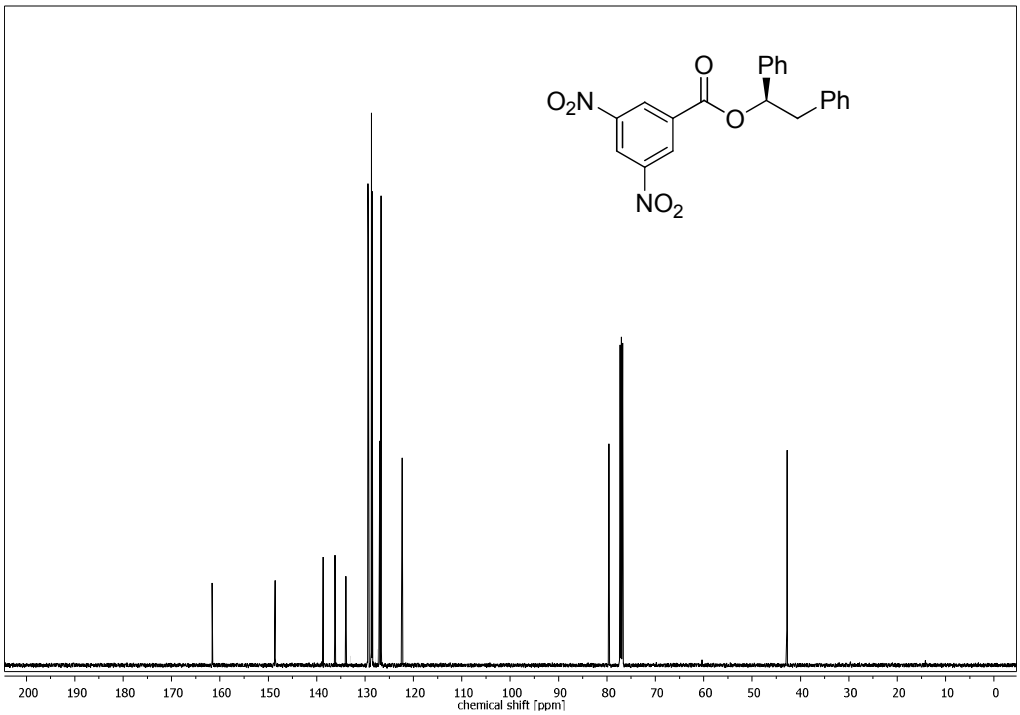
(–)-(*R*)-1,2-diphenylethanol (14)



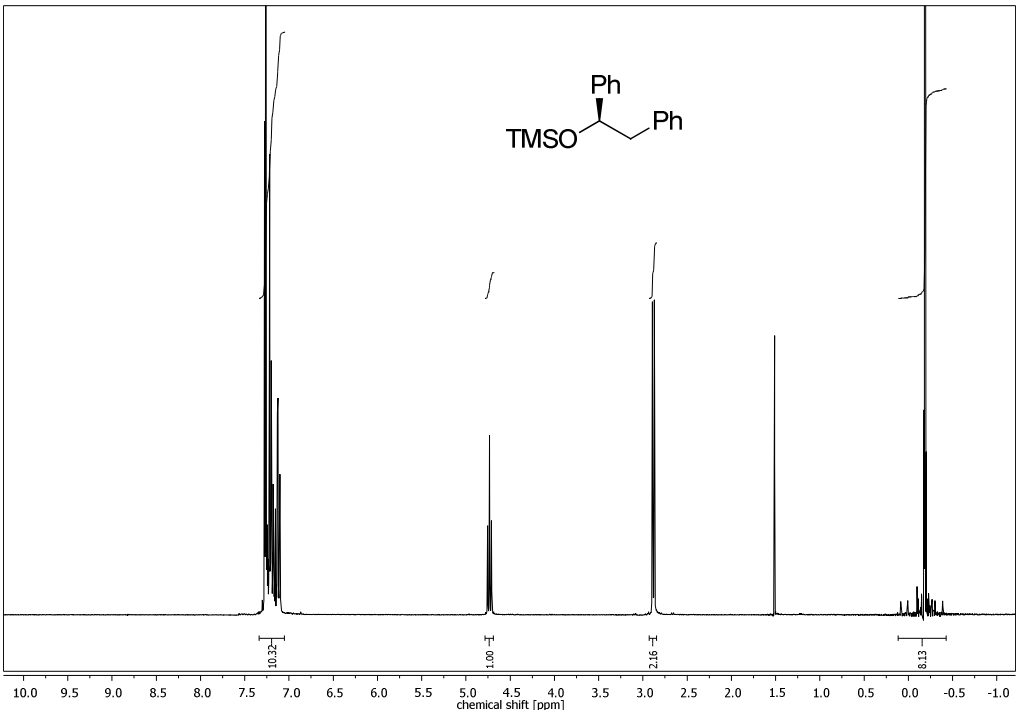


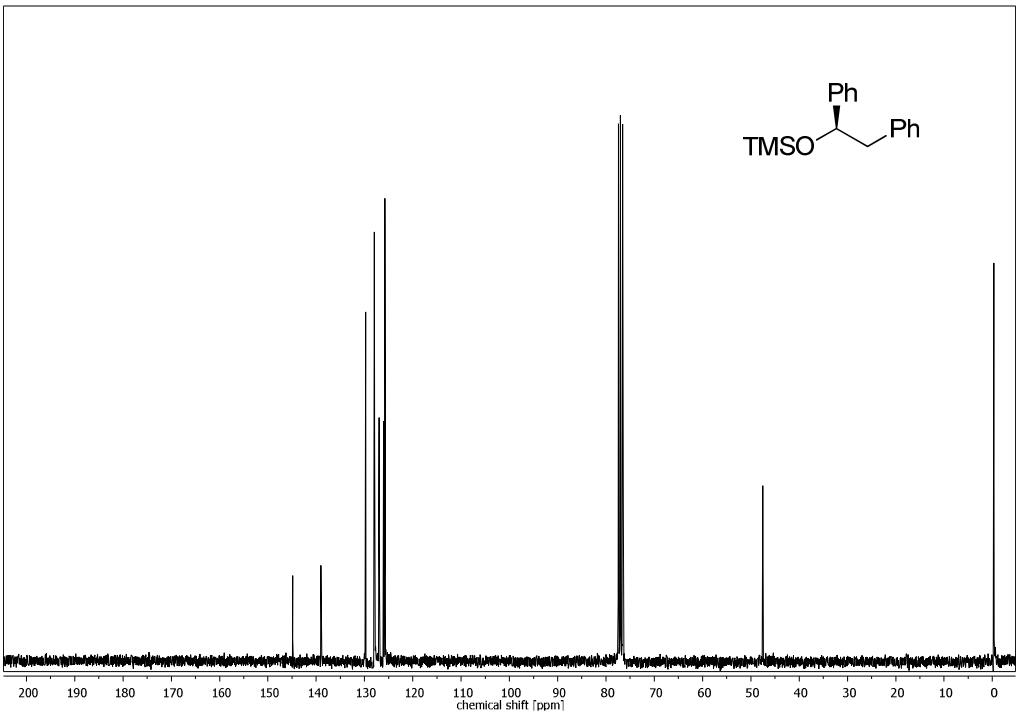
(+)-(*R*)-1,2-diphenylethyl 3,5-dinitrobenzoate (15)



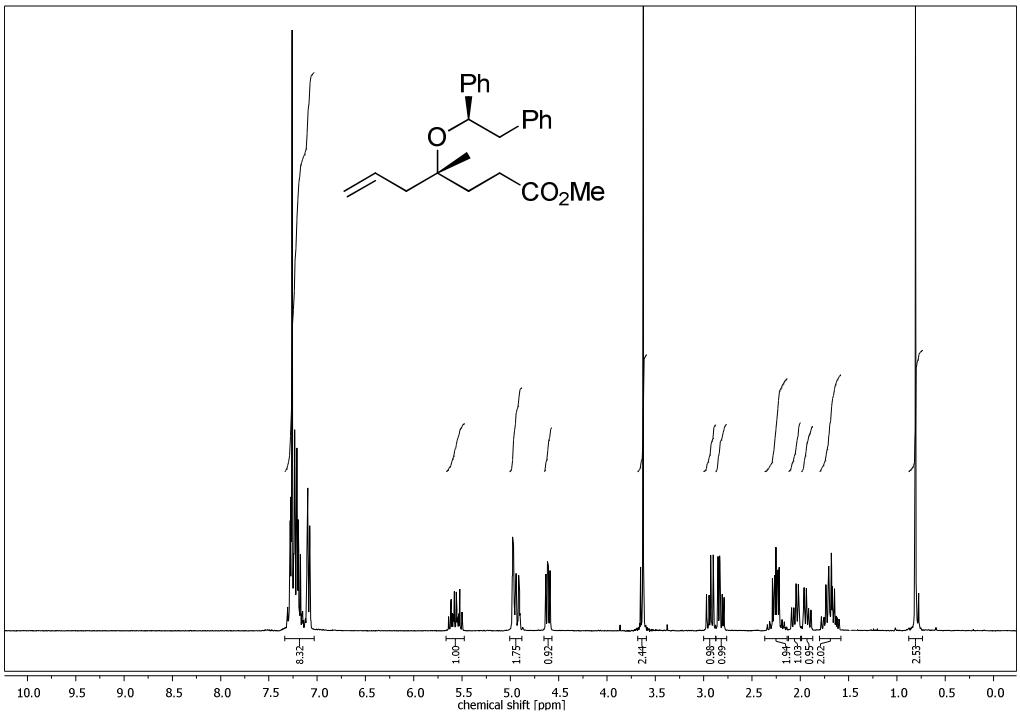


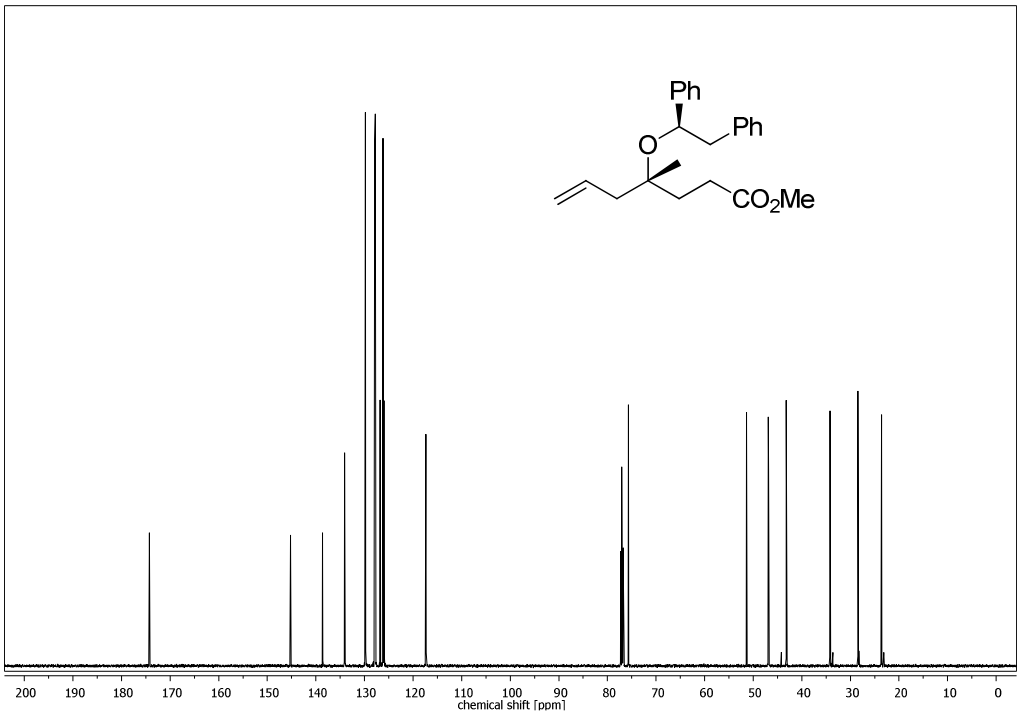
(+)-(*R*)-(1,2-diphenylethoxy)trimethylsilane (4)



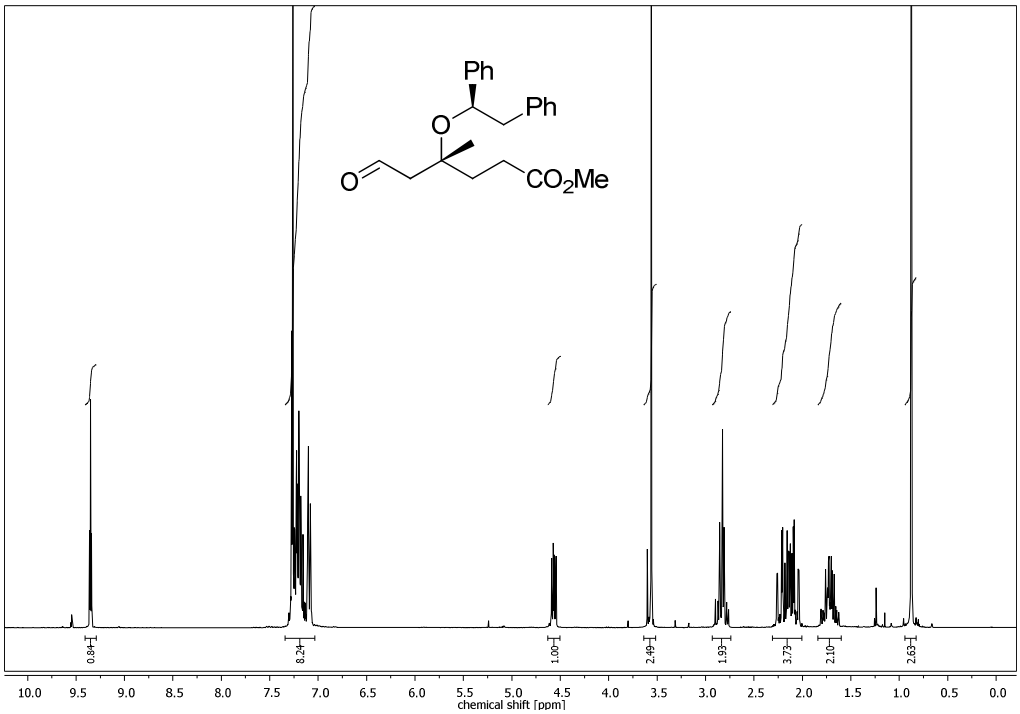


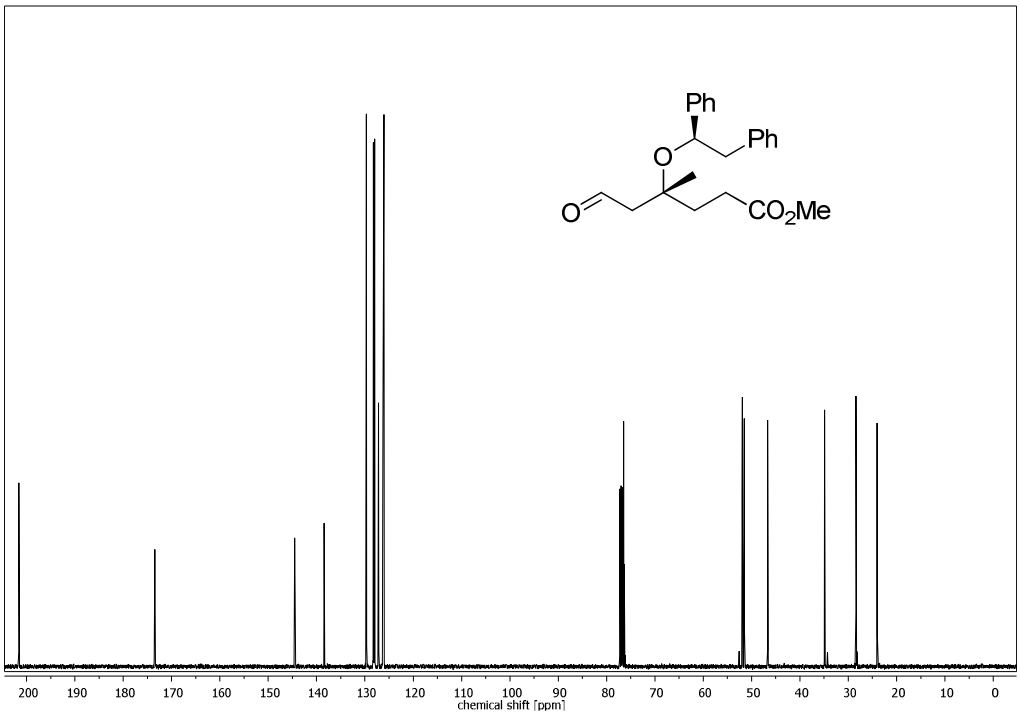
(+)-(*R*,*R*)-methyl 4-(1,2-diphenylethoxy)-4-methylhept-6-enoate (6)



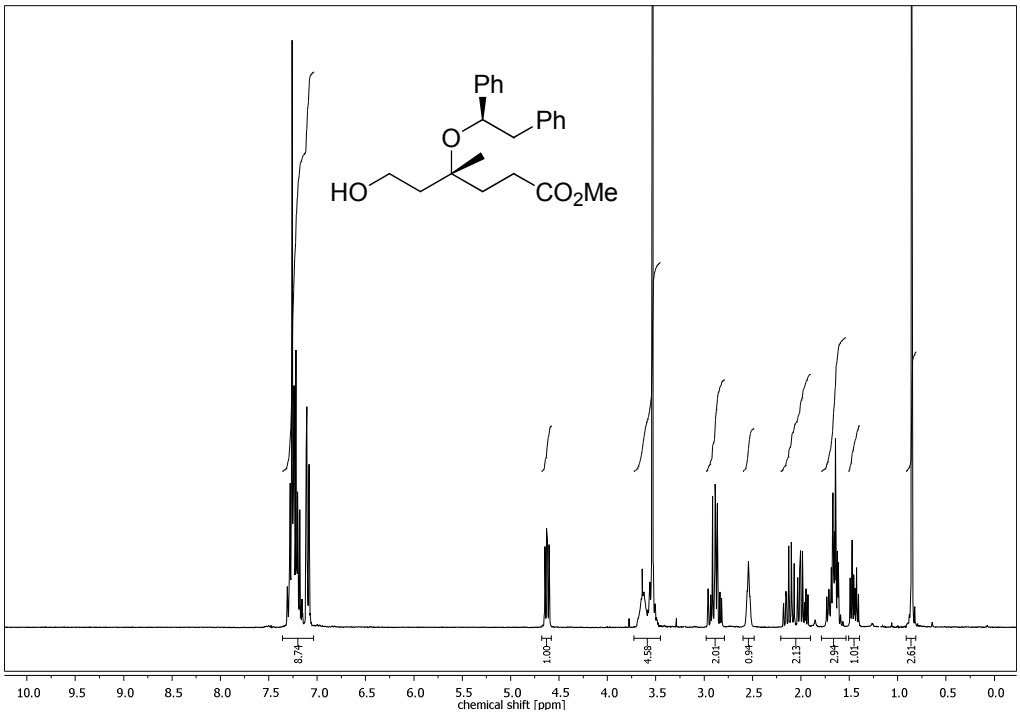


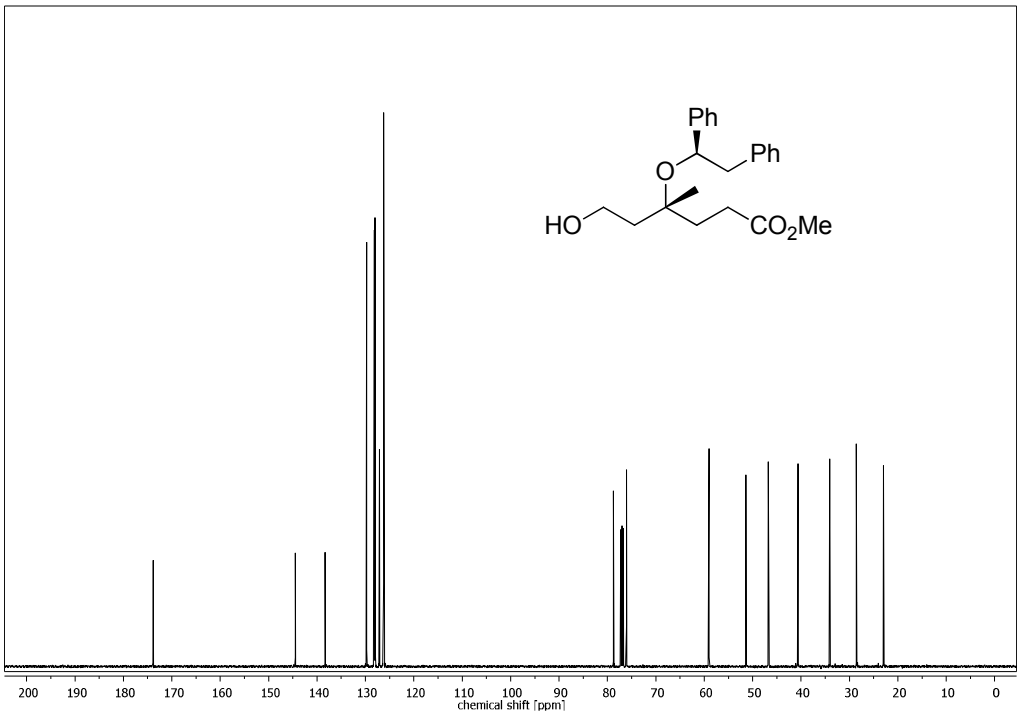
(+)-(*R*,*R*)-methyl 4-(1,2-diphenylethoxy)-4-methyl-6-oxohexanoate (7)



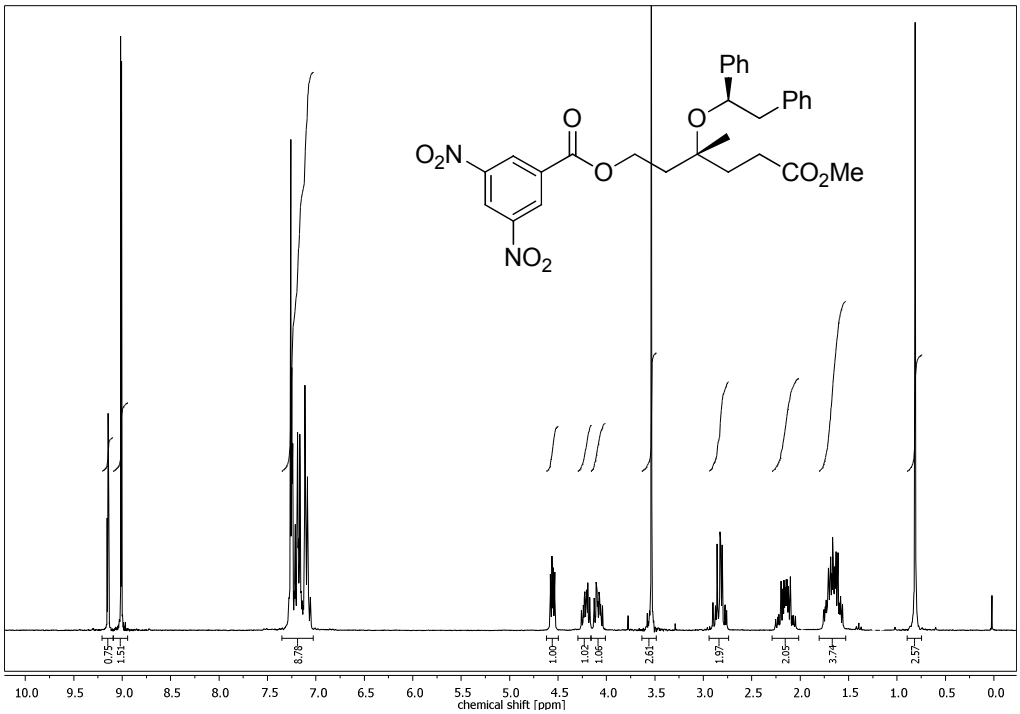


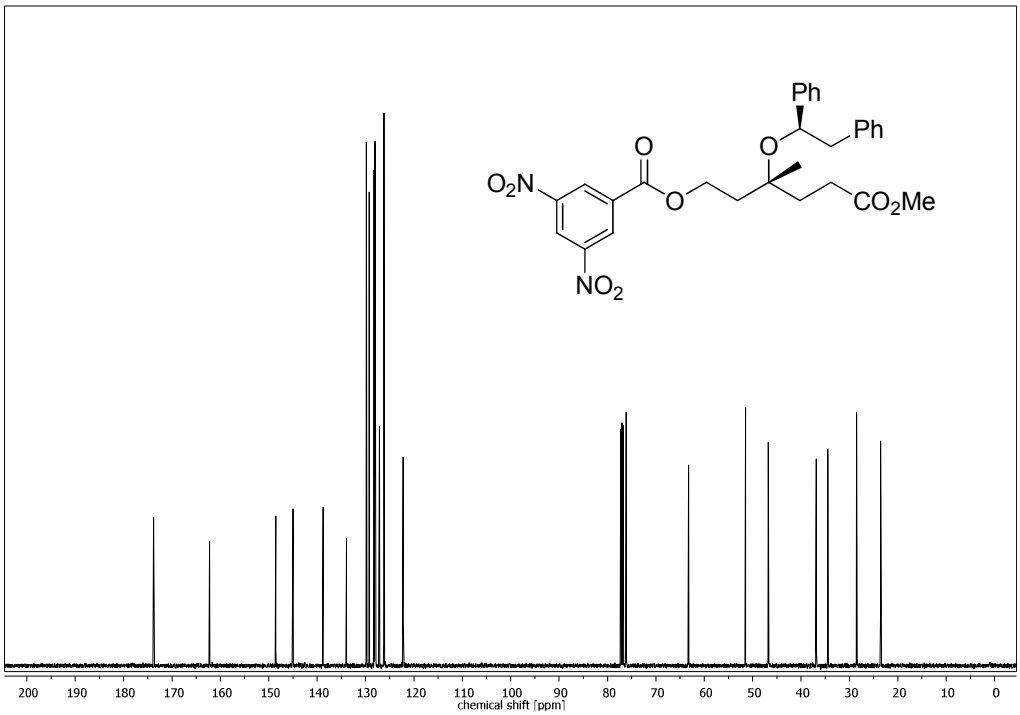
(+)-(*R*,*R*)-methyl 4-(1,2-diphenylethoxy)-6-hydroxy-4-methylhexanoate (10)



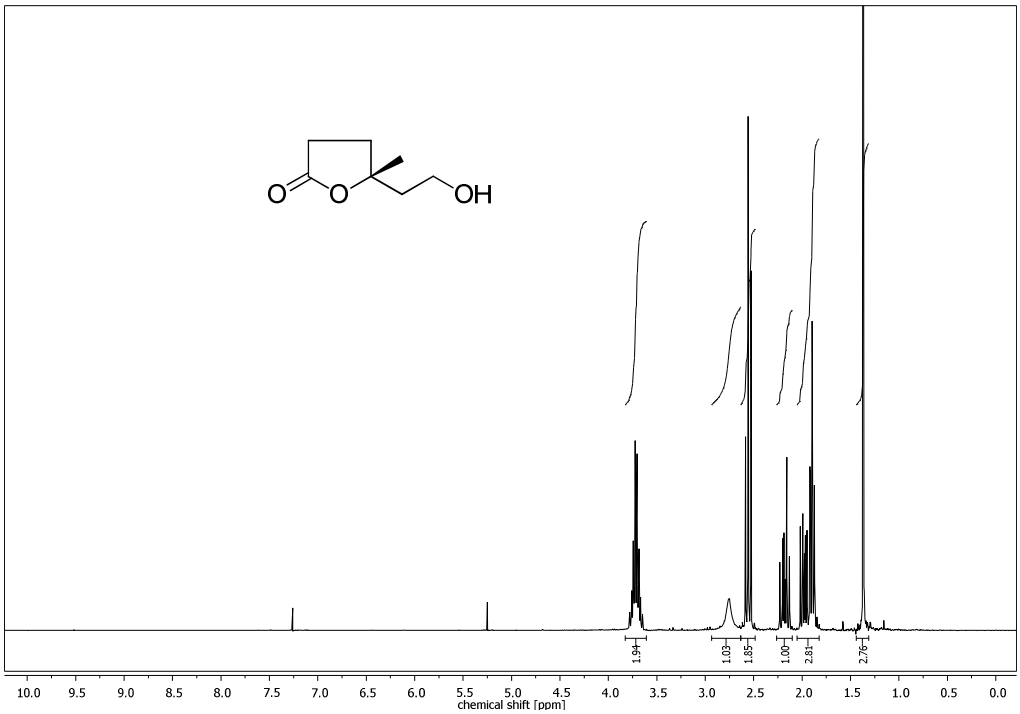


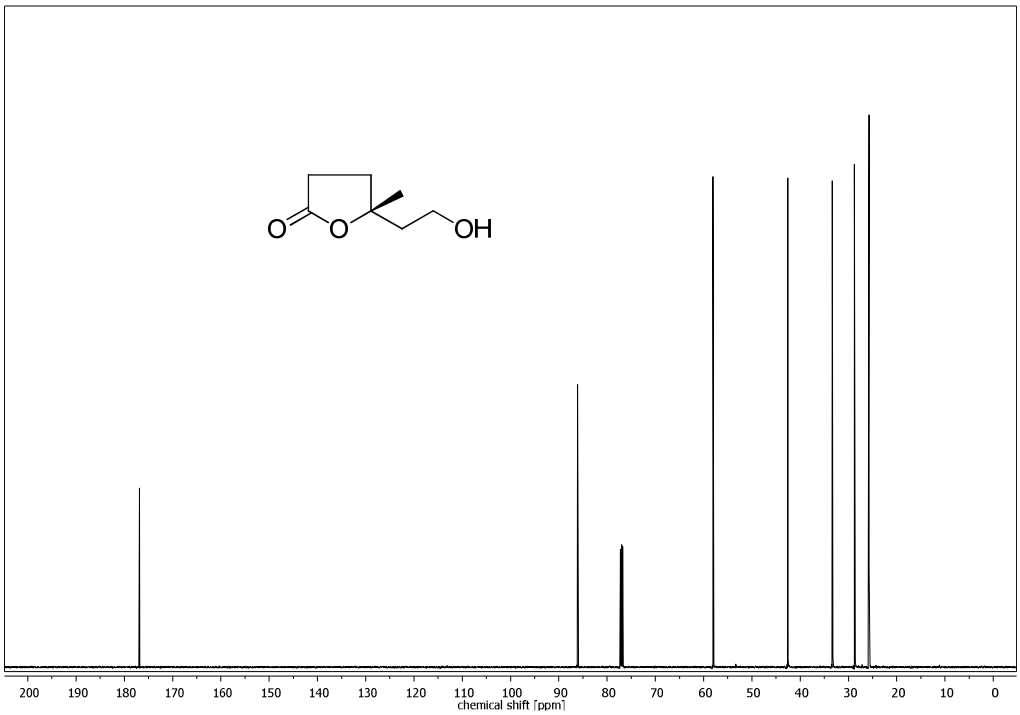
(+)-(*R*,*R*)-3-(1,2-diphenylethoxy)-6-methoxy-3-methyl-6-oxohexyl 3,5-dinitrobenzoate (11)



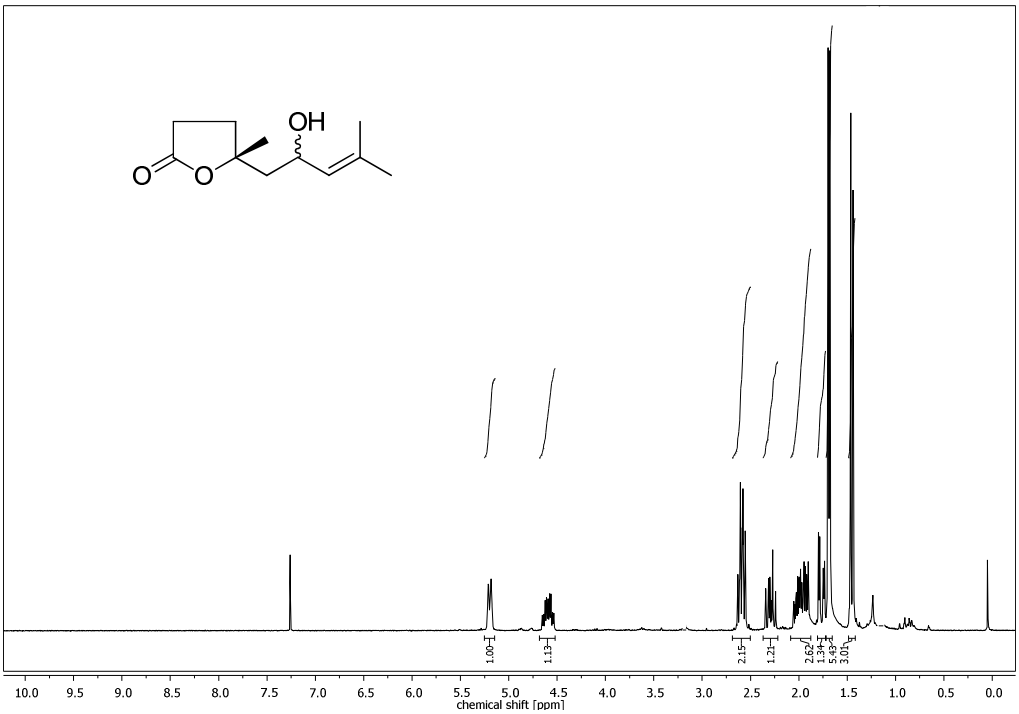


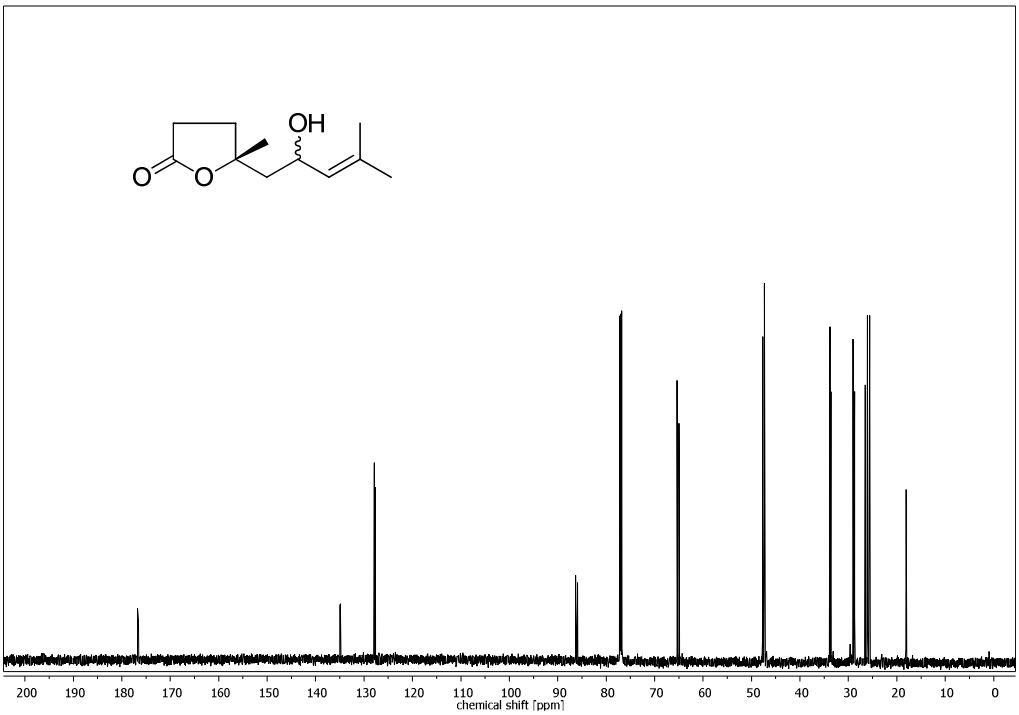
(–)-(*R*)-5-(2-hydroxyethyl)-5-methyldihydrofuran-2-one (9)



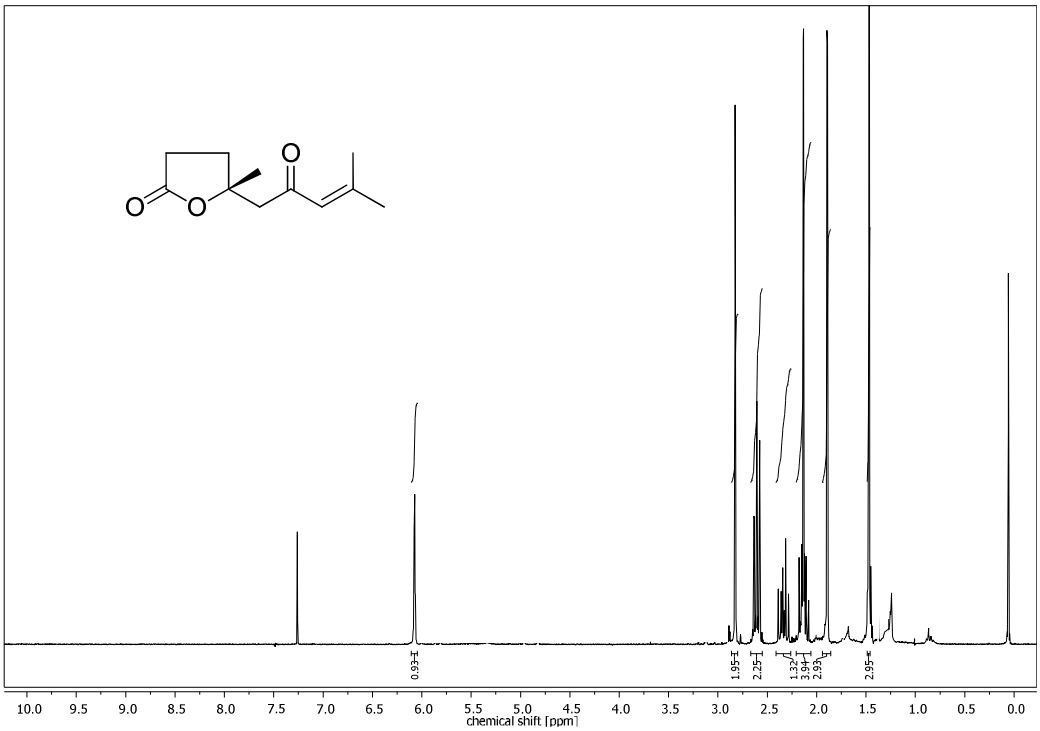


(–)-(5*R*)-5-(2-hydroxy-4-methylpent-3-en-1-yl)-5-methyldihydrofuran-2-one (13)





(+)-(*R*)-pinnatolide (1)



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