

Supporting Information

Reductive Aldol Coupling of Divinyl Ketones *via* Rhodium Catalyzed Hydrogenation: *syn*-Diastereoselective Construction of β -Hydroxyenones

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I. General Procedure

General: dichloromethane (DCM) was distilled from calcium hydride. Chemical reagents were purchased from Aldrich and Strem Chemicals, Inc. Commercially available aldehydes were purified immediately prior to use. Rh(COD)₂SbF₆¹, Rh(COD)₂BARF² and **1c**³ were prepared according to the previously reported procedures. Analytical thin-layer chromatography (TLC) was carried out using 0.2-mm commercial silica gel plates (DC-Fertigplatten Kieselgel 60 F₂₅₄). Flash chromatography was performed on silica gel 60 (200-400 mesh). NMR spectra were recorded on a Varian Gemini (300 MHz) spectrometer. ¹H NMR spectra were obtained at 300 MHz. ¹³C NMR spectra were obtained at 75 MHz. High resolution mass spectra were obtained on a Micromass ZAB-E spectrometer. FT-IR spectra were obtained using a Nicolet Impact 410 spectrometer. Melting points were obtained on a Thomas-Hoover Unimelt apparatus and are uncorrected.

General Procedure for the Coupling of Divinyl Ketones and Aldehydes: To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), aldehyde (0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) followed by H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and divinyl ketone (1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature until consumption of the aldehyde was observed, as revealed by TLC analysis, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the compound.

II. Procedures and Characterizations

Hexa-1,4-dien-3-one (1a)



To a solution of hexa-1,4-dien-3-ol⁴ (1.0 g, 10.2 mmol, 100 mol%) in CH₂Cl₂ (50 mL) at 0 °C was added MnO₂ (8.86 g, 101.9 mmol, 999 mol%). The reaction mixture was allowed to stir for 12 hours at ambient temperature, at which point the reaction mixture was filtered through a pad of celite with the aid of Et₂O. The resulting solution was evaporated and the residue was purified by flash chromatography (SiO₂: Et₂O/pentane) to afford the title compound (380 mg, 3.95 mmol) as a viscous yellow solid (39 % yield).

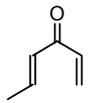
TLC: R_f 0.3 (Et₂O/pentane, 1/10).

¹H NMR (300 MHz, CDCl₃): δ 6.96 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.60 (dd, *J* = 17.4, 10.5 Hz, 1H), 6.40 (dq, *J* = 15.6, 1.8 Hz, 1H), 6.28 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.82 (dd, *J* = 10.5, 1.5 Hz, 1H), 1.95 (dd, *J* = 6.9, 1.8 Hz, 3H).

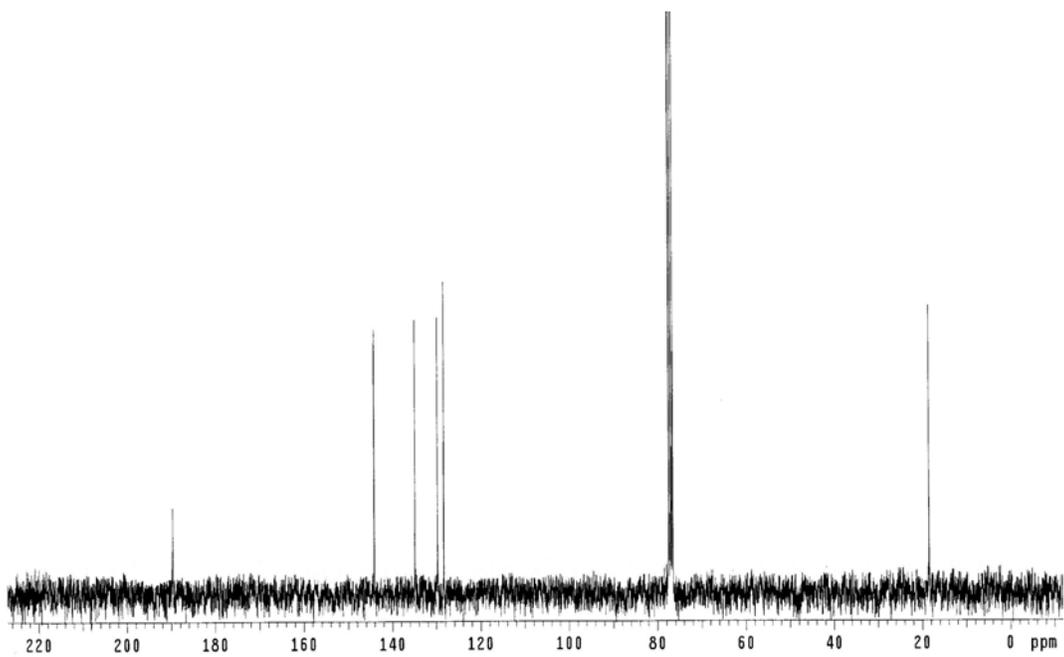
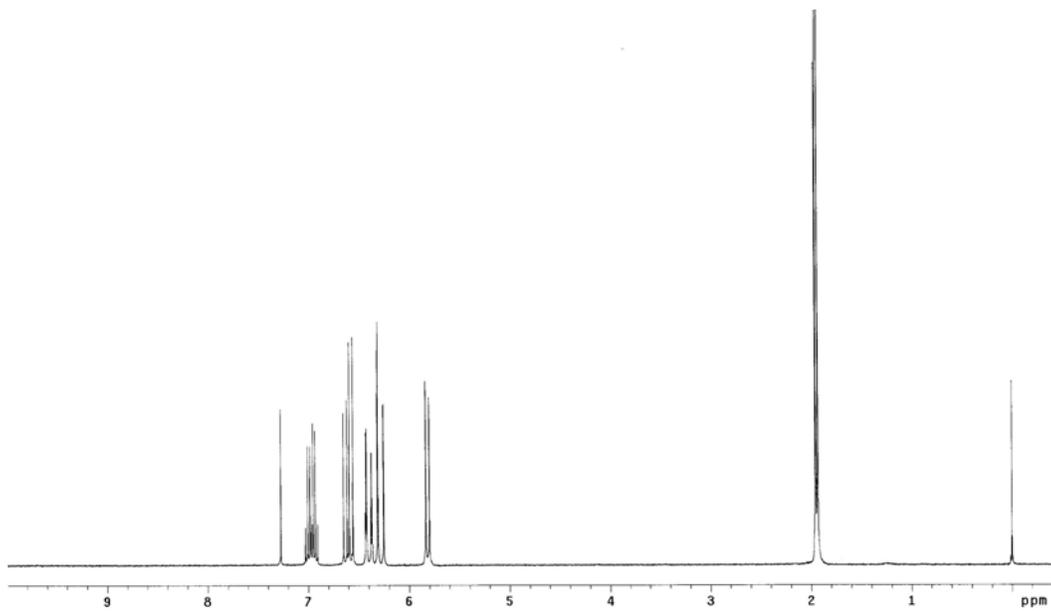
¹³C NMR (75 MHz, CDCl₃): δ 189.6, 144.1, 134.8, 129.7, 128.3, 18.5.

HRMS Calcd. for C₆H₈O (*M*+1): 97.0653, Found: 97.0653.

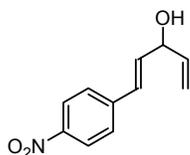
FTIR (NaCl film): 1666, 1635, 1611, 1443, 1403, 1276, 1216, 1135, 1090, 966, 749.



(1a)



1-(4-Nitro-phenyl)-penta-1,4-diene-3-ol



To a solution of vinylmagnesium bromide (1.0 M in THF, 25.6 mL, 25.6 mmol, 113 mol%) was added a solution of 3-(4-nitro-phenyl)-propenal (4.0 g, 22.6 mmol, 100 mol%) in THF (25 mL) at -78 °C. The reaction mixture was allowed to stir for 2 hours at ambient temperature, at which point the reaction mixture was cooled to 0 °C and saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ was added. The reaction mixture was extracted with Et_2O (3 times). The combined organic phases were dried (MgSO_4), filtered, and evaporated. The residue was purified by flash chromatography (SiO_2 : EtOAc/hexane) to afford the title compound (3.33 g, 16.2 mmol) as a yellow solid (72 % yield).

TLC: R_f 0.4 (EtOAc/hexane, 1/3).

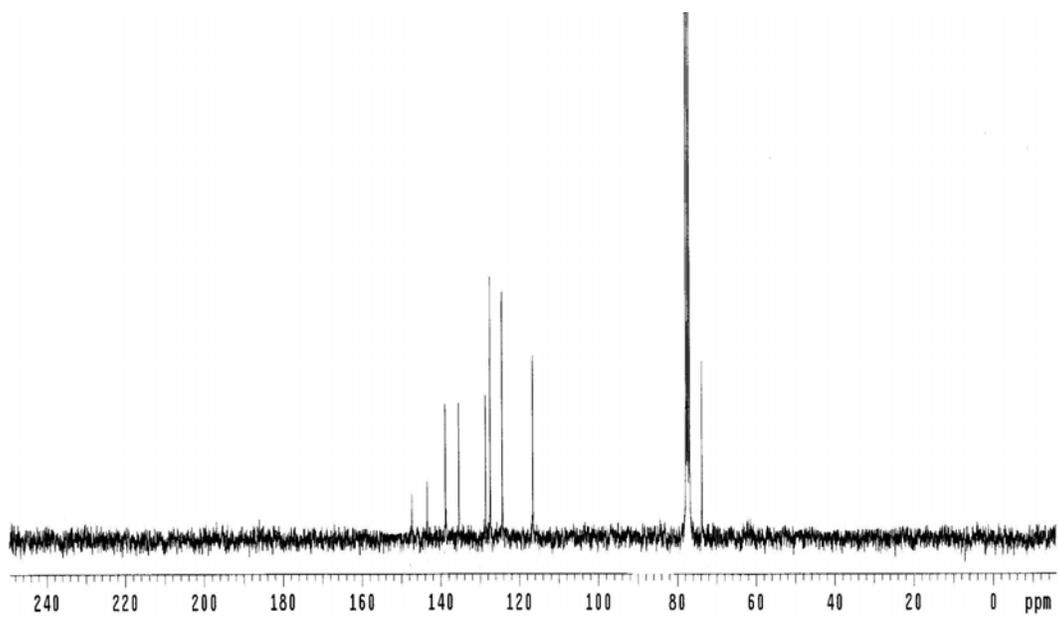
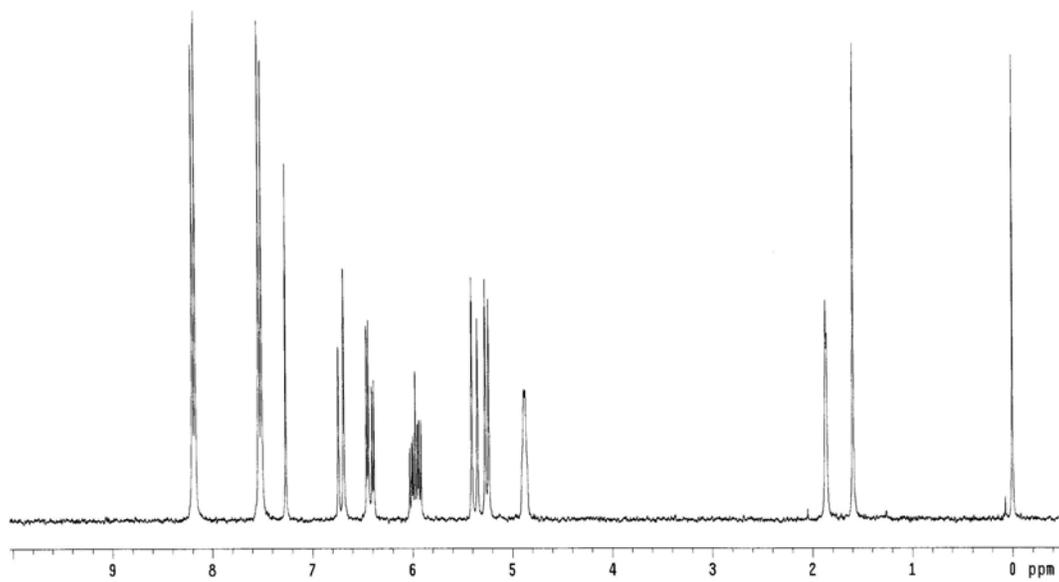
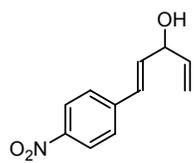
$^1\text{H NMR}$ (300 MHz, CDCl_3): δ 8.20-8.17 (m, 2H), 7.53-7.50 (m, 2H), 6.71 (d, $J = 15.9$ Hz, 1H), 6.42 (dd, $J = 15.9, 5.7$ Hz, 1H), 5.97 (ddd, $J = 17.1, 10.5, 6.0$ Hz, 1H), 5.38 (d, $J = 17.1$ Hz, 1H), 5.25 (d, $J = 10.5$ Hz, 1H), 4.88 (ddd, $J = 6.0, 5.7, 3.6$ Hz, 1H), 1.86 (d, $J = 3.6$ Hz, 1H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 147.3, 143.4, 138.8, 135.4, 128.5, 127.3, 124.3, 116.6, 73.7.

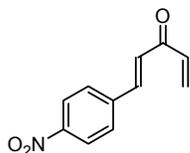
HRMS Calcd. for $\text{C}_{11}\text{H}_{11}\text{NO}_3$ ($M+1$): 206.0817, Found: 206.0816.

FTIR (NaCl film): 3384, 1595, 1513, 1343, 1109, 971, 928, 860, 748 cm^{-1} .

M.P.: 50-51 °C.



1-(4-Nitro-phenyl)-penta-1,4-dien-3-one (1b)



To a solution of 1-(4-nitro-phenyl)-penta-1,4-diene-3-ol (1.89 g, 9.21 mmol, 100 mol%) in CH₂Cl₂ (50 mL) at 0 °C was added MnO₂ (8.00 g, 92.1 mmol, 1000 mol%). The reaction mixture was allowed to stir for 12 hours at ambient temperature, at which point the reaction mixture was filtered through a pad of celite with the aid of Et₂O. The resulting solution was evaporated and the residue was purified by flash chromatography (SiO₂: EtOAc/hexane) to afford the title compound (590 mg, 2.90 mmol) as a yellow solid (32 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/7).

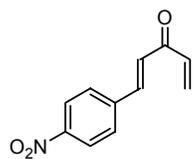
¹H NMR (300 MHz, CDCl₃): δ 8.28-8.26 (m, 2H), 7.75-7.73 (m, 2H), 7.69 (d, *J* = 12.0 Hz, 1H), 7.13 (d, *J* = 12.0 Hz, 1H), 6.71 (dd, *J* = 12.9, 8.1 Hz, 1H), 6.43 (dd, *J* = 12.9, 0.9 Hz, 1H), 5.98 (dd, *J* = 8.1, 0.9 Hz, 1H).

¹³C NMR (75 MHz, CDCl₃): δ 188.8, 140.8, 140.7, 135.4, 129.7, 128.9, 127.3, 124.2.

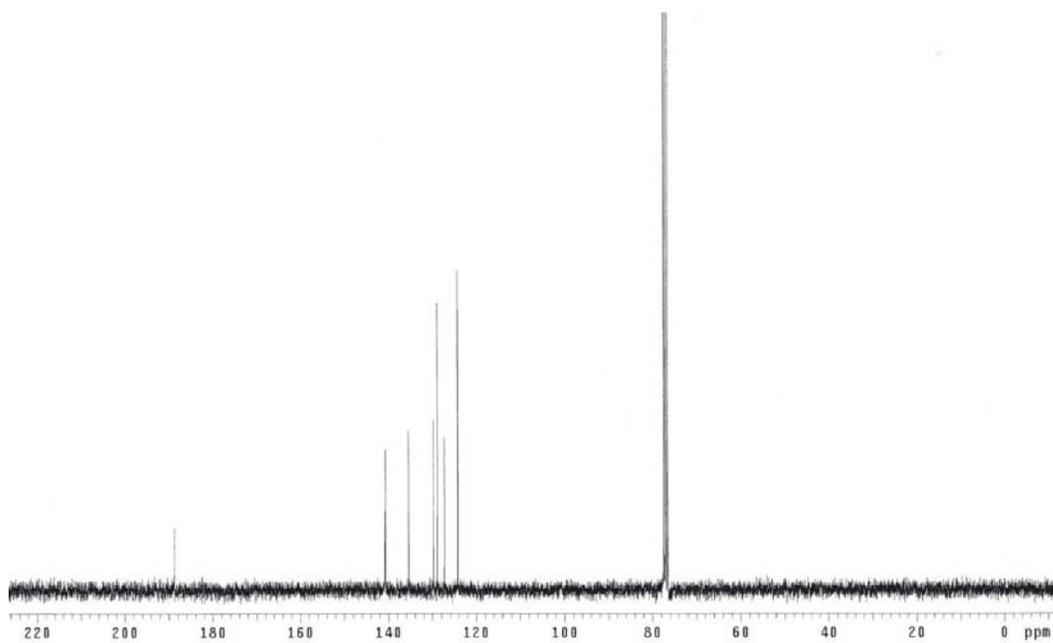
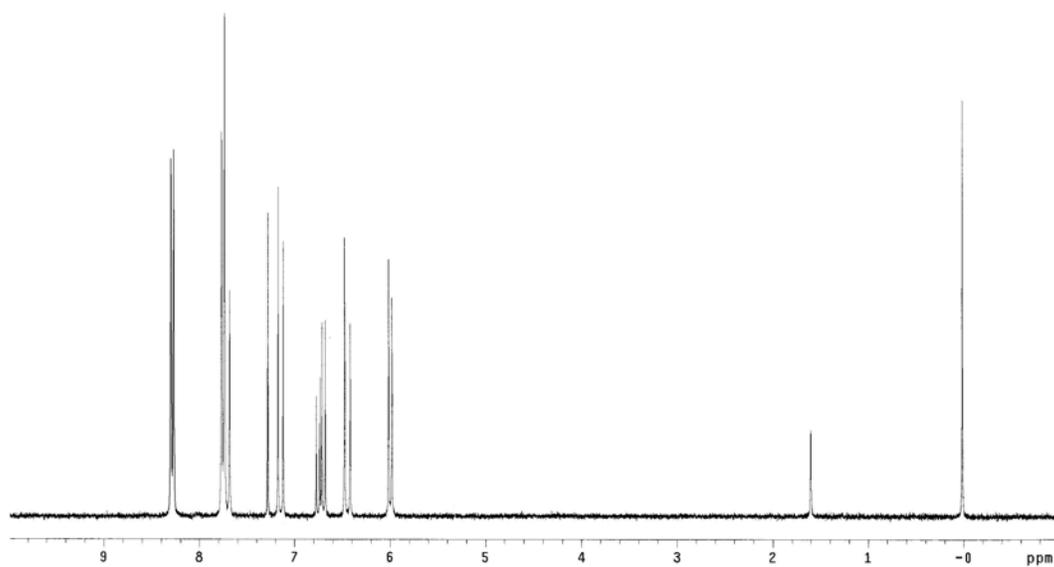
HRMS Calcd. for C₁₂H₁₄O₂ (M+1): 204.0661, Found: 204.0663.

FTIR (NaCl film): 2360, 1655, 1592, 1517, 1405, 1345, 1202, 1106, 982, 846 cm⁻¹.

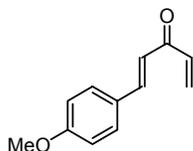
M.P.: 123-125 °C.



(1b)



1-(4-Methoxy-phenyl)-penta-1,4-dien-3-one (1d)



To a solution of 1-(4-methoxy-phenyl)-penta-1,4-dien-3-ol⁵ (2.32 g, 12.19 mmol, 100 mol%) in CH₂Cl₂ (50 mL) at 0 °C was added MnO₂ (10.60 g, 121.95 mmol, 1000 mol%). The reaction mixture was allowed to stir for 12 hours at ambient temperature, at which point the reaction mixture was filtered through a pad of celite with the aid of Et₂O. The resulting solution was evaporated and the residue was purified by flash chromatography (SiO₂: EtOAc/hexane) to afford the title compound (1.56 g, 8.29 mmol) as a yellow solid (68 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/4).

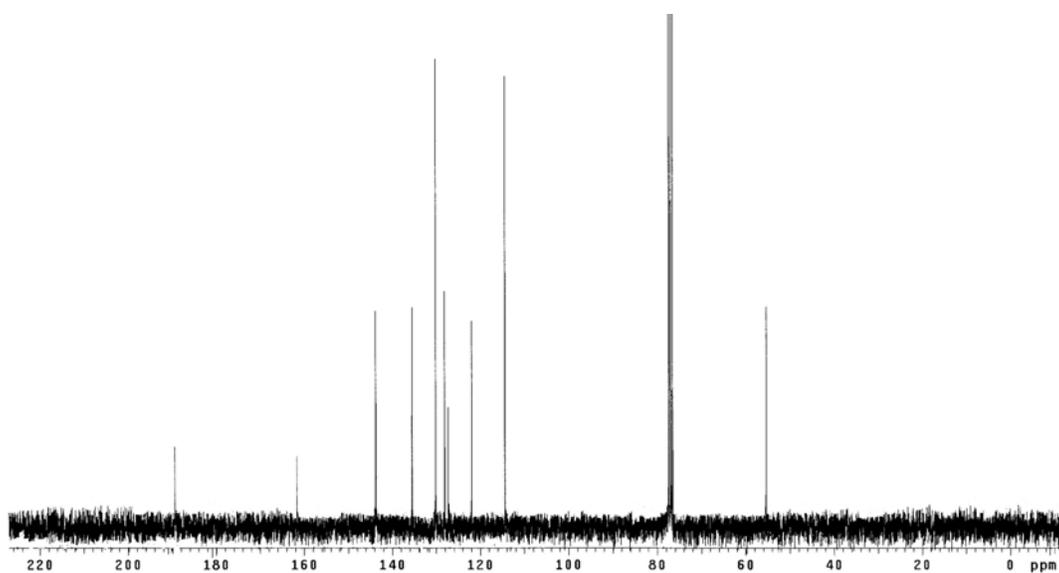
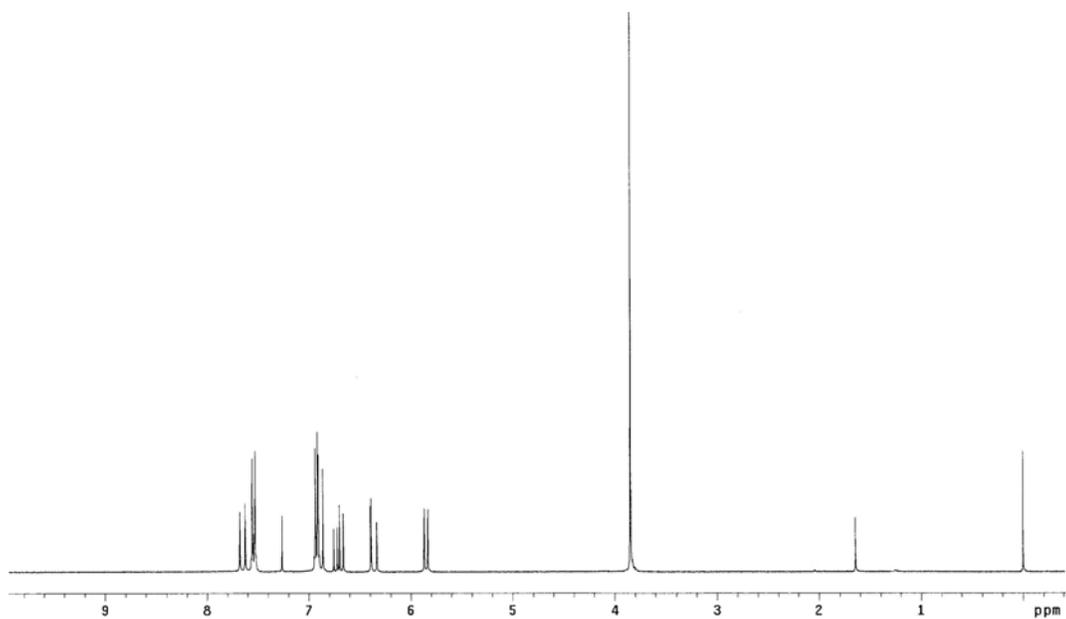
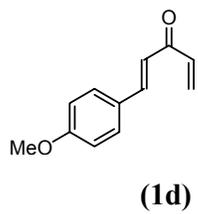
¹H NMR (300 MHz, CDCl₃): δ 7.65 (d, *J* = 15.9 Hz, 1H), 7.56-7.53 (m, 2H), 6.94-6.91 (m, 2H), 6.80 (d, *J* = 15.9 Hz, 1H), 6.71 (dd, *J* = 17.4, 10.5 Hz, 1H), 6.36 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.85 (dd, *J* = 10.5, 1.5 Hz, 1H), 3.85 (s, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 189.5, 161.7, 143.8, 135.5, 130.1, 128.1, 127.3, 122.0, 114.4, 55.4.

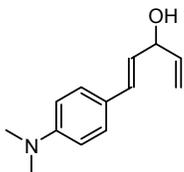
HRMS Calcd. for C₁₂H₁₂O₂ (M+1): 189.0916, Found: 189.0912.

FTIR (NaCl film): 2966, 1652, 1619, 1600, 1571, 1511, 1462, 1423, 1403, 1306, 1255, 1221, 1199, 1173, 1102, 1028, 987, 829 cm⁻¹.

M.P.: 67-69 °C.



1-(4-Dimethylamino-phenyl)-penta-1,4-dien-3-ol



To a solution of vinylmagnesium bromide (1.0 M in THF, 37.1 mL, 37.1 mmol, 130 mol%) was added a solution of 3-(4-dimethylamino-phenyl)-propenal (5.0 g, 28.5 mmol, 100 mol%) in THF (25 mL) at -78 °C. The reaction mixture was allowed to stir for 2 hours at ambient temperature, at which point the reaction mixture was cooled to 0 °C and saturated $\text{NH}_4\text{Cl}_{(\text{aq})}$ was added. The reaction mixture was extracted with Et_2O (3 times). The combined organic phases were dried (MgSO_4), filtered, and evaporated. The residue was purified by flash chromatography (SiO_2 : EtOAc/hexane) to afford the title compound (4.29 g, 21.1 mmol) as a viscous yellow oil (74 % yield).

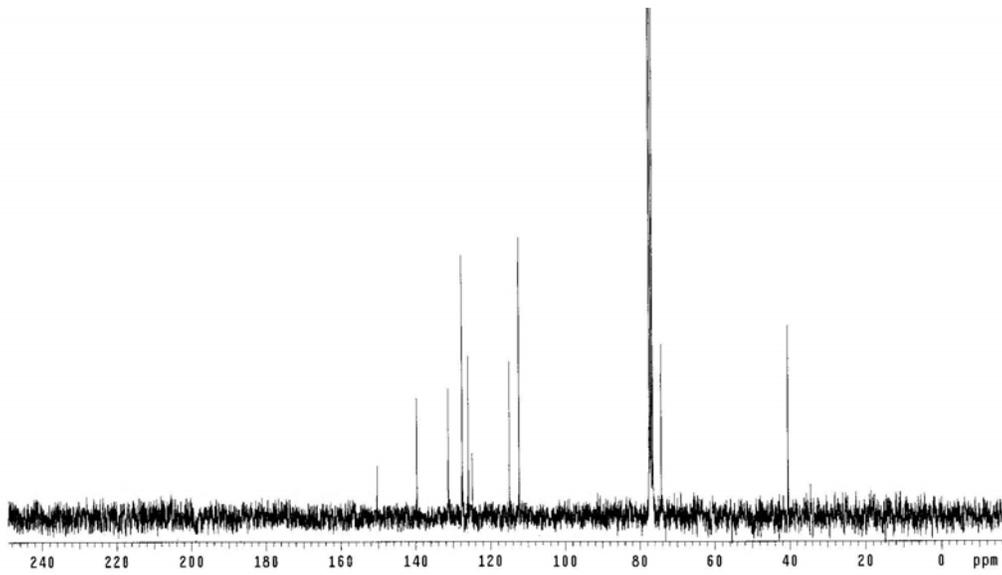
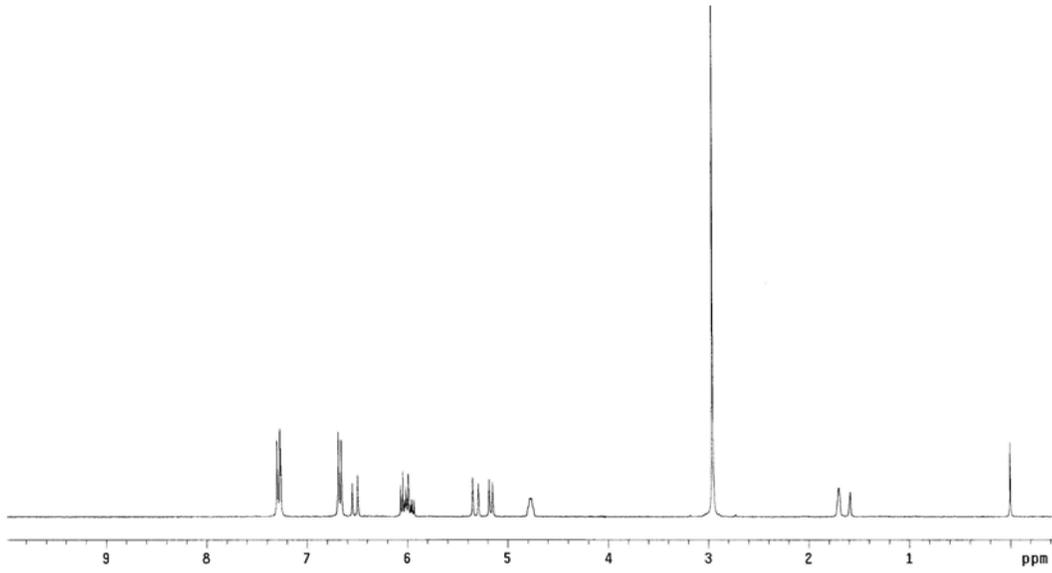
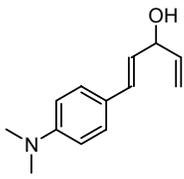
TLC: R_f 0.3 (EtOAc/hexane, 1/4).

$^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.29-7.26 (m, 2H), 6.68-6.66 (m, 2H), 6.52 (d, $J = 15.9$ Hz, 1H), 6.03 (dd, $J = 15.9, 7.2$ Hz, 1H), 5.99 (ddd, $J = 17.4, 10.5, 5.7$ Hz, 1H), 5.32 (d, $J = 17.4$ Hz, 1H), 5.17 (d, $J = 10.5$ Hz, 1H), 4.77 (dd, $J = 7.2, 5.7$ Hz, 1H), 2.96 (s, 6H).

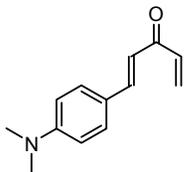
$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 150.2, 139.7, 131.3, 127.5, 125.9, 124.8, 114.9, 112.3, 74.3, 40.4.

HRMS Calcd. for $\text{C}_{13}\text{H}_{17}\text{NO}$ (M): 203.1310, Found: 203.1312.

FTIR (NaCl film): 3362, 2885, 2360, 1609, 1521, 1444, 1354, 1229, 1186, 1166, 965, 946, 805, 668 cm^{-1} .



1-(4-Dimethylamino-phenyl)-penta-1,4-dien-3-one (1e)



To a solution of 1-(4-dimethylamino-phenyl)-penta-1,4-dien-3-ol (2.12 g, 10.43 mmol, 100 mol%) in CH_2Cl_2 (50 mL) at 0 °C was added MnO_2 (9.06 g, 104.30 mmol, 1000 mol%). The reaction mixture was allowed to stir for 12 hours at ambient temperature, at which point the reaction mixture was filtered through a pad of celite with the aid of Et_2O . The resulting solution was evaporated and the residue was purified by flash chromatography (SiO_2 : EtOAc/hexane) to afford the title compound (1.47 g, 7.30 mmol) as a red solid (70 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/3).

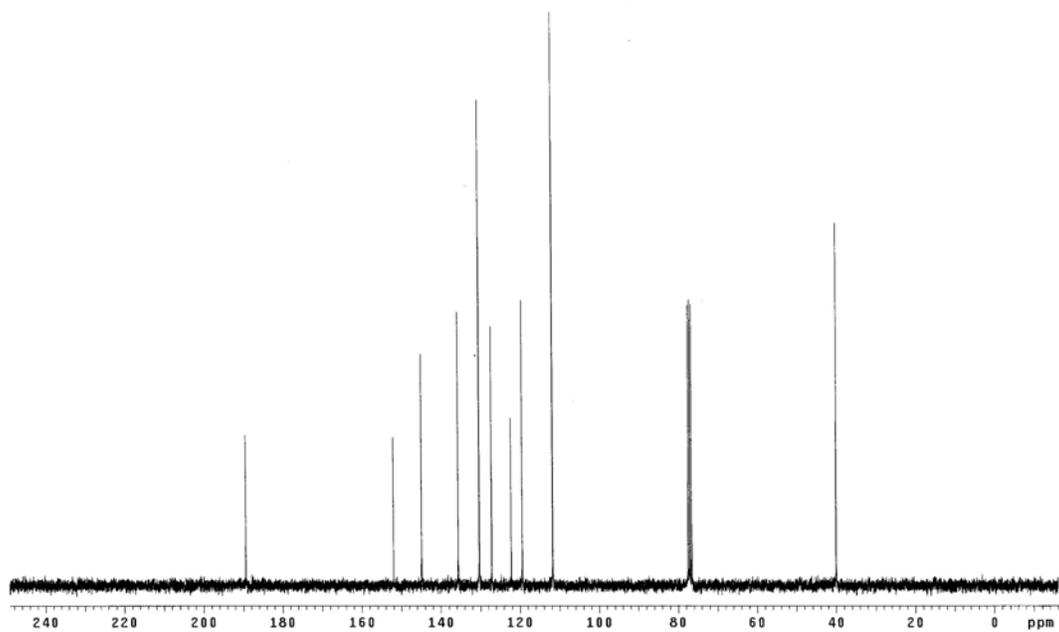
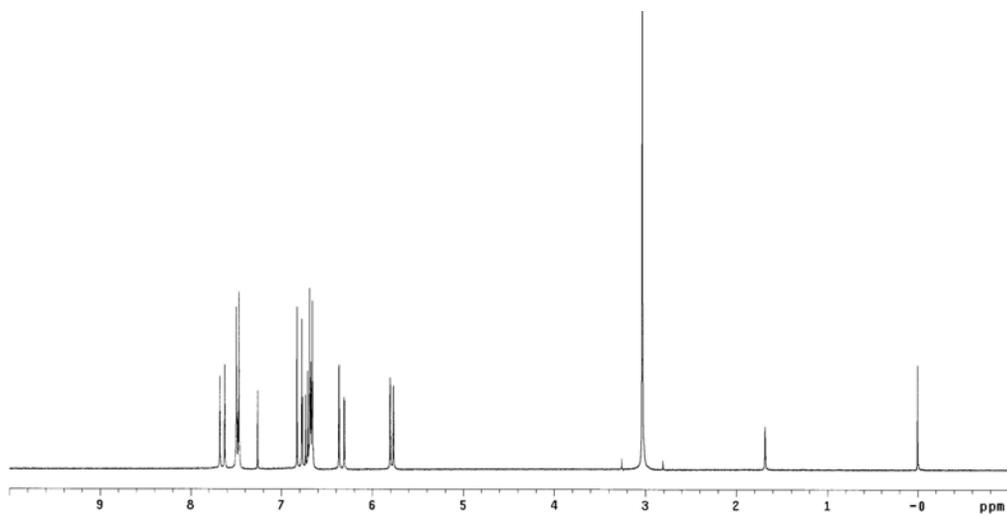
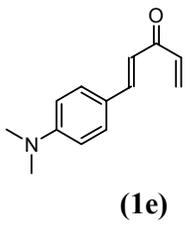
$^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.64 (d, J = 15.9 Hz, 1H), 7.48-7.45 (m, 2H), 6.79 (d, J = 15.9 Hz, 1H), 6.68 (dd, J = 17.4, 10.5 Hz, 1H), 6.67-6.64 (m, 2H), 6.33 (dd, J = 17.4, 1.5 Hz, 1H), 5.77 (dd, J = 10.5, 1.5 Hz, 1H), 3.01 (s, 6H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 189.3, 152.0, 144.8, 135.6, 130.2, 127.1, 119.4, 111.7, 40.0.

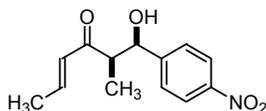
HRMS Calcd. for $\text{C}_{13}\text{H}_{15}\text{NO}$ ($M+1$): 202.1232, Found: 202.1231.

FTIR (NaCl film): 2916, 1648, 1605, 1572, 1522, 1455, 1226, 985, 814 cm^{-1} .

M.P.: 95-96 °C.



1-Hydroxy-2-methyl-1-(4-nitro-phenyl)-hex-4-en-3-one (3a)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 4-nitro-benzaldehyde (75.6 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and hexa-1,4-dien-3-one (96.1 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 7 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (102 mg, 0.41 mmol) as a viscous yellow oil (82 % yield).

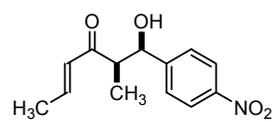
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 8.22-8.19 (m, 2H), 7.55-7.52 (m, 2H), 6.99 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.19 (dq, *J* = 15.6, 1.8 Hz, 1H), 5.24 (d, *J* = 2.7 Hz, 1H), 3.93 (br, 1H), 3.03 (dq, *J* = 7.2, 2.7 Hz, 1H), 1.95 (dd, *J* = 6.9, 1.8 Hz, 3H), 1.03 (d, *J* = 7.2 Hz, 3H).

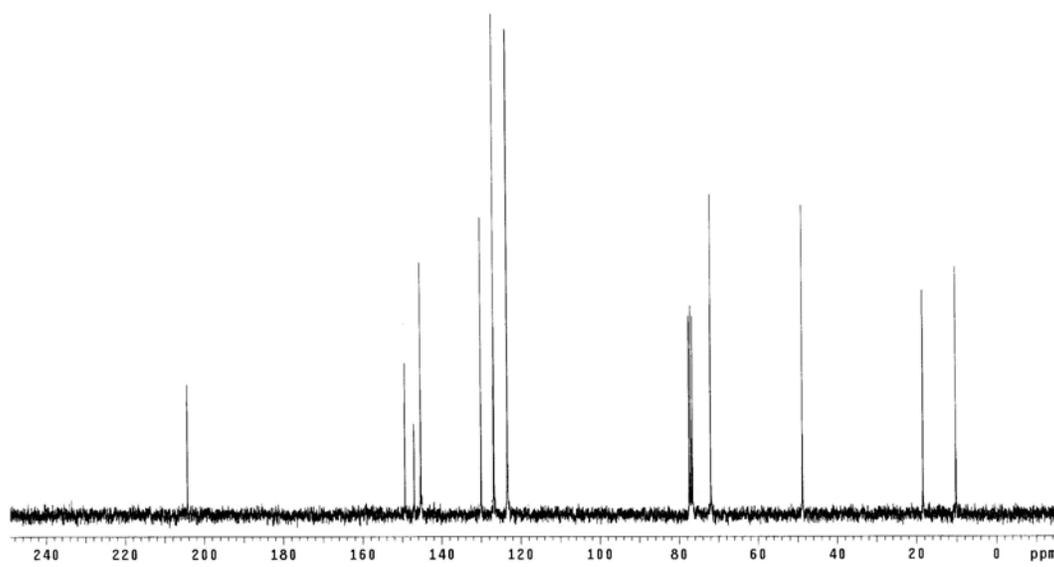
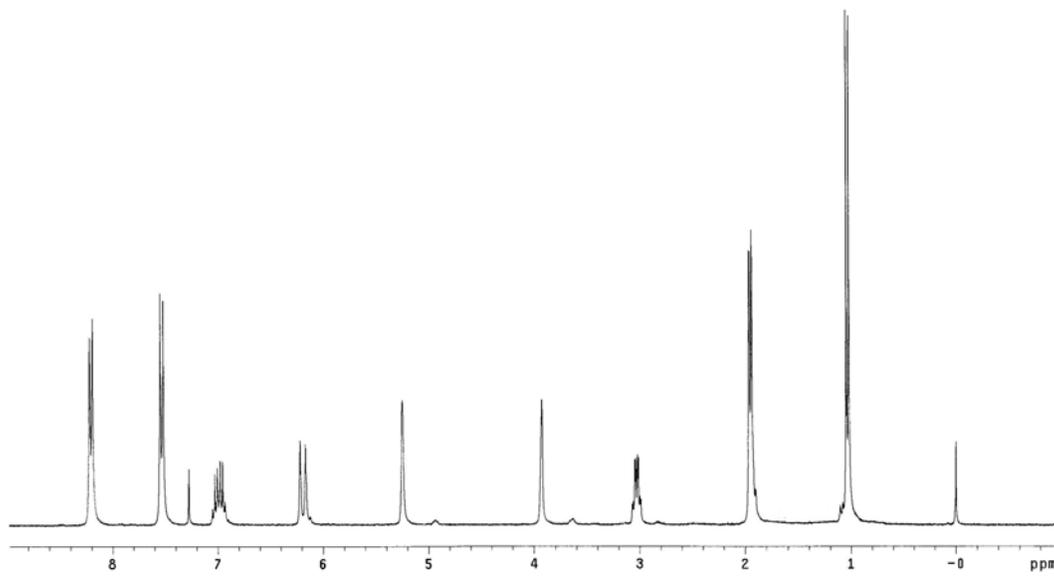
¹³C NMR (75 MHz, CDCl₃): δ 204.2, 149.3, 147.0, 145.3, 130.0, 126.7, 123.3, 71.9, 48.8, 18.3, 10.1.

HRMS Calcd. for C₁₃H₁₅NO₄ (M): 250.1079; Found: 250.1082.

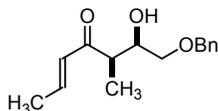
FTIR (NaCl film): 3461, 2975, 2937, 2369, 1683, 1651, 1624, 1605, 1519, 1441, 1375, 1347, 1201, 1108, 1056, 970, 854, 749, 707, 668 cm⁻¹.



(3a)



7-Benzyloxy-6-hydroxy-5-methyl-hept-2-en-4-one (3b)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), benzyloxy-acetaldehyde (75.1 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and hexa-1,4-dien-3-one (96.1 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 7 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (99 mg, 0.40 mmol) as a viscous yellow oil (80 % yield).

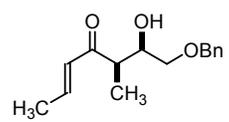
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 7.37-7.26 (m, 5H), 6.91 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.16 (dq, *J* = 15.6, 1.5 Hz, 1H), 4.52 (s, 2H), 4.04-4.14 (m, 1H), 3.53-3.41 (m, 2H), 3.01 (dq, *J* = 7.2, 5.4 Hz, 1H), 2.91 (d, *J* = 3.3 Hz, 1H), 1.90 (dd, *J* = 6.9, 1.5 Hz, 3H), 1.16 (d, *J* = 7.2 Hz, 3H).

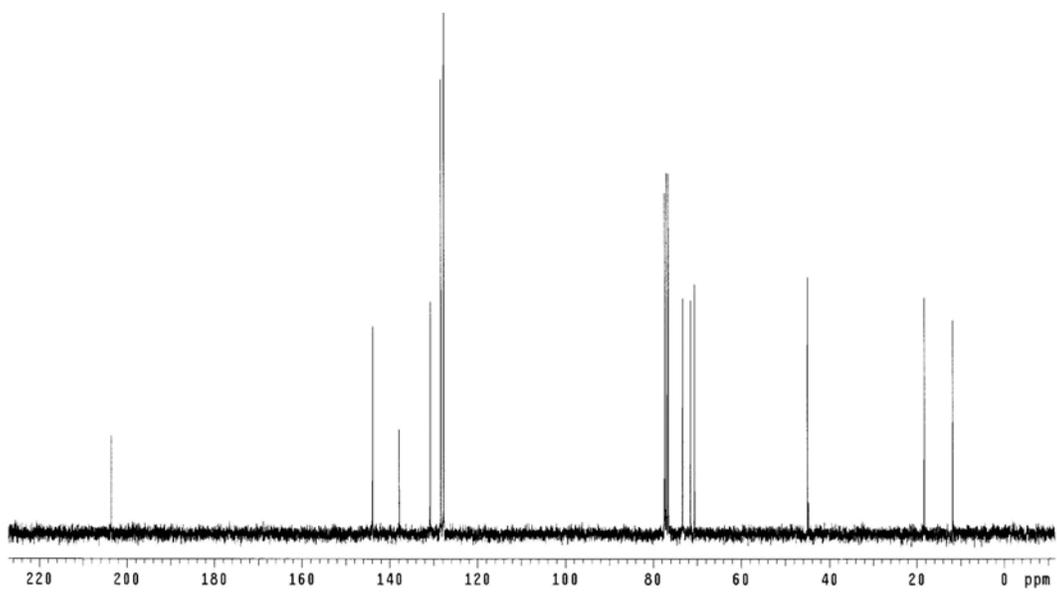
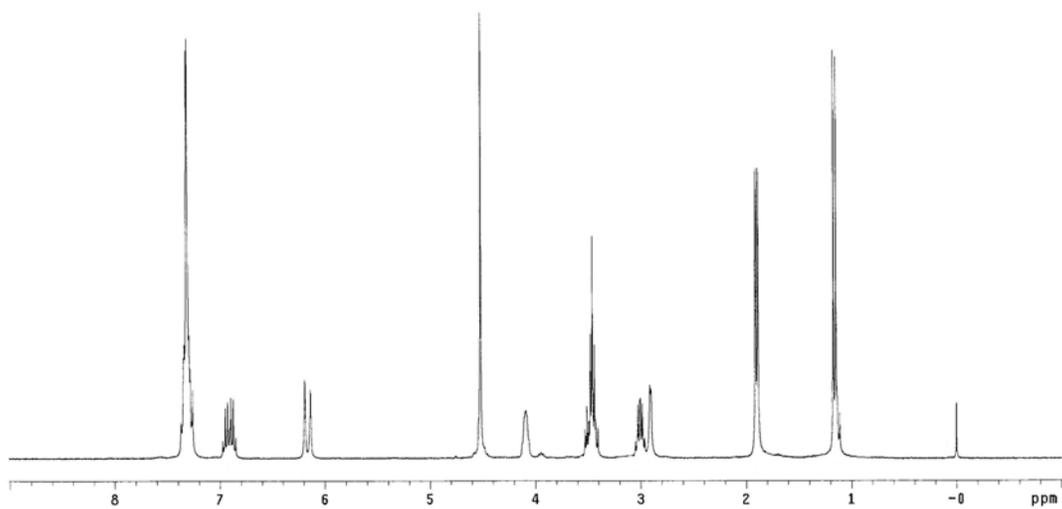
¹³C NMR (75 MHz, CDCl₃): δ 203.6, 143.9, 137.8, 130.8, 128.4, 127.7, 73.3, 71.5, 70.6, 45.0, 18.3, 11.8.

HRMS Calcd. for C₁₂H₂₀O₃ (M+1): 249.1491, Found: 249.1497.

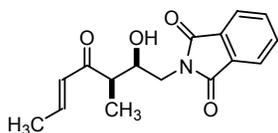
FTIR (NaCl film): 3447, 2912, 2360, 1654, 1626, 1453, 1374, 1101, 970, 738, 698, 668 cm⁻¹.



(3b)



2-(2-Hydroxy-3-methyl-4-oxo-hept-5-enyl)-isoindole-1,3-dione (3c)



To a 13 mm × 100 mm test-tube were added Li_2CO_3 (3.9 mg, 0.05 mmol, 10 mol%), $(2\text{-Fur})_3\text{P}$ (13.9 mg, 0.06 mmol, 12 mol%), $\text{Rh}(\text{COD})_2\text{SbF}_6$ (13.9 mg, 0.025 mmol, 5 mol%), (1,3-dioxo-1,3-dihydro-isoindol-2-yl)-acetaldehyde (94.6 mg, 0.5 mmol, 100 mol%) and CH_2Cl_2 (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with $\text{Ar}(\text{g})$ and $\text{H}_2(\text{g})$ for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and hexa-1,4-dien-3-one (96.1 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 7 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO_2 : EtOAc/hexane) to afford the title compound (122 mg, 0.42 mmol) as a white solid (85 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/3).

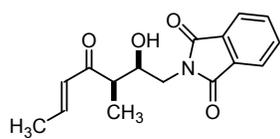
$^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.87-7.84 (m, 2H), 7.74-7.33 (m, 2H), 6.92 (dq, $J = 15.6, 6.9$ Hz, 1H), 6.19 (d, $J = 15.6$ Hz, 1H), 4.32-4.22 (m, 1H), 3.87 (dd, $J = 14.1, 4.5$ Hz, 1H), 3.73 (dd, $J = 14.1, 7.8$ Hz, 1H), 3.26 (br, 1H), 2.88 (m, 1H), 1.91 (d, $J = 6.9$ Hz, 3H), 1.29 (d, $J = 7.2$ Hz, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 203.2, 168.5, 144.3, 134.0, 131.9, 130.1, 123.3, 69.5, 45.8, 41.3, 18.3, 11.0.

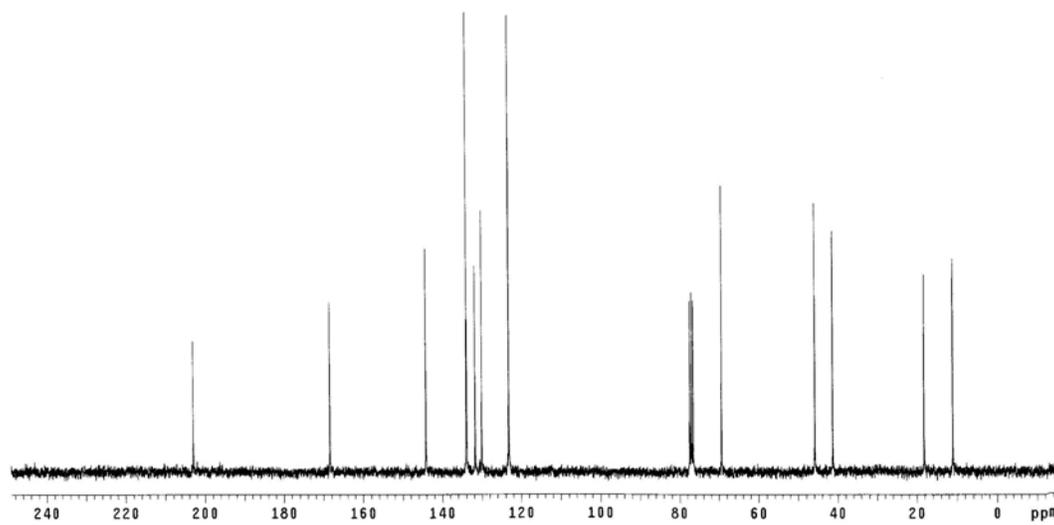
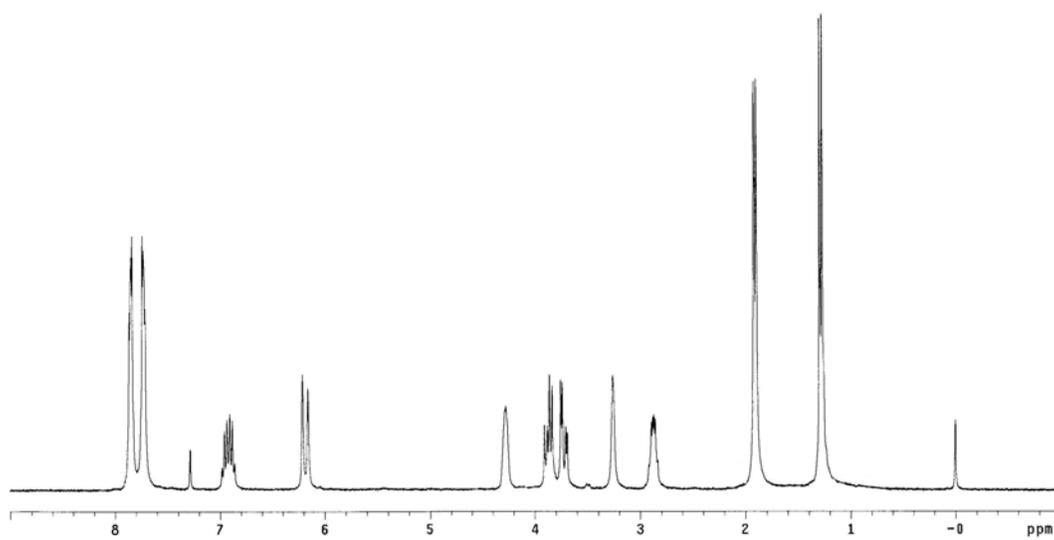
HRMS Calcd. for $\text{C}_{16}\text{H}_{17}\text{NO}_4$ ($M+1$): 288.1236, Found: 288.1234.

FTIR (NaCl film): 3472, 2937, 2360, 1772, 1712, 1625, 1431, 1395, 1190, 1034, 969, 714 cm^{-1} .

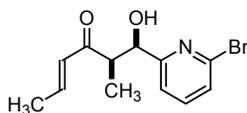
M.P.: 110-112 $^\circ\text{C}$.



(3c)



1-(6-Bromo-pyridin-2-yl)-1-hydroxy-2-methyl-hex-4-en-3-one (3d)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 6-bromo-pyridine-2-carbaldehyde (93.0 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and hexa-1,4-dien-3-one (96.1 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 7 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (134 mg, 0.47 mmol) as a viscous yellow oil (94 % yield).

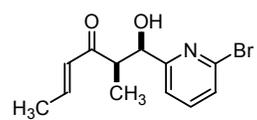
TLC: R_f 0.5 (EtOAc/hexane, 1/2).

¹H NMR (300 MHz, CDCl₃): δ 7.59-7.48 (m, 2H), 7.38-7.35 (m, 2H), 6.99 (dq, *J* = 15.6, 6.9 Hz, 1H), 6.20 (dq, *J* = 15.6, 1.5 Hz, 1H), 5.12 (dd, *J* = 3.3, 3.3 Hz, 1H), 4.04 (d, *J* = 3.3 Hz, 1H), 3.43 (dq, *J* = 6.9, 3.3 Hz, 1H), 1.93 (dd, *J* = 6.9, 1.5 Hz, 3H), 1.93 (dd, *J* = 6.9, 1.5 Hz, 3H), 1.00 (d, *J* = 6.9 Hz, 3H).

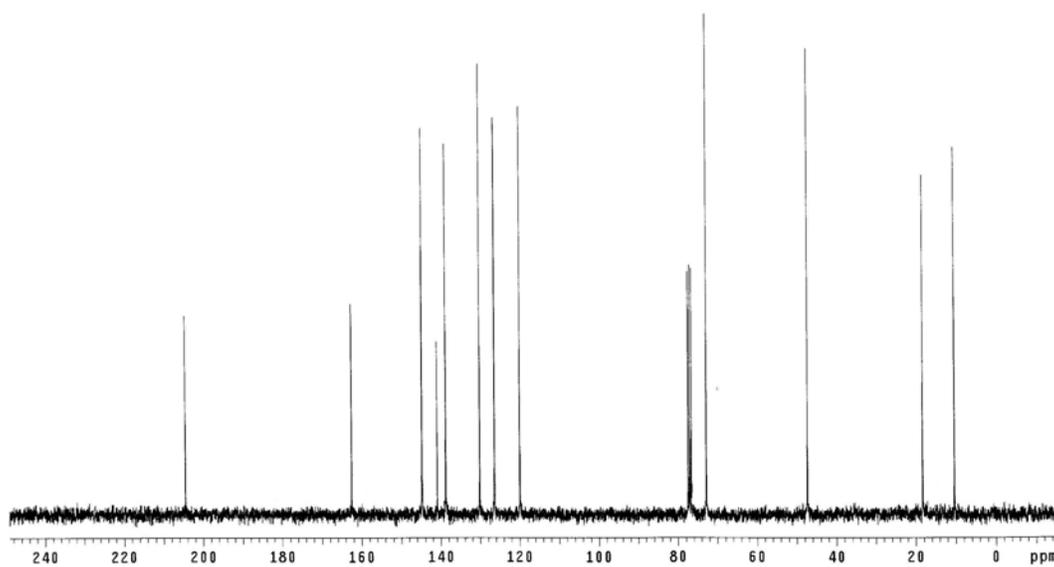
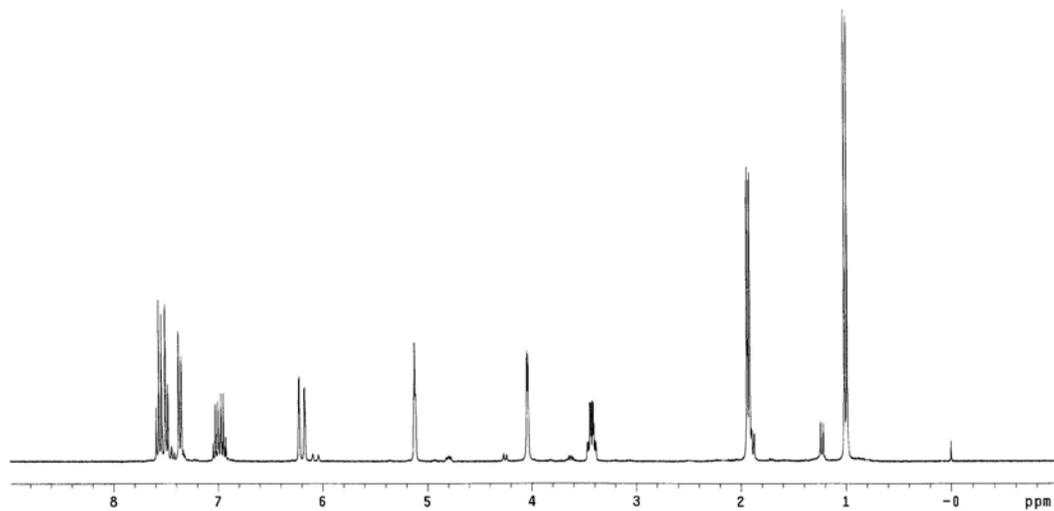
¹³C NMR (75 MHz, CDCl₃): δ 204.5, 162.5, 144.8, 140.9, 138.8, 130.1, 126.3, 119.9, 72.8, 47.3, 18.3, 10.3.

HRMS Calcd. for C₁₂H₁₄BrNO₂ (M+1): 284.0286, Found: 284.0283.

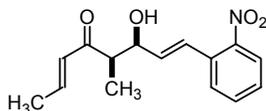
FTIR (NaCl film): 3443, 2973, 2935, 2360, 1684, 1653, 1626, 1582, 1555, 1437, 1406, 1375, 1290, 1199, 1157, 1127, 1044, 986, 969, 933, 788, 747, 697 cm⁻¹.



(3d)



6-Hydroxy-5-methyl-8-(2-nitro-phenyl)-octa-2,7-dien-4-one (3e)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 3-(2-nitro-phenyl)-propenal (88.6 mg, 1.0 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and hexa-1,4-dien-3-one (144.2 mg, 1.5 mmol, 300 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 7 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (103 mg, 0.37 mmol) as a viscous yellow oil (75 % yield).

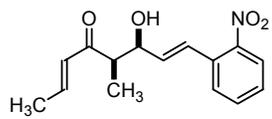
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 7.94-7.91 (m, 1H), 7.57-7.56 (m, 2H), 7.42-7.26 (m, 1H), 7.10 (d, *J* = 15.9 Hz, 1H), 6.98 (dq, *J* = 14.7, 6.9 Hz, 1H), 6.22 (d, *J* = 14.7 Hz, 1H), 6.16 (dd, *J* = 15.9, 5.7 Hz, 1H), 4.70 (dd, *J* = 5.7, 3.3 Hz, 1H), 3.24 (br, 1H), 3.01 (dq, *J* = 7.5, 3.3 Hz, 1H), 1.95 (d, *J* = 6.9 Hz, 3H), 1.23 (d, *J* = 7.5 Hz, 3H).

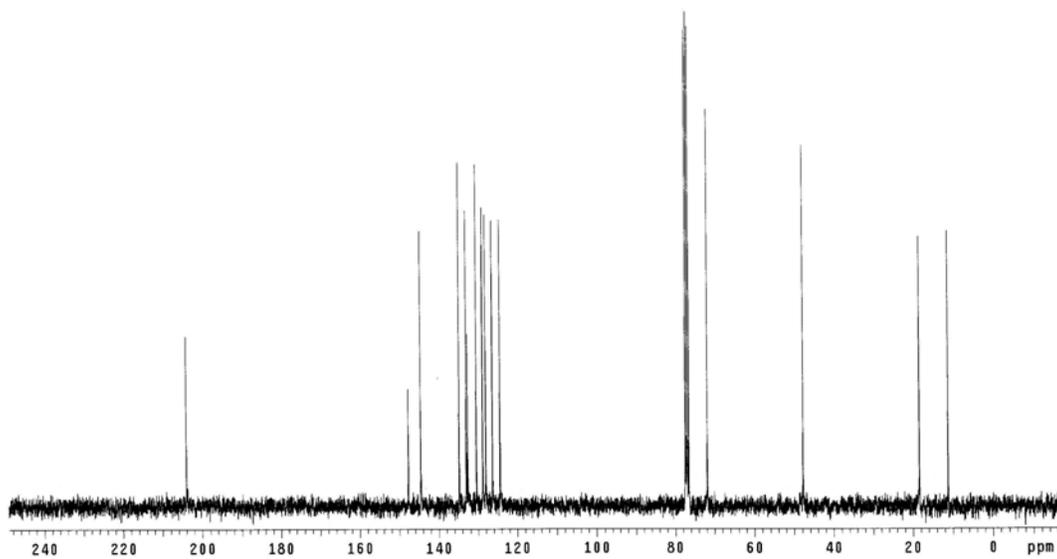
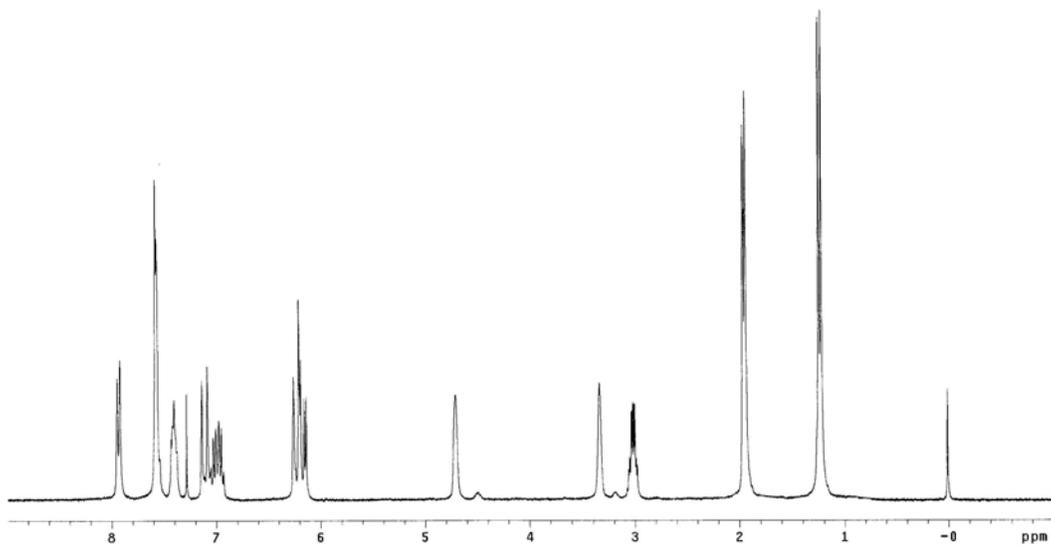
¹³C NMR (75 MHz, CDCl₃): δ 204.0, 147.7, 144.6, 134.8, 133.0, 132.6, 130.4, 128.8, 128.0, 126.3, 124.4, 71.8, 47.7, 18.3, 11.1.

HRMS Calcd. for C₁₅H₁₇NO₄ (M+1): 276.1236, Found: 276.1238.

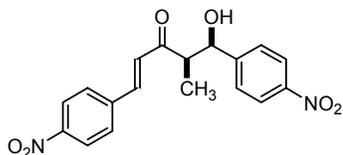
FTIR (NaCl film): 3447, 2973, 2933, 2359, 2341, 1685, 1654, 1624, 1570, 1522, 1441, 1345, 1302, 1199, 1042, 967, 860, 785, 742, 668 cm⁻¹.



(3e)



5-Hydroxy-4-methyl-1,5-bis-(4-nitro-phenyl)-pent-1-en-3-one (4b)



To a 13 mm × 100 mm test-tube were added Li_2CO_3 (3.9 mg, 0.05 mmol, 10 mol%), $(2\text{-Fur})_3\text{P}$ (13.9 mg, 0.06 mmol, 12 mol%), $\text{Rh}(\text{COD})_2\text{SbF}_6$ (13.9 mg, 0.025 mmol, 5 mol%), 4-nitro-benzaldehyde (75.6 mg, 0.5 mmol, 100 mol%) and CH_2Cl_2 (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with $\text{Ar}(\text{g})$ and $\text{H}_2(\text{g})$ for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-nitro-phenyl)-penta-1,4-dien-3-one (152.4 mg, 0.75 mmol, 150 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO_2 : EtOAc/hexane) to afford the title compound (78 mg, 0.22 mmol) as a white solid (44 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/2).

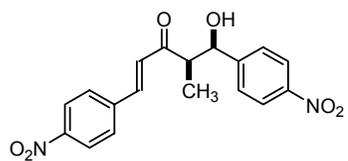
$^1\text{H NMR}$ (300 MHz, CDCl_3): δ 8.29-8.26 (m, 5H), 7.74-7.71 (m, 2H), 7.59-7.56 (m, 2H), 6.91 (d, $J = 15.9$ Hz, 1H), 3.61 (d, $J = 2.4$ Hz, 1H), 3.14 (dq, $J = 7.5, 2.7$ Hz, 1H), 1.15 (d, $J = 7.5$ Hz, 3H).

$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 203.5, 149.2, 149.1, 147.5, 141.5, 140.4, 129.4, 127.7, 127.1, 124.5, 124.0, 123.8, 72.2, 51.0, 10.3.

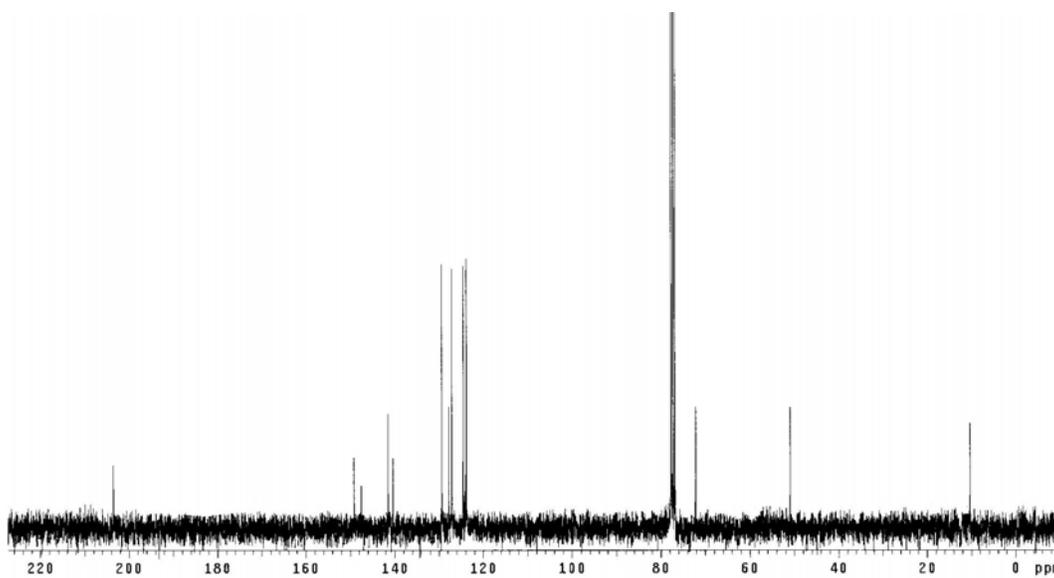
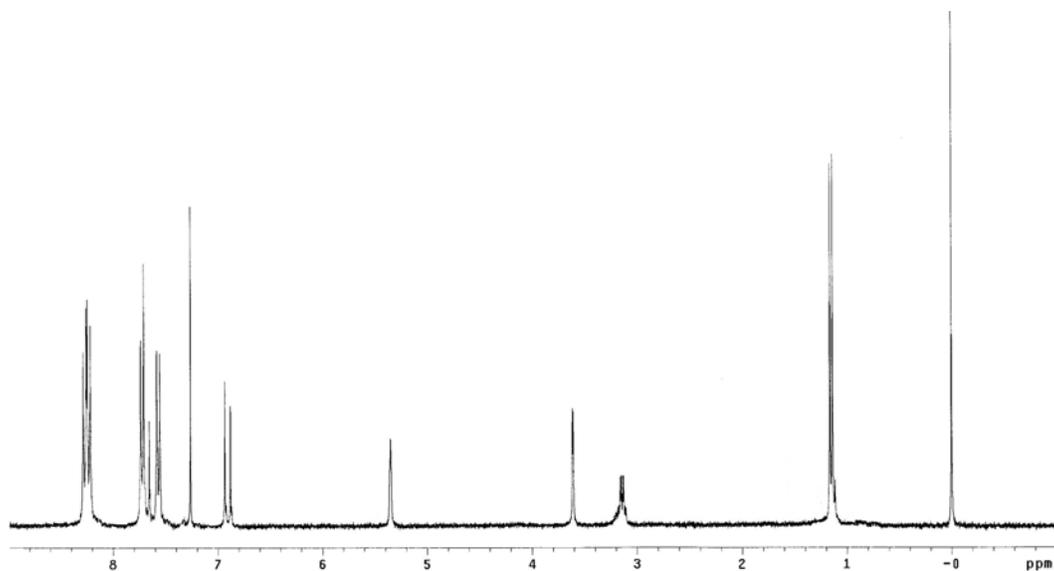
HRMS Calcd. for $\text{C}_{18}\text{H}_{16}\text{NO}_6$ ($M+1$): 357.1087, Found: 357.1083.

FTIR (NaCl film): 3495, 3107, 2360, 1684, 1596, 1516, 1344, 1108, 848 cm^{-1} .

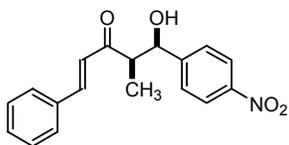
M.P.: 140-142 $^\circ\text{C}$.



(4b)



5-Hydroxy-4-methyl-5-(4-nitro-phenyl)-1-phenyl-pent-1-en-3-one (4c)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 4-nitro-benzaldehyde (75.6 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-phenyl-penta-1,4-dien-3-one (118.7 mg, 0.75 mmol, 150 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (78 mg, 0.025 mmol) as a viscous yellow oil (50 % yield).

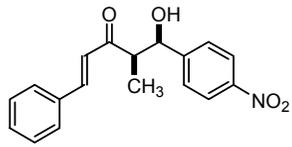
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 8.24-8.21 (m, 2H), 7.67 (d, *J* = 15.9 Hz, 1H), 7.59-7.56 (m, 4H), 7.45-7.41 (m, 3H), 6.80 (d, *J* = 15.9 Hz, 1H), 5.36-5.30 (m, 1H), 3.94 (br, 1H), 3.15 (dq, *J* = 7.5, 2.7 Hz, 1H), 1.12 (d, *J* = 7.5 Hz, 3H).

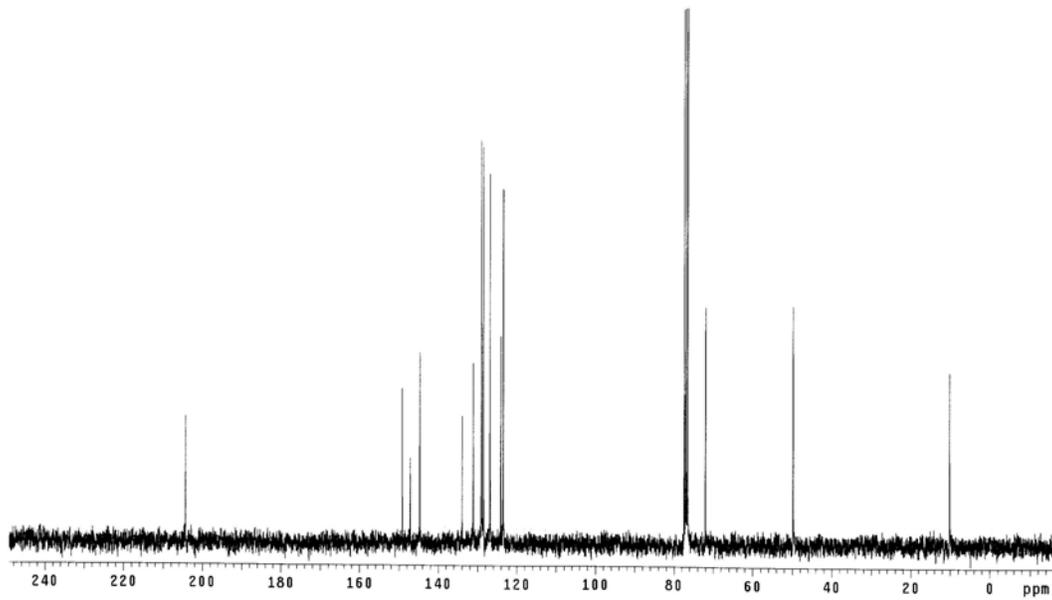
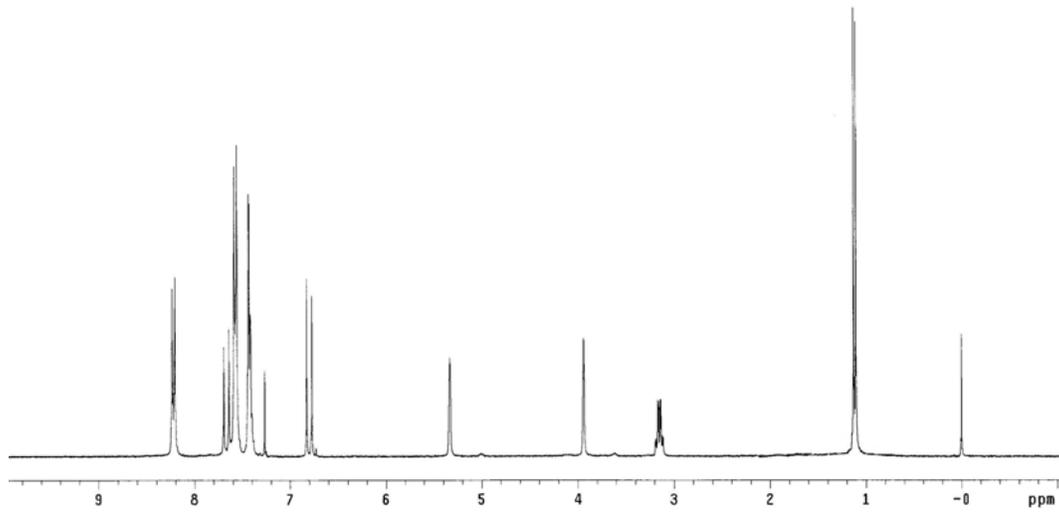
¹³C NMR (75 MHz, CDCl₃): δ 204.3, 149.2, 144.6, 133.9, 131.1, 129.0, 128.5, 126.8, 124.0, 123.4, 72.0, 49.8, 10.1.

HRMS Calcd. for C₁₈H₁₇NO₄ (M+1): 312.1236, Found: 312.1241.

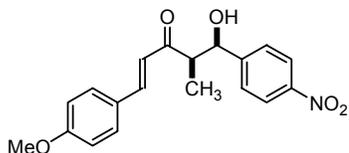
FTIR (NaCl film): 3445, 2941, 1678, 1603, 1575, 1517, 1449, 1345, 1184, 1107, 1051, 982, 852, 764, 707 cm⁻¹.



(4c)



5-Hydroxy-1-(4-methoxy-phenyl)-4-methyl-5-(4-nitro-phenyl)-pent-1-en-3-one (4d)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 4-nitro-benzaldehyde (75.6 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-methoxy-phenyl)-penta-1,4-dien-3-one (141.2 mg, 0.75 mmol, 150 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (110 mg, 0.32 mmol) as a white solid (64 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/3).

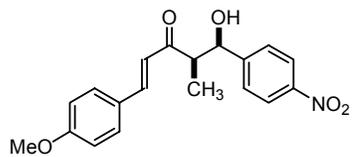
¹H NMR (300 MHz, CDCl₃): δ 8.23-8.20 (m, 2H), 7.63 (d, *J* = 15.9 Hz, 1H), 7.59-7.52 (m, 4H), 6.95-6.92 (m, 2H), 6.67 (d, *J* = 15.9 Hz, 1H), 5.34-5.30 (m, 1H), 4.08 (br, 1H), 3.86 (s, 3H), 3.12 (dq, *J* = 7.5, 2.7 Hz, 1H), 1.10 (d, *J* = 7.5 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 204.3, 162.1, 149.3, 147.0, 144.5, 130.4, 126.8, 126.5, 123.4, 121.7, 114.5, 72.1, 55.4, 49.5, 10.2.

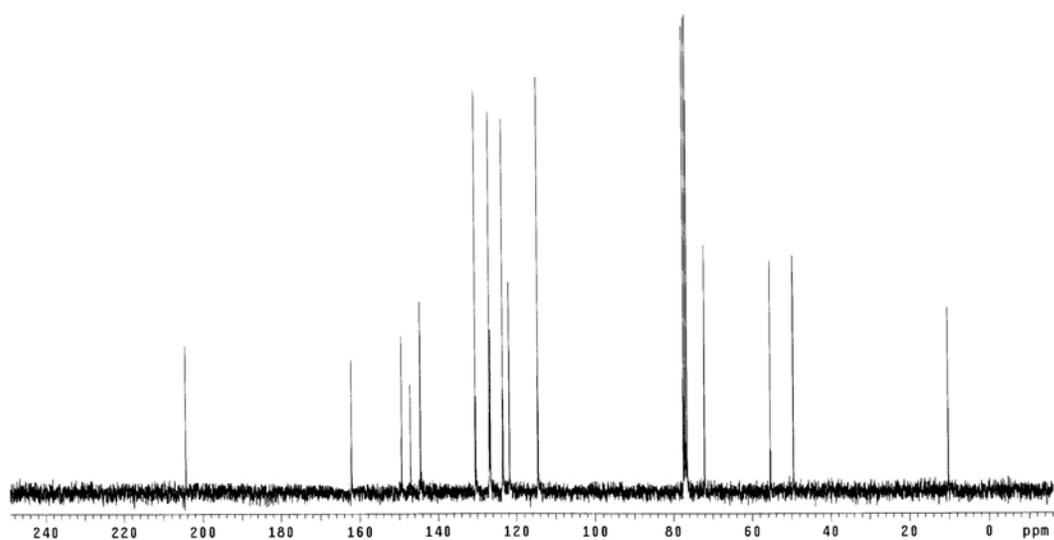
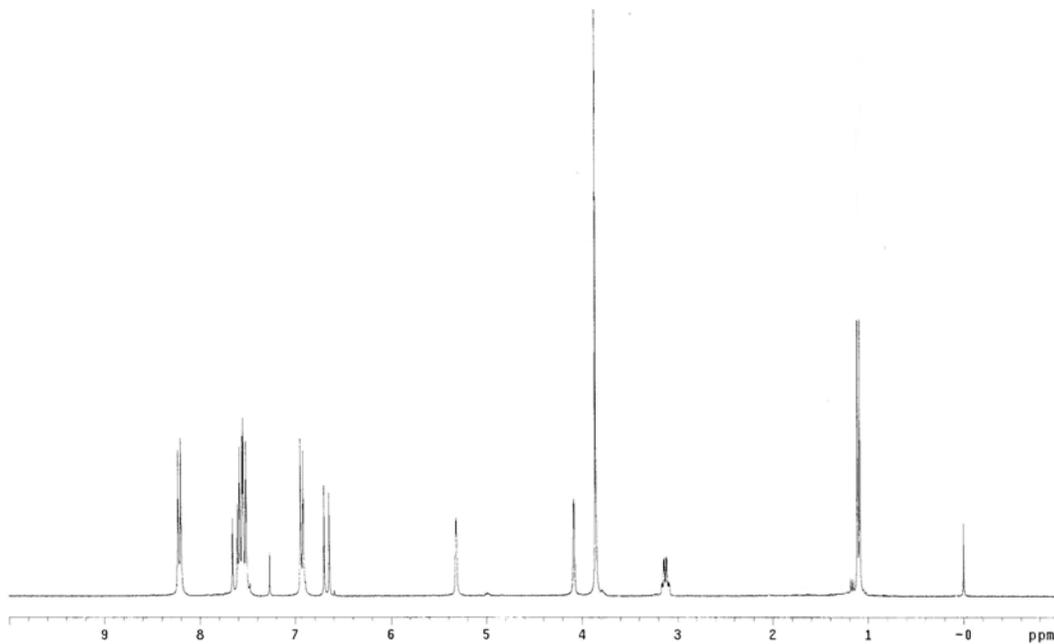
HRMS Calcd. for C₁₉H₁₉NO₅ (M+1): 342.1341, Found: 342.1344.

FTIR (NaCl film): 3448, 2935, 1596, 1571, 1511, 1458, 1422, 1345, 1255, 1172, 1108, 1028, 984, 853, 828, 705 cm⁻¹.

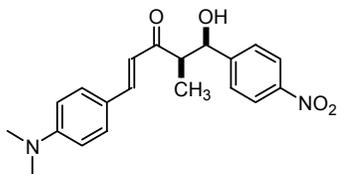
M.P.: 98-90 °C.



(4d)



1-(4-Dimethylamino-phenyl)-5-hydroxy-4-methyl-5-(4-nitro-phenyl)-pent-1-en-3-one (4e, 5a)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 4-nitro-benzaldehyde (75.6 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-dimethylamino-phenyl)-penta-1,4-dien-3-one (150.9 mg, 0.75 mmol, 150 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (164 mg, 0.46 mmol) as a yellow solid (93 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/3).

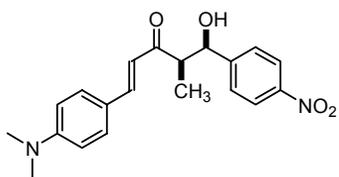
¹H NMR (300 MHz, CDCl₃): δ 8.24-8.21 (m, 2H), 7.63 (d, *J* = 15.9 Hz, 1H), 7.59-7.56 (m, 2H), 7.49-7.46 (m, 2H), 6.58 (d, *J* = 15.9 Hz, 1H), 5.24-5.26 (m, 1H), 4.34 (br, 1H), 3.12 (dd, *J* = 7.5, 2.7 Hz 1H), 3.06 (s, 6H), 1.08 (d, *J* = 7.5 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 204.3, 152.3, 149.5, 146.6, 130.6, 126.8, 123.3, 121.3, 118.6, 111.7, 72.2, 48.9, 39.9, 10.4.

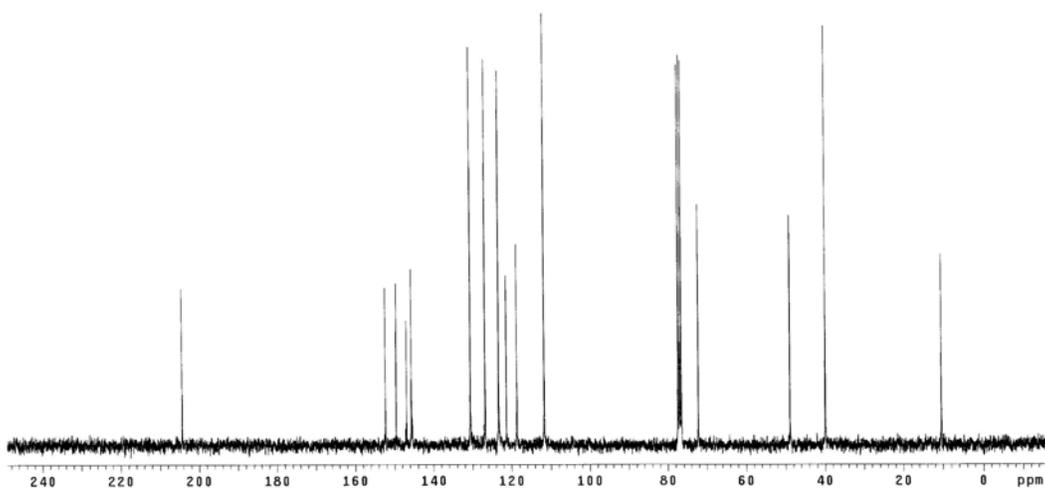
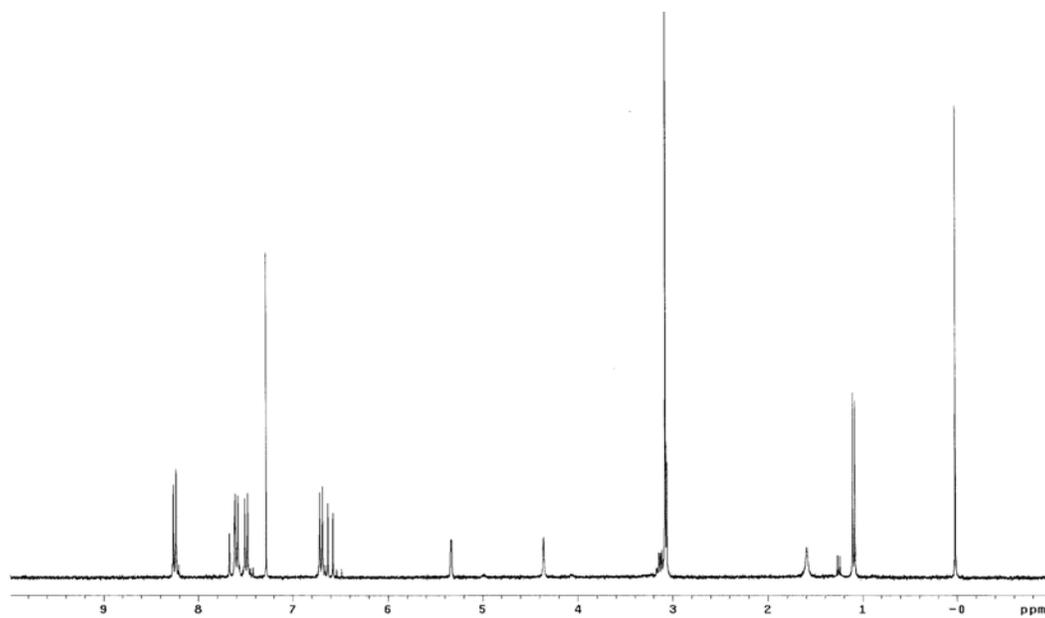
HRMS Calcd. for C₂₀H₂₂N₂O₄ (M): 354.1580, Found: 354.1581.

FTIR (NaCl film): 3421, 2916, 1574, 1523, 1434, 1369, 1344, 1182, 1052, 853, 815 cm⁻¹.

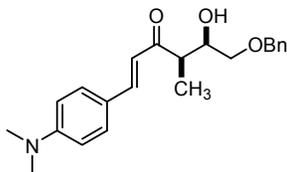
M.P.: 114-116 °C.



(4c, 5a)



6-Benzyloxy-1-(4-dimethylamino-phenyl)-5-hydroxy-4-methyl-hex-1-en-3-one (5b)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), benzyloxy-acetaldehyde (75.1 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-dimethylamino-phenyl)-penta-1,4-dien-3-one (201.3 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (159 mg, 0.45 mmol) as a viscous yellow oil (90 % yield).

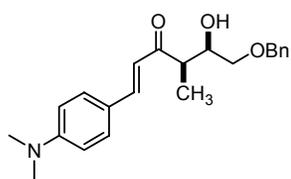
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 7.57 (d, *J* = 15.9 Hz, 1H), 7.46-7.43 (m, 2H), 7.33-7.26 (m, 5H), 6.68-6.65 (m, 2H), 6.58 (d, *J* = 15.9 Hz, 1H), 4.53 (s, 2H), 4.19-4.10 (m, 1H), 3.58-3.46 (m, 2H), 3.14-2.98 (m, 8H), 1.23 (d, *J* = 6.9 Hz, 3H).

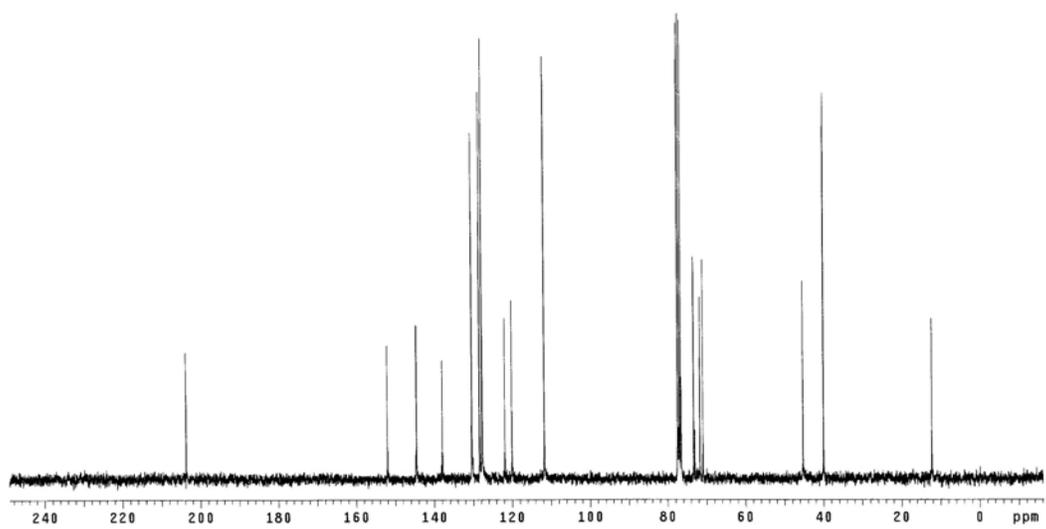
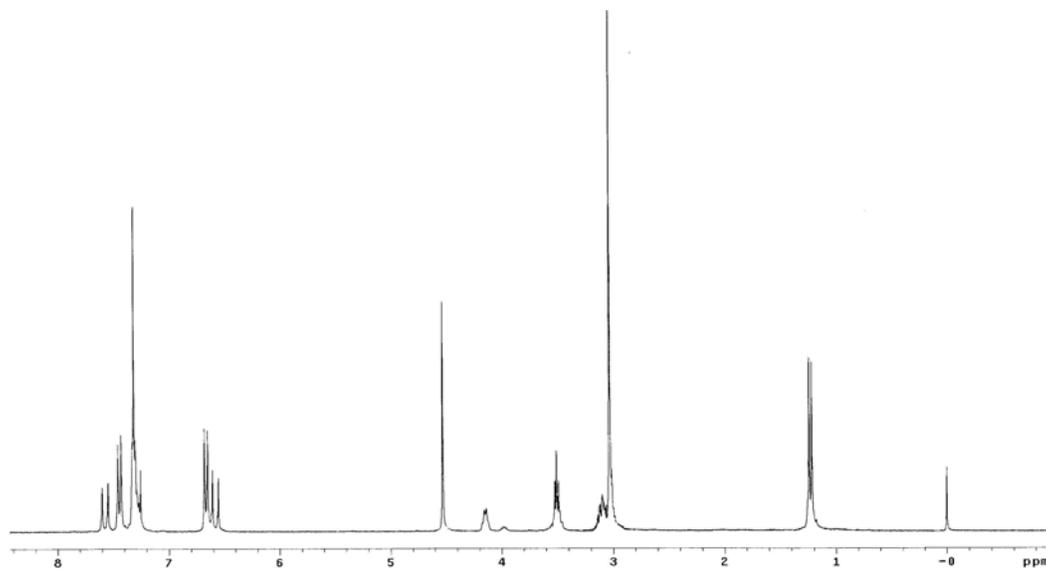
¹³C NMR (75 MHz, CDCl₃): δ 203.7, 152.0, 144.5, 137.9, 130.3, 128.3, 127.7, 127.6, 121.8, 120.0, 111.7, 73.3, 71.7, 70.9, 45.3, 40.0, 12.2.

HRMS Calcd. for C₂₂H₂₇NO₃ (M+1): 354.2069, Found: 354.2067.

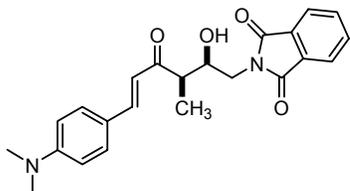
FTIR (NaCl film): 3454, 2921, 1579, 1525, 1433, 1365, 1227, 1182, 1063, 984, 945, 815, 737, 698 cm⁻¹.



(5b)



2-[6-(4-Dimethylamino-phenyl)-2-hydroxy-3-methyl-4-oxo-hex-5-enyl]-isoindole-1,3-dione (5c)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), (1,3-dioxo-1,3-dihydro-isoindol-2-yl)-acetaldehyde (94.6 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-dimethylamino-phenyl)-penta-1,4-dien-3-one (201.3 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (158 mg, 0.40 mmol) as a yellow solid (81 % yield).

TLC: R_f 0.5 (EtOAc/hexane, 1/1).

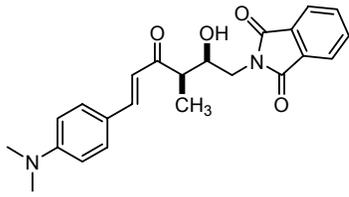
¹H NMR (300 MHz, CDCl₃): δ 7.86-7.83 (m, 2H), 7.72-7.69 (m, 2H), 7.56 (d, *J* = 15.6 Hz, 1H), 7.45-7.42 (m, 2H), 6.69-6.64 (m, 2H), 6.58 (d, *J* = 15.6 Hz, 1H), 4.36-4.31 (m, 1H), 3.91 (dd, *J* = 14.1, 8.1 Hz, 1H), 3.55 (dd, *J* = 14.1, 4.5 Hz, 1H), 3.53 (br, 1H), 3.03 (s, 6H), 3.03-2.90 (m, 1H), 1.36 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 203.3, 168.4, 152.0, 144.8, 133.9, 131.8, 130.3, 123.2, 121.6, 119.1, 111.6, 69.5, 46.0, 41.3, 39.9, 11.2.

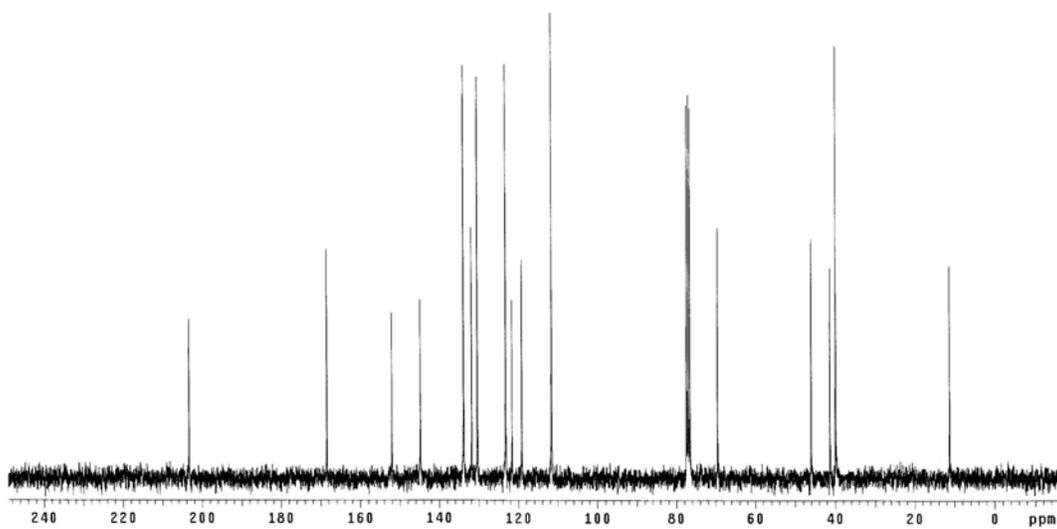
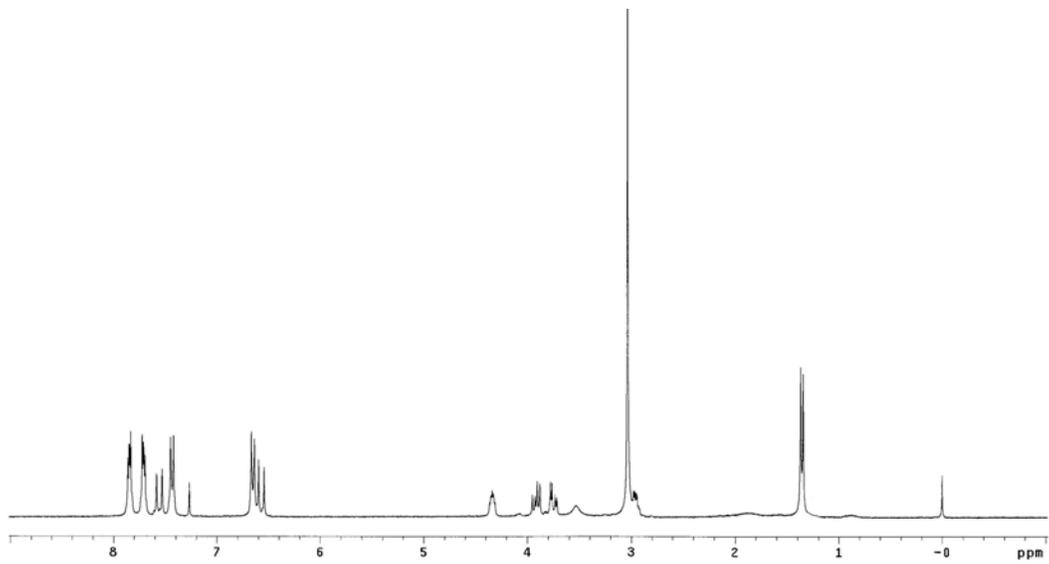
HRMS Calcd. for C₂₃H₂₄N₂O₄ (M+1): 393.1814, Found: 393.1810.

FTIR (NaCl film): 3463, 2922, 2368, 1710, 1577, 1524, 1432, 1394, 1366, 1183, 1033, 816, 714 cm⁻¹.

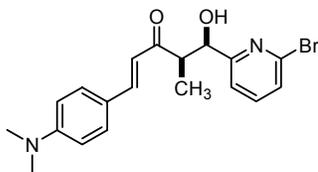
M.P.: 154-156 °C.



(5c)



5-(6-Bromo-pyridin-2-yl)-1-(4-dimethylamino-phenyl)-5-hydroxy-4-methyl-pent-1-en-3-one (5d)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 6-bromo-pyridine-2-carbaldehyde (93.0 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-dimethylamino-phenyl)-penta-1,4-dien-3-one (150.9 mg, 0.75 mmol, 150 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 12 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (169 mg, 0.43 mmol) as a yellow solid (87 % yield).

TLC: R_f 0.3 (EtOAc/hexane, 1/3).

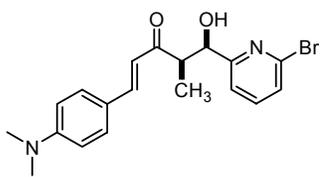
¹H NMR (300 MHz, CDCl₃): δ 7.62 (d, *J* = 15.9 Hz, 1H), 7.56-7.34 (m, 5H), 6.69-6.66 (m, 2H), 6.60 (d, *J* = 15.9 Hz, 1H), 5.19 (d, *J* = 3.0 Hz, 1H), 4.33 (br, 1H), 3.52 (dq, *J* = 7.2, 3.0 Hz, 1H), 3.04 (s, 6H), 1.05 (d, *J* = 7.2 Hz, 3H).

¹³C NMR (75 MHz, CDCl₃): δ 204.7, 162.8, 152.1, 145.2, 140.9, 138.7, 130.4, 126.2, 121.6, 119.2, 111.6, 73.2, 47.5, 39.9, 10.7.

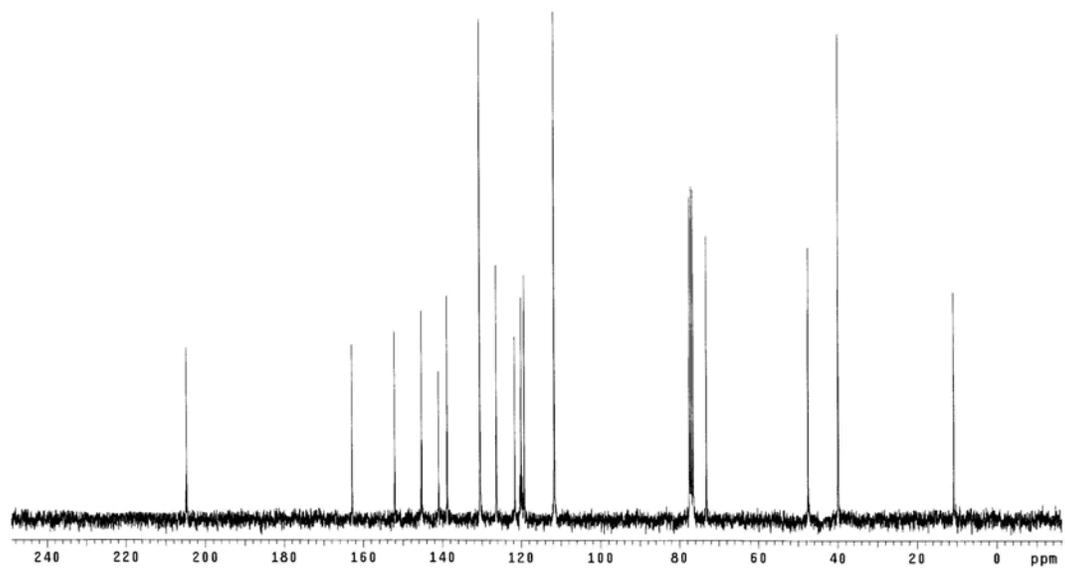
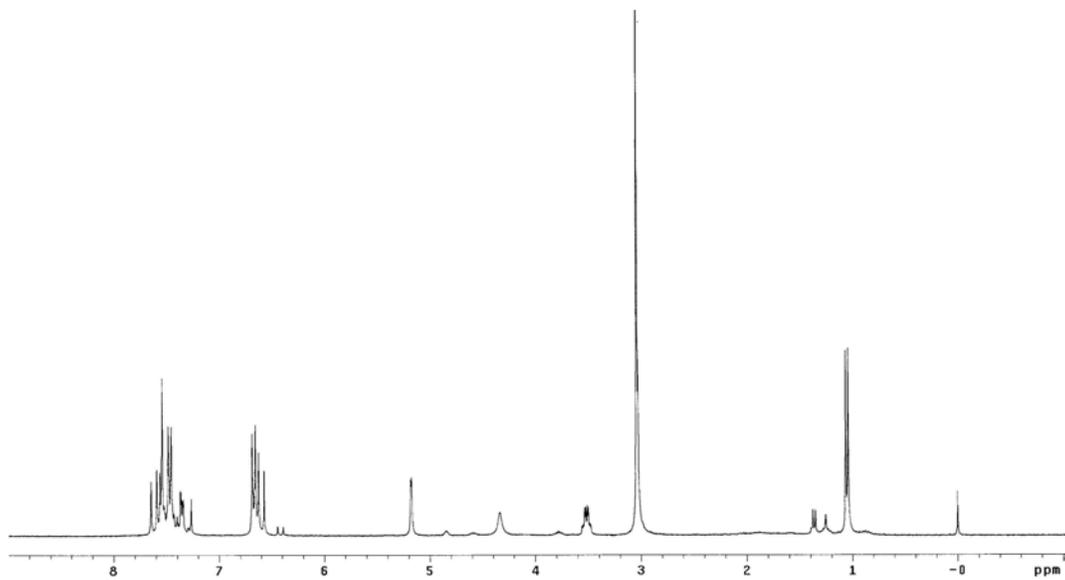
HRMS Calcd. for C₁₉H₂₁BrN₂O₂ (M+1): 389.0865, Found: 389.0865.

FTIR (NaCl film): 3425, 2917, 2360, 1597, 1524, 1434, 1366, 1182, 1052, 985, 945, 813 cm⁻¹.

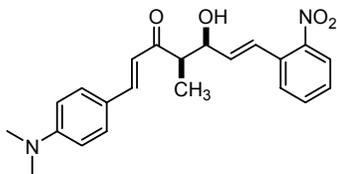
M.P.: 125-127 °C.



(5d)



1-(4-Dimethylamino-phenyl)-5-hydroxy-4-methyl-7-(2-nitro-phenyl)-hepta-1,6-dien-3-one (5e)



To a 13 mm × 100 mm test-tube were added Li₂CO₃ (3.9 mg, 0.05 mmol, 10 mol%), (2-Fur)₃P (13.9 mg, 0.06 mmol, 12 mol%), Rh(COD)₂SbF₆ (13.9 mg, 0.025 mmol, 5 mol%), 3-(2-nitro-phenyl)-propenal (88.6 mg, 0.5 mmol, 100 mol%) and CH₂Cl₂ (0.5 mL, 1.0 M). The test-tube was sealed and the reaction system was purged with Ar(g) and H₂(g) for 20 seconds each. The reaction system was placed under one atmosphere of hydrogen using a balloon and 1-(4-dimethylamino-phenyl)-penta-1,4-dien-3-one (201.3 mg, 1.0 mmol, 200 mol%) was added to the reaction mixture. The reaction mixture was allowed to stir at ambient temperature for 18 hours, at which point the reaction mixture was directly deposited onto a column of silica and purified chromatographically (SiO₂: EtOAc/hexane) to afford the title compound (136 mg, 0.35 mmol) as a red oil (71 % yield).

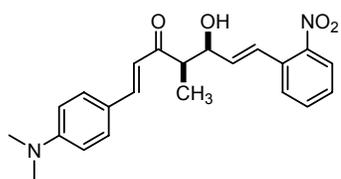
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 7.91-7.89 (m, 1H), 7.62 (d, *J* = 15.6 Hz, 1H), 7.59-7.33 (m, 6H), 7.13 (d, *J* = 15.9 Hz, 1H), 6.68-6.64 (m, 2H), 6.62 (d, *J* = 15.6 Hz, 1H), 6.21 (dd, *J* = 15.9, 5.7 Hz, 1H), 4.75 (dd, *J* = 5.7, 3.3 Hz, 1H), 3.10 (dq, *J* = 15.6, 3.3 Hz, 1H), 3.03 (s, 6H), 3.03-3.00 (br, 1H), 1.29 (d, *J* = 7.2 Hz, 3H).

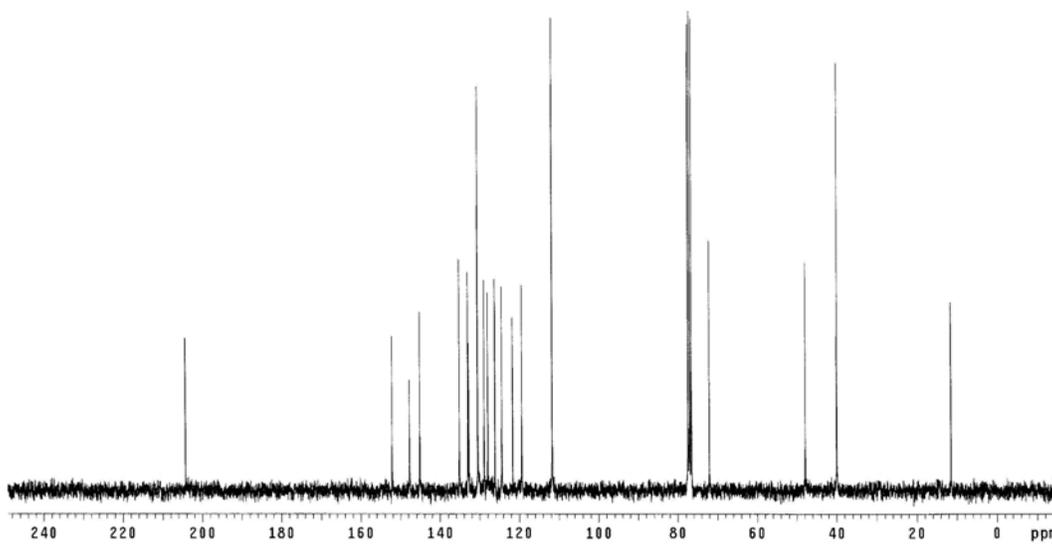
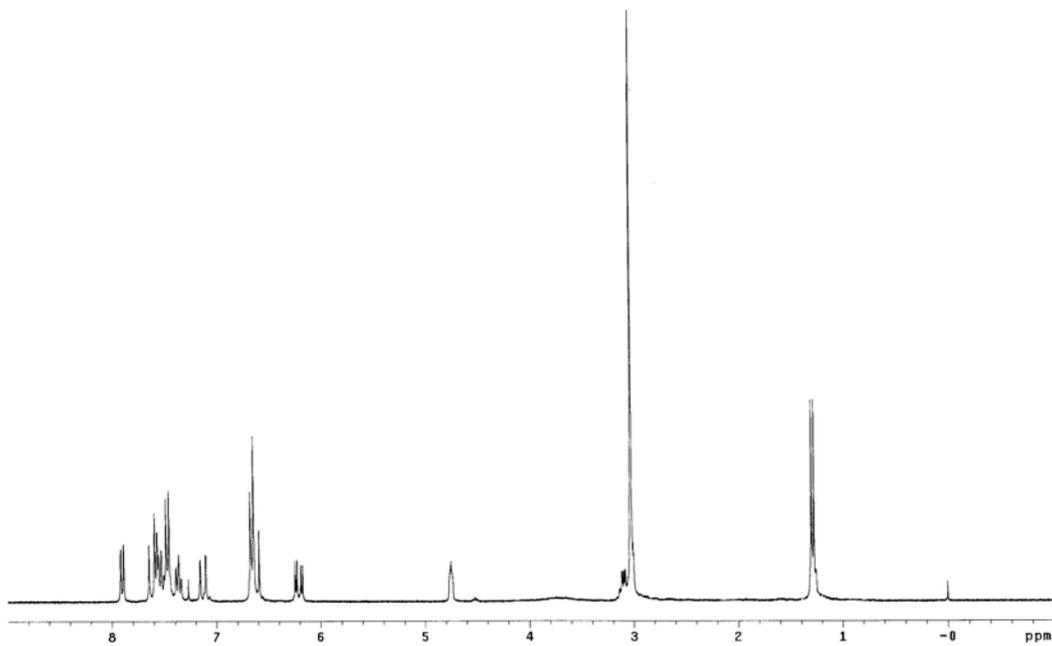
¹³C NMR (75 MHz, CDCl₃): δ 204.2, 152.1, 147.7, 145.1, 135.1, 133.0, 132.7, 130.5, 128.8, 127.9, 126.1, 124.3, 121.6, 119.3, 111.7, 72.1, 47.9, 40.0, 11.4.

HRMS Calcd. for C₂₂H₂₄N₂O₄ (M+1): 381.1814 ; Found: 381.1812

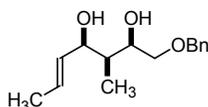
FTIR (NaCl film): 3424, 2926, 2359, 1577, 1523, 1434, 1344, 1182, 1168, 1053, 970, 946, 860, 815, 742 cm⁻¹.



(5e)



1-Benzyloxy-3-methyl-hept-5-ene-2,4-diol (**6a**)



A solution of Et₃B (1.0M in hexane, 0.46 mL, 0.46 mmol, 119 mol%) was added to a mixture of dry THF (1.5 mL) and MeOH (0.6 mL) at ambient temperature under nitrogen. After 1 hour, the mixture was cooled to -78 °C followed by the enone **3b** (96 mg, 0.39 mmol, 100 mol%) in THF (0.5 mL). The resulting solution was stirred for 1 hour. Then NaBH₄ (18 mg, 0.46 mmol, 120 mol%) was added, and the mixture was stirred for 5 hours. The reaction mixture was diluted with ether (15 mL), and treated with saturated NH₄Cl_(aq.) (15 mL). The layers were separated and the aqueous layer was extracted with ether (3x25 mL). The combined organic extracts were dried (MgSO₄) and concentrated. The residue was azeotroped a few times with MeOH until boron-containing compounds were removed. Flash chromatography (SiO₂: EtOAc/hexane) afforded the title compound (96 mg, 0.38 mmol) as colorless oil (98 % yield).

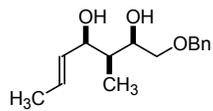
TLC: R_f 0.4 (EtOAc/hexane, 1/2).

¹H NMR (300 MHz, CDCl₃): δ 7.38-7.26 (m, 5H), 5.74 (ddq, *J* = 15.3, 6.3, 1.2 Hz, 1H), 5.51 (ddq, *J* = 15.3, 6.0, 1.5 Hz, 1H), 4.55 (d, *J* = 1.2, 2H), 4.34-4.26 (m, 1H), 4.10-4.02 (m, 1H), 3.54-3.44 (m, 2H), 2.85 (br, 1H), 2.62 (br, 1H) 1.70 (dd, *J* = 6.3, 1.5 Hz, 3H), 1.69-1.63 (m, 1H), 0.92 (d, *J* = 7.2 Hz, 3H).

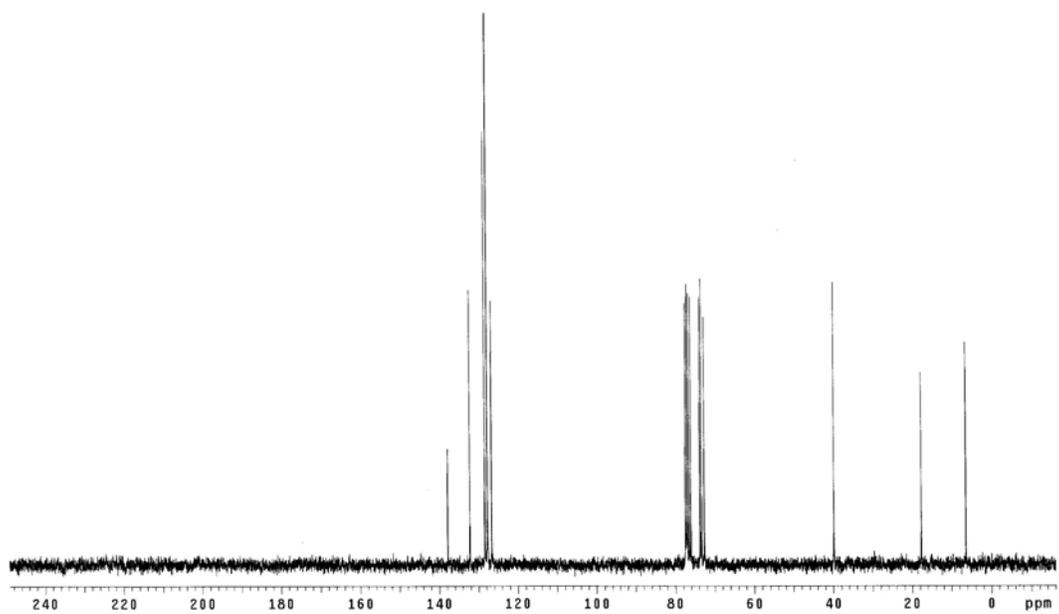
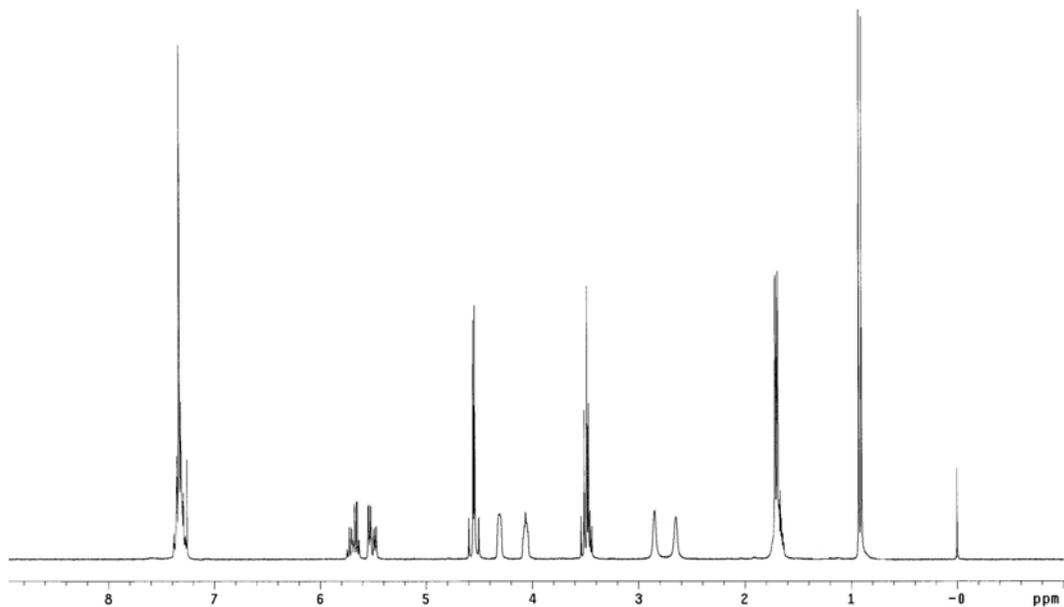
¹³C NMR (75 MHz, CDCl₃): δ 137.8, 132.2, 128.4, 127.7, 126.6, 76.1, 73.7, 73.4, 72.7, 39.9, 17.7, 6.4.

HRMS Calcd. for C₁₅H₂₂O₃ (M+1): 251.1647, Found: 251.1648.

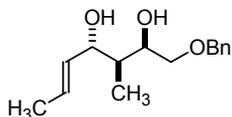
FTIR (NaCl film): 3395, 3029, 2968, 2914, 2858, 1670, 1496, 1453, 1377, 1253, 1094, 966, 736, 698 cm⁻¹.



(6a)



1-Benzyloxy-3-methyl-hept-5-ene-2,4-diol (**6b**)



A solution of $\text{Me}_4\text{NBH}(\text{OAc})_3$ (530 mg, 2.02 mmol, 1010 mol%) in AcOH (2.5 mL) and MeCN (2.5 mL) was prepared under Ar and stirred at ambient temperature for 20 min. The mixture was cooled to $-30\text{ }^\circ\text{C}$. A solution of the enone **3b** (50 mg, 0.20 mmol, 100 mol%) in MeCN (2.5 mL) at $0\text{ }^\circ\text{C}$ was added dropwise via cannular over 10 min. The resulting mixture was allowed to warm to $-20\text{ }^\circ\text{C}$ and stirred for 24 hours. CH_2Cl_2 was added to the reaction mixture, and then a saturated aqueous NaHCO_3 solution was slowly added. After 45 min at ambient temperature, the aqueous phase was extracted with CH_2Cl_2 (3 times), The organic phases were dried (MgSO_4), filtered, and evaporated, and the residue was purified by flash chromatography (SiO_2 : EtOAc/hexane) to afford the title compound (47 mg, 19 μmol) as a colorless oil (94 % yield).

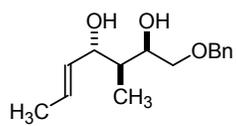
TLC: R_f 0.4 (EtOAc/hexane, 1/2).

$^1\text{H NMR}$ (300 MHz, CDCl_3): δ 7.38-7.27 (m, 5H), 5.68 (ddq, $J = 15.3, 6.3, 1.3$ Hz, 1H), 5.45 (ddq, $J = 15.3, 7.8, 1.5$ Hz, 1H), 4.57 (d, $J = 5.4$, 2H), 4.10-4.04 (m, 1H), 3.63 (dd, $J = 9.6, 2.7$ Hz, 1H), 3.46 (dd, $J = 9.3, 7.2$ Hz, 1H), 3.28 (br, 2H), 1.74-1.68 (m, 1H), 1.71 (dd, $J = 6.3, 1.5$ Hz, 3H), 0.77 (d, $J = 6.9$ Hz, 3H).

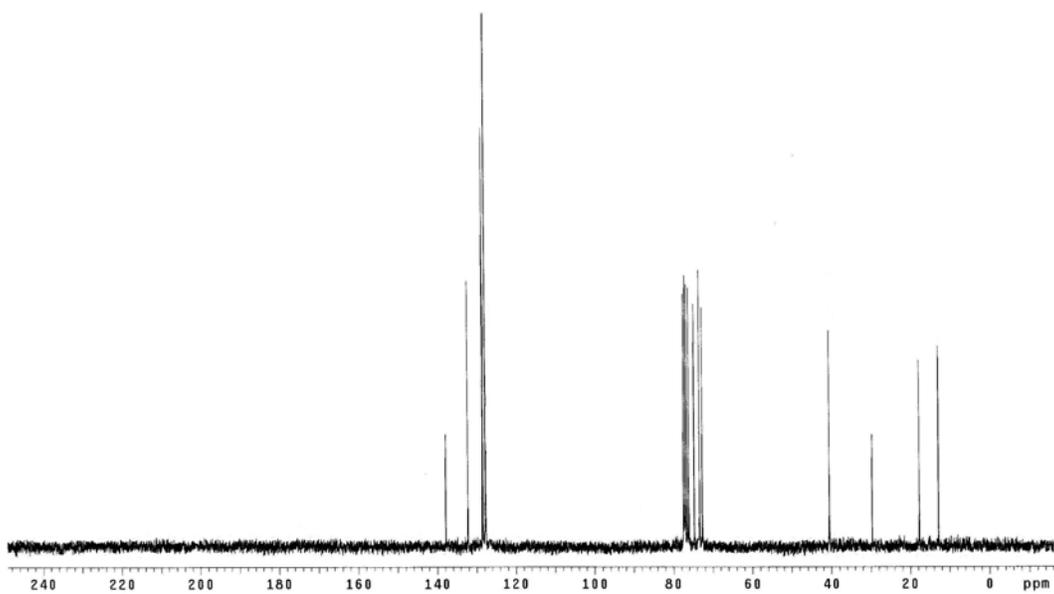
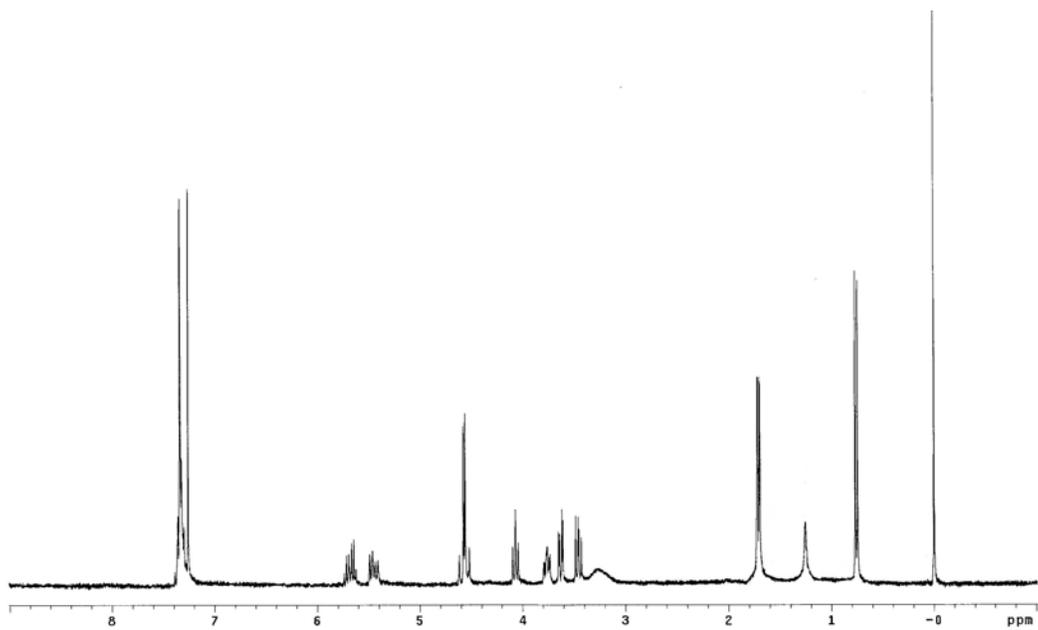
$^{13}\text{C NMR}$ (75 MHz, CDCl_3): δ 137.8, 132.3, 128.6, 128.5, 127.8, 127.7, 75.0, 73.4, 72.7, 41.0, 29.7, 17.7, 12.8.

HRMS Calcd. for $\text{C}_{15}\text{H}_{22}\text{O}_3$ ($M+1$): 251.1647, Found: 251.1648.

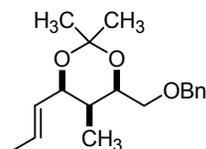
FTIR (NaCl film): 3385, 3029, 2918, 1720, 1496, 1453, 1376, 1326, 1101, 1005, 968, 927, 738, 698 cm^{-1} .



(6b)



4-Benzyloxymethyl-2,2,5-trimethyl-6-propenyl-[1,3]dioxane



To a solution of 1-benzyloxy-3-methyl-hept-5-ene-2,4-diol **6a** (54 mg, 0.22 mmol, 100 mol%) in 2,2-dimethoxypropane (5 mL) at 0 °C was added *p*-TsOH•H₂O (2 mg, 0.01 mmol, 5 mol%). After 3 hours at ambient temperature, the reaction mixture was quenched with saturated NaHCO_{3(aq.)}, extracted with EtOAc (3 times), The organic phases were dried (MgSO₄), filtered, and evaporated, and the residue was purified by flash chromatography (SiO₂: EtOAc/hexane) to afford the title compound (58 mg, 0.20 mmol) as a colorless oil (91 % yield).

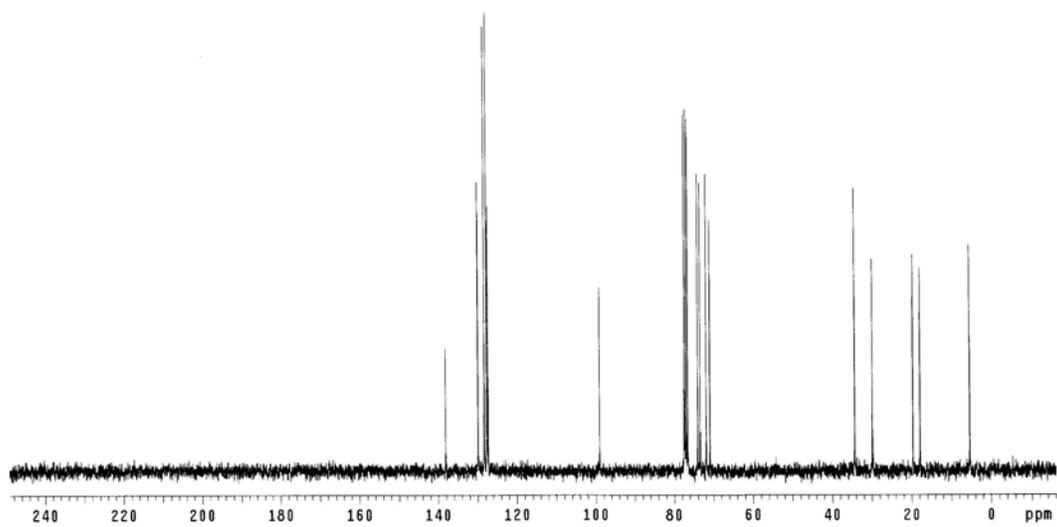
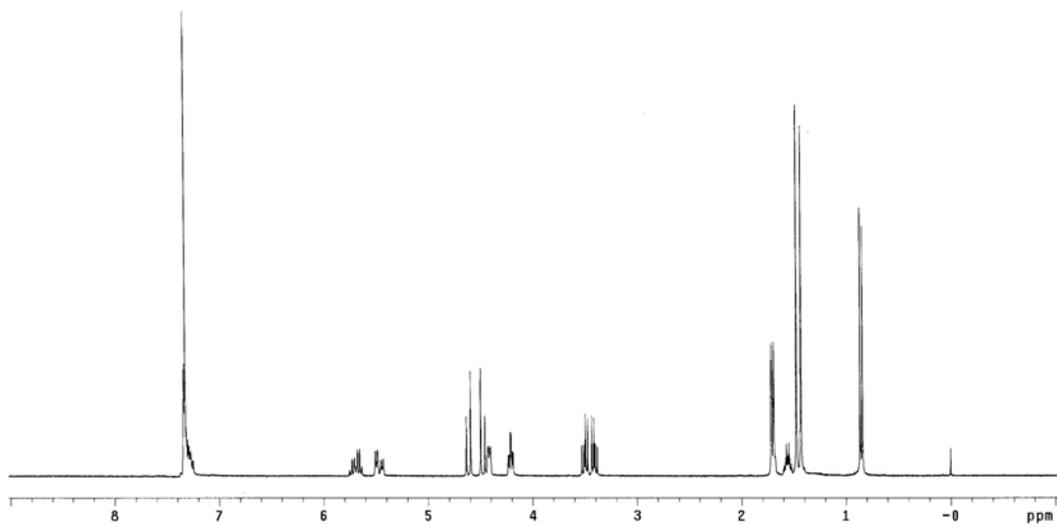
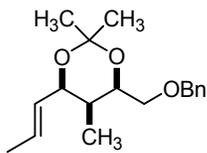
TLC: R_f 0.6 (EtOAc/hexane, 1/10).

¹H NMR (300 MHz, CDCl₃): δ 7.35-7.26 (m, 5H), 5.70 (ddq, *J* = 15.3, 6.6, 1.2 Hz, 1H), 5.47 (ddq, *J* = 15.3, 6.3, 1.5 Hz, 1H), 4.62 (d, *J* = 12, 1H), 4.48 (d, *J* = 12, 1H), 4.42 (ddd, *J* = 6.3, 5.7, 1.2, 1H), 4.21 (ddd, *J* = 6.6, 6.3, 2.4, 1H), 3.50 (dd, *J* = 9.9, 6.6, 1H), 3.41 (2.85 (dd, *J* = 9.9, 6.3, 1H), 1.71 (dd, *J* = 6.6, 1.5 Hz, 3H), 1.59-1.48 (m, 1H), 1.48 (s, 3H), 1.43 (s, 3H), 0.92 (d, *J* = 7.2 Hz, 3H).

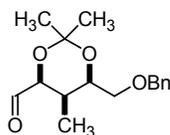
¹³C NMR (75 MHz, CDCl₃): δ 138.1, 129.9, 128.3, 127.7, 127.6, 127.3, 99.0, 74.0, 73.4, 71.8, 70.9, 34.3, 29.9, 19.6, 17.8, 5.4.

HRMS Calcd. for C₁₈H₂₆O₃ (M+1): 291.1960, Found: 291.1962.

FTIR (NaCl film): 2989, 2936, 1453, 1379, 1254, 1199, 1176, 1103, 1075, 1012, 967, 938, 735, 697 cm⁻¹.



6-Benzyloxymethyl-2,2,5-trimethyl-[1,3]dioxane-4-carbaldehyde (6c)



A solution of 4-benzyloxymethyl-2,2,5-trimethyl-6-propenyl-[1,3]dioxane (47 mg, 0.16 mmol, 100 mol%) in CH₂Cl₂ (30 mL) at -78 °C was bubbled with O₃ until blue color persisted. N₂ was bubbled for 10 min and PPh₃ (47 mg, 0.18 mmol, 113 mol%) was added to the reaction mixture, and stirred the reaction mixture overnight at ambient temperature. The reaction mixture was evaporated, and the residue was purified by flash chromatography (SiO₂: EtOAc/hexane) to afford the title compound (33 mg, 0.12 mmol) as a colorless oil (74 % yield).

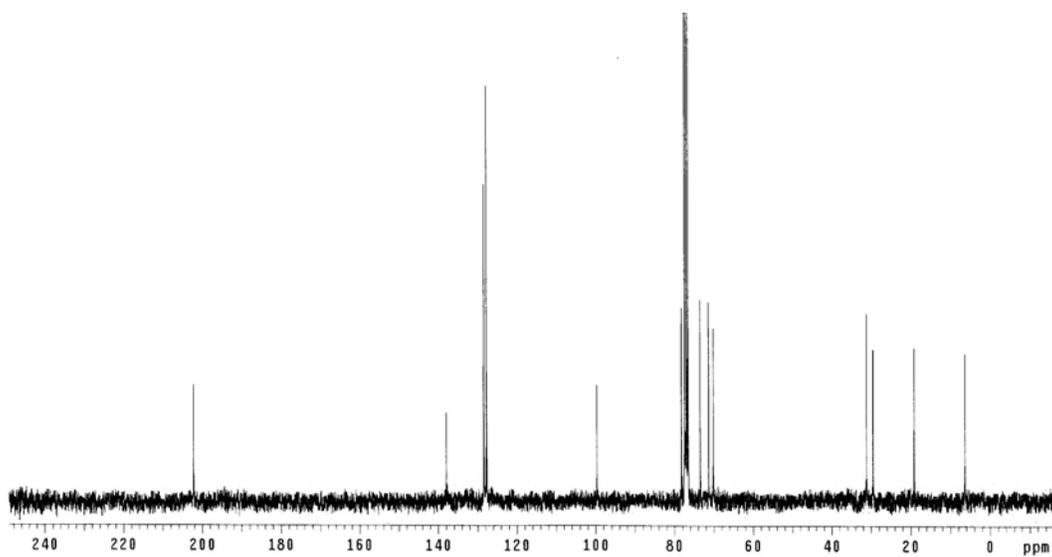
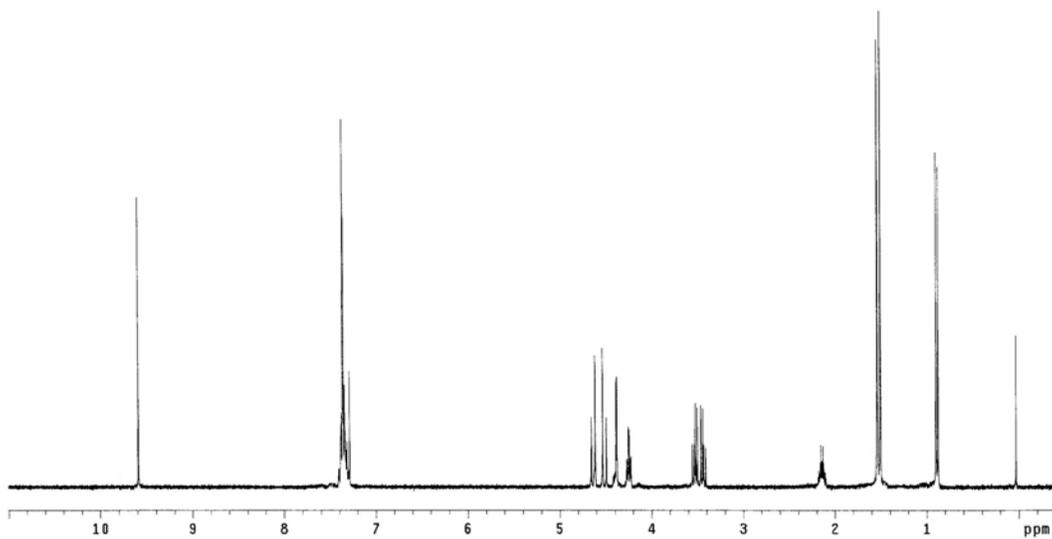
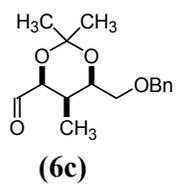
TLC: R_f 0.2 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 9.59 (s, 1H), 7.38-7.29 (m, 5H), 4.63 (d, *J* = 12.0 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.38 (d, *J* = 3.0 Hz, 1H), 4.25 (ddd, *J* = 6.6, 6.3, 2.4 Hz, 1H), 3.53 (dd, *J* = 9.6, 6.3 Hz, 1H), 3.44 (dd, *J* = 9.6, 6.6 Hz, 1H), 2.14 (ddq, *J* = 6.6, 3.0, 2.4 Hz, 1H), 1.54 (s, 3H), 1.50 (s, 3H), 0.89 (d, *J* = 6.6 Hz, 3H).

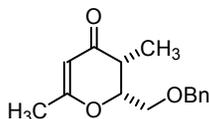
¹³C NMR (75 MHz, CDCl₃): δ 202.2, 137.9, 128.4, 127.7, 99.7, 78.2, 73.5, 71.3, 70.1, 31.2, 29.5, 19.1, 6.3.

HRMS Calcd. for C₁₆H₂₂O₄ (M+1): 279.1596, Found: 279.1598.

FTIR (NaCl film): 3454, 2933, 2869, 2359, 1720, 1626, 1453, 1374, 1274, 1201, 1099, 739, 698.



2-Benzyloxymethyl-3,6-dimethyl-2,3-dihydro-pyran-4-one (6d)



A 25 mL Schlenk tube was charged with PdCl₂ (7 mg, 0.04 mmol, 10 mol%), CuCl (4 mg, 0.04 mmol, 10 mol%), and Na₂HPO₄ (7 mg, 0.04 mmol, 10 mol%) and evacuated and backfilled with oxygen (3 times, balloon). A solution of the enone **3b** (100 mg, 0.40 mmol, 100 mol%) in DME (3 mL) was added via cannula. The resulting mixture was heated to 50 °C and allowed to stir at this temperature for 12 hours. The reaction mixture was allowed to cool to ambient temperature, diluted with Et₂O and filtered through a pad of silica, and concentrated *in vacuo* to give a crude residue that was further purified by flash column chromatography (SiO₂: EtOAc/hexane) to afford the title compound (70 mg, 0.28 mmol) as a colorless oil (71 % yield).

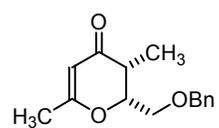
TLC: R_f 0.3 (EtOAc/hexane, 1/3).

¹H NMR (300 MHz, CDCl₃): δ 7.37-7.30 (m, 5H), 5.26 (s, 1H), 4.66-4.53 (m, 3H), 3.61 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.79 (dd, *J* = 10.5, 7.2 Hz, 1H), 2.41 (dq, *J* = 7.2, 3.6 Hz, 1H), 2.02 (s, 3H), 1.03 (d, *J* = 7.2 Hz, 3H).

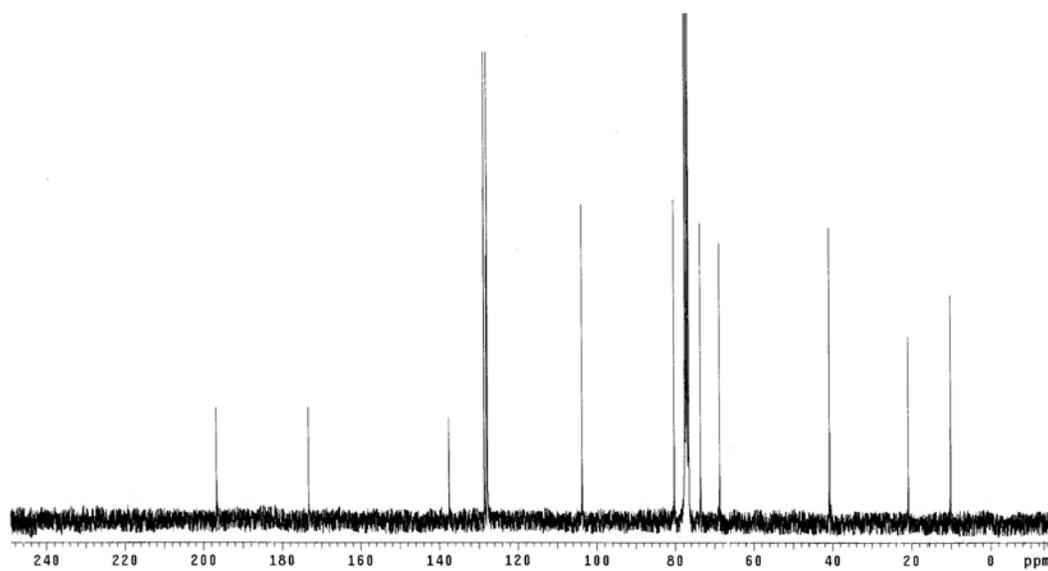
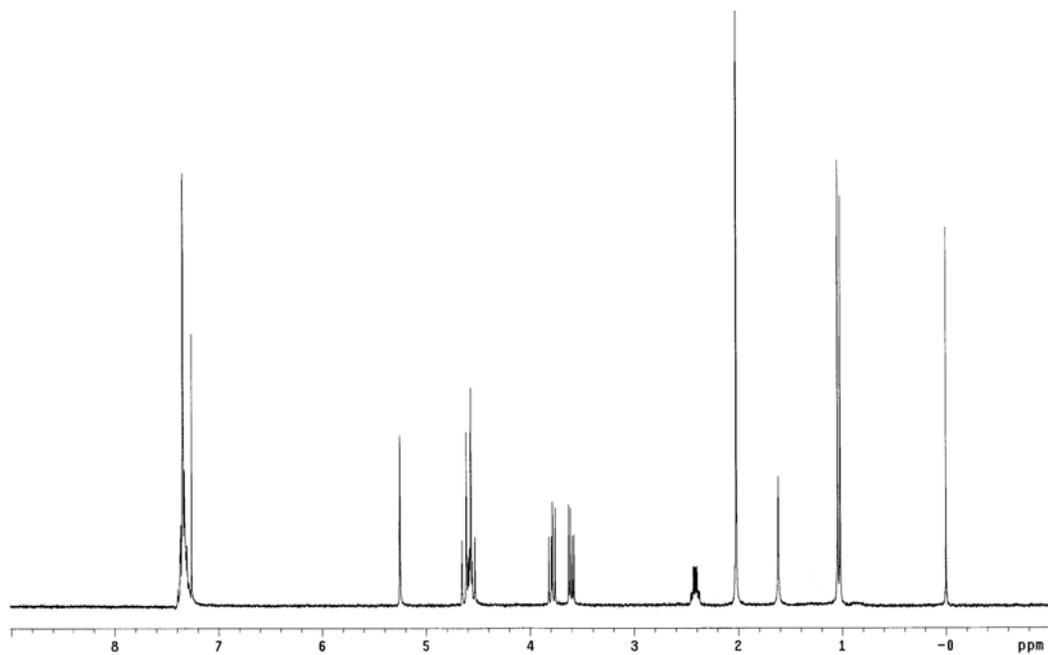
¹³C NMR (75 MHz, CDCl₃): δ 196.6, 173.3, 137.5, 128.5, 127.9, 127.7, 103.7, 80.2, 73.5, 68.7, 40.8, 20.8, 10.0.

HRMS Calcd. for C₁₅H₁₈O₈ (M+1): 247.1344, Found: 247.1346.

FTIR (NaCl film): 2919, 2360, 1668, 1610, 1453, 1393, 1337, 1240, 1175, 1090, 970, 827, 739, 697 cm⁻¹.



(6d)



III. References

- [1] RajanBabu, T. V.; Ayers, T. A.; Halliday, G. A.; You, K. K.; Calabrese, J. C. *J. Org. Chem.* **1997**, *62*, 6012.
- [2] (a) Brookhart, M.; Grant, B.; Volpe, A. F. Jr. *Organometallics* **1992**, *11*, 3920. (b) Reger, D. L.; Wright, T. D.; Little, C. A.; Lamba, J. J. S.; Smith, M. D. *Inorg. Chem.* **2001**, *40*, 3810. (c) Guzel, B.; Omary, M. A.; Fackler, J. P. Jr.; Akgerman, A. *Inorg. Chim. Acta* **2001**, *325*, 45.
- [3] Nenajdenko, V. G.; Lebedev, M. V.; Balenkova, E. S. *Tetrahedron* **2001**, *57*, 9017.
- [4] Birtwistle, D. H.; Brown, J. M.; Foxton, M. W. *Tetrahedron* **1988**, *44*, 7309.
- [5] Takaacs, J. M.; Jiang, X. T.; Leonov, A. P. *Tetrahedron Lett.* **2003**, *44*, 7075.