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Supporting Information

Dinuclear Zinc-Catalyzed Asymmetric Desymmetrization of Acyclic 2-Substituted-1,3-Propanediols: A Powerful Entry into Chiral Building Blocks

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SUPPORTING INFORMATION

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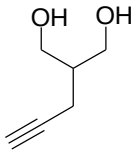
Experimental Section:

1. Preparation of 2-substituted-1,3-propanediols for desymmetrization studies:

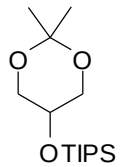
2-methylpropane-1,3-diol and 2-phenylpropane-1,3-diol are commercially available from Aldrich Chemical Company and were distilled prior to their use. 2-(benzyloxy)propane-1,3-diol is commercially available from Fluka. 2-ethyl-propane-1,3-diol **3**,[1] 2-allylpropane-1,3-diol **19**,[2] 2-benzylpropane-1,3-diol **23**, [3] 2-(4'-tolyl)propane-1,3-diol **31**, [4] 2-(4'-methoxyphenyl)propane-1,3-diol **33**,[4] 2-(4'-chlorophenyl)propane-1,3-diol **35**,[4] 2-(4'-biphenyl)propane-1,3-diol **37**,[5] 2-(1'-naphthyl)propane-1,3-diol **39**,[4] 2-(2'-naphthyl)propane-1,3-diol **41**,[4] 2-(3'-thiophene)propane-1,3-diol **43**,[4] and 2-(2'-thiophene)propane-1,3-diol **45** [4] were prepared according to literature procedures.

2-prop-2-yn-1-ylpropane-1,3-diol



Dimethyl propargylmalonate (10g, 59 mmol) was added dropwise to a suspension of lithium aluminum hydride (4.7 g, 124 mmol) in anhydrous diethyl ether (84 mL) at 0 ^{o}C. The reaction was stirred at 0 ^{o}C for 10 minutes and at room temperature for 20 hours. The reaction was quenched by adding $NaSO_4 \cdot 10H_2O$ (50g) in small portions until the mixture turned light gray. The resulting suspension was vacuum filtered, rinsed with diethyl ether, and concentrated. Flash chromatography of the resulting oil (60% ethyl acetate/hexanes→100% ethyl acetate) afforded the desired product (4.25 g, 48 %). R_f = 0.52 (100% ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$): d 3.89-3.76 (m, 4H), 2.32 (dd, *J* = 6.8, 2.7 Hz, 2H), 2.28-2.2 (m, *2*H), 2.01 (t, *J* = 2.7 Hz, 1H), 1.98 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 82.3, 70.2, 64.8, 41.5, 17.7. IR (neat): ?$_{max}$ 3299, 2933, 2886, 2116, 1648, 1637, 1467, 1431, 1187, 1099, 1031, 969, 865 cm^{-1}; Elemental Analysis: Theoretical C63.14, H8.83 Found C62.99, H8.75.

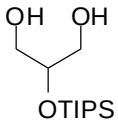
(2,2)-dimethyl-1,3-dioxan-5-yloxy)triisopropylsilane



To a solution of 5-Hydroxy-2,2-dimethyl-1,3-dioxane[6] (0.48 g, 3.65 mmol) in DMF (6 mL) was added imidazole (0.50 g, 7.31 mmol), and triisopropylsilyl chloride (0.84g , 4.38 mmol). The reaction mixture

was stirred for 12 h, quenched with saturated aqueous $NaHCO_3$, and extracted into diethyl ether (2 x 20 mL). The organic layers were combined, washed with brine, dried (Na_2SO_4), and concentrated. Silica gel chromatography of the resulting mixture using diethyl ether/hexanes mixtures afforded 0.84 g (80%) of the title compound as a clear oil. R_f = 0.78 (35 % diethyl ether/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): d 3.93 – 3.84 (m, 3H), 3.64 – 3.58 (m, 2H), 1.46 (s, 3H), 1.37 (s, 3H), 1.05 – 1.02 (m, 21H); ^{13}C NMR (125 MHz, $CDCl_3$): d 97.7, 65.7, 63.2, 27.9, 19.1, 18.0, 17.9, 12.1. IR (neat): ?$_{max}$ 2994, 2944, 2868, 1464, 1371, 1248, 1227, 1199, 1153, 1122, 1086, 1045, 882, 834, 683, 657, 640 cm^{-1}. HRMS (ESI, [$C_{15}H_{32}O_3Si$+H]) Calc'd for $C_{15}H_{33}O_3Si$ 289.2913 Found 289.2200.

2-(triisopropylsilyloxy)propane-1,3-diol



To a solution of (2,2-dimethyl-1,3-dioxan-5-yloxy)triisopropylsilane (0.2 g, 0.69 mmol) in methanol (10 mL) was added *p*-toluenesulfonic acid monohydrate (0.04 g, 0.21 mmol) at 0 °C. The reaction mixture was stirred at this temperature for 25 minutes, quenched with saturated aqueous $NaHCO_3$, and extracted into ethyl acetate (4 x 20 mL). The organic layers were combined, washed with brine, dried (Na_2SO_4), and concentrated. Silica gel chromatography of the resulting mixture using ethyl acetate/hexanes mixtures afforded 0.17 g (99%) of the title compound as a clear oil. R_f = 0.55 (50 % ethyl acetate/hexanes); ^{1}H NMR (100 MHz, $CDCl_3$): d 3.95 (p, *J* = 4.7 Hz, 1H), 3.72 (m, 4H), 2.03 (m, 2H), 1.10 – 1.06 (m, 21H). ^{13}C NMR (125 MHz, $CDCl_3$): d 72.4, 64.4, 18.2, 12.6; IR (neat): ?$_{max}$ 3392, 3944, 2867, 1055, 679. HRMS (ESI, [$C_{12}H_{28}O_3Si$ +H]) Calc'd for $C_{12}H_{29}O_3$ Si 249.1880 Found 249.1897.

2. Preparation of vinyl benzoates:

Vinyl 4-methoxybenzoate (8). To a flask containing 4-methoxybenzoic acid (1.00 g, 6.57 mmol), palladium (II) acetate (18.3 mg, 0.0818 mmol), 2,2'-dipyridyl (38.3 mg, 0.245 mmol), and phenothiazine (16.3 mg, 0.0818 mmol) was added vinyl acetate (3 mL). The reddish brown solution was refluxed for 3 hr under nitrogen, concentrated, and directly loaded onto a silica gel column. The column was eluted with 10% ethyl acetate/hexanes to give 0.88 g (75%) of the title compound as a white solid. R_f = 0.40 (20% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): d 8.06 (d, *J* = 9.0 Hz, 2H), 7.50 (dd, *J* = 14.1, 6.3 Hz, 1H), 6.94 (d, *J* = 9.0 Hz, 2H), 5.03 (dd, *J* = 13.8, 1.4 Hz, 1H), 4.67 (dd, *J* = 6.1, 1.6 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 164.2, 163.6, 141.8, 132.4, 121.4, 114.1, 98.0, 55.8. IR (neat): ?$_{max}$ 3106,

2980, 2844, 1931, 1724, 1649, 1609, 1516, 1456, 1426, 1302, 1273, 1182, 1147, 1102, 1024, 949, 875, 844, 764, 690 cm^{-1}. This compound has previously been reported. [7]

Vinyl 2-methoxybenzoate (7). The above procedure was used on 2-methoxybenzoic acid (1.00 g, 6.57 mmol), palladium (II) acetate (18.3 mg, 0.0818 mmol), 2,2'-dipyridyl (38.3 mg, 0.245 mmol), phenothiazine (16.3 mg, 0.0818 mmol), and vinyl acetate (3 mL). The desired product was obtained in a 70% yield (820 mg). R_f = 0.43 (20% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): d 7.90 (dd, *J* = 8.1, 1.9 Hz, 1H), 7.51 (m, 2H), 7.00 (m, 2H), 5.01 (dd, *J* = 14.2, 1.9 Hz, 1H), 4.66 (dd, *J* = 6.3, 1.5 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 162.9, 160.2, 141.7, 134.7, 132.3, 120.4, 118.6, 112.4, 98.1, 56.3; IR (neat): $?_{max}$ 3088, 2944, 2840, 1743, 1645, 1601, 1582, 1492, 1465, 1437, 1302, 1240, 1182, 1166, 1137, 1093, 1067, 1024, 949, 875, 755, 640, 659 cm^{-1}. EI HRMS m/z calc'd for $C_{10}H_{10}O_3$ 179.0708, found 179.0724. Elemental Analysis Theoretical C67.41, H5.66 Found C67.36, H5.42.

Vinyl 4-bromobenzoate (9). The above procedure was used on 4-bromobenzoic acid (1.00 g, 4.97 mmol), palladium (II) acetate (18.3 mg, 0.0818 mmol), 2,2'-dipyridyl (38.3 mg, 0.245 mmol), phenothiazine (16.3 mg, 0.0818 mmol), and vinyl acetate (3 mL). The desired product was obtained in a 55% yield (486 mg). R_f = 0.68 (20% ethyl acetate/hexanes); ^{1}H NMR (125 MHz, $CDCl_3$): d 7.99 (d, *J* = 8.9 Hz, 2H), 7.64 (d, *J* = 8.9 Hz, 2H), 7.51 (dd, *J* = 7.5, 6.2 Hz, 1H), 5.10 (dd, *J* = 14.2, 1.7 Hz, 1H), 4.75 (dd, *J* = 6.3, 1.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 163.2, 141.5, 132.2, 131.7, 129.2, 128.1, 98.9; IR (neat): $?_{max}$ 3094, 1927, 1736, 1651, 1590, 1486, 1398, 1303, 1259, 1177, 1148, 1094, 1070, 1012, 953, 887, 841, 750, 674 cm^{-1}. This compound has previously been reported.[8]

Vinyl 4-nitrobenzoate (10). The above procedure was used on 4-nitrobenzoic acid (1.00 g, 5.98 mmol), palladium (II) acetate (18.3 mg, 0.0818 mmol), 2,2'-dipyridyl (38.3 mg, 0.245 mmol), phenothiazine (16.3 mg, 0.0818 mmol), and vinyl acetate (3 mL). The desired product was obtained in a 20% yield (221 mg). R_f = 0.57 (20% ethyl acetate/hexanes); ^{1}H NMR (500 MHz, $CDCl_3$): d 8.33 (d, *J* = 8.5 Hz, 1H), 8.28 (d, *J* = 8.5 Hz, 1H), 7.50 (dd, *J* =14.0, 6.2 Hz, 1H), 5.16 (dd, *J* = 14.0, 2.0 Hz, 1H), 4.81 (dd, *J* = 6.2, 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 162.0, 151.1, 141.4, 134.6, 131.4, 124.0, 99.8; IR (neat): $?_{max}$ 3111, 1743, 1731, 1649, 1600, 1525, 1412, 1353, 1323, 1300, 1271, 1144, 1104, 1012, 948, 912, 878, 842, 781, 717, 698 cm^{-1}. This compound has previously been reported.[13]

3. Characterization data for desymmetrized products.

(-)-2-(hydroxymethyl)butyl 2-methoxybenzoate (12). The desymmetrization of 2-ethyl-propane-1,3-diol (32.5 mg, 0.312 mmol) was done at 0 ^{o}C with a 24h reaction time. This was done with vinyl 2-methoxybenzoate (278 mg, 1.56 mmol), anhydrous toluene (1.9 mL), and the stock catalyst solution (0.026 M, 0.6 mL, 0.0156 mmol). The desired product was obtained in an 88% yield (65 mg). R_f = 0.4 (50% ethyl acetate/hexanes); $[a]_D^{25}$ -4.57 (72% ee, *c*. 0.8, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): d 7.89-7.86 (m, 1H), 7.52-7.47 (m, 1H), 7.0 (dd, *J* = 17.0, 3.5 Hz, 2H), 4.51 (dd, *J* = 11.3, 4.0 Hz, 1H), 4.27 (dd, *J* = 11.0, 7.3 Hz, 1H), 3.90 (s, 3H), 3.75 (dd, *J* = 7.1, 10.8 Hz, 1H), 3.70-3.62 (m, 1H), 2.94 (s, 1H), 1.89 (m, 1H), 1.42 (m, 1H), 1.00 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 167.1, 159.1, 134.2, 132.7, 120.7, 112.2, 67.6, 64.7, 56.0, 42.1, 21.2, 11.9; IR (neat): $?_{max}$ 3508, 3078, 2962, 2878, 2840, 2041, 1710, 1601, 1583, 1491, 1464, 1437, 1383, 1303, 1251, 1182, 1132, 1084, 1050, 863, 757, 704, 660 cm^{-1}. t_r = 19.9 (major) and 21.7 min (Chiralcel® OJ Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 95:5, 1.0 mL/min). HRMS (ESI, [$C_{13}H_{18}O_4$+H]) Calc'd for $C_{13}H_{19}O_4$ 239.1278 Found 239.1288.

(-)-2-(hydroxymethyl)butyl 4-methoxybenzoate (13). The desymmetrization of 2-ethyl-propane-1,3-diol (32.5 mg, 0.312 mmol) was done at 0 ^{o}C with a 24h reaction time. This was done with vinyl 4-methoxybenzoate (278 mg, 1.56 mmol), anhydrous toluene (1.9 mL), and the stock catalyst solution (0.026 M, 0.6 mL, 0.0156 mmol). The desired product was obtained in an 88% yield (65 mg). R_f = 0.47 (50% ethyl acetate/hexanes); $[a]_D^{25}$ -5.63 (80% ee, *c*. 0.76, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): 7.99 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 4.45 (dd, *J* = 11.2, 4.4 Hz, 1H), 4.32 (dd, *J* = 11.2, 5.85 Hz, 1H), 3.86 (s, 3H), 3.67 (dd, *J* = 11.1, 4.7 Hz, 1H), 3.58 (dd, *J* = 11.4, 6.5, 1H), 1.85 (m, 1H), 1.45 (m, 2H), 1.01 (t, *J* = 7.48 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 167.2, 163.7, 131.9, 122.6, 113.9, 64.5, 62.6, 55.7, 42.8, 21.1, 11.8; IR (neat) $?_{max}$ 3452, 2963, 2879, 1712, 1607, 1581, 1512, 1463, 1383, 1317, 1278, 1258, 1169, 1104, 1031, 964, 848, 771, 697 cm^{-1}; t_r = 12.6 (major) and 14.4 min (Chiralcel® OD Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 90:10, 0.8 mL/min); Elemental Analysis Theoretical C65.53, H7.61 Found 65.39, H7.64. HRMS (ESI, [$C_{13}H_{18}O_4$+H]) Calc'd for $C_{13}H_{19}O_4$ 239.1278 Found 239.1287.

(+)- 2-(hydroxymethyl)butyl 4-bromobenzoate (14). The desymmetrization of 2-ethyl-propane-1,3-diol (32.5 mg, 0.312 mmol) was done at 0 ^{o}C with a 24h reaction time. This was done with vinyl 4-bromobenzoate (354 mg, 1.56 mmol), anhydrous toluene (1.9 mL), and the stock catalyst solution (0.026 M, 0.6 mL, 0.0156 mmol). The desired product was obtained in a 28% yield (25 mg). R_f = 0.18 (20% ethyl acetate/hexanes); $[a]_D^{25}$ 2.34 (68% ee, *c*. 0.75, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): d 7.89 (d, *J* =

8.8 Hz, 2H), 7.59 (d, *J* = 8.3 Hz, 2H), 4.46 (dd, *J* = 11.0, 4.5 Hz 1H), 4.36 (dd, *J* = 11.0, 6.3 Hz, 1H), 3.64 (m, 2H), 1.9 (m, 2H), 1.45 (m, 2H), 1.01 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 132.0, 131.4, 129.2, 128.5, 65.1, 62.6, 42.6, 21.1, 11.8; IR (neat): $?_{max}$ 3429, 2961, 2878, 1714, 1590, 1484, 1482, 1398, 1271, 1173, 1116, 1103, 1069, 1011, 960, 847, 755 cm^{-1}; t_r = 17.1(major) and 18.1 min (Chiralcel® OD Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 95:5, 0.8 mL/min); Elemental Analysis Theoretical C50.19 Found C50.69. HRMS (ESI, [$C_{12}H_{15}BrO_3$+H]) Calc'd for $C_{12}H_{16}BrO_3$ 287.0277 Found 287.0204.

(*S*)-3-hydroxy-2-methylpropyl benzoate (18). The desymmetrization of 2-methyl-propane-1,3-diol (36 mg, 0.4 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (296 mg, 2.0 mmol), anhydrous toluene (2.43 mL), and the stock catalyst solution (0.026 M, 0.8 mL, 0.02 mmol). The desired product was obtained in an 88% yield (68.2 mg). R_f = 0.34 (33% ethyl acetate/petroleum ether); $[a]_D^{25}$ 1.08 (90% ee, *c*. 0.98, CH_2Cl_2); $[a]_D^{25}$ 6.19 (90% ee, *c*. 1.02, MeOH); lit:[9] $[a]_D^{25}$ 7.9 (*c*. 1.0, MeOH); t_r = 42.7 (minor) and 44.4 (major) (Chirapak® OC Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 97:3, 0.8 mL/min); Spectral data matches literature values.[9]

(-)-2-(hydroxymethyl)pent-4-en-1-yl benzoate (20). The desymmetrization of 2-allylpropane-1,3-diol (46.5 mg, 0.4 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (296 mg, 2.0 mmol), anhydrous toluene (2.43 mL), and the stock catalyst solution (0.026 M, 0.8 mL, 0.02 mmol). The desired product was obtained in an 84% yield (73.6 mg). R_f = 0.18 (20% ethyl acetate/hexanes); $[a]_D^{25}$ -5.17 (84% ee, *c*. 0.87, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): d 8.04 (dd, *J* = 8.0, 1.3 Hz, 2H), 7.57 (tt, *J* =8.0, 1.3, 1H), 7.45 (dd, *J* = 8.0, 8.0 Hz, 2H), 5.84 (m, 1H), 5.15-5.06 (m, 1H), 4.46 (dd, *J* = 11.5, 4.7 Hz, 1H) 4.34 (dd, *J* = 11.5, 6.4 Hz, 1H), 3.69 (dd, *J* = 11.6, 4.6 Hz, 1H), 3.64 (dd, *J* = 11.6, 6.6 Hz, 1H), 2.21 (m, 2H), 2.06 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 167.3, 135.9, 133.4, 130.2, 129.8, 128.7, 117.4, 64.7, 62.6, 40.7, 32.9; IR (neat) $?_{max}$ 3475, 3076, 2927, 2252, 1716, 1642, 1602, 1452, 1389, 1316, 1277, 1178, 1118, 1071, 1027, 911, 733, 713 cm^{-1}. t_r = 9.57 (major) and 10.7 min (Chiralcel® OBH Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 95:5, 1.0 mL/min). This compound has previously been previously reported.[10]

(-)-2-(hydroxymethyl)pent-4-yn-1-yl benzoate (22). The desymmetrization of 2-prop-2-yn-1-ylpropane-1,3-diol (45.6 mg, 0.4 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (296 mg, 2.0 mmol), anhydrous toluene (2.43 mL), and the stock catalyst solution (0.026 M, 0.8 mL, 0.02 mmol). The desired product was obtained in a 90% yield (79 mg). R_f = 0.14 (20% ethyl

acetate/hexanes); $[a]_D^{25}$ -2.81 (80% ee, *c*. 0.88, CH_2Cl_2); ^{1}H NMR (125 MHz, $CDCl_3$): d 8.04 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.57 (tt, *J* =8.0, 1.4 Hz, 1H), 7.45 (dd, *J* =8.0, 8.0 Hz, 2H), 4.49 (dd, *J* = 11.2, 5.6 Hz, 2H), 4.45 (dd, *J* = 11.2, 6.1 Hz, 2H), 3.77 (dd, *J* = 11.3, 5.4 Hz, 1H), 3. 73 (dd, *J* = 11.3, 5.8 Hz, 1H), 4.43 (dd, *J* = 2.7, 0.8 Hz, 1H) 2.4 (d, *J* = 2.7, 1H), 2.24 (m, 1H), 2.03 (t, *J* = 2.7, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 167.2, 133.5, 129.9, 128.7, 81.9, 70.5, 64.3, 62.2, 40.2, 18.0; IR (neat) $?_{max}$ 3432, 3300, 2919, 1719, 1602, 1452, 1352, 1276, 1178, 1117, 1071, 1027, 974, 712 cm^{-1}. t_r = 18.3 (major) and 19.9 min (Chiralcel® OBH Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 95:5, 1.0 mL/min); HRMS (EI) Calc'd for $C_{13}H_{14}O_3$: 218.0943 Found: 218.0942.

(-)-2-benzyl-3-hydroxypropyl benzoate (24). The desymmetrization of 2-(benzyl)propane-1,3-diol (66.5 mg, 0.4 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (296 mg, 2.0 mmol), anhydrous toluene (2.43 mL), and the stock catalyst solution (0.026 M, 0.80 mL, 0.02 mmol). The desired product was obtained in an 85 % yield (92.3 mg). R_f = 0.13 (20% ethyl acetate/hexanes). $[a]_D^{25}$ -42.49 (90% ee, *c*. 0.65, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): d 8.05-8.02 (m, 2H), 7.60-7.54 (m, 1H), 7.48-7.43 (m, 2H), 7.33-7.18 (m, 5H), 4.45 (dd, *J* = 4.4 and 11.2 Hz, 1H), 4.33 (dd, *J* = 6.1, 11.2 Hz, 1H), 3.68 (dd, *J* = 4.6, 11.2 Hz, 1H), 3.58 (dd, *J* = 6.3, 11.5 Hz, 1H), 2.81-2.61 (m, 2H), 2.33-2.10 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): d 167.1, 139.3, 133.2, 129.9, 129.6, 129.1, 128.5, 128.4, 126.3, 64.2, 62.1, 42.8, 34.4; IR (neat): $?_{max}$ 3429, 3063, 3028, 2939, 2897, 1716, 1602, 1584, 1496, 1453, 1388, 1316, 1277, 1177, 1118, 1071, 1027, 978, 807, 745, 712 cm^{-1}; t_r = 46.9 min (major) and 42.8 min (Chiralcel® OC Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 97:3, 1.0 mL/min). This compound has previously been reported.[11]

(-)-2-(benzyloxy)-3-hydroxypropyl benzoate (26). The desymmetrization of 2-(benzyloxy)propane-1,3-diol (56.8 mg, 0.312 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (231 mg, 1.56 mmol), anhydrous toluene (1.9mL), and the stock catalyst solution (0.026 M, 0.6 mL, 0.0156 mmol). The desired product was obtained in a 36% yield (32 mg). R_f = 0.18 (20% ethyl acetate/hexanes); $[a]_D^{25}$ -4.8 (40 % ee, *c*. 0.94, $CHCl_3$): ^{1}H NMR (500 MHz, $CDCl_3$): d 8.04 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.58 (tt, *J* = 8.0, 1.3 Hz, 1H), 7.46 (dd, *J* = 8.0, 8.0 Hz, 2H), 7.38 - 7.21 (m, 5H), 4.78 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 12.0 Hz, 1H), 4.49 (dd, *J* =5.2, 17 Hz, 2H), 3.87 (m, 1H), 3.81 (dd, *J* = 11.8, 4.2, 1H), 3.74 (dd, *J* = 11.8, 5.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 166.8, 138.1, 133.5, 130.1, 130.0, 128.8, 128.7, 128.3, 128.2, 91.0, 72.5, 63.7, 62.4; IR (neat): $?_{max}$ 3436, 3064, 3008, 2934, 2880, 1716, 1602, 1584, 1496, 1453, 1316, 1274, 1177, 1110, 1070, 1026, 983, 739, 711 cm^{-1}; t_r = 28.5 (major)

and 30.3 min (Chiralcel® OC Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 95:5, 1.0 mL/min); HRMS (EI, $[MC_{17}H_{18}O_4 - (CH_3O)]^+$) Calc'd for $C_{16}H_{15}O_3$: 255.1099 Found: 255.1025 and (EI, $[MC_{17}H_{18}O_4 + H]^+$) Calc'd for $C_{17}H_{18}O_4$: 287.1205 Found: 287.1283. This compound has previously been reported.[12]

(-)-3-hydroxy-2-(triisopropylsilyloxy)propyl benzoate (28). The desymmetrization of 2-(triisopropylsilyloxy)propane-1,3-diol (77.4 mg, 0.312 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (231 mg, 1.56 mmol), anhydrous toluene (1.9 mL), and the stock catalyst solution (0.026 M, 0.6 mL, 0.0156 mmol). The desired product was obtained in a 22% yield (24 mg) along with 46.2 mg of the starting diol. Yield based on recovered starting material 54%. R_f = 0.33 (20% ethyl acetate/hexanes); $[a]_D^{25}$ -3.87 (60% ee, *c*. 2.8, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): d 8.04 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.57 (tt, *J* = 8.0, 1.3 Hz, 1H), 7.44 (dd, *J* = 8.8, 8.0 Hz, 2H), 4.50 (dd, *J* = 11.0, 4.7 Hz, 1H), 4.35 (dd, *J* = 11.0, 6.8, 1H), 4.20 (m, 1H), 3.73 (m, 2H), 2.17 (m, 1H), 1.14 – 1.06 (m, 22H) ^{13}C NMR (125 MHz, $CDCl_3$): d 166.5, 133.1, 129.8, 129.6, 128.4, 70.4, 64.8, 63.7, 17.9, 12.3; IR (neat): $?_{max}$ 3452, 2943, 2866, 1723, 1452, 1274, 1110, 1068, 882 cm^{-1}. t_r = 5.14 (major) and 6.48 min (Chiralcel® AS Chiral HPLC, ? = 220 nm, heptane : *i*-PrOH = 90:10 1.0 mL/min). HRMS (ESI, $[C_{19}H_{32}O_4Si+H]$) Calc'd for $C_{19}H_{33}O_4Si$ 353.2143 Found 253.2155.

(-)-2-benzyl-3-hydroxypropyl benzoate (40). The desymmetrization of 2-(naphthalen-1-yl)propane-1,3-diol (63.5 mg, 0.312 mmol) was done at -20 ^oC with a 24h reaction time. This was done with vinyl benzoate (231 mg, 1.56 mmol), anhydrous toluene (1.9 mL), and the stock catalyst solution (0.026 M, 0.60 mL, 0.016 mmol). The desired product was obtained in a 56 % yield (54 mg) and 26 mg of starting material was recovered. Based on this, the yield based on recovered starting material is 95%. Spectroscopic data matches literature values.[13] $[a]_D^{25}$ -28.86 (80% ee, *c*. 0.52, CH_2Cl_2); t_r = 26.1 (major) 29.5 min (Chiralcel® OD Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 90:10, 0.8 mL/min). This compound has previously been reported .[14]

4. Preparation of Chiral Building Blocks.

(-)-3-azido-2-methylpropyl benzoate (49). To a solution of (S)-3-hydroxy-2-methylpropyl benzoate (50 mg, 0.26 mmol, 91% ee) in toluene (1.5 mL) was added triphenylphosphine (137 mg, 0.53 mmol), $Zn(N_3)_2 \cdot Py$[15] (64 mg, 0.210 mmol). To the reaction mixture was added DIAD (106 mg, 0.53 mmol) dropwise. After 17 hours, the reaction mixture was diluted with 5 mL diethyl ether and 2 mL water and filtered through celite. The resulting layers were separated, the organic layer was dried (Na_2SO_4), filtered,

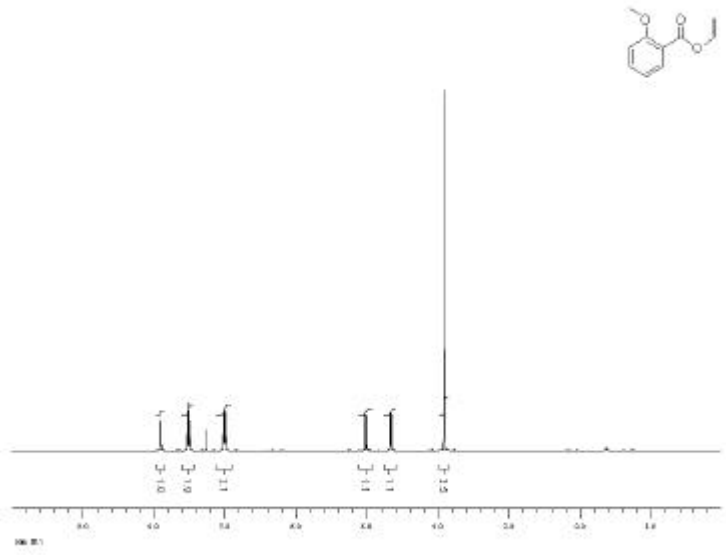
and concentrated. Chromatography of the resulting oil gave the 31 mg (52%, 91% ee) of the title compound as a clear oil. R_f = 0.7 (40% diethyl ether/hexanes); $[a]_D^{25}$ -19.85 (91% ee, *c*. 0.43, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): d 8.04 (dd, *J* = 8.0, 1.0 Hz, 2H), 7.58 (tt, *J* = 8.0, 1.0 Hz, 1H), 7.45 (dd, *J* = 8.0, 8.0 Hz, 2H), 4.35 (dd, *J* = 11.5, 4.7 Hz, 1H), 4.17 (dd, *J* = 11.5, 7.3 Hz, 1H), 2.6-2.35 (m, 3H), 1.21 (d, *J* = 7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): d 166.1, 133.2, 129.5, 128.4, 117.9, 67.4, 30.4, 21.6, 16.2; IR (neat): $?_{max}$ 2969, 1720, 1452, 1315, 1272, 1111, 1070, 1026, 711. t_r = 41.59 (major) and 43.82 min (Chiralcel® OD Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 99:1, 0.8 mL/min). HRMS (ESI, $[C_{11}H_{13}N_3O_2+2H]$) Calc'd for $C_{11}H_{15}N_3O_2$ 221.1153 Found 221.1307.

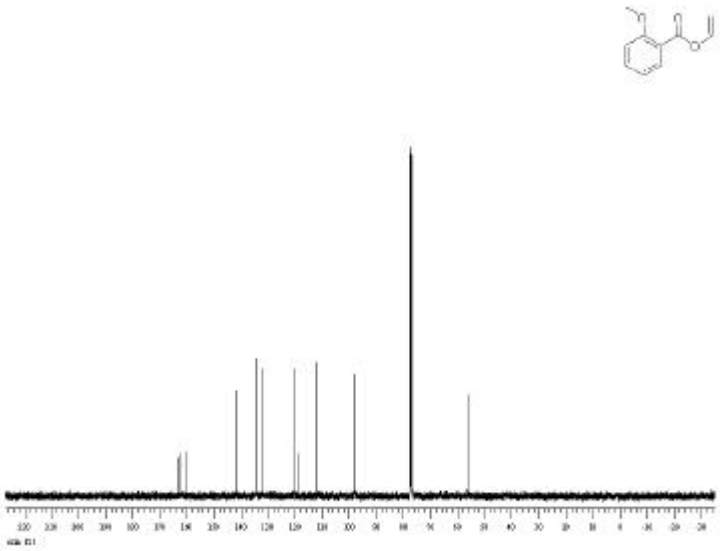
(+)-2-methyl-3-(triisopropylsilyloxy)propyl benzoate (50). A solution of (*S*)-3-hydroxy-2-methylpropyl benzoate (50 mg, 0.26 mmol, 91% ee) in DMF (0.5 mL) was added imidazole (34 mg, 0.51 mmol), and triisopropylsilyl chloride (59 mg, 0.31 mmol). The reaction mixture was stirred for 24 h, diluted with diethyl ether (10 mL), and washed with water. The organic layer was dried (Na_2SO_4) and concentrated. Silica gel chromatography of the resulting mixture using diethyl ether/hexanes mixtures afforded 73 mg (81%, 87% ee) of the title compound as a clear oil. R_f = 0.25 (5 % diethyl ether/hexanes); $[a]_D^{25}$ 2.25 (87% ee, *c*. 0.54, CH_2Cl_2); ^{1}H NMR (125 MHz, $CDCl_3$): d 8.07 (dd, *J* = 8.3, 1.3 Hz, 2H), 7.58 (dt, *J* = 7.4, 1.3 Hz, 1H), 7.46 (dd, *J* = 8.3, 7.4 Hz, 2H), 4.38 (dd, *J* = 10.7, 6.5 Hz, 1H), 4.29 (dd, *J* = 10.7, 5.8 Hz, 1H), 3.77 (dd, *J* = 9.6, 5.2 Hz, 1H), 3.73 (dd, *J* = 9.6, 6.0 Hz, 1H), 2.17 (m, 1H), 1.2 – 1.0 (m, 25H); ^{13}C NMR (125 MHz, $CDCl_3$): d 166.6, 132.7, 130.4, 129.5, 128.3, 66.7, 64.9, 35.8, 29.7, 17.9, 13.8, 11.9; IR (neat): $?_{max}$ cm^{-1} 2943, 2866, 1724, 1464, 1273, 1110, 1069, 711, 684; t_r = 8.78 (major) and 9.14 min (Chiralcel® OD Chiral HPLC, ? = 230 nm, heptane : *i*-PrOH = 1000:1, 0.8 mL/min). HRMS (ESI, $[C_{20}H_{34}O_3Si+H]$) Calc'd for $C_{20}H_{35}O_3Si$ 351.2350 Found 351.2361.

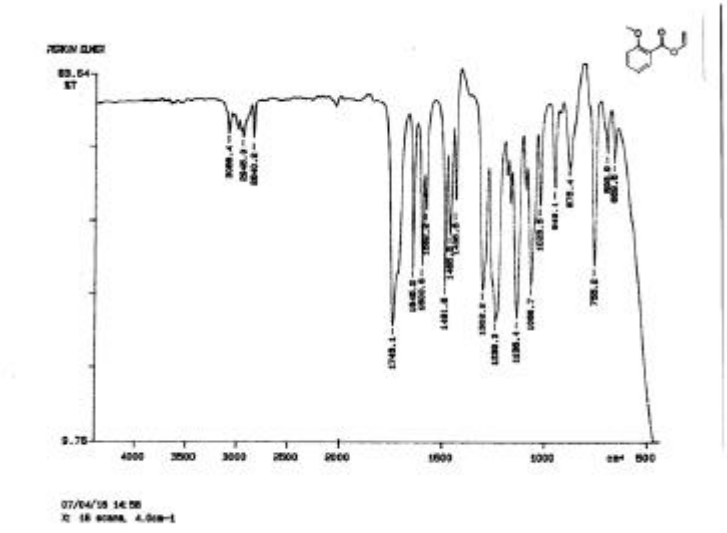
(-)-(6-oxotetrahydro-2H-pyran-3-yl)methyl benzoate (53). (S)-2-(hydroxymethyl)pent-4-yn-1-yl benzoate (50 mg, 0.23 mmol), $RuCp((p\text{-methoxytriphenylphoshine})_3)_2Cl$ (20.8 mg, 0.023 mmol), *p*-methoxytriphenylphoshine (32.4 mg, 0.092 mmol), N-hydroxysuccinimide (158.8 mg, 1.38 mmol), sodium bicarbonate (38.6 mg, 0.46 mmol), and tetrabutylammonium hexafluorophosphate (26.7 mg, 0.069 mmol) were combined in a flame-dried vial cooled under nitrogen. To this was added degassed DMF (0.6 mL) that had been degassed with argon. The mixture was placed in a pre-heated oil bath (85 ^oC) and was stirred 24 hr under nitrogen. The reaction was then cooled to room temperature, diluted with diethyl either, and washed with water 3 times. The aqueous layer was re-extracted with diethyl ether and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated to dryness. Silica gel column

chromatography (20% ethyl acetate/ toluene) was used to isolate the desired product (18 mg, 34% yield, 80% ee). R_f = 0.38 (20% ethyl acetate/ toluene); $[a]_D^{25}$ -2.88 (79% ee, *c*. 0.18, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): d 8.02 (dd, *J* = 8.4, 1.4 Hz, 2H), 7.58 (tt, *J* = 8.4, 1.4 Hz, 1H), 7.46 (m, 2H), 4.49 (ddd, *J* = 11.4, 4.7, 1.5 Hz, 1H), 4.37 (dd, *J* = 11.4, 5.5 Hz, 1H), 4.24 (m, 2H), 2.67 (m, 1H), 2.61 (m, 1H), 2.13 (m, 1H), 1.79 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): d 171.3, 166.5, 133.6, 129.8, 129.7, 128.8, 70.4, 64.8, 32.7, 28.8, 22.1. IR (neat): $?_{max}$ 2933, 2881, 1719, 1708, 1560, 1467, 1450, 1354, 1316, 1275, 1248, 1199, 1178, 1128, 1055, 1015, 975, 936, 892, 867, 716 cm^{-1}; t_r = 70.37 min and 76.48 min (major) (Chiralcel® AD Chiral HPLC, ? = 254 nm, heptane : *i*-PrOH = 97:3, 1 mL/min). HRMS (ESI, [$C_{13}H_{14}O_4$+H]) Calc'd for $C_{13}H_{15}O_4$ 235.0965 Found 235.0975.

5. ^{1}H, ^{13}C, and IR Spectra:



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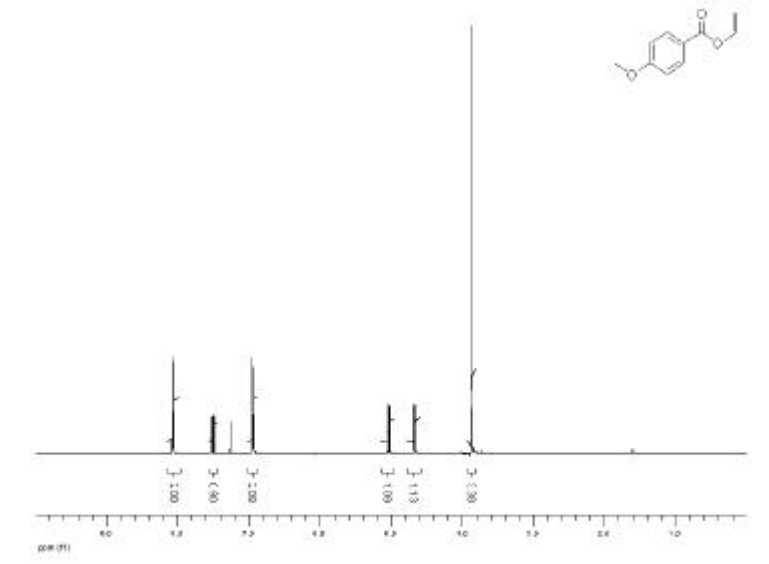

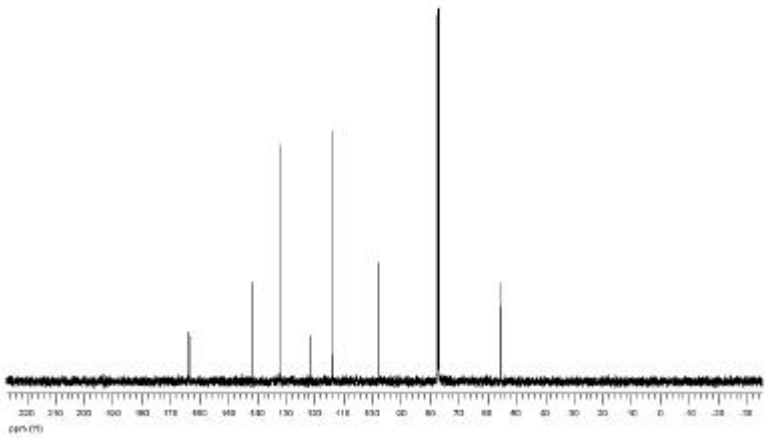

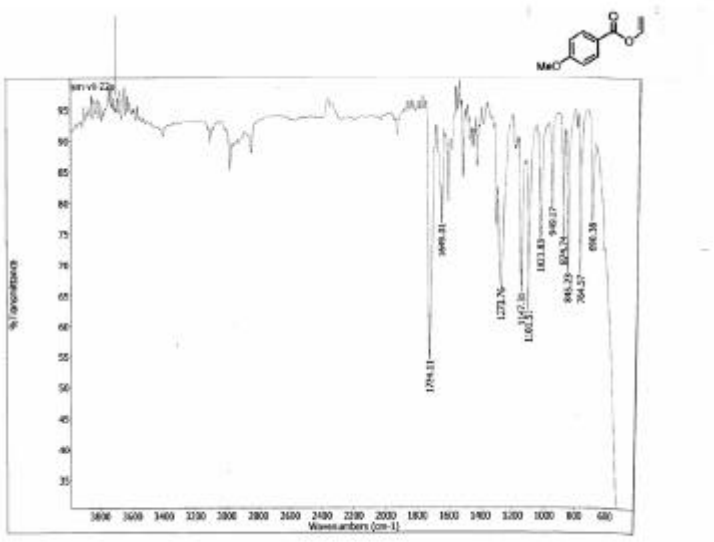

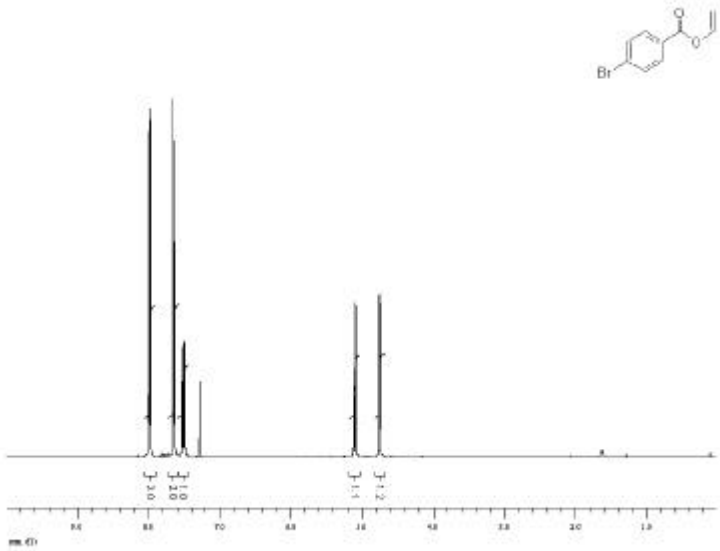

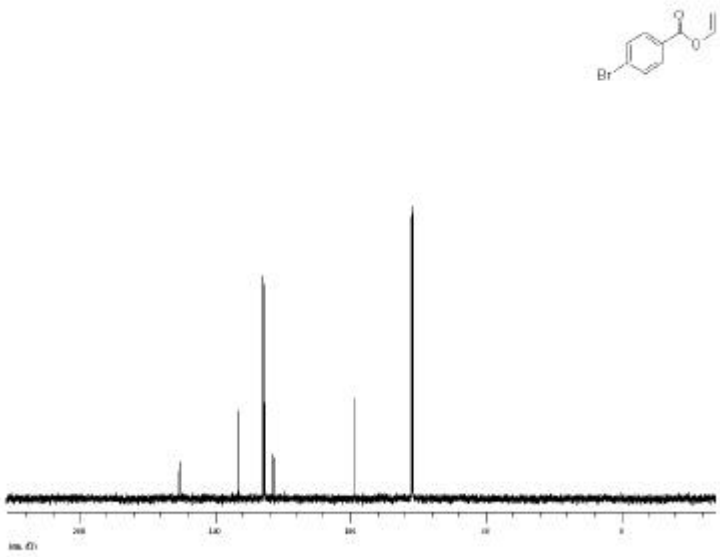

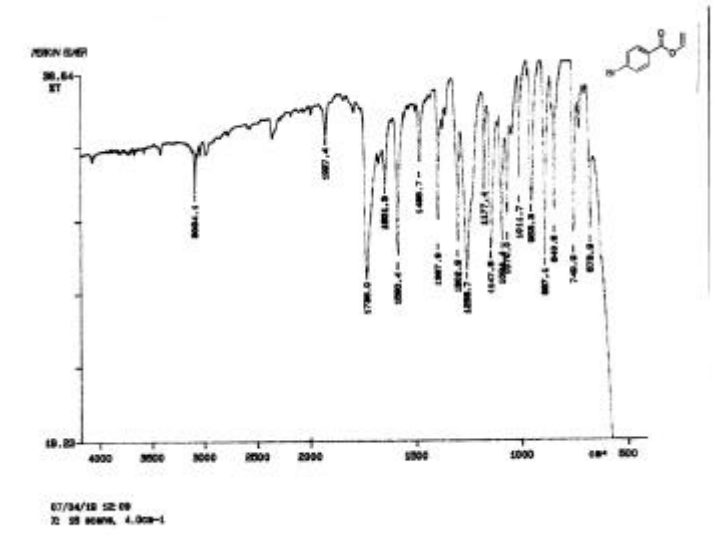

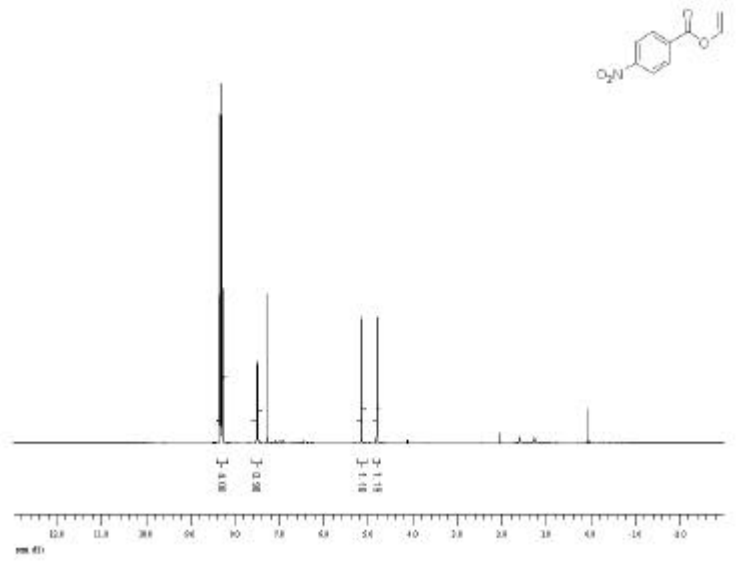

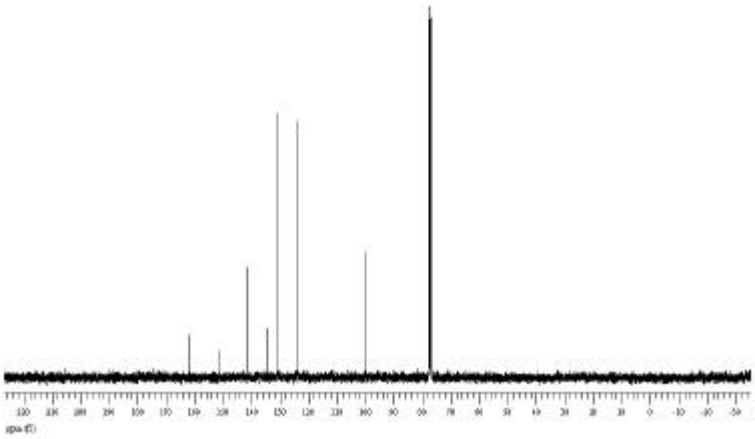

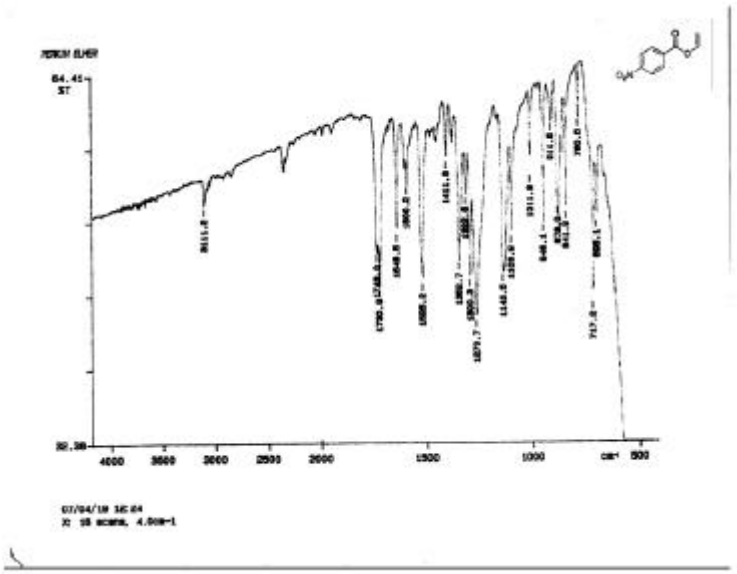

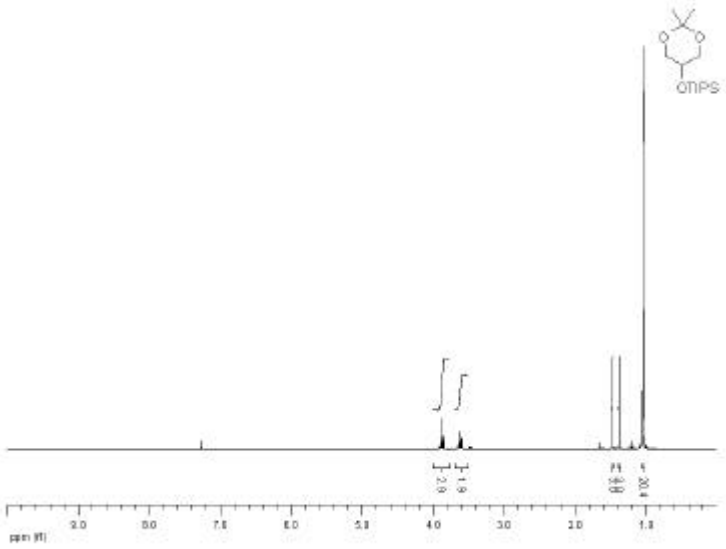
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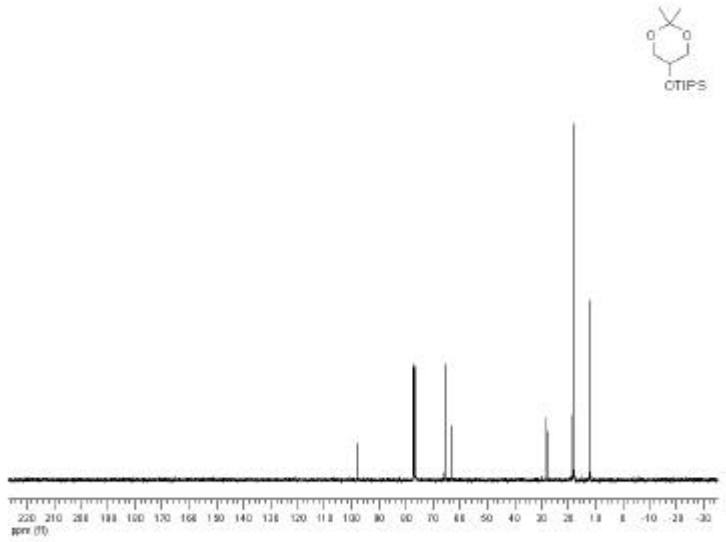
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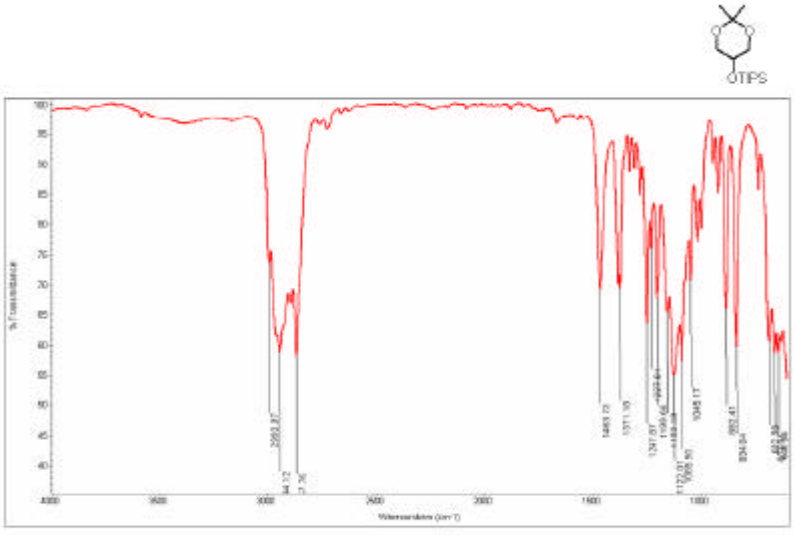
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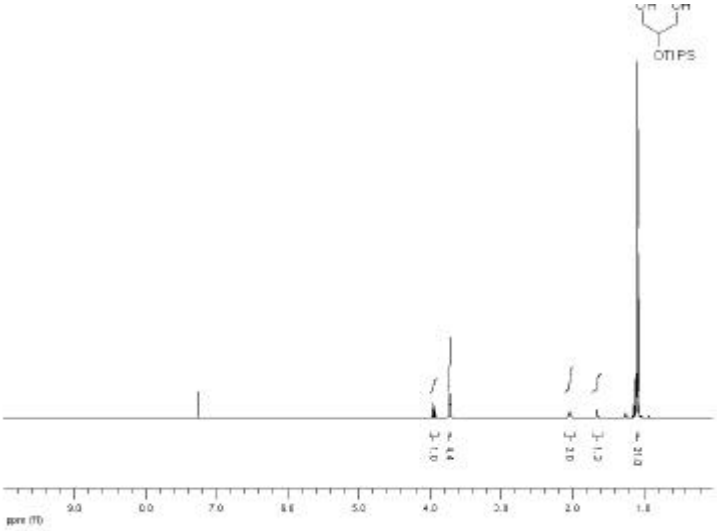
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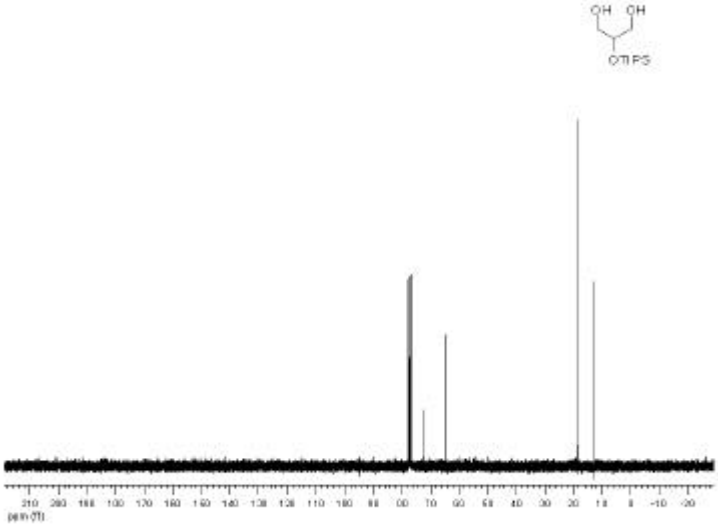
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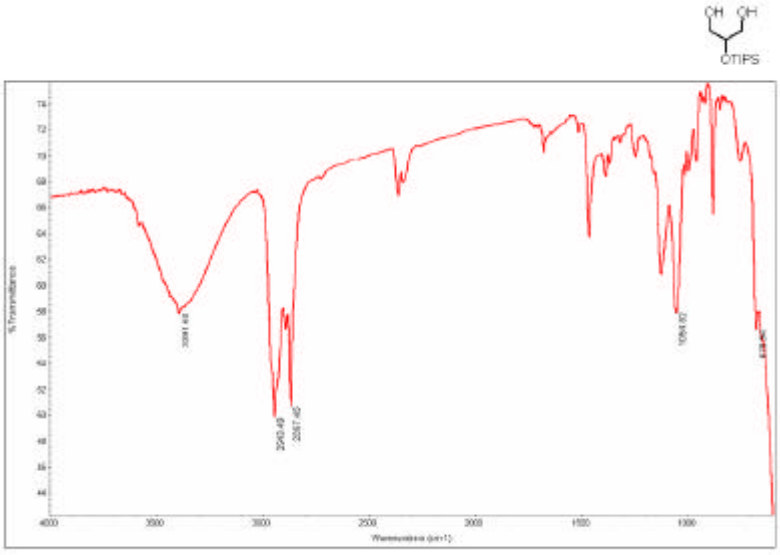
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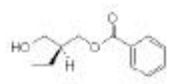
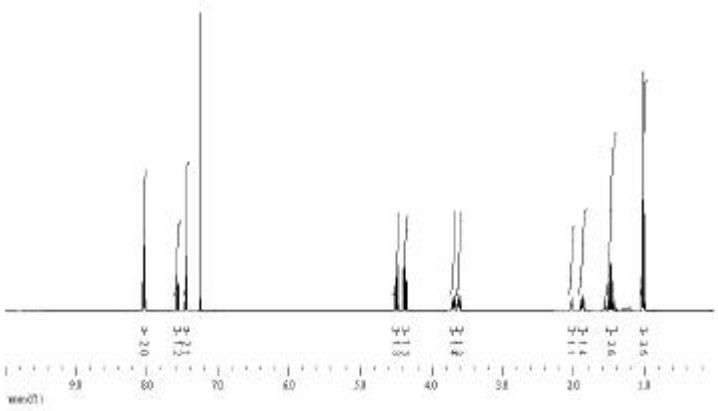
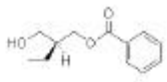
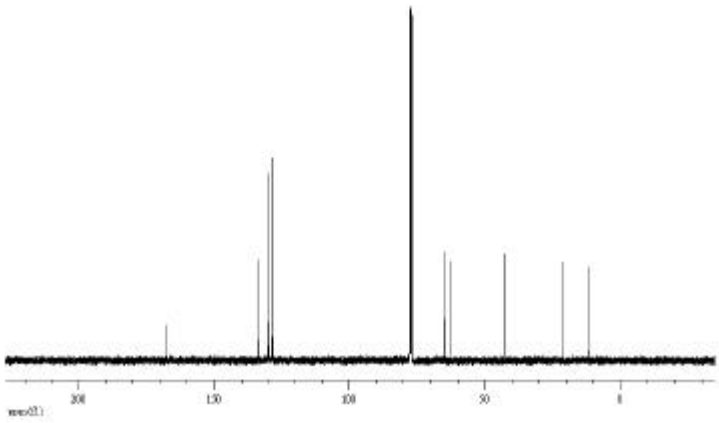
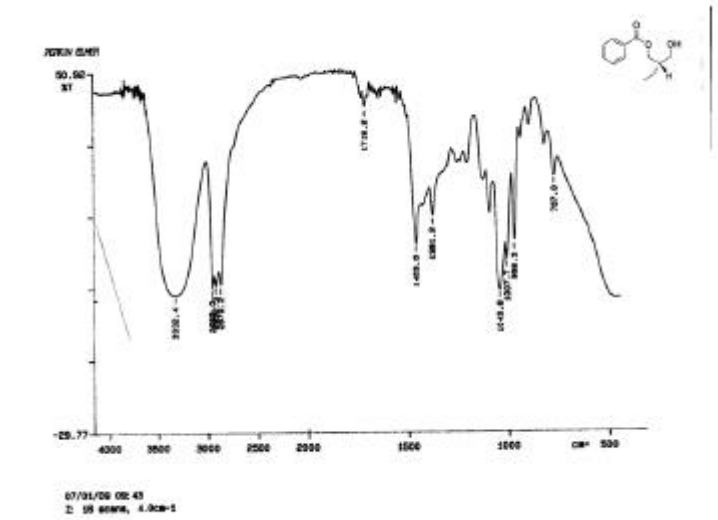
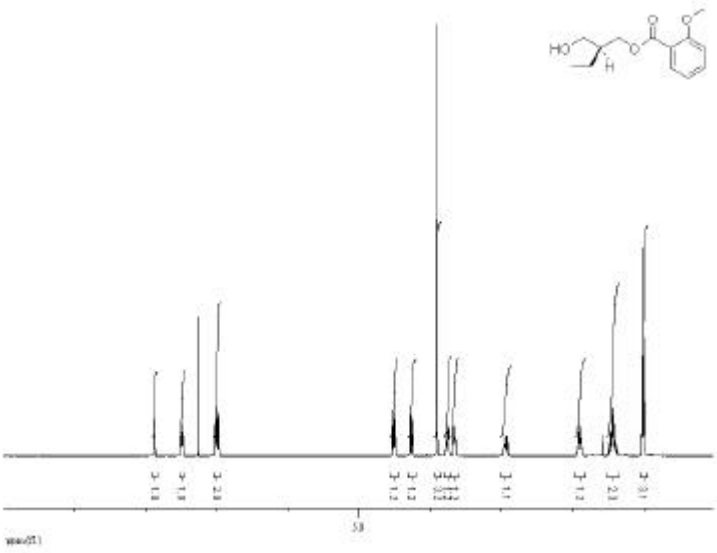


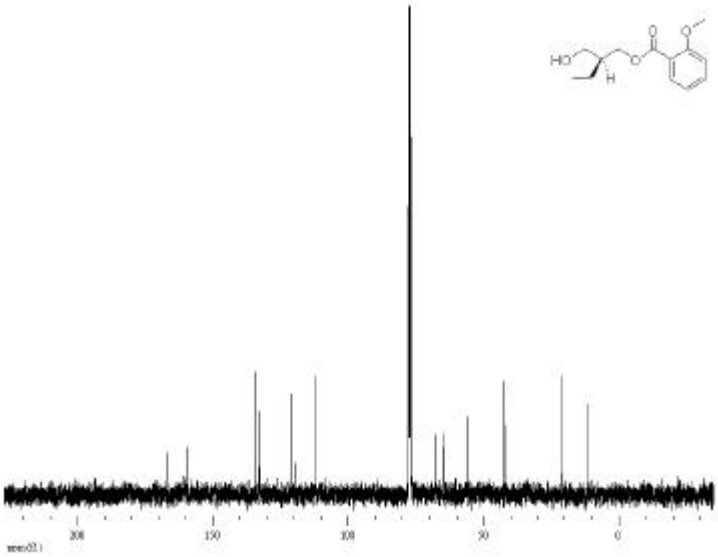


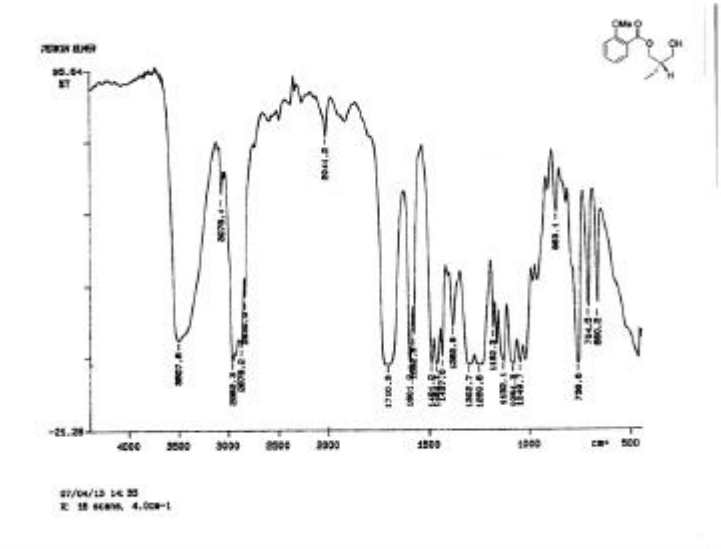


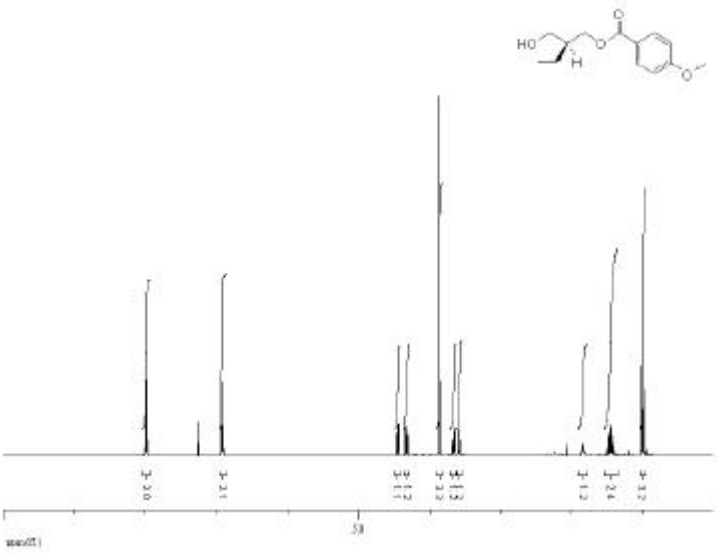


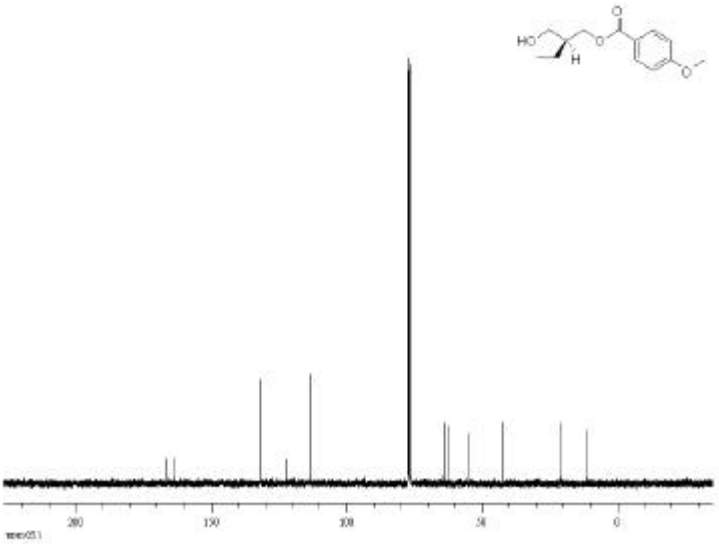


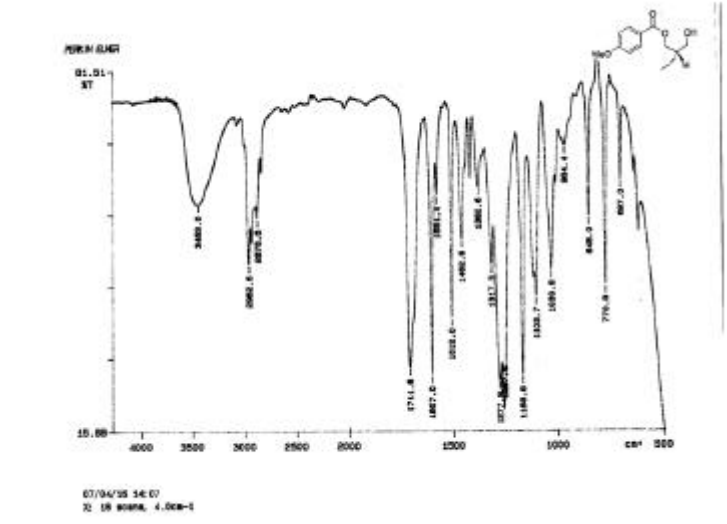


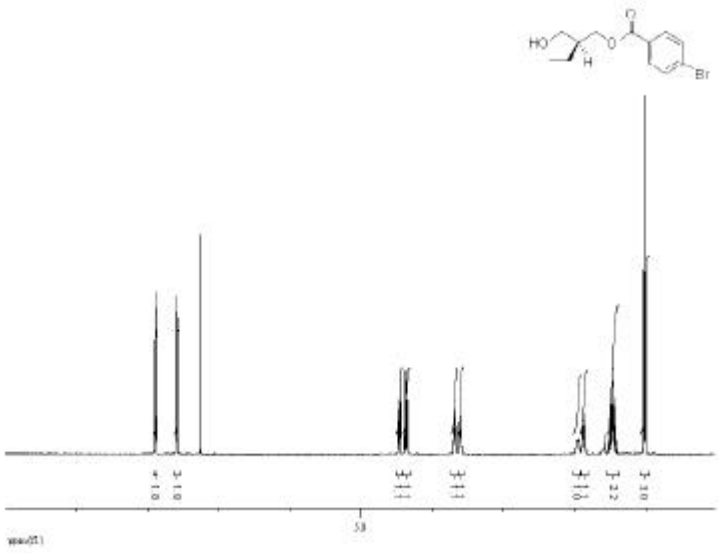


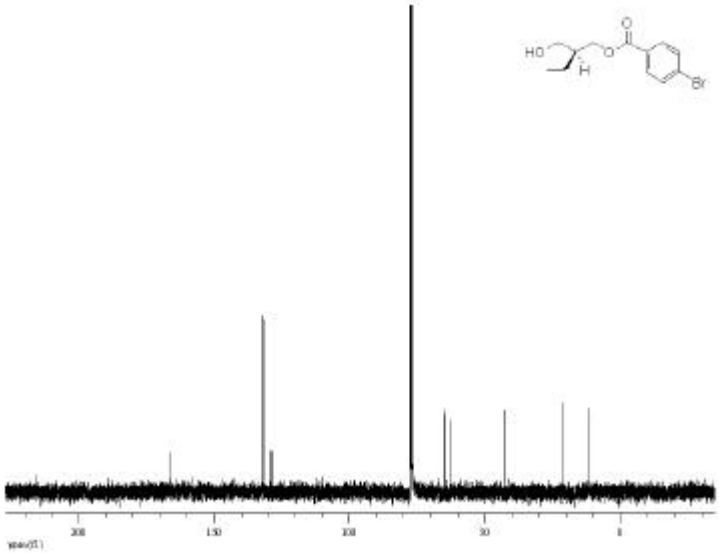


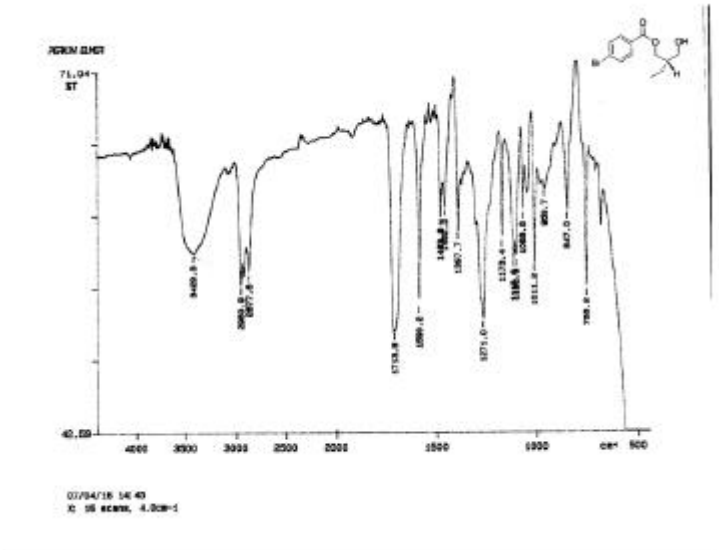


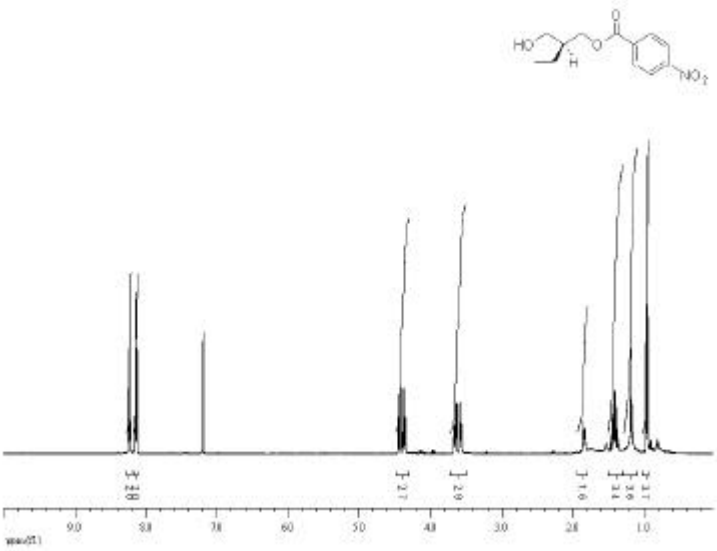


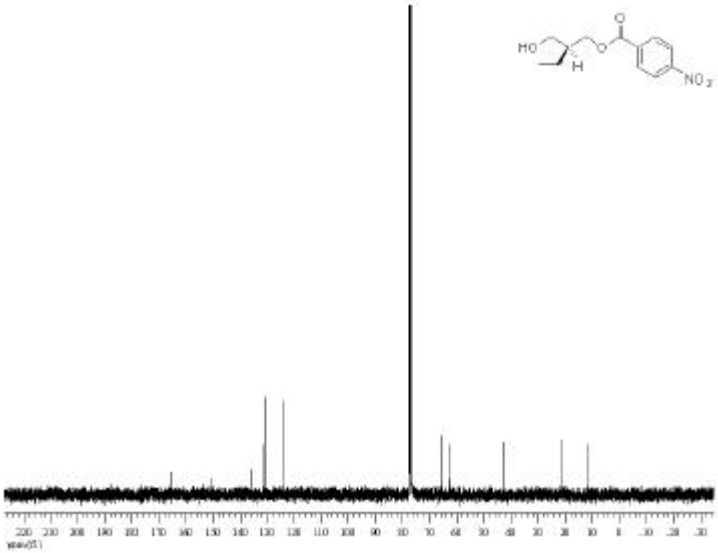


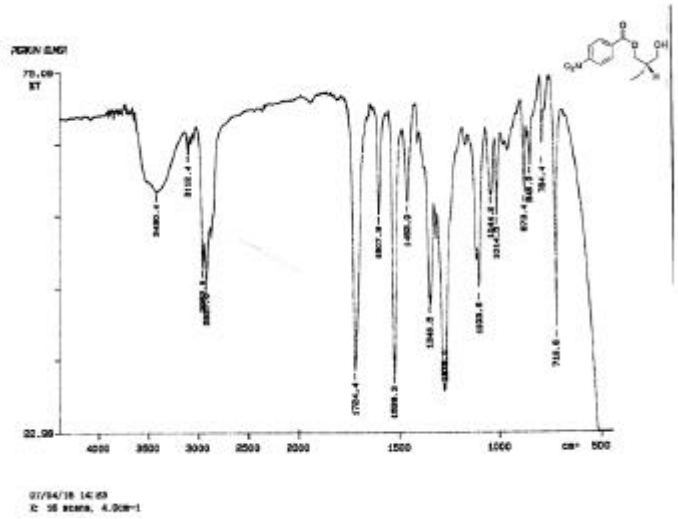


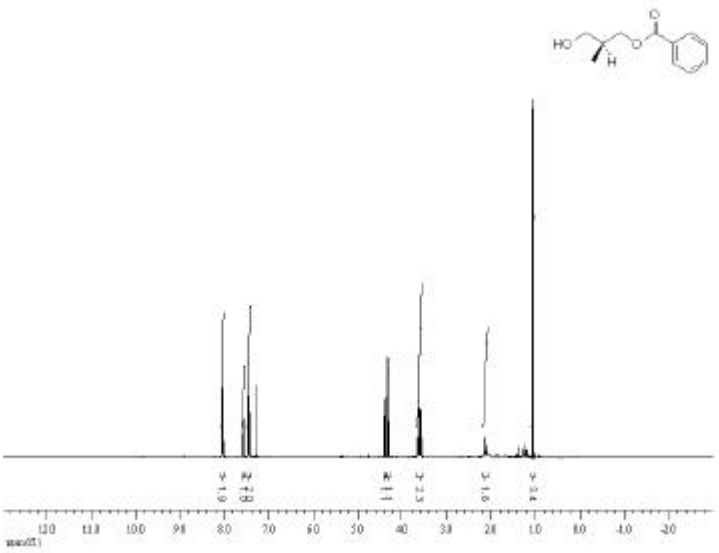


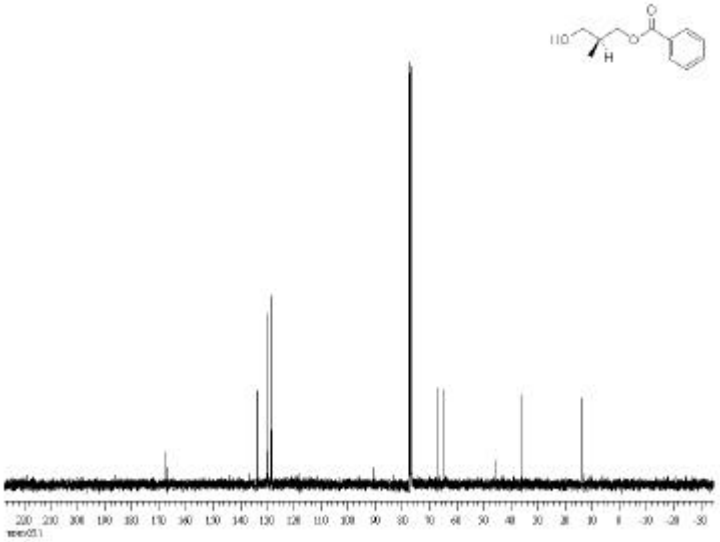


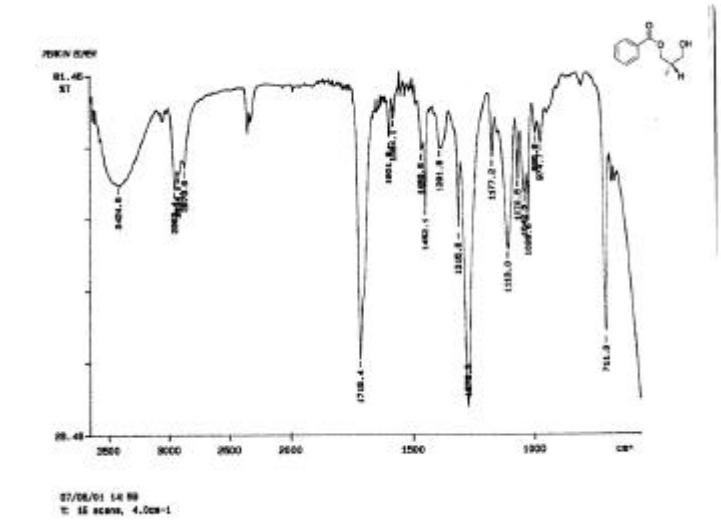


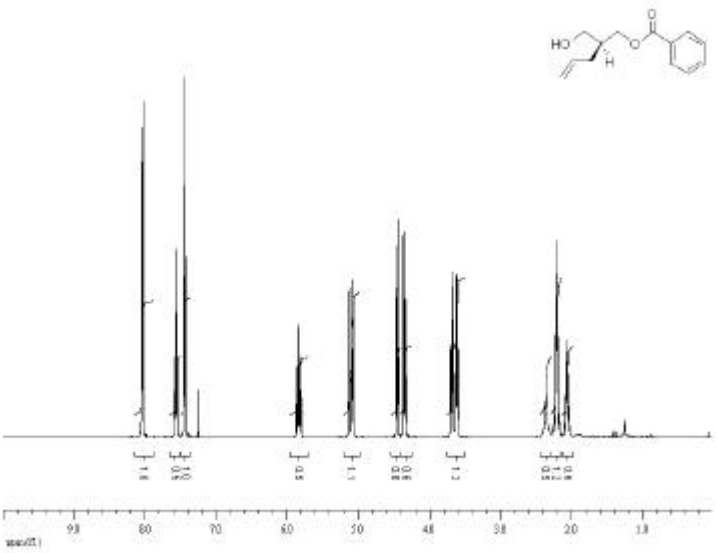


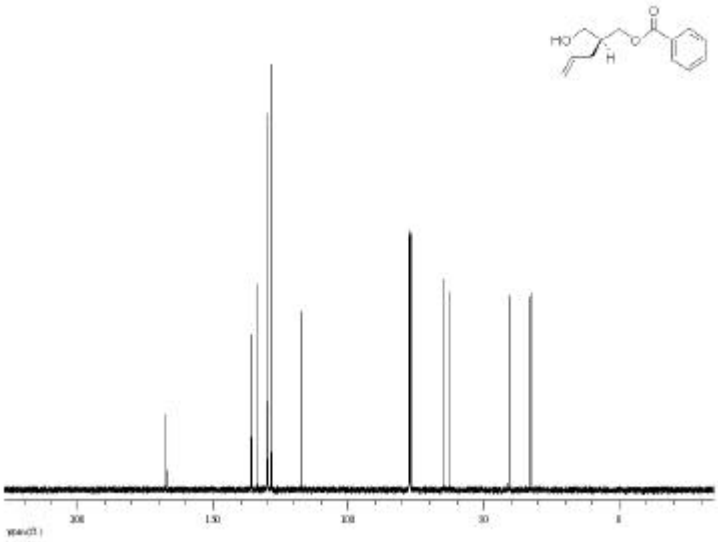


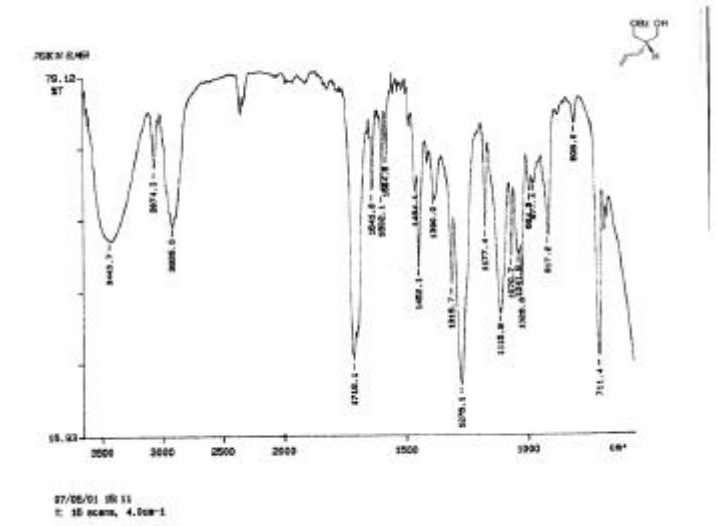


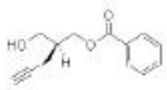


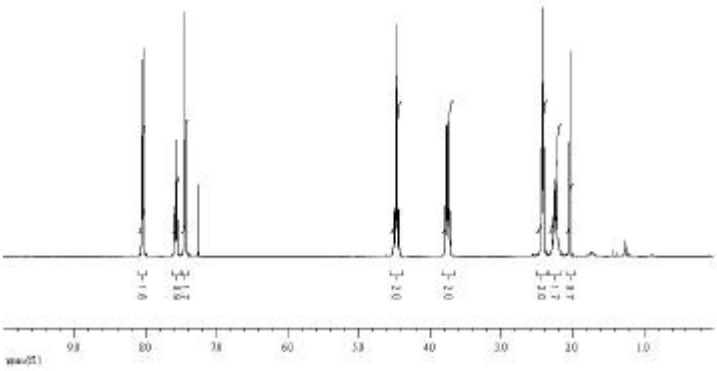


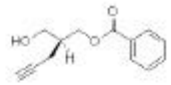


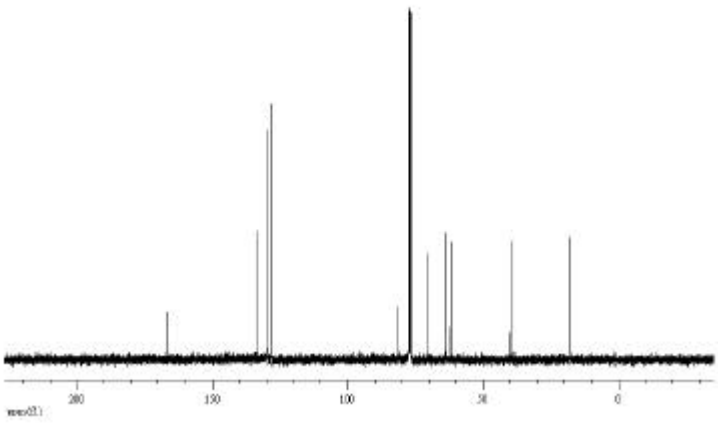


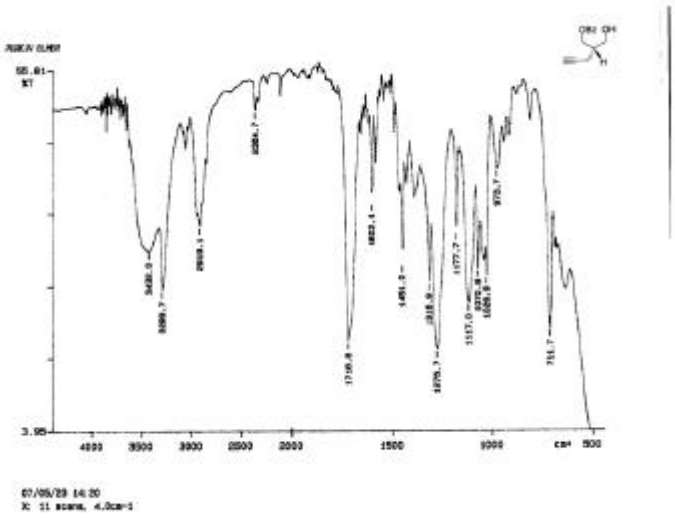


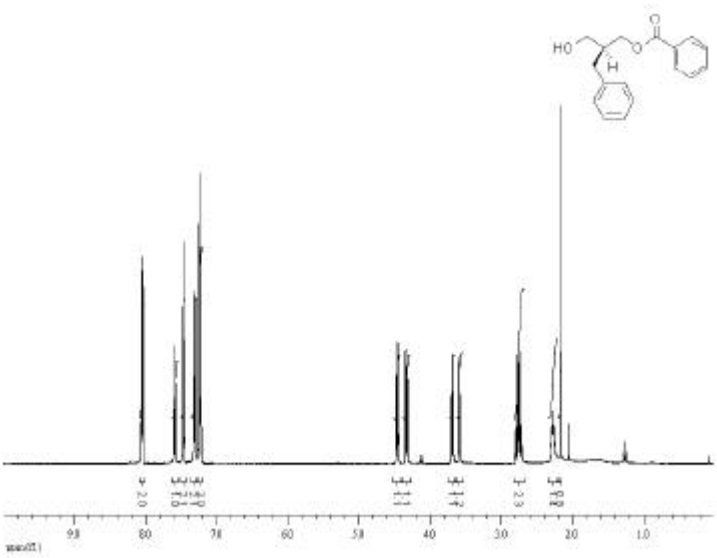


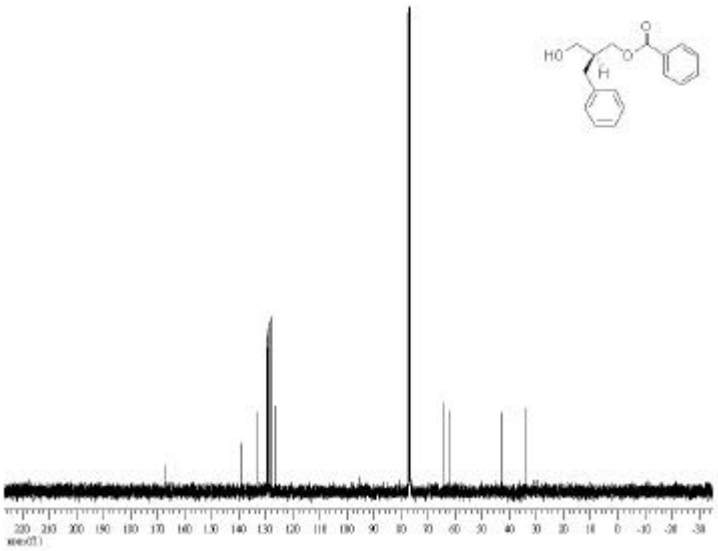


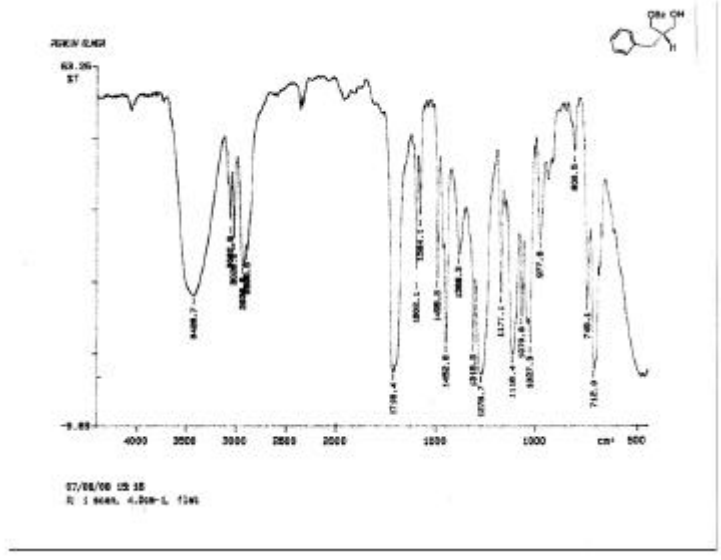


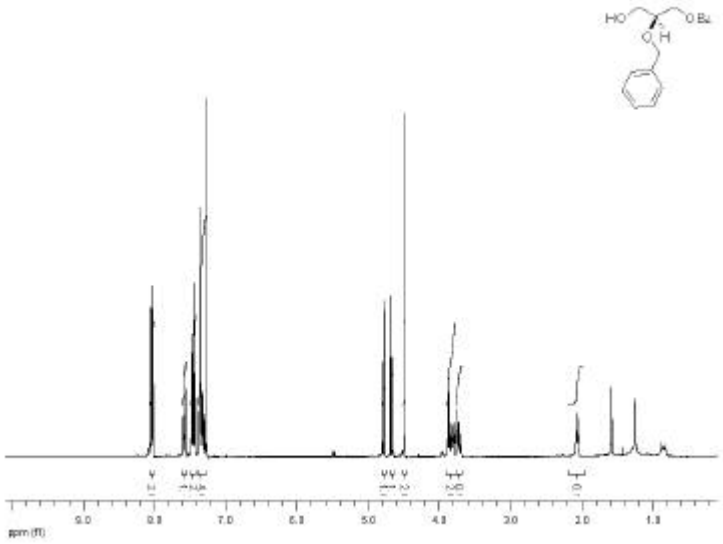


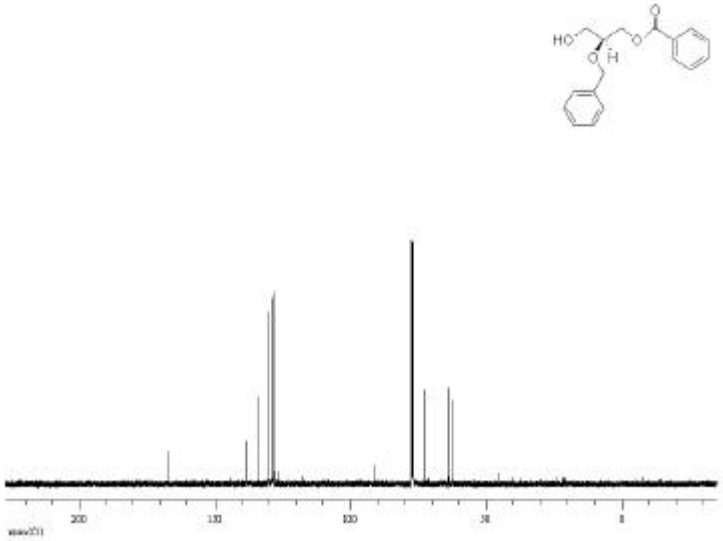


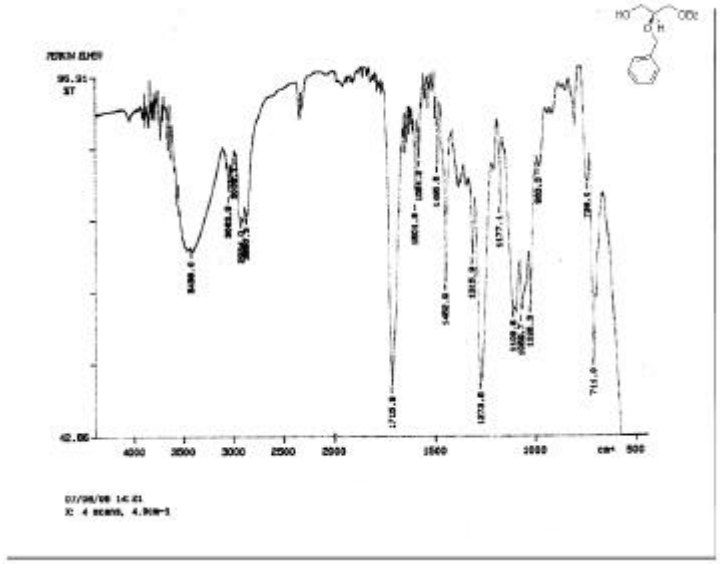


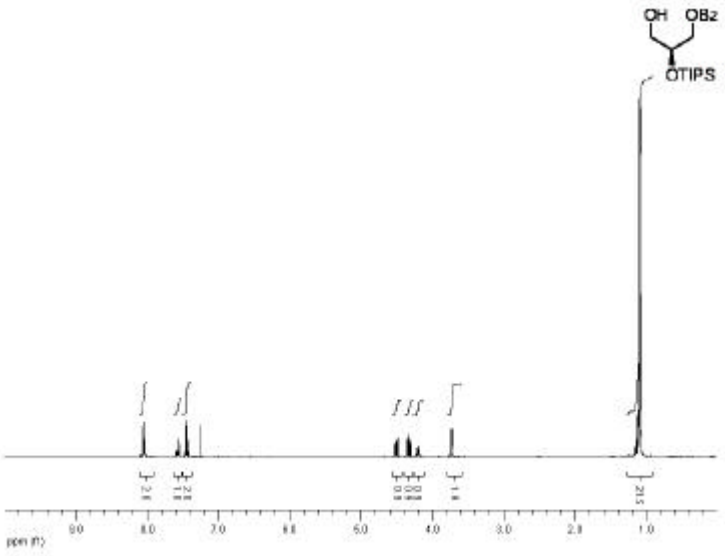


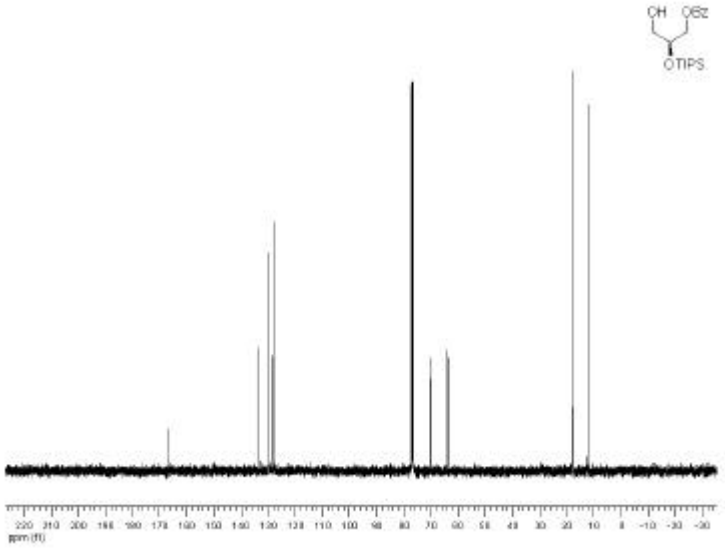









OH
OBz
OTIPS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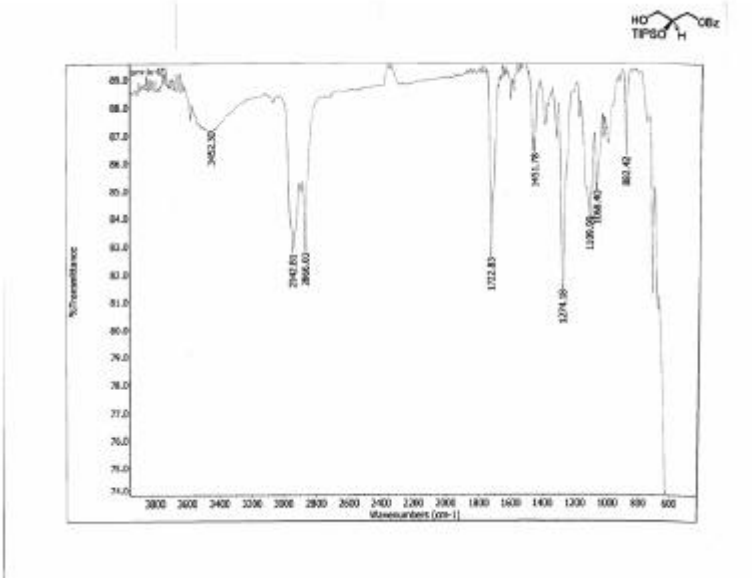
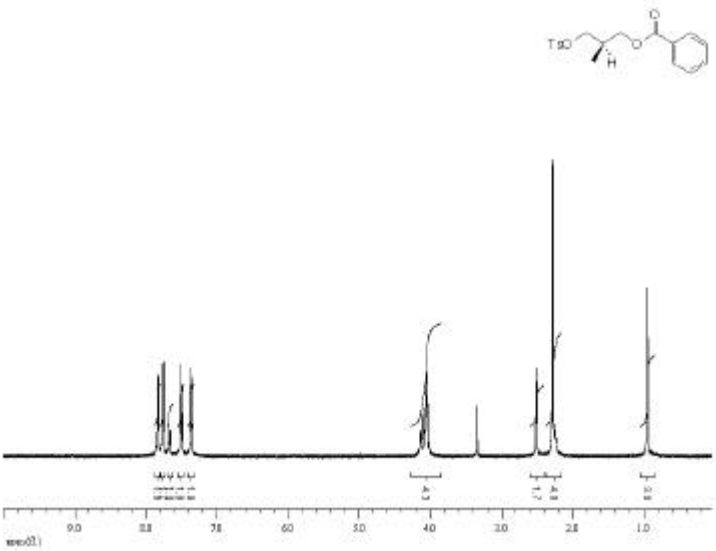
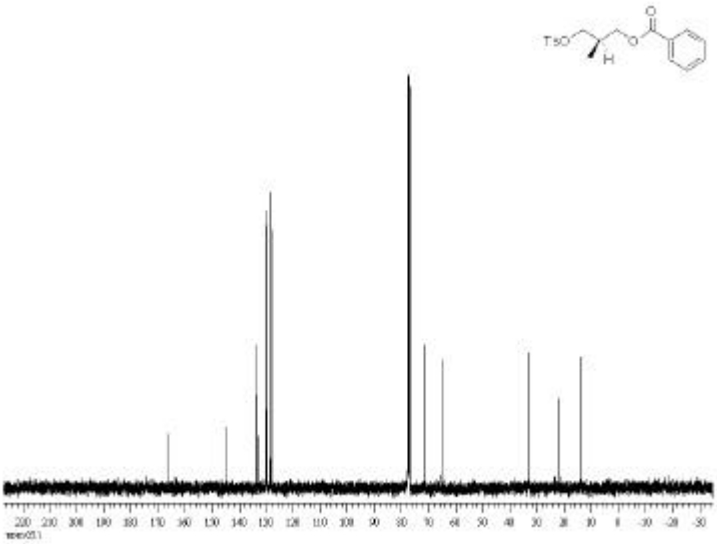
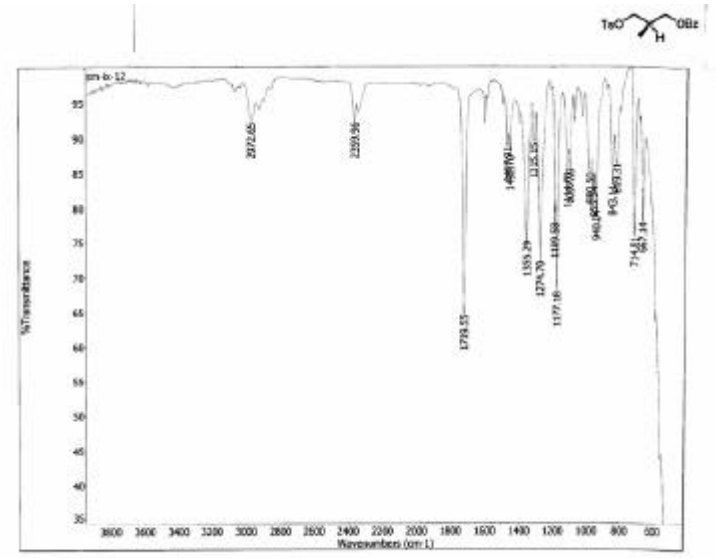
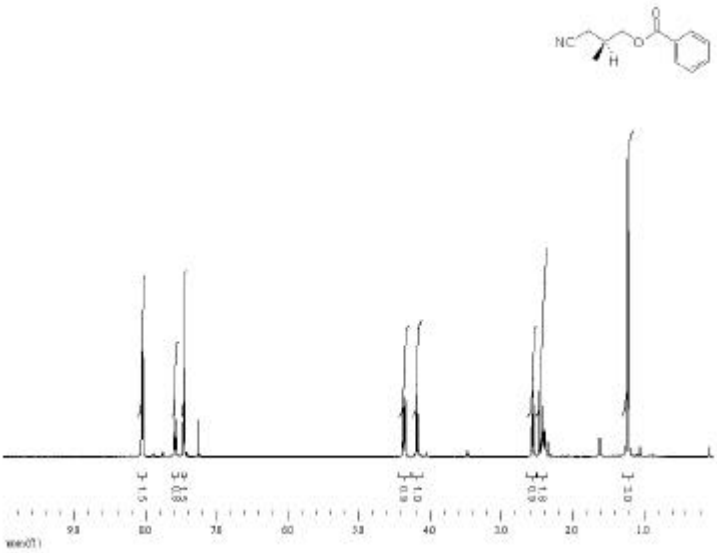
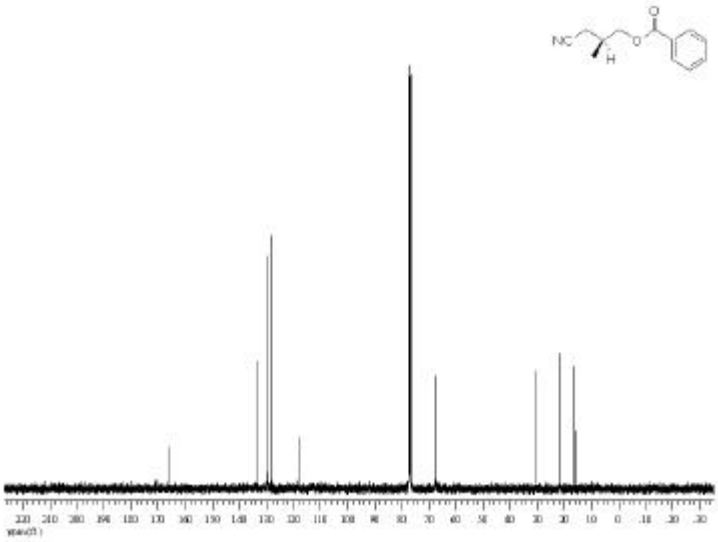

HO
TIPSO
OBz
H

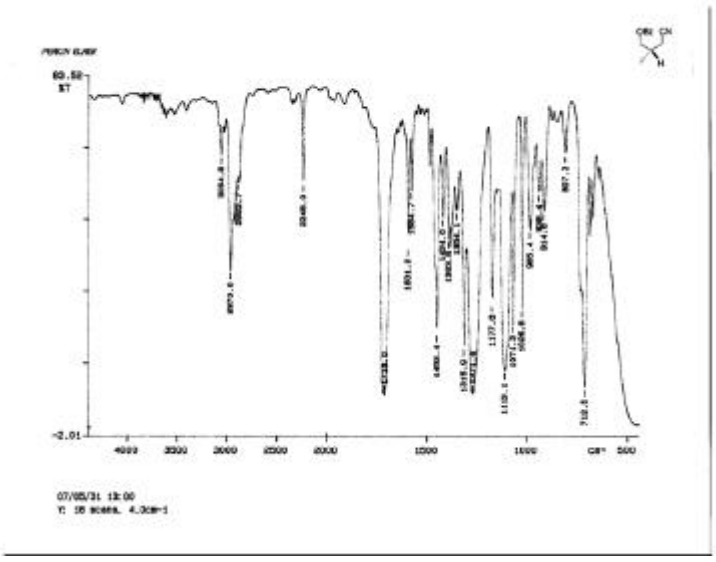


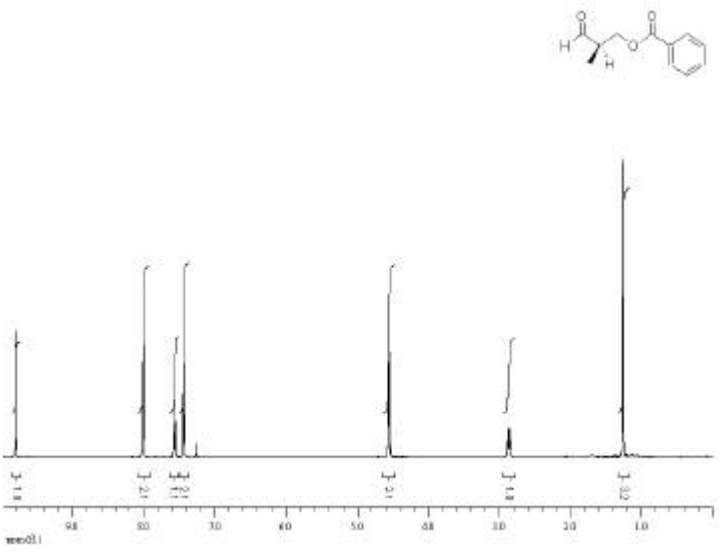


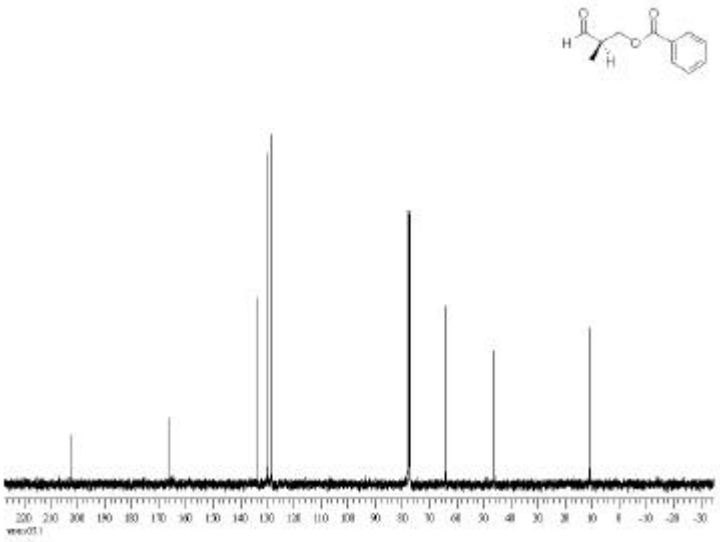


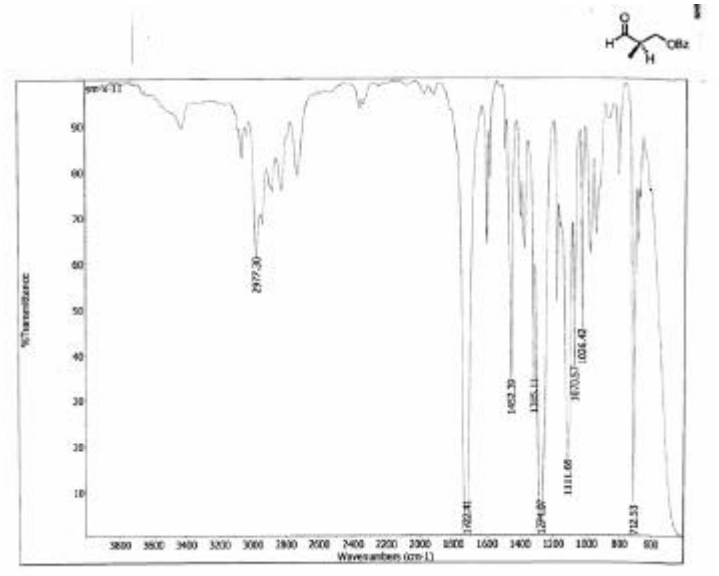


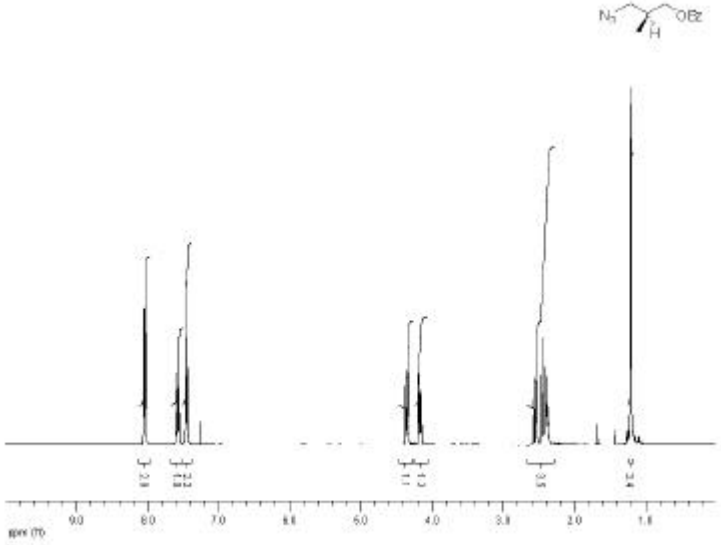


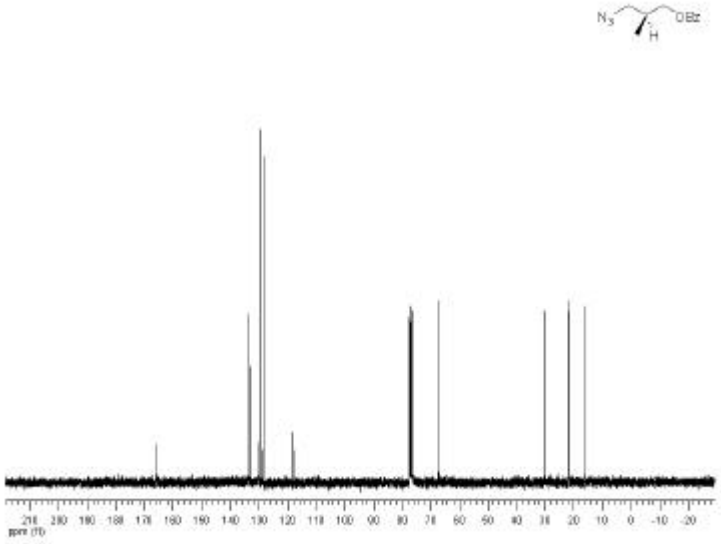


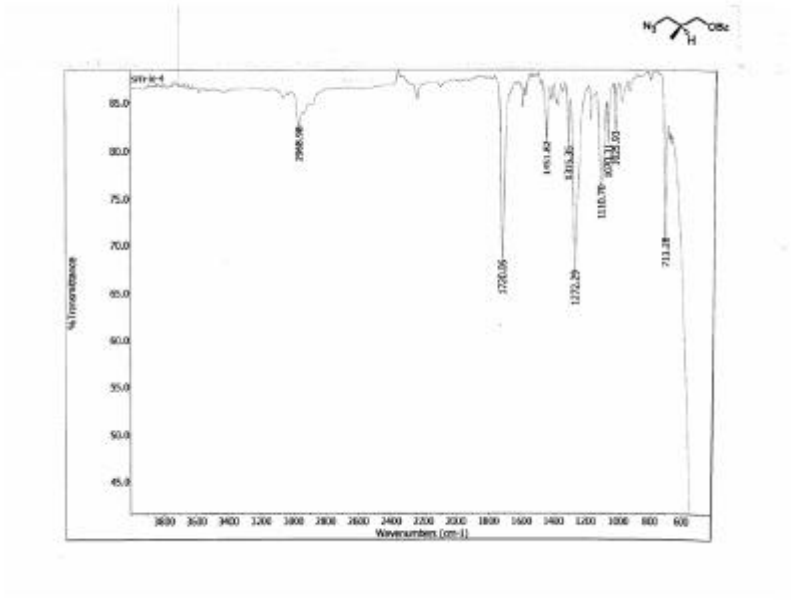


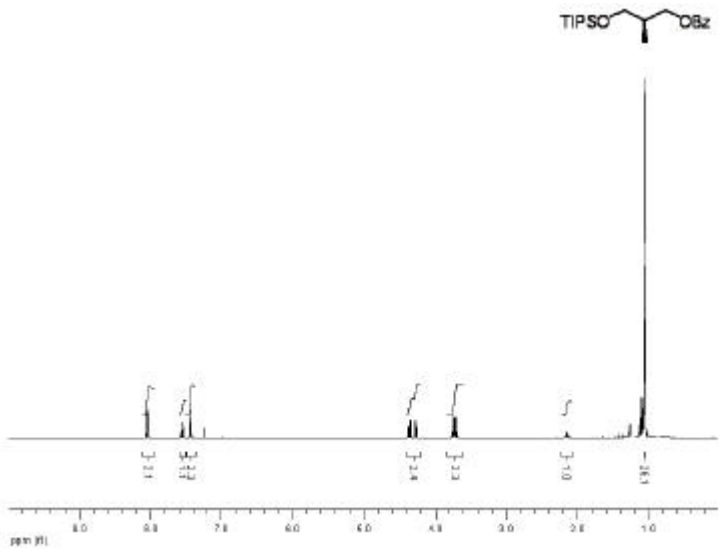


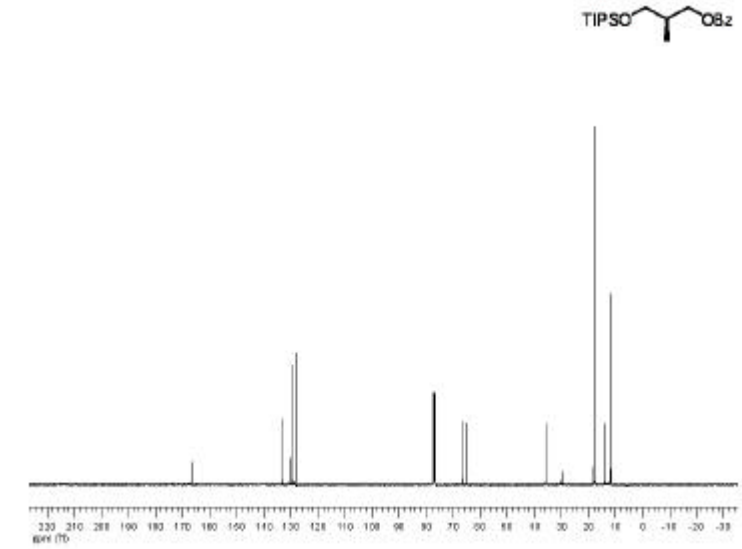

%Transmittance
Wavenumbers (cm-1)
2977.30
1702.41
1652.39
1325.11
1294.69
1170.57
1111.68
1024.42
712.53








TIPSO
OBz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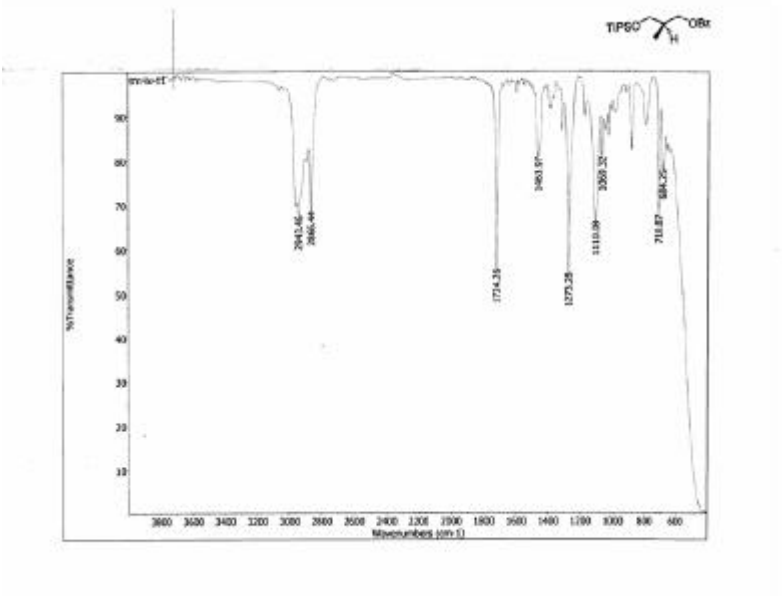
TIPSO
OBz
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2865.44
1734.35
1463.97
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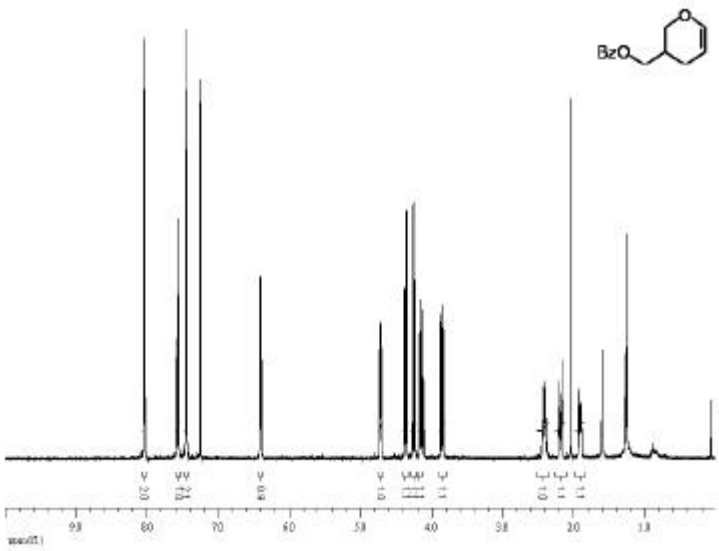
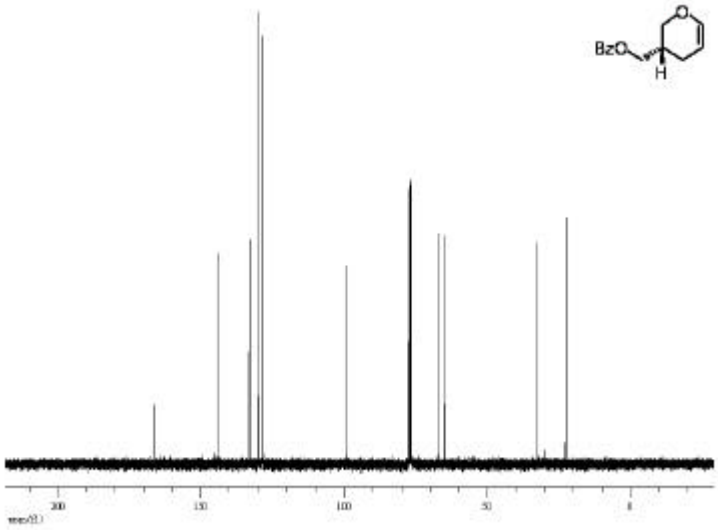
1110.09
1069.32
738.87
694.29


BzO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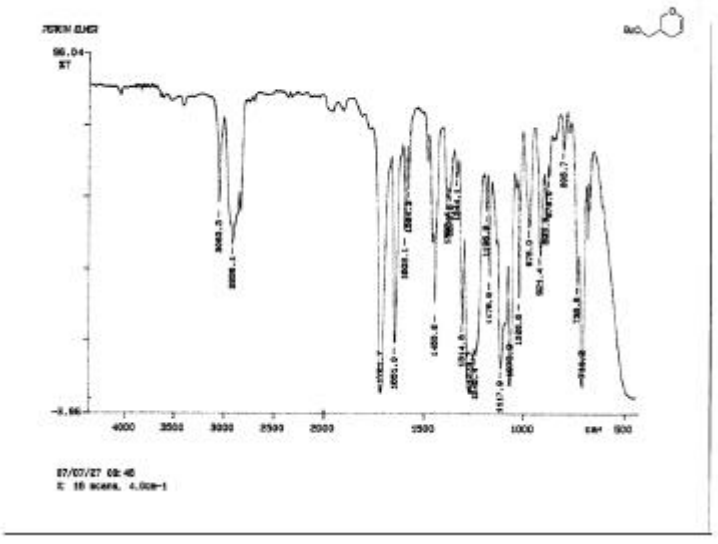

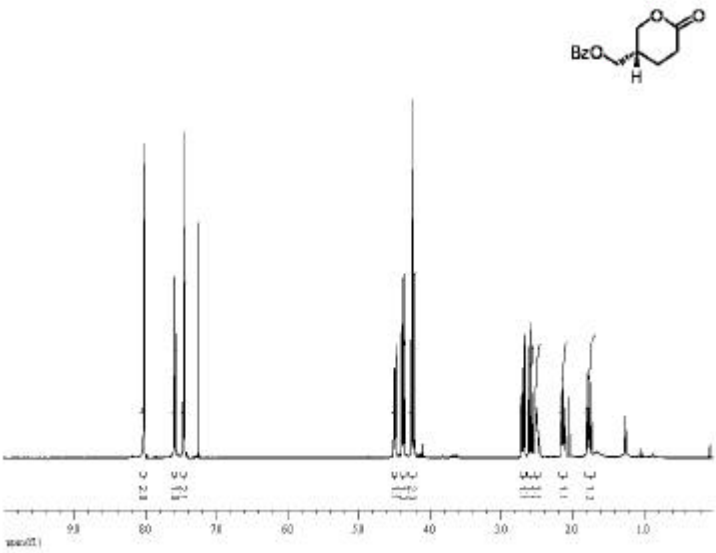
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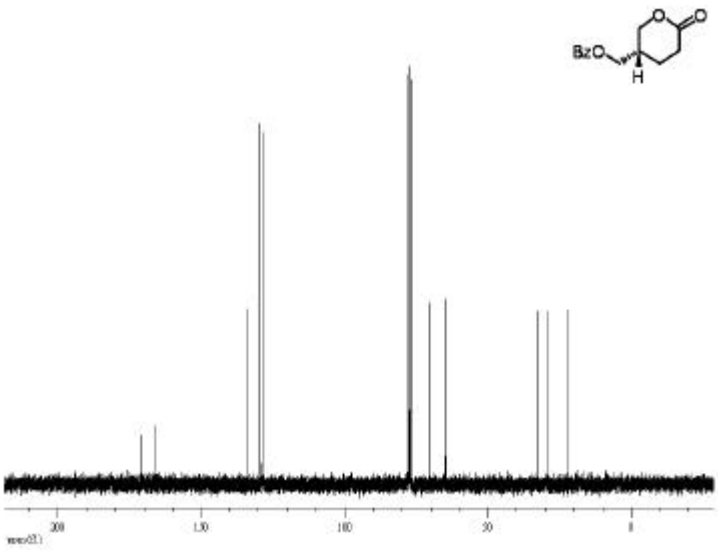
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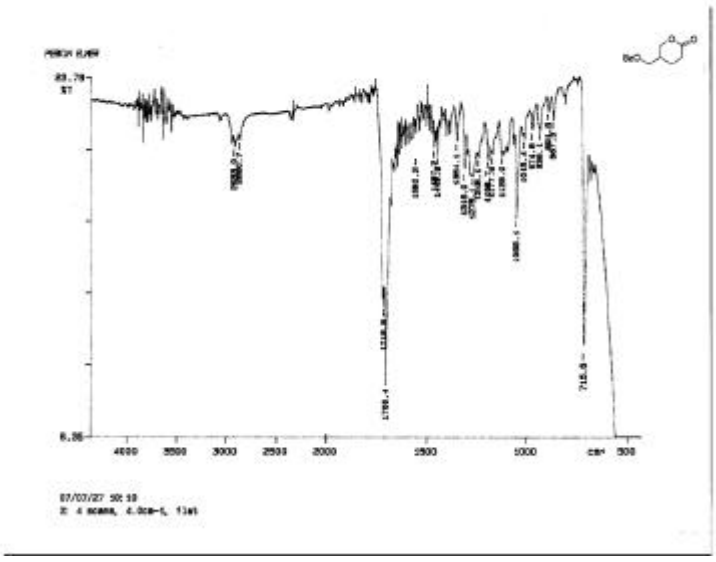

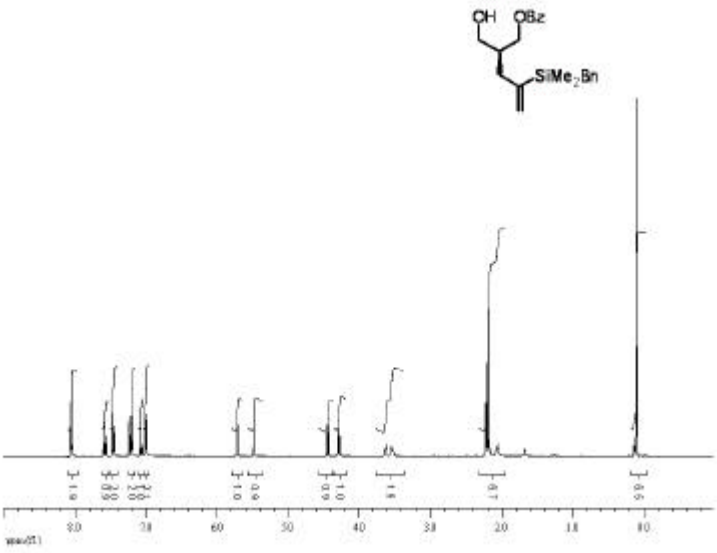
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OBz
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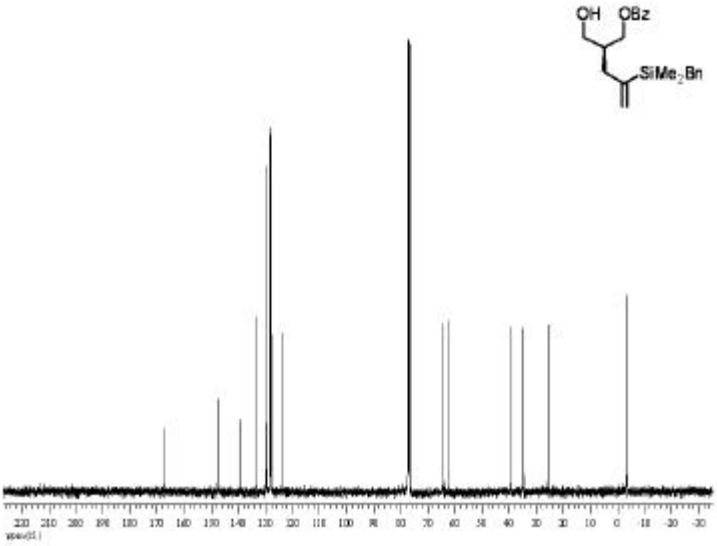
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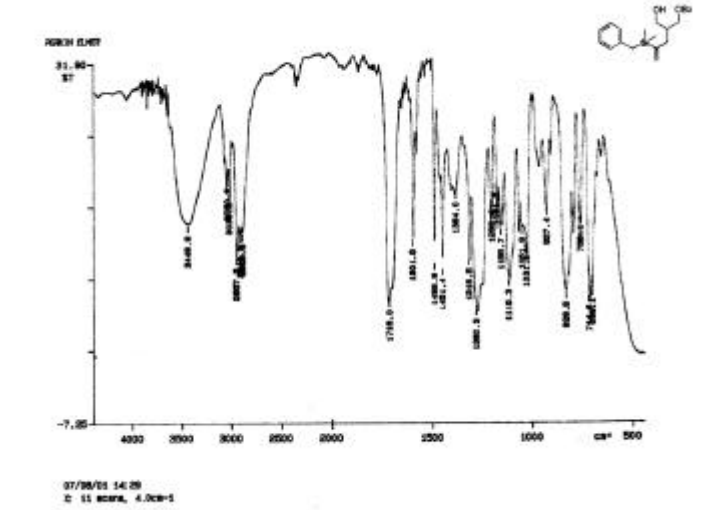

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