Electronic Supplementary Material (ESI) for Chemical Science

Catalytic C–H Hydroxylation by a Triazamacrocyclic Ruthenium Complex

Supplementary Material
(*33 pages*)

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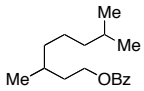
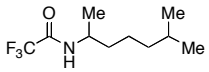
General. All reagents were obtained commercially unless otherwise noted. Moisture-sensitive reactions were performed using flame-dried glassware under an atmosphere of dry nitrogen. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Organic solutions were concentrated under reduced pressure (ca. 15 Torr) by rotary evaporation. Ethyl acetate and *tert*-butanol were used as received. Dichloromethane was dried by passage under 12 psi N_2 through columns containing activated alumina. Chromatographic purification of products was accomplished using forced-flow chromatography on Silicycle Ultra Pure Silica Gel Silia-P (40–63 μm). Compounds purified by chromatography on silica gel were typically applied to the adsorbent bed using the indicated solvent conditions with a minimum amount of added dichloromethane as needed for solubility. Thin layer chromatography was performed on EM Science silica gel 60 F254 plates (250 μm). Visualization of the developed chromatogram was accomplished by fluorescence quenching and by staining with aqueous ceric ammonium molybdate (CAM) solution.

NMR spectra were acquired on a Varian Mercury-300 operating at 300 and 75 MHz or a Varian Mercury-400 operating at 400 and 100 MHz for ^{1}H and ^{13}C, respectively, and are referenced internally according to residual solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s, singlet; bs, broad singlet; d, doublet, t, triplet; q, quartet; sept, septet; m, multiplet), integration, coupling constant (Hz). Data for ^{13}C are reported in terms of chemical shift (δ, ppm). Infrared spectra were recorded as thin films using NaCl salt plates on a Thermo-Nicolet IR300 spectrometer and are reported in frequency of absorption. High-resolution mass spectra were obtained the Vincent Coates Foundation Mass Spectrometry Laboratory, Stanford University.

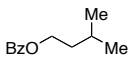
Characterization data for substrates appearing in Tables 1–3, S1:



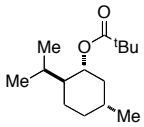
3,7-Dimethyloctyl benzoate (2, Table 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, 2H, J = 7.2 Hz), 7.55 (t, 1H, J = 7.6 Hz), 7.44 (t, 2H, J = 7.6 Hz), 4.42-4.32 (m, 2H), 1.86-1.76 (m, 1H), 1.70-1.46 (m, 3H), 1.42-1.12 (m, 6H), 0.96 (d, 3H, J = 6.4 Hz), 0.87 (d, 6H, J = 6.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 132.9, 130.6, 129.6, 128.4, 63.6, 39.3, 37.2, 35.6, 30.0, 28.0, 24.7, 22.8, 22.7, 19.7 ppm; IR (thin film) ν 2956, 2928, 2870, 1722, 1453, 1314, 1274, 1113, 1070 cm^{-1}.



2-Trifluoroacetamido-6-methylheptane (Table 2, entry 1)[1]: mp = 34–35 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.15 (br s, 1H), 4.03 (sept, 1H, J = 6.8 Hz), 1.58-1.45 (m, 3H), 1.30-1.25 (m, 2H), 1.22 (d, 3H, J = 6.4 Hz), 1.25-1.12 (m, 2H), 0.86 (d, 6H, J = 6.8 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6 (q, $J_{C–F}$ = 36 Hz), 116.0 (q, $J_{C–F}$ = 287 Hz), 46.6, 38.6, 36.6, 27.9, 23.7, 22.6, 20.4 ppm; IR (thin film) ν 3293, 3099, 2958, 2937, 2872, 1697, 1560, 1464, 1386, 1368, 1187, 1164 cm^{-1}.

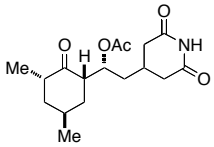


3-Methylbutyl benzoate (Table 2, entry 2): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, 2H, J = 7.2 Hz), 7.55 (t, 1H, J = 7.6 Hz), 7.44 (t, 2H, J = 7.6 Hz), 4.36 (t, 2H, J = 6.4 Hz), 1.80 (sept, 1H, J = 6.8 Hz), 1.66 (q, 2H, J = 6.8 Hz), 0.98 (d, 6H, J = 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 132.9, 130.5, 129.6, 128.4, 63.7, 37.5, 25.3, 22.6 ppm; IR (thin film) ν 2959, 2872, 1721, 1466, 1453, 1314, 1275, 1175, 1113, 1070, 1027 cm^{-1}.

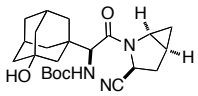


Menthyl pivalate (Table 2, entry 3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.61 (dt, 1H, *J* = 10.8, 4.4 Hz), 1.97-1.90 (m, 1H), 1.88 (dquintet, 1H, *J* = 6.8, 2.8 Hz), 1.71-1.62 (m, 2H), 1.53-1.33 (m, 2H), 1.17 (s, 9H), 1.10-0.80 (m, 3H), 0.88 (d, 6H, *J* = 6.8 Hz), 0.73 (d, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.1, 73.8, 47.1, 40.8, 38.9, 34.4, 31.4, 27.2, 26.2, 23.3, 22.1, 20.9, 16.1 ppm; IR (thin film) ν 2957, 2871, 1727, 1480, 1458, 1395, 1369, 1287, 1166, 1037, 984 cm^{-1}.

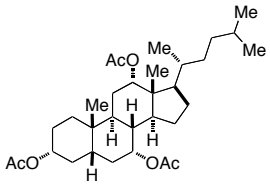
4-Oxatricyclo[4.3.1.1^{3,8}]undecan-5-one (Table 2, entry 4): mp >260 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.46 (quintet, 1H, *J* = 2.8 Hz), 3.04 (t, 1H, *J* = 6.0 Hz), 2.12-2.06 (m, 2H), 2.05-1.86 (m, 6H), 1.84-1.77 (m, 2H), 1.76-1.65 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.1, 73.2, 41.2, 35.7, 33.8, 30.9, 25.8 ppm; IR (thin film) ν 2916, 2853, 1716, 1393, 1265, 1169, 1107, 1082, 1035, 976 cm^{-1}.



Cycloheximide acetate (Table 2, entry 5): mp 136–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (br s, 1H), 5.32 (dt, 1H, *J* = 8.4, 3.6 Hz), 2.93 (ddd, 1H, *J* = 17.2, 4.0, 1.6 Hz), 2.70-2.53 (m, 3H), 2.37 (dd, 1H, *J* = 17.6, 10.4 Hz), 2.25 (dd, 1H, *J* = 17.2, 10.4 Hz), 2.20-2.10 (m, 2H), 2.05 (s, 3H), 1.92-1.82 (m, 2H), 1.73-1.55 (m, 4H), 1.23 (d, 3H, *J* = 7.2 Hz), 0.97 (d, 3H, *J* = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.4, 172.0, 171.8, 170.6, 69.5, 49.3, 42.8, 40.9, 38.9, 38.4, 37.0, 36.5, 27.4, 26.9, 21.1, 18.2, 14.3 ppm; IR (thin film) ν 3232, 2964, 2930, 1734, 1704, 1373, 1246, 1149 cm^{-1}.

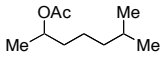


(*S*)-*N*-Boc-3-hydroxyadamantylglycine-L-*cis*-4,5-methanoprolinenitrile (Table 2, entry 6)[2]: mp 108–110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.36 (d, 1H, *J* = 10.0 Hz), 5.01 (dd, 1H, *J* = 10.8, 2.4 Hz), 4.43 (d, 1H, *J* = 10.0 Hz), 3.83 (q, 1H, *J* = 6.0 Hz), 2.55 (ddd, 1H, *J* = 13.6, 10.4, 5.6 Hz), 2.34 (dd, 1H, *J* = 13.6, 2.4), 2.22 (br s, 2H), 2.08 (br s, 1H), 1.86 (quintet, 1H, *J* = 7.2 Hz), 1.77 (d, 1H, *J* = 11.6 Hz), 1.74-1.58 (m, 6H), 1.56-1.38 (m, 5H), 1.41 (s, 9H), 1.08-1.00 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 155.8, 119.3, 79.9, 68.5, 58.6, 46.2, 45.1, 44.3, 44.2, 41.2, 38.0, 37.6, 37.0, 35.2, 30.4, 30.18, 30.16, 28.4, 17.8, 13.5 ppm; IR (thin film) ν 3440, 2922, 2853, 2250, 1702, 1645, 1503, 1450, 1427, 1367, 1314, 1249, 1168, 1048, 911 cm^{-1}.

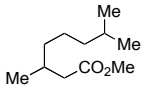


3α,7α,12α-Triacetoxy-5β-24-norcholestane (Table 2, entry 7): mp 62–64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.07 (t, 1H, *J* = 2.8 Hz), 4.88 (q, 1H, *J* = 2.8 Hz), 4.55 (tt, 1H, *J* = 11.2, 4.4 Hz), 2.12 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H),

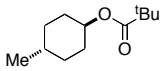
2.02-0.92 (m, 25H), 0.89 (s, 3H), 0.84 (d, 3H, J = 6.4 Hz), 0.82 (d, 3H, J = 6.4 Hz), 0.70 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.64, 170.58, 170.45, 75.6, 74.2, 70.8, 47.7, 45.0, 43.4, 41.0, 37.8, 35.3, 35.2, 34.7, 34.6, 34.4, 33.4, 31.3, 28.9, 28.4, 27.3, 26.9, 25.6, 23.1, 22.9, 22.6, 22.4, 21.7, 21.6, 21.5, 18.0, 12.3 ppm; IR (thin film) ν 2953, 2870, 1736, 1377, 1248, 1025 cm^{-1}.



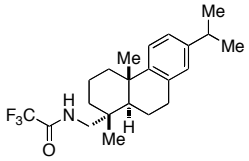
6-Methylheptan-2-yl acetate (Table S1, entry 2)[3]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87 (tq, 1H, J = 6.8, 6.8 Hz), 2.00 (s, 3H), 1.60-1.38 (m, 3H), 1.35-1.22 (m, 2H), 1.20-1.10 (m, 5H), 0.84 (d, 6H, J = 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 71.1, 38.7, 36.2, 27.9, 23.2, 22.60, 22.58, 21.4, 20.0 ppm; IR (thin film) ν 2955, 2870, 1739, 1466, 1371, 1247, 1126, 1042, 1020 cm^{-1}.



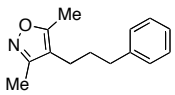
Methyl 3,7-dimethyloctanoate (Table S1, entry 3): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.66 (s, 3H), 2.30 (dd, 1H, J = 14.8, 6.0 Hz), 2.11 (dd, 1H, J = 14.4, 8.0 Hz), 1.94 (tq, 1H, J = 6.8, 6.8 Hz), 1.52 (sept, 1H, J = 6.8 Hz), 1.36-1.10 (m, 6H), 0.93 (d, 3H, J = 6.4 Hz), 0.86 (d, 6H, J = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 51.4, 41.8, 39.1, 37.0, 30.5, 28.0, 24.7, 22.7, 22.6, 19.8 ppm; IR (thin film) ν 2955, 2929, 2871, 1742, 1463, 1436, 1206, 1171 cm^{-1}.



***trans*-4-Methylcyclohexyl pivalate (Table S1, entry 5):** ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62 (tt, 1H, J = 11.2, 4.4 Hz), 1.91 (dd, 2H, J = 13.2, 4.4 Hz), 1.72 (d, 2H, J = 12.8 Hz), 1.41-1.25 (m, 3H), 1.17 (s, 9H), 1.03 (dq, 2H, J = 13.2, 3.2 Hz), 0.89 (d, 3H, J = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 72.9, 38.6, 33.0, 31.7, 31.4, 27.2, 21.9 ppm; IR (thin film) ν 2954, 2869, 1726, 1480, 1456, 1397, 1365, 1284, 1169, 1086, 1033, 1021, 995 cm^{-1}.

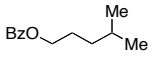


2,2,2-Trifluoro-*N*-(((1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)-methyl)acetamide (Table 3, entry 3): mp 48–50 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, 1H, J = 8.0 Hz), 7.04 (dd, 1H, J = 8.4, 2.0 Hz), 6.94 (d, 1H, J = 1.6 Hz), 6.43 (br s, 1H), 3.37-3.25 (m, 2H), 2.97 (dd, 1H, J = 17.6, 6.8 Hz), 2.91-2.79 (m, 2H), 2.35 (d, 1H, J = 12.4 Hz), 1.93-1.79 (m, 4H), 1.56-1.39 (m, 3H), 1.34-1.24 (m, 10H), 1.02 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6 (q, $J_{C–F}$ = 36 Hz), 146.7, 145.9, 134.5, 127.0, 124.2, 124.1, 116.0 (q, $J_{C–F}$ = 286 Hz), 50.4, 45.9, 38.2, 37.6, 36.2, 33.5, 30.2, 25.4, 24.02, 24.00, 19.1, 18.49, 18.47 ppm; IR (thin film) ν 3322, 2960, 2870, 1707, 1559, 1458, 1209, 1166, 910 cm^{-1}.

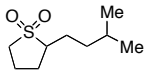


3,5-Dimethyl-4-(3-phenylpropyl)isoxazole (Table 3, entry 4): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (t, 2H, J = 7.2 Hz), 7.21 (d, 1H, J = 7.2 Hz), 7.17 (d, 2H, J = 7.2 Hz), 2.62 (t, 2H, J = 8.0 Hz), 2.33 (t, 2H, J = 7.6 Hz), 2.27 (s, 3H), 2.18 (s, 3H), 1.79 (tt, 2H, J = 7.6, 7.6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8, 259.8, 141.6, 128.5,

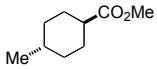
128.4, 126.1, 113.3, 35.4, 31.3, 21.8, 11.0, 10.3 ppm; IR (thin film) ν 3027, 2931, 2859, 1638, 1496, 1453, 1424, 1194, 892 cm^{-1}.



4-Methylpentyl benzoate (Table S1, entry 1): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, 2H, *J* = 6.8 Hz), 7.55 (t, 1H, *J* = 7.2 Hz), 7.44 (t, 2H, *J* = 7.6 Hz), 4.31 (t, 2H, *J* = 6.8 Hz), 1.76 (tt, 2H, *J* = 9.2, 6.8 Hz), 1.61 (sept, 1H, *J* = 6.8 Hz), 1.33 (dt, 2H, *J* = 9.2, 6.8 Hz), 0.92 (d, 6H, *J* = 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 132.9, 130.6, 129.6, 128.4, 65.5, 53.2, 27.8, 26.7, 22.6 ppm; IR (thin film) ν 2957, 2871, 1722, 1468, 1452, 1315, 1275, 1176, 1112, 1070, 1027 cm^{-1}.



2-(3-Methylbutyl)tetrahydrothiophene-1,1-dioxide (Table S1, entry 4): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.15 (ddd, 1H, *J* = 13.2, 8.8, 4.4 Hz), 2.97 (ddd, 1H, *J* = 13.2, 9.9, 8.1 Hz), 2.87 (dq, 1H, *J* = 11.1, 7.2 Hz), 2.36-2.24 (m, 1H), 2.20-2.07 (m, 1H), 2.06-1.94 (m, 1H), 1.94-1.80 (m, 1H), 1.77-1.62 (m, 1H), 1.64-1.20 (m, 4H), 0.90 (dd, 6H, *J* = 6.6, 2.1 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 61.4, 51.2, 36.1, 29.4, 27.9, 25.7, 22.4, 22.2, 20.1 ppm; IR (thin film) ν 2955, 2870, 1468, 1417, 1386, 1368, 1300, 1262, 1140, 1113 cm^{-1}.

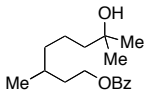


Methyl *trans*-4-methylcyclohexanecarboxylate (Table S1, entry 6)[4]: ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3H), 2.18 (tt, 1H, *J* = 12.3, 3.6 Hz), 1.96-1.87 (m, 2H), 1.77-1.68 (m, 2H), 1.47-1.33 (m, 3H), 0.97-0.82 (m, 2H), 0.85 (d, 3H, *J* = 6.3 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 51.5, 43.1, 34.3, 32.0, 29.1, 22.5 ppm; IR (thin film) ν 2950, 2929, 2868, 2847, 1738, 1450, 1435, 1377, 1318, 1270, 1252, 1194, 1164, 1140, 1084, 1038, 1014 cm^{-1}.

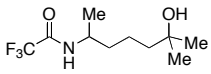
(1,4,7-Trimethyl-1,4,7-triazacyclononane)ruthenium(III) trichloride[5] and *trans*-(1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane)dichlororuthenium(III) chloride[6] were prepared according to literature procedures.

General Procedure for Catalytic C–H Hydroxylation. A 16 x 125 mm disposable test tube fitted with a rubber septum and stir bar was charged with $(Me_3tacn)RuCl_3$ (2 mg, 5.0 μmol, 0.02 equiv, unless otherwise noted), $AgClO_4$ (4 mg, 0.02 mmol, 0.08 equiv, unless otherwise noted), and 2.0 mL of H_2O. The mixture was stirred at 80 °C for 5 min, during which time AgCl precipitate formed. After cooling the reaction to room temperature, a solution of substrate (0.25 mmol unless otherwise noted) in 2.0 mL of *tert*-butanol was added, followed by solid ceric ammonium nitrate (411 mg, 0.75 mmol, 3.0 equiv). The resulting deep red mixture was stirred until the color faded to orange or yellow (generally 10–30 min), at which time an additional 411 mg of ceric ammonium nitrate was added. When TLC indicated that the reaction had ceased (see below for specific reaction times), the reaction was quenched with MeOH (~1 mL) and the contents transferred to a separatory funnel with 30 mL of H_2O. The aqueous mixture was extracted with 3 × 25 mL of EtOAc. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by chromatography on silica gel (conditions given below) afforded the desired alcohol product.

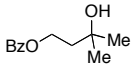
Characterization data for all products appearing in Tables 1–3:



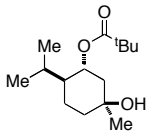
7-Hydroxy-3,7-dimethyloctyl benzoate (3, Table 1): The reaction was performed with 66 mg of substrate using 1 mg of (Me_3tacn)$RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 1.5 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). Colorless oil (35 mg, 50%); TLC R_f = 0.4 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, 2H, *J* = 8.4 Hz), 7.55 (t, 1H, *J* = 8.0 Hz), 7.44 (t, 2H, *J* = 8.4 Hz), 4.42-4.30 (m, 2H), 1.86-1.77 (m, 1H), 1.72-1.53 (m, 2H), 1.48-1.31 (m, 6H), 1.25-1.15 (m, 1H), 1.21 (s, 6H), 0.97 (d, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 132.9, 130.5, 129.6, 128.4, 71.0, 63.6, 44.2, 37.5, 35.6, 30.0, 29.4, 29.3, 21.7, 19.6 ppm; IR (thin film) ν 3421, 2965, 2935, 1719, 1453, 1378, 1275, 1114 cm^{-1}; HRMS (ES$^+$) calcd for $C_{17}H_{26}O_3$ 278.1882 found 301.1772 (MNa^+).



2-Hydroxy-2-methyl-6-trifluoroacetamidoheptane (Table 2, entry 1): The reaction was performed with 66 mg of substrate using 1 mg of (Me_3tacn)$RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 1.5 h. The product was purified by chromatography on silica gel (1:2 EtOAc/hexanes). Colorless oil (50 mg, 82%); TLC R_f = 0.15 (1:3 EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (br d, 1H, *J* = 6.3 Hz), 4.02 (sept, 1H, *J* = 6.9 Hz), 2.01 (br s, 1H), 1.62-1.32 (m, 6H), 1.21 (d, 3H, *J* = 6.9 Hz), 1.19 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.7 (q, J_{C-F} = 37 Hz), 115.9 (q, J_{C-F} = 286 Hz), 70.9, 46.5, 43.1, 36.6, 29.4, 29.2, 20.6, 20.4 ppm; IR (thin film) ν 3293, 3086, 2975, 2943, 1701, 1561, 1462, 1379, 1189, 1160, 939, 908, 724 cm^{-1}; HRMS (ES$^+$) calcd for $C_{10}H_{18}F_3NO_2$ 241.1290 found 242.1362 (MH^+).

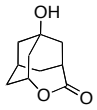


3-Hydroxy-3-methylbutyl benzoate (Table 2, entry 2): The reaction was performed with 48 mg of substrate and was stirred for 14 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). Colorless oil (30 mg, 58%); TLC R_f = 0.4 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, 2H, *J* = 6.8 Hz), 7.55 (t, 1H, *J* = 6.8 Hz), 7.43 (t, 2H, *J* = 6.8 Hz), 4.50 (t, 2H, *J* = 6.8 Hz), 1.98 (t, 2H, *J* = 6.8 Hz), 1.92 (br s, 1H), 1.32 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 133.0, 130.3, 129.6, 128.5, 70.2, 62.0, 41.8, 29.8 ppm; IR (thin film) ν 3425, 2972, 1719, 1452, 1316, 1278, 1176, 1117 cm^{-1}; HRMS (ES$^+$) calcd for $C_{12}H_{16}O_3$ 208.1099 found 231.0991 (MNa^+).

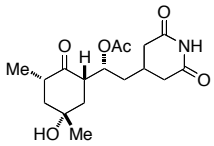


(1R,2S,5S)-5-Hydroxy-2-isopropyl-5-methylcyclohexyl pivalate (Table 2, entry 3): The reaction was performed with 60 mg of substrate and was stirred for 15 h. The product was purified by chromatography on silica gel (gradient elution: 1:7→1:3 EtOAc/hexanes). Colorless oil (29 mg, 45%); mp 59–60 °C; TLC R_f = 0.5 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.94 (dt, 1H, *J* = 10.8, 4.4 Hz), 1.99 (ddd, 1H, *J* = 12.8, 4.4, 2.4 Hz), 1.90 (d quintet, 1H, *J* = 7.2, 2.8 Hz), 1.68 (dq, 1H, *J* = 13.2, 2.8 Hz), 1.55-1.25 (m, 6H), 1.23 (s, 3H), 1.17 (s, 9H), 0.91 (d, 3H, *J* = 6.8 Hz), 0.78 (d, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.1, 71.6, 71.1, 47.1,

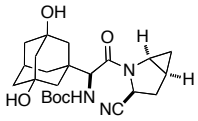
44.6, 38.9, 37.9, 31.5, 27.2, 26.2, 20.9, 19.2, 16.3 ppm; IR (thin film) ν 3454, 2961, 2874, 1726, 1705, 1481, 1462, 1370, 1293, 1175, 1157 cm^{-1}; HRMS (ES^+) calcd for $C_{15}H_{28}O_3$ 256.2038 found 279.1936 (MNa^+).



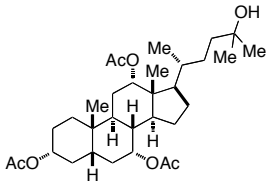
1-Hydroxy-4-oxatricyclo[4.3.1.1^{3,8}]undecan-5-one (Table 2, entry 4): The reaction was performed with 42 mg of substrate and was stirred for 22 h. The product was purified by chromatography on silica gel (5% MeOH/CH_2Cl_2). White solid (23 mg, 50%); mp >260 °C; TLC R_f = 0.3 (5% MeOH/CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66-4.60 (m, 1H), 3.22-3.16 (m, 1H), 2.44 (t, 1H, *J* = 3.2 Hz), 2.10 (dq, 1H, *J* = 14.4, 2.4 Hz), 1.99-1.89 (m, 4H), 1.88-1.82 (m, 2H), 1.79-1.69 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.8, 74.4, 66.9, 43.8, 42.3, 41.6, 39.0, 34.7, 30.4, 29.9 ppm; IR (thin film) ν 3406, 2926, 1721, 1396, 1361, 1171, 1148, 1116, 1069, 1036 cm^{-1}; HRMS (ES^+) calcd for $C_{10}H_{14}O_3$ 182.0943 found 205.0841 (MNa^+).



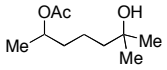
(R)-2-(2,6-Dioxopiperidin-4-yl)-1-((1S,3S,5R)-5-hydroxy-3,5-dimethyl-2-oxocyclohexyl)ethyl acetate (Table 2, entry 5): The reaction was performed with 40 mg (0.125 mmol) of substrate using 2 mg of (Me_3tacn)$RuCl_3$ (5.0 μmol, 0.04 equiv) and 4 mg of $AgClO_4$ (0.02 mmol, 0.16 equiv), and was stirred for 5 h. The product was purified by chromatography on silica gel (gradient elution: 2.5→5% MeOH/CH_2Cl_2). White foam (26 mg, 61%); mp = 96–98 °C; TLC R_f = 0.35 (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (br s, 1H), 5.35-5.28 (m, 1H), 2.90 (ddd, 1H, *J* = 17.2, 4.0, 1.6 Hz), 2.61 (ddd, 1H, *J* = 16.8, 4.0, 1.6 Hz), 2.56-2.42 (m, 2H), 2.35 (dd, 1H, *J* = 17.2, 10.0 Hz, 1H), 2.26 (dd, 1H, *J* = 16.8, 10.4 Hz), 2.20-2.09 (m, 1H), 2.07-1.97 (m, 2H), 2.05 (s, 3H), 1.76-1.58 (m, 4H), 1.56 (s, 3H), 1.00 (d, 3H, *J* = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.5, 172.1, 172.0, 170.6, 69.6, 68.9, 50.2, 49.0, 42.5, 42.1, 38.8, 38.3, 36.9, 27.3, 26.2, 21.0, 14.2 ppm; IR (thin film) ν 3451, 3237, 2971, 2933, 1703, 1375, 1261, 1151, 919 cm^{-1}; HRMS (ES^+) calcd for $C_{17}H_{25}NO_6$ 339.1682 found 362.1566 (MNa^+).



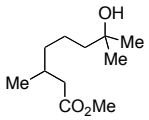
(*S*)-*N*-Boc-3,5-dihydroxyadamantylglycine-L-*cis*-4,5-methanoprolinenitrile (Table 2, entry 6): The reaction was performed with 52 mg (0.125 mmol) of substrate using 2 mg of (Me_3tacn)$RuCl_3$ (5.0 μmol, 0.04 equiv) and 4 mg of $AgClO_4$ (0.02 mmol, 0.16 equiv), and was stirred for 5 h. The product was purified by chromatography on silica gel (7.5% MeOH/CH_2Cl_2). White foam (27 mg, 50%); mp = 138–140 °C; TLC R_f = 0.6 (10% MeOH/CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.56 (d, 1H, *J* = 10.0 Hz), 5.02 (dd, 1H, *J* = 10.4, 2.4 Hz), 4.54 (d, 1H, *J* = 9.6 Hz), 3.85-3.81 (m, 1H), 2.60-2.52 (m, 1H), 2.44-2.30 (m, 4H), 1.93-1.85 (m, 1H), 1.82-1.67 (m, 4H), 1.66-1.44 (m, 8H), 1.42 (s, 9H), 1.40-1.32 (m, 1H), 1.12-1.04 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 155.9, 119.3, 80.1, 70.4, 58.0, 52.0, 45.4, 45.2, 45.1, 43.0, 42.9, 42.6, 38.1, 36.5, 30.4, 28.4, 17.9, 13.7 ppm; IR (thin film) ν 3433, 2932, 2246, 1697, 1644, 1504, 1454, 1427, 1367, 1334, 1249, 1163, 1049 cm^{-1}; HRMS (ES^+) calcd for $C_{23}H_{33}N_3O_5$ 431.2420 found 454.2318 (MNa^+).



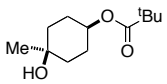
3α,7α,12α-Triacetoxy-5β-24-norcholestan-24-ol (Table 2, entry 7): The reaction was performed with 67 mg (0.125 mmol) of substrate using 5 mg of $(Me_3tacn)RuCl_3$ (0.0125 mmol, 0.1 equiv) and 10 mg of $AgClO_4$ (0.05 mmol, 0.4 equiv), and was stirred for 2 h. The product was purified by chromatography on silica gel (5% MeOH/CH_2Cl_2). White foam (39 mg, 57%); mp 80–82 °C; TLC R_f = 0.6 (5% MeOH/ CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (t, 1H, *J* = 2.8 Hz), 4.89 (d, 1H, *J* = 2.8 Hz), 4.56 (tt, 1H, *J* = 11.2, 4.4 Hz), 2.12 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H), 2.20-1.00 (m, 25H), 1.18 (s, 6H), 0.90 (s, 3H), 0.80 (d, 3H, *J* = 6.4 Hz), 0.72 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.64, 170.63, 170.5, 75.5, 74.2, 71.2, 70.8, 47.4, 45.1, 43.4, 41.0, 39.9, 37.8, 35.2, 34.74, 34.67, 34.4, 31.3, 30.1, 29.3, 29.2, 29.0, 27.3, 26.9, 25.6, 22.9, 22.6, 21.7, 21.6, 21.5, 18.0, 12.3 ppm; IR (thin film) ν 3454, 2943, 2871, 1735, 1378, 1249, 1025 cm^{-1}; HRMS (ES$^+$) calcd for $C_{32}H_{52}O_7$ 548.3713 found 571.3597 (MNa^+).



6-Hydroxy-6-methylheptan-2-yl acetate (Table S1, entry 2): The reaction was performed with 43 mg of substrate and was stirred for 3 h. The product was purified by chromatography on silica gel (25-50% EtOAc/hexanes). Colorless oil (30 mg, 63%); TLC R_f = 0.35 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.90 (tq, H, *J* = 6.8, 6.8 Hz), 2.02 (s, 3H), 1.64-1.54 (m, 1H), 1.52-1.30 (m, 6H), 1.21 (d, 3H, *J* = 6.4 Hz), 1.20 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 70.90, 70.89, 43.6, 36.4, 29.4, 29.3, 21.5, 20.2, 20.1 ppm; IR (thin film) ν 3445, 2972, 1736, 1718, 1374, 1245, 1130, 1026 cm^{-1}; HRMS (ES$^+$) calcd for $C_{10}H_{20}O_3$ 188.1412 found 211.1312 (MNa^+).

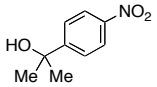


Methyl 7-hydroxy-3,7-dimethyloctanoate (Table S1, entry 3): The reaction was performed with 47 mg of substrate using 1 mg of $(Me_3tacn)RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 6 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). Colorless oil (23 mg, 46%); TLC R_f = 0.3 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65 (s, 3H), 2.30 (dd, 1H, *J* = 14.8, 6.0 Hz), 2.11 (dd, 1H, *J* = 14.8, 8.0 Hz), 1.96 (sept, 1H, *J* = 6.8 Hz), 1.49 (br s, 1H), 1.46-1.25 (m, 5H), 1.24-1.14 (m, 1H), 1.20 (s, 6H), 0.93 (d, 3H, *J* = 6.4 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 71.0, 51.5, 44.0, 41.7, 37.2, 30.4, 29.4, 29.3, 21.7, 19.8 ppm; IR (thin film) ν 3424, 2966, 1739, 1463, 1438, 1378, 1286, 1258, 1193 cm^{-1}; HRMS (ES$^+$) calcd for $C_{11}H_{22}O_3$ 202.1569 found 225.1460 (MNa^+).

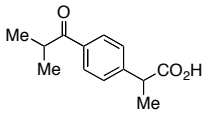


***cis*-4-Hydroxy-4-methylcyclohexyl pivalate (Table S1, entry 5):** The reaction was performed with 50 mg of substrate substrate using 1 mg of $(Me_3tacn)RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 12 h. The product was purified by chromatography on silica gel (1:7 EtOAc/hexanes). White solid (28 mg, 52%); mp = 31–32 °C, TLC R_f = 0.6 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.69 (sept, 1H, *J* = 4.8 Hz), 1.80-1.65 (m, 6H), 1.55-1.45 (m, 2H), 1.33 (br s, 1H), 1.24 (s, 3H), 1.17 (s, 9H) ppm; ^{13}C

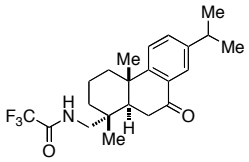
NMR (100 MHz, $CDCl_3$) δ 178.2, 71.3, 68.8, 38.8, 36.5, 29.7, 27.22, 27.20 ppm; IR (thin film) ν 3495, 2962, 2937, 2873, 1723, 1481, 1287, 1165, 1135, 996 cm^{-1}; HRMS (ES^+) calcd for $C_{12}H_{22}O_3$ 214.1569 found 237.1464 (MNa^+).



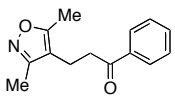
2-(4-Nitrophenyl)propan-2-ol (Table 3, entry 1): The reaction was performed with 41 mg of substrate and was stirred for 4 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). Colorless oil (29 mg, 63%); TLC R_f = 0.35 (1:3 EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, 2H, *J* = 8.8 Hz), 7.65 (d, 2H, *J* = 8.8 Hz), 2.00 (br s, 1H), 1.61 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.4, 146.7, 125.6, 123.6, 72.6, 31.8 ppm; IR (thin film) ν 3404, 2978, 1601, 1518, 1349, 1175, 1092, 856 cm^{-1}; HRMS (ES^+) calcd for $C_9H_{11}NO_3$ 181.0739.



2-(4-Isobutyrylphenyl)propanoic acid (Table 3, entry 2): The reaction was performed with 52 mg of substrate and was stirred for 3 h. The product was purified by chromatography on silica gel (gradient elution: 2.5→5% MeOH/CH_2Cl_2). White solid (30 mg, 54%); mp = 82–84 °C; TLC R_f = 0.4 (5% MeOH/CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 2H, *J* = 6.8 Hz), 7.41 (d, 2H, *J* = 6.4 Hz), 3.80 (q, 1H, *J* = 7.2 Hz), 3.53 (sept, 1H, *J* = 6.8 Hz), 1.53 (d, 3H, *J* = 7.2 Hz), 1.20 (d, 6H, *J* = 6.8 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.1, 179.9, 144.7, 135.4, 128.9, 128.0, 45.4, 35.4, 19.2, 18.1 ppm; IR (thin film) ν 3200, 2976, 2936, 1710, 1681, 1606, 1227, 1162, 982 cm^{-1}; HRMS (ES^+) calcd for $C_{13}H_{16}O_3$ 220.1099 found 243.0998 (MNa^+).

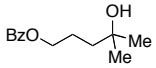


2,2,2-Trifluoro-*N*-(((1R,4aS,10aR)-7-isopropyl-1,4a-dimethyl-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenathren-1-yl)methyl)acetamide (Table 3, entry 3): The reaction was performed with 48 mg (0.125 mmol) of substrate using 2 mg of (Me_3tacn)$RuCl_3$ (5.0 μmol, 0.04 equiv) and 4 mg of $AgClO_4$ (0.02 mmol, 0.16 equiv), and was stirred for 0.5 h. The product was purified by chromatography on silica gel (10% EtOAc/hexanes). White foam (36 mg, 72%); mp = 174–176 °C; TLC R_f = 0.7 (25% EtOAc/hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (br s, 1H), 7.52 (d, 1H, *J* = 2.0 Hz), 7.32 (dd, 1H, *J* = 8.0, 2.0 Hz), 7.25 (d, 1H, *J* = 8.0 Hz), 3.48 (dd, 1H, *J* = 14.0, 8.4 Hz), 3.14 (dd, 1H, *J* = 14.0, 4.8 Hz), 2.80-2.60 (m, 3H), 2.36 (br d, 1H, *J* = 12.8 Hz), 2.07 (dd, 1H, *J* = 12.8, 4.4 Hz), 1.88-1.74 (m, 2H), 1.59-1.45 (m, 2H), 1.44-1.31 (m, 1H), 1.25 (s, 3H), 1.12 (d, 3H, *J* = 6.8 Hz), 1.07 (d, 3H, *J* = 6.8 Hz), 1.07 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 158.2 (q, J_{C-F} = 37 Hz), 153.4, 146.7, 133.1, 130.0, 124.7, 123.6, 116.1 (q, J_{C-F} = 286 Hz), 49.1, 44.1, 38.1, 37.8, 37.5, 36.1, 35.4, 33.4, 24.0, 23.6, 18.7, 18.1 ppm; IR (thin film) ν 3314, 2962, 2934, 1723, 1671, 1254, 1210, 1177, 1158 cm^{-1}; HRMS (ES^+) calcd for $C_{22}H_{28}F_3NO_2$ 395.2072 found 418.1966 (MNa^+).

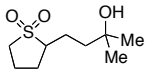


3-(3,5-Dimethylisoxazol-4-yl)-1-phenylpropan-1-one (Table 3, entry 4): The reaction was performed with 54 mg of substrate and was stirred for 16 h. The product was purified by chromatography on silica gel (20%

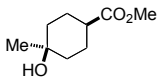
EtOAc/hexanes). Colorless oil (26 mg, 44%); TLC R_f = 0.4 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, *J* = 7.6 Hz), 7.57 (t, 1H, *J* = 7.2 Hz), 7.46 (t, 2H, *J* = 7.6 Hz), 3.13 (t, 2H, *J* = 7.6 Hz), 2.75 (t, 2H, *J* = 7.2 Hz), 2.34 (s, 3H), 2.25 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 165.3, 159.6, 136.6, 133.4, 128.8, 128.0, 112.6, 38.1, 16.5, 11.1, 10.4 ppm; IR (thin film) ν 2926, 1685, 1640, 1449, 1425, 1362, 1259, 1206 cm^{-1}; HRMS (ES$^+$) calcd for $C_{14}H_{15}NO_2$ 229.1103 found 252.0997 (MNa^+).



4-Hydroxy-4-methylpentyl benzoate (Table S1, entry 1): The reaction was performed on 52 mg of substrate using 1 mg of (Me_3tacn)$RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 2 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). Colorless oil (33 mg, 60%); TLC R_f = 0.3 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, 2H, *J* = 7.2 Hz), 7.55 (t, 1H, *J* = 7.2 Hz), 7.43 (t, 2H, *J* = 7.6 Hz), 4.34 (t, 2H, *J* = 6.4 Hz), 1.90-1.82 (m, 2H), 1.68 (br s, 1H), 1.64-1.59 (m, 2H), 1.26 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 133.0, 130.4, 129.6, 128.4, 70.7, 65.4, 40.0, 29.4, 23.9 ppm; IR (thin film) ν 3423, 2969, 1718, 142, 1380, 1315, 1278, 1176, 1115, 1070, 1027 cm^{-1}; HRMS (ES$^+$) calcd for $C_{13}H_{18}O_3$ 222.1256 found 245.1158 (MNa^+).

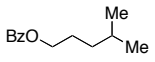
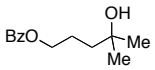
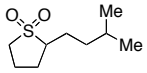
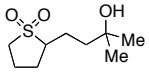
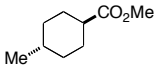
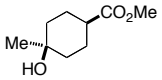


2-(3-Hydroxy-3-methylbutyl)tetrahydrothiophene-1,1-dioxide (Table S1, entry 4): The reaction was performed with 48 mg of substrate using 1 mg of (Me_3tacn)$RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 1.5 h. The product was purified by chromatography on silica gel (EtOAc). Colorless oil (36 mg, 70%); TLC R_f = 0.1 (1:1 EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.14 (ddd, 1H, *J* = 13.2, 8.8, 4.4 Hz), 3.02-2.86 (m, 2H), 2.40-2.28 (m, 1H), 2.24-2.11 (m, 1H), 2.10-1.91 (m, 2H), 1.84-1.51 (m, 5H), 1.22 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.5, 61.5, 51.5, 40.7, 29.7, 29.5, 29.0, 23.1, 20.2 ppm; IR (thin film) ν 3502, 2969, 1455, 1378, 1295, 1263, 1216, 1149, 1116, 933, 911 cm^{-1}; HRMS (ES$^+$) calcd for $C_9H_{18}O_3S$ 206.0977 found 229.0867 (MNa^+).



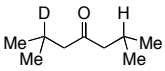
Methyl *cis*-4-hydroxy-4-methylcyclohexanecarboxylate (Table S1, entry 6): The reaction was performed with 39 mg of substrate using 1 mg of (Me_3tacn)$RuCl_3$ (2.5 μmol, 0.01 equiv) and 2 mg of $AgClO_4$ (0.01 mmol, 0.04 equiv), and was stirred for 4 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). White solid (25 mg, 58%); mp = 58–59 °C; TLC R_f = 0.35 (1:3 EtOAc/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (s, 3H), 2.22 (tt, 1H, *J* = 7.5, 7.5 Hz), 1.88-1.74 (m, 4H), 1.74-1.69 (m, 1H), 1.68-1.64 (m, 1H), 1.44-1.32 (m, 3H), 1.21 (s, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 68.5, 51.7, 42.4, 37.8, 31.1, 24.4 ppm; IR (thin film) ν 3429, 2930, 1733, 1436, 1376, 1321, 1259, 1199, 1149, 1041, 1008, 961, 912 cm^{-1}; HRMS (ES$^+$) calcd for $C_9H_{16}O_3$ 172.1099 found 173.1172 (MH^+).

Table S1. Additional examples of $(Me_3tacn)RuCl_3$-catalyzed C–H hydroxylation.[a]

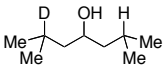
entry	substrate	product	% yield[b]
1			60[c]
2			70
3			58[c]

[a]Conditions: Reactions were performed on 0.25 mmol scale at ambient temperature with 2 mol% [$(Me_3tacn)RuCl_3$] **1**, 8 mol% $AgClO_4$, and 6 equiv. $(NH_4)_2Ce(NO_3)_6$ in 1:1 *t*-BuOH/H_2O. [b]Isolated yield of material purified by chromatography on SiO_2. [c]Reaction performed with 1 mol% **1**, 4 mol% $AgClO_4$.

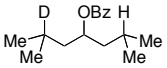
Synthesis and oxidation of 2,6-dimethylheptyl(2-d_1) benzoate (KIE substrate):



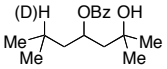
2,6-Dimethyl-(2-d_1)heptan-4-one:[7] A 10-mL round bottom flask with stir bar was charged with $Rh(PPh_3)_3Cl$ (31 mg, 0.034 mmol, 0.005 equiv). The flask was sealed with a rubber septum and the flask was briefly evacuated, then filled with N_2. This process was repeated two additional times. Both 2,6-dimethylhept-2-en-4-one (950 mg, 6.77 mmol) and $PhMe_2SiD$ (1.15 mL, 7.45 mmol, 1.1 equiv) were added via syringe, and the reaction was heated at 50 °C for 5 h. The reaction was cooled to room temperature before 2.0 mL of MeOH and K_2CO_3 (10 mg) were added. The mixture was stirred for 1 h then transferred to a separatory funnel with ~25 mL of H_2O. The aqueous layer was extratcted with 3 x 25 mL of Et_2O. The organic fractions were collected, dried over $MgSO_4$, and concentrated under reduced pressure to a volume of ~2 mL. The turbid mixture was filtered through a small pad of silica gel using 10% diethyl ether/hexanes as eluent. The isolated material was use in the subsequent reaction without additional purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.27 (d, 2H, J = 7.2 Hz), 2.25 (s, 2H), 2.12 (sept, 1H, J = 7.2 Hz), 0.92 (d, 6H, J = 7.2 Hz), 0.89 (s, 6H) ppm.



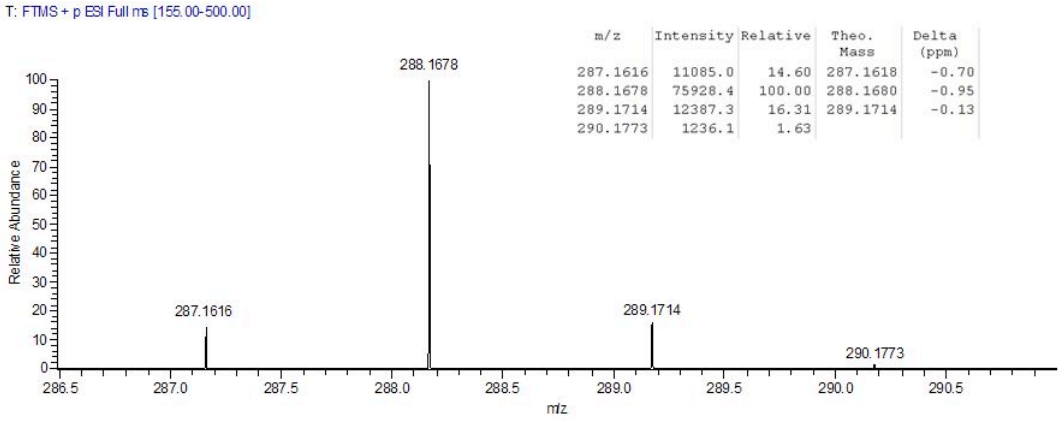
2,6-Dimethyl-(2-d_1)heptan-4-ol: Unpurified 2,6-dimethyl-(2-d_1)heptan-4-one (~6.77 mmol) was dissolved in 10 mL of MeOH to which a single portion of $NaBH_4$ (378 mg, 10.0 mmol, 1.5 equiv) was added. The reaction was stirred for 1 h, then quenched by the addition of X mL of H_2O. The aqueous mixture was transferred to a separatory funnel and extracted with 3 x 25 mL of Et_2O. The combined organic fractions were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of the oily residue by chromatography on silica gel (10% EtOAc/hexanes) afforded the desired product as a colorless oil (493 mg, 50% over two steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.75 (tt, 1H, J = 4.0, 4.0 Hz), 1.82-1.70 (m, 1H), 1.40-1.28 (m, 3H), 1.25-1.18 (m, 2H), 0.92 (d, 6H, J = 6.8 Hz), 0.90 (s, 6H) ppm.



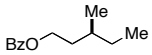
2,6-Dimethylheptyl(2-d_1) benzoate (Figure 2A): Neat 2,6-dimethyl-(2-d_1)heptan-4-ol (490 mg, 3.39 mmol) was dissolved in 5.0 mL of CH_2Cl_2. To this solution were added pyridine (0.42 mL, 5.09 mmol) and benzoyl chloride (0.43 mL, 3.73 mmol). The reaction was stirred for 16 h, then quenched by the addition of 10 mL of 1.0 M aqueous HCl. The solution was transferred to a separatory funnel and extracted with 3 x 25 mL of CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give a colorless oil. Purification by chromatography on silica gel (2% EtOAc/hexanes) furnished the desired product as a colorless oil (797 mg, 94%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, 2H, J = 8.8 Hz), 7.55 (t, 1H, J = 8.8 Hz), 7.44 (t, 2H, J = 8.8 Hz), 5.38-5.28 (m, 1H), 1.72-1.62 (m, 3H), 1.45-1.37 (m, 2H), 0.96-0.93 (m, 12H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 132.7, 130.9, 129.6, 128.4, 72.0, 44.2, 44.1, 24.8, 24.4 (t, J_{C-D} = 19 Hz), 23.3, 23.1, 22.5, 22.3 ppm; IR (thin film) ν 2957, 2928, 2869, 1717, 1314, 1274, 1113 cm^{-1}.



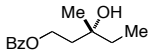
2-Hydroxy-2,6-dimethylheptan-4-yl benzoate and 2-hydroxy-2,6-dimethylheptan(6-d_1)-4-yl benzoate (Figure 2A): The reaction was performed following the General Procedure with 249 mg of substrate (1.0 mmol), and was stirred for 2.5 h. The product was purified by chromatography on silica gel (gradient elution: 10→25% EtOAc/hexanes). Colorless oil (136 mg, 51%); TLC R_f = 0.5 (25% EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, 2H, J = 7.2 Hz), 7.53 (t, 1H, J = 7.2 Hz), 7.42 (t, 2H, J = 7.2 Hz), 5.45-5.38 (m, 1H), 2.46 (br s, 1H), 1.95 (dd, 1H, J = 14.8, 8.0 Hz), 1.78 (dd, 1H, J = 15.2, 3.2 Hz), 1.71 (dd, 1H, J = 14.0, 8.4 Hz), 1.44 (dd, 1H, J = 14.0, 4.8 Hz), 1.25 (s, 3H), 1.22 (s, 3H), 0.93 (d, RCHMe_2) and 0.92 (s, 6H total, RCDMe_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 133.0, 130.4, 129.6, 128.4, 71.1, 69.9, 48.0, 45.3 (minor) and 45.1 (major), 30.0, 29.8, 24.7 (minor) and 24.3 (t, J_{C-D} = 18.9 Hz, major), 23.0 (minor) and 22.9 (major), 22.3 (minor) and 22.2 (major) ppm; IR (thin film) ν 3420, 2962, 2929, 1714, 1452, 1367, 1316, 1278, 1176, 1116, 1070, 1027 cm^{-1}; HRMS (ES$^+$) calcd for $C_{16}H_{24}O_3$ 264.1725 found 287.1616 (MNa$^+$, minor); calcd for $C_{16}H_{23}DO_3$ 265.1788 found 288.1678 (MNa$^+$, major). Ratio of deuterated to undeuterated compound was determined to be 6.7:1 by comparison of HRMS ion counts, after correction for natural isotopic abundance at other positions.



m/z	Intensity	Relative	Theo. Mass	Delta (ppm)
287.1616	11085.0	14.60	287.1618	-0.70
288.1678	75928.4	100.00	288.1680	-0.95
289.1714	12387.3	16.31	289.1714	-0.13
290.1773	1236.1	1.63		



(*S*)-3-Methylpentyl benzoate (Figure 2B): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, 2H, *J* = 6.8 Hz), 7.55 (t, 1H, *J* = 7.2 Hz), 7.46 (t, 2H, *J* = 6.8 Hz), 4.41-4.31 (m, 2H), 1.87-1.76 (m, 1H), 1.62-1.53 (m, 2H), 1.47-1.37 (m, 1H), 1.30-1.18 (m, 1H), 0.96 (d, 3H, *J* = 6.4 Hz), 0.91 (t, 3H, *J* = 7.2 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 132.9, 130.6, 129.6, 128.4, 63.7, 35.2, 31.6, 29.5, 19.2, 11.4 ppm; IR (thin film) ν 2962, 1721, 1274, 1112 cm^{-1}.



(*R*)-3-Hydroxy-3-methylpentyl benzoate (Figure 2B): The reaction was performed with 52 mg of substrate using 2 mg of $(Me_3tacn)RuCl_3$ (5 μmol, 0.02 equiv), 4 mg of $AgClO_4$ (0.02 mmol, 0.08 equiv), and 3 equiv of CAN, and was stirred for 1 h. The product was purified by chromatography on silica gel (1:3 EtOAc/hexanes). Colorless oil (19 mg, 34%); TLC R_f = 0.5 (1:3 EtOAc/hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, 2H, *J* = 8.0 Hz), 7.55 (t, 1H, *J* = 7.2 Hz), 7.43 (t, 2H, *J* = 7.2 Hz), 4.49 (t, 2H, *J* = 6.8 Hz), 1.96 (dt, 2H, *J* = 6.8, 2.8 Hz), 1.71 (br s, 1H), 1.62-1.58 (m, 2H), 1.26 (s, 3H), 0.95 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 133.0, 130.3, 129.6, 128.5, 72.2, 61.9, 39.4, 35.1, 26.6, 8.3 ppm; IR (thin film) ν 3481, 2970, 2937, 1719, 1453, 1277, 1116 cm^{-1}. The product %ee was estimated at 99% based on chiral HPLC analysis (ChiralCel OB column, 95:5 heptanes/iPrOH, 0.8 mL/min, see HPLC trances on pg. S13). A reaction performed using 6 equiv. CAN and stirred for 24 h gave 29 mg of the desired product (52%) having 50% ee.

(1) Brodsky, B. H.; Du Bois, J. *J. Am. Chem. Soc.* **2005**, *127*, 15391.

(2) Augeri, D. J.; Robl, J. A.; Betebenner, D. A.; Magnin, D. R.; Khanna, A.; Robertson, J. G.; Wang, A.; Simpkins, L. M.; Taunk, P.; Huang, Q.; Han, S.-P.; Abboa-Offei, B.; Cap, M.; Xin, L.; Tao, L.; Tozzo, E.; Welzel, G. E.; Egan, D. M.; Marcinkeviciene, J.; Chang, S. Y.; Biller, S. A.; Kirby, M. S.; Parker, R. A.; Hamann, L. G. *J. Med. Chem.* **2005**, *48*, 5025.

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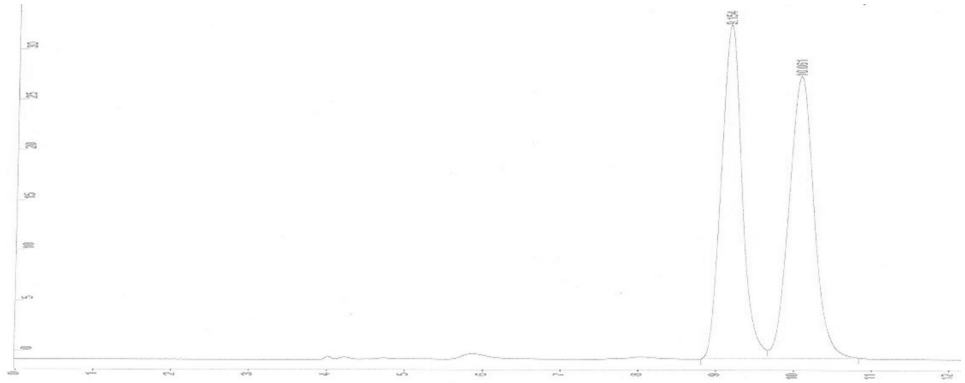
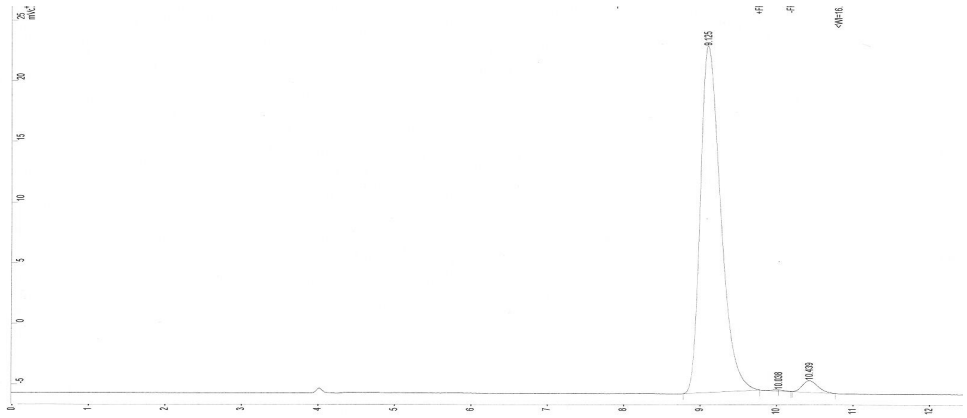
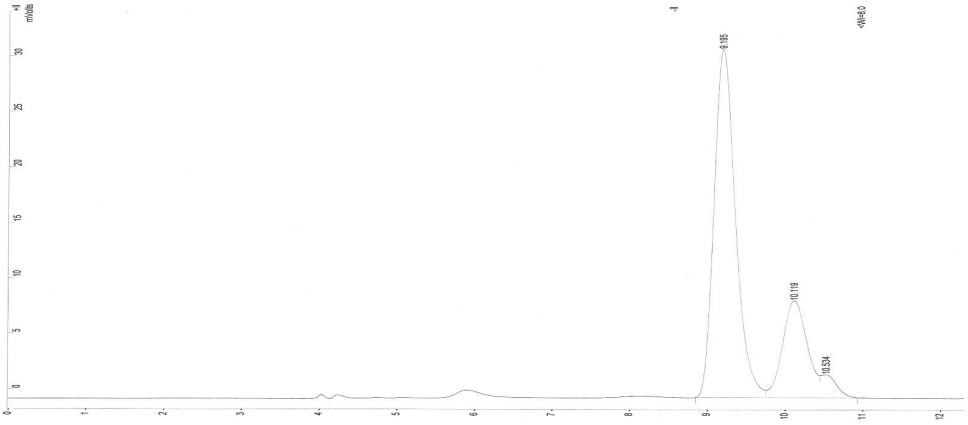


HPLC trace of racemic alcohol 6. Peaks: 9.15 min (49.7%), 10.06 min (50.3%).

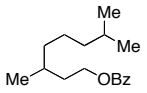


HPLC trace of reaction stirred for 1 h with 3 equiv. CAN. Peaks: 9.13 min (97.3%, major enantiomer), 10.04 min. (0.2%, minor enantiomer). The product having a retention time of 10.4 min was unassigned.

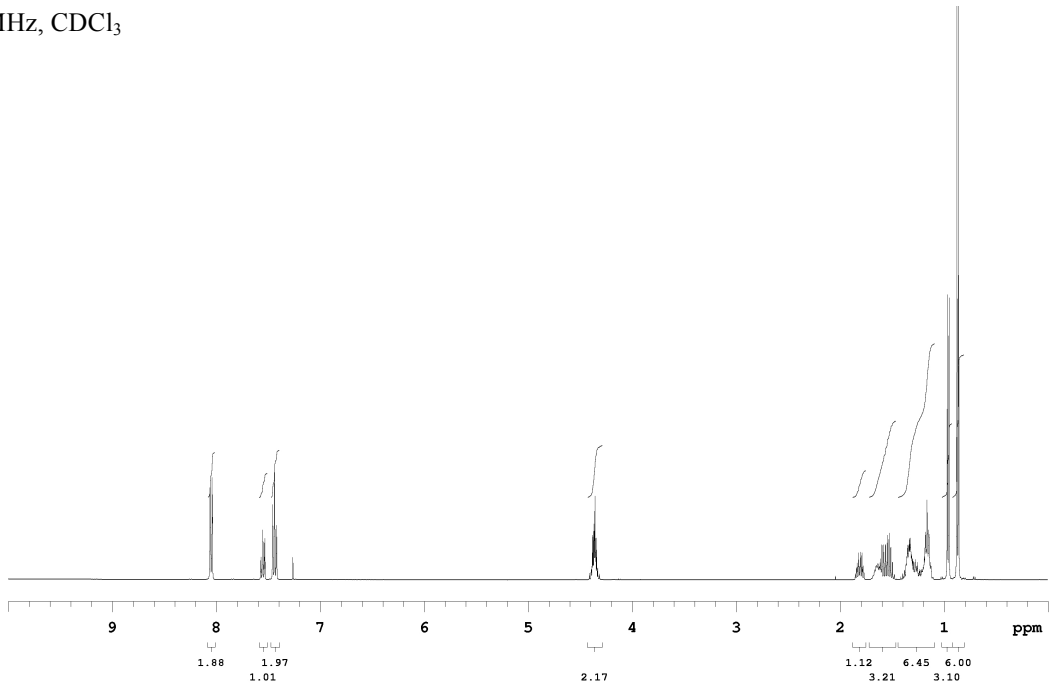


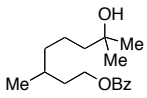
HPLC trace of reaction stirred for 24 h with 6 equiv. CAN. Peaks: 9.19 min. (73.1%, major enantiomer), 10.11 min (23.4%, minor enantiomer). The product having a retention time of 10.5 min. was unassigned.

^{1}H NMR spectra for all substrates and products in Tables 1–3, S1, and Figure 2

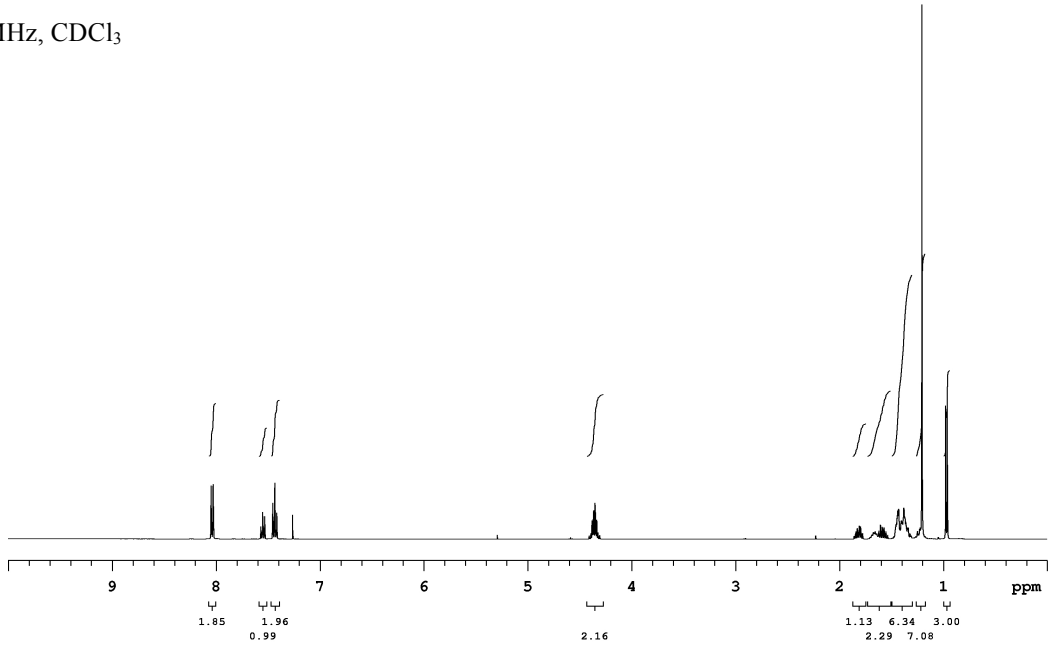


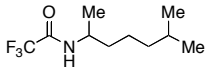
400 MHz, $CDCl_3$





400 MHz, $CDCl_3$





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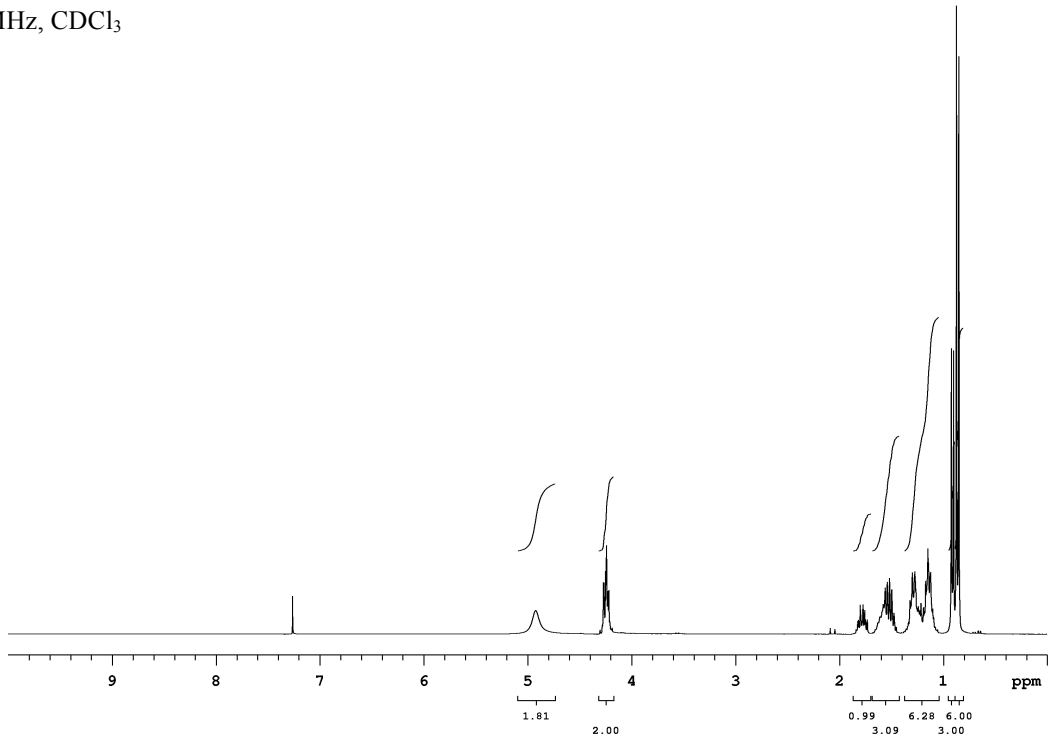

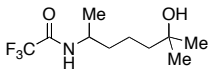

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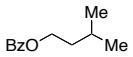

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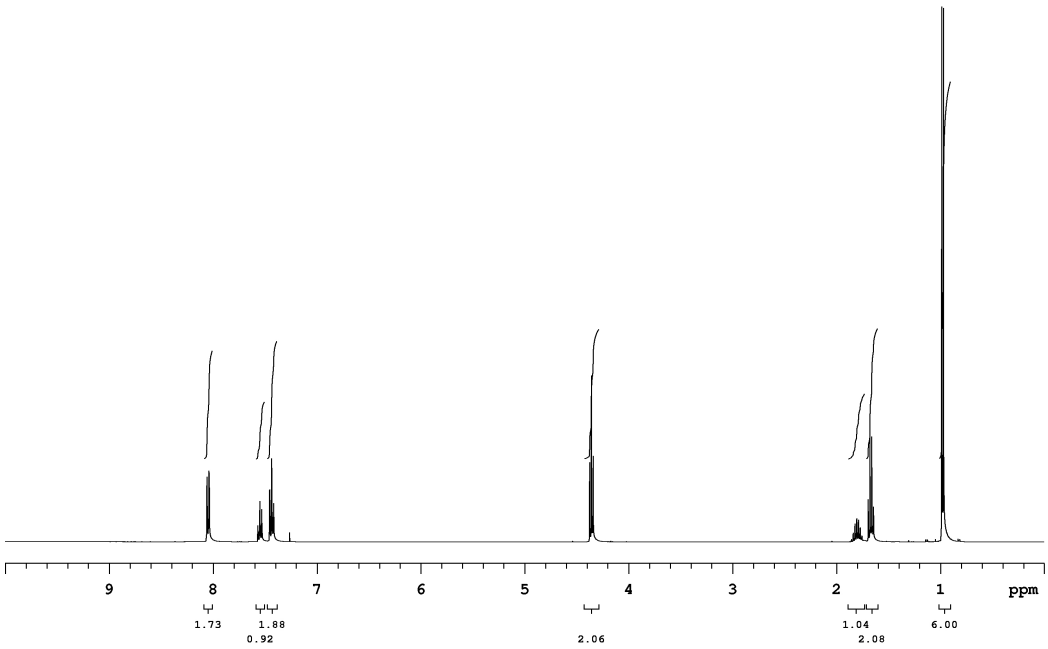

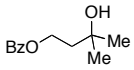

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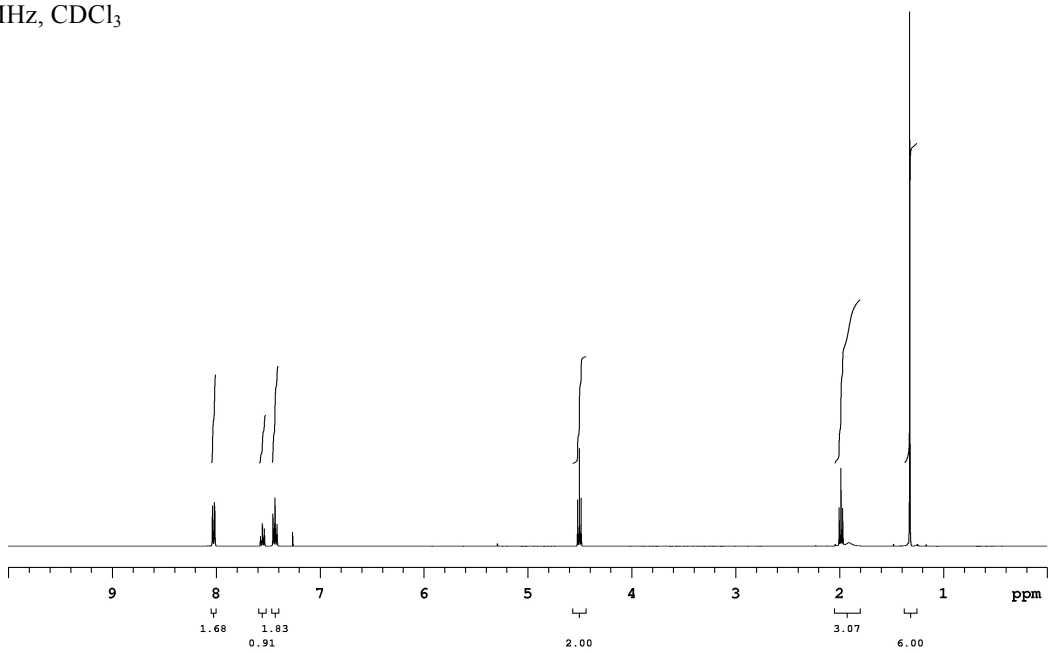

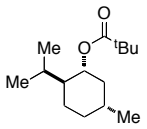

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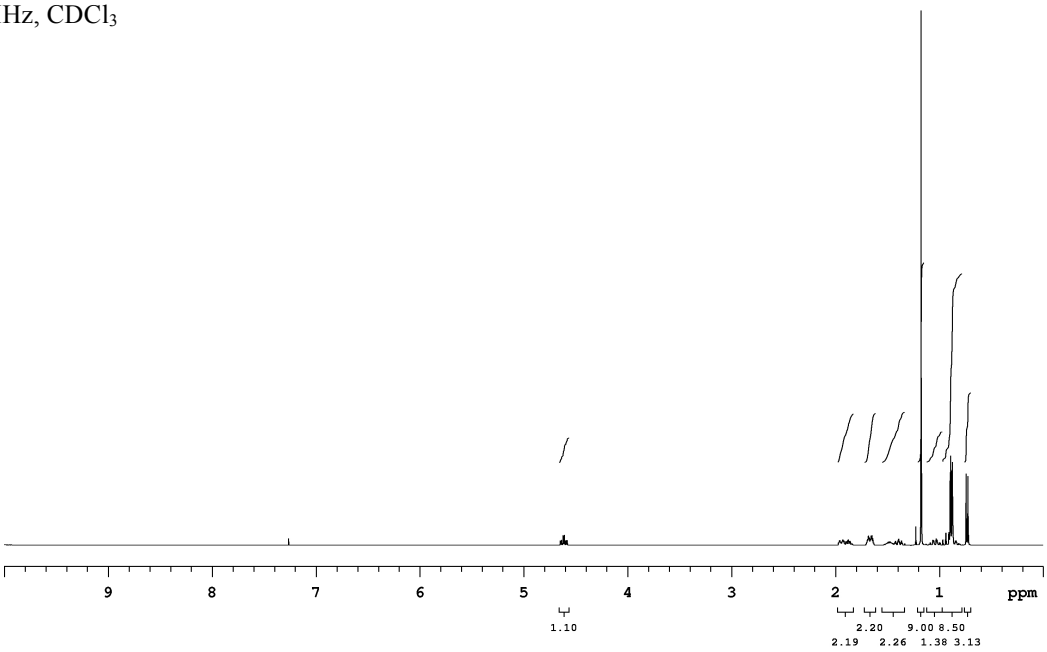

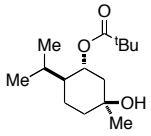

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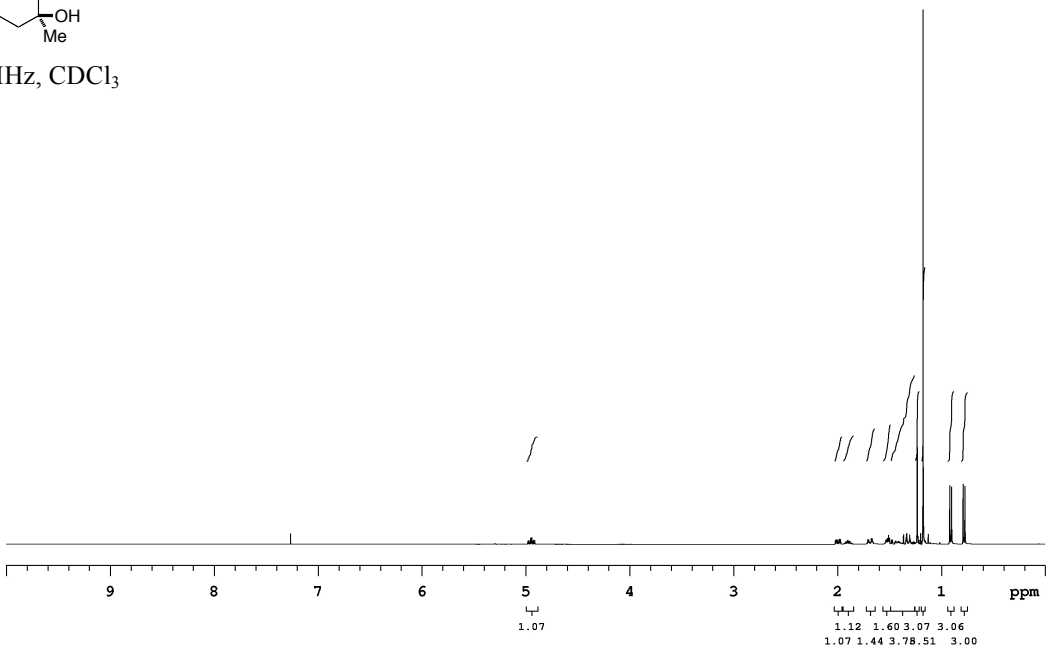

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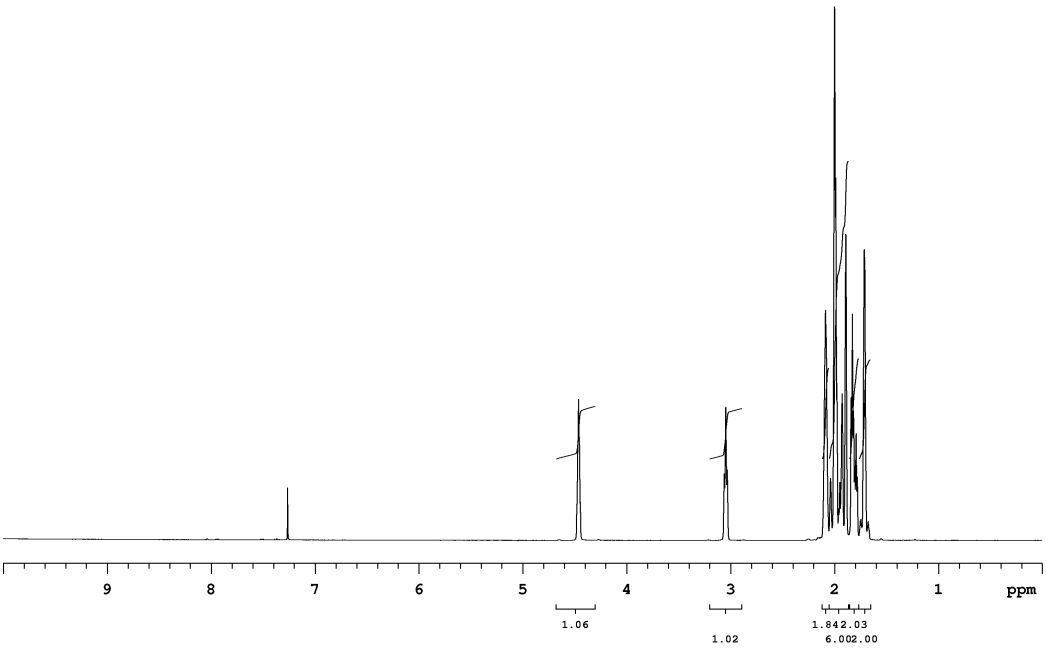

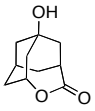

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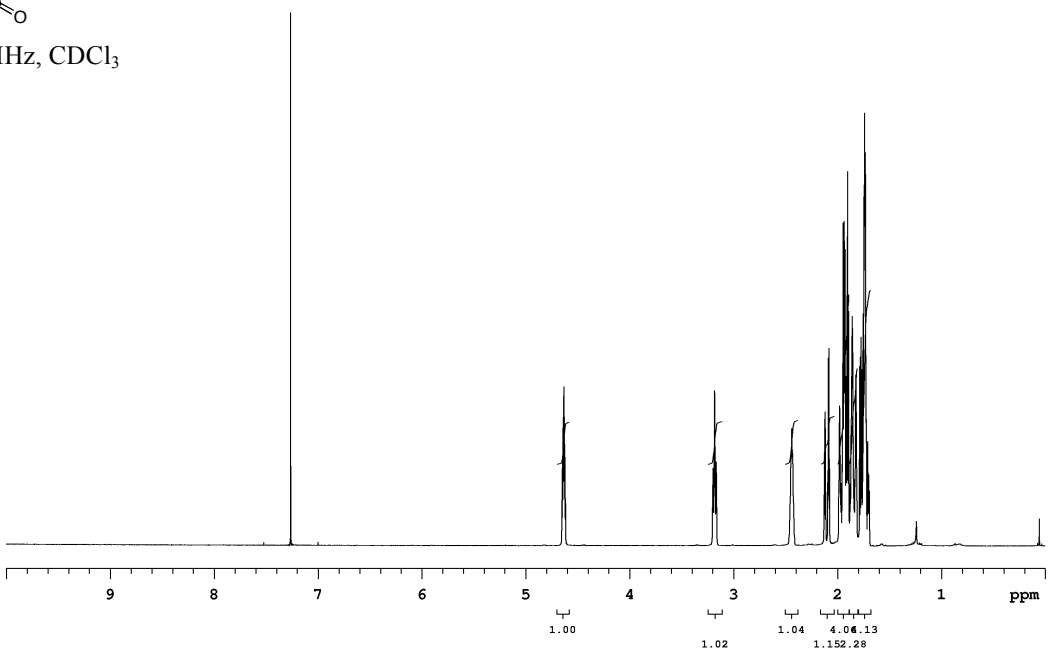

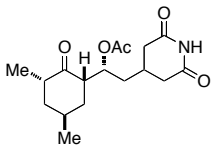

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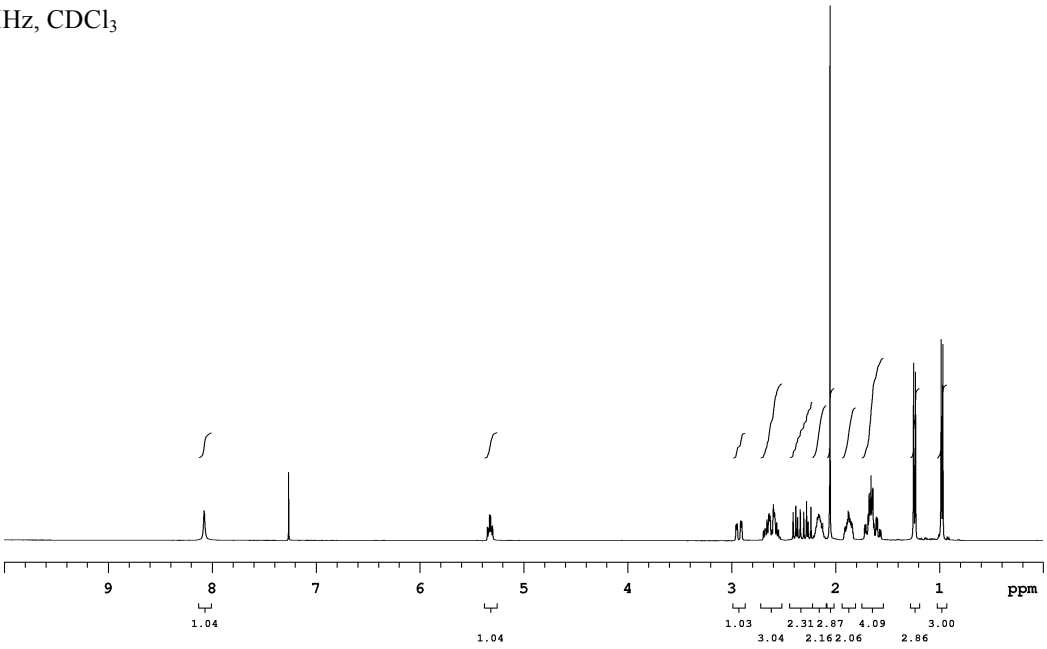

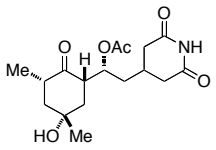

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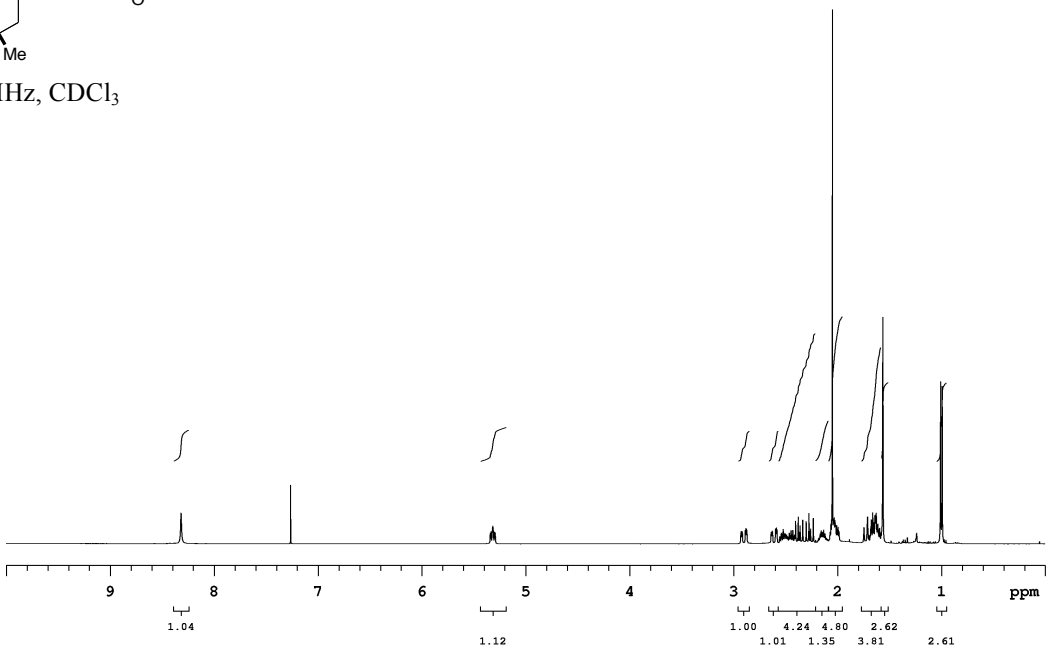

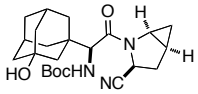

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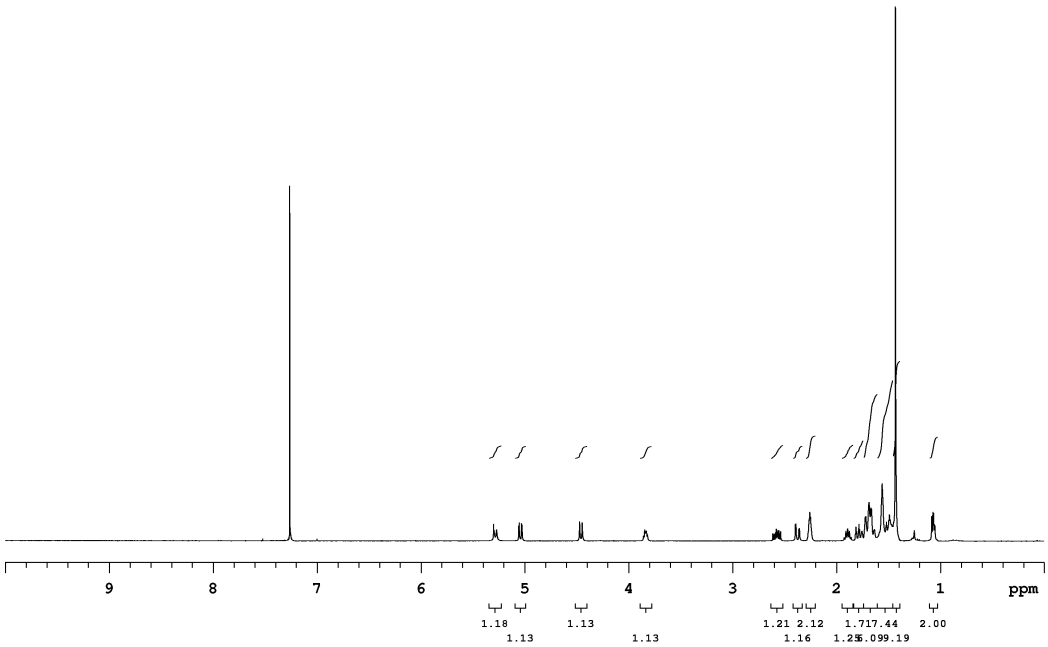

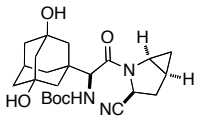

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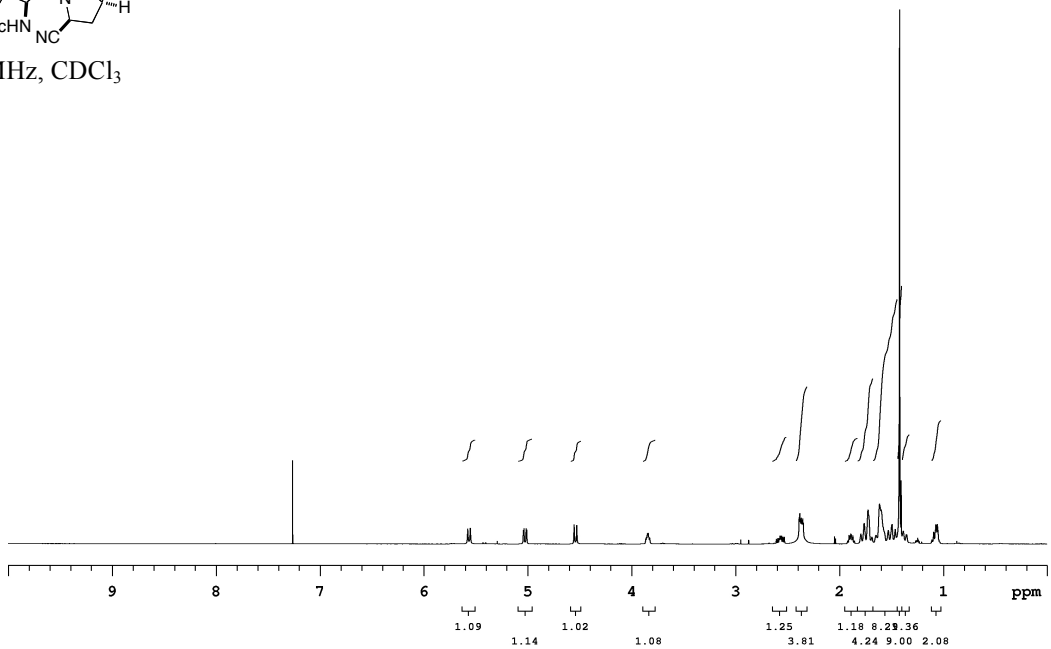

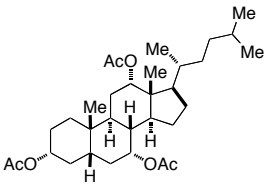

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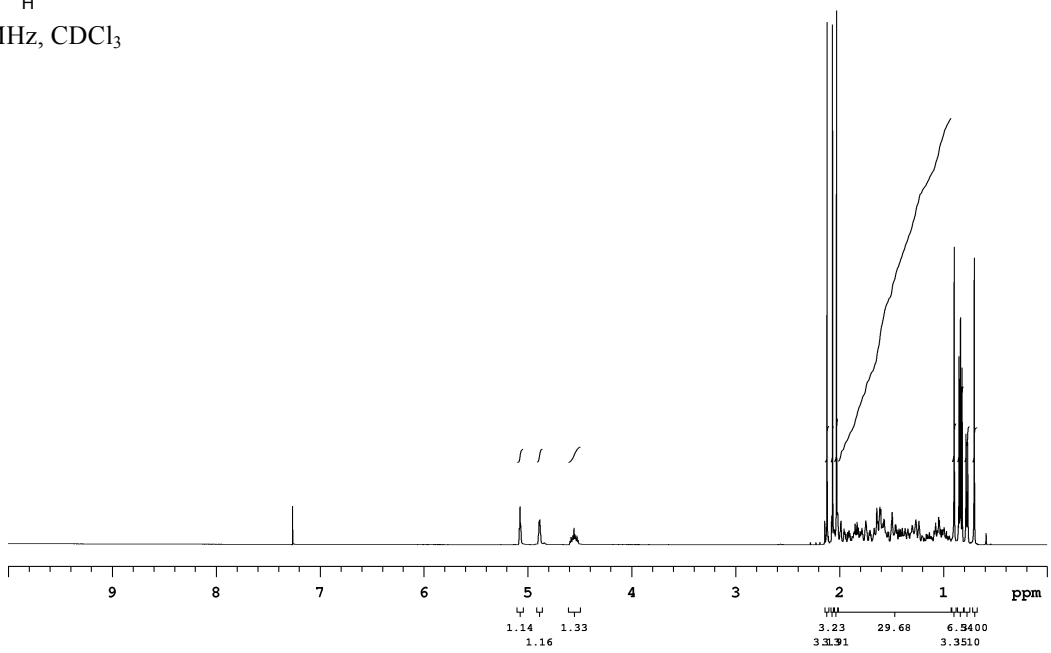

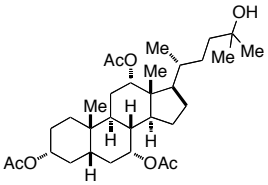

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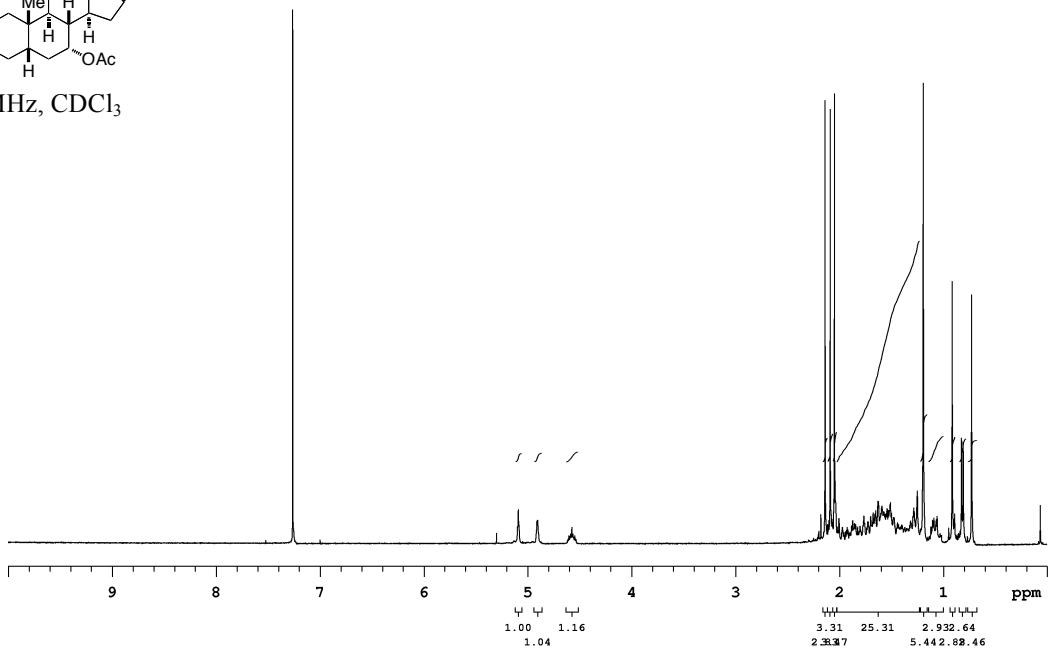

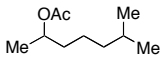

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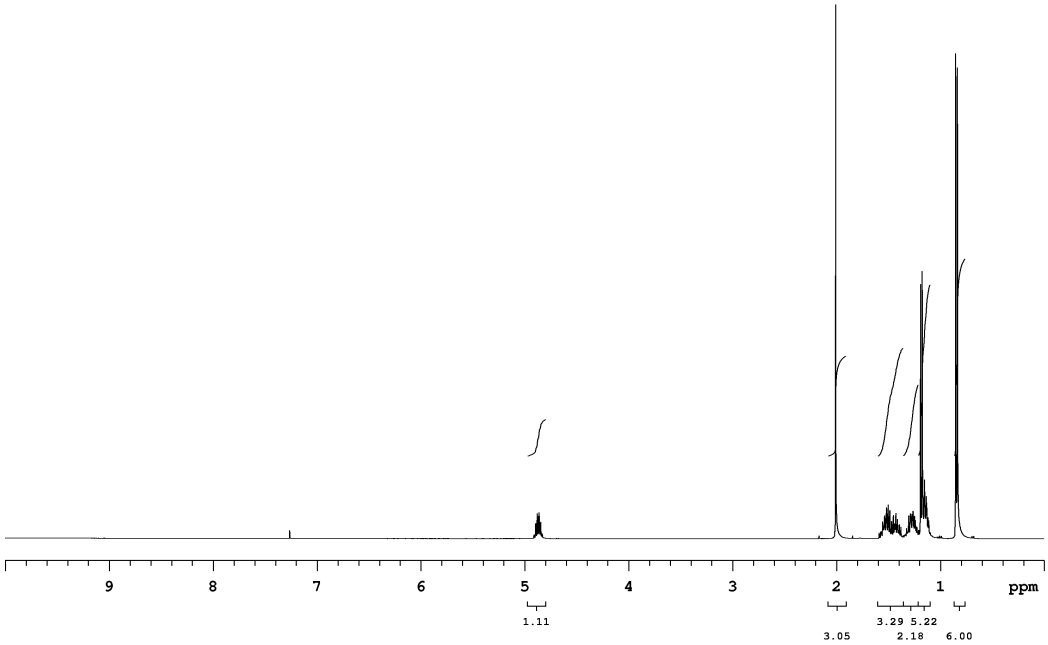

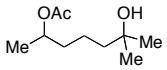

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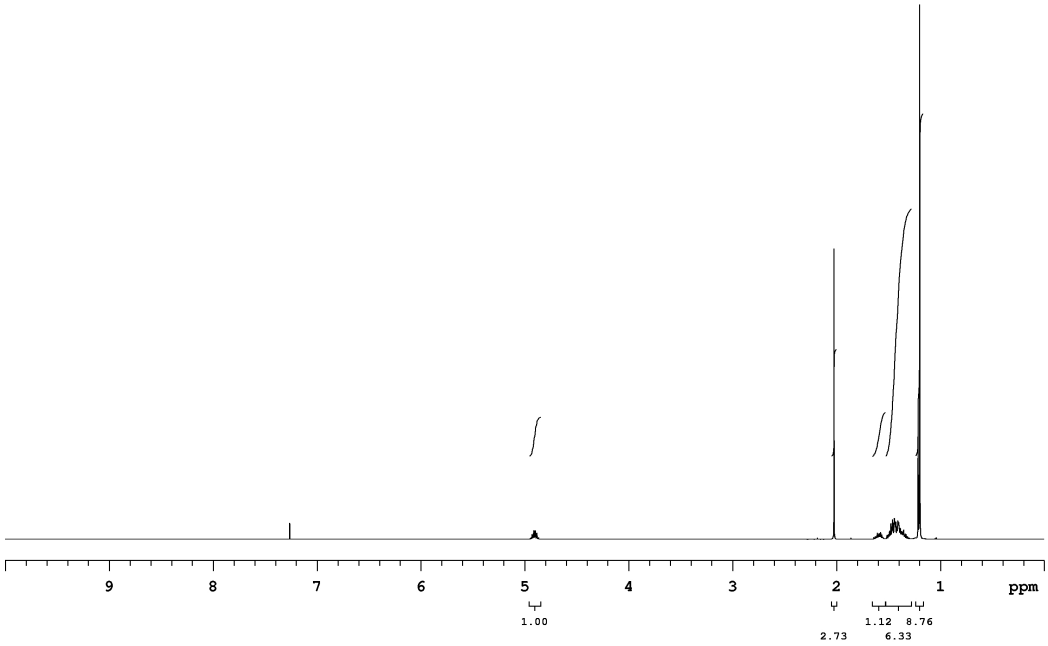

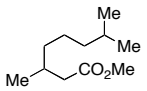

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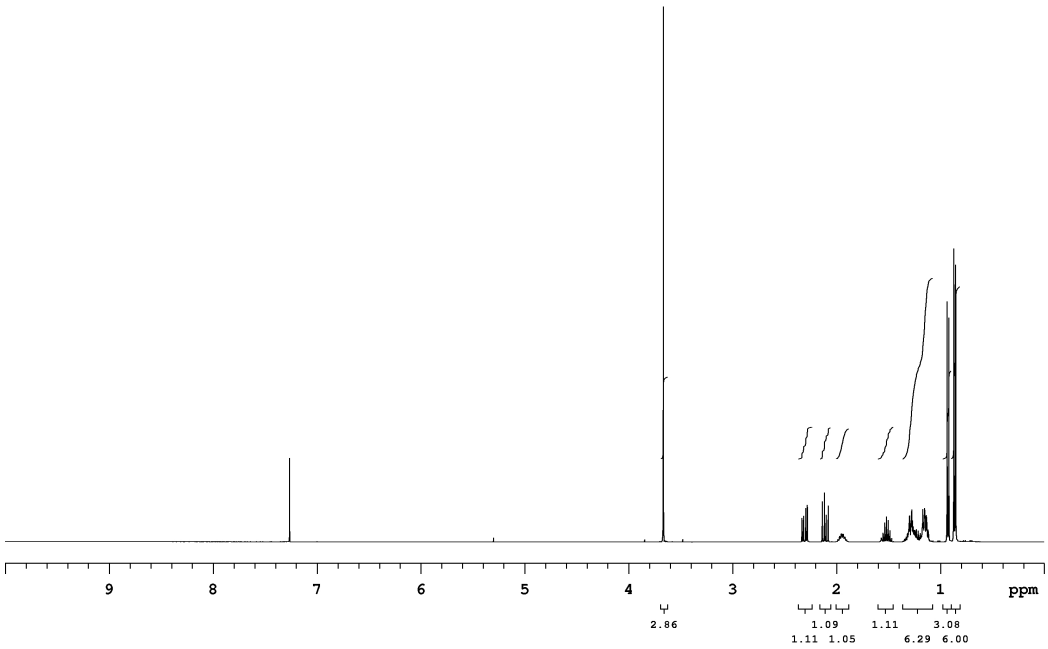

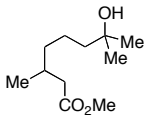

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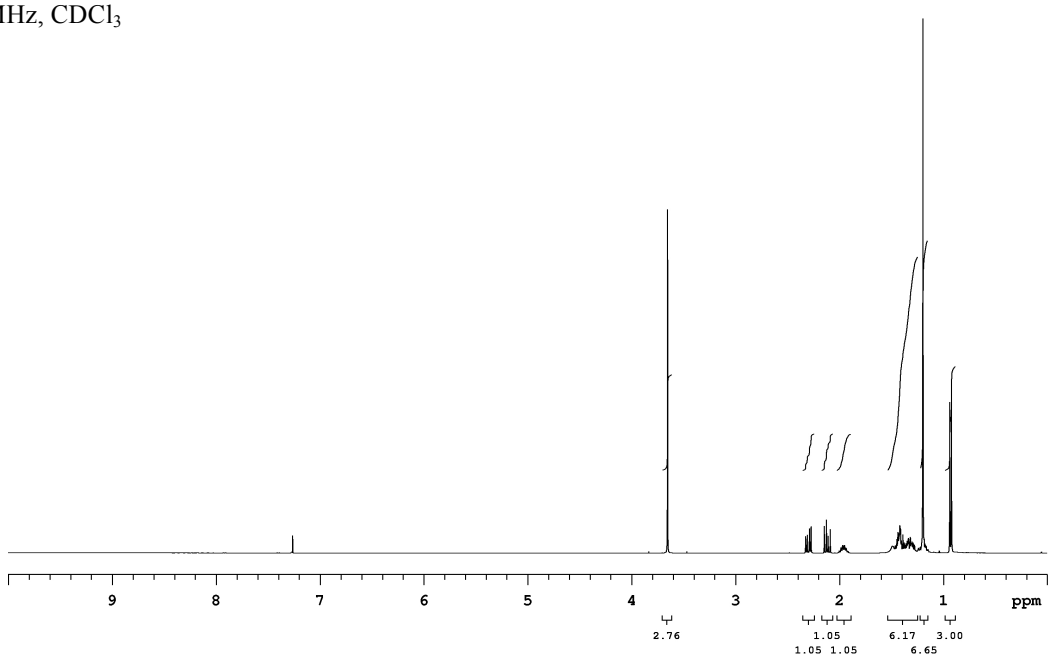

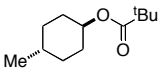

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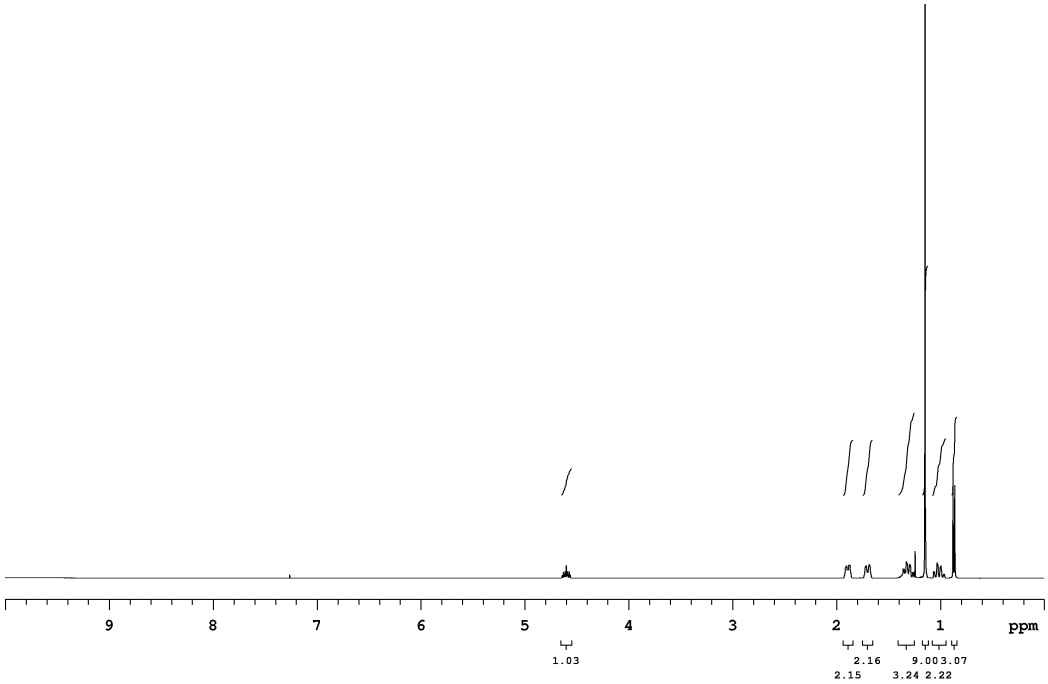

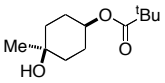

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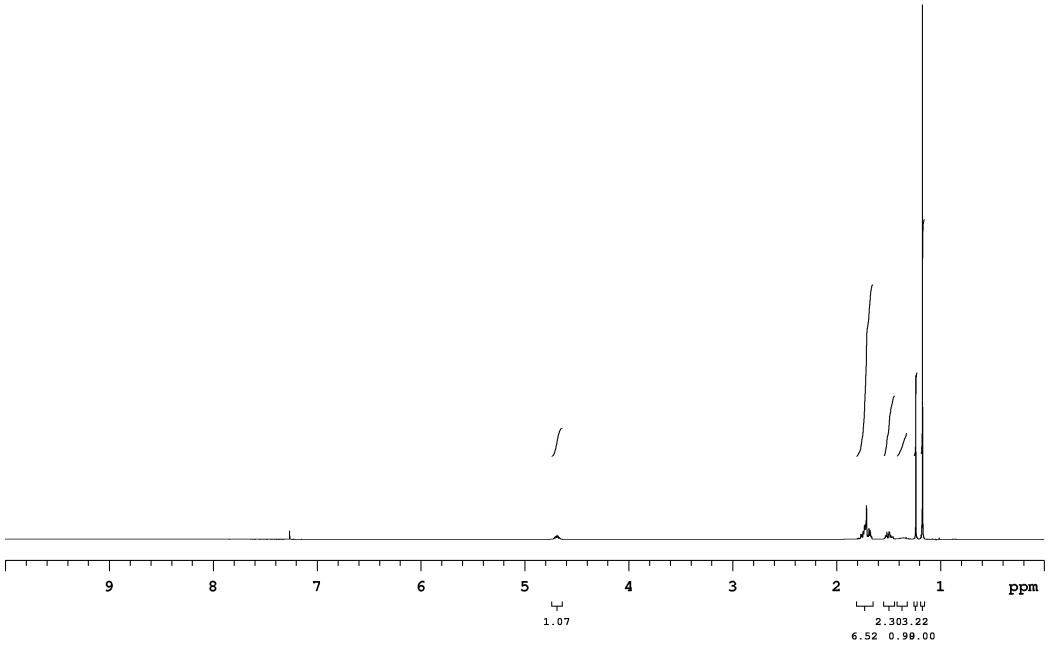

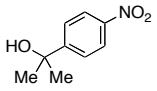

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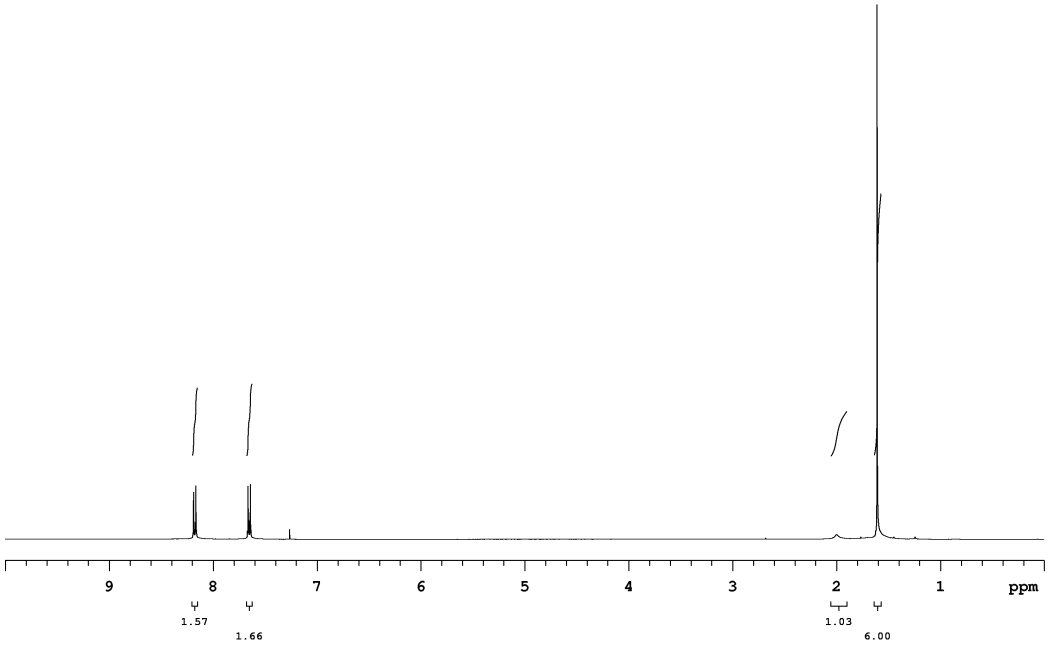

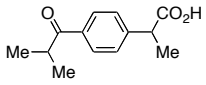

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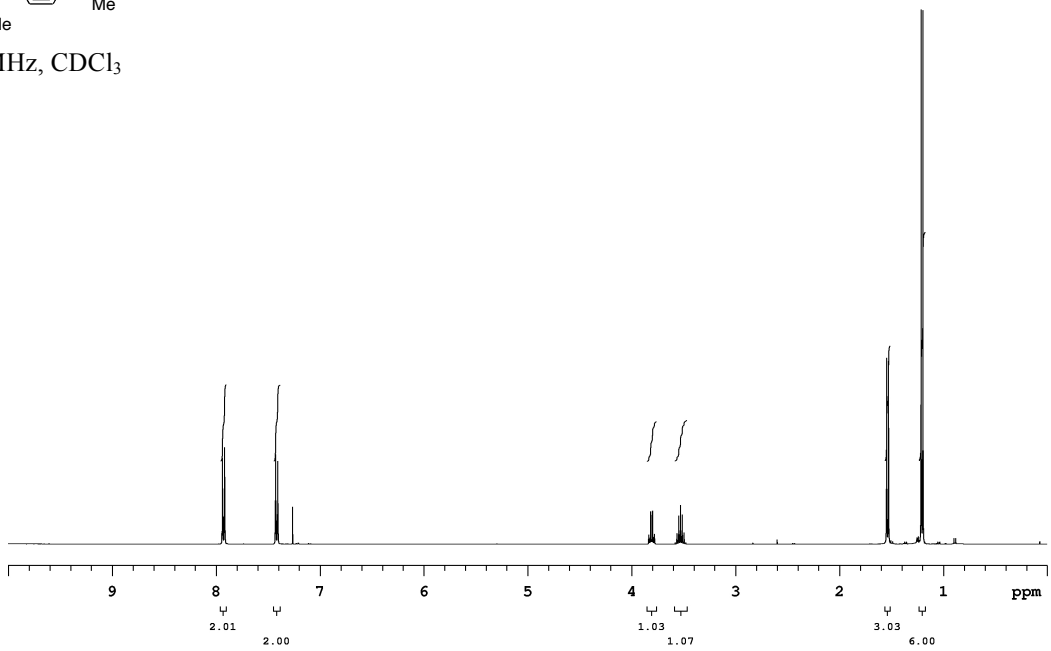

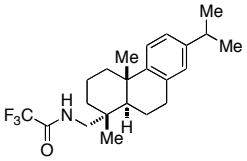

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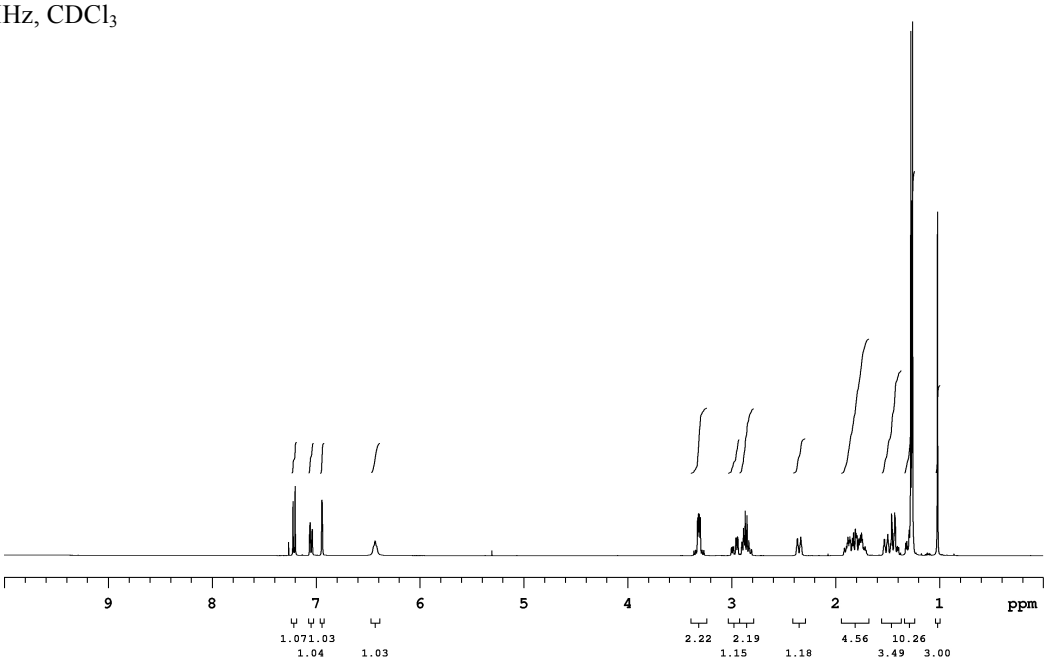

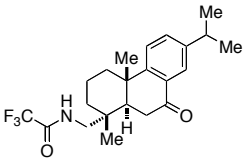

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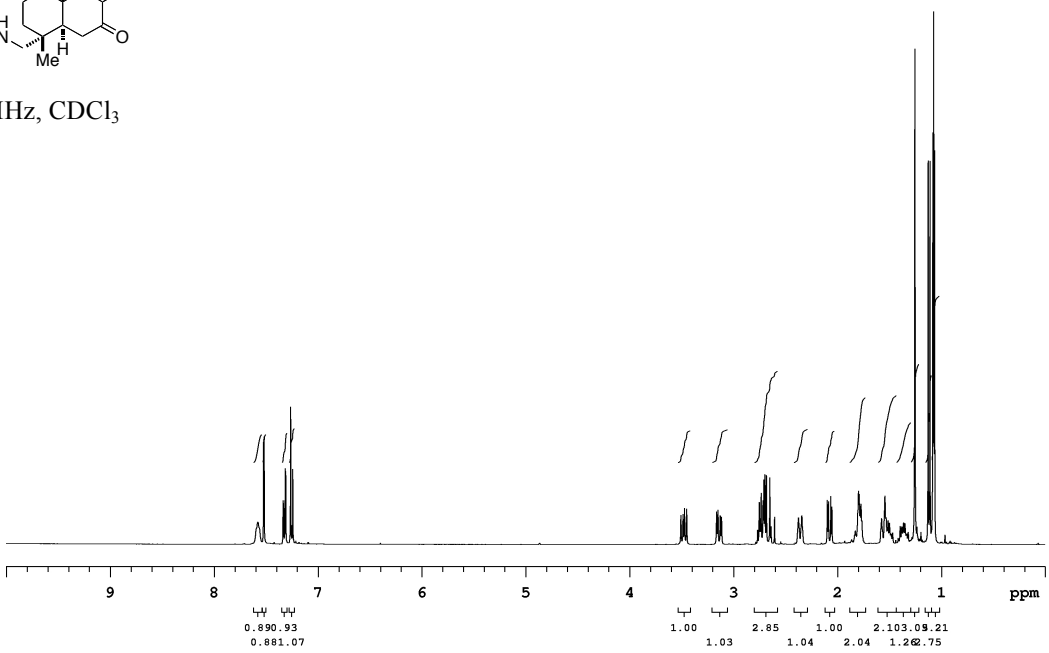

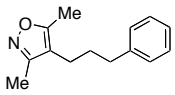

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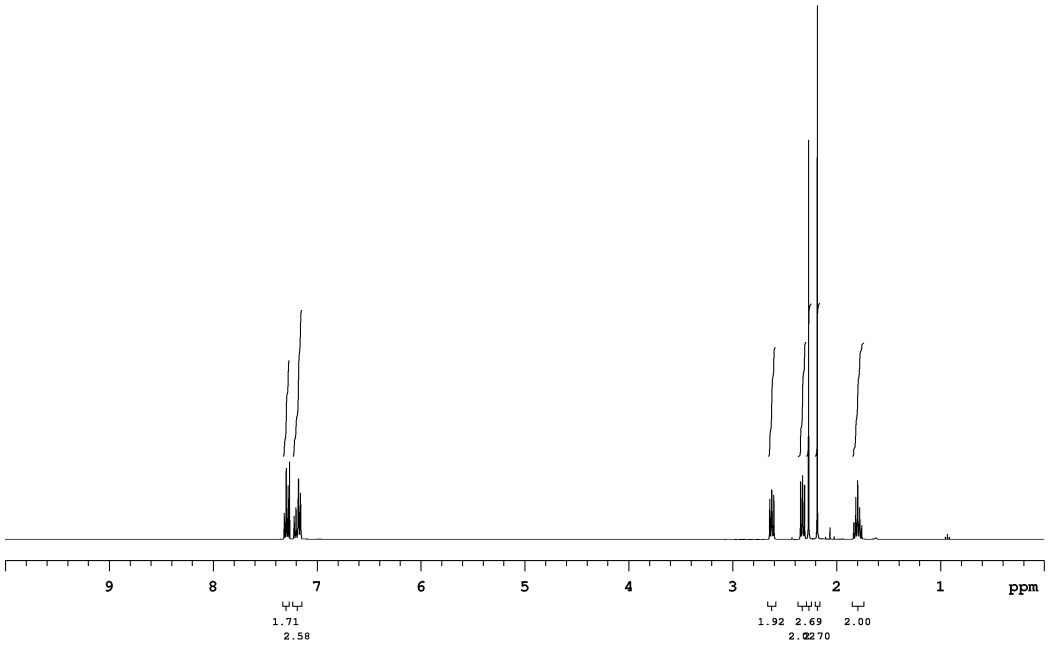

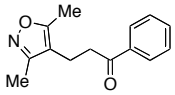

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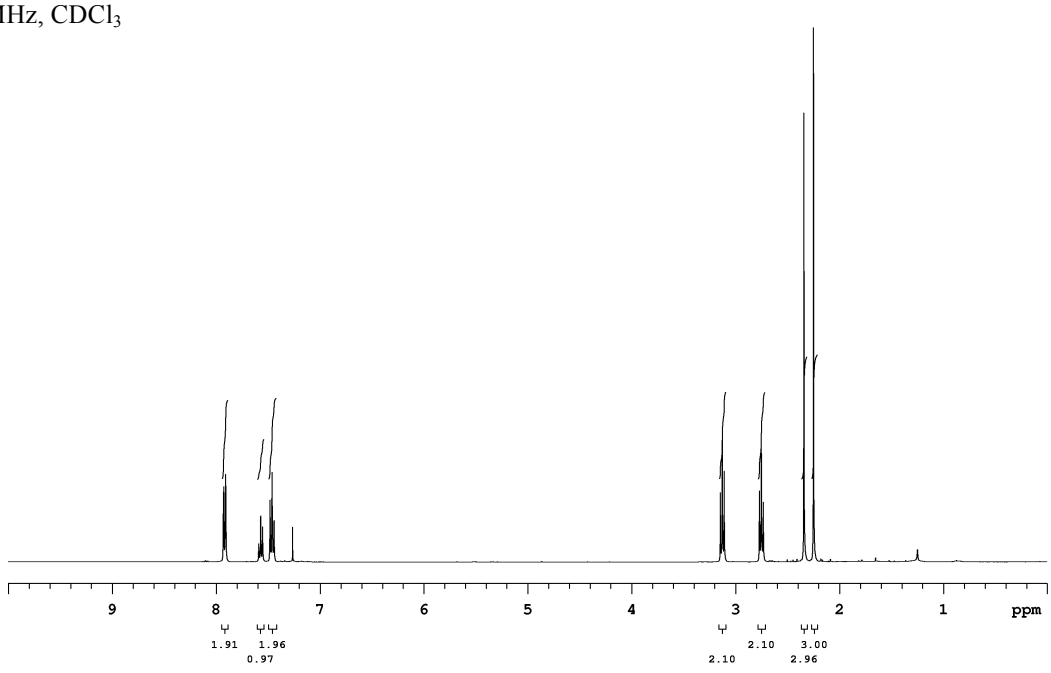

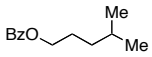

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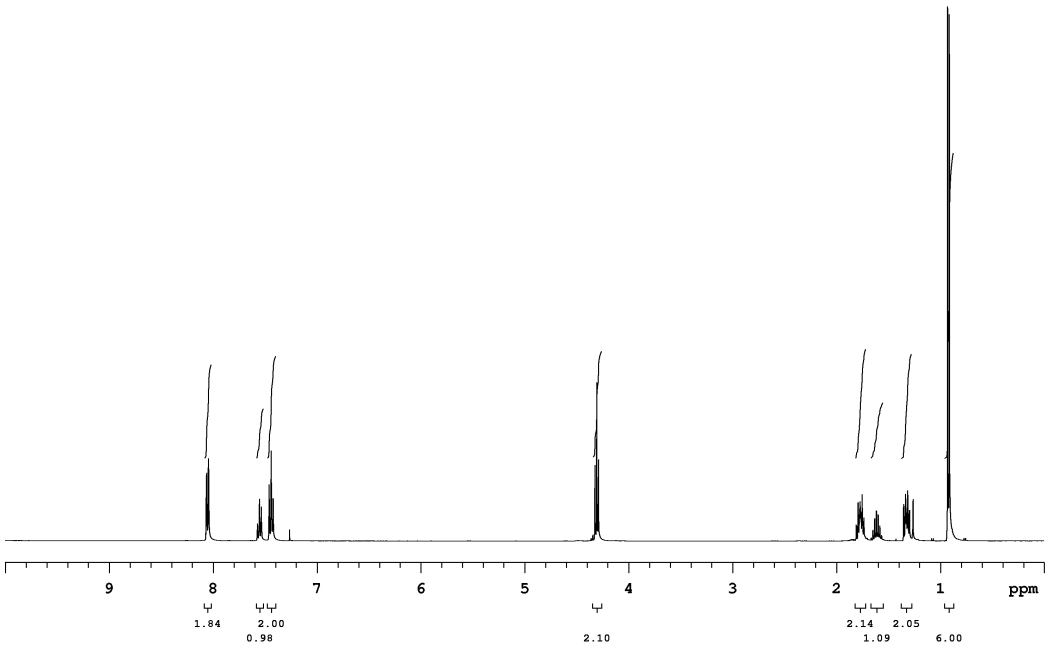

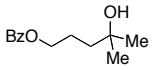

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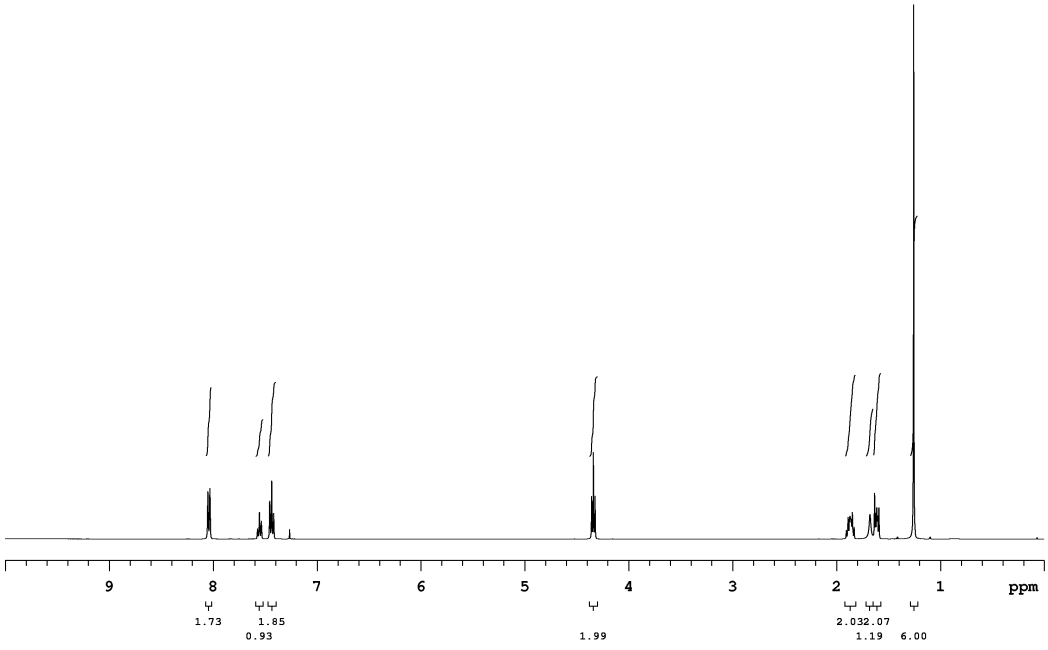

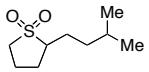

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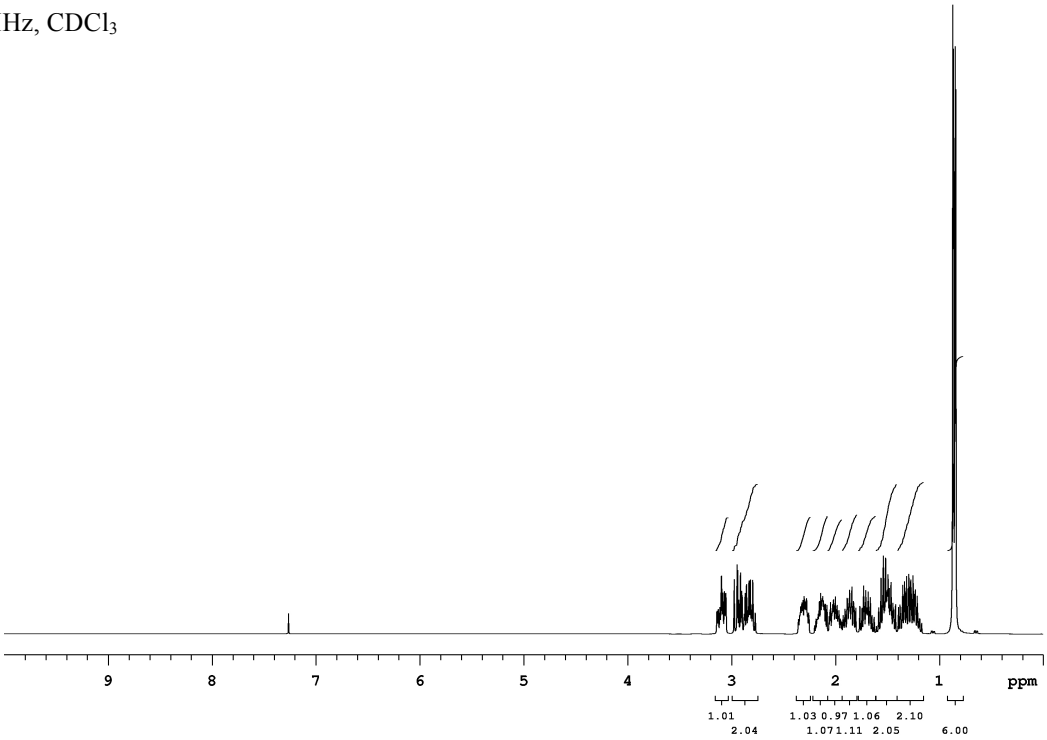

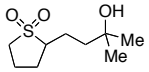

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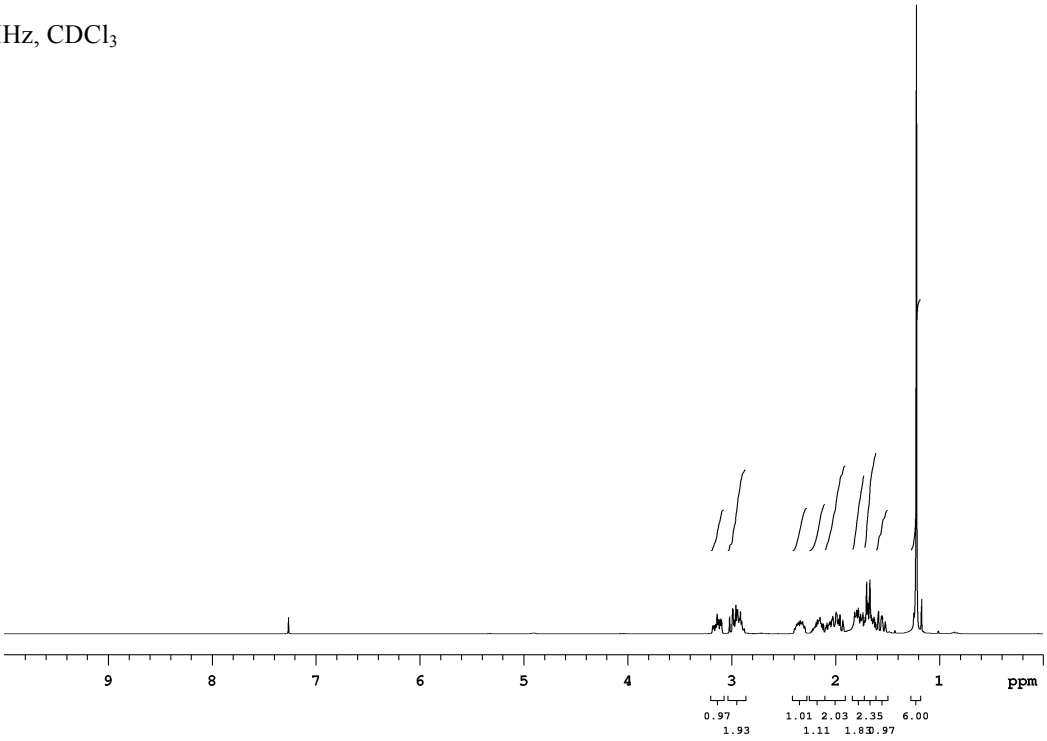
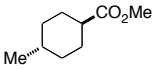
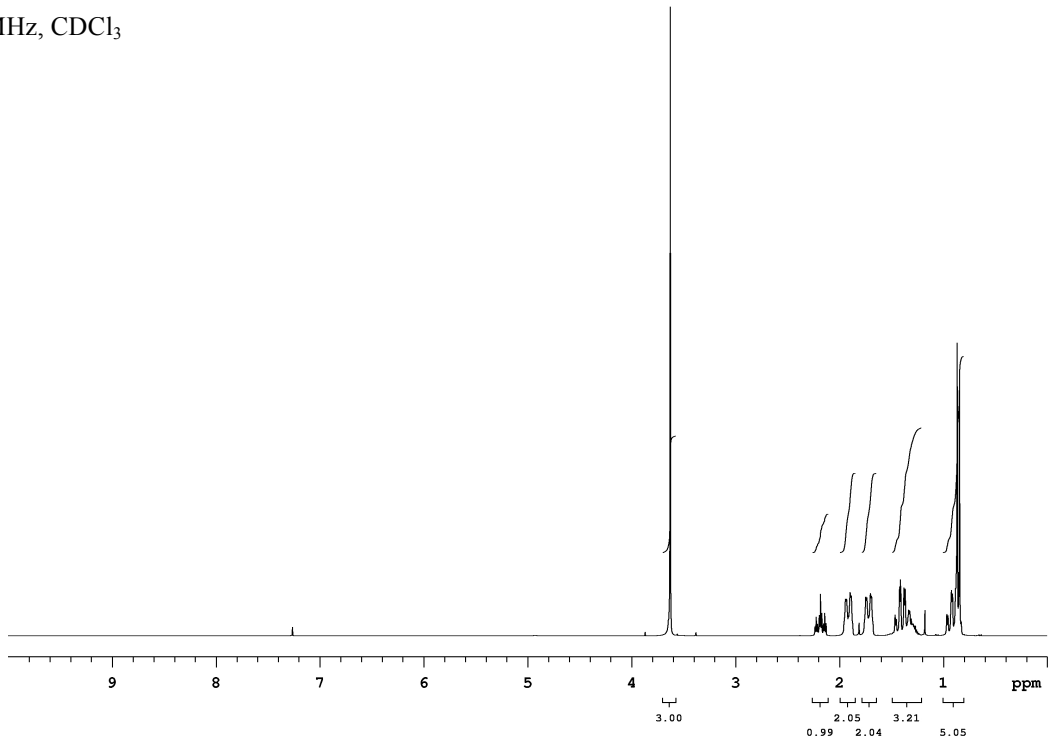
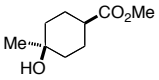


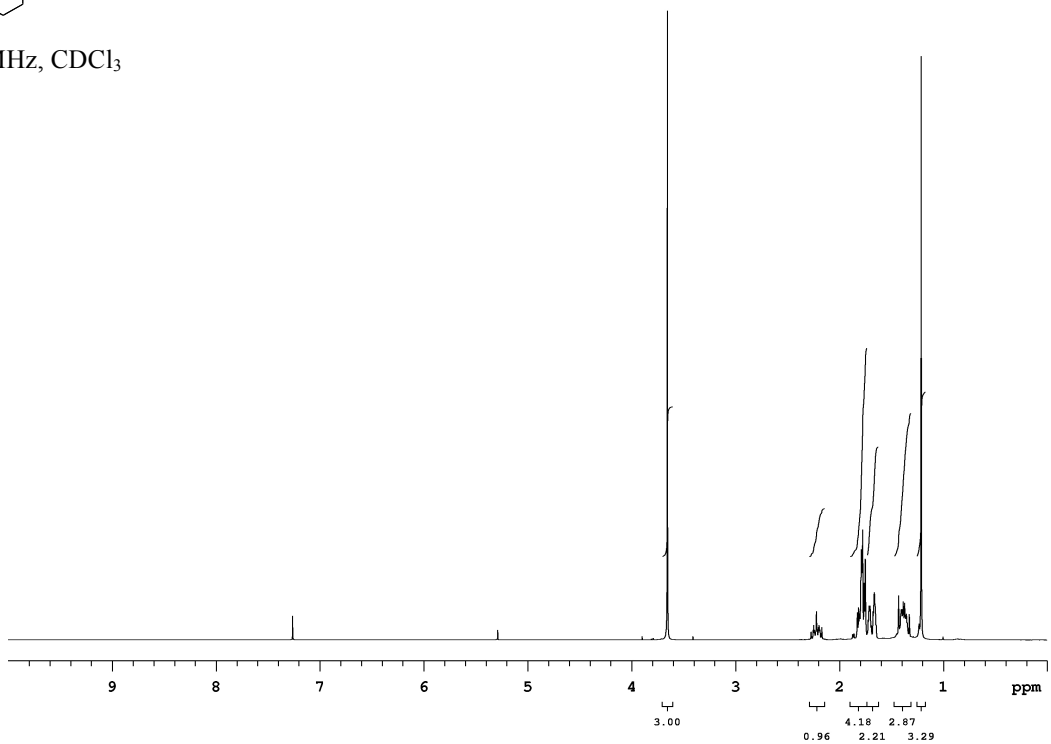


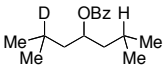
400 MHz, $CDCl_3$



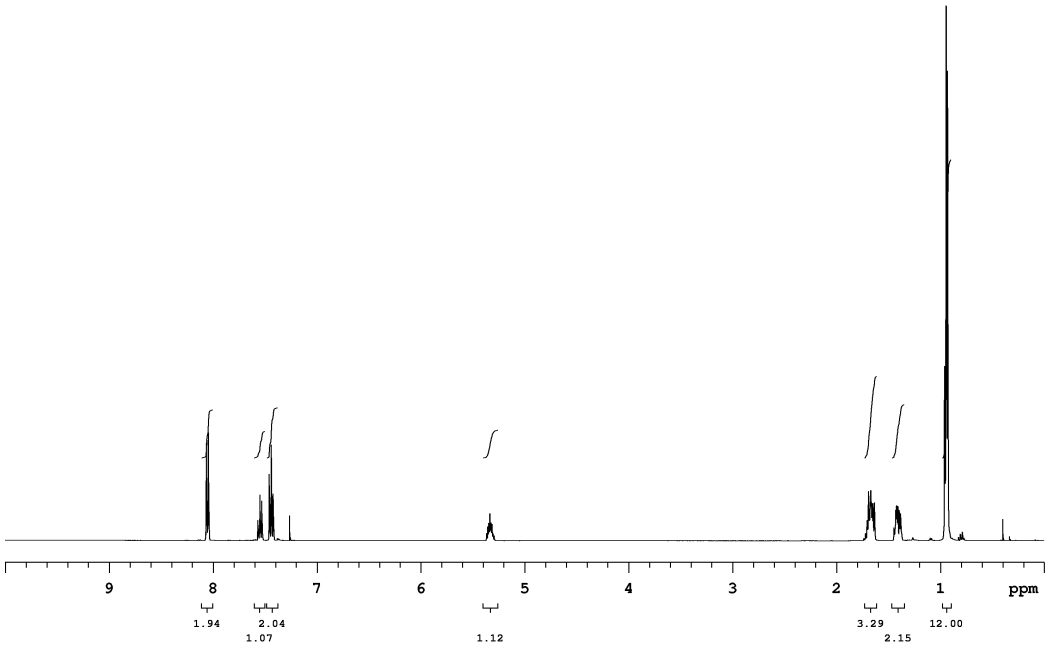


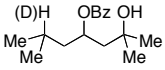
400 MHz, $CDCl_3$



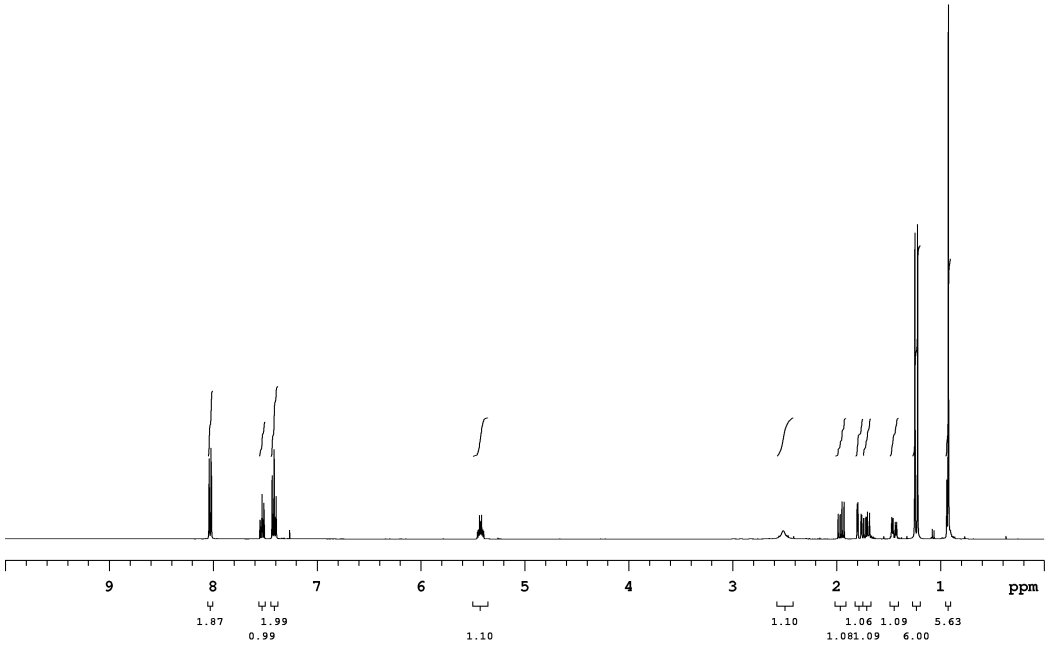


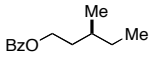
400 MHz, $CDCl_3$



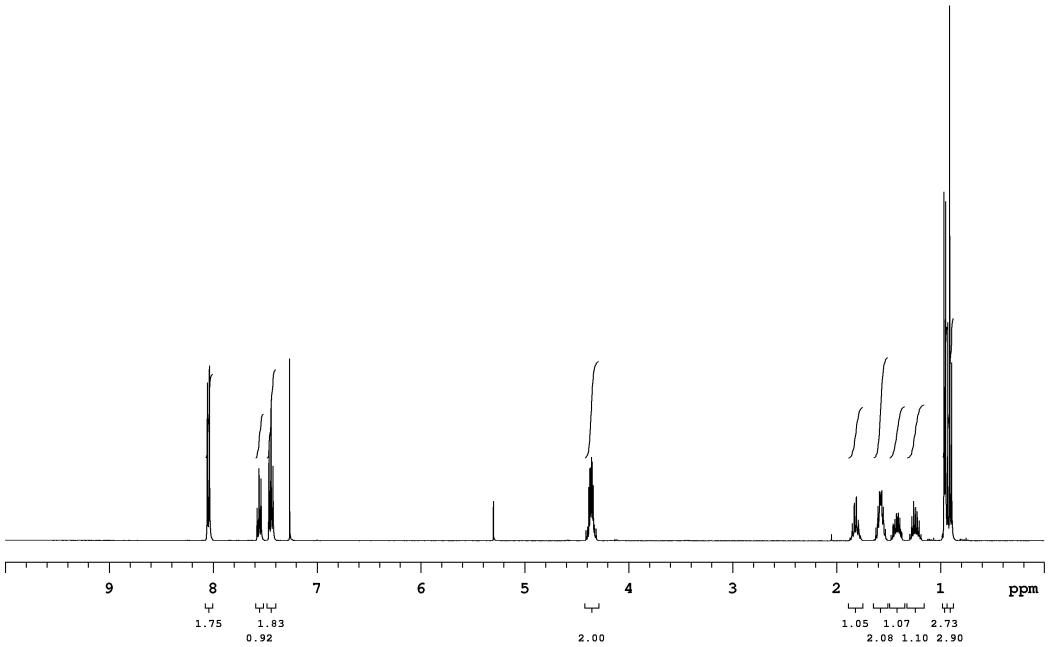


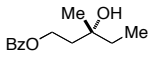
400 MHz, $CDCl_3$





400 MHz, $CDCl_3$





400 MHz, $CDCl_3$