A General Approach to the Enantioselective α-Oxidation of Aldehydes Via Synergistic Catalysis.

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Supporting Information

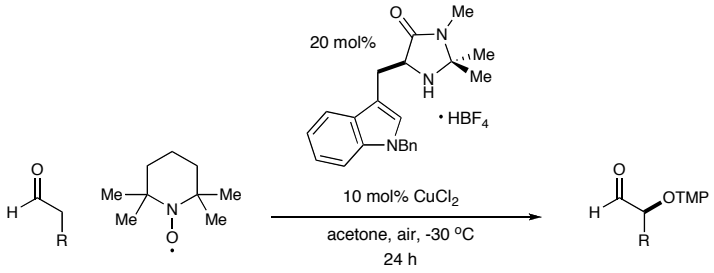
I. General Information. Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego[1]. All solvents were purified according to the method of Grubbs[2], unless otherwise noted. Organic solutions were concentrated under reduced pressure on a Büchi rotary evaporator. Chromatographic purification of products was accomplished using force-flow chromatography on Silicycle silica gel according to the method of Still[3]. Thin-layer chromatography (TLC) was performed on Silicycle 250 μm silica gel plates. TLC visualization was performed by ultraviolet light, $KMnO_4$, or CAM stain. All yields and selectivity reported are averages of at least two experimental runs.

^{1}H NMR spectra were recorded on a Bruker 500 (500 MHz) and are referenced relative to residual $CDCl_3$ proton signals at δ 7.27 ppm or residual C_6D_6 at δ 7.15 ppm. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ap = apparent), integration, coupling constant (Hz), and assignment. ^{13}C NMR spectra were recorded on a Bruker 500 (125 MHz) and are referenced relative to $CDCl_3$ at δ 77.23 ppm or C_6D_6 at δ 128.6 ppm. Data for ^{13}C NMR are reported in chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). High Resolution Mass spectra were obtained from the

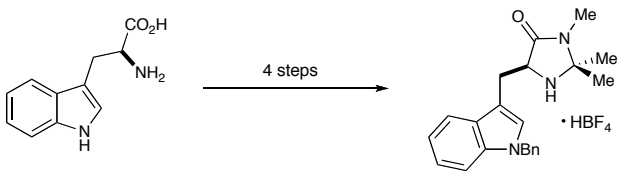
[1] Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; 3rd ed., Pergamon Press, Oxford, 1988.
[2] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.
[3] Still, W. C.; Kahn, M.; Mitra, A. J. *J. Org. Chem.* **1978**, *43*, 2923.

Princeton University Mass Spectral Facility. High Pressure Liquid chromatography (HPLC) was performed on a Hewlett-Packard 1100 Series chromatograph using a chiral column (25 cm) and guard column (5 cm) as noted for each compound. Optical rotations were measured on a Jasco P-1010 polarimeter with $[\alpha]_D$ values reported in degrees; concentration (c) is in g/100 mL. All aldehyde starting materials were commercially available or prepared from literature procedures *not* utilizing DMSO, as any residual dimethylsulfide inhibited the reaction.

II. Enantioselective α-Oxidation of Aldehydes



General Procedure for Enantioselective Oxidation: To an oven dried vial was added catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), oven-dried 4Å molecular sieves (5 mg), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.1 equiv.), and acetone (0.6 mL), which was taken from a bench-top solvent bottle and stored over oven-dried 4Å molecular sieves prior to use. Following the subsequent addition of aldehyde (1.0 mmol, 1.0 equiv.), the resulting brown solution was sealed with a septum cap and moved to a -30 °C bath and stirred for 5 min. A solution of TEMPO (187.5 mg, 1.20 mmol, 1.2 equiv.) in acetone (0.32 mL) was added dropwise to the reaction mixture. An ambient air inlet line (16G needle attached to rubber tubing) was then pierced through the septum cap and allowed to hang off the side of the cooling bath. After stirring for 24 h, the mixture was diluted with 2 mL of ether and quenched with 2 mL of saturated aqueous NH_4Cl. After the addition of 1 mL of water, the aqueous layer was extracted with ether (2 mL, x3), and the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude reaction mixture was purified by column chromatography to yield the α-oxyaminated aldehyde.

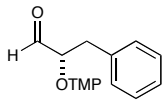


Catalyst 2. Benzylation of L-Tryptophan (20.0 g) was accomplished as previously reported by Magnus[4] to yield L-1-benzyl-Tryptophan (27.4 g, 93.1 mmol, 95% yield). To a dried round bottom flask was added the crude L-1-benzyl-Tryptophan (27.4 g, 93.1 mmol, 1.0 equiv.) and MeOH (200 mL), and the reaction mixture was cooled to 0 ºC. After 10 min., $SOCl_2$ (13.5 mL, 186.3 mmol, 2.0 equiv.) was added slowly to the vigorously stirring mixture. The resulting slurry was stirred vigorously at room temperature for 40 h, until complete by LCMS. After complete consumption of starting material, the mixture was concentrated under vacuum, and the solid was dissolved in minimal MeOH. The crude product was precipitated with ether and hexanes then filtered. The solid ester·HCl salt was dried under vacuum and used without further purification.

To a round bottom flask were added the crude ester·HCl salt (26.1 g, 75.7 mmol, 1.0 equiv.) and methyl amine (40% in MeOH, 60 mL), and the resulting solution was stirred overnight at room temperature until complete consumption of starting material was observed by LCMS. The mixture was then concentrated under vacuum, washed with ether, and concentrated again under vacuum. This procedure was performed three times to remove excess methylamine. The crude product was used without further purification. The crude amide·HCl salt was then suspended in 200 mL of CH_2Cl_2 and washed with 200 mL of sat. aq. $NaHCO_3$. The aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude, freebased amide (19.0 g, 61.9 mmol, 1.0 equiv.) was added to a dried round bottom flask with TSA·H_2O (590 mg, 3.09 mmol, 5 mol%), acetone (23 mL, 309.3 mmol, 5.0 equiv.), and MeOH (125 mL). The mixture was stirred at reflux overnight until complete consumption of starting material was observed by LCMS, after which it was cooled to room temperature and concentrated under vacuum. The crude

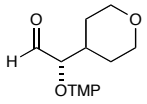
[4] Magnus, P.; Mugrage, B.; DeLuca, M. R.; Cain, G. A. *J. Am. Chem. Soc.* **1990**, *112*, 5220-5230.

catalyst was purified by flash chromatography with silica gel using EtOAc as an eluent to yield the freebase catalyst (17.4 g, 50.1 mmol, 51.2 % yield over four steps from L-Tryptophan) as a colorless oil. IR (thin film) 3588.4, 3517.1, 3263.0, 2939.9, 2682.6, 1702.4, 1593.5, 1465.6, 1406.6, 1344.5, 1315.3, 1108.2, 1032.2, 749.6, 703.3, 652.5 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.70 (d, 1H, J = 8.0 Hz, Ar**H**), 7.23-7.31 (m, 4H, Ar**H**), 7.19 (t, 1H, J = 7.0 Hz, Ar**H**), 7.14 (t, 1H, J = 7.5 Hz, Ar**H**), 7.05-7.11 (m, 3H, Ar**H**), 5.24-5.34 (m, 2H, NC**H**$_2$Ar), 3.86 (t, 1H, J = 5.5 Hz, 1H, C(=O)C**H**), 3.26-3.36 (m, 2H, C**H**$_2$Ar), 2.71 (s, 3H, NC**H**$_3$), 1.84 (bs, 1H, N**H**), 1.26 (s, 3H, C**H**$_3$), 1.01 (s, 3H, C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 174.1 (**C**(=O)), 137.7 (**Ar**), 136.4 (**Ar**), 128.8 (**Ar**), 128.7 (**Ar**), 127.6 (**Ar**), 127.5 (**Ar**), 127.0 (**Ar**), 122.0 (**Ar**), 119.5 (**Ar**), 119.2 (**Ar**), 109.7 (**Ar**), 109.5 (**Ar**), 75.5 (**C**(CH$_3$)$_2$), 59.1 (C(=O)**C**H), 49.9 (N**C**H$_2$Ar), 26.8 (C(**C**H$_3$)$_2$), 25.9 (**C**H$_2$Ar), 25.3 (C(**C**H$_3$)$_2$), 25.2 (N**C**H$_3$); HRMS (ESI-TOF) calculated for $C_{22}H_{25}ON_3$ $[M+H]^+$ m/z 347.1998, found 347.1998. $[\alpha]_D^{24}$ = -56.1 (c = 1.64, $CHCl_3$). The catalyst was then added to a dried round bottom flask with 400 mL of ether and cooled to -78 ºC. While stirring vigorously, $HBF_4 \cdot Et_2O$ (7.0 mL, 51.1 mmol, 1.02 equiv.) was added dropwise, and the cooling bath was removed. The mixture was stirred for 30 minutes, while slowly warming to room temperature, after which it was filtered, and the solid was recrystallized from a mixture of MeOH and 1:1 Et_2O : hexanes to yield the catalyst salt as a *white* solid.



***(S)*-3-phenyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal.** Prepared following the general procedure outlined above using 3-phenylpropionaldehyde (134.2 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular seives (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 10% Et_2O in hexanes to provide the title compound (251.3 mg, 89% yield, 92% ee) as a colorless liquid. IR (thin film) 2973.8, 2931.6, 1731.7, 1603.8, 1496.5, 1455.0,

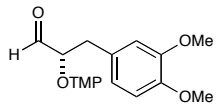
1375.2, 1361.8, 1259.2, 1241.8, 1208.2, 1182.6, 1132.9, 1074.0, 1044.6, 957.5, 749.1, 699.0 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.89 (d, 2H, J = 5.0 Hz, **H**C(=O)), 7.17-7.24 (m, 4H, Ar**H**), 7.12-7.17 (m, 1H, Ar**H**), 4.52 (dd, 1H, J = 5.0, 10.0 Hz, HC(=O)C**H**), 2.84-2.99 (m, 2H, C**H**Ph), 1.26-1.52 (m, 6H, $C(CH_3)_2C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$), 1.12-1.18 (m, 12H, $NC(C\mathbf{H_3})_2$); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.5 (H**C**(=O)), 136.5 (**Ar**), 130.1 (**Ar**), 128.6 (**Ar**), 126.9 (**Ar**), 88.7 (HC(=O)**C**), 60.9 ($N\mathbf{C}(CH_3)_2$), 59.8 ($N\mathbf{C}(CH_3)_2$), 40.3 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 40.2 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 36.8 ($\mathbf{C}H_2Ph$), 34.5 ($NC(\mathbf{C}H_3)_2$), 33.9 ($NC(\mathbf{C}H_3)_2$), 20.5 ($NC(\mathbf{C}H_3)_2$), 20.3 ($NC(\mathbf{C}H_3)_2$), 17.3 ($C(CH_3)_2CH_2\mathbf{C}H_2CH_2$); HRMS (ESI-TOF) calculated for $C_{18}H_{27}O_2N$ $[M+H]^+$ m/z 289.2042, found 289.2042. $[\alpha]_D^{25}$ = -97.0 (c = 1.06, $CHCl_3$). The enantiomeric excess was determined from the corresponding alcohol, which was prepared by treating the aldehyde (1.0 equiv.) with $NaBH_4$ (2.0 equiv.) in MeOH (0.5 M) at 0 ºC and slowly warming to room temperature over 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with saturated aqueous NH_4Cl. After the addition of water, the organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the alcohol (OD, 1% IPA/hexanes, 1.0 mL/min, 220 nm) indicated 92% ee: t_R (major) = 13.2 minutes, t_R (minor) = 15.8 minutes.



***(S)*-2-(tetrahydro-*2H*-pyran-4-yl)-2-(2,2,6,6-tetramethylpiperidin1-yloxy)acetaldehyde.** Prepared following the general procedure outlined above using 2-(tetrahydro-2*H*-pyran-4-yl)acetaldehyde[5] (128.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 15% Et_2O in

[5] Kitbunnadaj, R.; Hoffmann, M.; Fratantoni, S. A.; Bongers, G.; Bakker, R. A.; Wieland, K.; el Jilali, A.; De Esch, I. J. P.; Menge, W. M. P. B.; Timmerman, H.; Leurs, R. *Bioorganic & Medical Chemistry* **2005**, *13*, 6309.

petroleum ether to provide the title compound (253.3 mg, 90% yield, 95% ee) as a colorless liquid. IR (thin film) 2936.4, 2872.7, 2844.3, 1725.5, 1467.1, 1375.4, 1362.0, 1259.5, 1240.8, 1149.5, 1132.9, 1096.4, 1042.5, 1014.8, 989.6, 868.2, 749.9, 716.5 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.95 (d, 1H, J = 5.0 Hz, **H**C(=O)), 4.06 (dd, 1H, J = 10.0 Hz, J = 5.0 Hz, HC(=O)C**H**), 3.87-3.98 (m, 2H, C$\mathbf{H_2}$O), 3.11-3.23 (m, 2H, C$\mathbf{H_2}$O), 1.84-1.95 (m, 1H, $CH_2C\mathbf{H}(CH_2)_2$) 1.54-1.64 (m, 2H, $CH_2CH(C\mathbf{H_2})_2$), 1.10-1.54 (m, 20H, $CH_2CH(C\mathbf{H_2})_2$/OTMP); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.9 (H**C**(=O), 90.8 (HC(=O)**C**), 67.6 (**C**H_2O), 67.5(**C**H_2O), 61.3 (N**C**$(CH_3)_2$), 59.9 (N**C**$(CH_3)_2$), 40.4 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 40.1 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 37.1 ($CH_2\mathbf{C}H(CH_2)_2$), 34.6 (NC(**C**$H_3)_2$), 34.3 (NC(**C**$H_3)_2$), 29.1 ($CH_2CH(\mathbf{C}H_2)_2$), 28.6 ($CH_2CH(\mathbf{C}H_2)_2$), 20.5 (NC(**C**$H_3)_2$), 17.3 ($C(CH_3)_2CH_2\mathbf{C}H_2CH_2$); HRMS (ESI-TOF) calculated for $C_{16}H_{29}O_3N$ $[M+H]^+$ m/z 283.2147, found 283.2149. $[\alpha]_D^{25}$ = -139.9 (c = 0.51, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (OD, 2.0% IPA/hexanes, 1.0 mL/min, 254 nm) indicated 95% ee: t_R (major) = 13.0 minutes, t_R (minor) = 14.7 minutes.

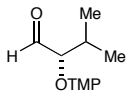


***(S)*-3-(3,4-dimethoxyphenyl)-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)propanal.**

Prepared following the general procedure outlined above using 3-(3,4-dimethoxyphenyl)propanal[6] (194.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure

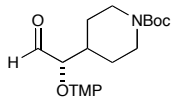
[6] Ermolatev, D. S.; Alifanov, V. L.; Rybakov, V. B.; Babaev, E. V.; Van der Eychen, E. V. *Synthesis* **2008**, *13*, 2083.

and was purified by flash chromatography using 18% EtOAc in hexanes to provide the title compound (305.8 mg, 88% yield, 92% ee) as a colorless liquid. IR (thin film) 2932.6, 2835.2, 1728.0, 1591.6, 1516.0, 1464.3, 1418.8, 1374.9, 1361.3, 1261.2, 1236.7, 1261.2, 1236.7, 1157.6, 1140.6, 1029.3, 957.0, 857.2, 805.2, 756.2, 713.2 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.96 (d, 1H, J = 5.0 Hz, **H**C(=O)), 6.78-6.85 (m, 2H, Ar**H**), 6.65 (d, 1H, Ar**H**), 4.54-4.60 (m, 1H, HC(=O)C**H**), 3.58 (s, 3H, OC**H**$_3$), 3.48 (s, 3H, OC**H**$_3$) 2.94-3.05 (m, 2H, C**H**$_2$Ar), 1.26-1.52 (m, 6H, C(CH$_3$)$_2$C**H**$_2$C**H**$_2$C**H**$_2$), 1.12-1.25 (m, 12H, NC(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.9 (H**C**(=O), 149.9 (**Ar**), 149.1 (**Ar**), 128.6 (**Ar**), 122.1 (**Ar**), 114.0 (**Ar**), 112.1 (**Ar**), 89.1 (HC(=O)**C**), 60.9 (N**C**(CH$_3$)$_2$), 59.9 (N**C**(CH$_3$)$_2$), 55.5 (O**C**H$_3$), 55.5 (O**C**H$_3$), 40.3 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 40.2 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 36.6 (**C**H$_2$Ar), 34.5 (NC(**C**H$_3$)$_2$), 33.9 (NC(**C**H$_3$)$_2$), 20.6 (NC(**C**H$_3$)$_2$), 20.4 (NC(**C**H$_3$)$_2$), 17.4 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$); HRMS (ESI-TOF) calculated for $C_{20}H_{31}O_4N$ $[M+H]^+$ m/z 349.2253, found 349.2243. $[\alpha]_D^{24}$ = -77.9 (c = 0.50, $CHCl_3$). The enantiomeric excess was determined from the corresponding alcohol, which was prepared by treating the aldehyde (1.0 equiv.) with $NaBH_4$ (2.0 equiv.) in MeOH (0.5 M) at 0 °C and slowly warming to room temperature over 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with saturated aqueous NH_4Cl. After the addition of water, the organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the alcohol (OJ, 2.0% IPA/hexanes, 1.0 mL/min, 220 nm) indicated 92% ee: t_R (minor) = 30.1 minutes, t_R (major) = 34.3 minutes.



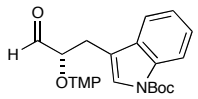
***(S)*-3-methyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)butanal.** Prepared following the general procedure outlined above using 3-methylbutanal (86.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography

using 3% Et_2O in hexanes to provide the title compound (212.4 mg, 88% yield, 94% ee) as a colorless liquid. IR (thin film) 2968.9, 2934.2, 2874.5, 1728.3, 1469.6, 1375.0, 1362.0, 1258.9, 1242.0, 1133.1, 1049.8, 1013.3, 956.7, 909.0, 709.3 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.98 (d, 1H, J = 5.0 Hz, **H**C(=O)), 4.06 (dd, 1H, J = 5.0 Hz, J = 5.0 Hz, HC(=O)C**H**), 2.00-2.11 (m, 1H, C**H**$_2$i-Pr), 1.15-1.53 (m, 18H, OTMP), 1.06 (d, 3H, J = 5.0 Hz, CH(C**H**$_3$)$_2$) 0.93 (d, 3H, J = 5.0 Hz, CH(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, C_6D_6) δ: 203.5 (H**C**(=O), 92.2 (HC(=O)**C**), 61.1 (N**C**(CH$_3$)$_2$), 59.8 (N**C**(CH$_3$)$_2$), 40.4 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 40.2 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 34.6 (NC(**C**H$_3$)$_2$), 34.2 (NC(**C**H$_3$)$_2$), 30.3 (**C**H(CH$_3$)$_2$), 20.5 (NC(**C**H$_3$)$_2$), 20.4 (NC(**C**H$_3$)$_2$), 18.7 (CH(**C**H$_3$)$_2$), 17.8 (CH(**C**H$_3$)$_2$), 17.4 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$); HRMS (ESI-TOF) calculated for $C_{14}H_{27}O_2N$ $[M+H]^+$ m/z 241.2042, found 241.2042. $[\alpha]_D^{25}$ = -148.6 (c = 0.84, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at 0 ºC room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (AD, 1.0% IPA/hexanes, 1.0 mL/min, 254 nm) indicated 94% ee: t_R (major) = 8.2 minutes, t_R (minor) = 10.2 minutes.



***(S)-tert*-butyl-4-(2-oxo-1-(2,2,6,6-tetramethylpiperidin1-yloxy)ethyl)piperidie-1-carboxylate.** Prepared following the general procedure outlined above using *tert*-butyl-4-(2-oxoethyl)piperidine-1-carboxylate (227.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 12% EtOAc in hexanes to provide the title compound (319.2 mg, 84% yield, 95% ee) as a colorless

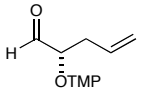
liquid. IR (thin film) 2974.9, 2932.1, 2870.1, 1725.9, 1694.5, 1466.9, 1450.7, 1421.9, 1364.9, 1278.7, 1249.7, 1172.4, 1139.0, 1042.9, 868.1, 767.6 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 9.90 (d, 1H, J = 5.0 Hz, **H**C(=O)), 4.15 (ap bs, 2H, C**H**$_2$N), 3.94-3.99 (m, 1H, HC(=O)C**H**), 2.69 (ap bs, 2H, C**H**$_2$N), 1.93-2.04 (m, 1H, CH_2C**H**$(CH_2)_2$) 1.25-1.93 (m, 20H, $CH_2CH(CH_2)_2$/OTMP), 1.10-1.25 (m, 11H, $CH_2CH(CH_2)_2$/$C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 204.8 (H**C**(=O), 154.7 (N**C**(=O)O), 90.2 (HC(=O)**C**), 79.5 (O**C**$(CH_3)_3$), 61.3 (N**C**$(CH_3)_2$), 60.0 (N**C**$(CH_3)_2$), 40.3 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 40.0 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 37.9 (CH_2**C**$H(CH_2)_2$), 34.5 (NC(**C**$H_3)_2$), 34.2 (NC(**C**$H_3)_2$), 28.5 (OC(**C**$H_3)_3$), 27.8 (N(**C**$H_2)_2$), 27.4 (CH_2CH(**C**$H_2)_2$), 20.5 (CH(**C**$H_3)_2$), 17.1 ($C(CH_3)_2CH_2$**C**H_2CH_2); HRMS (ESI-TOF) calculated for $C_{21}H_{38}O_4N_2$ $[M+H]^+$ m/z 382.2832, found 382.2831. $[\alpha]_D^{25}$ = -90.5 (c = 1.04, $CHCl_3$). The enantiomeric excess was determined from the corresponding benzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and benzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at 0 ºC room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (OD, 1.0% IPA/hexanes, 1.0 mL/min, 233 nm) indicated 95% ee: t_R (major) = 10.5 minutes, t_R (minor) = 13.7 minutes.



***(S)-tert*-butyl-3-(3-oxo-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propyl)-1*H*-indole-1-carboxylate.** Prepared following the general procedure outlined above using *tert*-butyl-3-(3-oxopropyl)-1*H*-indole-1-carboxylate[7] (273.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 5% EtOAc in hexanes

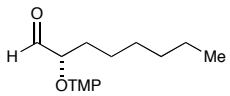
[7] Rendler, S.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 5027.

to provide the title compound (353.5 mg, 83% yield, 93% ee) as a colorless liquid. IR (thin film) 2975.7, 2932.7, 1729.4, 1610.9, 1570.0, 1451.7, 1368.5, 1308.7, 1254.6, 1155.7, 1087.7, 1045.1, 1015.5, 856.6, 764.8, 743.6, 713.6 cm^{-1}; ^1H NMR (500 MHz, C-DCl_3) δ: 9.87 (d, 1H, J = 5.0 Hz, **H**C(=O)), 8.16 (bs, 1H, Ar**H**), 7.52-7.59 (m, 2H, Ar**H**), 7.24-7.40 (m, 2H, Ar**H**), 4.46-4.52 (m, 1H, HC(=O)C**H**), 3.18 (apd, 2H, J = 5.0 Hz, C$\mathbf{H_2}$Ar), 1.69 (s, 9H, C(C$\mathbf{H_3}$)$_3$), 1.32-1.64 (m, 6H, C(CH$_3$)$_2$C$\mathbf{H_2}$C$\mathbf{H_2}$C$\mathbf{H_2}$), 1.12-1.29 (m, 12H, NC(C$\mathbf{H_3}$)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 204.0 (H**C**(=O), 149.6 (N**C**(=O)O), 135.4 (**Ar**), 130.6 (**Ar**), 128.4 (**Ar**), 124.5 (**Ar**), 122.6 (**Ar**), 119.0 (**Ar**), 115.2 (**Ar**), 114.6 (**Ar**), 87.5 (HC(=O)**C**), 83.5 (C(=O)O**C**(CH$_3$)$_3$), 60.7 (N**C**(CH$_3$)$_2$), 60.0 (N**C**(CH$_3$)$_2$), 40.1 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 40.1 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 34.3 (NC(**C**H$_3$)$_2$), 33.9 (NC(**C**H$_3$)$_2$), 28.2 (C(=O)OC(**C**H$_3$)$_3$), 25.9 (**C**H$_2$Ar), 20.6 (NC(**C**H$_3$)$_2$), 20.4 (NC(**C**H$_3$)$_2$), 17.1 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$) ; HRMS (ESI-TOF) calculated for $C_{25}H_{36}O_4N_2$ $[M+H]^+$ m/z 428.2662, found 428.2670. $[\alpha]_D^{24}$ = -38.0 (c = 1.04, $CHCl_3$). The enantiomeric excess was determined from the corresponding alcohol, which was prepared by treating the aldehyde (1.0 equiv.) with $NaBH_4$ (2.0 equiv.) in MeOH (0.5 M) at 0 °C and slowly warming to room temperature over 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with saturated aqueous NH_4Cl. After the addition of water, the organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the alcohol (OJ, 3% IPA/hexanes, 1.0 mL/min, 226 nm) indicated 93% ee: t_R (major) = 11.5 minutes, t_R (minor) = 15.0 minutes.



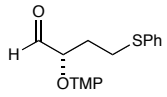
***(S)*-2-(2,2,6,6-tetramethylpiperidin-1-yloxy)pent-4-enal (19).** Prepared following the general procedure outlined above using 4-pentenal (84.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 5%

EtOAc in hexanes to provide the title compound (185.7 mg, 78% yield, 92% ee) as a colorless liquid. IR (thin film) 2975.3, 2935.3, 1733.3, 1642.8, 1470.6, 1375.4, 1361.9, 1259.3, 1209.1, 1183.2, 1133.4, 1047.0, 990.2, 957.8, 919.2, 785.3, 717.0 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.86 (d, 1H, J = 5.0 Hz, **H**C(=O)), 5.82 (ddt, J_{AB} = 7.5 Hz, J_{AC} = 11.0 Hz, J_{BD} = 7.0 Hz, J_{BE} = 3.0 Hz, $CH_2C\mathbf{H}CH_2$), 5.05-5.13 (m, 2H, $CH_2CHC\mathbf{H_2}$), 4.31 (ddd, 1H, J_{AB} = 4.0 Hz, J_{AC} = 5.0 Hz, J_{BD} = 3.0 Hz, HC(=O)C**H**), 2.37-2.53 (m, 2H, $C\mathbf{H_2}CHCH_2$), 1.07-1.53 (m, 18H, OTMP); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.5 (H**C**(=O), 132.5 ($CH_2\mathbf{C}HCH_2$), 118.3 ($CH_2CH\mathbf{C}H_2$), 88.2 (HC(=O)**C**), 60.6 ($N\mathbf{C}(CH_3)_2$), 59.9 ($N\mathbf{C}(CH_3)_2$), 40.3 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 40.2 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 35.0 ($\mathbf{C}H_2CHCH_2$), 34.4 ($NC(\mathbf{C}H_3)_2$), 34.0 ($NC(\mathbf{C}H_3)_2$), 20.4 ($CH(\mathbf{C}H_3)_2$), 20.3 ($CH(\mathbf{C}H_3)_2$), 17.4 ($C(CH_3)_2CH_2\mathbf{C}H_2CH_2$); HRMS (ESI-TOF) calculated for $C_{14}H_{25}O_2N$ $[M+H]^+$ m/z 239.1885, found 239.1885. $[\alpha]_D^{24}$ = -82.5 (c = 0.96, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at 0 °C room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (AD, 0.2% IPA/hexanes, 0.8 mL/min, 254 nm) indicated 92% ee: t_R (major) = 19.5 minutes, t_R (minor) = 22.7 minutes.



***(S)*-2-(2,2,6,6-tetramethylpiperidin1-yloxy)octanal.** Prepared following the general procedure outlined above using octanal (128.2 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml) at -40 °C. After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 3% Et_2O in hexanes to provide the title compound (291.9 mg, 86% yield, 90% ee) as a

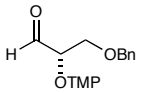
colorless liquid. IR (thin film) 2930.2, 2860.5, 1731.9, 1466.9, 1375.2, 1361.3, 1259.8, 1242.5, 1183.2, 1133.2, 10454.1, 972.6, 958.0, 917.5, 784.5, 713.5 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.91 (d, 1H, J = 5.0 Hz, **H**C(=O)), 4.28-4.33 (m, 1H, HC(=O)C**H**), 1.74-1.84 (m, 1H, HC(=O)CHC**H$_2$**), 1.62-1.72 (m, 1H, HC(=O)CHC**H$_2$**), 1.12-1.55 (m, 26H, C**H$_2$**C**H$_2$**C**H$_2$**C**H$_2$**CH$_3$**/OTMP**), 0.97 (t, 3H, J = 5.0 Hz, C**H$_3$**); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.9 (H**C**(=O), 89.0 (HC(=O)**C**), 60.6 (N**C**$(CH_3)_2$), 59.8 (N**C**$(CH_3)_2$), 40.3 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 40.2 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 34.5 (NC(**C**$H_3)_2$), 34.5 (NC(**C**$H_3)_2$), 31.9 (**C**H_2), 30.2 (**C**H_2), 29.7 (**C**H_2), 24.6 (CH_2), 22.9 (**C**H_2), 20.5 (NC(**C**$H_3)_2$), 20.3 (NC(**C**$H_3)_2$), 17.4 ($C(CH_3)_2CH_2$**C**H_2CH_2), 14.3 (**C**H_3); HRMS (ESI-TOF) calculated for $C_{17}H_{33}O_2N$ $[M+H]^+$ m/z 283.2511, found 283.2510. $[\alpha]_D^{26}$ = -61.4 (c = 0.73, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at 0 ºC room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (OD, 0.5% IPA/hexanes, 0.8 mL/min, 254 nm) indicated 90% ee: t_R (major) = 14.8 minutes, t_R (minor) = 16.4 minutes.



***(S)*-4-(phenylthiol)-2-(2,2,6,6-tetramethylpiperidin1-yloxy)butanal.** Prepared following the general procedure outlined above using 4-(phenylthio)butanal[8] (180.1 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 7% EtOAc in hexanes to provide the title compound (288.1 mg, 86% yield, 91% ee) as a colorless liquid. IR (thin film) 2972.6, 2933.5, 1727.4, 1584.8, 1481.0, 1439.2, 1375.1, 1361.5, 1259.8, 1132.8, 1053.3, 1025.5, 957.7, 738.1, 691.0 cm^{-1};

[8] Tius, M. A.; Trehan, S. *J. Org. Chem.* **1986**, *51*, 765.

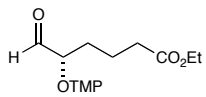
^{1}H NMR (500 MHz, C_6D_6) δ: 9.88 (d, 1H, J = 5.0 Hz, **H**C(=O)), 7.39 (d, 2H, J = 5.0 Hz, Ar**H**), 7.09-7.14 (m, 2H, Ar**H**), 6.99-7.04 (m, 1H, Ar**H**), 4.34-4.40 (m, 1H, HC(=O)C**H**), 2.91 (t, 2H, J = 7.5 Hz, C**H**$_2$SPh), 2.03-2.12 (m, 1H, HC(=O)CHC**H**$_2$), 1.90-2.00 (m, 1H, HC(=O)CHC**H**$_2$), 1.24-1.48 (m, 6H, C(CH$_3$)$_2$C**H**$_2$C**H**$_2$C**H**$_2$), 1.08-1.23 (m, 12H, NC(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.5 (H**C**(=O), 136.5 (**Ar**), 129.6 (**Ar**), 129.3 (**Ar**), 126.2 (**Ar**), 87.3 (HC(=O)**C**), 60.6 (N**C**(CH$_3$)$_2$), 59.9 (N**C**(CH$_3$)$_2$), 40.3 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 40.2 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 34.3 (NC(**C**H$_3$)$_2$), 34.1 (NC(**C**H$_3$)$_2$), 30.2 (**C**H$_2$SPh), 28.8 (HC(=O)C**C**H$_2$), 20.4 (CH(**C**H$_3$)$_2$), 20.3 (CH(**C**H$_3$)$_2$), 17.3 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$); HRMS (ESI-TOF) calculated for $C_{19}H_{29}O_2NS$ $[M+H]^+$ m/z 335.1919, found 335.1918. $[\alpha]_D^{26}$ = -86.9 (c = 0.60, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at 0 °C room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (OD, 1.0% IPA/hexanes, 1.0 mL/min, 254 nm) indicated 91% ee: t_R (major) = 18.7 minutes, t_R (minor) = 21.0 minutes.



***(S)*-3-(benzyloxy)-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal.** Prepared following the general procedure outlined above using 3-(benzyloxy)propanal[9] (164.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and ethyl acetate (0.92 mL). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 3% Et_2O in toluene to provide the title compound (247.3 mg, 77%

[9] Fonvielle, M.; Coincon, M.; Daher, R.; Desbenoit, N.; Kosieradzkak.; Barilone, N.; Gicquel, B.; Sygusch, J.; Jackson, M.; Therisod, M. *Chem. Eur. J.* **2008**, *14*, 852.

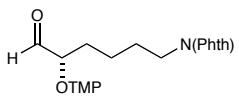
yield, 90% ee) as a colorless liquid. IR (thin film) 2973.7, 2932.3, 2871.3, 1733.1, 1454.4, 1375.6, 1361.4, 1260.0, 1208.4, 1183.8, 1132.4, 1094.9, 1046.0, 1028.2, 959.3, 747.8, 697.7 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 10.10 (d, 1H, J = 5.0 Hz, **H**C(=O)), 7.31-7.36 (m, 2H, Ar**H**), 7.24-7.29 (m, 2H, Ar**H**), 7.16-7.21 (m, 1H, Ar**H**), 4.36-4.40 (m, 1H, HC(=O)C**H**), 4.34 (ap s, 2H, C**H**$_2$OBn), 3.70-3.82 (m, 2H, OC**H**$_2$Ph), 1.14-1.52 (m, 18H, OTMP); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.7 (H**C**(=O), 138.4 (**Ar**), 128.6 (**Ar**), 127.8 (**Ar**), 127.8 (**Ar**), 89.1 (HC(=O)**C**), 73.4 (**C**H$_2$OBn), 69.7 (O**C**H$_2$Ph), 60.3 (N**C**(CH$_3$)$_2$), 60.3 (N**C**(CH$_3$)$_2$), 40.3 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 40.3 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 34.2 (NC(**C**H$_3$)$_2$), 33.8 (NC(**C**H$_3$)$_2$), 20.5 (CH(**C**H$_3$)$_2$), 20.4 (CH(**C**H$_3$)$_2$), 17.4 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$); HRMS (ESI-TOF) calculated for $C_{19}H_{29}O_3N$ $[M+H]^+$ m/z 319.2147, found 319.2148. $[\alpha]_D^{23}$ = -39.2 (c = 0.73, $CHCl_3$). The enantiomeric excess was determined from the corresponding alcohol after formation of the benzyl ester. This compound was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.), benzoyl chloride (1.2 equiv.), and DMAP (5 mol%) in CH_2Cl_2 (0.5 M) at 0 °C room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by flash chromatography. The ester was then treated with Zn (10 equiv.) and a 1:1 AcOH/H_2O mixture (0.5M) at 50 °C to cleave the N-O bond. The mixture was cooled to room temperature and extracted with CH_2Cl_2, and the organic layer was washed with sat. aq. $NaHCO_3$. The organic layer was then dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the alcohol (AS, 10% IPA/hexanes, 1.0 mL/min, 233 nm) indicated 90% ee: t_R (major) = 14.2 minutes, t_R (minor) = 17.0 minutes.



***(S)*-ethyl-6-oxo-5-(2,2,6,6-tetramethylpiperidin1-yloxy)hexanoate.** Prepared following the general procedure outlined above using ethyl-6-oxohexanoate[10] (158.2 mg, 1.00 mmol

[10] Wilson, J. E.; Casarez, A. D.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 11332.

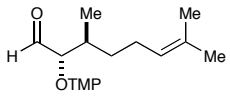
1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml) at -40 ºC. After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 8% Et_2O in hexanes to provide the title compound (255.8 mg, 82% yield, 89% ee) as a colorless liquid. IR (thin film) 2974.1, 2933.6, 2873.4, 1732.9, 1463.2, 1375.1, 13.62.0, 1242.0, 1163.9, 1133.5, 1097.2, 1063.4, 1044.5, 958.0, 877.6, 785.9, 714.7 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.85 (d, 1H, J = 4.5 Hz, **H**C(=O)), 4.20-4.25 (m, 1H, HC(=O)C**H**), 4.04 (q, 2H, J = 7.5, 14.5, 21.5 Hz, C(=O)OC**H$_2$**CH_3), 2.12-2.18 (m, 2H, C**H$_2$**C(=O)OCH_2CH_3), 1.58-1.80 (m, 4H, C**H$_2$**C**H$_2$**), 1.10-1.50 (m, 18H, OTMP), 1.06 (t, 3H, J = 7.0 Hz, C(=O)OCH_2C**H$_3$**); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.7 (**H**C(=O), 172.3 (**C**(=O)OCH_2CH_3), 88.6 (HC(=O)**C**), 60.6 (N**C**$(CH_3)_2$), 60.1 (C(=O)O**C**H_2CH_3), 59.8 (N**C**$(CH_3)_2$), 40.3 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 40.2 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 34.4 (NC(**C**$H_3)_2$), 34.0 (**C**H_2C(=O)OCH_2CH_3), 33.9 (NC(**C**$H_3)_2$), 29.5 (**C**H_2), 20.5 (CH(**C**$H_3)_2$), 20.3 (CH(**C**$H_3)_2$), 20.2 (**C**H_2), 17.4 ($C(CH_3)_2CH_2$**C**H_2CH_2) 14.3 (CH_2**C**H_3); HRMS (ESI-TOF) calculated for $C_{17}H_{31}O_4N$ $[M+H]^+$ m/z 313.2253, found 313.2249. $[\alpha]_D^{23}$ = -69.6 (c = 1.17, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the corresponding alcohol (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at 0 ºC room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the alcohol (OJ, 1.0% EtOH/hexanes, 0.8 mL/min, 254 nm) indicated 89% ee: t_R (major) = 24.0 minutes, t_R (minor) = 30.0 minutes.



***(S)*-6-(1,3-dioxoisoindolin-2-yl)-2-(2,2,6,6-tetramethylpiperidin1-yloxy)hexanal.**

Prepared following the general procedure outlined above using 6-(1,3-dioxoisoindolin-2-

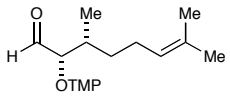
yl)hexanal[11] (245.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 15% EtOAc in hexanes to provide the title compound (345.8 mg, 86% yield, 90% ee) as a colorless liquid. IR (thin film) 2935.8, 2869.1, 1773.0, 1712.6, 1615.9, 1467.2, 1437.7, 1396.1, 1376.2, 1372.2, 1239.2, 1209.1, 1187.1, 1133.4, 1056.7, 999.5, 892.3, 791.3, 720.1 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 9.83 (d, 1H, J = 5.0 Hz, **H**C(=O)), 7.55-7.59 (m, 2H, Ar**H**), 6.95-7.01 (m, 2H, Ar**H**), 4.18-4.24 (m, 1H, HC(=O)C**H**), 3.56 (t, 2H, J = 7.5 Hz, C$\mathbf{H_2}$NAr), 1.65-1.74 (m, 1H, HC(=O)CHC$\mathbf{H_2}$), 1.50-1.64 (m, 3H, HC(=O)CHC$\mathbf{H_2}$/C$\mathbf{H_2}$), 1.10-1.50 (m, 20H, C$\mathbf{H_2}$/OTMP); ^{13}C NMR (125 MHz, C_6D_6) δ: 202.7 (H**C**(=O), 168.0 (**Ar**), 133.5 (**Ar**), 132.5 (**Ar**), 132.6 (**Ar**), 128.6 (**Ar**), 122.9 (**Ar**), 88.5 (HC(=O)**C**), 60.7 (N**C**$(CH_3)_2$), 59.7 (N**C**$(CH_3)_2$), 40.3 (C$(CH_3)_2$**C**$H_2CH_2CH_2$), 40.2 (C$(CH_3)_2$**C**$H_2CH_2CH_2$), 37.5 (**C**H_2NAr), 34.5 (NC(**C**$H_3)_2$), 34.0 (NC(**C**$H_3)_2$), 29.4 (**C**H_2), 28.7 (**C**H_2), 21.9 (**C**H_2), 20.5 (CH(**C**$H_3)_2$), 20.3 (CH(**C**$H_3)_2$), 17.4 (C$(CH_3)_2CH_2$**C**H_2CH_2); HRMS (ESI-TOF) calculated for $C_{23}H_{33}O_4N_2$ $[M+H]^+$ m/z 400.2362, found 400.2362. $[\alpha]_D^{25}$ = -52.9 (c = 0.91, $CHCl_3$). The enantiomeric excess was determined from the corresponding alcohol, which was prepared by treating the aldehyde (1.0 equiv.) with $NaBH_4$ (1.0 equiv.) in MeOH (0.5 M) at -78 ºC and slowly warming to room temperature overnight. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with saturated aqueous NH_4Cl. After the addition of water, the organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the alcohol (AD, 3.0% IPA/hexanes, 0.7 mL/min, 220 nm) indicated 90% ee: t_R (major) = 46.4 minutes, t_R (minor) = 52.2 minutes.



***(2S,3S)*-3,7-dimethyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)oct-6enal.** Prepared

[11] Vaismaa, M. J. P.; Yau, S. C.; Tomkinson, N. C. O. *Tetrahedron Lett.* **2009**, *50*, 3625.

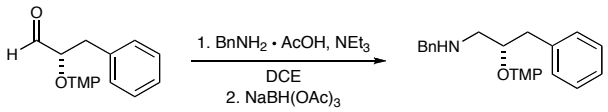
following the general procedure outlined above using *(S)*-Citronellal (154.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography using 5% Et_2O in hexanes to provide the title compound (246.7 mg, 80% yield, >20:1 dr) as a colorless liquid. IR (thin film) 2970.1, 2932.1, 1722.7, 1455.7, 1375.9, 1361.5, 1241.6, 1183.1, 1133.31, 046.4, 974.7, 957.4, 915.7, 711.4 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 10.04 (d, 1H, J = 5.0 Hz, **H**C(=O)), 5.26-5.32 (m, 1H, $CH_2C\mathbf{H}C(CH_3)_2$), 4.22 (dd, 1H, J = 6.0 Hz, J = 5.0 Hz, HC(=O)C**H**), 2.11-2.23 (m, 3H, C**H**$(CH_3)CH_2$/C**H**$_2$C$H(CH_3)_2$), 1.72-1.81 (m 4H, C**H**$_3$/C**H**$_2$), 1.68 (s, 3H, C**H**$_3$), 1.15-1.52 (m, 19H, C**H**$_2$/OTMP), 1.01 (d, 3H, J = 10.0 Hz, CH(C**H**$_3$)CH_2); ^{13}C NMR (125 MHz, C_6D_6) δ: 203.7 (H**C**(=O), 131.6 ($CH_2CH\mathbf{C}(CH_3)_2$), 124.8 ($CH_2\mathbf{C}HC(CH_3)_2$), 91.3 (HC(=O)**C**), 60.9 (N**C**$(CH_3)_2$), 60.0 (N**C**$(CH_3)_2$), 40.4 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 40.2 ($CH(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 35.1 (CHC**H**$(CH_3)CH_2$), 34.6 (NC(**C**$H_3)_2$), 34.1 (NC(**C**$H_3)_2$), 33.1 (**C**$H_2CHC(CH_3)_2$), 25.9 (CHC(**C**$H_3)_2$), 25.7 (**C**$H_2$), 20.6 (CH(**C**$H_3)_2$), 20.5 (CH(**C**$H_3)_2$), 17.8 (CH(**C**$H_3)_2$), 17.4 ($C(CH_3)_2CH_2\mathbf{C}H_2CH_2$), 15.1 (CH(**C**$H_3$)$CH_2$); HRMS (ESI-TOF) calculated for $C_{19}H_{35}O_2N$ $[M+H]^+$ m/z 309.2668, found 309.2666. $[\alpha]_D^{26}$ = -105.3 (c = 0.65, $CHCl_3$). The diastereomeric ratio (>20:1) was determined from the crude ^1H NMR aldehyde peaks.



***(2S,3R)*-3,7-dimethyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)oct-6enal.**[12] Prepared following the general procedure outlined above using *(R)*-Citronellal (154.0 mg, 1.00 mmol 1.00 equiv.), catalyst **2** (87.0 mg, 0.20 mmol, 0.2 equiv.), TEMPO (187.5 mg, 1.20 mmol, 1.20 equiv.), $CuCl_2$ (13.5 mg, 0.10 mmol, 0.10 equiv.), 4Å molecular sieves (5.0 mg), and acetone (0.92 ml). After 24 h the reaction mixture was subjected to the workup procedure outlined in the general procedure and was purified by flash chromatography

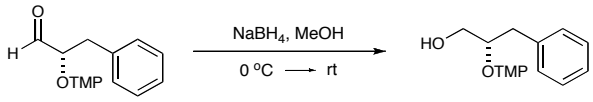
[12] The comericially available (*R*)-Citronellal (TCI) was sold as 93% ee, so chiral preprative HPLC was used to obtain enantiomeric pure starting material.

using 5% Et_2O in hexanes to provide the title compound (249.5 mg, 81% yield, 15:1 dr) as a colorless liquid. Major: IR (thin film) 2969.9, 2931.7, 1728.5, 1457.0, 1375.5, 1361.6, 1259.0, 1208.9, 1182.8, 1133.0, 1045.9, 974.9, 957.3, 913.8, 710.4 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 10.12 (d, 1H, J = 5.0 Hz, **H**C(=O)), 5.23-5.29 (m, 1H, $CH_2C\mathbf{H}C(CH_3)_2$), 4.19-4.25 (m, 1H, HC(=O)C**H**), 2.02-2.21 (m, 3H, C**H**$(CH_3)CH_2$/C$\mathbf{H_2}$CHC$(CH_3)_2$), 1.74-1.83 (m 4H, C$\mathbf{H_3}$/C$\mathbf{H_2}$), 1.66 (s, 3H, C$\mathbf{H_3}$), 1.14-1.54 (m, 19H, C$\mathbf{H_2}$/OTMP), 1.10 (d, 3H, J = 10.0 Hz, CH(C$\mathbf{H_3}$)CH_2); ^{13}C NMR (125 MHz, C_6D_6) δ: 204.2 (H**C**(=O), 131.7 ($CH_2CH\mathbf{C}(CH_3)_2$), 124.7 ($CH_2\mathbf{C}HC(CH_3)_2$), 91.4 (HC(=O)**C**), 61.0 (N**C**$(CH_3)_2$), 59.9 (N**C**$(CH_3)_2$), 40.5 ($C(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 40.2 ($CH(CH_3)_2\mathbf{C}H_2CH_2CH_2$), 35.7 (CHC**H**$(CH_3)CH_2$), 34.5 (NC(**C**$H_3)_2$), 34.2 (NC(**C**$H_3)_2$), 32.5 (**C**$H_2CHC(CH_3)_2$), 26.0 (CHC(**C**$H_3)_2$), 25.9 (**C**$H_2$), 20.5 (CH(**C**$H_3)_2$), 20.5 (CH(**C**$H_3)_2$), 17.7 (CH(**C**$H_3)_2$), 17.4 ($C(CH_3)_2CH_2\mathbf{C}H_2CH_2$), 15.5 (CH(**C**$H_3)CH_2$); HRMS (ESI-TOF) calculated for $C_{19}H_{35}O_2N$ $[M+H]^+$ m/z 309.2668, found 309.2666. $[\alpha]_D^{26}$ = -107.9 (c = 0.92, $CHCl_3$)[4]. Minor: See (*S*)-Citronllal entry above for data. $[\alpha]_D^{26}$ = +66.0 (c = 0.34, $CHCl_3$)[4]. The diastereomeric ratio (15:1) was determined from the crude ^1H NMR aldehyde peaks.



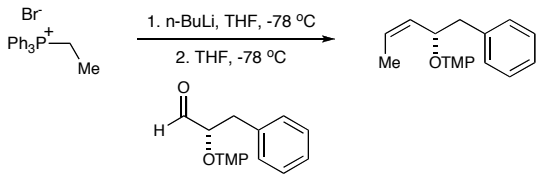
(*S*)-*N*-benzyl-3-phenyl-2-(2,2,6,6,-tetramethylpiperidin-1-yloxy)propan-1-amine. To a dried vial were added *(S)*-3-phenyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal (200 mg, 0.67 mmol, 1.0 equiv.), prepared from the procedure described above, triethylamine (125 μL, 0.91 mmol, 1.4 equiv.), benzylamine·acetic acid (146 mg, 0.87 mmol, 1.3 equiv.) and DCE (9.6 mL). The mixture was stirred vigorously for 15 minutes at room temperature before sodium triacetoxyborohydride (355 mg, 1.7 mmol, 2.5 equiv.) was added and stirred vigorously for an additional 3 h until starting material was consumed by TLC. The reaction was quenched with sat. aq. $NaHCO_3$ (5.0 mL) and water (3.0 mL). The aqueous layer was extracted with CH_2Cl_2 (2 x 8.0 mL) and EtOAc (2 x 8.0 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography with a 50%

EtOAc in hexanes eluent to provide the desired product (256.5 mg, 99% yield) as a colorless liquid. IR (thin film) 2971.2, 2930.8, 2870.7, 1602.9, 1495.3, 1453.4, 1375.2, 1360.2, 1207.9, 1132.0, 1029.7, 745.9, 698.2 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ: 7.15-7.36 (m, 10H, Ar**H**), 4.29-4.36 (m, 1H, C**H**OTMP), 3.62-3.76 (m, 2H, NHC**H**$_2$Ar), 3.19 (dd, 1H, J = 5.5, 13.0 Hz, NHC**H**$_2$CH), 2.86 (dd, 1H, J = 7.5, 12.0 Hz, C**H**$_2$Ar), 2.58-2.67 (m, 2H, C**H**$_2$Ar/NHC**H**$_2$CH), 0.95-1.71 (m, 18H, OTMP); ^{13}C NMR (125 MHz, CD_3OD) δ: 140.5 (**Ar**), 140.3 (**Ar**), 130.6 (**Ar**), 129.6 (**Ar**), 129.4 (**Ar**), 129.3 (**Ar**), 128.3 (**Ar**), 127.2 (**Ar**), 82.9 (NHCH$_2$**C**H), 61.3 (N**C**(CH$_3$)$_2$), 61.2 (N**C**(CH$_3$)$_2$), 54.5 (NH**C**H$_2$Ar), 53.6 (NH**C**H$_2$CH), 41.5 (bs, C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 39.9 (**C**H$_2$Ar), 35.0 (NC(**C**H$_3$)$_2$), 34.6 (NC(**C**H$_3$)$_2$), 21.2 (NC(**C**H$_3$)$_2$), 20.9 (NC(**C**H$_3$)$_2$), 18.3 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$); HRMS (ESI-TOF) calculated for $C_{25}H_{36}O_2N$ $[M+H]^+$ m/z 380.2828, found 380.2827. $[\alpha]_D^{23}$ = +23.8 (c = 0.98, $CHCl_3$). The enantiomeric excess was determined from the corresponding *m*-nitrobenzoyl ester, which was prepared by treating the product (1.0 equiv.) with triethylamine (2.0 equiv.) and *m*-nitrobenzoyl chloride (1.2 equiv.) in CH_2Cl_2 (0.5 M) at room temperature for 1 h. Upon complete consumption of starting material, the reaction mixture was diluted with CH_2Cl_2 and quenched with water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the ester (AD, 6% IPA/hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: t_R (major) = 16.7 minutes, t_R (minor) = 20.5 minutes.



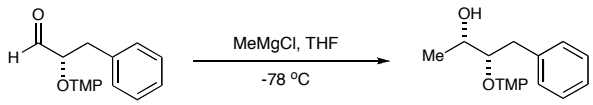
(*S*)-3-phenyl-2-(2,2,6,6,-tetramethylpiperidin-1-yloxy)propan-1-ol. To a dried vial were added *(S)*-3-phenyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal (150 mg, 0.52 mmol, 1.0 equiv.), prepared from the procedure described above, and MeOH (1.0 mL) and cooled to 0 °C, after which $NaBH_4$ (39.2 mg, 1.0 mmol, 2.0 equiv.) was added. The reaction was slowly warmed to room temperature over 1 h before being quenched with sat. aq. NH_4Cl (1.0 mL) and water (1.0 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2.0 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash

chromatography with a 10% EtOAc in hexanes eluent to provide the desired product (298.6 mg, 99% yield) as a colorless liquid. IR (thin film) 3410.7, 3317.5, 2924.5, 2898.1, 1728.4, 1610.0, 1470.2, 1404.4, 1394.7, 1221.3, 1220.0, 1156.6, 1072.0, 1019.9, 975.5, 790.1, 674.6 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.10-7.16 (m, 3H, Ar**H**), 7.18-7.23 (m, 2H, Ar**H**), 5.65 (bs, 1H, O**H**), 4.37-4.43 (m, 1H, C**H**OTMP), 3.90 (dd, 1H, J = 9.5, 12.0 Hz, C**H**$_2$OH), 3.58 (dd, 1H, J = 2.0, 12.0 Hz, C**H**$_2$OH), 2.65 (dd, 1H, J = 9.5, 13.5 Hz, C**H**$_2$Ar), 2.52 (dd, 1H, J = 5.5, 14.0 Hz, C**H**$_2$Ar), 1.18-1.56 (m, 9H, C**H**$_2$C**H**$_2$C**H**$_2$/NC(C**H**$_3$)$_2$), 1.14 (s, 3H, NC(C**H**$_3$)$_2$), 1.04 (s, 3H, NC(C**H**$_3$)$_2$), 0.90 (s, 3H, NC(C**H**$_3$)$_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 138.4 (**Ar**), 129.4 (**Ar**), 128.2 (**Ar**), 126.2 (**Ar**), 81.1 (HC(=O)**C**), 67.9 (**C**H$_2$OH), 61.5 (N**C**(CH$_3$)$_2$), 60.0 (N**C**(CH$_3$)$_2$), 40.3 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 39.9 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 37.7 (**C**H$_2$Ph), 34.6 (NC(**C**H$_3$)$_2$), 32.4 (NC(**C**H$_3$)$_2$), 20.6 (NC(**C**H$_3$)$_2$), 20.2 (NC(**C**H$_3$)$_2$), 17.2 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$); HRMS (ESI-TOF) calculated for $C_{18}H_{29}O_2N$ $[M+H]^+$ m/z 291.2198, found 291.2198. $[\alpha]_D^{22}$ = -56.4 (c = 1.30, $CHCl_3$). HPLC analysis as above indicated 93% ee.



(*S*, *Z*)-2,2,6,6,-tetramethyl-1-(1-phenylpent-3-en-2-yloxy)piperidine. To a dried vial were added (ethyl)triphenylphosphonium bromide (540 mg, 0.36 mmol, 2.1 equiv.) and THF (2.8 mL). The mixture was cooled to -78 °C, and n-BuLi (2.5M in THF, 0.55 mL, 0.35 mmol, 2.0 equiv.) was added dropwise. The mixture was warmed to 0 °C and stirred for 1 h, after which it was cooled to -78 °C, and the aldehyde (200 mg, 0.17 mmol, 1.0 equiv.) in THF (1.2 mL) was added dropwise. The mixture was stirred for 15 minutes then slowly warmed to 0 °C and stirred for an additional 40 minutes, after which it was warmed to room temperature, and stirred for an additional 30 minutes until starting material was consumed by TLC. The reaction was cooled to -78 °C and quenched with sat. aq. NH_4Cl (1.0 mL) and water (1.0 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2.0 mL), and the combined organic layers were dried over Na_2SO_4, filtered,

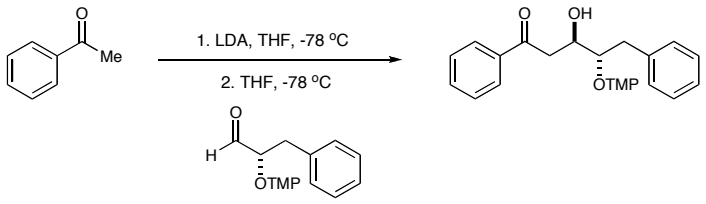
and concentrated under vacuum. The crude product was purified by flash chromatography with hexanes to provide the desired product (47 mg, 91% yield, 10:1 Z : E) as an inseparable mixture of olefin isomers as a colorless liquid. IR (thin film) 2972.2, 2929.1, 1604.3, 1495.9, 1453.9, 1374.0, 1359.8, 1258.0, 1241.4, 1182.0, 1132.8, 1004.6, 973.9, 956.4, 925.9, 724.2, 696.9 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 7.13-7.33 (m, 5H, Ar**H**), 5.58-5.65 (m, 1H, CH**C**HCH$_3$), 5.46-5.54 (m, 1H, **C**HCHCH$_3$), 4.95-5.03 (m, 1H, C**H**OTMP), 3.37 (dd, 1H, J = 4.5, 12.5 Hz, C**H**$_2$Ar), 2.78 (dd, 1H, J = 8.5, 13.0 Hz, C**H**$_2$Ar), 1.52-1.65 (m, 3H, C**H**$_3$), 1.21-1.51 (m, 18H, OTMP); ^{13}C NMR (125 MHz, C_6D_6) δ: 139.0 (**Ar**), 133.0 (CHCH**C**H$_3$), 130.3 (**Ar**), 128.3 (**Ar**), 126.2 (**Ar**), 125.5 (CHCH**C**H$_3$), 80.8 (**C**HOTMP), 60.3 (N**C**(CH$_3$)$_2$), 59.5 (N**C**(CH$_3$)$_2$), 42.0 (**C**H$_2$Ar), 42.0 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 40.7 (C(CH$_3$)$_2$**C**H$_2$CH$_2$CH$_2$), 35.4 (NC(**C**H$_3$)$_2$), 34.5 (NC(**C**H$_3$)$_2$), 20.8 (NC(**C**H$_3$)$_2$), 20.5 (NC(**C**H$_3$)$_2$), 17.7 (C(CH$_3$)$_2$CH$_2$**C**H$_2$CH$_2$) 13.3 (**C**H$_3$); HRMS (ESI-TOF) calculated for $C_{20}H_{31}ON$ $[M+H]^+$ m/z 301.2406, found 301.2407. The diastereomeric ratio was determined by the ratio of crude ^1H NMR peaks at 3.37 ppm and 3.24 ppm. The enantiomeric excess was determined from the corresponding diol, which was prepared by treating the product (1.0 equiv.) with Zn (10.0 equiv.) in a 1:1 mixture of AcOH : H_2O (0.5 M) at 50 °C. Upon complete consumption of starting material, the reaction mixture was cooled to room temperature and extracted with CH_2Cl_2 (x 3). The combined organic layers were washed with sat. aq. $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (x 3). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the major diol diastereomer (OJ, 3% IPA/hexanes, 1.0 mL/min, 220 nm) indicated 93% ee: t_R (major) = 46.7 minutes, t_R (minor) = 50.4 minutes.



(2*S*, 3*S*)-4-phenyl-2-(2,2,6,6,-tetramethylpiperidin-1-yloxy)butan-2-ol. To a dried vial were added *(S)*-3-phenyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal (200.0 mg, 0.69 mmol, 1.0 equiv.), prepared from the procedure described above, and THF (3.5 mL). The solution was cooled to -78 °C, and MeMgCl (3M in THF, 0.46 mL, 1.4 mmol, 2.0

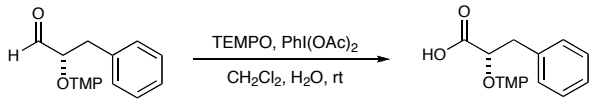
equiv.) was added dropwise. The reaction mixture was stirred at -78 ºC for 1.75 h then warmed to 0 ºC and stirred for an additional 15 minutes until starting material was consumed by TLC. The reaction was cooled to -78 ºC and quenched with sat. aq. NH_4Cl (1.0 mL) and water (1.0 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2.0 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography with a 20% EtOAc in hexanes eluent to provide the desired product (200.1 mg, 92% yield, 5:1 dr) as an inseparable mixture of diastereomers as a white solid. IR (thin film) 3458.2, 2971.6, 2930.2, 2871.3, 1604.3, 1495.6, 1454.3, 1378.5, 1360.7, 1256.7, 1242.2, 1181.1, 1132.0, 1053.3, 973.1, 910.5, 745.4, 698.8 cm^{-1}; Major: ^1H NMR (500 MHz, $CDCl_3$) δ: 7.18-7.33 (m, 5H, Ar**H**), 4.22-4.27 (m, 1H, C**H**OTMP), 3.89 (ap bs, 1H, C**H**OH), 3.43 (dd, 1H, J = 4.0, 13.0 Hz, C**H**$_2$Ar), 2.52-2.59 (m, 1H, C**H**$_2$Ar), 2.14 (s, 1H, O**H**), 1.00-1.70 (m, 21H, OTMP/C**H**$_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 139.4 (**Ar**), 129.3 (**Ar**), 128.4 (**Ar**), 126.0 (**Ar**), 86.0 (**C**HOTMP), 68.2 (**C**HOH), 60.7 (N**C**$(CH_3)_2$), 59.9 (N**C**$(CH_3)_2$), 40.7 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 40.5 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 35.8 (**C**H_2Ar), 34.6 (NC(**C**$H_3)_2$), 34.1 (NC(**C**$H_3)_2$), 20.8 (NC(**C**$H_3)_2$), 20.5 (NC(**C**$H_3)_2$), 17.4 (**C**H_3), 17.2 ($C(CH_3)_2CH_2$**C**H_2CH_2); Minor: ^1H NMR (500 MHz, $CDCl_3$) Peaks corresponding to major diastereomer in crude ^1H NMR overlapped except for δ: 4.01-4.12 (m, 2H, C**H**OH/C**H**OTMP), 3.47-3.53 (m, 1H, C**H**$_2$Ar), 2.79-2.86 (m, 1H, C**H**$_2$Ar). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 139.4 (**Ar**), 129.3 (**Ar**), 128.0 (**Ar**), 125.9 (**Ar**), 85.5 (**C**HOTMP), 71.5 (**C**HOH), 60.7 (N**C**$(CH_3)_2$), 59.9 (N**C**$(CH_3)_2$), 40.3 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 39.9 ($C(CH_3)_2$**C**$H_2CH_2CH_2$), 37.8 (**C**H_2Ar), 34.2 (NC(**C**$H_3)_2$), 32.0 (NC(**C**$H_3)_2$), 20.5 (NC(**C**$H_3)_2$), 20.3 (NC(**C**$H_3)_2$), 17.4 (**C**H_3), 17.2 ($C(CH_3)_2CH_2$**C**H_2CH_2). The diastereomeric ratio was determined by the ratio of crude ^1H NMR peaks at 3.43 ppm and 3.51 ppm. HRMS (ESI-TOF) calculated for $C_{19}H_{31}O_2N$ $[M+H]^+$ m/z 305.2355, found 305.2355. The enantiomeric excess was determined from the corresponding diol, which was prepared by treating the product (1.0 equiv.) with Zn (10.0 equiv.) in a 1:1 mixture of AcOH:H_2O (0.5 M) at 50 ºC. Upon complete consumption of starting material, the reaction mixture was cooled to room temperature and extracted with CH_2Cl_2 (x 3). The combined organic layers were washed with sat. aq. $NaHCO_3$, and the aqueous layer was extracted with CH_2Cl_2 (x 3). The combined organic layers were dried over Na_2SO_4 and

concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis of the diol major diastereomer (OJ, 3% IPA/hexanes, 1.0 mL/min, 220 nm) indicated 93% ee: t_R (major) = 46.7 minutes, t_R (minor) = 50.4 minutes.



(3*R*, 4*S*)-3-hydroxy-1,5-diphenyl-4-(2,2,6,6,-tetramethylpiperidin-1-yloxy)pentan-1-one. To a dried vial were added diisopropylamine (65 µL, 0.46 mmol, 1.0 equiv.) and THF (1.60 mL) and cooled to -78 °C, after which n-BuLi (2.5M in hexanes, 184 µL, 0.46 mmol, 1.0 equiv.) was added dropwise. After 30 minutes, acetophenone (54 µL, 0.46 mmol, 1.0 equiv.) was added dropwise, and the resulting solution was stirred at -78 °C for an additional 30 minutes. To the vial was added *(S)*-3-phenyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal (200 mg, 0.69 mmol, 1.5 equiv.), prepared from the procedure described above, in THF (0.4 mL) dropwise, and the reaction mixture was stirred at -78 °C until starting material was consumed by TLC (1.3 h). The reaction was quenched with sat. aq. NH_4Cl (1.0 mL) and slowly warmed to room temperature, followed by the addition of water (1.0 mL) and ether (1.0 mL). The aqueous layer was extracted with ether (3 x 2.0 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography with a 25% EtOAc in hexanes eluent to provide the desired product (164.0 mg, 87% yield, 13:1 dr) as an inseparable mixture of diastereomers as a white solid. IR (thin film) 2879.5, 1751.3, 1658.7, 1592.6, 1588.1, 1502.1, 1411.3, 19.96.4, 1377.2, 1225.1, 1199.9, 1185.1, 1111.2, 988.7, 973.0, 788.4, 676.4 cm^{-1}; ^1H NMR (500 MHz, C_6D_6) δ: 7.90 (d, 2H, J = 5.0 Hz, Ar**H**), 7.35-7.40 (m, 2H, Ar**H**), 7.09-7.31 (m, 6H, Ar**H**), 4.94-5.01 (m, 1H, C**H**OH), 4.41-4.47 (m, 1H, C**H**OTMP), 3.63 (dd, J = 6.0 Hz, J = 14.0 Hz, C**H**$_2$Ar), 3.16 (dd, 1H, J = 10.0 Hz, J = 18 Hz, C(=O)C**H**$_2$), 2.99-3.03 (m, 1H, C(=O)C**H**$_2$), 2.87-2.96 (m, 2H, C**H**$_2$Ar/O**H**), 1.10-1.64 (m, 18H, OTMP); ^{13}C NMR (125 MHz, C_6D_6) δ: 199.6 (**C**(=O)), 140.3 (**Ar**), 137.4 (**Ar**), 133.0 (**Ar**), 130.0

(**Ar**), 128.6 (**Ar**), 128.6 (**Ar**), 128.4 (**Ar**), 126.3 (**Ar**), 86.6 (**C**HOTMP), 68.2 (**C**HOH), 60.7 (N**C**$(CH_3)_2$), 60.3 (N**C**$(CH_3)_2$), 41.5 (**C**H_2), 40.9 (C$(CH_3)_2$**C**$H_2CH_2CH_2$), 40.8 (CH$(CH_3)_2$**C**$H_2CH_2CH_2$), 36.0 (**C**H_2Ar), 34.6 (NC(**C**$H_3)_2$), 34.4 (NC(**C**$H_3)_2$), 20.9 (CH(**C**$H_3)_2$), 20.8 (CH(**C**$H_3)_2$), 17.6 (C$(CH_3)_2$CH_2**C**H_2CH_2); HRMS (ESI-TOF) calculated for $C_{26}H_{35}O_3N$ $[M+H]^+$ m/z 409.2617, found 409.2617. HPLC analysis (OD, 2% IPA/hexanes, 1.0 mL/min, 254 nm) indicated 93% ee: t_R (major) = 10.8 minutes, t_R (minor) = 16.0 minutes. The relative stereochemical configuration was determined by NOE experiments of the corresponding cyclic carbonate after cleavage of the N-O bond and treatment with triphosgene.

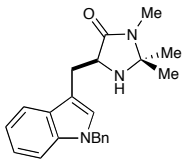


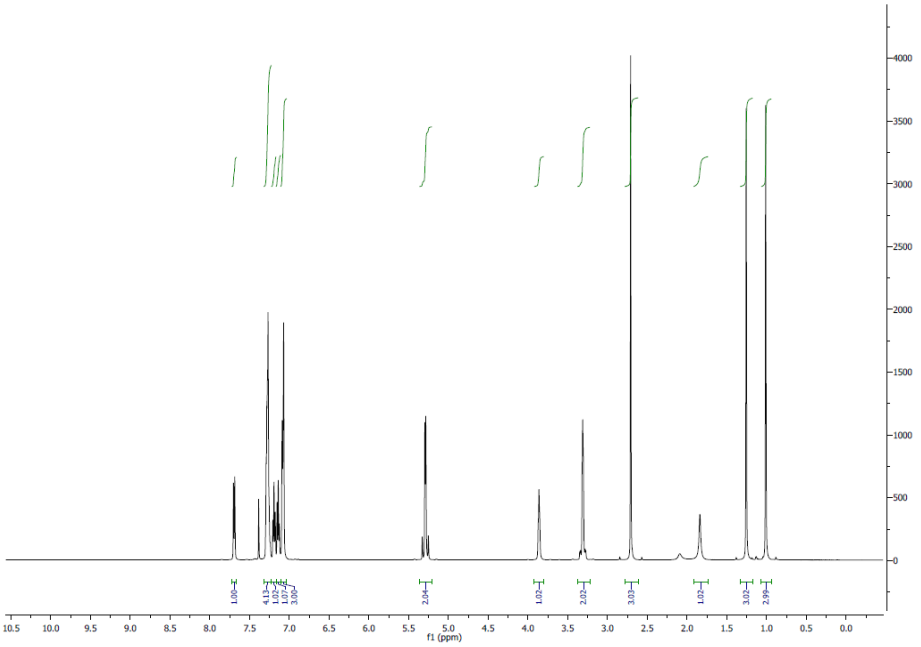
(*S*)-3-phenyl-2-(2,2,6,6,-tetramethylpiperidin-1-yloxy)propanoic acid. To a dried vial were added *(S)*-3-phenyl-2-(2,2,6,6-tetramethylpiperidin1-yloxy)propanal (125.5 mg, 0.43 mmol, 1.0 equiv.), prepared from the procedure described above, TEMPO (13.6 mg, 0.09 mmol, 0.2 equiv.), [bis(acetoxy)iodo]benzenebenzene (280 mg, 0.87 mmol, 2.0 equiv.), CH_2Cl_2 (1.5 mL), and water (0.7 mL). The mixture was stirred vigorously for 3 h at room temperature until starting material was consumed by TLC. The reaction was quenched with sat. aq. $NaHCO_3$ (1.0 mL) and water (1.0 mL). The aqueous layer was extracted with CH_2Cl_2 (3 x 2.0 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude product was purified by flash chromatography with a 35% EtOAc in hexanes eluent to provide the desired product (125.3 mg, 95% yield) as a colorless liquid. IR (thin film) 2970.2, 2921.8, 2547.0, 1766.9, 1720.1, 1452.4, 1373.1, 1213.0, 1122.4, 1021.7, 801.0, 755.9, 678.1 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.22-7.39 (m, 5H, Ar**H**), 4.69-4.73 (m, 1H, C**H**OTMP), 3.48 (dd, 1H, J = 5.0, 15.0 Hz, C**H**$_2$Ar), 3.17 (dd, 1H, J = 9.0, 15.0 Hz, C**H**$_2$Ar), 1.59-1.71 (m, 5H, C**H$_2$**), 1.45-1.53 (m, 1H, C**H$_2$**), 1.30 (s, 3H, C**H$_3$**), 1.20 (s, 3H, C**H$_3$**), 1.13 (s, 3H, C**H$_3$**), 1.11 (s, 3H, C**H$_3$**); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 173.4 (**C**(=O)OH), 137.7 (**Ar**), 129.7 (**Ar**), 128.3 (**Ar**), 126.5 (**Ar**), 80.5 (**C**HOTMP), 63.2 (N**C**$(CH_3)_2$), 62.9 (N**C**$(CH_3)_2$), 39.3 (C$(CH_3)_2$**C**$H_2CH_2CH_2$), 39.2 (CH$(CH_3)_2$**C**$H_2CH_2CH_2$), 37.7 (**C**H_2Ar),

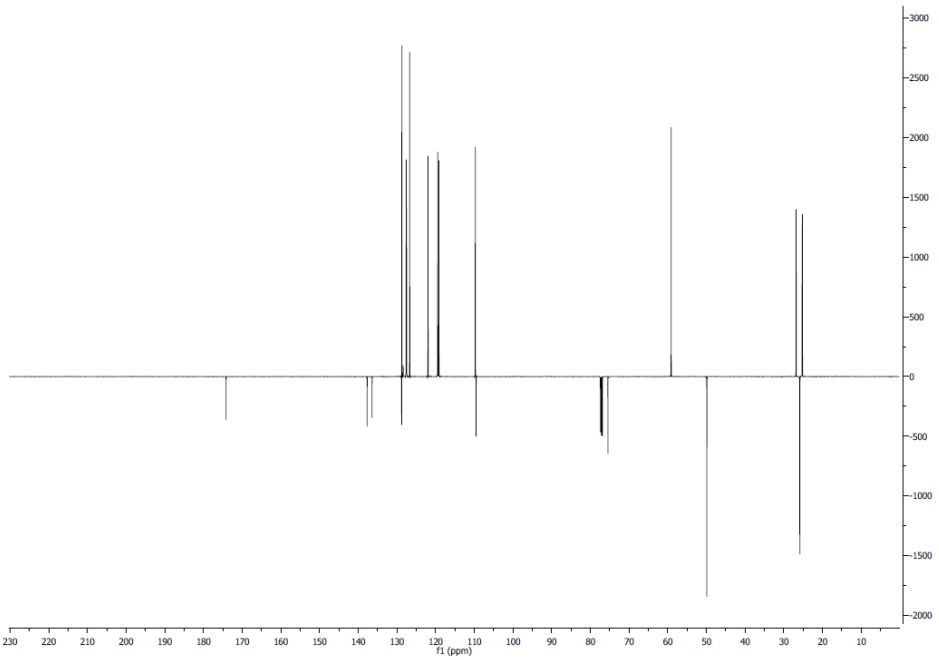
31.2 ($NC(\mathbf{C}H_3)_2$), 29.9 ($NC(\mathbf{C}H_3)_2$), 21.0 ($CH(\mathbf{C}H_3)_2$), 20.9 ($CH(\mathbf{C}H_3)_2$), 16.3 ($C(CH_3)_2CH_2\mathbf{C}H_2CH_2$); HRMS (ESI-TOF) calculated for $C_{18}H_{27}O_3N$ $[M+H]^+$ m/z 305.1991, found 305.1993. $[\alpha]_D^{24}$ = -77.4 (c = 0.80, $CHCl_3$). The enantiomeric excess was determined from the corresponding alcohol, which was prepared by treating the product (1.0 equiv.) with lithium aluminum hydride (3.0 equiv.) in THF (0.2 M) at 0 ºC with slow warming to room temperature over 1 h. Upon complete consumption of starting material, the reaction mixture was cooled to 0 ºC, diluted with ether, and slowly quenched by the dropwise addition of water. The slurry was stirred vigorously at room temperature for 30 minutes before extracting the aqueous layer with ether. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude mixture was purified by preparative TLC. HPLC analysis as above indicated 93% ee.

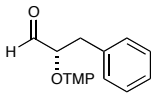
III. **Spectroscopic Data.**

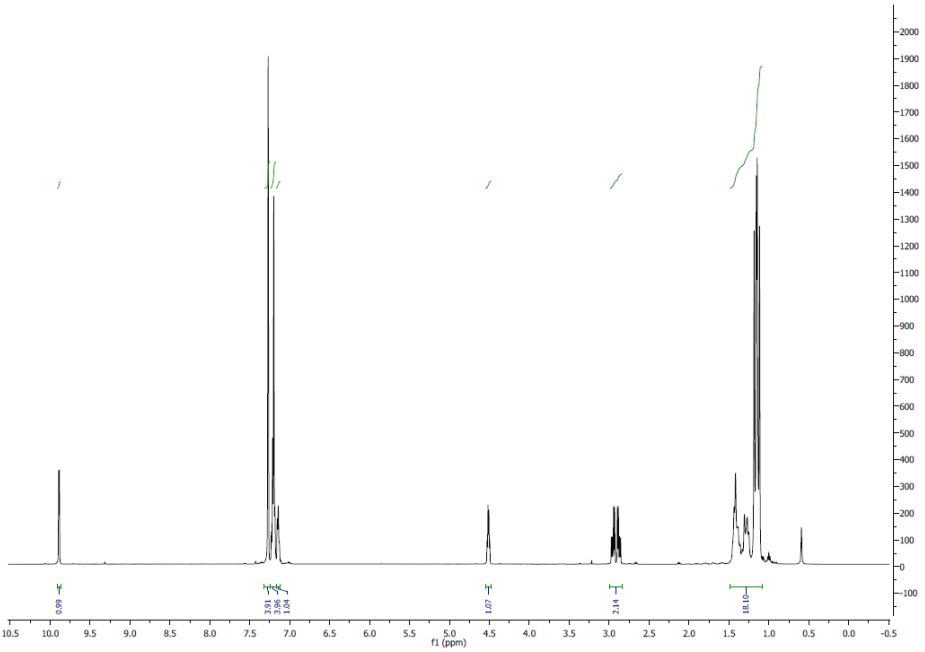
^1H and ^{13}C NMR spectra for all compounds are included below.








O
H
OTMP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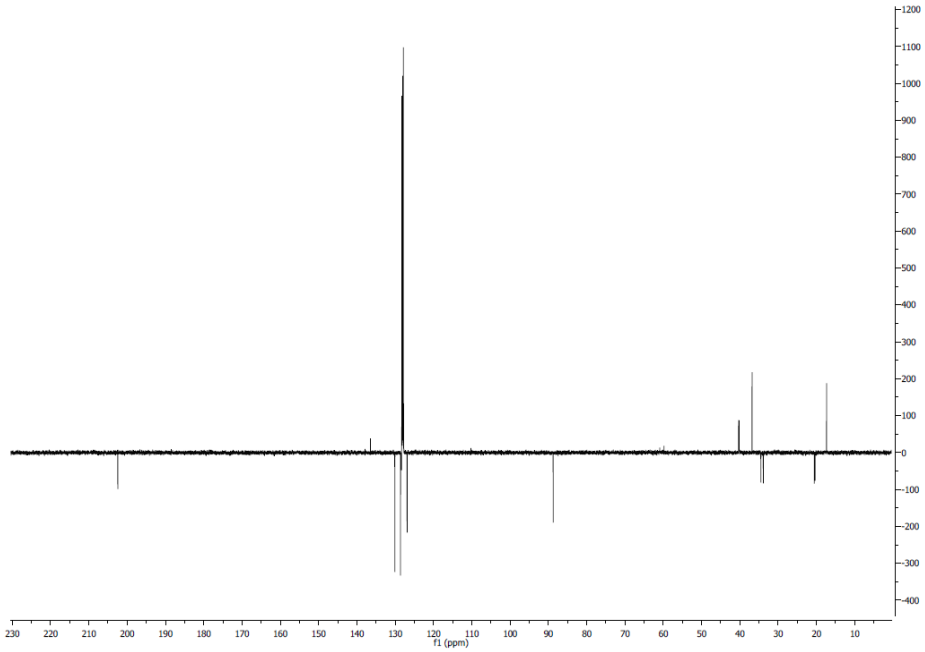
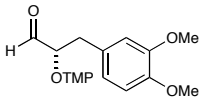
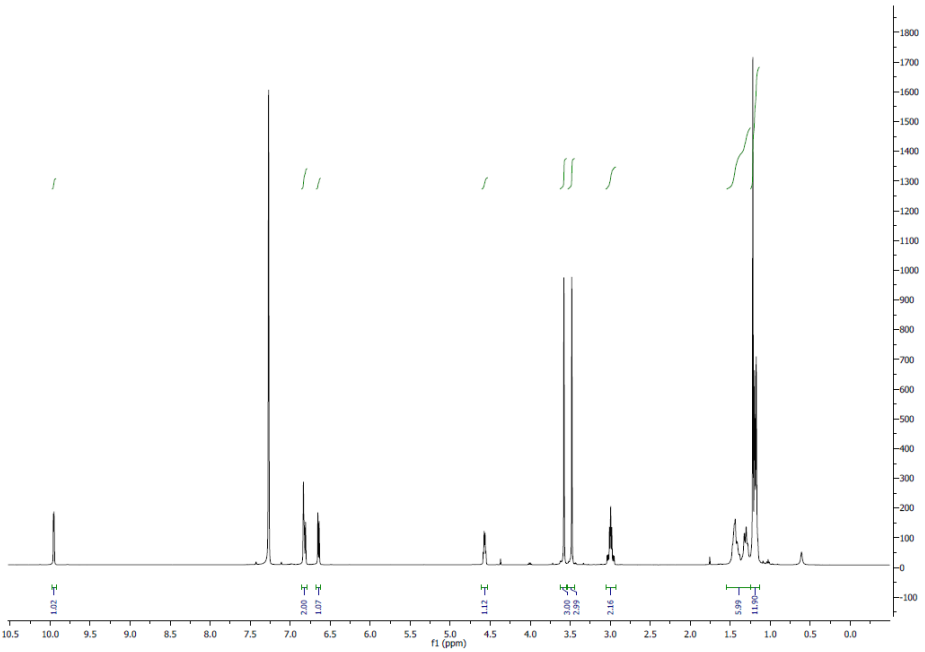
1.04
1.07
2.14
18.10
f1 (ppm)


f1 (ppm)


O
H
OTMP
OMe
OMe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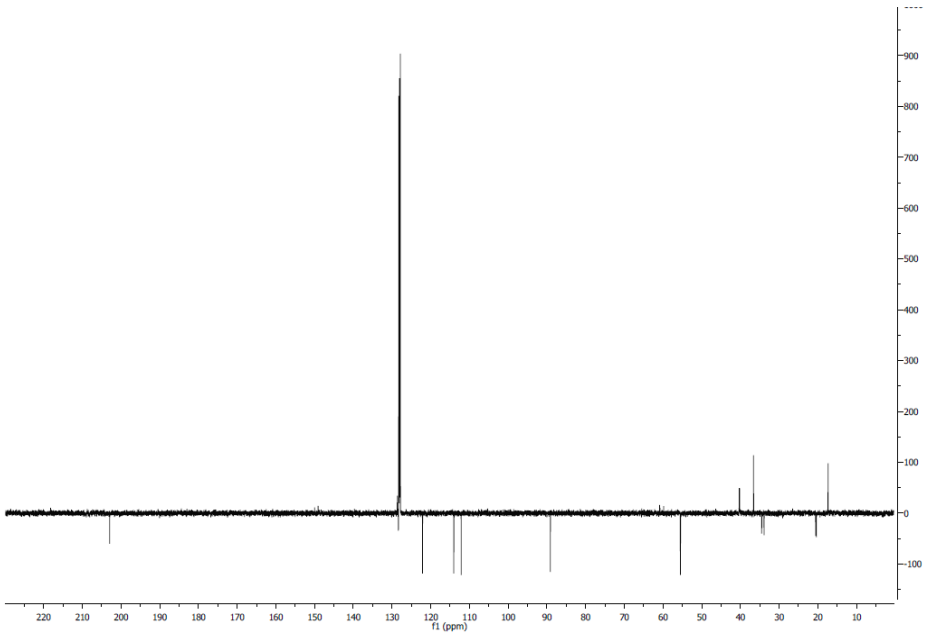
1.12
3.00
2.99
2.16
5.99
11.90
f1 (ppm)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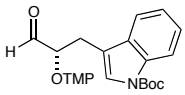

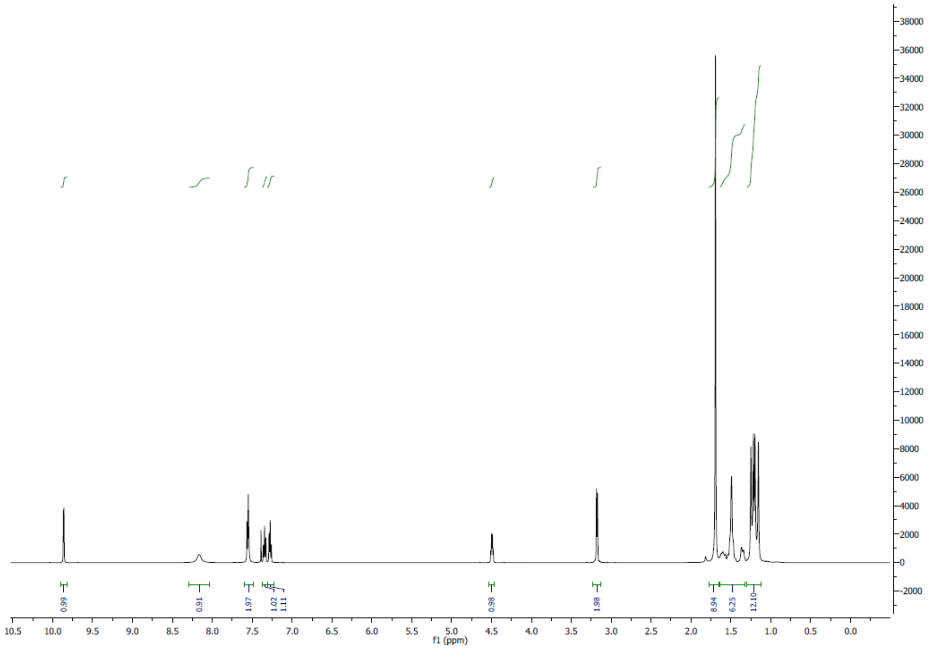

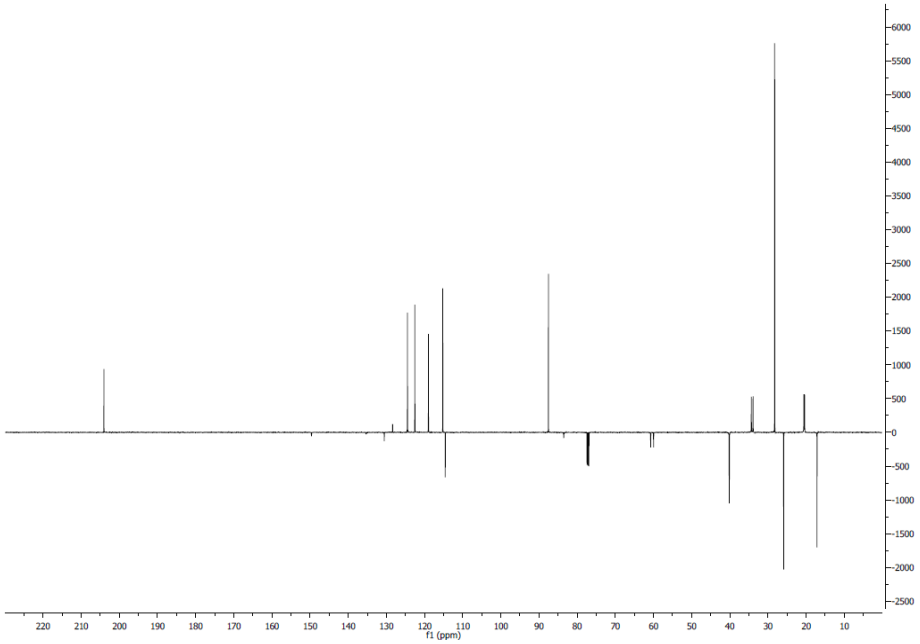

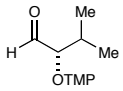

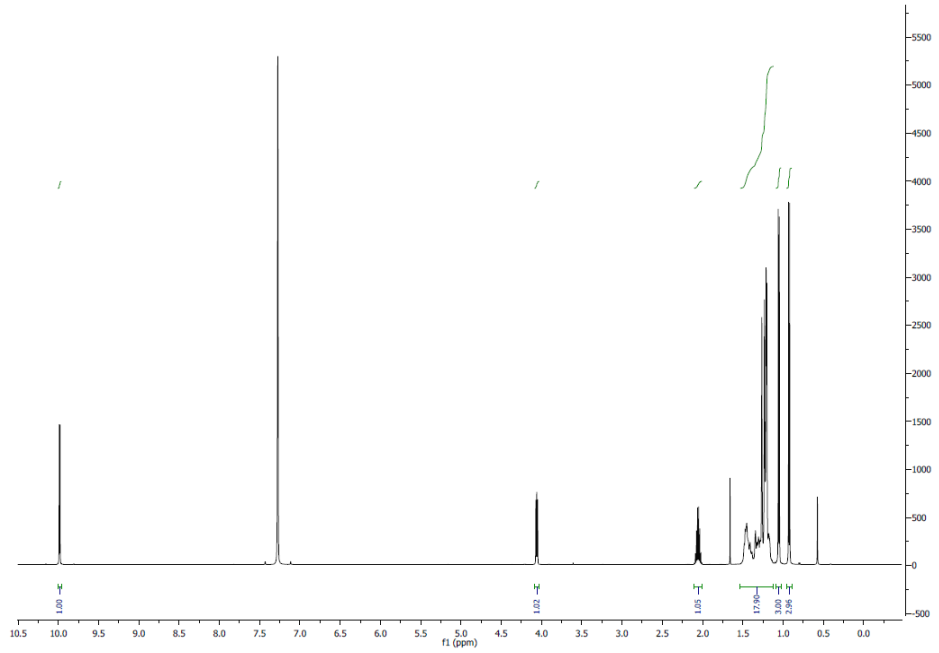

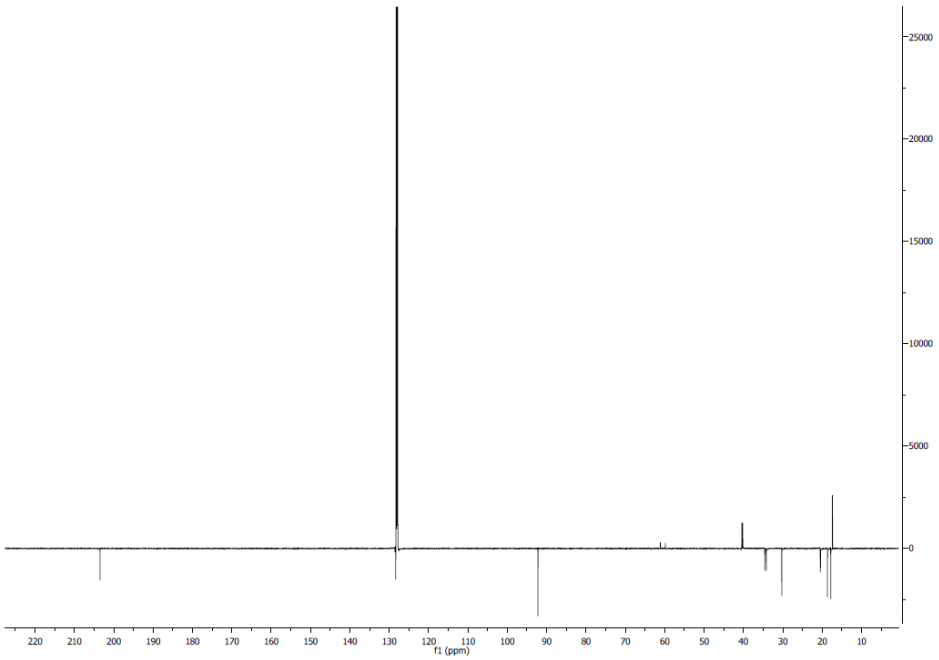

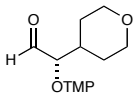

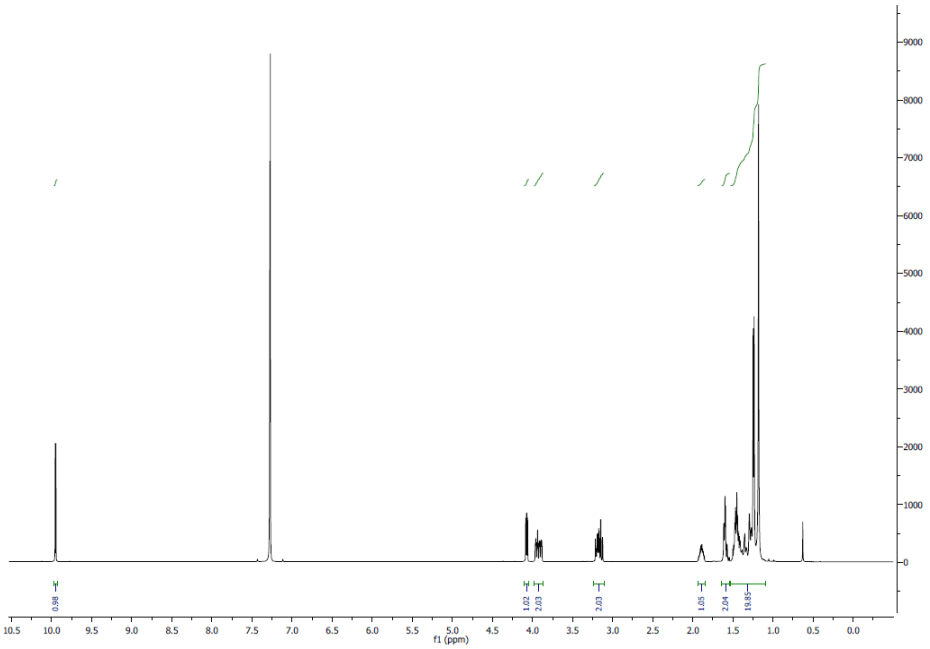

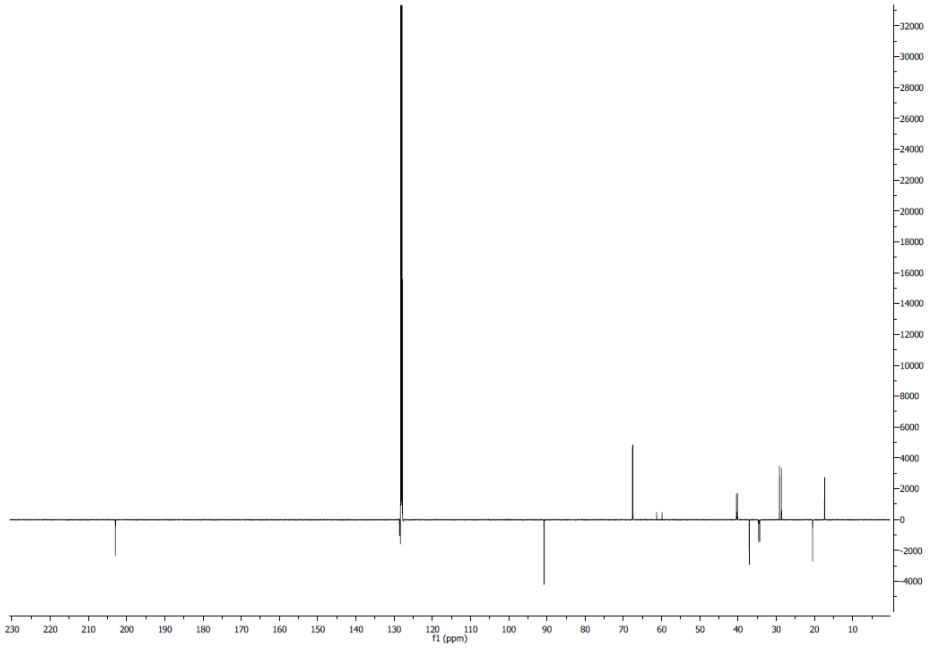

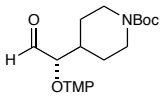

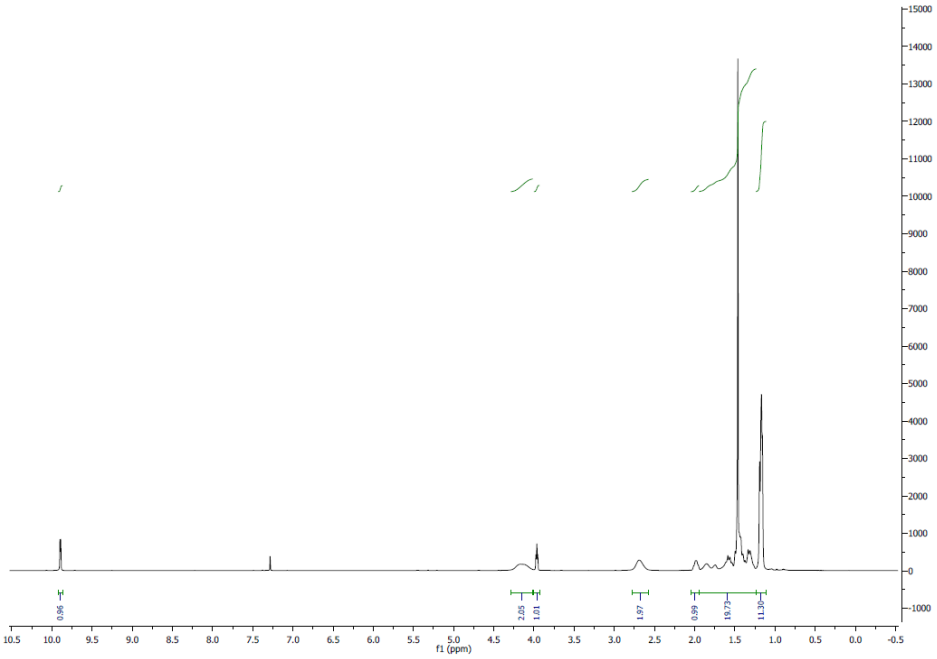

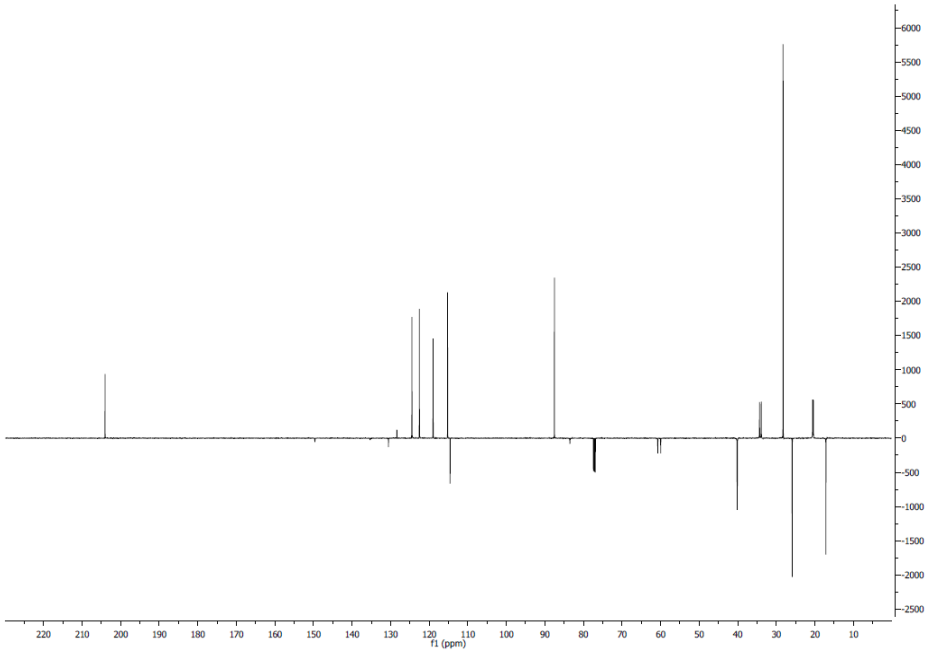

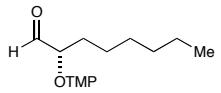

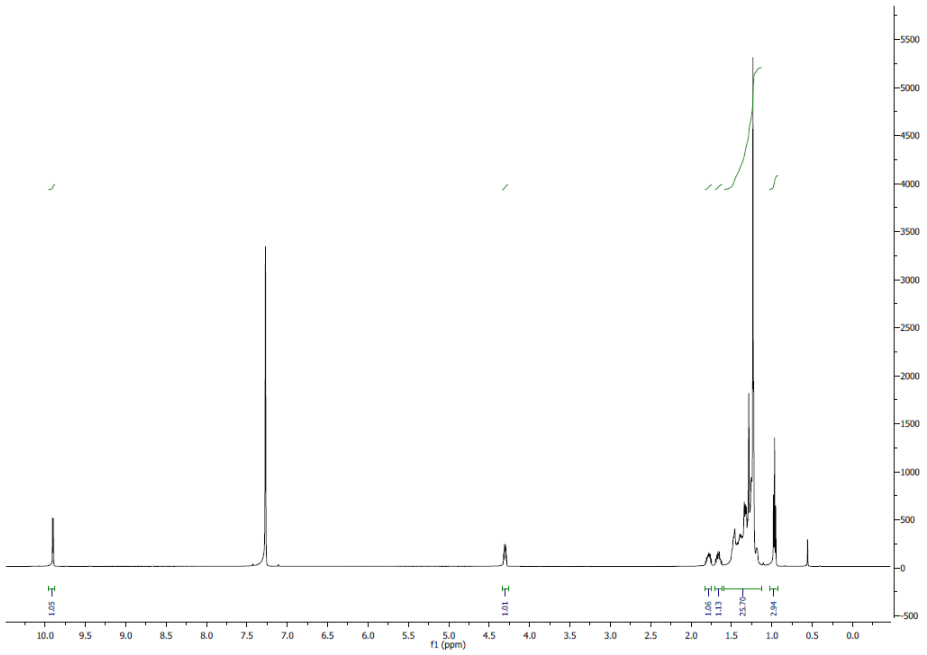

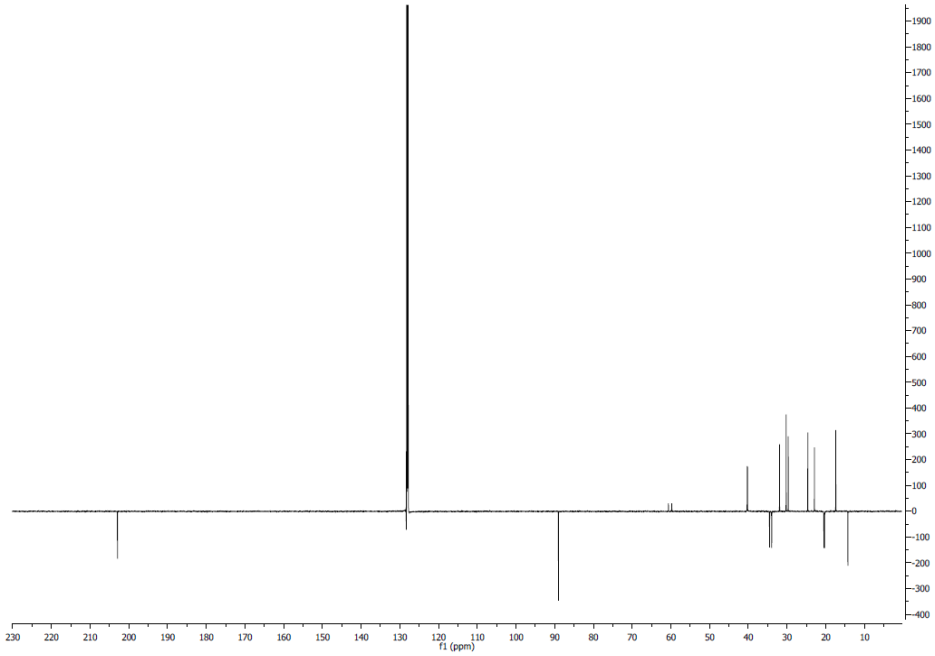

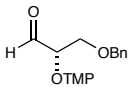

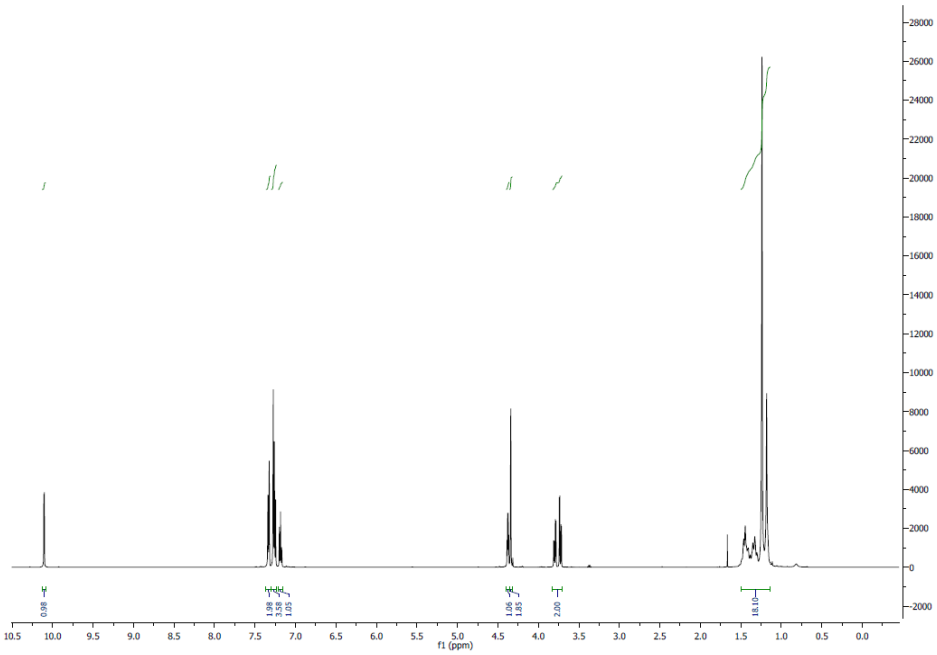

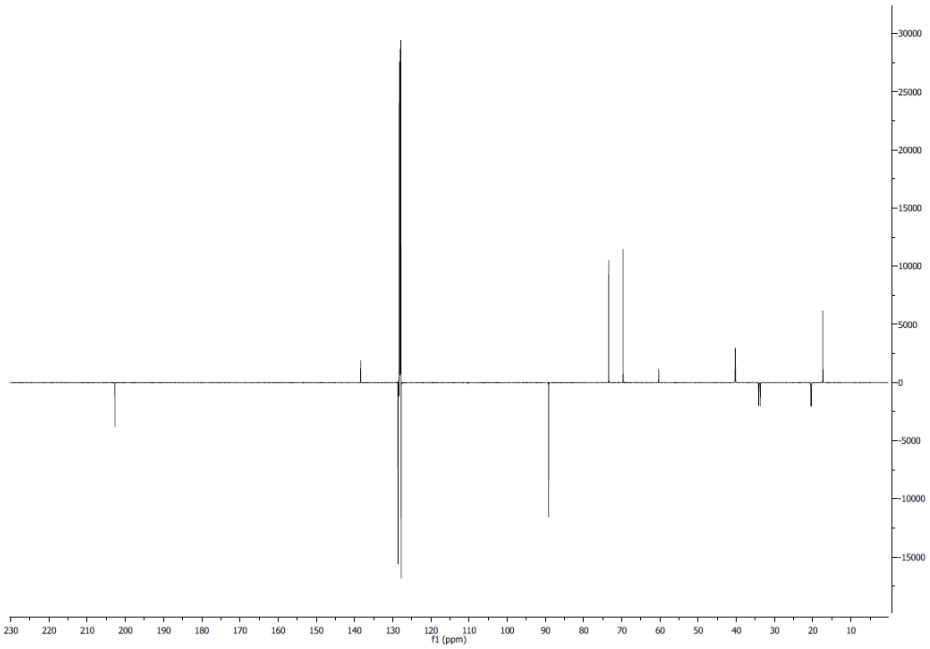

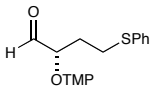

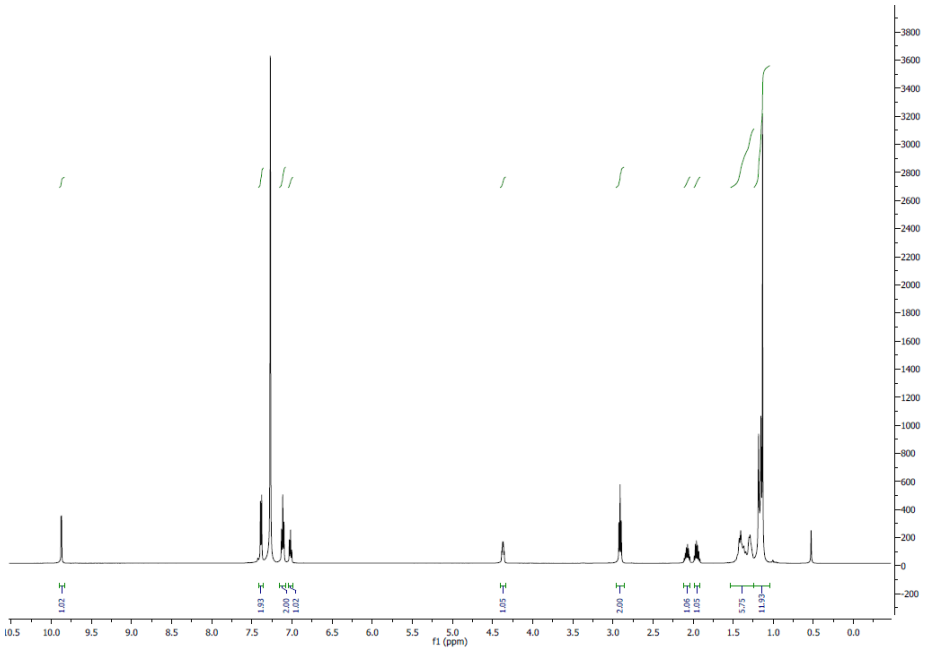

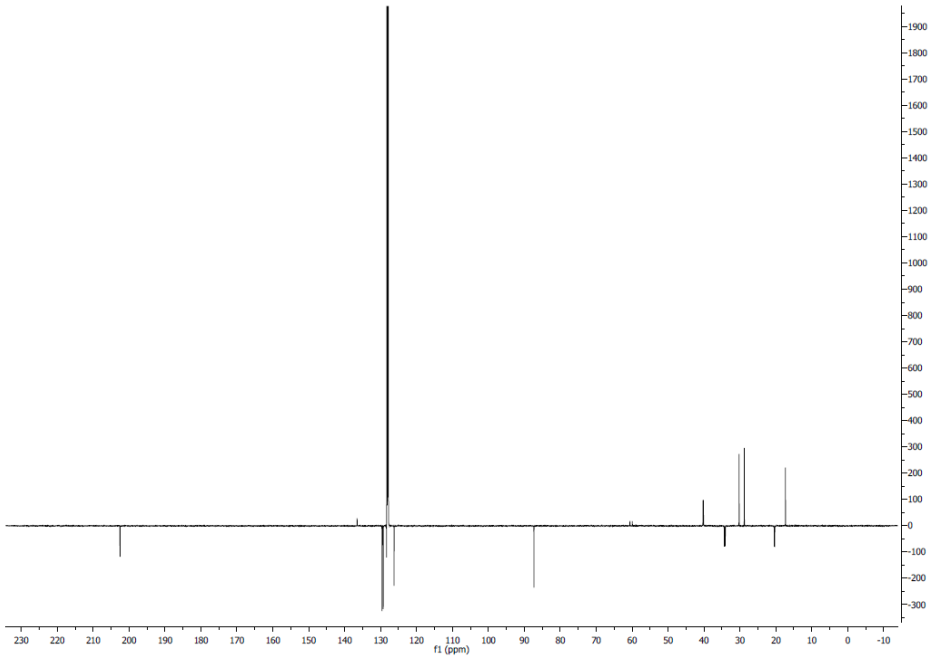

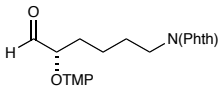

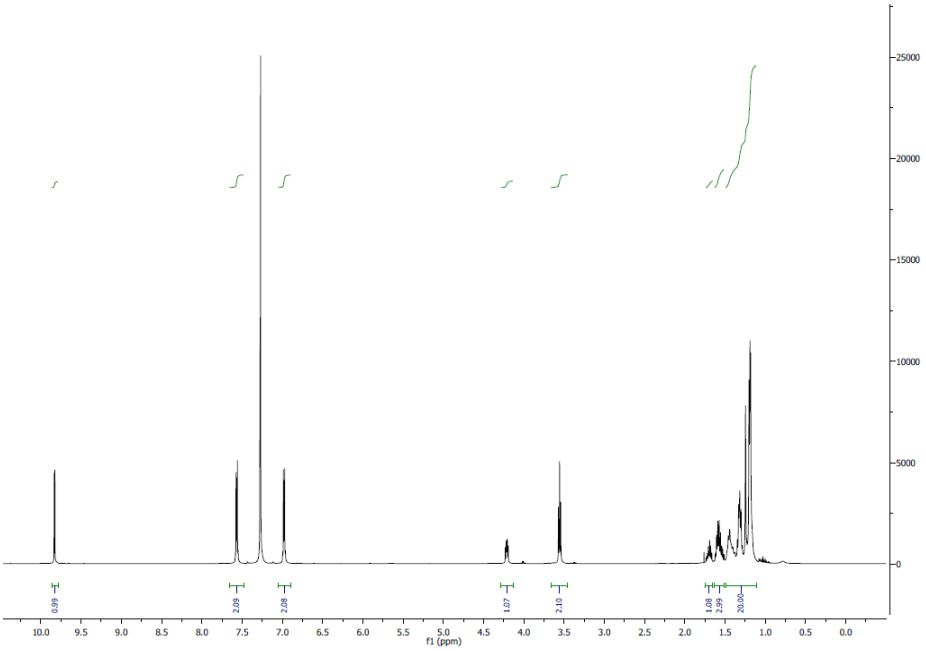

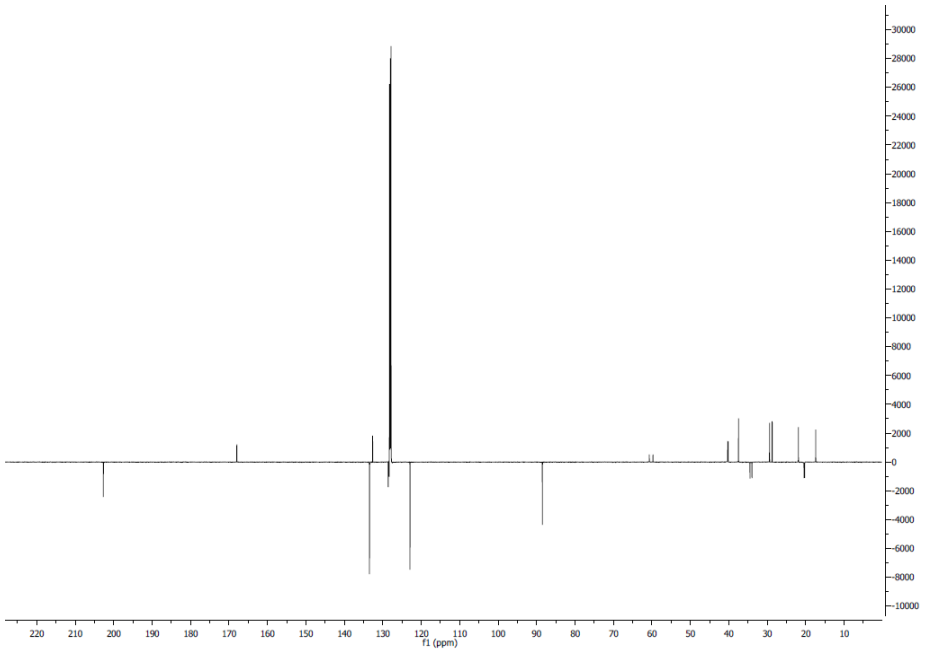

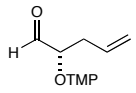
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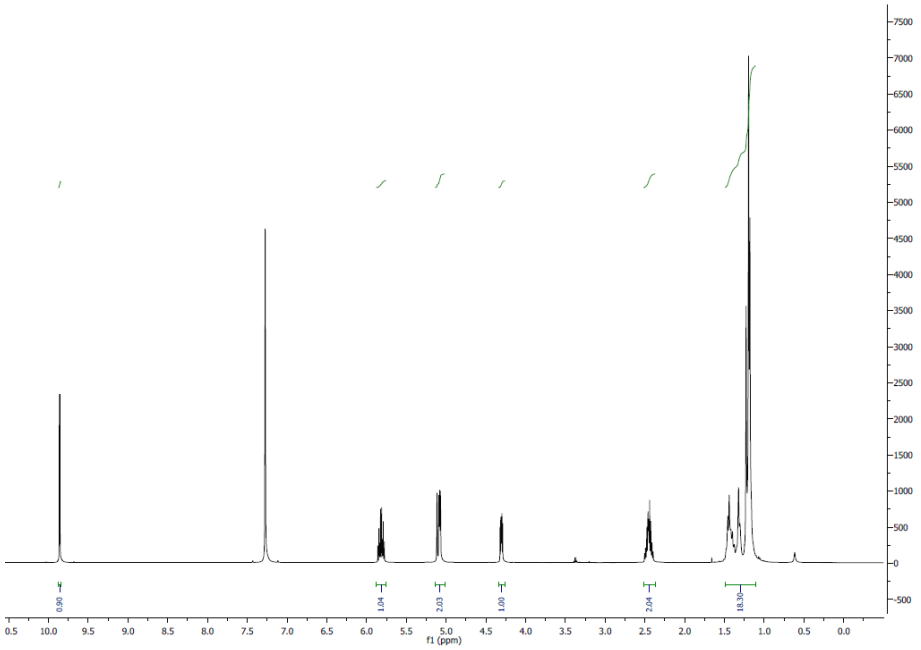
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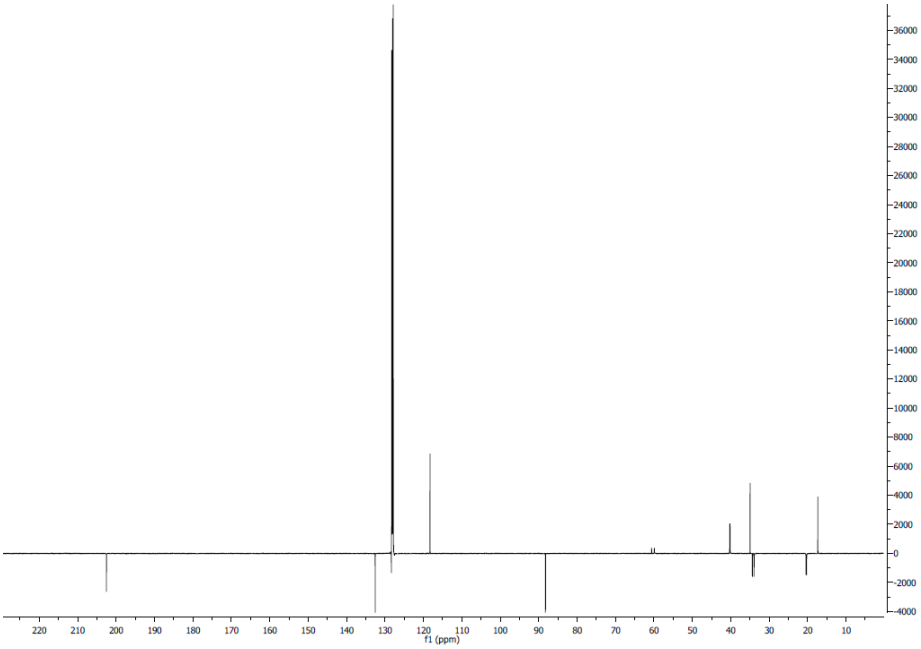
1.00
2.04
18.30
f1 (ppm)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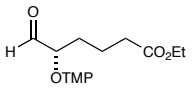
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CO2Et
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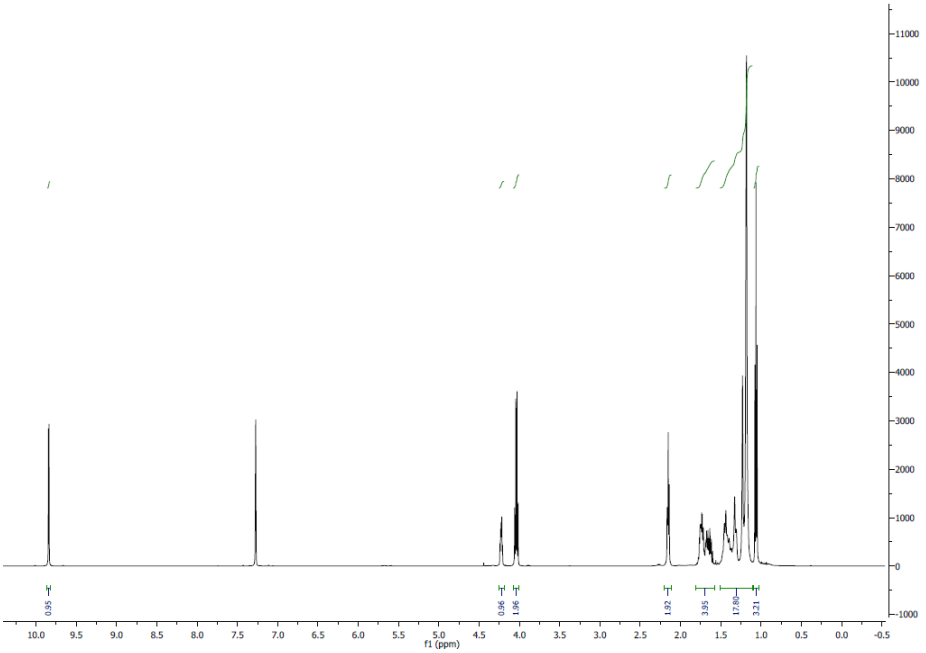
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1.96
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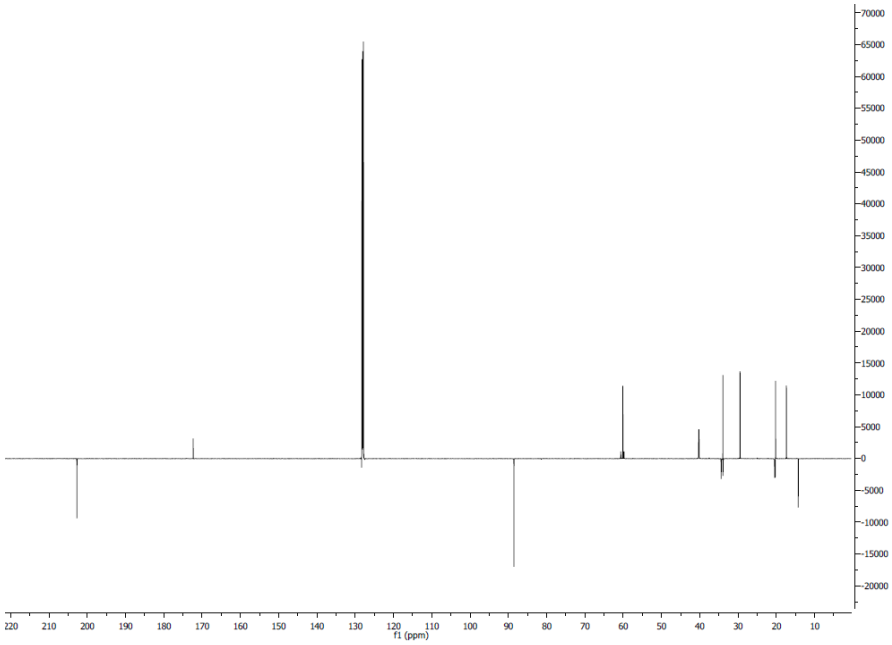
3.21
f1 (ppm)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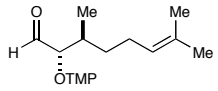
O
Me
Me
H
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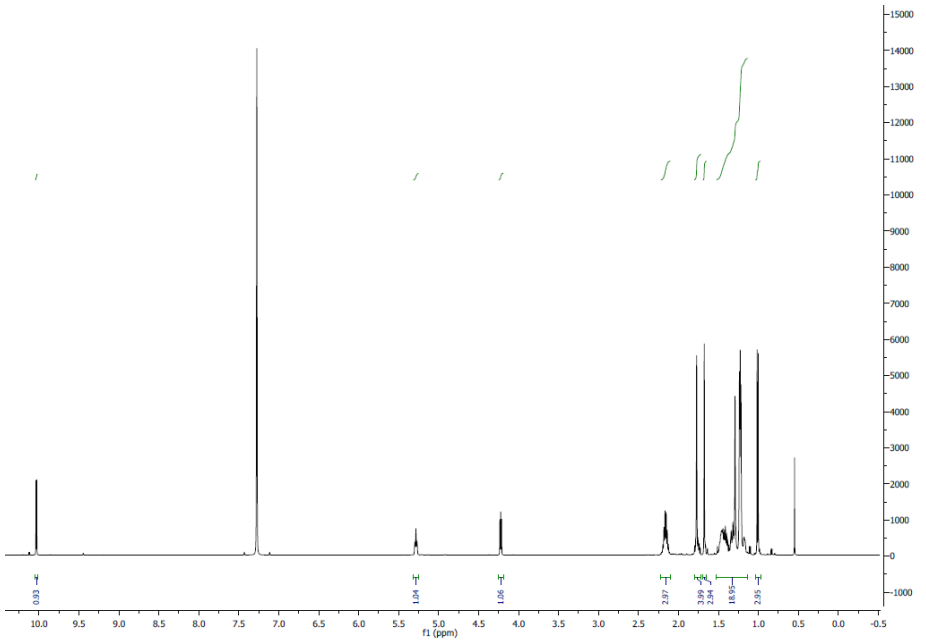
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2.94
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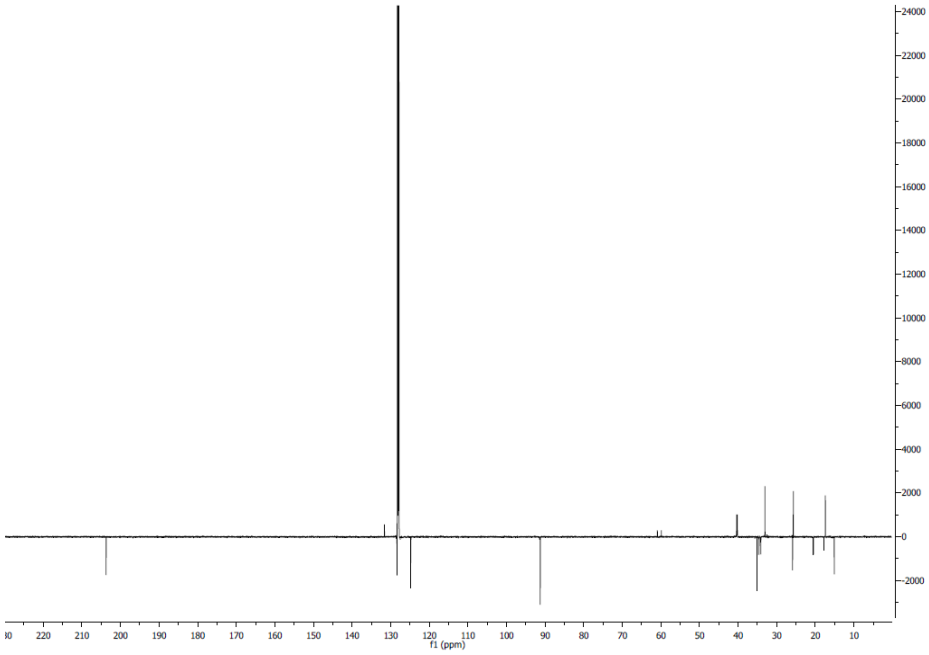
2.95
f1 (ppm)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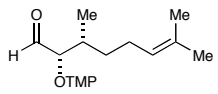
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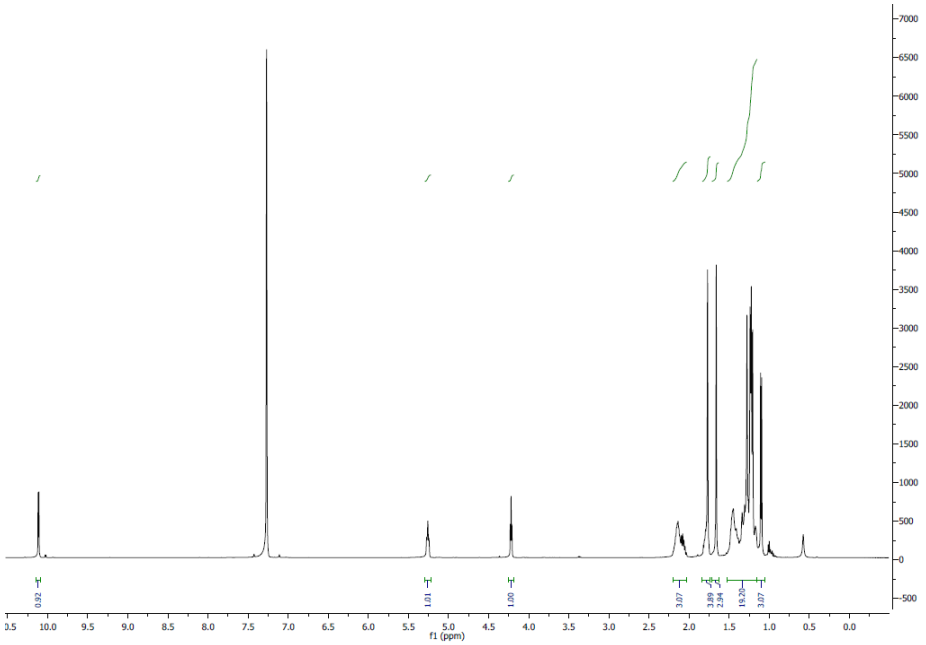
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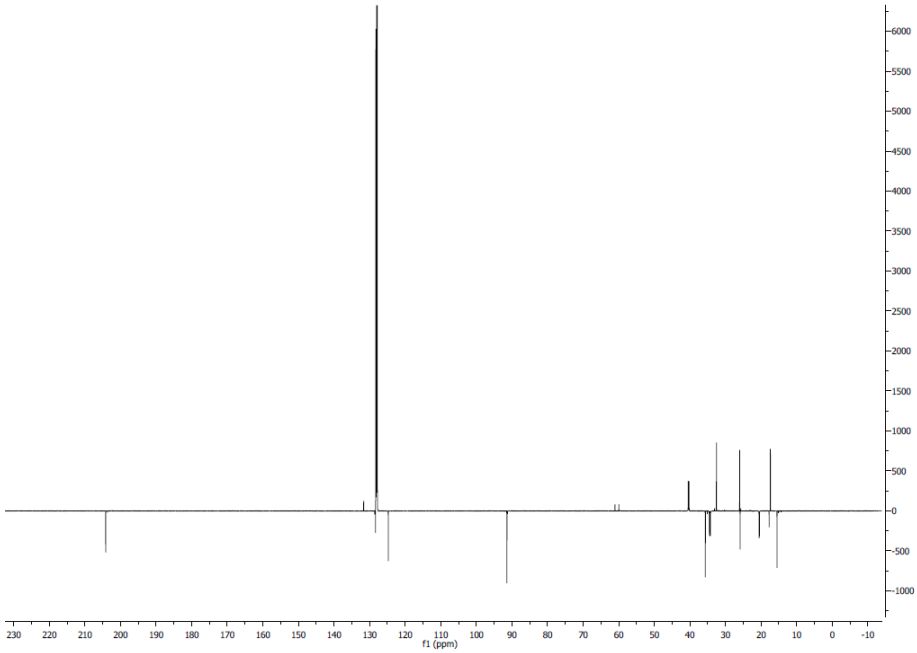
f1 (ppm)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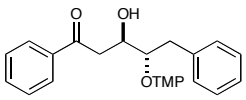
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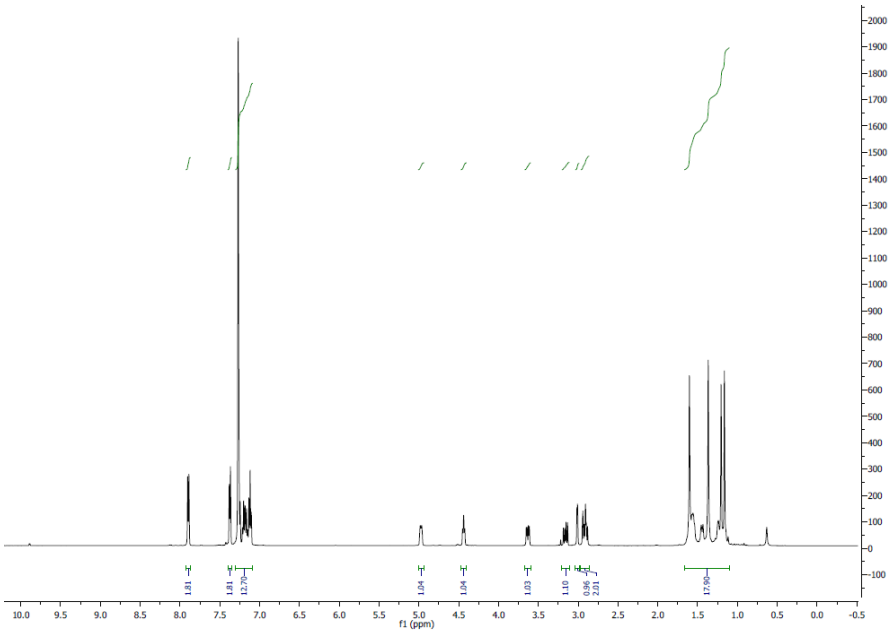
OTMP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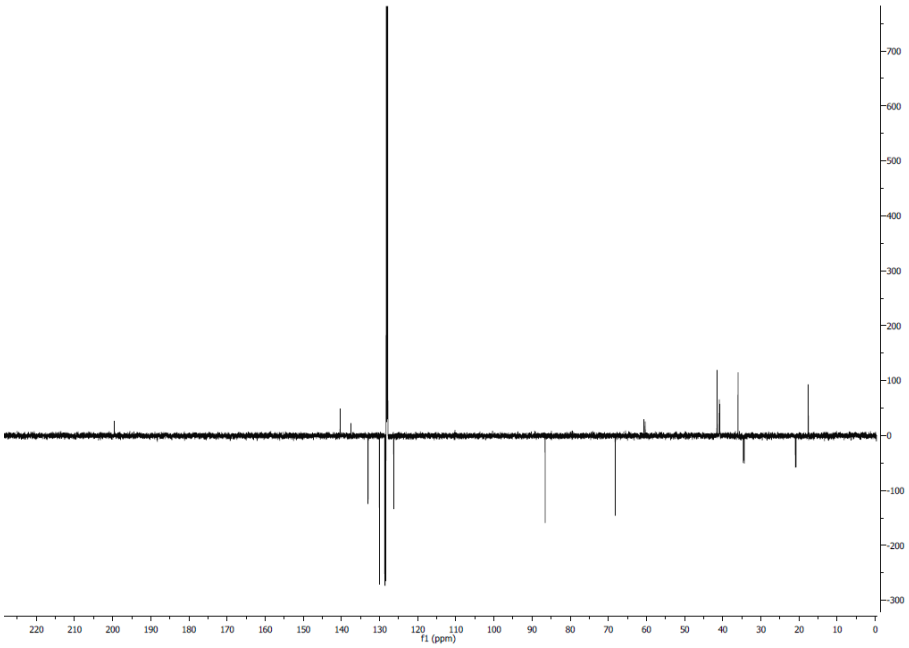
2.01
17.90
f1 (ppm)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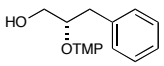

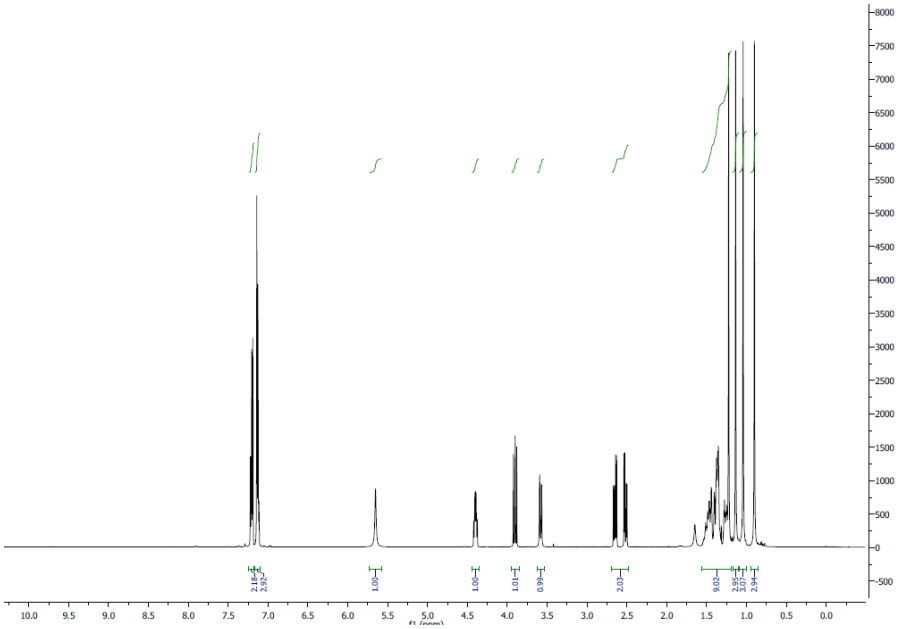

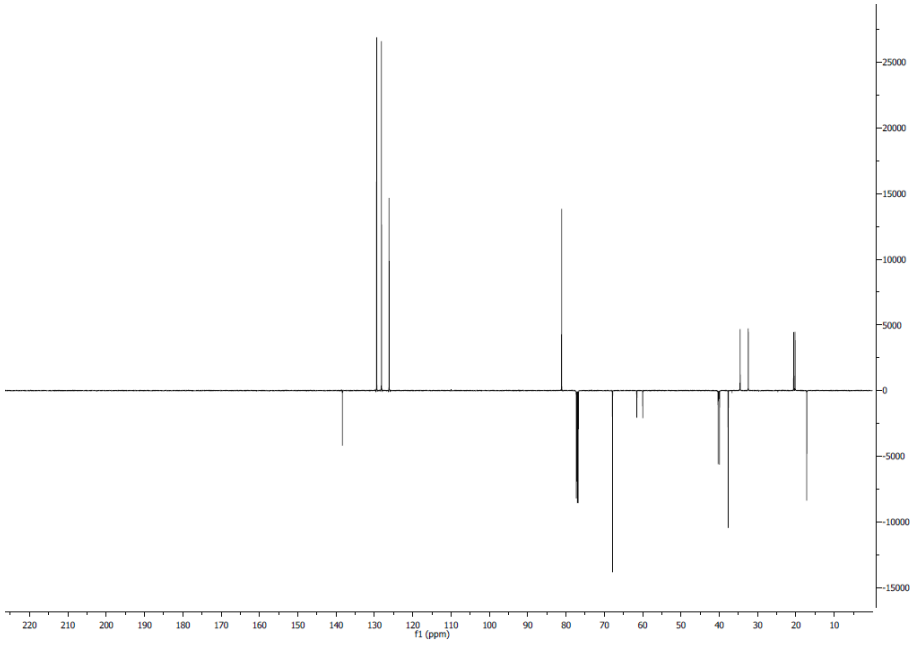

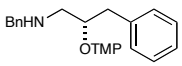

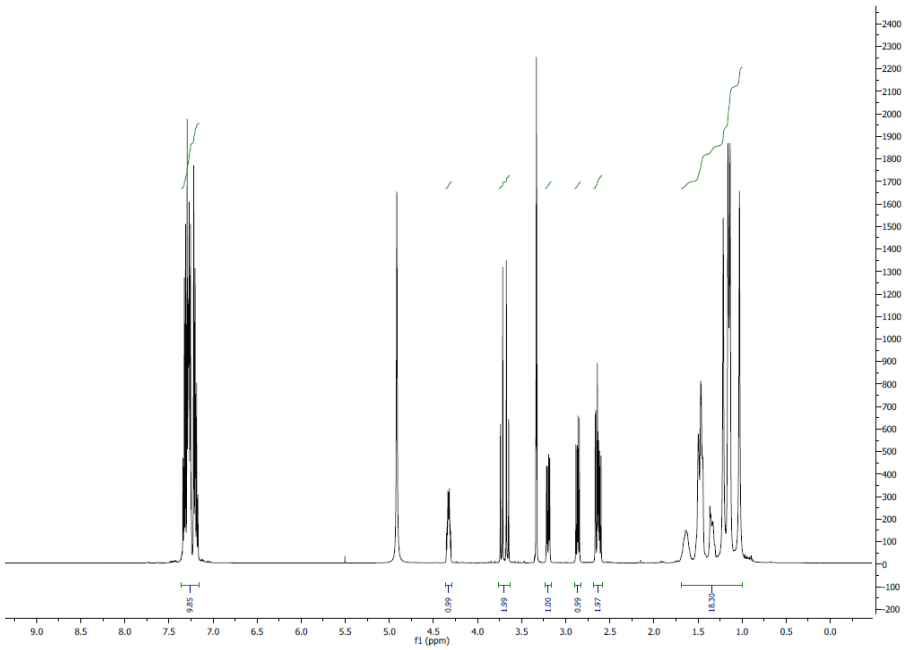

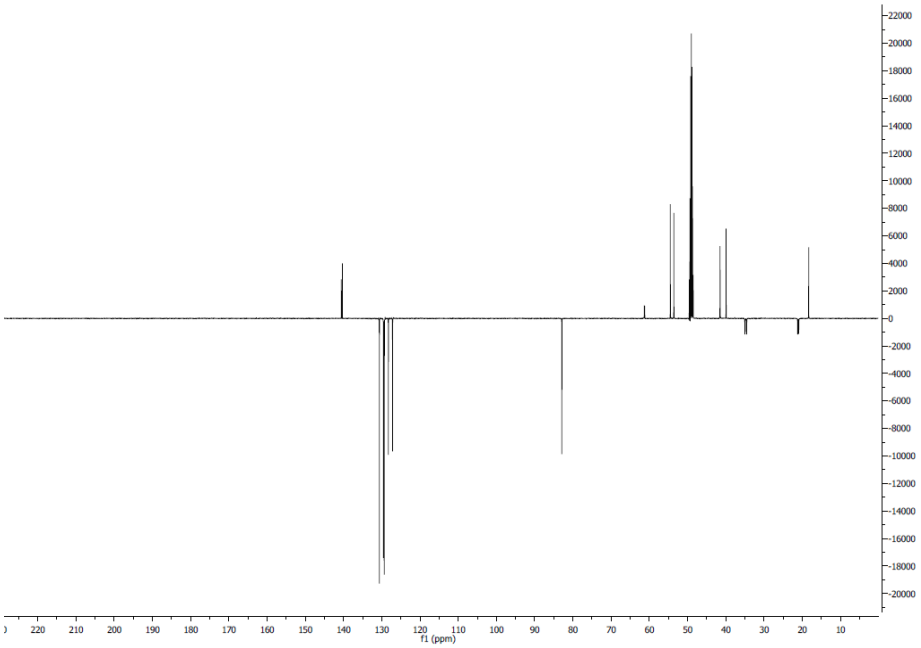

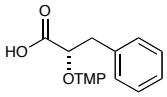
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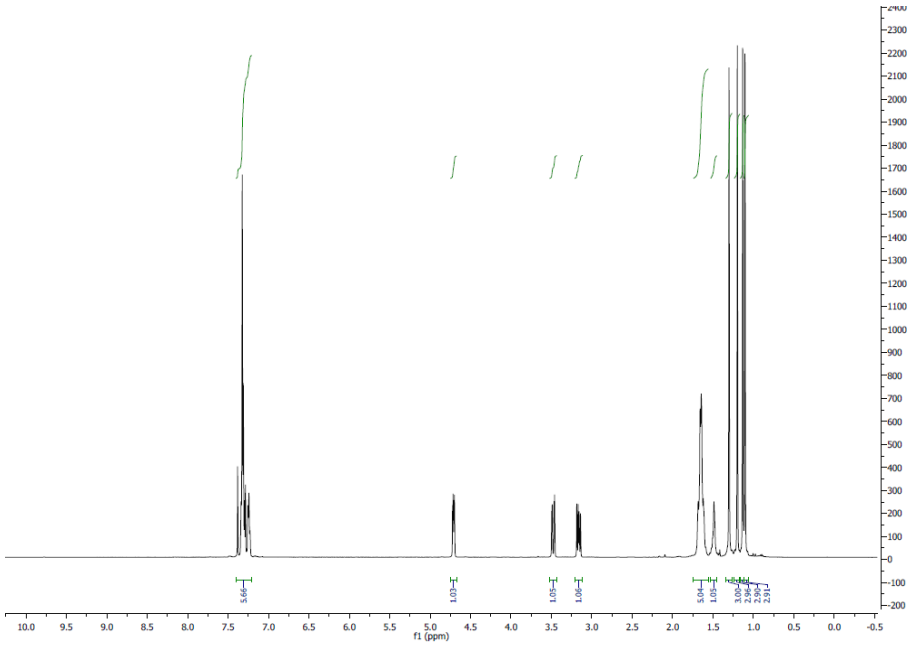
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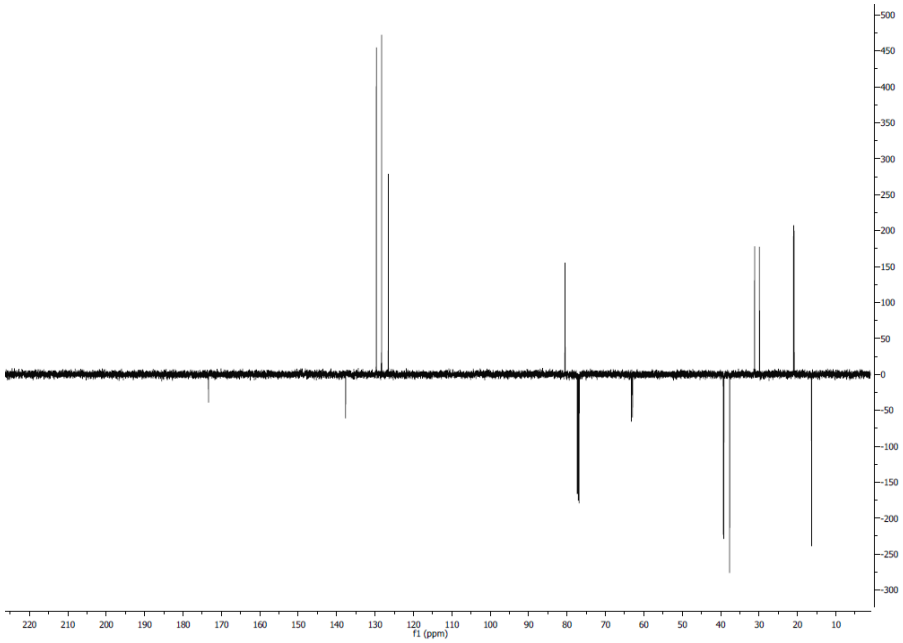
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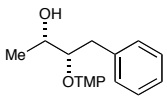

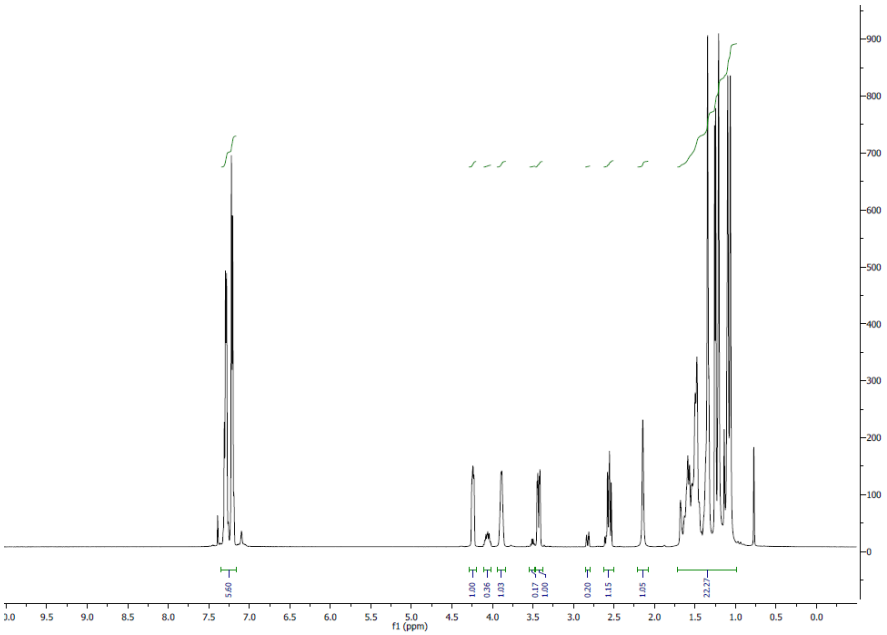

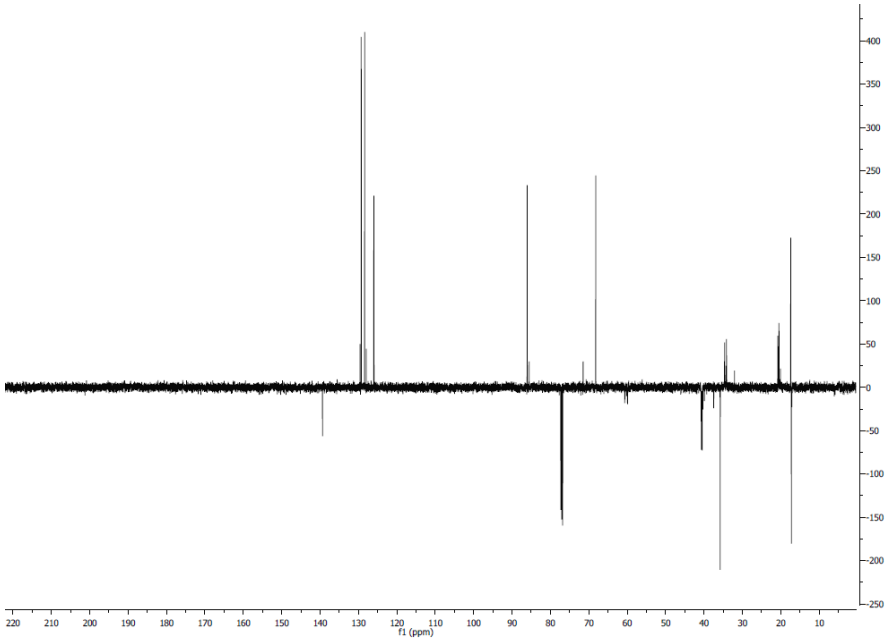

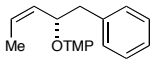
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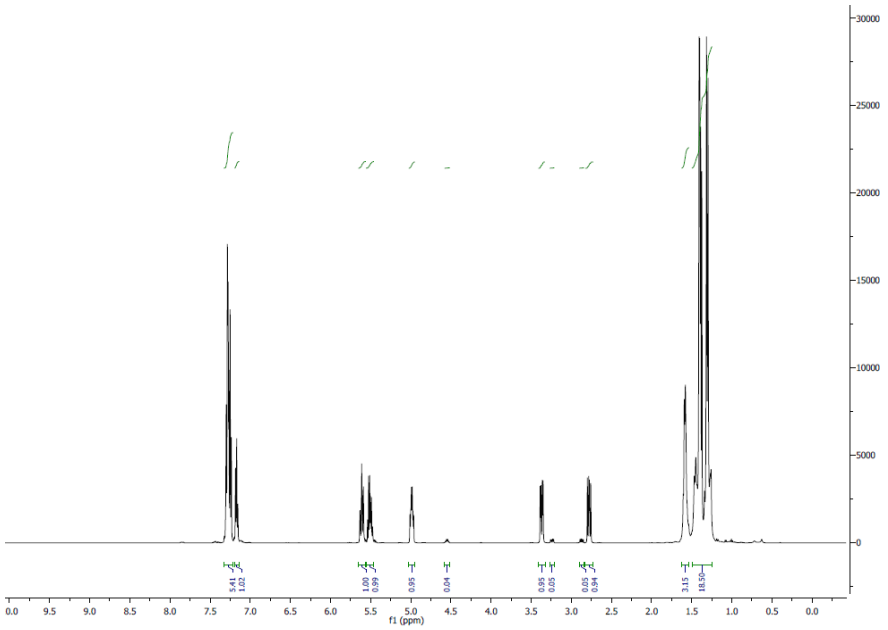
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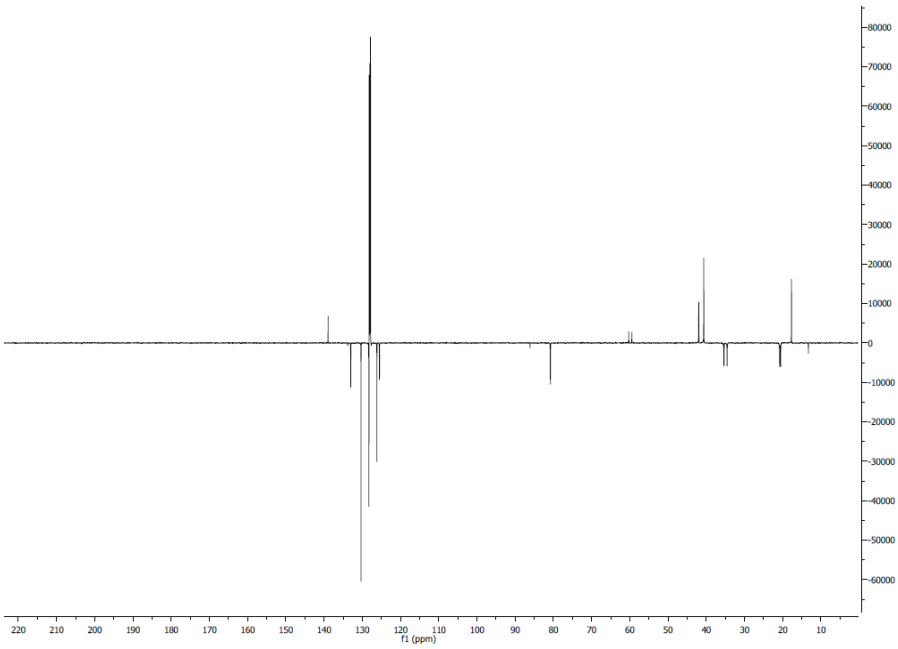
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