Supporting Information

Metal-free oxidative hydroxyalkylarylation of activated alkenes by direct sp^3 C-H functionalization of alcohols

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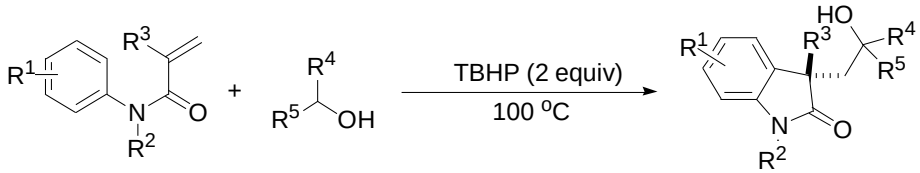
General Information

All Reactions were carried out under an atmosphere of nitrogen with the strict exclusion of air. Column chromatography was carried out on silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Advance III-400 in solvents as indicated. Chemical shift are reported in ppm from $CDCl_3$ using TMS as internal standard. IR spectra were recorded on a Bruker Tensor 27 spectrometer and only major peaks are reported in cm^{-1}. HRMS were obtained on a Q-TOF micro spectrometer. Melting points were determined on a microscopic apparatus and were uncorrected.

Starting Materials

All of acrylamides **1** were synthesized according to the literature, and the NMR spectroscopy were in full accordance with the data in the literature.[1]

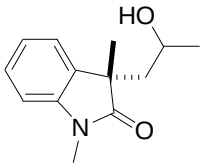
General Procedure for the Hydroxyalkylarylation of Acrylamides with Alcohols



1 **2** **3** or **4**

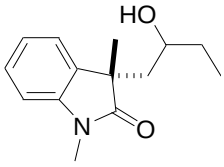
A 10 mL oven-dried Schlenk-tube were charged with acrylamide (**1**, 0.2 mmol, 1.0 equiv). The tube was evacuated and backfilled with nitrogen (three times). TBHP (0.4 mmol, 2.0 equiv) in 1 mL of alcohols were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred at 100 ^{o}C for 24 h. Upon completion of the reaction, the mixture was diluted with EtOAc, the solvent was then removed under vacuo. The residue was purified with chromatography column on silica gel (gradient eluent of EtOAc/petroleum ether: 1/15 to 1/10) to give the corresponding products **3** or **4** in yields listed in Scheme 2 and Scheme 3.

Characterization of Products 3



3a: A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:3); mp = 83-85 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.26 (t, *J* = 7.6 Hz, 1H), 7.19-7.17 (d, *J* = 7.2 Hz, 1H), 7.11-7.07 (t, *J* = 7.6 Hz, 1H), 6.87-6.86 (d, *J* = 7.6 Hz, 1H), 4.14-4.11 (m, 1H), 3.23 (s, 3H), 1.96-1.92 (d, *J* = 14.4 Hz, 1H), 1.78-1.72 (m, 2H), 1.44 (s, 3H), 1.16-1.15 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.0, 142.4, 135.0, 128.1, 123.0, 122.4, 108.4, 64.7, 47.4, 46.1, 26.4, 24.0, 22.8 ppm; IR (KBr): υ_{max} 3467, 3416, 2968, 1691, 1612, 1352 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{17}NNaO_2$ $[M+Na]^+$ 242.1151, found 242.1157.

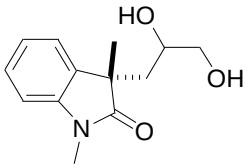
3a': A pale yellow oil, R_f 0.2 (EtOAc/petroleum ether = 1:3); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.25 (m, 1H), 7.16-7.14 (m, 1H), 7.08-7.04 (m, 1H), 6.87-6.85 (d, *J* = 8.0 Hz, 1H), 3.38-3.36 (m, 1H), 3.21 (s, 3H), 2.21-2.15 (m, 1H), 1.97-1.92 (m, 1H), 1.73 (s, 1H), 1.35 (s, 3H), 1.06-1.05 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.7, 143.5, 133.6, 127.8, 122.5, 122.3, 108.2, 65.5, 47.1, 46.9, 26.3, 25.4, 24.5 ppm; IR (KBr): υ_{max} 3478, 2966, 1697, 1612, 1380 cm^{-1}.



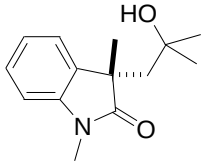
3b: A pale yellow oil, R_f 0.5 (EtOAc/petroleum ether = 1:2); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.27 (m, 1H), 7.20-7.18 (d, *J* = 7.2 Hz, 1H), 7.11-7.07 (m, 1H), 6.88-6.86 (d, *J* = 7.6 Hz, 1H), 3.85-3.80 (m, 1H), 3.23 (s, 3H), 1.98-1.94 (m, 1H), 1.75-1.69 (m, 2H), 1.49-1.40 (m, 5H), 0.94-0.91 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.0, 142.4, 135.2, 128.0, 123.0, 122.4, 108.4, 69.7, 47.3, 44.2, 30.8, 26.4, 22.9, 9.9 ppm; IR (KBr): υ_{max} 3458, 2929, 1688, 1612, 1352 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}NNaO_2$ $[M+Na]^+$ 256.1308, found 256.1313.

3b': A pale yellow oil, R_f 0.3 (EtOAc/petroleum ether = 1:2); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.25 (m, 1H), 7.15-7.13 (d, *J* = 7.2 Hz, 1H), 7.10-7.04 (m, 1H),

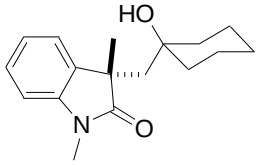
6.86-6.85 (d, *J* = 7.6 Hz, 1H), 3.21 (s, 3H), 3.09-3.07 (m, 1H), 2.21-2.11 (m, 1H), 2.02-1.95 (m, 1H), 1.75 (s, 1H), 1.35-1.29 (m, 5H), 0.83-0.79 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.9, 143.5, 133.6, 127.8, 122.5, 122.3, 108.2, 70.6, 46.9, 45.1, 31.2, 26.4, 25.5, 9.7 ppm; IR (KBr): υ_{max} 3455, 2926, 1670, 1612, 1349 cm^{-1}.



3d: A colorless oil, R_f 0.3 (EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31-7.27 (m, 1H), 7.20-7.18 (m, 1H), 7.12-7.08 (m, 1H), 6.89-6.87 (d, *J* = 8.0 Hz, 1H), 4.02-3.98 (m, 1H), 3.59-3.56 (d, *J* = 11.2 Hz, 1H), 3.43-3.39 (m, 1H), 3.24 (s, 3H), 2.27 (s, 1H), 1.95-1.91 (m, 1H), 1.84-1.78 (m, 1H), 1.72 (s, 1H), 1.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.1, 142.2, 134.8, 128.2, 123.2, 122.4, 108.4, 68.7, 66.8, 47.0, 40.1, 26.5, 22.9 ppm; IR (KBr): υ_{max} 3439, 2925, 1688, 1612, 1381 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{17}NNaO_3$ $[M+Na]^+$ 258.1101, found 258.1110.

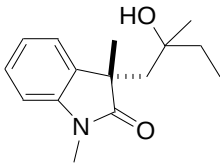


3e: A white solid, R_f 0.2 (EtOAc/petroleum ether = 1:2); mp = 103-105 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.21 (m, 2H), 7.07-7.03 (m, 1H), 6.88-6.86 (d, *J* = 8.0 Hz, 1H), 3.22 (s, 3H), 2.37-2.33 (d, *J* = 14.8 Hz, 1H), 2.14-2.10 (d, *J* = 14.8 Hz, 1H), 1.88 (s, 1H), 1.33 (s, 3H), 1.05 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.6, 142.8, 134.0, 127.9, 123.1, 122.4, 108.4, 70.8, 50.0, 46.7, 31.3, 29.8, 27.4, 26.3 ppm; IR (KBr): υ_{max} 3470, 2969, 1704, 1612, 1378 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}NNaO_2$ $[M+Na]^+$ 256.1308, found 256.1310.



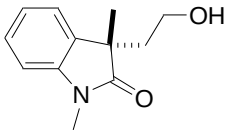
3f: A white solid, R_f 0.3 (EtOAc/petroleum ether = 1:2); mp = 70-72 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.23 (m, 2H), 7.07-7.03 (m, 1H), 6.88-6.86 (d, *J* = 8.0 Hz, 1H), 3.23 (s, 3H), 2.29-2.25 (d, *J* = 14.8 Hz, 1H), 2.15-2.12 (d, *J* = 14.8 Hz, 1H),

1.72 (s, 1H), 1.35-1.30 (m, 9H), 1.15-1.08 (m, 2H), 1.00-0.87 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.8, 142.7, 134.3, 127.8, 123.1, 122.3, 108.4, 71.5, 49.5, 46.4, 39.4, 37.8, 27.7, 26.4, 25.5, 22.0, 21.9 ppm; IR (KBr): υ_{max} 3475, 2929, 1698, 1612, 1379 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{23}NNaO_2$ $[M+Na]^+$ 296.1621, found 296.1629.



3g: A pale yellow solid, R_f 0.3 (EtOAc/petroleum ether = 1:2); mp = 89-91 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.25 (m, 2H), 7.08-7.04 (m, 1H), 6.88-6.86 (d, *J* = 7.6 Hz, 1H), 3.23 (s, 3H), 2.30-2.27 (d, *J* = 14.8 Hz, 1H), 2.14-2.11 (d, *J* = 14.8 Hz, 1H), 1.73 (s, 1H), 1.34 (s, 3H), 1.23-1.08 (m, 2H), 0.95 (s, 3H), 0.78-0.74 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.6, 142.8, 134.0, 127.9, 123.1, 122.4, 108.5, 72.9, 47.7, 46.7, 35.2, 27.5, 27.1, 26.4, 8.2 ppm; IR (KBr): υ_{max} 3472, 2988, 1703, 1612, 1378 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NNaO_2$ $[M+Na]^+$ 270.1465, found 270.1473.

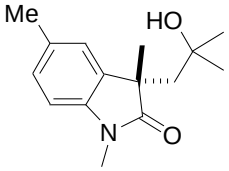
3g': A colorless oil, R_f 0.25 (EtOAc/petroleum ether = 1:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.26 (m, 1H), 7.22-7.20 (d, *J* = 7.2 Hz, 1H), 7.08-7.04 (m, 1H), 6.88-6.86 (d, *J* = 7.6 Hz, 1H), 3.24 (s, 3H), 2.34-2.31 (d, *J* = 14.8 Hz, 1H), 2.11-2.07 (d, *J* = 14.8 Hz, 1H), 1.77 (s, 1H), 1.42-1.29 (m, 5H), 0.86-0.82 (t, *J* = 7.6 Hz, 3H), 0.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.0, 142.9, 134.4, 128.0, 123.0, 122.3, 108.4, 72.7, 48.3, 46.6, 37.5, 27.5, 26.4, 25.9, 8.1 ppm; IR (KBr): υ_{max} 3482, 2967, 1700, 1610, 1378 cm^{-1}.



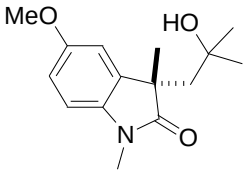
3h: A pale yellow oil, R_f 0.1 (EtOAc/petroleum ether = 1:2); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30-7.26 (m, 1H), 7.18-7.16 (m, 1H), 7.10-7.06 (m, 1H), 6.87-6.85 (d, *J* = 8.0 Hz, 1H), 3.69-3.66 (m, 1H), 3.47-3.46 (m, 1H), 3.22 (s, 3H), 2.35 (s, 1H), 2.19-2.12 (m, 1H), 2.02-1.95 (m, 1H), 1.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.5, 142.9, 134.1, 128.0, 122.8, 122.4, 108.3, 59.4, 47.0, 40.1, 26.3, 23.5 ppm; IR

(KBr): υ_{max} 3430, 2926, 1699, 1611, 1379 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{15}NNaO_2$ $[M+Na]^+$ 228.0995, found 228.1005.

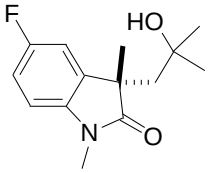
Characterization of Products 4



4a: A white solid, R_f 0.2 (EtOAc/petroleum ether = 1:2); mp = 98-100 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.07-7.05 (m, 2H), 6.76-6.75 (d, *J* = 7.6, 1H), 3.20 (s, 3H), 2.35-2.31 (d, *J* = 14.8 Hz, 1H), 2.32 (s, 3H), 2.12-2.08 (d, *J* = 14.8 Hz, 1H), 1.97 (s, 1H), 1.31 (s, 3H), 1.04 (s, 3H), 0.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.4, 140.4, 134.0, 132.0, 128.2, 123.9, 108.2, 70.8, 49.9, 46.8, 31.0, 30.0, 27.5, 26.3, 21.1 ppm; IR (KBr): υ_{max} 3460, 2925, 1696, 1623, 1379 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NNaO_2$ $[M+Na]^+$ 270.1465, found 270.1470.

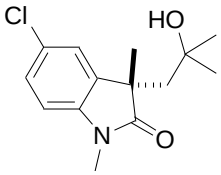


4b: A white solid, R_f 0.1 (EtOAc/petroleum ether = 1:2); mp = 99-101 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.83 (s, 1H), 6.80-6.75 (m, 2H), 3.78 (s, 3H), 3.20 (s, 3H), 2.35-2.31 (d, *J* = 14.8 Hz, 1H), 2.10-2.06 (d, *J* = 14.8 Hz, 1H), 2.03 (s, 1H), 1.32 (s, 3H), 1.06 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.2, 155.9, 136.3, 135.5, 111.9, 110.7, 108.7, 70.8, 55.8, 50.0, 47.2, 31.3, 29.8, 27.5, 26.4 ppm; IR (KBr): υ_{max} 3478, 2968, 1701, 1496, 1600, 1379 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NNaO_3$ $[M+Na]^+$ 286.1414, found 286.1423.

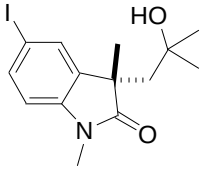


4c: A white solid, R_f 0.2 (EtOAc/petroleum ether = 1:2); mp = 123-125 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.00-6.95 (m, 2H), 6.80-6.76 (m, 1H), 3.22 (s, 3H), 2.37-2.34 (d, *J* = 14.8 Hz, 1H), 2.10-2.07 (d, *J* = 14.8 Hz, 1H), 1.80 (s, 1H), 1.33 (s, 3H), 1.09 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.3, 159.2 (d, J_{C-F} = 238.8 Hz), 138.7, 135.9 (d, J_{C-F} = 7.8 Hz), 114.0 (d, J_{C-F} = 23.2 Hz), 111.4 (d, J_{C-F} = 25.2 Hz), 108.8 (d, J_{C-F} = 7.8 Hz), 70.7, 50.0, 47.2, 31.8, 29.8, 27.3, 26.5 ppm; IR (KBr): υ_{max}

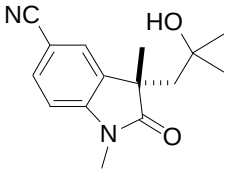
3474, 2970, 1702, 1620, 1495, 1378 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}FNNaO_2$ $[M+Na]^+$ 274.1214, found 274.1223.



4d: A white solid, R_f 0.2 (EtOAc/petroleum ether = 1:2); mp = 103-105 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.21 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.18 (d, *J* = 1.6 Hz, 1H), 6.78-6.76 (d, *J* = 8.4 Hz, 1H), 3.19 (s, 3H), 2.35-2.31 (d, *J* = 14.8 Hz, 1H), 2.09-2.05 (d, *J* = 14.8 Hz, 1H), 1.85 (s, 1H), 1.30 (s, 3H), 1.07 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.1, 141.4, 135.9, 127.7, 123.7, 109.2, 70.6, 50.0, 47.0, 31.7, 29.8, 27.2, 26.4 ppm; IR (KBr): υ_{max} 3465, 2969, 1706, 1609, 1490, 1346 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}ClNNaO_2$ $[M+Na]^+$ 290.0918, found 290.0927.

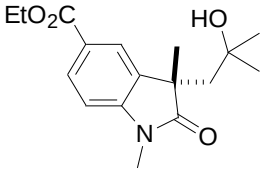


4e: A white solid, R_f 0.2 (EtOAc/petroleum ether = 1:2); mp = 126-128 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.59-7.57 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.50-7.49 (d, *J* = 1.6 Hz, 1H), 6.66-6.64 (d, *J* = 8.4 Hz, 1H), 3.20 (s, 3H), 2.35-2.31 (d, *J* = 14.8 Hz, 1H), 2.09-2.05 (d, *J* = 14.8 Hz, 1H), 1.74 (s, 1H), 1.32 (s, 3H), 1.09 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 180.8, 142.6, 136.7, 136.6, 132.0, 110.4, 84.8, 70.7, 50.0, 46.8, 31.8, 29.8, 27.3, 26.4 ppm; IR (KBr): υ_{max} 3474, 2968, 1706, 1602, 1486, 1362 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}INNaO_2$ $[M+Na]^+$ 382.0274, found 382.0279.

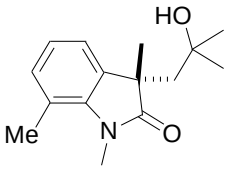


4f: A white solid, R_f 0.1 (EtOAc/petroleum ether = 1:2); mp = 145-147 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.60-7.58 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.46-7.45 (d, *J* = 1.6 Hz, 1H), 6.92-6.90 (d, *J* = 8.0 Hz, 1H), 3.23 (s, 3H), 2.39-2.35 (d, *J* = 14.8 Hz, 1H), 2.13-2.09 (d, *J* = 14.8 Hz, 1H), 1.60 (s, 1H), 1.31 (s, 3H), 1.09 (s, 3H), 0.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.3, 146.8, 135.2, 133.0, 126.7, 119.3, 108.7,

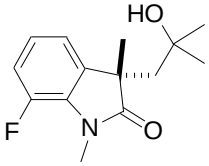
105.1, 70.5, 50.0, 46.4, 32.0, 29.9, 27.0, 26.5 ppm; IR (KBr): υ_{max} 3492, 2971, 2930, 1717, 1614, 1498, 1344 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{18}N_2NaO_2$ $[M+Na]^+$ 281.1260, found 281.1268.



4g: A white solid, R_f 0.1 (EtOAc/petroleum ether = 1:3); mp = 103-105 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02-8.00 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.87 (d, *J* = 1.6 Hz, 1H), 6.88-6.87 (d, *J* = 8.4 Hz, 1H), 4.37-4.32 (m, 2H), 3.24 (s, 3H), 2.38-2.34 (d, *J* = 14.8 Hz, 1H), 2.17-2.13 (d, *J* = 14.8 Hz, 1H), 1.74 (s, 1H), 1.39-1.36 (t, *J* = 7.2 Hz, 3H), 1.33 (s, 3H), 1.08 (s, 3H), 0.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.9, 166.4, 146.9, 134.1, 130.4, 124.5, 124.4, 107.8, 70.7, 60.8, 50.1, 46.5, 32.0, 29.6, 27.1, 26.5, 14.3 ppm; IR (KBr): υ_{max} 3505, 2971, 1707, 1614, 1499, 1374 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{23}NNaO_4$ $[M+Na]^+$ 328.1519, found 328.1523.

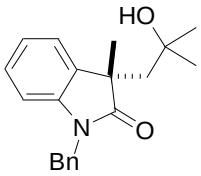


4h: A pale yellow oil, R_f 0.2 (EtOAc/petroleum ether = 1:3); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.06-7.04 (d, *J* = 7.6 Hz, 1H), 7.00-6.98 (d, *J* = 7.6 Hz, 1H), 6.95-6.91 (t, *J* = 7.2 Hz, 1H), 3.50 (s, 3H), 2.58 (s, 3H), 2.35-2.31 (d, *J* = 14.8 Hz, 1H), 2.11-2.07 (d, *J* = 14.8 Hz, 1H), 1.97 (s, 1H), 1.30 (s, 3H), 1.06 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.3, 140.5, 134.6, 131.6, 122.3, 121.0, 120.1, 70.8, 50.2, 46.1, 31.3, 29.8, 29.7, 27.8, 19.1 ppm; IR (KBr): υ_{max} 3464, 2970, 1698, 1601, 1460, 1338 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{21}NNaO_2$ $[M+Na]^+$ 270.1465, found 270.1472.

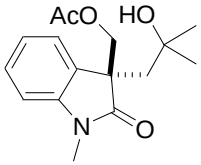


4i: A colorless oil, R_f 0.4 (EtOAc/petroleum ether = 1:3); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.02-6.95 (m, 3H), 3.44 (s, 3H), 2.37-2.34 (d, *J* = 14.8 Hz, 1H), 2.12-2.09 (d, *J* = 14.8 Hz, 1H), 1.77 (s, 1H), 1.32 (s, 3H), 1.08 (s, 3H), 0.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.2, 148.0 (d, J_{C-F} = 242.6 Hz), 137.0 (d, J_{C-F} = 2.9 Hz), 129.5 (d,

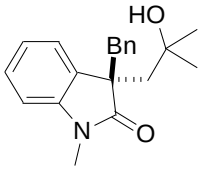
$J_{C\text{-}F}$ = 8.0 Hz), 122.8 (d, $J_{C\text{-}F}$ = 6.2 Hz), 119.0 (d, $J_{C\text{-}F}$ = 3.2 Hz), 115.7 (d, $J_{C\text{-}F}$ = 19.2 Hz), 70.8, 50.2, 47.1, 31.7, 29.7, 28.8, 27.6 ppm; IR (KBr): υ_{max} 3484, 2970, 1710, 1630, 1483, 1376 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{18}FNNaO_2$ $[M+Na]^+$ 274.1214, found 274.1220.



4j: A colorless oil, R_f 0.3 (EtOAc/petroleum ether = 1:3); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.22 (m, 6H), 7.17-7.13 (m, 1H), 7.04-7.00 (m, 1H), 6.76-6.74 (d, *J* = 8.0 Hz, 1H), 5.00-4.97 (d, *J* = 15.6 Hz, 1H), 4.91-4.88 (d, *J* = 15.6 Hz, 1H), 2.44-2.41 (d, *J* = 14.8 Hz, 1H), 2.20-2.16 (d, *J* = 14.8 Hz, 1H), 1.95 (s, 1H), 1.40 (s, 3H), 1.10 (s, 3H), 0.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 181.6, 141.9, 135.9, 134.1, 128.7, 127.7, 127.5, 127.4, 123.2, 122.4, 109.5, 70.9, 49.9, 46.8, 43.9, 31.7, 29.7, 28.0 ppm; IR (KBr): υ_{max} 3466, 2968, 1703, 1610, 1490, 1380 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NNaO_2$ $[M+Na]^+$ 332.1621, found 332.1624.



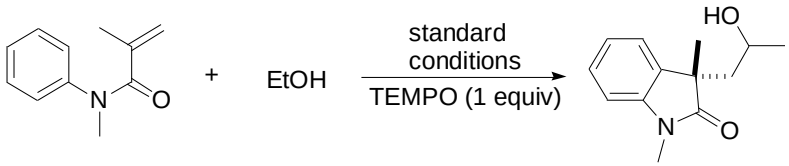
4l: A pale yellow oil, R_f 0.1 (EtOAc/petroleum ether = 1:3); ^1H NMR (400 MHz, $CDCl_3$): δ = 7.31-7.24 (m, 2H), 7.05-7.02 (m, 1H), 6.87-6.85 (d, *J* = 7.6 Hz, 1H), 4.41-4.38 (d, *J* = 10.4 Hz, 1H), 4.04-4.02 (d, *J* = 10.4 Hz, 1H), 3.33 (s, 3H), 2.32-2.29 (d, *J* = 14.8 Hz, 1H), 2.18-2.14 (d, *J* = 14.8 Hz, 1H), 1.89 (s, 1H), 1.83 (s, 3H), 1.07 (s, 3H), 0.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.3, 170.2, 143.7, 129.4, 128.6, 124.2, 122.3, 108.4, 70.6, 68.7, 50.7, 45.1, 31.6, 29.9, 26.4, 20.4 ppm; IR (KBr): υ_{max} 3472, 2970, 1744, 1707, 1612, 1494, 1378 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{21}NNaO_4$ $[M+Na]^+$ 314.1363, found 314.1370.



4m: A white solid, R_f 0.3 (EtOAc/petroleum ether = 1:2); mp = 141-143 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.24-7.16 (m, 2H), 7.07-6.72 (m, 4H), 6.72-6.70 (d, *J* = 8.0

Hz, 2H), 6.57-6.55 (d, *J* = 8.0 Hz, 1H), 3.10-3.07 (d, *J* = 12.8 Hz, 1H), 2.95-2.93 (d, *J* = 12.8 Hz, 1H), 2.91 (s, 3H), 2.54-2.50 (d, *J* = 14.8 Hz, 1H), 2.30-2.27 (d, *J* = 14.8 Hz, 1H), 1.94 (s, 1H), 1.08 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.9, 143.4, 134.7, 130.9, 129.9, 128.0, 127.2, 126.5, 124.2, 121.9, 108.1, 71.0, 52.8, 48.7, 47.0, 31.5, 30.0, 25.9 ppm; IR (KBr): υ_{max} 3461, 2964, 1706, 1612, 1470, 1379 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{23}NNaO_2$ $[M+Na]^+$ 332.1621, found 332.1625.

Investigation of the Reaction Mechanism



1a **2a** **3a**, trace

When the TEMPO was added to the reaction of **1a** with **2a** under the standard conditions, only a trace amount of the desired product **3a** was observed. The result indicates that the radical intermediate should be involved in the catalytic cycle of the reaction.

Isotope Labeling Experiment

a) Intramolecular Kinetic Isotope Effect (KIE) Experiment:

[D_1]-**1a** was synthesized according the literature procedure.[1] A 10 mL oven-dried Schlenk-tube were charged with [D_1]-**1a** (0.2 mmol, 1.0 equiv). The tube was evacuated and backfilled with nitrogen (three times). TBHP (0.4 mmol, 2 equiv) in 1 mL of isopropanol were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred at 100 ^{o}C for 24 h. Upon completion of the reaction, the mixture was diluted with EtOAc, and the solvent was then removed under vacuo. The residue was purified with chromatography column on silica gel to give the corresponding product. The product was analysis by ^{1}H NMR (Figure 1).

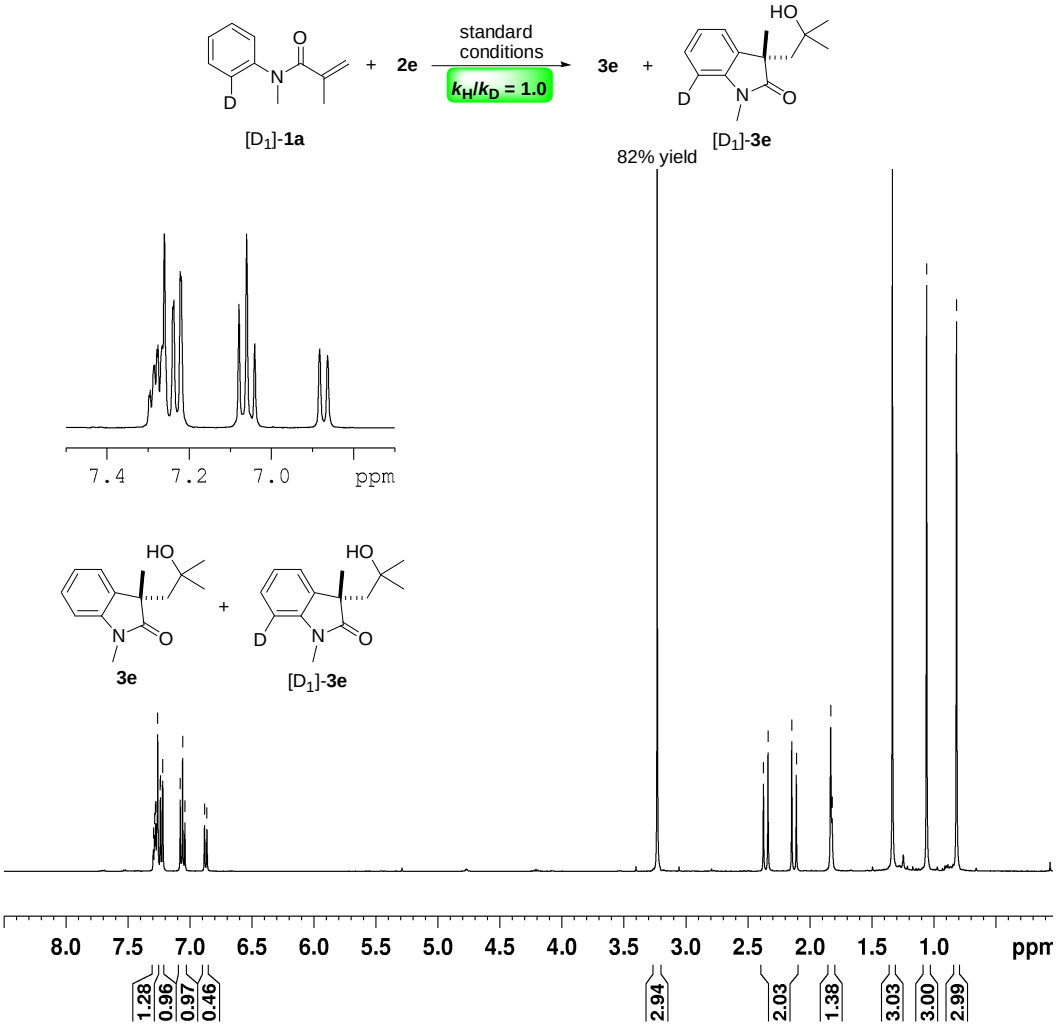


Figure 1. ^{1}H NMR spectra of the mixture of the product **3e** and [D_1]-**3e**.

b) Intermolecular Kinetic Isotope Effect (KIE) Experiment:

Aniline (ring-D_5, 98%, cat. No. DLM-862-0) were purchased from Cambridge Isotope Laboratories. The isotope reagent was used without further purification. [D_5]-**1a** was synthesized according the literature procedure using D_5-aniline as starting material.[1] A 10 mL oven-dried Schlenk-tube were charged with [D_5]-**1a** (0.1 mmol) and **1a** (0.1 mmol). The tube was evacuated and backfilled with nitrogen (three times). TBHP (0.4 mmol, 2 equiv) in 1 mL of isopropanol were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred for at 100 ^{o}C 24 h. Upon completion of the reaction, the mixture was diluted with EtOAc, and the solvent was then removed under vacuo. The residue was purified with chromatography column on silica gel to give the corresponding product. The product was analysis by ^{1}H NMR (Figure 2).

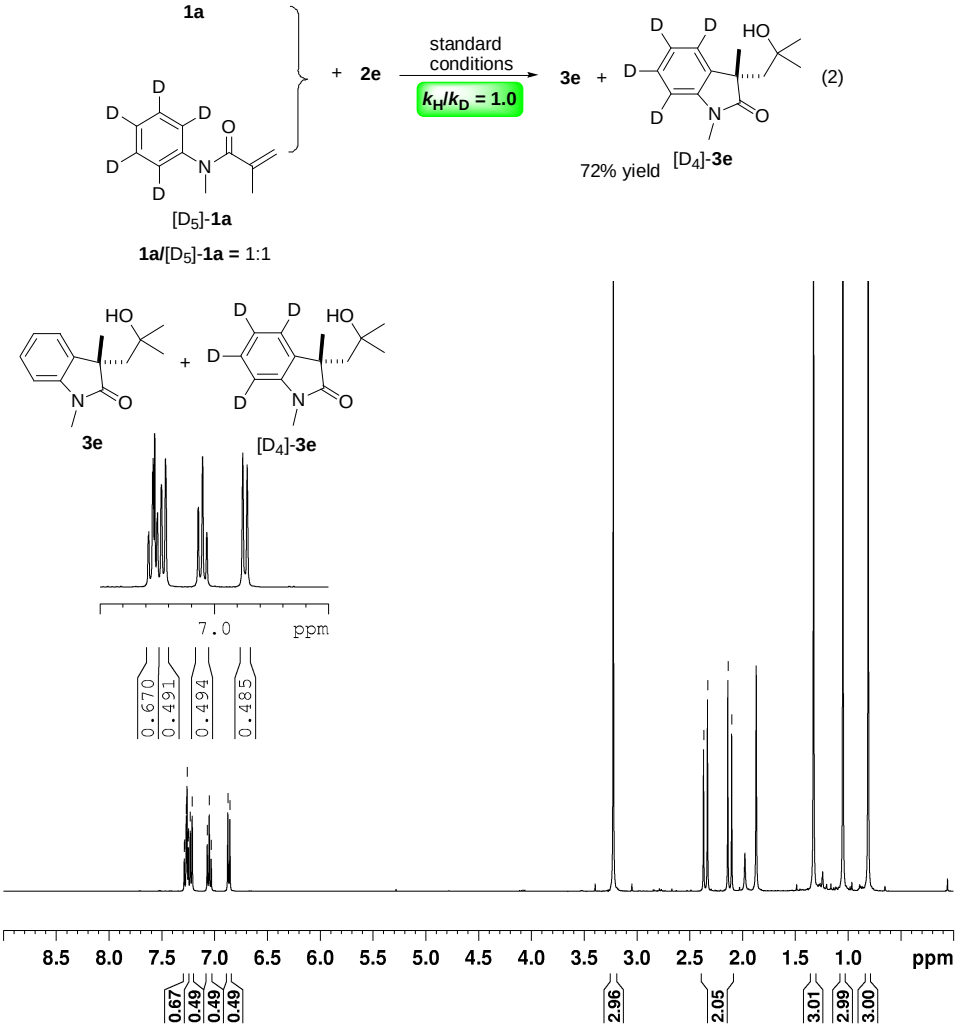


Figure 2. ^{1}H NMR spectra of the mixture of the product **3e** and [D_4]-**3e**.

c) Intermolecular Kinetic Isotope Effect (KIE) Experiment:

Methanol-D_4 (99.5%, cat. No. DLM-24TC-0) were purchased from Cambridge Isotope Laboratories. The isotope reagent was used without further purification. A 10 mL oven-dried Schlenk-tube were charged with **1a** (0.2 mmol). The tube was evacuated and backfilled with nitrogen (three times). TBHP (0.4 mmol, 2 equiv) in 1 mL of methanol/D_4-methanol (1:1) were added by syringe under nitrogen. The tube was then sealed and the mixture was stirred at 100 ^{o}C for 24 h. Upon completion of the reaction, the mixture was diluted with EtOAc, and the solvent was then removed under vacuo. The residue was purified with chromatography column on silica gel to give the corresponding product. The product was analysis by ^{1}H NMR (Figure 3).

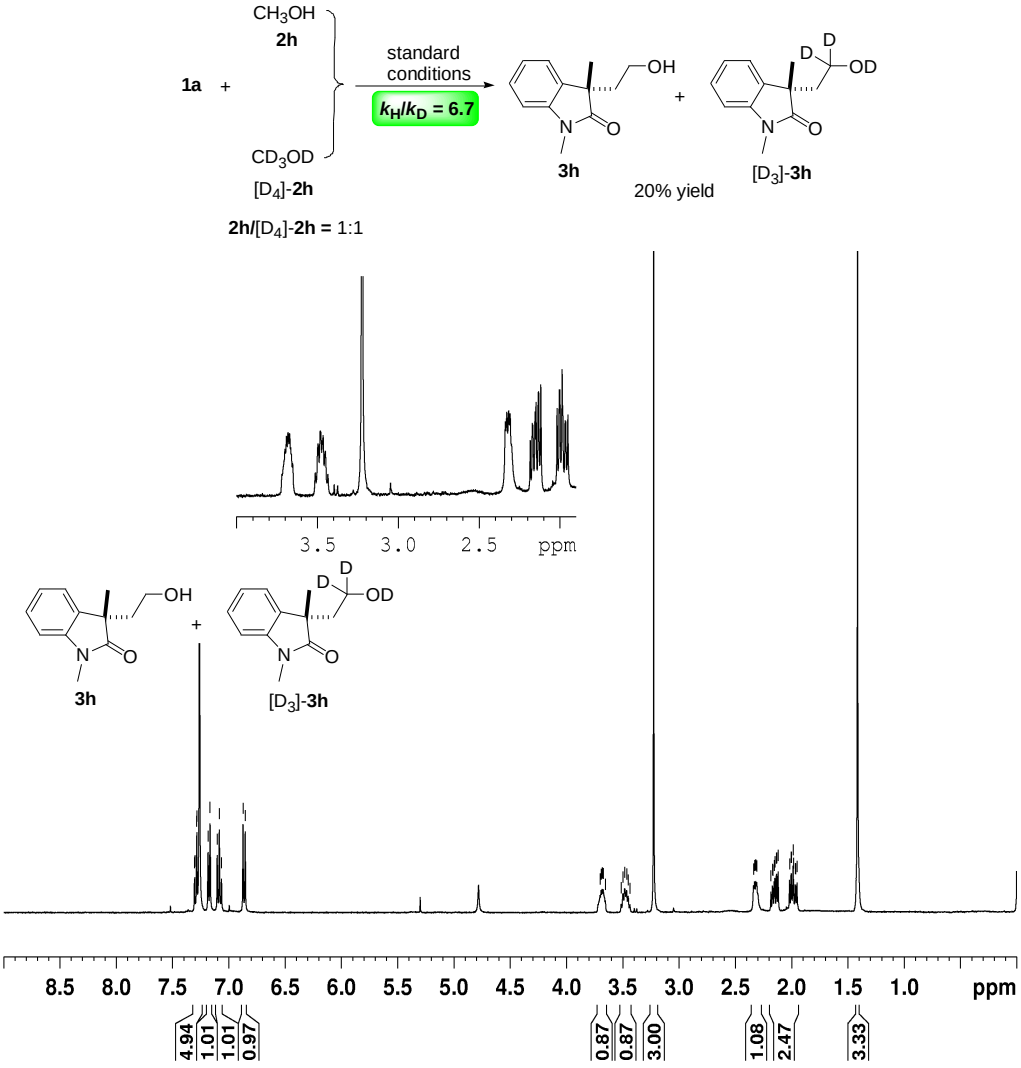
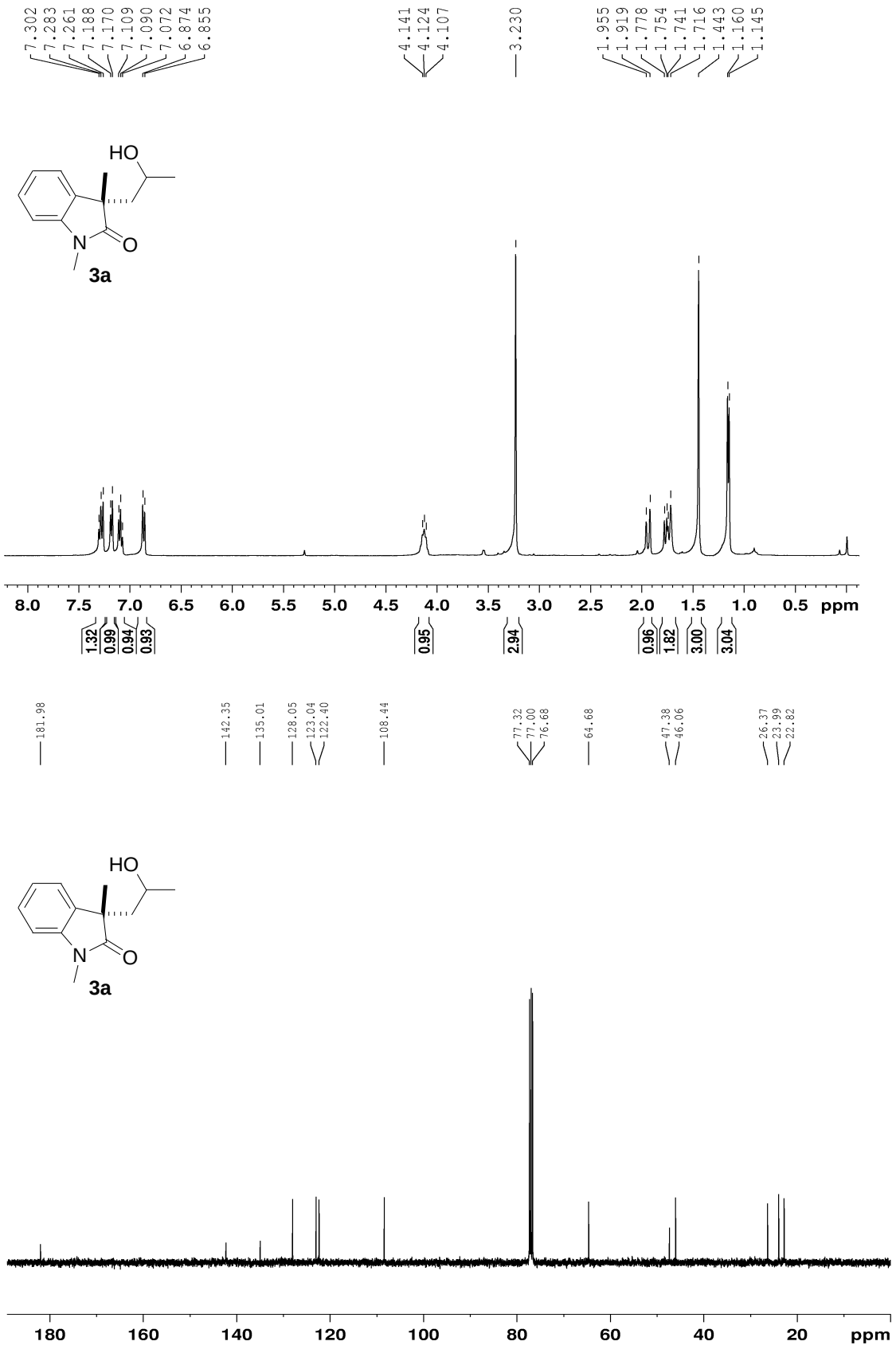


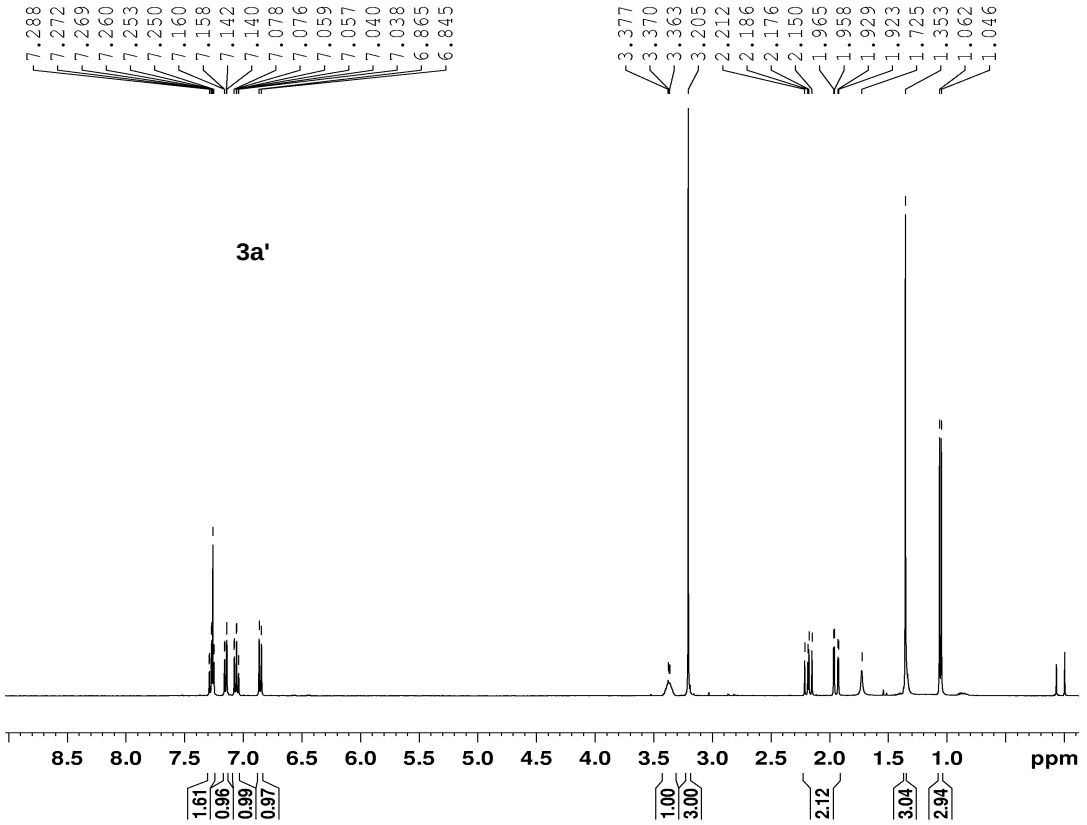
Figure 3. ^{1}H NMR spectra of the mixture of the product **3h** and [D_3]-**3h**.

References

(1) (a) T. Wu, X. Mu and G. Liu, *Angew. Chem., Int. Ed.*, 2011, **50**, 12578; (b) X. Mu, T. Wu, H.-Y. Wang, Y.-L. Guo and G. Liu, *J. Am. Chem. Soc.*, 2012, **134**, 878; (c) D. C. Fabry, M. Stodulski, S. Hoerner and T. Gulder, *Chem. Eur. J.*, 2012, **18**, 10834.

^{1}H NMR and ^{13}C NMR Spectra of the Products 3

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6.845
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3.370
3.363
3.205
2.212
2.186
2.176
2.150
1.965
1.958
1.929
1.923
1.725
1.353
1.062
1.046
3a'
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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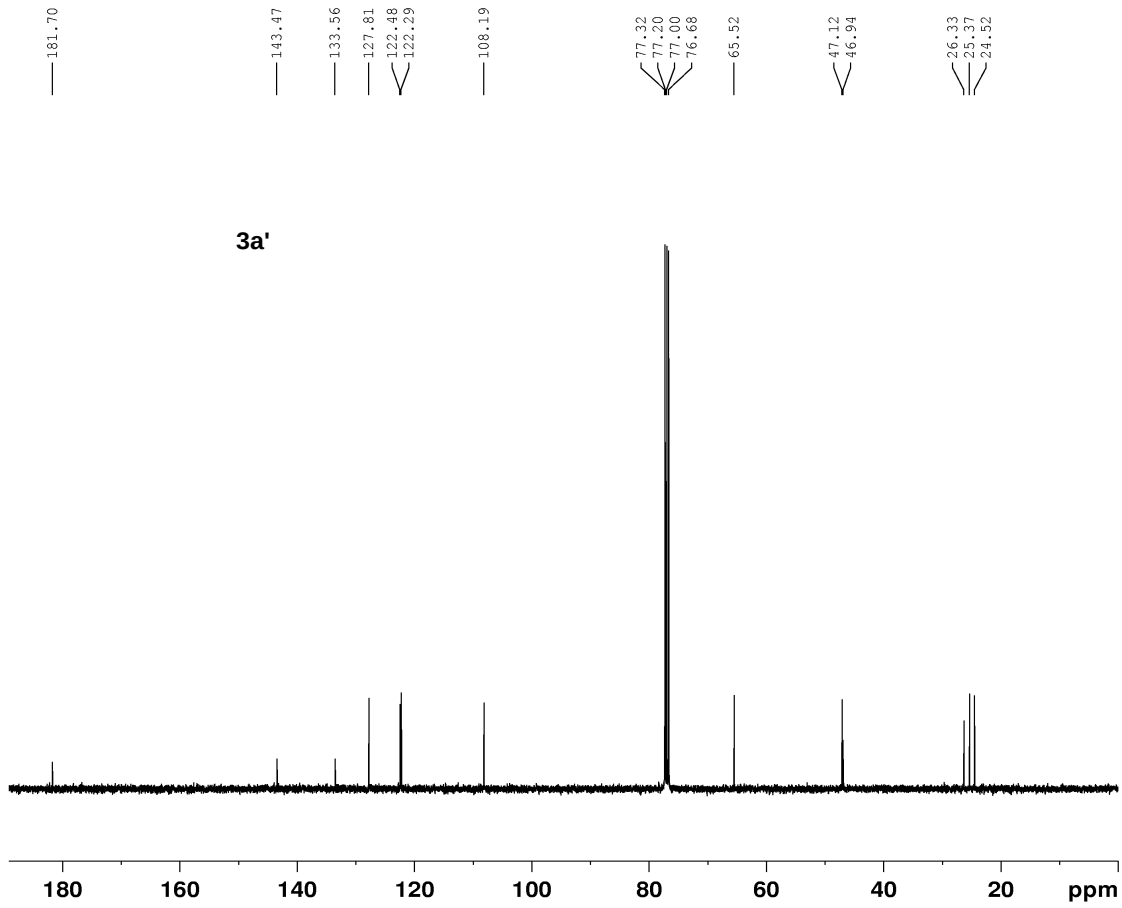
3.04
2.94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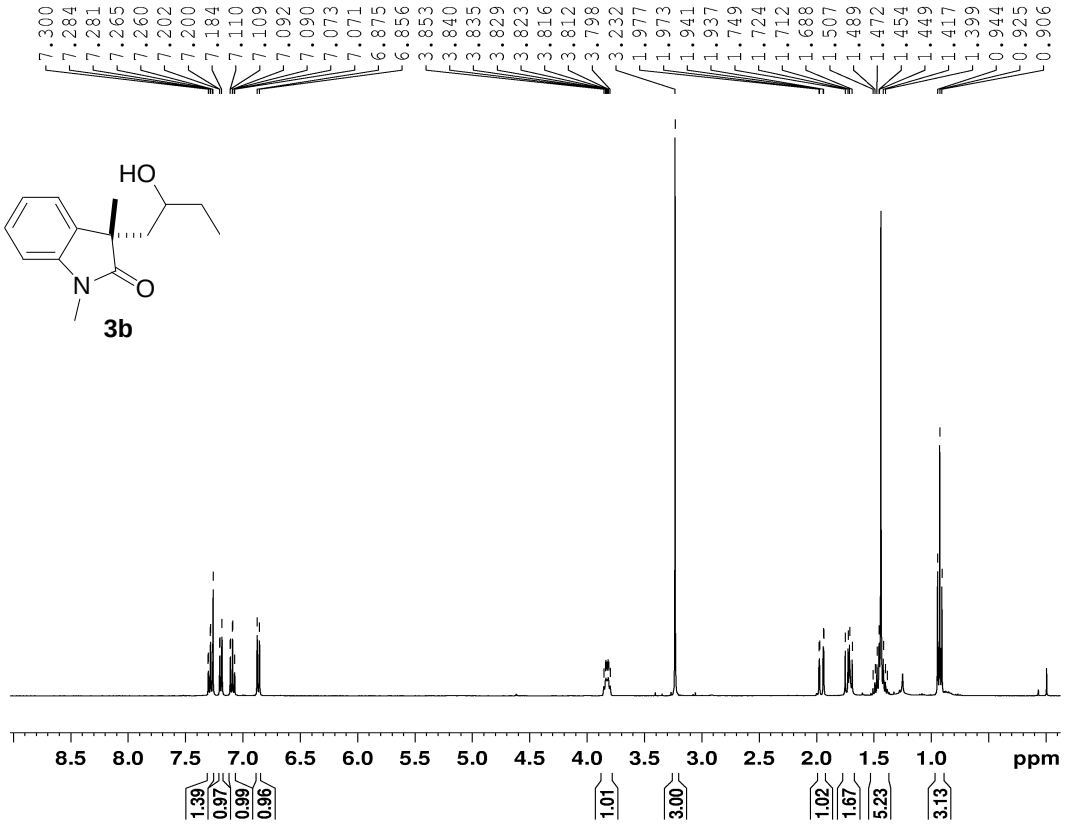
26.33
25.37
24.52
3a'
180 160 140 120 100 80 60 40 20 ppm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O
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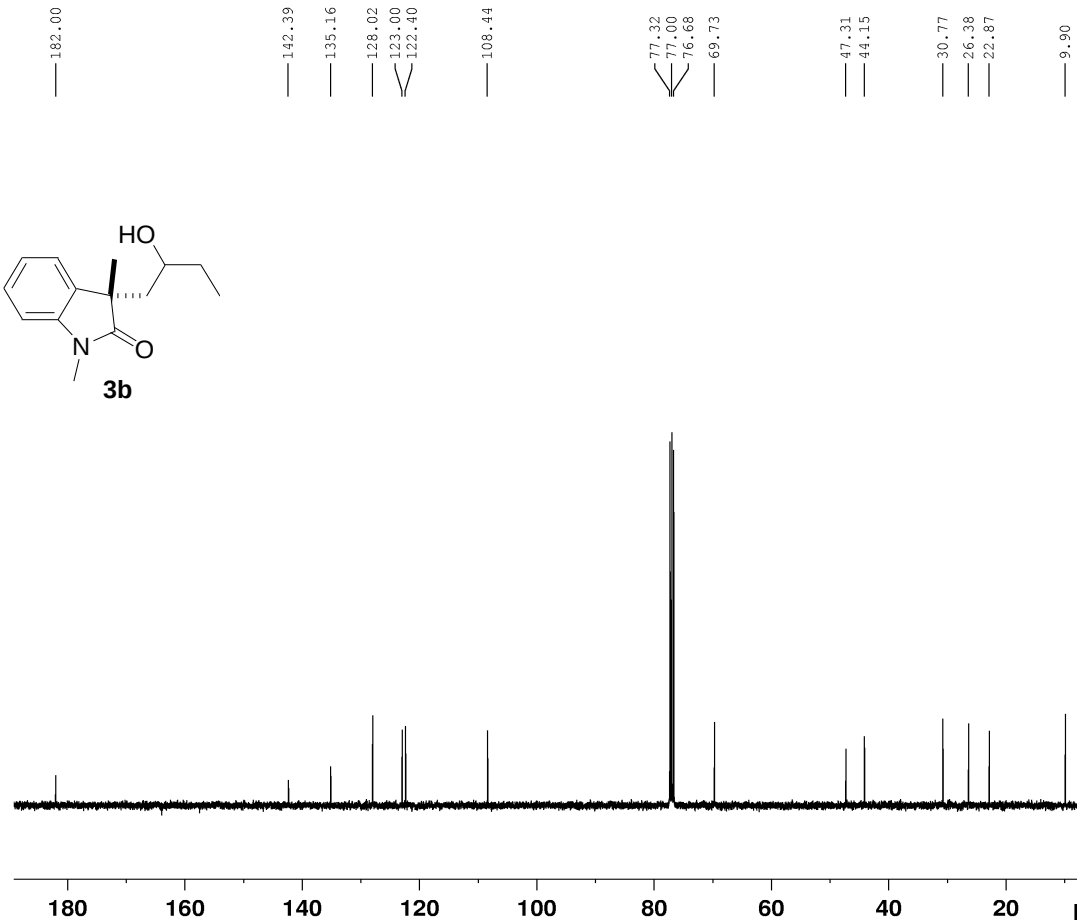
5.23
3.13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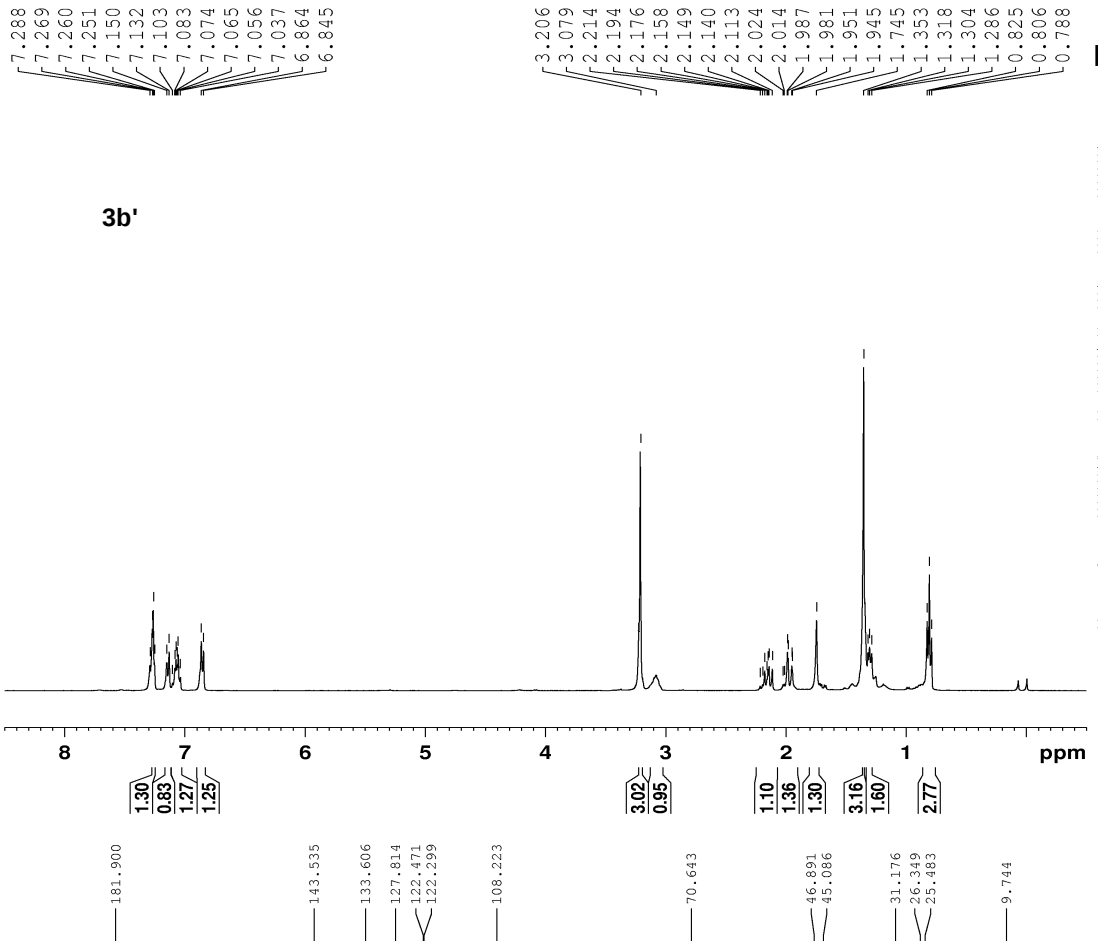
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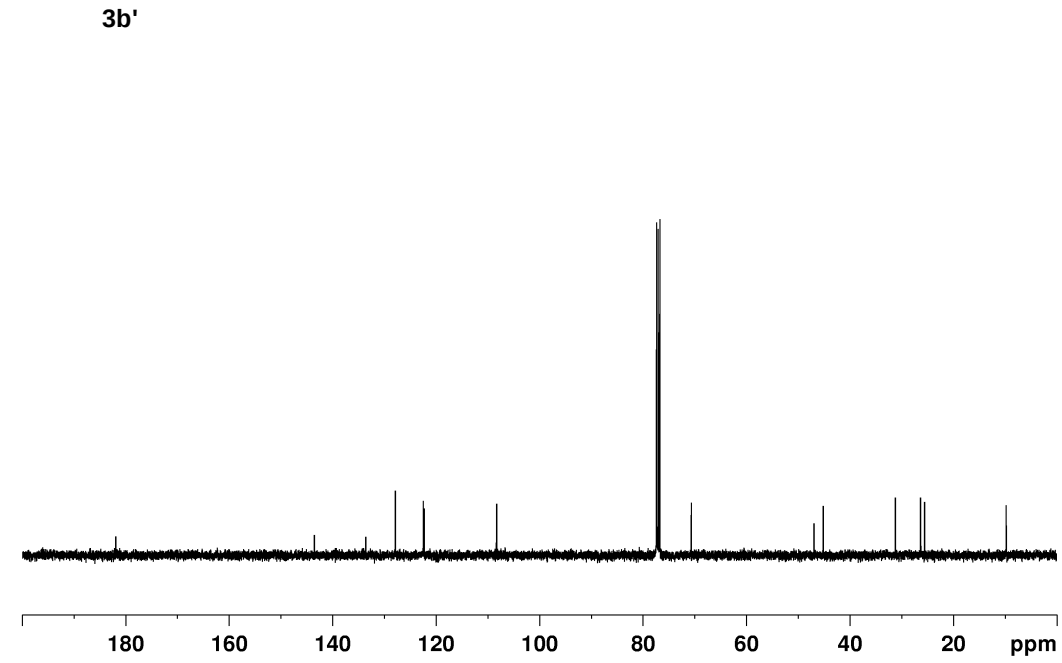
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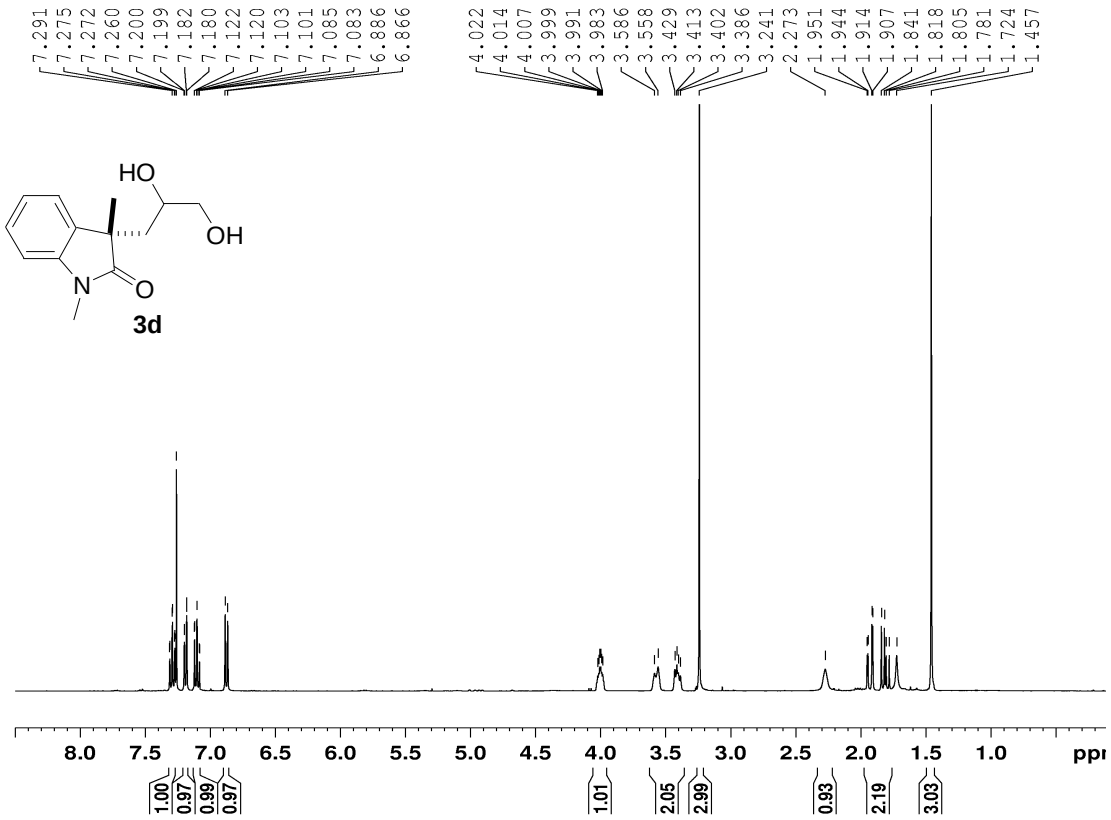
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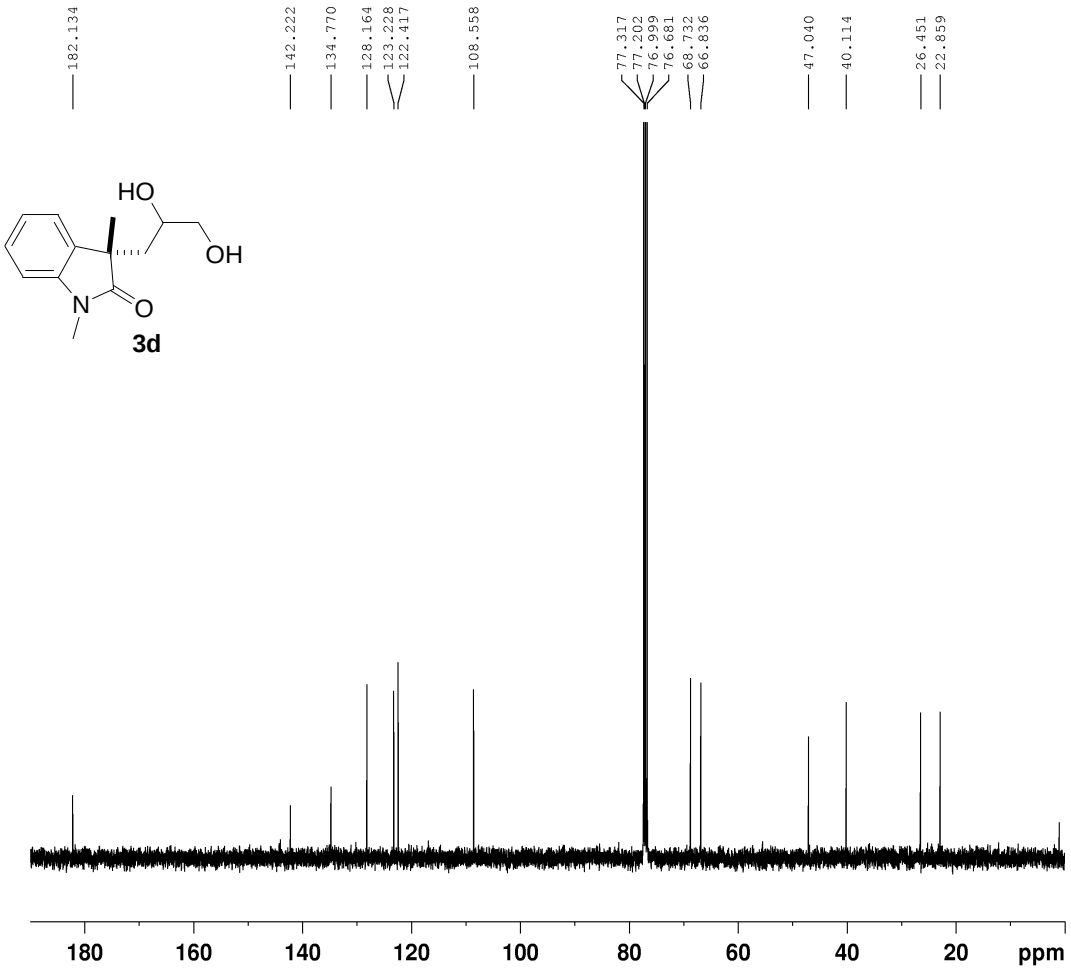
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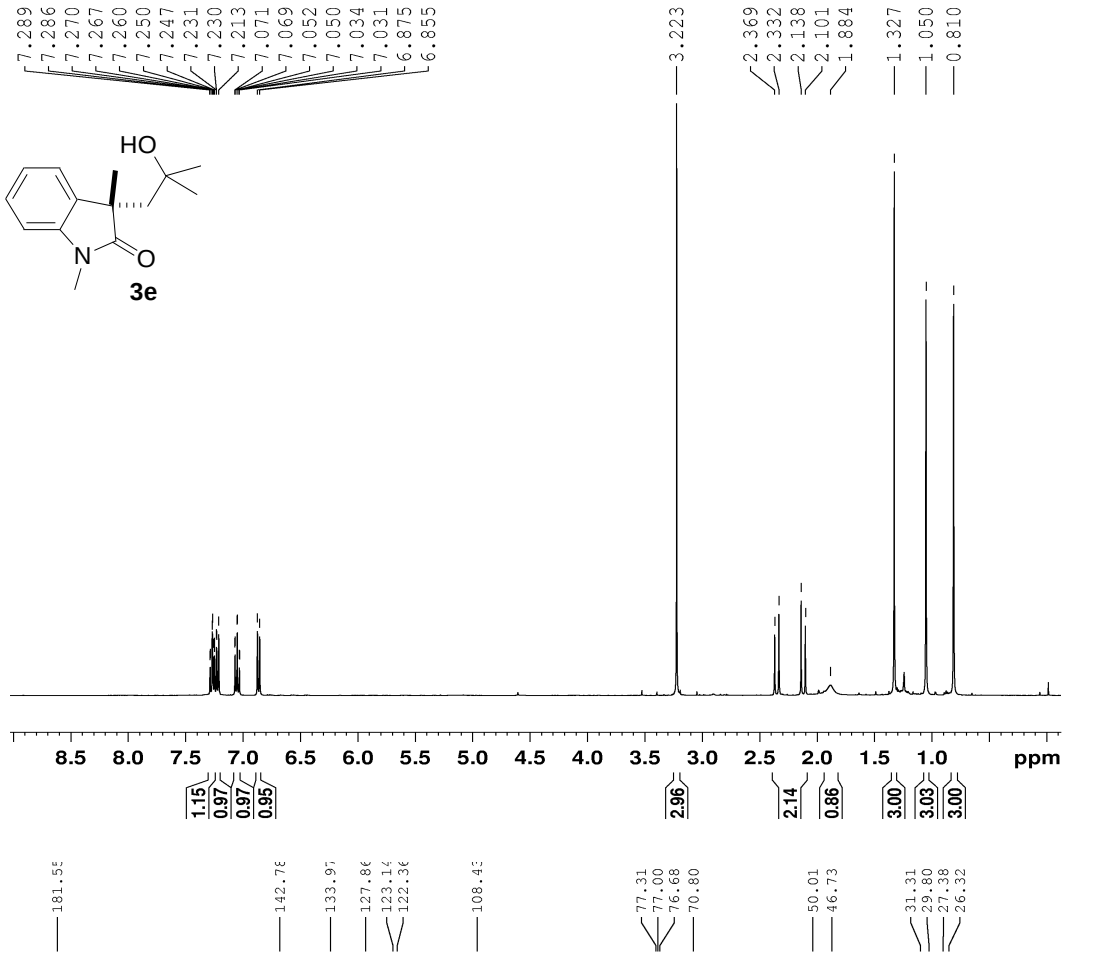

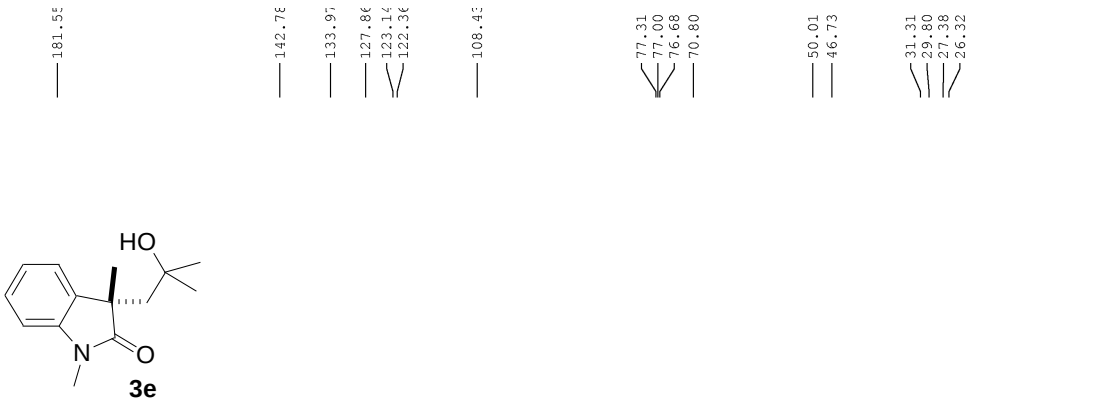

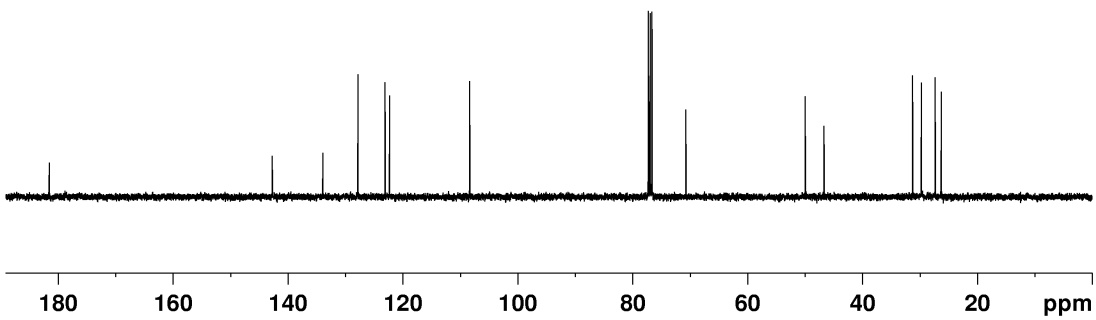

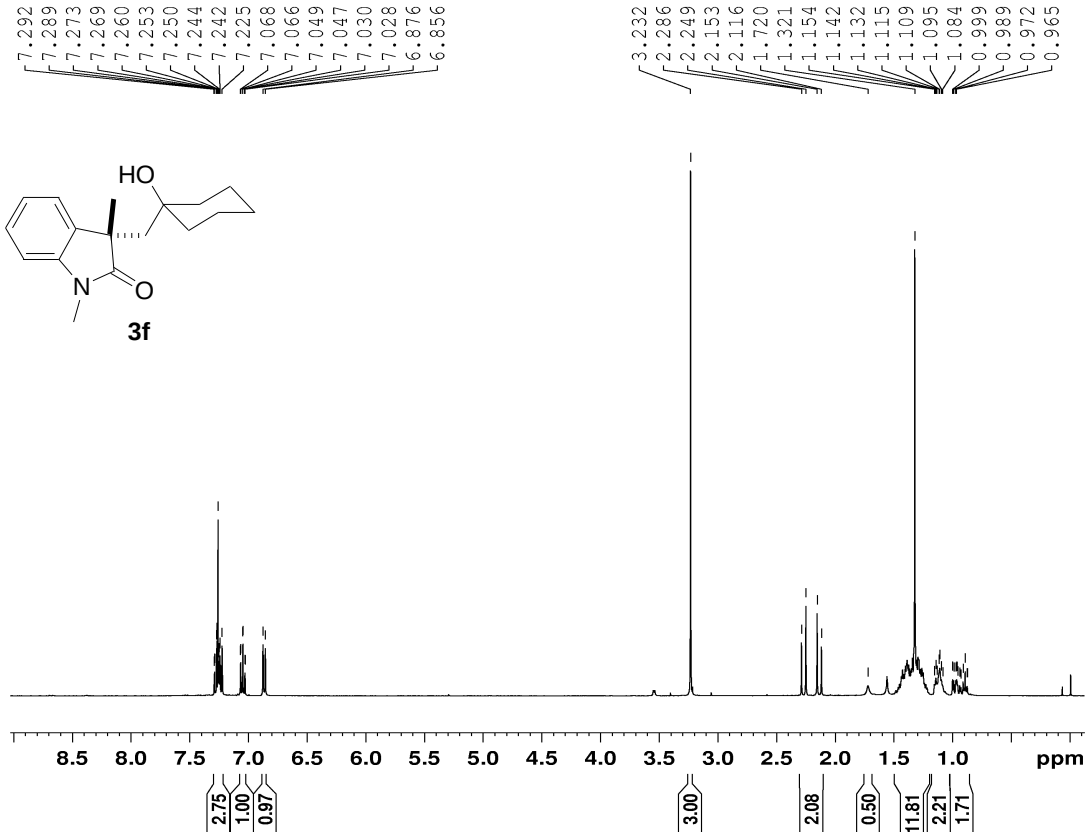
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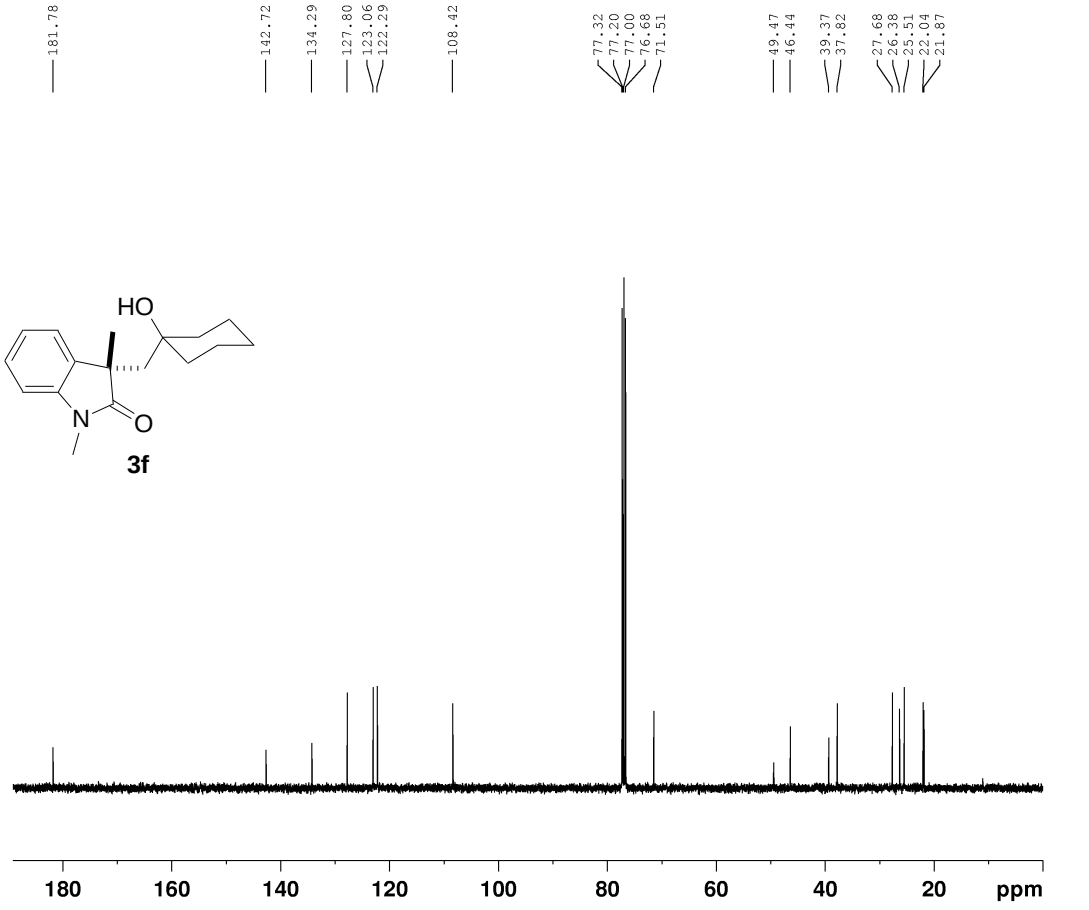
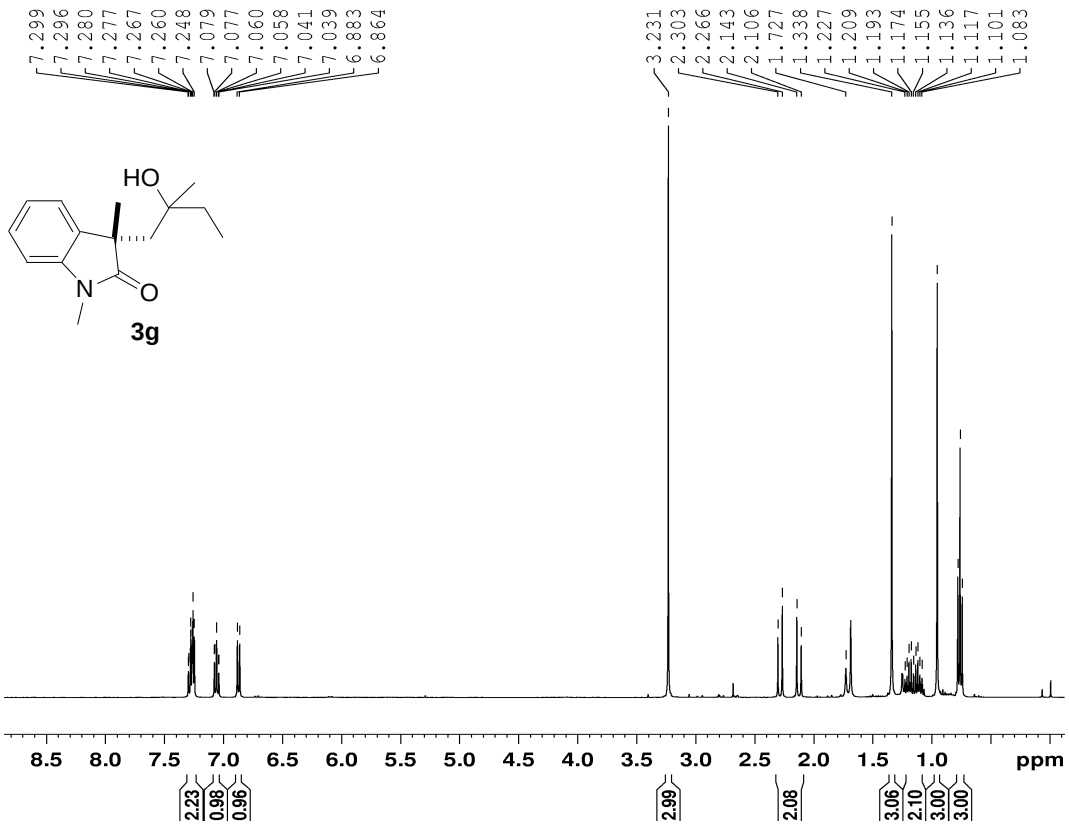
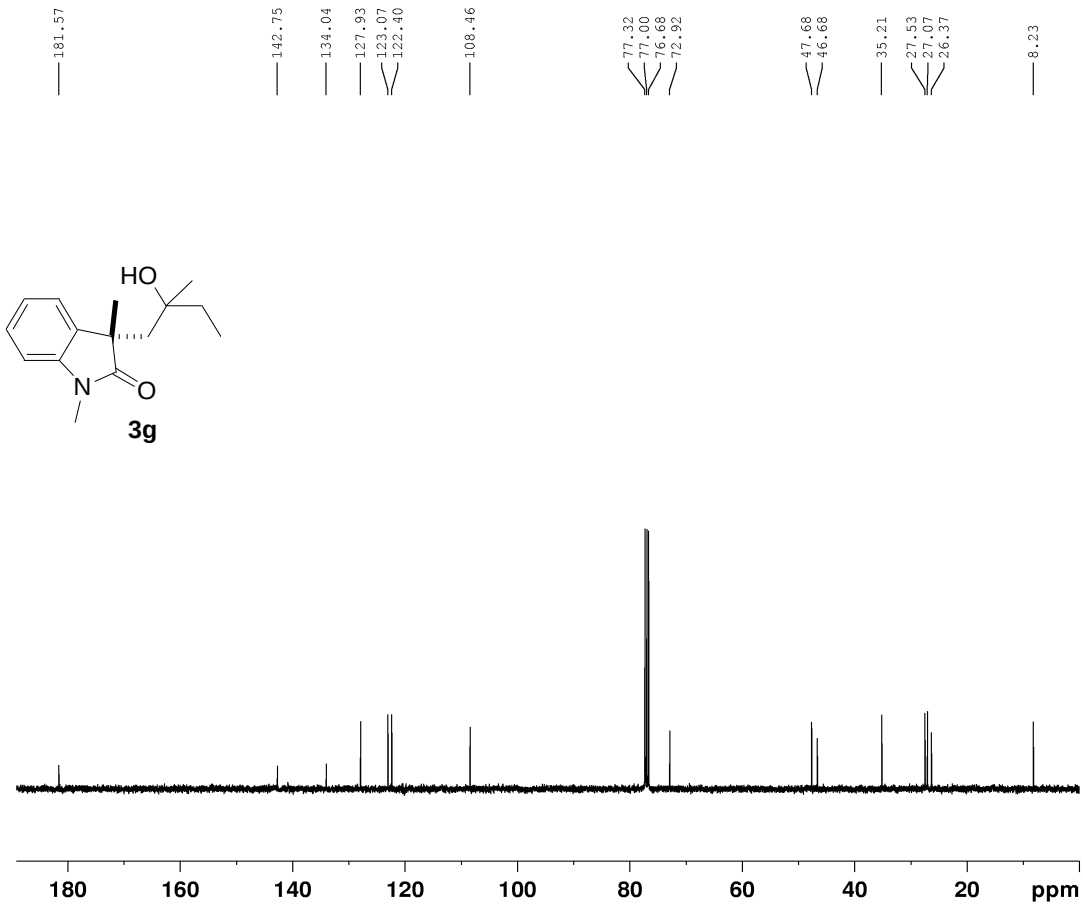
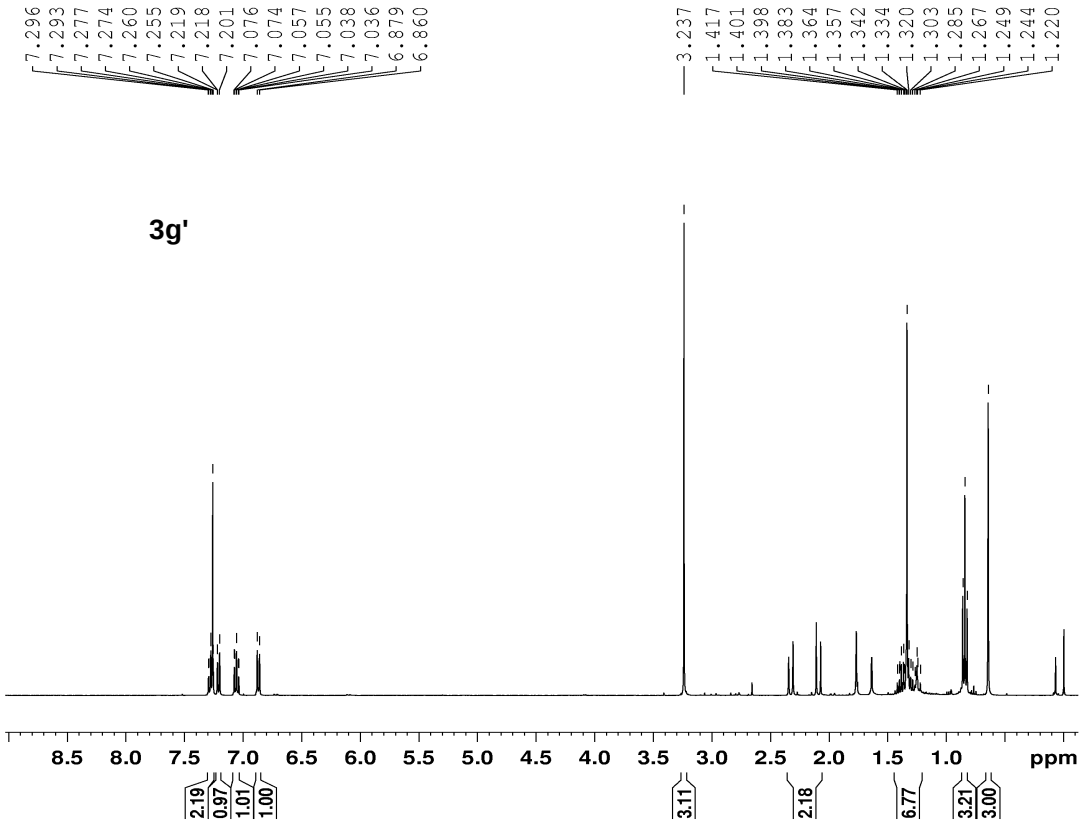
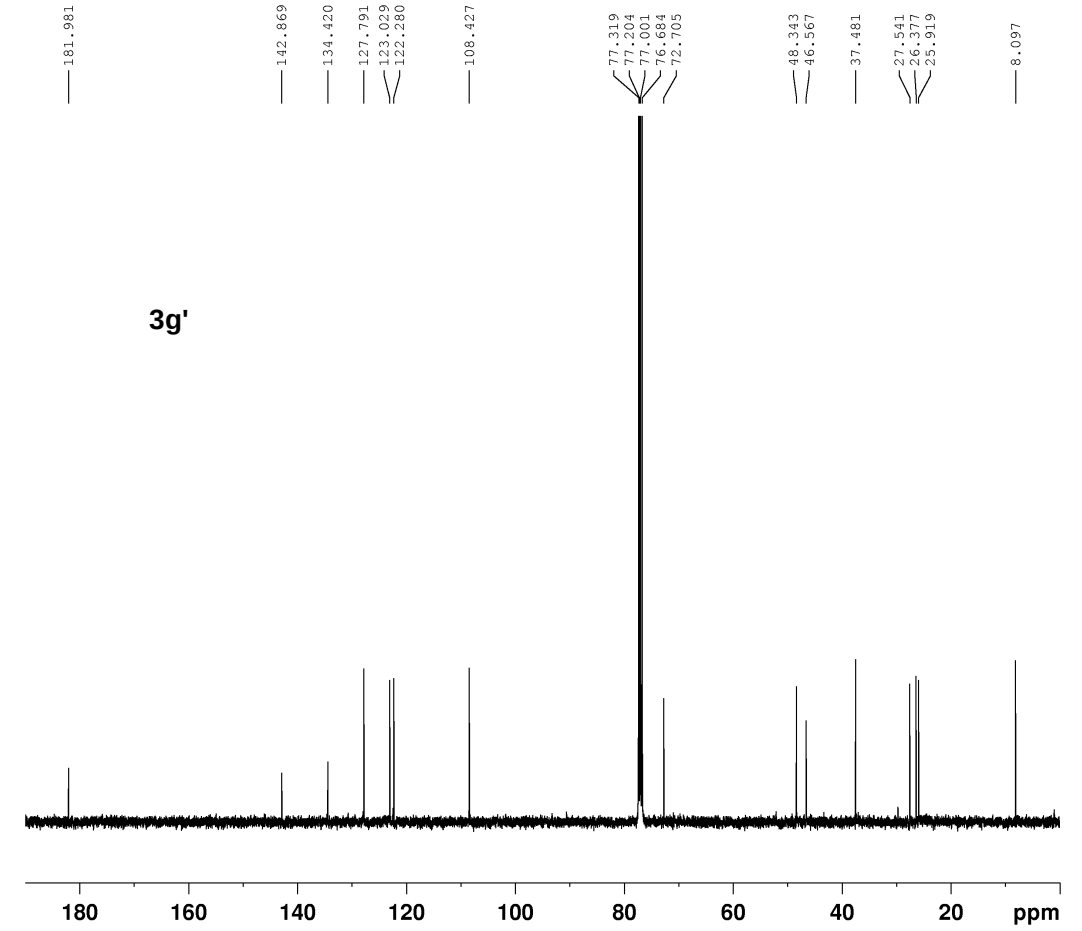
3.232
2.286
2.249
2.153
2.116
1.720
1.321
1.154
1.142
1.132
1.115
1.109
1.095
1.084
0.999
0.989
0.972
0.965
HO
N
O
3f
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.75
1.00
0.97
3.00
2.08
0.50
11.81
2.21
1.71

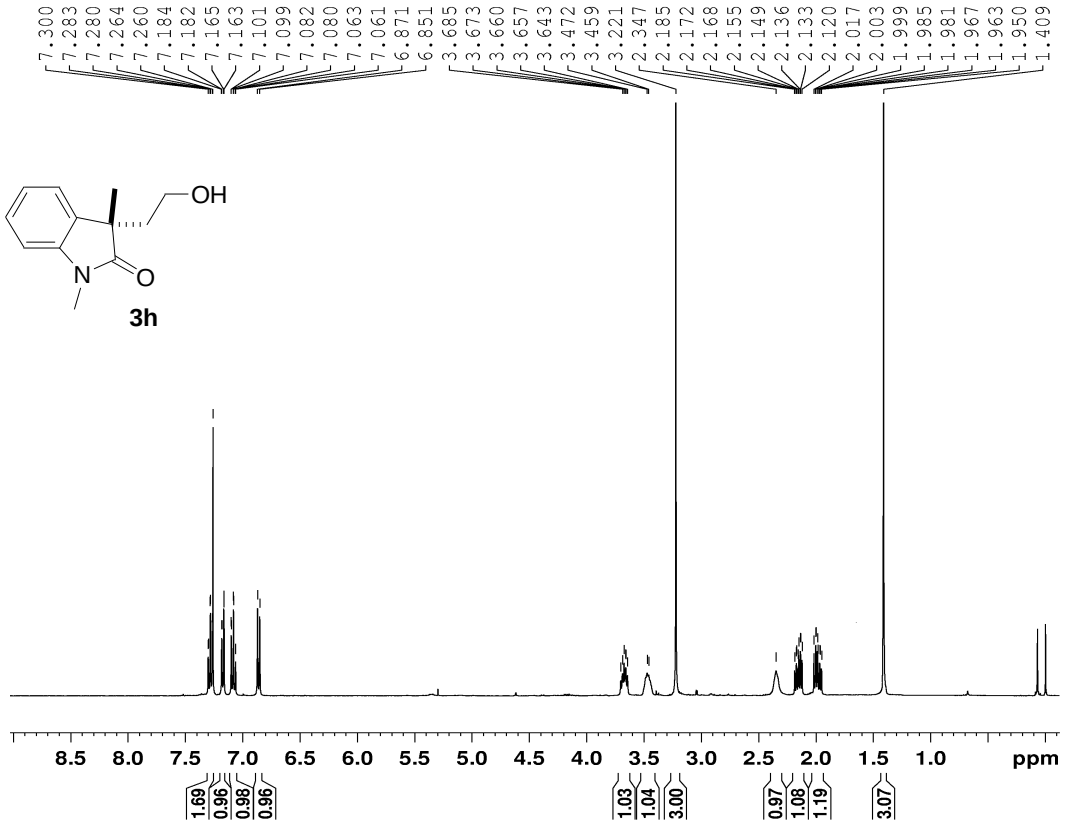

181.78
142.72
134.29
127.80
123.06
122.29
108.42
77.32
77.20
77.00
76.68
71.51
49.47
46.44
39.37
37.82
27.68
26.38
25.51
22.04
21.87
HO
N
O
3f
180 160 140 120 100 80 60 40 20 ppm

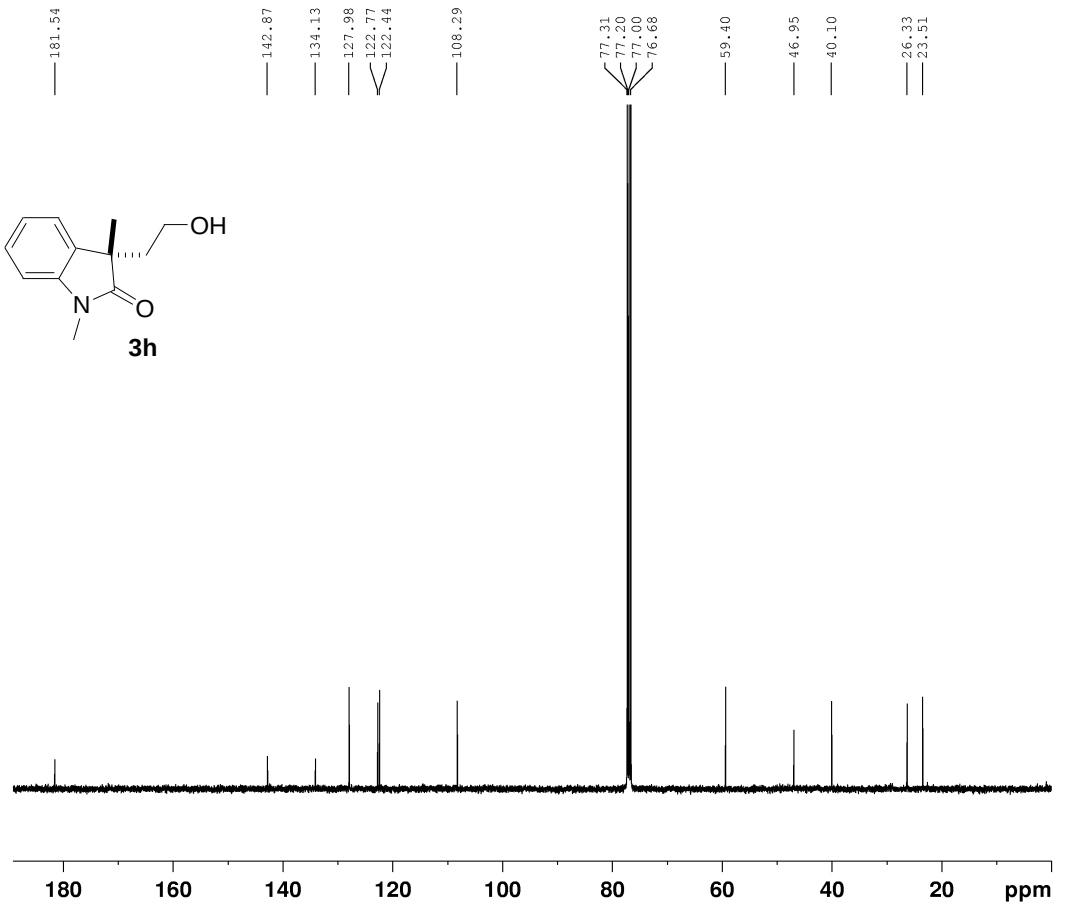

7.299
7.296
7.280
7.277
7.267
7.260
7.248
7.079
7.077
7.060
7.058
7.041
7.039
6.883
6.864
3.231
2.303
2.266
2.143
2.106
1.727
1.338
1.227
1.209
1.193
1.174
1.155
1.136
1.117
1.101
1.083
HO
N
O
3g
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.23
0.98
0.96
2.99
2.08
3.06
2.10
3.00
3.00


181.57
142.75
134.04
127.93
123.07
122.40
108.46
77.32
77.00
76.68
72.92
47.68
46.68
35.21
27.53
27.07
26.37
8.23
HO
N
O
3g
180 160 140 120 100 80 60 40 20 ppm

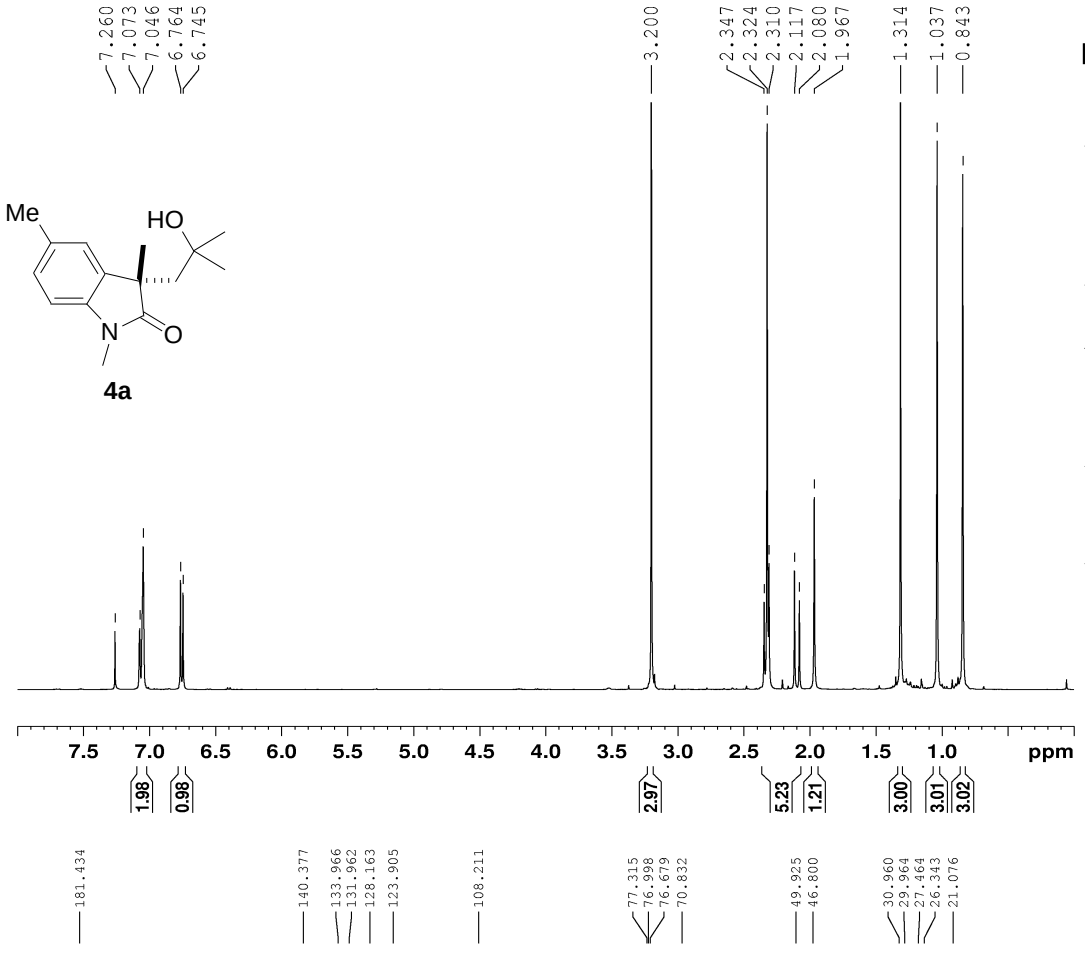

7.296
7.293
7.277
7.274
7.260
7.255
7.219
7.218
7.201
7.076
7.074
7.057
7.055
7.038
7.036
6.879
6.860
3.237
1.417
1.401
1.398
1.383
1.364
1.357
1.342
1.334
1.320
1.303
1.285
1.267
1.249
1.244
1.220
3g'
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.19
0.97
1.01
1.00
3.11
2.18
6.77
3.21
3.00

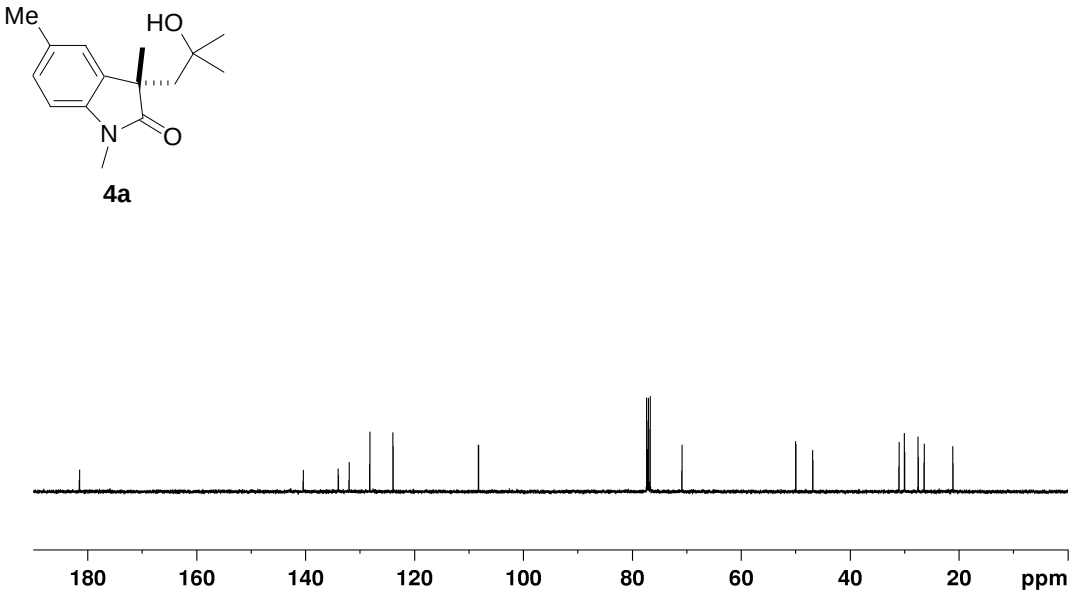

181.981
142.869
134.420
127.791
123.029
122.280
108.427
77.319
77.204
77.001
76.684
72.705
48.343
46.567
37.481
27.541
26.377
25.919
8.097
3g'
180 160 140 120 100 80 60 40 20 ppm

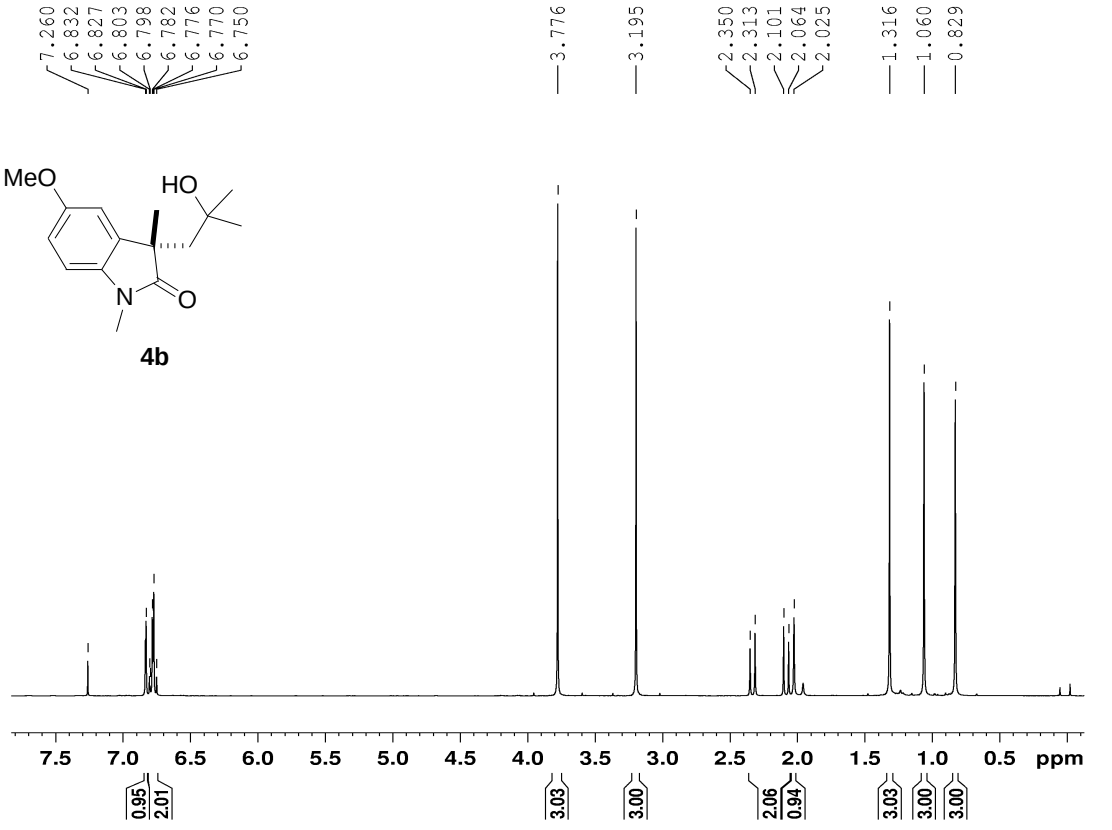

7.300
7.283
7.280
7.264
7.260
7.184
7.182
7.165
7.163
7.101
7.099
7.082
7.080
7.063
7.061
6.871
6.851
3.685
3.673
3.660
3.657
3.643
3.472
3.459
3.221
2.347
2.185
2.172
2.168
2.155
2.149
2.136
2.133
2.120
2.017
2.003
1.999
1.985
1.981
1.967
1.963
1.950
1.409
OH
N
O
3h
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.69
0.96
0.98
0.96
1.03
1.04
3.00
0.97
1.08
1.19
3.07


181.54
142.87
134.13
127.98
122.77
122.44
108.29
77.31
77.20
77.00
76.68
59.40
46.95
40.10
26.33
23.51
OH
N
O
3h
180 160 140 120 100 80 60 40 20 ppm

^{1}H NMR and ^{13}C NMR Spectra of the Products 4



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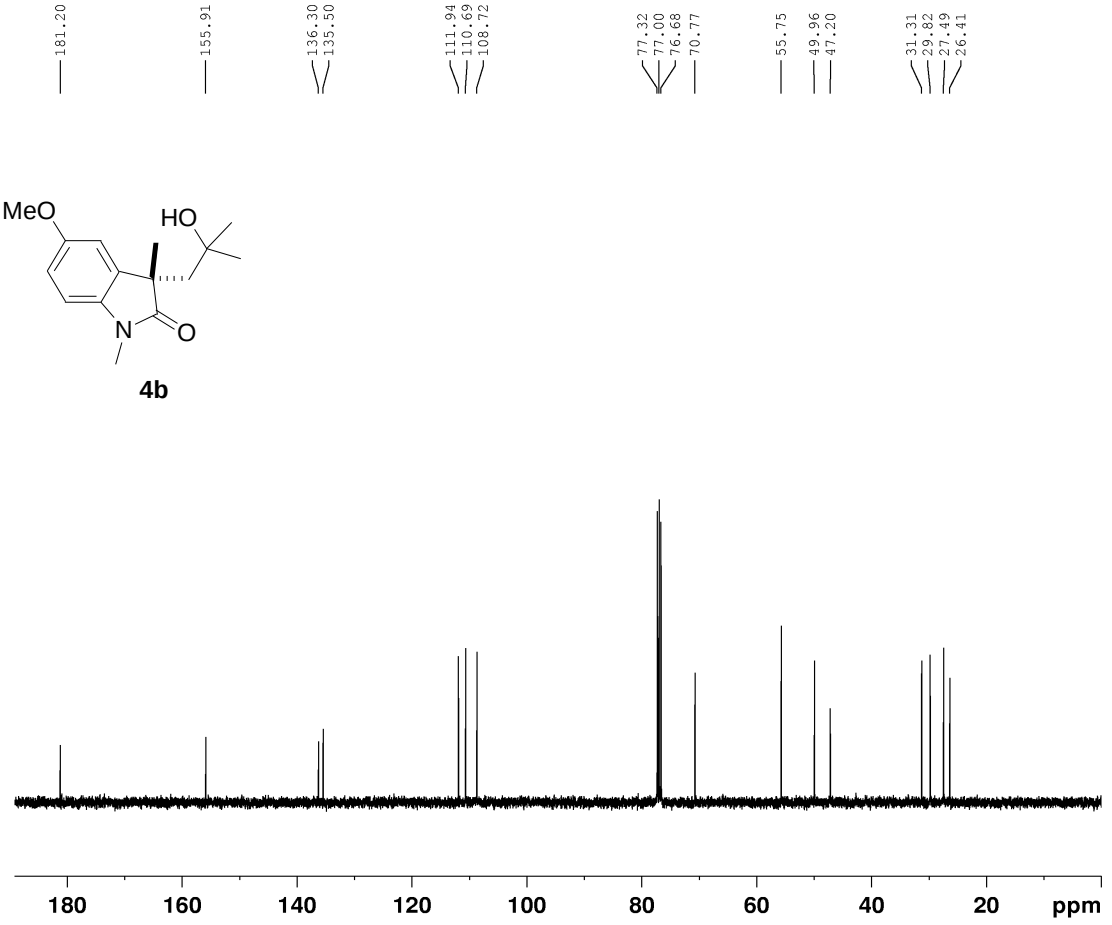
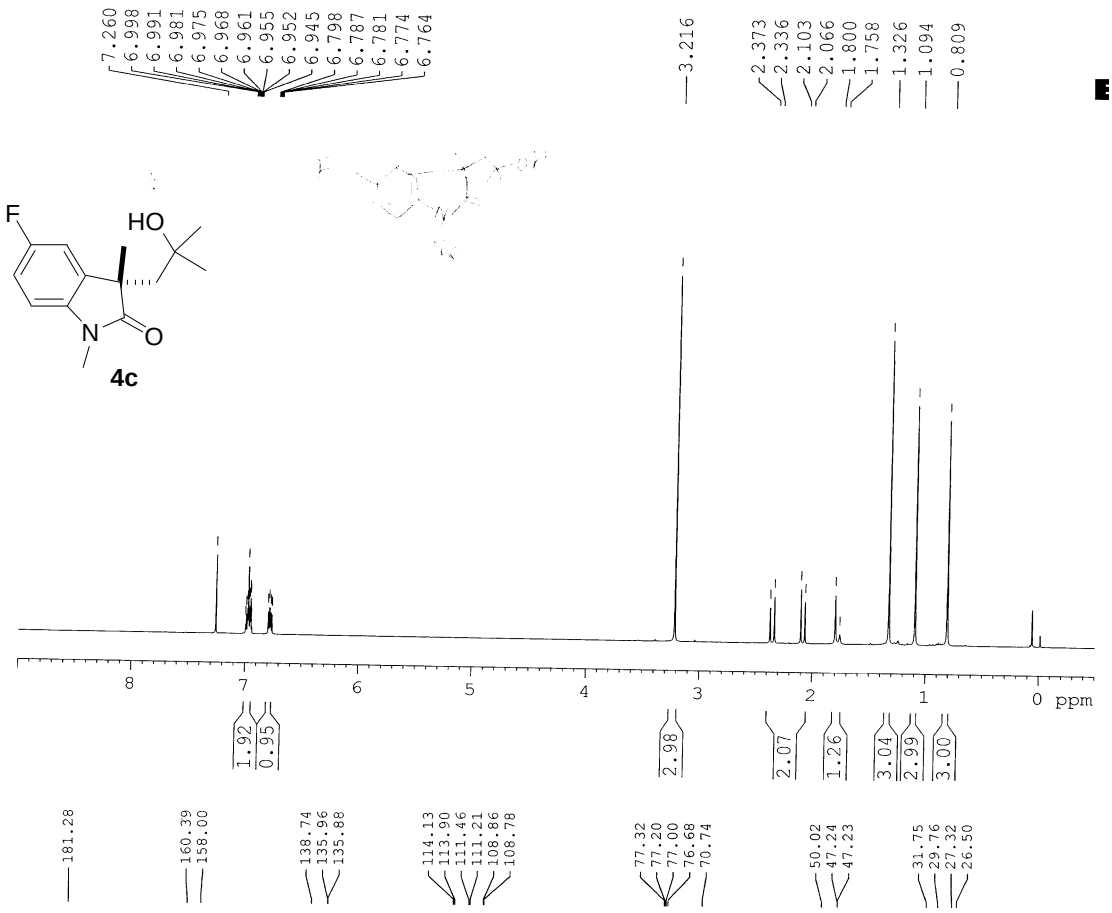
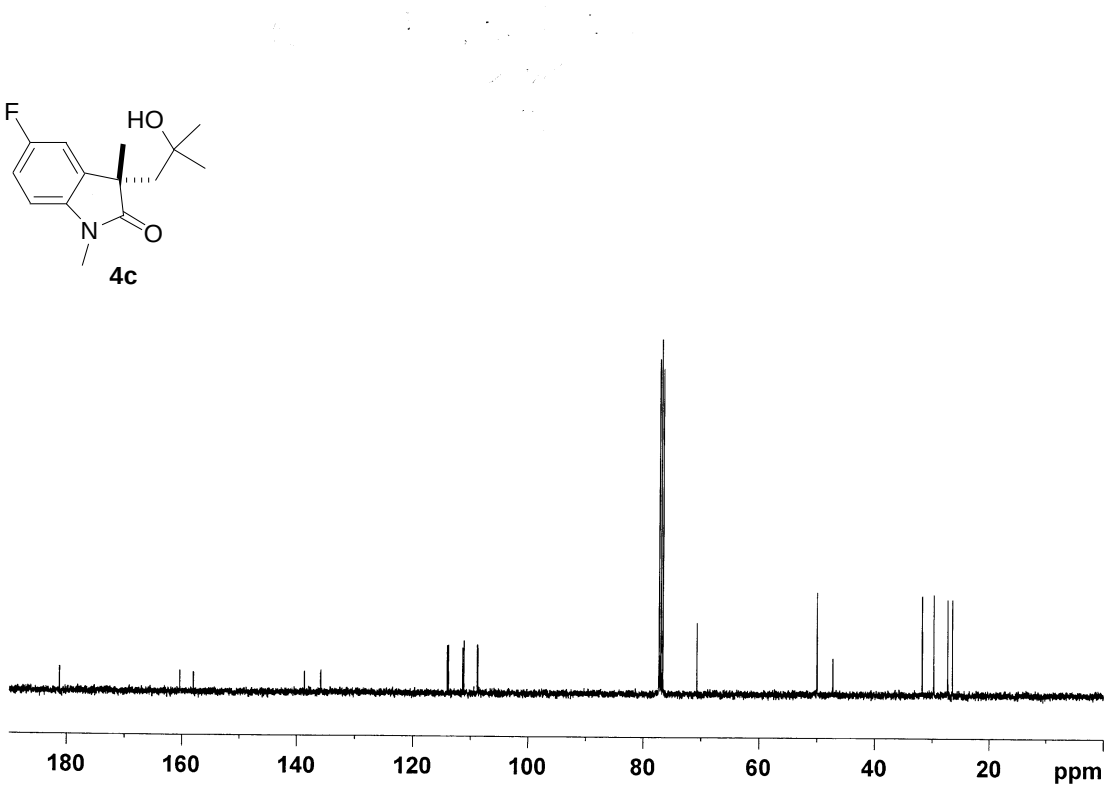
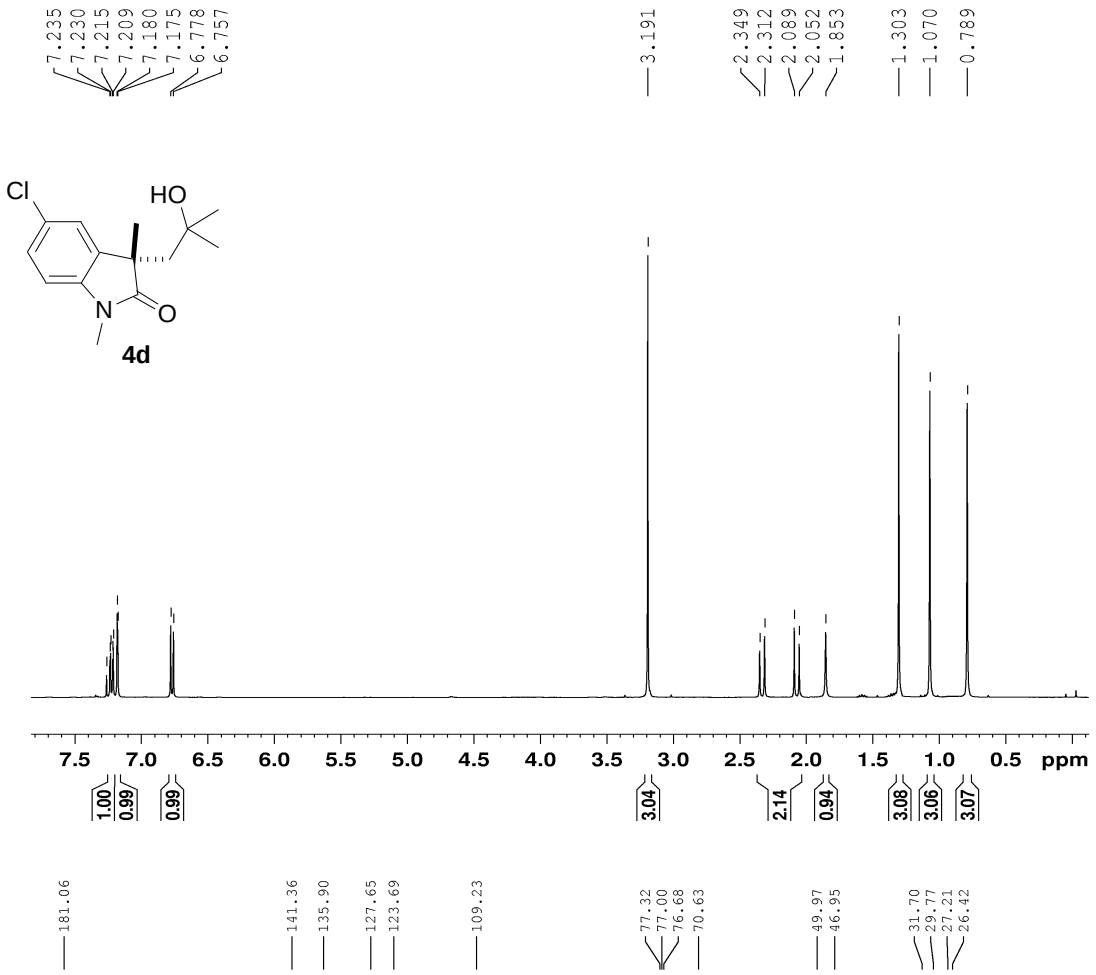
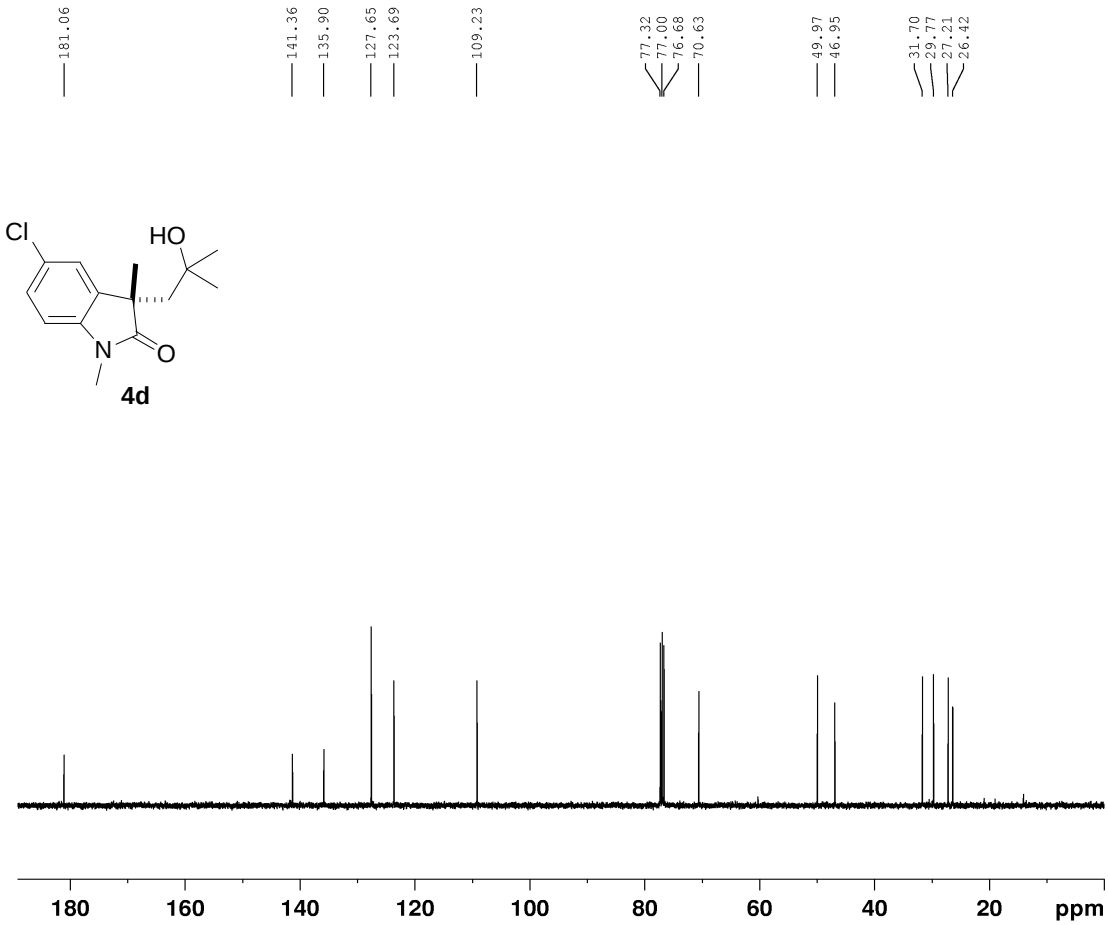
6.832
6.827
6.803
6.798
6.782
6.776
6.770
6.750
3.776
3.195
2.350
2.313
2.101
2.064
2.025
1.316
1.060
0.829
MeO
HO
N
O
4b
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.95
2.01
3.03
3.00
2.06
0.94
3.03
3.00
3.00

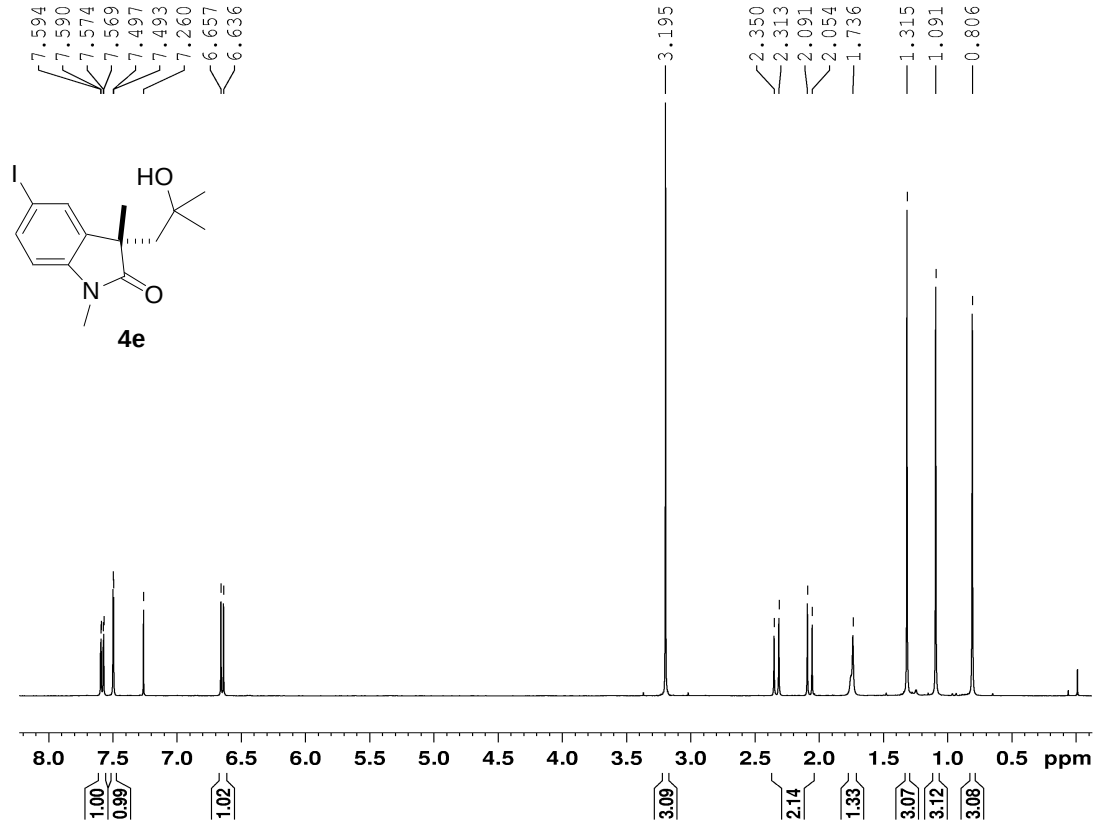

181.20
155.91
136.30
135.50
111.94
110.69
108.72
77.32
77.00
76.68
70.77
55.75
49.96
47.20
31.31
29.82
27.49
26.41
MeO
HO
N
O
4b
180
160
140
120
100
80
60
40
20
ppm


7.260
6.998
6.991
6.981
6.975
6.968
6.961
6.955
6.952
6.945
6.798
6.787
6.781
6.774
6.764
3.216
2.373
2.336
2.103
2.066
1.800
1.758
1.326
1.094
0.809
F
HO
N
O
4c
8
7
6
5
4
3
2
1
0 ppm
1.92
0.95
2.98
2.07
1.26
3.04
2.99
3.00


181.28
160.39
158.00
138.74
135.96
135.88
114.13
113.90
111.46
111.21
108.86
108.78
77.32
77.20
77.00
76.68
70.74
50.02
47.24
47.23
31.75
29.76
27.32
26.50
F
HO
N
O
4c
180
160
140
120
100
80
60
40
20
ppm


7.235
7.230
7.215
7.209
7.180
7.175
6.778
6.757
3.191
2.349
2.312
2.089
2.052
1.853
1.303
1.070
0.789
Cl
HO
N
O
4d
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.99
0.99
3.04
2.14
0.94
3.08
3.06
3.07


181.06
141.36
135.90
127.65
123.69
109.23
77.32
77.00
76.68
70.63
49.97
46.95
31.70
29.77
27.21
26.42
Cl
HO
N
O
4d
180
160
140
120
100
80
60
40
20
ppm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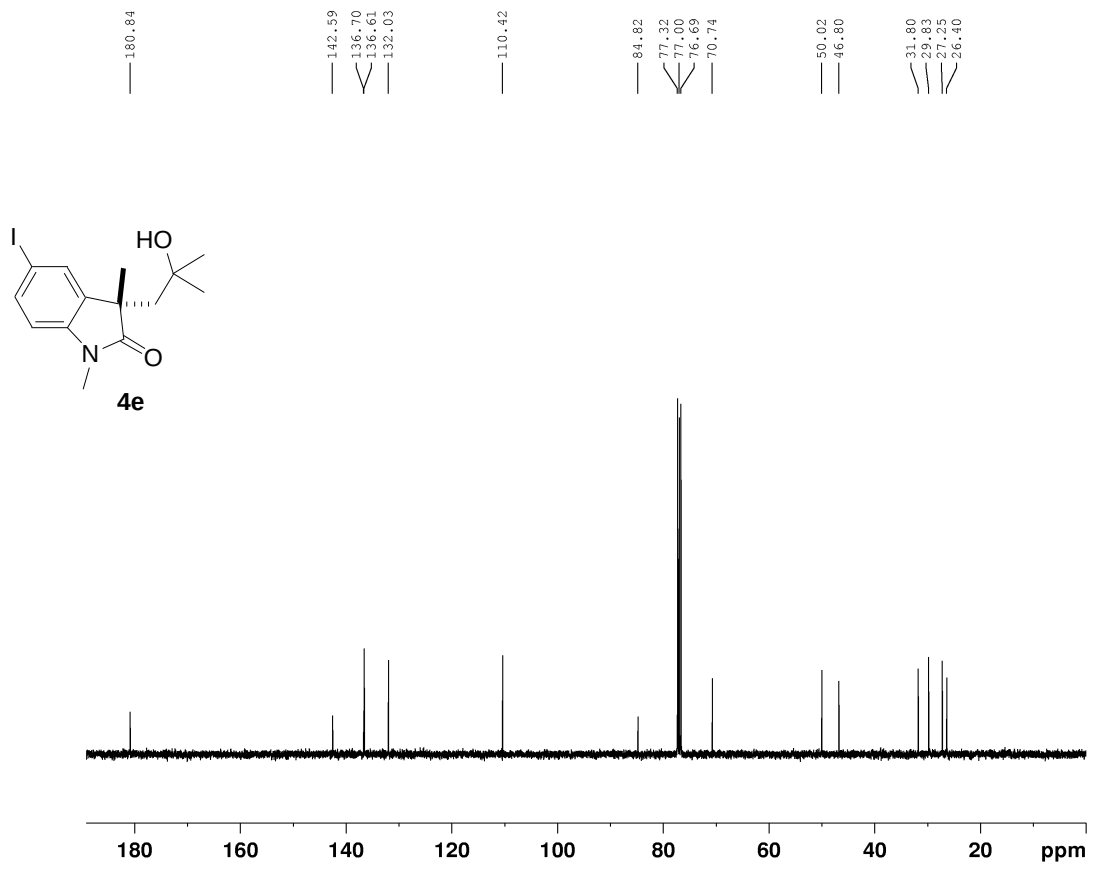
7.590
7.574
7.569
7.497
7.493
7.260
6.657
6.636
3.195
2.350
2.313
2.091
2.054
1.736
1.315
1.091
0.806
I
HO
N
O
4e
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.99
1.02
3.09
2.14
1.33
3.07
3.12
3.08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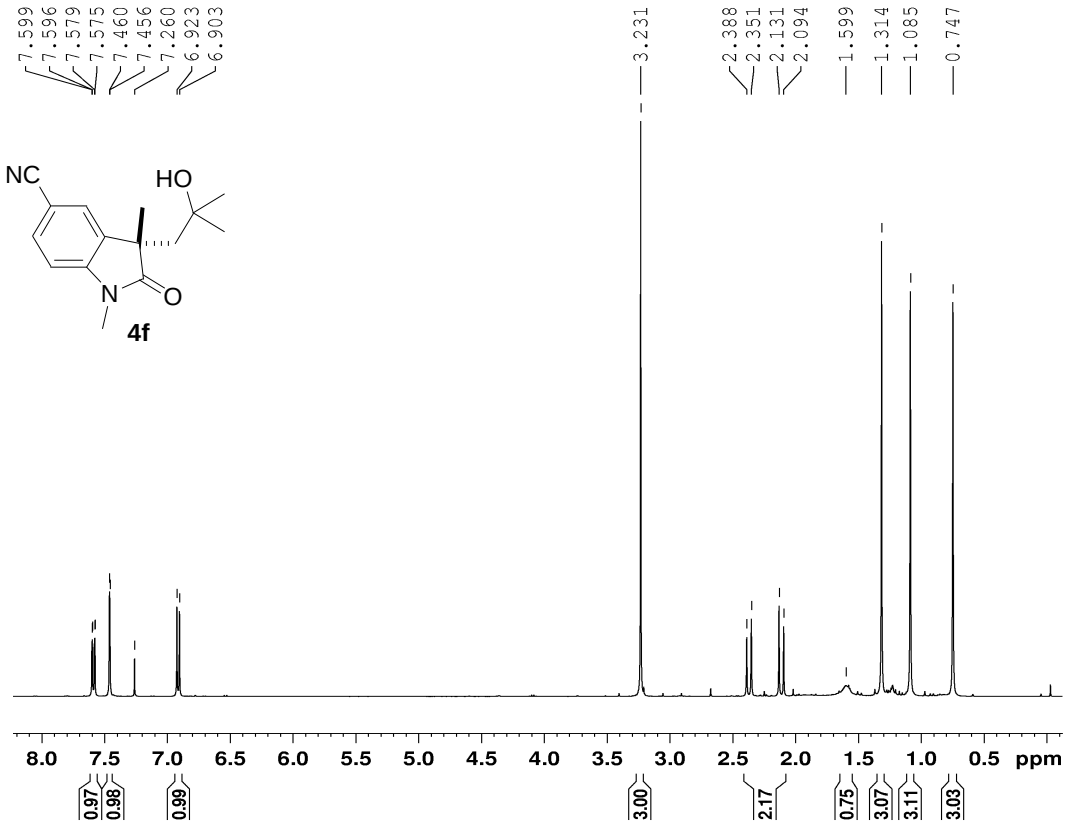
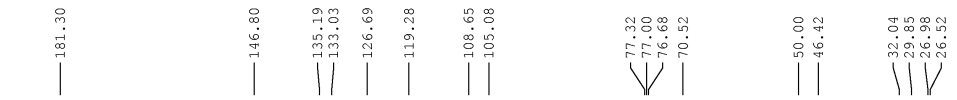
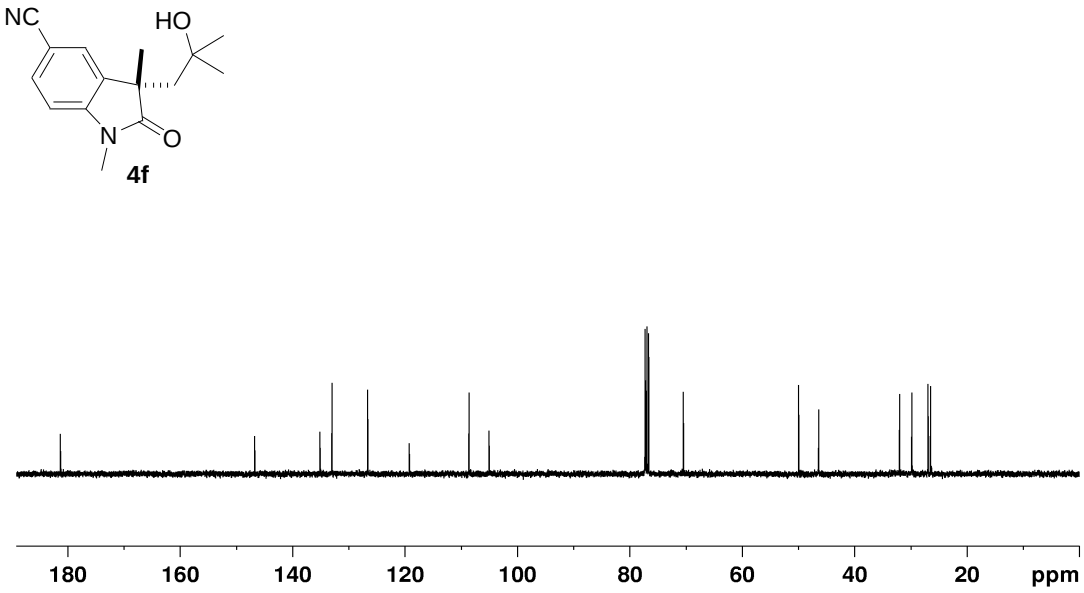
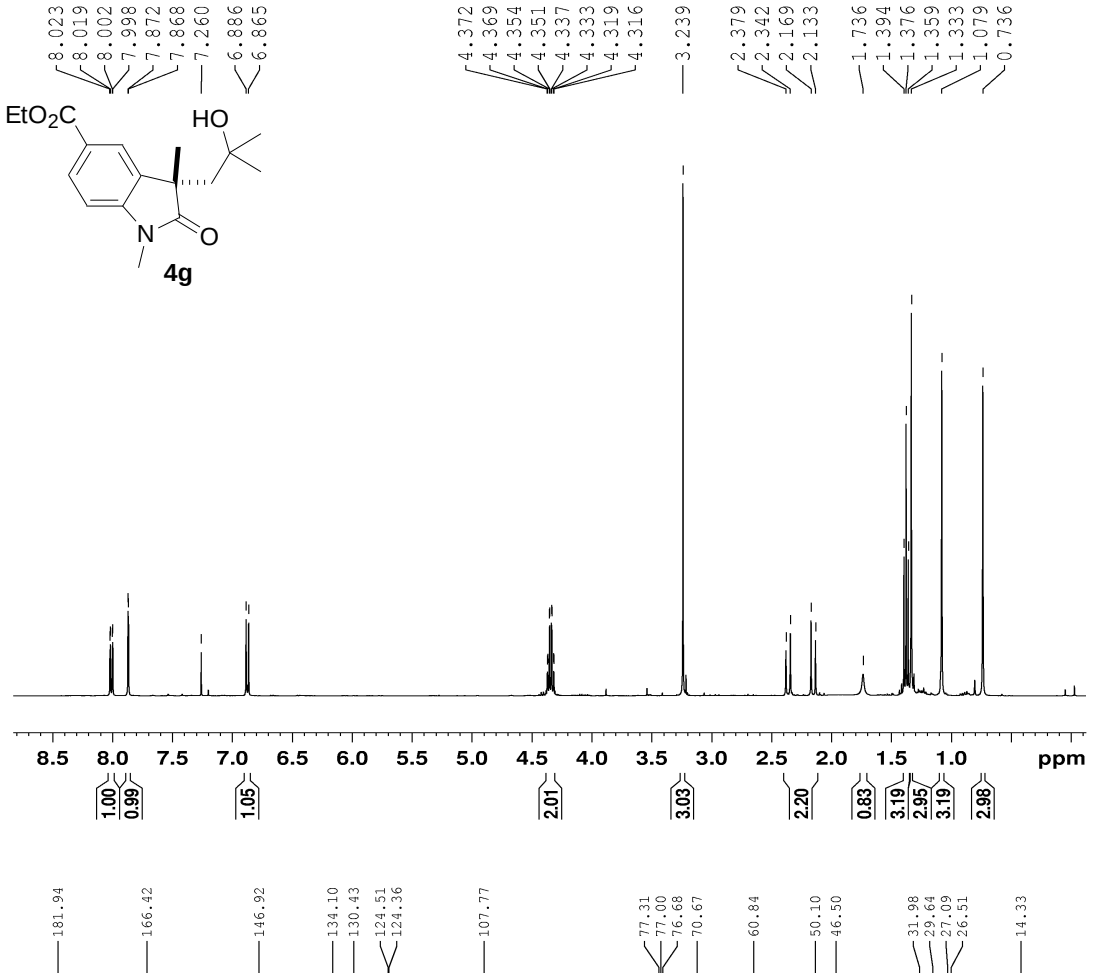
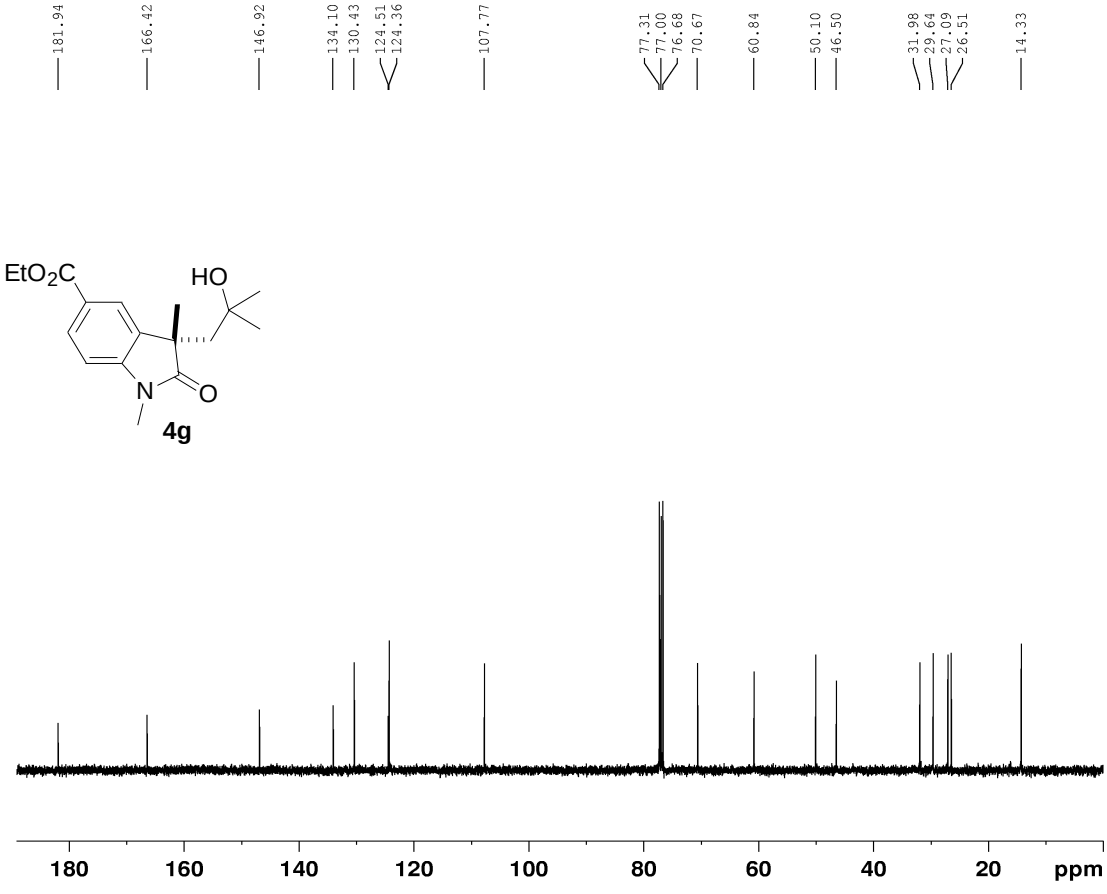
142.59
136.70
136.61
132.03
110.42
84.82
77.32
77.00
76.69
70.74
50.02
46.80
31.80
29.83
27.25
26.40
I
HO
N
O
4e
180
160
140
120
100
80
60
40
20
ppm


7.599
7.596
7.579
7.575
7.460
7.456
7.260
6.923
6.903
3.231
2.388
2.351
2.131
2.094
1.599
1.314
1.085
0.747
NC
HO
N
O
4f
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.97
0.98
0.99
3.00
2.17
0.75
3.07
3.11
3.03


181.30
146.80
135.19
133.03
126.69
119.28
108.65
105.08
77.32
77.00
76.68
70.52
50.00
46.42
32.04
29.85
26.98
26.32


NC
HO
N
O
4f
180
160
140
120
100
80
60
40
20
ppm


8.023
8.019
8.002
7.998
7.872
7.868
7.260
6.886
6.865
4.372
4.369
4.354
4.351
4.337
4.333
4.319
4.316
3.239
2.379
2.342
2.169
2.133
1.736
1.394
1.376
1.359
1.333
1.079
0.736
EtO2C
HO
N
O
4g
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
1.00
0.99
1.05
2.01
3.03
2.20
0.83
3.19
2.95
3.19
2.98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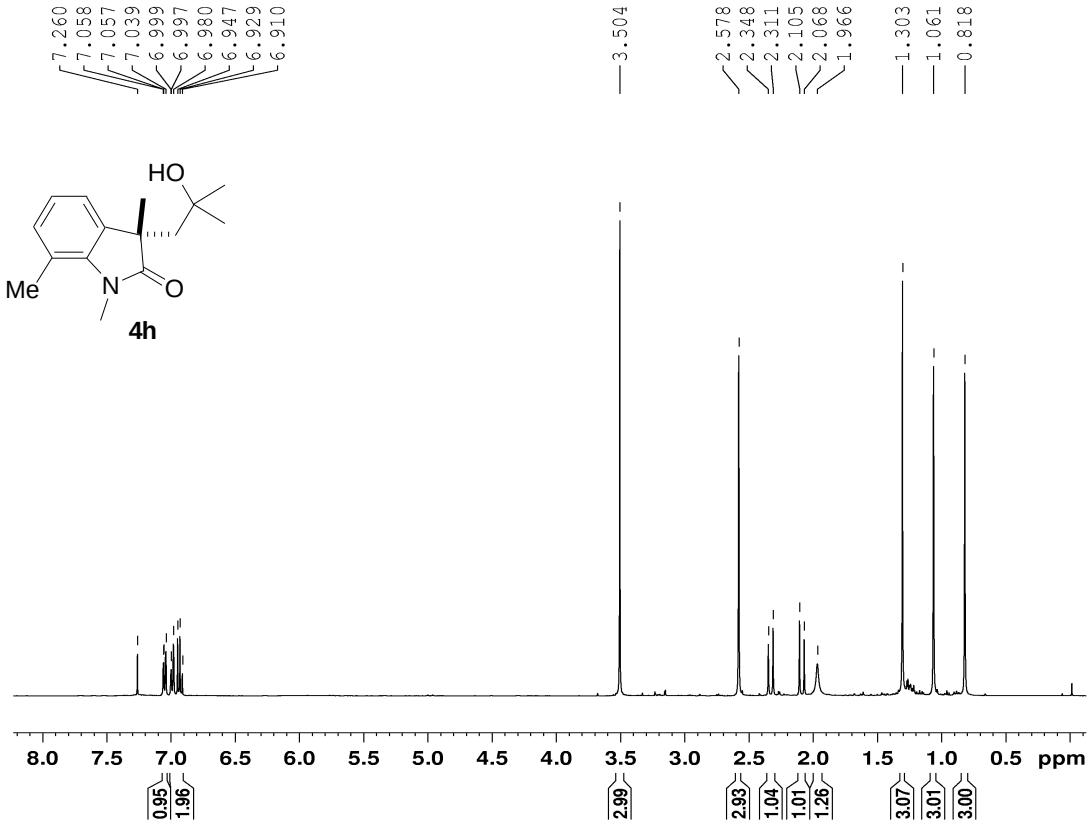
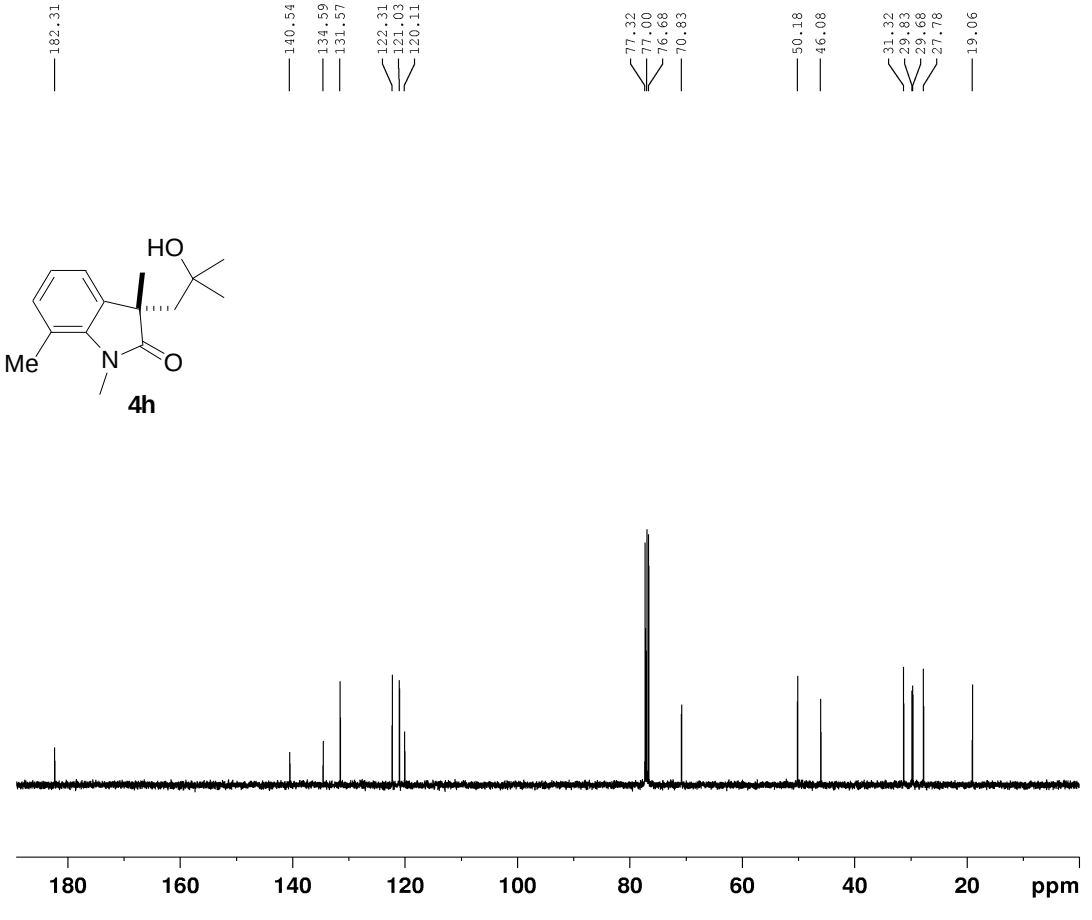
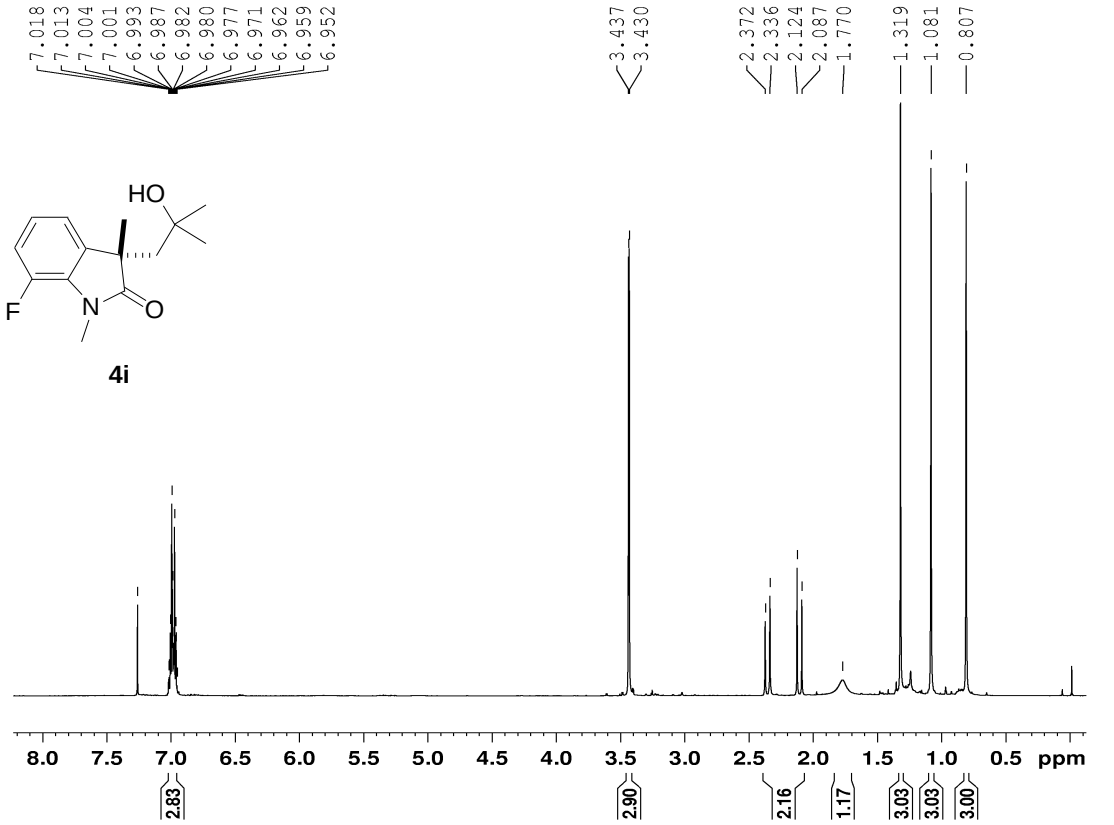
166.42
146.92
134.10
130.43
124.51
124.36
107.77
77.31
77.00
76.68
70.67
60.84
50.10
46.50
31.98
29.64
27.09
26.51
14.33
EtO2C
HO
N
O
4g
180
160
140
120
100
80
60
40
20
ppm



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7.004
7.001
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6.987
6.982
6.980
6.977
6.971
6.962
6.959
6.952
3.437
3.430
2.372
2.336
2.124
2.087
1.770
1.319
1.081
0.807
HO
F
N
O
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
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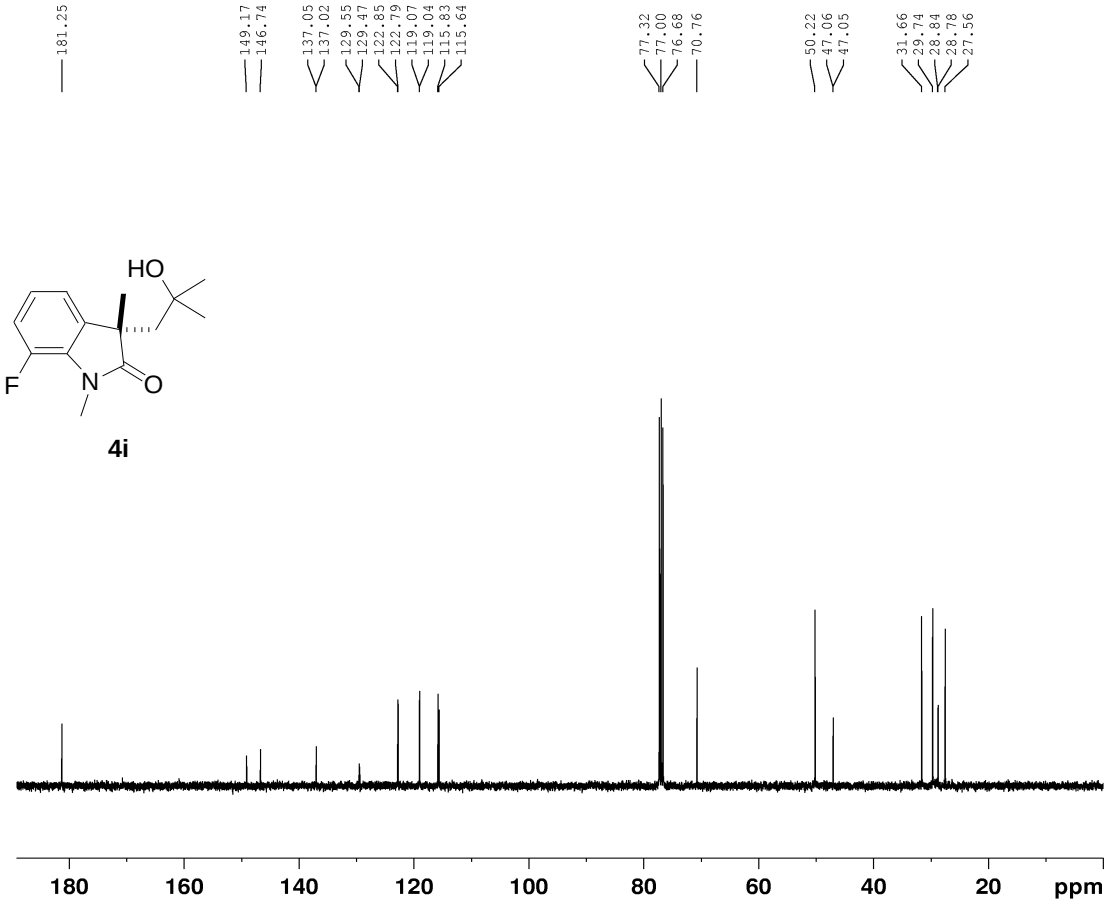
2.90
2.16
1.17
3.03
3.03
3.00

4i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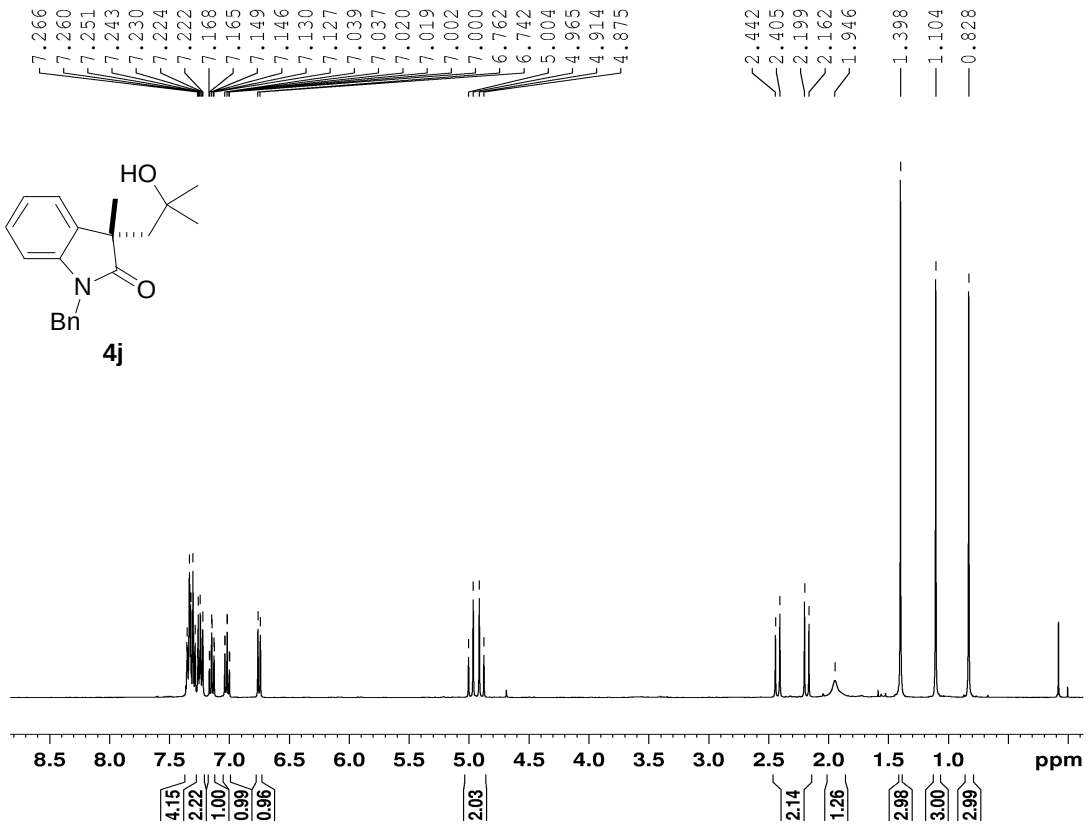
149.17
146.74
137.05
137.02
129.55
129.47
122.85
122.79
119.07
119.04
115.83
115.64
77.32
77.00
76.68
70.76
50.22
47.06
47.05
31.66
29.74
28.84
28.78
27.56
HO
F
N
O
180
160
140
120
100
80
60
40
20
ppm

4i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7.260
7.251
7.243
7.230
7.224
7.222
7.168
7.165
7.149
7.146
7.130
7.127
7.039
7.037
7.020
7.019
7.002
7.000
6.762
6.742
5.004
4.965
4.914
4.875
2.442
2.405
2.199
2.162
1.946
1.398
1.104
0.828
HO
N
O
Bn
4j
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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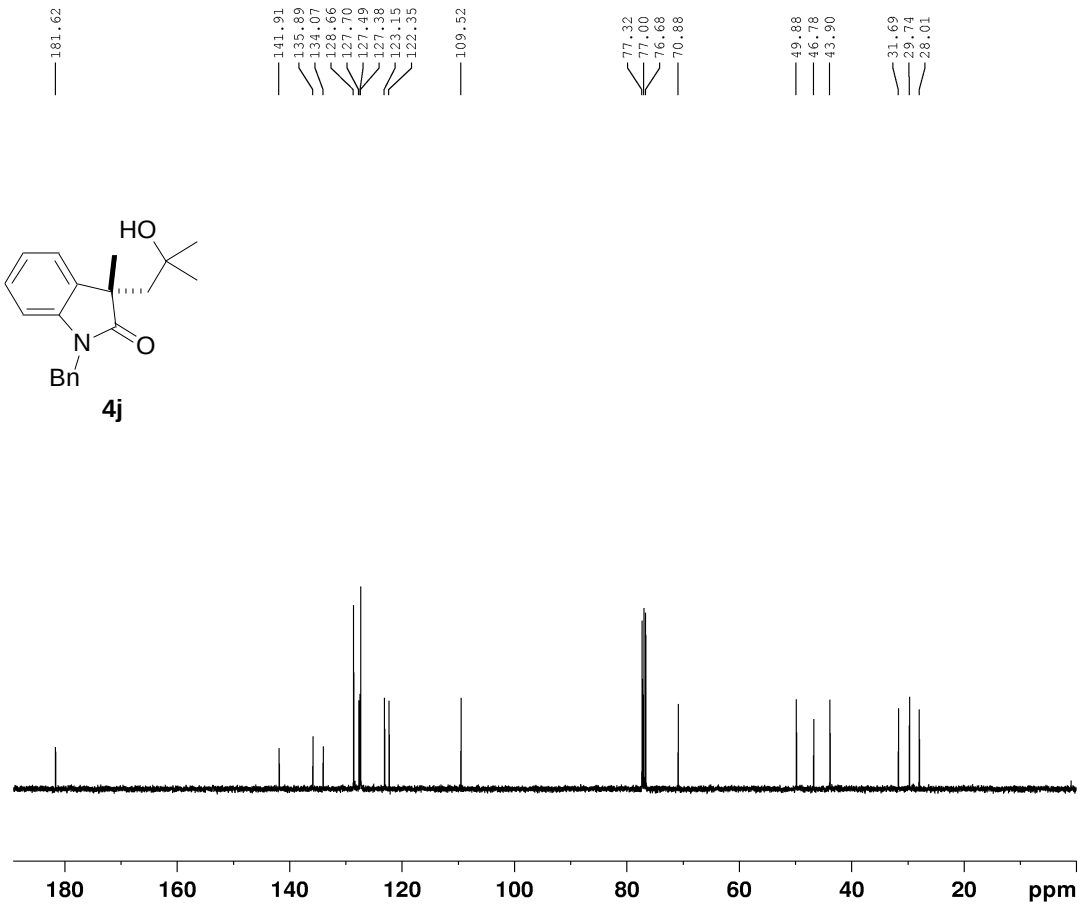
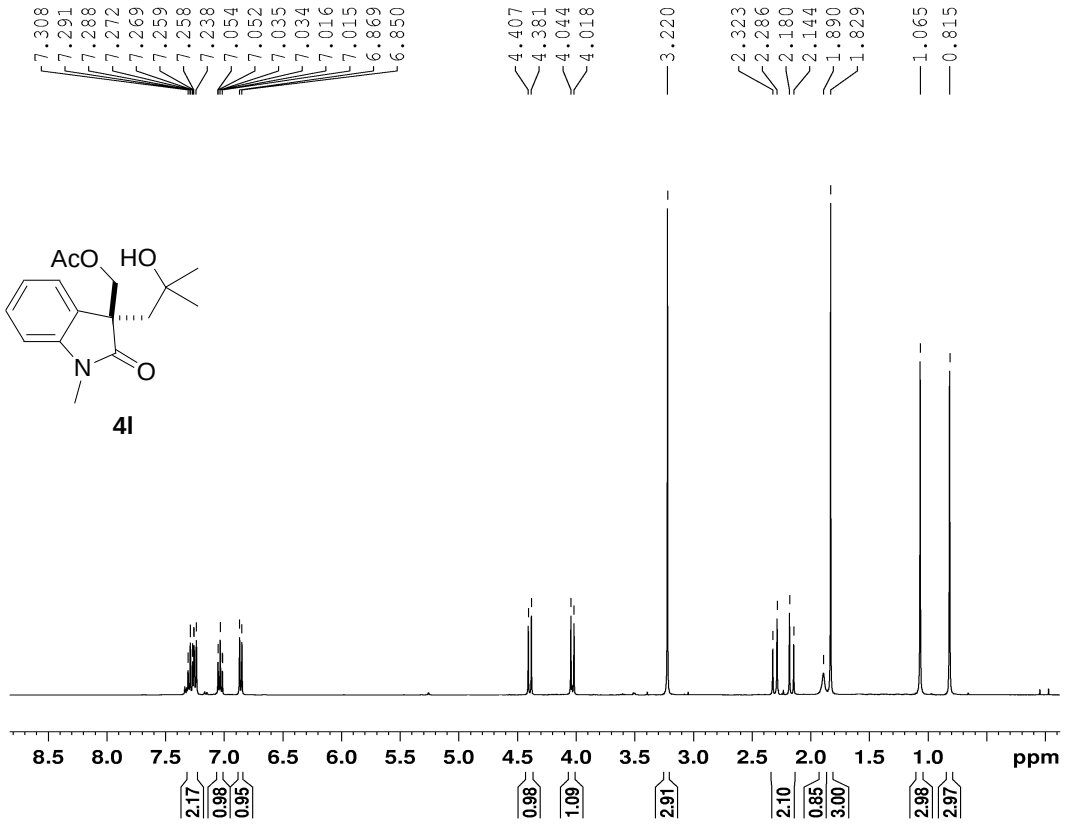
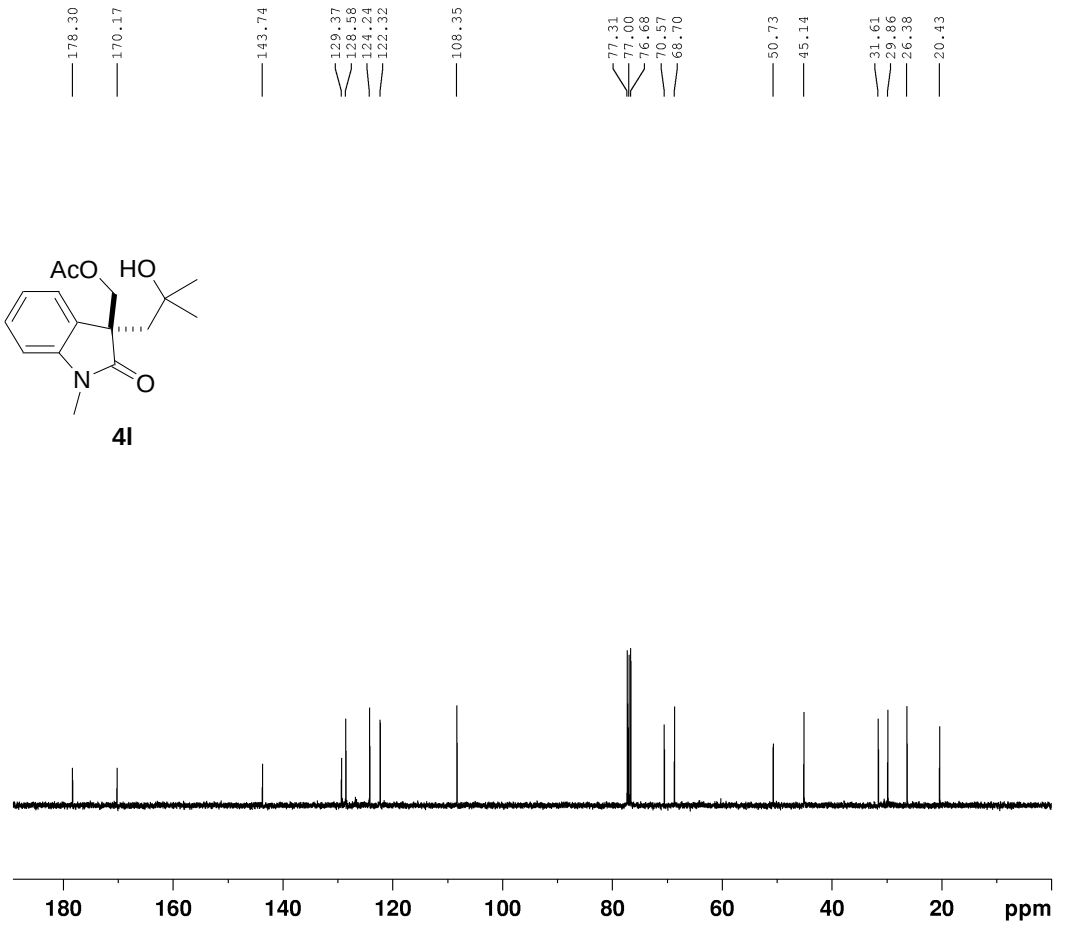
2.22
1.00
0.99
0.96
2.03
2.14
1.26
2.98
3.00
2.99

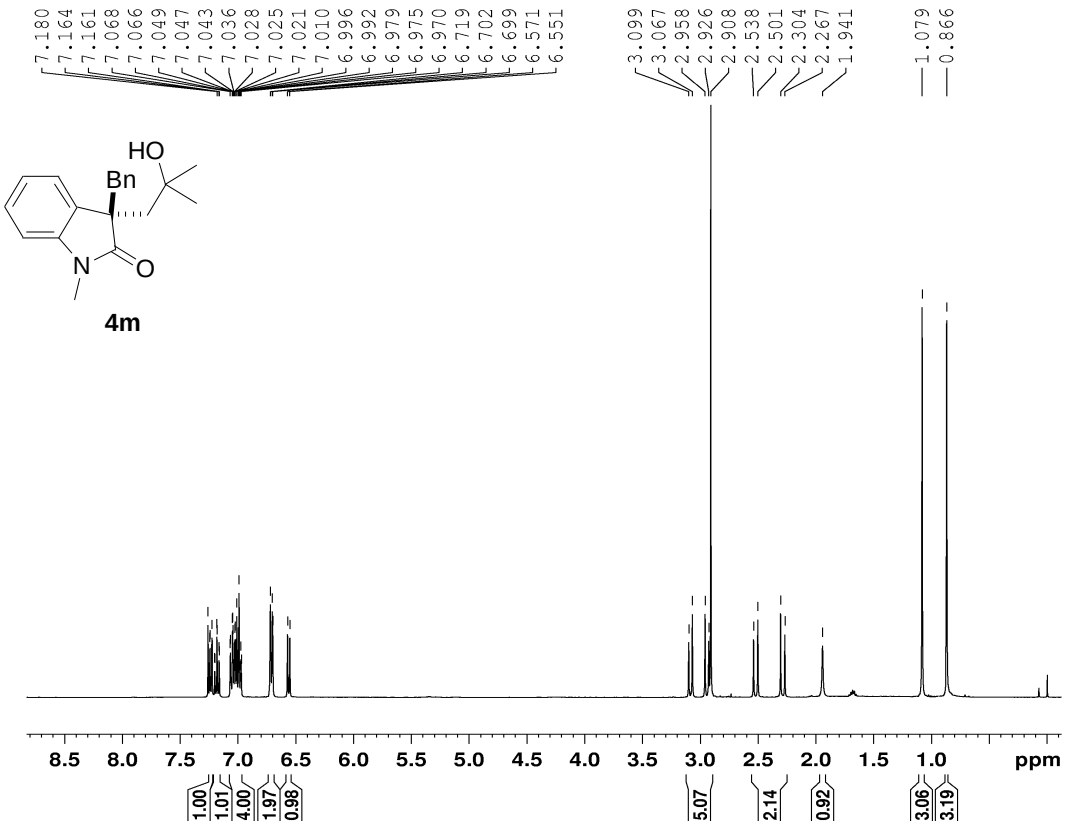

181.62
141.91
135.89
134.07
128.66
127.70
127.49
127.38
123.15
122.35
109.52
77.32
77.00
76.68
70.88
49.88
46.78
43.90
31.69
29.74
28.01
HO
N
O
Bn
4j
180 160 140 120 100 80 60 40 20 ppm


7.308
7.291
7.288
7.272
7.269
7.259
7.258
7.238
7.054
7.052
7.035
7.034
7.016
7.015
6.869
6.850
4.407
4.381
4.044
4.018
3.220
2.323
2.286
2.180
2.144
1.890
1.829
1.065
0.815
AcO
HO
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.17
0.98
0.95
0.98
1.09
2.91
2.10
0.85
3.00
2.98
2.97

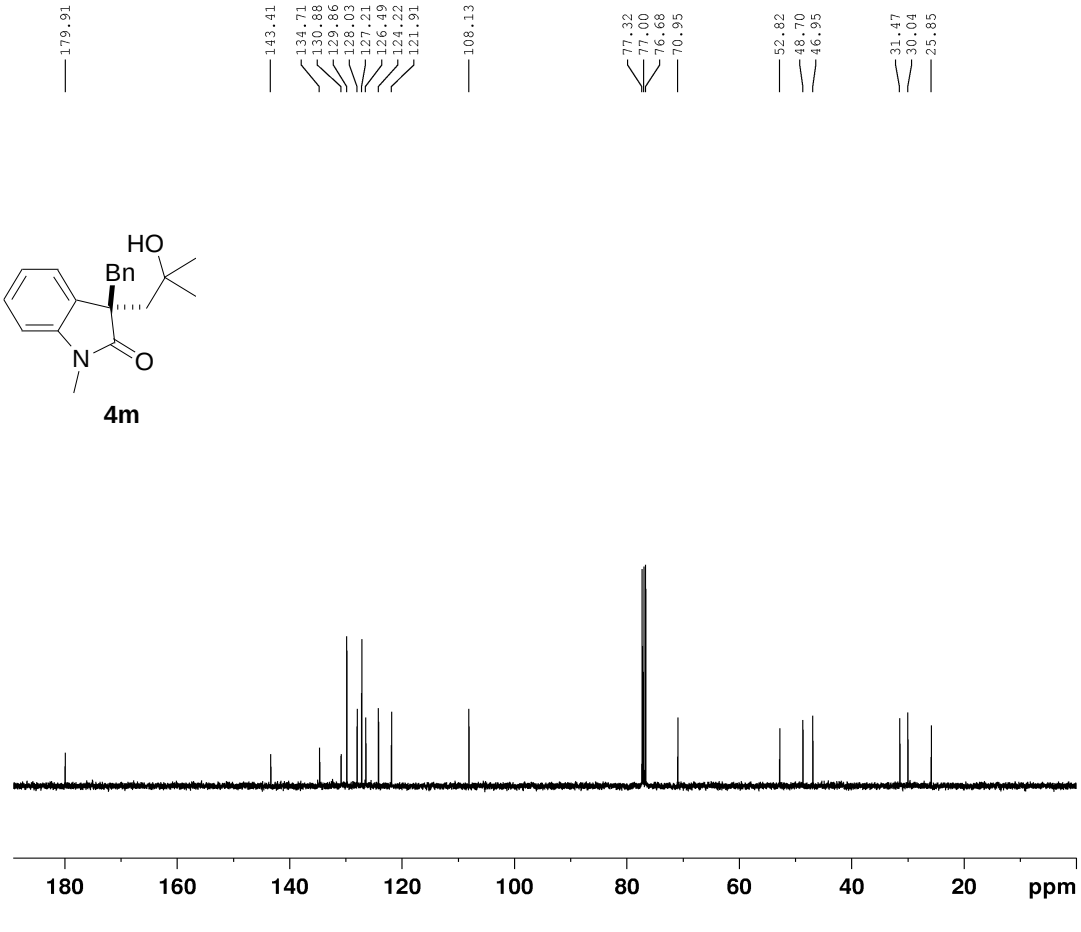
4l


178.30
170.17
143.74
129.37
128.58
124.24
122.32
108.35
77.31
77.00
76.68
70.57
68.70
50.73
45.14
31.61
29.86
26.38
20.43
AcO
HO
N
O
180 160 140 120 100 80 60 40 20 ppm

4l


7.180
7.164
7.161
7.068
7.066
7.049
7.047
7.043
7.036
7.028
7.025
7.021
7.010
6.996
6.992
6.979
6.975
6.970
6.719
6.702
6.699
6.571
6.551
3.099
3.067
2.958
2.926
2.908
2.538
2.501
2.304
2.267
1.941
1.079
0.866
HO
Bn
N
O
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00 1.01 4.00 1.97 0.98 5.07 2.14 0.92 3.06 3.19

4m


179.91
143.41
134.71
130.88
129.86
128.03
127.21
126.49
124.22
121.91
108.13
77.32
77.00
76.68
70.95
52.82
48.70
46.95
31.47
30.04
25.85
HO
Bn
N
O
180 160 140 120 100 80 60 40 20 ppm

4m