Electronic Supplementary Information

Access to 3,3-Disubstituted Oxindoles via Microwave-Assisted Cannizzaro and Aldol Reactions of Formaldehyde with Isatins and their Imines

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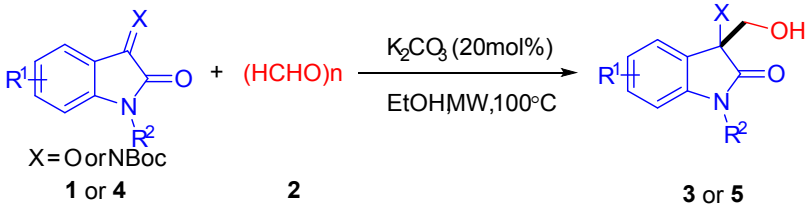
1. General Information

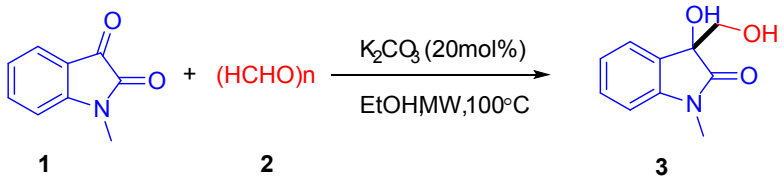
Commercially available materials purchased from Alfa Aesar or Aldrich was used as received. Proton nuclear magnetic resonance (^{1}H NMR; 400 MHz) spectra were recorded on a Bruker Avance 400 spectrometer. Chemical shifts were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). ^{1}H NMR splitting patterns were designated as singlet (s), doublet (d), triplet (t), quartet (q), dd (doublet of doublets); m (multiplets), and etc. All first order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted are designated as multiplet (m) or broad (br). Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruke AV400 (400 MHz) (100 MHz) spectrometer. High resolution mass spectral analysis (HRMS) was performed on Waters Q-tof Premier mass spectrometer. High-resolution mass spectra were obtained with a Finnigan MAT 95 XP mass spectrometer (Thermo Electron Corporation). Flash chromatography was performed using Merck silica gel 60 with distilled solvents. Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp.

2. Procedure for K_2CO_3 catalyzed Cannizzaro reaction between Isatins/Isatinketoimines and Formaldehyde



All substituted isatin and isatinketoimine substrates were synthesized according to literatures.[1-3] A standard microwave reaction vessel was charged with paraformaldehyde **2** (3.0 mmol, 15 equiv.), isatins/isatinketoimines **1** or **4** (0.2 mmol, 1 equiv.) and base K_2CO_3 (0.04 mmol, 20 mol%). Solvent EtOH (1.5 mL) was added and then the reaction mixture was placed in an was irradiated in a focused MW reactor (Discover by CEM Corporation, Matthews, NC) at 100 °C for 15 mins. After cooling to room temperature, the reaction mixture was directly evaporated and purified by column chromatography and gave the expected product **3** or **5**.

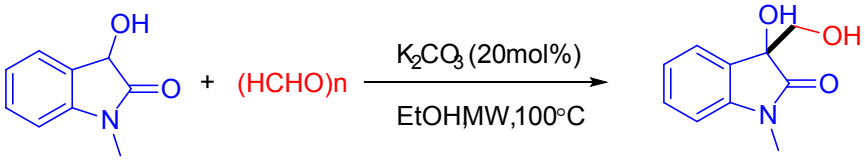
3. Gram-scale reaction between Isatin and Formaldehyde



1 2 3

A standard microwave reaction vessel was charged with paraformaldehyde **2** (2.79 g, 93.1 mmol, 15 equiv.), isatin **1** (1.0 g, 6.2 mmol, 1 equiv.) and base K_2CO_3 (172 mg, 1.24 mmol, 20 mol%). Solvent EtOH (20 mL) was added and then the reaction mixture was placed in an was irradiated in a focused microwave reactor at 100 °C for 1 hour. After cooling to room temperature, the reaction mixture was directly evaporated and purified by column chromatography and gave the expected product 66% yield (792 mg).

4. Control experiment

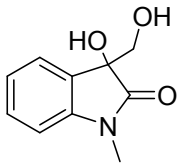


6 2 3

3-hydroxy-1-methylindolin-2-one was synthesized according to literatures.[4] A standard microwave reaction vessel was charged with paraformaldehyde **2** (2.0 mmol, 10 equiv.), 3-hydroxy-1-methylindolin-2-one **6** (0.2 mmol, 1 equiv.) and base K_2CO_3 (20 mol%). Solvent EtOH (1.5 mL) was added and then the reaction mixture was placed in an was irradiated in a focused MW reactor at 100 °C for 15 mins. After cooling to room temperature, the reaction mixture was directly evaporated and purified by column chromatography and gave the expected product **3** 90% yield.

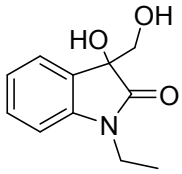
Reference

1. Calí, P.; Begtrup, M. *Synthesis* **2002**, *2002*, 63-66.
2. Lv, H.; Tiwari, B.; Mo, J.; Xing, C.; Chi, Y. R. *Organic Letters* **2012**，*14*， 5412-5415
3. Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R. *Organic Letters* **2012**, *14*, 2512-2515.
4. Trost, B. M.; Hirano, K. *Organic Letters* **2012**, *14*, 2446-2449.



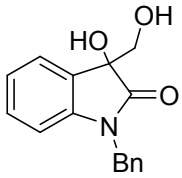
3a

1-Methyl-3-hydroxy-3-(hydroxymethyl)-oxindole 3a: The title compound was prepared according to general procedure. Colorless solid, 92% yield; ^{1}H NMR (Acetone-d_6, 400 MHz) δ 3.13 (s, 3 H), 3.78-3.87 (m, 2H), 3.94 (s, 1H), 4.92 (s, 1H), 6.93 (d, J = 8.0 Hz, 1H), 7.05 (t, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.41 (d, J = 7.9 Hz, 1H); ^{13}C NMR (Acetone-d_6, 100 MHz): δ 26.1, 67.1, 77.0, 108.8, 123.0, 125.1, 130.2, 130.9, 145.5, 177.5; HRMS (ESI) calcd. for $C_{10}H_{12}NO_3$ (M+H) $^{+}$: 194.0817 Found: 194.0819.



3b

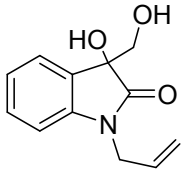
1-Ethyl-3-hydroxy-3-(hydroxymethyl)-oxindole 3b: The title compound was prepared according to general procedure. White solid, 83% yield; ^{1}H NMR (Acetone-d_6, 400 MHz) δ 1.18 (t, J = 9.6 Hz, 3H), 3.13 (q, J = 9.6 Hz, 2H), 3.77-3.88 (m, 2H), 3.93 (br s, 1H), 4.94 (s, 1H), 6.97 (d, J = 10.4 Hz, 1H), 7.03 (t, J = 10.0 Hz, 1H), 7.28-7.33 (m, 1H), 7.41 (d, J = 10.0 Hz, 1H); ^{13}C NMR (Acetone-d_6, 100 MHz): δ 12.9, 34.4, 67.1, 77.0, 109.0, 122.8, 125.3, 130.1, 131.2, 144.4, 177.2; HRMS (ESI) calcd. for $C_{11}H_{14}NO_3$ (M+H) $^{+}$: 208.0974 Found: 208.0974.



3c

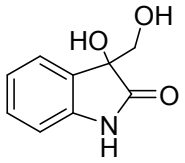
1-Benzyl-3-hydroxy-3-(hydroxymethyl)-oxindole 3c: The title compound was prepared according to general procedure. White solid, 94% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.90-3.96 (m, 2H), 4.01 (br s, 1H), 4.82 (d, J = 16 Hz, 1H), 5.01 (d, J = 16 Hz, 1H), 5.08 (br s, 1H), 6.76 (d, J = 8.0 Hz, 1H), 7.00-7.04 (m, 1H), 7.17-7.32 (m, 4H), 7.38-7.43 (m, 3H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 42.8, 66.3, 76.3, 108.9, 122.2, 124.3, 127.1,

127.2, 128.5, 129.1, 130.2, 136.5, 143.6, 177.0; HRMS (ESI) calcd. for $C_{16}H_{16}NO_3$ $(M+H)^+$: 270.1133 Found: 270.1130.



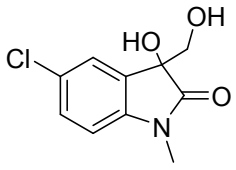
3d

1-Allyl-3-hydroxy-3-(hydroxymethyl)-oxindole 3d: The title compound was prepared according to general procedure. White solid, 84% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.86-3.87 (m, 1H), 3.91-3.94 (m, 1H), 4.16 (br s, 1H), 4.22-4.28 (m, 1H), 4.34-4.40 (m, 1H), 5.14 (dd, *J* = 10.4, 3.2 Hz, 1H), 5.21-5.27 (m, 2H), 5.80-5.87 (m, 1H), 6.85 (d, *J* = 8.4 Hz, 1H), 7.44-7.46 (m, 1H), 7.55-7.56 (m, 1H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 42.4, 66.9, 77.2, 111.5, 115.1, 117.2, 128.3, 132.3, 132.7, 133.5, 143.9, 176.8; HRMS (ESI) calcd. for $C_{12}H_{14}NO_3$ $(M+H)^+$: 220.0974 Found: 220.0973.



3e

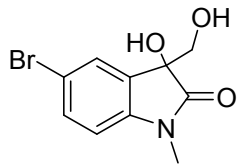
3-Hydroxy-3-hydroxymethyl-oxindole 3e: The title compound was prepared according to general procedure. Colorless solid, 74% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.82-3.88 (m, 2H), 4.00 (s, 1H), 4.96 (s, 1H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.99-7.01 (m, 1H), 7.20-7.23 (m, 1H), 7.38 (d, *J* = 7.2 Hz, 1H), 9.31 (br s, 1H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 67.1, 77.3, 110.4, 122.6, 125.6, 130.0, 131.5, 143.5, 179.4; HRMS (ESI) calcd. for $C_9H_{10}NO_3$ $(M+H)^+$: 180.0661 Found: 180.0661.



3f

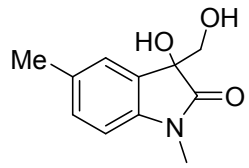
1-Methyl-3-hydroxy-3-(hydroxymethyl)-5-chloro-oxindole 3f: The title compound was prepared according to general procedure. White solid, 77% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.14 (s, 3H), 3.78-3.83 (m, 1H), 3.88-3.92 (m, 1H), 4.09 (br s, 1H), 5.11 (br s, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.41-7.42

(1H, m) ; ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 26.3, 66.9, 77.3, 110.2, 125.5, 129.9, 133.1, 144.3, 177.1; HRMS (ESI) calcd. for $C_{10}H_{11}ClNO_3$ (M+H) $^+$: 228.0427 Found: 228.0424.



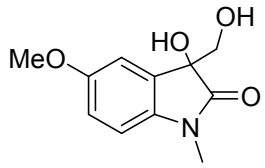
3g

1-Methyl-3-hydroxy-3-(hydroxymethyl)-5-bromo-oxindole 3g: The title compound was prepared according to general procedure. White solid, 76% yield; ^{1}H NMR (MeOD, 400 MHz) δ 3.07 (s, 3H), 3.70 (q, *J* = 10.4 Hz, 2H), 4.74 (s, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.38-7.41 (m, 1H), 7.44-7.45 (m, 1H); ^{13}C NMR (MeOD, 100 MHz): δ 26.5, 66.7, 77.8, 111.4, 116.6, 128.6, 133.5, 133.6, 144.7, 178.8; HRMS (ESI) calcd. for $C_{10}H_{11}BrNO_3$ (M+H) $^+$: 271.9922 Found: 271.9922.



3h

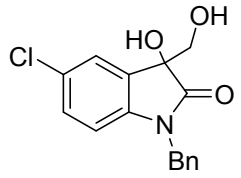
1-Methyl-3-hydroxy-3-(hydroxymethyl)-5-methyl-oxindole 3h: The title compound was prepared according to general procedure. White solid, 81% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 2.31 (s, 3H), 3.10 (s, 3H), 3.78-3.85 (m, 2H), 3.89 (br s, 1H), 4.85 (s, 1H), 6.81 (d, *J* = 8 Hz, 1H), 7.11-7.13 (m, 1H), 7.20-7.37 (m, 1H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 21.1, 26.1, 67.1, 77.1, 108.6, 125.9, 130.3, 130.9, 132.2, 143.1, 177.5; HRMS (ESI) calcd. for $C_{11}H_{14}NO_3$ (M+H) $^+$: 208.0974 Found: 208.0971.



3i

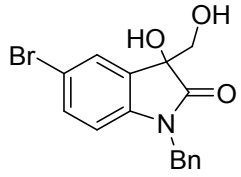
1-Methyl-3-hydroxy-3-(hydroxymethyl)-5-methoxy-oxindole 3i: The title compound was prepared according to general procedure. White solid, 88% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.10 (s, 3H), 3.78-3.89 (m, 5H), 3.97 (br s, 1H), 4.96 (s, 1H), 6.83-6.89 (m, 2H), 7.06-7.07 (m, 1H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 26.2, 56.03,

67.1, 77.4, 109.2, 112.6, 114.3, 132.2, 138.7, 156.9, 177.3; HRMS (ESI) calcd. for $C_{11}H_{14}NO_4$ $(M+H)^+$: 224.0923 Found: 224.0925.



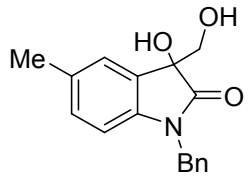
3j

1-Benzyl-3-hydroxy-3-(hydroxymethyl)-5-chloro-oxindole 3j: The title compound was prepared according to general procedure. White solid, 84% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.90-4.00 (m, 2H), 4.24 (br s, 1H), 4.83 (d, *J* = 16 Hz, 1H), 5.01 (d, *J* = 16 Hz, 1H), 5.29 (s, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 7.21-7.32 (m, 4H), 7.17-7.32 (m, 4H), 7.36-7.38 (m, 2H), 7.43-7.44 (m, 1H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 43.8, 67.0, 77.4, 111.1, 125.6, 128.1, 128.3, 129.5, 129.8, 133.3, 137.0, 143.4, 177.5; HRMS (ESI) calcd. for $C_{16}H_{15}ClNO_3$ $(M+H)^+$: 304.0740 Found: 304.0739.



3k

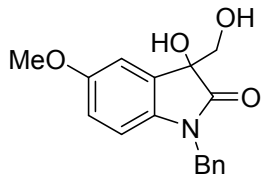
1-Benzyl-3-hydroxy-3-(hydroxymethyl)-5-bromo-oxindole 3k: The title compound was prepared according to general procedure. White solid, 81% yield; ^{1}H NMR (Acetone-*d*6, 400 MHz) δ 3.90-4.00 (m, 2H), 4.24 (br s, 1H), 4.83 (d, *J* = 16 Hz, 1H), 5.01 (d, *J* = 16 Hz, 1H), 5.28 (s, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 7.25-7.33 (m, 3H), 7.35-7.38 (m, 3H), 7.56-7.57 (m, 1H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 43.8, 67.1, 77.4, 111.7, 115.4, 128.1, 128.3, 128.5, 129.5, 132.8, 133.7, 136.9, 143.9, 177.4; HRMS (ESI) calcd. for $C_{16}H_{15}BrNO_3$ $(M+H)^+$: 348.0235 Found: 348.0232.



3l

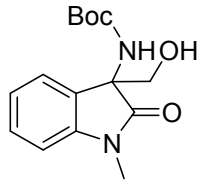
1-Benzyl-3-hydroxy-3-(hydroxymethyl)-5-methyl-oxindole 3l: The title compound was prepared according to general procedure. White solid, 87% yield; ^{1}H NMR

(Acetone-*d*6, 400 MHz) δ 2.26 (s, 3H), 3.91-3.93 (m, 2H), 4.07 (m, 1H), 4.79 (d, *J* = 16 Hz, 1H), 4.97 (d, *J* = 16 Hz, 1H), 5.06 (s, 1H), 6.63 (d, *J* = 8 Hz, 1H), 6.75-7.00 (m, 1H), 7.25-7.28 (m, 4H), 7.30-7.37 (m, 2H); ^{13}C NMR (Acetone-*d*6, 100 MHz): δ 20.2, 42.8, 66.3, 76.4, 108.7, 125.1, 127.1, 127.2, 128.5, 129.3, 130.2, 131.5, 136.6, 141.2, 177.0; HRMS (ESI) calcd. for $C_{17}H_{18}NO_3$ (M+H) $^+$: 284.1287 Found: 284.1284.



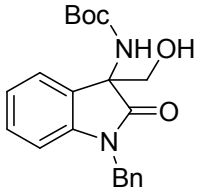
3m

1-Benzyl-3-hydroxy-3-(hydroxymethyl)-5-methoxy-oxindole 3m: The title compound was prepared according to general procedure. White solid, 91% yield; ^{1}H NMR (MeOD, 400 MHz) δ 3.63 (s, 3H), 3.78 (s, 2H), 4.69-4.75 (m, 3H), 4.84 (d, *J* = 16.0 Hz, 1H), 6.54 (d, *J* = 8.0 Hz, 1H), 6.55-6.65 (m, 1H), 6.97-6.98 (m, 1H), 7.11-7.18 (m, 1H), 7.19-7.24 (m, 1H); ^{13}C NMR (MeOD, 100 MHz): δ 43.0, 54.8, 65.6, 76.8, 109.7, 111.3, 113.5, 126.9, 127.1, 128.3, 131.1, 135.8, 136.3, 156.5, 177.9; HRMS (ESI) calcd. for $C_{17}H_{18}NO_4$ (M+H) $^+$: 300.1236 Found: 300.1238.



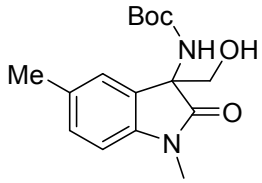
5a

***tert*-Butyl 3-(hydroxymethyl)-1-methyl-2-oxoindolin-3-ylcarbamate 5a:** The title compound was prepared according to general procedure. White solid, 84% yield; ^{1}H NMR (MeOD, 400 MHz) δ 1.00-1.45 (br s, 9H), 3.25 (s, 3H), 3.69 (d, *J* = 10.8 Hz, 1H), 3.78 (d, *J* = 10.8 Hz, 1H), 7.01 (d, *J* = 8.0 Hz, 1H), 7.11-7.14 (m, 1H), 7.32-7.38 (m, 2H); ^{13}C NMR (MeOD, 100 MHz): δ 25.6, 27.3, 63.8, 65.6, 80.1, 108.4, 122.8, 122.9, 128.9, 144.3, 155.4, 177.1; HRMS (ESI) calcd. for $C_{15}H_{21}N_2O_4$ (M+H) $^+$: 293.1501 Found: 293.1499.



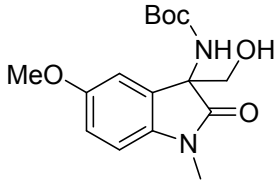
5b

***tert*-Butyl 3-(hydroxymethyl)-1-benzyl-2-oxoindolin-3-ylcarbamate 5b:** The title compound was prepared according to general procedure. White solid, 81% yield; ^{1}H NMR (MeOD, 400 MHz) δ 1.00-1.47 (br s, 9H), 3.79 (d, *J* = 10.4 Hz, 1H), 3.85 (d, *J* = 10.4 Hz, 1H), 4.88 (s, 2H), 5.15 (br s, 1H), 6.76 (br s, 1H), 7.06-7.09 (m, 1H), 7.18-7.27 (m, 2H), 7.30-7.33 (m, 3H), 7.44-7.46 (m, 2H); ^{13}C NMR (MeOD, 100 MHz): δ 28.5, 44.9, 65.0, 66.9, 80.9, 90.8, 110.5, 123.9, 124.0, 128.4, 138.5, 129.6, 129.7, 129.8, 137.4, 144.5, 156.3, 178.4; HRMS (ESI) calcd. for $C_{21}H_{25}N_2O_4$ (M+H) $^{+}$: 369.1814 Found: 369.1818.



5c

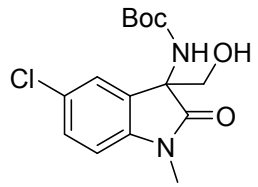
***tert*-Butyl 5-methyl-3-(hydroxymethyl)-1-methyl-2-oxoindolin-3-ylcarbamate 5c:** The title compound was prepared according to general procedure. White solid, 85% yield; ^{1}H NMR (MeOD, 400 MHz) δ 1.00-1.47 (br s, 9H), 2.37 (s, 3H), 3.23 (s, 3H), 3.67 (d, *J* = 10.4 Hz, 1H), 3.76 (d, *J* = 10.4 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 7.16-7.18 (m, 2H); ^{13}C NMR (MeOD, 100 MHz): δ 19.4, 25.0, 26.9, 63.6, 65.5, 79.7, 107.7, 123.2, 128.8, 129.7, 132.4, 141.6, 154.9, 176.8; HRMS (ESI) calcd. for $C_{16}H_{22}N_2O_4$ (M+H)$^{+}$: 307.1658 Found: 307.1660.



5d

***tert*-Butyl 5-methyl-3-(hydroxymethyl)-1-methoxy-2-oxoindolin-3-ylcarbamate 5d:** The title compound was prepared according to general procedure. White solid, 90% yield;

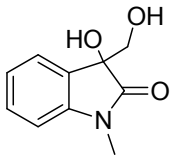
^{1}H NMR (MeOD, 400 MHz) δ 1.00-1.47 (br s, 9H), 3.23 (s, 3H), 3.67 (d, *J* = 10.4 Hz, 1H), 3.76 (d, *J* = 10.4 Hz, 1H), 3.81 (s, 3H), 6.92-6.97 (m, 3H); ^{13}C NMR (MeOD, 100 MHz): δ 25.4, 27.1, 54.9, 63.9, 65.3, 79.8, 108.5, 110.1, 112.8, 137.2, 154.8, 156.5, 176.4; HRMS (ESI) calcd for C16H23N2O5 (M+H) $^{+}$: 323.1607 Found: 323.1604.



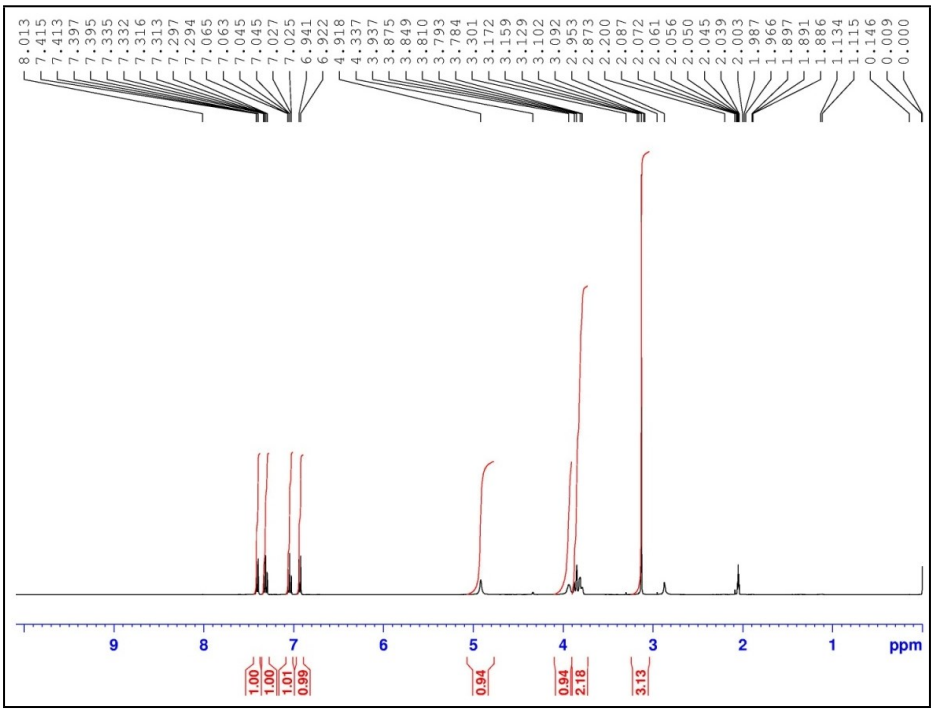
5e

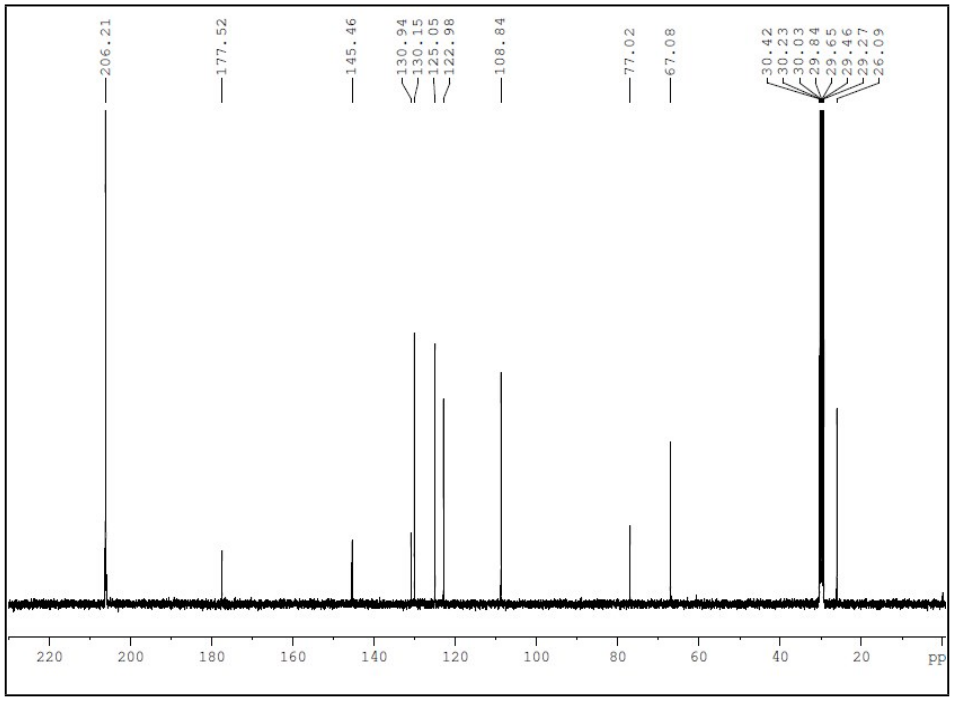
***tert*-Butyl 5-chloro-3-(hydroxymethyl)-1-methyl-2-oxoindolin-3-ylcarbamate 5e:** The title compound was prepared according to general procedure. White solid, 78% yield; ^{1}H NMR (MeOD, 400 MHz) δ 1.00-1.47 (br s, 9H), 3.24 (s, 3H), 3.68 (d, *J* = 10.4 Hz, 1H), 3.79 (d, *J* = 10.4 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 7.32-7.37 (m, 2H); ^{13}C NMR (MeOD, 100 MHz): δ 26.8, 28.5, 64.9, 66.5, 81.5, 110.7, 124.4, 129.2, 129.8, 144.6, 156.4, 177.7; HRMS (ESI) calcd. for $C_{15}H_{20}ClN_2O_4$ (M+H) $^{+}$: 327.1112 Found: 327.1107.

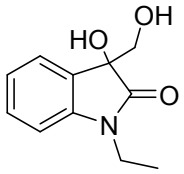
5. ^{1}H & ^{13}C NMR spectra for compound



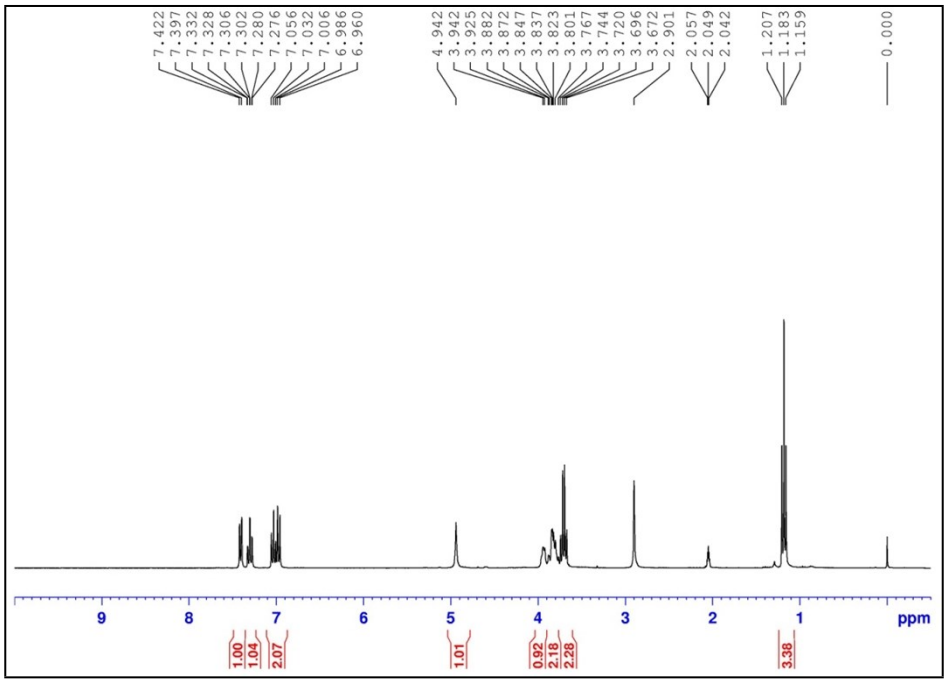
3a






OH
HO
O
N

3b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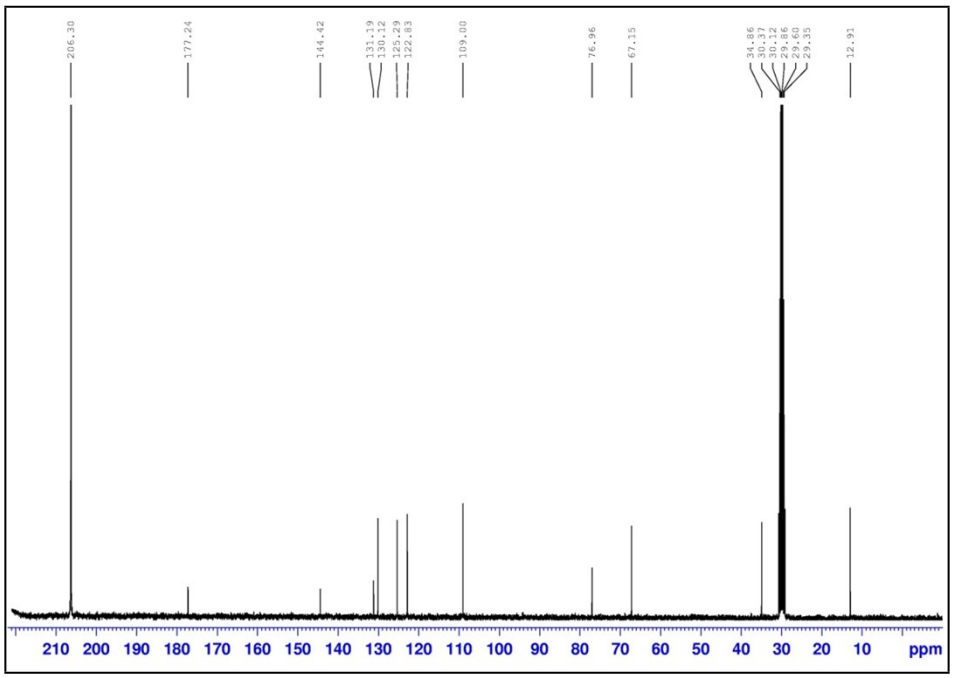
7.328
7.306
7.302
7.280
7.276
7.056
7.032
7.006
6.986
6.960
4.942
3.942
3.925
3.882
3.872
3.847
3.837
3.823
3.801
3.767
3.744
3.720
3.696
3.672
2.901
2.057
2.049
2.042
1.207
1.183
1.159
0.000
9
8
7
6
5
4
3
2
1
ppm
1.00
1.04
2.07
1.01
0.92
2.18
2.28
3.38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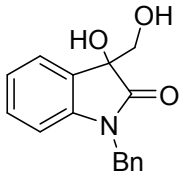
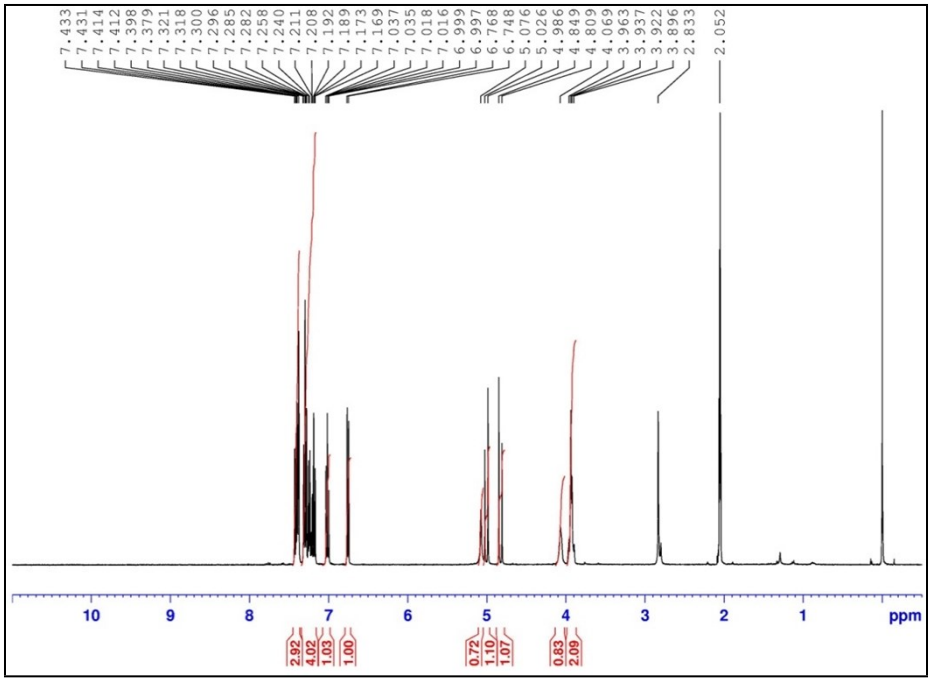
177.24
144.42
131.19
130.12
125.29
122.83
109.00
76.96
67.15
34.86
30.37
30.12
29.86
29.60
29.35
12.91
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
ppm


OH
HO
O
N
Bn

3c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7.321
7.318
7.300
7.296
7.285
7.282
7.258
7.240
7.211
7.208
7.192
7.189
7.173
7.169
7.037
7.035
7.018
7.016
6.999
6.997
6.768
6.748
5.076
5.026
4.986
4.849
4.809
4.069
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3.937
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3.896
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2.052
10
9
8
7
6
5
4
3
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ppm
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0.72
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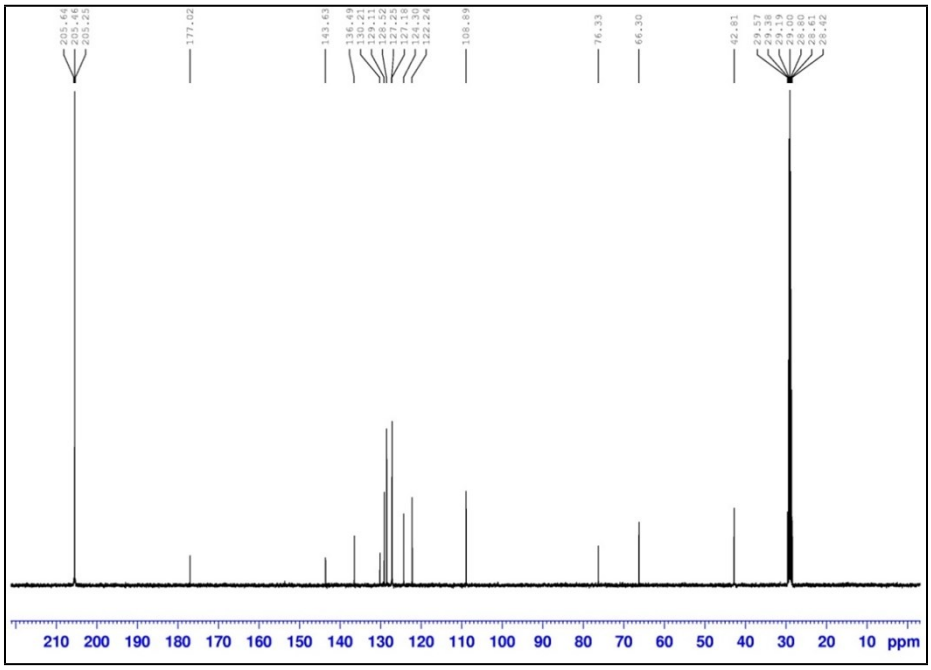
1.07
0.83
2.09


205.64
205.46
205.25
177.02
143.63
136.49
130.21
129.11
128.52
127.25
127.18
124.30
122.24
108.89
76.33
66.30
42.81
29.57
29.38
29.19
29.00
28.80
28.61
28.42
210
200
190
180
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150
140
130
120
110
100
90
80
70
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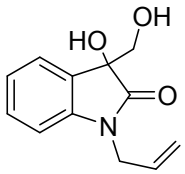
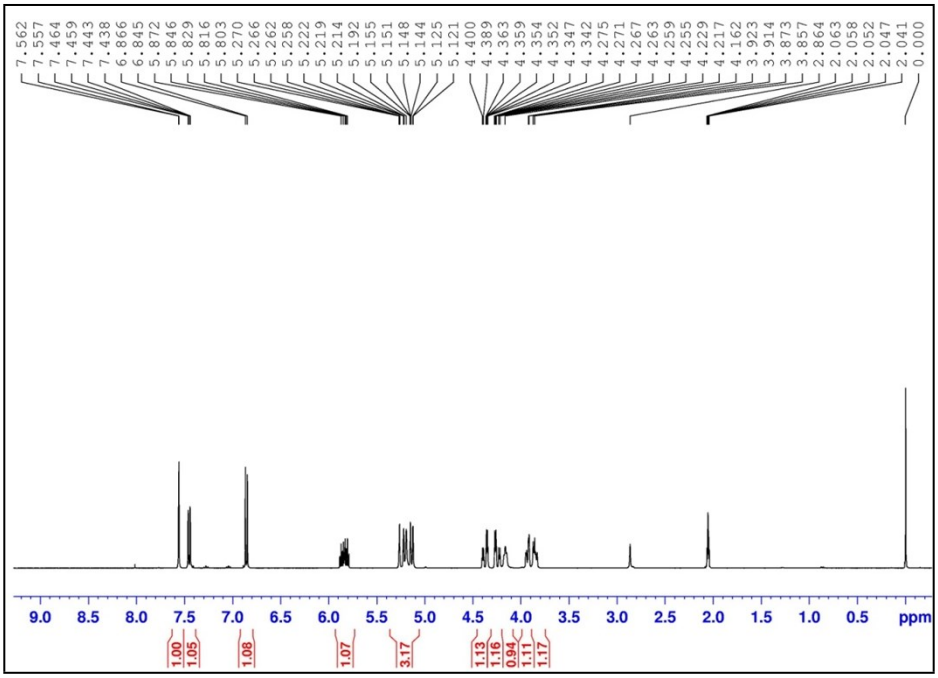
50
40
30
20
10
ppm


OH
HO
O
N

3d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7.438
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6.845
5.872
5.846
5.829
5.816
5.803
5.270
5.266
5.262
5.258
5.222
5.219
5.214
5.192
5.155
5.151
5.148
5.144
5.125
5.121
4.400
4.389
4.363
4.359
4.354
4.352
4.347
4.342
4.275
4.271
4.267
4.263
4.259
4.255
4.229
4.217
4.162
3.923
3.914
3.873
3.857
2.864
2.063
2.058
2.052
2.047
2.041
0.000
9.0 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 0.5 ppm
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1.05
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1.07
3.17
1.13
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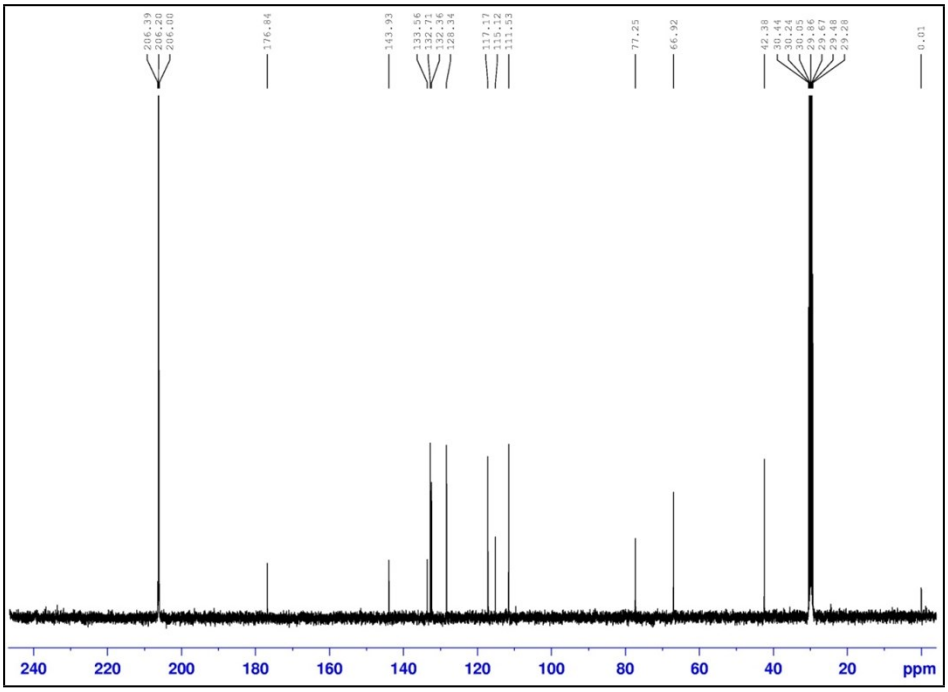
0.94
1.11
1.17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133.56
132.71
132.36
128.34
117.17
113.12
111.53
77.25
66.92
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30.24
30.05
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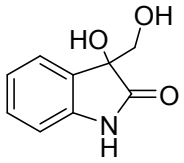
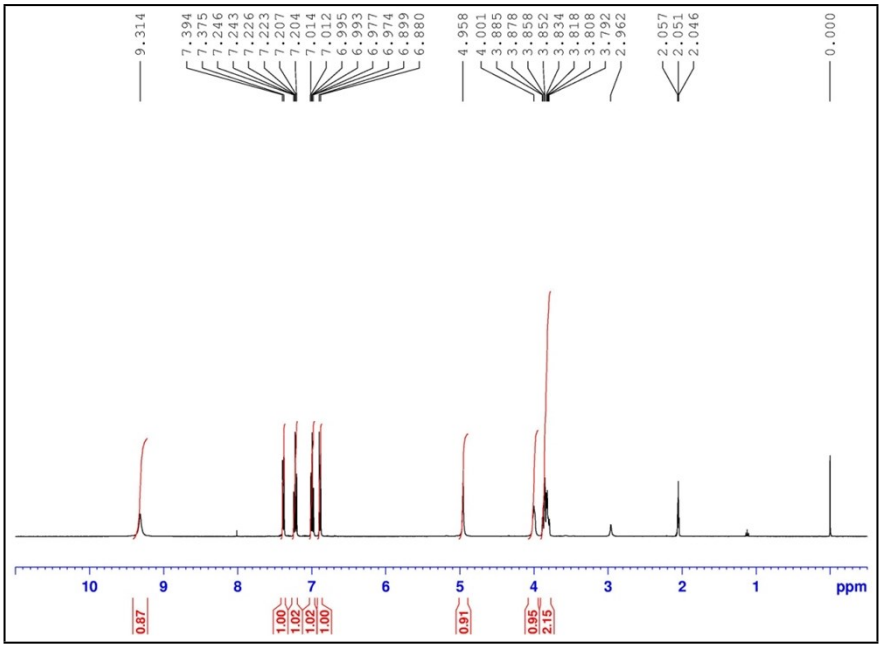
29.48
29.28
0.01
240 220 200 180 160 140 120 100 80 60 40 20 ppm


OH
HO
O
N
H

3e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7.375
7.246
7.243
7.226
7.223
7.207
7.204
7.014
7.012
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6.993
6.977
6.974
6.899
6.880
4.958
4.001
3.885
3.878
3.858
3.852
3.834
3.818
3.808
3.792
2.962
2.057
2.051
2.046
0.000
10
9
8
7
6
5
4
3
2
1
ppm
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1.00
1.02
1.02
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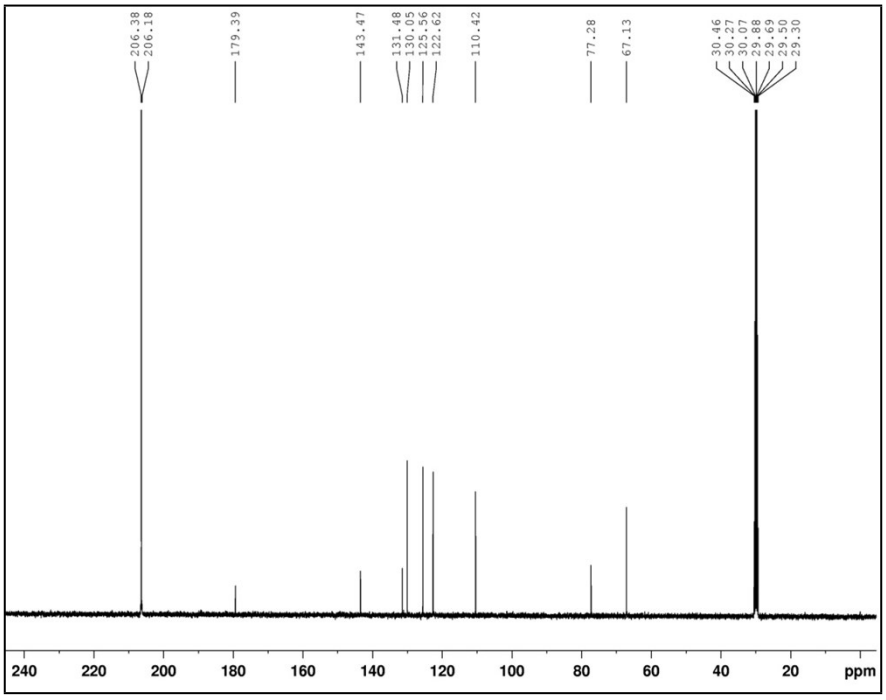
0.91
0.95
2.15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131.48
130.05
125.56
122.62
110.42
77.28
67.13
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30.07
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140
120
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80
60
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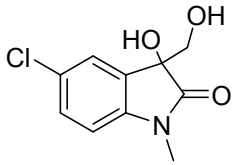
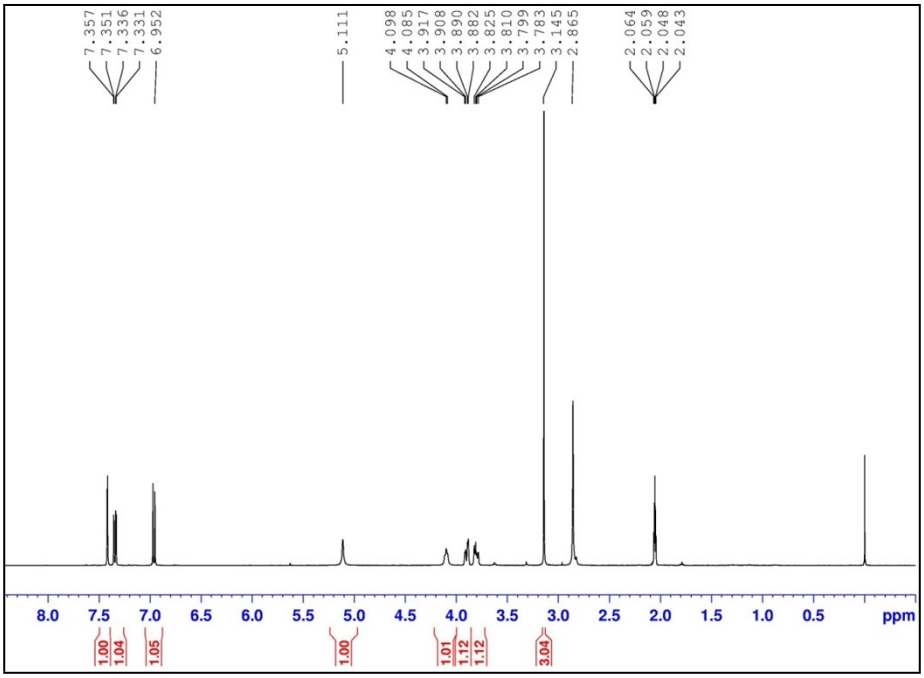
20
ppm


OH
HO
Cl
O
N

3f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7.336
7.331
6.952
5.111
4.098
4.085
3.917
3.908
3.890
3.882
3.825
3.810
3.799
3.783
3.145
2.865
2.064
2.059
2.048
2.043
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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0.5
ppm
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1.00
1.01
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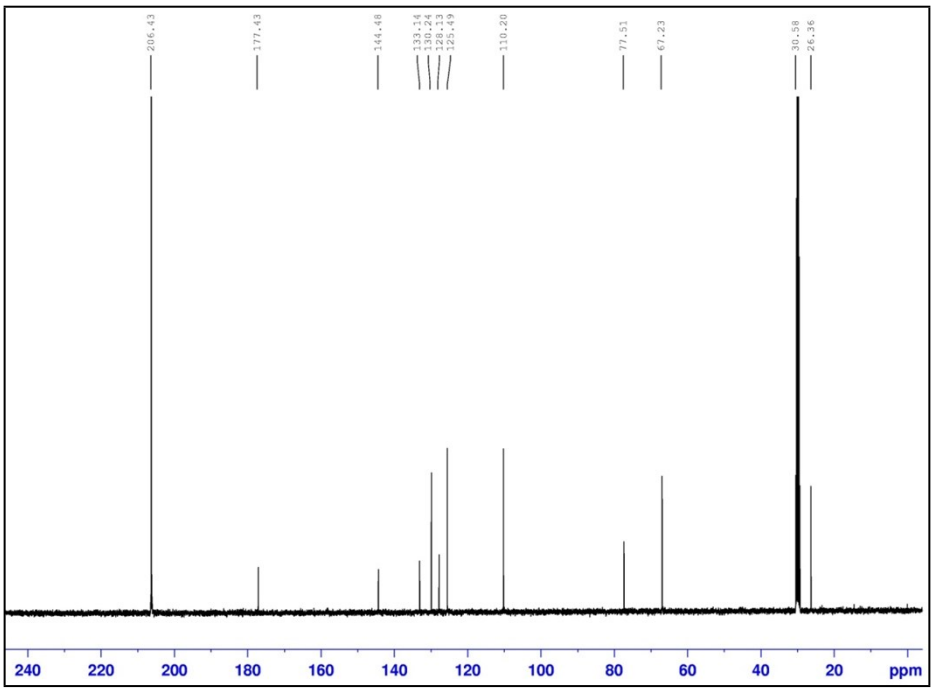
1.12
3.04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177.43
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133.14
130.24
128.13
125.49
110.20
77.51
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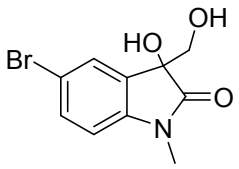
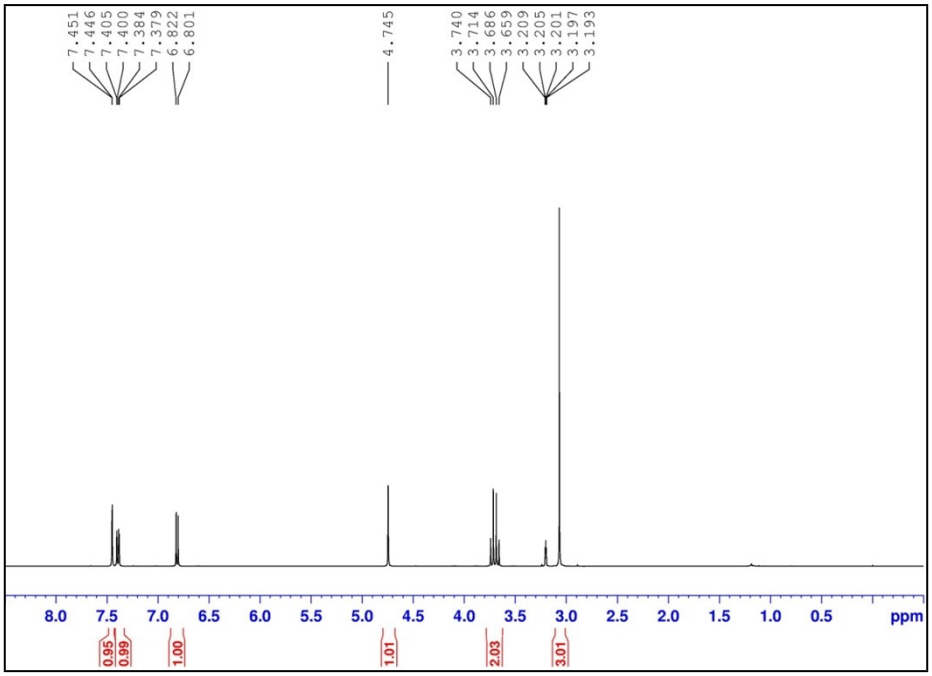
30.58
26.36
240
220
200
180
160
140
120
100
80
60
40
20
ppm


OH
HO
Br
O
N

3g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7.405
7.400
7.384
7.379
6.822
6.801
4.745
3.740
3.714
3.686
3.659
3.209
3.205
3.201
3.197
3.193
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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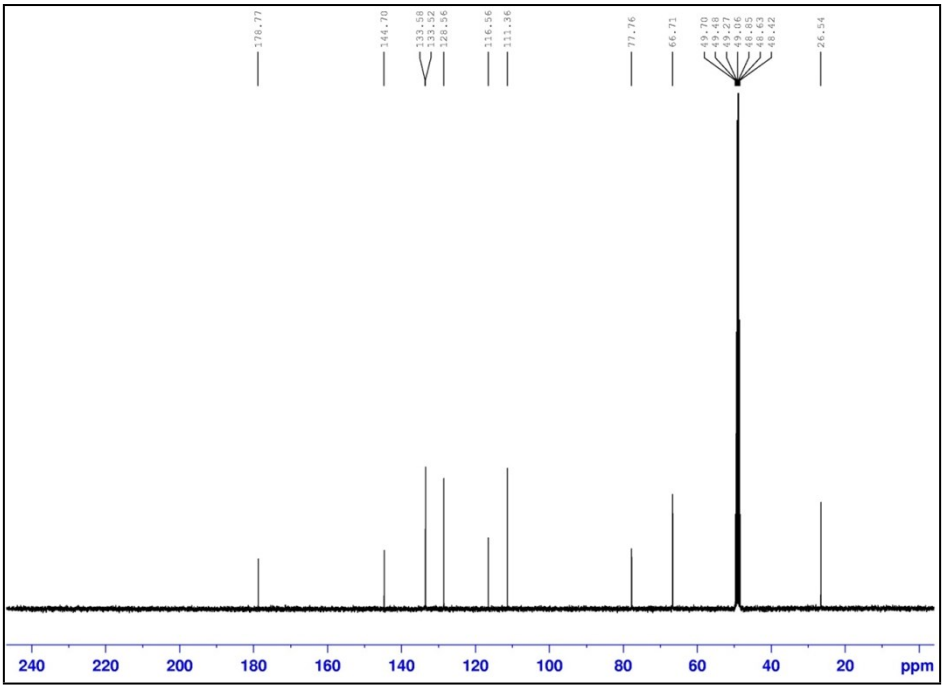
2.03
3.01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128.56
116.56
111.36
77.76
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49.70
49.48
49.27
49.06
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48.42
26.54
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180
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140
120
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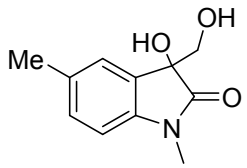
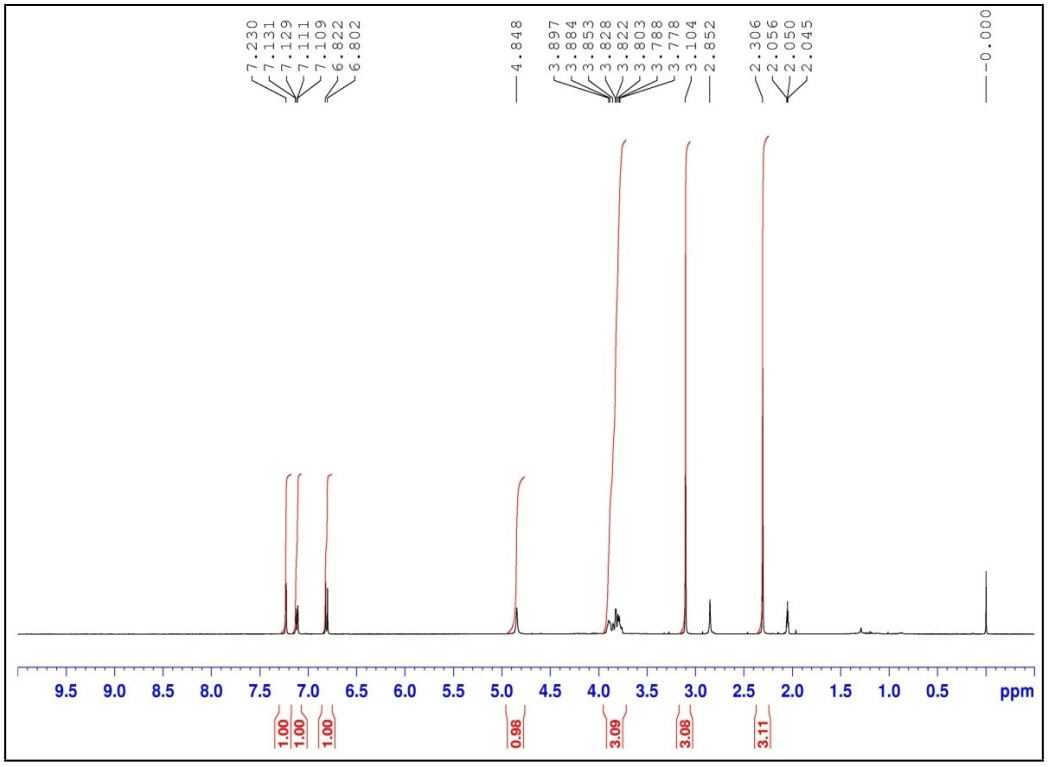
80
60
40
20
ppm


OH
HO
Me
O
N

3h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6.802
4.848
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3.853
3.828
3.822
3.803
3.788
3.778
3.104
2.852
2.306
2.056
2.050
2.045
0.000
9.5 9.0 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 0.5 ppm
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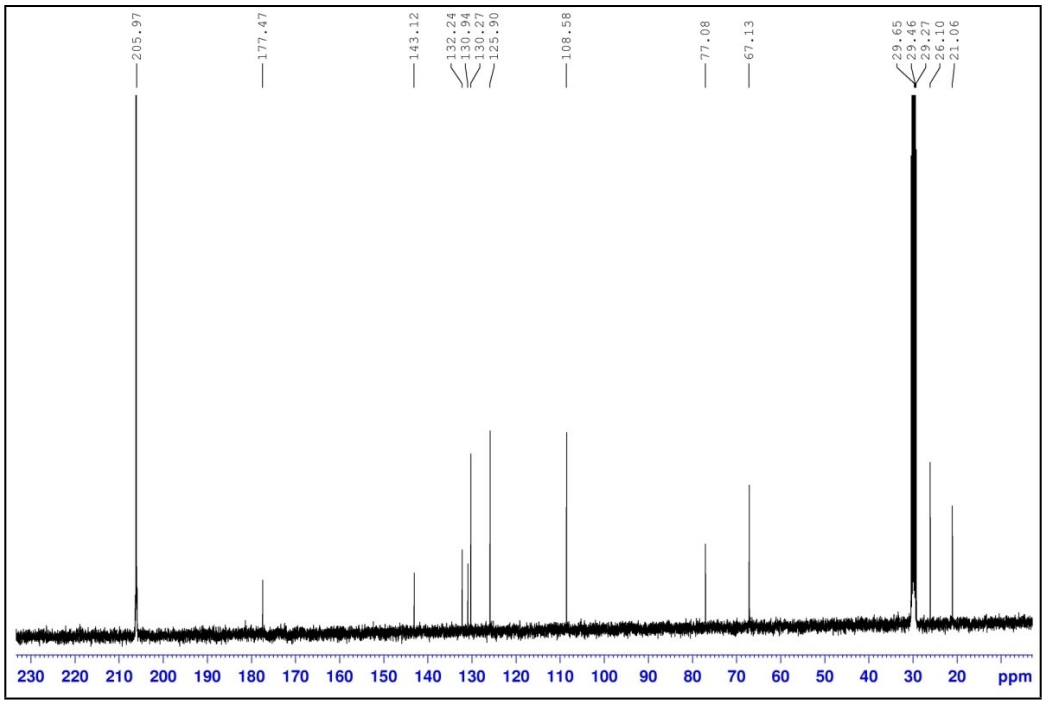
1.00
1.00
0.98
3.09
3.08
3.11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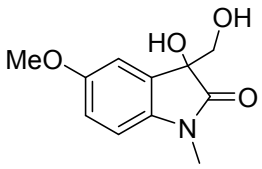
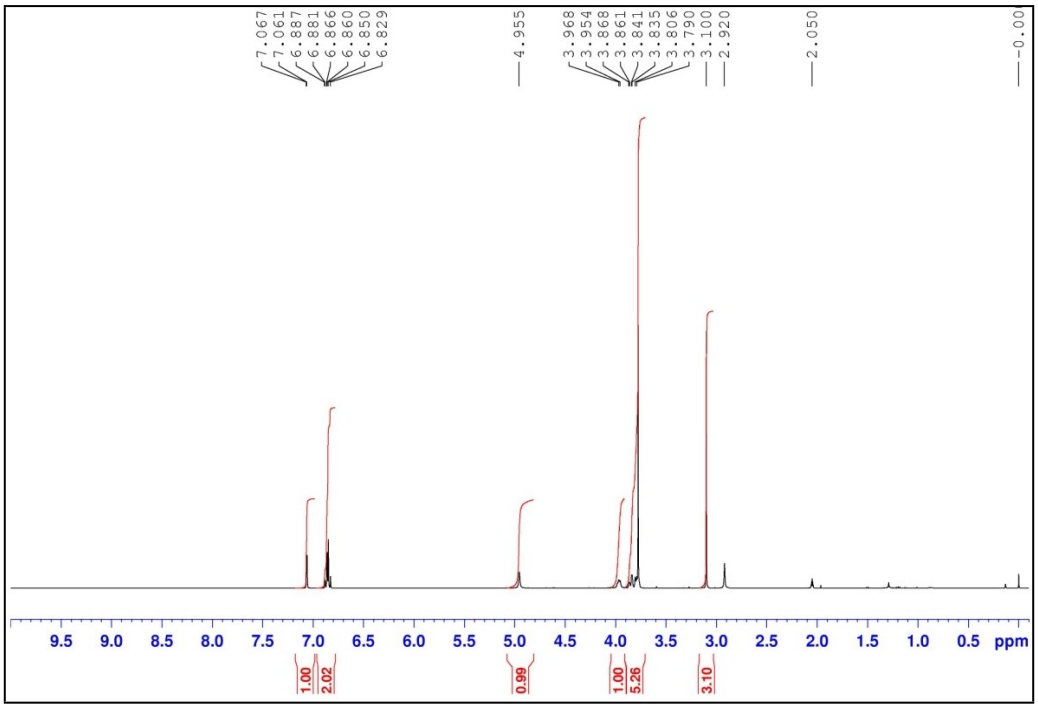
132.24
130.94
130.27
125.90
108.58
77.08
67.13
29.65
29.46
29.27
26.10
21.06
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


OH
HO
MeO
O
N

3i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6.860
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6.829
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3.861
3.841
3.835
3.806
3.790
3.100
2.920
2.050
0.00
9.5 9.0 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 0.5 ppm
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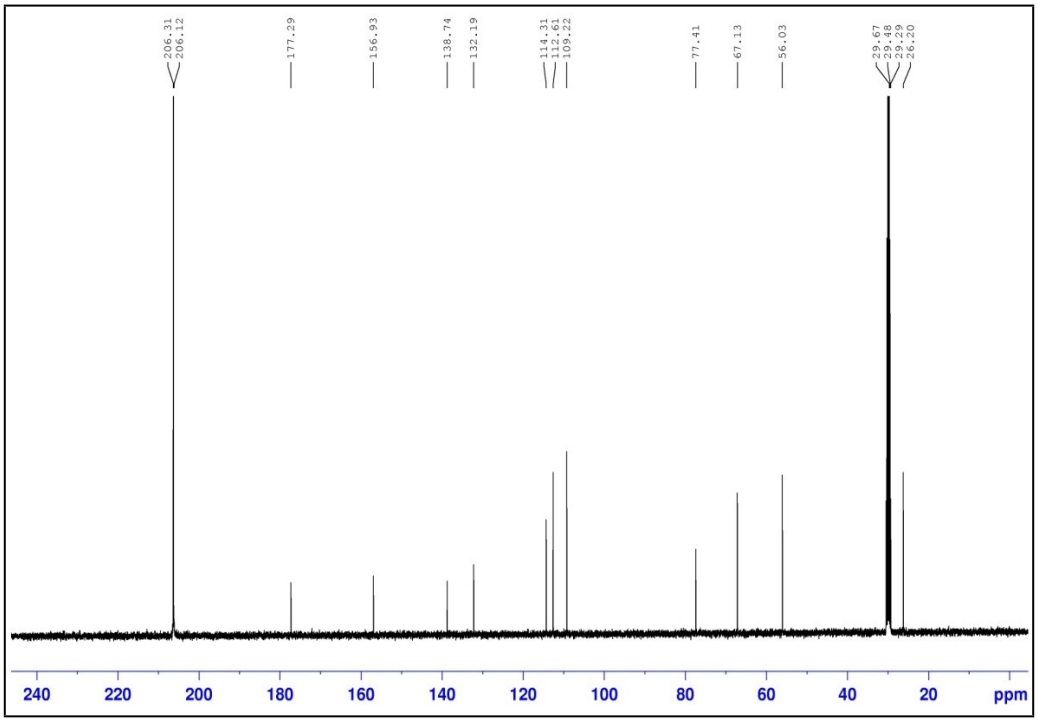
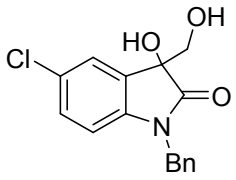
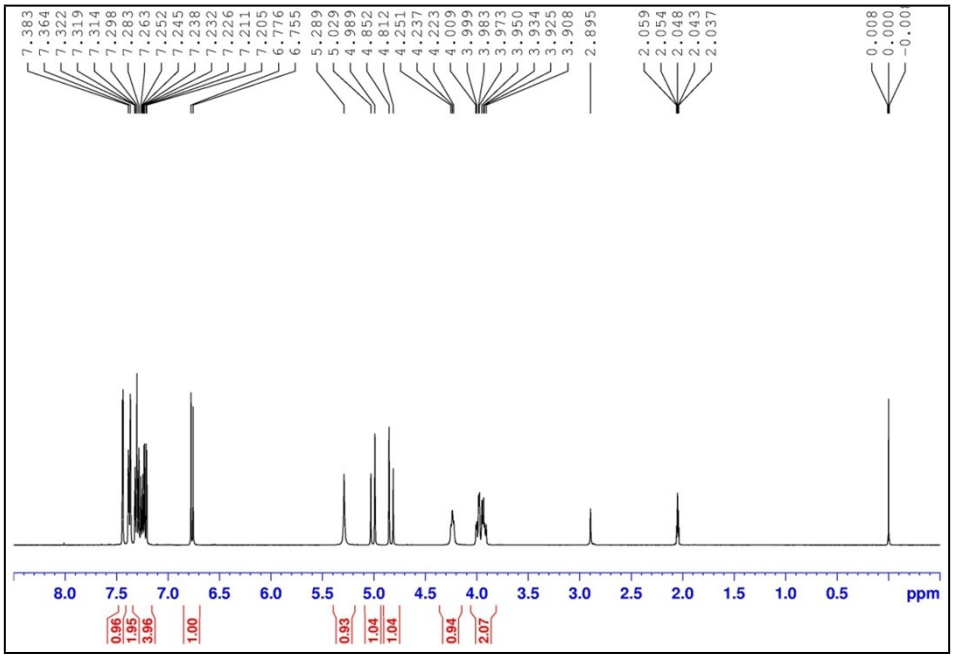
2.02
0.99
1.00
5.26
3.10


206.31
206.12
177.29
156.93
138.74
132.19
114.31
112.61
109.22
77.41
67.13
56.03
29.67
29.48
29.29
26.20
240 220 200 180 160 140 120 100 80 60 40 20 ppm


OH
HO
Cl
O
N
Bn

3j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7.364
7.322
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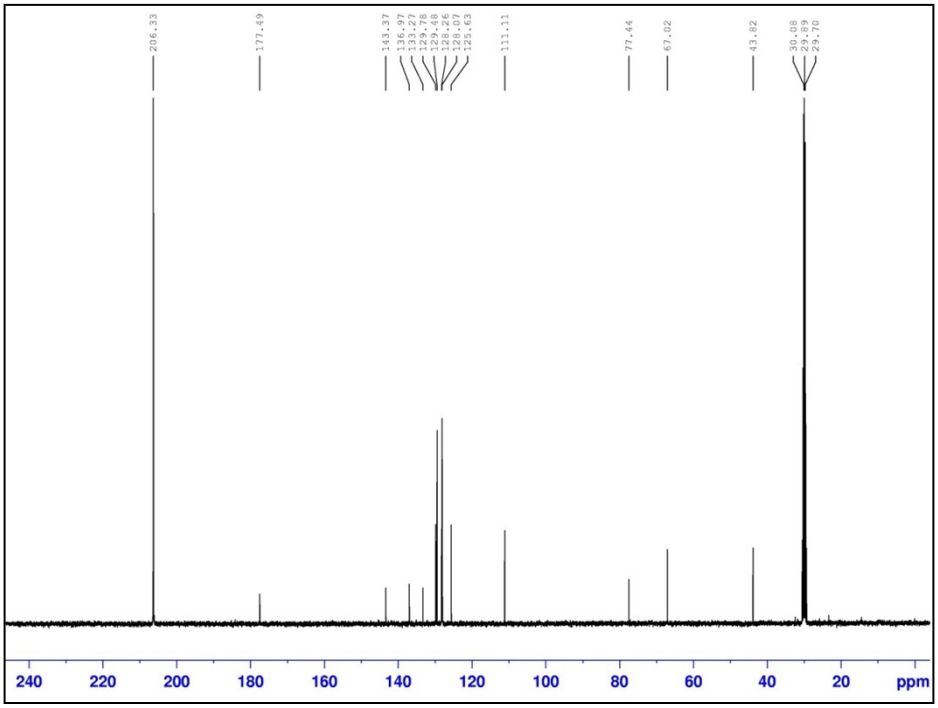
7.283
7.263
7.252
7.245
7.238
7.232
7.226
7.211
7.205
6.776
6.755
5.289
5.029
4.989
4.852
4.812
4.251
4.237
4.223
4.009
3.999
3.983
3.973
3.950
3.934
3.925
3.908
2.895
2.059
2.054
2.048
2.043
2.037
0.008
0.000
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.96
1.95
3.96
1.00
0.93
1.04
1.04
0.94
2.07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177.49
143.37
136.97
133.27
129.78
129.48
128.26
128.07
125.63
111.11
77.44
67.02
43.82
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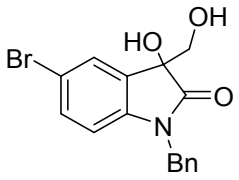
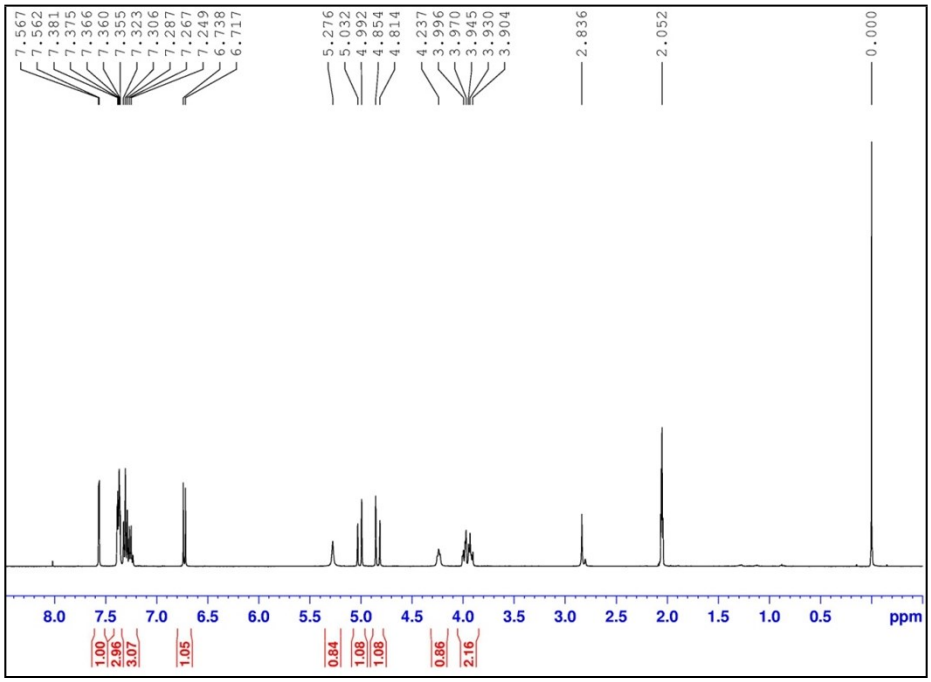
29.89
29.70
240
220
200
180
160
140
120
100
80
60
40
20
ppm


OH
HO
Br
O
N
Bn

3k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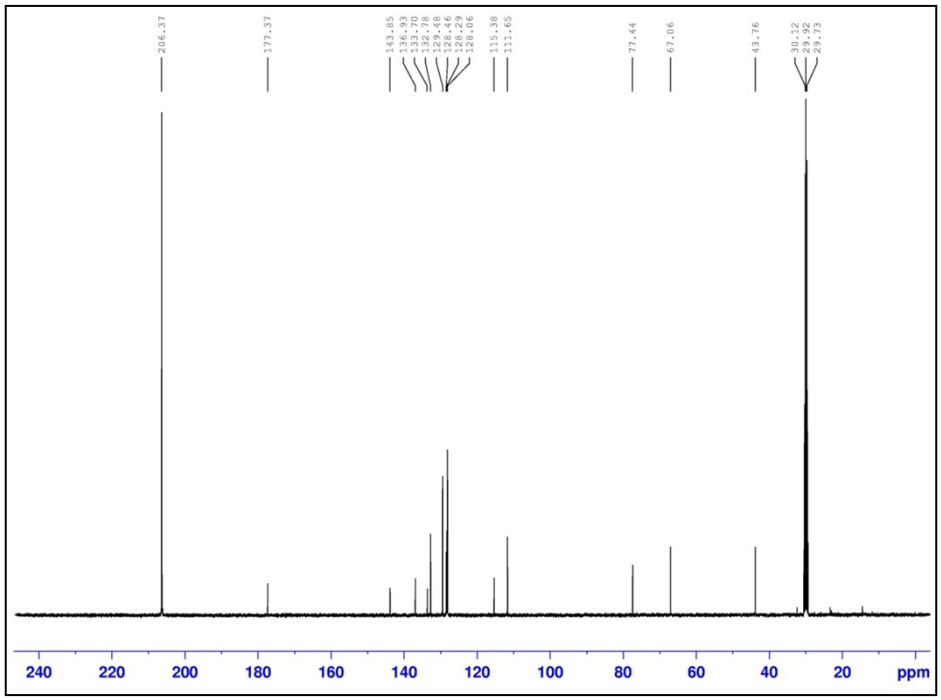
7.562
7.381
7.375
7.366
7.360
7.355
7.323
7.306
7.287
7.267
7.249
6.738
6.717
5.276
5.032
4.992
4.854
4.814
4.237
3.996
3.970
3.945
3.930
3.904
2.836
2.052
0.000
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
2.96
3.07
1.05
0.84
1.08
1.08
0.86
2.16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177.37
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133.70
132.78
129.48
128.46
128.29
128.06
115.38
111.65
77.44
67.06
43.76
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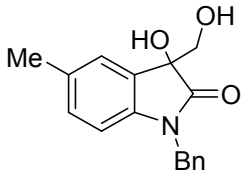
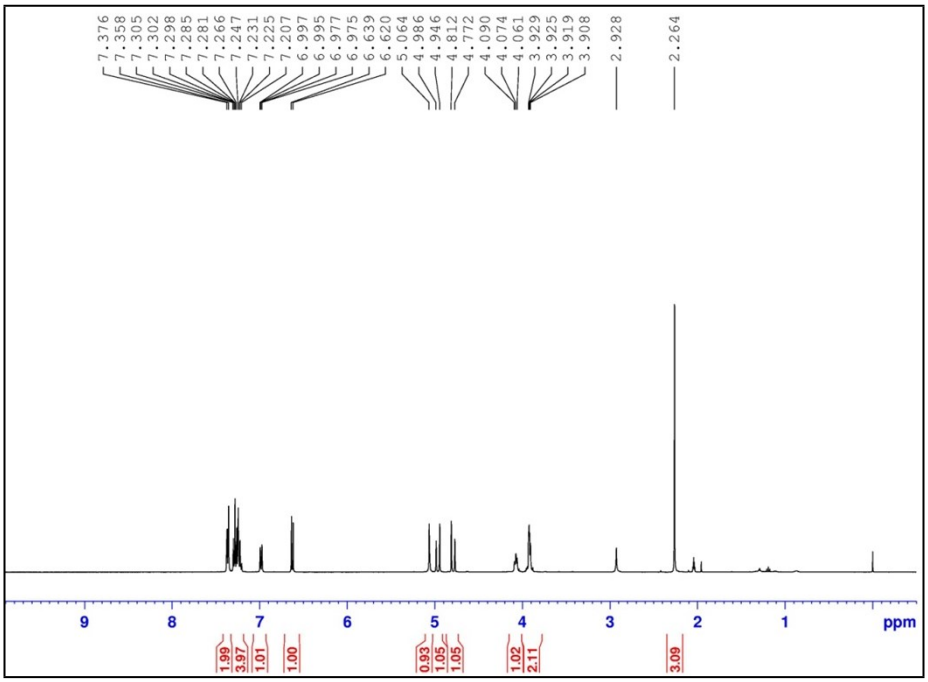
29.92
29.73
240
220
200
180
160
140
120
100
80
60
40
20
ppm


OH
HO
Me
O
N
Bn

3l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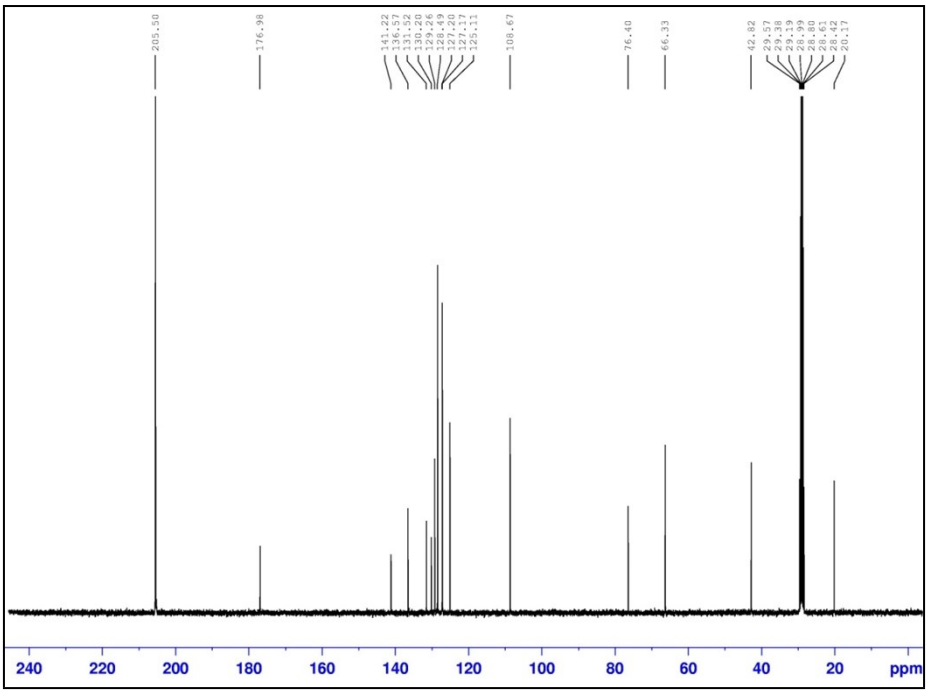
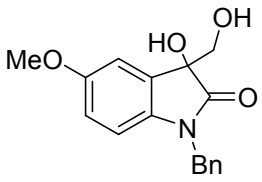
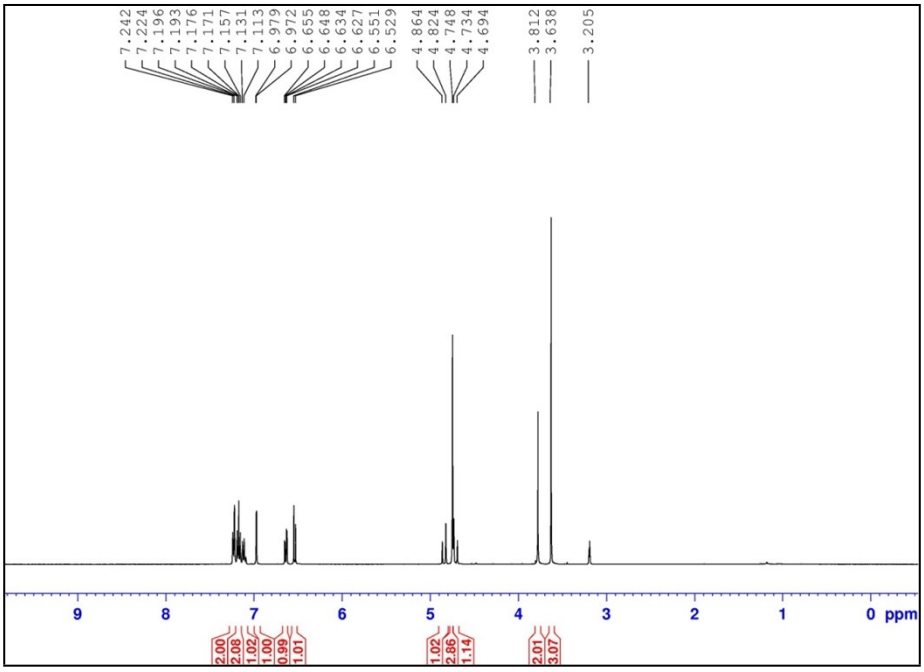
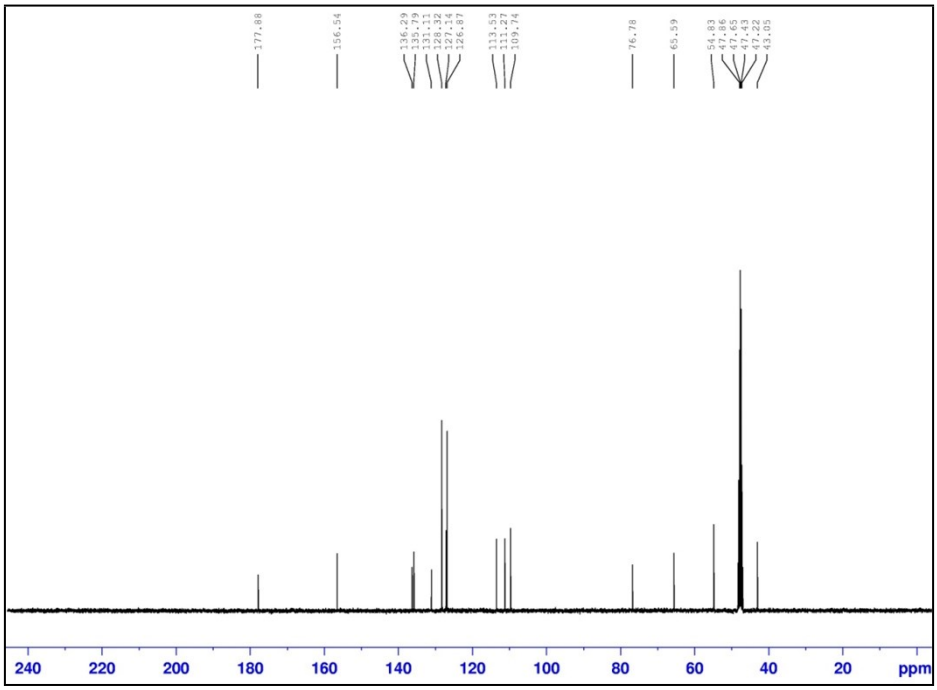
7.358
7.305
7.302
7.298
7.285
7.281
7.266
7.247
7.231
7.225
7.207
6.997
6.995
6.977
6.975
6.639
6.620
5.064
4.986
4.946
4.812
4.772
4.090
4.074
4.061
3.929
3.925
3.919
3.908
2.928
2.264
9
8
7
6
5
4
3
2
1
ppm
1.99
3.97
1.01
1.00
0.93
1.05
1.05
1.02
2.11
3.09

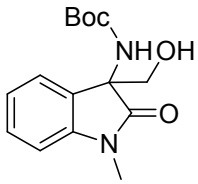

205.50
176.98
141.22
136.57
131.52
130.20
129.26
128.49
127.20
127.17
125.11
108.67
76.40
66.33
42.82
29.57
29.38
29.19
28.99
28.80
28.61
28.42
20.17
240
220
200
180
160
140
120
100
80
60
40
20
ppm


OH
HO
MeO
O
N
Bn

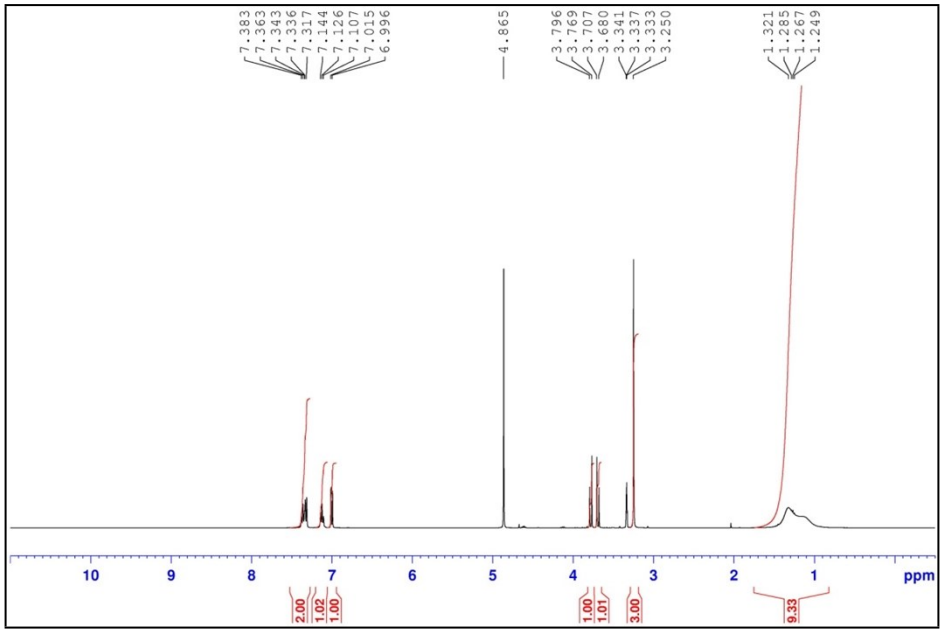
3m


7.242
7.224
7.196
7.193
7.176
7.171
7.157
7.131
7.113
6.979
6.972
6.655
6.648
6.634
6.627
6.551
6.529
4.864
4.824
4.748
4.734
4.694
3.812
3.638
3.205
9
8
7
6
5
4
3
2
1
0 ppm
2.00
2.08
1.02
1.00
0.99
1.01
1.02
2.86
1.14
2.01
3.07


177.88
156.54
136.29
135.79
131.11
130.32
127.74
126.87
113.53
111.27
109.74
76.78
65.59
54.83
47.86
47.65
47.43
47.22
43.05
240
220
200
180
160
140
120
100
80
60
40
20
ppm


Boc
NHOH
O
N

5a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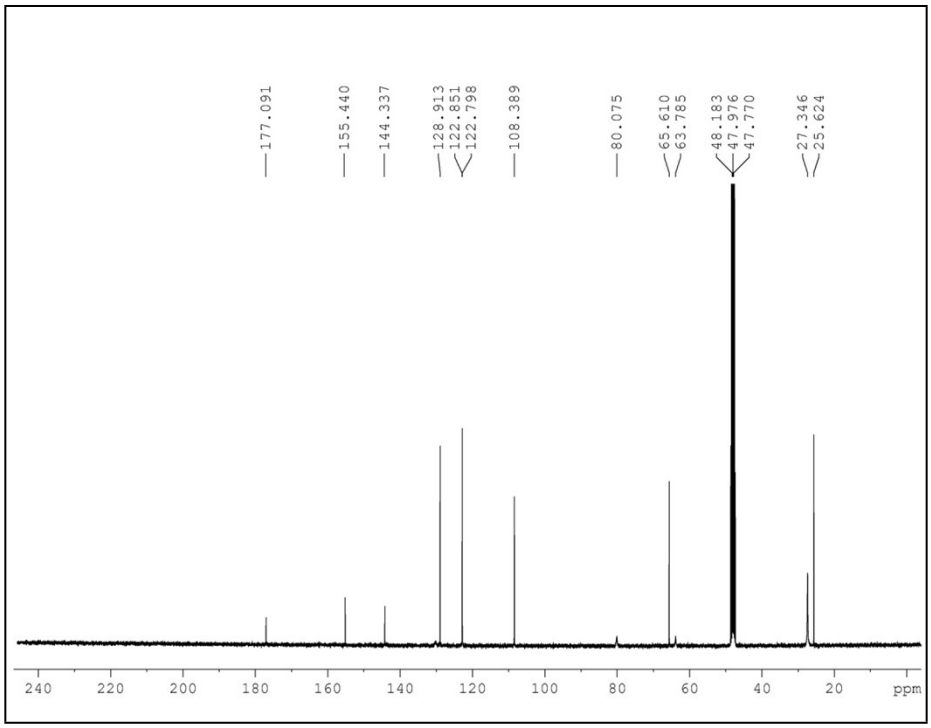
7.363
7.343
7.336
7.317
7.144
7.126
7.107
7.015
6.996
4.865
3.796
3.769
3.707
3.680
3.341
3.337
3.333
3.250
1.321
1.285
1.267
1.249
10
9
8
7
6
5
4
3
2
1
ppm
2.00
1.02
1.00
1.00
1.01
3.00
9.33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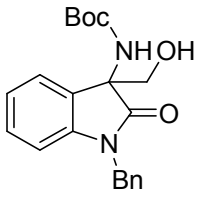
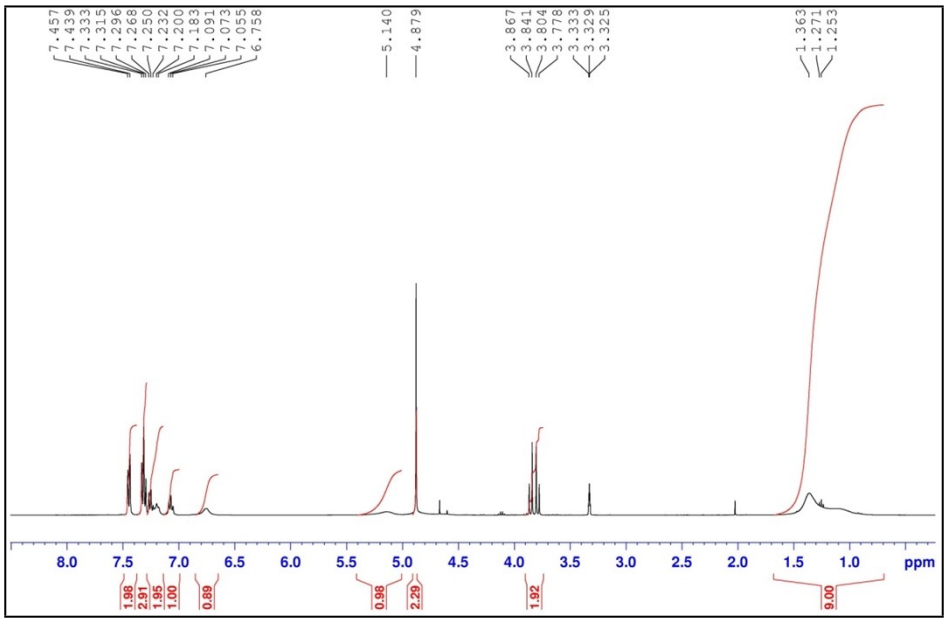
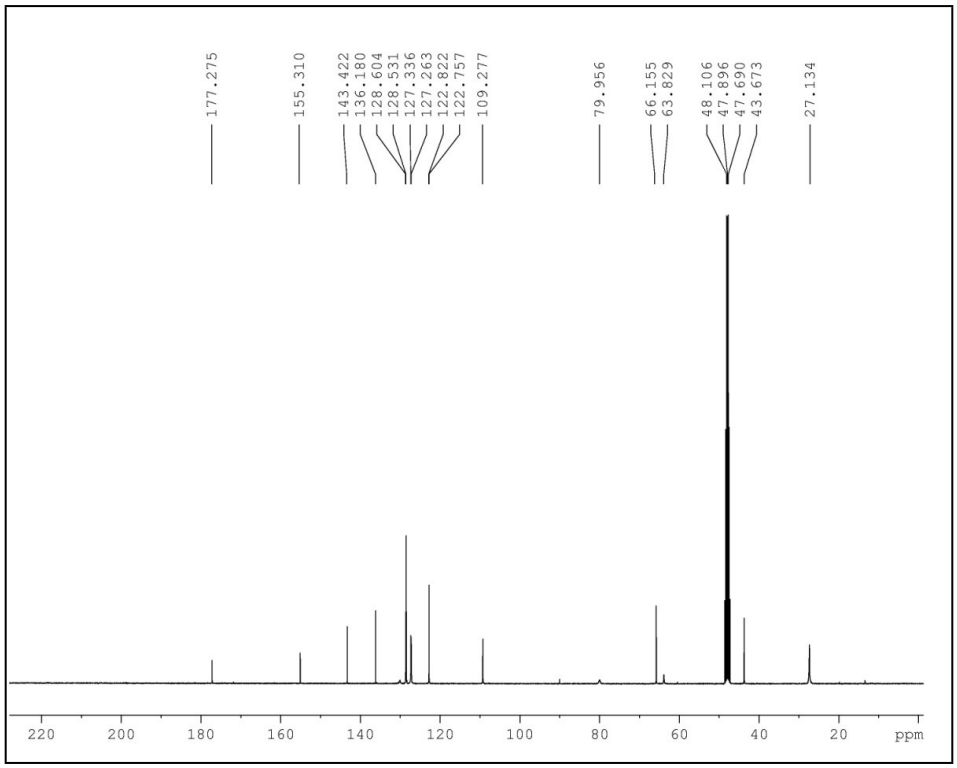
155.440
144.337
128.913
122.851
122.798
108.389
80.075
65.610
63.785
48.183
47.976
47.770
27.346
25.624
240
220
200
180
160
140
120
100
80
60
40
20
ppm


Boc
NH
OH
O
N
Bn

5b


7.457
7.439
7.333
7.315
7.296
7.268
7.250
7.232
7.200
7.183
7.091
7.073
7.055
6.758
5.140
4.879
3.867
3.841
3.804
3.778
3.333
3.329
3.325
1.363
1.271
1.253
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
1.98
2.91
1.95
1.00
0.89
0.98
2.29
1.92
9.00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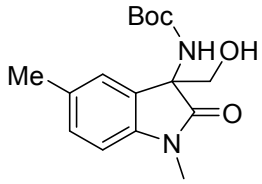
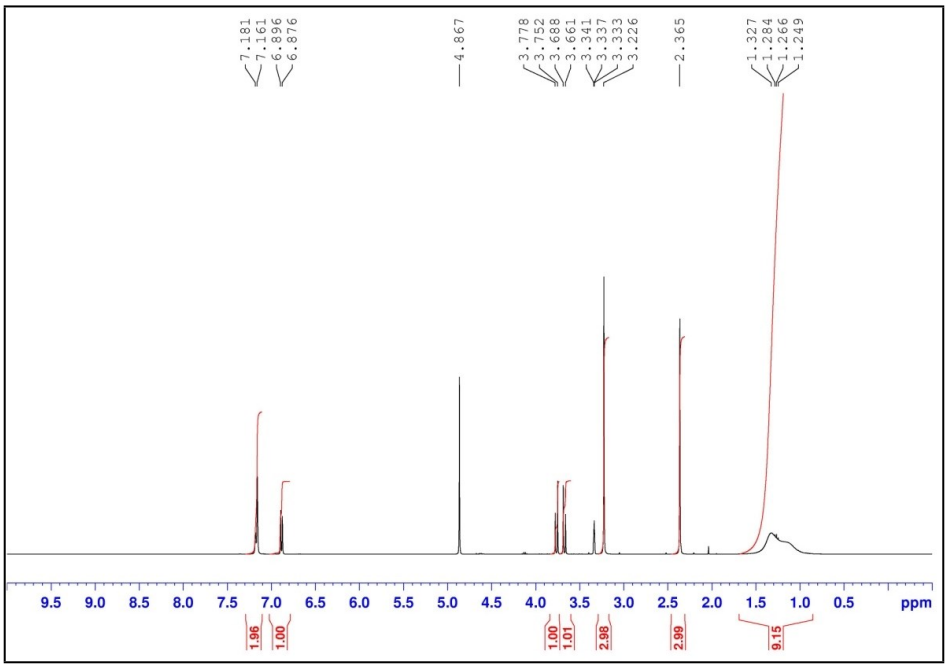
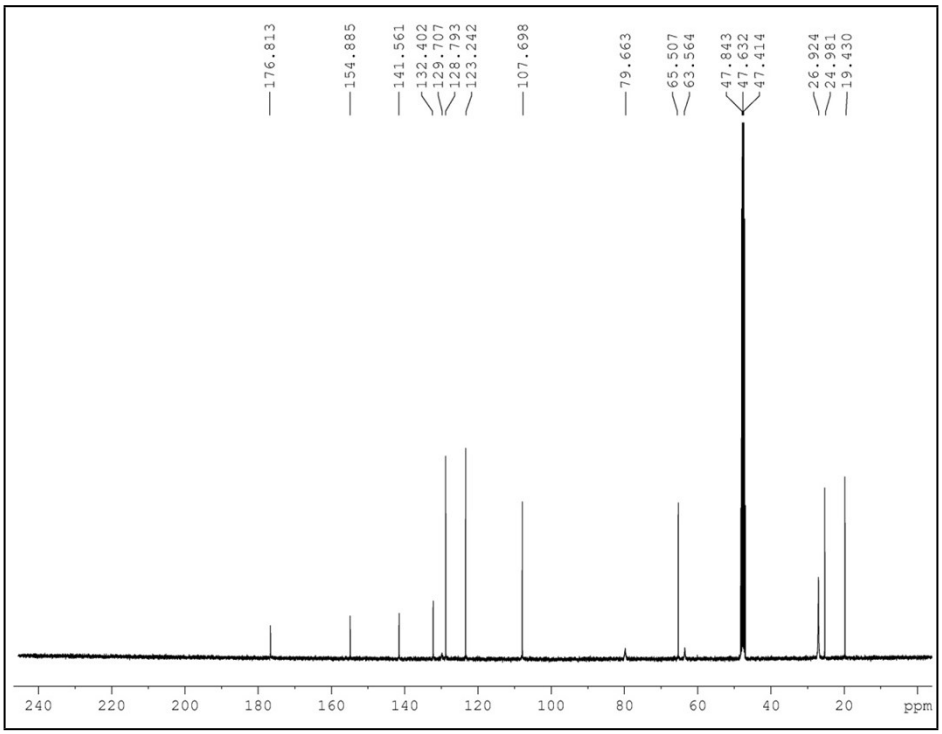
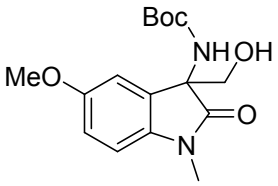
155.310
143.422
136.180
128.604
128.531
127.336
127.263
122.822
122.757
109.277
79.956
66.155
63.829
48.106
47.896
47.690
43.673
27.134
220
200
180
160
140
120
100
80
60
40
20
ppm


Boc
NH
OH
Me
O
N

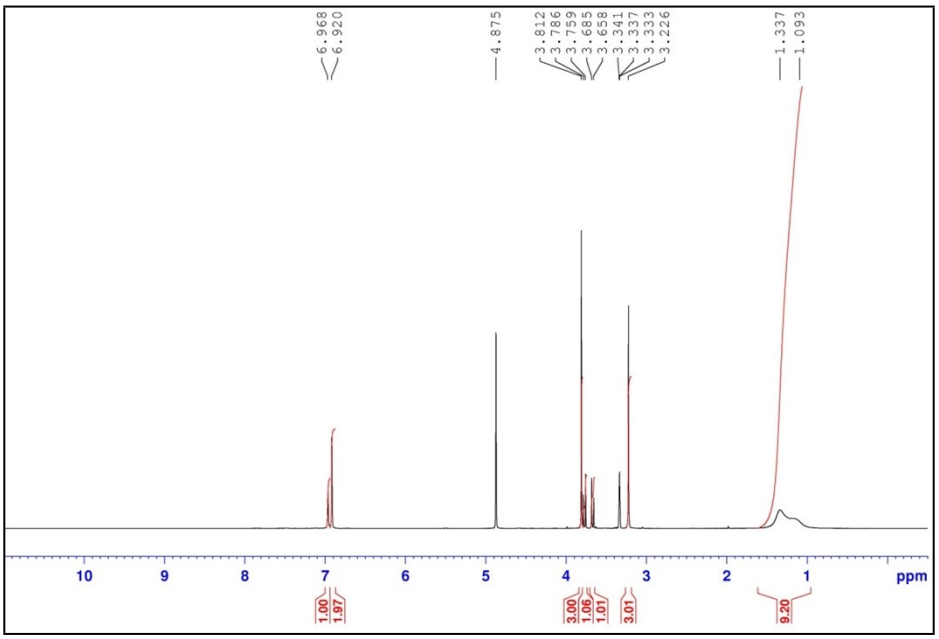
5c

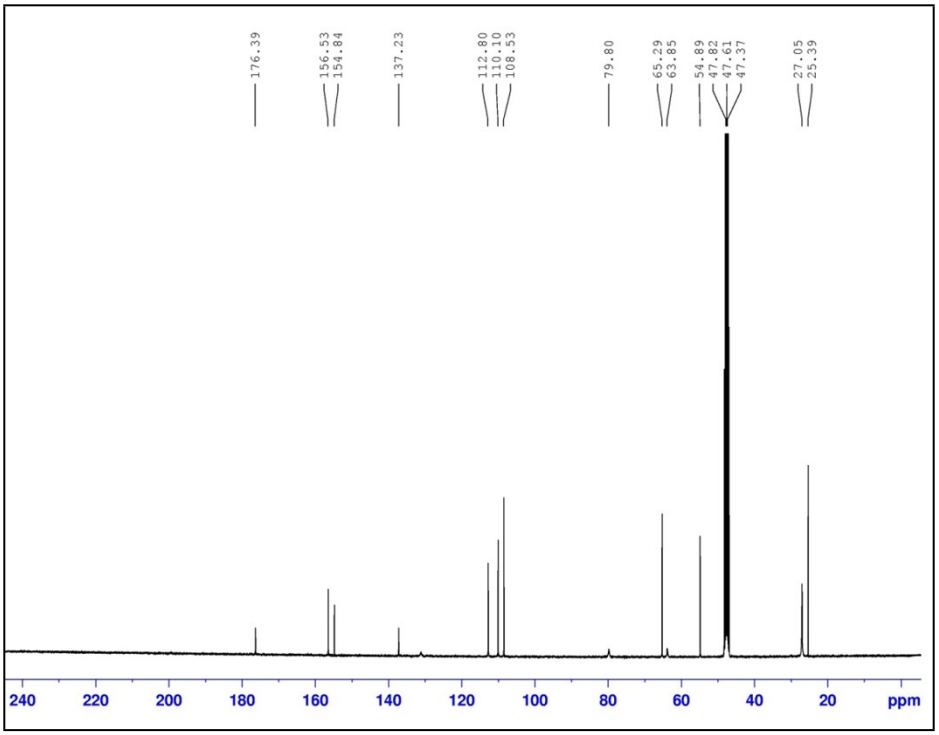

7.181
7.161
6.896
6.876
4.867
3.778
3.752
3.688
3.661
3.341
3.337
3.333
3.226
2.365
1.327
1.284
1.266
1.249
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.96
1.00
1.00
1.01
2.98
2.99
9.15

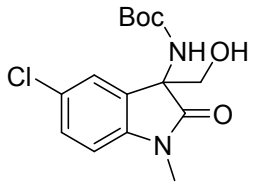

176.813
154.885
141.561
132.402
129.707
128.793
123.242
107.698
79.663
65.507
63.564
47.843
47.632
47.414
26.924
24.981
19.430
240 220 200 180 160 140 120 100 80 60 40 20 ppm


Boc
NH
OH
MeO
O
N

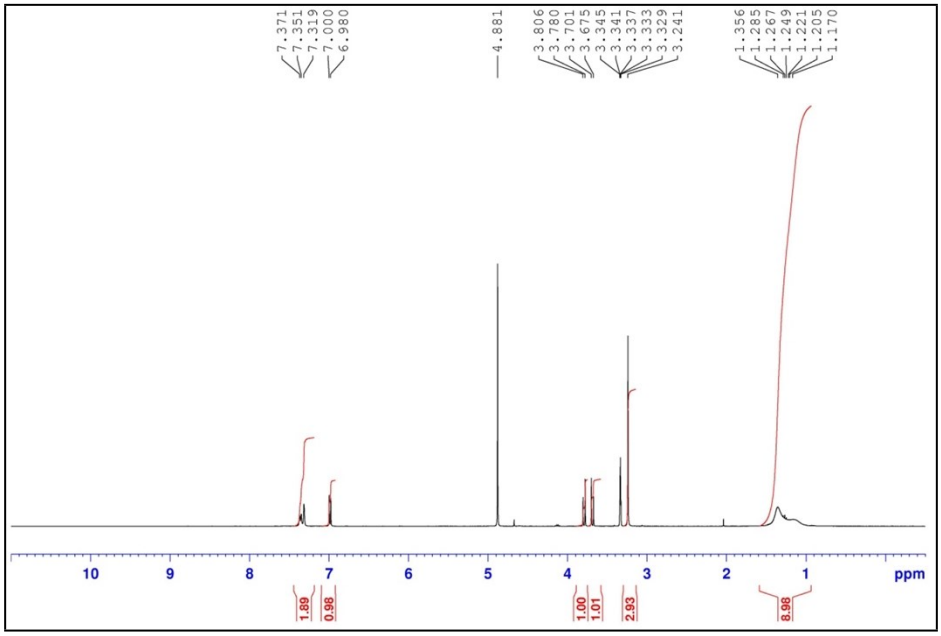
5d

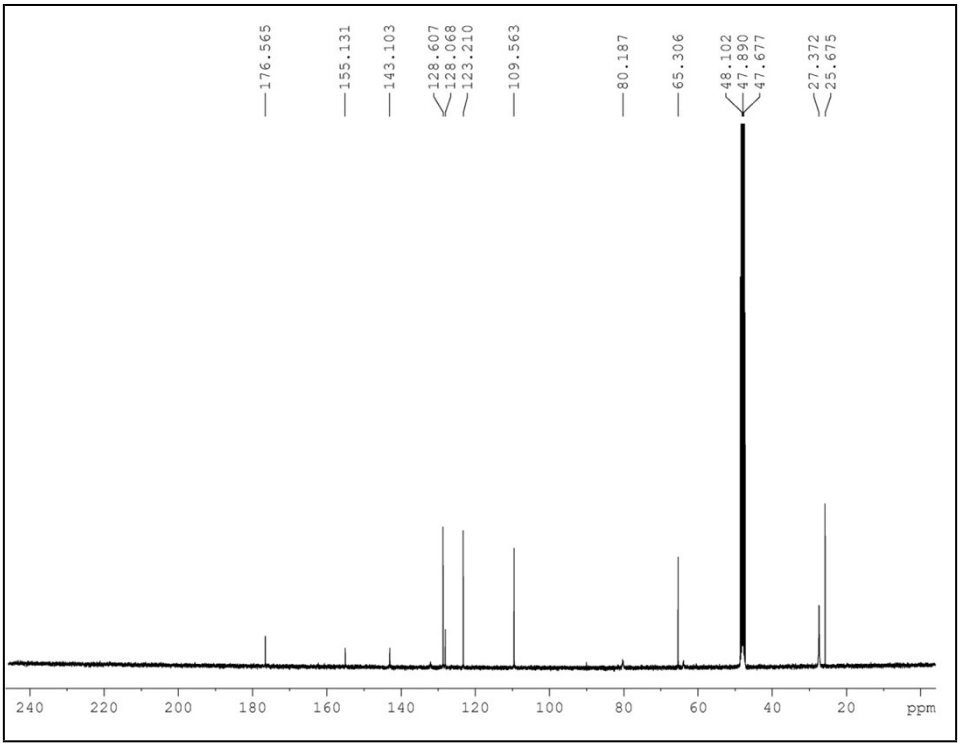

6.968
6.920
4.875
3.812
3.786
3.759
3.685
3.658
3.341
3.337
3.333
3.226
1.337
1.093
10
9
8
7
6
5
4
3
2
1
ppm
1.00
1.97
3.00
1.06
1.01
3.01
9.20


176.39
156.53
154.84
137.23
112.80
110.10
108.53
79.80
65.29
63.85
54.89
47.82
47.61
47.37
27.05
25.39
240
220
200
180
160
140
120
100
80
60
40
20
ppm


Boc
NH
OH
Cl
O
N

5e


7.371
7.351
7.319
7.000
6.980
4.881
3.806
3.780
3.701
3.675
3.345
3.341
3.337
3.333
3.329
3.241
1.356
1.285
1.267
1.249
1.221
1.205
1.170
10
9
8
7
6
5
4
3
2
1
ppm
1.89
0.98
1.00
1.01
2.93
8.98


176.565
155.131
143.103
128.607
128.068
123.210
109.563
80.187
65.306
48.102
47.890
47.677
27.372
25.675
240
220
200
180
160
140
120
100
80
60
40
20
ppm