Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Molecular iodine mediated oxidative cleavage of C-N bond of aryl and heteroaryl (dimethylamino)methyl groups into aldehydes

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Experimental

General: Commercial reagents were purchased from Sigma–Aldrich and used without further purification. Solvents were distilled before use. Reactions were monitored by thin-layer chromatography (TLC Silica gel 60 F254 purchased from Merck). Flash chromatography was performed on Combi*Flash Rf* lumen instrument with silica gel (230–400 mesh). 1H NMR (400 MHz) and 13C NMR (100 MHz) were recorded with a Bruker Avance 400 MHz instrument using $CDCl_3$ and DMSO- d6 as solvent and TMS as an internal standard. Melting points are recorded with a Thiele apparatus and are uncorrected.

General procedure for preparation of aldehydes (2a – 2r): To the solution of (*N, N*-dimethylamino)methyl substrate (1mmol) dissolved in 2 mL of 1, 4-dioxane was added sodium carbonate (1.5 equiv) and iodine (1.1 equiv) and the reaction was stirred for 12 h at room temperature. After the completion of the reaction (checked on TLC), 5 mL water was added and the mixture was stirred for another 3 h. The aqueous layer was extracted using ethyl acetate. Organic layer was dried over sodium sulfate and concentrated on rotary evaporator. The crude sample was purified by flash chromatography in DCM: MeOH (20:0.3) solvent mixture.

1*H*-indole-3-carbaldehyde (2a): Pale yellow solid, yield: 81 %, m.p. 189 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 9.93 (s, 1H), 8.30 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.20 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 185.54, 138.93, 137.53, 124.59, 123.97, 122.64, 121.32, 118.65, 112.90. Spectral data is in accordance with the literature.[1]

1-methyl-1*H*-indole-3-carbaldehyde (2b): Pale brown solid, yield: 83 %, m.p. 72 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.92 (s, 1H), 8.27 – 8.30 (m, 1H), 7.60 (s, 1H), 7.33 – 7.30 (m, 3H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.80, 139.42, 137.88, 124.93, 123.71, 122.70, 121.98, 117.99, 111.96, 33.67. Spectral data is in accordance with the literature.[1]

1-benzyl-1*H*-indole-3-carbaldehyde (2c): White solid, yield: 78 %, m.p. 105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 8.35 – 8.31 (m, 1H), 7.70 (s, 1H), 7.36 – 7.25 (m, 6H), 7.17 (d, *J*= 8 Hz, 2H), 5.34 (s, 2H).^{13}C NMR (100 MHz, $CDCl_3$) δ 184.70, 138.60, 137.48, 135.32, 129.15, 128.42, 127.36, 125.51, 124.19, 123.11, 122.18, 118.50, 110.42, 50.94. Spectral data is in accordance with the literature.[1]

5-methoxy-1H-indole-3-carbaldehyde (2d): Pale pink solid, yield: 71 %, m.p. 179 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.03 (s, 1H), 9.90 (s, 1H), 8.22 (s, 1H), 7.57 (d, *J* = 2.8 Hz, 1H), 7.41 (d, *J* = 8.8 Hz, 1H), 6.90 – 6.87 (dd, *J* = 8.8, 2.6 Hz, 1H), 3.79 (s, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 184.30, 156.09, 138.89, 132.26, 125.36, 118.50, 113.76, 113.66, 102.94, 55.73. Spectral data is in accordance with the literature.[3]

6-chloro-1H-indole-3-carbaldehyde (2e): White solid, yield: 75 %, m.p. 205 °C. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.23 (s, 1H), 9.94 (s, 1H), 8.34 (s, 1H), 8.08 (d, J = 8 Hz, 1H), 7.58 (s, 1H), 7.26 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-*d6*) δ 190.49, 144.54, 142.71, 133.12, 128.07, 127.67, 127.30, 123.19, 123.15, 117.44. Spectral data is in accordance with the literature.[4]

5-nitro-1H-indole-3-carbaldehyde (2f): Yellow solid, yield: 79 %, m.p. 290 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.73 (s, 1 H), 10.03 (s, 1H), 8.94 (s, 1H), 8.58 (s, 1H), 8.17 (d, *J*= 8.8 Hz, 1H), 7.74 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.05, 143.32, 141.96, 140.60, 123.97, 119.50, 119.28, 117.53, 113.71. Spectral data is in accordance with the literature.[1]

2-methyl-1H-indole-3-carbaldehyde (2g): Yellow solid, yield: 43 %, m.p. 196 °C. ^{1}H NMR (400 MHz, DMSO-*d6*): δ 11.98 (br s, 1H), 10.06 (s, 1H), 8.03 – 8.05 (t, J = 6.8 Hz, 1H), 7.40 – 7.37 (m, 1H), 7.19 – 7.13 (m, 2H), 2.68 (s, 3H). ^{13}C NMR (100 MHz, DMSO-*d6*): δ 184.66, 148.97, 135.80, 126.05, 123.06, 122.31, 120.43, 114.10, 111.82, 11.92. Spectral data is in accordance with the literature.[3]

2-phenyl-1H-indole-3-carbaldehyde (2h): White solid, yield: 63 %, m.p. 252 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.44 (s, 1H), 9.96 (s, 1H), 8.22 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J*= 7.2, 2H), 7.66 – 7.54 (m, 3H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.24 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 186.04, 149.61, 135.36, 130.33, 130.20, 129.47, 126.20, 124.22, 122.95, 121.51, 113.91, 112.49. Spectral data is in accordance with the literature.[1]

3-formyl-1H-indole-5-carbonitrile (2i): Yellow solid, yield: 61 %, m.p. 259 °C. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.58 (s, 1H), 10.00 (s, 1H), 8.51 (s, 1H), 8.46 (s, 1H), 7.71 (d, *J*= 8.4 Hz, 1H), 7.65 – 7.63 (m, 1H) . ^{13}C NMR (100 MHz, DMSO-*d6*) δ 185.91, 140.76, 139.28, 126.89, 126.16, 124.40, 120.39, 118.45, 114.43, 104.85. Spectral data is in accordance with the literature.[3]

Ethyl 3-formyl-1H-indole-2-carboxylate (2j): White powder, yield: 68 %, m.p. 183 °C. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 12.84 (s, 1H), 10.62 (s, 1H), 8.26 (d, 1H, *J* = 8.0 Hz), 7.59 (d, 1H, *J* = 8.4), 7.38 – 7.42 (m, 1H), 7.28 – 7.32 (m, 1H), 4.42 – 4.48 (q, 2H, *J* = 6.8 Hz), 1.38 – 1.41 (t, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, DMSO-*d6*) d: 188.0, 160.6, 136.2, 133.2, 126.4, 125.2, 124.0, 122.8, 118.9, 113.6, 62.3, 14.5. Spectral data is in accordance with the literature.[3]

4-hydroxy-2-oxo-2H-chromene-3-carbaldehyde (2k): White crystals, yield: 35 %, m.p. 138 °C. ^{1}H NMR (400 MHz, DMSO-*d6*), δ 10.34 (s, 1H), 10.00(s, 1H), 8.32 (d, *J*= 8.4, 1 H), 7.76 – 7.72 (t, *J*= 7.2, 1 H), 7.36 – 7.42 (m 2H). ^{13}C NMR (100 MHz, DMSO-*d6*): δ 191.07, 162.47, 158.31, 154.34, 135.42, 125.26, 124.72, 117.96, 114.04, 95.46. Spectral data is in accordance with the literature.[2]

Thiophene-2-carboxaldehyde (2l): Yellow liquid, yield: 59 %. ^{1}H NMR (400 MHz, CDCl3), δ 9.84 (s, 1H), 7.70 (d, *J*= 3.6, 1 H), 7.68 (d, *J*= 4.8, 1 H), 7.13 – 7.11 (t, *J*= 4.8, 2H). ^{13}C NMR (100 MHz, CDCl3): δ 183.14, 143.94, 136.59, 135.23, 128.43. Spectral data is in accordance with the literature.[8]

2-hydroxy-1-naphthaldehyde (2l): Yellow solid, yield: 56 %, m.p. 80 °C. ^{1}H NMR (400 MHz, CDCl3), δ 13.15 (s, 1H), 10.76 (s, 1H), 8.33 (d, *J*= 8.8 Hz, 1H,), 7.78 (d, *J*= 9.2 Hz, 1H,), 7.61 (d, *J*= 8 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.44 – 7.40 (m, 1H), 7.12 (d, *J*= 9.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.31, 164.93, 139.18, 132.87, 129.50, 129.14, 127.79, 124.53, 119.18, 118.61, 111.27. Spectral data is in accordance with the literature.[5]

3,4-dimethoxybenzaldehyde (2m): Off white solid, yield: 67 %, m.p. 46 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.86 (s, 1 H), 7.48 (d, *J* = 7.6 Hz, 1 H), 7.42 (s, 1 H), 7.00 (d, *J* = 8.4 Hz, 1 H), 3.98 (s, 3 H), 3.95 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.96, 154.49, 149.61, 130.12, 126.93, 110.37, 108.89, 56.19, 56.01 ppm. Spectral data is in accordance with the literature.[6]

2,3,4-trimethoxybenzaldehyde (2n): Colorless oil, yield: 64 %, b.p. 168 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.24 (s, 1 H), 7.61 (d *J*= 8.8 Hz, 1 H), 6.77 (d *J*= 8.8 Hz, 1 H), 4.04 (s, 1 H), 3.94 (s, 1 H), 3.89 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.87, 159.30, 156.94, 141.58, 124.23, 123.31, 107.40, 62.35, 60.98, 56.20 ppm. Spectral data is in accordance with the literature.[7]

3-methoxybenzaldehyde (2o): Colorless oil, yield: 59 %, b.p. 229 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.98 (s, 1H), 7.46-7.43 (m, 2H), 7.39 (s, 1H), 7.19-7.16 (m, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.23, 160.15, 137.79, 130.05, 123.57, 121.25, 112.05, 55.48. Spectral data is in accordance with the literature.[7]

Benzophenone (2p): White solid, yield: 89 %, m.p. 52 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.0 Hz, 4H), 7.60 (t, *J* = 7.3 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 137.6, 132.5, 130.1, 128.3. Spectral data is in accordance with the literature.[7]

Acetophenone (2q): Colorless oil, yield: 53 %, b.p. 200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 2.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.26, 137.10, 133.14, 128.59, 128.32, 26.63. Spectral data is in accordance with the literature.[7]

All copies of spectra:

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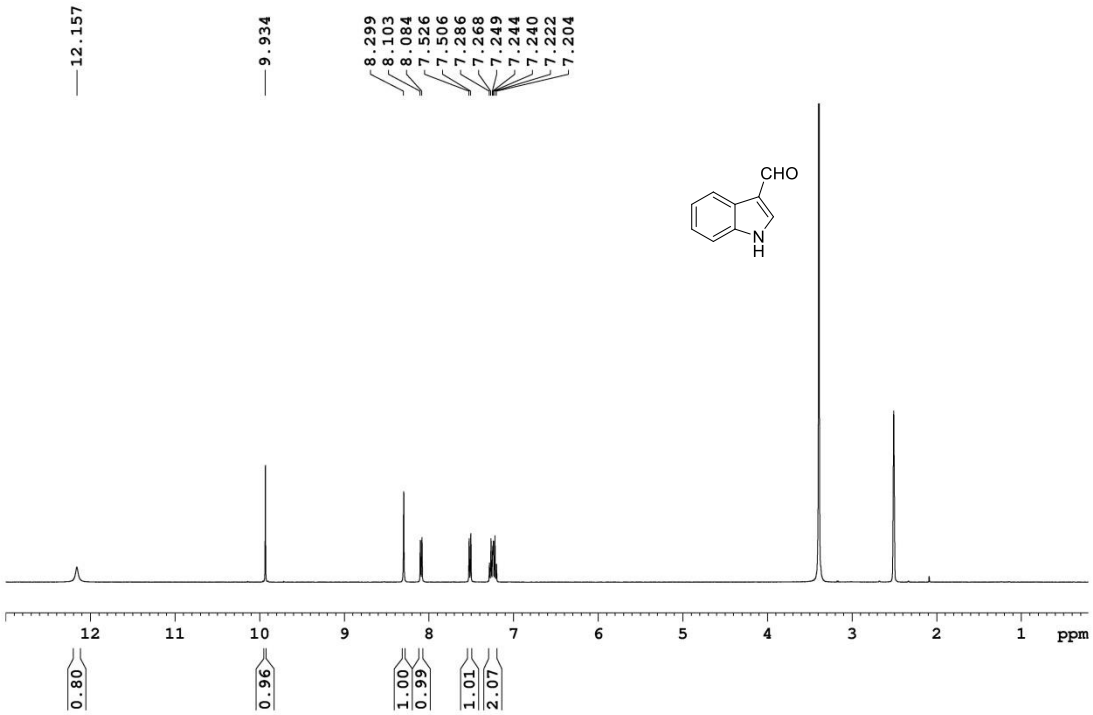

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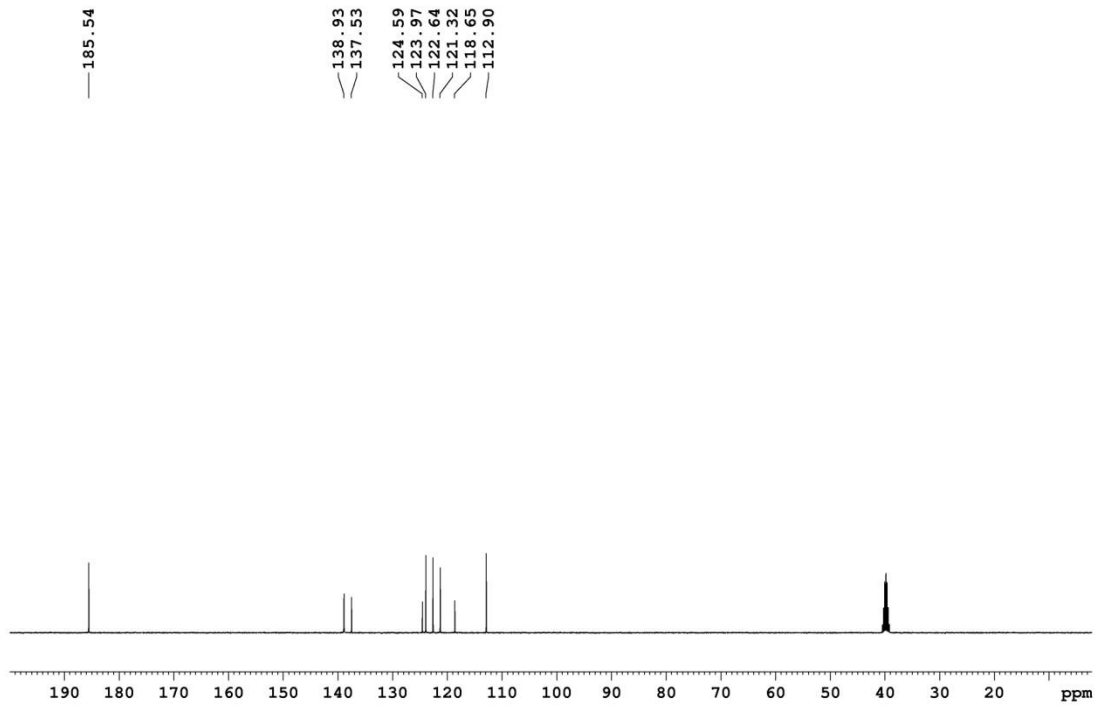

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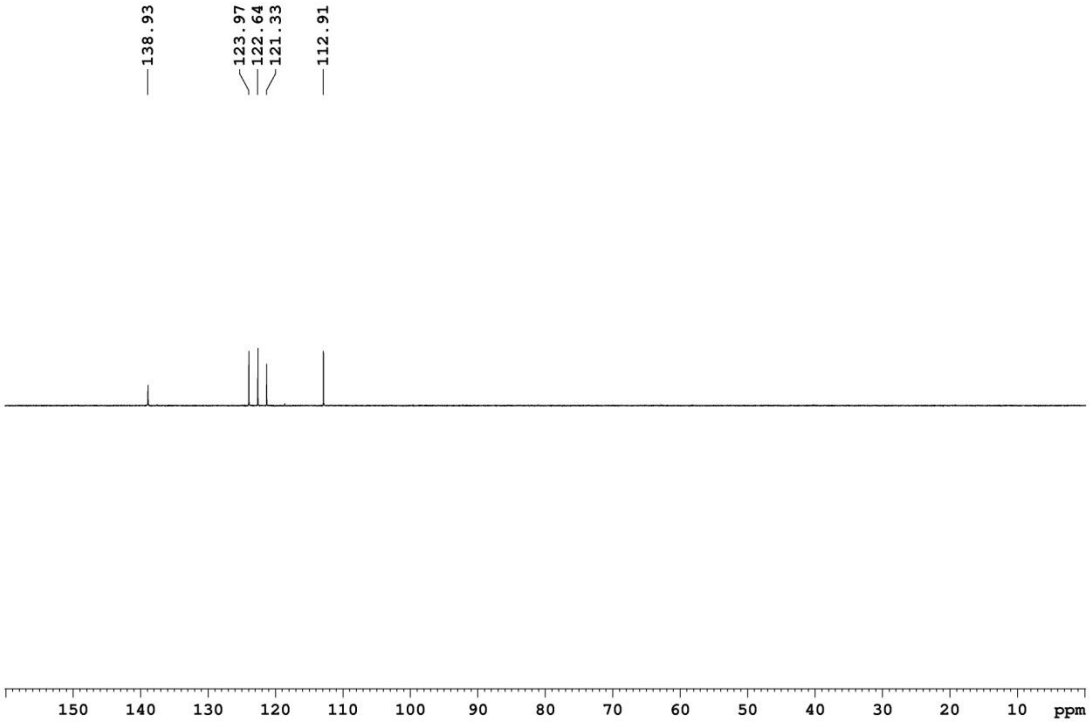

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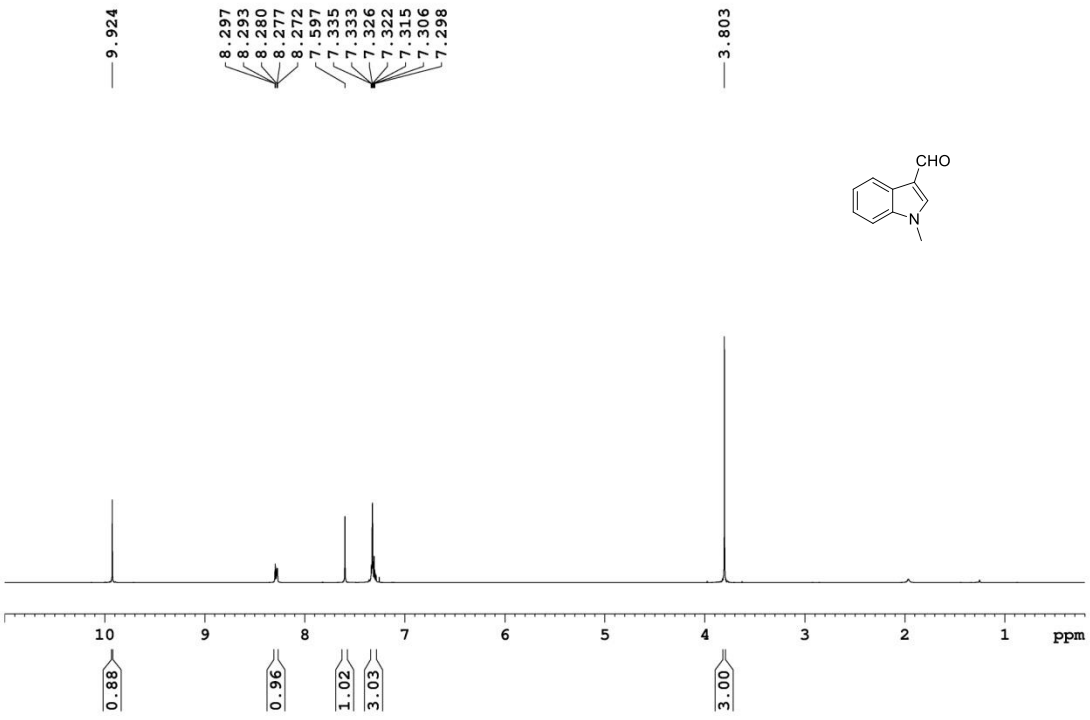

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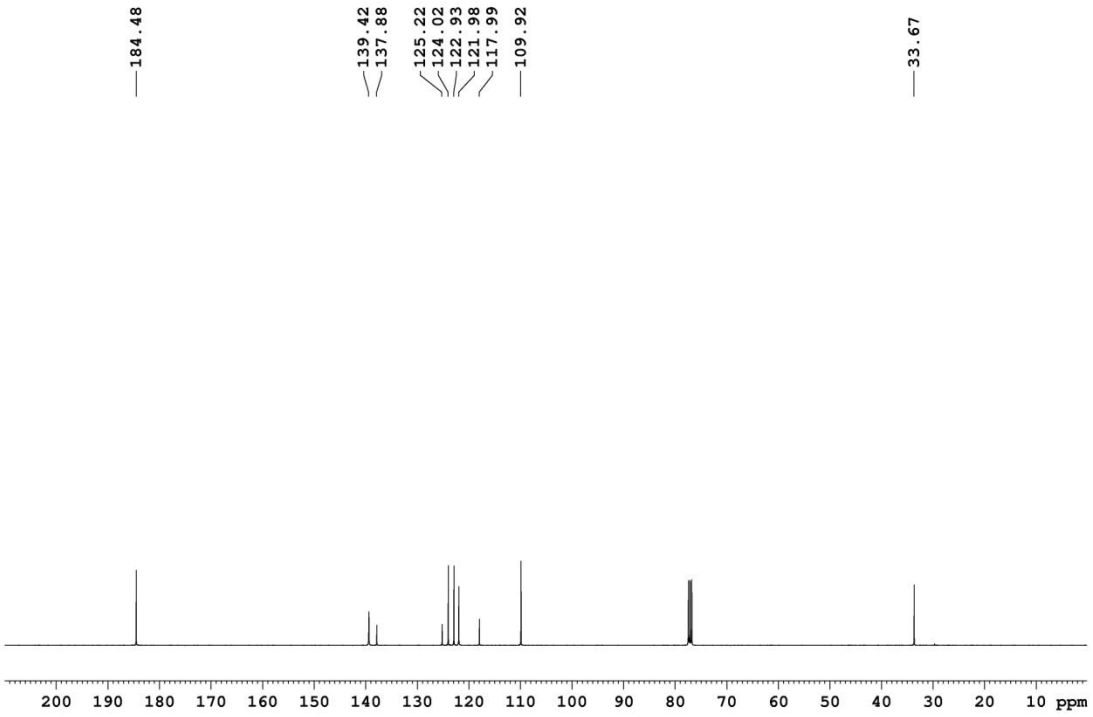

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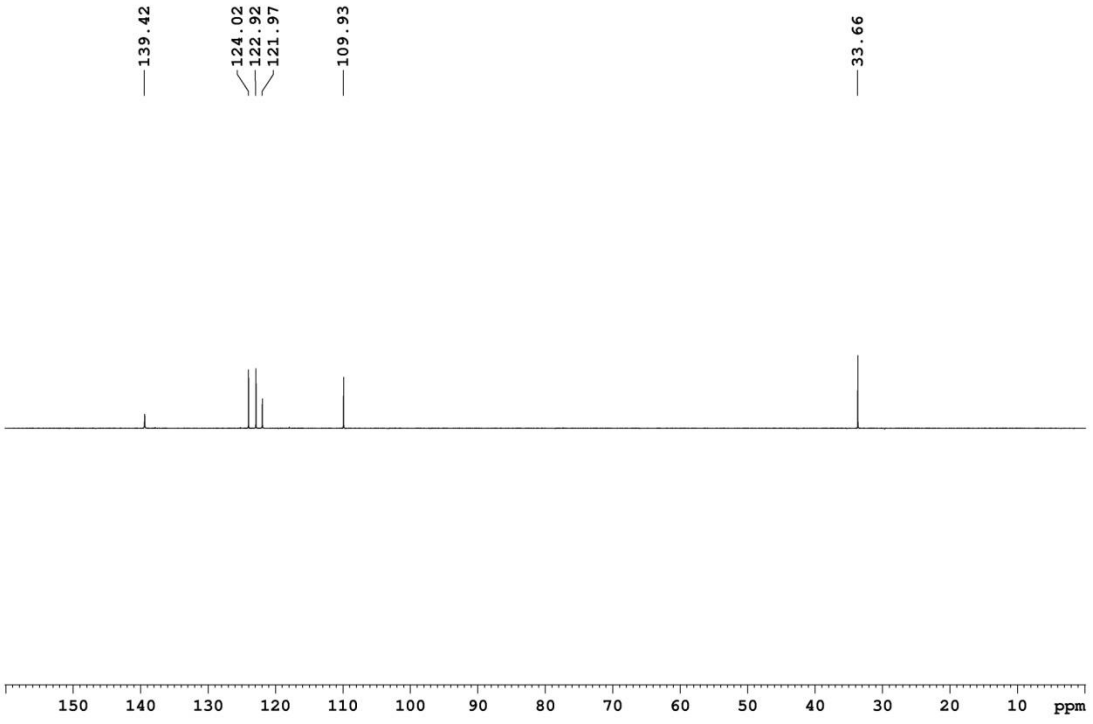

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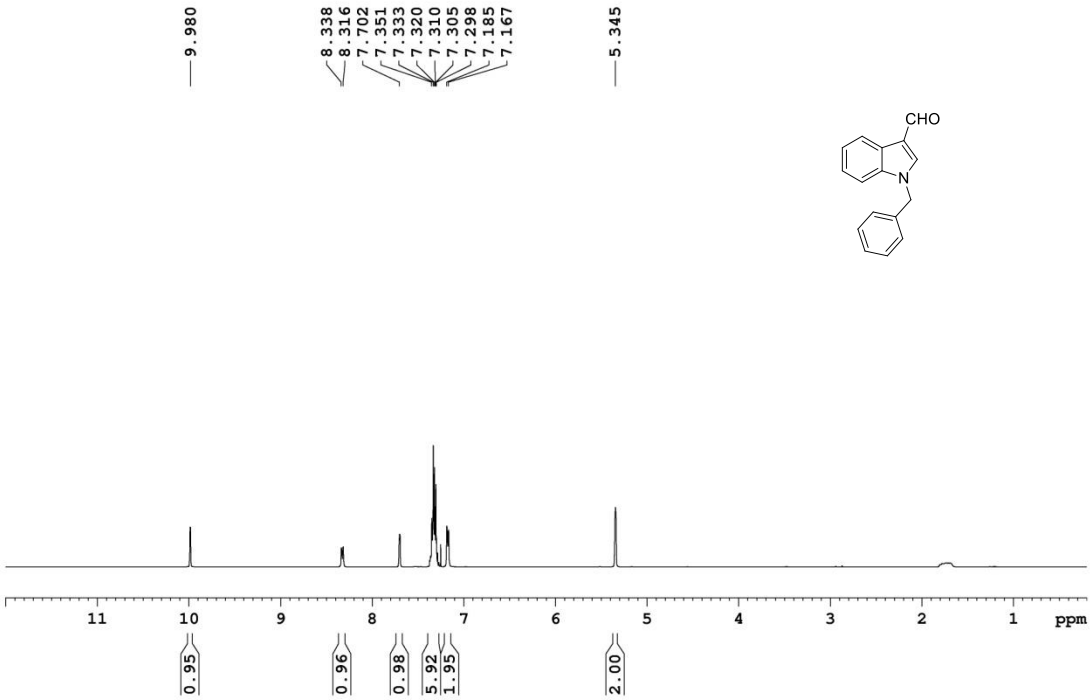

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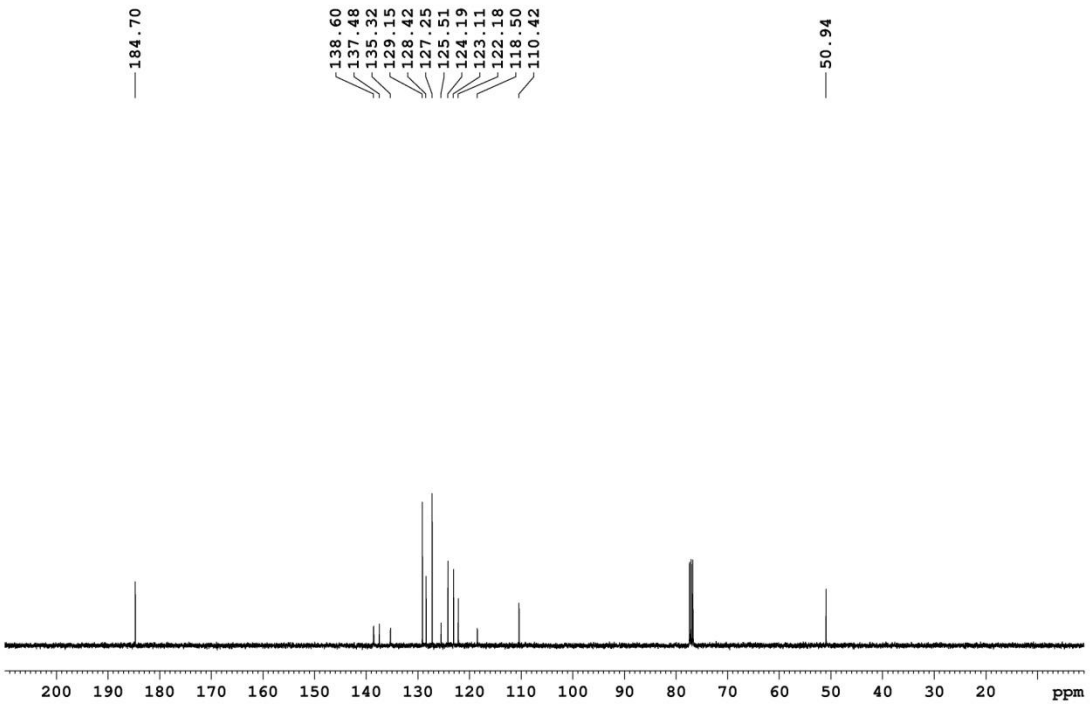

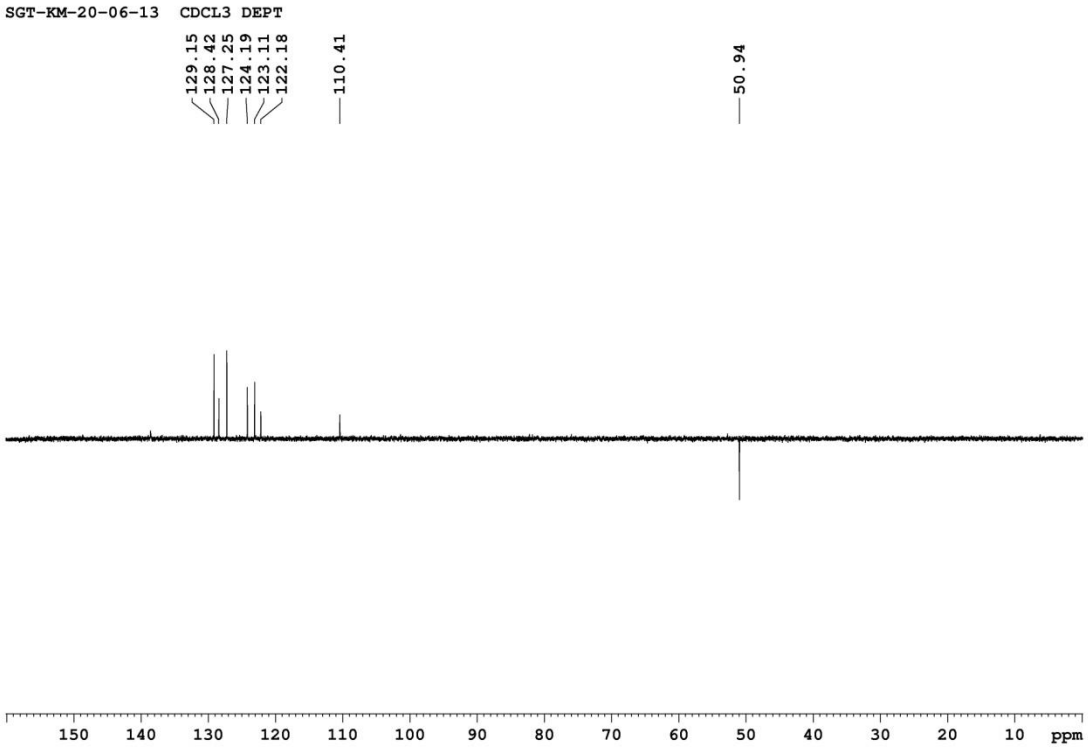
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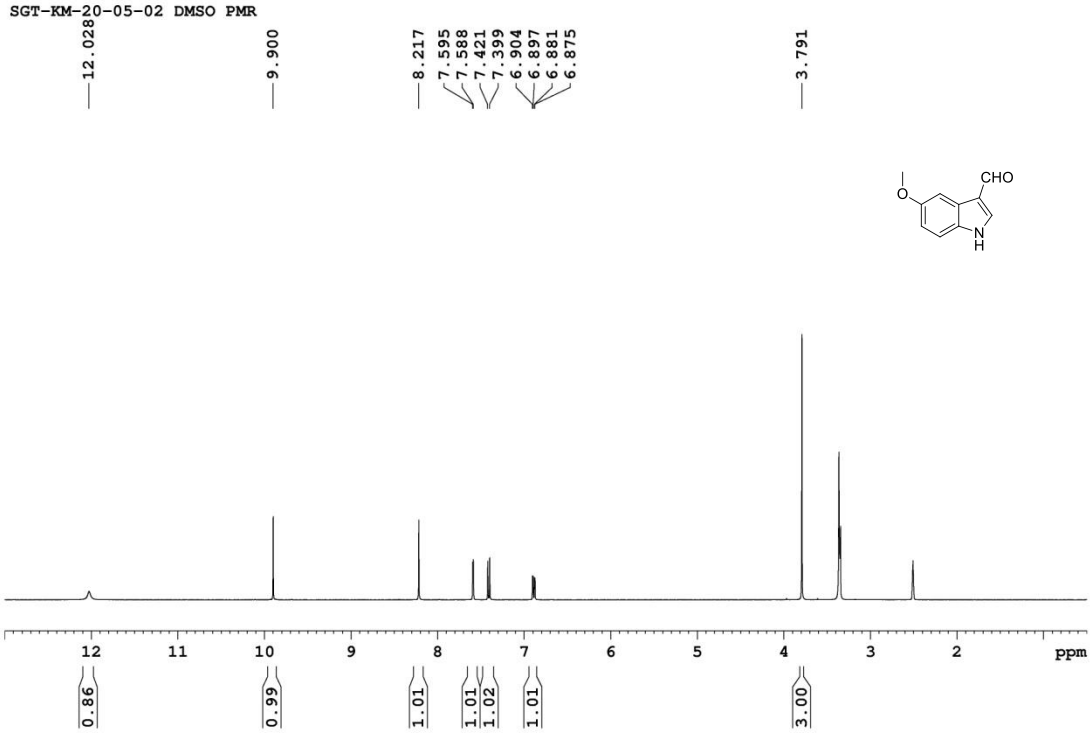
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6.875
3.791
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O
N
H
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1.01
1.02
1.01
3.00

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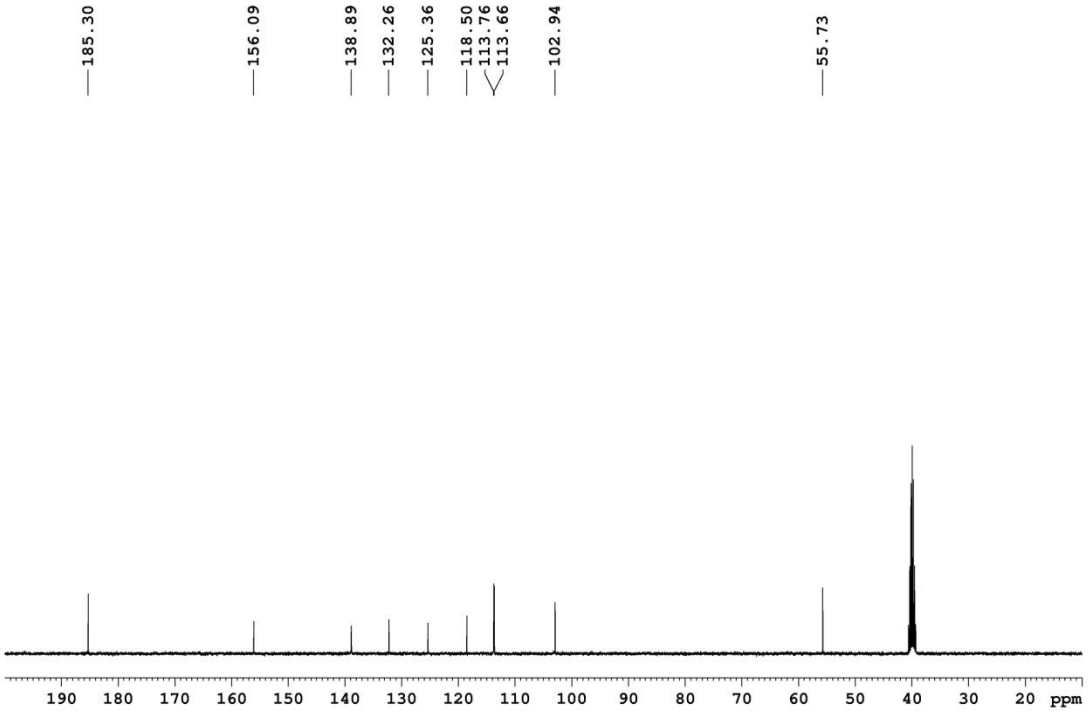

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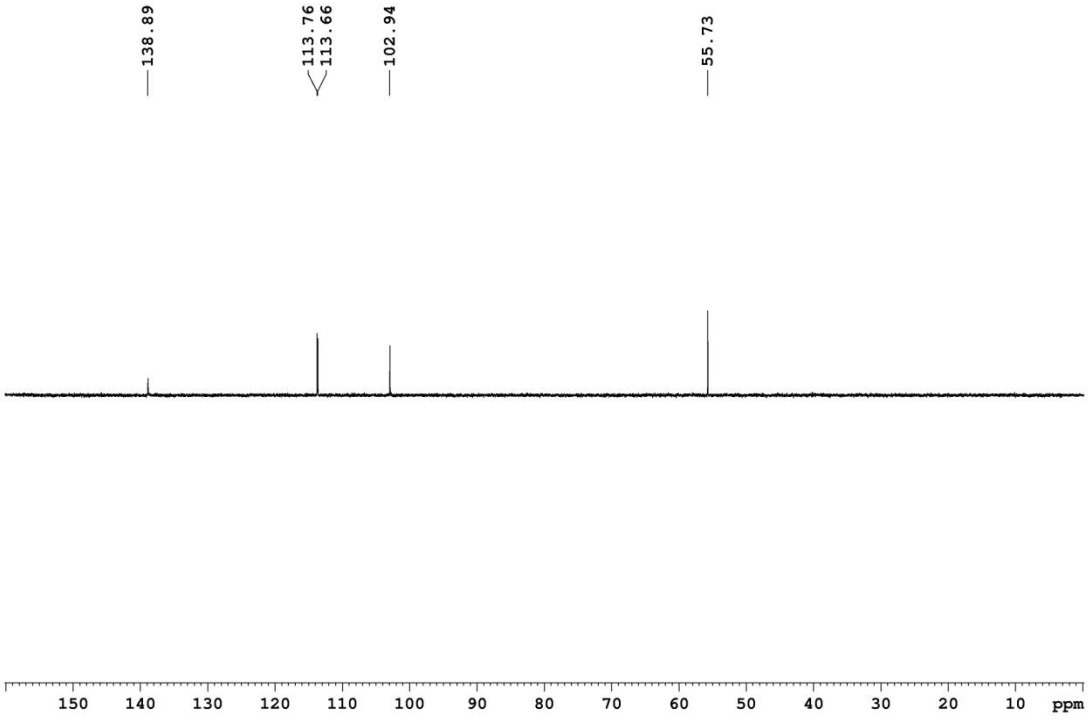

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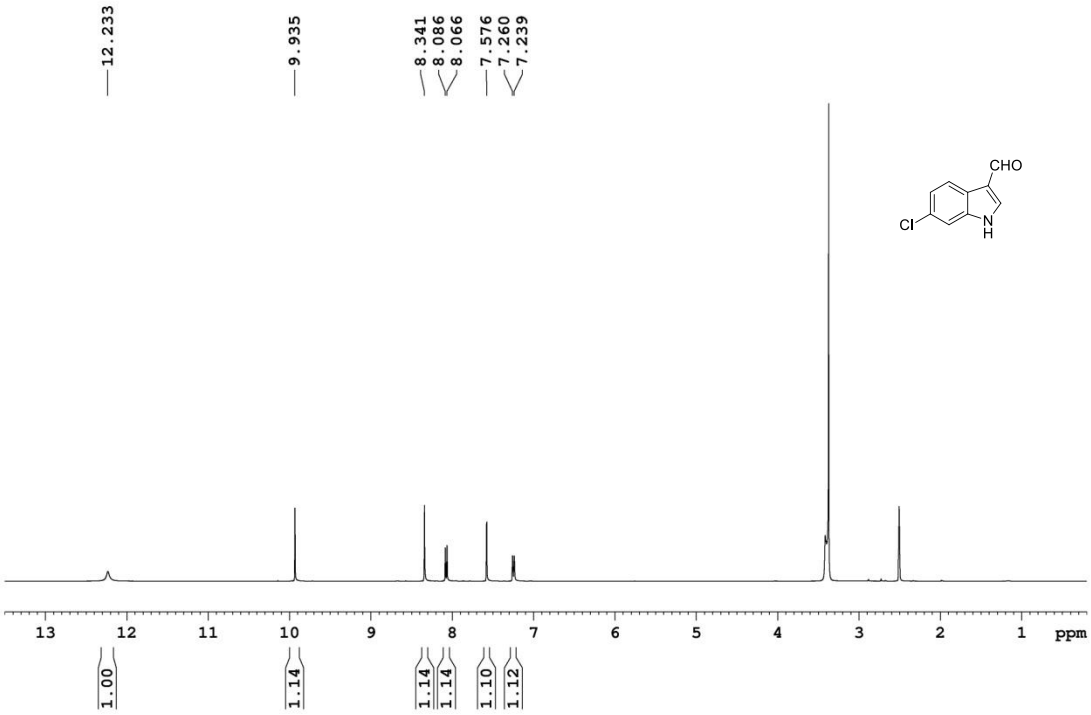

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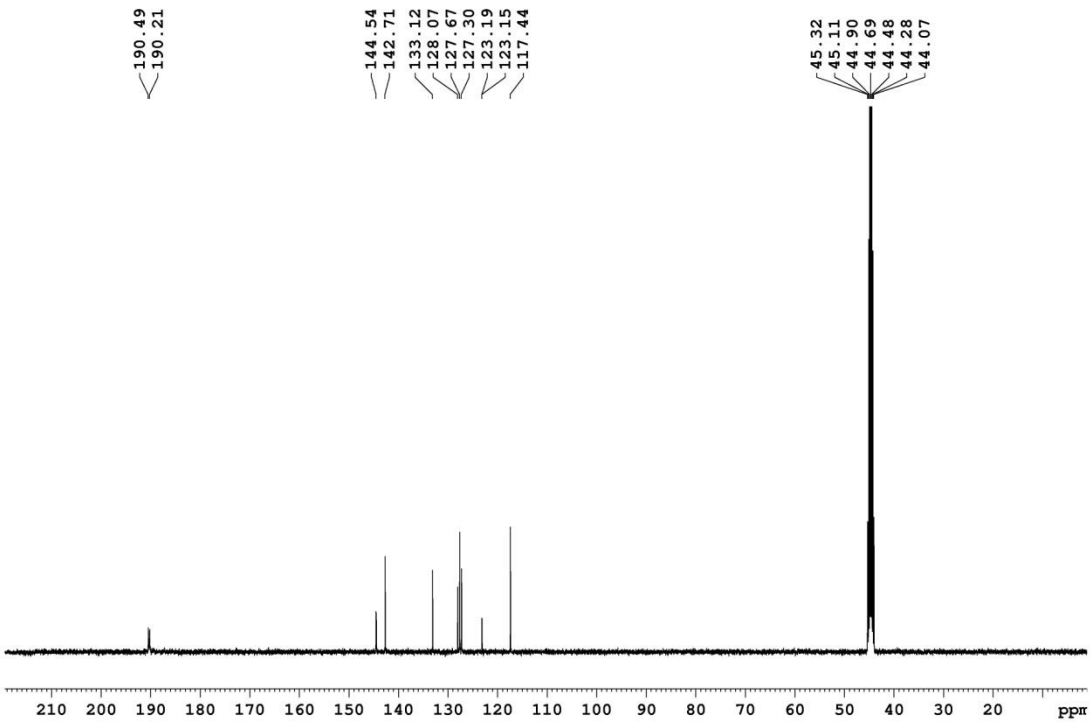

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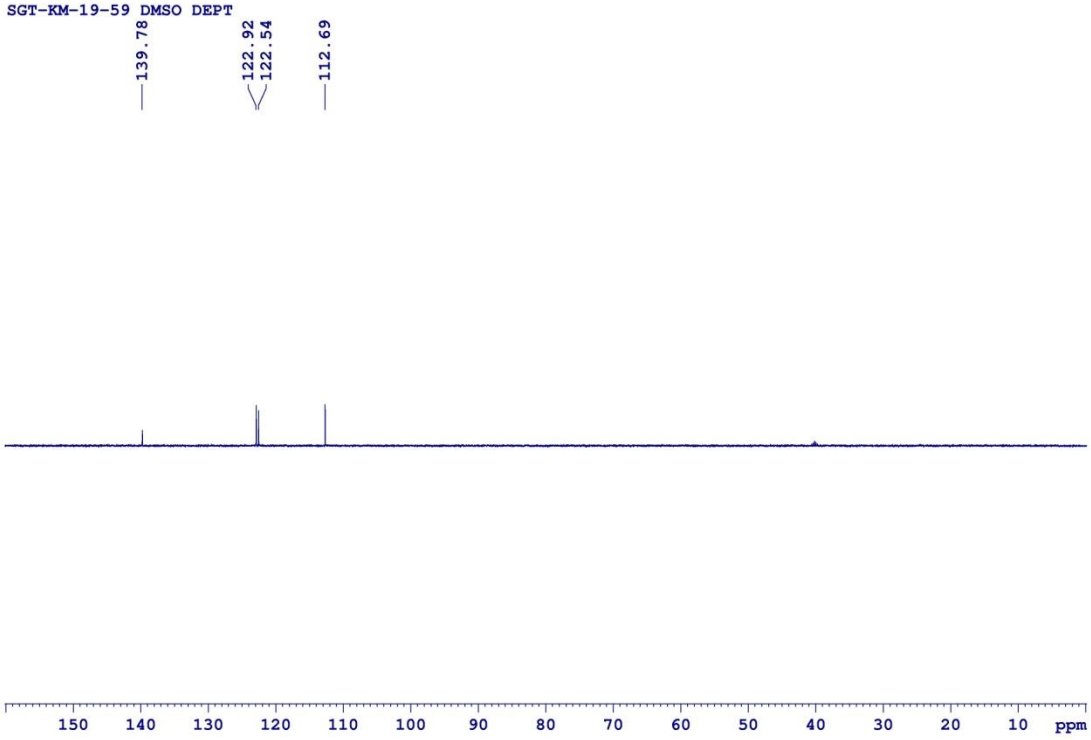

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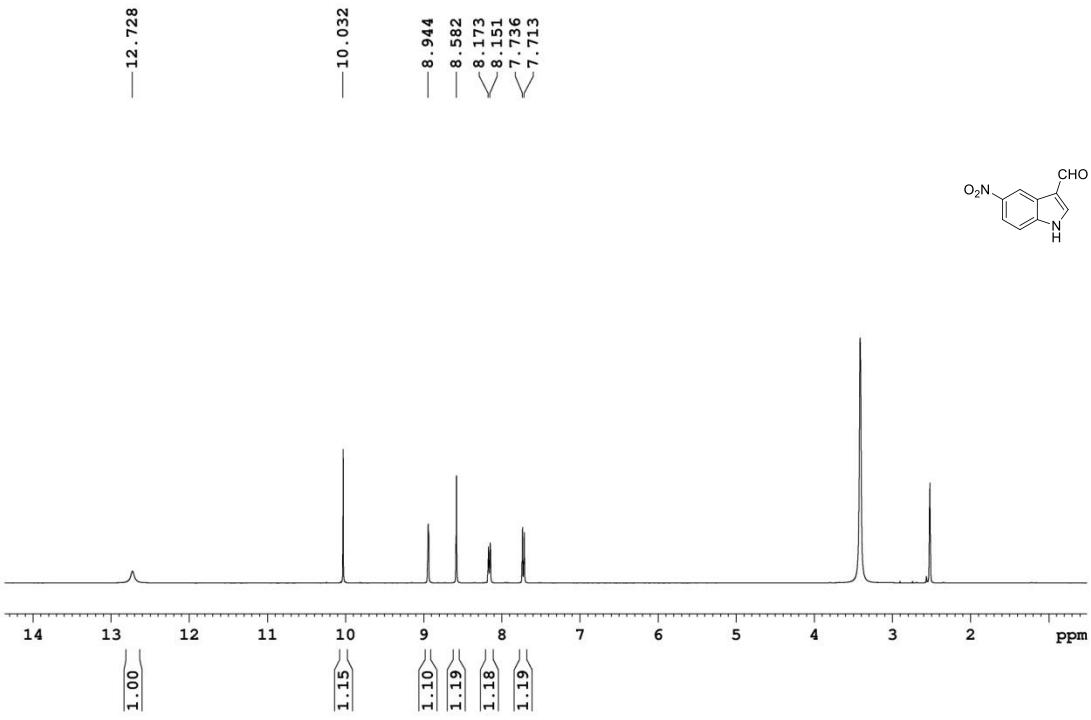

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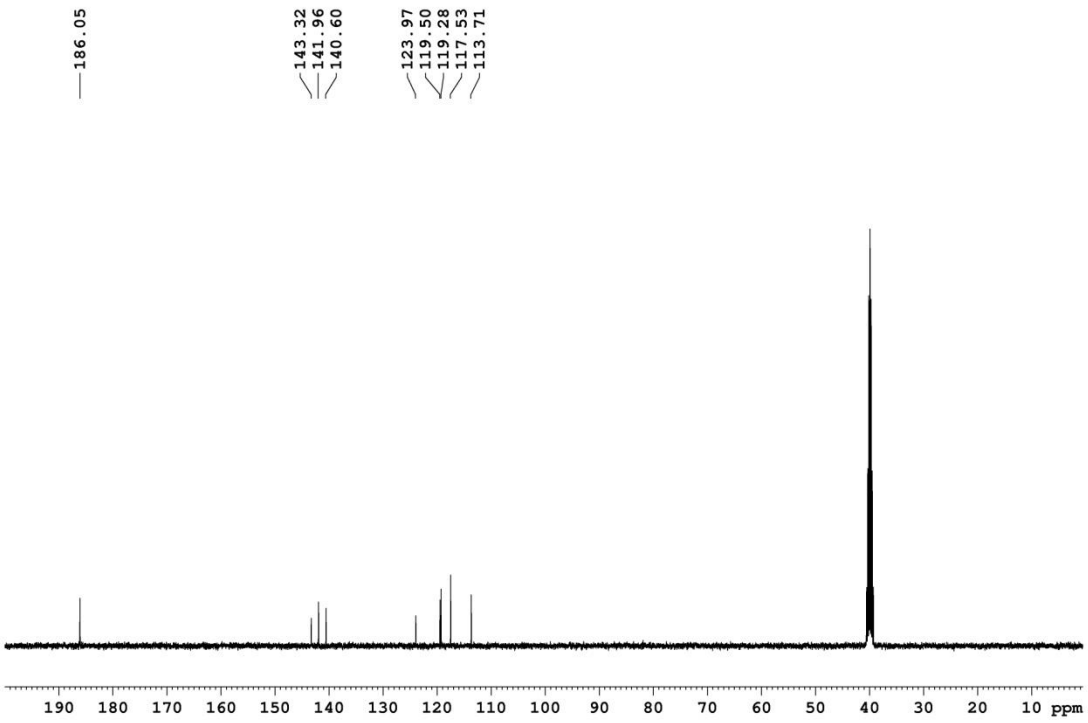

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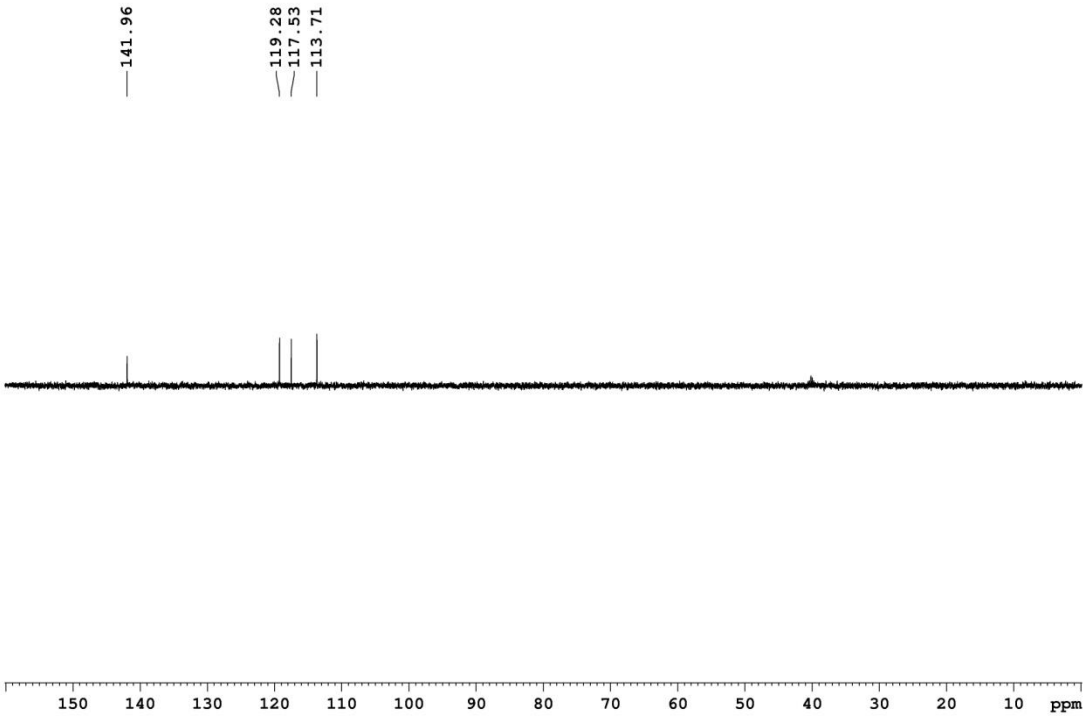

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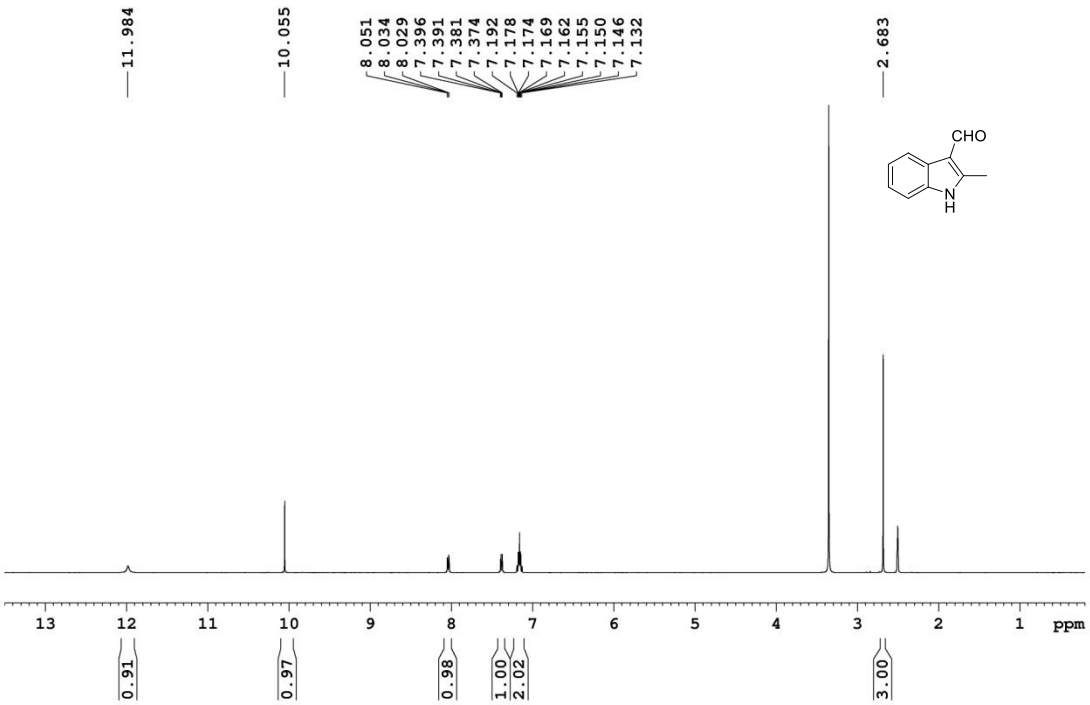

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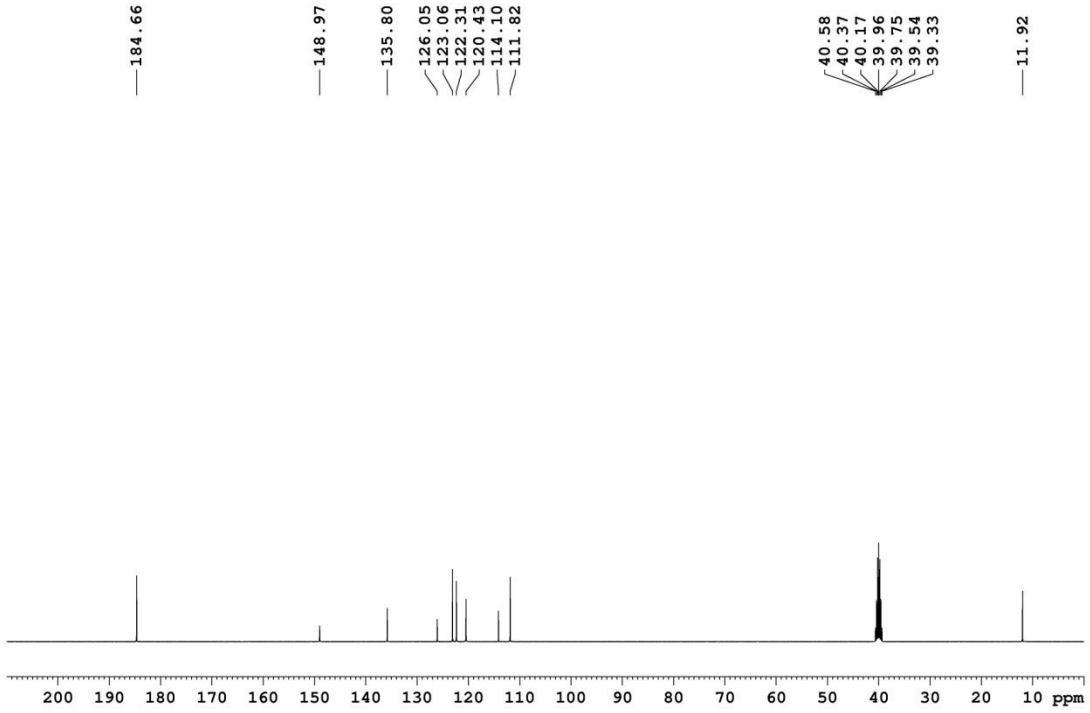

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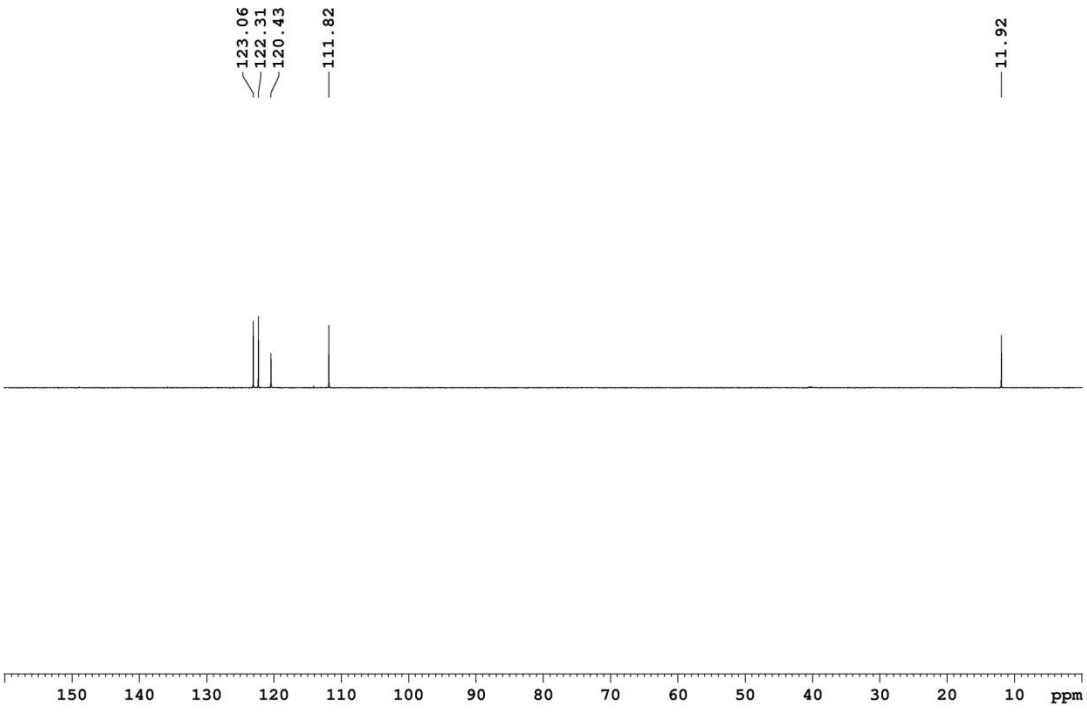

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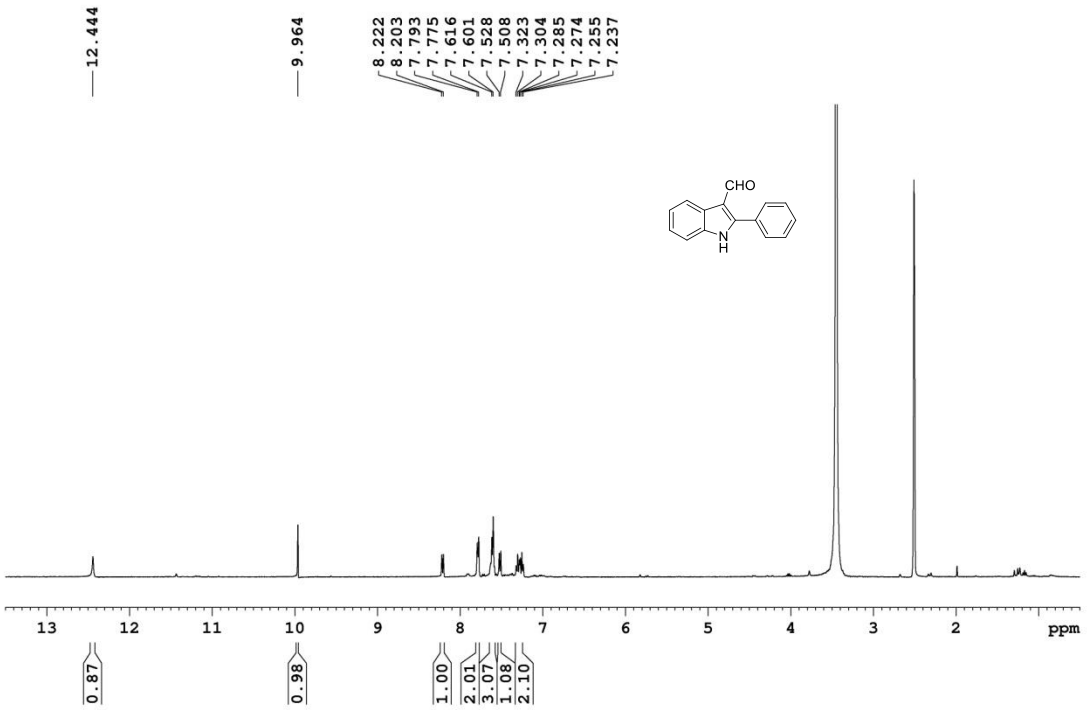

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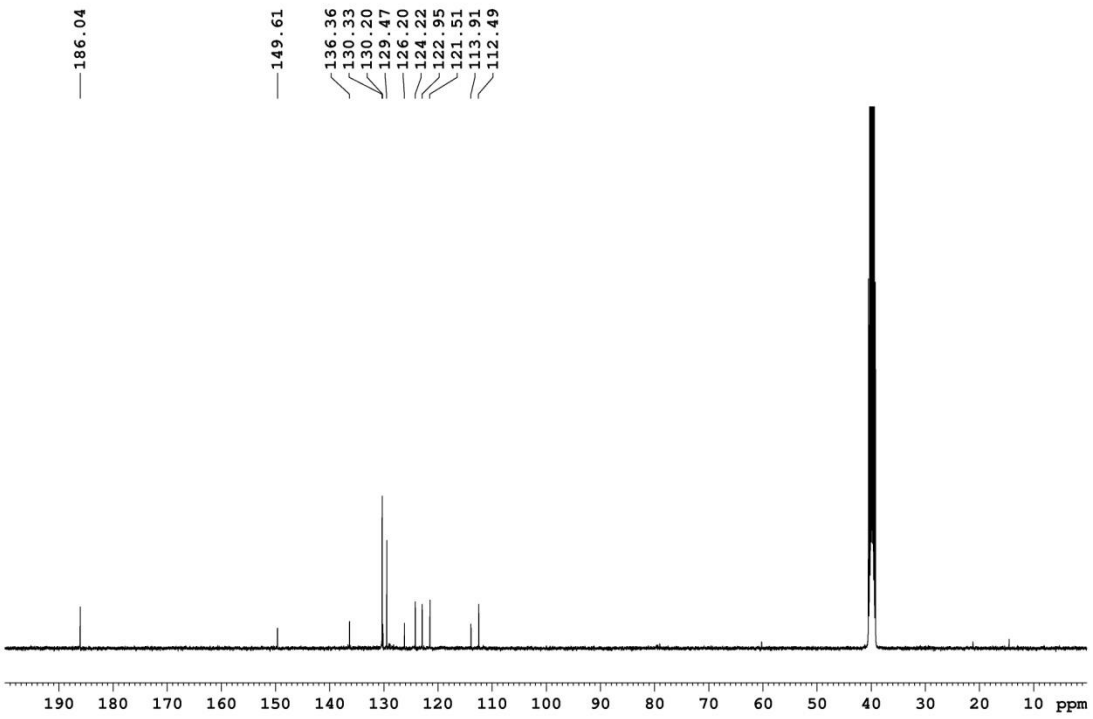

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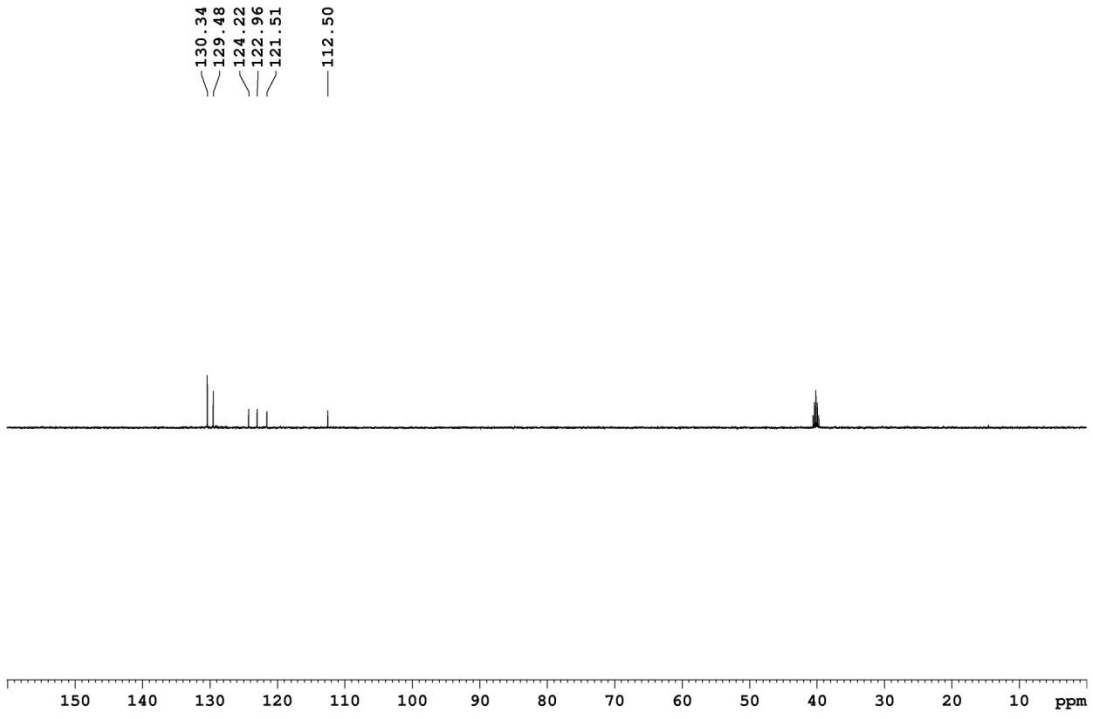

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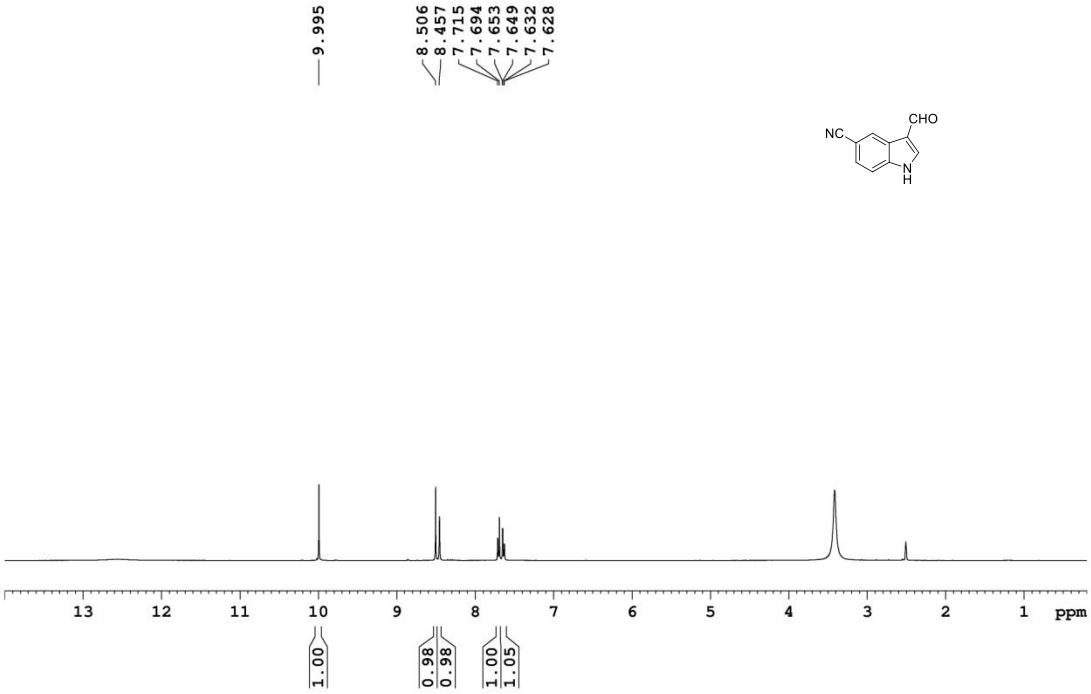

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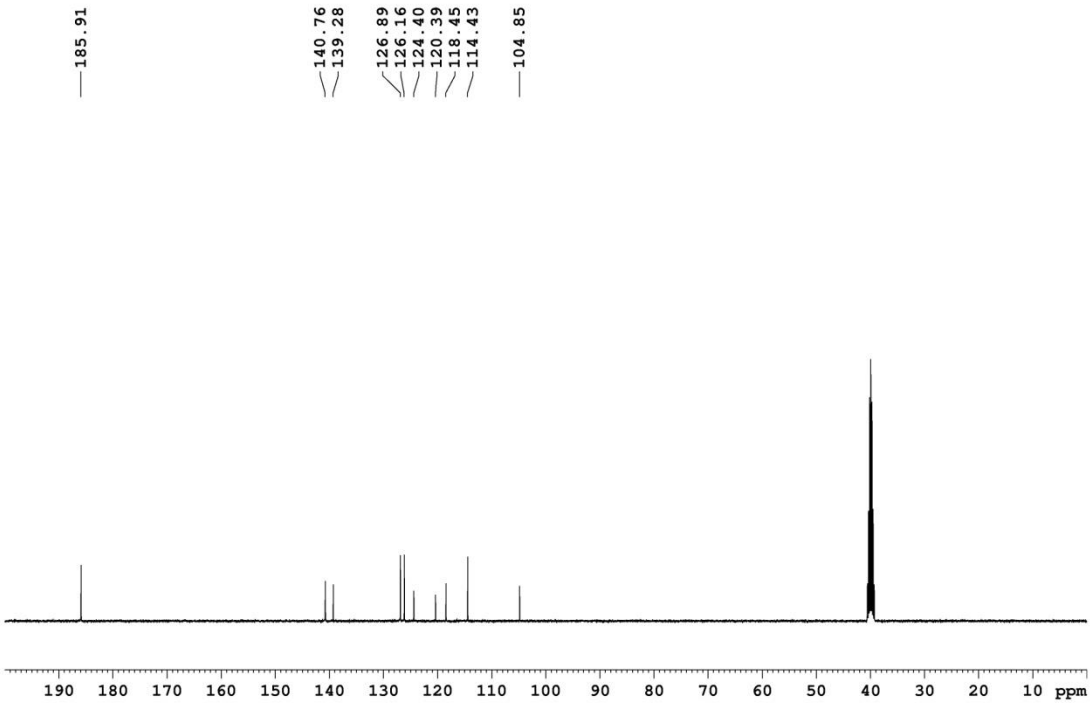

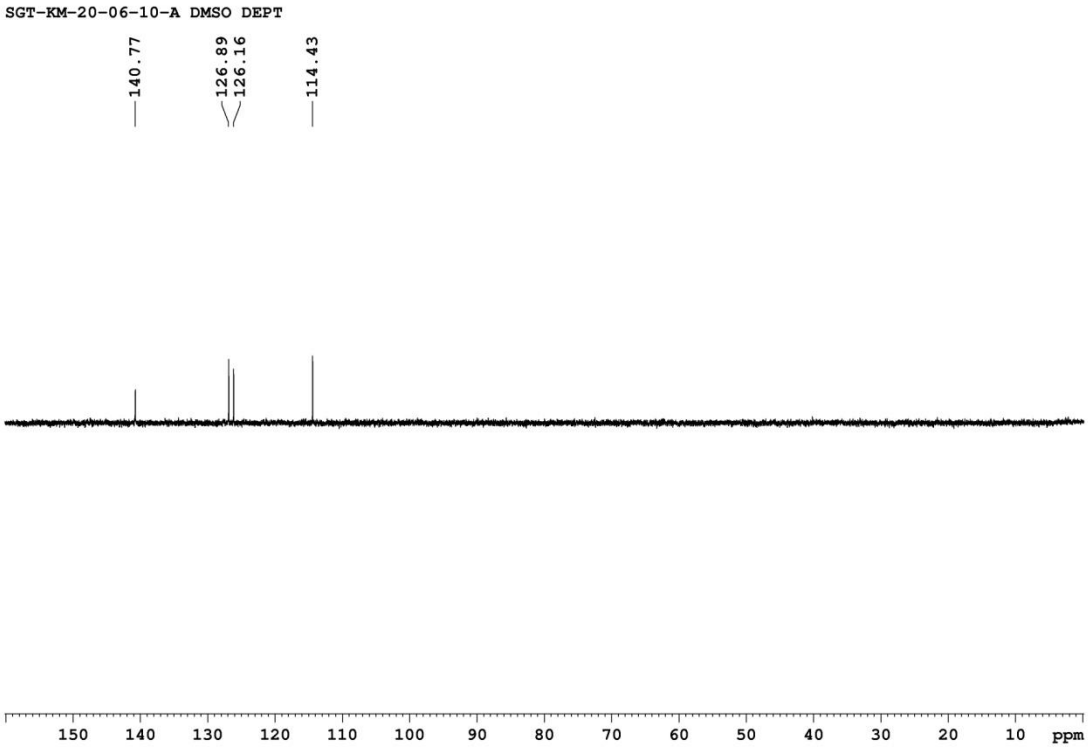
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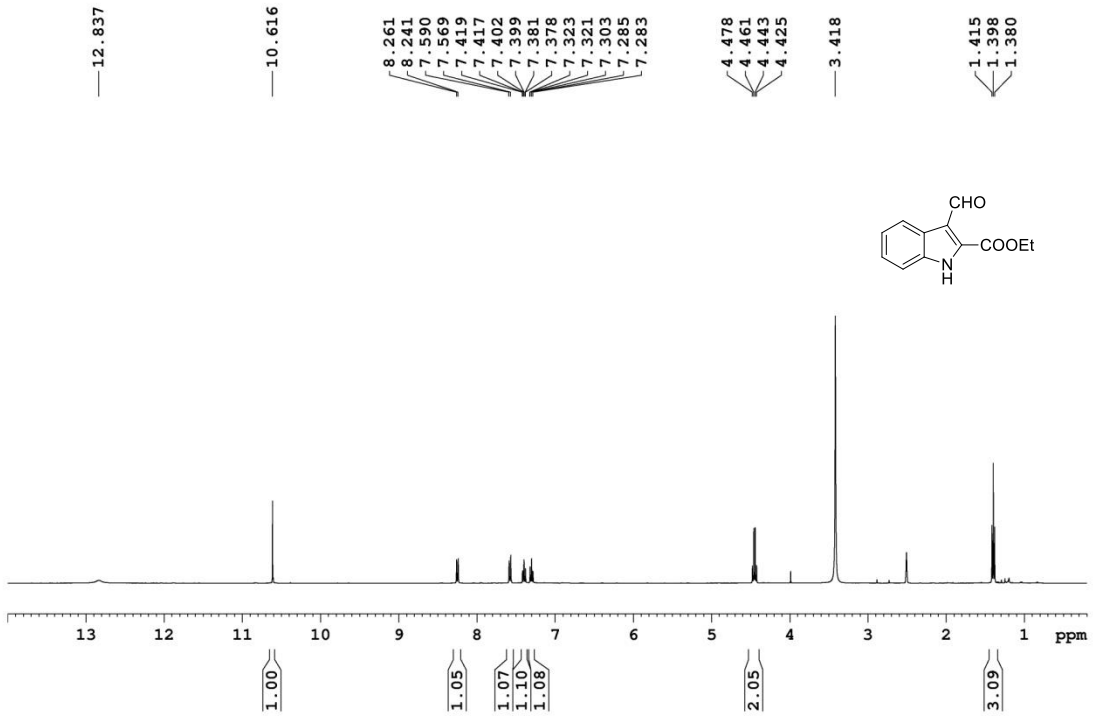
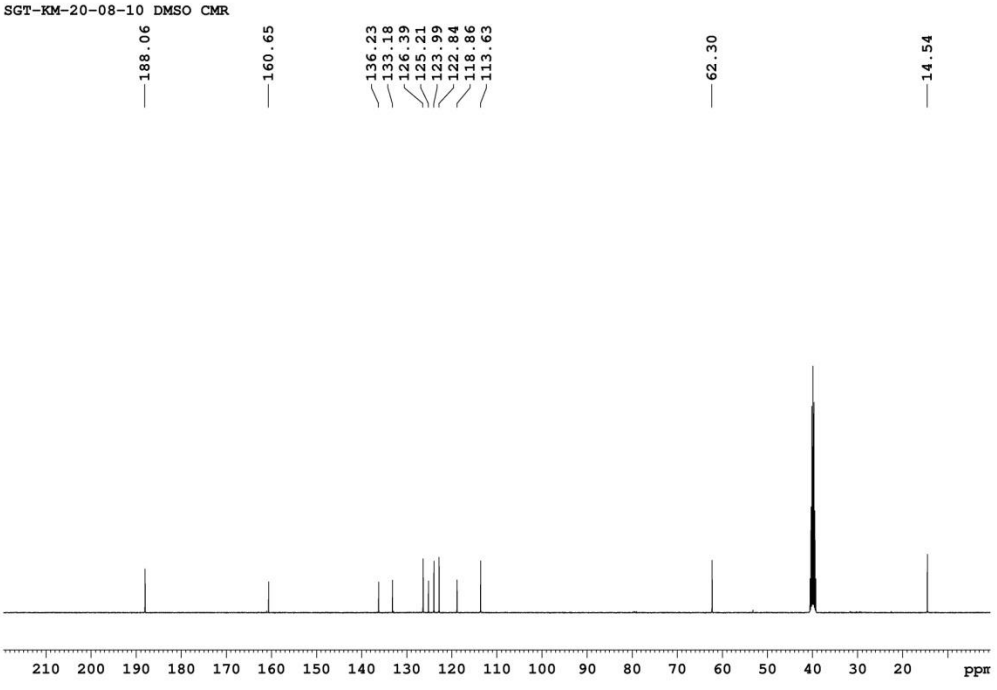
126.16
114.43
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

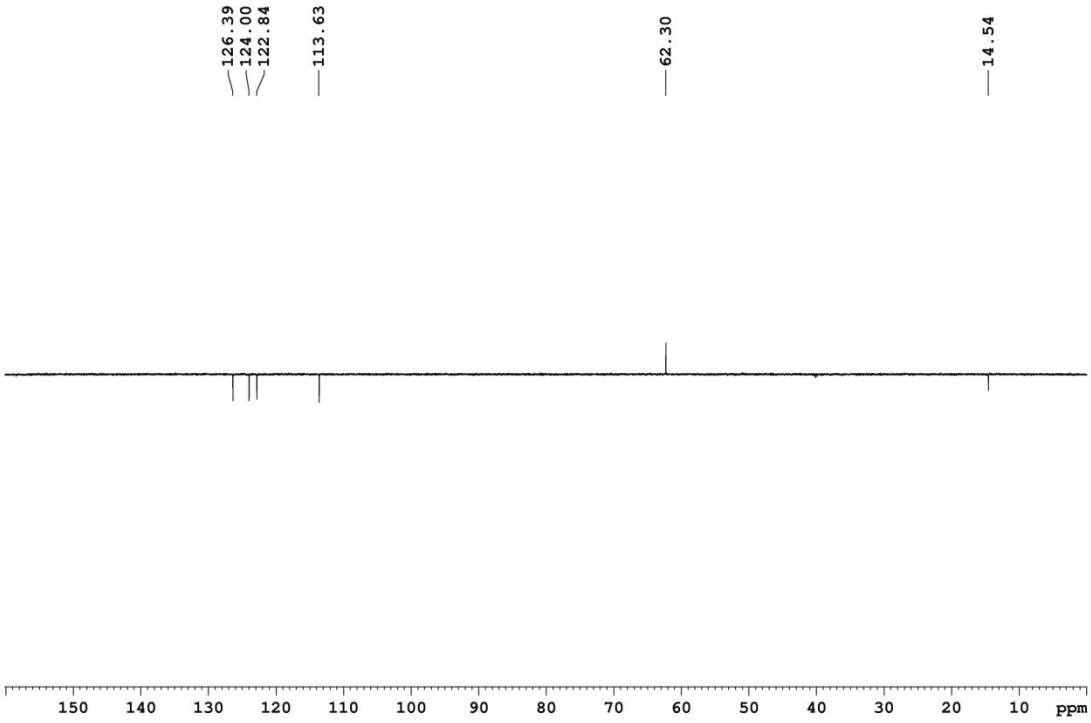
SGT-KM-20-08-10 DMSO PMR



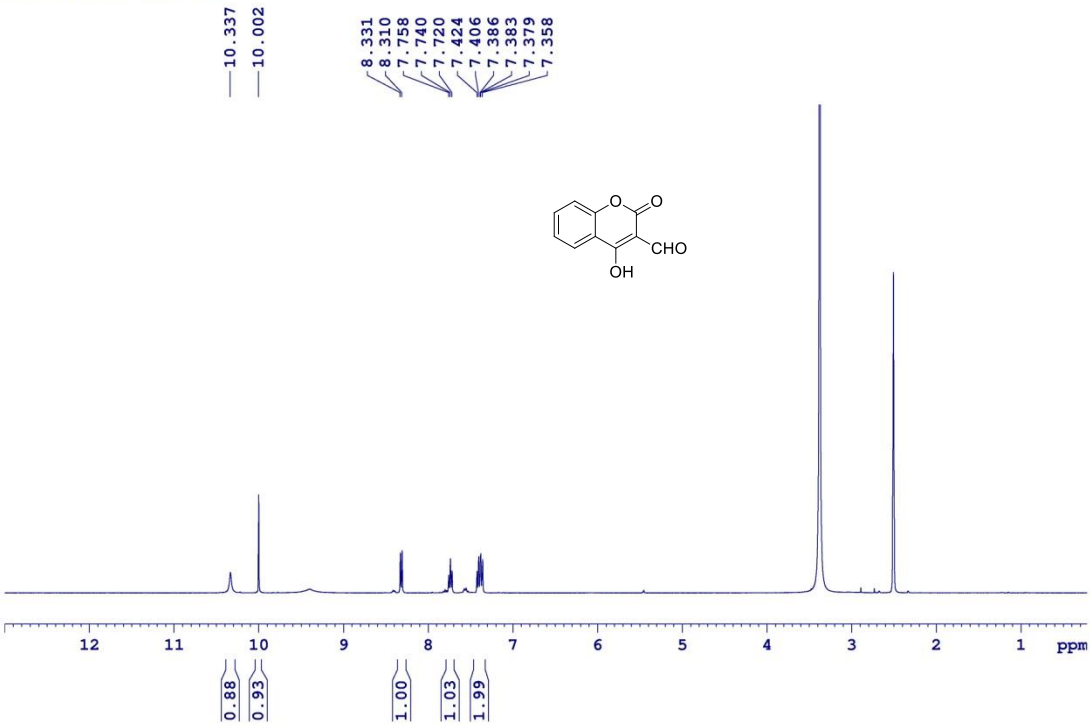
SGT-KM-20-08-10 DMSO CMR



SGT-KM-20-08-10 DMSO DEPT



SGT-KM-19-62 DMSO PMR



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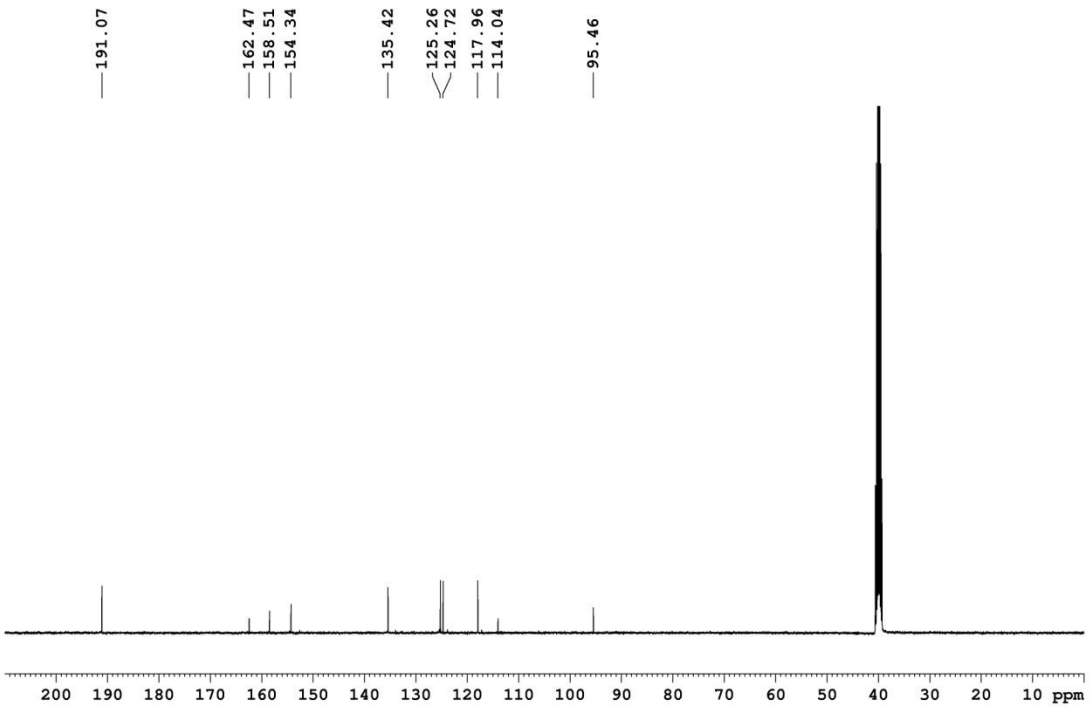
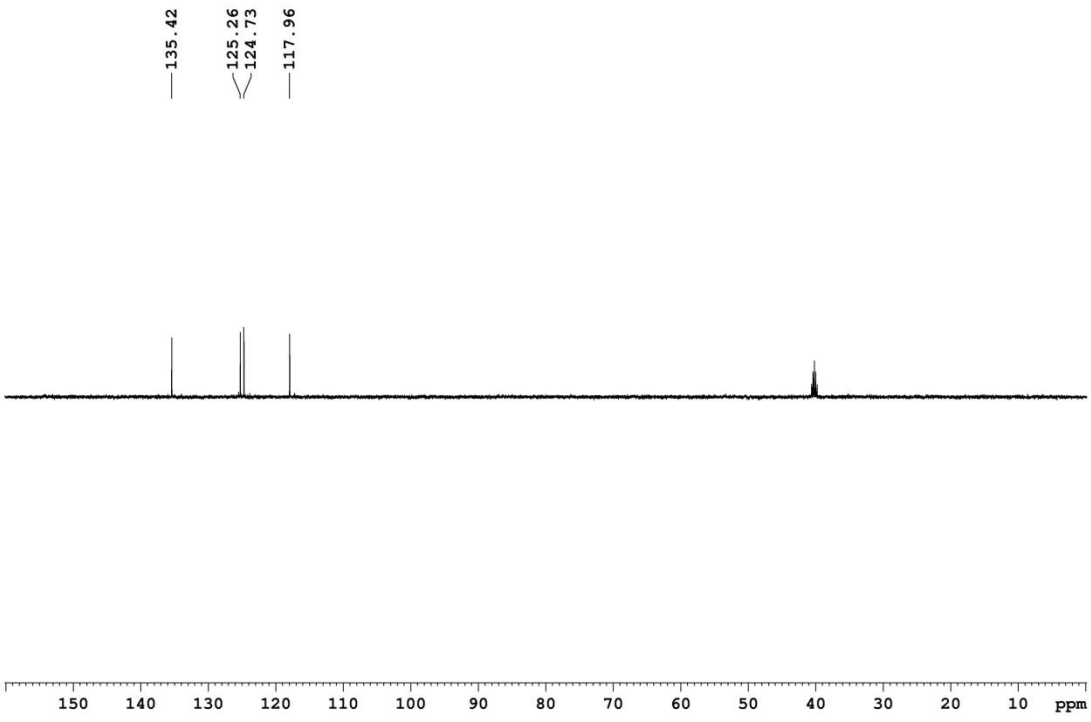
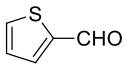
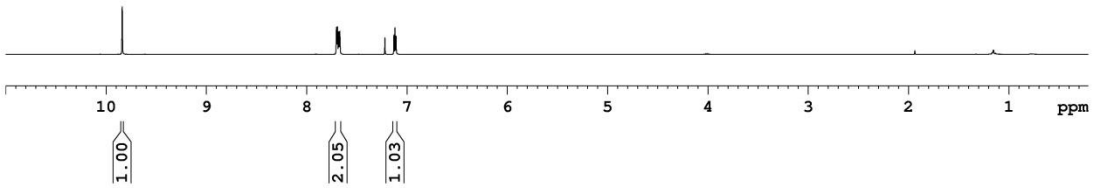


SGT-KM-19-62 DMSO DEPT

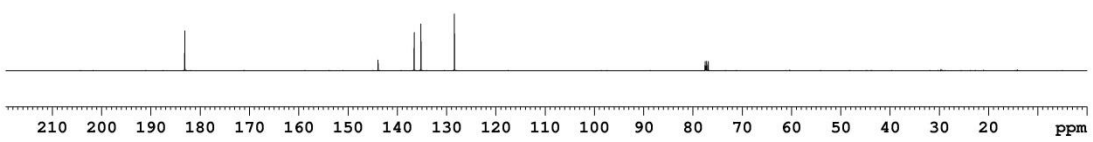


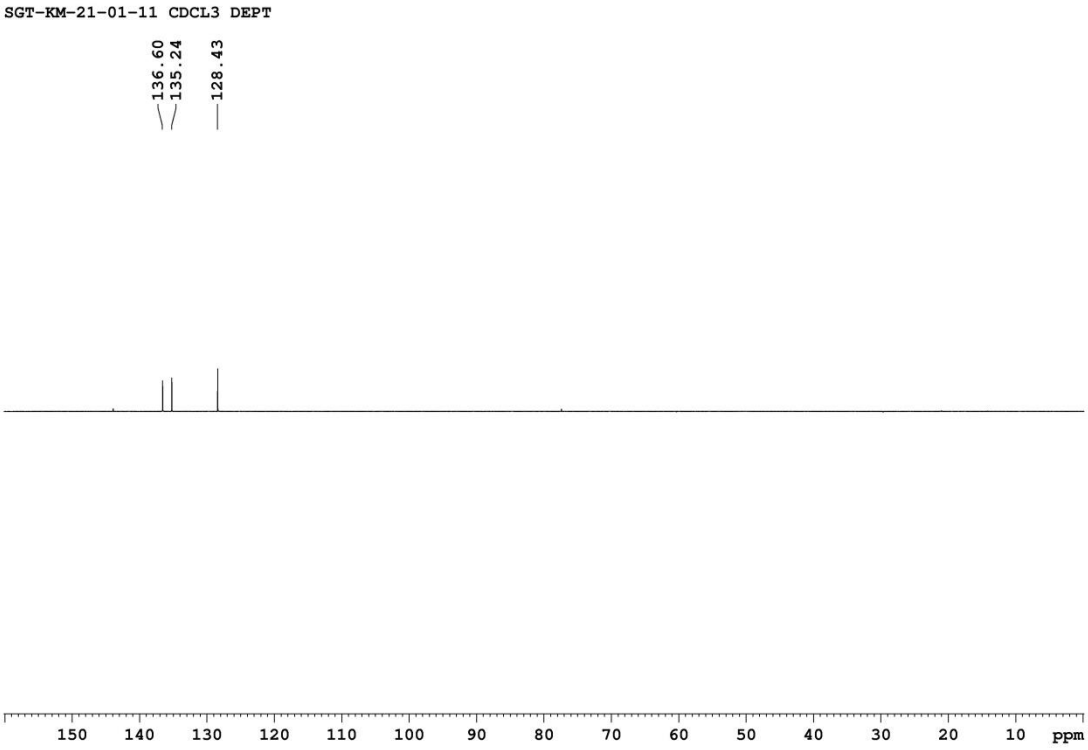
SGT-KM-21-01-11 CDCL3 PMR



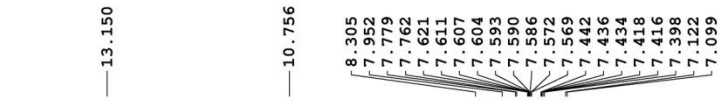


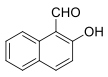
SGT-KM-21-01-11 CDCL3 CMR

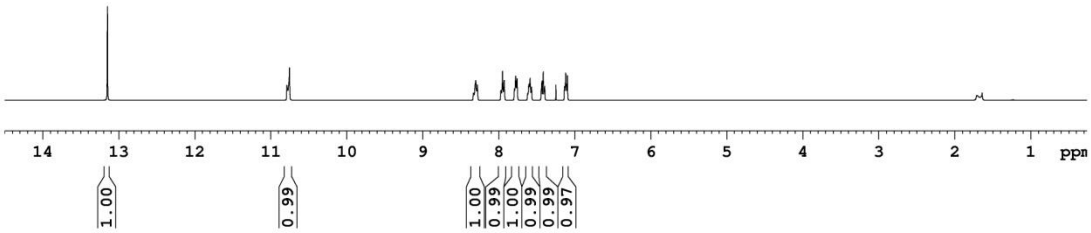



SGT-KM-21-01-11 CDCL3 DEPT
136.60
135.24
128.43
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

SGT-KM-20-06-12 CDCL3 PMR







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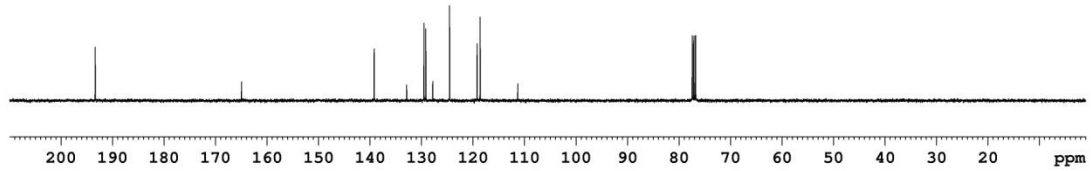

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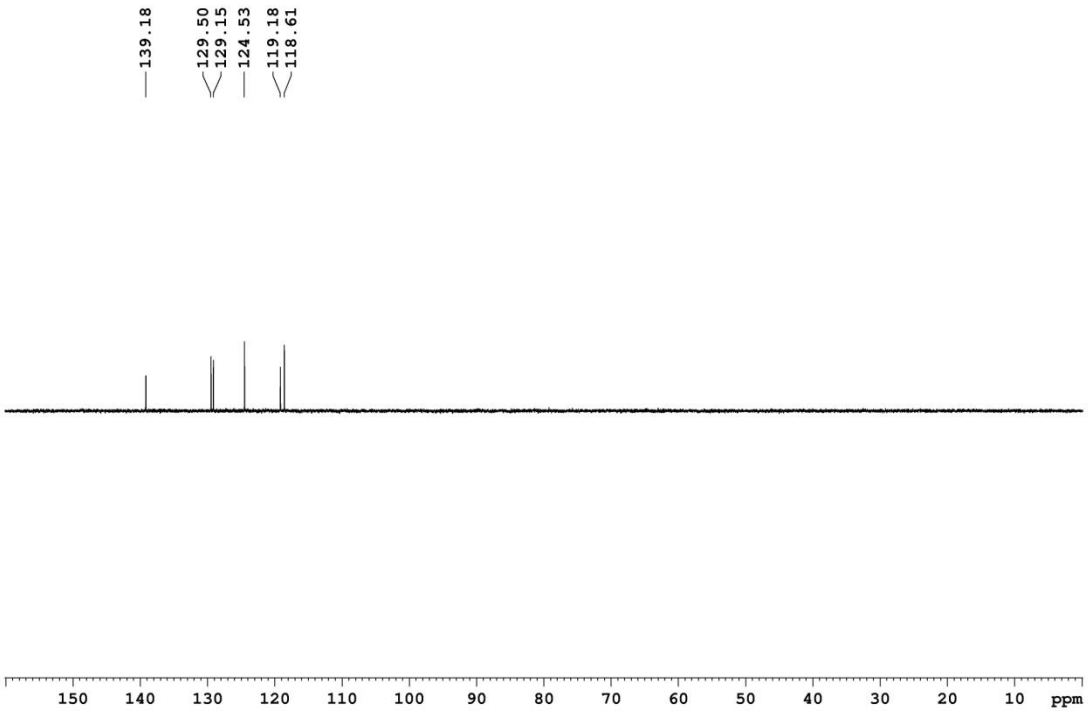
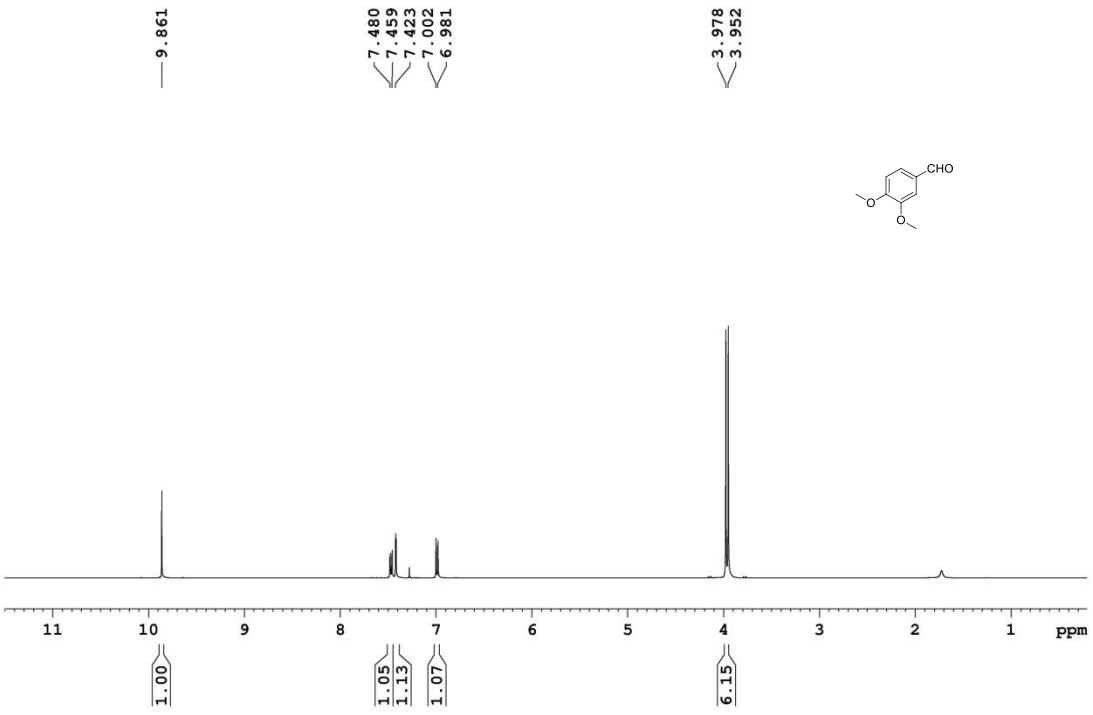
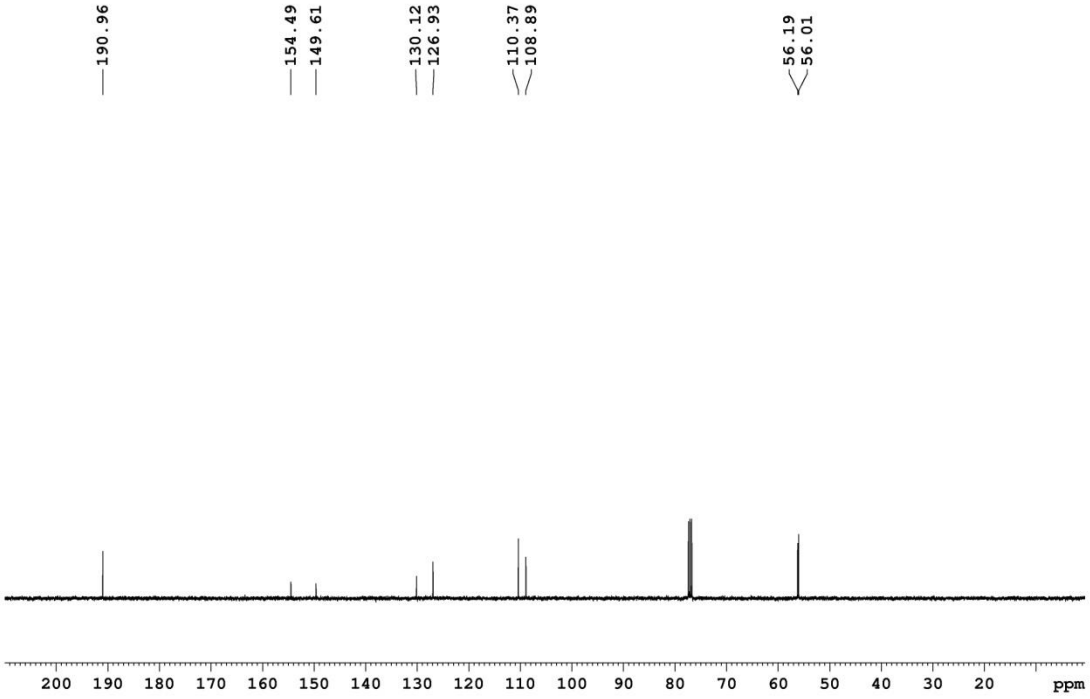


SGT-KM-20-07-07 CDCL3 PMR



SGT-KM-20-07-07 CDCL3 CMR



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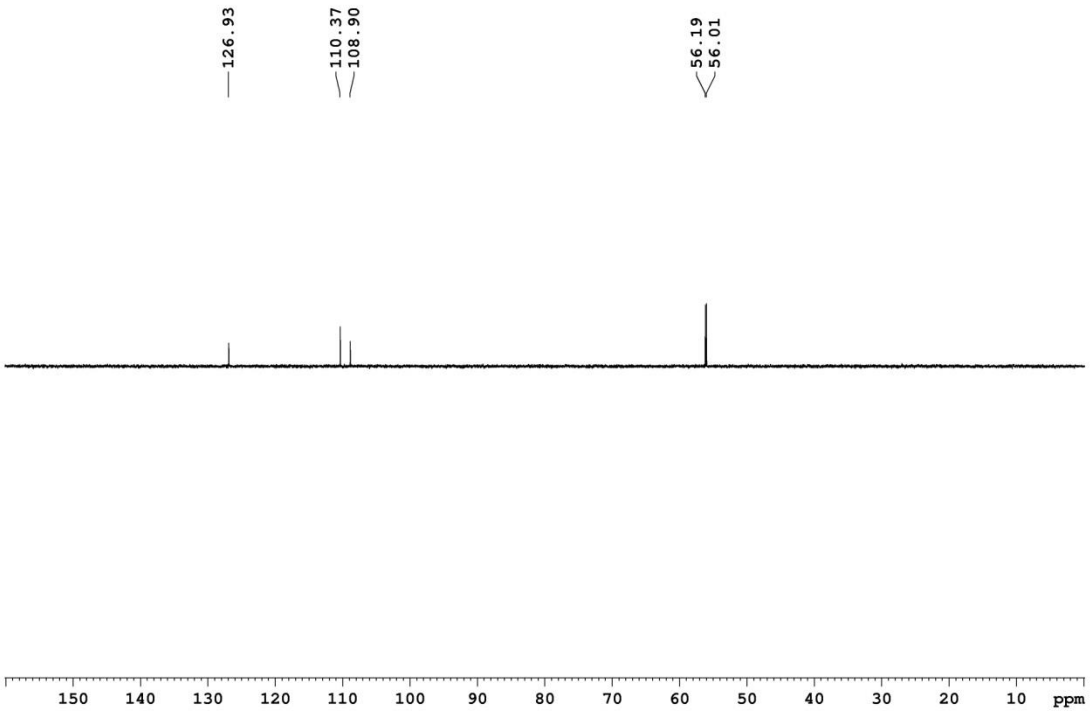
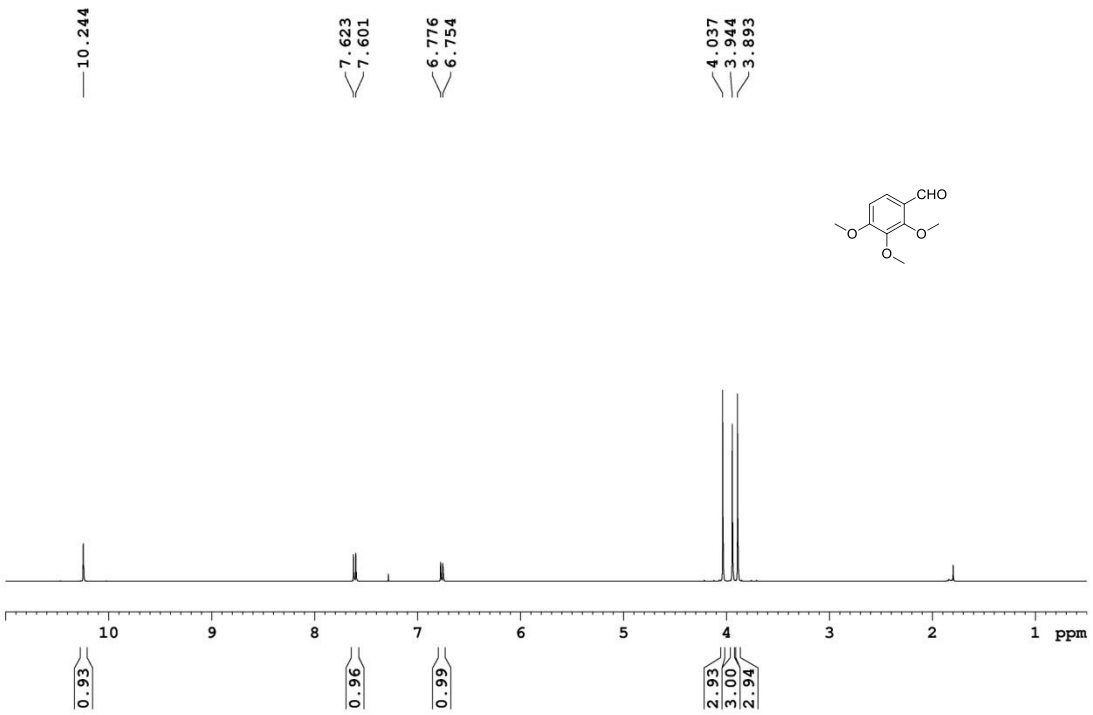


SGT-KM-20-07-06 CDCL3 PMR



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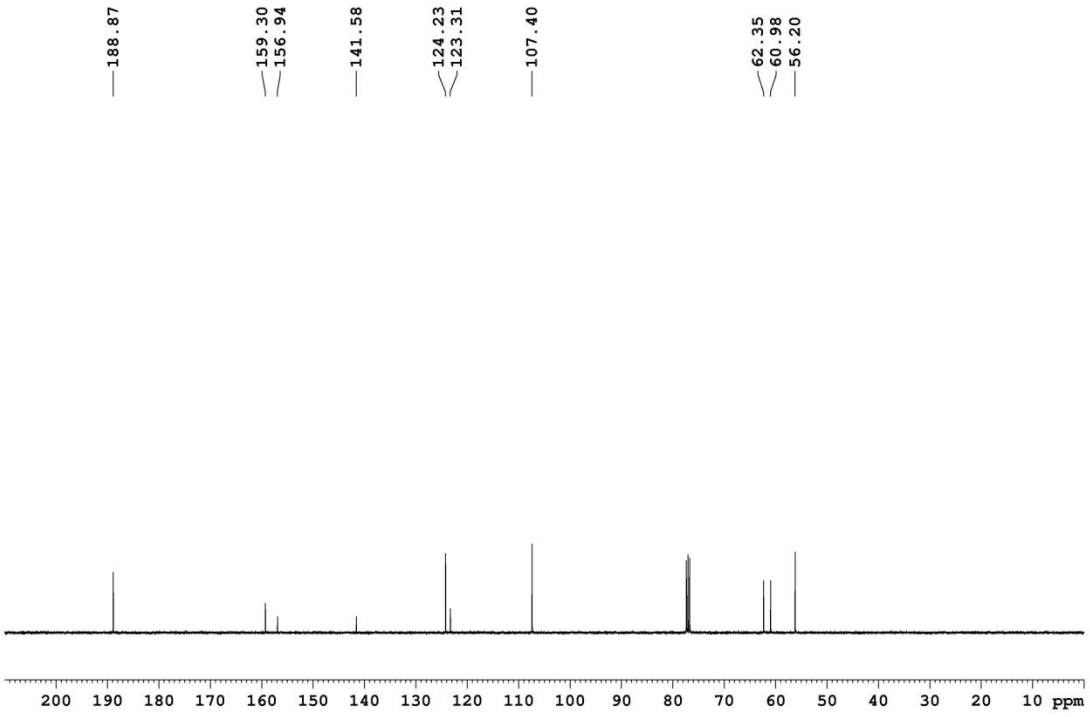

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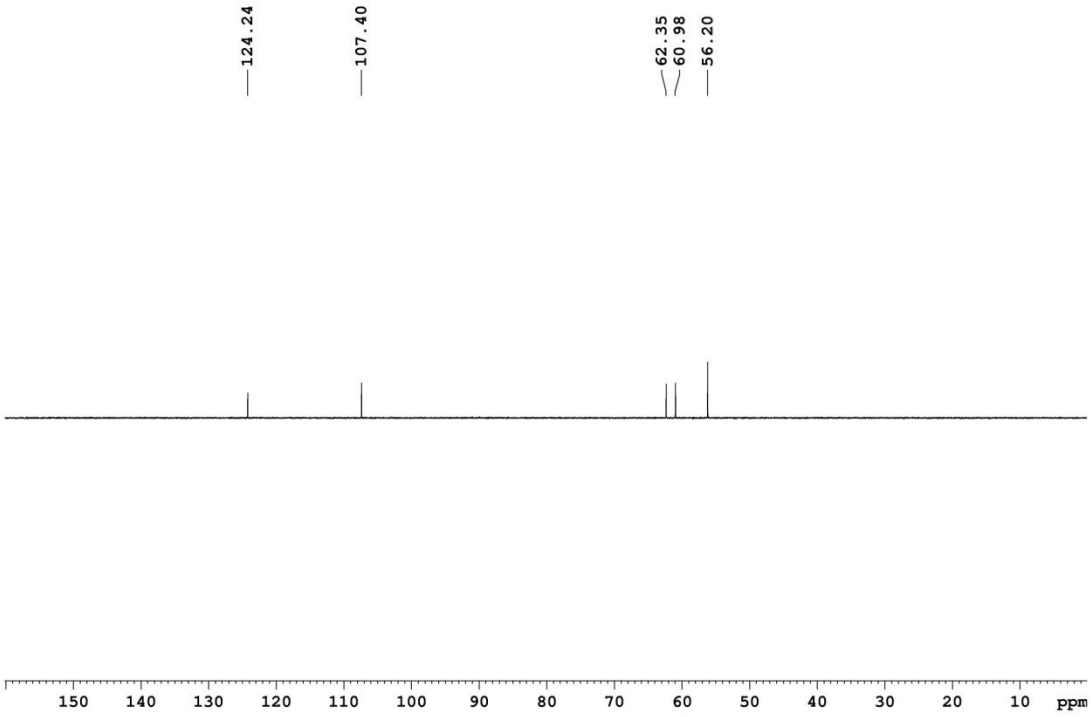
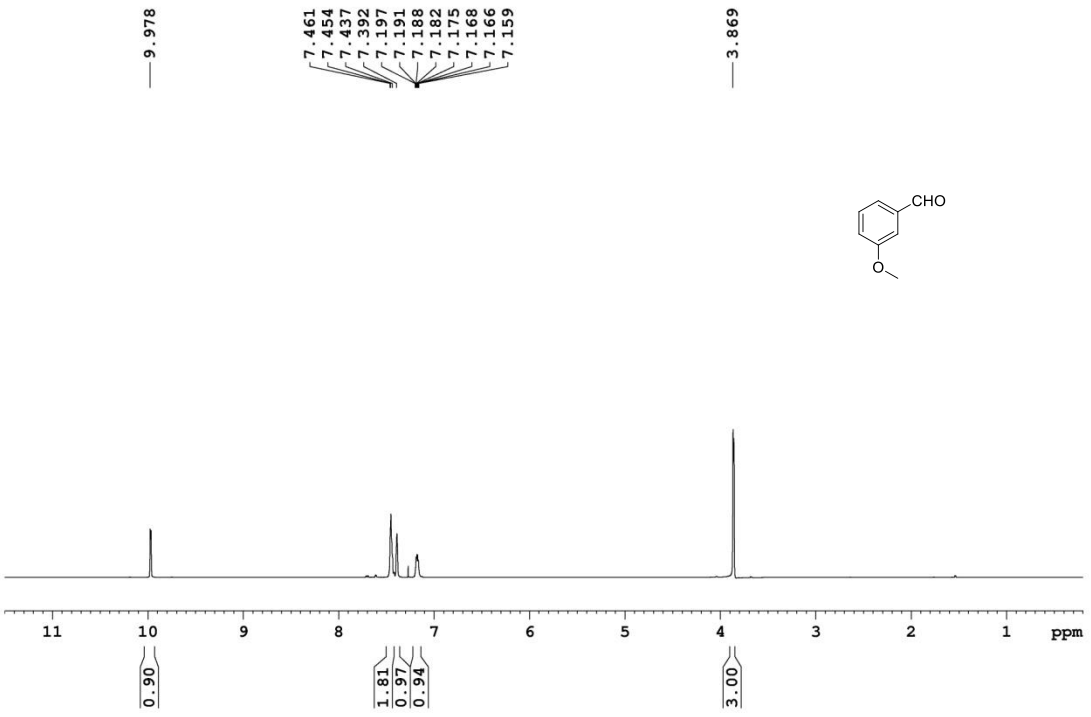


SGT-KM-20-07-03 CDCL3 PMR



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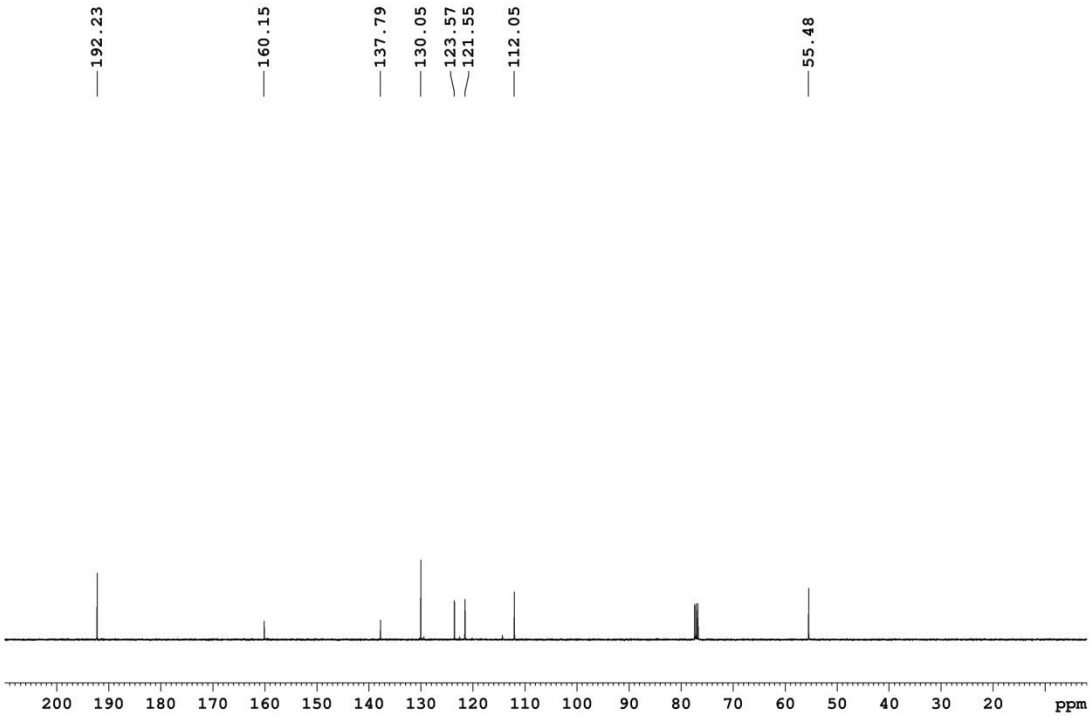

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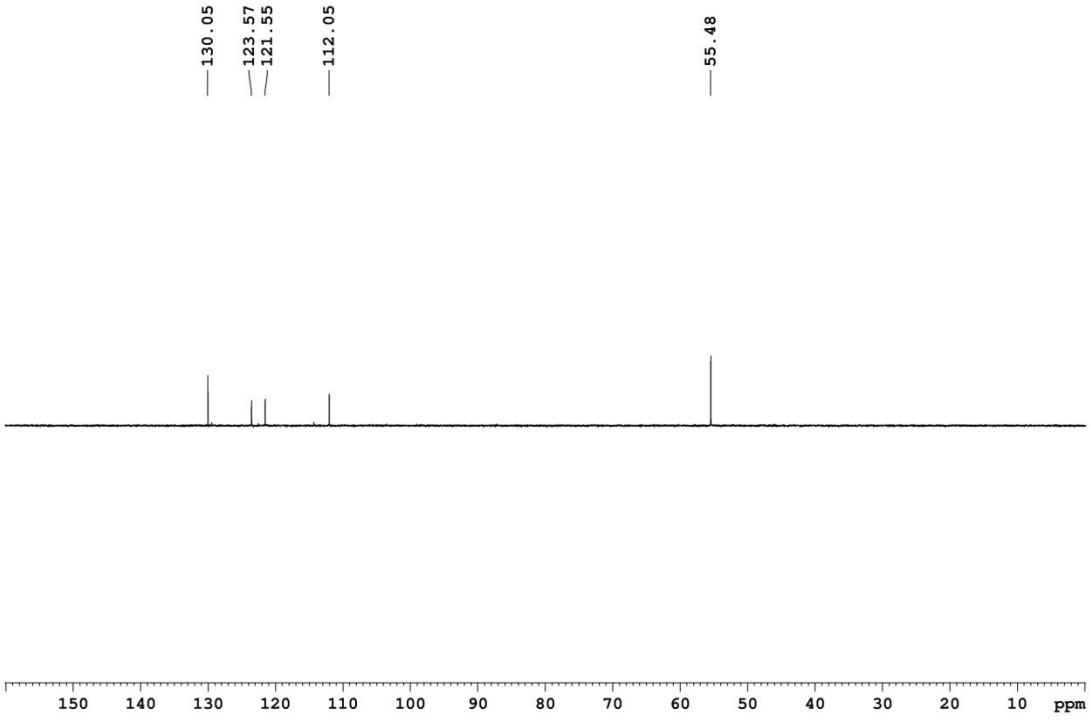
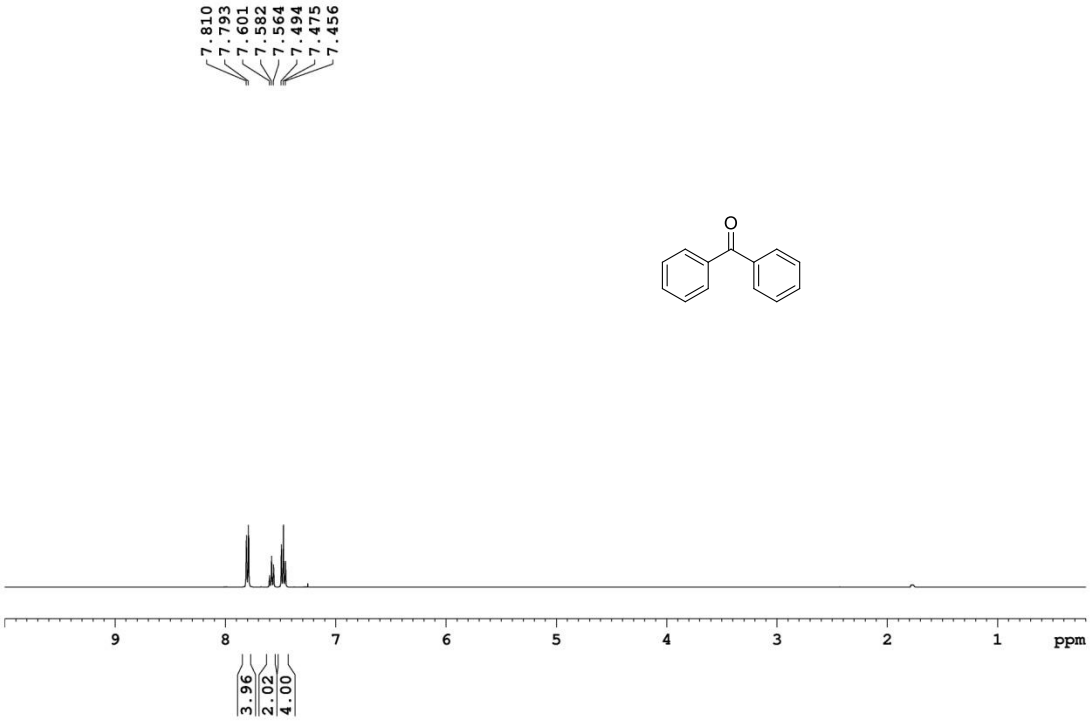


SGT-KM-20-08-31 CDCL3 PMR



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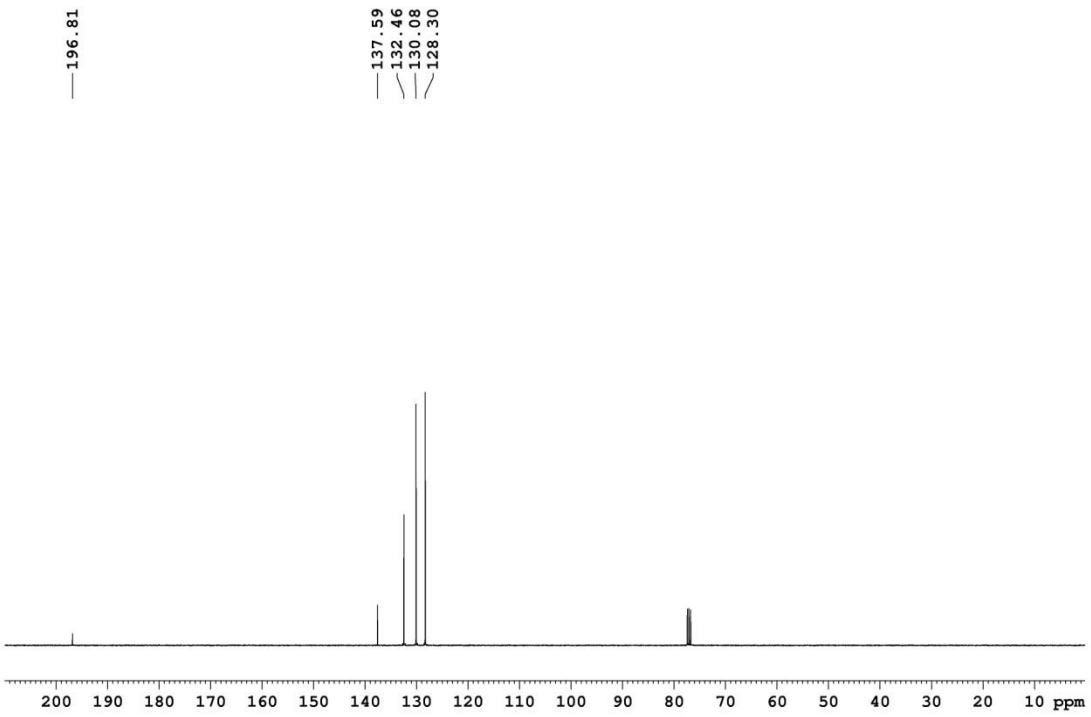

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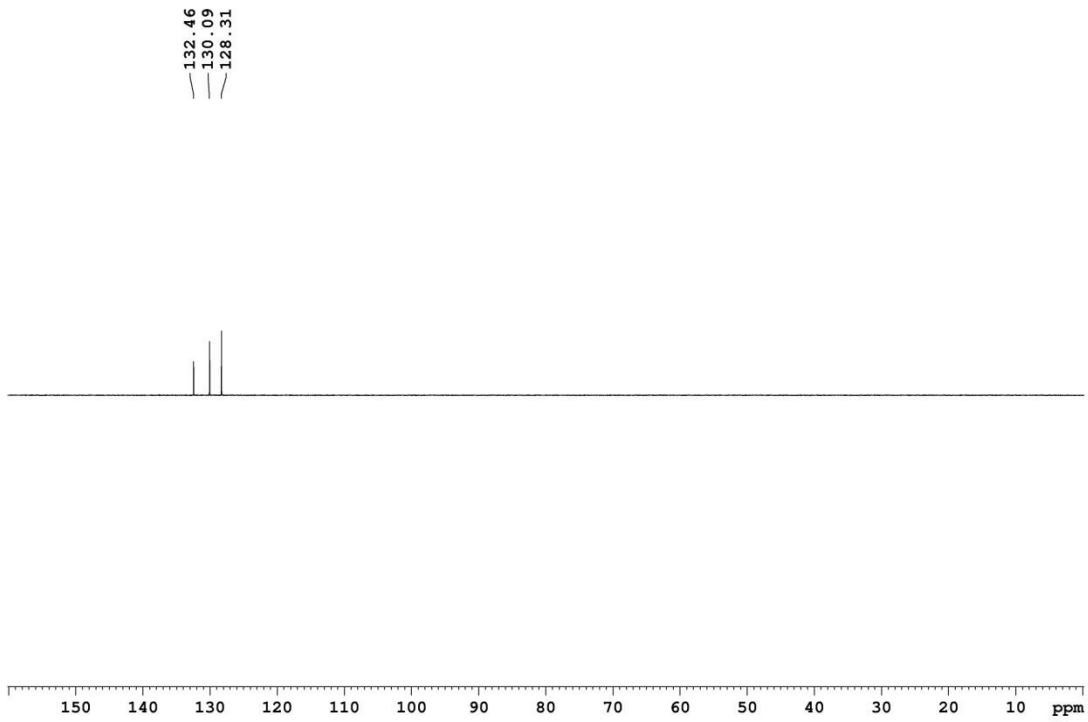

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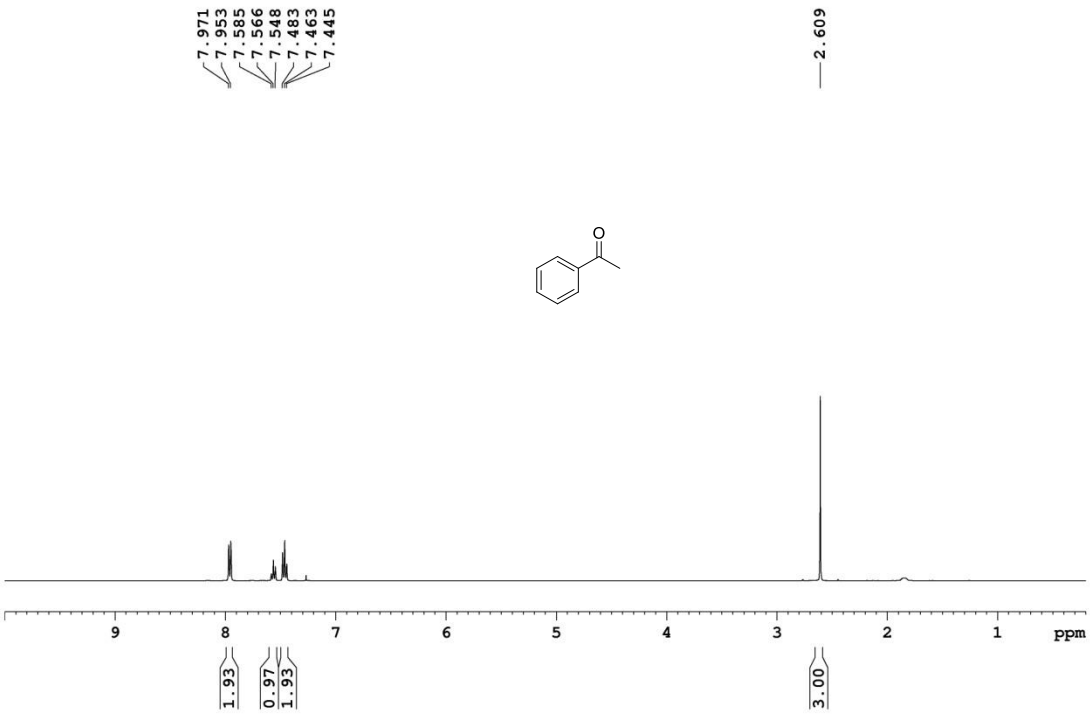

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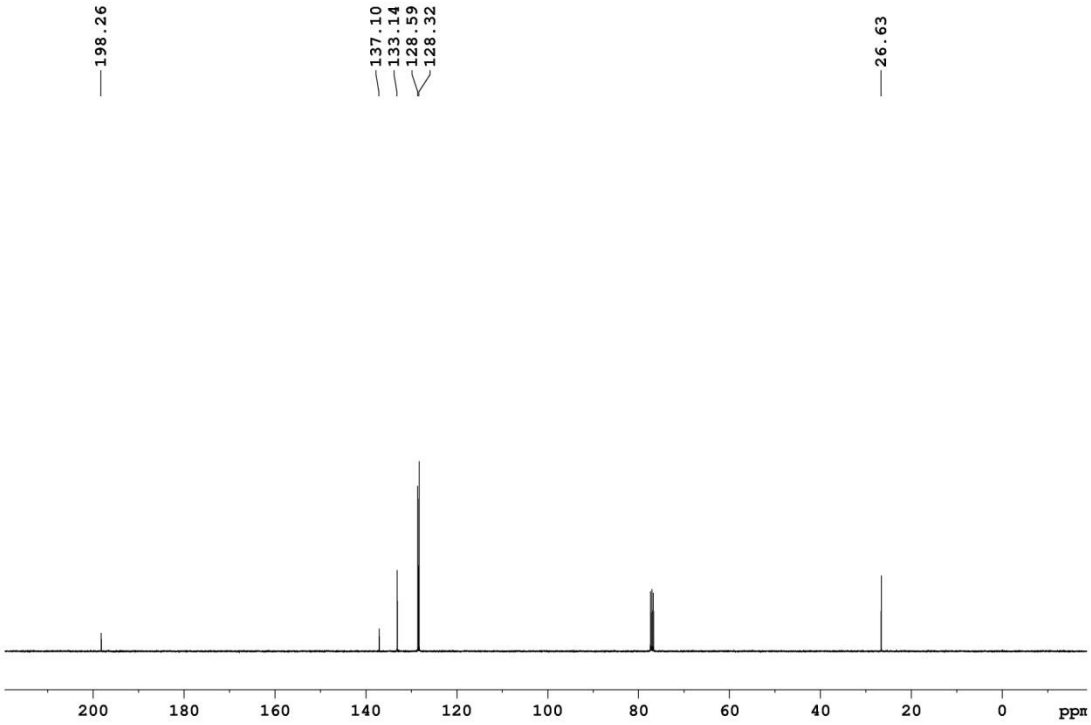

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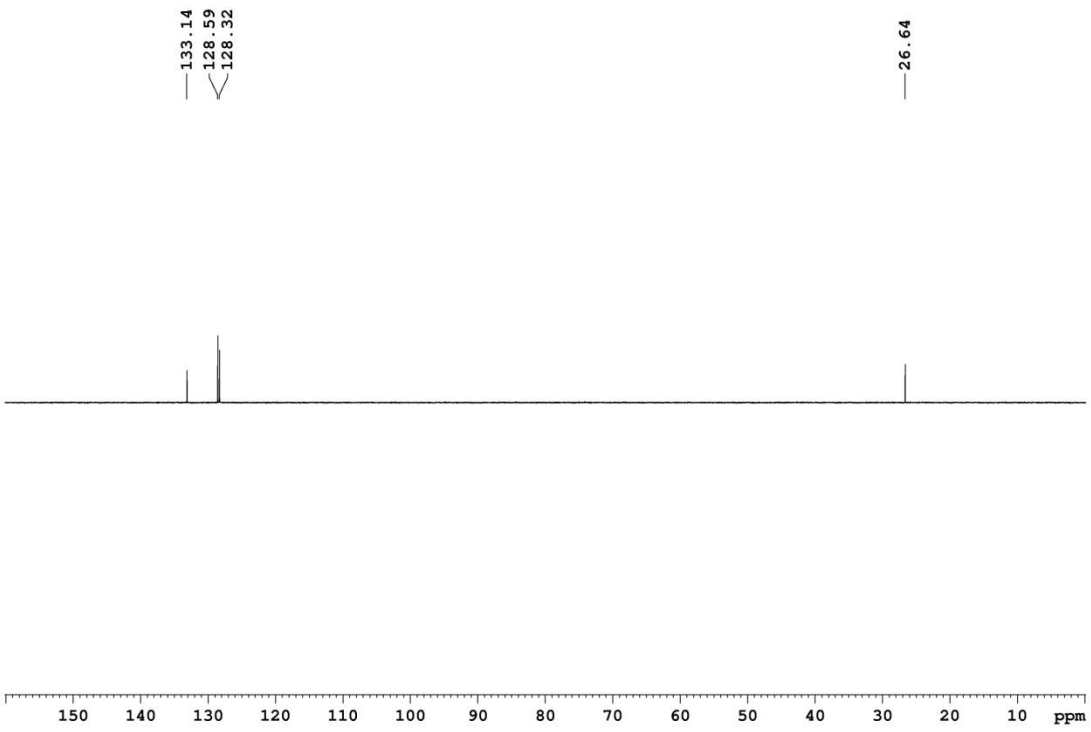

References:

(1) Q. D. Wang, J. M. Yang, D. F. J. Ren and B. B. Zeng, *Tetrahedron Letters*, 2017, **58**, 2877.

(2) M. A. Ibrahim, *Tetrahedron*, 2009, **65**, 7687.

(3) L. Lu, Q. Xiong, S. Guo, T. He, F. Xu, J. Gong, Z. Zhu and H. Cai, *Tetrahedron*, 2015, **71**, 3637.

(4) B. Zhang, B. Liu, J. Chen, J. Wang and M. Liu, *Tetrahedron Lett.,* 2014, **55**, 5618.

(5) M. L. Deb, C. D. Pegu, P. J. Borpatra and P.K. Baruah, *RSC Adv*., 2016, **6**, 40552.

(6) A. K. Das, S. Goswami, C. K. Quah and H. K. Fun, *New J. Chem.*, 2015, **39**, 5669.

(7) S. F. Adil, M. E. Assal, M. Rafi, S. M. Kuniyil, A. H. M. Khan, A. Khan, M. N. Tahir, A. Al-Warthan and M. R. H. Siddiqui, *Appl. Organomet. Chem.,* 2020, **34**, e5718.

(8) M. R. Baroneab and A. M. Jones, *Org. Biomol. Chem*., 2017, **15**, 10010-10015.