Electrochemical-induced hydroxylation of aryl halides in the presence of Et_3N in water

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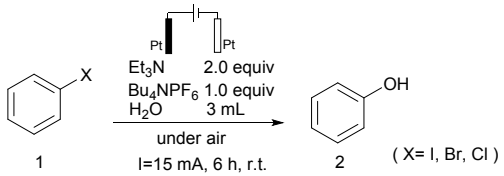
1. General information

All reagents were purchased from commercial sources and used without further purification. All solvents were dried in a standard manner. Reactions were monitored by TLC on silica gel plates. Column chromatography was performed over silica gel (200-300 mesh) and petroleum ether/ethyl acetate. Shanghai chenhua CHI600E electrochemical workstation was used in the standard configuration as delivered, including proprietary software. All products were characterized by NMR. ^{1}H NMR spectra were recorded at 500 and 400 MHz and ^{13}C NMR spectra were recorded at 101 and 125 MHz (Bruker DPX) with $CDCl_3$ and DMSO-d_6 as solvent. Chemical shifts are reported in ppm using TMS as internal standard. NMR by the services provided at the Shandong Liaocheng University. HPLC were recorded on an SHIMDZU LC-20A instrument with a HP5-MS 30 m x 0.25 mm capillary apolar columns.

2. General procedure for the catalytic reactions

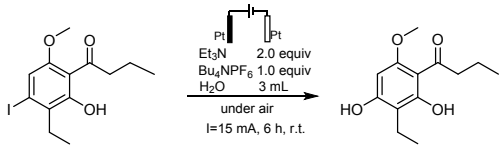


A dried 10 mL quartz tube equipped was charged with iodobenzene (or bromobenzene, chlorobenzene) (0.5 mmol), Et_3N (2.0 equiv), Bu_4NPF_6 (2.0 equiv) and water (3 mL) in the presence of the air balloon. The mixture was stirred at room temperature with a voltage range of 6-8 V for 6 h with 15 mA (Pt anode (10.0 mm × 10.0 mm), Pt cathode (10.0 mm × 10.0 mm)). After the reaction was completed, the reaction vessel was opened and the organic layer was collected by ethyl acetate extraction. The solution of the crude product was concentrated in vacuo, and the residue was purified by column chromatography on a silica gel (petroleum ether/ethyl acetate=5/1) to afford the target product as a white solid.

3. General procedure for the gram scale experiment

A dried 50 mL quartz tube equipped was charged with iodobenzene (or bromobenzene, chlorobenzene) (10 mmol), Et_3N (2.0 equiv), Bu_4NPF_6 (2.0 equiv) and water (20 mL) in the presence of the air balloon. The mixture was stirred at room temperature with a voltage range of 6-8 V for 24 h with 25 mA (Pt anode (15.0 mm × 15.0 mm), Pt cathode (15.0 mm × 15.0 mm)). After the reaction was completed, the reaction vessel was opened and the organic layer was collected by ethyl acetate extraction. The product was purified by flash column chromatography on silica gel.

4. Synthesis of 1-(3-ethyl-2,4-dihydroxy-6-methoxyphenyl)butan-1-one (D1)



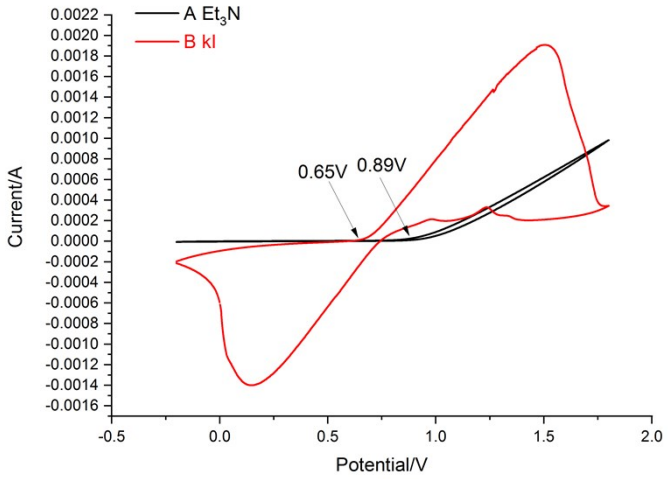
In a round-bottom flask, 1-(3-ethyl-2-hydroxy-4-iodo-6-methoxyphenyl)butan-1-one (0.5 mmol) was dissolved in 3 mL water and Et_3N (2.0 equiv), Bu_4NPF_6 (2.0 equiv) was added to the solution in the presence of the air balloon. The mixture was stirred at room temperature with a voltage range of 6-8 V for 6 h with 15 mA. After the reaction was completed, the reaction vessel was opened and the organic layer was collected by ethyl acetate extraction. The residue was purified by silica gel column chromatography to obtain the corresponding product 1-(3-ethyl-2,4-dihydroxy-6-methoxyphenyl)butan-1-one (D1) with the yield 86%.

5. Cyclic voltammetry experiment

Cyclic voltammograms were measured using Shanghai chenhua CHI600E electrochemical workstation with electrochemical analysis software, using a conventional three-electrode cell. The working electrode was a glassy carbon working electrode, the counter and reference electrodes consisted of a Pt wire and a SCE, espectively. The glassy carbon working electrode was polished with a polishing cloth before each measurement. The concentration of all tested compounds was 1 mmol L^{-1}. The scan rate was 0.1 V/s.

To prove that the anodic oxidation of iodide is preferable than the oxidation of Et_3N in the proposed mechanism, we have used potassium iodide and Et_3N to carry out cyclic voltammetry experiments with water as the solvent. From the following figure, we have observed that the onset potential of potassium

iodide oxidation (0.65 V) is lower than the onset potential for oxidation of Et_3N (0.89 V), which serves as evidence that iodide is more readily oxidized than Et_3N.



6. Cell cytotoxicity assay

MTT assay was used to tests cell cytotoxicity and a drug concentration required to inhibit cell growth by 50% (IC_{50}) was used to measure the sensitivity of cell to compound as described previously. Briefly, cells growing in logarithmic phase were seeded at a density of 3000~7000 cells per well in 96-well plates. After the cells adhered 24 h, a range of different concentrations of D1 and controll were added to the wells. After 48 h incubation, MTT (5 mg/mL, 20μL) was added into each well, and 4 h later, the medium was discarded and 150 μL DMSO was added into the wells to dissolve. Finally, optical density was measured at 570 nm by a Model 550 MicroplateReader (Bio-Rad, Hercules, CA, USA). IC_{50} was calculated from survival curves using the Bliss method. All experiments were repeated at least three times.

7. Characterization data

phenol (2a)[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.15 (m, 2H), 6.92 (t, J = 7.4 Hz, 1H), 6.83 (dd, J = 8.4, 0.8 Hz, 2H), 5.09 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.22, 129.67, 120.83, 115.34; MS (EI, m/z): 94 [M^+].

p-cresol (2b) [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10-6.95 (m, 2H), 6.79-6.69 (m, 2H), 5.70 (br, 1H), 2.29-2.23(m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.97, 130.06, 115.17, 115.14, 20.39; MS (EI, m/z): 108 [M^+].

4-methoxyphenol (2c) [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85-6.72 (m, 4H), 5.47 (br, 1H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.58, 149.52, 116.11, 114.96, 55.87; MS (EI, m/z): 124 [M^+].

hydroquinone (2d) [1]

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (s, 2H), 6.57 (s, 4H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.73, 115.67; MS (EI, m/z): 110 [M^+].

4-fluorophenol (2e)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98-6.84 (m, 2H), 6.82-6.68 (m, 2H), 6.12 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.53, 156.17, 150.98, 116.34, 116.26, 116.14, 115.91; MS (EI, m/z): 112 [M^+].

4-chlorophenol (2f) [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.14 (m, 2H), 6.80-6.72 (m, 2H), 5.09 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.99, 129.52,125.71, 116.64; MS (EI, m/z): 128 [M^+].

4-bromophenol (2g)[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.28 (m, 2H), 6.76-6.67 (m, 2H), 5.09 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.48, 132.47, 117.18, 112.96; MS (EI, m/z): 172 [M^+].

4-(tert-butyl) phenol (2h)[4]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.23 (m, 2H), 6.81-6.73 (m, 2H), 4.80 (broad, 1H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.05, 143.56,126.43, 114.74, 34.05, 31.51; MS (EI, m/z): 150 [M^+].

***p*-cyanophenol (2i) [1]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61-7.51 (m, 2H), 6.99-6.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.37, 134.31, 119.25, 116.48, 102.75; MS (EI, m/z): 119 [M^+].

4-hydroxybenzaldehyde (2j) [1]

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.58 (s, 1H), 9.77 (s, 1H), 7.79-7.70 (m, 2H), 6.96-6.87 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 190.86, 163.26, 132.04, 128.39, 115.79; MS (EI, m/z): 122 [M^+].

4-nitrophenol (2k)[2]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-8.12 (m, 2H), 7.00-6.89 (m, 2H), 6.47 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.60, 142.85, 126.30, 115.73; MS (EI, m/z): 139 [M^+].

1-(4-hydroxyphenyl) ethan-1-one (2l) [1]

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.31 (s, 1H), 7.82(d, J = 8.5 Hz, 2H), 6.84(d, J = 8.5 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.89, 161.91, 130.59, 128.53, 115.06, 26.11; MS (EI, m/z): 136 [M^+].

4-hydroxybenzoic acid (2m) [3]

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.44 (s, 1H), 10.23 (s, 1H), 7.88-7.75 (m, 2H), 6.92-6.78 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.18, 161.60, 131.54, 121.36, 115.12; MS (EI, m/z): 138 [M^+].

***o*-cresol (2n) [1]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16-7.03 (m, 2H), 6.88-6.80 (m, 1H), 6.78-6.71 (m, 1H), 4.86 (d, J = 2.0 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.68, 131.01, 127.09, 123.74, 120.74, 114.88, 15.66; MS (EI, m/z): 108 [M^+].

2-aminophenol (2o) [3]

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.92 (s, 1H), 6.64 (dd, J = 7.6, 1.2 Hz, 1H), 6.61-6.50 (m, 2H), 6.44-6.34 (m, 1H), 4.44 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 143.94, 136.45, 119.47, 116.43, 114.43, 114.34; MS (EI, m/z): 109 [M^+].

2-methoxyphenol (2p) [3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95-6.90 (m, 1H), 6.89-6.82 (m, 3H),5.69 (s, 1H) 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.54,145.61, 121.39, 120.08, 114.50, 110.70, 55.79; MS (EI, m/z): 124 [M^+].

2-hydroxybenzoic acid (2q)[5]

^{1}H NMR (500 MHz, DMSO-d_6) δ 13.85 (br, 1H), 11.48 (br, 1H), 7.79 (d, J = 7.5 Hz, 1H), 7.50 (t, J = 7.8 Hz, 1H), 6.98-6.85 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.83, 161.06, 135.54, 130.17, 119.07, 116.99, 112.82; MS (EI, m/z): 138 [M^+].

pyrocatechol (2r) [3]

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92-6.85 (m, 2H), 6.84-6.78 (m, 2H), 5.31 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.50, 121.29, 115.53; MS (EI, m/z): 110 [M^+].

2-nitrophenol (2s) [3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.58 (d, J = 1.2 Hz, 1H), 8.11(d, J =8.4 Hz, 1H), 7.65-7.53 (m, 1H), 7.16 (d, J = 8.4 Hz, 1H), 7.04-6.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.11, 137.51, 125.04,

122.99, 120.19, 119.95; MS (EI, m/z): 139 [M^+].

5-methylbenzene-1,3-diol (2t)[6]

^{1}H NMR (400 MHz, DMSO-d_6) δ 9.03 (s, 2H), 6.05-5.97 (m, 3H), 2.10 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.22, 139.19, 107.09, 99.75, 21.22; MS (EI, m/z): 124 [M^+].

3-methoxyphenol (2u) [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.6 Hz, 1H), 6.53-6.46 (m, 1H), 6.45-6.37 (m, 2H), 5.99 (br, 1H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.70, 156.61, 130.19, 107.99, 106.47, 101.59, 55.26; MS (EI, m/z): 124 [M^+].

3,4-dimethylphenol (2v)[7]

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95(d, *J* =8.0 Hz, 1H), 6.62(d, *J* =2.5 Hz, 1H),6.56(dd, *J* =8.2, 2.5 Hz, 1H), 5.32 (s, 1H), 2.18 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.27, 137.93, 130.45, 128.65, 116.62, 112.39, 19.75, 18.68; MS (EI, m/z): 122 [M^+].

***m*-cresol (2w) [1]**

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.6 Hz, 1H), 6.74(d, *J* =7.6 Hz, 1H), 6.68-6.59 (m, 2H), 5.54 (s, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.18, 139.82, 129.40, 121.66, 116.05, 112.30, 21.25; MS (EI, m/z): 108 [M^+].

4,6-dimethylpyrimidin-2-ol (2x)[8]

^{1}H NMR (400 MHz, D_2O) δ 6.77–6.70(m, 1H), 2.74–2.37(m, 6H); ^{13}C NMR (100 MHz, D_2O) δ 170.34, 148.45, 106.43, 19.32; MS (EI, m/z): 124 [M^+].

pyridin-3-ol (2y) [3]

^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.86 (s, 1H), 8.27 – 7.85 (m, 2H), 7.36 – 6.94 (m, 2H); ^{13}C NMR (101 MHz, DMSO-*d6*) δ 154.14, 140.72, 138.48, 124.56, 122.47; MS (EI, m/z): 95 [M^+].

quinolin-8-ol (2z)[9]

^{1}H NMR (400 MHz, DMSO-*d6*) δ 9.79 (s, 1H), 8.85 (dd, *J* = 4.2, 1.7 Hz, 1H), 8.31 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.60 – 7.35 (m, 3H), 7.10 (dd, *J* = 7.4, 1.5 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-*d6*) δ 153.78, 148.60, 138.97, 136.51, 129.27, 127.96, 122.29, 118.19, 111.74; MS (EI, m/z): 145 [M^+].

pyridin-2-ol (3a)[11]

^{1}H NMR (400 MHz, $CDCl_3$) δ 13.50 (s, 1H), 7.45 (dd, J = 2.8, 0.8 Hz, 1H), 7.34 (dd, J = 4.4, 1.6 Hz, 1H), 6.61 – 6.42 (d, J = 8.7 Hz, 1H), 5.78 – 5.57 (d, J = 8.6 Hz, 1H); ^{13}C NMR (101 MHz, DMSO-*d6*) δ 165.40, 136.32, 134.08, 120.16, 118.06; MS (EI, m/z): 95 [M^+].

hydroquinone (3b) [1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 2H), 6.57 (s, 4H). ^{13}C NMR (101 MHz, DMSO-*d6*) δ 150.21, 116.14; MS (EI, m/z): 110 [M^+].

1-(3-ethyl-2,4-dihydroxy-6-methoxyphenyl)butan-1-one (D1)[10]

^{1}H NMR (400 MHz, MeOD) δ 6.00 (s, 1H), 3.86 (s, 3H), 2.96 (t, *J* = 7.4 Hz, 2H), 2.57 (q, *J* = 7.4 Hz, 2H), 1.69 (m, 2H), 1.06 (t, *J* = 7.4 Hz, 3H), 1.00 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, MeOD) δ 205.6, 164.3, 162.1, 161.7, 110.0, 104.4, 89.8, 54.4, 45.8, 18.2, 14.9, 13.0, 12.4; MS (EI, m/z): 238[M^+].

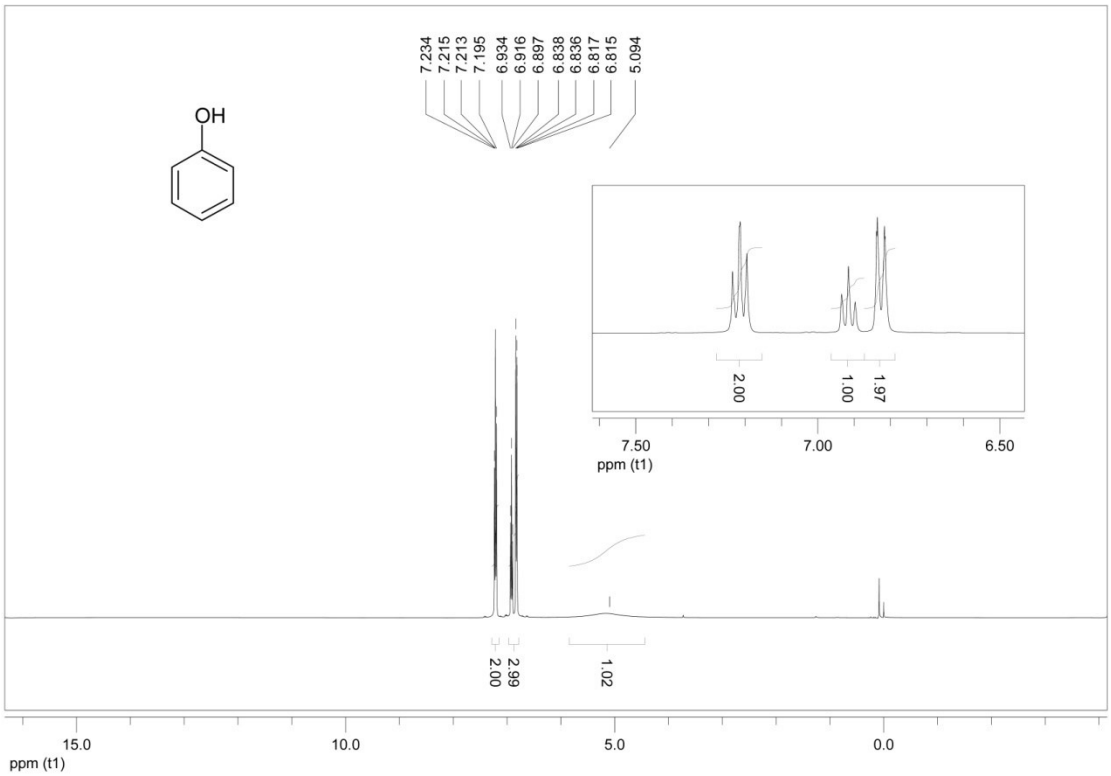
8. References

1. M. Jiang, H. Yang, H. Fu, *Org. Lett.* 2016, **18**, 5248.
2. Y.-M. Cai, Y.-T. Xu, X. Zhang, W.-X. Gao, X.-B. Huang, Y.-B. Zhou, M.-C. Liu, H.-Y. Wu, *Org. Lett.* 2019, **21,** 8479.
3. L. Jing, J. Wei, L. Zhou, Z. Li, X. Zhou, *Chem. Commun*., 2010, **46**, 4767.

4. N. Sun, C. Wang, H. Wang, L. Yang, P. Jin, W. Zhang, J. Jiang, *Angew. Chem. Int. Ed.,* 2019, **58**, 18011.
5. R. K. Sodhi, S. Paul, J. H. Clark, *Green Chem*., 2012, **14**, 1649.
6. H. Richter, S. Beckendorf, O. G. Mancheño, *Adv. Synth. Catal*., 2011, **353,** 295.
7. A. Sridhar, R. Rangasamy, M. Selvaraj, *New J. Chem*., 2019, **43**, 17974.
8. F. Ke, X. Chen, Z. Li, H. Xiang, X. Zhou, *RSC Adv.,* 2013, **3**, 22837.
9. A. Takacs, A. Szilagyi, P. Acs, L. Mark, A. F. Peixoto, M. M. Pereira, L. Kollar, *Tetrahedron*, **2011**, *67*, 2402.
10. W. A. Ayer, L. D. Jimenez, *Can. J. Chem*., 1994, **72**. 2326.
11. L. Wang, D.-Y. Dai, Q. Chen, M.-Y. He, *Asian. J. Org. Chem.,* 2013, **2**, 1040.

9 ^{1}H NMR and ^{13}C NMR spectra for the products

2a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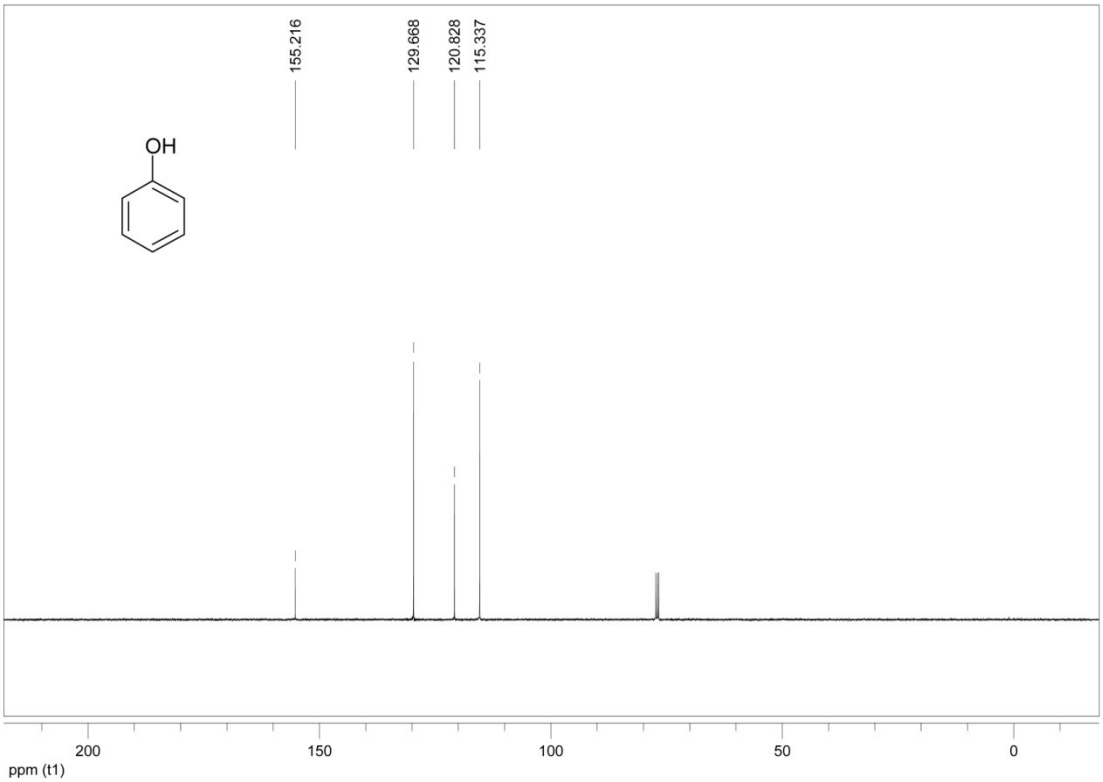
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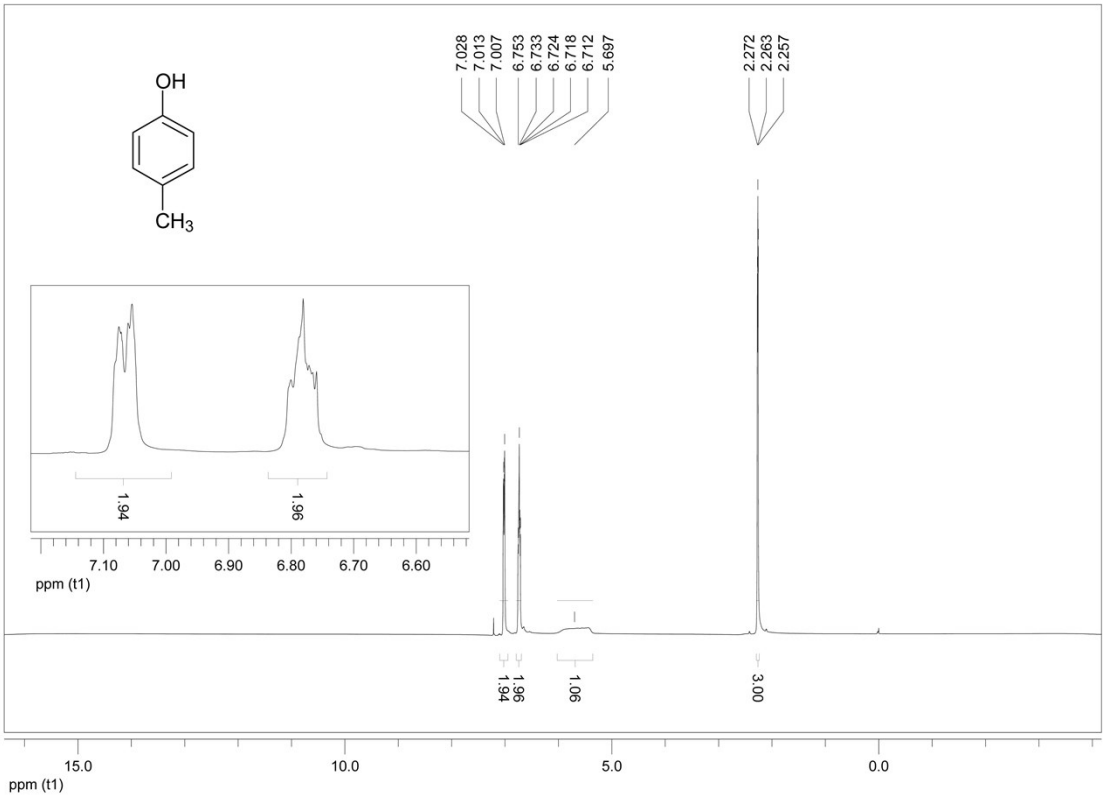
2b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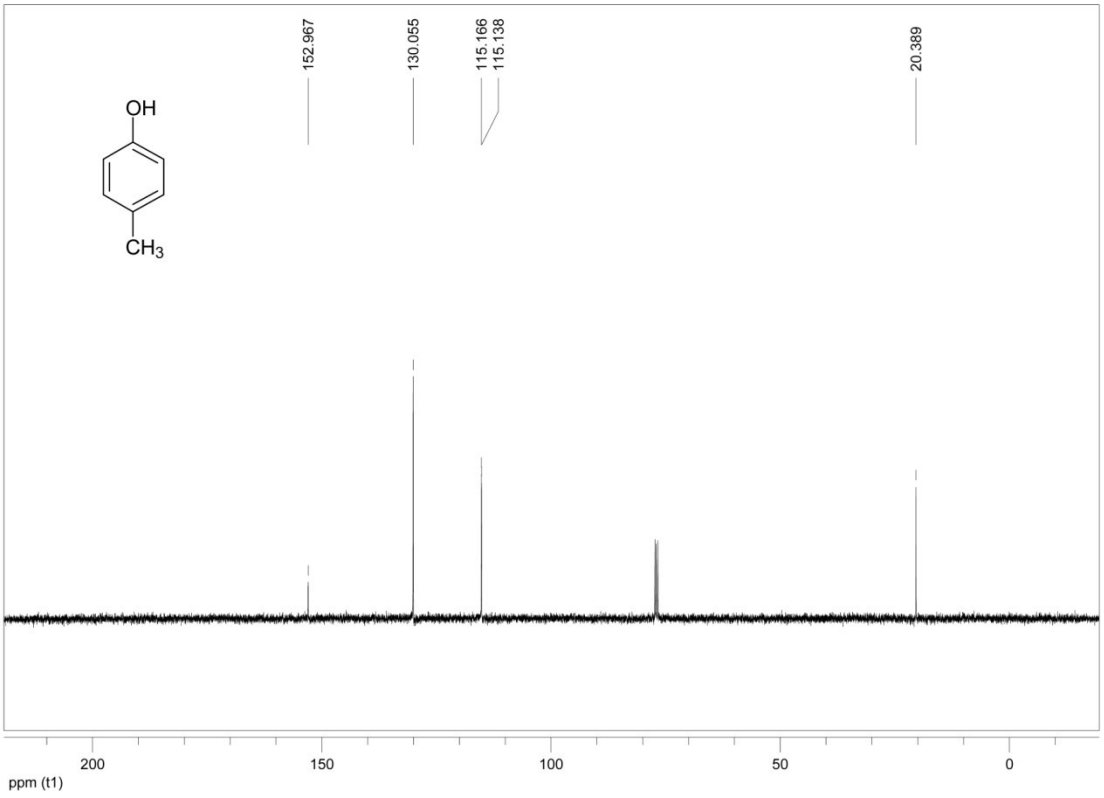
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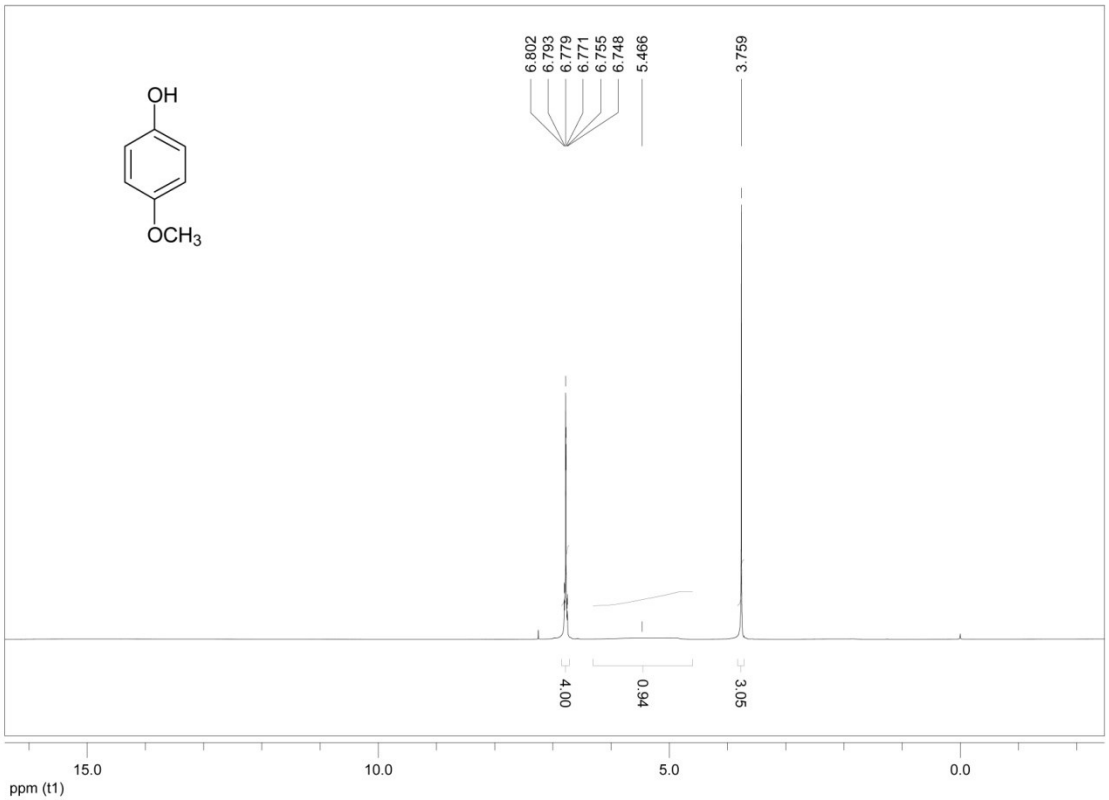
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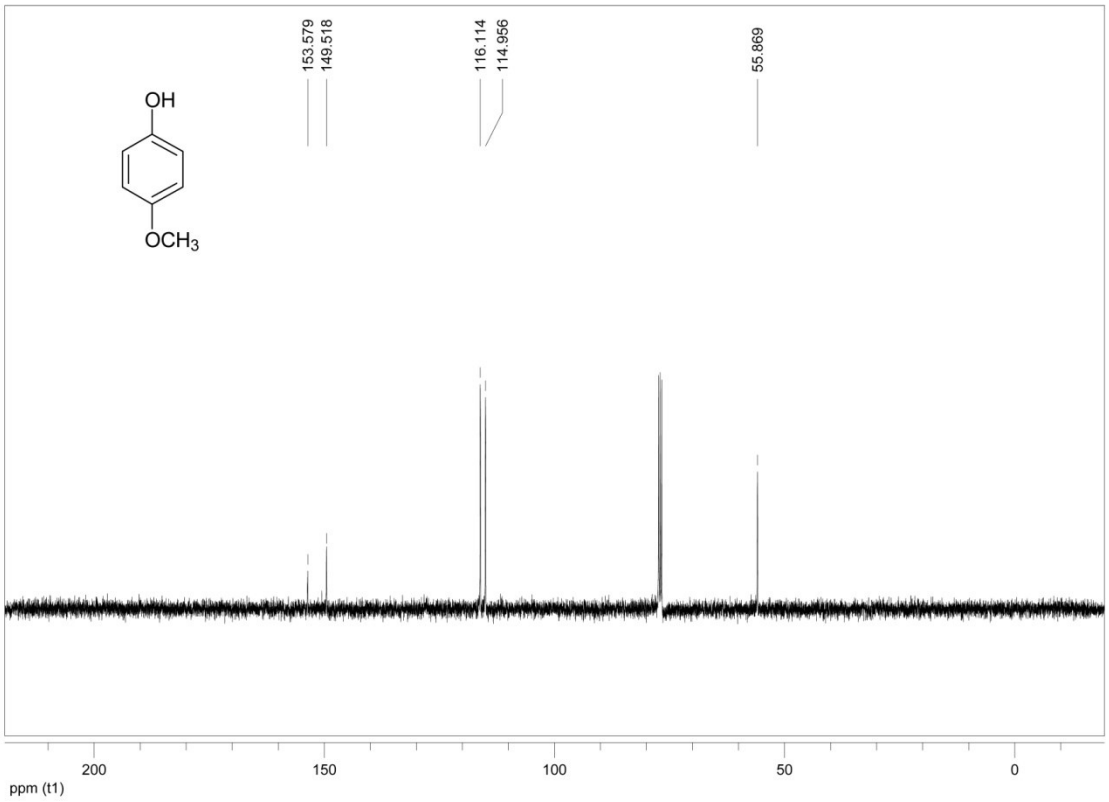
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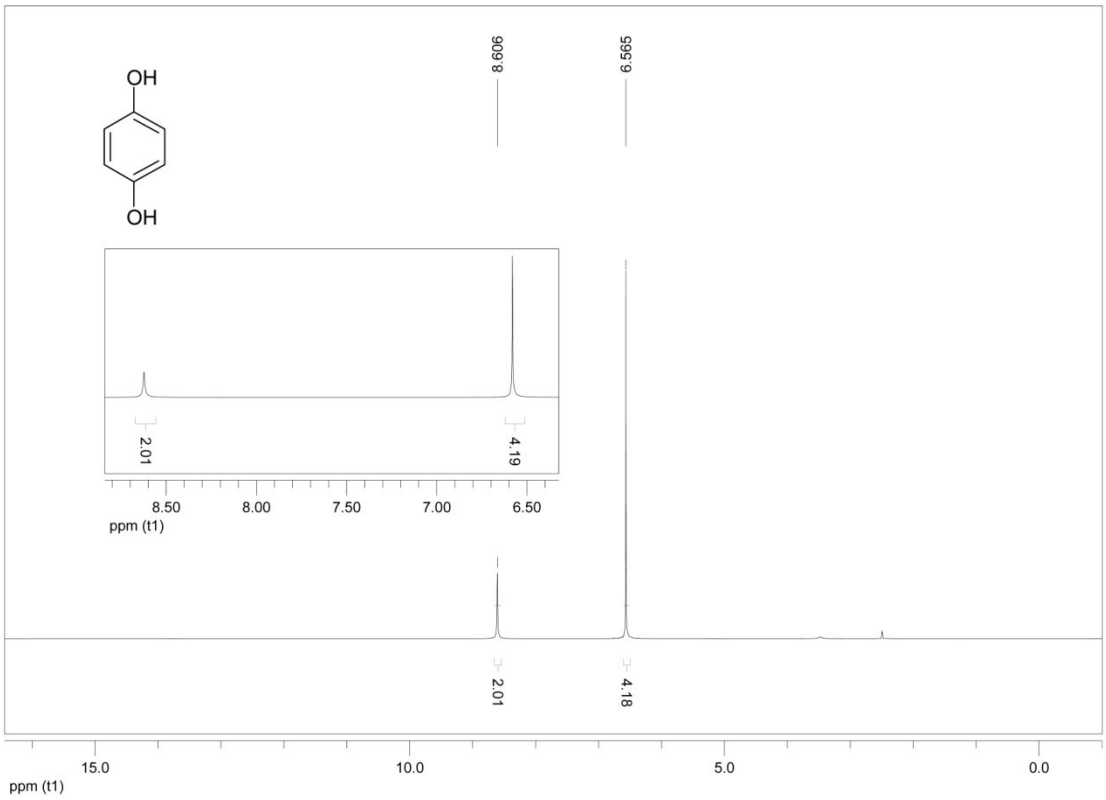
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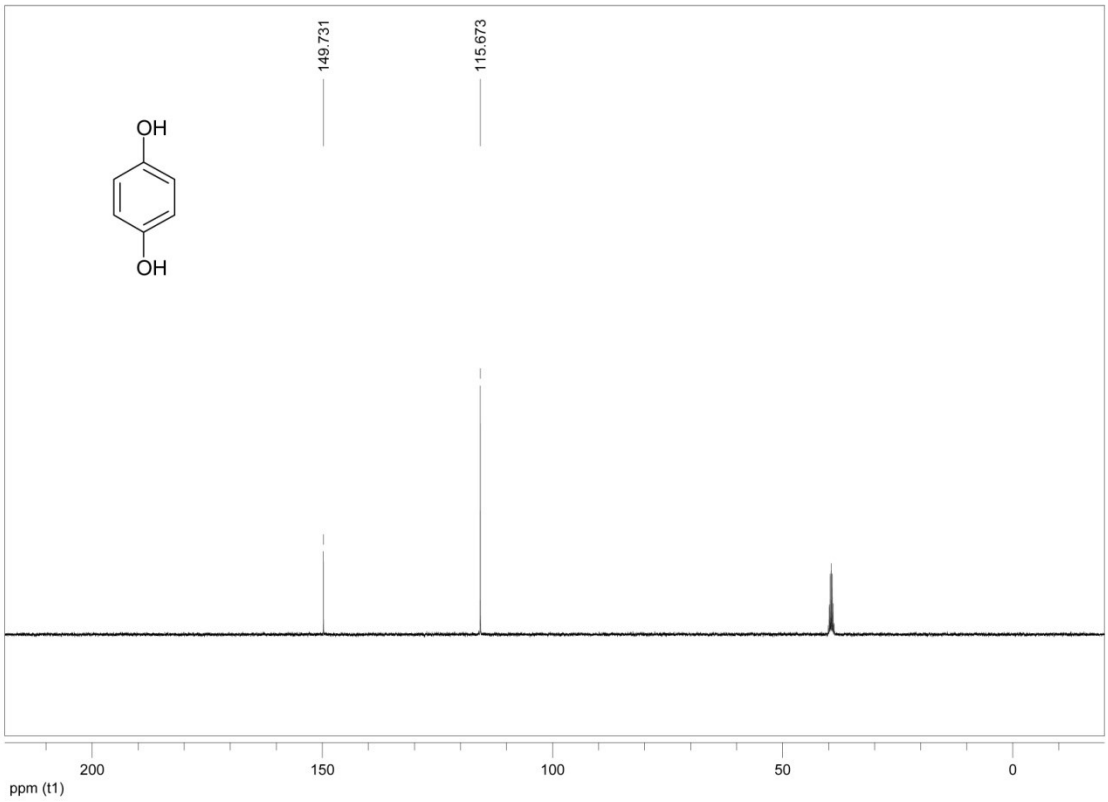
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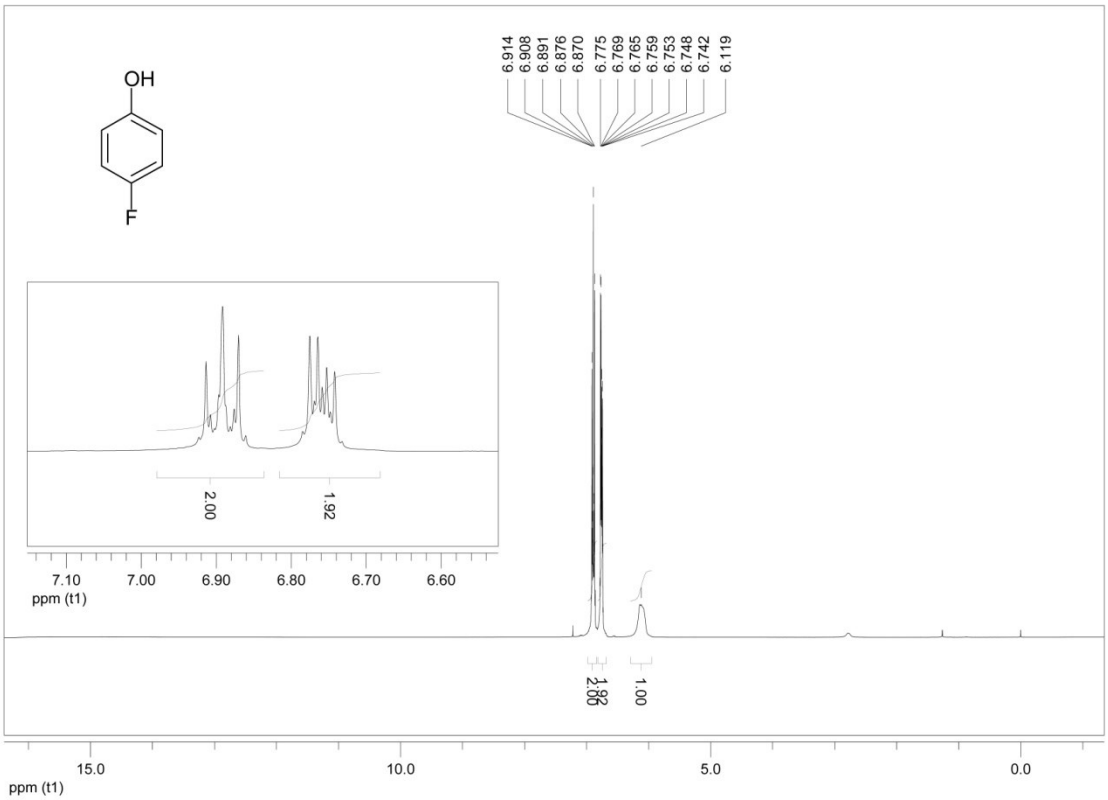
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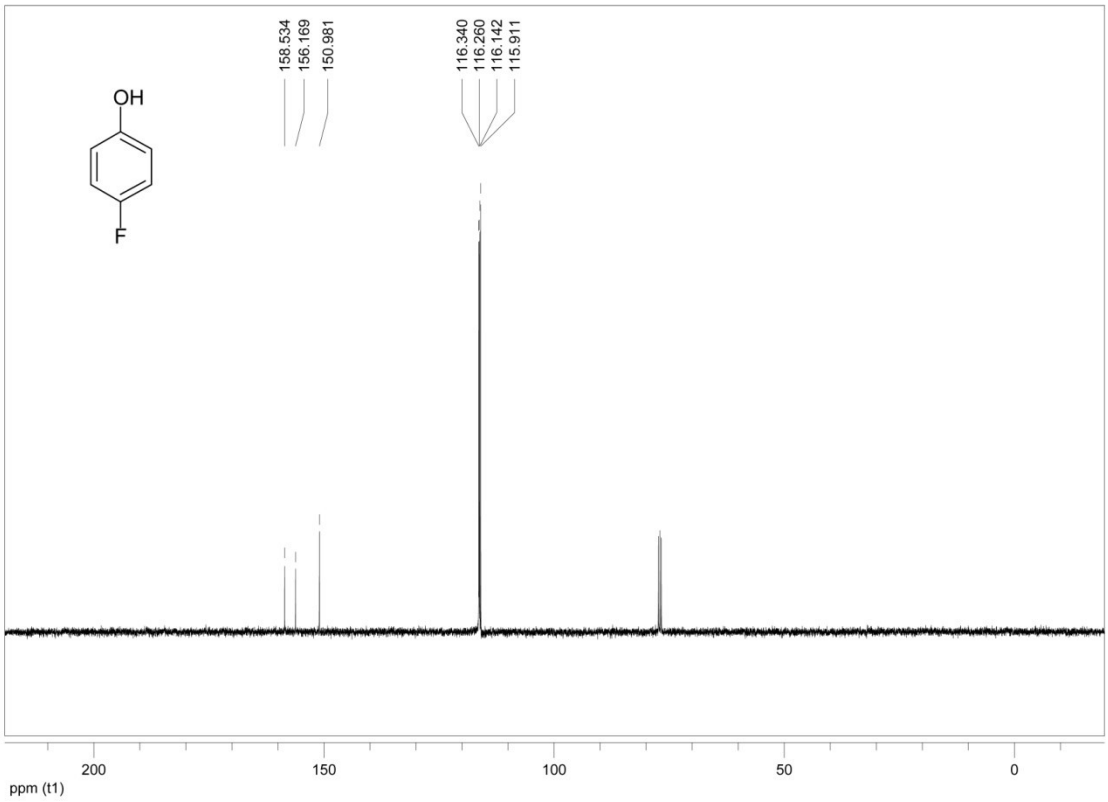
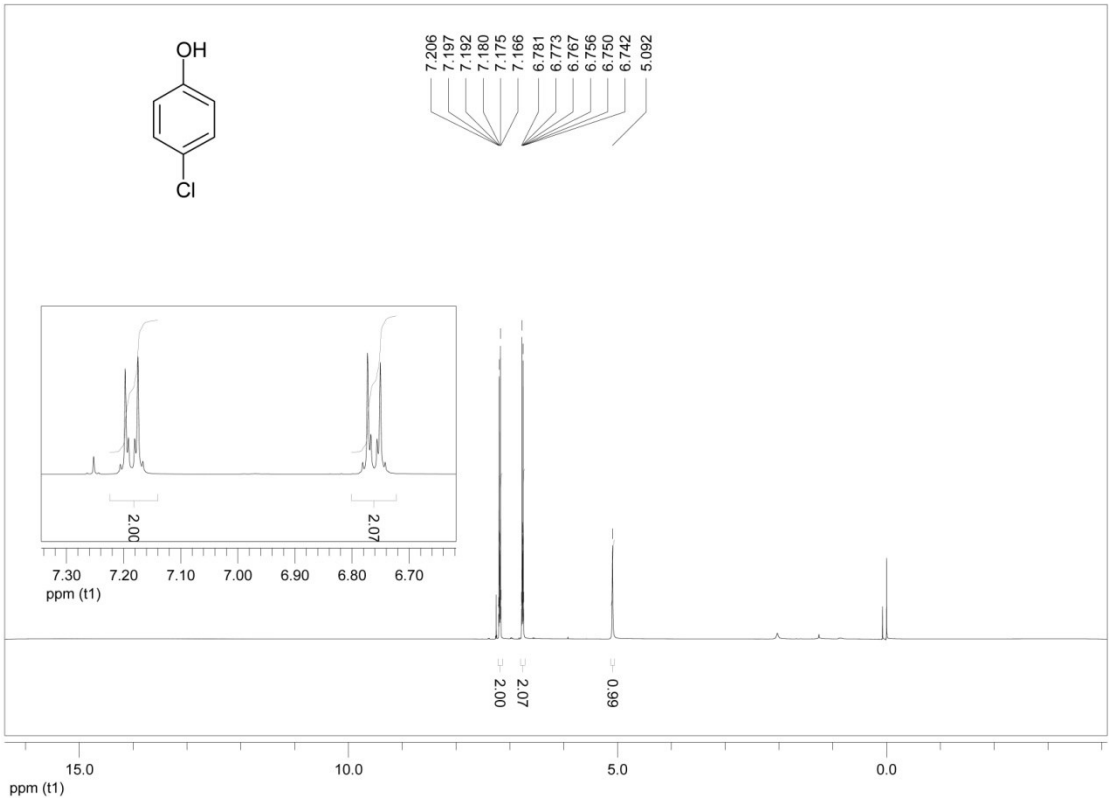
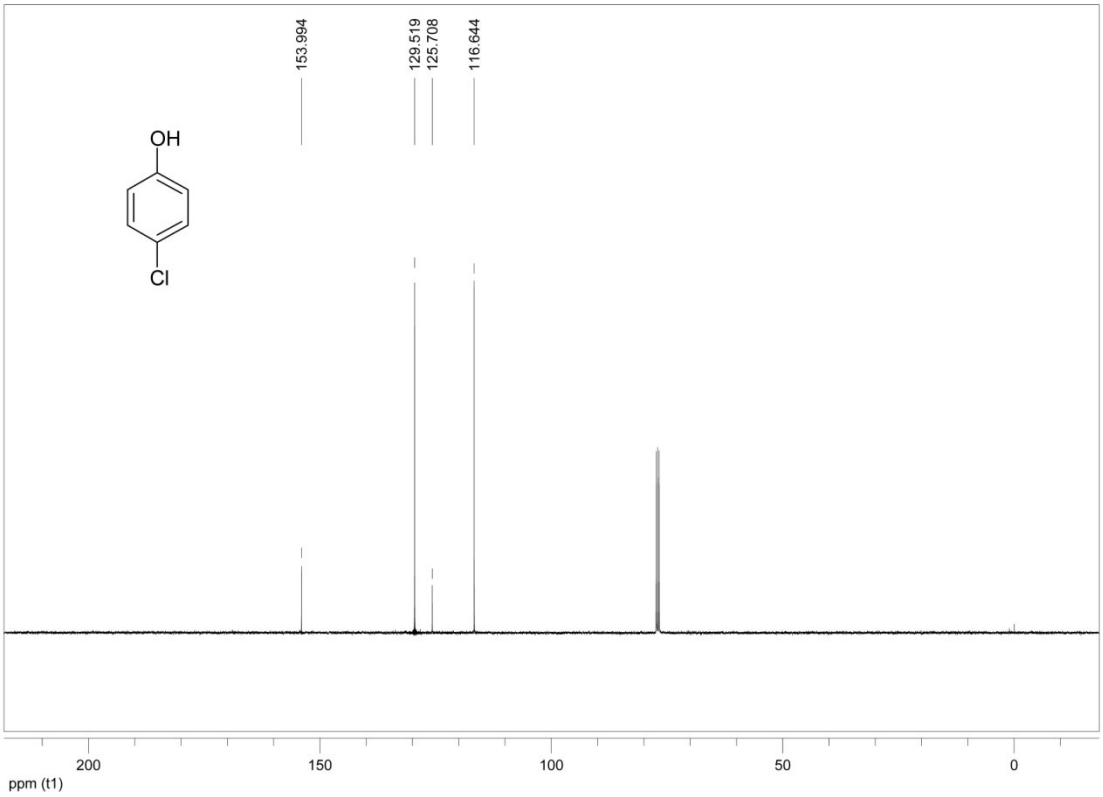
6.876
6.870
6.775
6.769
6.765
6.759
6.753
6.748
6.742
6.119
2.00
1.92
7.10
7.00
6.90
6.80
6.70
6.60
ppm (t1)
2.00
1.92
1.00
15.0
10.0
5.0
0.0
ppm (t1)

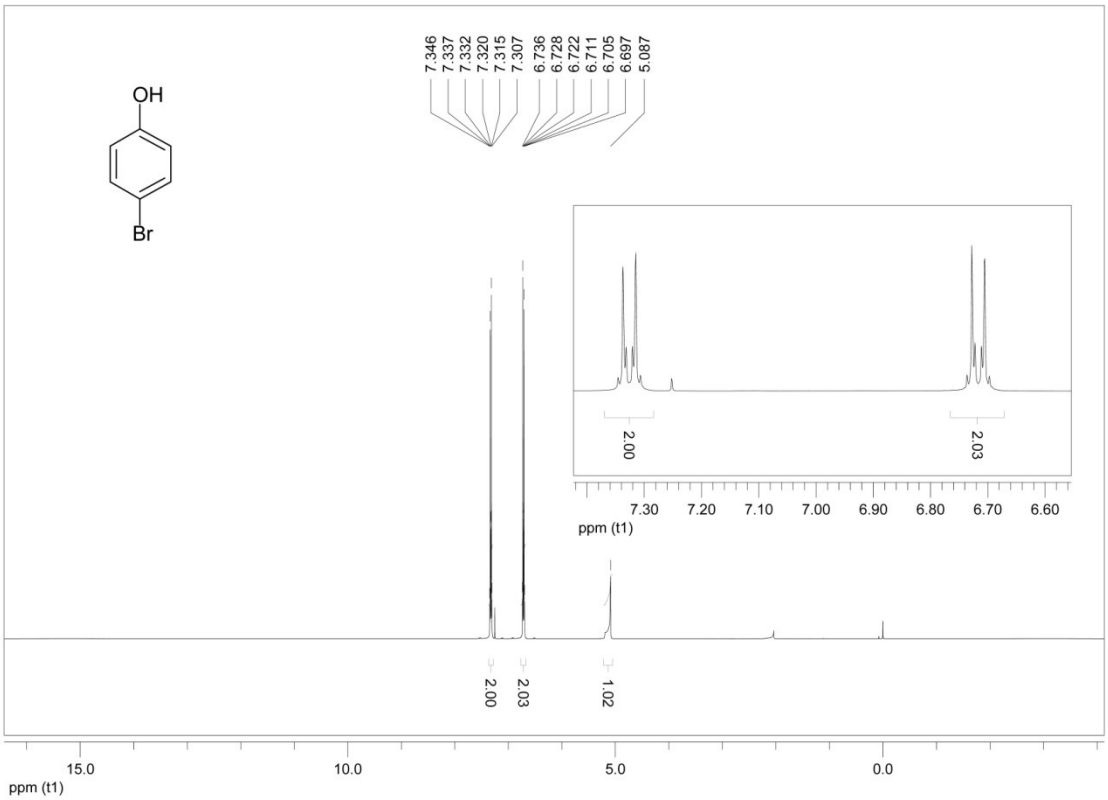

OH
F
158.534
156.169
150.981
116.340
116.260
116.142
115.911
200
150
100
50
0
ppm (t1)

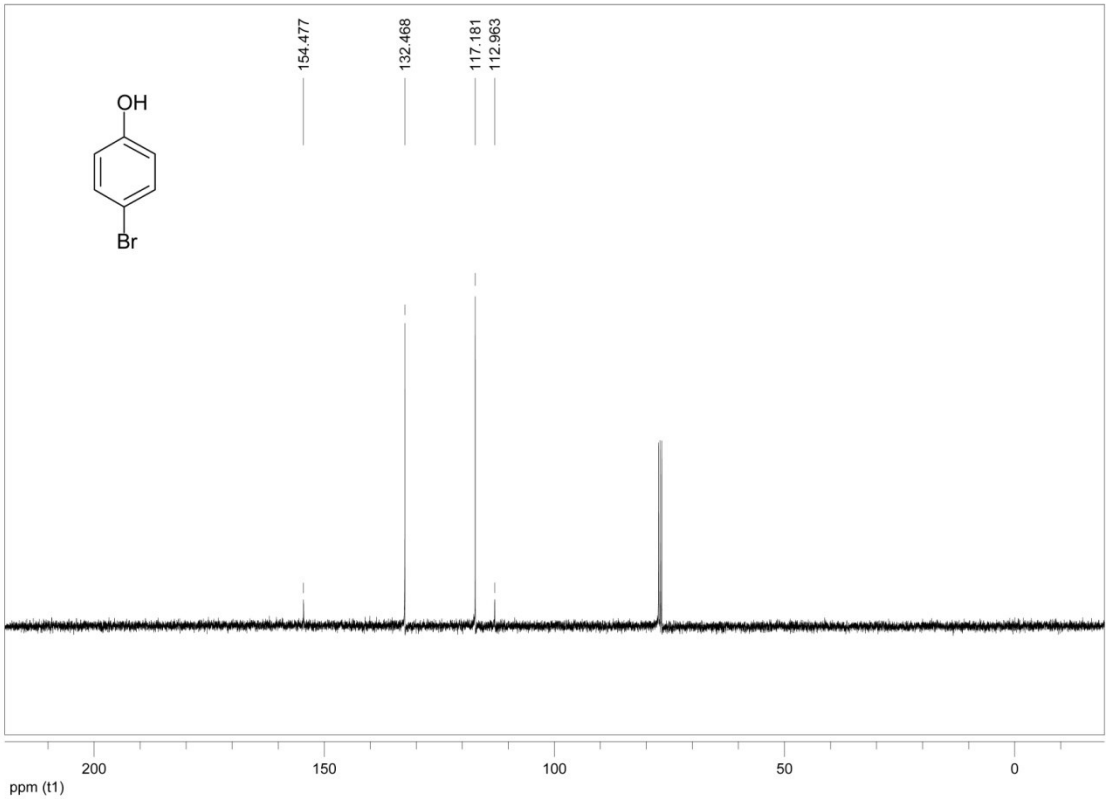
2f


OH
Cl
7.206
7.197
7.192
7.180
7.175
7.166
6.781
6.773
6.767
6.756
6.750
6.742
5.092
2.00
2.07
7.30
7.20
7.10
7.00
6.90
6.80
6.70
ppm (t1)
2.00
2.07
0.99
15.0
10.0
5.0
0.0
ppm (t1)

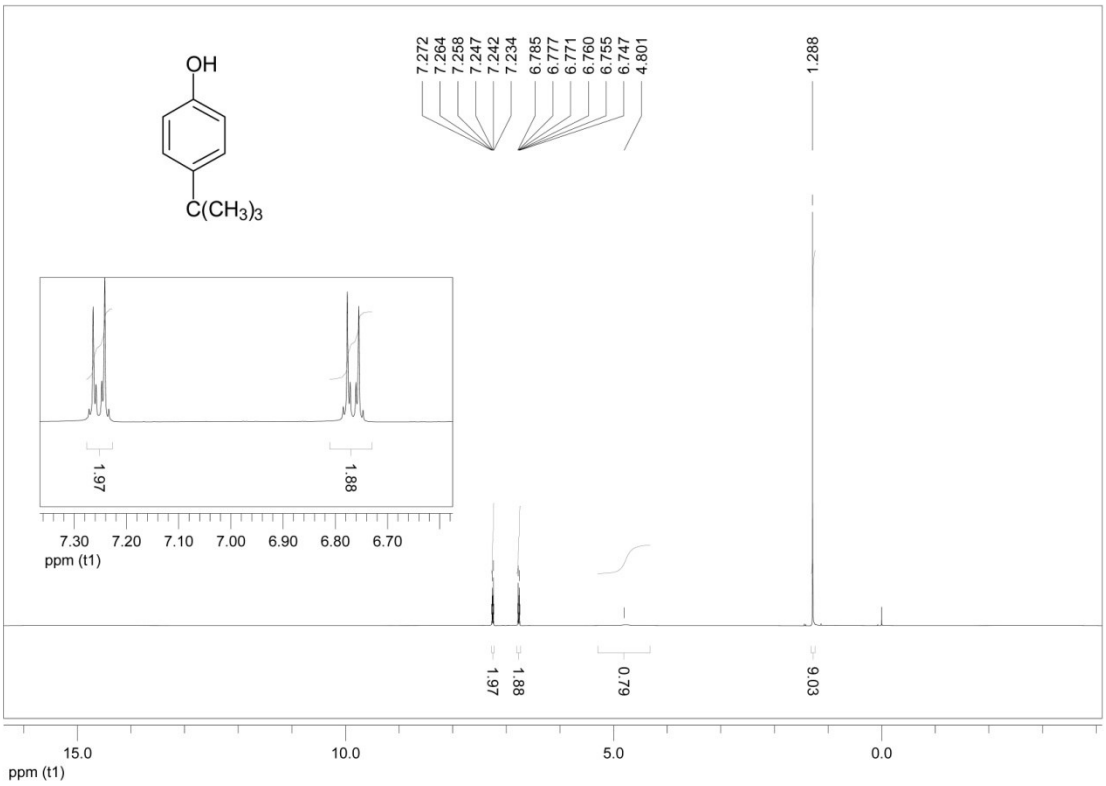

153.994
129.519
125.708
116.644
OH
Cl
200
150
100
50
0
ppm (t1)

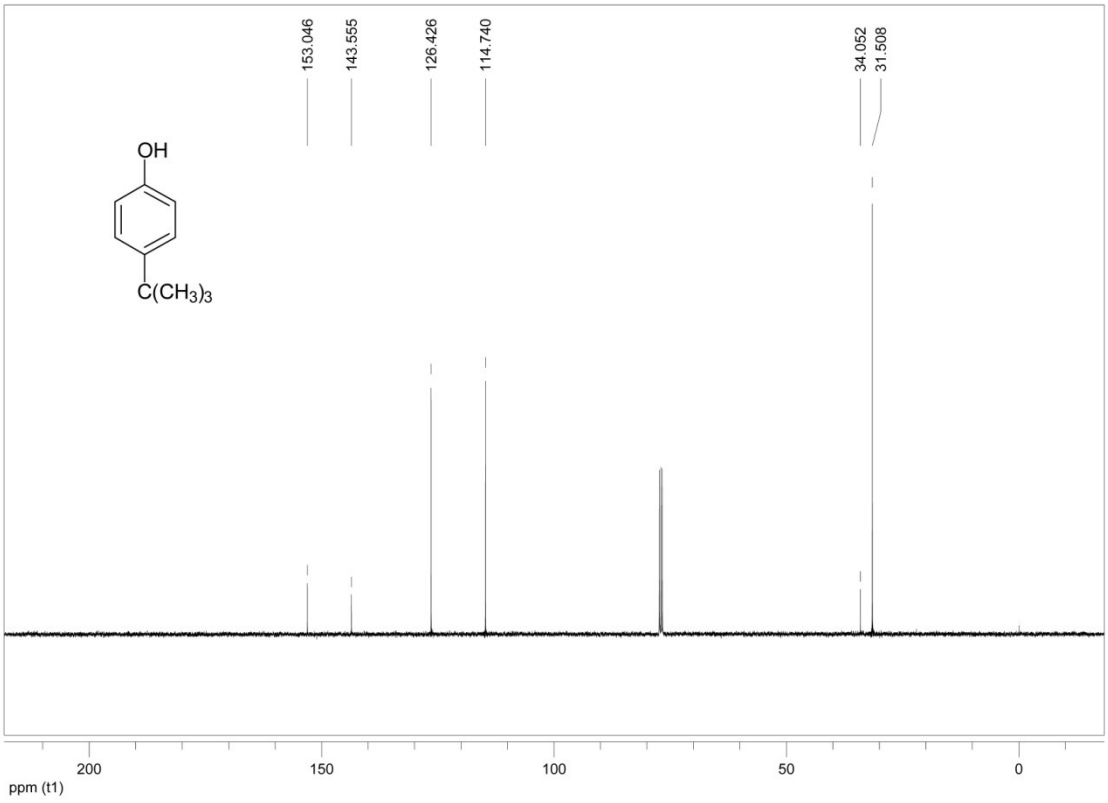
2g


7.346
7.337
7.332
7.320
7.315
7.307
6.736
6.728
6.722
6.711
6.705
6.697
5.087
OH
Br
2.00
2.03
7.30
7.20
7.10
7.00
6.90
6.80
6.70
6.60
ppm (t1)
2.00
2.03
1.02
15.0
10.0
5.0
0.0
ppm (t1)

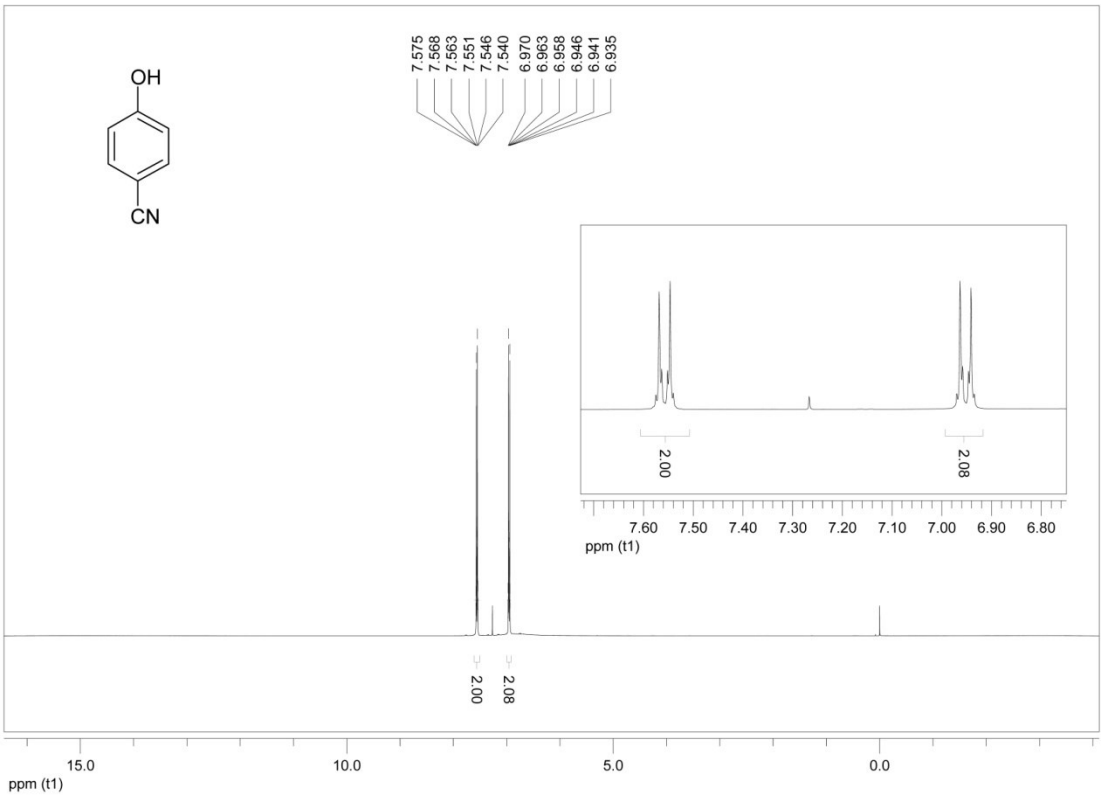

154.477
132.468
117.181
112.963
OH
Br
200
150
100
50
0
ppm (t1)

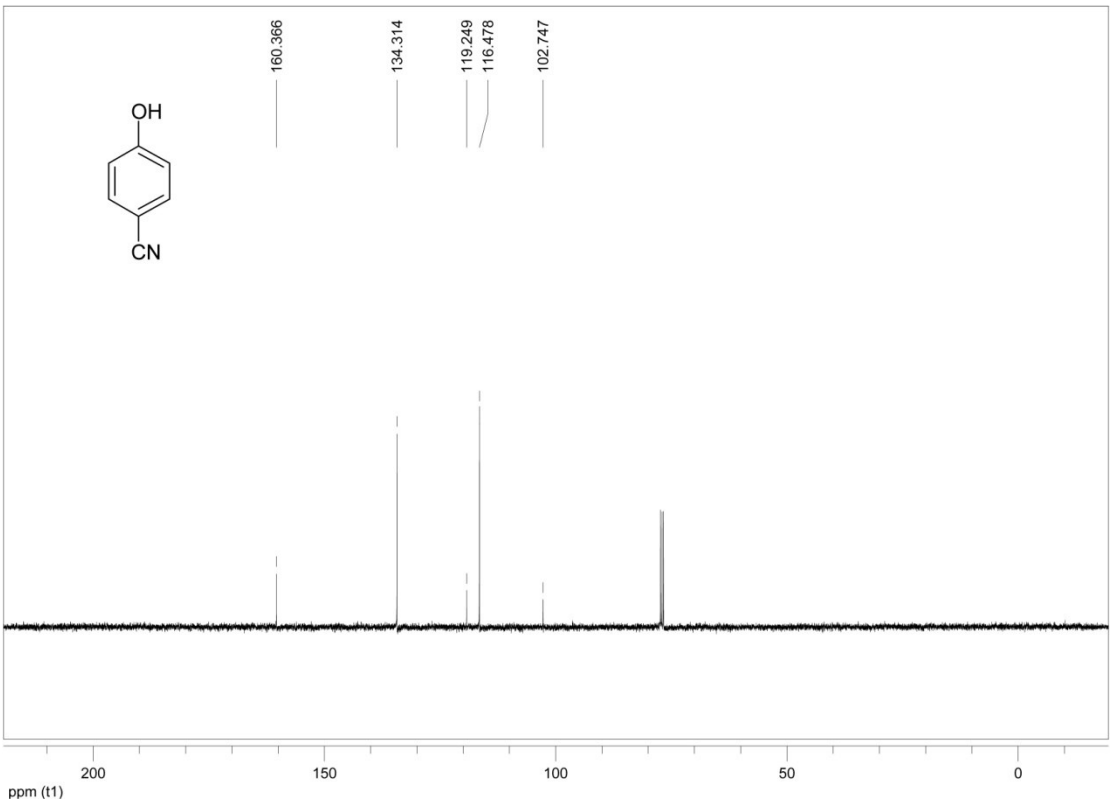
2h


OH
C(CH3)3
7.272
7.264
7.258
7.247
7.242
7.234
6.785
6.777
6.771
6.760
6.755
6.747
4.801
1.288
1.97
1.88
7.30
7.20
7.10
7.00
6.90
6.80
6.70
ppm (t1)
1.97
1.88
0.79
9.03
15.0
10.0
5.0
0.0
ppm (t1)

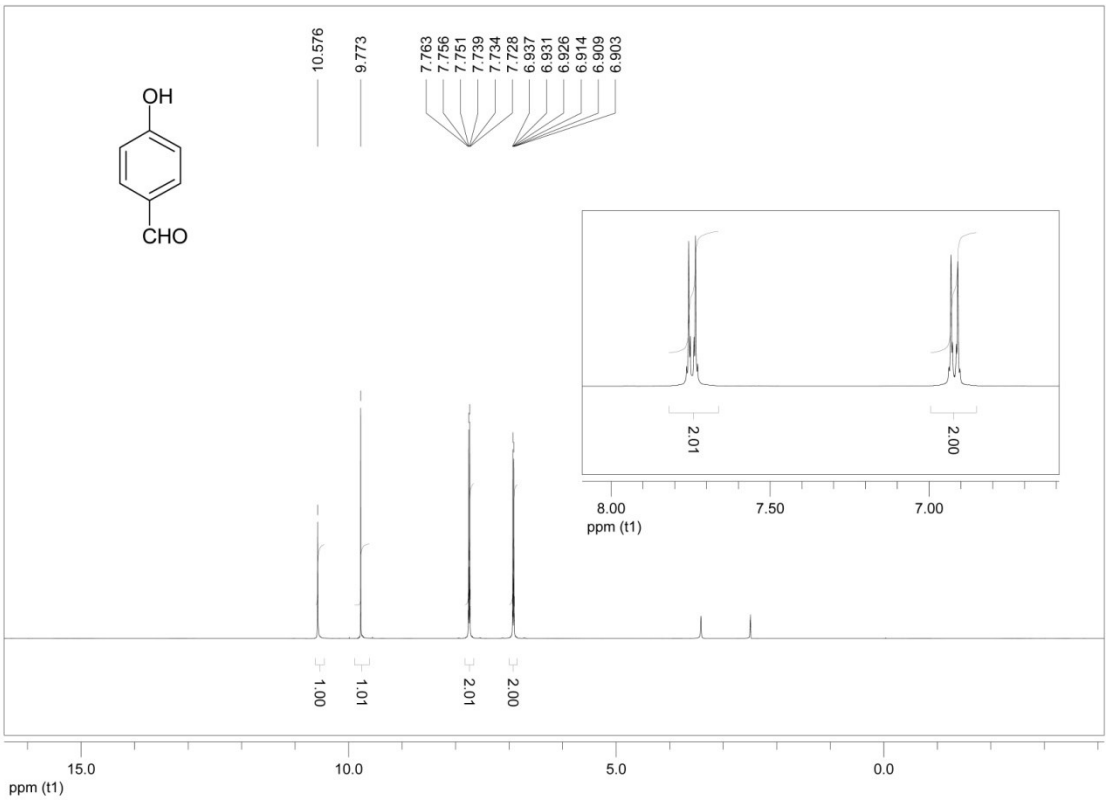

153.046
143.555
126.426
114.740
34.052
31.508
OH
C(CH3)3
200
150
100
50
0
ppm (t1)

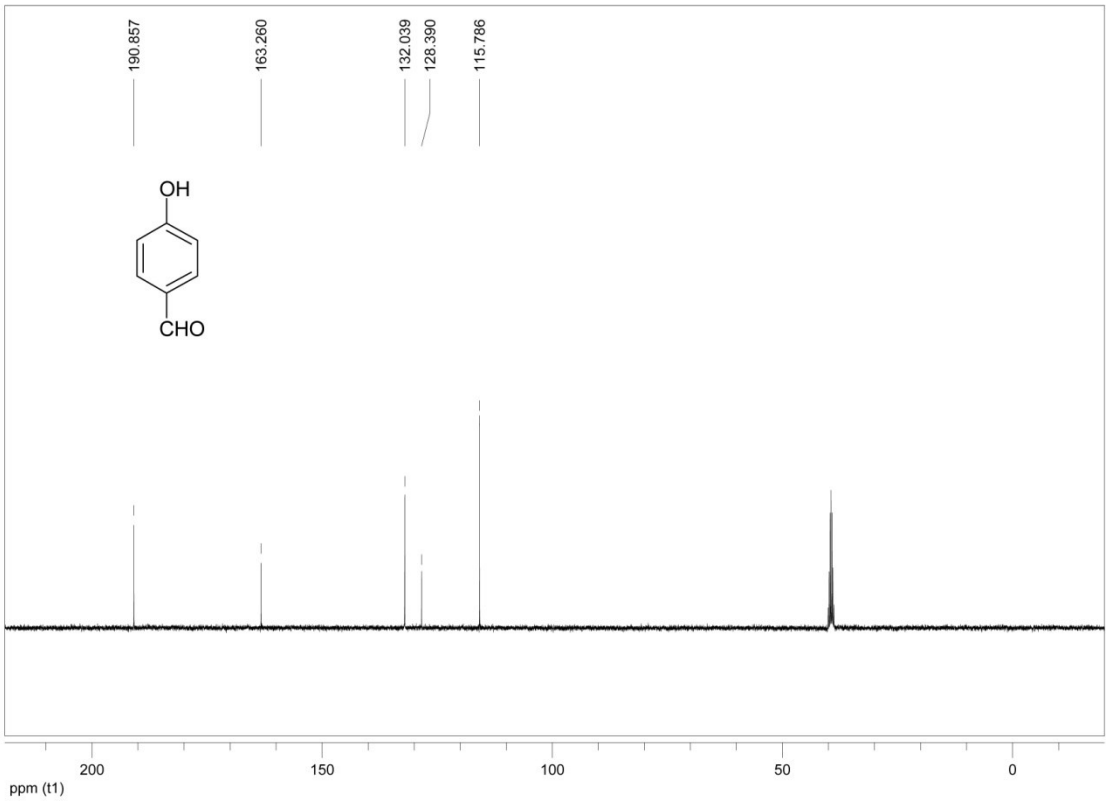
2i


7.575
7.568
7.563
7.551
7.546
7.540
6.970
6.963
6.958
6.946
6.941
6.935
OH
CN
2.00
2.08
7.60 7.50 7.40 7.30 7.20 7.10 7.00 6.90 6.80
ppm (t1)
2.00
2.08
15.0 10.0 5.0 0.0
ppm (t1)

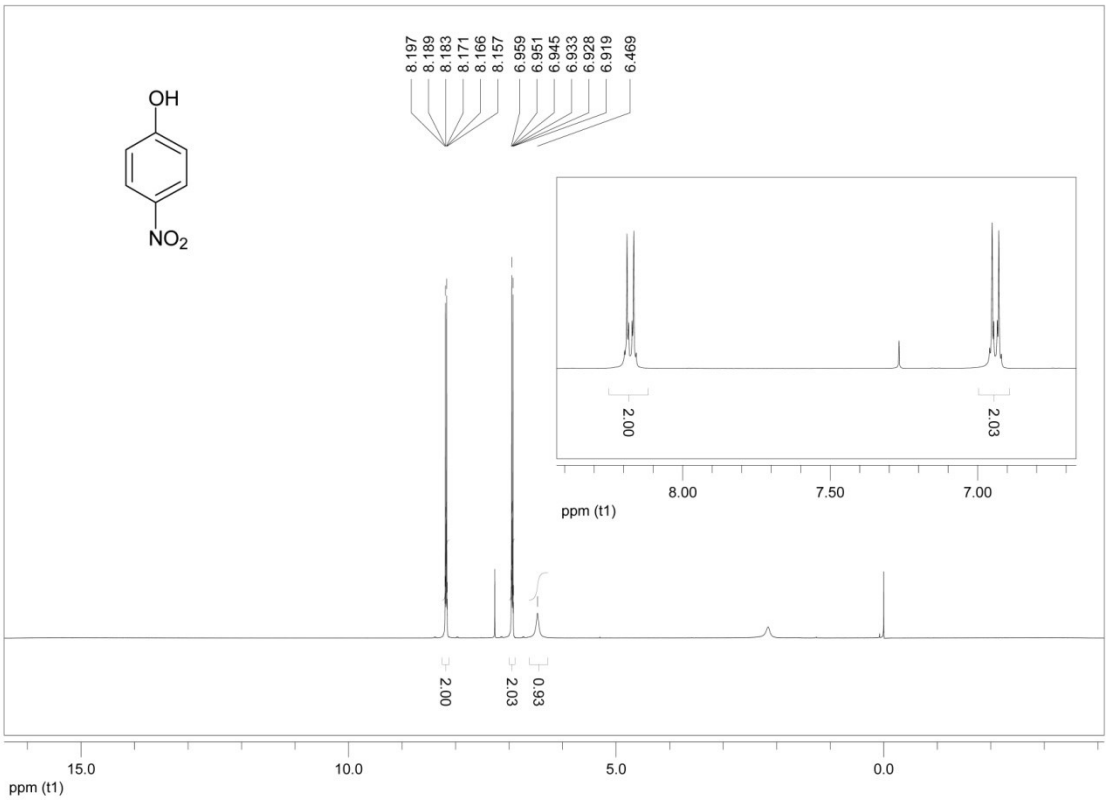

160.366
134.314
119.249
116.478
102.747
OH
CN
200 150 100 50 0
ppm (t1)

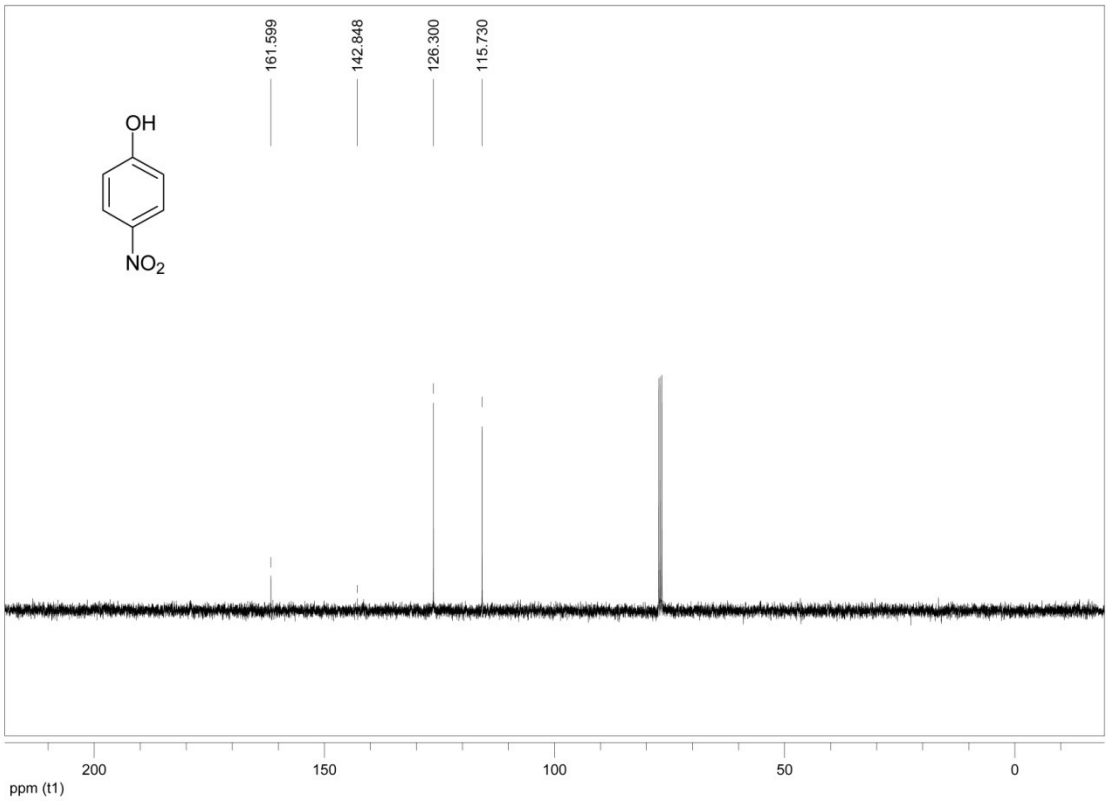
2j


10.576
9.773
7.763
7.756
7.751
7.739
7.734
7.728
6.937
6.931
6.926
6.914
6.909
6.903
OH
CHO
2.01
2.00
8.00
7.50
7.00
ppm (t1)
1.00
1.01
2.01
2.00
15.0
10.0
5.0
0.0
ppm (t1)

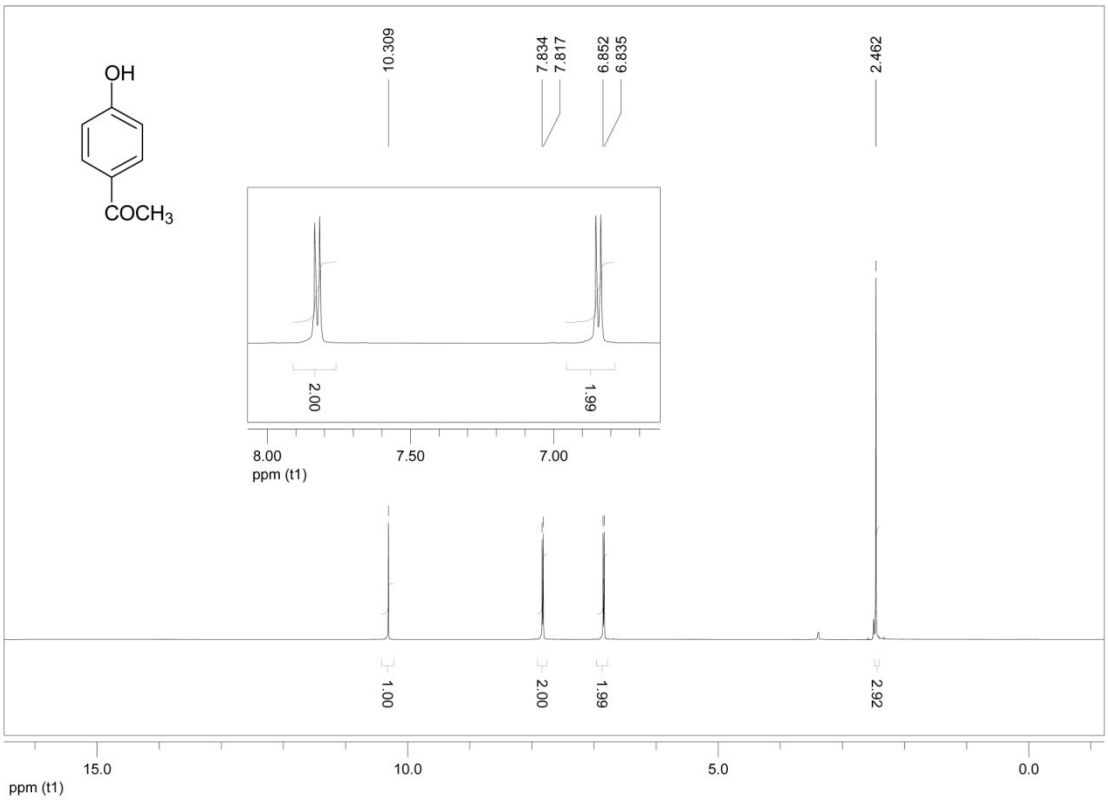

190.857
163.260
132.039
128.390
115.786
OH
CHO
200
150
100
50
0
ppm (t1)

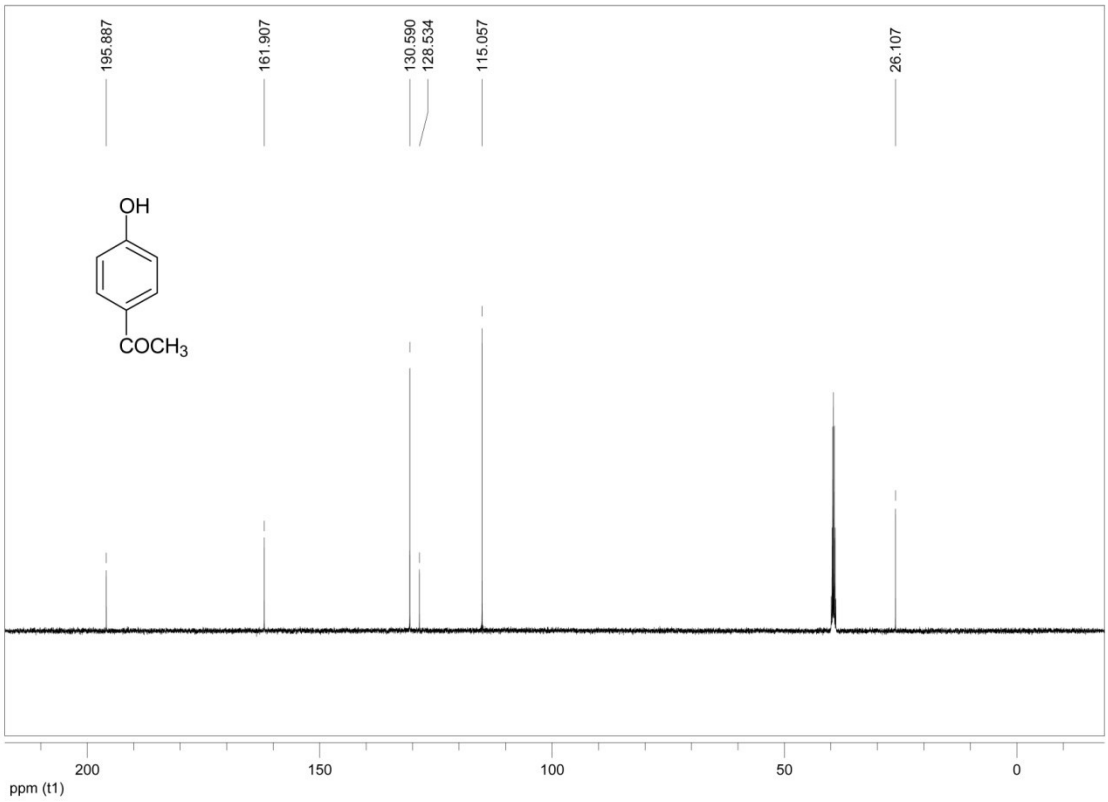
2k


8.197
8.189
8.183
8.171
8.166
8.157
6.959
6.951
6.945
6.933
6.928
6.919
6.469
OH
NO2
2.00
2.03
8.00
7.50
7.00
ppm (t1)
2.00
2.03
0.93
15.0
10.0
5.0
0.0
ppm (t1)

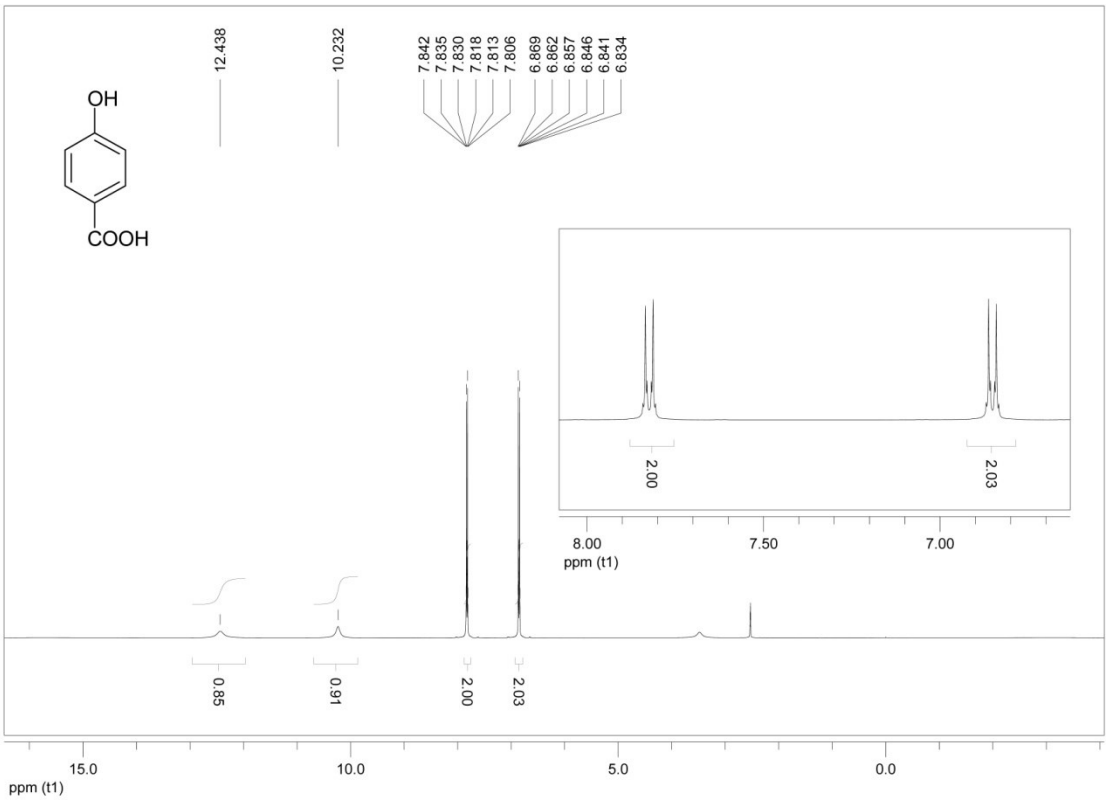

161.599
142.848
126.300
115.730
OH
NO2
200
150
100
50
0
ppm (t1)

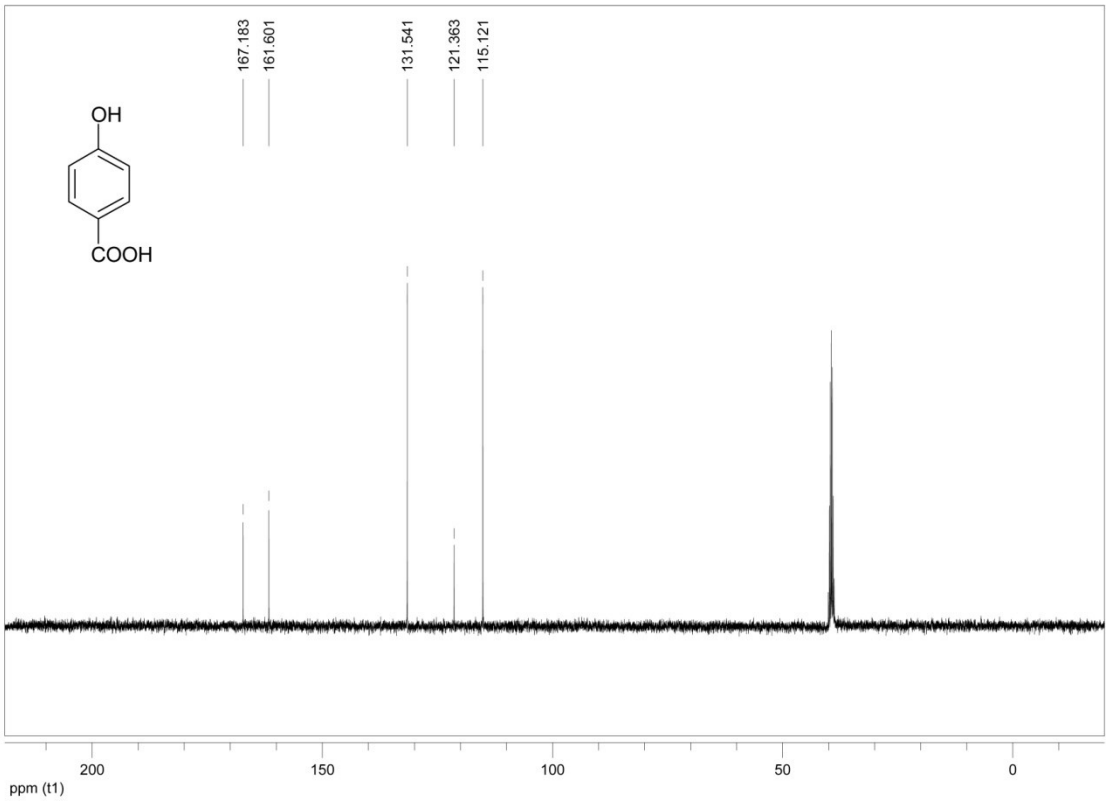
2l


OH
COCH3
10.309
7.834
7.817
6.852
6.835
2.462
2.00
1.99
8.00
7.50
7.00
ppm (t1)
1.00
2.00
1.99
2.92
15.0
10.0
5.0
0.0
ppm (t1)

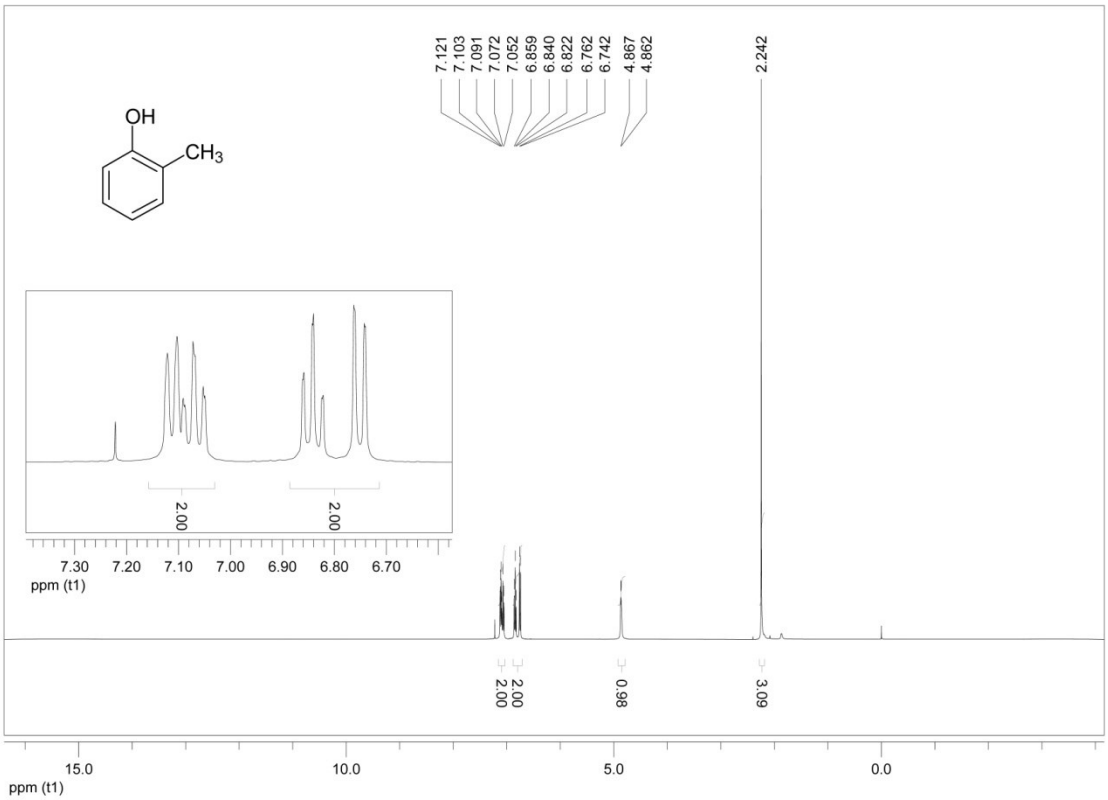

195.887
161.907
130.590
128.534
115.057
26.107
OH
COCH3
200
150
100
50
0
ppm (t1)

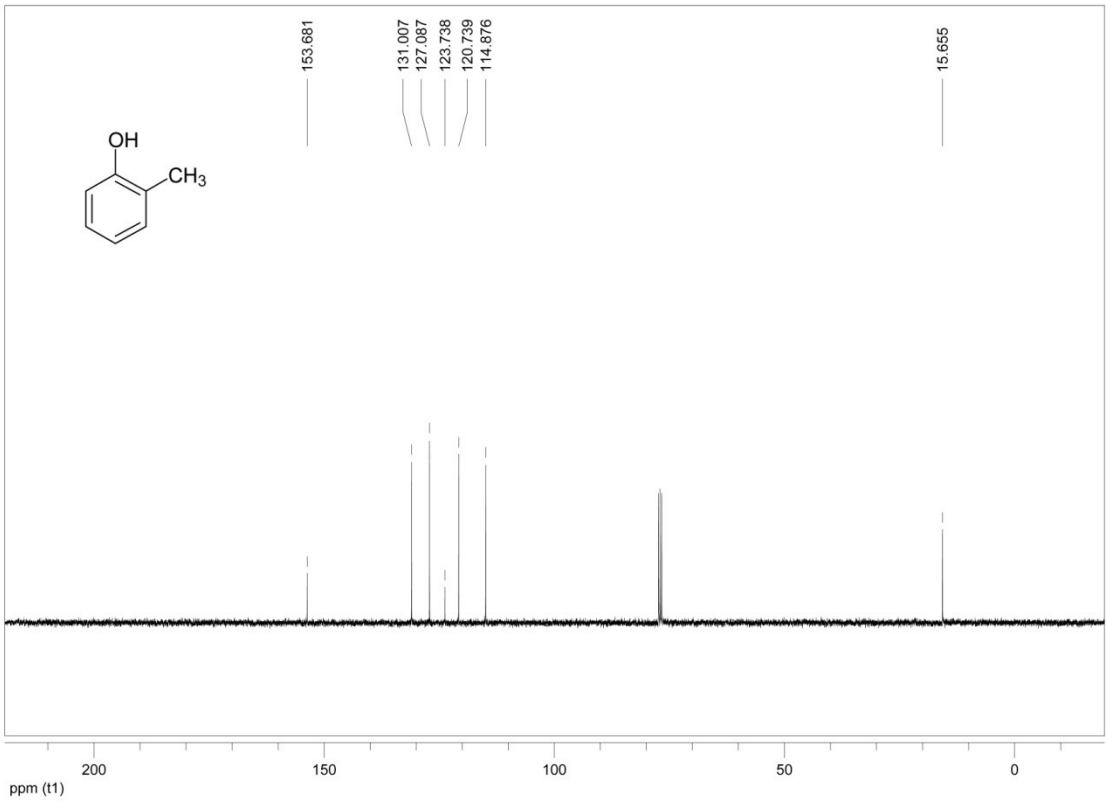
2m


12.438
10.232
7.842
7.835
7.830
7.818
7.813
7.806
6.869
6.862
6.857
6.846
6.841
6.834
OH
COOH
2.00
2.03
8.00
7.50
7.00
ppm (t1)
0.85
0.91
2.00
2.03
15.0
10.0
5.0
0.0
ppm (t1)

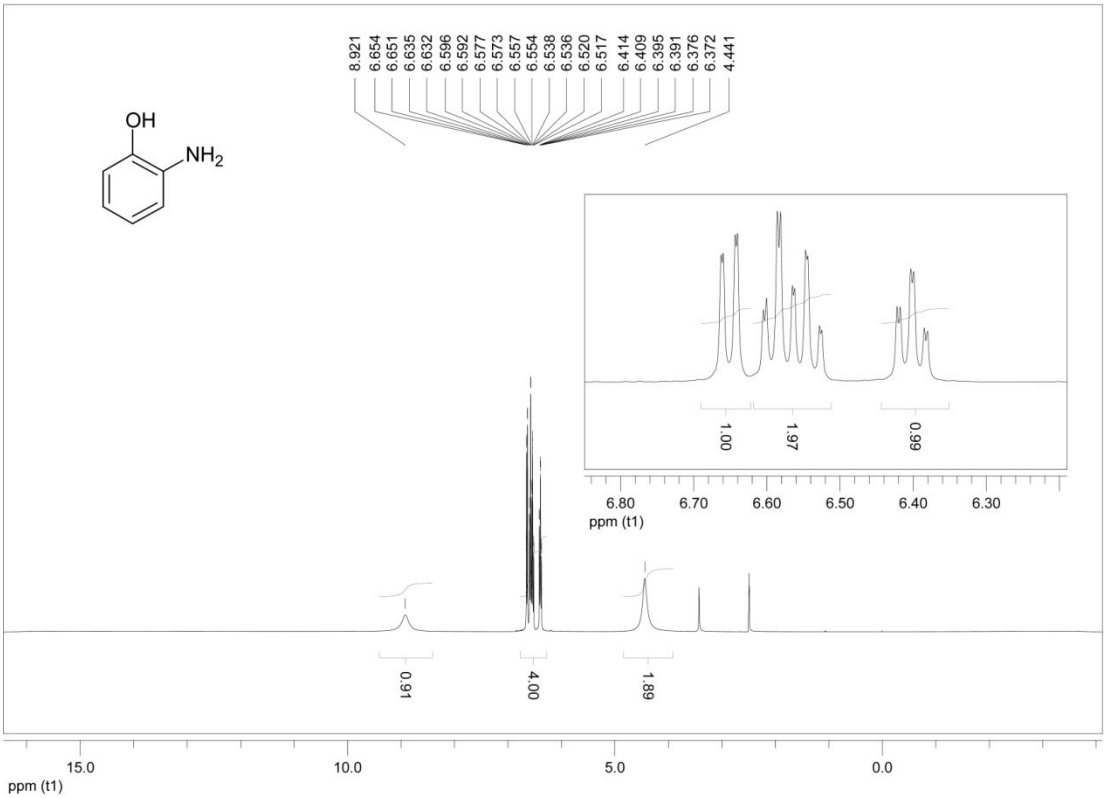

167.183
161.601
131.541
121.363
115.121
OH
COOH
200
150
100
50
0
ppm (t1)

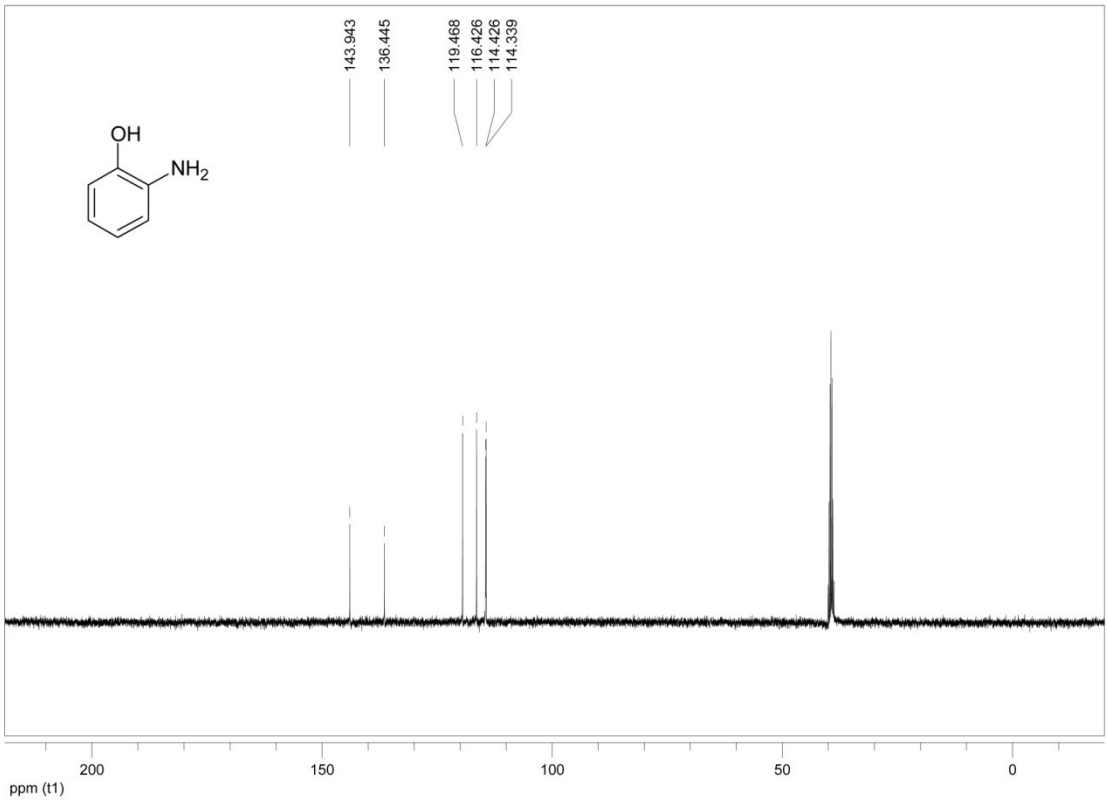
2n


7.121
7.103
7.091
7.072
7.052
6.859
6.840
6.822
6.762
6.742
4.867
4.862
2.242
OH
CH3
2.00
2.00
7.30
7.20
7.10
7.00
6.90
6.80
6.70
ppm (t1)
2.00
2.00
0.98
3.09
15.0
10.0
5.0
0.0
ppm (t1)

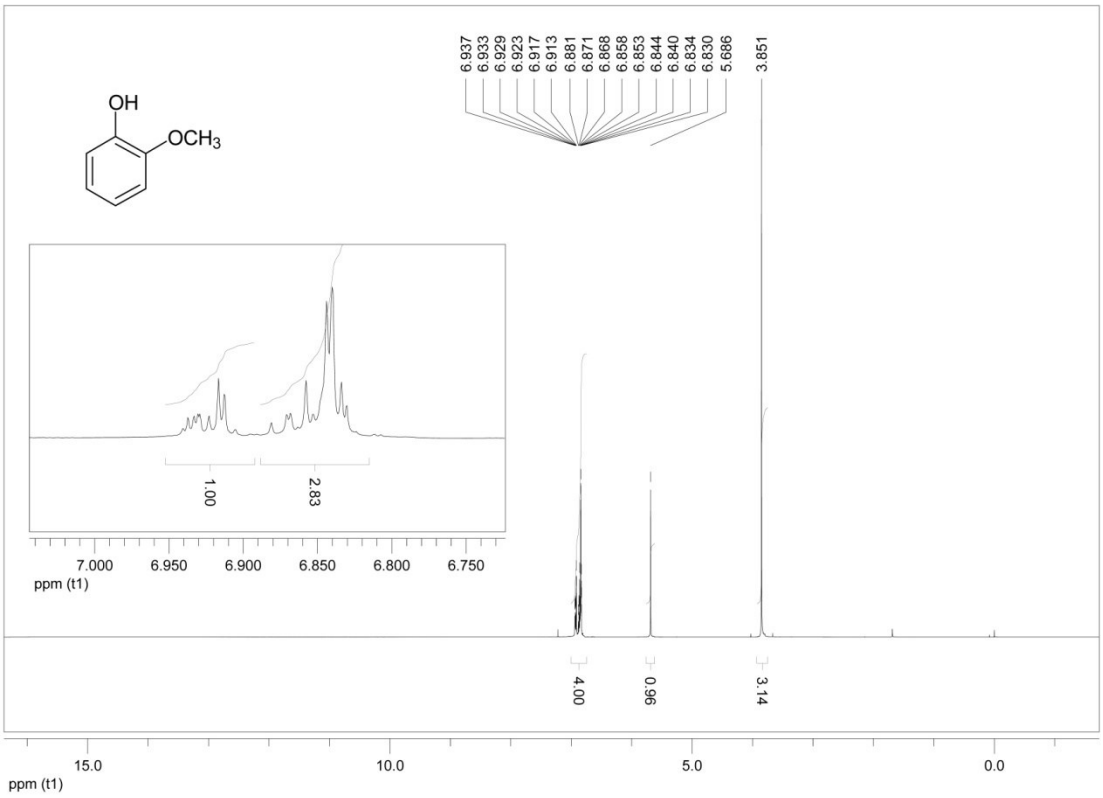

153.681
131.007
127.087
123.738
120.739
114.876
15.655
OH
CH3
200
150
100
50
0
ppm (t1)

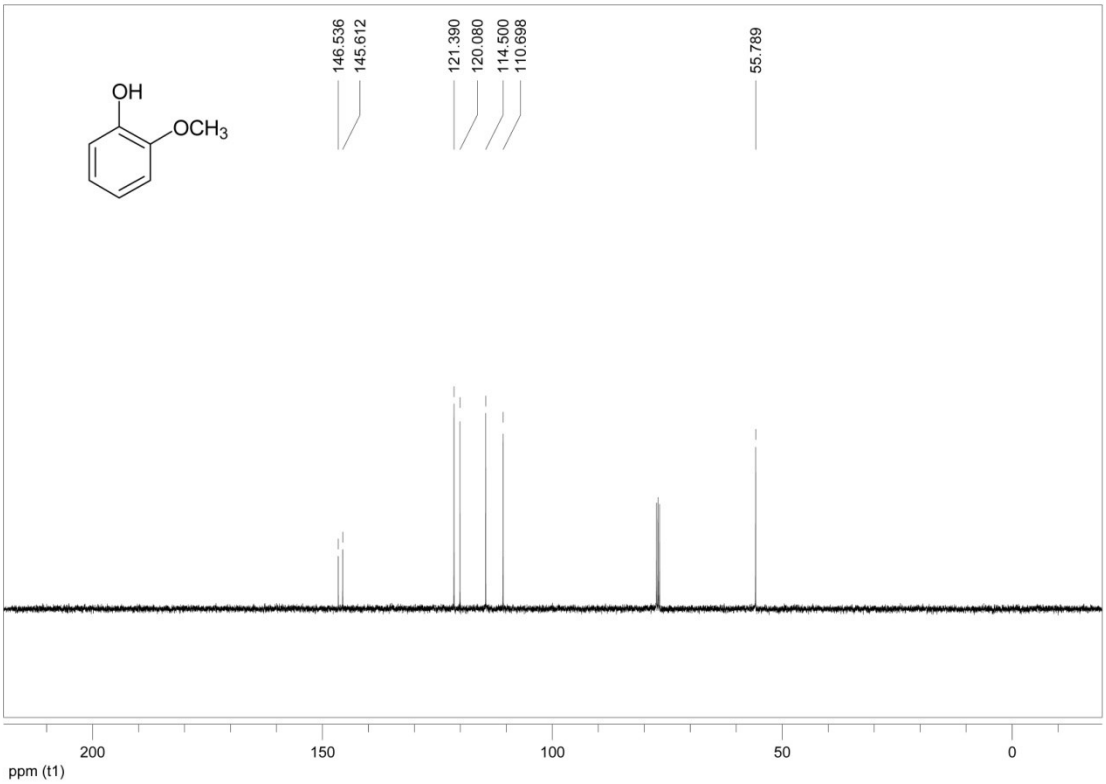
2o


8.921
6.654
6.651
6.635
6.632
6.596
6.592
6.577
6.573
6.557
6.554
6.538
6.536
6.520
6.517
6.414
6.409
6.395
6.391
6.376
6.372
4.441
OH
NH2
1.00
1.97
0.99
6.80
6.70
6.60
6.50
6.40
6.30
ppm (t1)
0.91
4.00
1.89
15.0
10.0
5.0
0.0
ppm (t1)

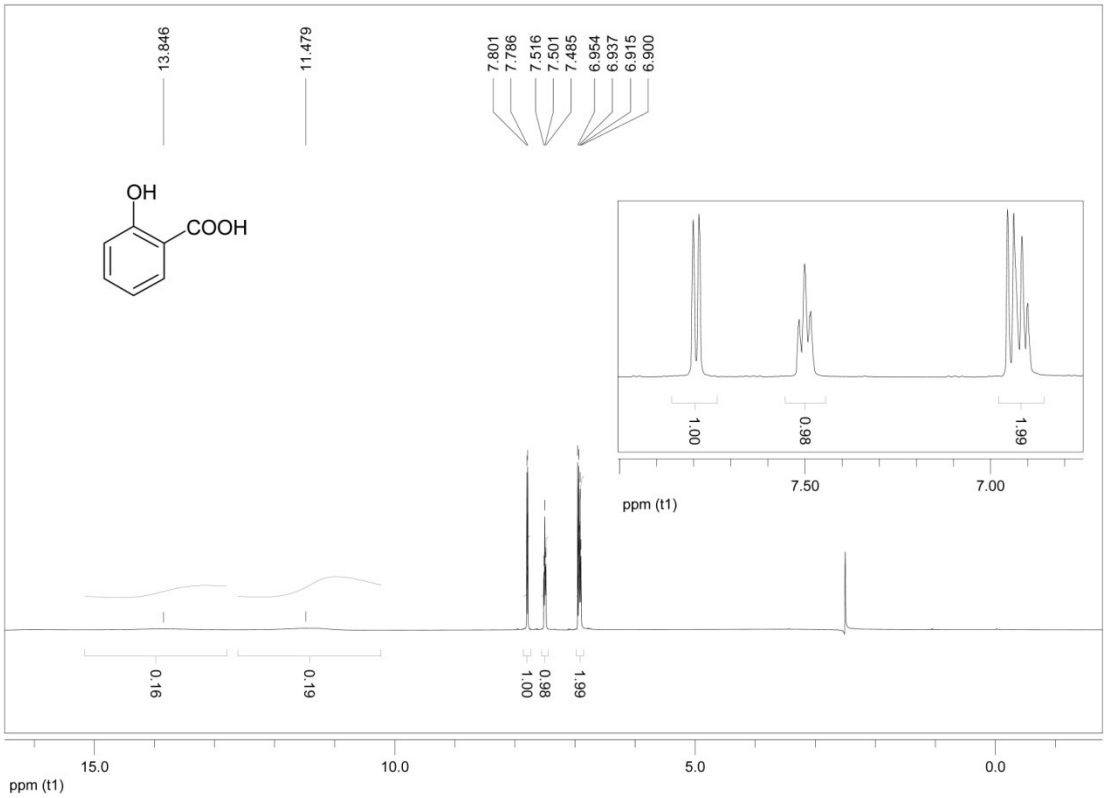

143.943
136.445
119.468
116.426
114.426
114.339
OH
NH2
200
150
100
50
0
ppm (t1)

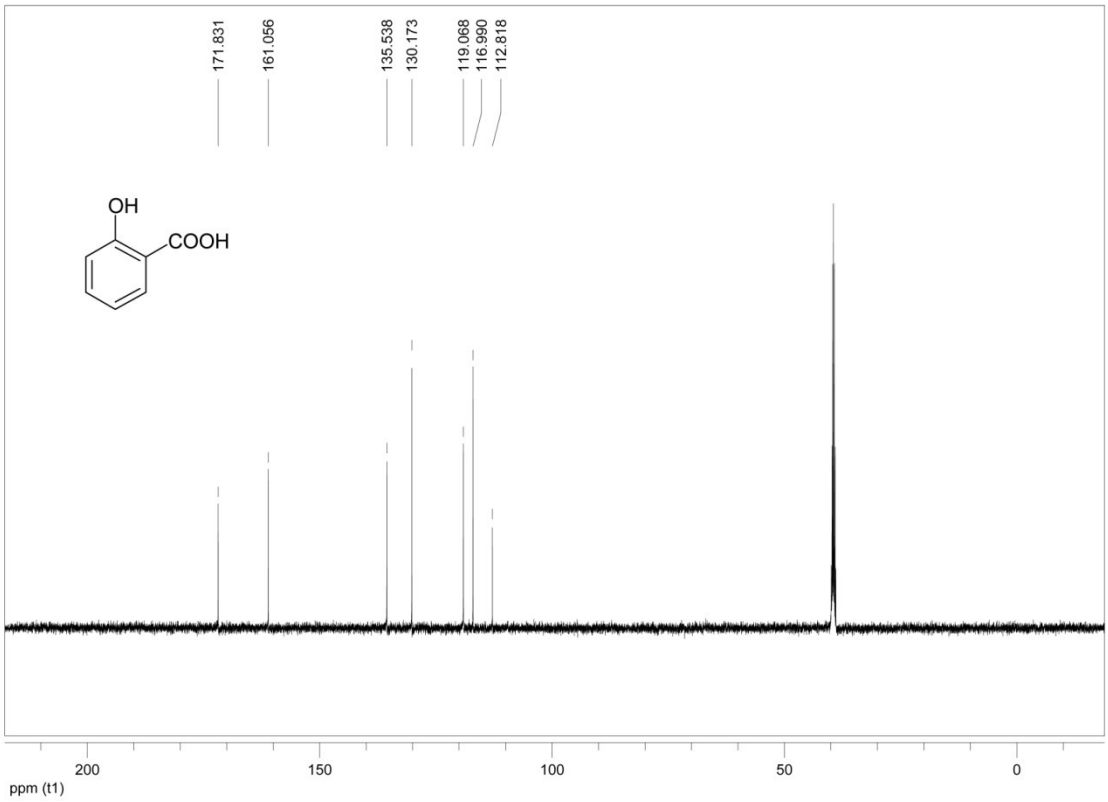
2p


6.937
6.933
6.929
6.923
6.917
6.913
6.881
6.871
6.868
6.858
6.853
6.844
6.840
6.834
6.830
5.686
3.851
OH
OCH3
1.00
2.83
7.000
6.950
6.900
6.850
6.800
6.750
ppm (t1)
4.00
0.96
3.14
15.0
10.0
5.0
0.0
ppm (t1)

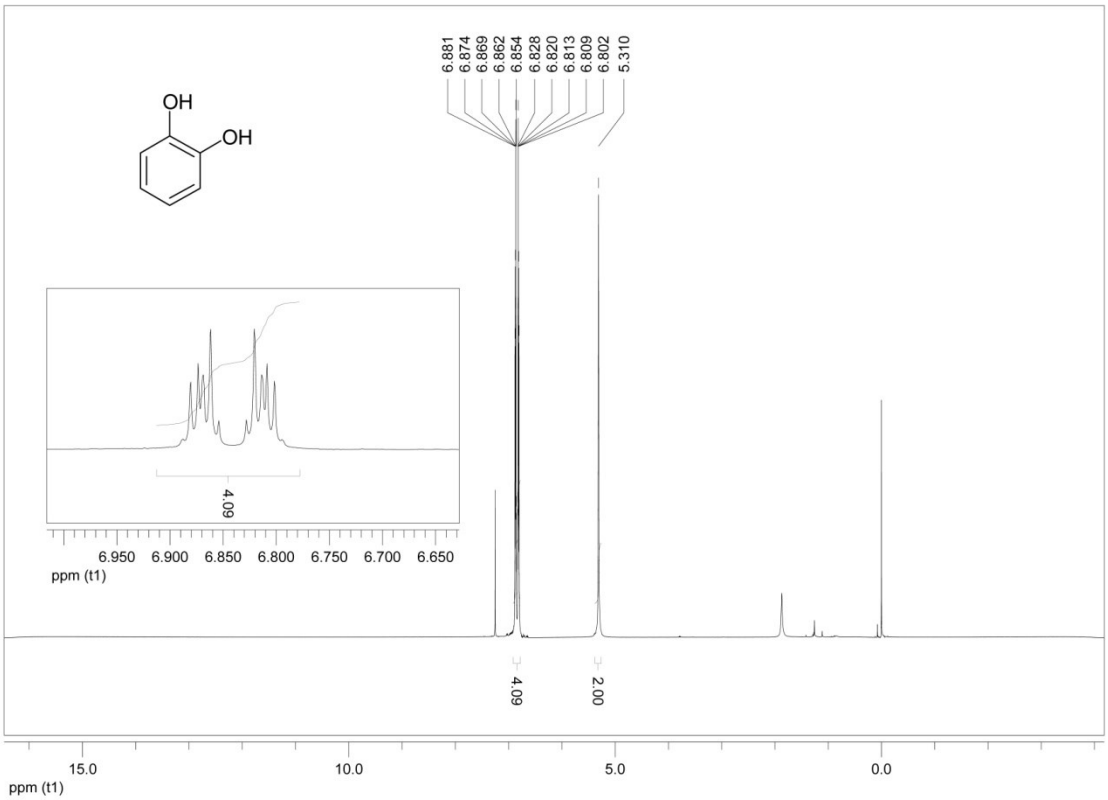

146.536
145.612
121.390
120.080
114.500
110.698
55.789
OH
OCH3
200
150
100
50
0
ppm (t1)

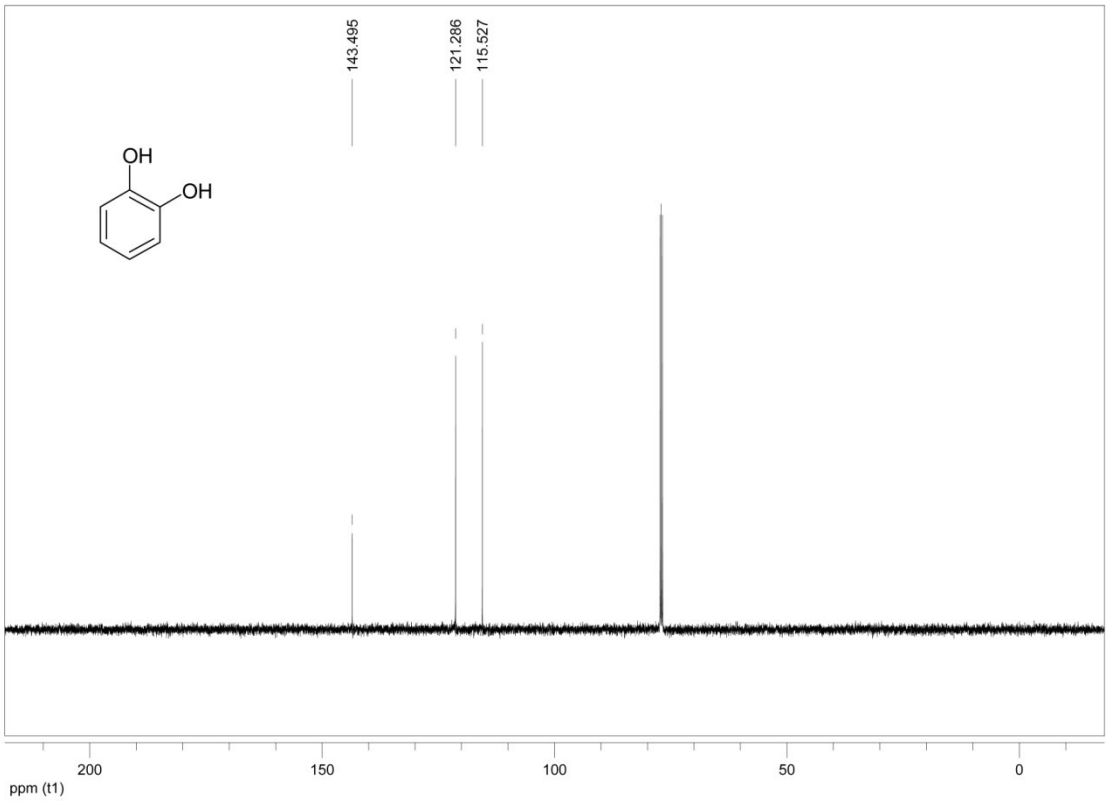
2q


13.846
11.479
7.801
7.786
7.516
7.501
7.485
6.954
6.937
6.915
6.900
OH
COOH
1.00
0.98
1.99
7.50
7.00
ppm (t1)
0.16
0.19
1.00
0.98
1.99
15.0
10.0
5.0
0.0
ppm (t1)

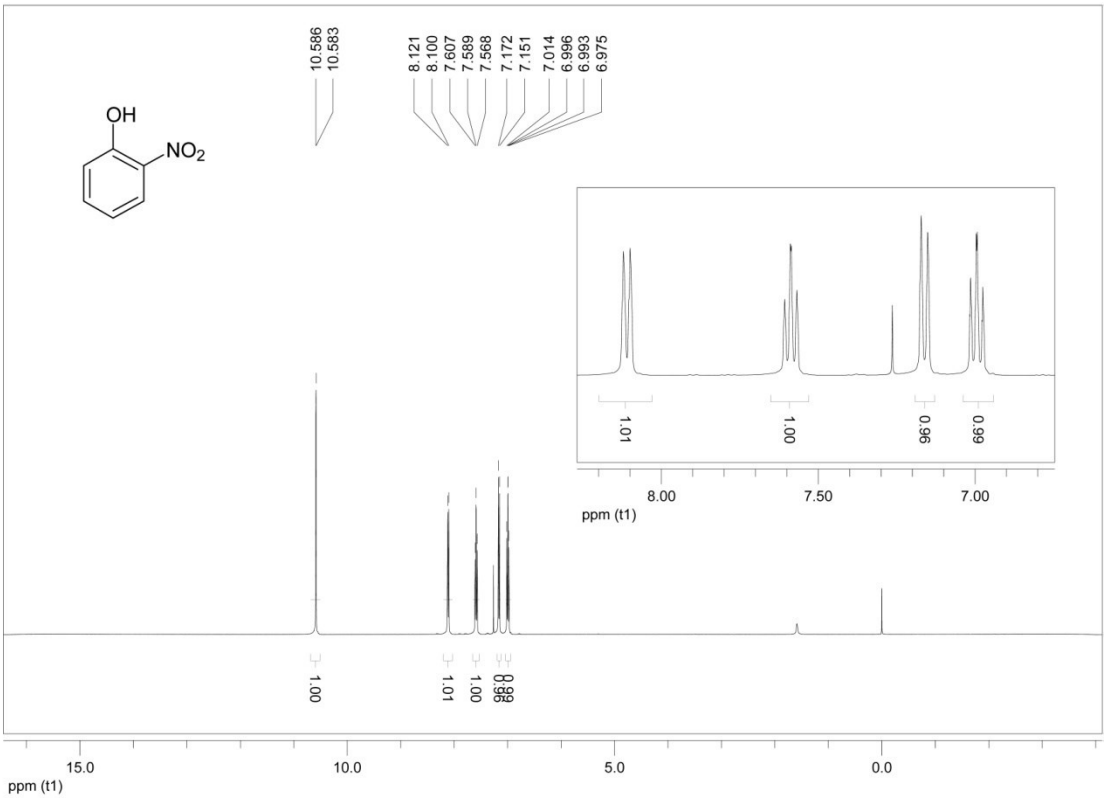

171.831
161.056
135.538
130.173
119.068
116.990
112.818
OH
COOH
200
150
100
50
0
ppm (t1)

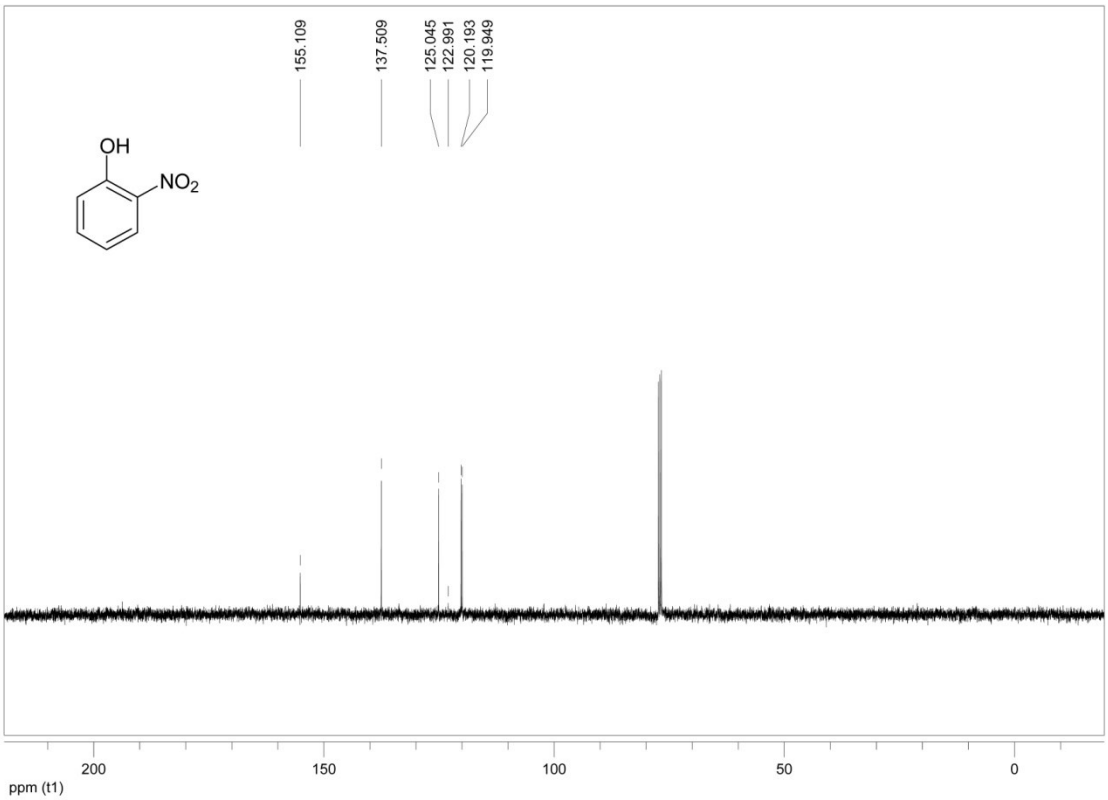
2r


6.881
6.874
6.869
6.862
6.854
6.828
6.820
6.813
6.809
6.802
5.310
OH
OH
4.09
6.950 6.900 6.850 6.800 6.750 6.700 6.650
ppm (t1)
4.00
2.00
15.0
10.0
5.0
0.0
ppm (t1)

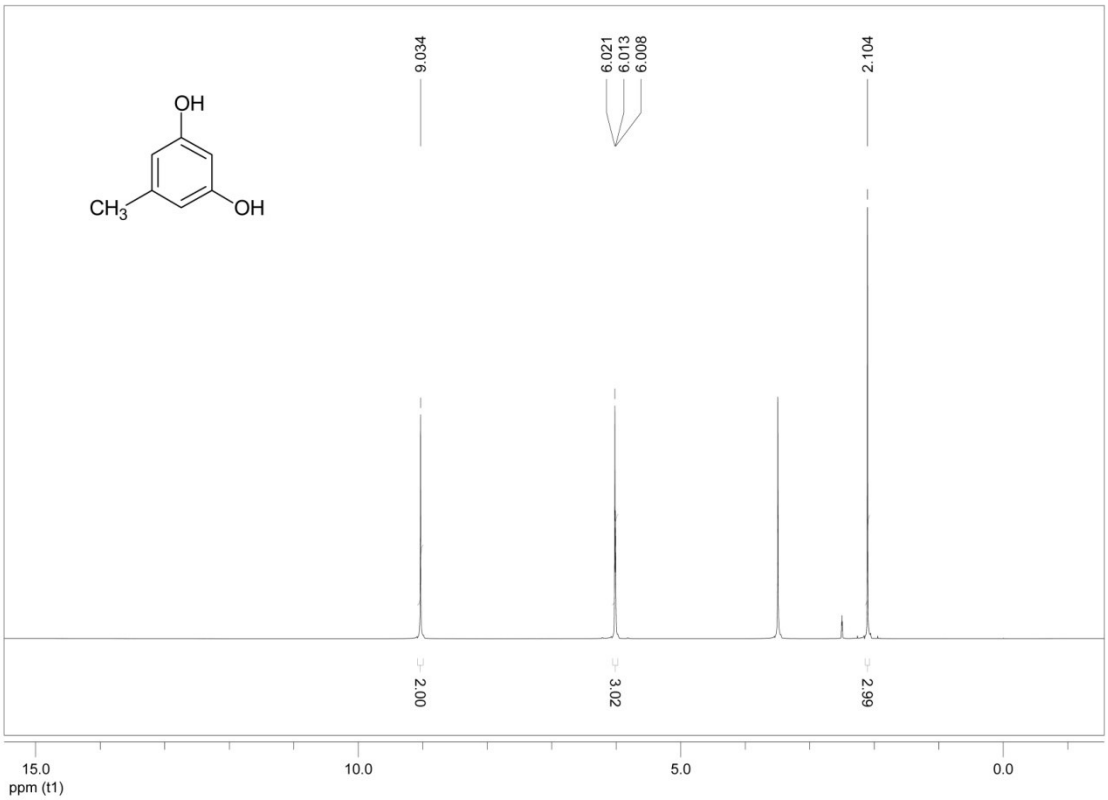

143.495
121.286
115.527
OH
OH
200
150
100
50
0
ppm (t1)

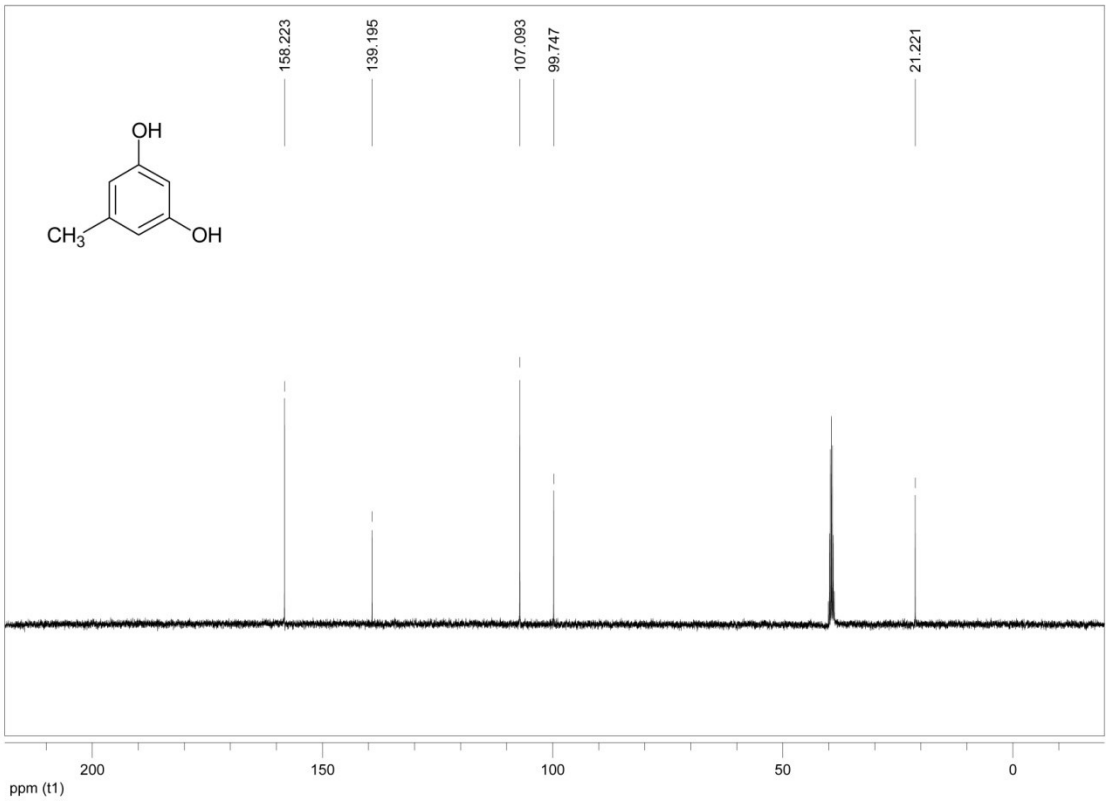
2s


10.586
10.583
8.121
8.100
7.607
7.589
7.568
7.172
7.151
7.014
6.996
6.993
6.975
OH
NO2
1.01
1.00
0.99
0.99
8.00
7.50
7.00
ppm (t1)
1.00
1.01
1.00
0.99
0.99
15.0
10.0
5.0
0.0
ppm (t1)

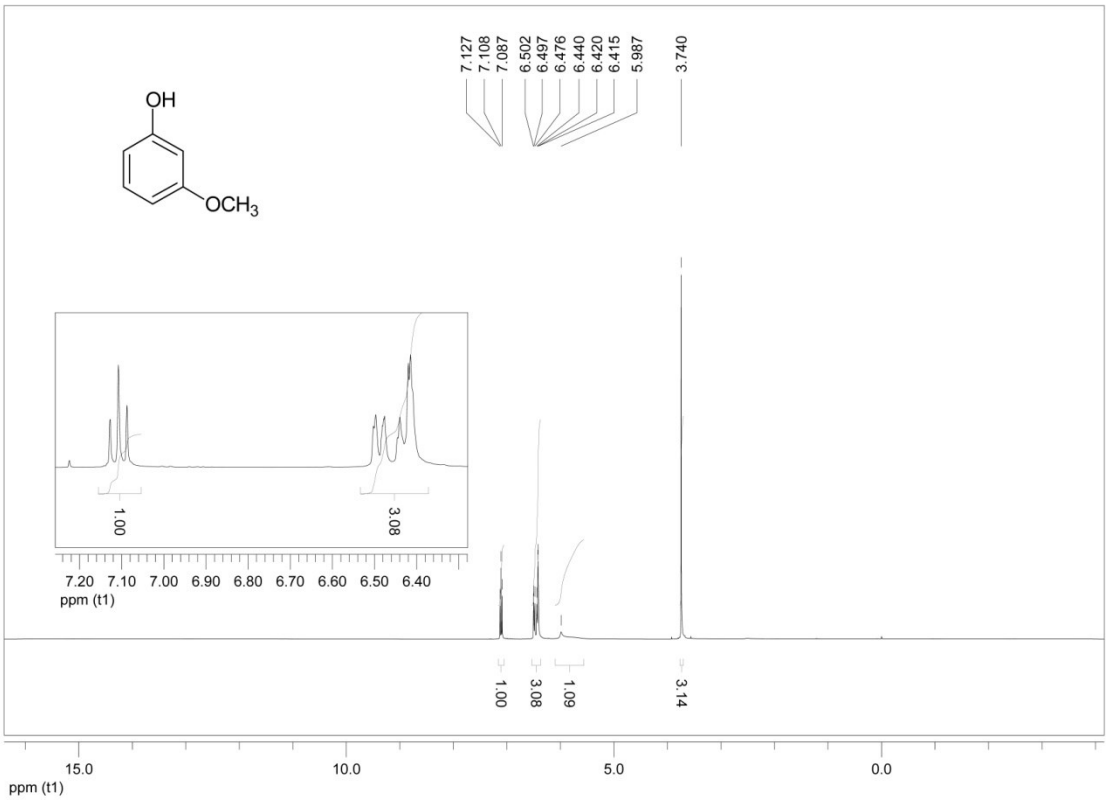

155.109
137.509
125.045
122.991
120.193
119.949
OH
NO2
200
150
100
50
0
ppm (t1)

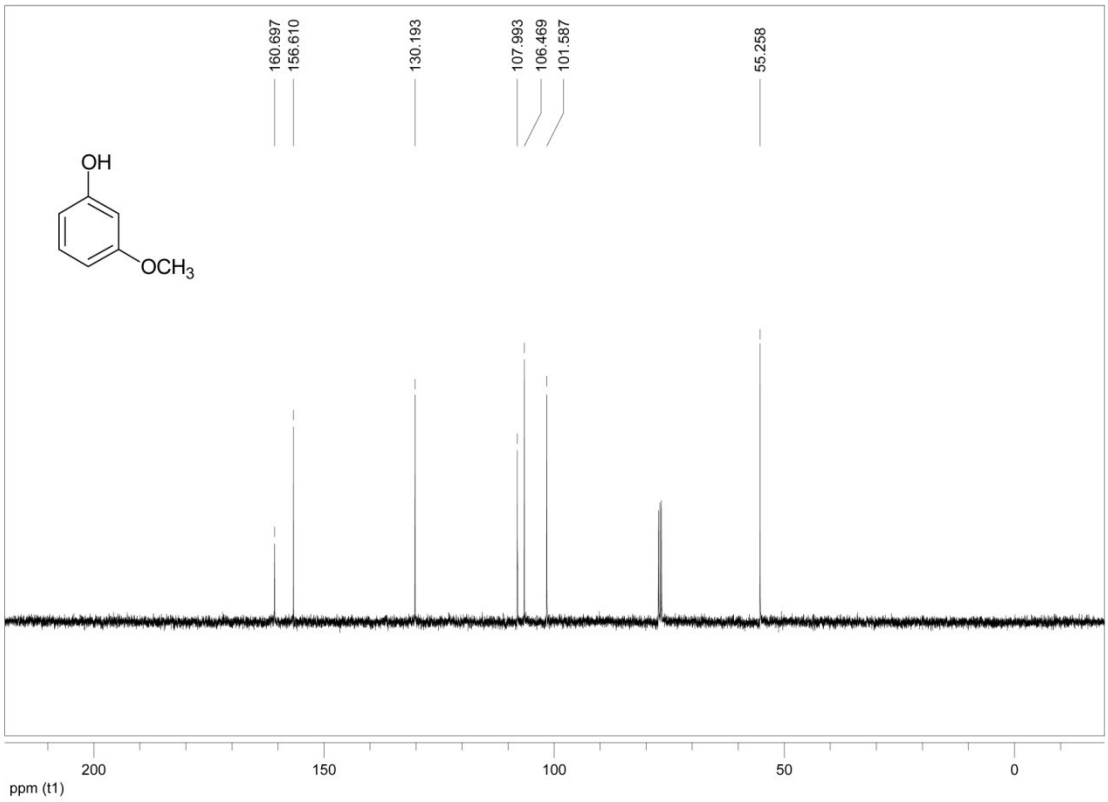
2t


9.034
6.021
6.013
6.008
2.104
OH
CH3
OH
2.00
3.02
2.99
15.0
10.0
5.0
0.0
ppm (t1)

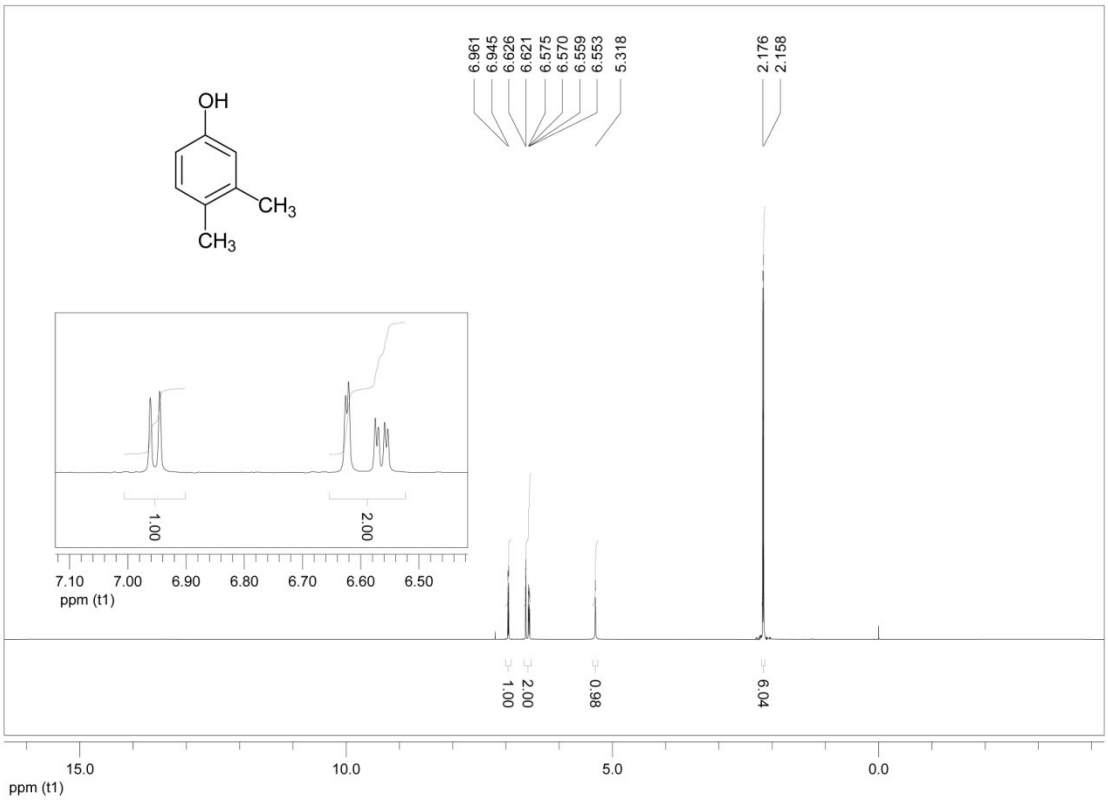

158.223
139.195
107.093
99.747
21.221
OH
CH3
OH
200
150
100
50
0
ppm (t1)

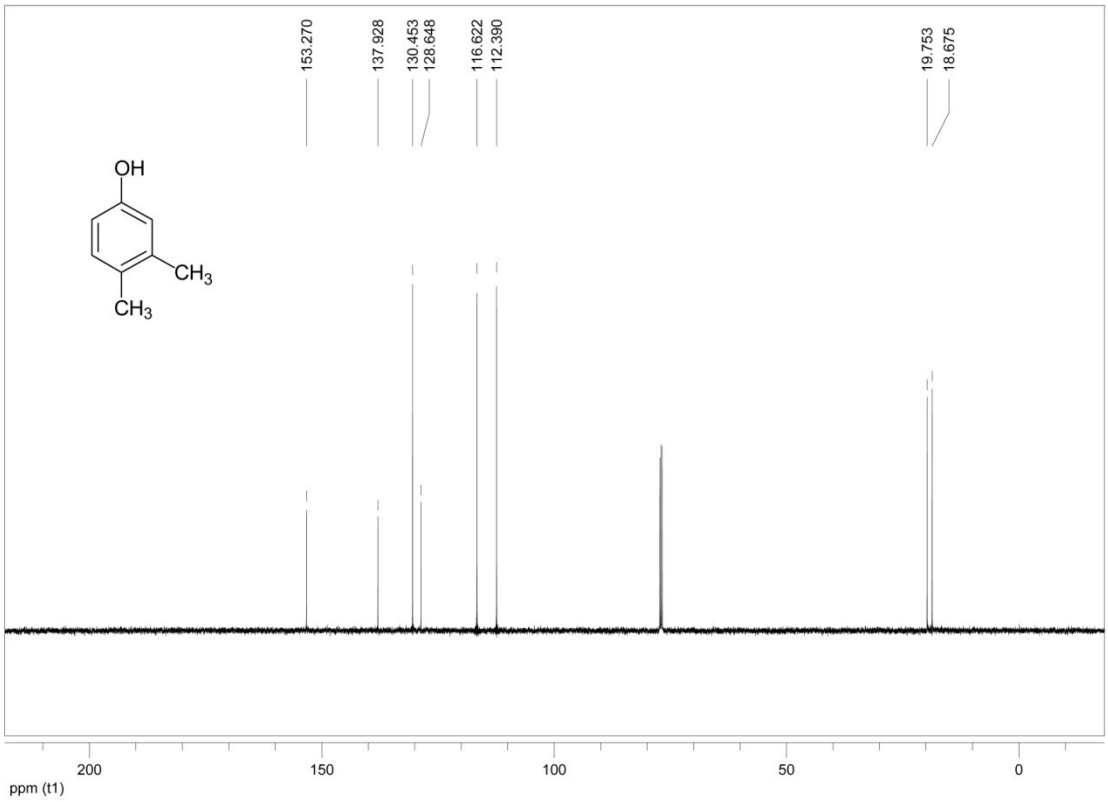
2u


7.127
7.108
7.087
6.502
6.497
6.476
6.440
6.420
6.415
5.987
3.740
OH
OCH3
1.00
3.08
7.20 7.10 7.00 6.90 6.80 6.70 6.60 6.50 6.40
ppm (t1)
1.00
3.08
1.09
3.14
15.0
10.0
5.0
0.0
ppm (t1)

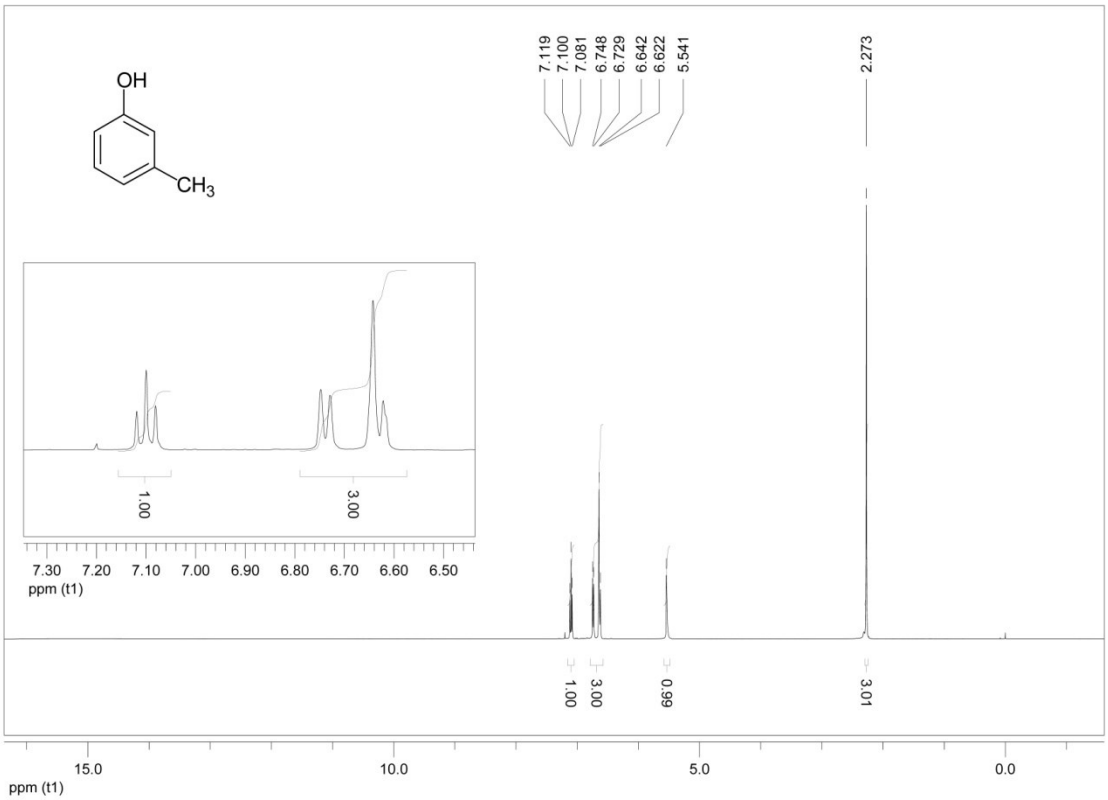

160.697
156.610
130.193
107.993
106.469
101.587
55.258
OH
OCH3
200
150
100
50
0
ppm (t1)

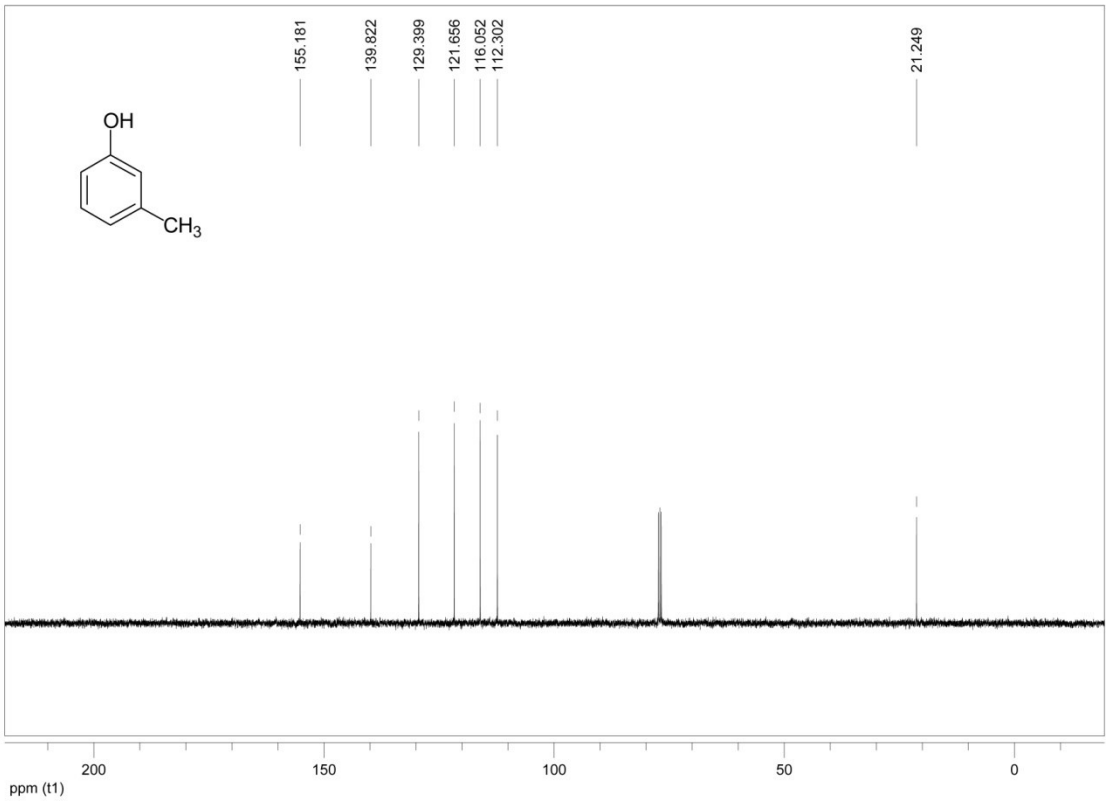
2v


6.961
6.945
6.626
6.621
6.575
6.570
6.559
6.553
5.318
2.176
2.158
OH
CH3
CH3
1.00
2.00
7.10
7.00
6.90
6.80
6.70
6.60
6.50
ppm (t1)
1.00
2.00
0.98
6.04
15.0
10.0
5.0
0.0
ppm (t1)

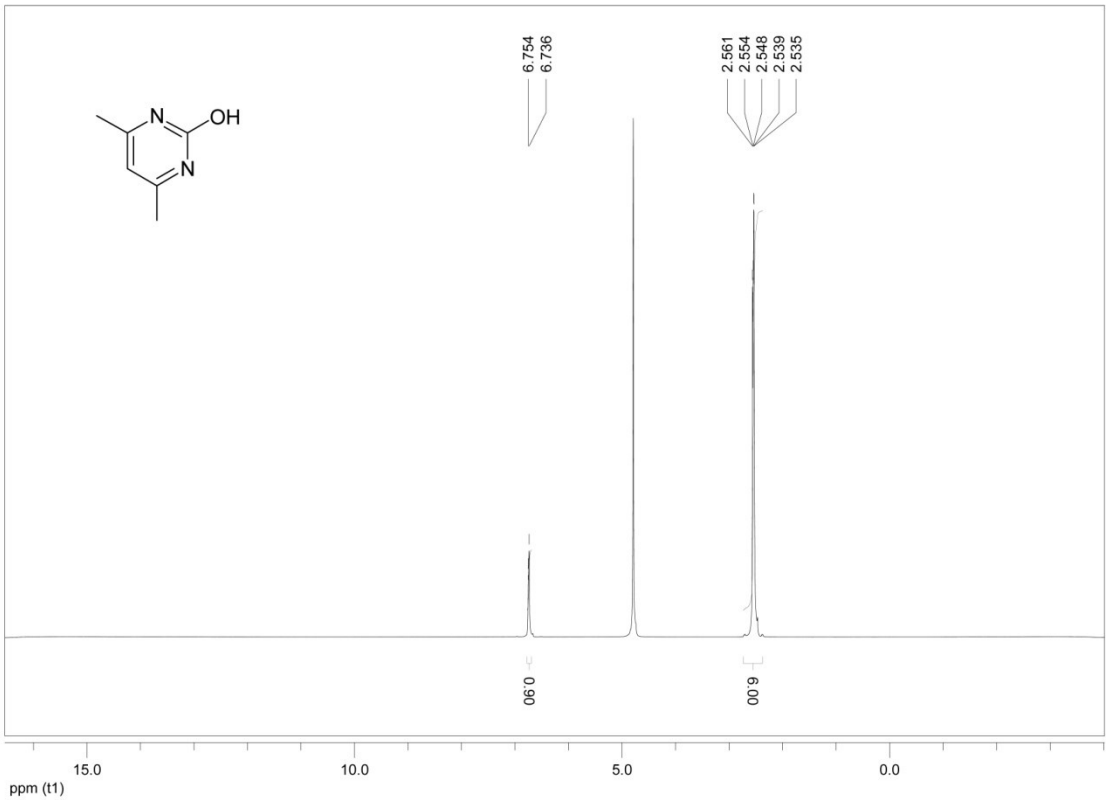

153.270
137.928
130.453
128.648
116.622
112.390
19.753
18.675
OH
CH3
CH3
200
150
100
50
0
ppm (t1)

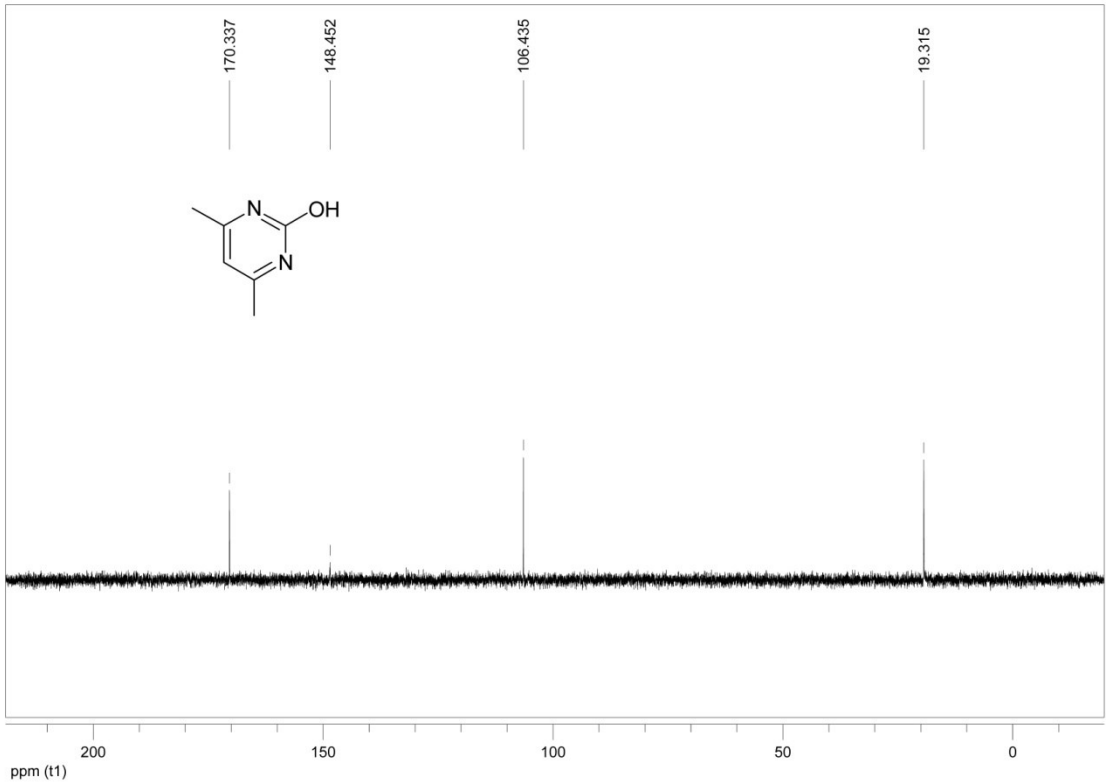
2w


OH
CH3
7.119
7.100
7.081
6.748
6.729
6.642
6.622
5.541
2.273
1.00
3.00
7.30 7.20 7.10 7.00 6.90 6.80 6.70 6.60 6.50
ppm (t1)
1.00
3.00
0.99
3.01
15.0
10.0
5.0
0.0
ppm (t1)

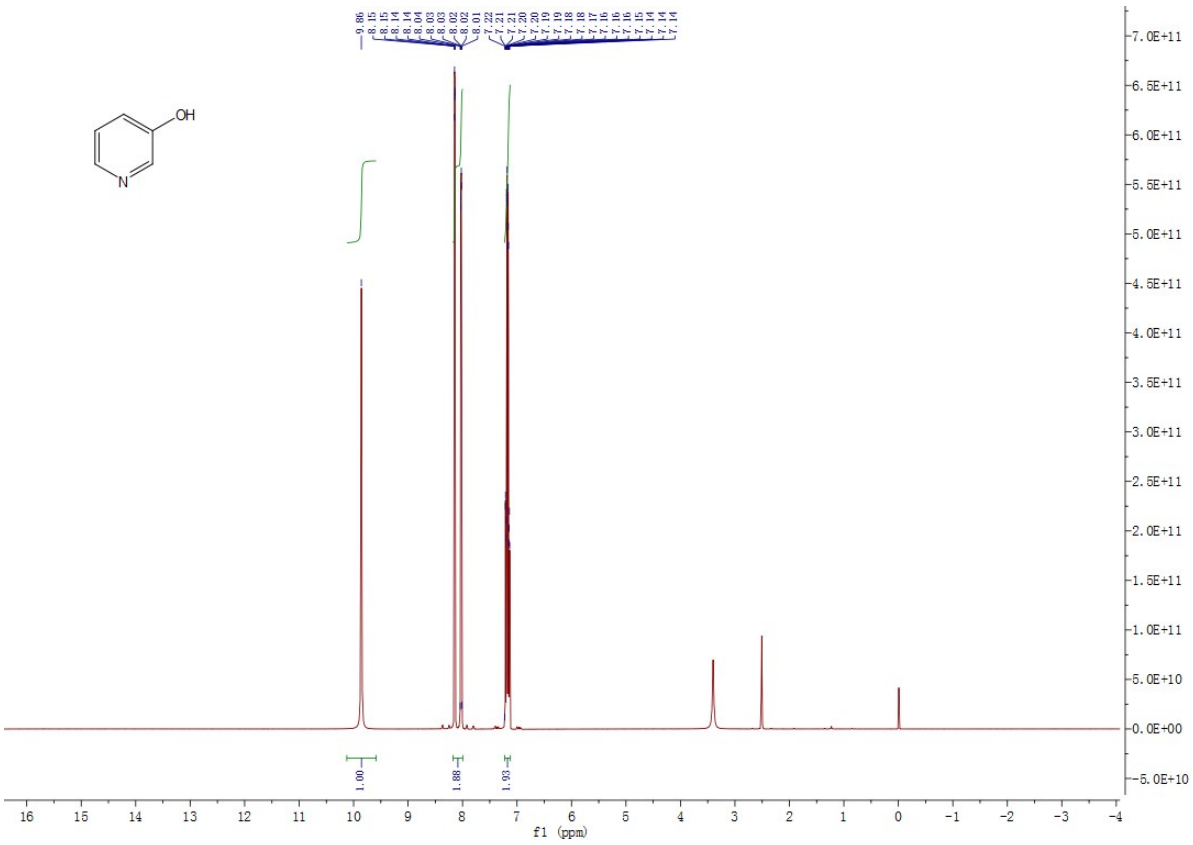

155.181
139.822
129.399
121.656
116.052
112.302
21.249
OH
CH3
200
150
100
50
0
ppm (t1)

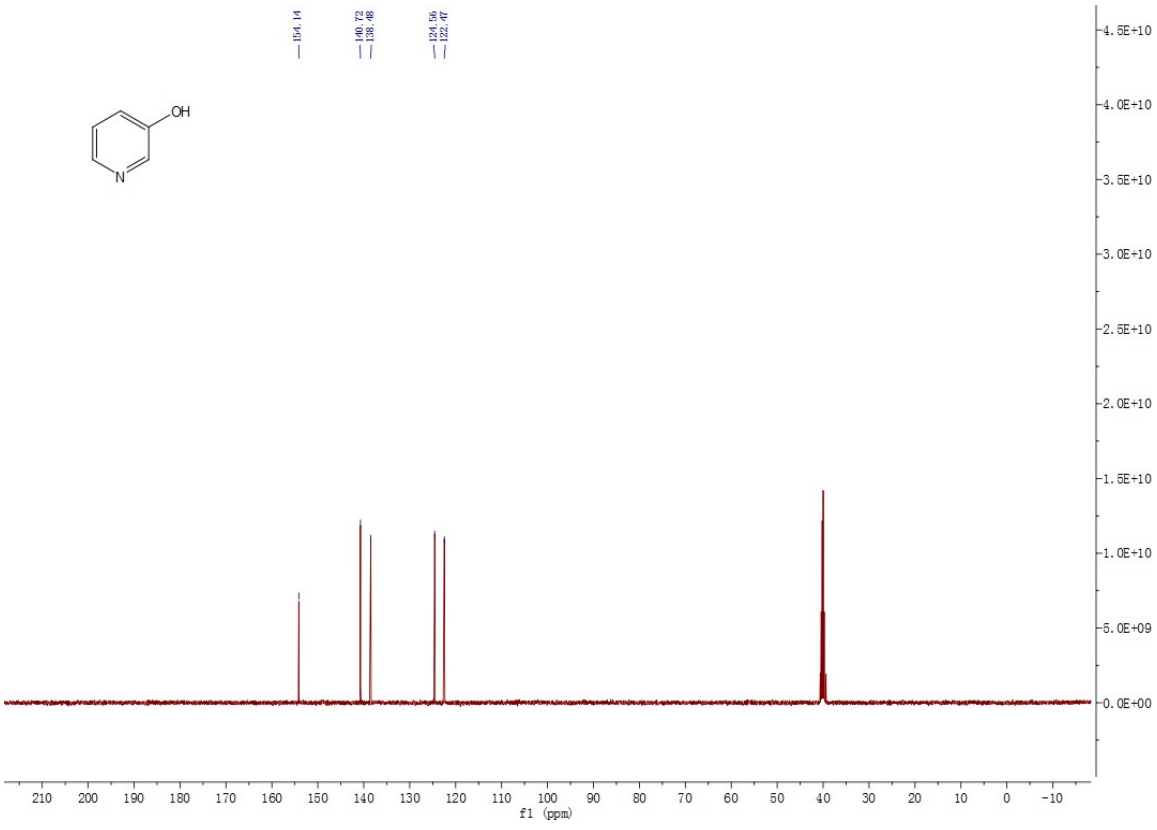
2x


6.754
6.736
2.561
2.554
2.548
2.539
2.535
N
OH
N
0.90
6.00
15.0
10.0
5.0
0.0
ppm (t1)

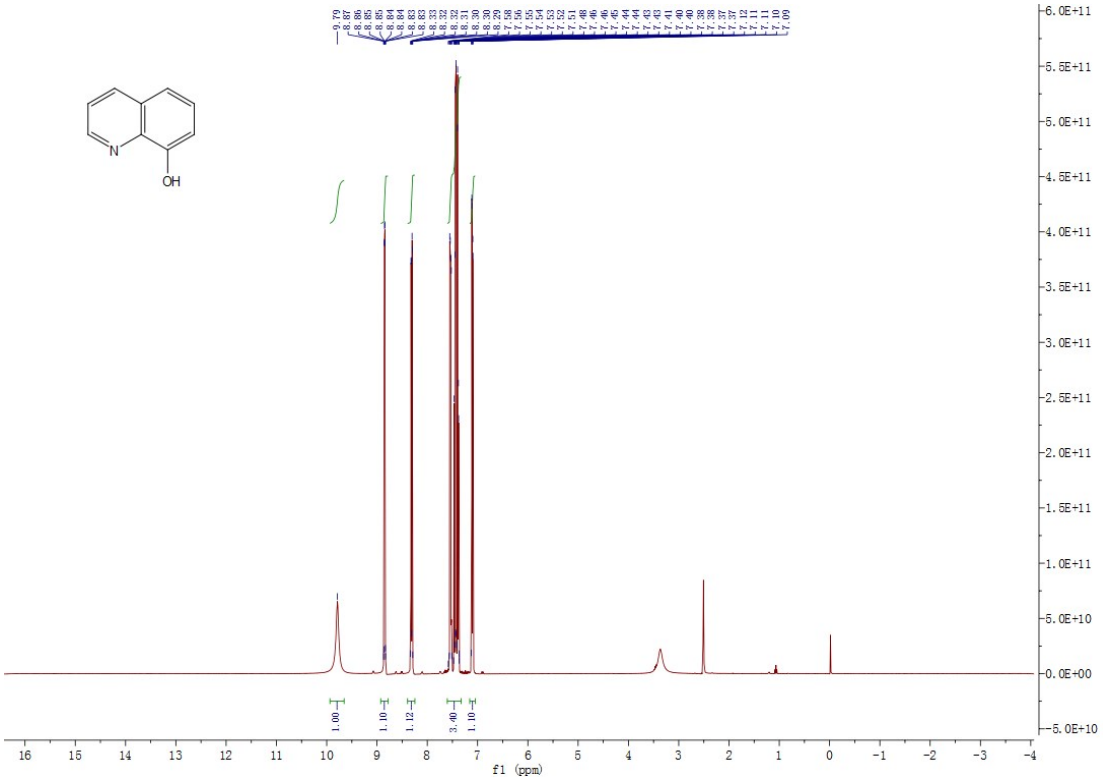

170.337
148.452
106.435
19.315
N
OH
N
200
150
100
50
0
ppm (t1)

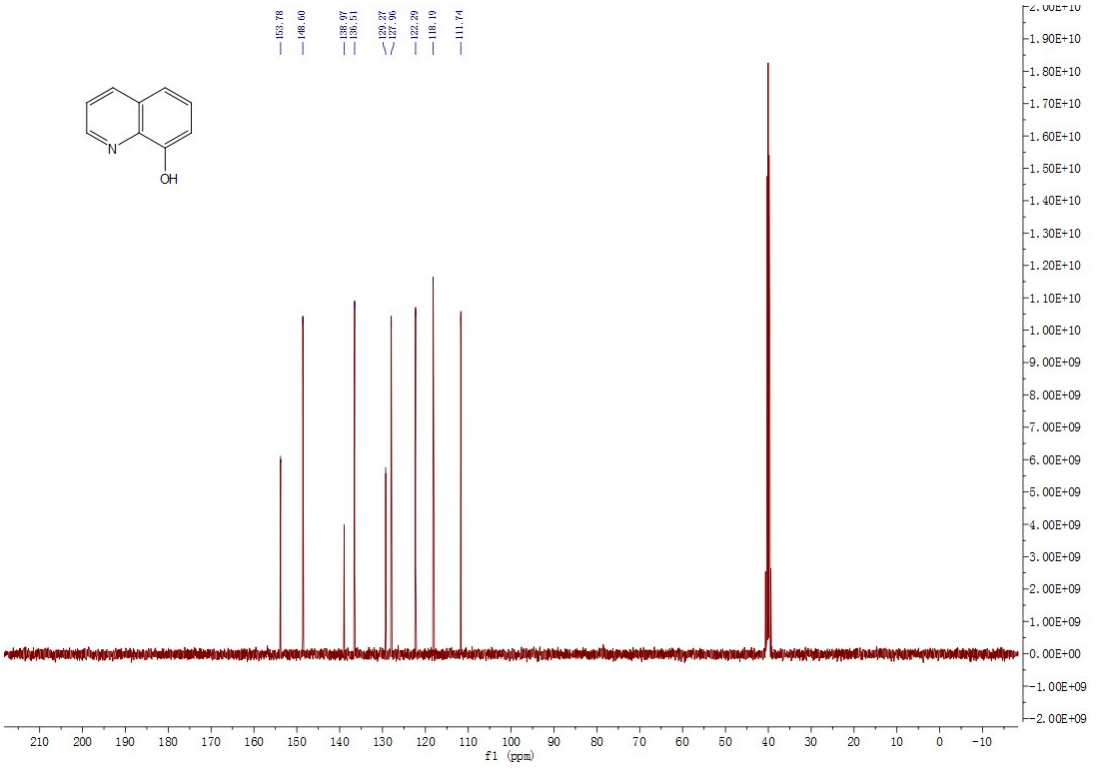
2y


OH
N
9.86
8.15
8.14
8.14
8.04
8.04
8.03
8.03
8.02
8.02
8.01
8.01
7.22
7.21
7.21
7.20
7.20
7.19
7.19
7.18
7.18
7.17
7.17
7.16
7.16
7.16
7.15
7.14
7.14
7.14
1.00
1.88
1.93
f1 (ppm)

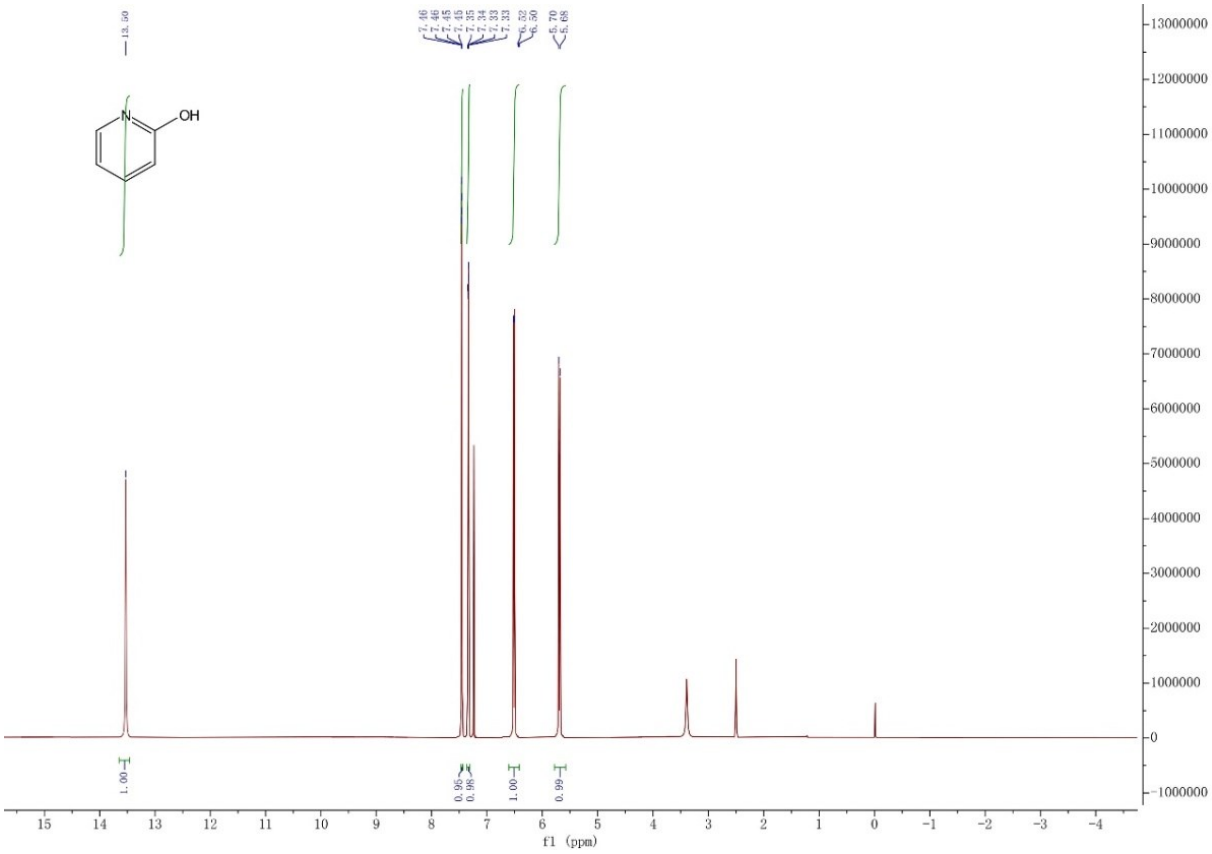

OH
N
154.14
140.72
138.48
124.56
122.47
f1 (ppm)

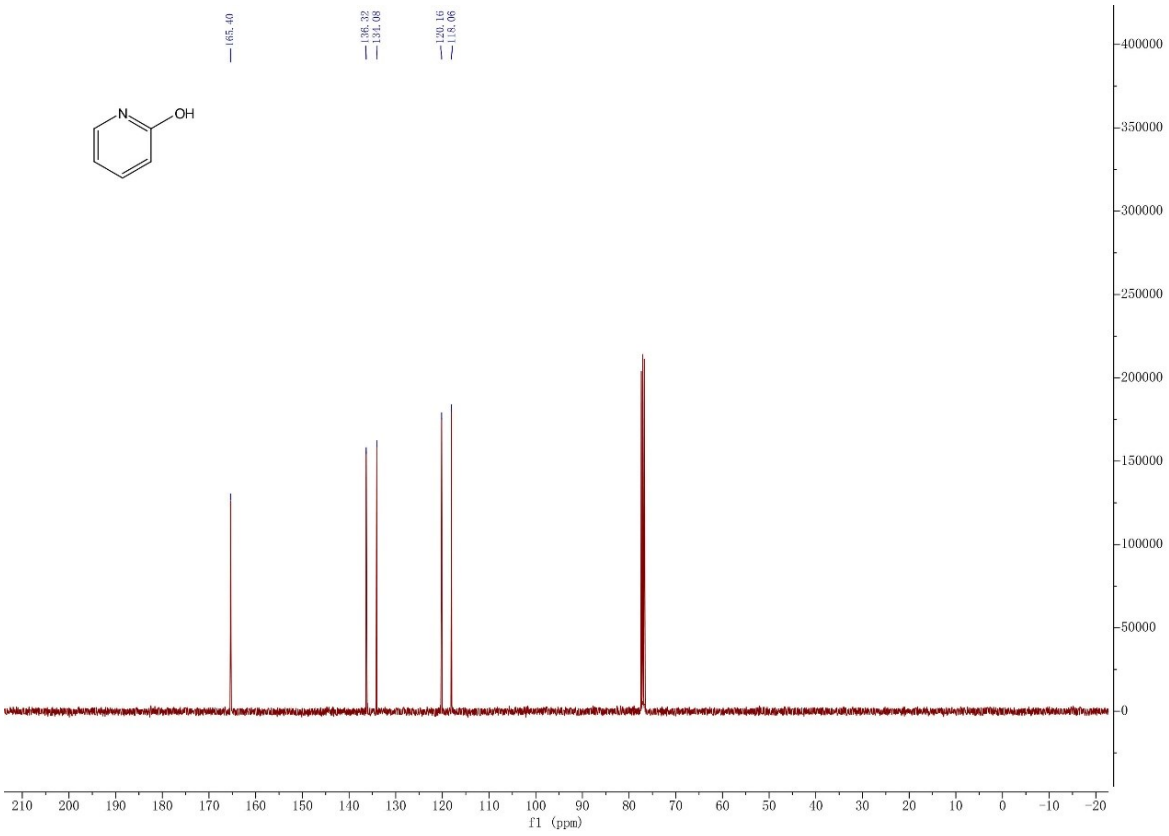
2z


N
OH
f1 (ppm)

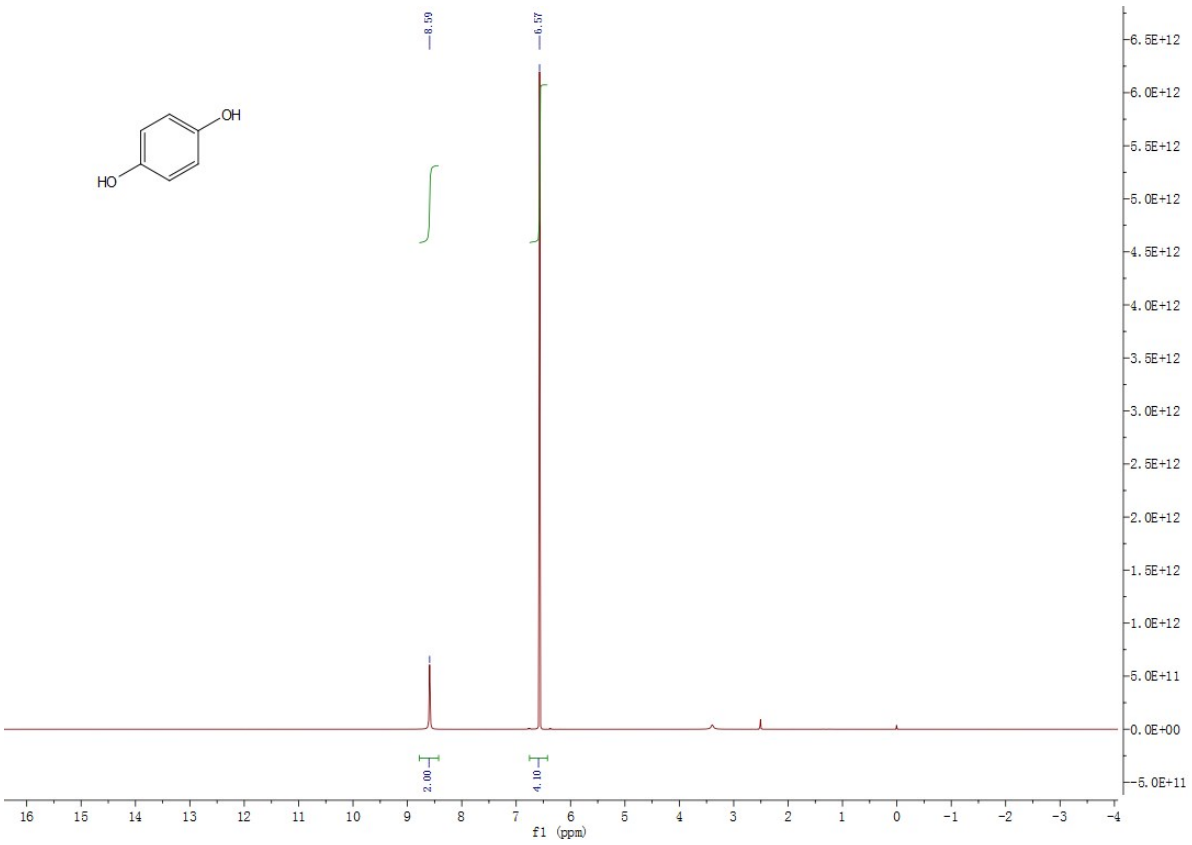

153.78
148.60
138.97
136.51
129.27
127.96
122.29
118.19
111.74
N
OH
f1 (ppm)

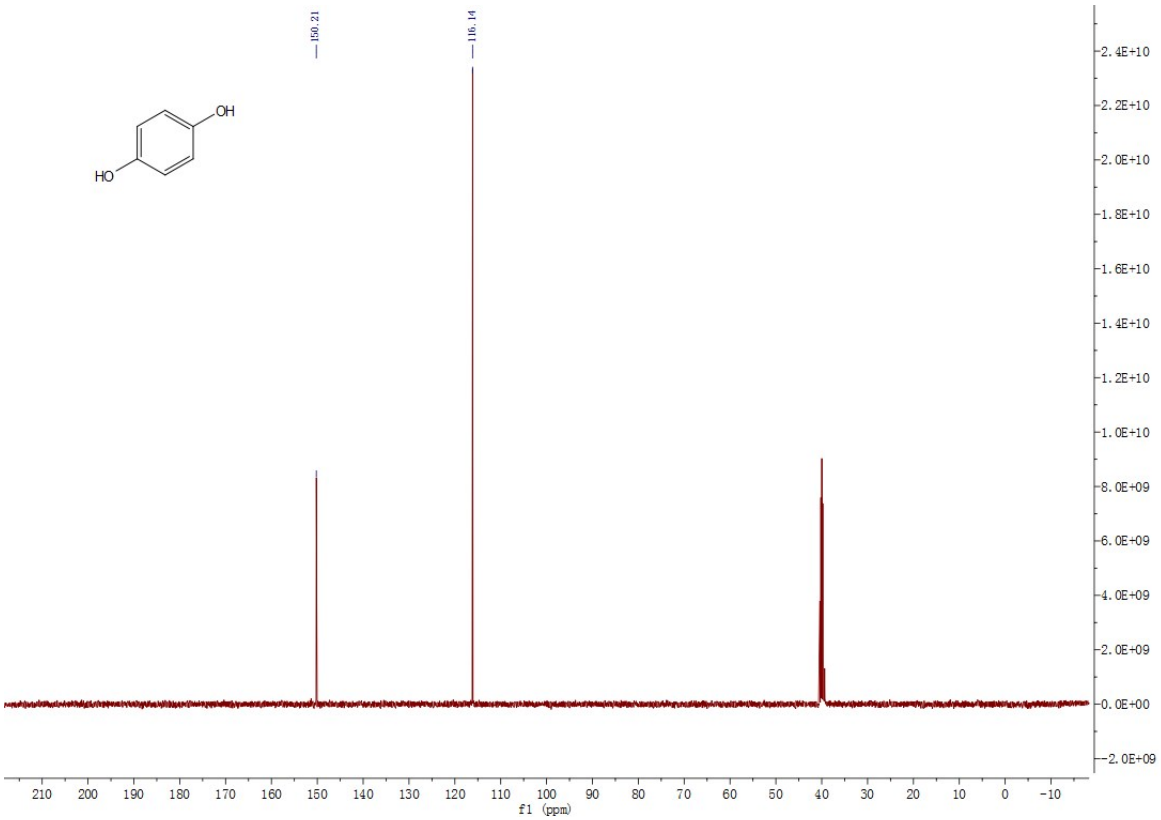
3a


13.69
7.46
7.46
7.45
7.45
7.35
7.34
7.33
7.33
6.32
6.30
5.70
5.68
OH
1.00
0.96
0.96
1.00
0.99
f1 (ppm)

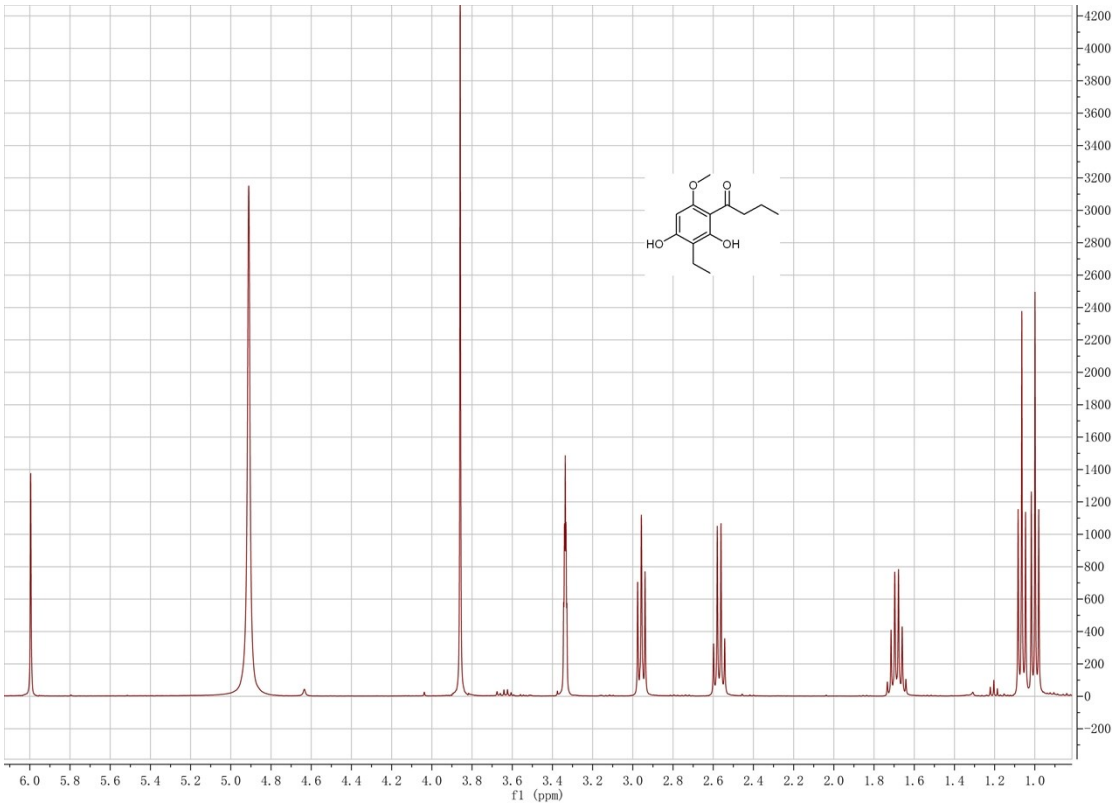

165.40
136.32
134.08
120.16
118.06
OH
f1 (ppm)

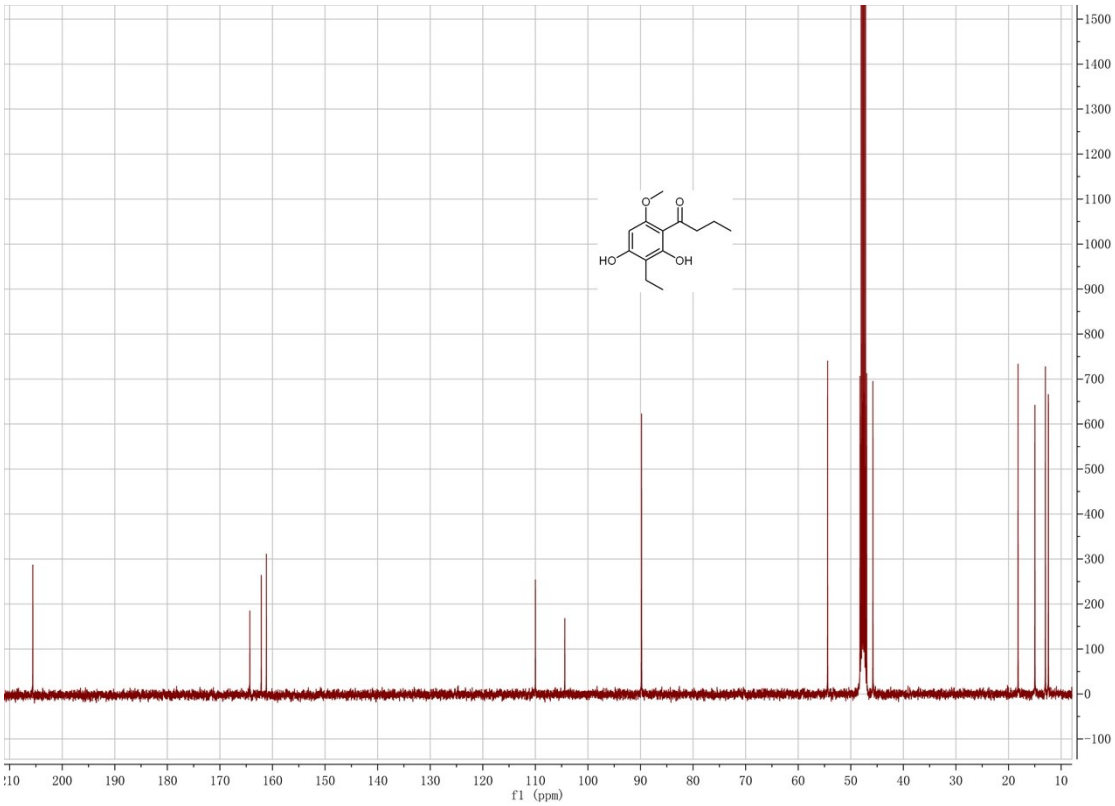
3b





D1


HO
OH
O
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)


HO
OH
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)