Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

A Facile Hydroxylation of Arylboronic Acids Mediated by Sodium Ascorbate

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Supporting Information

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General methods: ^{1}H NMR spectra were recorded on Varian Mercury 400 spectrometer. Chemical shifts are reported in ppm from TMS with the solvent resonance as the internal standard (deuterochloroform: δ = 7.27 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = duplet, t = triplet, q = quartet, dd = double duplet, dt = double triplet, bs = broad signal, m = multiplet), coupling constants (Hz). ^{13}C NMR spectra were recorded on Varian MR400 spectrometer. Chemical shifts are reported in ppm from TMS with the solvent as the internal standard (deuterochloroform: δ = 77.0 ppm). Chromatographic purification was done with 240-400 mesh silica gel. Purification on preparative thin layer chromatography was done on Merck TLC silica gel 60 F_{254}.

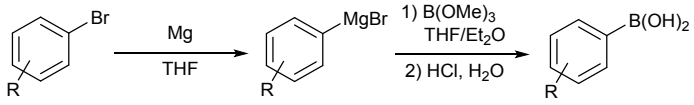
EPR spectra were recorded at room temperature using an ELEXYS E500 spectrometer equipped with a NMR gaussmeter for the calibration of the magnetic field and a frequency counter for the determination of g-factors that were corrected against that of the perylene radical cation in concentrated sulfuric acid (g = 2.002583). The instrument settings were as follows: microwave power 5.0 mW, modulation amplitude 0.2 G, modulation frequency 100 kHz, scan time 180 s.

Materials. If not otherwise stated, all reactions were carried out in flame dried glassware under nitrogen atmosphere. Anhydrous solvents were supplied by Merck in Sureseal® bottles and were used as received avoiding further purification.

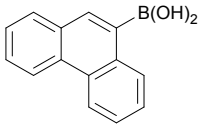
Boronic acids commercially available were purchase from Merck, TCI or AlfaAesar or prepared by the following reported procedure.

Compounds **3**[1] and **4**[2] were prepared according to reported literature.

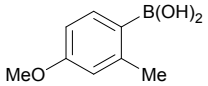
Synthesis of boronic acids



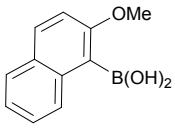
To a stirred suspension of magnesium turnings (0.096 g, 4 mmol, 1 equiv) in anhydrous THF (4 mL) under nitrogen atmosphere some drops of a solution of aryl bromide (4 mmol, 1 equiv) in THF (2 mL) were slowly added. When the mixture temperature increase, due to the reaction start, the solution was added dropwise in 10 min. (if not increase of the reaction temperature was observed, the mixture was gently heated). The mixture was vigorously stirred for 40 min and was cannulated to a solution of $B(OMe)_3$ (0.44 mL, 4 mmol, 1 equiv) in diethyl ether (4 mL) at -78°C. After 20 min the reaction mixture was slowly warmed up until room temperature was reached and stirring was continued for 24 h. HCl (1M, 10 mL) was added dropwise and the reaction was stirred for 1h. Diethyl ether (15 mL) was added and the phases were separated. Aqueous layer was extracted with Et_2O (3 × 20 mL). The collected organic layers were washed with NaOH (1M, 3 x 5 mL). The basic solution was treated with HCl (37%) at 0°C until pH = 1 and the desired boronic acid precipitated from the solution. Filtration gave the pure product.



(**1d**) 9-phenanthrenboronic acid (0.75 g, 85%); The general procedure was applied using 9-bromophenanthrene (1.03 g, 4 mmol). ^{1}H-NMR (401 MHz, DMSO + 2 drops of D_2O): δ = 8.79 (dd, *J* = 12.6, 4.9 Hz, 2H), 8.42 (s, 2H), 8.35 (dd, *J* = 7.8, 1.6 Hz, 1H), 8.00 (s, 1H), 7.94 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.72–7.36 (m, 4H). ^{13}C-NMR (101 MHz, DMSO): δ = 134.2, 133.5, 131.2, 130.7, 129.8, 129.8, 129.0, 127.5, 127.1, 126.8, 126.6, 123.3, 123.1, 120.6.



(**1k**) 4-methoxy-2-methylphenylboronic acid (0.352 g, 53%); The general procedure was applied using - 1-bromo-4-methoxy-2-methylbenzene (0.804 g, 4 mmol). ^{1}H-NMR(401 MHz, DMSO + 2 drops of D_2O): δ = 7.73 (s, 1H), 7.43–7.36 (m, 1H), 6.65 (s, 2H), 6.64 (s, 1H), 4.59 (s, 3H), 3.74 (s, 3H). ^{13}C-NMR(101 MHz, DMSO + 2 drops of D_2O): δ = 160.0, 144.0, 135.5, 116.4, 115.1, 109.9, 54.8, 22.4.

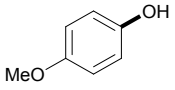


(**1l**) (2-methoxynaphthalen-1-yl)boronic (0.525 g, 65%) . The general procedure was applied using - 1-bromo-4-methoxy-2-methylbenzene (0.948 g, 4 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$ + 2 drops of D_2O): δ = 8.80 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 9.1 Hz, 1H), 7.77 (d, *J* = 7.4 Hz, 1H), 7.49 (ddd, *J* = 8.7, 6.8, 1.5 Hz, 1H), 7.36 (dd, *J* = 10.9, 4.0 Hz, 1H), 7.27 (d, *J* = 9.1 Hz, 1H), 5.94 (s, 2H), 4.02 (s, 3H).

General procedure for oxidation of arylboronic acids

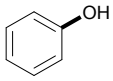
To a 25 mL round bottom flask at open air, arylboronic acid (0.3 mmol), sodium ascorbate (0.6 mmol, 0.119 g) and DMF (1.5 mL) were added. The suspension was vigorously stirred for 18 h, and it was diluted with water (10 mL) and extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, and the solvent was removed under reduced pressure. Title compounds were purified by column chromatography on SiO_2 using cyclohexane/ethyl acetate mixture as eluent.

Screening test were performed on 0.1 mmol scale.

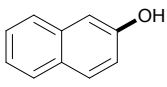


(**2a**) 4-methoxyphenol (0.035 g, 95%); The general procedure was applied using 4-methoxyphenylboronic acid **1a** (0.045 mg, 0.3 mmol).

^{1}H-NMR (401 MHz, $CDCl_3$): δ = 6.79-6.73 (m, 4H), 4.96 (bc, 1H), 3.74 (s, 3H). 13C- NMR (101 MHz, CDCl3): δ = 153.7, 149.4, 116.0 (2C), 114.8 (2C), 55.8.

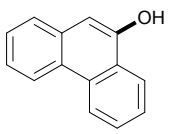


(**2b**) phenol (0.026 g, 92%); The general procedure was applied using phenylboronic acid **1b** (0.037 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 7.33 – 7.16 (m, 2H), 6.99 – 6.88 (m, 1H), 6.88 – 6.79 (m, 2H), 5.05 (s, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ =155.3, 129.7 (2C), 120.9, 115.3 (2C).

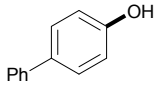


(**2c**) 2-naphtol (0.038 g, 89%); The general procedure was applied using 2-naphtylboronic acid **1c** (0.053 mg, 0.3 mmol).

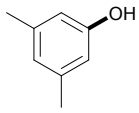
^{1}H-NMR (401 MHz, $CDCl_3$): δ = 7.79 – 7.70 (m, 2H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.16–7.05 (m, 2H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 153.3, 134.6, 129.8, 128.92, 127.7, 126.5, 126.3, 123.6, 117.7, 109.5.



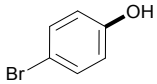
(**2d**) 9-phenanthrol (0.027 g, 46%); The general procedure was applied using 9-phenanthrenboronic acid **1d** (0.066 g, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 8.67 (d, *J* = 8.1 Hz, 1H), 8.59 (d, *J* = 7.3 Hz, 1H), 8.31 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.76 – 7.57 (m, 3H), 7.57 – 7.42 (m, 2H), 7.00 (s, 1H), 5.36 (s, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 149.5, 132.7, 131.5, 127.2, 126.9, 126.7, 126.4, 125.5, 124.3, 122.7, 122.6, 122.3, 106.1.



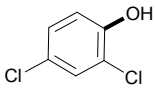
(**2e**) 4-phenylphenol (0.059 g, 96%); The general procedure was applied using 4-biphenylboronic acid **1e** (0.061 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, CD_3CN): δ =7.57 (d, *J* = 7.7, 2H), 7.49 (d, *J* = 8.7, 2H), 7.41 (t, *J* = 7.6, 2H), 7.30 (t, *J* = 7.4, 1H), 7.11 (s, 1H), 6.90 (d, *J* = 8.7, 2H); ^{13}C-NMR (101 MHz, CD_3CN) δ =157.5, 141.6, 133.4, 129.8 (2C), 129.0 (2C), 127.6, 127.3 (2C), 116.6 (2C).



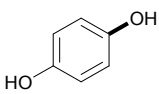
(**2f**) 3,5-dimethylphenol; (0.030 g, 81%); The general procedure was applied using 3,5-dimethylphenylboronic acid **1f** (0.045 g, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 6.64 (s, 1H), 6.53 (s, 2H), 5.86 (s, 1H), 2.30 (s, 6H); ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 155.0, 139.5, 122.6 (2C), 113.1 (2C), 21.1 (2C).



(**2g**) 4-bromophenol; (0.035 g, 68%); The general procedure was applied using 4-bromophenylboronic acid **1g** (0.060 g, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 7.36 – 7.28 (m, 2H), 6.76 – 6.60 (m, 2H), 5.47 (s, 1H); ^{13}C-NMR (101 MHz, $CDCl_3$) δ =154.2, 132.5 (2C), 117.2 (2C), 113.1.

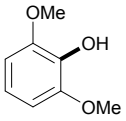


(**2h**) 2,4-dichlorophenol; (0.035 g, 72%); The general procedure was applied using 2,4-dichlorophenylboronic acid **1h** (0.058 g, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 7.31 (d, *J* = 2.5 Hz, 1H), 7.13 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.93 (d, *J* = 8.7 Hz, 1H), 5.48 (bs, 1H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 150.1, 128.5, 128.4, 125.3, 120.3, 117.1

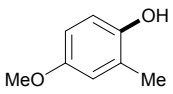


(**2i**) hydroxyquinone; (0.033 g, 98%); The general procedure was applied using 4-

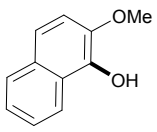
hydroxyphenylboronic acid **1i** (0.043 g, 0.3 mmol). ^{1}H-NMR (401 MHz, CD_3CN): δ = 6.64 (s, 4H), 6.39 (s, 2H); ^{13}C-NMR (101 MHz, CD_3CN): δ = 151.0 (2C), 116.8 (4C).



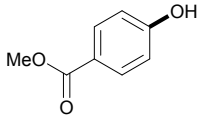
(**2j**) 2,6-dimethoxyphenol; (0.035 g, 76%); The general procedure was applied using 2,6-dimethoxyphenylboronic acid **1j** (0.055 g, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 6.78 (t, *J* = 8.3 Hz, 1H), 6.57 (d, *J* = 8.3 Hz, 2H), 5.50 (s, 1H), 3.87 (s, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 147.2, 134.9, 119.0 (2C), 104.9 (2C), 56.3 (2C).



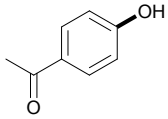
(**2k**) 4-methoxy-2-methylphenol, (0.039 g, 93%); The general procedure was applied using 4-methoxy-2-methylphenylboronic acid **1k** (49 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 6.76–6.65 (m, 2H), 6.62 (d, *J* = 3.0 Hz, 1H), 4.59 (bs, 1H), 3.74 (s, 3H), 2.24 (s, 3H). ^{13}C-NMR (101MHz, $CDCl_3$) δ = 153.5, 147.8, 124.9, 116.6, 115.5, 111.8, 55.7, 16.1.



(**2l**) 2-methoxy-1-naphtol, (0.051 g, 98%); The general procedure was applied using 2-methoxy-1-naphthylboronic acid **1l** (60 mg, 0.3 mmol). ^{1}H-NMR (401MHz, $CDCl_3$) δ = 8.18 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.53–7.32 (m, 3H), 7.25 (d, *J* = 8.9 Hz, 1H), 6.10 (bs, 1H), 3.97 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 141.2, 139.7, 129.6, 127.5, 125.3, 124.2, 124.0, 121.2, 119.6, 113.3, 57.1.

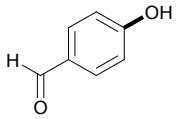


(**2m**) methyl 4-hydroxybenzoate, 0.041 mg, 89%); The general procedure was applied using 4-methoxycarbonylphenylboronic acid **1m** (54 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 7.94 (d, *J* = 14.2 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 3.87 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 167.5, 160.3, 131.9 (2C), 122.2, 115.3 (2C), 52.1.

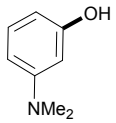


(**2n**) 4'-hydroxyacetophenone, (0.040 g, 97%); The general procedure was applied using

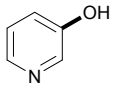
4-acetylphenylboronic acid **1n** (48 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 8.15 (s, 1H), 7.89 (d, *J* = 8.7 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 2.57 (s, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ = 198.8, 161.6, 131.2 (2C), 129.4, 115.6 (2C), 26.3.



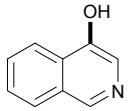
(**2o**) 4-hydroxybenzaldehyde, (0.023 g, 62%); The general procedure was applied using 4-formylphenylboronic acid **1o** (60 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, CD_3CN): δ = 9.80 (s, 1H), 7.76 (d, *J* = 8.6, 2H), 6.95 (d, *J* = 8.6, 2H). ^{13}C-NMR (101 MHz, CD_3CN) δ = 192.0, 163.7, 133.0 (2C), 130.4, 16.8 (2C).



(**2p**) 3-(N,N-dimethylamino)phenol, (0.037 g, 82%); The general procedure was applied using 3-(N.N-dimethylamino)boronic acid **1p** (50 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, $CDCl_3$): δ = 7.07 (t, *J* = 8.1 Hz, 1H), 6.33 (s, 1H), 6.24 – 6.14 (m, 2H), 2.90 (s, 6H). ^{13}C-NMR (101 MHz, $CDCl_3$) δ = 156.6, 152.1, 130.0, 105.7, 104.2, 100.2, 40.7 (2C).



(**2q**) 3-hydroxypyridine, (0.022 g, 76%); The general procedure was applied using 3-pyridineboronic acid **1q** (37 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, CD_3OD): δ = 8.08 (d, *J* = 1.7 Hz, 1H), 8.00 (dd, *J* = 4.1, 1.8 Hz, 1H), 7.28–7.21 (m, 2H). ^{13}C-NMR (101 MHz, CD_3OD) δ = 156.2, 141.1, 138.5, 126.2, 124.8.



(**2r**) 4-hydroxyisoquinoline, (0.019 g, 44%); The general procedure was applied using 4-isoquinolineboronic acid **1r** (52 mg, 0.3 mmol). ^{1}H-NMR (401 MHz, CD_3OD): δ = 8.70 (s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.91 (s, 1H), 7.76–7.69 (m, 1H), 7.67–7.60 (m, 1H). ^{13}C-NMR (101 MHz, CD_3OD); δ = 151.3, 143.5, 131.0, 130.9, 129.5, 129.1, 128.2, 126.1, 122.4.

General procedure for oxidation of arylboronic acids in the presence of "additives"

To a DMF (0.5 mL) solution of 4-methoxy-2-methylphenylboronic acid (0.017 g, 0.1 mmol) in 10 mL round bottom flask equipped with magnetic stirring bar, sodium ascorbate (0.040 g, 0.2 mmol, 2 equiv) and "additive" (0.1 mmol) were added. The mixture was vigorously stirred for 18 h at open air. Water (5 mL) was added and the mixture was extracted with AcOEt (3 x 15 mL). The collected organic layers were dried over Na_2SO_4, and concentrated under reduced pressure. Crude reaction mixture was analysed by ^{1}H-NMR and HPLC-MS analysis.

^{11}B NMR experiments

The reaction mechanism was investigated by performing the reaction of $PhB(OH)_2$ **1b** with sodium ascorbate in d_{10}-DMF inside a NMR tube, under bubbling of air and monitoring the progress of the reaction by ^{11}B NMR spectroscopy. The reaction proceeds with 29% of conversion after 8 h of bubbling. After addition of sodium ascorbate to the solution of **1b** a new peak at 5.5 ppm appears and the signal remains unvaried during the course of the reaction. We speculate, on the basis of literature values for related compounds,[3] that this signal is relative to intermediates **I** or **II** (see Scheme 3 main text). During the progress of the reaction the peaks relative to boronic acid decreased and a new species appears at 11.1 ppm which we assigned to intermediate **III** (see Scheme 3 main text) or $X\text{-}B(OH)_2$.

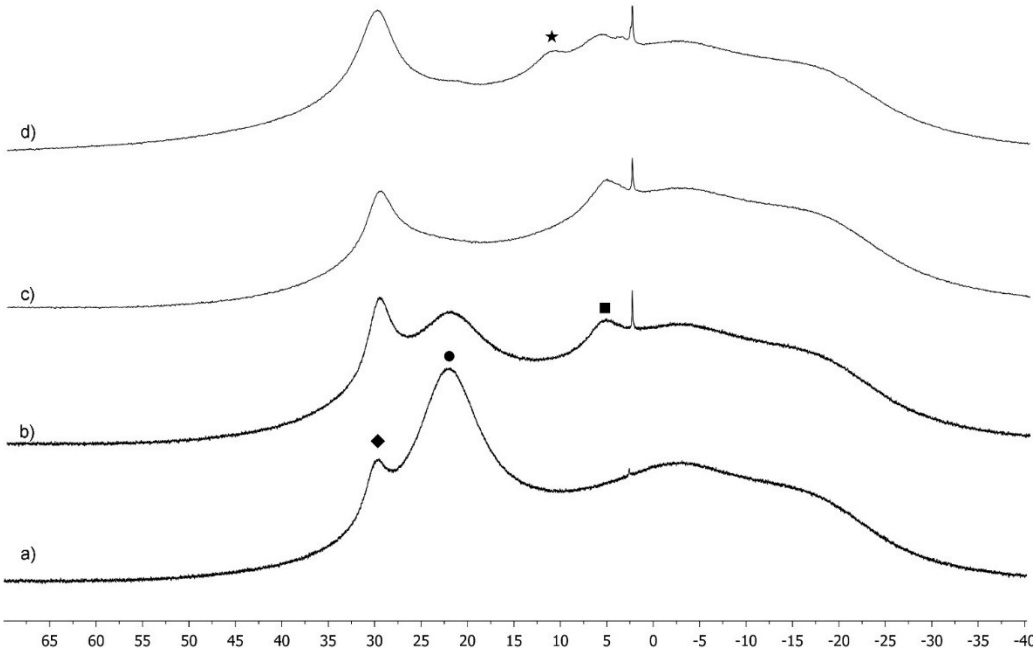


Figure S1. ^{11}B NMR (127 MHz, d_{10}-DMF) spectra: a) **1b**; b) **1b** + 2 equiv. of sodium ascorbate after 10 min. without bubbling air; c) after 1 h bubbling air; d) after 8 h bubbling air. ◆ NMR tube; ● **1b**; ■ **I** or **II** (see Scheme 3 main text); ★ **III** (see Scheme 3 main text) or H_3BO_3.

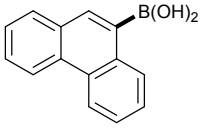
References

1 P. W. Tan, M. Haughey and D. J. Dixon, *Chem. Commun.*, 2015, **51**, 4406.

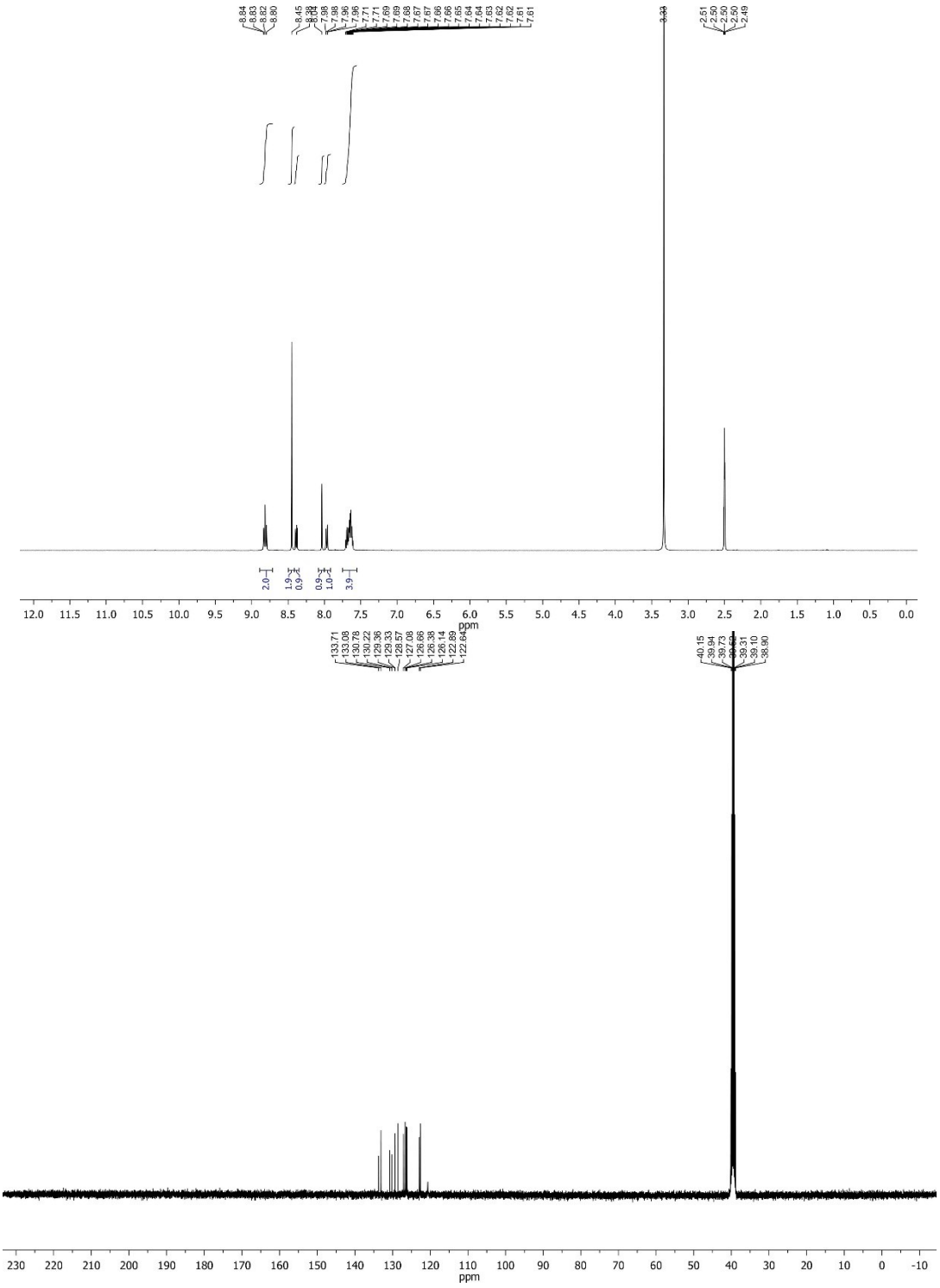
2 G. A. Molander and B. Biolatto, *Org. Lett.*, 2002, **4**, 1867.

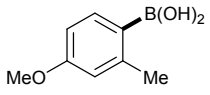
3 (a) R. Frauenlob, C. García, G. A. Bradshaw, H. M. Burke and E. Bergin, *J. Org. Chem.*, 2012, **77**, 4445; (b) R. Wada, T. Shibuguchi, S. Makino, K. Oisaki, M. Kanai and M. Shibasaki, *J. Am. Chem. Soc.*, 2006, **128**, 7687; (c) H. Kotoucova, I. Strnadova, M. Kovandova, J. Chudoba, H. Dvorakova and R. Cibulka, *Org. Biomol. Chem.*, 2014, **12**, 2137.

Copies of NMR spectra



1d

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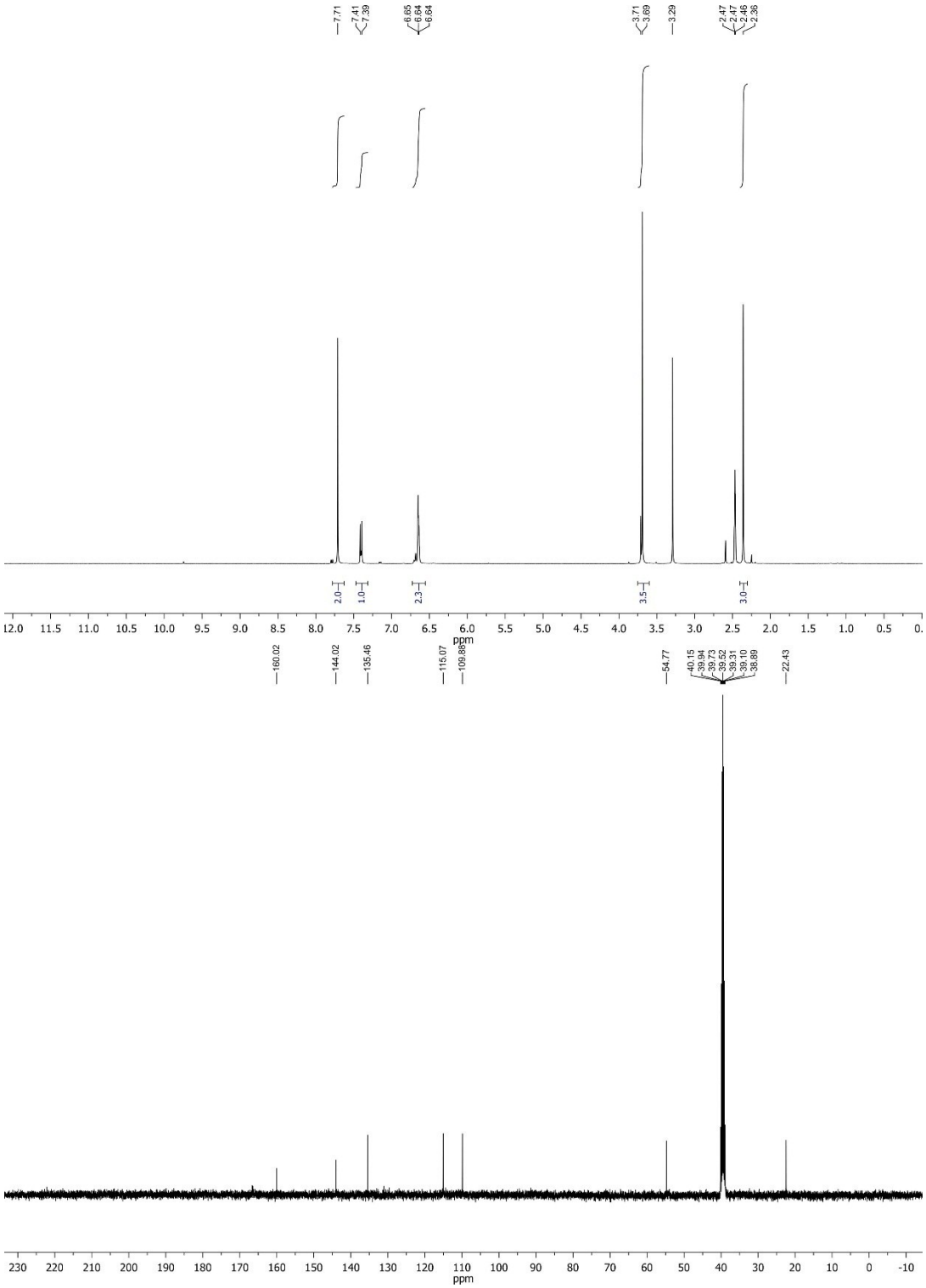
MeO
Me

1k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7.39
6.65
6.64
6.64
3.71
3.69
3.29
2.47
2.47
2.46
2.36
2.0
1.0
2.3
3.5
3.0
ppm
160.02
144.02
135.46
115.07
109.88
54.77
40.15
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39.73
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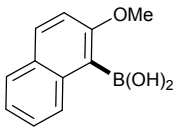
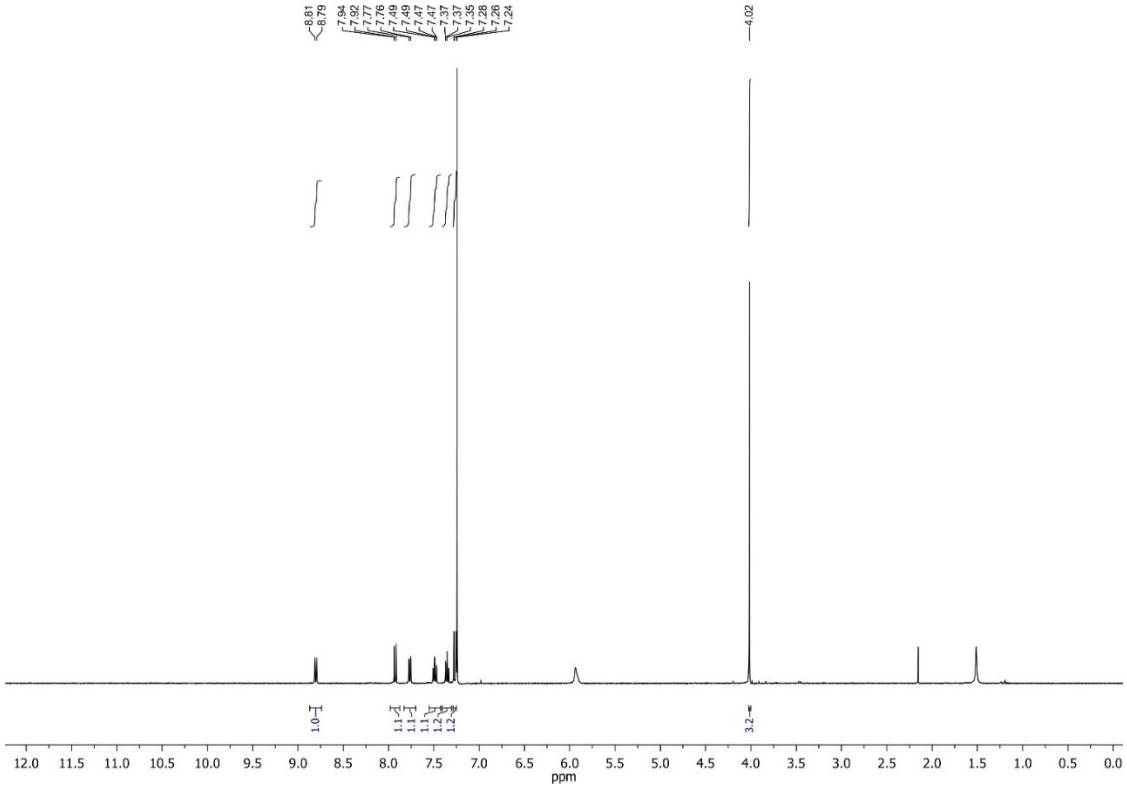
39.31
39.10
38.89
22.43
ppm


OMe
B(OH)2

1l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7.76
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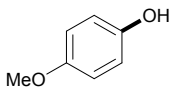
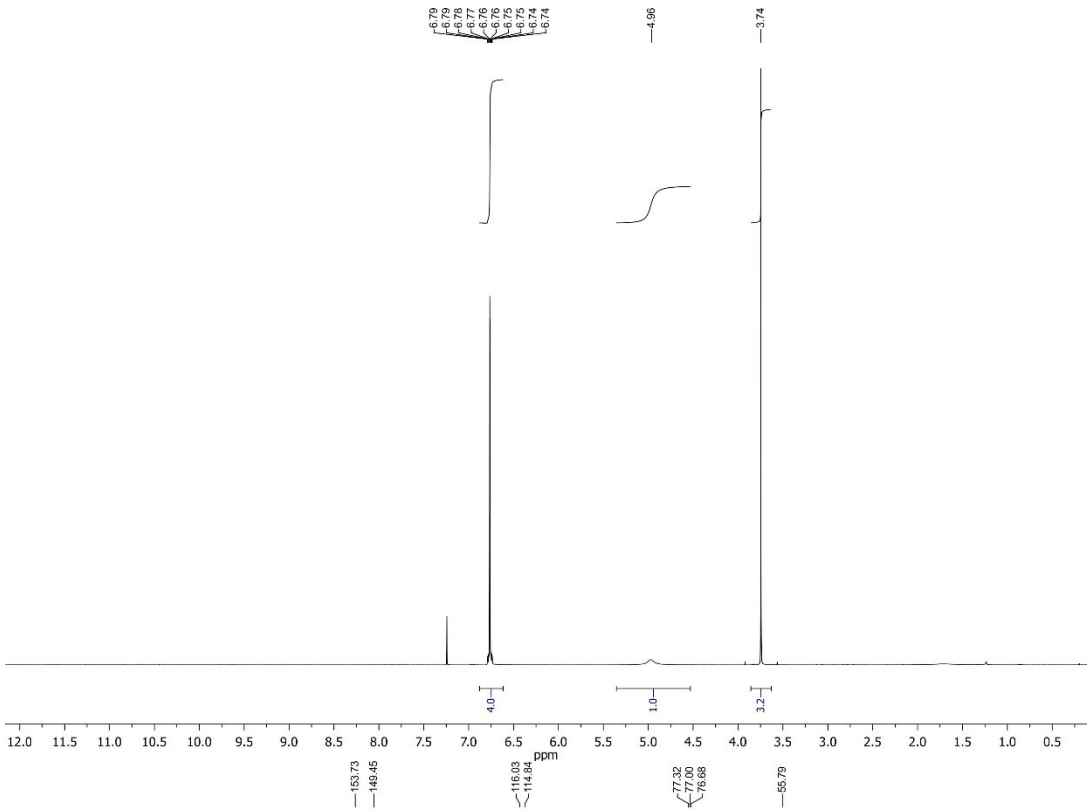
7.49
7.47
7.47
7.37
7.35
7.28
7.26
7.24
4.02
1.0
1.1
1.1
1.1
1.2
1.2
3.2
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm


OH
MeO

2a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6.76
6.76
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6.75
6.74
6.74
4.96
3.74
4.0
1.0
3.2
12.0 11.5 11.0 10.5 10.0 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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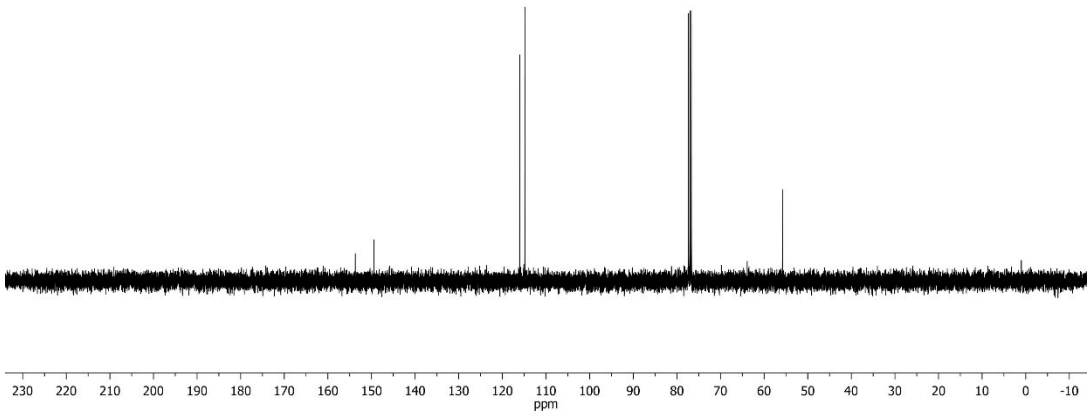
116.03
114.84
77.32
77.00
76.68
55.79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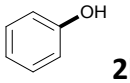
ppm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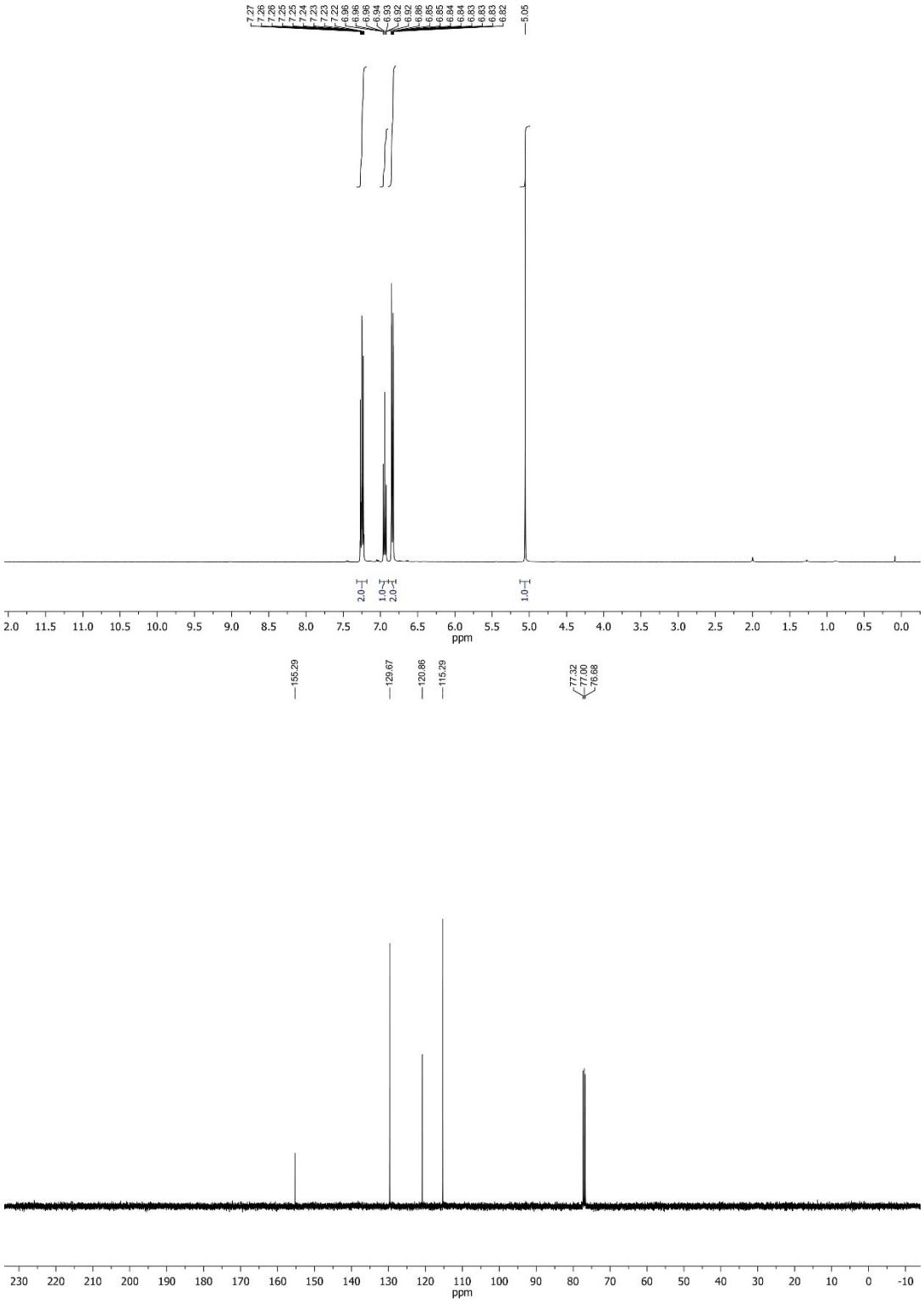
2b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7.23
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6.96
6.96
6.96
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6.92
6.92
6.86
6.85
6.84
6.84
6.83
6.83
6.82
5.05
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ppm
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115.29
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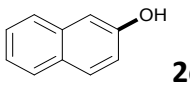
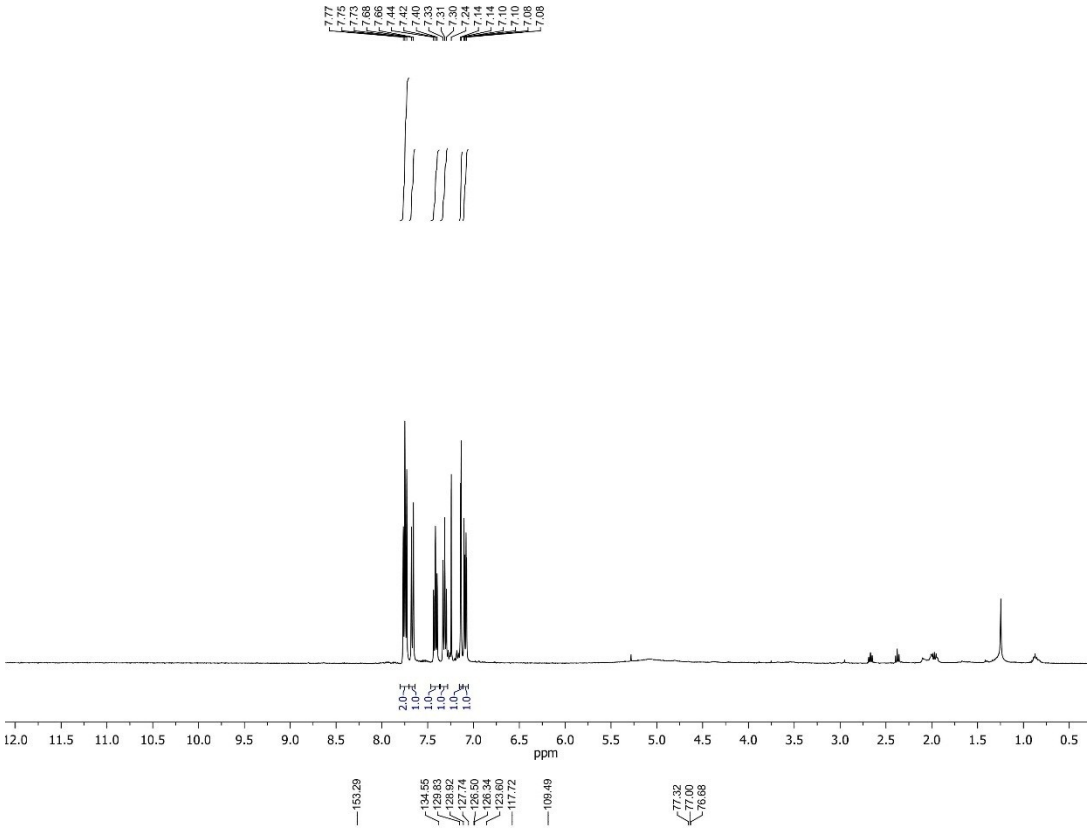
77.00
76.68
ppm


OH

2c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7.40
7.33
7.31
7.30
7.24
7.14
7.14
7.10
7.10
7.08
7.08
2.0
1.0
1.0
1.0
1.0
ppm

153.29
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128.92
127.74
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123.60
117.72
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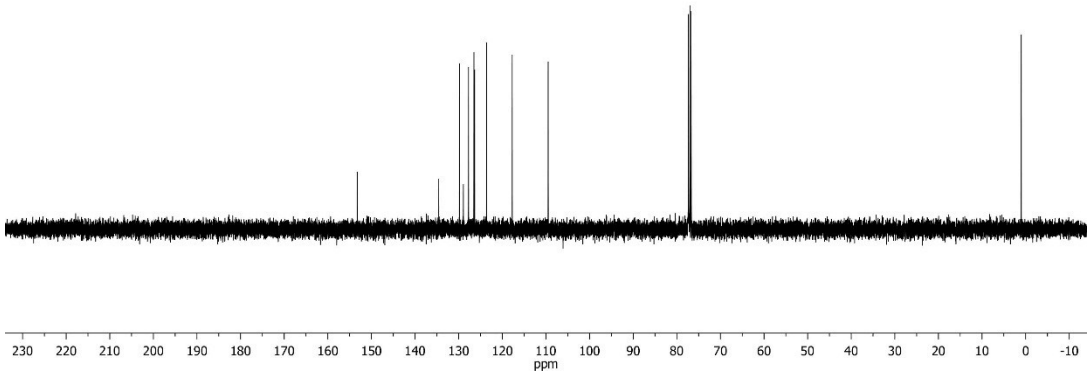
77.32
77.00
76.68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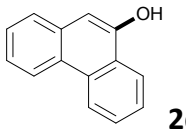
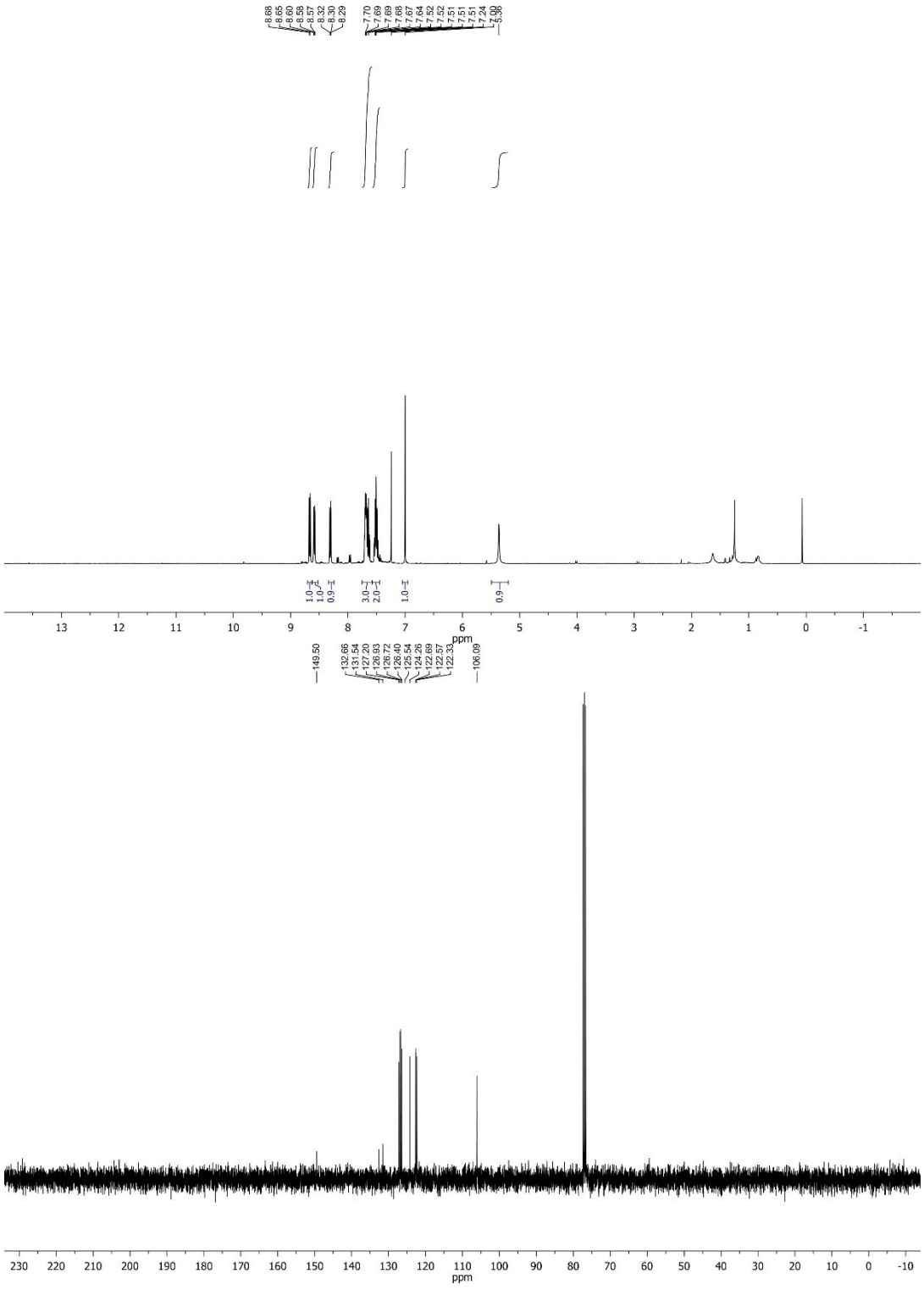

OH

2d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7.64
7.52
7.52
7.51
7.51
7.51
7.24
7.00
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1.0
1.0
0.9
3.0
2.0
1.0
0.9
ppm
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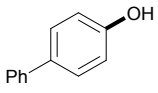
ppm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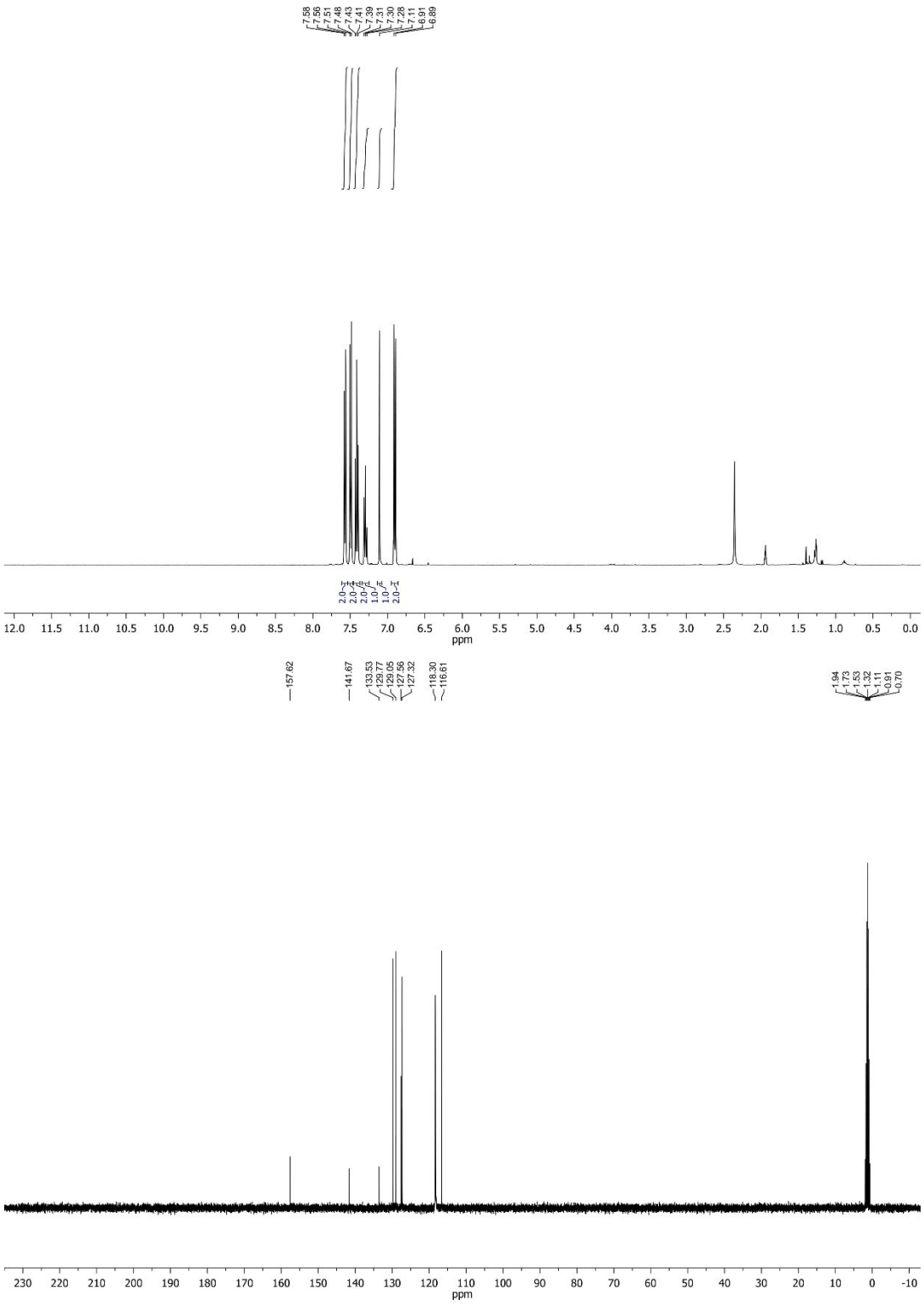
Ph

2e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1.0
2.0
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ppm
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129.77
129.05
127.56
127.32
118.30
116.61
1.94
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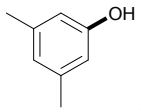
ppm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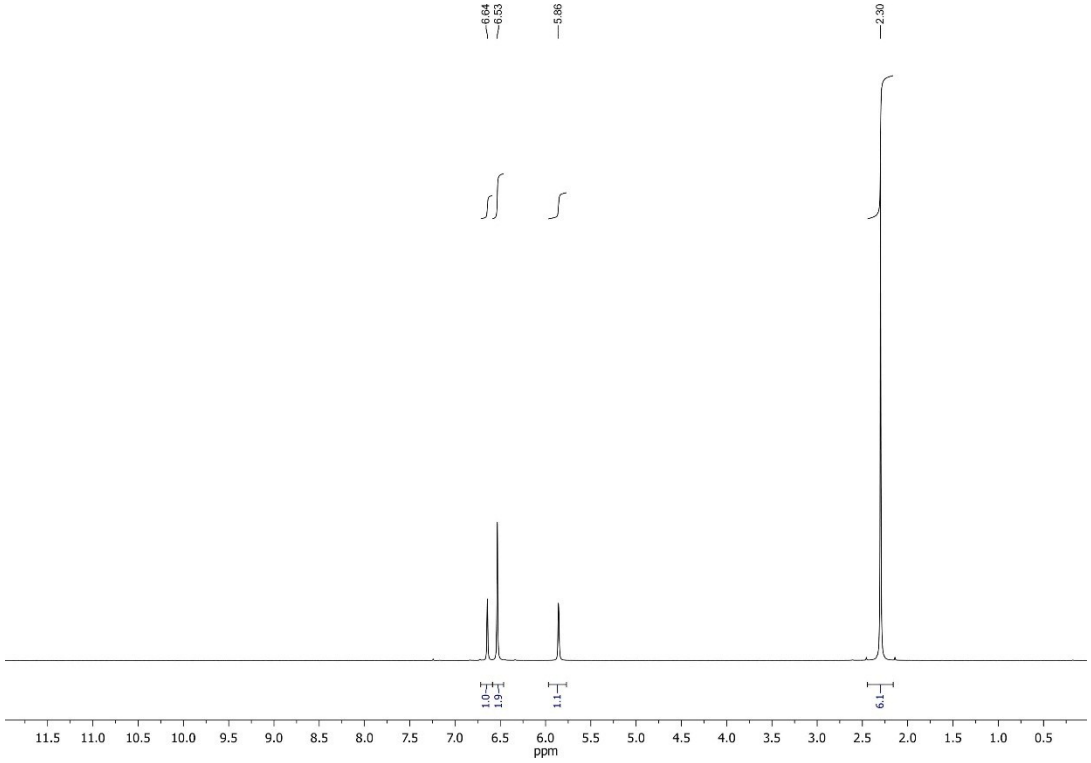
2f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1.9
1.1
6.1
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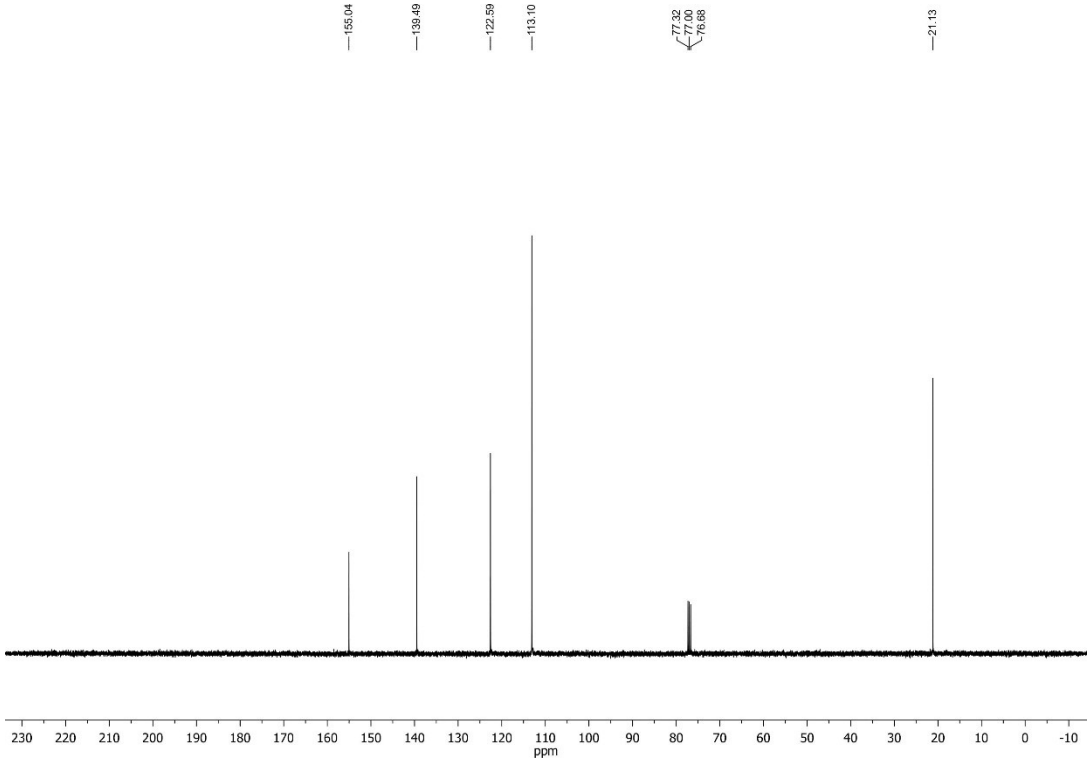
ppm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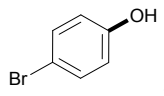
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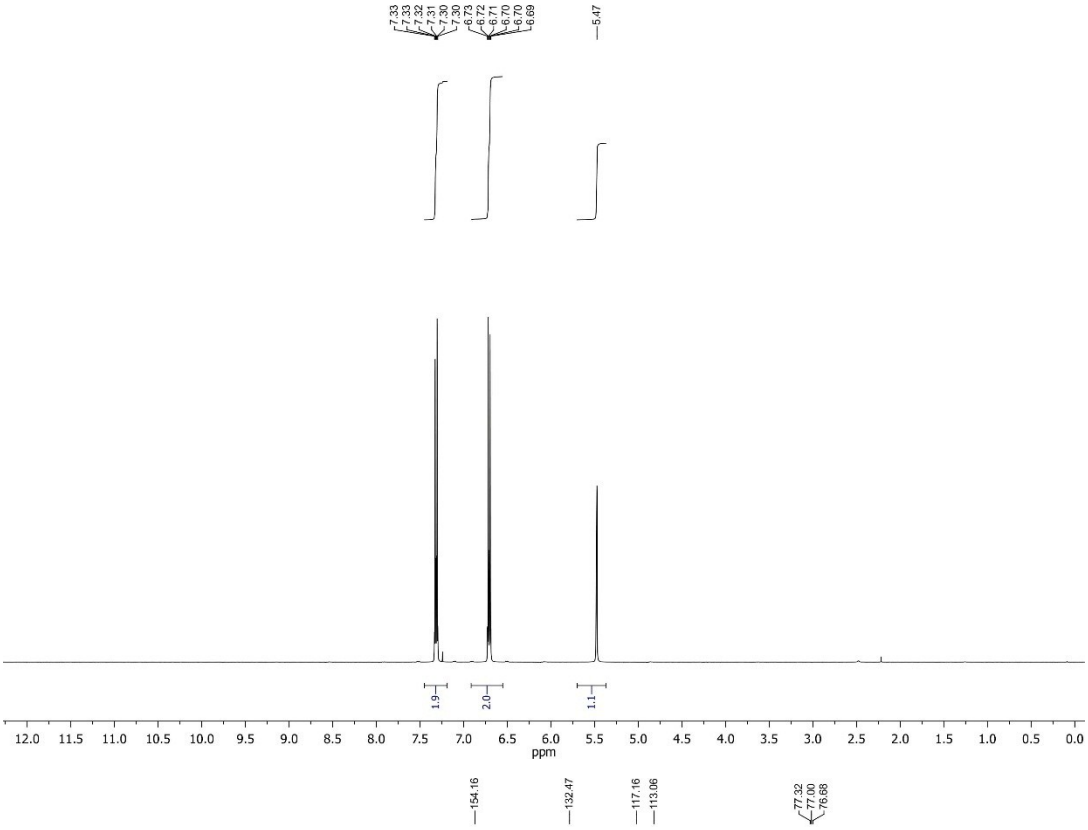
Br

2g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6.70
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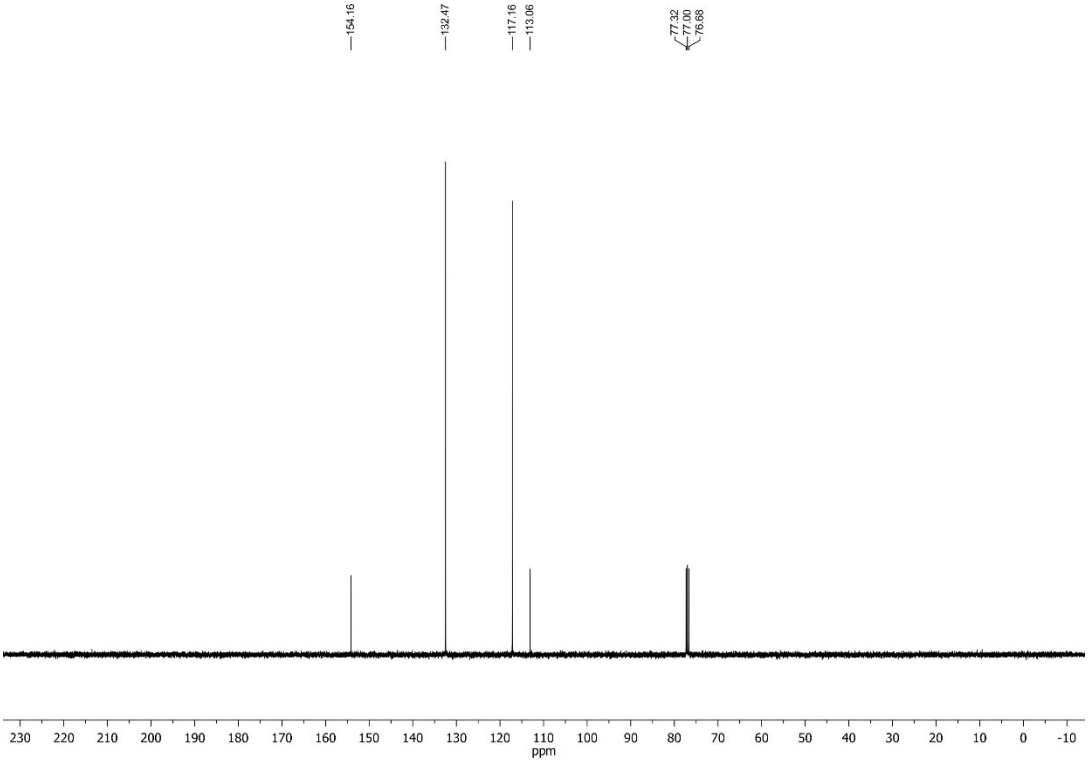
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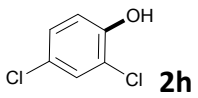
ppm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Cl

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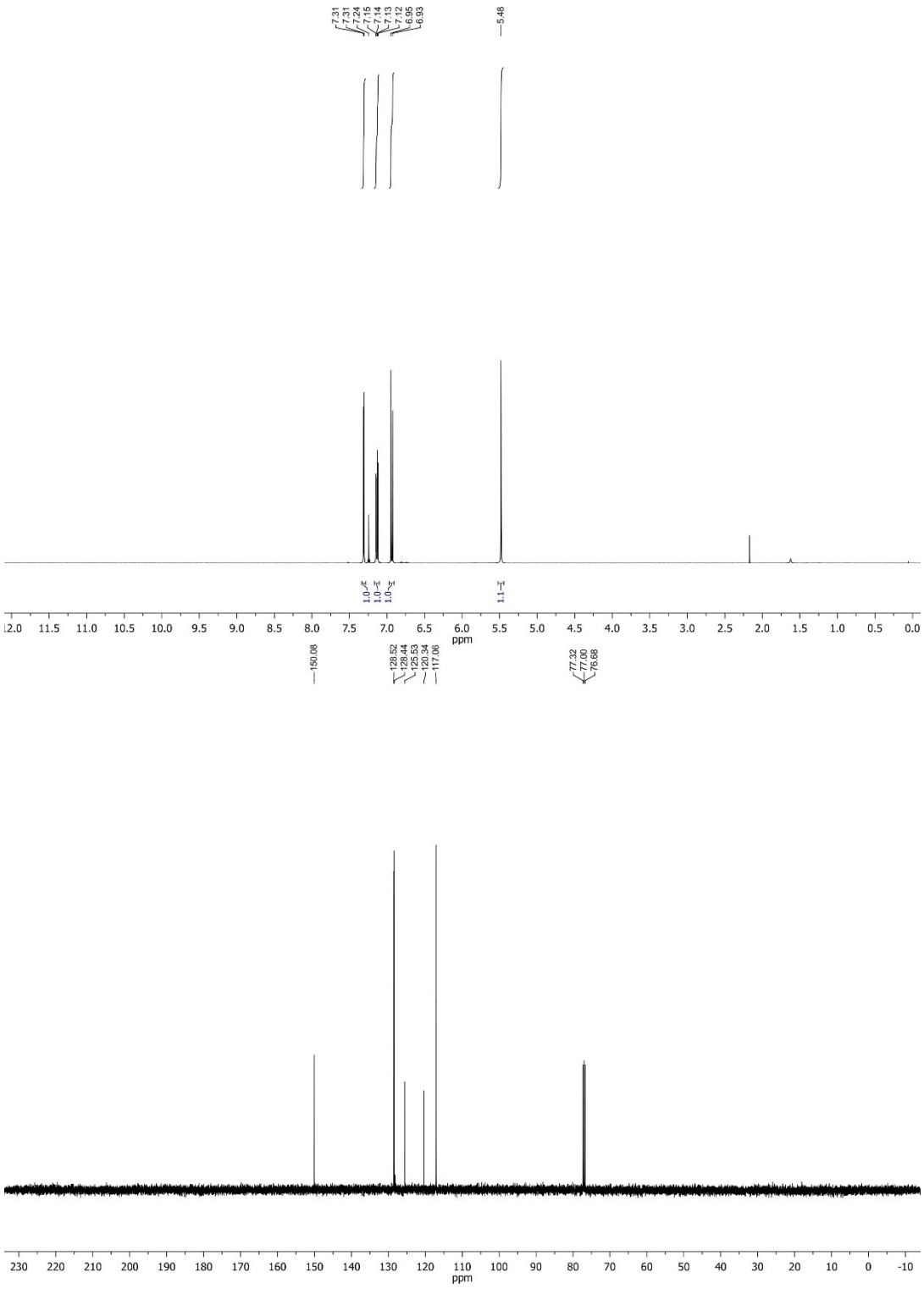
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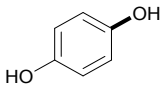
77.00
76.68
ppm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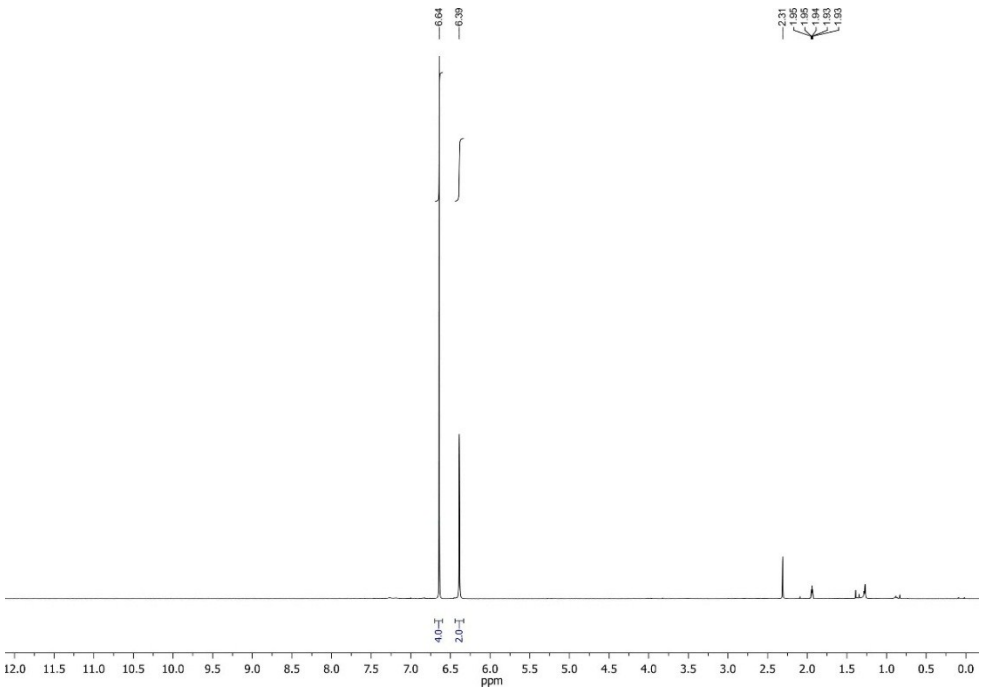
HO

2i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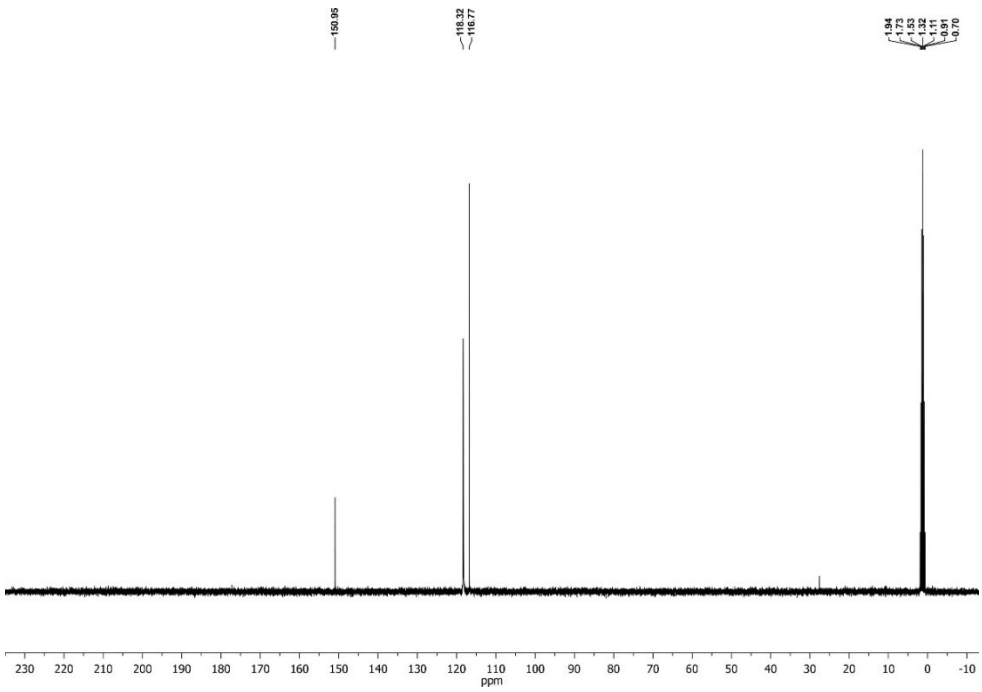
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1.53
1.32
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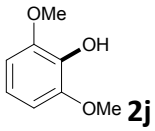
ppm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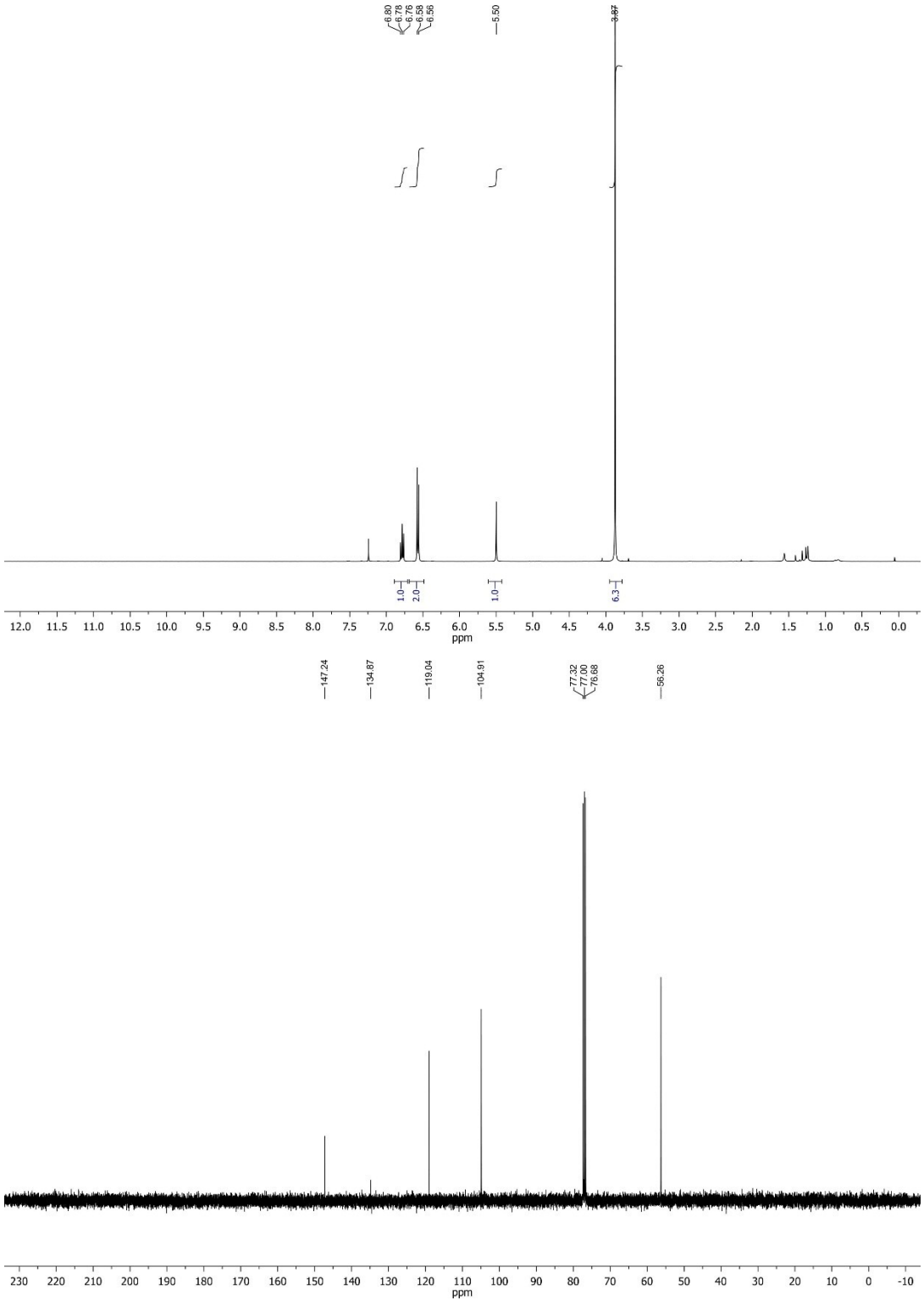
OH
OMe

2j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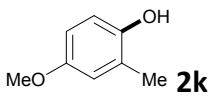
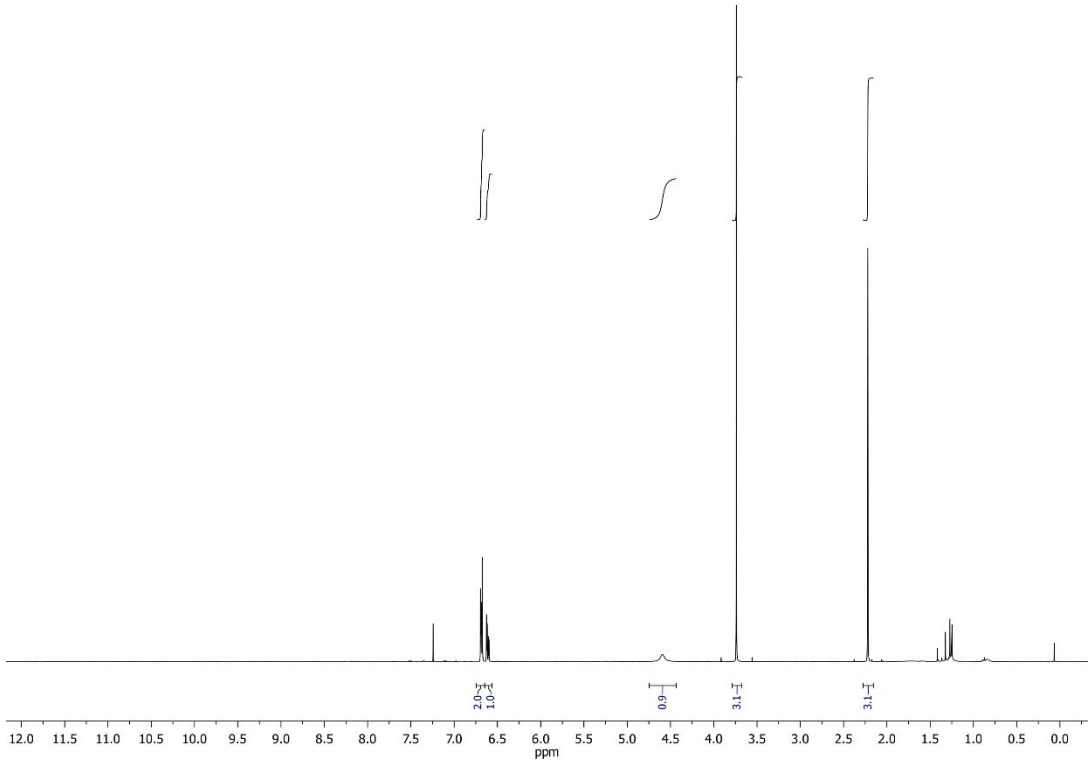
ppm


OH
MeO
Me

2k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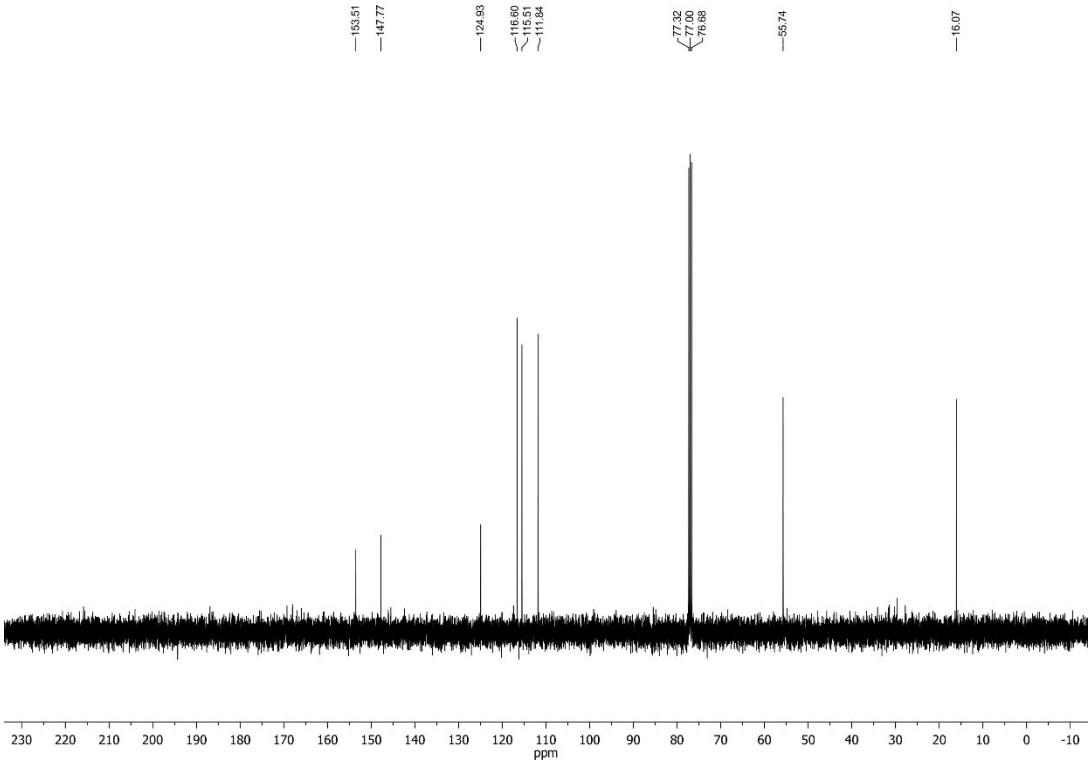
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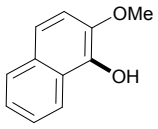
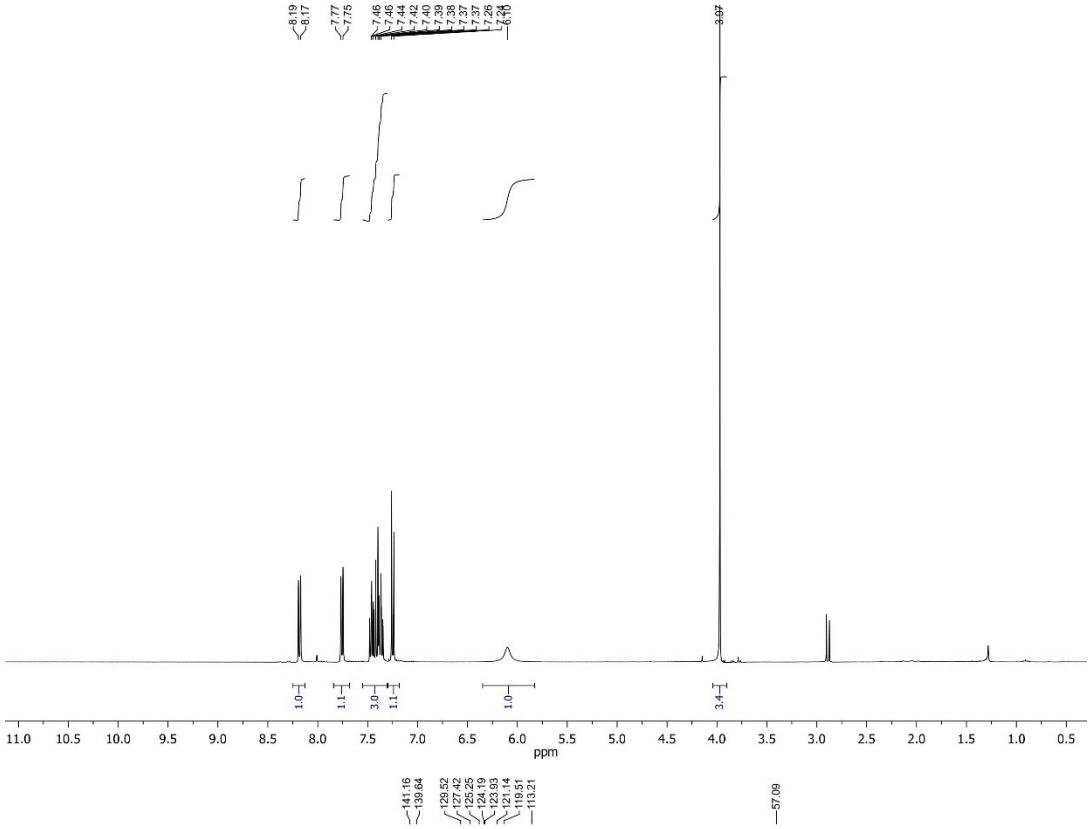
ppm


OMe
OH

2l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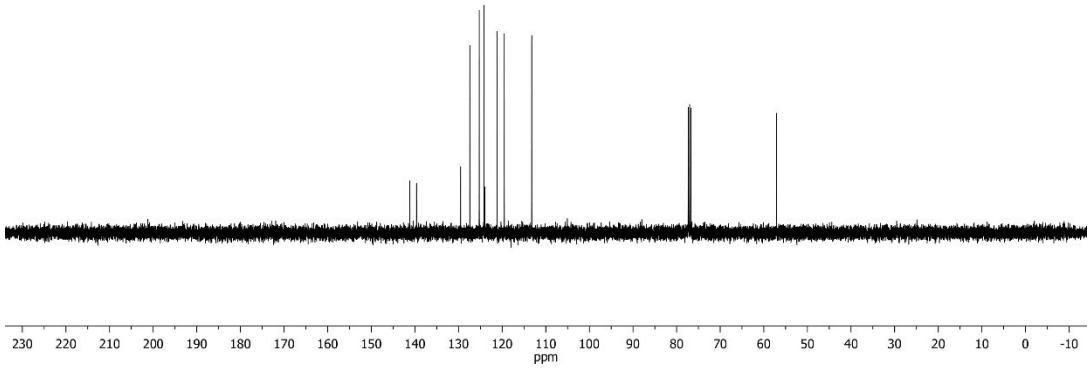
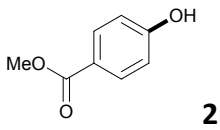
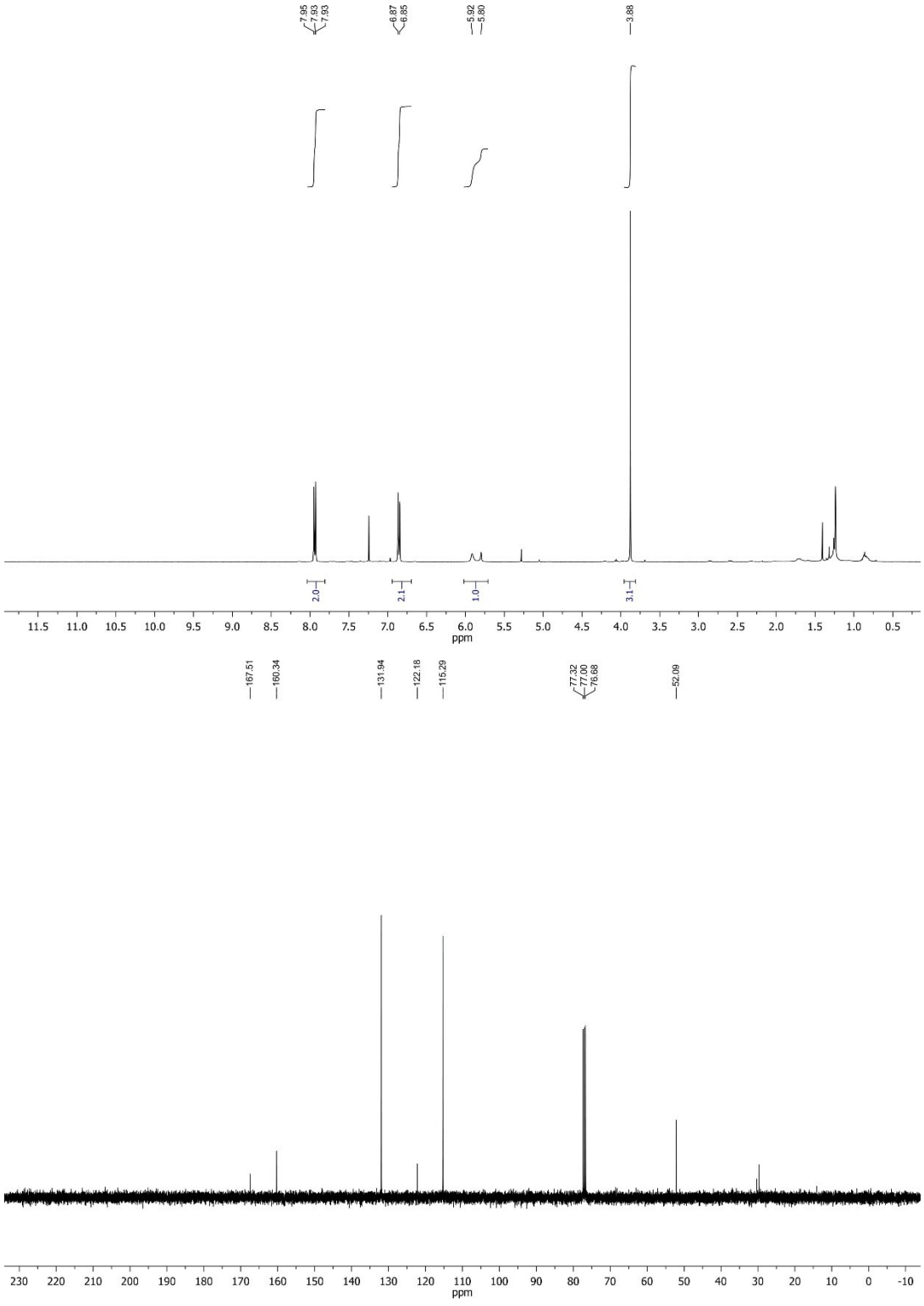
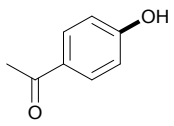
7.26
7.10
6.41
3.97
1.0
1.1
3.0
1.1
1.0
3.4
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
ppm
141.16
139.64
129.52
127.42
125.25
124.19
123.93
121.14
119.51
113.21
57.09


230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

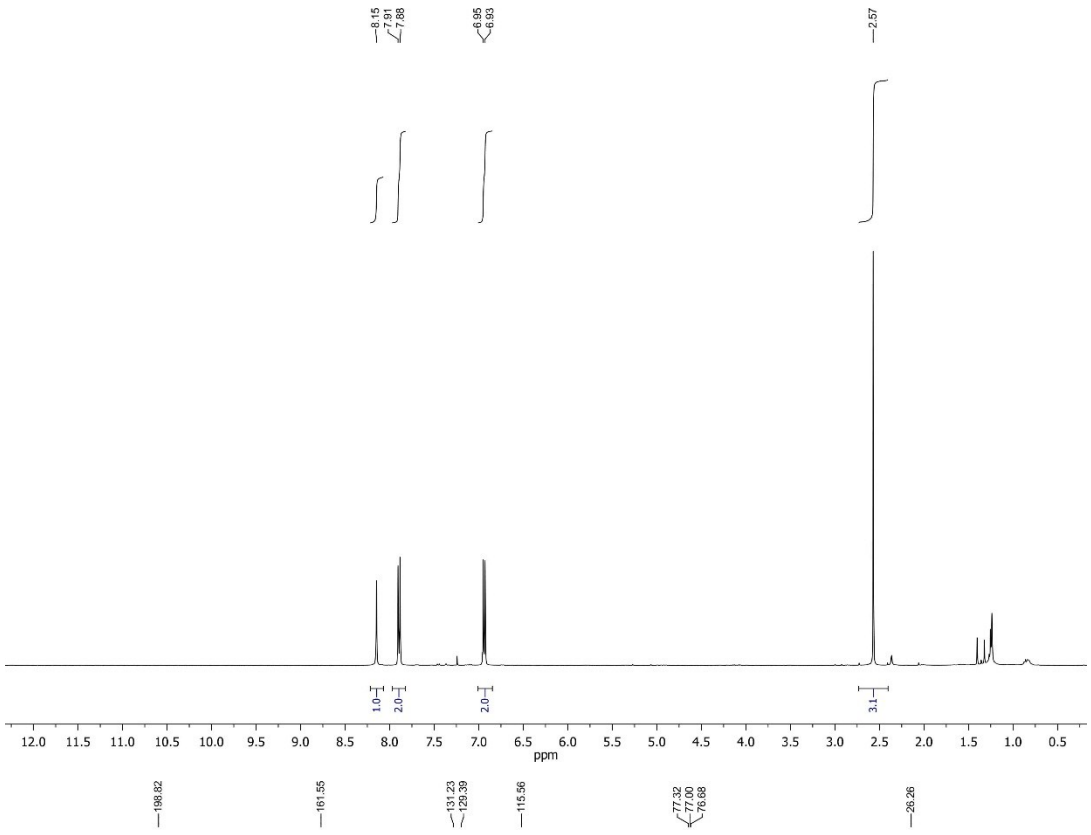

OH
MeO
O

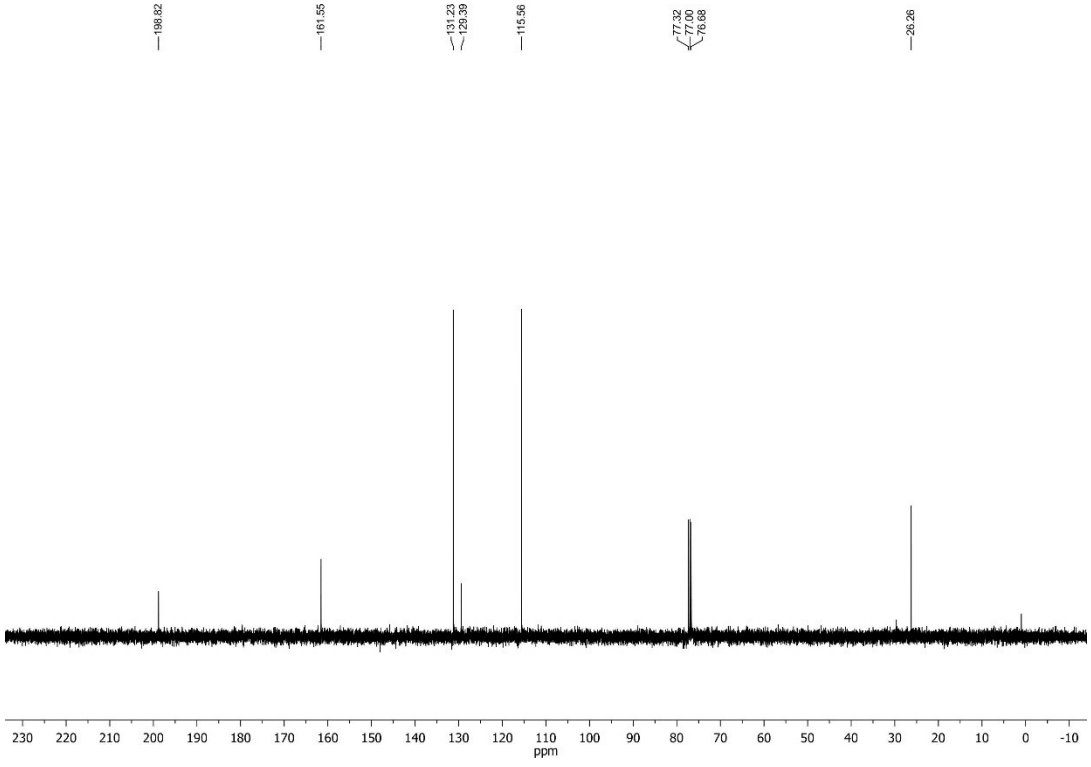
2m

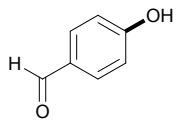

7.95
7.93
7.93
6.87
6.85
5.92
5.80
3.88
2.0
2.1
1.0
3.1
ppm
167.51
160.34
131.94
122.18
115.29
77.32
77.00
76.68
52.09
ppm


OH
O

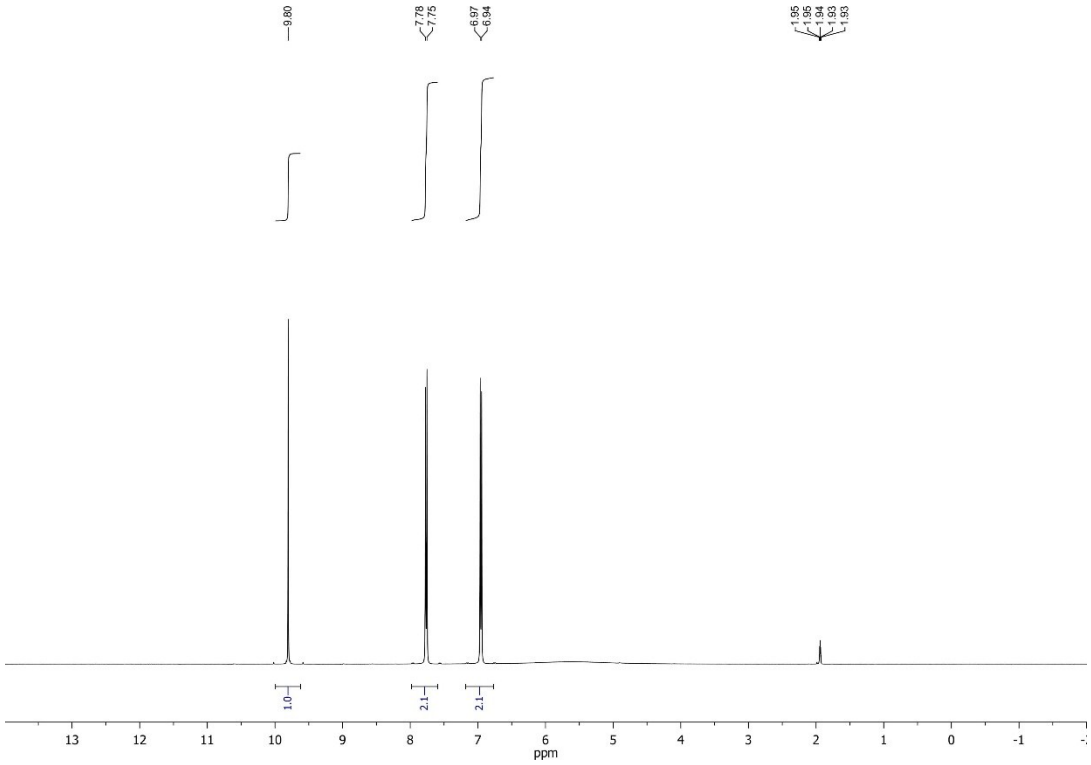
2n

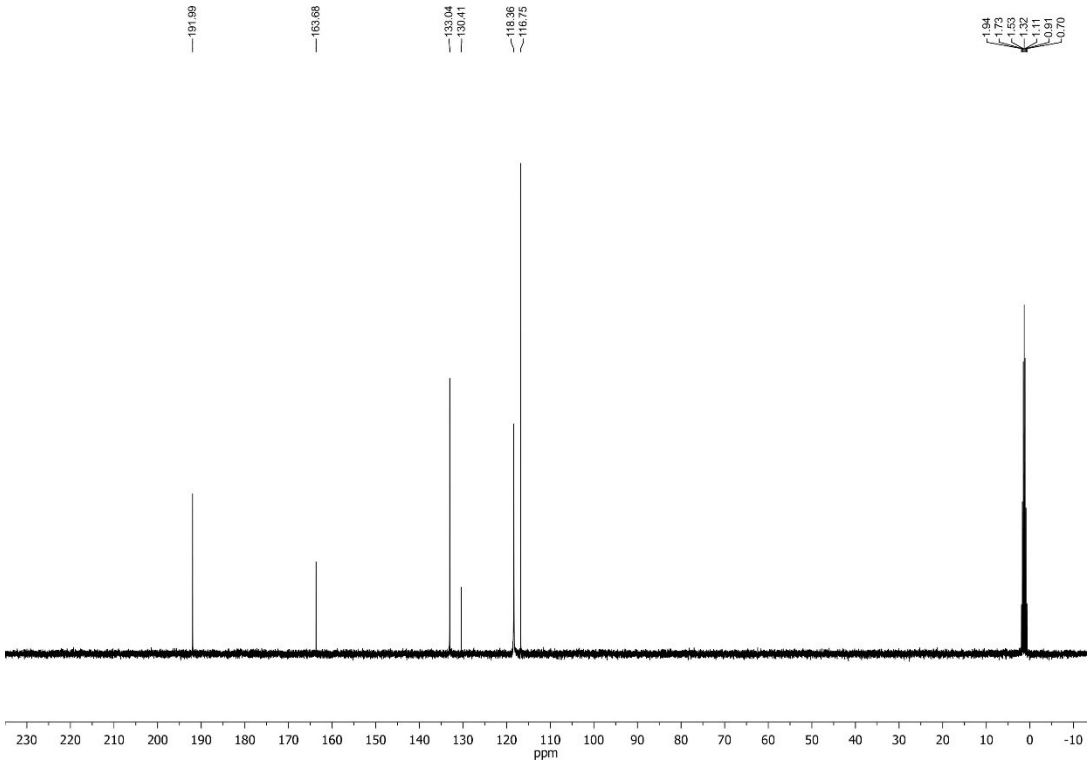

8.15
7.91
7.88
6.95
6.93
2.57
1.0
2.0
2.0
3.1
ppm

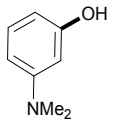

198.82
161.55
131.23
129.39
115.56
77.32
77.00
76.68
26.26
ppm


OH
H
O

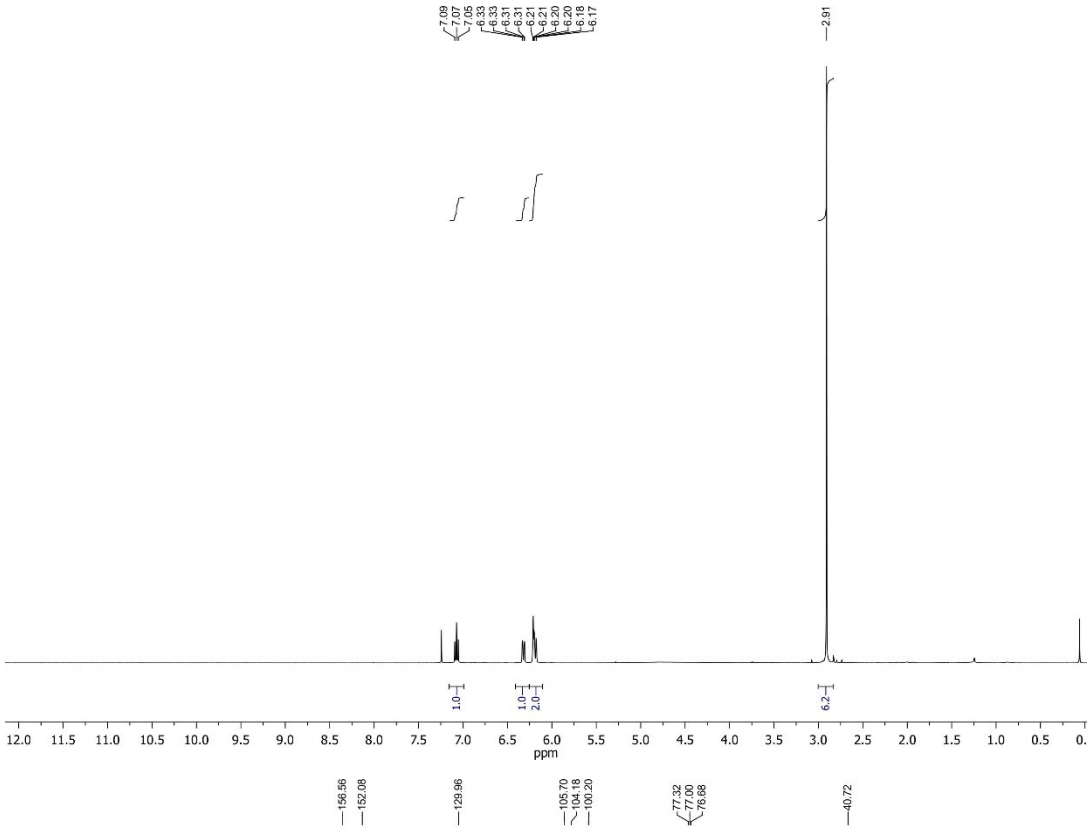
2o

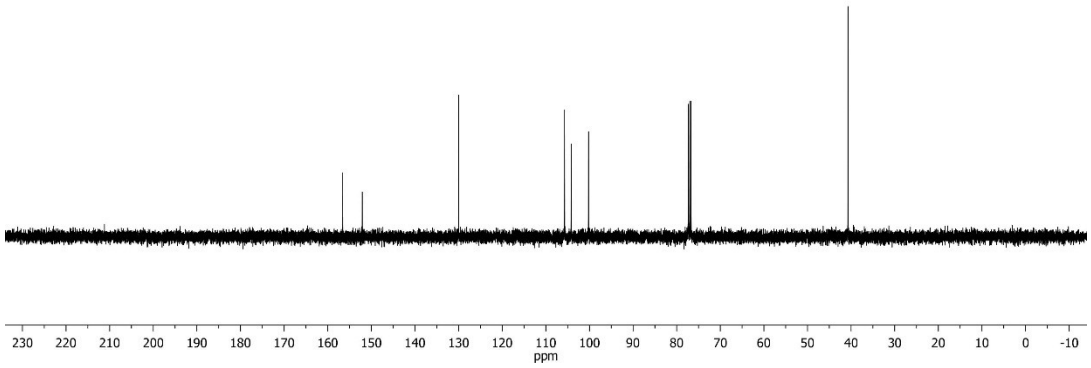

9.80
7.78
7.75
6.97
6.94
1.95
1.95
1.94
1.93
1.93
1.0
2.1
2.1
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm

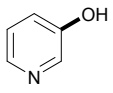

191.89
163.68
133.04
130.41
118.36
116.75
1.94
1.73
1.53
1.32
1.11
0.91
0.70
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
ppm


OH
NMe2

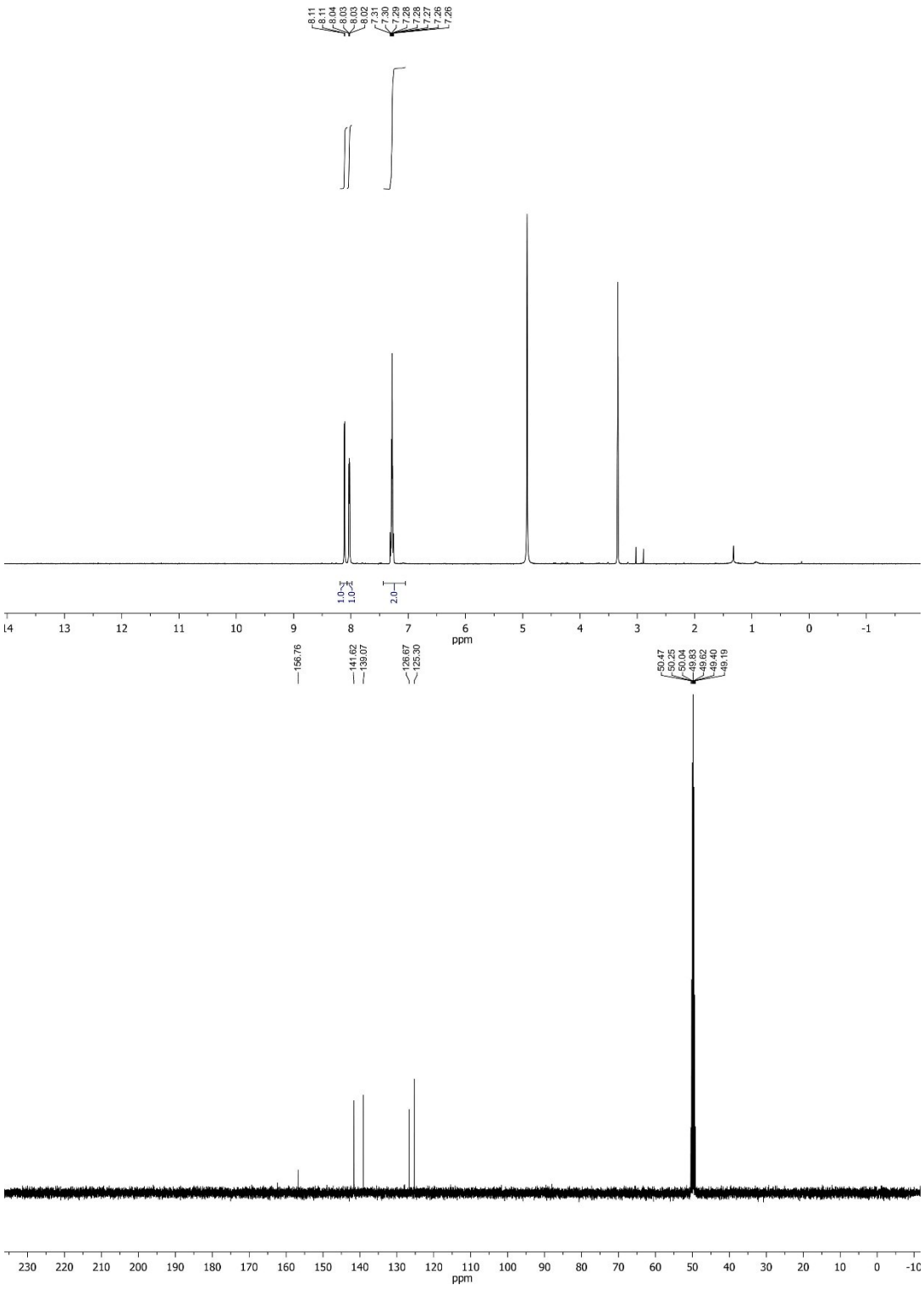
2p

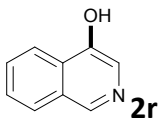

7.09
7.07
7.05
6.33
6.31
6.31
6.21
6.21
6.20
6.20
6.18
6.17
2.91
1.0
1.0
2.0
6.2
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
ppm
156.56
152.08
129.96
105.70
104.18
100.20
77.32
77.00
76.68
40.72


230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
ppm

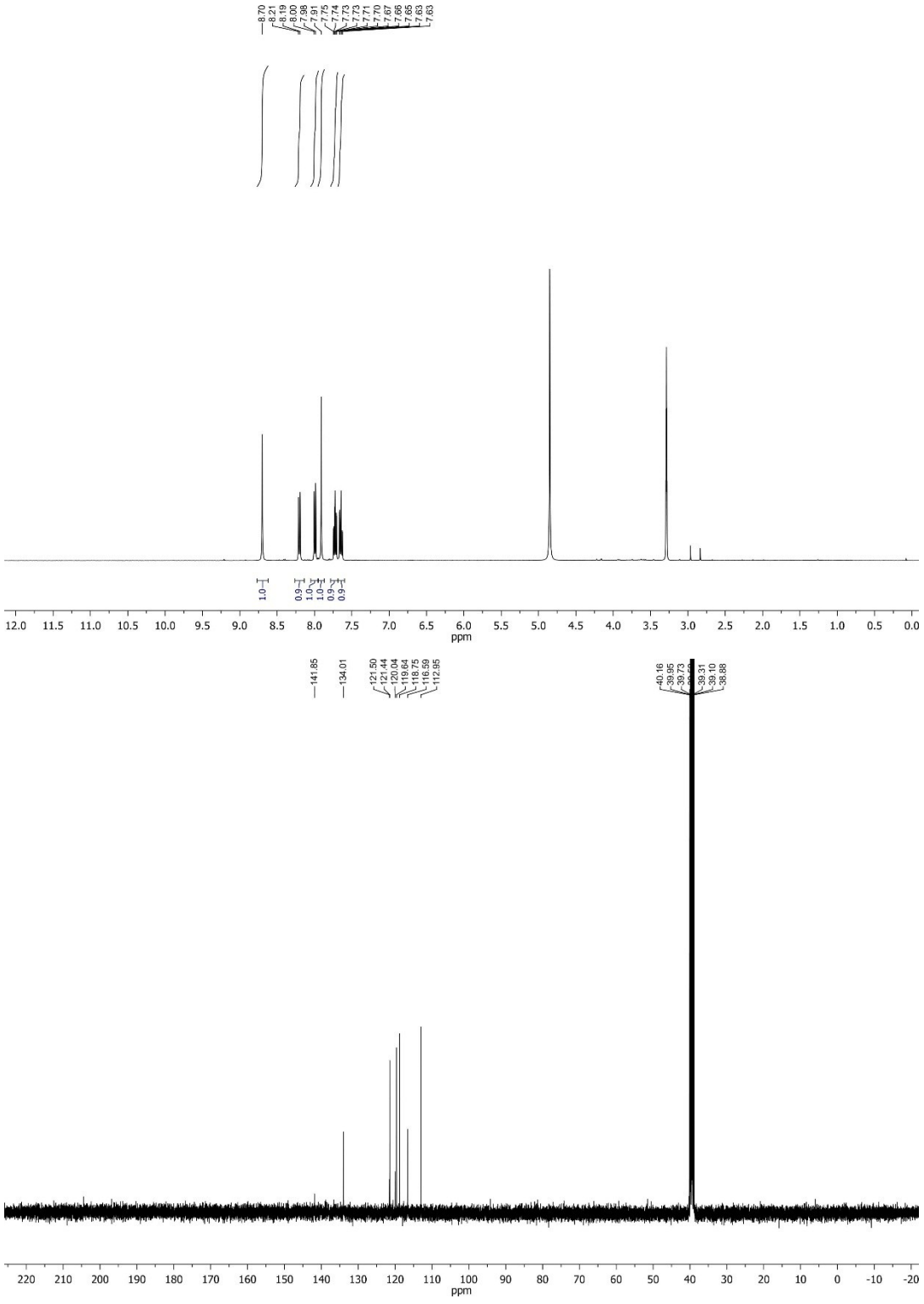

OH
N

2q


8.11
8.11
8.04
8.03
8.03
8.02
7.31
7.30
7.29
7.28
7.28
7.27
7.26
7.26
1.0
1.0
2.0
ppm
156.76
141.62
139.07
126.67
125.30
50.47
50.25
50.04
49.83
49.62
49.40
49.19
ppm


OH
N

2r


8.70
8.21
8.19
8.00
7.98
7.91
7.75
7.74
7.73
7.73
7.71
7.70
7.67
7.67
7.66
7.63
7.63
1.0
0.9
1.0
1.0
0.9
0.9
ppm
141.85
134.01
121.50
121.44
120.04
119.64
118.75
116.59
112.95
40.16
39.95
39.73
39.31
39.10
38.88
ppm