Electronic Supplementary Material (ESI) for ChemComm.

Organocatalytic enantioselective formal arylation of azlactones using quinones as aromatic partner

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Index:

General methods:

Unless stated otherwise, all reactions were carried out in flame dried glassware. All solvents were purified and dried according to standard methods prior to use. Azlactone **2**[1] and catalysts **3**[2] were prepared according to literature. Naphthoquinone **1a**, benzoquinone **1b** and juglone **1c** were purchased from *A*lfa *A*esar *A Johnson Matthey Company*. ^{1}H and ^{13}C NMR spectra were recorded on a Varian instrument (300 MHz and 75 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet or unresolved, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). IR spectra were recorded on a FT-IR spectrometer and only major peaks were reported in cm^{-1}. Optical rotations were reported as follows: $[\alpha]_D^{rt}$ (c: g/100 mL, in solvent). High resolution mass spectra (HRMS) were obtained by the ESI ionization sources. The ee value determination was carried out using chiral HPLC with Daicel Chiracel column on Waters with a 996 UV-detector.

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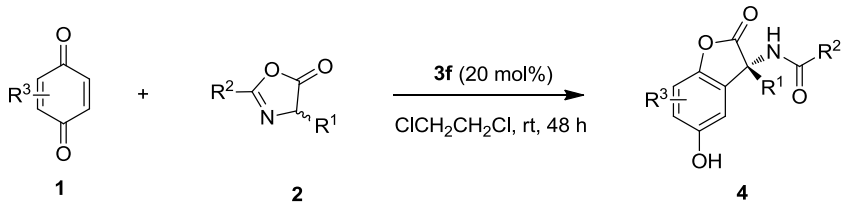
(1) S. Cabrera, E. Reyes, J. Alemán, A. Milelli, S. Kobbelgaard, K. A. Jørgensen, *J. Am. Chem. Soc.*, 2008, **130**, 12031.

(2) T. Okino, Y. Hoashi, Y. Takemoto, *J. Am. Chem. Soc.* 2003, **125**, 12672.

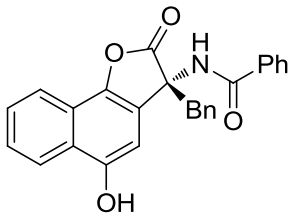
General procedure and spectral data for the synthesis of **4**



1 **2** **4**

To a solution of naphthoquinone **1** (0.10 mmol) in $ClCH_2CH_2Cl$ (1.0 mL) was added azlactone **2** (0.10 mmol) and catalyst **3f** (0.02 mmol). The reaction mixture was stirred for 48 h at room temperature. After the reaction performed completely, the solvent was removed under vacuum and residue was purified by flash column chromatography (petroleum ether/AcOEt 3:1 - 1:1) to give the pure desired products **4**.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4a**



^{1}H NMR (300 MHz, DMSO) δ 10.17 (s, 1H), 9.61 (s, 1H), 8.13 (dd, *J* = 7.0, 2.2 Hz, 1H), 7.88 (d, *J* = 7.1 Hz, 2H), 7.61 (dd, *J* = 13.1, 4.9 Hz, 2H), 7.56 – 7.33 (m, 4H), 7.03 (dd, *J* = 9.5, 6.2 Hz, 3H), 6.89 (s, 1H), 6.82 (dd, *J* = 6.4, 2.8 Hz, 2H), 3.62 (d, *J* = 12.9 Hz, 1H), 3.39 (d, *J* = 12.9 Hz, 1H).

^{13}C NMR (75 MHz, DMSO) δ 175.1, 165.8, 150.2, 141.0, 132.8, 132.3, 132.1, 130.0, 128.4, 127.8, 127.6, 127.0, 125.3, 124.7, 122.9, 121.7, 120.0, 119.3, 101.7, 63.5, 41.8.

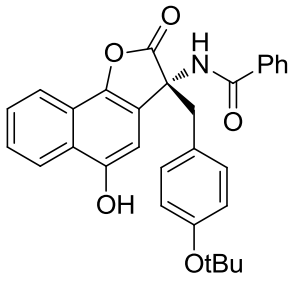
IR: 3314, 1808, 1706, 1644, 1529, 1363, 1228, 1061 cm-1;

$[\alpha]_D^{rt}$ = +323 (c = 1.00, MeOH);

HRMS (ESI): $C_{26}H_{19}NO_4$+H, Calc: 410.1386, Found: 410.1387;

HPLC: DAICEL CHIRALCEL OJ, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} =10.8, t_{minor} = 15.8, 99% ee.

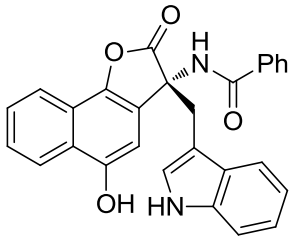
(R)-N-(3-(4-(tert-butoxy)benzyl)-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benz amide, **4b**



^{1}H NMR (300 MHz, DMSO) δ 10.14 (s, 1H), 9.60 (s, 1H), 8.10 (d, *J* = 7.3 Hz, 1H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.73 – 7.20 (m, 6H), 6.83 (s, 1H), 6.66 (d, *J* = 8.4 Hz, 2H), 6.55 (d, *J* = 8.4

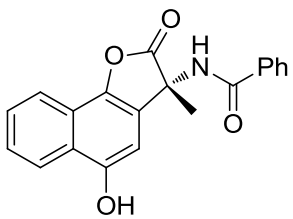
Hz, 2H), 3.53 (d, *J* = 12.8 Hz, 1H), 3.32(d, *J* = 12.8 Hz, 1H), 1.00 (s, 9H).
^{13}C NMR (75 MHz, DMSO) δ 175.3, 165.8, 153.9, 150.2, 140.8, 132.3, 132.1, 130.3, 128.4, 127.6, 127.4, 126.8, 125.2, 124.6, 123.1, 122.8, 121.9, 119.8, 119.3, 101.7, 77.7, 63.8, 28.2.
IR: 3361, 3274, 2970, 2926, 2371, 1794, 1701, 1657, 1227, 1155 cm-1;
$[\alpha]_D^{rt}$ = +289.77 (c = 0.88, MeOH);
HRMS (ESI): $C_{30}H_{27}NO_5$+H, Calc: 482.1970, Found: 482.1962;
HPLC: DAICEL CHIRALCEL IA, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 8.0, t_{minor} = 5.2, 99% ee.

(R)-N-(3-((1H-indol-3-yl)methyl)-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4c**



^{1}H NMR (300 MHz, DMSO) δ 10.70 (d, *J* = 1.8 Hz, 1H), 10.16 (s, 1H), 9.60 (s, 1H), 8.11 (dd, *J* = 7.1, 2.0 Hz, 1H), 7.90 (d, *J* = 7.1 Hz, 2H), 7.59 (t, *J* = 7.6 Hz, 2H), 7.55 – 7.39 (m, 4H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.03 – 6.90 (m, 2H), 6.85 (t, *J* = 7.2 Hz, 1H), 6.43 (d, *J* = 2.3 Hz, 1H), 3.73 (d, *J* = 14.0 Hz, 1H), 3.60 (d, *J* = 13.9 Hz, 1H).
^{13}C NMR (75 MHz, DMSO) δ 175.7, 165.7, 150.2, 141.4, 135.2, 132.4, 132.0, 128.4, 127.6, 127.3, 126.9, 125.2, 124.6, 124.2, 122.9, 122.8, 120.8, 120.1, 119.3, 118.3, 118.0, 111.2, 105.2, 101.8, 63.1, 31.8.
IR: 3370, 2917, 1805, 1702, 1267, 1230, 1097 cm-1;
$[\alpha]_D^{rt}$ = +283.17 (c = 1.12, MeOH);
HRMS (ESI): $C_{28}H_{20}N_2O_4$+H, Calc: 449.1503, Found: 449.1496;
HPLC: DAICEL CHIRALCEL IC, Hexane/EtOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{major} = 5.4, >99% ee.

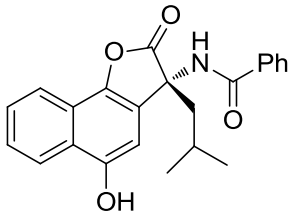
(R)-N-(5-hydroxy-3-methyl-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4d**



^{1}H NMR (300 MHz, DMSO) δ 10.21 (s, 1H), 9.53 (s, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.88 (dd, *J* = 17.3, 7.7 Hz, 3H), 7.68 – 7.39 (m, 5H), 6.74 (s, 1H), 1.71 (s, 3H).
^{13}C NMR (75 MHz, DMSO) δ 176.2, 165.5, 150.2, 139.9, 131.8, 131.7, 128.1, 127.3, 126.9, 125.1, 124.4, 124.3, 122.6, 119.9, 119.5, 100.8, 57.8, 23.3.
IR: 3395, 3340, 1803, 1783, 1704, 1643, 1529, 1413, 1046, 688 cm-1;

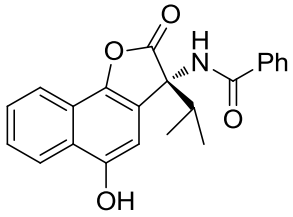
[α]$_D^{rt}$ = +166.04 (c = 1.00, MeOH);
HRMS (ESI): $C_{20}H_{15}NO_4$+H, Calc: 334.1080, Found: 334.1074;
HPLC: DAICEL CHIRALCEL AD, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 10.9, >99% ee.

(R)-N-(5-hydroxy-3-isobutyl-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4e**



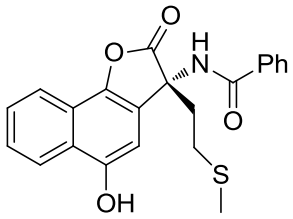
^{1}H NMR (300 MHz, DMSO) δ 10.19 (s, 1H), 9.27 (s, 1H), 8.18 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 7.4 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.51 (dt, *J* = 14.8, 7.2 Hz, 4H), 6.75 (s, 1H), 2.31 (dd, *J* = 13.7, 5.2 Hz, 1H), 2.03 (dd, *J* = 13.6, 6.9 Hz, 1H), 1.48 – 1.04 (m, 1H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.63 (d, *J* = 6.6 Hz, 3H).
^{13}C NMR (75 MHz, DMSO) δ 176.1, 165.6, 150.4, 141.1, 132.3, 132.0, 128.4, 127.6, 127.3, 125.5, 124.8, 123.0, 122.5, 120.2, 119.7, 101.6, 61.7, 44.5, 23.9, 23.6, 23.0.
IR: 3341, 1809, 1708, 1413, 1364, 1223, 1057 cm-1;
[α]$_D^{rt}$ = +206.69 (c = 0.99, MeOH);
HRMS (ESI): $C_{23}H_{21}NO_4$+H, Calc: 376.1550, Found: 376.1543;
HPLC: DAICEL CHIRALCEL AD, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 6.9, t_{minor} = 5.3, 98% ee.

(R)-N-(5-hydroxy-3-isopropyl-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4f**



^{1}H NMR (300 MHz, DMSO) δ 10.15 (s, 1H), 9.33 (s, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 7.89 (d, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 7.1 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.59 – 7.51 (m, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 6.70 (s, 1H), 2.60 – 2.52 (m, 1H), 1.02 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.8 Hz, 3H).
^{13}C NMR (75 MHz, DMSO) δ 174.8, 166.4, 150.2, 141.2, 132.5, 132.0, 128.3, 127.7, 127.2, 125.4, 124.5, 122.9, 122.1, 120.2, 119.4, 101.8, 65.1, 33.4, 16.5, 15.8.
IR: 3004, 2969, 2925, 1811, 1714, 1668, 1363, 1222, 1092, 1059, 530 cm-1;
[α]$_D^{rt}$ = +168.93 (c = 1.03, MeOH);
HRMS (ESI): $C_{22}H_{19}NO_4$+H, Calc: 362.1397, Found: 362.1387;
HPLC: DAICEL CHIRALCEL IC, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 7.2, >99% ee.

(R)-N-(5-hydroxy-3-(2-(methylthio)ethyl)-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4g**



^{1}H NMR (300 MHz, DMSO) δ 10.22 (s, 1H), 9.47 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 7.4 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.60 – 7.51 (m, 2H), 7.47 (t, *J* = 7.3 Hz, 2H), 6.74 (s, 1H), 2.45 – 2.11 (m, 4H), 2.00 (s, 3H).

^{13}C NMR (75 MHz, DMSO) δ 175.3, 166.0, 150.6, 140.9, 132.1, 128.4, 127.6, 127.3, 125.5, 124.8, 123.0, 120.3, 119.7, 101.2, 61.4, 35.8, 26.6, 14.6.

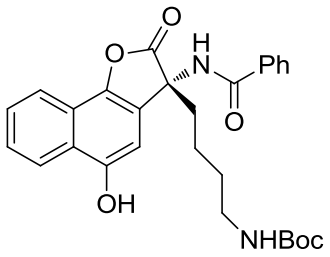
IR: 3407, 2921, 1809, 1710, 1364, 1223, 1093, 531 cm-1;

$[\alpha]_D^{rt}$ = -128.16 ℃ (c =1.03, MeOH);

HRMS (ESI): $C_{22}H_{19}NO_4S$+H, Calc: 394.1118, Found: 394.1108;

HPLC: DAICEL CHIRALCEL IC, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 5.8, t_{minor} = 6.7, 87% ee.

(R)-tert-butyl (4-(3-benzamido-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)butyl) carbamate, **4h**



^{1}H NMR (300 MHz, DMSO) δ 10.15 (s, 1H), 9.40 (s, 1H), 8.17 (d, *J* = 8.3 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.64 (t, *J* = 7.5 Hz, 1H), 7.56 (dd, *J* = 7.1, 4.7 Hz, 2H), 7.48 (t, *J* = 7.5 Hz, 2H), 6.72 (s, 2H), 2.81 (d, *J* = 6.0 Hz, 2H), 2.19 (t, *J* = 10.8 Hz, 1H), 2.13 – 1.92 (m, 1H), 1.43 – 1.21 (m, 10H), 1.18 (s, 1H), 1.15-1.00 (m, 1H), 1.00 – 0.86 (m, 1H).

^{13}C NMR (75 MHz, DMSO) δ 175.8, 165.8, 155.4, 150.4, 140.9, 132.2, 132.0, 128.4, 127.6, 127.1, 125.4, 124.7, 122.9, 122.7, 120.2, 119.6, 101.3, 77.3, 61.8, 35.9, 29.4, 28.1, 19.7.

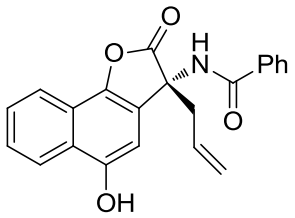
IR: 3340,2924, 1809, 1705, 1526, 1366, 1226, 1169, 1059 cm-1;

$[\alpha]_D^{rt}$ = -116.19 ℃ (c = 1.01, MeOH);

HRMS (ESI): $C_{28}H_{30}N_2O_6$+H, Calc: 491.2191491.2177, Found: 491.2177;

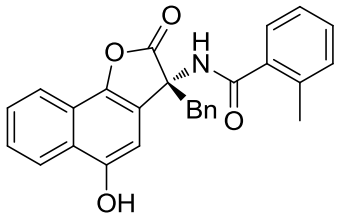
HPLC: DAICEL CHIRALCEL IC, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 6.8, t_{minor} = 7.9, 92% ee.

(R)-N-(3-allyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4i**



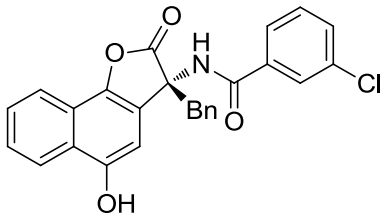
^{1}H NMR (300 MHz, DMSO) δ 10.19 (s, 1H), 9.48 (s, 1H), 8.18 (d, *J* = 8.3 Hz, 1H), 7.87 (dd, *J* = 14.0, 7.7 Hz, 3H), 7.75 – 7.31 (m, 5H), 6.76 (s, 1H), 5.34 (dt, *J* = 16.9, 7.3 Hz, 1H), 5.06 (dd, *J* = 22.4, 13.5 Hz, 2H), 3.04 (dd, *J* = 13.4, 6.3 Hz, 1H), 2.81 (dd, *J* = 13.5, 7.9 Hz, 1H).
^{13}C NMR (75 MHz, DMSO) δ 175.1, 165.9, 150.4, 140.8, 132.2, 132.1, 129.7, 128.4, 127.6, 127.2, 125.4, 124.7, 122.9, 122.3, 121.0, 120.2, 119.6, 101.3, 61.9.
IR: 3327, 2923, 1808, 1704, 1641, 1527, 1444, 1413, 1364, 1228, 1059, 779, 531 cm-1;
$[\alpha]_D^{rt}$ = +219.54 ℃ (c = 0.99, MeOH);
HRMS (ESI): $C_{22}H_{17}NO_4$+H, Calc: 360.1234, Found: 360.1230;
HPLC: DAICEL CHIRALCEL IA, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 5.3, t_{minor} = 4.6, 99% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-2-methylbenzamide, **4j**



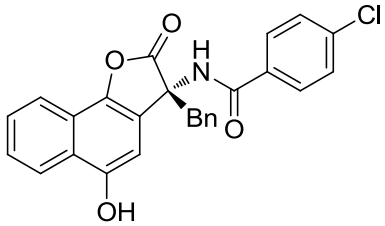
^{1}H NMR (300 MHz, DMSO) δ 10.24 (s, 1H), 9.63 (s, 1H), 8.52 – 7.97 (m, 1H), 7.61 (d, *J* = 7.1 Hz, 1H), 7.56 – 7.43 (m, 2H), 7.43 – 7.33 (m, 2H), 7.28 (t, *J* = 8.3 Hz, 2H), 7.03 (d, *J* = 4.7 Hz, 3H), 6.93 (s, 1H), 6.85 – 6.72 (m, 2H), 3.48 (d, *J* = 12.9 Hz, 1H), 3.30 (d, *J* = 12.9 Hz, 1H), 2.26 (s, 3H).
^{13}C NMR (75 MHz, DMSO) δ 175.2, 168.5, 150.3, 141.0, 135.6, 134.8, 132.7, 130.5, 129.9, 127.8, 127.2, 127.1, 127.0, 125.6, 125.3, 124.7, 122.9, 121.7, 120.1, 119.4, 101.6, 63.3, 41.8, 19.2.
IR: 3344, 1805, 1655, 1639, 1594, 1384, 1229, 1098, 1067, 772 cm-1;
$[\alpha]_D^{rt}$ = +187.68 ℃ (c = 0.682, MeOH);
HRMS (ESI): $C_{27}H_{21}NO_4$+H, Calc: 424.1548, Found: 424.1543;
HPLC: DAICEL CHIRALCEL IA, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 14.4, t_{minor} = 12.6, 98% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-3-chlorobenzamide, **4k**



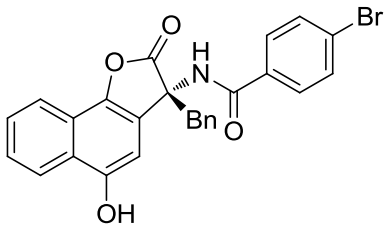
^{1}H NMR (300 MHz, DMSO) δ 10.21 (s, 1H), 9.74 (s, 1H), 8.13 (dd, *J* = 6.7, 2.6 Hz, 1H), 7.98 (d, *J* = 1.7 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.74 – 7.65 (m, 1H), 7.61 (dd, *J* = 6.7, 2.6 Hz, 1H), 7.55 (dd, *J* = 7.9, 4.8 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.20 – 6.96 (m, 3H), 6.91 (s, 1H), 6.81 (dd, *J* = 6.4, 2.8 Hz, 2H), 3.62 (d, *J* = 12.9 Hz, 1H), 3.40 (d, *J* = 12.9 Hz, 1H).
^{13}C NMR (75 MHz, DMSO) δ 175.0, 164.4, 150.3, 141.1, 134.2, 133.3, 132.7, 131.9, 130.5, 129.9, 127.8, 127.3, 127.1, 127.0, 126.5, 125.4, 124.8, 122.9, 121.5, 120.0, 119.3, 101.7, 63.6, 41.7.
IR: 3337, 3067, 1806, 1702, 1639, 1528, 1412, 1232, 1097, 1061, 1001, 678 cm-1;
$[\alpha]_D^{rt}$ = +298.00 ٩(c = 1.00, MeOH);
HRMS (ESI): $C_{26}H_{18}ClNO_4$+H, Calc: 444.0999, Found: 444.0997;
HPLC: DAICEL CHIRALCEL OJ, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 14.6, t_{minor} = 21.8, 99% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-4-chlorobenzamide, **4l**



^{1}H NMR (300 MHz, DMSO) δ 10.20 (s, 1H), 9.70 (s, 1H), 8.48 – 8.04 (m, 1H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.76 – 7.56 (m, 3H), 7.56 – 7.37 (m, 2H), 7.04 (d, *J* = 3.5 Hz, 3H), 6.89 (s, 1H), 6.81 (d, *J* = 3.7 Hz, 2H), 3.61 (d, *J* = 12.9 Hz, 1H), 3.39 (d, *J* = 12.9 Hz, 1H).
^{13}C NMR (75 MHz, DMSO) δ 175.1, 164.8, 150.3, 141.1, 137.0, 132.7, 131.0, 130.0, 129.6, 128.6, 127.8, 127.1, 127.0, 125.4, 124.8, 122.9, 121.6, 120.0, 119.3, 101.7, 63.6, 41.8.
IR: 3324, 3065, 1807, 1701, 1639, 1595, 1531, 1485, 1233, 1096 cm-1;
$[\alpha]_D^{rt}$ = +301.01 ٩(c = 0.99, MeOH);
HRMS (ESI): $C_{26}H_{18}ClNO_4$+H, Calc: 444.0999, Found: 444.0997;
HPLC: DAICEL CHIRALCEL OJ, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 14.7, t_{minor} = 25.2, >99% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-4-bromobenzamide, **4m**



^{1}H NMR (300 MHz, DMSO) δ 10.20 (s, 1H), 9.70 (s, 1H), 8.13 (dd, *J* = 6.8, 2.5 Hz, 1H), 7.84 (d, *J* = 8.6 Hz, 2H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.61 (dd, *J* = 6.8, 2.5 Hz, 1H), 7.49 (tt, *J* = 6.9, 5.2 Hz, 2H), 7.21 – 6.95 (m, 3H), 6.89 (s, 1H), 6.81 (dd, *J* = 6.4, 2.8 Hz, 2H), 3.61 (d, *J* = 13.0 Hz, 1H), 3.38 (d, *J* = 13.0 Hz, 1H).

^{13}C NMR (75 MHz, DMSO) δ 175.0, 164.8, 150.3, 141.1, 132.7, 131.5, 131.3, 130.0, 129.7, 127.8, 127.1, 127.0, 126.0, 125.4, 124.8, 122.9, 121.5, 120.0, 119.3, 101.7, 63.6, 41.8.

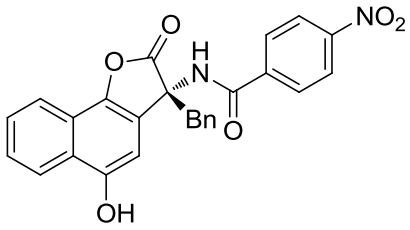
IR: 3409, 1809, 1709, 1364, 1224, 1095, 1065, 531 cm-1;

$[\alpha]_D^{rt}$ = +244.23 ℃ (c = 1.04, MeOH);

HRMS (ESI): $C_{26}H_{18}BrNO_4$+H, Calc: 488.0497, Found: 488.0492;

HPLC: DAICEL CHIRALCEL IA, Hexane/EtOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{major} = 11.3, t_{minor} = 13.9, 97% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-4-nitrobenzamide, **4n**



^{1}H NMR (300 MHz, DMSO) δ 10.23 (s, 1H), 9.99 (s, 1H), 8.37 (d, *J* = 8.8 Hz, 2H), 8.24 – 8.04 (m, 3H), 7.62 (dd, *J* = 6.7, 2.5 Hz, 1H), 7.50 (tt, *J* = 6.8, 5.2 Hz, 2H), 7.12 – 6.98 (m, 3H), 6.92 (s, 1H), 6.82 (dd, *J* = 6.4, 2.7 Hz, 2H), 3.64 (d, *J* = 12.9 Hz, 1H), 3.42 (d, *J* = 12.9 Hz, 1H).

^{13}C NMR (75 MHz, DMSO) δ 174.9, 164.2, 150.3, 149.5, 141.1, 137.7, 132.6, 129.9, 129.2, 127.8, 127.2, 127.1, 125.4, 124.8, 123.7, 122.9, 121.3, 120.0, 119.3, 101.6, 63.7, 41.7.

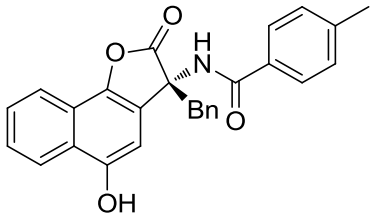
IR: 3328, 1809, 1709, 1603, 1529, 1361, 1224, 1062, 531 cm-1;

$[\alpha]_D^{rt}$ = +212.74 ℃ (c = 0.97, MeOH);

HRMS (ESI): $C_{26}H_{18}N_2O_6$+H, Calc: 455.1251, Found: 455.1238;

HPLC: DAICEL CHIRALCEL AD, Hexane/EtOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{major} = 11.6, t_{minor} = 13.8, 98% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-4-methylbenzamide, **4o**



^{1}H NMR (300 MHz, DMSO) δ 10.18 (s, 1H), 9.52 (s, 1H), 8.28 – 7.93 (m, 1H), 7.79 (d, *J* = 8.1 Hz, 2H), 7.68 – 7.57 (m, 1H), 7.48 (tt, *J* = 6.8, 5.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.14 – 6.95 (m, 3H), 6.88 (s, 1H), 6.81 (dd, *J* = 6.3, 2.7 Hz, 2H), 3.61 (d, *J* = 13.0 Hz, 1H),3.38 (d, *J* = 13.0 Hz, 1H), 2.37 (s, 3H).

^{13}C NMR (75 MHz, DMSO) δ 175.2, 165.6, 150.2, 142.1, 141.0, 132.8, 130.0, 129.5, 128.9, 127.8, 127.7, 127.1, 127.0, 125.3, 124.7, 122.9, 121.8, 120.0, 119.3, 101.7, 63.5, 41.8, 21.0.

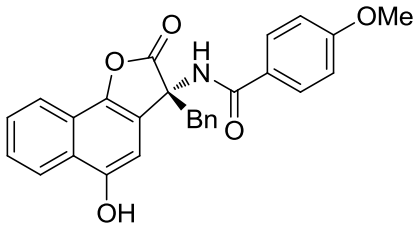
IR: 3334, 3034, 1808, 1704, 1638, 1535, 1498, 1414, 1364, 1230, 1096, 1001 cm-1;

$[\alpha]_D^{rt}$ = +258.23 ٩(c = 1.00, MeOH);

HRMS (ESI): $C_{27}H_{21}NO_4$+H, Calc: 424.1548, Found: 424.1543;

HPLC: DAICEL CHIRALCEL IA, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 7.4, t_{minor} = 5.6, 99% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)-4-methoxybenzamid e, **4p**



^{1}H NMR (300 MHz, DMSO) δ 10.17 (s, 1H), 9.43 (s, 1H), 8.12 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 2H), 7.61 (dd, *J* = 6.9, 2.1 Hz, 1H), 7.48 (tt, *J* = 6.8, 5.3 Hz, 2H), 7.04 (dd, *J* = 5.3, 3.3 Hz, 5H), 6.88 (s, 1H), 6.81 (dd, *J* = 6.3, 2.8 Hz, 2H), 3.61 (d, *J* = 12.9 Hz, 1H), 3.37 (d, *J* = 12.9 Hz, 1H).

^{13}C NMR (75 MHz, DMSO) δ 175.3, 165.2, 162.1, 150.2, 141.0, 132.9, 130.0, 127.7, 127.0, 126.9, 125.2, 124.7, 124.4, 122.9, 122.0, 120.0, 119.4, 113.6, 101.7, 63.4, 55.4, 41.8.

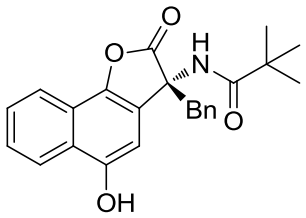
IR: 3344, 2848, 1808, 1710, 1607, 1500, 1364, 1258, 1223, 1095, 530 cm-1;

$[\alpha]_D^{rt}$ = +219.54 ٩(c = 0.99, MeOH);

HRMS (ESI): $C_{27}H_{21}NO_5$+H, Calc: 440.1497, Found: 440.1492;

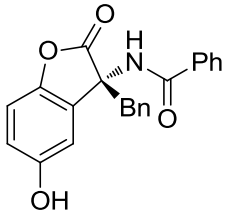
HPLC: DAICEL CHIRALCEL AD, Hexane/EtOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{major} = 14.8, t_{minor} = 11.8, 99% ee.

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)pivalamide, **4q**



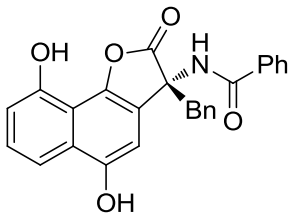
^{1}H NMR (300 MHz, DMSO) δ 10.17 (s, 1H), 8.57 (s, 1H), 8.11 (dd, *J* = 6.1, 3.0 Hz, 1H), 7.55 (dd, *J* = 6.1, 3.0 Hz, 1H), 7.51 – 7.28 (m, 2H), 6.99 (d, *J* = 3.6 Hz, 3H), 6.83 (s, 1H), 6.74 (d, *J* = 3.9 Hz, 2H), 3.51 (d, *J* = 12.9 Hz, 1H), 3.23 (d, *J* = 12.9 Hz, 1H), 1.08 (s, 9H).
^{13}C NMR (75 MHz, DMSO) δ 177.2, 175.2, 150.1, 140.9, 132.9, 129.9, 127.7, 127.0, 126.9, 125.2, 124.6, 122.8, 122.0, 120.0, 119.3, 101.4, 63.1, 41.7, 37.6, 26.9.
IR: 3354, 2967, 1807, 1705, 1647, 1516, 1414, 1365, 1228, 1095, 1062, 1001, 701 cm-1;
$[\alpha]_D^{rt}$ = +158.89 (c = 1.01, MeOH);
HRMS (ESI): $C_{24}H_{23}NO_4$+H, Calc: 390.1710, Found: 390.1700;
HPLC: DAICEL CHIRALCEL IA, Hexane/EtOH = 85/15, flow rate = 1.0 mL/min, retention time: t_{major} = 5.2, t_{minor} = 6.1, >99% ee

(R)-N-(3-benzyl-5-hydroxy-2-oxo-2,3-dihydrobenzofuran-3-yl)benzamide, **4r**



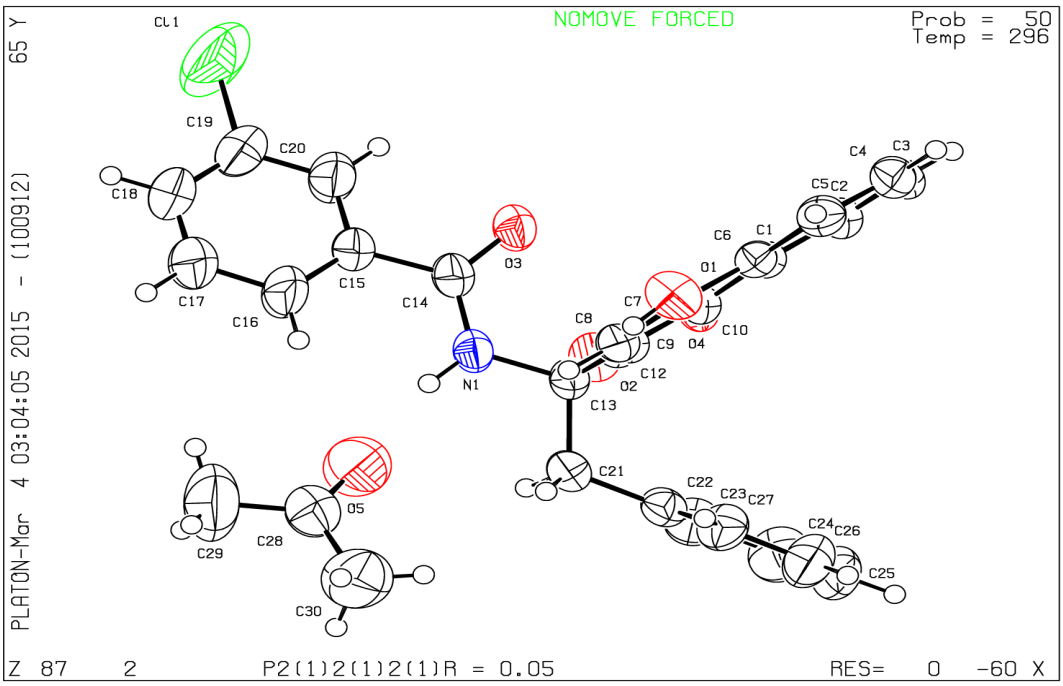
^{1}H NMR (300 MHz, DMSO) δ 9.54 (s, 1H), 9.36 (s, 1H), 8.05 – 7.73 (m, 2H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.50 (t, *J* = 7.3 Hz, 2H), 7.09 (dt, *J* = 5.5, 4.1 Hz, 3H), 6.91 – 6.73 (m, 3H), 6.67 (d, *J* = 8.6 Hz, 1H), 6.58 (dd, *J* = 8.6, 2.5 Hz, 1H), 3.48 (d, *J* = 12.9 Hz, 1H), 3.29 (d, *J* = 12.9 Hz, 1H).
^{13}C NMR (75 MHz, DMSO) δ 175.1, 165.8, 153.9, 145.6, 132.6, 123.2, 132.1, 130.0, 128.8, 128.4, 127.8, 127.6, 127.1, 115.4, 110.4, 110.0, 62.7, 42.0.
IR: 3517, 3412, 3005, 2925, 1807, 1714, 1528, 1363, 1221, 1092, 902, 529 cm-1;
HRMS (ESI): $C_{22}H_{17}NO_4$+H, Calc: 360.1235, Found: 360.1230;
HPLC: DAICEL CHIRALCEL OJ, Hexane/EtOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{major} = 12.1, >99% ee.

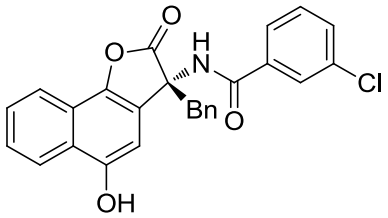
(R)-N-(3-benzyl-5,9-dihydroxy-2-oxo-2,3-dihydronaphtho[1,2-b]furan-3-yl)benzamide, **4s**



^{1}H NMR (300 MHz, DMSO) δ 9.95 (s, 1H), 9.87 (s, 1H), 9.49 (s, 1H), 7.86 (d, *J* = 7.3 Hz, 2H), 7.70 – 7.39 (m, 4H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.13 – 6.92 (m, 3H), 6.88 – 6.65 (m, 4H), 3.56 (d, *J* = 12.9 Hz, 1H), 3.33 (d, *J* = 12.9 Hz, 1H).
^{13}C NMR (75 MHz, DMSO) δ 175.9, 165.6, 152.3, 149.7, 141.2, 133.0, 132.4, 132.0, 128.4, 127.8, 127.8, 127.6, 127.1, 125.8, 121.3, 113.0, 112.0, 110.2, 102.1, 62.2, 41.9.
IR: 3411, 3005, 1806, 1785, 1711, 1670, 1421, 1363, 1223, 1092, 530 cm-1;
$[\alpha]_D^{rt}$ = +224.80 ℃ (c = 0.99, MeOH);
HRMS (ESI): $C_{26}H_{19}NO_5$+H, Calc: 426.1339, Found: 426.1336;
HPLC: DAICEL CHIRALCEL OJ, Hexane/EtOH = 80/20, flow rate = 1.0 mL/min, retention time: t_{major} = 10.4, t_{minor} = 15.9, 92% ee.

X-ray Structure of **4k:**





Datablock: 2

Bond precision: C-C = 0.0041 A Wavelength=0.71073

Cell: a=6.6033(11) b=13.917(2) c=27.990(5)
alpha=90 beta=90 gamma=90

Temperature: 296 K

	Calculated	Reported
Volume	2572.2(7)	2572.2(8)
Space group	P 21 21 21	P2(1)2(1)2(
Hall group	P 2ac 2ab	?
Moiety formula	C26 H18 Cl N O4, C3 H6 O	?
Sum formula	C29 H24 Cl N O5	C29 H24 Cl N O5
Mr	501.94	501.94
Dx,g cm-3	1.296	1.296
Z	4	4
Mu (mm-1)	0.188	0.188

F000	1048.0	1048.0
F000'	1049.08	
h,k,lmax	8,18,36	8,18,36
Nref	6024[3444]	5979
Tmin,Tmax	0.956,0.963	0.946,0.963
Tmin'	0.945	

Correction method= # Reported T Limits: Tmin=0.946 Tmax=0.963 AbsCorr = MULTI-SCAN

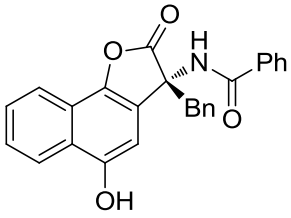
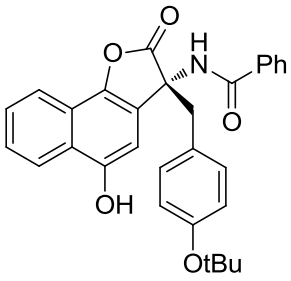
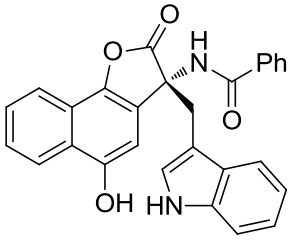
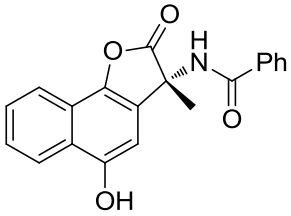
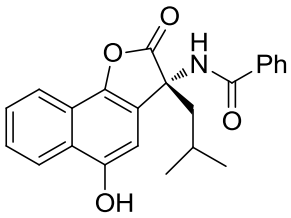
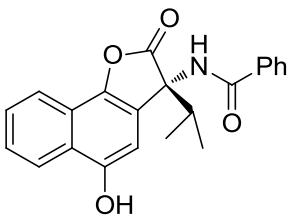
Data completeness= 1.74/0.99 Theta(max)= 27.660

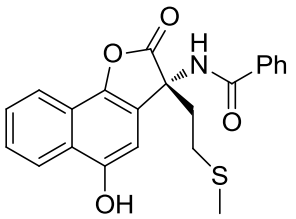
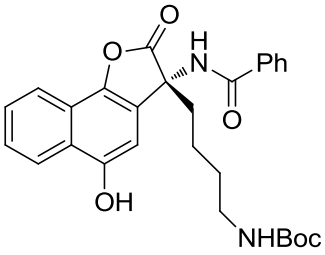
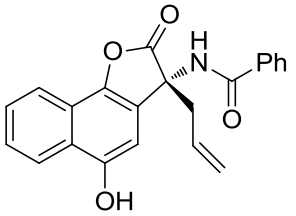
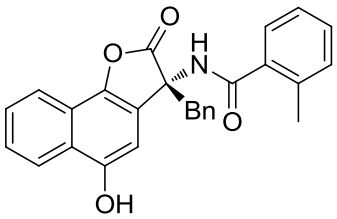
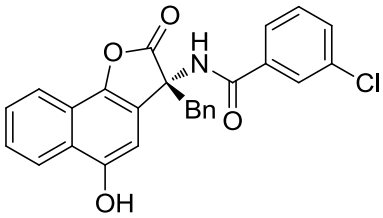
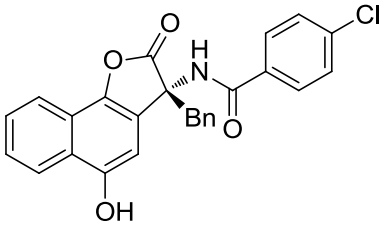
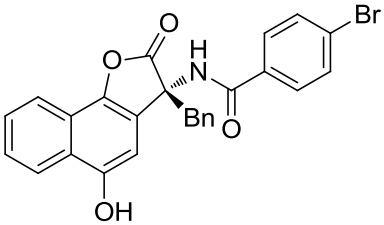
R(reflections)= 0.0485(3769) wR2(reflections)= 0.1251(5979)

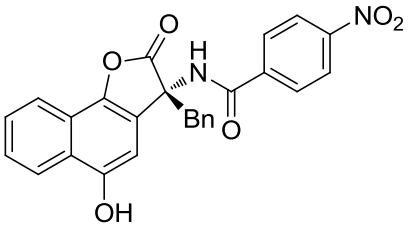
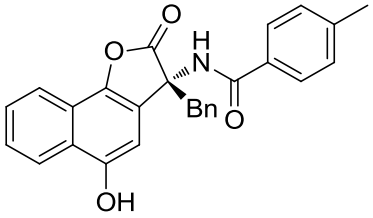
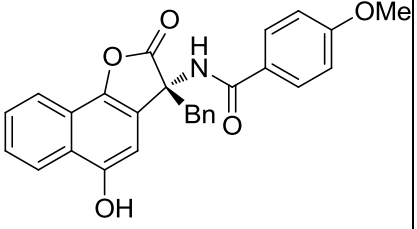
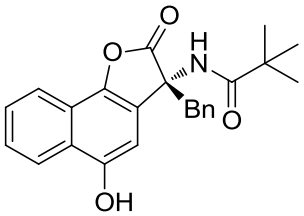
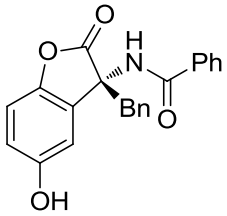
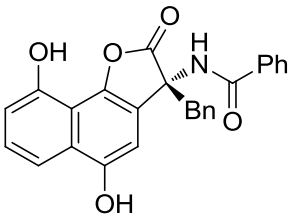
S = 1.018 Npar= 329

HPLC Analytic Conditions:

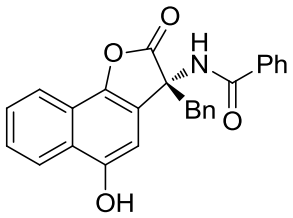
All products are separated by using DAICEL CHIRALCEL column.

entry	product	Chiralcel column	Mobile phase	flow rate ml/min	Retention time	ee (%)
1		OJ	H:E = 85:15	1.0	t_{major} =10.8 t_{minor} = 15.8	99
2		IA	H:E = 85:15	1.0	t_{major} = 8.0 t_{minor} = 5.2	99
3		IC	H:E = 80:20	1.0	t_{major} = 5.4	>99
4		AD	H:E = 85:15	1.0	t_{major} = 10.9	>99
5		AD	H:E = 85:15	1.0	t_{major} = 6.9 t_{minor} = 5.3	98
6		IC	H:E = 85:15	1.0	t_{major} = 7.2	>99

7		IC	H:E = 85:15	1.0	t_{major} = 5.8 t_{minor} = 6.7	87
8		IC	H:E = 85:15	1.0	t_{major} = 6.8 t_{minor} = 7.9	92
9		IA	H:E = 85:15	1.0	t_{major} = 5.3 t_{minor} = 4.6	99
10		IA	H:E = 85:15	1.0	t_{major} = 14.4 t_{minor} = 12.6,	98
11		OJ	H:E = 85:15	1.0	t_{major} = 14.6 t_{minor} = 21.8	99
12		OJ	H:E = 85:15	1.0	t_{major} = 14.7 t_{minor} = 25.2	>99
13		IA	H:E = 80:20	1.0	t_{major} = 11.3 t_{minor} = 13.9	97

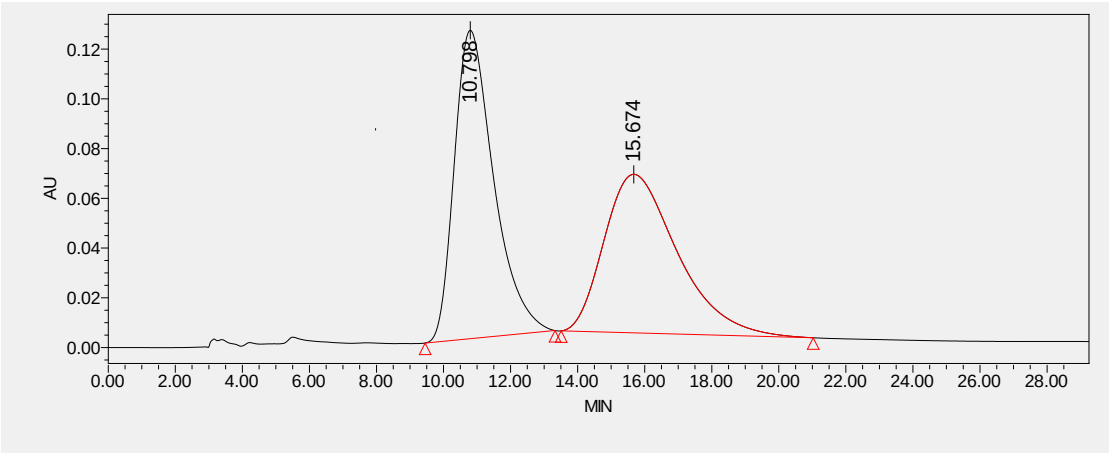
14		AD	H:E = 80:20	1.0	t_{major} = 11.6 t_{minor} = 13.8	98
15		IA	H:E = 85:15	1.0	t_{major} = 7.4 t_{minor} = 5.6	99
16		AD	H:E = 80:20	1.0	t_{major} = 14.8 t_{minor} = 11.8	99
17		IA	H:E = 85:15	1.0	t_{major} = 5.2 t_{minor} = 6.1	>99
18		OJ	H:E = 80:20	1.0	t_{major} = 12.1	>99
19		OJ	H:E = 80:20	1.0	t_{major} = 10.4 t_{minor} = 15.9	92

4a (Table 2, entry 1)

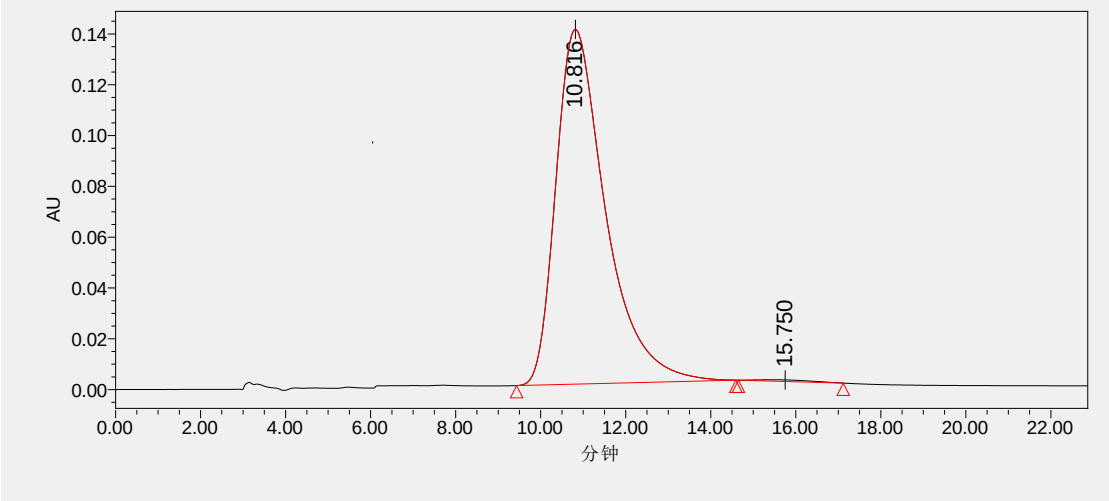


4a

Chiralpak OJ column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

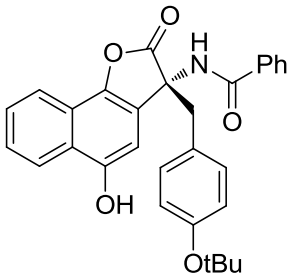


	Retention time	Area	% Area	Height	Integral type
1	10.798	10134628	51.16	123998	bb
2	15.674	9675220	48.84	63741	bb



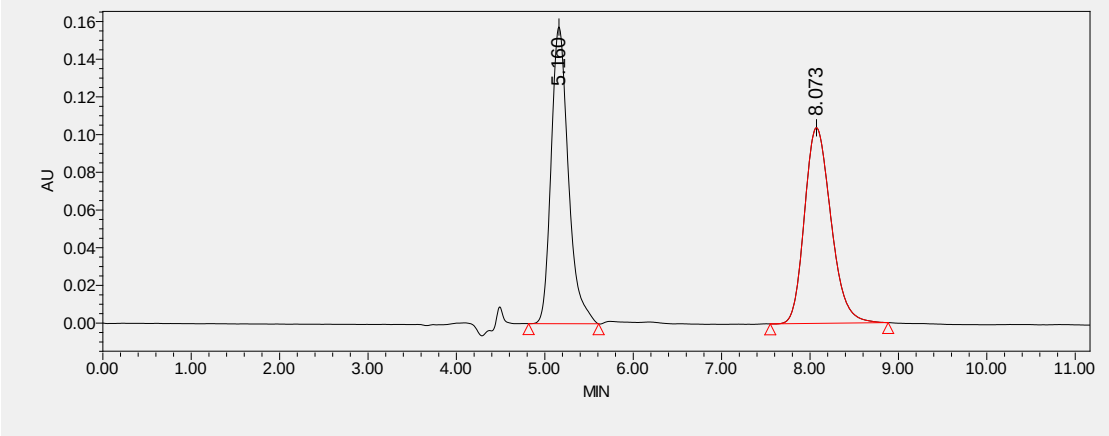
	Retention time	Area	% Area	Height	Integral type
1	10.816	11342744	99.54	139615	bb
2	15.750	52736	0.46	615	bb

4b (Table 2, entry 2)

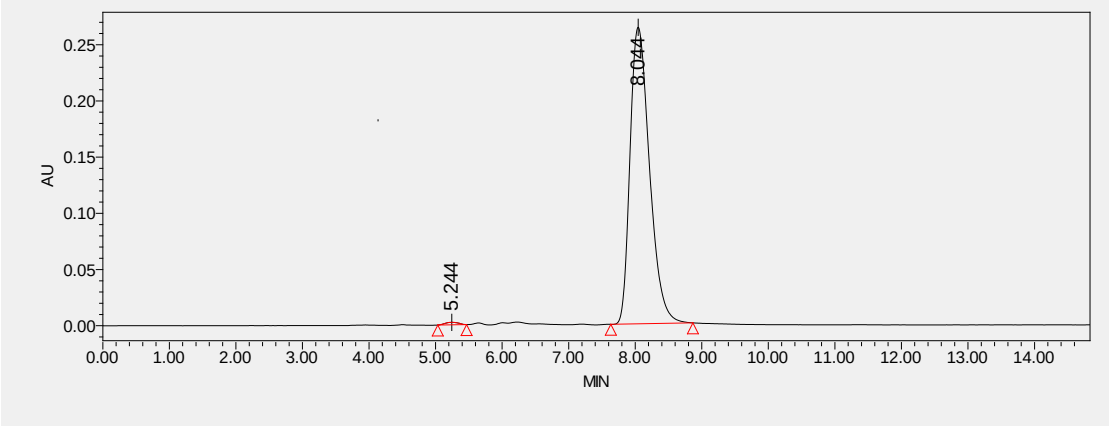


4b

Chiralpak IA column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

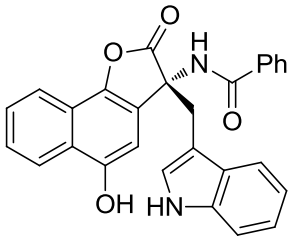


	Retention time	Area	% Area	Height	Integral type
1	5.160	2134566	49.71	157479	bb
2	8.073	2159706	50.29	103816	bb



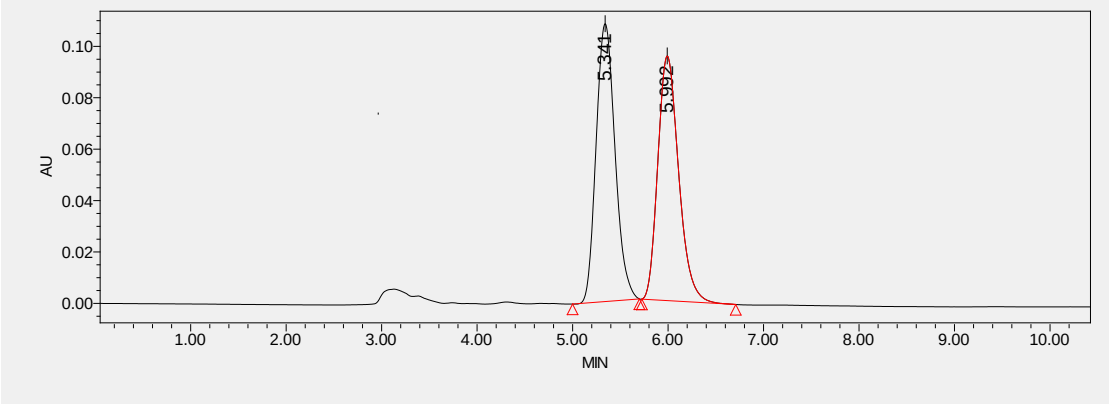
	Retention time	Area	% Area	Height	Integral type
1	5.244	30889	0.57	2207	bb
2	8.044	5363231	99.43	263943	bb

4c (Table 2, entry 3)

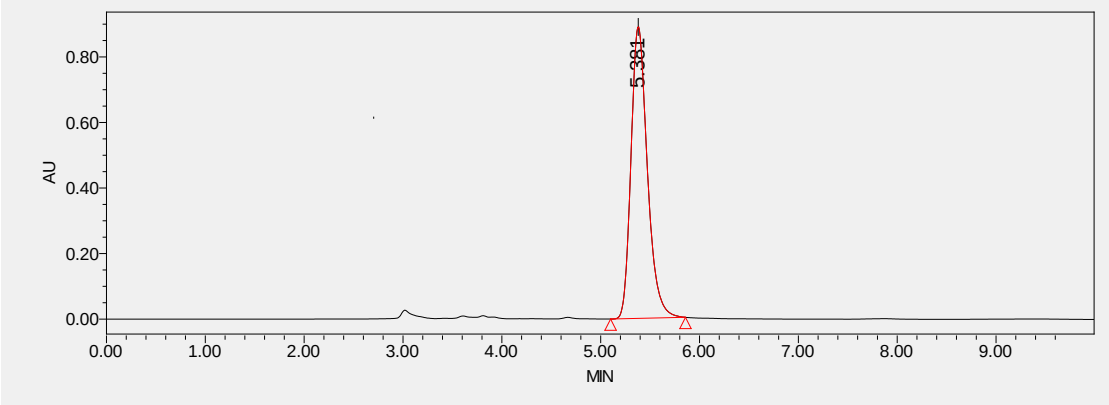


4c

Chiralpak IC column, hexane/ EtOH (80:20), flow rate 1.0 mL/min

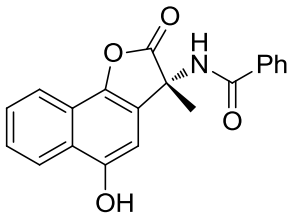


	Retention time	Area	% Area	Height	Integral type
1	5.341	1488380	50.80	108112	bb
2	5.992	1441327	49.20	95158	bb



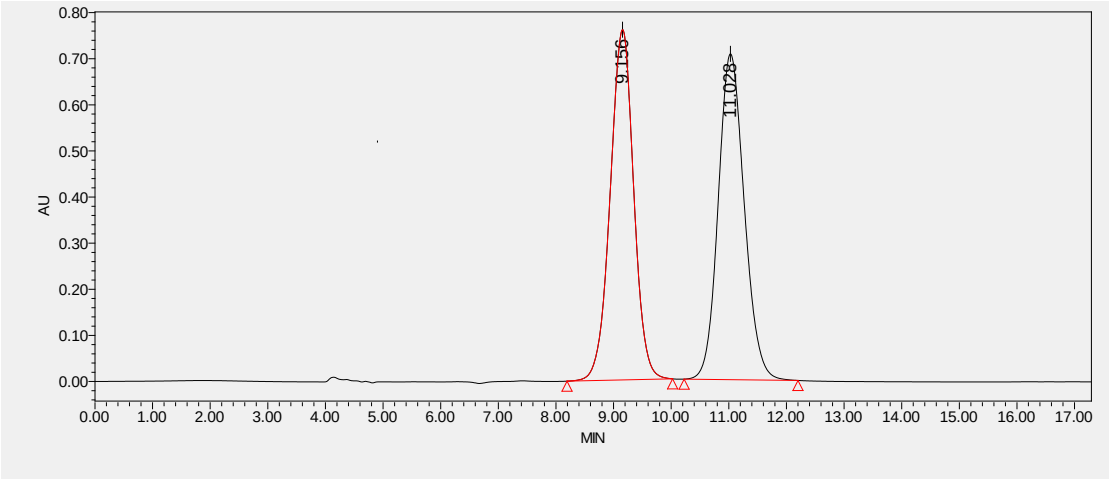
	Retention time	Area	% Area	Height	Integral type
1	5.381	10240499	100.00	890319	bb

4d (Table 2, entry 4)

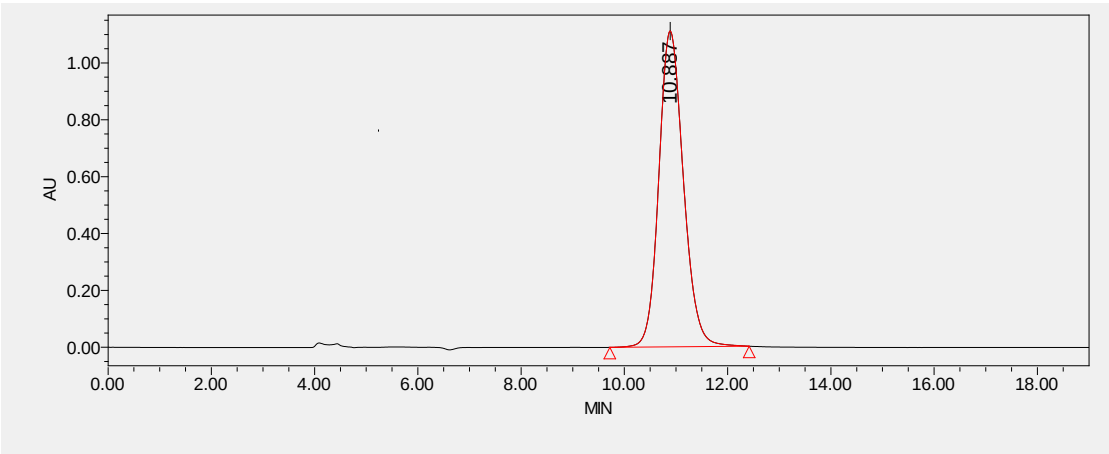


4d

Chiralpak AD column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

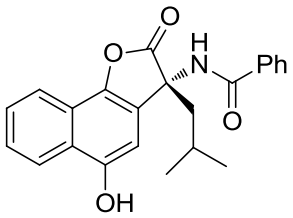


	Retention time	Area	% Area	Height	Integral type
1	9.156	21531309	49.27	759774	bb
2	11.028	22173201	50.73	706649	bb



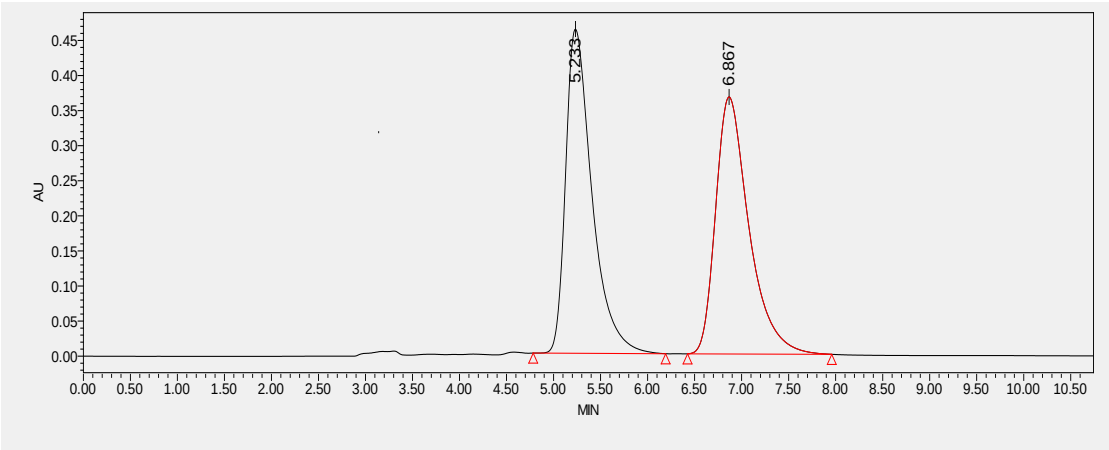
	Retention time	Area	% Area	Height	Integral type
1	10.887	36687239	100.00	1110889	bb

4e (Table 2, entry 5)

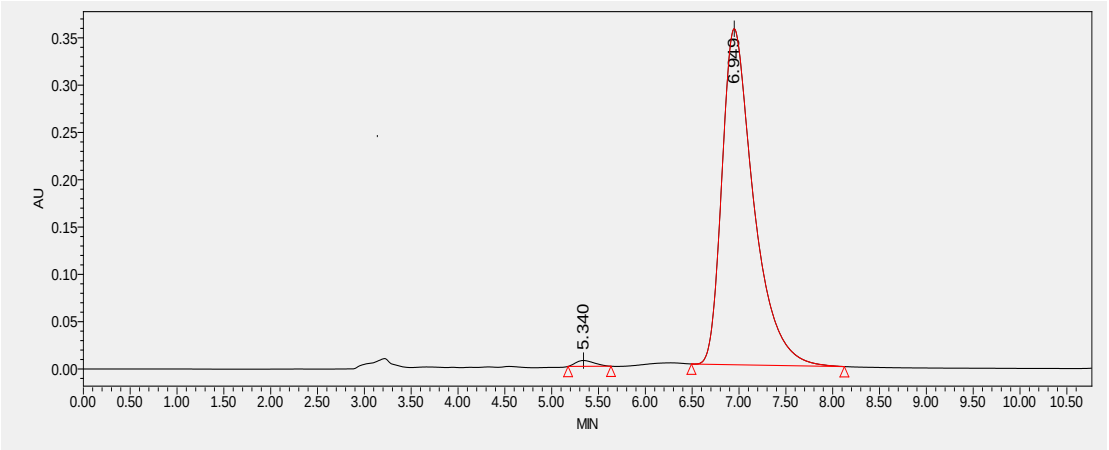


4e

Chiralpak AD column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

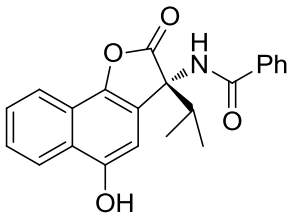


	Retention time	Area	% Area	Height	Integral type
1	5.233	8994103	49.93	462070	bb
2	6.867	9017571	50.07	366382	bb



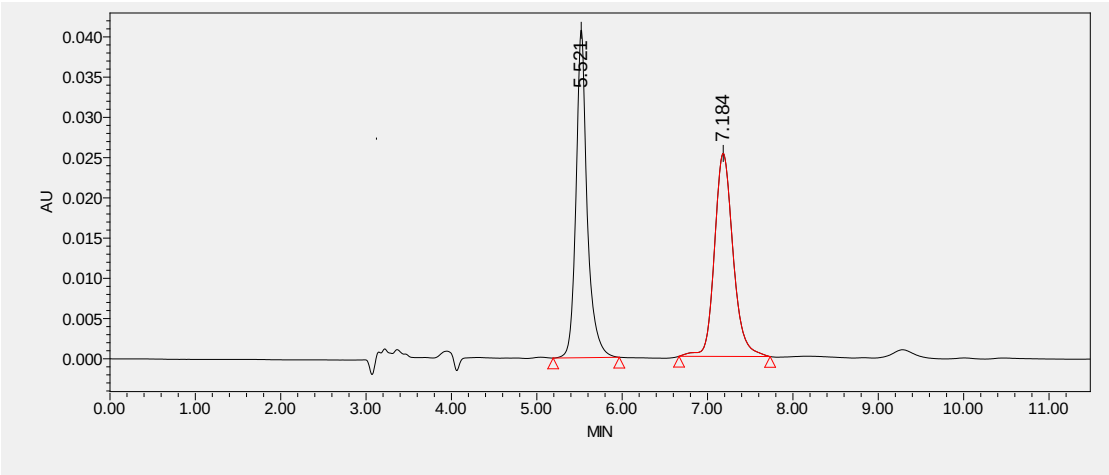
	Retention time	Area	% Area	Height	Integral type
1	5.340	85030	1.00	6159	bb
2	6.949	8384291	99.00	355265	bb

4f (Table 2, entry 6)

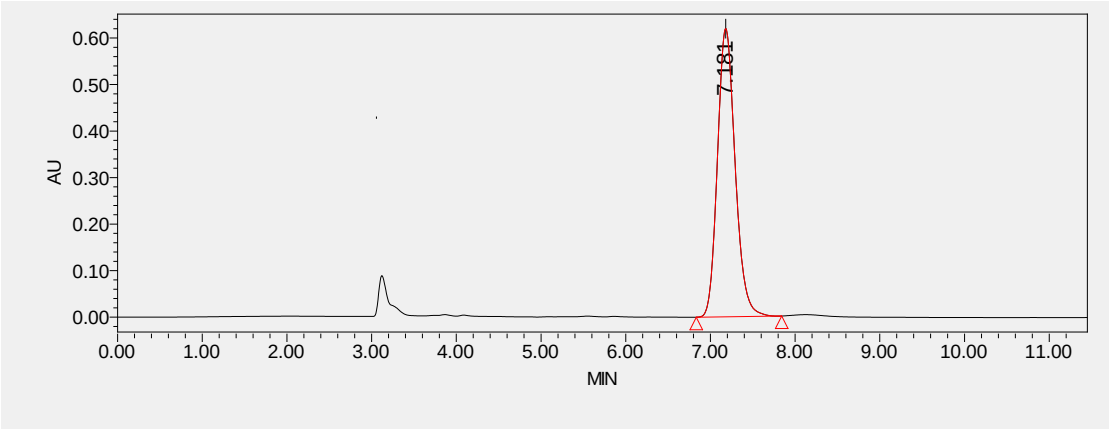


4f

Chiralpak IC column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

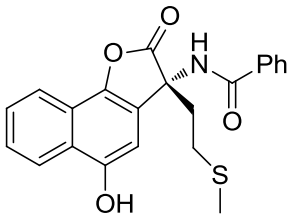


	Retention time	Area	% Area	Height	Integral type
1	5.521	369259	49.10	40807	bb
2	7.184	382838	50.90	25233	bb



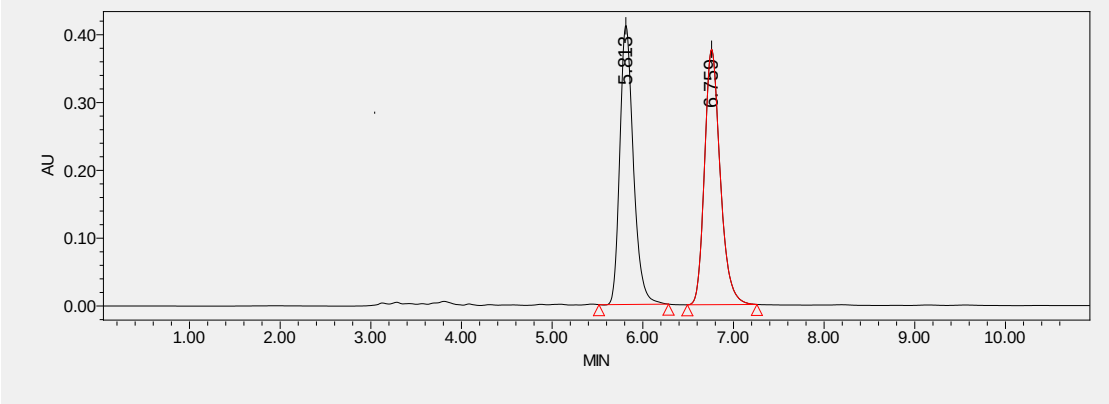
	Retention time	Area	% Area	Height	Integral type
1	7.181	9002397	100.00	619691	bb

4g (Table 2, entry 7)

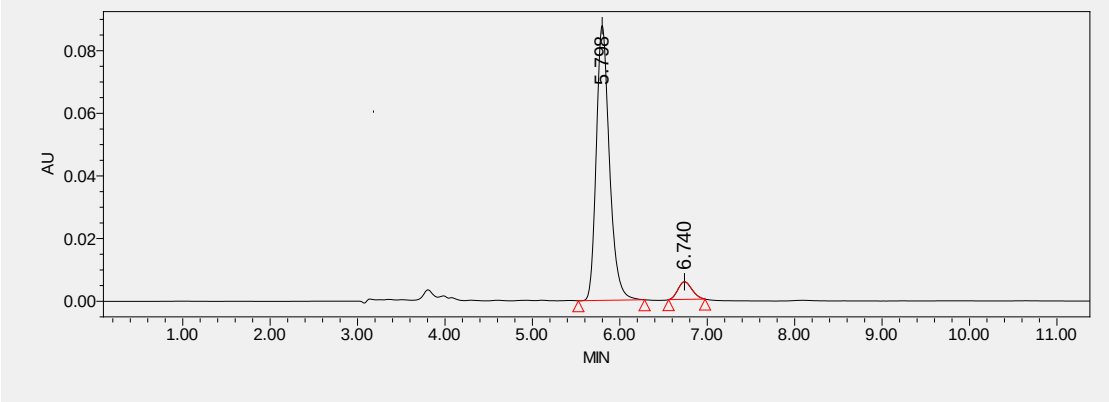


4g

Chiralpak IC column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

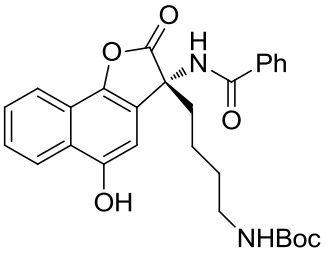


	Retention time	Area	% Area	Height	Integral type
1	5.813	4275165	48.62	411504	bb
2	6.759	4518564	51.38	376754	bb



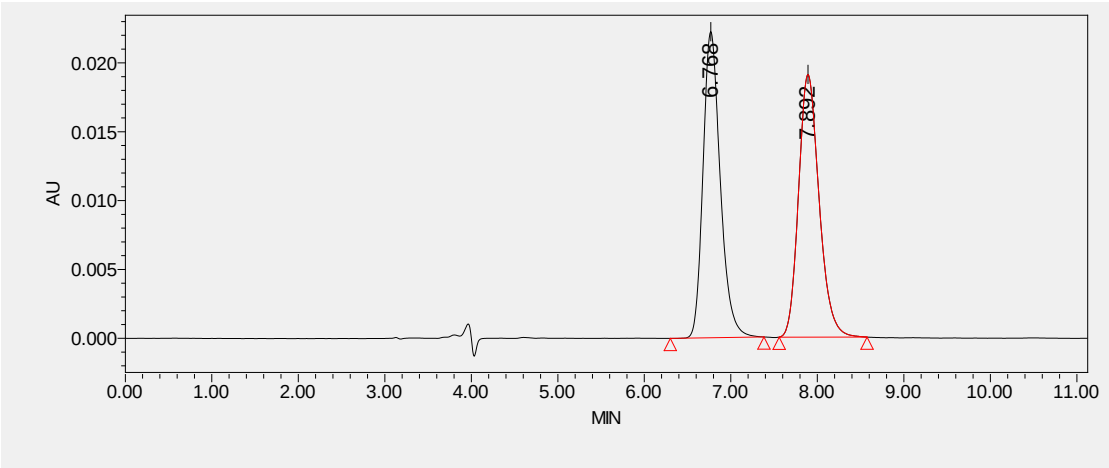
	Retention time	Area	% Area	Height	Integral type
1	5.798	916723	93.57	87809	bb
2	6.740	62980	6.43	5650	bb

4h (Table 2, entry 8)

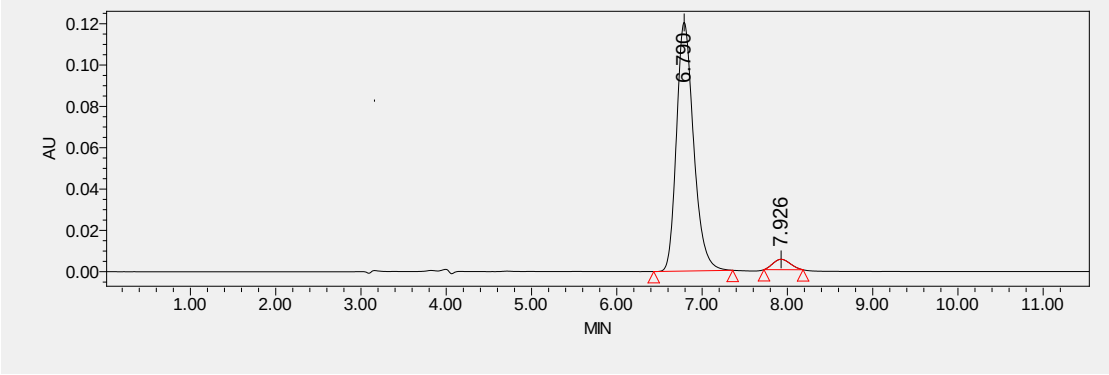


4h

Chiralpak IC column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

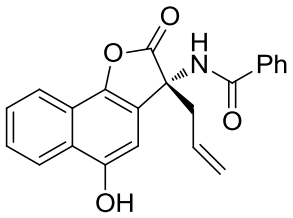


	Retention time	Area	% Area	Height	Integral type
1	6.768	307868	49.45	22239	bb
2	7.892	314657	50.55	19069	bb



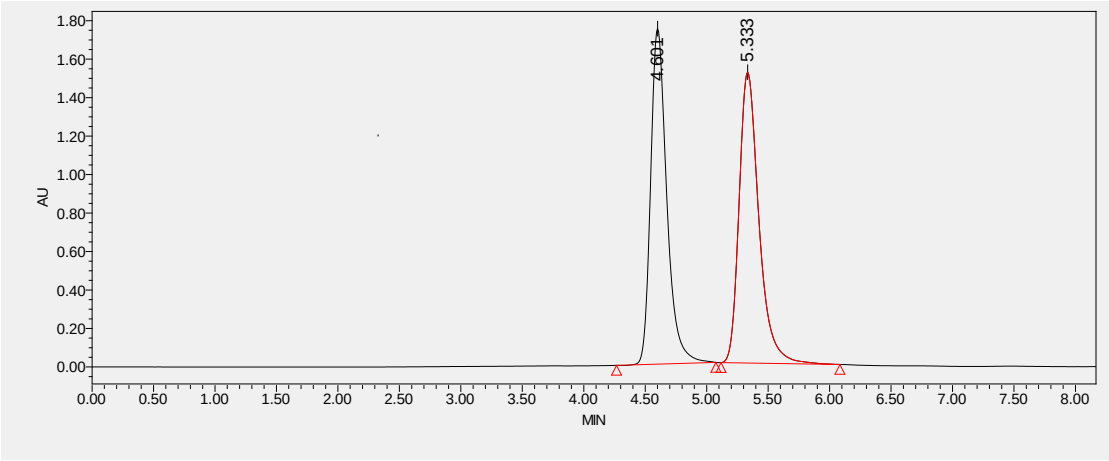
	Retention time	Area	% Area	Height	Integral type
1	6.790	1678049	95.94	120390	bb
2	7.926	71077	4.06	5033	bb

4i (Table 2, entry 9)

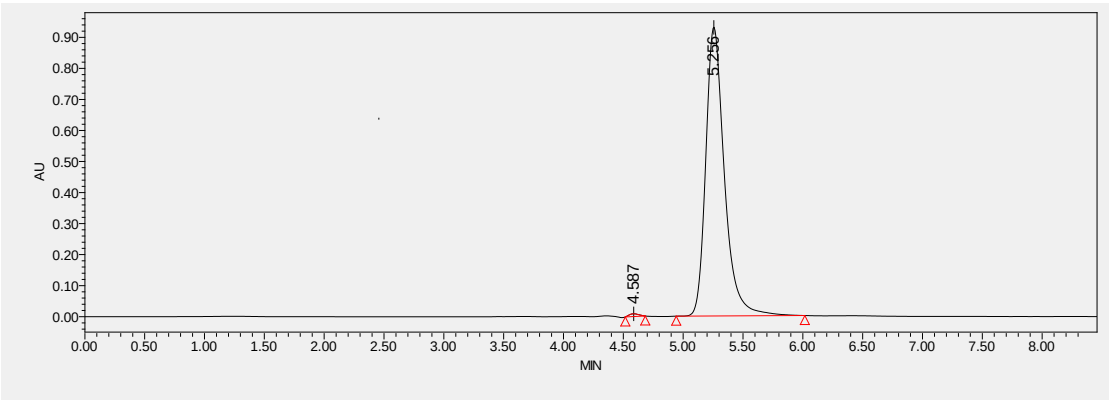


4i

Chiralpak IA column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

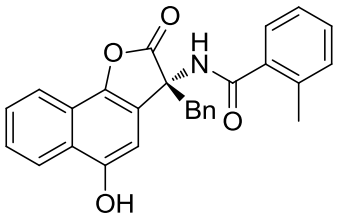


	Retention time	Area	% Area	Height	Integral type
1	4.601	15931395	48.48	1745539	bb
2	5.333	16927284	51.52	1512327	bb



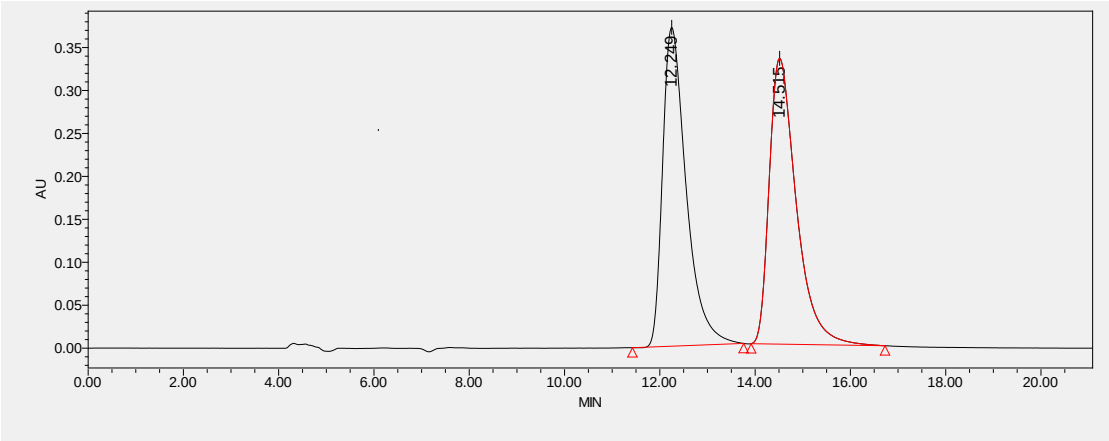
	Retention time	Area	% Area	Height	Integral type
1	4.587	50037	0.49	8882	bb
2	5.256	10072440	99.51	930691	bb

4j (Table 2, entry 10)

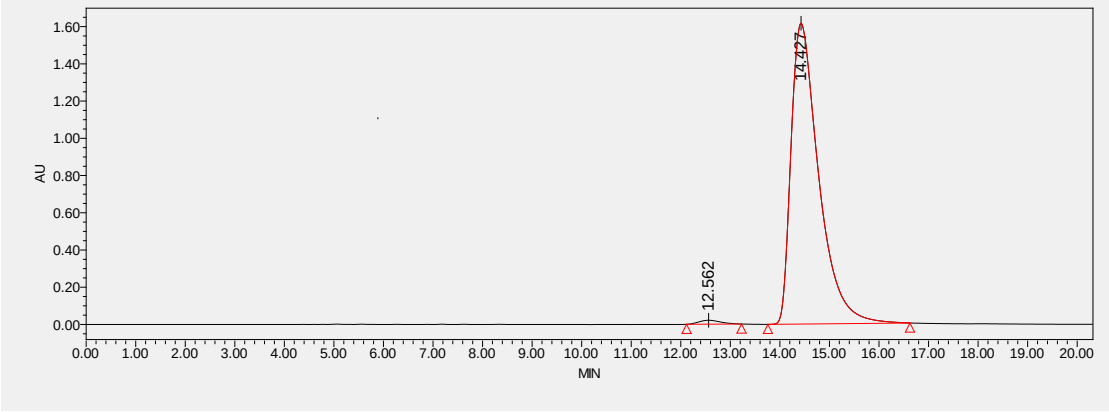


4j

Chiralpak IA column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

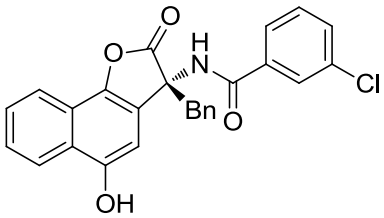


	Retention time	Area	% Area	Height	Integral type
1	12.249	12767780	49.35	371180	bb
2	14.515	13103404	50.65	332719	bb



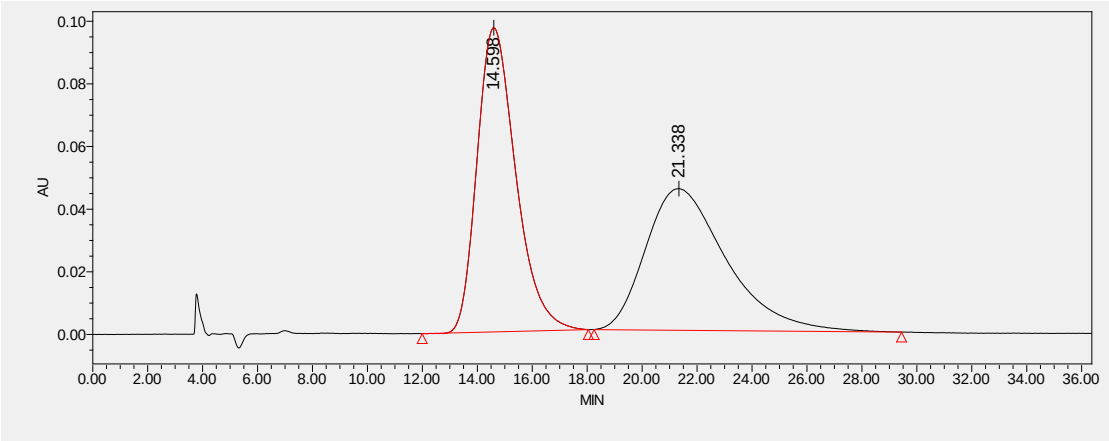
	Retention time	Area	% Area	Height	Integral type
1	12.562	638033	1.01	20975	bb
2	14.427	62646149	98.99	1615714	bb

4k (Table 2, entry 11)

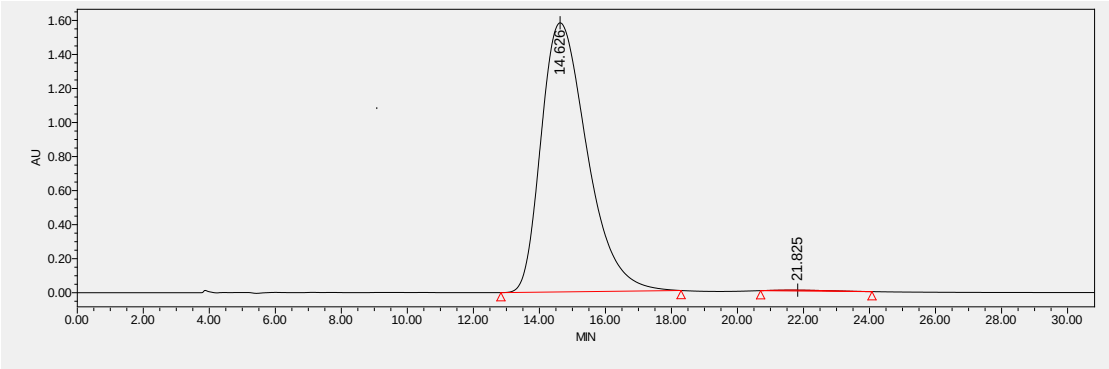


4k

Chiralpak OJ column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

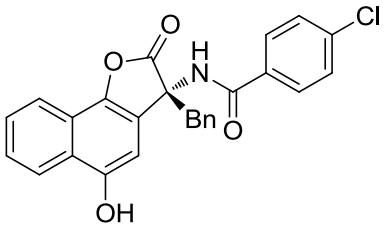


	Retention time	Area	% Area	Height	Integral type
1	14.598	9511334	50.78	97118	bb
2	21.338	9219019	49.22	45232	bb



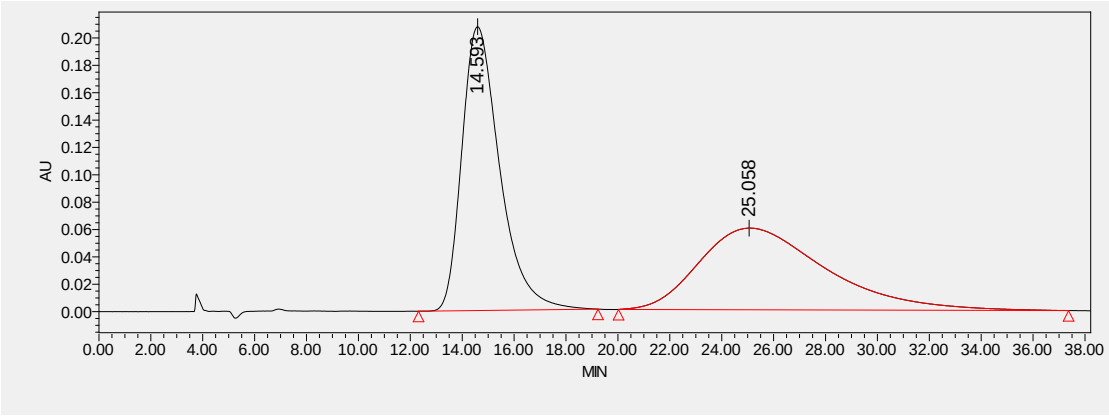
	Retention time	Area	% Area	Height	Integral type
1	14.626	152923148	99.62	1580713	bb
2	21.825	582650	0.38	4978	bb

4l (Table 2, entry 12)

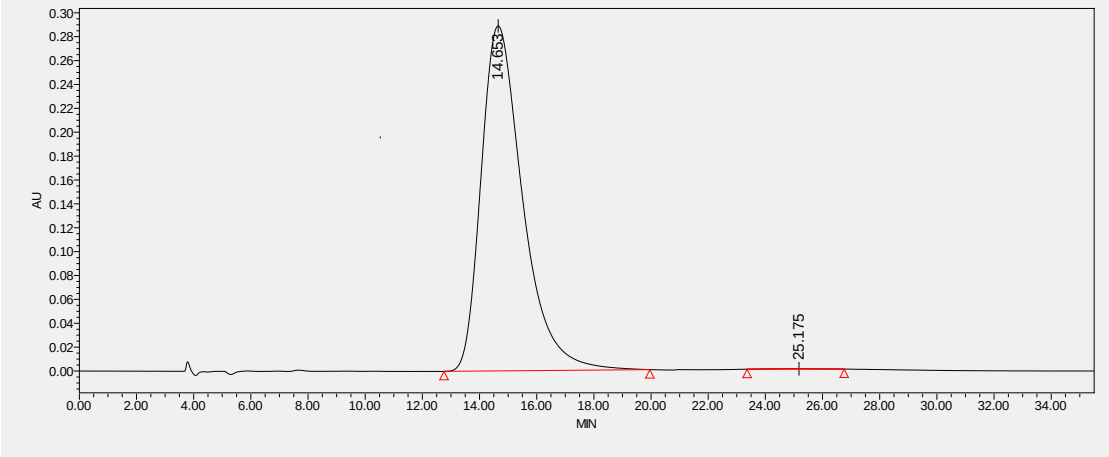


4l

Chiralpak OJ column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

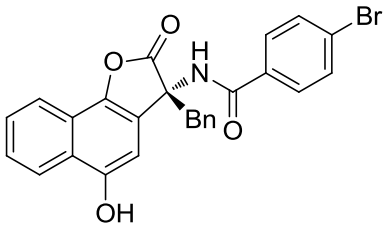


	Retention time	Area	% Area	Height	Integral type
1	14.593	21048204	51.01	207435	bb
2	25.058	20216061	48.99	59705	bb



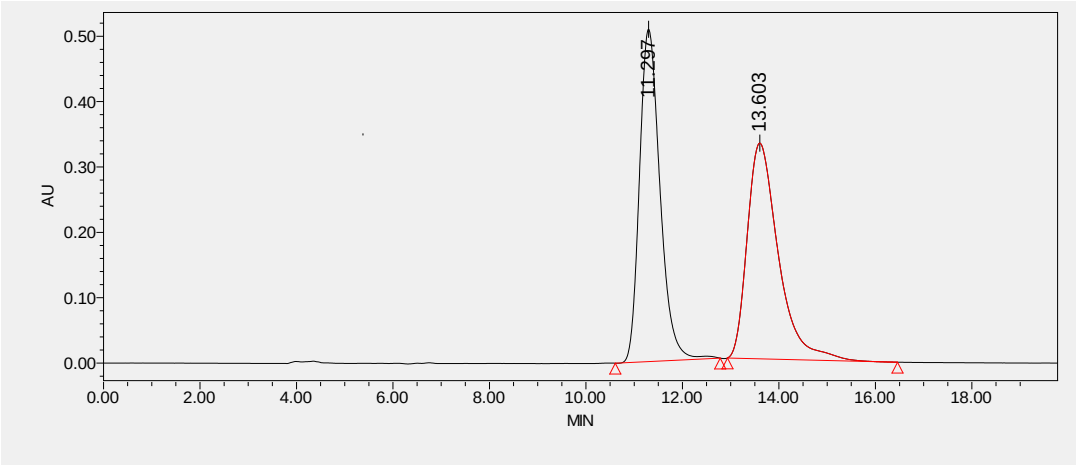
	Retention time	Area	% Area	Height	Integral type
1	14.653	29190528	99.84	288915	bb
2	25.175	45583	0.16	373	bb

4m (Table 2, entry 13)

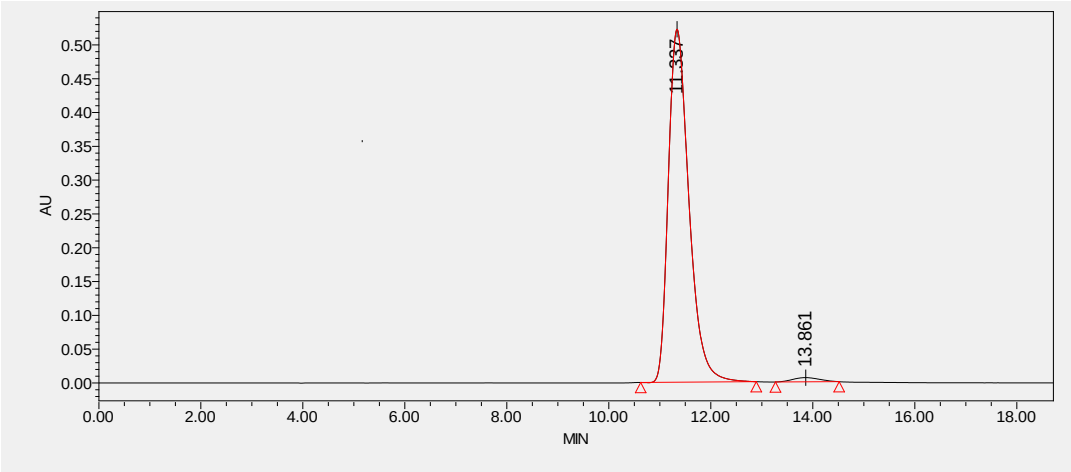


4m

Chiralpak IA column, hexane/ EtOH (80:20), flow rate 1.0 mL/min

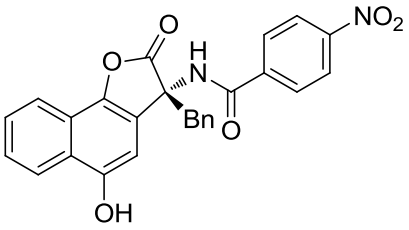


	Retention time	Area	% Area	Height	Integral type
1	11.297	15030347	50.39	508394	bb
2	13.603	14796485	49.61	329909	bb



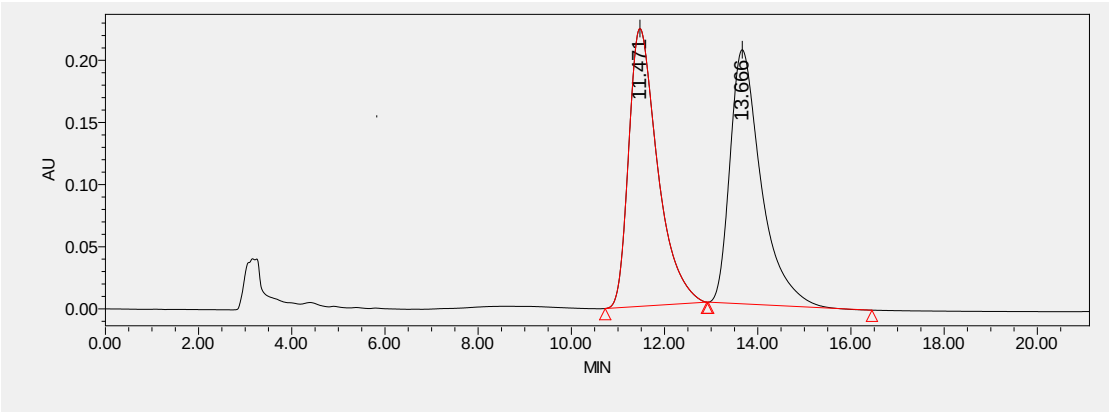
	Retention time	Area	% Area	Height	Integral type
1	11.337	14664909	98.46	522109	bb
2	13.861	229940	1.54	6257	bb

4n (Table 2, entry 14)

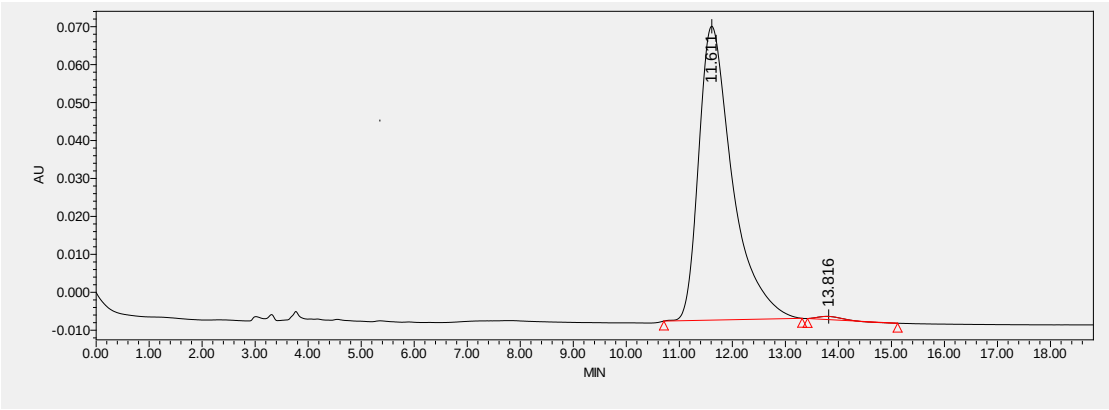


4n

Chiralpak AD column, hexane/ EtOH (80:20), flow rate 1.0 mL/min

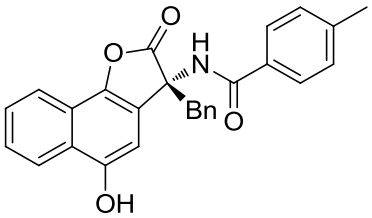


	Retention time	Area	% Area	Height	Integral type
1	11.471	9647610	50.35	223585	bb
2	13.666	9515371	49.65	204508	bb



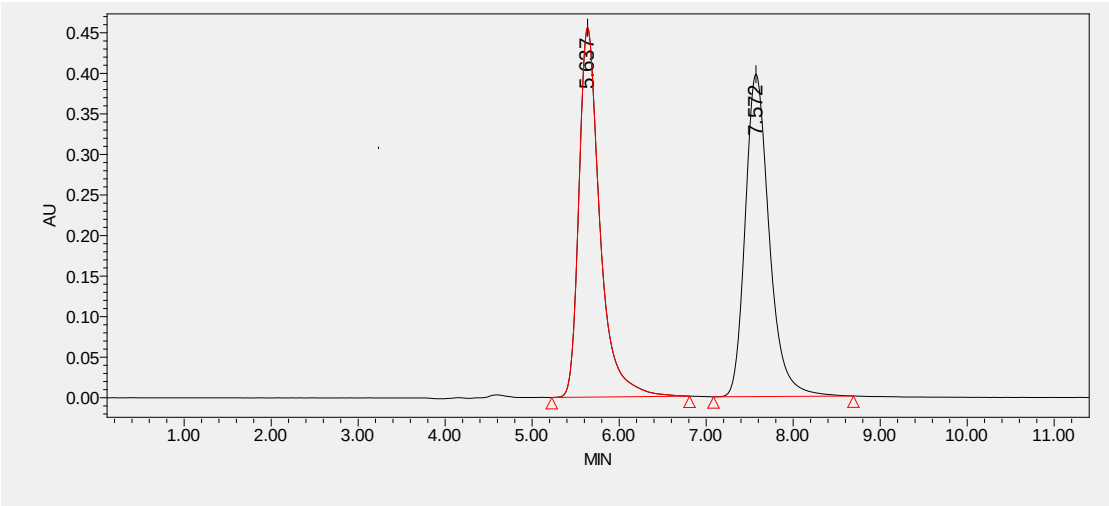
	Retention time	Area	% Area	Height	Integral type
1	11.611	3416393	99.19	77428	bb
2	13.816	27863	0.81	843	bb

4o (Table 2, entry 15)

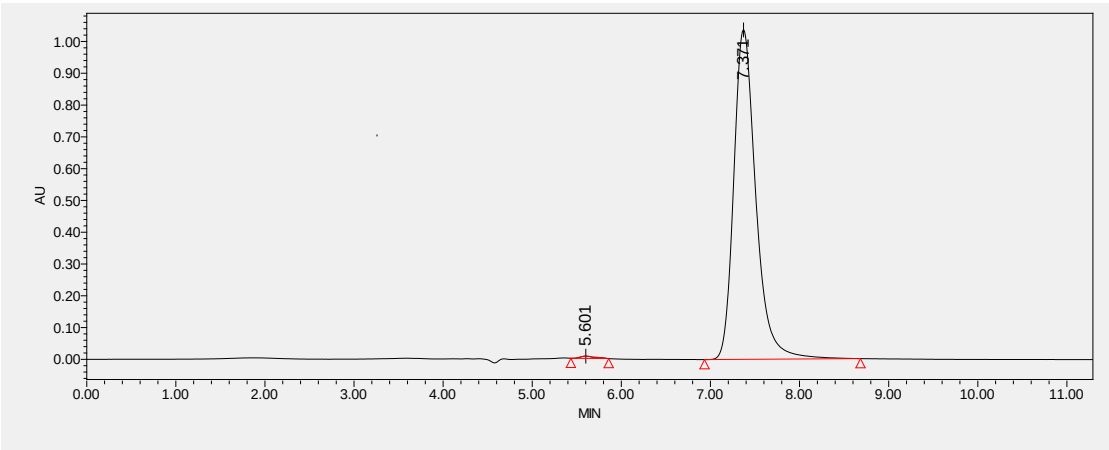


4o

Chiralpak IA column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

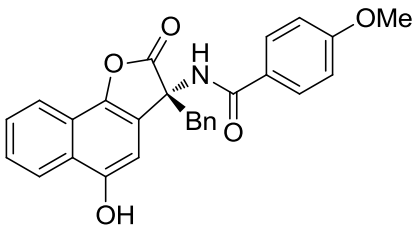


	Retention time	Area	% Area	Height	Integral type
1	5.637	7654843	50.05	455872	bb
2	7.572	7638878	49.95	397551	bb



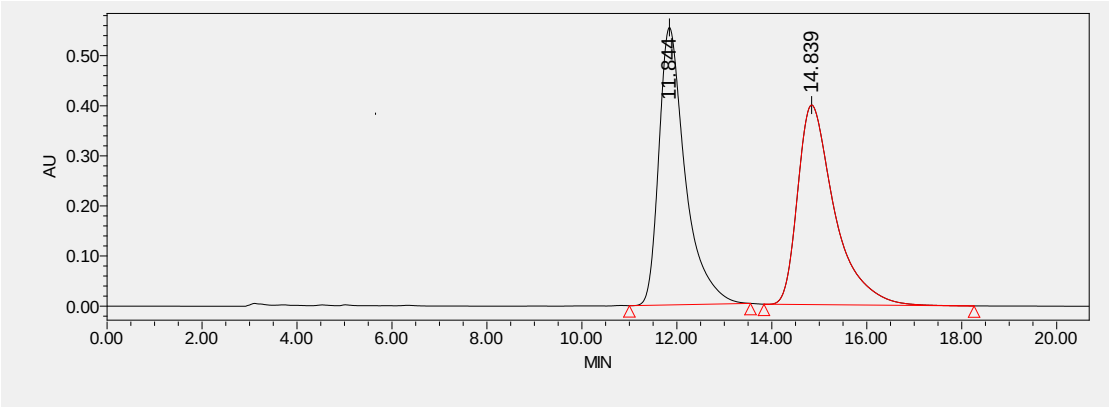
	Retention time	Area	% Area	Height	Integral type
1	5.601	82899	0.46	7220	bb
2	7.371	17858854	99.54	1036895	bb

4p (Table 2, entry 16)

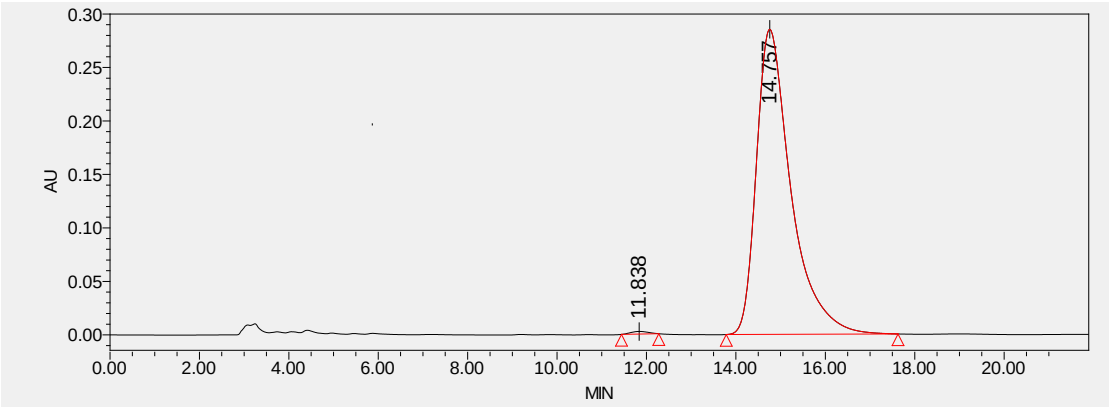


4p

Chiralpak AD column, hexane/ EtOH (80:20), flow rate 1.0 mL/min

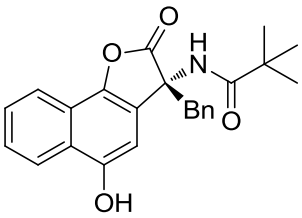


	Retention time	Area	% Area	Height	Integral type
1	11.844	21296317	49.78	554070	bb
2	14.839	21481412	50.22	398460	bb



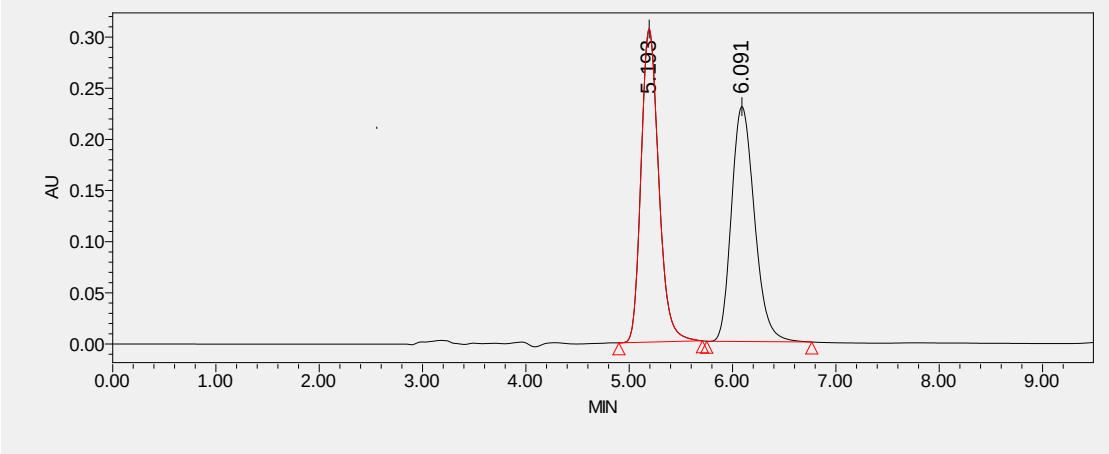
	Retention time	Area	% Area	Height	Integral type
1	11.838	67235	0.44	2480	bb
2	14.757	15321852	99.56	285164	bb

4q (Table 2, entry 17)

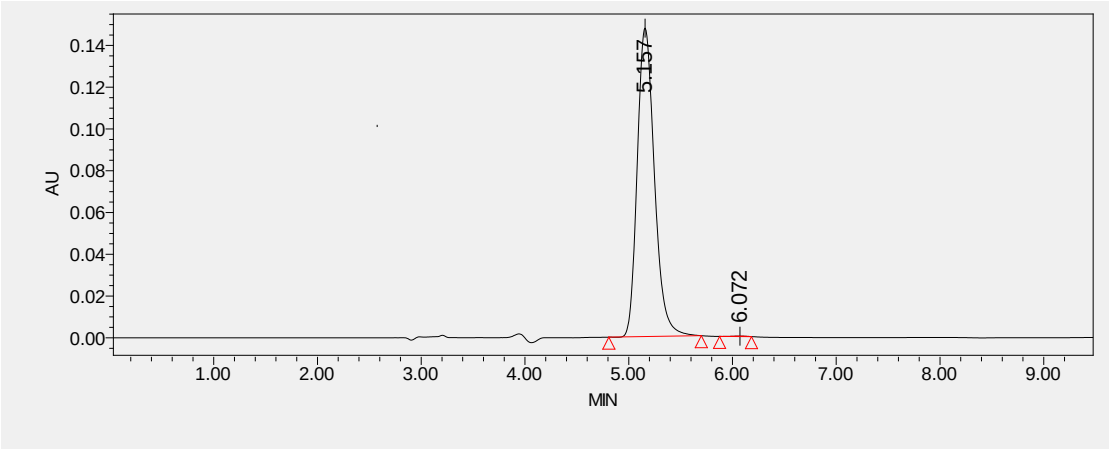


4q

Chiralpak IA column, hexane/ EtOH (85:15), flow rate 1.0 mL/min

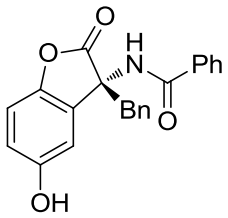


	Retention time	Area	% Area	Height	Integral type
1	5.193	3627902	50.49	306168	bb
2	6.091	3557563	49.51	229679	bb



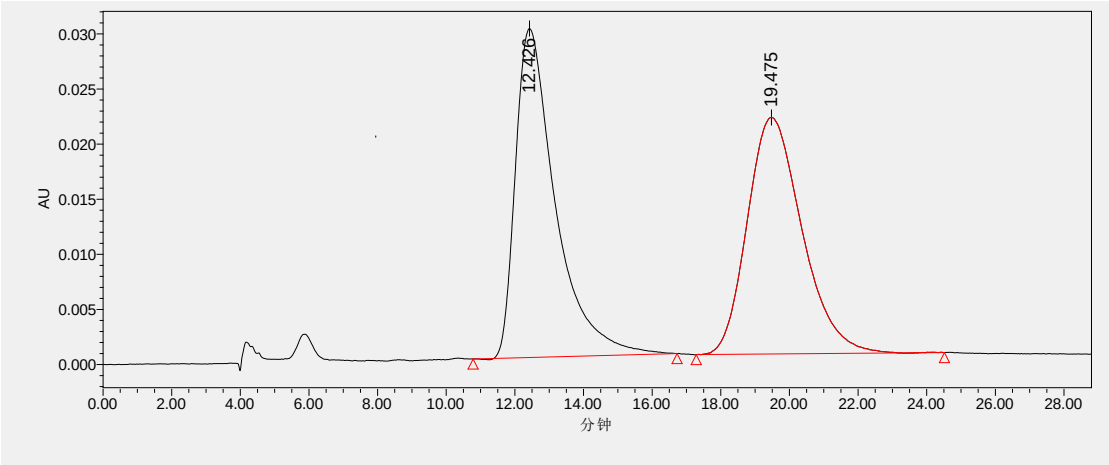
	Retention time	Area	% Area	Height	Integral type
1	5.157	1702612	99.89	147739	bb
2	6.072	1815	0.11	196	bb

4r (Scheme 4)

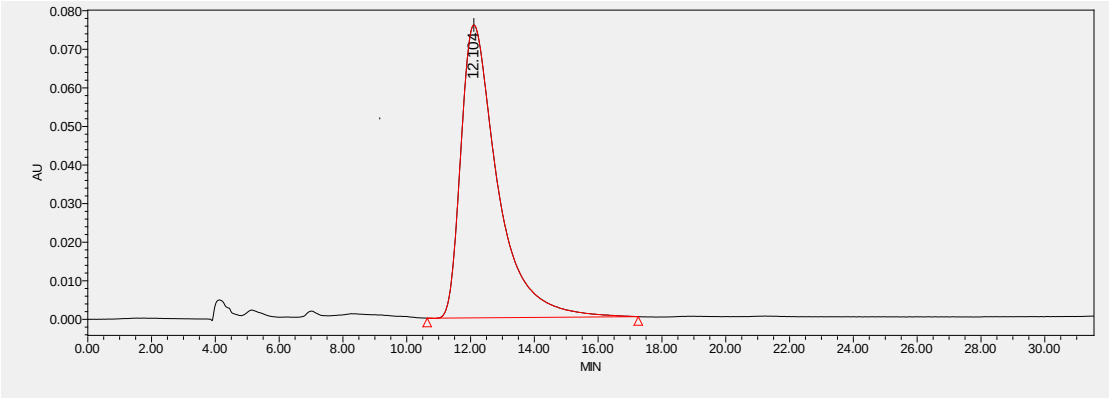


4r

Chiralpak OJ column, hexane/ EtOH (80:20), flow rate 1.0 mL/min

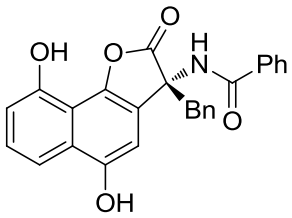


	Retention time	Area	% Area	Height	Integral type
1	12.426	2411581	50.37	29846	bb
2	19.475	2376090	49.63	21456	bb



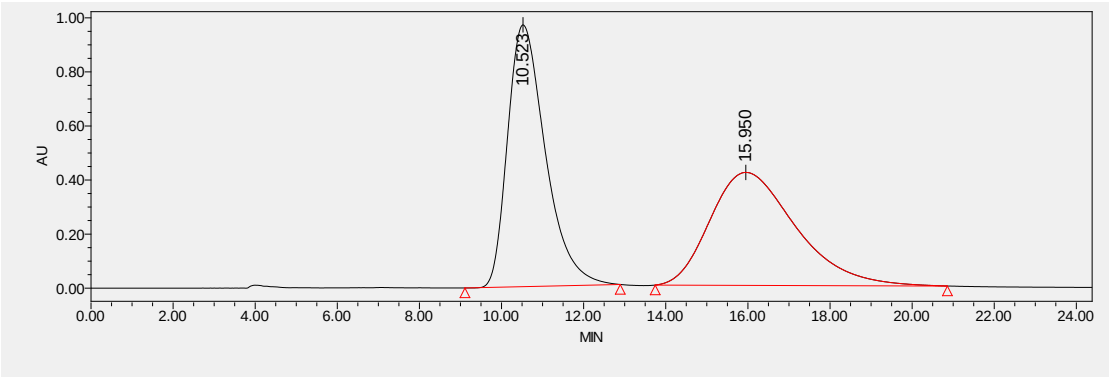
	Retention time	Area	% Area	Height	Integral type
1	12.104	6079604	100.00	75927	bb

4s (Scheme 4)

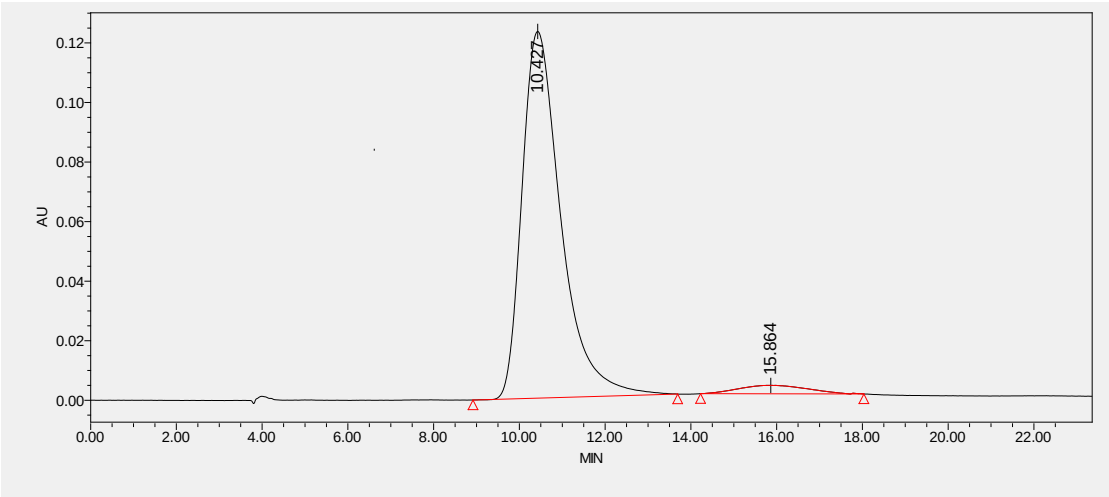


4s

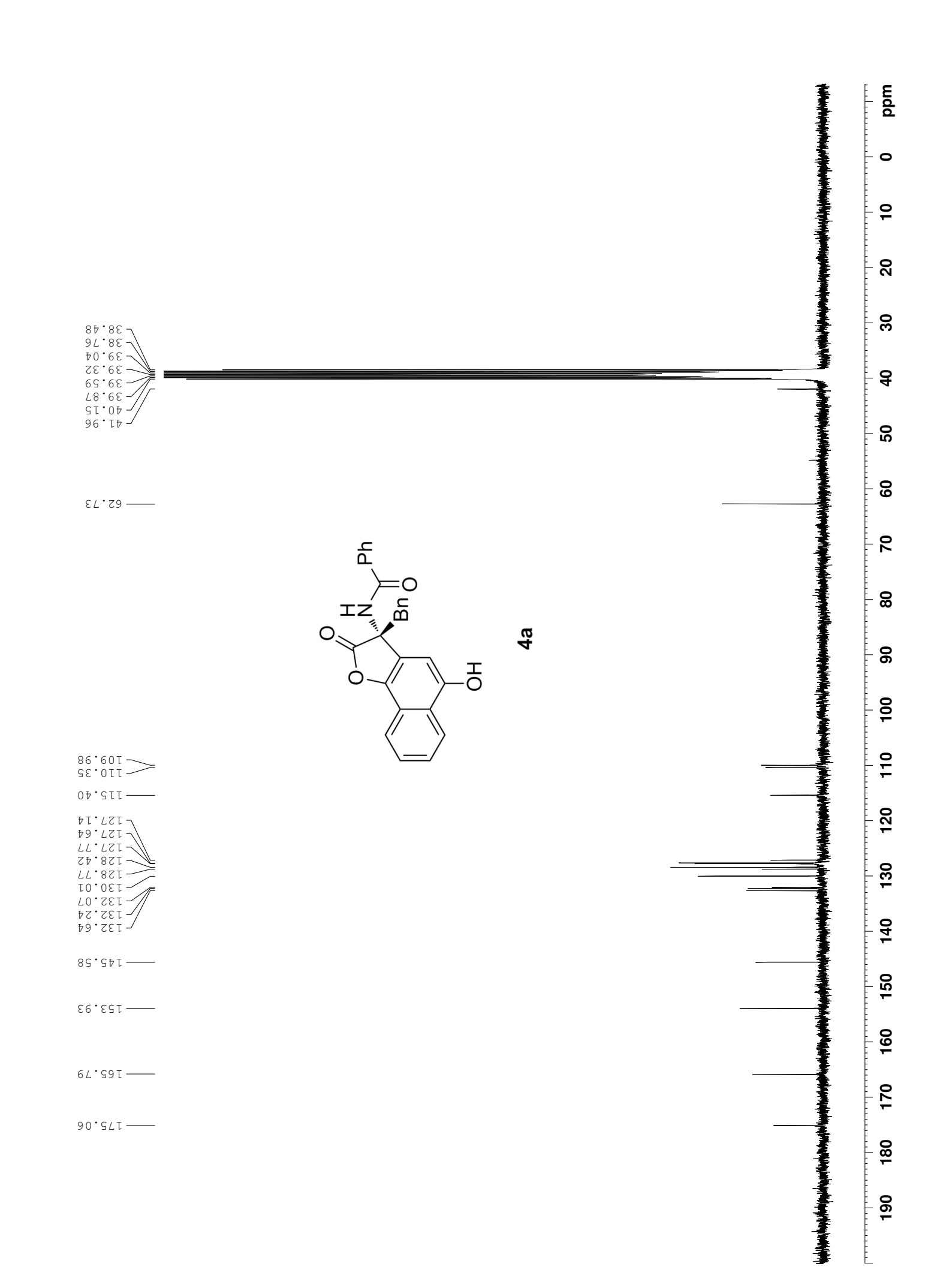
Chiralpak OJ column, hexane/ EtOH (80:20), flow rate 1.0 mL/min

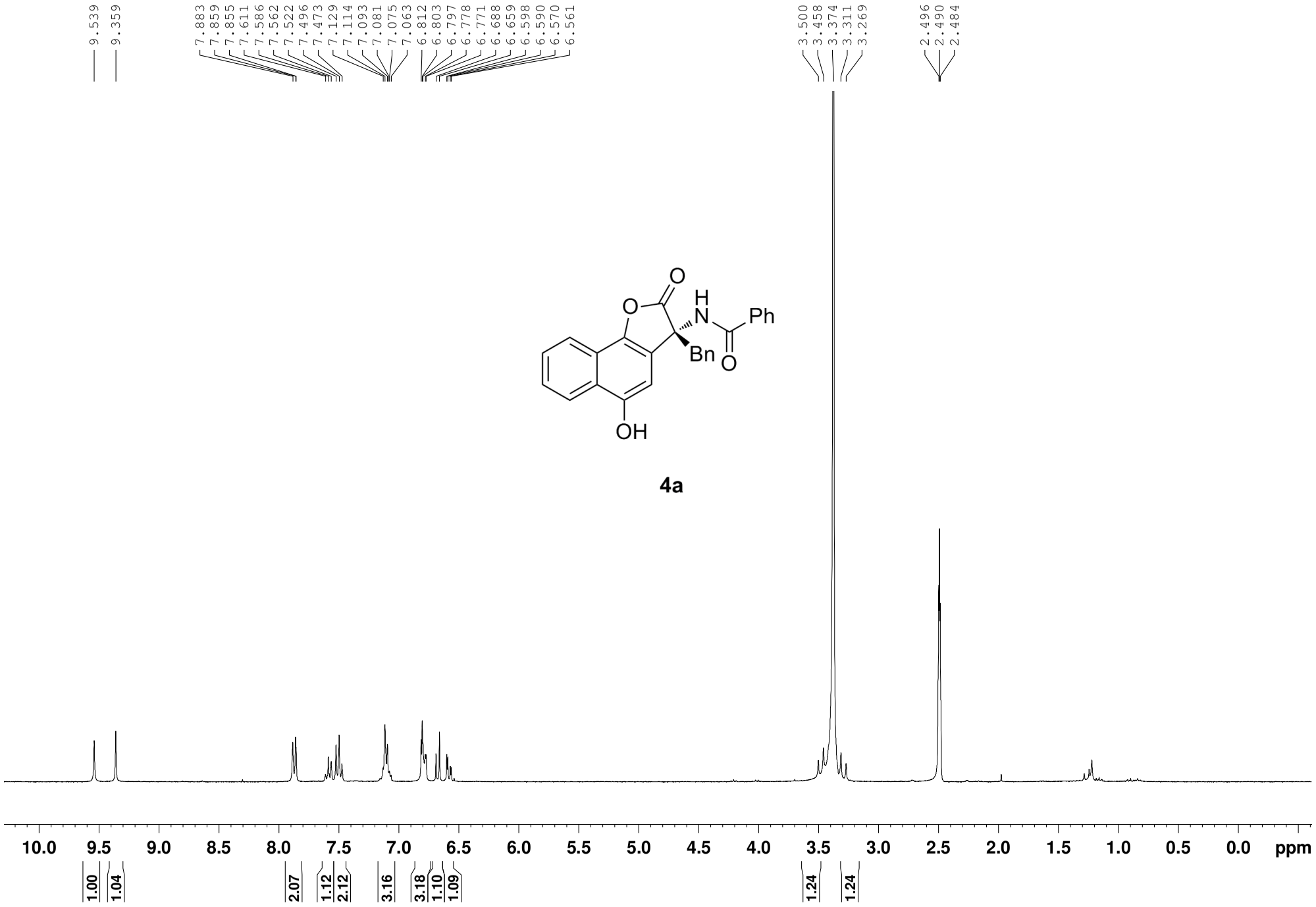


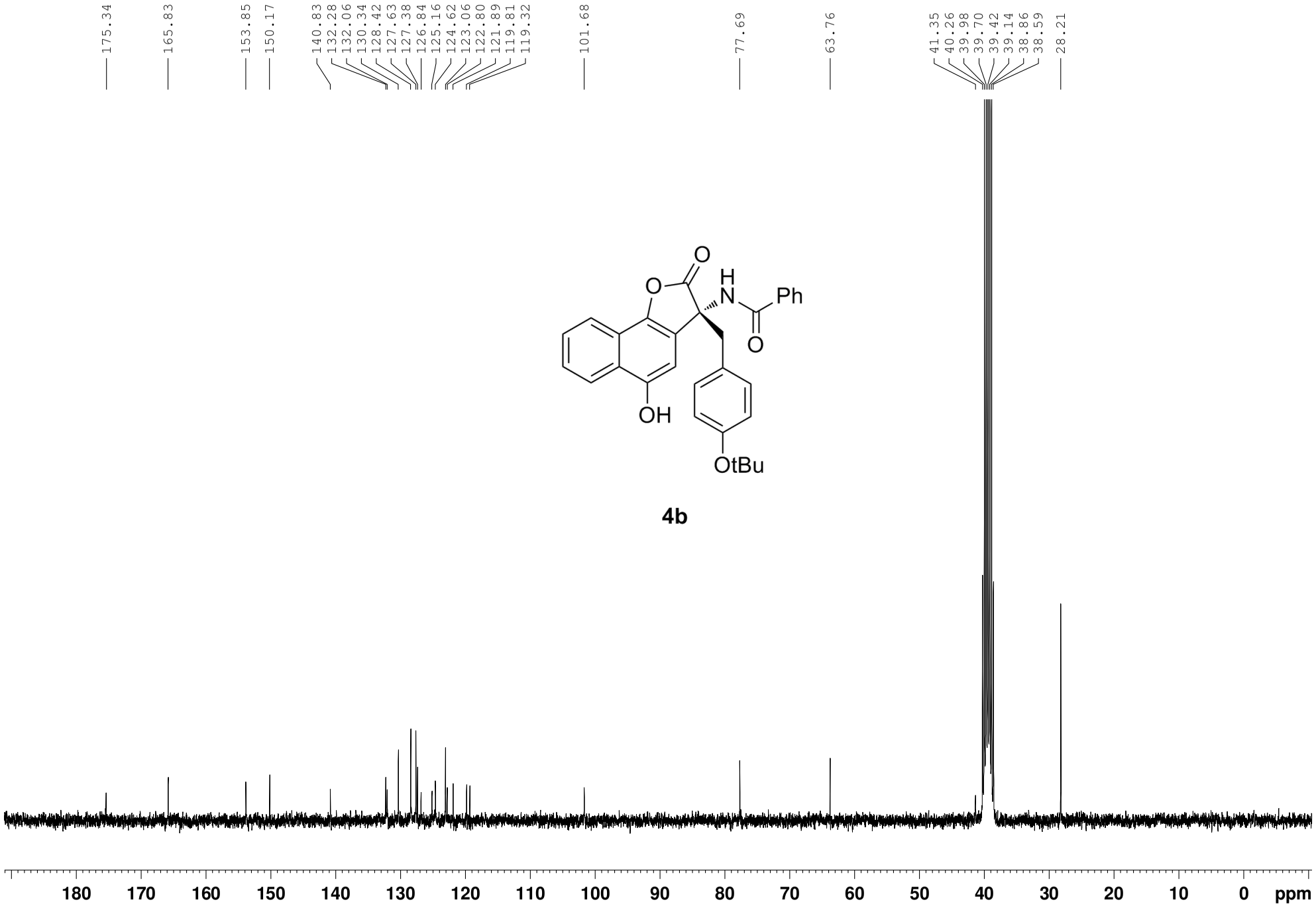
	Retention time	Area	% Area	Height	Integral type
1	10.523	61964468	50.52	968413	bb
2	15.950	60686641	49.48	417821	bb

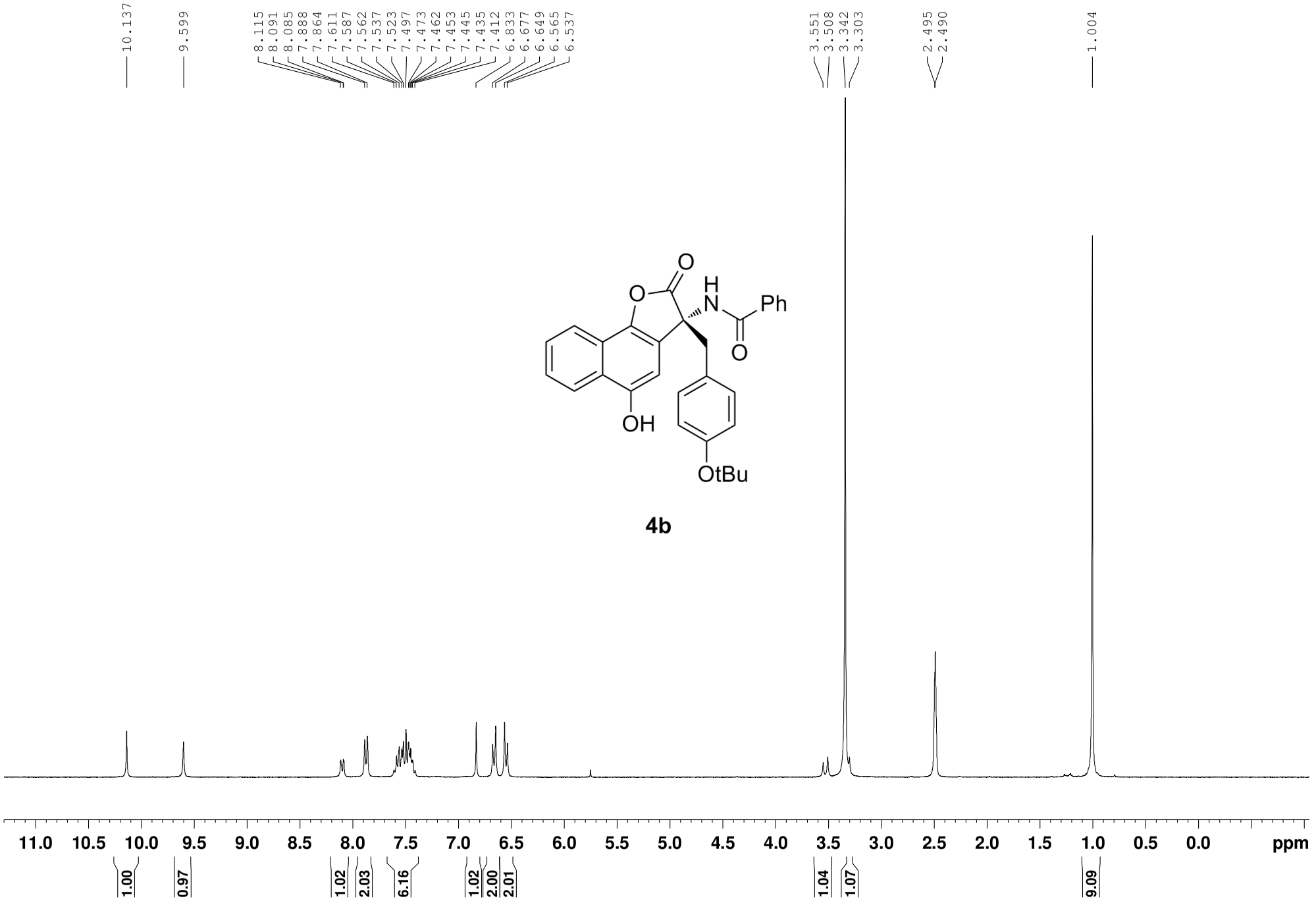


	Retention time	Area	% Area	Height	Integral type
1	10.427	7771427	96.08	123132	bb
2	15.864	316673	3.92	2830	bb

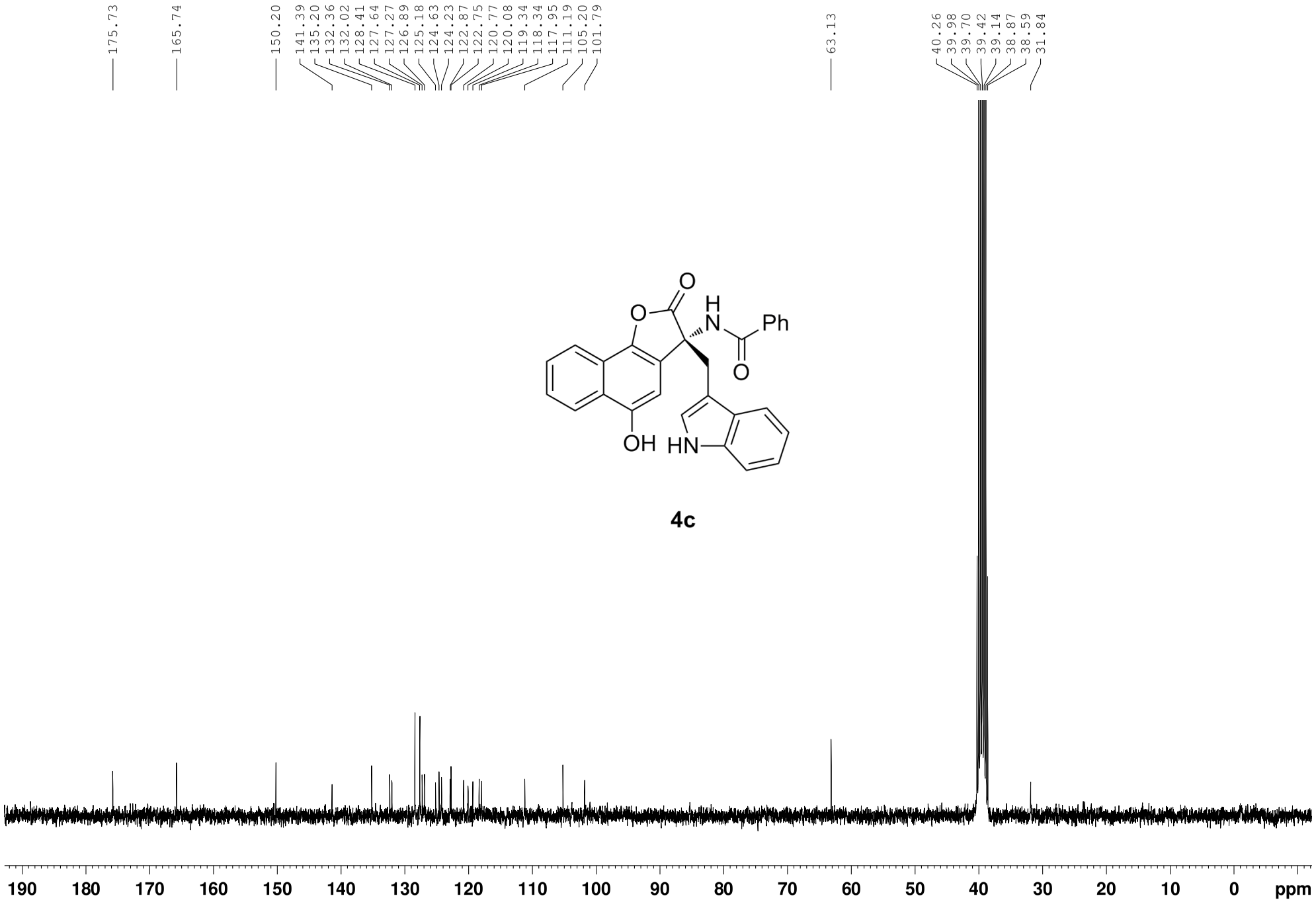

38.48
38.76
39.04
39.32
39.59
39.87
40.15
41.96
62.73
109.98
110.35
115.40
127.14
127.64
127.77
128.42
128.77
130.01
132.07
132.24
132.64
145.58
153.93
165.79
175.06
Ph
O
H
N
Bn
O
O
O
OH
4a
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190

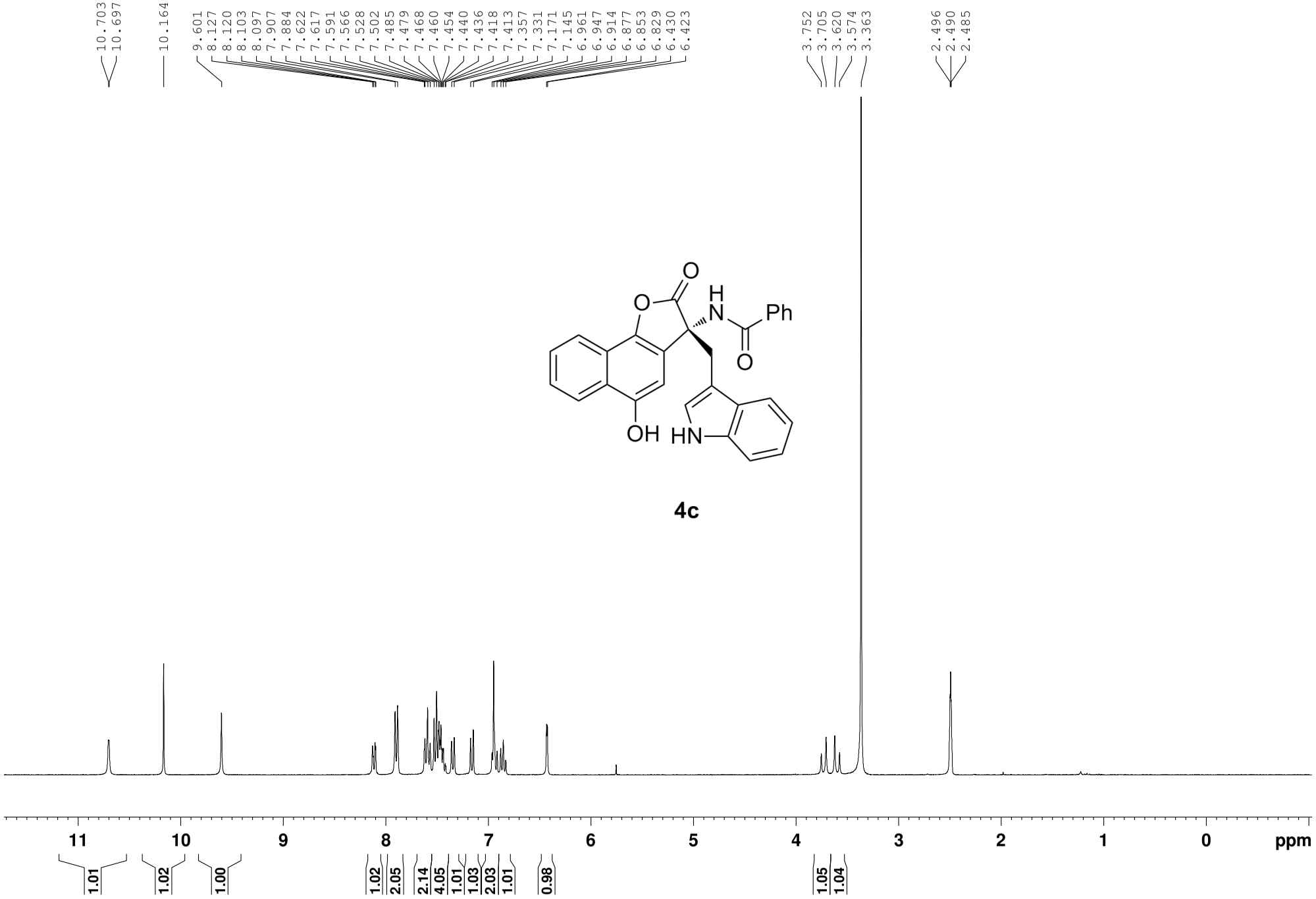

9.539
9.359
7.883
7.859
7.855
7.611
7.586
7.562
7.522
7.496
7.473
7.129
7.114
7.093
7.081
7.075
7.063
6.812
6.803
6.797
6.778
6.771
6.688
6.659
6.598
6.590
6.570
6.561
3.500
3.458
3.374
3.311
3.269
2.496
2.490
2.484
O
O
H
N
Ph
Bn
O
OH
4a
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.04
2.07
1.12
2.12
3.16
3.18
1.10
1.09
1.24
1.24


175.34
165.83
153.85
150.17
140.83
132.28
132.06
130.34
128.42
127.63
127.38
126.84
125.16
124.62
123.06
122.80
121.89
119.81
119.32
101.68
77.69
63.76
41.35
40.26
39.98
39.70
39.42
39.14
38.86
38.59
28.21
O
O
H
N
Ph
O
OH
OtBu
4b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

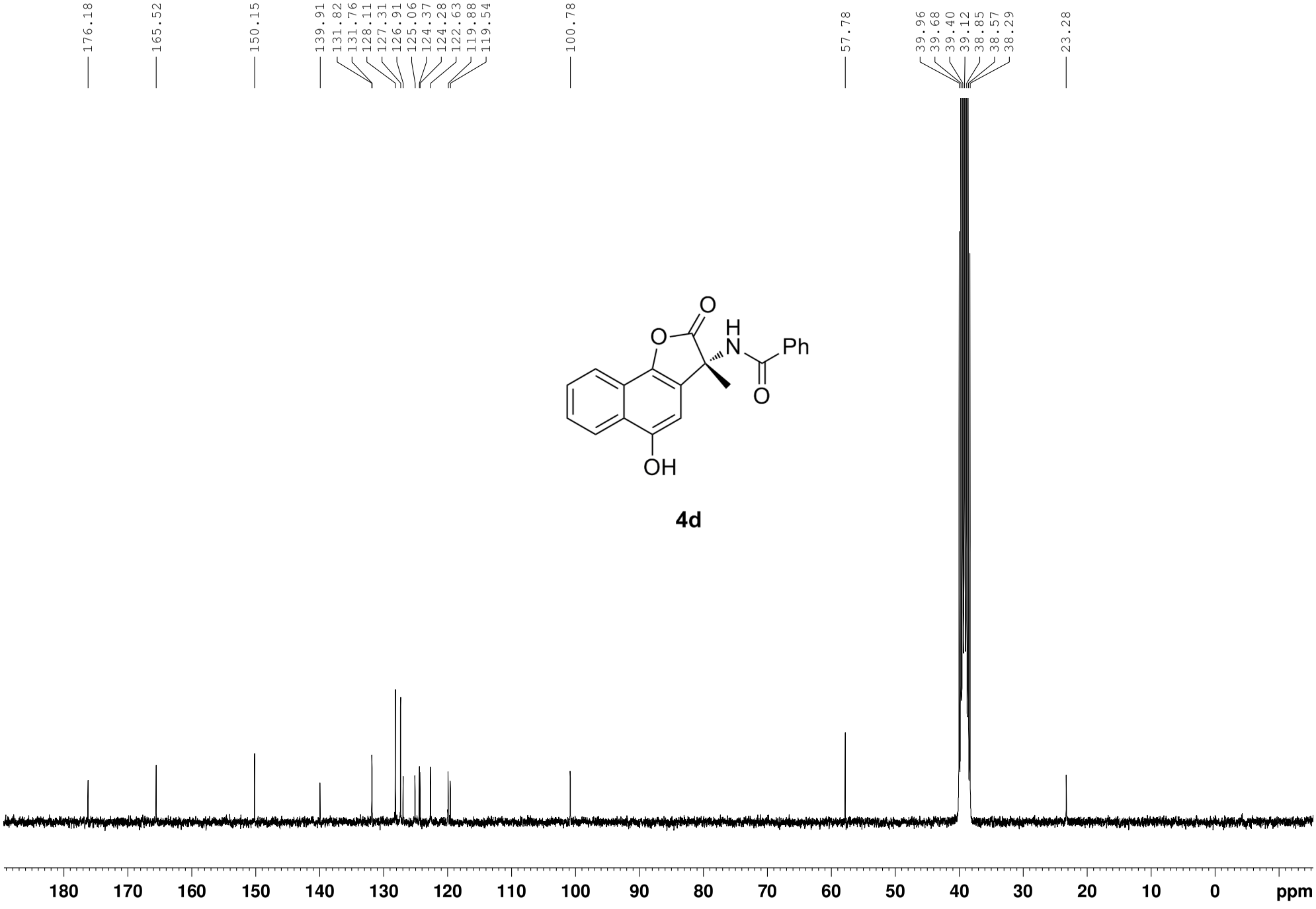

10.137
9.599
8.115
8.091
8.085
7.888
7.864
7.611
7.587
7.562
7.537
7.523
7.497
7.473
7.462
7.453
7.445
7.435
7.412
6.833
6.677
6.649
6.565
6.537
3.551
3.508
3.342
3.303
2.495
2.490
1.004
O
O
H
N
Ph
O
OH
OtBu
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
0.97
1.02
2.03
6.16
1.02
2.00
2.01
1.04
1.07
9.09

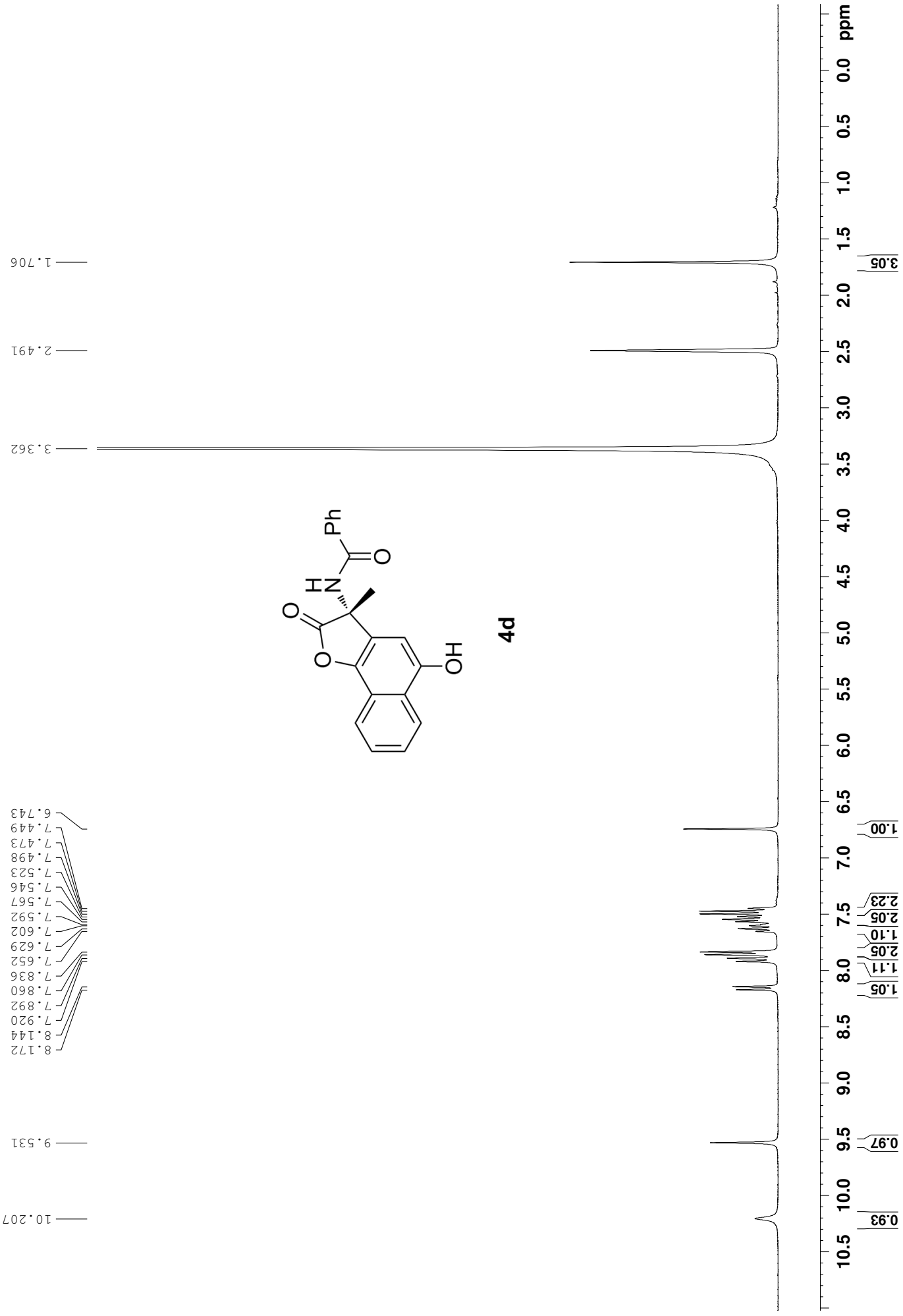
4b

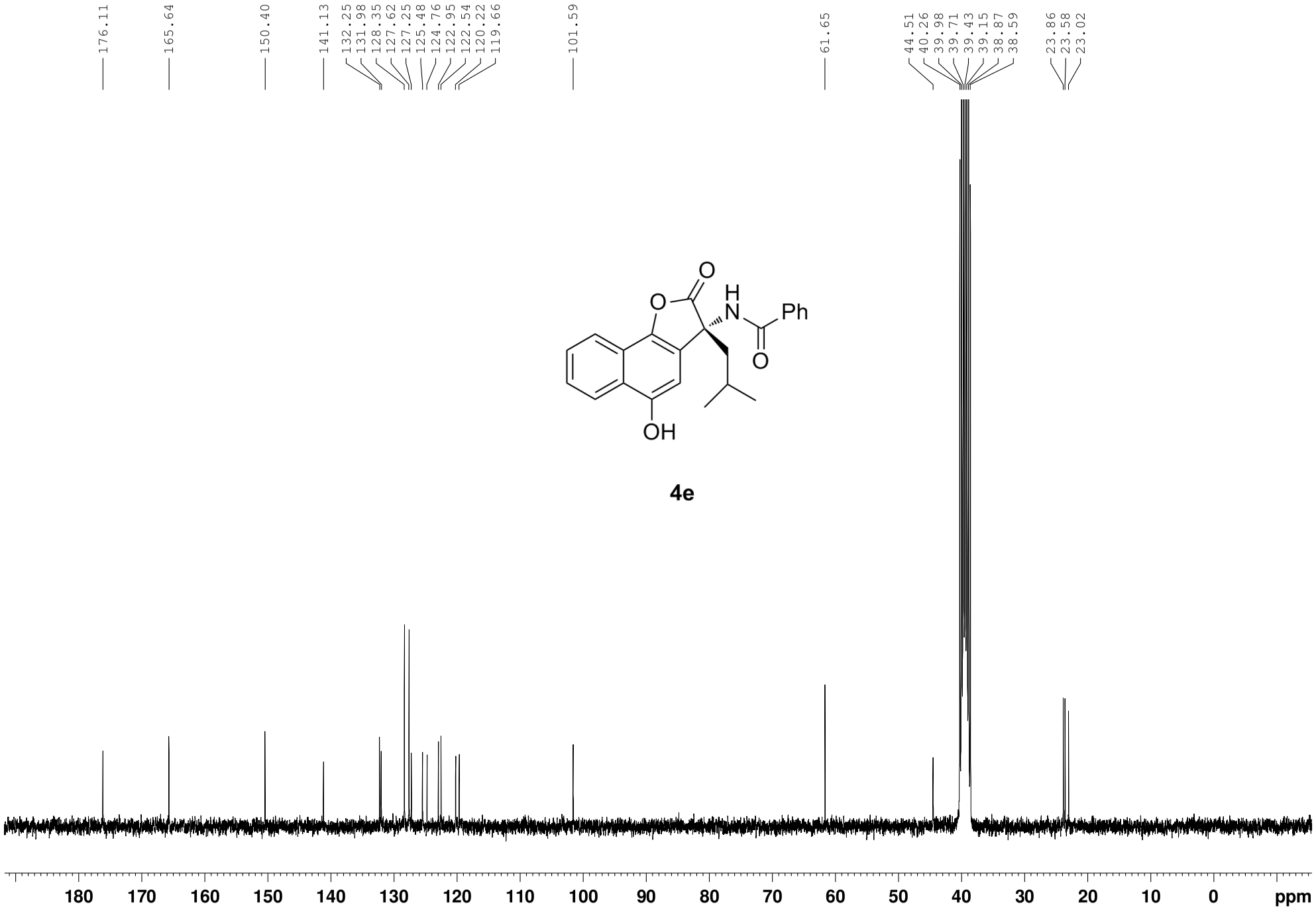

175.73
165.74
150.20
141.39
135.20
132.36
132.02
128.41
127.64
127.27
126.89
125.18
124.63
124.23
122.87
122.75
120.77
120.08
119.34
118.34
117.95
111.19
105.20
101.79
63.13
40.26
39.98
39.70
39.42
39.14
38.87
38.59
31.84
O
O
H
N
Ph
O
OH
HN
4c
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


10.703
10.697
10.164
9.601
8.127
8.120
8.103
8.097
7.907
7.884
7.622
7.617
7.591
7.566
7.528
7.502
7.485
7.479
7.468
7.460
7.454
7.440
7.436
7.418
7.413
7.357
7.331
7.171
7.145
6.961
6.947
6.914
6.877
6.853
6.829
6.430
6.423
3.752
3.705
3.620
3.574
3.363
2.496
2.490
2.485
O
O
H
N
Ph
O
OH
HN
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.01
1.02
1.00
1.02
2.05
2.14
4.05
1.01
1.03
2.03
1.01
0.98
1.05
1.04

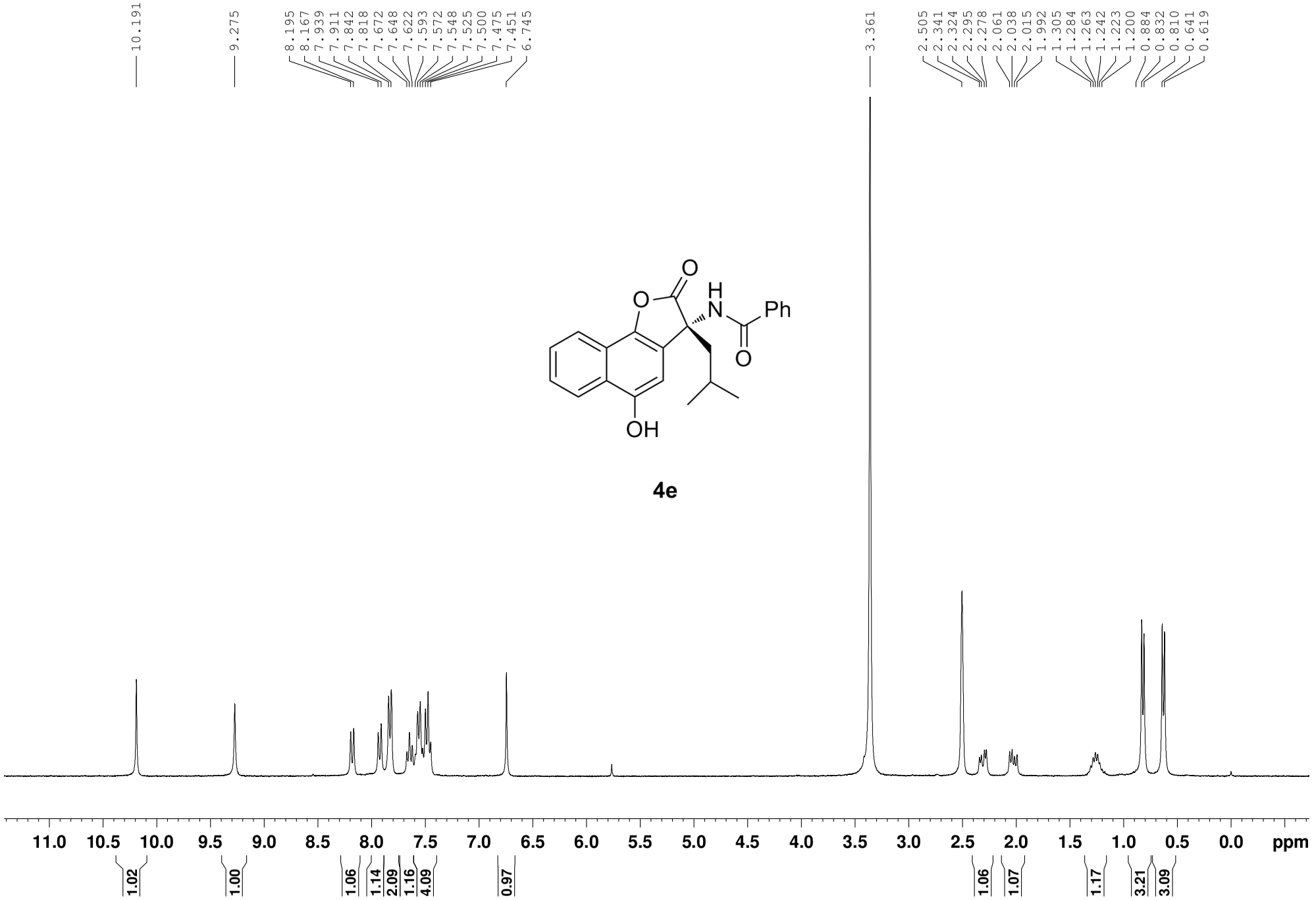
4c

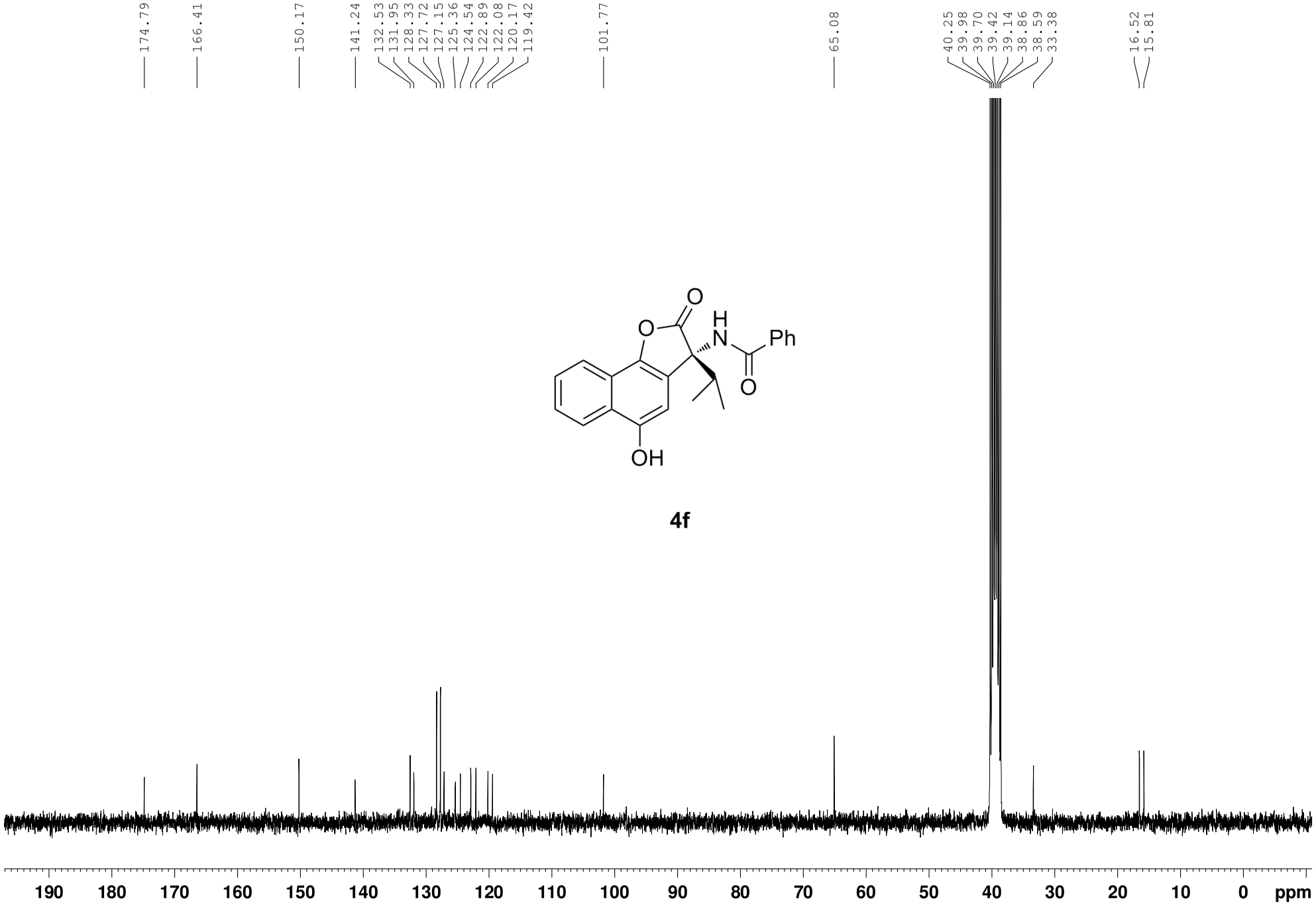

176.18
165.52
150.15
139.91
131.82
131.76
128.11
127.31
126.91
125.06
124.37
124.28
122.63
119.88
119.54
100.78
57.78
39.96
39.68
39.40
39.12
38.85
38.57
38.29
23.28
O
O
H
N
Ph
O
OH
4d
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


10.207
9.531
8.172
8.144
7.920
7.892
7.860
7.836
7.652
7.629
7.602
7.592
7.567
7.546
7.523
7.498
7.473
7.449
6.743
3.362
2.491
1.706
Ph
O
H
N
O
O
OH
4d
ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
9.5
10.0
10.5
0.93
0.97
1.05
1.11
2.05
1.10
2.05
2.23
1.00
3.05

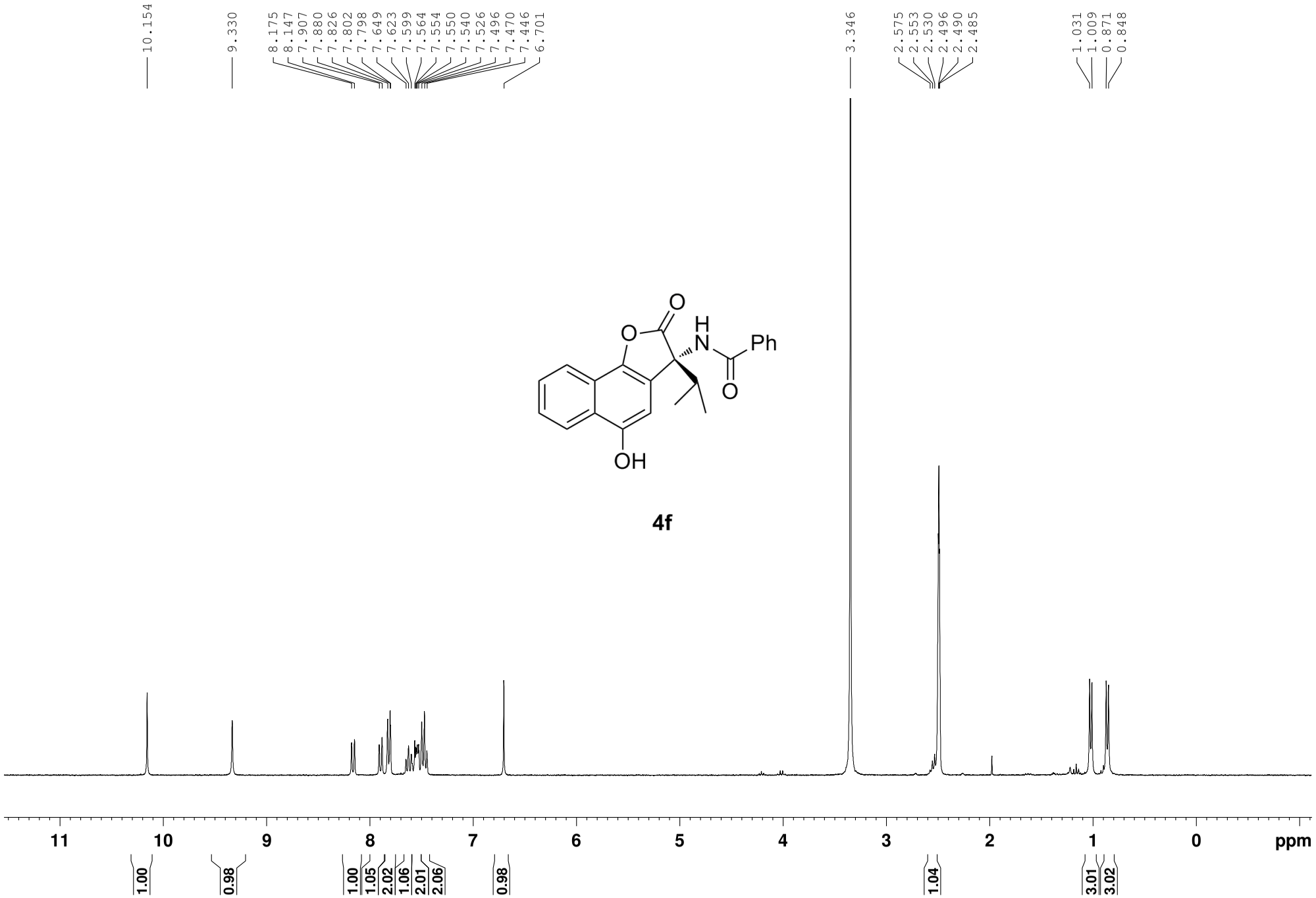

176.11
165.64
150.40
141.13
132.25
131.98
128.35
127.62
127.25
125.48
124.76
122.95
122.54
120.22
119.66
101.59
61.65
44.51
40.26
39.98
39.71
39.43
39.15
38.87
38.59
23.86
23.58
23.02
O
O
H
N
Ph
O
OH
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

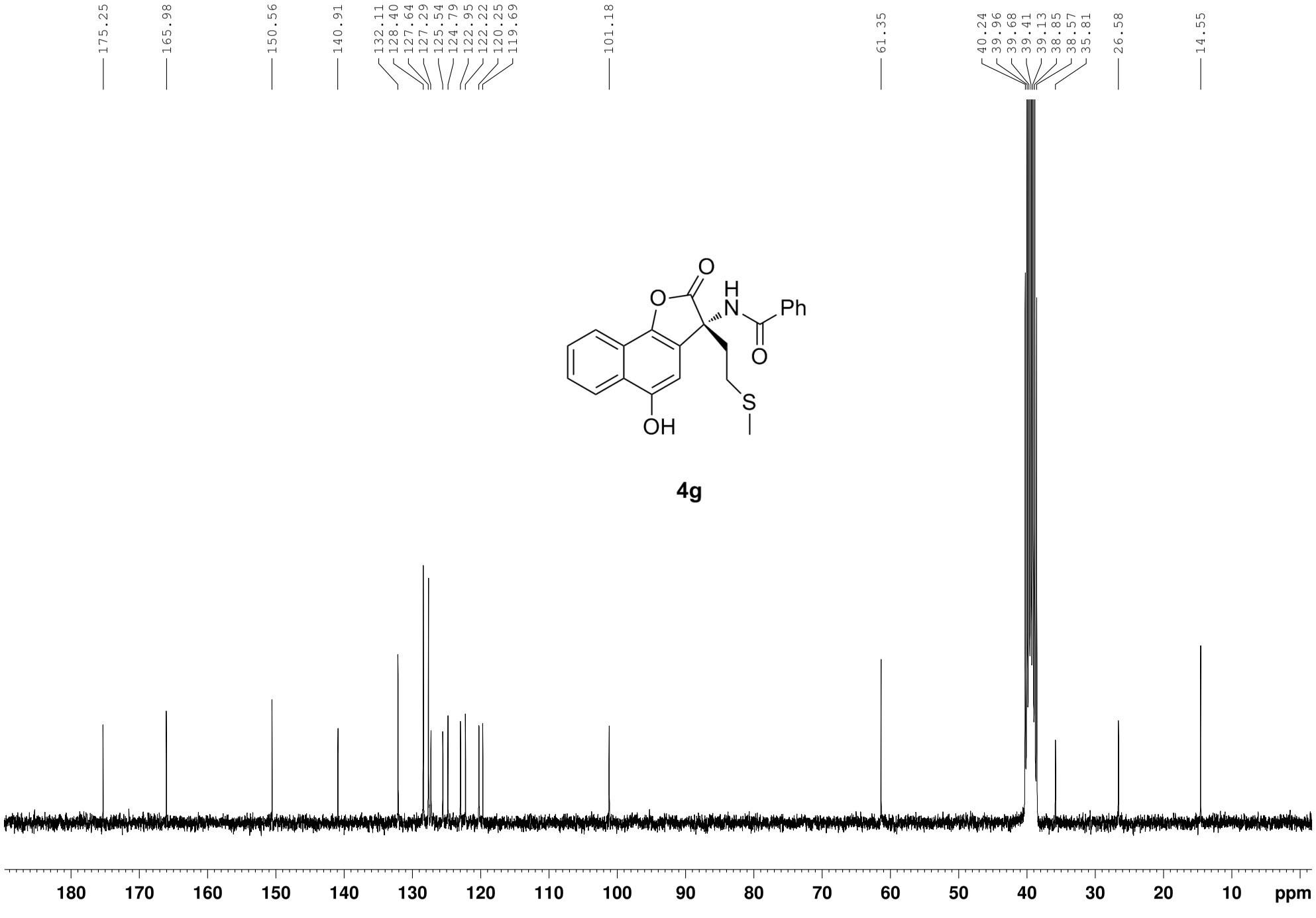
4e


10.191
9.275
8.195
8.167
7.939
7.911
7.842
7.818
7.672
7.648
7.622
7.593
7.572
7.548
7.525
7.500
7.475
7.451
6.745
3.361
2.505
2.341
2.324
2.295
2.278
2.061
2.038
2.015
1.992
1.305
1.284
1.263
1.242
1.223
1.200
0.884
0.832
0.810
0.641
0.619
O
O
H
N
Ph
O
OH
4e
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
1.02
1.00
1.06
1.14
2.09
1.16
4.09
0.97
1.06
1.07
1.17
3.21
3.09


174.79
166.41
150.17
141.24
132.53
131.95
128.33
127.72
127.15
125.36
124.54
122.89
122.08
120.17
119.42
101.77
65.08
40.25
39.98
39.70
39.42
39.14
38.86
38.59
33.38
16.52
15.81
O
O
H
N
Ph
O
OH
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

4f


10.154
9.330
8.175
8.147
7.907
7.880
7.826
7.802
7.798
7.649
7.623
7.599
7.564
7.554
7.550
7.540
7.526
7.496
7.470
7.446
6.701
3.346
2.575
2.553
2.530
2.496
2.490
2.485
1.031
1.009
0.871
0.848
O
O
H
N
Ph
O
OH
4f
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.98
1.00
1.05
2.02
1.06
2.01
2.06
0.98
1.04
3.01
3.02


175.25
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122.22
120.25
119.69
101.18
61.35
40.24
39.96
39.68
39.41
39.13
38.85
38.57
35.81
26.58
14.55
O
O
H
N
Ph
O
S
OH
4g
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150
140
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120
110
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70
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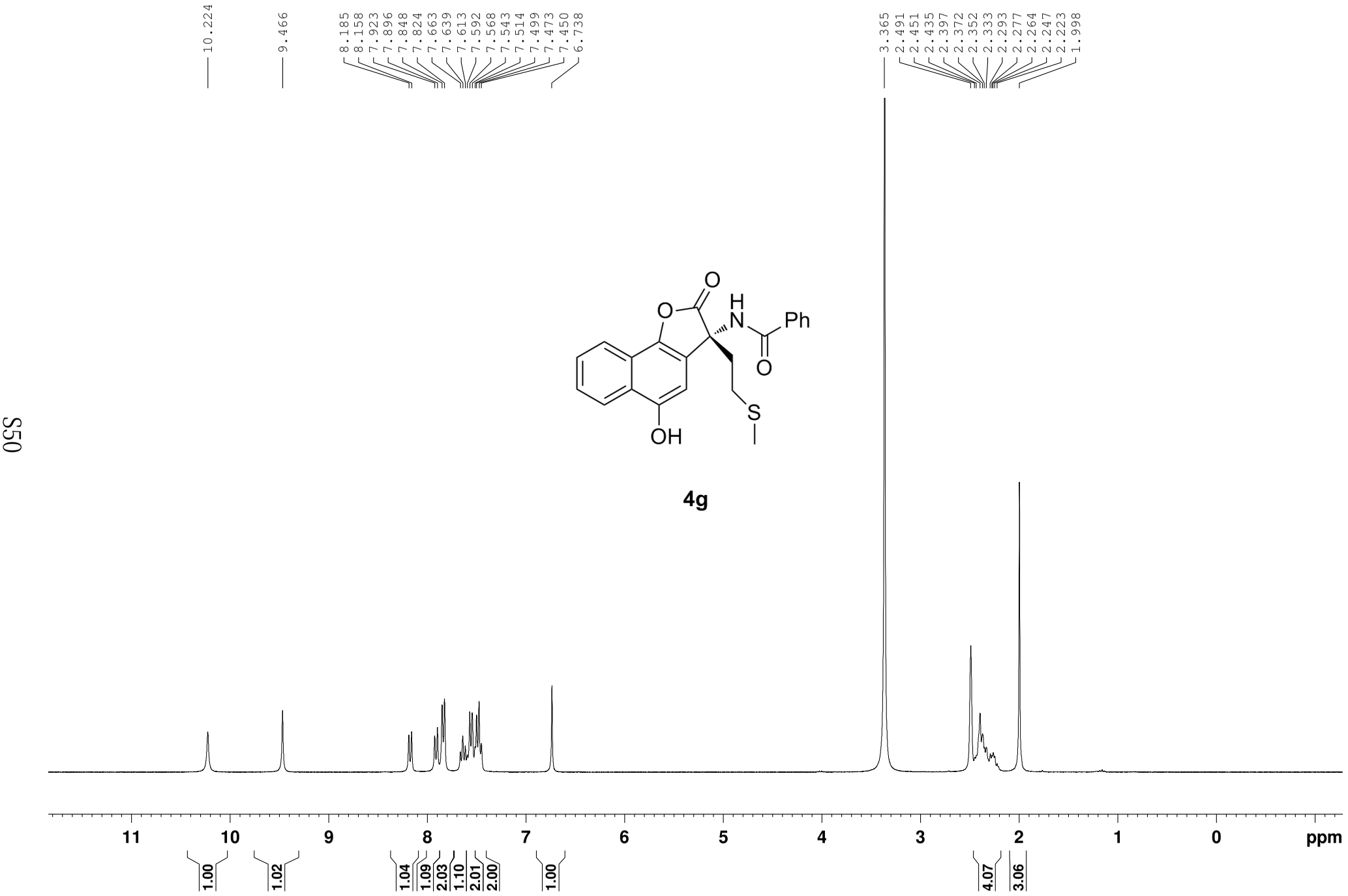
30
20
10
ppm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7.592
7.568
7.543
7.514
7.499
7.473
7.450
6.738
3.365
2.491
2.451
2.435
2.397
2.372
2.352
2.333
2.293
2.277
2.264
2.247
2.223
1.998
O
O
H
N
Ph
O
S
OH
4g
11
10
9
8
7
6
5
4
3
2
1
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1.00
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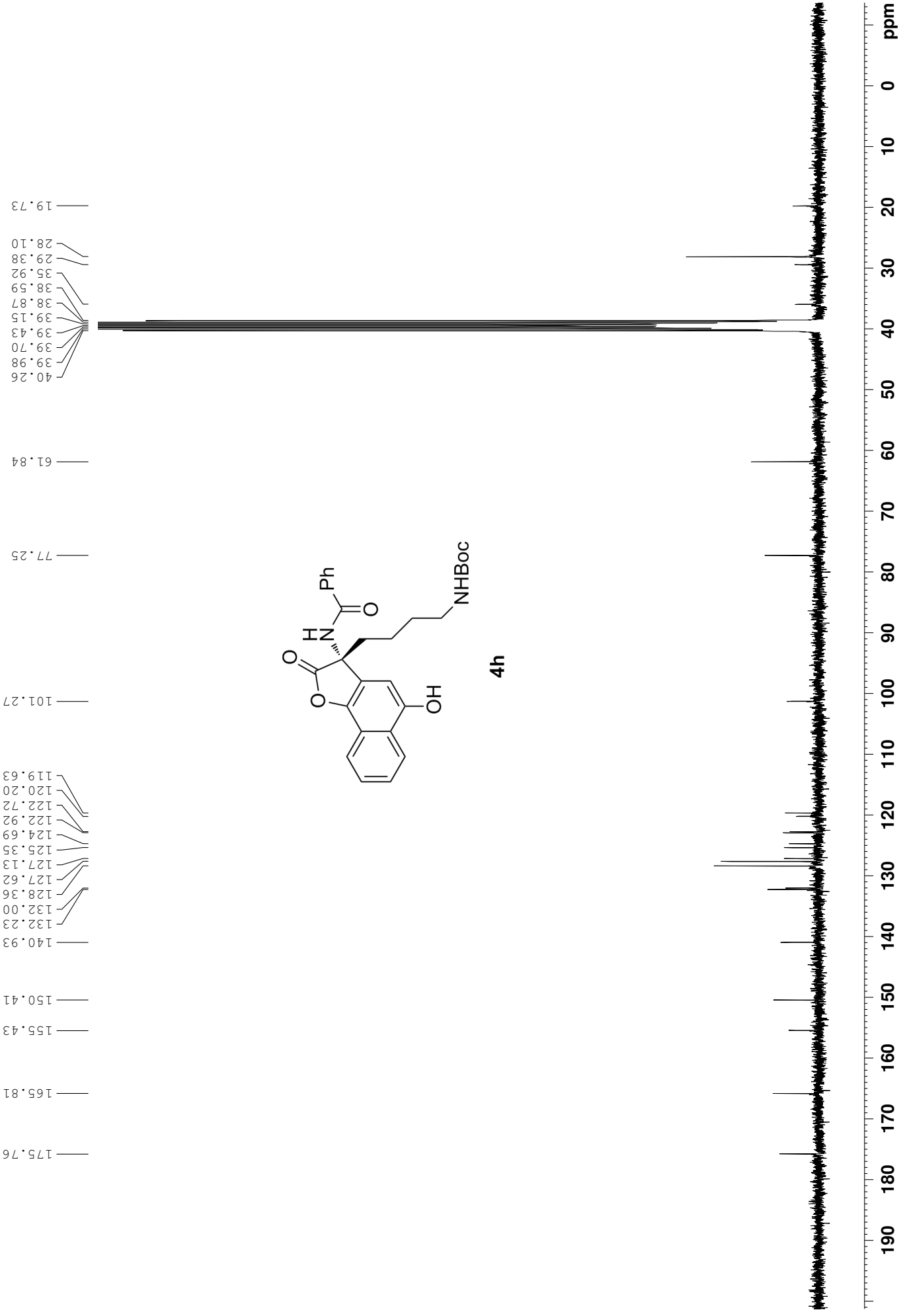
3.06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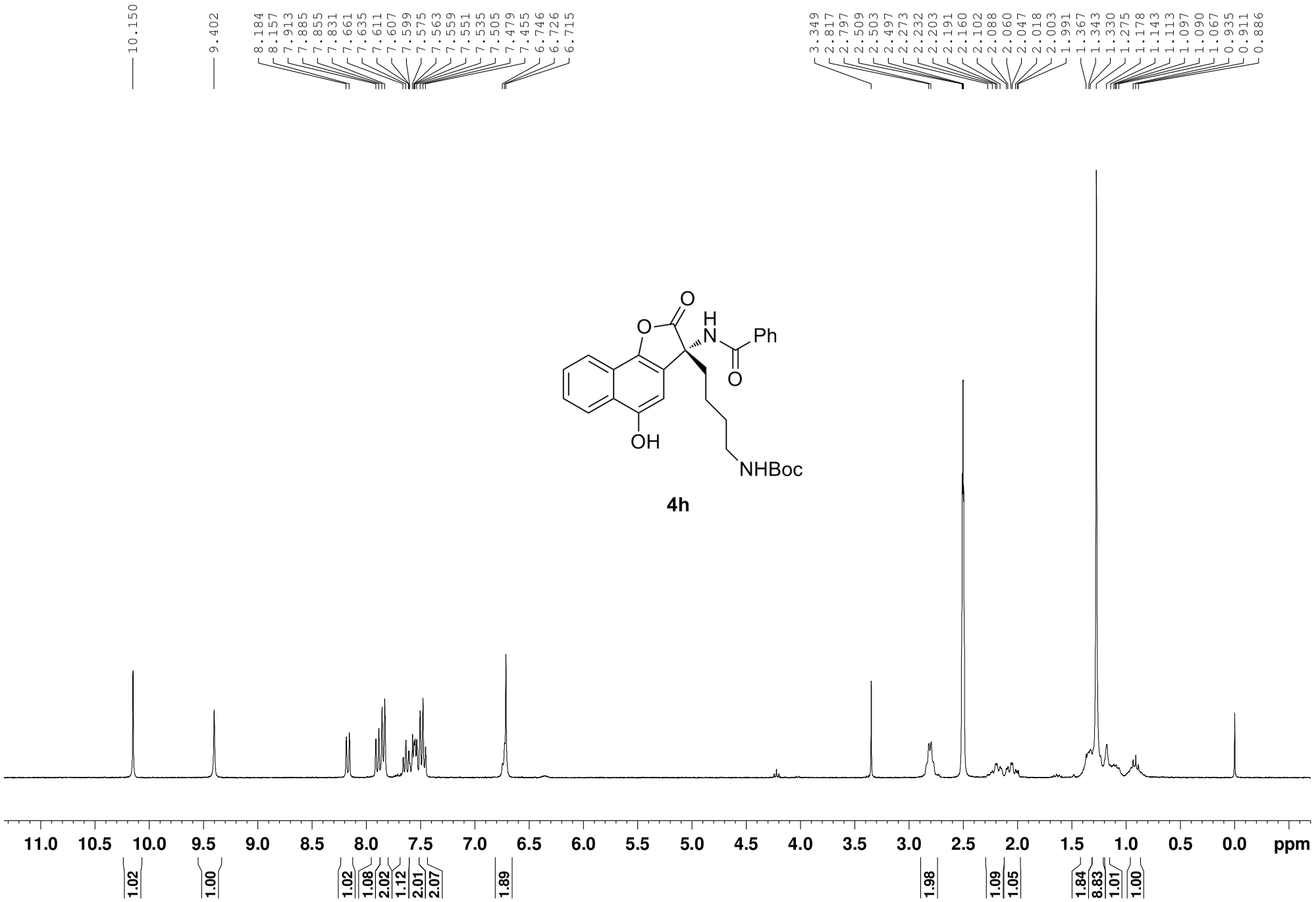
175.76
Ph
NHBoc
OH
4h
ppm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7.599
7.575
7.563
7.559
7.551
7.535
7.505
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7.455
6.746
6.726
6.715
3.349
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2.797
2.509
2.503
2.497
2.273
2.232
2.203
2.191
2.160
2.102
2.088
2.060
2.047
2.018
2.003
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1.367
1.343
1.330
1.275
1.178
1.143
1.113
1.097
1.090
1.067
0.935
0.911
0.886
O
O
H
N
Ph
O
OH
NHBoc
4h
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
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1.00
1.02
1.08
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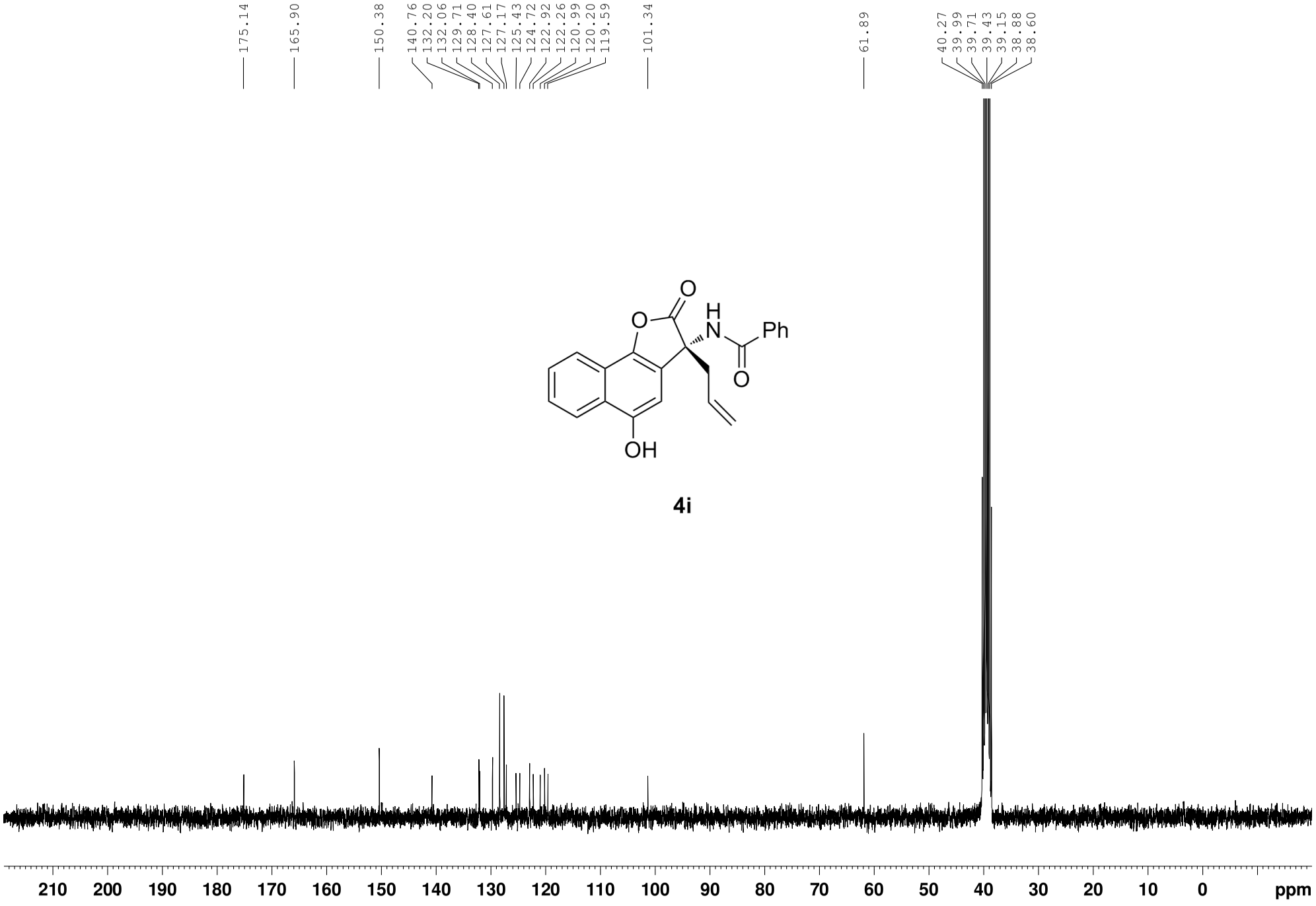
1.00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120.20
119.59
101.34
61.89
40.27
39.99
39.71
39.43
39.15
38.88
38.60
O
O
H
N
Ph
O
OH
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200
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100
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60
50
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30
20
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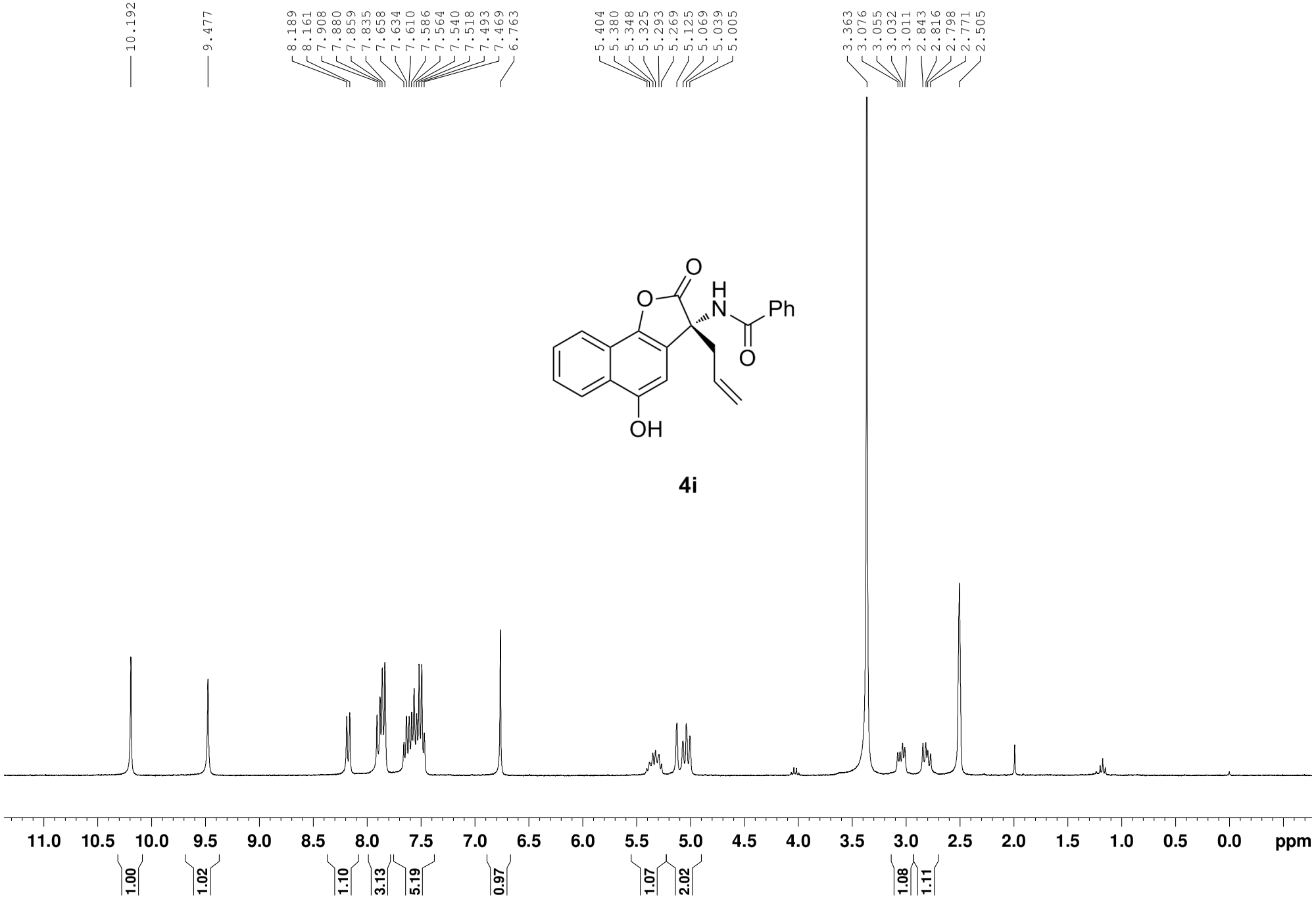
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7.564
7.540
7.518
7.493
7.469
6.763
5.404
5.380
5.348
5.325
5.293
5.269
5.125
5.069
5.039
5.005
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3.076
3.055
3.032
3.011
2.843
2.816
2.798
2.771
2.505
O
O
H
N
Ph
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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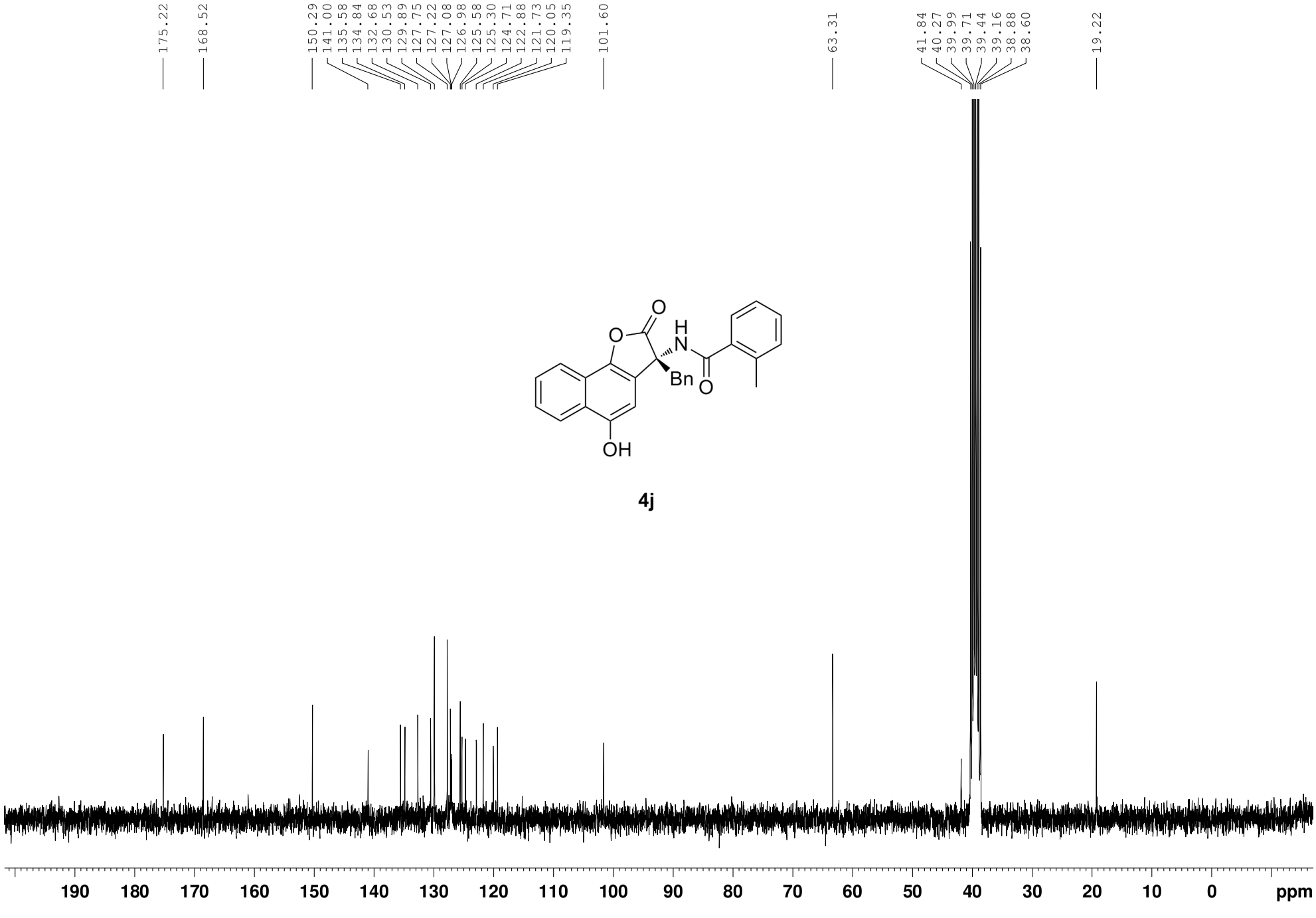
1.08
1.11

4i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120.05
119.35
101.60
63.31
41.84
40.27
39.99
39.71
39.44
39.16
38.88
38.60
19.22
O
O
H
N
Bn
O
OH
4j
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140
130
120
110
100
90
80
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60
50
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20
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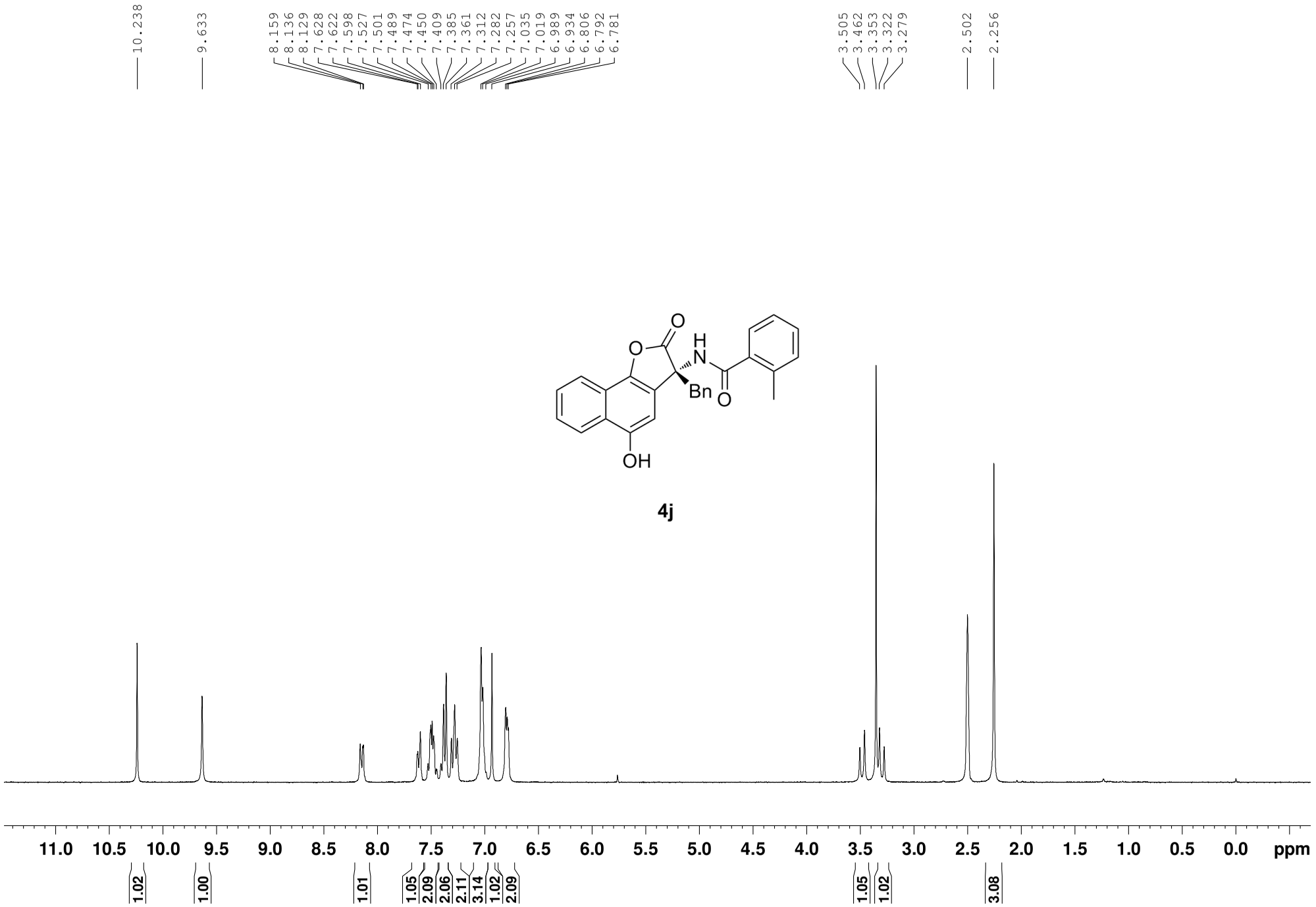
ppm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7.361
7.312
7.282
7.257
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7.019
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6.792
6.781
3.505
3.462
3.353
3.322
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2.502
2.256
O
O
H
N
Bn
O
OH
4j
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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
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2.0
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0.0
ppm
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2.06
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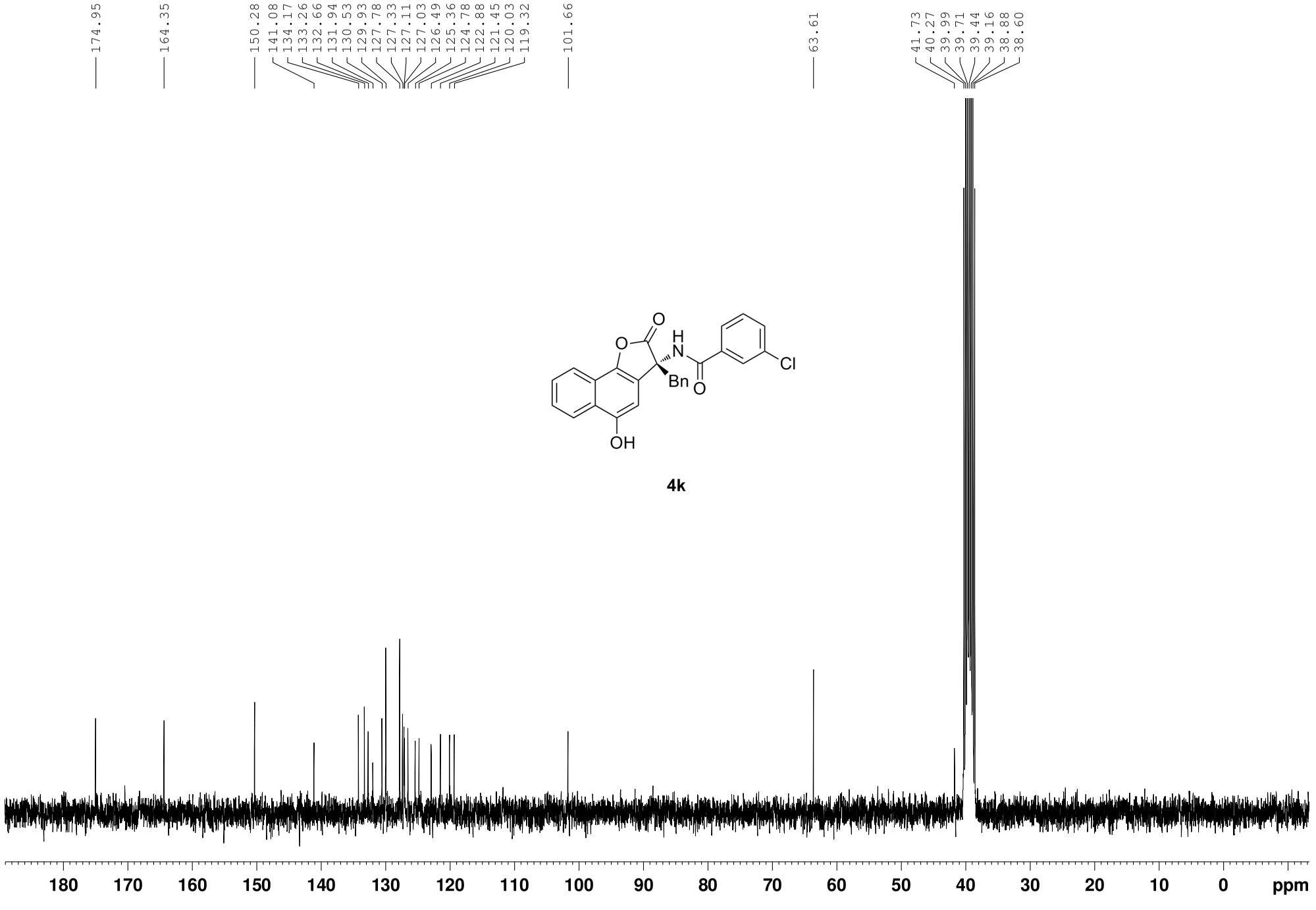
1.05
1.02
3.08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127.11
127.03
126.49
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124.78
122.88
121.45
120.03
119.32
101.66
63.61
41.73
40.27
39.99
39.71
39.44
39.16
38.88
38.60
O
O
H
N
Cl
Bn
O
OH
4k
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130
120
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100
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50
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20
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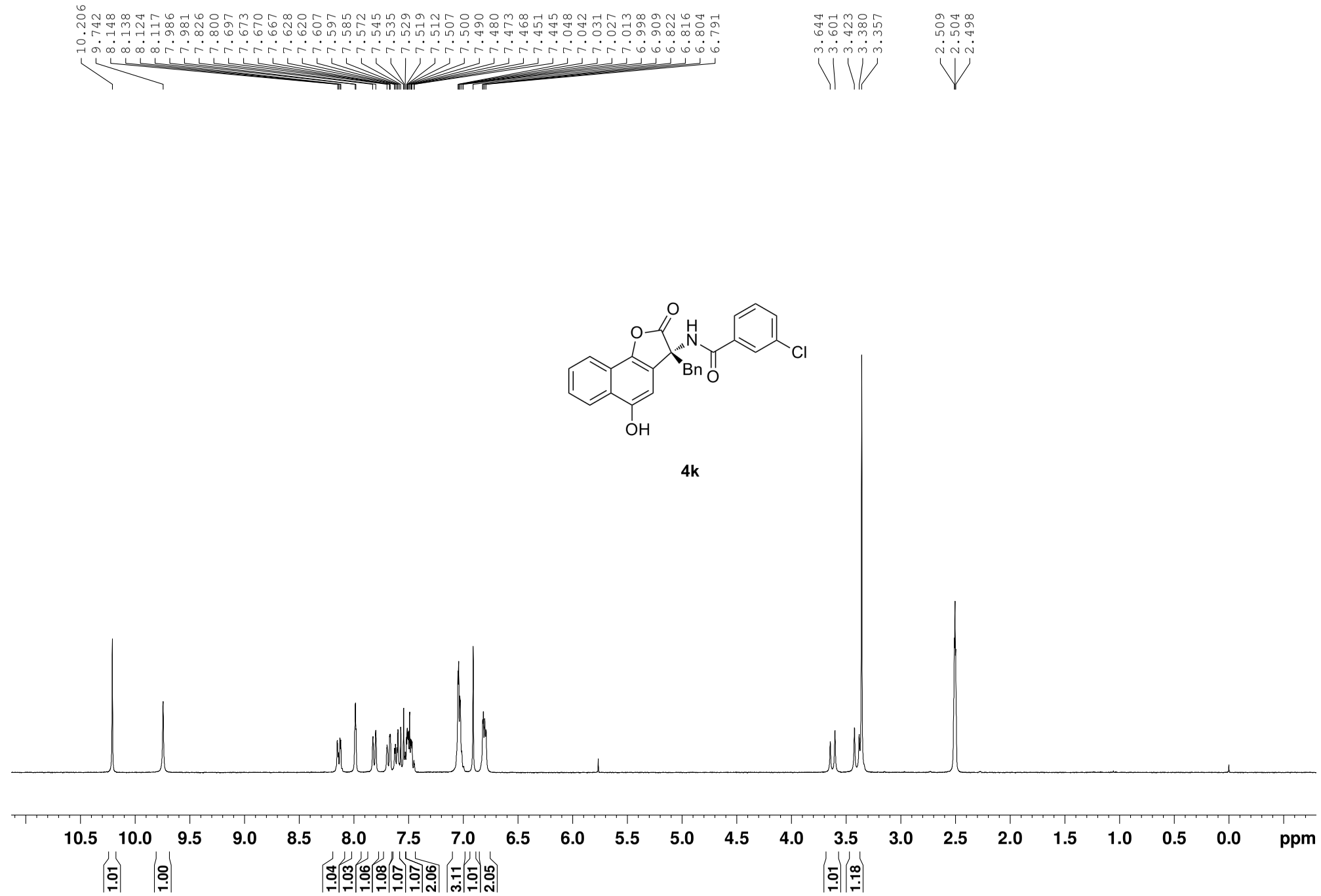
0
ppm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7.670
7.667
7.628
7.620
7.607
7.597
7.585
7.572
7.545
7.535
7.529
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7.512
7.507
7.500
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7.480
7.473
7.468
7.451
7.445
7.048
7.042
7.031
7.027
7.013
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6.909
6.822
6.816
6.804
6.791
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3.423
3.380
3.357
2.509
2.504
2.498
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O
H
N
Cl
Bn
O
OH
4k
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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
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1.00
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1.08
1.07
1.07
2.06
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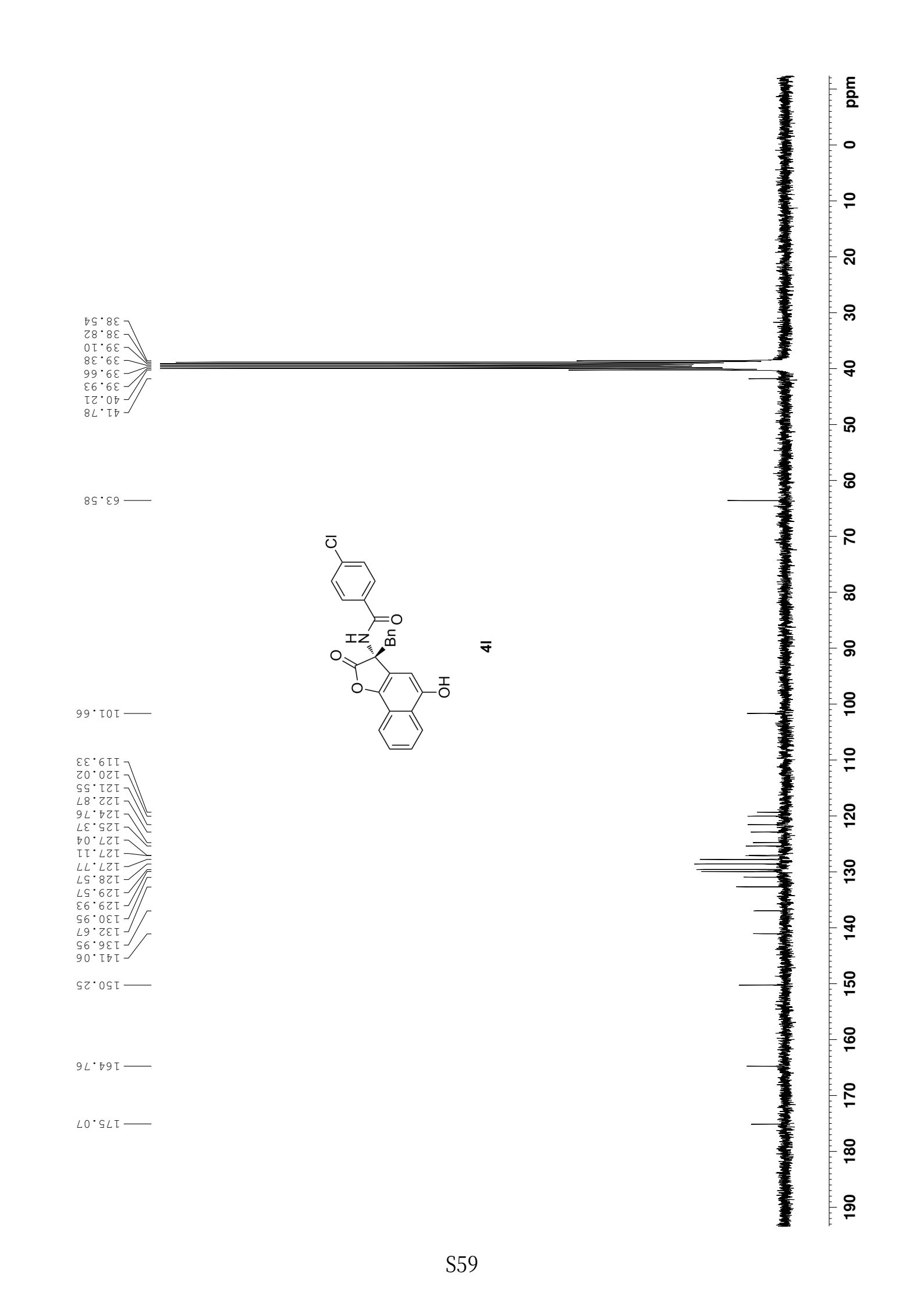
1.01
1.18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124.76
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127.04
127.11
127.77
128.57
129.57
129.93
130.95
132.67
136.95
141.06
150.25
164.76
175.07
Cl
O
H
N
Bn
O
O
O
HO
4l
ppm
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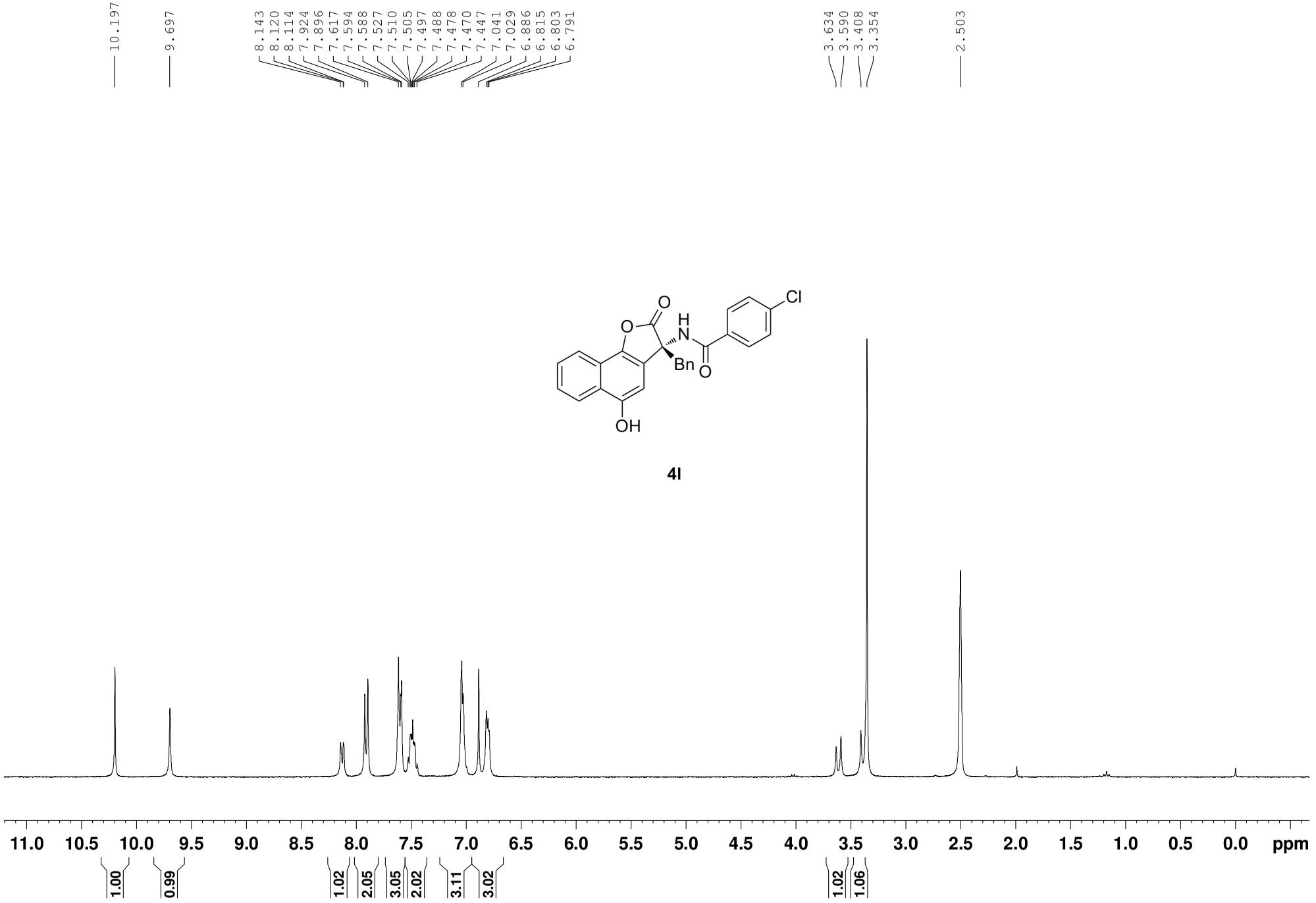
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7.497
7.488
7.478
7.470
7.447
7.041
7.029
6.886
6.815
6.803
6.791
3.634
3.590
3.408
3.354
2.503
O
O
H
N
Cl
Bn
O
OH
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10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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3.0
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2.0
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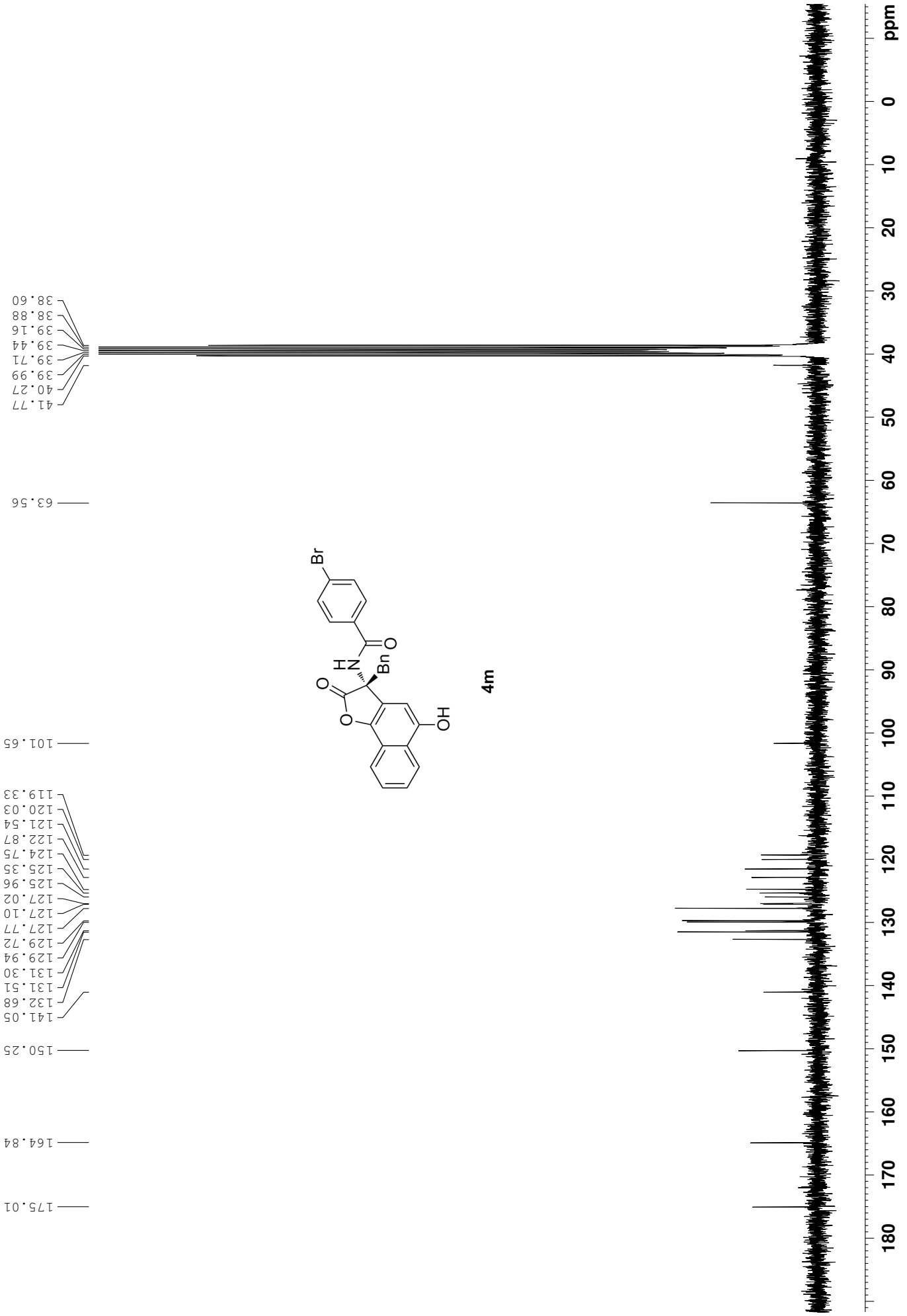
1.02
1.06

4l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131.30
131.51
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O
Bn
O
O
OH
4m
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170
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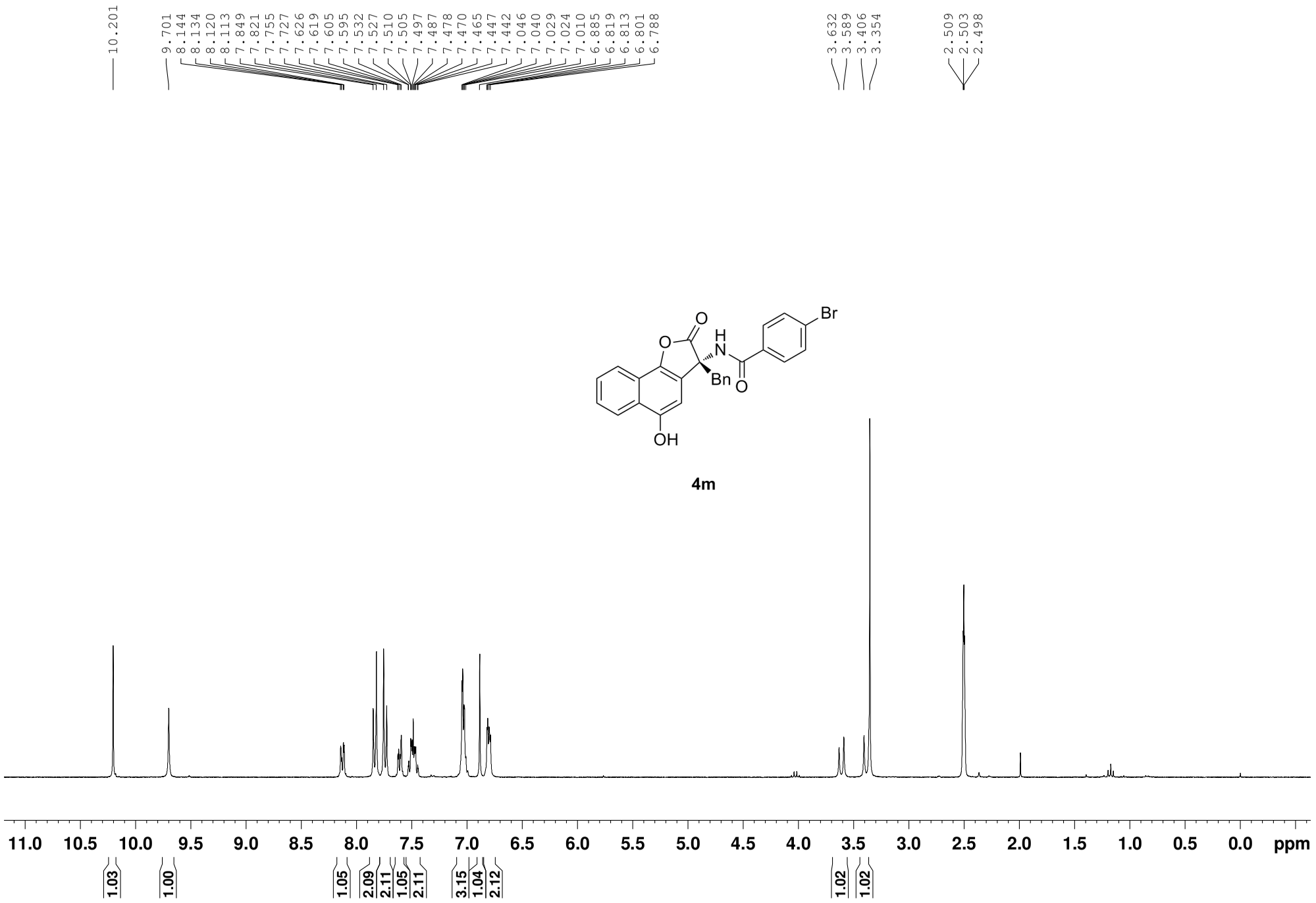
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7.510
7.505
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7.470
7.465
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2.503
2.498
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O
H
N
Br
Bn
O
OH
4m
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10.0
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
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5.0
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4.0
3.5
3.0
2.5
2.0
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3.15
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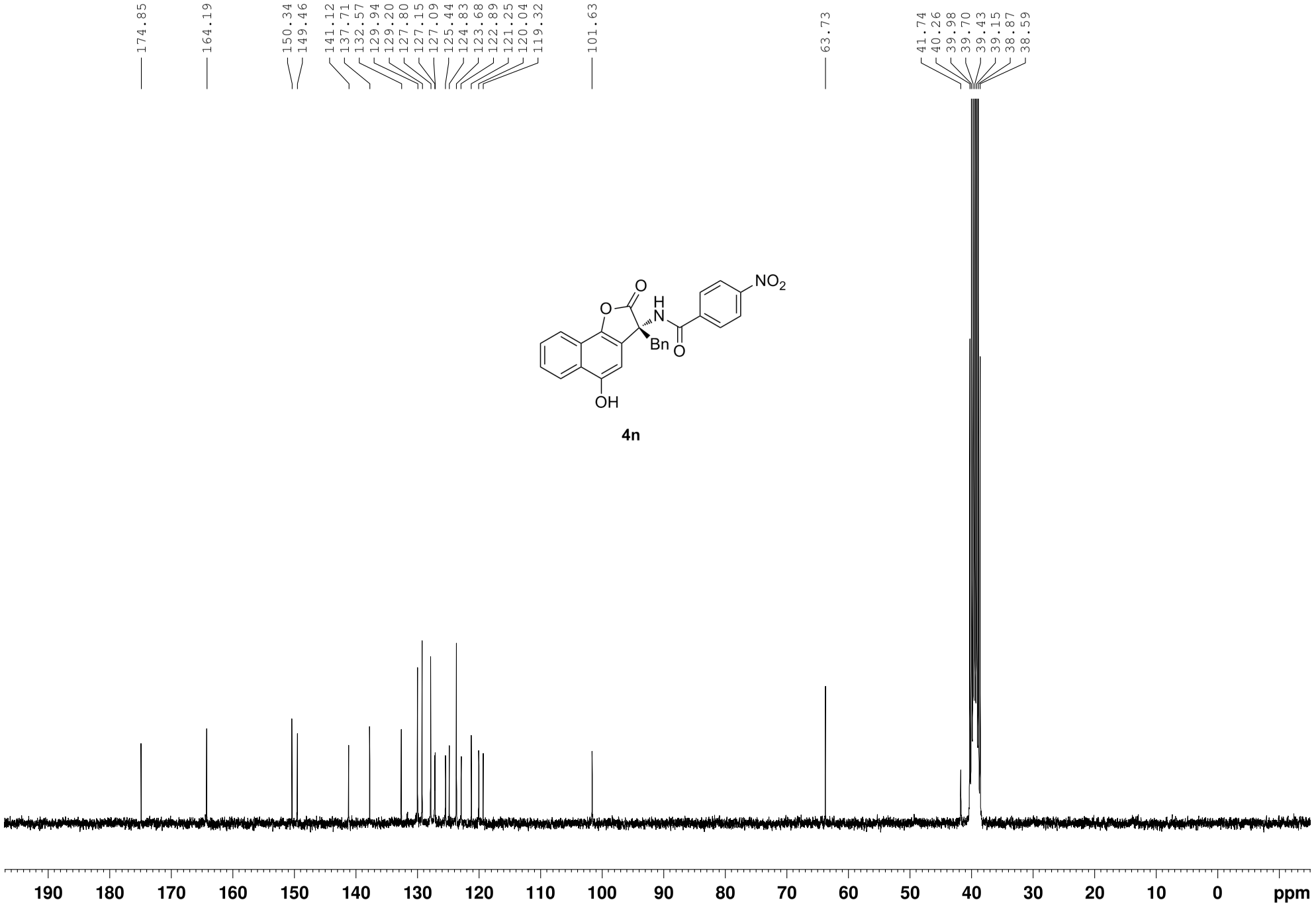
1.02
1.02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123.68
122.89
121.25
120.04
119.32
101.63
63.73
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39.70
39.43
39.15
38.87
38.59
O
O
H
N
O
Bn
NO2
OH
4n
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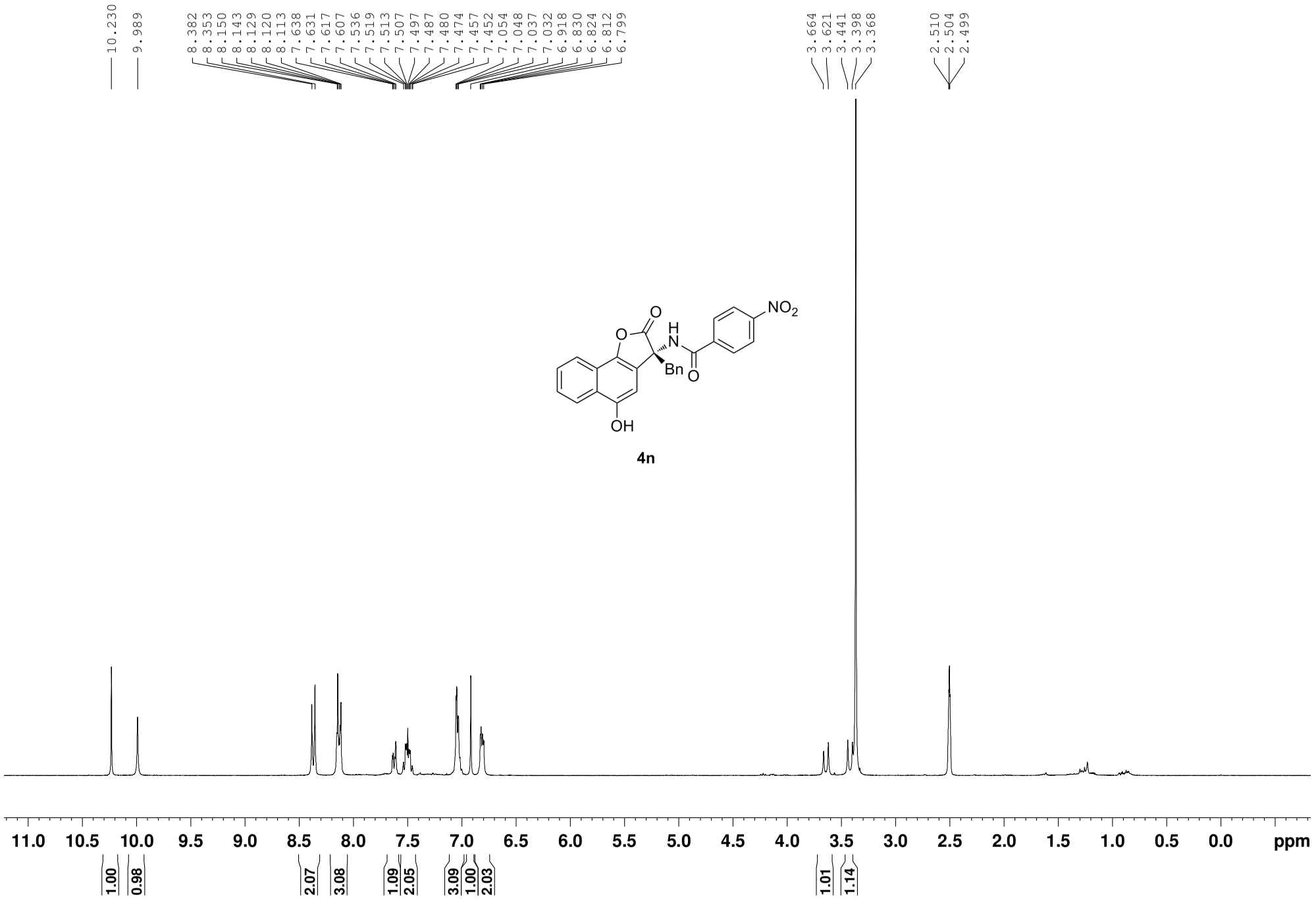
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7.536
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7.497
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7.474
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OH
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9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
2.0
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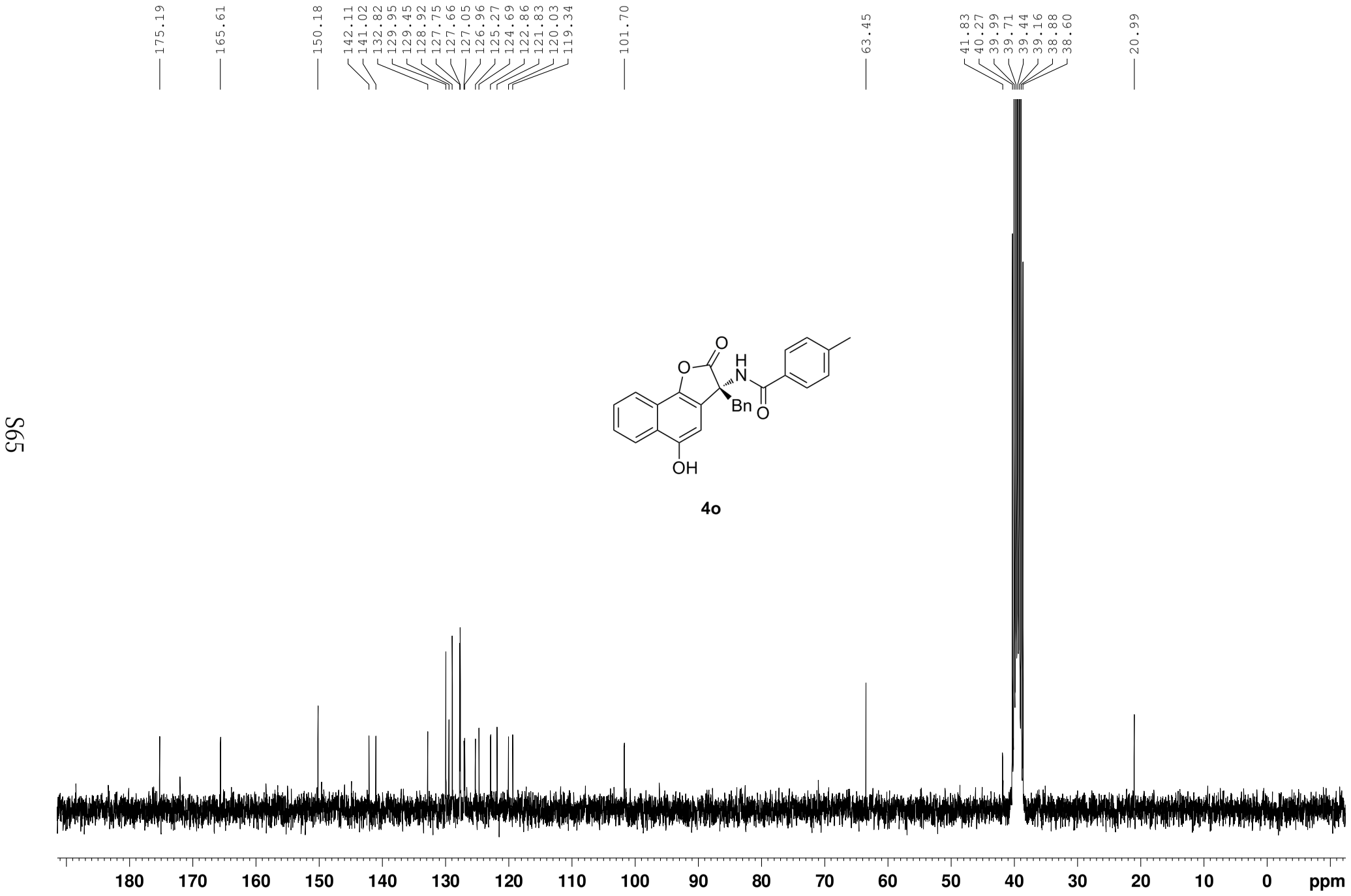
1.14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40.27
39.99
39.71
39.44
39.16
38.88
38.60
20.99
O
O
H
N
Bn
O
OH
180
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130
120
110
100
90
80
70
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50
40
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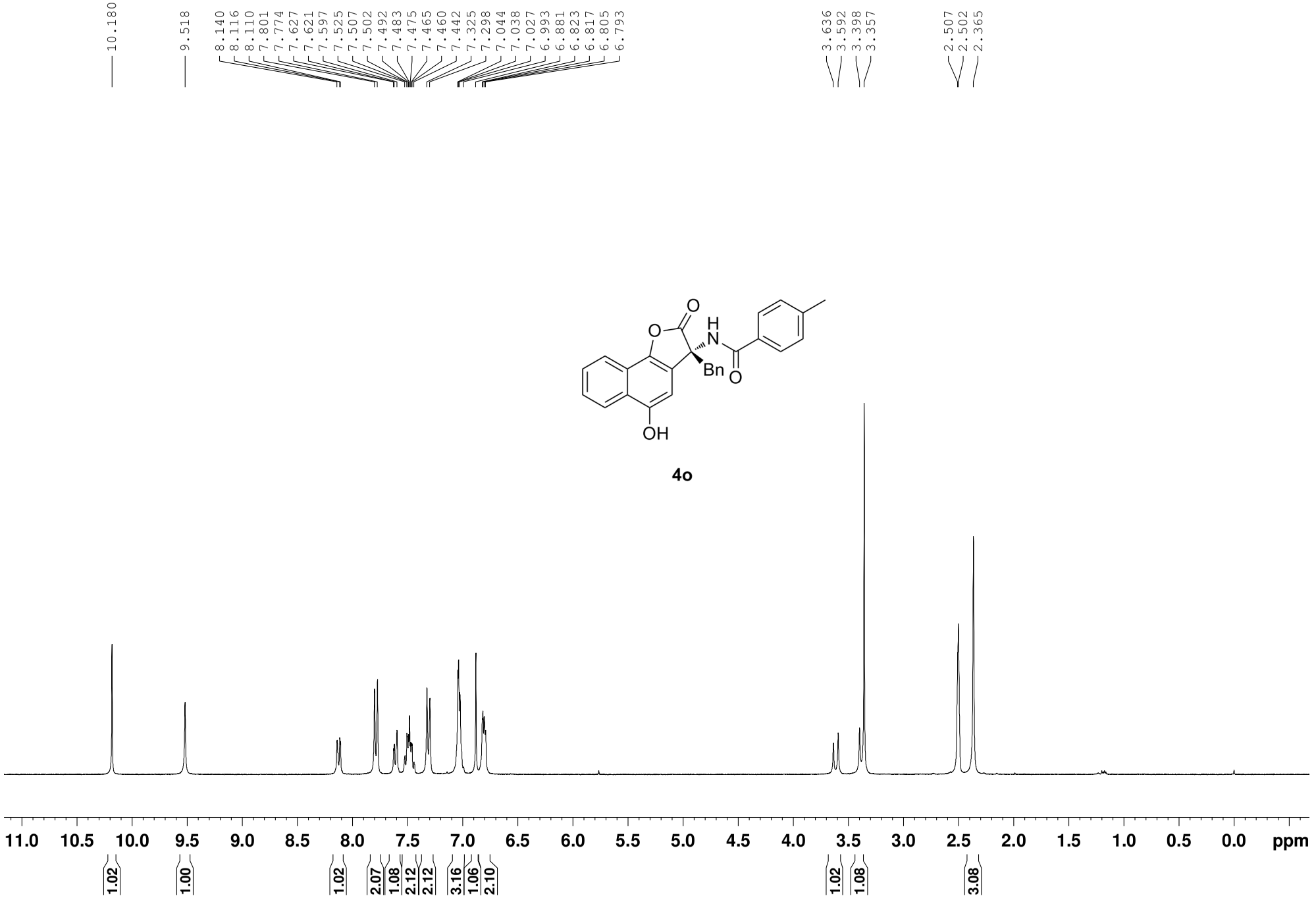
20
10
0
ppm

4o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7.465
7.460
7.442
7.325
7.298
7.044
7.038
7.027
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6.881
6.823
6.817
6.805
6.793
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3.592
3.398
3.357
2.507
2.502
2.365
O
O
H
N
Bn
O
OH
4o
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10.0
9.5
9.0
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8.0
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
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0.0
ppm
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2.12
3.16
1.06
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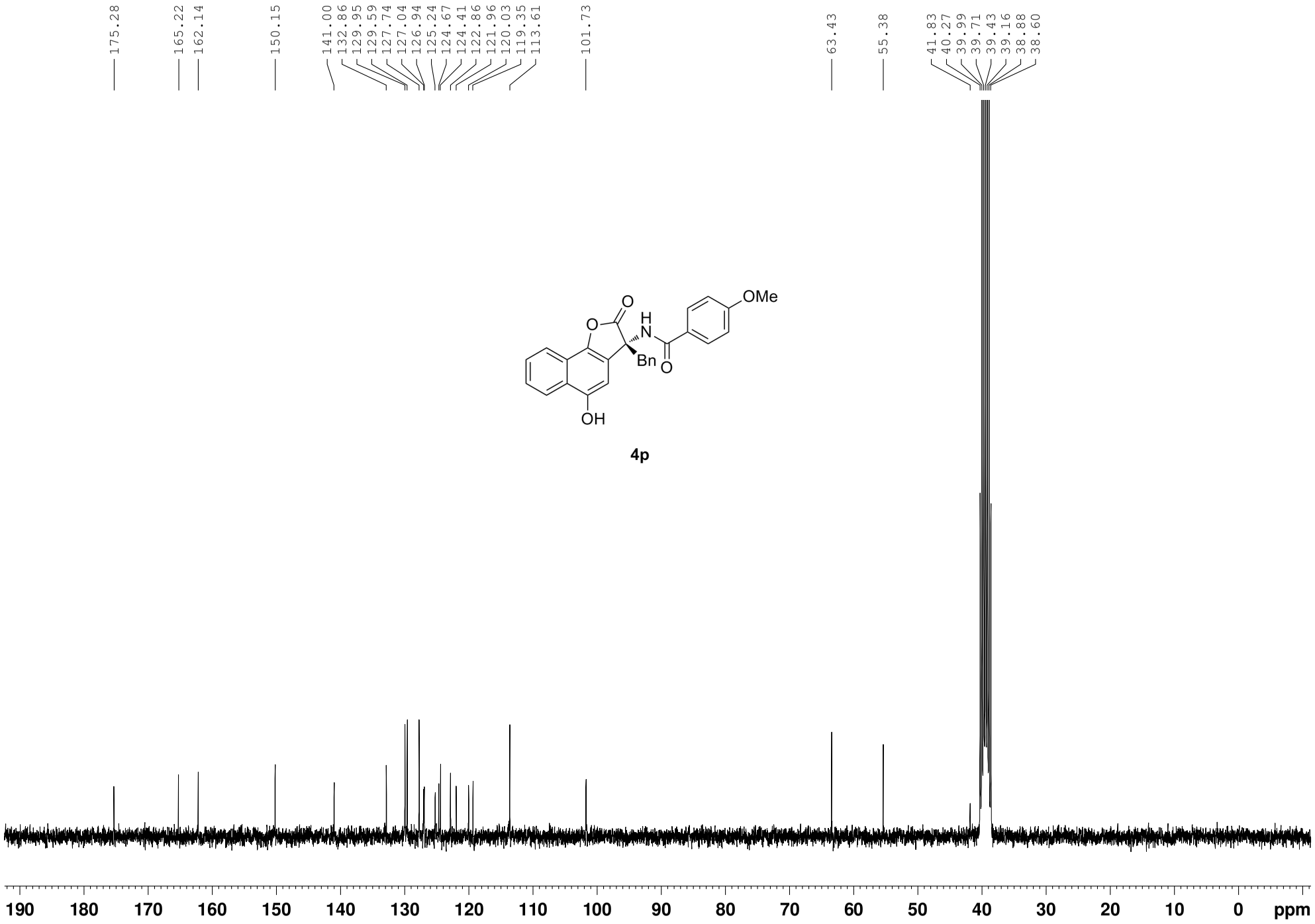
1.08
3.08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120.03
119.35
113.61
101.73
63.43
55.38
41.83
40.27
39.99
39.71
39.43
39.16
38.88
38.60
O
O
H
N
OMe
Bn
O
OH
4p
190
180
170
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140
130
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100
90
80
70
60
50
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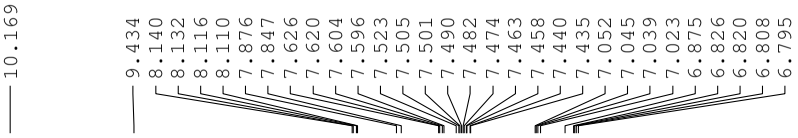
30
20
10
0
ppm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7.505
7.501
7.490
7.482
7.474
7.463
7.458
7.440
7.435
7.052
7.045
7.039
7.023
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6.808
6.795
3.819
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3.358
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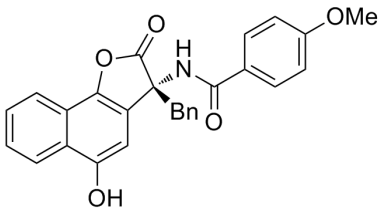
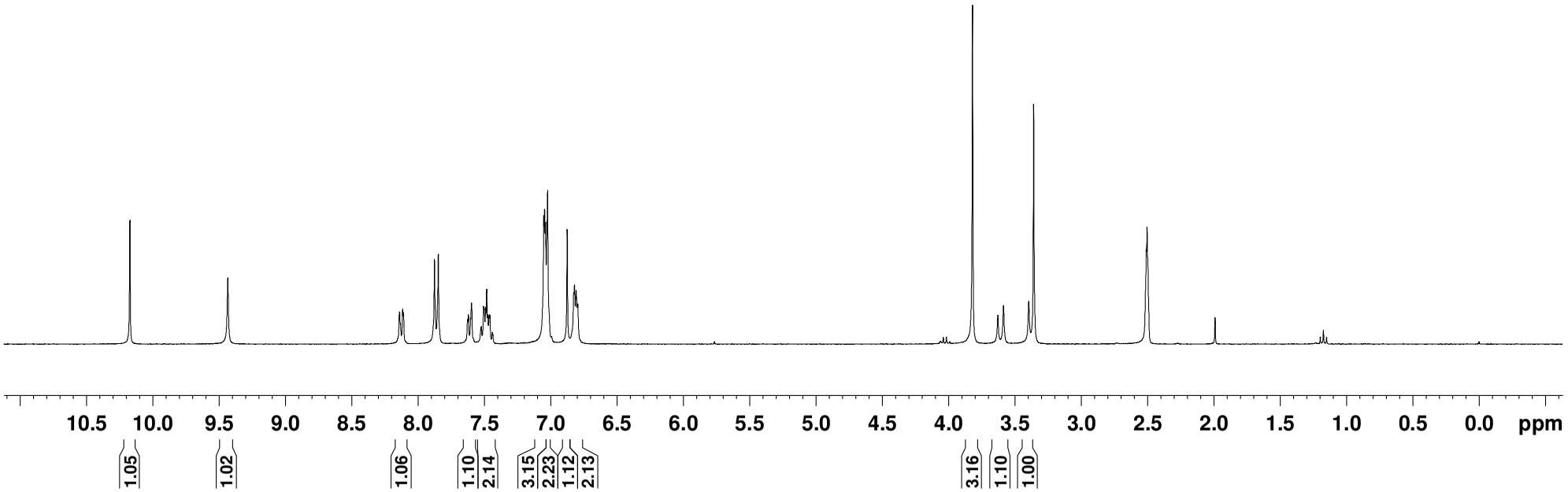
2.503


O
O
H
N
OMe
Bn
O
OH

4p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10.0
9.5
9.0
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8.0
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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
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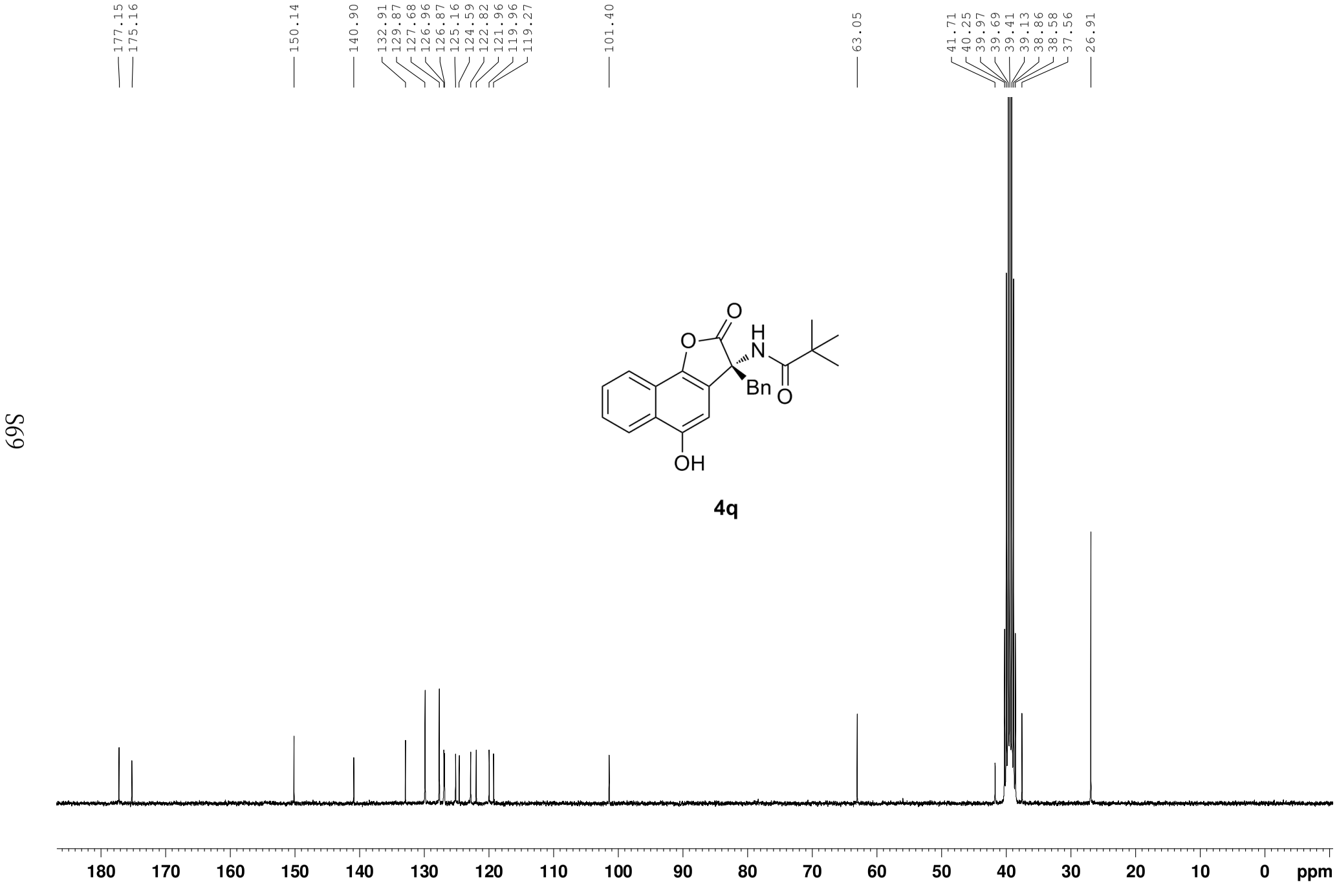
1.02
1.06
1.10
2.14
3.15
2.23
1.12
2.13
3.16
1.10
1.00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175.16
150.14
140.90
132.91
129.87
127.68
126.96
126.87
125.16
124.59
122.82
121.96
119.96
119.27
101.40
63.05
41.71
40.25
39.97
39.69
39.41
39.13
38.86
38.58
37.56
26.91
O
O
H
N
Bn
O
OH
4q
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

10.172
8.568
8.122
8.110
8.099
8.091
7.559
7.551
7.540
7.528
7.486
7.463
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7.437
6.995
6.983
6.835
6.748
6.735
6.724
3.528
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3.366
3.247
3.204
2.491
1.081
4q
ppm
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1.01
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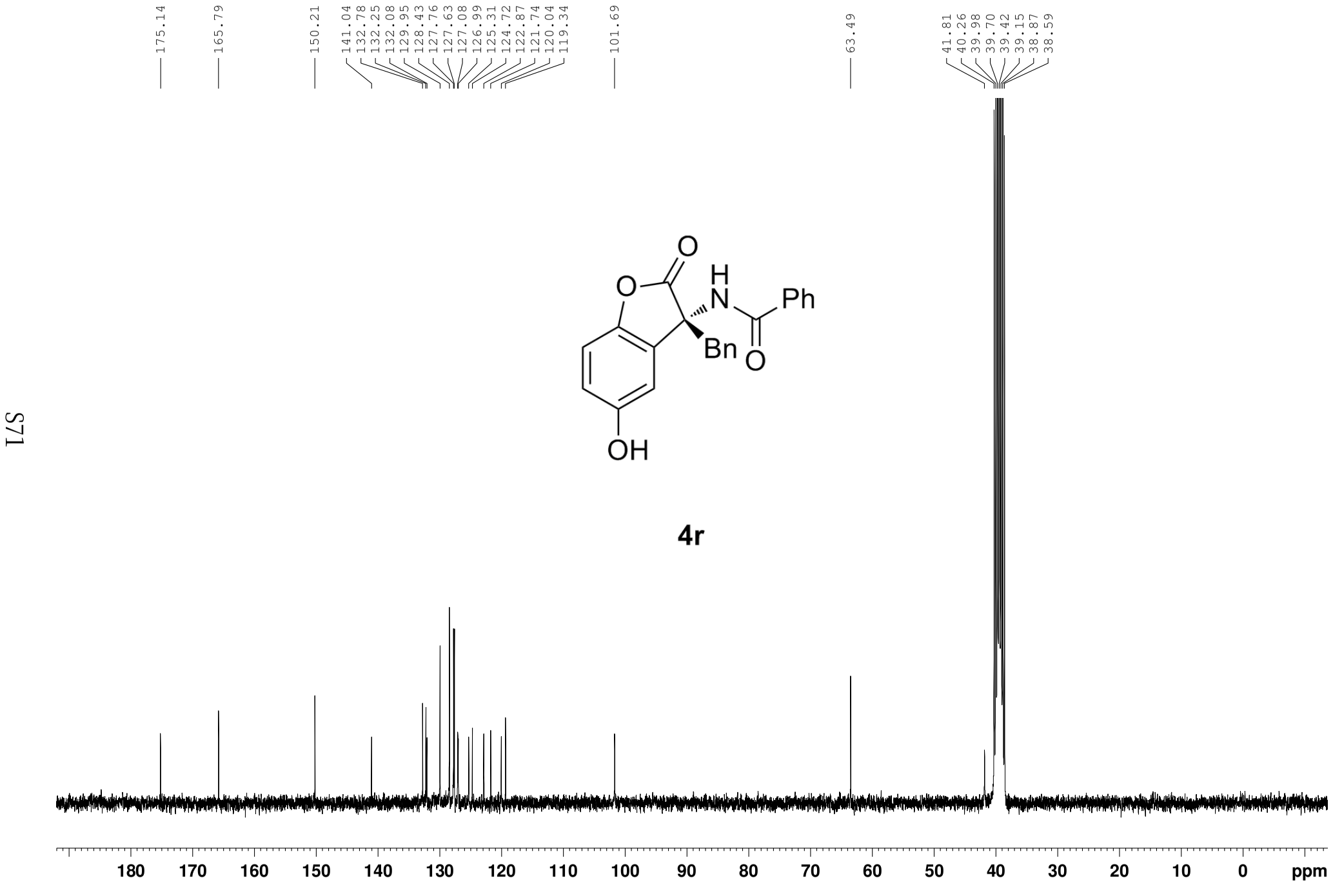
1.05
3.09
1.05
2.03
1.04
1.13
9.07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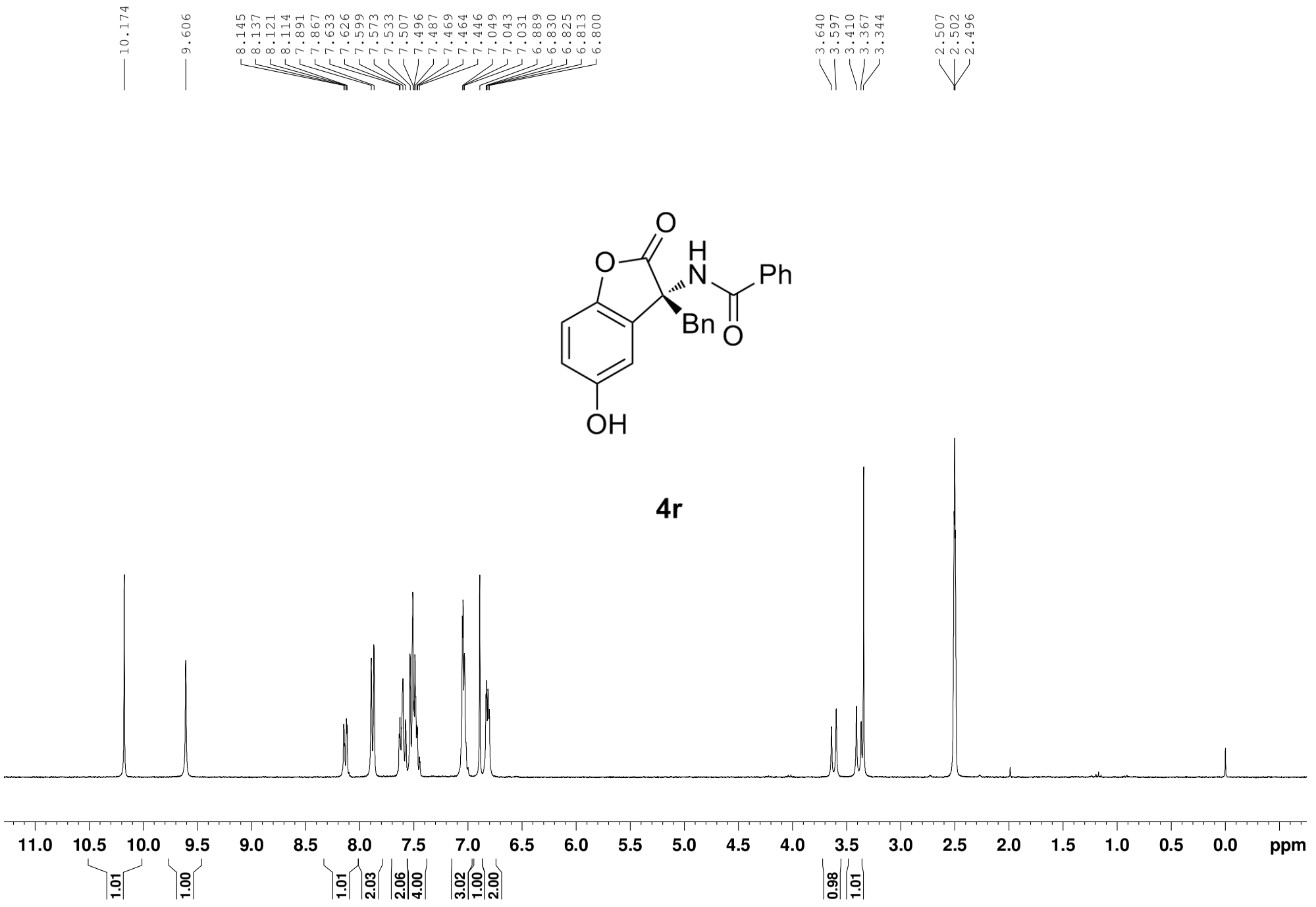
129.95
128.43
127.76
127.63
127.08
126.99
125.31
124.72
122.87
121.74
120.04
119.34
101.69
63.49
41.81
40.26
39.98
39.70
39.42
39.15
38.87
38.59
O
O
H
N
Ph
Bn
O
OH
4r
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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8.121
8.114
7.891
7.867
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7.626
7.599
7.573
7.533
7.507
7.496
7.487
7.469
7.464
7.446
7.049
7.043
7.031
6.889
6.830
6.825
6.813
6.800
3.640
3.597
3.410
3.367
3.344
2.507
2.502
2.496
O
O
H
N
Ph
Bn
O
OH
4r
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
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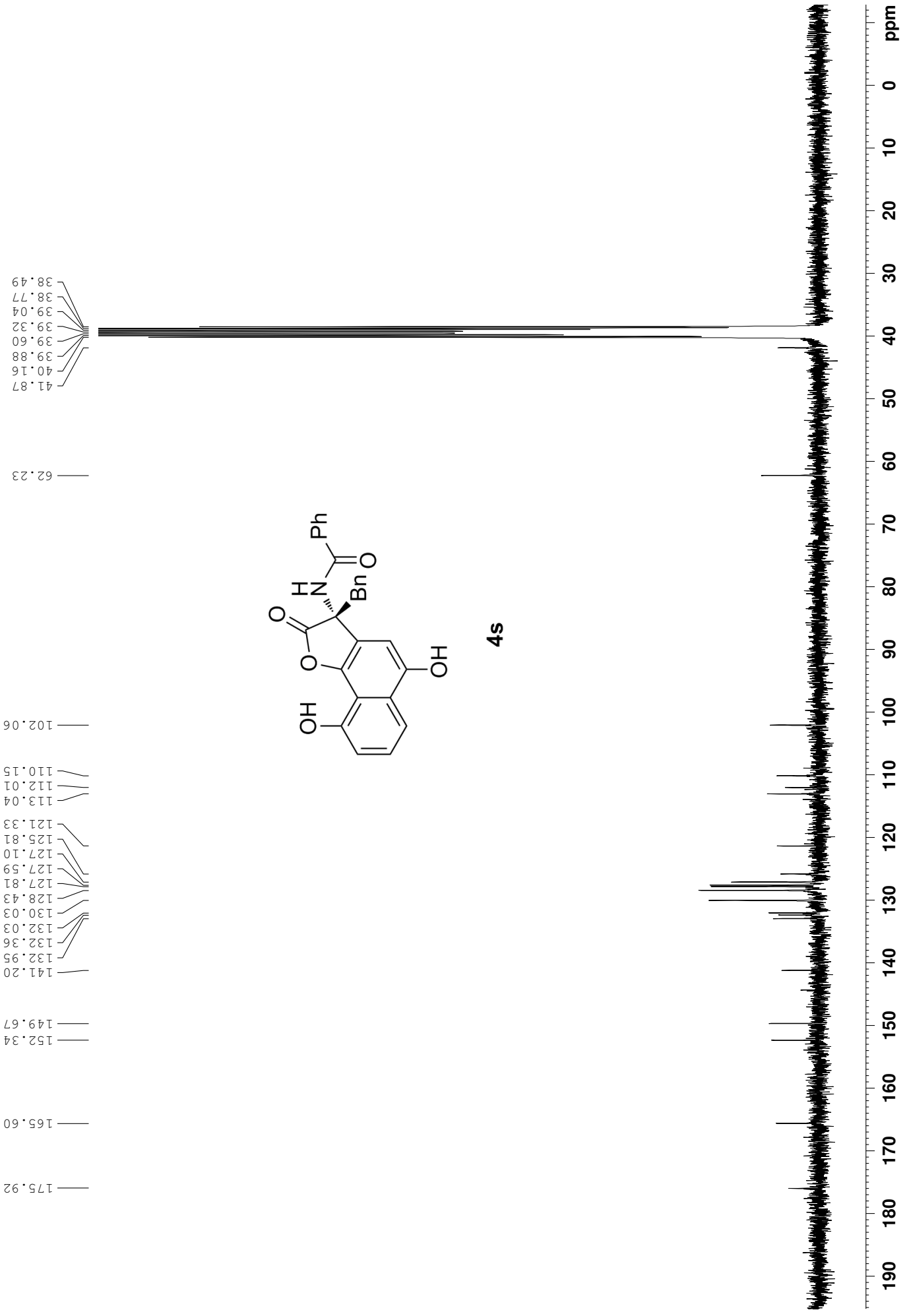
1.00
1.01
2.03
2.06
4.00
3.02
1.00
2.00
0.98
1.01


ppm
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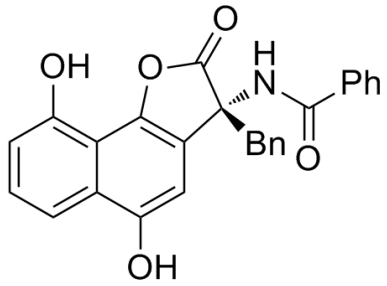
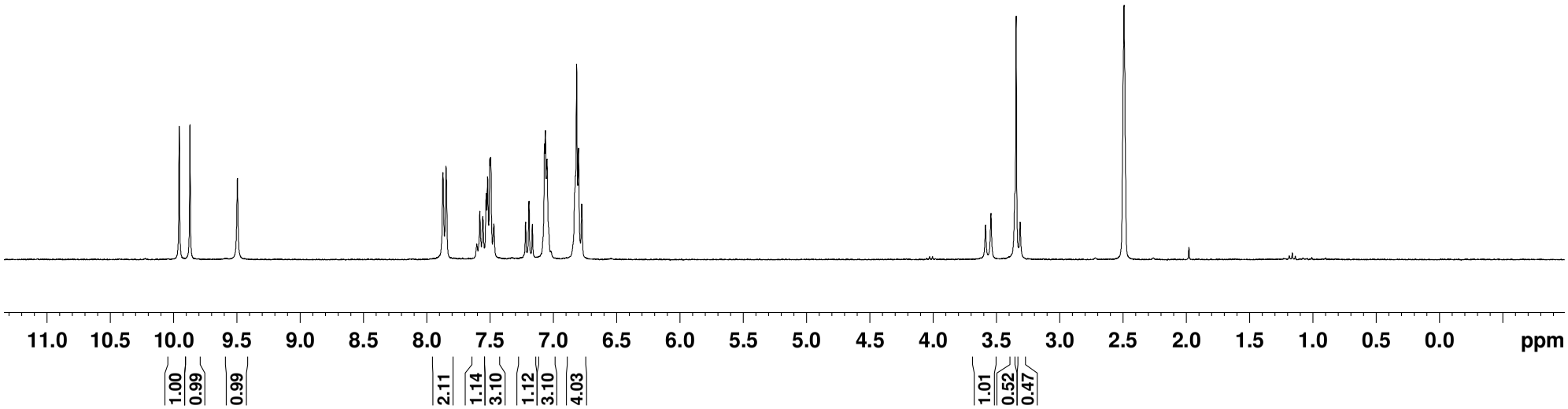
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190
38.49
38.77
39.04
39.32
39.60
39.88
40.16
41.87
62.23
102.06
110.15
112.01
113.04
121.33
125.81
127.10
127.59
127.81
128.43
130.03
132.03
132.36
132.95
141.20
149.67
152.34
165.60
175.92
Ph
O
H
N
Bn
O
O
O
OH
OH
4s

9.952
9.867
9.492
7.872
7.847
7.604
7.580
7.556
7.530
7.519
7.500
7.494
7.470
7.218
7.192
7.165
7.069
7.062
7.049
7.019
6.824
6.815
6.800
6.774
3.585
3.542
3.343
3.311
2.490



4s



Cell culture

Both human leukemia HL-60 cells and human cervical cancer Hela cells were maintained in PRMI 1640 medium (Gibco) supplemented with 10% fetal bovine serum (FBS). All the cells were maintained at 37 ℃ under a humidified atmosphere of 5% CO_2.

General procedure for cytotoxicity testing of the compounds / resazurin reduction assay

The cytotoxicity of the studied compounds was determined using resazurin reduction assay. Briefly, HL-60 and Hela cells were seeded in 96-well plate with 5×10^3 cells/well 24 h before treatment. Then different concentrations of compounds were treated for 48 h in a humidified 5% CO_2 atmosphere at 37 ℃. Phosphate buffered saline (PBS) buffer alone treated cells were the control. After that, 10 μL of 5 mg/mL Resazurin solution was added into each well, and then incubated for 2 h at 37 ℃. The fluorescence intensity was measured using FlexStation 3 (Molecular Devices) at excitation/emission wavelength of 555/585 nm. Each assay was done at least three times, with three replicates each. IC_{50} values represent the compound's concentrations required to inhibit 50% of cell proliferation and were calculated by GraphPad Prism.

General procedure for antibacterial activity testing of the compounds

The MIC (minimum inhibitory concentration) values were determined using a standard serial dilution method with minor modification. The antibacterial activity was tested in Mueller-Hinton Broth(MH-broth) against *S. aureus* ATCC 29213 and *B. subtilis* ATCC 23857. The final concentrations of these compounds were ranged from 1-256 μM with MH-broth. The inoculum sizes contained approximately 1×10^5 CFU mL^{-1}. MIC values were observed after 18h for *S. aureus* ATCC 29213 and *B. subtilis* ATCC 23857 at 37 ℃. The MIC value was defined as the lowest concentration of the antibacterial angent, which was shown no visible turbidity comparing with drug-free control group.