Supporting information

Efficient Synthesis of Isochromanones and Isoquinolines via $Yb(OTf)_3$-Catalyzed Tandem Oxirane/Aziridine Ring Opening/ Friedel-Crafts Cyclization.

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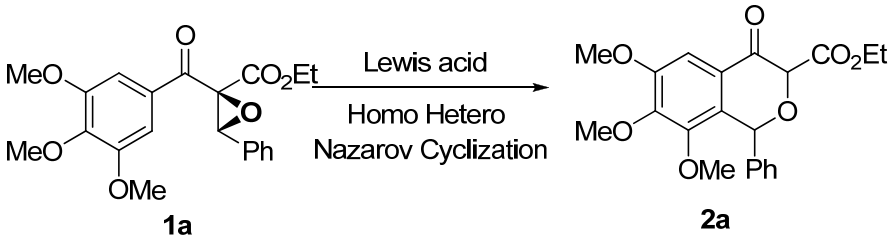
Contents

SI-Table 1. Screening reaction conditions [a].



1a **2a**

Entry	Catalyst	Solvent	Time/h	Yield (%)[b]
1	$Sc(OTf)_3$	CH_2Cl_2	10	73
2	$Cu(OTf)_2$	CH_2Cl_2	10	Trace
3	$In(OTf)_3$	CH_2Cl_2	10	72
4	$Yb(OTf)_3$	CH_2Cl_2	10	99
5	$Y(OTf)_3$	CH_2Cl_2	16	43
6	$Fe(OTf)_3$	CH_2Cl_2	9	sluggish
7	$Sn(OTf)_2$	CH_2Cl_2	11	sluggish
8	$Mg(OTf)_2$	CH_2Cl_2	16	trace
9[c]	$Yb(OTf)_3$	CH_2Cl_2	10	83
10	$Yb(OTf)_3$	toluene	15	41
11	$Yb(OTf)_3$	DCE	10	57
12	$Yb(OTf)_3$	DMF	9	trace
13	$Yb(OTf)_3$	THF	10	trace
14[d]	$Yb(OTf)_3$	CH_2Cl_2	10	sluggish

[a] Reaction conditions: **1a** (racemic, 0.2 mmol), 10 mol % of catalyst, and 70 mg of activated 4 Å MS in 3 mL of solvent at room temperature. [b] Determined by ^{1}H NMR (CH_2Br_2 as a standard). [c] 5 mol % of catalyst was added. [d] No 4 Å MS was added.

General information

Infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer. ^{1}H NMR spectra, ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer in chloroform-d_3. All signals are reported in ppm with the internal TMS signal at 0 ppm as a standard. The data is being reported as (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration). All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware with magnetic stirring. $ClCH_2CH_2Cl$ (DCE), CH_2Cl_2 (DCM) were freshly distilled from CaH_2; toluene was freshly distilled from sodium metal prior to use. Solid aldehydes were used directly without purification. Lewis-acid purchased from Alfa or Aldrich were used directly. 4 Å molecular sieves purchased from Sinopharm Chemical Reagent Co., Ltd were powdered and dried at 300 ºC in muffle furnace for 8-10 hours prior to use. α, β-Unsaturated-1,3-carboxylates[1]

and oxiranyl carboxylates **1a-1l** and **1a'-1k'** [2] were prepared according to the literatures. The procedure of methylation of the compounds **2a-2l** and ethylation of the intermediate **2a** is same as the reference 3. Ethyl 2-bromo-3-oxo-3-(3,4,5-trimethoxyphenyl)propanoate[5] and aziridines (**1n-1r**)[6] were also prepared according to literatures.

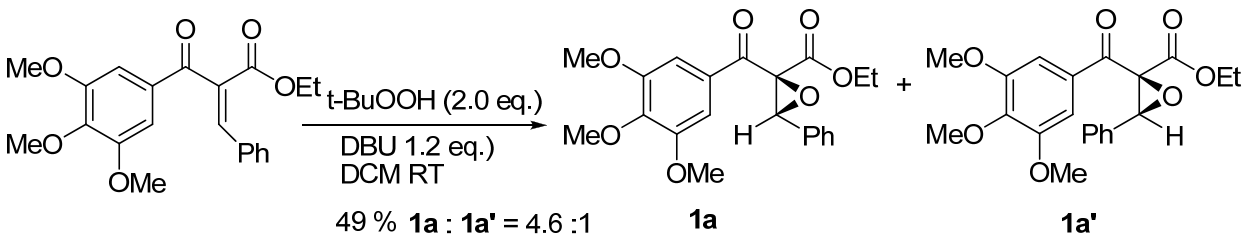
Experimental Procedures and Characterization Data

Synthesis of substrates 1.

General Procedure for expoxidation of α-arylidene β-keto esters.

In a flame dried flask, a solution of the *α*-arylidene *β*-keto ester in DCM was slowly added to a solution of *t*-BuOOH (2 equiv, 65% aqueous), DBU (1.2 equiv.) in DCM at 0 ^{o} under N_2 atmosphere. And then the reaction temperature was then allowed to room temperature. After the reaction was complete which was determined by TLC analysis, the reaction mixture was treated with saturated aqueous solution of $Na_2S_2O_3$•$5H_2O$ (5 mL) and stirred for another 5 mins. The reaction mixtire was extracted three times with DCM. The combined organic phase was washed with brine and then dried with Na_2SO_4. After filteration and evaporated, the residue was purified by column chromatography on silica gel.

1. Ethyl 3-phenyl-2-(3,4,5-trimethoxybenzoyl)oxirane-2-carboxylate(1a/1a').

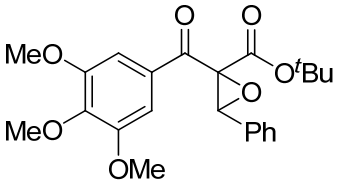


Yield 49%, dr = 4.6 : 1.

The major isomer, **1a** as white solid , m.p. 78-80 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 7.2 Hz, 2 H), 7.45- 7.30 (m, 5 H), 4.61 (s, 1 H), 4.10-3.90 (m, 11 H), 0.91 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8, 164.8, 153.1, 143.4, 131.8, 129.0, 128.7, 128.0, 126.4, 106.5, 67.7, 62.0, 61.7, 60.8, 56.1, 13.6. MS (EI): m/z (%) = 386 (M^+, 14.64), 195 (100). HRMS calcd for $C_{21}H_{22}O_7$: 386.1366, found: 386.1364. IR (neat) *ν*/cm^{-1} 2975, 2909, 2841, 2657, 2251, 1957, 1744, 1679, 1582, 1503, 1452, 1246, 998, 825, 700, 614.

The minor isomer, **1a'** as light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.21 (m, 5 H), 7.16 (s, 2 H), 4.69 (s, 1 H), 4.29 (q, *J* = 7.2 Hz, 2 H), 3.92 (s, 3 H), 3.87 (s, 6 H), 1.24 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.5, 166.5, 153.0, 143.4, 132.3, 130.4, 129.1, 128.5, 126.3, 106.4, 65.9, 63.1, 62.9, 60.9, 56.2, 13.9. MS (EI): m/z (%) = 386 (M^+, 38.54), 195 (100). HRMS calcd for $C_{21}H_{22}O_7$: 386.1366, found: 386.1368. IR (neat) *v*/cm^{-1} 2998, 2942, 2839, 2255, 1746, 1683, 1584, 1502, 1458, 1339, 1249, 1123, 1000, 858, 700, 612.

2. *t*ert-butyl 3-phenyl-2-(3,4,5-trimethoxybenzoyl)oxirane-2-carboxylate (1b/1b').



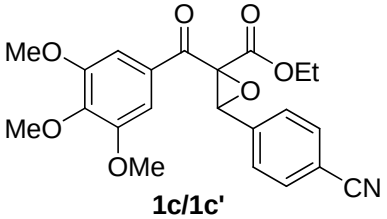
1b/1b'

Yield 55%, dr = 1 : 1,

1b as white solid, m.p. 99-101 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 6.8 Hz, 2 H), 7.45-7.30 (m, 5 H), 4.62 (s, 1 H), 3.95-3.94 (m, 9 H), 1.12 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.2, 163.9, 153.0, 143.2, 132.1, 129.3, 128.5, 127.9, 126.5, 106.4, 83.5, 67.4, 61.3, 60.8, 56.1, 27.3. MS (EI): m/z (%) = 414 (M^+, 9.07), 195 (100). HRMS calcd for $C_{23}H_{26}O_7$: 414.1679, found: 414.1681. IR (neat) *v*/cm^{-1} 3037, 2939, 2841, 2655, 1958, 1747, 1686, 1583, 1504, 1460, 1340, 1251, 1127, 996, 861, 714, 613.

1b' as white solid, m.p. 61-64 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.24 (m, 5 H), 7.10 (s, 2 H), 4.67 (s, 1 H), 3.90 (s, 3 H), 3.86 (s, 6 H), 1.39 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 165.1, 152.7, 142.8, 132.2, 130.4, 128.7, 128.2, 126.0, 105.7, 84.1, 66.4, 62.5, 60.6, 55.9, 27.4. MS (EI): m/z (%) = 414 (M^+, 4.63), 57 (100). HRMS calcd for $C_{23}H_{26}O_7$: 414.1679, found: 414.1680. IR (neat) *v*/cm^{-1} 2982, 2939, 2842, 2639, 1972, 1729, 1683,1585, 1502, 1458, 1340, 1236, 1127, 995, 862, 711.

3. Ethyl 3-(4-cyanophenyl)-2-(3,4,5-trimethoxybenzoyl)oxirane-2-carboxylate (1c/1c').



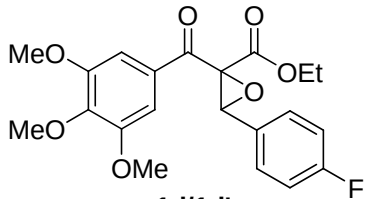
1c/1c'

Yield 43%, dr = 3.9 : 1,

1c as white solid, m.p. 115-118 °C**,** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2 H), 7.66 (d, *J* = 8.0 Hz, 2H), 7.36 (s, 2 H), 4.66 (s, 1 H), 4.06-3.91 (m, 11 H), 0.93 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9, 164.3, 153.1, 143.7, 137.1, 131.8, 128.6, 127.4, 118.1, 112.6, 106.5, 67.6, 62.3, 60.8, 60.8, 56.1, 13.6. MS (EI): m/z (%) = 411 (M^+, 12.21), 195 (100). HRMS calcd for $C_{22}H_{21}NO_7$: 411.1318, found: 400.1319. IR (neat) *v*/cm^{-1} 3097, 2925, 2853, 2649, 2231, 1949, 1745, 1685, 1582, 1460, 1414, 1343, 1250, 1124, 1000, 806, 771.

1c' as yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 7.17 (s, 2 H), 4.70 (s, 1 H), 4.31 (q, *J* = 7.2 Hz, 2 H), 3.94 (s, 3 H), 3.89 (s, 6 H), 1.25 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.7, 166.0, 153.2, 144.0, 137.8, 132.2, 129.8, 127.1, 118.2, 112.9, 106.5, 65.9, 63.3, 61.9, 61.0, 56.3, 13.9. MS (EI): m/z (%) = 411 (M^+, 1.70), 84 (100). HRMS calcd for $C_{22}H_{21}NO_7$: 411.1318, found: 400.1317. IR (neat) *v*/cm^{-1} 3097, 2941, 2840, 2651, 2230, 1939, 1747, 1684, 1583, 1503, 1461, 1416, 1340, 1251, 999, 855, 730.

4. Ethyl 2-(3,4,5-trimethoxybenzoyl)-3-(4-fluorophenyl)oxirane-2-carboxylate (1d/1d').



1d/1d'

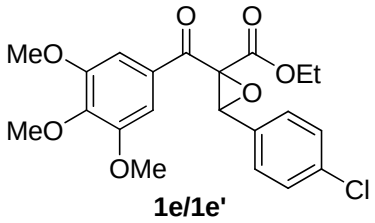
Yield 55%, dr = 4.3 : 1,

1d as white solid, m.p. 100-103 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.50 (m, 2 H), 7.38 (s, 2 H), 7.08 (t, *J* = 8.0 Hz, 2 H), 4.59 (s, 1 H), 4.04-3.99 (m, 2 H), 3.95 (s, 9 H), 0.94 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 162.9 (d, $J_{C,F}$ = 246 Hz), 161.7, 153.2, 143.6, 129.0, 128.4 (d, $J_{C,F}$ = 8 Hz), 127.7, 115.2 (d, $J_{C,F}$ = 22 Hz), 106.6, 67.7, 62.2, 61.2, 60.9, 56.2, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$): -112.4 ppm. MS (EI): m/z (%) = 404 (M^+, 22.51), 195 (100). HRMS calcd for $C_{21}H_{21}O_7F$: 404.1271, found: 404.1275. IR (neat) *v*/cm^{-1} 2986, 2841, 2256, 1746, 1680, 1585, 1505, 1460, 1419, 1332, 1235, 998, 829, 698, 629.

1d' as yellow solid, m.p. 73-75 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19-7.17 (m, 4 H), 6.95 (t, *J* = 7.6 Hz, 2 H), 4.67 (s, 1 H), 4.29 (q, *J* = 6.8 Hz, 2 H), 3.93 (s, 3 H), 3.88 (s, 6 H), 1.24 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 166.4, 163.0 (d, $J_{C,F}$ = 247

Hz), 161.8, 153.0, 143.6, 130.2, 128.2, 128.1, 115.7, 115.6 (d, $J_{C,F}$ = 21), 106.4, 65.9, 62.9, 62.4, 60.9, 56.3, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$): -111.9 ppm. MS (EI): m/z (%) = 404 (M^+, 7.91), 107 (100). HRMS calcd for $C_{21}H_{21}O_7F$: 404.1271, found: 404.1270. IR (neat) ν/cm^{-1} 3080, 2989, 2942, 2840, 2258, 1742, 1684, 1584, 1509, 1464, 1417, 1340, 1226, 1000, 841, 715, 676.

5. Ethyl 3-(4-chlorophenyl)-2-(3,4,5-dimethoxybenzoyl)oxirane-2-carboxylate (1e/1e').



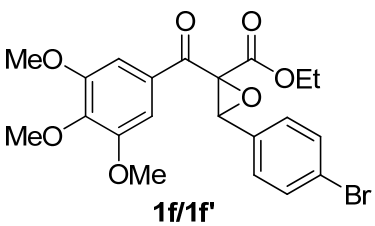
1e/1e'

Yield 43%, dr = 3.1 :1

1e as white solid, m.p. 85-87 °C**,** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.0 Hz, 2 H), 7.40-7.30 (m, 4 H), 4.59 (s, 2 H), 4.08-3.98 (m, 2 H), 3.95 (s, 3 H), 3.93 (s, 6 H), 0.94 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3, 164.5, 153.0, 143.4, 134.6, 130.3, 128.7, 128.2, 127.9, 106.4, 67.5, 62.1, 61.0, 60.7, 56.0, 13.5. MS (EI): m/z (%) = 422 (M+2, 4.85), 420 (M^+, 15.28), 195 (100). HRMS calcd for $C_{21}H_{21}O_7Cl$: 420.0976, found: 420.0976. IR (neat) ν/cm^{-1} 3089, 3000, 2941, 2838, 2662, 1901, 1745, 1678, 1582, 1504, 1458, 1416, 1235, 1003, 825, 742, 701.

1e' as yellow solid, m.p. 96-97 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 7.6 Hz, 2H), 7.20-7.10 (m, 4 H), 4.66 (s, 1 H), 4.29 (q, J = 7.2 Hz, 2 H), 3.93 (s, 3 H), 3.88 (s, 6 H), 1.24 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2, 166.3, 153.0, 143.5, 135.0, 130.9, 130.1, 128.7, 127.6, 106.3, 65.8, 63.0, 62.3, 60.9, 56.2, 13.9. MS (EI): m/z (%) = 422 (M+2, 4.62), 420 (M^+, 12.84), 89 (100). HRMS calcd for $C_{21}H_{21}O_7Cl$: 420.0976, found: 420.0979. IR (neat) v/cm-1 3095, 2999, 2980, 2937, 2838, 2838, 2656, 1934, 1741, 1680, 1586, 1503, 1464, 1420, 1250, 1131, 1006, 851, 710.

6. Ethyl 3-(4-bromophenyl)-2-(3,4,5-trimethoxybenzoyl)oxirane-2-carboxylate (1f/1f').



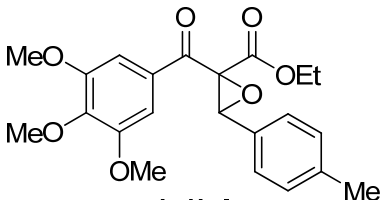
1f/1f'

Yield 73%, dr = 2.8 : 1,

1f as white solid, m.p. 93-94 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 6.4 Hz, 2 H), 7.42-7.34 (m, 4 H), 4.55 (s, 1 H), 4.10-3.88 (m, 11 H), 0.95 (m, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 164.7, 153.2, 143.7, 131.4, 131.0, 128.9, 128.3, 123.0, 106.7, 67.7, 62.3, 61.3, 61.0, 56.3, 13.8. MS (EI): m/z (%) = 466 (M+2, 9.13), 464 (M^+, 9.69), 195 (100). HRMS calcd for $C_{21}H_{21}O_7Br$: 464.0471, found: 464.0471. IR (neat) v/cm-1 3090,2941, 2843, 2656, 1915, 1752, 1691, 1582, 1503, 1446, 1418, 1335, 1237, 1124, 1011, 855, 765, 702.

1f' as white solid, m.p. 132-134 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.0 Hz, 2 H), 7.17 (s, 2 H), 7.08 (d, *J* = 8.0 Hz, 2 H), 4.64 (s, 1 H), 4.29 (q, *J* = 7.2 Hz, 2 H), 3.93 (s, 3 H), 3.88 (s, 6 H), 1.24 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2, 166.3, 153.1, 143.7, 131.7, 131.4, 130.1, 127.9, 123.2, 106.4, 65.8, 63.0, 62.4, 60.9, 56.3, 13.9. MS (EI): m/z (%) = 466 (M+2, 6.10), 464 (M^+, 7.13), 195 (100). HRMS calcd for $C_{21}H_{21}O_7Br$: 464.0471, found: 464.0472. IR (neat) *v*/cm-1 3093, 2938, 2839, 2661, 1934, 1739, 1678, 1586, 1503, 1463, 1419, 1342, 1252, 1131, 1010, 848, 764, 709.

7. Ethyl 2-(3,4,5-trimethoxybenzoyl)-3-p-tolyloxirane-2-carboxylate (1g/1g').



1g/1g'

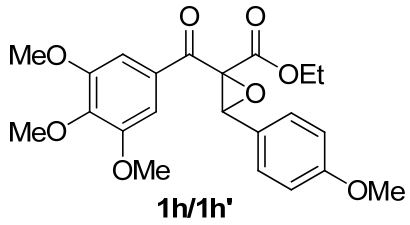
Yield 32%, dr = 7.5 : 1,

1g as white solid, m.p. 99-101 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.34 (m, 4 H), 7.18-7.17 (d, *J* = 7.6 Hz, 2 H), 4.56 (s, 1 H), 4.05- 3.96 (m, 2 H), 3.95 (s, 3H), 3.94 (s, 9 H), 2.36 (s, 3 H), 0.94 (t, *J* =6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.1, 165.0, 153.2, 143.6, 138.7, 129.2, 129.0, 128.9, 128.4 , 126.5, 106.8, 67.9, 62.1, 62.0, 61.0, 56.3, 21.2, 13.7. MS (EI): m/z (%) = 400 (M^+, 29.92), 43 (100). HRMS calcd for $C_{22}H_{24}O_7$: 400.1522, found: 400.1524. IR (neat) *v*/cm^{-1} 3103, 3014, 2944, 2841, 2662, 1988, 1722, 1675, 1580, 1504, 1457, 1416, 1332, 1233, 1125, 1000, 861, 773.

1g' as white solid, m.p. 92-95 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 2 H), 7.09 (d, *J* = 6.8 Hz, 2 H), 7.05 (d, *J* = 6.8 Hz, 2H), 4.67 (s, 1 H), 4.28 (q, *J* = 6.8 Hz, 2 H), 3.92 (s, 3 H), 3.87 (s, 6 H), 2.26 (s, 3 H), 1.23 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6, 166.5, 152.9, 143.2, 138.9, 130.3, 129.1, 129.1, 126.1, 106.2, 65.8, 63.1, 62.7, 60.8, 56.1,

21.1, 13.8. MS (EI): m/z (%) = 400 (M^+, 0.57), 195 (100). HRMS calcd for $C_{22}H_{24}O_7$: 400.1522, found: 400.1523. IR (neat) ν/cm^{-1} 2979, 2841, 2647, 1937, 1741, 1683, 1587, 1503, 1464, 1419, 1340, 1248, 1007, 830, 707.

8. Ethyl 2-(3,4,5-trimethoxybenzoyl)-3-(4-methoxyphenyl)oxirane-2-carboxylate (1h/1h').



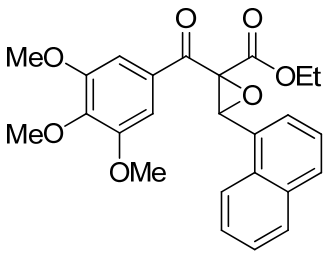
1h/1h'

Yield 52%, dr = 2.3 : 1,

1h as white solid, m.p. 112-114 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 7.6 Hz, 2 H), 7.39 (s, 2 H), 6.90 (d, J = 7.6 Hz, 2 H), 4.54 (s, 1 H), 4.04-4.00 (m, 2 H), 3.95 (s, 3 H), 3.94 (s, 6 H), 3.82 (s, 3 H), 0.96 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.1, 165.0, 160.1, 153.2, 143.5, 129.2, 127.9, 123.9, 113.7, 106.7, 68.0, 62.1, 61.9, 61.0, 56.3, 55.3, 13.8. MS (EI): m/z (%) = 416 (M^+, 11.79), 195 (100). HRMS calcd for $C_{22}H_{24}O_8$: 416.1471, found: 416.1470. IR (neat) ν/cm^{-1} 3101, 3035, 2941, 2839, 2669, 1721, 1672, 1611, 1580, 1503, 1414, 1336, 1246, 1129, 996, 834, 758, 664.

1h' as yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (s, 2 H), 7.12 (d, J = 8.0 Hz, 2 H), 6.76 (d, J = 8.0 Hz, 2 H), 4.64 (s, 1H), 4.26 (q, J = 7.2 Hz, 2 H), 3.92 (s, 3H), 3.87 (s, 6 H), 3.74 (s, 3 H), 1.23 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8, 166.6, 160.1, 153.0, 143.4, 130.4, 127.6, 124.1, 114.0, 106.4, 66.0, 63.1, 62.8, 60.9, 56.2, 55.2, 13.9. MS (EI): m/z (%) = 416 (M^+, 7.49), 195 (100). HRMS calcd for $C_{22}H_{24}O_8$: 416.1471, found: 416.1475. IR (neat) ν/cm^{-1} 3076, 2940, 2840, 2647, 1996, 1741, 1685, 1582, 1506, 1461, 1416, 1332, 1124, 1001, 833, 763.

9. Ethyl 3-(naphthalen-1-yl)-2-(3,4,5-trimethoxybenzoyl)oxirane-2-carboxylate (1i/1i').



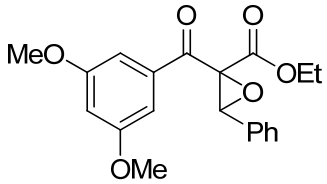
1i/1i'

Yield 61%, dr= 3.3 :1,

1i as white solid, m.p. 106-108 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.4 Hz, 1 H), 7.85 (t, *J* = 9.6 Hz, 2 H), 7.69 (d, *J* = 6.4 Hz, 1 H), 7.60 (t, *J* = 6.8 Hz, 1 H), 7.53-7.44 (m, 2 H), 7.44 (s, 2 H), 5.12 (s, 1 H), 3.95 (m, 3 H), 3.94 (s, 6 H), 3.83-3.72 (m, 2 H), 0.53 (t, *J* = 6.0 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.0, 164.9, 153.2, 143.6, 132.8, 130.6, 129.0, 128.8, 128.4, 127.8, 126.6, 126.0, 124.8, 124.3, 123.1, 106.5, 66.7, 61.8, 60.83, 60.79, 56.1, 13.2. MS (EI): m/z (%) = 436 (M^+, 10.15), 195 (100). HRMS calcd for $C_{25}H_{24}O_7$: 436.1522, found: 436.1523. IR (neat) *v*/cm^{-1} 3052, 2941, 2581, 1948, 1745, 1670, 1584, 1503, 1461, 1417, 1335, 1248, 1127, 999, 784, 674.

1i' as white solid, m.p. 114-116 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 8.0 Hz, 1 H), 7.83 (d, *J* = 8.0 Hz, 1 H), 7.73 (d, *J* = 7.2 Hz, 1 H), 7.59 (t, *J* = 7.2 Hz, 1 H), 7.51 (t, *J* = 7.2 Hz, 1 H), 7.29 (t, *J* = 8.4 Hz, 1 H), 7.31-7.27 (m, 2 H), 7.05 (s, 2 H), 5.36 (s, 1 H), 4.35 (q, *J* = 6.8 Hz, 2 H), 3.83 (s, 3 H), 3.74 (s, 6 H), 1.27 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.2, 166.6, 152.7, 143.0, 133.1, 130.9, 130.2, 129.1, 128.8, 127.6, 126.6, 125.9, 125.0, 123.2, 122.3, 106.1, 66.3, 62.8, 61.0, 60.7, 56.0, 13.8. MS (EI): m/z (%) = 436 (M^+, 11.40), 139 (100). HRMS calcd for $C_{25}H_{24}O_7$: 436.1522, found: 436.1529. IR (neat) *v*/cm^{-1} 3047, 2943, 2838, 2639, 1970, 1747, 1674, 1584, 1503, 1455, 1416, 1337, 1238, 1125, 996, 775, 709.

10. **Ethyl 2-(3,5-dimethoxybenzoyl)-3-phenyloxirane-2-carboxylate (1j/1j').**



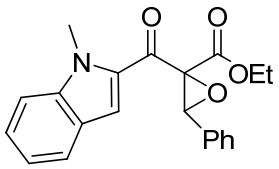
1j/1j'

Yield 50%, dr= 6.9 : 1.

1j as white solid, m.p. 88-91 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 6.8 Hz, 2 H), 7.39-7.34 (m, 3 H), 7.24 (s, 2 H), 6.71 (s, 1 H), 4.60 (s, 1 H), 4.05- 3.90 (m, 2 H), 3.85 (s, 6 H), 0.90 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1, 164.7, 161.0, 136.0, 131.9, 128.8, 128.2, 126.6, 107.1, 106.7, 67.6, 62.1, 61.9, 55.6, 13.7. MS (EI): m/z (%) = 356 (M^+, 17.58), 165 (100). HRMS calcd for $C_{20}H_{20}O_6$: 356.1260, found: 356.1258. IR (neat) *v*/cm^{-1} 2998, 2915, 2661, 1968, 1754, 1684, 1592, 1455, 1359, 1242, 1211, 1175, 1043, 858, 777, 669.

1j' as yellow oil**,** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (s, 5 H), 6.99 (s, 2 H), 6.61 (s, 1 H), 4.72 (s, 1 H), 4.26 (q, *J* = 6.8 Hz, 2 H), 3.76 (s, 6 H), 1.20 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) 189.5, 166.4, 160.7, 137.0, 132.1, 129.0, 128.4, 126.3, 106.5, 106.4, 66.0, 63.0, 62.8, 55.5, 13.8. MS (EI): m/z (%) = 356 (M^+, 13.88), 165 (100). HRMS calcd for $C_{20}H_{20}O_6$: 356.1260, found: 356.1261. IR (neat) *v*/cm^{-1} 3092, 2940, 2841, 2651, 1964, 1746, 1692, 1593, 1457, 1353, 1252, 1205, 1157, 1015, 853, 788, 699.

11. Ethyl 2-(1-methyl-1H-indole-2-carbonyl)-3-phenyloxirane-2-carboxylate (1k/1k').



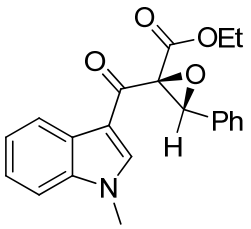
1k/1k'

Yield 59%, dr= 4.1 : 1,

1k red oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78-7.70 (m, 2 H), 7.53 (d, *J* = 7.2 Hz, 2 H), 7.45-7.38 (m, 5 H), 7.19 (t, *J* = 6.8 Hz, 1 H), 4.67 (s, 1 H), 4.10 (s, 3 H), 4.09-3.95 (m, 2 H), 0.94 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.7, 164.9, 140.6, 132.0, 131.8, 128.7, 128.1, 127.1, 126.4, 125.9, 123.6, 121.0, 114.9, 110.3, 68.4, 62.0, 61.9, 32.0, 13.6. MS (EI): m/z (%) = 436 (M^+, 10.15), 195 (100). HRMS calcd for $C_{21}H_{19}NO_4$: 349.1314, found: 349.1312. IR (neat) *v*/cm^{-1} 3063, 2523, 1523, 1750, 1615, 1464, 1426, 1392, 1295, 1014, 845, 621.

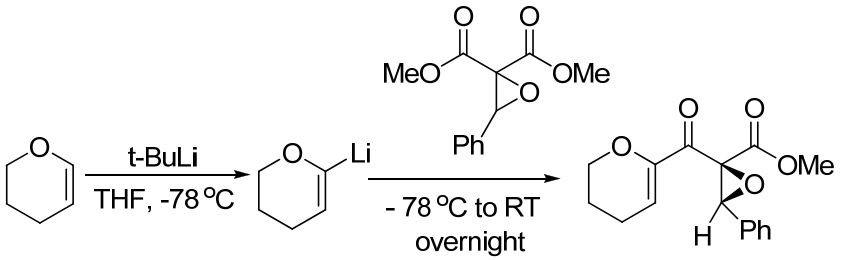
1k' red oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.6 Hz, 1 H), 7.50 (s, 1 H), 7.35-7.13 (m, 8 H), 4.70 (s, 1 H), 4.27-4.25 (m, 2 H), 3.85 (s, 3 H), 1.22 (t, *J* = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.1, 166.6, 140.2, 133.3, 132.5, 128.8, 128.2, 126.6, 126.2, 125.9, 123.4, 120.8, 114.2, 110.3, 66.1, 62.8, 62.7, 31.6, 13.8. MS (EI): m/z (%) = 349 (M^+, 5.94), 89 (100). HRMS calcd for $C_{21}H_{19}NO_4$: 349.1314, found: 349.1311. IR (neat) *v*/cm^{-1} 2986, 2551, 1742, 1659, 1615, 1513, 1464, 1395, 1255, 1050, 875, 738, 627.

12. Ethyl 2-(1-methyl-1H-indole-3-carbonyl)-3-phenyloxirane-2-carboxylate (1l).



Yield 19%, **1l** as yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (d, *J* = 1.6 Hz, 1 H), 8.23 (s, 1 H), 7.45-7.30 (m, 8 H), 4.51 (s, 1 H), 4.12-4.04 (m, 1 H), 4.04-3.90 (m, 1 H), 3.81 (s, 3 H), 0.90 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.4, 165.0, 137.8, 137.0, 132.7, 128.7, 128.1, 126.8, 126.1, 123.8, 123.1, 122.5, 112.6, 109.7, 69.6, 62.2, 61.8, 33.6, 13.6. MS (EI): m/z (%) = 349 (M^+, 0.57), 89 (100). HRMS calcd for $C_{21}H_{19}NO_4$: 349.1314, found: 349.1314. IR (neat) *v*/cm^{-1} 3125, 3060, 2982, 2937, 2910, 2678, 1959, 1742, 1629, 1520, 1463, 1368, 1239, 1311, 1239, 1124, 1090, 1024, 937, 863, 746, 698, 623.

13. Methyl 2-(3,4-dihydro-2H-pyran-6-carbonyl)-3-phenyloxirane-2-carboxylate (1m)[3].

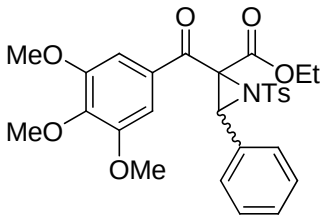


To a solution of 3,4-dihydro-2*H*-pyran (1.2 equiv.) in THF was added *t*-BuLi (1.3 M in hexane, 1.2 equiv.) at –78 °C. After it was stirred for 10 min at–78 °C, the reaction mixture was allowed to warm to 0 °C and stirred for 50 mins at 0 °C . The resulting 2-lithiodihydropyran solution was then cooled to -78 °C and treated rapidly dropwise with dimethyl 3-phenyloxirane-2, 2-dicarboxylate in THF. The mixture was stirred at –78 °C overnight. The reaction was quenched by water. The mixture was extracted with CH_2C1_2 (2X) and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel.

Yield 43%, as white solid, m.p. 154-157 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 6.8 Hz, 2 H), 7.38-7.28 (m, 3 H), 6.25 (s, 1 H), 4.58 (s, 1 H), 4.19-4.10 (m, 1 H), 4.10-4.04 (m, 1 H), 3.55 (s, 3 H), 2.29-2.28 (m, 2 H), 1.92-1.90 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.8, 165.1, 149.4, 131.7, 128.7, 128.0, 126.6, 114.9, 66.5, 65.8, 61.6, 52.5, 21.4, 20.8. MS (EI): m/z (%) = 288 (M^+, 23.51), 55 (100). HRMS calcd for $C_{16}H_{16}O_5$: 288.0998, found: 288.0997. IR (neat) *v*/cm^{-1} 2990, 2959, 2876, 1768, 1708, 1626, 1438, 1403, 1333, 1265, 1132, 1045, 989, 863, 718.

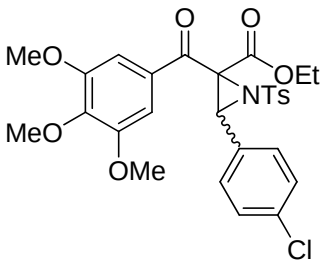
Synthesis of aziridines 1n-1r[7].

14. Ethyl 3-phenyl-1-tosyl-2-(3,4,5-trimethoxybenzoyl)aziridine-2-carboxylate(1n).



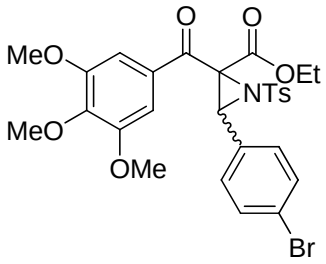
White solid, unstable, crude dr = 3.3 :1.0, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* =7.2 Hz, 2.11 H), 7.84 (d, *J* = 7.6 Hz, 2.30 H), 7.32-7.31 (m, 7.96 H), 7.28 (s, 4.91 H), 7.22 (s, 2.32 H), 7.22 (s, 2.32 H), 7.19 (s, 3.30 H), 7.10 (s, 2.22 H), 5.01 (s, 1.00 H), 4.83 (s, 1.05 H), 4.42 -4.38 (m, 1.07), 4.34-4.29 (m, 1.19 H), 3.95 (s, 3,26 H), 3.91 (s, 3.63 H), 3.86 (s, 7.33 H), 3.83 (s, 7.26 H), 2.43 (s, 6.69 H), 1.28 (t, *J* = 6.8 Hz, 3.88 H), 0.71 (t, *J* = 7.2 Hz, 3.18 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6, 164.1, 163.9, 152.9, 145.2, 144.7, 143.3, 143.0, 136.9, 134.8, 131.4, 130.8, 130.1, 129.9, 129.7, 129.7, 128.8, 128.6, 128.5, 128.4, 128.2, 127.4, 127.1, 126.8, 107.0, 106.6, 63.5, 62.4, 61.9, 60.9, 56.3, 56.0, 51.5, 47.4, 21.6, 13.8, 13.5. MS (ESI): m/z (%) = 562.2 [$(M+Na)^+$], HRMS-ESI calcd for $C_{28}H_{29}NO_8SNa$ [$(M+Na)^+$]: 562.1523, found: 562.1506. IR (neat) *ν*/cm^{-1} 3659, 3476, 3379, 3056, 2987, 2943, 2844, 2507, 1928, 1748, 1696, 1585, 1461, 1333, 1161, 927, 865, 764, 682.

15. Ethyl 3-(4-chlorophenyl)-1-tosyl-2-(3,4,5-trimethoxybenzoyl) aziridine-2-carboxylate (1o).



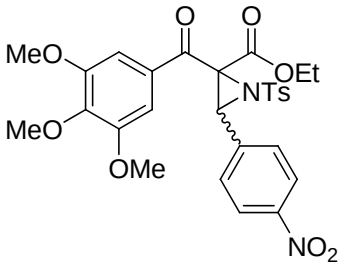
White solid, dr = 2.3 : 1, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 2.12 H), 7.81 (d, *J* = 7.2 Hz, 1.82 H), 7.33-7.26 (m, 10.00 H), 7.15 (d, *J* = 6.8 Hz, 2.37 H), 7.02 (d, *J* = 7.6 Hz, 2.04 H), 4.96 (s, 1.00 H), 4.78 (s, 0.82 H), 4.42-4.37 (m, 1.07 H), 4.34-4.26 (m, 1.13 H), 3.95-3.93 (m, 5.92 H), 3.88-3.86 (m, 7.74 H), 3.82 (s, 5.98 H), 2.42 (s, 6.10 H), 1.28 (t, *J* = 6.8 Hz, 3.26 H), 0.76 (t, *J* = 6.8 Hz, 2.54 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2, 185.2, 163.8, 163.6, 152.91, 152.85, 145.4, 144.8, 143.3, 143.1, 136.5, 134.7, 134.6, 134.5, 130.0, 129.7, 129.7, 129.6, 129.3, 128.7, 128.5, 128.4, 128.3, 128.1, 127.4, 127.3, 126.7, 106.8, 106.6, 63.5, 62.5, 61.9, 60.9, 60.7, 56.3, 55.9, 50.6, 46.6, 21.5, 13.7, 13.5. MS (ESI): m/z (%) = 598.1 [$(M+2+Na)^+$], 596.1 [$(M+Na)^+$], HRMS-ESI calcd for $C_{28}H_{28}NO_8SClNa$ [$(M+Na)^+$]: 596.1119, found: 596.1116. IR (neat) *ν*/cm^{-1} 3670, 2987, 2906, 2371, 2309, 1733, 1685, 1582, 1334, 1162, 1123, 929, 858, 774, 677.

16. Ethyl 3-(4-bromophenyl)-1-tosyl-2-(3,4,5-trimethoxybenzoyl)aziridine-2-carboxylate (1p).



White solid, dr = 2 :1, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 2.07 H), 7.82 (d, *J* = 6.8 Hz, 0.99 H), 7.42 (d, *J* = 7.2 Hz, 0.95 H), 7.31-7.29 (m, 6.18 H), 7.22 (d, *J* = 7.6 Hz, 0.99 H), 6.97 (d, *J* = 7.6 Hz, 2.03 H), 4.95 (s, 1.00 H), 4.77 (s, 0.43 H), 4.43-4.37 (m, 1.05 H), 4.32-4.27 (m, 1.14 H), 3.94-3.93 (m, 4.73 H), 3.88 (s, 6.71 H), 3.83 (s, 3.47 H), 2.41 (s, 4.36 H), 1.28 (t, *J* = 6.4 Hz, 3.16 H), 0.77 (t, *J* = 6.0 Hz, 1.31 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.3, 185.3, 163.9, 163.7, 153.0, 152.9, 145.4, 144.9, 143.4, 143.3, 136.2, 134.6, 131.7, 131.5, 130.6, 130.0, 129.8, 129.8, 129.7, 128.9, 128.5, 128.3, 128.3, 127.5, 127.3, 123.0, 122.9, 106.9, 106.7, 63.6, 62.6, 62.0, 60.9, 60.7, 56.4, 56.2, 56.0, 50.7, 46.8, 21.6, 13.7, 13.5. MS (ESI): m/z (%) = 642.1 [$(M+2+Na)^+$], 640.1 [$(M+Na)^+$], HRMS-ESI calcd for $C_{28}H_{28}NO_8SBrNa$ [$(M+Na)^+$]: 640.0622, found: 640.0611. IR (neat) ν/cm^{-1} 3667, 2977, 2902, 2252, 1920, 1741, 1691, 1586, 1332, 1164, 1126, 1005, 927, 833, 758, 680.

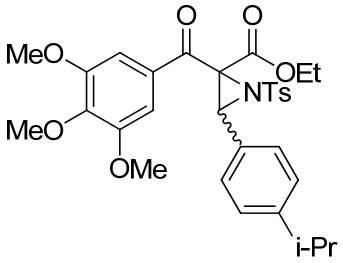
17. Ethyl 3-(4-nitrophenyl)-1-tosyl-2-(3,4,5-trimethoxybenzoyl)aziridine-2-carboxylate(1q).



White solid, dr about 3: 1, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.6 Hz, 1.45 H), 8.04 (d, *J* = 7.6 Hz, 1.04H), 7.86 (d, *J* = 7.6 Hz, 1.07 H), 7.82 (d, *J* = 6.8 Hz, 1.81 H), 7.53 (d, *J* = 8.0 Hz, 1.46 H), 7.34-7.24 (m, 6.83 H), 5.02 (s, 0.51 H), 4.87 (s, 1.00 H), 4.48 -4.40 (m, 0.52 H), 4.37-4.29 (m, 0.56 H), 3.95-3.94 (m, 3.75 H), 3.89 (s, 3.10 H), 3.85-3.82 (m, 6.06 H), 2.44 (s, 4.13 H), 1.30 (t, *J* = 6.8 Hz, 1.58 H), 0.75 (t, *J* = 6.8 Hz, 2.22 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9, 184.7, 163.6, 163.4, 153.1, 153.0, 148.1, 145.8, 145.2, 143.6, 138.9, 138.1, 136.4, 134.3, 130.0, 129.9, 129.7, 129.5, 129.4, 128.4, 128.3, 127.9, 127.4, 126.4, 123.7, 123.5, 106.9, 106.8, 63.9, 62.8, 62.3, 61.0, 60.8, 56.4, 56.0, 50.2, 46.4, 21.7, 13.8, 13.6. MS (ESI): m/z (%) = 607.1 [$(M+Na)^+$], HRMS-ESI calcd for $C_{28}H_{28}N_2O_{10}SNa$

[(M+Na)$^+$]: 607.1367, found: 607.1357. IR (neat) ν/cm^{-1} 3662, 2988, 2969, 2901, 2460, 2264, 1935, 1754, 1688, 1583, 1524, 1336, 1241, 1163, 1123, 931, 857, 815, 765, 679.

18. Ethyl 3-(4-isopropylphenyl)-1- tosyl-2- (3, 4, 5-trimethoxybenzoyl)aziridine-2- carboxylate (1r).

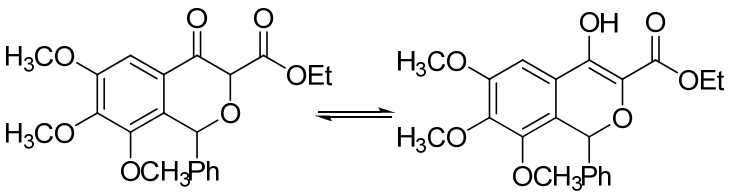


White solid, dr =5: 1, 1H NMR (400 MHz, CDCl3) δ 7.89 (d, *J* = 7.6 Hz, 2.08 H), 7.83 (d, *J* = 7.6 Hz, 3.96 H), 7.54 (d, *J* = 7.2 Hz, 3.31 H), 7.30-7.21 (m, 13.16 H), 7.18 (s, 3.26 H), 7.14-7.12 (m, 0.56 H), 7.04-6.99 (m, 4.16 H), 6.81 (s, 1.65 H), 4.99 (s, 1.00 H), 4.81 (s, 0.21 H), 4.41-4.21 (m, 5.95 H), 3.97-3.91 (m, 7.19 H), 3.85-3.83 (m, 22.86 H), 2.94-2.87 (m, 1.72 H), 2.80-2.76 (m, 1.09 H), 2.41 (s, 3.82 H), 2.38 (s, 4.87 H), 1.35 (t, J = 6.8 Hz, 5.02 H), 1.28-1.23 (m, 14.45 H), 1.18 (d, J = 6.8 Hz, 1.81 H), 1.13 (d, J = 6.8 Hz, 6.22 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.8, 164.2, 162.1, 157.1, 153.1, 152.9, 152.4, 150.3, 149.5, 144.7, 144.5, 142.9, 140.9, 136.9, 133.7, 132.4, 130.2, 129.6, 129.5, 128.6, 128.3, 128.2, 128.1, 127.3, 127.0, 126.8, 126.6, 126.5, 126.3, 125.7, 121.4, 109.5, 107.4, 106.9, 106.5, 106.0, 92.9, 63.4, 61.2, 60.9, 60.8, 60.7, 56.3, 56.1, 55.9, 51.6, 33.8, 33.6, 23.8, 23.6, 21.6, 21.6, 14.1, 13.7. MS (ESI): m/z (%) = 604.2 [(M+Na)$^+$], HRMS-ESI calcd for $C_{31}H_{35}NO_8SNa$ [(M+Na)$^+$]: 604.1968, found: 604.1976. IR (neat) ν/cm^{-1} 3670, 2962, 2940, 2874, 2594, 2254, 1920, 1704, 1579, 1503, 1354, 1294, 1168, 1126, 1101, 1047, 947, 816, 731, 678.

Geneal Procedure for Lewis acid catalyzed tandem cyclization.

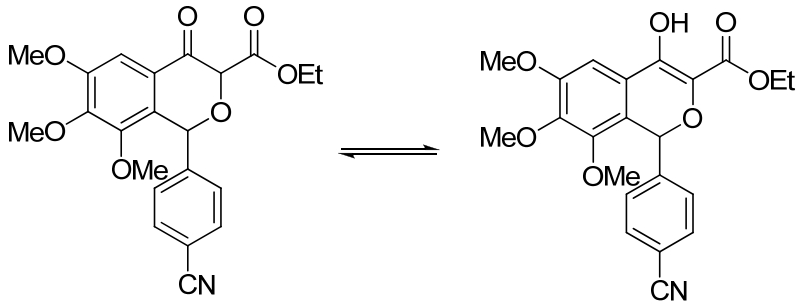
The reaction was carried out at RT with 1 (0.3 mmol), 4A MS (120 mg), 10 mol % $Yb(OTf)_3$ in CH_2Cl_2(4 ml) at 25 ^oC and completed within 15 h, the mixture was passed through a short pad of silicon gel to afford **2**.

19. Ethyl 6,7,8-trimethoxy-4-oxo-1-phenylisochroman-3-carboxylate and its isomers (2a).



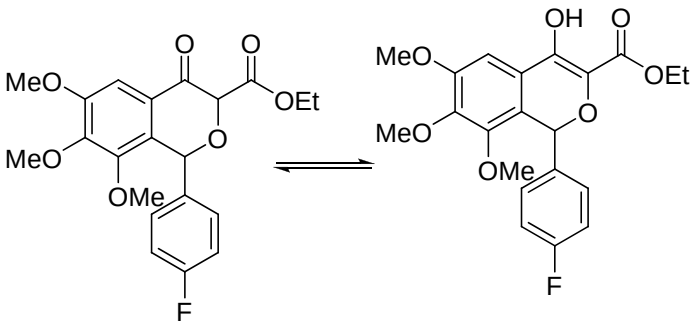
2a, 99% isolated yield, ratio of ketone and enolate 1 : 2, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (s, 0.63 H), 7.42 (s, 0.48 H), 7.35 (s, 1.50 H), 7.26-7.25 (m, 4 H), 7.09 (s, 0.72 H), 6.41 (s, 1.00 H), 4.73 (s, 0.32 H), 4.33-4.30 (m, 2.26 H), 3.94 (s, 7.26 H), 3.78 (s, 2.12 H), 3.60 (s, 1.05 H), 1.36 (t, J = 6.4 Hz, 2.13 H), 1.33-1.29 (m, 1.33 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.15, 168.12, 166.27, 153.64, 151.54, 149.11, 148.78, 147.85, 143.96, 139.06, 136.88, 129.68, 128.95, 128.79, 128.64, 128.52, 128.38, 128.24, 128.10, 127.97, 127.18, 124.18, 121.85, 120.64, 120.31, 104.62, 101.73, 75.92, 73.12, 72.50, 61.87, 61.12, 60.87, 60.44, 56.05, 14.24, 14.00. MS (EI): m/z (%) = 386 (M^+, 9.36), 84 (100). HRMS calcd for $C_{21}H_{22}O_7$: 386.1366, found: 386.1366. IR (neat) ν/cm^{-1} 2981, 2941, 2840, 2255, 1749, 1694, 1657, 1621, 1592, 1572, 1491, 1460, 1410, 1382, 1339, 1299, 1243, 1182, 1118, 998, 699.

20. Ethyl 1-(4-cyanophenyl)-6,7,8-trimethoxy-4-oxoisochroman-3-carboxylate (2c).



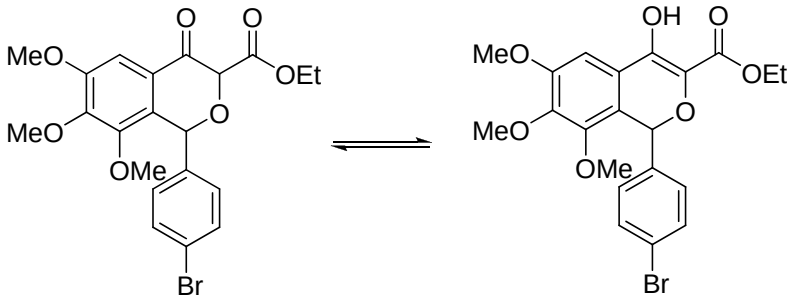
2c, 89% isolated yield, ratio of ketone and enolate 1 : 3, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.38 (s, 0.73 H), 7.68 (d, J = 7.6 Hz, 1.11 H), 7.59 (d, J = 7.6 Hz, 1.93 H), 7.50-7.45 (m, 0.57 H), 7.42- 7.40 (m, 0.74 H), 7.39-7.37 (m, 1.99 H), 7.30-7.28 (m, 0.28 H), 7.09 (s, 0.87 H), 6.38 (s, 1 H), 4.66 (s, 0.24 H), 4.37-4.36 (m, 1.85 H), 4.31-4.29 (m, 0.60 H), 3.96-3.92 (s, 8.96 H), 3.87-3.85 (s, 3.40 H), 3.64 (s, 0.66 H), 1.39 (t, J = 6.0 Hz, 2.59 H), 1.33-1.26 (m, 1.27 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 187.14, 167.71, 165,87, 154.03, 151.45, 148.95, 148.70, 148.60, 147.72, 144.63, 143.92, 142.72, 141.19, 132.27, 132.01, 131.82, 129.43, 129.28, 129.16, 127.85, 127.61, 127.42, 123.90, 121.49, 120.19, 119.18, 118.47, 118.17, 112.58, 111.76, 110.25, 105.44, 104.69, 101.90, 100.47, 93.22, 76.18, 72.45, 71.70, 62.00, 61.28, 60.95, 60.87, 60.63, 60.38, 59.26, 56.04, 14.21, 13.92. MS (EI): m/z (%) = 411 (M^+, 32.41), 43 (100). HRMS calcd for $C_{22}H_{21}NO_7$: 411.1318, found: 411.1321. IR (neat) ν/cm^{-1}.3424, 2981, 2942, 2842, 2254, 2230, 1748, 1699, 1658, 1592, 1572, 1238, 1117, 1009, 775, 730.

21. Ethyl 1-(4-fluorophenyl)-6,7,8-trimethoxy-4-oxoisochroman-3-carboxylate (2d).



2d, 99% isolated yield, ratio of ketone and enolate 1 : 2, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 0.56 H), 7.42 (s, 0.42 H), 7.29-7.21 (m, 1.56 H), 7.10 (s, 0.68 H), 7.05 (t, *J* = 8.0 Hz, 0.95 H), 6.96 (t, *J* =8.0 Hz, 1.39 H), 6.37 (s, 1.00 H), 4.70 (s, 0.35 H), 4.34-4.30 (m, 2.19 H), 3.95 (s, 6.80 H), 3.79 (s, 1.96 H), 3.63 (s, 1.28 H), 1.36 (t, *J* = 6.8 Hz, 2.12 H), 1.32-1.30 (m, 1.23 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 187.89, 168.04, 166.17, 163.68, 161.57, 161.23, 153.76, 151.51, 148.99, 148.69, 147.85, 143.98, 134.82, 132.91, 130.45, 130.37, 129.33, 129.06, 128.97, 124.06, 121.73, 120.38, 120.03, 115.59, 115.38, 114.99, 114.78, 104.64, 101.76, 75.82, 72.44, 71.88, 61.95, 61.18, 60.87, 60.47, 56.06, 14.23, 13.99. MS (EI): m/z (%) = 404 (M^+, 58.40), 157 (100). HRMS calcd for $C_{21}H_{21}O_7F$: 404.1271, found: 404.1268. IR (neat) ν/cm^{-1} 3673, 2986, 2942, 2902, 2256, 1750, 1694, 1656, 1408, 1232, 1117, 1072, 922, 848, 822, 774, 733.

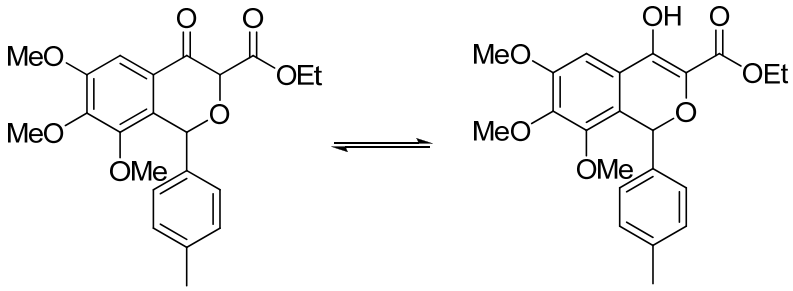
22. Ethyl 1-(4-bromophenyl)-6,7,8-trimethoxy-4-oxoisochroman-3-carboxylate (2f).



2f, 99% isolated yield, ratio of ketone and enolate 1 : 2, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (s, 0.63 H), 7.49 (d, *J* = 7.6 Hz, 0.76 H), 7.40 (d, *J* = 8.0 Hz, 1.97 H), 7.12-7.09 (m, 2.89 H), 6.34 (s, 1.00 H), 4.68 (s, 0.28 H), 4.34-4.29 (m, 2.20 H), 3.95 (s, 6.88 H), 3.81 (s, 2.15 H), 3.64 (s, 0.88 H), 1.37 (t, *J* = 6.8 Hz, 2.21 H), 1.32 (t, *J* = 6.8 Hz, 1.12 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 187.74, 167.97, 166.11, 153.82, 151.51, 149.01, 148.70, 147.80, 143.96, 138.20, 136.15, 131.71, 131.38, 131.29, 131.23, 131.14, 130.55, 130.26, 128.94, 128.28, 127.86, 124.07, 122.98, 122.13, 121.70, 120.13, 120.01, 104.67, 104.22, 101.81, 75.89, 72.52, 71.90, 61.95, 61.22, 60.93, 60.89, 60.51, 60.27, 56.19, 56.08, 14.26, 14.01. MS (EI): m/z (%) = 466 (M+2, 8.20), 464 (M^+,7.58), 84 (100). HRMS calcd

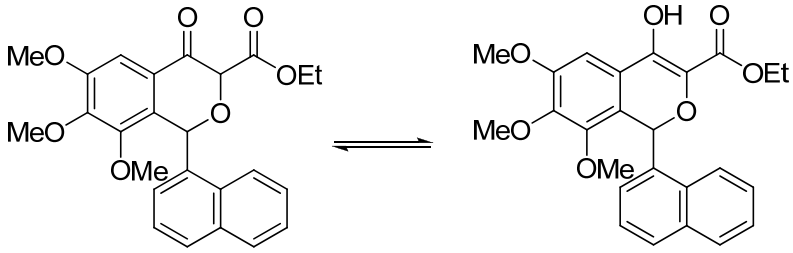
for $C_{21}H_{21}O_7Br$: 464.0471, found: 464.0471. IR (neat) ν/cm^{-1} 2982, 2942, 2840, 2255, 1749, 1695, 1591, 1572, 1140, 1237, 1118, 1071, 920, 859, 804, 775, 732.

23. **Ethyl 1-(4-methylphenyl)-6,7,8-trimethoxy-4-oxoisochroman-3-carboxylate (2g).**



2g, 99% isolated yield, ratio of ketone and enolate 1 : 1, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.40 (s, 0.49 H), 7.41 (s, 0.51 H), 7.17-7.07 (m, 5.48 H), 6.38 (s, 1.00 H), 4.73 (s, 0.41 H), 4.34-4.29 (m, 2.26 H), 3.94 (s, 7.33 H), 3.77 (s, 1.93 H), 3.61 (s, 1.28 H), 2.34 (s, 1.73 H), 2.30 (s, 2.10 H), 1.36 (t, J = 6.8 Hz, 1.92 H), 1.33-1.29 (m, 1.66 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 188.32, 168.19, 166.34, 153.59, 151.54, 149.09, 148.78, 147.87, 143.98, 138.71, 137.78, 136.09, 133.74, 129.99, 129.22, 128.93, 128.71, 128.63, 128.48, 127.24, 124.22, 121.89, 120.84, 120.28, 104.63, 101.71, 75.82, 72.98, 72.44, 61.85, 61.11, 60.87, 60.52, 59.33, 56.08, 21.08, 21.02, 14.26, 14.03. MS (EI): m/z (%) = 400 (M^+, 2.99), 84 (100). HRMS calcd for $C_{22}H_{24}O_7$: 400.1522, found: 400.1523. IR (neat) ν/cm^{-1} 2982, 2942, 2255, 1911, 1750, 1694, 1592, 1572, 1461, 1243, 1116, 1073, 1020, 993, 922, 860, 803, 774, 733.

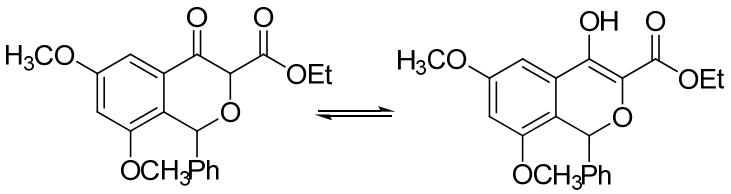
24. Ethyl 6,7,8-trimethoxy-1-(naphthalen-1-yl)-4-oxoisochroman-3-carboxylate (2i).



2i , 99% isolated yield, ratio of ketone and enolate 1 : 1, yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 0.60 H), 8.75 (d, J = 8.4 Hz, 0.68 H), 8.56 (d, J = 8.4 Hz, 0.90 H), 7.89 (d, J = 7.6 Hz, 1.36 H), 7.84 (d, J = 7.6 Hz, 1.95 H), 7.75 (d, J = 8.0 Hz, 0.95 H), 7.63-7.48 (m, 5.35 H), 7.28-7.21 (m, 1.80 H), 7.16 (t, J = 8.4 Hz, 2.51 H), 6.83 (d, J = 6.8 Hz, 0.89 H), 6.69 (d, J = 6.8 Hz, 0.67 H), 4.64 (s, 0.78 H), 4.28-4.17 (m, 2.00 H), 3.97-3.92 (m, 12.23 H), 3.85-3.74 (m, 2.05 H), 3.63 (s, 2.08 H), 3.61 (s, 0.63 H), 3.55 (s, 2.49 H), 3.46 (s, 0.58 H), 1.24 (t, J = 7.2 Hz, 2.98 H), 1.00 (t, J = 6.8 Hz, 2.01 H). ^{13}C NMR (400

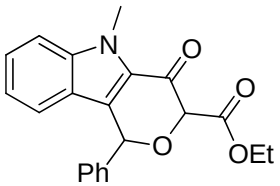
MHz, $CDCl_3$) δ 188.59, 168.11, 166.16, 153.72, 153.67, 151.95, 151.61, 149.14, 148.74, 147.82, 144.06, 133.98, 133.83, 132.38, 132.21, 131.92, 129.93, 129.36, 128.48, 128.17, 126.71, 126.38, 126.15, 126.11, 125.85, 125.56, 125.33, 124.64, 124.50, 124.24, 124.16, 123.79, 123.63, 122.82, 120.16, 104.57, 101.55, 76.15, 70.20, 70.14, 61.68, 60.79, 60.69, 60.58, 60.44, 56.00, 13.86, 13.61. MS (EI): m/z (%) = 436 (M^+,22.83), 43 (100). HRMS calcd for $C_{25}H_{24}O_7$: 436.1522, found: 436.1526. IR (neat) ν/cm^{-1} 2981, 2940, 2839, 2254, 1949, 1749, 1691, 1657, 1591, 1461, 1411, 1347, 1236, 1119, 1015, 991, 921, 858, 777, 731.

25. Ethyl 6,8-dimethoxy-4-oxo-1-phenylisochroman-3-carboxylate (2j).



2j, 99% isolated yield, ratio of ketone and enolate 1 : 3, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.35 (s, 0.87 H), 7.32 (s, 1.19 H), 7.28-7.18 (m, 6.70 H), 6.88 (s, 0.94 H), 6.72 (s, 0.37 H), 6.59 (s, 1.00 H), 6.44 (s, 0.89 H), 6.38 (s, 0.34 H), 4.71 (s, 0.32 H), 4.38-4.29 (m, 2.78 H), 3.87 (s, 4.38 H), 3.77 (s, 2.90 H), 3.69 (s, 1.12 H), 1.37 (t, J = 5.2 Hz, 2.90 H), 1.35-1.28 (m, 1.33 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 189.17, 168.16, 166.25, 160.69, 160.51, 156.52, 156.01, 151.60, 139.12, 136.52, 130.33, 128.59, 128.50, 128.44, 128.36, 127.96, 127.90, 127.82, 127.04, 124.38, 121.17, 115.55, 105.27, 101.06, 99.98, 98.10, 76.00, 72.84, 72.10, 61.89, 61.20, 55.82, 55.60, 55.52, 14.28, 14.02 MS (EI): m/z (%) = 356 (M^+, 2.94), 84 (100). HRMS calcd for $C_{20}H_{20}O_6$: 356.1260, found: 356.1261. IR (neat) ν/cm^{-1}.3664, 2987, 2973, 2902, 2255, 1750, 1700, 1658, 1584, 1409, 1221, 1076,1025, 1050, 911, 735, 697.

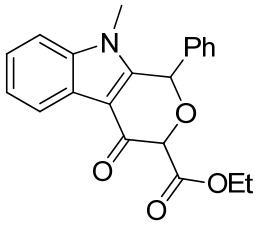
26. Ethyl 5-methyl-4-oxo-1-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indole-3-carboxylate (2k)



2k, yellow oil, 99% isolated yield, dr 3:1, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (S, 0.61 H), 7.32-7.26 (m, 6.45 H), 6.91-6.87 (m, 1.43 H), 6.80 (s, 0.28 H), 6.59 (s, 0.81 H), 6.56 (s, 0.11 H), 4.91 (s, 0.24 H), 4.88 (s, 0.65 H), 4.26-4.18 (m, 2.00 H), 4.04-4.02 (m, 2.94 H), 1.24 (t, J = 6.4 Hz, 3.00 H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 183.65, 182.60, 167.13, 166.43,

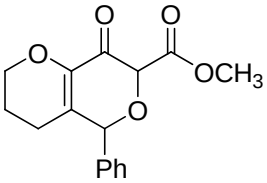
140.13, 140.03, 138.59, 138.31, 129.21, 129.07, 128.99, 128.80, 128.66, 127.96, 127.46, 127.26, 126.45, 122.73, 122.49, 122.08, 120.96, 120.86, 110.44, 110.38, 82.00, 78.98, 77.79, 74.54, 61.91, 61.79, 31.55, 14.10. MS (EI): m/z (%) = 349 (M^+,5.83), 43 (100). HRMS calcd for $C_{21}H_{19}NO_4$: 349.1314, found: 349.1318. IR (neat) ν/cm^{-1} 3362, 2986, 2902, 2254, 1741, 1669, 1530, 1478, 1429, 1227, 1186, 1097, 1016, 953, 900, 746, 699.

27. Ethyl 9-methyl-4-oxo-1-phenyl-1,3,4,9-tetrahydropyrano[3,4-b]indole-3-carboxylate (2l)



2l, crude yield 96% in 1.54 : 1 dr, isolated yield 80% in 2.64 : 1 dr, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ7.50-7.34 (m, 7.00 H), 6.96-6.94 (m, 1.43 H), 6.91-6.88 (m, 0.28 H), 6.67 (s, 0.84 H), 6.64 (s, 0.15 H), 6.09 (s, 0.27 H), 5.00 (s, 0.25 H), 4.96 (s, 0.66 H), 4.34-4.26 (m, 2 H), 4.13 (s, 2.11 H), 4.11 (s, 0.81 H), 1.33 (t, J = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.66, 182.60, 167.14, 166.45, 140.11, 140.02, 138.55, 138.26, 129.24, 129.09, 129.00, 128.80, 128.67, 127.96, 127.48, 127.28, 127.21, 126.43, 122.71, 122.47, 122.08, 120.97, 120.87, 110.45, 110.39, 81.99, 78.95, 77.81, 74.52, 61.96, 61.84, 31.57, 31.46, 14.11, 14.07. MS (EI): m/z (%) = 349 (M^+, 2.83), 77 (100). HRMS calcd for $C_{21}H_{19}NO_4$: 349.1314, found: 349.1316. IR (neat) ν/cm^{-1} 3466, 3064, 2983, 2254, 1740, 1668, 1528, 1477, 1268, 1225, 1127, 1015, 902, 772, 698.

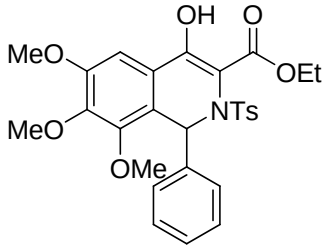
28. Methyl 8-oxo-5-phenyl-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran-7-carboxylate (2m).



2m, crude yield 82% in 2 : 1 dr, isolated yield 60% in 5 : 4 dr, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (s, 6.95 H), 5.80 (s, 1.00 H), 5.32 (s, 0.39 H), 4.90 (s, 0.38 H), 4.87 (s, 0.84 H), 4.32-4.29 (m, 0.46 H), 4.25-4.23 (m, 1.07 H), 4.00-3.98 (m, 1.10 H), 3.87-3.78 (m, 4.29 H), 2.01-1.96 (m, 1.25 H), 1.88-1.75 (m, 5.78 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 183.61, 183.01, 166.94, 166.00, 143.99, 143.04, 137.50, 137.05, 131.21, 131.09, 129.20, 129.13, 128.85, 128.76, 128.33, 128.17, 80.56, 79.83, 78.10, 77.49, 77.32, 66.00, 65.87,

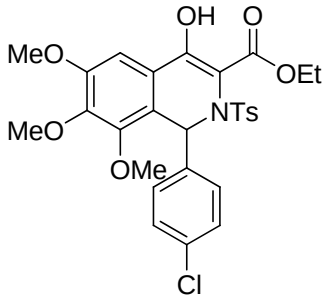
52.78, 52.68, 22.71, 22.63, 21.30, 21.17. MS (EI): m/z (%) = 288 (M^+, 1.38), 43 (100). HRMS calcd for $C_{16}H_{16}O_5$: 288.0998, found: 288.0999. IR (neat) ν/cm^{-1} 3660, 3466, 2970, 2901, 2254, 1746, 1693, 1635, 1494, 1453, 1270, 1133, 1039, 917, 732, 701, 642.

29. Ethyl 4-hydroxy-6,7,8-trimethoxy-1-phenyl-2-tosyl-1,2-dihydroisoquinoline-3-carboxylate (2n).



The reaction of substrate **1n** with dr 1.1 : 1 afforded **2n** 80% yield, while **1n** with dr 3 :1 yielded 2n 83%, white solid, m.p. 111-113 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.94 (s, 1 H), 7.48 (d, J = 7.6 Hz, 2 H), 7.22 (s, 2 H), 6.99 (d, J = 7.6 Hz, 4 H), 6.72 (s, 1 H), 6.36 (s, 1 H), 4.29 (q, J = 6.8 Hz, 2 H), 3.87 (s, 3 H), 3.82 (s, 3 H), 3.78 (s, 3 H), 2.26 (s, 3 H), 1.33 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 162.9, 153.2, 149.3, 144.5, 143.1, 137.7, 134.1, 128.8, 127.9, 127.8, 127.7, 127.5, 123.3, 122.1, 103.1, 101.3, 61.3, 60.8, 60.6, 56.1, 55.1, 21.3, 14.1. MS (ESI): m/z (%) = 562.2 [$(M+Na)^+$], HRMS-ESI calcd for $C_{28}H_{29}NO_8SNa$ [$(M+Na)^+$]: 562.1518, found: 562.1506. IR (neat) ν/cm^{-1} 3062, 3032, 2982, 2944, 2916, 2842, 2816, 2587, 1920, 1646, 1620, 1592, 1564, 1492, 1454, 1408, 1383, 1344, 1248, 1201, 1163, 1119, 1021, 990, 810, 766, 673.

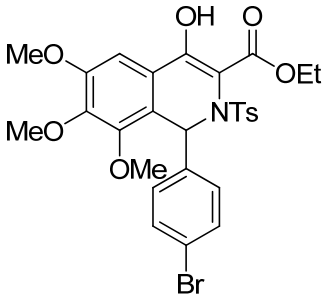
31. Ethyl 1-(4-chlorophenyl)-4-hydroxy-6,7,8-trimethoxy-2-tosyl-1,2-dihydroisoquinoline-3-carboxylate (2o).



The reaction of substrate **1o** with dr 4.6 :1 afforded **2o** in 85 % yield as white solid, m.p. 113-115 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.93 (s, 1 H), 7.46 (d, J = 7.6 Hz, 2 H), 7.17 (dd, J = 8.4 Hz and 23.2 Hz, 4 H), 6.98 (d, J = 7.2 Hz, 2 H), 6.71 (s, 1 H), 6.31 (s, 1 H), 4.31-4.30 (m, 2 H), 3.86 (s, 3 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 2.25 (s, 3 H), 1.34 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.7, 153.3, 149.1, 144.3, 143.2, 136.3,

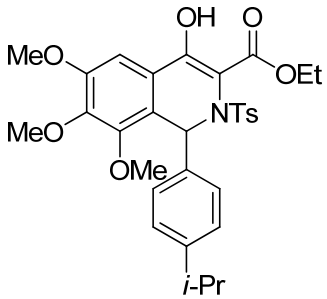
133.7, 133.6, 128.8, 128.7, 128.1, 127.5, 122.4, 121.8, 103.1, 101.0, 61.4, 60.8, 60.6, 56.0, 54.4, 21.2, 14.1. MS (ESI): m/z (%) = 596.1 [(M+Na)$^+$], HRMS-ESI calcd for $C_{28}H_{28}NO_8SClNa$ [(M+Na)$^+$]: 596.1135, found: 596.1116. IR (neat) ν/cm^{-1} 2998, 2943, 2849, 2580, 1974, 1745, 1643, 1564, 1490, 1459, 1411, 1344, 1241, 1168, 1121, 1016, 989, 914, 842, 784, 676.

32. Ethyl 1-(4-bromophenyl)-4-hydroxy-6, 7, 8-trimethoxy-2-tosyl-1,2-dihydroisoquinoline-3-carboxylate (2p).



The reaction of substrate **1p** with dr 2.4 : 1 afforded **2p** in 89% yield as white solid, m.p. 124-126 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1H), 7.47 (d, J = 7.6 Hz, 2 H), 7.35 (d, J = 7.2 Hz, 2 H), 7.08 (d, J = 7.6 Hz, 2 H), 6.98 (d, J = 7.6 Hz, 2 H), 6.71 (s, 1 H), 6.28 (s, 1 H), 4.35-4.26 (m, 2 H), 3.86 (s, 3 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 2.26 (s, 3 H), 1.35 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 162.7, 153.3, 149.2, 144.4, 143.2, 136.9, 133.8, 131.1, 129.3, 128.8, 127.6, 122.5, 121.9, 121.9, 103.1, 101.1, 61.5, 60.8, 60.7, 56.1, 54.5, 21.3, 14.2. MS (ESI): m/z (%) = 640.1 [(M+Na)$^+$], HRMS-ESI calcd for $C_{28}H_{28}NO_8SBrNa$ [(M+Na)$^+$]: 640.0593, found: 640.0611. IR (neat) ν/cm^{-1} 3093, 3057, 3001, 2959, 2939, 2858, 2583, 1930, 1643, 1595, 1562, 1489, 1457, 1409, 1345, 1255, 1203, 1167, 1119, 1074, 1055, 1020, 990, 929, 803, 751, 676.

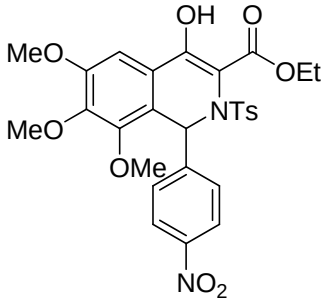
33. Ethyl 4-hydroxy-1-(4-isopropylphenyl)-6,7,8-trimethoxy-2-tosyl-1,2-dihydroisoquinoline-3-carboxylate (2q).



The reaction of substrate **1q** with dr 5 : 1 afforded **2q** 71% yield as white solid, m.p. 136-137 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1 H), 7.48 (d, J = 7.6 Hz, 2 H),

7.11-7.05 (m, 4 H), 6.99 (d, *J* = 8.0 Hz, 2 H), 6.71 (s, 1 H), 6.32 (s, 1 H), 4.32-4.29 (m, 2 H), 3.87 (s, 3 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 2.85-2.80 (m, 1 H), 2.26 (s, 3 H), 1.32 (t, *J* = 6.8 Hz, 3 H), 1.19 (d, *J* = 6.8 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 162.9, 153.1, 149.3, 148.3, 144.4, 143.0, 134.8, 134.2, 128.7, 127.7, 127.3, 126.0, 123.6, 122.0, 103.1, 101.3, 61.3, 60.8, 60.6, 56.1, 54.9, 33.6, 23.8, 21.3, 14.1. MS (ESI): m/z (%) = 604.2 [$(M+Na)^+$], HRMS-ESI calcd for $C_{31}H_{35}NO_8SNa$ [$(M+Na)^+$]: 604.1986, found: 604.1976. IR (neat) v/cm^{-1} 3428, 3171, 2960, 2925, 2854, 2737, 2589, 1907, 1649, 1584, 1489, 1463, 1320, 1207, 1177, 1124, 1070, 1017, 989, 931, 842, 813, 797, 698.

34. ethyl 4-hydroxy-6,7,8-trimethoxy-1-(4-nitrophenyl)-2-tosyl-1,2-dihydroisoquinoline-3-carboxylate(2r).

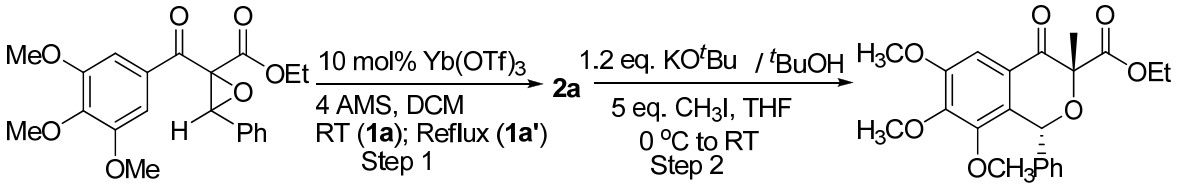


The reaction of substrate **1r** with dr 2.7 : 1 afforded **2r** 55% yield , as white solid, m.p 164-165 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.91 (s, 1 H), 8.09 (d, *J* = 7.6 Hz, 2 H), 7.46 (d, *J* = 7.2 Hz, 4 H), 7.42 (d, *J* = 8.0 Hz, 2 H), 7.01 (d, *J* = 7.6 Hz, 2 H), 6.72 (s, 1 H), 6.38 (s, 1 H), 4.34-4.31 (m, 2 H), 3.88 (s, 3 H), 3.86 (s, 3 H), 3.83 (s, 3 H), 2.27 (s, 3 H), 1.37 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 162.7, 153.6, 149.1, 147.5, 145.4, 144.4, 143.5, 133.5, 128.9, 128.4, 127.6, 123.1, 121.7, 121.5, 103.2, 101.1, 61.6, 60.8, 60.7, 56.1, 54.6, 21.3, 14.2. MS (ESI): m/z (%) = 607.1 [$(M+Na)^+$], HRMS-ESI calcd for $C_{28}H_{28}N_2O_{10}SNa$ [$(M+Na)^+$]: 607.1364, found: 607.1357. IR (neat) v/cm^{-1} 3111, 3077, 2961, 2928, 2851, 2633, 1939, 1707, 1580, 1523, 1502, 1459, 1413, 1346, 1293, 1168, 1124, 1045, 1015, 914, 855, 815, 743, 702.

'One –Pot' synthesis of 3-methyl-4-oxo-1-phenylisochroman-3-carboxylate (3a-3j).

The reaction was carried out at RT with **1** (0.3 mmol), 4 Å MS (120 mg), 10 mol % Yb(OTf)3 in CH_2Cl_2 at 25 ^{o}C for 15 h , and after filtration to remove catalyst, the crude product 2 was reacted with 5 eq.CH_3I with t-BuOK (1.2 eq.) and t-BuOH (a drop) in THF at RT for 15 h . Flash chlomataghraghy to afford **3**.

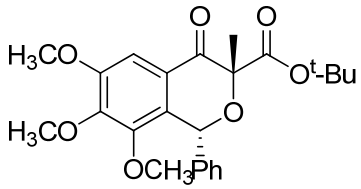
35. Ethyl 6,7,8-trimethoxy-3-methyl-4-oxo-1-phenylisochroman-3-carboxylate(3a).



1a or 1a' **3a**

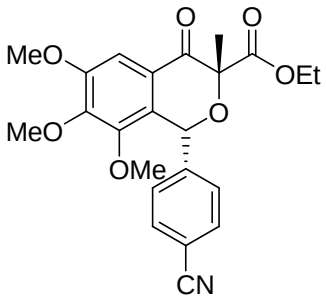
3a, 86% total yield from **1a**, 74% total yield from **1a'**, dr > 50 : 1; yellow solid, m.p. 86-88 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1 H), 7.30-7.29 (m, 3 H), 7.24-7.22 (m, 2 H), 6.21 (s, 1H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.59-3.53 (m, 1 H), 3,44 (s, 3 H), 3.39-3.35 (m, 1 H), 1.66 (s, 3 H), 0.98 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.2, 170.0, 153.6, 148.6, 147.6, 138.9, 129.3, 129.2, 128.4, 127.9, 123.6, 104.7, 80.1, 72.6, 61.3, 60.7, 60.1, 56.1, 22.8, 13.4. MS (EI): m/z (%) = 400 (M^+, 5.47), 43 (100). HRMS calcd for $C_{22}H_{24}O_7$: 400.1522, found: 400.1522. IR (neat) ν/cm^{-1} 3089, 3066, 3002, 2963, 2934, 2895, 2839, 2665, 1952, 1747, 1686, 1591, 1488, 1416, 1355, 1331, 1257, 1121, 1085, 1018, 950, 919, 803, 766, 697.

36. tert-butyl 6,7,8-trimethoxy-3-methyl-4-oxo-1-phenylisochroman-3-carboxylate (3b).



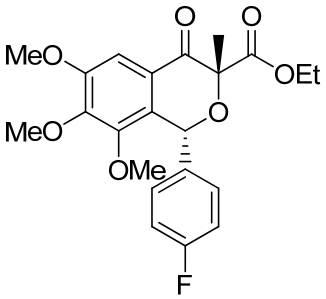
3b, 69% total yield, dr > 50 :1, white solid, m.p. 78-80 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) 7.47 (s, 1 H), 7.32-7.26 (m, 5 H), 6.12 (s, 1 H), 3.95 (s, 3 H), 3.89 (s, 3 H), 3.28 (s, 3 H), 1.64 (s, 3 H), 1.19 (s, 9 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.7, 168.7, 153.6, 148.8, 147.8, 140.4, 129.9, 129.4, 128.3, 128.2, 123.6, 106.8, 104.6, 82.1, 81.4, 72.5, 60.8, 59.9, 56.2, 56.1, 27.5, 22.3. MS (EI): m/z (%) = 428 (M^+, 0.61), 57 (100). HRMS calcd for $C_{24}H_{28}O_7$: 428.1835, found: 428.1834. IR (neat) ν/cm^{-1} 3091, 3060, 2986, 2932, 2851, 2667, 1944, 1738, 1687, 1590, 1486, 1462, 1350, 1320, 1257, 1189, 1123, 1020, 950, 864, 743, 698, 653.

37. Ethyl 1-(4-cyanophenyl)-6,7,8-trimethoxy-3-methyl-4-oxoisochroman-3-carboxylate(3c).



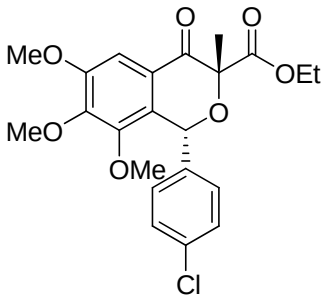
3c, 75% total yield ,dr > 50 : 1, yellow solid, m.p. 160-161 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63(d, *J* = 7.6 Hz, 2 H), 7.49 (s, 1 H), 7.38 (d, *J* = 7.2 Hz, 2 H), 6.16 (s, 1 H), 3.66 (s, 3 H), 3.64 (s, 3 H), 3.63-3.61 (m, 1 H), 3.54-3.49 (m, 1 H), 3.49 (s, 3H), 1.67 (s, 3 H), 1.04 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.7, 169.5, 154.1, 148.5, 147.5, 144.5, 131.7, 129.8, 127.4, 123.5, 118.4, 112.1, 104.9, 80.5, 71.9, 61.5, 60.9, 60.2, 56.1, 22.0, 13.5. MS (EI): m/z (%) = 425 (M^+, 3.11), 43 (100). HRMS calcd for $C_{23}H_{23}NO_7$: 425.1475, found: 425.1474. IR (neat) *v*/cm^{-1} 3102, 2995, 2944, 2834, 2669, 2227, 1935, 1748, 1686, 1594, 1488, 1463, 1361, 1332, 1227, 1119, 1022.

38. Ethyl 1-(4-fluorophenyl)-6,7,8-trimethoxy-3-methyl-4-oxoisochroman-3-carboxylate(3d).



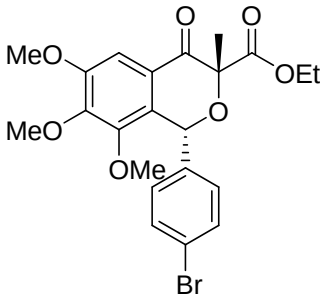
3d, 74% total yield, dr >50 :1, yellow solid, m.p. 111-112 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1 H), 7.24-7.22 (m, 2 H), 6.99 (t, *J* = 8.0 Hz, 2 H), 6.18 (s, 1 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.84 -3.60 (m, 1 H), 3.52-3.40 (m, 4 H), 1.66 (s, 3 H), 1.03 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.1, 170.0, 162.6 (d, $J_{C,F}$ = 246 Hz), 153.8, 148.6, 147.6, 135.0, 131.0 (d, $J_{C,F}$ = 8 Hz), 128.9, 123.6, 114.8 (d, $J_{C,F}$ = 21 Hz), 104.8, 80.1, 71.8, 61.4, 60.8, 60.2, 56.1, 22.7, 13.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -113.2 ppm. MS (EI): m/z (%) = 418 (M^+, 1.61), 43 (100). HRMS calcd for $C_{22}H_{23}O_7F$: 418.1428, found: 400.1429. IR (neat) *v*/cm^{-1} 3084, 2975, 2952, 2845, 2666, 1918, 1730, 1693, 1593, 1489, 1467, 1411, 1360, 1330, 1245, 1216, 1120, 1086, 1016, 920, 854, 795, 763, 667, 615.

39. Ethyl 1-(4-chlorophenyl)-6,7,8-trimethoxy-3-methyl-4-oxoisochroman-3-carboxylate(3e).



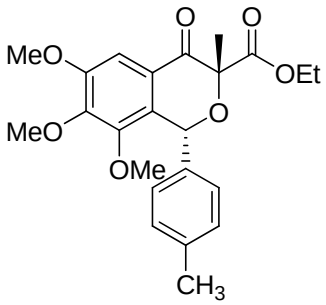
3e, 78% total yield, dr >50 :1, yellow solid, m.p. 122-124 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 6.15 (s, 1 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.68-3.57 (m, 1 H), 3.49 (s, 3 H), 3.49-3.44 (m, 1 H), 1.65 (s, 3 H) 1.02 (t, *J* = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 169.9, 153.8, 148.6, 147.6, 137.7, 134.2, 130.6, 128.6, 128.1, 123.6, 104.8, 80.2, 71.9, 61.5, 60.8, 60.3, 56.1, 22.6, 13.5. MS (EI): m/z (%) = 436 (M+2, 1.00), 434 (M^+, 2.43), 43 (100). HRMS calcd for $C_{22}H_{23}O_7Cl$: 434.1132, found: 434.1134 IR (neat) *v*/cm^{-1} 3096, 3063, 2974, 2952, 2845, 2665, 1922, 1728, 1694, 1591, 1488, 1466, 1405, 1359, 1329, 1245, 1119, 1086, 1014, 954, 919, 854, 806, 765, 665.

40. Ethyl 1-(4-bromophenyl)-6,7,8-trimethoxy-3-methyl-4-oxoisochroman-3-carboxylate(3f).



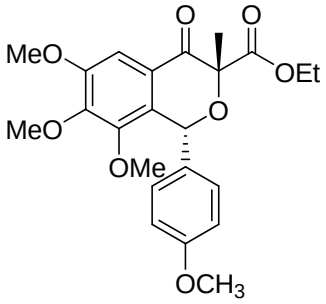
3f, 79% total yield ,dr >50 :1, yellow solid, m.p. 100-102 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1 H), 7.43 (d, *J* = 7.2 Hz, 2 H), 7.12 (d, *J* = 7.2 Hz, 2 H), 6.14 (s, 1 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.65-3.59 (m, 1 H), 3.50 (s, 3 H), 3.50-3.45 (m, 1 H), 1.65 (s, 3 H), 1.03 (t, *J* = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.9, 169.8, 153.8, 148.5, 147.5, 138.1, 131.0, 130.9, 128.4, 123.5, 122.4, 104.7, 80.2, 71.9, 61.4, 60.8, 60.2, 56.1, 22.6, 13.5. MS (EI): m/z (%) = 480 (M+2, 3.00), 478 (M^+, 3.46), 43 (100). HRMS calcd for $C_{22}H_{23}O_7Br$: 478.0627, found: 478.0633. IR (neat) *v*/cm^{-1} 3093, 3058, 2947, 2842, 2660, 1921, 1728, 1694, 1590, 1487, 1330, 1244, 1119, 1011, 919, 853, 803, 765, 665.

41. Ethyl 1-(4-methylphenyl)-6,7,8-trimethoxy-3-methyl-4-oxoisochroman-3-carboxylate(3g).



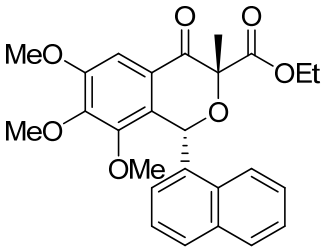
3g, 68% total yield, dr > 50 :1, yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.08 (s, 4 H), 6.17 (s, 1 H), 3.95 (s, 3 H), 3.90 (s, 3 H), 3.58-3.50 (m, 1 H), 3.44 (s, 3 H), 3.38-3.30 (m, 1 H), 2.29 (s, 3 H), 1.63 (s, 3 H), 0.97 (t, J = 7.2 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3, 170.1, 153.6, 148.7, 147.6, 138.1, 135.9, 129.6, 129.2, 128.5, 123.7, 104.7, 80.0, 72.4, 61.3, 60.8, 60.3, 56.1, 23.0, 21.1, 13.4. MS (EI): m/z (%) = 414 (M^+, 1.92), 43 (100). HRMS calcd for $C_{23}H_{26}O_7$: 414.1679, found: 414.1680. IR (neat) ν/cm^{-1} 2974, 2940, 2890, 2485, 1929, 1746, 1687, 1590, 1456, 1414, 1356, 1328, 1306, 1247, 1120, 1087, 1049, 1017, 1004, 951, 879, 800, 764, 679.

42. Ethyl 6, 7, 8-trimethoxy-1-(4-methoxyphenyl)-3-methyl-4-oxoisochroman-3-carboxylate (3h).



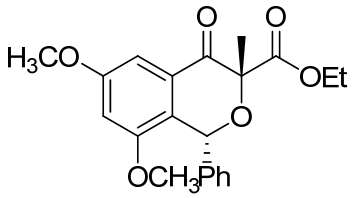
3h, 40% total yield, dr > 50 : 1, yellow solid, m.p. 65-66 ^{o}C, 1H NMR (400 MHz, CDCl3) δ 7.50 (s, 1 H), 7.13 (d, J = 8.0 Hz, 2 H), 6.81 (d, J = 7.6 Hz, 2 H), 6.18 (s, 1 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.77 (s, 3 H), 3.65 -3.58 (m, 1 H), 3.47 (s, 3 H), 3.45-3.40 (m, 1 H), 1.65 (s, 3 H), 1.01 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.3, 170.2, 159.6, 153.6, 148.6, 147.7, 131.1, 130.7, 130.2, 129.7, 123.7, 114.2, 113.2, 104.8, 80.0, 72.1, 61.4, 60.8, 60.3, 56.2, 56.1, 55.2, 23.2, 13.5. MS (EI): m/z (%) = 430 (M^+, 2.91), 43 (100). HRMS calcd for $C_{23}H_{26}O_8$: 430.1628, found: 430.1627. IR (neat) ν/cm^{-1} 3102, 2939, 2840, 2660, 1920, 1726, 1693, 1590, 1510, 1463, 1304, 1246, 1119, 1011, 818, 771, 673, 617.

43. Ethyl 6,7,8-trimethoxy-3-methyl-1-(naphthalen-1-yl)-4-oxoisochroman-3-carboxylate(3i).



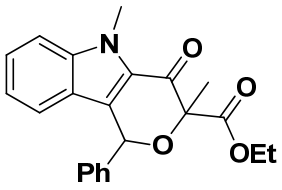
3i , 66% total yield, dr> 50 : 1, white solid, m.p. 164-167 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, *J* = 7.6 Hz, 1 H), 7.88 (d, *J* = 7.6 Hz, 1 H), 7.77 (d, *J* = 7.6 Hz, 1 H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.58 -7.56 (m, 2 H), 7.21 (t, *J* = 7.2 Hz, 1 H), 6.99 (s, 1H), 6.76 (d, *J* = 6.4 Hz, 1 H), 3.99 (s, 3 H), 3.92 (s, 3 H), 3.47 (s, 3H), 3.30-3.20 (m, 1 H), 2.46-2.36 (m, 1 H), 1.62 (s, 3 H), 0.39 (t, *J* = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.4, 170.1, 153.7, 148.7, 147.5, 134.0, 133.7, 132.9, 129.7, 129.5, 128.3, 127.1, 126.5, 125.8, 125.0, 124.2, 104.9, 80.2, 69.4, 60.8, 60.4, 56.1, 23.8, 12.6. MS (EI): m/z (%) = 450 (M^+, 8.93), 43 (100). HRMS calcd for $C_{26}H_{26}O_7$: 450.1679, found: 450.1681. IR (neat) *v*/cm^{-1} 3074, 3006, 2980, 2943, 2870, 2843, 2652, 1956, 1734, 1683, 1589, 1463, 1352, 1271, 1250, 1117, 1088, 1005, 925, 859, 778, 660.

44. Ethyl 6,8-dimethoxy-3-methyl-4-oxo-1-phenylisochroman-3-carboxylate(3j).



3j, 85% total yield, dr > 50 : 1, white solid, m.p. 93-95 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.25 (m, 4 H), 7.19-7.17 (m, 2 H), 6.70 (s, 1 H), 6.21 (s, 1 H), 3.90 (s, 3 H), 3.63 (s, 3 H), 3.50-3.38 (m, 1 H), 3.30-3.20 (m, 1 H), 1.65 (s, 3 H), 0.95 (t, *J* = 7.2 Hz, 3 H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.2, 170.1, 160.4, 156.4, 138.2, 129.7, 129.1, 128.1, 127.7, 123.8, 105.1, 100.0, 79.9, 72.3, 61.2, 55.7, 55.6, 23.2, 13.4. MS (EI): m/z (%) = 370 (M^+, 1.31), 43 (100). HRMS calcd for $C_{21}H_{22}O_6$: 370.1416, found: 370.1419. IR (neat) *v*/cm^{-1} 3092, 3058, 2999, 2978, 2941, 2902, 2843, 2675, 1964, 1723, 1693, 1608, 1451, 1372, 1307, 1266, 1208, 1121, 1058, 847, 747, 698, 663.

45. ethyl 3,5-dimethyl-4-oxo-1-phenyl-1,3,4,5-tetrahydropyrano[4,3-b]indole-3-carboxylate (3k/3k')

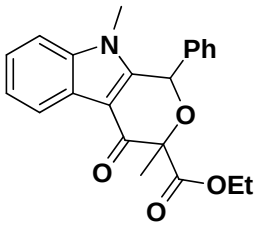


88% total yield, dr 3 : 1,

3k, major isomer, white solid, m.p. 140-142 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.45 (m, 2 H), 7.44-7.31 (m, 5 H), 7.00-6.90 (m, 1 H), 6.85 (d, *J* = 8.0 Hz, 1 H), 6.26 (s, 1 H), 4.14 (s, 3 H), 4.10-3.96 (m, 2 H), 1.81 (s, 3 H), 1.20 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2, 169.3, 140.2, 139.1, 129.0, 128.9, 128.5, 127.3, 127.2, 125.8, 122.5, 122.0, 120.8, 110.4, 83.7, 73.2, 61.7, 31.6, 18.9, 13.8. MS (EI): m/z (%) = 363 (M^+, 37.09), 218 (100). HRMS calcd for $C_{22}H_{21}NO_4$: 363.1471, found: 363.1471. IR (neat) *v*/cm^{-1} 2988, 2901, 1920, 1744, 1662, 1613, 1533, 1475, 1419, 1291, 1261, 1137, 1117, 1050, 980, 772, 713, 697.

3k', minor isomer, white solid, m.p. 104-106 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50-7.45 (m, 2 H), 7.45-7.36 (m, 3 H), 7.35-7.30 (m, 2 H), 6.95-6.85 (m, 1 H), 6.72 (d, *J* = 8.0 Hz, 1 H), 6.44 (s, 1 H), 4.35-4.25 (m, 1 H), 4.35-4.15 (m, 1 H), 4.14 (s, 3 H), 1.79 (s, 3 H), 1.29 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6, 169.7, 140.3, 139.8, 129.04, 128.96, 128.7, 128.2, 127.0, 126.7, 122.6, 122.2, 120.7, 110.4, 83.8, 74.8, 61.8, 31.5, 22.0, 14.2. MS (EI): m/z (%) = 363 (M^+, 4.49), 43 (100). HRMS calcd for $C_{22}H_{21}NO_4$: 363.1471, found: 363.1471. IR (neat) *v*/cm^{-1} 2988, 2923, 2851, 1961, 1726, 1681, 1536, 1480, 1447, 1345, 1258, 1129, 1058, 1018, 976, 895, 780, 742, 700.

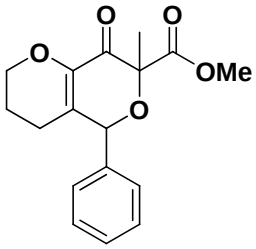
46. ethyl 3,9-dimethyl-4-oxo-1-phenyl-1,3,4,9-tetrahydropyrano[3,4-b]indole-3-carboxylate (3l/3l').



3l/3l', 63 % total yield, dr 3 : 1, white solid, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.45 (m, 3,17 H), 7.44-7.35 (m, 7.15 H), 7.00-6.90 (m, 2.68 H), 6.74 (d, *J* = 8.4 Hz, 0.38 H), 6.47 (s, 0.37 H), 6.28 (s, 1.00 H), 4.35-4.20 (m, 0.74 H), 4.19-4.12 (m, 4.11 H), 4.12-4.00 (m, 1.98 H), 1.85-1.78 (m, 4.11 H), 1.30 (t, *J* = 7.2 Hz, 1.11 H), 1.21 (t, *J* = 7.2 Hz, 3.00 H). ^{13}C NMR

(100 MHz, $CDCl_3$) δ 187.2, 185.5, 169.6, 169.3, 140.2, 139.6, 139.0, 129.0, 128.94, 128.90, 128.7, 128.5, 128.1, 127.8, 127.3, 127.2, 127.0, 126.6, 125.8, 122.49, 122.45, 122.1, 122.0, 120.8, 120.6, 110.41, 110.35, 83.73, 83.68, 74.7, 73.2, 61.9, 61.8, 31.6, 31.4, 21.9, 18.9, 14.1, 13.8. MS (EI): m/z (%) = 363 (M^+, 20.08), 290 (100). HRMS calcd for $C_{22}H_{21}NO_4$: 363.1471, found: 363.1470. IR (neat) ν/cm^{-1} 3675, 2988, 2901, 2883, 2828, 1942, 1908, 1743, 1727, 1681, 1662, 1613, 1476, 1420, 1260, 1117, 1052, 979, 909, 742, 713, 613.

47. methyl 7-methyl-8-oxo-5-phenyl-2,3,4,5,7,8-hexahydropyrano[4,3-b]pyran-7-carboxylate (3m/3m').

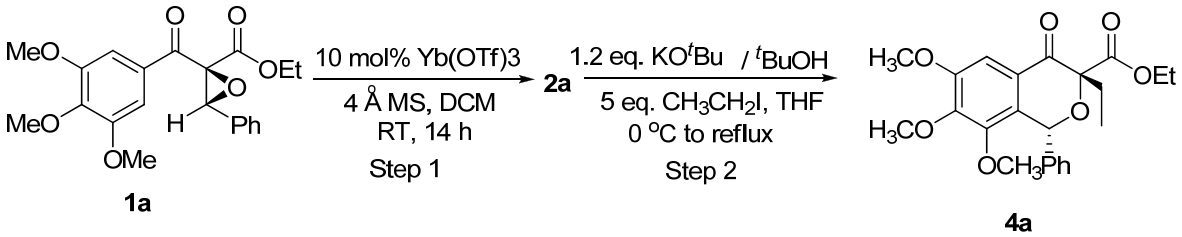


66% total yield, dr 6:1,

3m, major isomer, white solid, m.p.96-99 °C , ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.35 (m, 5 H), 5.38 (s, 1 H), 4.30-4.20 (m, 1 H), 4.00-3.90 (m, 1 H), 3.58 (s, 3 H), 2.00-1.82 (m, 3 H), 1.80-1.72 (m , 1 H), 1.71 (s, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.3, 169.1, 142.3, 137.5, 129.8, 129.0, 128.7, 128.4, 82.8, 75.9, 65.9, 52.7, 22.6, 21.1, 19.3. MS (EI): m/z (%) = 302 (M^+, 14.23), 115 (100). HRMS calcd for $C_{17}H_{18}O_5$: 302.1154, found: 302.1157. IR (neat) ν/cm^{-1} 2988, 2970, 2884, 2833, 1990, 1922, 1910, 1744, 1687, 1664, 1639, 1476, 1457, 1378, 1289, 1260, 1109, 1065, 978, 931, 741, 700, 619.

3m', minor isomer, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.35 (m, 5 H), 5.63 (s, 1 H), 4.32-4.29 (m, 1 H), 3.85-3.75 (m, 4 H), 1.90-1.75 (m, 3 H), 1.68 (s, 3 H), 1.66-1.60 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6, 169.7, 142.5, 138.7, 130.3, 129.0, 128.8, 128.1, 82.4, 77.1, 65.9, 52.8, 22.5, 22.0, 21.3. MS (EI): m/z (%) = 302 (M^+, 0.38), 243(100). HRMS calcd for $C_{17}H_{18}O_5$: 302.1154, found: 302.1152. IR (neat) ν/cm^{-1} 2987, 2971, 2901, 2252, 1959, 1743, 1698, 1637, 1445, 1386, 1251, 1108, 1071, 910, 764, 729, 700, 612.

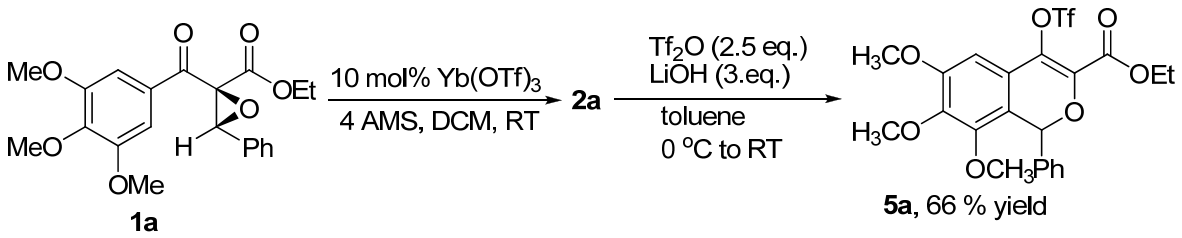
48. Sythesis ethyl 3-ethyl-6,7,8-trimethoxy-4-oxo-1-phenylisochroman-3-carboxylate(4a)[6].



1a **4a**

yield 64%, yellow solid,dr > 50 :1, m.p. 98-100 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1 H), 7.35-7.15 (m, 5 H), 6.23 (s, 1 H), 3.97 (s, 3 H), 3.92 (s, 3 H), 3.62-3.55 (m, 1 H), 3.42 (s, 3 H), 3.40-3.33 (m, 1 H), 2.20-2.10 (m, 1 H), 2.08-1.97 (m, 1 H), 1.05-0.95 (m, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.0, 169.8, 153.6, 148.6, 147.7, 139.3, 129.5, 129.3, 128.4, 128.0, 124.5, 104.5, 83.8, 72.6, 61.2, 60.8, 60.2, 56.1, 30.0, 13.6, 8.0. MS (EI): m/z (%) = 414 (M^+, 1.31), 57 (100). HRMS calcd for $C_{23}H_{26}O_7$: 414.1679, found: 414.1678. IR (neat) ν/cm^{-1} 3094, 2991, 2978, 2938, 2880, 2835, 2649, 1991, 1748, 1686, 1591, 1487, 1460, 1346, 1220, 1122, 1025, 966, 924, 864, 707.

49. Ethyl 6, 7, 8-trimethoxy -1- phenyl -4- (trifluoromethylsulfonyloxy)- 1H -isochromene-3-carboxylate (5a).



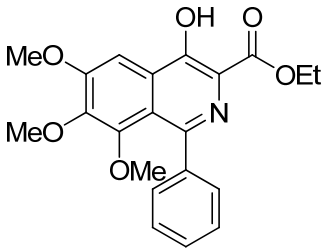
1a **5a**, 66 % yield

66% yield, red solid, m.p.75-77 °C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (s, 3 H), 7.26 (s, 2 H), 6.82 (s, 1 H), 6.60 (s, 1 H), 4.35-4.30 (m, 2 H), 3.63-3.91 (m, 6 H), 3.77 (s, 3 H), 1.34 (t, J = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 154.1, 149.4, 143.9, 137.6, 137.0, 136.1, 128.8, 128.2, 127.4, 121.3, 118.4 (q, $J_{C,F}$ = 319 Hz), 117.7, 100.4, 74.4, 62.2, 61.0, 56.0, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -73.1 ppm. MS (EI): m/z (%) = 518 (M^+, 4.80), 69 (100). HRMS calcd for $C_{22}H_{21}O_9SF_3$: 518.0858, found: 518.0860. IR (neat) v/cm^{-1} 3013, 2984, 2944, 2850, 1726, 1630, 1597, 1573, 1495, 1461, 1414, 1362, 1307, 1203, 1133, 1054, 985, 825, 753, 696, 614.

Synthesis of isoquinoline-3-carboxylate 6a-6e.

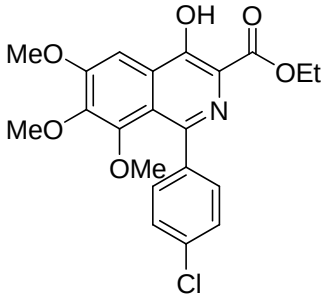
The reaction was carried out at RT with **1** (0.3 mmol), 4 Å MS (120 mg), 10 mol % $Yb(OTf)_3$ in CH_2Cl_2 at 25 °C for 15 h , then the mixture of unpurified **2** was carried out with 1.05 eq. of K_2CO_3 at 40 °C overnight. Flash chlomataghraghy to afford **6**.

50. Ethyl 4-hydroxy-6,7,8-trimethoxy-1-phenylisoquinoline-3-carboxylate (6a).



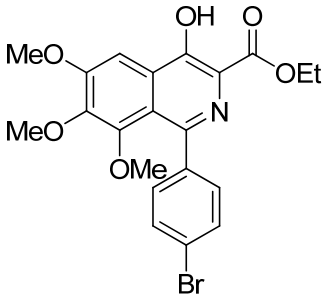
The reaction of substrate **1n** with dr 1.1 :1 afforded **6a** in 78% total yield as white solid, m.p. 183-185 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.91 (s, 1 H), 7.60 (s, 1 H), 7.48 (d, *J* = 6.4 Hz, 2 H), 7.42-7.31 (m, 3 H), 4.53 (q, *J* = 6.8 Hz, 2 H), 4.07 (s, 3 H), 3.94 (s, 3 H), 3.27 (s, 3 H), 1.46 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 156.0, 154.5, 149.9, 149.2, 145.2, 142.8, 128.9, 127.1, 127.0, 126.4, 121.2, 119.5, 98.4, 62.1, 61.1, 60.9, 56.1, 14.2. MS (EI): m/z (%) = 383 (M^+, 49.72), 43 (100). HRMS calcd for $C_{21}H_{21}NO_6$: 383.1369, found: 383.1367. IR (neat) *v*/cm^{-1} 3304, 3107, 2994, 2939, 2855, 2496, 1958, 1650, 1565, 1490, 1465, 1407, 1319, 1206, 1122, 1074, 1024, 983, 813, 714.

51. Ethyl 1-(4-chlorophenyl)-4-hydroxy-6,7,8-trimethoxyisoquinoline-3-carboxylate（6b）



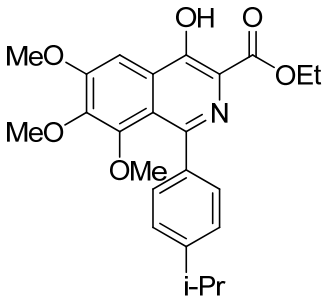
The reaction of substrate **1o** with dr 4.6 :1 afforded **6b** in 84% yield as white solid, m.p. 221-223 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1 H), 7.59 (s, 1 H), 7.44 (d, *J* = 7.6 Hz, 2 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 4.53 (q, *J* = 6.8 Hz, 2H), 4.07 (s, 3H), 3.96 (s, 3 H), 3.31 (s, 3 H), 1.47 (t, 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 156.1, 154.6, 149.6, 147.7, 145.3, 141.2, 133.1, 130.4, 127.2, 126.4, 121.0, 119.6, 98.5, 62.2, 61.2, 61.0, 56.2, 14.3. MS (EI): m/z (%) = 417 (M^+, 6.63), 45 (100). HRMS calcd for $C_{21}H_{20}NO_6Cl$: 417.0979, found: 417.0979 IR (neat) *v*/cm^{-1} 3435, 3110, 3088, 3020, 2979, 2937, 2863, 2824, 2584, 1914, 1650, 1566, 1491, 1461, 1406, 1317, 1206, 1181, 1124, 1074, 1012, 984, 843, 731, 688, 619.

52. Ethyl 1-(4-bromophenyl)-4-hydroxy-6,7,8-trimethoxyisoquinoline-3-carboxylate(6c)



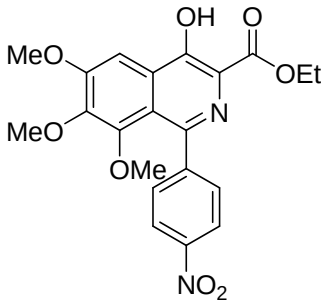
The reaction of substrate **1p** with dr 2.4 : 1 afford **6c** in 89% yield as white solid, m.p. 228-230 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.92 (s, 1 H), 7.59 (s, 1 H), 7.53 (d, *J* = 7.2 Hz, 2 H), 7.37 (d, *J* = 7.2 Hz, 2 H), 4.53 (q, *J* = 6.4 Hz, 2 H), 4.07 (s, 3 H), 3.95 (s, 3 H), 3.31 (s, 3 H), 1.46 (t, *J* = 6.4 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 156.1, 154.7, 149.6, 147.7, 145.3, 141.7, 130.8, 130.2, 126.4, 121.4, 120.9, 119.6, 98.5, 62.2, 61.2, 61.0, 56.2, 14.3. MS (ESI): m/z (%) = 464 [$(M+2+H)^+$], 462 [$(M+H)^+$]. HRMS-ESI calcd for $C_{21}H_{21}NO_6BrNa$ [$(M+H)^+$]: 462.0542, found: 462.0547. IR (neat) *v*/cm^{-1} 3327, 3271, 3106, 3087, 2980, 2936, 2853, 2579, 1914, 1649, 1607, 1583, 1567, 1490, 1465, 1407, 1317, 1206, 1181, 1125, 1074, 1010, 983, 853, 841, 794, 730, 685, 613.

53. Ethyl 4-hydroxy-1-(4-isopropylphenyl)-6,7,8-trimethoxyisoquinoline-3-carboxylate(6d).



The reaction of substrate **1q** with dr 5 : 1 afforded **6d** in 70% yiled, as white solid, m.p. 173-175 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.89 (s, 1 H), 7.59 (s, 1 H), 7.40 (d, *J* = 7.2 Hz, 2 H), 7.25 (d, *J* = 7.6 Hz, 2 H), 4.53 (q, *J* = 6.4 Hz, 2 H), 4.07 (s, 3 H), 3.94 (s, 3 H), 3.26 (s, 3 H), 3.00-2.90 (m, 2 H), 1.46 (t, *J* = 6.8 Hz, 3 H), 1.29 (d, *J* = 6.4 Hz, 6 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 156.0, 154.4, 150.0, 149.4, 147.8, 145.3, 140.3, 129.0, 126.5, 125.2, 121.3, 119.6, 98.4, 62.2, 61.2, 61.1, 56.2, 34.0, 24.1, 14.3. MS (EI): m/z (%) =425 (M^+, 43.28), 308 (100). HRMS calcd for $C_{21}H_{20}NO_6Cl$: 425.1838, found: 425.1836. IR (neat) v/cm^{-1} 3470, 3202, 3181, 3042, 3011, 2961, 2595, 1908, 1650, 1584, 1488, 1453, 1319, 1207, 1154, 932, 842, 796, 696.

54. Ethyl 4-hydroxy-6,7,8-trimethoxy-1-(4-nitrophenyl)isoquinoline-3-carboxylate(6e).



The reaction of substrate **1r** with dr 2.7 : 1 afforded **6e** 42% yield as white solid, m.p. 225-226 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.99 (s, 1 H), 8.28 (d, *J* = 7.6 Hz, 2 H), 7.65 (d, *J* = 7.6 Hz, 2 H), 7.61 (s, 1 H), 4.54 (q, *J* = 6.8 Hz, 2 H), 4.09 (s, 3 H), 3.96 (s, 3 H), 3.31 (s, 3 H), 1.47 (t, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 156.4, 155.1, 149.4, 149.1, 146.9, 146.4, 145.3, 130.0, 126.4, 122.4, 120.8, 119.8, 98.7, 62.4, 61.2, 60.9, 56.3, 14.3. MS (EI): m/z (%) = 428 (M^+, 90.16), 356 (100). HRMS calcd for $C_{21}H_{20}N_2O_8$: 428.1220, found: 428.1220. IR (neat) *v*/cm^{-1} 3297, 3108, 3058, 2988, 2926, 2851, 2595, 1946, 1661, 1594, 1563, 1511, 1448, 1412, 1344, 1229, 1129, 1080, 973, 851, 728, 693, 612.

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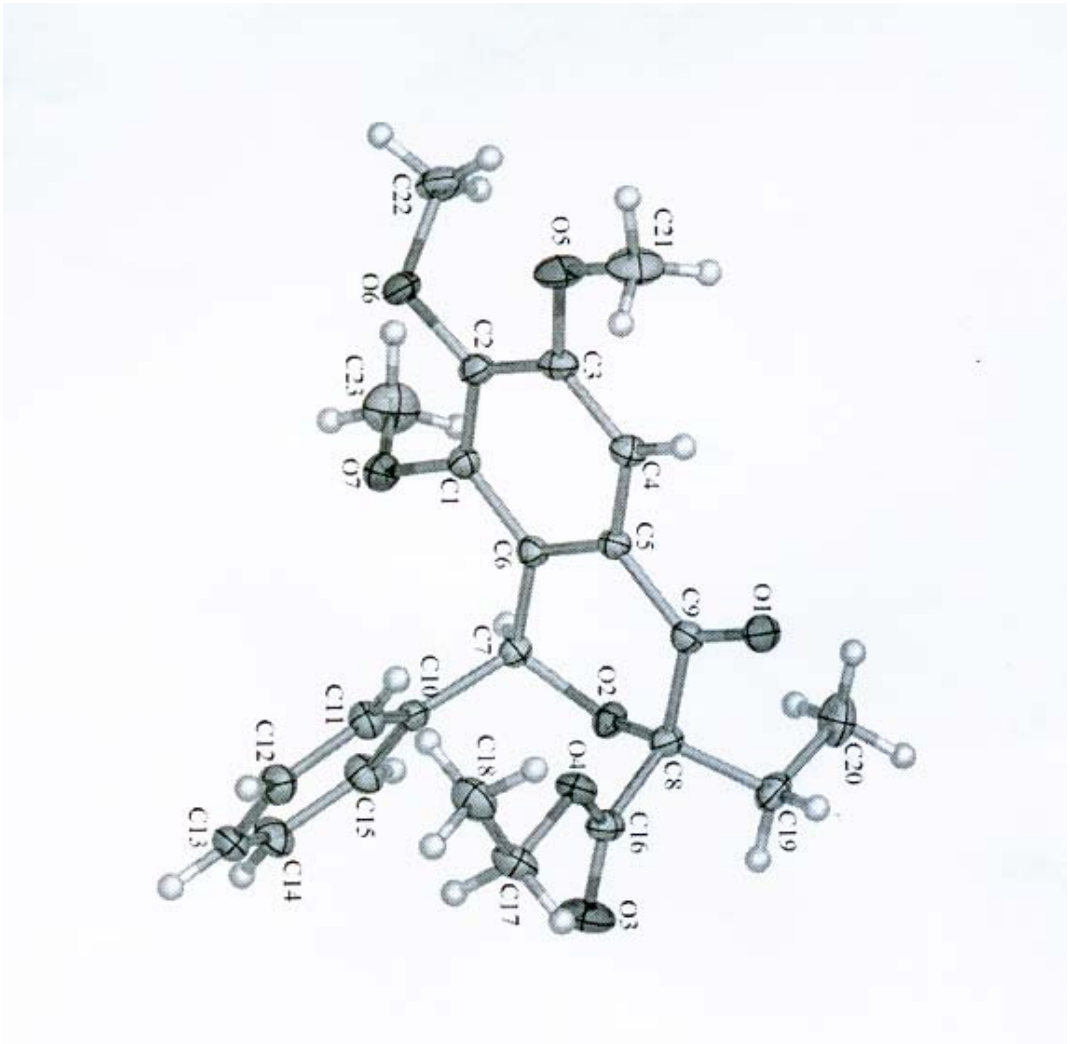
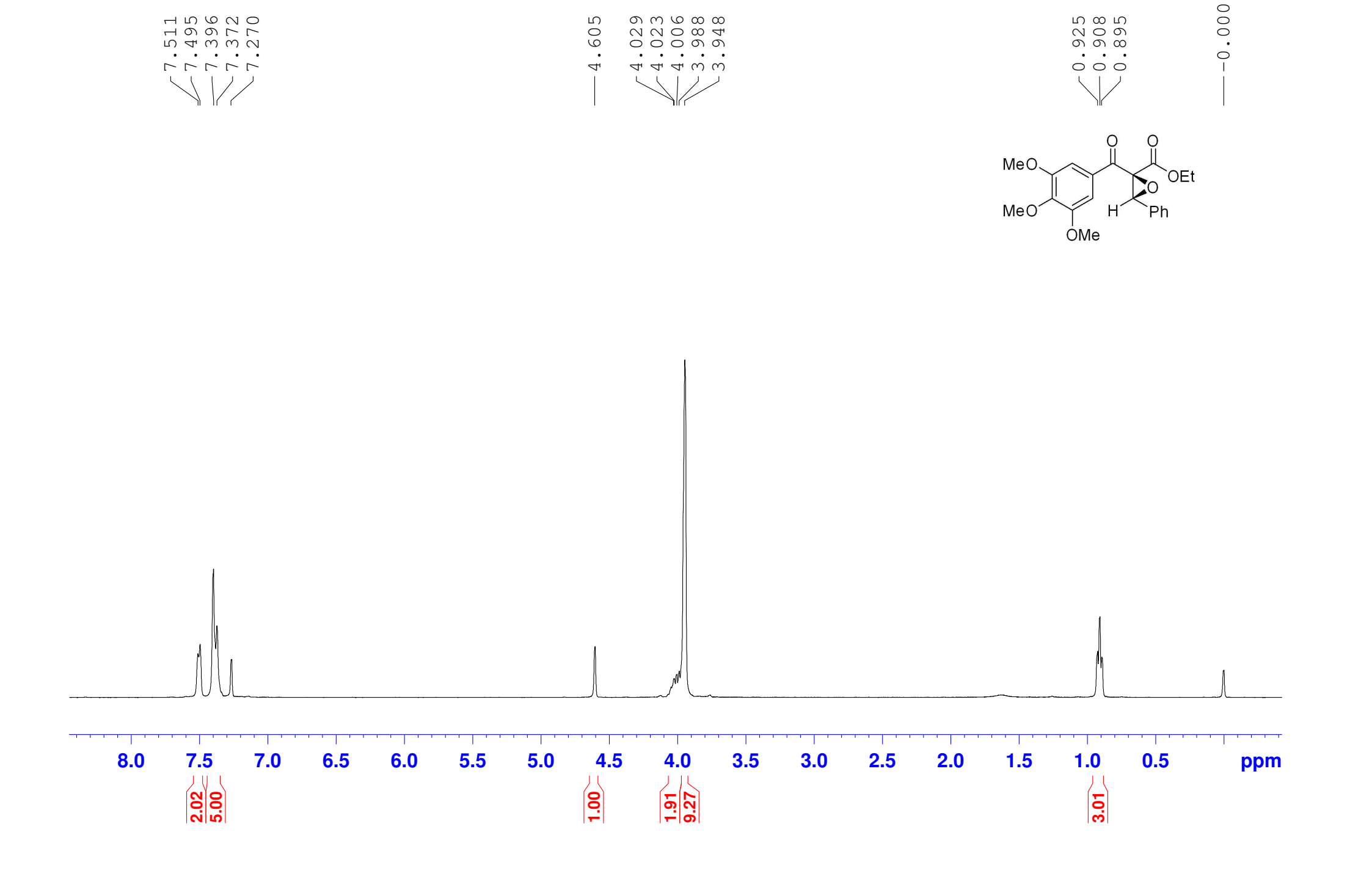
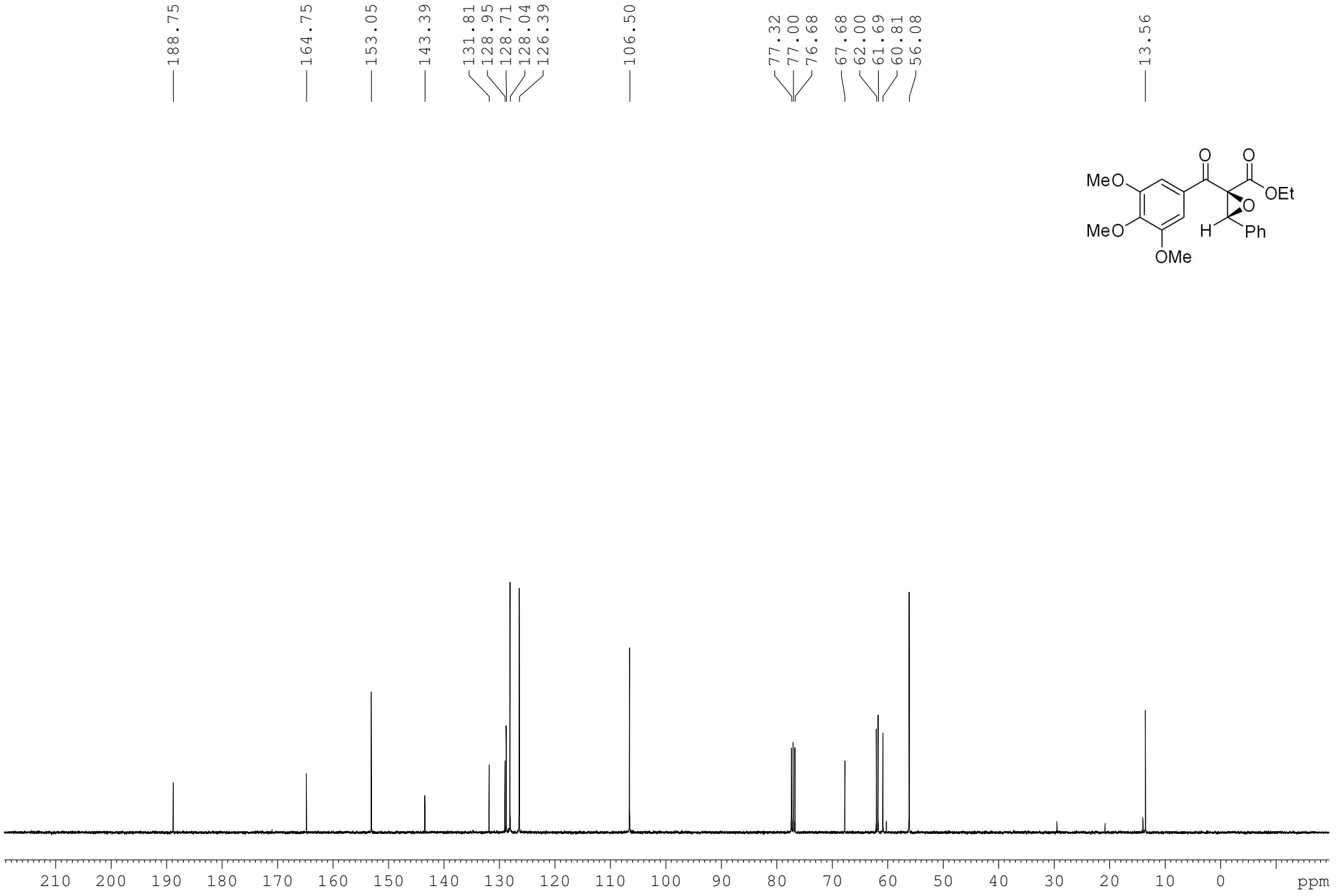
Crystal Structure of 4a

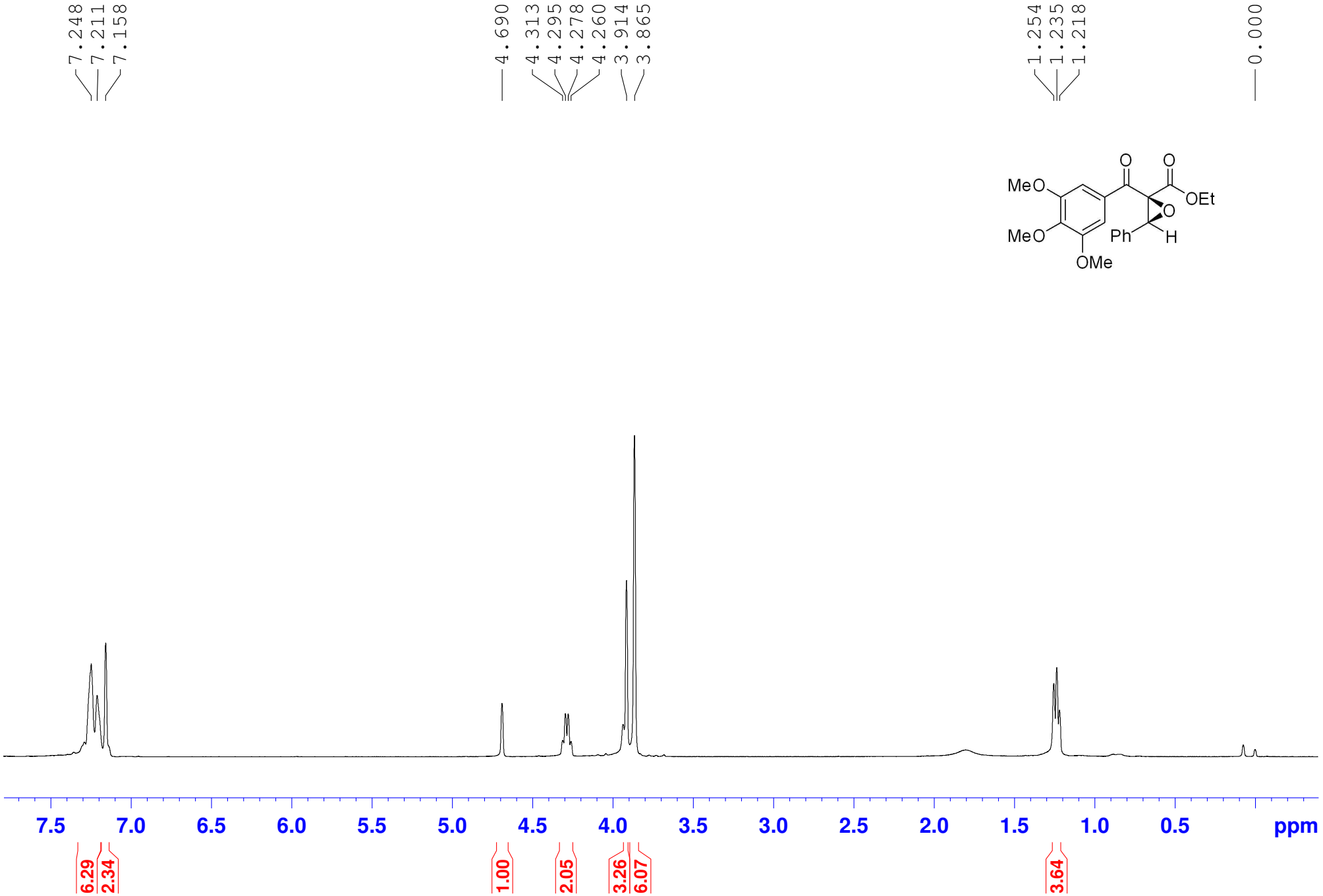
4a

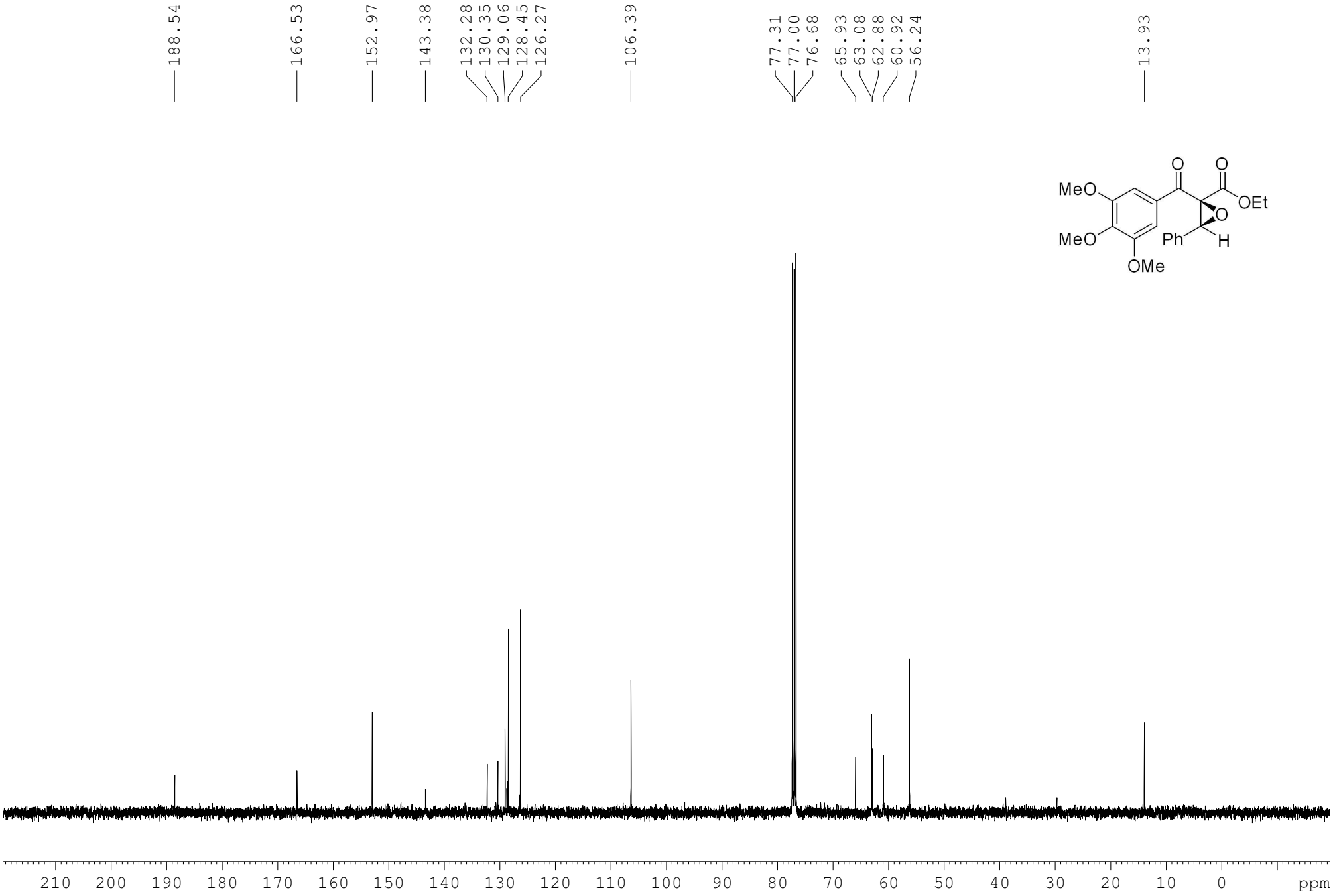


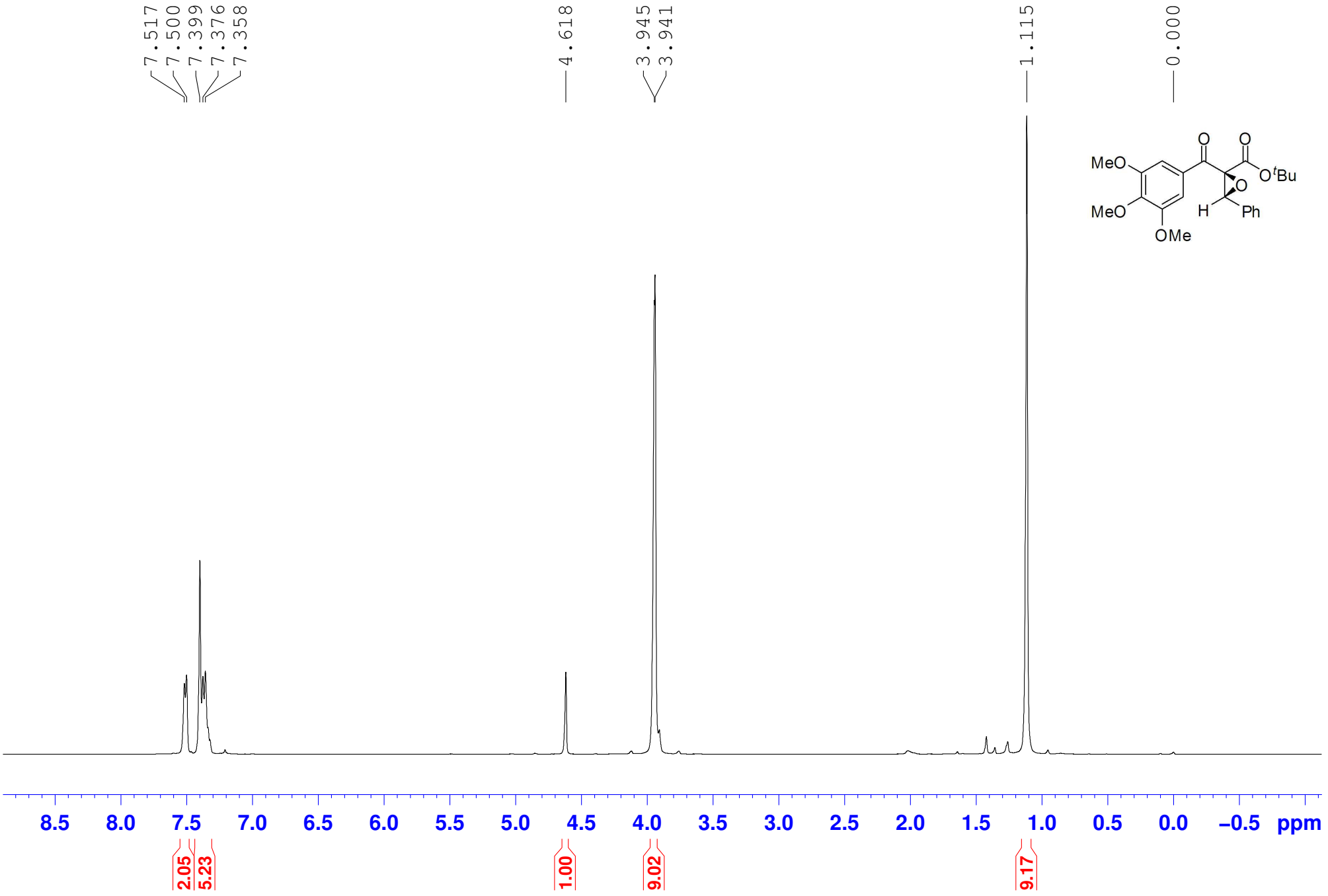
^{1}H and ^{13}C NMR Spectra for New Compounds

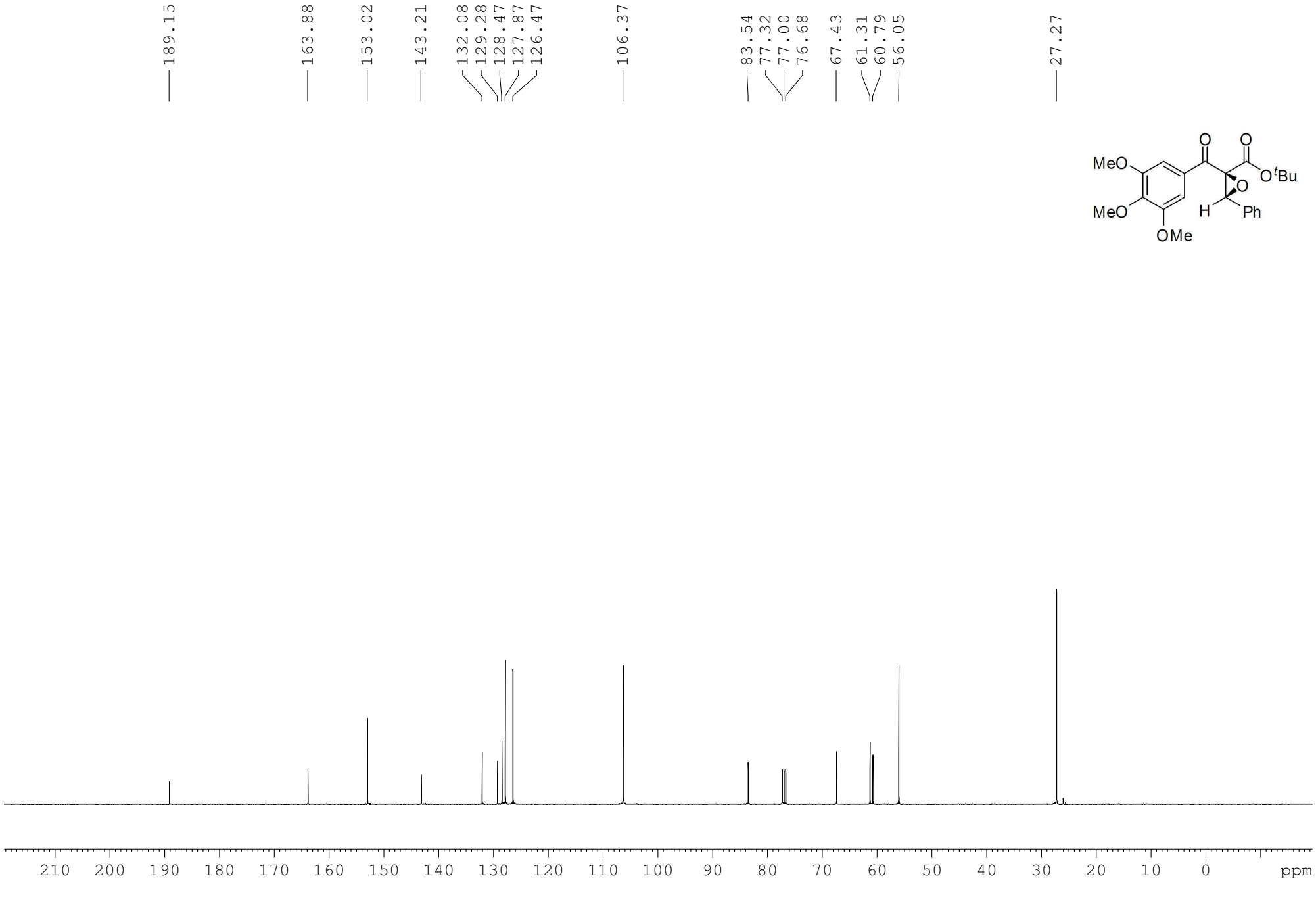


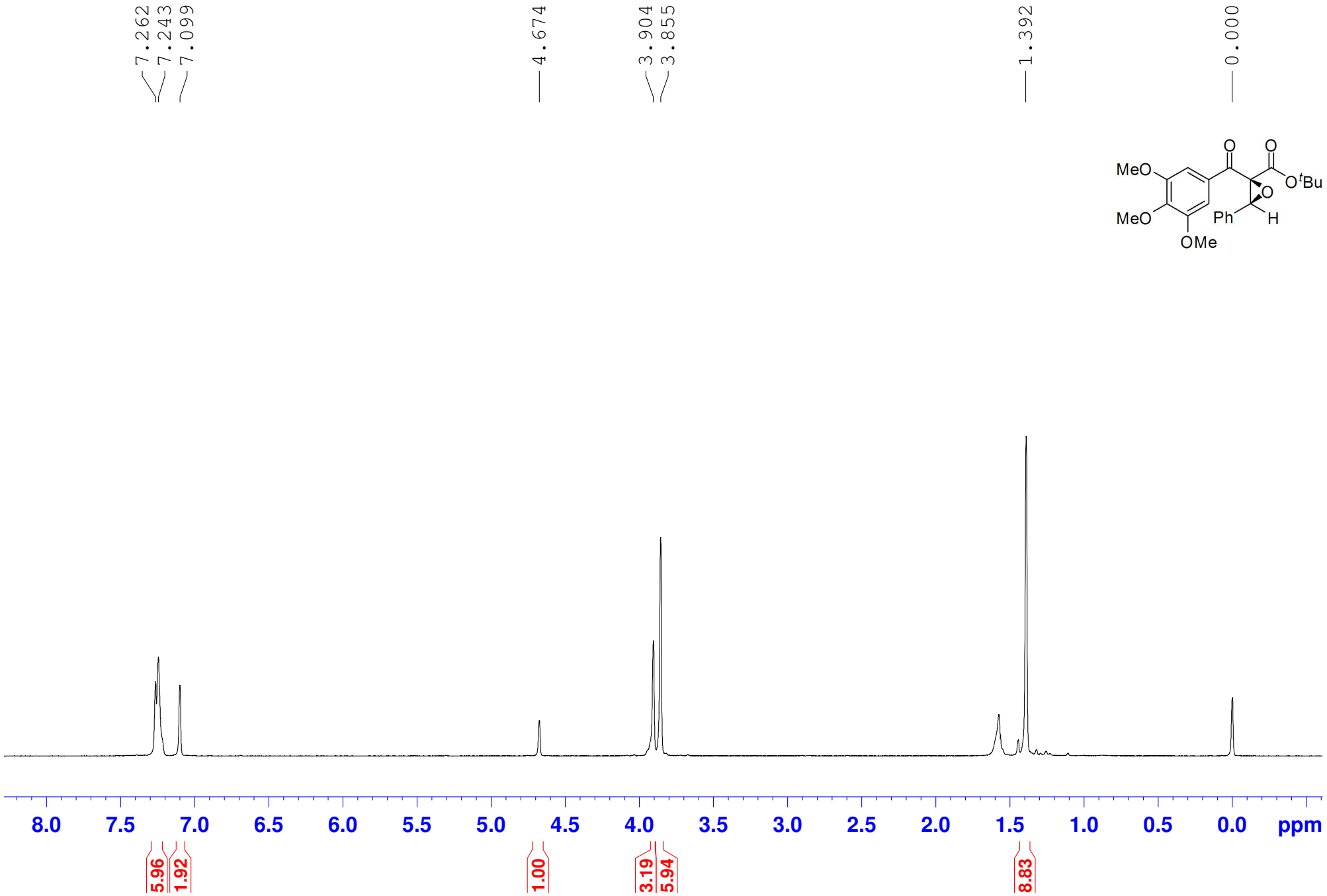


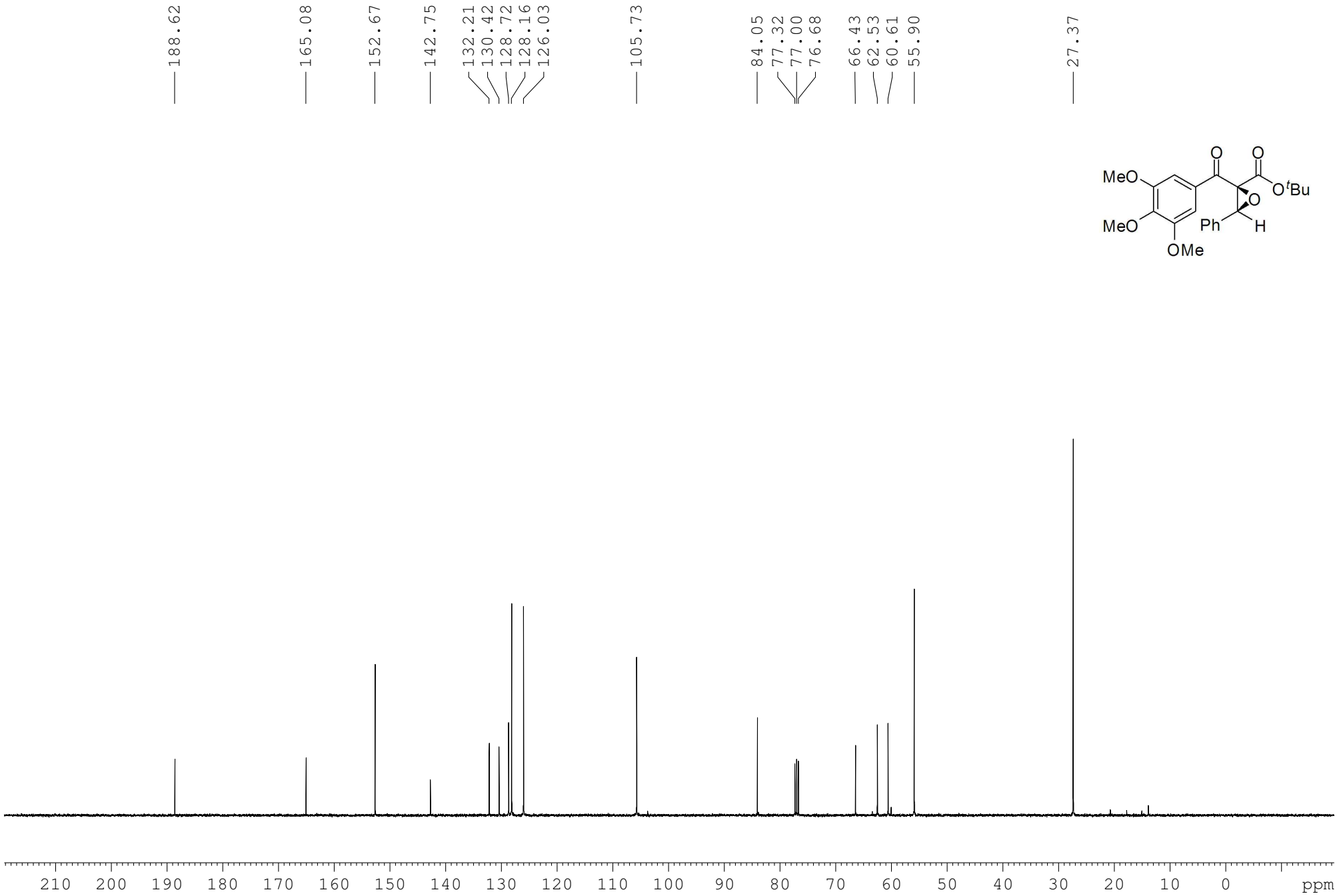


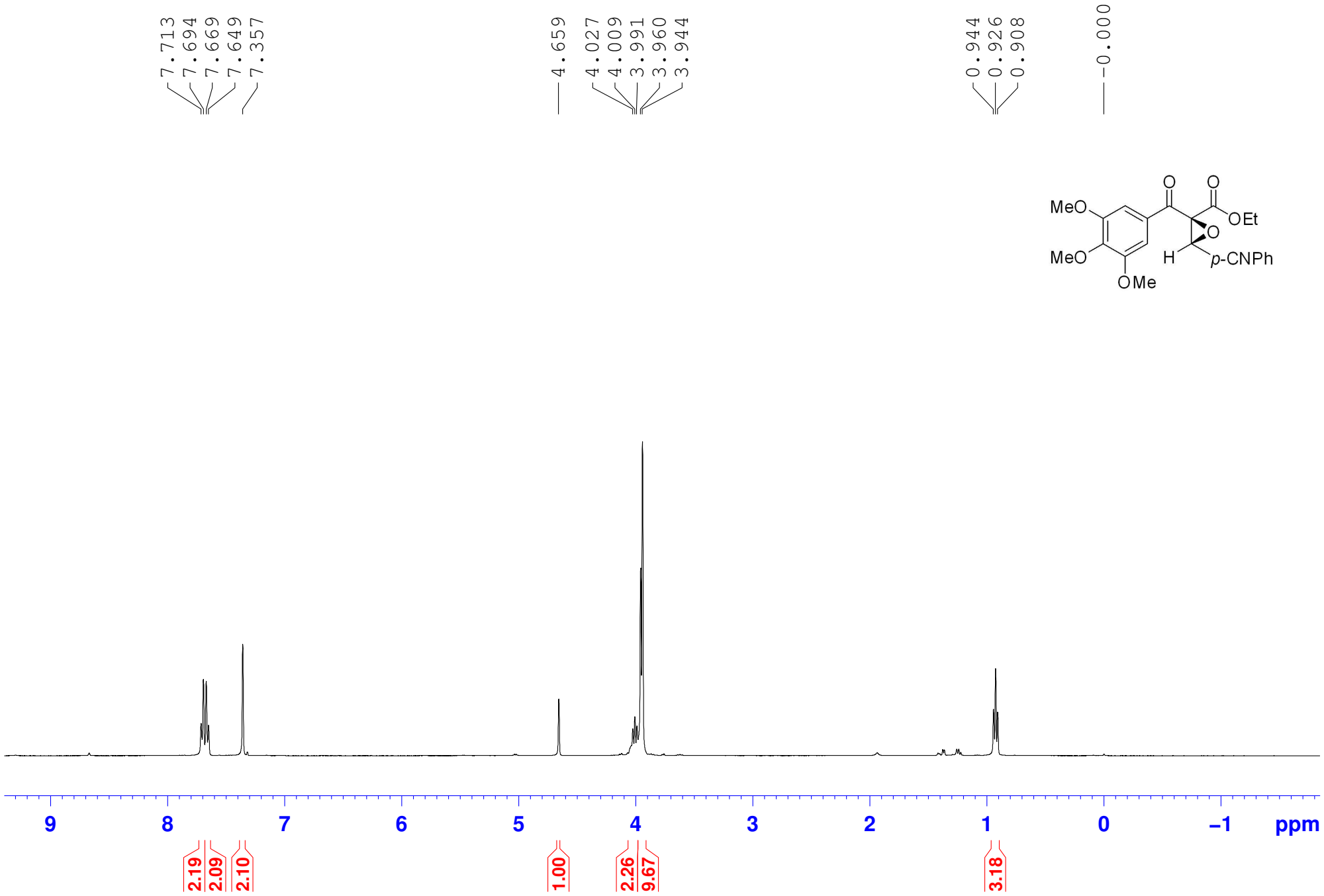


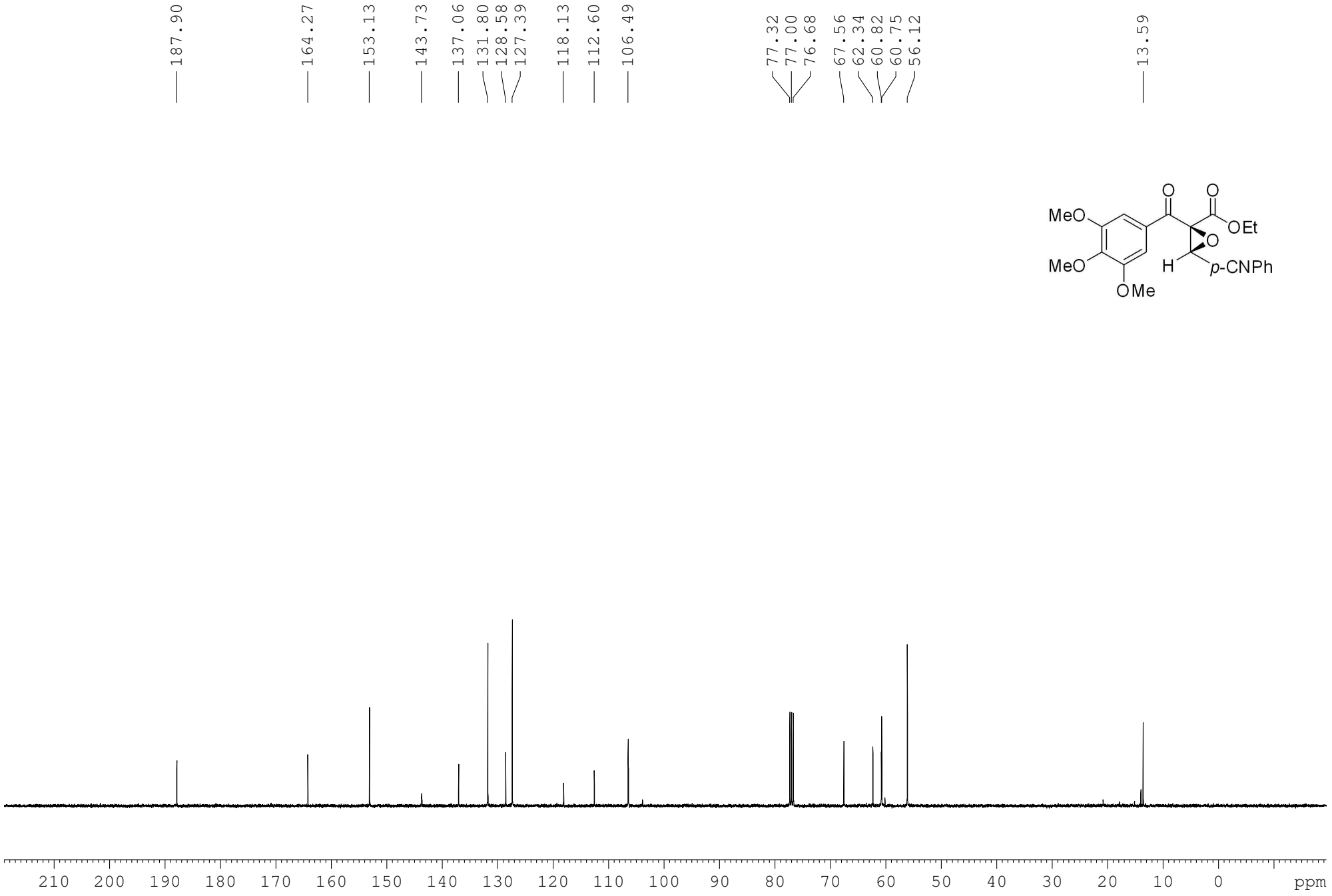


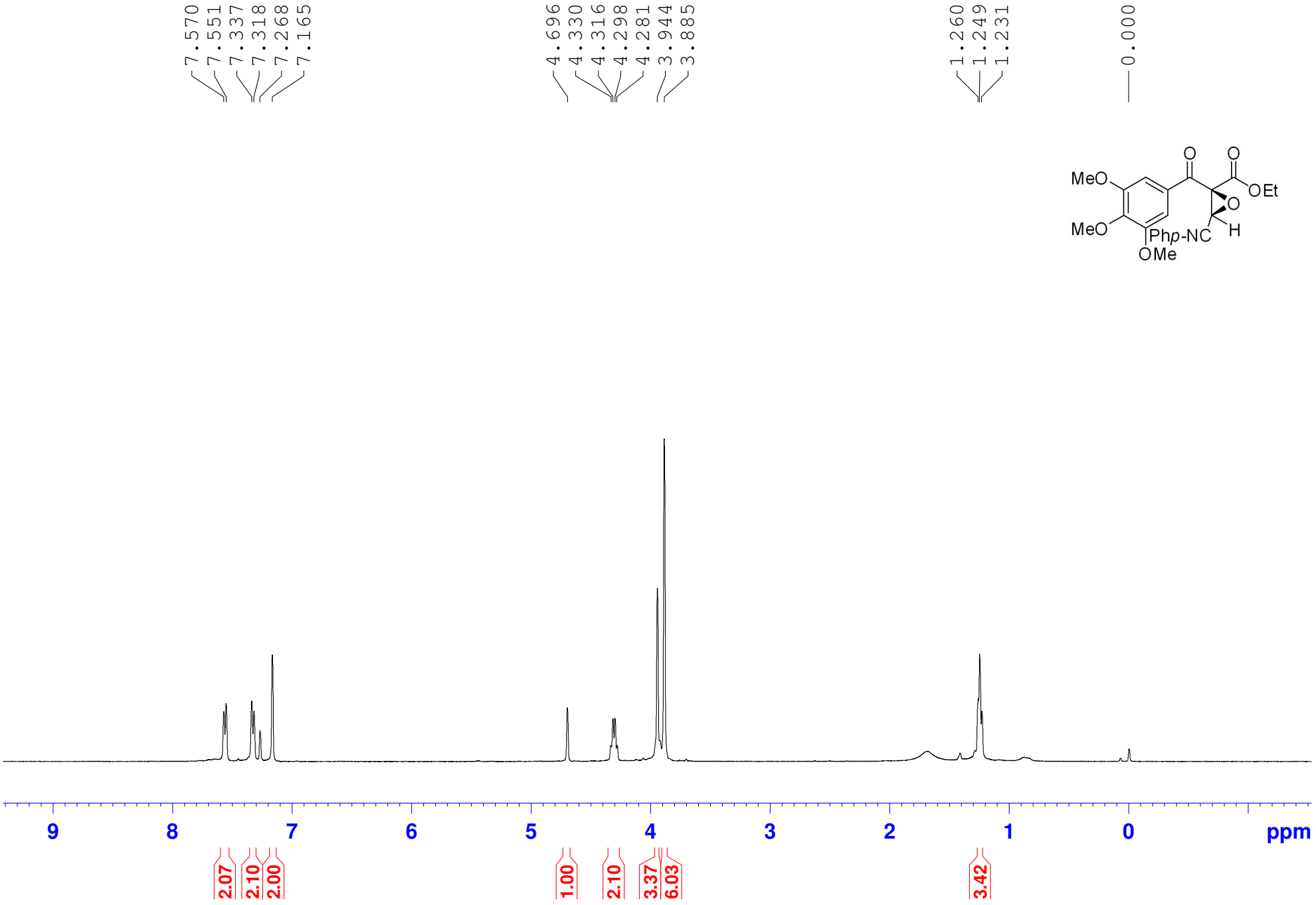


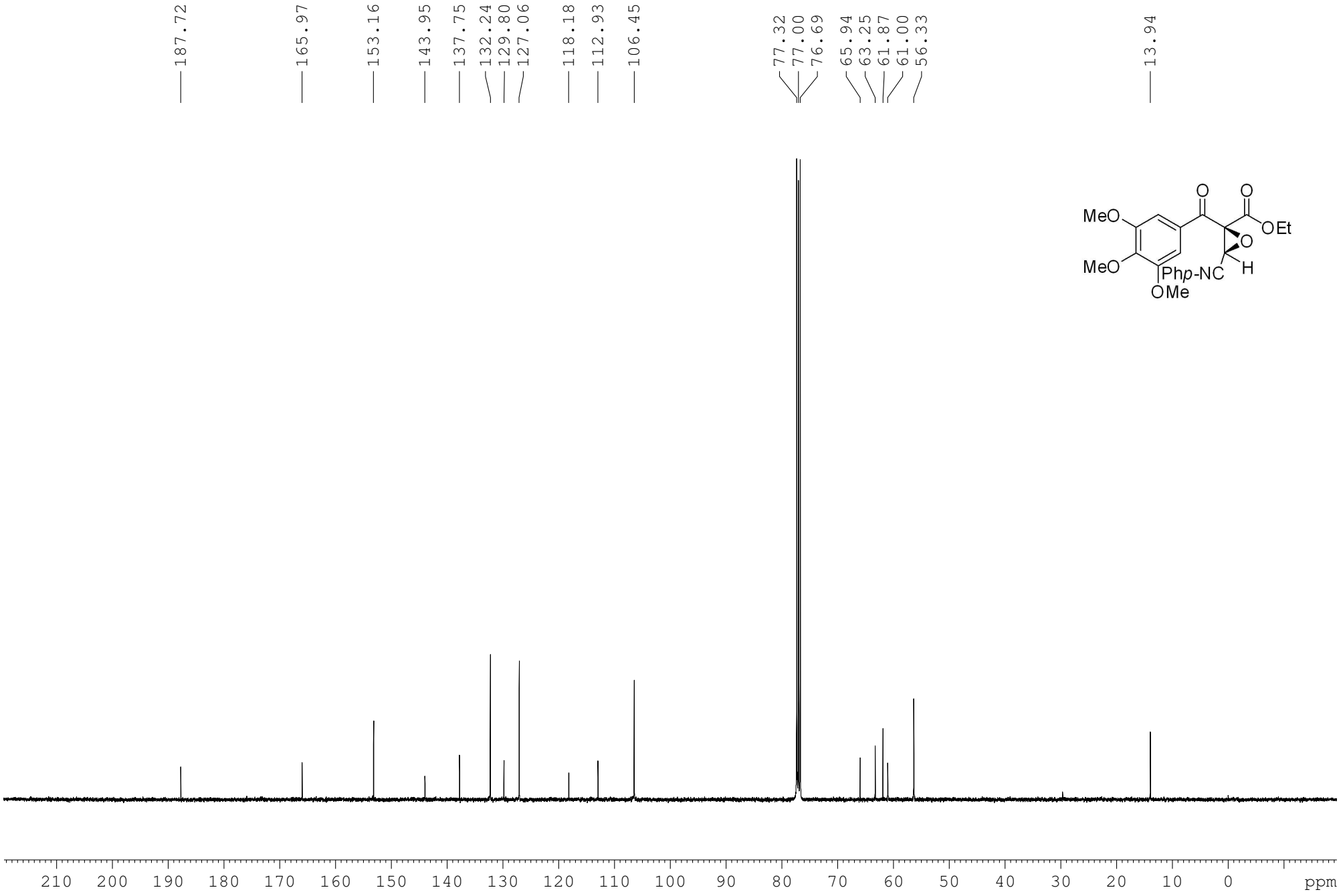


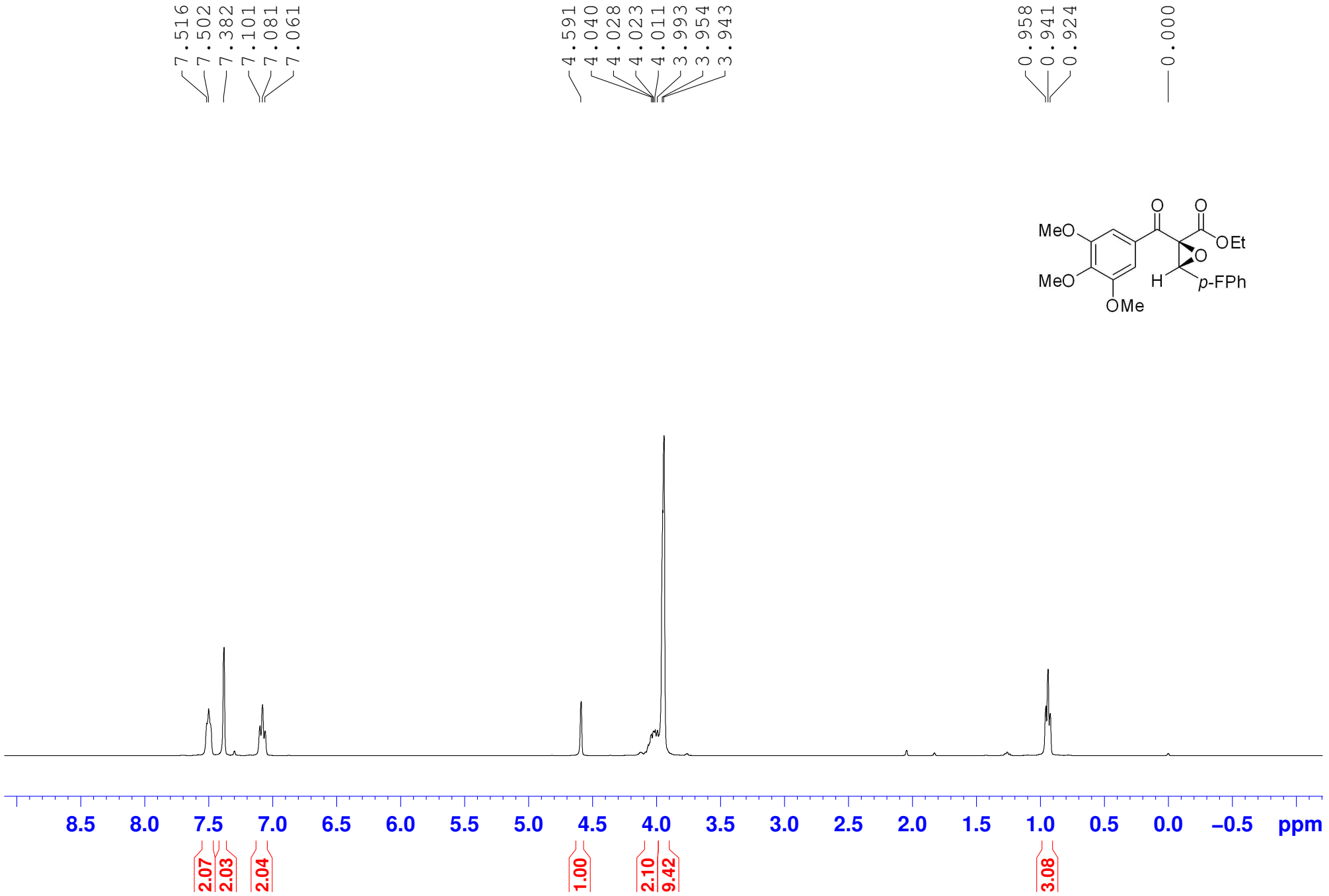


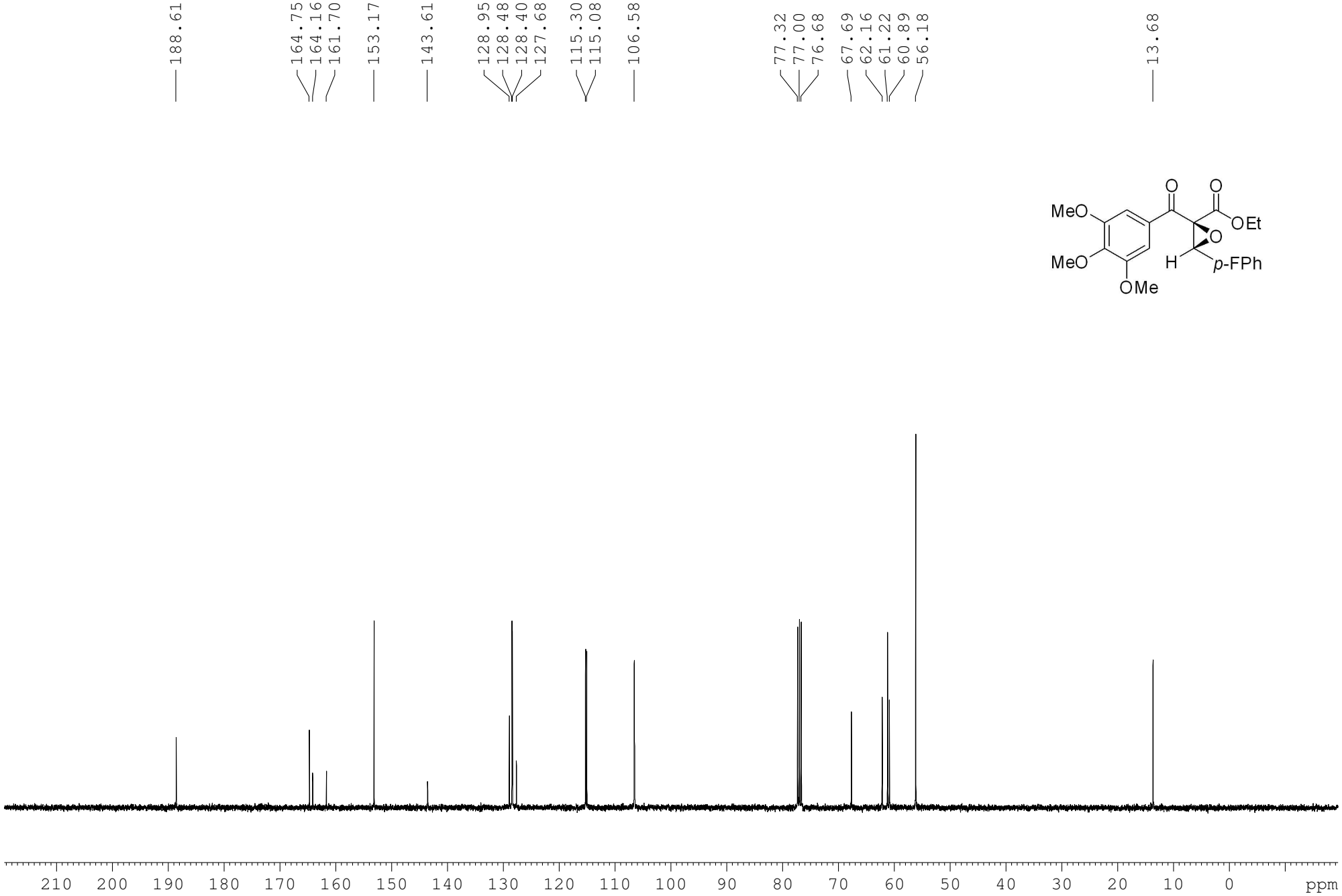


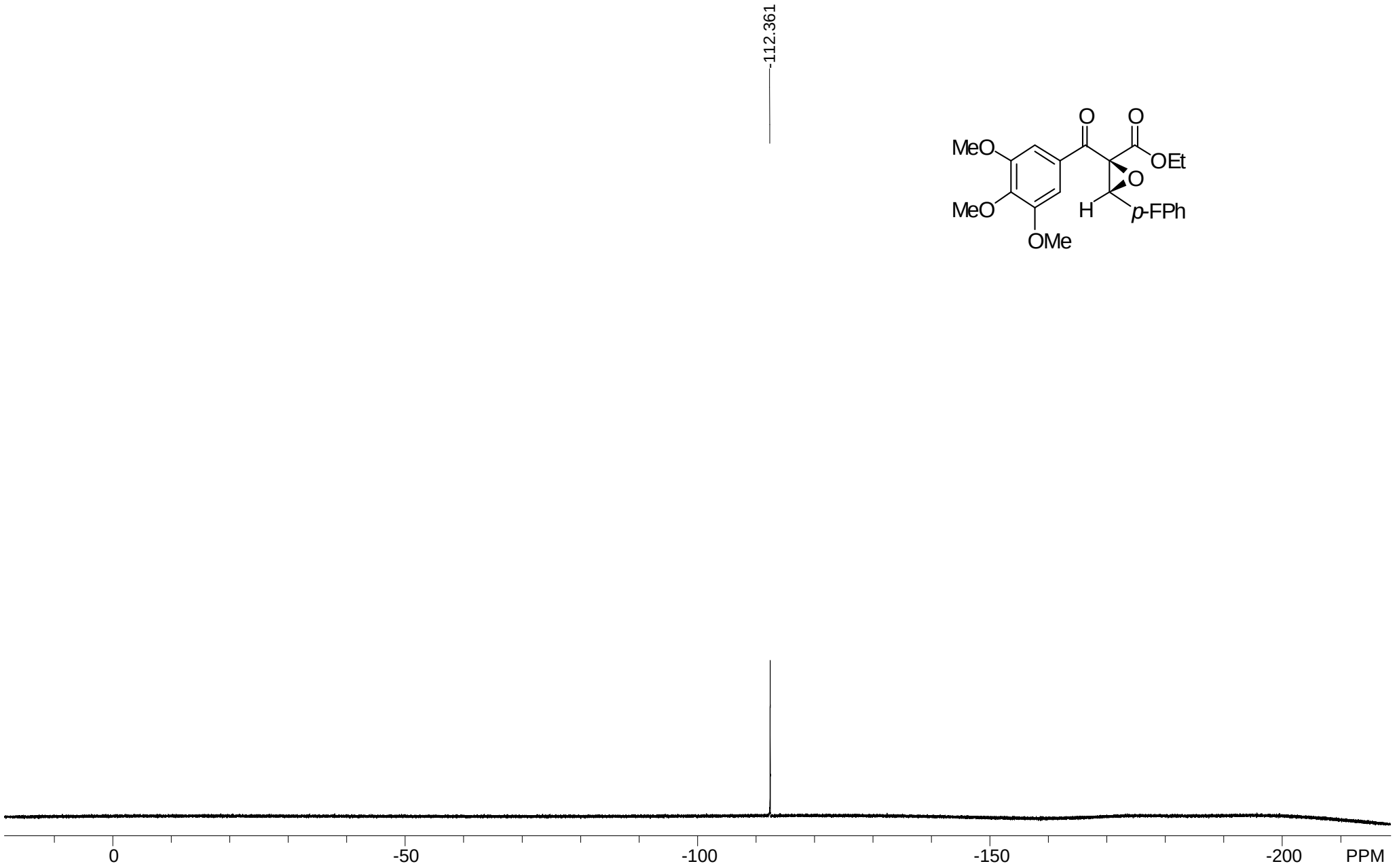


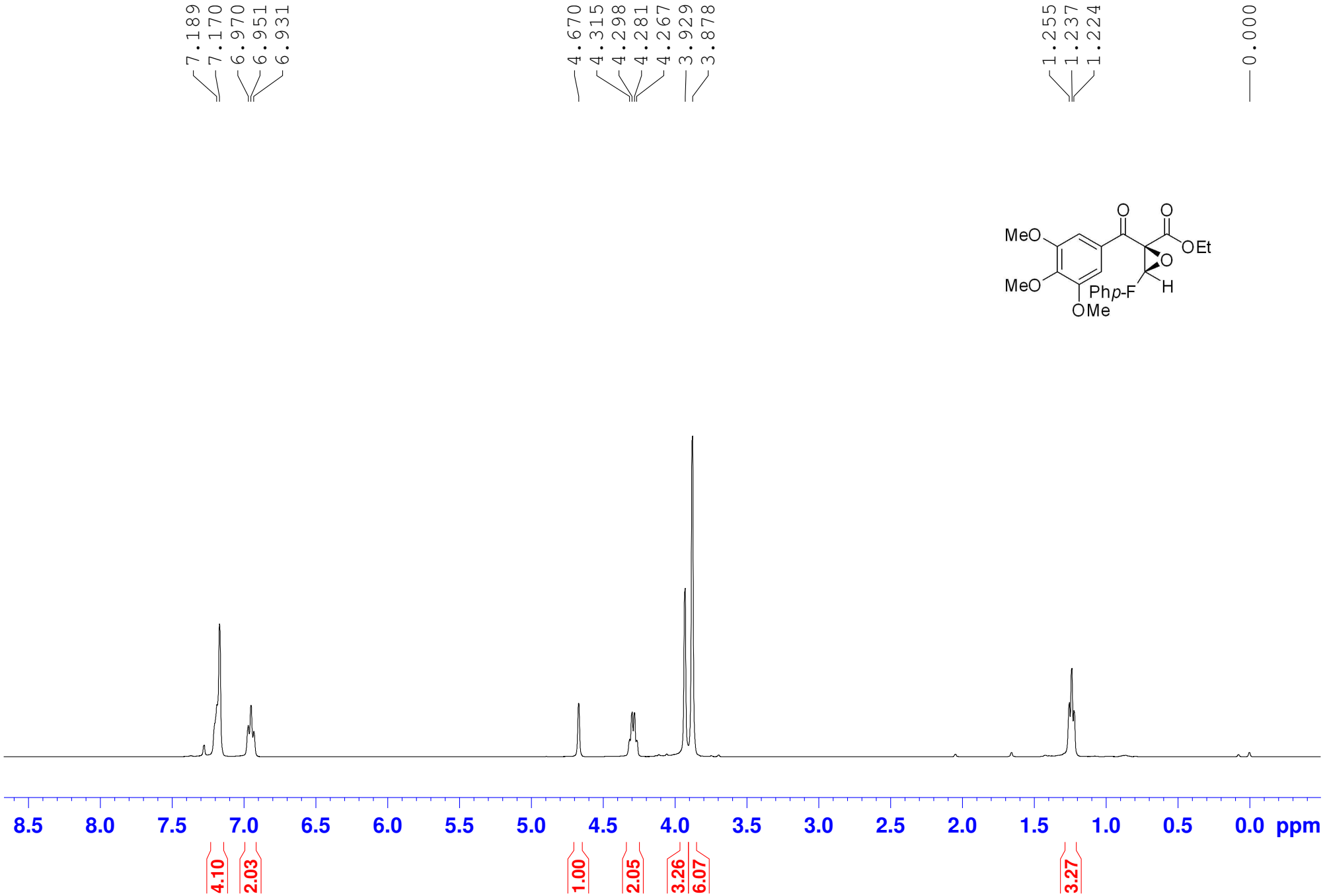


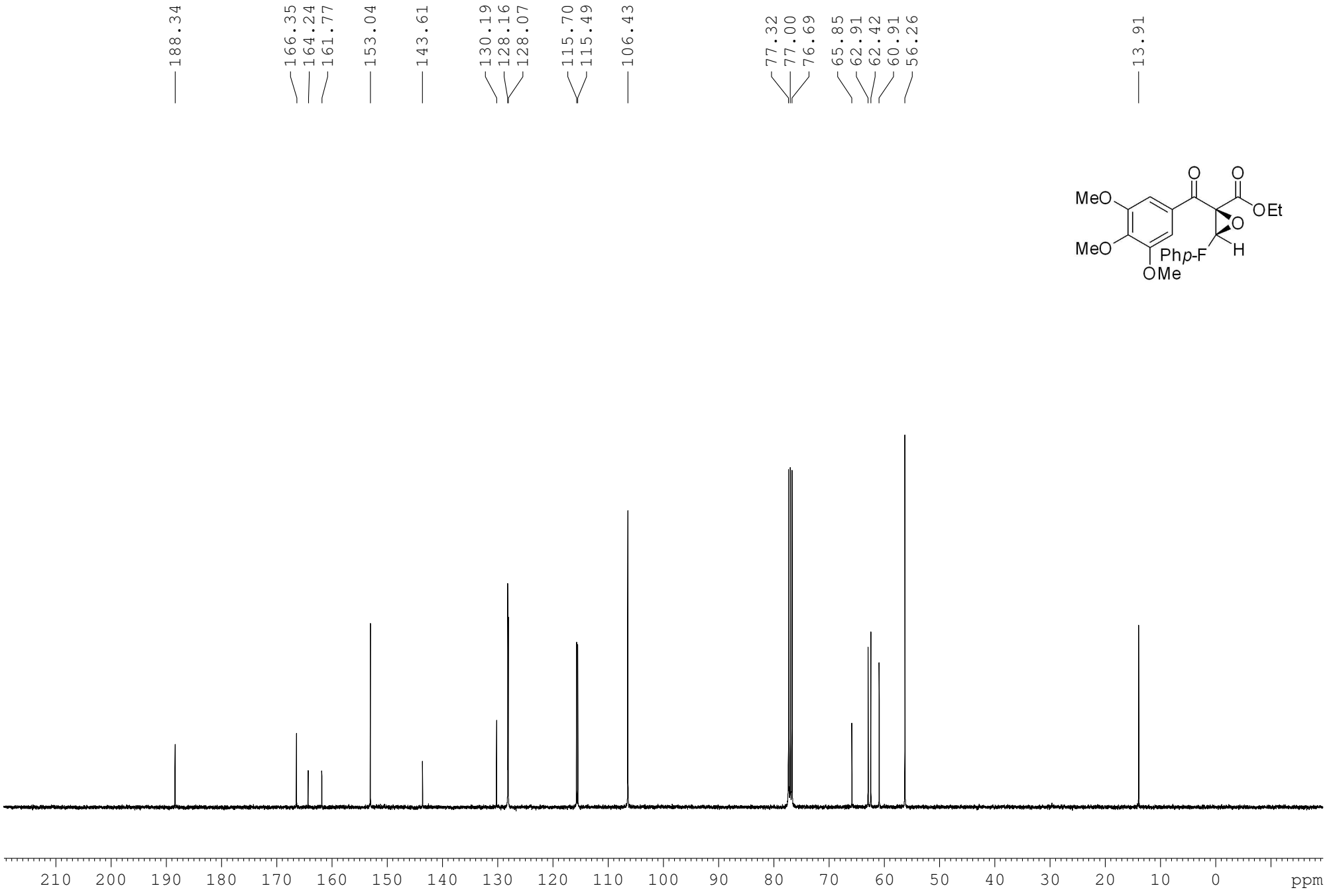


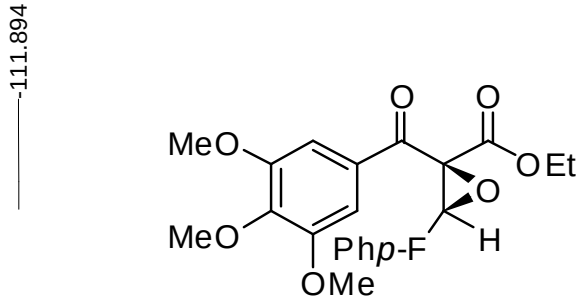


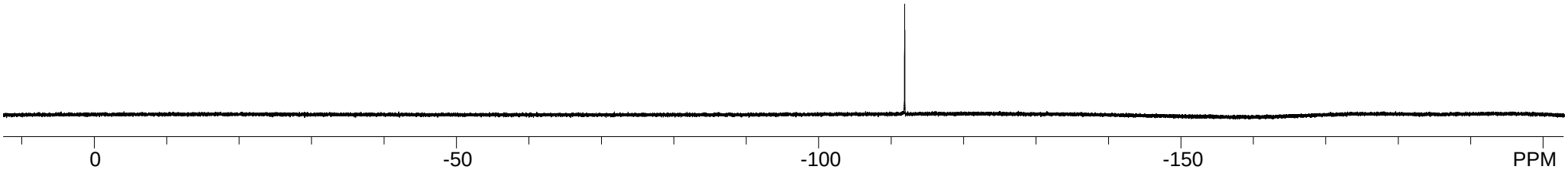


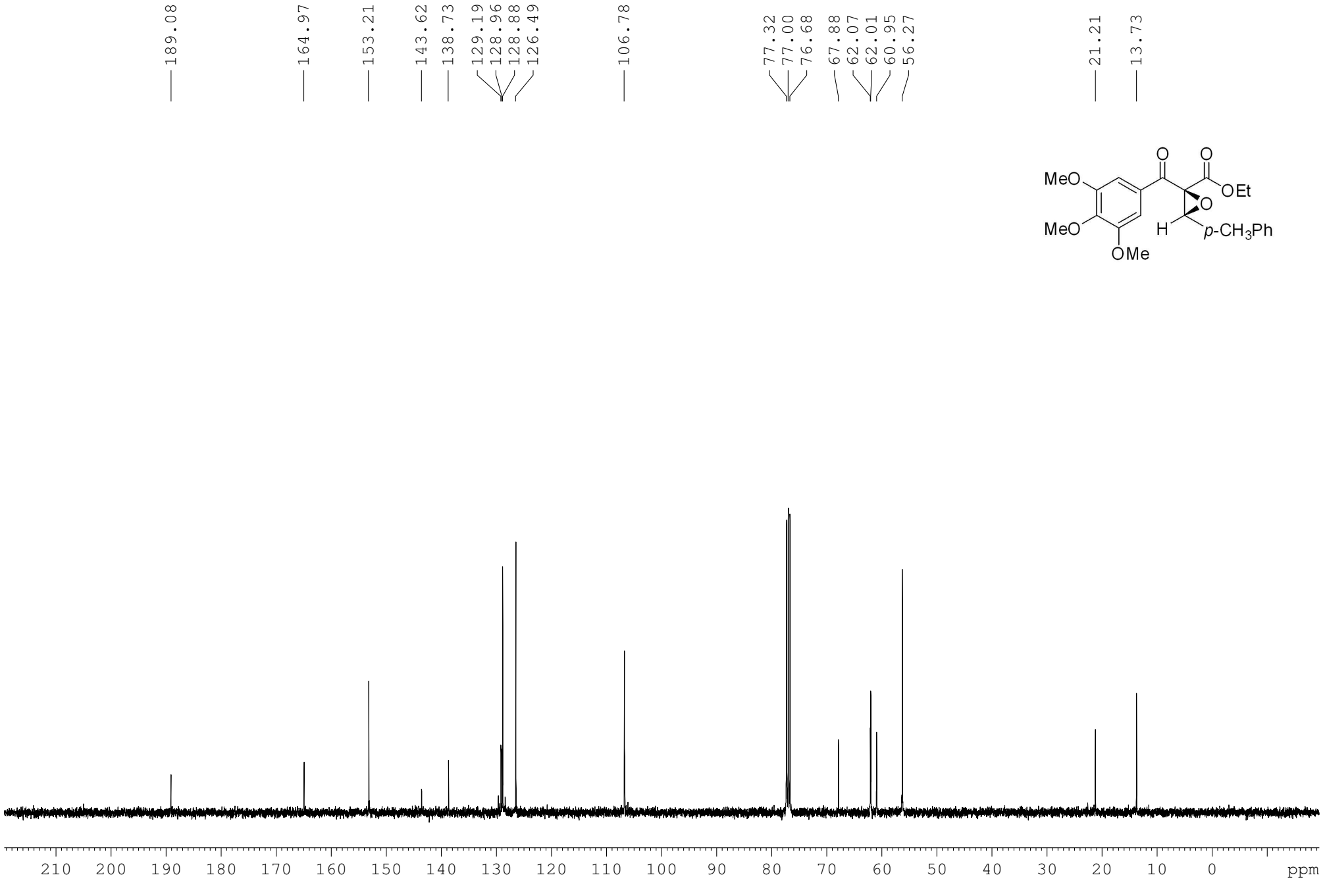


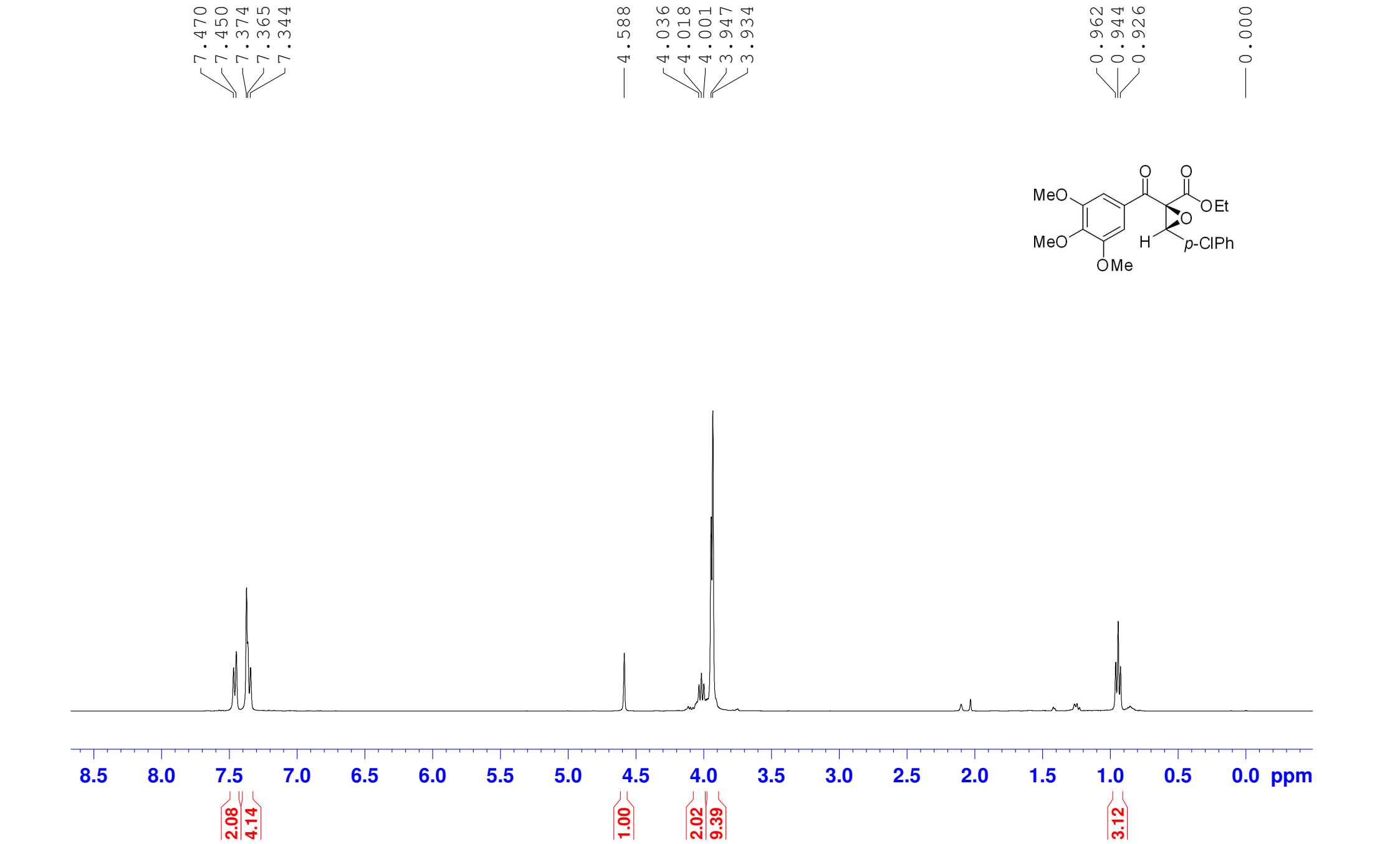


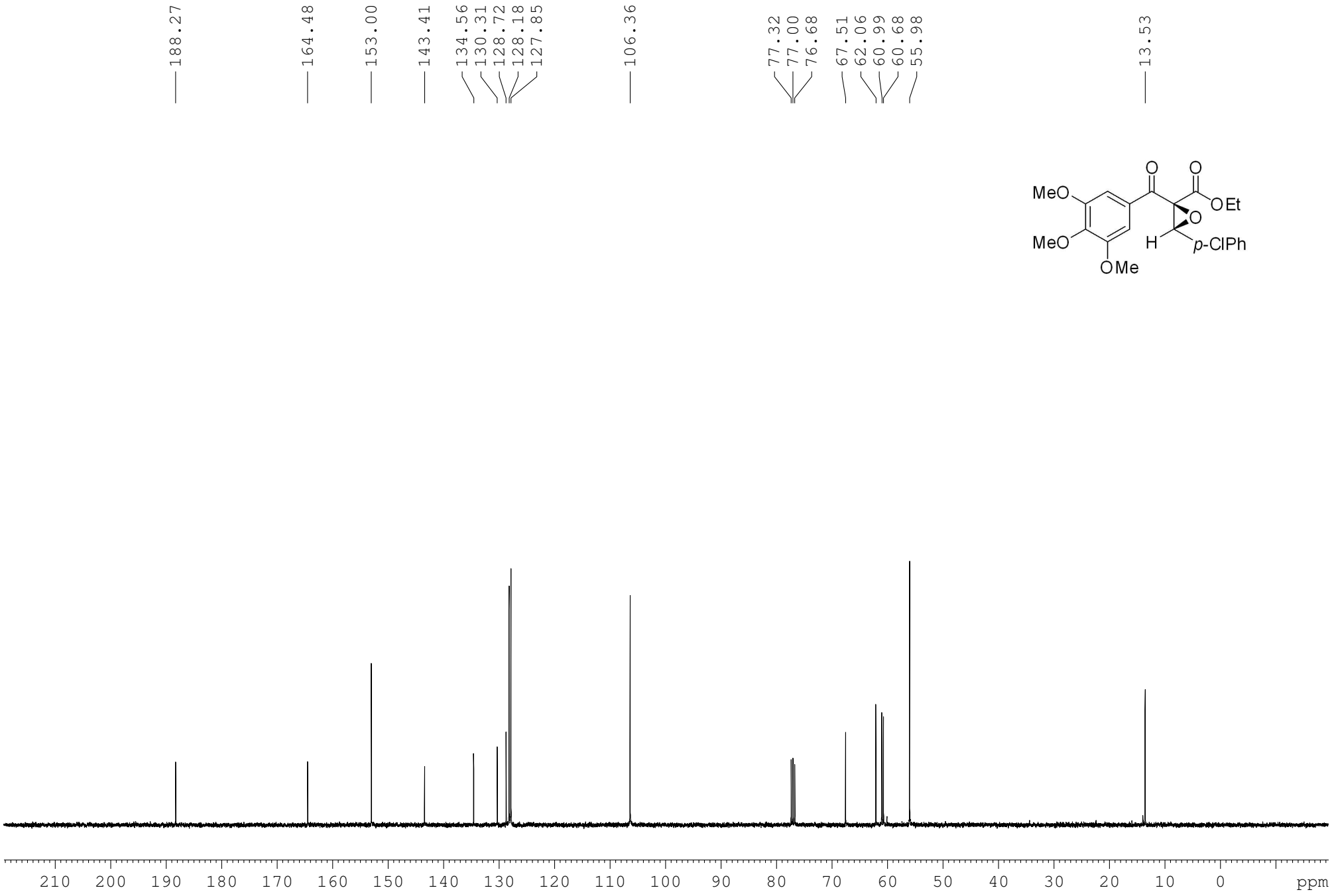


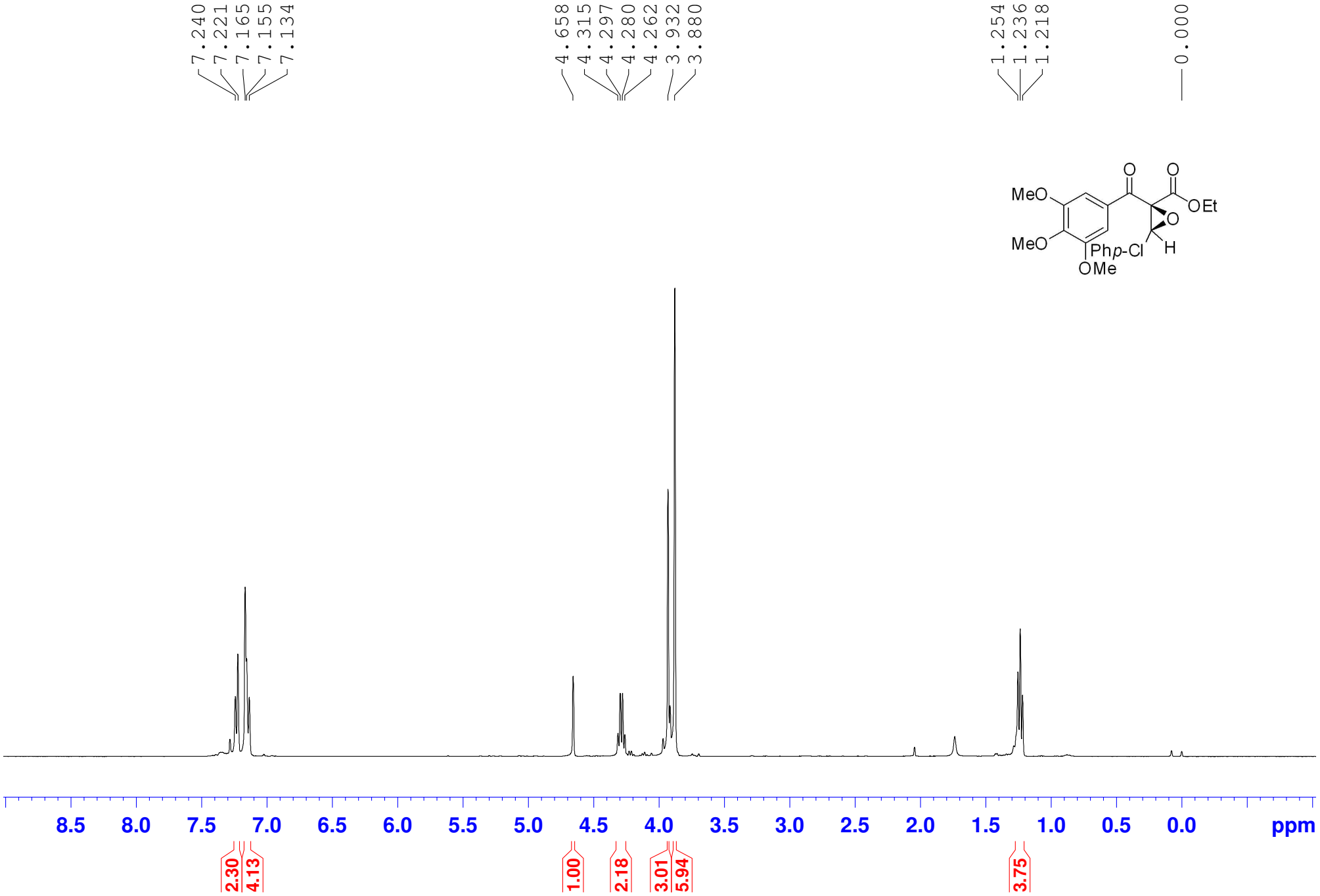


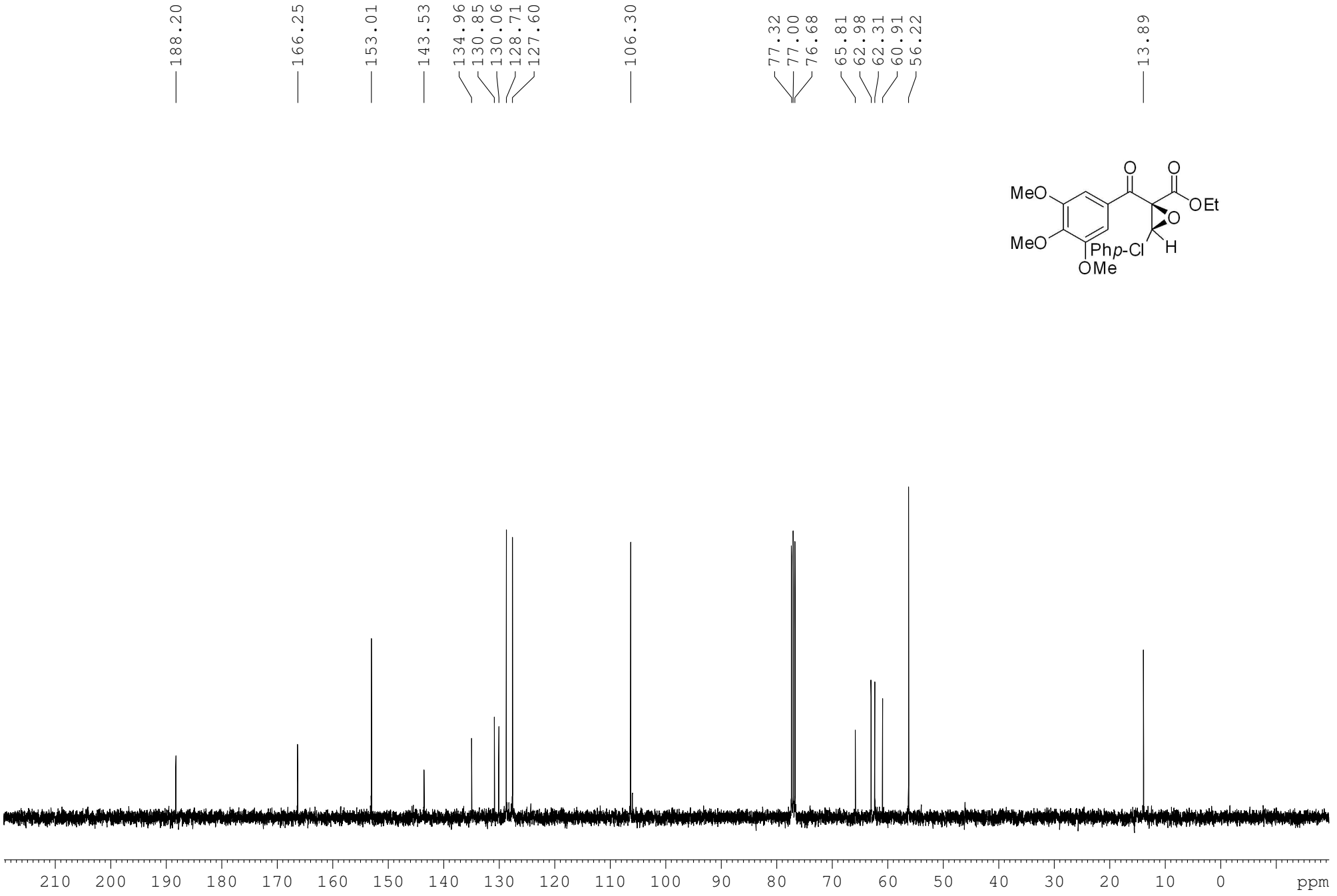


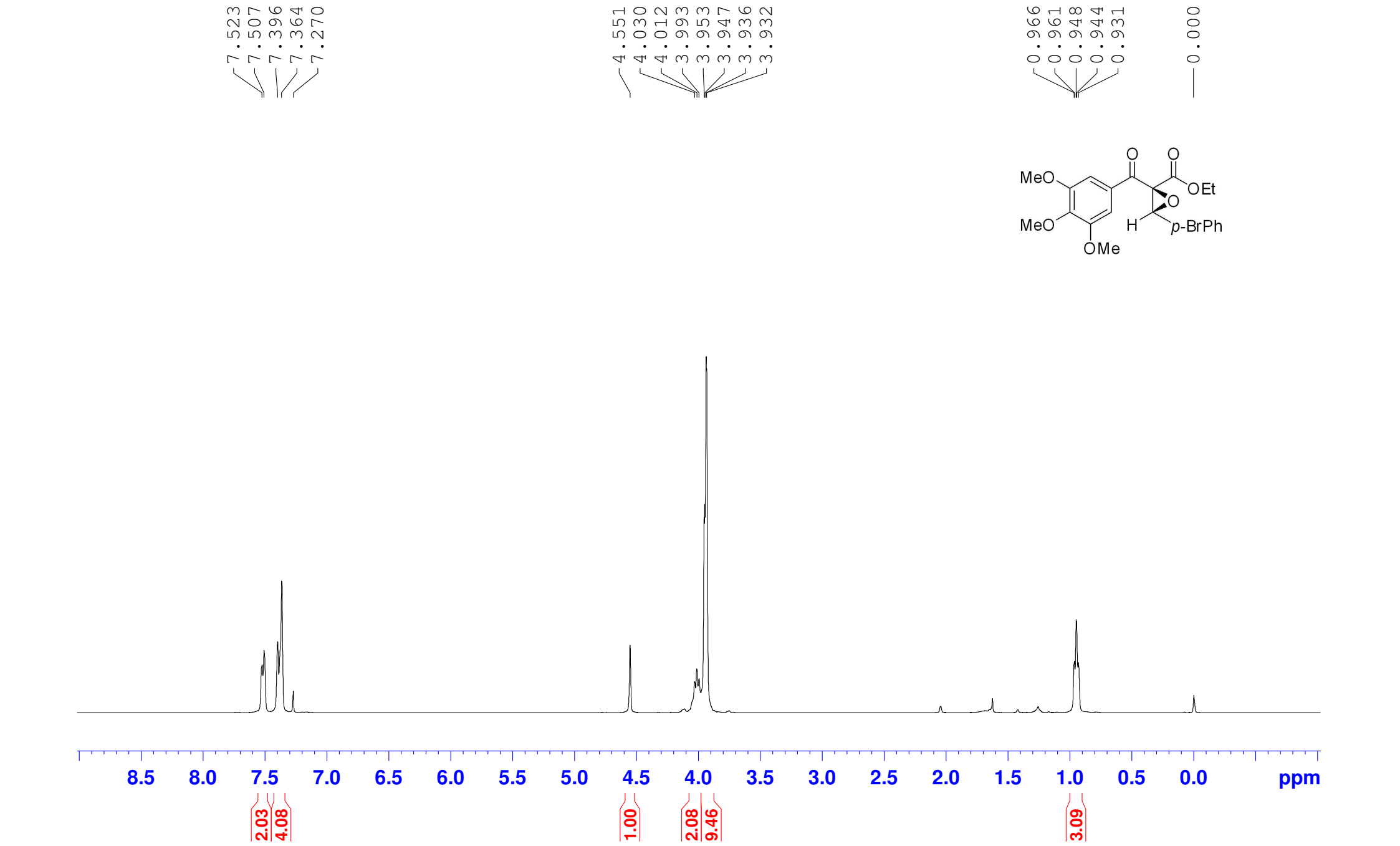


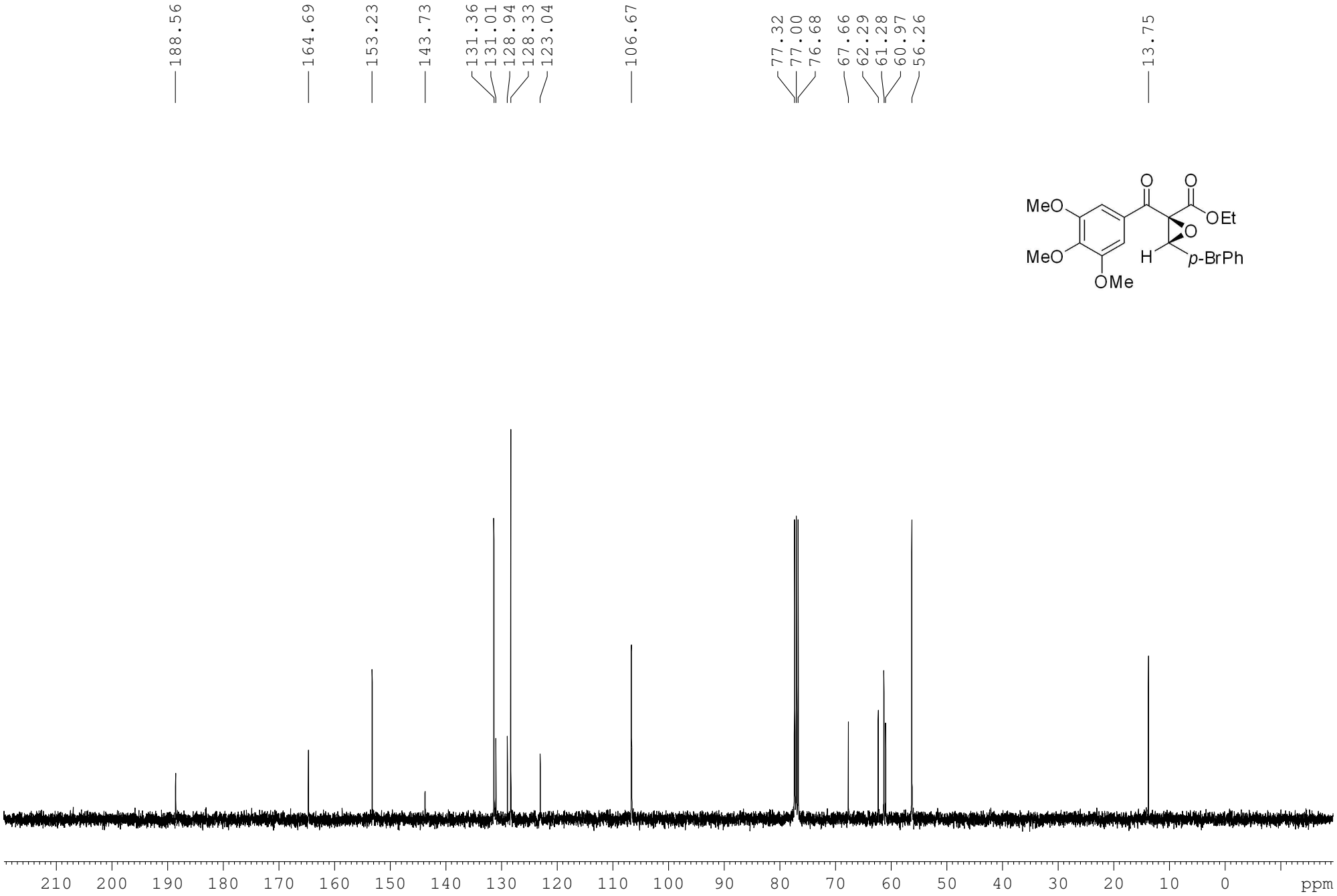


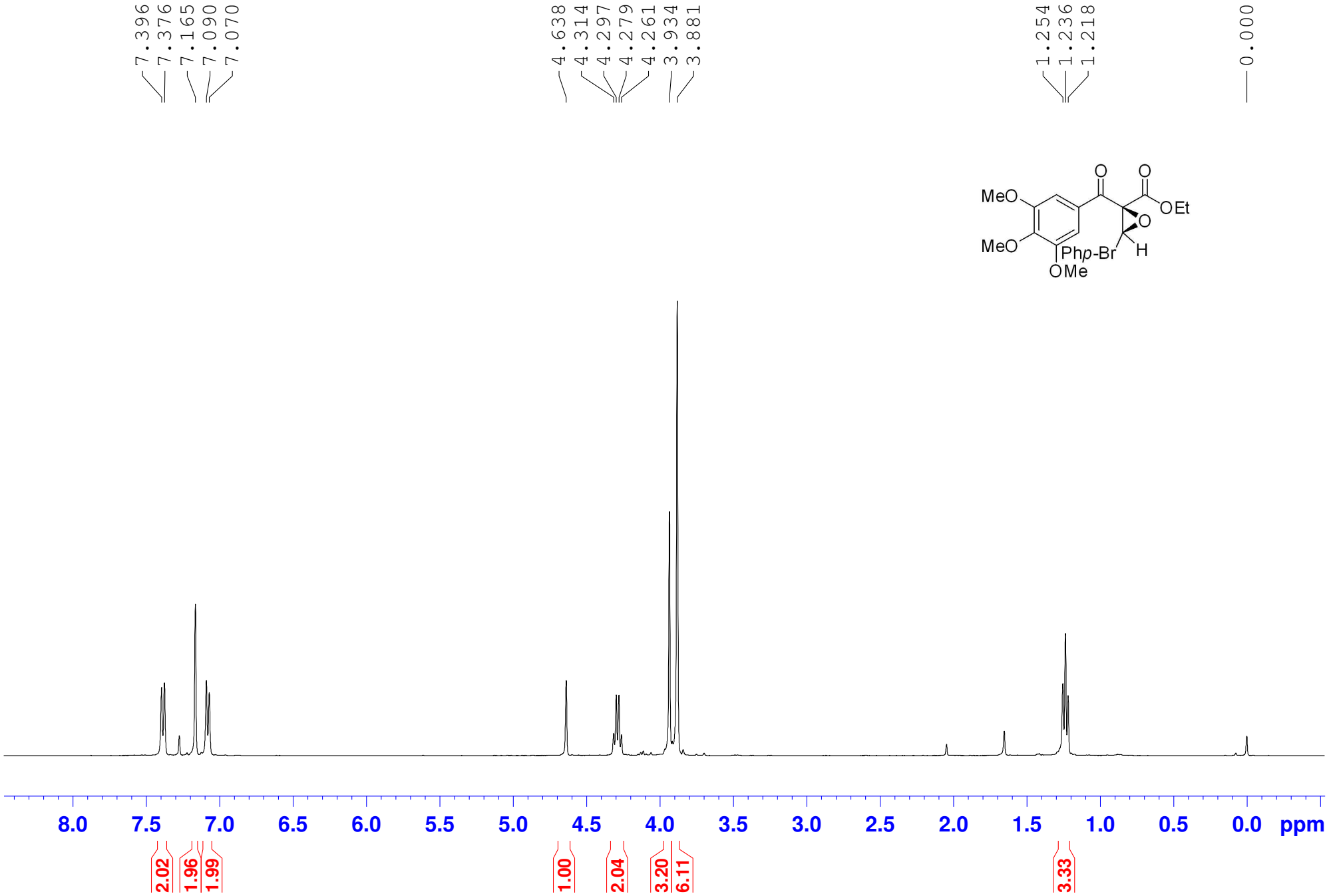


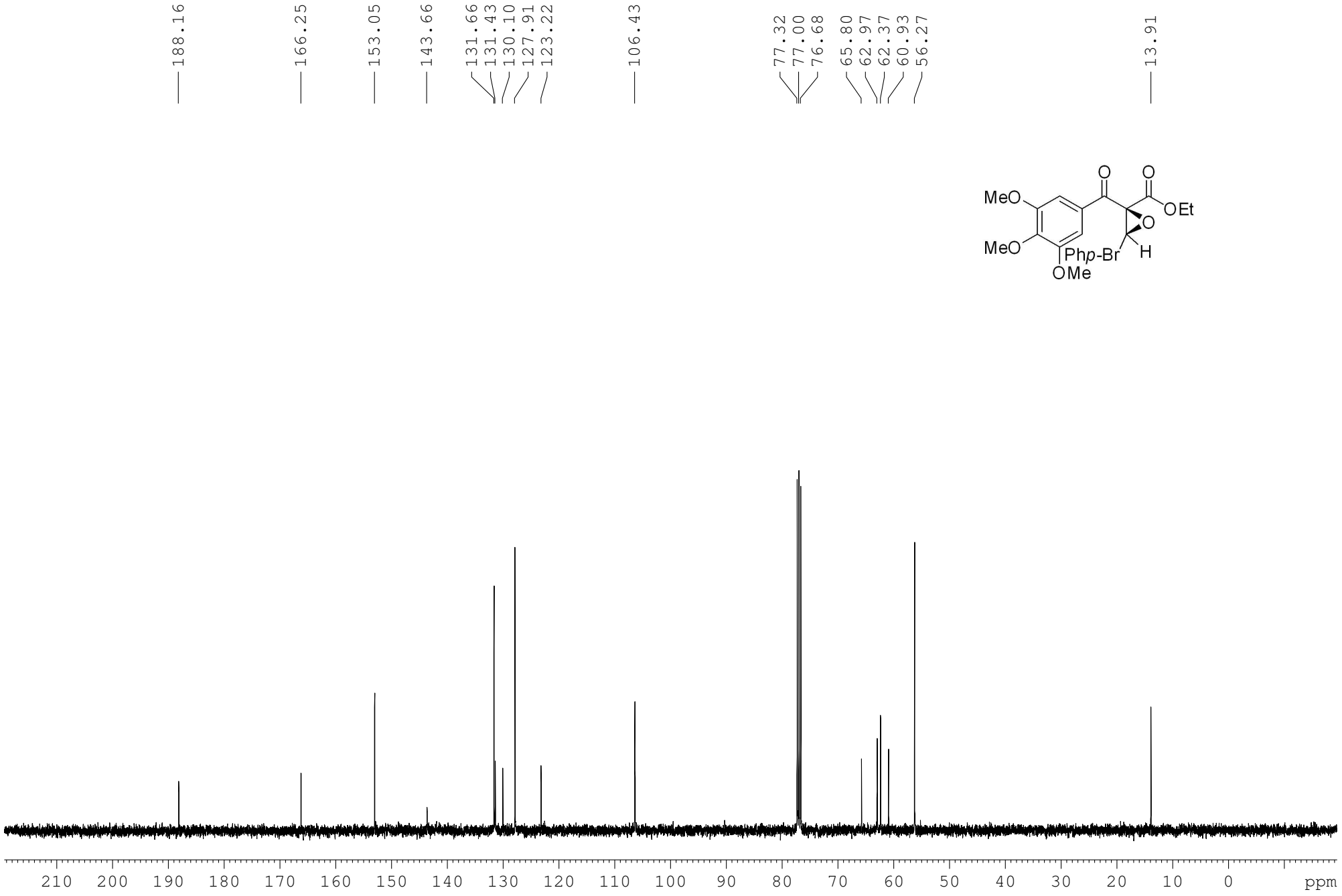


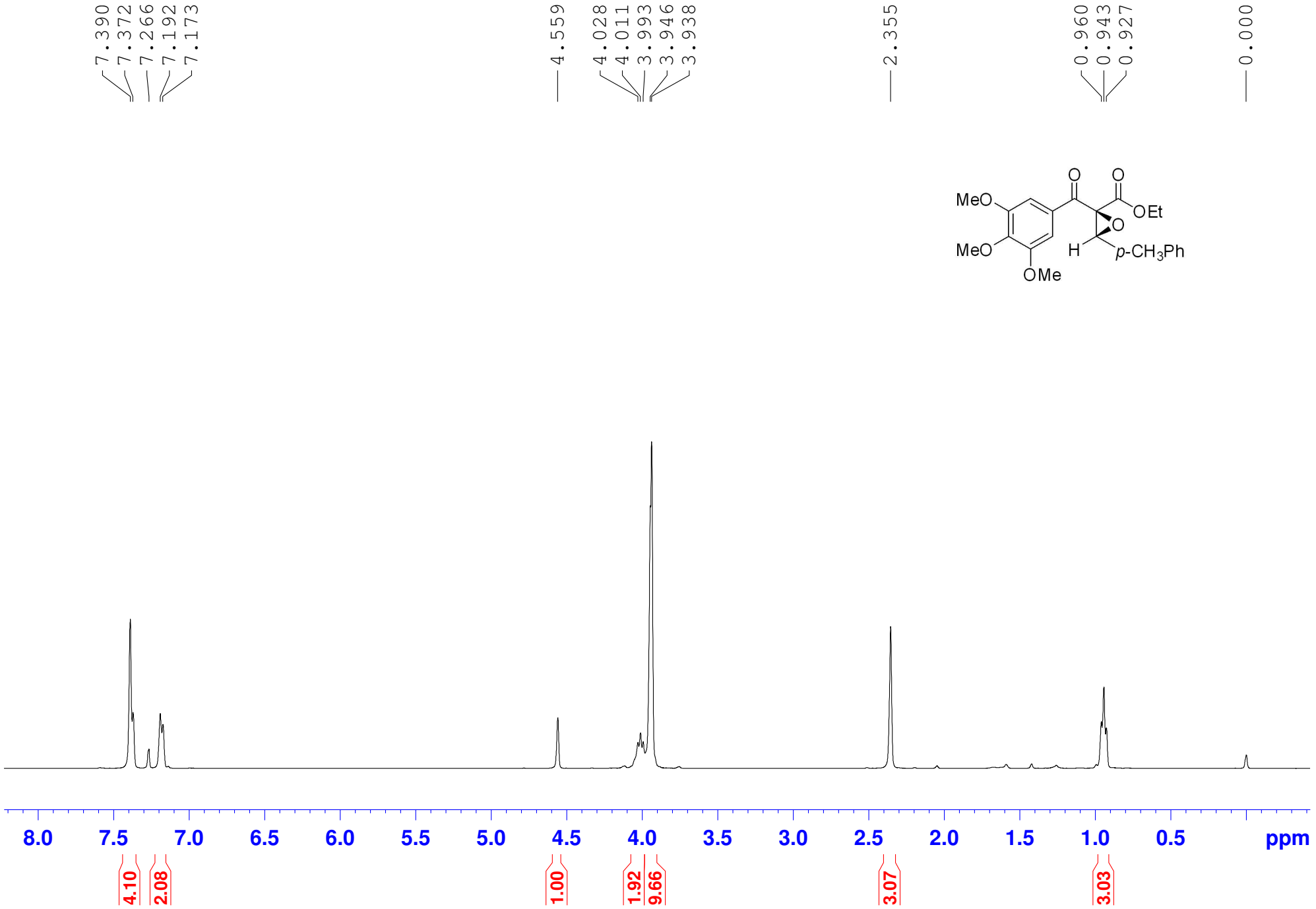


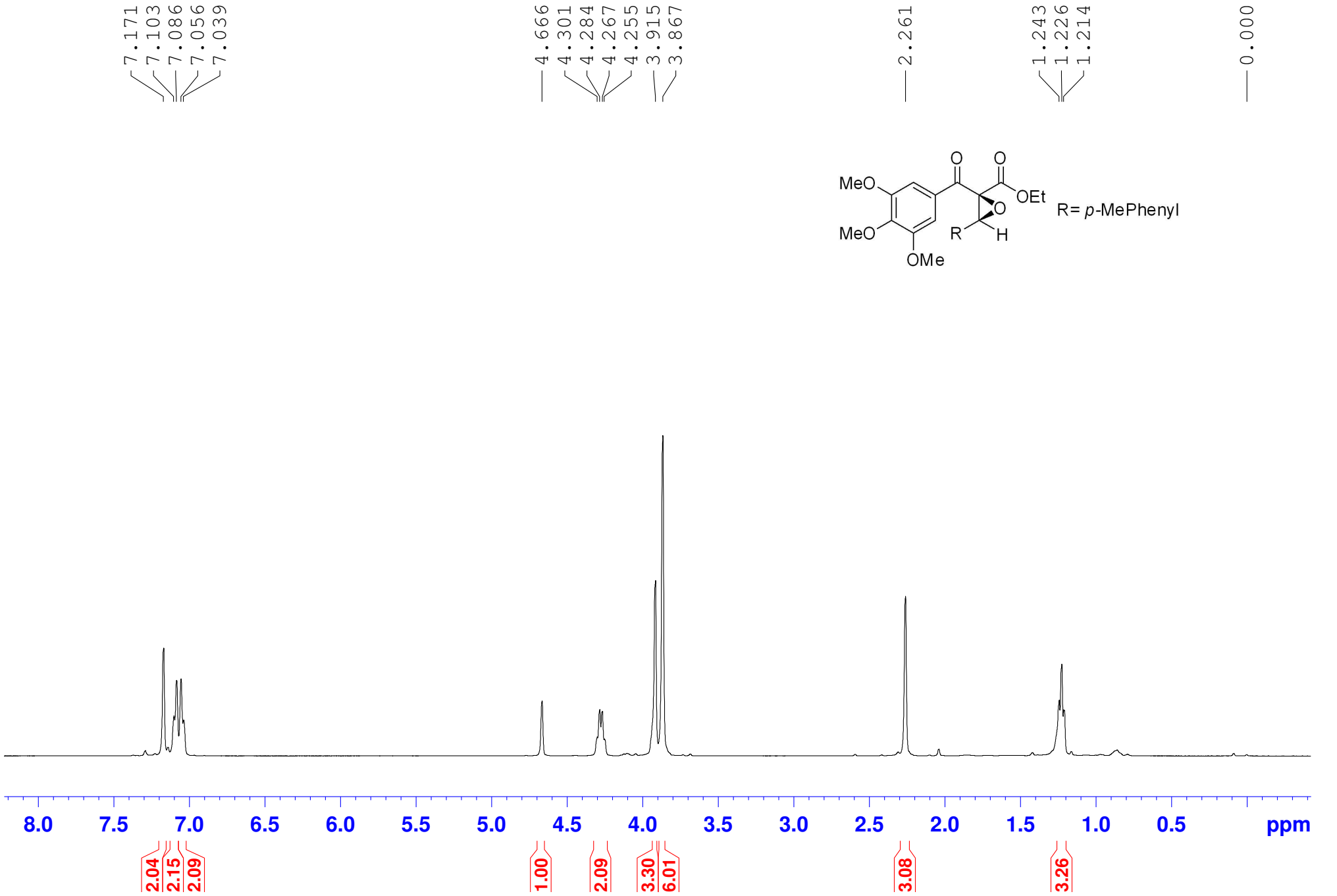


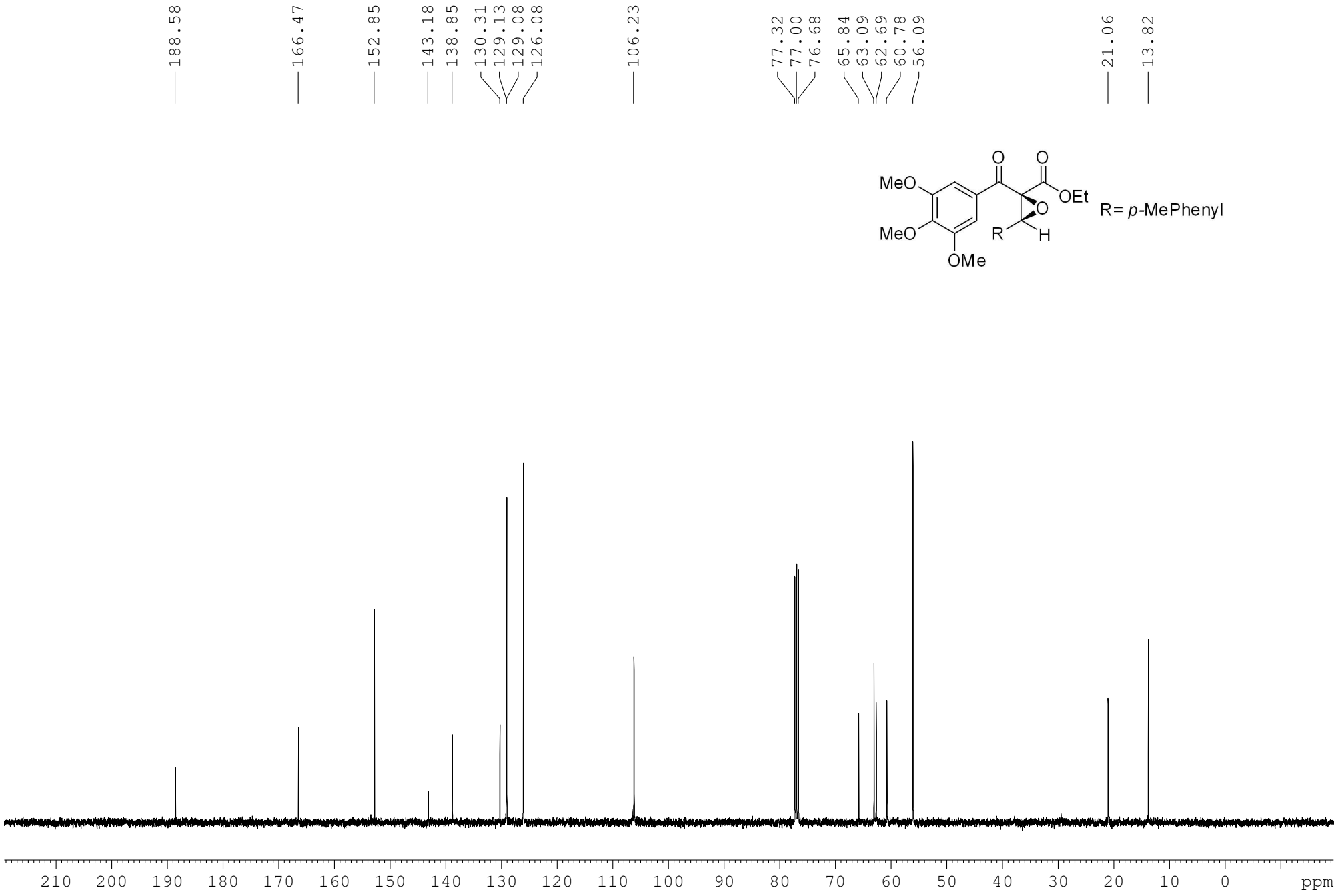


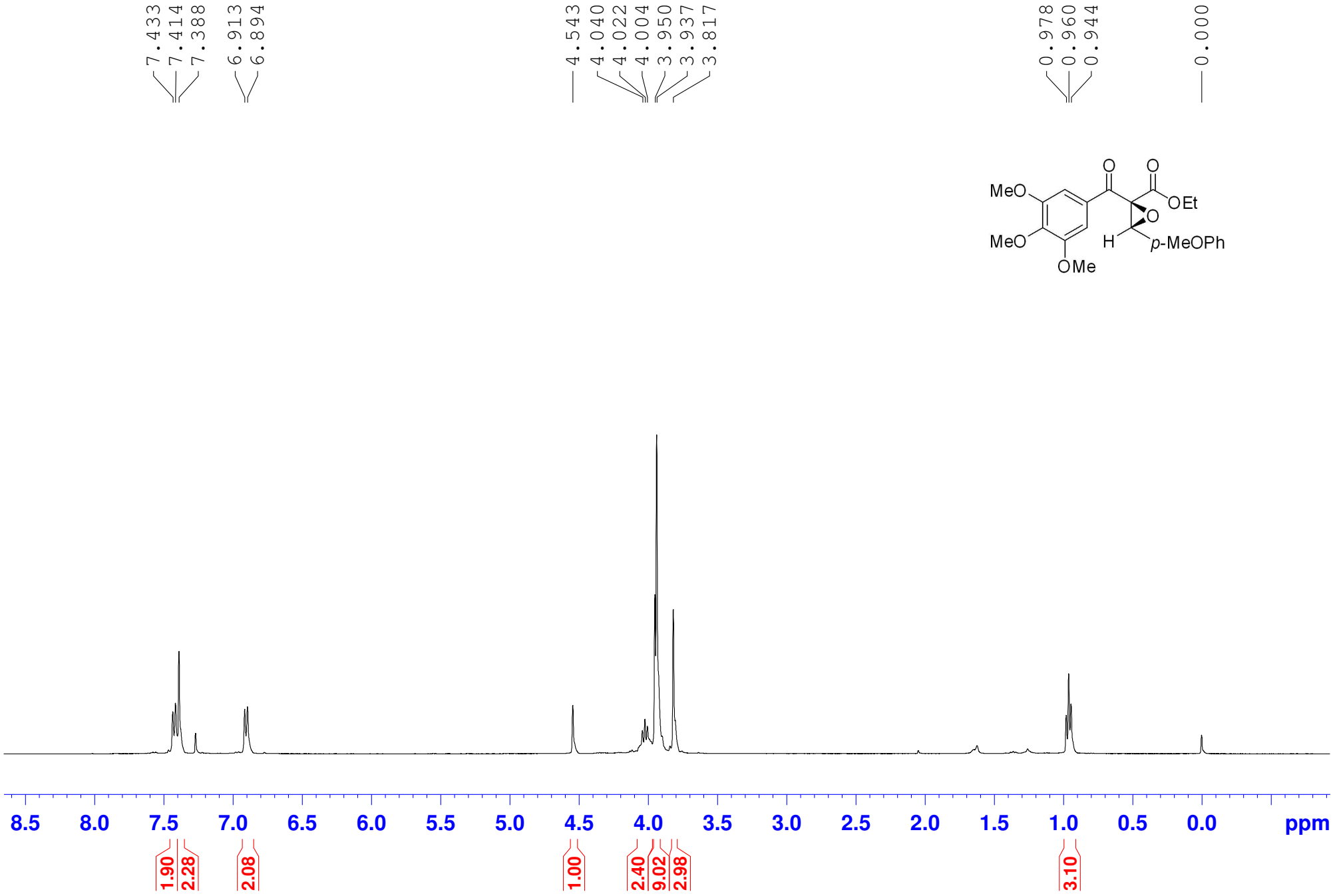


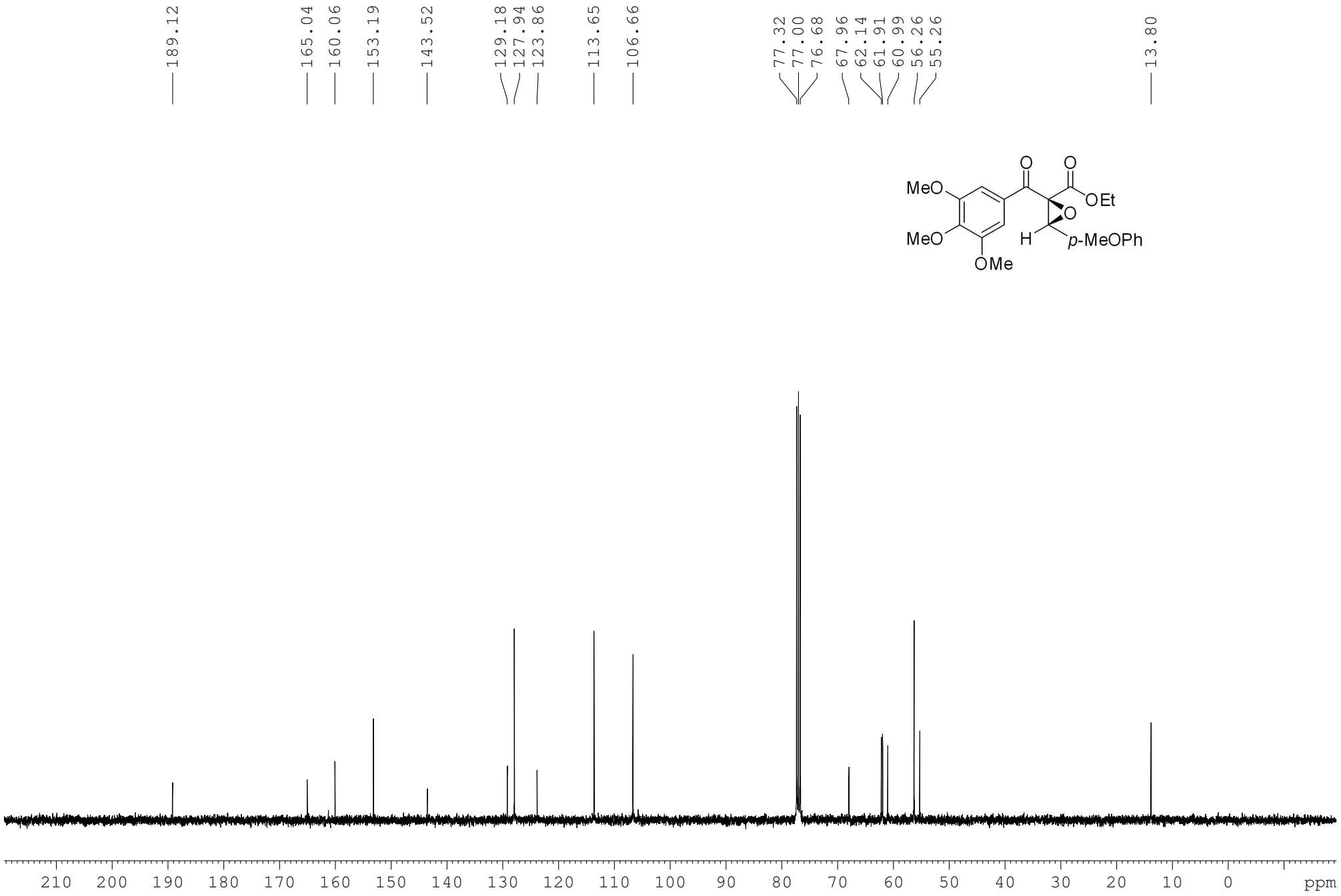


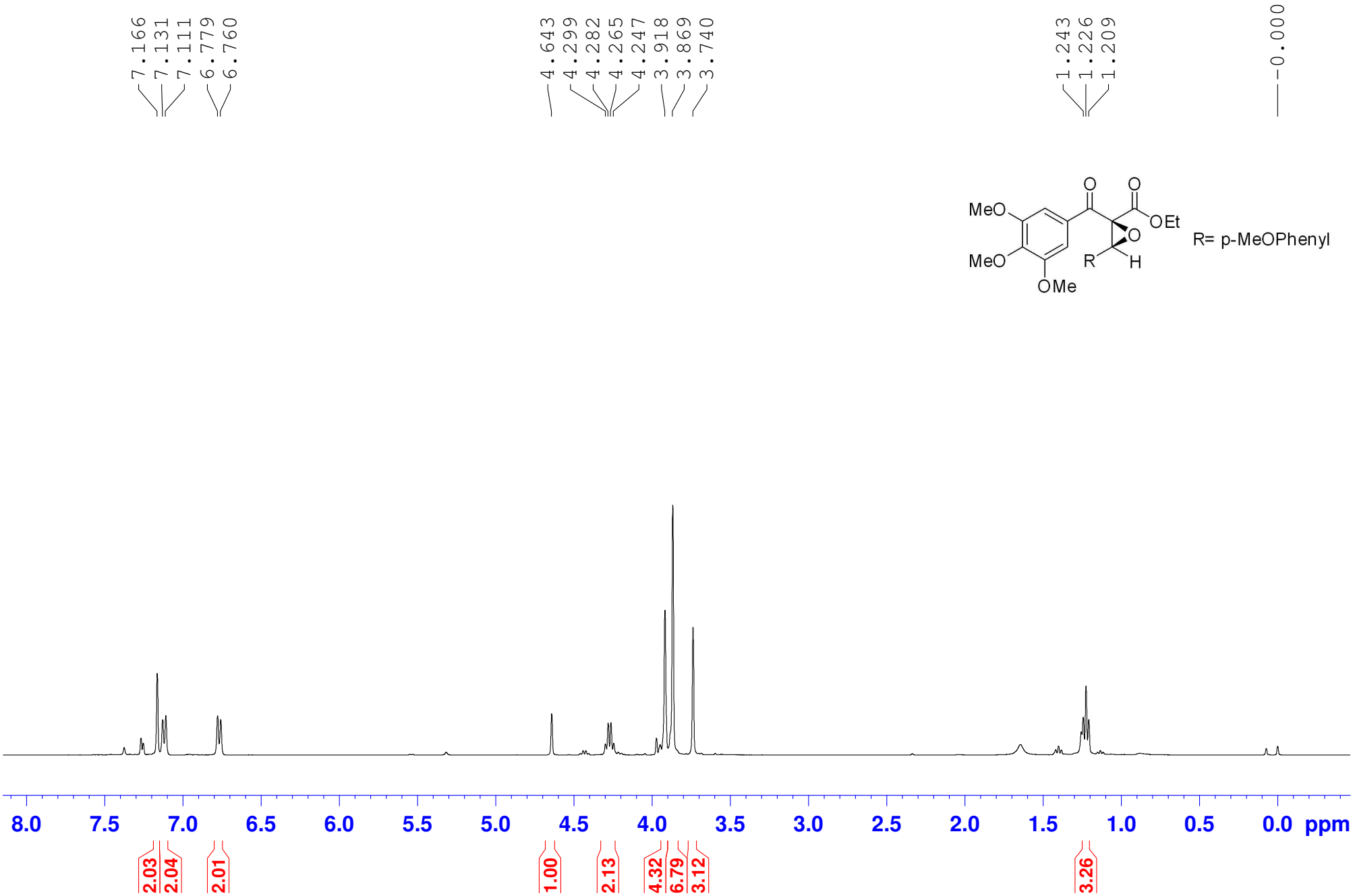


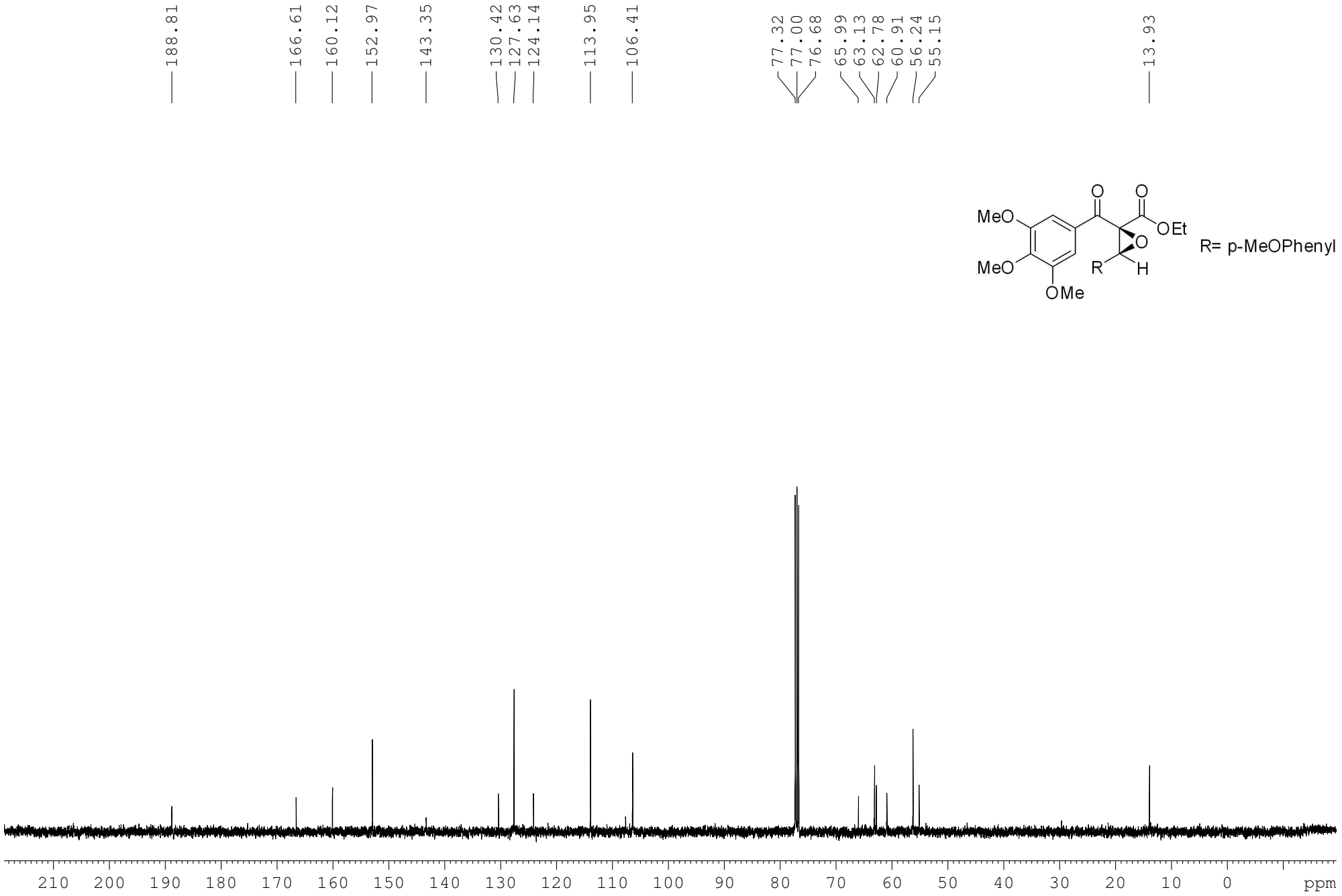












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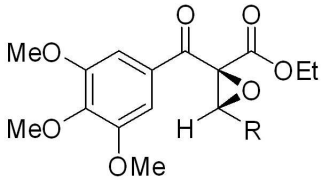

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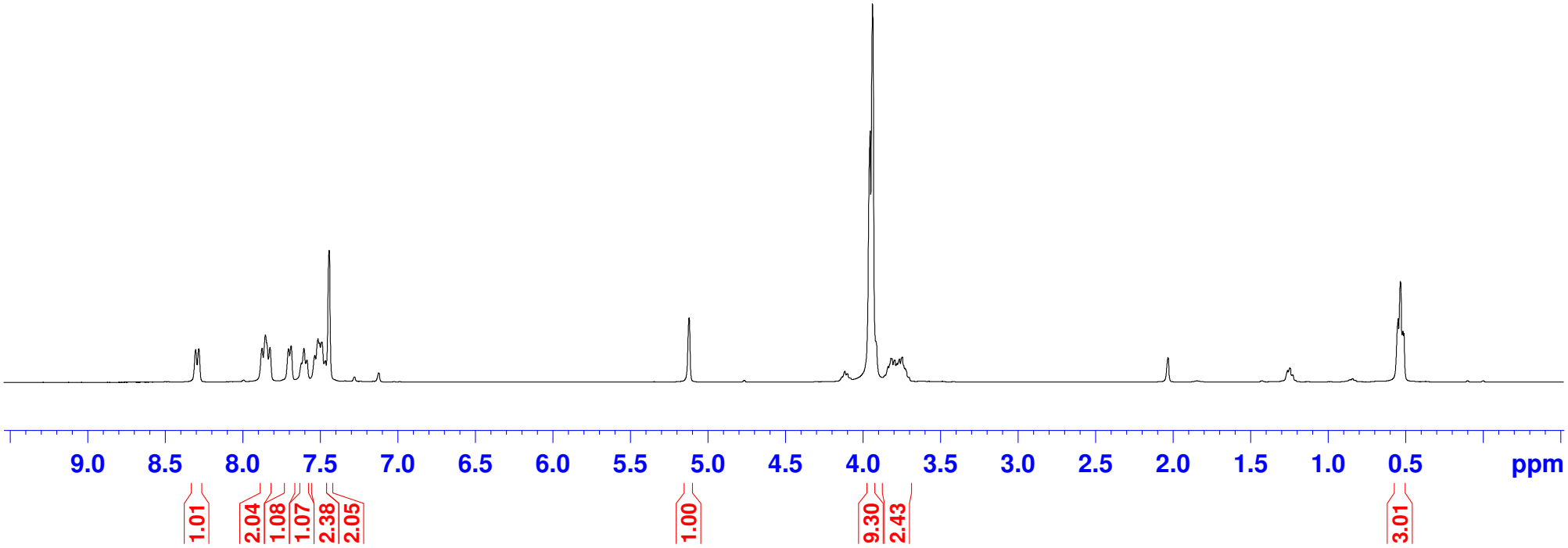

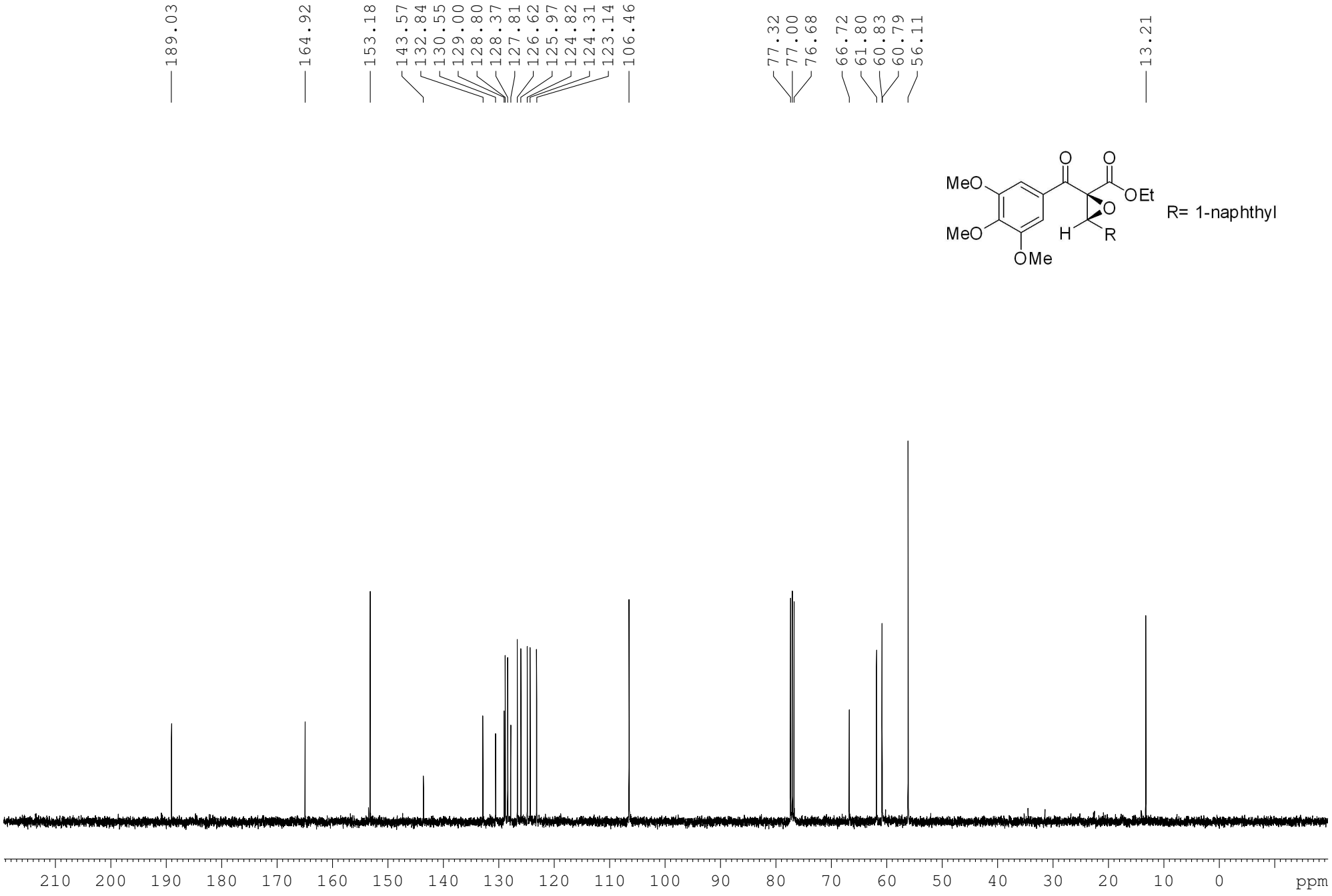

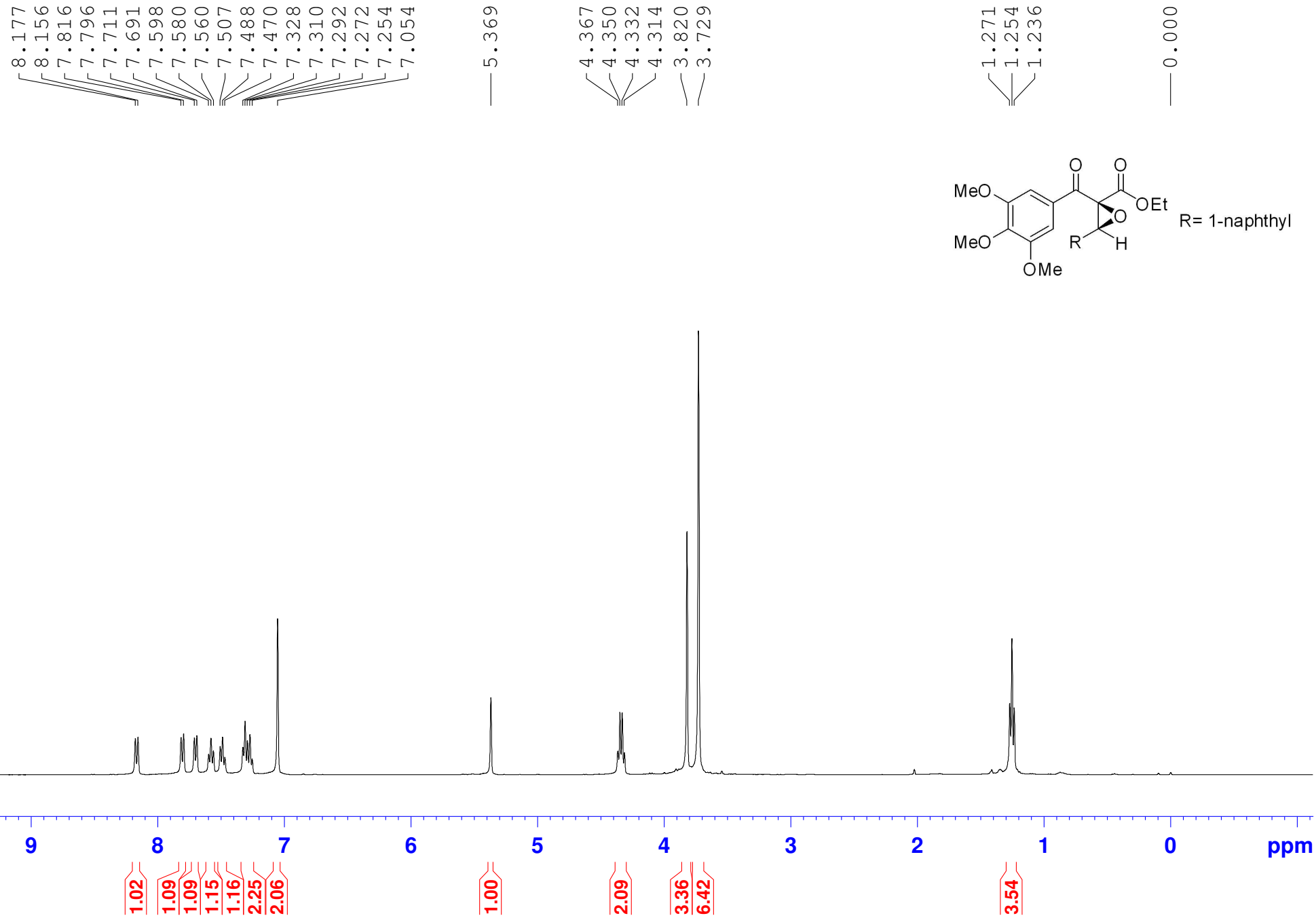

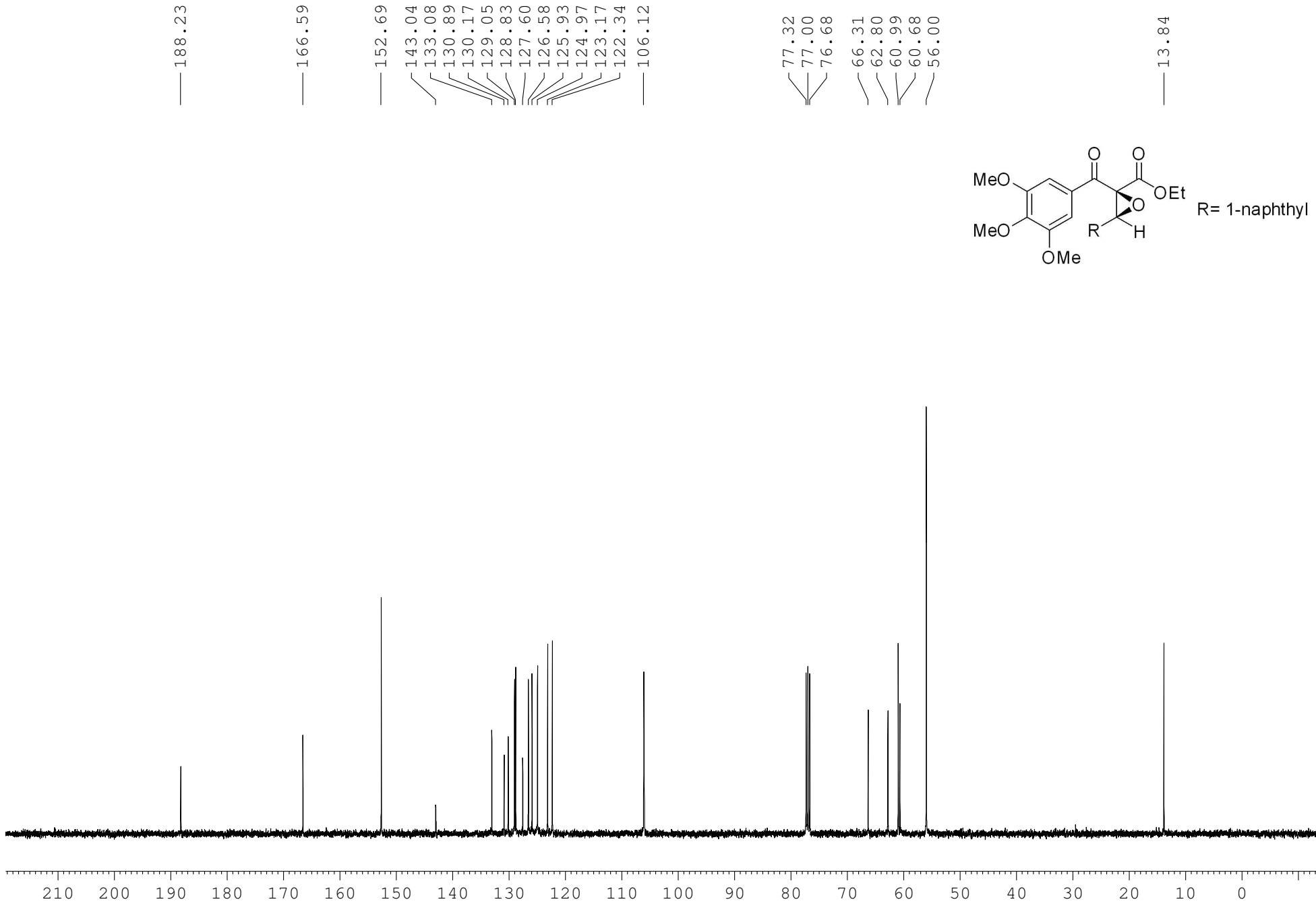

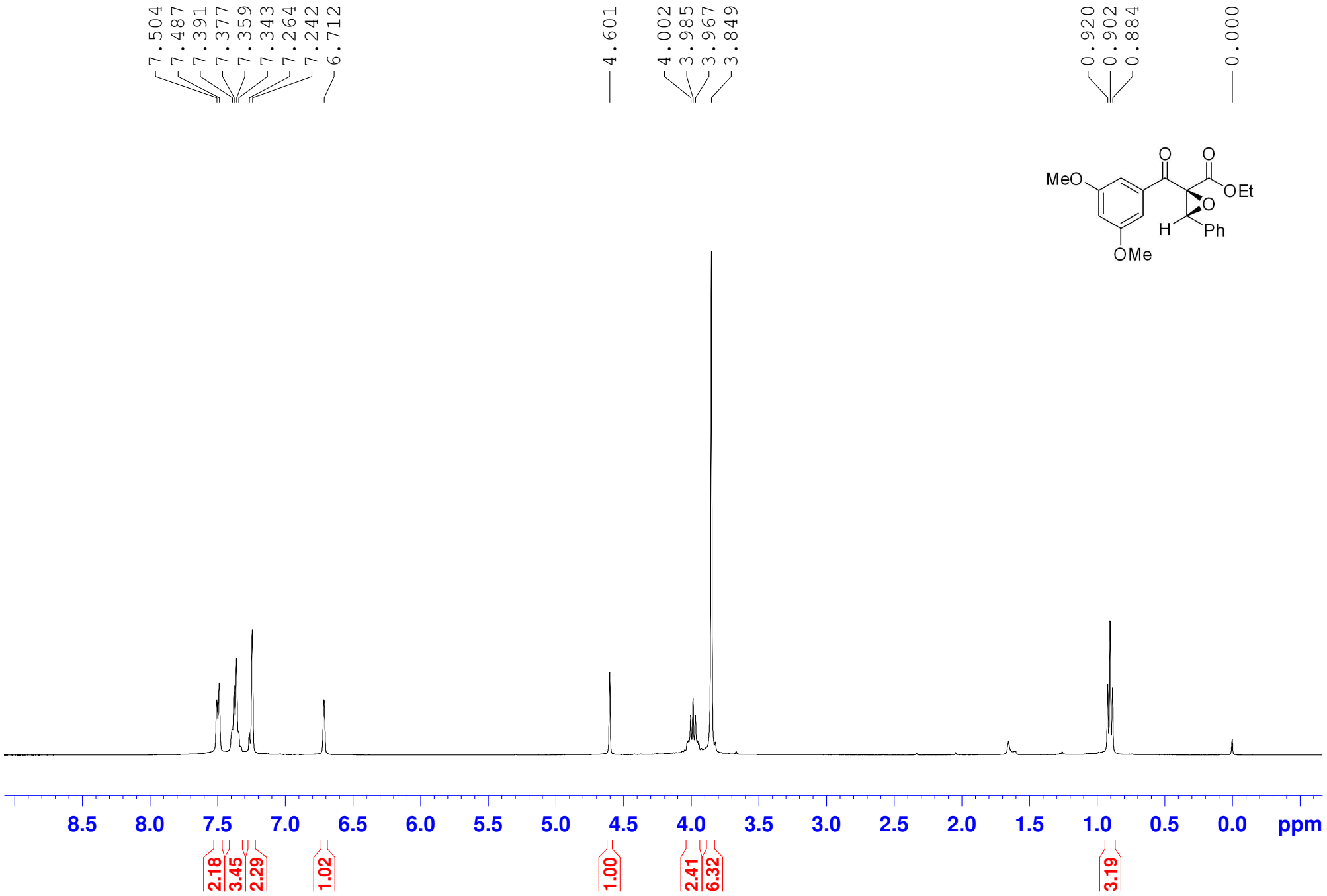

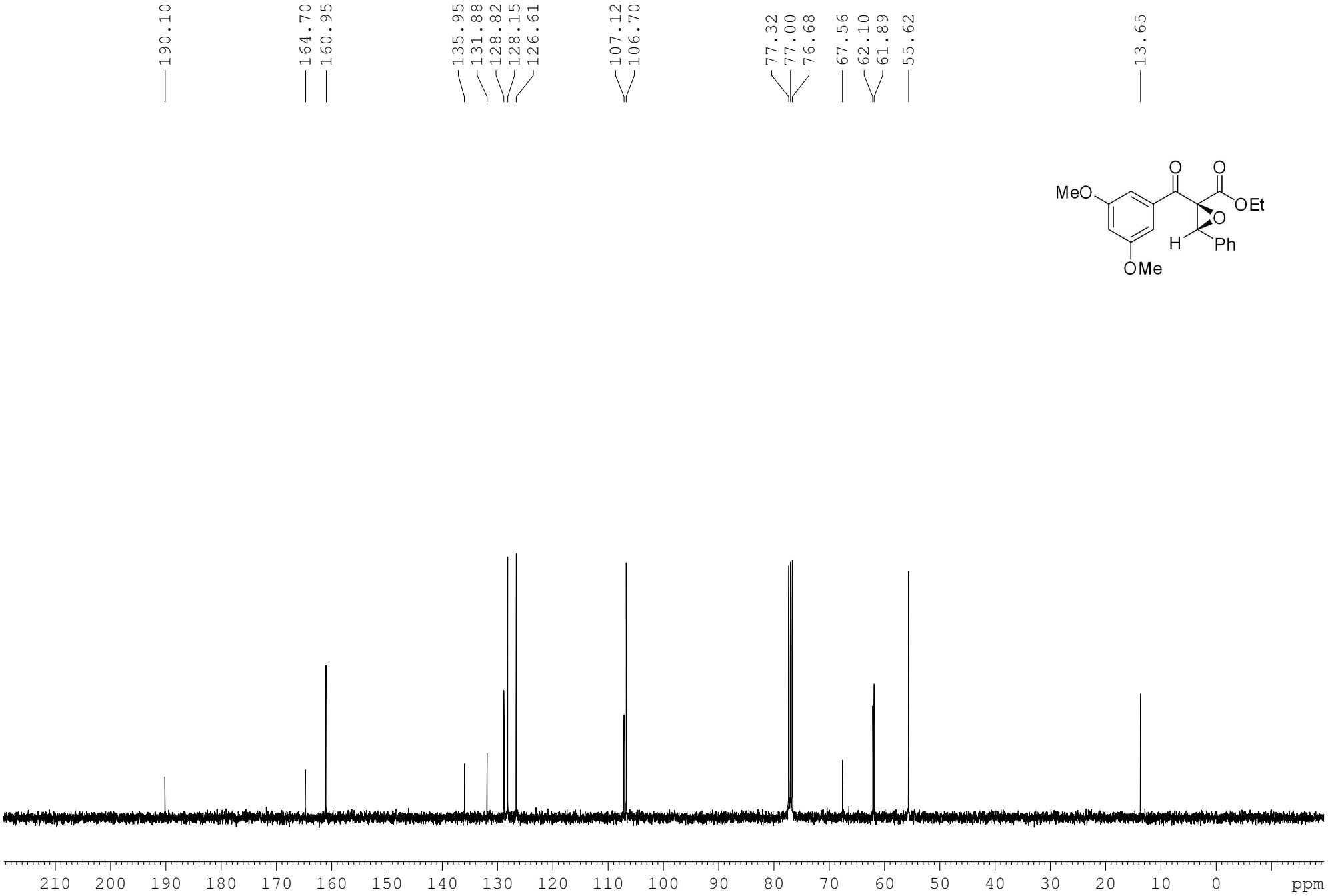

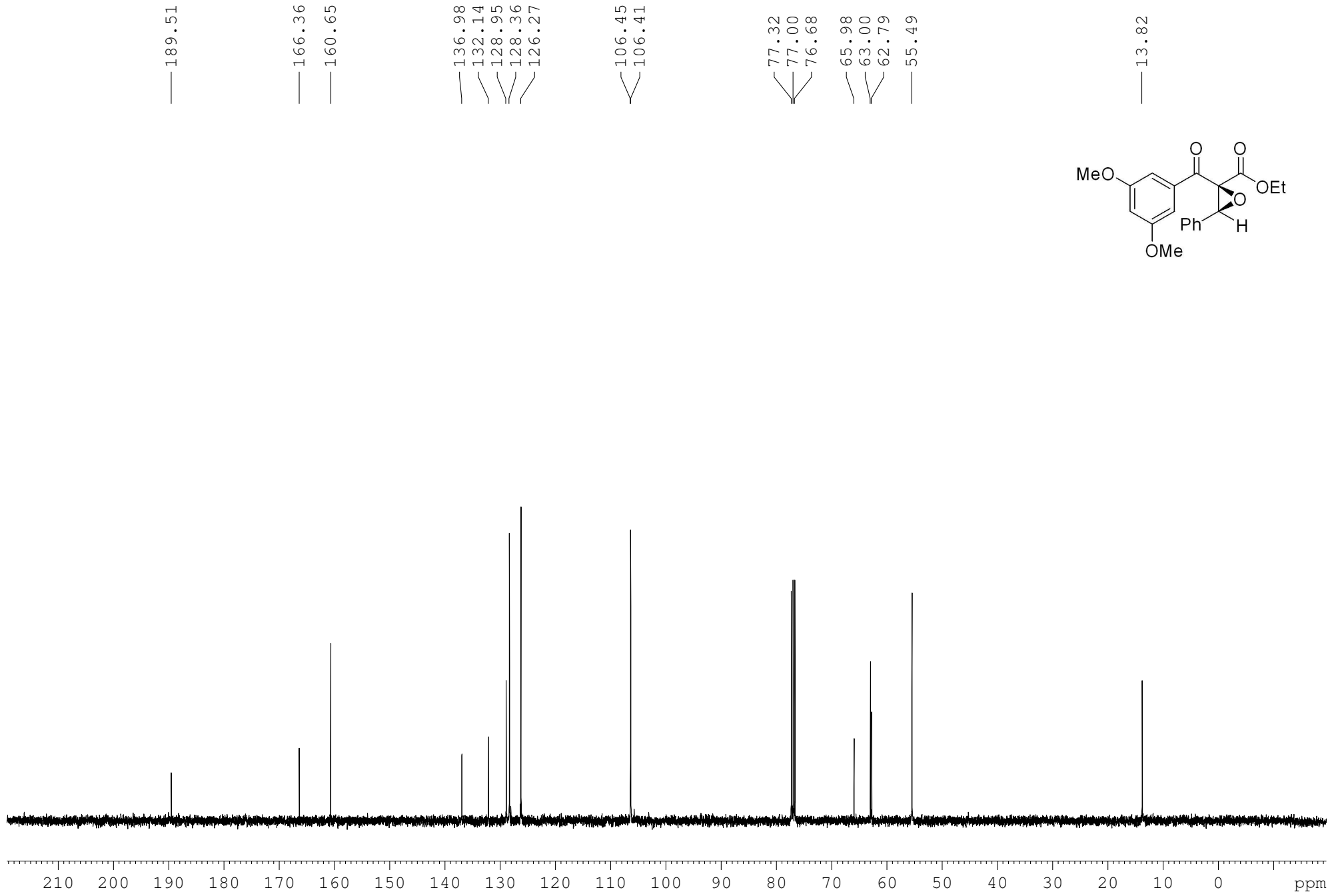

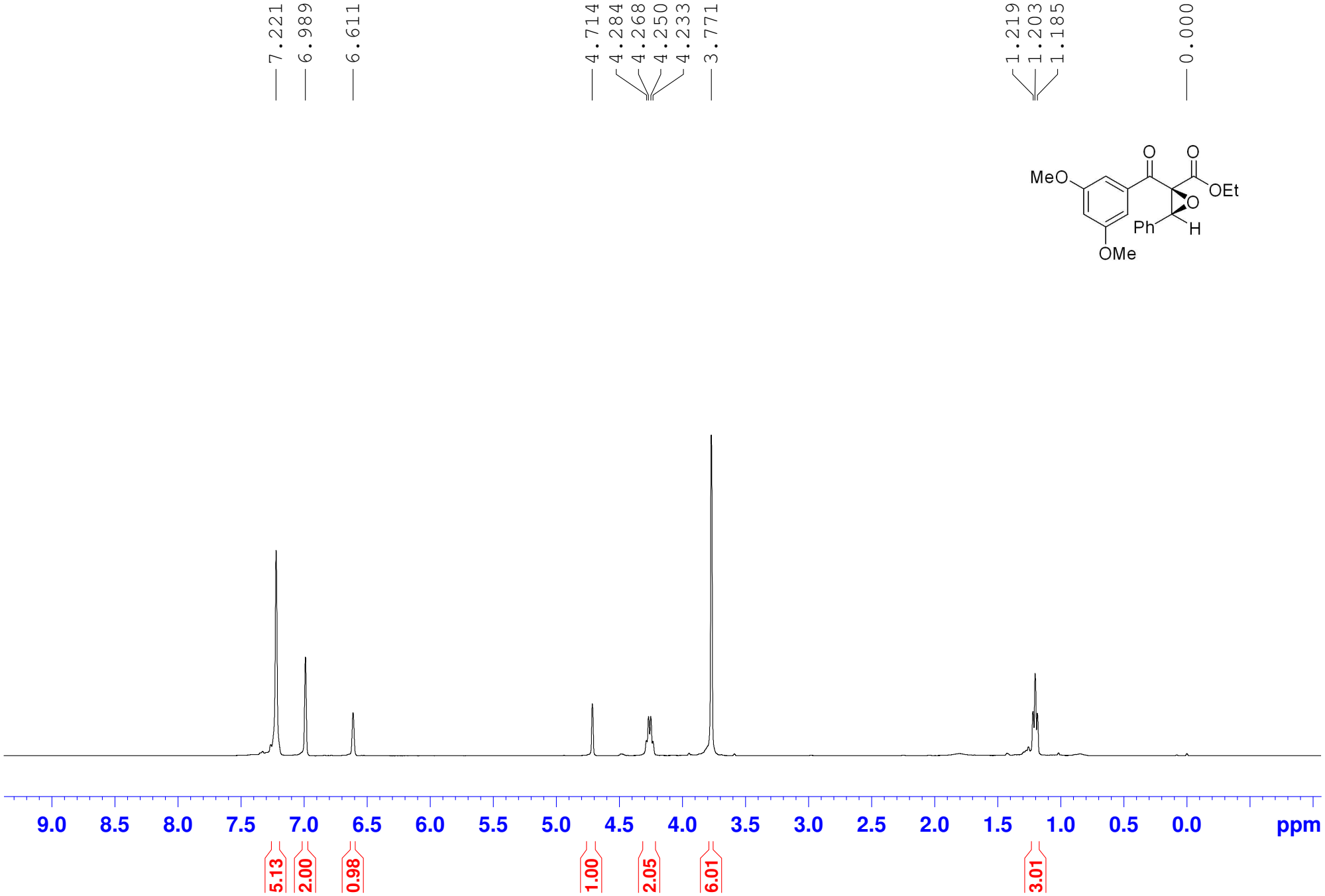

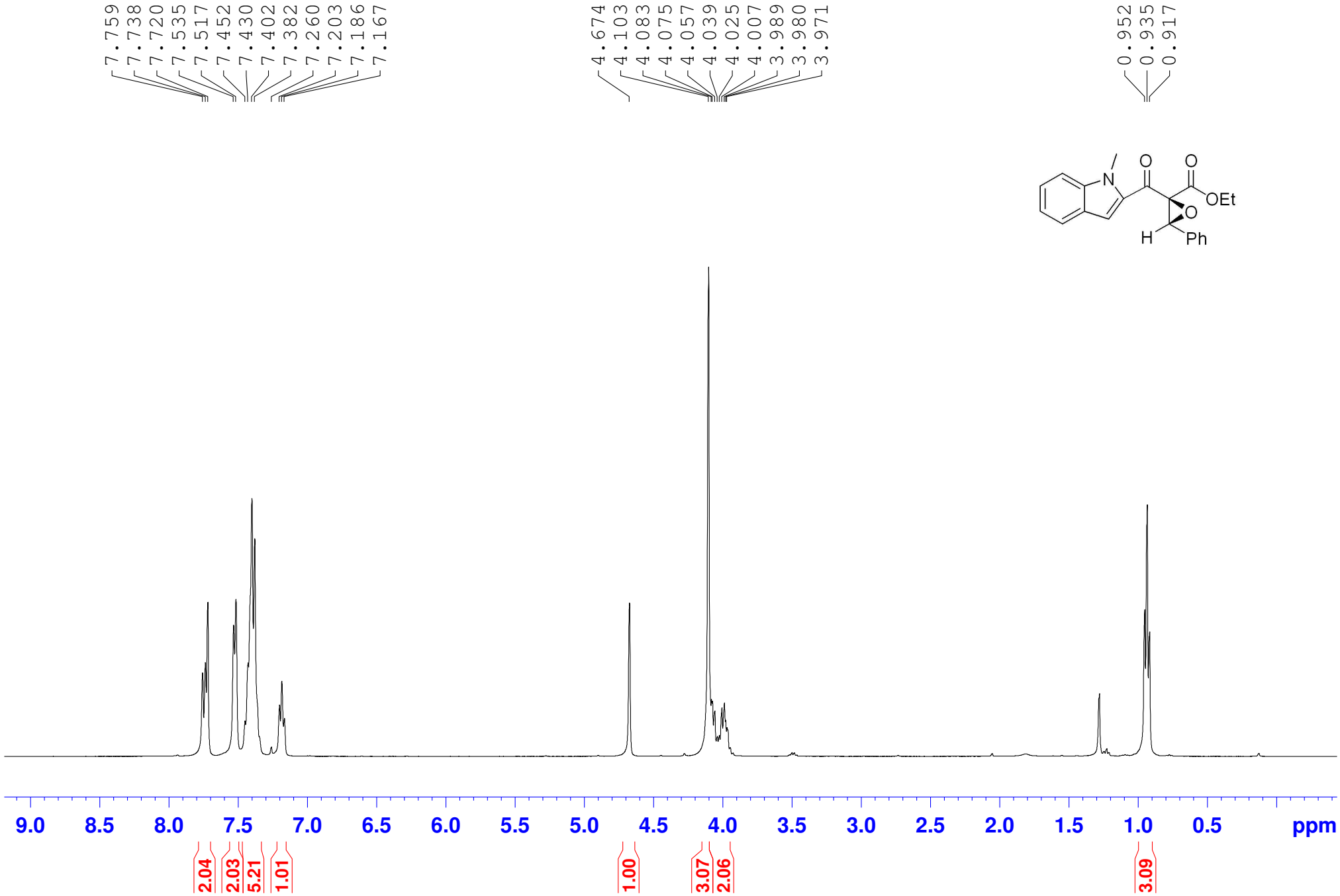

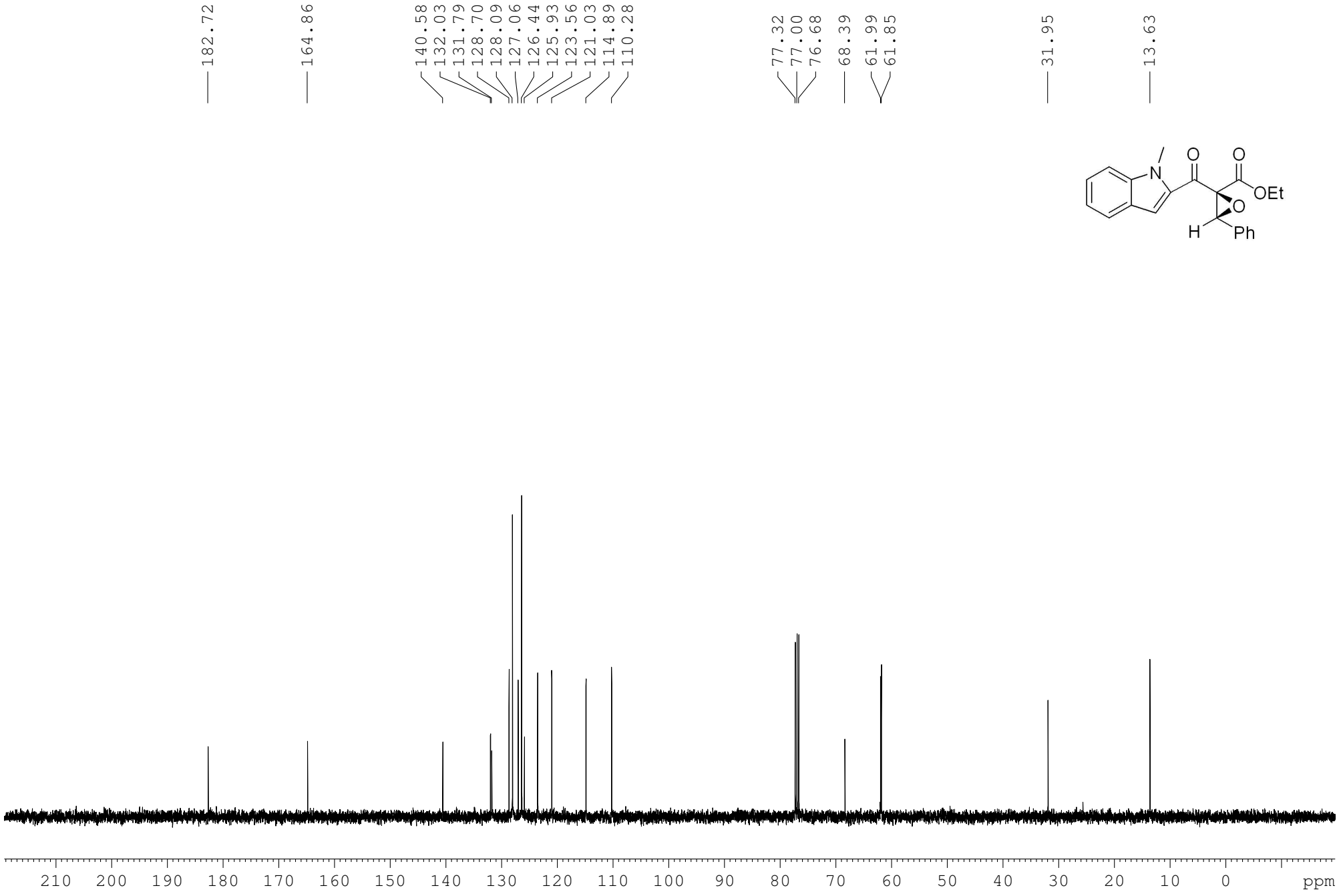

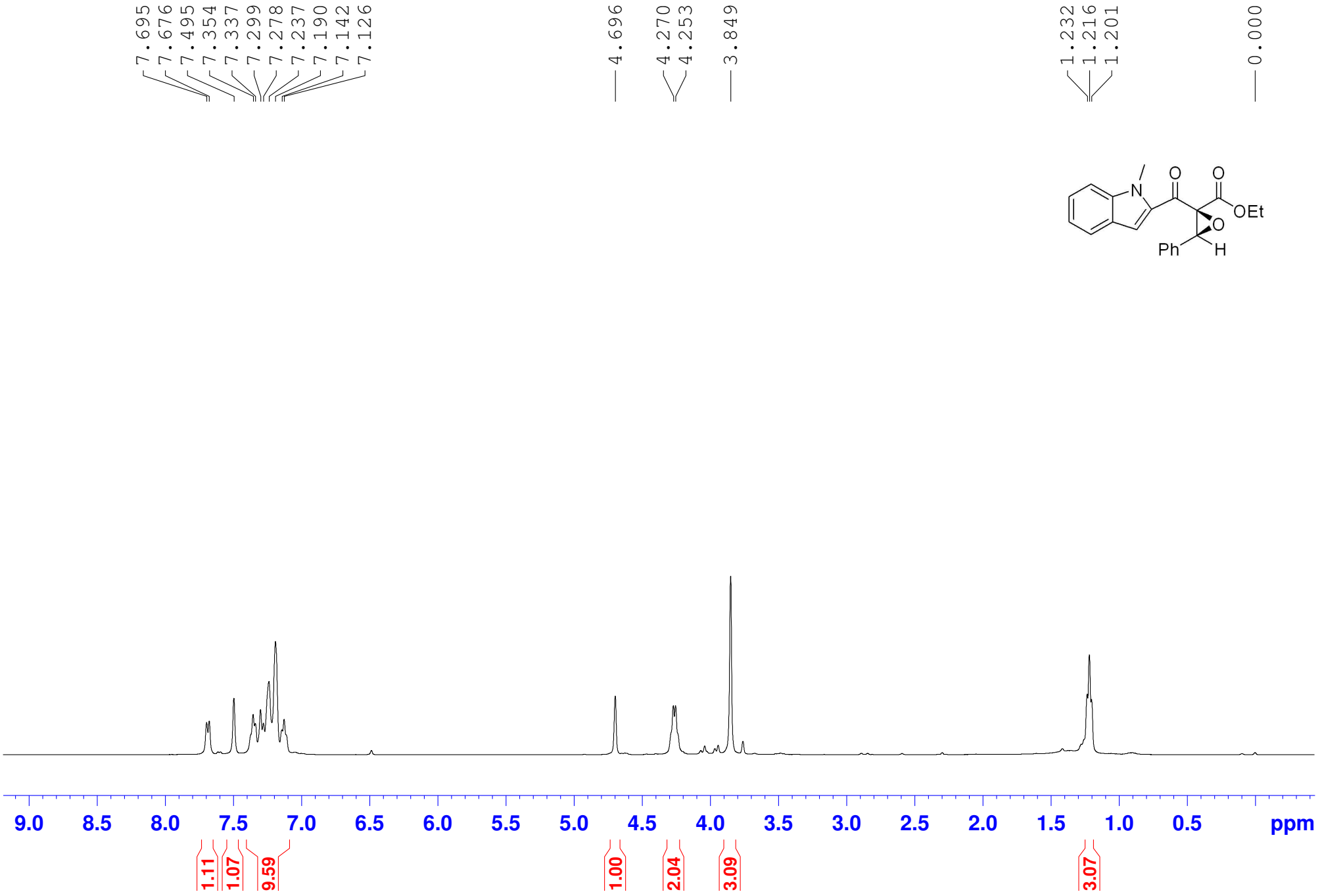

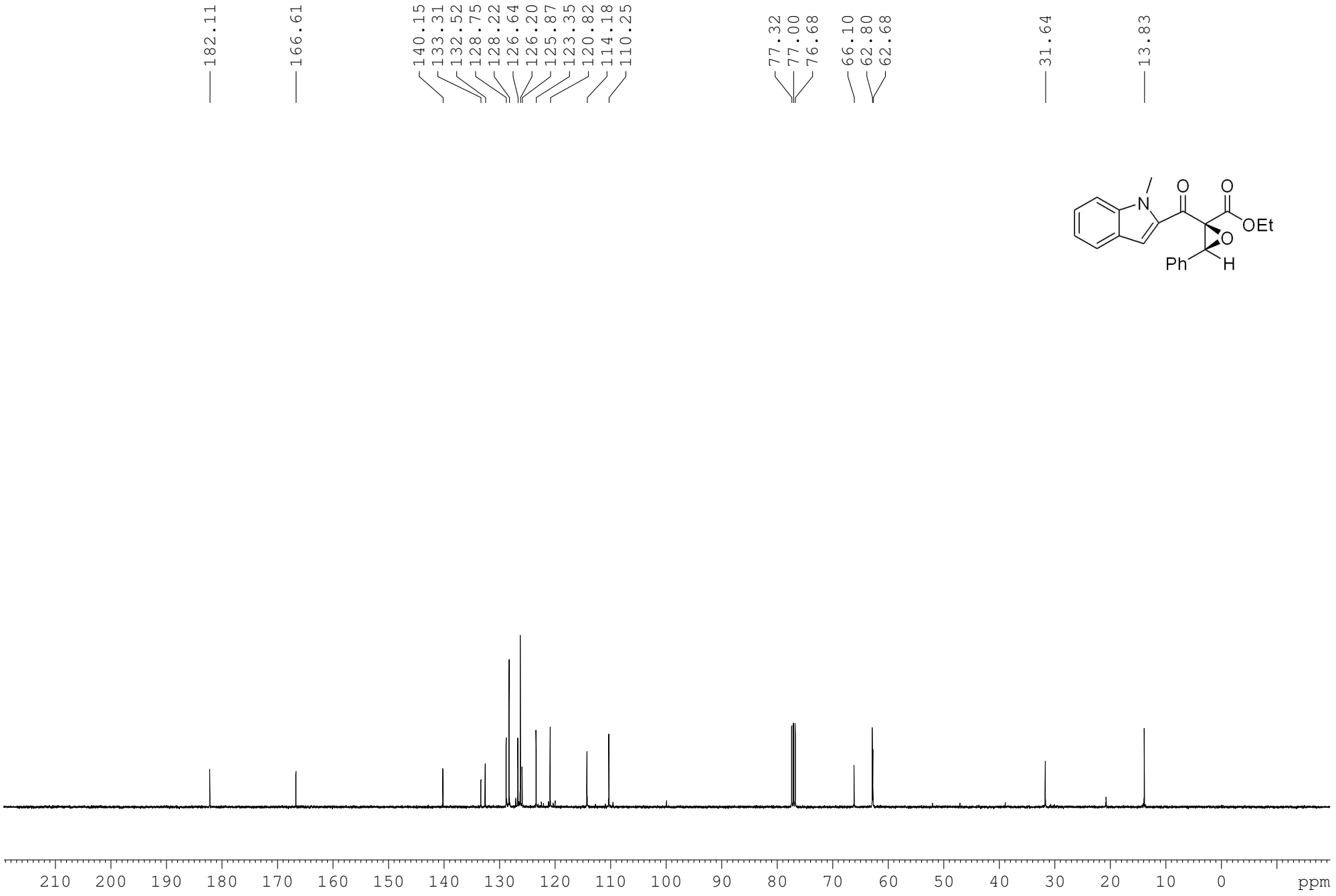

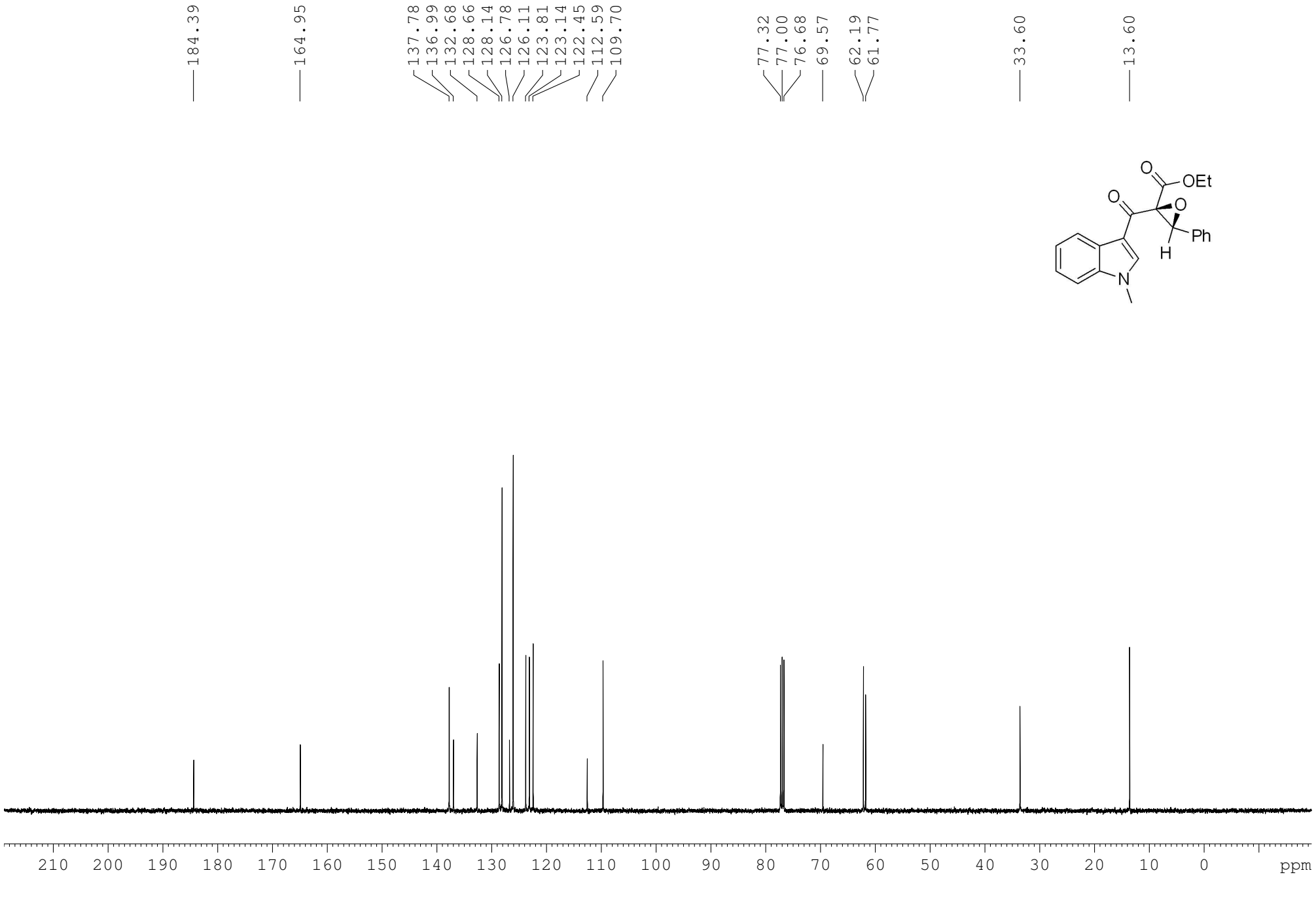

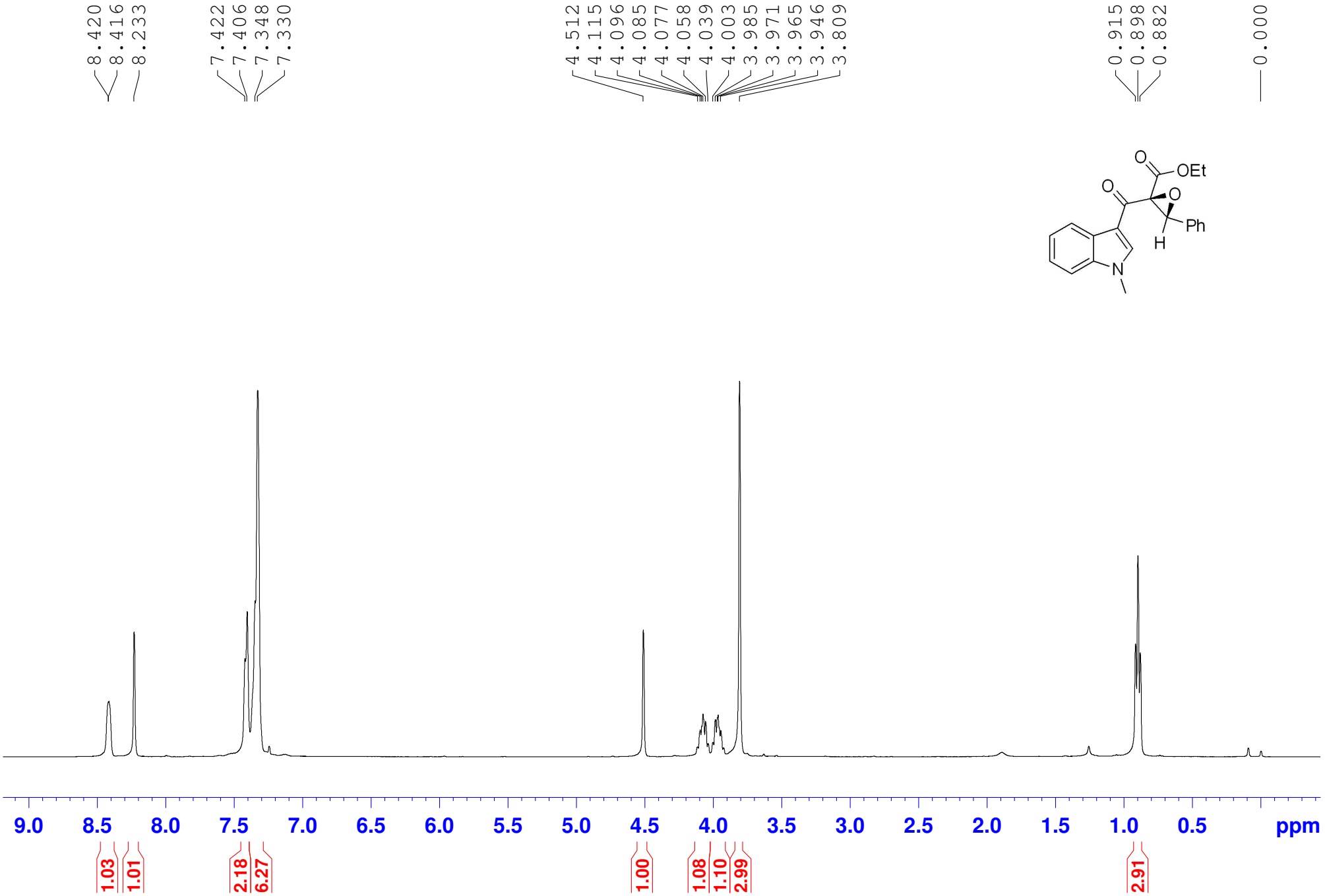

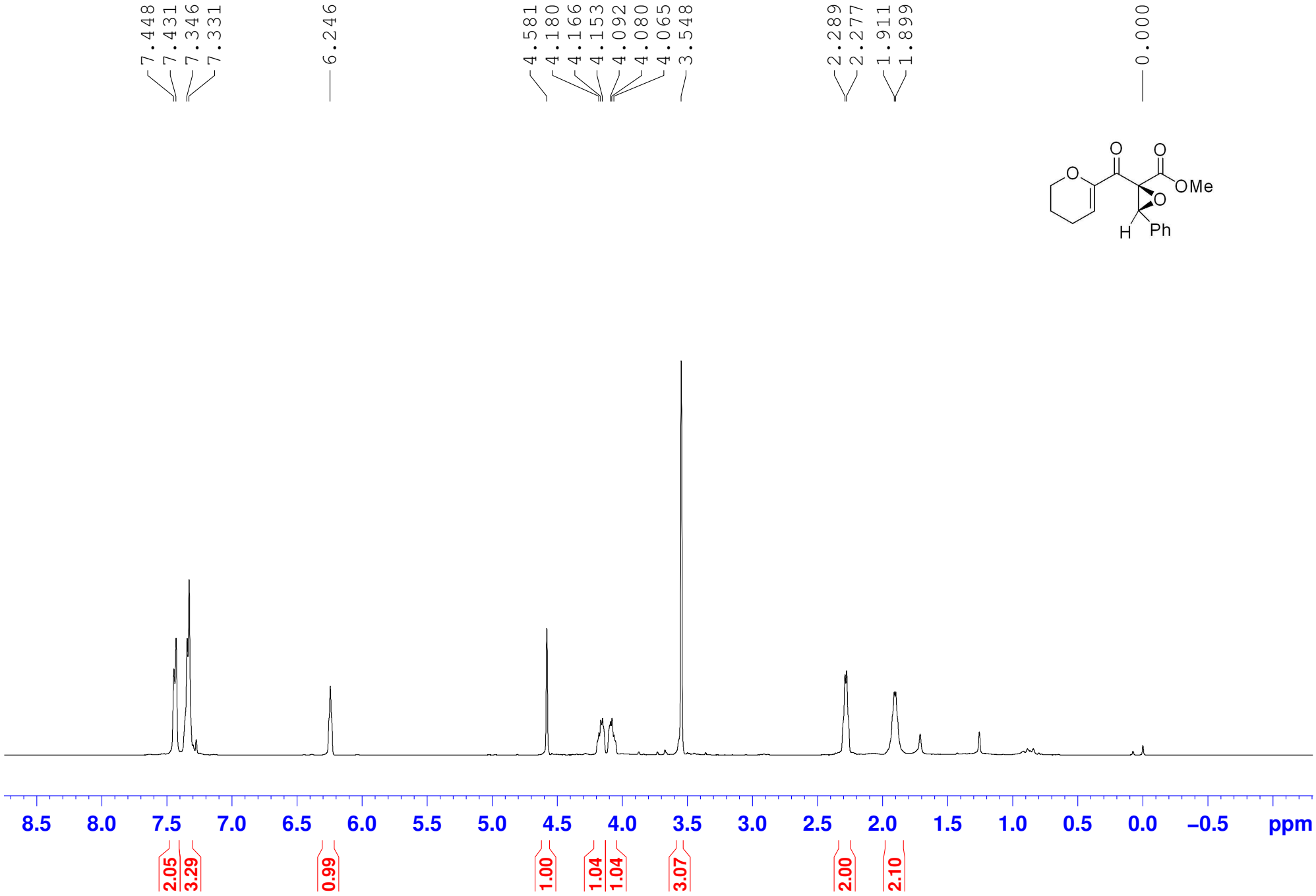

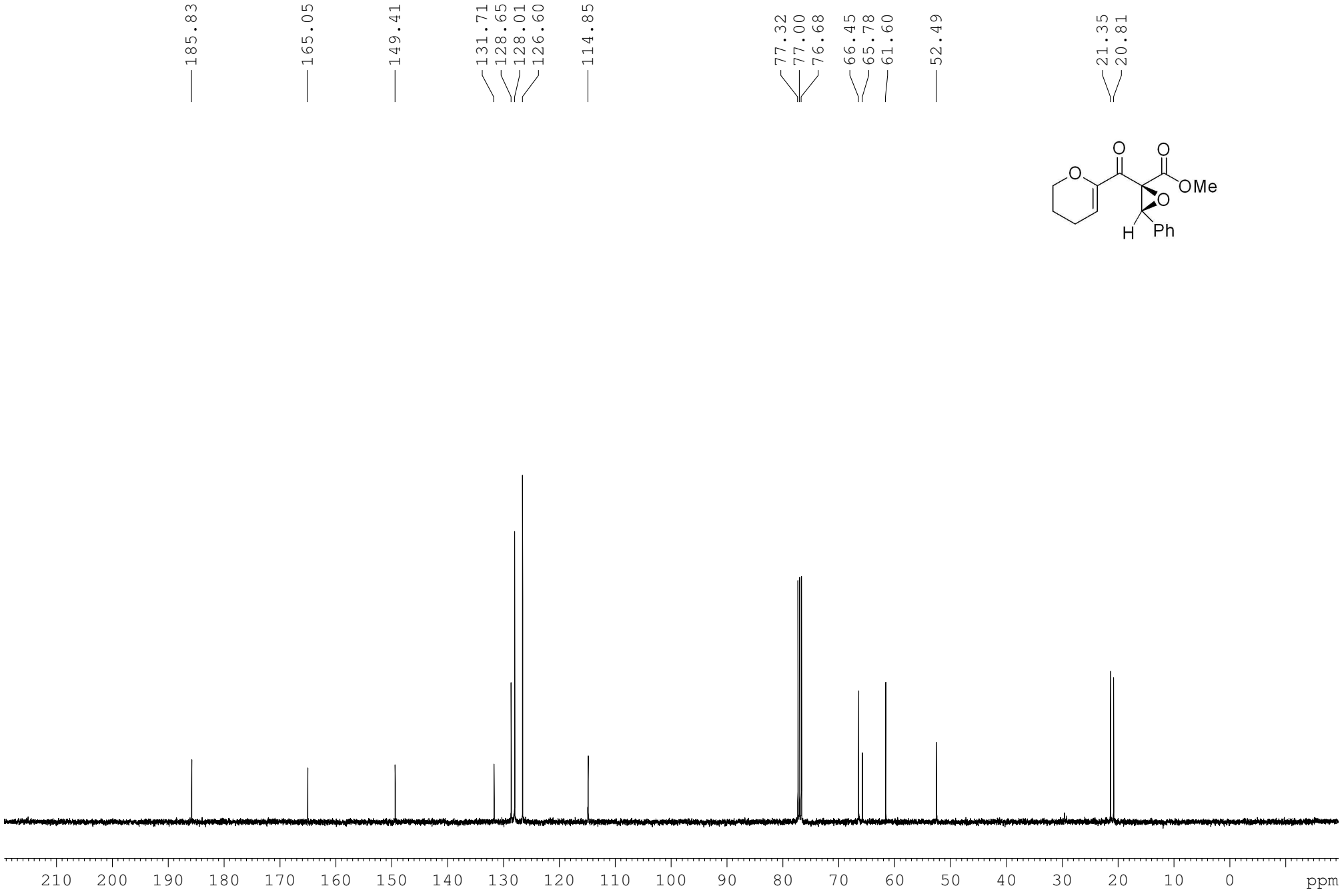

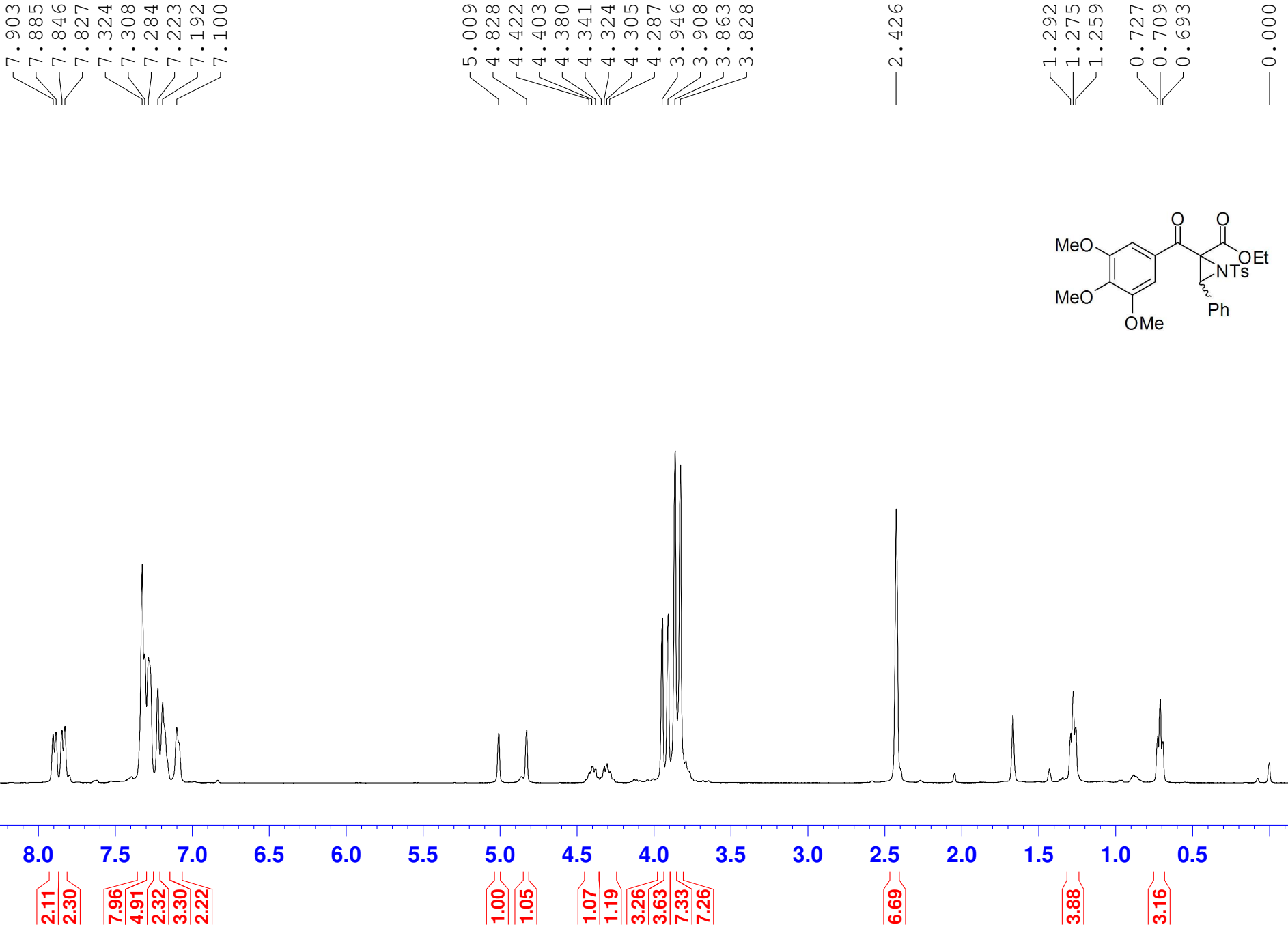

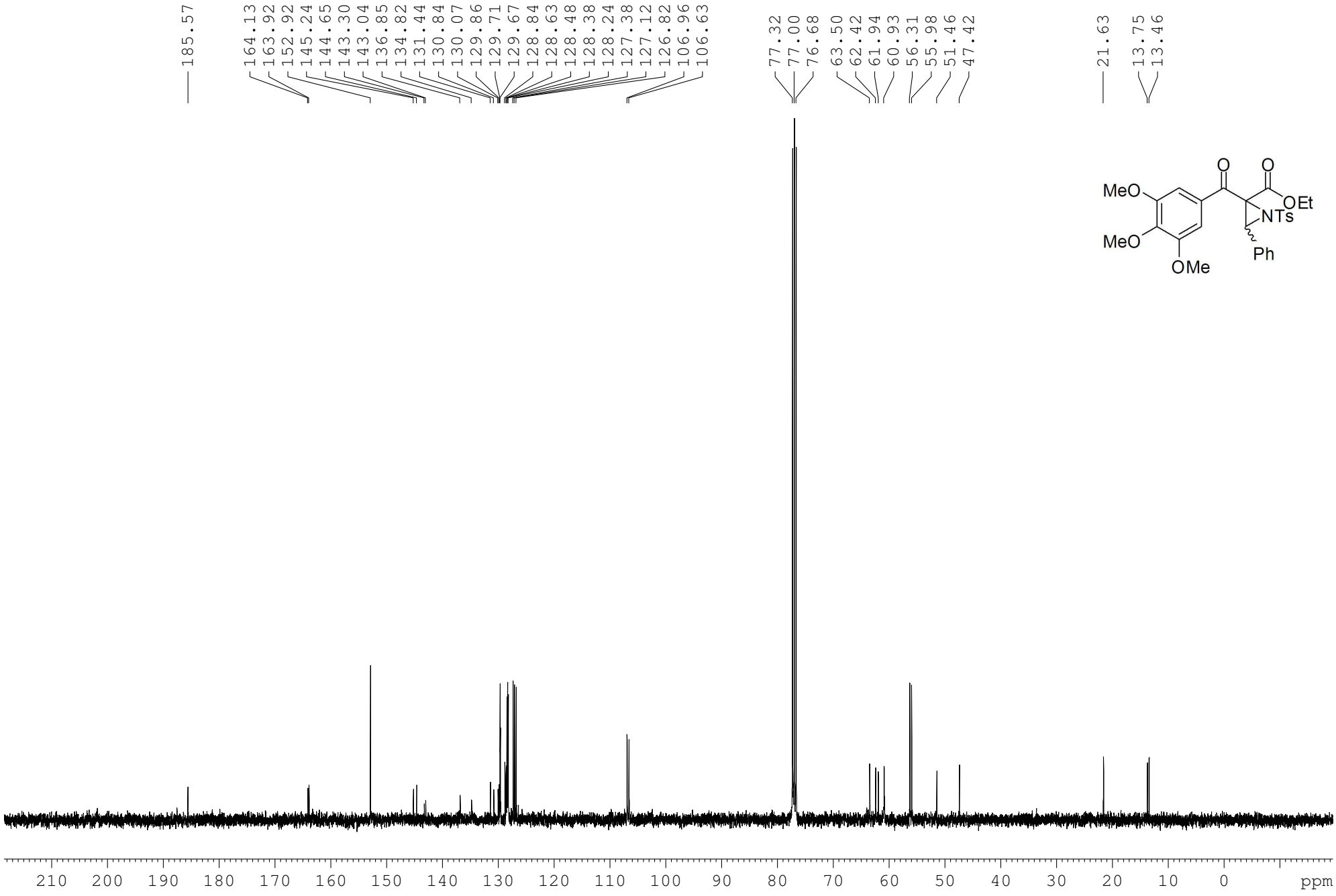

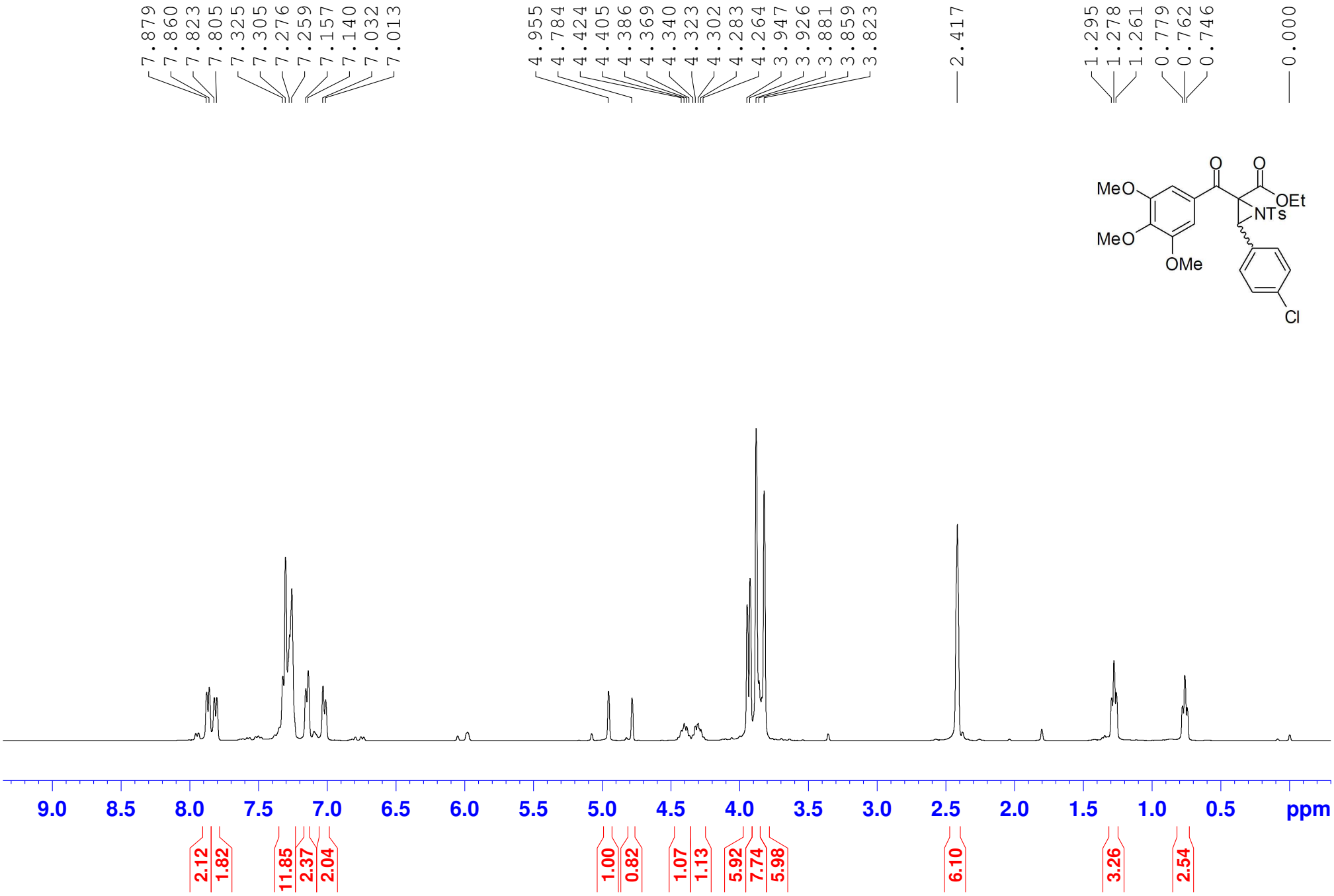

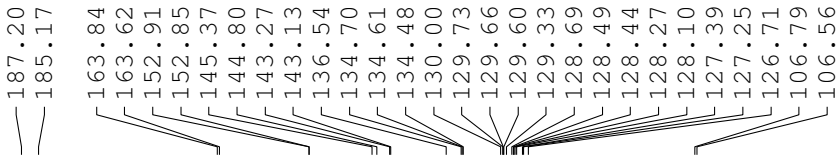

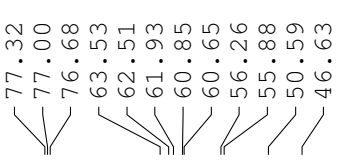

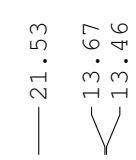

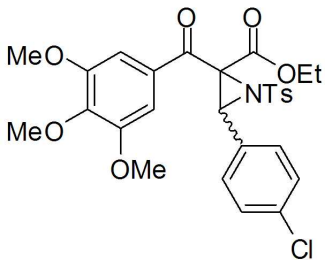

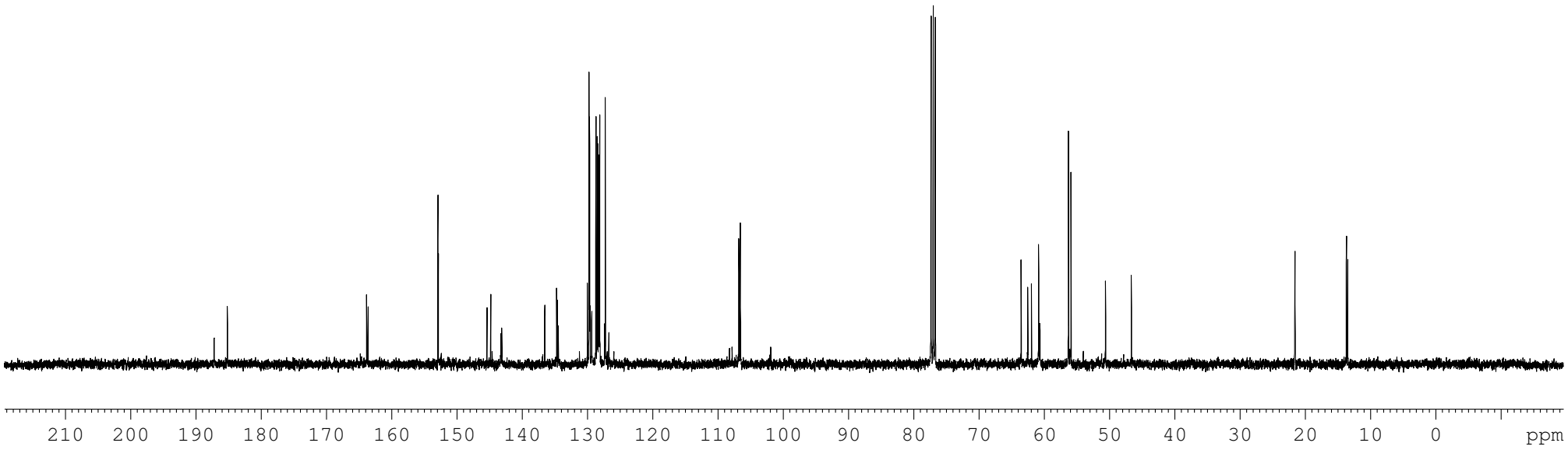

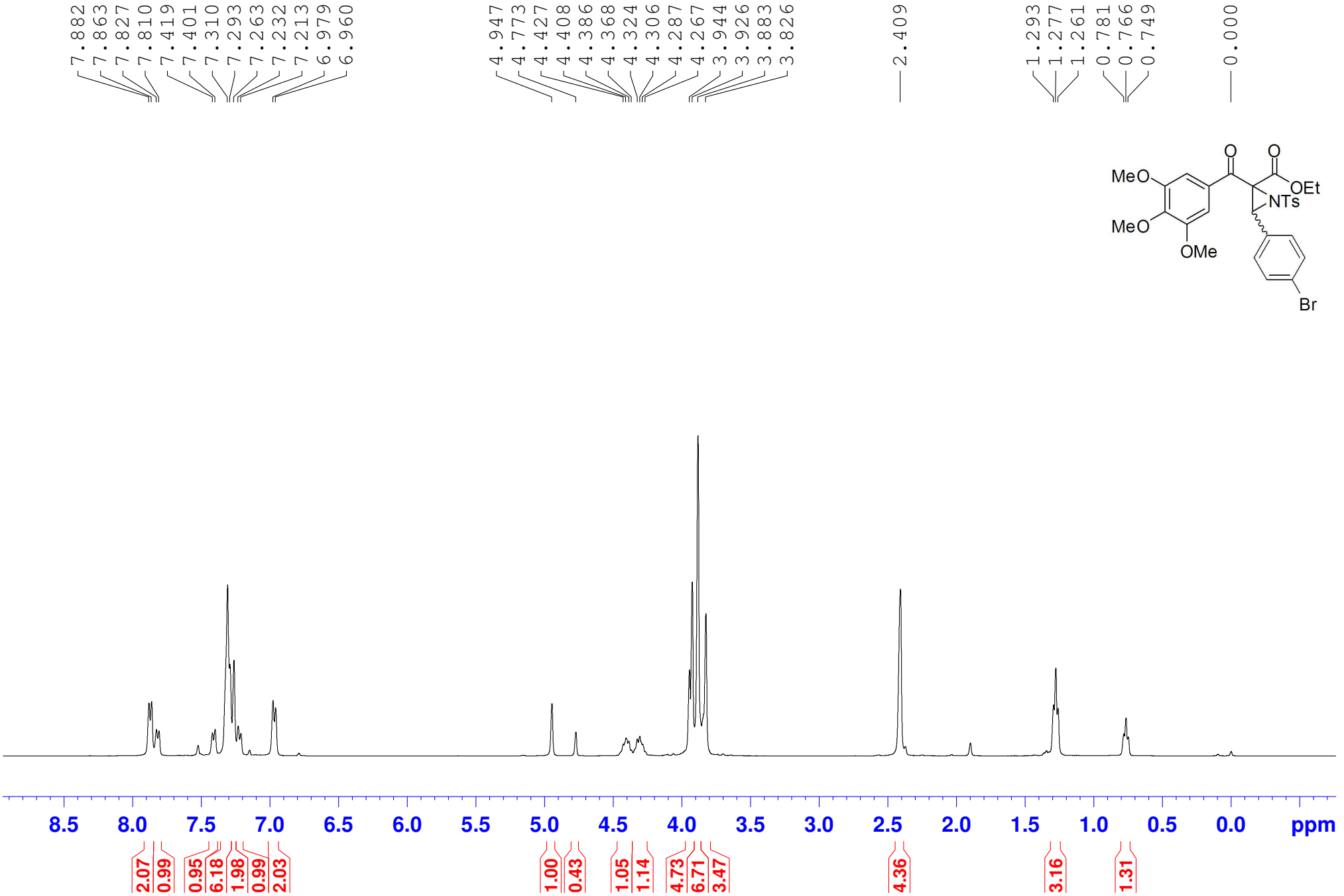

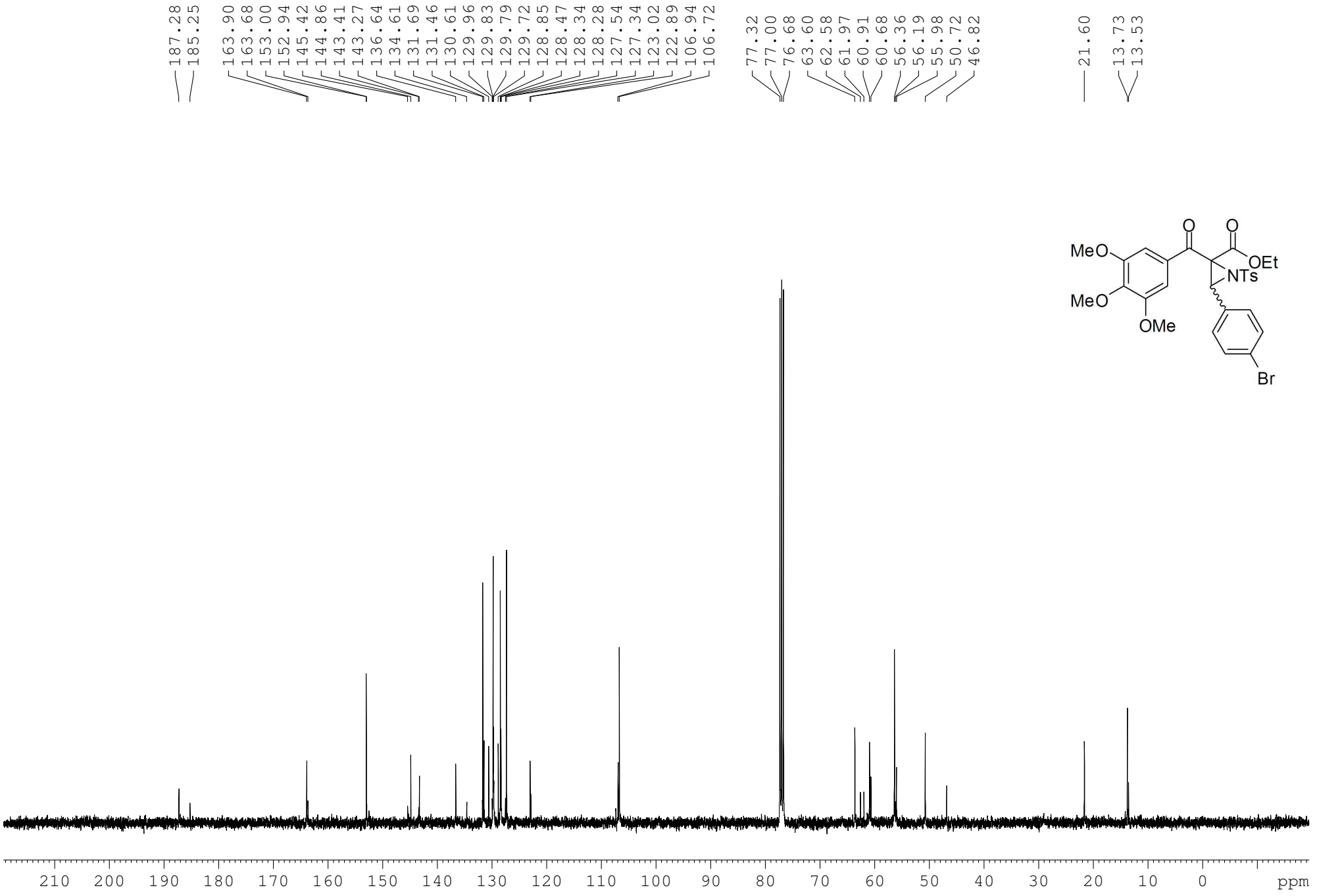

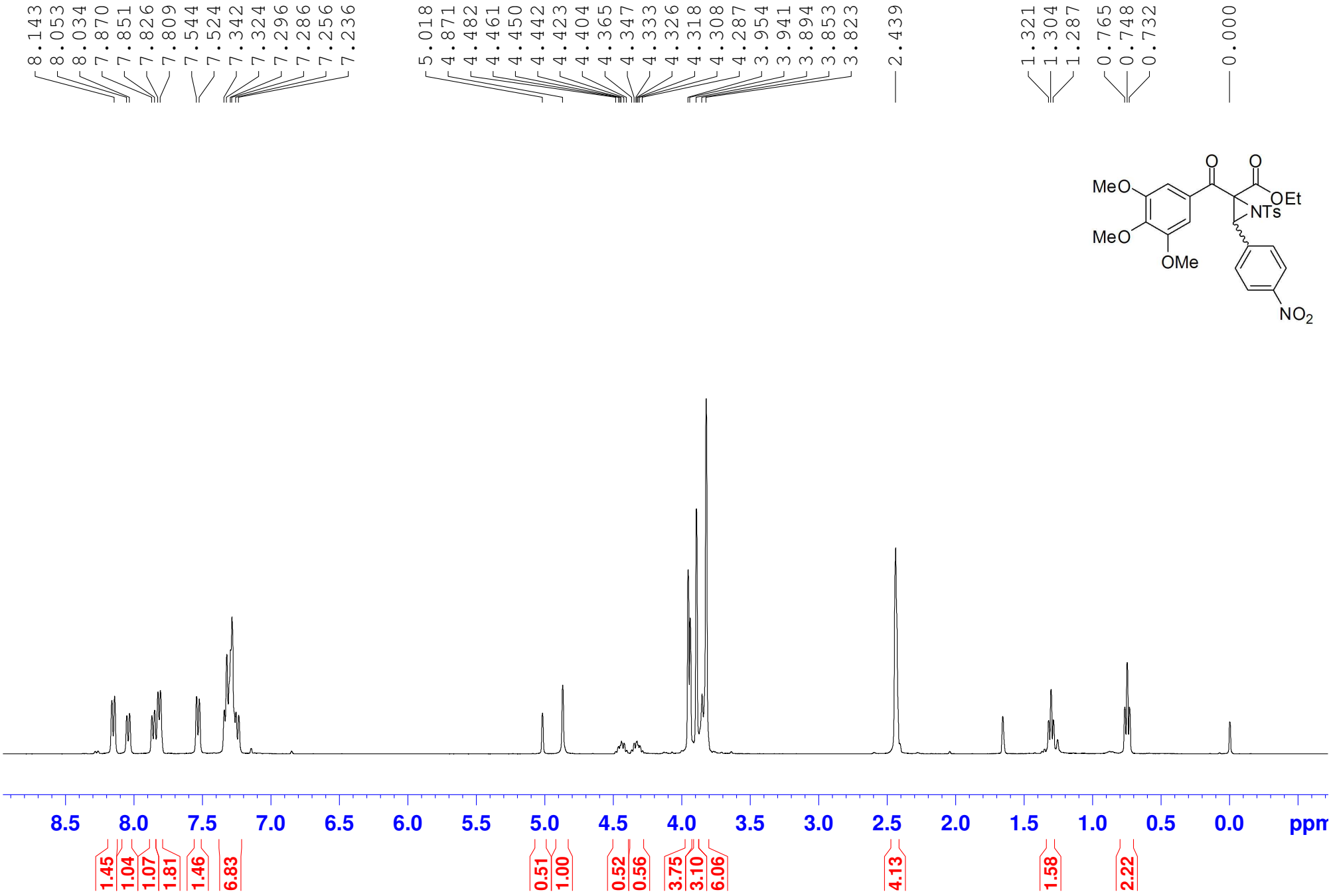

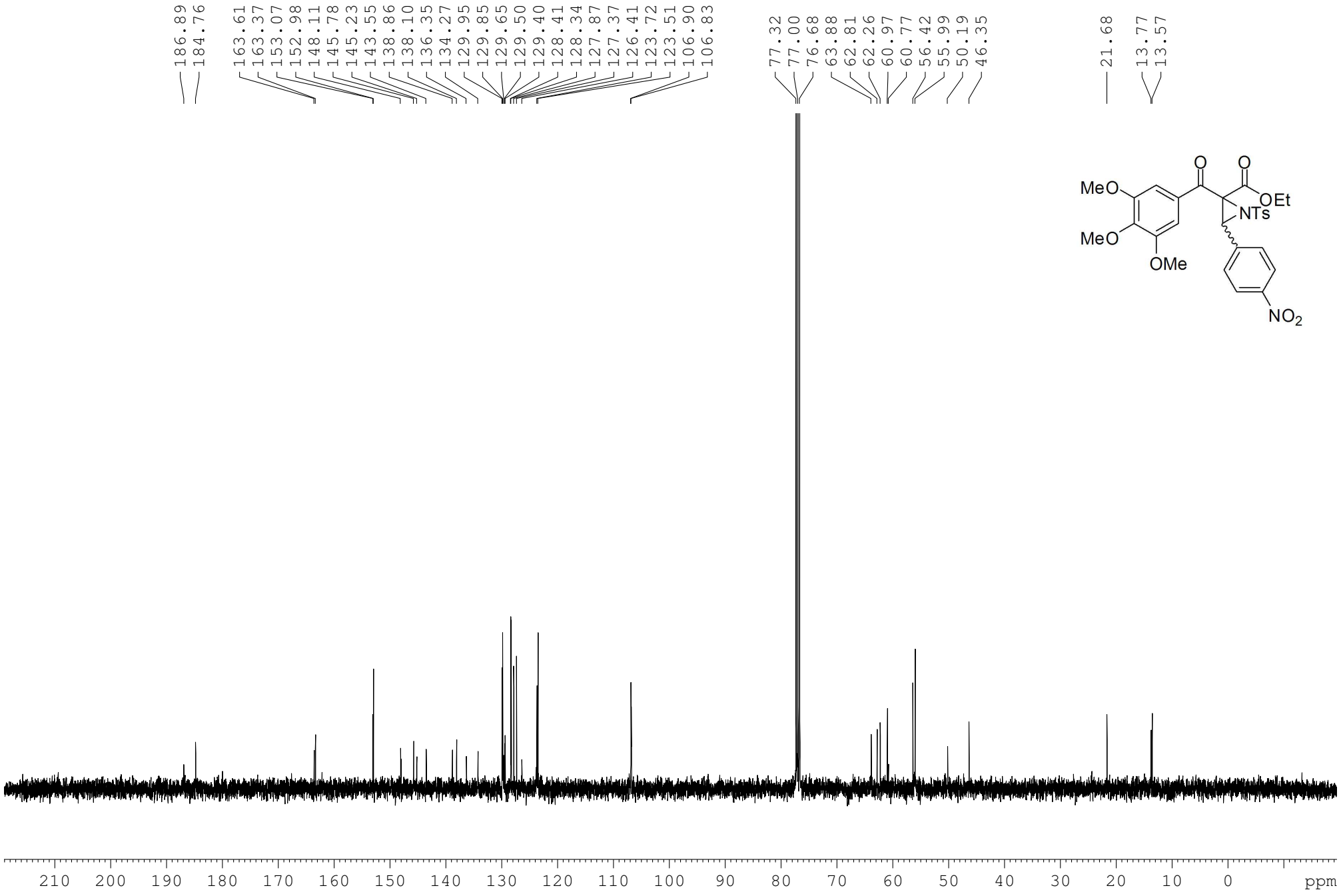

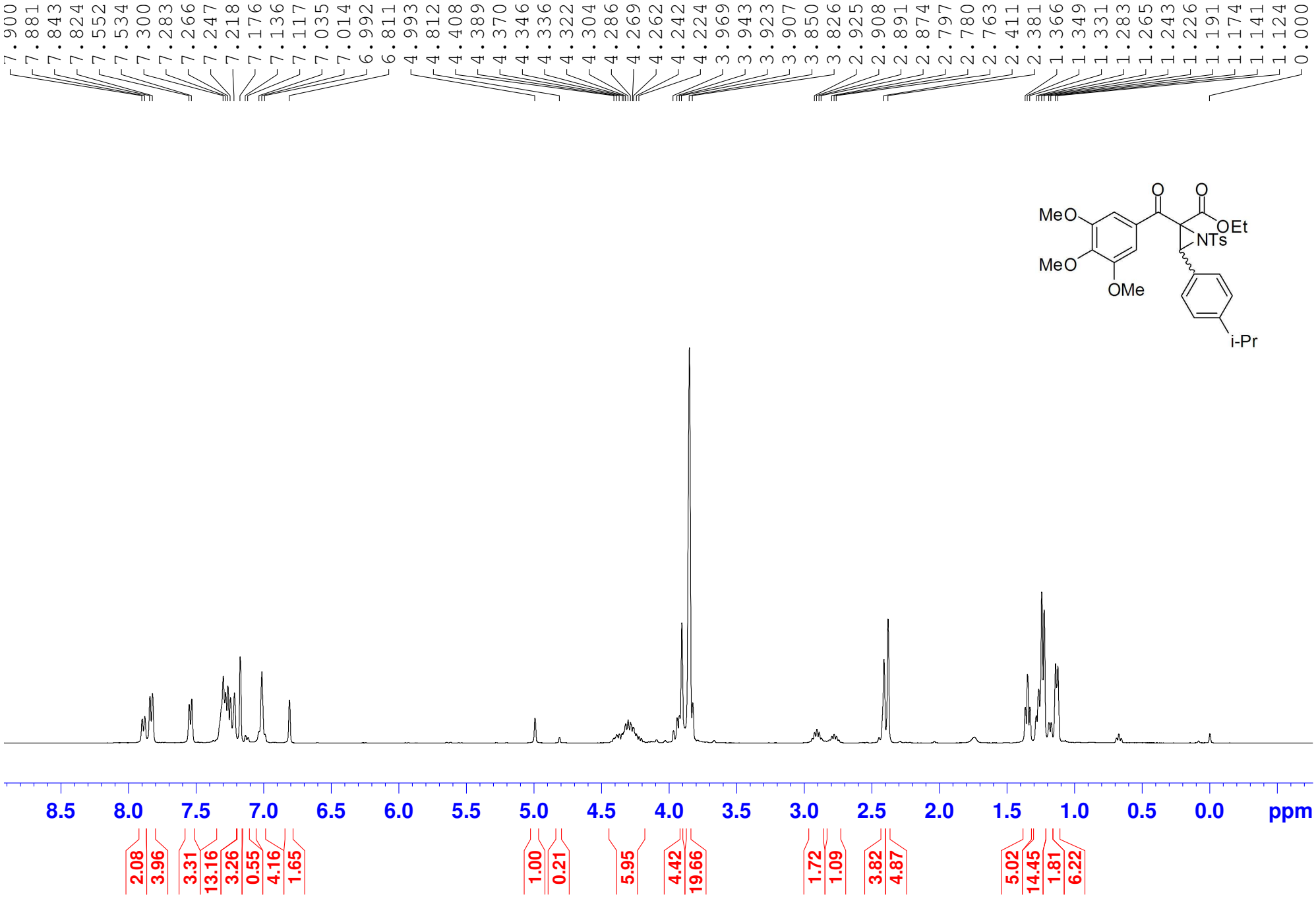

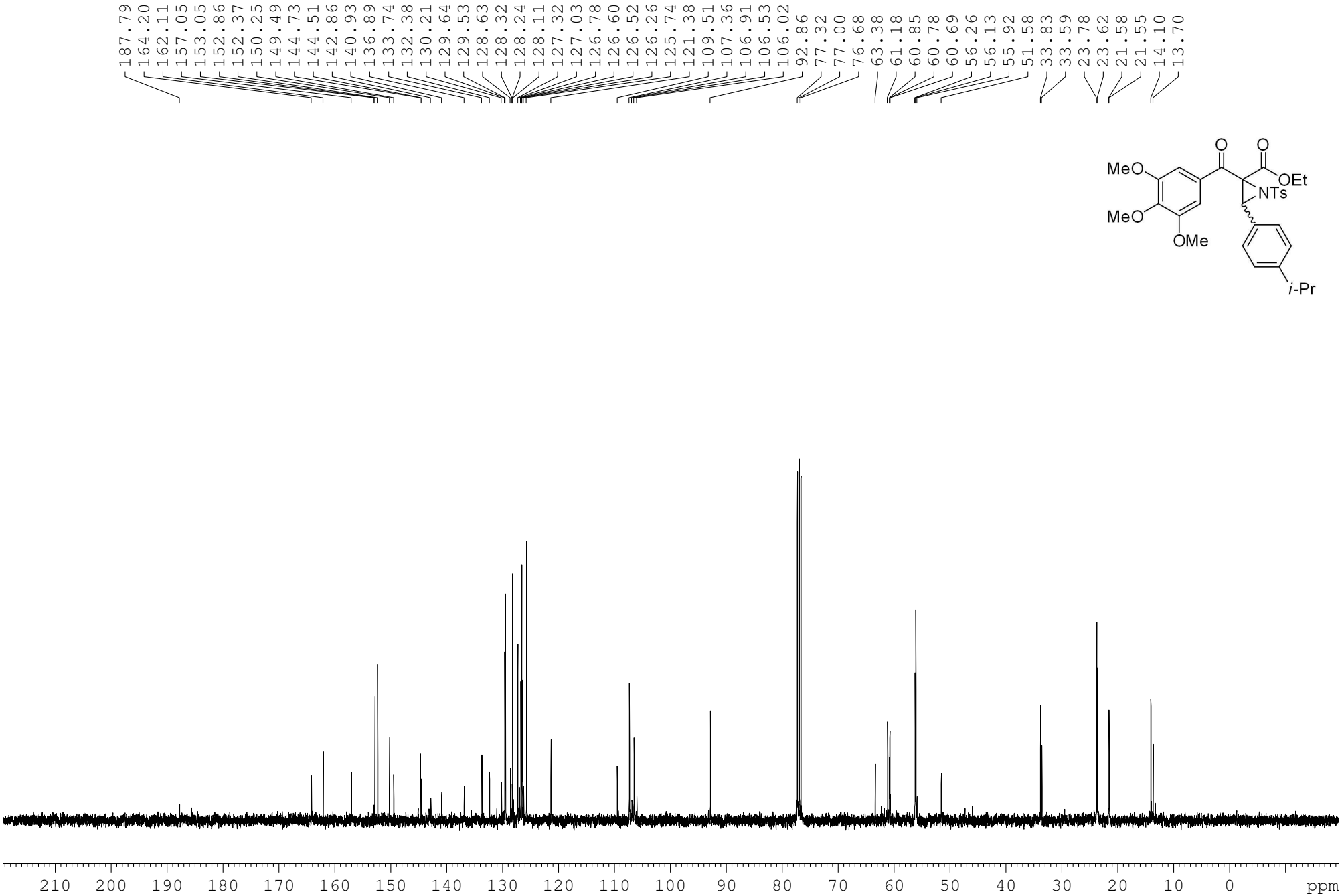

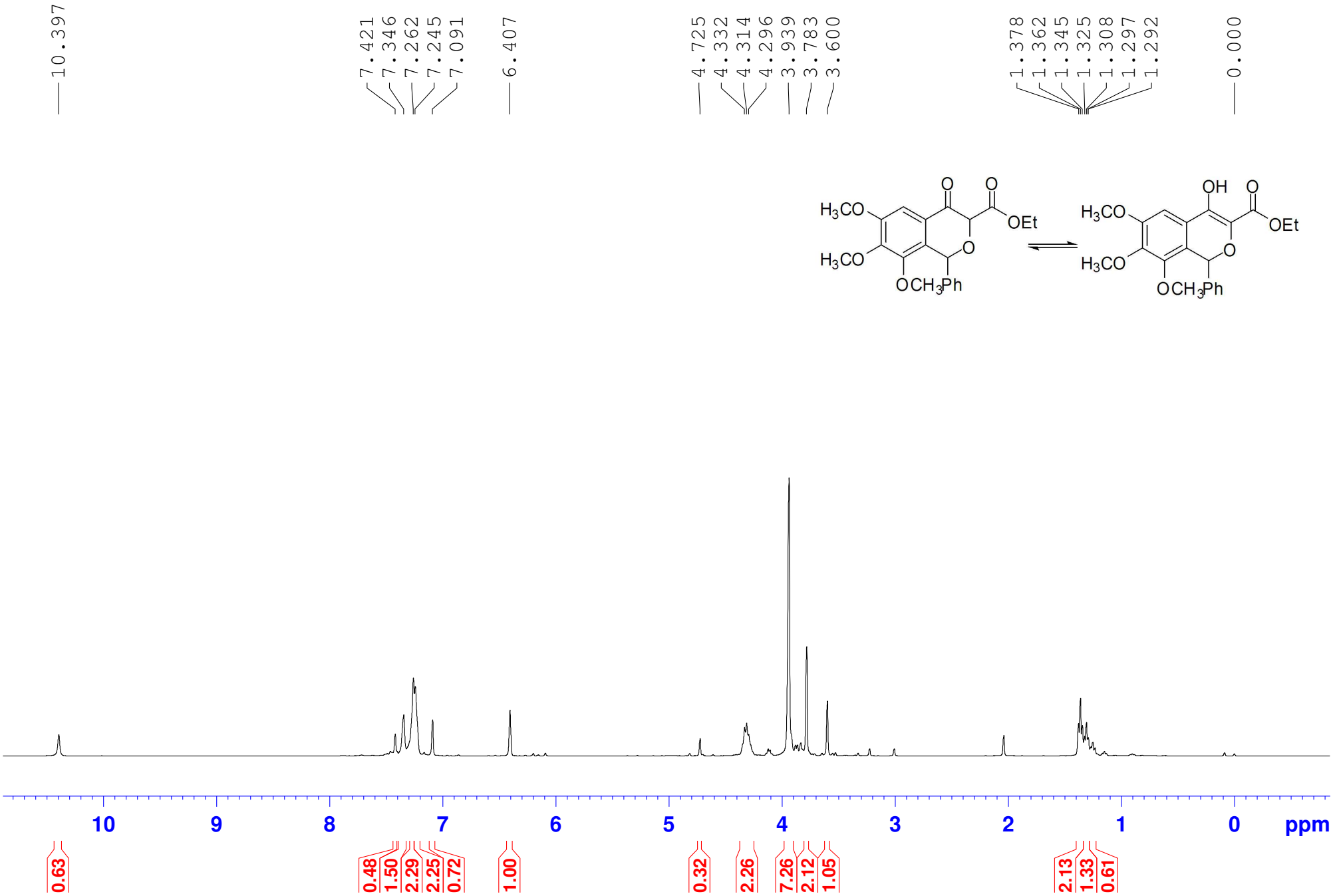

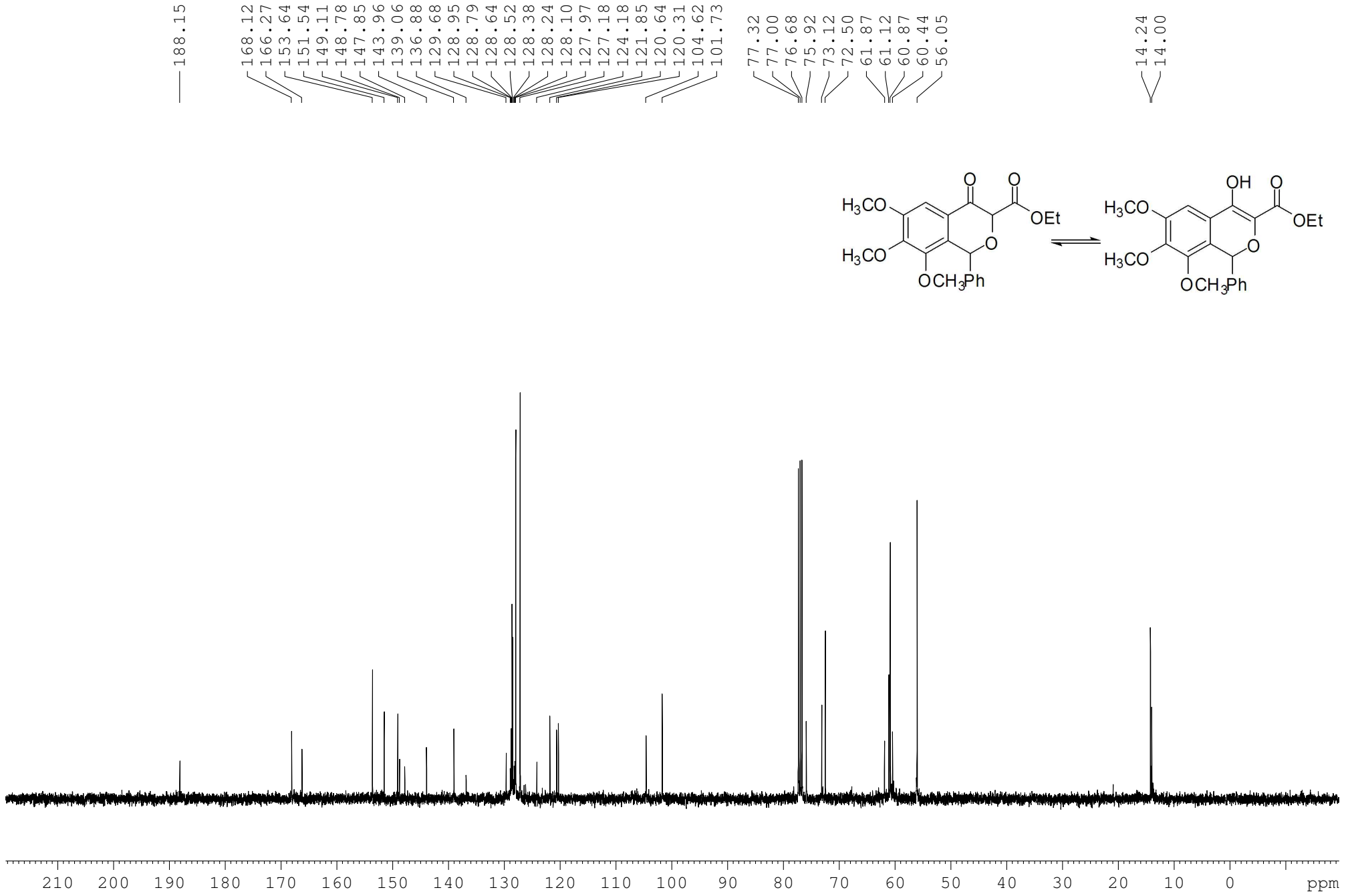

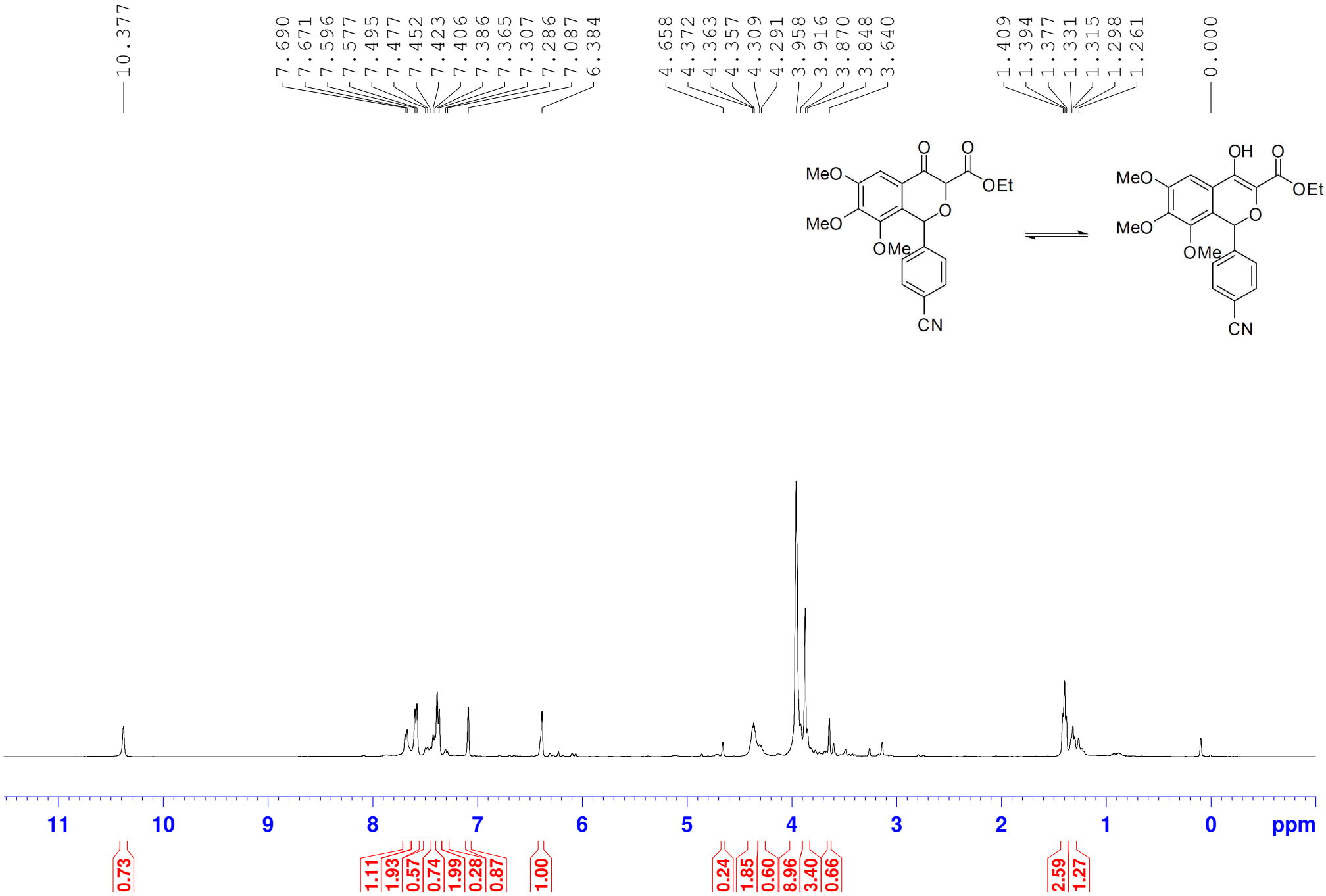

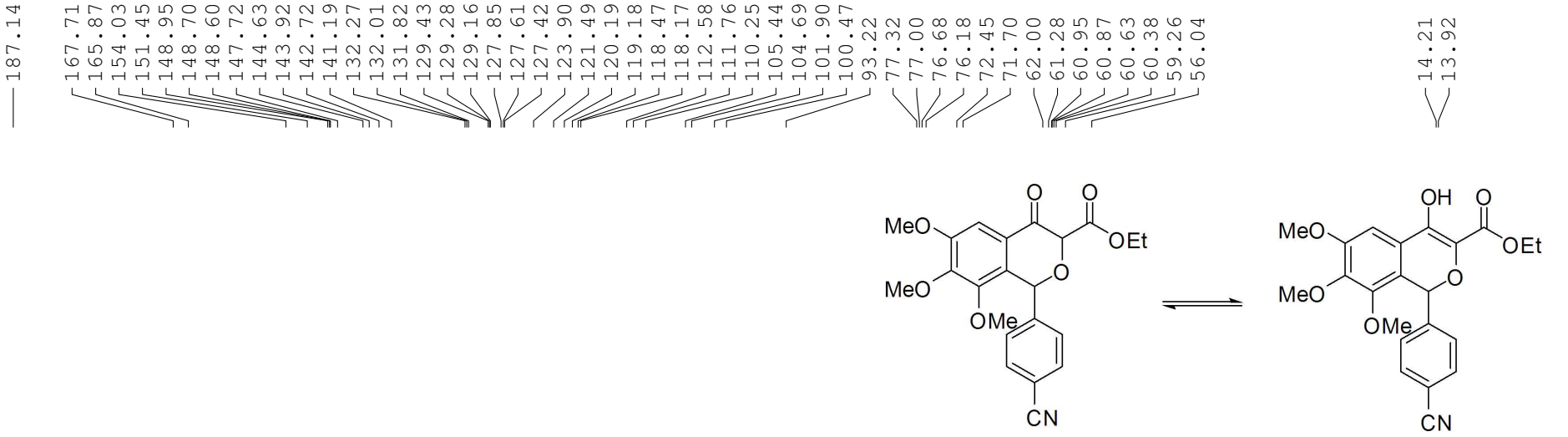

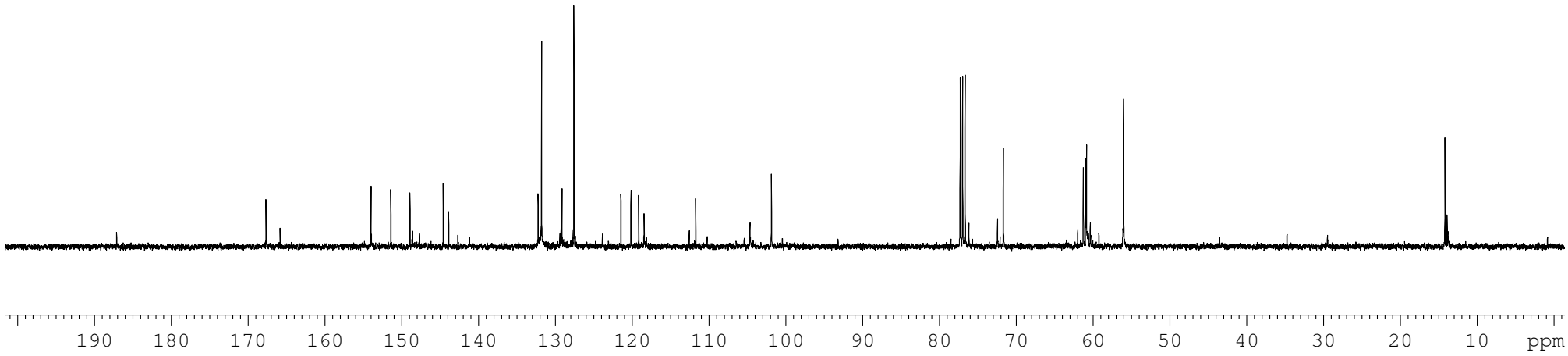

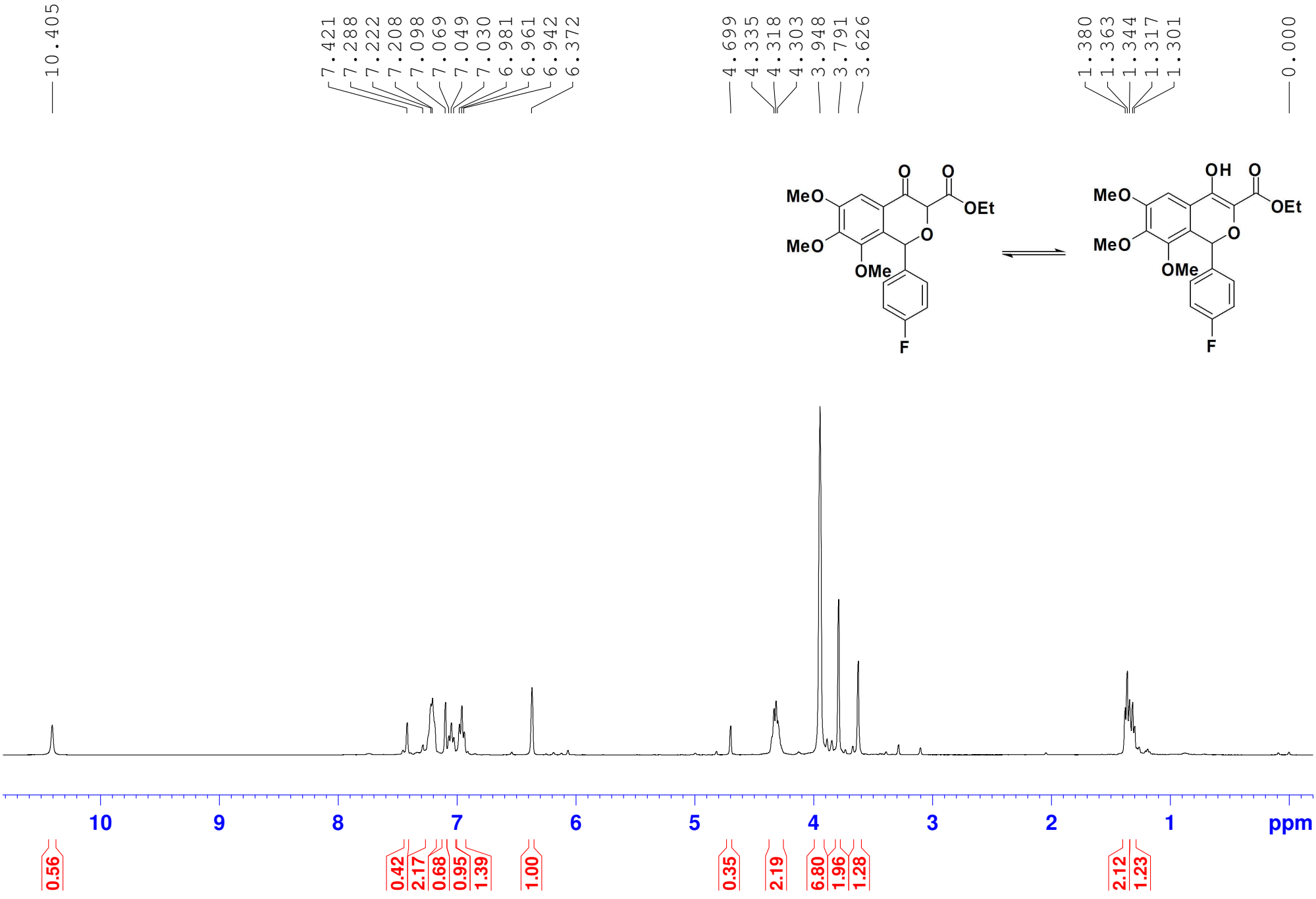

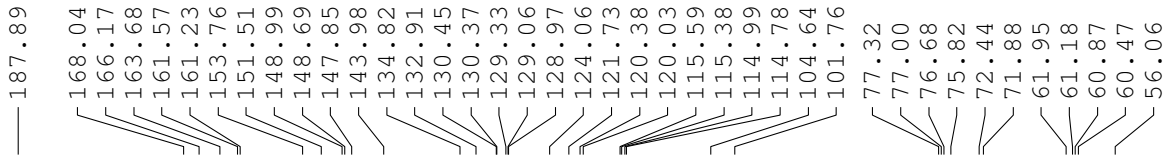

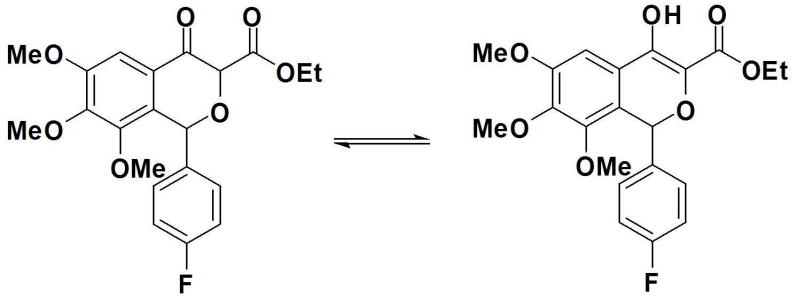

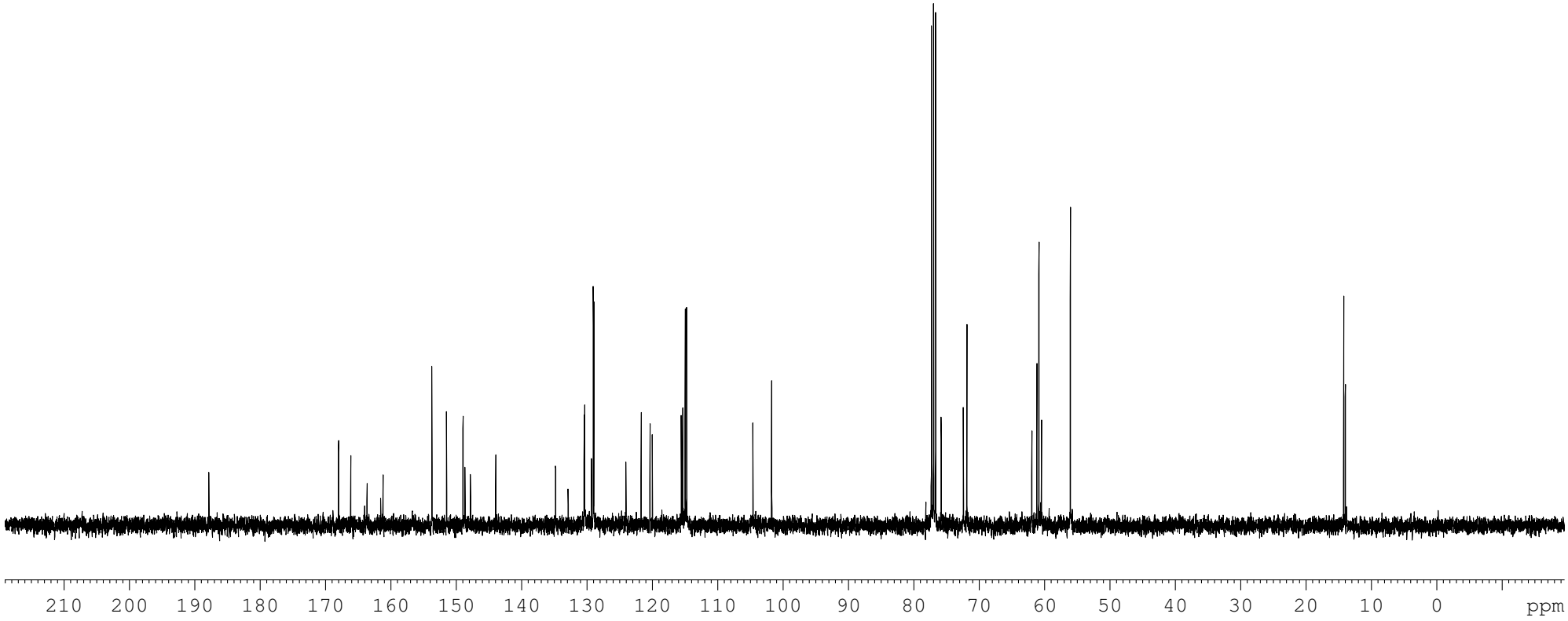

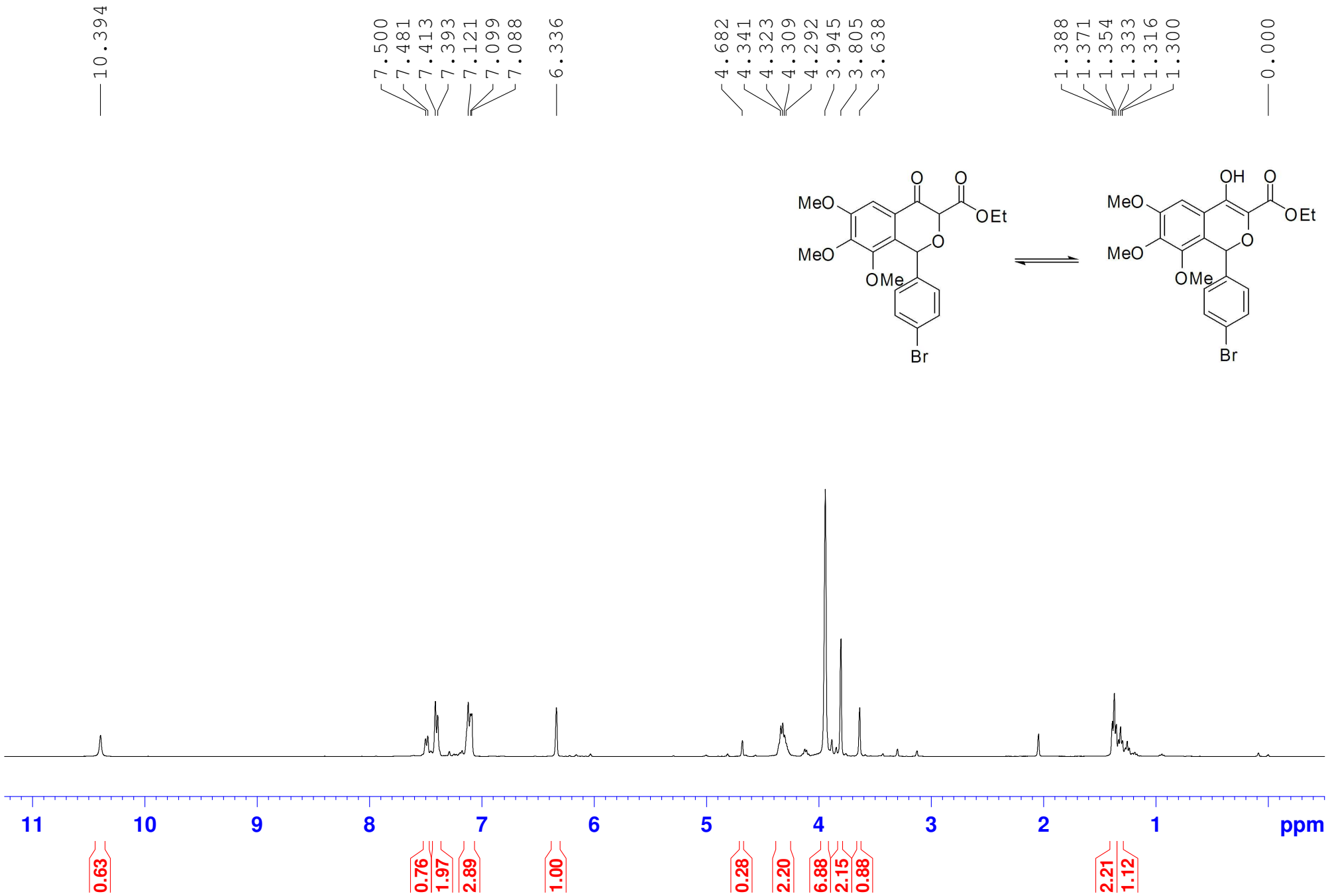

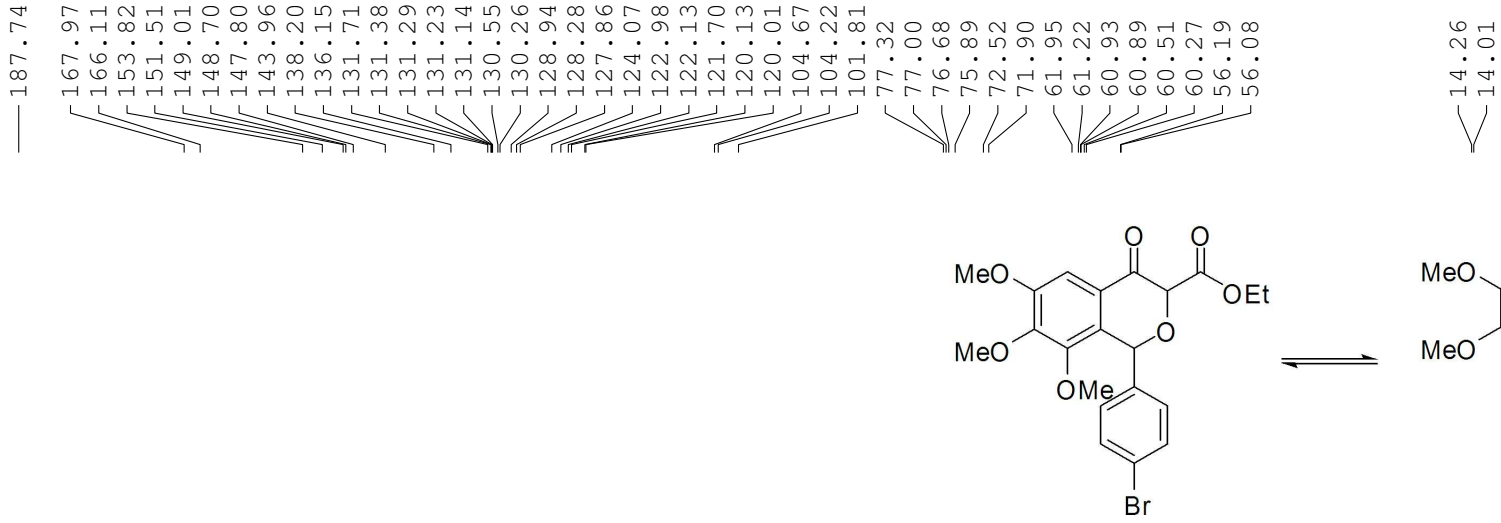

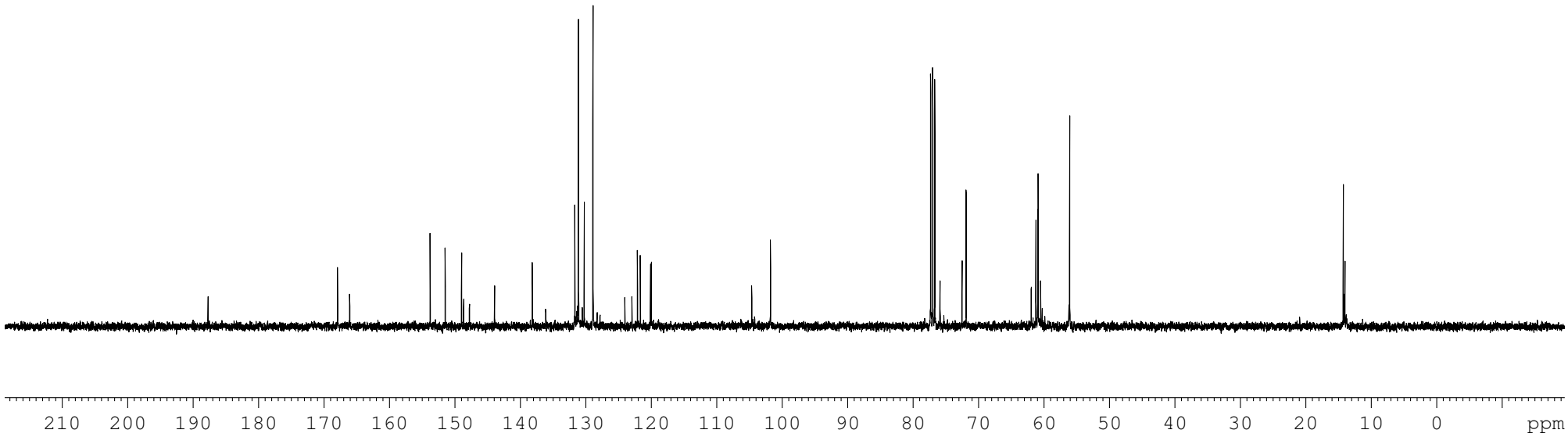

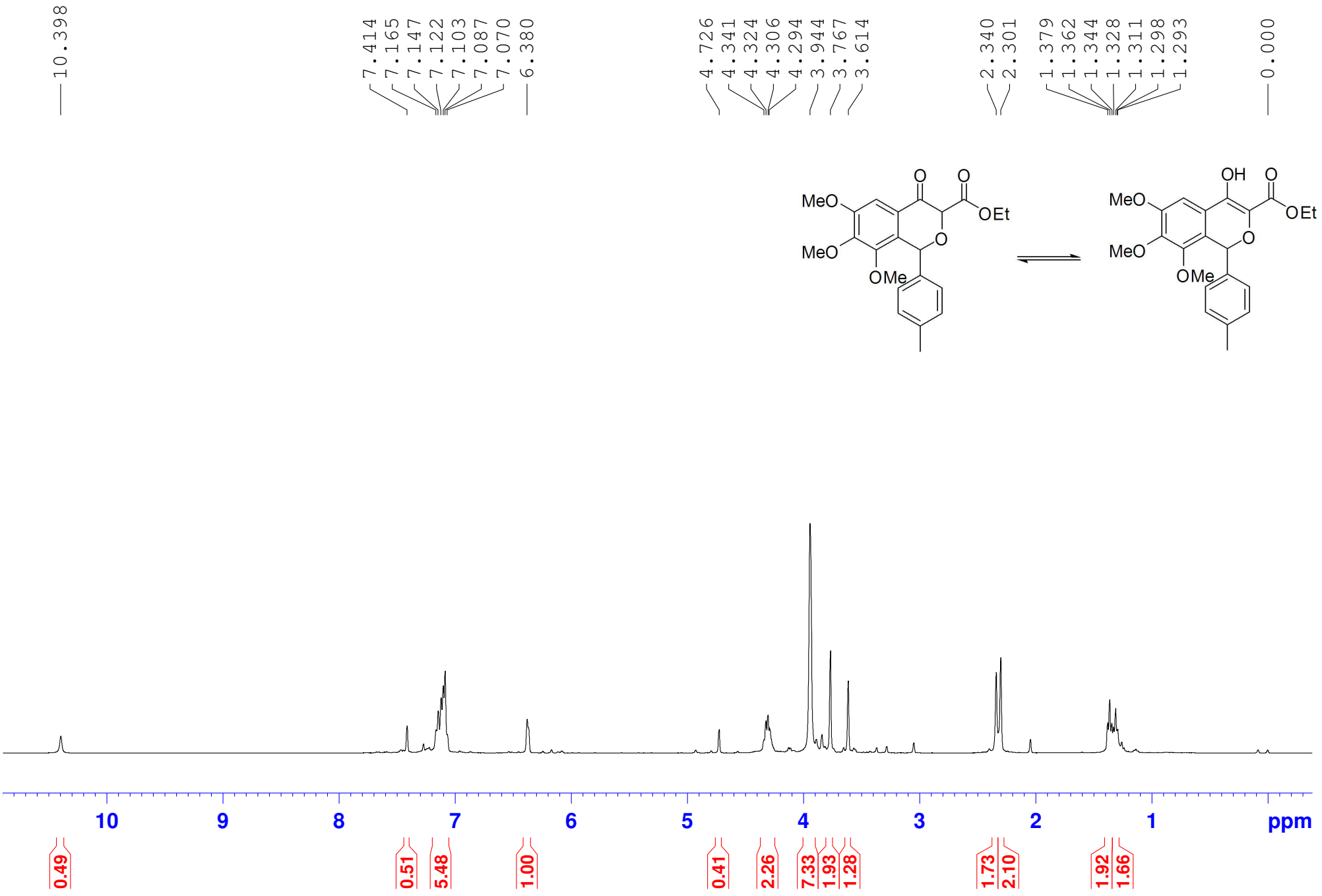

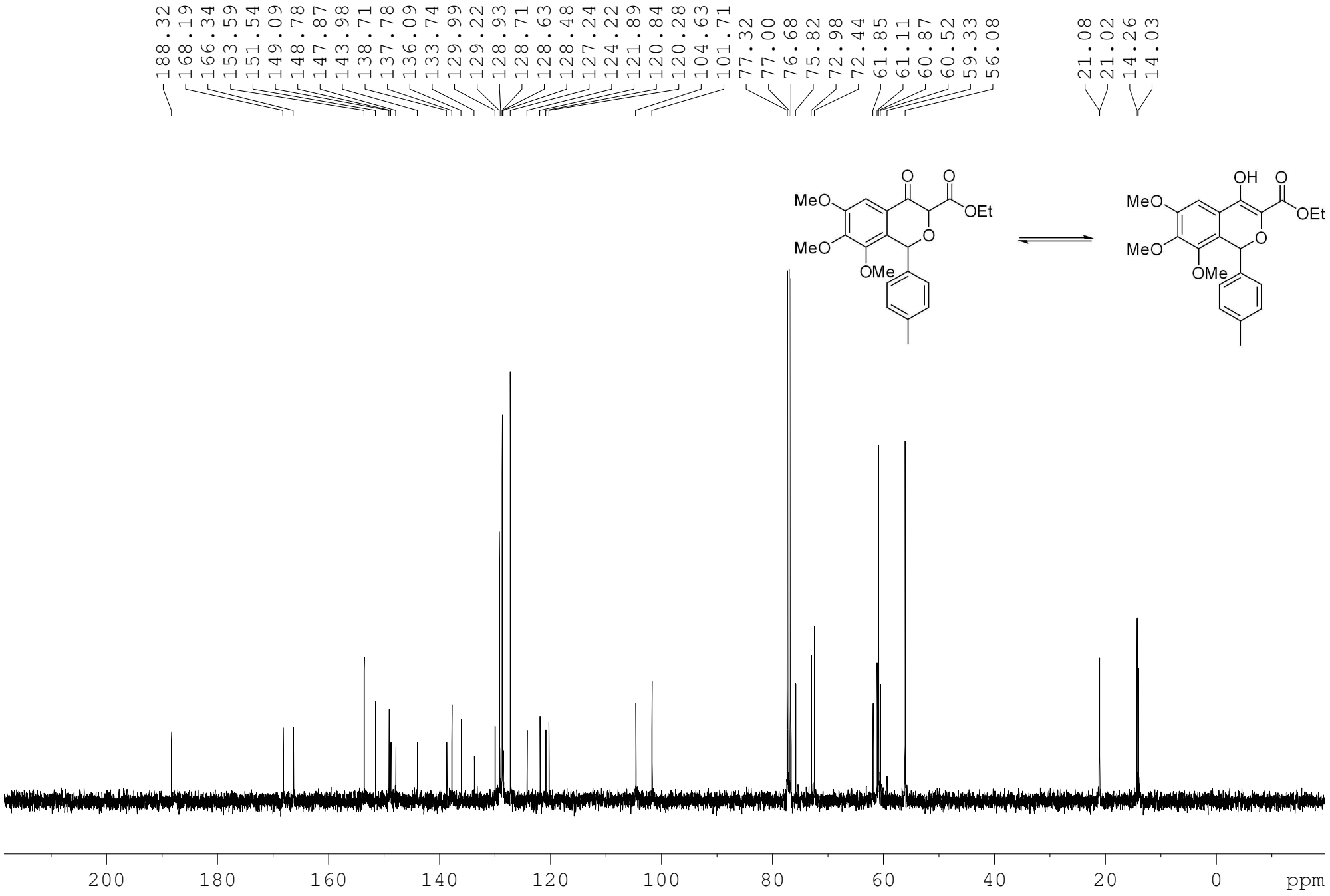

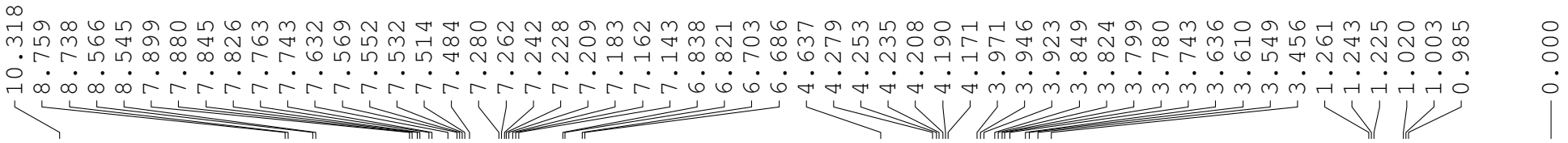

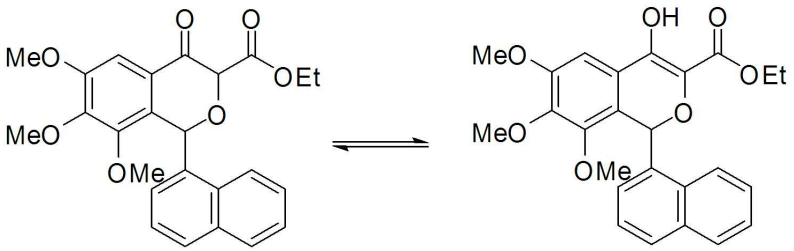

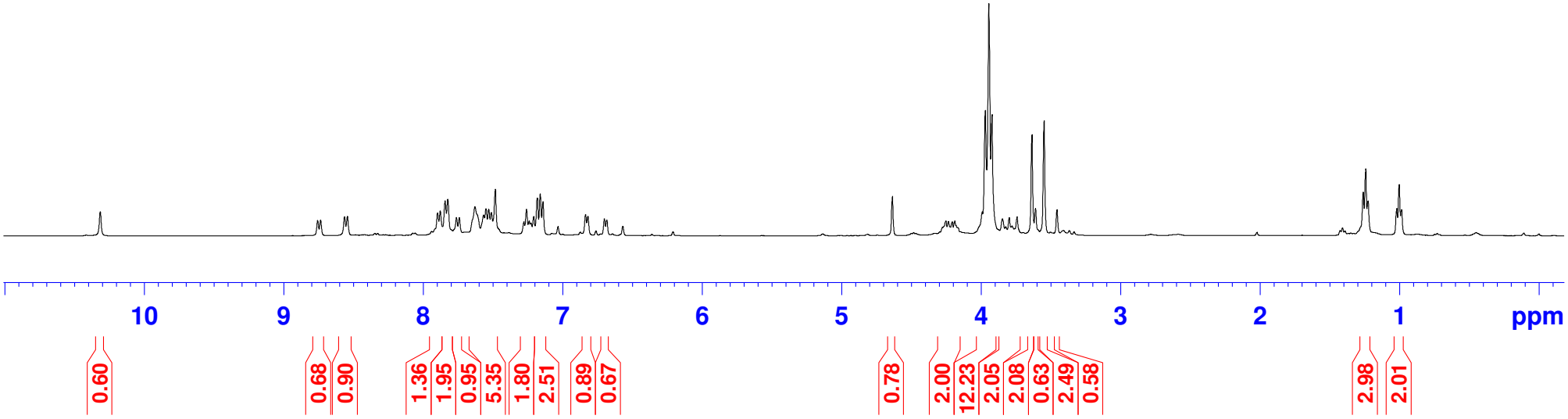

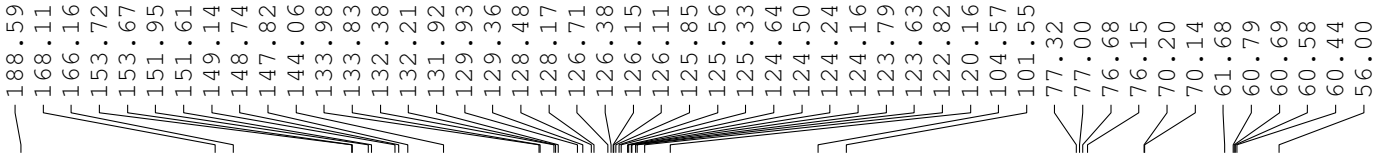

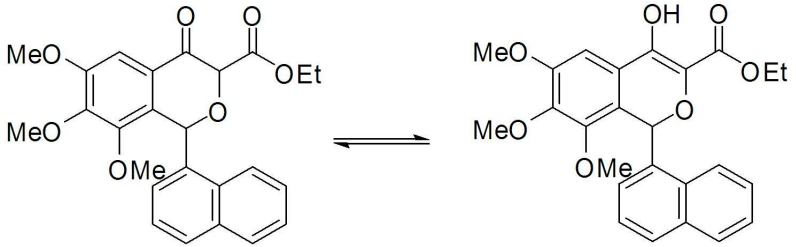

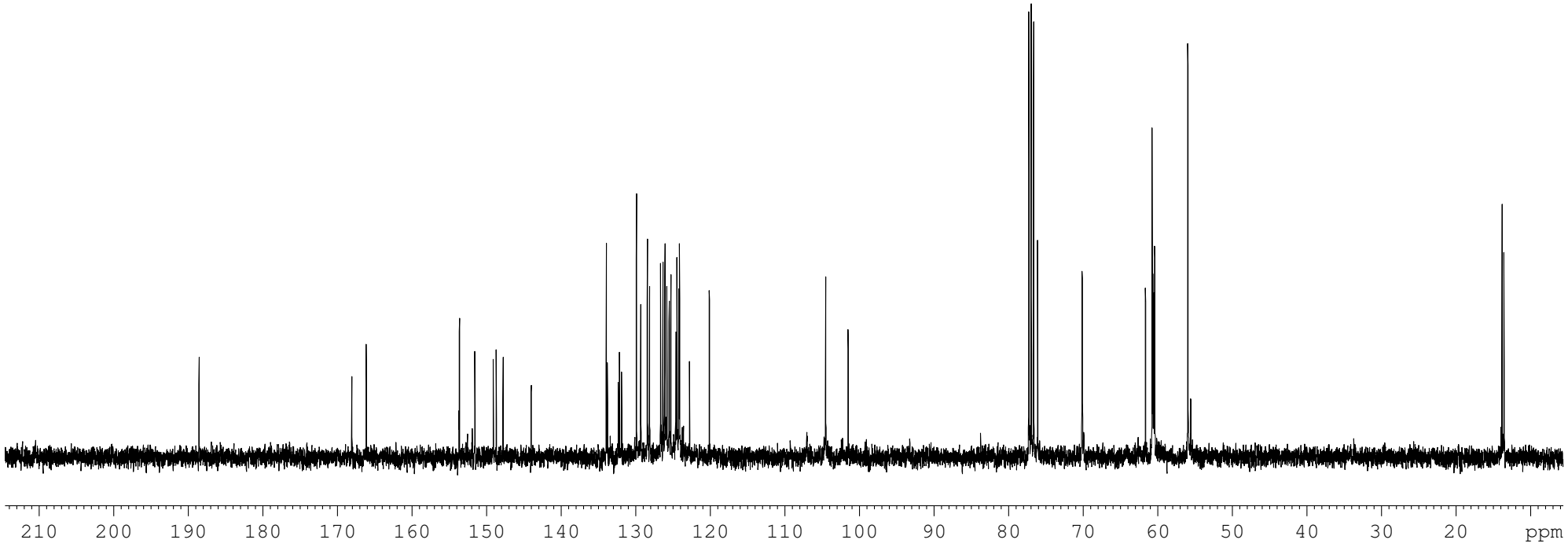

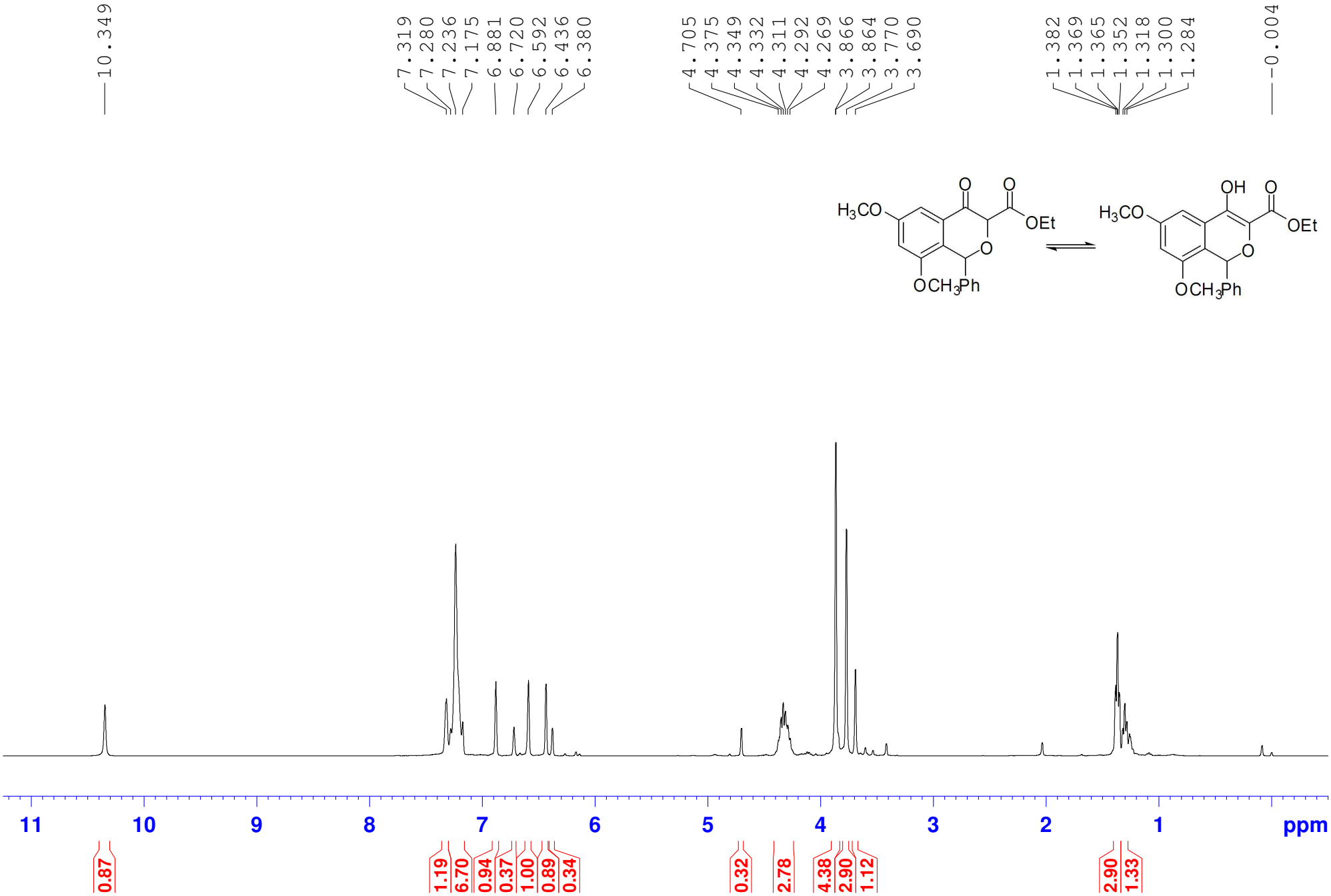

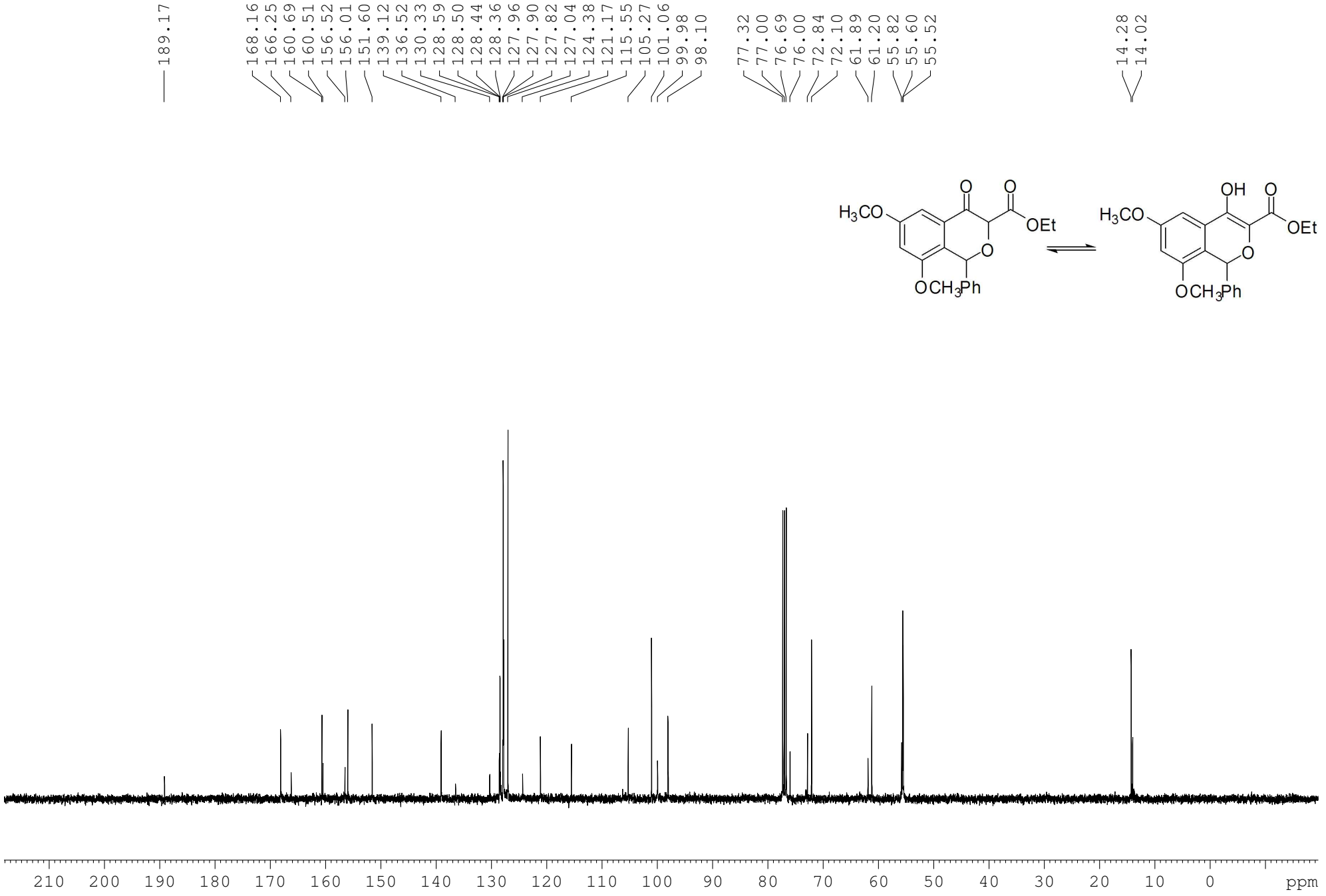

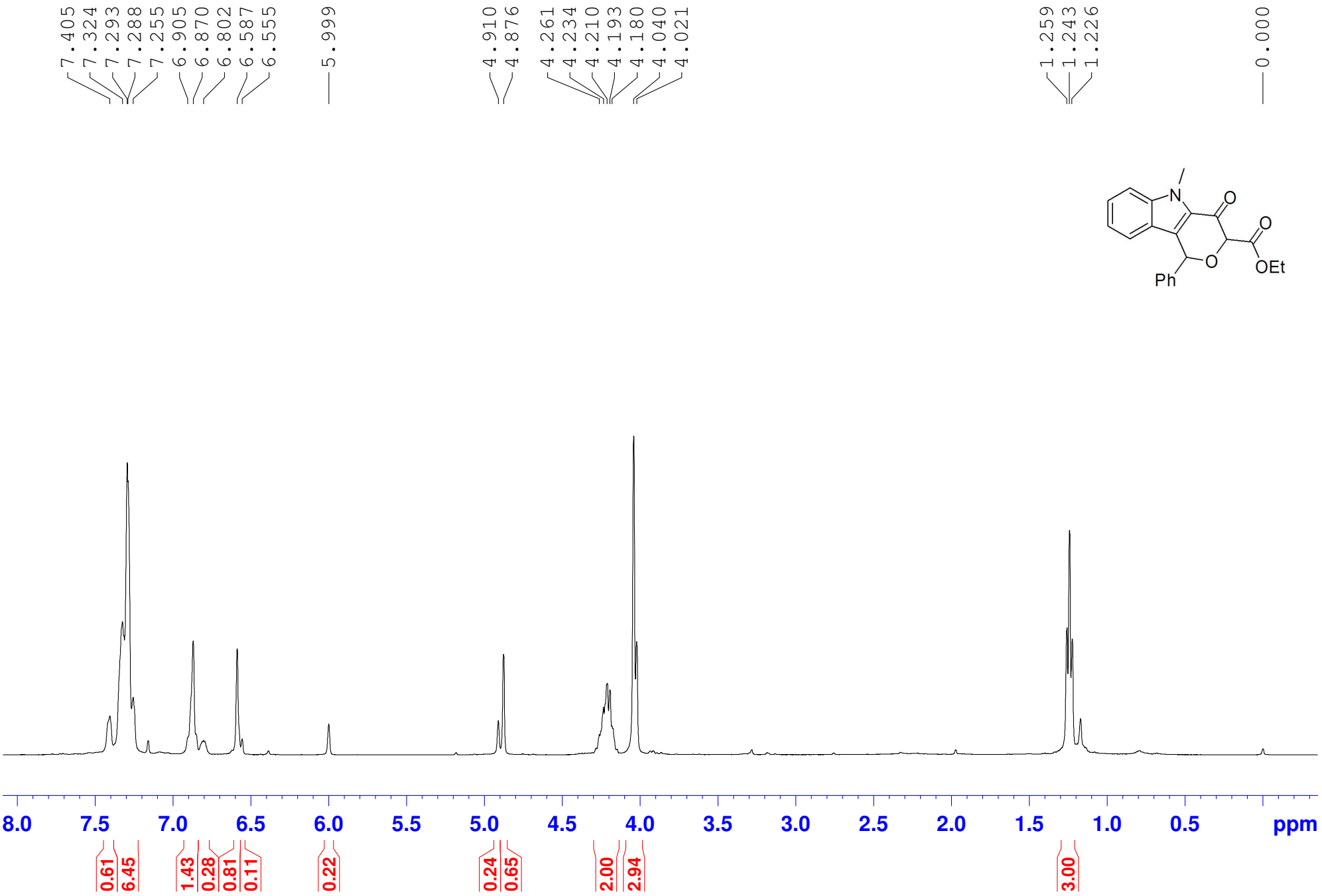

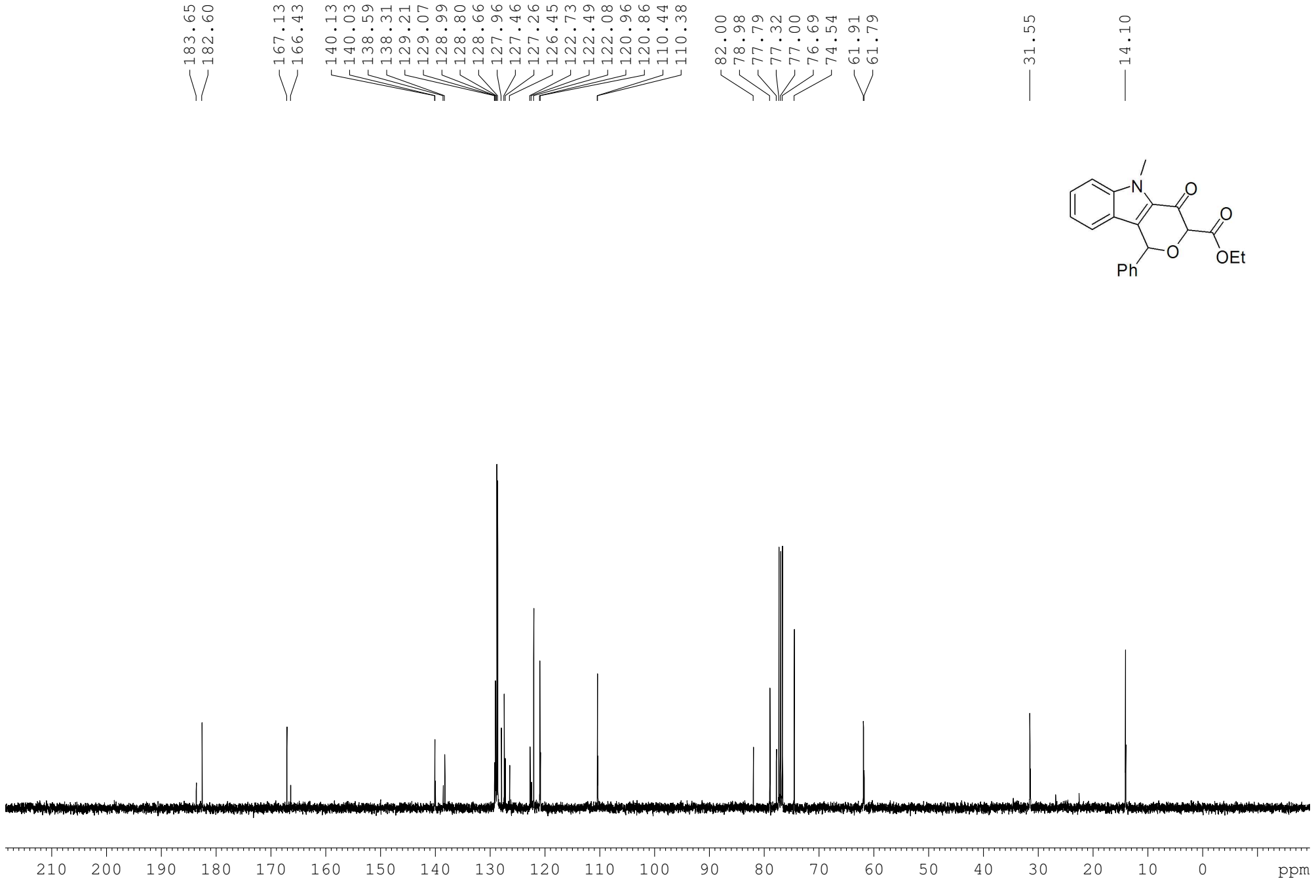

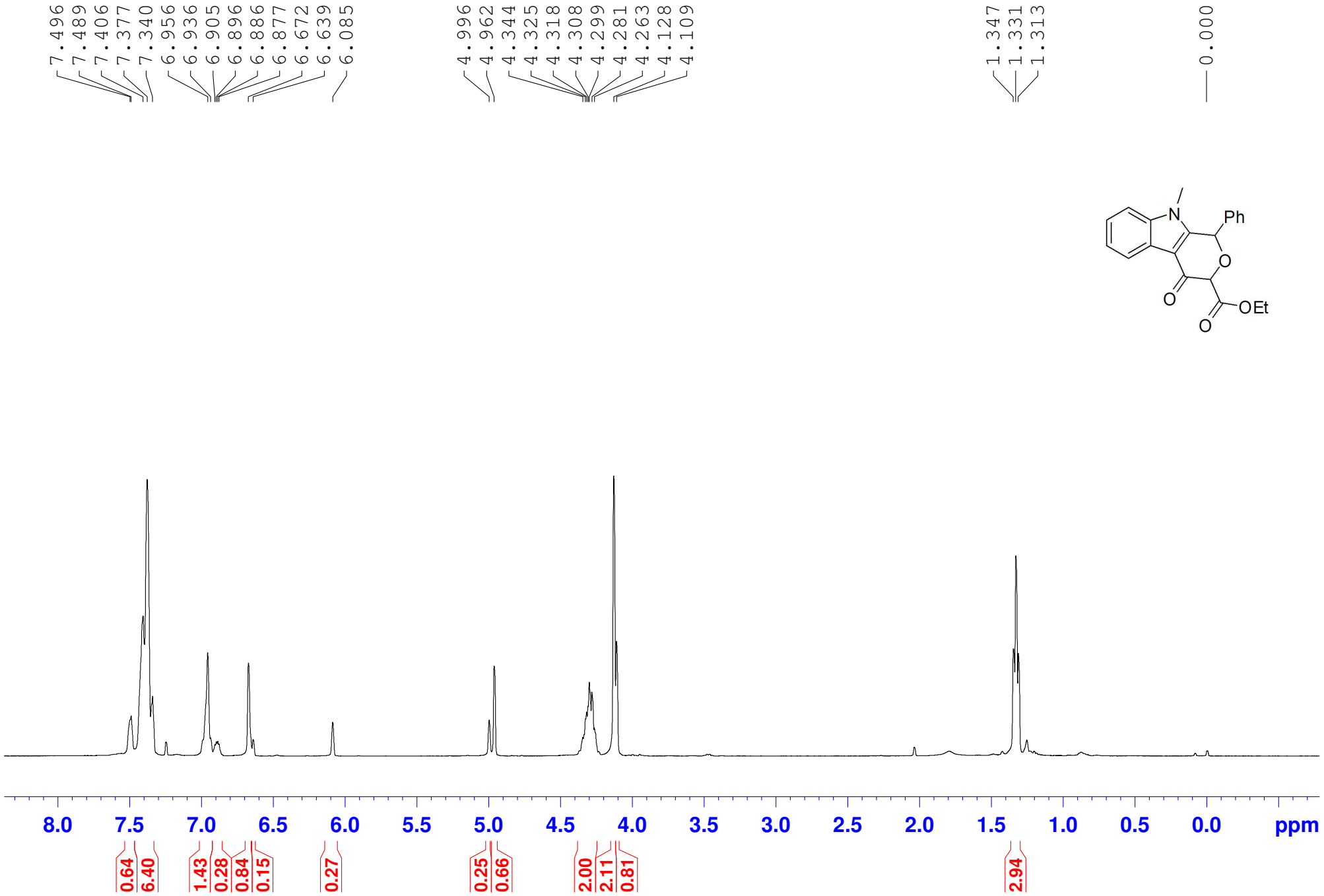

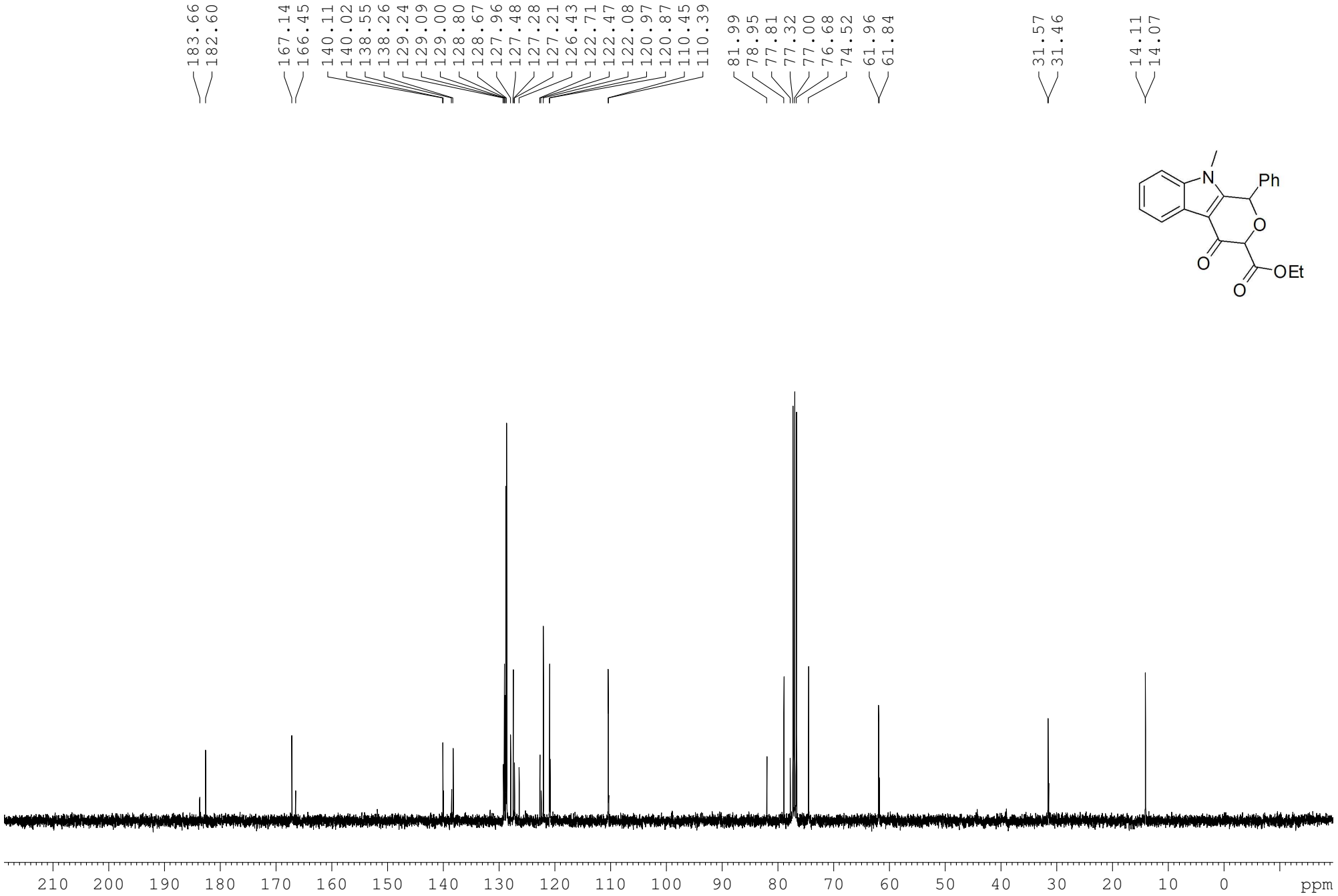

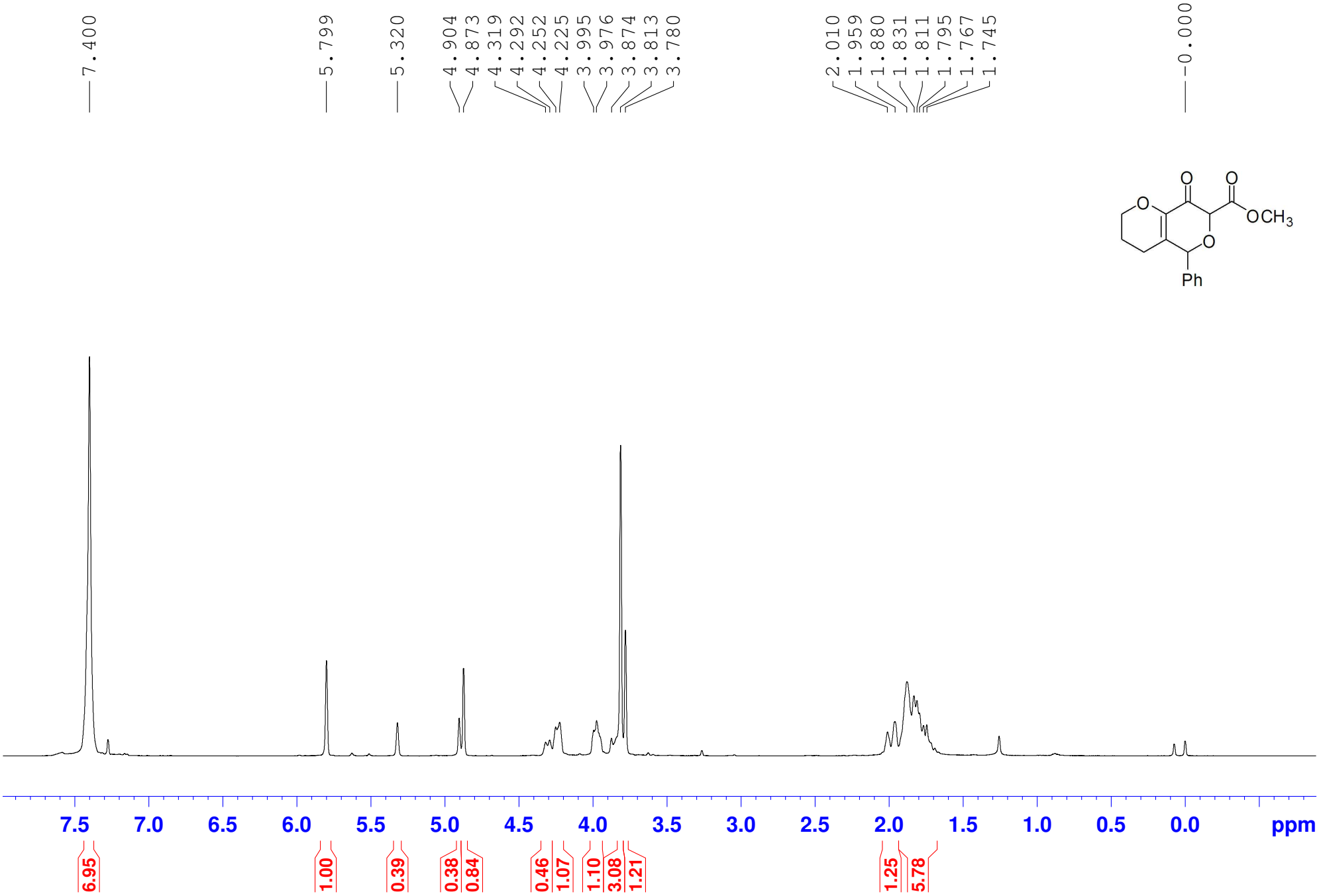

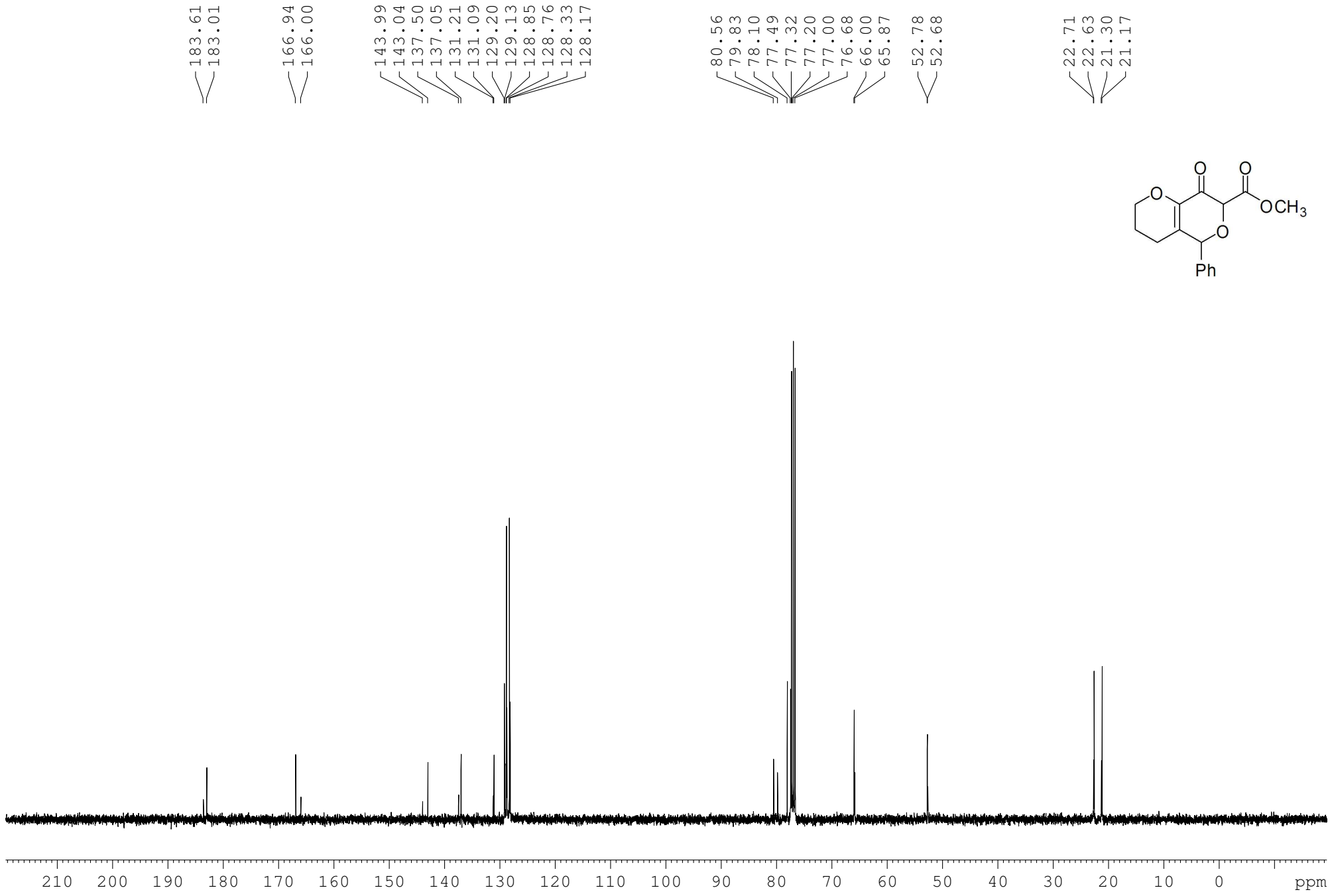

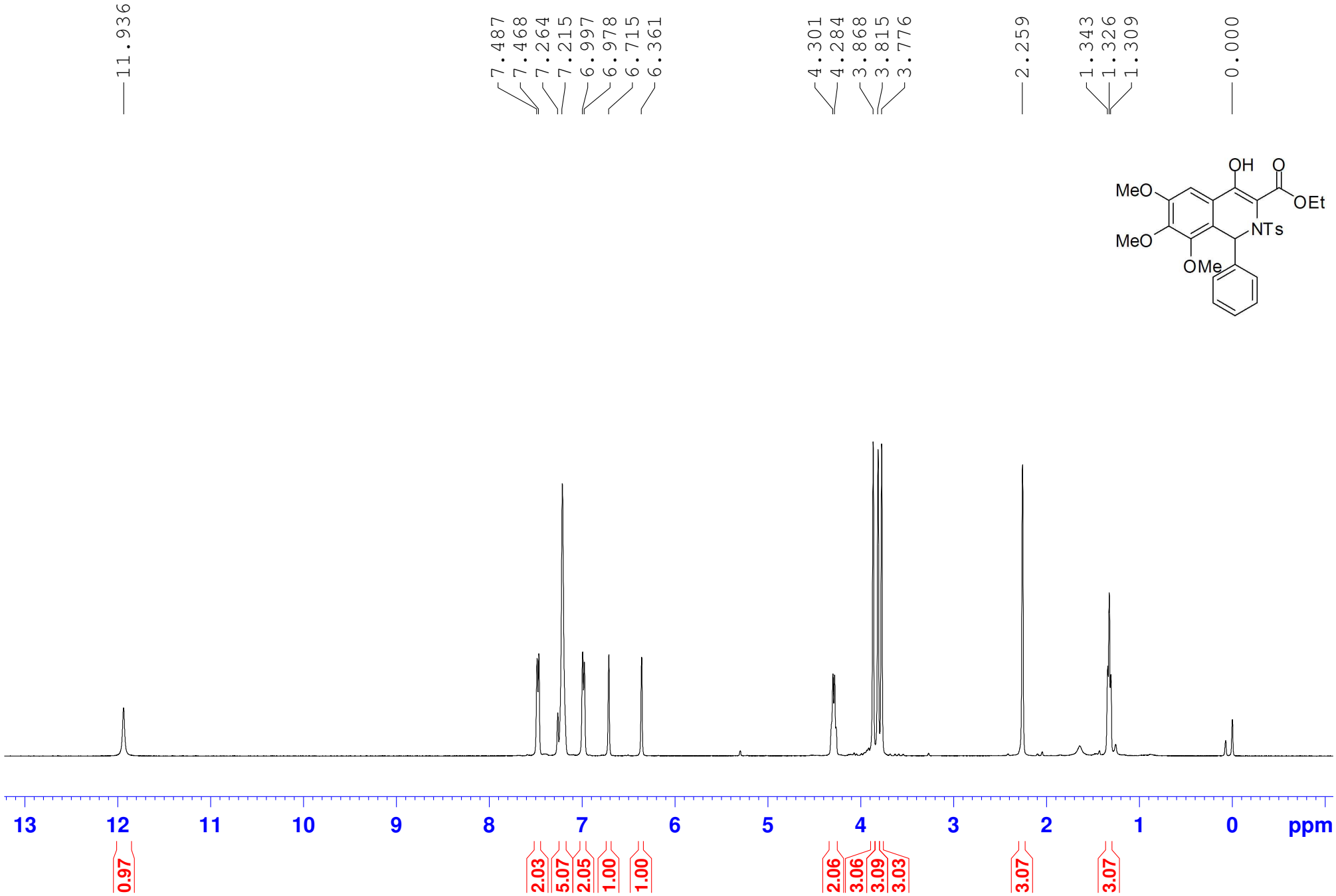

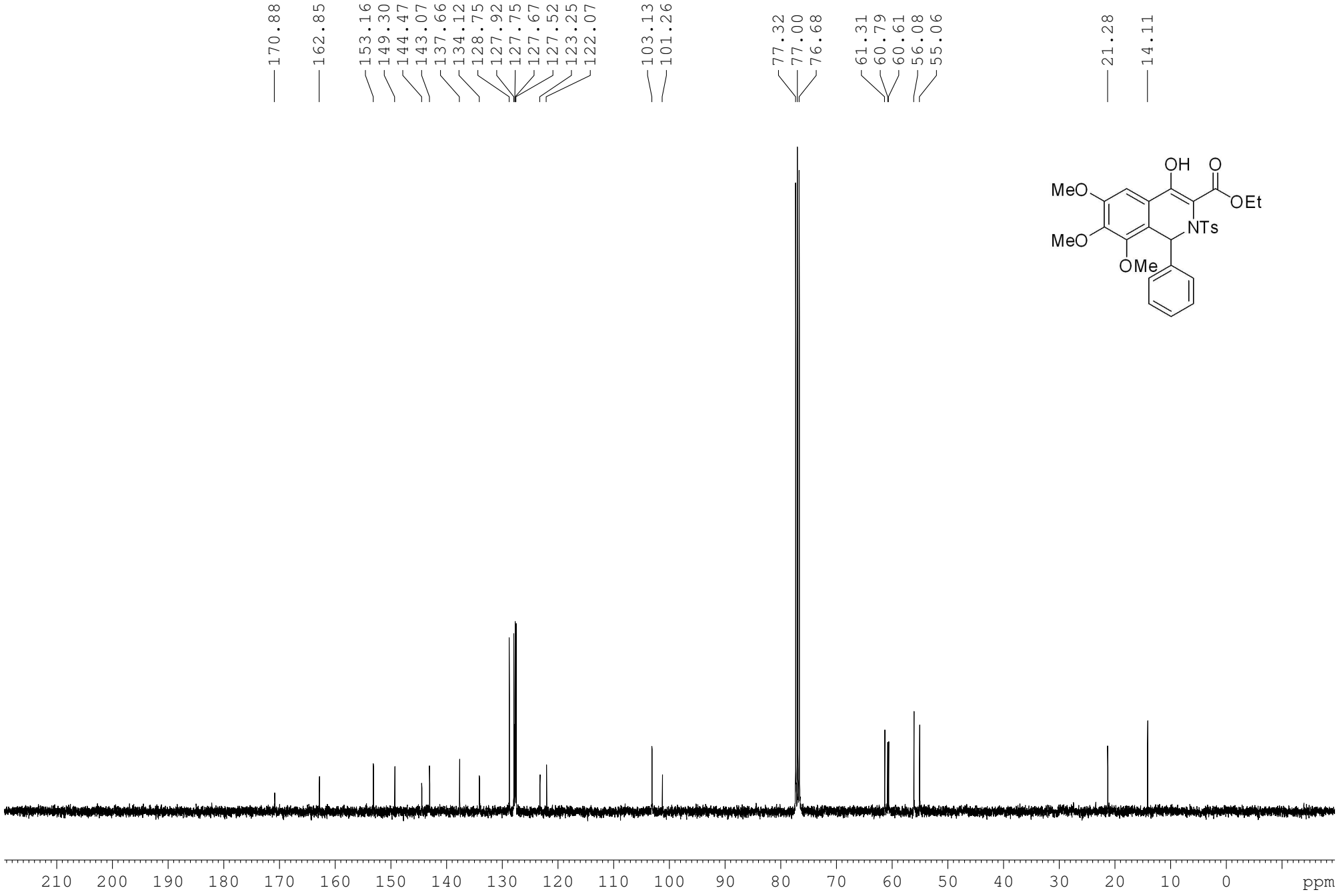

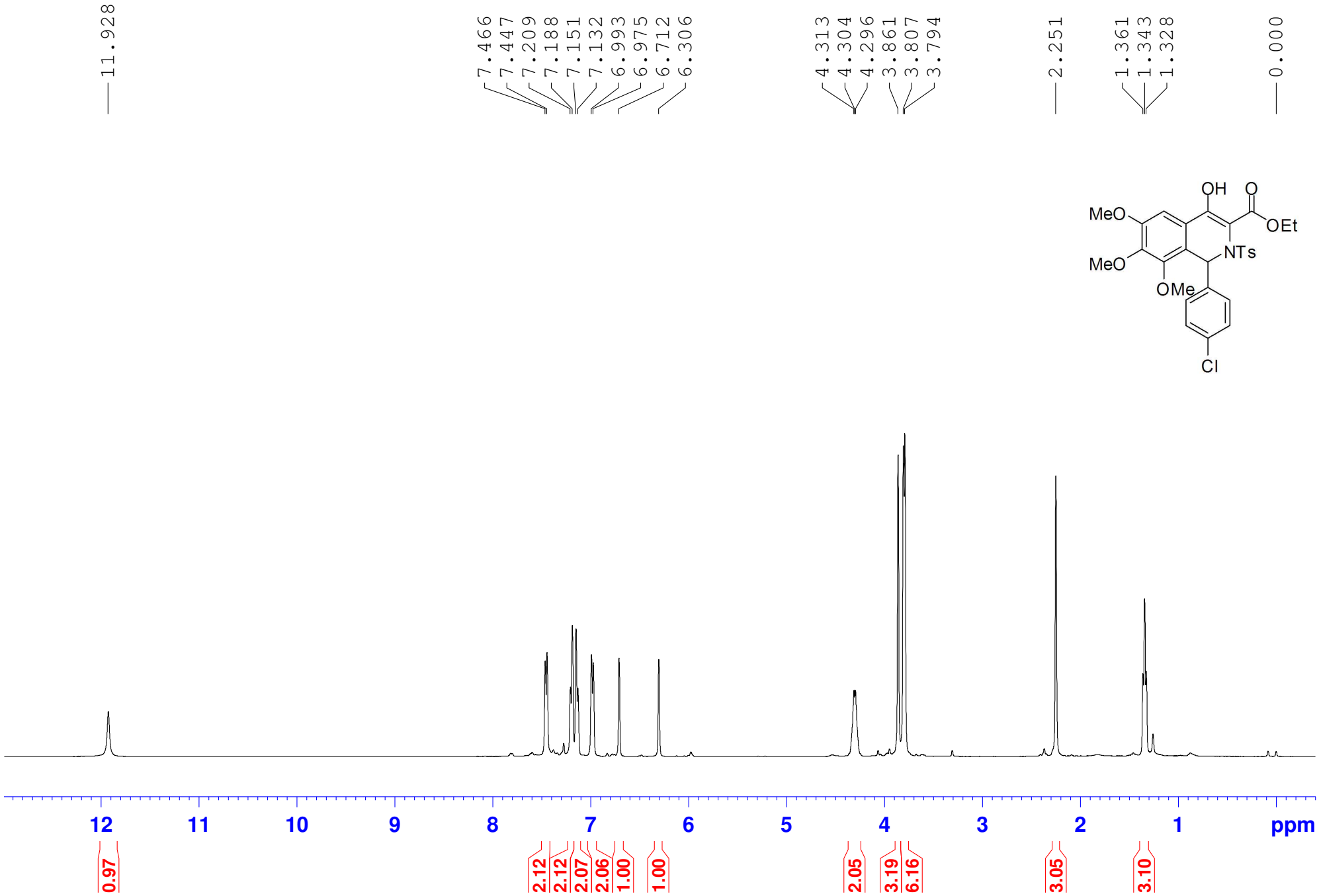

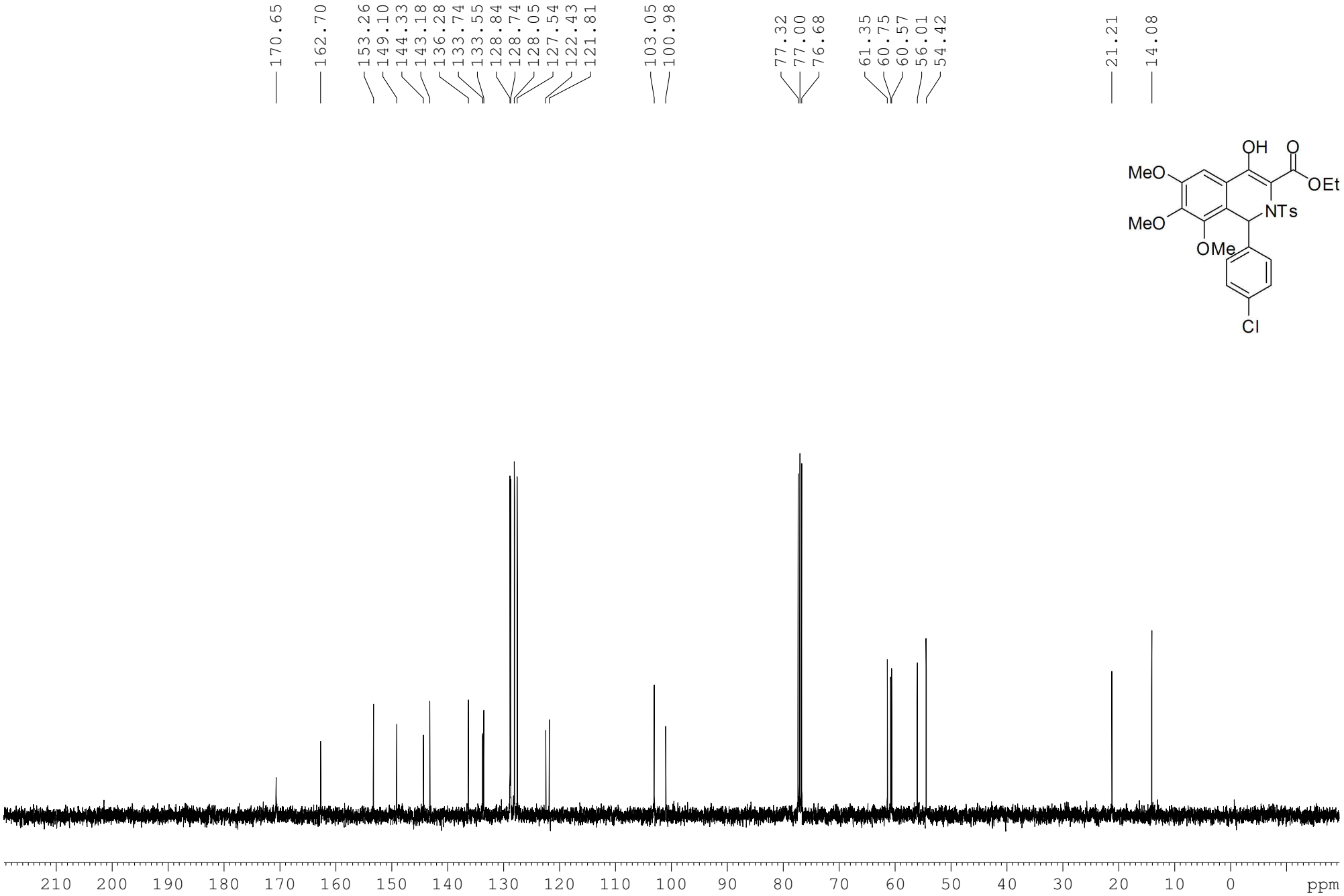

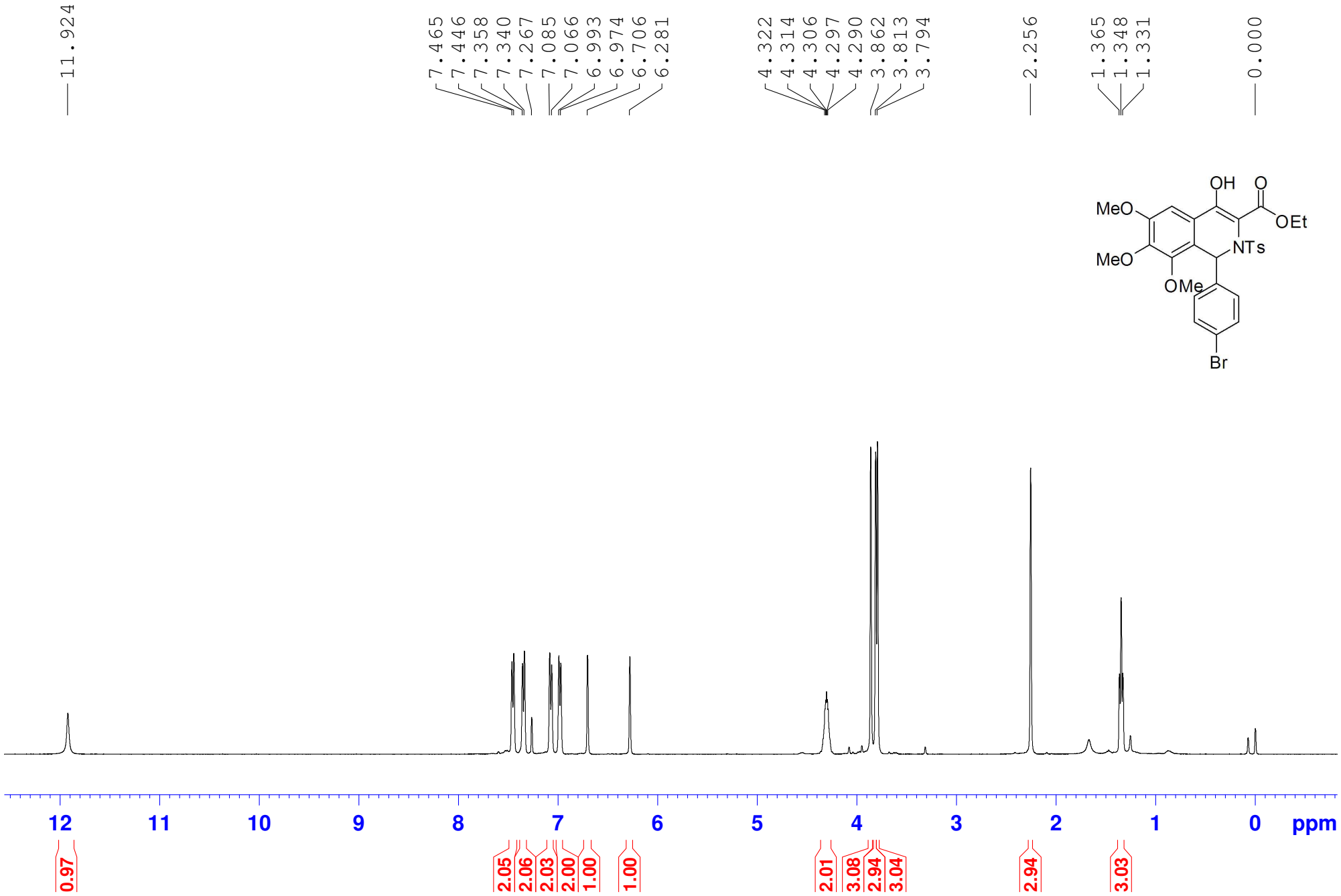

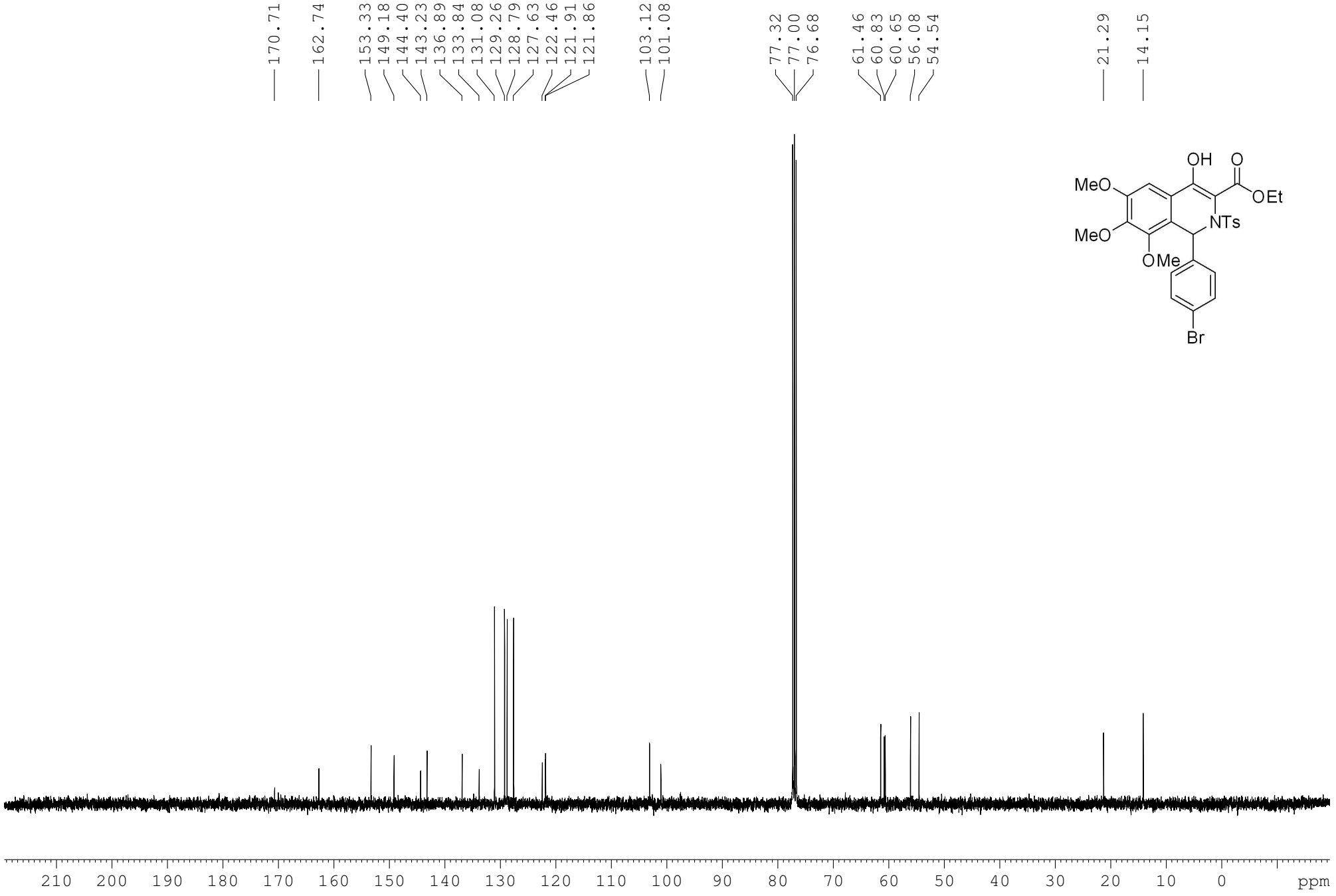

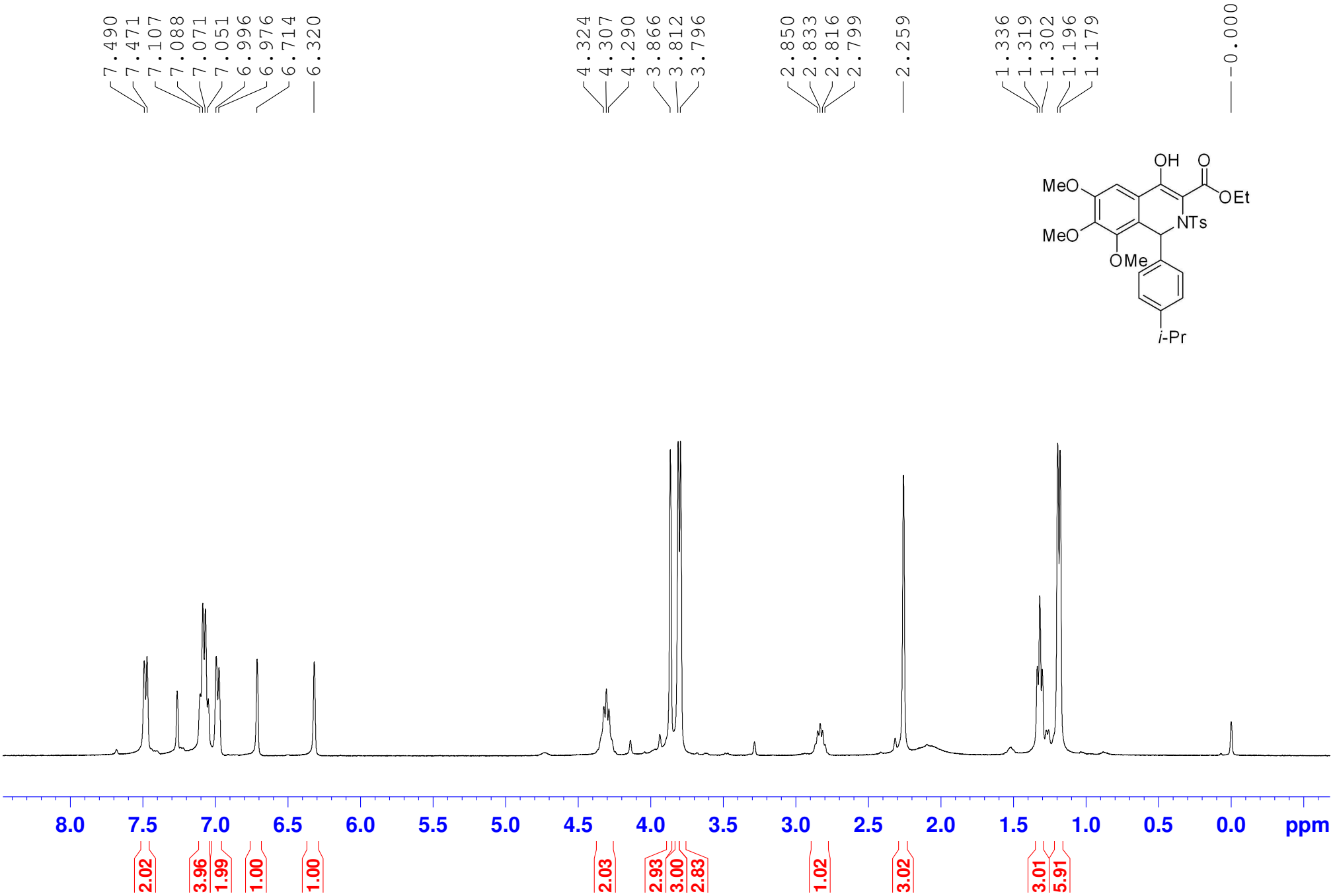

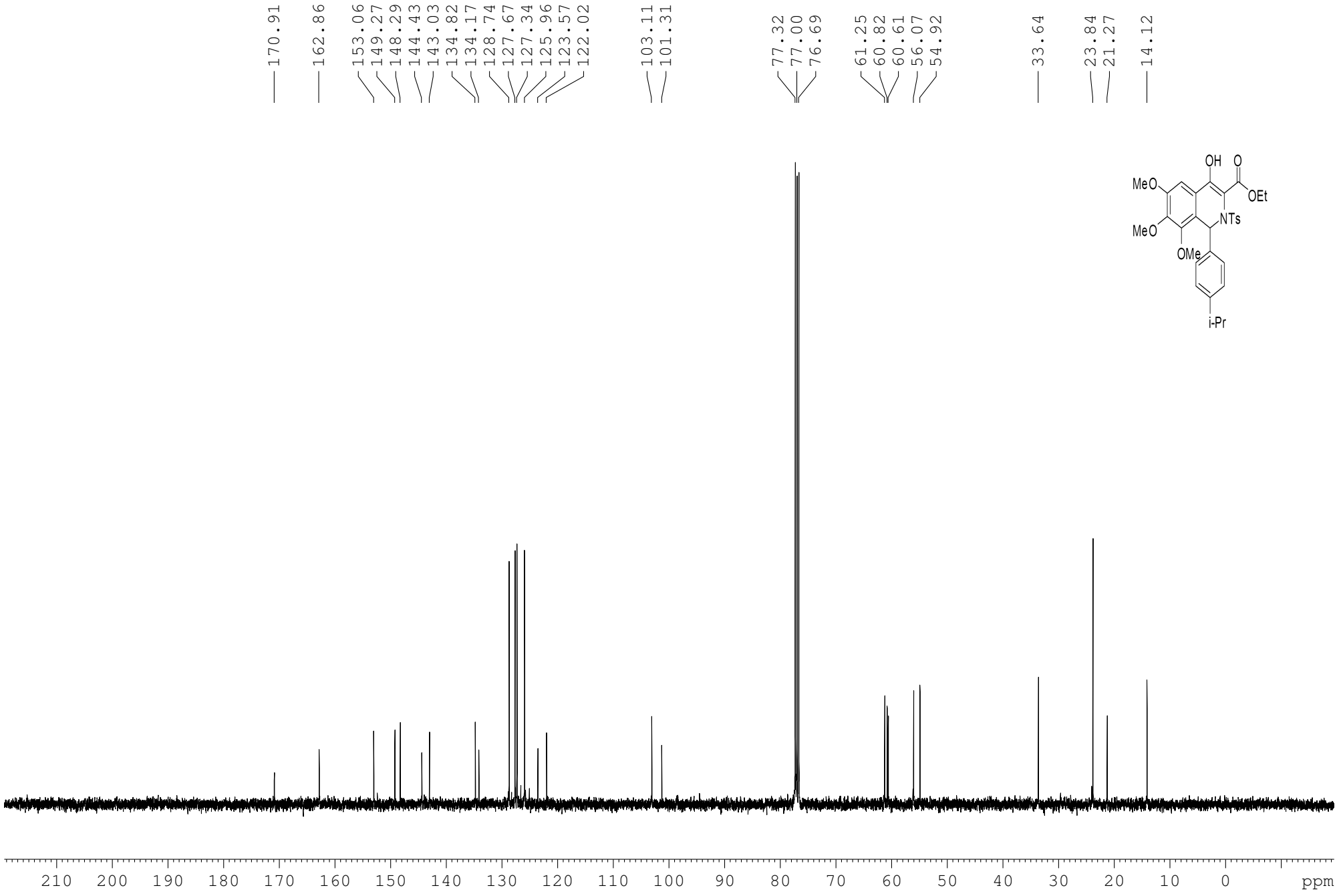

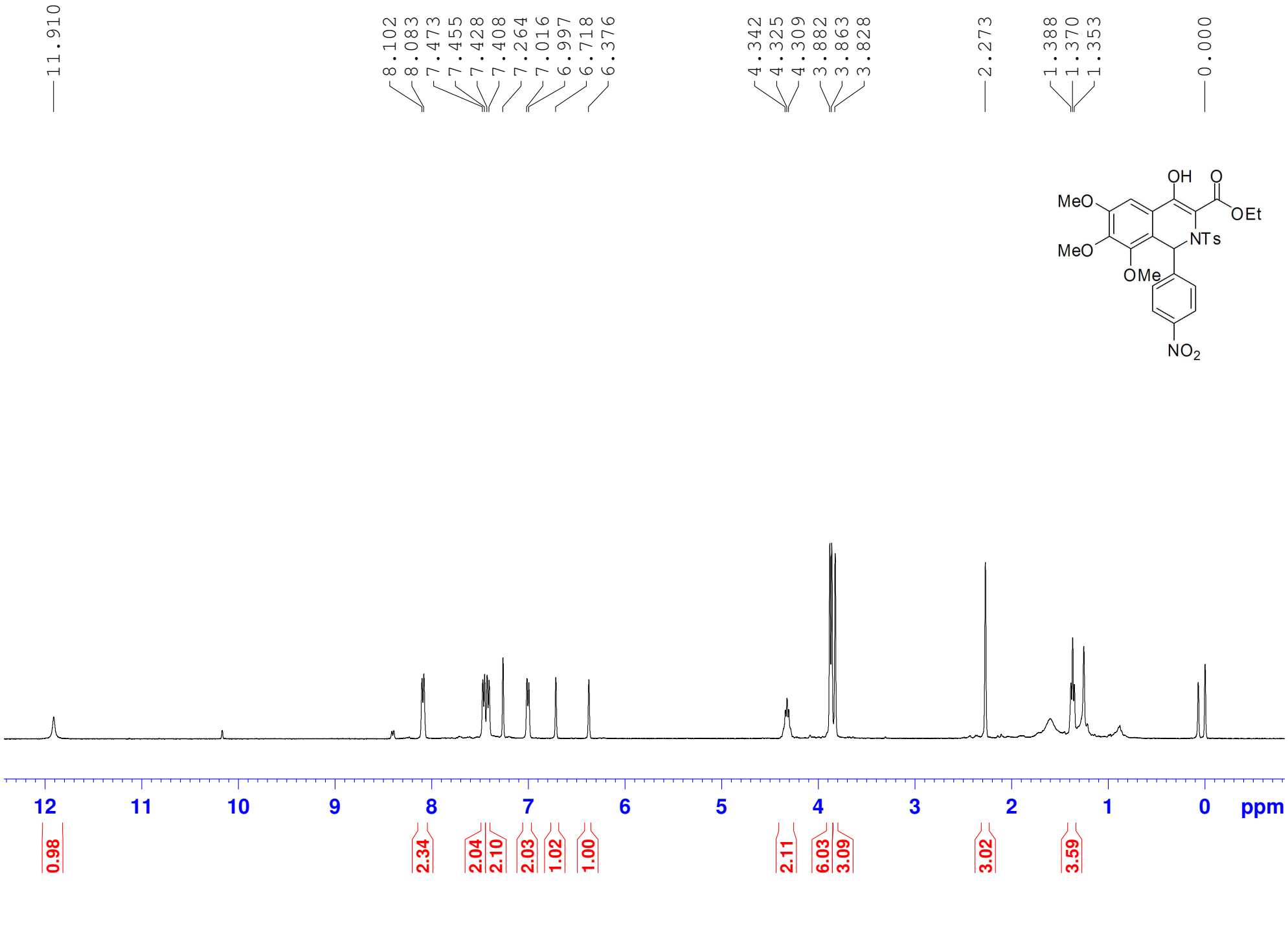

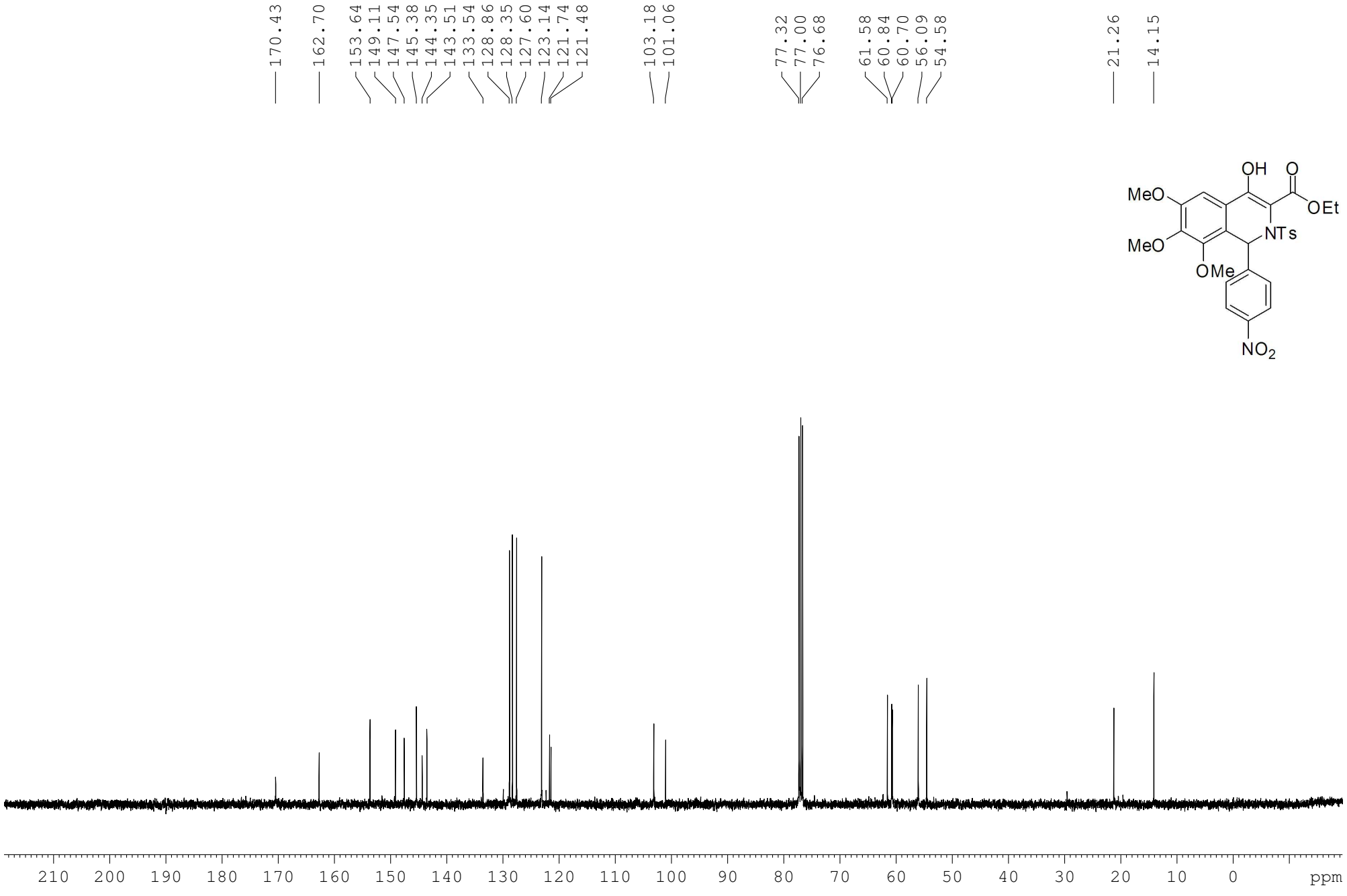

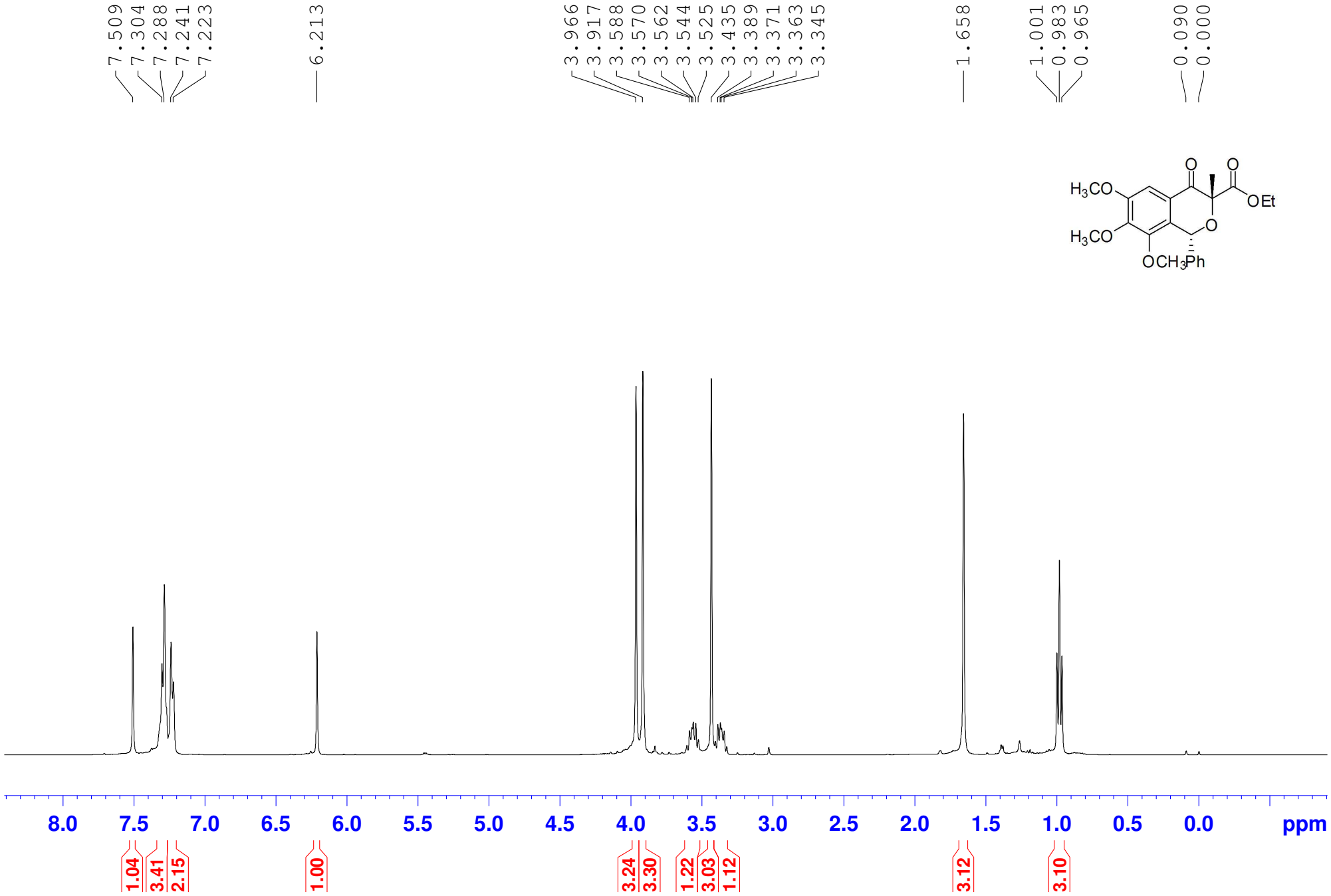

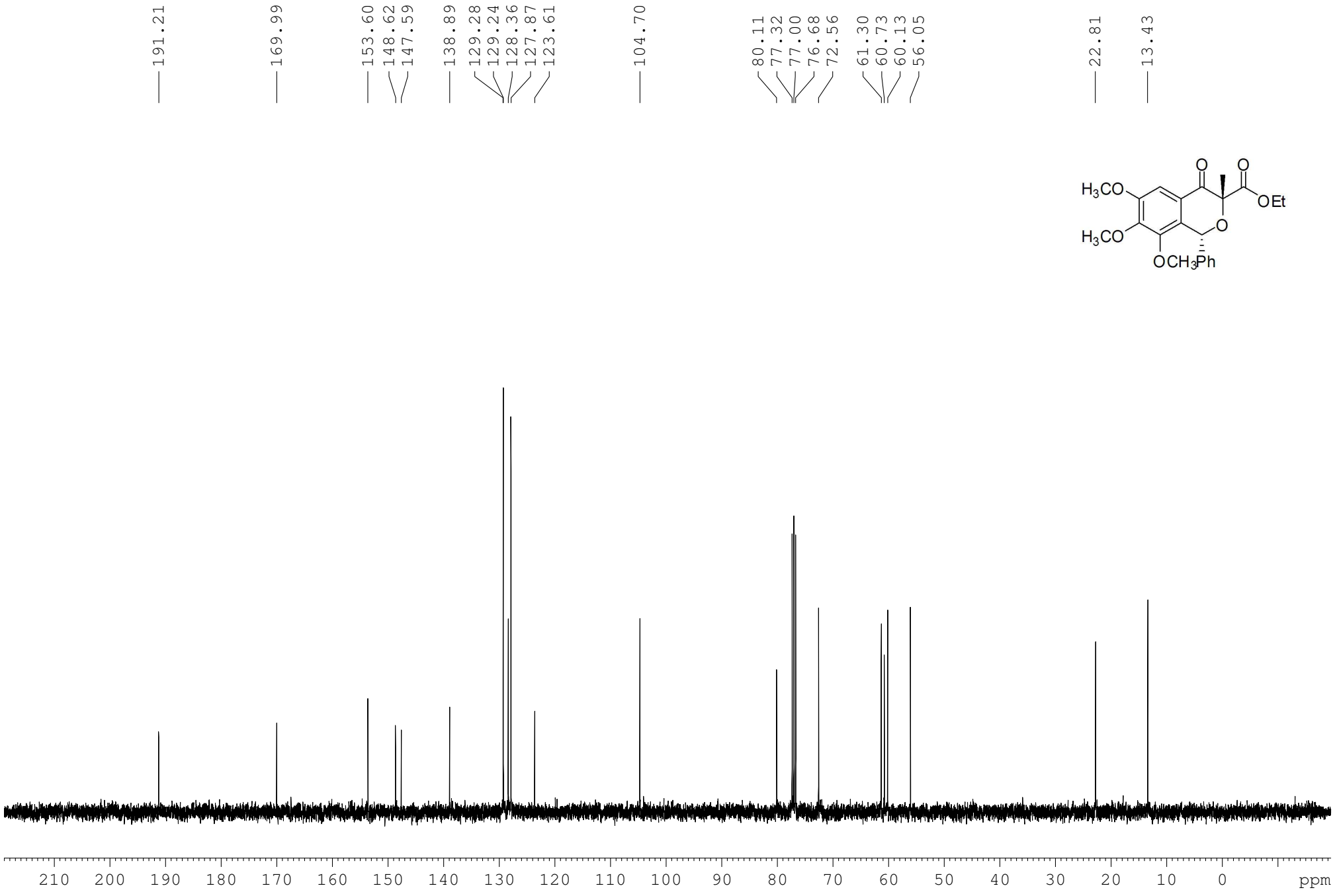

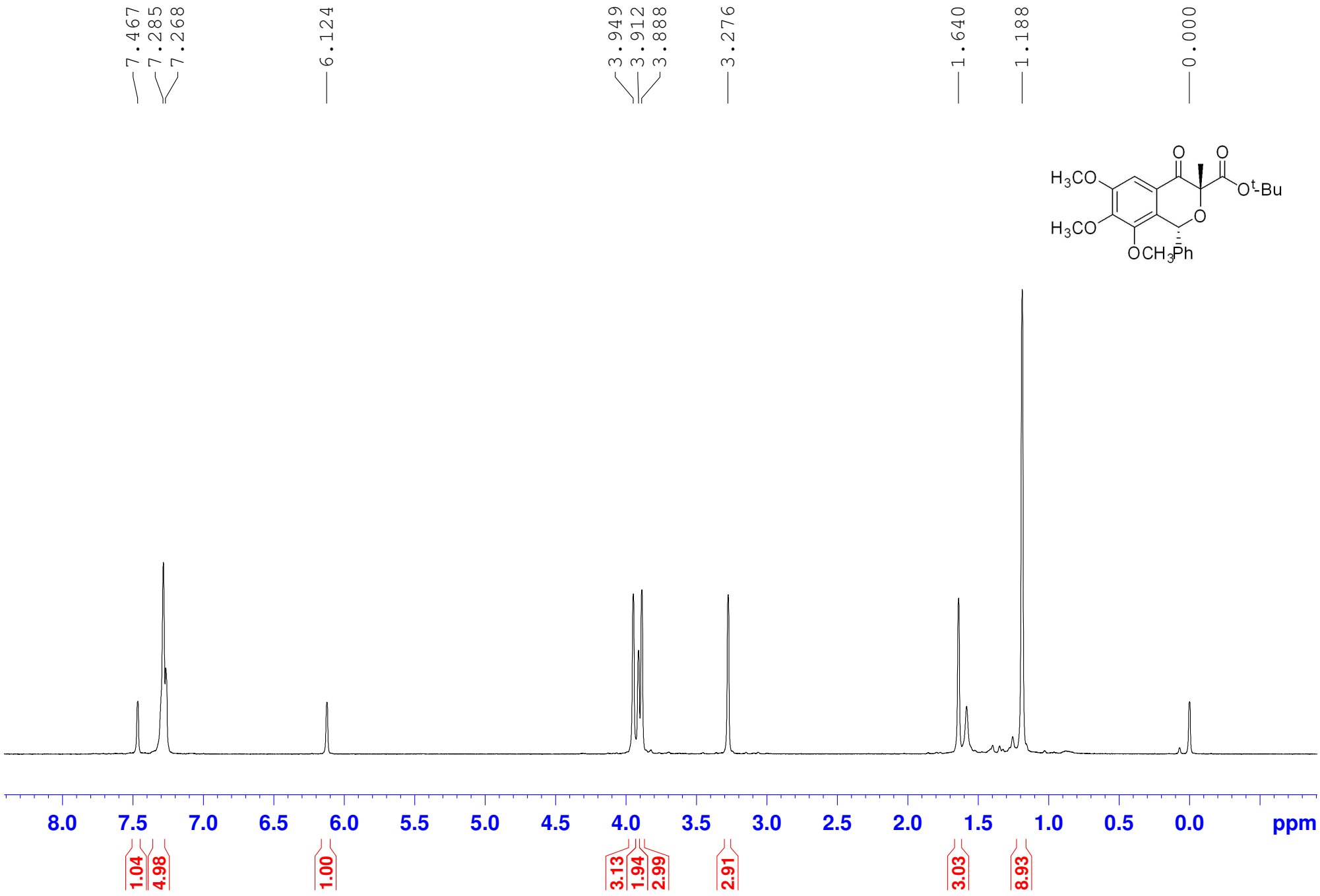

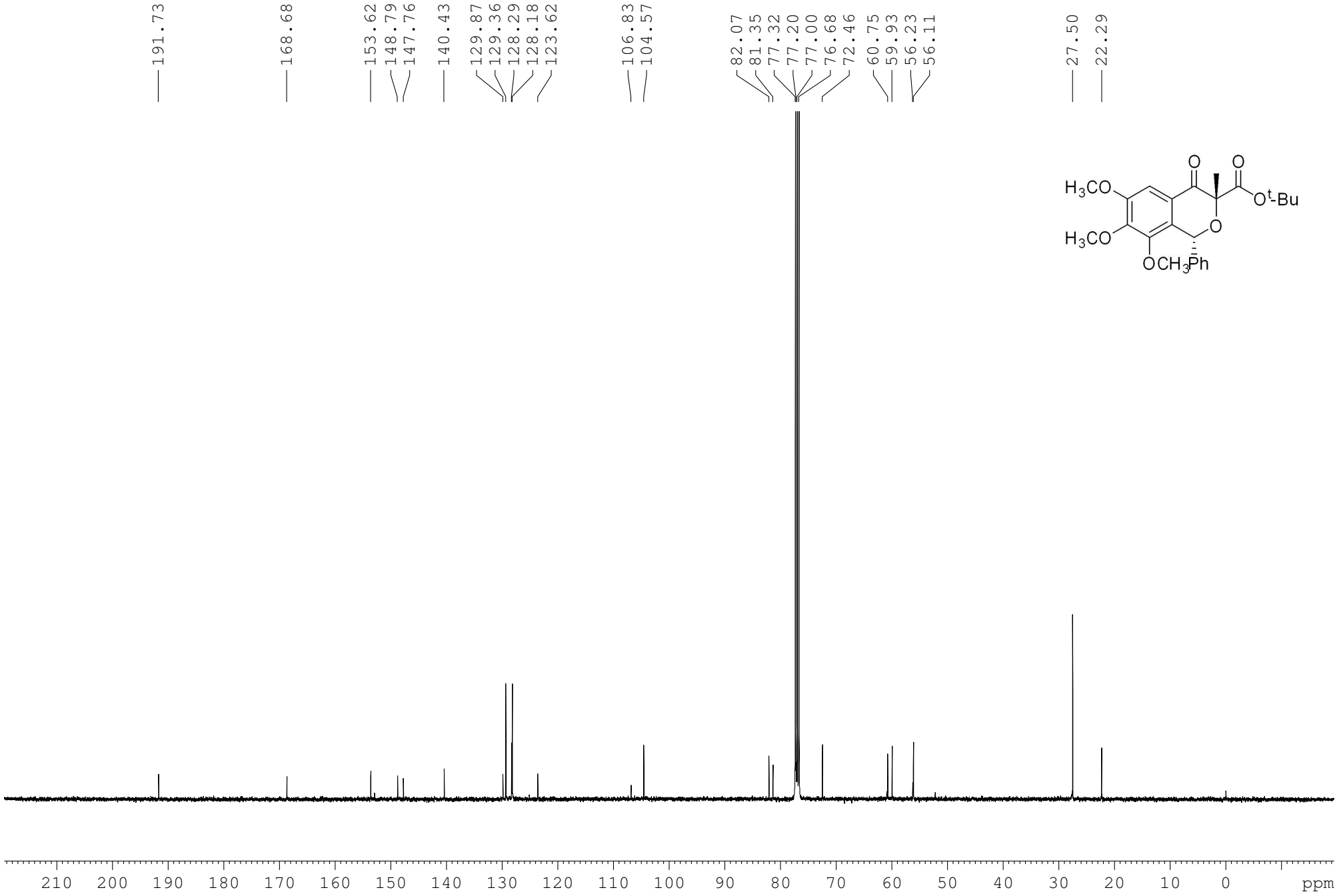

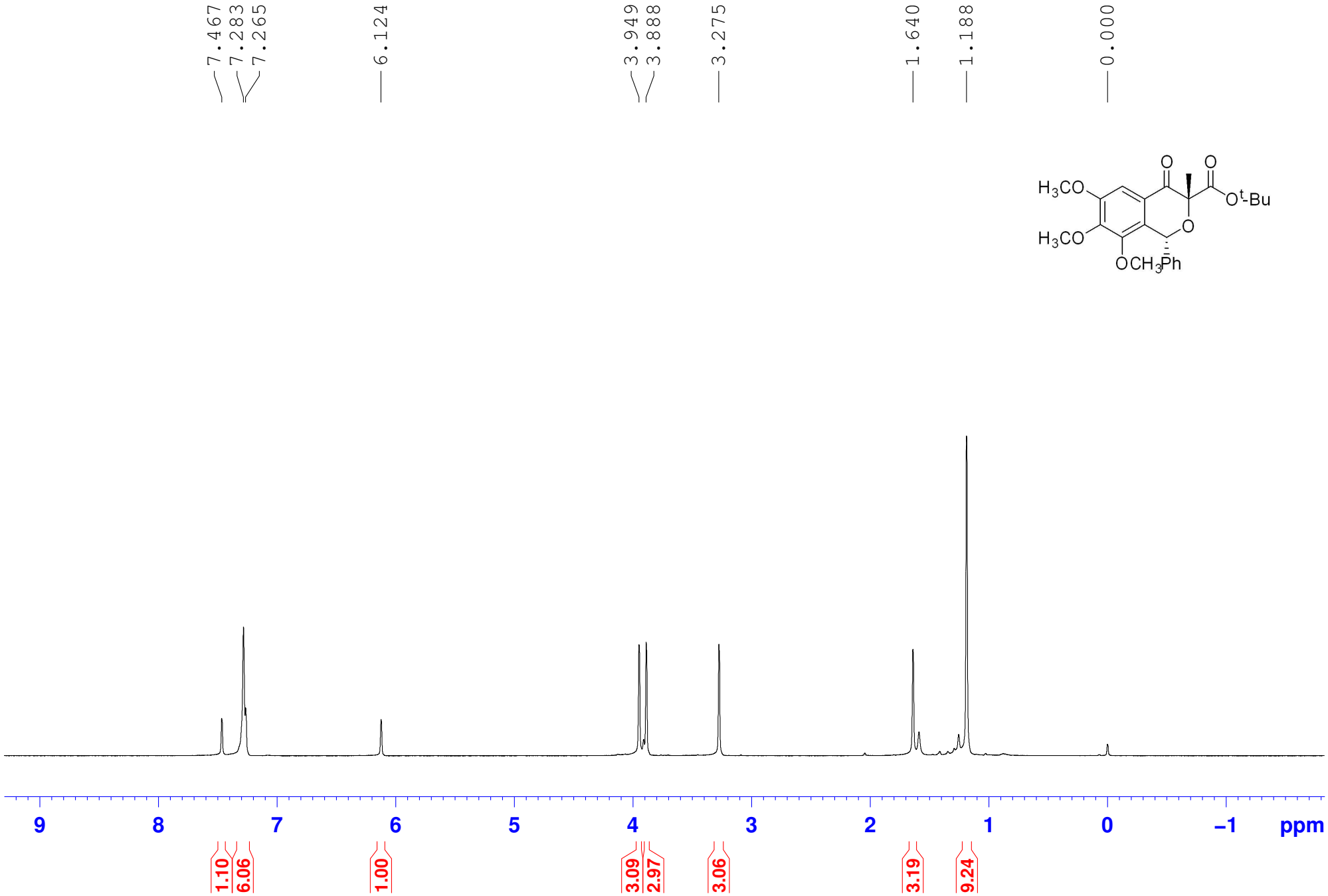

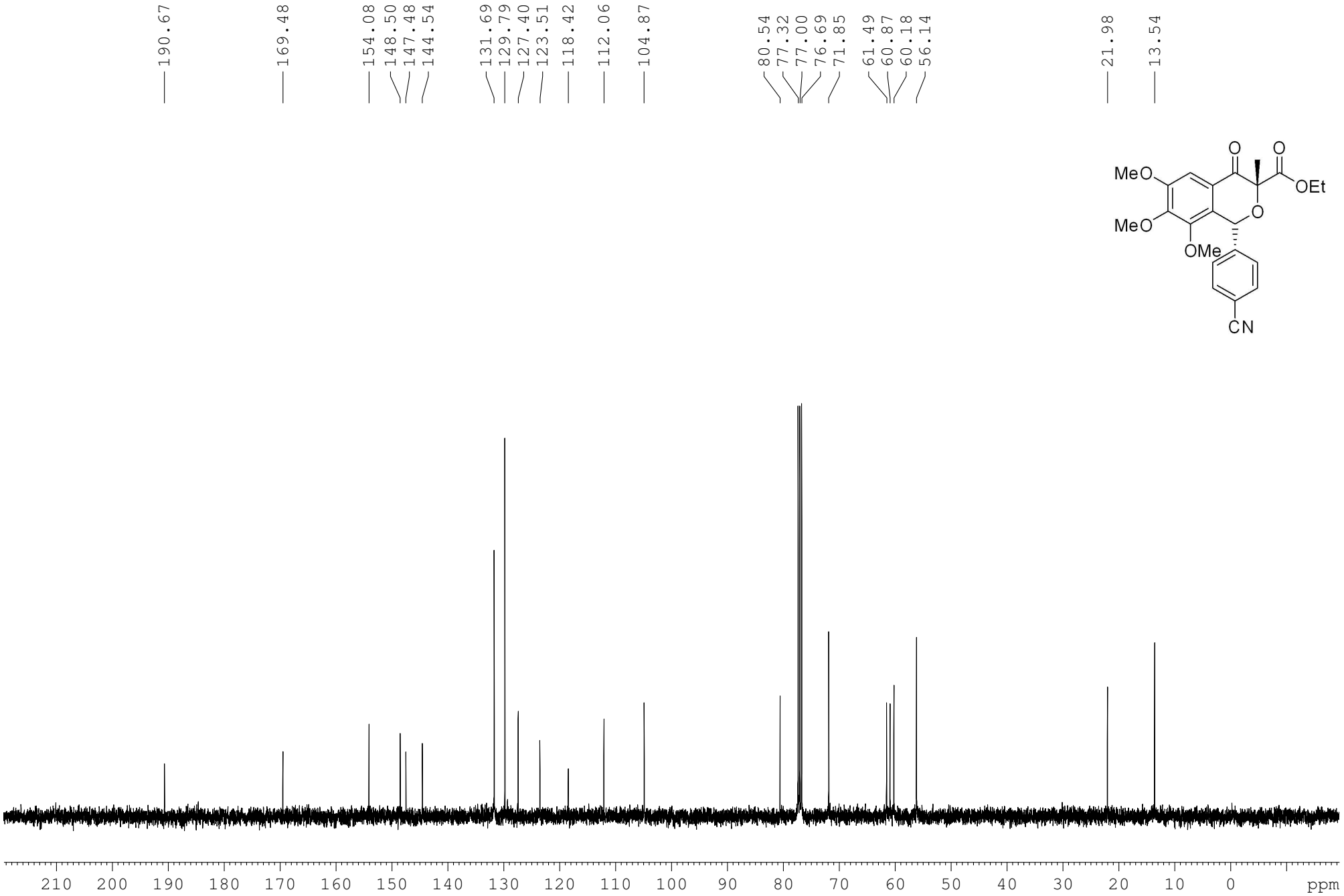

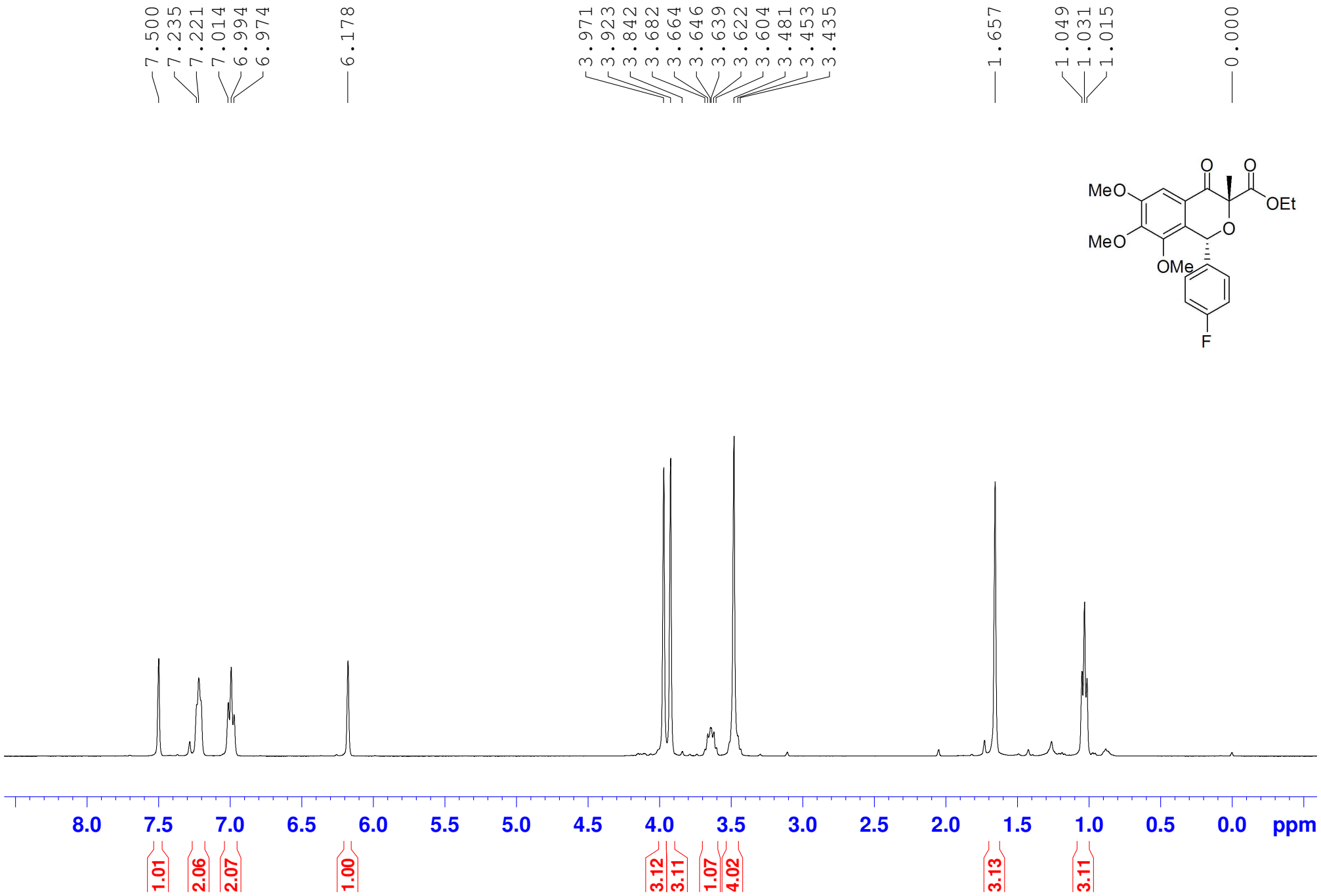

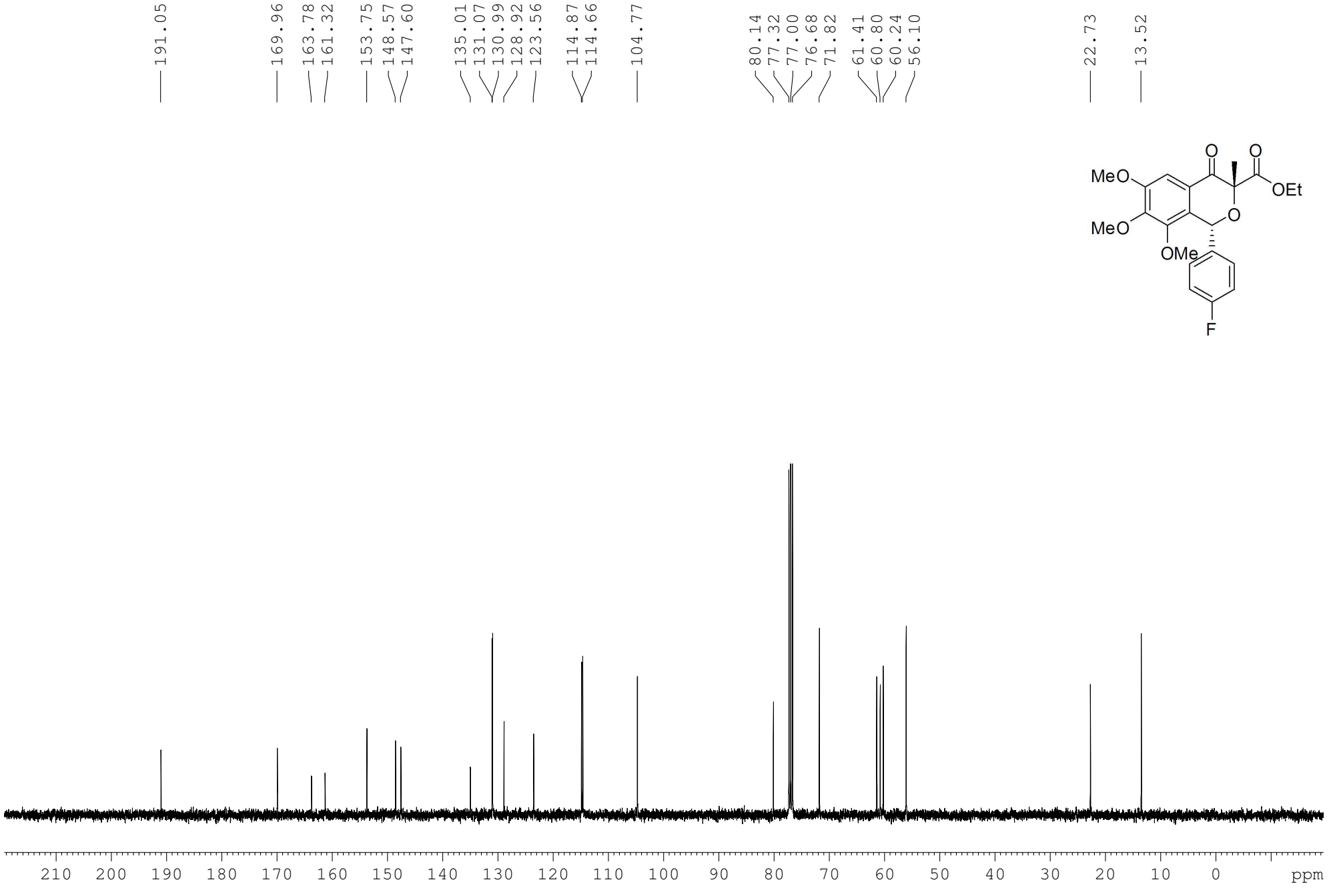

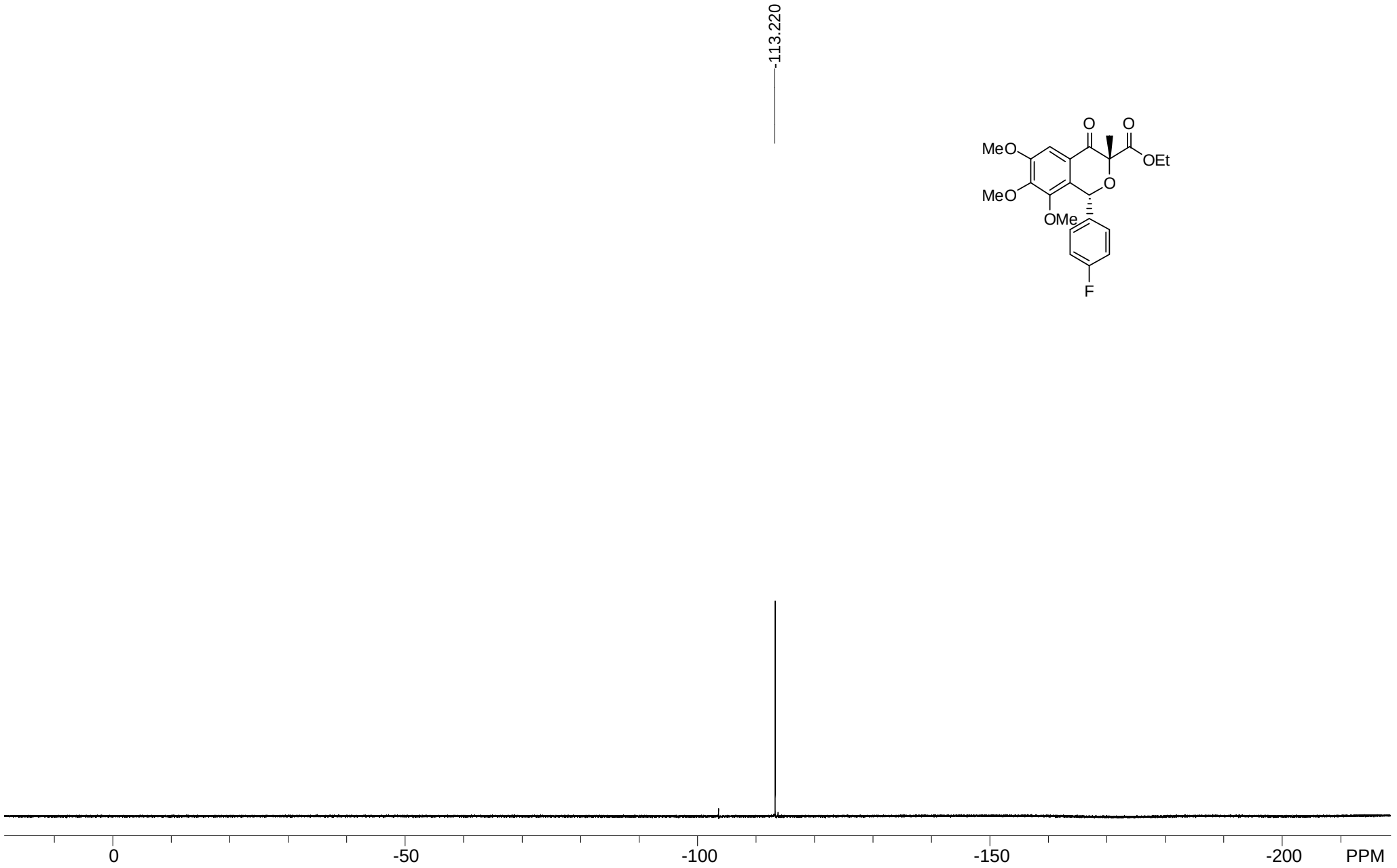

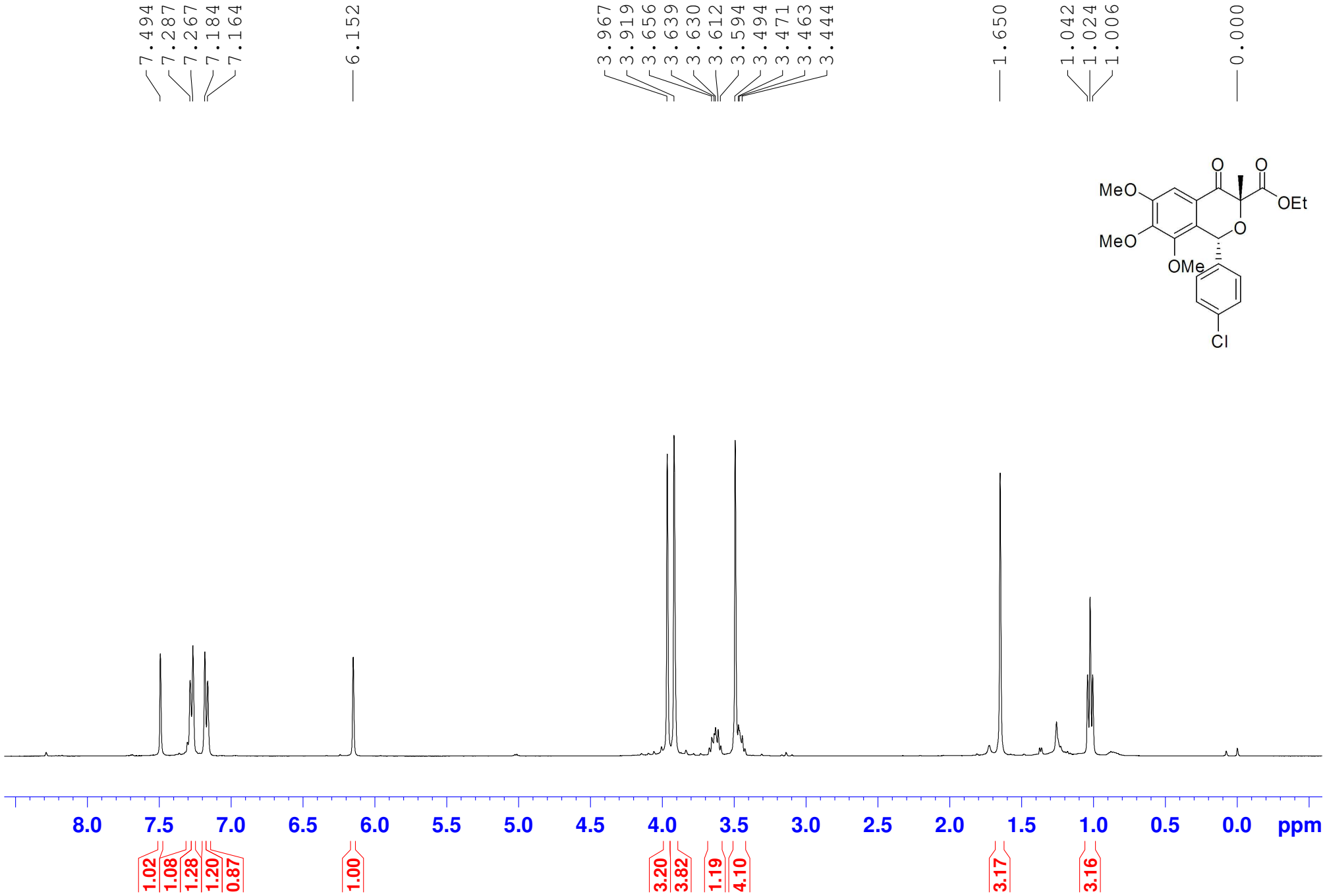

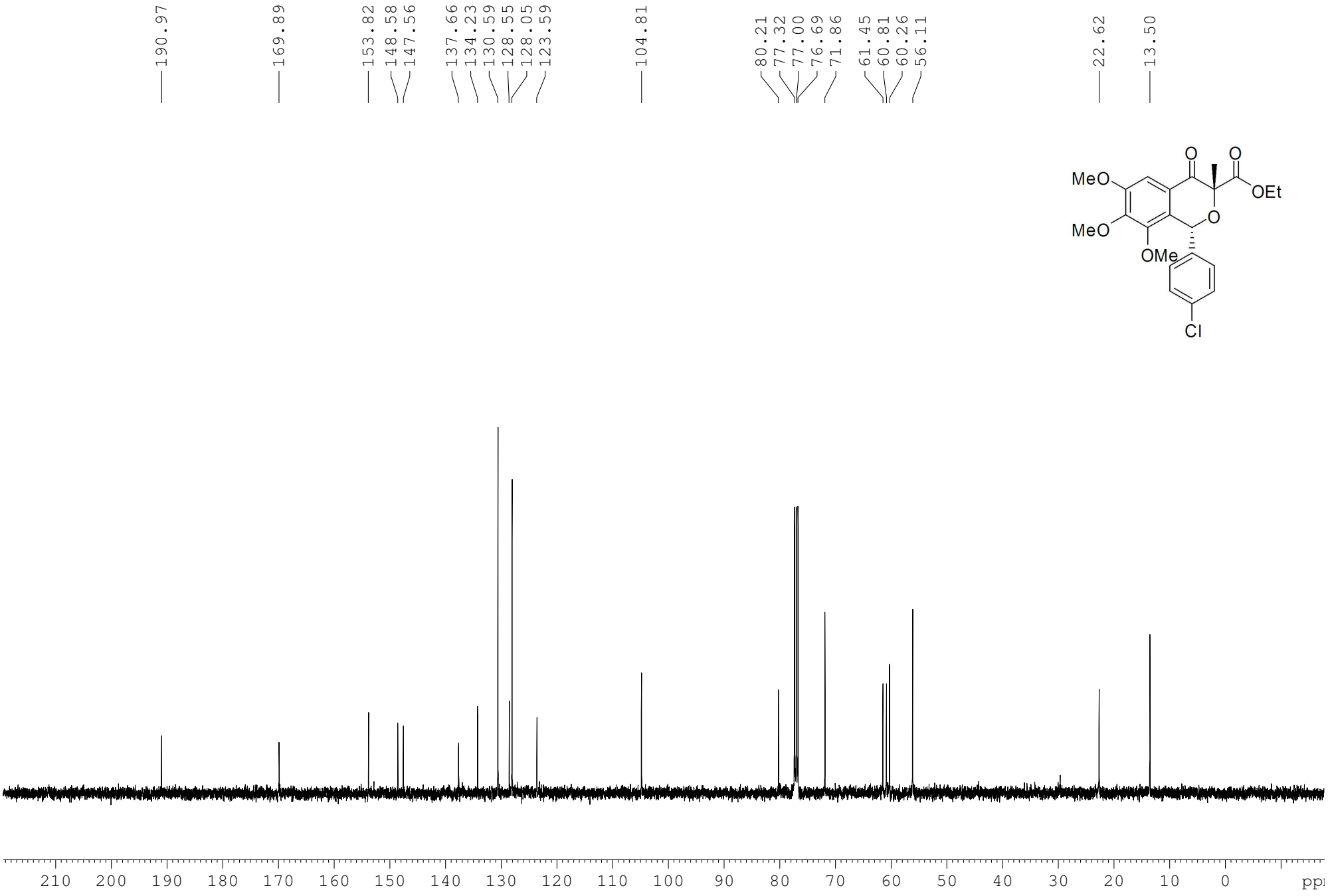

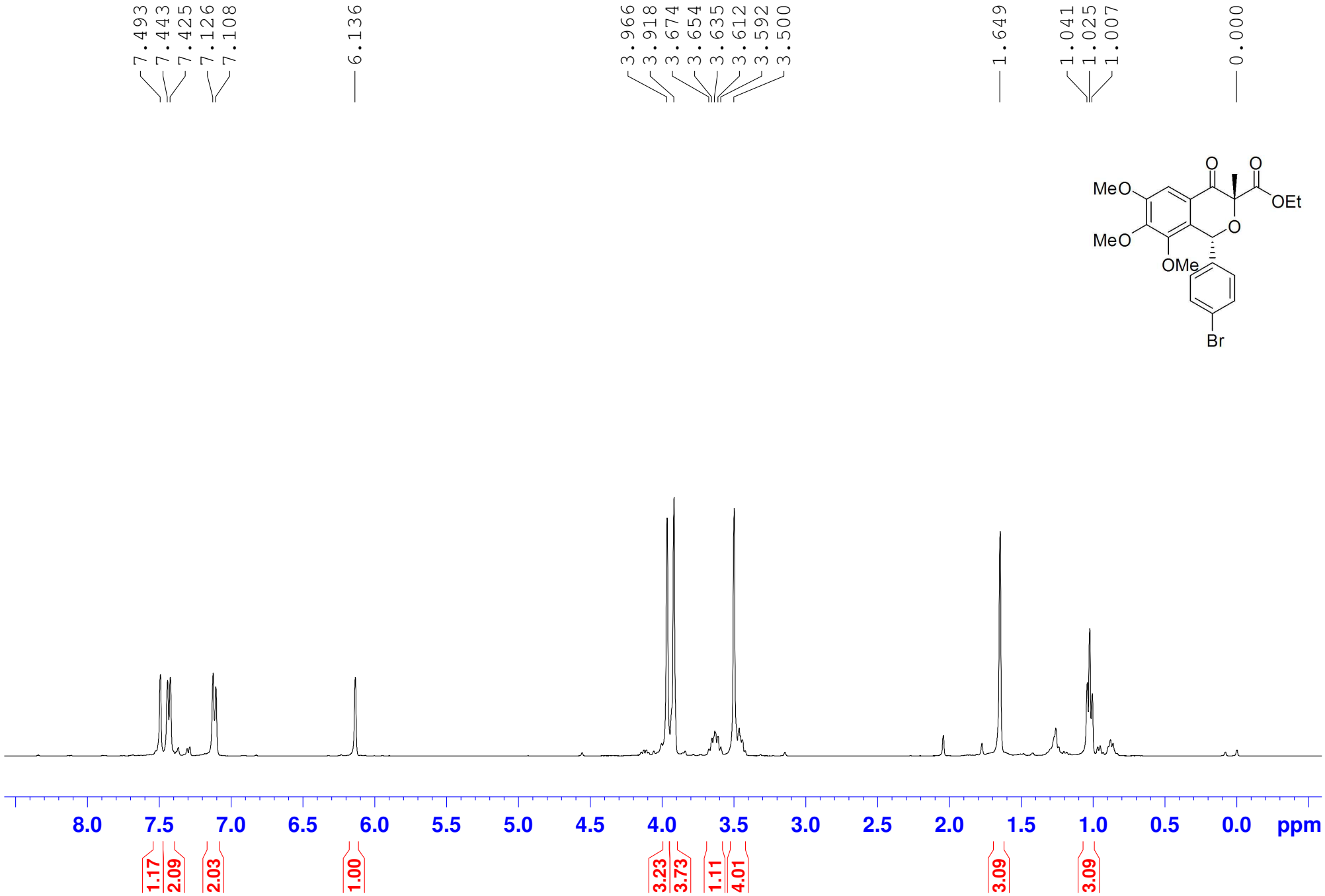

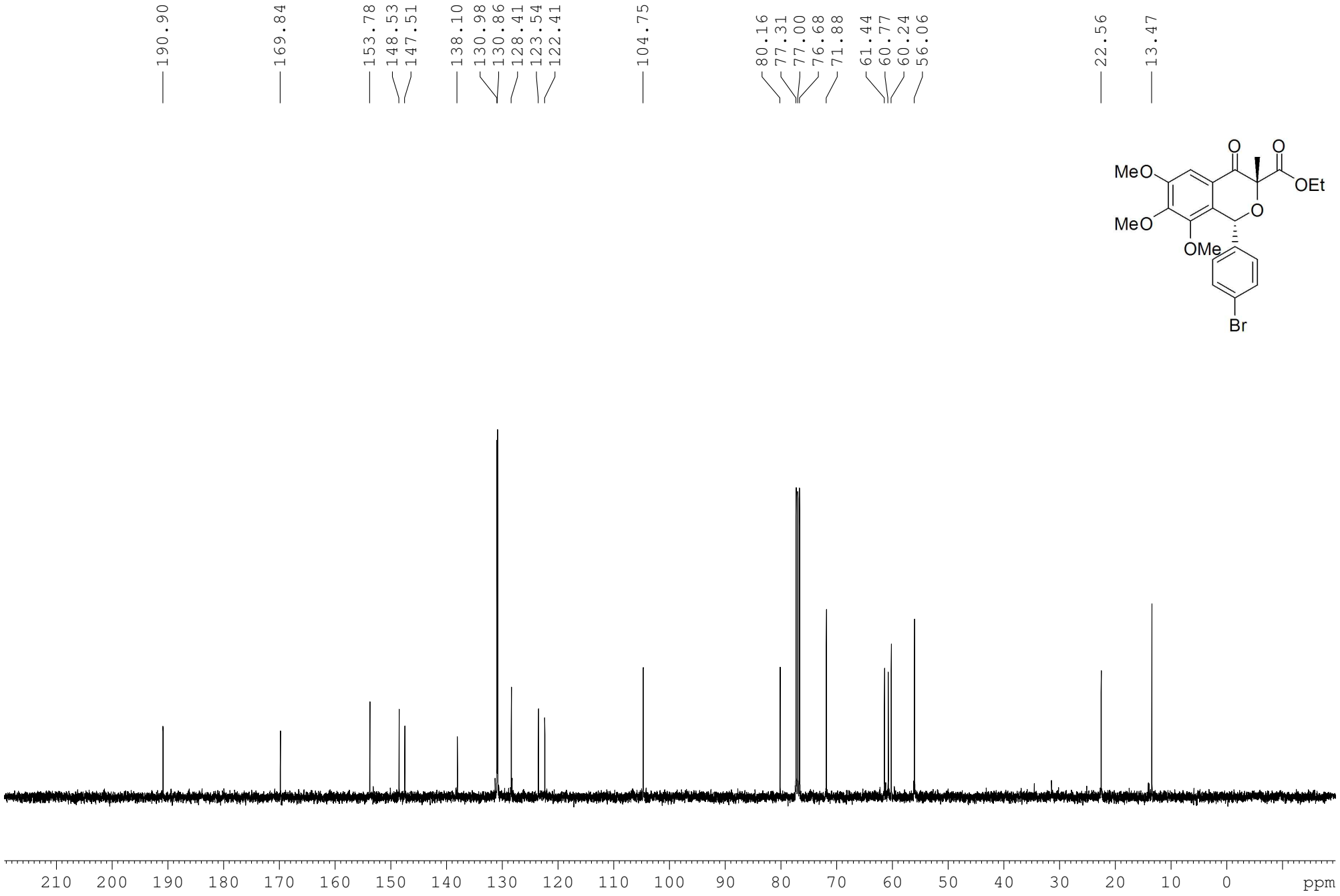

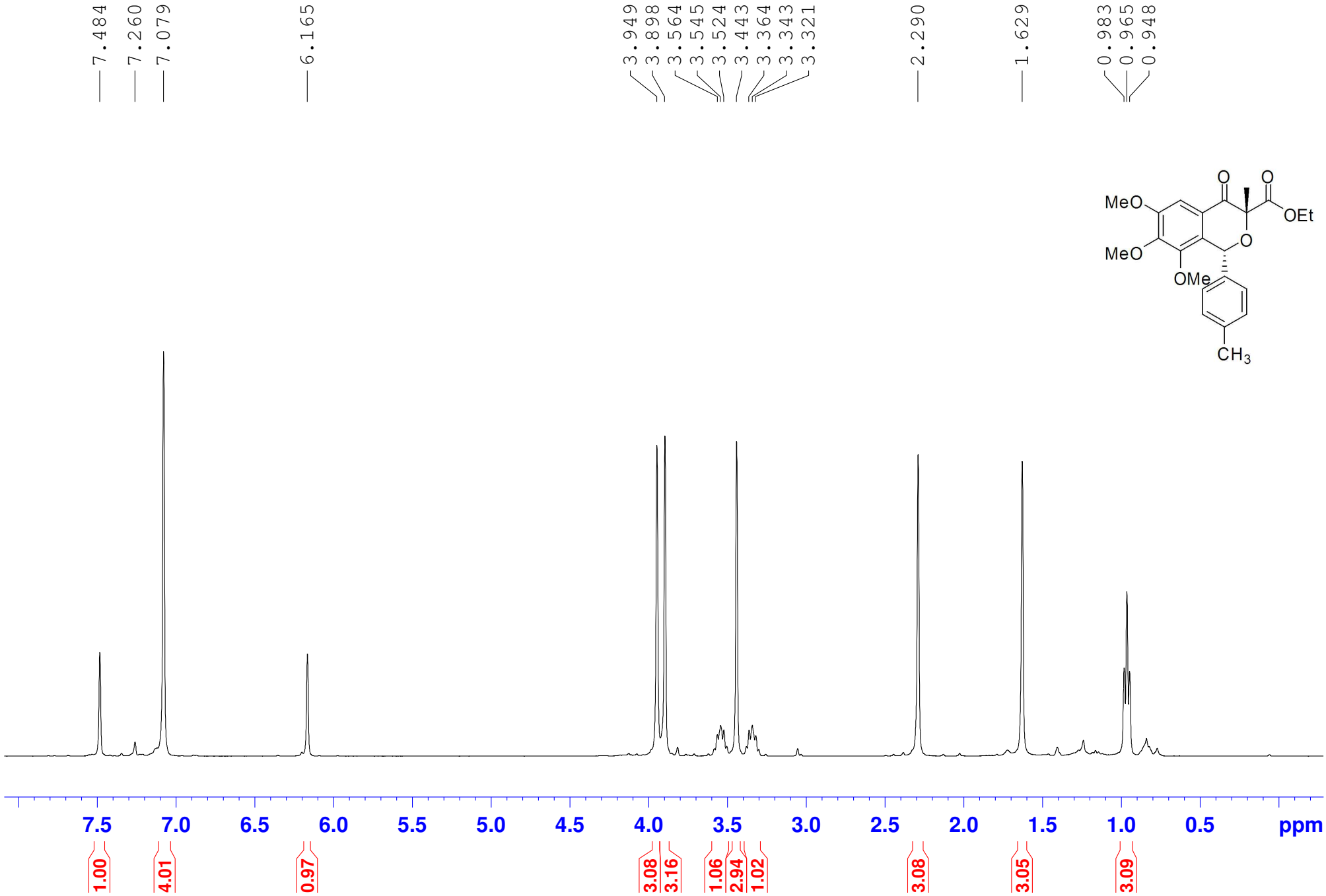

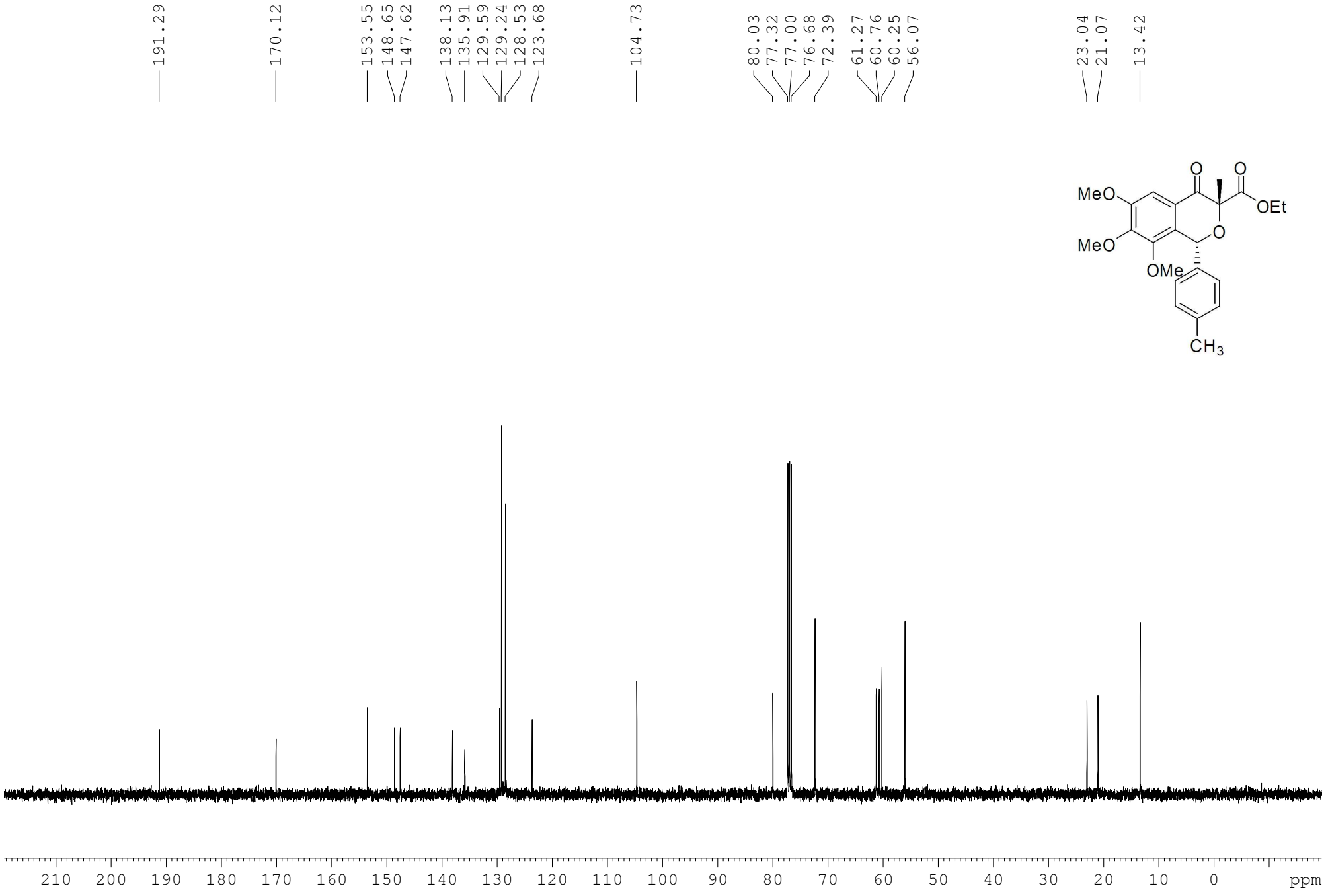

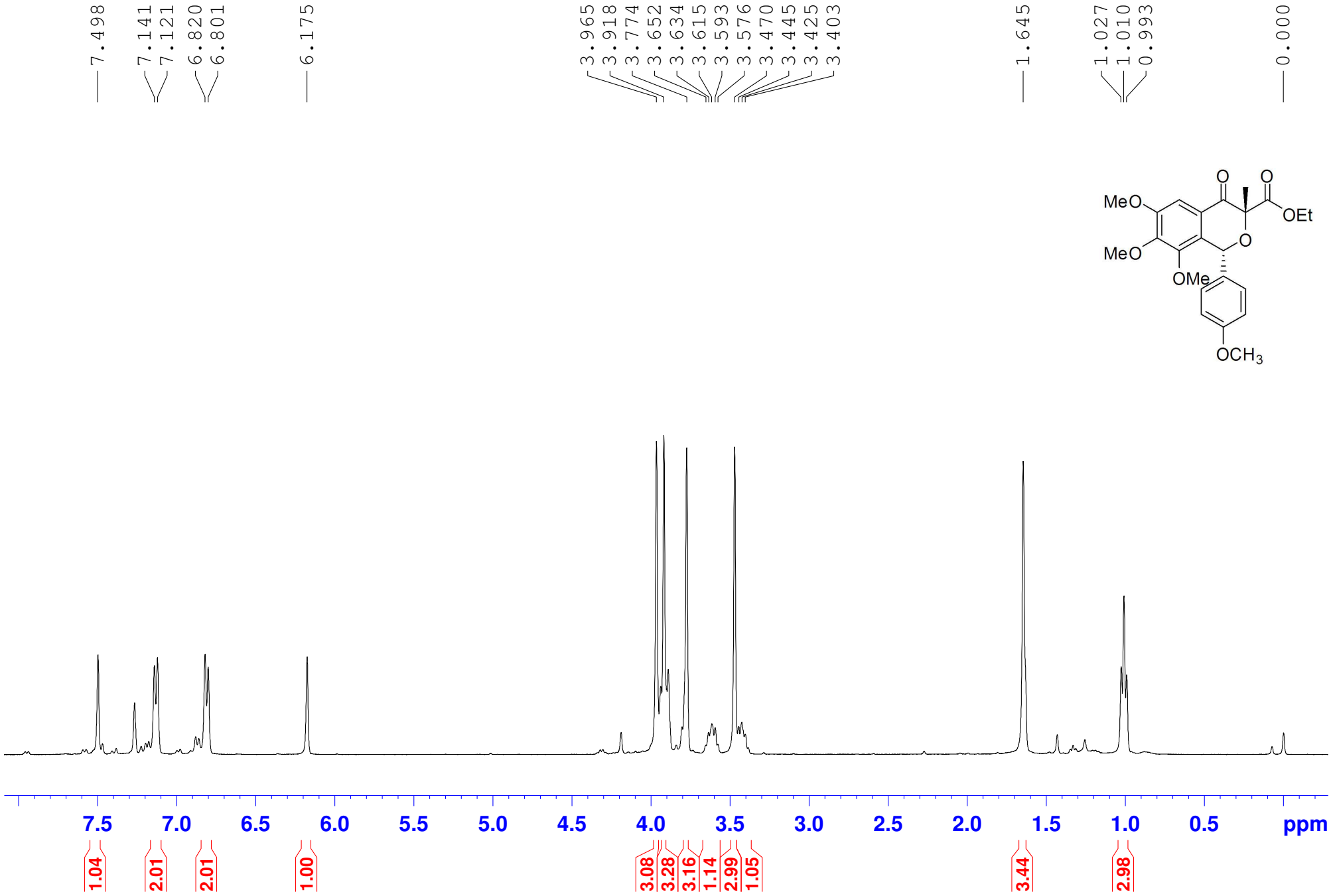

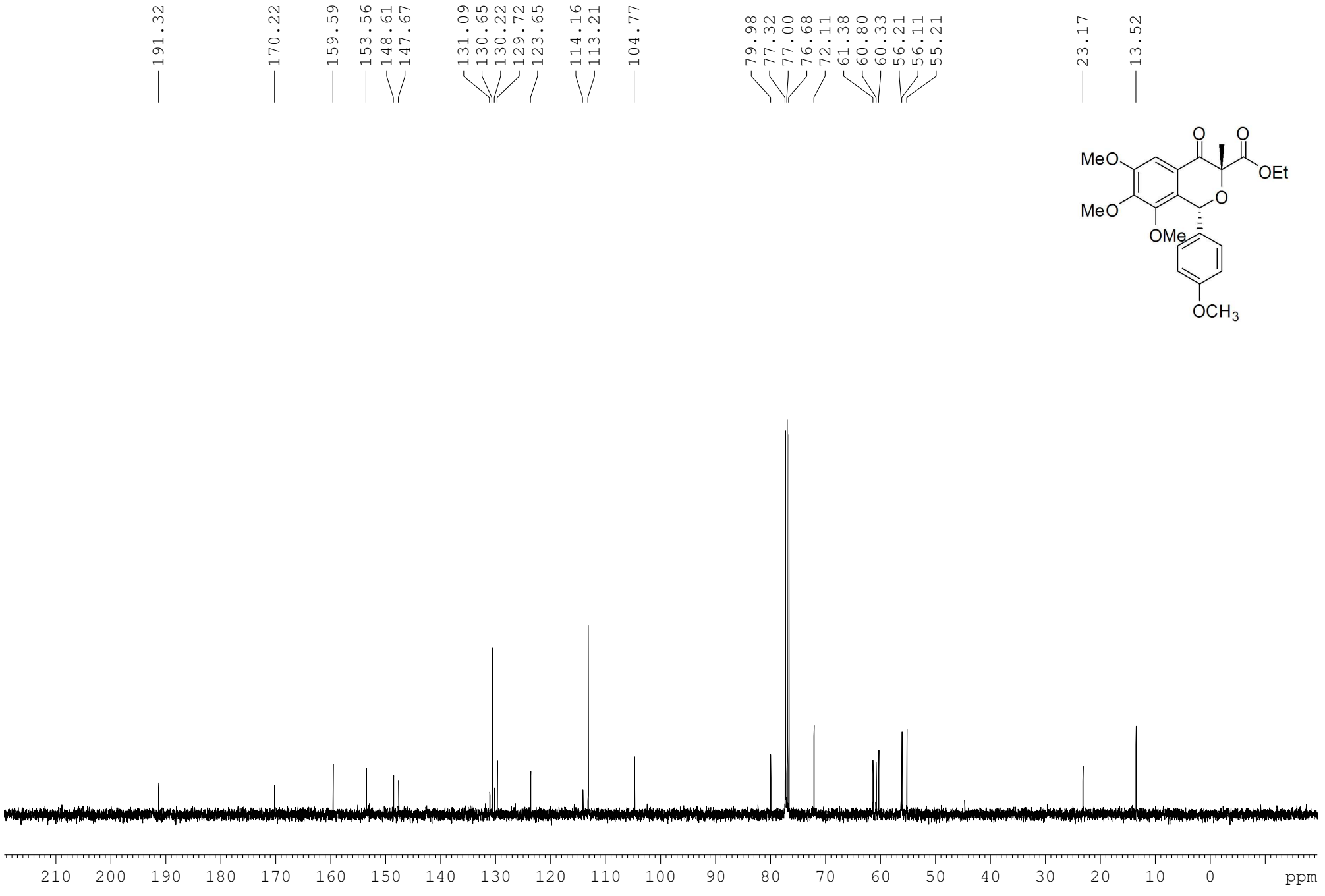

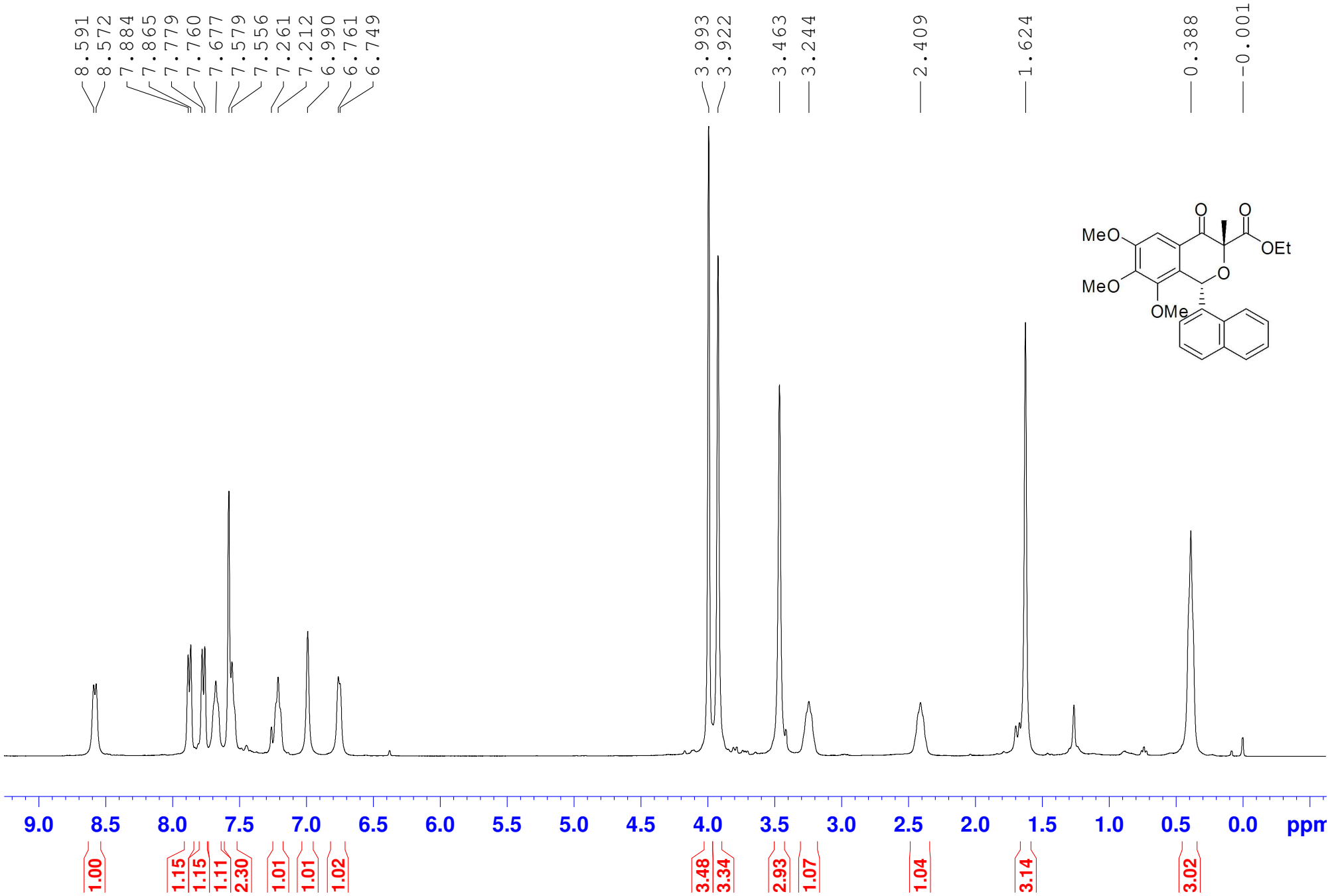

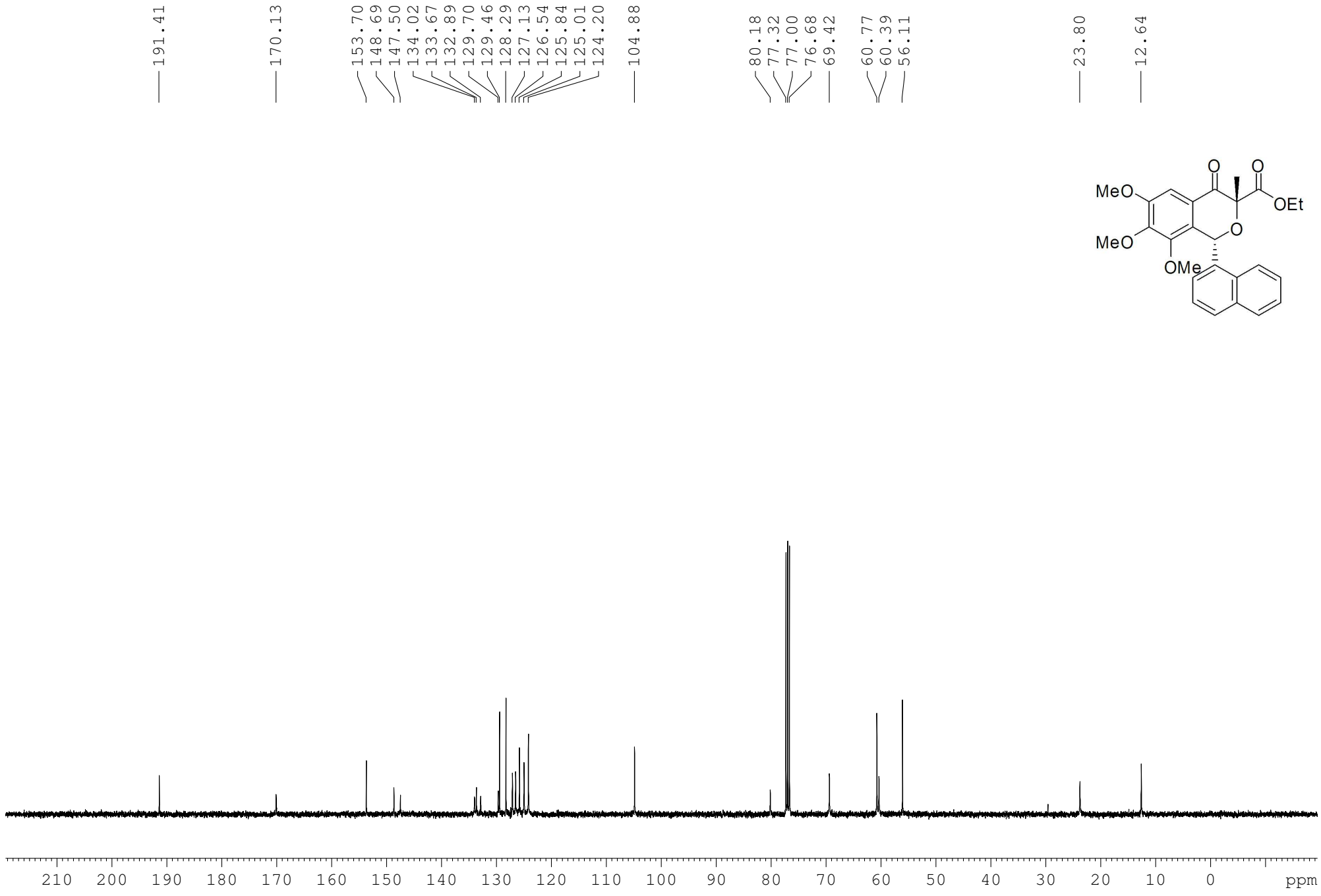

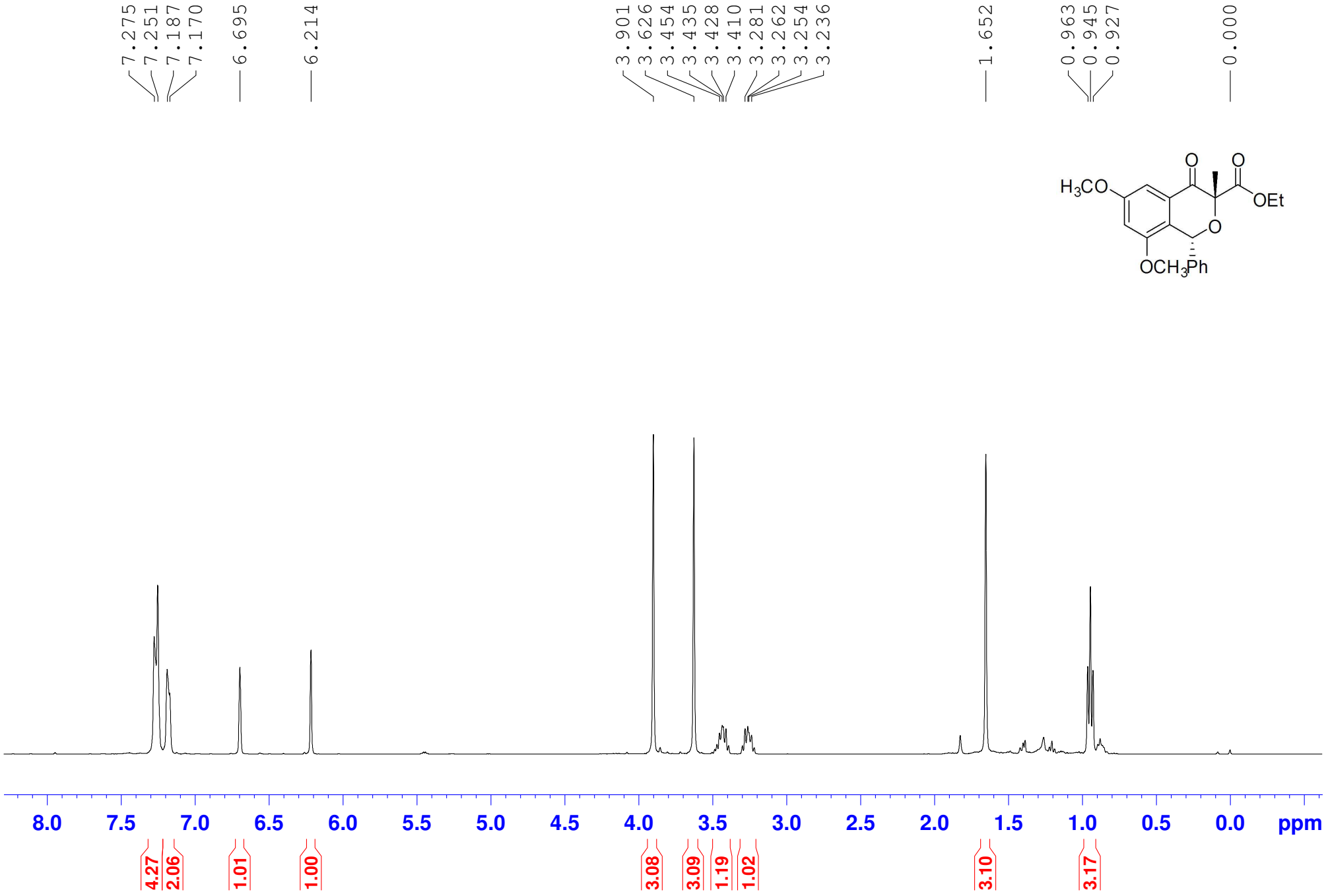

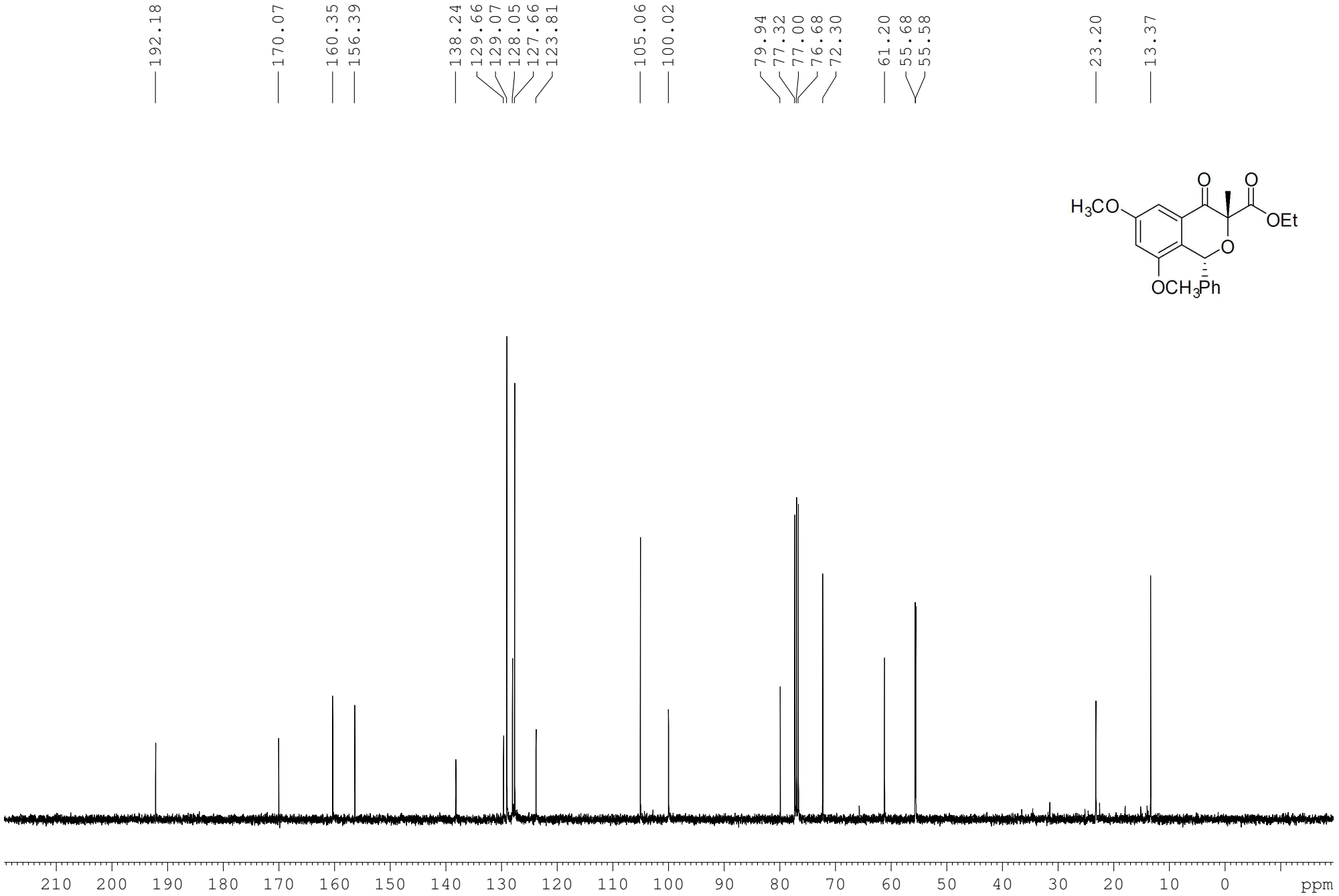

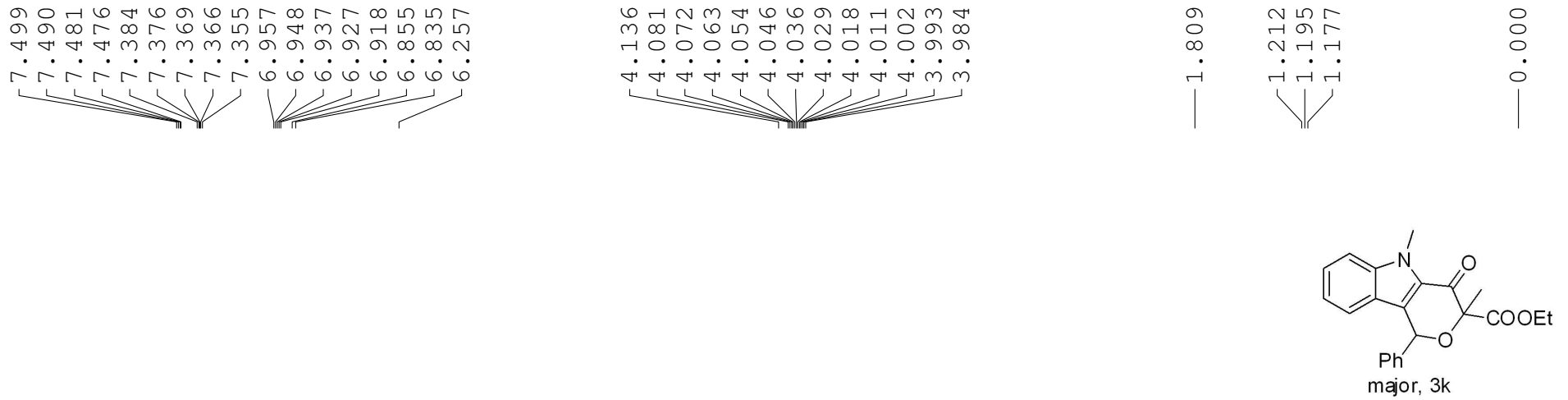

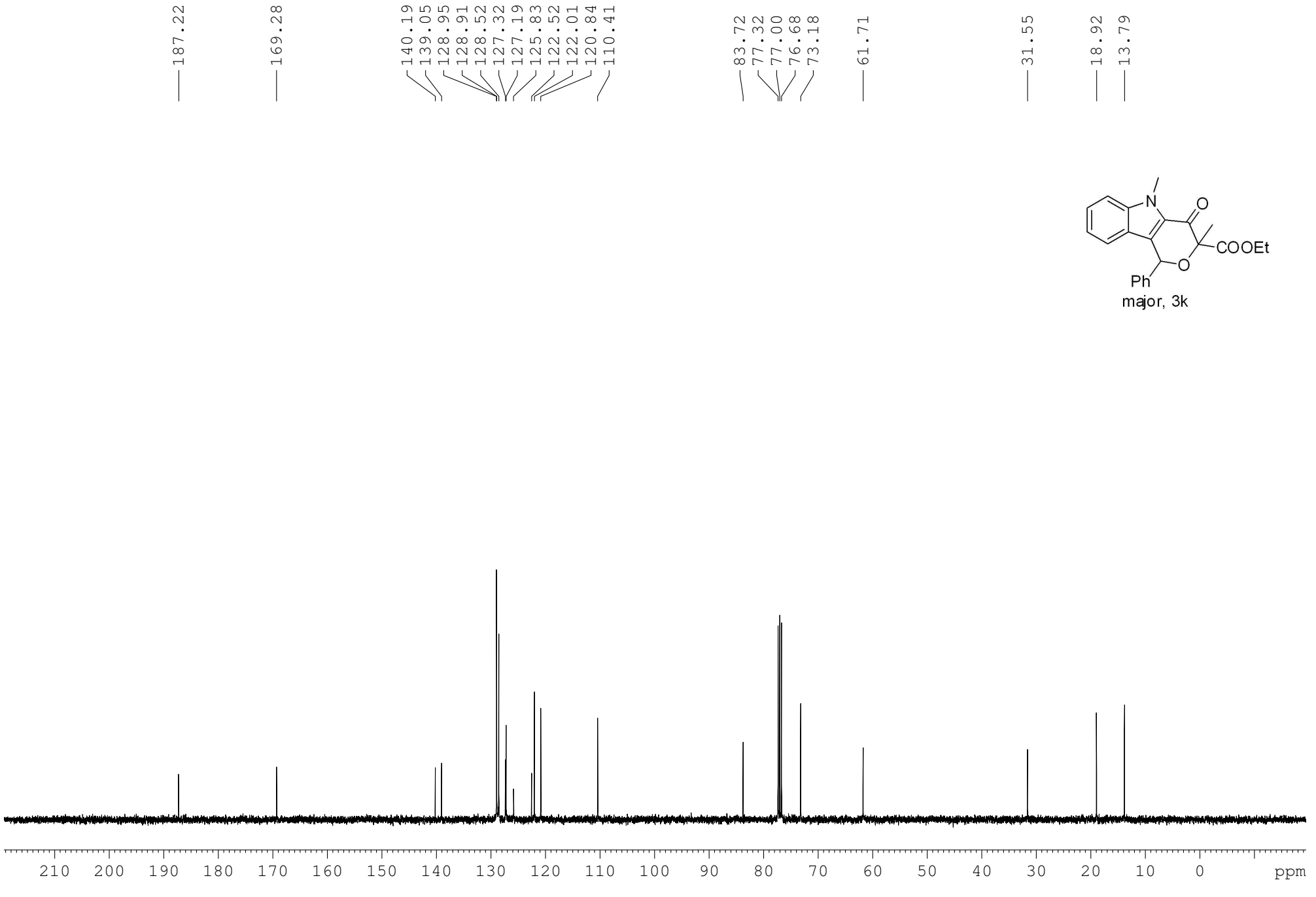

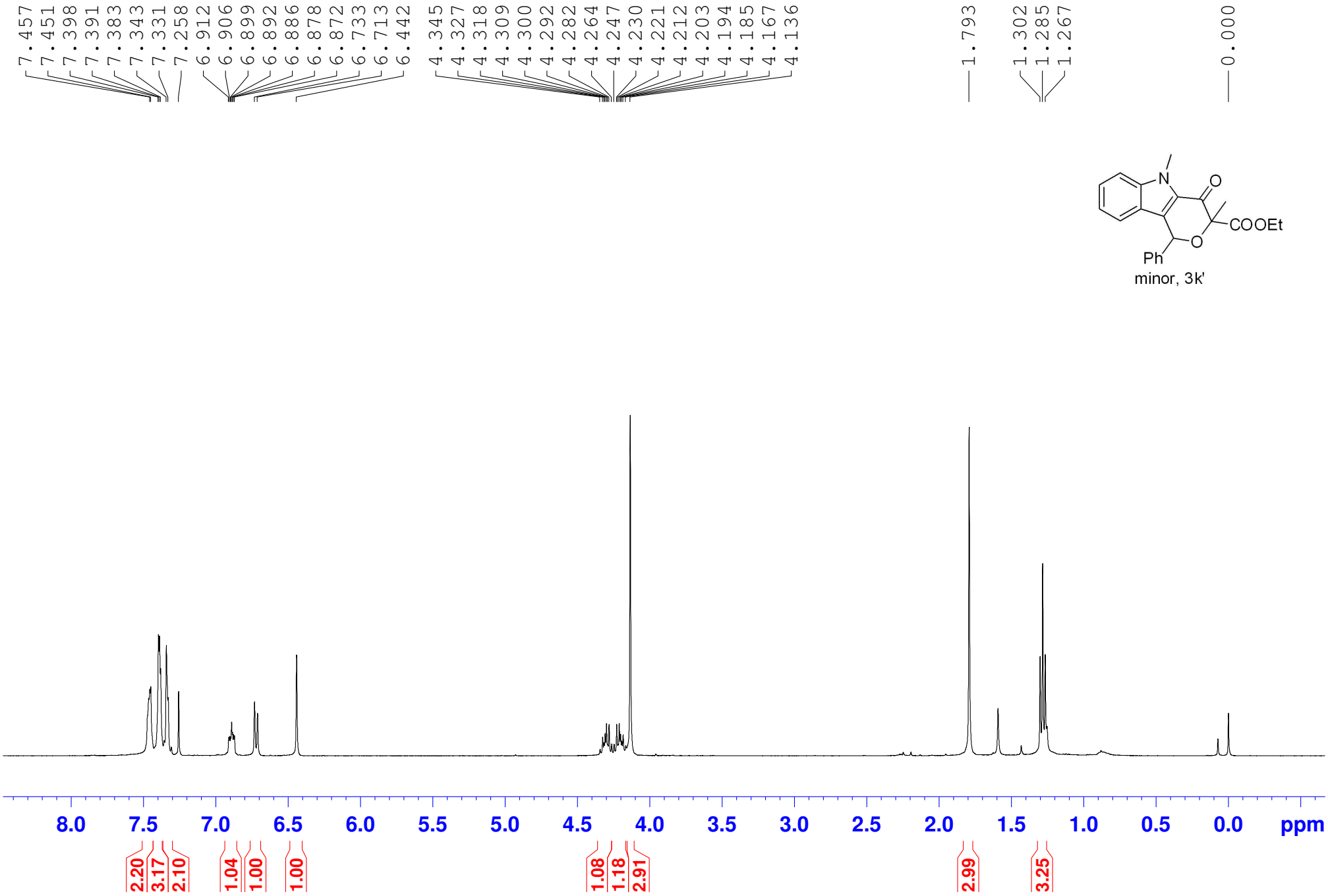

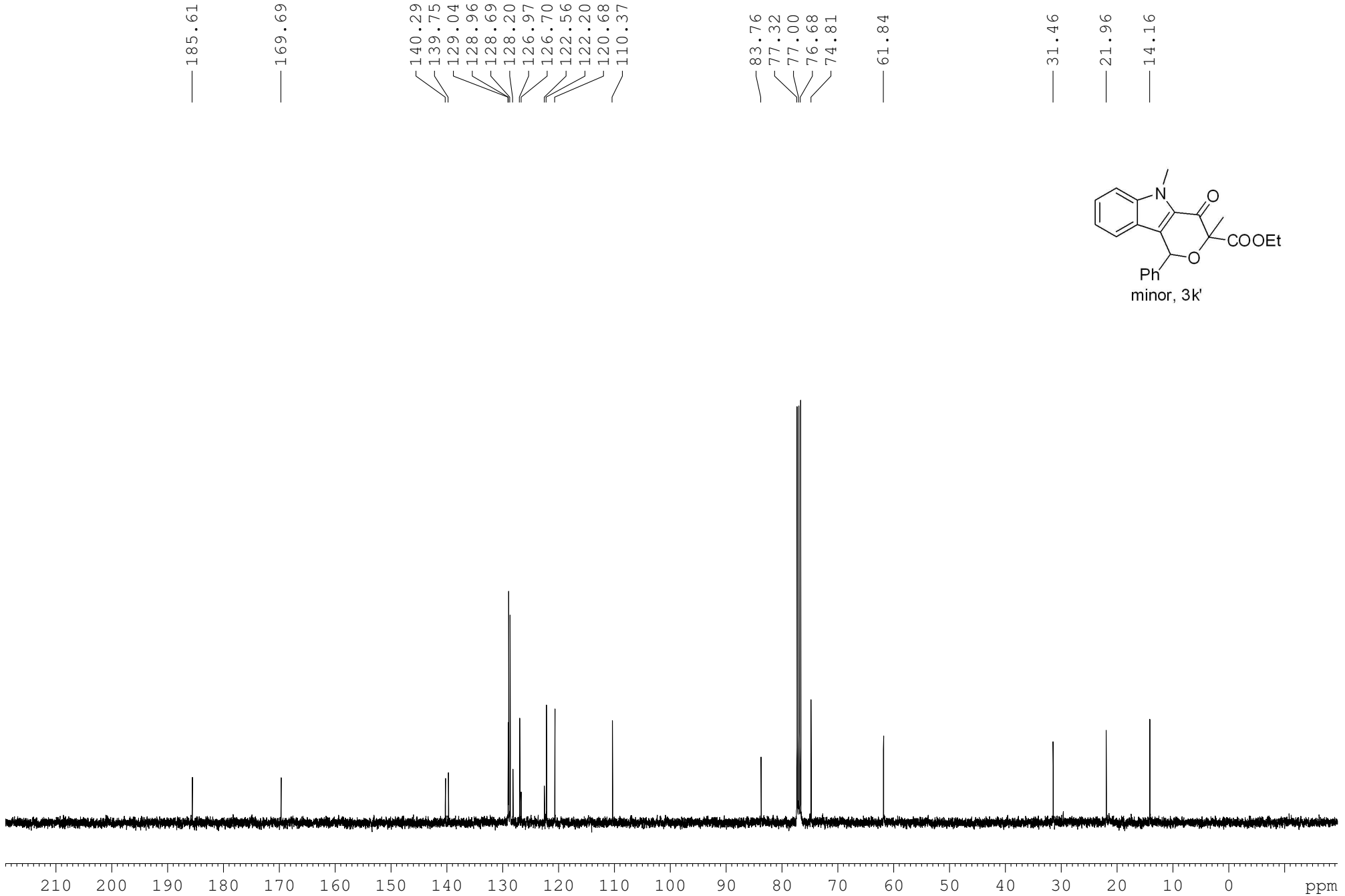

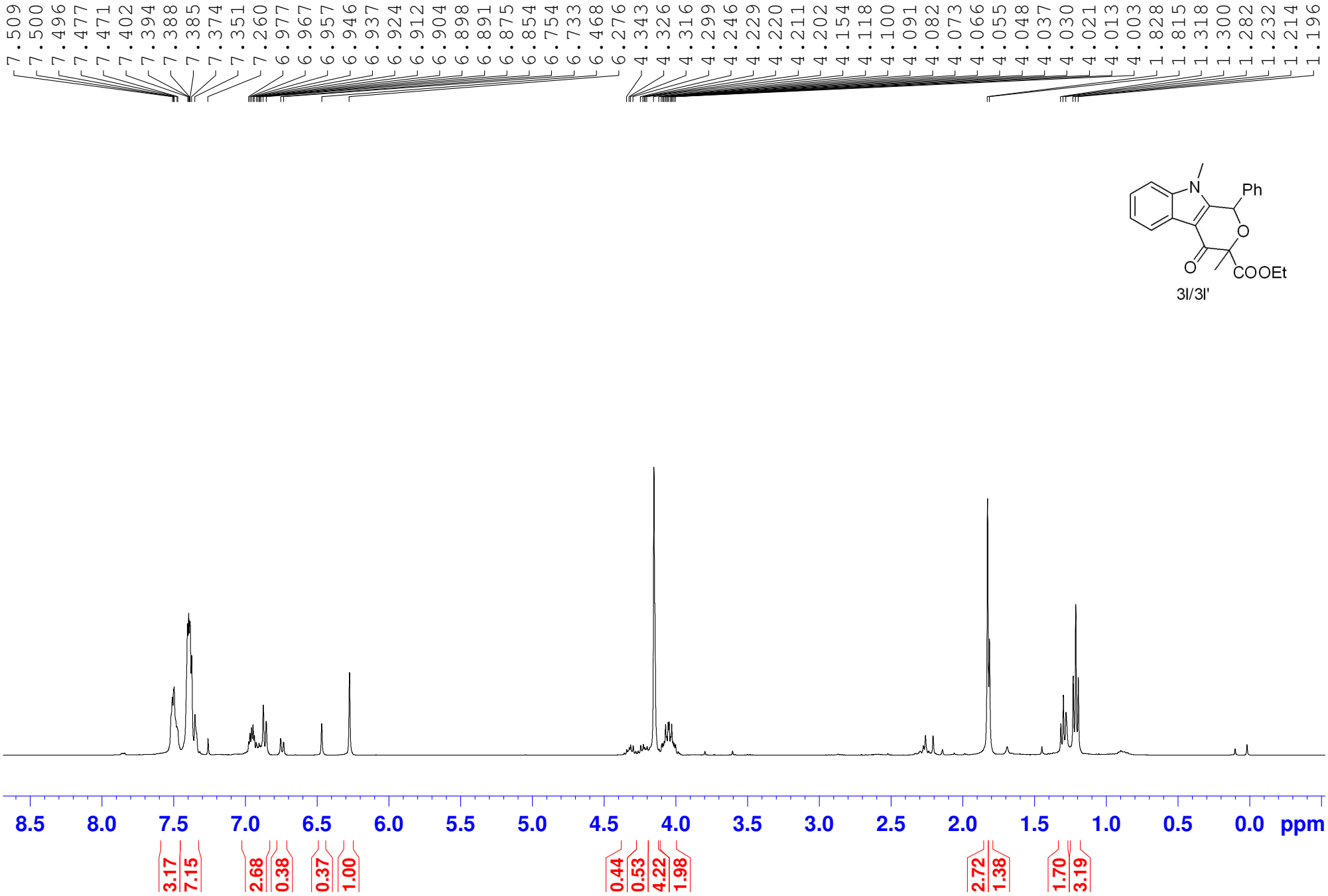

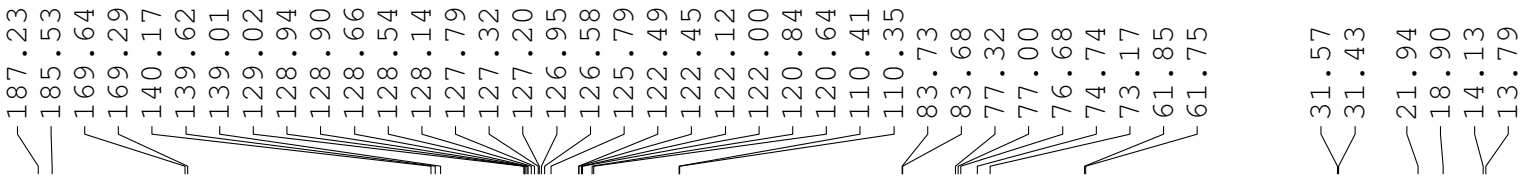

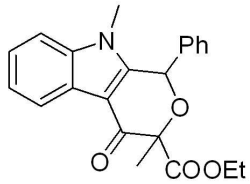

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