TFP as Ligand in Au(I)-catalyzed Dihydropyran Synthesis. Unprecedented Rearrangement of Dihydropyrans into Cyclopentenones

Eliška Matoušová,[a] Aleš Růžička,[b] Jiří Kuneš,[a] Jarmila Králová[a] and Milan Pour*[a]

[a] Centre for New Antivirals and Antineoplastics, Department of Inorganic and Organic Chemistry, Charles University in Prague, Faculty of Pharmacy in Hradec Králové, Heyrovského 1203, CZ-500 03 Hradec Králové, Czech Republic

[b] Department of General and Inorganic Chemistry, University of Pardubice, Faculty of Chemical Technology, Studentská 573, CZ-53210 Pardubice, Czech Republic

*Corresponding author. Tel.: +420 49 5067277; fax: +420 49 5067166. E-mail address: milan.pour@faf.cuni.cz

Supporting information

General Methods

All reagents were purchased from Sigma-Aldrich. CH_2Cl_2 was distilled from CaH_2, THF was distilled from sodium and benzophenone, MeOH was distilled over 3A molecular sieves. Silica gel 60 (Merck) was used for column chromatography. TLC was performed on Silica gel 60 F_{254} aluminum sheets (Merck).

^1H and ^{13}C NMR spectra were recorded on a VNMR S500 and a VARIAN MERCURY Vx BB 300 spectrometers. Chemical shifts were recorded as δ values in parts per million (ppm), and were indirectly referenced to tetramethylsilane (TMS) *via* the solvent signal (3.30 ppm for ^1H and 49.0 ppm for ^{13}C). Coupling constants (*J*) are given in Hz. Melting points

were determined on a Büchi B-545 apparatus without correction. Mass spectra were recorded on a ZAB-SEQ (VG-Analytical) and a LCMS Agilent 500 instruments. Infrared spectra were recorded on a NICOLET 6700 FT-IR/ATR-Ge spectrometer and are reported in wave numbers (cm^{-1}). Elemental analyses were recorded on a CHNS-OCE FISONS EA 1110 instrument.

Preparation of Gold Catalyst

Chloro(tetrahydrothiophene)gold(I) was prepared according to a literature procedure.[1]
Tetrahydrothiophene (0.19 ml, 2.1 mmol) was added dropwise to a solution of $HAuCl_4 \cdot 3H_2O$ (394 mg, 1 mmol) in a mixture of water (0.7 ml) and ethanol (3.3 ml). The reaction mixture was stirred for 30 min at room temperature until the yellow precipitate was transformed to a white solid. The resulting white precipitate was filtred, washed with ethanol and vacuum dried. Yield 95 %.

Chloro(trifurylphoshine)gold(I) was prepared according to a literature procedure.[2]
(tht)AuCl (64 mg, 0.2 mmol) and trifurylphosphine (47 mg, 0.2 mmol) were stirred together in CH_2Cl_2 (3 ml) at room temperature for 1 hour. The solvent was removed, the resulting powder dissolved in a minimum amount of CH_2Cl_2, and precipitated by petroleum ether. The precipitate was filtred, washed with petroleum ether and vacuum dried. Yield 90 %.
The spectral data of the catalyst were identical with those reported in the literature.[3]

Formation of Propargylic Alcohols. 3-Phenylprop-2-yn-1-ol, oct-2-yn-1-ol, but-2-yn-1-ol, 4-phenylbut-3-yn-2-ol, hex-5-en-2-yn-1-ol and hex-2-yn-1-ol were obtained commercially from Sigma-Aldrich.
3-(Naphthalen-1-yl)prop-2-yn-1-ol, 3-(thiophen-3-yl)prop-2-yn-1-ol, 4-phenylbut-2-yn-1-ol, 3-(4-methoxyphenyl)prop-2-yn-1-ol and 4-(3-hydroxyprop-1-ynyl)benzonitrile were synthesized from the corresponding alkynes: generally, an alkyne (5 mmol) was dissolved in anhydrous THF (10 ml) under argon atmosphere and cooled to - 78 °C. Then butyllithium (2 ml of 2.5 M solution in hexanes, 5 mmol) was added dropwise and after 30 min of stirring at

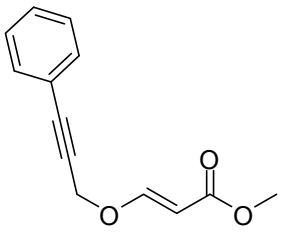
[1] R. Usón, A. Laguna, M. Laguna, *Inorg. Synth.*, 1989, **26**, 85.
[2] T. L. Stott, M. O. Wolf, B. O. Patrick, *Inorg. Chem.*, 2005, **44**, 620.
[3] M. R. Karver, D. Krishnamurthy, R. A. Kulkarni, N. Bottini, A. M. Barrios, *J. Med. Chem.*, 2009, **52**, 6912.

this temperature, paraformaldehyde (275 mg, 5 mmol) was added. The reaction mixture was warmed to room temperature and stirred for approx. 2 hours until a dissolution of paraformaldehyde was observed. The mixture was diluted with ethyl acetate and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel.

4-(Benzyloxy)but-2-yn-1-ol was prepared by the protection of but-2-yn-1,4-diol according to a literature procedure.[4]

General Procedure for the Addition of Propargylic Alcohols to Methyl Propiolate.

Methyl propiolate (0.09 ml, 1 mmol) and triethylamine (0.42 ml, 3 mmol) were added to a solution of propargylic alcohol (1 mmol) in 5 ml of anhydrous CH_2Cl_2 under argon atmosphere. The reaction mixture was stirred at room temperature for approx. 0.5 - 2 hours (conversion was monitored by TLC analysis). The mixture was diluted with ethyl acetate and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel.

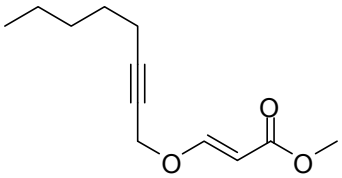


(*E*)-Methyl 3-(3-phenylprop-2-ynyloxy)acrylate 3a: Prepared according to general procedure in 99 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellow oil.

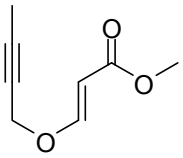
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 12.6 Hz, 1H, H3), 7.47-7.43 (m, 2H, Ar), 7.36-7.30 (m, 3H, Ar), 5.39 (d, J = 12.6 Hz, 1H, H2), 4.75 (s, 2H, OCH_2), 3.72 (s, 3H, OCH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.8, 160.9, 131.9, 129.0, 128.3, 121.7, 98.0, 88.4, 81.8, 59.1, 51.2; **IR** ν_{max} [cm^{-1}] 2952, 2230, 1711, 1644, 1626, 1491, 1441, 1377, 1329, 1259, 1190, 1129; **MS (TOF CI)** *m/z* (relative intensity) 217.1 $[M+H]^+$ (48), 185.1 (49), 157.1 (18), 115.1

[4] M. M. Faul, L. L. Winneroski, C. A. Krumrich, *J. Org. Chem.*, 1999, **64**, 2465.

(100), 105.0 (4), 71.0 (3); **HRMS (TOF CI)** *m/z* calcd. for $C_{13}H_{13}O_3$: 217.0865, found: 217.0858.

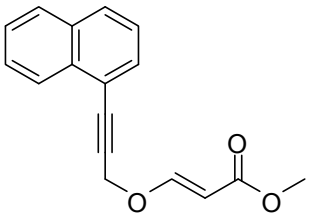


(*E*)-Methyl 3-(oct-2-ynyloxy)acrylate 3b: Prepared according to general procedure in 98 % yield, purified by column chromatography (petroleum ether/ethyl acetate 98:2), yellowish oil. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 12.6 Hz, 1H, H3), 5.31 (d, *J* = 12.6 Hz, 1H, H2), 4.50 (t, *J* = 2.2 Hz, 2H, OCH_2), 3.69 (s, 3H, OCH_3), 2.25-2.17 (m, 2H, CH_2), 1.55-1.44 (m, 2H, CH_2), 1.39-1.22 (m, 4H, CH_2), 0.88 (t, *J* = 7.1 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.9, 161.0, 97.6, 89.9, 73.0, 59.1, 51.1, 30.9, 28.0, 22.1, 18.7, 13.9; **IR** ν_{max} [cm^{-1}] 2933, 2861, 2229, 1715, 1646, 1626, 1461, 1435, 1379, 1327, 1286, 1258, 1188, 1159, 1126; **MS (TOF CI)** *m/z* (relative intensity) 211.1 $[M+H]^+$ (100), 179.1 (24), 151.1 (10), 125.1 (6), 109.1 (27), 103.0 (19), 67.1 (12); **HRMS (TOF CI)** *m/z* calcd. for $C_{12}H_{19}O_3$: 211.1334, found: 211.1327.



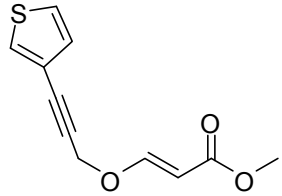
(*E*)-Methyl 3-(but-2-ynyloxy)acrylate 3c: Prepared according to general procedure in 99 % yield, purified by column chromatography (petroleum ether/ethyl acetate 85:15), white amorphous solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57 (d, *J* = 12.6 Hz, 1H, H3), 5.30 (d, *J* = 12.6 Hz, 1H, H2), 4.47 (q, *J* = 2.4 Hz, 2H, OCH_2), 3.69 (s, 3H, OCH_3), 1.86 (t, *J* = 2.4 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.9, 161.0, 97.7, 85.3, 72.3, 59.0, 51.1, 3.6; **IR** ν_{max} [cm^{-1}] 2953, 2231, 1711, 1645, 1625, 1437, 1330, 1287, 1255, 1187, 1163, 1127; **LRMS (APCI)** *m/z* (relative intensity) 155.0 $[M+H]^+$ (100), 140.2 (18), 123.1 (40), 102.4 (20), 84.9 (31), 52.6 (19).



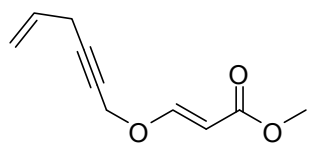
(*E*)-Methyl 3-(3-(naphthalen-1-yl)prop-2-ynyloxy)acrylate 3d: Prepared according to general procedure in 96 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellow solid, mp 39.4 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.13-8.08 (m, 1H, Ar), 7.71-7.69 (m, 2H, Ar), 7.58-7.51 (d, J = 12.6 Hz, m, 2H, H3, Ar, overlapped), 7.43-7.34 (m, 2H, Ar), 7.30-7.24 (m, 1H, Ar), 5.32 (d, J = 12.6 Hz, 1H, H2), 4.73 (s, 2H, OCH_2), 3.56 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.7, 160.9, 133.2, 133.0, 131.0, 129.5, 128.3, 127.0, 126.5, 125.9, 125.1, 119.3, 98.1, 86.7, 86.6, 59.2, 51.2; **IR** ν_{max} [cm^{-1}] 3088, 3057, 3044, 2947, 2237, 1703, 1640, 1435, 1397, 1339, 1230, 1196, 1169, 1138; **MS (TOF EI)** *m/z* (relative intensity) 266.1 $[M]^+$ (57), 250.1 (44), 234.1 (100), 218.1 (16), 206.1 (76), 190.1 (18), 125.0 (10), 79.0 (18); **HRMS (ESI)** *m/z* calcd. for $C_{17}H_{15}O_3$: 267.1016, found: 267.1016.



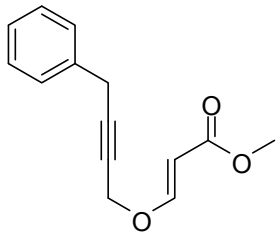
(*E*)-Methyl 3-(3-(thiophen-3-yl)prop-2-ynyloxy)acrylate 3e: Prepared according to general procedure in 99 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellowish solid, mp 35.0 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 12.6 Hz, 1H, H3), 7.53-7.50 (m, 1H, Ar), 7.30-7.25 (m, 1H, Ar), 7.14-7.11 (m, 1H, Ar), 5.37 (d, J = 12.6 Hz, 1H, H2), 4.73 (s, 2H, OCH_2), 3.72 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.7, 160.9, 130.1, 129.8, 125.5, 120.7, 98.0, 83.6, 81.6, 59.1, 51.2; **IR** ν_{max} [cm^{-1}] 3107, 2950, 2228, 1708, 1647, 1625, 1434, 1372, 1328, 1257, 1188, 1125; **MS (TOF EI)** *m/z* (relative intensity) 222.0 $[M]^+$ (6), 207.0 (6), 193.0 (15), 163.0 (92), 134.0 (17), 121.0 (100), 111.0 (10), 63.0 (13); **HRMS (TOF EI)** *m/z* calcd. for $C_{11}H_{10}O_3S$: 222.0351, found: 222.0357.



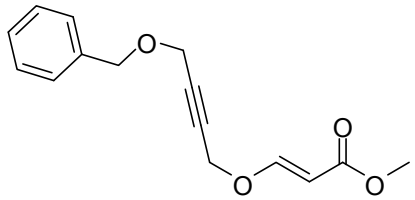
(*E*)-Methyl 3-(hex-5-en-2-ynyloxy)acrylate 3f: Prepared according to general procedure in 87 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 12.6 Hz, 1H, H3), 5.84-5.72 (m, 1H, H5'), 5.37-5.25 (m, 2H, H2, H6', overlapped), 5.13 (m, 1H, H6'), 4.54 (s, 2H, OCH_2), 3.70 (s, 3H, OCH_3), 3.04-2.98 (m, 2H, H4'); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.8, 160.9, 131.5, 116.6, 97.8, 86.2, 75.4, 58.9, 51.2, 23.0; **IR** ν_{max} [cm^{-1}] 2951, 2240, 1712, 1645, 1626, 1436, 1328, 1287, 1259, 1188, 1158, 1127; **MS (TOF EI)** *m/z* (relative intensity) 280.1 $[M]^+$ (4), 165.1 (2), 151.1 (12), 139.0 (9), 121.1 (14), 111.0 (10), 93.1 (7), 77.0 (100), 51.0 (9); **HRMS (ESI)** *m/z* calcd. for $C_{10}H_{13}O_3$: 181.0859, found: 181.0857.



(*E*)-Methyl 3-(4-phenylbut-2-ynyloxy)acrylate 3g: Prepared according to general procedure in 31 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellow oil.

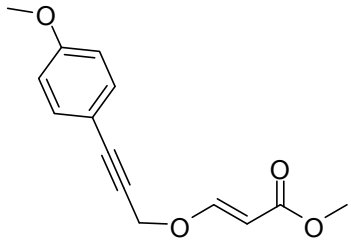
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 12.6 Hz, 1H, H3), 7.31-7.16 (m, 5H, Ar), 5.30 (d, *J* = 12.6 Hz, 1H, H2), 4.52 (t, *J* = 2.2 Hz, 2H, OCH_2), 3.66 (s, 3H, OCH_3), 3.61 (t, *J* = 2.2 Hz, 2H, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.8, 160.9, 135.8, 128.6, 127.8, 126.8, 97.8, 87.1, 75.2, 58.9, 51.2, 25.1; **IR** ν_{max} [cm^{-1}] 2950, 1712, 1646, 1625, 1495, 1453, 1436, 1328, 1288, 1258, 1188, 1128; **MS (TOF EI)** *m/z* (relative intensity) 230.1 $[M]^+$ (2), 201.1 (15), 170.1 (14), 141.1 (24), 128.1 (100), 115.1 (7), 102.0 (5); **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{15}O_3$: 231.1016, found: 231.1015.



(*E*)-Methyl 3-(4-(benzyloxy)but-2-ynyloxy)acrylate 3h: Prepared according to general procedure in 98 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), colourless amorphous solid.

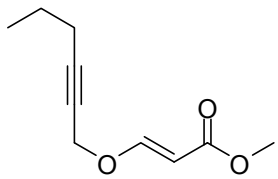
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 12.6 Hz, 1H, H3), 7.37-7.27 (m, 5H, Ar), 5.35 (d, *J* = 12.6 Hz, 1H, H2), 4.60-4.57 (m, 4H, OCH_2), 4.22 (t, *J* = 1.8 Hz, 2H, OCH_2), 3.71 (s, 3H, OCH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.7, 160.7, 137.1, 128.4, 128.1, 127.9, 98.0, 84.9,

79.5, 71.8, 58.5, 57.1, 51.2; **IR** ν_{max} [cm^{-1}] 2950, 1711, 1645, 1626, 1437, 1329, 1288, 1259, 1188, 1129; **MS (TOF EI)** *m/z* (relative intensity) 260.1 $[M]^+$ (1), 186.1 (21), 155.0 (36), 127.0 (23), 116.0 (48), 111.0 (32), 98.0 (16), 85.0 (100), 71.0 (21), 59.0 (48); **HRMS (ESI)** *m/z* calcd. for $C_{15}H_{17}O_4$: 261.1121, found: 261.1121.



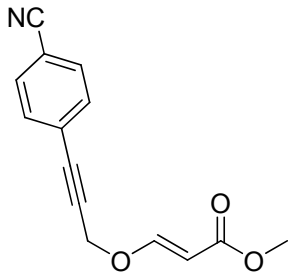
(*E*)-Methyl 3-(3-(4-methoxyphenyl)prop-2-ynyloxy)acrylate 3i: Prepared according to general procedure in 95 % yield, purified by column chromatography (petroleum ether/ethyl acetate 85:15), yellowish solid, mp 39.9 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 12.6 Hz, 1H, H3), 7.41-7.36 (m, 2H, AA', BB', Ar), 6.86-6.80 (m, 2H, AA', BB', Ar), 5.38 (d, *J* = 12.6 Hz, 1H, H2), 4.73 (s, 2H, OCH_2), 3.80 (s, 3H, OCH_3), 3.71 (s, 3H, $COOCH_3$); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.8, 161.0, 160.1, 133.4, 114.0, 113.7, 97.9, 88.5, 80.5, 59.3, 55.3, 51.2; **IR** ν_{max} [cm^{-1}] 2956, 2840, 2233, 1706, 1626, 1605, 1511, 1443, 1433, 1379, 1335, 1294, 1246, 1227, 1186, 1177, 1142; **LRMS (APCI)** *m/z* (relative intensity) 246.8 $[M+H]^+$ (100), 219.6 (30), 216.6 (6), 205.6 (16), 187.6 (6), 168.1 (65), 145.3 (13).



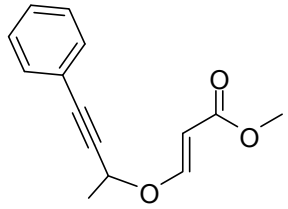
(*E*)-Methyl 3-(hex-2-ynyloxy)acrylate 3j: Prepared according to general procedure in 95 % yield, purified by column chromatography (petroleum ether/ethyl acetate 95:5), colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 12.6 Hz, 1H, H3), 5.31 (d, *J* = 12.6 Hz, 1H, H2), 4.50 (t, *J* = 2.2 Hz, 2H, OCH_2), 3.70 (s, 3H, OCH_3), 2.20 (tt, *J* = 7.0 Hz, *J* = 2.2 Hz, 2H, CH_2), 1.60-1.47 (m, 2H, CH_2), 0.97 (t, *J* = 7.4 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.9, 161.0, 97.6, 89.7, 73.2, 59.1, 51.2, 21.7, 20.7, 13.4; **IR** ν_{max} [cm^{-1}] 2964, 2874, 2232, 1713, 1645, 1626, 1438, 1380, 1328, 1286, 1259, 1189, 1159, 1128; **LRMS (APCI)** *m/z* (relative intensity) 382.8 $[M+H]^+$ (100), 168.9 (12), 164.2 (14), 152.5 (8), 142.5 (7), 131.7 (7), 124.4 (15), 104.9 (9), 91.9 (11).



(*E*)-Methyl 3-(3-(4-cyanophenyl)prop-2-ynyloxy)acrylate 3l: Prepared according to general procedure in 95 % yield, purified by column chromatography (petroleum ether/ethyl acetate 8:2), yellow solid, mp 107.6 °C.

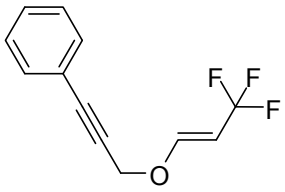
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.59 (m, 3H, H3, AA', BB', Ar, overlapped), 7.55-7.50 (m, 2H, AA', BB', Ar), 5.38 (d, *J* = 12.6 Hz, 1H, H2), 4.76 (s, 2H, OCH_2), 3.71 (s, 3H, OCH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 167.5, 160.6, 132.3, 132.0, 126.5, 118.1, 112.5, 98.2, 86.5, 86.1, 58.7, 51.3; **IR** ν_{max} [cm^{-1}] 2222, 1706, 1618, 1503, 1430, 1338, 1325, 1231, 1191, 1146; **LRMS (APCI)** *m/z* (relative intensity) 242.3 $[M+H]^+$ (80), 228.5 (7), 210.4 (18), 140.4 (100), 87.5 (34), 75.5 (18), 59.3 (13).



(*E*)-Methyl 3-(4-phenylbut-3-yn-2-yloxy)acrylate 6: Prepared according to general procedure in 99 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellowish oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 12.4 Hz, 1H, H3), 7.46-7.41 (m, 2H, Ar), 7.35-7.29 (m, 3H, Ar), 5.43 (d, *J* = 12.4 Hz, 1H, H2), 4.91 (q, J = 6.6 Hz, 1H, CH), 3.71 (s, 3H, OCH_3), 1.65 (d, *J* = 6.6 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 168.1, 160.3, 131.8, 128.9, 128.3, 121.7, 98.6, 87.1, 86.1, 68.0, 51.1, 21.9; **IR** ν_{max} [cm^{-1}] 2991, 2950, 2229, 1712, 1644, 1624, 1491, 1436, 1330, 1191, 1138, 1111; **MS (TOF CI)** *m/z* (relative intensity) 253.1 $[M+Na]^+$ (1), 239.1 (4), 227.1 (12), 199.1 (100), 171.1 (45), 143.1 (5), 131.1 (4), 77.0 (1); **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{14}O_3Na$: 253.0835, found: 253.0834.

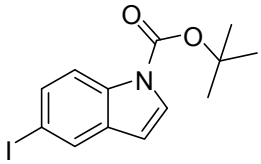
Addition of Propargylic Alcohol to 3,3,3-Trifluoroprop-1-yne.



(*E*)-3,3,3-Trifluoro-1-(3-phenylprop-2-ynyloxy)prop-1-ene 5: Trifluoropropyne gas was bubbled into anhydrous CH_2Cl_2 at - 60 °C and 3-phenylprop-2-yn-1-ol (0.65 ml, 5 mmol) and triethylamine (2.1 ml, 15 mmol) were added. The reaction mixture was stirred for 30 min at - 60 °C and then warmed to room temperature. After 2.5 hours the mixture turned black and complete consumption of the starting material was observed. The mixture was diluted with ethyl acetate and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/ethyl acetate 95:5). Yield 100 %, yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.43 (m, 2H, Ar), 7.38-7.30 (m, 3H, Ar), 7.11 (dq, J = 12.8 Hz, J = 2.0 Hz, 1H, H1), 5.18 (dq, J = 12.8 Hz, J = 6.5 Hz, 1H, H2), 4.71 (s, 2H, OCH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 153.0 (q, J = 7.8 Hz), 131.8, 129.1, 128.4, 124.5 (q, J = 266.9 Hz), 121.7, 96.1 (q, J = 33.8 Hz), 88.6, 81.7, 58.7; **IR** ν_{max} [cm^{-1}] 2870, 2228, 1682, 1662, 1491, 1444, 1371, 1346, 1327, 1260, 1207, 1179, 1093; **MS (TOF EI)** *m/z* (relative intensity) 225.1 $[M]^+$ (18), 157.1 (27), 115.0 (100), 105.0 (18), 89.0 (17), 63 (10); **HRMS (TOF EI)** *m/z* calcd. for $C_{12}H_8OF_3$: 225.0527, found: 225.0533.

Preparation of Methyl 3-(Boc-indol-5-yl-prop-2-ynyloxy)acrylate.



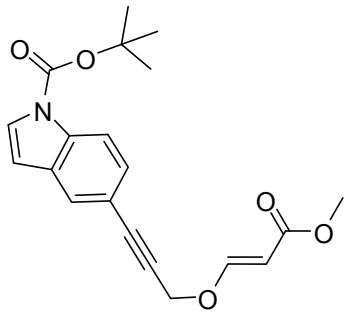
***tert*-Butyl 5-iodo-1*H*-indole-1-carboxylate:** Prepared from 5-iodo-1*H*-indole according to literature procedure.[5] Yield 100 %, white solid, mp 51.0 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95-7.88 (m, 2H, Ar), 7.60-7.53 (m, 2H, Ar), 6.50-6.47 (m, 1H, Ar), 1.67 (s, 9H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 180.6, 149.4, 134.4, 132.6, 129.7, 126.6, 117.0, 106.2, 86.6, 84.1, 28.1; **IR** ν_{max} [cm^{-1}] 3163, 2982, 1734, 1531, 1443, 1367, 1362, 1341, 1325, 1276, 1249, 1200, 1184, 1157, 1130, 1084.

MS spectra were identical with literature.[6]

---

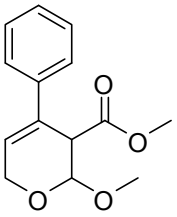
[5] S. D. Erickson, J. A. Simon, W. C. Still, *J. Org. Chem.*, 1993, **58**, 1305.
[6] *Eu. Pat.*, 2 108 642 (A1), 2009.



(*E*)-*tert*-Butyl 5-(3-(3-methoxykarbonylprop-1-enyloxy)prop-1-ynyl)-1*H*-indole-1-carboxylate 3k: To a solution of *tert*-butyl 5-iodo-1*H*-indole-1-carboxylate (344 mg, 1 mmol) in anhydrous THF (7.5 ml) $(PPh_3)_2PdCl_2$ (35 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), triethylamine (1.4 ml, 10 mmol) and (*E*)-methyl 3-(prop-2-ynyloxy)acrylate (155 mg, 1.1 mmol) were added. The reaction mixture was stirred at room temperature for 20 hours. The mixture was diluted with ethyl acetate and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography (petroleum ether/ethyl acetate 9:1). Yield 49 %, brown oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13-8.06 (m, 1H, Ar), 7.70-7.64 (m, 2H, CH, Ar, overlapped), 7.63-7.59 (m, 1H, Ar), 7.42-7.36 (m, 1H, Ar), 6.55-6.52 (m, 1H, Ar), 5.41 (d, J = 12.6 Hz, 1H, CH), 4.77 (s, 2H, OCH_2), 3.72 (s, 3H, OCH_3), 1.67 (s, 9H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 180.6, 167.8, 161.0, 149.4, 130.4, 127.8, 126.9, 124.9, 115.7, 115.2, 107.0, 97.9, 89.2, 84.1, 80.5, 59.3, 51.2, 28.1; **IR** ν_{max} [cm^{-1}] 2980, 2229, 1732, 1645, 1625, 1468, 1437, 1366, 1331, 1286, 1257, 1231, 1154, 1132, 1084; **LRMS (APCI)** *m/z* (relative intensity) 355.8 $[M+H]^+$ (100), 327.9 (15), 299.8 (24), 253.7 (28), 199.4 (11).

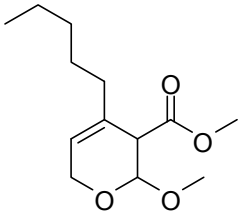
General Procedure for Gold(I)-Catalyzed Cyclisation to Dihydropyrans. (TFP)AuCl (23 mg, 0.05 mmol) and $AgBF_4$ (10 mg, 0.05 mmol) were placed into a dry flask under argon atmosphere and 10 ml of anhydrous CH_2Cl_2 and 0.13 ml of anhydrous methanol (3 mmol) were added. Subsequently, a solution of propargyl vinyl ether (1 mmol) in anhydrous CH_2Cl_2 (6.5 ml) was added. The reaction mixture was stirred at room temperature for approx. 0.5 - 4 hours (conversion was monitored by TLC analysis). The mixture was filtered and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel.



Methyl 3,6-dihydro-2-methoxy-4-phenyl-2*H*-pyran-3-carboxylate 4a: Prepared according to general procedure in 98 % yield (66 % *trans*, 32 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellowish amorphous solid.

***trans* isomer:** **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.36-7.22 (m, 5H, Ar), 6.22 (t, *J* = 3.0 Hz, 1H, H5), 5.15 (d, *J* = 2.2 Hz, 1H, H2), 4.38 (t, *J* = 2.2 Hz, 2H, H6), 3.73-3.69 (m, 1H, H3), 3.63 (s, 3H, $COOCH_3$), 3.51 (s, 3H, OCH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.9, 139.1, 130.1, 128.4, 127.5, 125.2, 123.7, 98.6, 60.7, 55.8, 52.3, 48.0; **IR** ν_{max} [cm^{-1}] 2926, 2851, 1723, 1652, 1598, 1496, 1437, 1364, 1240, 1194, 1136, 1093, 1072; **MS (TOF EI)** *m/z* (relative intensity) 248.1 $[M]^+$ (4), 216.1 (15), 184.1 (15), 157.1 (100), 129.1 (68), 115.1 (19), 77 (10); **HRMS (ESI)** *m/z* calcd. for $C_{14}H_{16}O_4Na$: 271.0946, found: 271.0941; **Anal** calcd. for $C_{14}H_{16}O_4$: C, 67.7; H, 6.5; O, 25.8; found: C, 67.7; H, 6.6; O, 25.7 %.

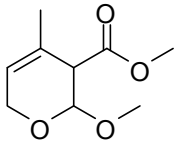
***cis* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.33-7.22 (m, 5H, Ar), 6.24-6.21 (m, 1H, H5), 4.98 (d, *J* = 4.2 Hz, 1H, H2), 4.54 (dt, *J* = 17.0 Hz, *J* = 2.6 Hz, 1H, H6), 4.32 (dt, *J* = 17.0 Hz, *J* = 2.6 Hz, 1H, H6), 3.98-4.00 (m, 1H, H3), 3.59 (s, 3H, $COOCH_3$), 3.52 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.0, 139.1, 131.2, 128.5, 127.5, 124.8, 124.2, 98.5, 62.0, 56.4, 52.2, 47.5; **IR** ν_{max} [cm^{-1}] 2936, 2838, 1730, 1654, 1492, 1446, 1438, 1366, 1249, 1238, 1206, 1135, 1101, 1079; **MS (TOF CI)** *m/z* (relative intensity) 249.1 $[M+H]^+$ (3), 231.1 (6), 217.1 (37), 189.1 (100), 157.1 (23), 129.1 (4); **HRMS (TOF CI)** *m/z* calcd. for $C_{14}H_{17}O_4$: 249.1127, found: 249.1124; **Anal** calcd. for $C_{14}H_{16}O_4$: C, 67.7; H, 6.5; O, 25.8; found: C, 67.9; H, 6.65; O, 25.5 %.



Methyl 3,6-dihydro-2-methoxy-4-pentyl-2*H*-pyran-3-carboxylate 4b: Prepared according to general procedure in 83 % yield (62 % *trans*, 21 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 98:2), colourless oil.

***trans* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.63-5.53 (m, 1H, H5), 4.94 (d, *J* = 2.8 Hz, 1H, H2), 4.21-4.13 (m, 2H, H6), 3.72 (s, 3H, $COOCH_3$), 3.45 (s, 3H, OCH_3), 3.08-3.05 (m, 1H, H3), 2.08-1.90 (m, 2H, CH_2), 1.48-1.19 (m, 6H, CH_2), 0.87 (t, *J* = 7.0 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.3, 130.9, 120.6, 98.9, 60.9, 55.8, 52.1, 49.2, 35.2, 31.4, 26.5, 22.4, 14.0; **IR** ν_{max} [cm^{-1}] 2953, 2929, 2857, 1736, 1435, 1383, 1312, 1244, 1193, 1138, 1118, 1097, 1069; **MS (TOF CI)** *m/z* (relative intensity) 243.2 $[M+H]^+$ (6), 225.1 (8), 211.1 (100), 193.1 (32), 183.1 (27), 179.1 (13), 151.1 (28); **HRMS (TOF CI)** *m/z* calcd. for $C_{13}H_{23}O_4$: 243.1596, found: 243.1599; **Anal** calcd. for $C_{13}H_{22}O_4$: C, 64.4; H, 9.15; O, 26.4; found: C, 64.5; H, 9.3; O, 26.2 %.

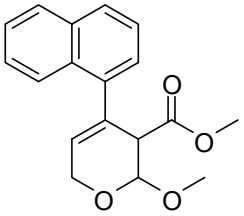
***cis* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.62-5.59 (m, 1H, H5), 4.80 (d, *J* = 4.3 Hz, 1H, H2), 4.31 (d, *J* = 16.1 Hz, 1H, H6), 4.07 (d, *J* = 16.1 Hz, 1H, H6), 3.70 (s, 3H, $COOCH_3$), 3.48 (s, 3H, OCH_3), 3.34-3.30 (m, 1H, H3), 2.05 (t, *J* = 7.7 Hz, 2H, CH_2), 1.40-1.18 (m, 6H, CH_2), 0.84 (t, *J* = 7.0 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.1, 131.7, 121.3, 98.3, 61.4, 56.1, 51.9, 48.3, 34.8, 31.3, 26.7, 22.4, 13.9; **IR** ν_{max} [cm^{-1}] 2953, 2929, 2857, 1750, 1677, 1435, 1382, 1363, 1306, 1270, 1246, 1193, 1139, 1119, 1090, 1059; **LRMS (APCI)** *m/z* (relative intensity) 243.1 $[M+H]^+$ (6), 224.8 (30), 212.4 (48), 210.8 (100), 192.9 (25), 183.8 (8), 162.7 (9), 151.0 (14), 134.7 (12), 121.7 (9); **Anal** calcd. for $C_{13}H_{22}O_4$: C, 64.4; H, 9.15; O, 26.4; found: C, 64.2; H, 9.1; O, 26.7 %.



Methyl 3,6-dihydro-2-methoxy-4-methyl-2*H*-pyran-3-carboxylate 4c: Prepared according to general procedure in 70 % yield (57 % *trans*, 13 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellowish oil.

***trans* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.60-5.57 (m, 1H, H5), 4.96 (d, *J* = 2.7 Hz, 1H, H2), 4.16-4.11 (m, 2H, H6), 3.71 (s, 3H, $COOCH_3$), 3.44 (s, 3H, OCH_3), 2.98 (s, 1H, H3), 1.73-1.75 (m, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.0, 126.6, 121.7, 98.6, 60.6, 55.8, 52.1, 50.2, 22.0; **IR** ν_{max} [cm^{-1}] 2918, 2848, 1736, 1436, 1388, 1325, 1306, 1194, 1157, 1137, 1110, 1082, 1073; **MS (TOF CI)** *m/z* (relative intensity) 209.1 $[M+Na]^+$ (3), 183.1 (22), 169.0 (100), 155.1 (1), 141.1 (3), 112.1 (3); **HRMS (ESI)** *m/z* calcd. for $C_9H_{14}O_4Na$: 209.0784, found: 209.0784; **Anal** calcd. for $C_9H_{14}O_4$: C, 58.05; H, 7.6; O, 34.4; found: C, 58.1; H, 7.7; O, 34.2 %.

***cis* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.65-5.62 (m, 1H, H5), 4.87 (d, *J* = 4.4 Hz, 1H, H2), 4.32-4.25 (m, 1H, H6), 4.07-4.01 (m, 1H, H6), 3.72 (s, 3H, $COOCH_3$), 3.45 (s, 3H, OCH_3), 3.33-3.28 (m, 1H, H3), 1.76 (s, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.0, 127.4, 122.3, 98.0, 60.8, 56.1, 52.0, 49.5, 21.3; **LRMS (APCI)** *m/z* (relative intensity) 187.2 $[M+H]^+$ (1), 169.2 (100), 155.2 (21), 141.3 (15), 128.2 (9), 111.9 (6); **Anal** calcd. for $C_9H_{14}O_4$: C, 58.05; H, 7.6; O, 34.4; found: C, 58.3; H, 7.5; O, 34.2 %.



Methyl 3,6-dihydro-2-methoxy-4-(naphthalen-1-yl)-2*H*-pyran-3-carboxylate 4d:

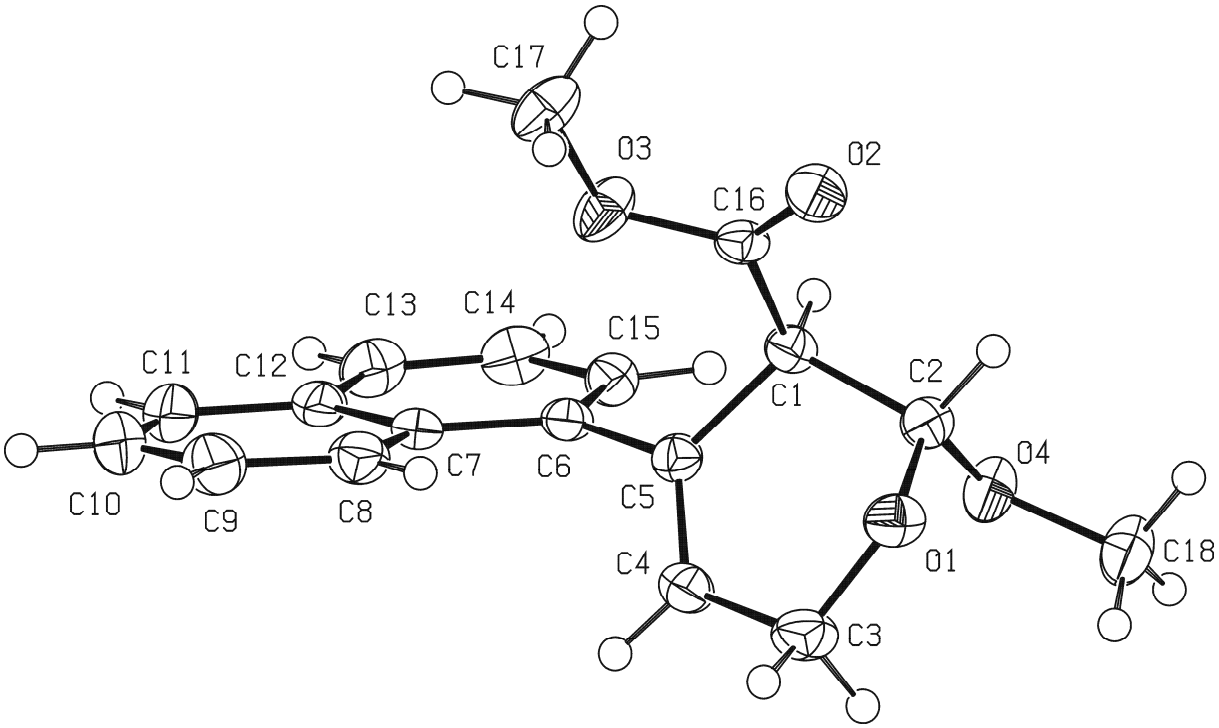
Prepared according to general procedure in 84 % yield (61 % *trans*, 23 % *cis*), purified by column chromatography (gradient elution, petroleum ether/ethyl acetate 95:5 – 9:1), yellowish solid, mp 110.5 °C (*trans*), 95.0 °C (*cis*).

***trans* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.18-8.14 (m, 1H, Ar), 7.87-7.83 (m, 1H, Ar), 7.81-7.86 (m, 1H, Ar), 7.52-7.35 (m, 4H, Ar), 5.98-5.96 (m, 1H, H5), 5.24-5.22 (m, 1H, H2), 4.47-4.43 (m, 2H, H6), 3.70-3.66 (m, 1H, H3), 3.61 (s, 3H, $COOCH_3$), 3.50 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.6, 138.4, 133.6, 131.4, 130.1, 128.2, 127.7, 127.2, 126.1, 126.0, 125.7, 125.4, 125.2, 98.5, 60.6, 55.9, 52.0, 50.4; **IR** ν_{max} [cm^{-1}] 3061, 3003, 2945, 2917, 2856, 1732, 1591, 1506, 1441, 1360, 1321, 1274, 1218, 1190, 1136, 1069; **MS (TOF EI)** *m/z* (relative intensity) 298.1 $[M]^+$ (19), 266.1 (7), 234.1 (20), 207.1 (98), 195.1 (17), 179.1 (100), 165.1 (32), 152.1 (28), 127.1 (3), 89.0 (7); **HRMS (TOF EI)** *m/z* calcd. for $C_{18}H_{18}O_4$: 298.1205, found: 298.1200; **Anal** calcd. for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1; O, 21.45; found: C, 72.2; H, 6.2; O, 21.6 %.

***cis* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.09-8.03 (m, 1H, Ar), 7.86-7.82 (m, 1H, Ar), 7.79-7.75 (m, 1H, Ar), 7.51-7.39 (m, 3H, Ar), 7.32-7.28 (m, 1H, Ar), 6.02-6.00 (m, 1H, H5), 5.11 (d, *J* = 4.1 Hz, 1H, H2), 4.65 (dt, *J* = 16.7 Hz, *J* = 2.3 Hz, 1H, H6), 4.41-4.35 (dt, *J* = 16.7 Hz, *J* = 2.3 Hz, 1H, H6), 3.98-3.94 (m, 1H, H3), 3.58 (s, 3H, $COOCH_3$), 3.49 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.5, 138.0, 133.8, 131.3, 130.8, 128.3, 128.1, 127.7, 126.0, 125.7, 125.3, 125.2, 125.1, 98.7, 62.1, 56.4, 51.9, 50.0; **IR** ν_{max} [cm^{-1}] 3042, 3006, 2928, 2831, 1739, 1506, 1442, 1384, 1358, 1259, 1244, 1211, 1193, 1156, 1137, 1110, 1102; **MS (TOF EI)** *m/z* (relative intensity) 298.1 $[M]^+$ (9), 266.1 (4), 234.1 (7), 207.1 (100),

195.1 (8), 179.1 (75), 165.1 (22), 152.1 (17), 127.1 (2), 89.0 (5); **HRMS (TOF EI)** *m/z* calcd. for $C_{18}H_{18}O_4$: 298.1205, found: 298.1193; **Anal** calcd. for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1; O, 21.45; found: C, 72.7; H, 6.0; O, 21.3 %.

Crystallografic data for *trans*-4d



Molecular structure of **4d**, an ORTEP view, 50% probability level.

4d crystallizes in orthorhombic centrosymmetric space group *P*bca. The molecular structure of **4d** consists of two ring systems where one is the planar aromatic naphthyl moiety and the second one is the skewed partially saturated six membered heterocycle. All interatomic distances are in line with the standard single and double bond distances.[7]

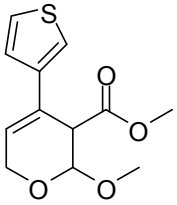
The X-ray data for colourless crystals of **4d** were obtained at 150K using Oxford Cryostream low-temperature device on a Nonius KappaCCD diffractometer with MoK_α radiation (λ = 0.71073 Å), a graphite monochromator, and the ϕ and χ scan mode. Data reductions were performed with DENZO-SMN.[8] The absorption was corrected by integration methods.[9] Structures were solved by direct methods (Sir92)[10] and refined by full matrix least-square

[7] F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, R. Taylor, *J. Chem. Soc. Perkin. Trans. II*, 1987, **12**, S1.
[8] Z. Otwinowski, W. Minor, *Methods in Enzymology*, 1997, **276**, 307.
[9] P. Coppens, in: *Crystallographic Computing*, ed. F. R. Ahmed, S. R. Hall, C. P. Huber Editors, Copenhagen, Munksgaard, 1970, pp. 255-270.
[10] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, *J. Appl. Crystallogr.*, 1993, **26**, 343.

based on F^2 (SHELXL97).[11] Hydrogen atoms were mostly localized on a difference Fourier map, however to ensure uniformity of the treatment of the crystal, all hydrogen atoms were recalculated into idealized positions (riding model) and assigned temperature factors $H_{iso}(H) = 1.2\ U_{eq}$(pivot atom) or of $1.5U_{eq}$ for the methyl moiety with C-H = 0.96, 0.97, 0.98 and 0.93 Å for methyl, methylene, methine and hydrogen atoms in aromatic rings or unsaturated carbon atom, respectively.

Crystallographic data for structural analysis have been deposited with the Cambridge Crystallographic Data Centre. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EY, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http:// www.ccdc.cam.ac.uk).

Crystallographic data for **4d**: $C_{18}H_{18}O_4$, M = 298.32, orthorhombic, *P*bca, a = 12.9230(7), b = 7.4390(12), c = 30.766(2) Å, α = β = γ = 90°, Z = 8, V = 2957.7(6) $Å^3$, D_c = 1.340 g.cm-3, μ = 0.094 mm^{-1}, T_{min} = 0.977, T_{max} = 0.986; 16499 reflections measured (θ_{max} = 27.5°), 16377 independent (R_{int} = 0.0567), 3373 with I > 2σ(I), 199 parameters, S = 1.140, R_1(obs. data) = 0.0548, wR_2(all data) = 0.1065; max., min. res. El. density = 0.356, -0.239 e $Å^{-3}$. CCDC Deposition number: 829174.



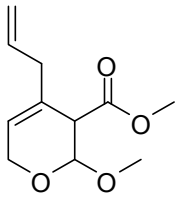
Methyl 3,6-dihydro-2-methoxy-4-(thiophen-3-yl)-2*H*-pyran-3-carboxylate 4e: Prepared according to general procedure in 87 % yield (61 % *trans*, 26 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellowish solid, mp 82.5 °C (*trans*), yellowish amorphous solid (*cis*).

***trans* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.27-7.24 (m, 1H, Ar), 7.21-7.18 (m, 1H, Ar), 7.10-7.08 (m, 1H, Ar), 6.24 (t, *J* = 2.9 Hz, 1H, H5), 5.11 (d, *J* = 1.7 Hz, 1H, H2), 4.37-4.34 (m, 2H, H6), 3.69 (s, 3H, $COOCH_3$), 3.62-3.59 (m, 1H, H3), 3.49 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.9, 140.8, 125.8, 125.1, 124.7, 122.3, 119.4, 98.2, 60.1, 55.8, 52.5, 48.2; **IR** ν_{max} [cm^{-1}] 3104, 2950, 2842, 1729, 1435, 1386, 1364, 1321, 1246, 1197, 1165,

[11] G. M. Sheldrick, SHELXL-97, University of Göttingen, Göttingen, 1997.

1134, 1070; **MS (TOF EI)** *m/z* (relative intensity) 254.1 $[M]^+$ (19), 222.0 (15), 190.0 (27), 179.0 (15), 163.0 (100), 135.0 (62), 121.0 (11), 109.0 (13), 91.1 (21); **HRMS (TOF EI)** *m/z* calcd. for $C_{12}H_{14}O_4S$: 254.0613, found: 254.0612; **Anal** calcd. for $C_{12}H_{14}O_4S$: C, 56.7; H, 5.55; O, 25.2; S, 12.6; found: C, 56.7; H, 5.7; O, 25.3; S, 12.3 %.

***cis* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.29-7.25 (m, 1H, Ar), 7.21-7.13 (m, 2H, Ar), 6.27 (t, *J* = 2.5 Hz, 1H, H5), 4.85 (d, *J* = 3.9 Hz, 1H, H2), 4.63 – 4.57 (m, 1H, H6), 4.39-4.33 (m, 1H, H6), 3.84-3.81 (m, 1H, H3), 3.69 (s, 3H, $COOCH_3$), 3.54 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.2, 140.3, 126.9, 126.0, 124.5, 122.9, 119.5, 98.9, 63.1, 56.5, 52.3, 48.0; **IR** ν_{max} $[cm^{-1}]$ 3103, 2952, 2923, 2851, 1724, 1428, 1380, 1370, 1251, 1238, 1203, 1136, 1108, 1076; **MS (TOF EI)** *m/z* (relative intensity) 254.1 $[M]^+$ (5), 222.0 (12), 195.0 (13), 179.0 (12), 163.0 (100), 135.0 (47), 121.0 (7), 109.0 (10), 91.1 (13); **HRMS (TOF EI)** *m/z* calcd. for $C_{12}H_{14}O_4S$: 254.0613, found: 254.0621; **Anal** calcd. for $C_{12}H_{14}O_4S$: C, 56.7; H, 5.55; O, 25.2; S, 12.6; found: C, 56.9; H, 5.3; O, 25.5; S, 12.3 %.

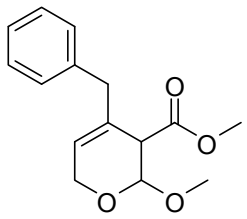


Methyl 4-allyl-3,6-dihydro-2-methoxy-2*H*-pyran-3-carboxylate 4f: Prepared according to general procedure in 67 % yield (52 % *trans*, 15 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 98:2), colourless oil.

***trans* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.80-5.69 (m, 1H, H2'), 5.63 (s, 1H, H5), 5.09-5.04 (m, 2H, H3'), 5.02-4.95 (m, 1H, H2), 4.18-4.14 (m, 2H, H6), 3.70 (s, 3H, $COOCH_3$), 3.43 (s, 3H, OCH_3), 3.06 (s, 1H, H3), 2.86-2.71 (m, 2H, CH_2); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.0, 134.6, 128.9, 122.2, 117.3, 98.5, 60.4, 55.7, 52.1, 48.5, 39.7; **IR** ν_{max} $[cm^{-1}]$ 2951, 2847, 1737, 1638, 1435, 1385, 1364, 1312, 1257, 1194, 1171, 1136, 1107, 1080, 1070; **MS (TOF EI)** *m/z* (relative intensity) 212.1 $[M]^+$ (1), 180.1 (19), 171.1 (7), 152.1 (50), 139.0 (53), 121.1 (100), 91.0 (79), 77.0 (47), 65.0 (13), 59.0 (12); **HRMS (ESI)** *m/z* calcd. for $C_{11}H_{16}O_4Na$: 235.0941, found: 235.0940; **Anal** calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.6; O, 30.15; found: C, 62.4; H, 7.6; O, 30.0 %.

***cis* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.77-5.63 (m, 2H, H2', H5, overlapped), 5.08-5.00 (m, 2H, H3'), 4.86 (d, *J* = 4.3 Hz, 1H, H2), 4.36-4.29 (m, 1H, H6), 4.12-4.04 (m, 1H, H6), 3.71 (s, 3H, $COOCH_3$), 3.45 (s, 3H, OCH_3), 3.39-3.35 (m, 1H, H3), 2.92-2.78 (m, 2H, CH_2); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.9, 134.9, 129.9, 122.8, 117.4, 98.1, 61.0, 56.1, 52.0, 47.9,

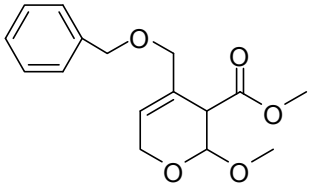
39.4; **IR** ν_{max} [cm^{-1}] 2951, 2926, 2854, 1749, 1638, 1435, 1383, 1362, 1312, 1267, 1191, 1170, 1136, 1113, 1087, 1059; **LRMS (APCI)** *m/z* (relative intensity) 213.0 $[M+H]^+$ (4), 181.0 (30), 153.1 (41), 140.0 (38), 121.9 (91), 92.0 (100), 78.0 (5), 60.0 (7); **Anal** calcd. for $C_{11}H_{16}O_4$: C, 62.25; H, 7.6; O, 30.15; found: C, 61.9; H, 7.9; O, 30.2 %.



Methyl 4-benzyl-3,6-dihydro-2-methoxy-2*H*-pyran-3-carboxylate 4g: Prepared according to general procedure in 75 % yield (57 % *trans*, 18 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 98:2), colourless oil.

***trans* isomer:** ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.16 (m, 5H, Ar), 5.52 (s, 1H, H5), 5.00 (d, *J* = 2.2 Hz, 1H, H2), 4.20-4.16 (m, 2H, H6), 3.68 (s, 3H, $COOCH_3$), 3.47-3.32 (m, 5H, OCH_3, CH_2), 3.04 (bs, 1H, H3); ^{13}**C NMR** (125 MHz, $CDCl_3$) δ 171.0, 138.0, 130.1, 129.3, 128.3, 126.3, 123.1, 98.5, 60.4, 55.7, 52.1, 48.5, 41.8; **IR** ν_{max} [cm^{-1}] 3027, 2930, 2848, 1736, 1602, 1495, 1453, 1435, 1384, 1364, 1311, 1255, 1195, 1168, 1134, 1107, 1081, 1070; **MS (TOF EI)** *m/z* (relative intensity) 262.1 $[M]^+$ (1), 230.1 (21), 202.1 (92), 171.1 (100), 143.1 (96), 139.0 (61), 128.1 (79), 115.1 (42), 91.1 (49), 65.0 (15), 59.0 (6); **HRMS (ESI)** *m/z* calcd. for $C_{15}H_{19}O_4$: 263.1278, found: 263.1278; **Anal** calcd. for $C_{15}H_{18}O_4$: C, 68.7; H, 6.9; O, 24.4; found: C, 68.8; H, 6.8; O, 24.4 %.

***cis* isomer:** ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 7.32-7.13 (m, 5H, Ar), 5.69-5.65 (m, 1H, H5), 4.83 (d, *J* = 4.4 Hz, 1H, H2), 4.39-4.30 (m, 1H, H6), 4.14-4.07 (m, 1H, H6), 3.72-3.70 (m, 5H, $COOCH_3$, CH_2, overlapped), 3.45 (s, 3H, OCH_3), 3.28-3.25 (m, 1H, H3); ^{13}**C NMR** (125 MHz, $CDCl_3$) δ 169.9, 138.2, 131.2, 129.2, 128.4, 126.4, 123.4, 98.1, 60.9, 56.1, 52.0, 47.5, 41.5; **IR** ν_{max} [cm^{-1}] 2954, 2923, 2853, 1739, 1642, 1494, 1462, 1378, 1364, 1312, 1248, 1189, 1161, 1136, 1112, 1083, 1061; **MS (TOF EI)** *m/z* (relative intensity) 262.1 $[M]^+$ (1), 230.1 (19), 202.1 (89), 171.1 (98), 143.1 (100), 139.0 (60), 128.1 (75), 115.1 (38), 91.1 (44), 65.0 (15), 59.0 (7); **HRMS (ESI)** *m/z* calcd. for $C_{15}H_{19}O_4$: 263.1278, found: 263.1278; **Anal** calcd. for $C_{15}H_{18}O_4$: C, 68.7; H, 6.9; O, 24.4; found: C, 69.0; H, 6.65; O, 24.3 %.

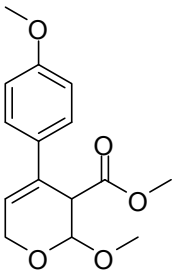


Methyl 4-((benzyloxy)methyl)-3,6-dihydro-2-methoxy-2*H*-pyran-3-carboxylate 4h:

Prepared according to general procedure in 70 % yield (49 % *trans*, 21 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 95:5), colourless amorphous solid.

***trans* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H, Ar), 5.93-5.90 (m, 1H, H5), 5.08 (d, *J* = 2.0 Hz, 1H, H2), 4.51 (d, *J* = 11.7 Hz, 1H, OCH_2), 4.41 (d, *J* = 11.7 Hz, 1H, OCH_2), 4.24-4.21 (m, 2H, OCH_2), 4.12-4.08 (m, 1H, H6), 3.99-3.94 (m, 1H, H6), 3.68 (s, 3H, $COOCH_3$), 3.47 (s, 3H, OCH_3), 3.28-3.25 (m, 1H, H3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.7, 138.1, 128.3, 127.8, 127.8, 127.5, 124.6, 98.3, 72.0, 71.7, 60.0, 55.8, 52.2, 46.2; **IR** ν_{max} [cm^{-1}] 2923, 2853, 1737, 1496, 1453, 1356, 1311, 1259, 1196, 1156, 1136, 1082; **LRMS (APCI)** *m/z* (relative intensity) 293.4 $[M+H]^+$ (2), 261.4 (100), 243.4 (30), 229.4 (38), 211.4 (28), 183.4 (38), 153.4 (7), 129.4 (11), 91.4 (20); **Anal** calcd. for $C_{16}H_{20}O_5$: C, 65.7; H, 6.9; O, 27.4; found: C, 65.9; H, 6.9; O, 27.2 %.

***cis* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H, Ar), 5.93 (s, 1H, H5), 4.91 (d, *J* = 4.3 Hz, 1H, H2), 4.50-4.40 (m, 2H, OCH_2), 4.34 (d, *J* = 16.5 Hz, 1H, H6), 4.20 (d, *J* = 12.0 Hz, 1H, OCH_2), 4.14 (d, *J* = 16.5 Hz, 1H, H6), 4.00 (d, *J* = 12.0 Hz, 1H, OCH_2), 3.68 (s, 3H, $COOCH_3$), 3.55 (s, 1H, H3), 3.46 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 169.7, 138.0, 128.9, 128.3, 127.6, 127.6, 124.6, 97.9, 72.2, 71.9, 60.6, 56.1, 52.0, 45.9; **IR** ν_{max} [cm^{-1}] 2954, 2923, 2853, 1741, 1462, 1454, 1378, 1309, 1264, 1169, 1137, 1092; **LRMS (APCI)** *m/z* (relative intensity) 293.4 $[M+H]^+$ (3), 260.9 (100), 243.0 (33), 228.9 (24), 210.9 (17), 183.9 (8), 153.1 (9), 91.9 (3); **Anal** calcd. for $C_{16}H_{20}O_5$: C, 65.7; H, 6.9; O, 27.4; found: C, 66.0; H, 6.7; O, 27.3 %.

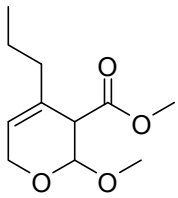


Methyl 3,6-dihydro-2-methoxy-4-(4-methoxyphenyl)-2*H*-pyran-3-carboxylate 4i:

Prepared according to general procedure in 89 % yield (63 % *trans*, 26 % *cis*), purified by column chromatography (gradient elution, petroleum ether/ethyl acetate 9:1 – 8:2), white solid, mp 75.4 °C (*trans*), 127.8 °C (*cis*).

***trans* isomer:** **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.30-7.23 (m, 2H, AA', BB', Ar), 6.88-6.81 (m, 2H, AA', BB', Ar), 6.12 (t, *J* = 2.5 Hz, 1H, H5), 5.13-5.11 (m, 1H, H2), 4.38-4.34 (m, 2H, H6), 3.79 (s, 3H, OCH_3), 3.68-3.65 (m, 1H, H3), 3.64 (s, 3H, $COOCH_3$), 3.50 (s, 3H, OCH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 171.0, 159.1, 131.7, 129.5, 126.3, 122.0, 113.8, 98.7, 60.7, 55.8, 55.2, 52.4, 48.1; **IR** ν_{max} [cm^{-1}] 2943, 2843, 1722, 1608, 1515, 1439, 1367, 1302, 1272, 1238, 1181, 1138, 1095, 1072; **LRMS (APCI)** *m/z* (relative intensity) 279.1 $[M+H]^+$ (3), 248.3 (12), 219.4 (100), 217.1 (9), 188.1 (6); **Anal** calcd. for $C_{15}H_{18}O_5$: C, 64.7; H, 6.5; O, 28.7; found: C, 64.9; H, 6.5; O, 28.6 %.

***cis* isomer:** **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.29-7.23 (m, 2H, AA', BB', Ar), 6.87-6.81 (m, 2H, AA', BB', Ar), 6.17-6.12 (m, 1H, H5), 4.94 (d, *J* = 4.1 Hz, 1H, H2), 4.54 (dt, *J* = 16.9 Hz, *J* = 2.7 Hz, 1H, H6), 4.31 (dt, *J* = 16.9 Hz, *J* = 2.7 Hz, 1H, H6), 3.96-3.90 (m, 1H, H3), 3.79 (s, 3H, OCH_3), 3.62 (s, 3H, $COOCH_3$), 3.52 (s, 3H, OCH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 170.1, 159.1, 131.5, 130.7, 125.9, 122.5, 113.9, 98.7, 62.3, 56.4, 55.2, 52.2, 47.6; **IR** ν_{max} [cm^{-1}] 2945, 2842, 1729, 1607, 1514, 1462, 1428, 1379, 1300, 1265, 1250, 1239, 1202, 1183, 1139, 1108, 1082; **LRMS (APCI)** *m/z* (relative intensity) 279.2 $[M+H]^+$ (1), 260.9 (17), 248.2 (34), 219.1 (100), 217.1 (21), 188.1 (8); **Anal** calcd. for $C_{15}H_{18}O_5$: C, 64.7; H, 6.5; O, 28.7; found: C, 64.55; H, 6.7; O, 28.7 %.

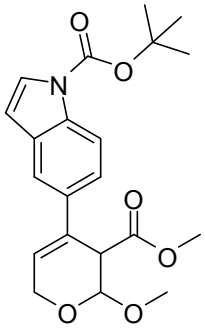


Methyl 3,6-dihydro-2-methoxy-4-propyl-2*H*-pyran-3-carboxylate 4j: Prepared according to general procedure in 77 % yield (65 % *trans*, 12 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 95:5), colourless oil.

***trans* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 5.60-5.56 (m, 1H, H5), 4.94 (d, *J* = 2.8 Hz, 1H, H2), 4.19-4.16 (m, 2H, H6), 3.72 (s, 3H, $COOCH_3$), 3.45 (s, 3H, OCH_3), 3.07-3.04 (m, 1H, H3), 2.01-1.96 (m, 2H, CH_2), 1.53-1.36 (m, 2H, CH_2), 0.89 (t, *J* = 7.3 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 171.3, 130.6, 120.8, 98.8, 60.8, 55.8, 52.1, 49.1, 37.3, 20.0, 13.6; **IR** ν_{max} [cm^{-1}] 2956, 2873, 2843, 1738, 1462, 1435, 1383, 1310, 1257, 1193, 1140, 1116, 1093, 1066; **LRMS (APCI)** *m/z* (relative intensity) 215.1 $[M+H]^+$ (1), 197.2 (11), 184.2 (18),

165.2 (100), 133.2 (63), 106.1 (8); **Anal** calcd. for $C_{11}H_{18}O_4$: C, 61.7; H, 8.5; O, 29.9; found: C, 61.8; H, 8.2; O, 30.0 %.

***cis* isomer:** ^{1}**H NMR** (500 MHz, $CDCl_3$) δ 5.61-5.58 (m, 1H, H5), 4.79 (d, *J* = 4.3 Hz, 1H, H2), 4.34-4.28 (m, 1H, H6), 4.10-4.04 (m, 1H, H6), 3.69 (s, 3H, $COOCH_3$), 3.43 (s, 3H, OCH_3), 3.33-3.29 (m, 1H, H3), 2.08-1.97 (m, 2H, CH_2), 1.46-1.30 (m, 2H, CH_2), 0.85 (t, *J* = 7.3 Hz, 3H, CH_3); ^{13}**C NMR** (125 MHz, $CDCl_3$) δ 170.1, 131.4, 121.5, 98.3, 61.4, 56.1, 51.9, 48.2, 36.9, 20.1, 13.6; **IR** ν_{max} [cm^{-1}] 2958, 2874, 1737, 1462, 1439, 1383, 1309, 1265, 1198, 1141, 1120, 1094, 1057; **LRMS (APCI)** *m/z* (relative intensity) 215.2 $[M+H]^+$ (1), 197.4 (45), 184.2 (25), 165.2 (76), 133.2 (100), 106.0 (11); **Anal** calcd. for $C_{11}H_{18}O_4$: C, 61.7; H, 8.5; O, 29.9; found: C, 62.0; H, 8.25; O, 29.8 %.

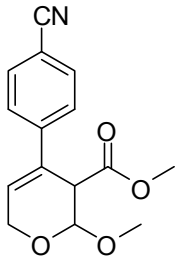


***tert*-Butyl 5-(2-methoxy-3-(methoxycarbonyl)-3,6-dihydro-2*H*-pyran-4-yl)-1*H*-indole-1-carboxylate 4k:** Prepared according to general procedure in 38 % yield (25 % *trans*, 13 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellowish solid, mp 115.3 °C (*trans*), 124.8 °C (*cis*)

***trans* isomer:** ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 8.10-8.02 (m, 1H, Ar), 7.59-7.55 (m, 1H, Ar), 7.51-7.48 (m, 1H, Ar), 7.35-7.29 (m, 1H, Ar), 6.55-6.52 (m, 1H, Ar), 6.21 (t, *J* = 2.8 Hz, 1H, H5), 5.16 (d, *J* = 2.2 Hz, 1H, H2), 4.40 (t, *J* = 2.4 Hz, 2H, H6), 3.80-3.76 (m, 1H, H3), 3.61 (s, 3H, $COOCH_3$), 3.53 (s, 3H, OCH_3), 1.66 (s, 9H, CH_3); ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 180.6, 171.0, 149.6, 134.1, 130.7, 130.4, 126.3, 123.1, 122.0, 117.7, 115.0, 107.4, 98.8, 83.7, 60.8, 55.9, 52.3, 48.5, 28.2; **IR** ν_{max} [cm^{-1}] 2931, 2853, 1736, 1471, 1439, 1366, 1339, 1286, 1246, 1193, 1160, 1137, 1089, 1072; **LRMS (APCI)** *m/z* (relative intensity) 388.3 $[M+H]^+$ (16), 370.4 (7), 329.4 (100), 300.4 (78), 272.4 (23), 268.4 (63), 256.4 (16), 224.4 (11), 197.4 (14); **Anal** calcd. for $C_{21}H_{25}NO_6$: C, 65.1; H, 6.5; N, 3.6; O, 24.8; found: C, 65.0; H, 6.4; N, 3.9; O, 24.7 %.

***cis* isomer:** ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 8.09-8.01 (m, 1H, Ar), 7.59-7.55 (m, 1H, Ar), 7.51-7.47 (m, 1H, Ar), 7.33-7.27 (m, 1H, Ar), 6.55-6.51 (m, 1H, Ar), 6.25-6.21 (m, 1H, H5),

5.01 (d, J = 4.2 Hz, 1H, H2), 4.57 (dt, J = 16.9 Hz, J = 2.6 Hz, 1H, H6), 4.34 (dt, J = 16.9 Hz, J = 2.6 Hz, 1H, H6), 4.08-4.03 (m, 1H, H3), 3.58 (s, 3H, $COOCH_3$), 3.54 (s, 3H, OCH_3), 1.66 (s, 9H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 180.8, 170.4, 149.9, 134.2, 131.8, 131.0, 126.6, 123.9, 121.8, 117.5, 115.4, 107.7, 98.9, 84.0, 62.4, 56.6, 52.4, 48.1, 28.4; **IR** ν_{max} [cm^{-1}] 2930, 2856, 1732, 1470, 1439, 1369, 1336, 1276, 1257, 1237, 1194, 1159, 1138, 1112, 1084, 1056; **LRMS (APCI)** *m/z* (relative intensity) 388.2 $[M+H]^+$ (9), 370.2 (12), 329.2 (100), 300.2 (53), 272.2 (18), 268.3 (70), 256.2 (8), 224.2 (18), 197.1 (6); **Anal** calcd. for $C_{21}H_{25}NO_6$: C, 65.1; H, 6.5; N, 3.6; O, 24.8; found: C, 64.85; H, 6.7; N, 3.7; O, 24.8 %.

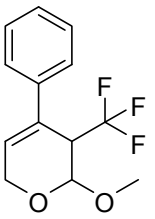


Methyl 4-(4-cyanophenyl)-2-methoxy-3,6-dihydro-2*H*-pyran-3-carboxylate 4l: Prepared according to general procedure in 92 % yield (68 % *trans*, 24 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 9:1), white solid, mp 121.2 °C (*trans*), yellowish amorphous solid (*cis*)

***trans* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.63-7.58 (m, 2H, AA', BB', Ar), 7.44-7.40 (m, 2H, AA', BB', Ar), 6.35-6.31 (m, 1H, H5), 5.21-5.18 (m, 1H, H2), 4.40-4.36 (m, 2H, H6), 3.67-3.62 (m, 4H, H3, $COOCH_3$, overlapped), 3.50 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.2, 143.7, 132.3, 128.9, 127.0, 125.9, 118.7, 111.0, 98.1, 60.4, 55.8, 52.5, 47.4; **IR** ν_{max} [cm^{-1}] 2923, 2848, 2227, 1603, 1438, 1362, 1274, 1247, 1136, 1093, 1074; **LRMS (APCI)** *m/z* (relative intensity) 274.1 $[M+H]^+$ (1), 256.3 (23), 243.2 (18), 210.3 (100), 215.2 (50), 183.3 (12), 154.3 (29), 75.2 (3); **Anal** calcd. for $C_{15}H_{15}NO_4$: C, 65.9; H, 5.5; N, 5.1; O, 23.4; found: C, 65.8; H, 5.4; N, 5.1; O, 23.7 %.

***cis* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.62-7.58 (m, 2H, AA', BB', Ar), 7.41-7.36 (m, 2H, AA', BB', Ar), 6.33 (s, 1H, H5), 5.09-5.05 (m, 1H, H2), 4.51 (d, J = 17.3 Hz, 1H, H6), 4.32 (d, J = 17.3 Hz, 1H, H6), 4.00 (s, 1H, H3), 3.60 (s, 3H, $COOCH_3$), 3.51 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 144.0, 132.4, 130.0, 127.4, 125.4, 118.7, 111.0, 97.8, 60.9, 56.3, 52.3, 46.9; **IR** ν_{max} [cm^{-1}] 2924, 2851, 2227, 1734, 1605, 1558, 1507, 1437, 1385, 1362, 1307, 1250, 1197, 1168, 1134, 1112, 1057; **LRMS (APCI)** *m/z* (relative intensity) 274.1 $[M+H]^+$ (3), 256.4 (100), 242.4 (98), 226.4 (28), 210.4 (29), 182.4 (41), 85.5 (9), 75.5

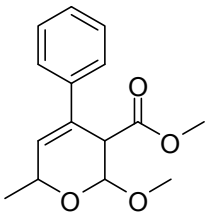
(14), 61.3 (6); **Anal** calcd. for $C_{15}H_{15}NO_4$: C, 65.9; H, 5.5; N, 5.1; O, 23.4; found: C, 66.0; H, 5.4; N, 5.3; O, 23.3 %.



3-(Trifluoromethyl)-3,6-dihydro-2-methoxy-4-phenyl-2*H*-pyran 7: Prepared according to general procedure in 38 % yield (20 % *trans*, 18 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 9:1), white solid, mp 82.1 °C (*trans*), white amorphous solid (*cis*).

***trans* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H, Ar), 6.21 (t, *J* = 2.5 Hz, 1H, H5), 5.21 (s, 1H, H2), 4.39-4.34 (m, 2H, H6), 3.51 (s, 3H, OCH_3), 3.51-3.47 (m, 1H, H3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.7, 128.5, 127.7, 127.7, 127.4 (q, *J* = 2.0 Hz), 125.7, 124.8 (q, *J* = 281.2 Hz), 95.0 (q, *J* = 3.7 Hz), 60.0, 55.6, 44.8 (q, *J* = 25.6 Hz); **IR** ν_{max} [cm^{-1}] 2932, 2886, 2851, 1600, 1495, 1447, 1393, 1365, 1320, 1260, 1160, 1144, 1117, 1110, 1069; **LRMS (APCI)** *m/z* (relative intensity) 259.2 $[M+H]^+$ (100), 241.0 (24), 208.5 (9), 190.5 (19), 185.0 (17), 85.2 (6); **Anal** calcd. for $C_{13}H_{13}F_3O_2$: C, 60.5; H, 5.1; F, 22.1; O, 12.4; found: C, 60.7; H, 5.0; F, 22.2; O, 12.1 %.

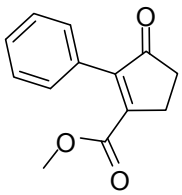
***cis* isomer:** **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39-7.24 (m, 5H, Ar), 6.05 (s, 1H, H5), 4.97-4.94 (m, 1H, H2), 4.51 (dt, *J* = 17.2 Hz, *J* = 2.4 Hz, 1H, H6), 4.34 (dt, *J* = 17.2 Hz, *J* = 2.4 Hz, 1H, H6), 3.75-3.67 (m, 1H, H3), 3.59-3.57 (m, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 139.5, 130.2 (q, *J* = 2.1 Hz), 128.4, 128.2, 127.6, 126.5, 124.9 (q, *J* = 281.7 Hz), 97.6 (q, *J* = 2.3 Hz), 62.3, 56.6, 44.7 (q, *J* = 25.1 Hz); **IR** ν_{max} [cm^{-1}] 2939, 2850, 1600, 1498, 1446, 1397, 1362, 1329, 1256, 1245, 1155, 1144, 1112, 1069; **LRMS (APCI)** *m/z* (relative intensity) 259.4 $[M+H]^+$ (100), 241.3 (35), 208.4 (17), 190.3 (8), 185.4 (23), 85.2 (11); **Anal** calcd. for $C_{13}H_{13}F_3O_2$: C, 60.5; H, 5.1; F, 22.1; O, 12.4; found: C, 60.8; H, 4.7; F, 22.5; O, 12.0 %.



Methyl 3,6-dihydro-2-methoxy-6-methyl-4-phenyl-2*H*-pyran-3-carboxylate 8: Prepared according to general procedure in 71 % yield, purified by column chromatography (gradient elution, petroleum ether/ethyl acetate 95:5 – 9:1), colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.20 (m, 5H, Ar), 6.16 (d, J = 2.0 Hz, 1H, H5), 5.21-5.19 (m, 1H, H2), 4.50-4.44 (m, 1H, H6), 3.67-3.65 (m, 4H, $COOCH_3$, H3), 3.48 (s, 3H, OCH_3), 1.39 (d, J = 6.8 Hz, 3H, CH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.9, 139.1, 129.1, 128.4, 128.3, 127.5, 125.2, 98.7, 65.1, 55.6, 52.4, 47.7, 20.4; **IR** ν_{max} [cm^{-1}] 3025, 2977, 2951, 2951, 2838, 1744, 1728, 1600, 1496, 1445, 1435, 1347, 1313, 1246, 1192, 1155, 1118, 1070, 1045; **MS (TOF CI)** *m/z* (relative intensity) 285.1 $[M+Na]^+$ (1), 261.1 (7), 249.1 (7), 245.1 (10), 231.1 (44), 221.1 (13), 203.1 (100), 189.1 (48), 171.1 (23), 105.0 (4); **HRMS (ESI)** *m/z* calcd. for $C_{15}H_{18}O_4Na$: 285.1097, found: 285.1098; **Anal** calcd. for $C_{15}H_{18}O_4$: C, 68.7; H, 6.9; O, 24.4; found: C, 68.6; H, 6.9; O, 24.5 %.

General Procedure for the Rearrangement of Dihydropyrans to Cyclopentenones. Methanol (0.03 ml, 0.2 mmol) and anhydrous *p*-toluenesulfonic acid (138 mg, 0.8 mmol) were added to a solution of dihydropyran (0.2 mmol) in toluene (1.5 ml). The reaction mixture was heated to 80 °C and stirred overnight at this temperature. The mixture was diluted with ethyl acetate and washed with a saturated aqueous $NaHCO_3$ solution. The organic layer was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by column chromatography on silica gel.

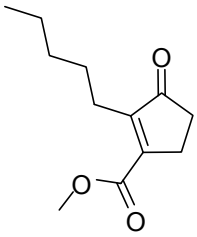


Methyl 3-oxo-2-phenylcyclopent-1-enecarboxylate 9a: Prepared according to general procedure in 69 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), yellow oil. The spectral data were identical with those in the literature.[12]

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-7.28 (m, 5H, Ar), 3.74 (s, 3H, OCH_3), 2.98-2.91 (m, 2H, H5), 2.69-2.63 (m, 2H, H4); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 207.2, 166.2, 156.4, 146.3, 130.1, 128.9, 128.8, 127.9, 52.2, 34.5, 27.0; **MS (TOF CI)** *m/z* (relative intensity) 217.1 $[M+H]^+$

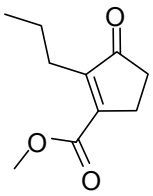
[12] J. T. Kuethe, A. Wong, J. Wu, I. W. Davies, P. G. Dormer, C. J. Welch, M. C. Hillier, D. L. Hughes, P. J. Reider, *J. Org. Chem.*, 2002, **67**, 5993.

(100), 185.1 (34), 129.1 (3); **HRMS (TOF CI)** *m/z* calcd. for $C_{13}H_{13}O_3$: 217.0865, found: 217.0863.



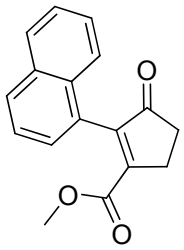
Methyl 3-oxo-2-pentylcyclopent-1-enecarboxylate 9b: Prepared according to general procedure in 20 % yield, purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H, OCH_3), 2.78-2.72 (m, 2H, H5), 2.52 (t, J = 7.7 Hz, 2H, CH_2), 2.48-2.43 (m, 2H, H4), 1.46-1.34 (m, 2H, CH_2), 1.34-1.22 (m, 4H, CH_2), 0.87 (t, J = 6.9 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 209.6, 165.8, 154.0, 151.8, 52.0, 34.0, 31.9, 28.1, 26.4, 24.0, 22.4, 13.9; **IR** ν_{max} [cm^{-1}] 2955, 2928, 2859, 1713, 1679, 1461, 1436, 1274, 1224, 1182, 1101; **MS (TOF CI)** *m/z* (relative intensity) 211.1 $[M+H]^+$ (100), 195.1 (5), 151.1 (4); **HRMS (TOF CI)** *m/z* calcd. for $C_{12}H_{19}O_3$: 211.1334, found: 211.1328.



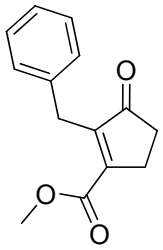
Methyl 3-oxo-2-propylcyclopent-1-enecarboxylate 9c: Prepared according to general procedure in 44 % yield, purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 3H, OCH_3), 2.78-2.72 (m, 2H, H5), 2.54-2.43 (m, 4H, H4, CH_2), 1.50-1.37 (m, 2H, CH_2), 0.90 (t, J = 7.4 Hz, 3H, CH_3); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 209.6, 165.8, 154.2, 151.4, 52.0, 34.0, 26.4, 25.9, 21.8, 14.1; **IR** ν_{max} [cm^{-1}] 2958, 2929, 2872, 1712, 1693, 1462, 1439, 1366, 1256, 1237, 1207, 1190, 1179, 1129, 1100; **LRMS (APCI)** *m/z* (relative intensity) 183.7 $[M+H]^+$ (100), 151.6 (5), 123.6 (13), 105.7 (4), 75.7 (5), 59.5 (3).



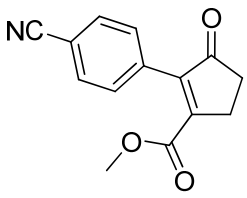
Methyl 2-(naphthalen-1-yl)-3-oxocyclopent-1-enecarboxylate 9d: Prepared according to general procedure in 40 % yield, purified by column chromatography (petroleum ether/ethyl acetate 9:1), brown amorphous solid.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91-7.85 (m, 2H, Ar), 7.55-7.39 (m, 5H, Ar), 3.50 (s, 3H, OCH_3), 3.22-2.99 (m, 2H, CH_2), 2.83-2.75 (m, 2H, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 207.5, 165.4, 158.6, 147.4, 133.4, 131.1, 129.0, 128.5, 128.2, 126.7, 126.1, 125.8, 125.0, 124.7, 52.1, 34.7, 27.2; **IR** ν_{max} [cm^{-1}] 2925, 2854, 1729, 1709, 1507, 1436, 1395, 1259, 1231, 1201, 1161, 1108, 1047; **LRMS (APCI)** *m/z* (relative intensity) 267.4 $[M+H]^+$ (12), 235.5 (100), 85.5 (5), 59.1 (4).



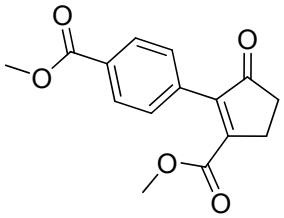
Methyl 2-benzyl-3-oxocyclopent-1-enecarboxylate 9e: Prepared according to general procedure in 38 % yield, purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellowish oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.14 (m, 5H, Ar), 3.92 (s, 2H, CH_2), 3.87 (s, 3H, OCH_3), 2.82-2.75 (m, 2H, CH_2), 2.50-2.44 (m, 2H, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 209.1, 165.6, 154.6, 149.6, 138.3, 129.0, 128.4, 126.3, 52.1, 34.0, 29.6, 26.6; **IR** ν_{max} [cm^{-1}] 2951, 2922, 2852, 1754, 1710, 1494, 1453, 1435, 1292, 1252, 1233, 1173, 1109, 1077, 1051; **LRMS (APCI)** *m/z* (relative intensity) 230.9 $[M+H]^+$ (100), 198.9 (34), 182.5 (12), 158.7 (24), 137.1 (3).



Methyl 2-(4-cyanophenyl)-3-oxocyclopent-1-enecarboxylate 9f: Prepared according to general procedure in 22 % yield, purified by column chromatography (petroleum ether/ethyl acetate 85:15), yellow oil.

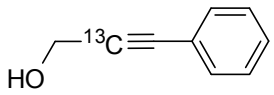
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72-7.63 (m, 2H, AA', BB', Ar), 7.46-7.38 (m, 2H, AA', BB', Ar), 3.76 (s, 3H, OCH_3), 3.02-2.92 (m, 2H, CH_2), 2.73-2.62 (m, 2H, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 206.1, 165.2, 158.0, 145.1, 134.9, 131.6, 129.8, 118.5, 112.4, 52.4, 34.5, 27.2; **IR** ν_{max} [cm^{-1}] 2927, 2852, 2222, 1730, 1712, 1437, 1343, 1214, 1183, 1161, 1091; **LRMS (APCI)** *m/z* (relative intensity) 242.3 $[M+H]^+$ (100), 210.3 (50), 156.4 (3), 75.6 (5).



Methyl 2-(4-(methoxycarbonylphenyl)-3-oxocyclopent-1-enecarboxylate 9g: Prepared according to general procedure in 20 % yield, purified by column chromatography (petroleum ether/ethyl acetate 85:15), yellow oil.

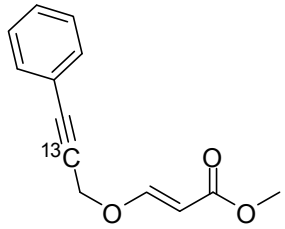
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08-8.03 (m, 2H, AA', BB', Ar), 7.40-7.35 (m, 2H, AA', BB', Ar), 3.92 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3), 2.99-2.94 (m, 2H, CH_2), 2.71-2.65 (m, 2H, CH_2); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 206.6, 166.7, 165.8, 157.5, 145.7, 134.8, 130.2, 129.1, 129.0, 52.3, 52.2, 34.6, 27.1; **IR** ν_{max} [cm^{-1}] 2923, 2852, 1715, 1436, 1277, 1227, 1183, 1161, 1111; **LRMS (APCI)** *m/z* (relative intensity) 274.9 $[M+H]^+$ (100), 256.9 (2), 243.9 (16), 148.5 (3).

Preparation of ^{13}C-labelled compounds.



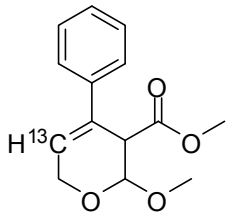
3-phenylprop-2-yn-1-ol-2-^{13}C: Prepared according to general procedure for formation of propargylic alcohols from alkynes in 92 % yield, purified by column chromatography (petroleum ether/ethyl acetate 8:2), colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46-7.41 (m, 2H, Ar), 7.34-7.28 (m, 3H, Ar), 4.50 (d, *J* = 7.5 Hz, 2H, OCH_2), 1.95 (bs, 1H, OH); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 131.6 (d, *J* = 2.5 Hz), 128.4, 128.3, 122.5 (d, *J* = 12.4 Hz), 87.2 (^{13}C), 86.4 (d, *J* = 83.1 Hz), 51.6 (d, *J* = 73.7 Hz).



(*E*)-Methyl 3-(3-phenylprop-2-ynyloxy)acrylate-2'-^{13}C: Prepared according to general procedure for the addition of propargylic alcohols to methyl propiolate in 99 % yield, purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellowish oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 12.6 Hz, 1H, H3), 7.47-7.43 (m, 2H, Ar), 7.37-7.29 (m, 3H, Ar), 5.39 (d, *J* = 12.6 Hz, 1H, H2), 4.75 (d, *J* = 7.9 Hz, 2H, OCH_2), 3.72 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 167.7, 160.9 (d, *J* = 2.5 Hz), 131.8 (d, *J* = 2.6 Hz), 129.0, 128.3, 121.7 (d, *J* = 12.8 Hz), 98.0, 82.1 (d, *J* = 92.9 Hz), 81.8 (^{13}C), 59.1 (d, *J* = 79.2 Hz), 51.2.



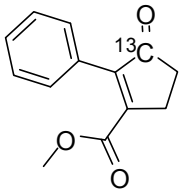
Methyl 3,6-dihydro-2-methoxy-4-phenyl-2*H*-pyran-3-carboxylate-5-^{13}C:

Prepared according to general procedure for gold(I)-catalyzed cyclisation to dihydropyrans in 80 % yield (58 % *trans*, 22 % *cis*), purified by column chromatography (petroleum ether/ethyl acetate 95:5), white amorphous solid.

***trans* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.22 (m, 5H, Ar), 6.21 (dt, *J* = 157.9 Hz, *J* = 2.8 Hz, 1H, H5), 5.15 (d, *J* = 2.2 Hz, 1H, H2), 4.38 (dt, *J* = 5.2 Hz, *J* = 2.2 Hz, 2H, H6), 3.72-3.69 (m, 1H, H3), 3.63 (s, 3H, $COOCH_3$), 3.51 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.9 (d, *J* = 2.9 Hz), 139.1, 130.1 (d, *J* = 74.2 Hz), 128.4, 127.5, 125.2 (d, *J* = 3.8 Hz), 123.7 (^{13}C), 98.6 (d, *J* = 4.5 Hz), 60.7 (d, *J* = 42.6 Hz), 55.8, 52.3, 48.0.

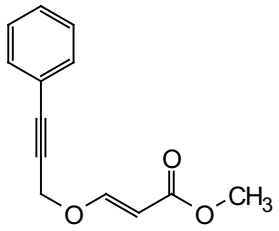
***cis* isomer: ^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34-7.22 (m, 5H, Ar), 6.23 (d, *J* = 158.1 Hz, 1H, H5), 4.99 (d, *J* = 4.2 Hz, 1H, H2), 4.55 (ddt, *J* = 17.0 Hz, *J* = 5.4 Hz, *J* = 2.6 Hz, 1H, H6), 4.32 (ddt, *J* = 17.0 Hz, *J* = 5.4 Hz, *J* = 2.6 Hz, 1H, H6), 4.01-3.97 (m, 1H, H3), 3.60 (s, 3H,

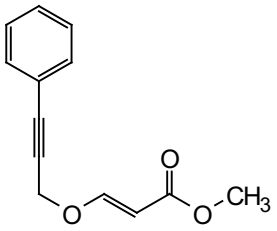
$COOCH_3$), 3.53 (s, 3H, OCH_3); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 170.0 (d, *J* = 2.7 Hz), 139.1, 131.2 (d, *J* = 74.0 Hz), 128.5, 127.5, 124.8 (d, *J* = 3.8 Hz), 124.2 (^{13}C), 98.5 (d, *J* = 4.8 Hz), 62.0 (d, *J* = 42.9 Hz), 56.4, 52.2, 47.5.

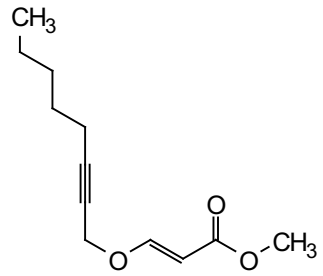


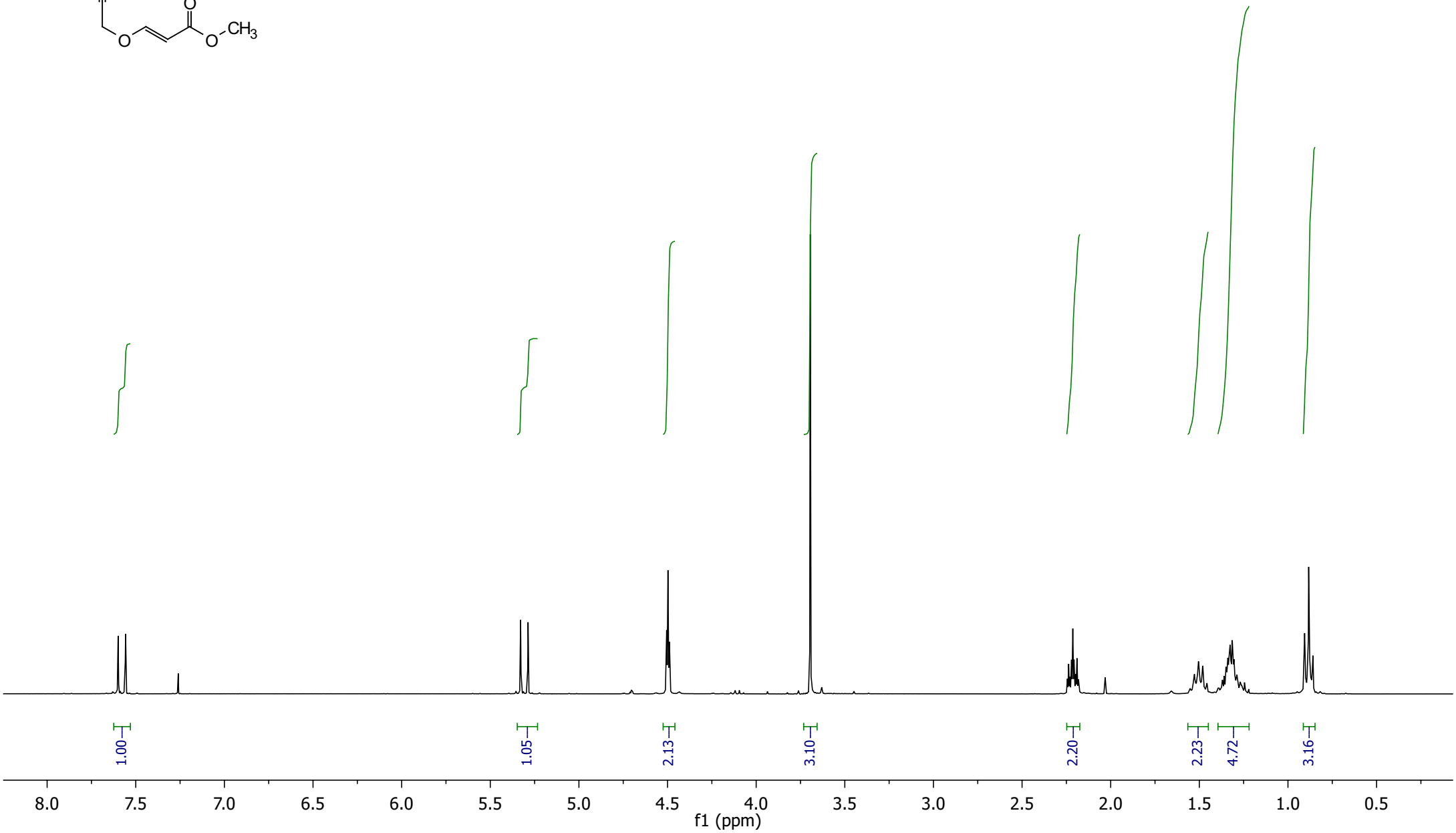
Methyl 3-oxo-2-phenylcyclopent-1-enecarboxylate-3-^{13}C: Prepared according to general procedure for the rearrangement of dihydropyrans to cyclopentenones in 69 % yield, purified by column chromatography (petroleum ether/ethyl acetate 95:5), yellow oil.

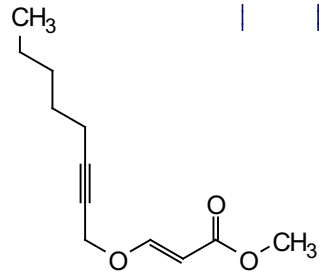
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.27 (m, 5H, Ar), 3.74 (s, 3H, OCH_3), 2.96-2.91 (m, 2H, H5), 2.68-2.63 (m, 2H, H4); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 207.2 (^{13}C), 166.2 (d, *J* = 8.0 Hz), 156.4 (d, *J* = 12.0 Hz), 146.2 (d, *J* = 46.9 Hz), 130.1 (d, *J* = 2.0 Hz), 128.9, 128.8, 127.9, 52.2, 34.5 (d, *J* = 39.6 Hz), 27.0 (d, *J* = 3.3 Hz).

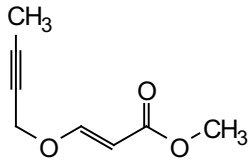


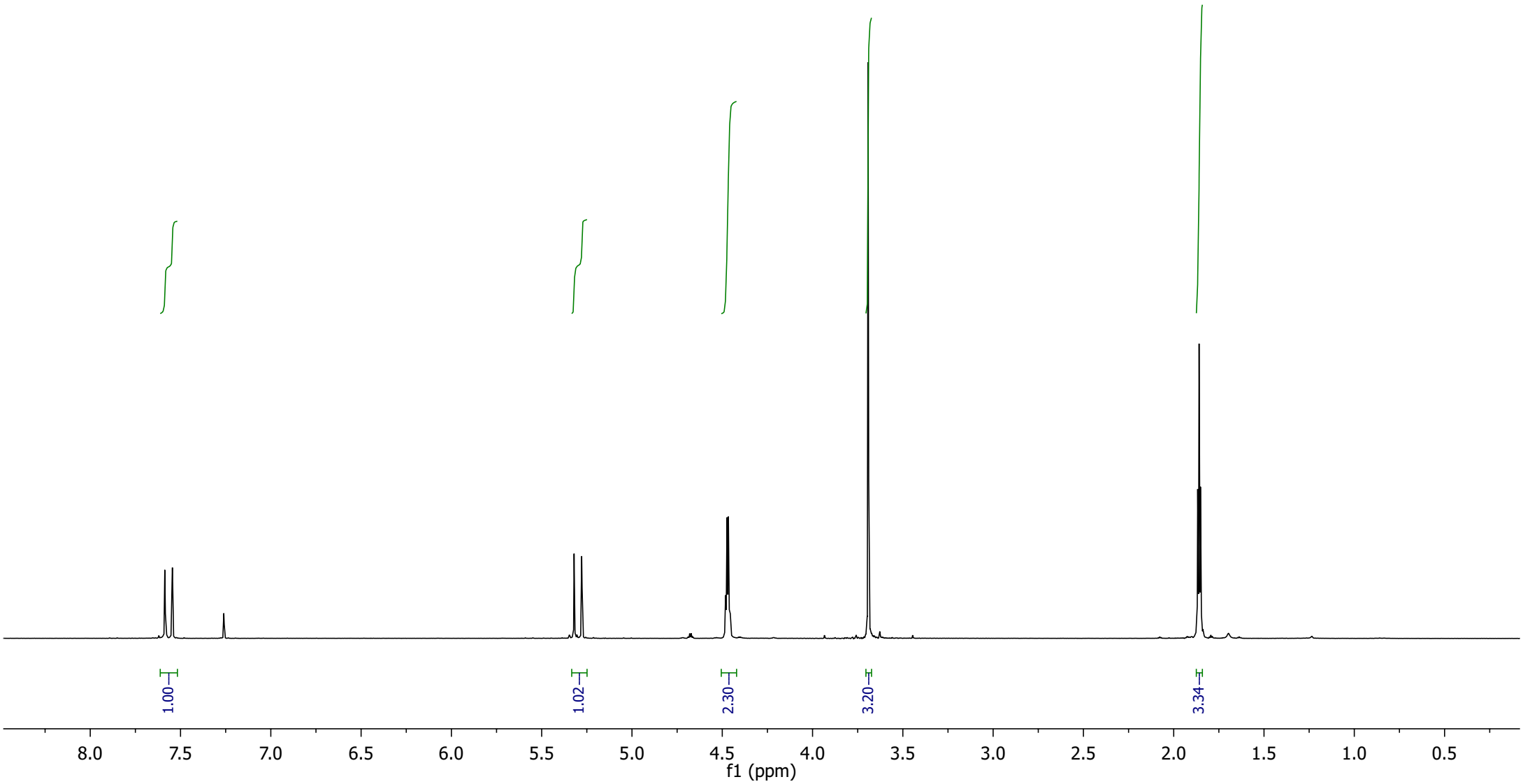


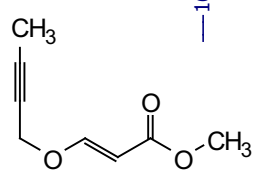


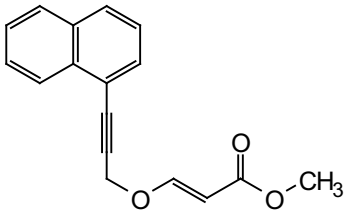


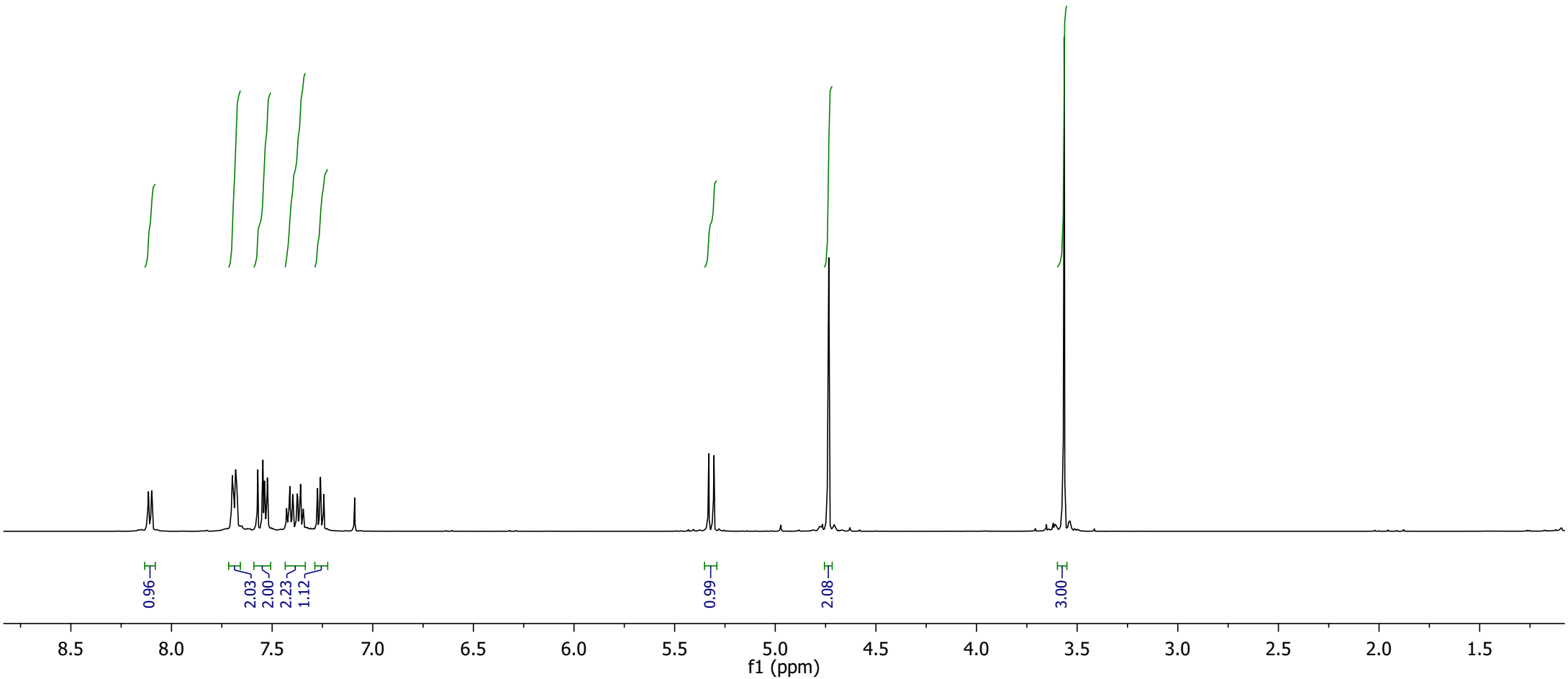


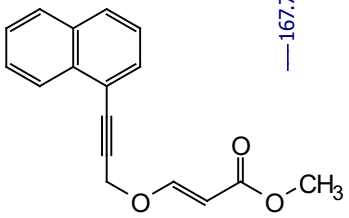


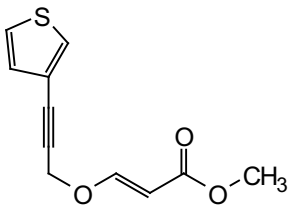


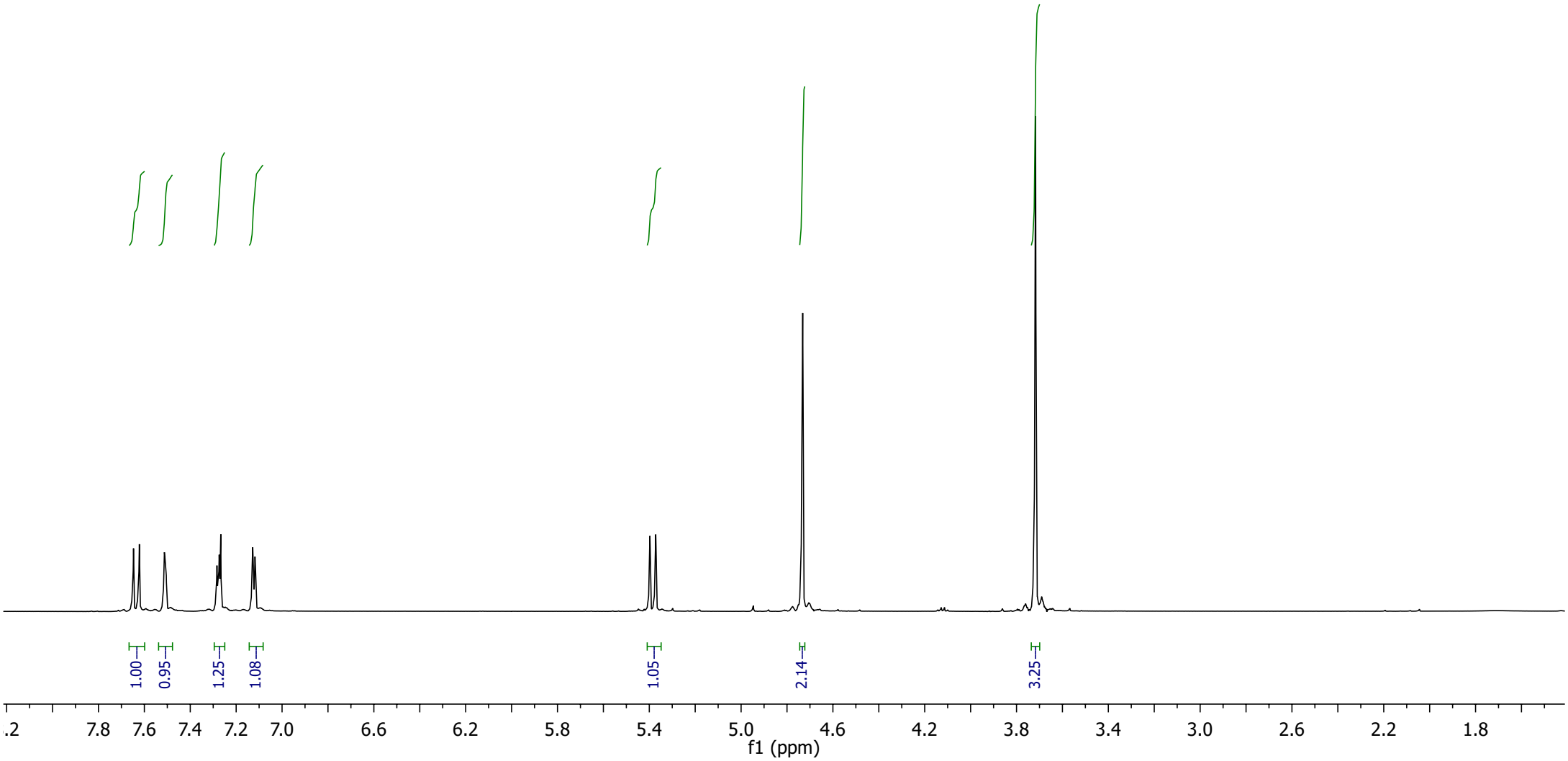


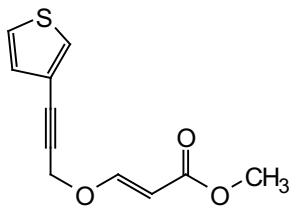


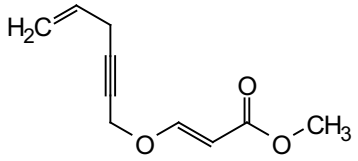


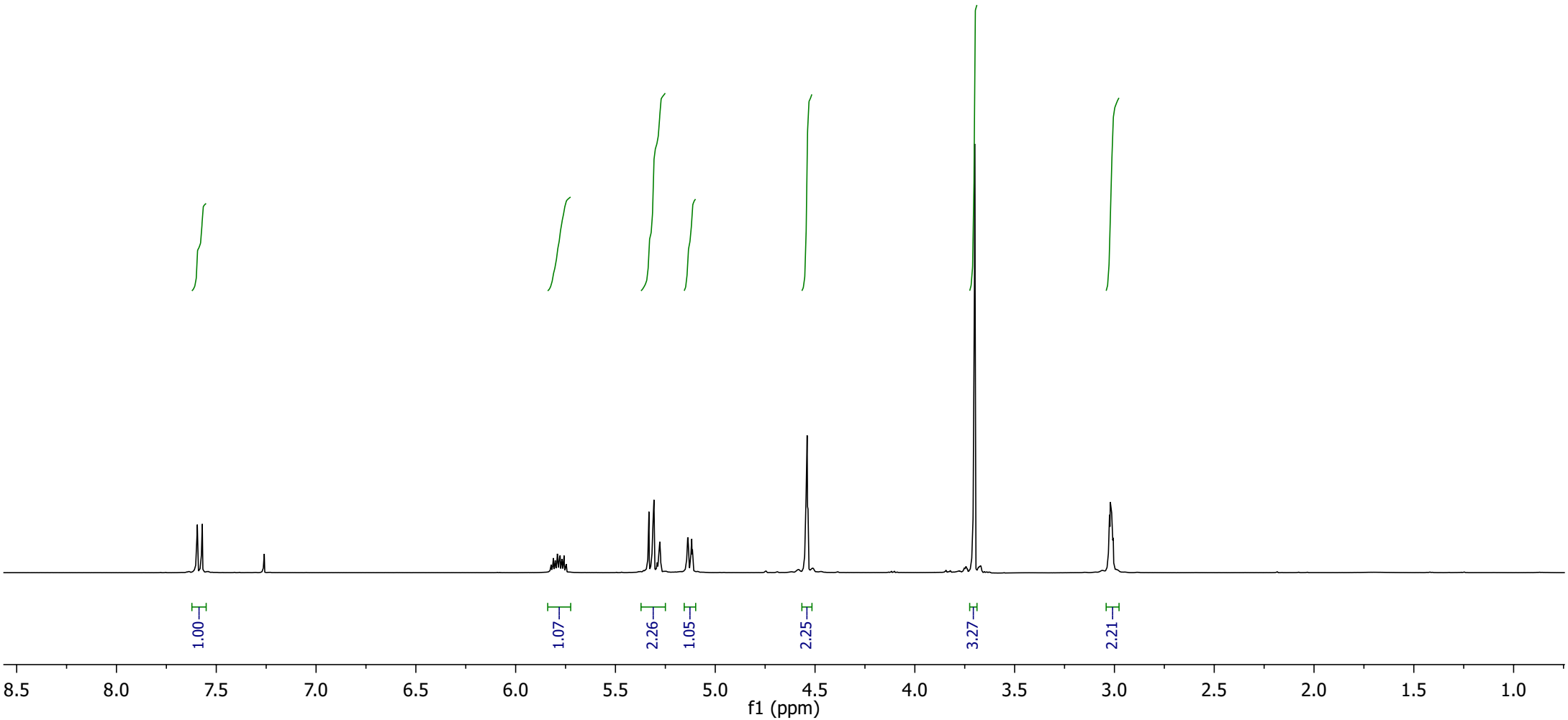


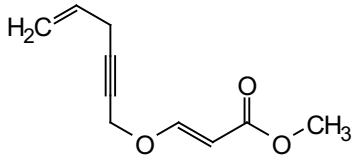


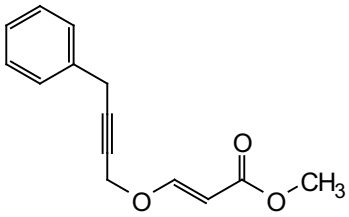


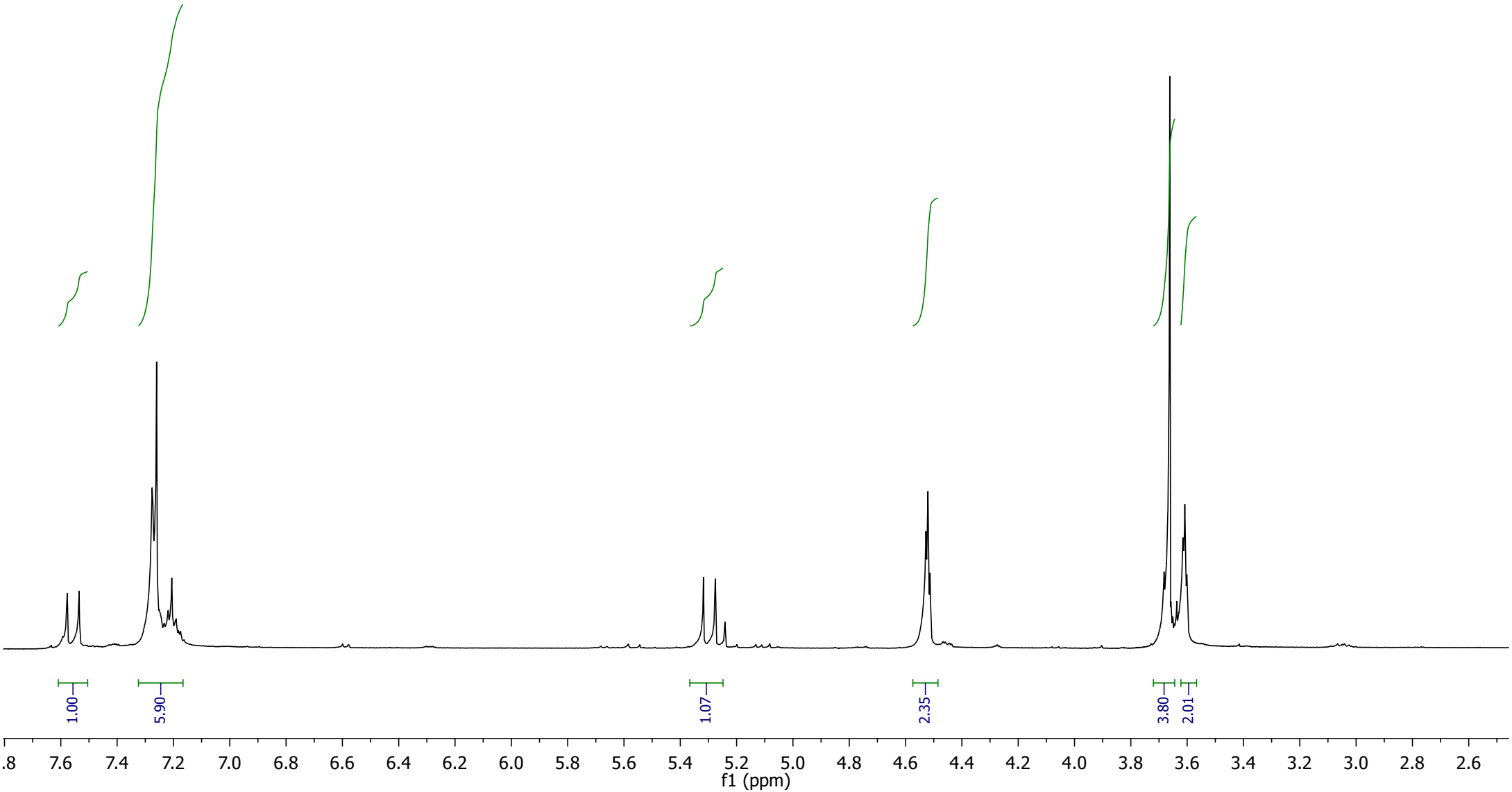


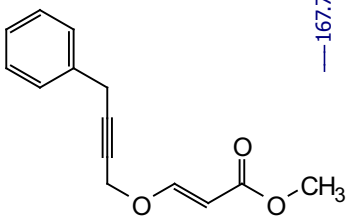


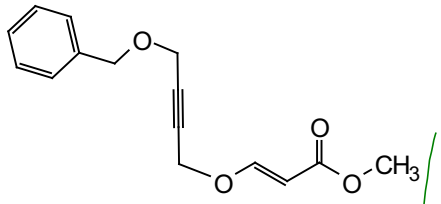


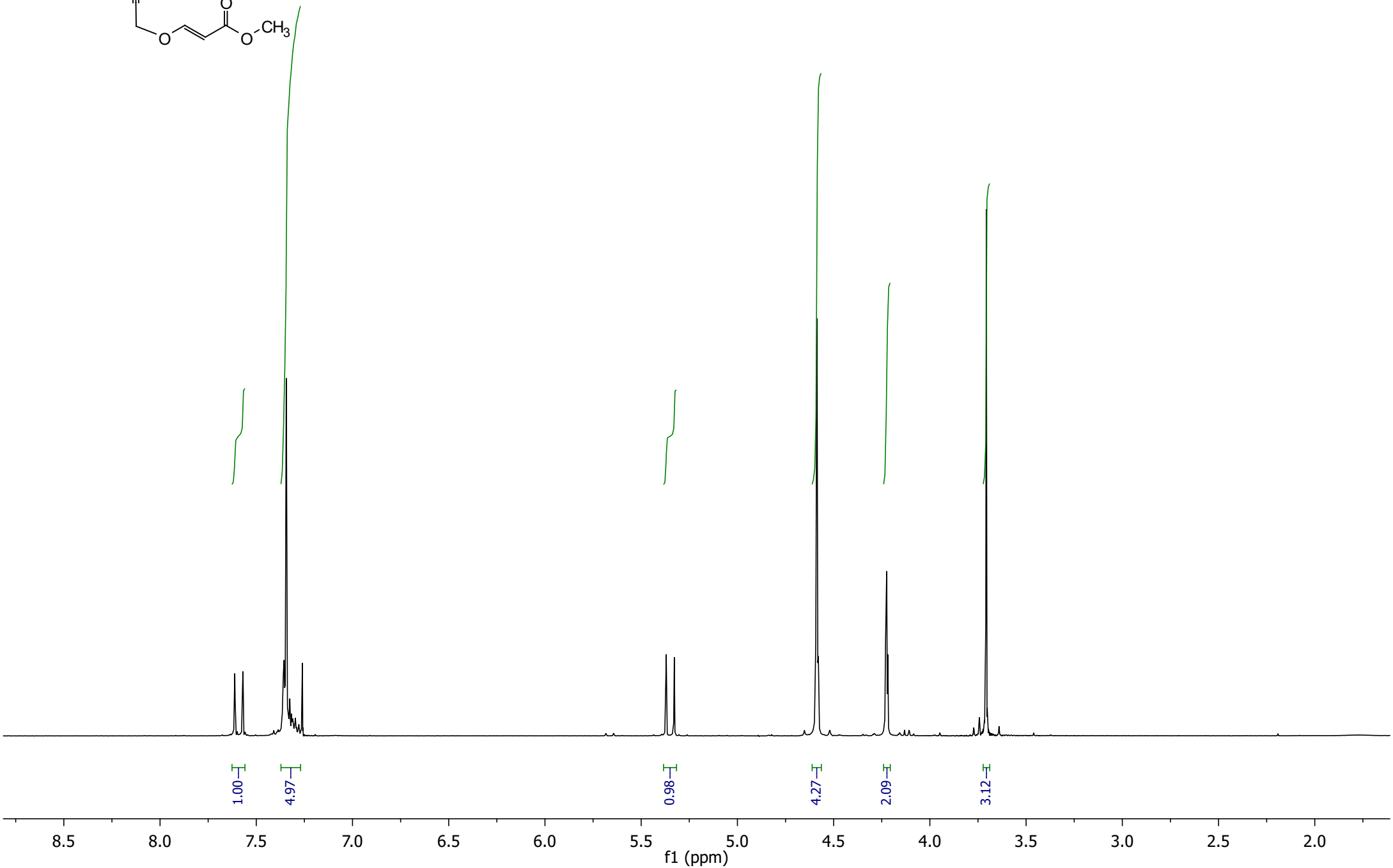


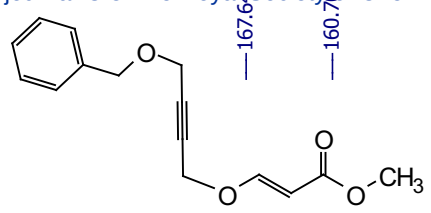


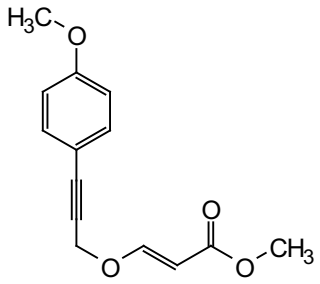


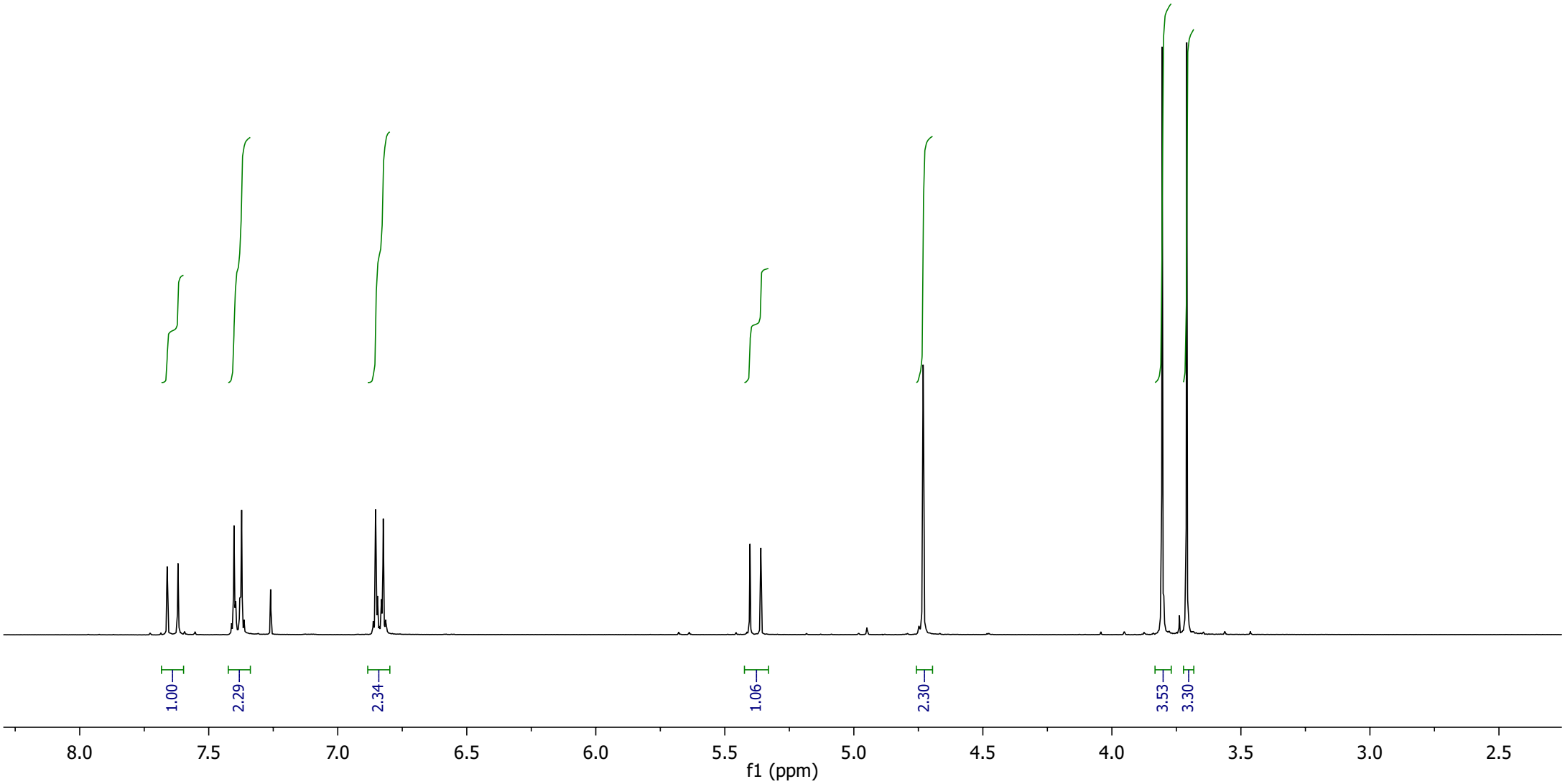


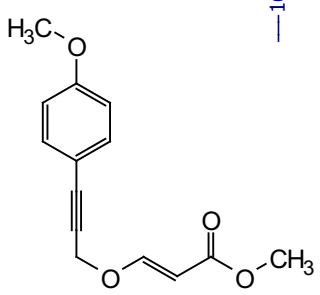


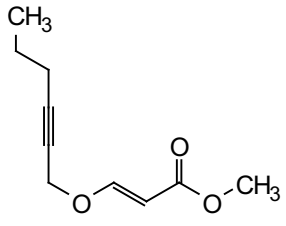


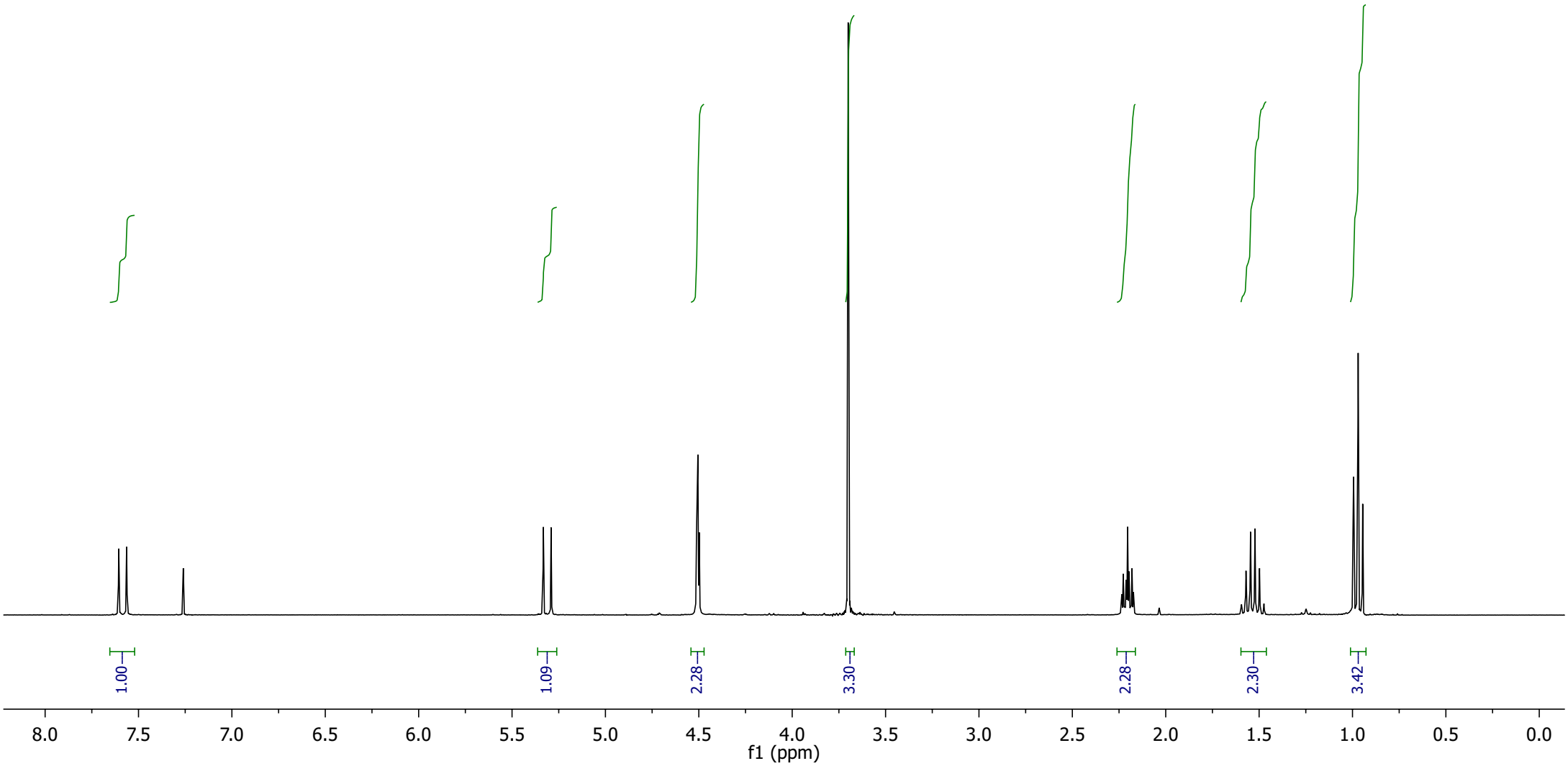


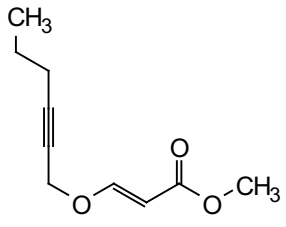


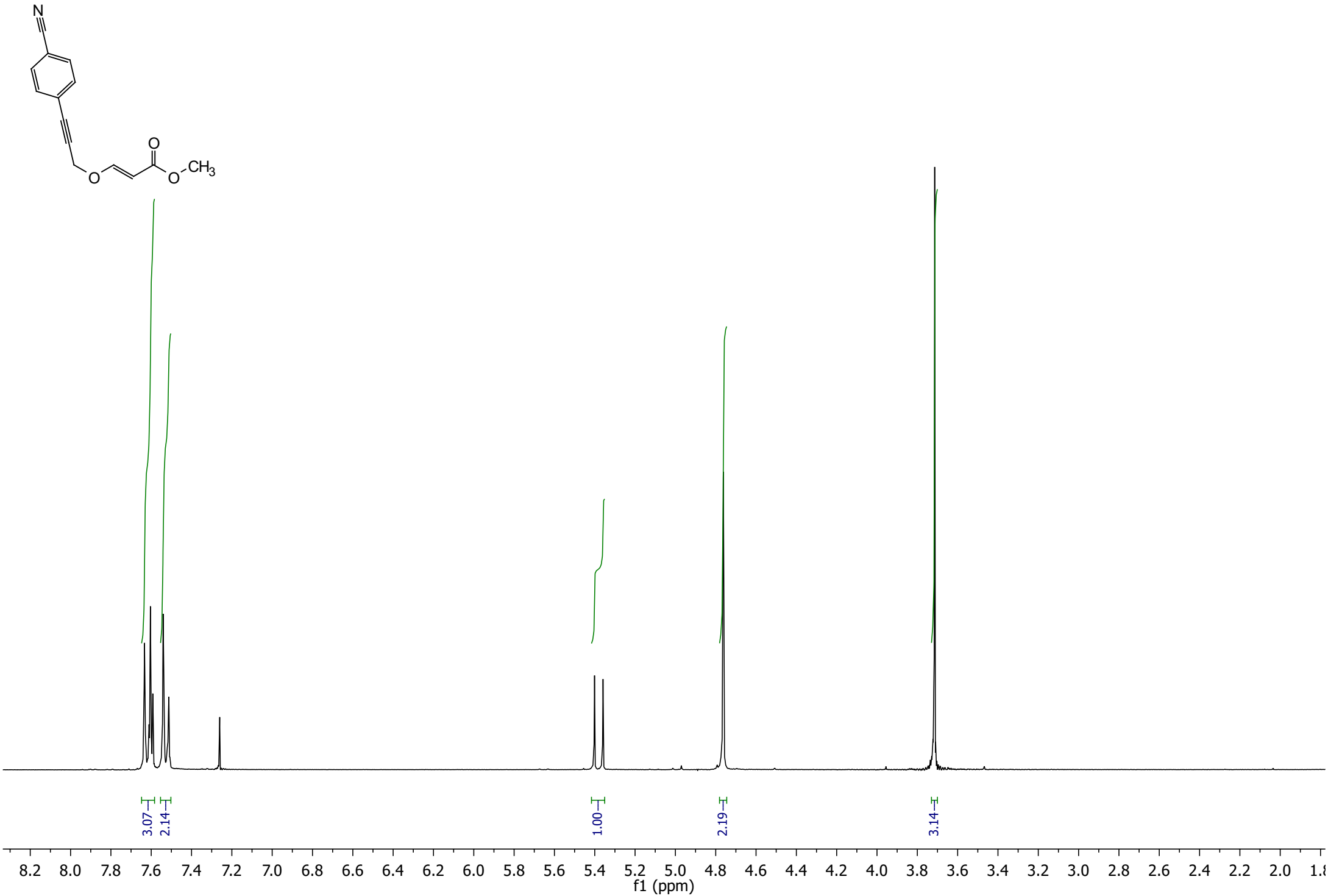


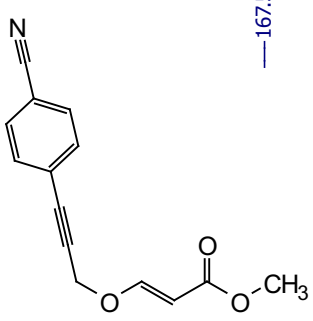


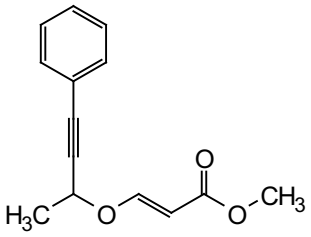


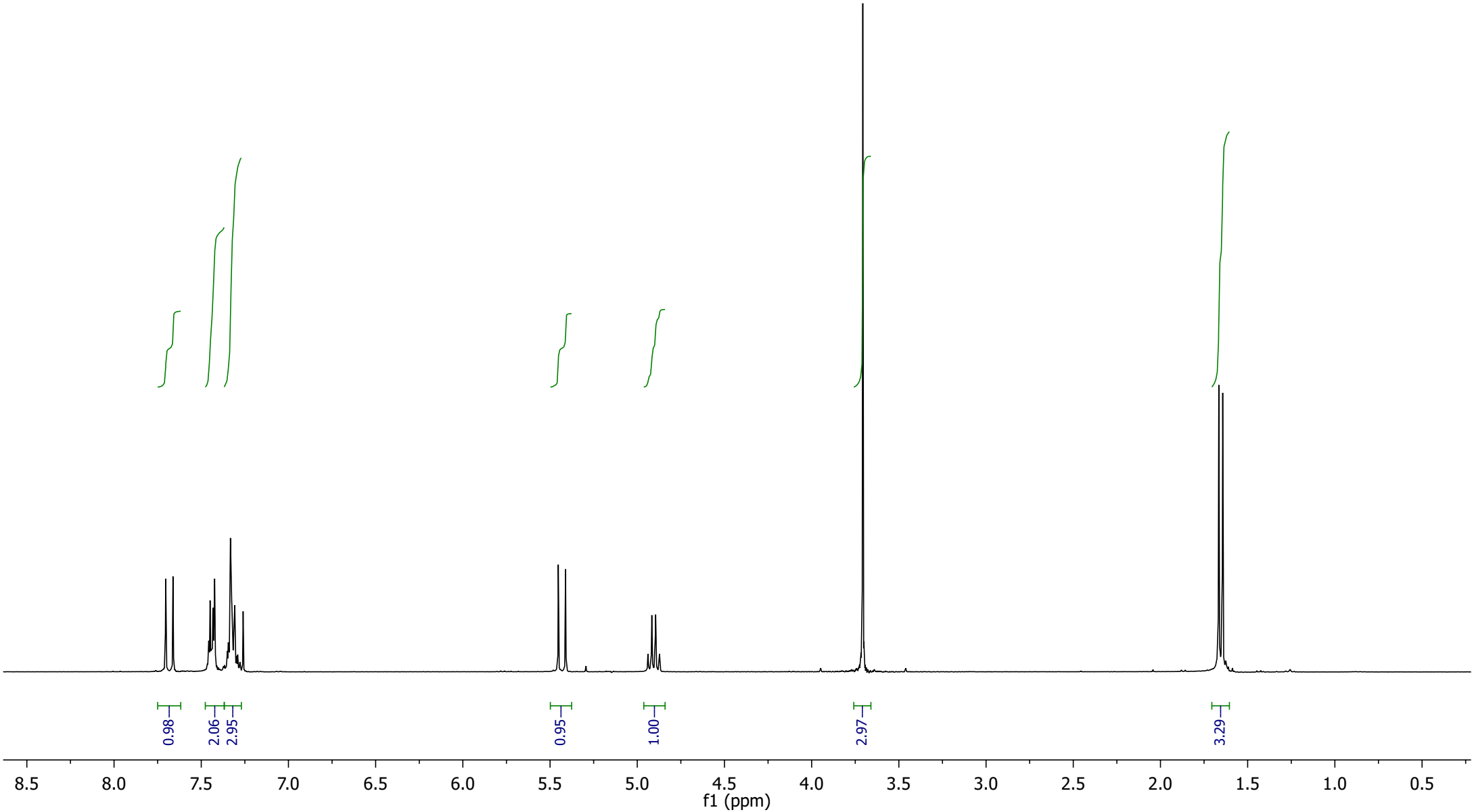


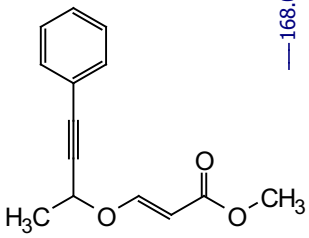


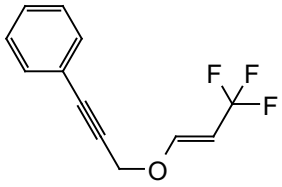


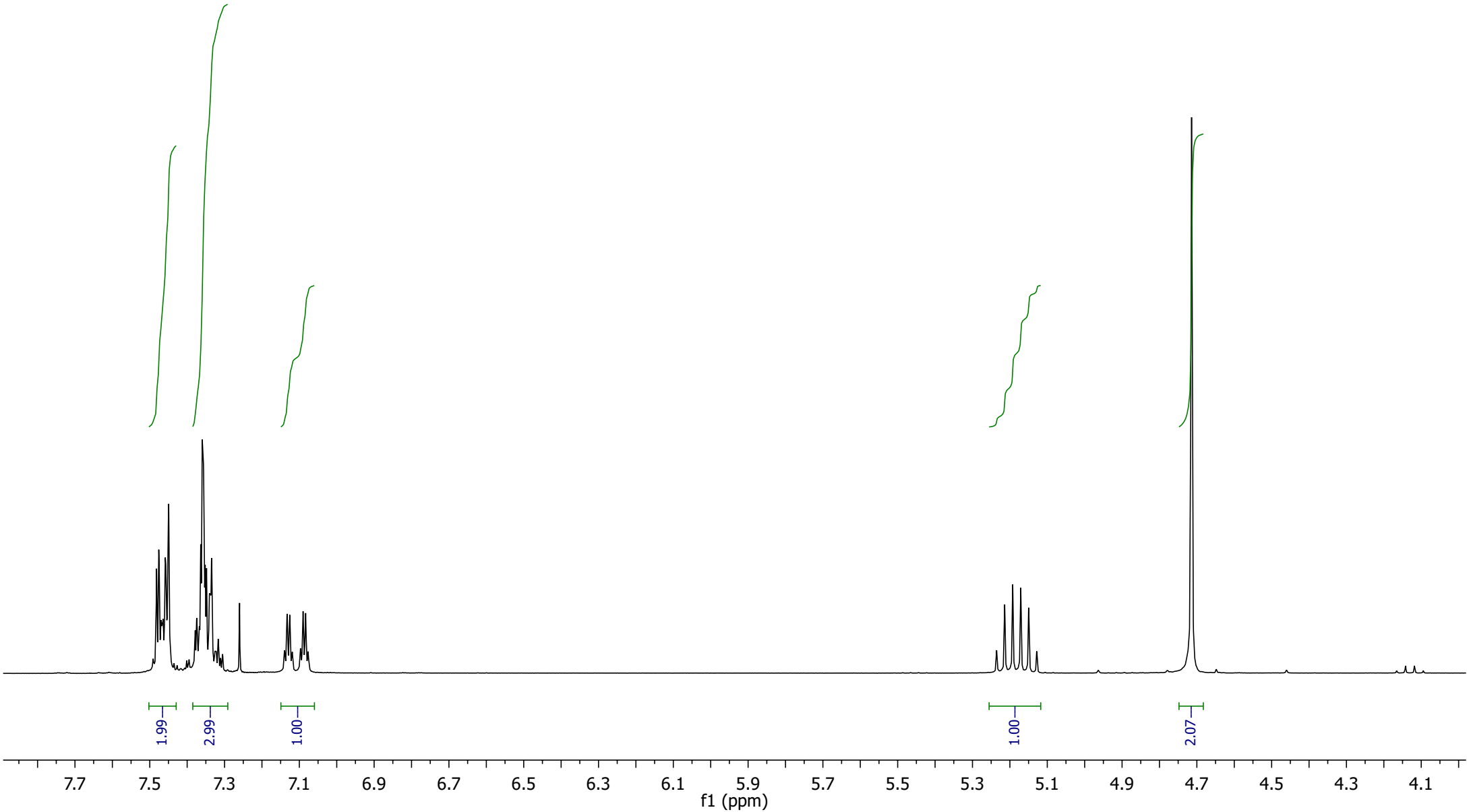


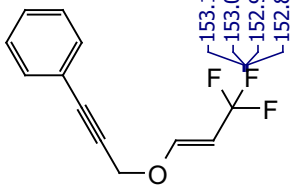


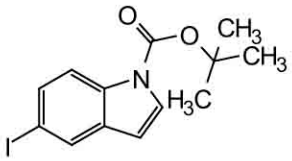


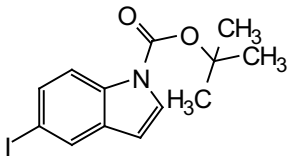


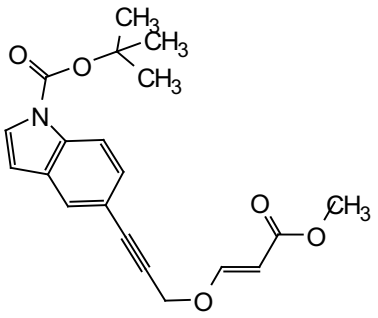


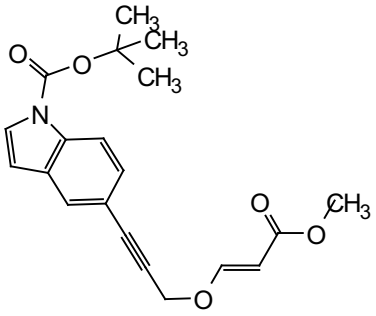


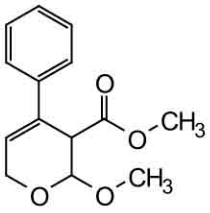




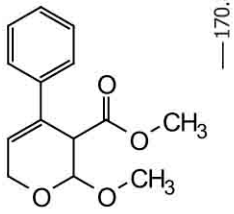




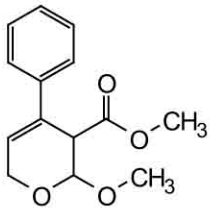




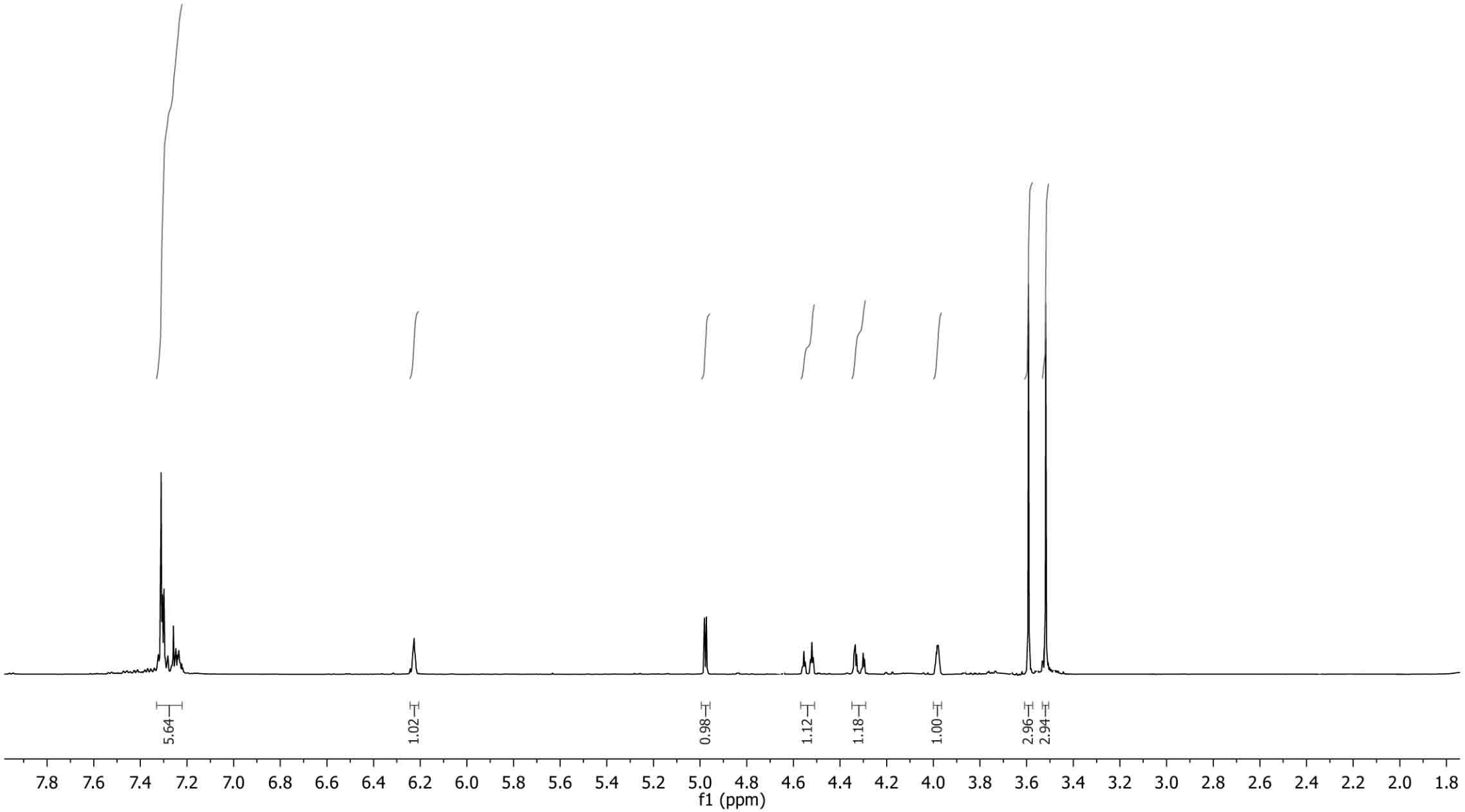
trans isomer

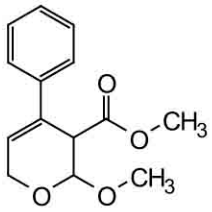


trans isomer

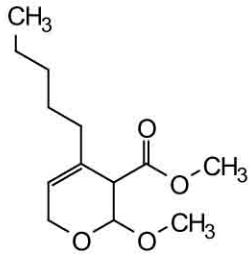


cis isomer

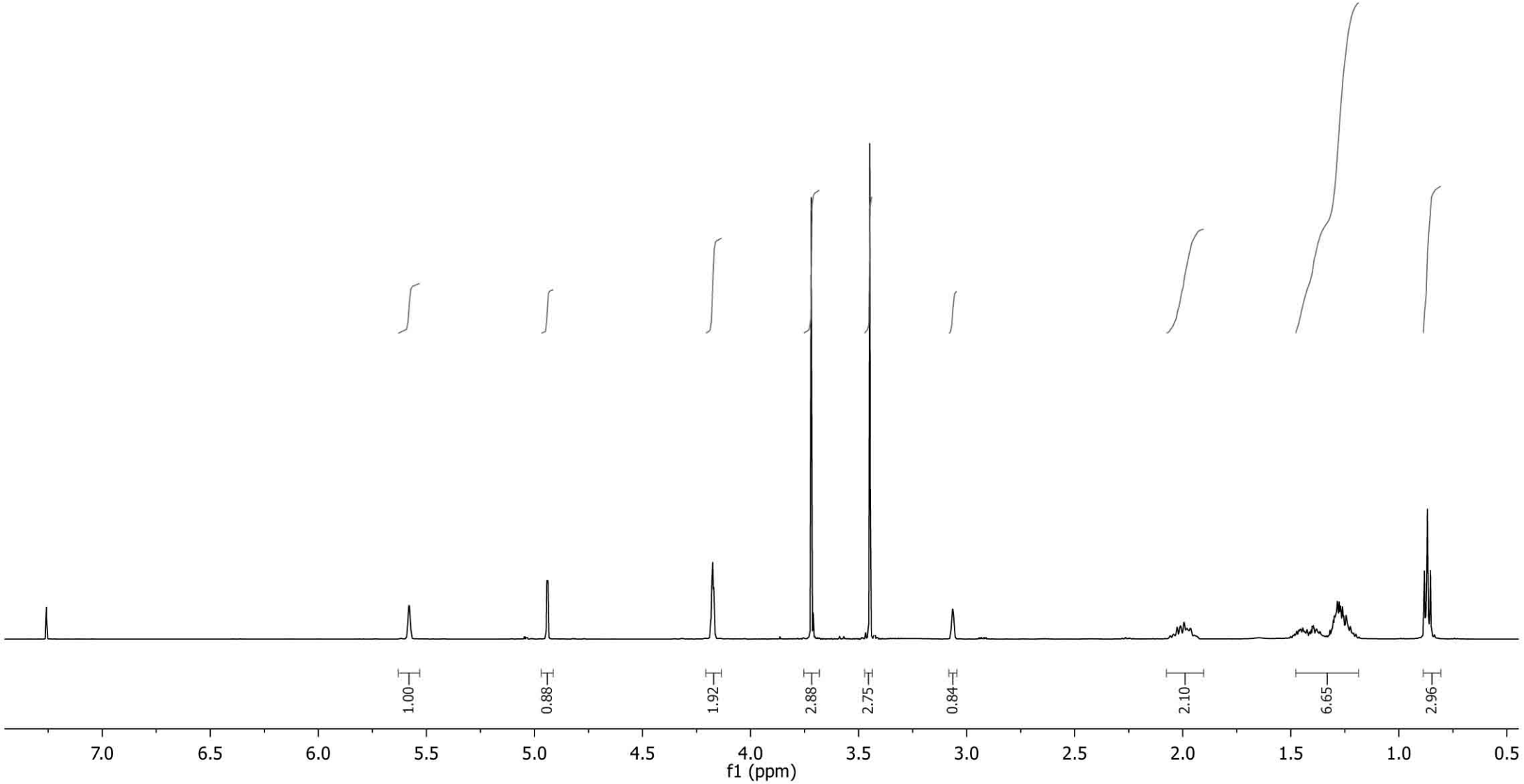


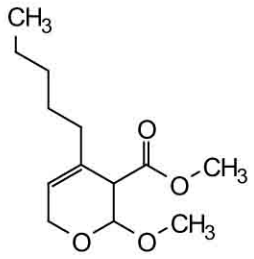


cis isomer

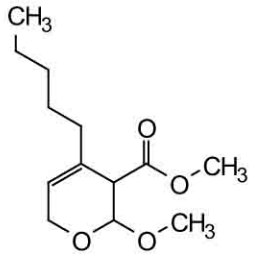


trans isomer

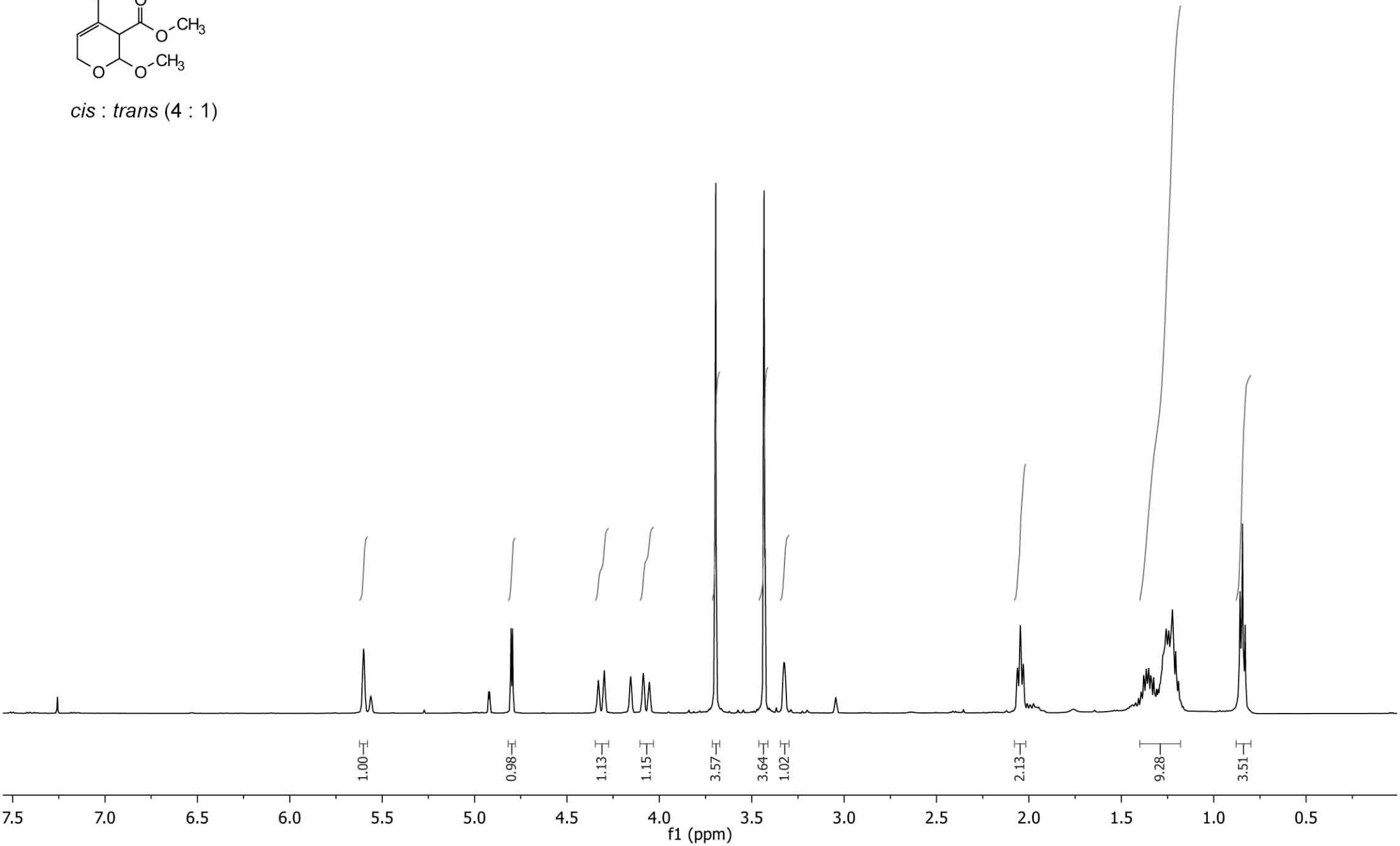


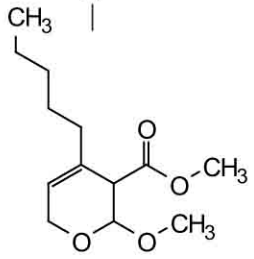


trans isomer

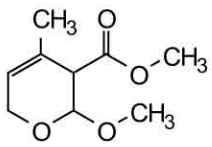


cis : *trans* (4 : 1)

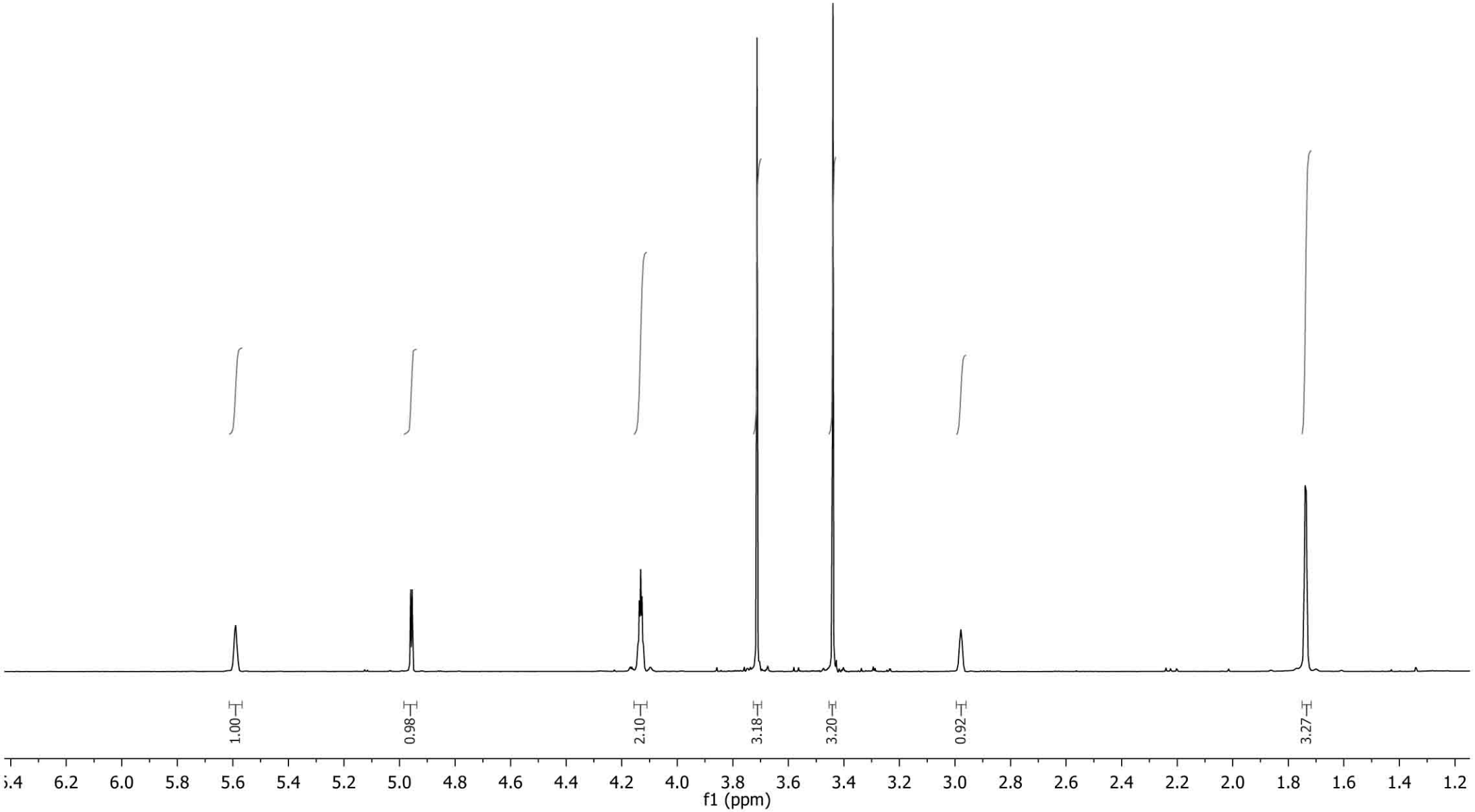


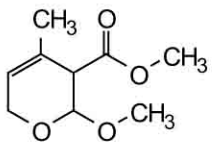


cis : *trans* (4 : 1)

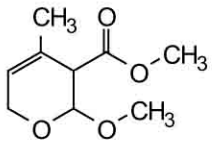


trans isomer

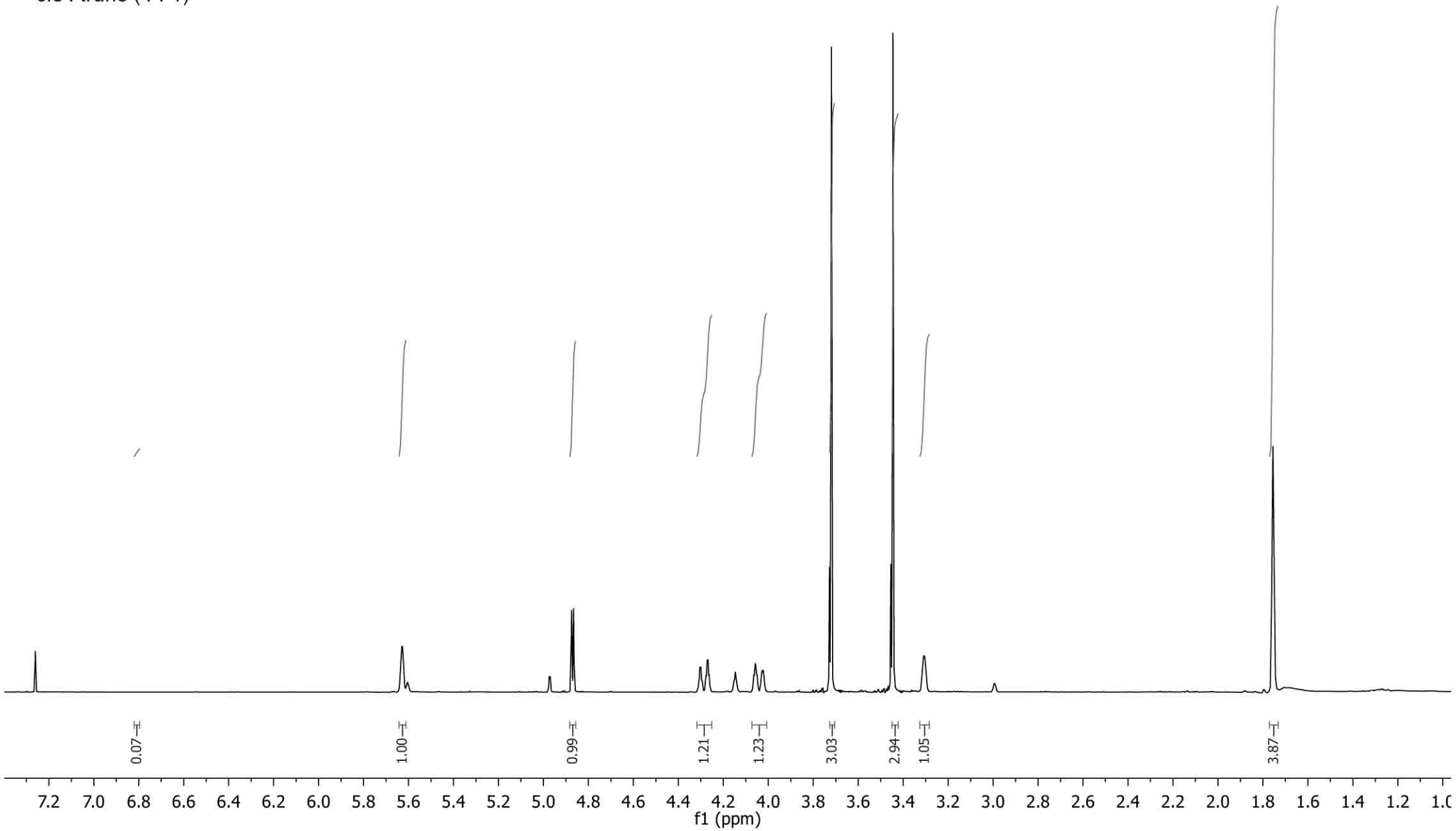


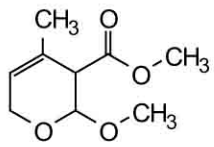


trans isomer

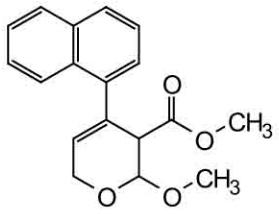


cis : *trans* (4 : 1)

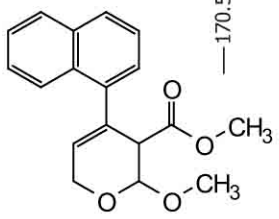




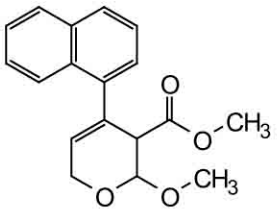
cis : *trans* (4 : 1)



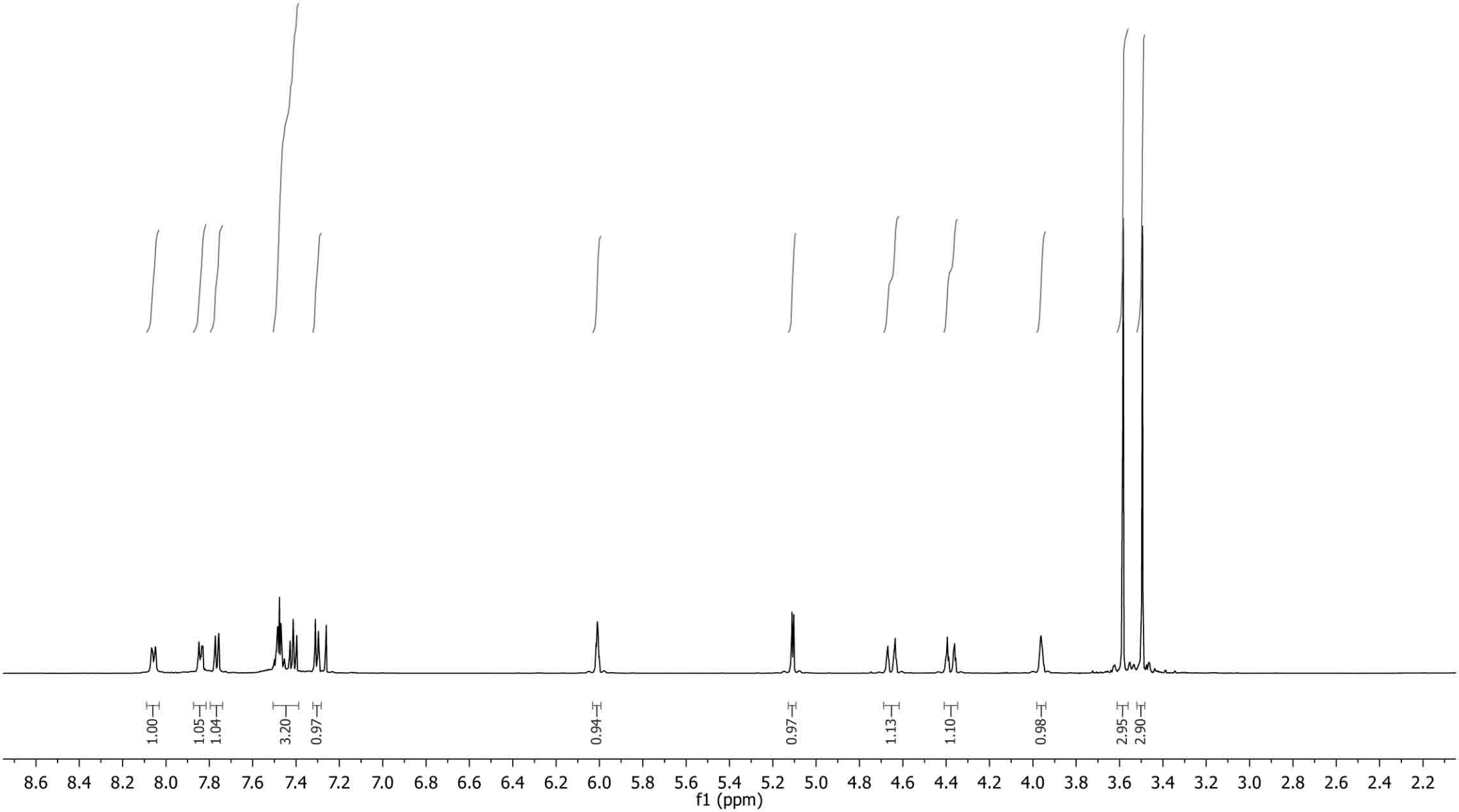
trans isomer

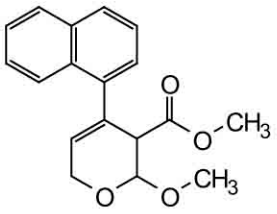


trans isomer

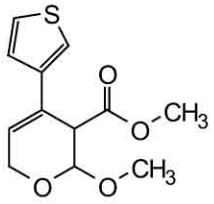


cis isomer

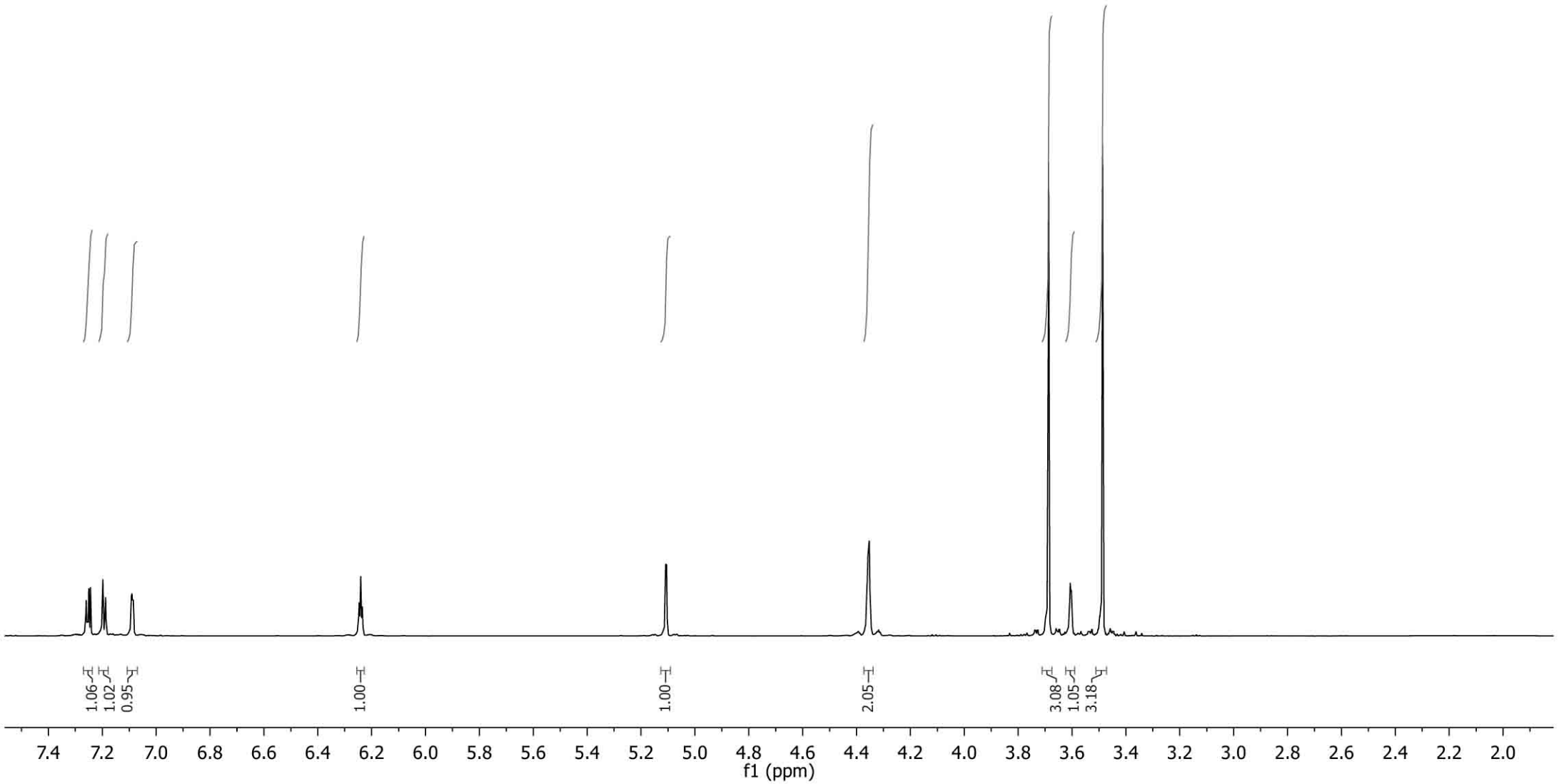


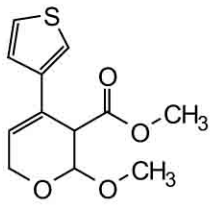


cis isomer

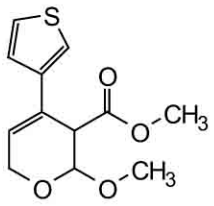


trans isomer

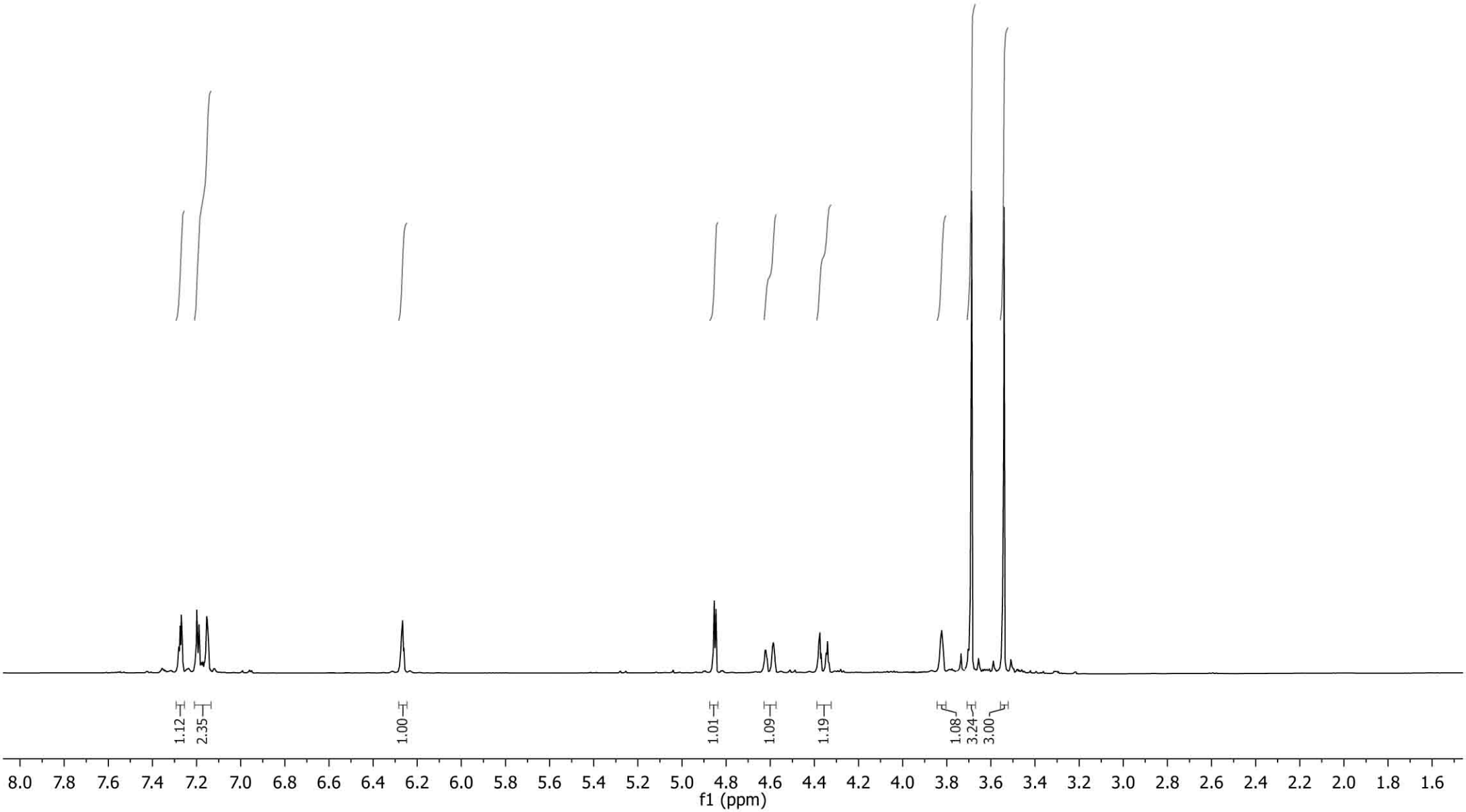


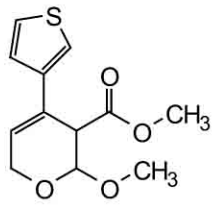


trans isomer

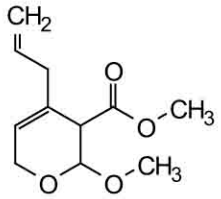


cis isomer

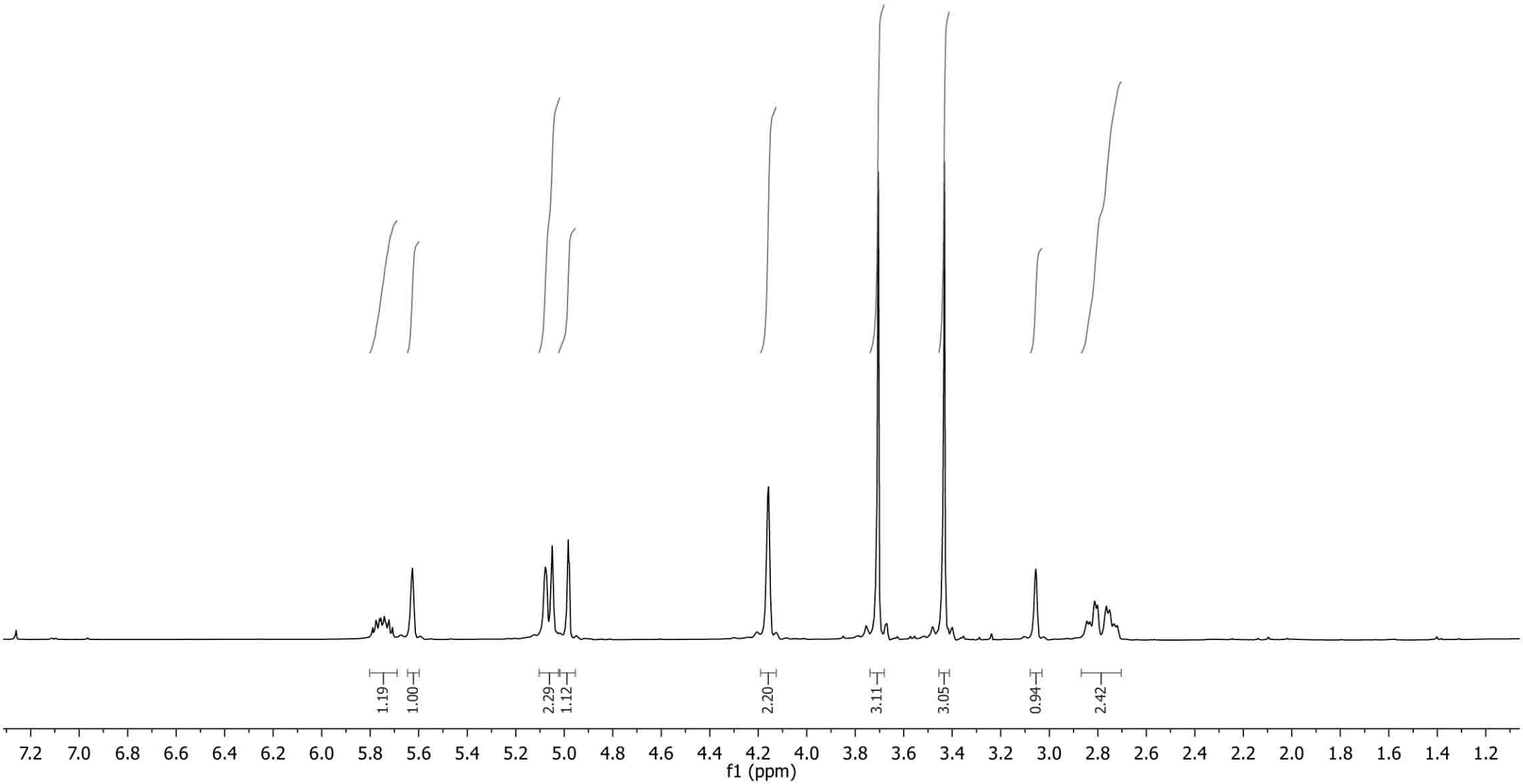


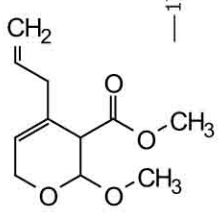


cis isomer

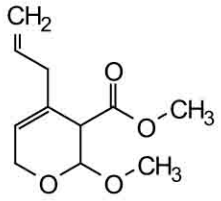


trans isomer

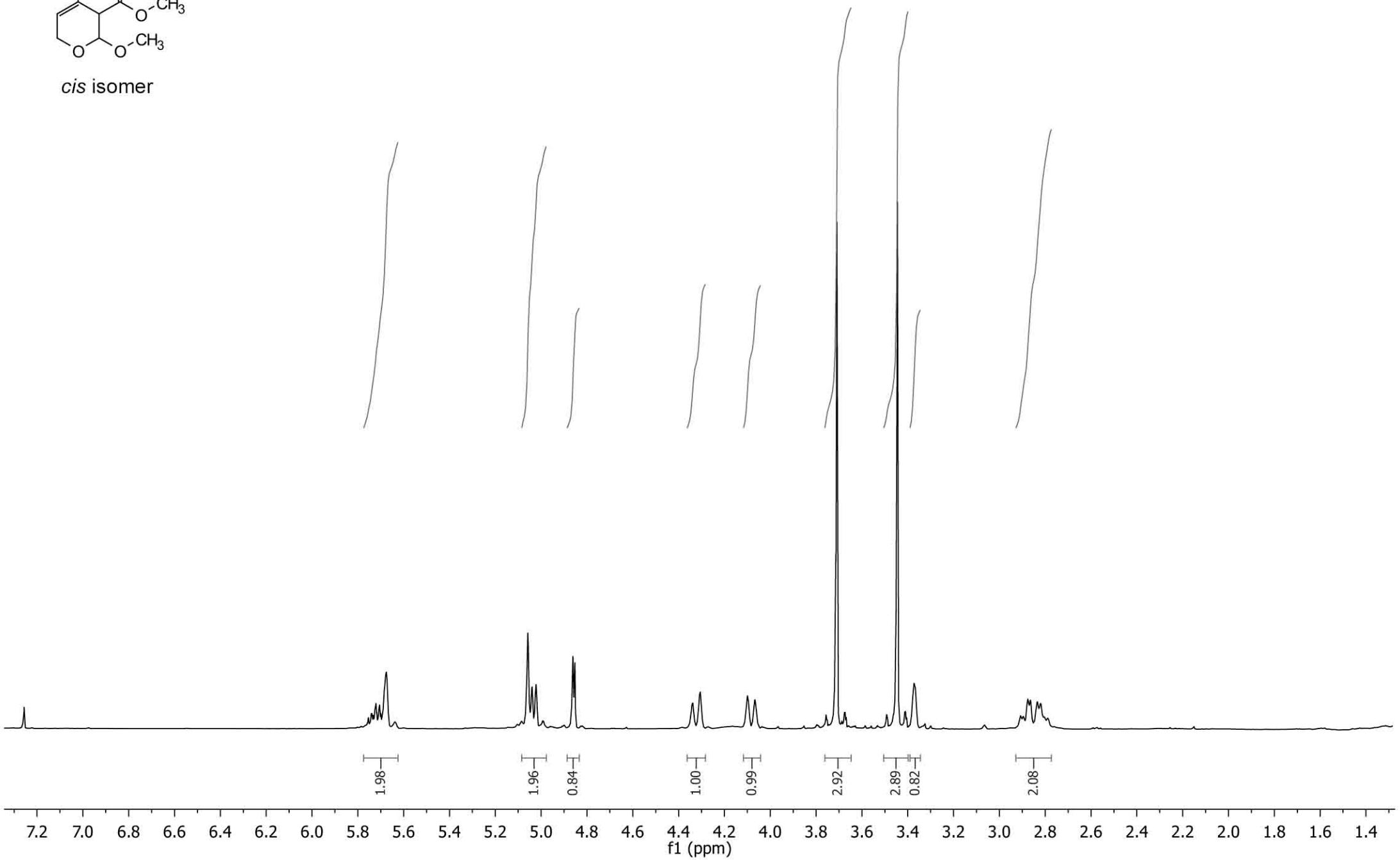


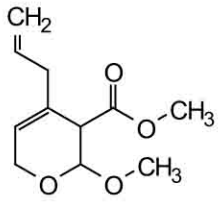


trans isomer

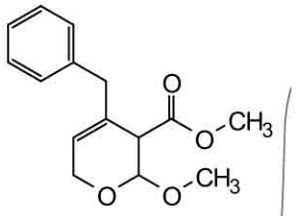


cis isomer

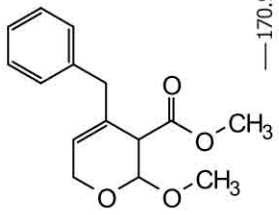




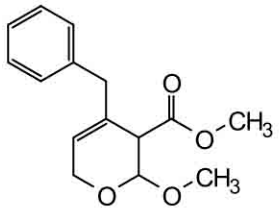
cis isomer



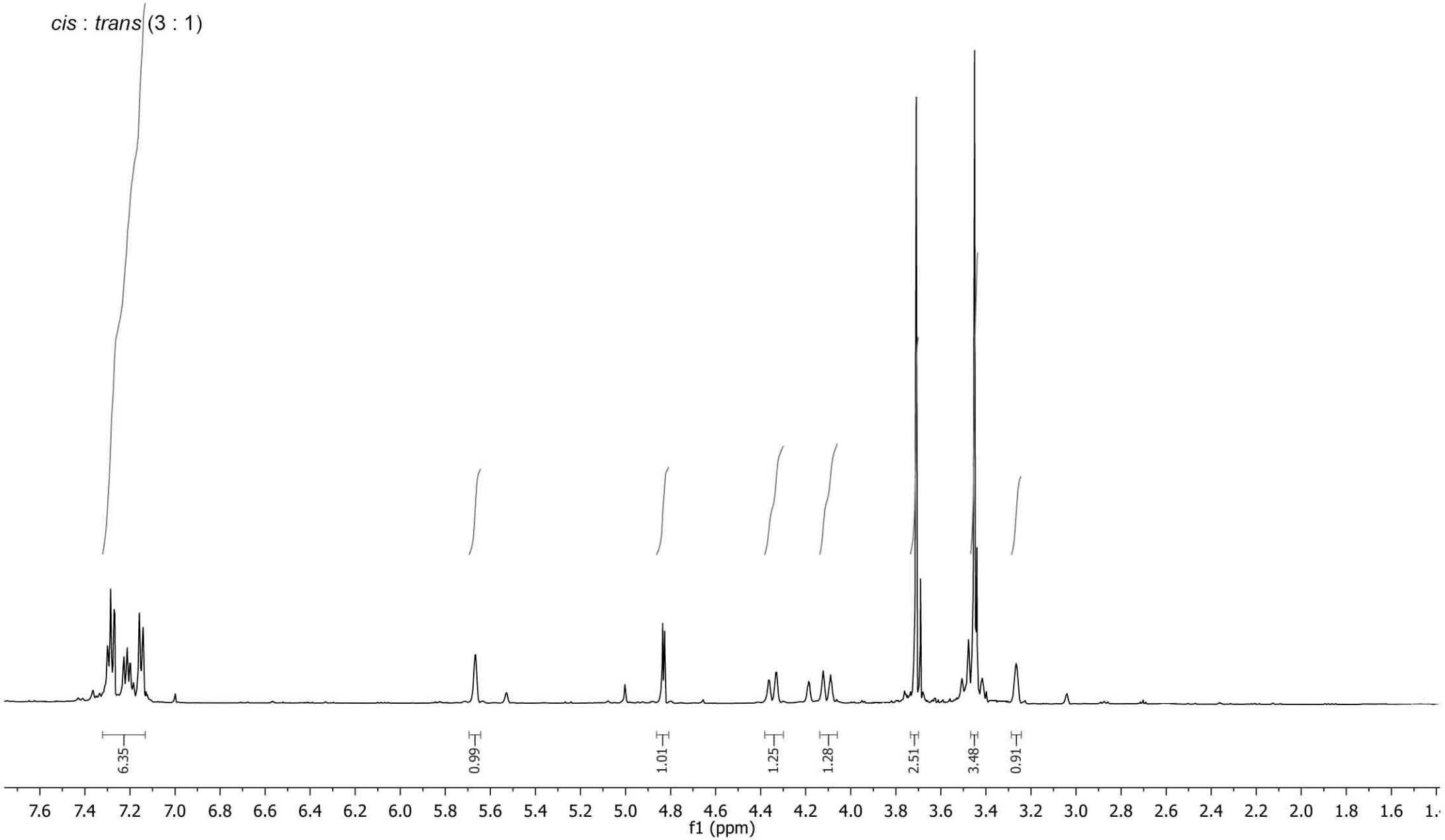
trans isomer

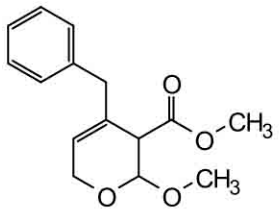


trans isomer

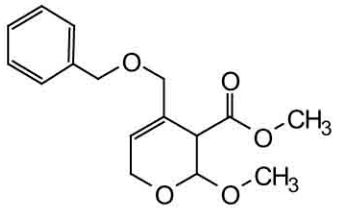


cis : *trans* (3 : 1)

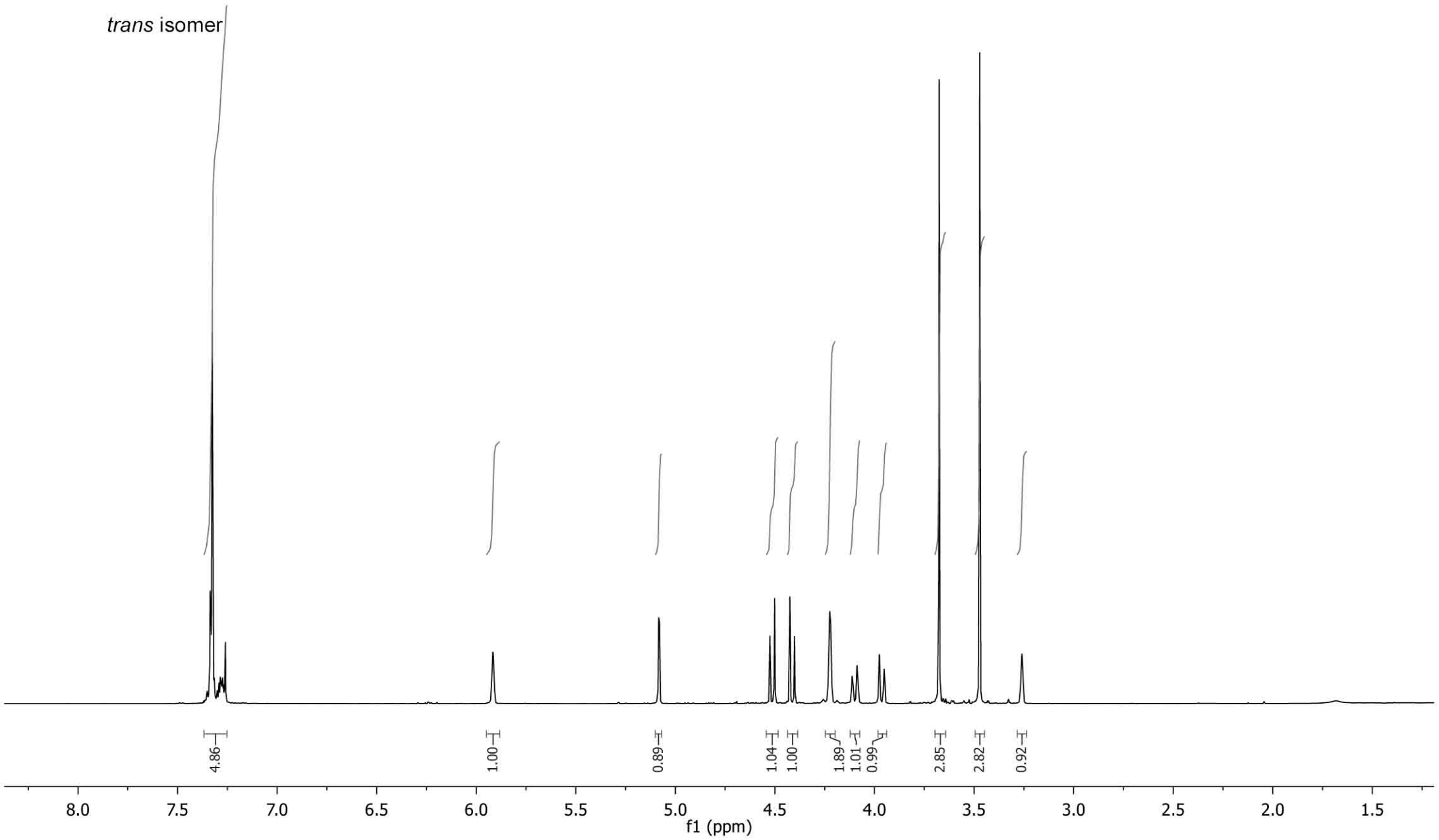


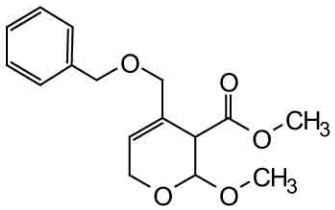


cis : *trans* (3 : 1)

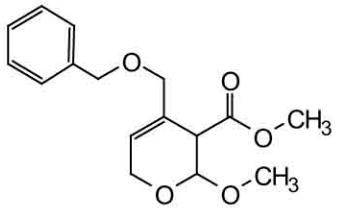


trans isomer

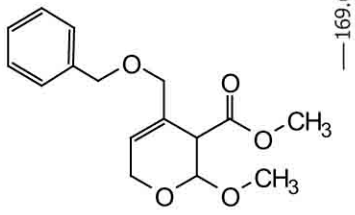




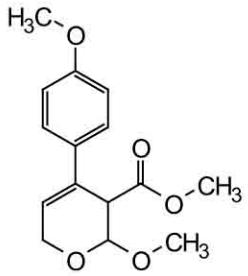
trans isomer



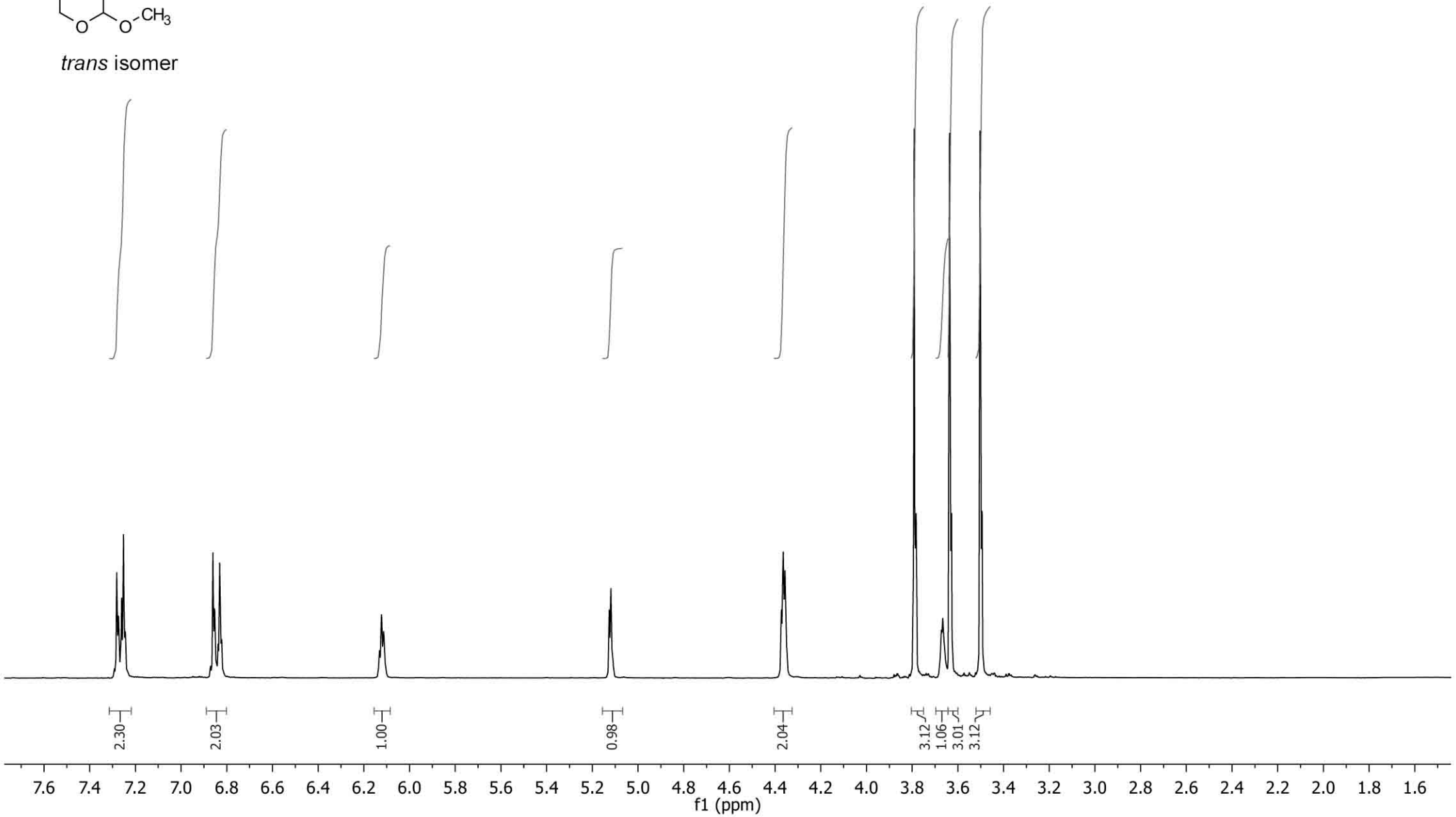
cis isomer

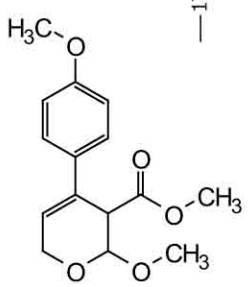


cis isomer

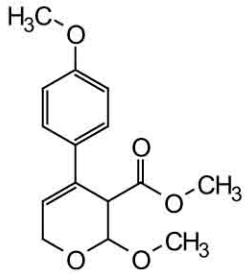


trans isomer

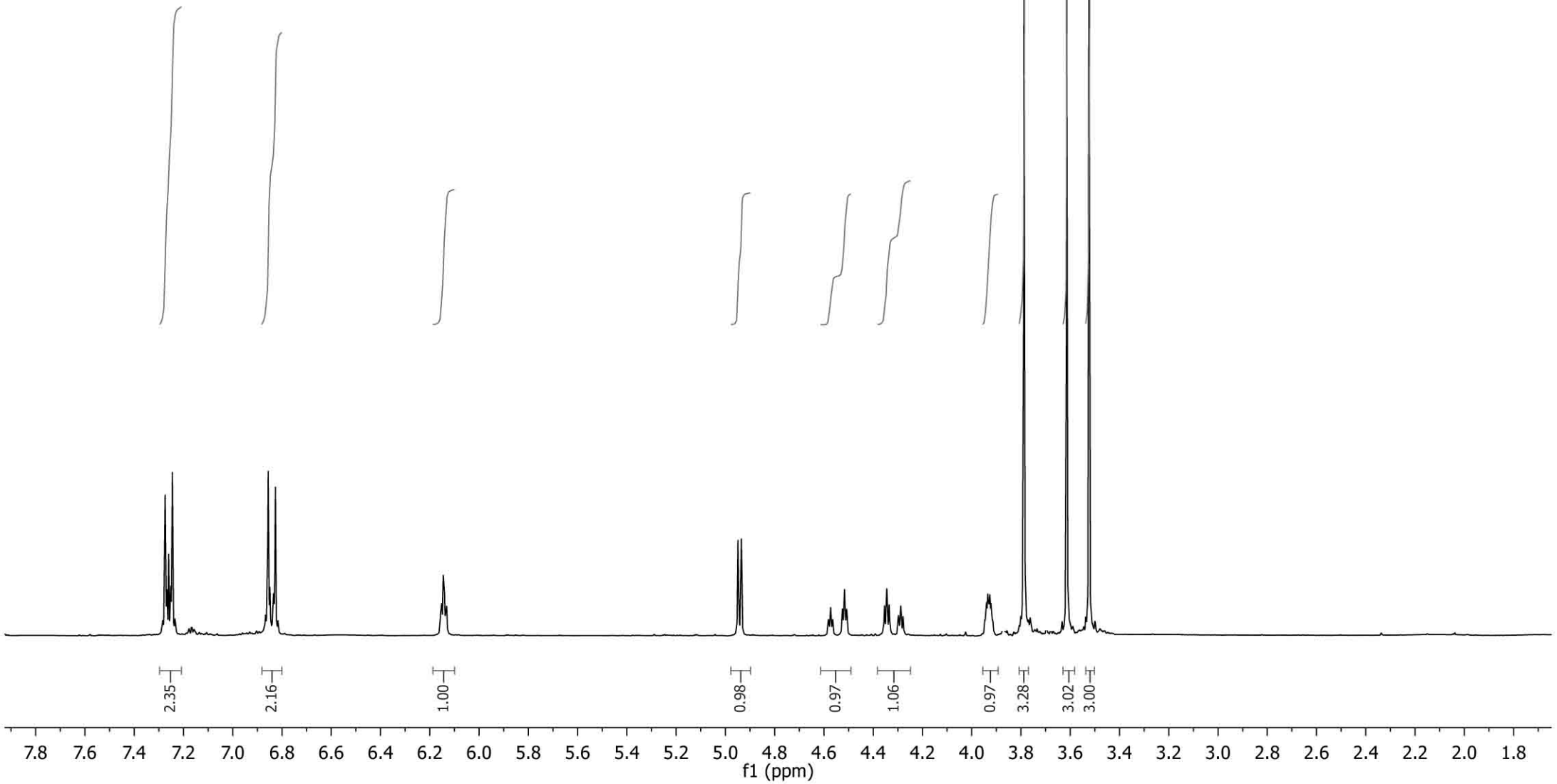


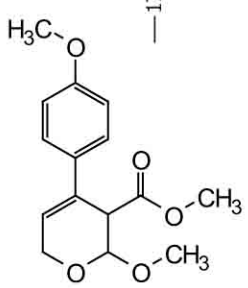


trans isomer

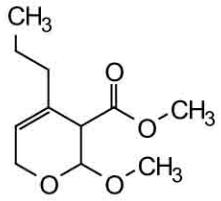


cis isomer

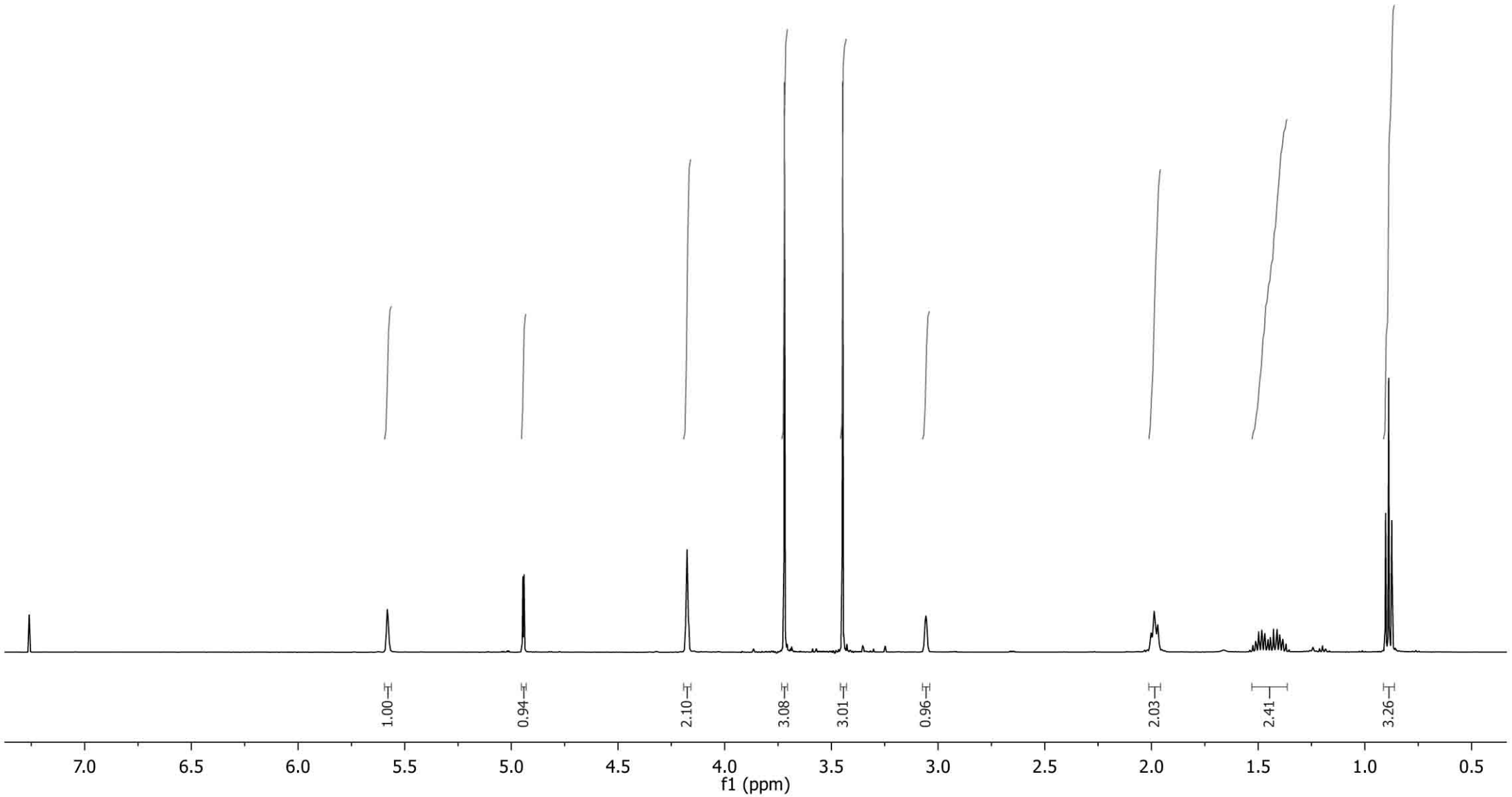


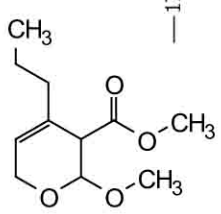


cis isomer

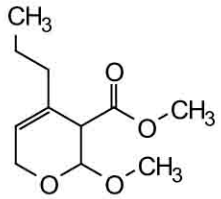


trans isomer

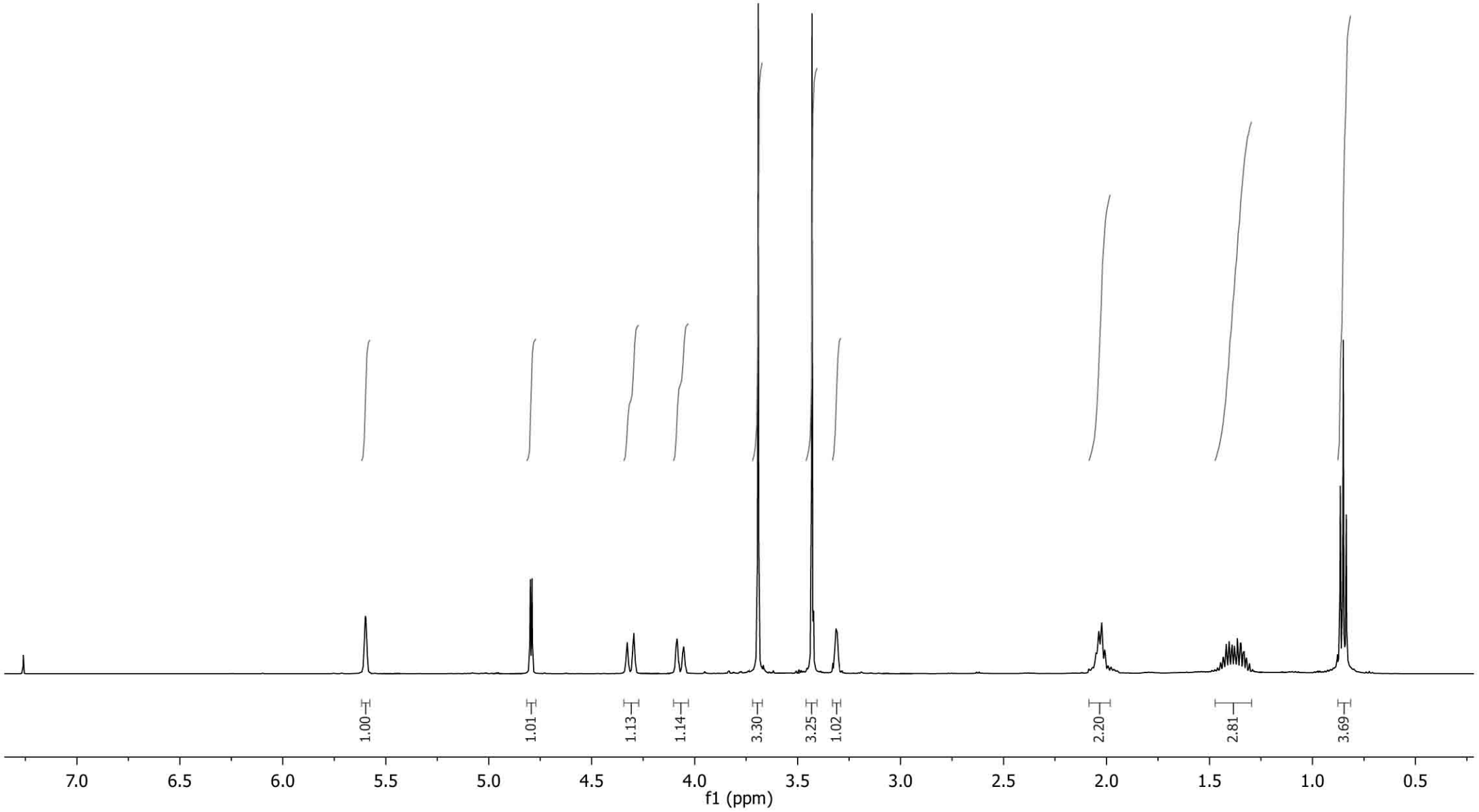


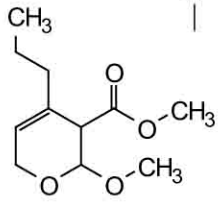


trans isomer

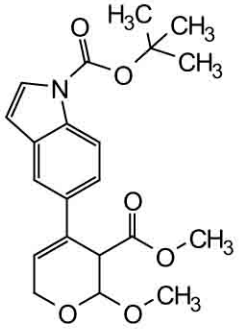


cis isomer

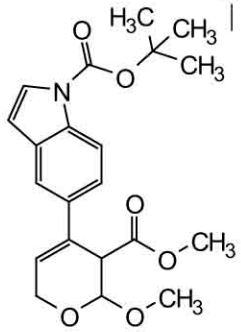




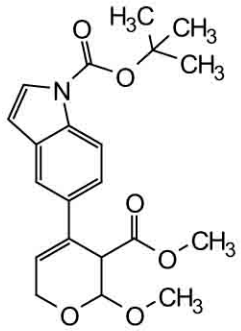
cis isomer



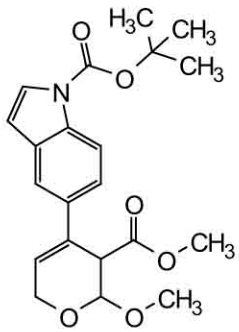
trans isomer



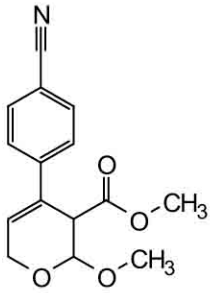
trans isomer



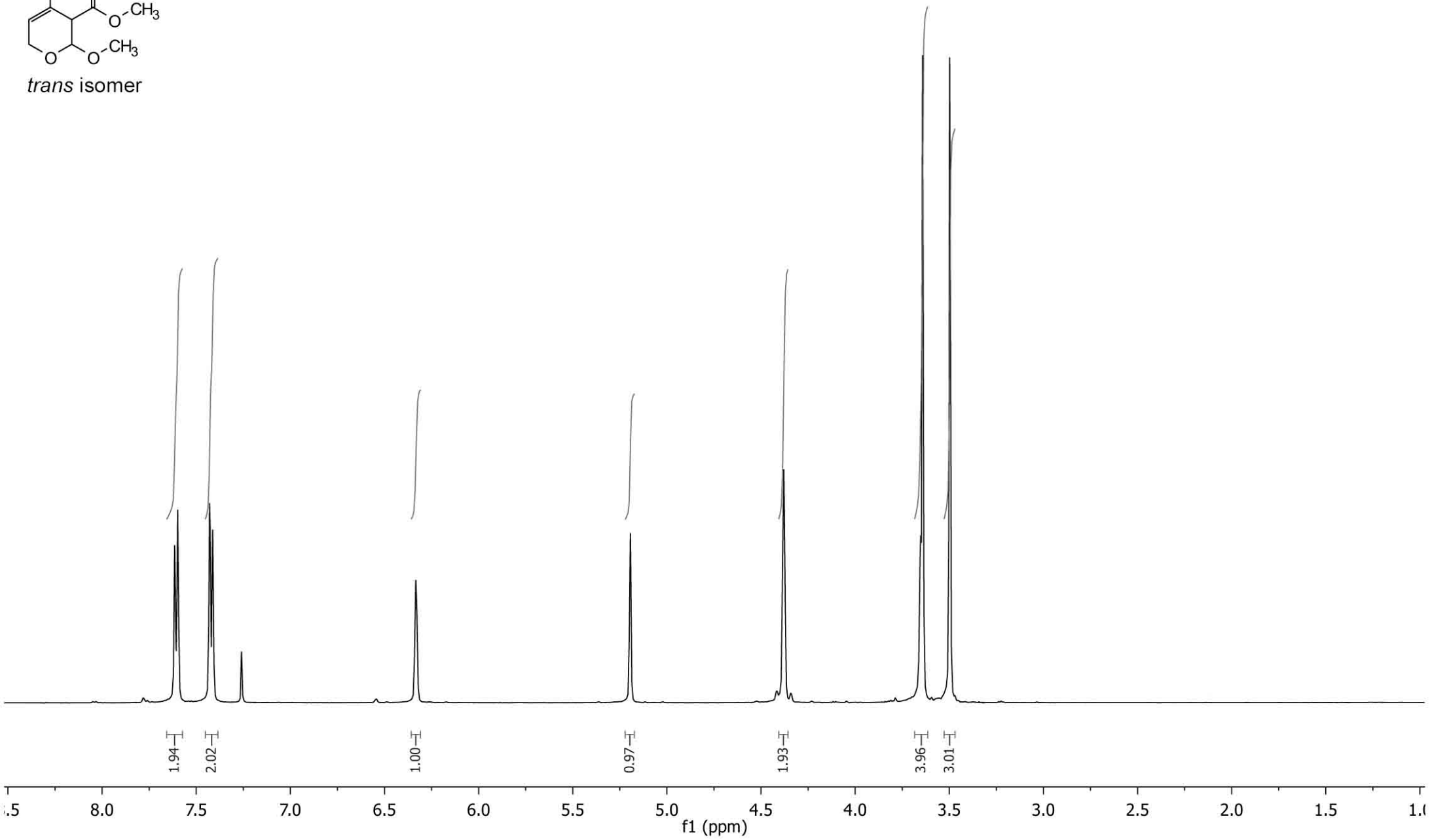
cis isomer

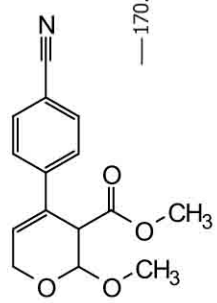


cis isomer

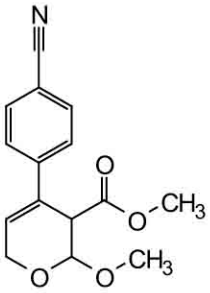


trans isomer

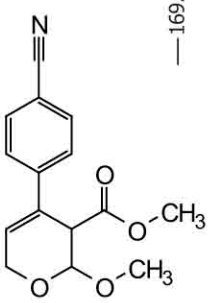




trans isomer

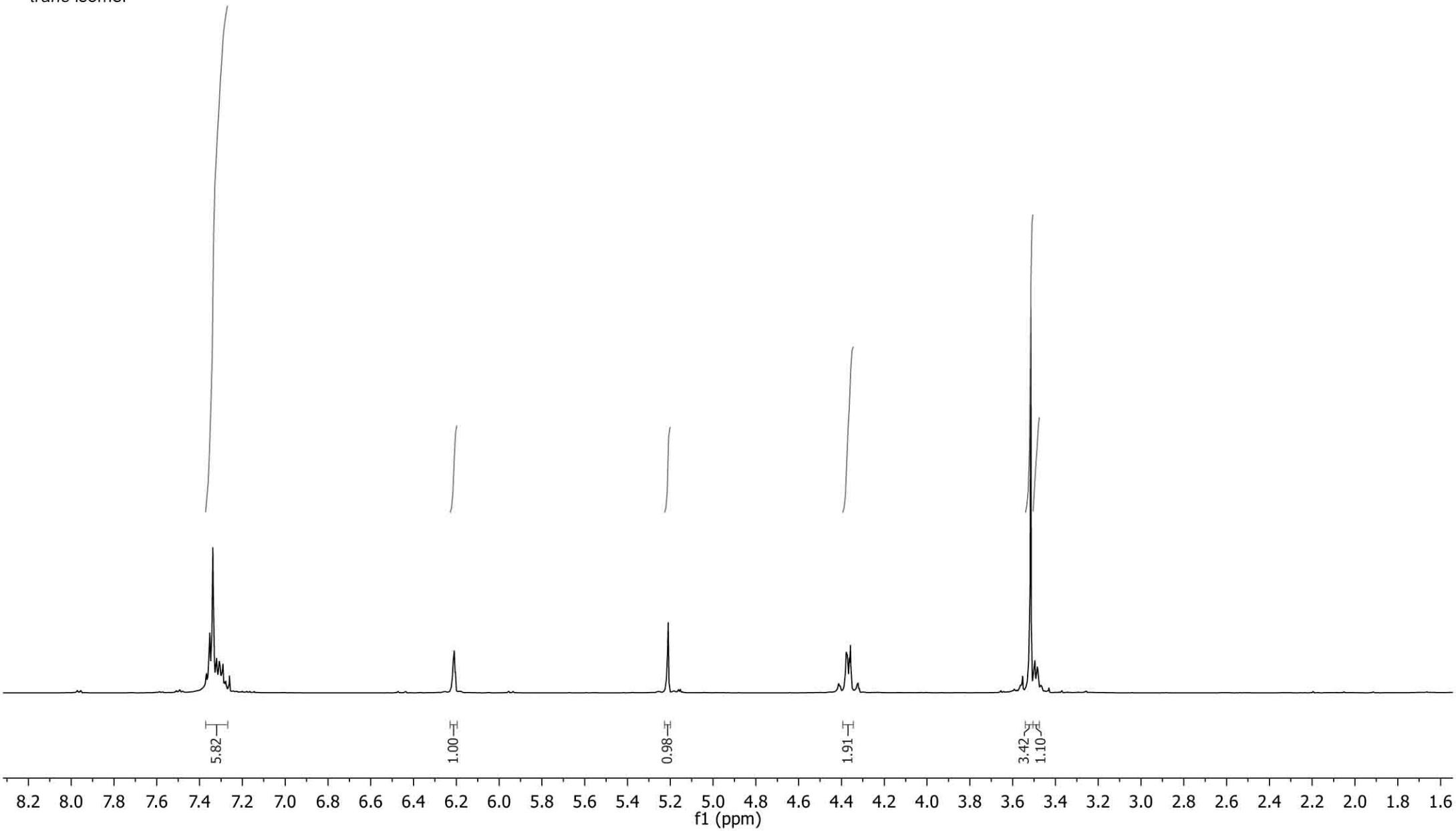


cis isomer



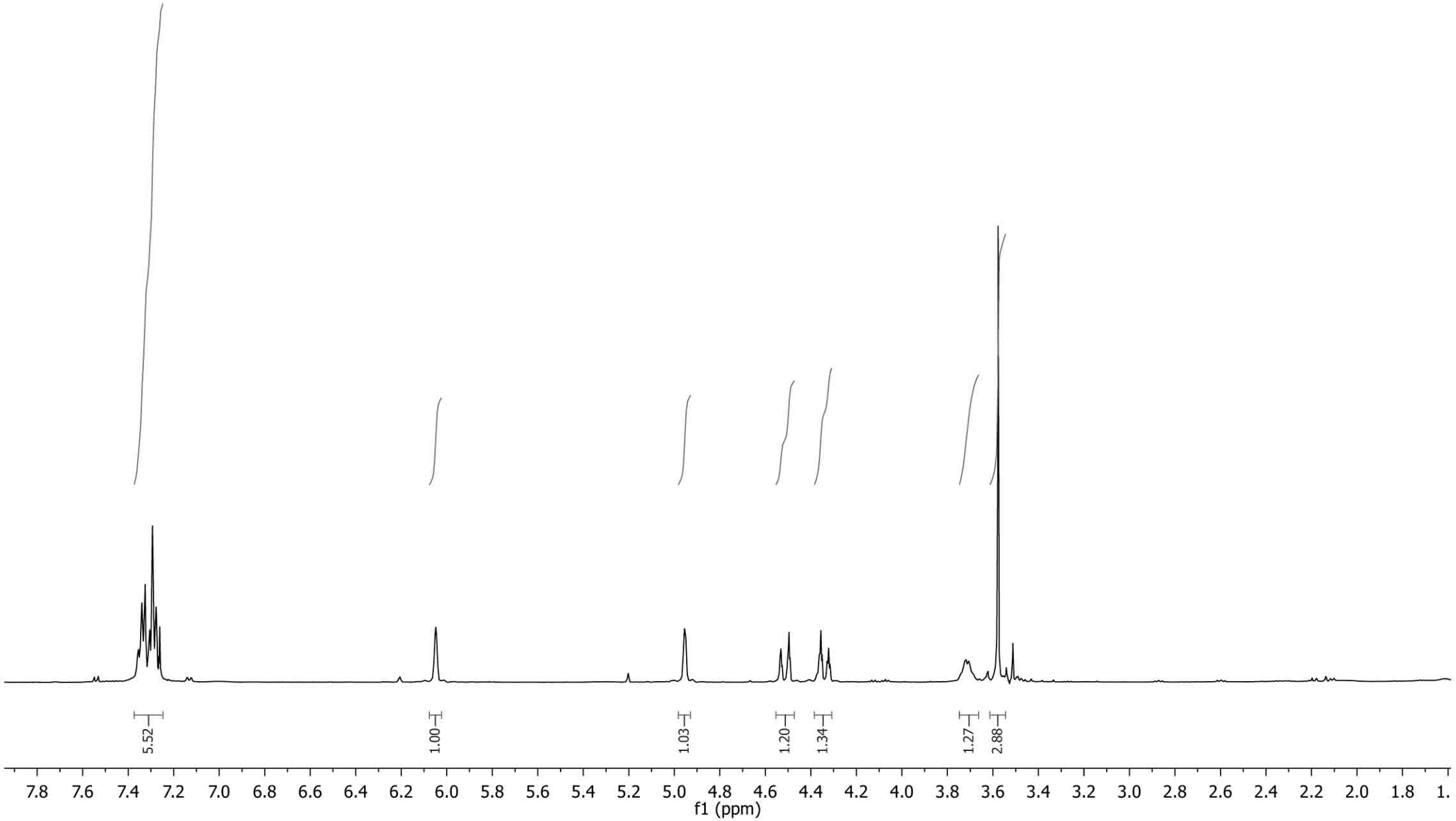
cis isomer

trans isomer

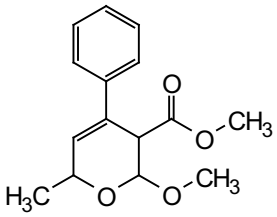


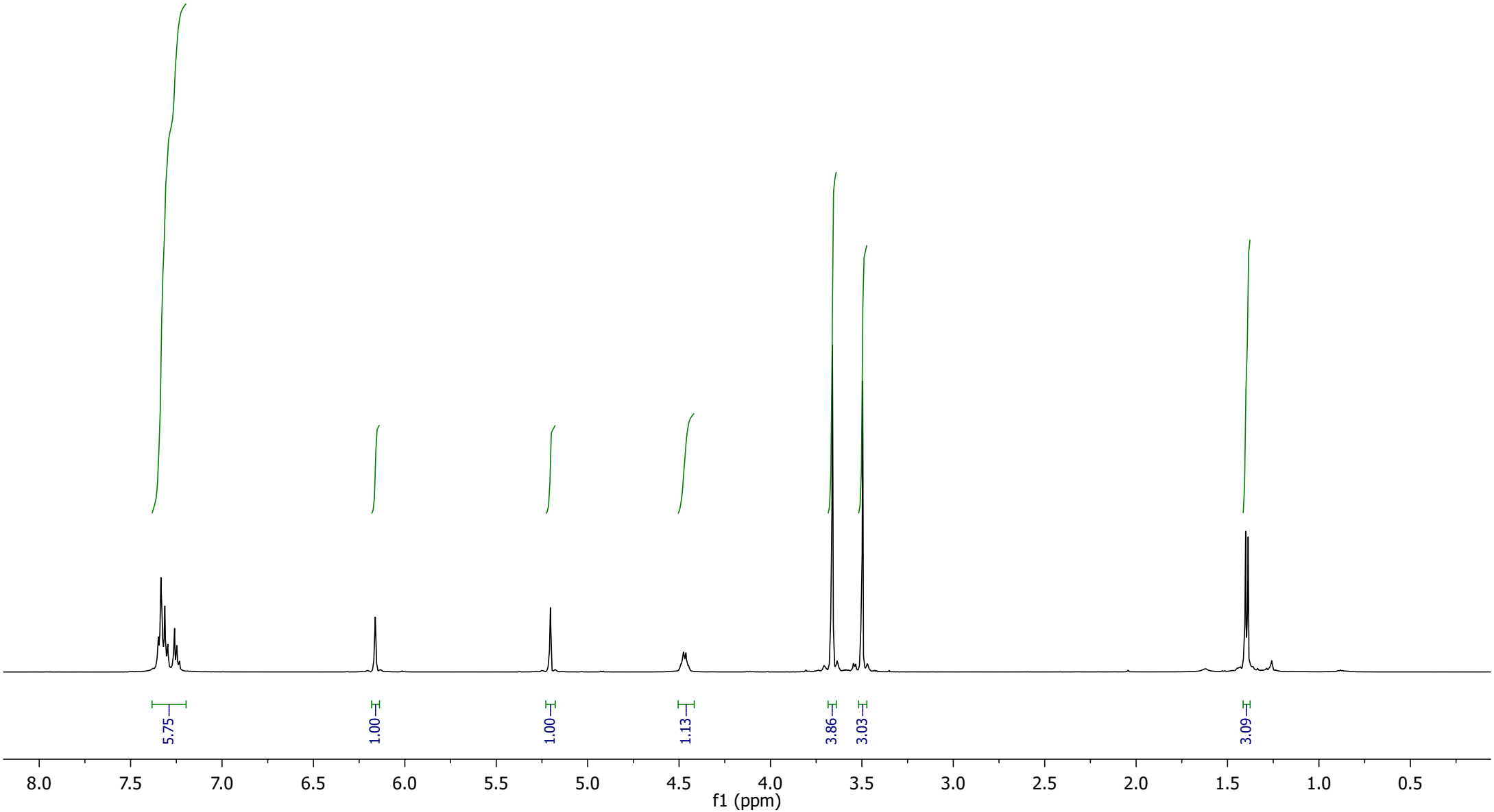
trans isomer

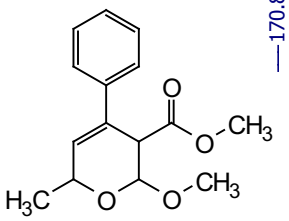
cis isomer

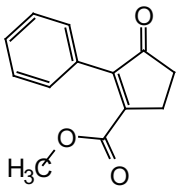


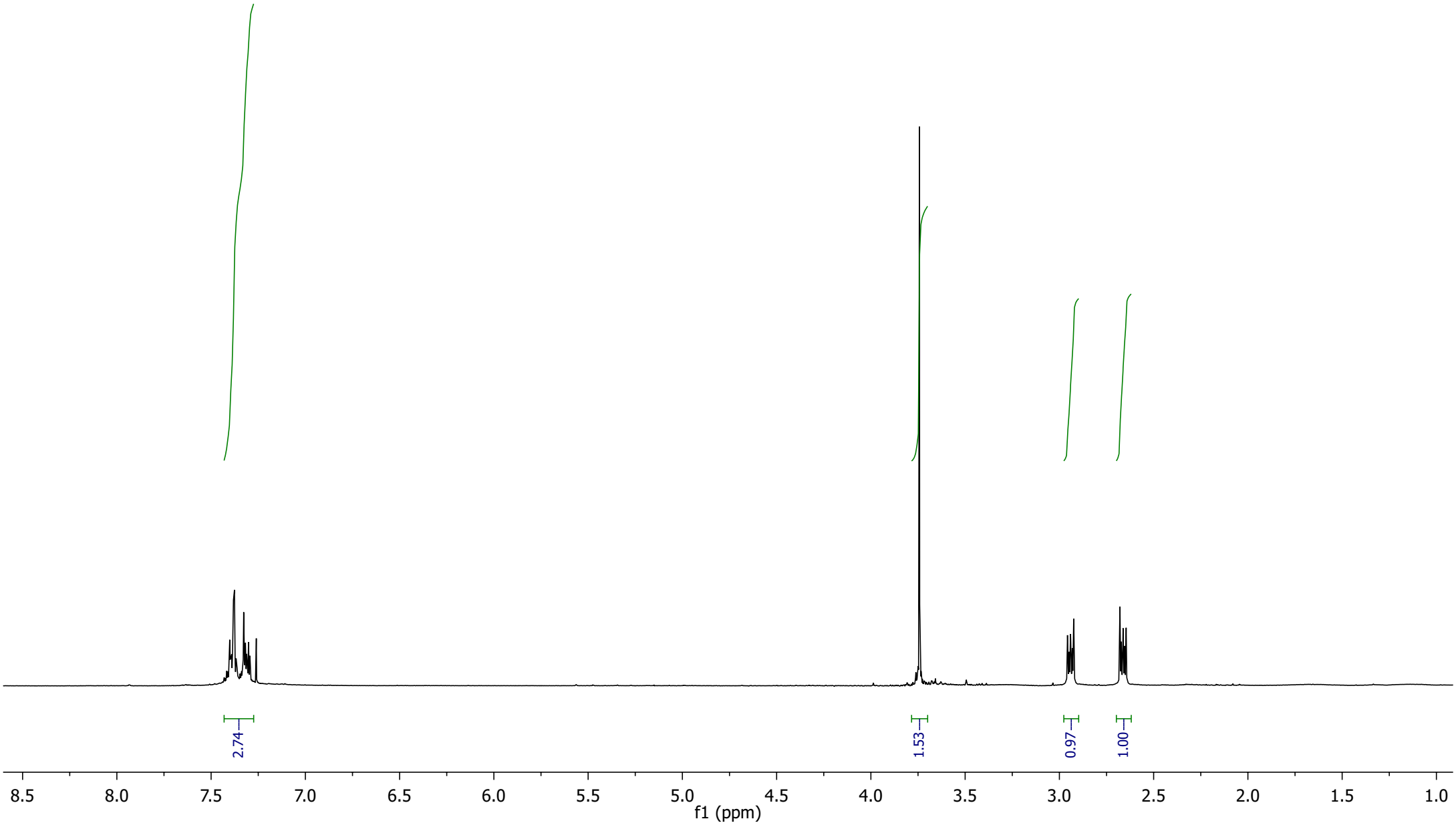
cis isomer

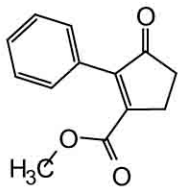


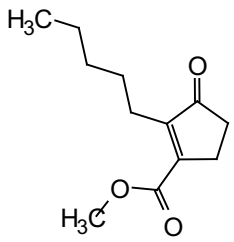


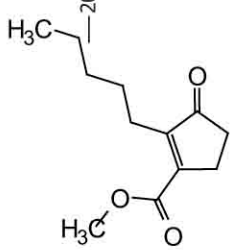


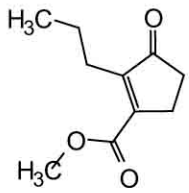


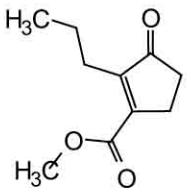




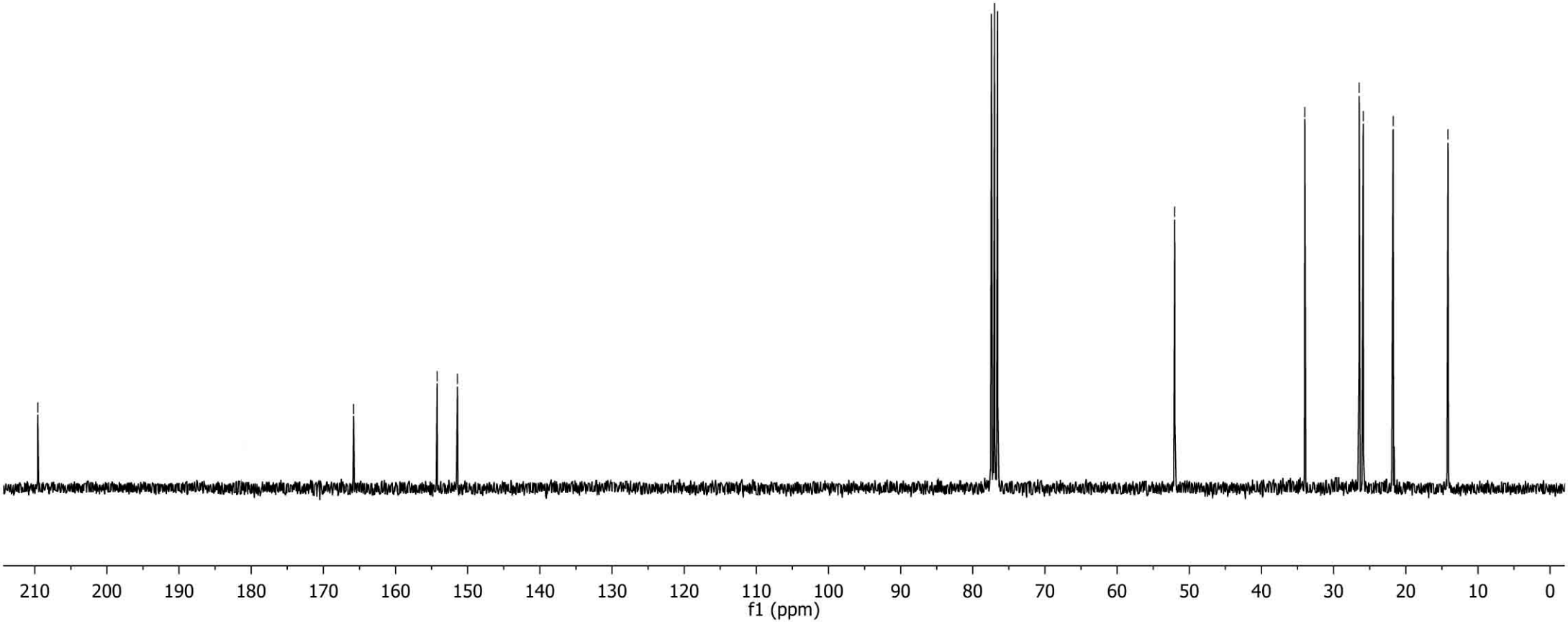


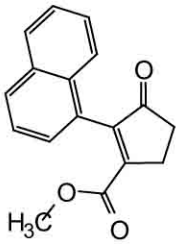


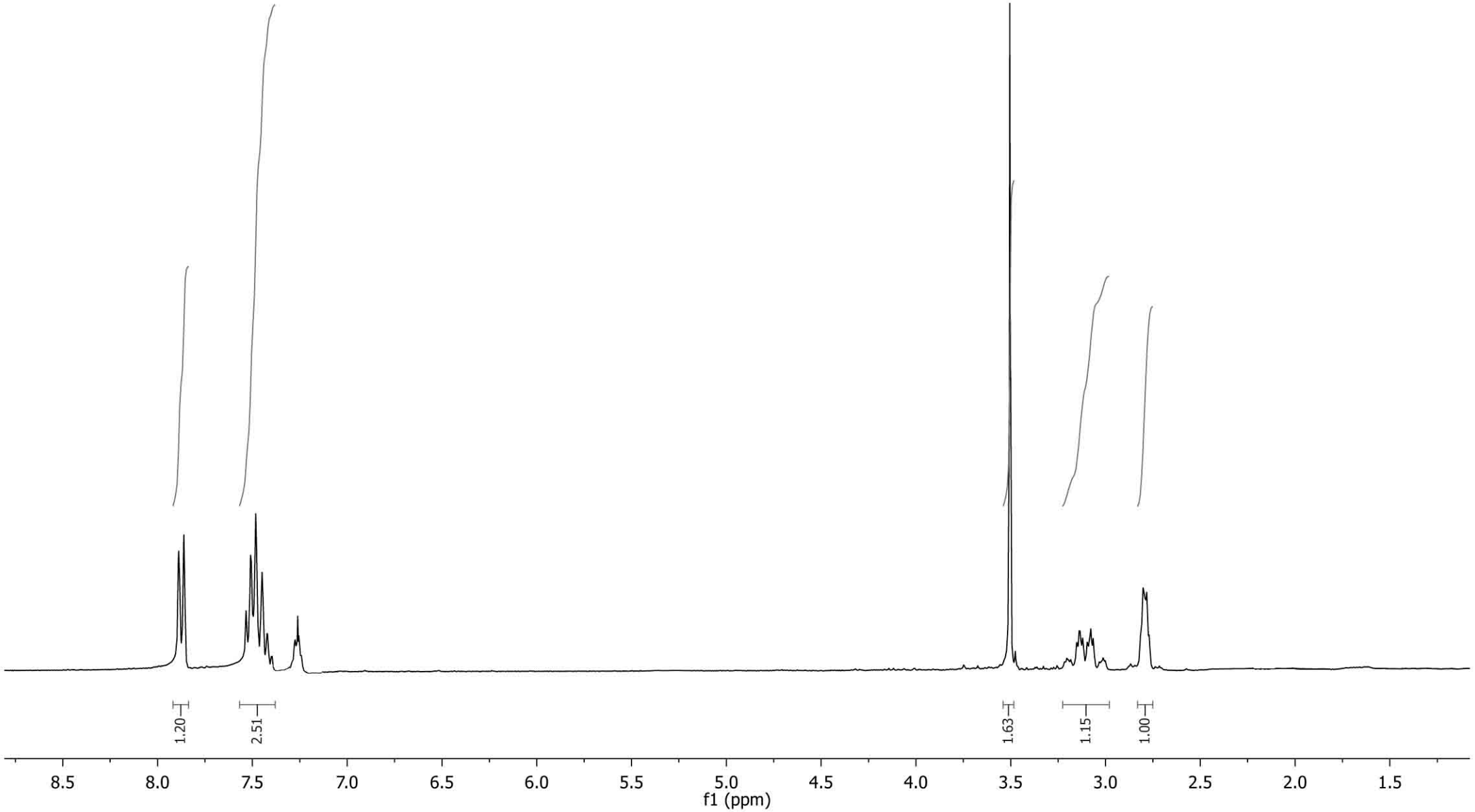


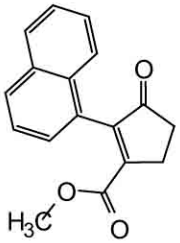


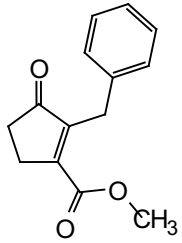
209.58
165.80
154.23
151.42
52.02
33.99
26.45
25.89
21.75
14.14

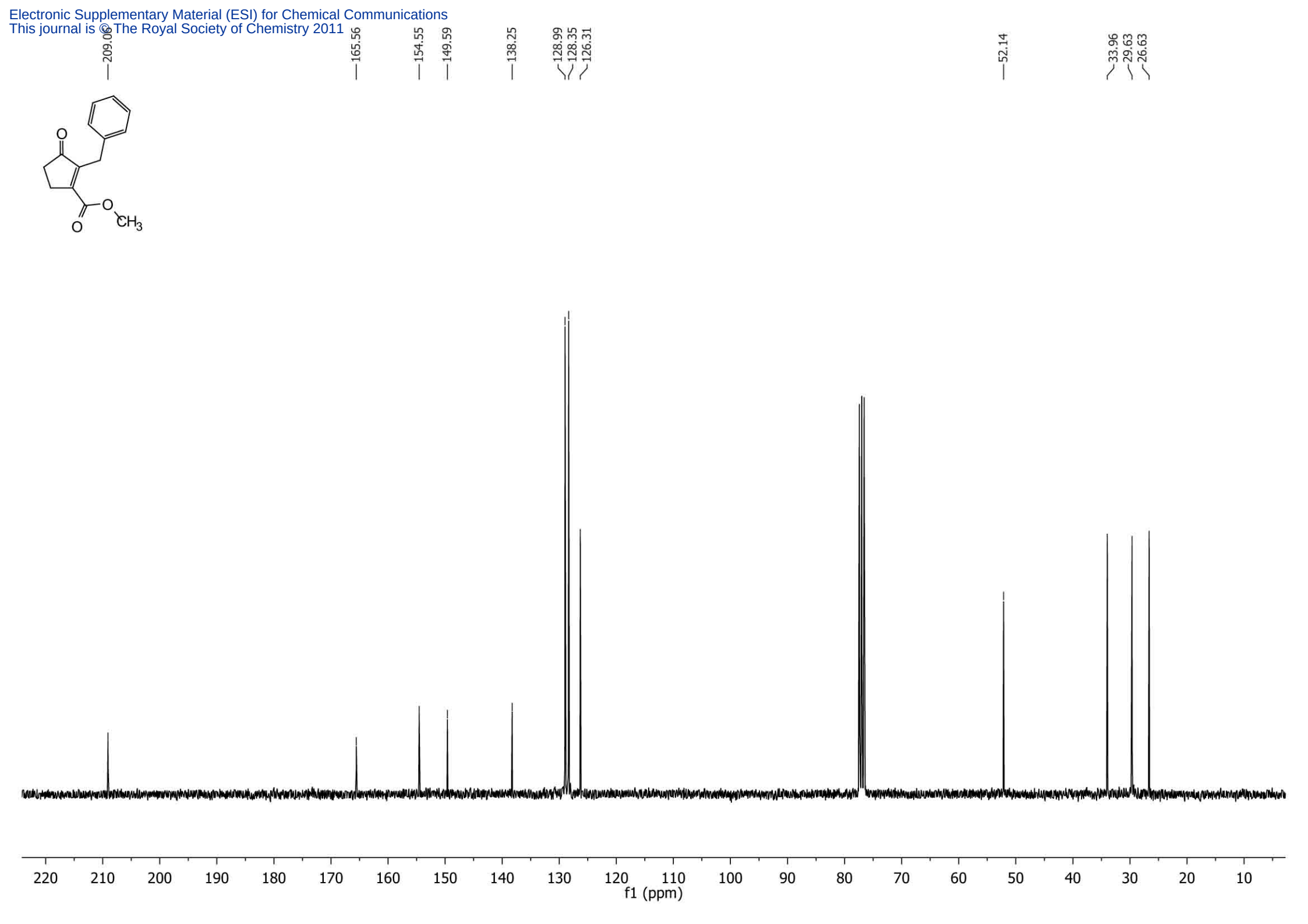


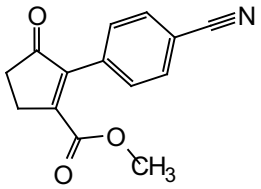


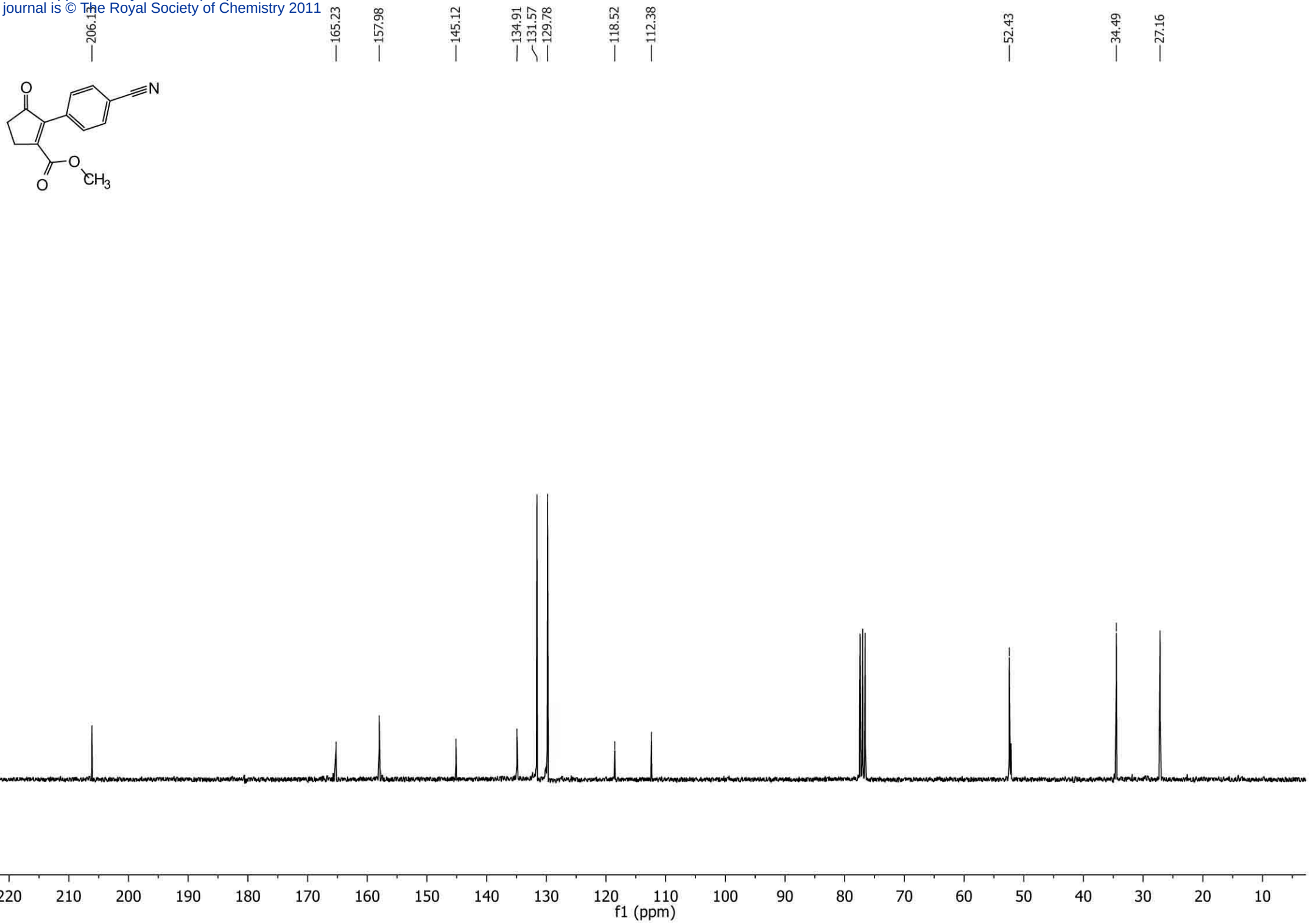


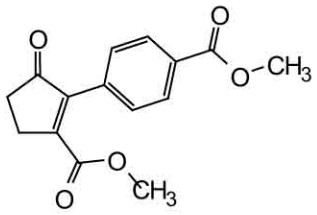


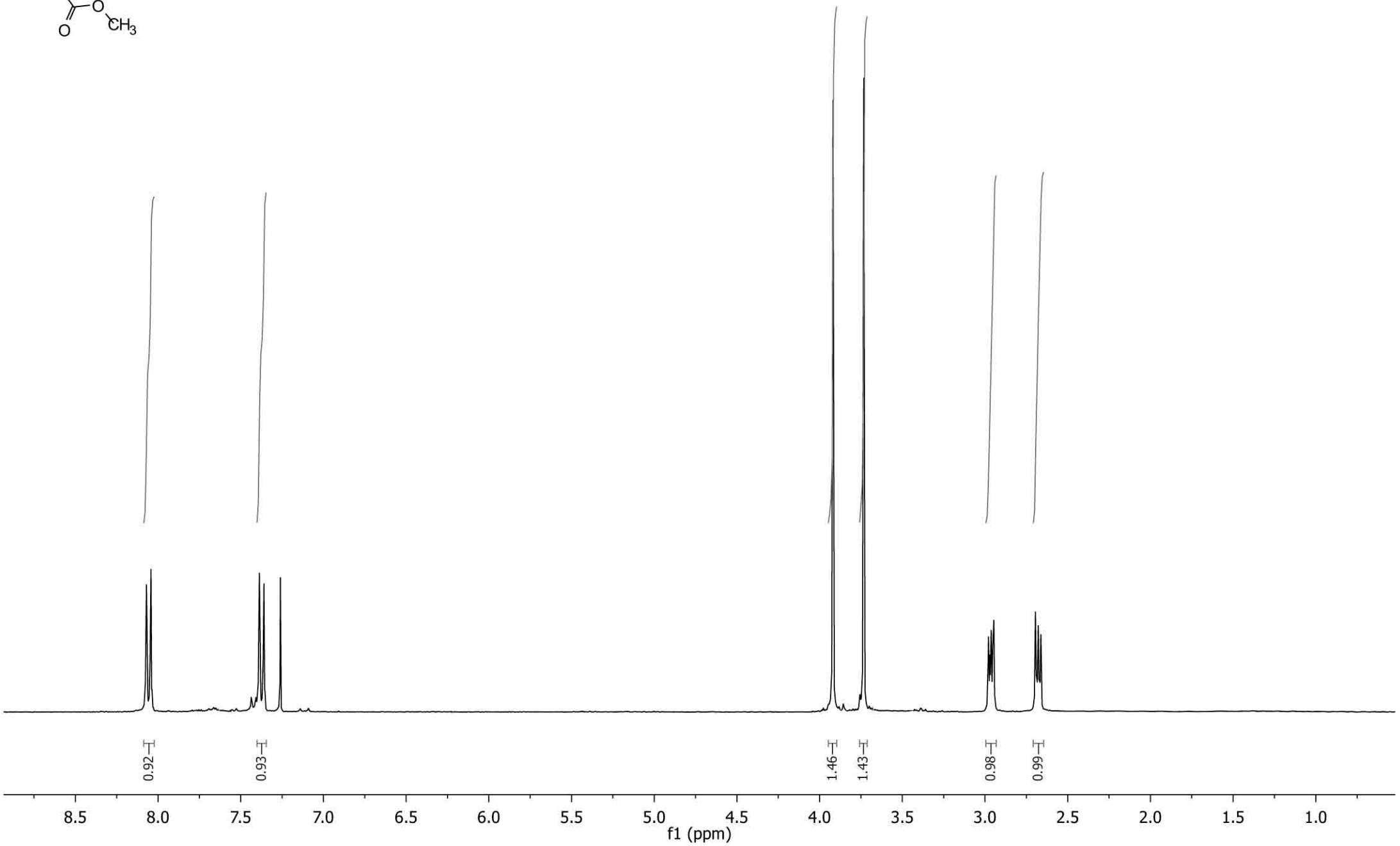


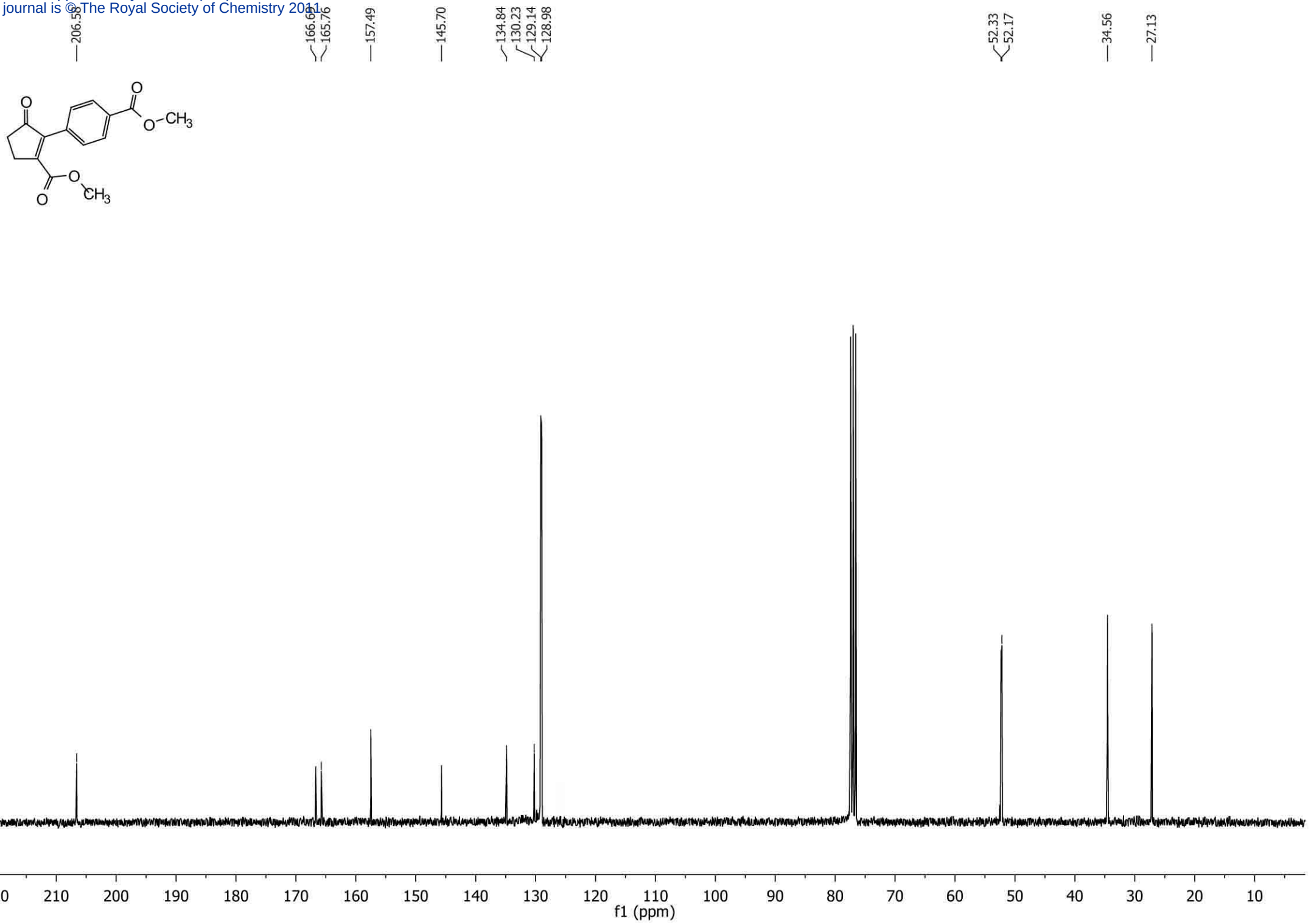


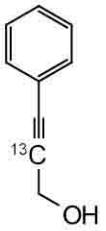


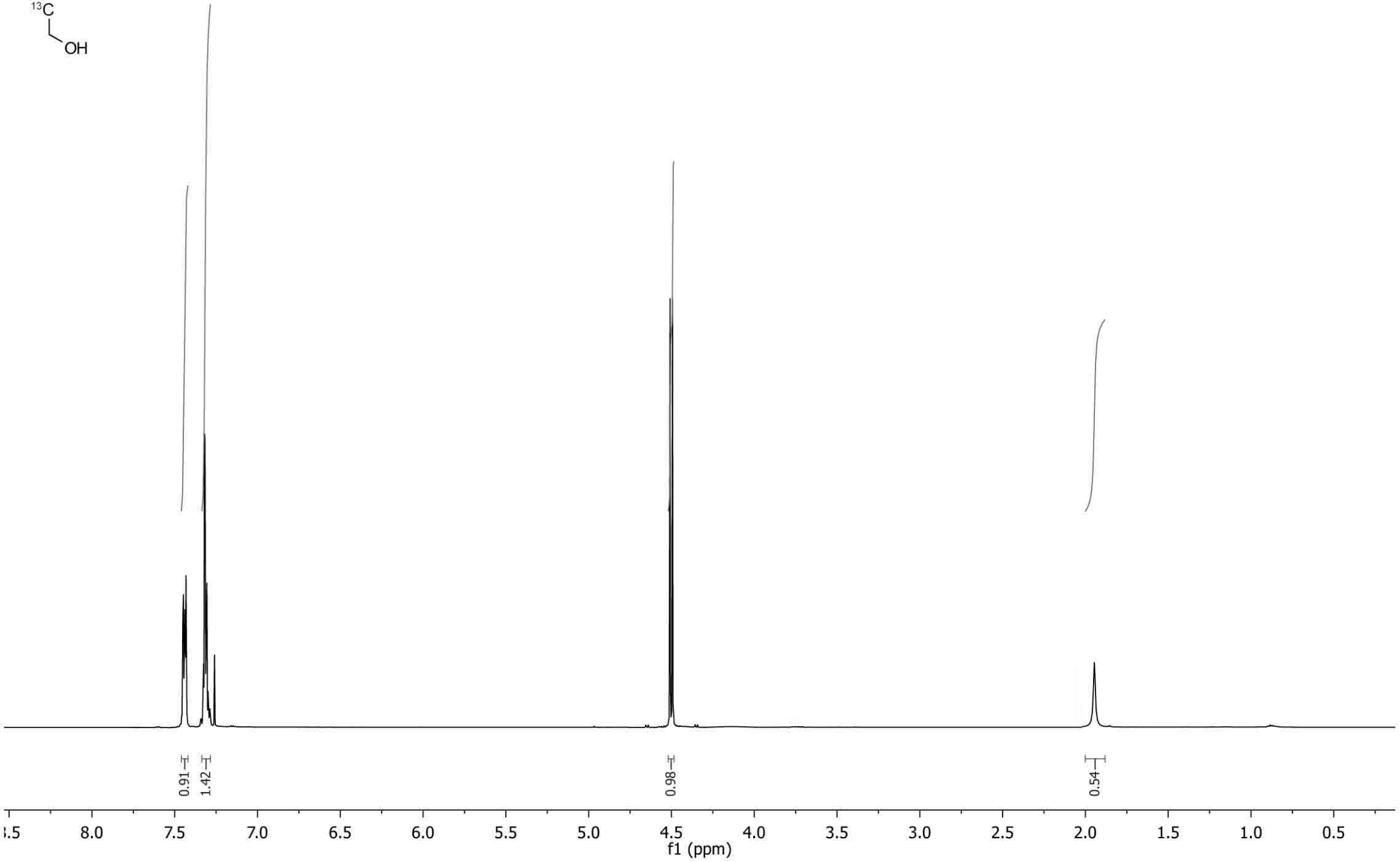


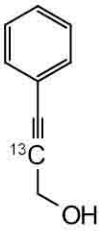


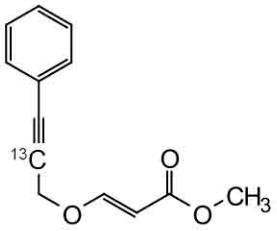


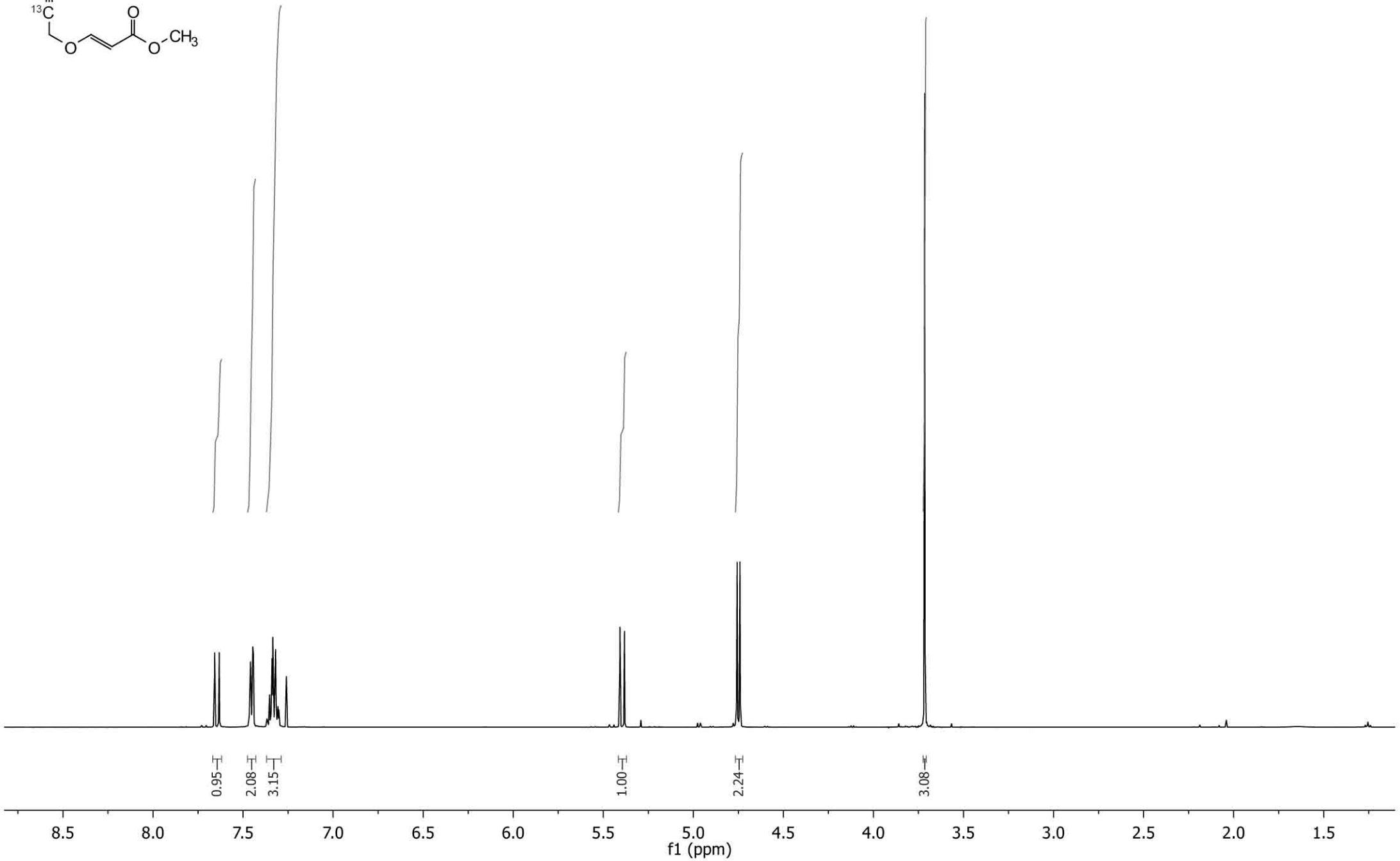


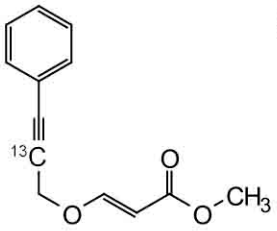


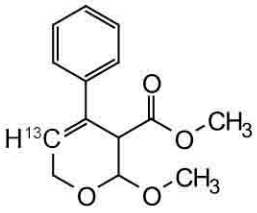




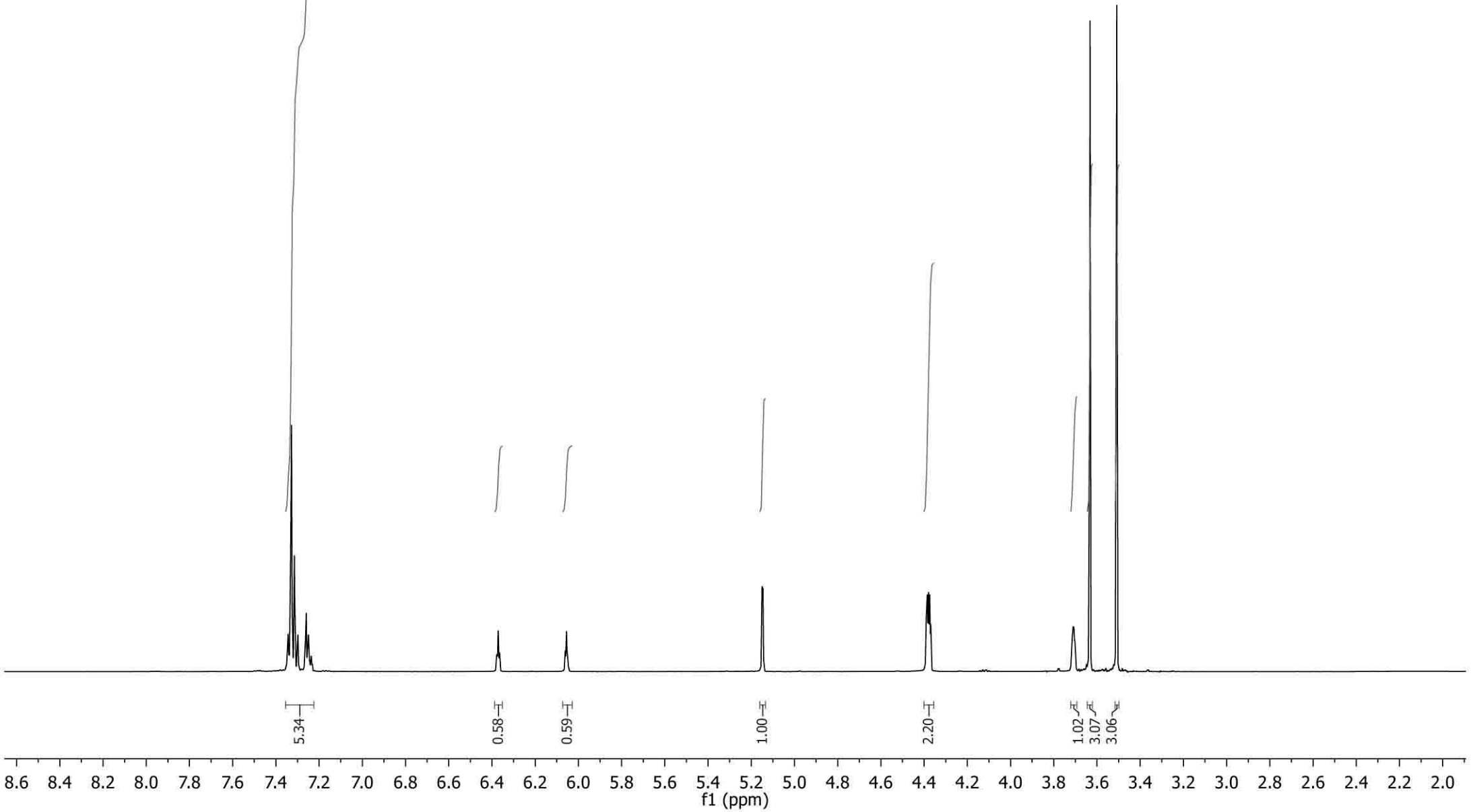


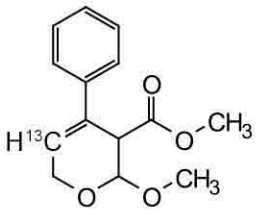




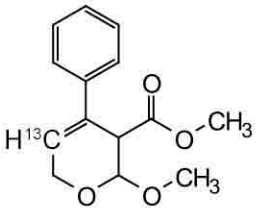


trans isomer

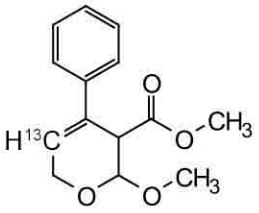




trans isomer



cis isomer



cis isomer