

Highly Regio- and Stereoselective Heck Reaction of Allylic Esters with Arenediazonium Salts: Application to the Synthesis of Kavalactones

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SUPPORTING INFORMATION

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Materials and Methods

Hydrogen nuclear magnetic resonance spectra (^1H NMR) were obtained at 250 MHz and 500 MHz. Spectra were recorded in CDCl_3 solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of residual CHCl_3 or tetramethylsilane (TMS) as reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 62.5 MHz and 125 MHz. Spectra were recorded in CDCl_3 solutions. Chemical shifts are reported in ppm, referenced to the solvent peak CDCl_3 . Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), q (quartet), dd (double doublet), dt (double triplet), ddd (double double doublet), tdd (triple double doublet) and m (multiplet). Microwave reactions were conducted on a CEM Discover[®] Microwave synthesizer. The equipment consists of a continuous focused microwave-power delivery system with operator-selectable power output from 0 to 300 W. Reactions were performed in glass vessels (capacity 10 mL) sealed with a septum. Temperature measurements were conducted using an infrared temperature sensor mounted under the reaction vessel. All experiments were performed using a stirring option whereby the contents of the vessel were stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel. All experiments were carried out with simultaneous cooling by passing compressed air through the microwave cavity while heating (option PowerMAX enabled). Column chromatography was performed using silica gel (230-400 mesh) following the methods described by Still.¹ Thin layer chromatography (TLC) was performed using silica gel GF₂₅₄, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or phosphomolibdic acid, followed by heating. Air- and moisture-sensitive reaction was conducted in flame-dried or oven dried glassware equipped with tightly fitted rubber septa and under a positive atmosphere of dry argon. Reagents and solvents were handled using standard syringe techniques. Temperatures above room temperature were maintained by use of a mineral oil bath heated on a hotplate. Allylic ester **1b** ($\text{R}^1 = \text{Bu}$) was prepared according to literature procedure.² The allylic ester **1c** ($\text{R}^1 = \text{CH}_2\text{OAc}$) was purchased from Aldrich.

¹ Still, W.C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

² Felluga, F.; Forzato, C.; Ghelfi, F. Nitti, P.; Pitacco, G.; Pagnoni, U. M.; Roncaglia, F. *Tetrahedron; Asymmetry* **2007**, *18*, 527.

General Procedure for the Heck Arylations of the Allylic Esters

To a round-bottomed flask (or a test tube) were added $\text{Pd}_2(\text{dba})_3 \cdot \text{dba}$ (4 mol%, 12 mg), sodium acetate (3 equiv, 0.9 mmol, 81 mg) and benzonitrile (2 mL). To the resulting suspension were then added the appropriate allylic ester (0.3 mmol) and the arenediazonium salt (1.1 equiv, 0.33 mmol). The reaction was stirred at room temperature and the reaction progress was monitored by the evolution of N_2 . After the nitrogen bubbling has stopped, the crude reaction mixture was filtered through a plug of silica and concentrated under reduced pressure. The product was purified by flash chromatography (hexanes:ethyl acetate as eluent) to provide the arylated allylic ester.

(*E*)-3-(4-methoxyphenyl)allyl acetate – 3a

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 2.09 (s, 3H), 3.81 (s, 3H), 4.70 (dd, $J^1 = 6.75$ Hz, $J^2 = 1.25$ Hz, 2H), 6.15 (dt, $J^1 = 15.75$ Hz, $J^2 = 6.75$ Hz, 1H), 6.61 (d, $J = 15.75$ Hz, 1H), 6.85 (d, $J = 6.75$ Hz, 2H), 7.33 (d, $J = 6.75$ Hz, 2H).

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 21.0, 55.2, 65.3, 114.0, 120.8, 127.8, 128.9, 134.0, 159.6, 170.9.

IR (film, cm^{-1}): 1737, 1513, 1245.

MS (ESI): 207 ($\text{M}+1$), 206 (M), 163, 147, 103.

HRMS calc for $\text{C}_{12}\text{H}_{14}\text{O}_3$: 206.0942, found: 206.0943.

(*E*)-1-(4-methoxyphenyl)hept-1-en-3-yl acetate – 3b

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 0.9 (t, $J = 6.5$ Hz, 3H), 1.26-1.43 (m, 4H), 1.61-1.80 (m, 2H), 2.06 (s, 3H), 3.80 (s, 3H), 5.38 (q, $J = 6.75$ Hz, 1H), 5.98 (dd, $J^1 = 16.0$ Hz, $J^2 = 7.5$ Hz, 1H), 6.55 (d, $J = 16.0$ Hz, 1H), 6.85 (d, $J = 8.75$ Hz, 2H), 7.31 (d, $J = 8.75$ Hz, 2H).

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 14.0, 21.4, 22.5, 27.4, 34.3, 55.3, 75.1, 113.9, 125.6, 127.7, 129.1, 132.1, 159.4, 170.4.

IR (film, cm^{-1}): 1735, 1512, 1245.

MS (EI): 262 (M), 202 ($\text{M}-\text{AcOH}$), 173, 159, 121.

HRMS calc for $\text{C}_{14}\text{H}_{18}\text{O}$ ($\text{M}-\text{AcOH}$): 202.1358, found: 202.1355.

(E)-4-(4-methoxyphenyl)but-3-ene-1,2-diyl diacetate – 3c

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 2.08 (s, 3H), 2.11 (s, 3H), 3.81 (s, 3H), 4.17 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.25$ Hz, 1H), 4.32 (dd, $J^1 = 11.75$ Hz, $J^2 = 3.75$ Hz, 1H), 5.64 (tdd, $J^1 = 7.25$ Hz, $J^2 = 3.75$ Hz, $J^3 = 0.75$ Hz, 1H), 5.98 (dd, $J^1 = 16.0$ Hz, $J^2 = 7.5$ Hz, 1H), 6.65 (d, $J = 16.0$ Hz, 1H), 6.85 (d, $J = 8.75$ Hz, 2H), 7.32 (d, $J = 8.75$ Hz, 2H).

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 20.8, 21.2, 55.3, 65.1, 72.3, 114.0, 120.6, 127.9, 128.5, 134.2, 159.8, 170.1, 170.7.

IR (KBr, cm^{-1}): 1733, 1254, 1232.

MS (ESI): 219, 218, 176, 159.

HRMS calc for $\text{C}_{15}\text{H}_{18}\text{O}_5$: 278.1154, found: 278.1154.

(E)-4-phenylbut-3-ene-1,2-diyl diacetate – 3d

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 2.08 (s, 3H), 2.12 (s, 3H), 4.18 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.0$ Hz, 1H), 4.33 (dd, $J^1 = 11.75$ Hz, $J^2 = 3.75$ Hz, 1H), 5.67 (tdd, $J^1 = 7.12$ Hz, $J^2 = 4.0$ Hz, $J^3 = 1.0$ Hz, 1H), 6.12 (dd, $J^1 = 16.0$ Hz, $J^2 = 7.0$ Hz, 1H), 6.71 (d, $J = 16.0$ Hz, 1H), 7.28-7.34 (m, 5H).

^{13}C NMR: CDCl_3 , 125 MHz, $\delta(\text{ppm})$: 20.7, 21.1, 64.9, 72.0, 123.0, 126.7, 128.3, 128.6, 134.4, 135.8, 170.0, 170.6.

IR (film, cm^{-1}): 1740, 1221.

MS (ESI): 188 (M-AcOH), 146, 145, 115.

HRMS calc for $\text{C}_{12}\text{H}_{12}\text{O}_2$ (M-AcOH): 188.0837, found: 188.0837.

(E)-4-p-tolylbut-3-ene-1,2-diyl diacetate – 3e

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 2.08 (s, 3H), 2.11 (s, 3H), 2.34 (s, 3H), 4.17 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.0$ Hz, 1H), 4.32 (dd, $J^1 = 11.75$ Hz, $J^2 = 3.75$ Hz, 1H), 5.65 (tdd, $J^1 = 7.12$ Hz, $J^2 = 3.75$ Hz, $J^3 = 0.75$ Hz, 1H), 6.06 (dd, $J^1 = 16.0$ Hz, $J^2 = 7.25$ Hz, 1H), 6.67 (d, $J = 16.0$ Hz, 1H), 7.13 (d, $J = 7.75$ Hz, 2H), 7.28 (d, $J = 7.75$ Hz, 2H).

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 20.8, 21.1, 21.2, 65.0, 72.2, 121.9, 126.5, 129.3, 133.0, 134.4, 138.3, 170.2, 170.8.

IR (KBr, cm^{-1}): 1742, 1242, 1224.

MS (ESI): 202 (M-AcOH), 160, 129, 128, 115.

HRMS calc for $\text{C}_{13}\text{H}_{14}\text{O}_2$ (M-AcOH): 202.0994, found: 202.0994.

(E)-4-(naphthalen-2-yl)but-3-ene-1,2-diyl diacetate – 3f

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.09 (s, 3H), 2.14 (s, 3H), 4.22 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.0$ Hz, 1H), 4.38 (dd, $J^1 = 11.75$ Hz, $J^2 = 4.0$ Hz, 1H), 5.72 (tdd, $J^1 = 7.0$ Hz, $J^2 = 4.0$ Hz, $J^3 = 1.0$ Hz, 1H), 6.24 (dd, $J^1 = 16.0$ Hz, $J^2 = 7.25$ Hz, 1H), 6.87 (d, $J = 16.0$ Hz, 1H), 7.41-7.51 (m, 2H), 7.57 (dd, $J^1 = 8.62$ Hz, $J^2 = 1.5$ Hz, 1H), 7.75-7.82 (m, 4H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.1, 65.0, 72.1, 123.3, 123.3, 126.2, 126.4, 127.1, 127.6, 128.1, 128.3, 133.23, 133.24, 133.4, 134.5, 170.1, 170.7.

IR (KBr, cm⁻¹): 1738, 1726, 1251, 1227, 1041.

MS (ESI): 299 (M+1), 298, 264, 263.

HRMS calc for C₁₈H₁₈O₄: 298.1205, found: 298.1205.

(E)-4-(3,4-dimethoxyphenyl)but-3-ene-1,2-diyl diacetate – 3g

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.08 (s, 3H), 2.11 (s, 3H), 3.88 (s, 3H), 3.90 (s, 3H), 4.17 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.25$ Hz, 1H), 4.33 (dd, $J^1 = 11.75$ Hz, $J^2 = 3.75$ Hz, 1H), 5.65 (tdd, $J^1 = 7.0$ Hz, $J^2 = 4.0$ Hz, $J^3 = 1.0$ Hz, 1H), 5.98 (dd, $J^1 = 15.75$ Hz, $J^2 = 7.25$ Hz, 1H), 6.65 (d, $J = 15.75$ Hz, 1H), 6.82 (d, $J = 8.75$ Hz, 1H), 6.92-6.95 (m, 2H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.2, 55.8, 55.9, 65.0, 72.2, 108.9, 111.0, 120.1, 120.9, 128.8, 134.4, 149.0, 149.4, 170.1, 170.7.

IR (film, cm⁻¹): 1739, 1513, 1224.

MS (EI): 308 (M), 248 (M-AcOH), 206, 193, 175, 115.

HRMS calc for C₁₆H₂₀O₆: 308.1260, found: 308.1242.

(E)-4-(4-fluorophenyl)but-3-ene-1,2-diyl diacetate – 3h

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.08 (s, 3H), 2.12 (s, 3H), 4.17 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.0$ Hz, 1H), 4.33 (dd, $J^1 = 11.75$ Hz, $J^2 = 4.0$ Hz, 1H), 5.64 (tdd, $J^1 = 7.12$ Hz, $J^2 = 3.87$ Hz, $J^3 = 1.0$ Hz, 1H), 6.04 (dd, $J^1 = 16.0$ Hz, $J^2 = 7.25$ Hz, 1H), 6.67 (d, $J = 16.0$ Hz, 1H), 7.02 (t, $J = 8.75$ Hz, 2H), 7.35 (dd, $J^1 = 8.62$ Hz, $J^2 = 5.5$ Hz, 2H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.1, 64.9, 72.0, 115.6 (d, $J = 21.2$ Hz), 122.7 (d, $J = 1.9$ Hz), 128.3 (d, $J = 8.1$ Hz), 131.9 (d, $J = 3.1$ Hz), 133.3, 162.7 (d, $J = 246.2$ Hz), 170.1, 170.7.

IR (film, cm⁻¹): 1741, 1510, 1226.

MS (ESI): 206 (M-AcOH), 164, 151, 133.

HRMS calc for C₁₂H₁₁FO₂ (M-AcOH): 206.0743, found: 206.0743.

(E)-4-(4-chlorophenyl)but-3-ene-1,2-diyl diacetate – 3i

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.08 (s, 3H), 2.12 (s, 3H), 4.17 (dd, *J*¹ = 11.75 Hz, *J*² = 7.0 Hz, 1H), 4.33 (dd, *J*¹ = 11.75 Hz, *J*² = 3.75 Hz, 1H), 5.65 (tdd, *J*¹ = 6.75 Hz, *J*² = 3.87 Hz, *J*³ = 1.0 Hz, 1H), 6.09 (dd, *J*¹ = 16.0 Hz, *J*² = 7.25 Hz, 1H), 6.65 (dd, *J*¹ = 16.0 Hz, *J*² = 1.0 Hz, 1H), 7.30 (s, 4H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.1, 64.8, 71.9, 123.7, 127.9, 128.8, 133.1, 134.0, 134.3, 170.1, 170.7.

IR (film, cm⁻¹): 1741, 1221.

MS (EI): 282 (M), 222 (M-AcOH), 180, 167, 145.

HRMS calc for C₁₄H₁₅ClO₄: 282.0659, found: 282.0659.

(E)-4-(4-bromophenyl)but-3-ene-1,2-diyl diacetate – 3j

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.08 (s, 3H), 2.12 (s, 3H), 4.17 (dd, *J*¹ = 11.75 Hz, *J*² = 7.0 Hz, 1H), 4.35 (dd, *J*¹ = 11.75 Hz, *J*² = 3.75 Hz, 1H), 5.64 (tdd, *J*¹ = 7.0 Hz, *J*² = 3.75 Hz, *J*³ = 1.0 Hz, 1H), 6.11 (dd, *J*¹ = 16.0 Hz, *J*² = 7.0 Hz, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.1, 64.8, 71.9, 122.2, 123.9, 128.2, 131.7, 133.1, 134.7, 170.0, 170.6.

IR (KBr, cm⁻¹): 1731, 1251, 1226.

MS (EI): 326 (M), 266 (M-AcOH), 226, 211, 145, 128.

HRMS calc for C₁₂H₁₁BrO₂ (M-AcOH): 265.9942, found: 265.9958.

(E)-4-(4-iodophenyl)but-3-ene-1,2-diyl diacetate – 3k

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.08 (s, 3H), 2.12 (s, 3H), 4.17 (dd, *J*¹ = 11.75 Hz, *J*² = 7.0 Hz, 1H), 4.32 (dd, *J*¹ = 11.75 Hz, *J*² = 3.75 Hz, 1H), 5.64 (tdd, *J*¹ = 7.0 Hz, *J*² = 3.5 Hz, *J*³ = 1.0 Hz, 1H), 6.12 (dd, *J*¹ = 16.0 Hz, *J*² = 7.0 Hz, 1H), 6.62 (d, *J* = 16.0 Hz, 1H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 2H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.1, 64.8, 71.8, 93.8, 124.0, 128.4, 133.2, 135.3, 137.7, 170.1, 170.7.

IR (KBr, cm⁻¹): 1731, 1251, 1226.

MS (EI): 374 (M), 314 (M-AcOH), 259, 145, 128.

HRMS calc for C₁₄H₁₅IO₄: 374.0015, found: 374.0015.

(E)-4-(3-nitrophenyl)but-3-ene-1,2-diyl diacetate – 3l

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.09 (s, 3H), 2.14 (s, 3H), 4.19 (dd, $J^1 = 12.0$ Hz, $J^2 = 6.75$ Hz, 1H), 4.35 (dd, $J^1 = 12.0$ Hz, $J^2 = 3.75$ Hz, 1H), 5.68 (tdd, $J^1 = 6.75$ Hz, $J^2 = 3.94$ Hz, $J^3 = 1.12$ Hz, 1H), 6.28 (dd, $J^1 = 16.0$ Hz, $J^2 = 6.75$ Hz, 1H), 6.75 (d, $J = 16.0$ Hz, 1H), 7.53 (d, $J = 8.0$ Hz, 1H), 7.68 (d, $J = 7.75$ Hz, 1H), 8.12 (ddd, $J^1 = 8.14$ Hz, $J^2 = 2.2$ Hz, $J^3 = 1.0$ Hz, 1H), 8.25 (t, $J = 2.0$ Hz, 1H).

¹³C NMR: CDCl₃, 125 MHz, δ(ppm): 20.7, 21.0, 64.6, 71.5, 121.2, 122.8, 126.6, 129.6, 131.7, 132.5, 137.6, 148.6, 170.0, 170.6.

IR (KBr, cm⁻¹): 1732, 1534, 1351, 1250, 1223.

MS (EI): 233 (M-AcOH), 191, 178, 144, 115.

(E)-4-(2-methoxyphenyl)but-3-ene-1,2-diyl diacetate – 3m

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.09 (s, 3H), 2.11 (s, 3H), 3.84 (s, 3H), 4.18 (dd, $J^1 = 11.75$ Hz, $J^2 = 7.25$ Hz, 1H), 4.34 (dd, $J^1 = 11.75$ Hz, $J^2 = 3.75$ Hz, 1H), 5.68 (tdd, $J^1 = 7.25$ Hz, $J^2 = 3.87$ Hz, $J^3 = 1.0$ Hz, 1H), 6.16 (dd, $J^1 = 16.25$ Hz, $J^2 = 7.25$ Hz, 1H), 6.86 (d, $J = 7.5$ Hz, 1H), 6.92 (t, $J = 7.5$ Hz, 1H), 7.02 (d, $J = 16.0$ Hz, 1H), 7.24 (td, $J^1 = 7.5$ Hz, $J^2 = 1.5$ Hz, 1H), 7.40 (dd, $J^1 = 7.5$ Hz, $J^2 = 1.5$ Hz, 1H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.2, 55.3, 65.1, 72.5, 110.8, 120.5, 123.4, 124.7, 127.2, 129.4, 129.5, 156.9, 170.1, 170.7.

IR (KBr, cm⁻¹): 1742, 1245, 1224.

MS (EI): 278 (M), 218 (M-AcOH), 163, 145, 115.

(E)-4-(benzo[d][1,3]dioxol-5-yl)but-3-ene-1,2-diyl diacetate – 3n

¹H NMR: CDCl₃, 250 MHz, δ(ppm): 2.07 (s, 3H), 2.10 (s, 3H), 4.15 (dd, $J^1 = 11.5$ Hz, $J^2 = 7.0$ Hz, 1H), 4.31 (dd, $J^1 = 11.5$ Hz, $J^2 = 3.75$ Hz, 1H), 5.62 (tdd, $J^1 = 7.1$ Hz, $J^2 = 3.8$ Hz, $J^3 = 1.0$ Hz, 1H), 5.94 (dd, $J^1 = 15.75$ Hz, $J^2 = 7.25$ Hz, 1H), 5.95 (s, 3H), 6.61 (d, $J = 15.75$ Hz, 1H), 6.75 (d, $J = 8.0$ Hz, 1H), 6.82 (dd, $J^1 = 8.0$ Hz, $J^2 = 1.5$ Hz, 1H), 6.91 (d, $J = 1.5$ Hz, 1H).

¹³C NMR: CDCl₃, 62.5 MHz, δ(ppm): 20.8, 21.1, 65.0, 72.1, 101.1, 105.7, 108.3, 121.1, 121.7, 130.2, 134.2, 147.8, 148.1, 170.1, 170.7.

IR (KBr, cm^{-1}): 1742, 1248, 1039.

MS (EI): 292 (M), 232 (M-AcOH), 190, 177, 115.

Procedure for the Heck Arylation of Olefin 4

To a microwave test tube were added $\text{Pd}_2(\text{dba})_3 \cdot \text{dba}$ (4 mol%, 6 mg), sodium acetate (3 equiv, 0.45 mmol, 40 mg) and benzonitrile (2 mL). To the resulting suspension were then added the lactone **4** (0.15 mmol, 23.5 mg) and the arenediazonium salt (1.1 equiv, 0.17 mmol). The reaction was stirred in a microwave reactor, at 80 °C under a 300 w power, for 1 h. After this time, the crude reaction mixture was filtered in a plug of silica and concentrated under reduced pressure. The product was purified by flash chromatography (hexanes:ethyl acetate 1:1) to provide the Heck adduct.

(*E*)-4-methoxy-6-(4-methoxystyryl)-5,6-dihydro-2H-pyran-2-one – 5.³

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 2.52 (dd, $J^1 = 17.0$ Hz, $J^2 = 4.75$ Hz, 1H), 2.67 (ddd, $J^1 = 17.0$ Hz, $J^2 = 10.0$ Hz, $J^3 = 1.25$ Hz, 1H), 3.76 (s, 3H), 3.80 (s, 3H), 4.98-5.07 (m, 1H), 5.18 (d, $J = 1.25$ Hz, 1H), 6.11 (dd, $J^1 = 17.0$ Hz, $J^2 = 6.5$ Hz, 1H), 6.66 (d, $J = 17.0$ Hz, 1H), 6.86 (d, $J = 8.75$ Hz, 2H), 7.32 (d, $J = 8.75$ Hz, 2H).

^{13}C NMR: CDCl_3 , 125 MHz, $\delta(\text{ppm})$: 33.6, 55.5, 56.3, 90.8, 114.3, 123.4, 128.2, 128.6, 133.1, 160.0, 167.1, 172.6, 199.7.

I.R. (film, cm^{-1}) 3015, 2970, 2946, 1739, 1366, 1228, 1217.

MS (EI) m/z = 260 (M), 232, 161, 134, 121, 98, 68.

(*E*)-6-(2-(benzo[*d*][1,3]dioxol-5-yl)vinyl)-4-methoxy-5,6-dihydro-2H-pyran-2-one – 7.²

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 2.52 (dd, $J^1 = 17.0$ Hz, $J^2 = 4.5$ Hz, 1H), 2.66 (ddd, $J^1 = 17.0$ Hz, $J^2 = 10.75$ Hz, $J^3 = 1.25$ Hz, 1H), 3.77 (s, 3H), 4.98-5.07 (m, 1H), 5.19 (d, $J = 1.25$ Hz, 1H), 5.97 (s, 2H), 6.08 (dd, $J^1 = 15.75$ Hz, $J^2 = 6.25$ Hz, 1H), 6.64 (dd, $J^1 = 15.75$ Hz, $J^2 = 1.0$ Hz, 1H), 6.76 (d, $J = 8.0$ Hz, 1H), 6.83 (dd, $J^1 = 8.0$ Hz, $J^2 = 1.5$ Hz, 1H), 6.92 (d, $J = 1.5$ Hz, 1H).

³ (a) Amaral, P. A.; Gouault, N.; Le Roch, M.; Eifler-Lima, V.; David, M. *Tetrahedron Lett.* **2008**, 49, 6607. (b) Hashimoto, T.; Suganuma, M.; Fujiki, H.; Yamada, M.; Kohno, T.; Asakawa, Y. *Phytomedicine* **2003**, 10, 309. (c) Lygo, B. *Tetrahedron* **1995**, 51, 12859.

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 33.3, 56.1, 76.0, 90.5, 101.2, 105.8, 108.3, 121.7, 123.6, 130.1, 132.9, 147.8, 148.1, 166.8, 172.3.
I.R. (film, cm^{-1}) 1706, 1624, 1249, 1220.

Procedure for the DDQ oxidation of Heck adduct 5

To a round-bottomed flask, under argon atmosphere, were added the Heck adduct **5** (0.15 mmol, 40 mg) and dry benzene (2 mL). To this solution, DDQ (0.18 mmol, 42 mg) was added and the reaction was refluxed for 2 h. After this time, the crude reaction mixture was filtered through a plug of Celite and concentrated under reduced pressure. The product was purified by flash chromatography (hexanes:ethyl acetate 1:1) to provide iangonine in 85 % yield.

(*E*)-4-methoxy-6-(4-methoxystyryl)-2H-pyran-2-one – **6**.²

^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 3.82 (s, 3H), 3.83 (s, 3H), 5.47 (d, $J = 2.0$ Hz, 1H), 5.89 (d, $J = 2.0$ Hz, 1H), 6.45 (d, $J = 16.0$ Hz, 1H), 6.90 (d, $J = 8.75$ Hz, 2H), 7.43-7.48 (m, 3H).

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 55.3, 55.9, 88.3, 100.5, 114.3, 116.3, 128.0, 129.0, 135.4, 159.1, 160.7, 164.2, 171.2.

I.R. (film, cm^{-1}) 3016, 2970, 1736, 1366, 1229, 1216.

MS (EI) $m/z = 258$ (M), 230, 215, 187, 159, 115, 89, 69.

Procedure for the Hydrogenation of Heck adduct 7.⁴

To a round-bottomed flask, under hydrogen atmosphere, were added the Heck adduct **7** (0.15 mmol, 41 mg) and dry methanol (3 mL), followed by the addition of Pd/C 10 % (20% w/w, 9 mg). The reaction was stirred at room temperature for 12 h. After this time, the crude reaction mixture was filtered through a plug of Celite and concentrated under reduced pressure. The product was purified by flash chromatography (hexanes:ethyl acetate 1:1) to provide ($\pm$)-dihydromethysticin in 95 % yield.

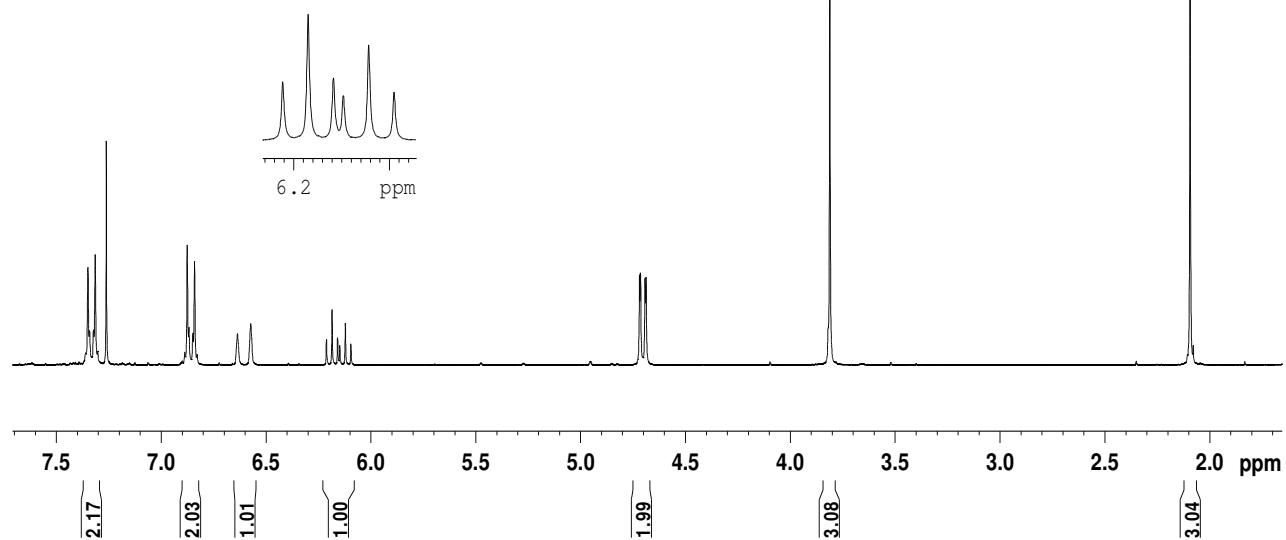
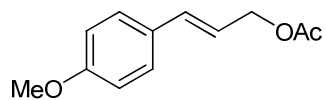
⁴ Pierres, C.; George, P.; van Hijfte, L.; Ducep, J. B.; Hibert, M.; Mann, A. *Tetrahedron Lett.* **2003**, *44*, 3645.

6-(2-(benzo[d][1,3]dioxol-5-yl)ethyl)-4-methoxy-5,6-dihydro-2H-pyran-2-one - 8

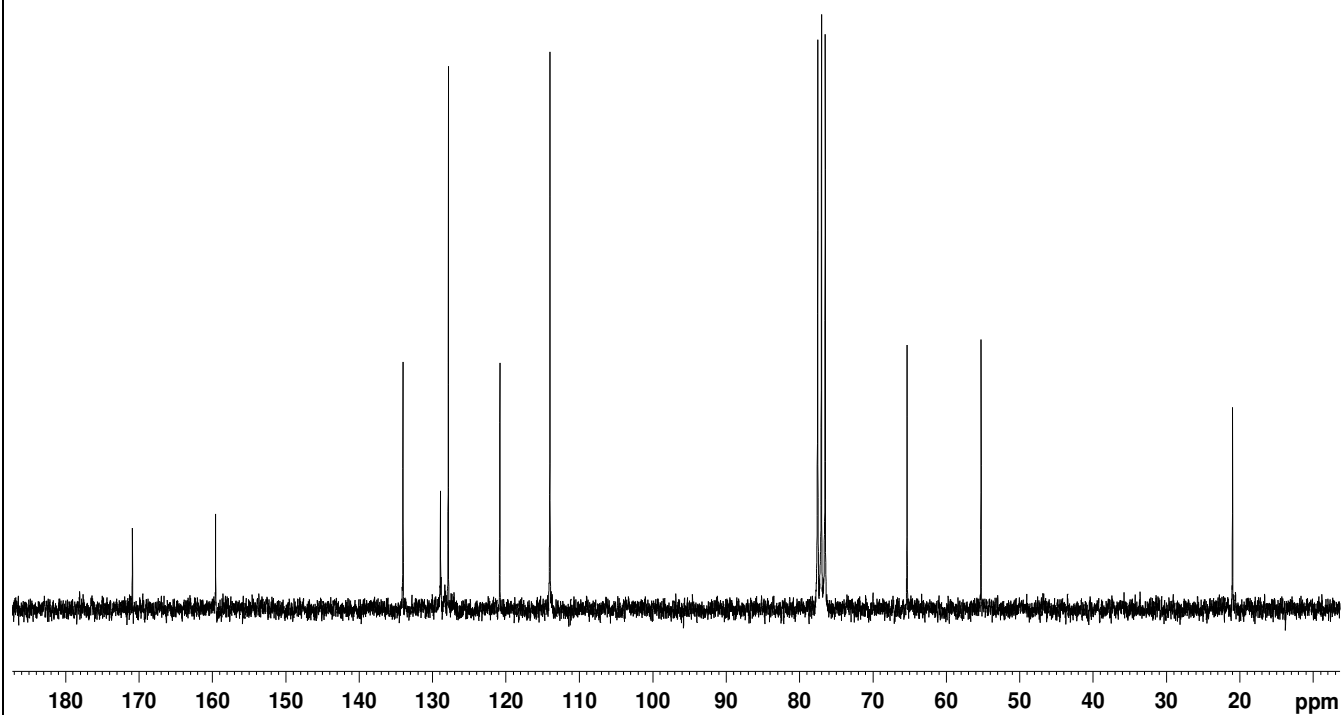
^1H NMR: CDCl_3 , 250 MHz, $\delta(\text{ppm})$: 1.79-1.93 (m, 1H), 2.01-2.17 (m, 1H), 2.28 (dd, $J^1 = 17.0$ Hz, $J^2 = 4.0$ Hz, 1H), 2.50 (ddd, $J^1 = 17.0$ Hz, $J^2 = 12.0$ Hz, $J^3 = 1.5$ Hz, 1H), 2.64-2.86 (m, 2H), 3.73 (s, 3H), 4.29-4.40 (m, 1H), 5.13 (d, $J = 1.5$ Hz, 1H), 5.92 (s, 2H), 6.63-6.75 (m, 3H).

^{13}C NMR: CDCl_3 , 62.5 MHz, $\delta(\text{ppm})$: 30.7, 36.6, 56.0, 74.6, 90.3, 100.8, 108.3, 108.8, 121.3, 134.6, 145.8, 147.7, 167.3, 172.7.

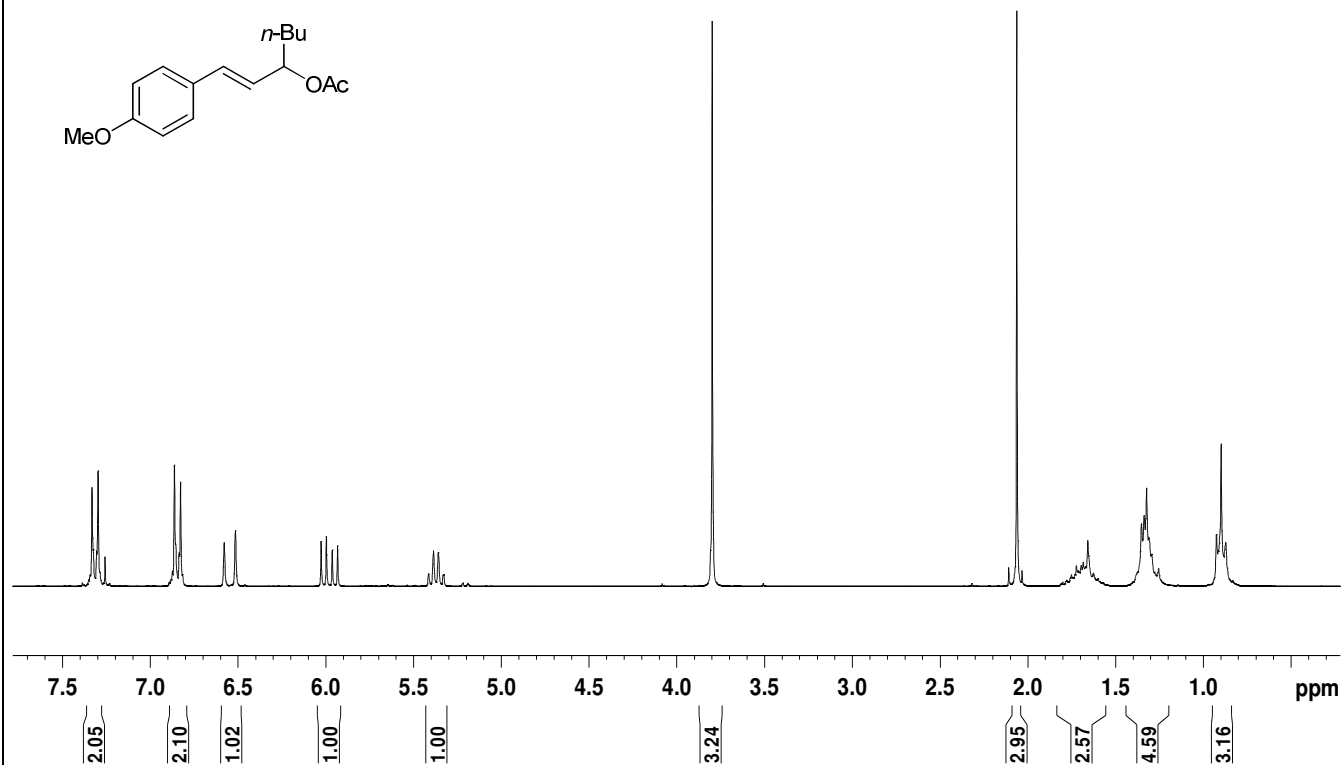
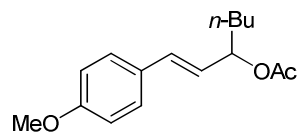
SELECTED SPECTRA



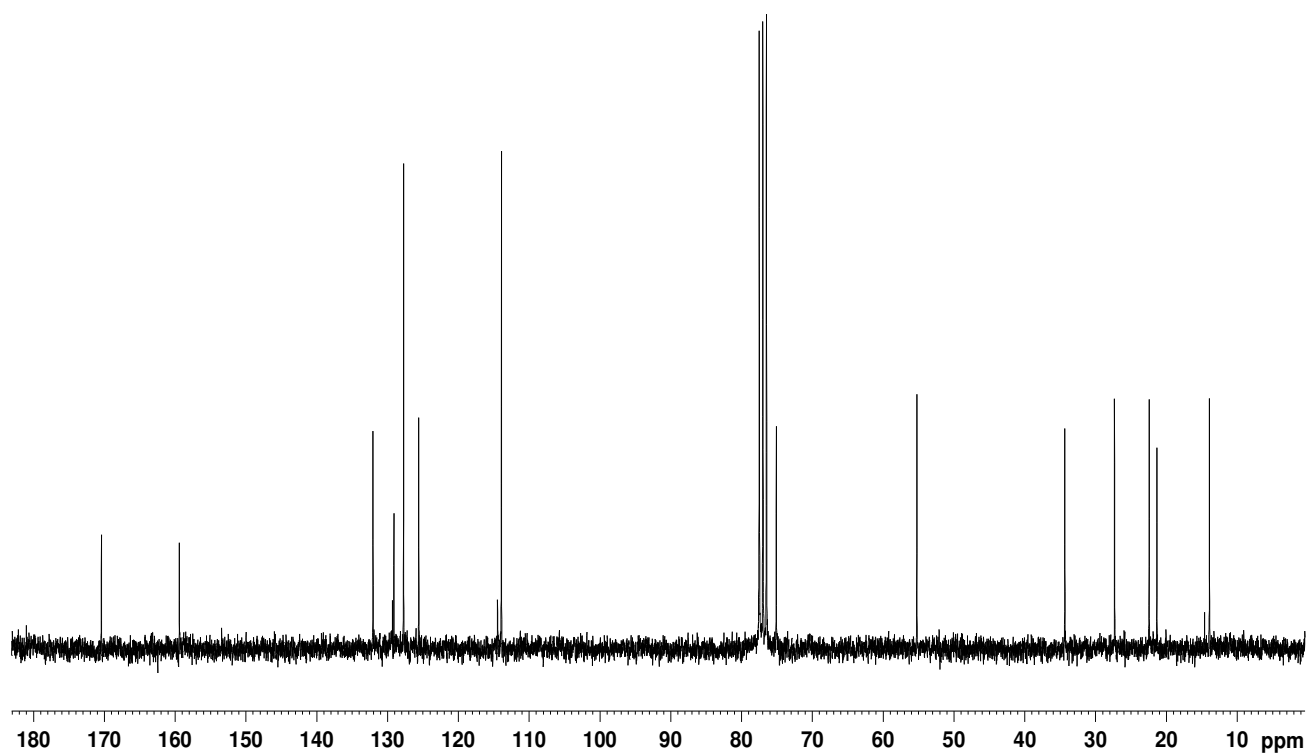
Spectrum of ^1H NMR of the compound **3a** in CDCl_3 , 250 MHz



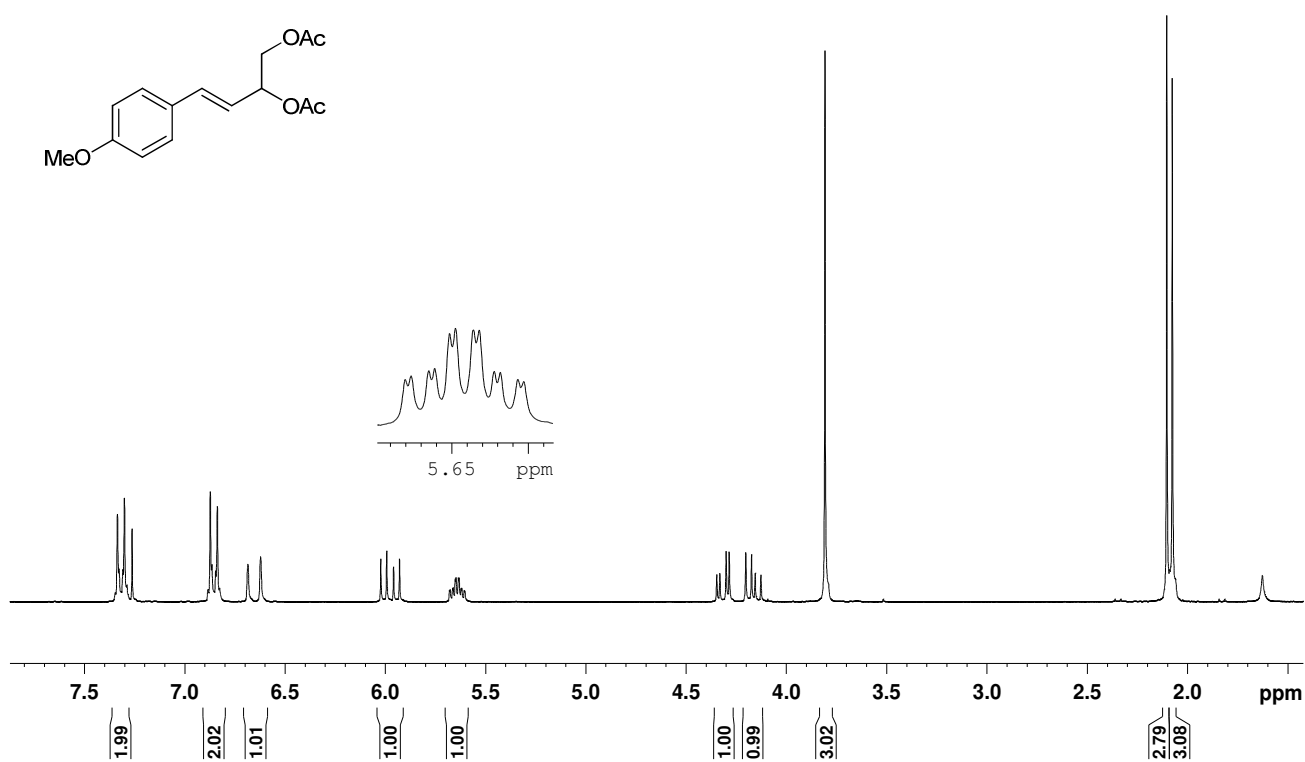
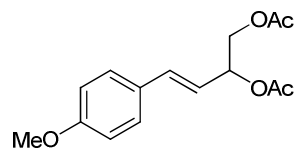
Spectrum of ^{13}C NMR of the compound **3a** in CDCl_3 , 62.5 MHz



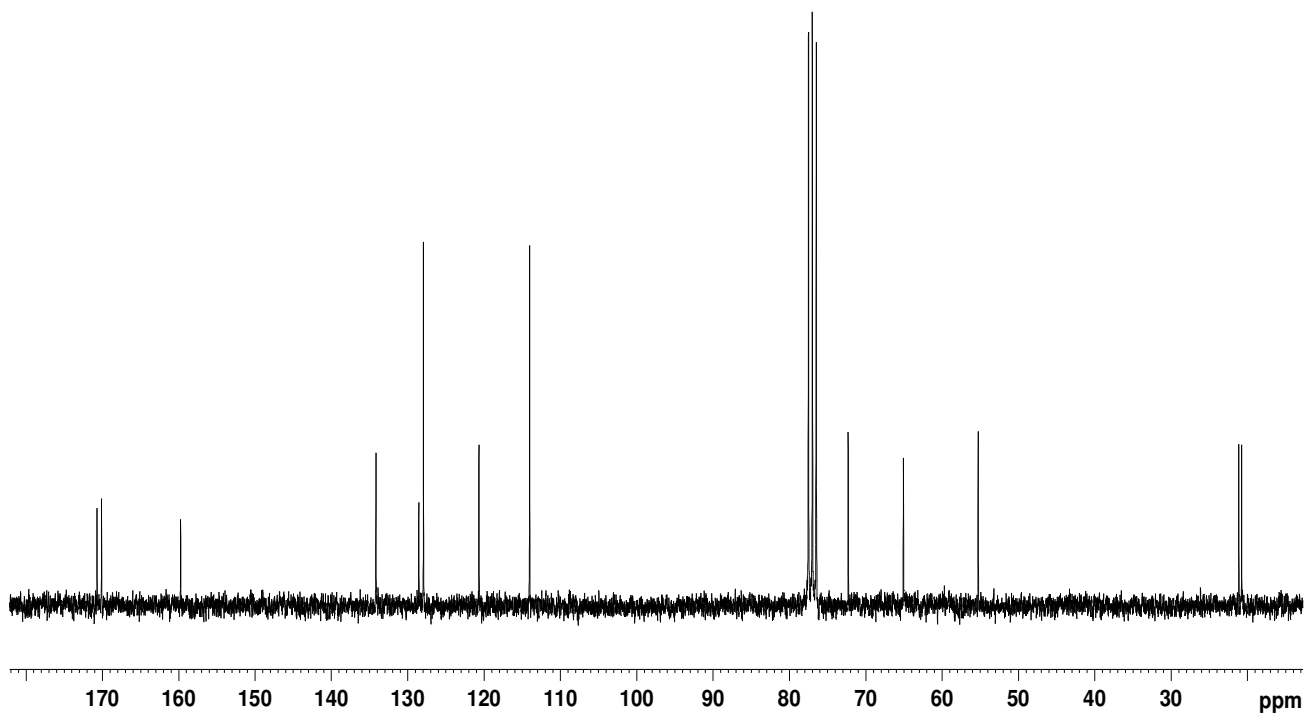
Spectrum of ^1H NMR of the compound **3b** in CDCl_3 , 250 MHz



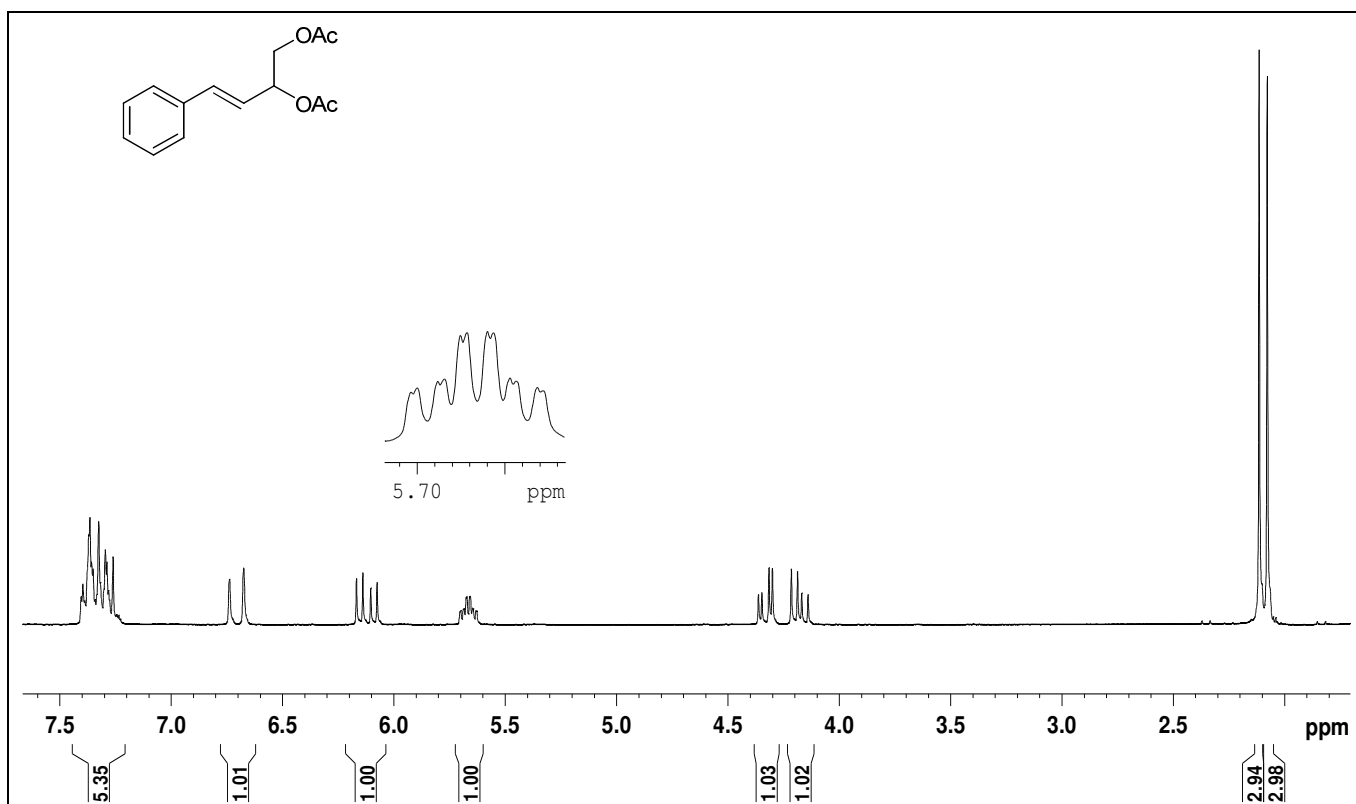
Spectrum of ^{13}C NMR of the compound **3b** in CDCl_3 , 62.5 MHz



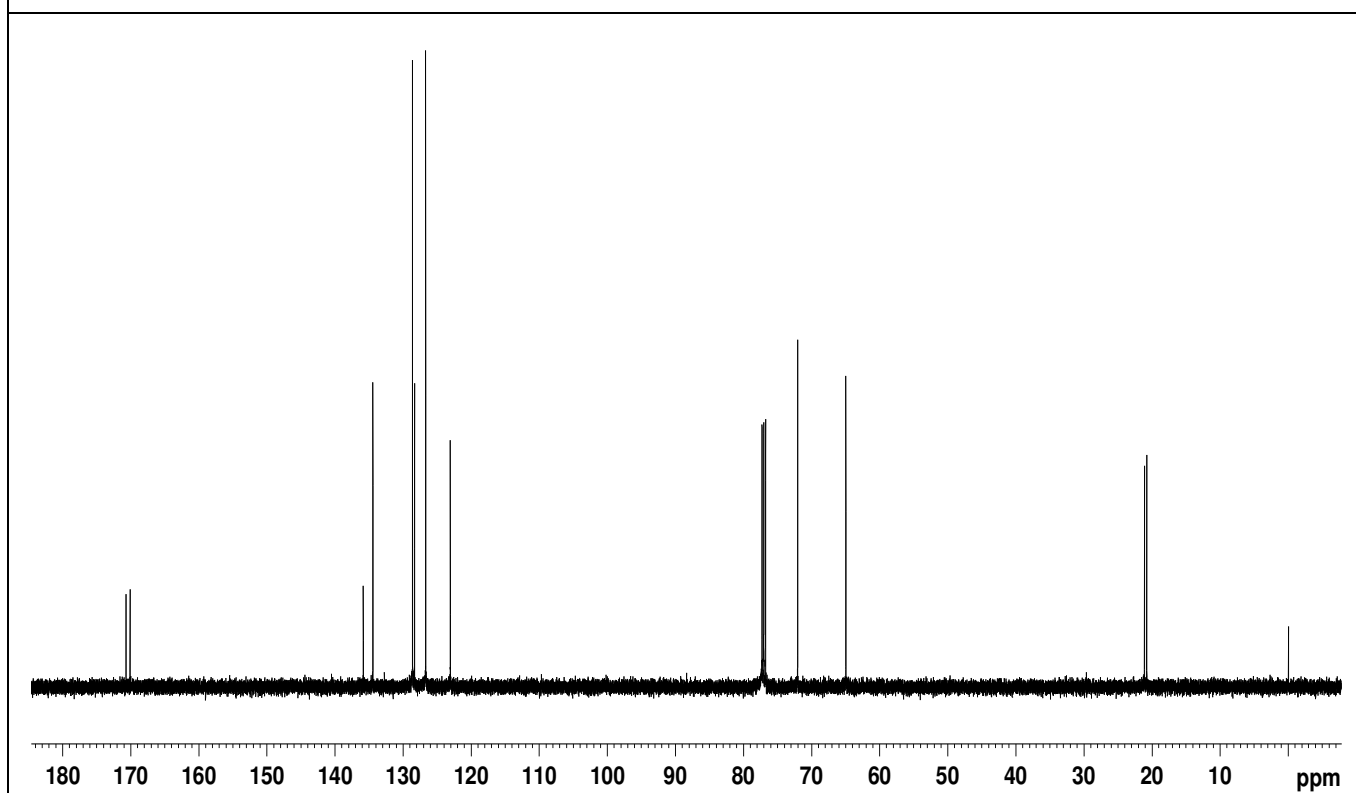
Spectrum of ^1H NMR of the compound **3c** in CDCl_3 , 250 MHz



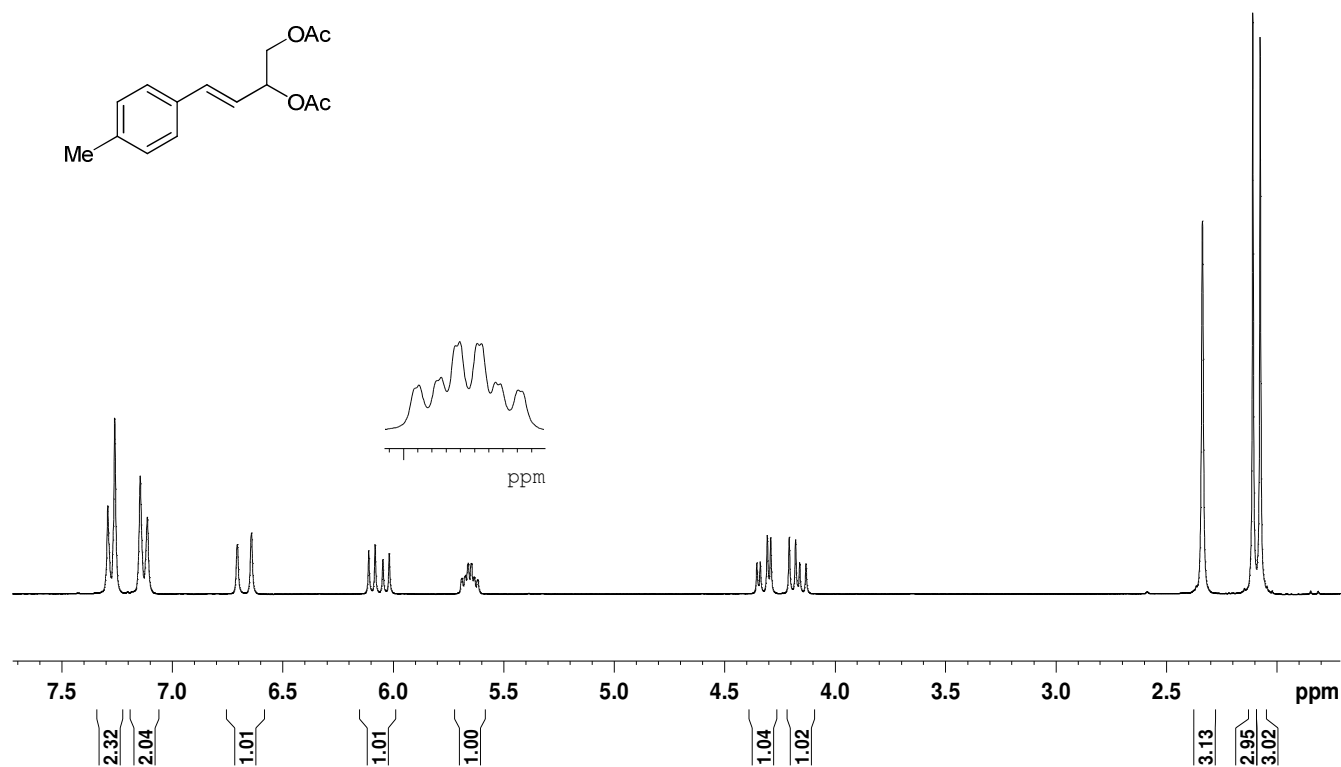
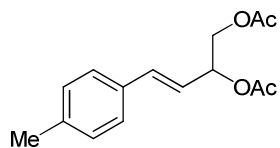
Spectrum of ^{13}C NMR of the compound **3c** in CDCl_3 , 62.5 MHz



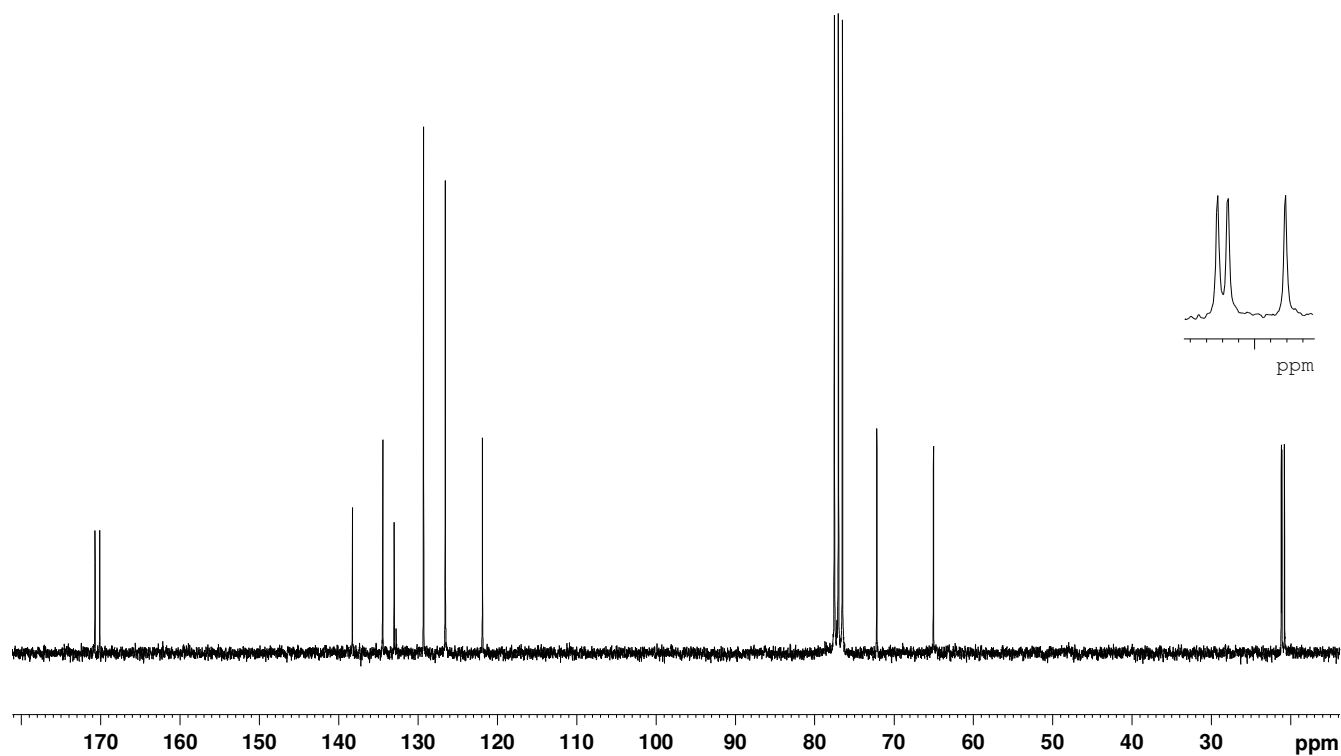
Spectrum of ¹H NMR of the compound **3d** in CDCl₃, 250 MHz



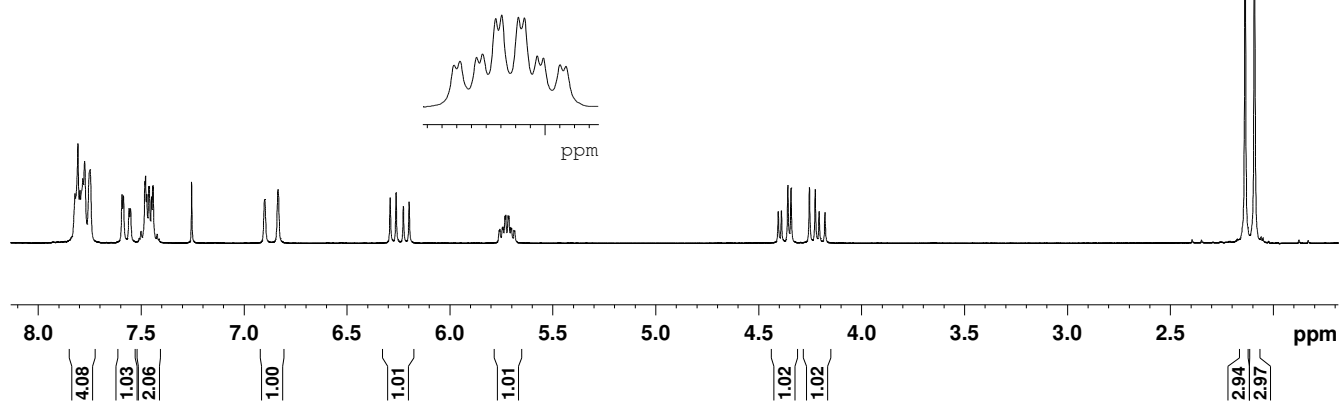
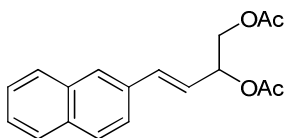
Spectrum of ¹³C NMR of the compound **3d** in CDCl₃, 125 MHz



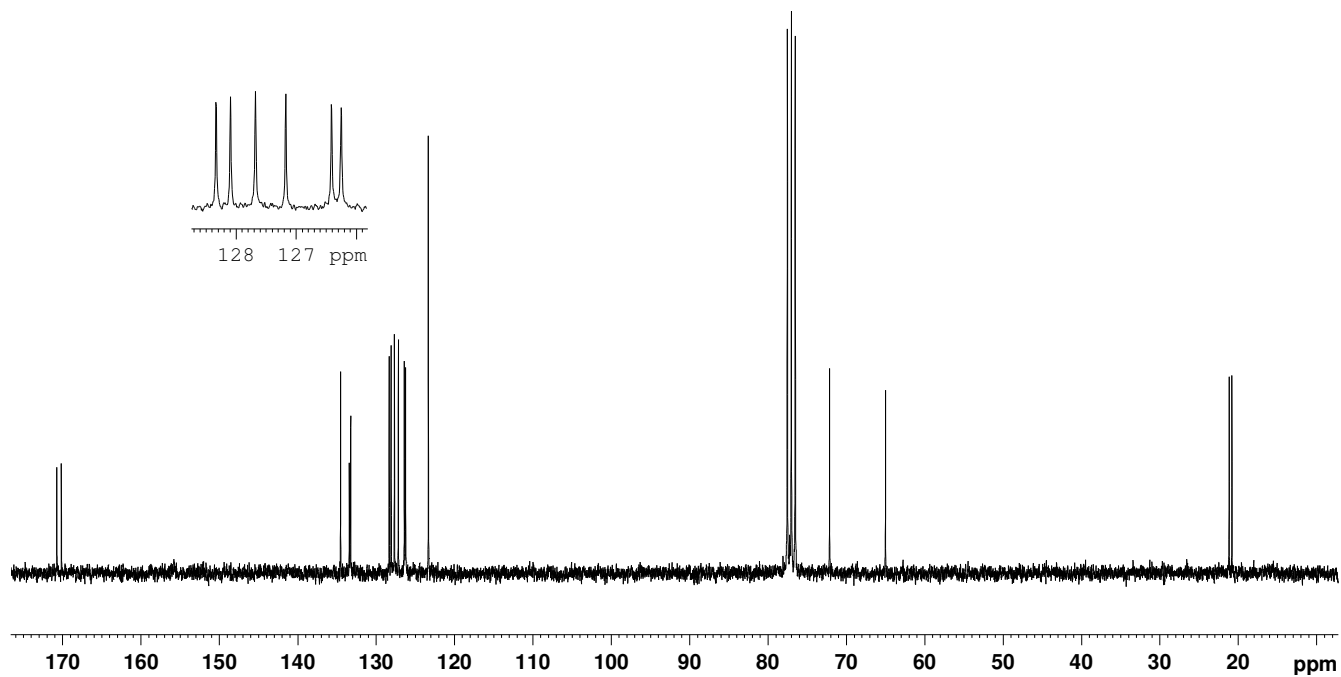
Spectrum of ^1H NMR of the compound **3e** in CDCl_3 , 250 MHz



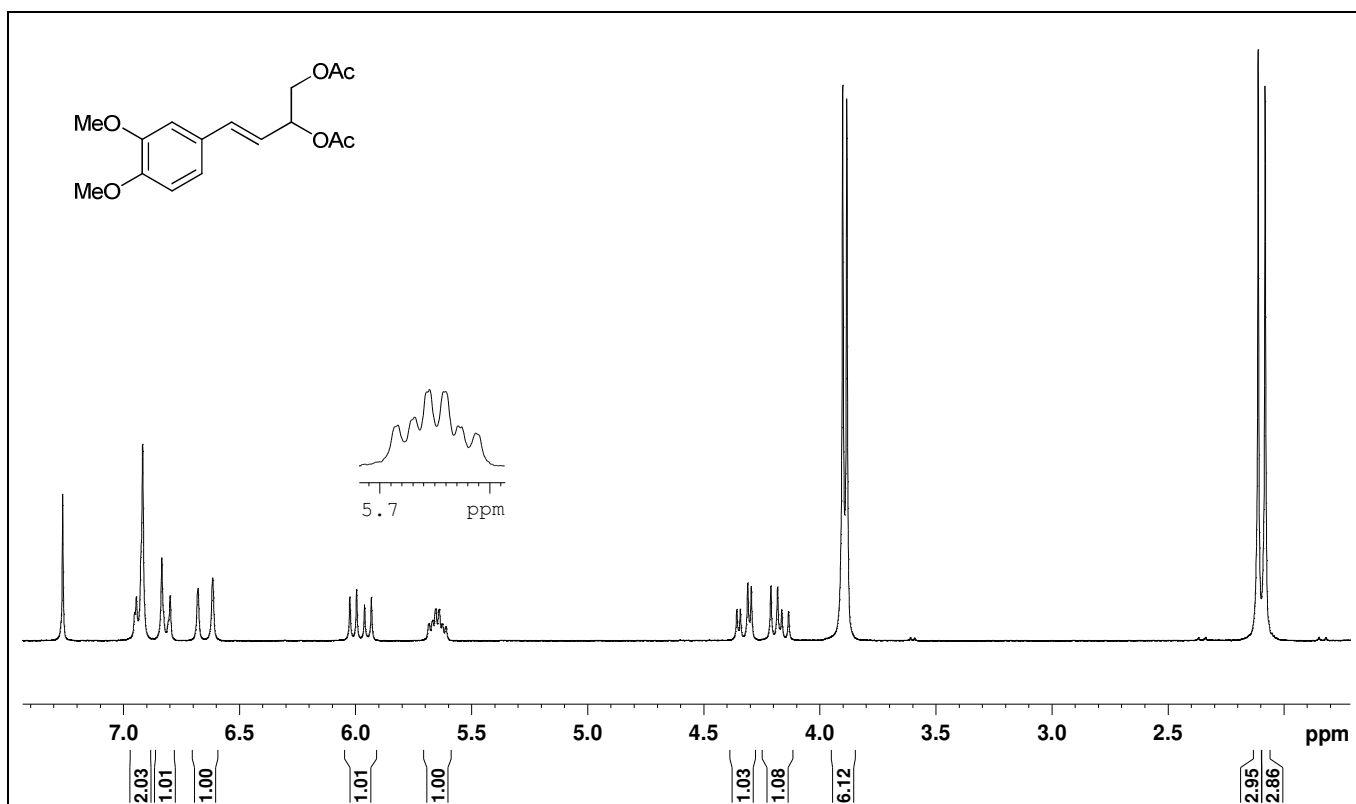
Spectrum of ^{13}C NMR of the compound **3e** in CDCl_3 , 62.5 MHz



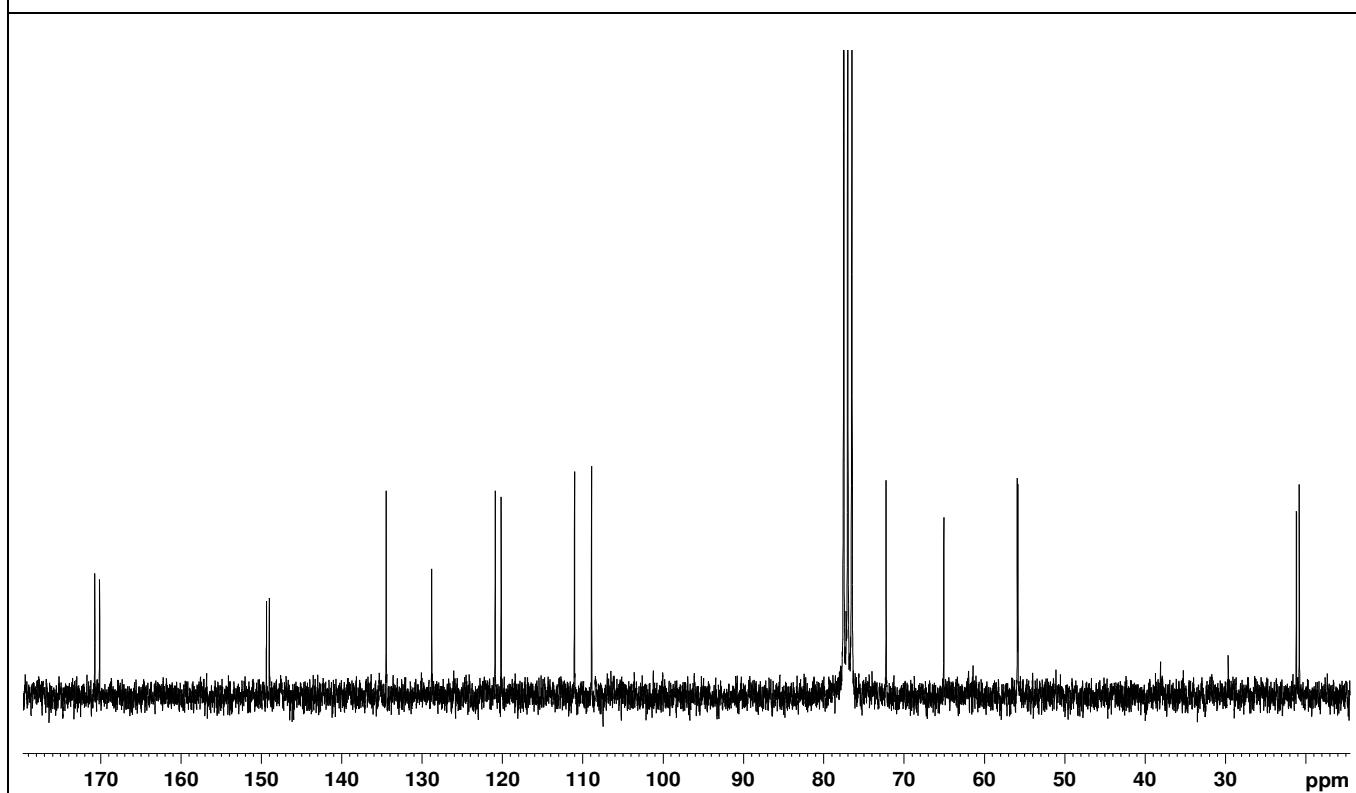
Spectrum of ^1H NMR of the compound **3f** in CDCl_3 , 250 MHz



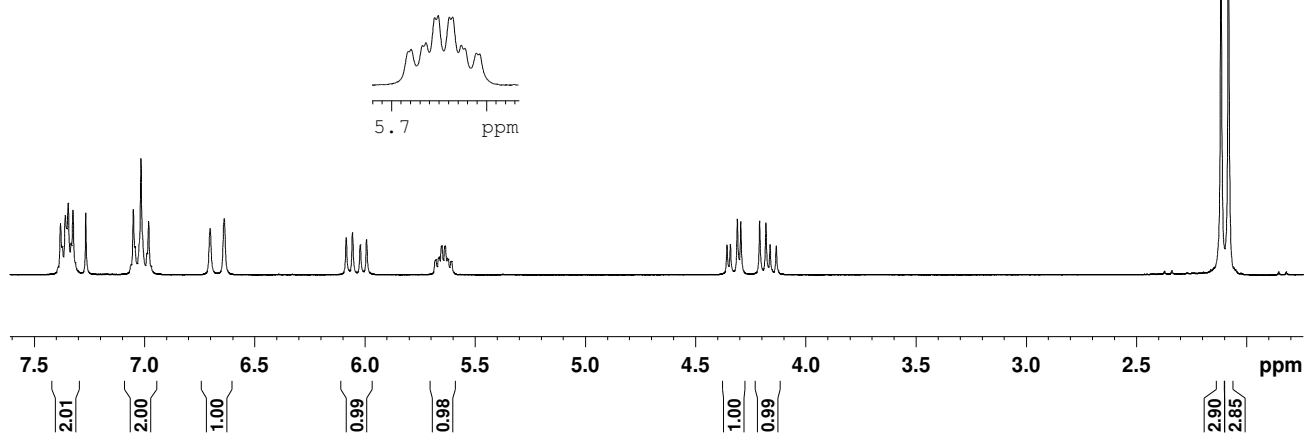
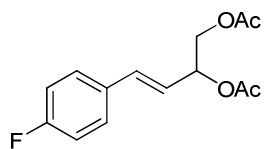
Spectrum of ^{13}C NMR of the compound **3f** in CDCl_3 , 62.5 MHz



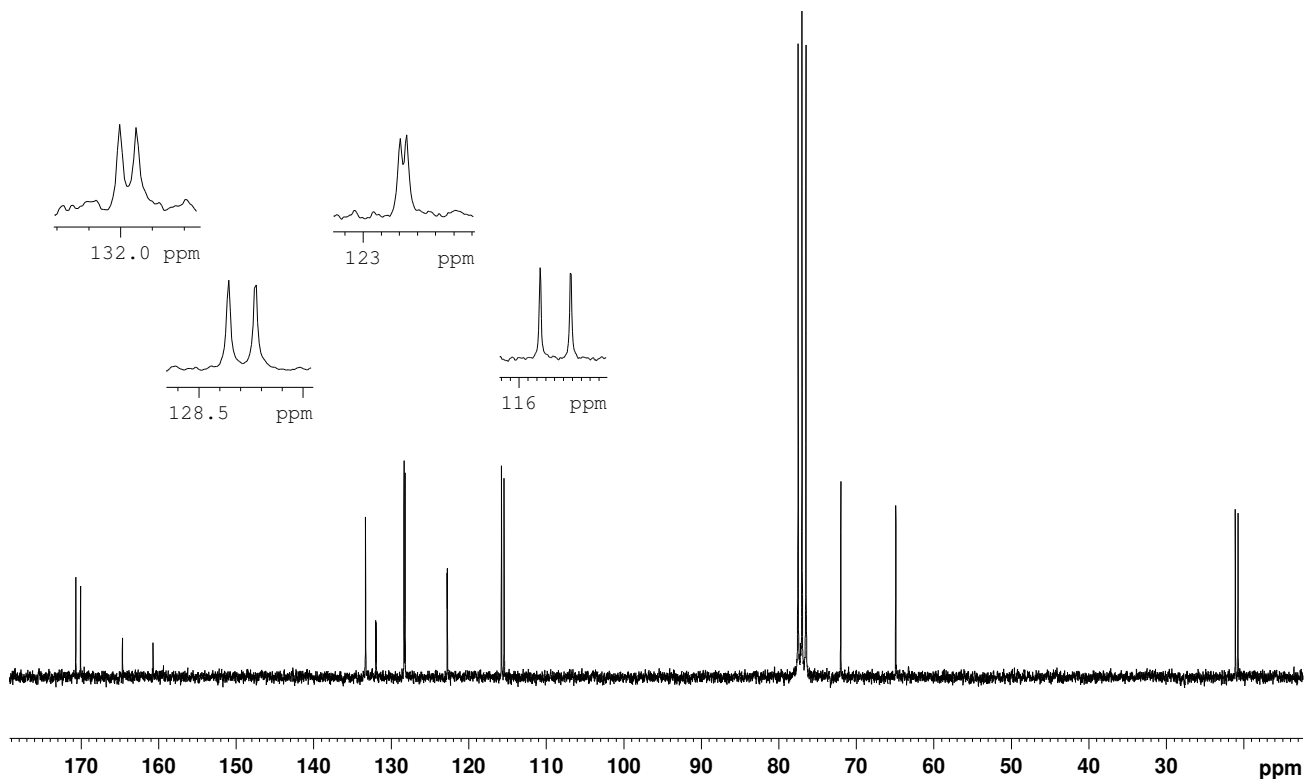
Spectrum of ¹H NMR of the compound **3g** in CDCl₃, 250 MHz



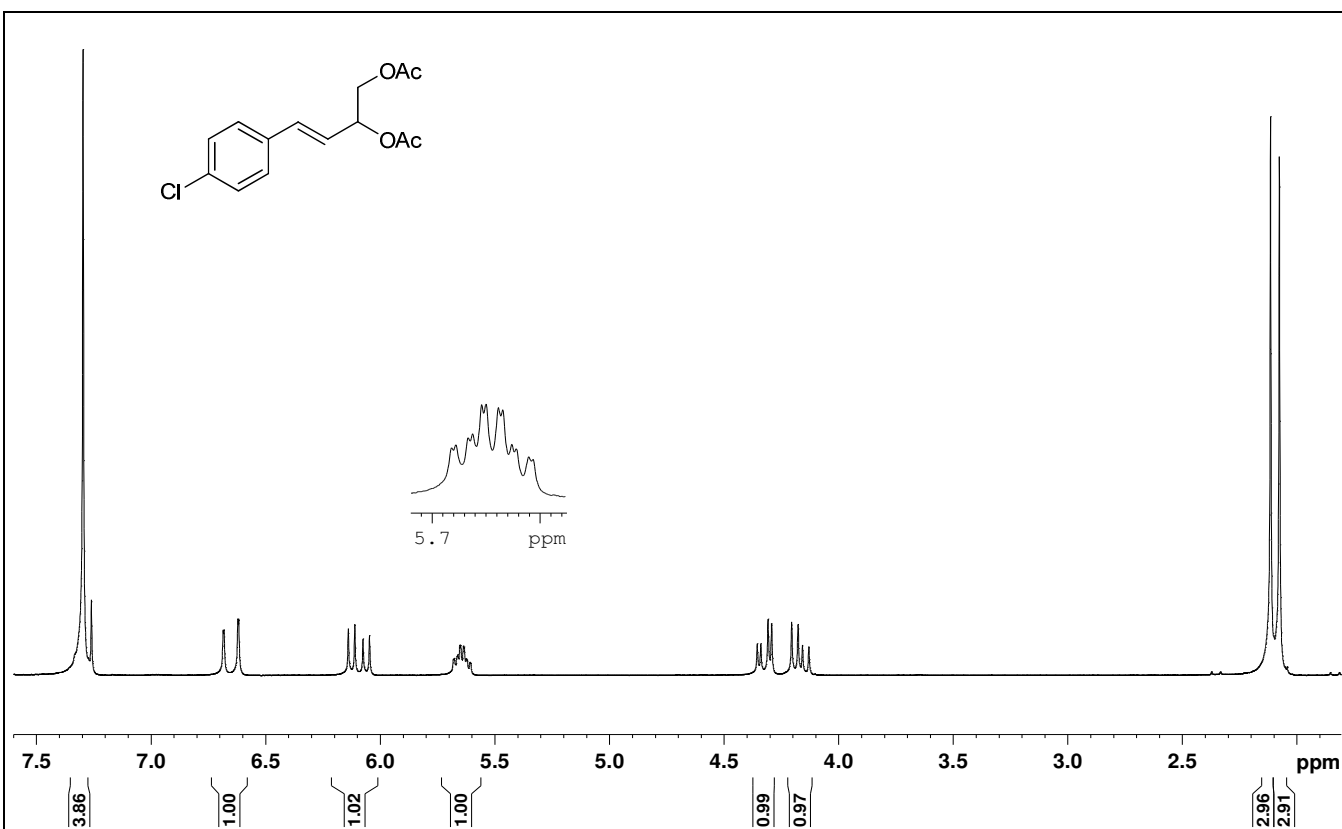
Spectrum of ¹³C NMR of the compound **3g** in CDCl₃, 62.5 MHz



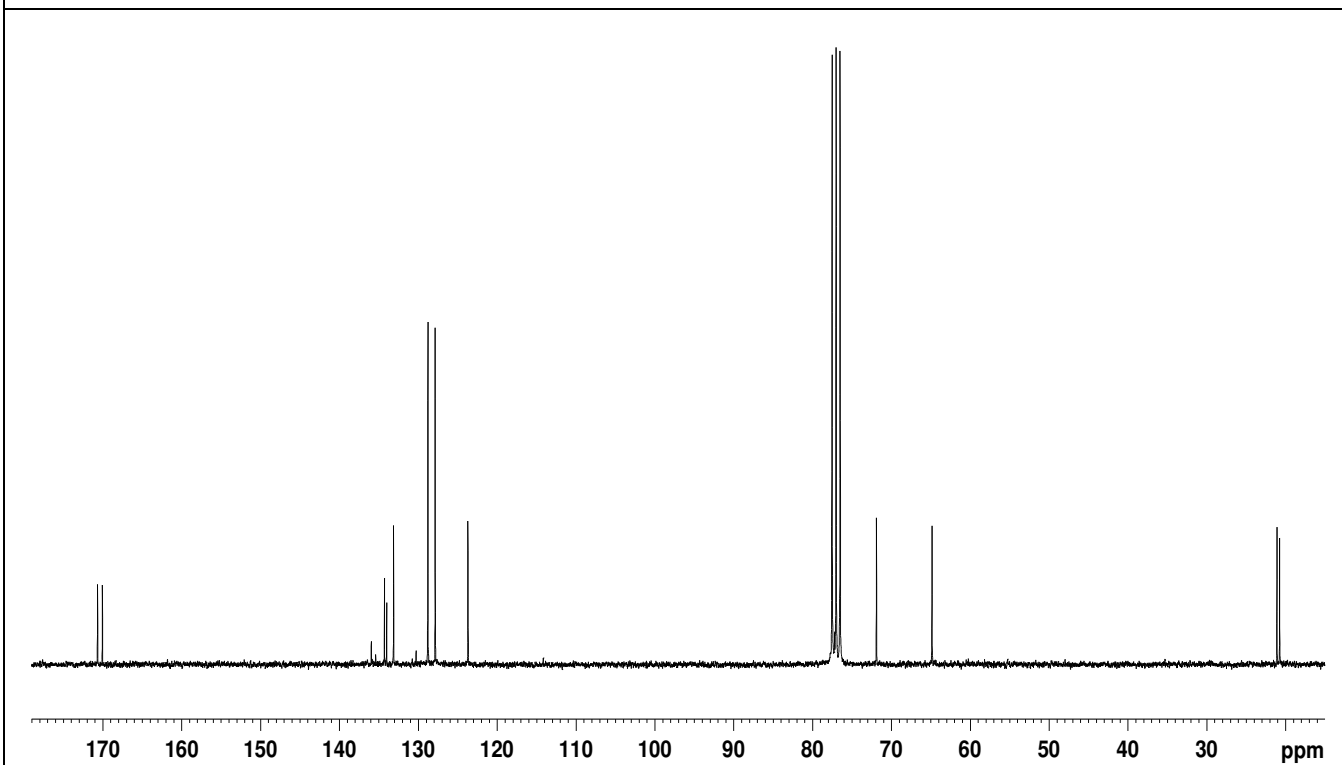
Spectrum of ^1H NMR of the compound **3h** in CDCl_3 , 250 MHz



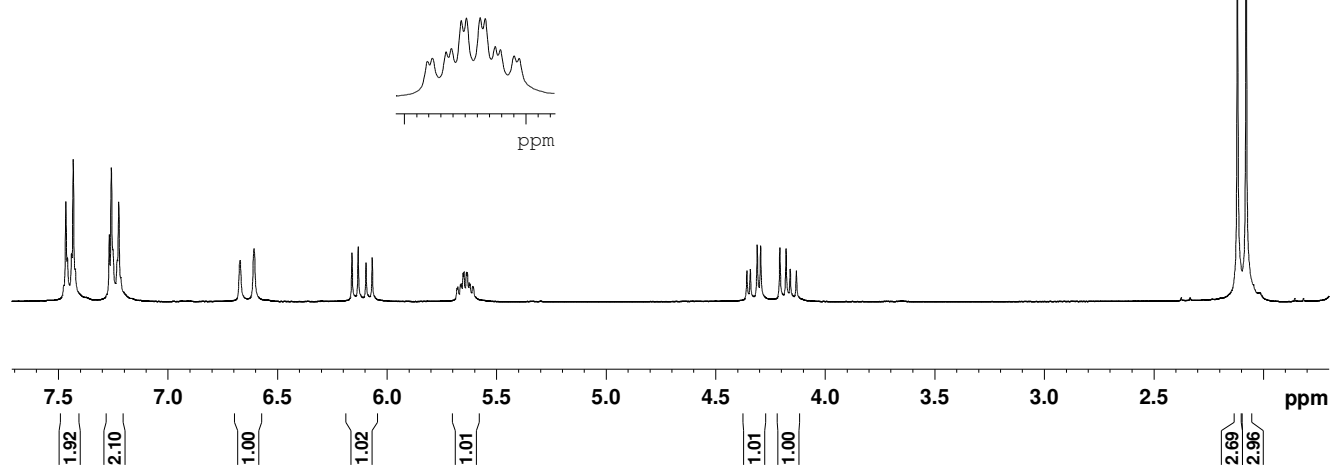
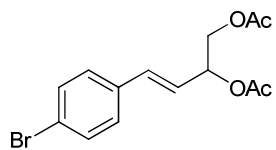
Spectrum of ^{13}C NMR of the compound **3h** in CDCl_3 , 62.5 MHz



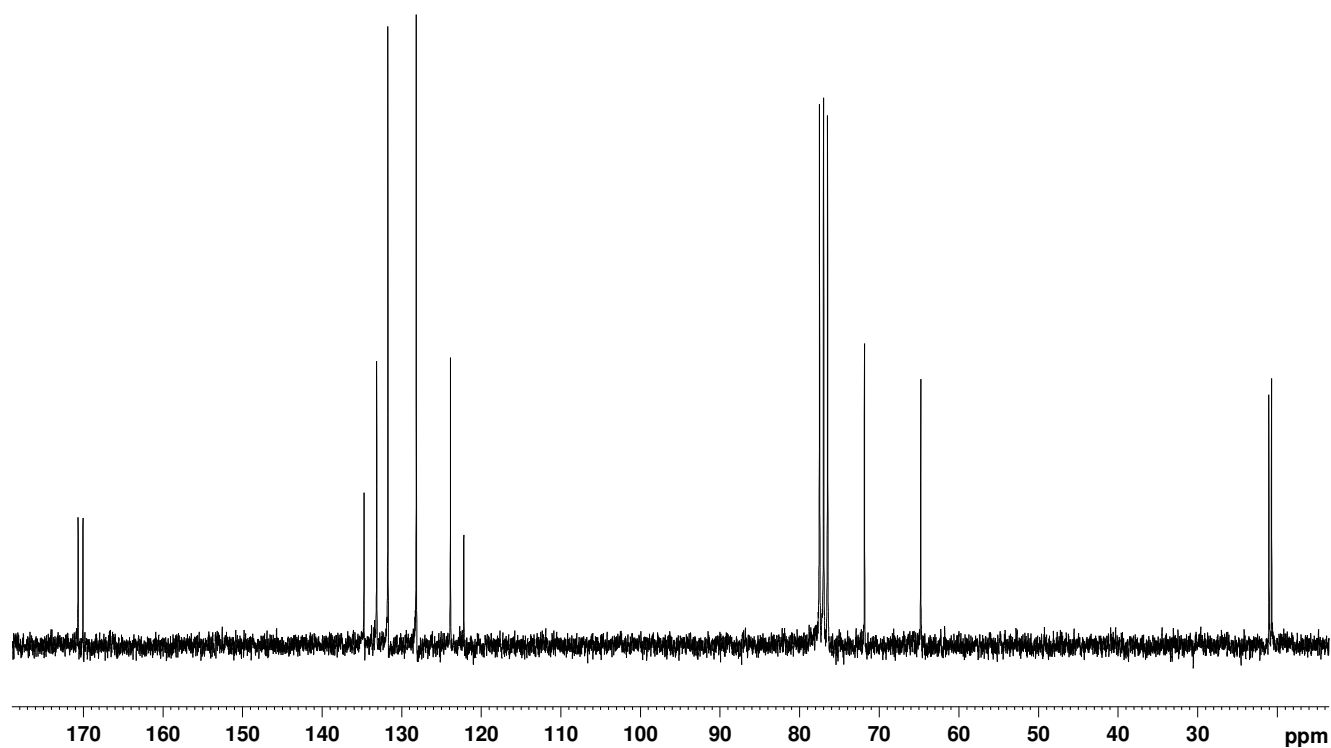
Spectrum of ¹H NMR of the compound **3i** in CDCl₃, 250 MHz



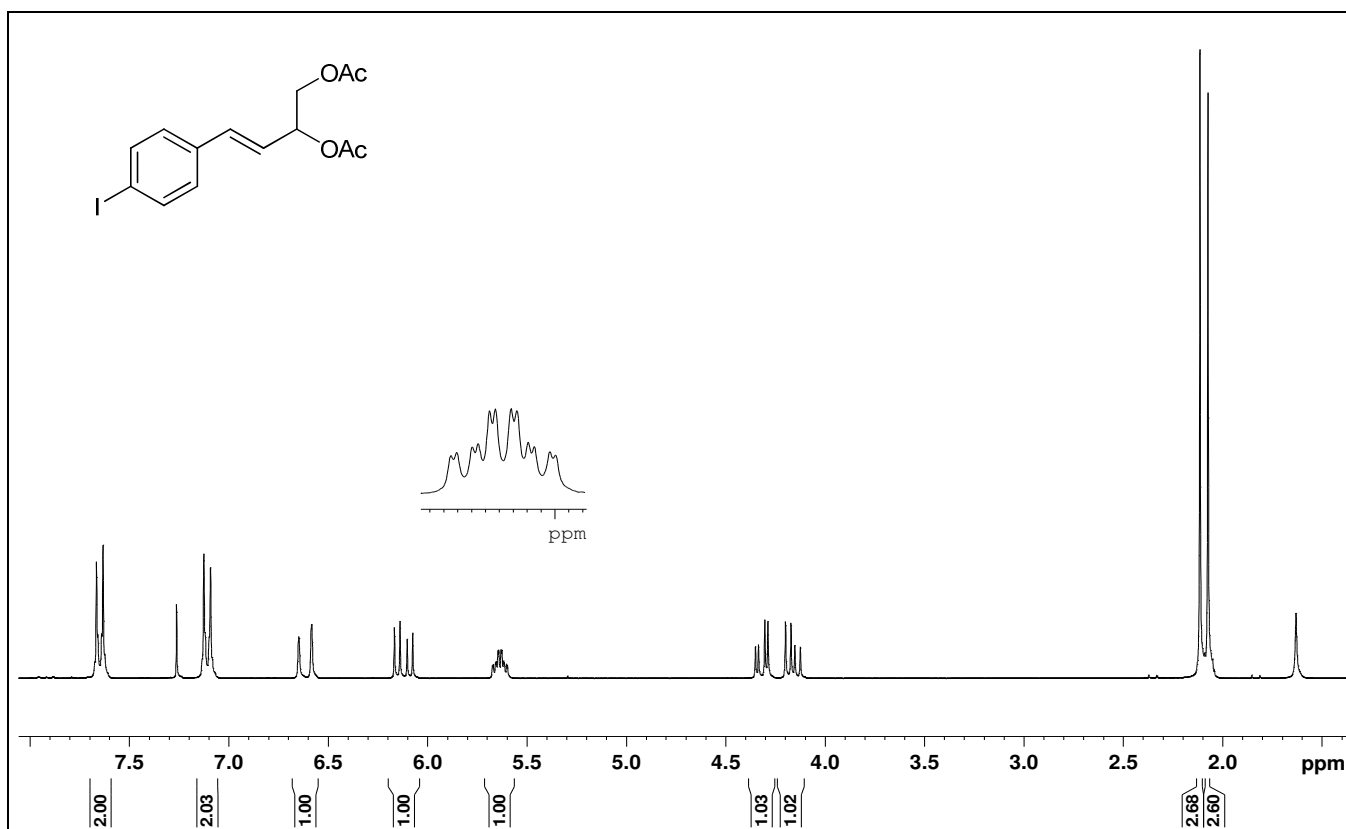
Spectrum of ¹³C NMR of the compound **3i** in CDCl₃, 62.5 MHz



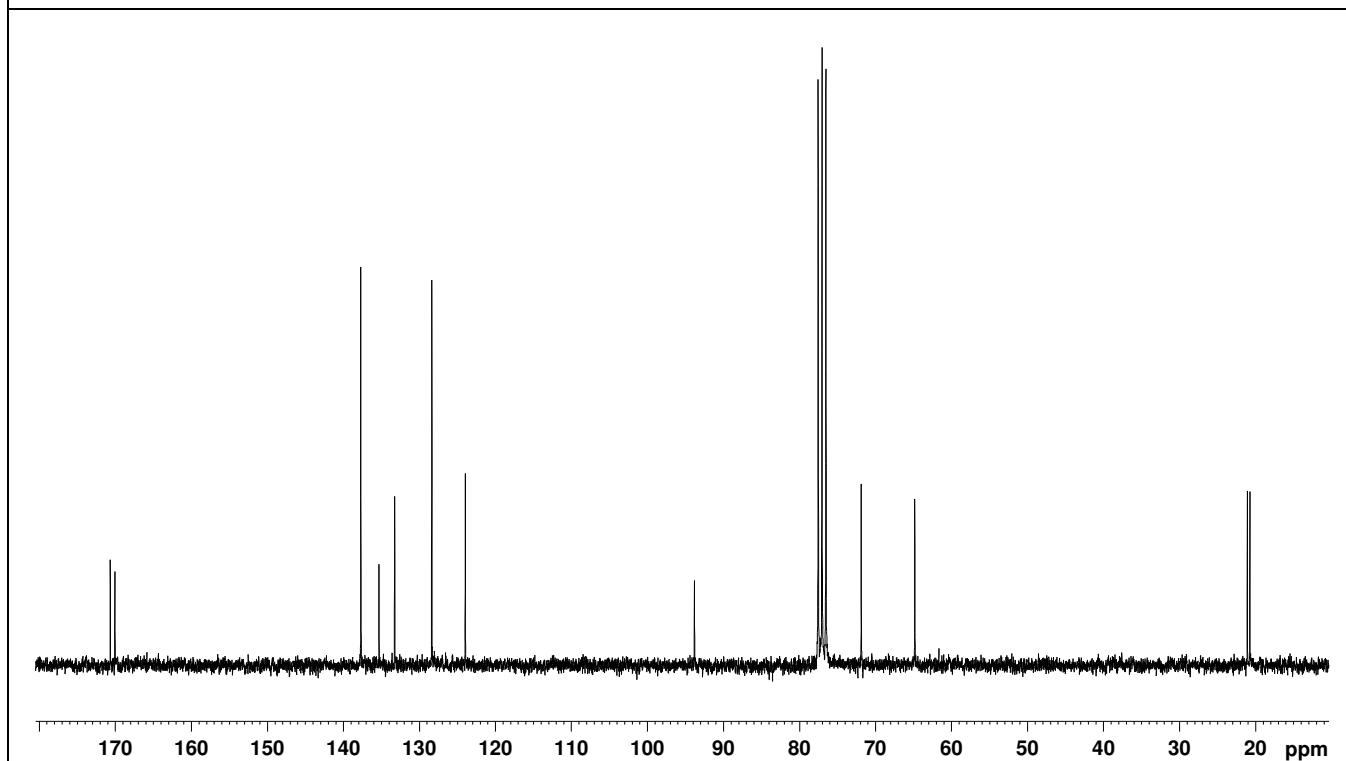
Spectrum of ^1H NMR of the compound **3j** in CDCl_3 , 250 MHz



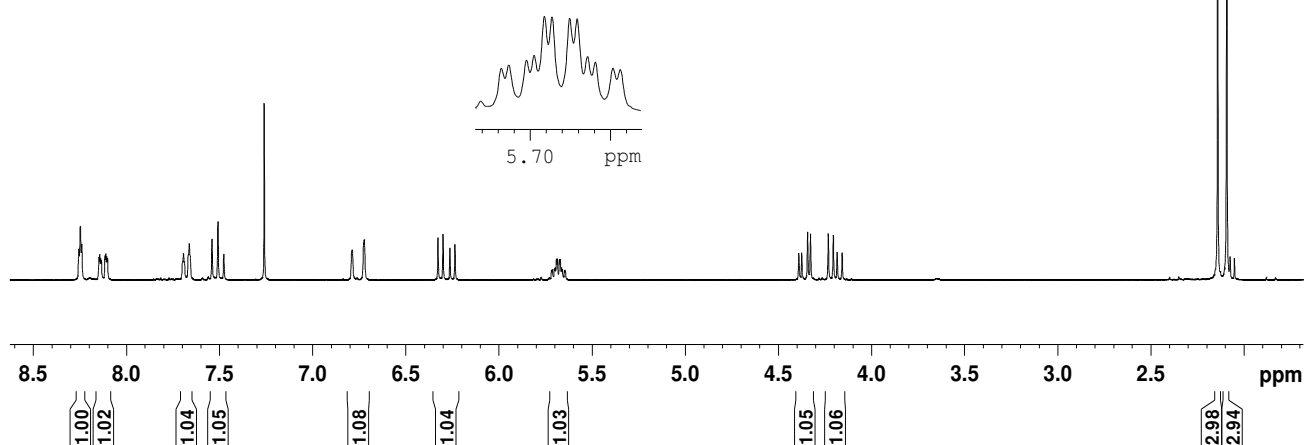
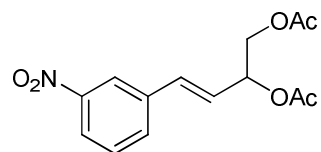
Spectrum of ^{13}C NMR of the compound **3j** in CDCl_3 , 62.5 MHz



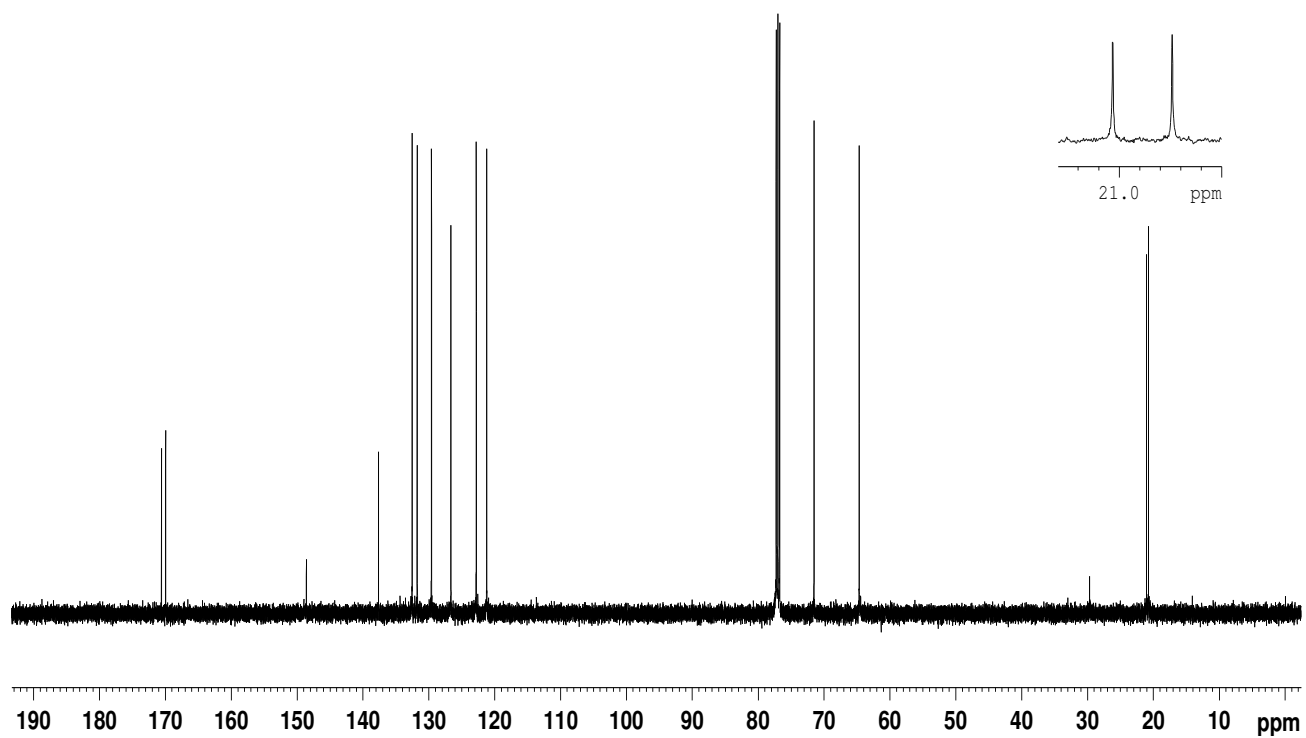
Spectrum of ^1H NMR of the compound **3k** in CDCl_3 , 250 MHz



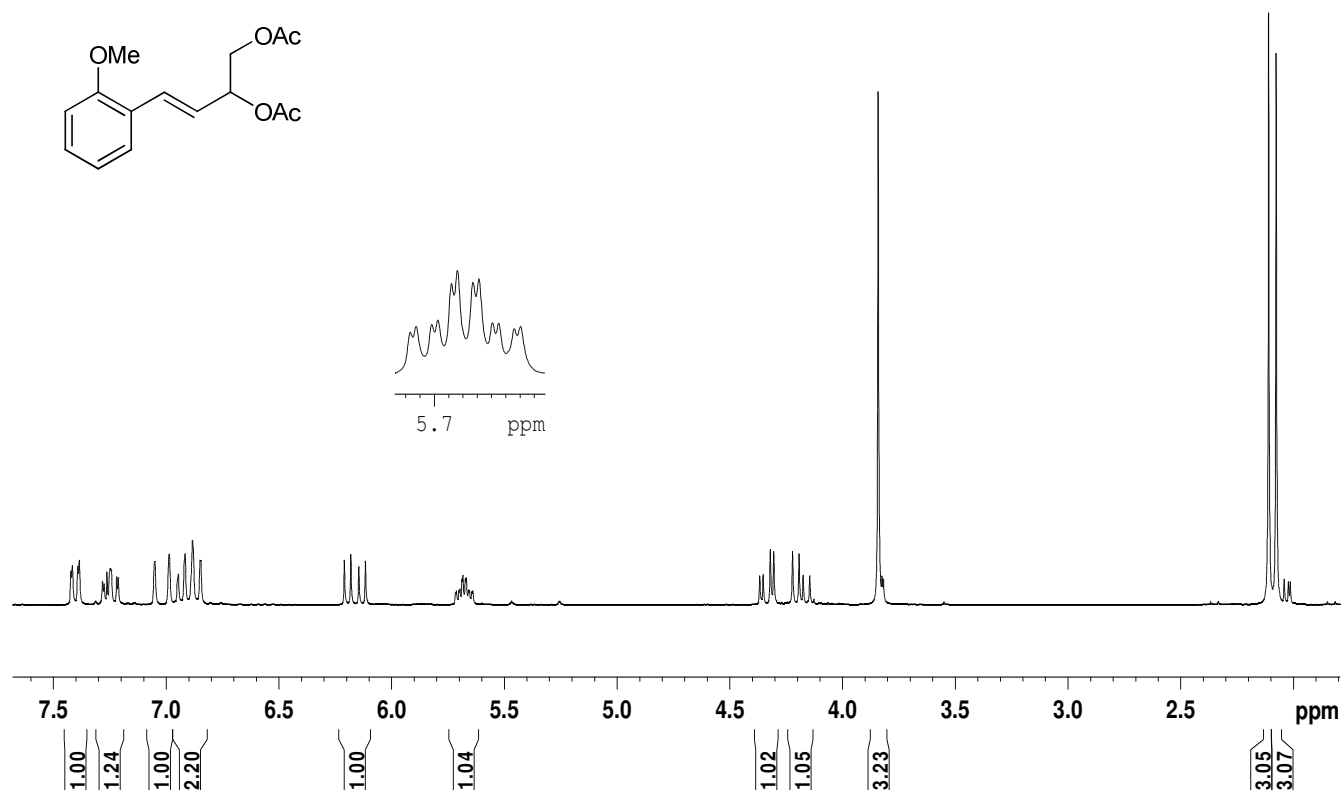
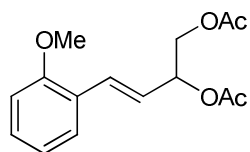
Spectrum of ^{13}C NMR of the compound **3k** in CDCl_3 , 62.5 MHz



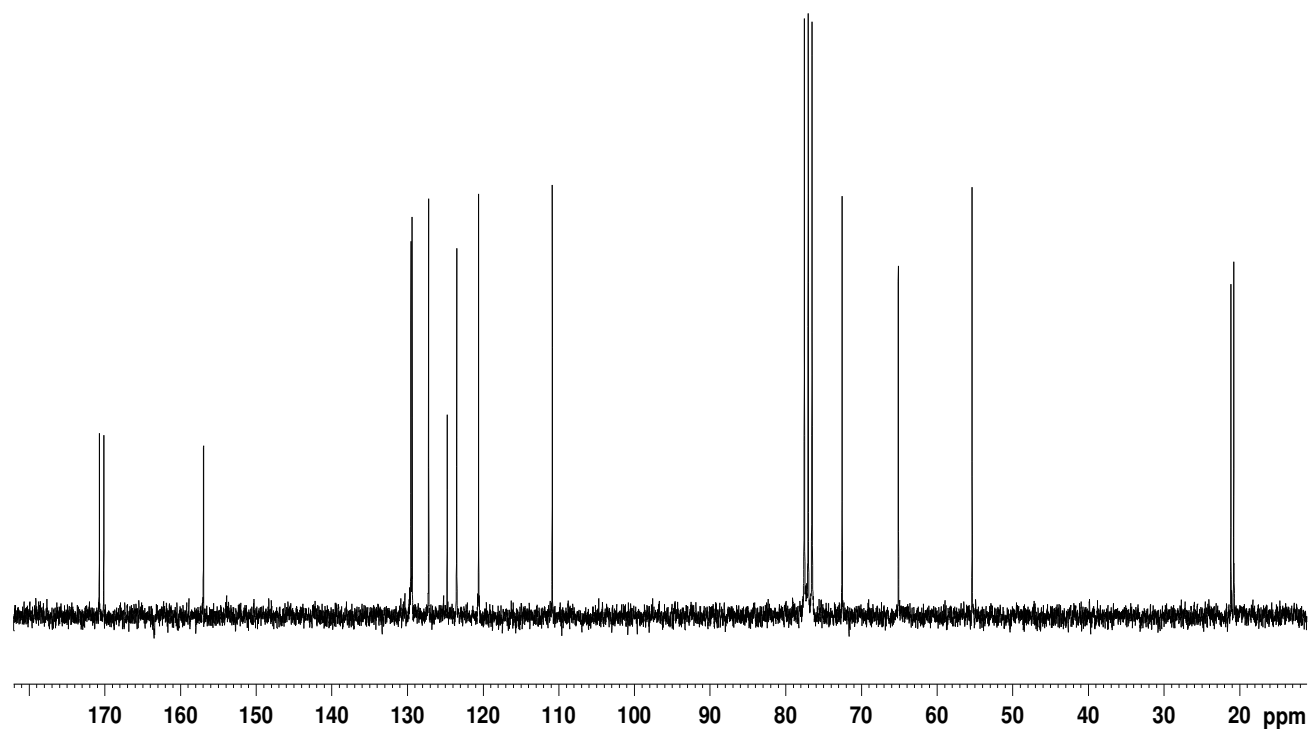
Spectrum of ^1H NMR of the compound **3I** in CDCl_3 , 250 MHz



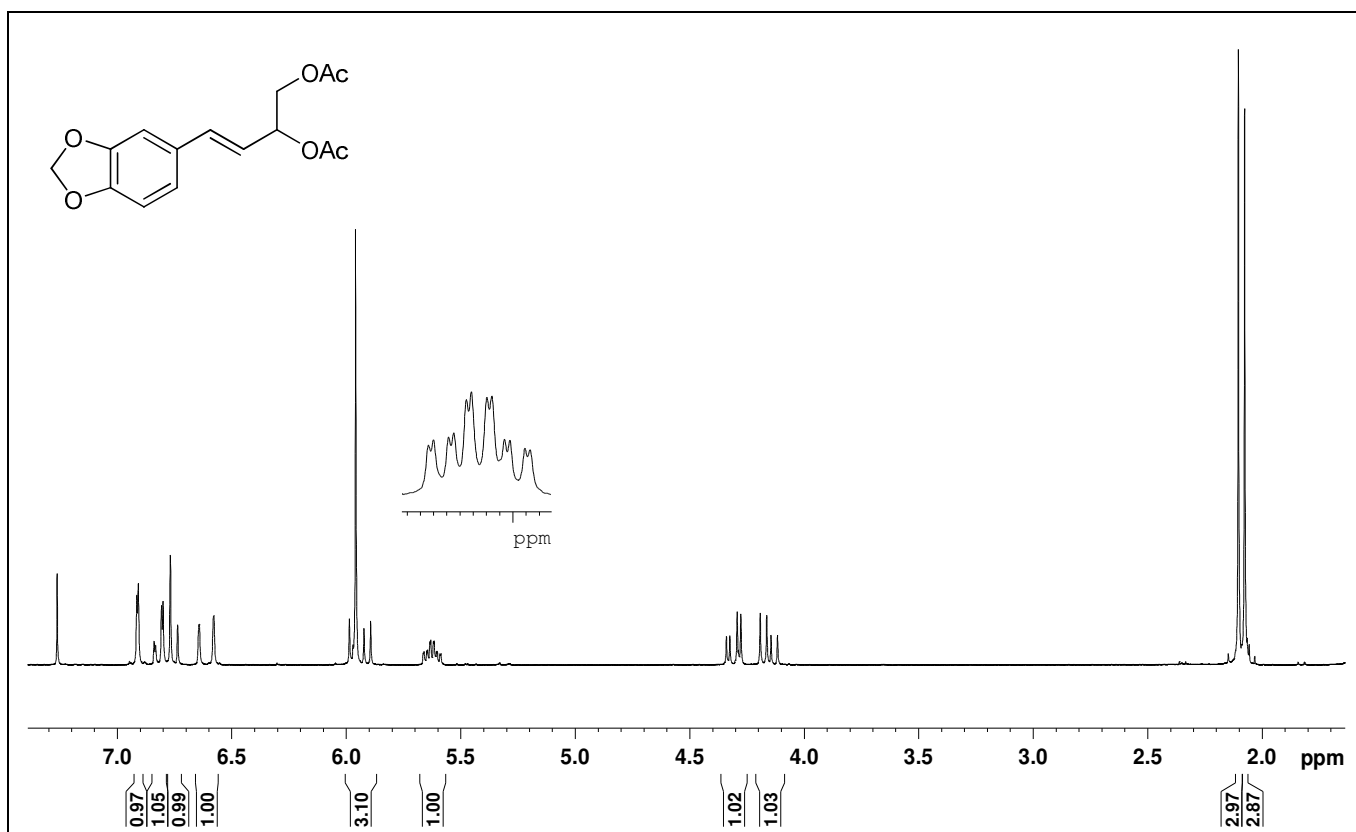
Spectrum of ^{13}C NMR of the compound **3I** in CDCl_3 , 125 MHz



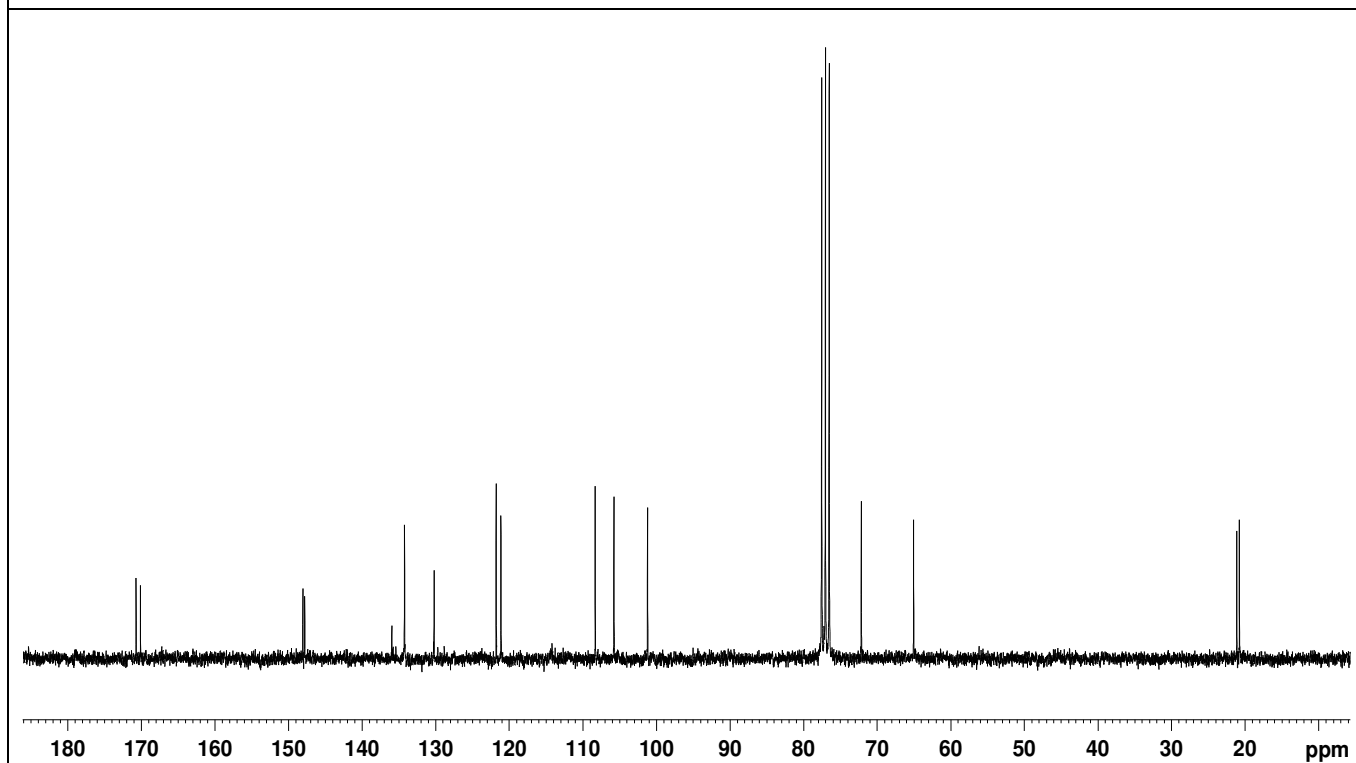
Spectrum of ^1H NMR of the compound **3m** in CDCl_3 , 250 MHz



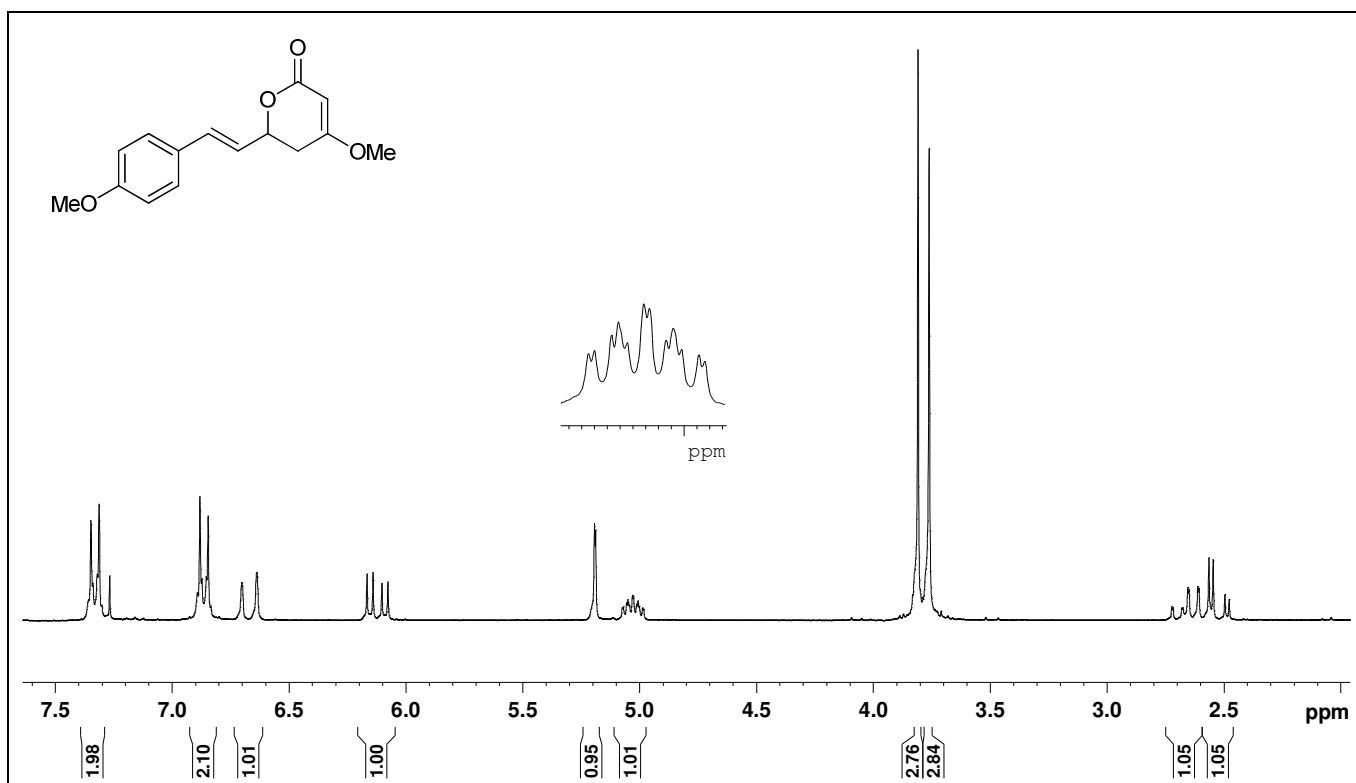
Spectrum of ^{13}C NMR of the compound **3m** in CDCl_3 , 62.5 MHz



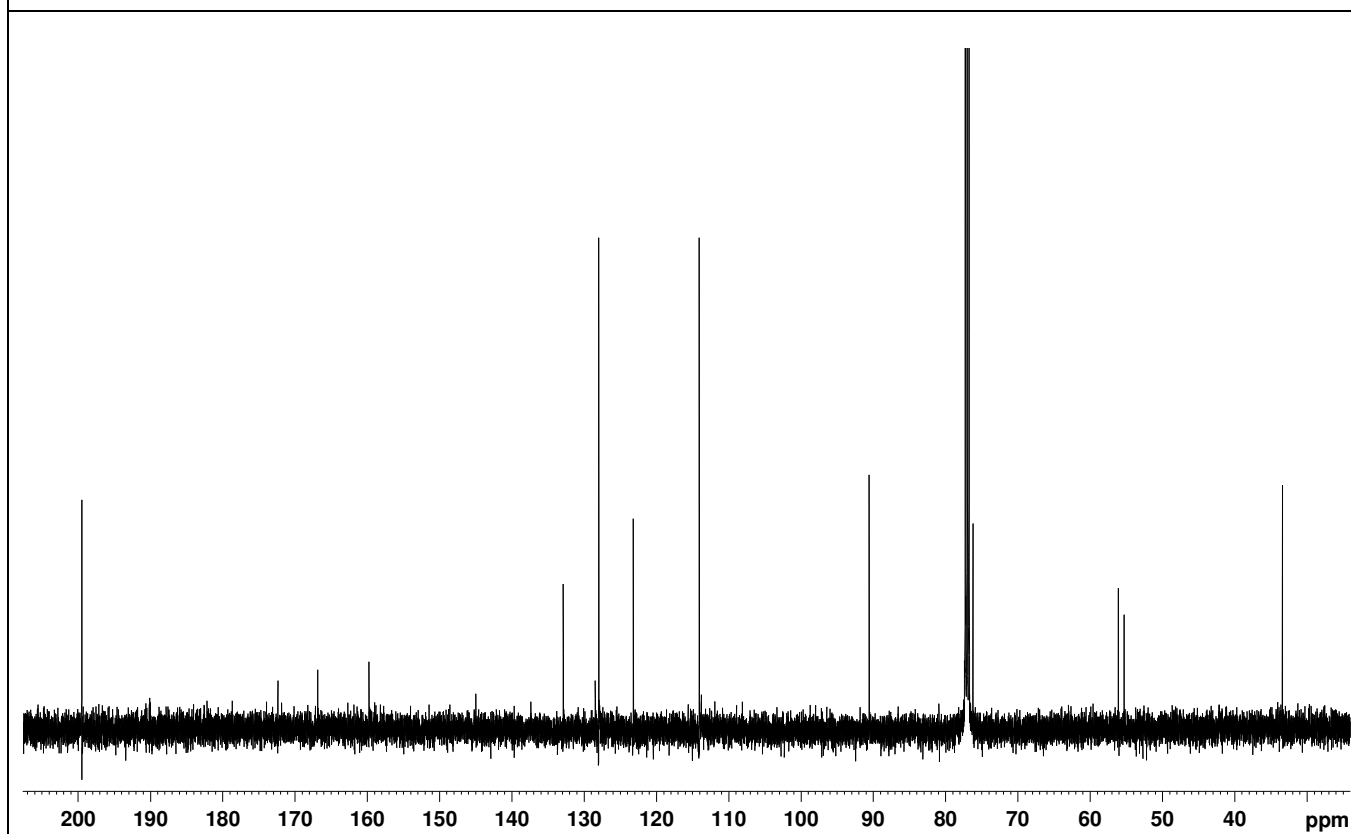
Spectrum of ¹H NMR of the compound **3n** in CDCl₃, 250 MHz



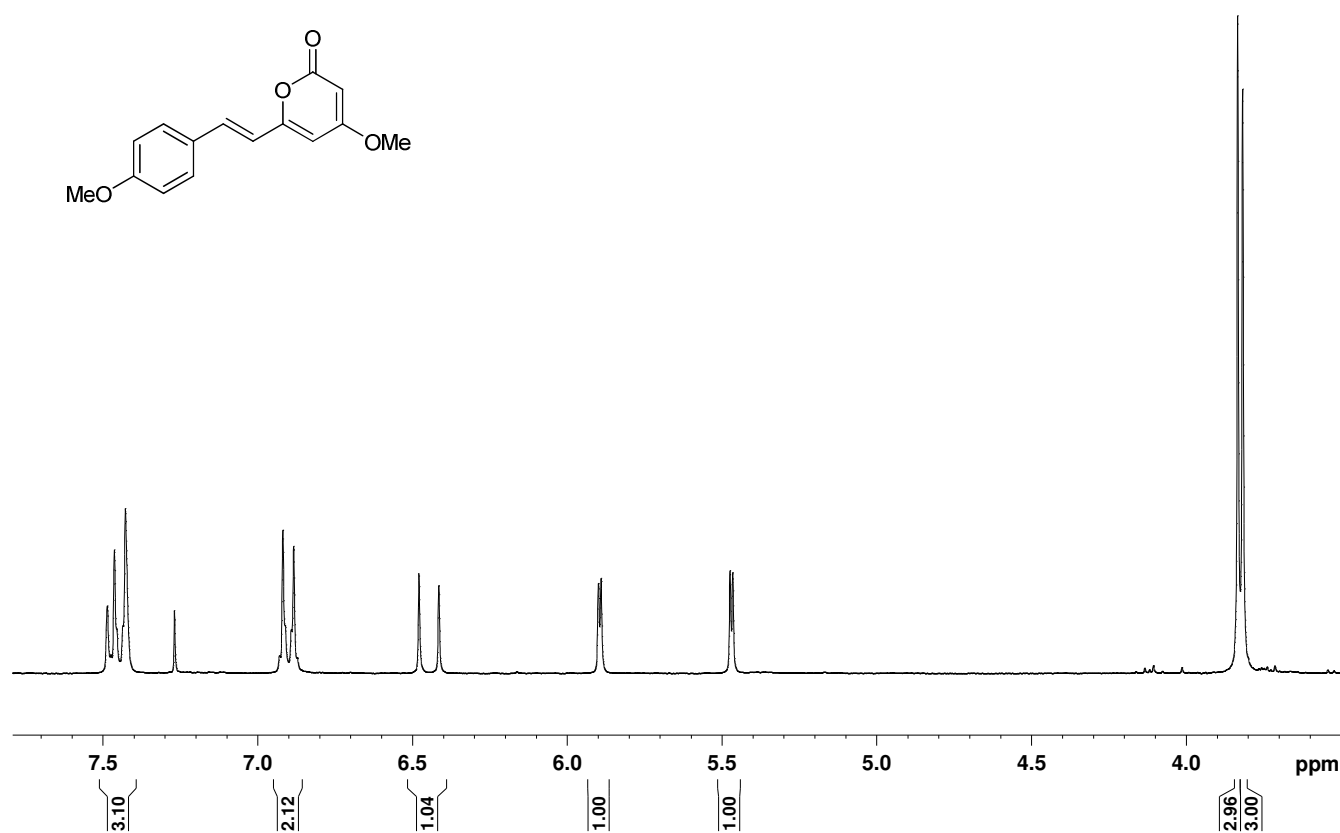
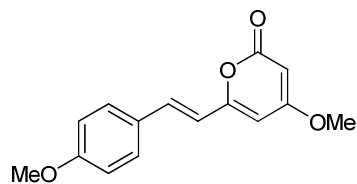
Spectrum of ¹³C NMR of the compound **3n** in CDCl₃, 62.5 MHz



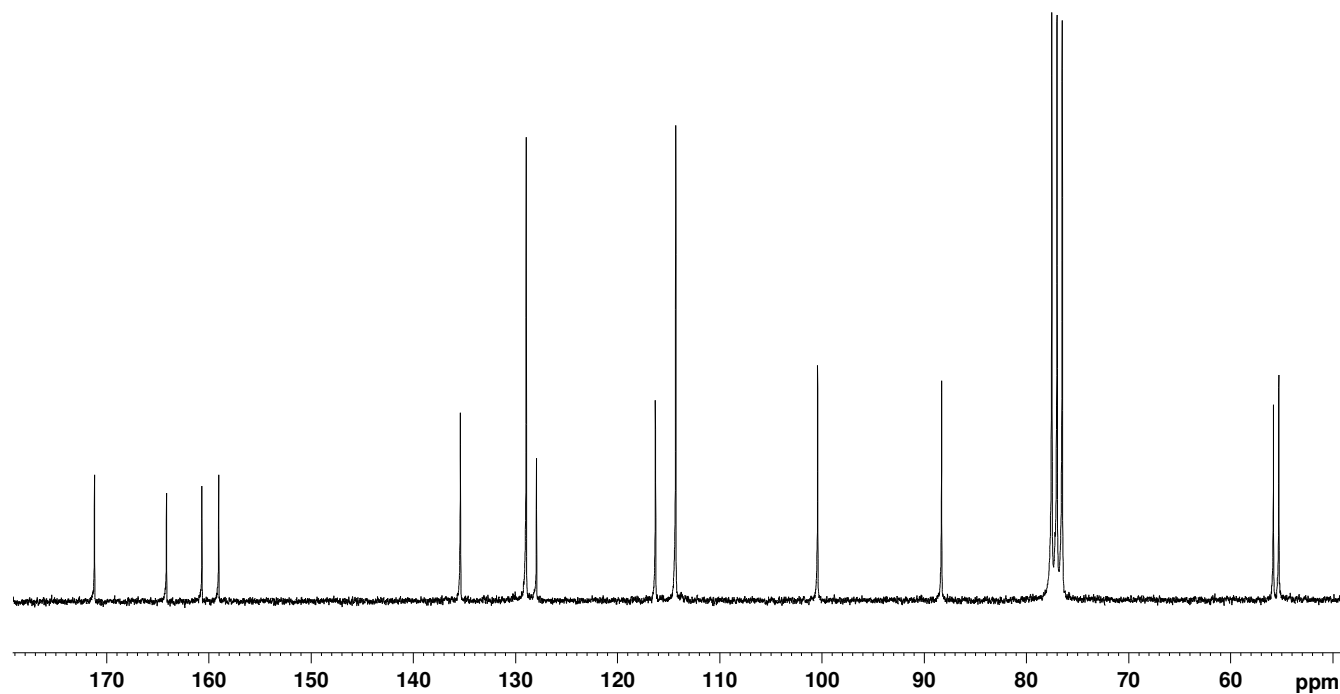
Spectrum of ^1H NMR of the compound **5** in CDCl_3 , 250 MHz



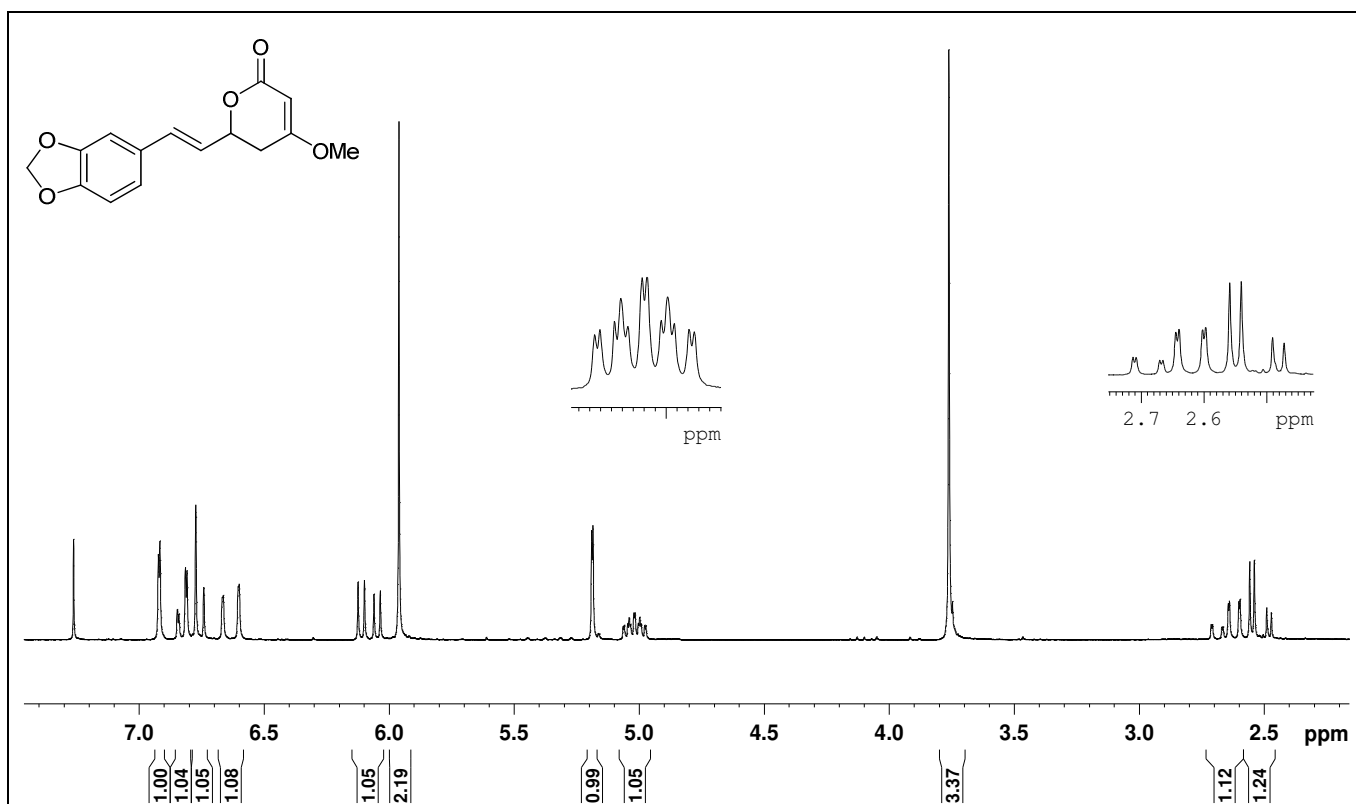
Spectrum of ^{13}C NMR of the compound **5** in CDCl_3 , 125 MHz



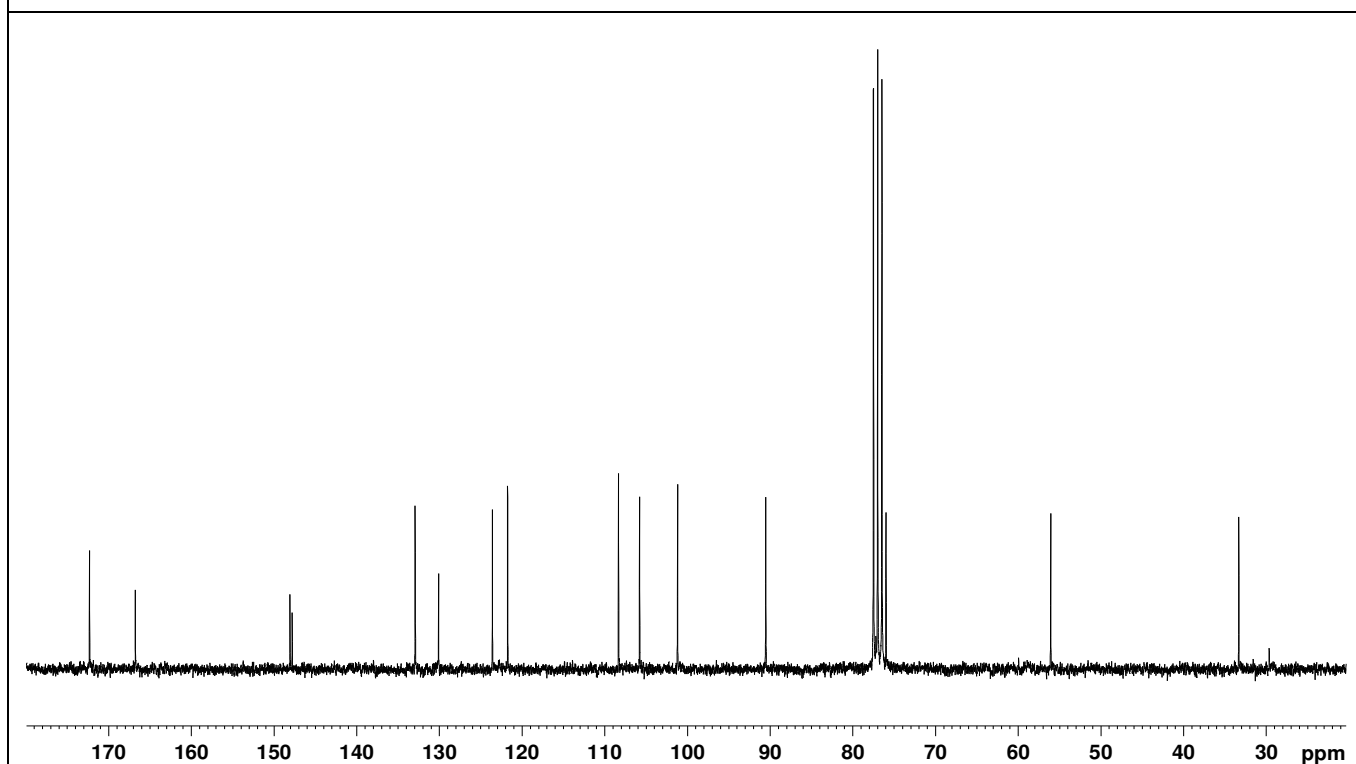
Spectrum of ^1H NMR of the compound **6** in CDCl_3 , 250 MHz



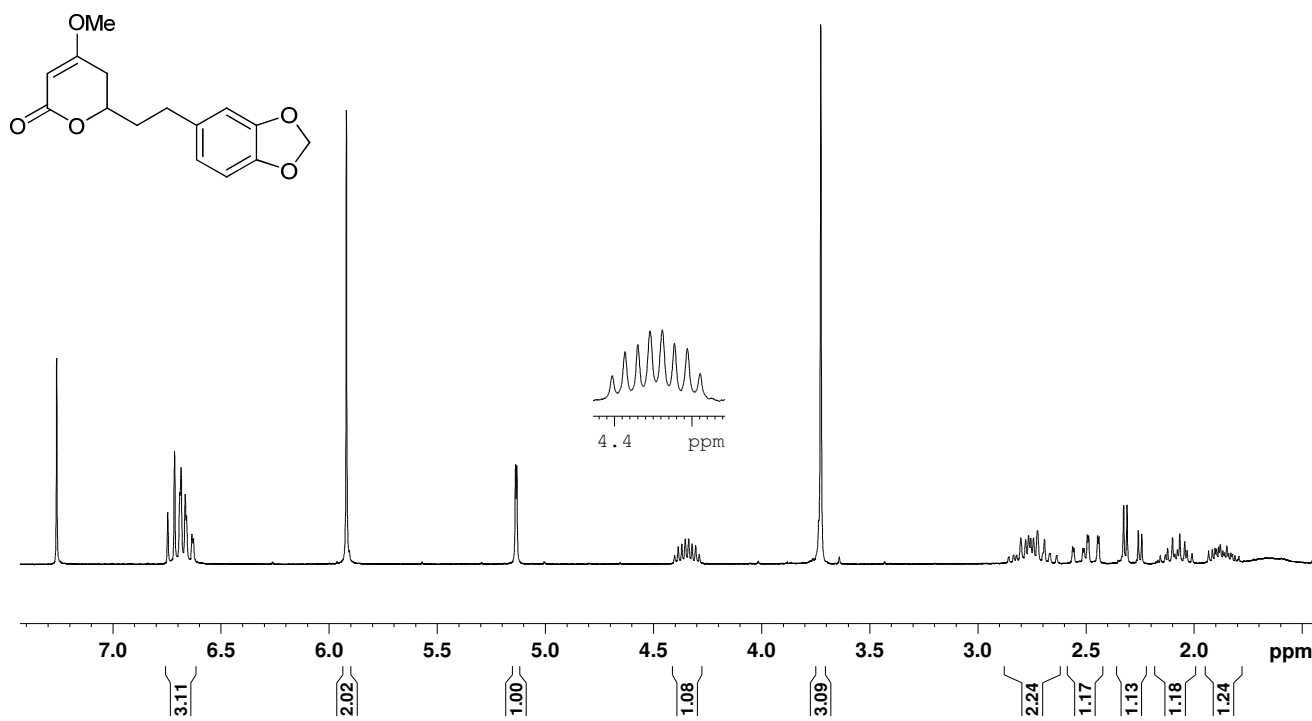
Spectrum of ^{13}C NMR of the compound **6** in CDCl_3 , 62.5 MHz



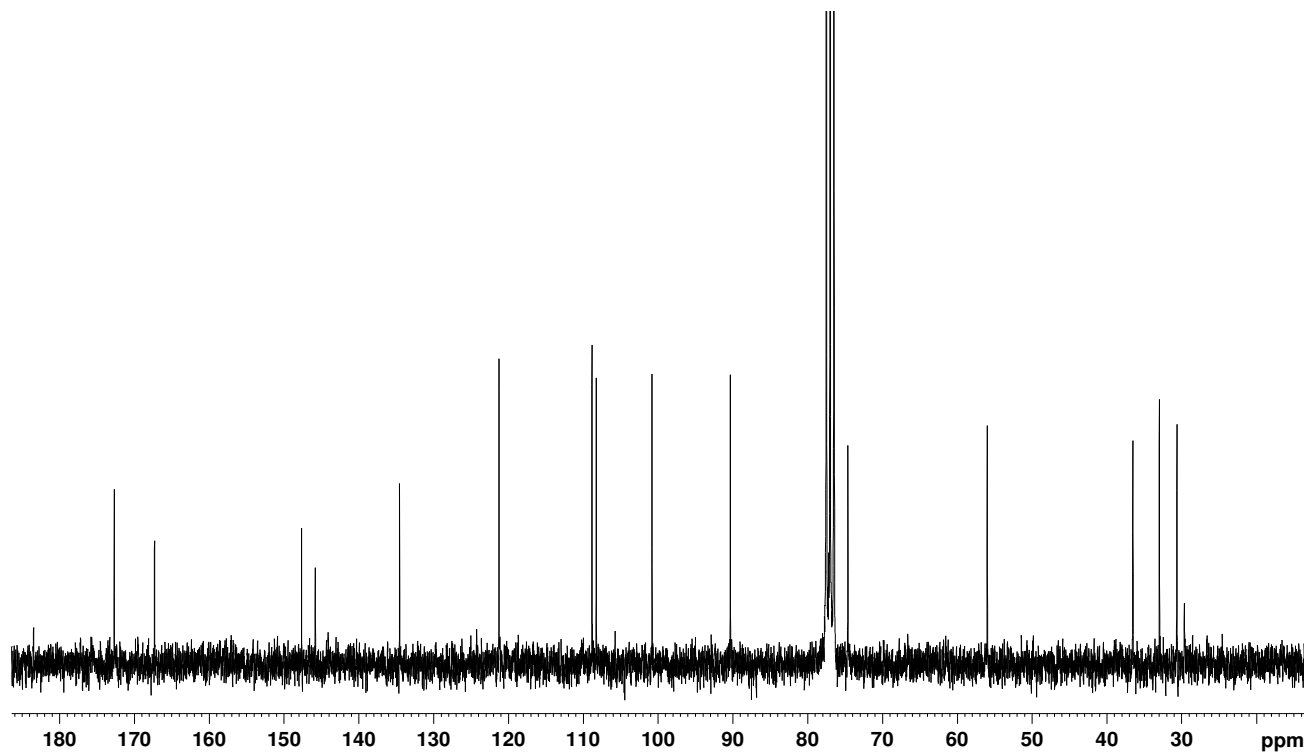
Spectrum of ¹H NMR of the compound 7 in CDCl₃, 250 MHz



Spectrum of ¹³C NMR of the compound 7 in CDCl₃, 62.5 MHz



Spectrum of ¹H NMR of the compound **8** in CDCl₃, 250 MHz



Spectrum of ¹³C NMR of the compound **8** in CDCl₃, 62.5 MHz