Electronic Supplementary Information (ESI)

# Structure-Activity Relationship and Bioactivity Studies of Neurotrophic *trans*-Banglene

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## General Information

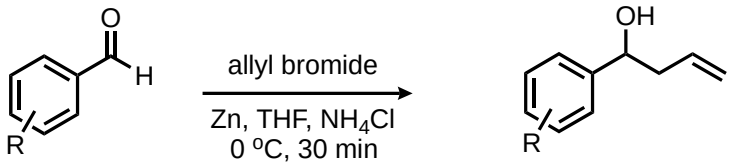
All reactions were performed under a nitrogen atmosphere unless stated otherwise. Dichloromethane ($CH_2Cl_2$) and toluene were passed through a column of activated molecular sieves (4Å, LC technologies SP-1 solvent purification system). HPLC purification was performed using an Agilent 1260 preparatory system, using one of the following: a C8 Zorbax column (PrepHT, 21.2x150mm, 7 µm particle size), Lux® 5 µm i-Amylose-3 column (250 x 10 mm, 5 µm particle size) or Daicel CHIRALPAK AD-H (250 x 30 mm). Chiral HPLC analysis was performed using a normal-phase Agilent 1260 system, with UV detection using a standard diode-array- detector, and one of the following: a Daicel CHIRALPAK IG column (150 x 4.6 mm, 5 µm particle size), IC Daicel CHIRALPAK IC column (150 x 4.6 mm, 5 µm particle size), or a Daicel CHIRALPAK AD-H (250 x 4.6 mm).

NMR spectra were obtained from one of the following Varian spectrometers: DD2 MR 400MHz, VNMRS 500MHz, VNMRS 600MHz, VNMRS 700MHz. NMR spectra chemical shifts (δ) are reported in ppm and are referenced to residual protonated solvent ($^1H$) or deuterated solvent ($^{13}C$) chemical shifts. Coupling constants (*J*) are reported in Hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dq = doublet of quartets, ddd = doublet of doublet of doublets, tdd = triplet of doublet of doublets, m = multiplet, app. = apparent, br. = broad. HSQC was used to determine $^{13}C$ NMR multiplicities, which are reported as follows: C = no attached hydrogens, CH = one attached hydrogen, $CH_2$ = two attached hydrogens, $CH_3$ = three attached hydrogens.

HRMS were obtained from a Kratos Analytical MS50G EI-MS. FTIR were obtained using a Thermo Nicolet 8700 with an attached continuum microscope. Optical rotation data was obtained using a Perkin Elmer 241 Polarimeter at 589 nm at 25 °C, using a 10 cm path-length cell.

## General Procedures

### *Synthesis of allyl alcohols (2a-d)*[1]




**1a-d** **2a-d**

The aldehyde **1** (30 mmol) was dissolved in tetrahydrofuran (25 mL). Allyl bromide (8 mL, 90 mmol) and saturated aqueous $NH_4Cl$ solution (125 mL) were then added, and the reaction mixture was cooled to 0 °C. Zinc power (12 g, 180 mmol) was added, and the reaction mixture was stirred at 0 °C for 30 minutes. The precipitate was filtered, and the filtrate was extracted with ethyl acetate (25 mLx4). The organic layers were combined and washed with brine (25 mLx1), then dried over $Na_2SO_4$, filtered, and then concentrated in vacuo. The resulting product was used without further purification.

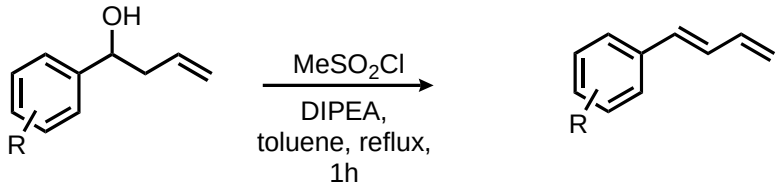
**2a. 1-(3,4-Dimethoxyphenyl)but-3-en-1-ol:** White solid (91%). **$^1$H NMR** ($CDCl_3$, 400 MHz) δ: 6.94–6.83 (m, 3H), 5.85–5.76 (m,1H), 5.20–5.14 (m, 2H), 4.70 (td, *J* = 6.5 Hz, 3.0 Hz, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 2.51 (t, *J* = 6.9 Hz, 2H), 1.96 (d, *J* = 3.0 Hz, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 149.1, 148.2, 134.6, 118.4, 118.1, 111.0, 109.0, 73.3, 56.0, 55.9, 43.9. Characterization data is consistent with literature.[2]

**2b. 1-(3-Methoxyphenyl)but-3-en-1-ol:** Yellow oil (99%). **$^1$H NMR** ($CDCl_3$, 400 MHz) δ: 7.29–7.25 (t, *J* = 8.0, 1H), 6.95–6.93 (m, 2H), 6.82 (ddd, *J* = 8.4 Hz, 2.6 Hz, 1.2 Hz, 1H), 5.87–5.77 (m, 1H), 5.20–5.14 (m, 1H), 4.73 (dd, *J* = 7.7 Hz, 4.2 Hz, 1H), 3.82 (s, 3H), 2.56–2.45 (m, 2H), 2.03 (s, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.8, 145.7, 134.5, 129.5, 118.5, 118.2, 113.1, 111.4, 73.3, 55.3, 43.9. Characterization data is consistent with literature.[3]

**2c. 1-(4-Methoxyphenyl)but-3-en-1-ol:** Yellow oil (99%). **$^1$H NMR** ($CDCl_3$, 700 MHz) δ: 7.29–7.28 (app. d, *J* = 8.3 Hz, 2H), 6.89–6.88 (app. d, *J* = 8.7 Hz, 2H), 5.83–5.77 (m, 1H), 5.17–5.12 (m, 2H), 4.70 (t, *J* = 6.5 Hz, 1H), 3.81 (s, 3H), 2.52–2.49 (app. t, *J* = 6.5 Hz, 2H), 1.94 (s, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.0, 136.0, 134.6, 127.0, 118.2, 113.8, 72.9, 55.3, 43.7. Characterization data is consistent with literature.[3]

**2d. 1-(3-hydroxy-4-methoxy)but-3-en-1-ol:** Colourless oil **(**99%). **$^1$H-NMR** ($CDCl_3$, 600 MHz) δ: 6.93–6.82 (m, 3H), 5.84–5.78 (m, 1H), 5.58 (s, 1H), 5.19–5.13 (m, 2H), 4.69–4.66 (td, *J* = 4.8 Hz, 3.0 Hz, 1H), 3.91 (s, 3H), 2.51–2.49 (m, 2H), 1.99 (d, *J* = 3.0 Hz, 1H). **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ: 146.6, 145.1, 136.0, 134.6, 118.9, 118.3, 114.1, 108.3, 73.3, 55.9, 43.9. Characterization data is consistent with literature.[1] (*this compound decomposes at room temperature*).

***Synthesis of dienes (3a and 3c)[1]***




**2a,c** **3a,c**

In a flame dried RBF, the alcohol **2** (14 mmol) was dissolved in toluene (40 mL). N,N-diisopropylethylamine (72 mmol) and methanesulfonyl chloride (22 mmol) were slowly added and the reaction mixture was heated at reflux for 1 hour. The mixture was diluted with $CH_2Cl_2$ (45 mL), washed with sodium bicarbonate (15 mLx3), water (15 mLx3), and brine (15 mLx2). Then the organic layer dried over $Na_2SO_4$, filtered, and then concentrated in vacuo. The resultant oil was purified by column chromatography (silica; isocratic: 8% ethyl acetate/hexane).

**3a. 4-((*E*)-Buta-1,3-dienyl)-1,2-dimethoxybenzene:** Yellow oil (45%). $R_f$ = 0.1. **$^1$H NMR** ($CDCl_3$, 500 MHz) δ: 6.97–6.94 (m, 2H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.67 (dd, *J* = 15.4 Hz, 10.6 Hz, 1H), 6.53–6.45 (m, 2H), 5.29 (d, *J* = 16.7 Hz, 1H), 5.13 (d, *J* = 10.0 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 149.1, 148.9, 137.3, 132.7, 130.3, 128.0, 119.9, 116.7, 111.2, 108.7, 60.0, 55.9. Characterization data are consistent with literature.[4]

**3c. (*E*)-1-(buta-1,3-dien-1-yl)-4-methoxybenzene:** Yellow oil (45%). $R_f$ = 0.3. **$^1$H NMR** ($CDCl_3$, 400 MHz) δ: 7.34 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.67 (dd, *J* = 15.6 Hz, 10.5 Hz, 1H), 6.53–6.45 (m, 2H), 5.28 (d, *J* = 16.9 Hz, 1H), 5.11 (d, *J* = 10.1 Hz, 1H), 3.81 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.3, 137.4, 132.4, 129.9, 127.6, 116.4, 114.1, 55.3. Characterization data are consistent with literature.[5]

***Synthesis of 3b: (E)-1-(buta-1,3-dien-1-yl)-3-methoxybenzene***

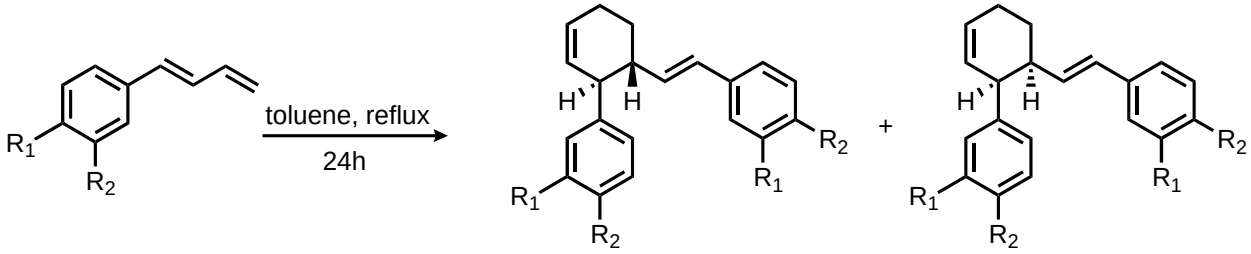
In a flame dried RBF, 1-(3 methoxy)-but-3-en-1-ol (**2b**, 170 mg, 1.0 mmol) was dissolved in 4 mL toluene, followed by the addition of 3Å molecular sieves. Pyridine (0.6 mL, 7.0 mmol) and phosphoryl chloride (0.16 mL, 2.10 mmol) were slowly added, and the reaction mixture was heated at reflux overnight. The reaction mixture was diluted with $CH_2Cl_2$ (15 mL), washed with 0.01 M HCl (5 mLx2), $NaHCO_3$ (sat. aq.)(5 mLx1), water (5 mLx2), and brine (10 mLx1). The organic layer was dried over $Na_2SO_4$, filtered, and then concentrated in vacuo. The resultant oil was purified with column chromatography (silica; isocratic: 15% ethyl acetate/hexane, $R_f$ = 0.3) to remove residual starting alcohol, and the yellow oil (107 mg, 70% 3b) was then carried forward to synthesise 20 and 22.

### *Synthesis of 3d: (E)-4-(Buta-1, 3-dienyl)-2-methoxyphenol*

In a flame dried RBF, alcohol **2d** (4.50 mmol) was dissolved in toluene (40.0 mL), followed by the addition of p-toluenesulphonic acid (0.09 mmol). The reaction mixture was then heated at reflux for 50 mins. The reaction solution was washed with aq. sat. sodium bicarbonate (10 mLx2), brine (10 mL) and then the organic layer was dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The resulting residue was purified by column chromatography (silica; 5-10 % ethyl acetate/hexane, $R_f$ = 0.4 in 10% ethyl acetate/hexane).

Low melting white solid (12%). **$^1$H NMR** ($CDCl_3$, 400 MHz,): 6.94–6.88 (m, 3H), 6.70–6.64 (m, 1H), 6.55–6.46 (m, 2H), 5.77 (s, 1H), 5.31 (dd, *J* = 17.6 Hz, 1.6 Hz, 1H), 5.14 (dd, *J* = 10.0 Hz, 2.0 Hz, 1H), 3.90 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ: 146.8, 145.7, 137.4, 132.9, 129.9, 127.6, 120.5, 116.5, 114.7, 108.4, 55.9. Characterization data are consistent with literature.[1]

### *Synthesis of Banglenes (c–BG, t–BG) and homo-dimeric Banglene derivatives (20-23)*[6]




**3a-c** ***t*-BG,20,21** ***c*-BG,22,23**

In a flame dried RBF, the corresponding diene (0.62 mmol) was dissolved in toluene (2 mL). Hydroquinone (0.12 mmol) was added only for synthesis of (**20-23**), and the reaction was allowed to stir at reflux, for 18 hours. Toluene was removed in vacuo, and the resulting residue was purified by column chromatography (silica). The cis/trans diastereomers were then separated by preparative HPLC.

| product | silica column conditions | product mass (% yield) | HPLC separation conditions | HPLC injection | isolated components | | |
|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) |
| ***c*–BG**<br>***t*-BG** | 20% EtOAc/hex<br>$R_f$ = 0.3 | 390 mg<br>(40%) | C8 column. 50→100% ACN/$H_2O$ (20 min) | 350 mg | ***t*–BG**<br>***c*-BG** | 164 mg<br>166 mg | 10.8<br>11.3 |
| **20**<br>**22** | 20% EtOAc/hex<br>$R_f$ = 0.4 | 90 mg<br>(90%) | i-amylose-3 column. 97% hex/EtOH (15 min) | 70 mg | **20**<br>**22** | 10 mg<br>5 mg | 9.4<br>8.6 |
| **21**<br>**23** | 5% EtOAc/hex<br>$R_f$ = 0.2 | 47 mg<br>(47%) | i-amylose-3 column. 97% hex/EtOH (15 min) | 40 mg | **(-) 21**<br>**(+) 23** | 5 mg<br>4 mg | 14.5<br>11.3 |

**(±) 3(*S*/*R*)-(3,4-Dimethoxyphenyl)-4(*S*/*R*)-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (*c*-BG):**

Colourless oil. **$^1$H NMR** ($CDCl_3$, 700MHz) δ : 6.79 (d, *J* = 8.2 Hz, 1H), 6.75–6.72 (m, 4H), 6.69 (d, *J* =

1.9 Hz, 1H), 6.24 (d, *J* = 15.8 Hz, 1H), 5.97 (tdd, *J* = 2.3 Hz, 4.4 Hz, 10.0 Hz, 1H), 5.79 (tdd, *J* = 2.3 Hz, 4.4 Hz, 10 Hz, 1H), 5.58 (dd, *J* = 9.2 Hz, 15.8 Hz), 3.85 (s, 3H), 3.84 (s, 3H), 3.82 (s, 3H), 3.74 (s, 3H), 3.50 (br. s, 1H), 2.70 (dddd, *J* = 3.1 Hz, 5.5 Hz, 9.1 Hz, 10.9 Hz, 1H), 2.27–2.16 (m, 2H), 1.68–1.59 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 149.0, 148.3, 148.2, 147.6, 133.9, 132.5, 131.1, 129.2, 128.6, 128.1, 122.0, 118.8, 113.7, 111.2, 110.4, 108.8, 56.0, 55.9, 55.8, 45.8, 42.7, 24.9, 24.4. Characterization data are consistent with literature.[7]

**(±) 3(*S*/*R*)-(3,4-Dimethoxyphenyl)-4(*R*/*S*)-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (*t*–BG):** Yellow oil. **$^{1}$H NMR** ($CDCl_3$, 700MHz) δ: 6.82 (d, *J* = 1.8 Hz, 1H), 6.8 (dd, *J* = 1.9 Hz, 8.3 Hz, 1H), 6.77 (t, *J* = 7.8 Hz, 2H), 6.72 (dd, *J* = 1.9 Hz, 8.2 Hz, 1H), 6.7 (d, *J* = 1.9 Hz, 1H), 6.09 (d, *J* = 15.9 Hz, 1H), 6.02 (dd, *J* = 7.6 Hz, 15.9 Hz), 5.90 (tdd, *J* = 2.5 Hz, 4.3 Hz, 10.0 Hz, 1H), 5.68 (dq, *J* = 10.2 Hz, 2.2 Hz, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 3.82 (s, 3H), 3.18 (dq, *J* = 8.6 Hz, 2.8 Hz), 2.36 (dq, *J* = 9.0 Hz, 2.8 Hz 1H), 2.24–2.20 (m, 2H), 1.92 (dq, *J* = 13.3 Hz, 4.1 Hz), 1.70–1.65 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 149.0, 148.6, 148.3, 147.4, 137.6, 132.2, 131.0, 130.3, 128.9, 127.6, 120.5, 118.8, 111.7, 111.2, 110.9, 108.8, 55.98, 55.92, 55.89, 55.88 48.1, 45.5, 27.9, 24.2. Characterization data are consistent with literature.[7]

**(±) 3(*S*/*R*)-(3-methoxyphenyl)-4(*R*/*S*)-[(*E*)-3-methoxystyryl]cyclohex-1-ene (20):** Yellow oil. **$^{1}$H NMR** ($CDCl_3$, 600MHz) δ: 7.18 (q, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.80–6.78 (m, 2H), 6.74–6.72 (m, 3H), 6.17–6.16 (m, 2H), 5.90 (tdd, *J* = 2.4 Hz, 4.4 Hz, 10 Hz, 1H), 5.70 (dq, *J* = 10.0 Hz, 2.2 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.23 (dq, *J* = 11.0 Hz, 2.7 Hz, 1H), 2.45–2.41 (1.0 Hz, 2H), 2.26–2.19 (m, 2H), 1.92 (tdd, *J* = 3.2 Hz, 5.2 Hz, 12.6 Hz, 1H), 1.70–1.64 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.8 (C), 159.6 (C), 146.6 (C), 139.4 (C), 134.4 (CH), 129.9 (CH), 129.4 (CH), 129.2 (CH), 129.1 (CH), 127.6 (CH), 121.1 (CH), 118.7 (CH), 114.2 (CH), 112.4 (CH), 111.5 (CH), 111.5 (CH), 55.2 ($CH_3$), 55.2 ($CH_3$), 48.4 (CH), 45.2 (CH), 27.8 ($CH_2$), 24.5 ($CH_2$). **HRMS** (EI, $C_{22}H_{24}O_2$, $M^+$): calcd.: 320.1776, found: 320.1782. **FTIR** (cast film): 3021, 2928, 2834, 1599, 1488, 1264, 1156, 1050, 777 $cm^{-1}$.

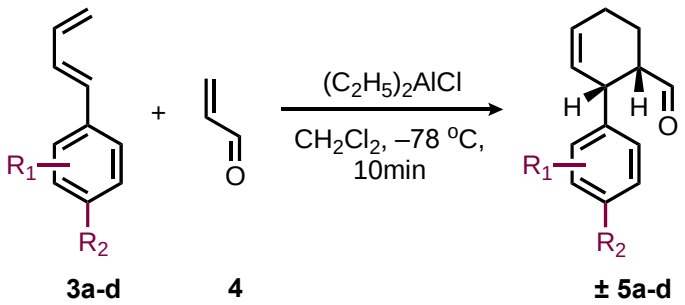
**(–) 3(*R*)-(4-methoxyphenyl)-4(*S*)-[(*E*)-4-methoxystyryl]cyclohex-1-ene (21):** Yellow oil. $[\alpha]^{25}_{D}$ –237 (*c* = 0.7, $CH_2Cl_2$). **$^{1}$H NMR** ($CDCl_3$, 700MHz) δ: 7.19 (d, *J* = 8.7 Hz, 2H), 7.10 (d, *J* = 8.6 Hz, 2H), 6.82–6.80 (m, 4H), 6.11 (d, *J* = 15.9 Hz, 2H), 6.02 (dd, *J* = 7.6 Hz, 15.9 Hz, 1H), 5.88 (tdd, *J* = 2.5 Hz, 4.2 Hz, 10.0 Hz, 1H), 5.65 (dq, *J* = 9.8 Hz, 2.2 Hz, 1H), 3.78 (s, 3H), 3.78 (s, 3H), 3.18 (dq, *J* = 11.0 Hz, 2.7 Hz 1H), 2.35 (dq, *J* = 2.7 Hz, 8.9 Hz, 1H), 2.23–2.18 (m, 2H), 1.91 (dq, *J* = 12.5 Hz, 4.2 Hz, 1H), 1.68–1.63 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 158.7 (C), 158.0 (C), 137.2 (C), 132.1 (C), 130.8 (CH), 130.5 (CH), 129.4 (CH), 128.5 (CH), 127.4 (CH), 127.1 (CH), 113.9 (CH), 113.6 (CH), 55.3 ($CH_3$), 55.3 ($CH_3$), 47.7 (CH), 45.5 (CH), 27.9 ($CH_2$), 24.6 ($CH_2$). **FTIR** (cast film): 3020, 2927, 2835, 1609, 1511, 1249,

1175, 1037 $cm^{-1}$. **HRMS** (EI, $C_{22}H_{24}O_2$, $M^+$): calcd.: 320.1776, found: 320.1774. **FTIR** (cast film): 3018, 2929, 2835, 1609, 1511, 1249, 1176, 1037 $cm^{-1}$.

**(±) 3(*S/R*)-(3-methoxyphenyl)-4(*S/R*)-[(*E*)-3-methoxystyryl]cyclohex-1-ene (22):** Colourless oil. **$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.20–7.17 (m, 1H), 7.15 (t, *J* = 7.9 Hz, 1H), 6.79 (dd, *J* = 7.5 Hz, 13.2 Hz, 2H), 6.67–6.75 (m, 2H), 6.73–6.71 (m, 2H), 6.27 (d, *J* = 15.8 Hz, 1H), 5.98 (tdd, *J* = 2.4 Hz, 3.4 Hz, 10.1 Hz, 1H), 5.82–5.76 (m, 2H), 3.77 (s, 3H), 3.74 (s, 3H), 3.57 (br. s, 1H), 2.76 (dddd, *J* = 3.1 Hz, 5.6 Hz, 9.1 Hz, 10.4 Hz, 1H), 2.28–2.17 (m, 2H), 1.74–1.64 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ 159.7 (C), 159.2 (C), 143.1 (C), 139.5 (C), 134.3 (CH), 129.4 (CH), 129.0 (CH), 128.9 (CH), 128.5 (CH), 128.2 (CH), 122.6 (CH), 118.8 (CH), 115.8 (CH), 112.5 (CH), 111.7 (CH), 111.4 (CH), 55.2 ($CH_3$), 46.0 (CH), 42.5 (CH), 24.6 ($CH_2$), 24.6 ($CH_2$). **HRMS** (EI, $C_{22}H_{24}O_2$, $M^+$): calcd.: 320.1776, found: 320.1775. **FTIR** (cast film): 3021, 2926, 2835, 1599, 1486, 1264, 1155, 1049, 776 $cm^{-1}$.

**(+) 3(*S*)-(4-methoxyphenyl)-4(*R*)-[(*E*)-4-methoxystyryl]cyclohex-1-ene (23):** Colorless oil. $[\alpha]^{25}_D$ +212 (*c* = 0.6, $CH_2Cl_2$). **$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.14 (d, *J* = 8.6 Hz, 1H), 7.10 (d, *J* = 8.6 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.79 (d, *J* = 8.8 Hz, 2H), 6.25 (d, *J* = 15.9 Hz, 1H), 5.95 (tdd, *J* = 2.4 Hz, 3.8 Hz, 10.0 Hz, 1H), 5.8 (tdd, *J* = 2.2 Hz, 4.5 Hz, 10.0 Hz, 1H), 5.60 (dd, *J* = 9.1 Hz, 15.9 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.52 (br. s, 1H), 2.70 (dddd, *J* = 3.3 Hz, 5.5 Hz, 9.0 Hz, 10.5 Hz, 1H), 2.27–2.14 (m, 2H), 1.68–1.58 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 158.7 (C), 158.1 (C), 133.4 (C), 132.1 (C), 131.0 (CH), 130.9 (CH), 129.4 (CH), 128.4 (CH), 127.9 (CH), 127.1 (CH), 113.9 (CH), 113.1 (CH), 55.3 ($CH_3$), 55.3 ($CH_3$), 43.3 (CH), 42.8 (CH), 24.8 ($CH_2$), 24.4 ($CH_2$). **HRMS** (EI, $C_{22}H_{24}O_2$, $M^+$): calcd.: 320.1776, found: 320.1775. **FTIR** (cast film): 3018, 2929, 2835, 1609, 1511, 1249, 1176, 1037 $cm^{-1}$.

### *Synthesis of cis-aldehydes (5a-d)[1]*




**3a-d** **4** **± 5a-d**

In a flame dried RBF, the corresponding diene (4 mmol) was dissolved in $CH_2Cl_2$ (12 mL) and cooled to –78 °C. Acrolein (6 mmol) was added, followed by the dropwise addition of $Et_2AlCl$ (3.8 mmol). The reaction mixture was stirred at –78 °C for 10 minutes and then warmed to 0 °C. The reaction was quenched with 1N HCl (15 mL) and extracted with $CH_2Cl_2$ (20 mLx2). The combined organic layers were washed with $NaHCO_3$(sat. aq.) (15 mLx2), then brine(10mLx1), dried over $Na_2SO_4$, filtered, and then

concentrated in vacuo. The crude residue was purified with column chromatography (silica; isocratic: 20 % ethyl acetate/hexane).

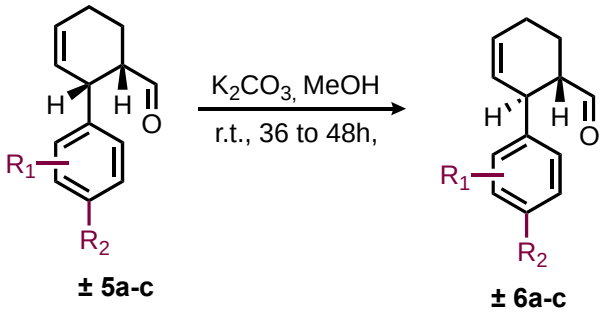
**(±) (1*S*, 2*R*)-2-(3,4-Dimethoxyphenyl)cyclohex-3-ene-1-carboxyaldehyde (5a):** White semi-solid (46%). $R_f$ = 0.36. **$^1$H NMR** ($CDCl_3$, 600 MHz) δ: 9.50 (d, *J* = 2.1 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.76 (dd, *J* = 8.2 Hz, 2.1 Hz, 1H), 6.72 (d, *J* = 1.9 Hz, 1H), 5.99–5.97 (m, 1H), 5.83–5.80 (m, 1H), 3.93–3.91 (m,1H), 3.85 (s, 6H), 2.76–2.72 (m, 1H), 2.32–2.26 (m, 1H), 2.19–2.12 (m, 1H), 1.88–1.85 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 205.0, 148.8, 148.1, 132.6, 128.5, 128.1, 121.4, 112.6, 111.1, 55.9, 50.9, 41.2, 23.7, 18.9. Characterization data are consistent with literature.[7]

**(±) (1*S*, 2*R*)-2-(3-Dimethoxyphenyl)cyclohex-3-ene-1-carboxyaldehyde (5b):** Yellow oil (22%), $R_f$ = 0.6. **$^1$H NMR** ($CDCl_3$, 500MHz) δ: 9.51 (d, *J* = 2.1 Hz, 1H), 7.23–7.20 (m, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 6.77–6.76 (m, 2H), 6.00–5.97 (m, 1H), 5.84–5.81 (m,1H), 3.95–3.94 (m, 1H), 3.79 (s, 3H), 2.77–2.74 (m, 1H), 2.30–2.26 (m, 1H), 2.18–2.12 (m, 1H), 1.92–1.85 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 126MHz) δ: 204.7 (CH), 159.7 (C) ,141.8 (C), 129.4 (CH), 128.8 (CH), 127.8 (CH), 121.7 (CH), 115.5 (CH), 112.0 (CH), 55.2 ($CH_3$), 50.7 (CH), 41.5 (CH), 23.6 ($CH_2$), 19.0 ($CH_2$). **HRMS** (EI, $C_{14}H_{16}O_2$, $M^+$): calcd.: 216.1150, found: 216.1148.

**(±) (1*S*, 2*R*)-2-(4-Dimethoxyphenyl)cyclohex-3-ene-1-carboxyaldehyde (5c)**. Yellow oil (44%). $R_f$ = 0.3. **$^1$H NMR** ($CDCl_3$, 700MHz) δ: 9.51 (d, *J* = 1.9 Hz, 1H), 7.13 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 5.98–5.96 (m, 1H), 5.80 (m, 1H), 3.95–3.92 (m, 1H), 3.78 (s, 3H), 2.75–2.72 (m, 1H), 2.31–2.25 (m, 1H), 2.18–2.11 (m,1H), 1.89–1.80 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 126MHz) δ: 158.7, 132.1, 130.3, 128.4, 128.2, 113.8, 112.9, 55.3, 51.0, 40.8, 23.7, 18.6. **HRMS** (EI, $C_{14}H_{16}O_2$, $M^+$): calcd.: 216.1150, found: 216.1153.

**(±) (1*S*, 2*R*)-2-(4-hydroxy-3-methoxyphenyl)-cyclohex-3-ene-1-carboxaldehyde (5d):** Yellow oil (30%). **$^1$H NMR** ($CDCl_3$, 400 MHz) δ: 9.49 (d, *J* = 2 Hz, 1H), 6.82 (d, *J* = 8.4 Hz, 1H), 6.72–6.68 (m, 2H), 5.98–5.93 (m, 1H), 5.81–5.77 (m, 1H), 5.65 (br. s, 1H), 3.91–3.87 (m, 1H), 3.83 (s, 3H), 2.74–2.69 (m, 1H), 2.30–2.24 (m, 1H), 2.17–2.12 (m, 1H), 1.87–1.81 (m, 2H). **$^{13}$C NMR** ($CDCl_3$, 125 MHz) δ: 205.2, 146.5, 144.7, 131.9, 128.5, 128.2, 122.1, 114.4, 111.9, 55.9, 50.9, 41.2, 23.6, 18.8. Characterization data are consistent with literature.[1]

***Racemization of cis-aldehydes to trans-aldehydes (6a-c)***[7]




**± 5a-c** **± 6a-c**

The corresponding *cis*-aldehyde **5** (1.4 mmol) was dissolved in methanol (15 mL), followed by the addition of $K_2CO_3$ (1.6 mmol). The reaction solution was stirred at room temperature for 48 hours. The reaction mixture was diluted with $CH_2Cl_2$ (20 mL) and washed with water (10 mL) and brine (10 mL). The organic layer was dried over $Na_2SO_4$ and concentrated in vacuo.

**(±) (1*R*, 2*R*)-2-(3,4-Dimethoxyphenyl)cyclohex-3-ene-1-carboxyaldehyde (6a)**: Yellow oil (85%, 87:13 **6a:5a**). **$^1$H NMR** ($CDCl_3$, 500 MHz) δ: 9.69 (d, *J* = 1.5 Hz, 1H), 6.81–6.72 (m, 3H), 5.92 (dq, *J* = 10.0 Hz, 3.3 Hz, 1H), 5.70 (dq, *J* = 2.5 Hz, 10.0 Hz, 1H), 3.86 (d, *J* = 5.6 Hz, 6H), 3.76–3.72 (m, 1H), 2.60 (dddd, *J* = 1.6 Hz, 3.5 Hz, 7.6 Hz, 9.4 Hz, 1H), 2.23–2.18 (m, 2H), 2.01–1.95 (m, 1H), 1.81–1.74 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 205.0, 148.8, 148.1, 132.6, 128.5, 128.1, 121.4, 112.6, 111.1, 55.9, 50.9, 41.2, 23.7, 18.9. Characterization data are consistent with literature.[7]

**(±) (1*R*, 2*R*)-2-(3-Dimethoxyphenyl)cyclohex-3-ene-1-carboxyaldehyde (6b):** Yellow oil (71%, 90:10 **6b:5b**). **$^1$H NMR** ($CDCl_3$, 500MHz) δ: 9.70 (d, *J* = 1.3 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.79–6.75 (m, 2H), 5.90 (dq, *J* = 9.5Hz, 3.3 Hz, 1H), 5.68 (dq, *J* = 10.0 Hz, 2.4 Hz, 1H), 3.80 (s, 3H), 3.77–3.73 (m, 1H), 2.61 (ddt, *J* = 1.3 Hz, 3.5 Hz, 8.5 Hz, 1H), 2.20–2.15 (m, 2H), 2.0–1.93 (m, 1H), 1.80–1.72 (m,1H). **$^{13}$C NMR** ($CDCl_3$, 126MHz) δ: 203.8 (CH), 159.8 (C), 145.3 (C), 129.6 (CH), 128.7 (CH), 127.8 (CH), 120.7 (CH), 114.2 (CH), 111.9 (CH), 55.3 ($CH_3$), 53.9 (CH), 41.4 (CH), 23.5 ($CH_2$), 20.9 ($CH_2$). **HRMS** (EI, $C_{14}H_{16}O_2$, $M^+$): calcd.: 216.1150, found: 216.1150.

**(±) (1*R*, 2*R*)-2-(4-Dimethoxyphenyl)cyclohex-3-ene-1-carboxyaldehyde (6c):** Yellow oil (87%, 90:10 **6c:5c**). **$^1$H NMR** ($CDCl_3$, 500MHz) δ: 9.69 (d, *J* = 1.2 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.88 (dq, *J* = 9.5 Hz, 3.3 Hz, 1H), 5.66 (dq, *J* = 9.5 Hz, 2.4 Hz, 1H), 3.79 (s, 3H), 3.74–3.70 (m, 1H), 2.56 (ddt, *J* = 1.5 Hz, 4.3 Hz, 8.5 Hz, 1H), 2.21–2.15 (m, 2H), 1.95 (dq, 1H, *J* = 13.5 Hz, 4.3 Hz), 1.78-1.71 (m,1H). **$^{13}$C NMR** ($CDCl_3$, 126MHz) δ: 204.0 (CH), 158.4 (C) ,135.6 (C), 129.3 ($CH_2$), 129.2 ($CH_2$), 127.5 (CH), 114.0 (CH), 55.3 ($CH_3$), 54.2 (CH), 40.7 ($CH_2$), 23.5 ($CH_2$), 21.0 ($CH_2$). **HRMS** (EI, $C_{14}H_{16}O_2$, $M^+$): calcd.: 216.1150, found: 216.1148.

### *Synthesis of Wittig Salts (7a-f)*

In a flame dried RBF, the corresponding bromide (5.4 mmol) was dissolved in toluene (20 mL), followed by addition of triphenylphosphine (5.4 mmol). The reaction solution was then heated at reflux overnight. The organic layer was concentrated in vacuo to afford a crude white solid which was then purified by recrystallization in ethanol (7a), or ethanol/diethyl ether (7b-f).

**3,4-Methoxybenzyltriphenylphosphonium bromide (7a)**: White powder (61%). **$^{1}$H NMR** ($CDCl_3$, 400MHz) δ: 7.78–7.74 (m, 9H), 7.65–7.62 (m, 6H), 6.86 (s, 1H), 6.62–6.61 (m, 2H), 5.37 (d, *J* = 13.8 Hz, 2H), 3.80 (s, 3H), 3.55 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 126MHz) δ: 148.9, 148.8, 134.8 (d, *J* = 3.1 Hz), 134.6 (d, *J* = 9.5 Hz), 130.0 (d, *J* = 12.6 Hz), 123.7 (d, *J* = 6.2 Hz), 119.0 (d, *J* = 9.0 Hz), 118.3, 117.8, 115.0, (d, *J* = 4.8 Hz), 111.0 (d, *J* = 3.4 Hz), 56.1, 55.80, 30.5, 30.2. **$^{31}$P{$^{1}$H} NMR** ($CDCl_3$, 201.64 MHz) δ: 22.5 (s). Characterization data is consistent with literature.[8]

**Benzyltriphenylphosphonium bromide (7b):** White powder (76%). **$^{1}$H NMR** ($CDCl_3$, 400MHz) δ: 7.78–7.72 (m, 9H), 7.65–7.60 (td, *J* = 7.8 Hz, 3.6 Hz, 6H), 7.23–7.19 (m, 1H), 7.14–7.09 (m, 4H), 5.43 (d, *J* = 14.4 Hz, 2H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 135.0 (d, *J* = 3.1 Hz), 134.5 (d, *J* = 9.8 Hz), 131.6 (d, *J* = 5.6 Hz), 130.2 (d, *J* = 12.3 Hz), 128.9 (d, *J* = 3.4 Hz), 128.4 (d, *J* = 3.9 Hz), 127.2 (d, *J* = 8.7 Hz), 118.0 (d, *J* = 85.6 Hz), 31.0 (d, *J* = 46.6 Hz). **$^{31}$P{$^{1}$H}** NMR ($CDCl_3$, 162 MHz) δ: 23.2 (s). Characterization data is consistent with literature.[9]

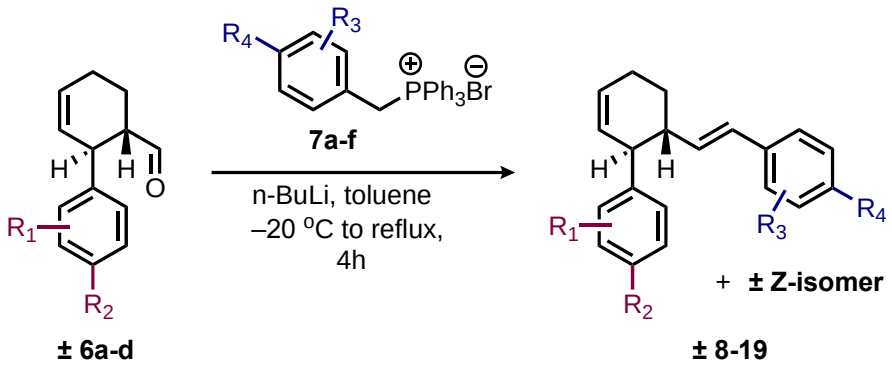
**3-Methoxybenzyltriphenylphosphonium bromide (7c)**: White powder (65%). **$^{1}$H NMR** ($CDCl_3$, 400MHz) δ: 7.78–7.73 (m, 9H), 7.63 (td, *J* = 7.7 Hz, 3.4 Hz, 6H), 7.02 (t, *J* = 8.0 Hz, 1H), 6.82 (q, *J* = 1.8 Hz, 1H), 6.76 (dt, *J* = 8.2 Hz, 2.1 Hz, 1H), 6.63 (d, *J* = 7.5, 1H), 5.40 (d, *J* = 14.4 Hz, 2H), 3.55 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.7, 135.0 (d, *J* = 3.1 Hz), 134.6 (d, *J* = 9.8 Hz), 130.1 (d, *J* = 12.6 Hz), 129.7 (d, *J* = 3.1 Hz), 123. 5 (d, *J* = 5.9 Hz), 118.2, 117.7, 116.3 (d, *J* = 5.3 Hz), 115.4 (d, *J* = 3.9 Hz), 55.5, 31.9 (d, *J* = 46.8 Hz). **$^{31}$P{$^{1}$H}** NMR ($CDCl_3$, 161.913 MHz) δ: 23.23 (s). Characterization data is consistent with literature.[10]

**4-Methoxybenzyltriphenylphosphonium bromide (7d)**: White powder (65%). **$^{1}$H NMR** ($CDCl_3$, 400MHz) δ: 7.77–7.71 (m, 9H), 7.64–7.61 (m, 6H), 7.03 (dd, *J* = 2.5 Hz, 8.8 Hz, 2H), 6.65 (d, *J* = 8.6 Hz, 2H), 5.35 (dd, *J* = 3.2 Hz, 14.0 Hz, 2H), 3.72 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.7, 134.9 (d, *J* = 3.1 Hz), 134.5 (d, *J* = 9.5 Hz), 132.8 (d, *J* = 5.3 Hz), 130.2 (d, *J* = 12.6 Hz), 118.3, 117.8, 114.3 (d, *J* = 3.1 Hz), 55.3, 30.2 (d, *J* = 46.6 Hz). **$^{31}$P{$^{1}$H}** NMR ($CDCl_3$, 161.913 MHz) δ: 22.4 (s). Characterization data is consistent with literature.[11]

**2-Methylbenzyltriphenylphosphonium bromide (7e):** White powder (71%). **$^{1}$H NMR** ($CDCl_3$, 400MHz) δ: 7.81–7.76 (m, 3H), 7.72–7.61 (m, 12H), 7.15 (t, *J* = 7.3 Hz, 1H), 7.09 (d, *J* = 7.2 Hz, 1H), 7.0–6.96 (m, 2H), 5.37 (d, *J* = 14.1 Hz, 2H), 1.68 (s, 3H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 138.6, 135.1 (d, *J* = 2.8 Hz), 134.4 (d, *J* = 9.8 Hz), 131.6, 131.0, 130.22 (d, *J* = 12.6 Hz), 128.8, 126.7, 125.7, 122.0, 118.2, 117.8, 28.5 (d, *J* = 46.6 Hz). **$^{31}$P{$^{1}$H}** NMR (CDCl3, 161.913 MHz) δ: 22.2 (s). Characterization data is consistent with literature.[12]

**2-Bromobenzyltriphenylphosphonium bromide (7f):** White powder (87%). **$^{1}$H NMR** ($CDCl_3$, 400MHz) δ: 7.81–7.77 (m, 3H), 7.75–7.70 (m, 6H), 7.66–7.59 (m, 7H), 7.37 (d, *J* = 7.9 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (tt, *J* = 7.7 Hz, 2.0 Hz, 1H), 5.75 (d, *J* = 14.3 Hz, 2H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 135.2 (d, *J* = 2.8 Hz), 134.5 (d, *J* = 9.8 Hz), 133.5 (d, *J* = 4.9 Hz), 132.9, 130.2 (d, *J* = 12.6 Hz), 128.5 (d, *J* = 3.6 Hz), 118.0, 117.3, 31.1 (d, *J* = 48.2 Hz). Characterization data is consistent with literature.[13]

### *Synthesis of Banglenes and Derivatives (8-19) via a Wittig reaction*[1]




In a flame dried RBF, the corresponding Wittig salt **7** (0.6 mmol) was dissolved in toluene (5 mL) and tetrahydrofuran (5 mL) and cooled to –70 °C. n-Butyl lithium (0.73 mmol) was added slowly, and the reaction mixture was allowed to stir at –70 °C for 1 hour. The reaction solution was then warmed up to –20° C, the corresponding aldehyde (**6**) was added, and the reaction was then heated at reflux for 3 hours. The reaction mixture was quenched with saturated aqueous $NH_4Cl$ (5 mL), and then concentrated in vacuo. The crude oil was dissolved in ethyl acetate (30 mL), washed with water (10 mLx2), and $NaHCO_3$ (sat. aq.) (10 mLx2), was dried over $Na_2SO_4$ and then concentrated in vacuo. The resulting oil was purified with column chromatography.

**(±) 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*E*)-styryl]cyclohex-1-ene (8):**

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | | ee |
|---|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) | |
| **8E** **8Z** | 20% EtOAc/hex $R_f$ = 0.4 | 93 mg (48%) | i-amylose-3 column. 97% hex/EtOH (15 min) | 80 mg | (+) **8E** | 10 mg | 5.8 | 99% |
| | | | | | (–) **8E** | 19 mg | 8.0 | >99% |
| | | | | | (+) **8Z** | *not isolated* | 5.5 | - |
| | | | | | (–) **8Z** | | 7.2 | - |

**$^1$H NMR** ($CDCl_3$, 500MHz) δ: 7.26–7.25 (m, 4H, *overlaps with CDCl$_3$*), 7.16 (m, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.72 (dd, *J* = 2.0 Hz, 8.1 Hz, 1H), 6.70 (d, *J* = 1.9 Hz, 1H), 6.16 (d, *J* = 3.3 Hz, 2H), 5.90 (tdd, *J* = 2.4 Hz, 4.1 Hz, 10.0 Hz, 1H), 5.68 (dq, *J* = 10.0 Hz, 2.2 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.78 (s, 3H), 3.19 (dq, *J* = 11.2 Hz, 2.7 Hz, 1H), 2.41–2.35 (m, 1H), 2.27–2.17 (m, 2H), 1.95–1.91 (m, 1H), 1.72–1.64 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 148.6 (C), 147.4 (C), 137.8 (C), 137.5 (C), 134.1 (CH), 130.3 (CH), 129.3 (CH), 128.5 (CH), 127.6 (CH), 126.9 (CH), 126.0 (2xCH), 120.4 (CH), 111.7 (CH), 110.9 (CH), 55.9 ($CH_3$), 55.9 ($CH_3$), 48.0 (CH), 45.5 (CH), 27.8 ($CH_2$), 24.6 ($CH_2$).

**(+) 8E:** White oil; $[\alpha]^{25}_D$ +296 (*c* = 0.10, $CH_2Cl_2$). **HRMS** (EI, $C_{22}H_{24}O_2$, $M^+$): calcd.: 320.1776, found: 320.1771. **FTIR** (cast film): 3022, 2929, 2835, 1516, 1261, 1139, 1030 $cm^{-1}$.

**(–) 8E:** White oil; $[\alpha]^{25}_D$ –290 (*c* = 0.99, $CH_2Cl_2$). **HRMS** (EI, $C_{22}H_{24}O_2$, $M^+$): calcd.: 320.1776, found: 320.1774. **FTIR** (cast film): 3022, 2929, 2835, 15l16, 1261, 1139, 1030 $cm^{-1}$.

**(±) 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*E*)-3-methoxystyryl]cyclohex-1-ene (9)**:

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | | ee |
|---|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) | |
| **9E** **14Z** | 15% EtOAc/hex $R_f$ = 0.3 | 123 mg (58%) | i-amylose-3 column. 95% hex/EtOH (15 min) | 110 mg | (+) **9E** | 13 mg | 5.8 | 99% |
| | | | | | (–) **9E** | 25 mg | 7.8 | >99% |
| | | | | | (+) **14Z** | 9 mg | 5.2 | >99% |
| | | | | | (–) **14Z** | 9 mg | 6.3 | >99% |

**$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.17 (t, *J* = 7.9 Hz, 1H), 6.87 (bd, *J* = 7.7 Hz, 1H), 6.80 (t, *J* = 2.0 Hz, 1H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.74–6.72 (m, 2H), 6.80 (d, *J* = 1.9 Hz, 1H), 6.18–6.12 (m, 2H), 5.90 (tdd, *J* = 2.4 Hz, 4.4 Hz, 10.0 Hz, 1H), 5.68 (dq, *J* = 10.0 Hz, 2.2 Hz, 1H), 3.85 (s, 3H), 3.83 (s, 3H), 3.79 (s, 3H), 3.19 (dq, *J* = 11.0 Hz, 2.7 Hz, 1H), 2.40–2.36 (m, 1H), 2.28–2.18 (m, 2H), 1.93 (tdd, *J* = 3.1 Hz, 5.2 Hz, 12.8 Hz 1H), 1.71–1.65 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.8 (C), 148.7 (C), 147.4 (C), 139.3 (C), 137.5 (C), 134.5 (CH), 130.3 (CH), 129.4 (CH), 129.2 (CH), 127.6 (CH), 120.4 (CH), 118.7 (CH),

112.4 (CH), 111.7 (CH), 111.5 (CH), 110.9 (CH), 55.9 ($CH_3$), 55.9 ($CH_3$), 55.2 ($CH_3$), 48.0 (CH), 45.5 (CH), 27.8 ($CH_2$), 24.5 ($CH_2$).

**(+) 9:** White oil; $[\alpha]^{25}_D$ +300 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1878. **FTIR** (cast film): 3018, 2931, 2835, 1598, 1515, 1464, 1261, 1155, 1030 $cm^{-1}$.

**(–) 9:** White oil; $[\alpha]^{25}_D$ -294 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1875. **FTIR** (cast film): 3019, 2931, 2835, 1598, 1515, 1464, 1261, 1155, 1030 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*Z*)-3-methoxystyryl]cyclohex-1-ene (14): $^1$H NMR** ($CDCl_3$, 500MHz) δ: 7.10 (t, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.69 (dd, *J* = 2.2 Hz, 8.2 Hz, 1H), 6.64 (dd, *J* = 2.0 Hz, 8.2 Hz, 1H), 6.54 (d, *J* = 2.0 Hz, 1H), 6.45 (br. d, *J* = 7.6 Hz, 1H), 6.42 (br. s, 1H), 6.31 ( d, *J* = 11.7 Hz, 1H), 5.83 (tdd, *J* = 2.4 Hz, 4.3 Hz, 10 Hz, 1H), 5.64 (dq, *J* = 10.0 Hz, 2.2 Hz, 1H), 5.56 (dd, *J* = 10.5 Hz, 11.6 Hz, 1H), 3.83 (s, 3H), 3.72 (s, 3H), 3.72 (s, 3H), 3.14 (dq, *J* = 11.2 Hz, 2.8 Hz, 1H), 2.85 (dq, *J* = 2.5 Hz, 10.0 Hz, 1H), 2.23–2.12 (m, 2H), 1.82 (tdd, *J* = 3.1 Hz, 5.2 Hz, 13.0 Hz, 1H), 1.67–1.59 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 159.3 (C), 148.8 (C), 147.4 (C), 139.1 (C), 137.3 (C), 136.9 (CH), 130.4 (CH), 128.8 (CH), 128.8 (CH), 127.3 (CH), 120.9 (CH), 120.4 (CH), 113.9 (CH), 111.9 (CH), 111.2 (CH), 110.8 (CH), 55.9 (CH3), 55.7 ($CH_3$), 55.1 ($CH_3$), 48.1 (CH), 40.6 (CH), 28.5 ($CH_2$), 24.3 ($CH_2$).

**(+) 14:** White solid; $[\alpha]^{25}_D$ +23 (*c* = 0.85, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1876. **FTIR** (cast film): 3000, 2930, 2834, 1576, 1515, 1464, 1260, 1140, 1030 $cm^{-1}$.

**(–) 14:** White solid; $[\alpha]^{25}_D$ –12 (*c* = 0.78, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1882. **FTIR** (cast film): 2999, 2931, 2834, 1577, 1515, 1464, 1260, 1140, 1030 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*E*)-4-methoxystyryl]cyclohex-1-ene (10)**:

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | | | ee |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | mass | $R_{ta}$ (min) | $R_{tb}$ (min) | |
| **10E**<br>**15Z** | 20% EtOAc/hex<br>$R_f$ = 0.4 | 100 mg<br>(48%) | *sequential runs:*<br>i-amylose-3 column.<br>a. 95% hex/EtOH (30 min)<br>b. 97% hex/EtOH (20 min) | 90 mg | (+) **10E** | 13 mg | 16.3 | 10.6 | >99% |
| | | | | | (–) **10E** | 20 mg | 20.1 | - | 99% |
| | | | | | (+) **15Z** | 9 mg | 16.3 | 11.9 | 98% |
| | | | | | (–) **15Z** | 109mg | 16.3 | 9.3 | 99% |

**$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.20 (d, *J* = 8.7 Hz, 2H), 6.79 (dd, *J* = 17.0 Hz, 8.5 Hz, 3H), 6.72 (dd, *J* = 1.8 Hz, 8.1 Hz, 1H), 6.70 (d, *J* = 1.8 Hz, 1H), 6.11 (d, *J* = 15.9 Hz, 1H), 6.02 (dd, 7.5 Hz, 15.9 Hz, 1H), 5.89 (tdd, *J* = 2.5 Hz, 4.5 Hz, 10.0 Hz, 1H), 5.68 (dq, *J* = 9.8 Hz, 2.3 Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 3.17 (dq, *J* = 11.2 Hz, 2.8 Hz, 1H), 2.35 (dq, *J* = 2.6 Hz, 8.9 Hz, 1H), 2.24–2.18 (m, 2H), 1.92 (tdd, *J* = 3.1 Hz, 5.3 Hz, 12.8 Hz, 1H), 1.69–1.64 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 158.7

(C), 148.6 (C), 147.4 (C), 137.7 (C), 132.0 (C), 130.7 (CH), 130.4 (CH), 128.6 (CH), 127.6 (CH), 127.1 (2 CH), 120.4 (CH), 113.9 (2 CH), 111.8 (CH), 110.9 (CH), 55.9 ($CH_3$), 55.9 ($CH_3$), 55.3 ($CH_3$), 48.1 (CH), 45.4 (CH), 27.9 ($CH_2$), 24.6 ($CH_2$).

**(+) 10:** White oil; $[\alpha]^{25}_D$ +335 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1875. **FTIR** (cast film): 3018, 2931, 2835, 1607, 1512, 1250, 1139, 1031 $cm^{-1}$.

**(–) 10:** White oil; $[\alpha]^{25}_D$ –303 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): 350.1882, found: 350.1879. **FTIR** (cast film): 3018, 2931, 2835, 1607, 1512, 1250, 1139, 1031 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*Z*)-4-methoxystyryl]cyclohex-1-ene (15): $^1$H NMR** ($CDCl_3$, 500MHz) δ: 6.78 (d, *J* = 8.6 Hz, 2H), 6.73 (t, *J* = 5.5 Hz, 3H), 6.66 (dd, *J* = 2.0 Hz, 8.2 Hz, 1H), 6.55 (d, *J* = 1.9 Hz, 1H), 6.27 (d, *J* = 11.7 Hz, 1H), 5.84 (tdd, *J* = 2.4 Hz, 4.3 Hz, 10.0 Hz, 1H), 5.65 (dq, *J* = 10.0 Hz, 2.2 Hz, 1H), 5.49 (dd, *J* = 10.4 Hz, 11.6 Hz, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 3.72 (s, 3H), 3.14 (dq, *J* = 11.1 Hz, 2.8 Hz, 1H), 2.81 (dq, *J* = 2.3 Hz, 10.0 Hz, 1H), 2.23–2.12 (m, 2H), 1.82 (tdd, *J* = 3.1 Hz, 5.3 Hz, 13.0 Hz, 1H), 1.67–1.59 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 158.1(C), 148.8 (C), 147.4 (C), 137.4 (C), 135.5 (CH), 130.4 (CH), 130.3 (C), 129.5 (CH), 128.3 (CH), 127.4 (CH), 120.5 (CH), 113.3 (CH), 111.3 (CH), 110.8 (CH), 56.0 ($CH_3$), 55.7 ($CH_3$), 55.2 ($CH_3$), 48.1 (CH), 40.5 (CH), 28.4 ($CH_2$), 24.4 ($CH_2$).

**(+) 15:** White solid; $[\alpha]^{25}_D$ +16 (*c* = 1.10, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1876. **FTIR** (cast film): 350.1882, found: 350.1878. **FTIR** (cast film): 2999, 2929, 2835, 1607, 1512, 1249, 1139, 1031 $cm^{-1}$.

**(–) 15:** White solid; $[\alpha]^{25}_D$ –8 (*c* = 1.10, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): 350.1882, found: 350.1878. **FTIR** (cast film): 2999, 2929, 2835, 1607, 1512, 1249, 1139, 1031 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*E*)-2-methylstyryl]cyclohex-1-ene (11):**

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | amount | $R_t$ (min) | ee |
|---|---|---|---|---|---|---|---|---|
| **11E 16Z** | 20% EtOAc/hex $R_f$ = 0.4 | 141 mg (70%) | i-amylose-3 column. 97% hex/EtOH (20 min) | 140 mg | **(+) 11E** | 20 mg | 10.7 | 98% |
| | | | | | **(–) 11E** | 24 mg | 12.6 | 99% |
| | | | | | **(+) 16Z** | 20 mg | 9.7 | 99% |
| | | | | | **(–) 16Z** | 19 mg | 11.7 | 99% |

**$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.33 (d, *J* = 8.4 Hz, 1H), 7.12–7.07 (m, 3H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.73 (dd, *J* = 8.4 Hz, 2.0 Hz, 1H), 6.71 (d, *J* = 2.1 Hz, 1H), 6.31 (d, *J* = 15.7 Hz, 1H), 5.98 (dd, *J* = 7.9 Hz, 15.9 Hz, 1H), 5.89 (tdd, *J* = 2.5 Hz, 4.6 Hz, 2.5 Hz, 1H), 5.69 (dq, 10.1 Hz, 2.2 Hz, 1H), 3.85 (s, 3H), 3.84 (s, 3H), 3.19 (dq, *J* = 8.8 Hz, 2.8 Hz, 1H), 2.40 ( dq, *J* = 2.6 Hz, 9.3 Hz, 1H), 2.29–2.19 (m, 2H),

2.15 (s, 3H), 2.0 (tdd, *J* = 3.1 Hz, 5.4 Hz, 12.9 Hz, 1H), 1.73–1.67 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 148.7 (C), 147.4 (C), 137.6 (C), 137.1 (C), 135.5 (C), 135.1 (CH), 130.5 (CH), 130.1(CH), 127.5 (CH), 127.5 (CH), 126.8 (CH), 125.9 (CH), 125.5 (CH), 120.6 (CH), 111.7 (CH), 111.0 (CH), 56.0 ($CH_3$), 55.9 ($CH_3$), 48.2 (CH), 46.0 (CH), 28.2 ($CH_2$), 24.7 ($CH_2$), 19.8 ($CH_3$).

**(+)11.** Colourless oil; $[\alpha]^{25}_D$ +266 (*c* = 1, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_2$, $M^+$): calcd.: 334.1933, found: 334.1930. **FTIR** (cast film): 3018, 2931, 2835, 1515, 1261, 1030 $cm^{-1}$.

**(–)11.** Colourless oil; $[\alpha]^{25}_D$ –201 (*c* = 1, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_2$, $M^+$): 334.1933, found: 334.1928. **FTIR** (cast film): 3018, 2931, 2835, 1515, 1261, 1030 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*Z*)-2-methylstyryl]cyclohex-1-ene (16): $^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.07 (t, *J* = 7.4 Hz, 1H), 7.04 (d, *J* = 7.3, 1H) 7.0 (t, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 8.0 Hz, 1H), 6.58 (dt, *J* = 1.7 Hz, 8.4 Hz, 2H), 6.38 (d, *J* = 2.0 Hz, 1H), 6.27 (d, *J* = 11.3 Hz, 1H), 5.78 (dq, *J* = 9.8 Hz, 3.2 Hz, 1H), 5.60–5.57 (m, 2H), 3.85 (s, 3H), 3.64 (s, 3H), 3.10 (dq, *J* = 9.0 Hz, 2.8 Hz, 1H), 2.58 (dq, *J* = 2.8 Hz, 10.3 Hz, 1H), 2.16–2.13 (m, 2H), 1.87 (s, 3H), 1.81–1.77 (m, 1H), 1.66–1.60 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 148.8 (C), 147.4 (C), 137.6 (C), 137.0 (C), 136.3 ($CH_2$), 130.6 ($CH_2$), 129.3 (CH), 128.8 ($CH_2$), 128.4 (CH), 127.1 (CH), 126.6 (CH), 125.0 (CH), 120.5 ($CH_2$), 110.9 (CH), 110.8 (CH), 56.0 ($CH_3$), 55.7 ($CH_3$), 48.2 (CH), 40.7 (CH), 28.7 ($CH_2$), 24.4 ($CH_2$), 19.5 ($CH_3$).

**(+) 16.** White solid; $[\alpha]^{25}_D$ +64 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_2$, $M^+$): calcd.: 334.1933, found: 334.1934. **FTIR** (cast film): 3018, 2924, 2835, 1516, 1261, 1031 $cm^{-1}$.

**(–)16.** White solid; $[\alpha]^{25}_D$ –43 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{23}H_{26}O_2$, $M^+$): calcd.: 334.1933, found: 334.1928. **FTIR** (cast film): 3018, 2928, 2834, 1516, 1261, 1031 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*E*)-2-bromostyryl]cyclohex-1-ene (12):**

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | | ee |
|---|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) | |
| **12E** **12Z** | 20% EtOAc/hex $R_f$ = 0.3 | 71 mg (29%) | i-amylose-3 column. 97% hex/EtOH (30 min) | 70 mg | (+) **12E** | 18 mg | 13.1 | >99% |
| | | | | | (–) **12E** | 18 mg | 17.0 | 99% |
| | | | | | (+) **12Z** | *not isolated* | 11.4 | - |
| | | | | | (–) **12Z** | | 14.8 | - |

**$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.48 (dd, *J* = 7.9 Hz, 1.2 Hz, 1H), 7.40 (dd, *J* = 7.8Hz, 1.5 Hz, 1H), 7.20 (dt, *J* = 0.8 Hz, 7.5 Hz, 1H), 7.03 (dt, *J* = 1.5 Hz, 7.7 Hz, 1H), 6.80 (d, *J* = 8.2 Hz, 1H), 6.74 (dd, *J* = 8.1 Hz, 2.0 Hz, 1H), 6.72 (d, *J* = 2.1 Hz, 1H), 6.53 (d, *J* = 15.8 Hz, 1H), 6.10 (dd, *J* = 7.6 Hz, 15.9 Hz, 1H), 5.9 (tdd, *J* = 2.5 Hz, 4.6 Hz, 10.0 Hz, 1H), 5.68 (dq, *J* = 10.0 Hz, 2.2 Hz, 1H), 3.85 (s, 3H), 3.85 (s, 3H),

3.22 (dq, *J* = 11.1 Hz, 2.8 Hz, 1H), 2.46 (dq, *J* = 2.1 Hz, 9.0 Hz, 1H), 2.29–2.19 (m, 2H), 1.97 (tdd, *J* = 3.1 Hz, 5.1 Hz, 12.9 Hz, 1H), 1.74–1.68 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 148.8 (C), 147.5(C), 137.7 (C), 137.4 (C), 137.2 (CH), 132.8 (CH), 130.4 (CH), 128.3 (CH), 128.2 (CH), 127.5 (CH), 127.3 (CH), 126.9 (CH), 123.3 (C), 120.5 (CH), 111.6 (CH), 111.1 (CH), 55.9 ($CH_3$), 55.9 ($CH_3$), 48.0 (CH), 45.3 (CH), 27.7 ($CH_2$), 24.6 ($CH_2$).

**(+)12E:** Colourless oil; $[\alpha]^{25}_D$ +214 (*c* = 1.00, $CH_2Cl_2$). **HRMS** (EI, $C_{22}H_{23}BrO_2$, $M^+$): calcd.: 400.0861, found: 400.0861. **FTIR** (cast film): 3018, 2930, 2834, 1515, 1465, 1261, 1139, 1029 $cm^{-1}$.

**(–)12E:** Colourless oil; $[\alpha]^{25}_D$ –230 (*c* = 0.99, $CH_2Cl_2$). **HRMS** (EI, $C_{22}H_{23}BrO_2$, $M^+$): calcd.: 400.0861, found: 400.0871. **FTIR** (cast film): 3018, 2930, 2834, 1515, 1465, 1261, 1139, 1029 $cm^{-1}$.

**(±) 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*Z*)-3,4-dimethoxystyryl]cyclohex-1-ene (13):**

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | | | | ee |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | $mass_a$ | $R_{ta}$ (min) | $mass_b$ | $R_{tb}$ (min) | |
| **t-BG 13** | 20% EtOAc/hex $R_f$ = 0.3 | 527 mg (77%) | *sequential runs:* a. AD-H column. 18% $^i$PrOH/$CO_2$ b. C8 column. 50→100% ACN/$H_2O$ (30 min) | 479 mg | **(+) t-BG** | 144 mg | 12.0 | 67 mg | 11.9 | 99% |
| | | | | | **(–) t-BG** | 146 mg | 15.2 | 50 mg | 11.9 | 93% |
| | | | | | **(+) 13Z** | 44 mg | 9.4 | 12 mg | 10.1 | 96% |
| | | | | | **(–) 13Z** | 50 mg | 10.8 | 18 mg | 10.1 | 95% |

**HPLC Method B used to remove minor impurities*

**$^1$H NMR** ($CDCl_3$, 700MHz) δ: 6.72 (d, *J* = 8.2 Hz, 1H), 6.70 (d, *J* = 8.1 Hz, 1H), 6.65 (dd, *J* = 2.1 Hz, 8.2 Hz, 1H), 6.56 (d, *J* = 2.1 Hz, 1H), 6.43–6.41 (m, 2H), 6.27 (d, *J* = 11.5 Hz, 1H), 5.84 (tdd, *J* = 2.4 Hz, 4.2 Hz, 10.1 Hz, 1H), 5.65 (dq, *J* = 2.2 Hz, 9.8 Hz, 1H), 5.51 (dd, *J* = 10.4 Hz, 11.5 Hz), 3.84 (s, 3H), 3.83 (s, 3H), 3.76 (s, 3H), 3.73 (s, 3H), 3.15 (dq, *J* = 8.8 Hz, 2.8 Hz, 1H), 2.84 (dq, *J* = 2.5 Hz, 10.1 Hz, 1H), 2.19–2.15 (m, 2H), 1.83 (tdd, *J* = 3.1 Hz, 5.0 Hz, 12.8 Hz, 1H), 1.67–1.61 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 148.7, 148.4, 147.6, 147.4, 137.4, 135.9, 130.7, 130.5, 128.5, 127.3, 120.8, 120.3, 111.8, 111.3, 110.8, 110.8, 55.9, 55.8, 55.7, 48.1, 40.7, 28.6, 24.5. Characterization data is consistent with literature.[7]

**(+) t- BG:** Colourless oil: $[\alpha]^{25}_D$ +325 (*c* = 1.00, $CH_2Cl_2$).
**(–) t-BG:** Colourless oil: $[\alpha]^{25}_D$ –275 (*c* = 1.00, $CH_2Cl_2$).
**(+)13:** Colourless oil: $[\alpha]^{25}_D$ +6.4(*c* = 1.00, $CH_2Cl_2$).
**(–)13:** Colourless oil: $[\alpha]^{25}_D$ –3.3 (*c* = 1.90, $CH_2Cl_2$).

**(±) 3(*S/R*)-(3-methoxyphenyl)-4(*R/S*)-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (17):**

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | |
|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) |
| **17E** **17Z** | 15% EtOAc/hex $R_f$ = 0.2 | 66 mg (52%) | i-amylose-3 column. 97% hex/EtOH (20 min) | 50 mg | **(±) 17E** | 22 mg | 7.8 |
| | | | | | **(±) 17Z** | *not isolated* | |

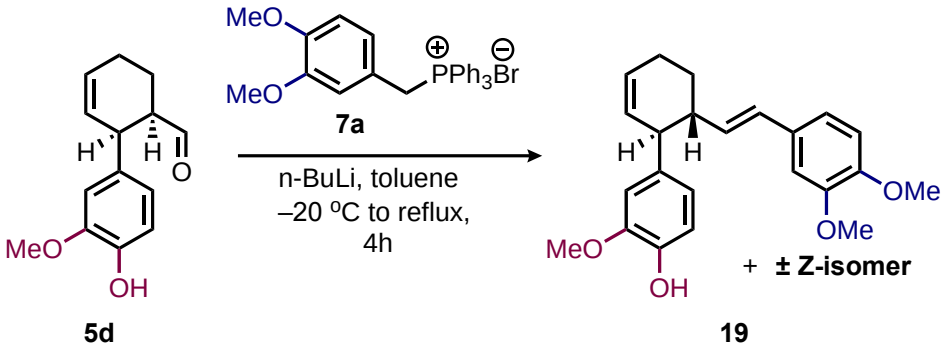
**17E:** White oil. **$^1$H NMR** ($CDCl_3$, 700MHz) δ: 7.19 (t, *J* = 7.8 Hz, 1H), 6.82–6.73 (m, 6H), 6.13 (d, *J* = 15.9 Hz, 1H), 6.03 (dd, *J* = 7.6 Hz, 16.0 Hz 1H), 5.90 (tdd, *J* = 2.4 Hz, 4.0 Hz, 10.0 Hz, 1H), 5.68 (dq, *J* = 10.0 Hz, 2.1 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.77 (s, 3H), 3.23 (dq, *J* = 9.4 Hz, 2.7 Hz, 1H), 2.41 (dq, *J* = 2.6 Hz, 9.3 Hz, 1H), 2.26–2.18 (m, 2H), 1.92 (dq, *J* = 12.5 Hz, 4.2 Hz, 1H), 1.70–1.64 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 176 MHz) δ: 159.5 (C), 149.0 (C), 148.3 (C), 146.7 (C), 132.2 (CH), 131.1 (C), 130.0 (CH), 129.0 (CH), 128.9 (CH), 127.6 (CH), 121.1 (CH), 118.9 (CH), 114.3 (CH), 111.5 (CH), 111.2 (CH), 108.8 (CH), 56.0 ($CH_3$), 55.8 ($CH_3$), 55.2 ($CH_3$), 48.5 (CH), 45.1 (CH), 27.8 ($CH_2$), 24.5 ($CH_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1874. **FTIR** (cast film): 3019, 2931, 2835, 1601, 1515, 1465, 1263, 1157, 1028 $cm^{-1}$.

**(±) (3(*S/R*)-(4-methoxyphenyl)-4(*R/S*)-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (18):**

| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | |
|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) |
| **18E** **18Z** | 20% EtOAc/hex $R_f$ = 0.2 | 206 mg (85%) | i-amylose-3 column. 97% hex/EtOH (10 min) | 100 mg | **(±) 18E** | 22 mg | 9.2 |
| | | | | | **(±) 18Z** | *not isolated* | |

**$^1$H NMR** ($CDCl_3$, 500MHz) δ: 7.12–7.09 (m, 2H), 6.83–6.76 (m, 5H), 6.11 (d, *J* = 16.0 Hz, 1H), 6.02 (dd, *J* = 7.4 Hz, 16.0 Hz, 1H), 5.89 (dq, *J* = 10.0, 3.3 Hz, 1H), 5.66 (dq, *J* = 10 Hz, 2.2 Hz, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.78 (s, 3H), 3.20 (dq, *J* = 11.0 Hz, 2.8 Hz, 1H), 2.36 (dq, *J* = 2.9 Hz, 9.8 Hz, 1H), 2.24–2.19 (m, 2H), 1.91 (dq, *J* = 12.5 Hz, 4.2 Hz, 1H), 1.70–1.63 (m, 1H). **$^{13}$C NMR** ($CDCl_3$, 126 MHz) δ: 158.0 (C), 149.0 (C), 148.3 (C), 137.1 (C), 132.3 (C), 131.1 (CH), 130.5 (CH), 129.4 (2 CH), 128.8 (CH), 127.4 (CH), 118.8 (CH), 113.6 (2 CH), 111.2 (CH), 108.8 (CH), 56.0 ($CH_3$), 55.9 ($CH_3$), 55.263 ($CH_3$), 47.6 (CH), 45.5 (CH), 27.9 ($CH_2$), 24.6 ($CH_2$). **HRMS** (EI, $C_{23}H_{26}O_3$, $M^+$): calcd.: 350.1882, found: 350.1878. **FTIR** (cast film): 3018, 2931, 2835, 1608, 1513, 1262, 1139, 1029 $cm^{-1}$.

**(±) 3(*S*/*R*)-(3-methoxy-4-hydroxyphenyl)-4(*R*/*S*)-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (19)**:




| product | silica column conditions | product mass (% yield) | separation method | HPLC injection | isolated components | | |
|---|---|---|---|---|---|---|---|
| | | | | | | amount | $R_t$ (min) |
| **19E** **19Z** | 10 → 25% EtOAc/hex $R_f$ = 0.2 | 40 mg (32%) | C8 column. 50→100% ACN/$H_2O$ (30 min) | 40 mg | **(±) 19E** | 8 mg | 18.0 |
| | | | | | **(±) 19Z** | *not isolated* | |

**$^1$H NMR** ($CDCl_3$, 500MHz) δ: 6.83–6.76 (m, 4H), 6.70–6.67 (m, 2H), 6.10 (d, *J* = 16.0 Hz, 1H), 6.02 (dd, *J* = 16.0 Hz, 7.5 Hz, 1H), 5.91–5.87 (m, 1H), 5.67 (dq, *J* = 10.5 Hz, 2.5 Hz, 1H), 5.45 (s, 1H), 3.87 (s, 3H), 3.86 (s, 3H), 3.82 (s, 3H), 3.17–3.15 (m, 1H), 2.35–2.33 (m, 1H), 2.22–2.20 (m, 2H), 1.93–1.90 (m, 1H), 1.69–1.64 (m, 1H). Characterization data are consistent with literature.[7]

**Synthesized via **5d** without racemization to **6d***

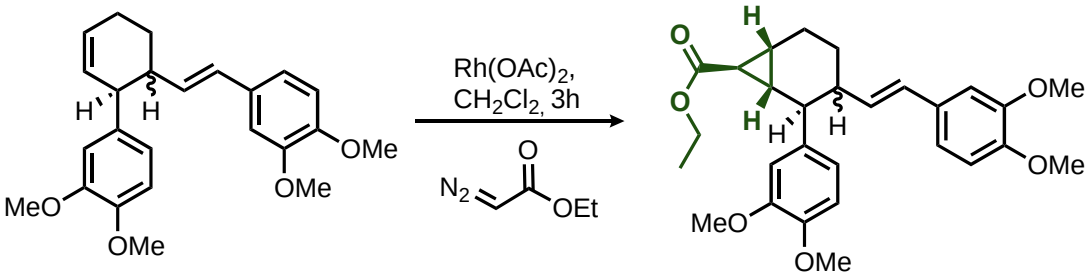
### *Synthesis of 24 and 25:*

Pd/C (5 mg) was added to a flame dried flask under $N_2$ followed by (±) *t*-BG or (±)*c*-BG (25.0 mg, 0.06 mmol) in ethyl acetate. After a quick exposure to vacuum, then $N_2$, the flask was placed under reduced pressure. A hydrogen ($H_2$) balloon was inserted, and the reaction was then stirred for 18 hours. The contents of the flask were filtered through celite and rinsed with $CH_2Cl_2$. The solvent was concentrated in vacuo, providing products **24** and **25** without the need for further purification.

**(±) 4-((1*R*,2*S*)-2-(3,4-dimethoxyphenylethy)cyclohexyl)-1,2-dimethoxy benzene (24):** White solid (99%). **$^1$H NMR** ($CDCl_3$,700 MHz) δ: 6.75 (d, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 7.7 Hz, 1H), 6.62 (dd, *J* = 7.7 Hz, 1.4 Hz, 1H), 6.59 (d, *J* = 1.4 Hz, 1H), 6.51 (dd, *J* = 7.7 Hz, 1.4 Hz, 1H), 6.46 (d, *J* = 1.4 Hz, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H), 2.56–2.52 (m, 1H), 2.32–2.27 (m, 1H), 2.17–2.14 (m, 1H), 2.06–2.02 (m, 1H), 1.82–.77 (m, 3H), 1.52–1.42 (m, 2H), 1.39–1.31 (m, 3H), 1.20–1.16 (m, 1H), 1.10, 1.04 (m, 1H). **$^{13}$C NMR** ($CDCl_3$,175 MHz) δ: 148.7, 148.6, 147.0, 146.9, 139.4, 135.4, 120.0, 119.5, 111.6, 111.0, 110.6, 55.9, 55.8, 55.7, 55.7, 50.4, 41.5, 36.3, 35.9, 32.2, 32.1, 26.9, 26.5. **HRMS** (EI, $C_{24}H_{32}O_4$, $M^+$): calcd: 385.2301, found: 385.2342.

**(±) 4-((1S,2S)-2-(3,4-dimethoxyphenylethy)cyclohexyl)-1,2-dimethoxy benzene (25):** White solid (95%). **$^1$H NMR** ($CDCl_3$,700 MHz) δ: 6.77 (d, *J* = 8.4 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H ), 6.67 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.65 (d, *J* = 1.4 Hz, 1H), 6.49 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.45 (d, *J* = 1.4 Hz, 1H), 3.85 (s, 3H), 3.82 (app s, 6H), 3.77 (s, 3H), 2.80-2.77 (m, 1H), 2.48-2.45 (m, 1H), 2.14-2.11 (m, 1H), 1.89-1.85 (m, 3H), 1.75-1.67 (m, 2H), 1.59-1.46 (m, 4H), 1.41-1.37 (m, 1H), 1.31-1.26 (m, 1H) ppm. **$^{13}$C-NMR** ($CDCl_3$,175 MHz) δ: 148.6, 148.5, 146.9, 146.9, 138.5, 135.3, 120.0, 119.2, 111.6, 111.2, 111.0, 110.7, 55.9, 55.9, 55.8, 55.7, 45.9, 39.3, 33.6, 29.6, 27.3, 26.5, 25.7, 20.6**HRMS** (EI, $C_{24}H_{32}O_4$, $M^+$): calcd: 385.2301, found: 385.2342.

***Synthesis of 26 and 27*** [14]




**± *c*-BG or ± *t*-BG**

**± 26 or ± 27**
> 95:5 E:Z

Rhodium acetate dimer (1 mg) and a solution of (±)*t*-BG (50 mg, 0.13 mmol) or (±)*c*-BG (24 mg, 0.06 mmol) in $CH_2Cl_2$ (0.50 mL) was added to a flame dried round bottom flask. The reaction solution was stirred while ethyl diazoacetate (33 wt% $CH_2Cl_2$ solution, 16 μL dissolve in 0.5 mL $CH_2Cl_2$ for t-BG and 8 μL dissolve in 0.5 mL $CH_2Cl_2$ for c-BG) was added dropwise. The reaction was stirred at rt for 3 hours and then concentrated in vacuo. The residue was dissolved in acetonitrile and was purified by HPLC

| product | separation method | product mass (% yield) | $R_t$ (min) |
|---|---|---|---|
| 26 | C8 column. 50→100% ACN/$H_2O$ (20 min) | 9.4 mg (16%) | 17.8 |
| 27 | | 4.5 mg (15%) | 9.9 |

(±) **1-((1*R*,2*S*,3*S*,6*R*,7*S*)-3-(3,4-dimethoxyphenethyl)-2-(3,4-dimethoxyphenyl)bicyclo[4.1.0]heptan-7-yl)-2-methoxyethanone (26):** Yellow oil (16%). **$^1$H NMR** ($CDCl_3$,700 MHz) δ: 6.80 (m, 2H), 6.73–6.72 (m, 2H), 6.70–6.69 (m, 2H), 5.92 (d, *J* = 16.1 Hz, 1H), 5.73 (dd, *J* = 16.1 Hz, 7.7 Hz, 1H), 4.10–4.05 (m, 2H), 3.83 (s, 6H), 3.83 (s, 3H), 3.82 (s, 3H), 2.55 (dd, *J* = 10.5 Hz, 0.7 Hz, 1H), 2.16–2.14 (m, 1H), 2.05–1.98 (m, 2H), 1.86–1.84 (m, 1H), 1.75–1.69 (m, 2H), 1.59 (app t, *J* = 4.2 Hz, 1H), 1.23 (t, *J* = 7 Hz, 3H),1.16 (dd, *J* = 12.6 Hz, 4.2 Hz, 1H). **$^{13}$C NMR** ($CDCl_3$,175 MHz) δ: 174.1, 148.9, 148.7, 148.3, 147.3, 139.0, 131.8, 130.8, 129.0, 120.2, 118.7, 111.4, 111.1, 111.0, 108.7, 60.4, 55.9, 55.9, 55.8, 55.7, 28.2, 25.7, 25.4, 23.3, 22.5, 14.3. **HRMS** (EI, $C_{28}H_{35}O_6$, $[M+H]^+$): calcd: 467.2355, found: 467.2439.

**(±) 1-((1*R*,2*R*,3*S*,6*R*,7*S*)-3-(3,4-dimethoxyphenethyl)-2-(3,4-dimethoxyphenyl)bicyclo[4.1.0]heptan-7-yl)-2-methoxyethanone (27):** Yellow oil (15%). **$^{1}$H NMR** ($CDCl_3$, 700 MHz) δ: 6.88 (dd, *J* = 7.7 Hz, 2.1 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 6.76 (d, *J* = 2.1 Hz, 2H), 6.74 (dd, *J* = 7.7 Hz, 2.1 Hz, 2H), 6.17 (d, *J* = 16.1 Hz, 1H), 5.60 (dd, *J* = 16.1 Hz, 9.1 Hz, 1H), 4.12 (q, *J* = 7 Hz, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.83 (s, 3H), 3.74 (s, 3H), 3.23 (app. d, *J* = 4.9 Hz, 1H), 2.29–2.23 (m, 2H), 1.89 (appt, *J* = 4.2 Hz, 2H), 1.82–1.78 (m, 1H), 1.60 (t, *J* = 4.2 Hz, 1H), 1.52–1.48 (m, 1H), 1.27–1.21 (m, 4H). **$^{13}$C NMR** ($CDCl_3$ ,175 MHz) δ: 174.2, 148.9, 148.4, 148.1, 147.5, 134.9, 131.3, 130.7, 129.1, 121.3, 118.8, 113.3, 111.2, 110.5, 108.6, 60.4, 55.9, 55.8, 55.8, 55.7, 43.7, 40.0, 28.3, 26.2, 23.1, 20.9, 20.8, 14.3. **HRMS** (EI, $C_{28}H_{36}O_6$, $[M+H]^+$): calcd: 467.2355, found: 467.2442.

## *Optical Purity Data*

Enantiomeric excess (% ee) was determined by chiral HPLC analysis, with one of the following methods:

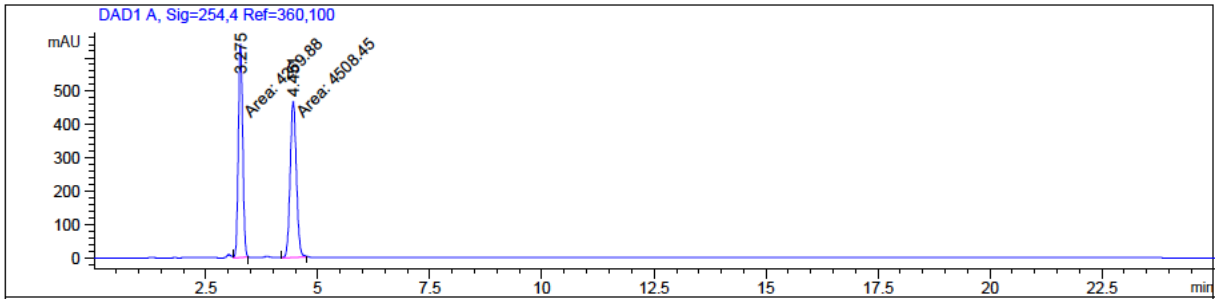
(a) 5% IPA: Hexane. Daicel CHIRALPAK IG column.

(b) 20% isopropanol/$CO_2$, 100 bar. Daicel CHIRALPAK AD-H column.

(c) 10% IPA: Hexane. Daicel CHIRALPAK IC column.

** Absolute stereochemistry was assigned according to published data in ref. 7*

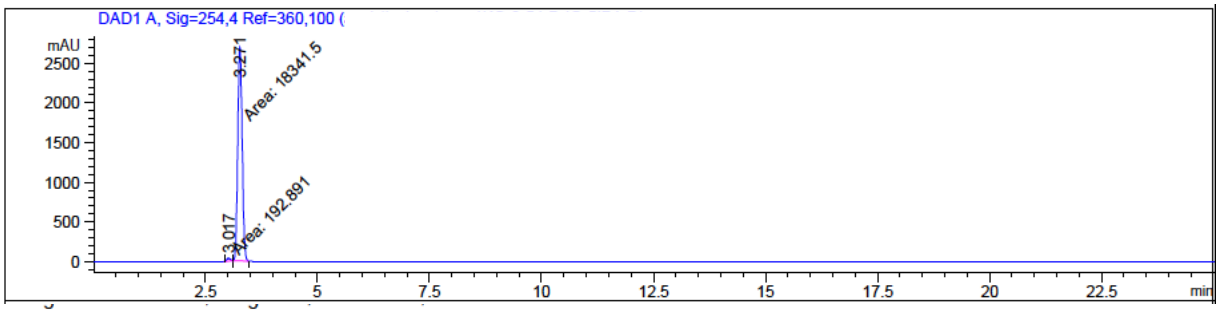
**8. (±) 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*E*)-styryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

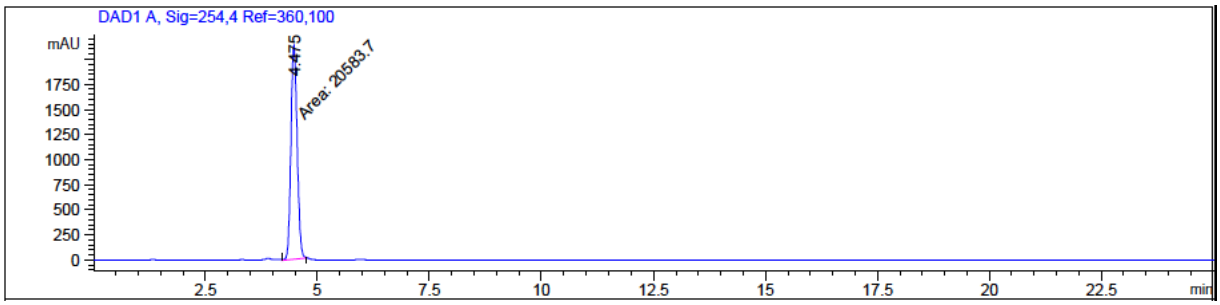
| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 3.275 | MM | 0.1110 | 4269.88037 | 640.98907 | 48.6412 |
| 2 | 4.451 | MM | 0.1608 | 4508.44580 | 467.26389 | 51.3588 |
| Totals : | | | | 8778.32617 | 1108.25296 | |

**(+)8. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*E*)-styryl]cyclohex-1-ene (99% ee): (Method a)**




| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 3.017 | MM | 0.0932 | 192.89052 | 34.49250 | 1.0407 | Impurity |
| 2 | 3.271 | MM | 0.1134 | 1.83415e4 | 2694.58887 | 98.9593 | (+)8 |
| Totals : | | | | 1.85344e4 | 2729.08137 | | |

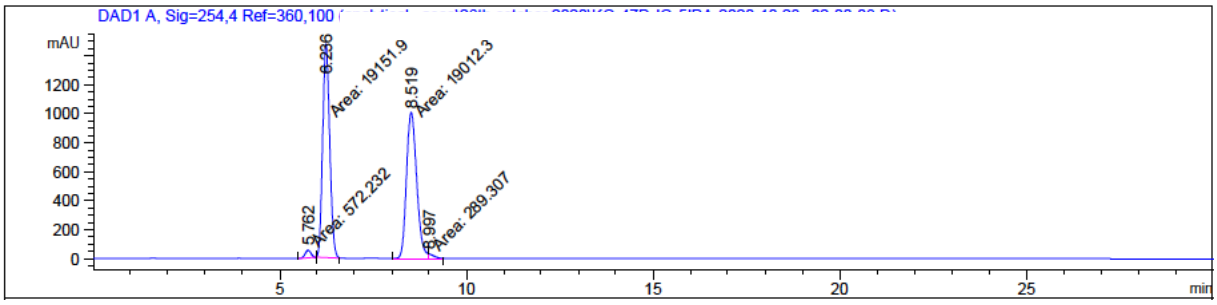
**(–)8. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*E*)-styryl]cyclohex-1-ene (> 99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 4.475 | MM | 0.1612 | 2.05837e4 | 2128.18555 | 100.0000 | (–)8 |
| Totals : | | | | 2.05837e4 | 2128.18555 | | |

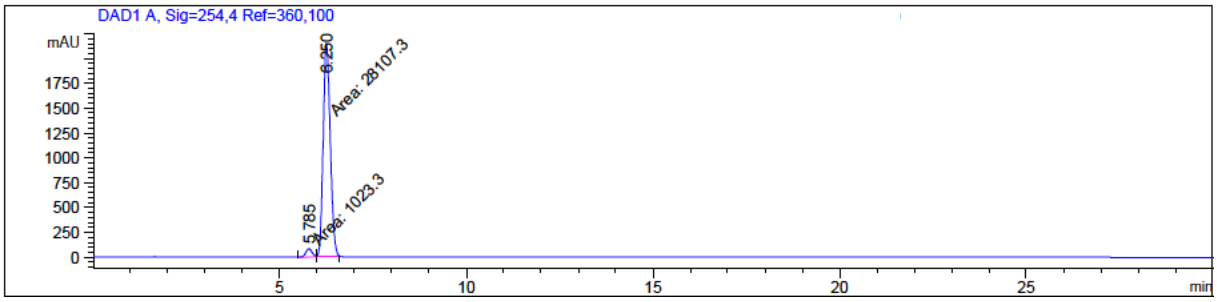
**9. 3(*S*/*R*)-(3,4-dimethoxyphenyl)-4(*R*/*S*)-[(*E*)-3-methoxystyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.762 | MM | 0.1832 | 572.23199 | 52.04971 | 1.4663 |
| 2 | 6.236 | MM | 0.2170 | 1.91519e4 | 1471.11340 | 49.0750 |
| 3 | 8.519 | MF | 0.3142 | 1.90123e4 | 1008.52759 | 48.7173 |
| 4 | 8.997 | FM | 0.1510 | 289.30722 | 31.94090 | 0.7413 |
| Totals : | | | | 3.90258e4 | 2563.63160 | |

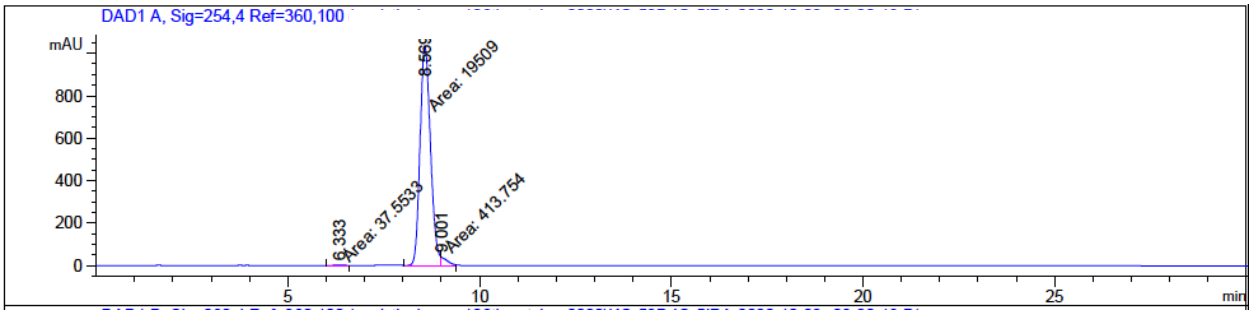
**(+)9. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*E*)-3-methoxystyryl]cyclohex-1-ene(>99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 5.785 | MM | 0.2057 | 1023.30310 | 82.91499 | 3.5128 | Impurity |
| 2 | 6.250 | MM | 0.2190 | 2.81073e4 | 2139.51660 | 96.4872 | (+)9 |
| Totals : | | | | 2.91306e4 | 2222.43159 | | |

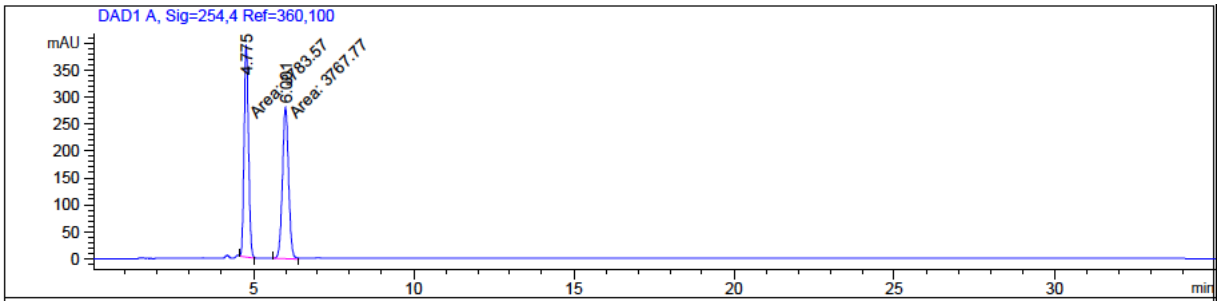
**(–)9. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*E*)-3-methoxystyryl]cyclohex-1-ene(>99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 6.333 | MM | 0.2538 | 37.55331 | 2.46581 | 0.1881 | (+)9 |
| 2 | 8.569 | MF | 0.3149 | 1.95090e4 | 1032.60400 | 97.7390 | (–)9 |
| 3 | 9.001 | FM | 0.1763 | 413.75418 | 39.11983 | 2.0729 | Impurity |
| Totals : | | | | 1.99603e4 | 1074.18965 | | |

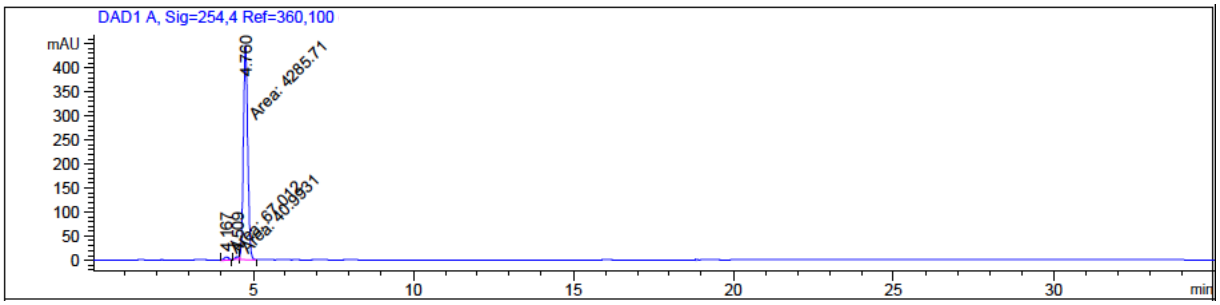
**14. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*Z*)-3-methoxystyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 4.775 | MM | 0.1600 | 3783.56592 | 394.04947 | 50.1046 |
| 2 | 6.001 | MM | 0.2238 | 3767.76880 | 280.64569 | 49.8954 |
| Totals : | | | | 7551.33472 | 674.69516 | |

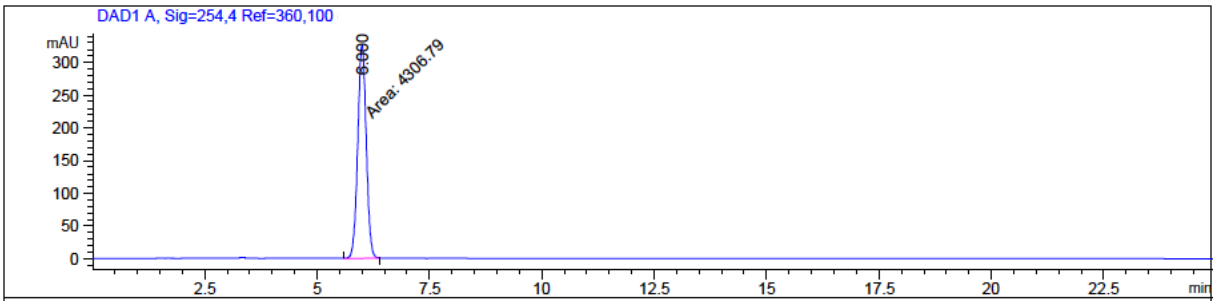
**(+)14. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*Z*)-3-methoxystyryl]cyclohex-1-ene (>99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 4.167 | MM | 0.1578 | 67.01202 | 7.07963 | 1.5252 | Impurity |
| 2 | 4.509 | MF | 0.1259 | 40.99306 | 5.42767 | 0.9330 | Impurity |
| 3 | 4.760 | FM | 0.1605 | 4285.70508 | 444.97592 | 97.5418 | (+)14 |
| Totals : | | | | 4393.71016 | 457.48322 | | |

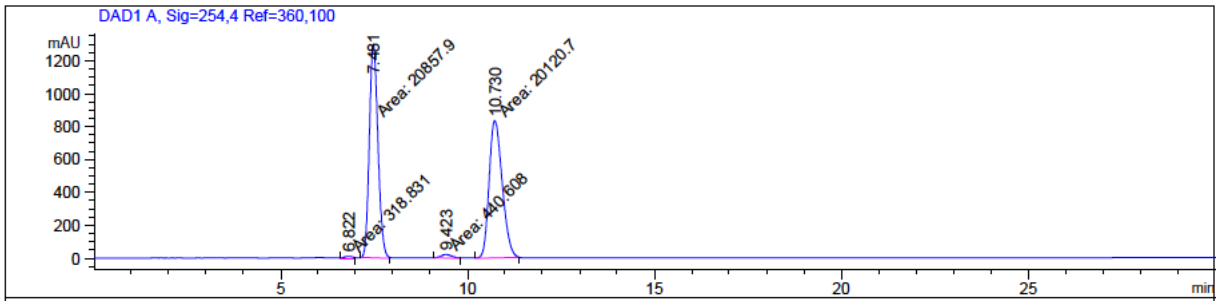
**(–)14. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*Z*)-3-methoxystyryl]cyclohex-1-ene (>99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 6.000 | MM | 0.2197 | 4306.78857 | 326.78674 | 100.0000 | (–)14 |
| Totals : | | | | 4306.78857 | 326.78674 | | |

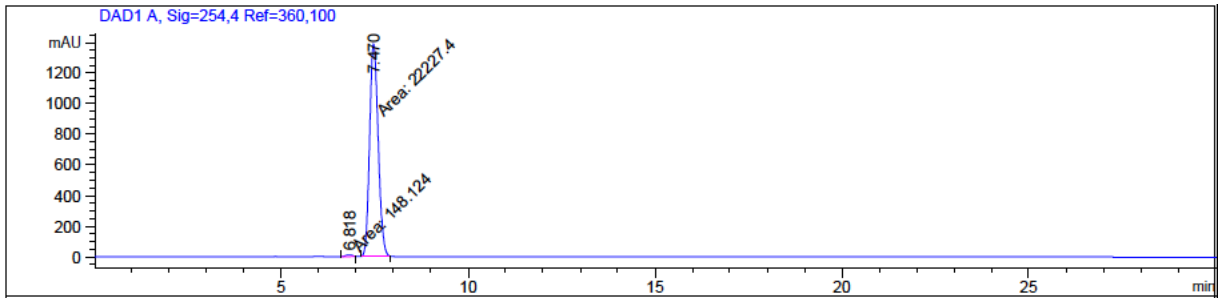
**10. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*E*)-4-methoxystyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 6.822 | MM | 0.2920 | 318.83115 | 18.19932 | 0.7639 |
| 2 | 7.481 | MM | 0.2679 | 2.08579e4 | 1297.71582 | 49.9733 |
| 3 | 9.423 | MM | 0.3424 | 440.60825 | 21.44956 | 1.0557 |
| 4 | 10.730 | MM | 0.4021 | 2.01207e4 | 833.89203 | 48.2072 |
| Totals : | | | | 4.17381e4 | 2171.25673 | |

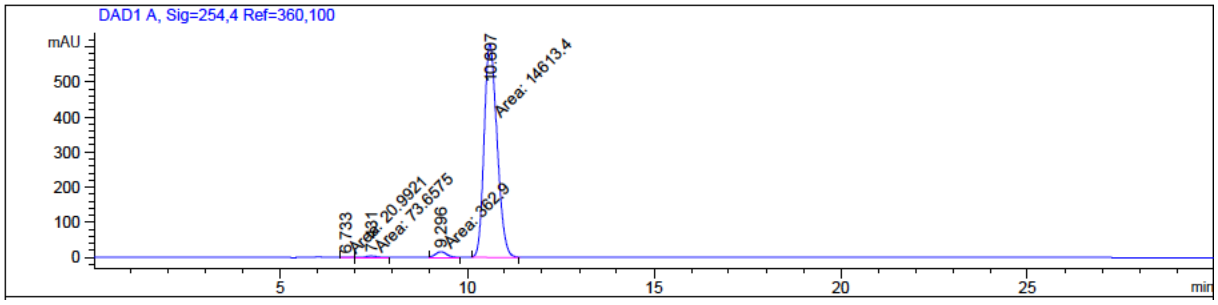
**(+)10. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*E*)-4-methoxystyryl]cyclohex-1-ene (>99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 6.818 | MM | 0.2138 | 148.12431 | 11.54741 | 0.6620 | Impurity |
| 2 | 7.470 | MM | 0.2671 | 2.22274e4 | 1386.85339 | 99.3380 | (+)10 |
| Totals : | | | | 2.23755e4 | 1398.40080 | | |

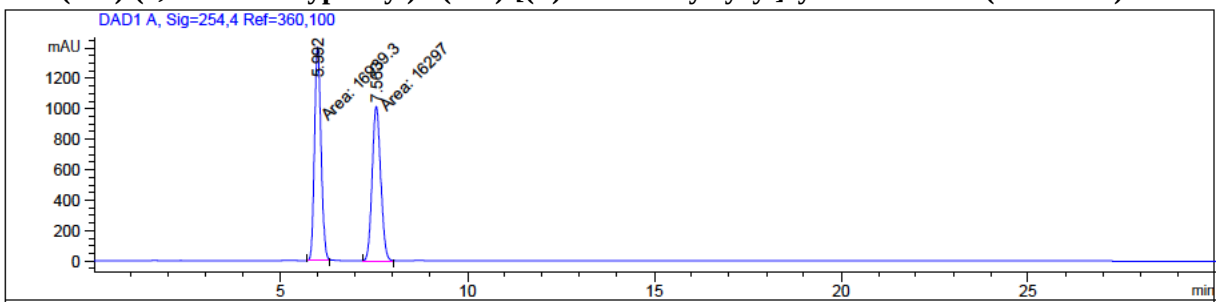
**(–)10. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*E*)-4-methoxystyryl]cyclohex-1-ene (99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 6.733 | MM | 0.2292 | 20.99214 | 1.10117 | 0.1393 | Impurity |
| 2 | 7.431 | MM | 0.3088 | 73.65749 | 3.97611 | 0.4887 | (+)10 |
| 3 | 9.296 | MM | 0.3646 | 362.90045 | 16.59074 | 2.4080 | Impurity |
| 4 | 10.607 | MM | 0.4010 | 1.46134e4 | 607.34192 | 96.9640 | (–)10 |
| Totals : | | | | 1.50709e4 | 629.00994 | | |

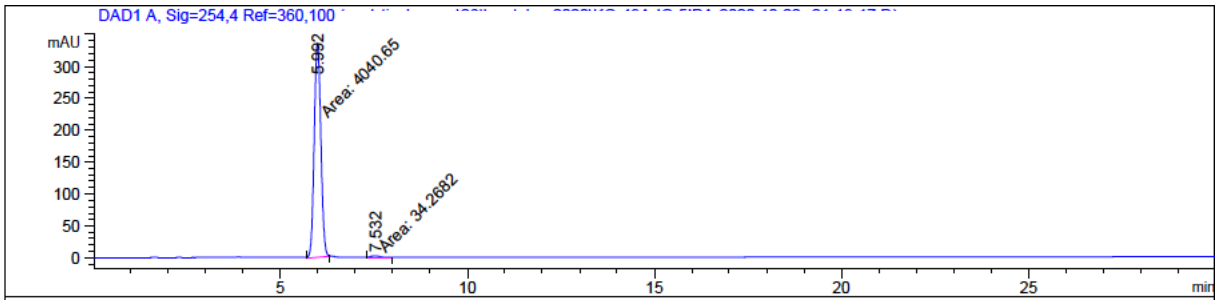
**15. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*Z*)-4-methoxystyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 5.992 | MM | 0.2023 | 1.69393e4 | 1395.22888 | 50.9662 |
| 2 | 7.563 | MM | 0.2668 | 1.62970e4 | 1017.92480 | 49.0338 |
| Totals : | | | | 3.32363e4 | 2413.15369 | |

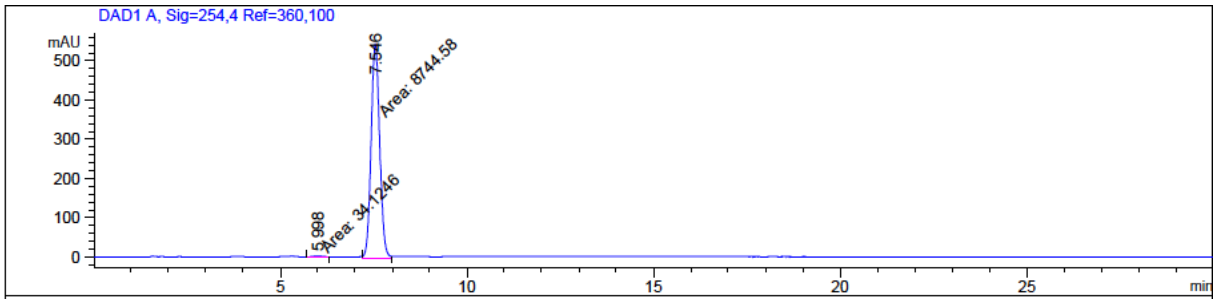
**(+) 15. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*Z*)-4-methoxystyryl]cyclohex-1-ene (98% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 5.992 | MM | 0.2014 | 4040.65259 | 334.44958 | 99.1590 | (–)15 |
| 2 | 7.532 | MM | 0.2558 | 34.26825 | 2.23308 | 0.8410 | (+)15 |
| Totals : | | | | 4074.92084 | 336.68266 | | |

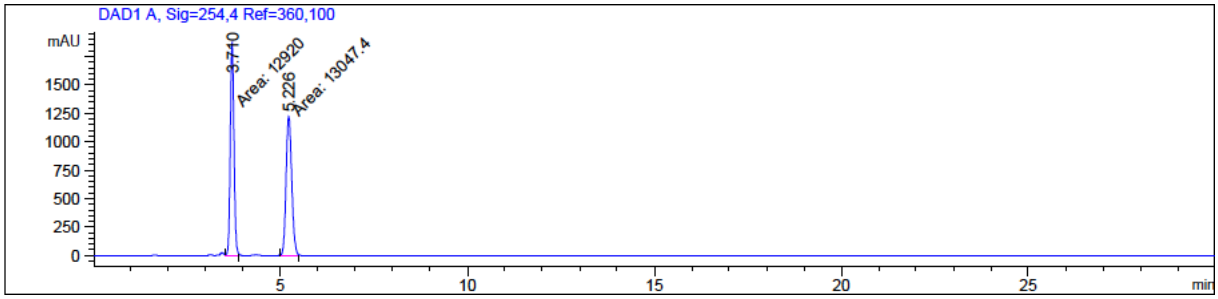
**(–) 15. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*Z*)-4-methoxystyryl]cyclohex-1-ene (99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 5.998 | MM | 0.2191 | 34.12463 | 2.59597 | 0.3887 | (–)15 |
| 2 | 7.546 | MM | 0.2669 | 8744.57520 | 546.10803 | 99.6113 | (+)15 |
| Totals : | | | | 8778.69983 | 548.70400 | | |

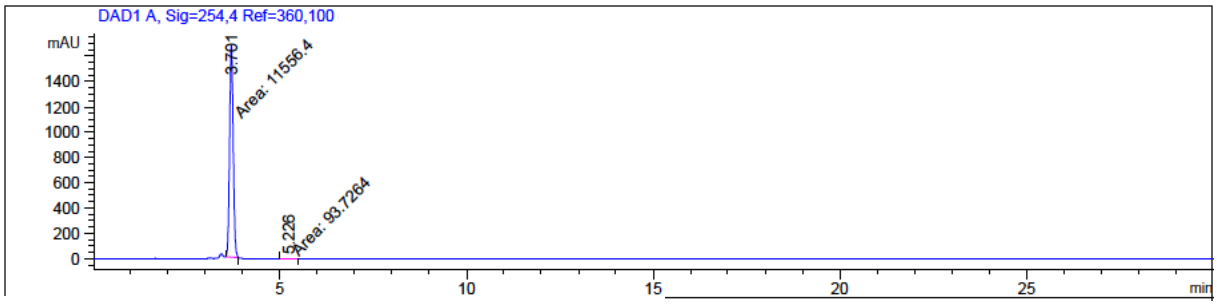
**11. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*E*)-2-methylstyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 3.710 | MM | 0.1154 | 1.29200e4 | 1865.38831 | 49.7547 |
| 2 | 5.226 | MM | 0.1773 | 1.30474e4 | 1226.50244 | 50.2453 |
| Totals : | | | | 2.59673e4 | 3091.89075 | |

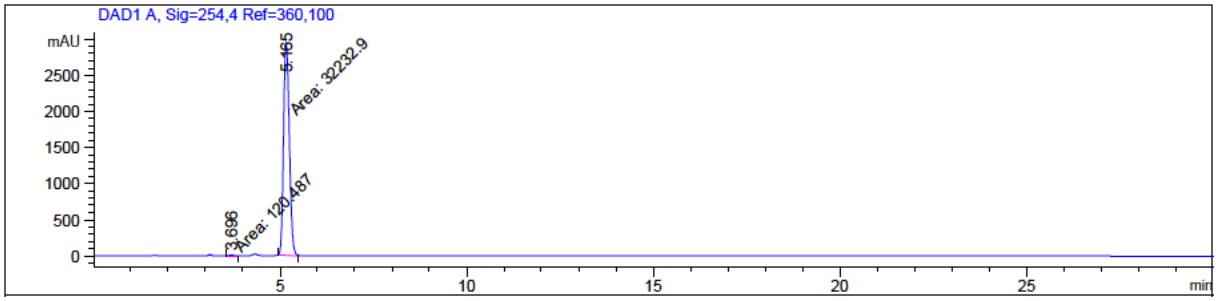
**(+) 11. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*E*)-2-methylstyryl]cyclohex-1-ene (98%ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 3.701 | MM | 0.1144 | 1.15564e4 | 1684.34827 | 99.1955 | (+)11 |
| 2 | 5.226 | MM | 0.4766 | 93.72644 | 3.27791 | 0.8045 | (–)11 |
| Totals : | | | | 1.16501e4 | 1687.62618 | | |

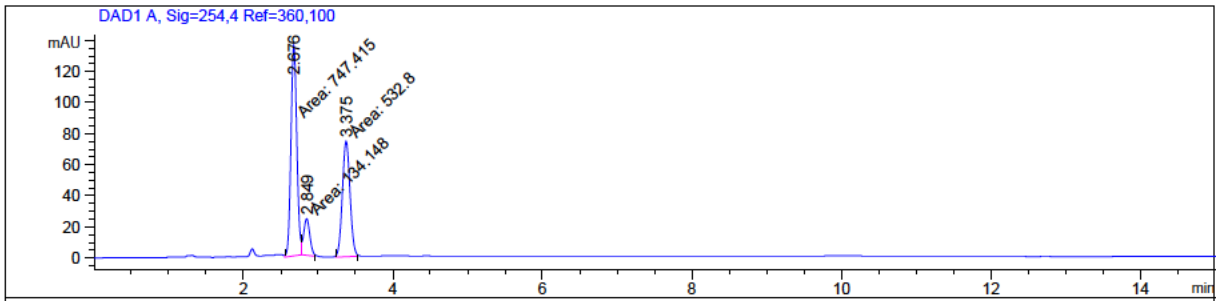
**(–) 11. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*E*)-2-methylstyryl]cyclohex-1-ene (99%ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 3.696 | MM | 0.1361 | 120.48663 | 14.74946 | 0.3724 | (+)11 |
| 2 | 5.165 | MM | 0.1827 | 3.22329e4 | 2940.39087 | 99.6276 | (–)11 |
| Totals : | | | | 3.23534e4 | 2955.14033 | | |

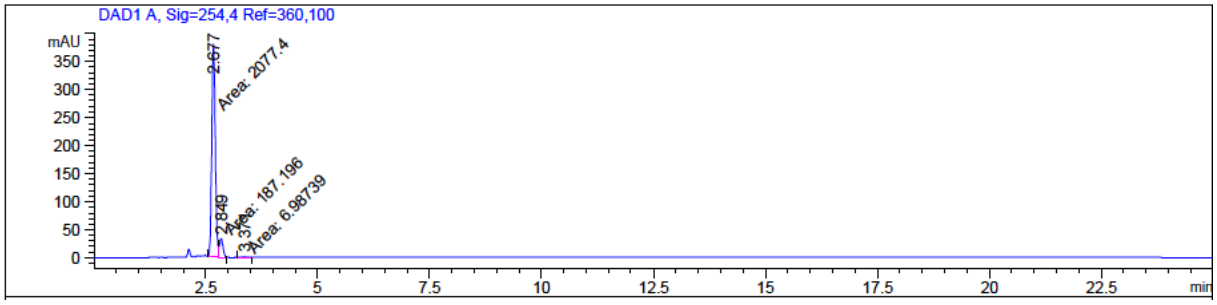
**16. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*Z*)-2-methylstyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.676 | MM | 0.0916 | 747.41486 | 135.98724 | 52.8446 |
| 2 | 2.849 | MM | 0.0947 | 134.14784 | 23.60262 | 9.4847 |
| 3 | 3.375 | MM | 0.1194 | 532.80042 | 74.35267 | 37.6707 |
| Totals : | | | | 1414.36311 | 233.94253 | |

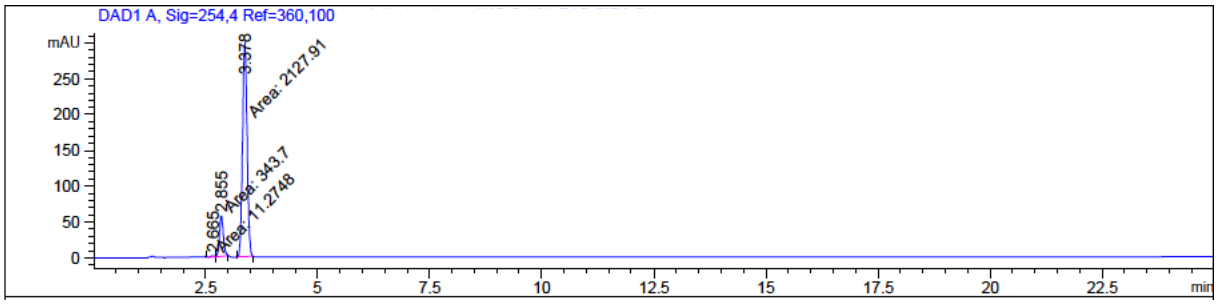
**(+)16. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*Z*)-2-methylstyryl]cyclohex-1-ene (99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 2.677 | MM | 0.0911 | 2077.39697 | 380.17612 | 91.4516 | (+)16 |
| 2 | 2.849 | MM | 0.0947 | 187.19553 | 32.93308 | 8.2408 | impurity |
| 3 | 3.371 | MM | 0.1600 | 6.98739 | 7.27885e-1 | 0.3076 | (–)16 |
| Totals : | | | | 2271.57989 | 413.83708 | | |

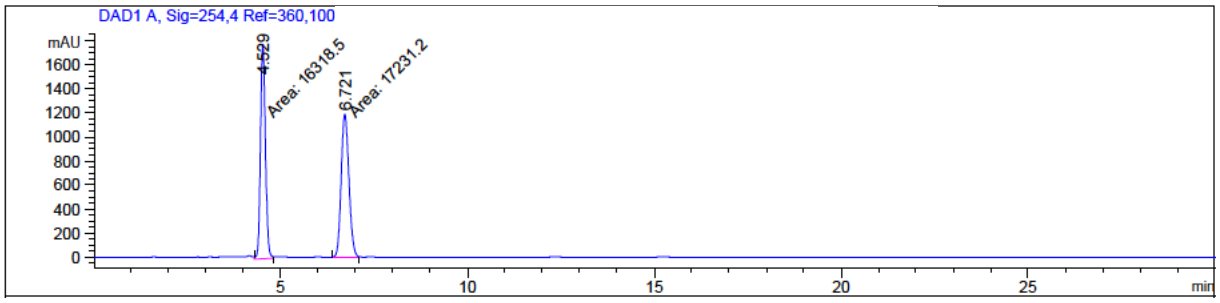
**(–)16. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*Z*)-2-methylstyryl]cyclohex-1-ene (99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 2.665 | MM | 0.1076 | 11.27477 | 1.74601 | 0.4541 | (+)16 |
| 2 | 2.855 | MM | 0.1014 | 343.70029 | 56.51110 | 13.8428 | impurity |
| 3 | 3.378 | MM | 0.1196 | 2127.91309 | 296.63055 | 85.7031 | (–)16 |
| Totals : | | | | 2482.88815 | 354.88767 | | |

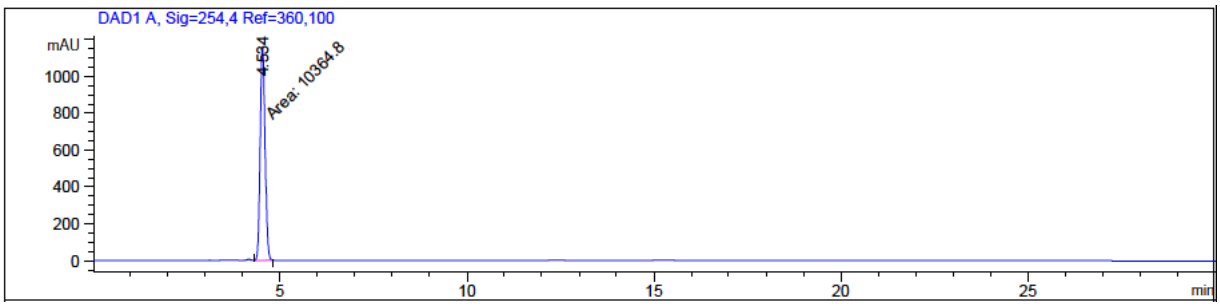
**12. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*E*)-2-bromostyryl]cyclohex-1-ene: (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 4.529 | MM | 0.1522 | 1.63185e4 | 1787.35388 | 48.6397 |
| 2 | 6.721 | MM | 0.2411 | 1.72312e4 | 1191.35974 | 51.3603 |
| Totals : | | | | 3.35496e4 | 2978.71362 | |

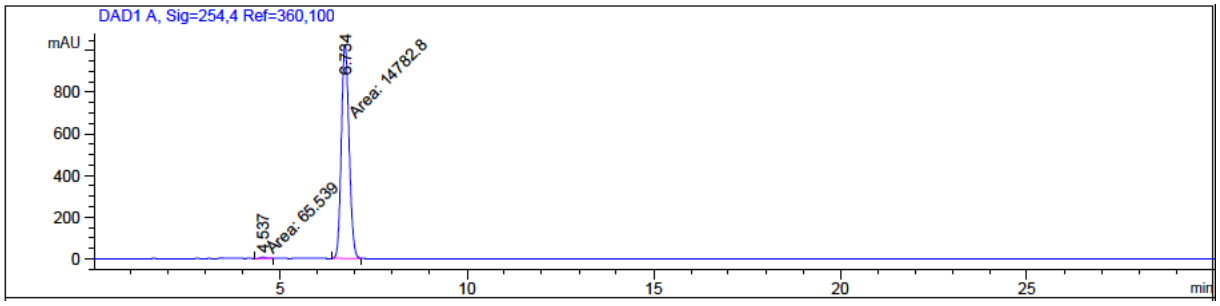
**(+)12. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*E*)-2-bromostyryl]cyclohex-1-ene (>99% ee): (Method a)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 4.534 | MM | 0.1487 | 1.03648e4 | 1161.68628 | 100.0000 | (+)12 |
| Totals : | | | | 1.03648e4 | 1161.68628 | | |

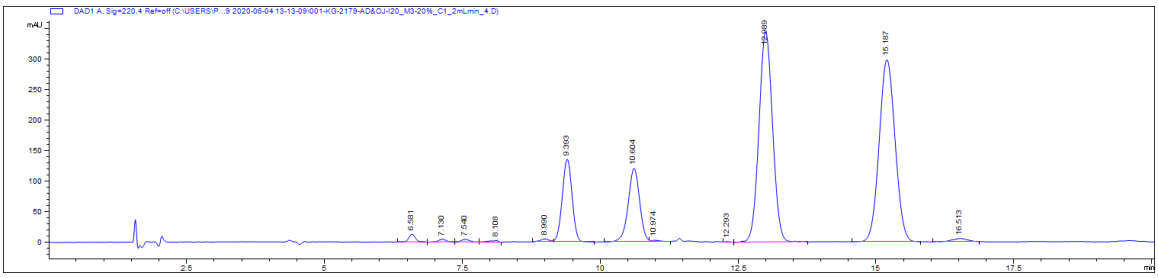
**(–)12. 3(*R*)-(3,4-dimethoxyphenyl)-4(*S*)-[(*E*)-2-bromostyryl]cyclohex-1-ene (99% ee): (Method a)**



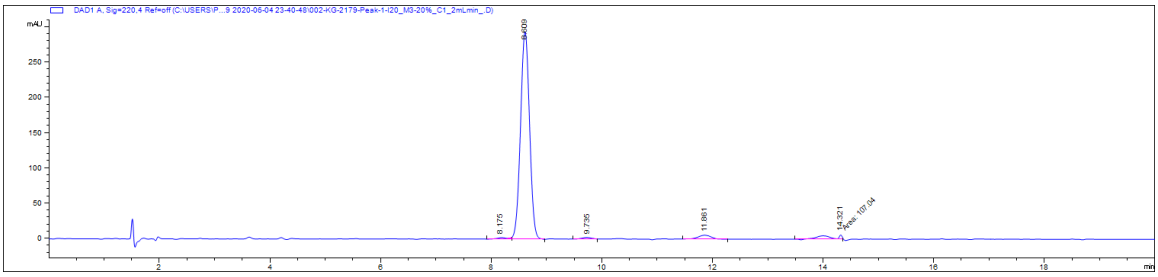

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 4.537 | MM | 0.1676 | 65.53897 | 6.51827 | 0.4414 | (+)12 |
| 2 | 6.734 | MM | 0.2394 | 1.47828e4 | 1029.02100 | 99.5586 | (–)12 |
| Totals : | | | | 1.48483e4 | 1035.53927 | | |

**13. 3(*S/R*)-(3,4-dimethoxyphenyl)-4(*R/S*)-[(*Z*)-3,4-dimethoxystyryl]cyclohex-1-ene: (Method b)**

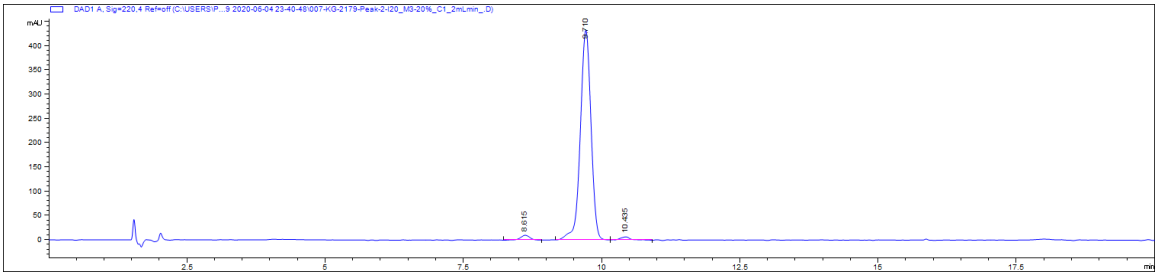


**(+)13. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*Z*)-3,4-dimethoxystyryl]cyclohex-1-ene: (Method b)**



| Index | Time (min) | Area (%) 220 nm |
|---|---|---|
| *impurity* | 8.18 | 0.715 |
| (+)13 | 8.61 | 93.027 |
| (–)13 | 9.74 | 0.717 |
| (+) *t*-BG | 11.86 | 2.579 |
| (–) *t*-BG | 14.32 | 2.961 |
| Total | | 100.00 |

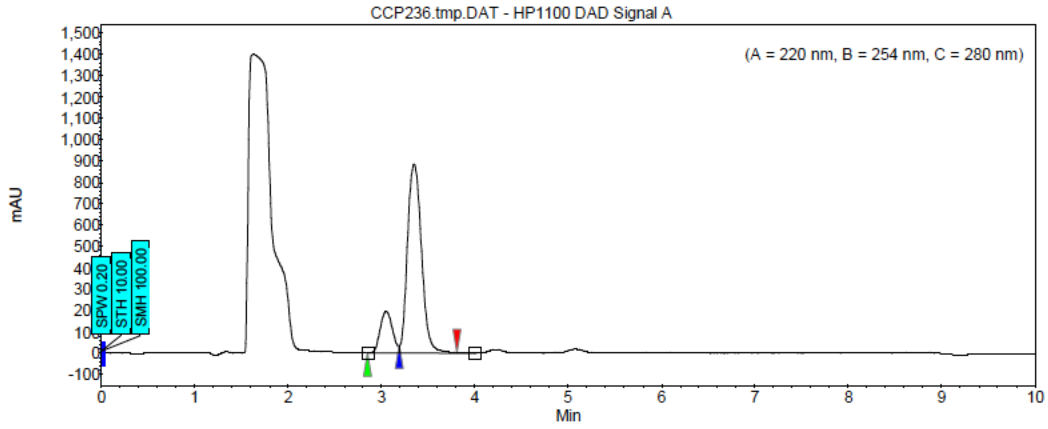
**(–)13. 3(*R*)-(3,4-dimethoxyphenyl)-4(S)-[(*Z*)-3,4-dimethoxystyryl]cyclohex-1-ene: (Method b)**



| Index | Time (min) | Area (%) 220 nm |
|---|---|---|
| (+)13 | 8.82 | 2.051 |
| (–)13 | 9.71 | 96.518 |
| *impurity* | 10.43 | 1.368 |
| Total | | 100.00 |

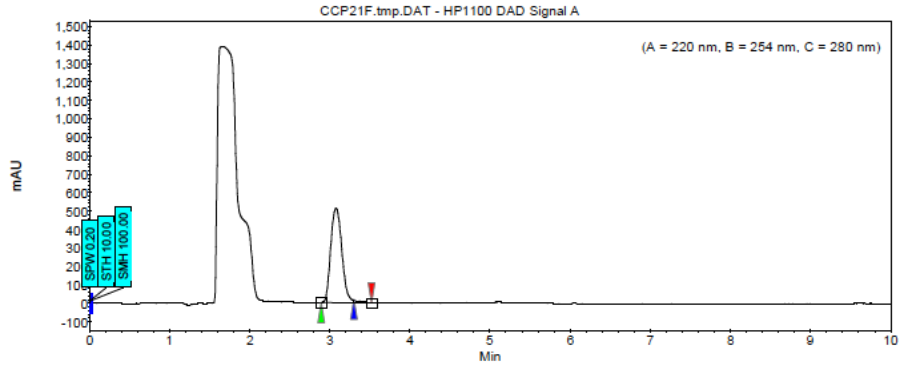
Since this analytical method led to different retention times for (+) **13** and (–) **13** as compared to the trace **13** (which is a mixture of (+) **13**, (–) **13**, (+) **t-BG** and (–) **t-BG**) another round of analytical validation was done to establish the enantiomeric purity (spectra shown below). Due to limited material remaining, a mixture containing 85:15 of the two enantiomers was prepared. These enantiomers were dissolved in DMSO which results in a solvent peak at ~1.6 min, this peak was ignored while integrating these spectra.

**15:85 of (+) 13: (–) 13: (Method b)**



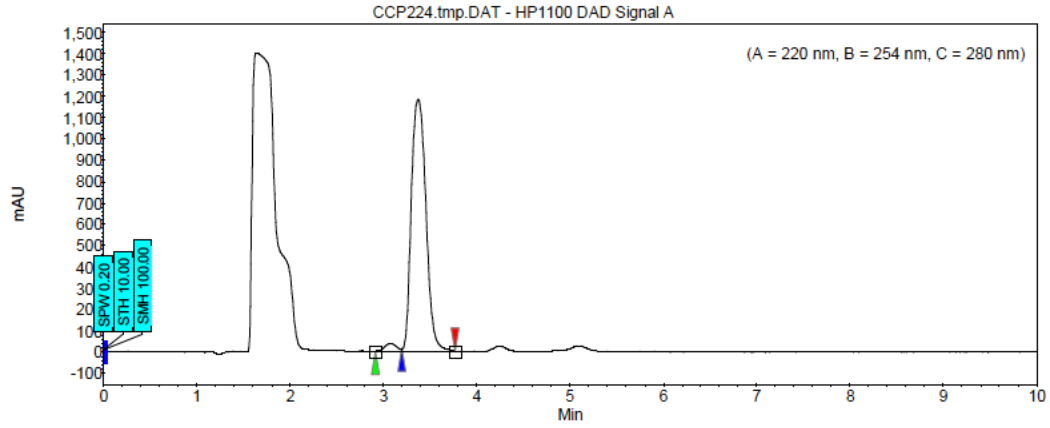

| | Index | Name | Start | Time | End | RT Offset | Quantity | Height | Area | Area |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | [Min] | [Min] | [Min] | [Min] | [% Area] | [µV] | [µV.Min] | [%] |
| (+)13 | 1 | UNKNOWN | 2.85 | 3.05 | 3.19 | 0.00 | 15.95 | 192.6 | 29.1 | 15.946 |
| (–)13 | 2 | UNKNOWN | 3.19 | 3.35 | 3.81 | 0.00 | 84.05 | 883.9 | 153.3 | 84.054 |
| | | | | | | | | | | |
| | Total | | | | | | 100.00 | 1076.5 | 182.4 | 100.000 |

**(+)13. 3(*S*)-(3,4-dimethoxyphenyl)-4(*R*)-[(*Z*)-3,4-dimethoxystyryl]cyclohex-1-ene (96% ee): (Method b-round 2)**



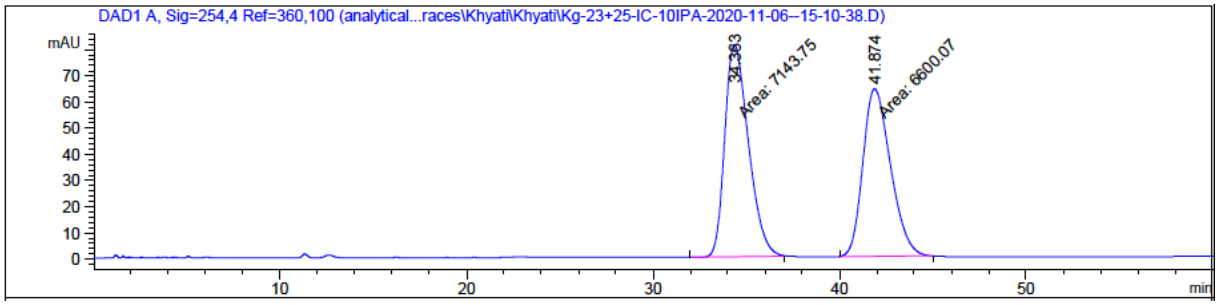

| | Index | Name | Start | Time | End | RT Offset | Quantity | Height | Area | Area |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | [Min] | [Min] | [Min] | [Min] | [% Area] | [µV] | [µV.Min] | [%] |
| (+)13 | 1 | UNKNOWN | 2.90 | 3.08 | 3.30 | 0.00 | 98.31 | 511.5 | 82.2 | 98.311 |
| (–)13 | 2 | UNKNOWN | 3.30 | 3.30 | 3.52 | 0.00 | 1.69 | 13.3 | 1.4 | 1.689 |
| | | | | | | | | | | |
| | Total | | | | | | 100.00 | 524.8 | 83.6 | 100.000 |

**(–)13. 3(*R*)-(3,4-dimethoxyphenyl)-4(S)-[(*Z*)-3,4-dimethoxystyryl]cyclohex-1-ene (95% ee) : (Method b-round 2)**




| | Index | Name | Start | Time | End | RT Offset | Quantity | Height | Area | Area |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | [Min] | [Min] | [Min] | [Min] | [% Area] | [µV] | [µV.Min] | [%] |
| (+)13 | 1 | UNKNOWN | 2.92 | 3.08 | 3.20 | 0.00 | 2.42 | 36.2 | 5.3 | 2.416 |
| (–)13 | 2 | UNKNOWN | 3.20 | 3.37 | 3.77 | 0.00 | 97.58 | 1182.0 | 213.9 | 97.584 |
| | | | | | | | | | | |
| | Total | | | | | | 100.00 | 1218.2 | 219.2 | 100.000 |

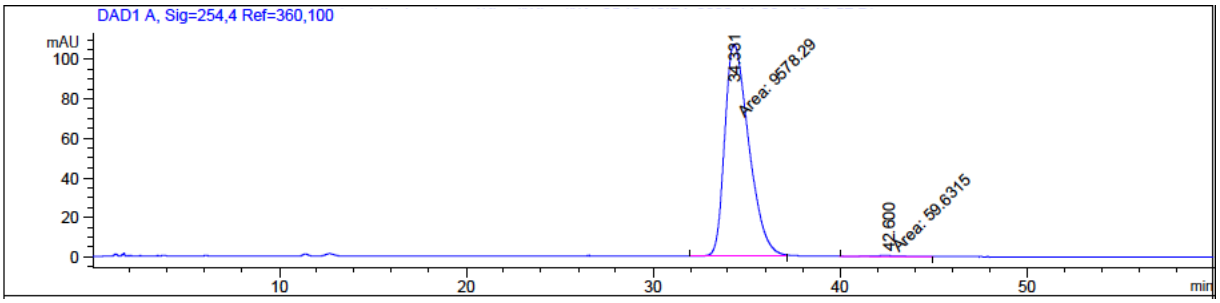
**_t_–BG– 3(_S/R_)-(3,4-Dimethoxyphenyl)-4(_R/S_)-[(_E_)-3,4-dimethoxystyryl]cyclohex-1-ene: (Method c)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % |
|---|---|---|---|---|---|---|
| 1 | 34.363 | MM | 1.4701 | 7143.75244 | 80.99113 | 51.9779 |
| 2 | 41.874 | MM | 1.7187 | 6600.07324 | 64.00153 | 48.0221 |
| Totals : | | | | 1.37438e4 | 144.99266 | |

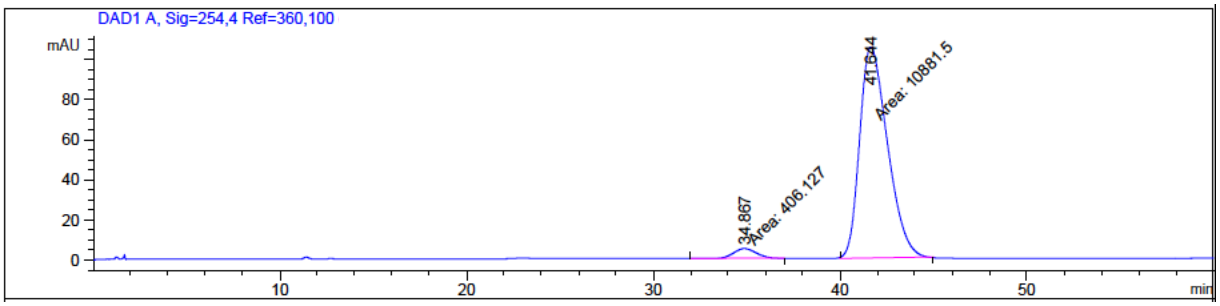
**(+)_t_–BG– 3(_S_)-(3,4-Dimethoxyphenyl)-4(_R_)-[(_E_)-3,4-dimethoxystyryl]cyclohex-1-ene (99% ee): (Method c)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 34.331 | MM | 1.4894 | 9578.29492 | 107.18334 | 99.3813 | +_t_-BG |
| 2 | 42.600 | MM | 2.3143 | 59.63152 | 4.29444e-1 | 0.6187 | -_t_-BG |
| Totals : | | | | 9637.92644 | 107.61279 | | |

**(–) *t*–BG– 3(*R*)-(3,4-Dimethoxyphenyl)-4(*S*)-[(*E*)-3,4-dimethoxystyryl]cyclohex-1-ene (93% ee): (Method c)**




Signal 1: DAD1 A, Sig=254,4 Ref=360,100

| Peak # | RetTime [min] | Type | Width [min] | Area [mAU*s] | Height [mAU] | Area % | Description |
|---|---|---|---|---|---|---|---|
| 1 | 34.867 | MM | 1.3973 | 406.12741 | 4.84431 | 3.5980 | (+)*t*-BG |
| 2 | 41.644 | MM | 1.7276 | 1.08815e4 | 104.97392 | 96.4020 | (–)*t*-BG |
| Totals : | | | | 1.12876e4 | 109.81823 | | |

## *PC-12 cell assays procedures*

### *Cell line maintenance*

PC-12 cells (CRL-1721) were obtained from ATCC and maintained in Dulbecco's modified Eagle's medium (DMEM) (Gibco™ LS11965092) containing 5% horse serum (HS) (Gibco™ LS10438018), 5% fetal bovine serum (FBS) (Gibco™ LS26050070) and 100 U/mL penicillin with 100 µg/mL streptomycin (1% Pen-Strep) (Gibco™ LS15140148). Cells were cultured for a month to reach passage 4 and then used for neuritogenesis assays. Living cells were counted using trypan blue exclusion staining.

### *Coating with collagen IV*

The assay to determine neuritogenesis was carried out in 96 well plates (Ibidi USA µ-Plate 96 Well, ibiTreat -#1.5 polymer coverslip, #89626). Each well was coated with 4-6 µg/cm$^2$ of Collagen IV (Sigma-C5533 - Collagen from human placenta Bornstein and Traub Type IV) dissolved in Hanks' balanced salt solution (HBSS). After overnight incubation at 8°C, the plates were sterilized with 70% ethanol and then washed with HBSS (3 times) to remove any residual ethanol.

### *Neuritogenesis assay*[15]

Passage 4 PC-12 cells (at 70% confluency) were seeded in the collagen-IV coated wells at a density of 2 × 10$^4$ cells/cm$^2$ and cultured in DMEM medium containing 5% HS, 5% FBS and 1% Pen-Strep for 24 hours, then the medium was changed to DMEM containing 2% HS, 1% FBS and a given treatment was added (see below). The cells were cultured for a further 48 hours and then visualized and/or stained for analysis.

*Treatments*: All the test compounds and commercial inhibitors were dissolved in DMSO and added as a solution. Compounds were tested at 30 µM concentration, unless otherwise noted. The final concentration of DMSO does not exceed 0.6% in any test. NGF (10ng/mL) with 0.6% DMSO was used as the positive control and 0.6% DMSO as the negative control.

For testing the perturbation of pathways associated with Nerve growth factor (NGF) mediated signalling, the following chemical inhibitors were used – triciribine hydrate (**iAkt,** 5 µM; Sigma T3830), Gö 6983 (**iPkc,** 0.5 µM; Sigma G1918), and SCH772984 (**iErk,** 10 µM; AbMole BioScience M2084).

All compounds and controls were tested as triplicate independent experiments. Importantly, to reduce inter-assay variations caused by evaporation of cell culture medium, cells were cultured only in wells B2-G11, the wells on the outer boundary of the plate were flooded with 300 µl of HBSS over the time course of the entire assay.

### *Immunofluorescence staining procedure*[16,17]

48 hours after addition of test compounds and controls, the cells were fixed with 4:1 ratio of 20% formaldehyde and 5% sucrose for 30 min. After aspirating, the fixative was washed with HBSS (2 times), and the residual formaldehyde was treated with 0.1% $NaBH_4$ for 7 min and washed with HBSS (2 times). The cells were blocked and permeabilized with 5% goat serum in 0.3% Triton X-100 for 25 min. Cells were incubated with primary mouse anti-β-tubulin III antibody (Sigma T8578), 1:1000 diluted in antibody buffer (5% goat serum in 0.1% Triton X-100) overnight at 4°C. The primary antibody was aspirated and washed with HBSS (2 times). Neurites were stained with secondary antibody goat anti-mouse, Alexa Fluor Plus 488, Secondary Antibody (Invitrogen™ A28175) and the nuclei were stained with 0.5 µg/well of Hoechst 33342 (Invitrogen™ LSH3570) for 1h at 37°C. After the secondary antibody was aspirated and washed with HBSS (2 times), mounting solution (80% glycerol and 0.5% n-propyl gallate) was added.

### *Imaging acquisition parameters and data analyses*

Images were acquired on a high content analysis system (Metaxpress XLS, Molecular Devices) with a Nikon 10× Plan Fluor lens. 25 sites per well (covering the entire well) with 0 µm between images in X and Y direction were taken with a 100 ms exposure time for DAPI filter set and an 1800 ms exposure time for Alexa 488 filter set. A digital confocal mode was used to image neurites with five Z sections separated by 2 µm steps which were combined into a single stack for analysis. Proper image acquisition was confirmed in several wells to ensure that gain and exposure levels didn't result in images with saturated regions. The images were segmented and analyzed using Metaxpress' Neurite Outgrowth module, the parameters were set as shown:

| Segemented region | Parameter | Measurement |
|---|---|---|
| Cell bodies | Approximate maximum width | 25 µm |
| | Minimum area | 90 $\mu m^2$ |
| Nuclear stain | Approximate minimum width | 4 µm |
| | Approximate maximum width | 15 µm |
| Outgrowth | Maximum width | 4 µm |
| | Minimum cell growth to log as significant | 5 µm |

For each well, the data generated for 25 images was added up to give the total number of cells and the total number of cells with significant outgrowth. An average cell body area was also calculated. Statistical analyses and graphing were done using GraphPad Prism version 9.2.0. p-values were determined by One-way ANOVA followed by Dunnett's multiple comparisons test or unpaired t-tests as mentioned in figures. Bar graphs have been plotted to show data as mean ± standard deviation.

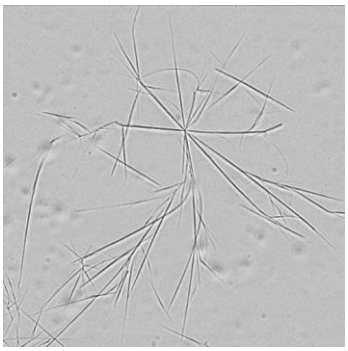


**Fig S1**. Image of *cis*-BG crystal at 10X magnification taken 24 h after addition of *cis*-BG in DMEM medium with 5% HS and 5% FBS. Similar results were seen when *cis*-BG was added to DMEM medium without any serum proteins.

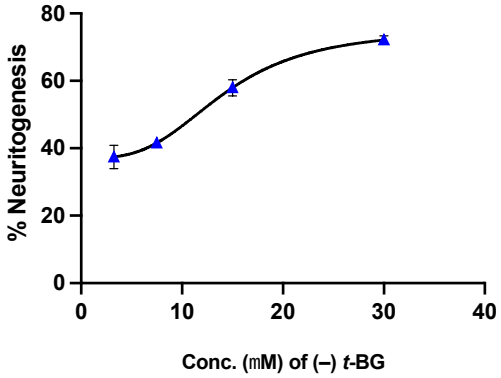



**Fig S2**. Dose response curve of the potentiating effect of (–) *trans*-banglene when dosed along with 10 ng/mL of NGF. Curve simulated by GraphPad Prism using a dose-response curve model with variable slope (four parameters) with least squares fit.

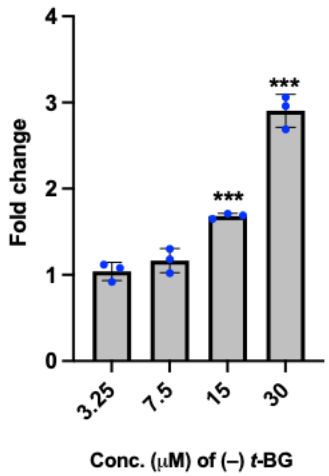



**Fig S3**. Fold change of neuritogenesis after treatment with increasing (μM) concentrations of (–) *trans*-banglene for 48 h. % Neuritogenesis was calculated as a percentage of total number of cells that had neurites > 5 μm. Fold change was calculated as %neuritogenesis (Compound) / % neuritogenesis (DMSO). p-value measured by unpaired t-test vs. DMSO ***p<0.001

| Treatments compared | Figure ref. | p-Value |
|---|---|---|
| Vitamin E vs NGF + 0.6% DMSO | 4a | 0.8440 |
| (–) 13 vs DMSO | 4c | 0.3061 |
| (+) 13 vs DMSO | 4c | 0.4437 |
| (+) *t*-BG vs NGF + 0.6% DMSO | 4d | 0.0788 |
| (–) 10 vs DMSO | 6 | 0.4035 |
| (±) 18 vs DMSO | 6 | 0.3440 |

**Table S1**. p-Values for key treatment comparisons which were not statistically significant

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**Figure S4:** $^{1}$H NMR spectrum of compound **2a** ($CDCl_3$, 400 MHz)

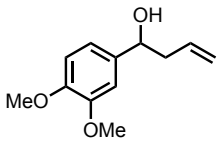
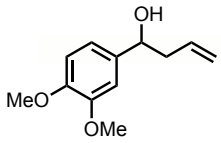


**Figure S5:** $^{13}C$ NMR spectrum of compound **2a** ($CDCl_3$, 176 MHz)



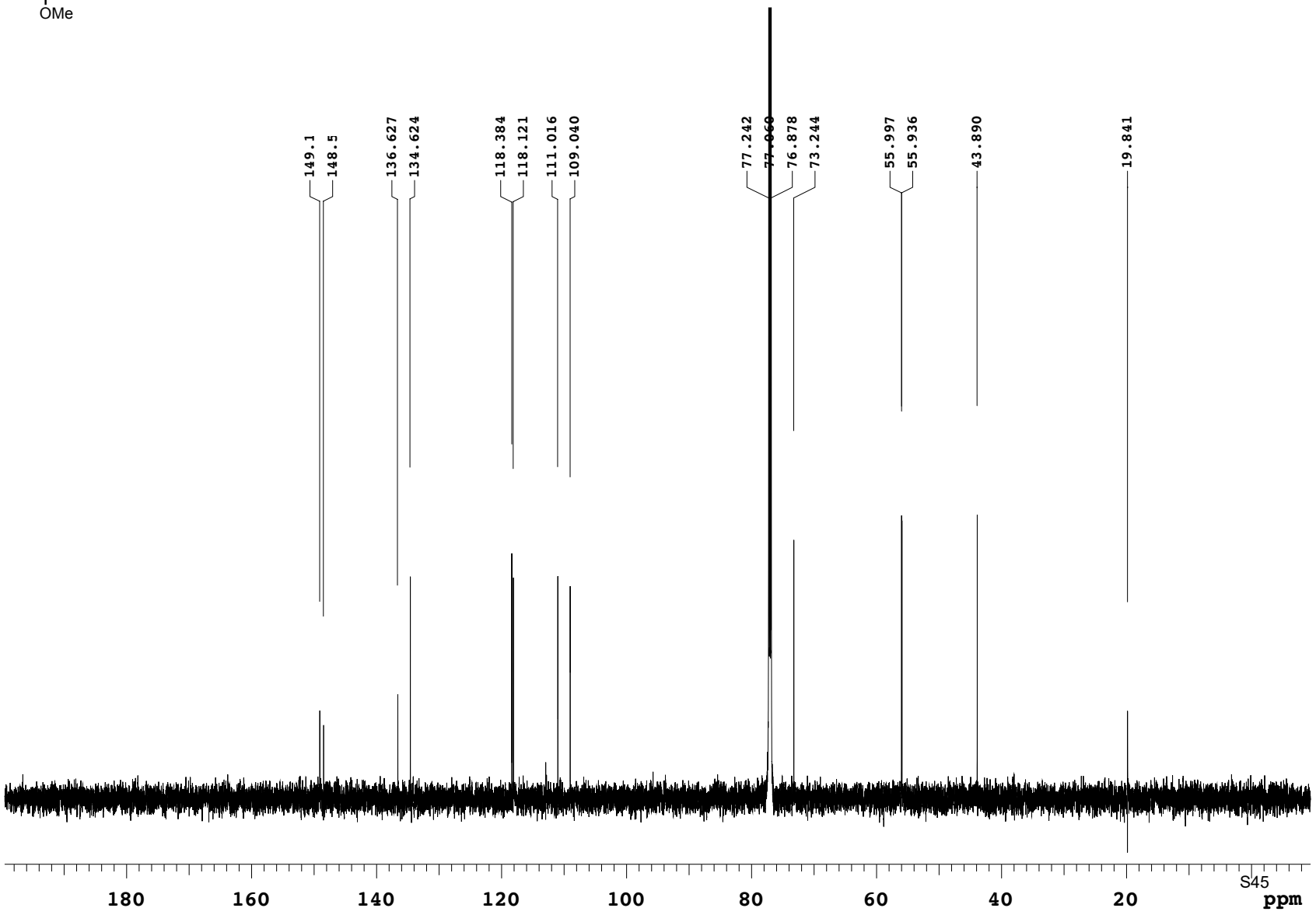
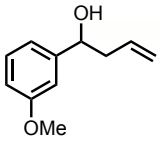



**Figure S6:** $^{1}H$ NMR spectrum of compound **2b** ($CDCl_3$, 400 MHz)




Recorded on: **mr400, Jul 11 2020** Sweep Width(Hz): **4807.69** Acquisiton Time(s): **5** Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** Digital Res.(Hz/pt): **0.07** Hz per mm(Hz/mm): **16.67** Completed Scans **16**

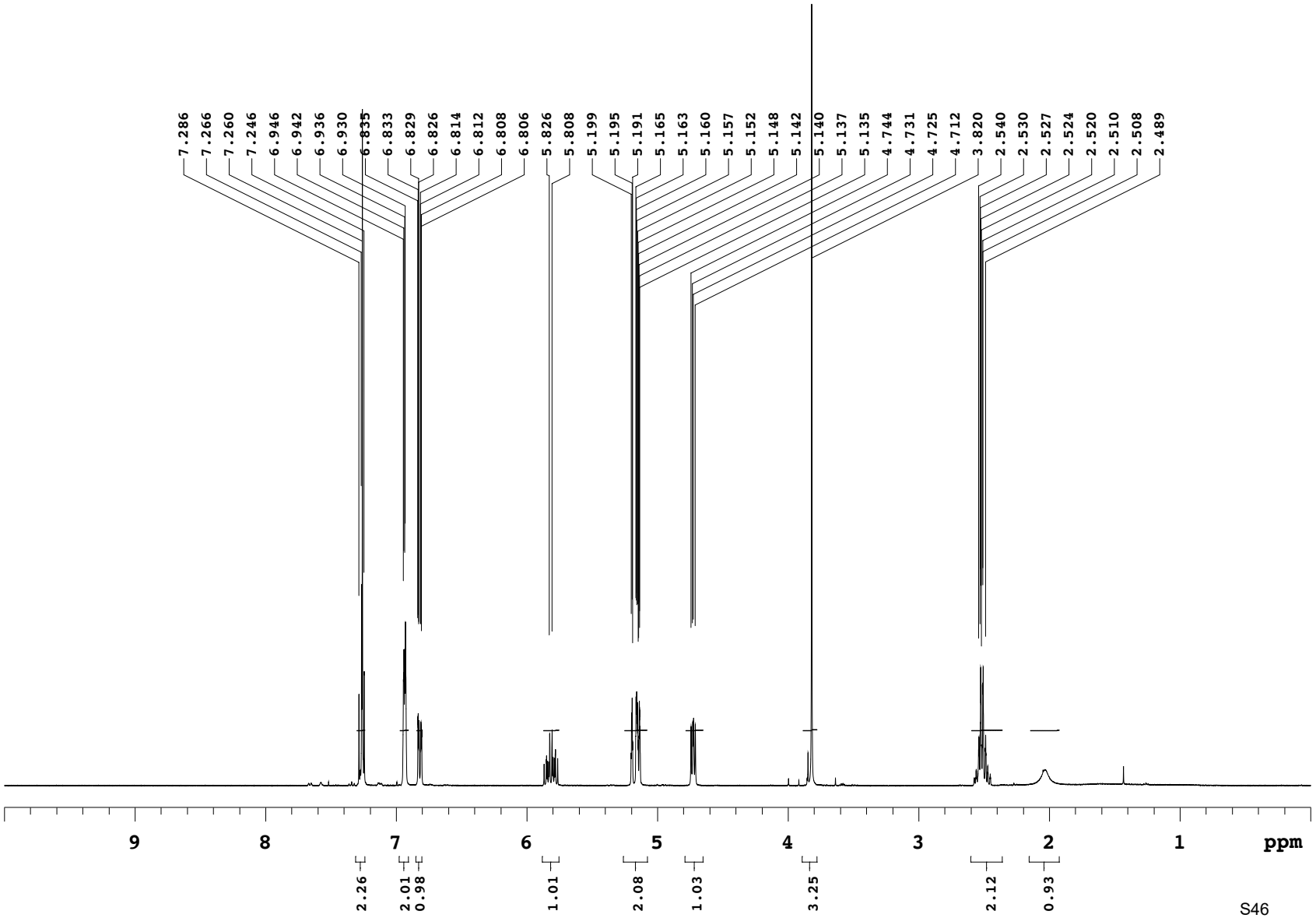
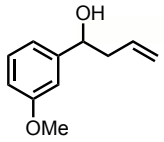


**Figure S7:** $^{13}C$ NMR spectrum of compound **2b** ($CDCl_3$, 176 MHz)



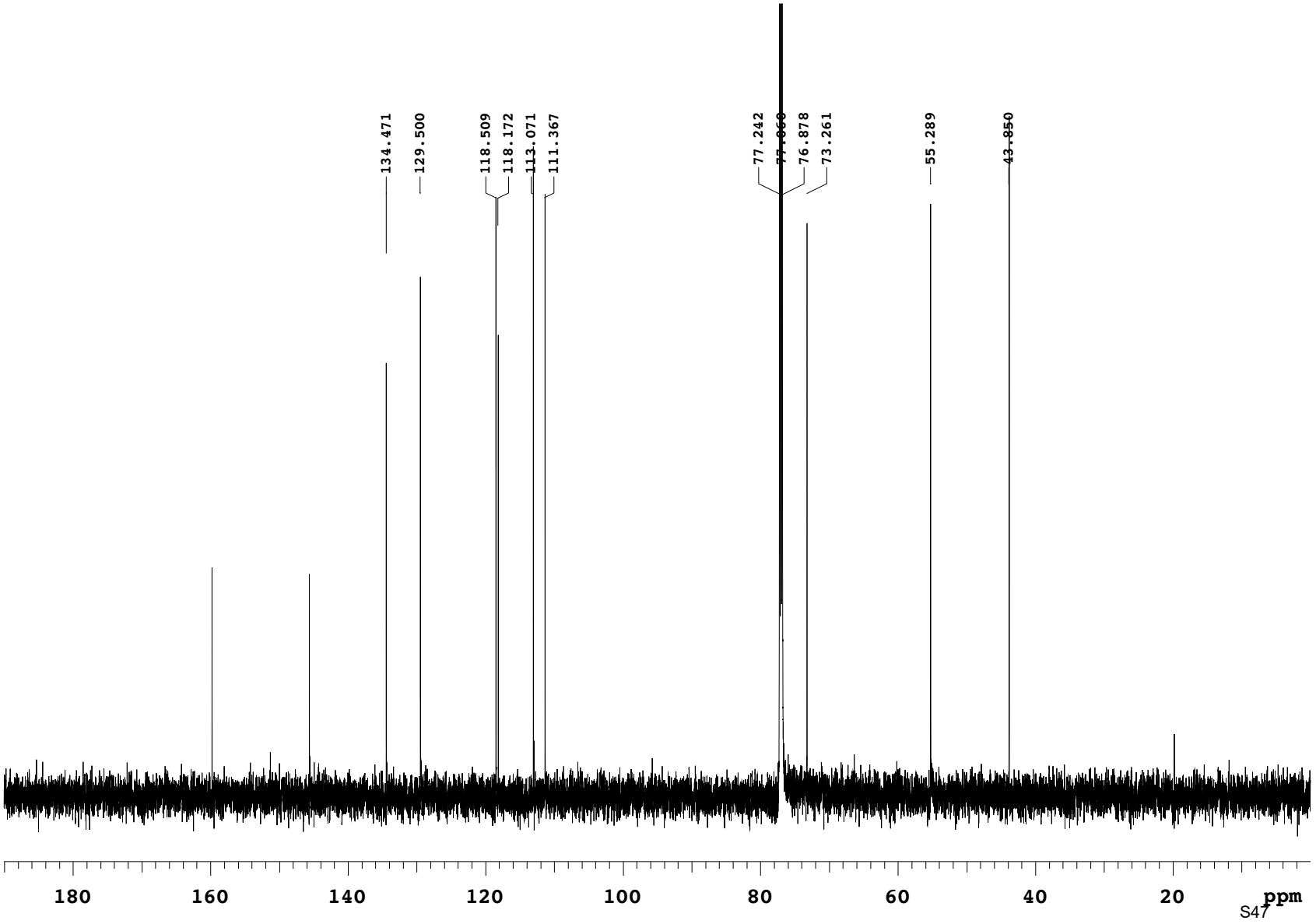
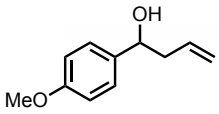



**Figure S8:** $^{1}H$ NMR spectrum of compound **2c** ($CDCl_3$, 700 MHz)



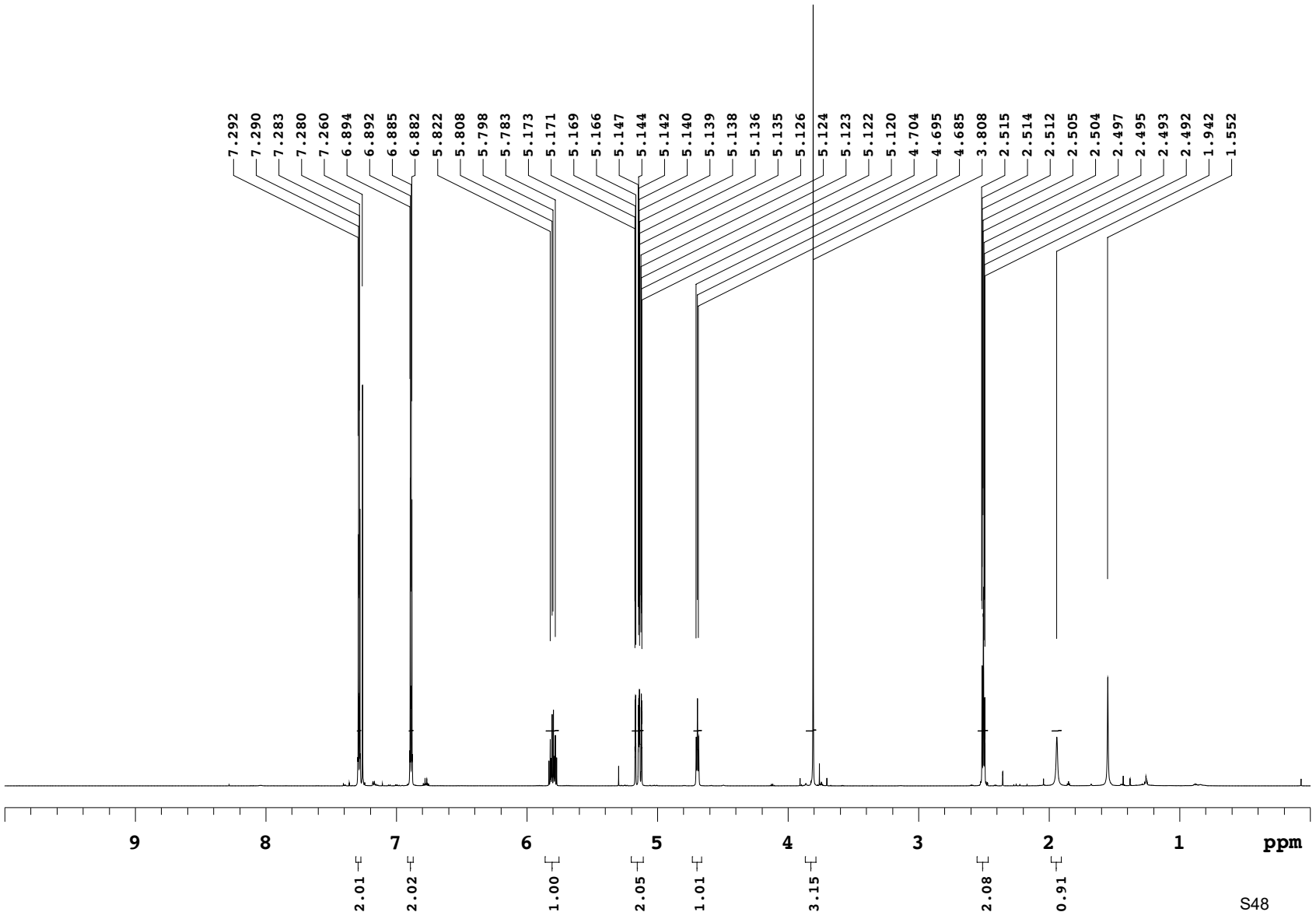
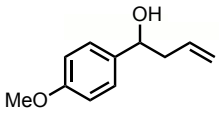



**Figure S9:** $^{13}C$ NMR spectrum of compound **2c** ($CDCl_3$, 176 MHz)



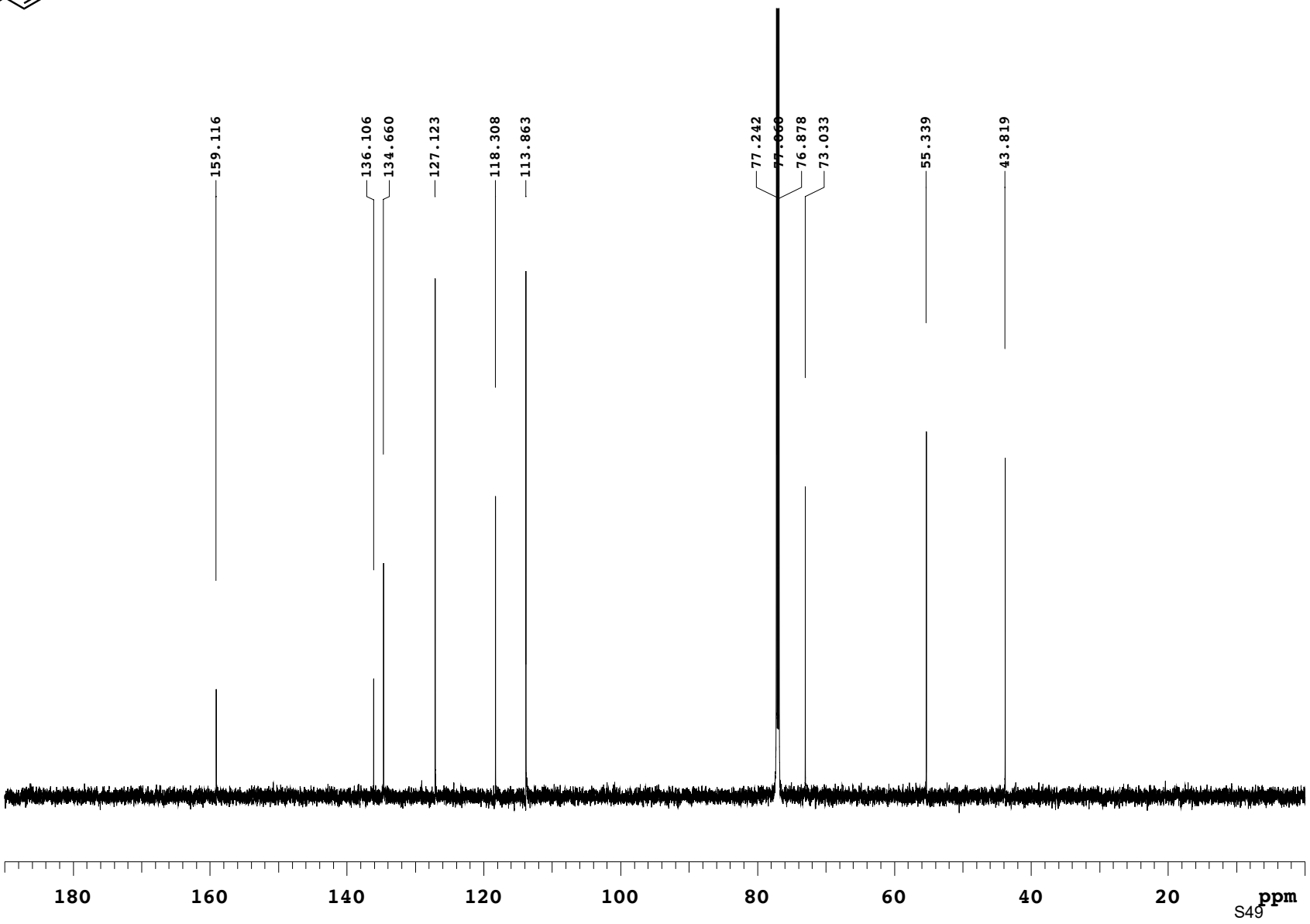



**Figure S10:** $^{1}$H NMR spectrum of compound **2d** ($CDCl_3$, 600 MHz)

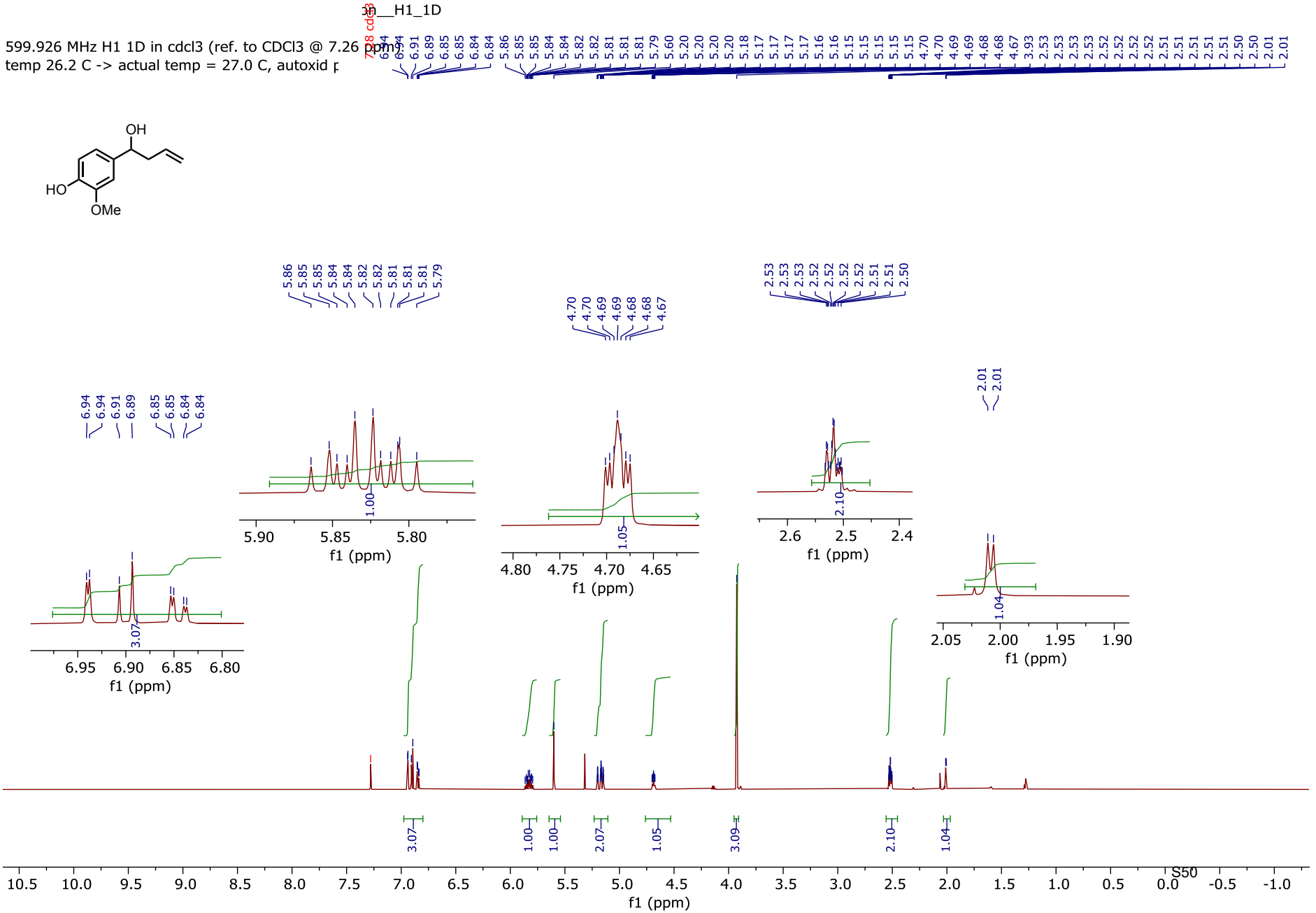


**Figure S11:** $^{13}C$ NMR spectrum of compound **2d** ($CDCl_3$, 126 MHz)

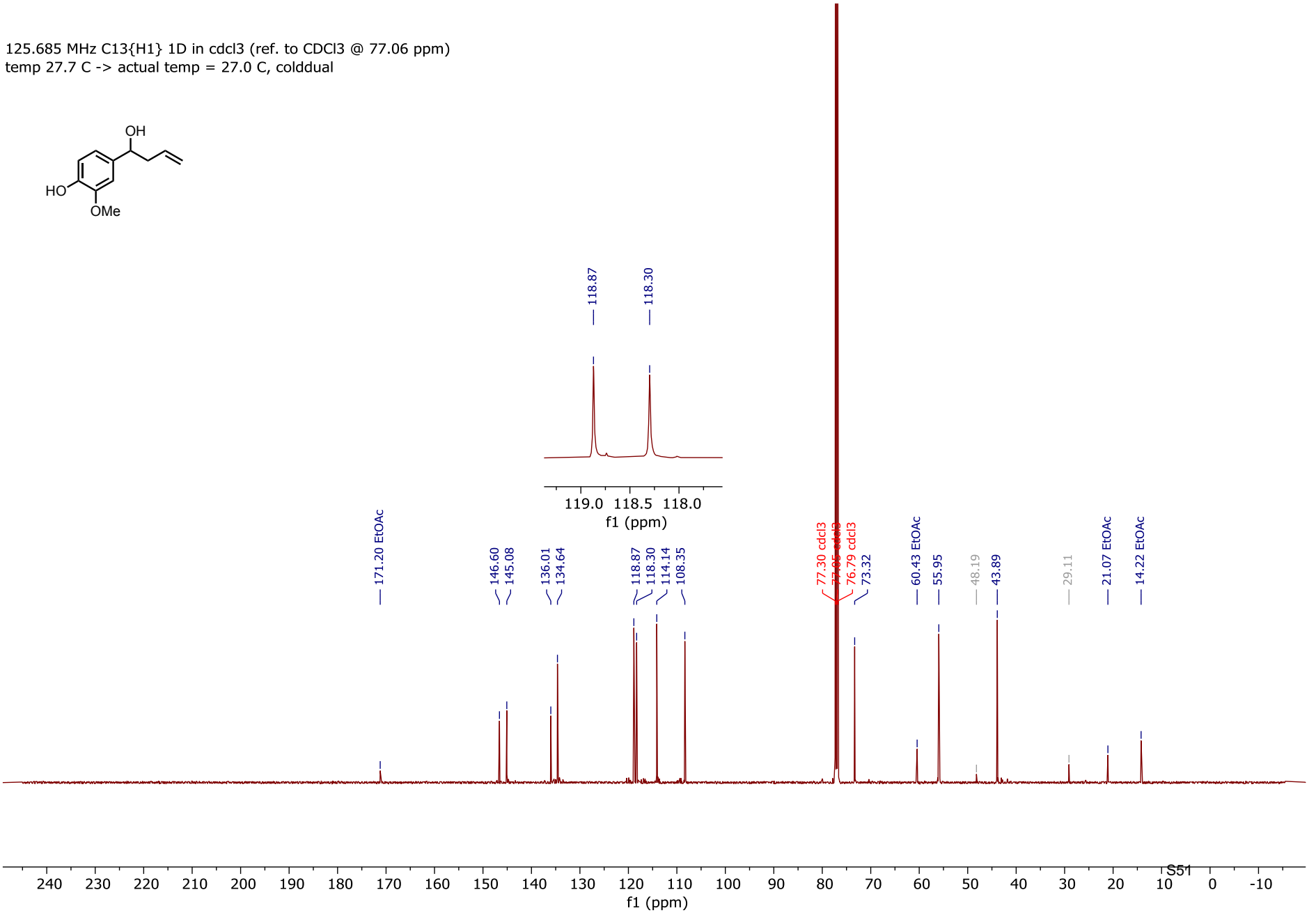
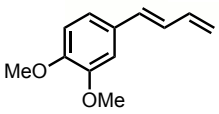


**Figure S12:** $^1$H NMR spectrum of compound **3a** ($CDCl_3$, 500 MHz)

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| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8** |

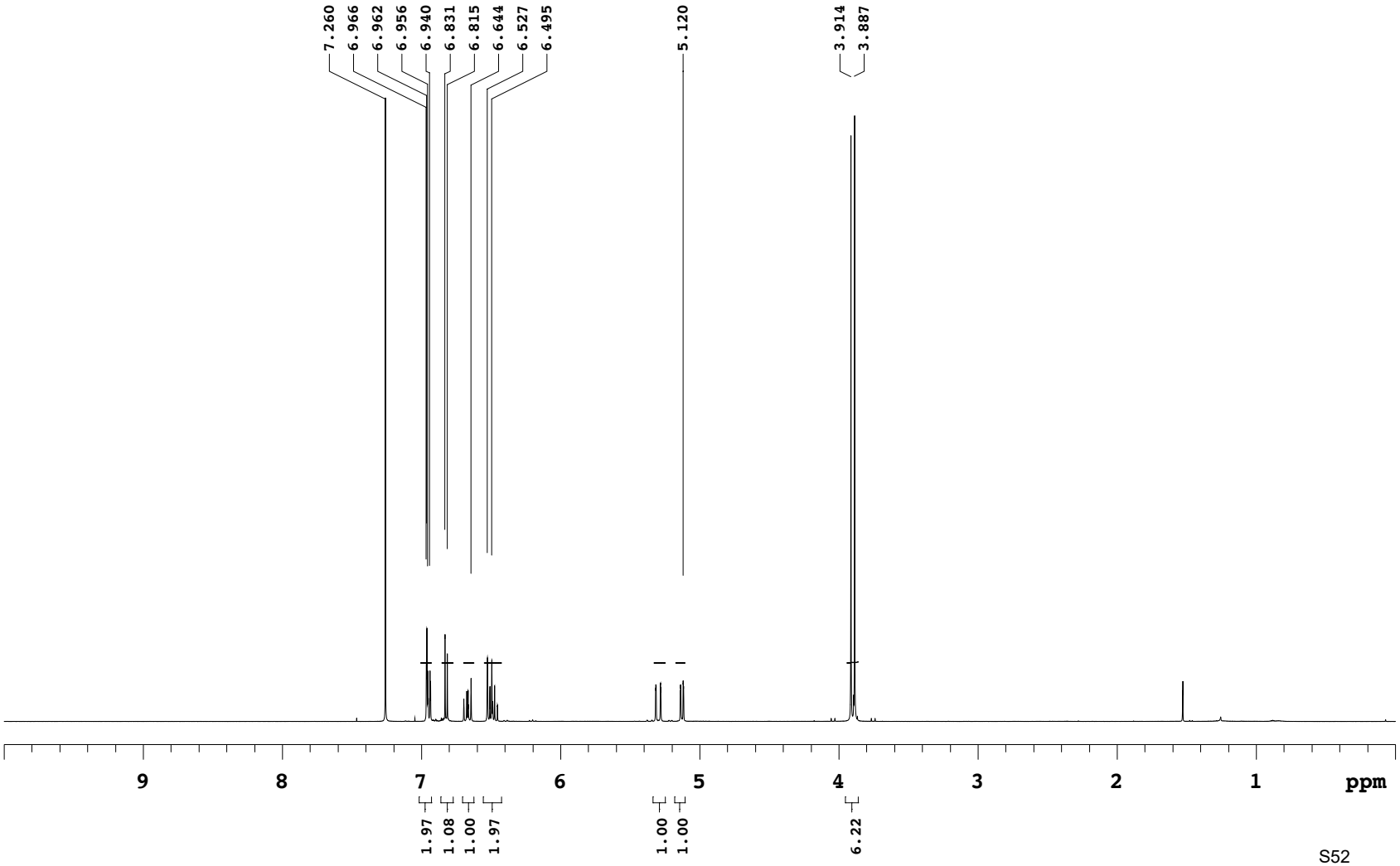
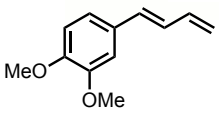


**Figure S13:** $^{13}C$ NMR spectrum of compound **3a** ($CDCl_3$, 126 MHz)




Recorded on: **u500, Jul 3 2018** | Sweep Width(Hz): **33783.8** | Acquisiton Time(s): **1** | Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.26** | Hz per mm(Hz/mm): **99.5** | Completed Scans **128**

149.141
149.007
137.300
132.690
130.319
127.940
119.900
116.703
111.243
108.741
77.314
77.060
76.806
55.989
55.886

180 160 140 120 100 80 60 40 20 ppm

**Figure S14:** $^{1}H$ NMR spectrum of compound **3c** ($CDCl_3$, 500 MHz)

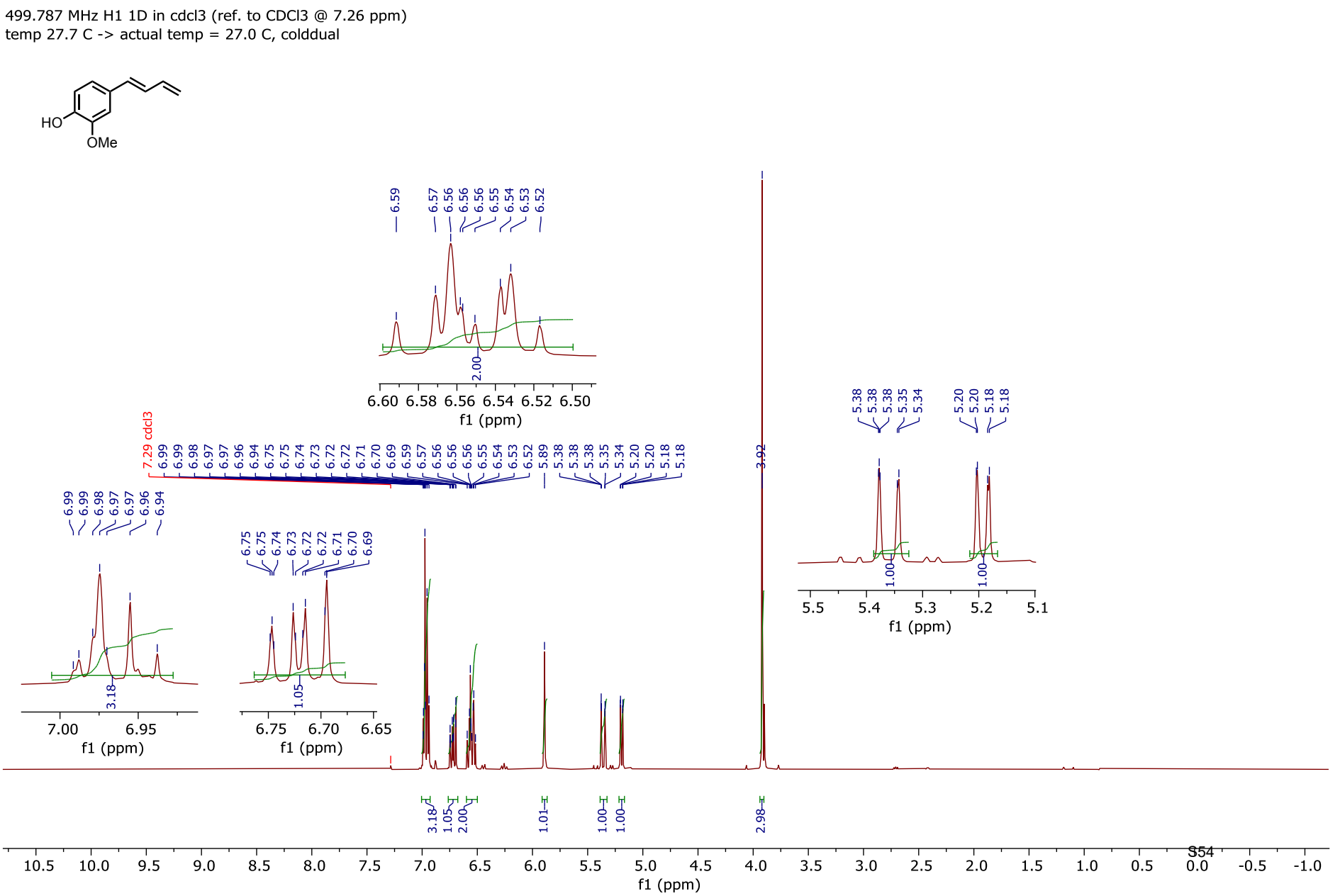


**Figure S15:** $^{13}C$ NMR spectrum of compound **3c** ($CDCl_3$, 126 MHz)

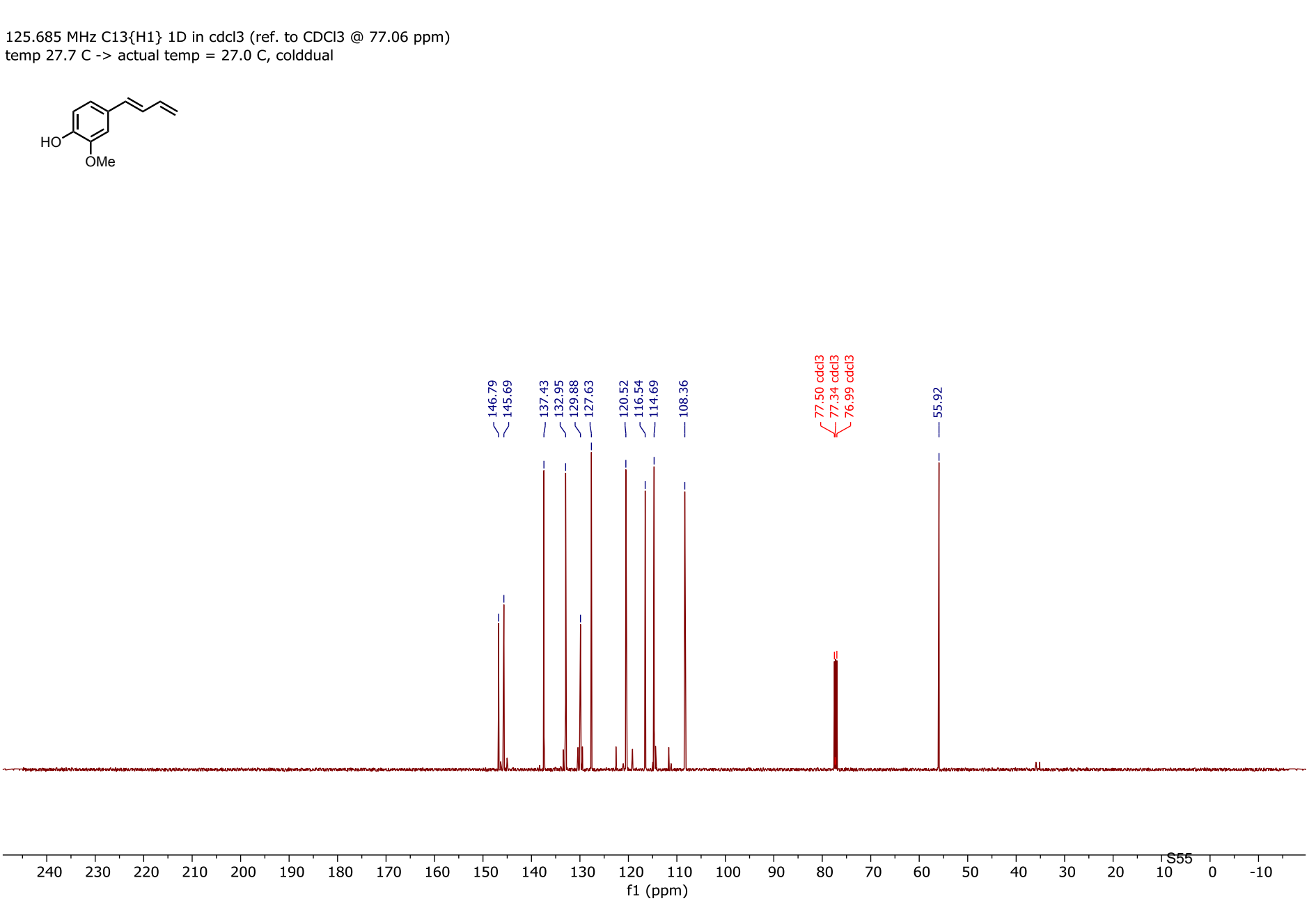
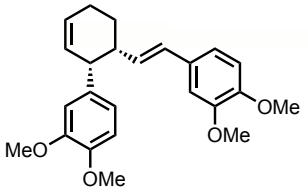


**Figure S16:** $^{1}$H NMR spectrum of compound ***c*–BG** ($CDCl_3$, 700 MHz)



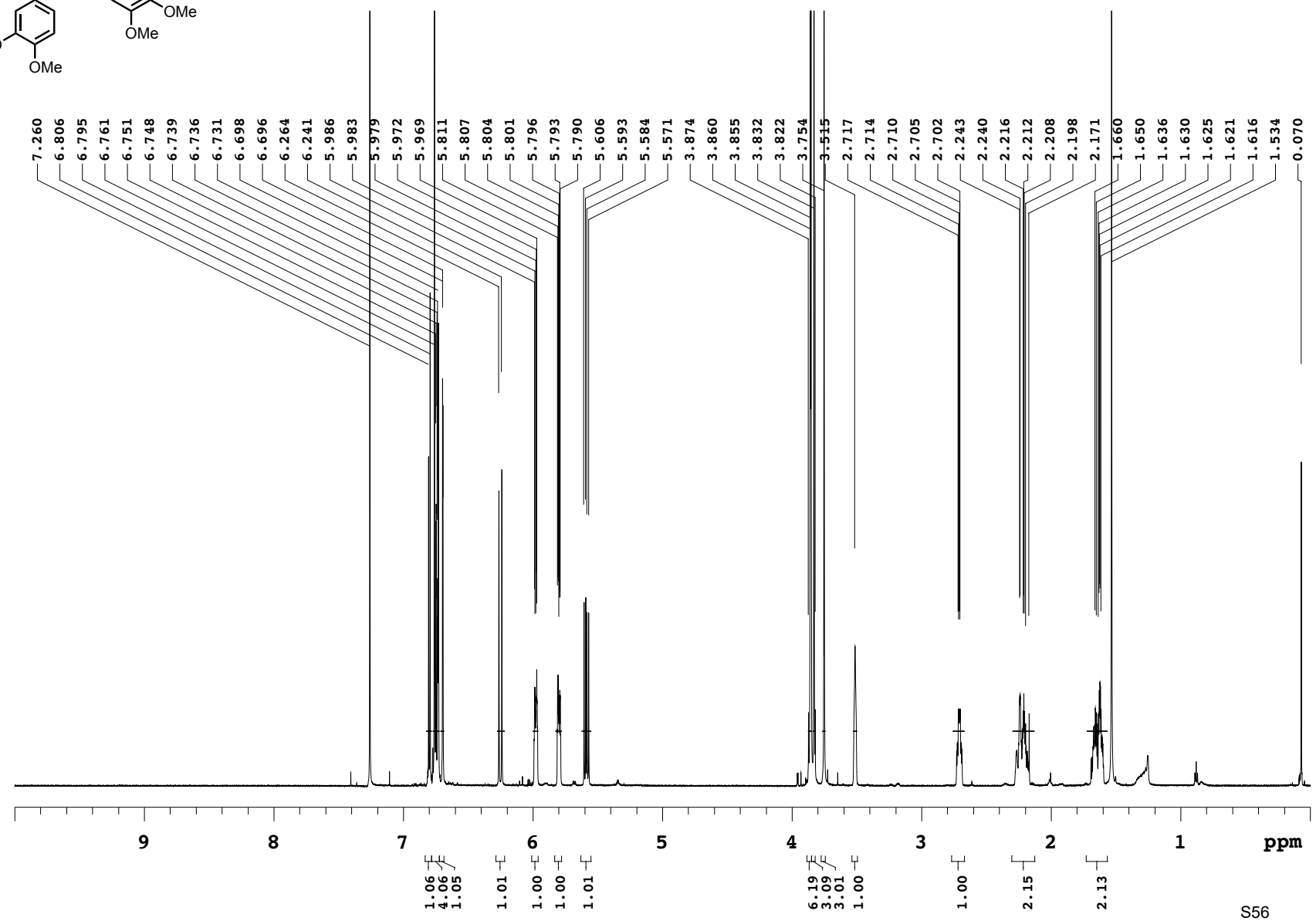
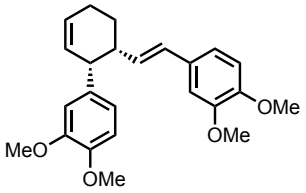



**Figure S17:** $^1$H NMR magnified spectrum of compound ***c*–BG** ($CDCl_3$, 700 MHz)

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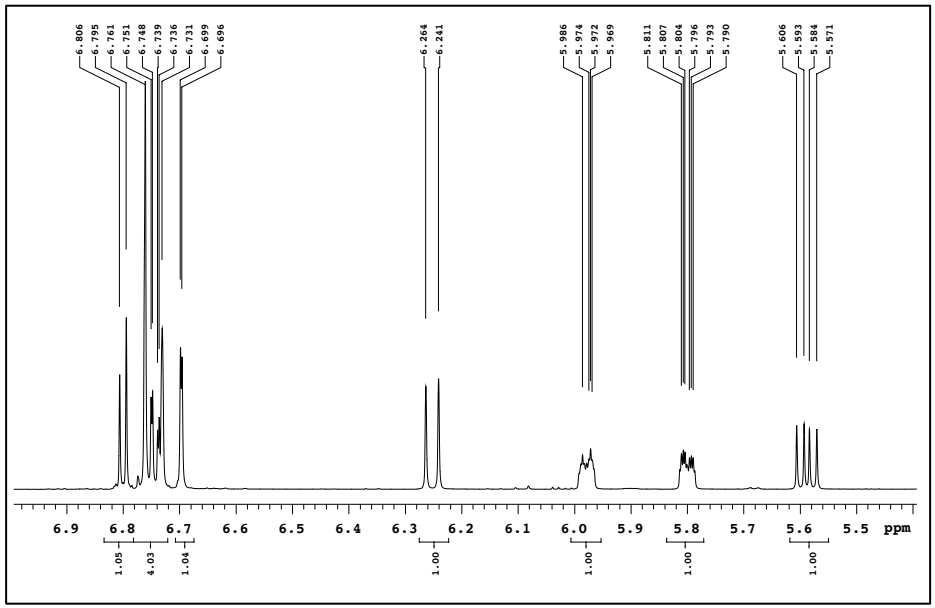
|---|---|---|---|
| Recorded on: **v700, Nov 1 2019** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



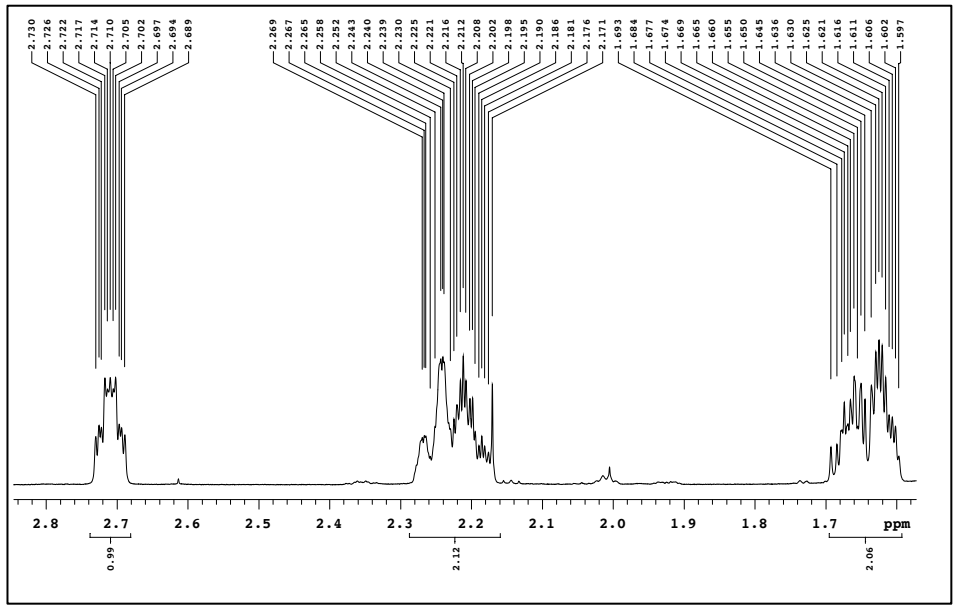
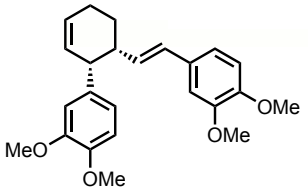



**Figure S18:** $^{13}C$ NMR spectrum of compound ***c*–BG** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Nov 1 2019** Sweep Width(Hz): **36764.7** Acquisiton Time(s): **1** Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** Digital Res.(Hz/pt): **0.28** Hz per mm(Hz/mm): **117.28** Completed Scans **256**

148.996 148.164 147.576 133.871 132.518 131.133 129.202 128.561 128.094 122.006 118.789 113.658 111.225 110.415 108.761 77.242 77.060 76.878 55.981 55.925 55.828 45.804 42.675 24.859 24.366

150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

**Figure S19:** $^{1}$H NMR spectrum of compound ***t*–BG** ($CDCl_3$, 700 MHz)

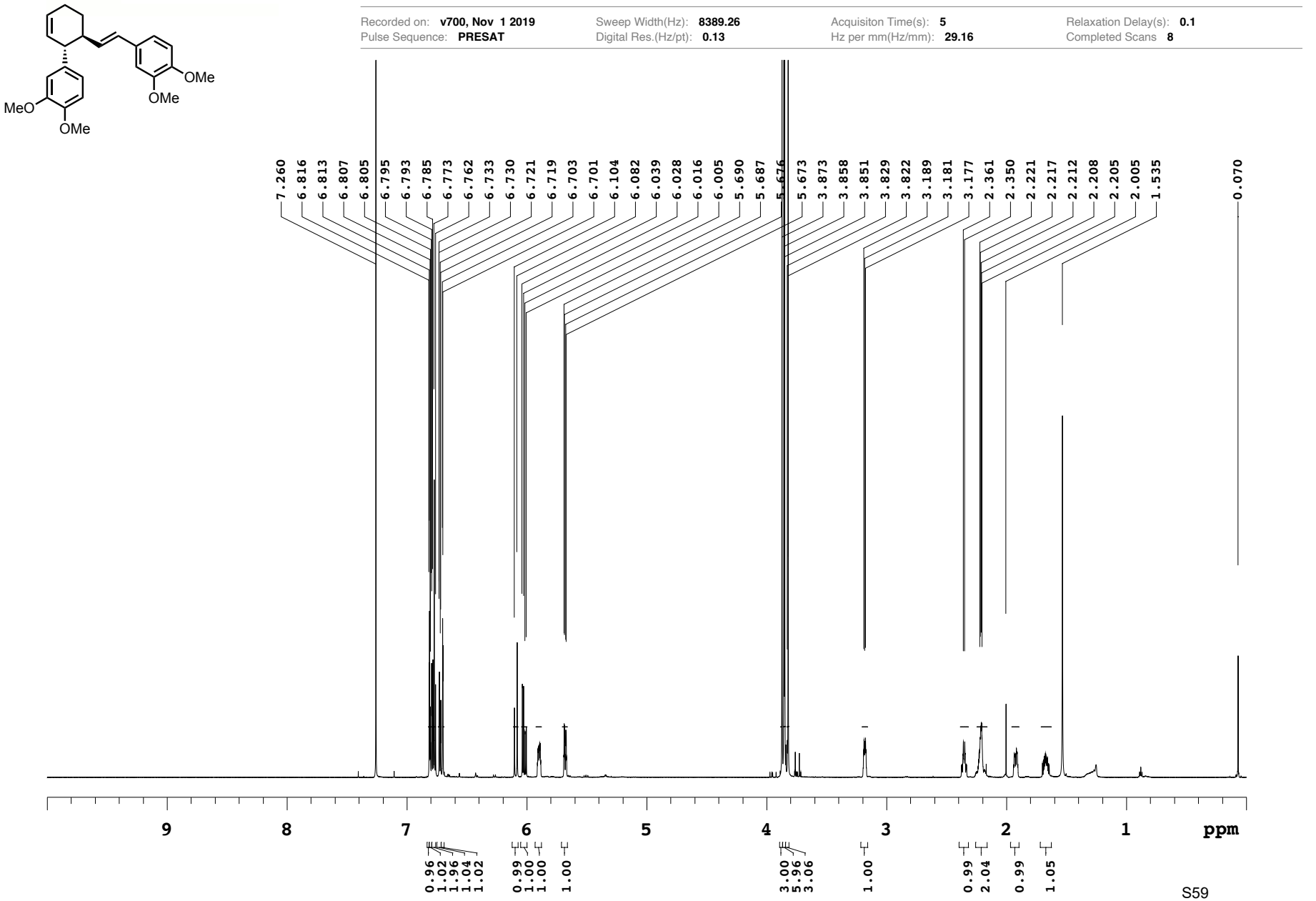
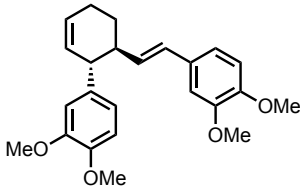
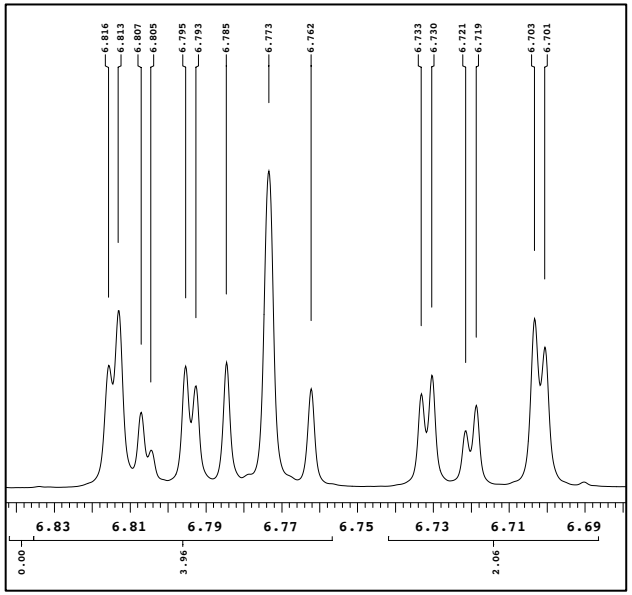


**Figure S20:** $^1$H NMR magnified spectrum of compound ***t*–BG** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Nov 1 2019** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



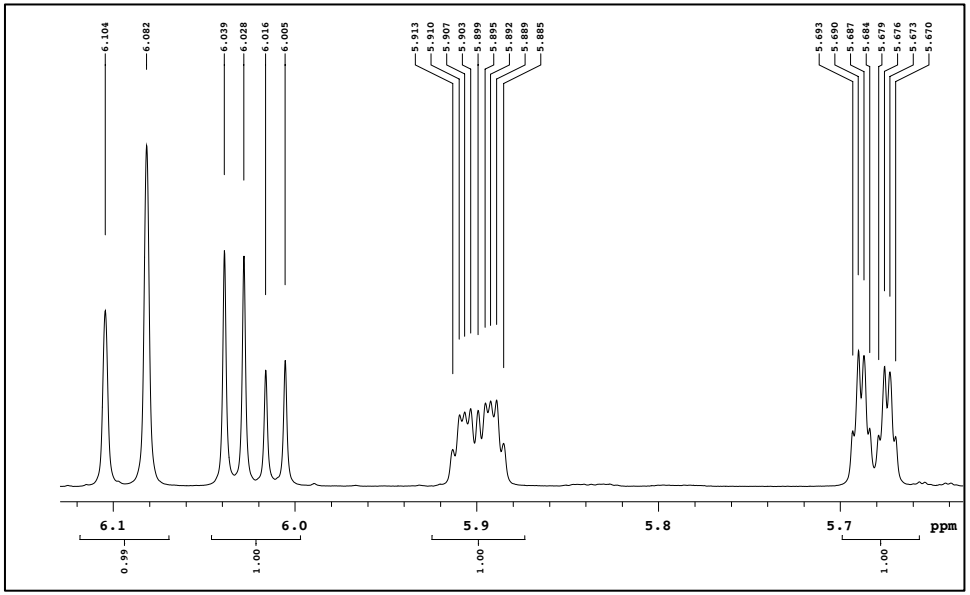
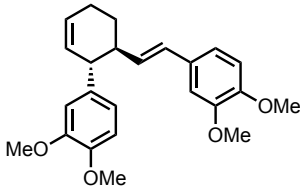
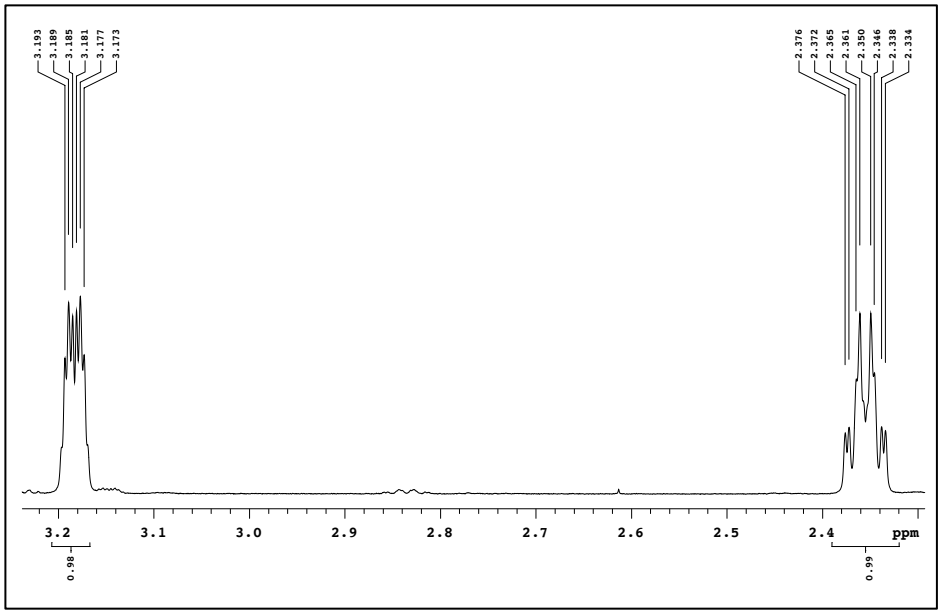



**Figure S21:** $^1$H NMR magnified spectrum of compound ***t*–BG** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Nov 1 2019** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



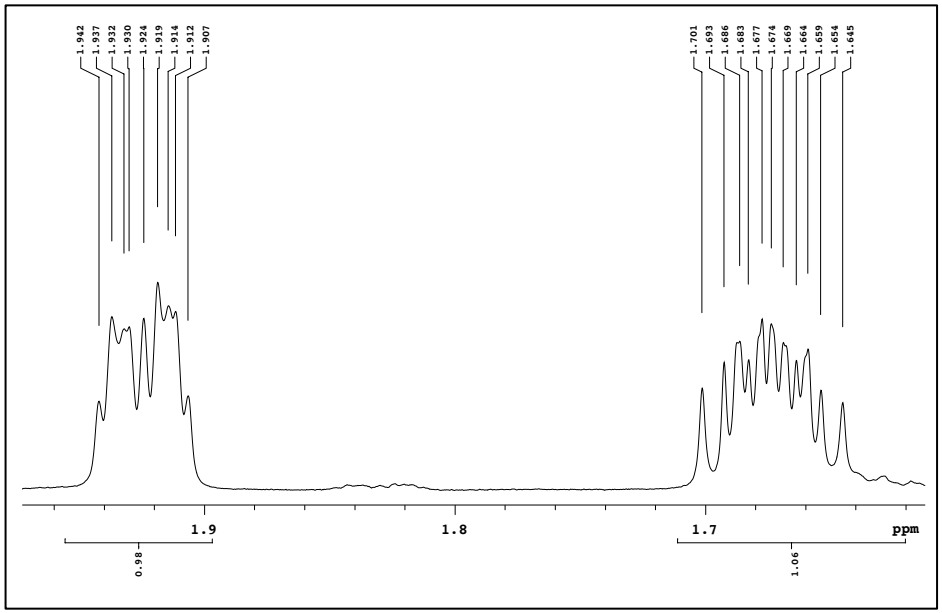



**Figure S22:** $^{13}C$ NMR spectrum of compound ***t*–BG** ($CDCl_3$, 176 MHz)

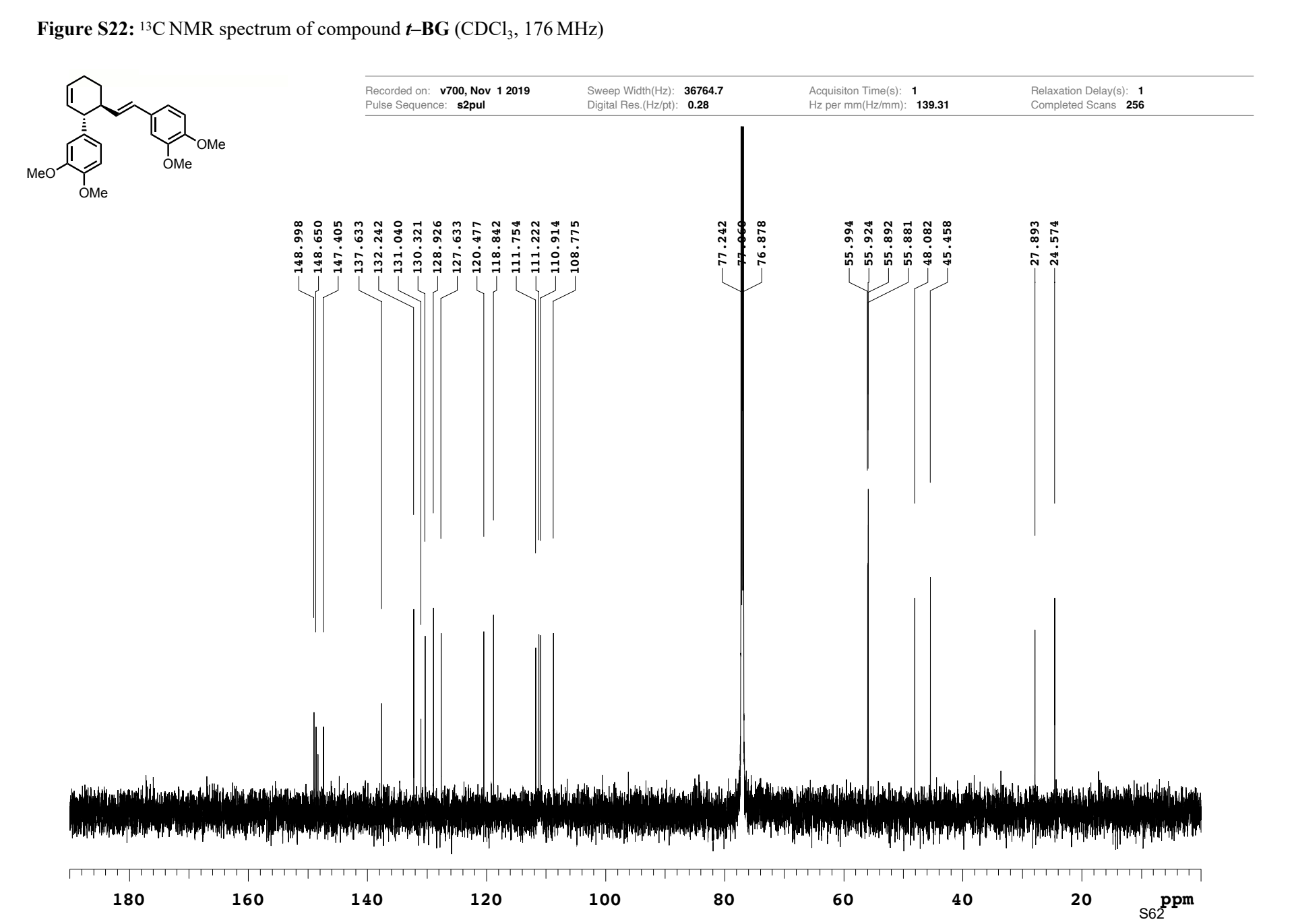


**Figure S23:** $^1$H NMR spectrum of compound **5a** ($CDCl_3$, 500 MHz)

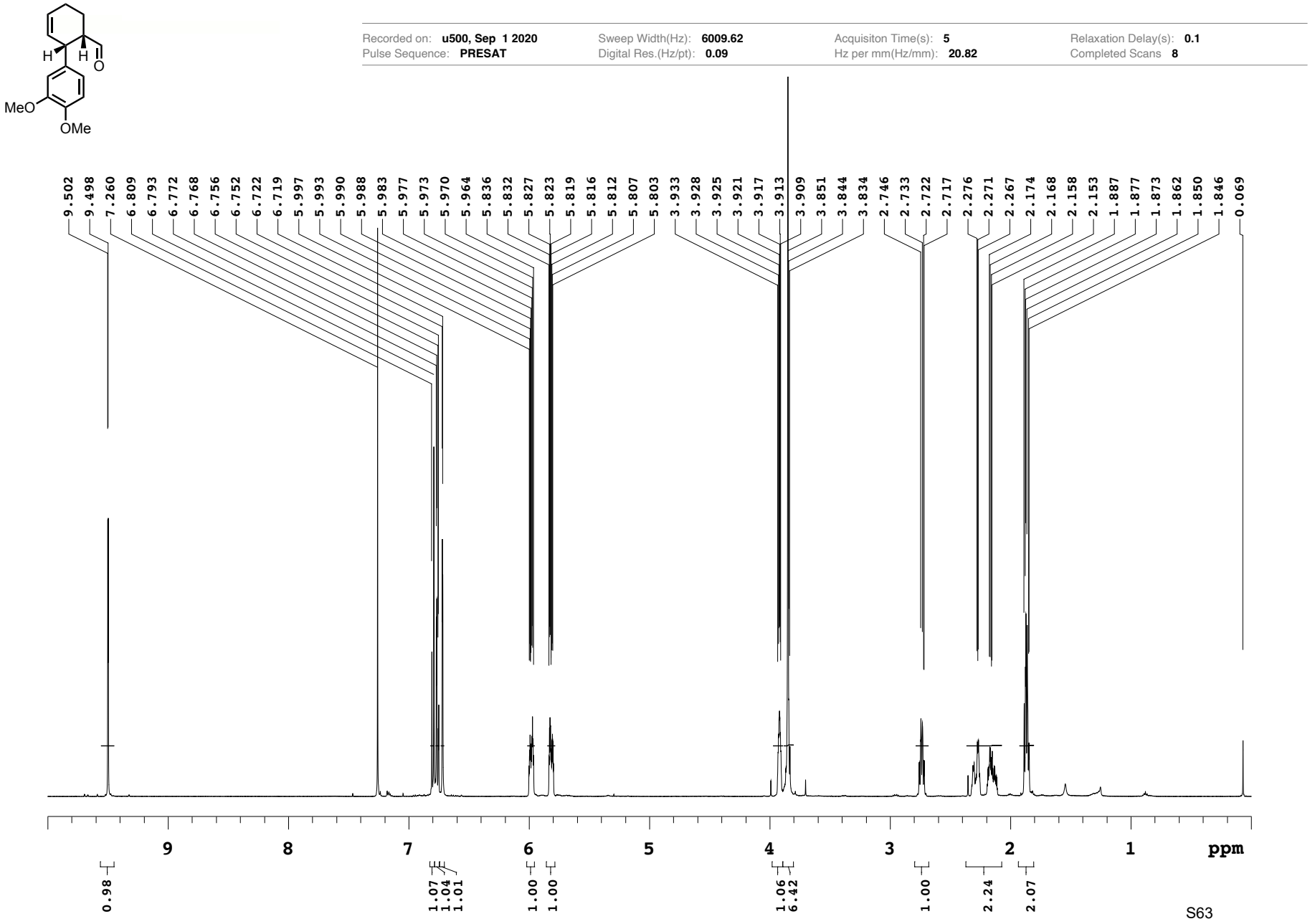
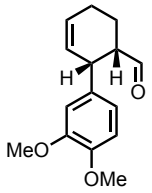
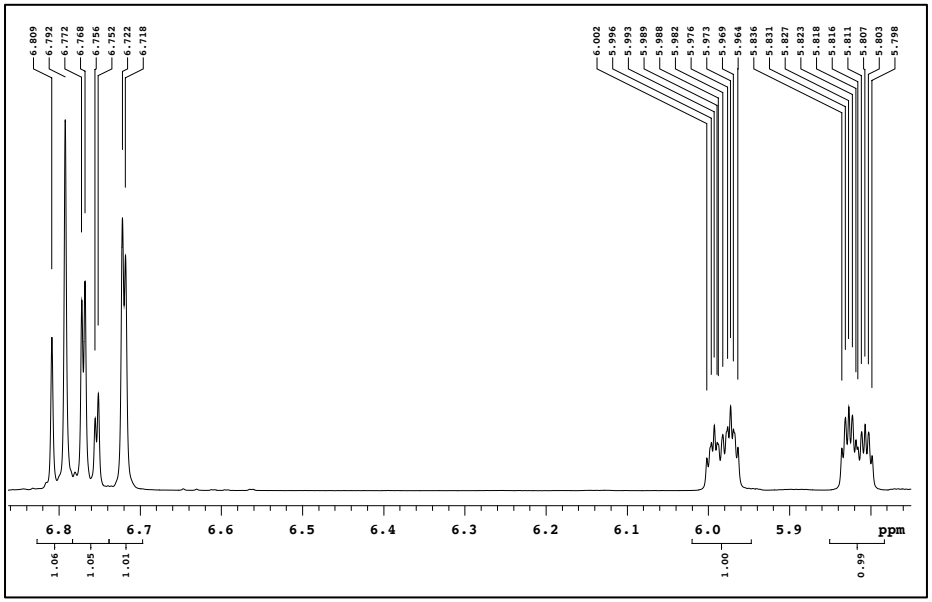


**Figure S24:** $^1$H NMR magnified spectrum of compound **5a** ($CDCl_3$, 500 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **u500, Sep 1 2020** | Sweep Width(Hz): **6009.62** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8** |



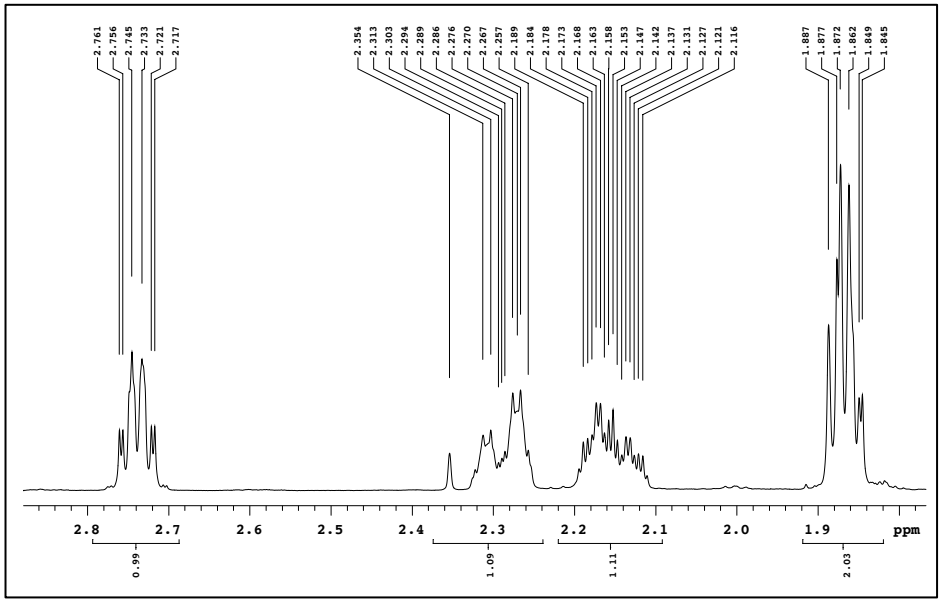
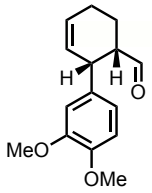



**Figure S25:** $^{13}C$ NMR spectrum of compound **5a** ($CDCl_3$, 126 MHz)

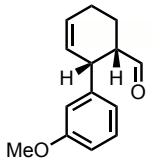



Recorded on: u500, Sep 1 2020 | Sweep Width(Hz): 33783.8 | Acquisiton Time(s): 1 | Relaxation Delay(s): 1
Pulse Sequence: s2pul | Digital Res.(Hz/pt): 0.26 | Hz per mm(Hz/mm): 125.69 | Completed Scans 128

121.417
77.314
77.060
76.806
55.935
50.902
23.648

220 200 180 160 140 120 100 80 60 40 20 ppm

**Figure S26:** $^1$H NMR spectrum of compound **5b** ($CDCl_3$, 500 MHz)



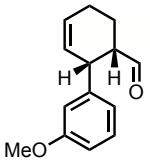

Recorded on: **u500, Jul 17 2020** Sweep Width(Hz): **6009.62** Acquisiton Time(s): **5** Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** Digital Res.(Hz/pt): **0.09** Hz per mm(Hz/mm): **20.82** Completed Scans **8**

9.514 9.510 7.260 7.232 7.216 7.199 6.814 6.798 6.774 6.762 5.998 5.994 5.988 5.982 5.978 5.974 5.970 5.840 5.836 5.831 5.827 5.820 5.816 5.812 3.944 3.785 2.768 2.764 2.758 2.753 2.749 2.273 2.264 2.172 2.167 2.156 2.151 1.903 1.891 1.885 1.874 1.868 1.858 1.544 0.071

9 8 7 6 5 4 3 2 1 ppm

0.96 1.02 1.02 1.99 1.00 1.00 1.02 3.16 1.00 1.05 1.10 2.07

**Figure S27:** $^{13}C$ NMR spectrum of compound **5b** ($CDCl_3$, 176 MHz)



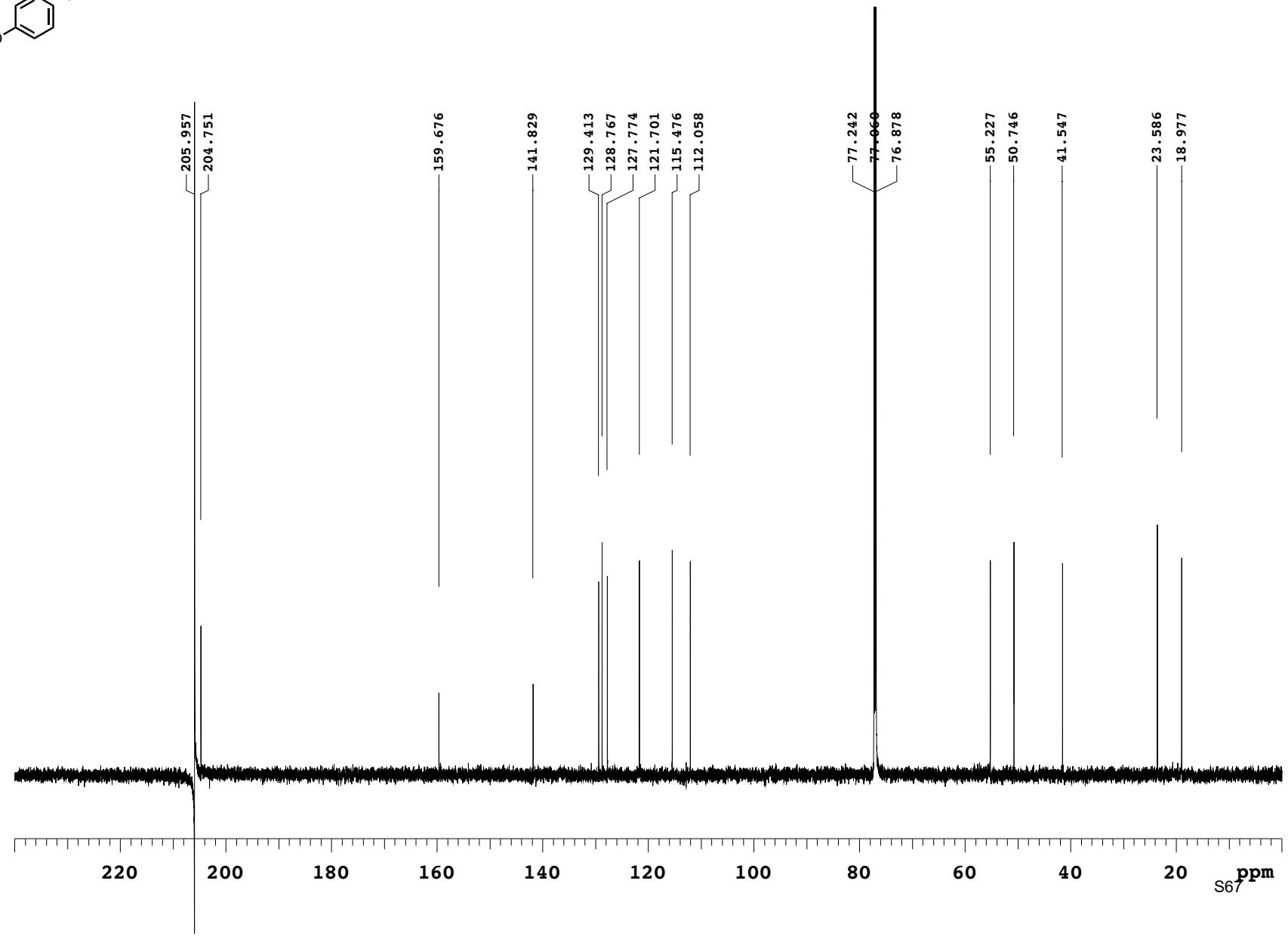



**Figure S28:** $^{1}$H NMR spectrum of compound **5c** ($CDCl_3$, 700 MHz)

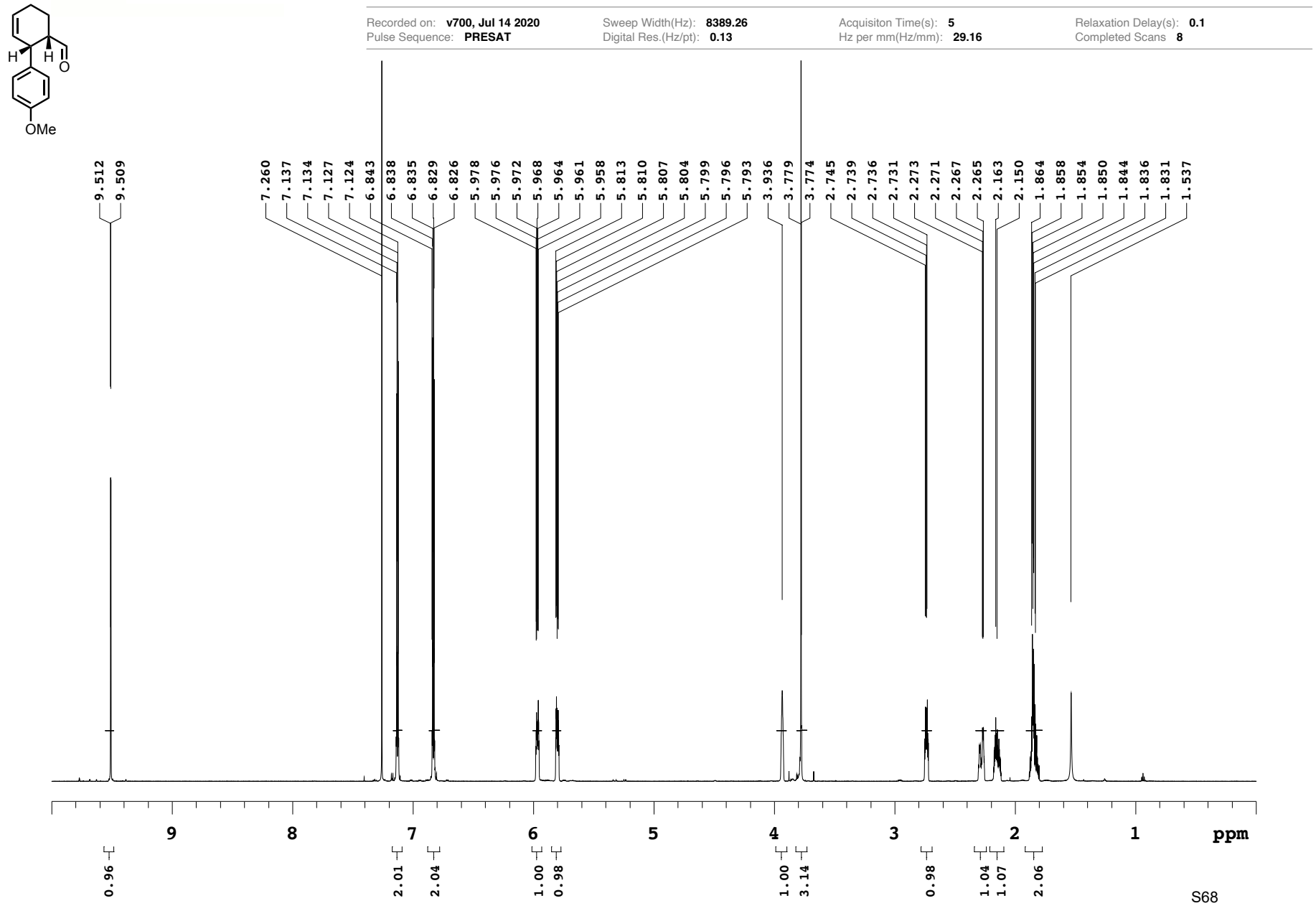


**Figure S29:** $^{13}C$ NMR spectrum of compound **5c** ($CDCl_3$, 176 MHz)

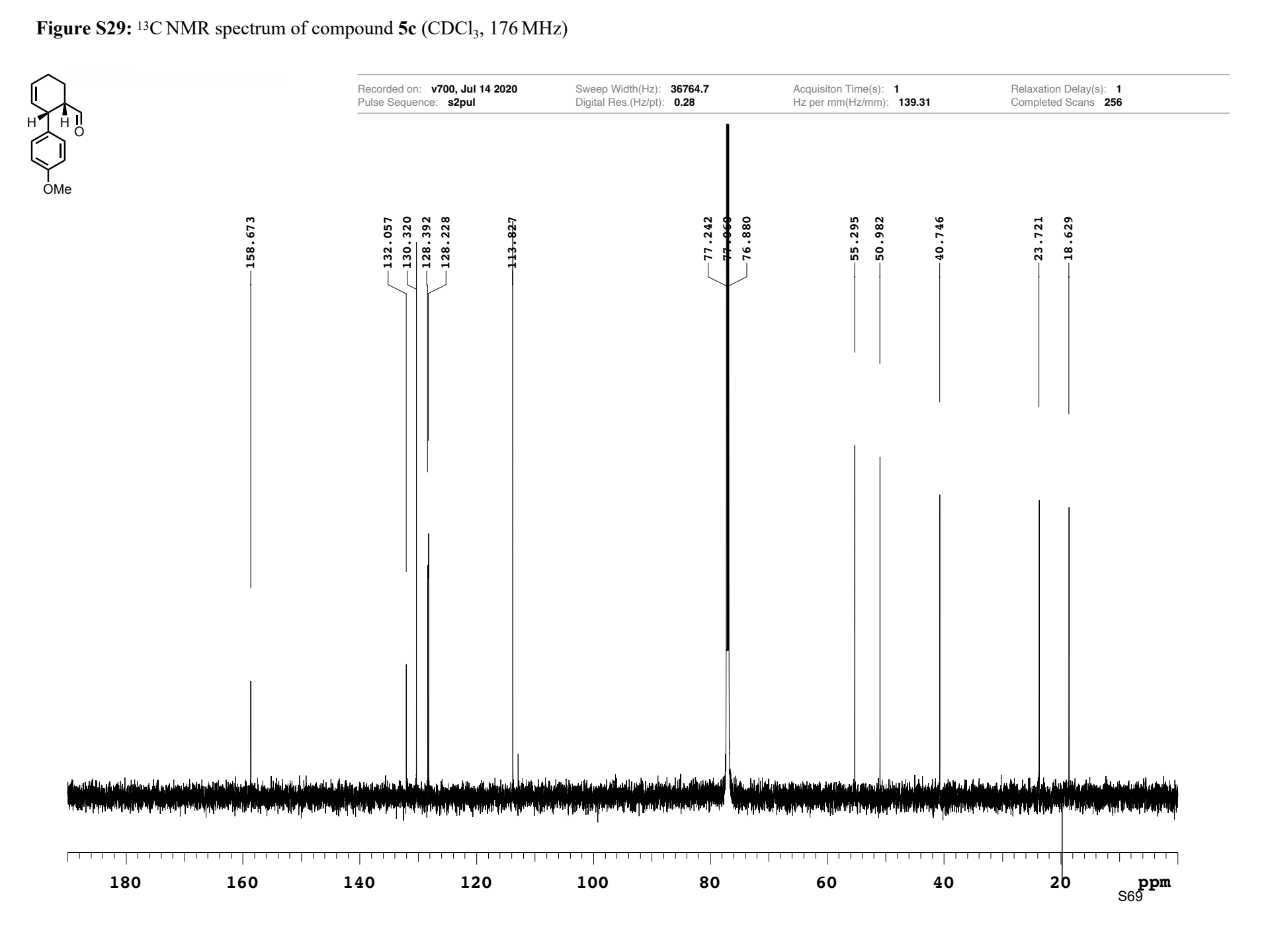


**Figure S30:** $^{1}$H NMR spectrum of compound **5d** ($CDCl_3$, 500 MHz)

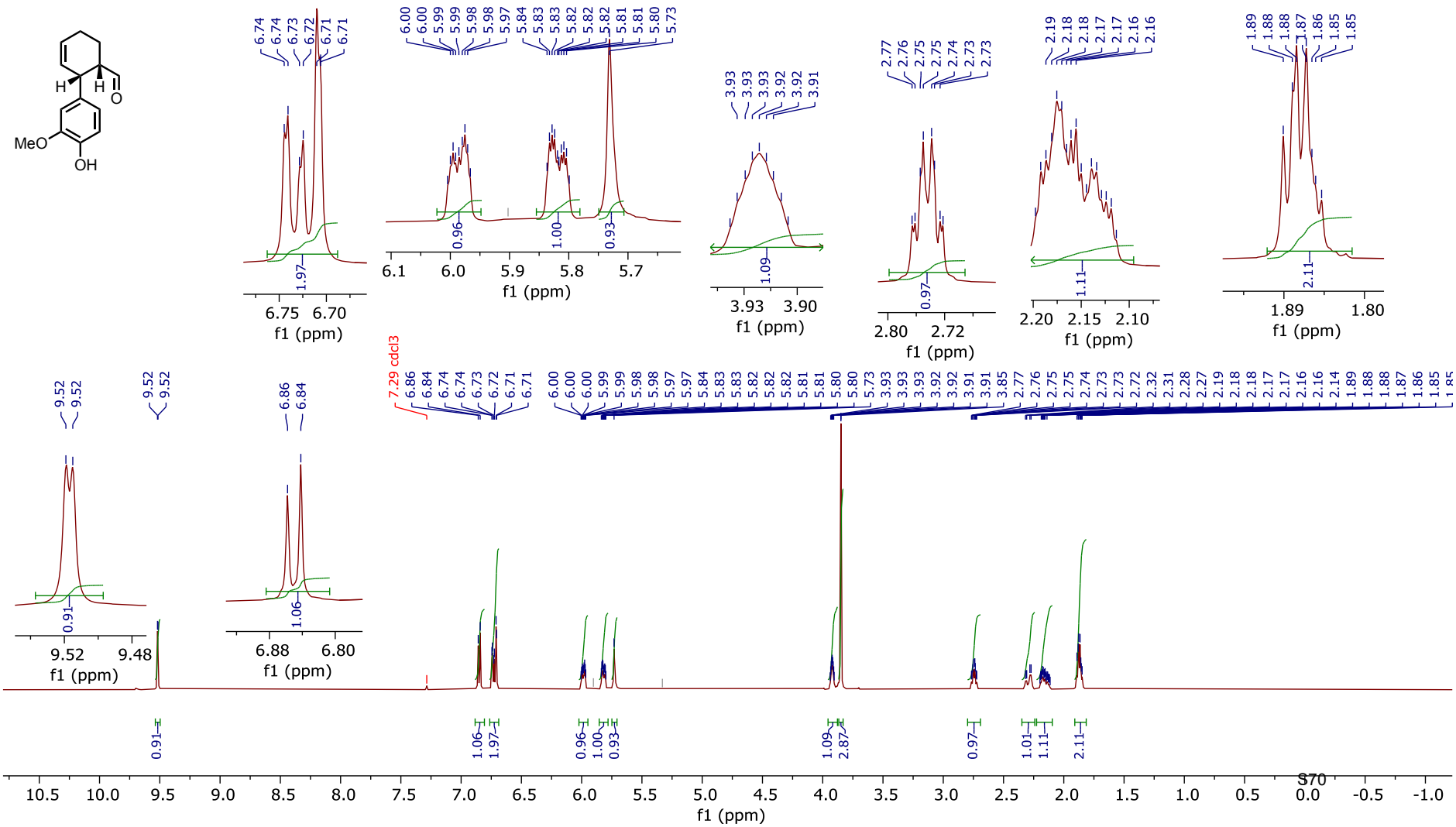


**Figure S31:** $^{13}C$ NMR spectrum of compound **5d** ($CDCl_3$, 126 MHz)

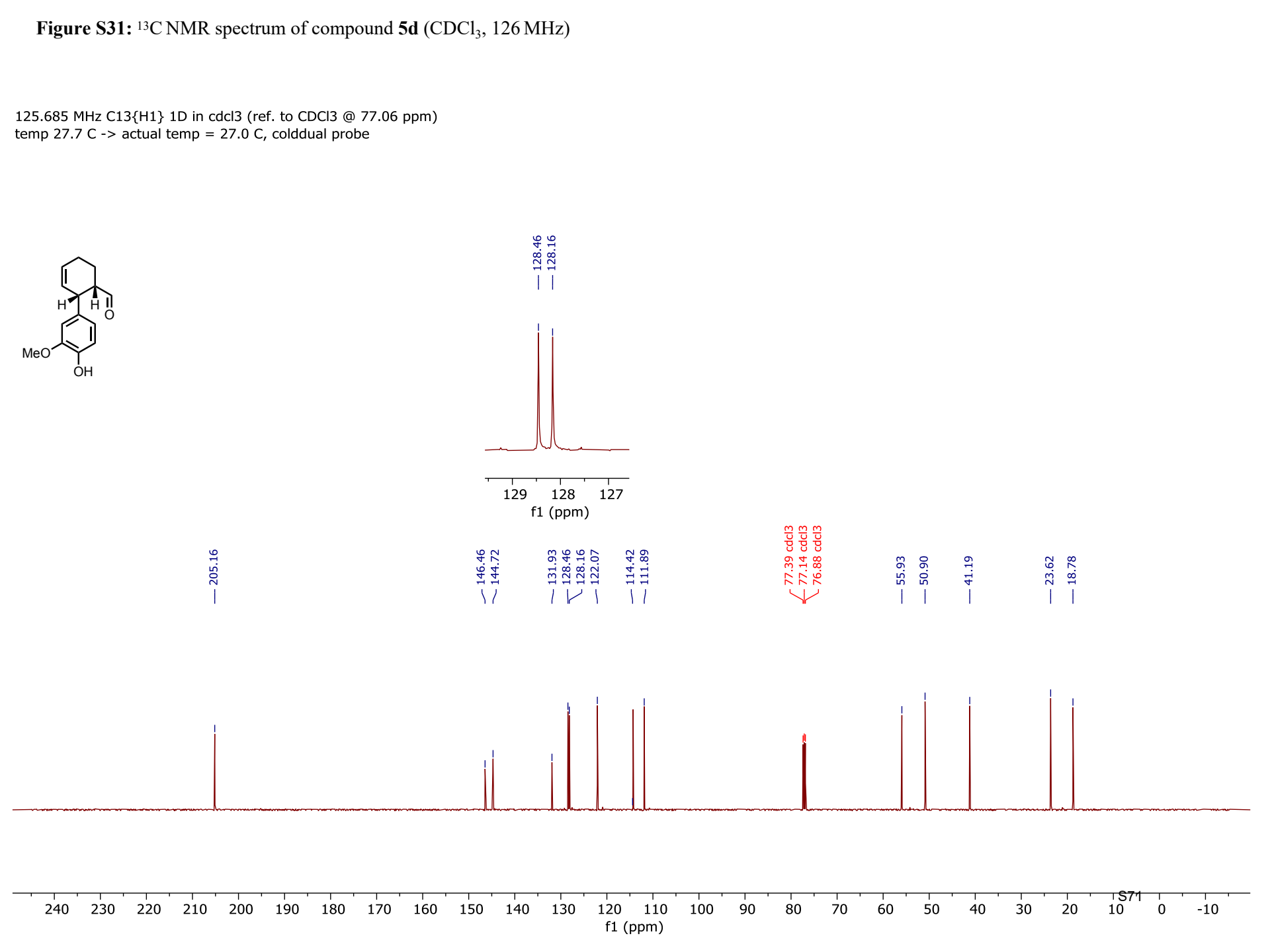
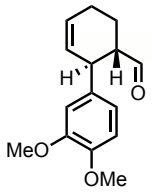


**Figure S32:** $^1$H NMR spectrum of compound **6a** ($CDCl_3$, 500 MHz)



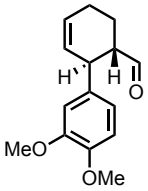

Recorded on: **u500, Sep 1 2020** | Sweep Width(Hz): **6009.62** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8**

9.692 7.260 6.814 6.797 6.791 6.774 6.762 6.758 6.739 6.721 6.717 5.903 5.898 5.890 5.883 5.878 5.695 5.691 5.685 5.681 5.671 5.665 3.867 3.856 3.849 3.766 3.743 3.727 3.721 3.716 3.712 3.707 3.701 2.593 2.585 2.578 2.571 2.563 2.200 2.195 2.190 2.185 2.180 2.174 2.169 2.163 1.972 1.965 1.956 1.949 1.945 1.939 1.774 1.768 1.759 1.748 1.740

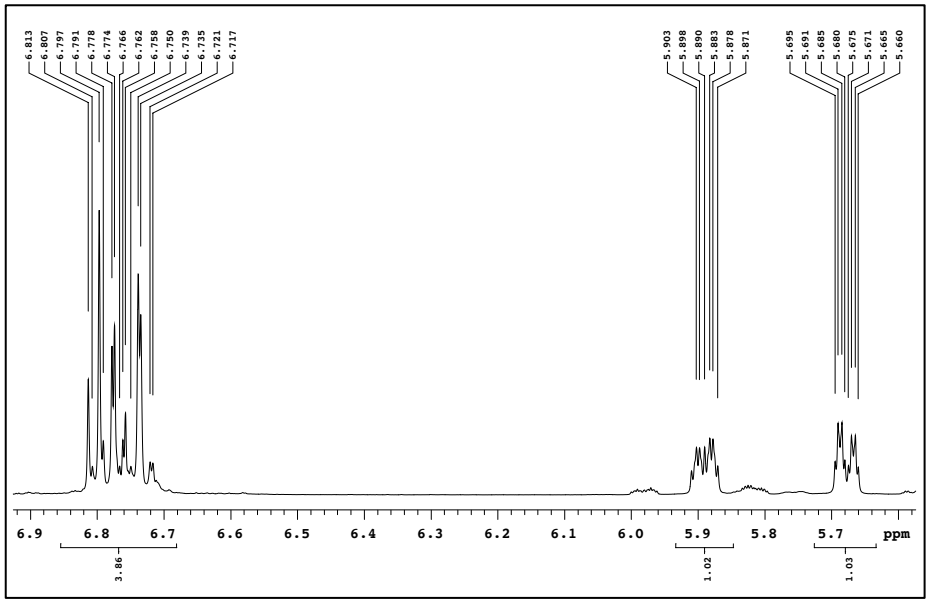
9 8 7 6 5 4 3 2 1 ppm

0.94 0.10 3.81 0.11 1.00 0.20 1.01 0.14 7.80 1.61 0.15 1.01 2.52 1.13 0.28 1.23

**Figure S33:** $^1$H NMR magnified spectrum of compound **6a** ($CDCl_3$, 500 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **u500, Sep 1 2020** | Sweep Width(Hz): **6009.62** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8** |



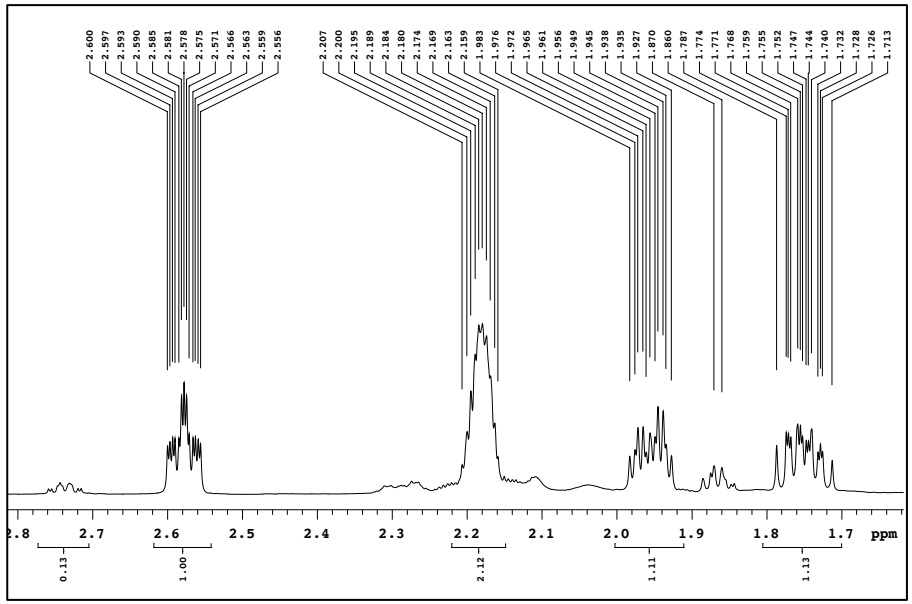
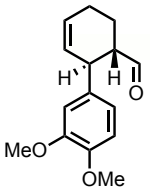



**Figure S34:** $^{13}C$ NMR spectrum of compound **6a** ($CDCl_3$, 126 MHz)




Recorded on: u500, Sep 1 2020 | Sweep Width(Hz): 33783.8 | Acquisiton Time(s): 1 | Relaxation Delay(s): 1
Pulse Sequence: s2pul | Digital Res.(Hz/pt): 0.26 | Hz per mm(Hz/mm): 125.69 | Completed Scans 128

204.010
129.155
127.639
120.297
111.396
111.242
77.314
77.060
76.806
55.961
55.943
54.118
41.086
23.496
21.078

220 200 180 160 140 120 100 80 60 40 20 ppm

**Figure S35:** $^1$H NMR spectrum of compound **6b** ($CDCl_3$, 500 MHz)

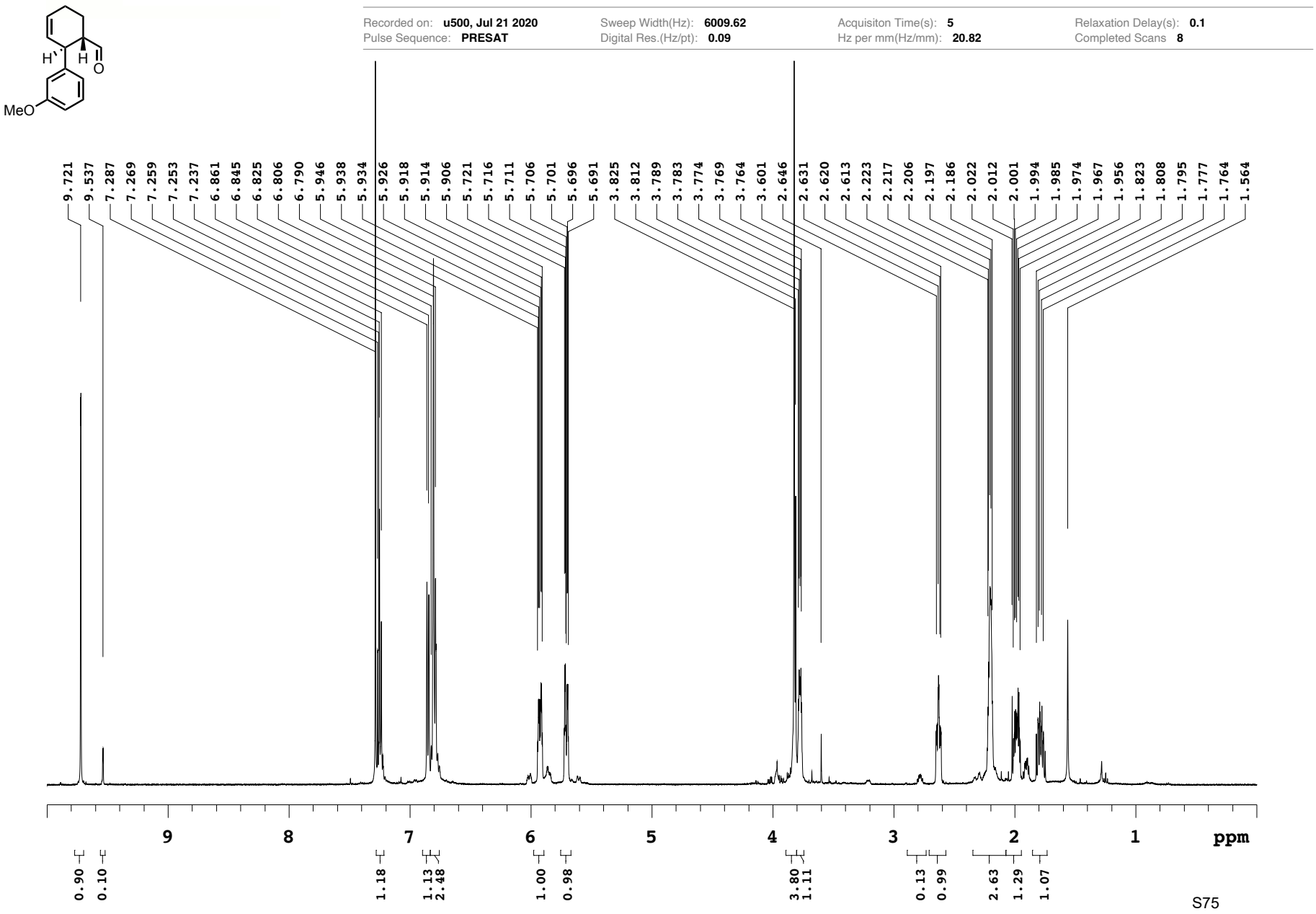
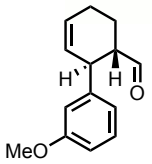
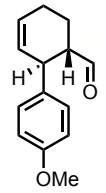


**Figure S36:** $^{13}C$ NMR spectrum of compound **6b** ($CDCl_3$, 126 MHz)




Recorded on: **u500, Jul 21 2020** Sweep Width(Hz): **33783.8** Acquisiton Time(s): **1** Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** Digital Res.(Hz/pt): **0.26** Hz per mm(Hz/mm): **125.69** Completed Scans **128**

**Figure S37:** $^{1}$H NMR spectrum of compound **6c** ($CDCl_3$, 500 MHz)




Recorded on: **u500, Jul 17 2020** Sweep Width(Hz): **6009.62** Acquisiton Time(s): **5** Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** Digital Res.(Hz/pt): **0.09** Hz per mm(Hz/mm): **20.82** Completed Scans **8**

9.686 9.513 7.260 7.155 7.138 7.122 6.856 6.839 6.824 5.900 5.893 5.888 5.880 5.873 5.868 5.861 5.677 5.671 5.667 5.661 5.657 5.651 5.647 3.789 3.779 3.732 3.727 3.721 3.717 3.712 3.706 2.577 2.573 2.558 2.543 2.539 2.182 2.177 2.172 2.167 2.155 1.965 1.958 1.954 1.949 1.938 1.931 1.782 1.768 1.763 1.754 1.749 1.741 1.735 1.726 1.722 1.542

9 8 7 6 5 4 3 2 1 ppm

0.94 0.11 2.27 2.29 1.01 1.01 3.52 0.98 0.11 1.00 2.21 1.06 1.05

**Figure S38:** $^{13}C$ NMR spectrum of compound **6c** ($CDCl_3$, 126 MHz)

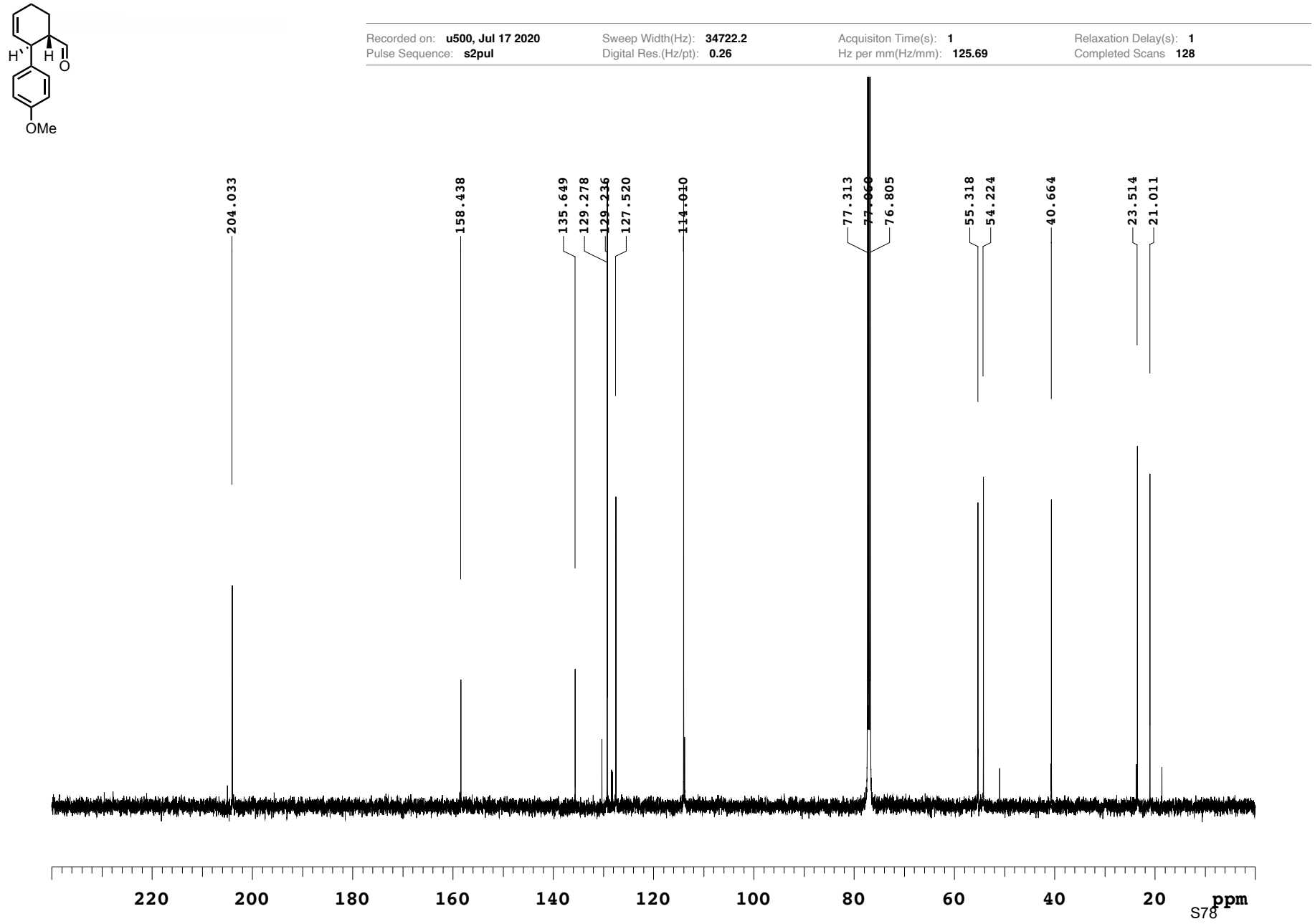
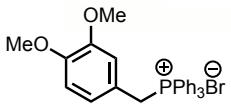
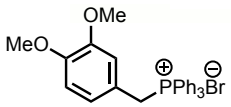


**Figure S39:** $^1$H NMR spectrum of compound **7a** ($CDCl_3$, 400 MHz)




Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **4807.69** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.07** | Hz per mm(Hz/mm): **16.67** | Completed Scans **16**

**Figure S40:** $^{13}C$ NMR spectrum of compound **7a** ($CDCl_3$, 176 MHz)

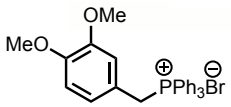



Recorded on: u500, Sep 27 2021 | Sweep Width(Hz): 33783.8 | Acquisiton Time(s): 1 | Relaxation Delay(s): 1
Pulse Sequence: s2pul | Digital Res.(Hz/pt): 0.26 | Hz per mm(Hz/mm): 99.5 | Completed Scans 128

148.968, 148.935, 148.855, 134.853, 134.830, 134.664, 134.586, 130.111, 130.012, 123.755, 123.704, 119.155, 119.085, 118.424, 117.746, 115.100, 115.061, 111.029, 77.314, 77.060, 76.806, 58.474, 56.140, 55.849, 30.554, 30.185, 18.482

180 160 140 120 100 80 60 40 20 ppm

**Figure S41:** $^{31}P\{^{1}H\}$ NMR spectrum of compound **7a** ($CDCl_3$, 162 MHz)




Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **11363.6** | Acquisiton Time(s): **1** | Relaxation Delay(s): **0.1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **47.35** | Completed Scans **64**

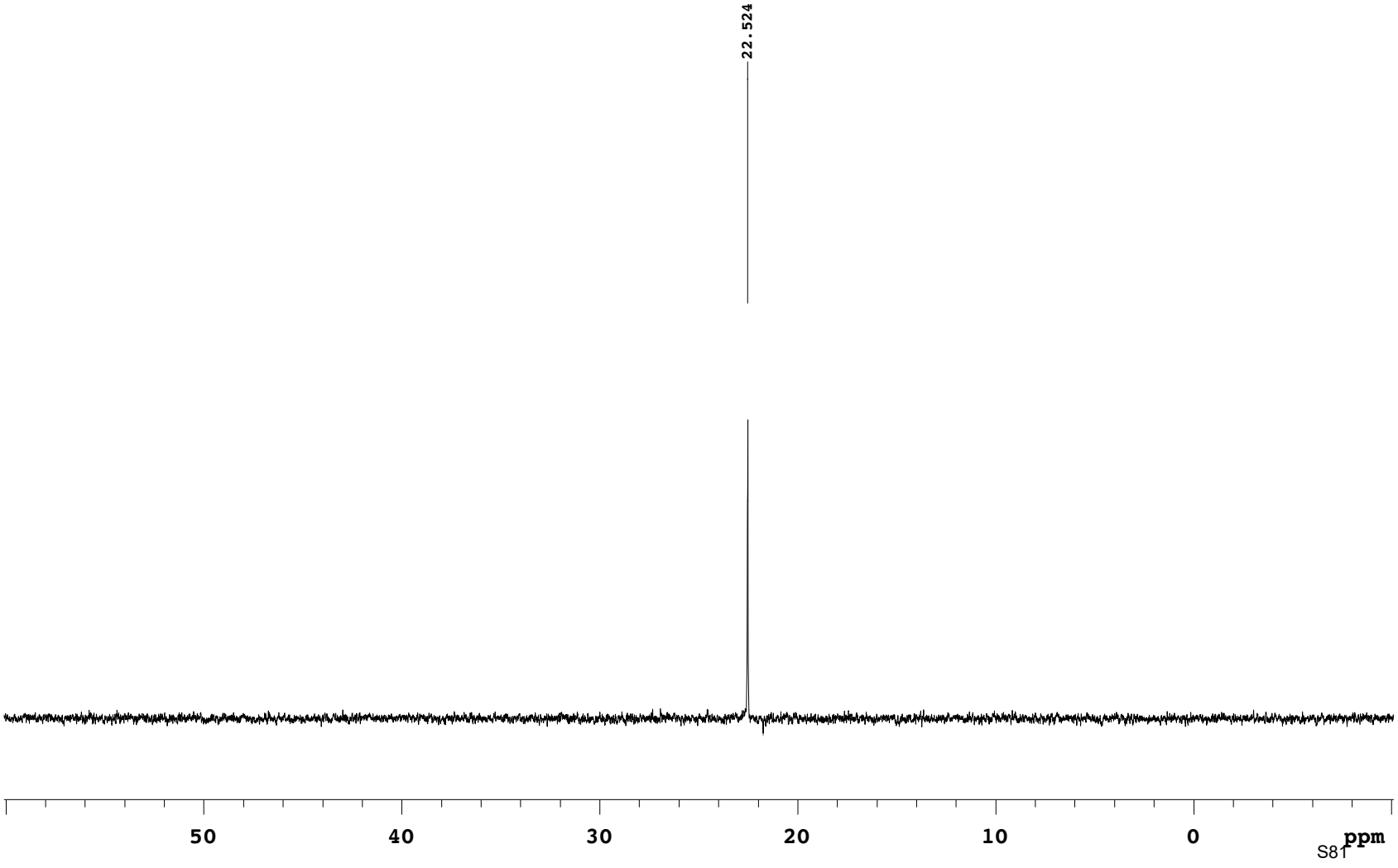
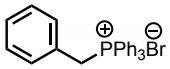


**Figure S42:** $^1$H NMR spectrum of compound **7b** ($CDCl_3$, 400 MHz)




Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **4807.69** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.07** | Hz per mm(Hz/mm): **16.67** | Completed Scans **16**

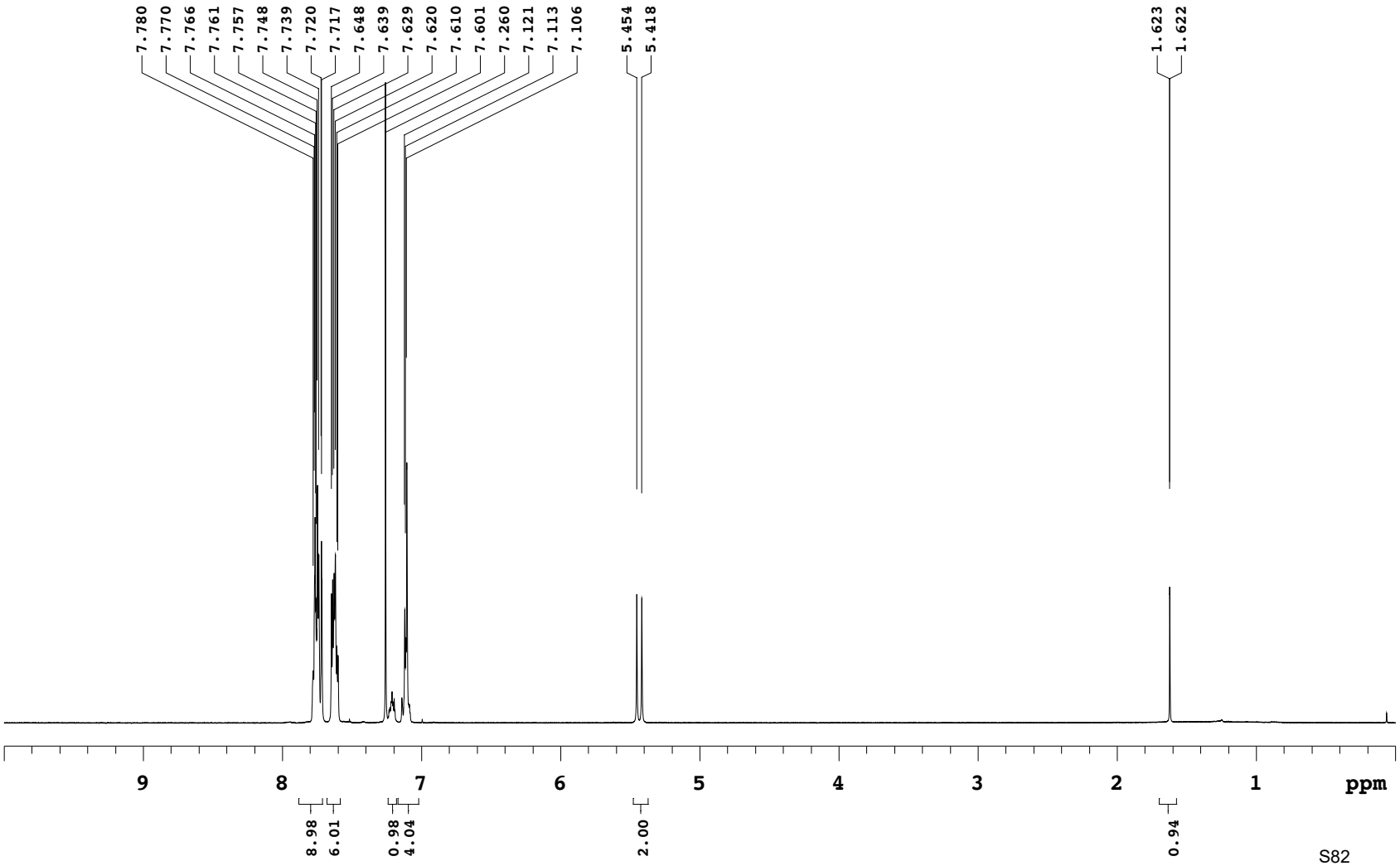
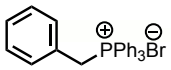


**Figure S43:** $^{13}C$ NMR spectrum of compound **7b** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Jul 25 2020** | Sweep Width(Hz): **36764.7** | Acquisiton Time(s): **1** | Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.28** | Hz per mm(Hz/mm): **139.31** | Completed Scans **256**

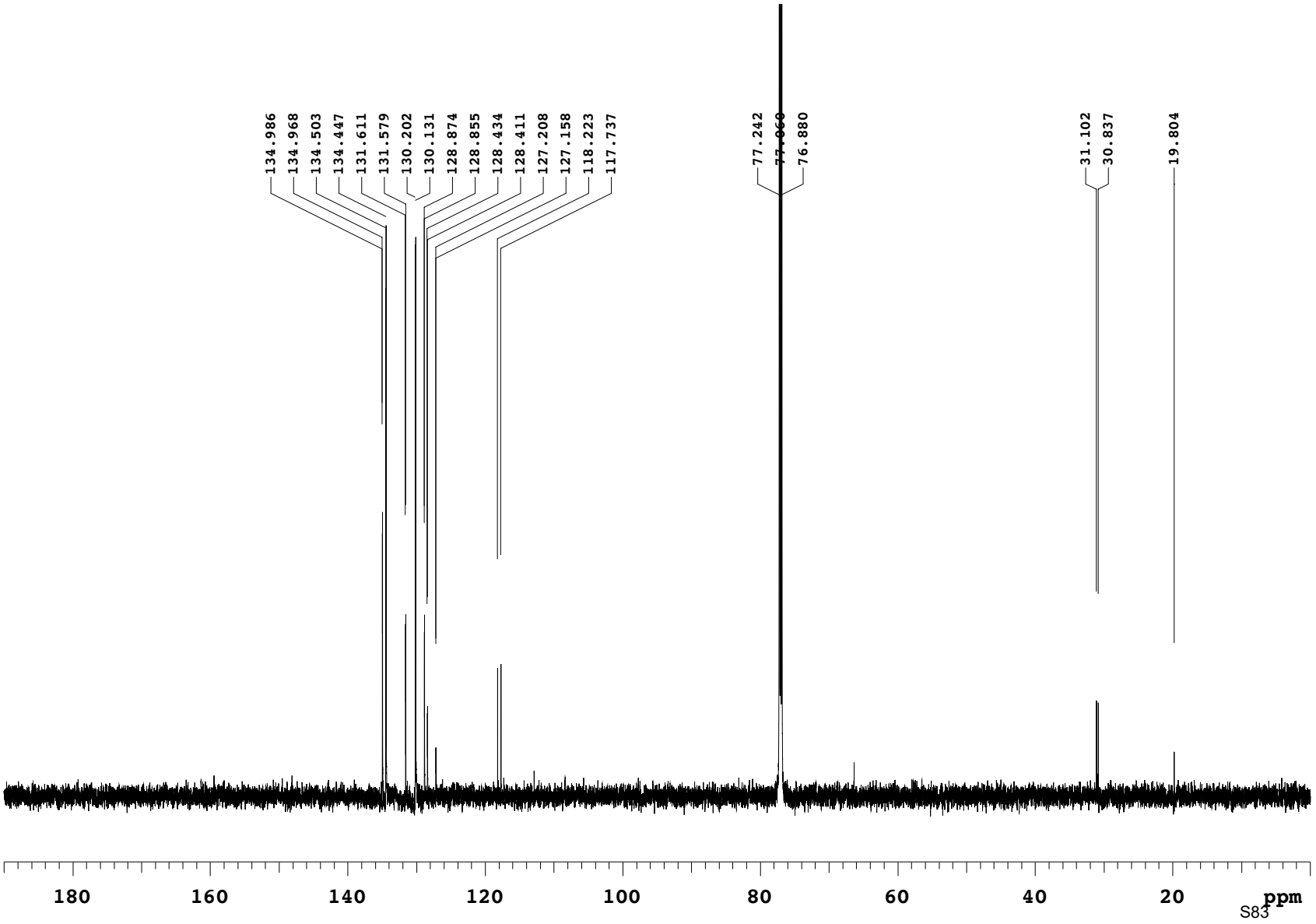
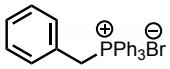


**Figure S44:** $^{31}P\{^{1}H\}$ NMR spectrum of compound **7b** ($CDCl_3$, 162 MHz)




Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **11363.6** | Acquisiton Time(s): **1** | Relaxation Delay(s): **0.1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **47.35** | Completed Scans **64**

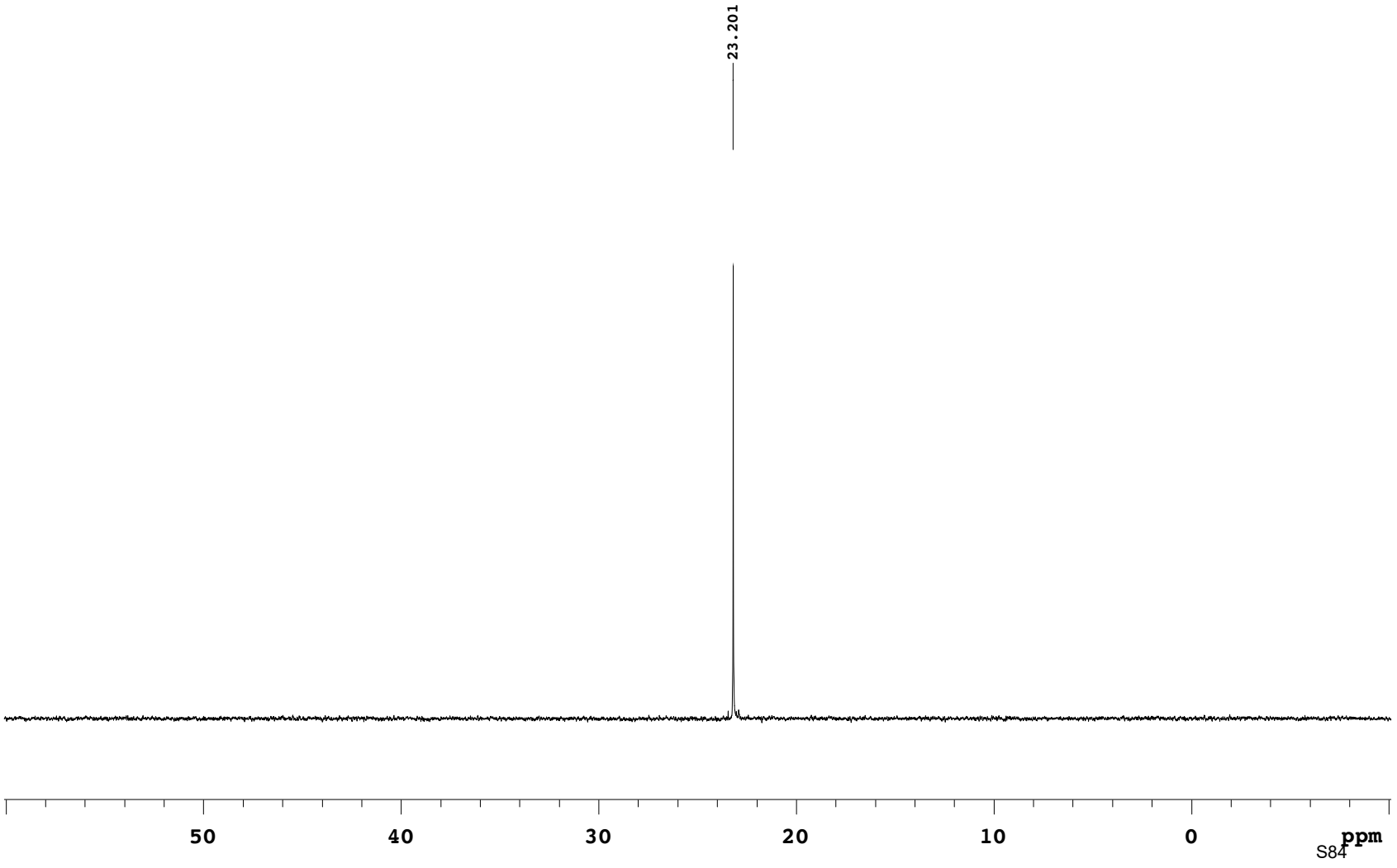
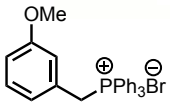


**Figure S45:** $^1$H NMR spectrum of compound **7c** ($CDCl_3$, 400 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **4807.69** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.07** | Hz per mm(Hz/mm): **16.67** | Completed Scans **16** |

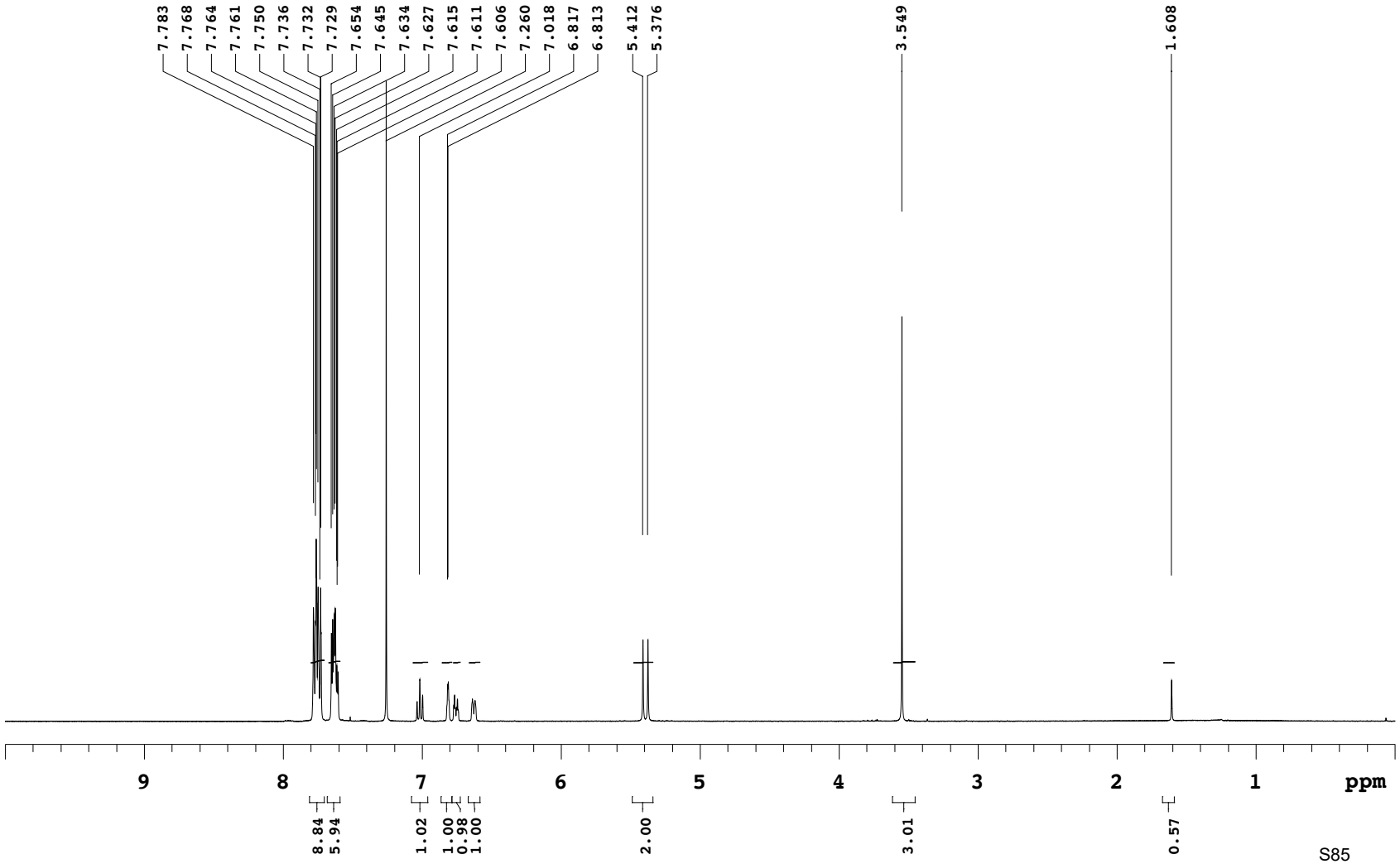
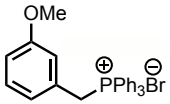


**Figure S46:** $^{13}C$ NMR spectrum of compound **7c** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Jul 25 2020** | Sweep Width(Hz): **36764.7** | Acquisiton Time(s): **1** | Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.28** | Hz per mm(Hz/mm): **139.31** | Completed Scans **256**

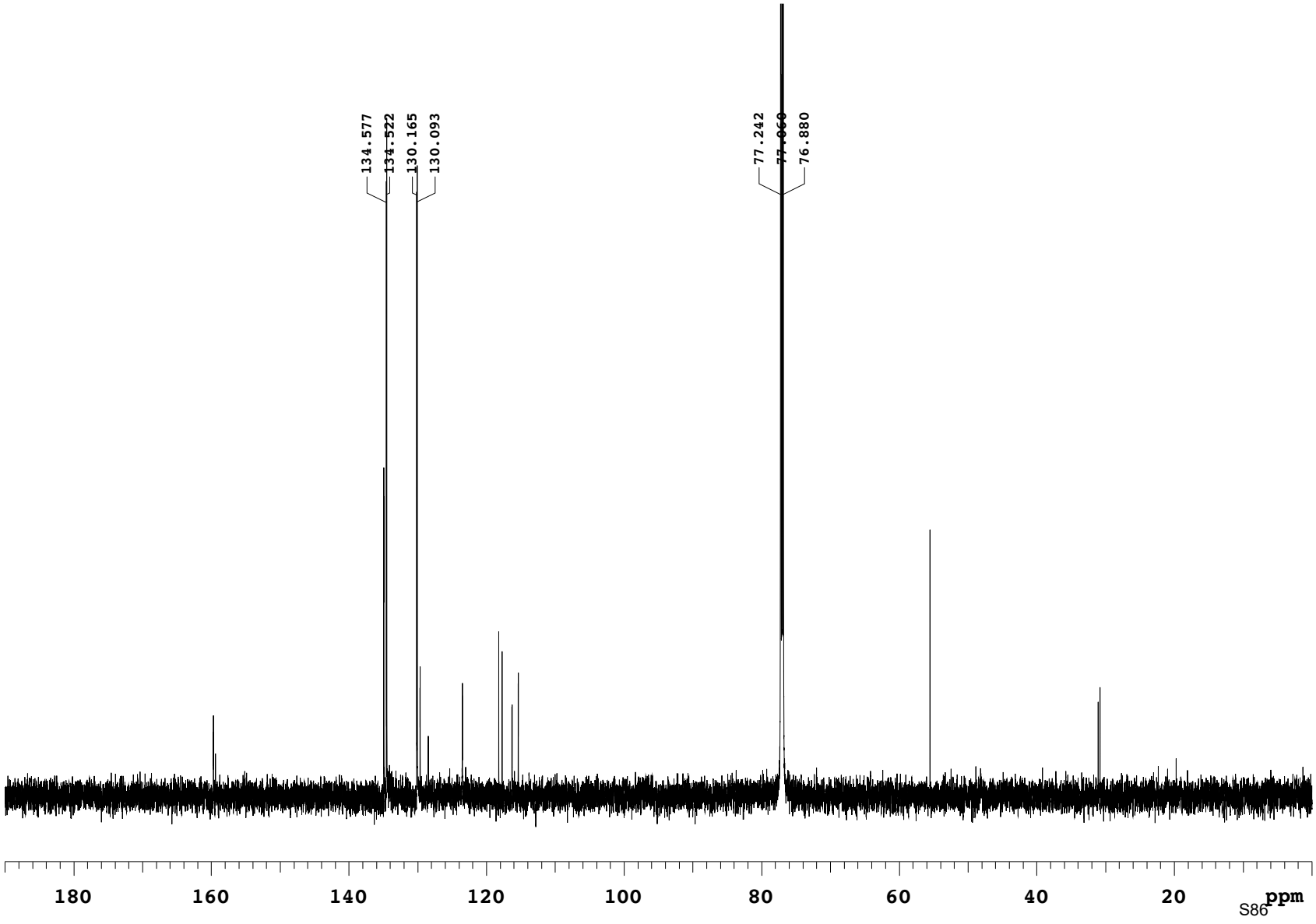
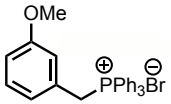


**Figure S47:** $^{31}P\{^{1}H\}$ NMR spectrum of compound **7c** ($CDCl_3$, 162 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **11363.6** | Acquisiton Time(s): **1** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **47.35** | Completed Scans **64** |

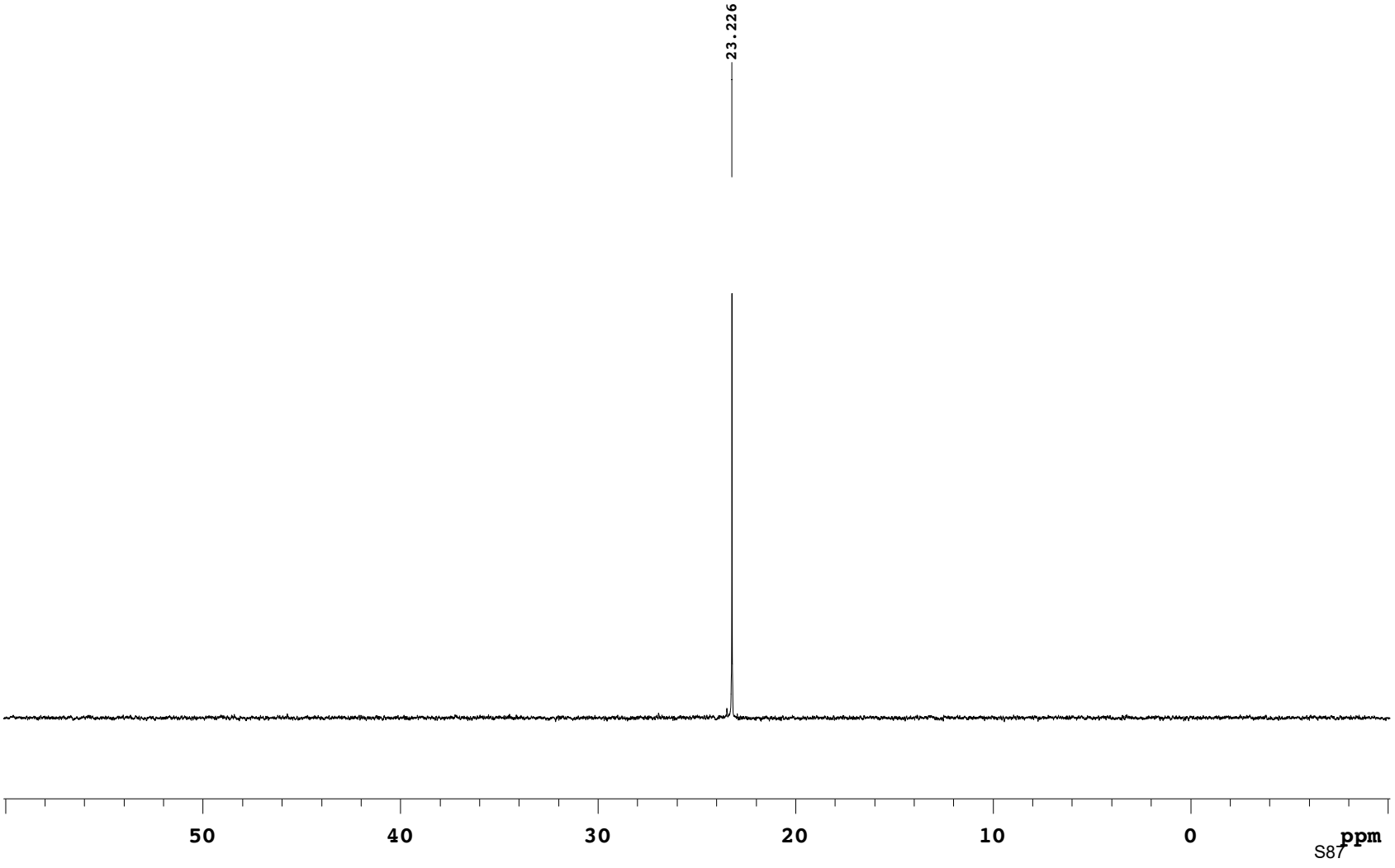
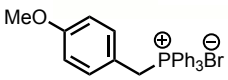


**Figure S48:** $^1$H NMR spectrum of compound **7d** ($CDCl_3$, 400 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **4807.69** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.07** | Hz per mm(Hz/mm): **16.67** | Completed Scans **16** |

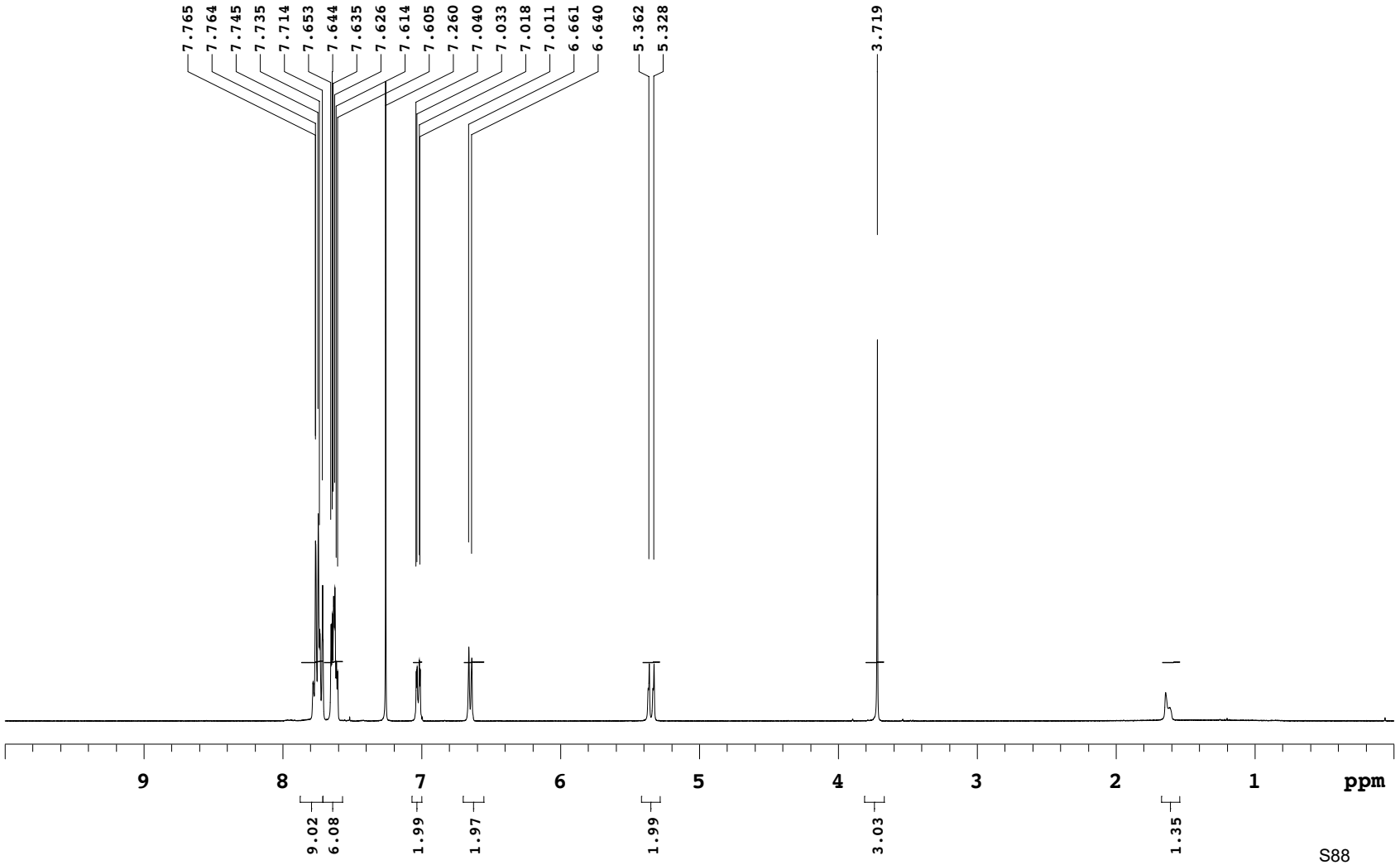


**Figure S49:** $^{13}C$ NMR spectrum of compound **7d** ($CDCl_3$, 176 MHz)

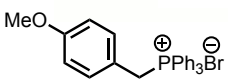
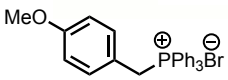


**Figure S50:** $^{31}P\{^{1}H\}$ NMR spectrum of compound **7d** ($CDCl_3$, 162 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **11363.6** | Acquisiton Time(s): **1** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **47.35** | Completed Scans **64** |

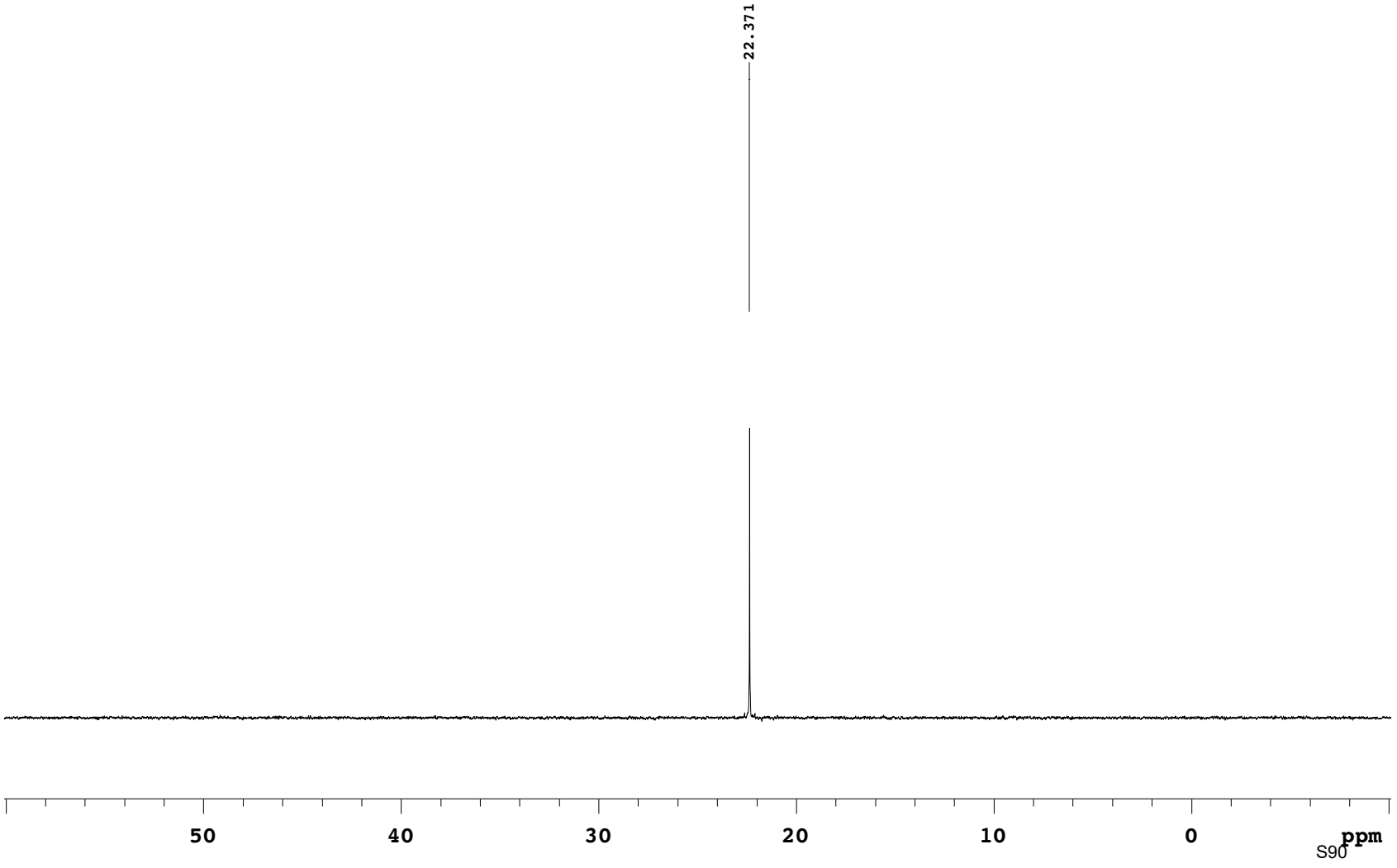
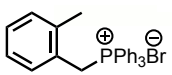


**Figure S51:** $^{1}H$ NMR spectrum of compound **7e** ($CDCl_3$, 400 MHz)




Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **4807.69** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.07** | Hz per mm(Hz/mm): **16.67** | Completed Scans **16**

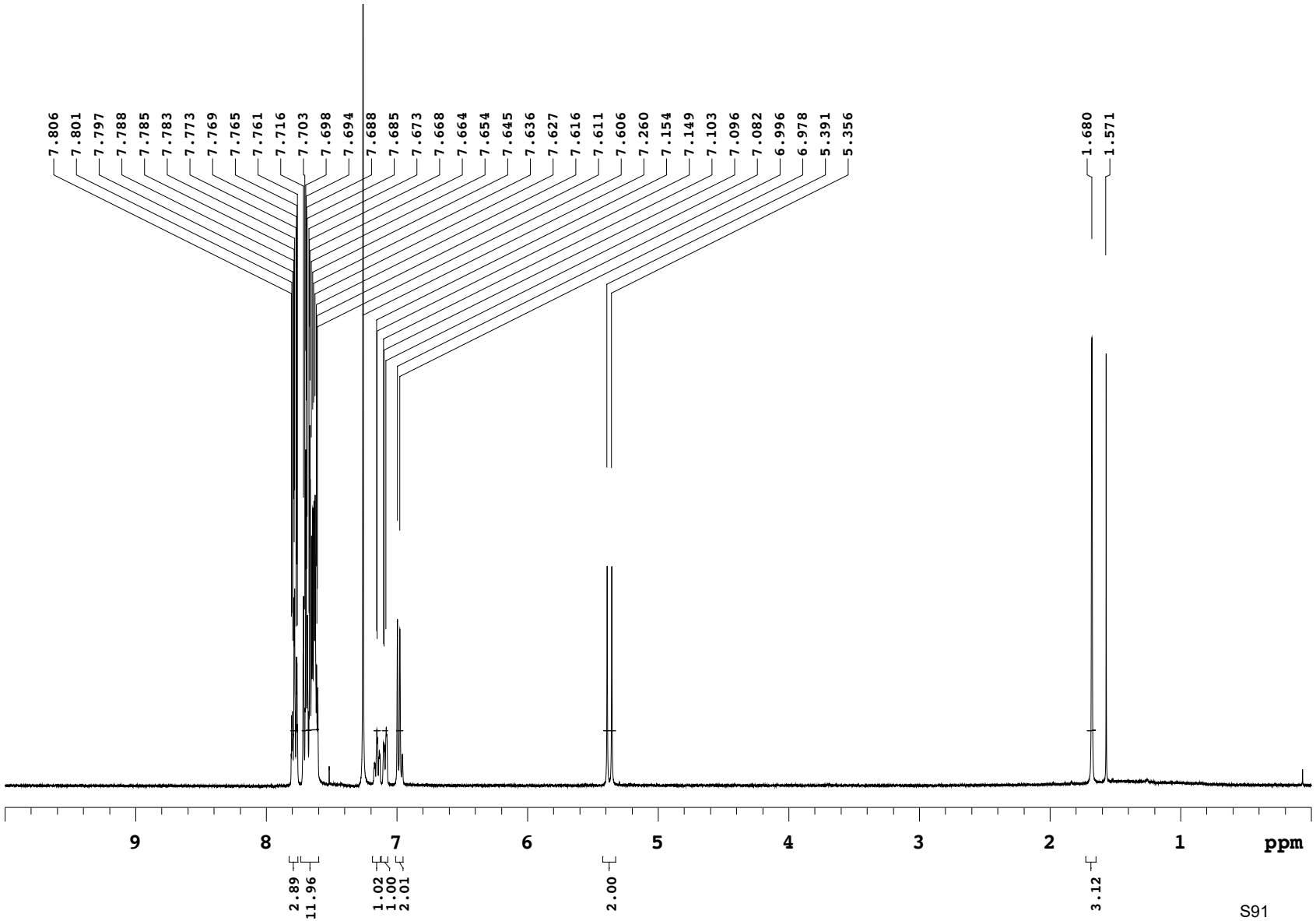
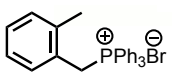


**Figure S52:** $^{13}C$ NMR spectrum of compound **7e** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Jul 25 2020** | Sweep Width(Hz): **36764.7** | Acquisiton Time(s): **1** | Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.28** | Hz per mm(Hz/mm): **139.31** | Completed Scans **256**

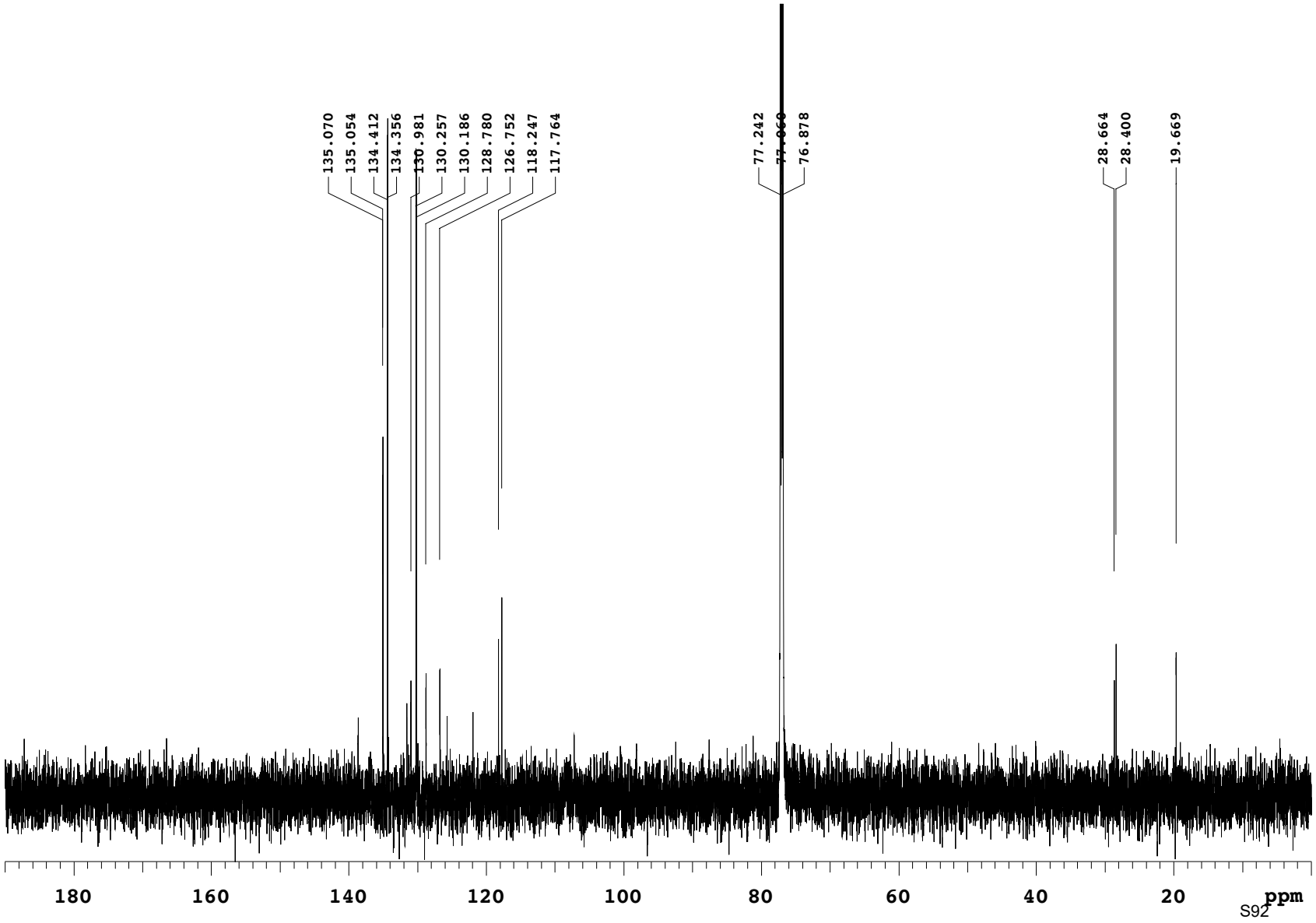
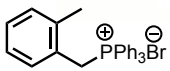


**Figure S53:** $^{31}P\{^{1}H\}$ NMR spectrum of compound **7e** ($CDCl_3$, 162 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **mr400, Jul 25 2020** | Sweep Width(Hz): **11363.6** | Acquisiton Time(s): **1** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **47.35** | Completed Scans **72** |

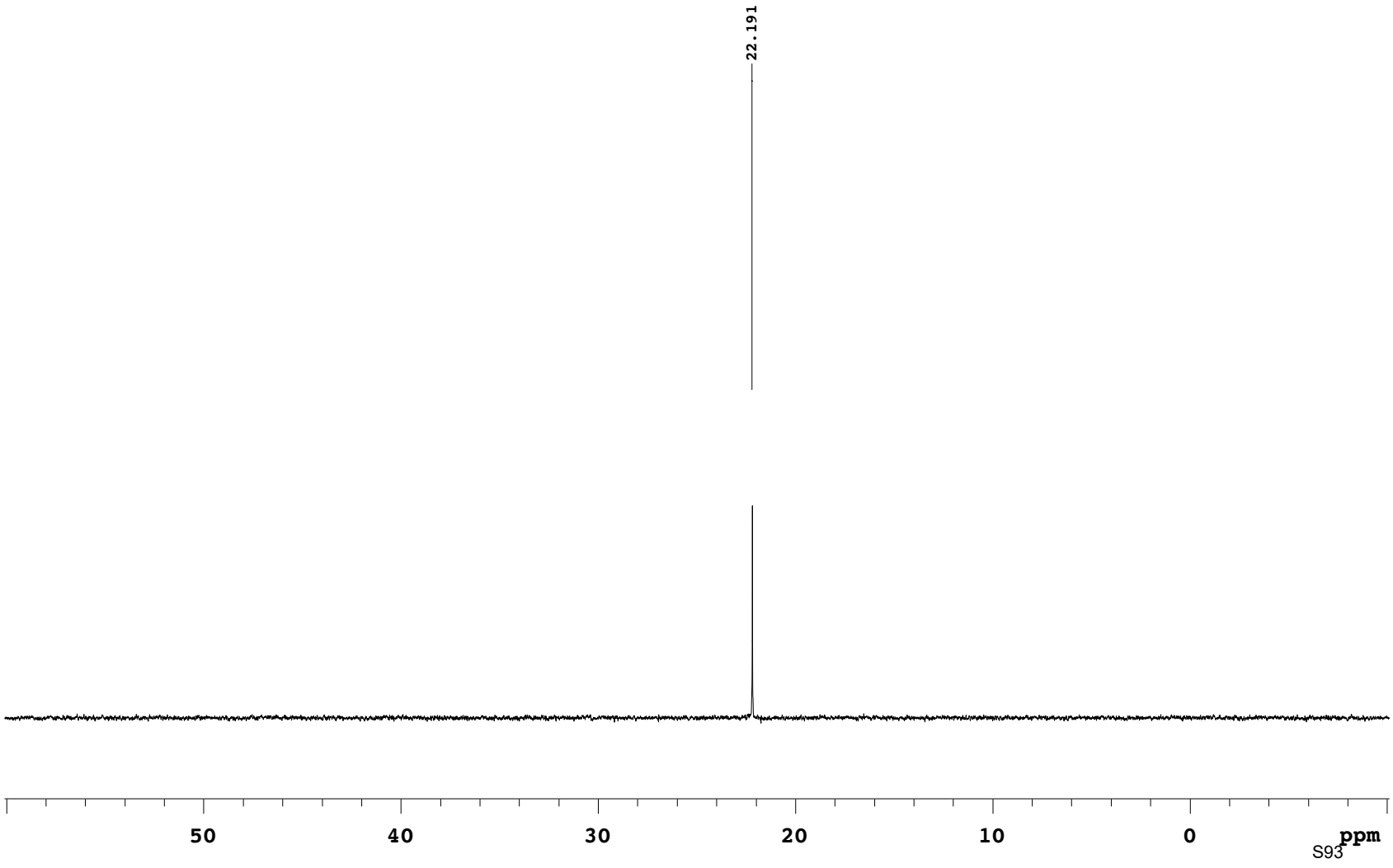
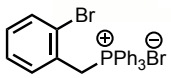


**Figure S54:** $^1$H NMR spectrum of compound **7f** ($CDCl_3$, 500 MHz)




Recorded on: **u500, Sep 1 2020** | Sweep Width(Hz): **6009.62** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8**

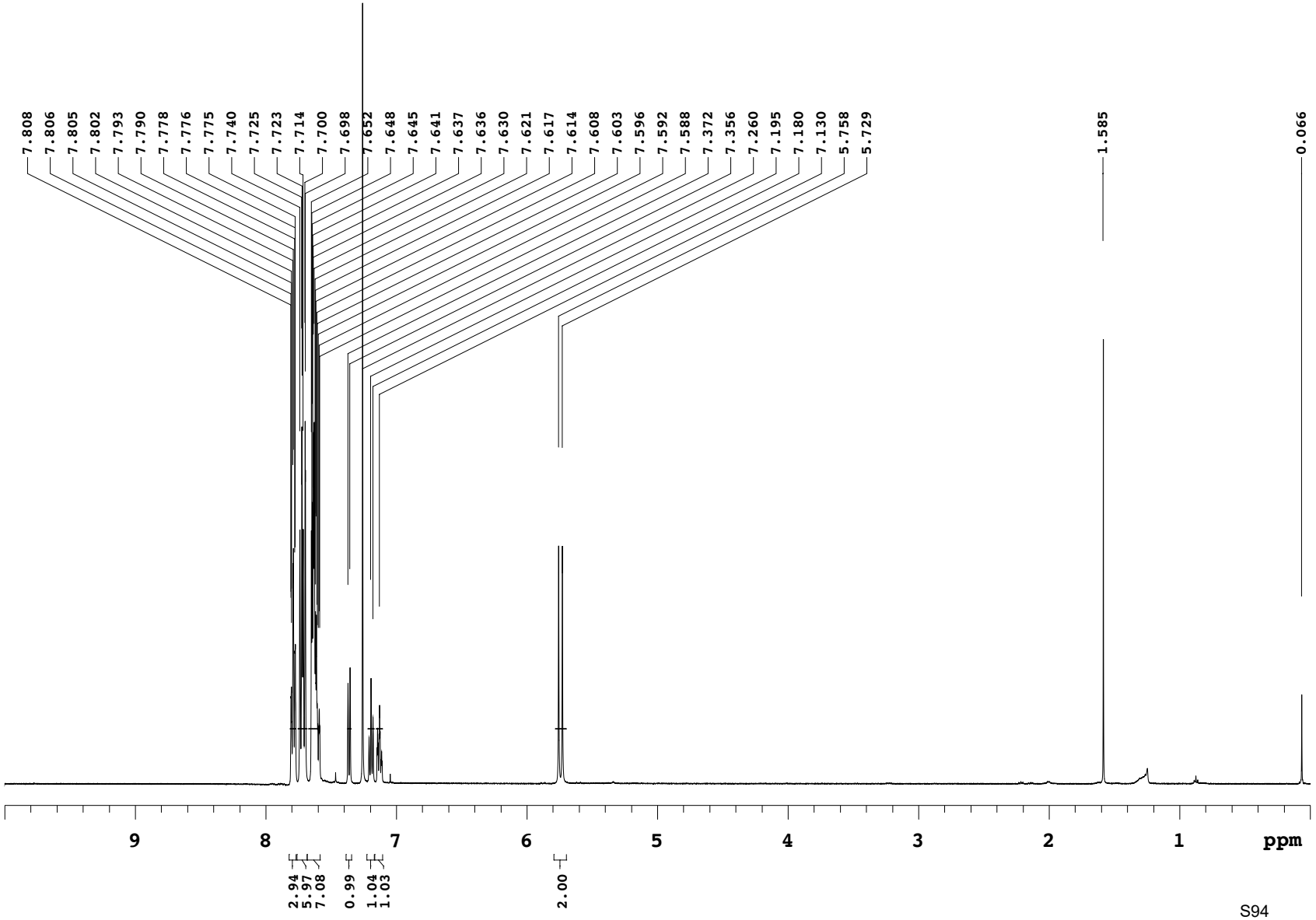
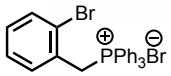


**Figure S55:** $^{13}C$ NMR spectrum of compound **7f** ($CDCl_3$, 126 MHz)




Recorded on: **u500, Sep 1 2020** | Sweep Width(Hz): **33783.8** | Acquisiton Time(s): **1** | Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** | Digital Res.(Hz/pt): **0.26** | Hz per mm(Hz/mm): **99.5** | Completed Scans **128**

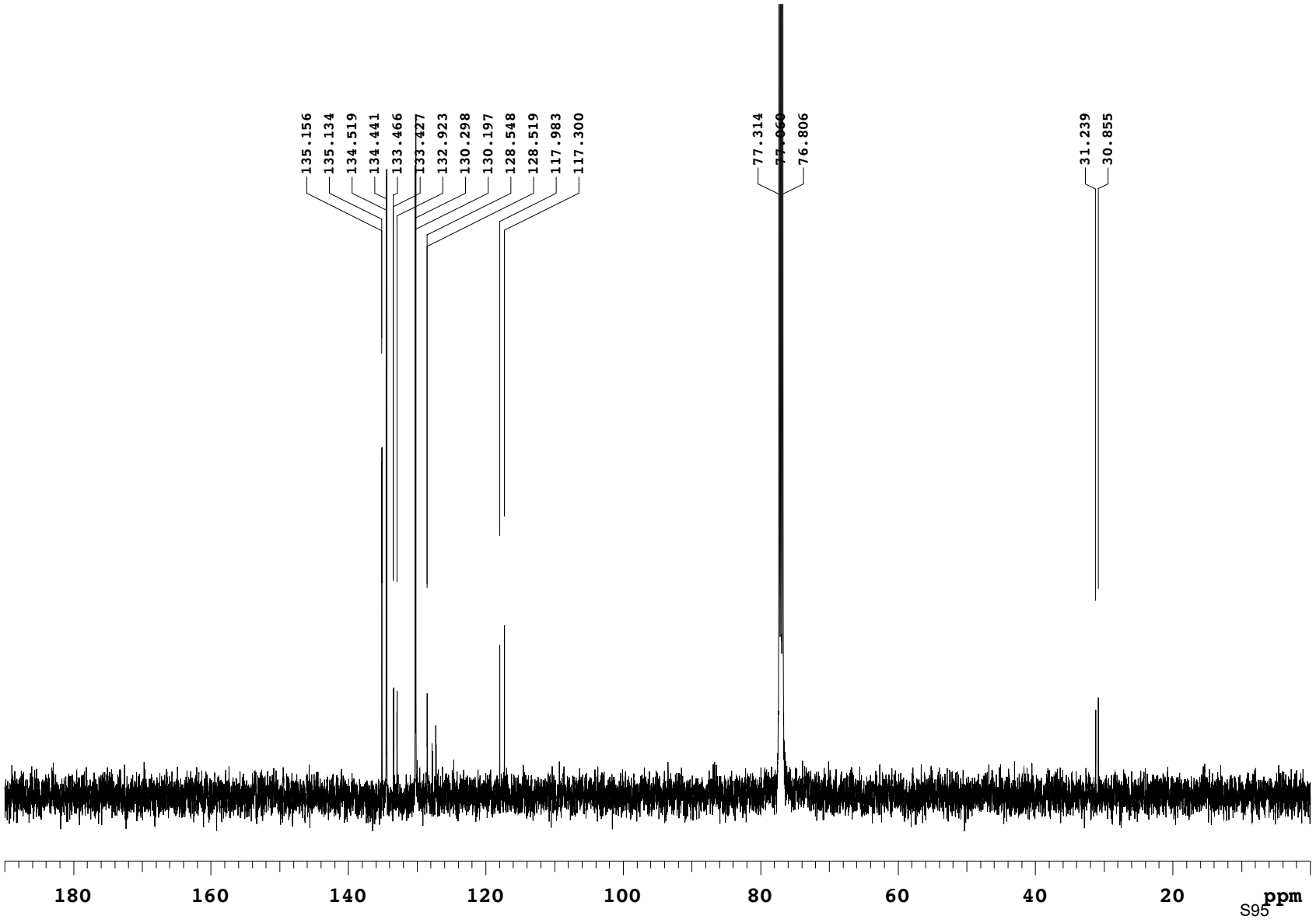


**Figure S56:** $^1$H NMR spectrum of compound **8** ($CDCl_3$, 500 MHz)

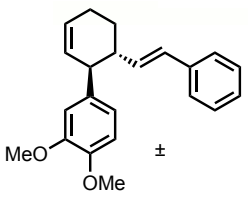
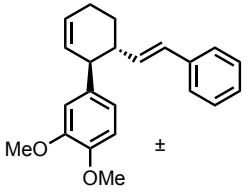
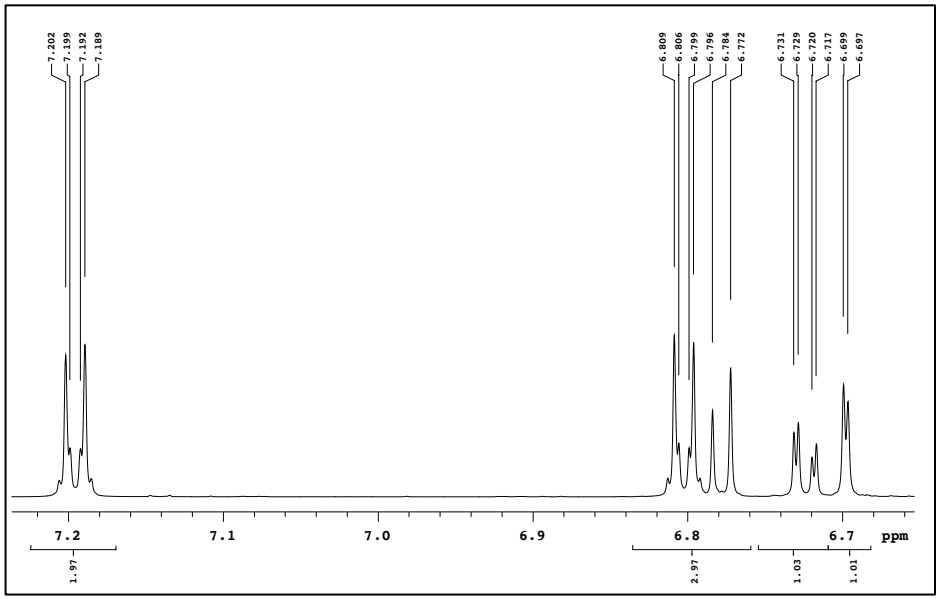


**Figure S57:** $^1$H NMR magnified spectrum of compound **8** ($CDCl_3$, 500 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **u500, Aug 15 2020** | Sweep Width(Hz): **6009.62** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8** |



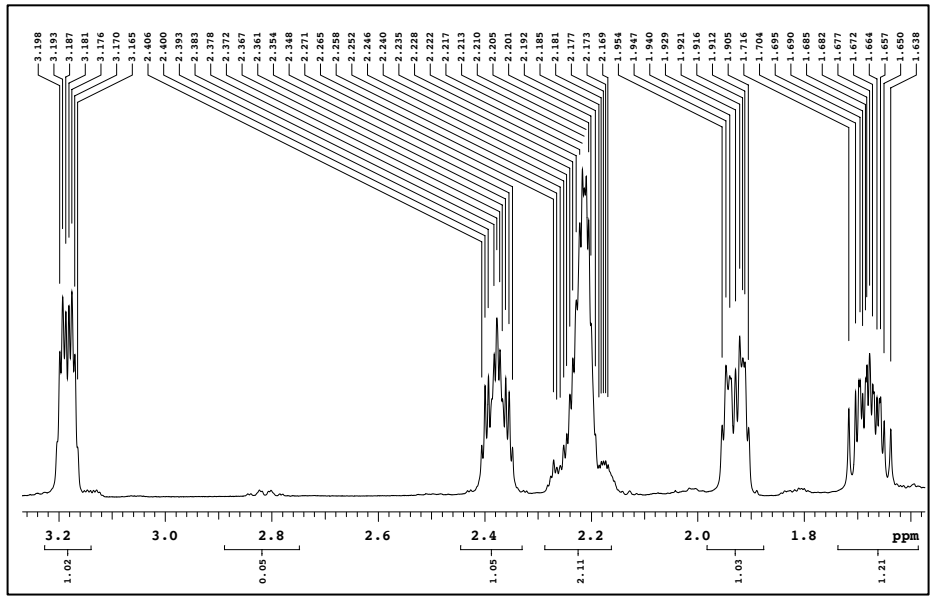
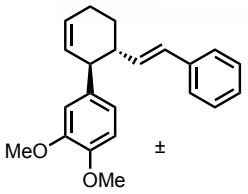



**Figure S58:** $^{13}C$ NMR spectrum of compound **8** ($CDCl_3$, 126 MHz)

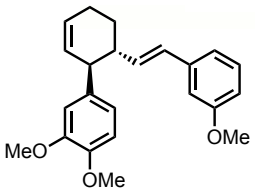



Recorded on: **u500, Aug 15 2020** Sweep Width(Hz): **33783.8** Acquisiton Time(s): **1** Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** Digital Res.(Hz/pt): **0.26** Hz per mm(Hz/mm): **99.5** Completed Scans **128**

148.656 147.415 137.860 137.542 134.129 130.326 129.270 128.464 127.592 126.893 126.017 120.436 111.738 110.949 77.314 77.060 76.806 55.910 55.877 48.043 45.479 29.754 27.820 24.565

180 160 140 120 100 80 60 40 20 ppm

**Figure S59:** $^1$H NMR spectrum of compound **9** ($CDCl_3$, 700 MHz)



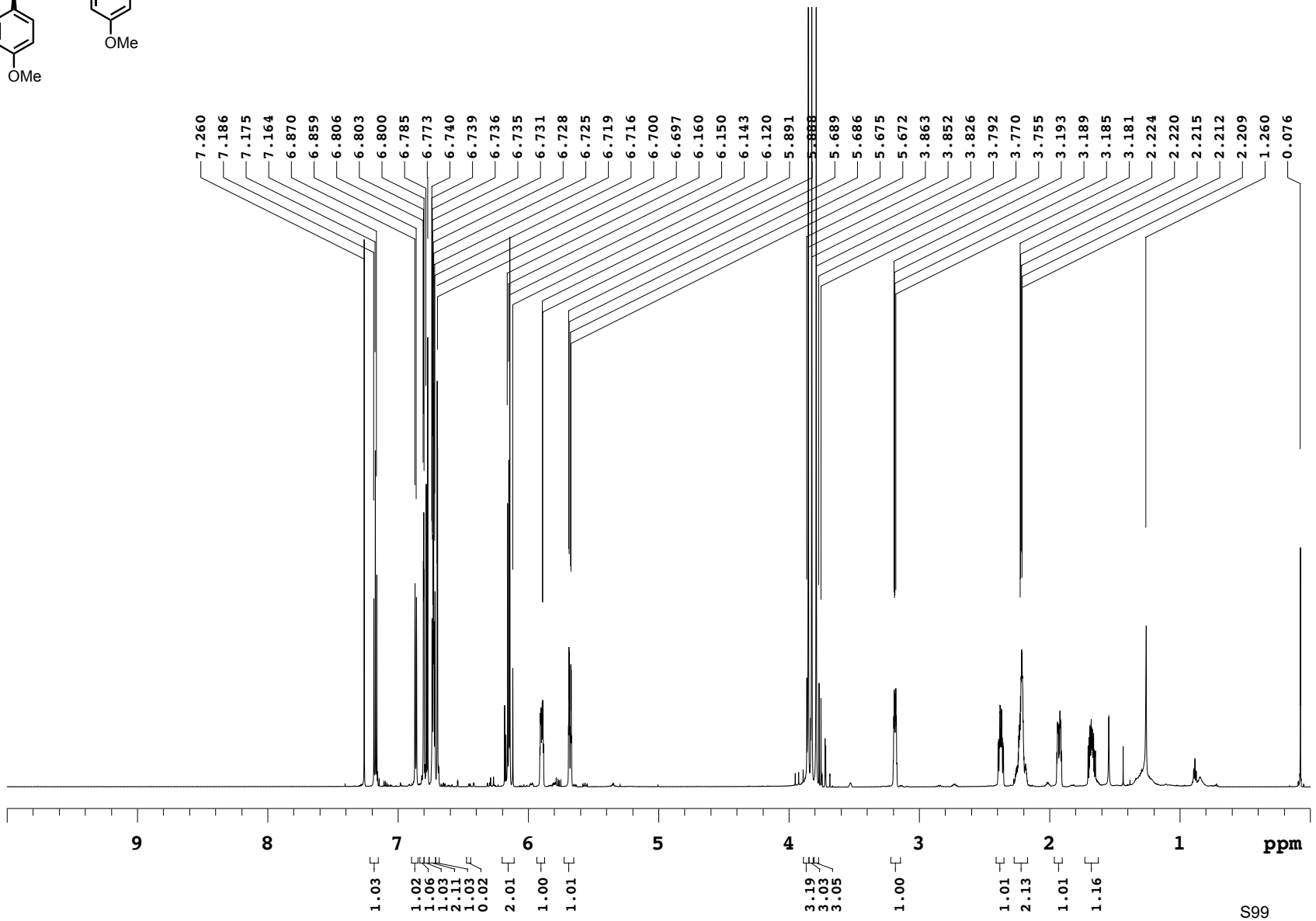
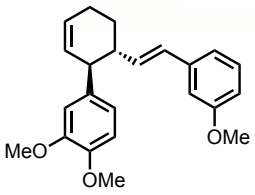



**Figure S60:** $^{13}C$ NMR spectrum of compound **9** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Aug 15 2020** Sweep Width(Hz): **36764.7** Acquisiton Time(s): **1** Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** Digital Res.(Hz/pt): **0.28** Hz per mm(Hz/mm): **139.31** Completed Scans **256**

159.787 148.669 147.421 139.349 137.499 134.483 130.292 129.414 129.173 127.589 120.450 118.684 112.429 111.699 111.511 110.943 77.240 77.060 76.878 55.904 55.882 55.227 47.982 45.458 27.797 24.534

180 160 140 120 100 80 60 40 20 ppm

**Figure S61:** $^{1}H$ NMR spectrum of compound **10** ($CDCl_3$, 700 MHz)

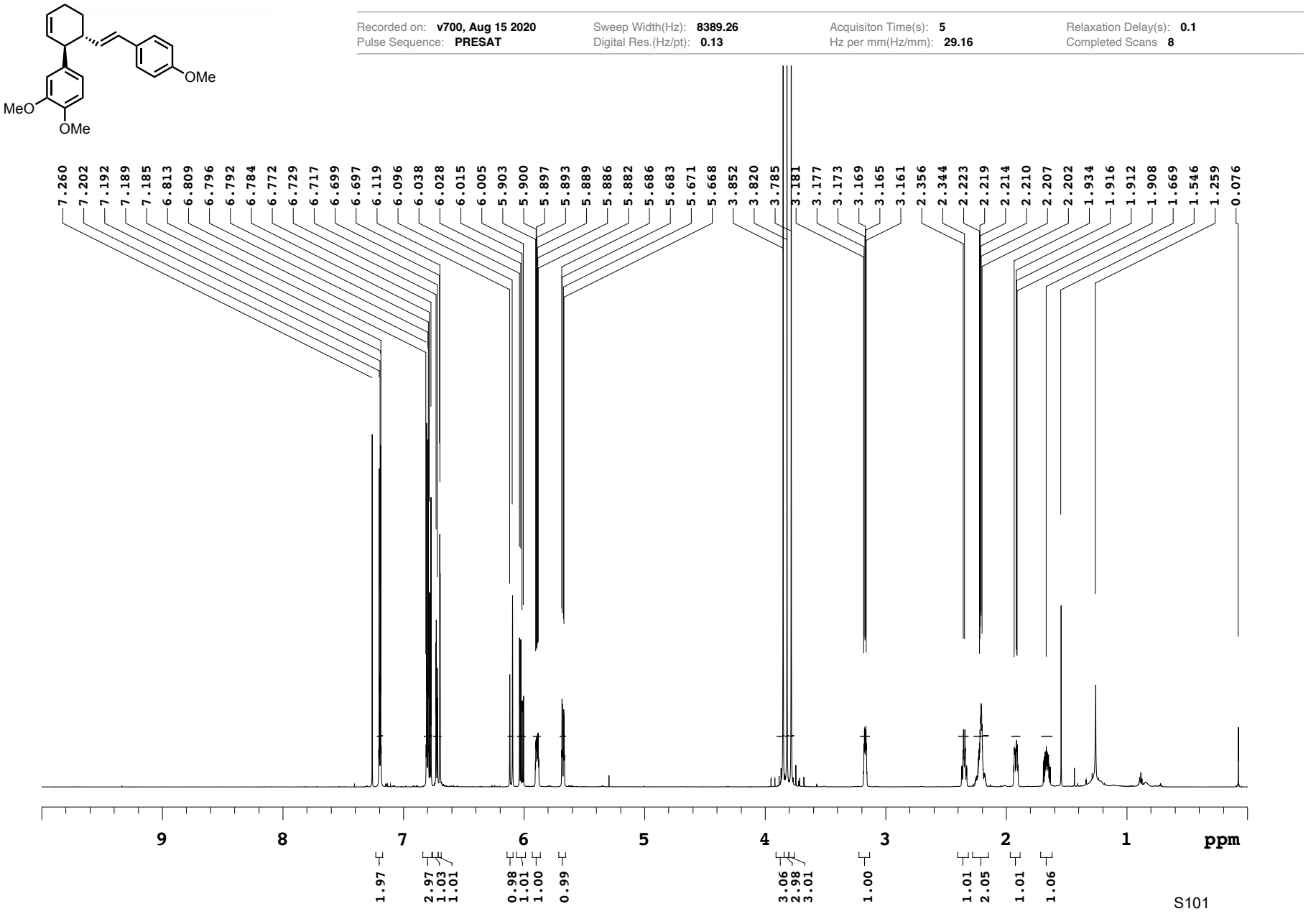
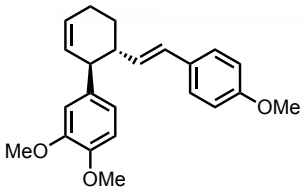


**Figure S62:** $^{13}C$ NMR spectrum of compound **10** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Aug 15 2020** Sweep Width(Hz): **36764.7** Acquisiton Time(s): **1** Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** Digital Res.(Hz/pt): **0.28** Hz per mm(Hz/mm): **139.31** Completed Scans **256**

158.728 148.622 147.372 137.651 131.997 130.701 130.366 128.584 127.586 127.079 120.431 113.899 111.777 110.922 77.242 77.060 76.880 55.903 55.876 55.321 48.136 45.414 27.889 24.591

180 160 140 120 100 80 60 40 20 ppm

**Figure S63:** $^{1}H$ NMR spectrum of compound **11** ($CDCl_3$, 700 MHz)

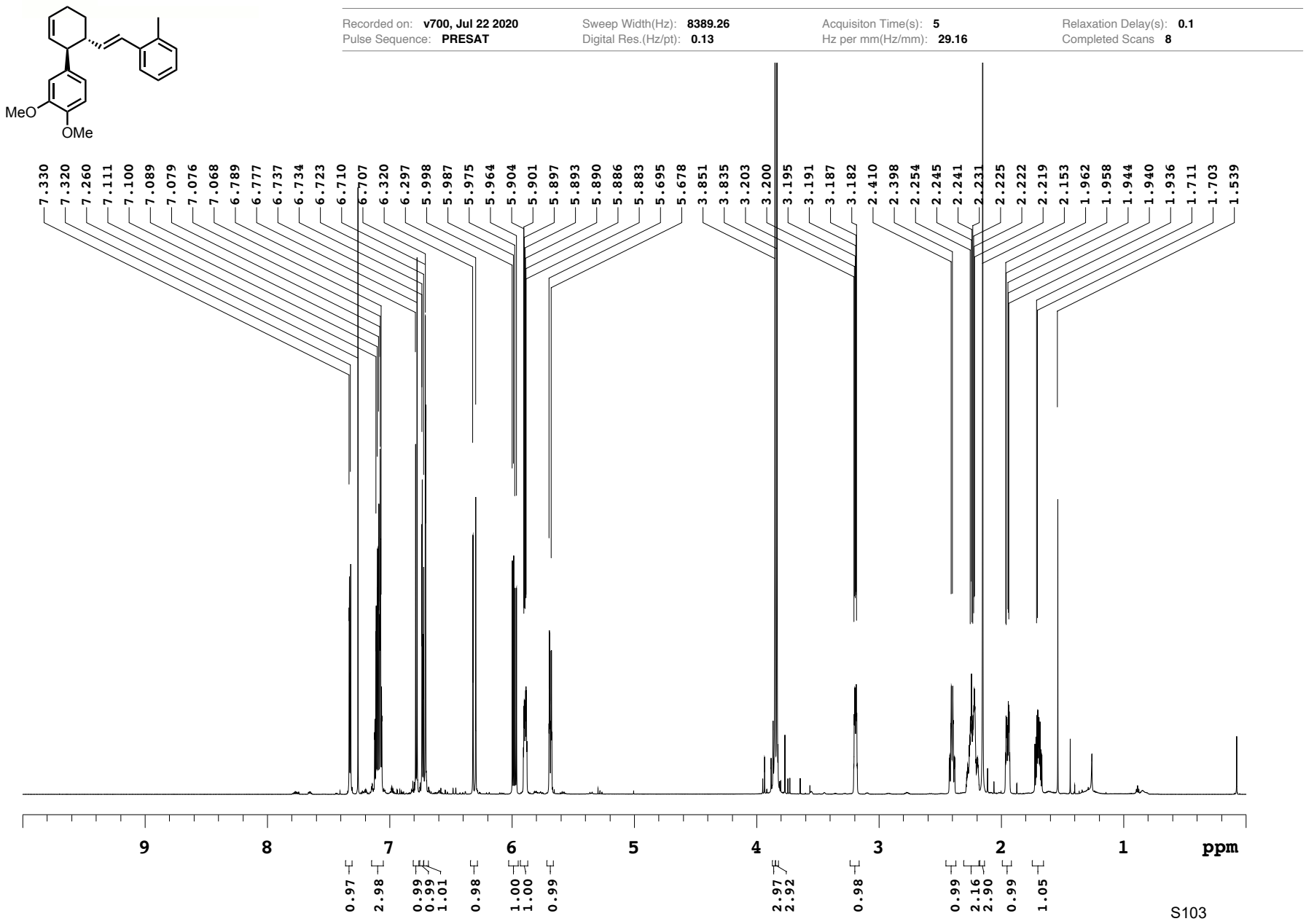


**Figure S64:** $^{13}C$ NMR spectrum of compound **11** ($CDCl_3$, 176 MHz)

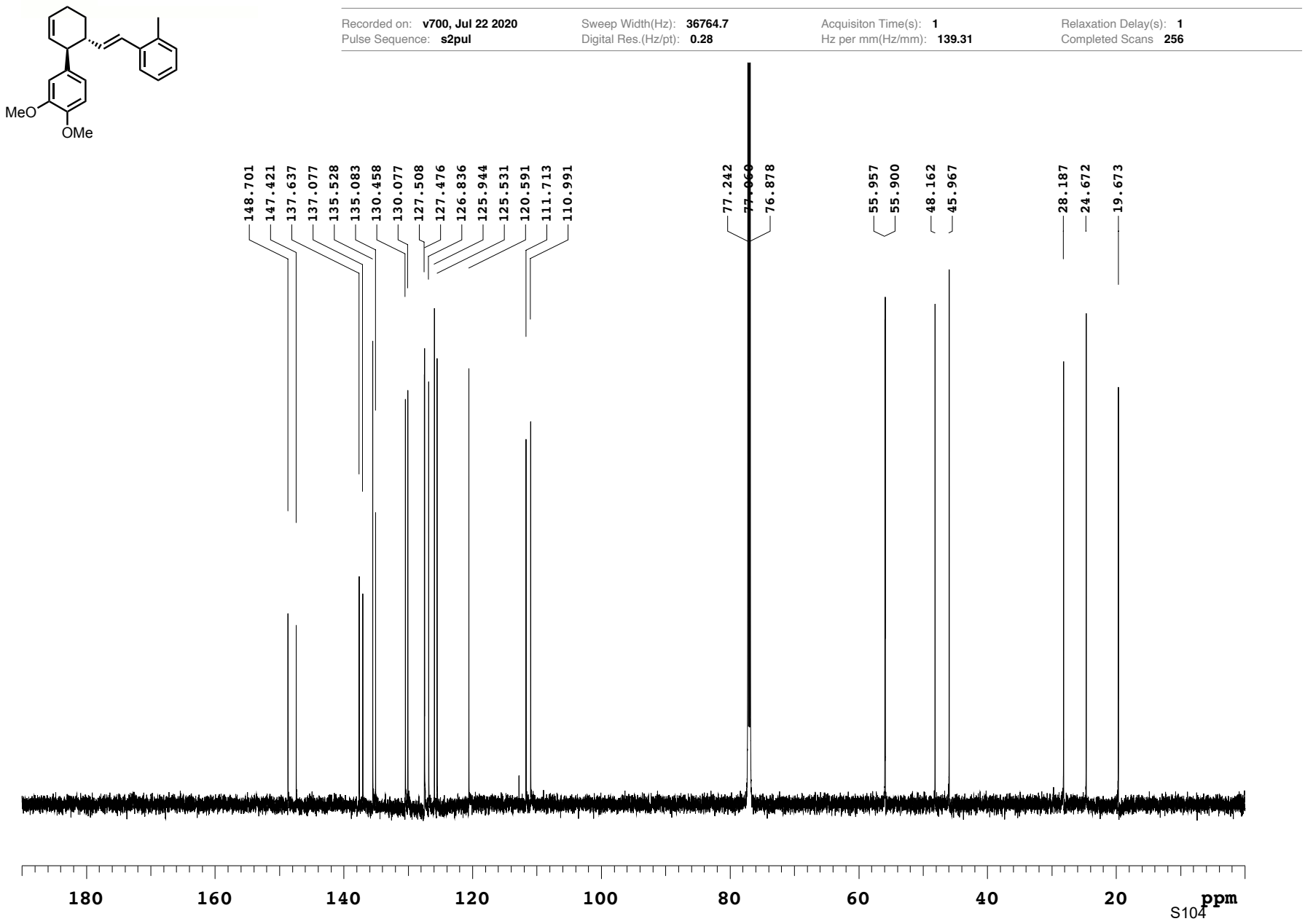


**Figure S65:** $^1$H NMR spectrum of compound **12** ($CDCl_3$, 700 MHz)

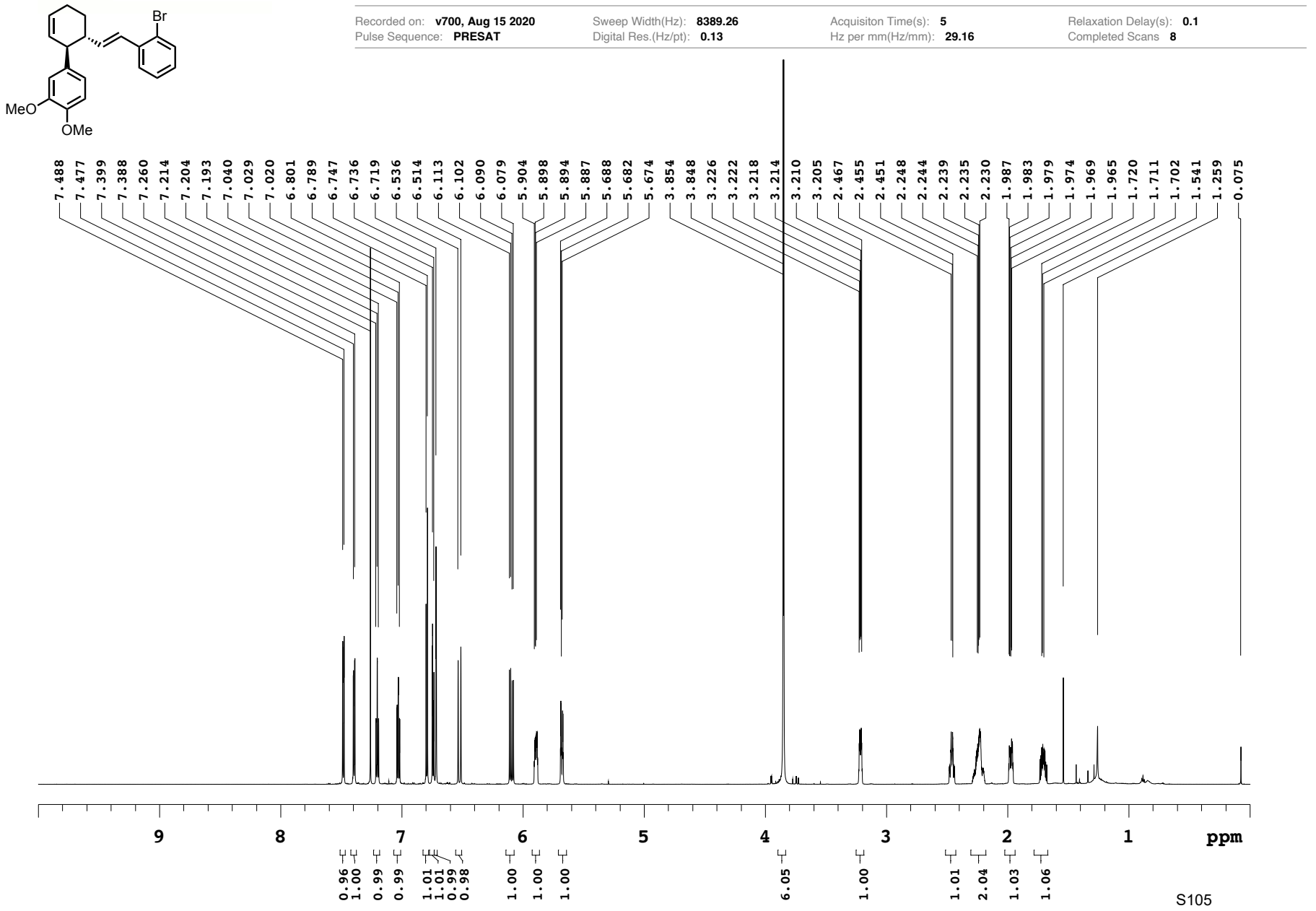


**Figure S66:** $^{13}C$ NMR spectrum of compound **12** ($CDCl_3$, 176 MHz)

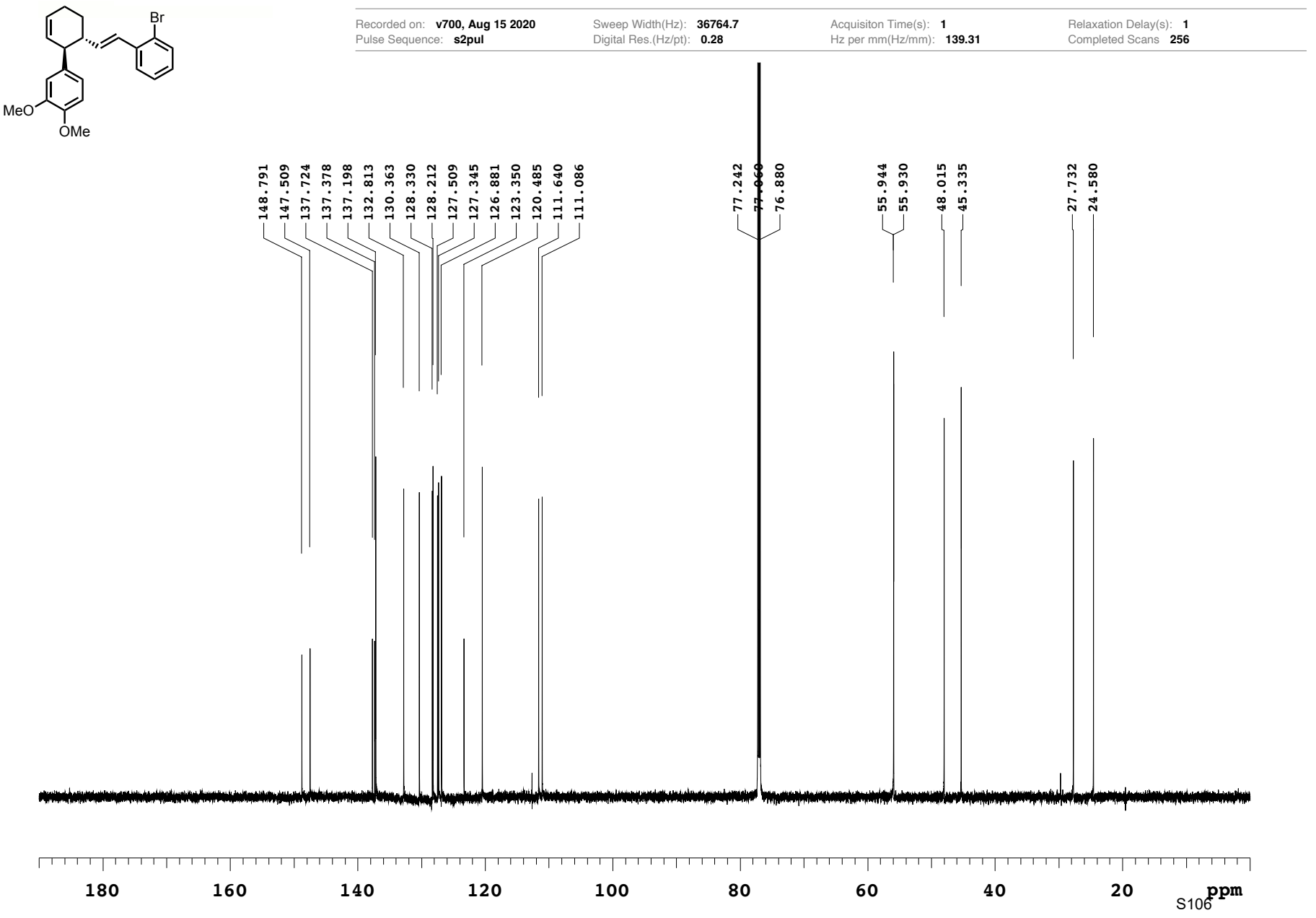


**Figure S67:** $^{1}H$ NMR spectrum of compound **13** ($CDCl_3$, 700 MHz)

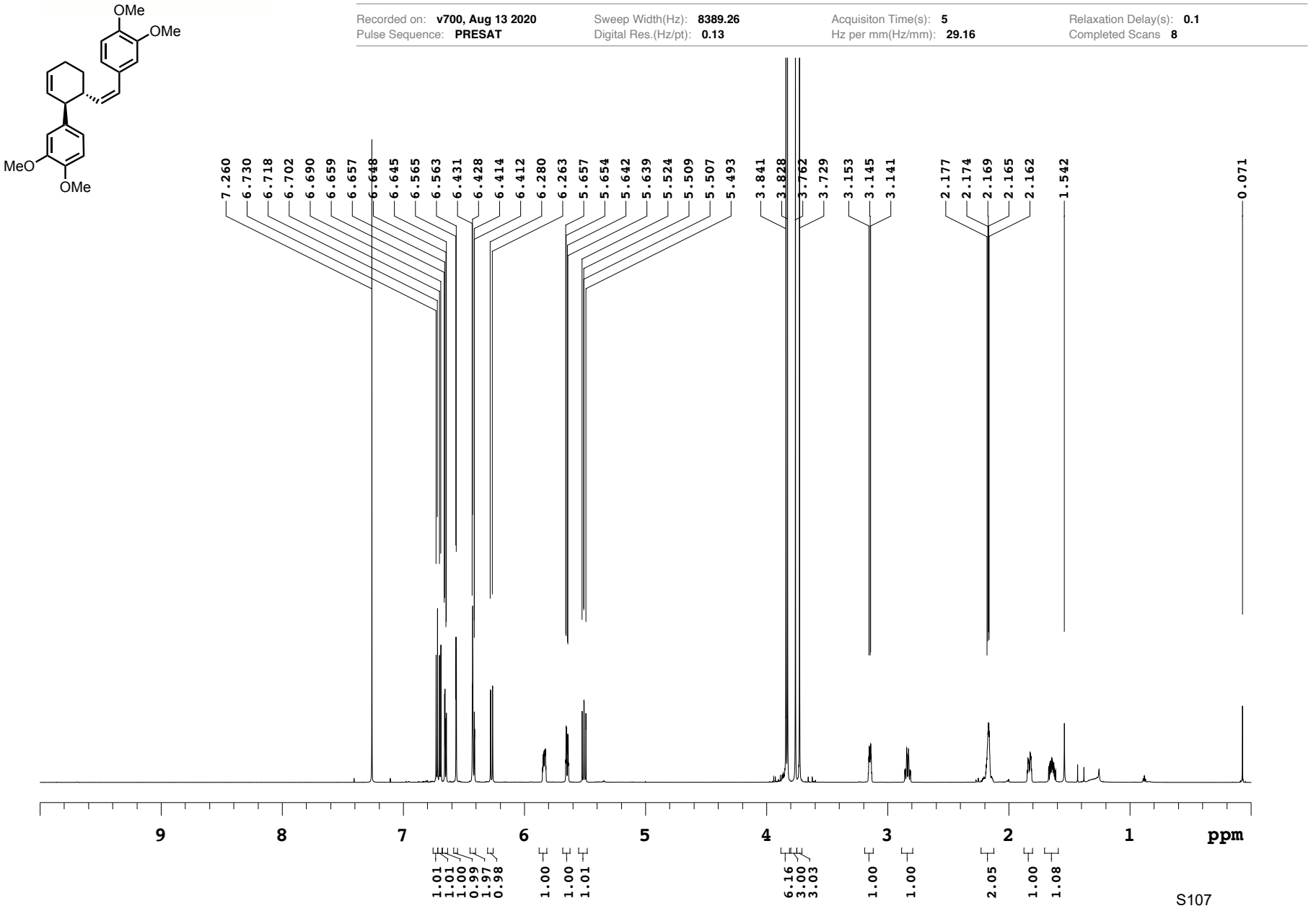
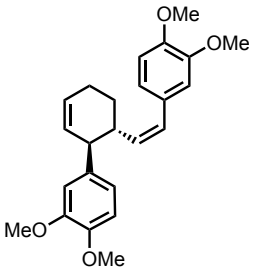
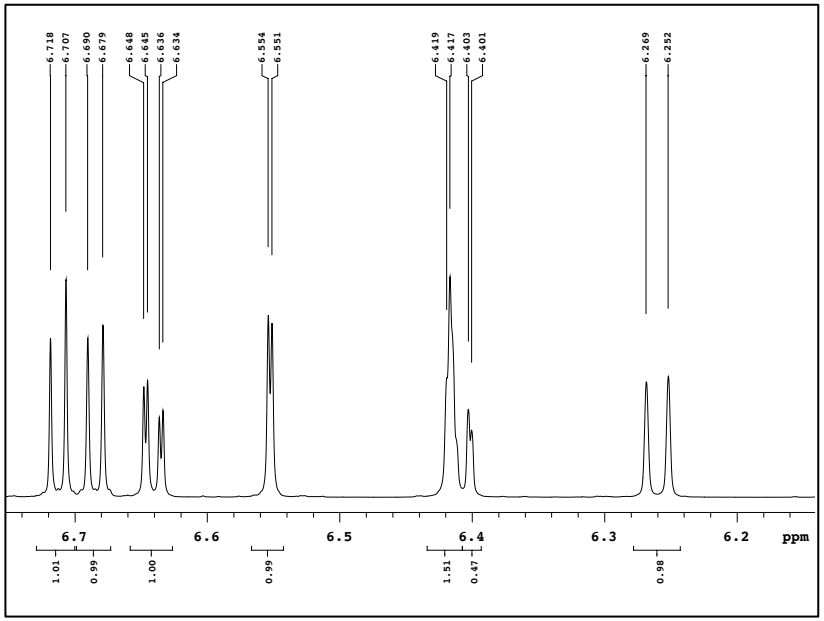


**Figure S68:** $^{1}$H NMR magnified spectrum of compound **13** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 13 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



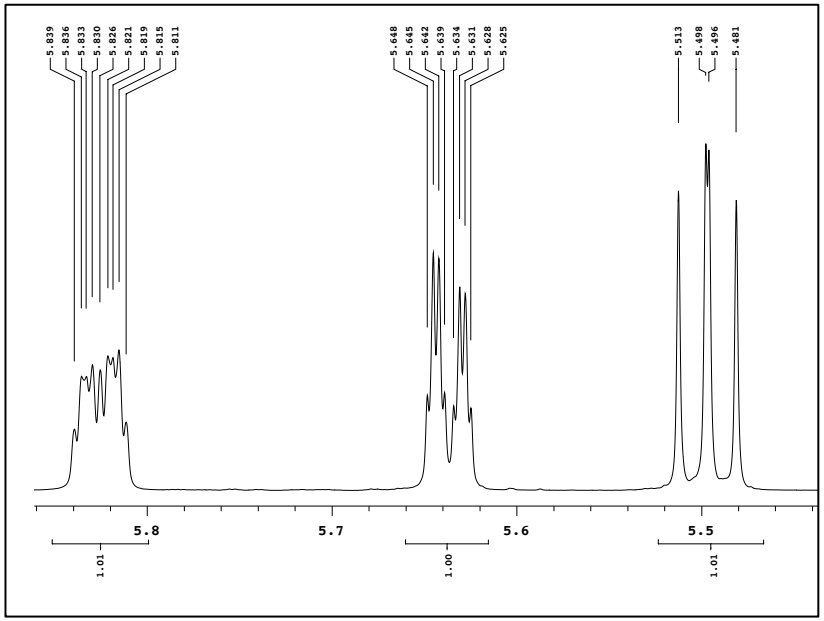
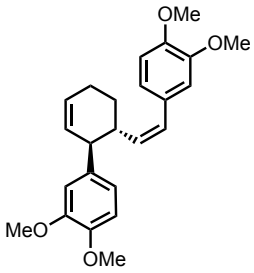
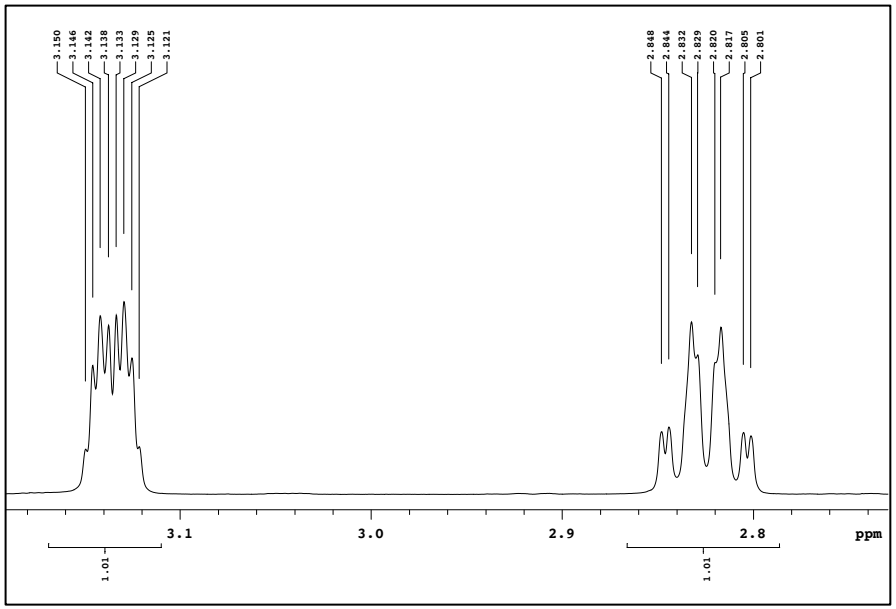



**Figure S69:** $^1$H NMR magnified spectrum of compound **13** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 13 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



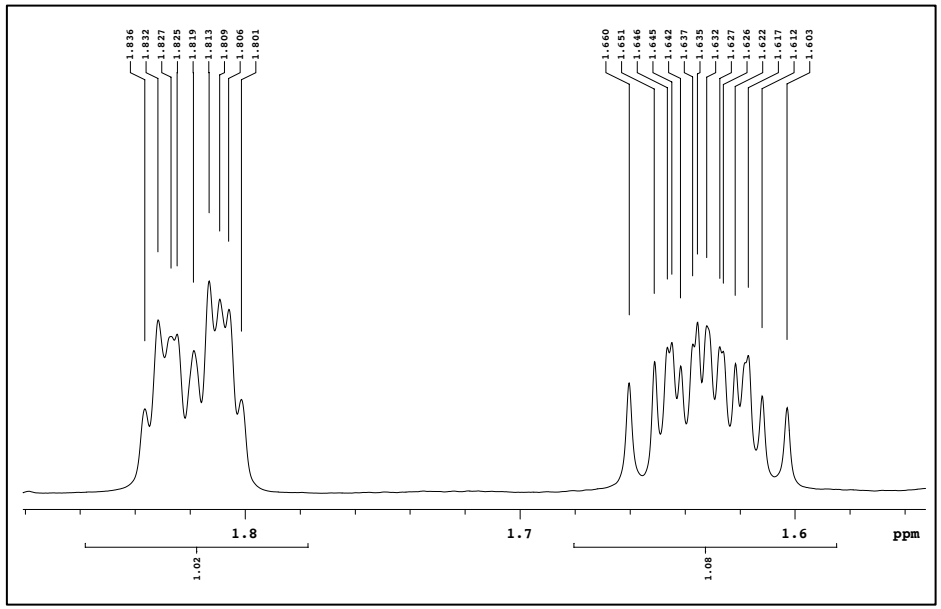



**Figure S70:** $^{13}C$ NMR spectrum of compound **13** ($CDCl_3$, 176 MHz)

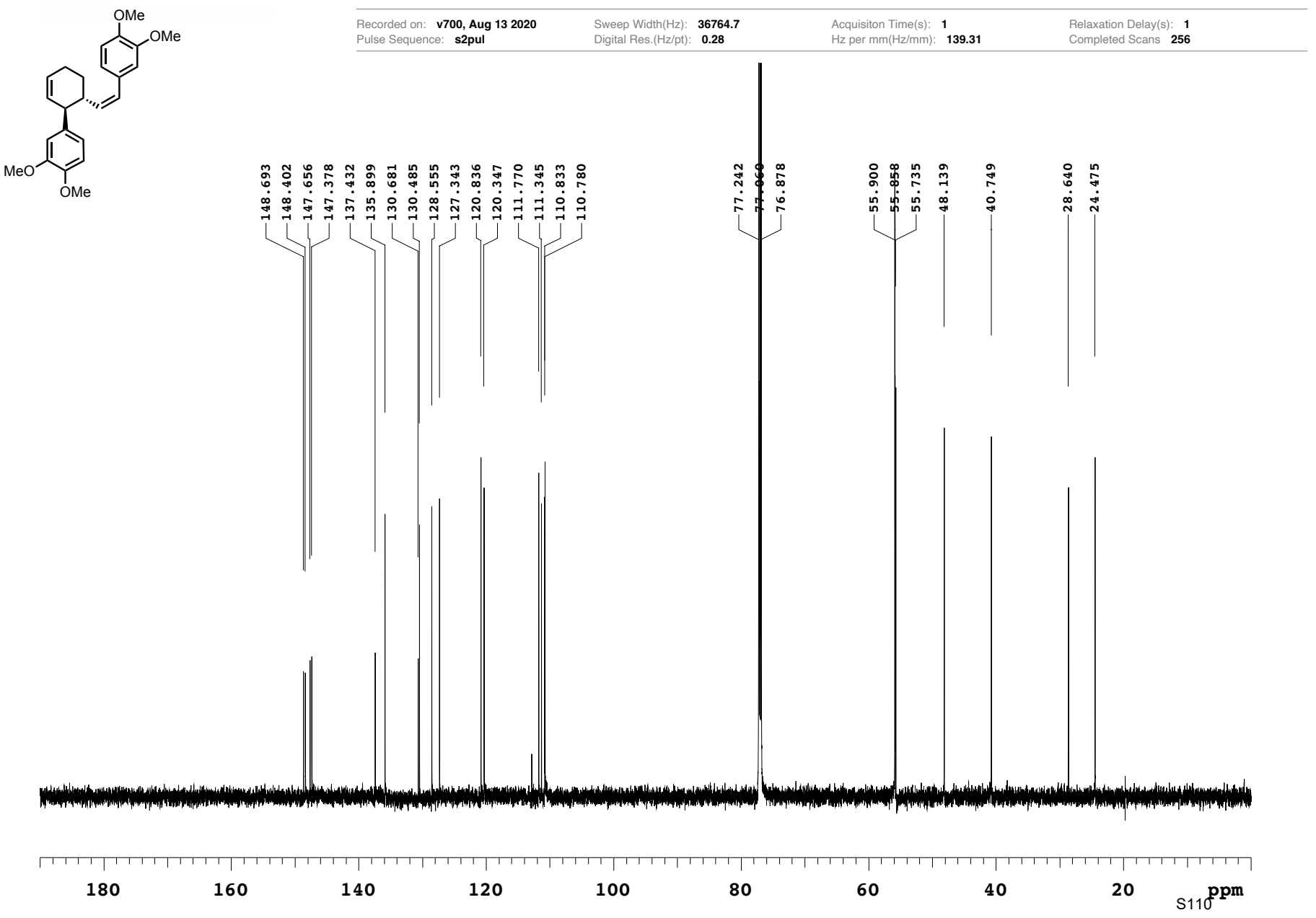


**Figure S71:** $^{1}H$ NMR spectrum of compound **14** ($CDCl_3$, 500 MHz)

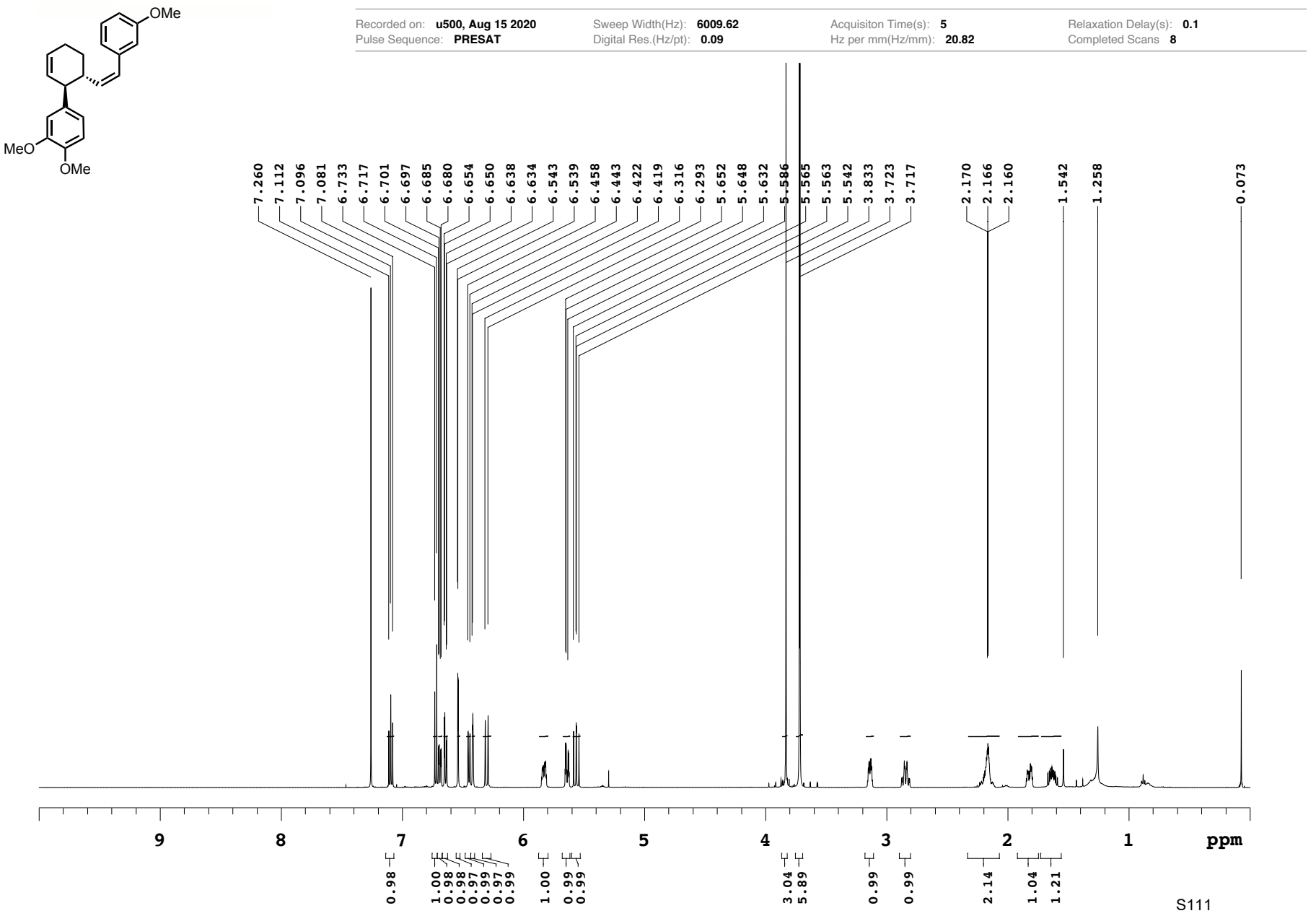


**Figure S72:** $^{13}C$ NMR spectrum of compound **14** ($CDCl_3$, 126 MHz)

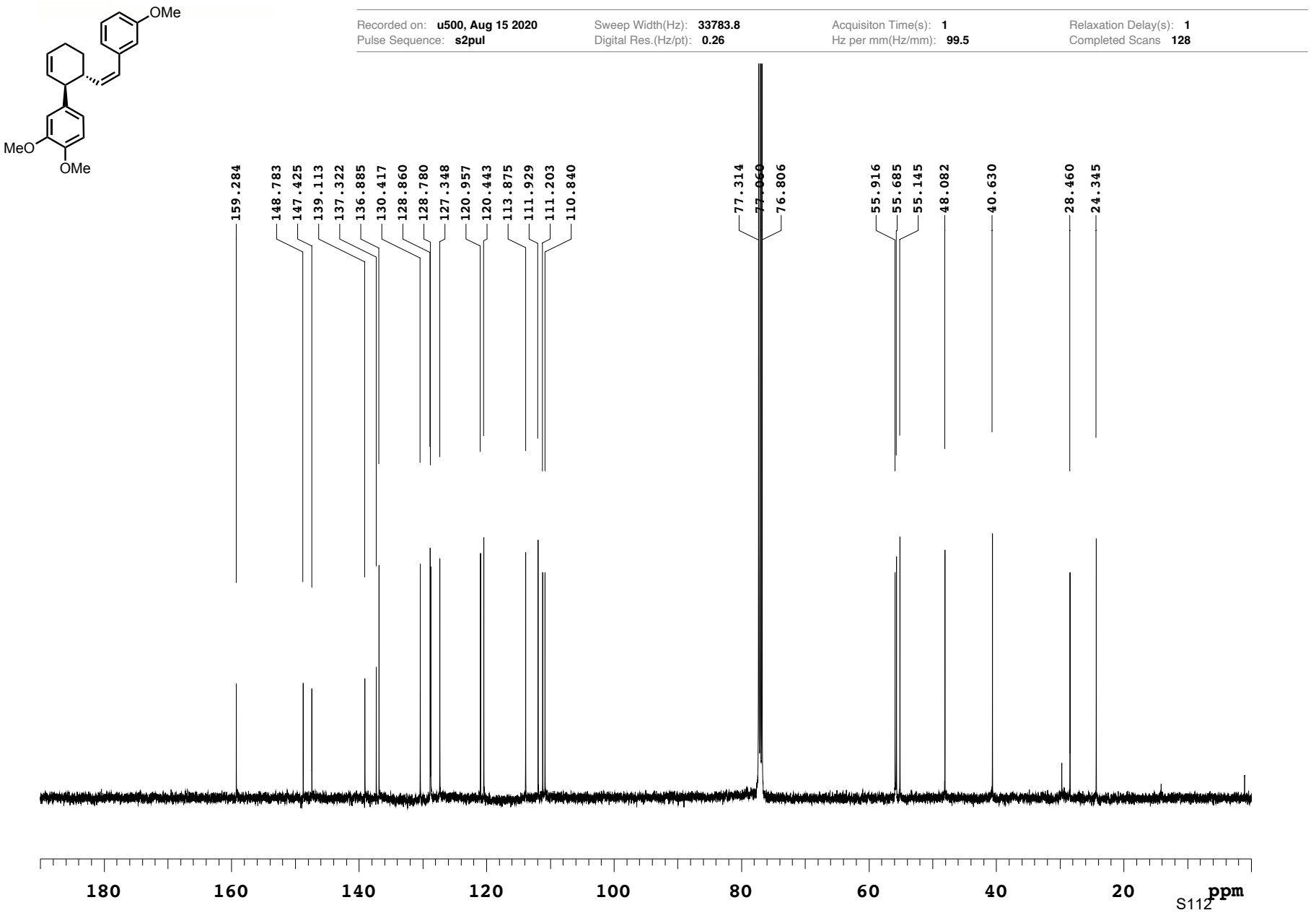


**Figure S73:** $^{1}H$ NMR spectrum of compound **15** ($CDCl_3$, 500 MHz)

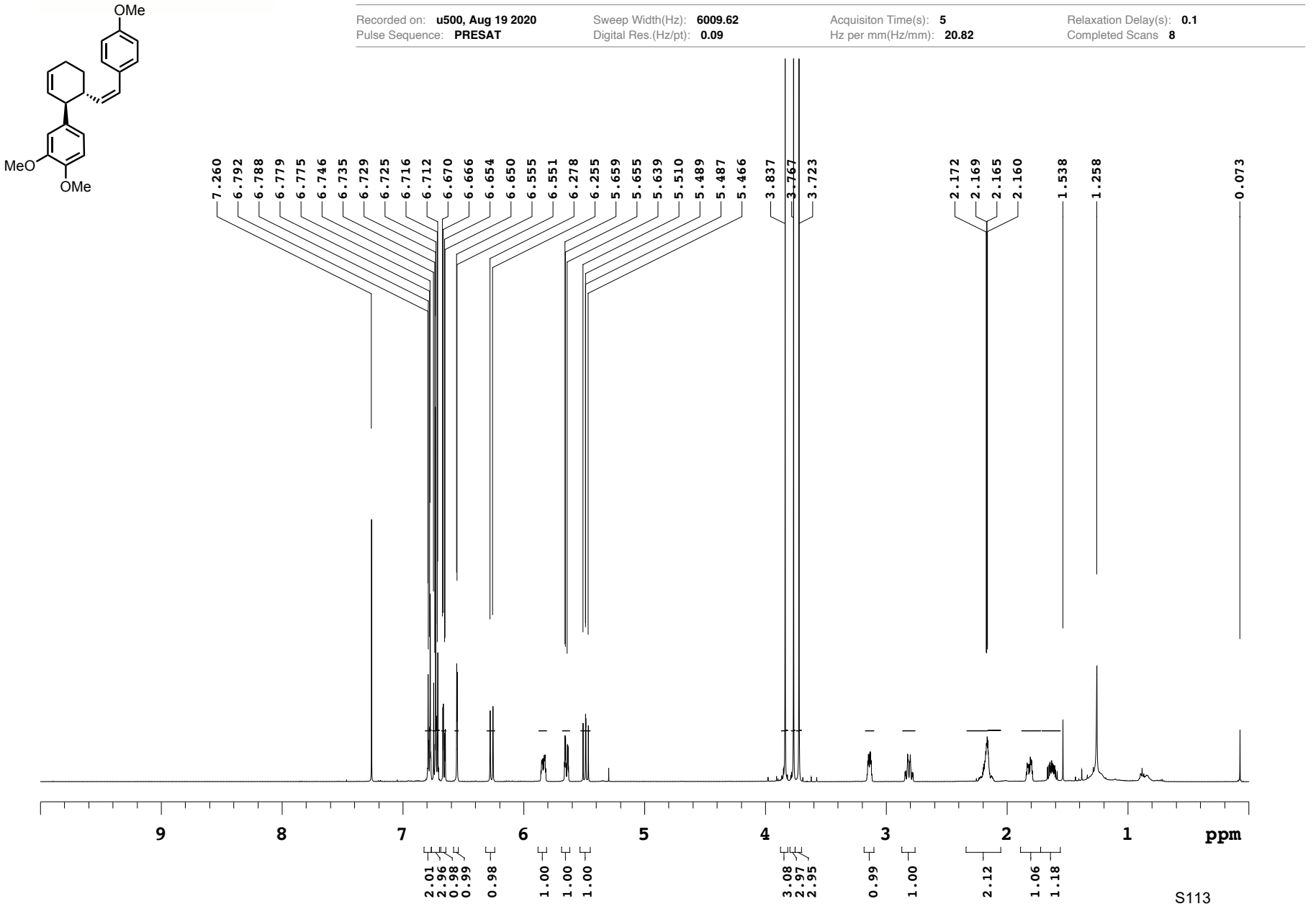


**Figure S74:** $^{13}C$ NMR spectrum of compound **15** ($CDCl_3$, 126 MHz)

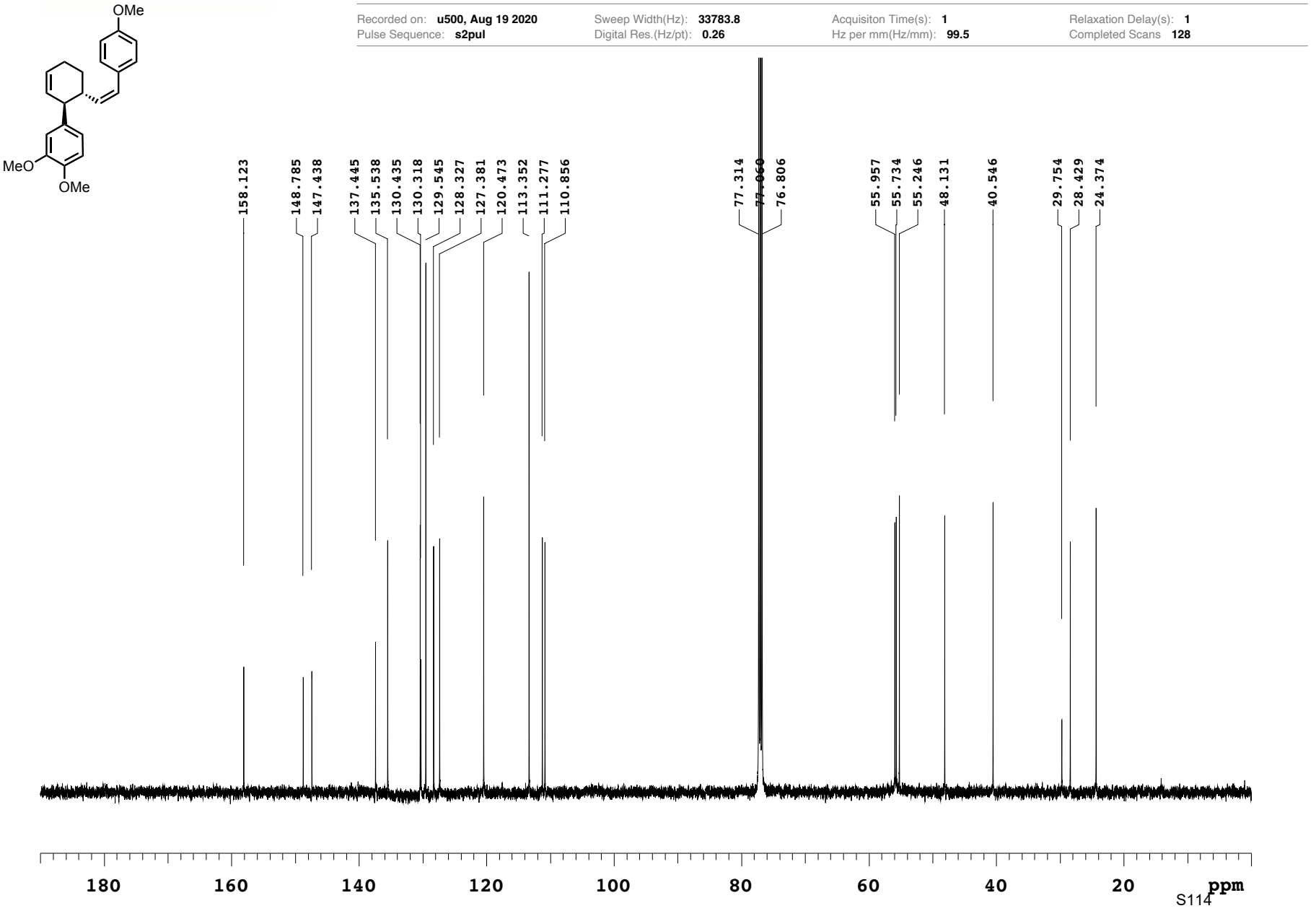


**Figure S75:** $^{1}H$ NMR spectrum of compound **16** ($CDCl_3$, 700 MHz)

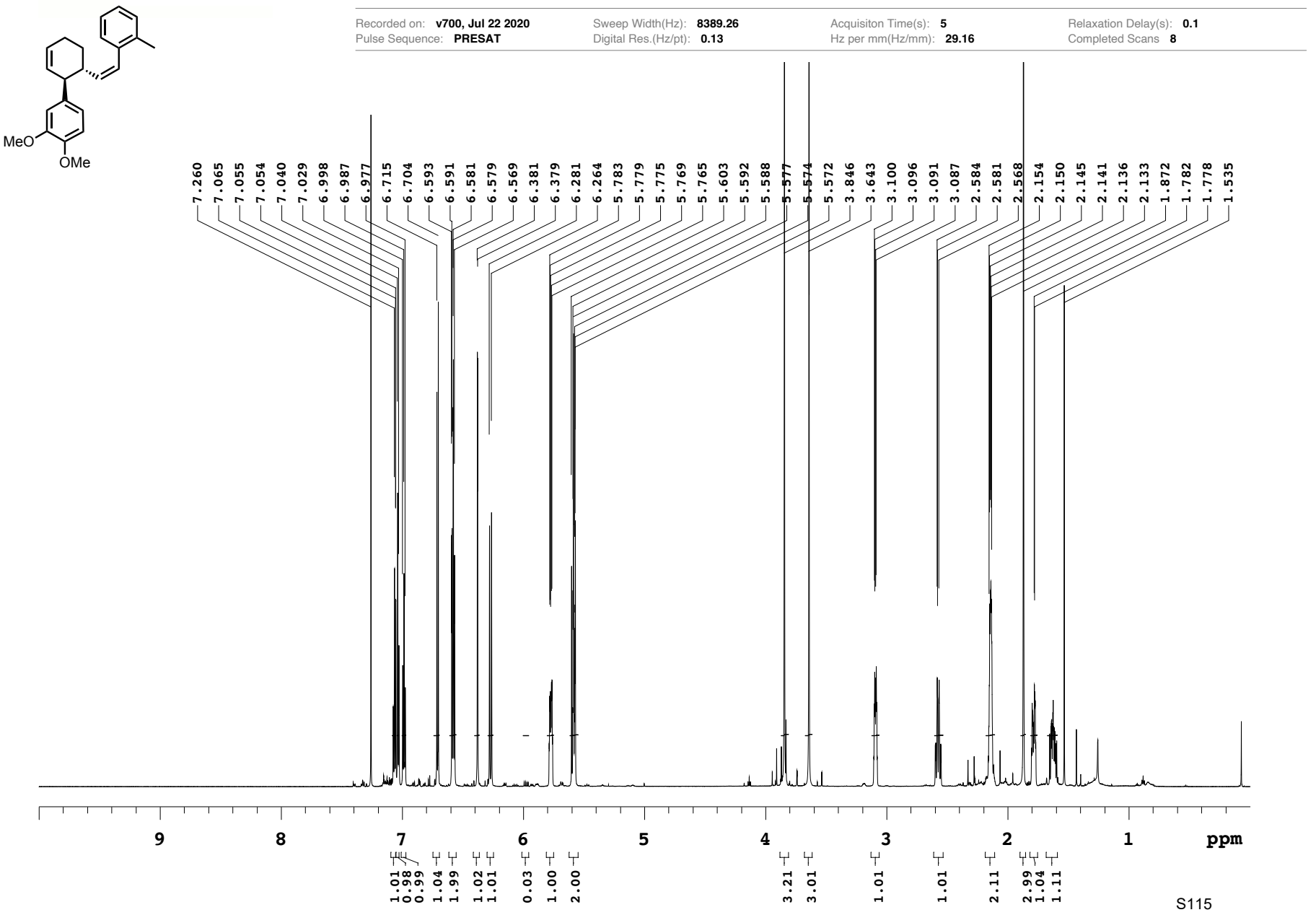


**Figure S76:** $^{13}C$ NMR spectrum of compound **16** ($CDCl_3$, 176 MHz)

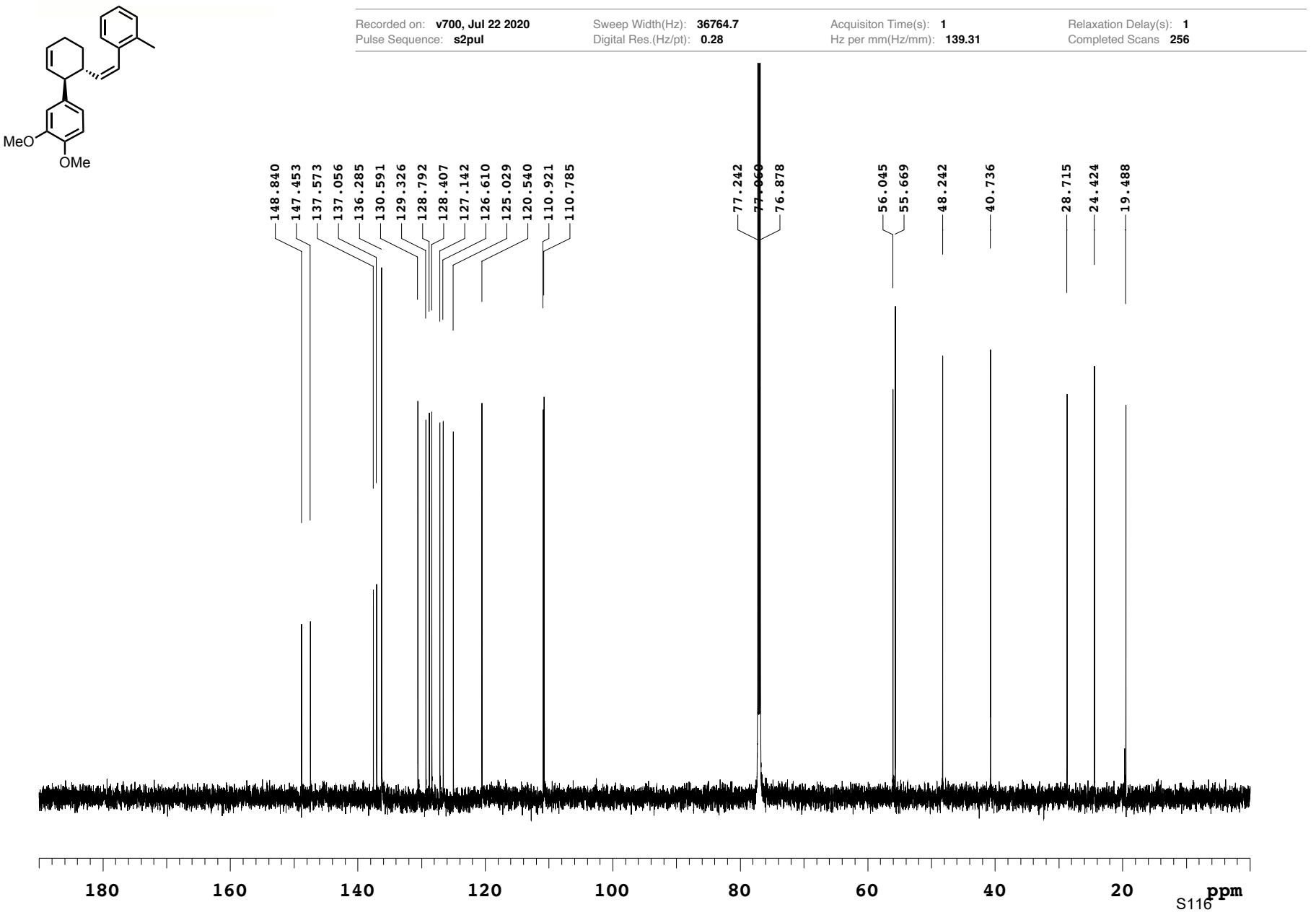


**Figure S77:** $^{1}H$ NMR spectrum of compound **17** ($CDCl_3$, 700 MHz)

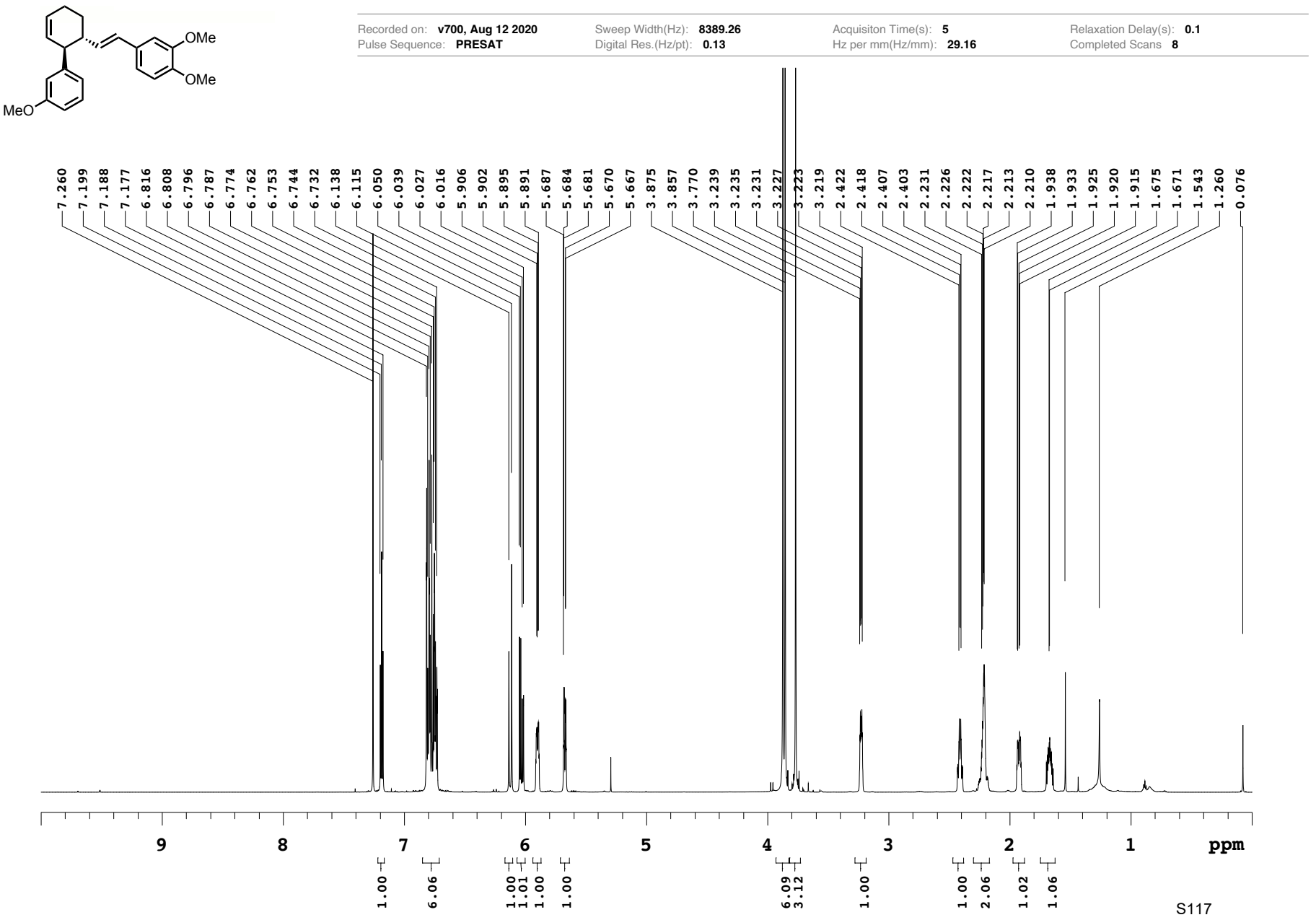
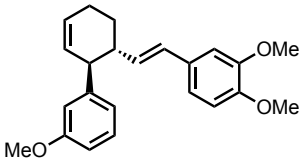


**Figure S78:** $^1$H NMR magnified spectrum of compound **17** ($CDCl_3$, 700 MHz)

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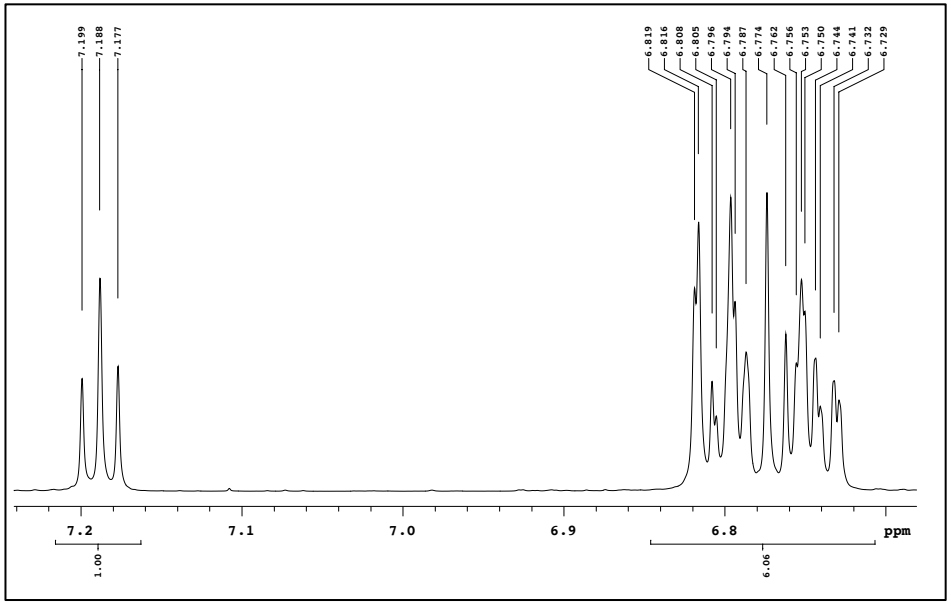
|---|---|---|---|
| Recorded on: **v700, Aug 12 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



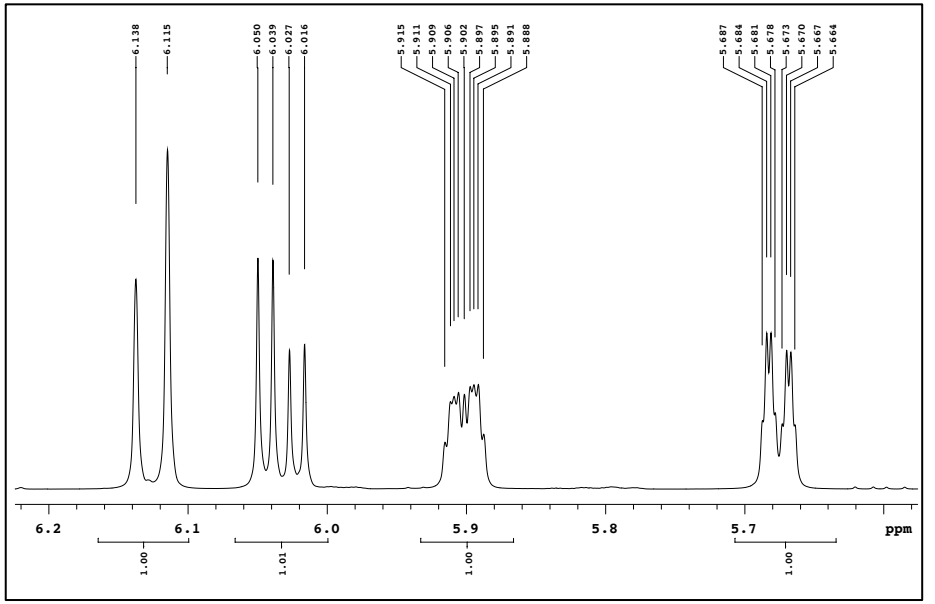
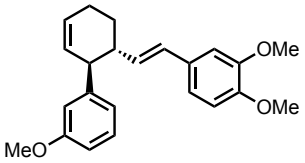
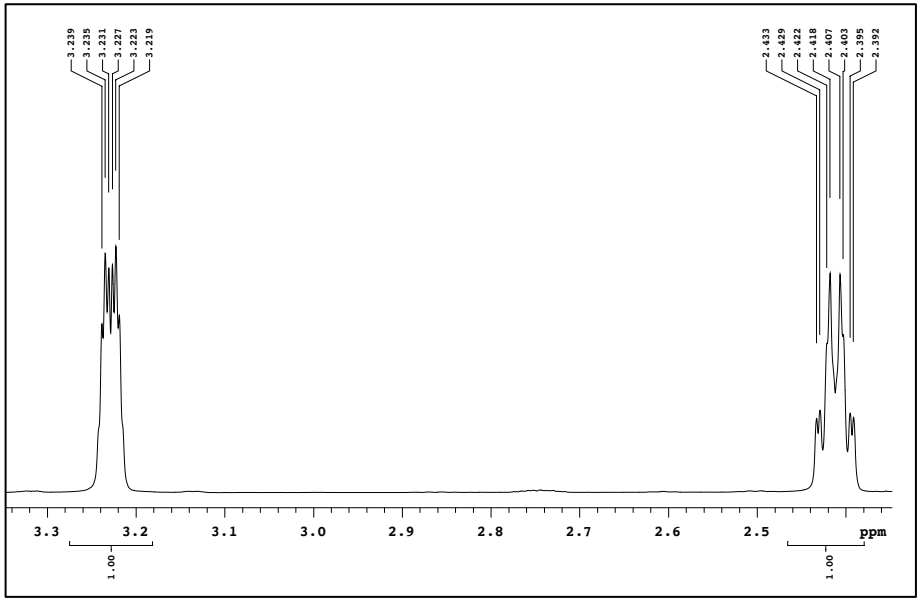



**Figure S79:** $^1$H NMR magnified spectrum of compound **17** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 12 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



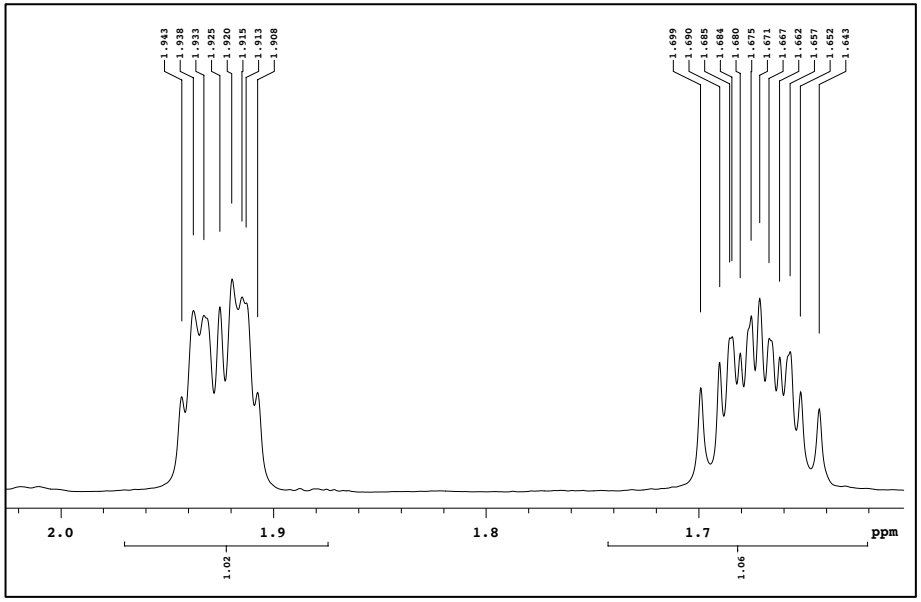



**Figure S80:** $^{13}C$ NMR spectrum of compound **17** ($CDCl_3$, 176 MHz)

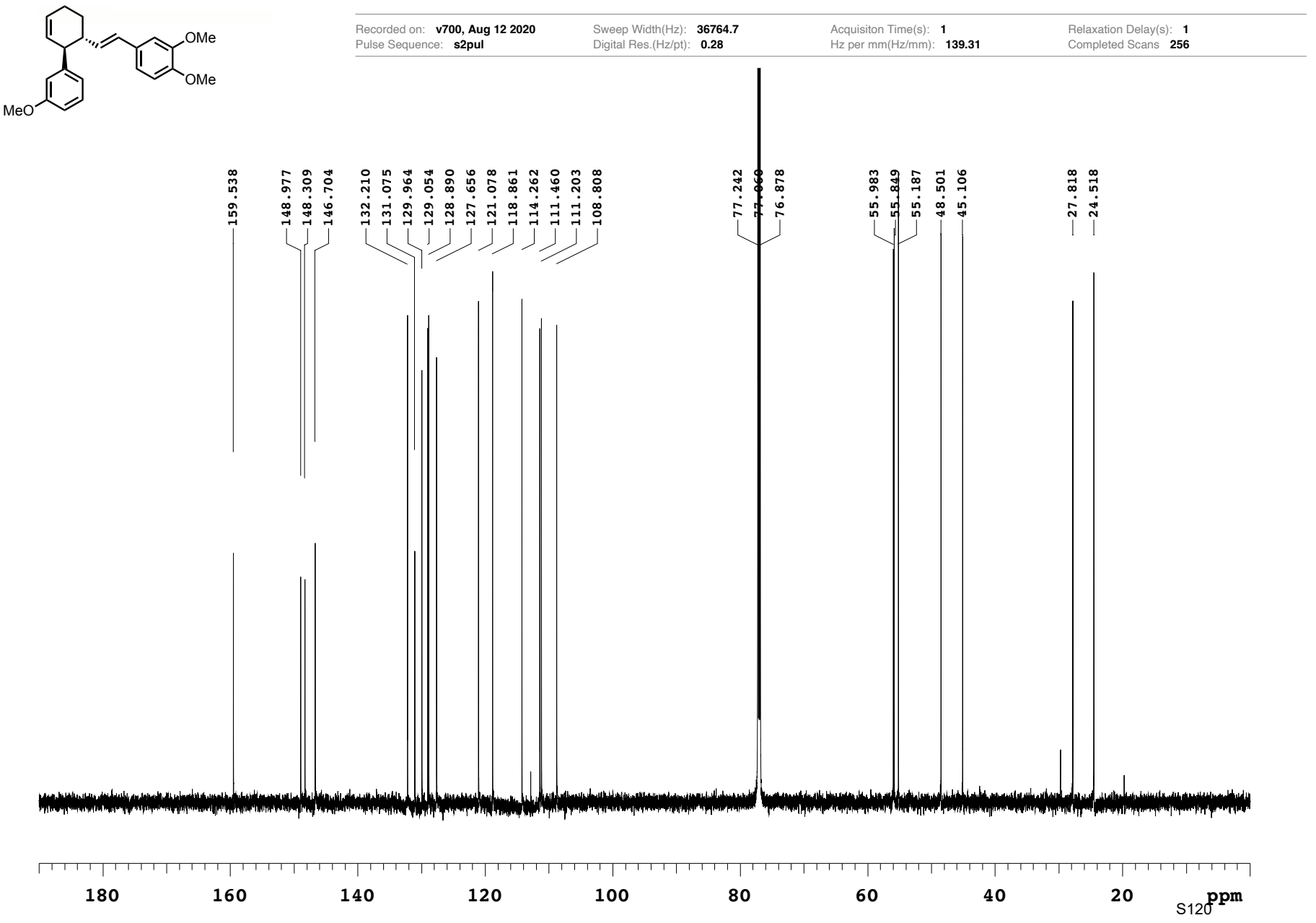
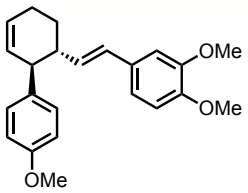


**Figure S81:** $^{1}H$ NMR spectrum of compound **18** ($CDCl_3$, 500 MHz)




Recorded on: **u500, Aug 14 2020** | Sweep Width(Hz): **6009.62** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.09** | Hz per mm(Hz/mm): **20.82** | Completed Scans **8**

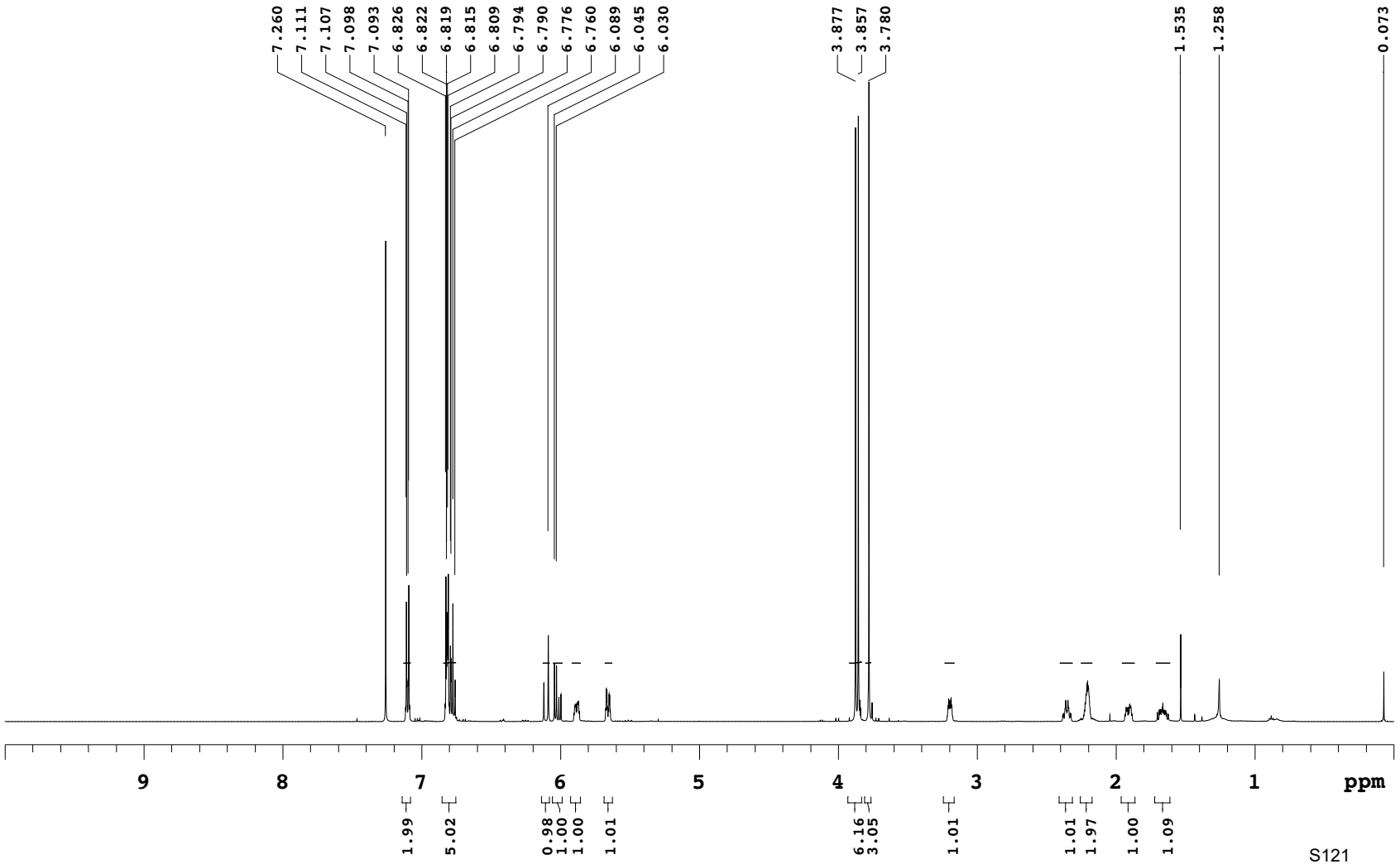


**Figure S82:** $^{13}C$ NMR spectrum of compound **18** ($CDCl_3$, 126 MHz)

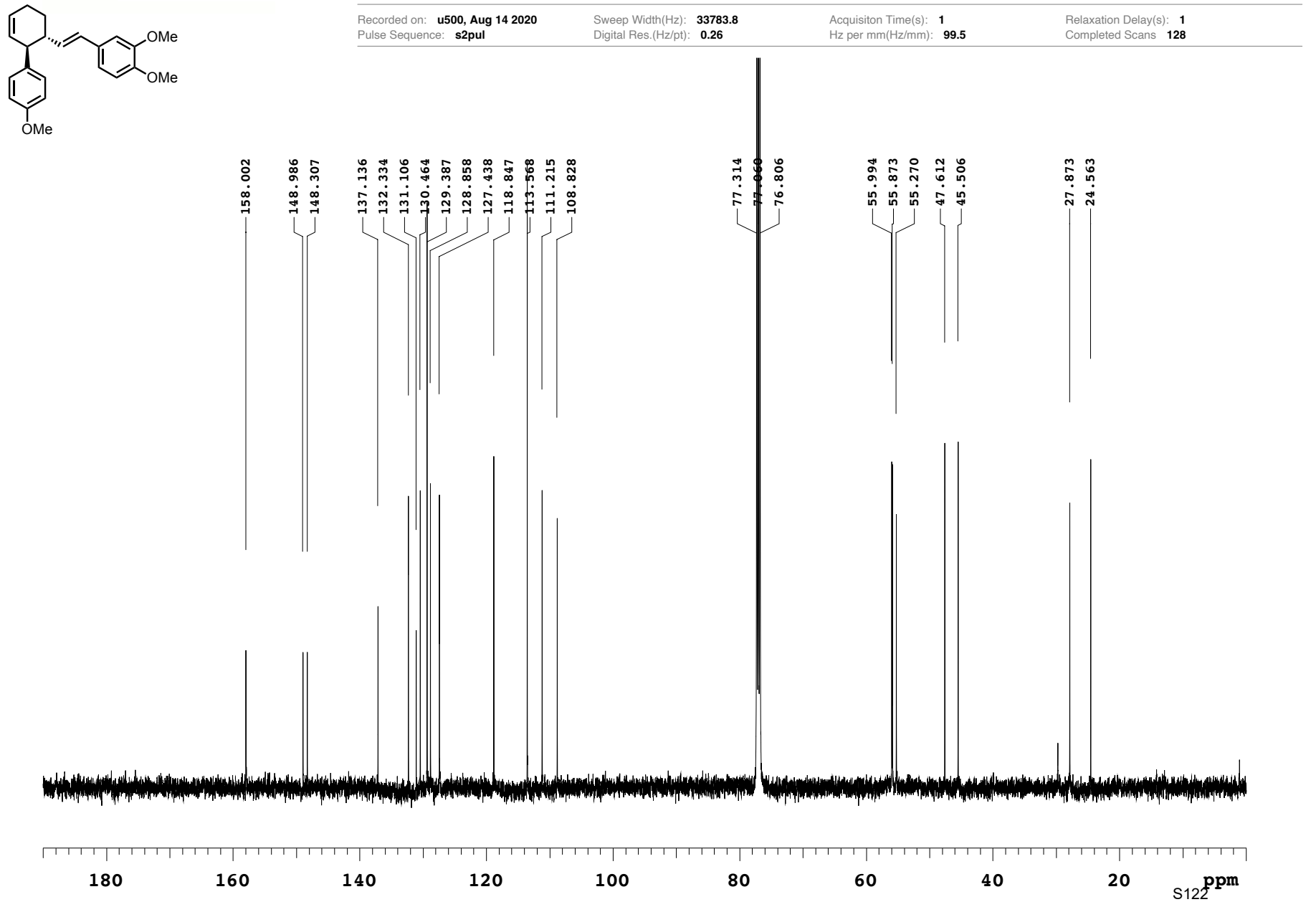


**Figure S83:** $^{1}$H NMR spectrum of compound **19** ($CDCl_3$, 500 MHz)

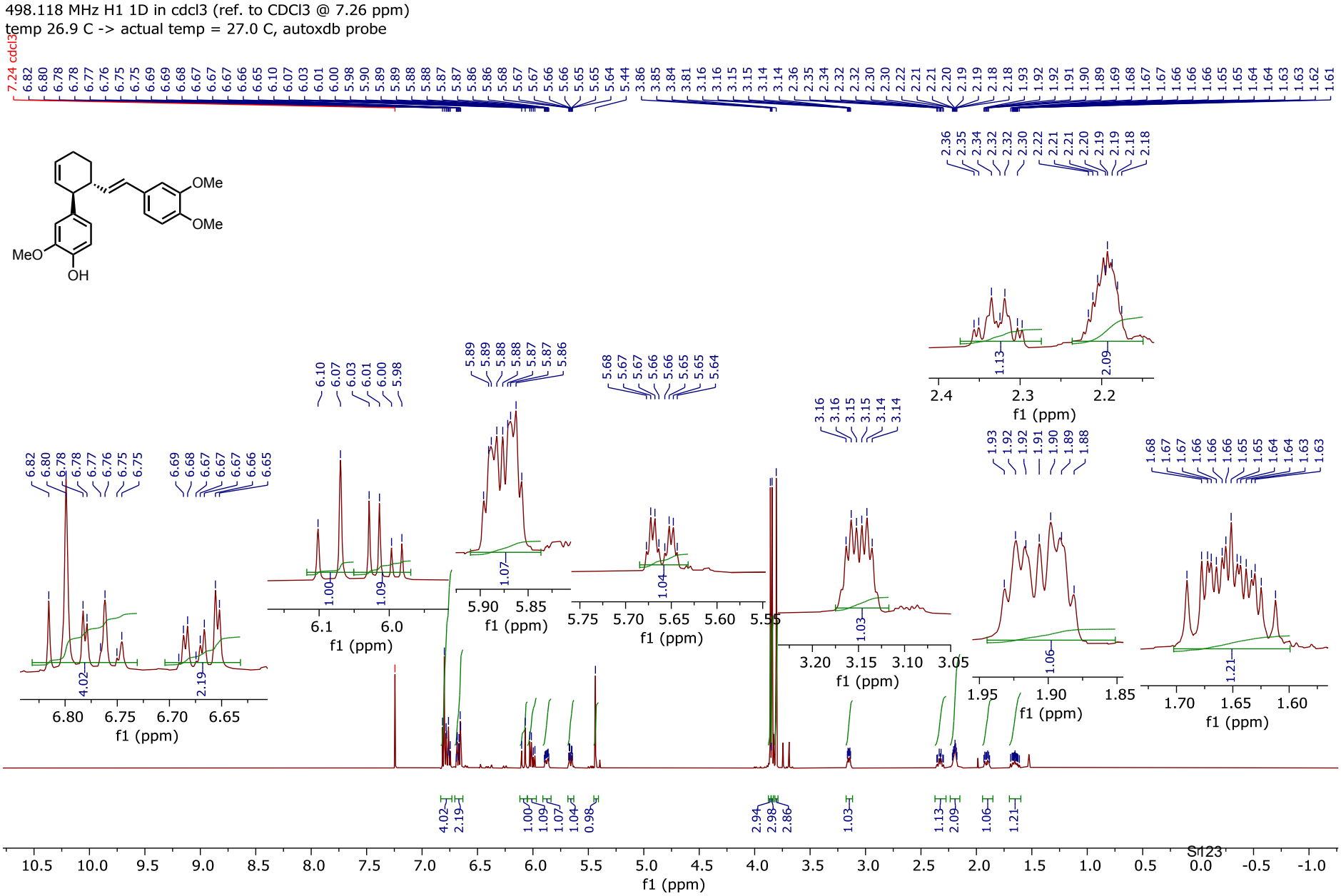


**Figure S84:** $^{13}C$ NMR spectrum of compound **19** ($CDCl_3$, 126 MHz)

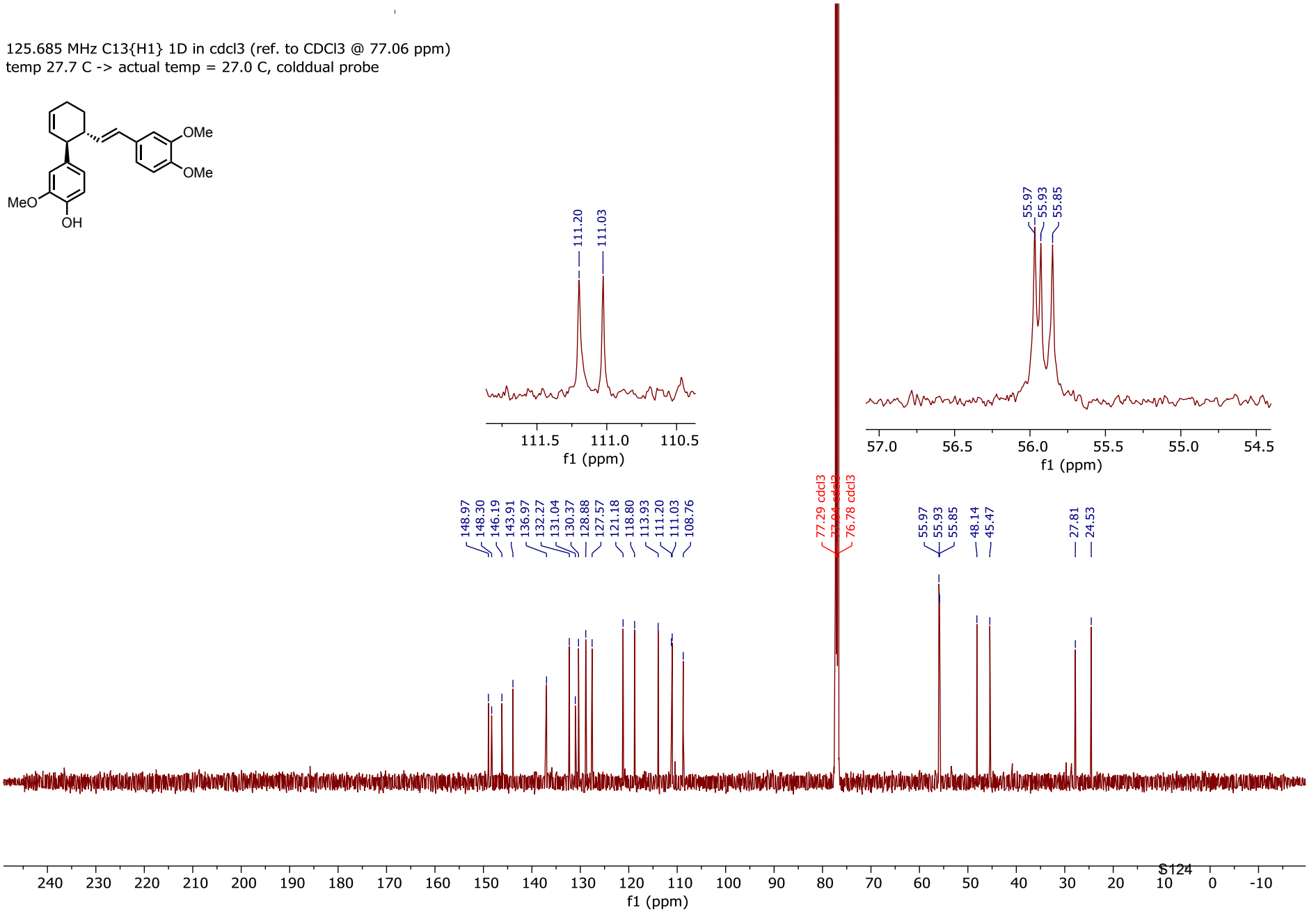


**Figure S85:** $^{1}H$ NMR spectrum of compound **20** ($CDCl_3$, 700 MHz)

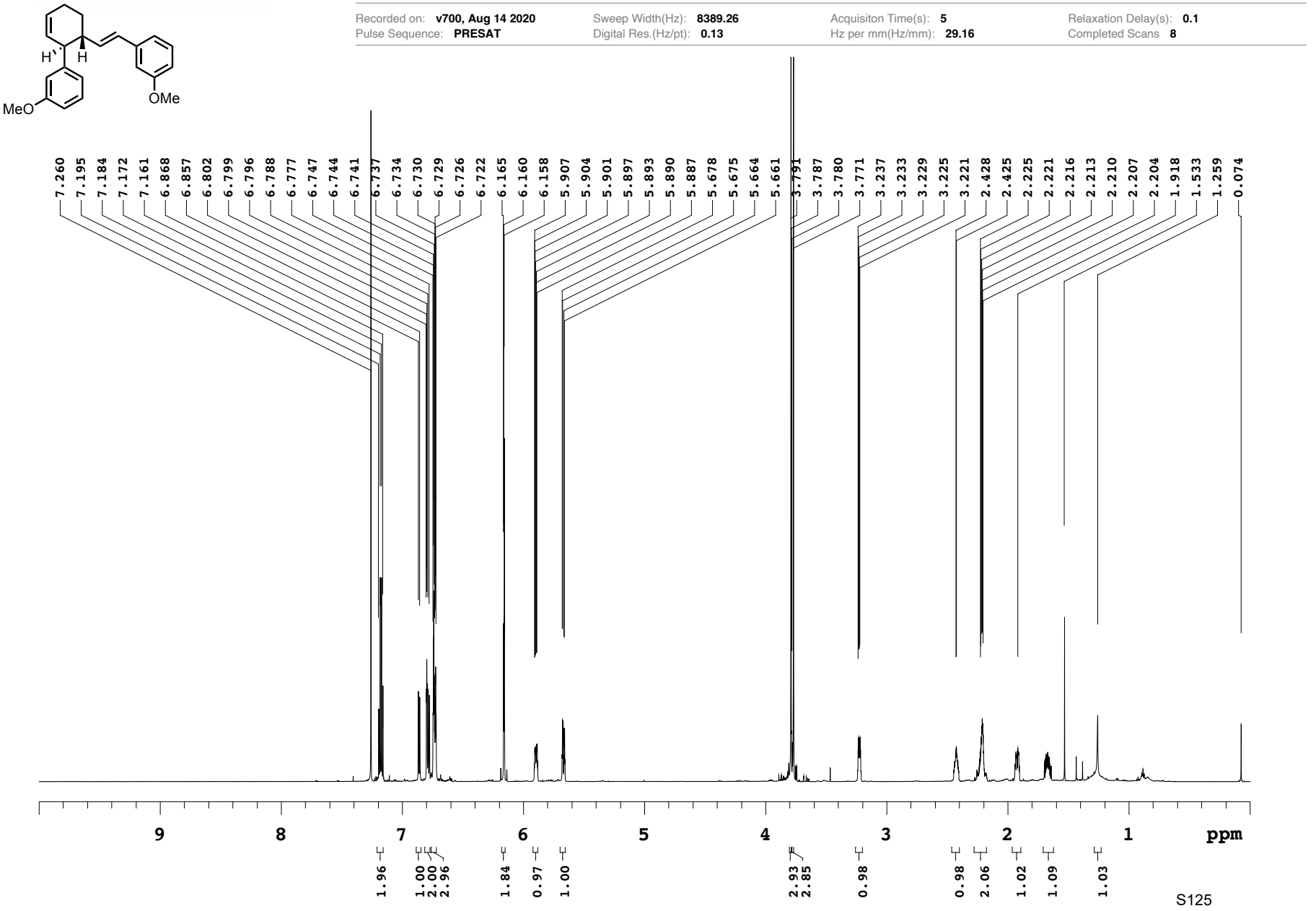
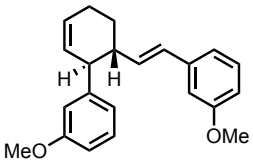
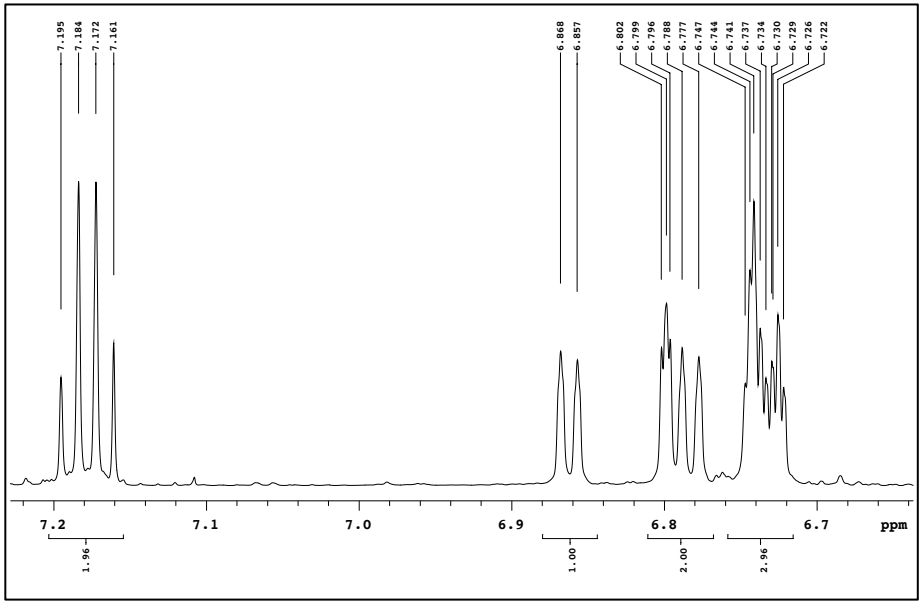


**Figure S86:** $^1$H NMR magnified spectrum of compound **20** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 14 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



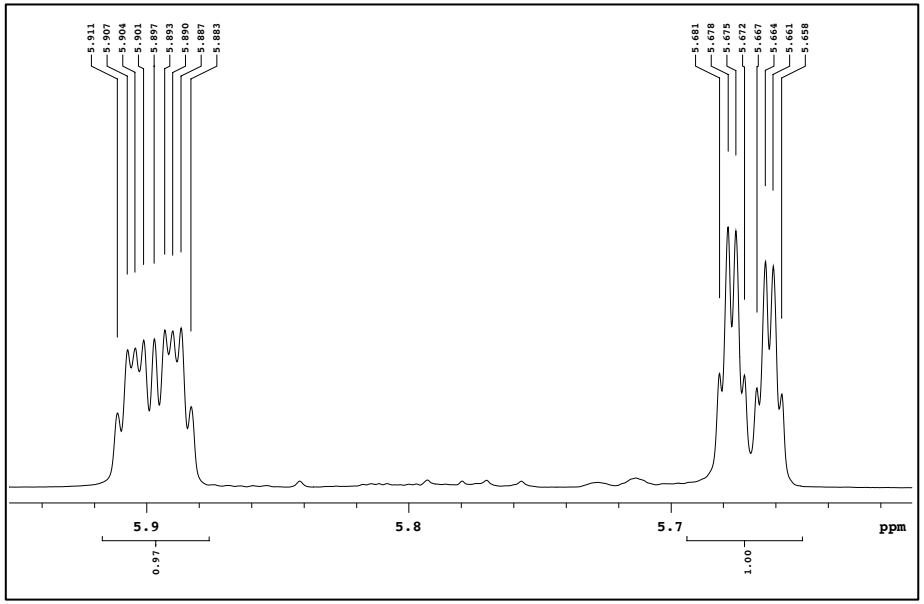
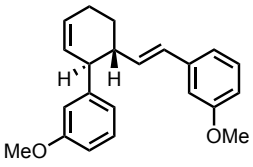
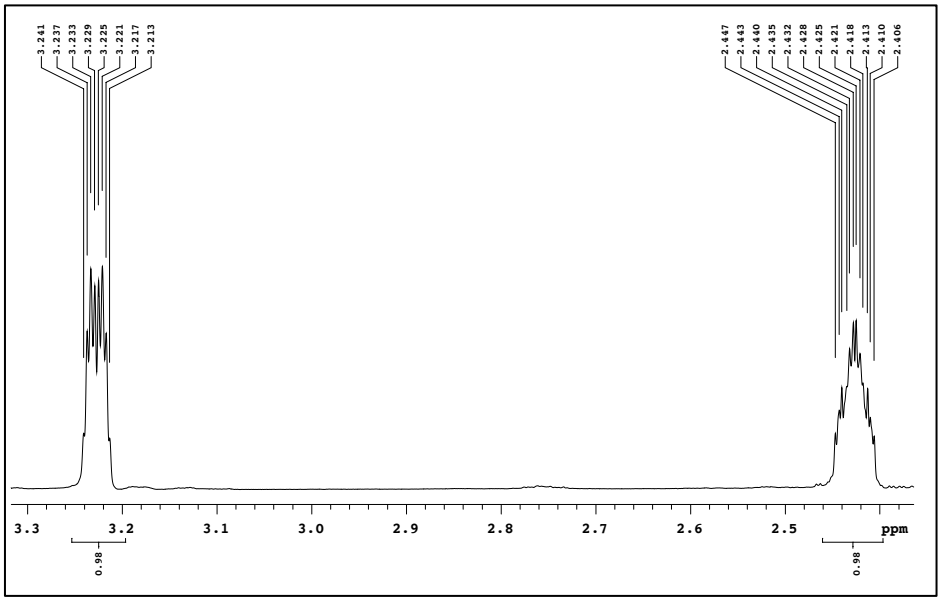



**Figure S87:** $^1$H NMR magnified spectrum of compound **20** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 14 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



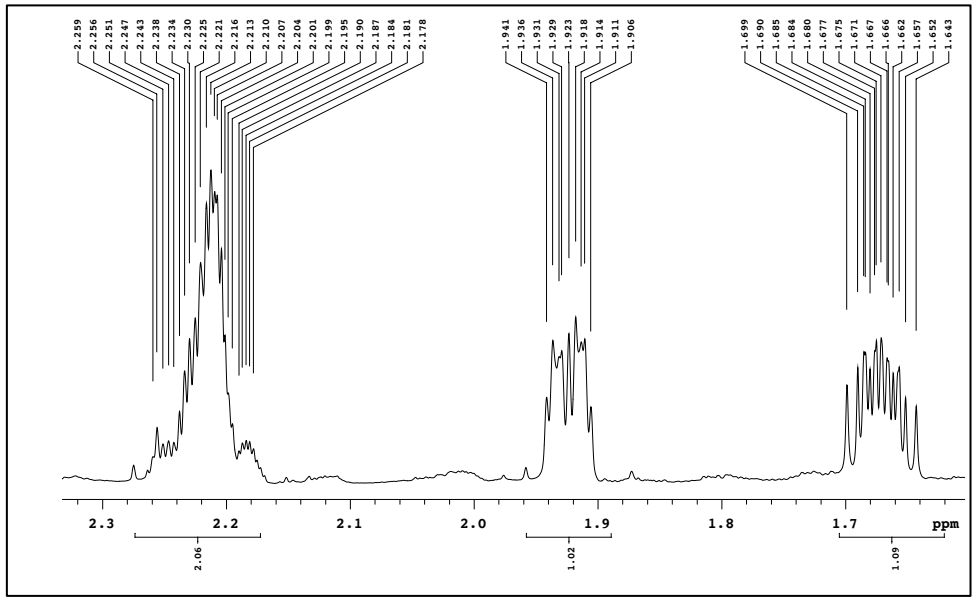



**Figure S88:** $^{13}C$ NMR spectrum of compound **20** ($CDCl_3$, 176 MHz)

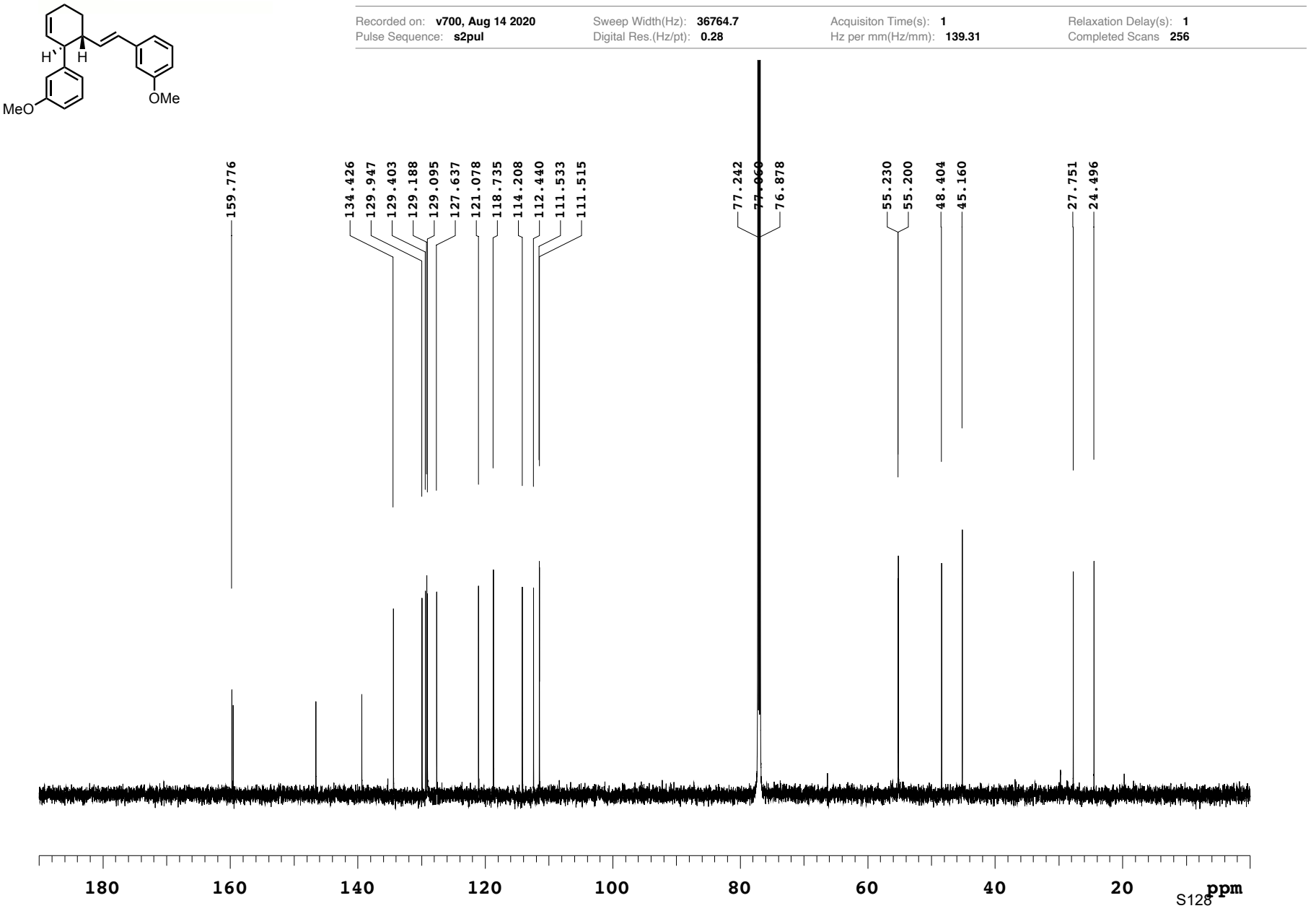


**Figure S89:** $^{1}H$ NMR spectrum of compound **21** ($CDCl_3$, 700 MHz)

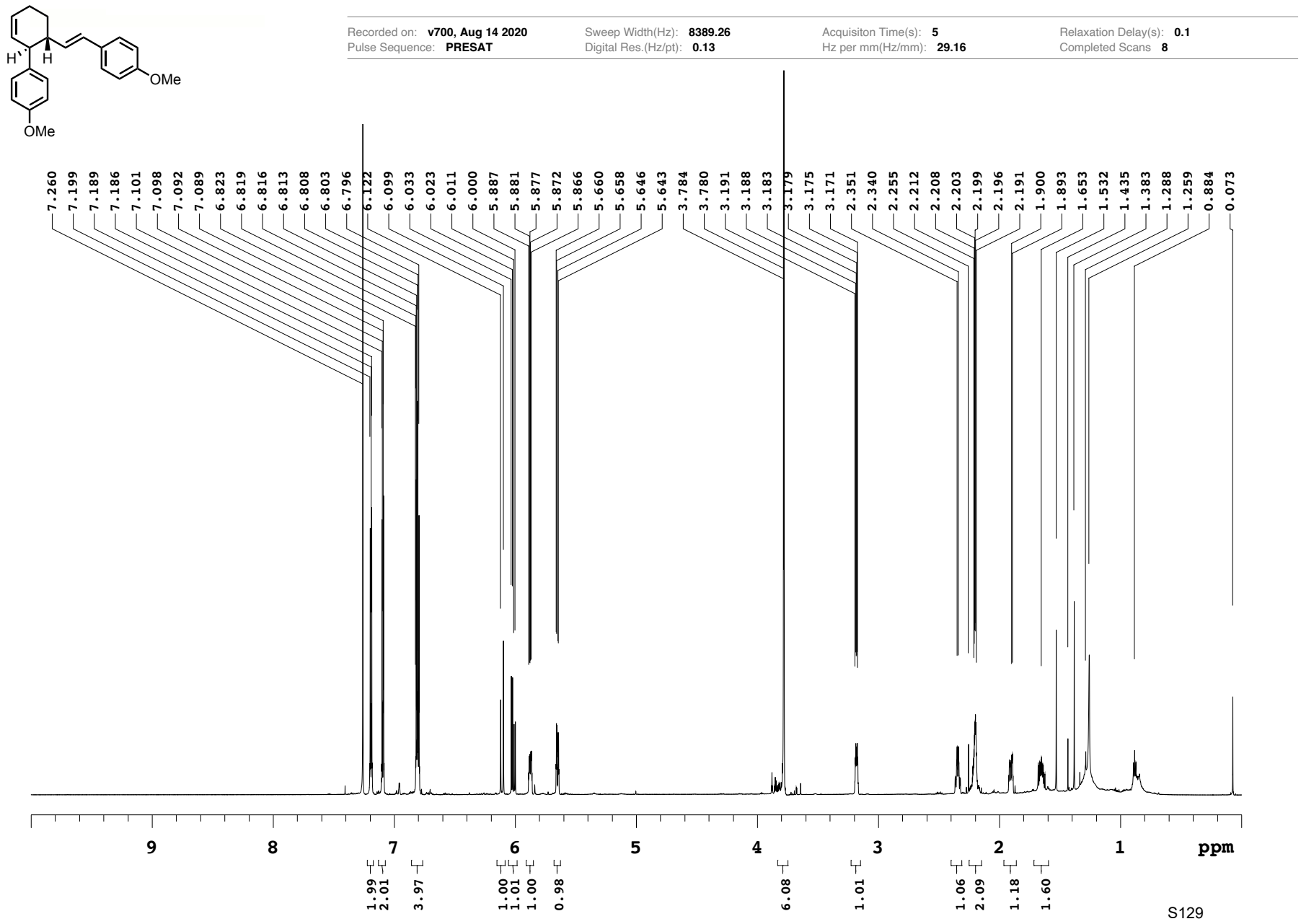
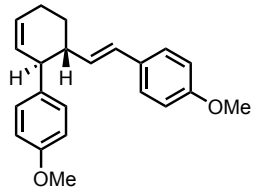
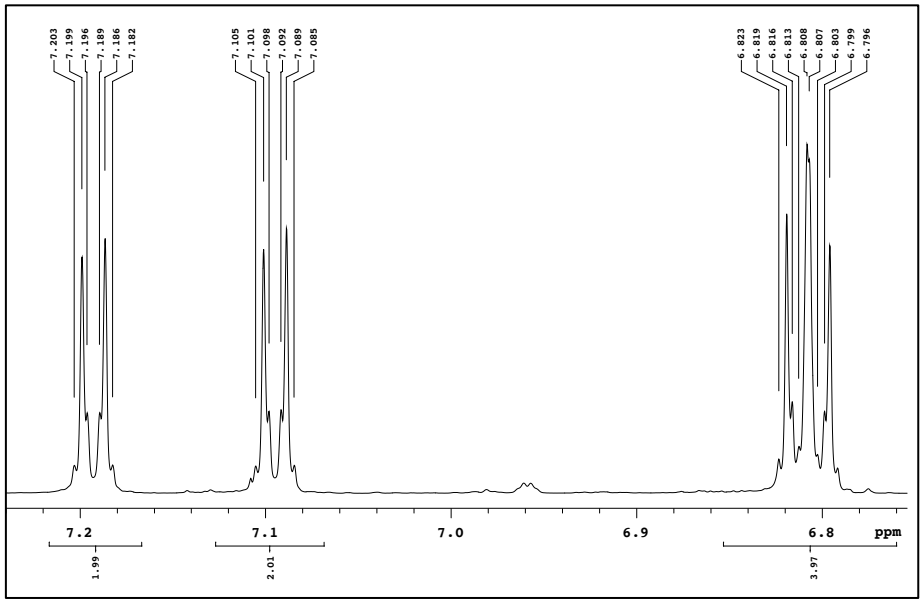


**Figure S90:** $^1$H NMR magnified spectrum of compound **21** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 14 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



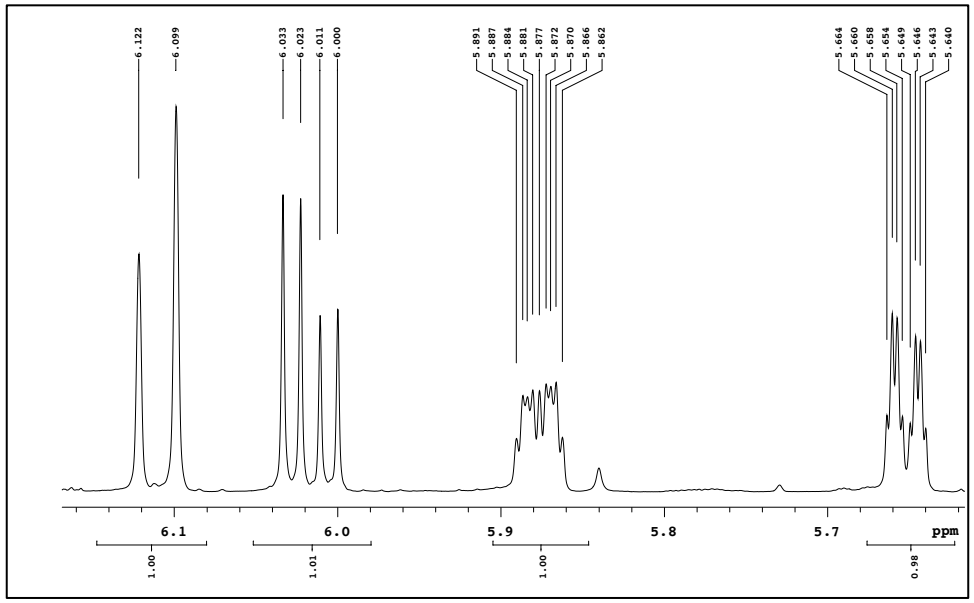
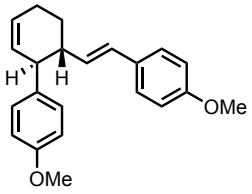



**Figure S91:** $^{1}$H NMR magnified spectrum of compound **21** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 14 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |

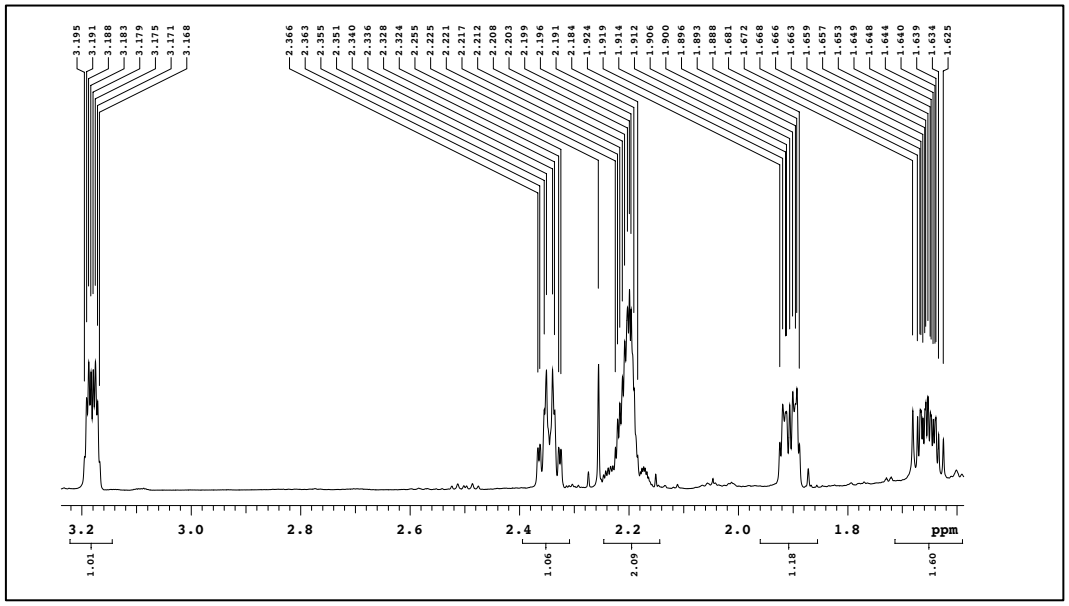
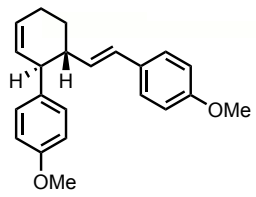


**Figure S92:** $^{13}C$ NMR spectrum of compound **21** ($CDCl_3$, 176 MHz)




Recorded on: **v700, Aug 14 2020** Sweep Width(Hz): **36764.7** Acquisiton Time(s): **1** Relaxation Delay(s): **1**
Pulse Sequence: **s2pul** Digital Res.(Hz/pt): **0.28** Hz per mm(Hz/mm): **139.31** Completed Scans **256**

158.714 157.981 137.169 132.091 130.780 130.517 129.384 128.536 127.413 127.115 113.894 113.567 77.242 77.060 76.878 55.339 55.267 47.679 45.484 27.881 24.598

180 160 140 120 100 80 60 40 20 ppm

**Figure S93:** $^{1}H$ NMR spectrum of compound **22** ($CDCl_3$, 700 MHz)

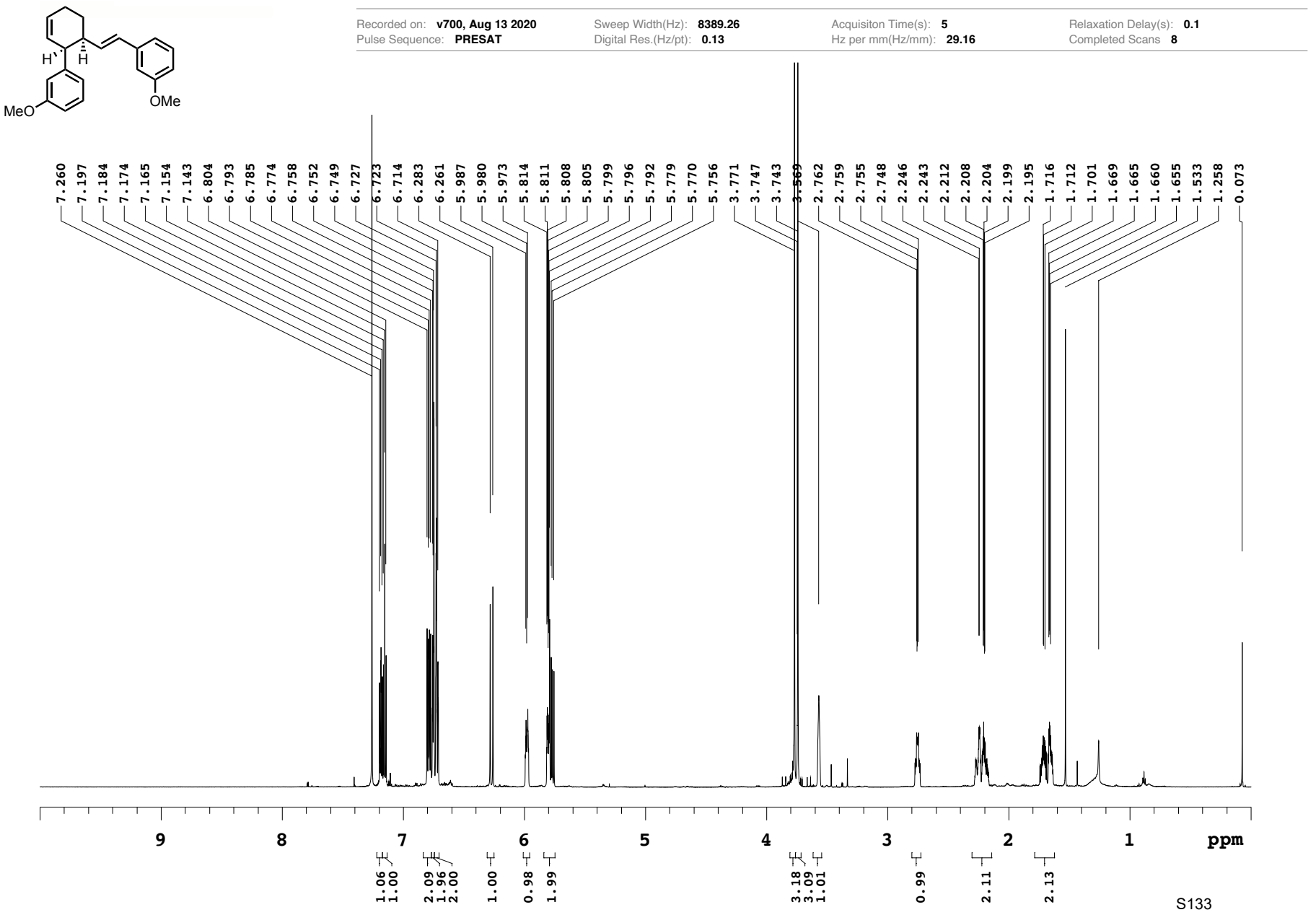
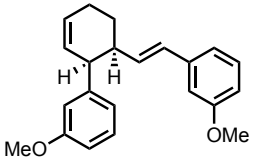
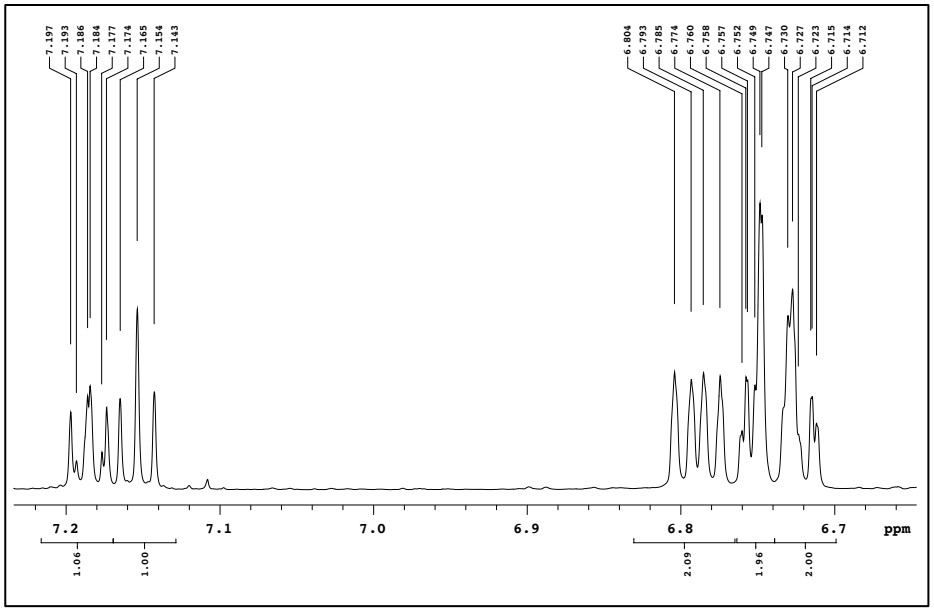


**Figure S94:** $^1$H NMR magnified spectrum of compound **22** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 13 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



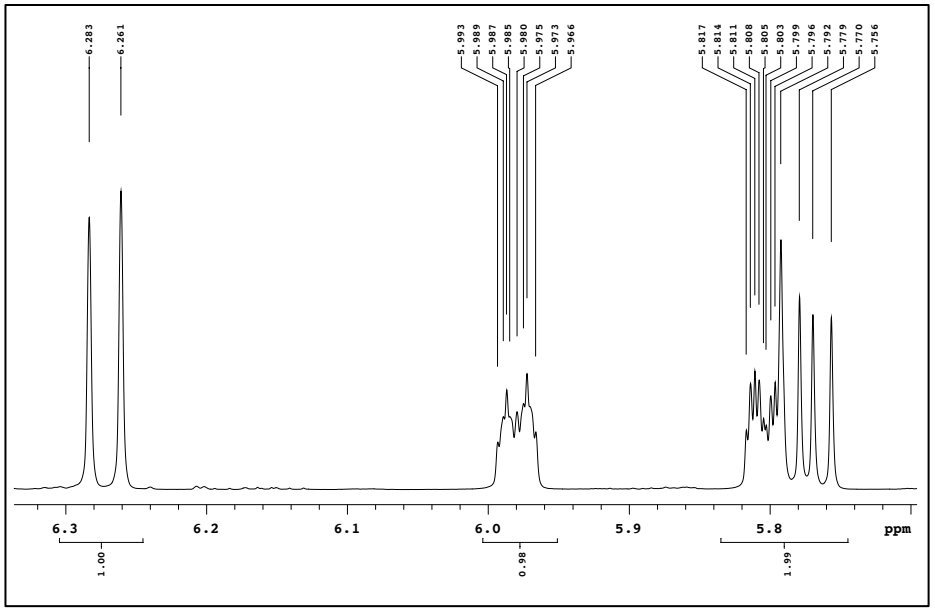
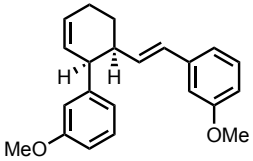
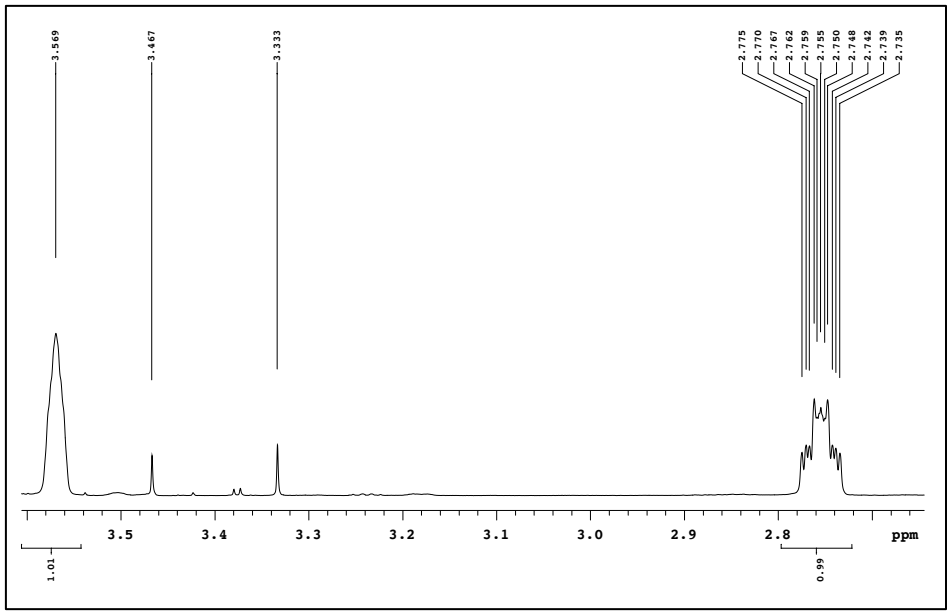



**Figure S95:** $^1$H NMR magnified spectrum of compound **22** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 13 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



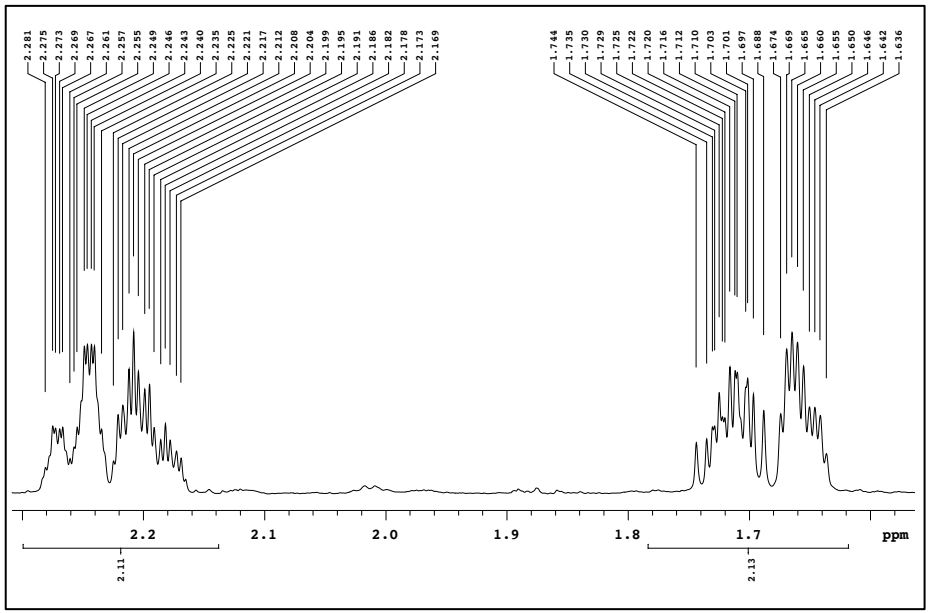



**Figure S96:** $^{13}C$ NMR spectrum of compound **22** ($CDCl_3$, 176 MHz)

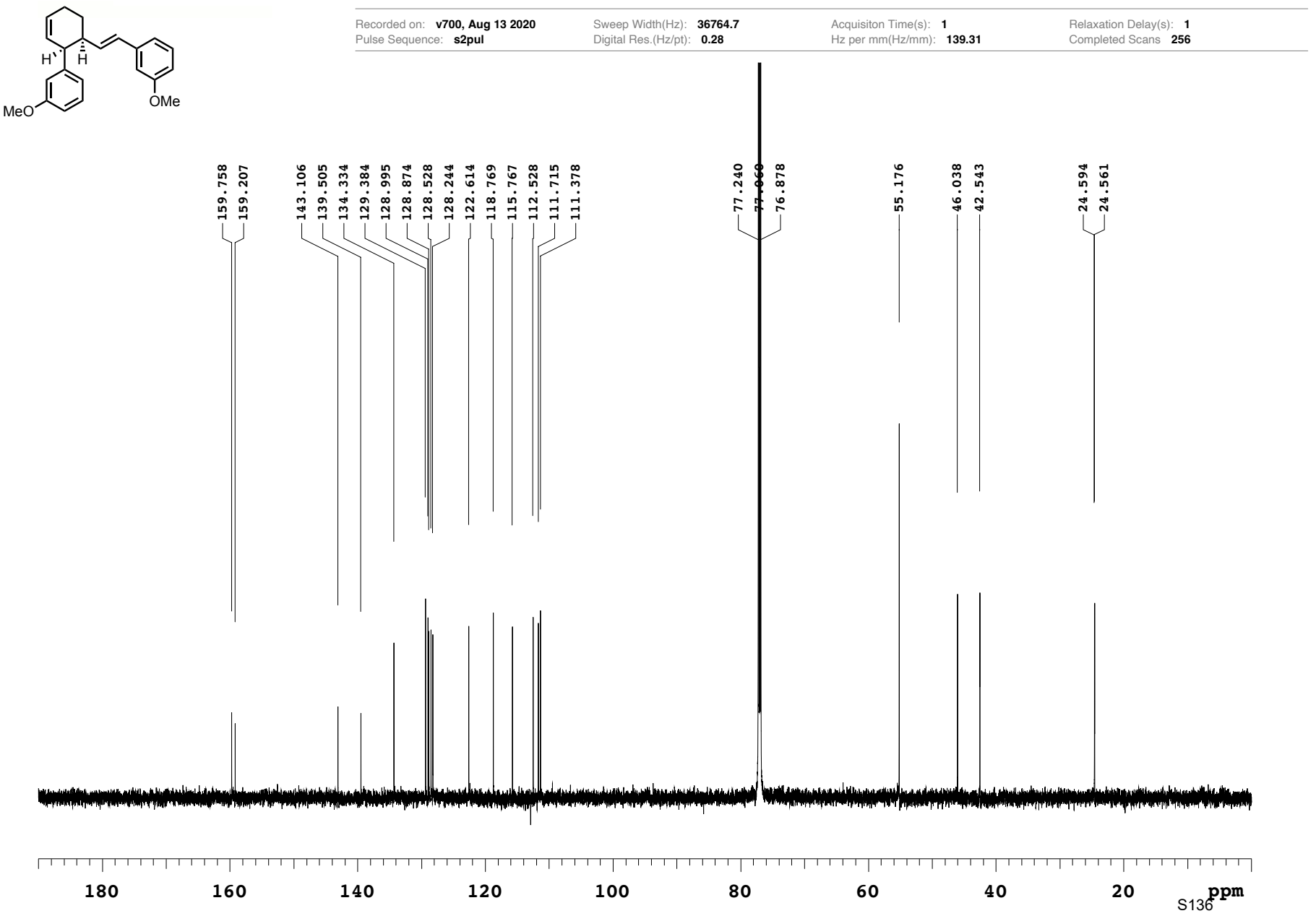
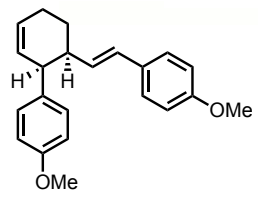


**Figure S97:** $^{1}H$ NMR spectrum of compound **23** ($CDCl_3$, 700 MHz)



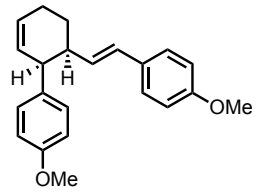

Recorded on: **v700, Aug 14 2020** Sweep Width(Hz): **8389.26** Acquisiton Time(s): **5** Relaxation Delay(s): **0.1**
Pulse Sequence: **PRESAT** Digital Res.(Hz/pt): **0.13** Hz per mm(Hz/mm): **29.16** Completed Scans **8**

7.260 7.142 7.139 7.133 7.130 7.101 7.098 7.092 7.089 6.825 6.822 6.816 6.813 6.797 6.794 6.788 6.785 6.259 6.236 5.946 5.793 5.618 5.605 5.596 5.583 3.794 3.783 3.772 3.766 3.519 1.531 1.258

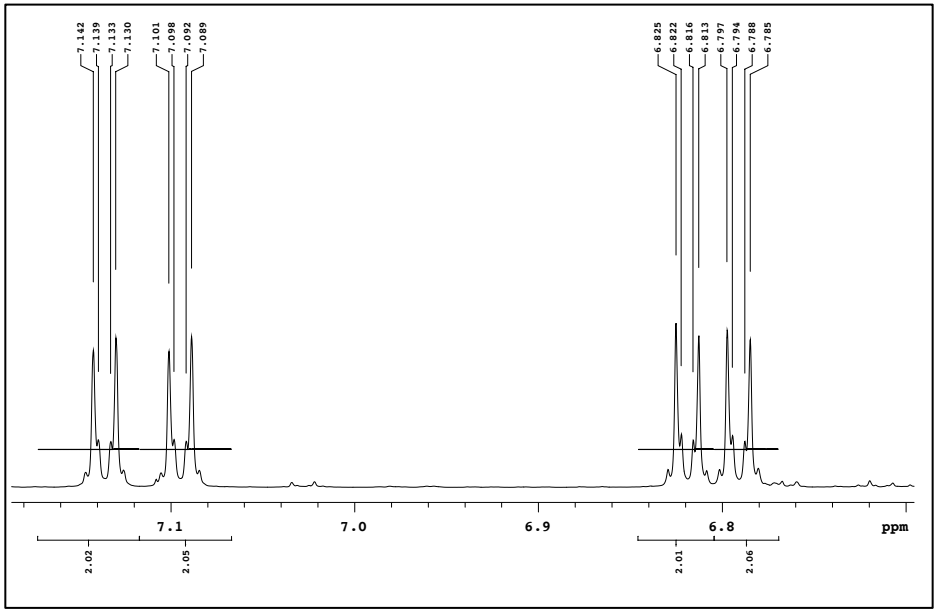
9 8 7 6 5 4 3 2 1 ppm

2.02 2.05 2.01 2.06 1.04 1.00 1.01 1.02 6.29 1.01 1.01 2.21 2.23

**Figure S98:** $^{1}$H NMR spectrum of compound **23** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 14 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |



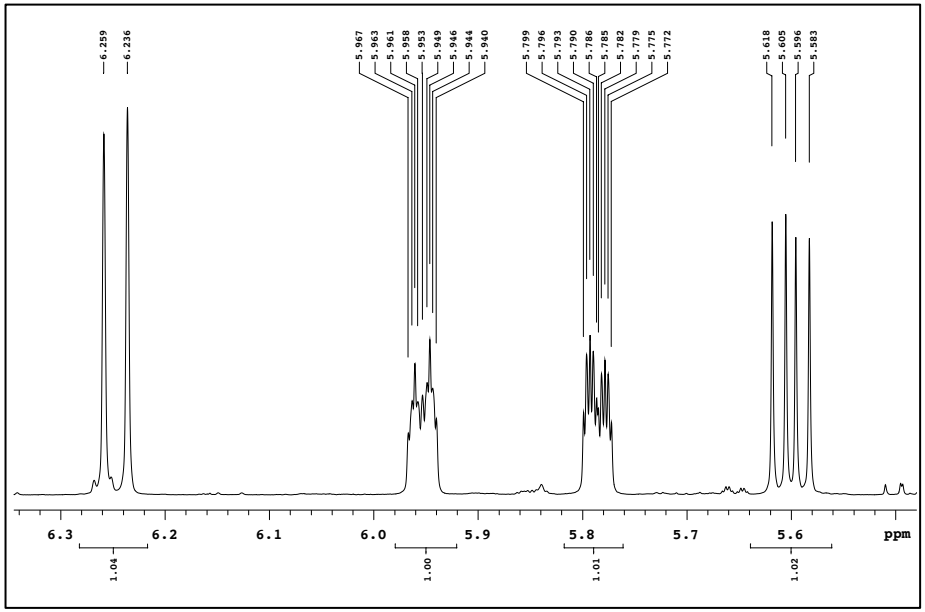
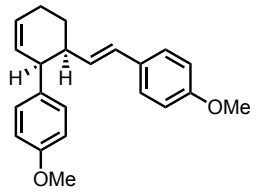



**Figure S99:** $^{1}$H NMR spectrum of compound **23** ($CDCl_3$, 700 MHz)




| | | | |
|---|---|---|---|
| Recorded on: **v700, Aug 14 2020** | Sweep Width(Hz): **8389.26** | Acquisiton Time(s): **5** | Relaxation Delay(s): **0.1** |
| Pulse Sequence: **PRESAT** | Digital Res.(Hz/pt): **0.13** | Hz per mm(Hz/mm): **29.16** | Completed Scans **8** |

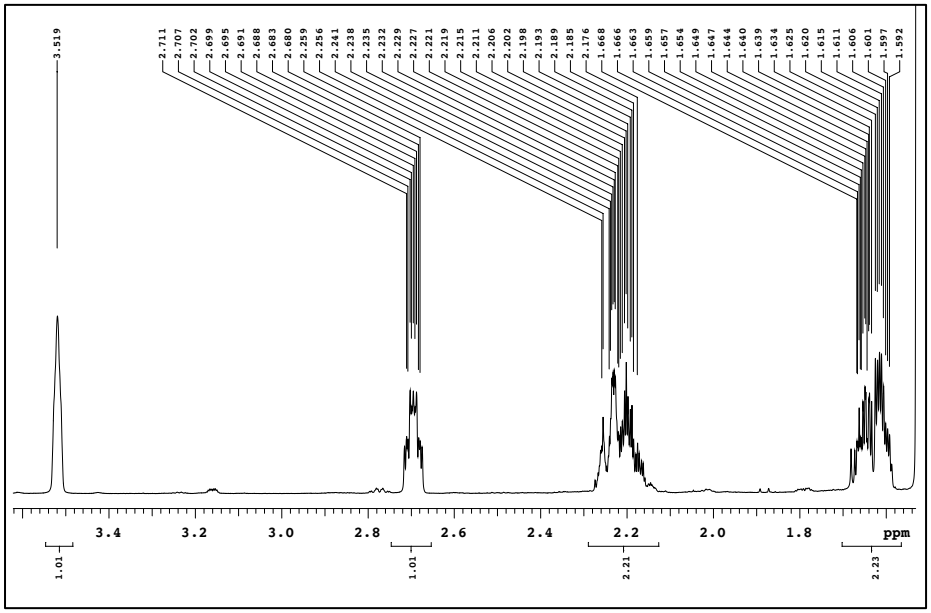


**Figure S100:** $^{13}C$ NMR spectrum of compound **23** ($CDCl_3$, 176 MHz)

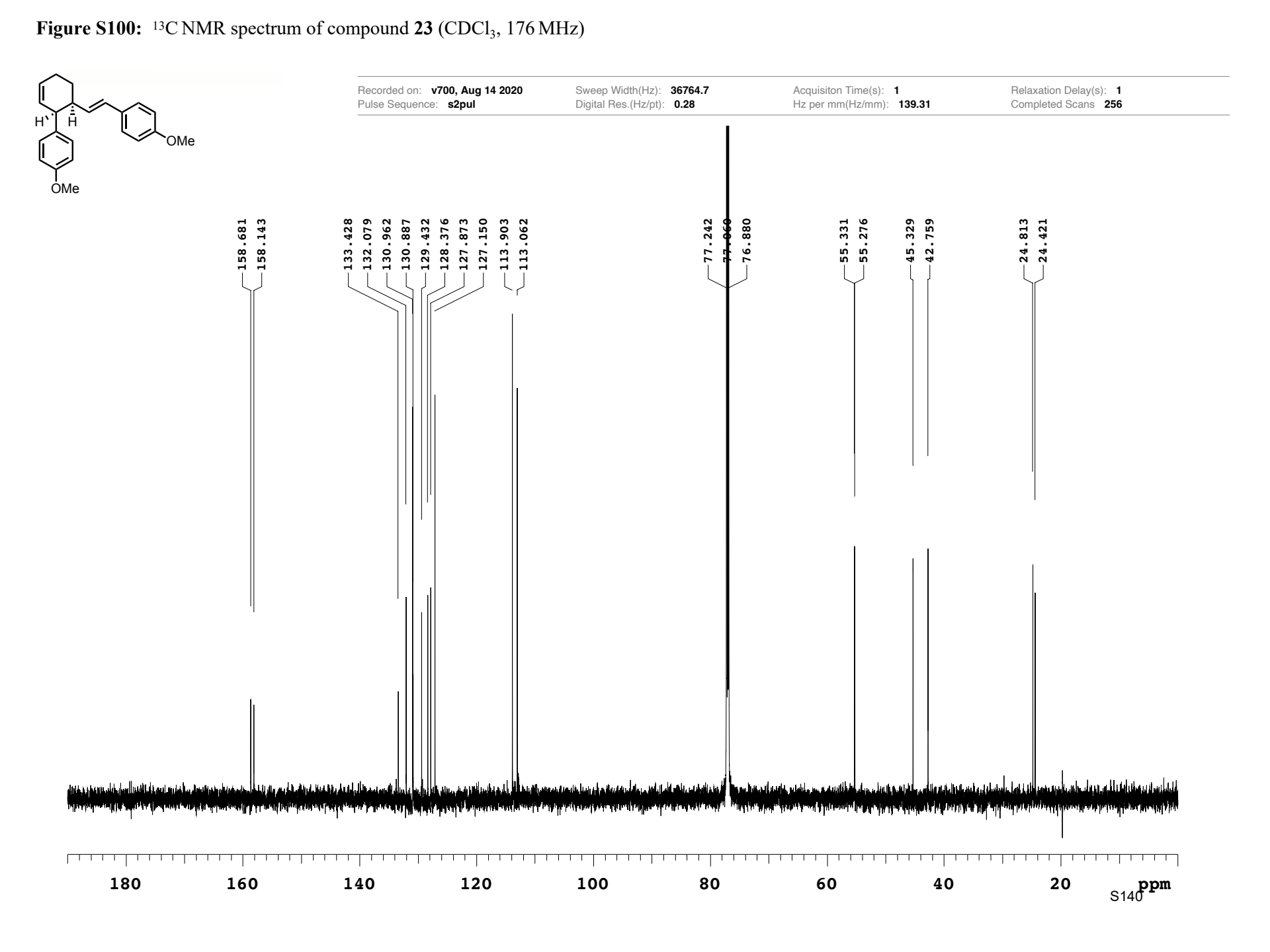


**Figure S101:** $^{1}H$ NMR spectrum of compound **24** ($CDCl_3$, 700 MHz)

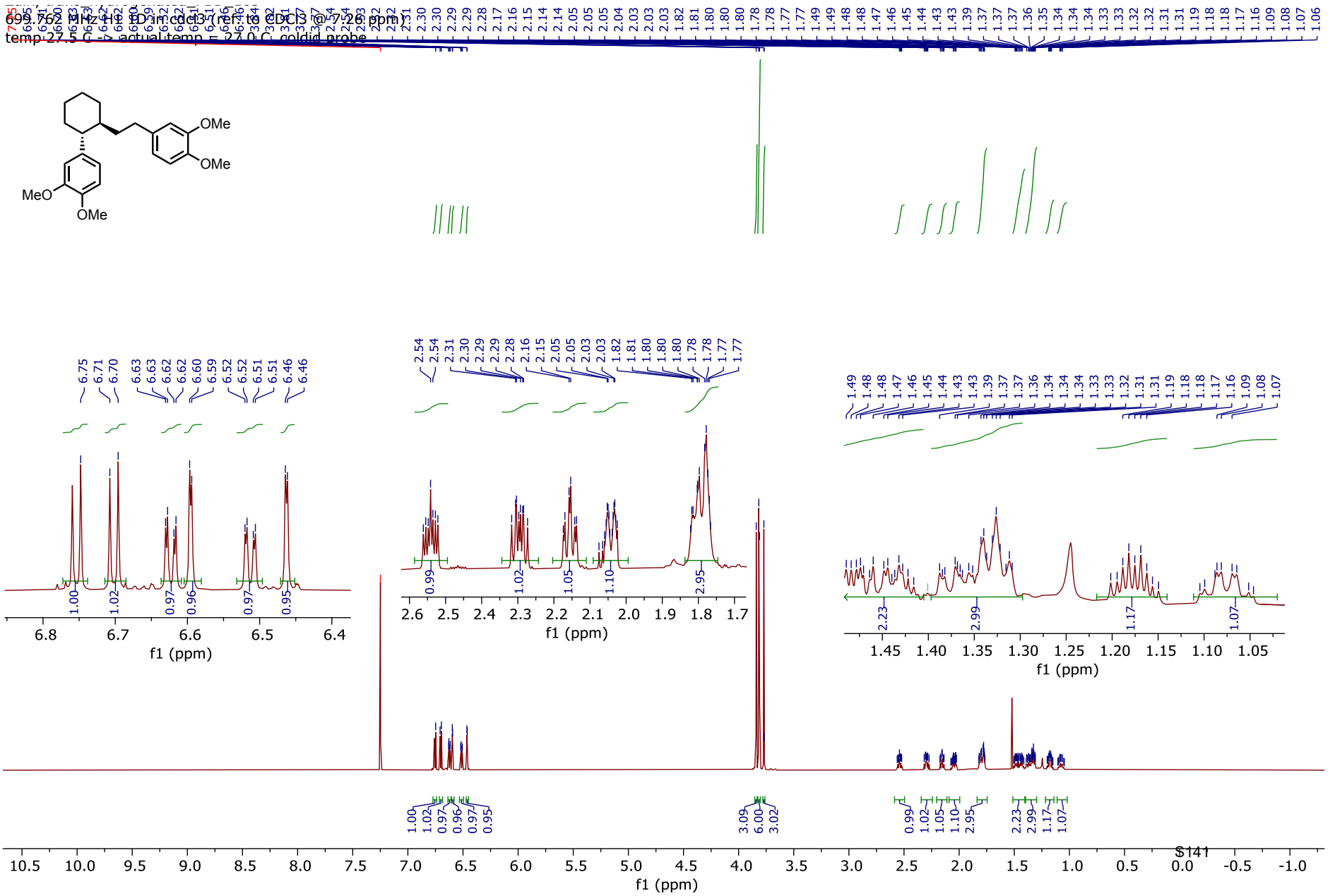


**Figure S102:** $^{13}C$ NMR spectrum of compound **24** ($CDCl_3$, 176 MHz)

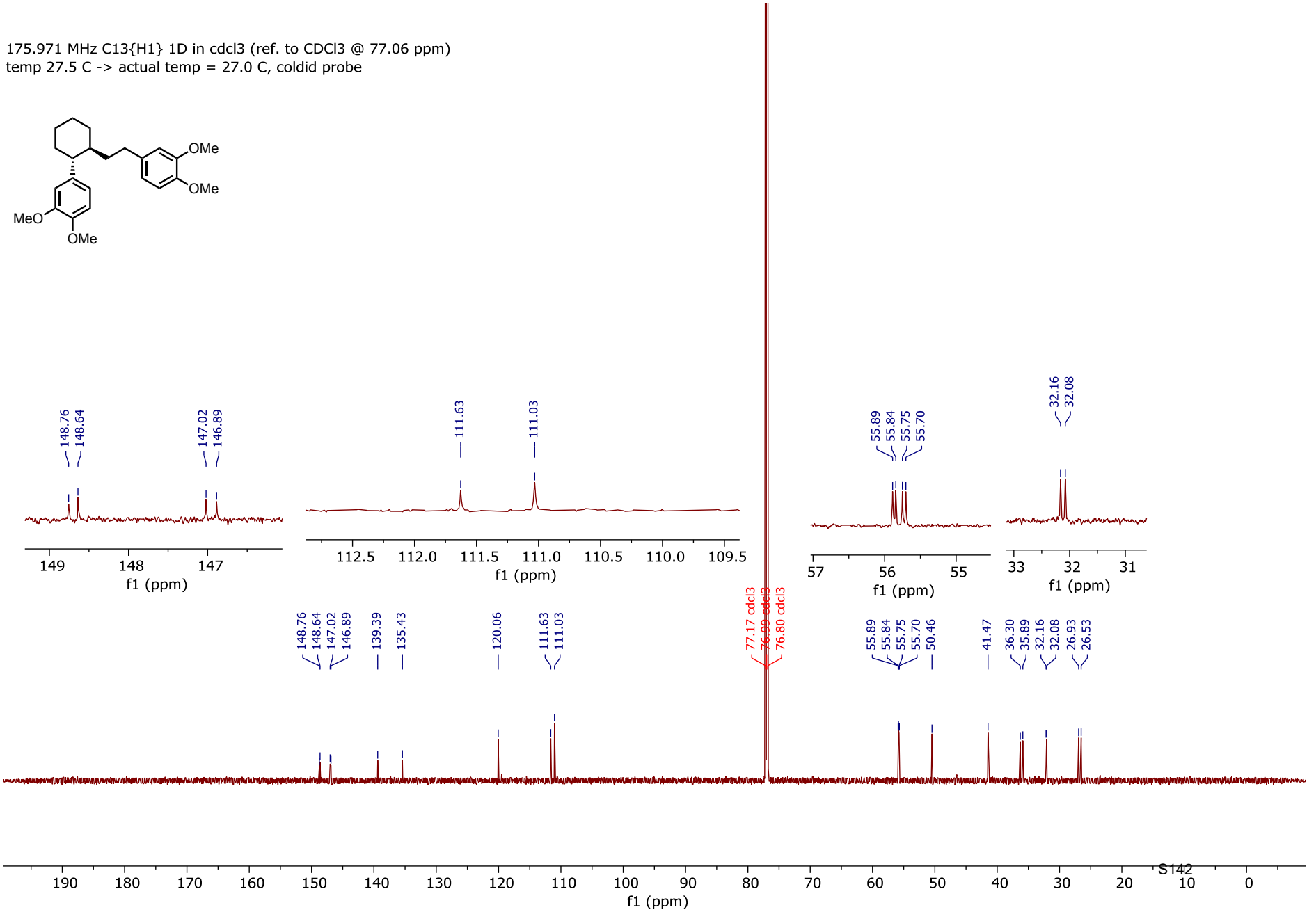


**Figure S103:** $^{1}H$ NMR spectrum of compound **25** ($CDCl_3$, 700 MHz)

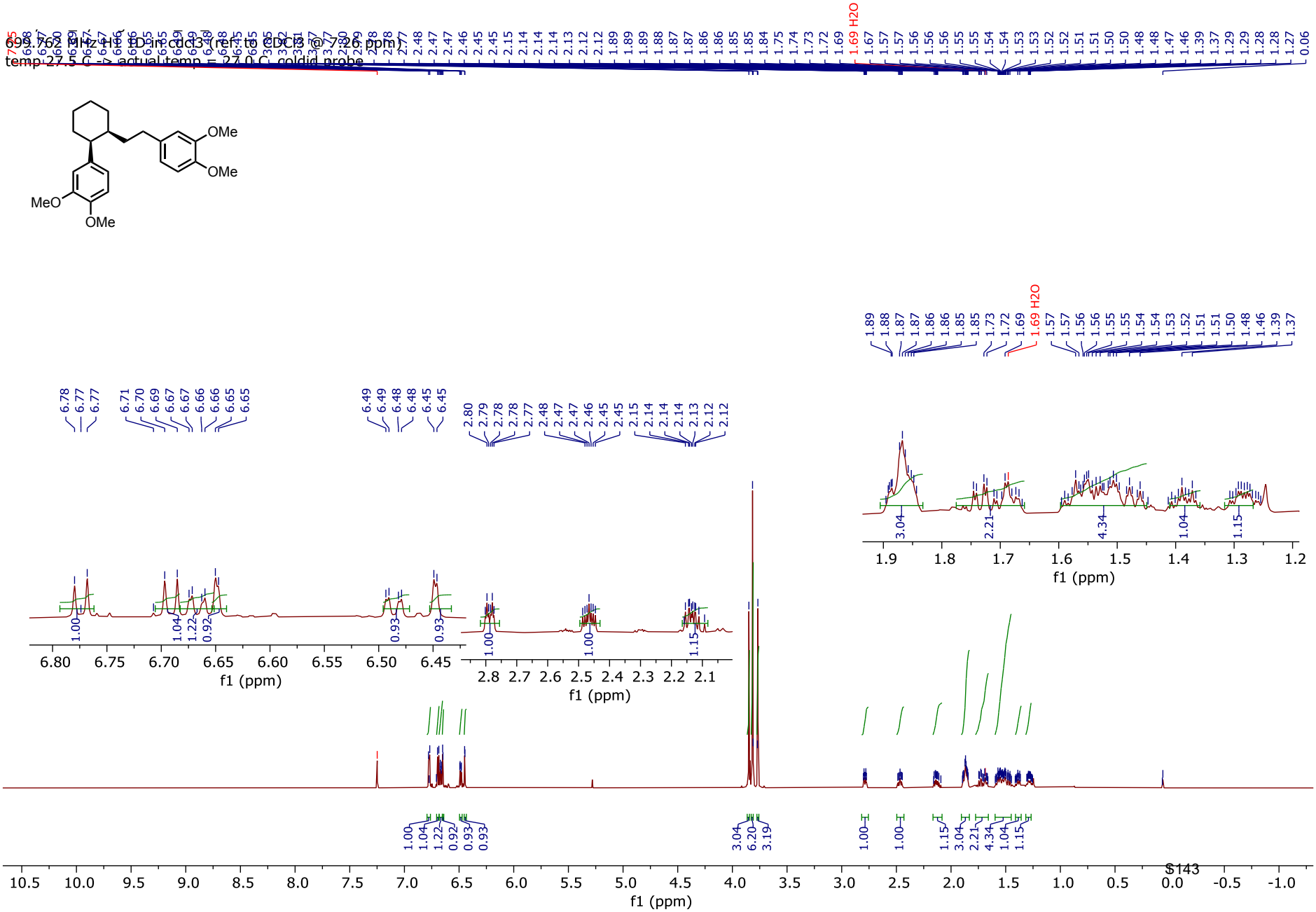


**Figure S104:** $^{13}C$ NMR spectrum of compound **25** ($CDCl_3$, 176 MHz)

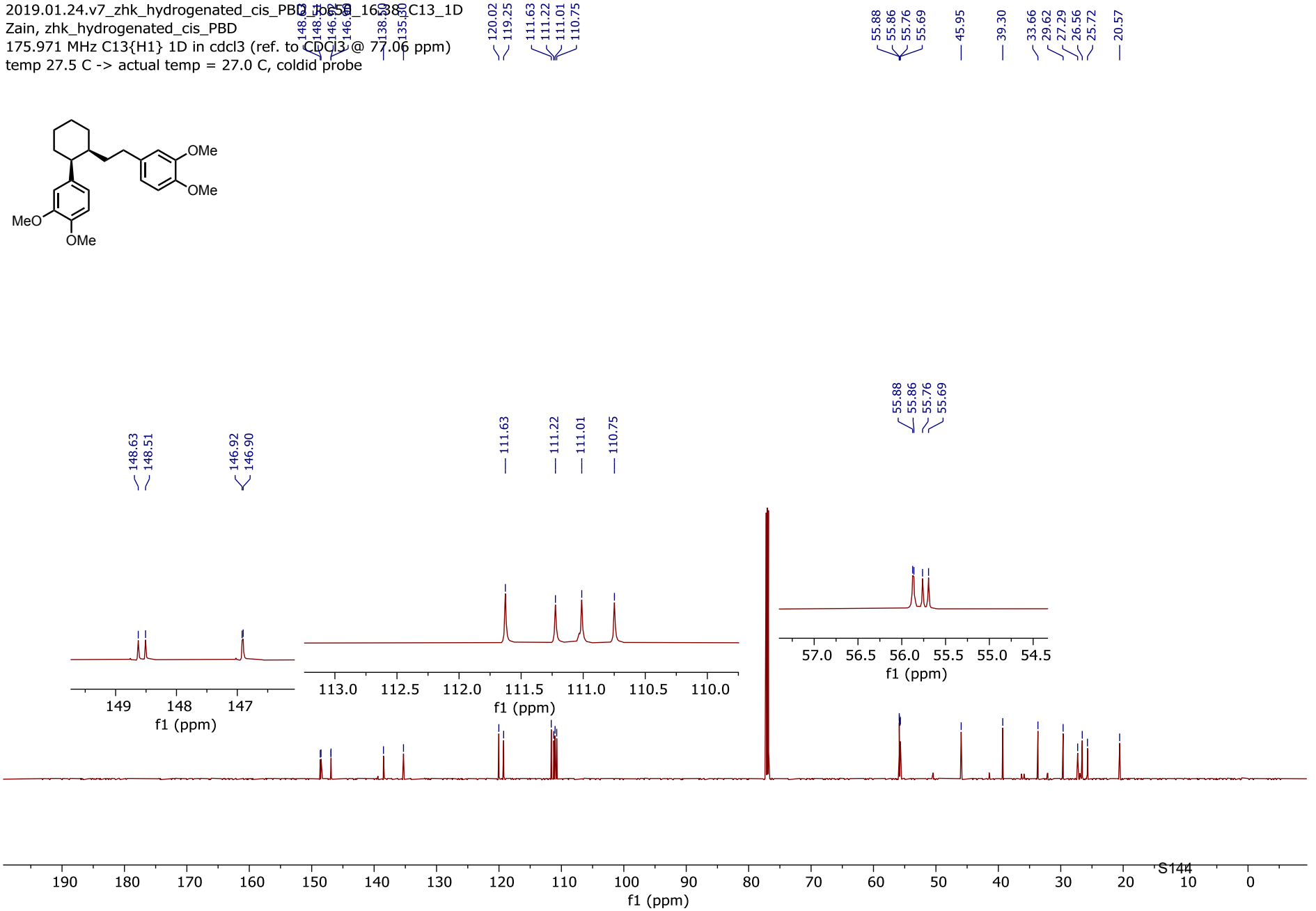


**Figure S105:** $^{1}H$ NMR spectrum of compound **26** ($CDCl_3$, 700 MHz)

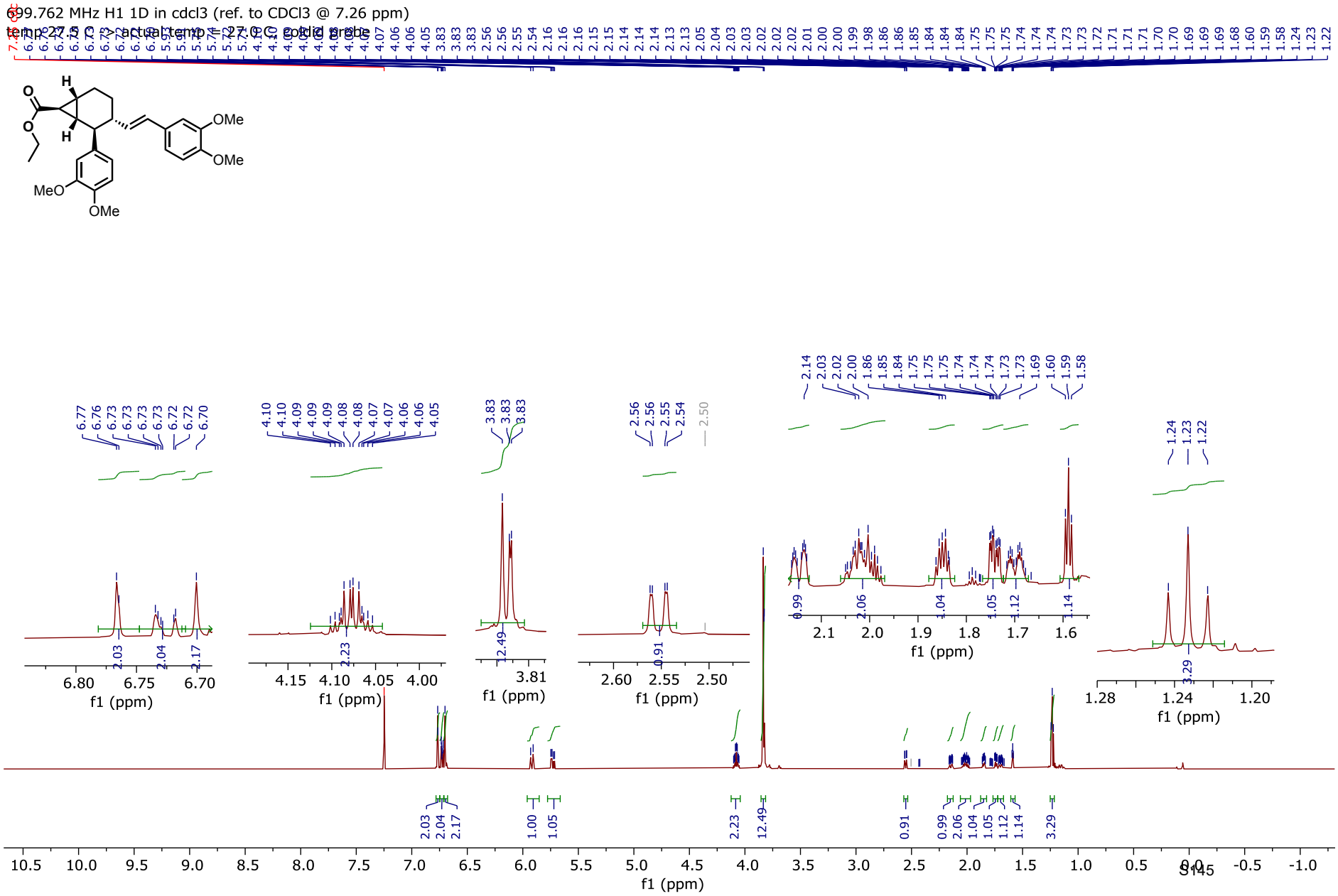


**Figure S106:** $^{13}C$ NMR spectrum of compound **26** ($CDCl_3$, 176 MHz)

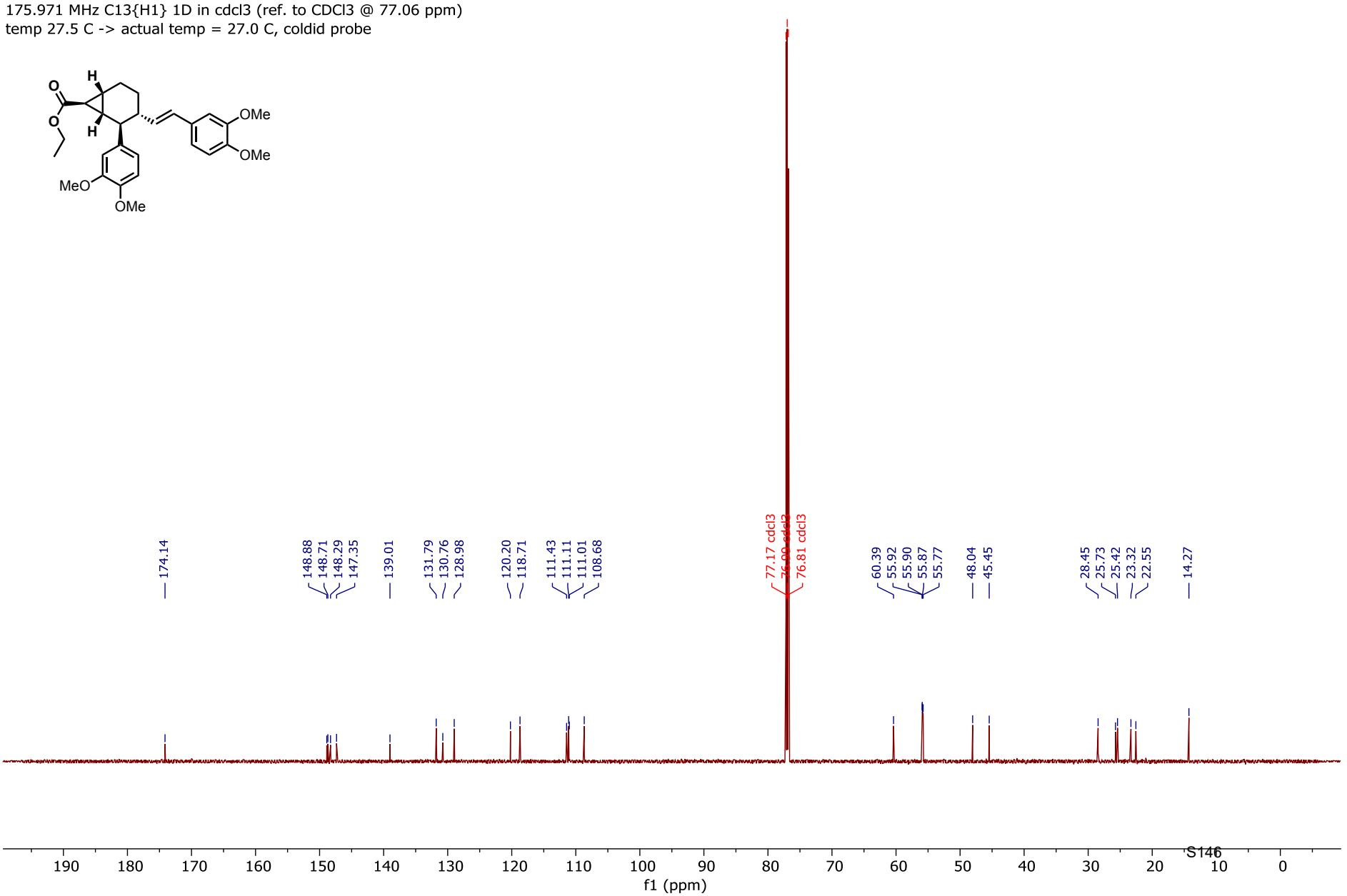


**Figure S107:** $^{1}$H NMR spectrum of compound **27** ($CDCl_3$, 700 MHz)

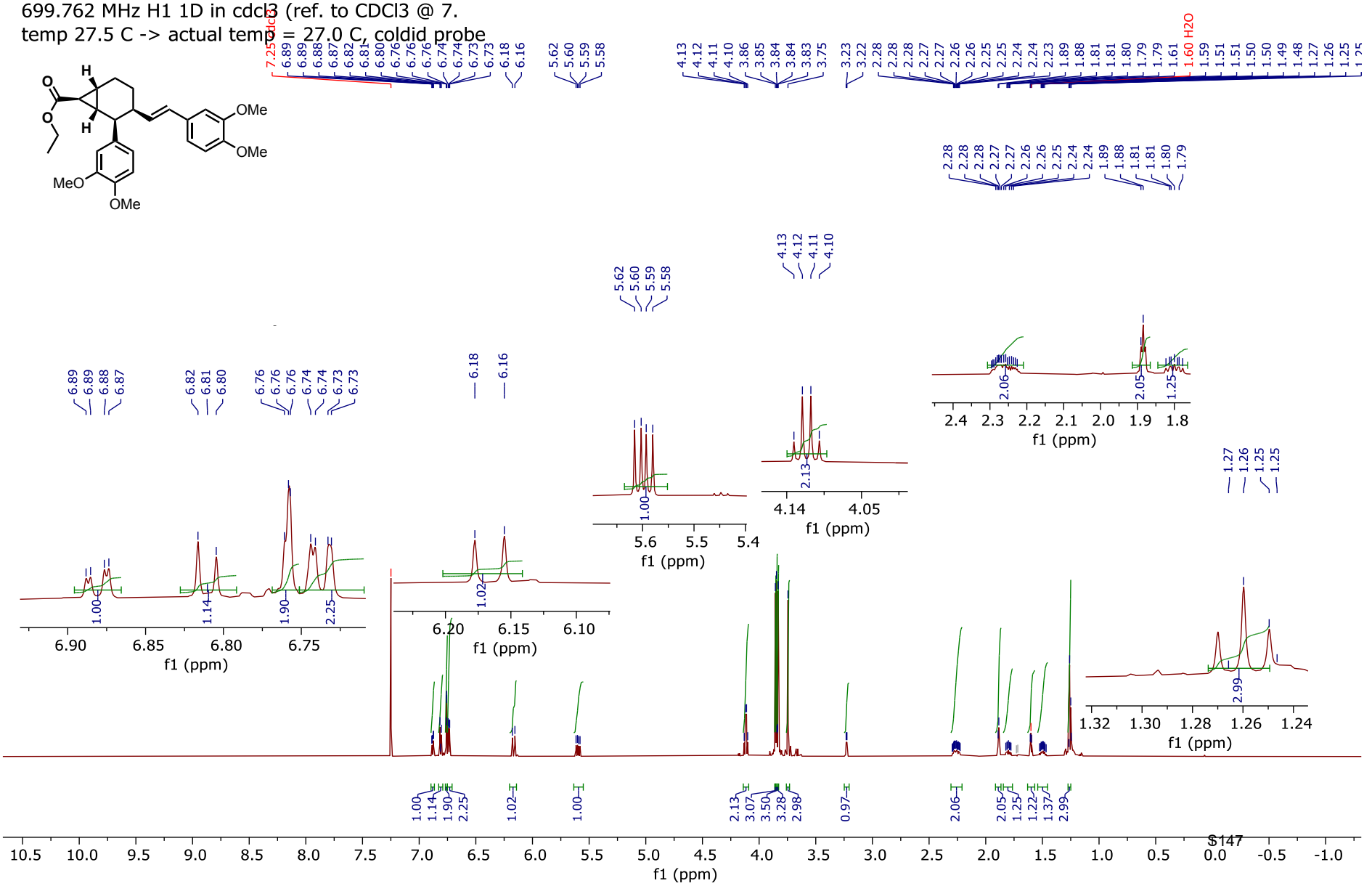


**Figure S108:** $^{13}C$ NMR spectrum of compound **27** ($CDCl_3$, 176 MHz)