Electronic Supplementary Material (ESI) for Medicinal Chemistry Communications

Supporting Information

3,4,2'-trimethoxy-*trans*-stilbene - a potent CYP1B1 inhibitor

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1. Materials and instrumentation

All reactions were performed in oven dried glassware under nitrogen under inert atmosphere of argon. Reaction temperatures were measured for external bath. Organic solvents were rotary evaporated under reduced pressure at or below 50 ºC. Solvents and all reagents were obtained from commercial suppliers and used without further purification. Melting points were obtained on a "Stuart" Bibby apparatus without correction. Thin layer chromatography (TLC) was performed on silica gel Merck Kieselgel 60 F_{254} plates and visualized with UV (λ_{max} 254 or 365 nm). Mass spectrometry experiments (ESI – electrospray) was determined by the Advanced Chemical Equipment and Instrumentation Facility at the Faculty of Chemistry, Adam Mickiewicz University in Poznan. NMR experiments were recorded using a Bruker 400 spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm) and are referred to a residual solvent peak. The abbreviation s, d, t, m, o, and h means singlet, doublet, triplet, multiplet, overlay and hidden.

2. Synthesis

2.1. Synthesis of 3,4,-dimethoxybenzyl chloride (2)

3,4,-Dimethoxybenzyl alcohol (**1**) (3.00 g, 17.6 mmol) was dissolved in 30 mL of anhydrous CH_2Cl_2, placed in ice-water bath and vigorously stirred. Next 3.85 mL of thionyl chloride (6.32 g, mmol) dissolved in 20 mL of anhydrous CH_2Cl_2 was slowly dropped into reaction mixture. Resulting reaction mixture was vigorously stirred in room temperature during 1 h. After this time mixture was once again cooled in ice-water bath and reaction was quenched by slowly dropping of 20 mL of anhydrous ethanol. Solvents were distilled off under reduced pressure and residue was purified by flash column chromatography with $CHCl_3$ as eluent. It gave pale yellow oil of 3,4,-dimethoxybenzyl chloride (2.59 g, 78%) M. p. 49-51 °C . (lit. 50-52°C,[1])TLC R_f ($CHCl_3$) 0.56. MS(ESI) m/z 186 $[M]^+$.

2.2 Synthesis of diethyl (3,4,-dimethoxybenzyl)phosphonate (3)

In a round-flask with a $CaCl_2$ tube 3,4-dimethoxybenzyl chloride **2** (2.57 g, 13.8 mmol) and triethyl phosphite (2.64 mL, 15.2 mmol) were placed and heated at 130°C for 24h. Resulting

product (**3**) diethyl (3,4-dimethoxybenzyl)phosphonate was isolated from reaction mixture by distillation at reduced pressure (fraction 200 - 201 °C /7 Torr, lit. 189 - 190 °C/3 Torr [Fresneda]) to yield pale, viscous oil of compound **2** (2.12 g, 53%). TLC R_f (EtOAc) 0.23. ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.88-6.87 (m, 2H), 6.80-6.78 (m, 1H), 3.98-3.90 (m, 4H), 3.72 (s, 6H), 3.13 ($J_{H,P}$ = 22.1 Hz), 1.17 (t, J= 7.2 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.8 ($J_{C,P}$ = 3.0 Hz), 148.0 ($J_{C,P}$ = 4.0 Hz), 124.8 ($J_{C,P}$ = 9.0 Hz), 122.3 ($J_{C,P}$ = 7.0 Hz), 114.0 ($J_{C,P}$ = 6.0 Hz), 112.2 ($J_{C,P}$ = 3.0 Hz), 66.7 ($J_{C,P}$ = 8.0 Hz), 55.9, 55.9, 32.1 ($J_{C,P}$ = 135.0 Hz), 16.7 ($J_{C,P}$ = 5.0 Hz). MS(ESI) m/z 288 $[M]^+$.

2.3. General procedure for the preparation of trans-stilbenes

2.3.1. Synthesis of 3,4-dimethoxy-trans-stilbene (5a)

Diethyl (3,4-dimethoxybenzyl)phosphonate **3** (3.47 g, 12.0 mmol) and 15 mL of dry DMF were placed in round-flask and cooled to 0°C in ambient atmosphere (under nitrogen). Next sodium methoxide (1.30 g, 24.0 mmol) and benzaldehyde **(4a)** (1.27 g, 12.0 mmol) was added and resulting reaction mixture was strongly stirred under nitrogen for 1h in room temperature and 1.5 h in 100°C. After cooling to room temperature reaction mixture was poured into 500 mL of water with crushed ice and left overnight. Resulting precipitate was filtered off, washed with distilled water (2×25 mL) and purified by crystallization from 95% ethanol. It gave 3,4-dimethoxystilbene **(5a)** as white crystalline solid (1.74 g, 60%) M.p. = 109-110 °C. TLC R_f ($CHCl_3$)= 0.45. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 (d, J = 7.5 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.25 (so, 1H), 7.24 (to, J = 7.5 Hz, 1H), 7.19 (d, J = 16.5 Hz, 1H), 7.13 (do, J = 16.5 Hz, 1H), 7.10 (ddo, J=8.3 Hz, J=1.7 Hz, 1H), 6.95 (d, J = 8.3 Hz, 1H), 3.83 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 148.9, 148.8, 137.4, 130.0, 128.6, 128.4, 127.1, 126.2, 126.1, 119.9, 111.8, 109.2, 55.5, 55.5h . (graphical presentation of signal-structure allocation - Figure X1S). MS(ESI) m/z 240 $[M]^+$. Anal. cal. for $C_{16}H_{16}O_2$ × 1/3 H_2O C(78.02%) H(6.82%). Found C(77.86%) H(6.99%)

Crystal data for **5a** Table 1, Table 2, Figures 1-3, A1S, CCDC 962067

2.3.2. Synthesis of 3,4,2'-trimethoxy-trans-stilbene (5b)

Compound **5b** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (5.00 g, 17.3 mmol) sodium methoxide (1.89 g, 34.6 mmol) and 2-methoxybenzaldehyde (**4b**) (2.36g 17.3 mmol) gave

after crystallization from 95% ethanol white solid of 3,4,2'-trimethoxystilbene **5b** (1.50 g, 32%). M. p. = 102 - 103 °C. TLC R_f ($CHCl_3$)= 0.52. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.28 (d, *J* = 16.7 Hz, 1H), 7.25 – 7.21 (mo, 1H), 7.16 (do, *J* = 2.0 Hz, 1H), 7.15 (do, *J* = 16.5 Hz, 2H), 7.08 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.02 (dd, *J* = 8.2, 0.7 Hz, 1H), 6.95 (to, *J* = 8.6 Hz, 1H), 6.94 (do, *J* = 8.4 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.3, 148.9, 148.6, 130.4, 128.9, 128.4, 126.1, 125.8, 120.9, 120.6, 119.5, 111.8, 111.3, 109.34, 55.5, 55.5, 55.4. (graphical presentation of signal-structure allocation - Figure X2S). LRMS(EI) m/z 270 $[M]^+$, HRMS(EI) calculated for $C_{17}H_{18}O_3$ 270.12558. Found 270.12590.

Crystal data for **5b** Table 1, Table 3, Fig.4, Fig. 5, CCDC 962068

2.3.3. Synthesis of 3,4,2',3'-tetramethoxy-trans-stilbene (5c)

Compound **5c** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (5.00 g, 17.3 mmol) sodium methoxide (1.89 g, 34.6 mmol) and 2,3-dimethoxybenzaldehyde (**4c**) (2.87g 17.3 mmol) gave after crystallization from methanol white solid of 3,4,2',3'-tetramethoxy-trans-stilbene **5c** (2.70 g, 52%). M. p. = 110 - 111 °C. TLC R_f ($CHCl_3$) 0.24. ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.27 (ddo, *J* =7.7, 0.9 Hz, 1H), 7.24 (d, *J* = 16.2 Hz, 1H), 7.19 (sh, 1H), 7.17 (d, *J* = 16.6 Hz, 1H), 7.12 (dd, *J* = 8.3, 1.8 Hz, 1H), 7.06 (t, *J* = 8.0 Hz, 1H), 6.96 (do, *J* = 8.4 Hz, 1H), 6.94 (ddo, *J* = 8.3, 1.0 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H), 3.77 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.3, 149.4, 149.3, 146.6, 131.4, 130.6, 130.2, 124.6, 120.7, 120.1, 117.9, 112.3, 112.0, 110.1, 60.9, 56.1, 56.0, 56.0h. (graphical presentation of signal-structure allocation - Figure X3S). MS(ESI) m/z 300 $[M]^+$. Anal. cal. for $C_{18}H_{20}O_4$ C(71.98%) H(6.71%). Found C(72.08%) H(6.93%).

2.3.4. Synthesis of 3,4,2',4'-tetramethoxy-trans-stilbene (5d)

Compound **5d** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (5.00 g, 17.3 mmol) sodium methoxide (1.89 g, 34.6 mmol) and 2,4-dimethoxybenzaldehyde (**4d**) (2.87g 17.3 mmol) gave after crystallization from methanol white solid of 3,4,2',4'-tetramethoxy-trans-stilbene **5d** (2.34 g, 45%). M. p. = 115 - 116 °C. TLC R_f ($CHCl_3$) 0.30. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.53 (d, *J* = 8.5 Hz, 1H), 7.21 (d, *J* = 16.5 Hz, 1H), 7.13 (d, *J* = 1.5 Hz, 1H), 7.04 (do, *J* = 1.6

Hz, 1H), 7.02 (do, *J* = 16.7 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 6.59 (d, *J* = 2.2 Hz, 1H), 6.56 (dd, *J* = 8.5, 2.3 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.5, 158.0, 149.4, 148.8, 131.3, 127.5, 127.1, 121.4, 119.6, 119.2, 112.3, 109.6, 106.0, 98.8, 55.9, 55.9, 55.9, 55.7. (graphical presentation of signal-structure allocation - Figure X4S). MS(ESI) m/z 300 $[M]^+$. Anal. cal. for $C_{18}H_{20}O_4$ C(71.98%) H(6.71%). Found C(71.82%) H(7.15%).

2.3..5. Synthesis of 3,4,2',5'-tetramethoxy-trans-stilbene (5e)

Compound **5e** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (3.20 g, 11.1 mmol), sodium methoxide (1.20 g, 22.2 mmol) and 2,5-dimethoxybenzaldehyde (**4e**) (1.85g 11.1 mmol) gave after crystallization from 95% ethanol yellow solid of 3,4,2',5'-tetramethoxy-trans-stilbene **5e** (1.10 g, 33%). M. p. = 86 - 88 °C. TLC R_f ($CHCl_3$) 0.26. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 (d, *J* = 16.5 Hz, 1H), 7.21 (so, 1H), 7.19 (do, *J* = 16.9 Hz, 3H), 7.17 (so, 1H), 7.10 (d, *J* = 8.3 Hz, 1H), 6.95 (do, *J* = 9.1 Hz, 1H), 6.95h (do, *J* = 9.1 Hz, 1H) 6.82 (dd, *J* = 8.9, 2.7 Hz, 1H), 3.82 (s, 3H), 3.80 (s, 3H), 3.78 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.8, 151.2, 149.4, 149.2, 130.8, 129.7, 127.0, 121.1, 120.0, 114.1, 113.0, 112.3, 111.6, 109.9, 56.5, 56.0, 55.9, 55.8 (graphical presentation of signal-structure allocation - Figure X5S). MS(ESI) m/z 300 $[M]^+$. Anal. cal. for $C_{18}H_{20}O_4 \times 1/3\ H_2O$ C(70.57%) H(6.80%). Found C(70.61%) H(6.33%)

2.3.6. Synthesis of 3,4,2',6'-tetramethoxy-trans-stilbene (5f)

Compound **5f** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (3.47 g, 12.0 mmol), sodium methoxide (1.30 g, 24.0 mmol) and 2,6-dimethoxybenzaldehyde (**4f**) (2.00 g 12.0 mmol) gave after crystallization from 95% ethanol white solid of 3,4,2',6'-tetramethoxy-trans-stilbene **5f** (2.60 g, 72%). M. p. = 112-113 °C. TLC R_f ($CHCl_3$) 0.38. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.43 (d, J = 16.7 Hz, 1H), 7.22 (do, J = 16.6 Hz, 1H), 7.18 (to, J = 8.3 Hz, 1H), 7.07 (d, J=1.2 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 6.69 (d, J = 8.4 Hz, 2H), 3.84 (s, 6H), 3.81 (s, 3H), 3.76 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.0, 148.9, 148.4, 131.7, 131.6, 128.1, 118.7, 117.6, 113.8, 111.9, 109.4, 104.2, 55.7, 55.7h, 55.5, 55.4 (graphical

presentation of signal-structure allocation - Figure X6S). MS(ESI) m/z 300 $[M]^+$. Anal. cal. for $C_{18}H_{20}O_4 \times 1/3\ H_2O$ C(70.57%) H(6.80%). Found C(70.72%) H(7.00%)

Crystal data for **5f** Table 1, Table 4, Figures 6 - 8, CCDC 962069

2.3.7. Synthesis of 3,4,2',3',4'-pentamethoxy-trans-stilbene (5g)

Compound **5g** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (2.89 g, 10.0 mmol), sodium methoxide (1.08 g, 20.0 mmol) and 2,3,4-trimethoxybenzaldehyde (**4g**) (1.96 g 10.0 mmol) gave after crystallization from 95% ethanol white solid of 3,4,2',3',4'-pentamethoxy-trans-stilbene **5g** (1.35 g, 41%). M. p. = 104-105 °C. TLC R_f ($CHCl_3$) 0.14. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.36 (d, J = 8.8 Hz, 1H), 7.17 (so, 1H), 7.16 (do, J = 16.4 Hz, 2H), 7.08 (do, J = 5.9 Hz, 2H), 7.07 (do, J = 16.7 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 6.83 (d, J = 8.8 Hz, 1H), 3.83 (so, 3H), 3.82 (so, 6H), 3.77 (s, 6H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 153.2, 151.5, 149.4, 149.0, 142.4, 131.0, 128.2, 124.4, 121.0, 121.0, 119.7, 112.3, 109.9, 108.9, 61.5, 60.8, 56.3, 55.9 (graphical presentation of signal-structure allocation - Figure X7S). MS(ESI) m/z 330 $[M]^+$.

Crystal data for **5g** Table 1, Table 4, Fig. 9, Fig. 10, CCDC 962070

2.3.8. Synthesis of 3,4,2',4',5'-pentamethoxy-trans-stilbene (5h)

Compound **5h** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (2.89 g, 10.0 mmol), sodium methoxide (1.08 g, 20.0 mmol) and 2,4,5-trimethoxybenzaldehyde (**4h**) (1.96 g 10.0 mmol) gave after crystallization from methanol yellow solid of 3,4,2',4',5'-pentamethoxy-trans-stilbene **5h** (1.64 g, 50%). M. p. = 124-125 °C. TLC R_f ($CHCl_3$) 0.15. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.23 (do, J = 16.4 Hz, 1H), 7.23 (so, 1H), 7.13 (s, 1H), 7.08 (do, J = 17.7 Hz, 1H), 7.07 (do, J = 6.5 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 6.71 (s, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 3.81 (sh, 3H), 3.79 (s, 3H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.6, 149.8, 149.4, 148.74, 143.5, 131.3, 127.0, 121.0, 119.4, 117.8, 112.37, 110.4, 109.7, 98.7, 56.8, 56. 7, 56.2, 55.9, 55.9 (graphical presentation of signal-structure allocation - Figure X8S). LRMS(EI) m/z 330 $[M]^+$, HRMS(EI) calculated for $C_{19}H_{22}O_5$ 330.14673. Found 330.14529.

2.3.9. Synthesis of 3,4,2',4',6'-pentamethoxy-trans-stilbene (5i)

Compound **5i** was prepared according to procedure described for the synthesis of **5a**. Reaction of diethyl (3,4-dimethoxybenzyl)phosphonate **3** (5.88 g, 20.4 mmol), sodium methoxide (2.20 g, 40.8 mmol) and 2,4,6-trimethoxybenzaldehyde (**4i**) (4.00 g 20.4 mmol) gave after crystallization from methanol white solid of 3,4,2',4',6'-pentamethoxy-trans-stilbene **5i** (3.40 g, 51%). M. p. = 129-131 °C. TLC R_f ($CHCl_3$) 0.25. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.32 (d, J = 16.6 Hz, 1H), 7.16 (d, J = 16.6 Hz, 1H), 7.03 (d, J = 1.5 Hz, 1H), 6.99 (dd, J = 8.3, 1.5 Hz, 1H), 6.91 (d, J = 8.3 Hz, 1H), 6.29 (s, 2H), 3.85 (s, 6H), 3.81 (s, 3H), 3.80 (s, 3H), 3.75 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.9, 158.9, 148.9, 148.0, 132.1, 129.1, 118.3, 117.7, 112.0, 109.2, 107.0, 91.0, 55.7, 55.5, 55.4, 55.2. (graphical presentation of signal-structure allocation - Figure X9S). MS(ESI) m/z 330 $[M]^+$. Anal. cal. for $C_{19}H_{22}O_5$ C(69.07%) H(6.71%). Found C(69.42%) H(6.84%)
Crystal data for **5i** Table 1, Table 5, Figures 11-13, CCDC 962071

3. Crystallographic data

X-ray

The crystals of stilbenes were crystalized by slow evaporation respectively: 5g, 5f and 5b from ethanol, 5i and 5a from methanol. The crystal structures of all compounds in solid state were analyzed by single crystal X-ray diffraction. Diffraction data were collected with Oxford Diffraction Atlas Xcaliburusing graphite-monochromatedMoKα radiation (compound 5g, 5i, 5a, and 5f) at room temperature, Oxford Diffraction Eos Xcalibur using graphite-monochromated MoKα radiation (compound 5b) at 100K and processed with the Agilent Technologies CrysAlis Pro software.[2] The structures were solved by direct methods and refined by the full-matrix least-squares method based on F^2 (SIR92),[3] (SHELXS, SHELXL).[4] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms for compound 5f were found in difference Fourier maps and freely refined with isotropic displacement parameters. The C-bound hydrogen atoms of compounds 5g, 5i, 5a and 5b were generated geometrically with C-H = 0.93 - 0.98Å and refined as riding on their corresponding carbon

atoms. Summary of structure determination is given in Table 1. Torsion angles are given in Tables 2 to 6.

Computing details

Data collection: *CrysAlis PRO*;[2] cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97*;[4] program(s) used to refine structure: *SHELXL97*;[4] molecular graphics: *SHELXTL*[4] and Mercury;[5] software used to prepare material for publication: *SHELXL97*

Table 1. Crystal data and refinement details of stilbens 5a, 5b, 5f, 5g and 5i.

	5a	**5b**	**5f**	**5g**	**5i**
Empirical formula	$C_{16}H_{16}O_2$	$C_{17}H_{18}O_3$	$C_{18}H_{20}O_4$	$C_{19}H_{22}O_5$	$C_{19}H_{22}O_5$
Formula weight	240.29	270.31	300.34	330.37	330.37
Temperature, K	293(2)	100(2)	293(2)	293(2)	293(2)
Wavelength, Å	0.71073	0.71073	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Monoclinic	Monoclinic	Monoclinic	Monoclinic
Space group	Aba2	$P2_1/c$	$P2_1/n$	$P2_1/c$	$P2_1/c$
Unit cell dimentions, Å and °	a = 17.2254(13) b = 24.9655(18) c = 6.1462(4) α = β =γ = 90°	a = 13.969(3) b =5.1099(10) c =20.095(4) β= 105.24(3) °	a = 16.0340(3) b = 5.04530(10) c = 19.5669(4) β= 95.835(2)°	a = 26.3492(8) b = 8.1624(3) c = 8.1890(2) β = 97.079(2)°	a = 7.7187(4) b = 16.2257(6) c = 13.7254(6) β = 93.205(4)°
Volume, A^3	2643.1(3)	1383.9(5)	1574.69(5)	1747.80(9)	1716.30(13)
Z	8	4	4	4	4
Calculated density, g/cm^3	1.208	1.297	1.267	1.255	1.289
Absorption coefficient, mm^{-1}	0.078	0.088	0.089	0.090	0.092
Reflections collected	4056	12911	15140	11884	13002
Independent reflections	1998	2423	2740	3071	3024
Data/restraints/parameters	1998 / 1 / 163	2423 / 0 / 182	2740 / 0 / 280	3071 / 0 / 306	3024/ 0 / 217
Goodness-of-fit on F^2	0.888	1.064	1.039	1.005	1.031
Final R indices [I>2σ(I)]	R1 = 0.0353, wR2 = 0.0545	R1 = 0.0399, wR2 = 0.1068	R1 = 0.0314, wR2 = 0.0856	R_1 = 0.0390, wR_2 = 0.0988	R_1 = 0.0557, wR_2 = 0.1360
R indices (all data)	R_1 = 0.0936, wR_2 = 0.0592	R_1 = 0.0477, wR_2 = 0.1147	R_1 = 0.0474, wR_2 = 0.0908	R_1 = 0.0543, wR_2 = 0.1058	R_1 = 0.1008, wR_2 = 0.1516
Largest peak and hole $eÅ^{-3}$	0.172, -0.133	0.232,-0.223	0.131, -0.098	0.146, -0.133	0.274, -0.168

3.1. X-ray structure of 3,4-dimethoxy-trans-stilbene (5a)

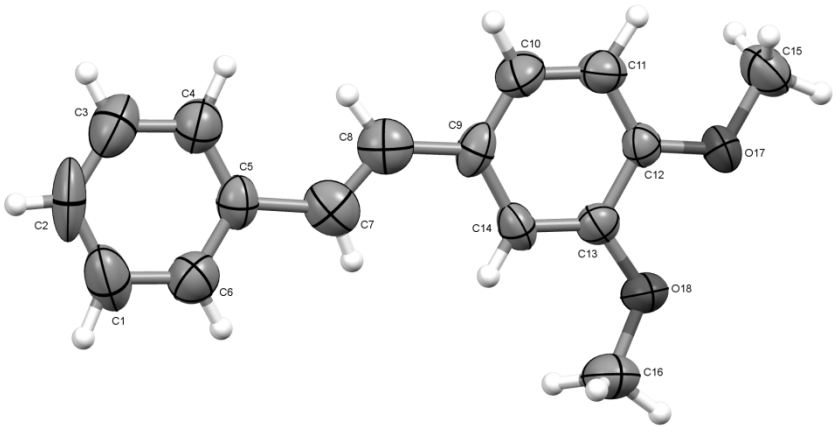


Fig. 1. A view of 5a, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

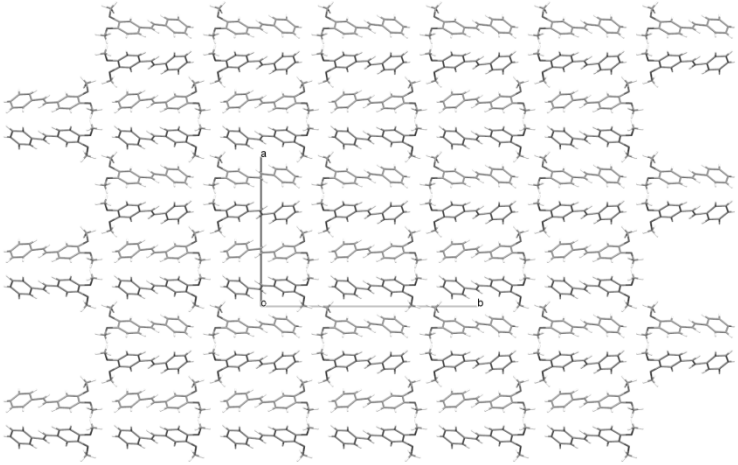


Fig. 2. The crystal packing as seen along [001]direction

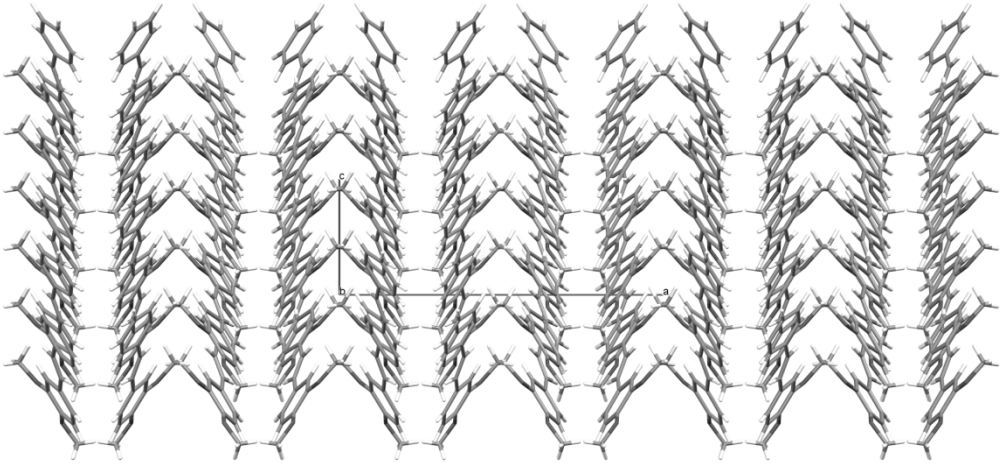


Fig. 3. The crystal packing as seen along [010] direction

Table 2. Torsion angles [°] for 5a.

C(6)-C(1)-C(2)-C(3)	0.2(5)
C(1)-C(2)-C(3)-C(4)	0.2(5)
C(2)-C(3)-C(4)-C(5)	-1.5(5)
C(3)-C(4)-C(5)-C(6)	2.5(5)
C(3)-C(4)-C(5)-C(7)	-177.5(3)
C(4)-C(5)-C(6)-C(1)	-2.1(5)
C(7)-C(5)-C(6)-C(1)	177.9(3)
C(2)-C(1)-C(6)-C(5)	0.8(5)
C(4)-C(5)-C(7)-C(8)	10.1(4)
C(6)-C(5)-C(7)-C(8)	-169.9(3)
C(5)-C(7)-C(8)-C(9)	-176.6(3)
C(7)-C(8)-C(9)-C(10)	171.9(3)
C(7)-C(8)-C(9)-C(14)	-5.2(4)
C(14)-C(9)-C(10)-C(11)	2.1(4)
C(8)-C(9)-C(10)-C(11)	-175.2(2)
C(9)-C(10)-C(11)-C(12)	-0.9(4)
C(10)-C(11)-C(12)-O(17)	178.5(2)
C(10)-C(11)-C(12)-C(13)	-1.0(4)
C(11)-C(12)-C(13)-O(18)	-179.1(2)
O(17)-C(12)-C(13)-O(18)	1.4(3)
C(11)-C(12)-C(13)-C(14)	1.6(3)
O(17)-C(12)-C(13)-C(14)	-177.9(2)
O(18)-C(13)-C(14)-C(9)	-179.5(2)
C(12)-C(13)-C(14)-C(9)	-0.3(4)
C(10)-C(9)-C(14)-C(13)	-1.5(4)
C(8)-C(9)-C(14)-C(13)	175.7(2)
C(11)-C(12)-O(17)-C(15)	-5.1(3)
C(13)-C(12)-O(17)-C(15)	174.3(2)
C(14)-C(13)-O(18)-C(16)	-11.0(3)
C(12)-C(13)-O(18)-C(16)	169.7(2)

3.2 X-ray structure of 3,4,2'-trimethoxy-trans-stilbene (5b)

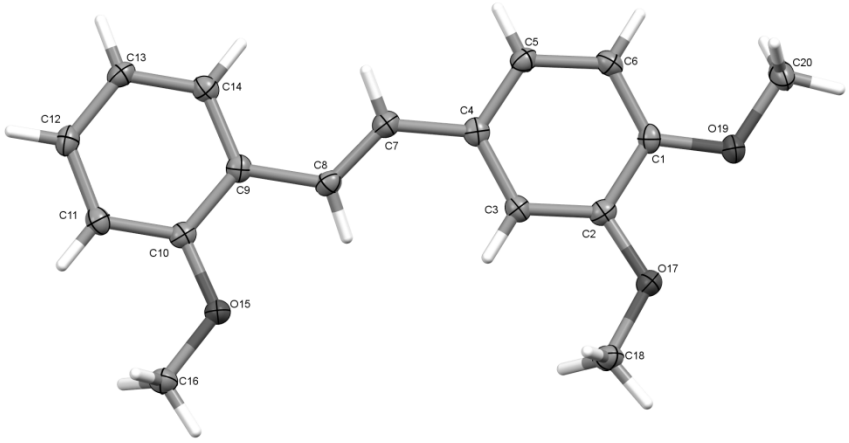


Fig. 4 .A view of **5b**, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

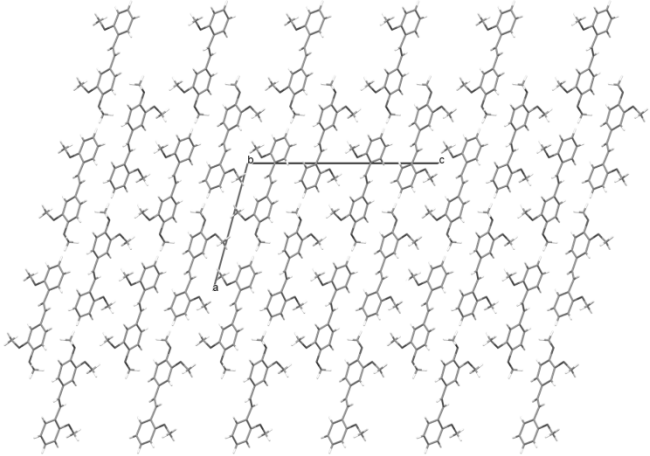


Fig. 5. The crystal packing as seen along [010] direction

Table 3.Torsion angles [°] for 5b.

C(20)-O(19)-C(1)-C(6)	3.1(2)
C(20)-O(19)-C(1)-C(2)	-175.22(12)
C(16)-O(15)-C(10)-C(11)	-1.99(19)
C(16)-O(15)-C(10)-C(9)	177.32(11)
O(19)-C(1)-C(6)-C(5)	-179.32(12)
C(2)-C(1)-C(6)-C(5)	-1.1(2)
C(5)-C(4)-C(3)-C(2)	-1.0(2)
C(7)-C(4)-C(3)-C(2)	178.16(12)
C(1)-C(6)-C(5)-C(4)	-1.3(2)
C(3)-C(4)-C(5)-C(6)	2.3(2)
C(7)-C(4)-C(5)-C(6)	-176.84(13)
C(18)-O(17)-C(2)-C(3)	-10.5(2)

C(18)-O(17)-C(2)-C(1)	168.90(12)
C(4)-C(3)-C(2)-O(17)	178.02(12)
C(4)-C(3)-C(2)-C(1)	-1.4(2)
O(19)-C(1)-C(2)-O(17)	1.36(18)
C(6)-C(1)-C(2)-O(17)	-177.06(12)
O(19)-C(1)-C(2)-C(3)	-179.19(12)
C(6)-C(1)-C(2)-C(3)	2.4(2)
O(15)-C(10)-C(11)-C(12)	179.91(13)
C(9)-C(10)-C(11)-C(12)	0.6(2)
C(13)-C(14)-C(9)-C(10)	1.6(2)
C(13)-C(14)-C(9)-C(8)	-177.78(13)
O(15)-C(10)-C(9)-C(14)	178.99(12)
C(11)-C(10)-C(9)-C(14)	-1.7(2)
O(15)-C(10)-C(9)-C(8)	-1.62(19)
C(11)-C(10)-C(9)-C(8)	177.71(13)
C(7)-C(8)-C(9)-C(14)	14.0(2)
C(7)-C(8)-C(9)-C(10)	-165.35(14)
C(9)-C(14)-C(13)-C(12)	-0.5(2)
C(9)-C(8)-C(7)-C(4)	-177.69(13)
C(5)-C(4)-C(7)-C(8)	167.25(15)
C(3)-C(4)-C(7)-C(8)	-11.9(2)
C(10)-C(11)-C(12)-C(13)	0.6(2)
C(14)-C(13)-C(12)-C(11)	-0.7(2)

3.3 X-ray structure of 3,4,2',6'-tetramethoxy-trans-stilbene (5f)

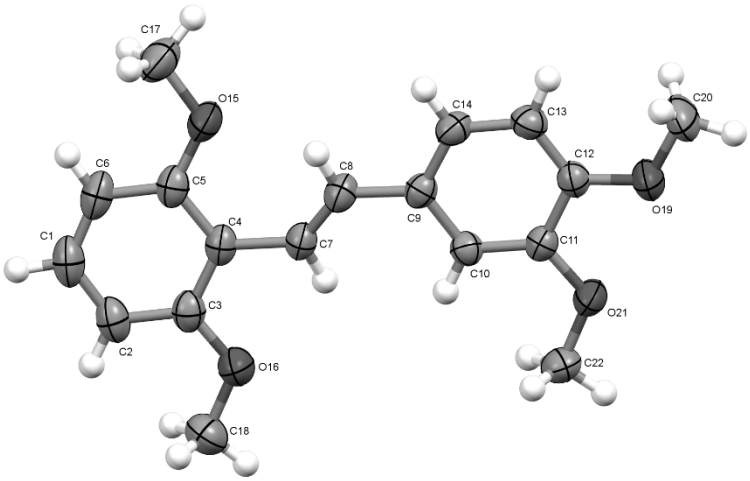


Fig. 6. A view of **5f**, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

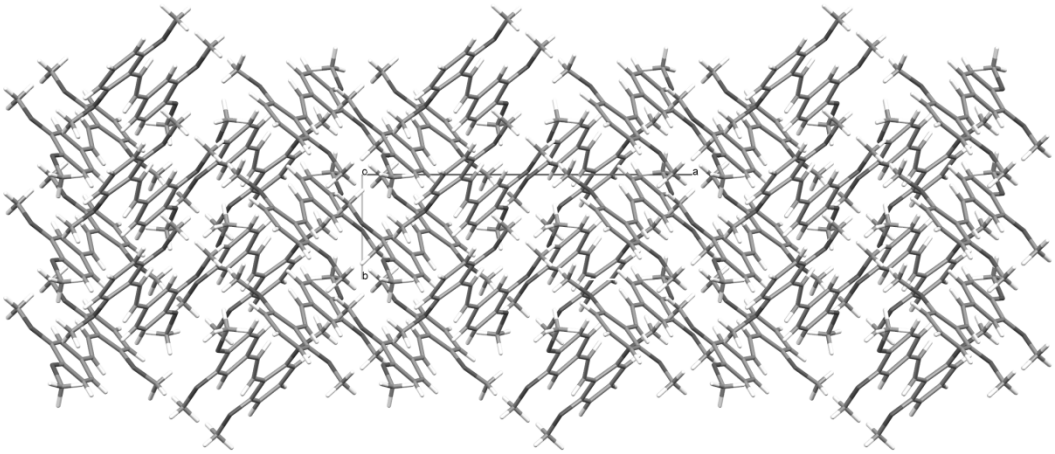


Fig. 7. The crystal packing as seen along [001]direction

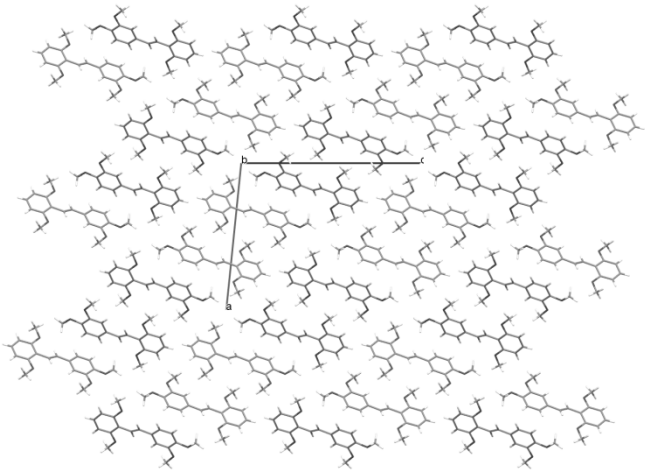


Fig. 8. The crystal packing as seen along [010] direction

Table 4.Torsion angles [°] for 5f.

C(6)-C(1)-C(2)-C(3)	1.4(2)
C(1)-C(2)-C(3)-O(16)	179.43(12)
C(1)-C(2)-C(3)-C(4)	0.39(19)
O(16)-C(3)-C(4)-C(5)	178.41(10)
C(2)-C(3)-C(4)-C(5)	-2.49(17)
O(16)-C(3)-C(4)-C(7)	-2.11(16)
C(2)-C(3)-C(4)-C(7)	176.99(11)
C(3)-C(4)-C(5)-O(15)	-176.71(10)
C(7)-C(4)-C(5)-O(15)	3.83(17)
C(3)-C(4)-C(5)-C(6)	2.99(17)
C(7)-C(4)-C(5)-C(6)	-176.46(12)
C(2)-C(1)-C(6)-C(5)	-0.9(2)
O(15)-C(5)-C(6)-C(1)	178.29(12)

C(4)-C(5)-C(6)-C(1)	-1.40(19)
C(3)-C(4)-C(7)-C(8)	-161.80(12)
C(5)-C(4)-C(7)-C(8)	17.6(2)
C(4)-C(7)-C(8)-C(9)	179.29(12)
C(7)-C(8)-C(9)-C(14)	167.71(12)
C(7)-C(8)-C(9)-C(10)	-11.8(2)
C(14)-C(9)-C(10)-C(11)	-0.39(16)
C(8)-C(9)-C(10)-C(11)	179.11(11)
C(9)-C(10)-C(11)-O(21)	178.57(10)
C(9)-C(10)-C(11)-C(12)	-0.70(17)
O(21)-C(11)-C(12)-O(19)	-0.28(15)
C(10)-C(11)-C(12)-O(19)	179.06(10)
O(21)-C(11)-C(12)-C(13)	-178.69(10)
C(10)-C(11)-C(12)-C(13)	0.65(17)
O(19)-C(12)-C(13)-C(14)	-177.74(11)
C(11)-C(12)-C(13)-C(14)	0.50(18)
C(10)-C(9)-C(14)-C(13)	1.58(17)
C(8)-C(9)-C(14)-C(13)	-177.95(11)
C(12)-C(13)-C(14)-C(9)	-1.66(19)
C(6)-C(5)-O(15)-C(17)	-0.41(19)
C(4)-C(5)-O(15)-C(17)	179.28(13)
C(2)-C(3)-O(16)-C(18)	2.84(19)
C(4)-C(3)-O(16)-C(18)	-178.07(12)
C(13)-C(12)-O(19)-C(20)	3.6(2)
C(11)-C(12)-O(19)-C(20)	-174.73(14)
C(10)-C(11)-O(21)-C(22)	-2.67(18)
C(12)-C(11)-O(21)-C(22)	176.63(11)

3.4. X-ray structure of 3,4,2',3',4'-pentamethoxy-trans-stilbene (5g)

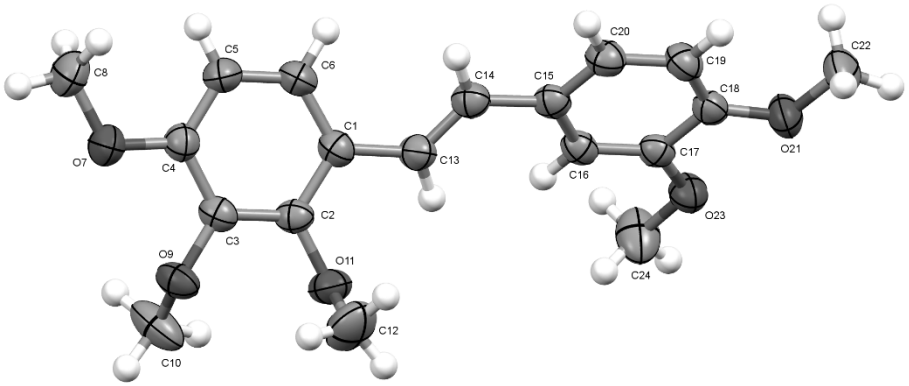


Fig. 9. A view of **5g**, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

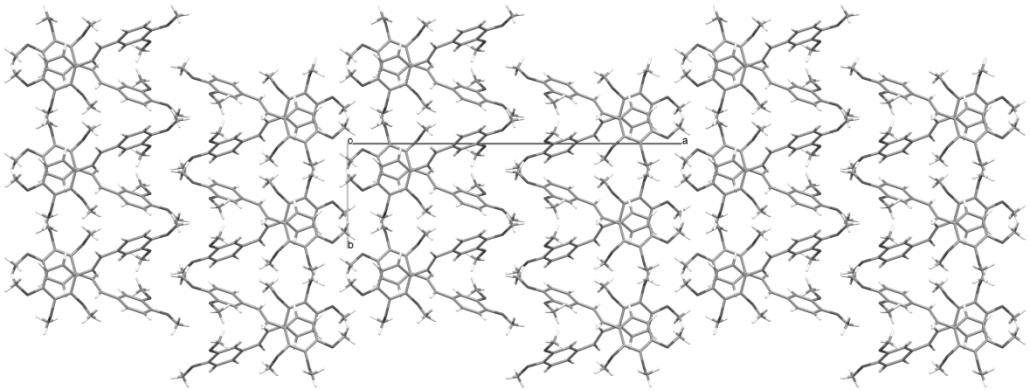


Fig. 10. The crystal packing as seen along the chain direction, i.e. along [001]

Table 5.Torsion angles [°] for 5g.

C(6)-C(1)-C(2)-O(11)	178.07(14)
C(13)-C(1)-C(2)-O(11)	-2.6(2)
C(6)-C(1)-C(2)-C(3)	-0.3(2)
C(13)-C(1)-C(2)-C(3)	179.07(14)
O(11)-C(2)-C(3)-O(9)	3.5(2)
C(1)-C(2)-C(3)-O(9)	-178.17(14)
O(11)-C(2)-C(3)-C(4)	-179.29(13)
C(1)-C(2)-C(3)-C(4)	-1.0(2)
O(9)-C(3)-C(4)-O(7)	-2.5(2)
C(2)-C(3)-C(4)-O(7)	-179.76(13)
O(9)-C(3)-C(4)-C(5)	178.38(14)
C(2)-C(3)-C(4)-C(5)	1.1(2)
O(7)-C(4)-C(5)-C(6)	-179.05(15)
C(3)-C(4)-C(5)-C(6)	0.0(2)
C(4)-C(5)-C(6)-C(1)	-1.3(3)
C(2)-C(1)-C(6)-C(5)	1.4(2)
C(13)-C(1)-C(6)-C(5)	-177.91(15)
C(5)-C(4)-O(7)-C(8)	-4.6(2)
C(3)-C(4)-O(7)-C(8)	176.30(15)
C(2)-C(3)-O(9)-C(10)	-73.1(2)
C(4)-C(3)-O(9)-C(10)	109.64(18)
C(3)-C(2)-O(11)-C(12)	-75.3(2)
C(1)-C(2)-O(11)-C(12)	106.35(18)
C(6)-C(1)-C(13)-C(14)	31.2(2)
C(2)-C(1)-C(13)-C(14)	-148.06(17)
C(1)-C(13)-C(14)-C(15)	179.93(15)
C(13)-C(14)-C(15)-C(20)	-159.33(16)
C(13)-C(14)-C(15)-C(16)	18.8(3)
C(20)-C(15)-C(16)-C(17)	1.3(2)

C(14)-C(15)-C(16)-C(17)	-176.92(14)
C(15)-C(16)-C(17)-O(23)	-179.11(14)
C(15)-C(16)-C(17)-C(18)	0.4(2)
O(23)-C(17)-C(18)-O(21)	-1.3(2)
C(16)-C(17)-C(18)-O(21)	179.14(14)
O(23)-C(17)-C(18)-C(19)	178.35(14)
C(16)-C(17)-C(18)-C(19)	-1.2(2)
O(21)-C(18)-C(19)-C(20)	179.90(16)
C(17)-C(18)-C(19)-C(20)	0.3(2)
C(16)-C(15)-C(20)-C(19)	-2.2(2)
C(14)-C(15)-C(20)-C(19)	176.02(15)
C(18)-C(19)-C(20)-C(15)	1.4(3)
C(19)-C(18)-O(21)-C(22)	-2.2(3)
C(17)-C(18)-O(21)-C(22)	177.39(15)
C(16)-C(17)-O(23)-C(24)	1.7(2)
C(18)-C(17)-O(23)-C(24)	-177.86(16)

3.5. X-ray structure of 3,4,2',4',6'-pentamethoxy-trans-stilbene (5i)

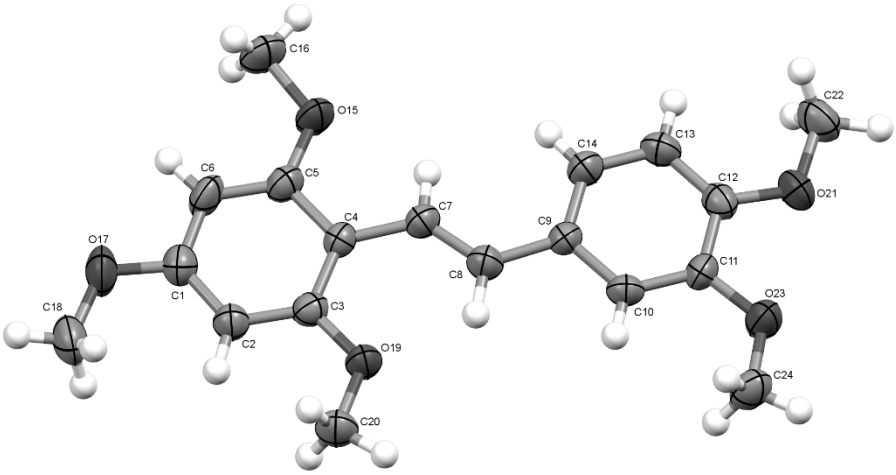


Fig. 11. A view of **5i**, showing the atom-labeling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii.

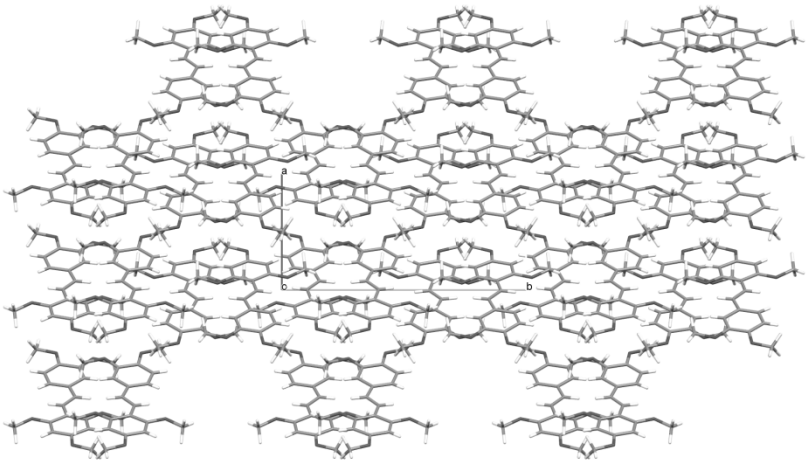


Fig. 12.The crystal packing as seen along [001]direction

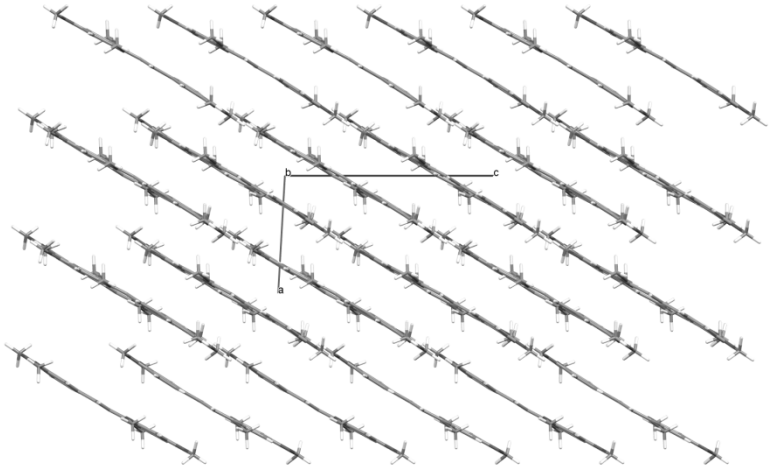


Fig. 13. The crystal packing as seen along [010] direction

Table 6. Torsion angles [°] for 5i.

C(20)-O(19)-C(3)-C(2)	8.2(3)
C(20)-O(19)-C(3)-C(4)	-171.6(2)
C(5)-C(4)-C(3)-O(19)	178.9(2)
C(7)-C(4)-C(3)-O(19)	-0.9(3)
C(5)-C(4)-C(3)-C(2)	-1.0(3)
C(7)-C(4)-C(3)-C(2)	179.2(2)
C(3)-C(4)-C(7)-C(8)	-3.5(5)
C(5)-C(4)-C(7)-C(8)	176.7(3)
C(24)-O(23)-C(11)-C(12)	-173.7(2)
C(24)-O(23)-C(11)-C(10)	6.5(4)
O(23)-C(11)-C(10)-C(9)	179.9(2)
C(12)-C(11)-C(10)-C(9)	0.2(4)
C(22)-O(21)-C(12)-C(13)	2.4(4)
C(22)-O(21)-C(12)-C(11)	-177.9(2)
O(23)-C(11)-C(12)-C(13)	178.5(2)
C(10)-C(11)-C(12)-C(13)	-1.7(4)

O(23)-C(11)-C(12)-O(21)	-1.2(3)
C(10)-C(11)-C(12)-O(21)	178.5(2)
C(18)-O(17)-C(1)-C(6)	177.9(2)
C(18)-O(17)-C(1)-C(2)	-1.0(4)
C(11)-C(10)-C(9)-C(14)	1.2(4)
C(11)-C(10)-C(9)-C(8)	-177.2(2)
C(4)-C(7)-C(8)-C(9)	-177.2(2)
C(14)-C(9)-C(8)-C(7)	0.8(4)
C(10)-C(9)-C(8)-C(7)	179.2(3)
C(16)-O(15)-C(5)-C(6)	-5.2(4)
C(16)-O(15)-C(5)-C(4)	174.0(2)
C(3)-C(4)-C(5)-O(15)	-179.1(2)
C(7)-C(4)-C(5)-O(15)	0.8(3)
C(3)-C(4)-C(5)-C(6)	0.2(4)
C(7)-C(4)-C(5)-C(6)	-180.0(2)
O(17)-C(1)-C(2)-C(3)	178.4(2)
C(6)-C(1)-C(2)-C(3)	-0.5(4)
O(19)-C(3)-C(2)-C(1)	-178.7(2)
C(4)-C(3)-C(2)-C(1)	1.1(4)
C(10)-C(9)-C(14)-C(13)	-1.1(4)
C(8)-C(9)-C(14)-C(13)	177.2(3)
O(17)-C(1)-C(6)-C(5)	-179.2(2)
C(2)-C(1)-C(6)-C(5)	-0.2(4)
O(15)-C(5)-C(6)-C(1)	179.6(2)
C(4)-C(5)-C(6)-C(1)	0.4(4)
O(21)-C(12)-C(13)-C(14)	-178.5(3)
C(11)-C(12)-C(13)-C(14)	1.8(4)
C(9)-C(14)-C(13)-C(12)	-0.4(4)

4. Biological assay

To assess CYP1 enzyme activities 7-ethoxyresorufin *O*-deethylase (EROD) activity was measured according to the method of Burke *et al.*.[6] The test compounds were freshly dissolved in dimethylsulfoxide (DMSO) on the day of experiment.

The reaction mixture (1 ml total volume) contained the various concentrations of a test compound, 1.3 mM $NADP^+$, 3.3 mM glucose-6-phosphate, 0.5 U/ml glucose-6-phosphate dehydrogenase, 3.3 mM magnesium chloride and 2 µM 7-ethoxyresorufin in 100 mM potassium phosphate (pH 7.4). The reactions were initiated by the addition of human recombinant cytochromes (1.25 pmole CYP1A1, 5 pmole CYP1A2 or 5 pmole CYP1B1) and samples were incubated at 37°C for 15 min. The fluorescence of the product was determined on a HITACHI Model F 2500 fluorescence spectrophotometer (λ_{ex}550 and λ_{em}585). The quantitation of the deethylated metabolite was based on comparison of its fluorescence with resorufin as a standard. Control incubations did not contain the test compounds. The IC_{50}

values for the activity-concentration curves from individual experiments were calculated with GraphPad Prism software (San Diego, CA, USA).

5. Molecular docking

Analyzed molecules were docked to the active sites of CYP1A2 (PDB: 2HI4) and CYP1B1 (PDB: 3PM0) with the use of Accelrys Discovery Studio 3.5 suite of programs by LigandFit procedure.

Receptors were prepared for docking by 'Prepare protein' procedure. Water molecules were removed, hydrogen atoms added and aminoacid residues were protonated at the specified pH (pH = 7.4 for protonation).

For both targets the binding site was defined from the volume of a cocrystallized α-naphthoflavone ligand. The grid resolution was set to default value of 0.5 Å. Conformations of ligands were generated with use of a Monte Carlo method. During conformational search internal ligand electrostatic energy was not included and the constant number of trials equal to 5000 was set.

For docking and DockScore function calculations CFF forcefield was used. Twenty poses were saved for each ligand after docking and then minimized *in situ* with use of adopted basis Newton-Raphson algorithm. For further evaluation DockScore function was chosen as exhibiting the best correlation with experimental data.

All calculations were performed with use of CHARMm forcefield. Partial charges for receptors were set according to Momany-Rone method, but for ligands MMFF94 partial charge rules were used, except for interaction energy calculations, where Momany-Rone charges was also used for ligands.

For the best poses, these characterized by the highest values of DockScore function, binding, interaction and strain energies were calculated (Table XX). The binding free energies for selected receptor-ligand complexes were estimated by the 'Calculate binding energies' protocol. Poisson-Boltzmann with non-polar surface area (PBSA) implicit solvent model was used in these calculations and the parameter 'use non-polar surface area' was set to 'True'. Interaction energy was calculated between ligands and residues surrounding binding site,

within 5Å radius from cocrystallized α-naphthoflavone ligand, including heme. Strain energy, as a difference between energy of docked conformation and energy of optimized ligand structure was calculated with aid of 'Calculate molecular properties' protocol.

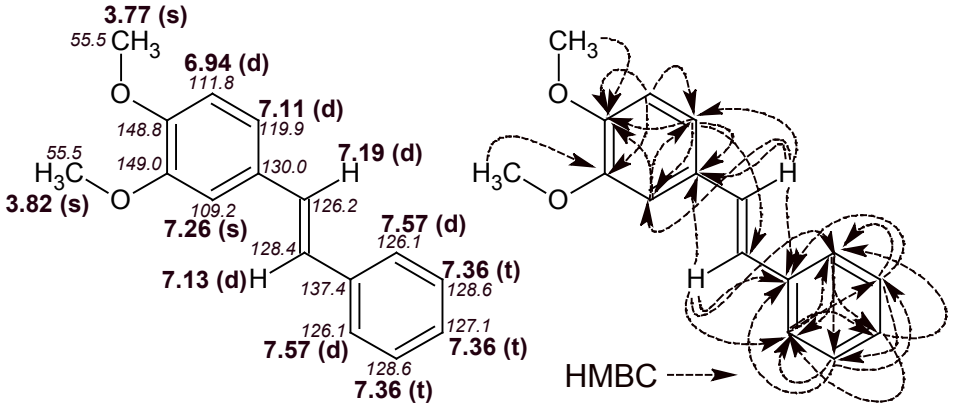
Table 7. Characteristic of ligand-receptor complexes calculated for best poses of ligands

Compound	DockScore		Binding energy [kcal/mol]		Interaction energy [kcal/mol]		Strain energy [kcal/mol]	
	CYP1A2	CYP1B1	CYP1A2	CYP1B1	CYP1A2	CYP1B1	CYP1A2	CYP1B1
5a	52.6	56.8	–295.6	–399.6	–40.3	–41.2	32.7	45.12
5b pose A*	53.0	57.1	–299.2	–443.1	–43.4	–59.0	94.03	48.87
5b pose B**	——	55.6	——	–403.0	——	–47.2	——	74.08
5c	26.8	48.7	–328.4	–428.4	–58.6	–60.3	108.81	80.32
5d	24.0	52.5	–304.3	–409.4	–47.5	–53.3	115.52	60.11
5e	34.5	57.6	–319.4	–406.9	–52.9	–53.3	65.77	71.21
5f	42.2	63.1	–302.3	–434.4	–44.6	–63.8	140.76	46.02
5g	——	32.2	——	–415.9	——	–59.4	——	76.57
5h	——	21.9	——	–412.9	——	–55.1	——	70.07
5i	9.0	26.8	–328.3	–426.1	–62.9	–55.8	129.72	117.15

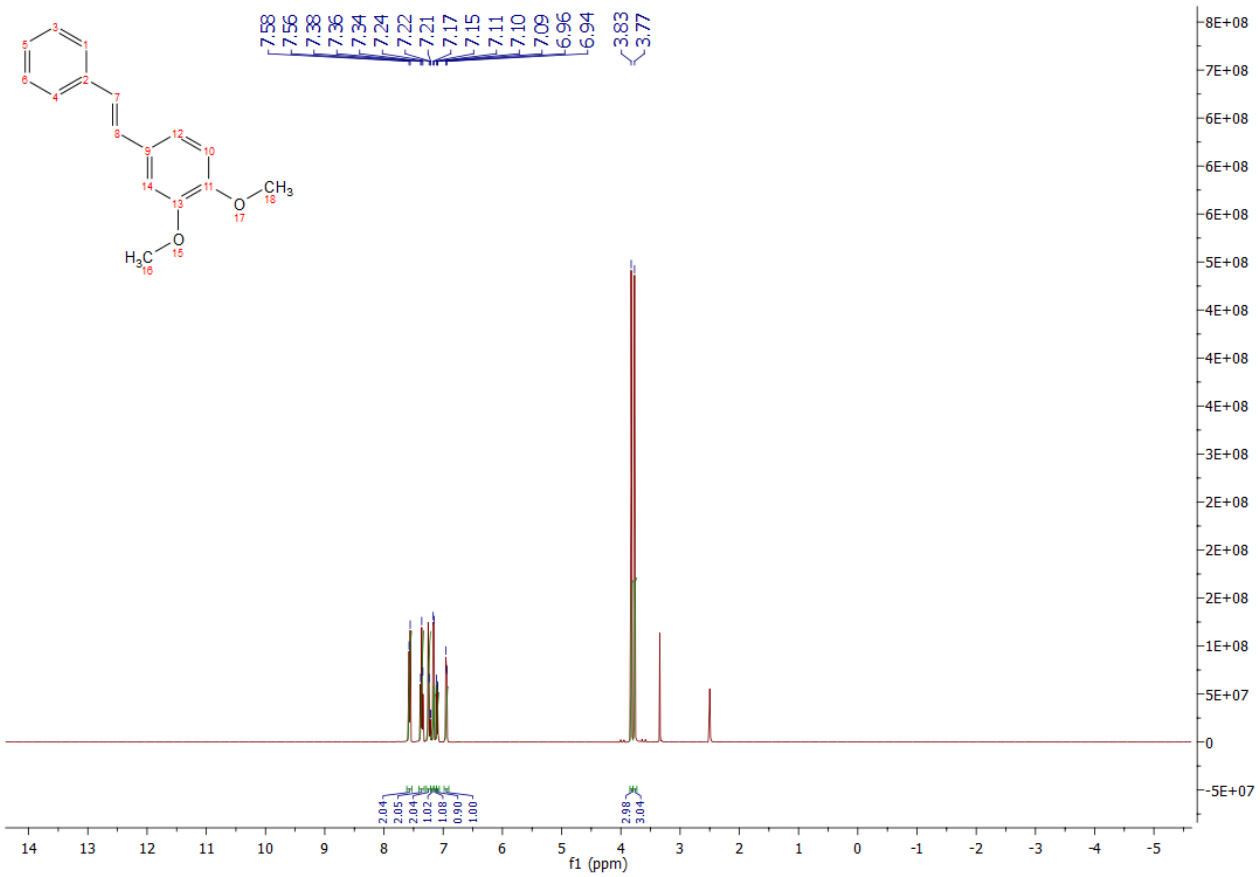
* ring A directed to the heme
** ring B directed to the heme

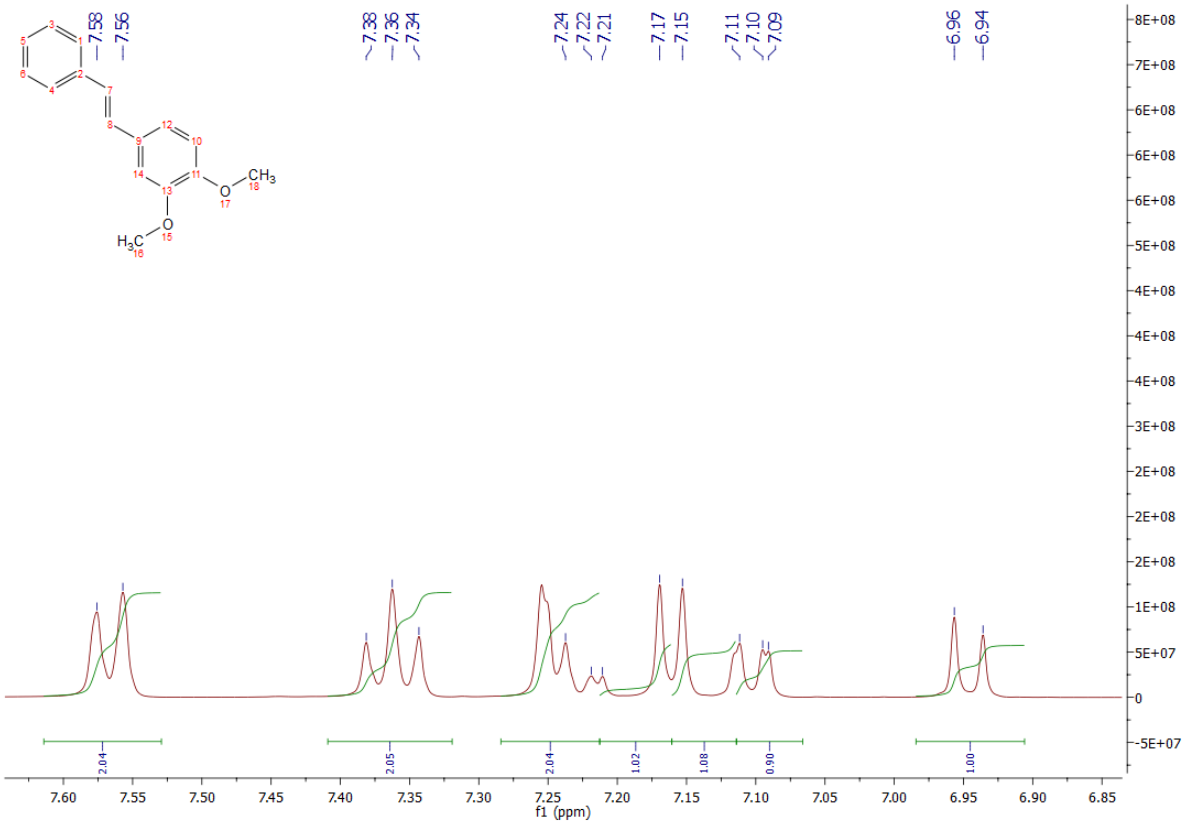
6. NMR 1D and 2D experiments

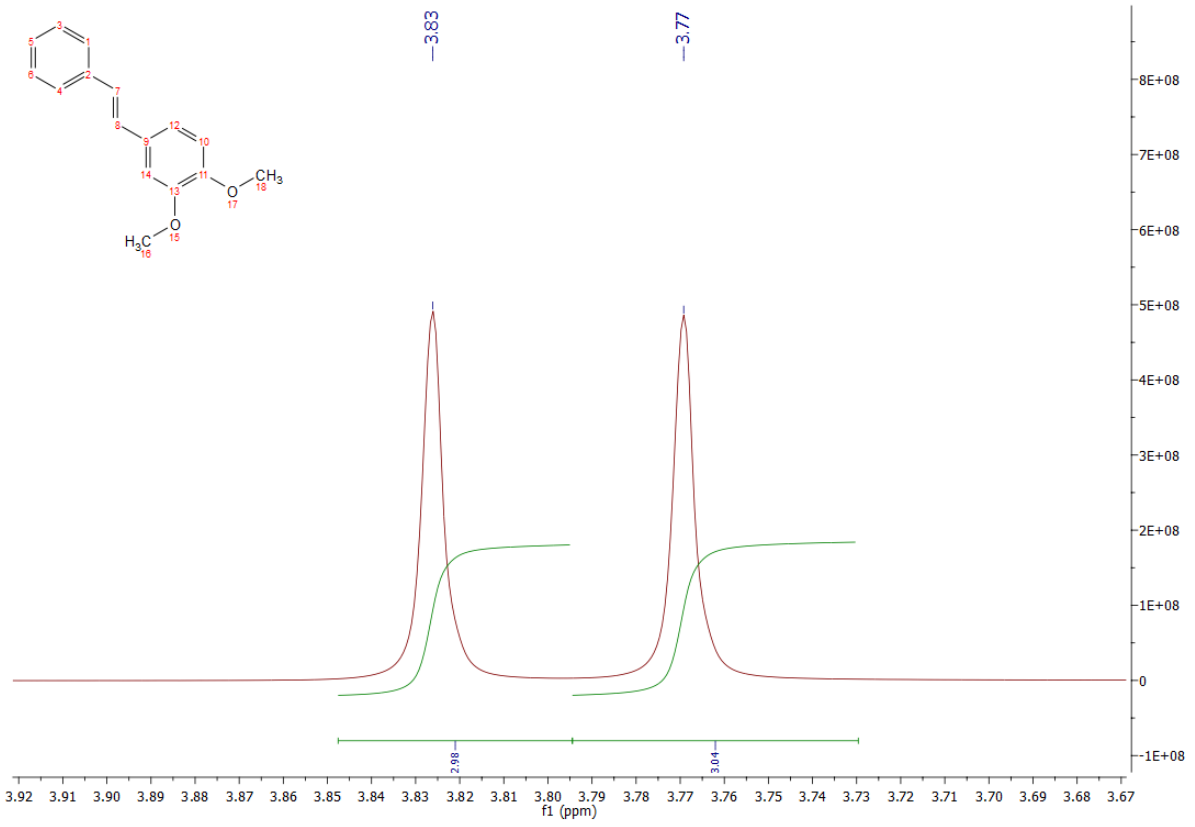
6.1 NMR data for 3,4-dimethoxy-trans-stilbene (5a)



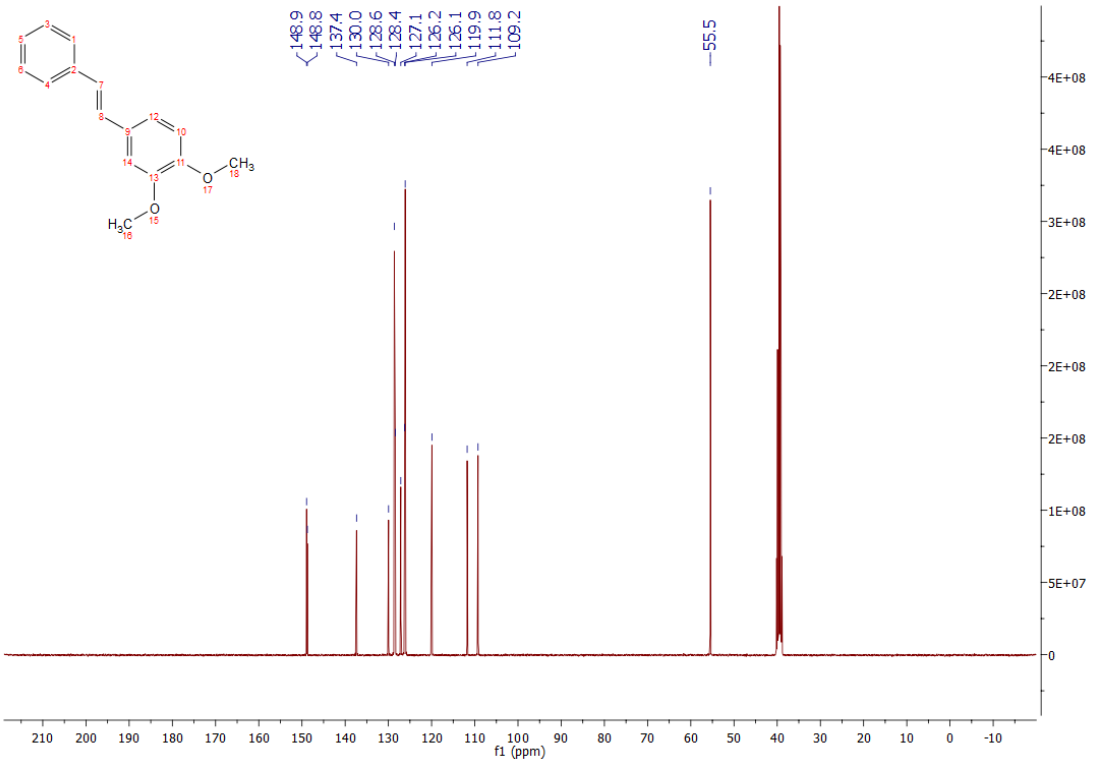
Scheme 1. Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

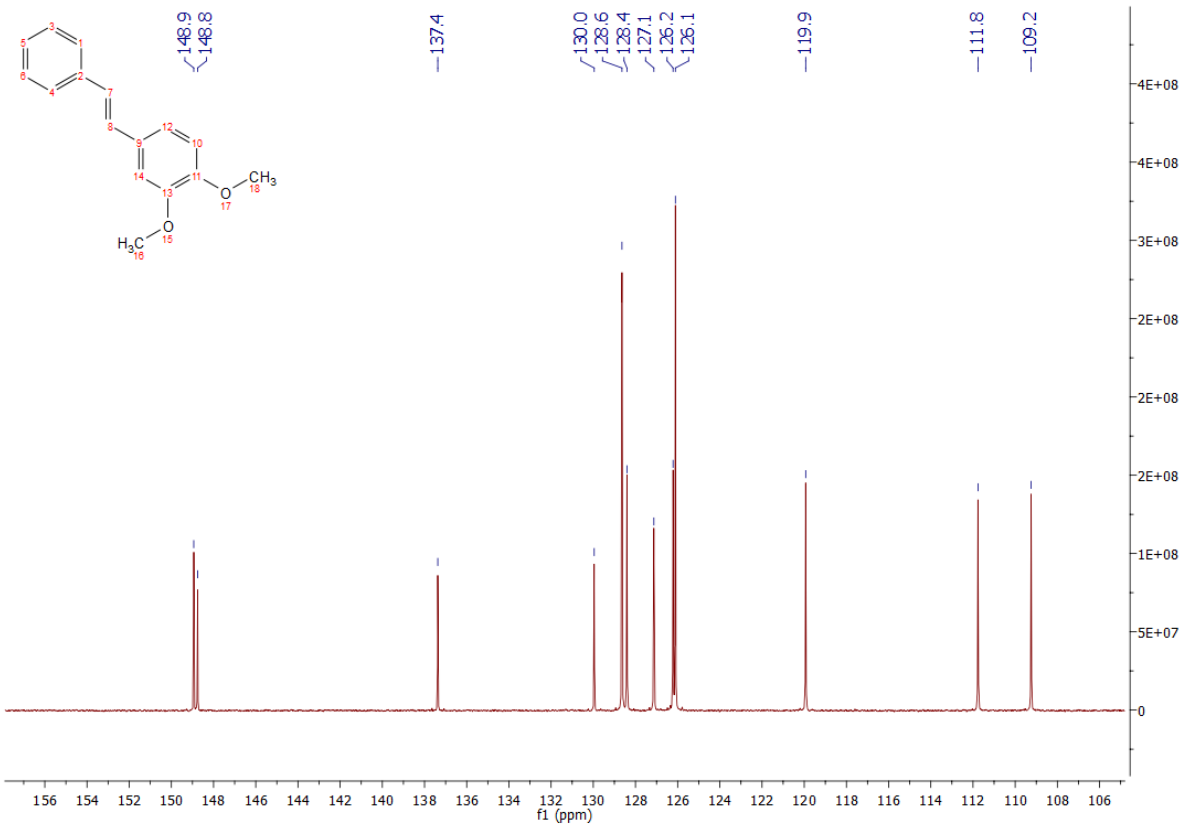


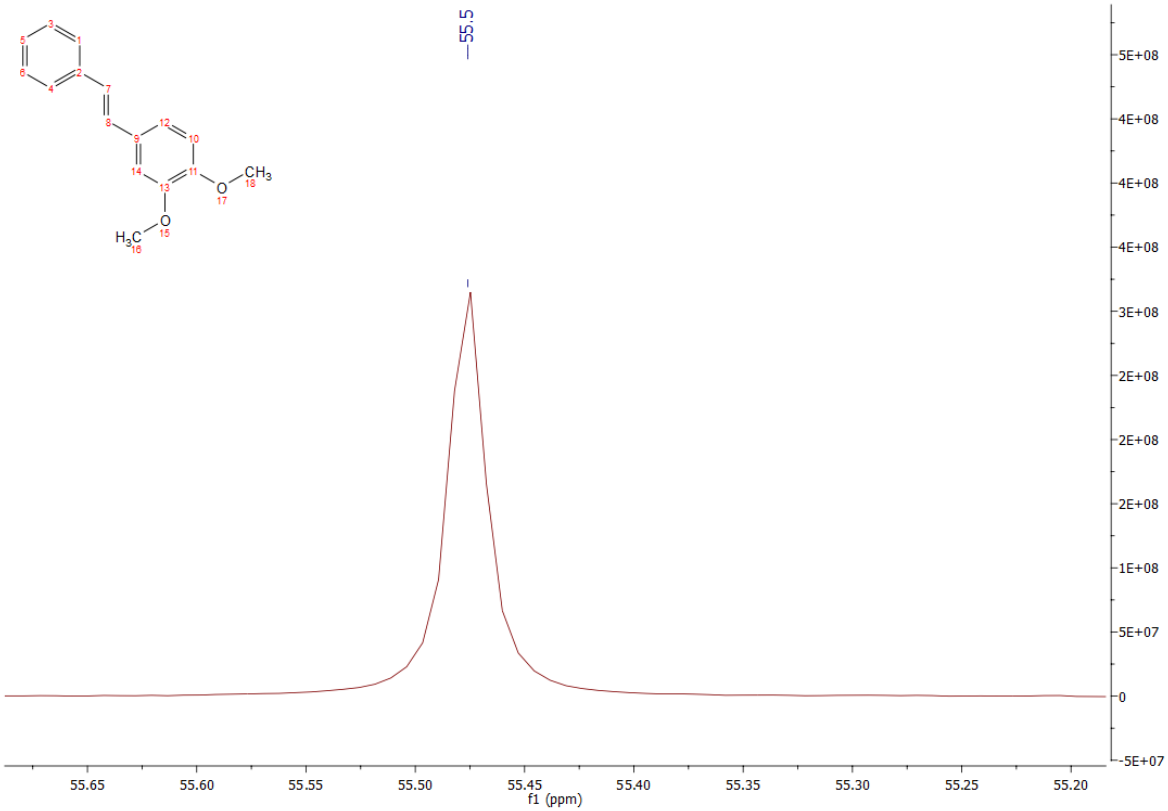

7.58
7.56
7.38
7.36
7.34
7.24
7.22
7.21
7.17
7.15
7.11
7.10
7.09
6.96
6.94
f1 (ppm)


3.83
3.77
f1 (ppm)

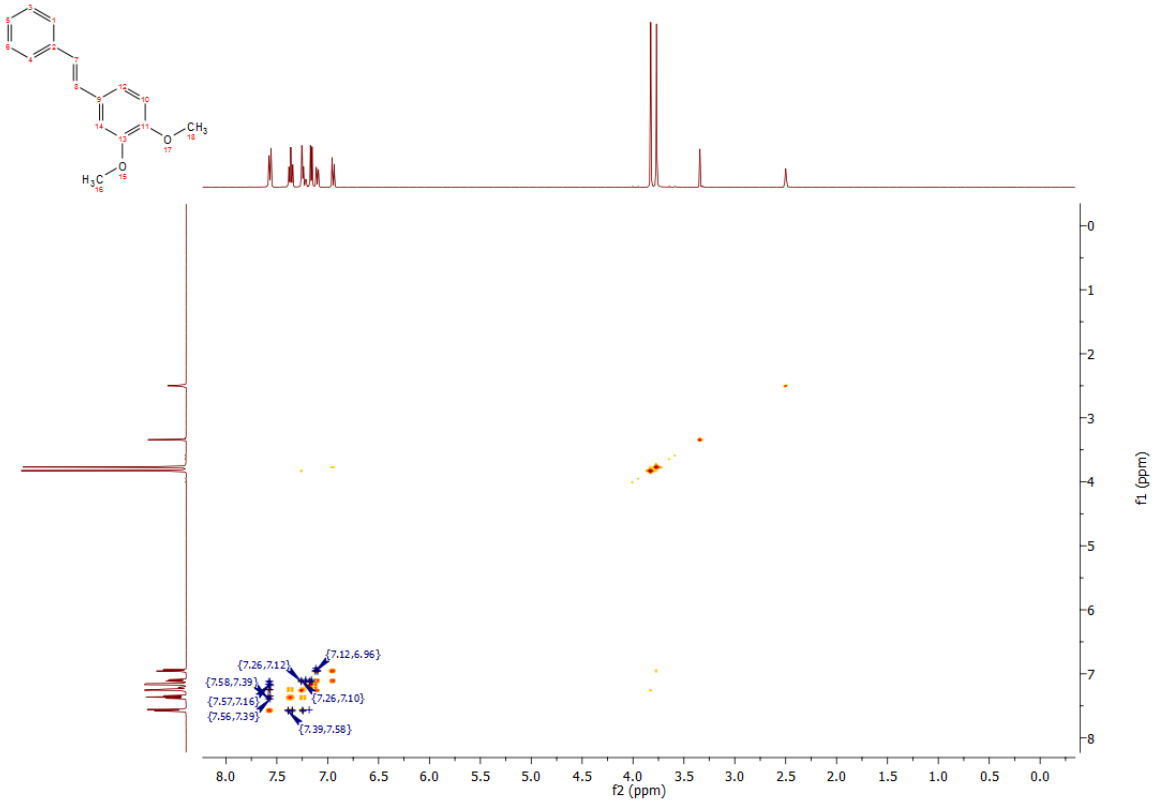
13C

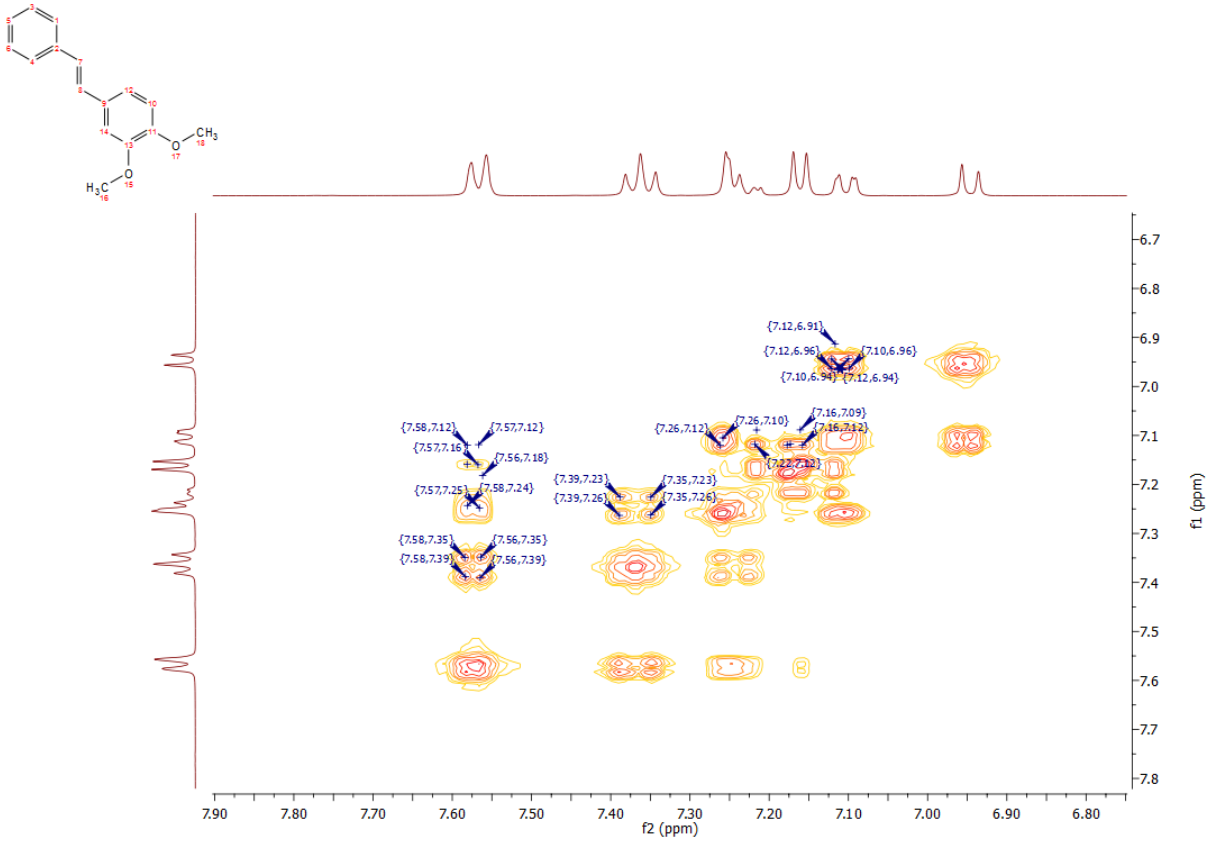

148.9
148.8
137.4
130.0
128.6
128.4
127.1
126.2
126.1
119.9
111.8
109.2
55.5
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


148.9
148.8
137.4
130.0
128.6
128.4
127.1
126.2
126.1
119.9
111.8
109.2
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
156 154 152 150 148 146 144 142 140 138 136 134 132 130 128 126 124 122 120 118 116 114 112 110 108 106
f1 (ppm)

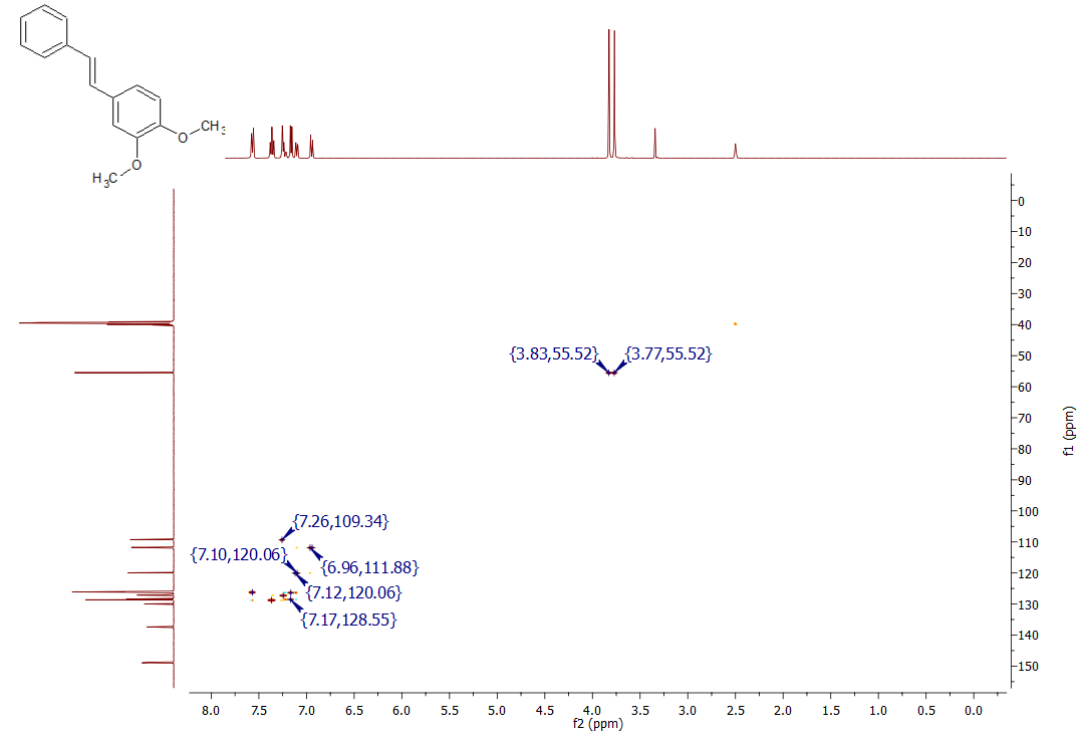

55.5
5E+08
4E+08
4E+08
4E+08
3E+08
2E+08
2E+08
2E+08
1E+08
5E+07
0
-5E+07
55.65
55.60
55.55
55.50
55.45
55.40
55.35
55.30
55.25
55.20
f1 (ppm)

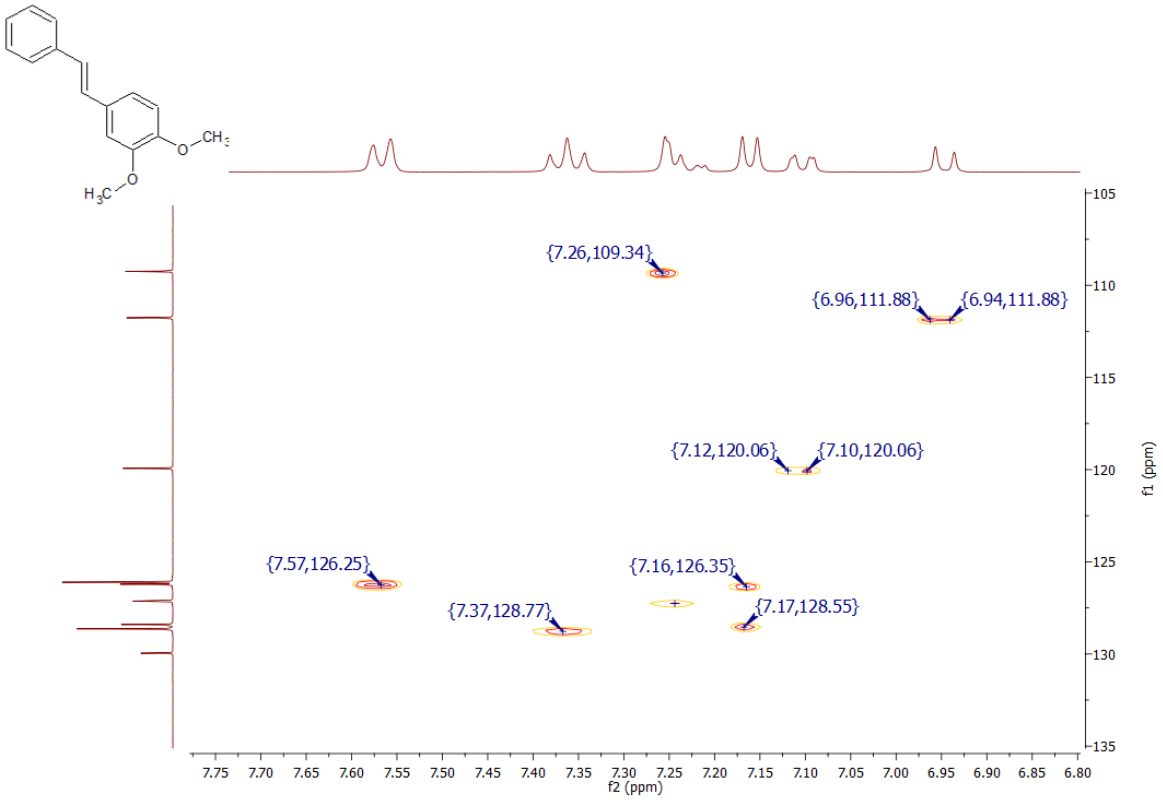
1H1H COSY


{7.26,7.12}
{7.12,6.96}
{7.58,7.39}
{7.57,7.16}
{7.26,7.10}
{7.56,7.39}
{7.39,7.58}
f1 (ppm)
f2 (ppm)

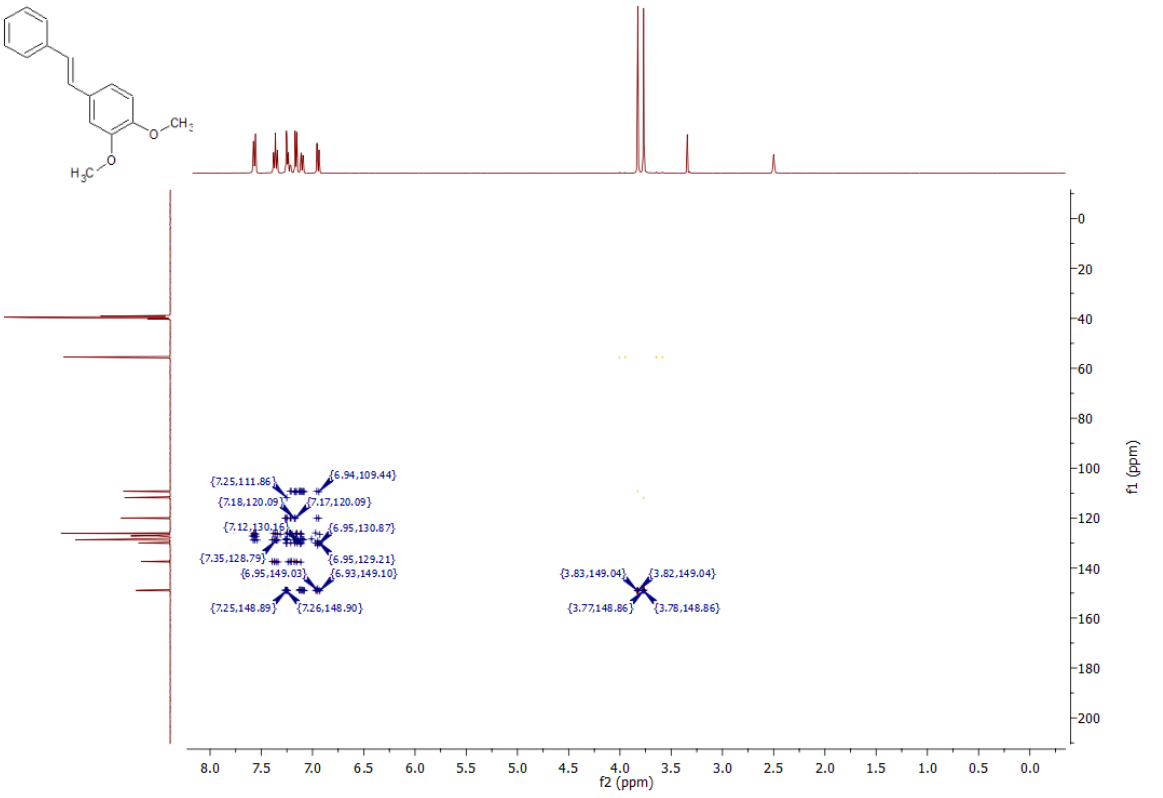

{7.12,6.91}
{7.12,6.96}
{7.10,6.96}
{7.10,6.94}
{7.12,6.94}
{7.58,7.12}
{7.57,7.12}
{7.57,7.16}
{7.56,7.18}
{7.57,7.25}
{7.58,7.24}
{7.58,7.35}
{7.58,7.39}
{7.56,7.35}
{7.56,7.39}
{7.26,7.12}
{7.26,7.10}
{7.16,7.09}
{7.16,7.12}
{7.22,7.12}
{7.39,7.23}
{7.39,7.26}
{7.35,7.23}
{7.35,7.26}
f1 (ppm)
f2 (ppm)

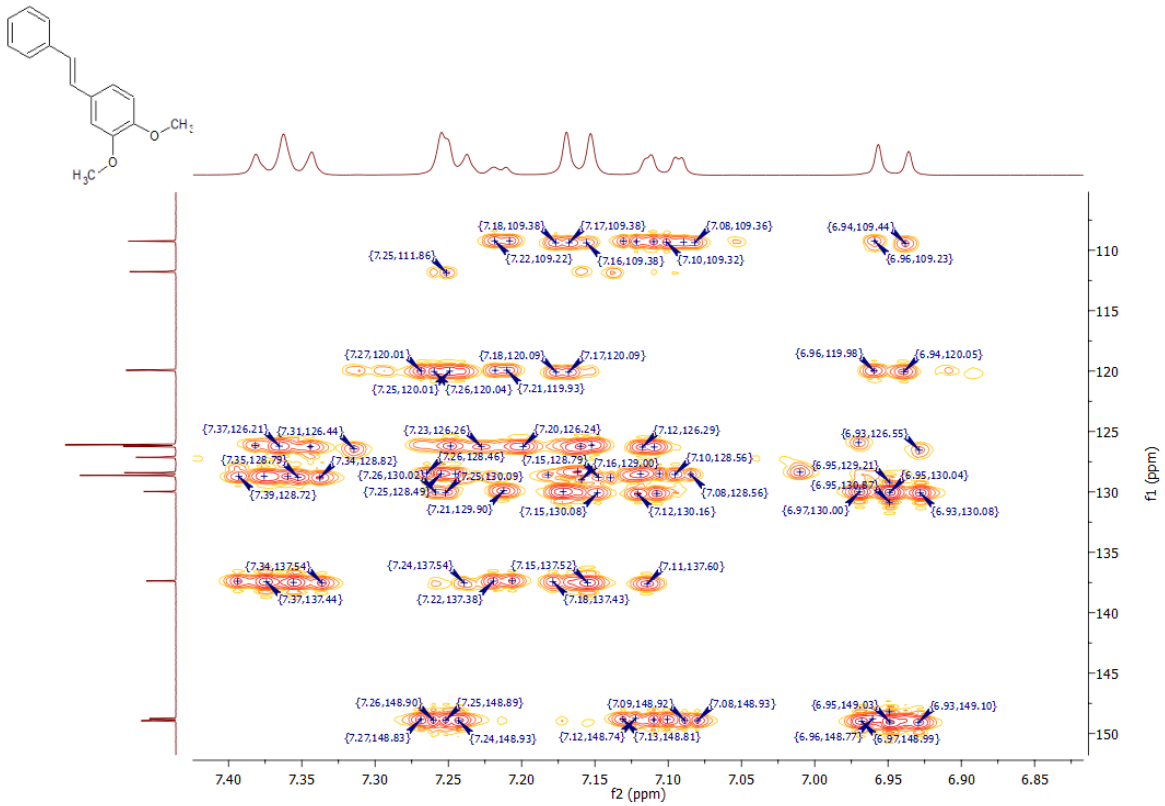
HSQC


{3.83,55.52}
{3.77,55.52}
{7.26,109.34}
{7.10,120.06}
{6.96,111.88}
{7.12,120.06}
{7.17,128.55}
f1 (ppm)
f2 (ppm)

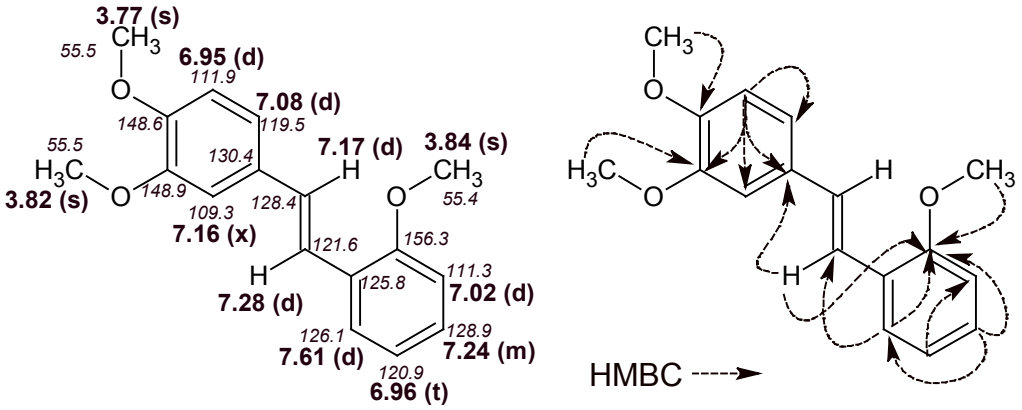

{7.26,109.34}
{6.96,111.88}
{6.94,111.88}
{7.12,120.06}
{7.10,120.06}
{7.57,126.25}
{7.16,126.35}
{7.37,128.77}
{7.17,128.55}
f1 (ppm)
f2 (ppm)

HMBC


{7.25,111.86}
{6.94,109.44}
{7.18,120.09}
{7.17,120.09}
{7.12,130.15}
{6.95,130.87}
{7.35,128.79}
{6.95,129.21}
{6.95,149.03}
{6.93,149.10}
{7.25,148.89}
{7.26,148.90}
{3.83,149.04}
{3.82,149.04}
{3.77,148.86}
{3.78,148.86}
f1 (ppm)
f2 (ppm)

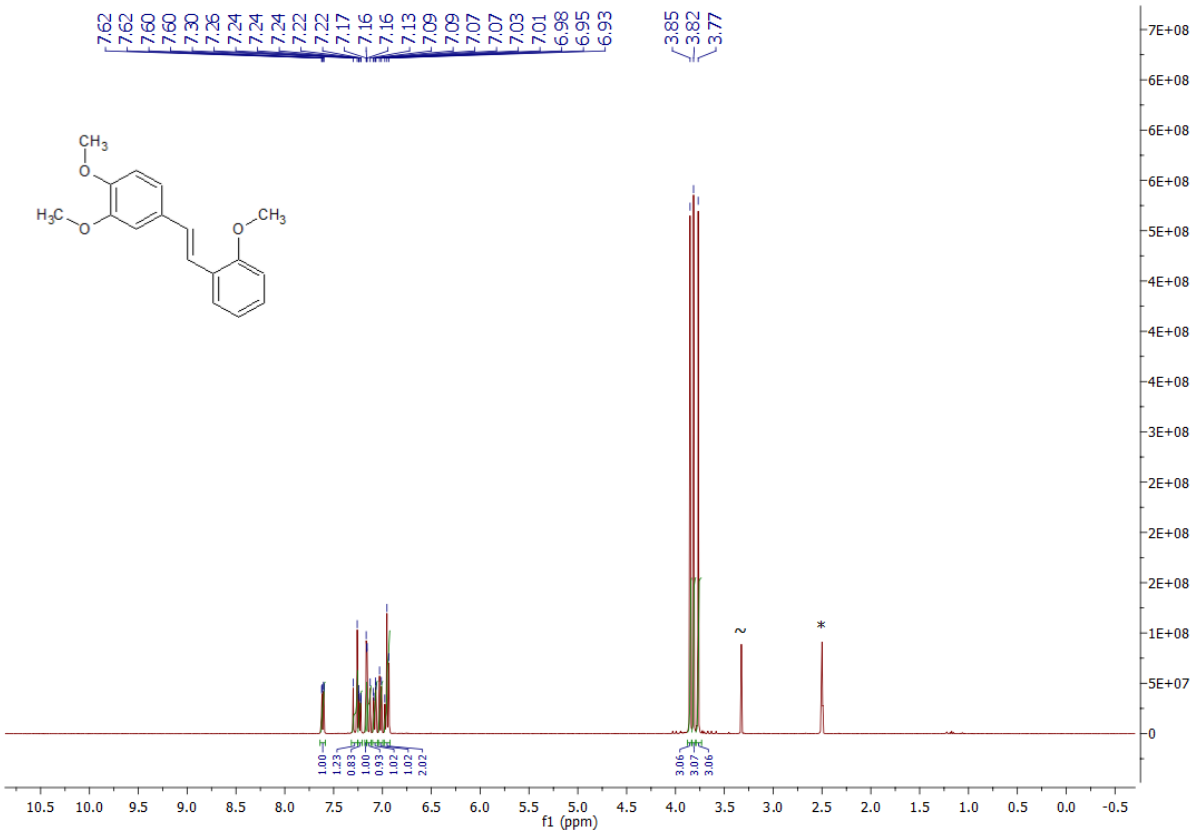


6.2 NMR data for 3,4,2'-trimethoxy-trans-stilbene (5b).

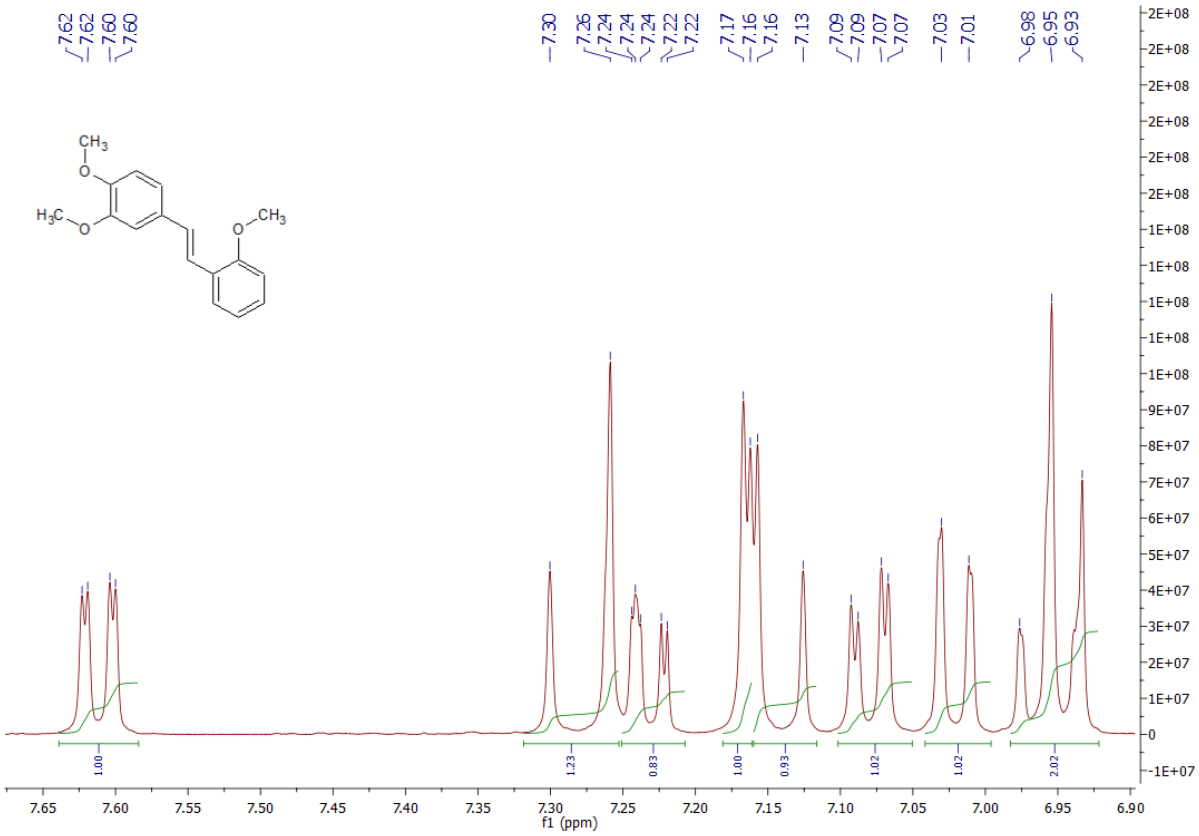


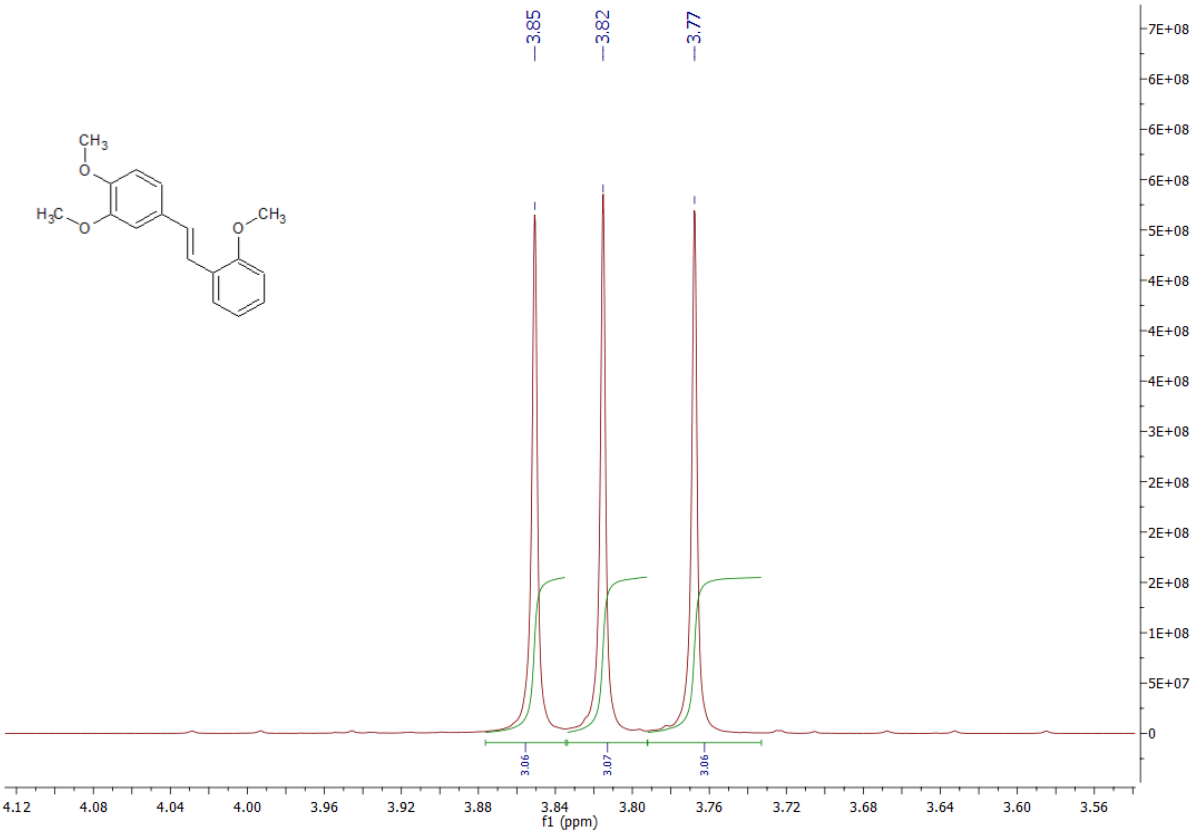
Scheme X2 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

1H

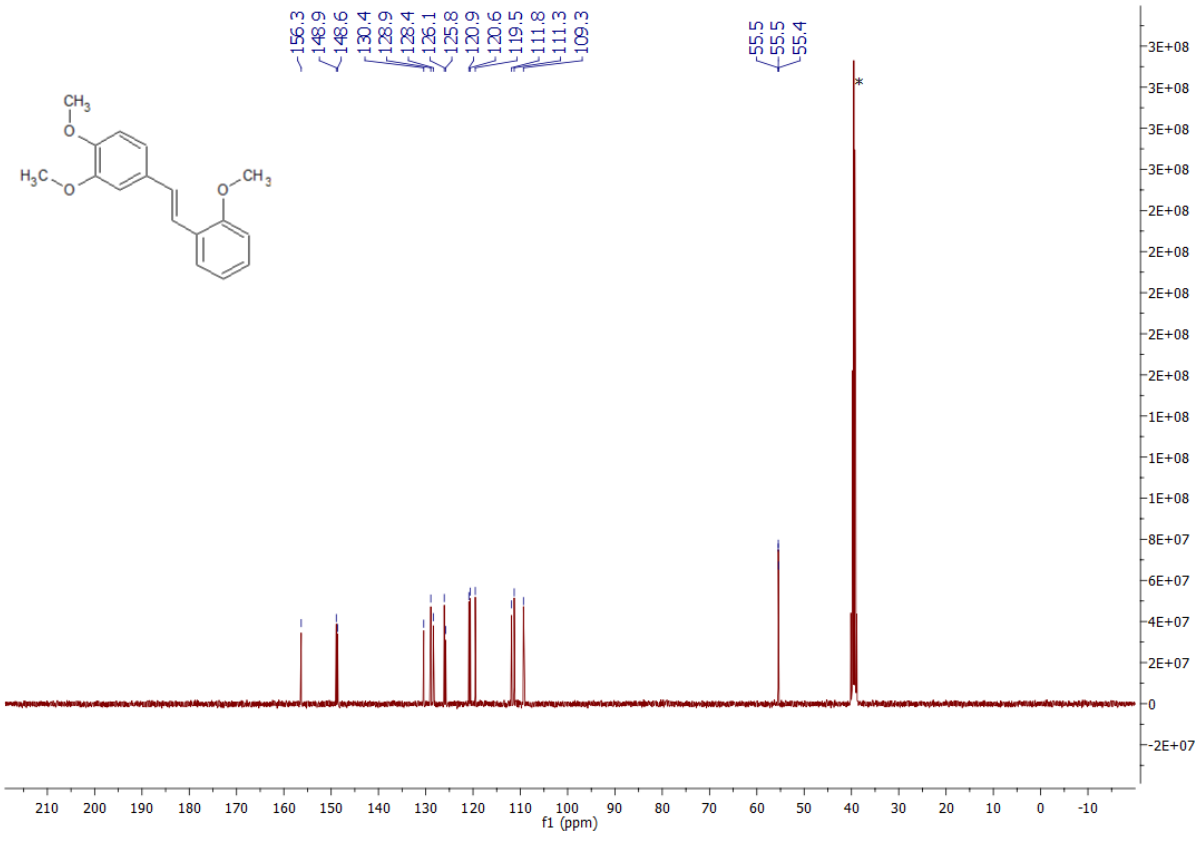


Symbol * and ~ indicates DMSO and water residuals peaks.

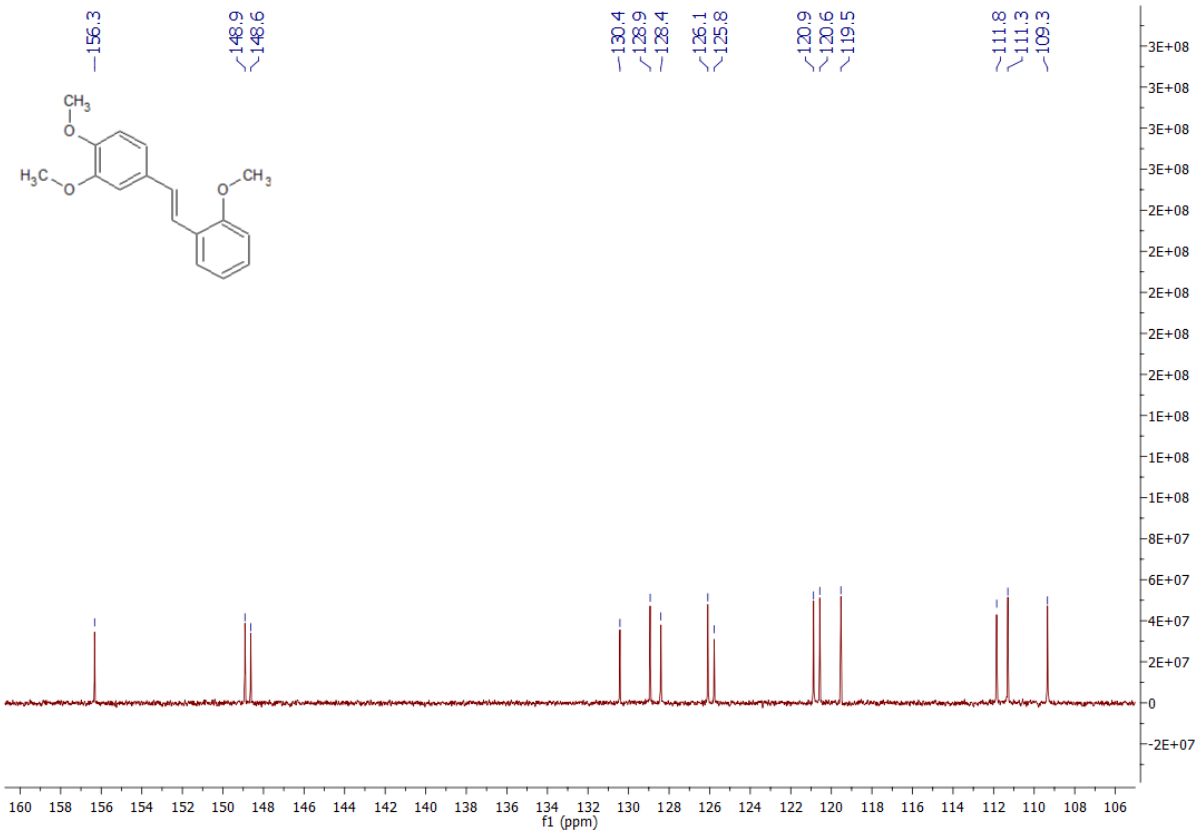


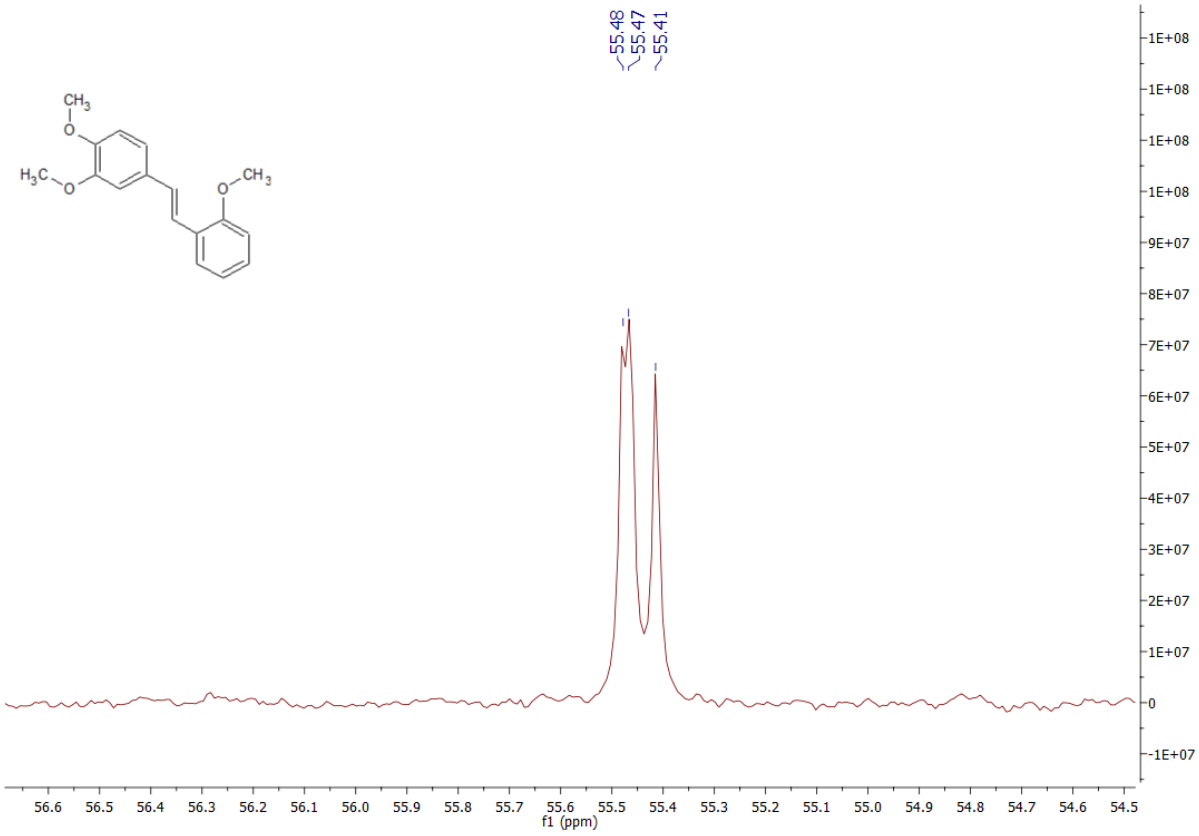

3.85
3.82
3.77
3.06
3.07
3.06
f1 (ppm)

13C

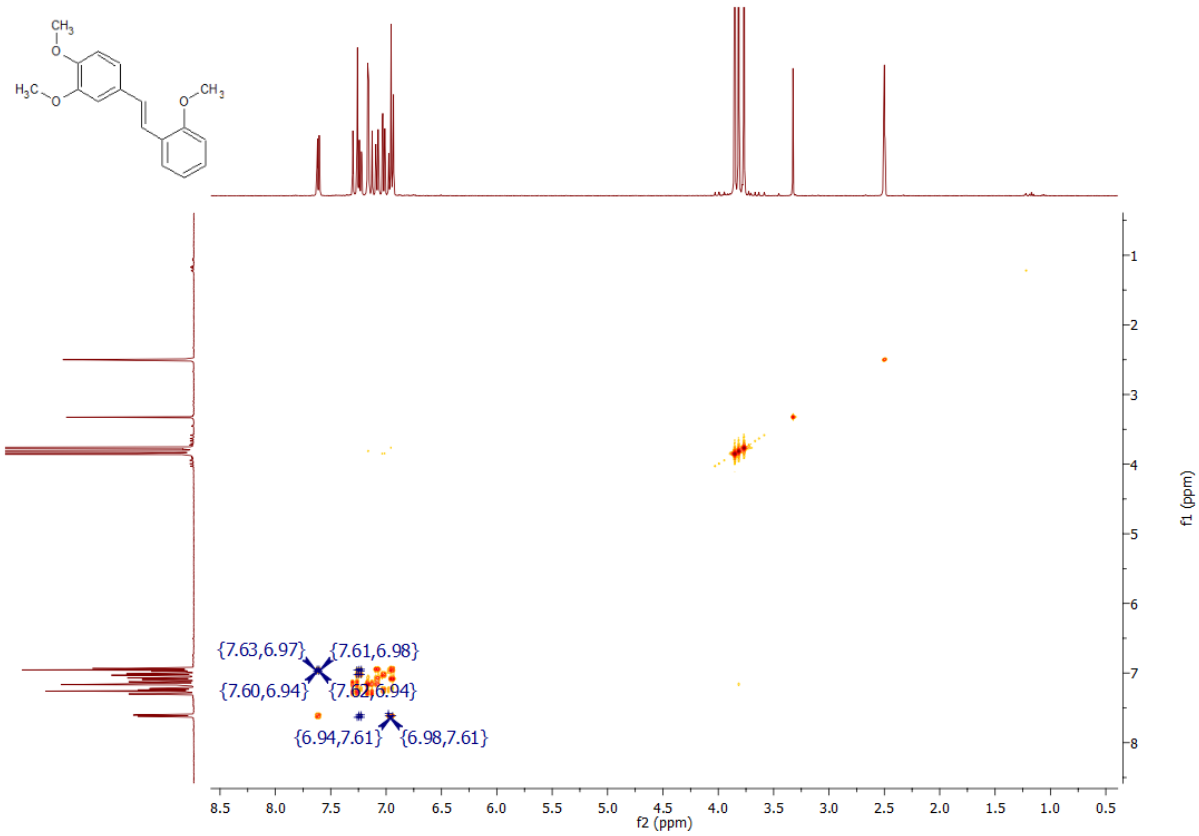

156.3
148.9
148.6
130.4
128.9
128.4
126.1
125.8
120.9
120.6
119.5
111.8
111.3
109.3
55.5
55.5
55.4
*
f1 (ppm)

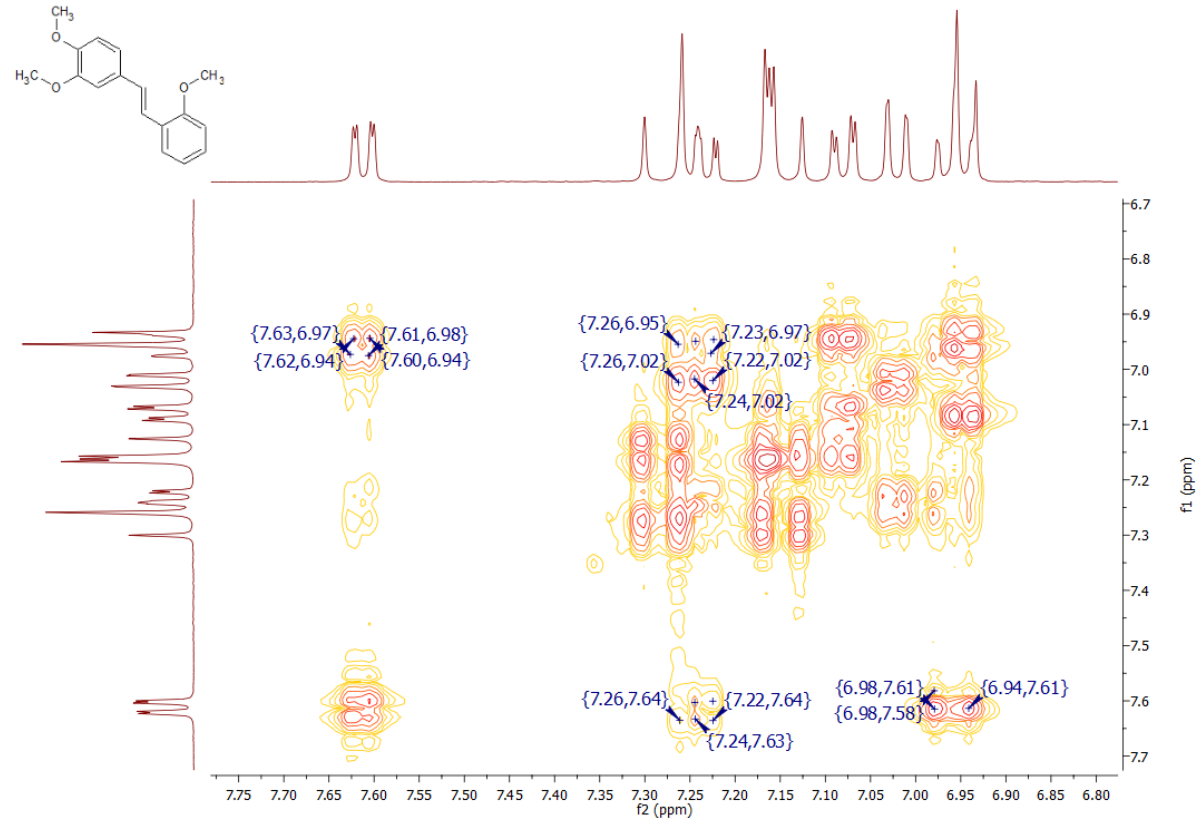
Symbol * indicates DMSO residual peaks.



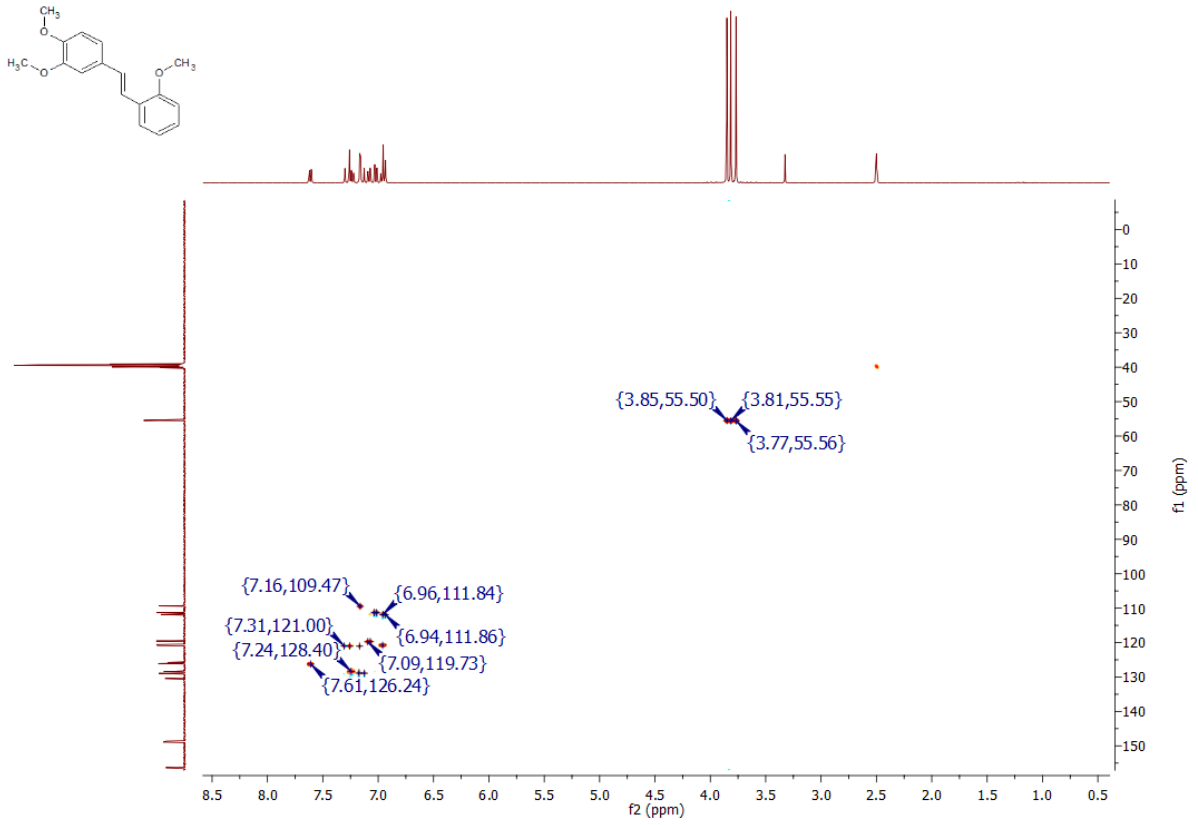


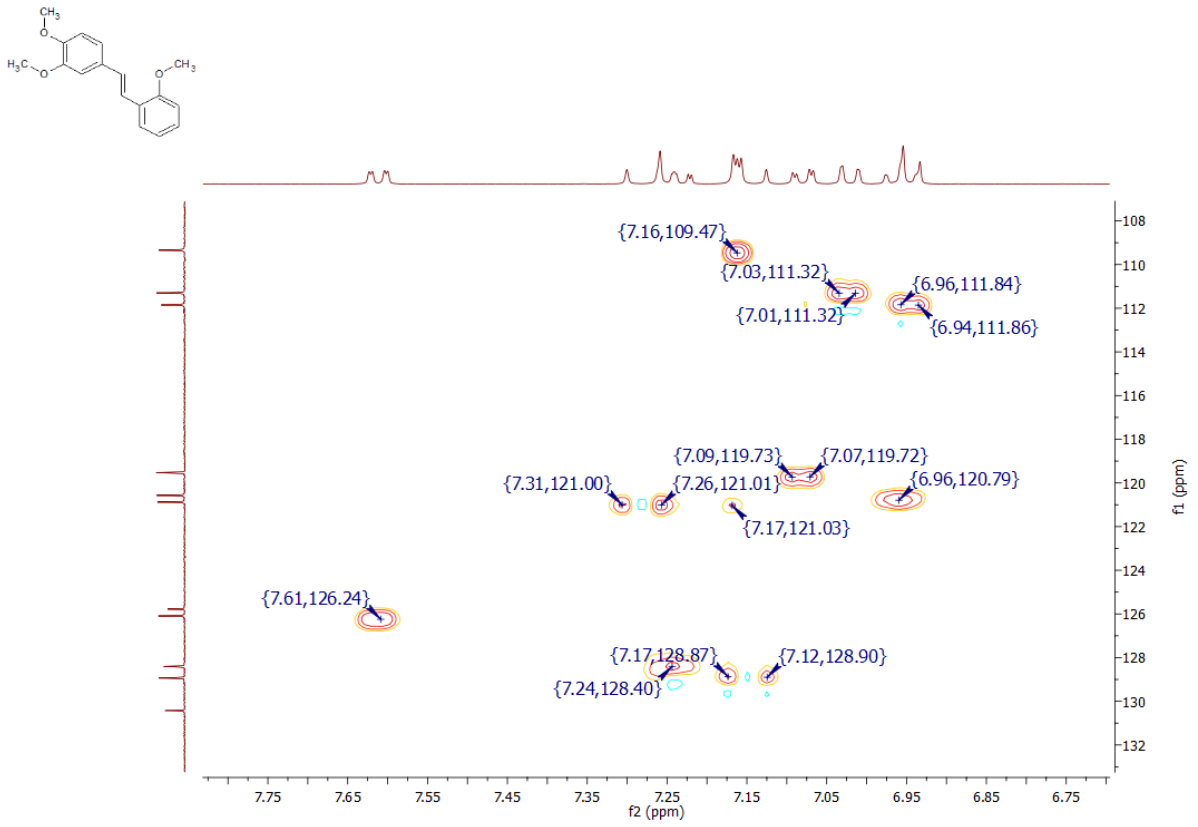
1H1H COSY

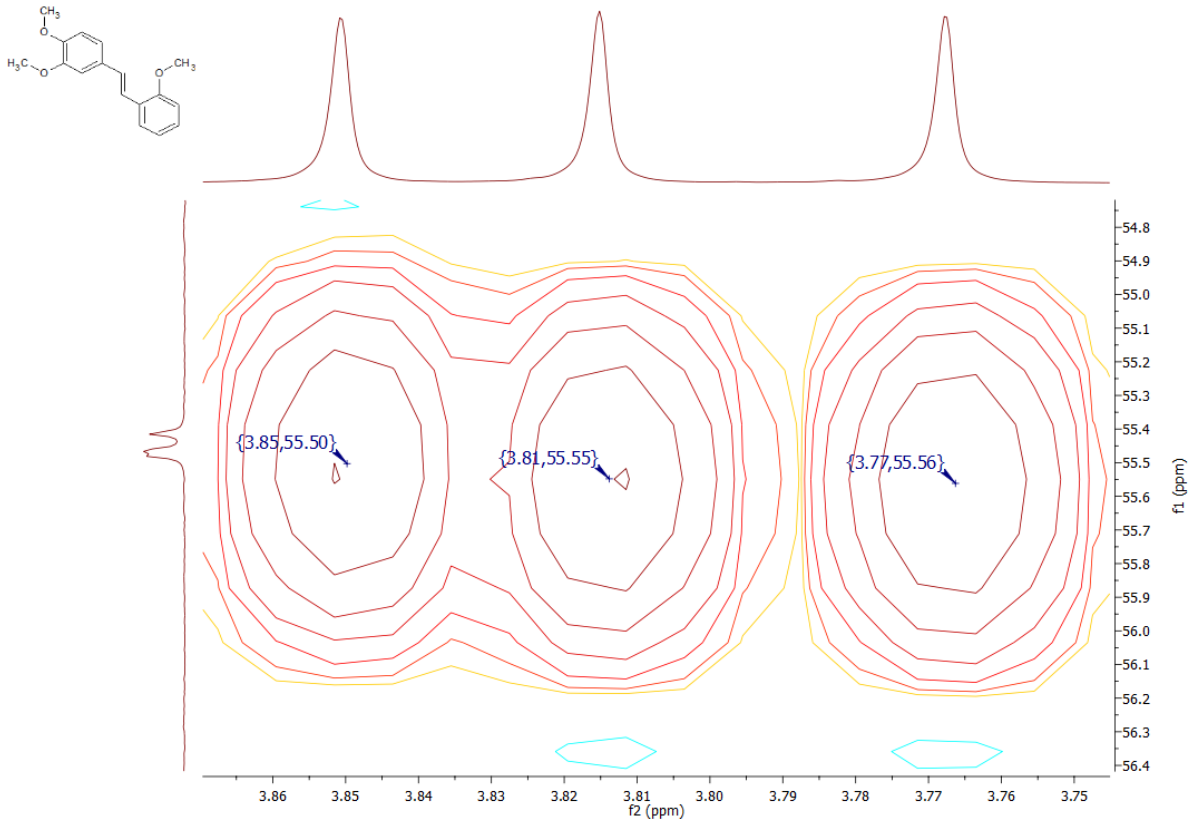

{7.63,6.97}
{7.61,6.98}
{7.60,6.94}
{7.62,6.94}
{6.94,7.61}
{6.98,7.61}
f1 (ppm)
f2 (ppm)


{7.63,6.97}
{7.61,6.98}
{7.62,6.94}
{7.60,6.94}
{7.26,6.95}
{7.23,6.97}
{7.26,7.02}
{7.22,7.02}
{7.24,7.02}
{7.26,7.64}
{7.22,7.64}
{7.24,7.63}
{6.98,7.61}
{6.94,7.61}
{6.98,7.58}
f1 (ppm)
f2 (ppm)

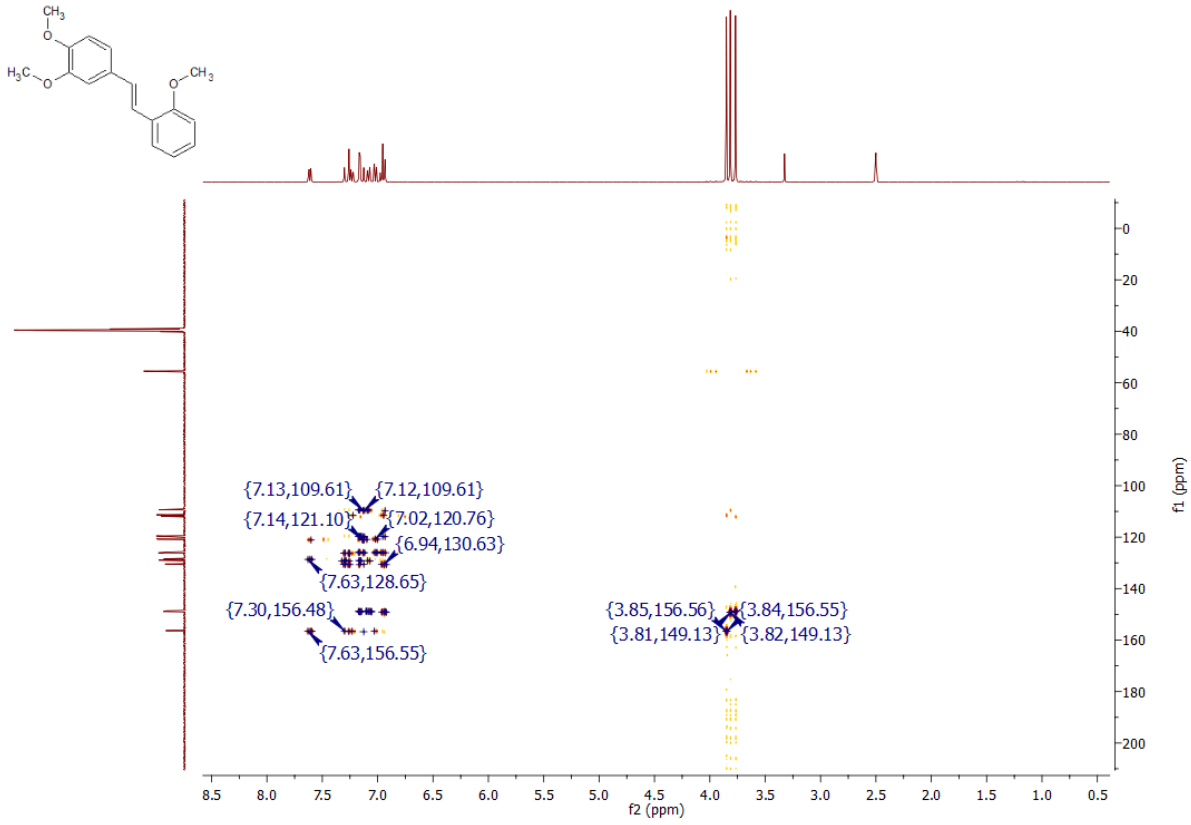
HSQC

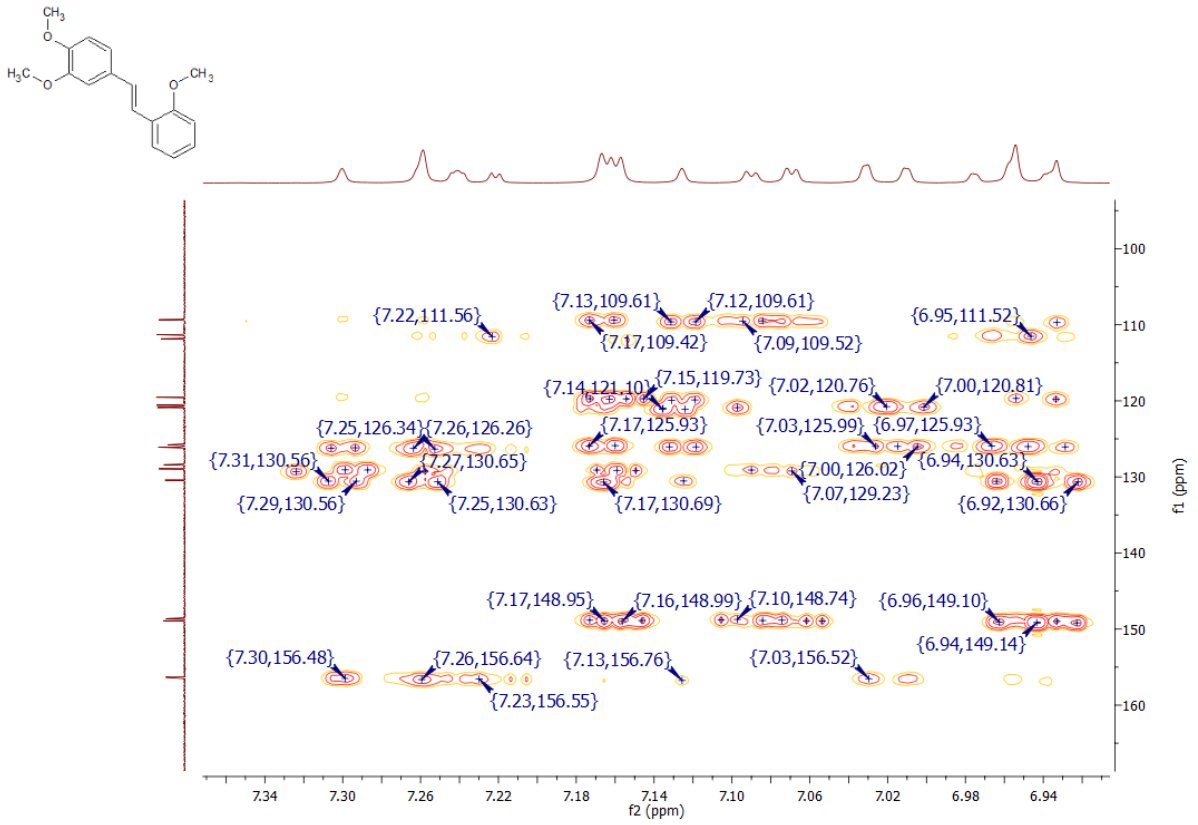


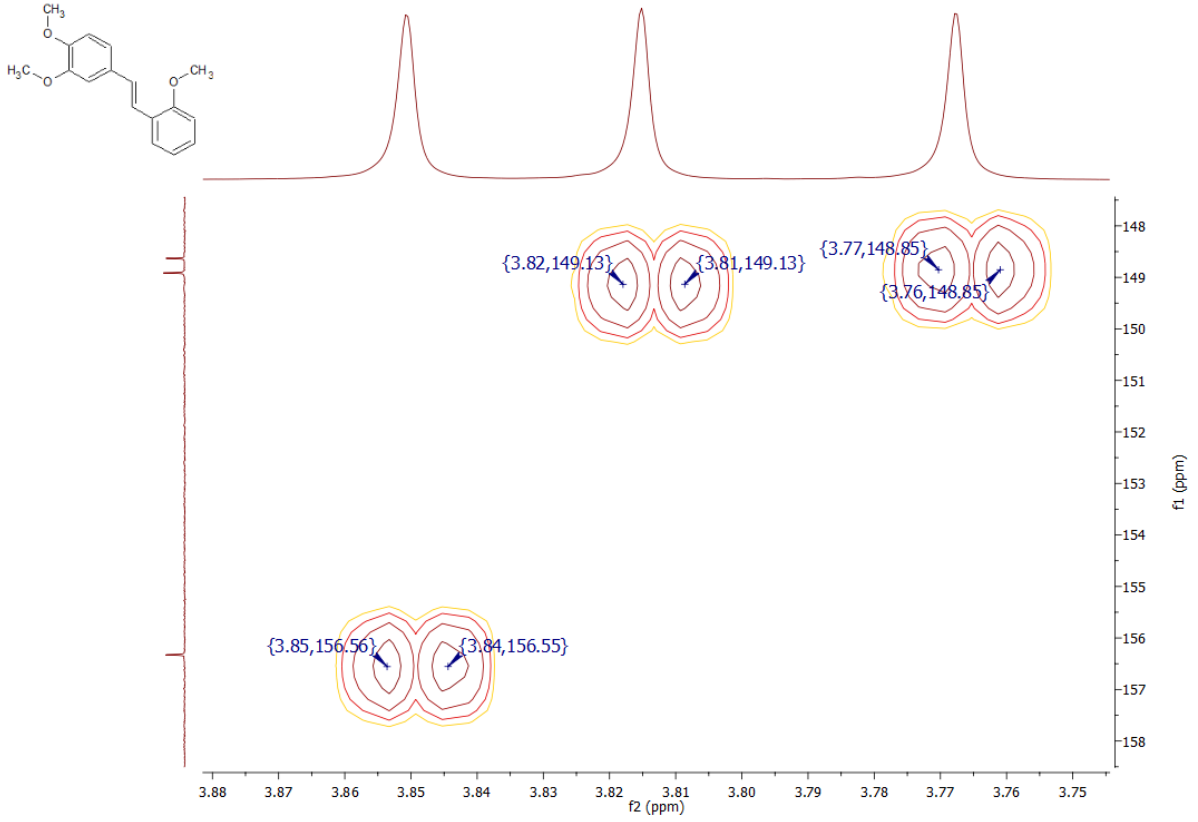



{3.85,55.50}
{3.81,55.55}
{3.77,55.56}
f2 (ppm)
f1 (ppm)

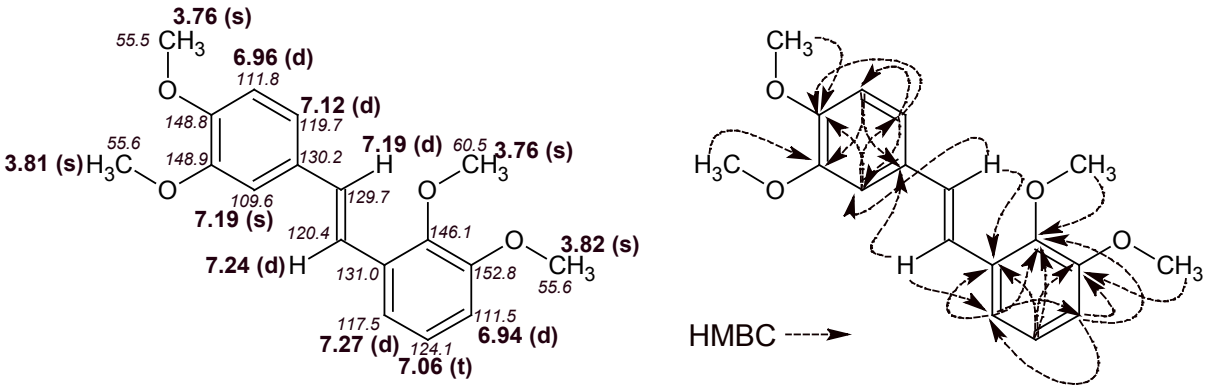
HMBC


{7.13,109.61}
{7.12,109.61}
{7.14,121.10}
{7.02,120.76}
{6.94,130.63}
{7.63,128.65}
{7.30,156.48}
{7.63,156.55}
{3.85,156.56}
{3.84,156.55}
{3.81,149.13}
{3.82,149.13}
f2 (ppm)
f1 (ppm)


{7.22,111.56}
{7.13,109.61}
{7.12,109.61}
{7.17,109.42}
{7.09,109.52}
{6.95,111.52}
{7.14,121.10}
{7.15,119.73}
{7.02,120.76}
{7.00,120.81}
{7.25,126.34}
{7.26,126.26}
{7.17,125.93}
{7.03,125.99}
{6.97,125.93}
{7.31,130.56}
{7.27,130.65}
{7.00,126.02}
{6.94,130.63}
{7.07,129.23}
{7.29,130.56}
{7.25,130.63}
{7.17,130.69}
{6.92,130.66}
{7.17,148.95}
{7.16,148.99}
{7.10,148.74}
{6.96,149.10}
{6.94,149.14}
{7.30,156.48}
{7.26,156.64}
{7.13,156.76}
{7.03,156.52}
{7.23,156.55}
7.34
7.30
7.26
7.22
7.18
7.14
7.10
7.06
7.02
6.98
6.94
f2 (ppm)
100
110
120
130
140
150
160
f1 (ppm)

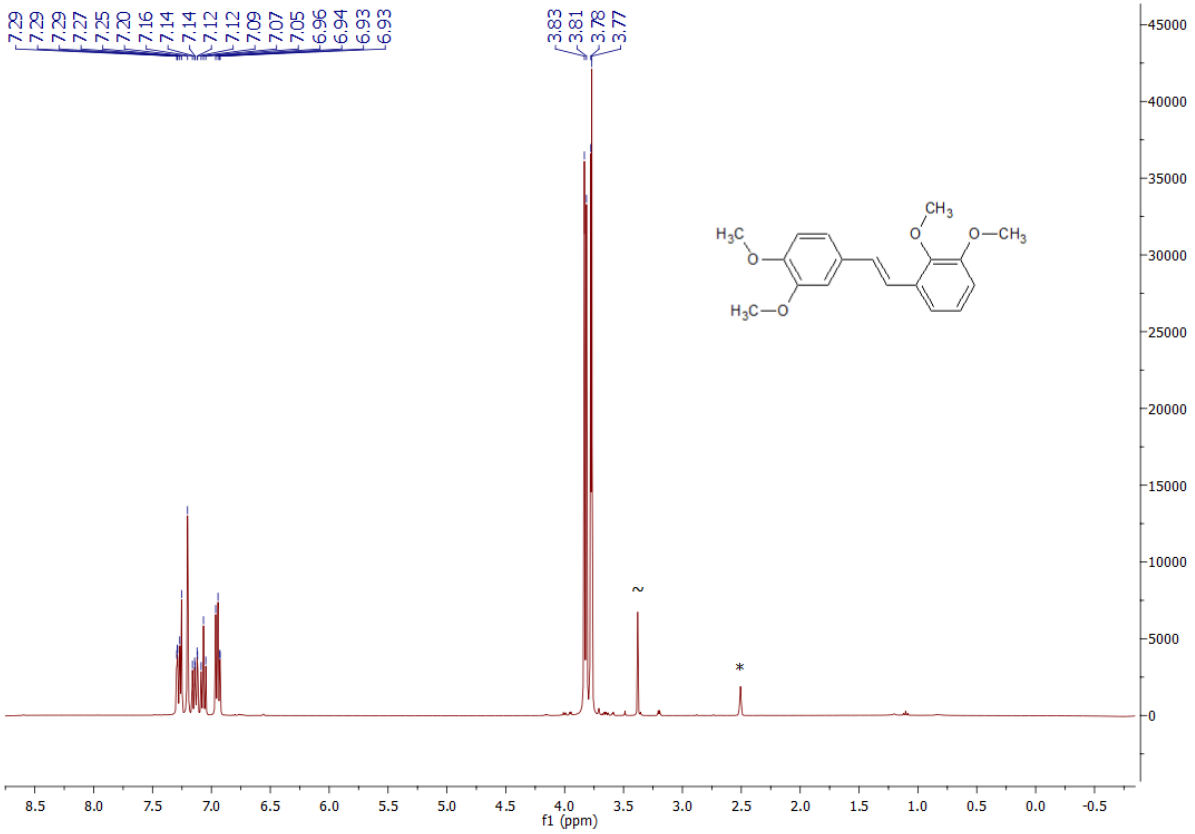

{3.82,149.13}
{3.81,149.13}
{3.77,148.85}
{3.76,148.85}
{3.85,156.56}
{3.84,156.55}
3.88
3.87
3.86
3.85
3.84
3.83
3.82
3.81
3.80
3.79
3.78
3.77
3.76
3.75
f2 (ppm)
148
149
150
151
152
153
154
155
156
157
158
f1 (ppm)

6.3 NMR data for 3,4,2',3'-tetramethoxy-trans-stilbene (5c).

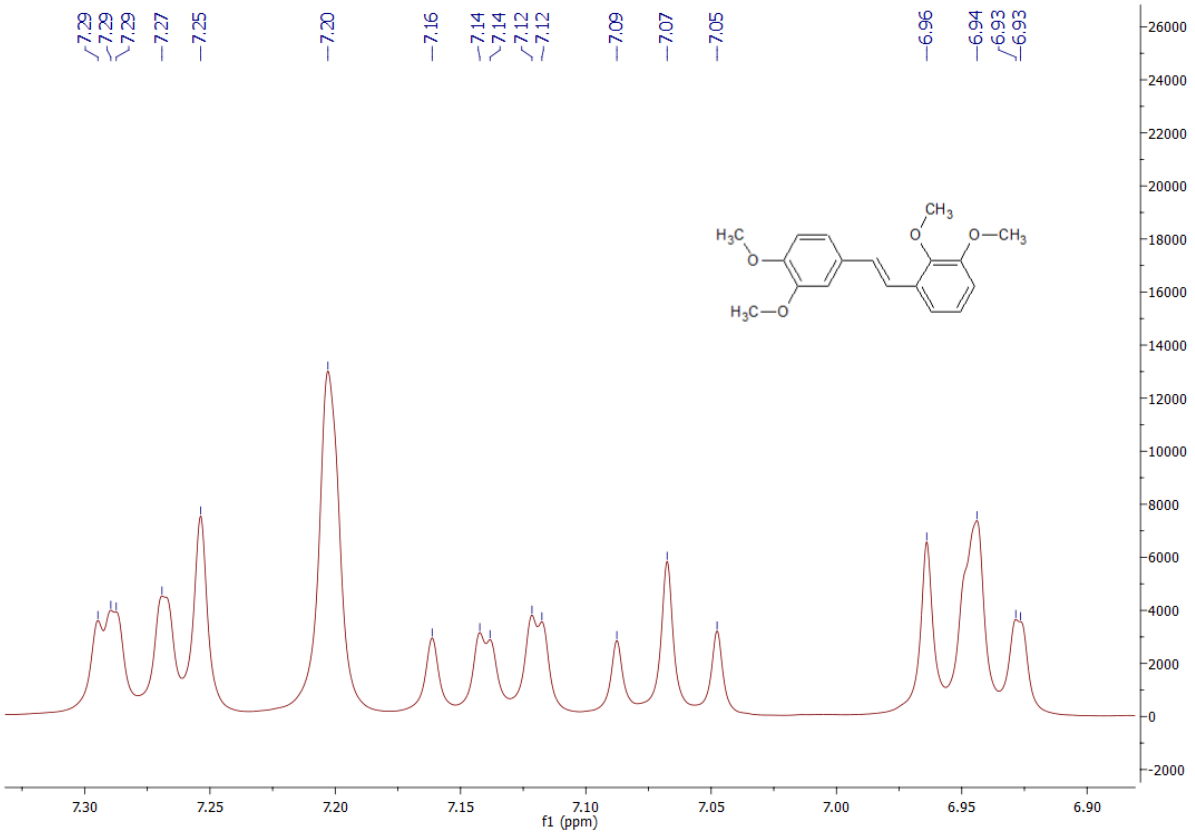


Scheme X3 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

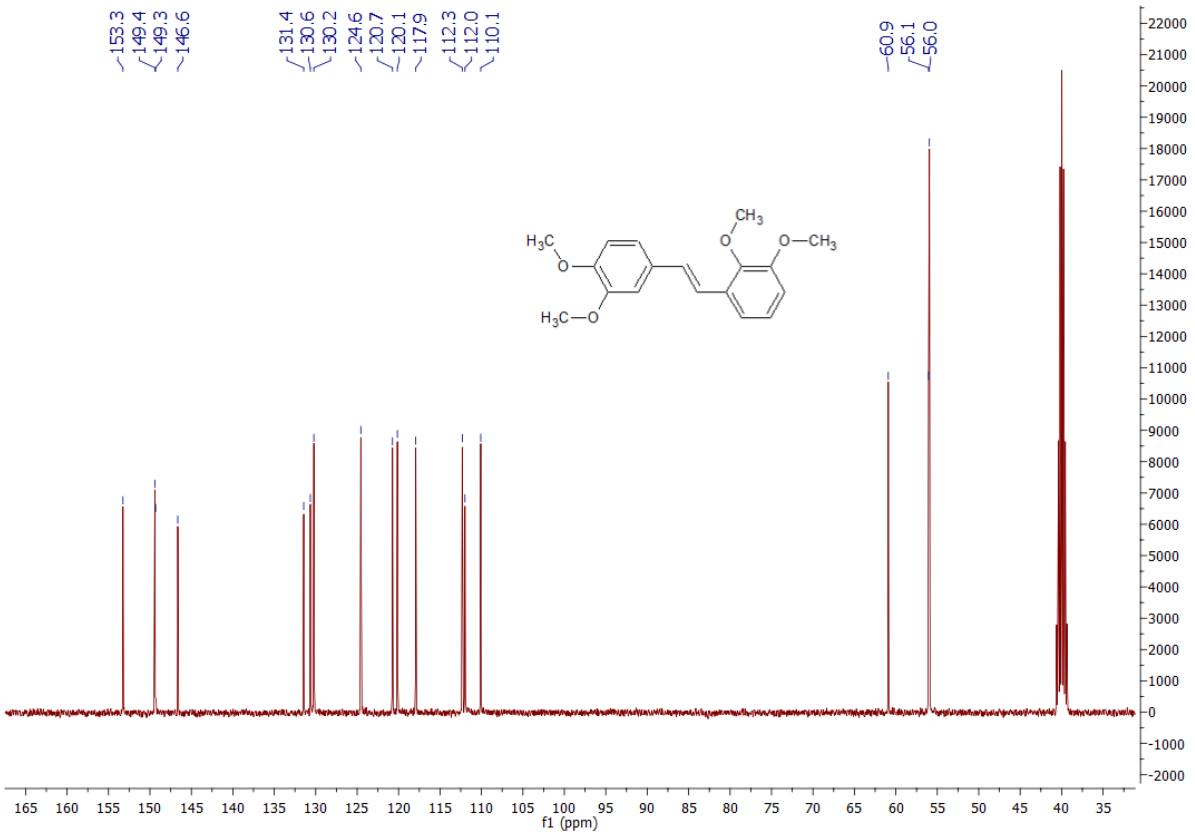
1H

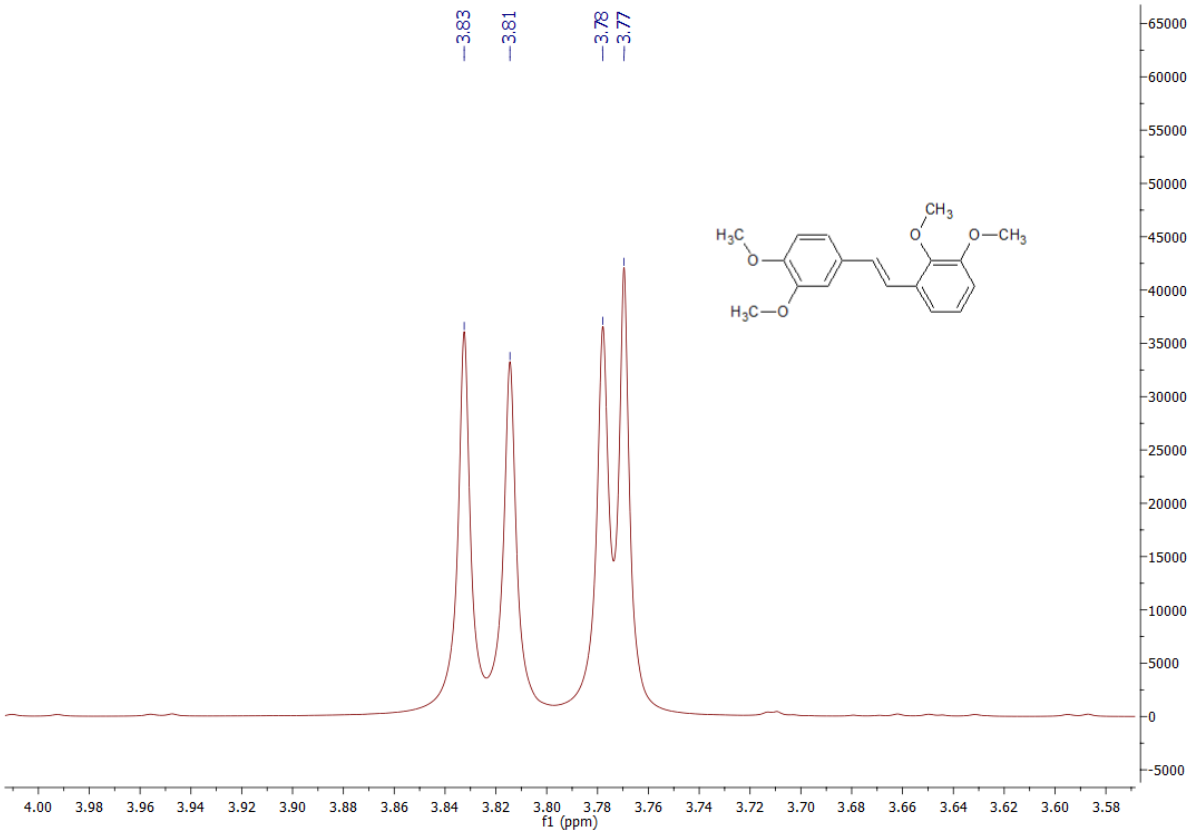


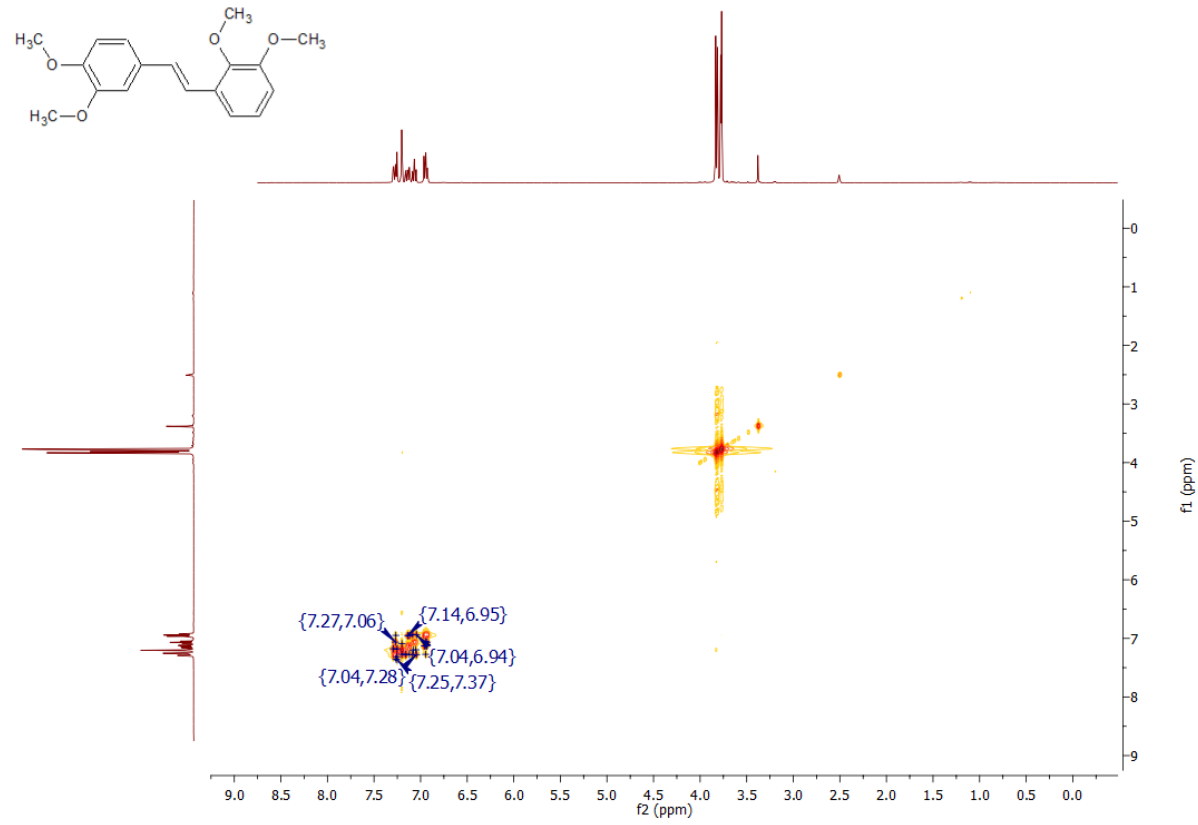
Symbol * and ~ indicates DMSO and water residuals peaks.

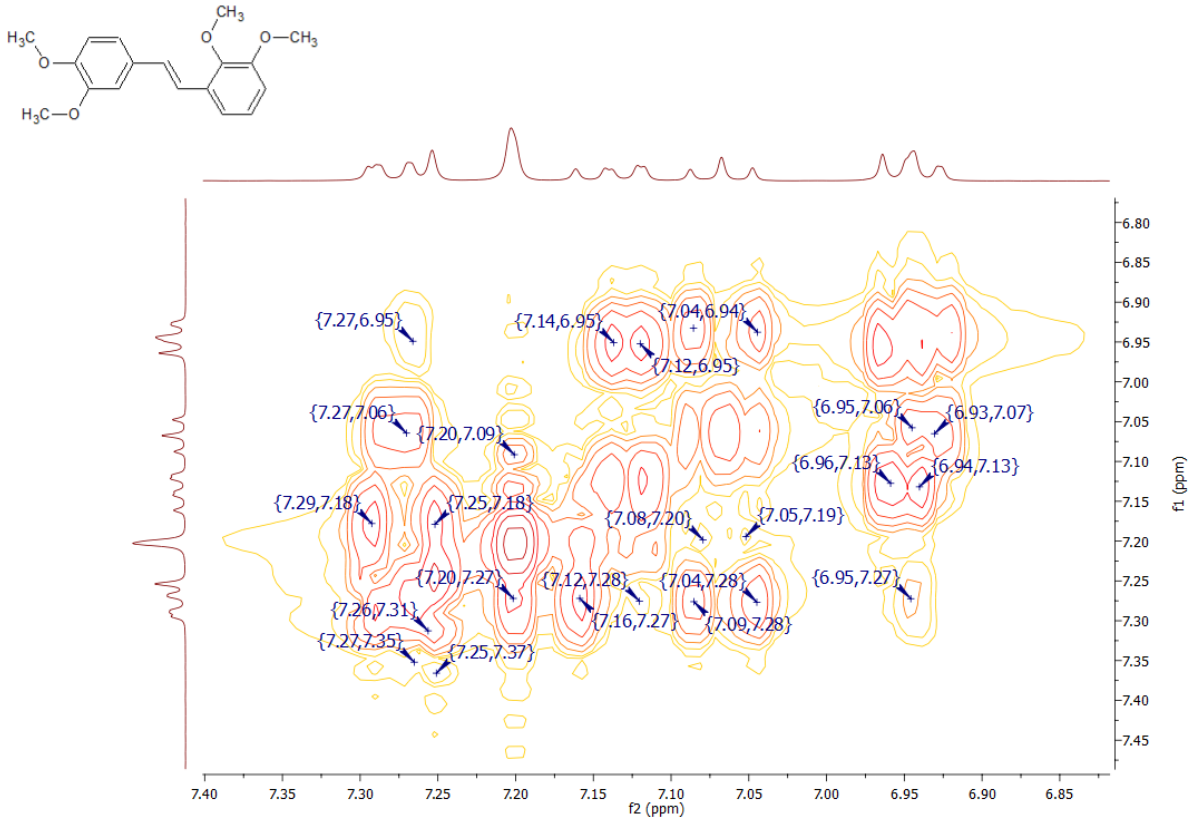

7.29
7.29
7.29
7.27
7.25
7.20
7.16
7.14
7.14
7.12
7.12
7.09
7.07
7.05
6.96
6.94
6.93
6.93
CH3
O
H3C
O
O—CH3
H3C—O
f1 (ppm)

13C

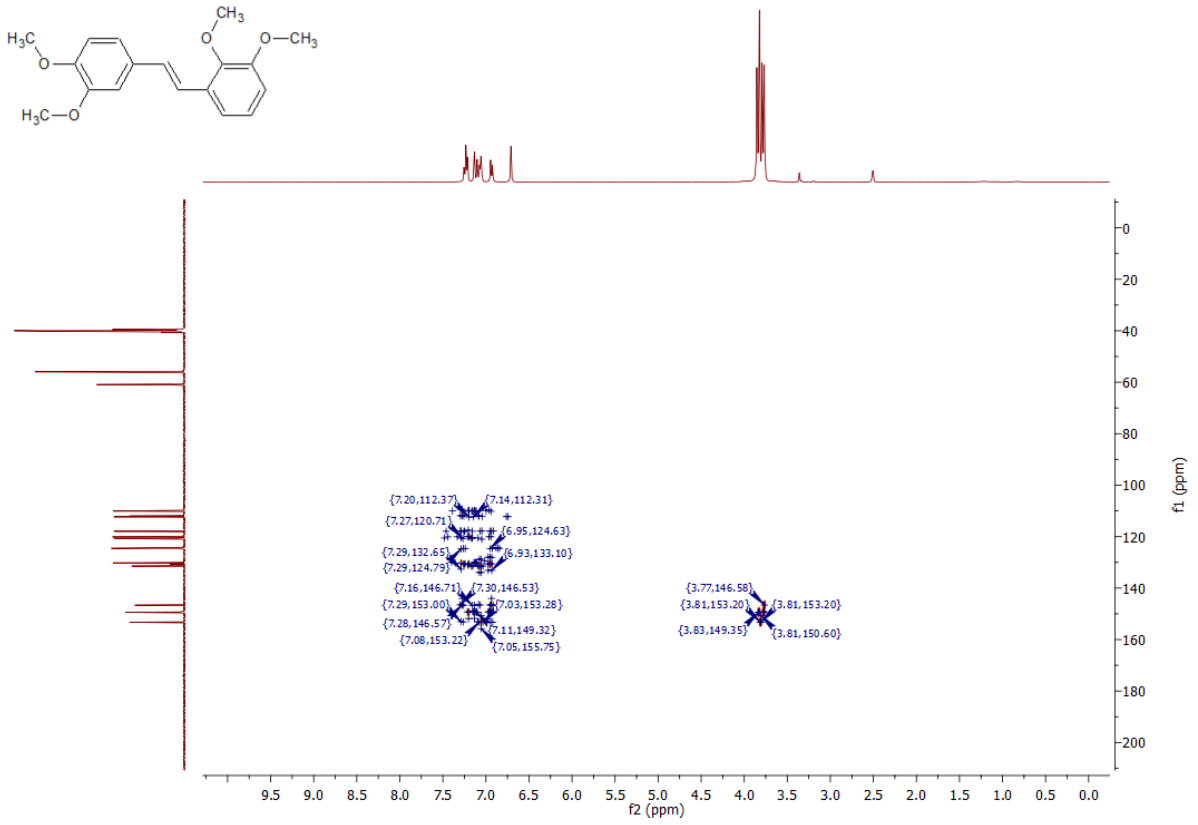

153.3
149.4
149.3
146.6
131.4
130.6
130.2
124.6
120.7
120.1
117.9
112.3
112.0
110.1
60.9
56.1
56.0
CH3
O
H3C
O
O—CH3
H3C—O
f1 (ppm)

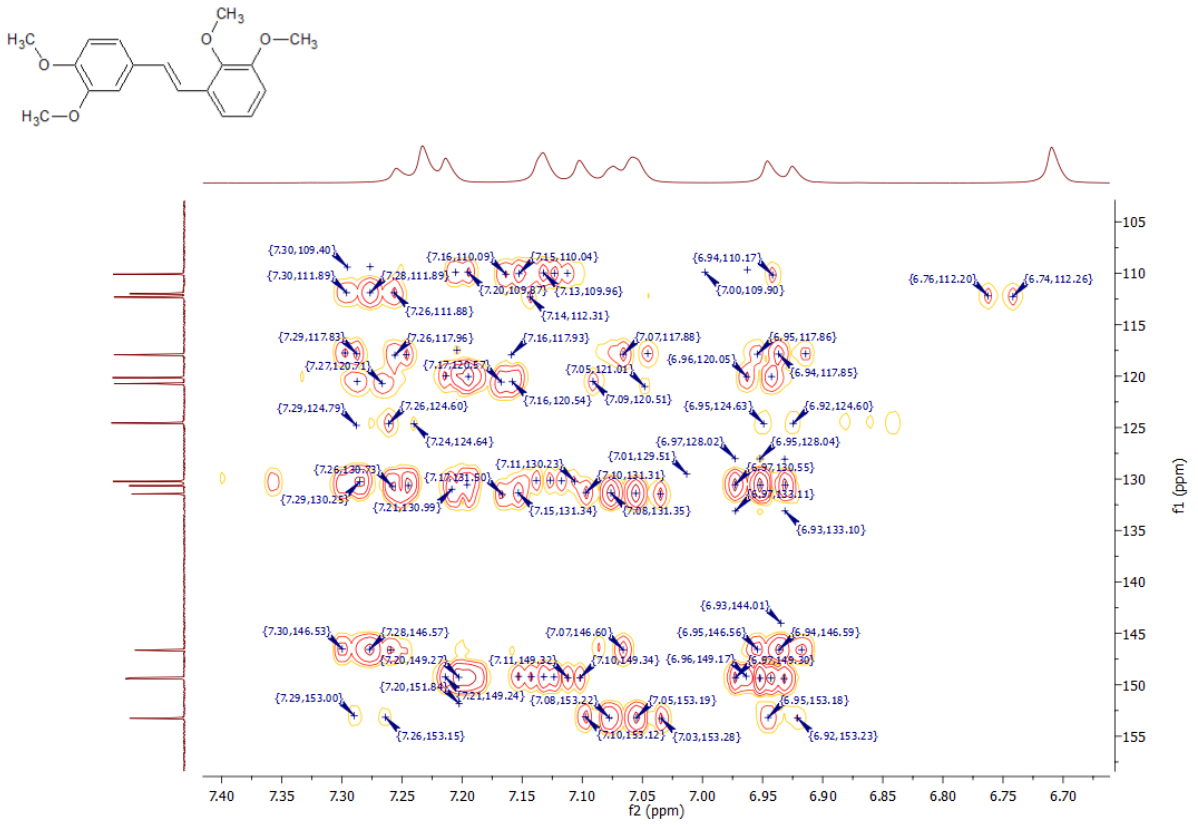

3.83
3.81
3.78
3.77
f1 (ppm)

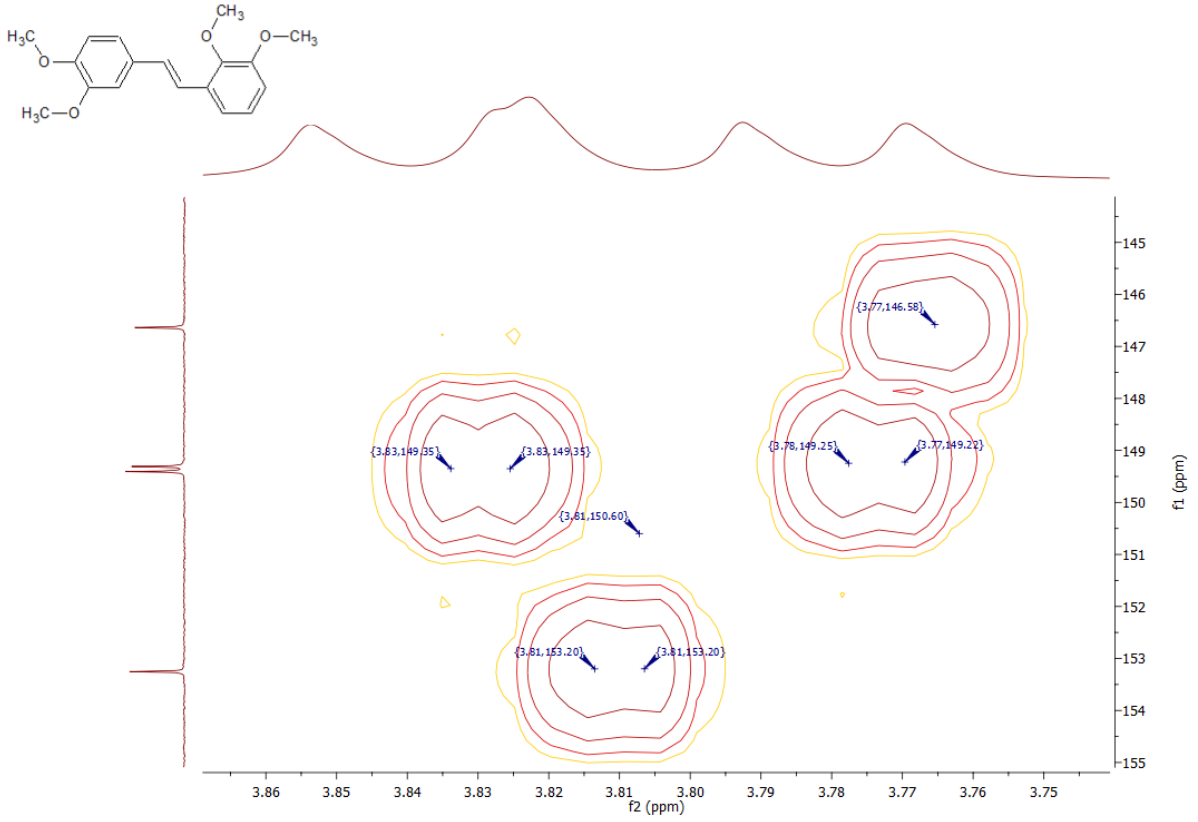

{7.27,7.06}
{7.14,6.95}
{7.04,6.94}
{7.04,7.28}
{7.25,7.37}
f2 (ppm)
f1 (ppm)


{7.27,6.95}
{7.14,6.95}
{7.04,6.94}
{7.12,6.95}
{7.27,7.06}
{7.20,7.09}
{6.95,7.06}
{6.93,7.07}
{6.96,7.13}
{6.94,7.13}
{7.29,7.18}
{7.25,7.18}
{7.08,7.20}
{7.05,7.19}
{7.20,7.27}
{7.12,7.28}
{7.04,7.28}
{6.95,7.27}
{7.26,7.31}
{7.16,7.27}
{7.09,7.28}
{7.27,7.35}
{7.25,7.37}
f2 (ppm)
f1 (ppm)

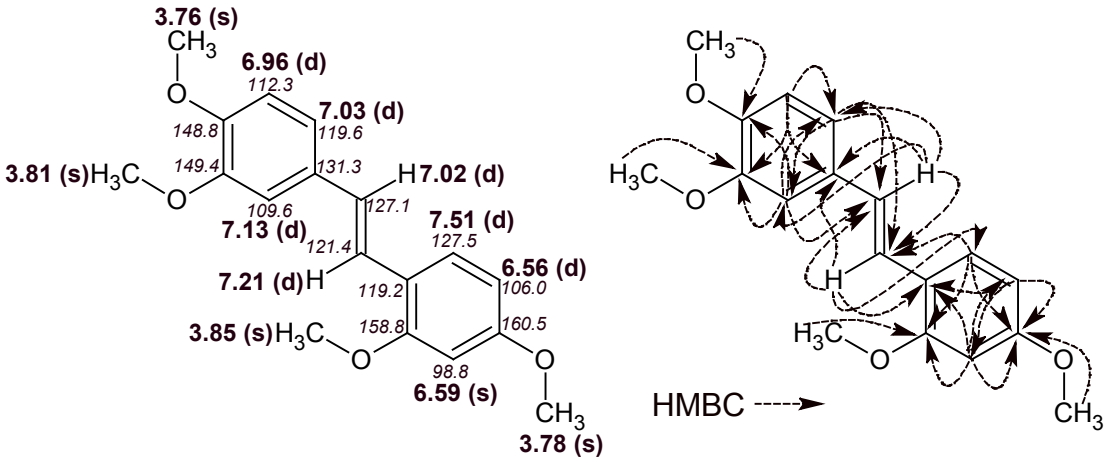
HMBC


{7.20,112.37}
{7.14,112.31}
{7.27,120.71}
{6.95,124.63}
{7.29,132.65}
{6.93,133.10}
{7.29,124.79}
{7.16,146.71}
{7.30,146.53}
{7.29,153.00}
{7.03,153.28}
{7.28,146.57}
{7.11,149.32}
{7.08,153.22}
{7.05,155.75}
{3.77,146.58}
{3.81,153.20}
{3.83,149.35}
{3.81,150.60}
f2 (ppm)
f1 (ppm)


f2 (ppm)
f1 (ppm)

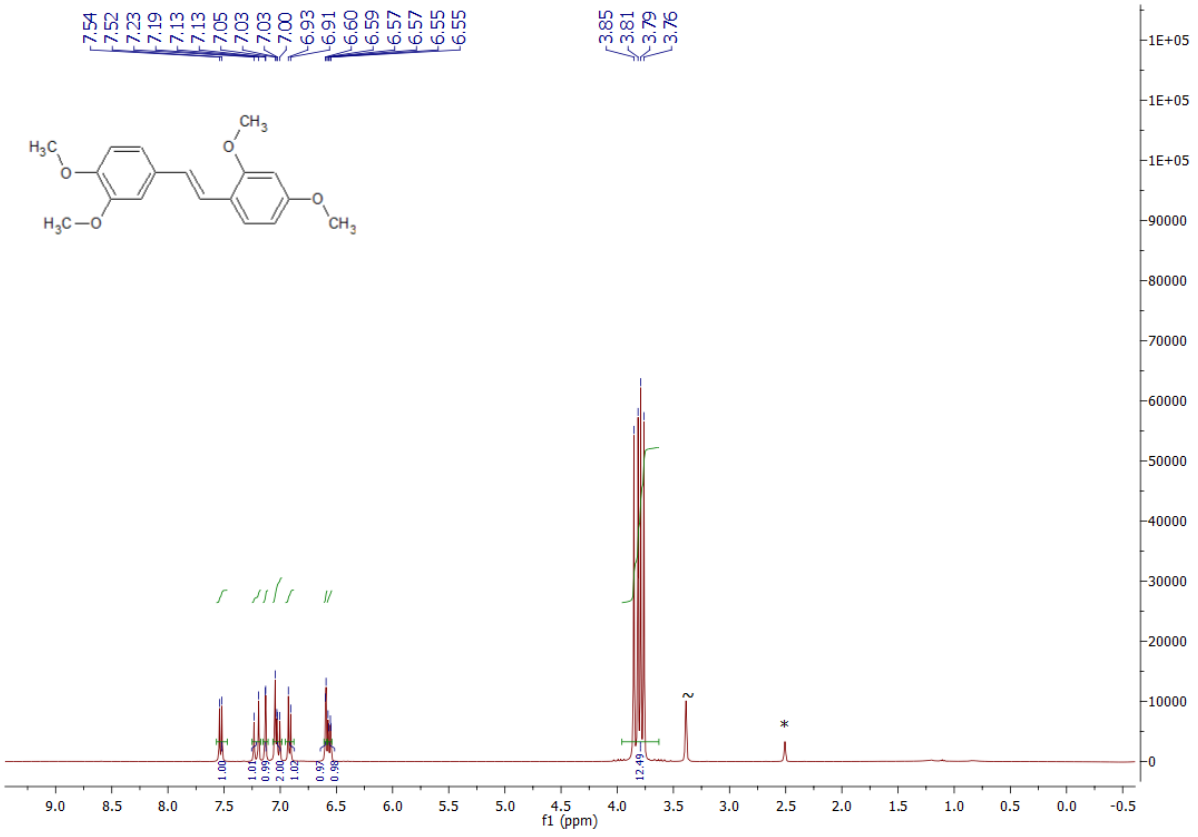

f2 (ppm)
f1 (ppm)

6.4 NMR data for 3,4,2',4'-tetramethoxy-trans-stilbene (5d)

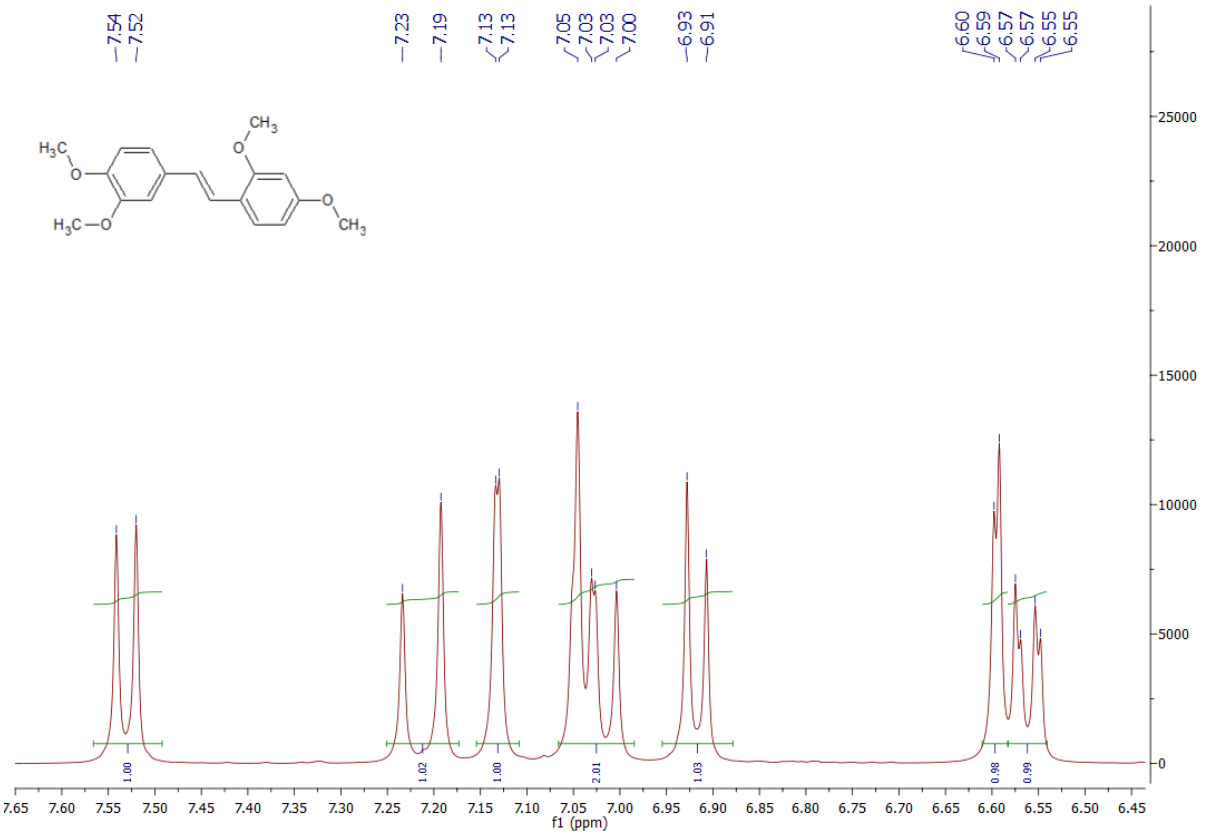


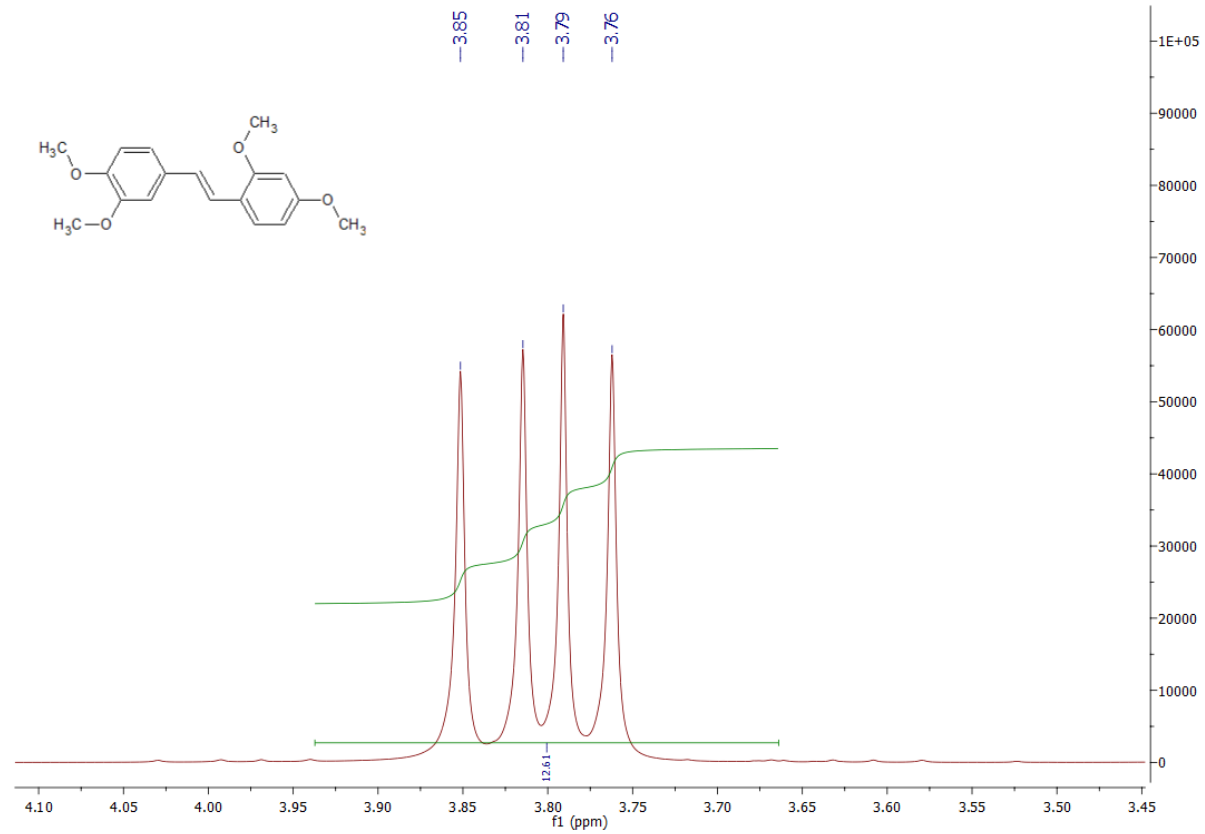
Scheme X4 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

1H

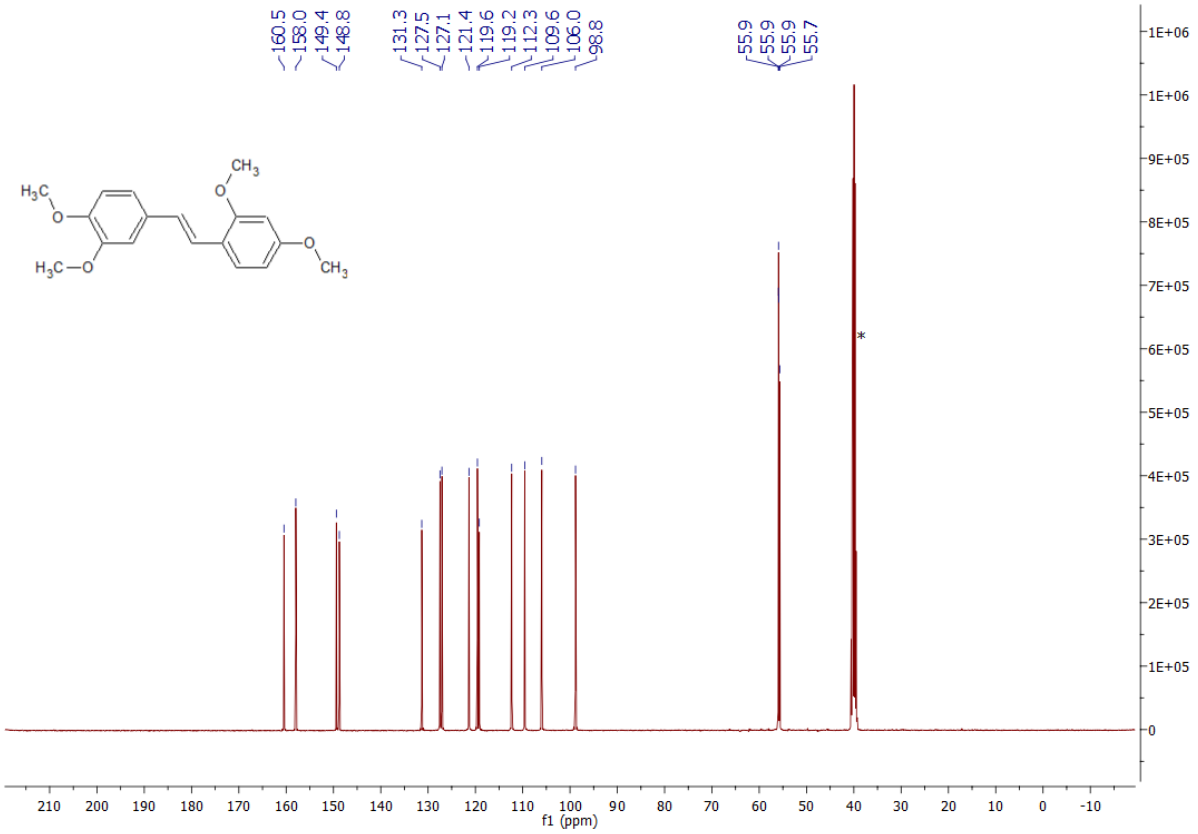


Symbol * and ~ indicates DMSO and water residuals peaks.

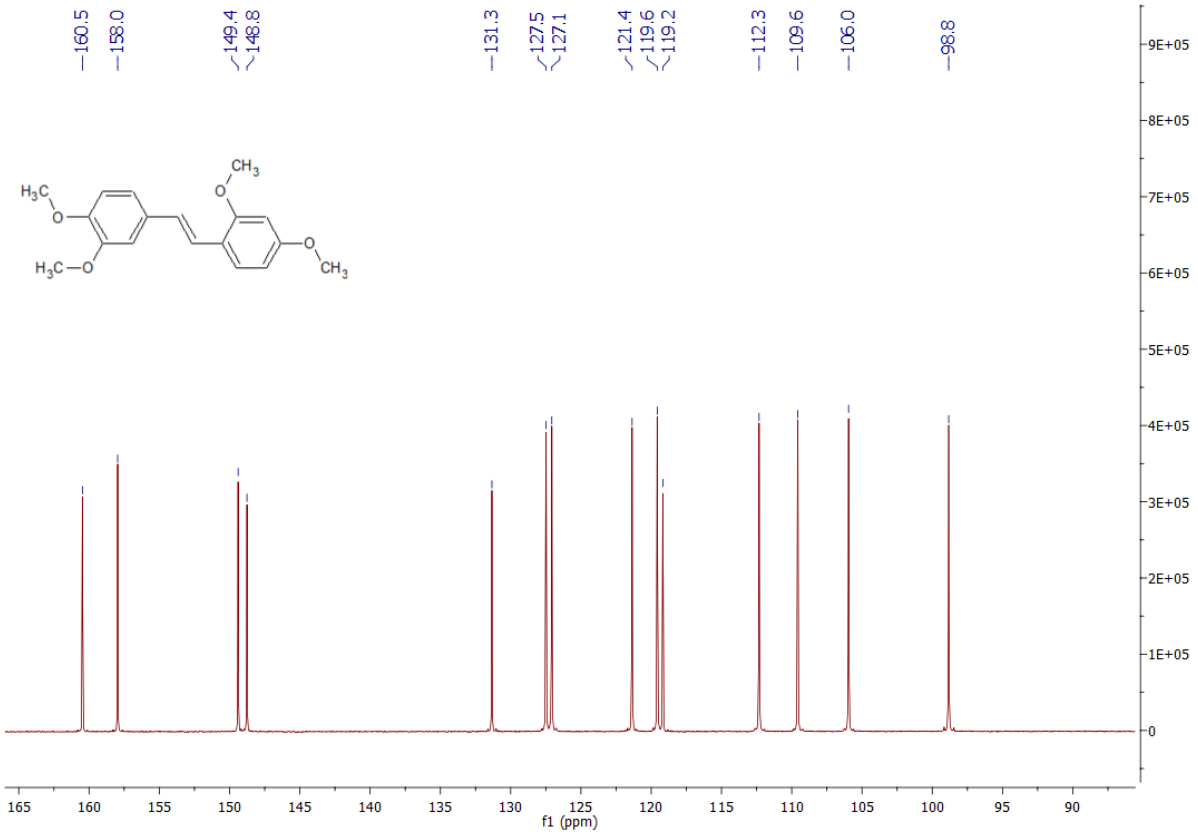

7.54
7.52
7.23
7.19
7.13
7.13
7.05
7.03
7.03
7.00
6.93
6.91
6.60
6.59
6.57
6.57
6.55
6.55
H3C
O
CH3
O
H3C—O
O
CH3
25000
20000
15000
10000
5000
0
1.00
1.02
1.00
2.01
1.03
0.98
0.99
7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95 6.90 6.85 6.80 6.75 6.70 6.65 6.60 6.55 6.50 6.45
f1 (ppm)

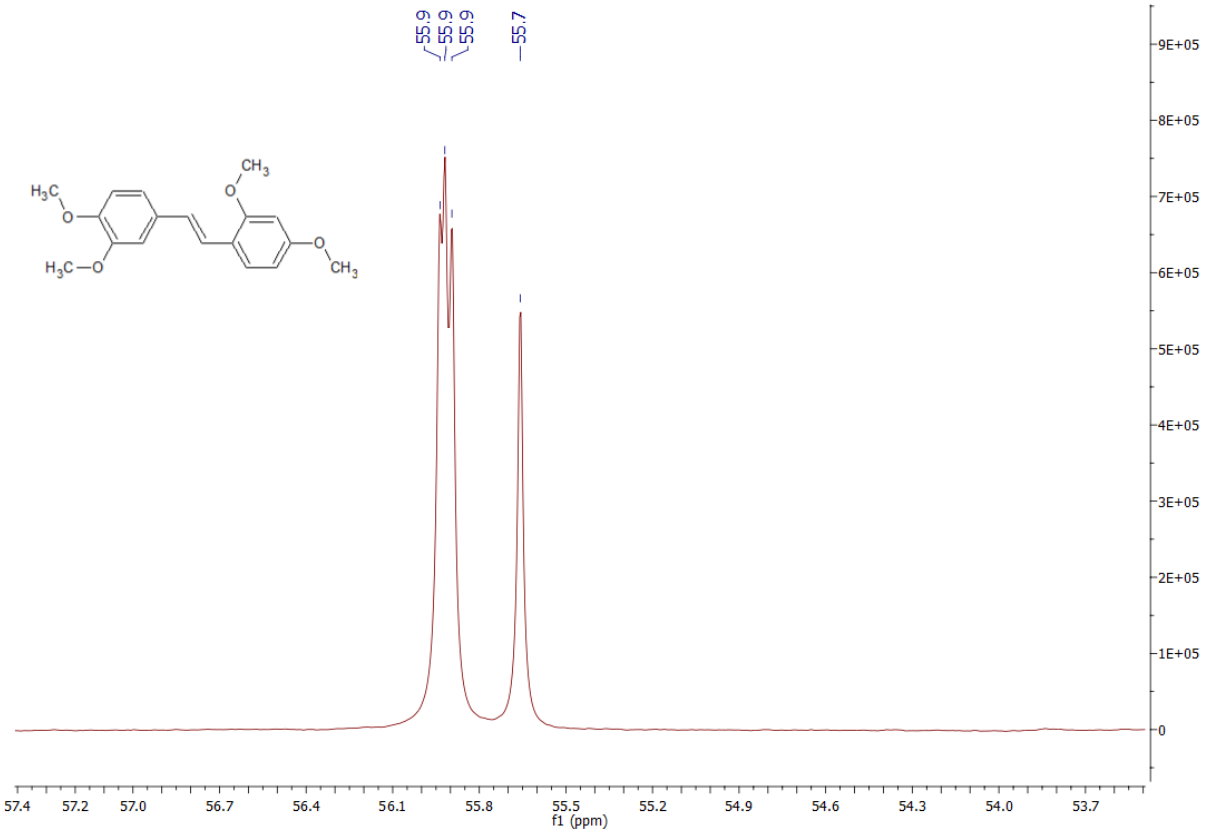

3.85
3.81
3.79
3.76
H3C
O
CH3
O
H3C—O
O
CH3
1E+05
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
12.61
4.10 4.05 4.00 3.95 3.90 3.85 3.80 3.75 3.70 3.65 3.60 3.55 3.50 3.45
f1 (ppm)

13C

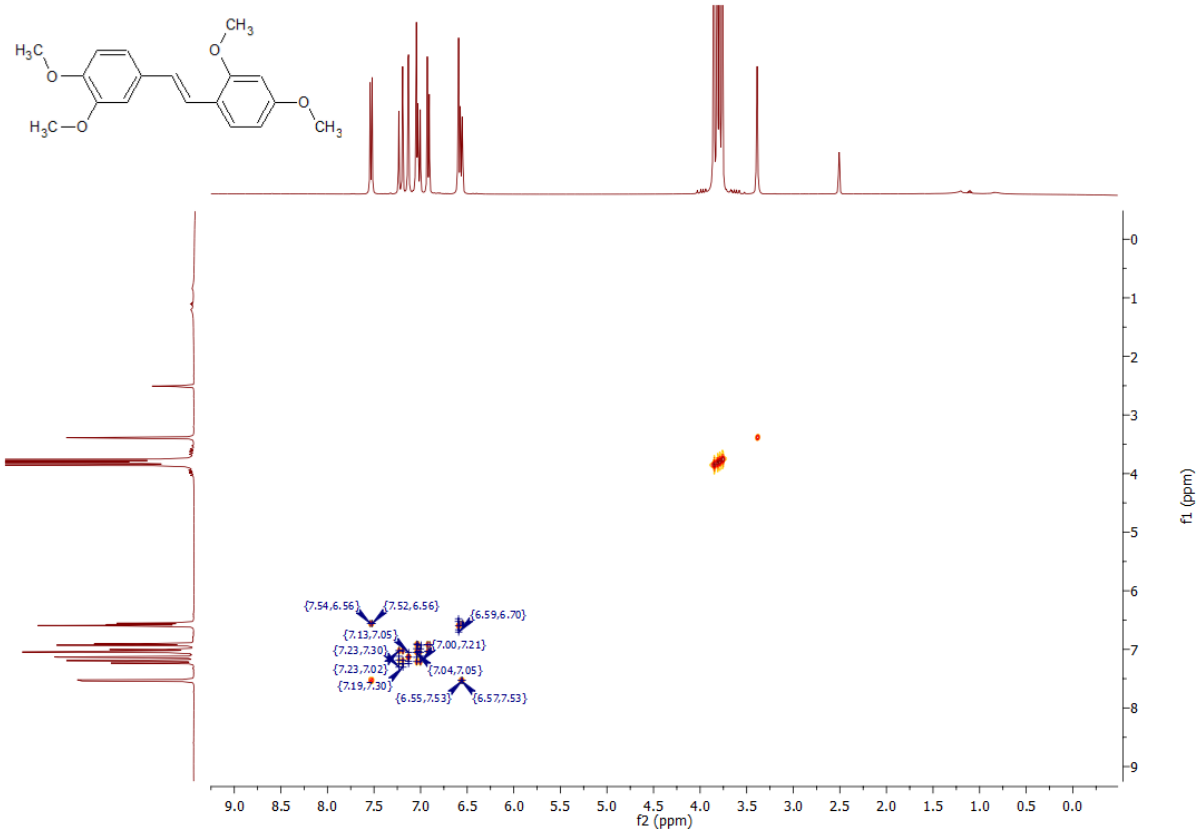


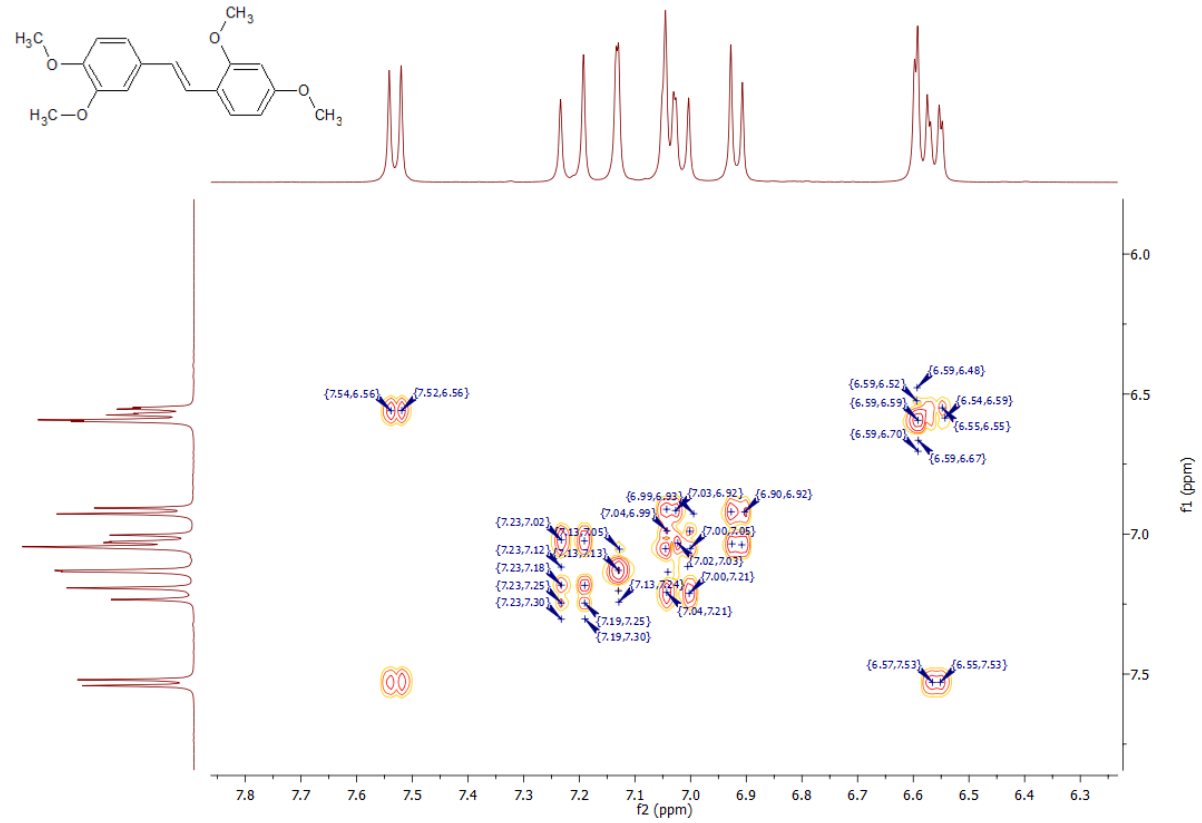
Symbol * indicates DMSO residual peaks.



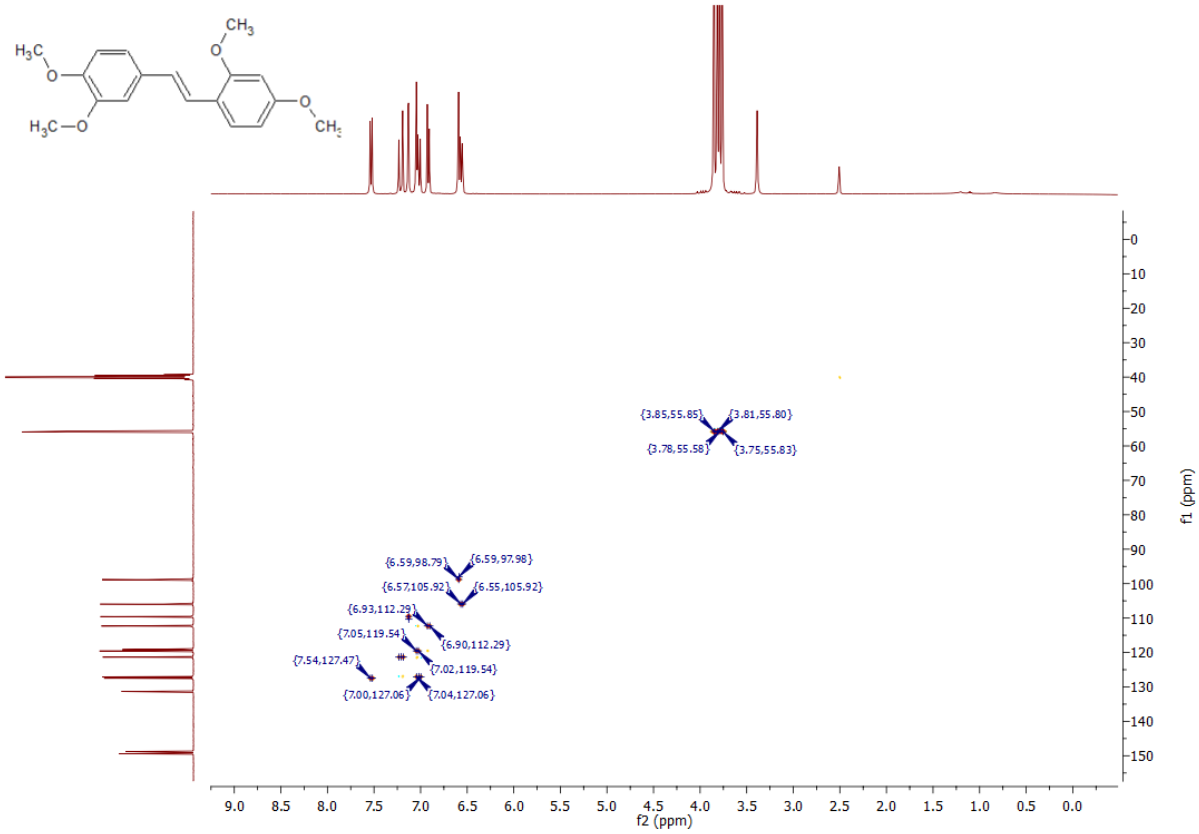


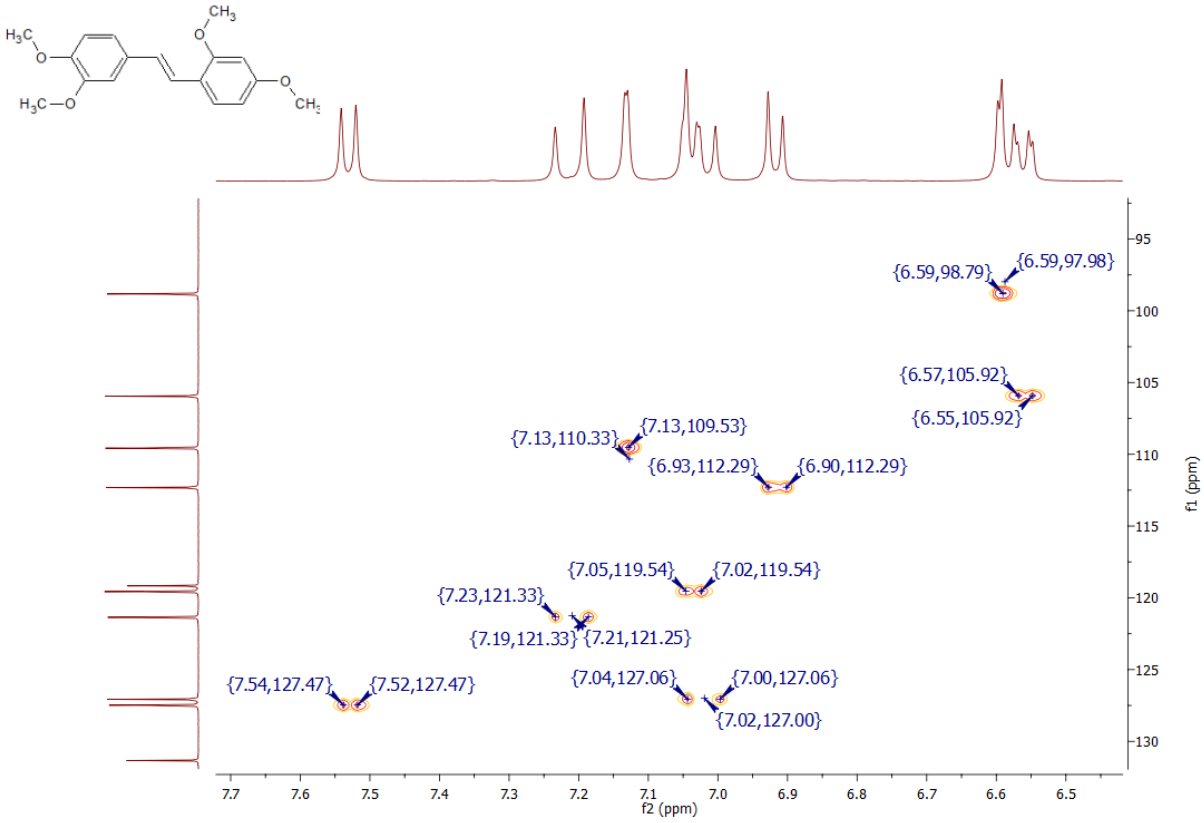
1H1H COSY

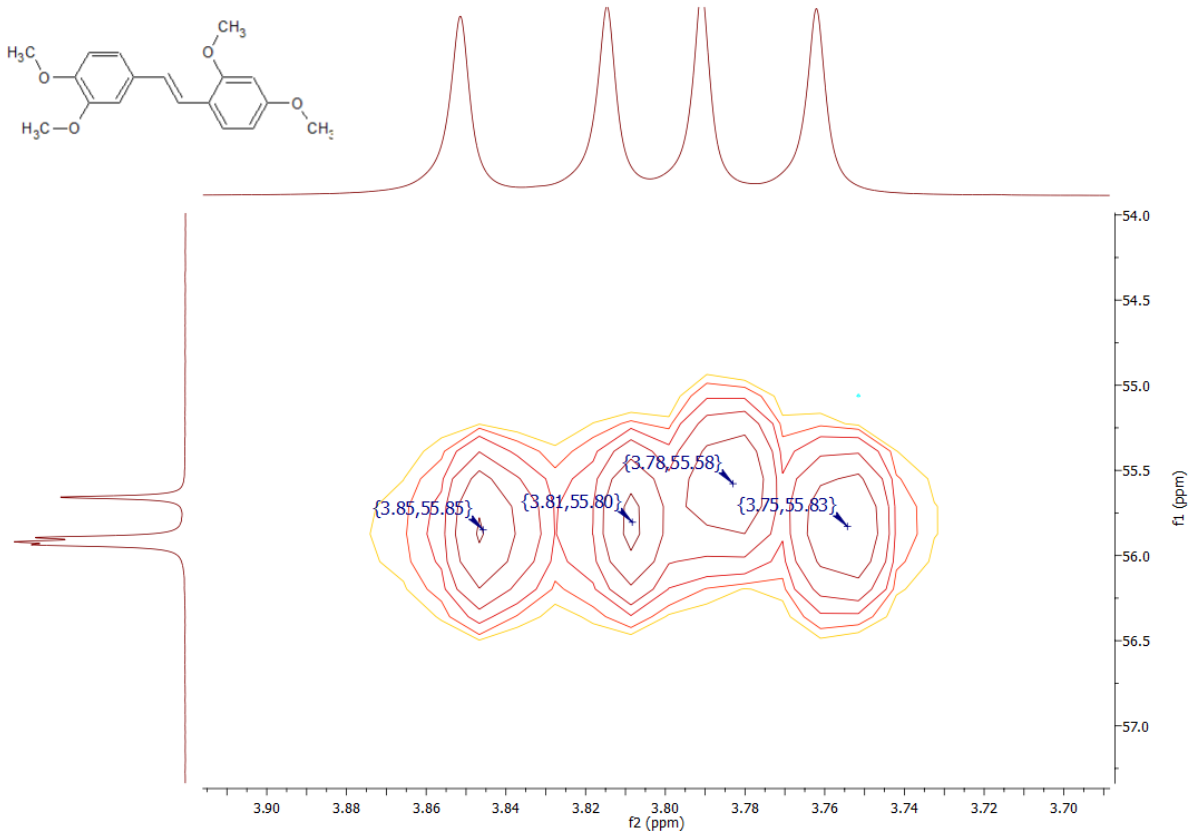




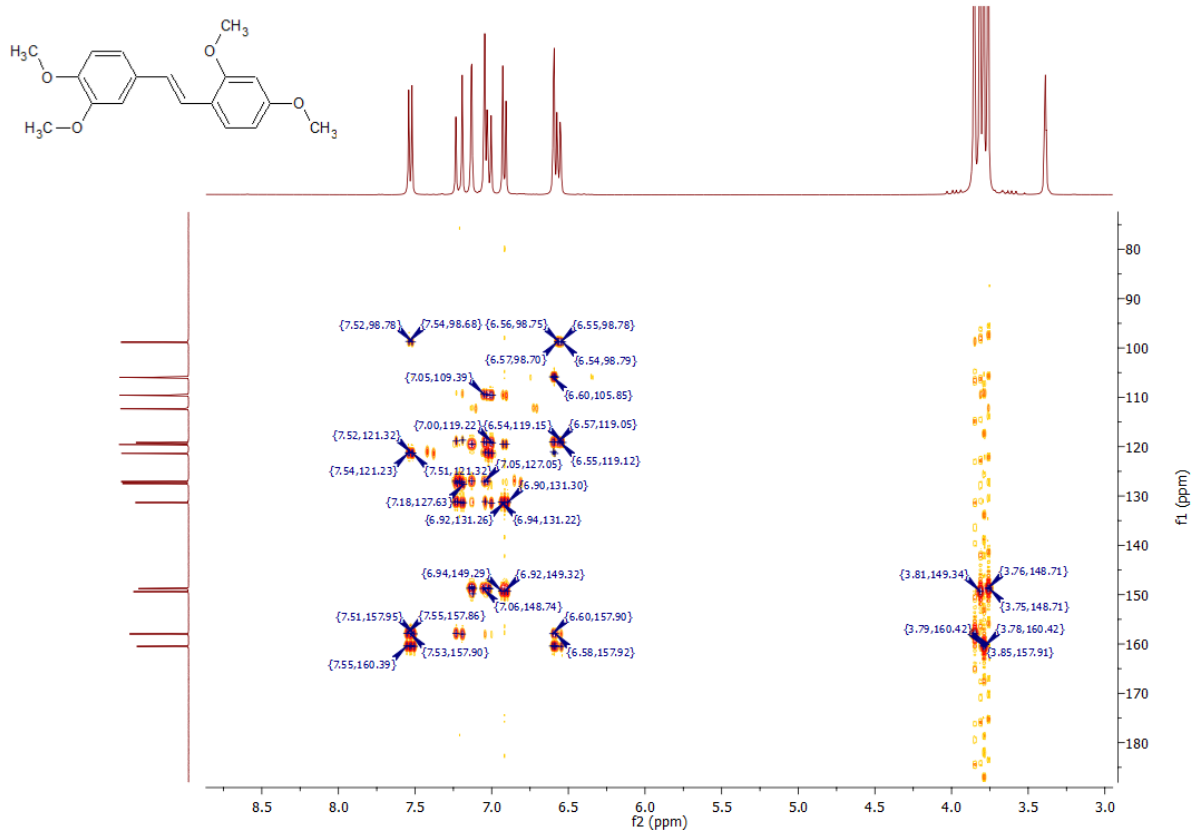
HSQC

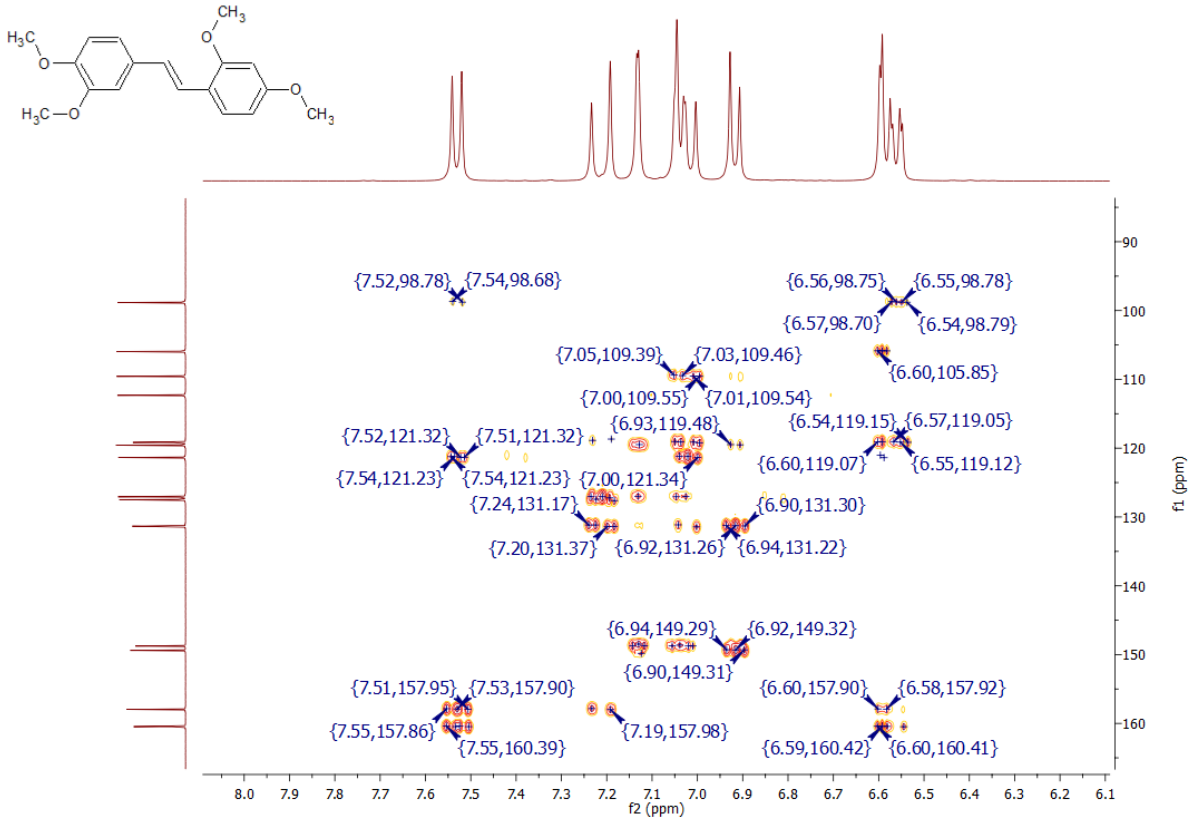


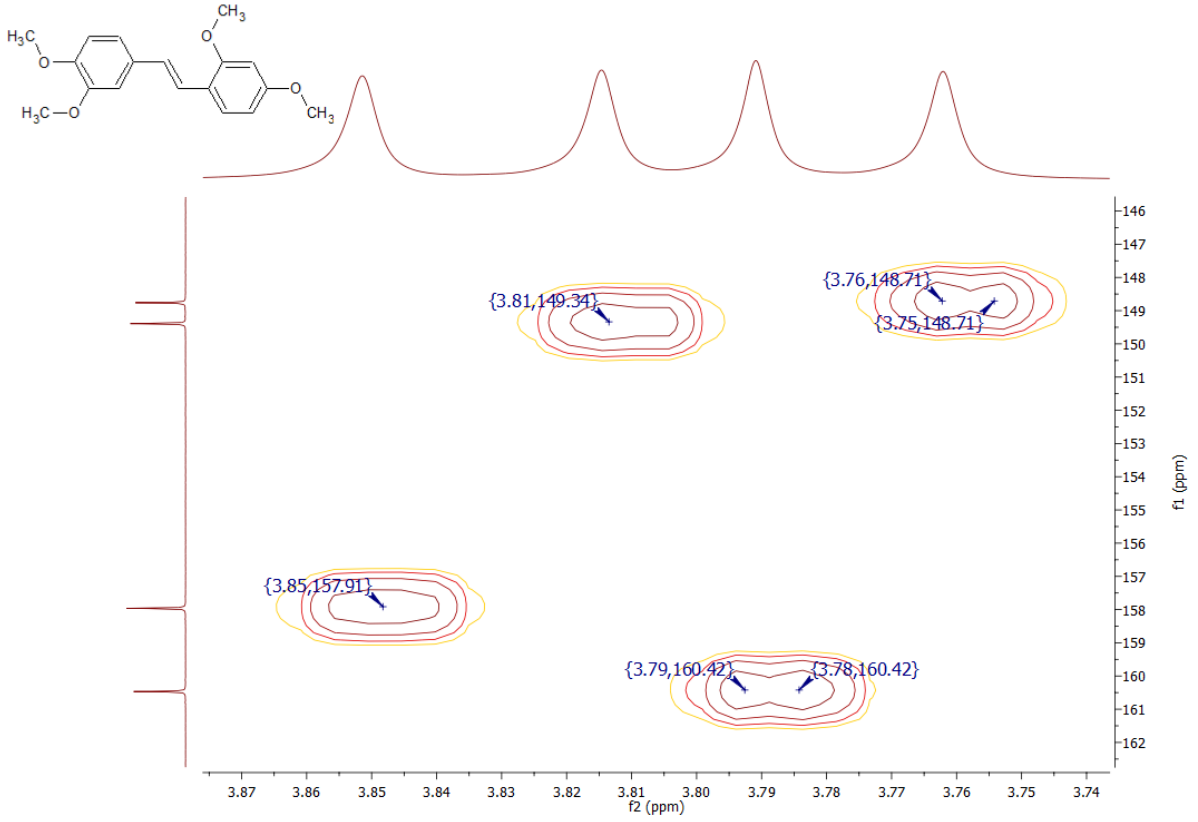

{6.59,98.79}
{6.59,97.98}
{6.57,105.92}
{6.55,105.92}
{7.13,110.33}
{7.13,109.53}
{6.93,112.29}
{6.90,112.29}
{7.05,119.54}
{7.02,119.54}
{7.23,121.33}
{7.19,121.33}
{7.21,121.25}
{7.54,127.47}
{7.52,127.47}
{7.04,127.06}
{7.00,127.06}
{7.02,127.00}
f2 (ppm)
f1 (ppm)


{3.78,55.58}
{3.85,55.85}
{3.81,55.80}
{3.75,55.83}
f2 (ppm)
f1 (ppm)

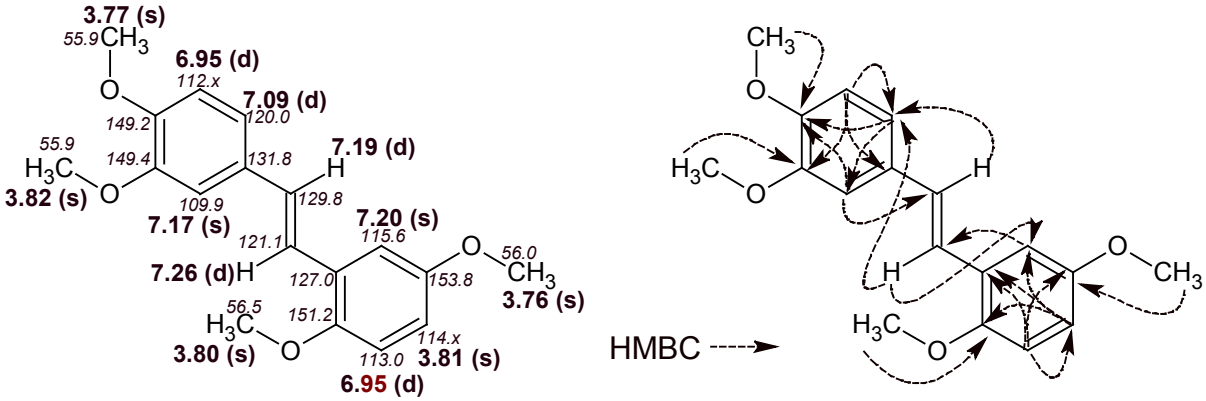
HMBC


H3C
O
CH3
O
H3C—O
O
CH3
{7.52,98.78}
{7.54,98.68}
{6.56,98.75}
{6.55,98.78}
{6.57,98.70}
{6.54,98.79}
{7.05,109.39}
{6.60,105.85}
{7.00,119.22}
{6.54,119.15}
{6.57,119.05}
{7.52,121.32}
{7.54,121.23}
{7.51,121.32}
{7.05,127.05}
{6.55,119.12}
{6.90,131.30}
{7.18,127.63}
{6.92,131.26}
{6.94,131.22}
{6.94,149.29}
{6.92,149.32}
{7.06,148.74}
{7.51,157.95}
{7.55,157.86}
{6.60,157.90}
{7.55,160.39}
{7.53,157.90}
{6.58,157.92}
{3.81,149.34}
{3.76,148.71}
{3.75,148.71}
{3.79,160.42}
{3.78,160.42}
{3.85,157.91}
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
f2 (ppm)
80
90
100
110
120
130
140
150
160
170
180
f1 (ppm)


{7.52,98.78} {7.54,98.68}
{6.56,98.75} {6.55,98.78}
{6.57,98.70} {6.54,98.79}
{7.05,109.39} {7.03,109.46}
{6.60,105.85}
{7.00,109.55} {7.01,109.54}
{6.93,119.48}
{6.54,119.15} {6.57,119.05}
{7.52,121.32} {7.51,121.32}
{6.60,119.07} {6.55,119.12}
{7.54,121.23} {7.54,121.23} {7.00,121.34}
{7.24,131.17} {6.90,131.30}
{7.20,131.37} {6.92,131.26} {6.94,131.22}
{6.94,149.29} {6.92,149.32}
{6.90,149.31}
{7.51,157.95} {7.53,157.90}
{6.60,157.90} {6.58,157.92}
{7.55,157.86} {7.19,157.98}
{7.55,160.39}
{6.59,160.42} {6.60,160.41}
f2 (ppm)
f1 (ppm)

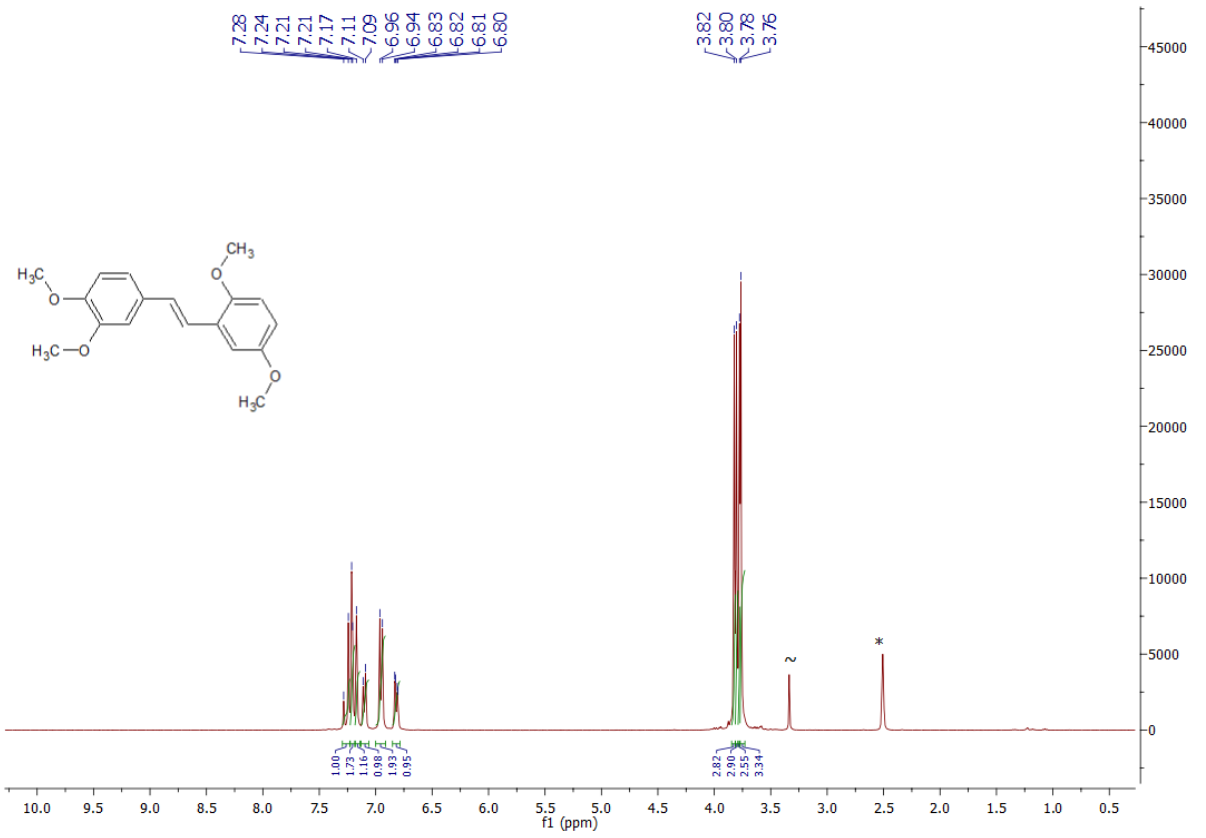

{3.81,149.34}
{3.76,148.71}
{3.75,148.71}
{3.85,157.91}
{3.79,160.42} {3.78,160.42}
f2 (ppm)
f1 (ppm)

6.5 NMR data for 3,4,2',5'-tetramethoxy-trans-stilbene (5e)

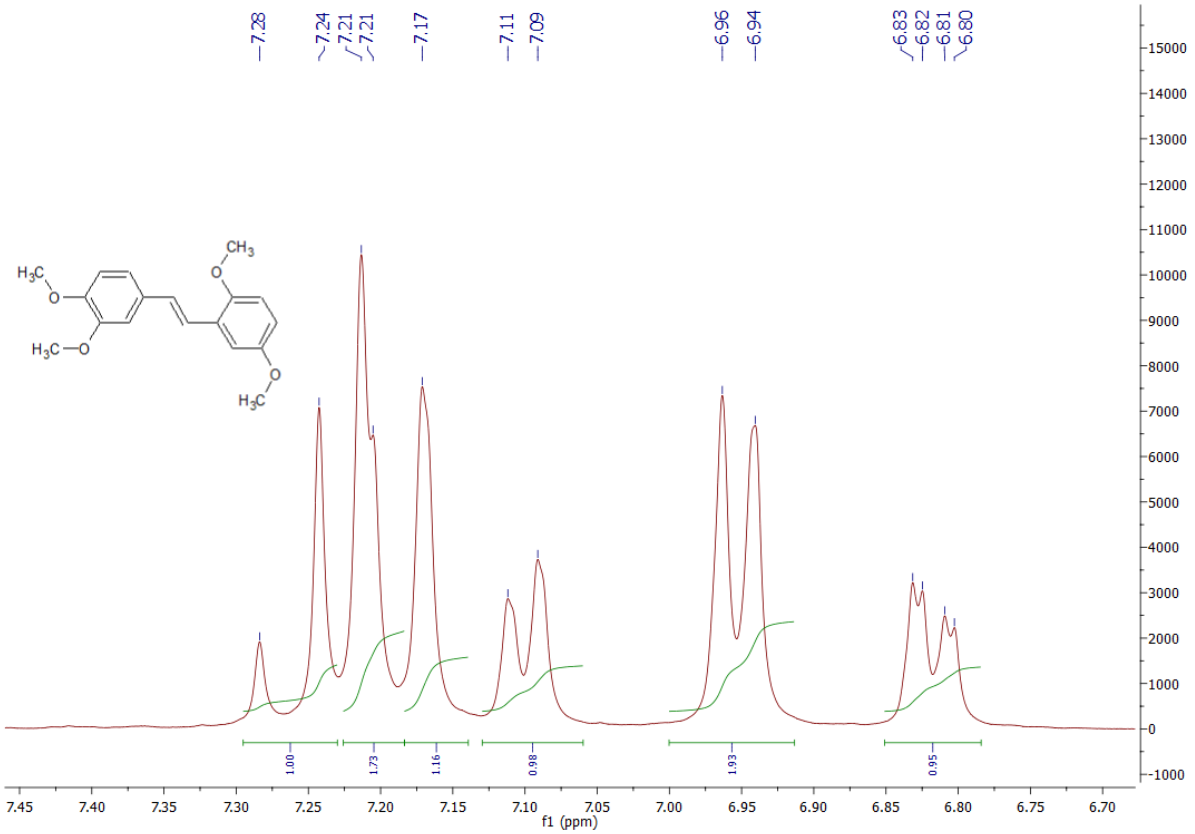


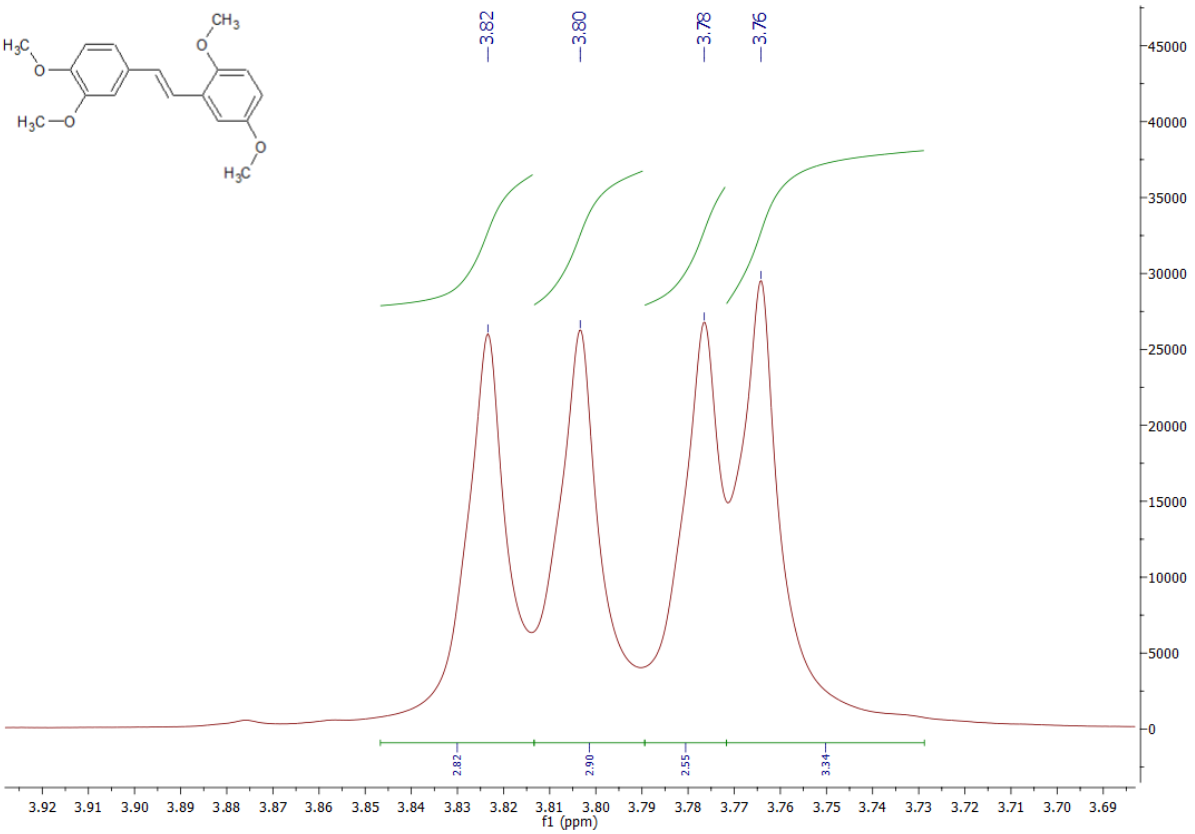
Scheme X5 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

1H

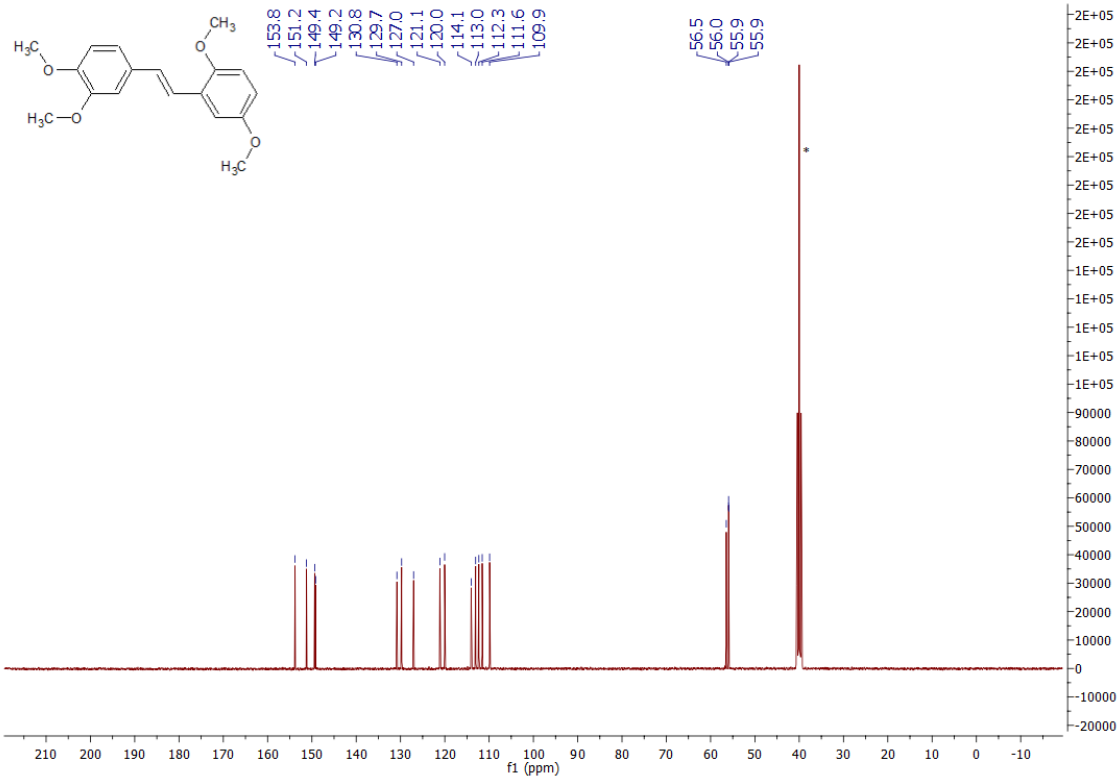


Symbol * and ~ indicates DMSO and water residuals peaks.

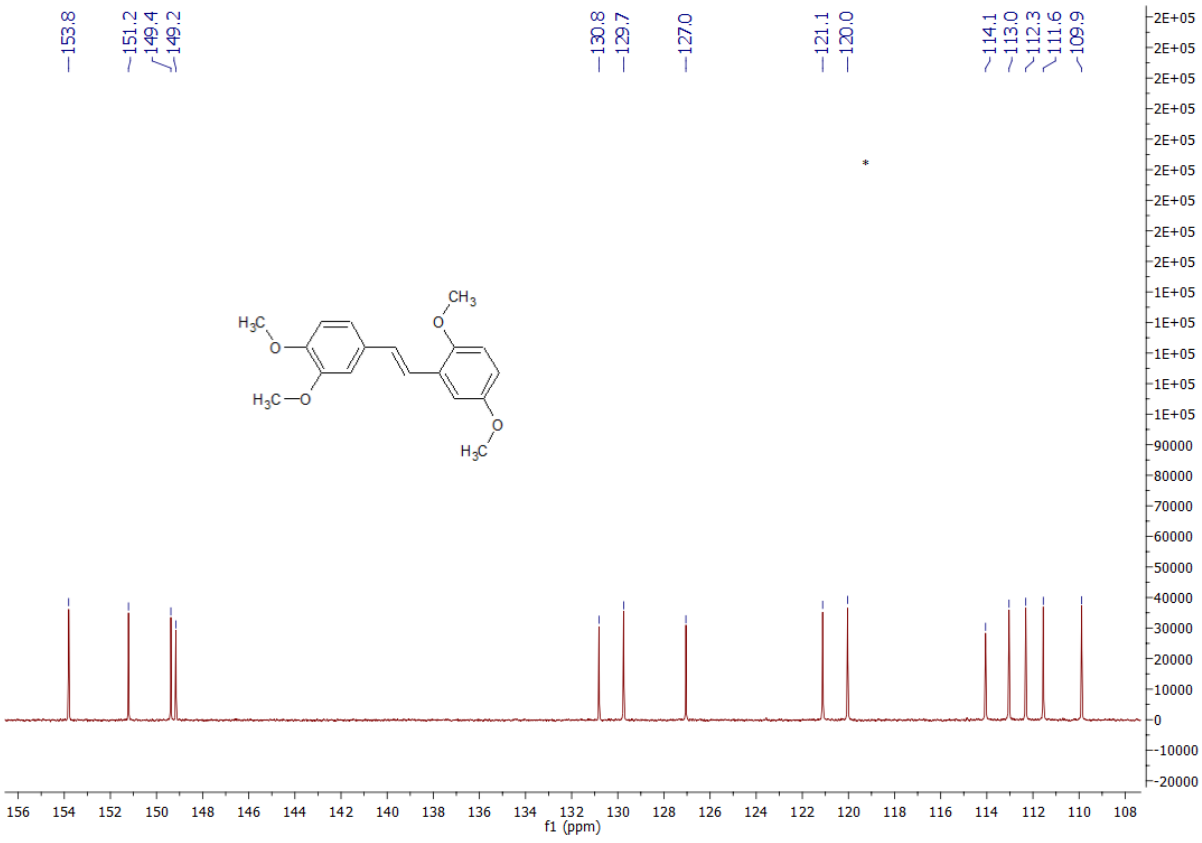


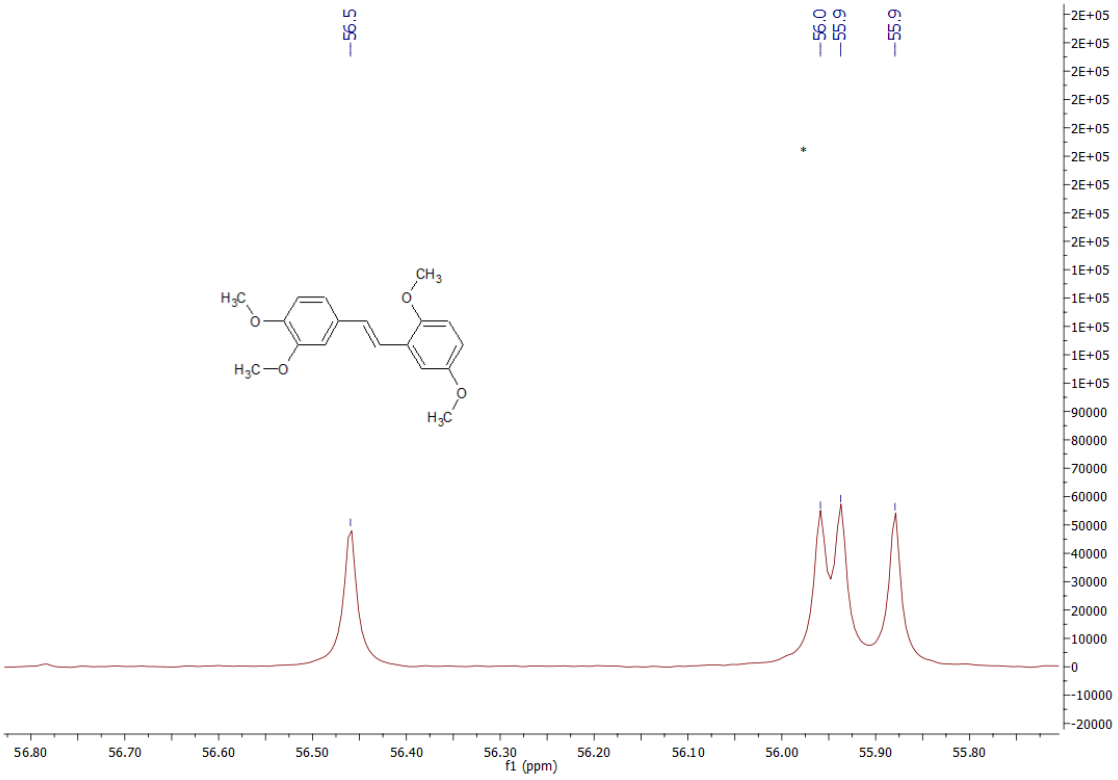


13C

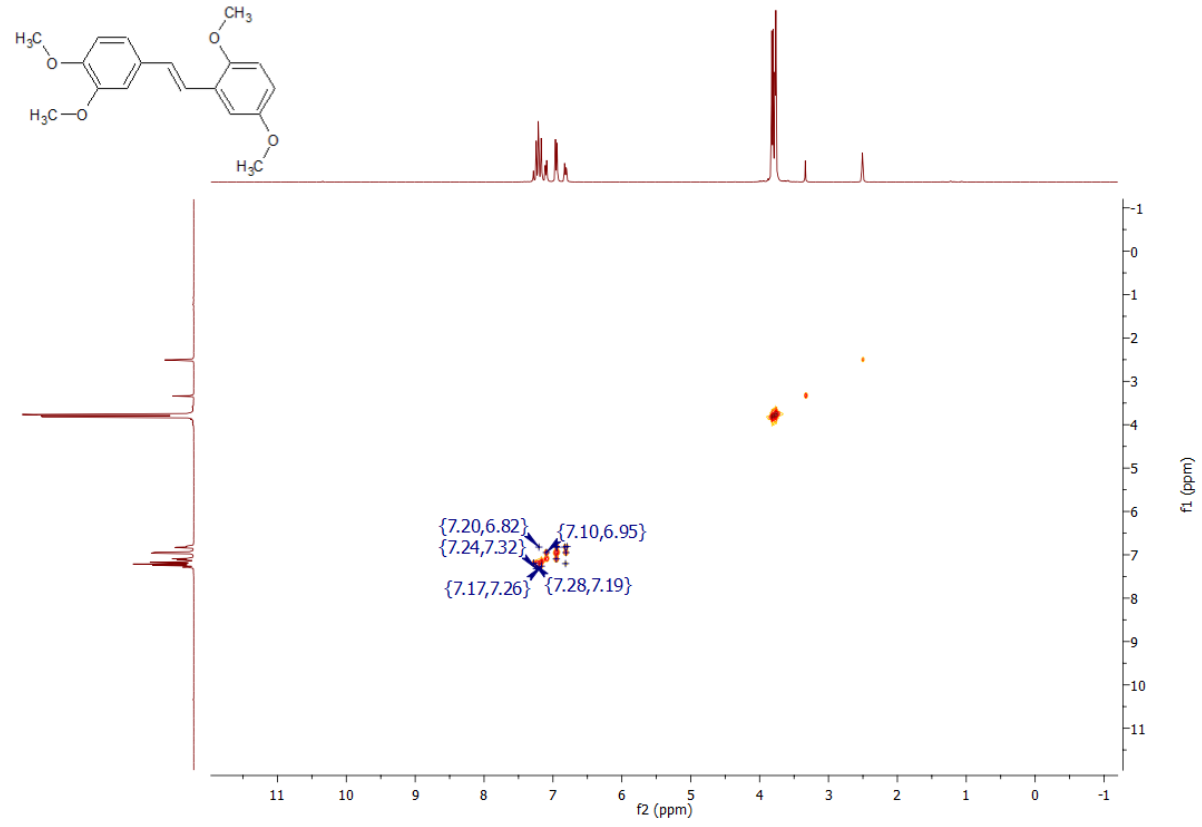


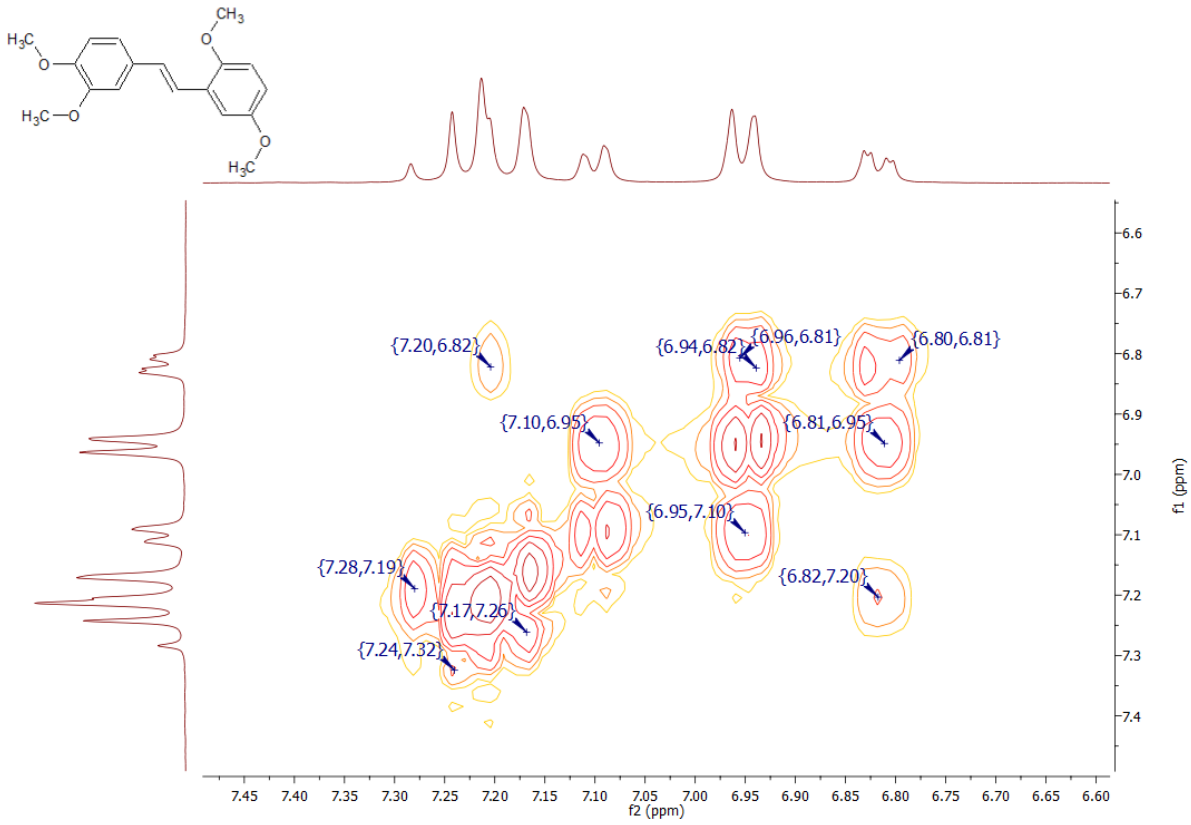
Symbol * indicates DMSO residual peaks.



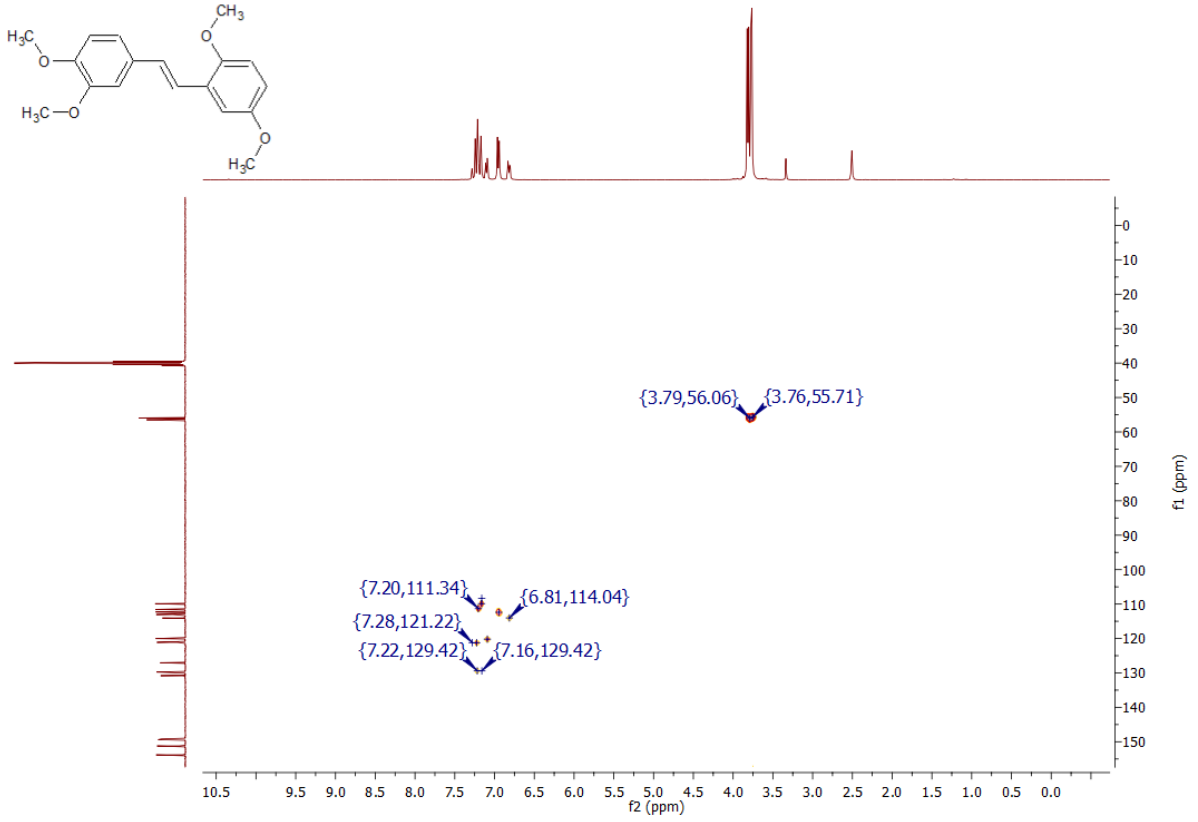

56.5
56.0
55.9
55.9
f1 (ppm)

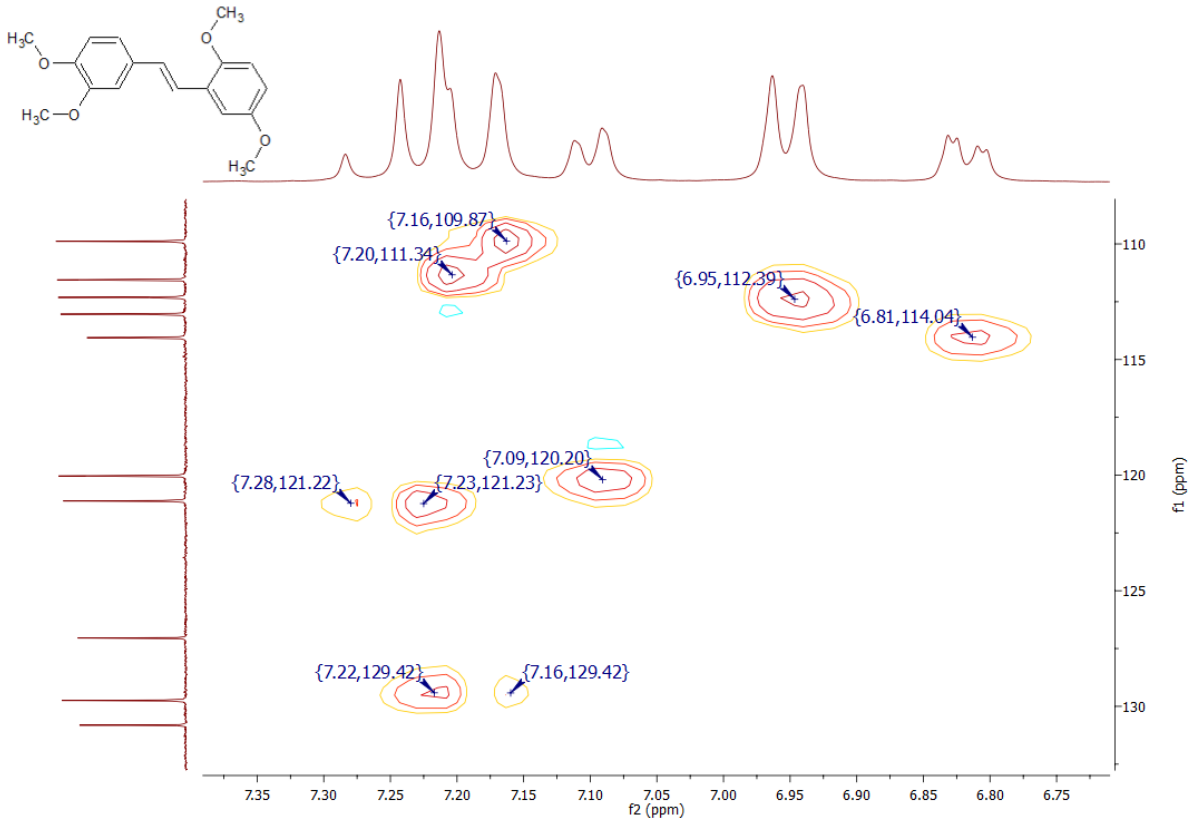
1H1H COSY

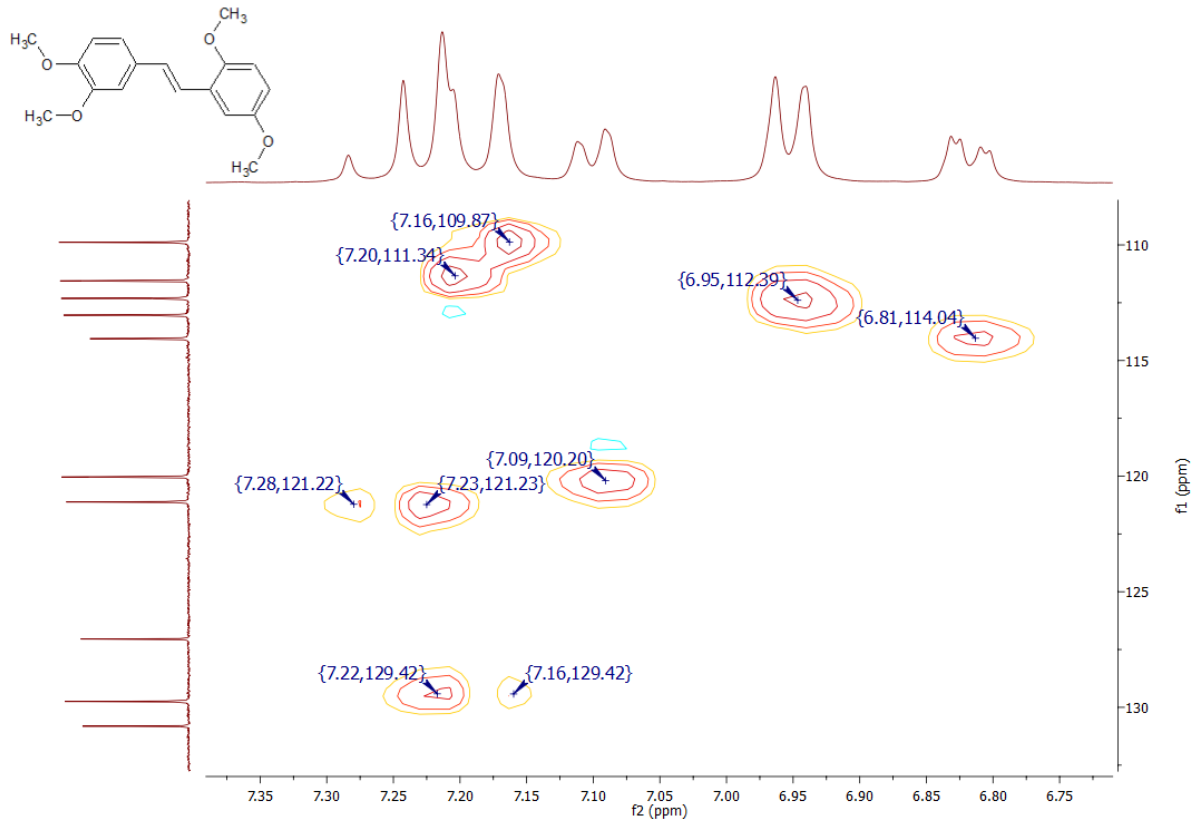

{7.20,6.82}
{7.24,7.32}
{7.10,6.95}
{7.17,7.26}
{7.28,7.19}
f2 (ppm)
f1 (ppm)



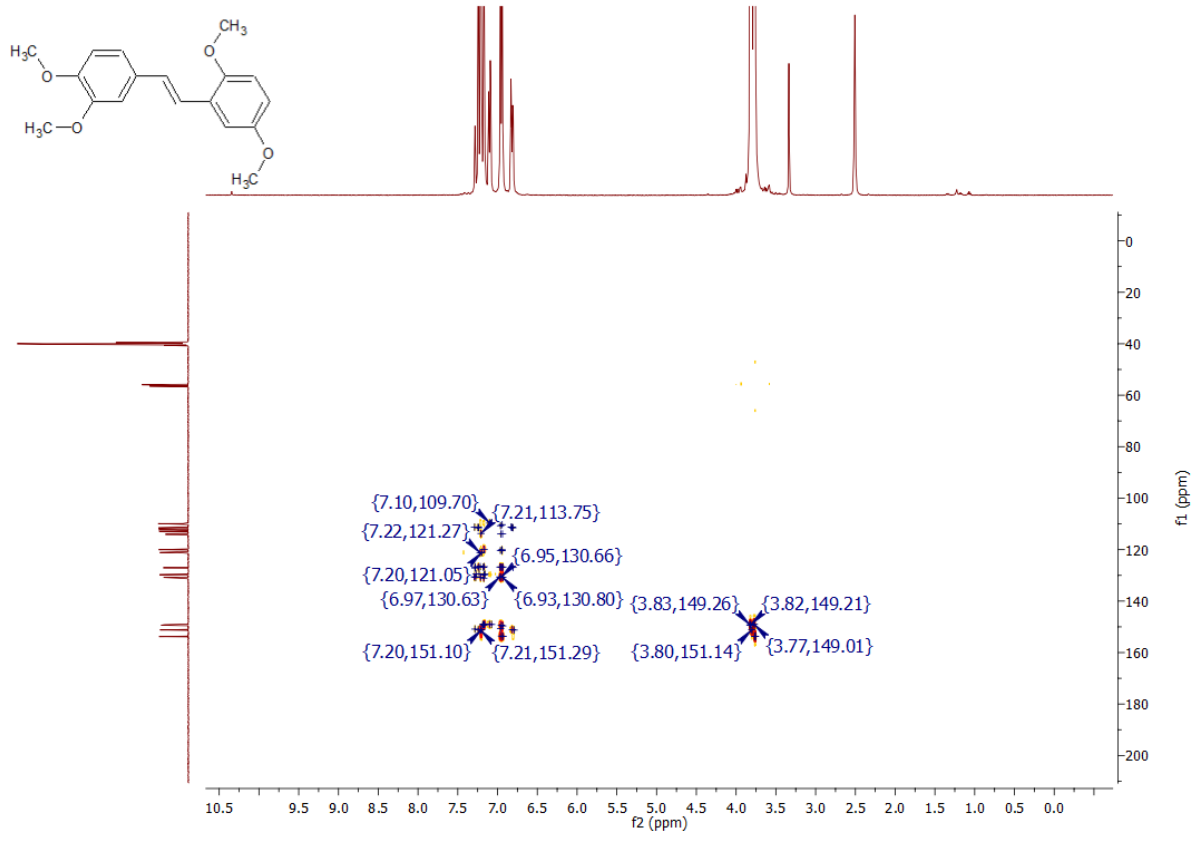
HSQC

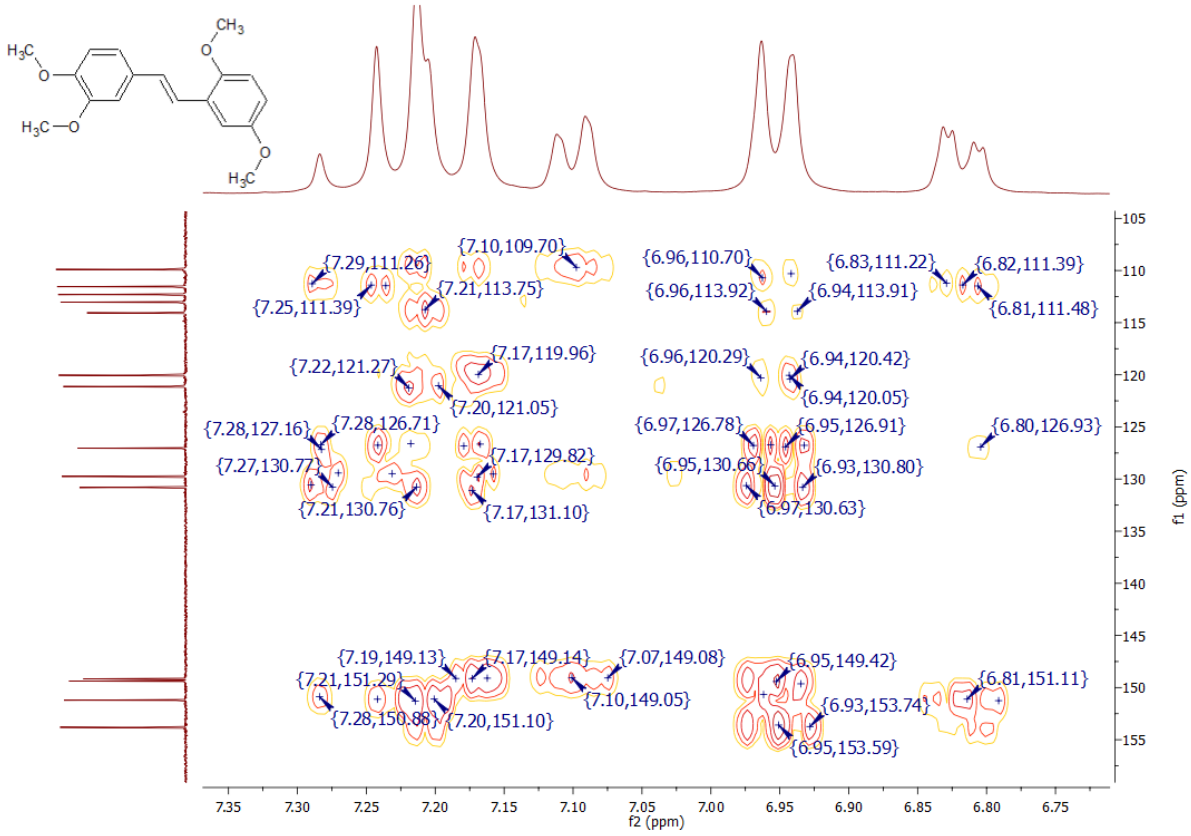


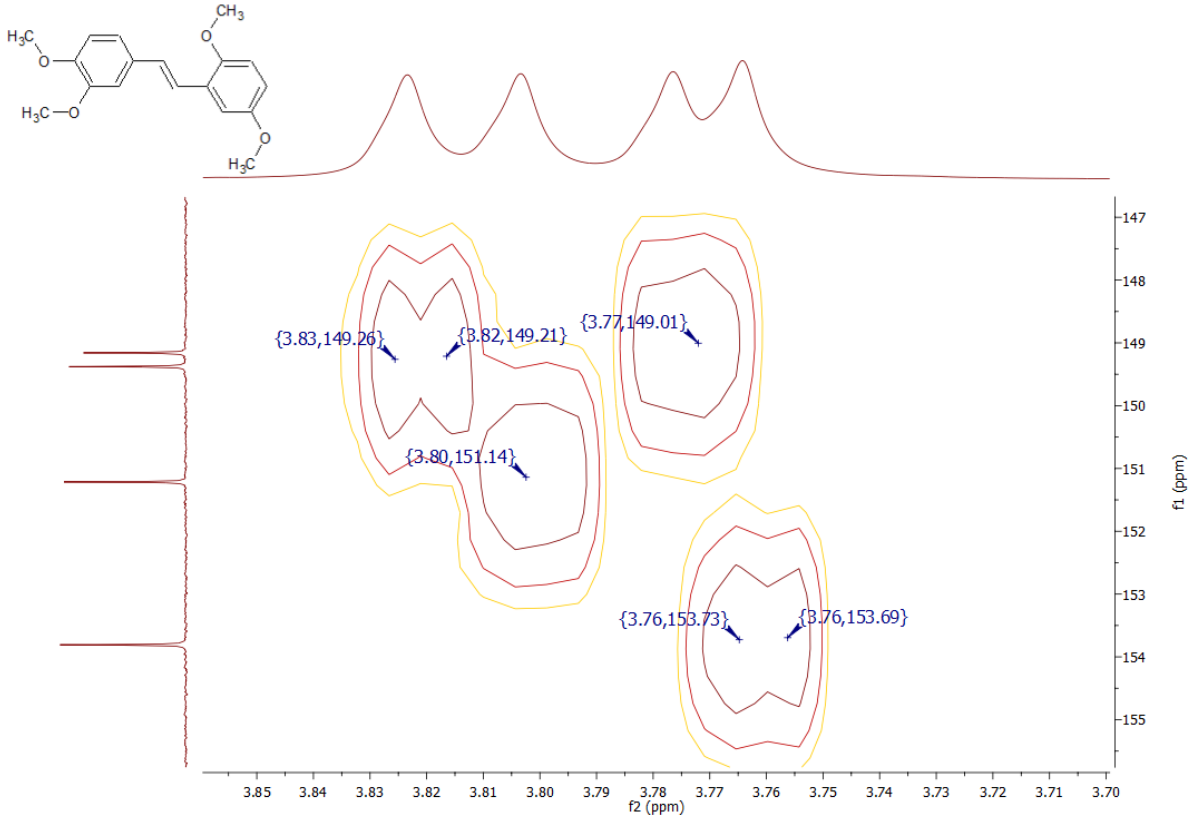




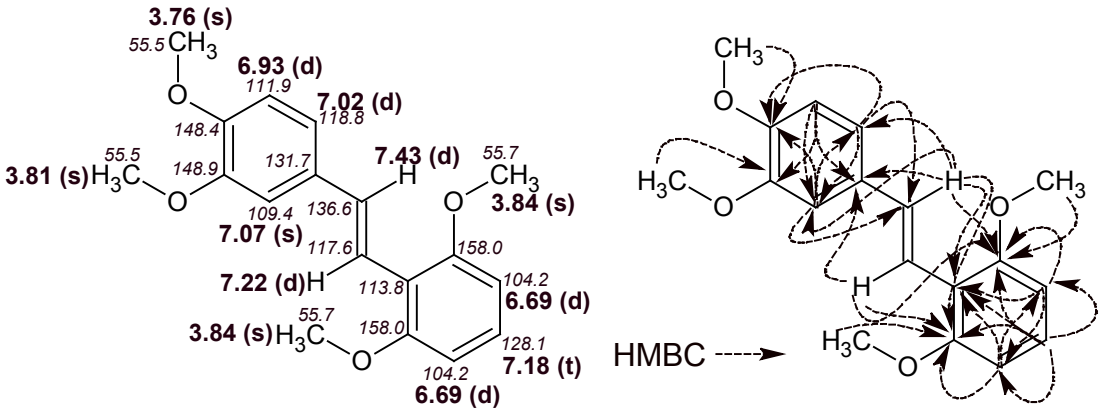
HMBC




{7.29,111.26}
{7.10,109.70}
{7.25,111.39}
{7.21,113.75}
{6.96,110.70}
{6.83,111.22}
{6.82,111.39}
{6.96,113.92}
{6.94,113.91}
{6.81,111.48}
{7.22,121.27}
{7.17,119.96}
{7.20,121.05}
{6.96,120.29}
{6.94,120.42}
{6.94,120.05}
{7.28,127.16}
{7.28,126.71}
{6.97,126.78}
{6.95,126.91}
{6.80,126.93}
{7.27,130.77}
{7.17,129.82}
{6.95,130.66}
{6.93,130.80}
{7.21,130.76}
{7.17,131.10}
{6.97,130.63}
{7.19,149.13}
{7.17,149.14}
{7.07,149.08}
{6.95,149.42}
{7.21,151.29}
{6.81,151.11}
{7.10,149.05}
{6.93,153.74}
{7.28,150.88}
{7.20,151.10}
{6.95,153.59}
f1 (ppm)
f2 (ppm)

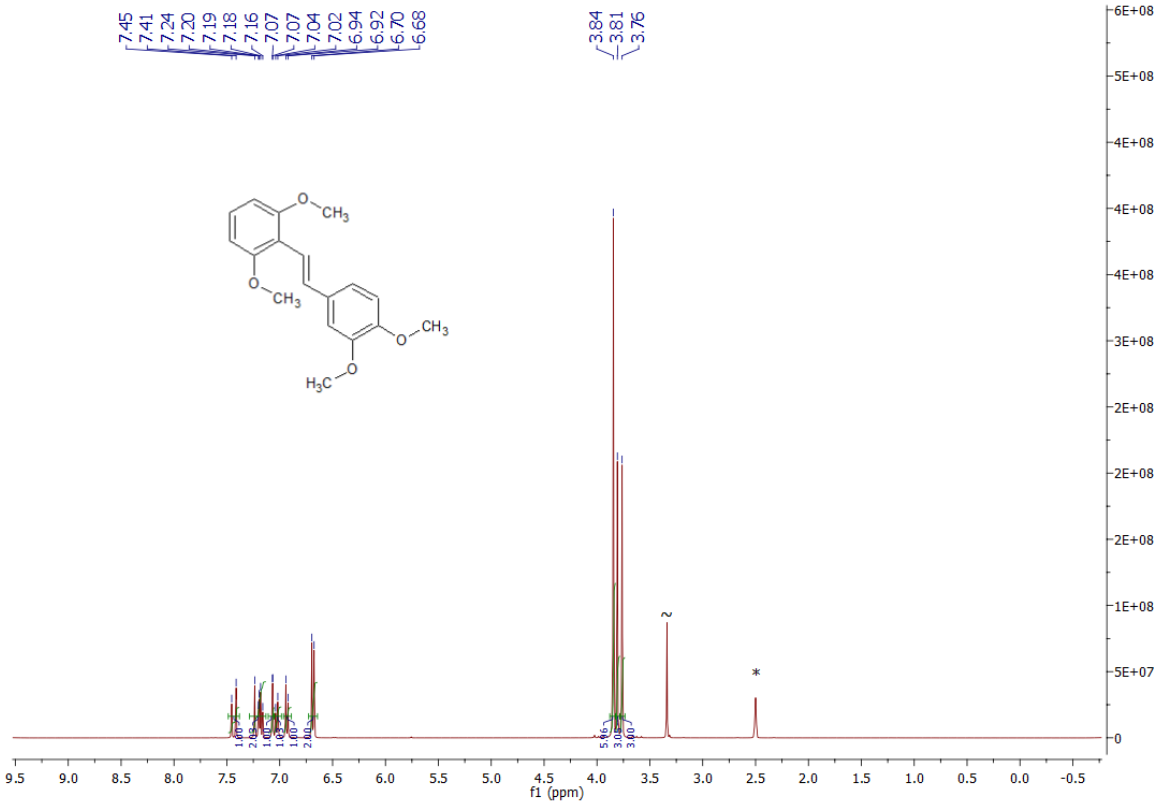

{3.83,149.26}
{3.82,149.21}
{3.77,149.01}
{3.80,151.14}
{3.76,153.73}
{3.76,153.69}
f1 (ppm)
f2 (ppm)

6.6 NMR data for 3,4,2',6'-tetramethoxy-trans-stilbene (5f)

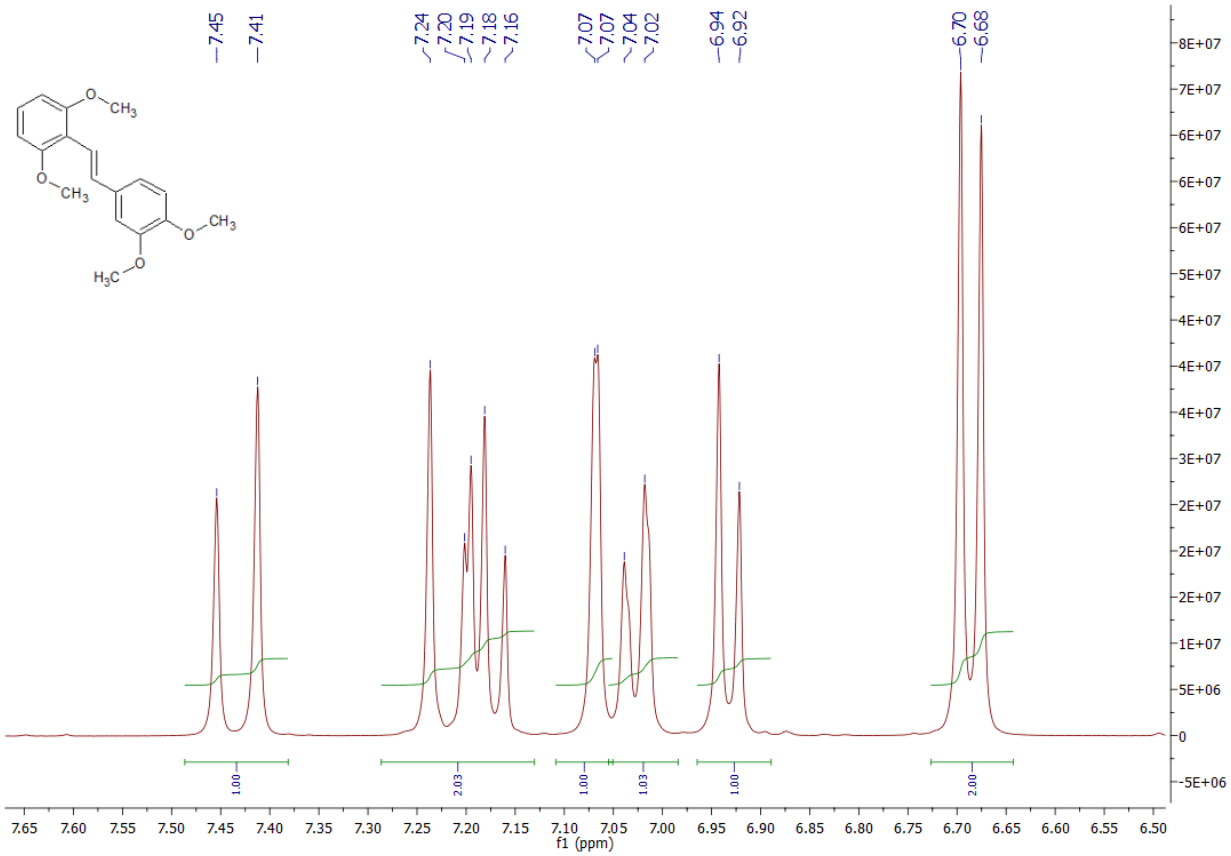


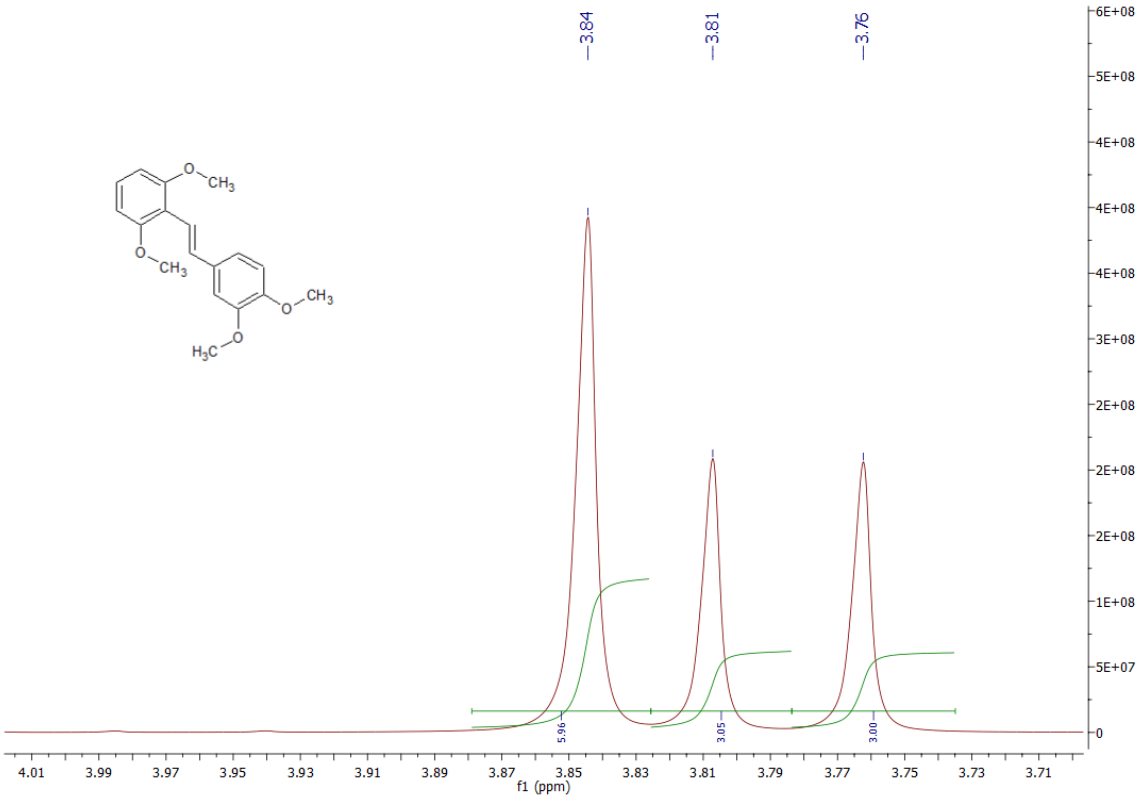
Scheme X6 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

1H

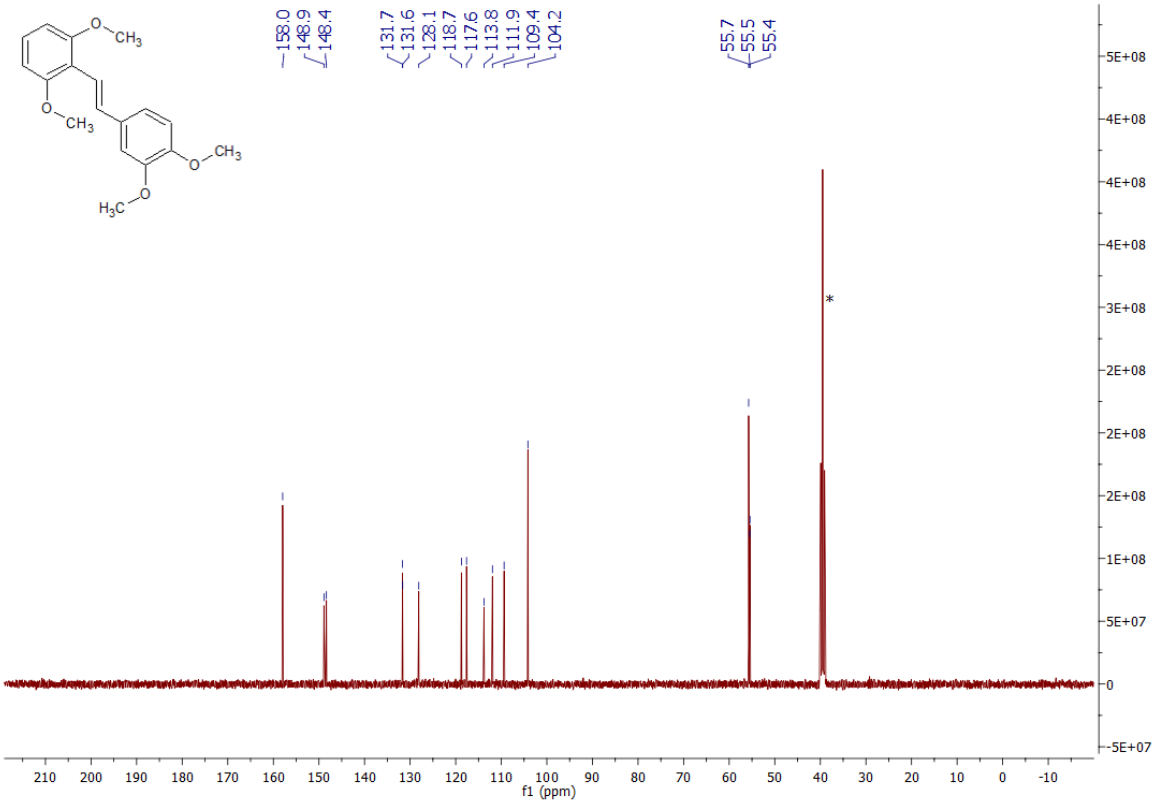


Symbol * and ~ indicates DMSO and water residuals peaks.

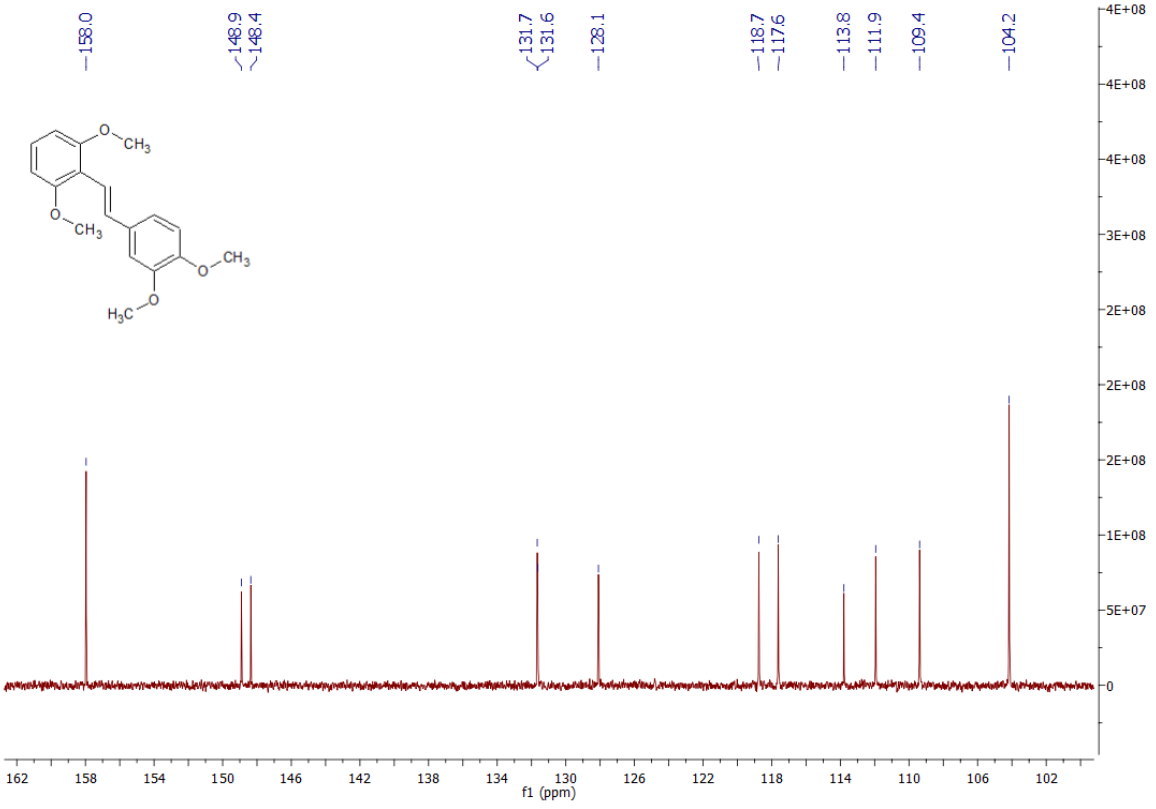

7.45
7.41
7.24
7.20
7.19
7.18
7.16
7.07
7.07
7.04
7.02
6.94
6.92
6.70
6.68
1.00
2.03
1.00
1.03
1.00
2.00
f1 (ppm)

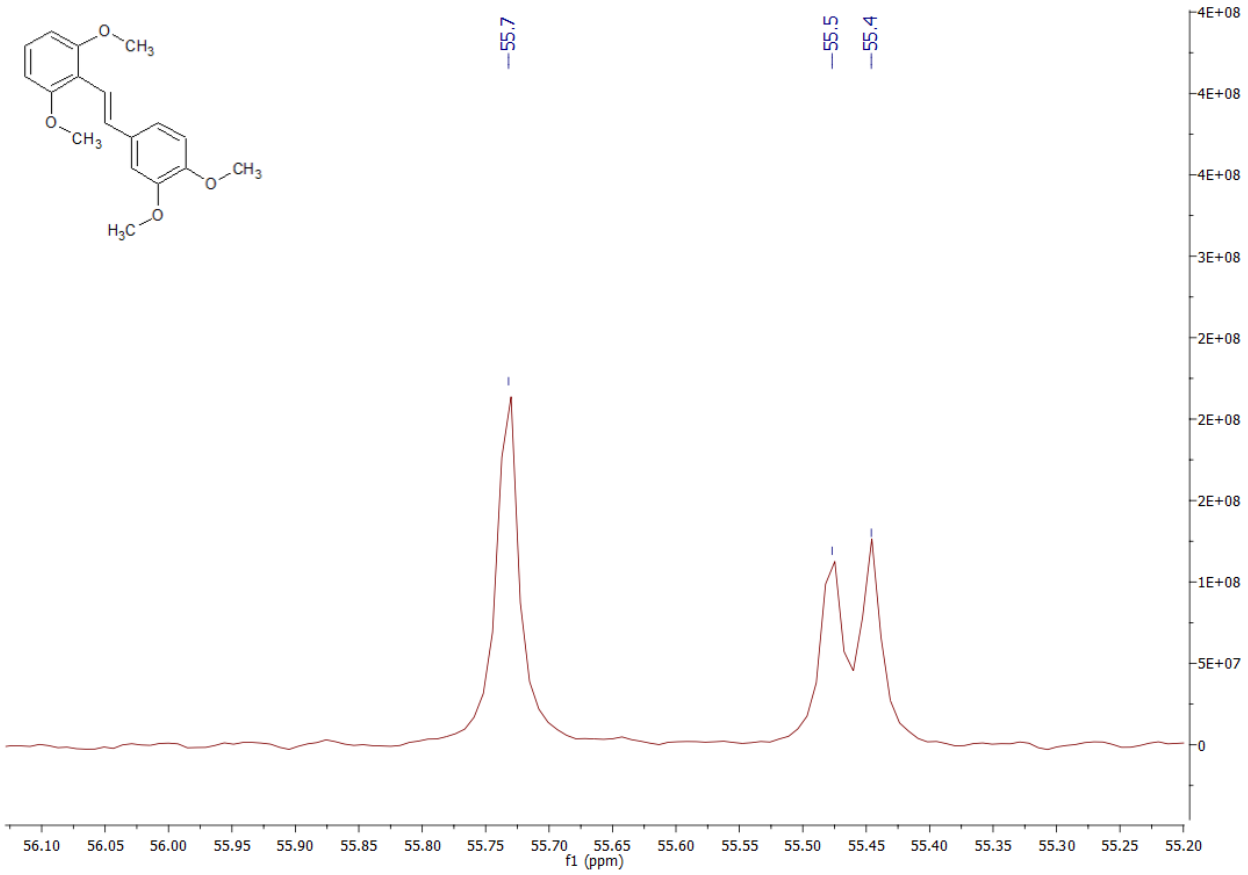

3.84
3.81
3.76
5.96
3.05
3.00
f1 (ppm)

13C

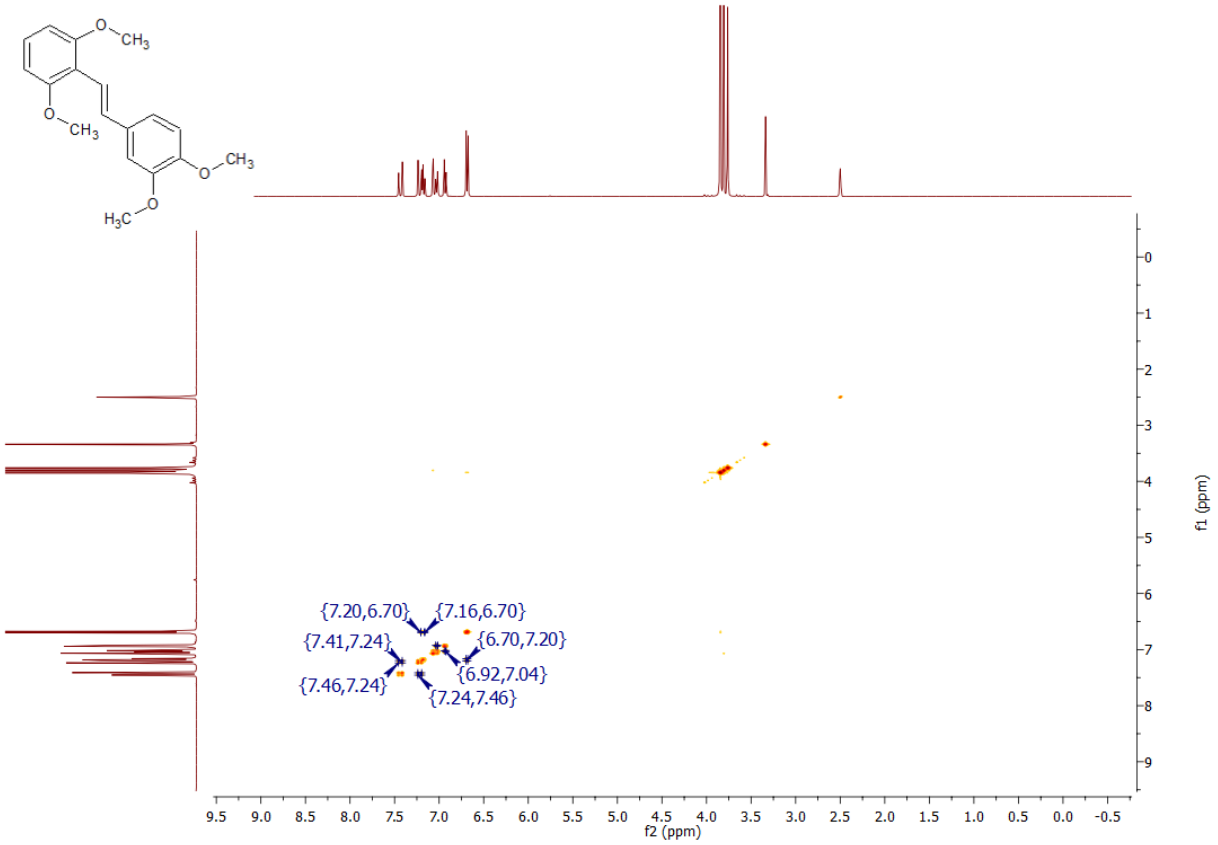


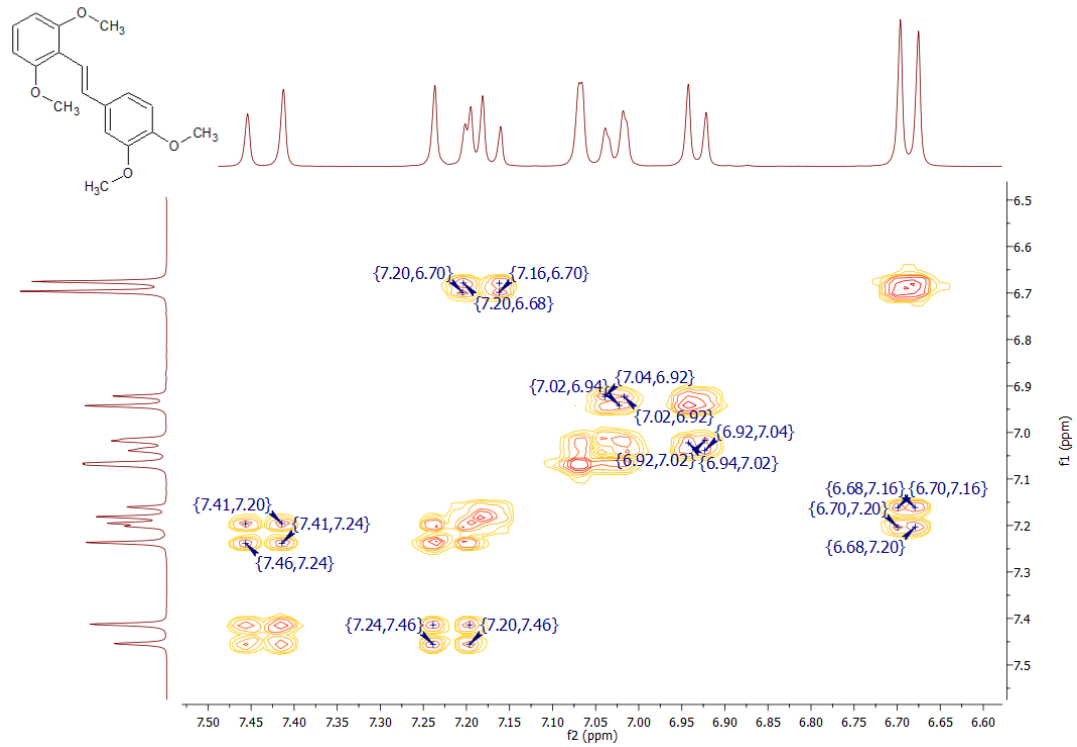
Symbol * indicates DMSO residual peaks.



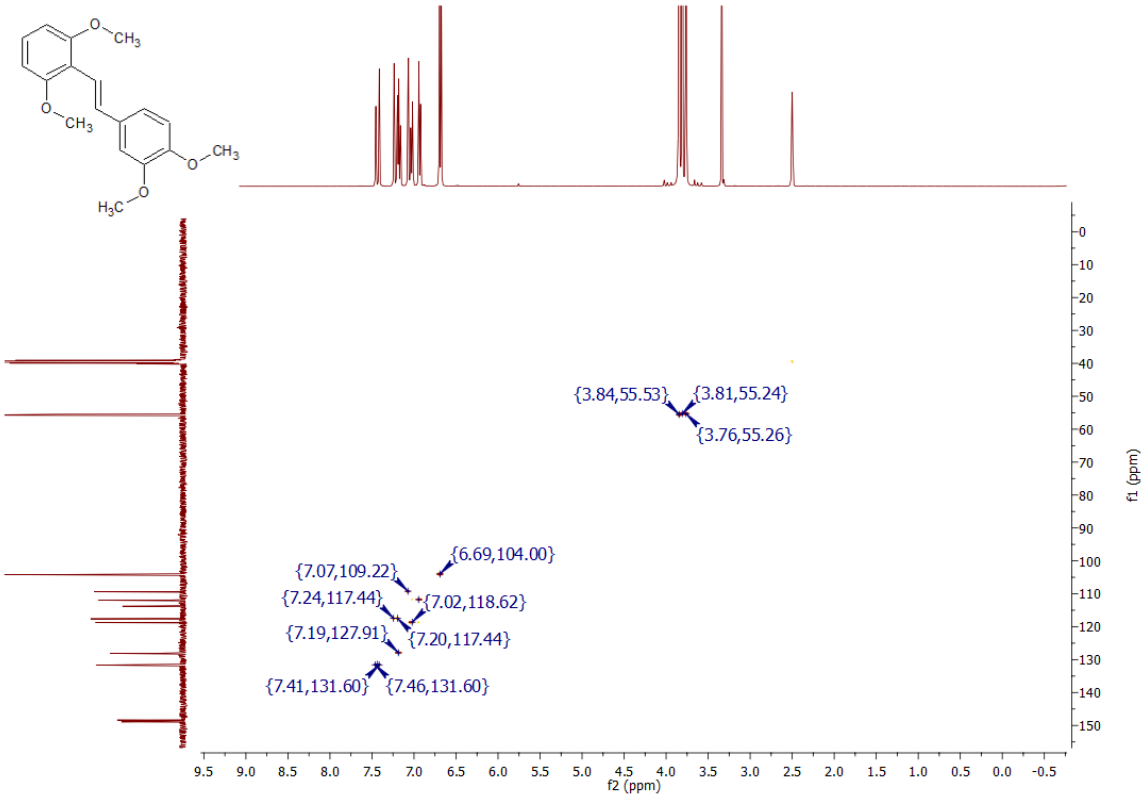


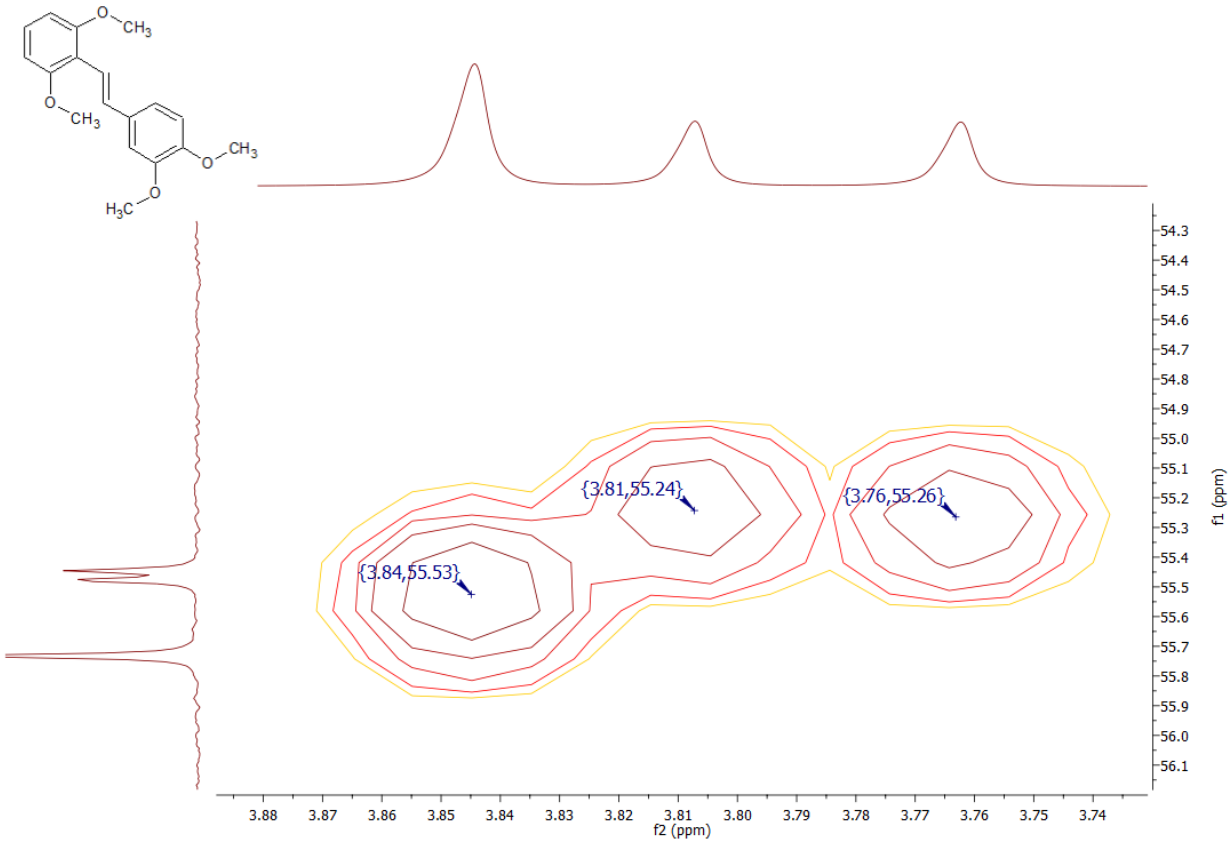
1H1H COSY

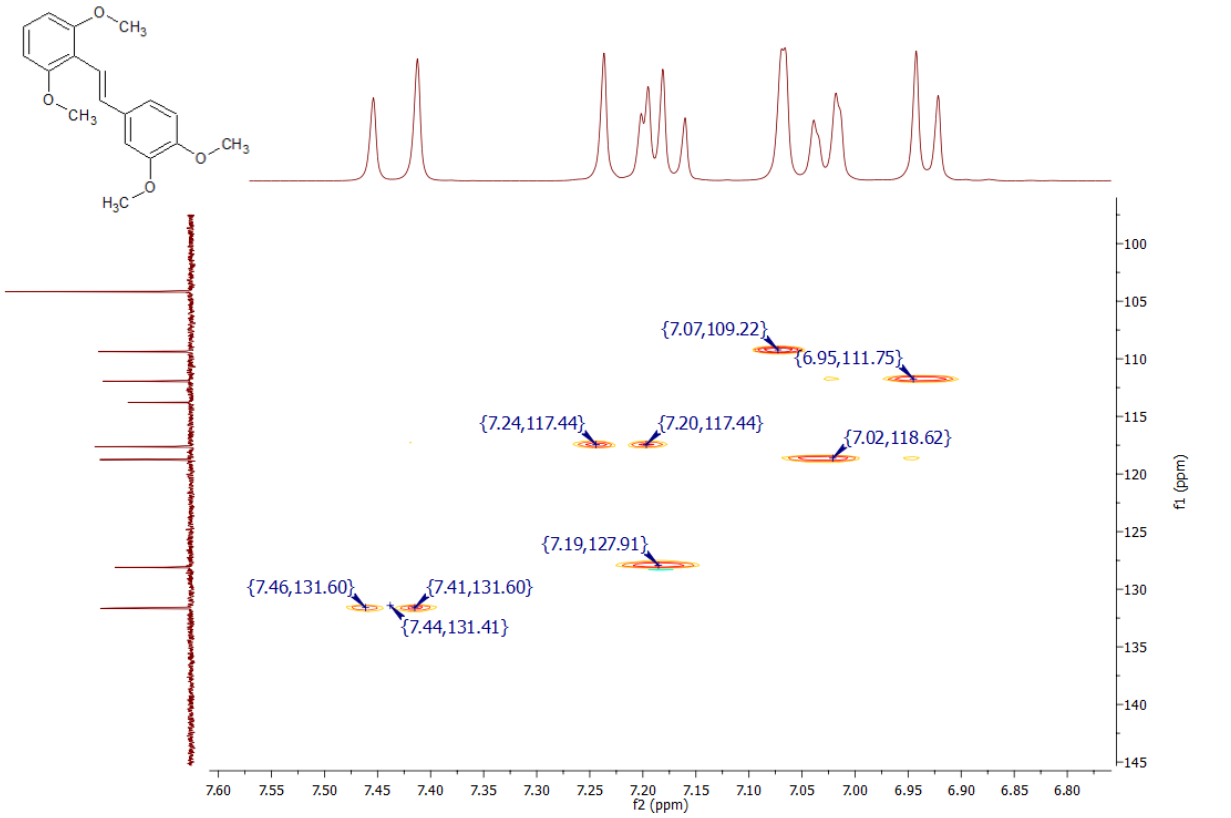



{7.20,6.70}
{7.16,6.70}
{7.20,6.68}
{7.02,6.94}
{7.04,6.92}
{7.02,6.92}
{6.92,7.04}
{6.92,7.02}
{6.94,7.02}
{6.68,7.16}
{6.70,7.16}
{6.70,7.20}
{6.68,7.20}
{7.41,7.20}
{7.41,7.24}
{7.46,7.24}
{7.24,7.46}
{7.20,7.46}
f1 (ppm)
f2 (ppm)

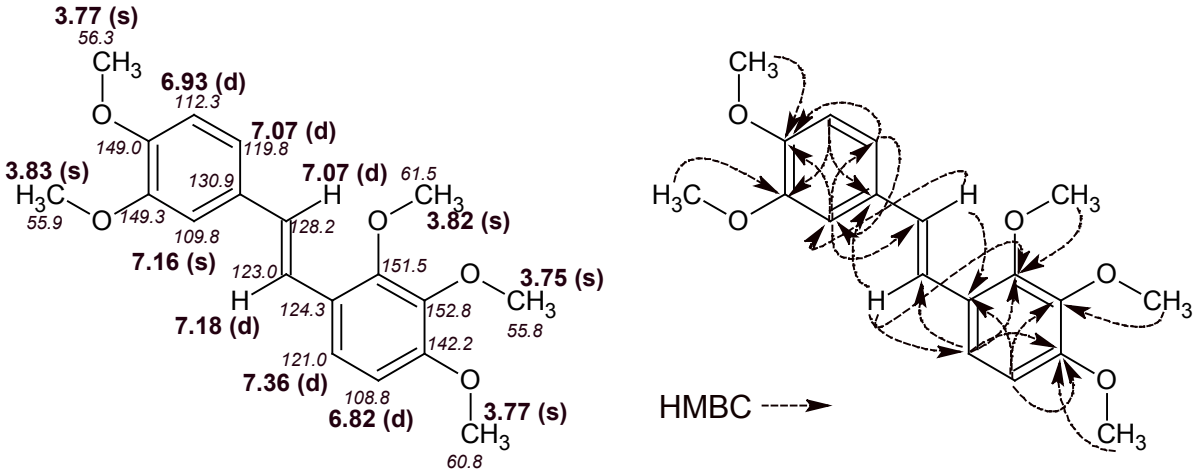
HSQC


{3.84,55.53}
{3.81,55.24}
{3.76,55.26}
{6.69,104.00}
{7.07,109.22}
{7.24,117.44}
{7.02,118.62}
{7.19,127.91}
{7.20,117.44}
{7.41,131.60}
{7.46,131.60}
f1 (ppm)
f2 (ppm)


{3.81,55.24}
{3.76,55.26}
{3.84,55.53}
f1 (ppm)
f2 (ppm)

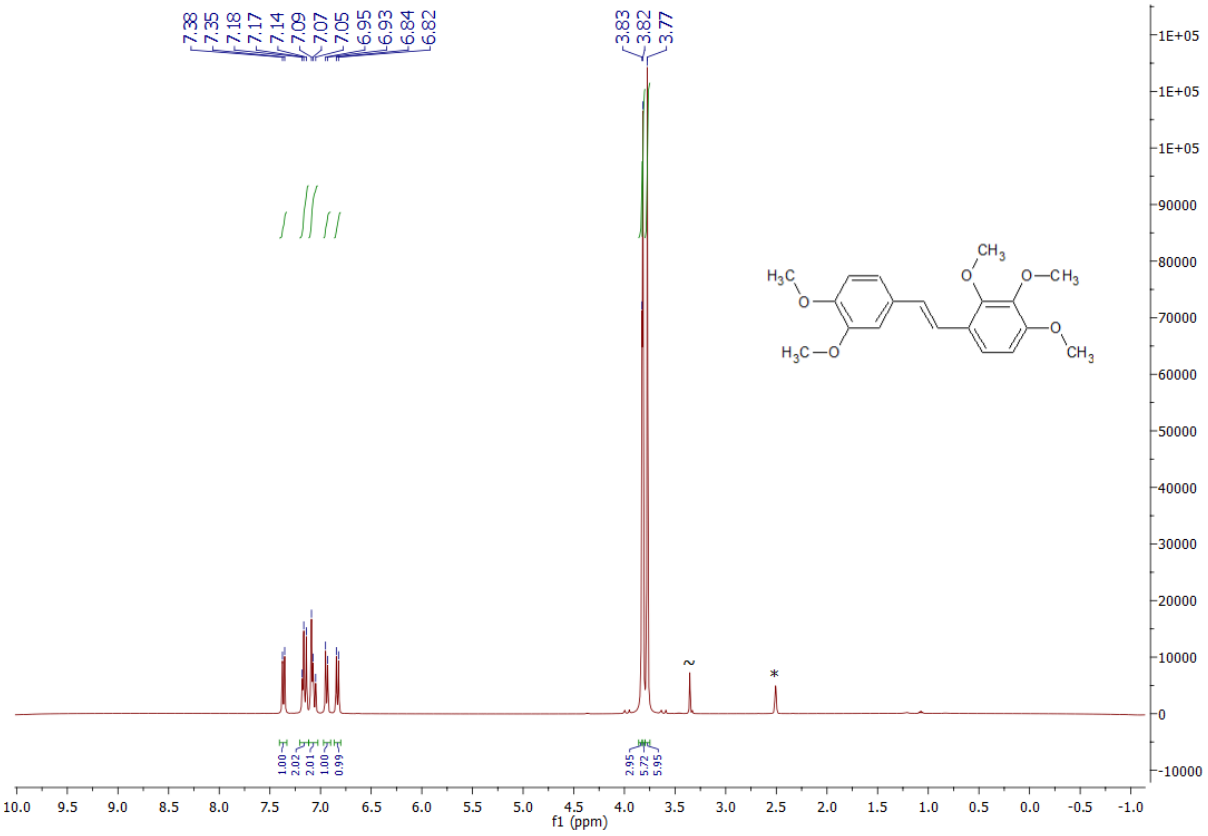

{7.07,109.22}
{6.95,111.75}
{7.24,117.44}
{7.20,117.44}
{7.02,118.62}
{7.19,127.91}
{7.46,131.60}
{7.41,131.60}
{7.44,131.41}
f1 (ppm)
f2 (ppm)

6.7 NMR data for 3,4,2',3',4'-pentamethoxy-trans-stilbene (5g)

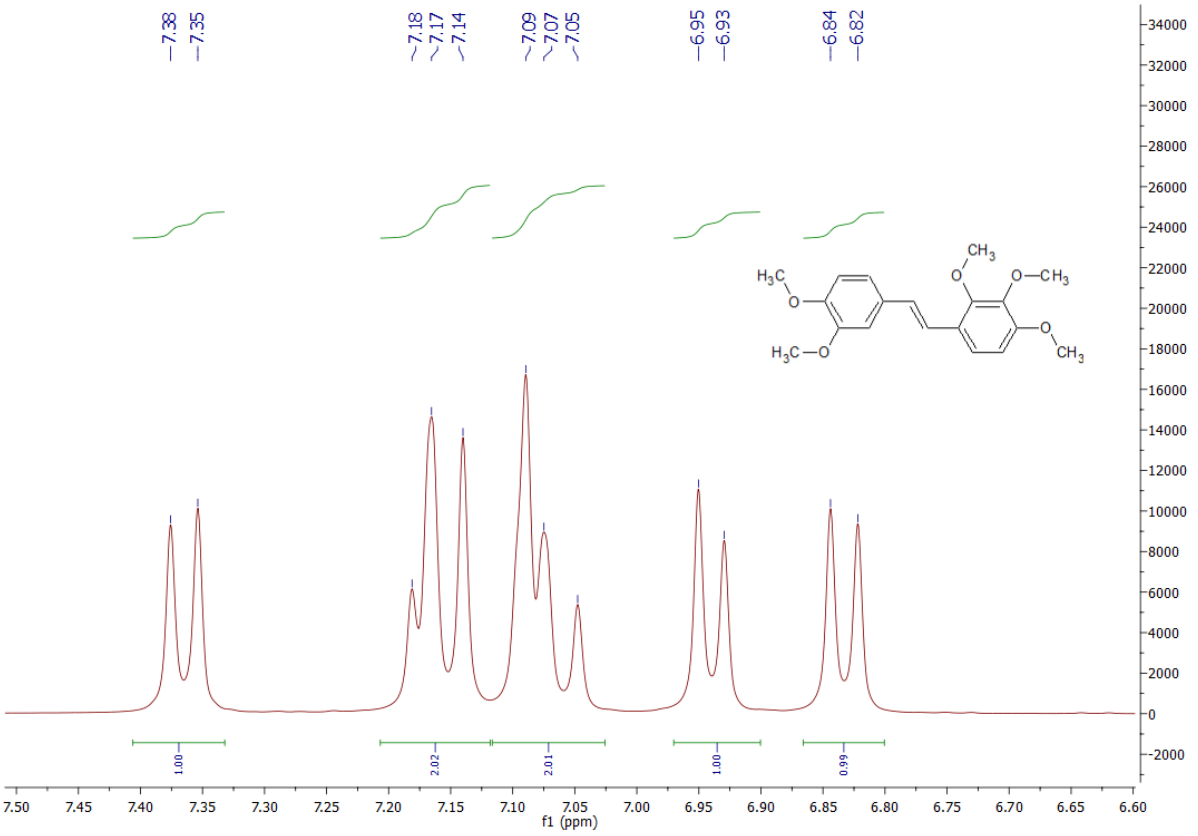


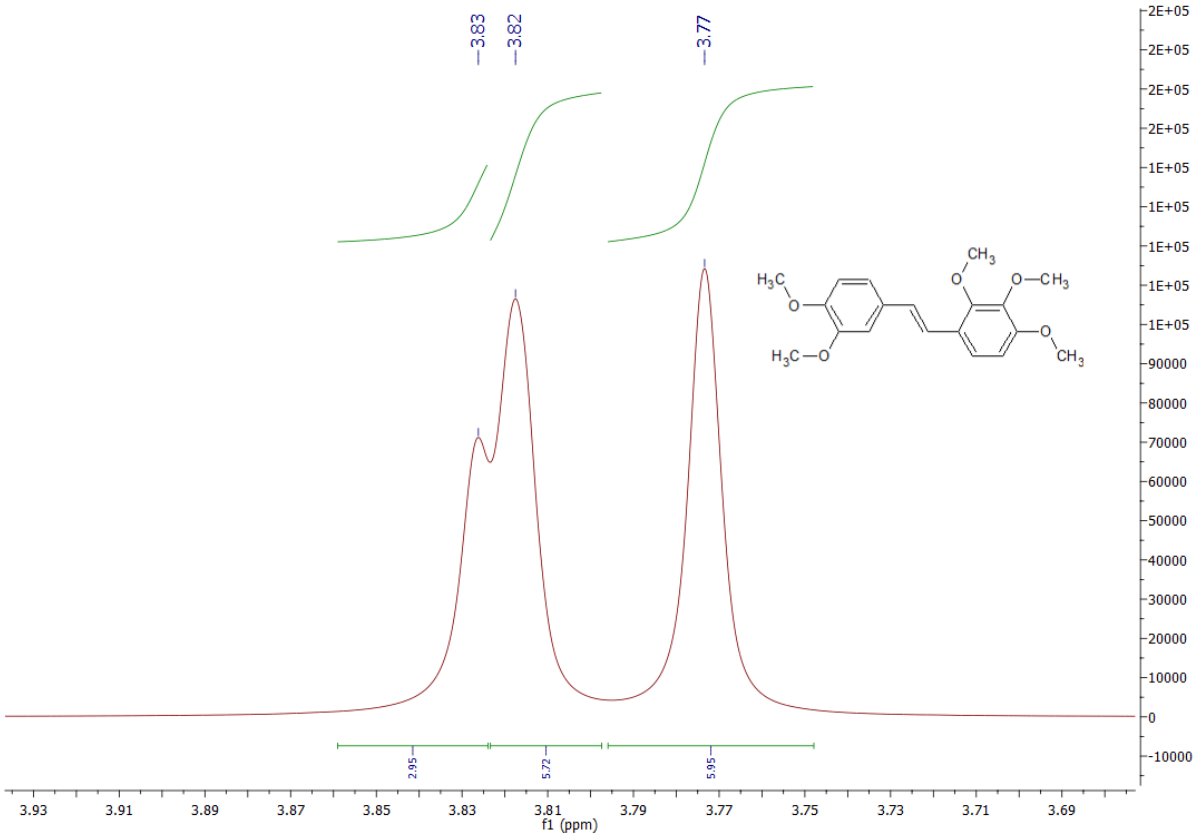
Scheme X7 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

1H

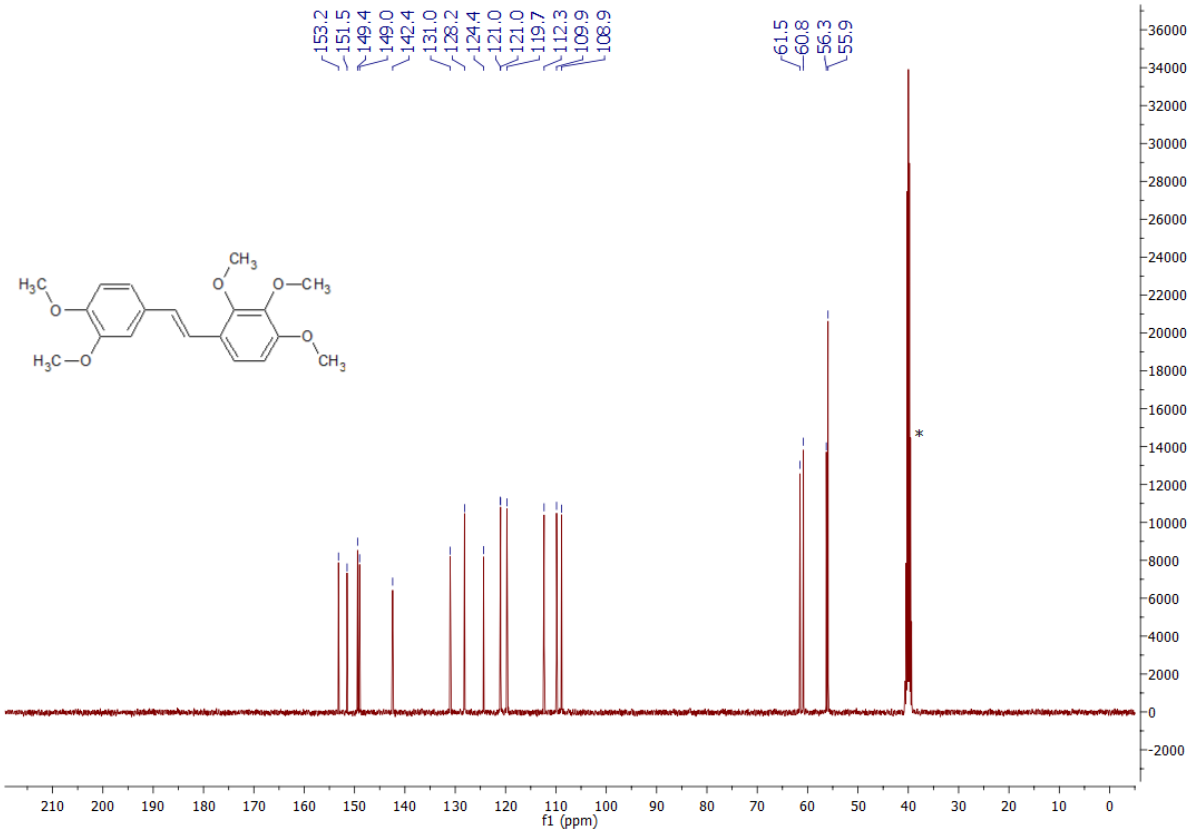


Symbol * and ~ indicates DMSO and water residuals peaks.

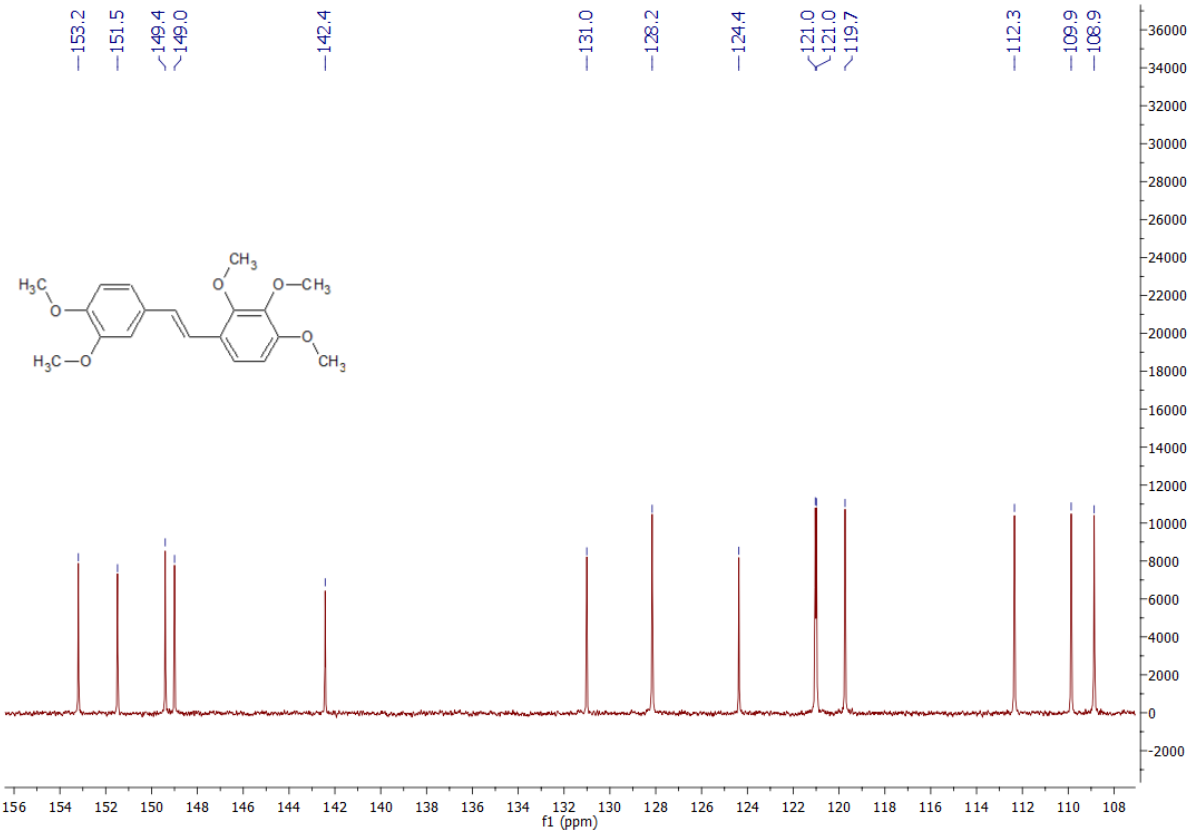

7.38
7.35
7.18
7.17
7.14
7.09
7.07
7.05
6.95
6.93
6.84
6.82
1.00
2.02
2.01
1.00
0.99
f1 (ppm)

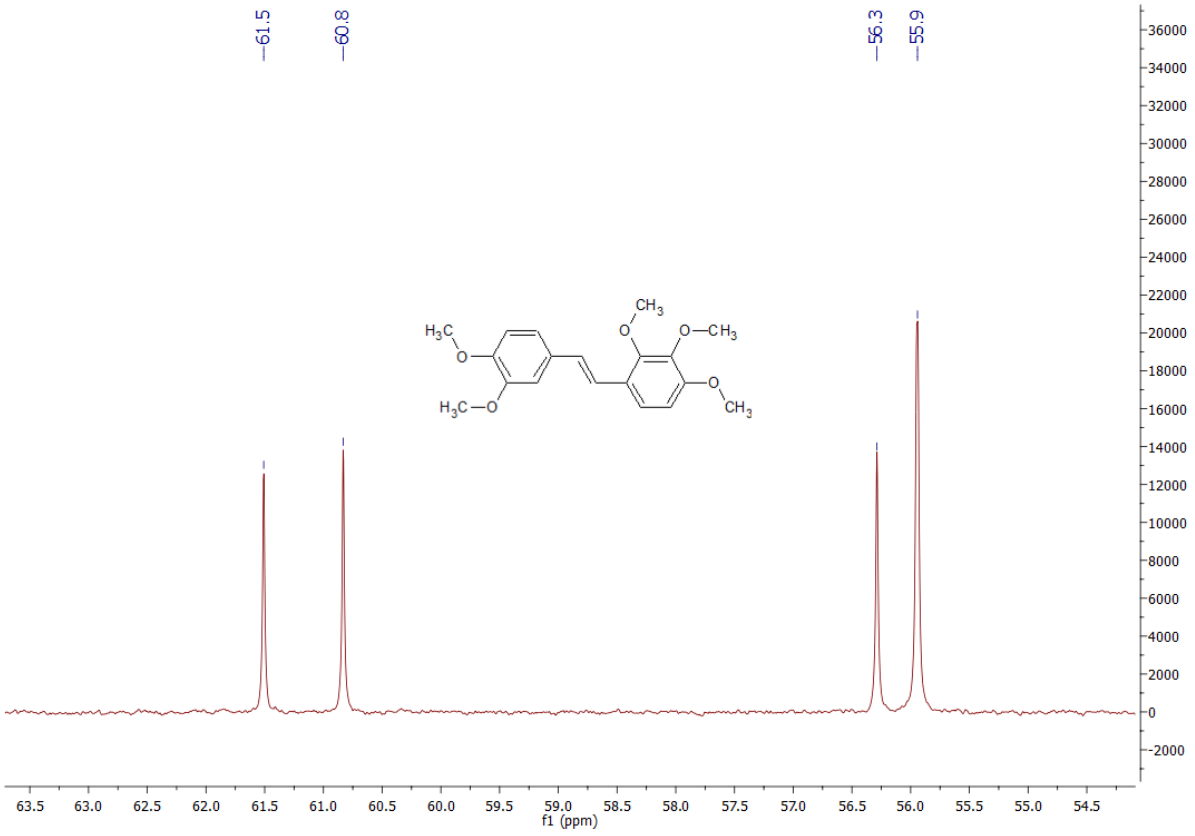

3.83
3.82
3.77
2.95
5.72
5.95
f1 (ppm)

13C

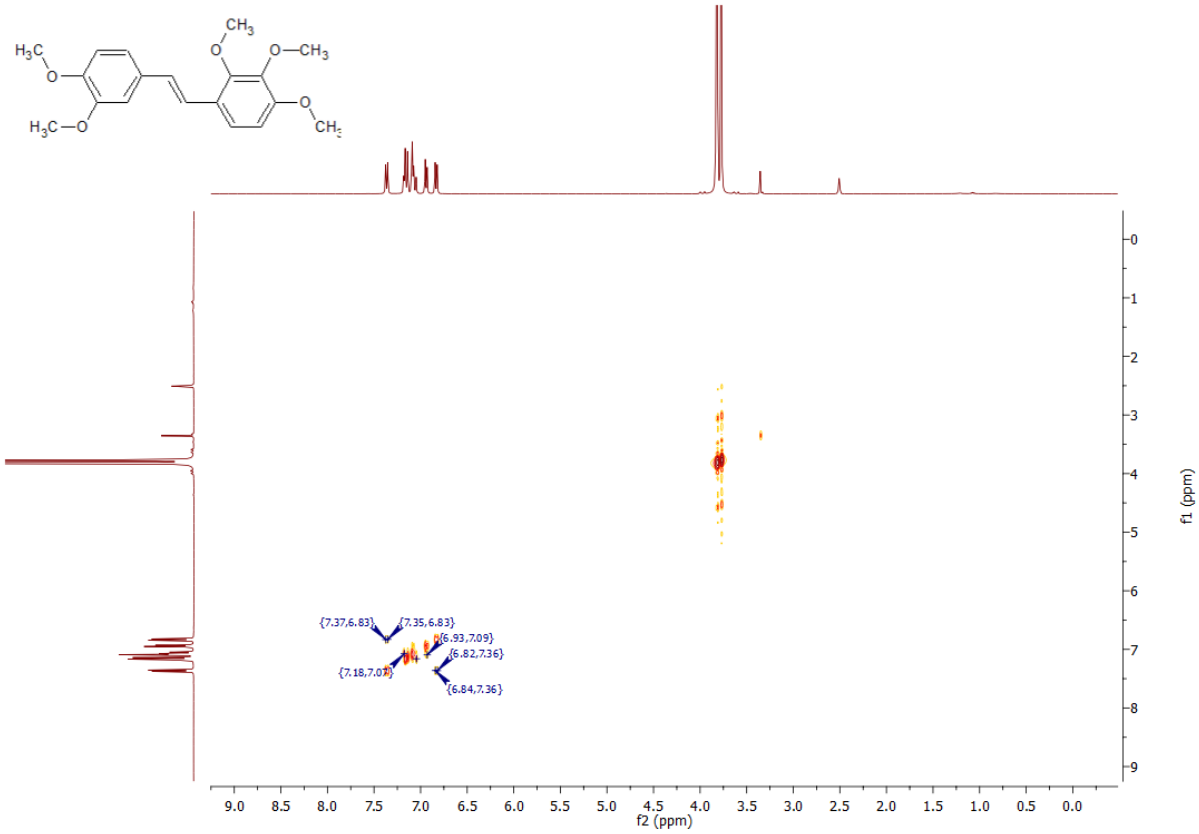


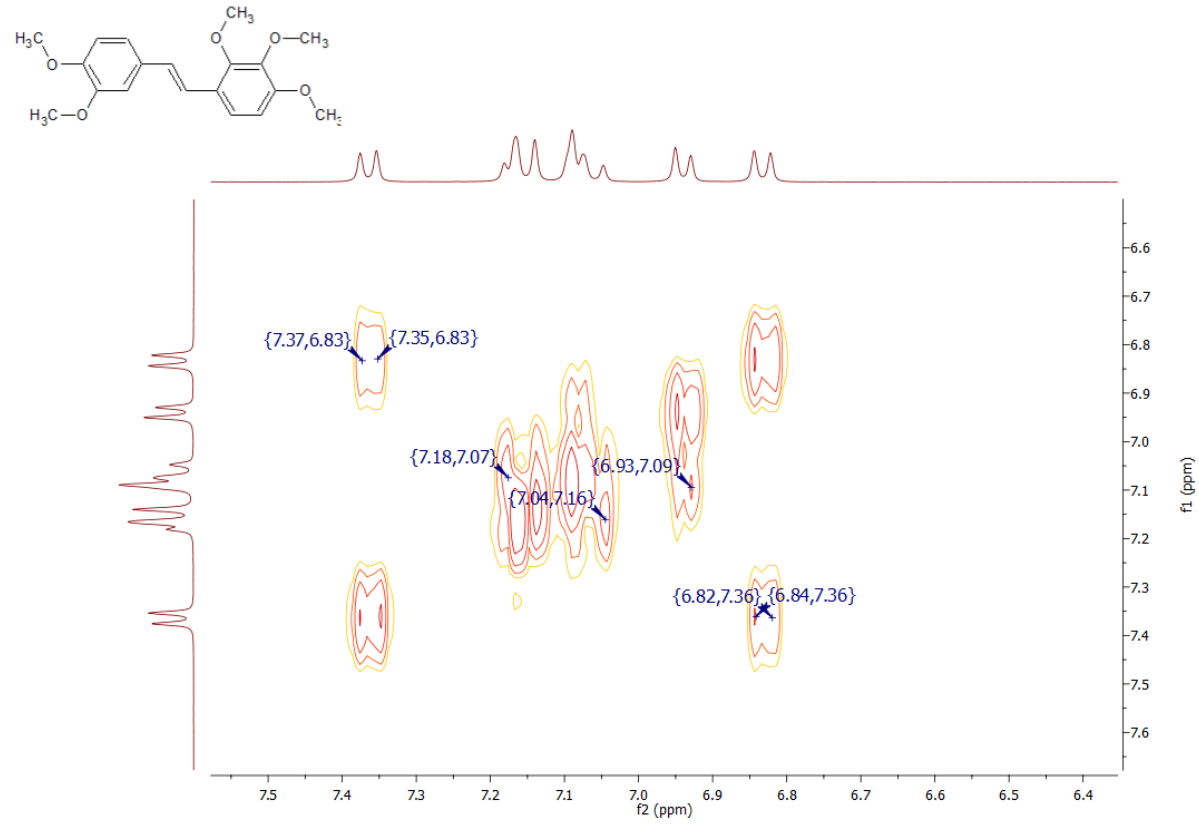
Symbol * indicates DMSO residual peaks.


153.2
151.5
149.4
149.0
142.4
131.0
128.2
124.4
121.0
121.0
119.7
112.3
109.9
108.9
f1 (ppm)

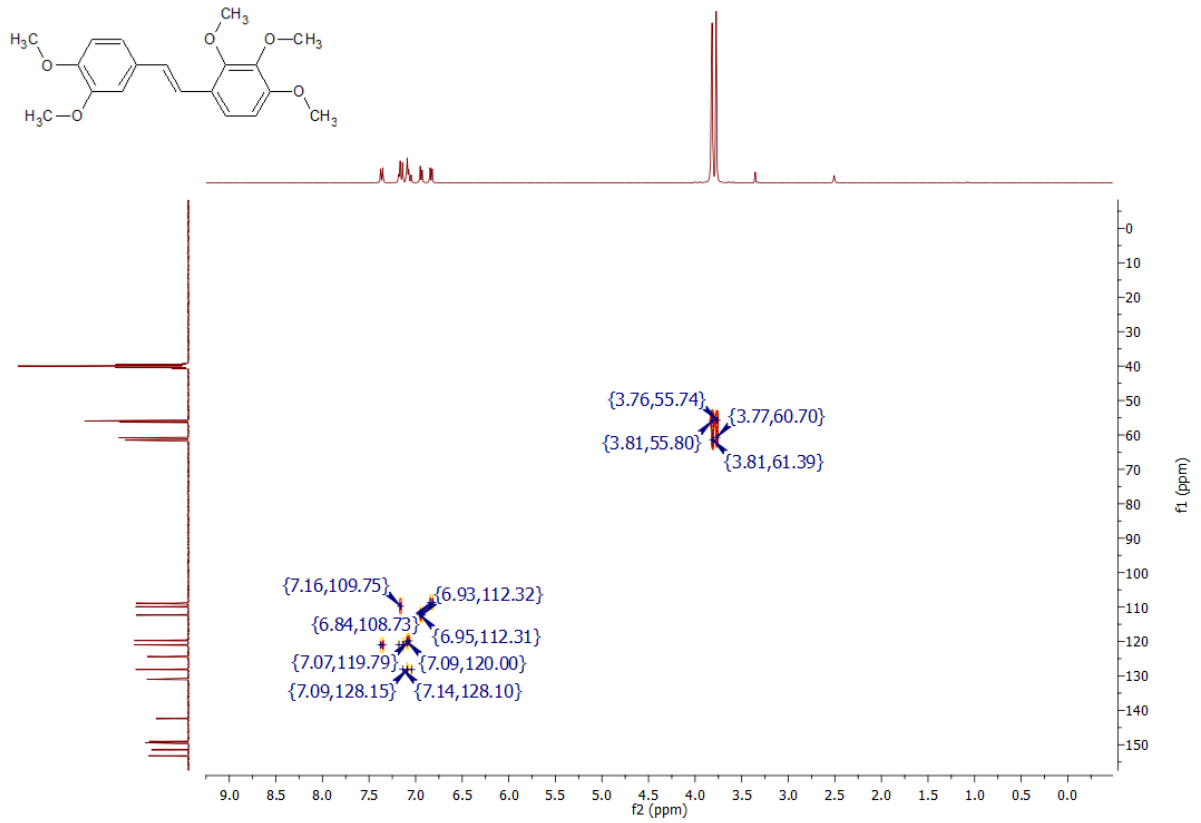

61.5
60.8
56.3
55.9
f1 (ppm)

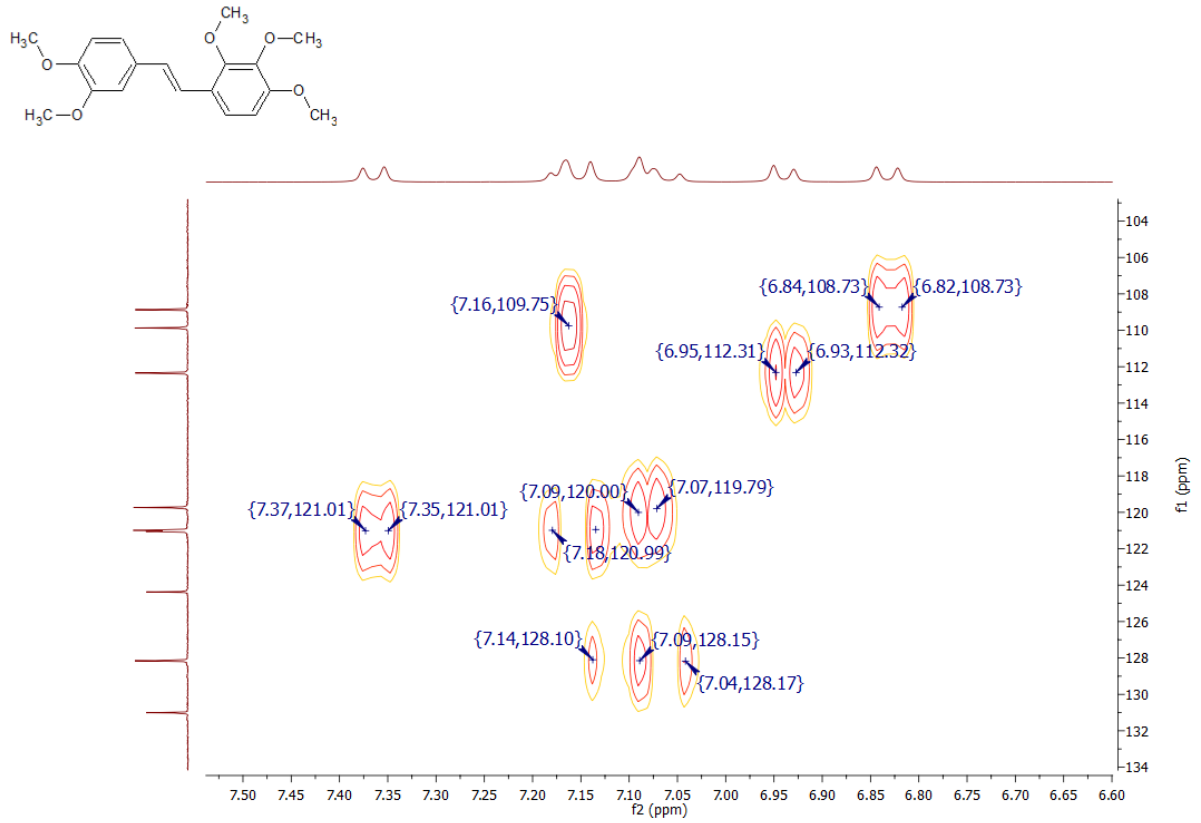
1H1H COSY

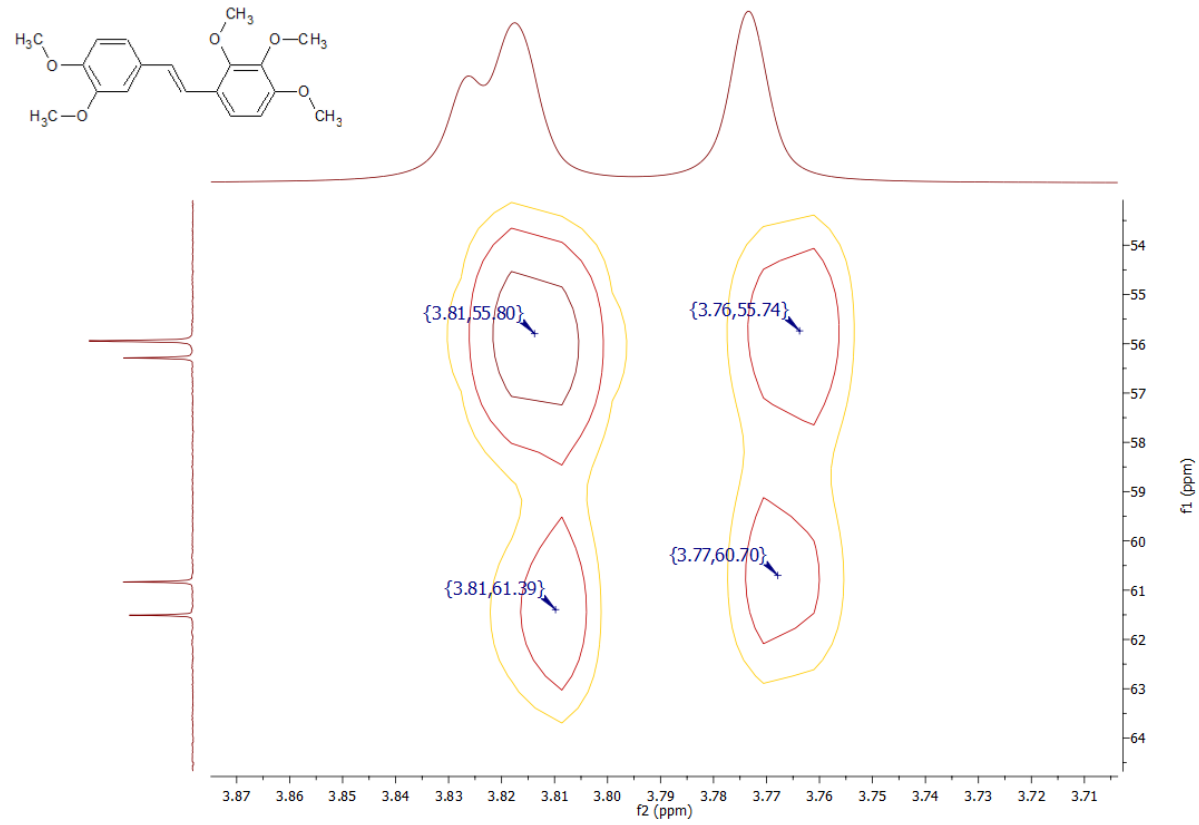

{7.37,6.83}
{7.35,6.83}
{6.93,7.09}
{6.82,7.36}
{7.18,7.07}
{6.84,7.36}
f2 (ppm)
f1 (ppm)


{7.37,6.83}
{7.35,6.83}
{7.18,7.07}
{6.93,7.09}
{7.04,7.16}
{6.82,7.36}
{6.84,7.36}
f2 (ppm)
f1 (ppm)

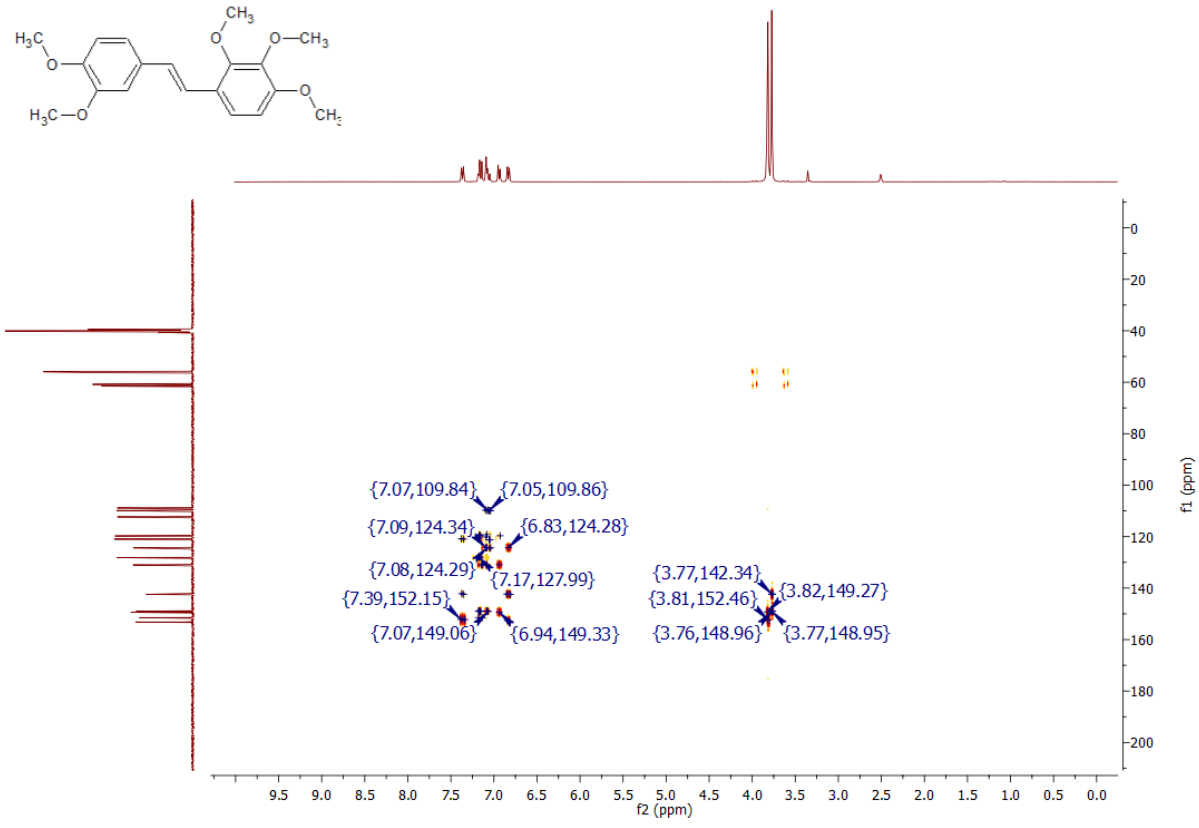
HSQC

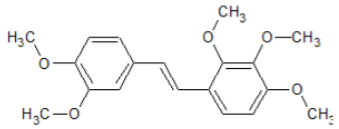

{3.76,55.74}
{3.77,60.70}
{3.81,55.80}
{3.81,61.39}
{7.16,109.75}
{6.93,112.32}
{6.84,108.73}
{6.95,112.31}
{7.07,119.79}
{7.09,120.00}
{7.09,128.15}
{7.14,128.10}
f2 (ppm)
f1 (ppm)

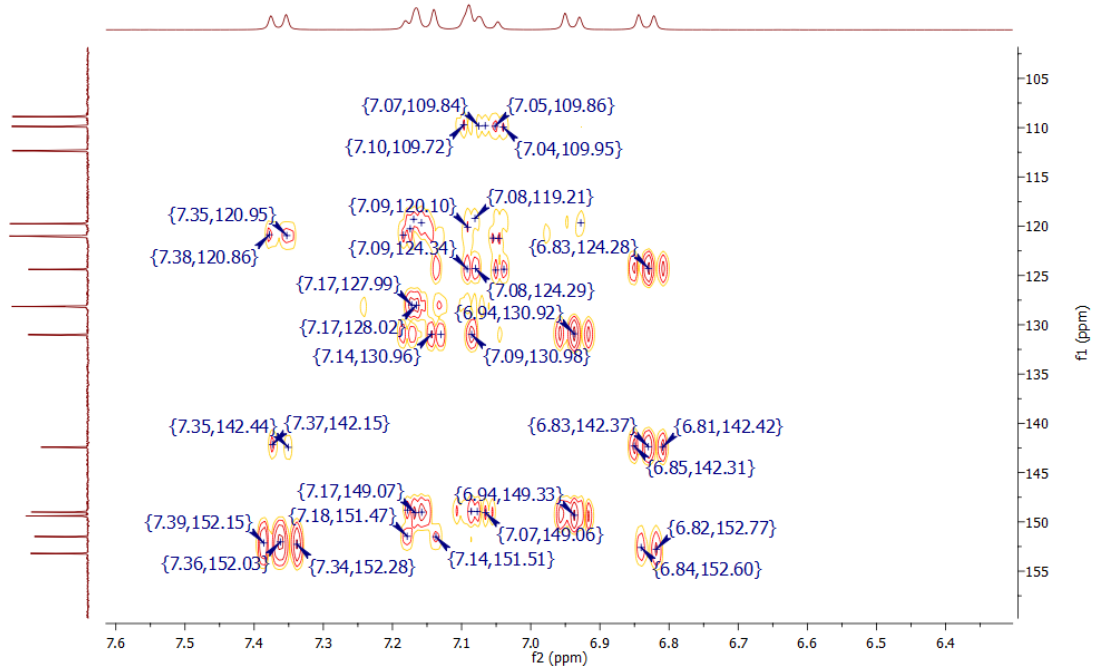

{7.16,109.75}
{6.84,108.73}
{6.82,108.73}
{6.95,112.31}
{6.93,112.32}
{7.37,121.01}
{7.35,121.01}
{7.09,120.00}
{7.07,119.79}
{7.18,120.99}
{7.14,128.10}
{7.09,128.15}
{7.04,128.17}
f2 (ppm)
f1 (ppm)

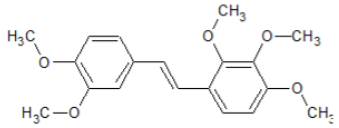

{3.81,55.80}
{3.76,55.74}
{3.77,60.70}
{3.81,61.39}
f2 (ppm)
f1 (ppm)

HMBC


{7.07,109.84}
{7.05,109.86}
{7.09,124.34}
{6.83,124.28}
{7.08,124.29}
{7.17,127.99}
{7.39,152.15}
{7.07,149.06}
{6.94,149.33}
{3.77,142.34}
{3.82,149.27}
{3.81,152.46}
{3.76,148.96}
{3.77,148.95}
f2 (ppm)
f1 (ppm)

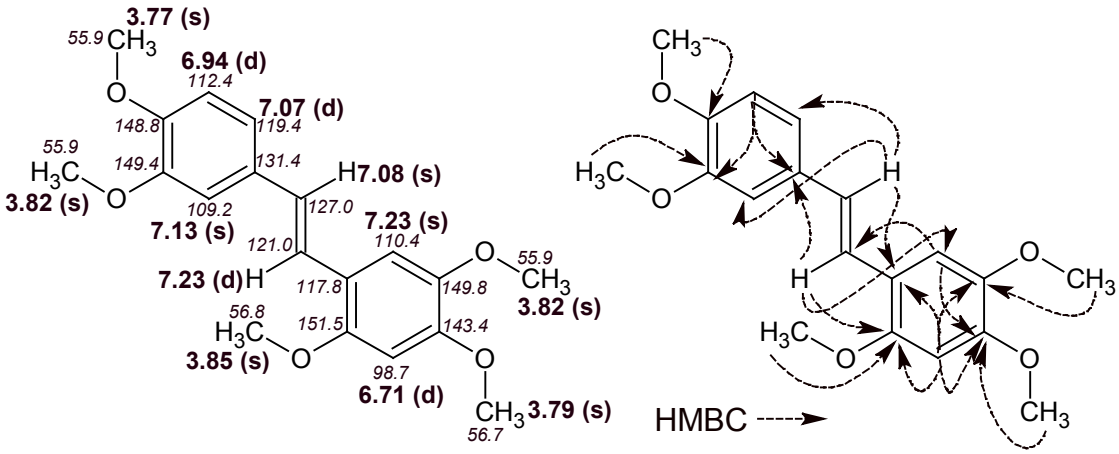



{7.07,109.84}
{7.05,109.86}
{7.10,109.72}
{7.04,109.95}
{7.35,120.95}
{7.09,120.10}
{7.08,119.21}
{7.38,120.86}
{7.09,124.34}
{6.83,124.28}
{7.17,127.99}
{7.08,124.29}
{6.94,130.92}
{7.17,128.02}
{7.14,130.96}
{7.09,130.98}
{7.35,142.44}
{7.37,142.15}
{6.83,142.37}
{6.81,142.42}
{6.85,142.31}
{7.17,149.07}
{6.94,149.33}
{7.39,152.15}
{7.18,151.47}
{7.07,149.06}
{6.82,152.77}
{7.36,152.03}
{7.34,152.28}
{7.14,151.51}
{6.84,152.60}
f1 (ppm)
f2 (ppm)



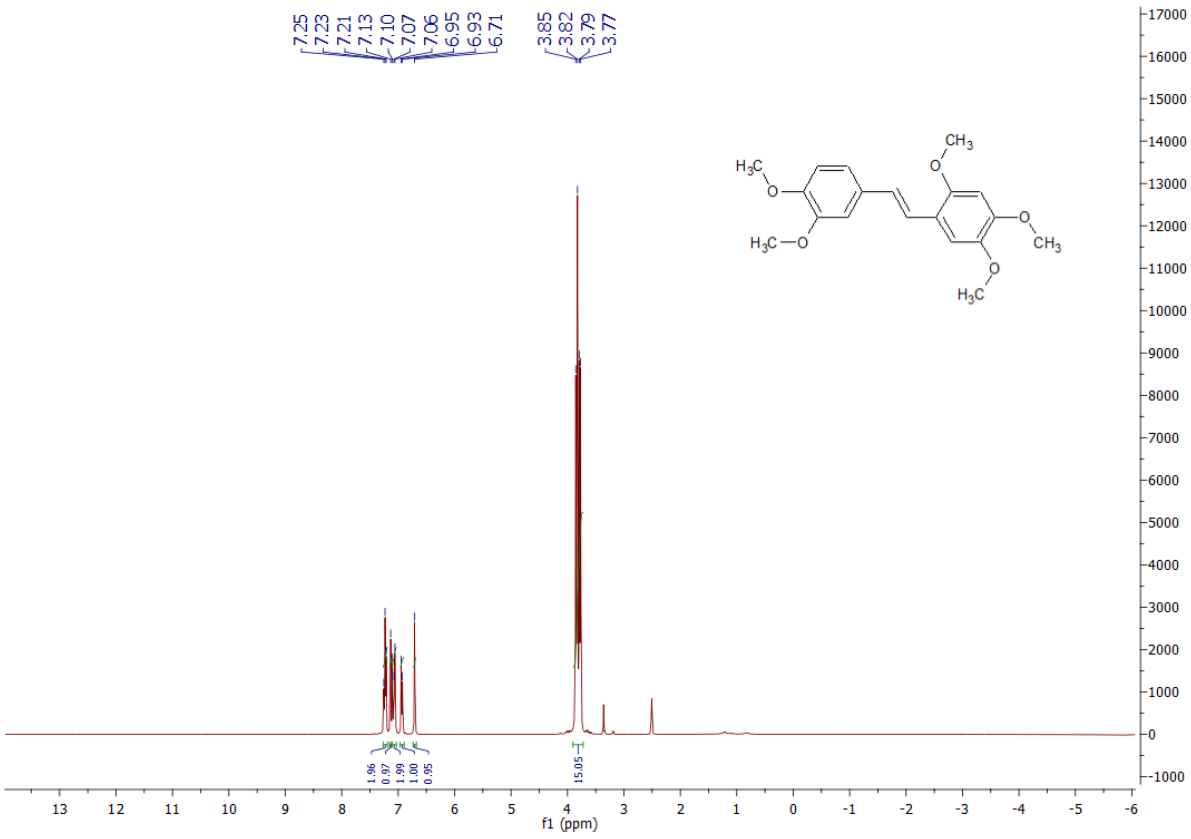
{3.77,142.34}
{3.77,142.32}
{3.82,149.27}
{3.77,148.95}
{3.76,148.96}
{3.81,152.46}
f1 (ppm)
f2 (ppm)

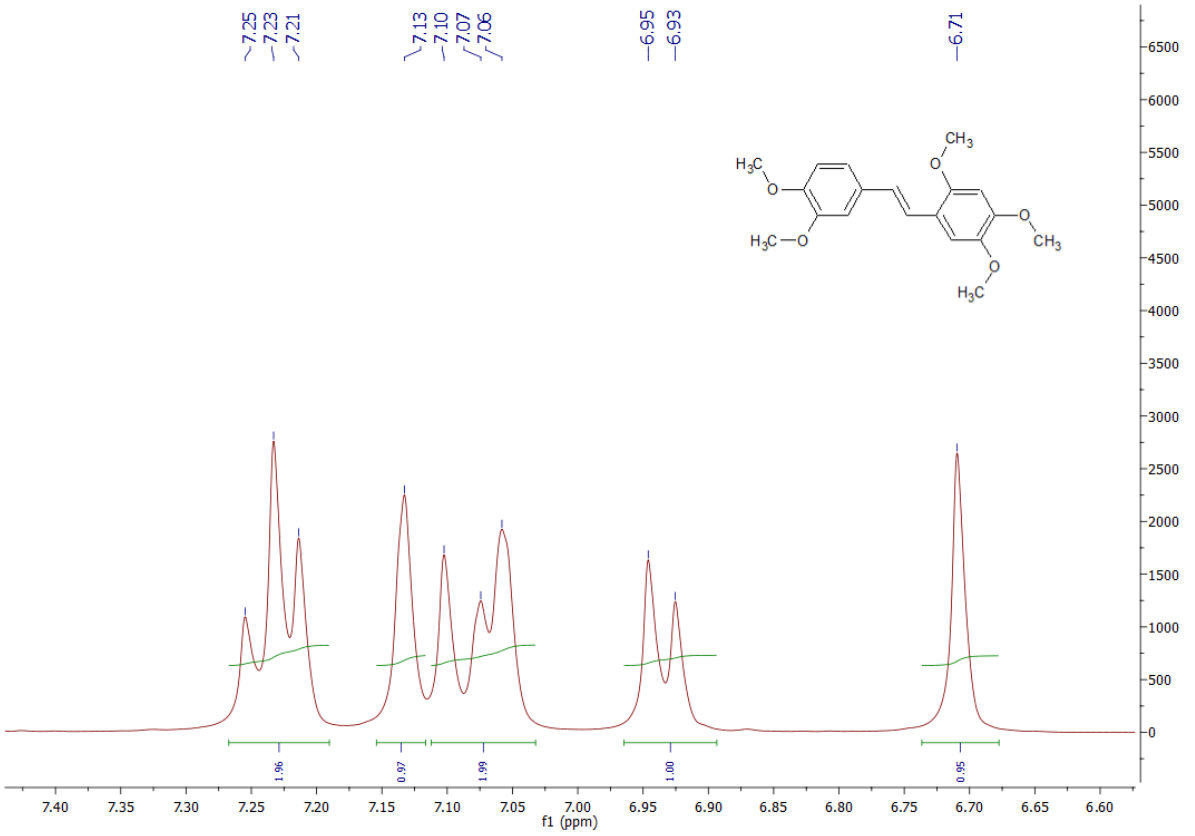
6.8 NMR data for 3,4,2',4',5'-pentamethoxy-trans-stilbene (5h)

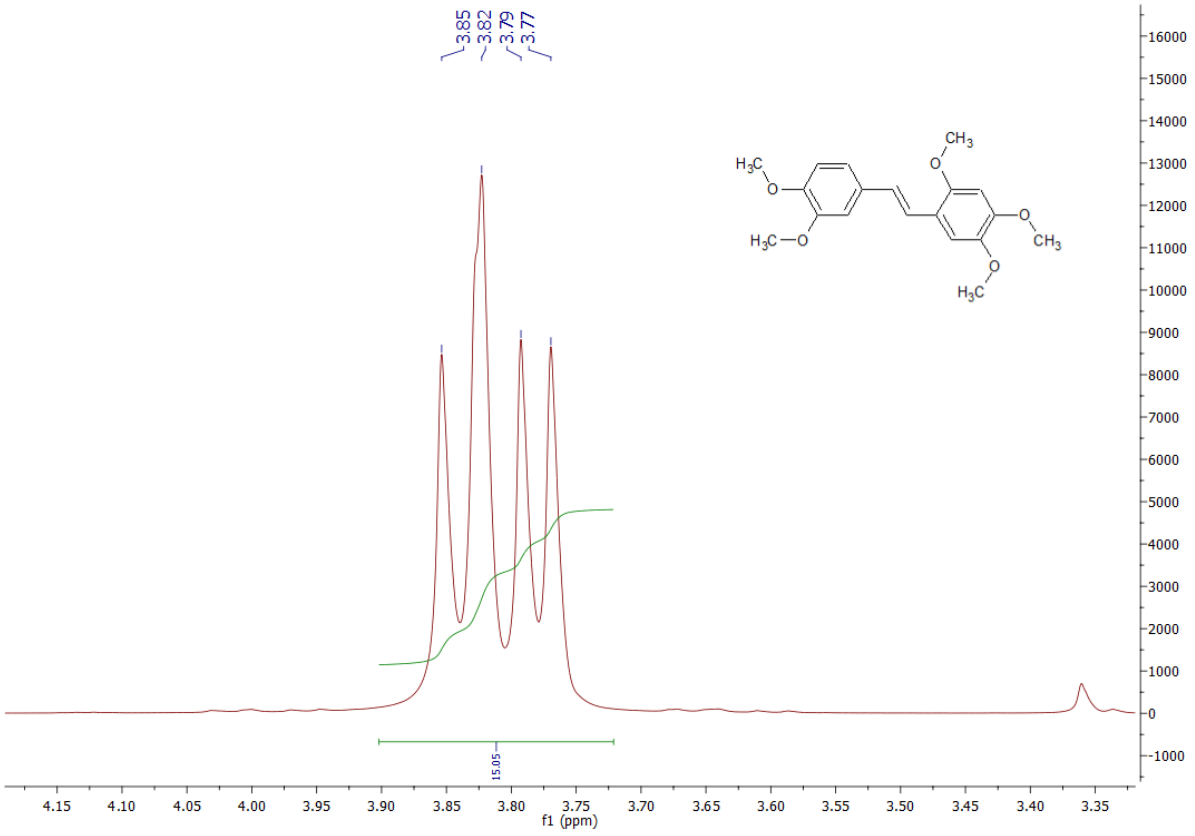


Scheme X8 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

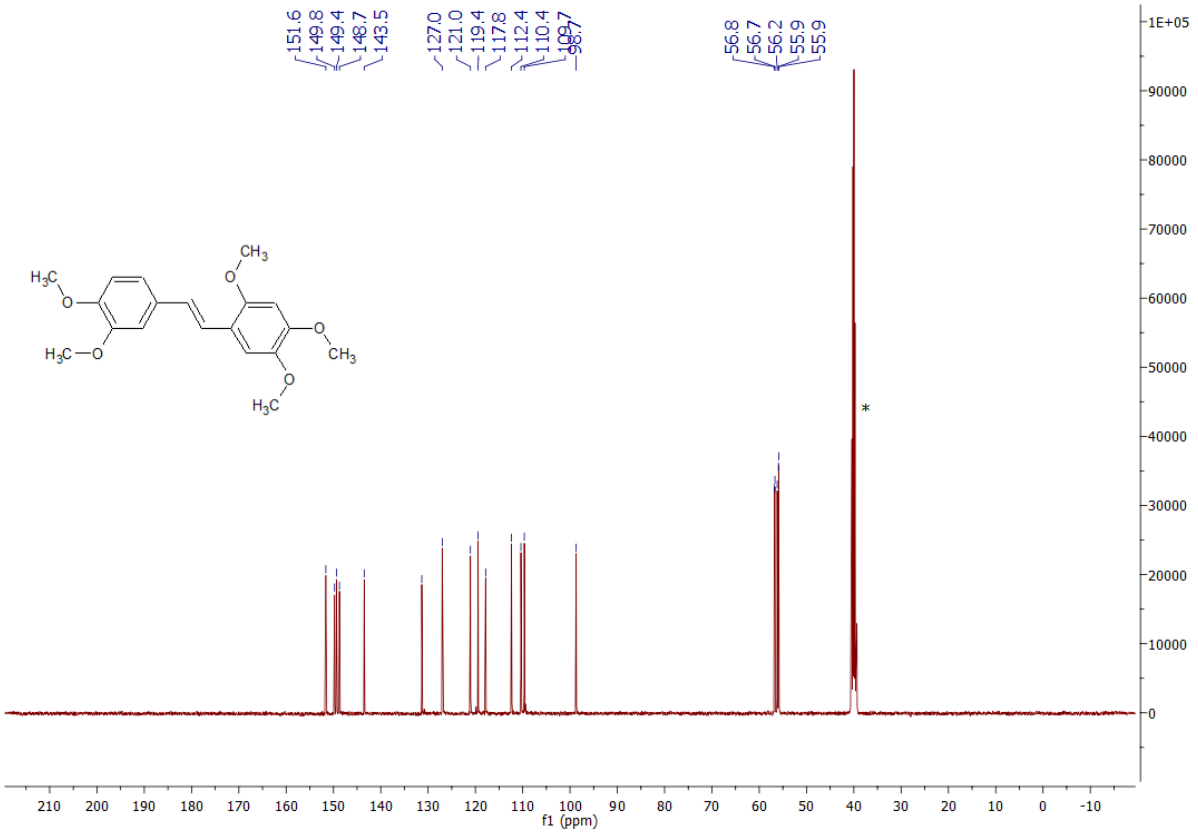
1H



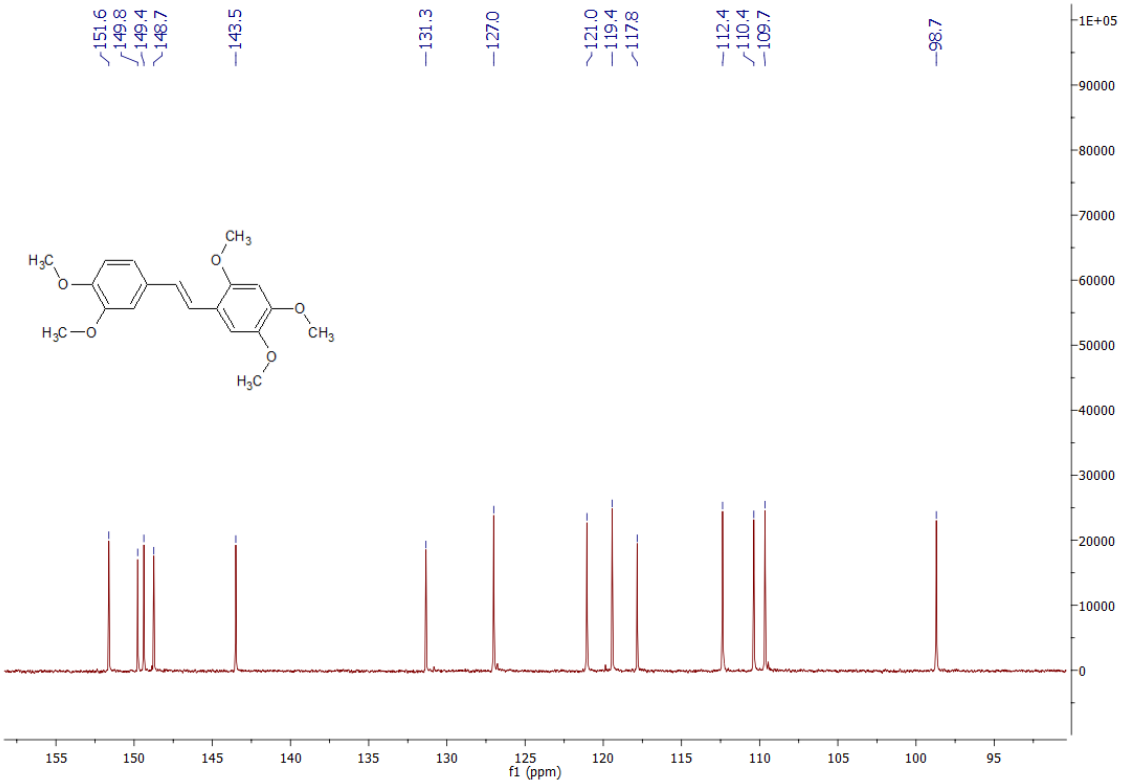

7.25
7.23
7.21
7.13
7.10
7.07
7.06
6.95
6.93
6.71
1.96
0.97
1.99
1.00
0.95
f1 (ppm)

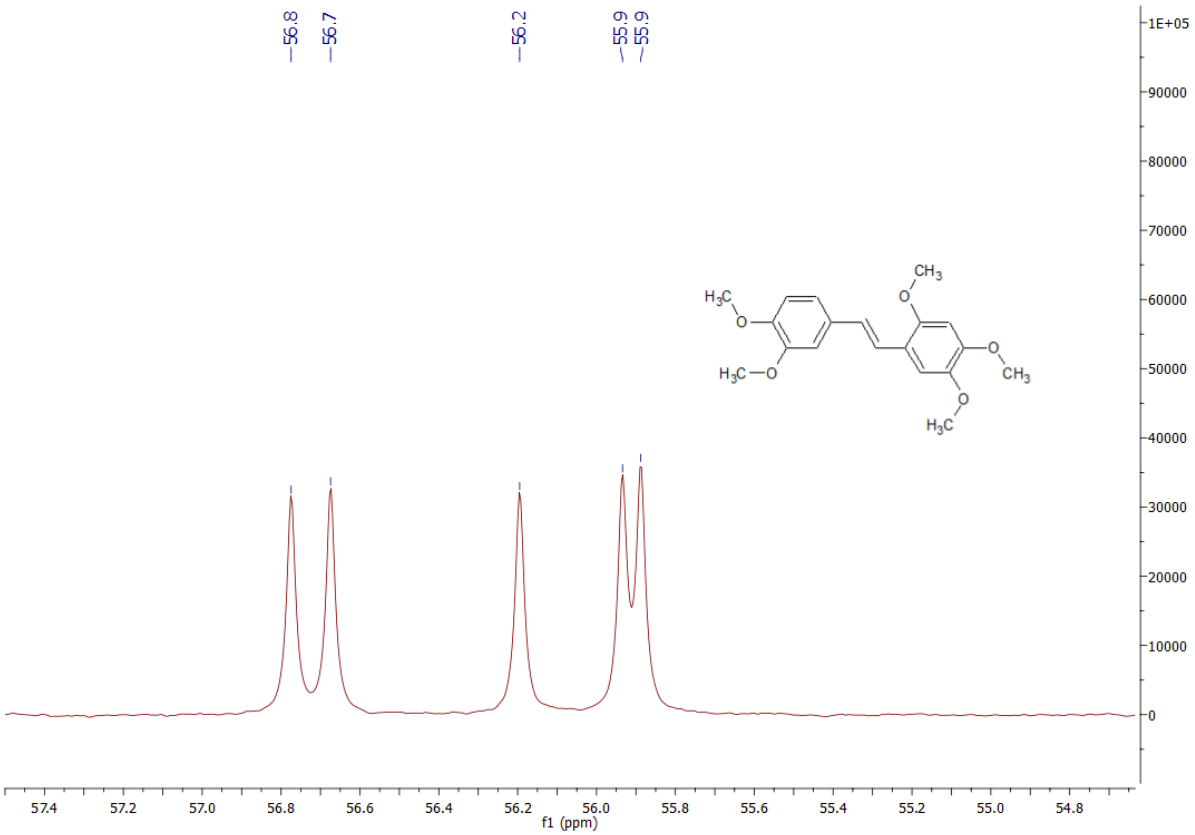

3.85
3.82
3.79
3.77
15.05
f1 (ppm)

13

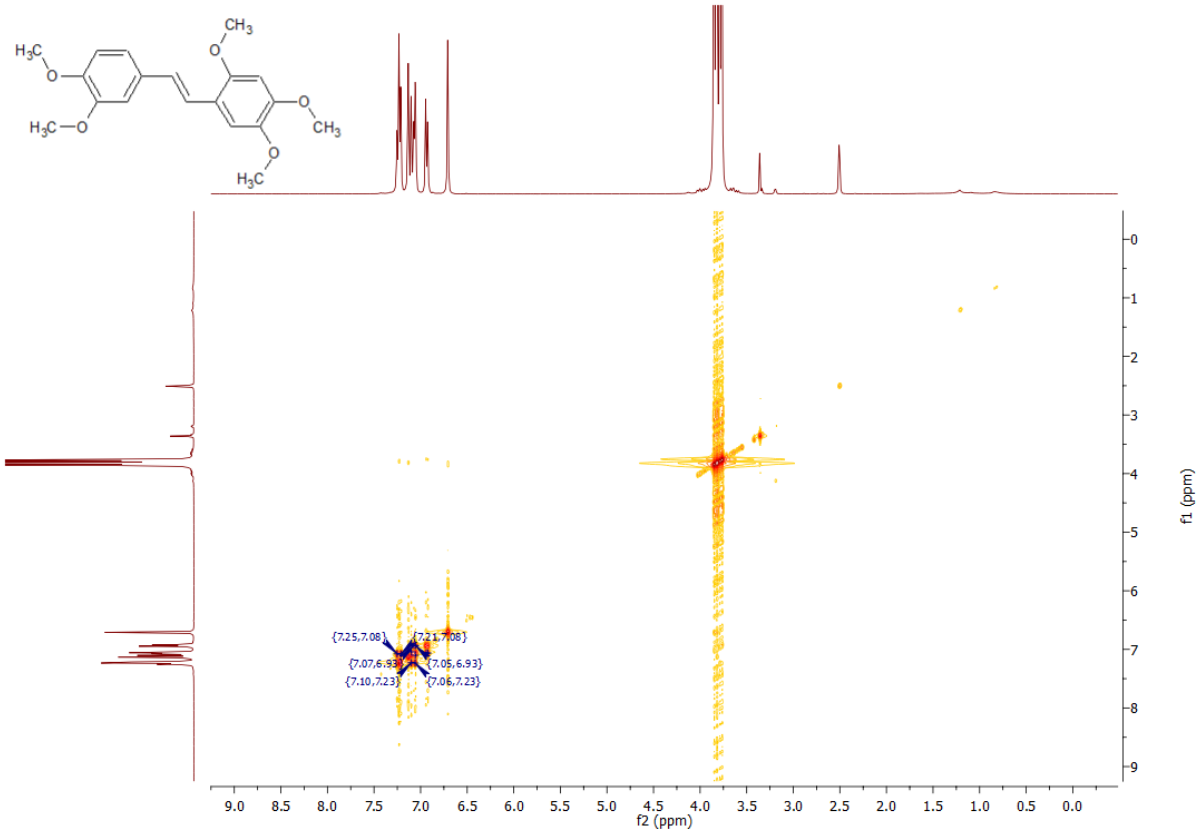


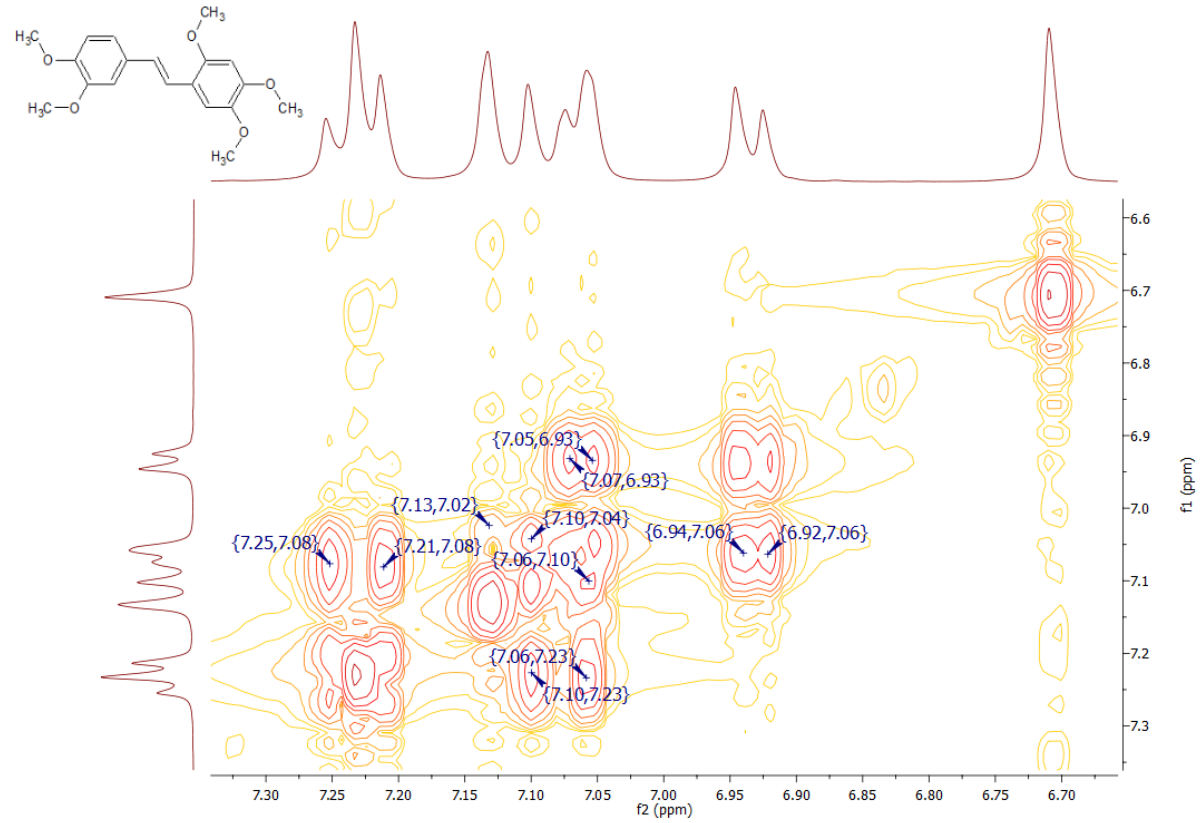
Symbol * indicates DMSO residual peaks.


151.6
149.8
149.4
148.7
143.5
131.3
127.0
121.0
119.4
117.8
112.4
110.4
109.7
98.7
f1 (ppm)

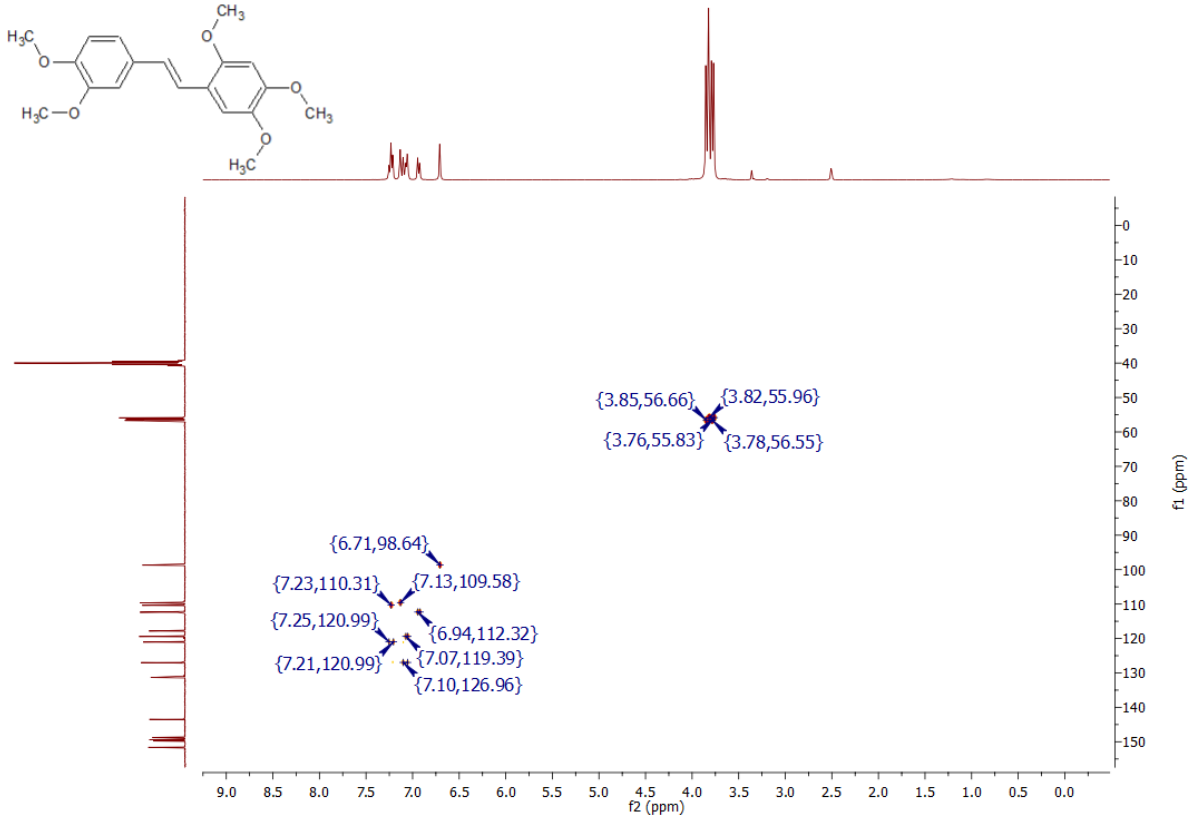

56.8
56.7
56.2
55.9
55.9
f1 (ppm)

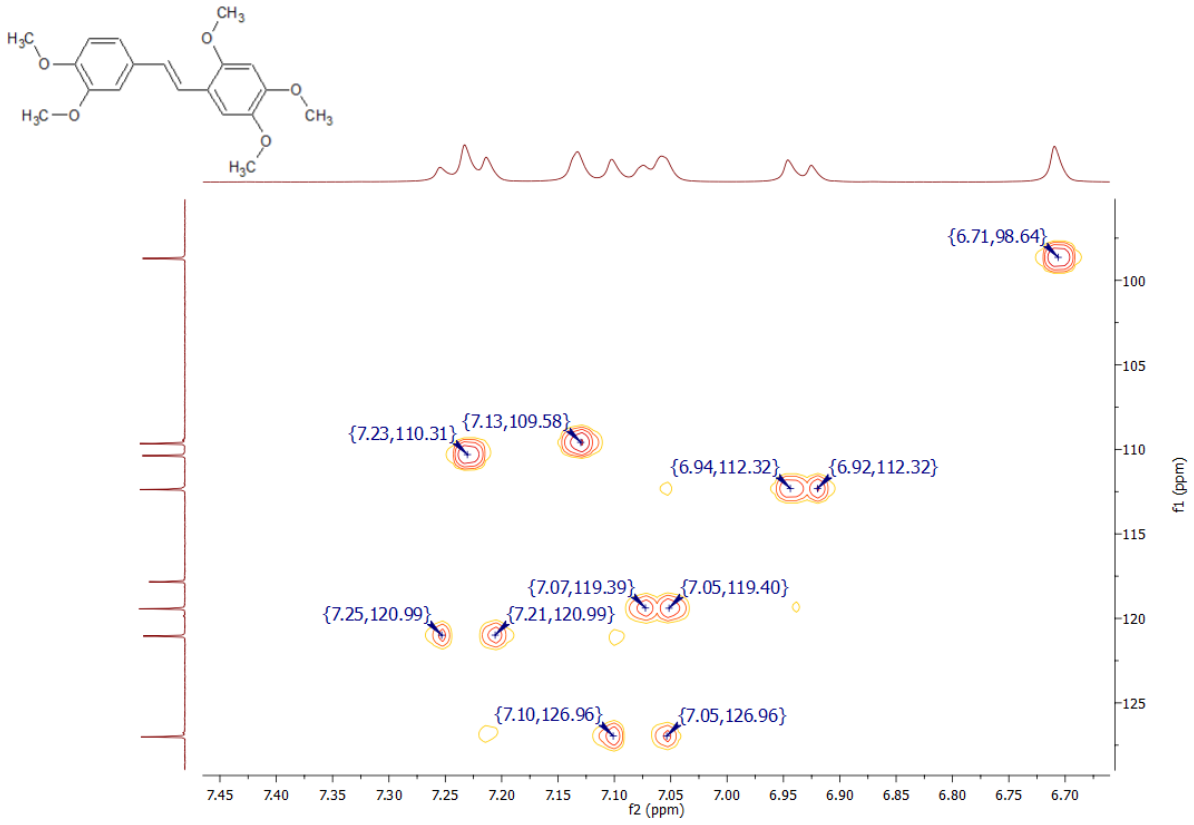
1H1HCOSY

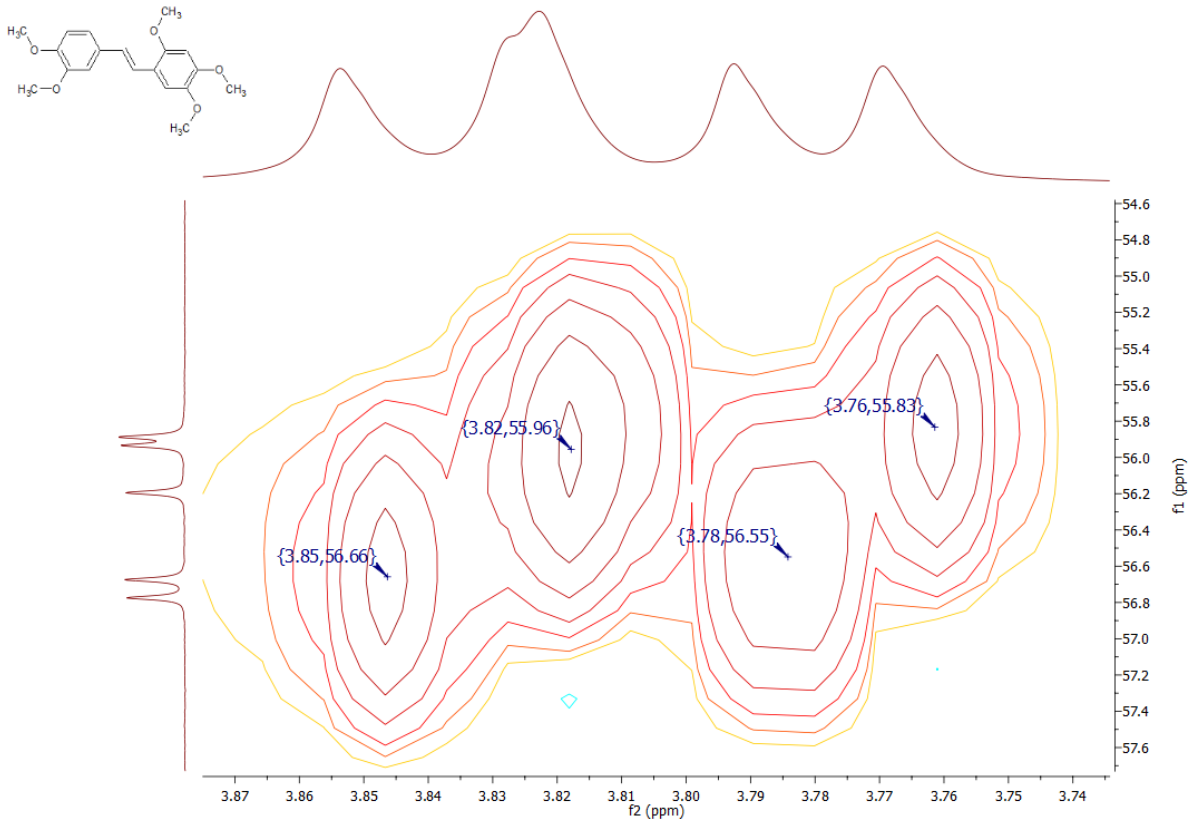

{7.25,7.08}
{7.21,7.08}
{7.07,6.93}
{7.05,6.93}
{7.10,7.23}
{7.06,7.23}
f2 (ppm)
f1 (ppm)


{7.05,6.93}
{7.07,6.93}
{7.13,7.02}
{7.10,7.04}
{6.94,7.06}
{6.92,7.06}
{7.25,7.08}
{7.21,7.08}
{7.06,7.10}
{7.06,7.23}
{7.10,7.23}
f2 (ppm)
f1 (ppm)

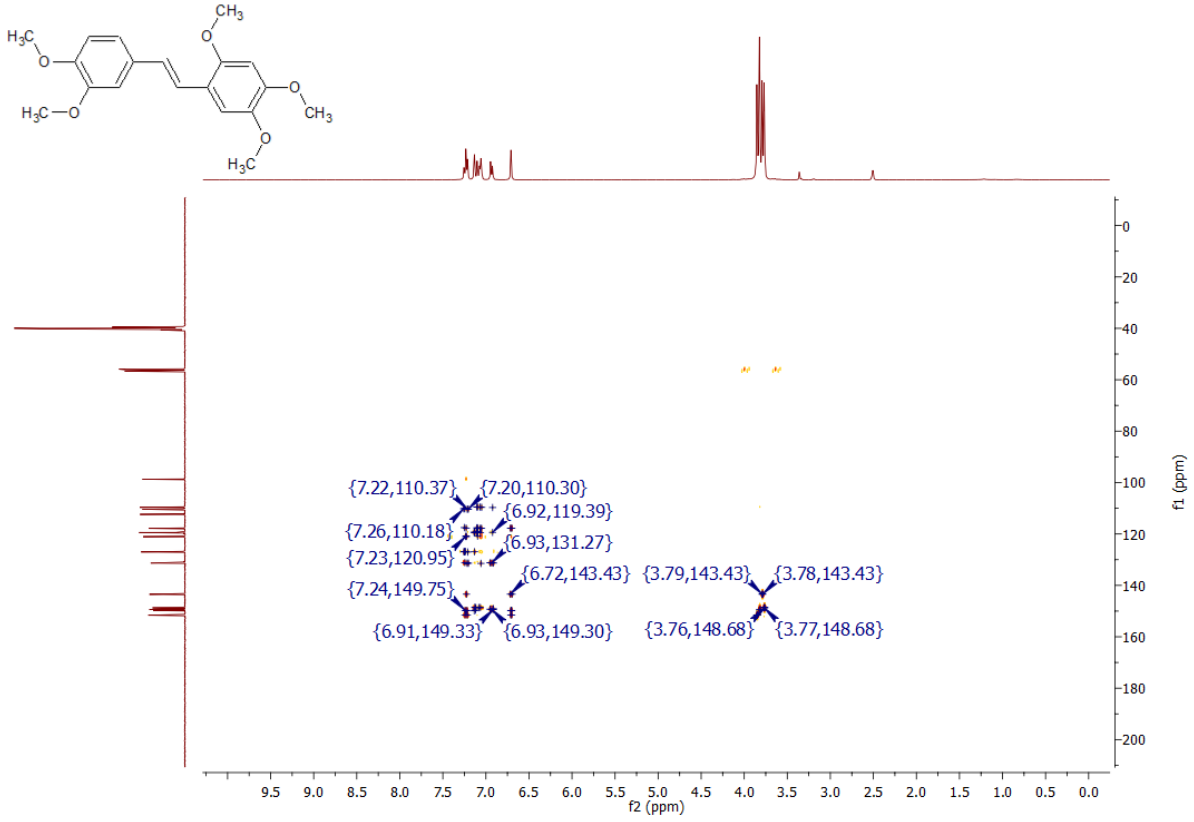
HSQC

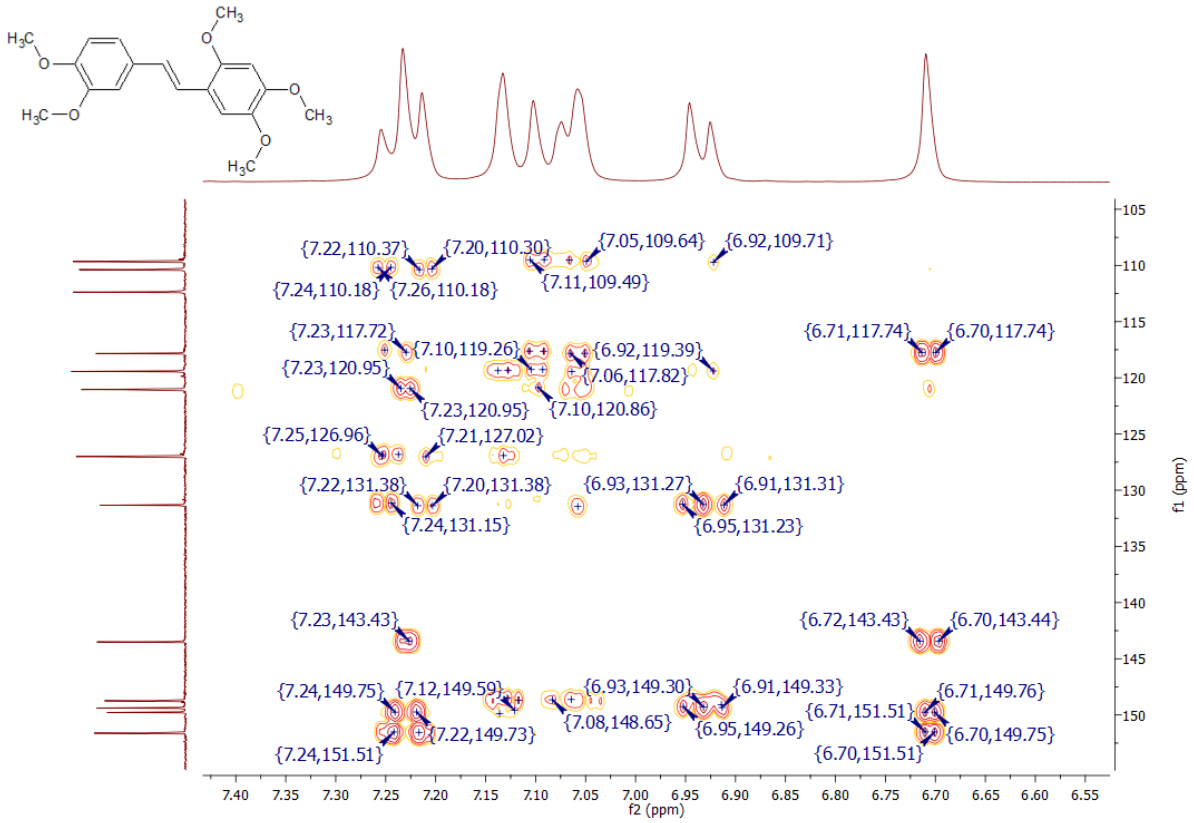

{3.85,56.66}
{3.82,55.96}
{3.76,55.83}
{3.78,56.55}
{6.71,98.64}
{7.23,110.31}
{7.13,109.58}
{7.25,120.99}
{6.94,112.32}
{7.21,120.99}
{7.07,119.39}
{7.10,126.96}
f1 (ppm)
f2 (ppm)

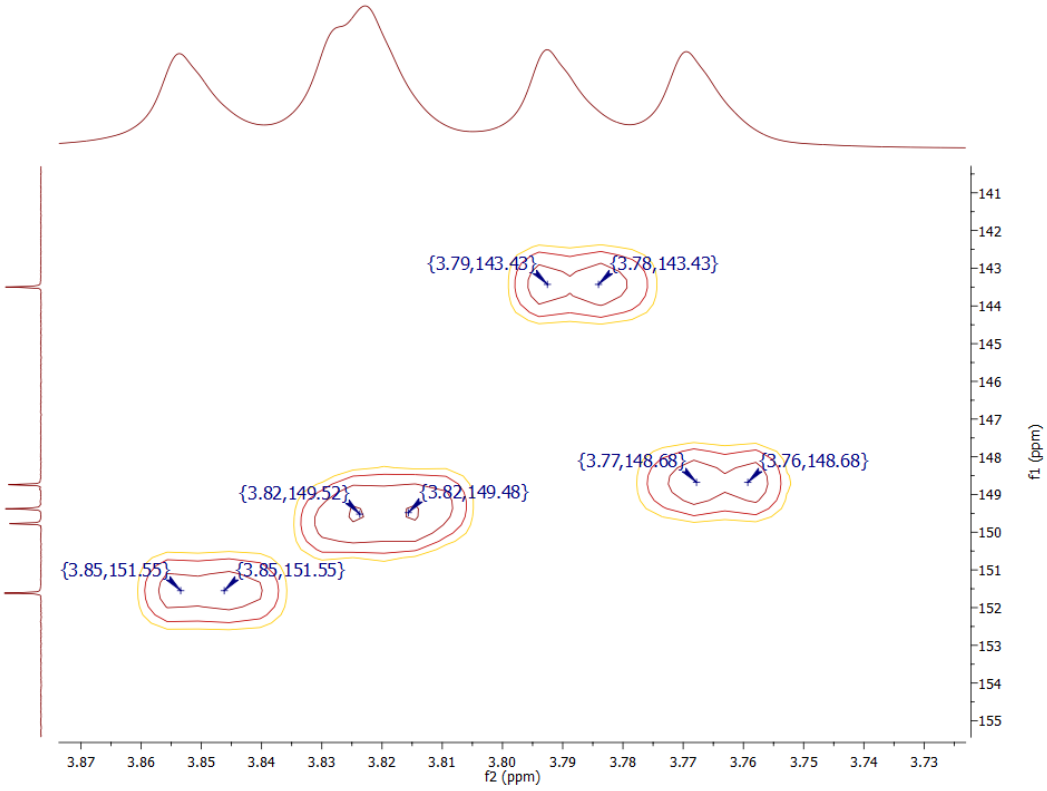

{6.71,98.64}
{7.23,110.31}
{7.13,109.58}
{6.94,112.32}
{6.92,112.32}
{7.07,119.39}
{7.05,119.40}
{7.25,120.99}
{7.21,120.99}
{7.10,126.96}
{7.05,126.96}
f1 (ppm)
f2 (ppm)


{3.82,55.96}
{3.76,55.83}
{3.85,56.66}
{3.78,56.55}
f1 (ppm)
f2 (ppm)

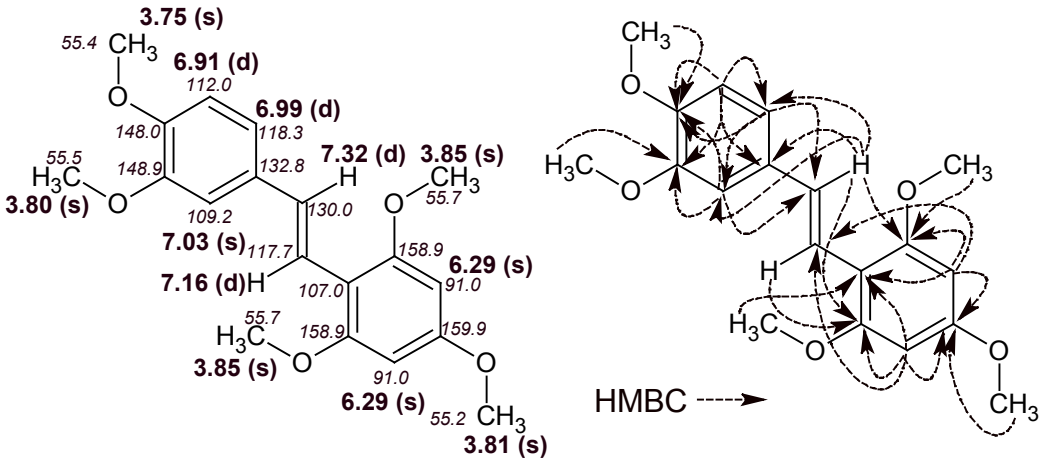
HMBC


{7.22,110.37}
{7.20,110.30}
{6.92,119.39}
{7.26,110.18}
{6.93,131.27}
{7.23,120.95}
{6.72,143.43}
{3.79,143.43}
{3.78,143.43}
{7.24,149.75}
{6.91,149.33}
{6.93,149.30}
{3.76,148.68}
{3.77,148.68}
f2 (ppm)
f1 (ppm)


{7.22,110.37}
{7.20,110.30}
{7.05,109.64}
{6.92,109.71}
{7.24,110.18}
{7.26,110.18}
{7.11,109.49}
{7.23,117.72}
{7.10,119.26}
{6.92,119.39}
{6.71,117.74}
{6.70,117.74}
{7.23,120.95}
{7.06,117.82}
{7.23,120.95}
{7.10,120.86}
{7.25,126.96}
{7.21,127.02}
{7.22,131.38}
{7.20,131.38}
{6.93,131.27}
{6.91,131.31}
{7.24,131.15}
{6.95,131.23}
{7.23,143.43}
{6.72,143.43}
{6.70,143.44}
{7.24,149.75}
{7.12,149.59}
{6.93,149.30}
{6.91,149.33}
{6.71,149.76}
{6.71,151.51}
{7.08,148.65}
{7.22,149.73}
{6.95,149.26}
{6.70,149.75}
{7.24,151.51}
{6.70,151.51}
f2 (ppm)
f1 (ppm)

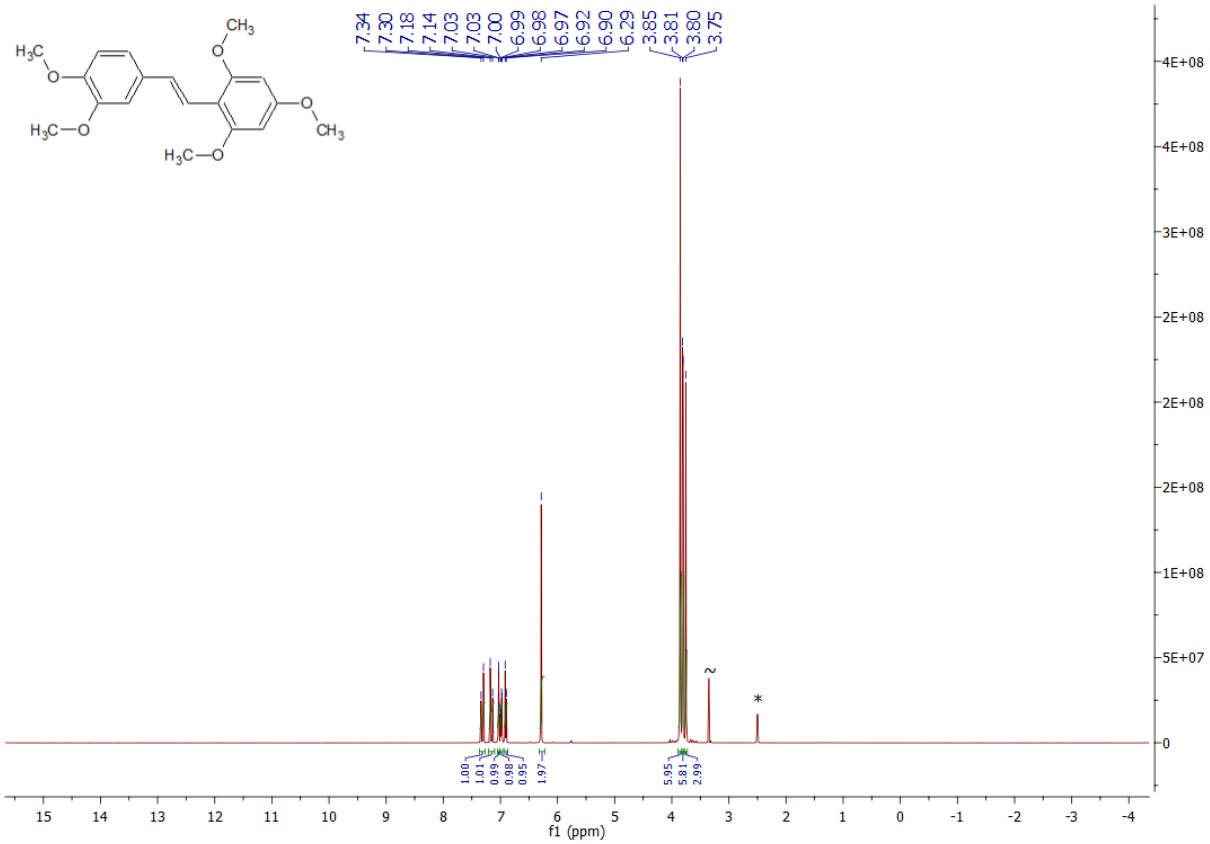

{3.79,143.43}
{3.78,143.43}
{3.77,148.68}
{3.76,148.68}
{3.82,149.52}
{3.82,149.48}
{3.85,151.55}
{3.85,151.55}
f1 (ppm)
f2 (ppm)

6.9 NMR data for 3,4,2',4',6'-pentamethoxy-trans-stilbene (5i)

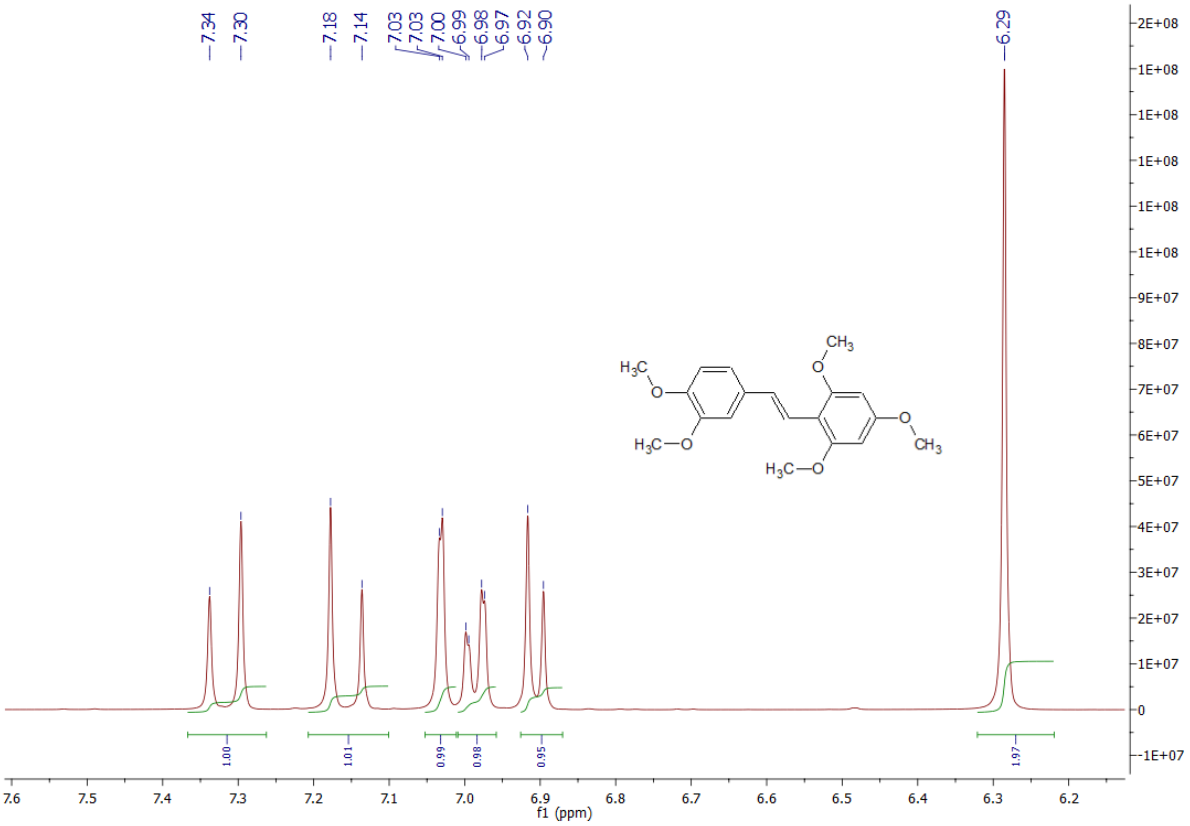


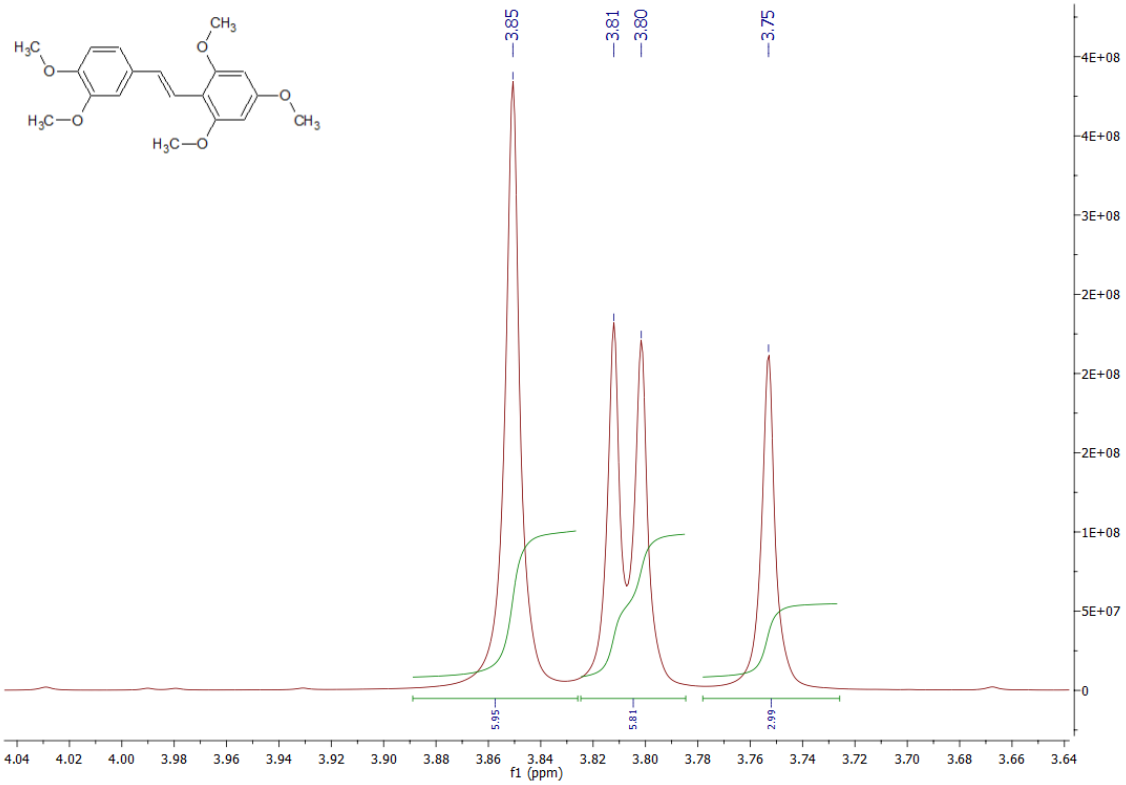
Scheme X9 Annotated signals ^{1}H and ^{13}C NMR spectra according to 2D experiments (^{1}H-^{1}H COSY, HSQC and HMBC).

1H

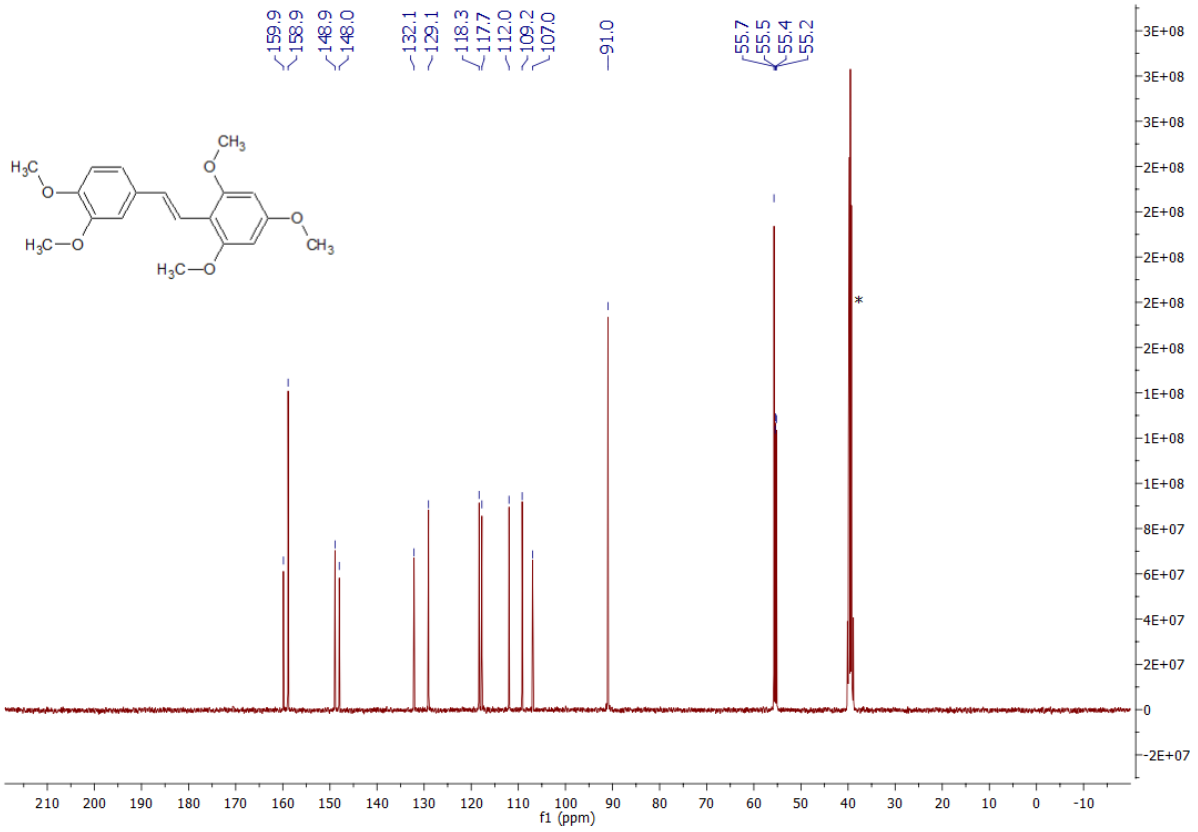


Symbol * and ~ indicates DMSO and water residuals peaks.

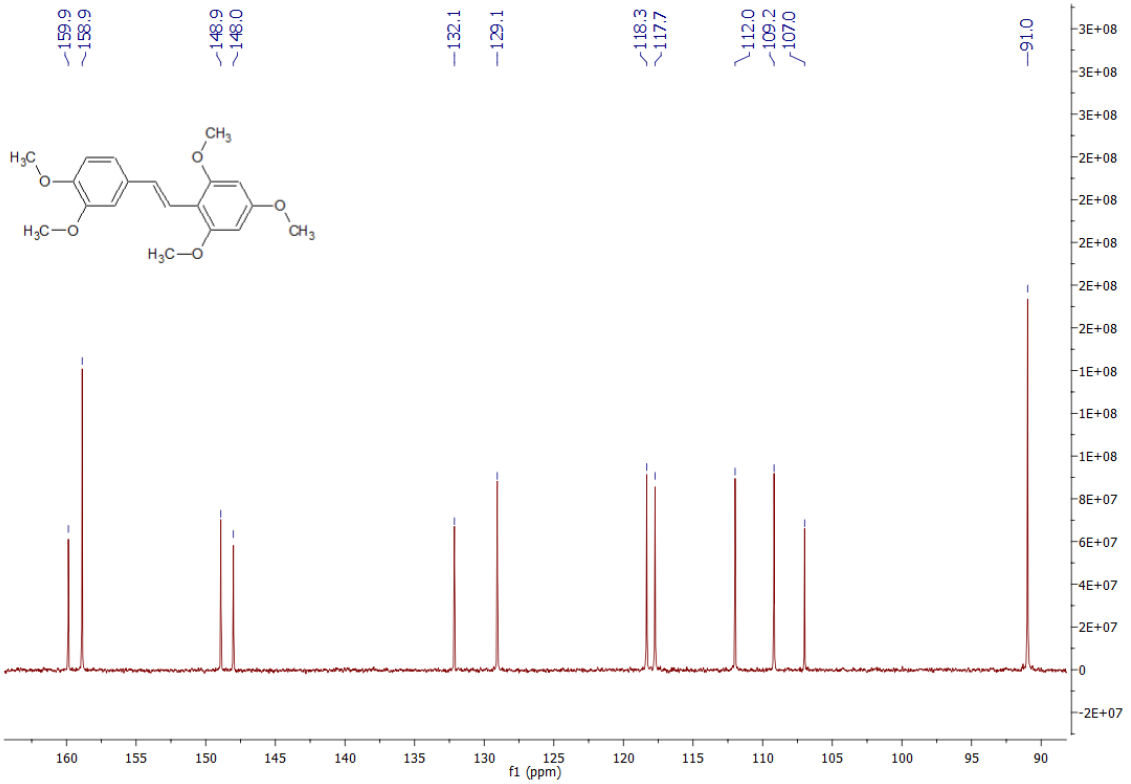


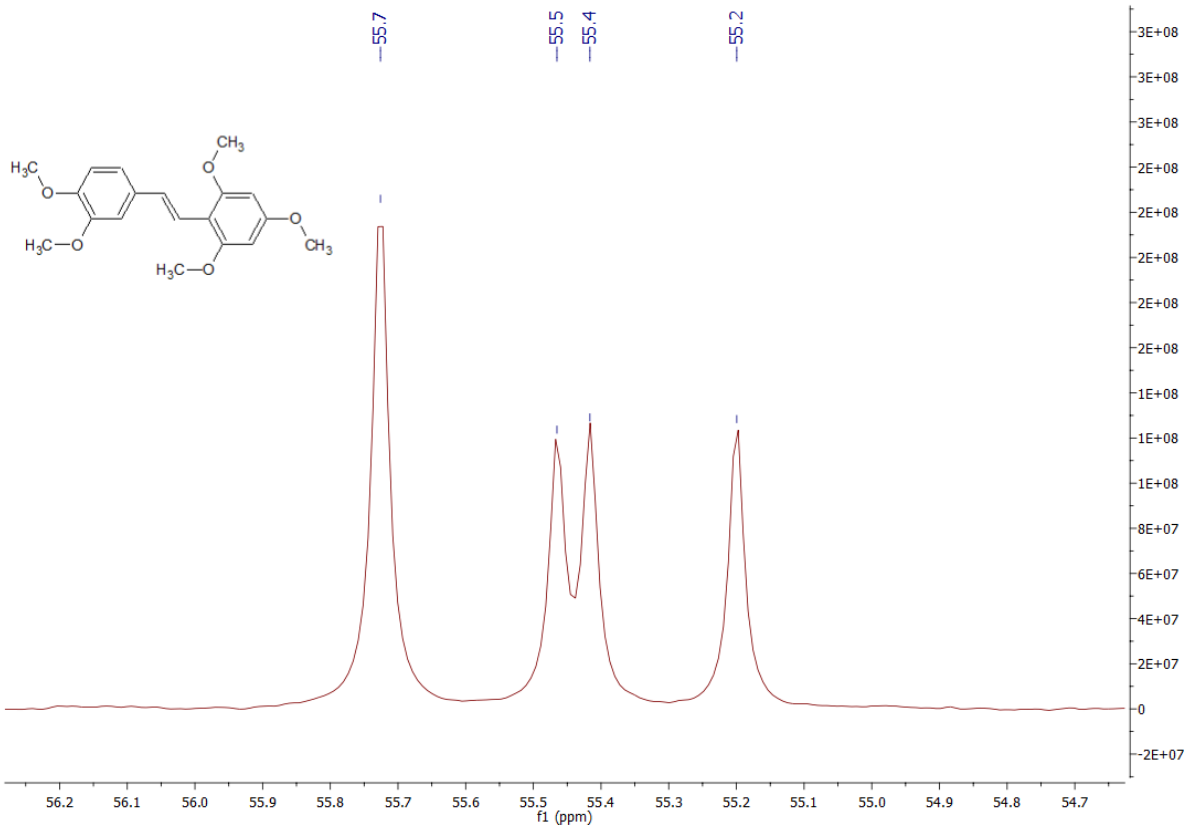


13C

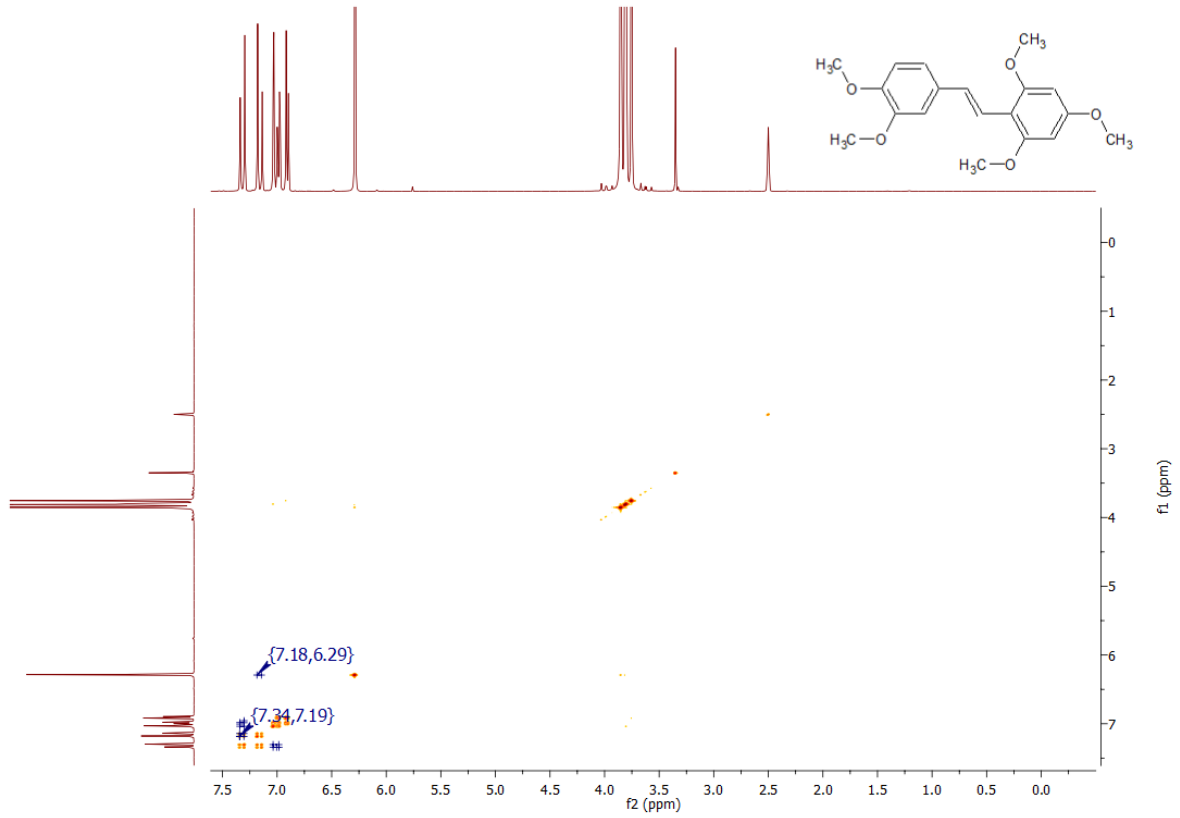


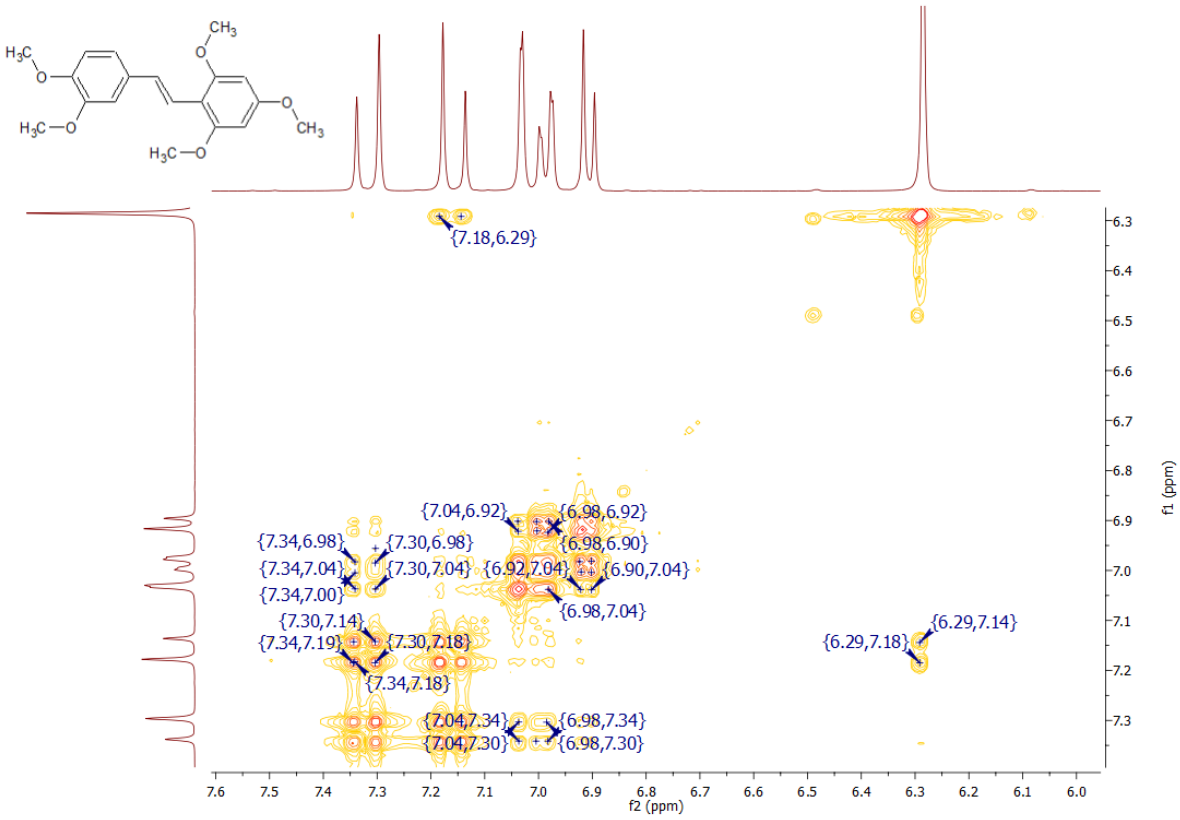
Symbol * indicates DMSO residual peaks.


159.9
153.9
148.9
148.0
132.1
129.1
118.3
117.7
112.0
109.2
107.0
91.0
f1 (ppm)

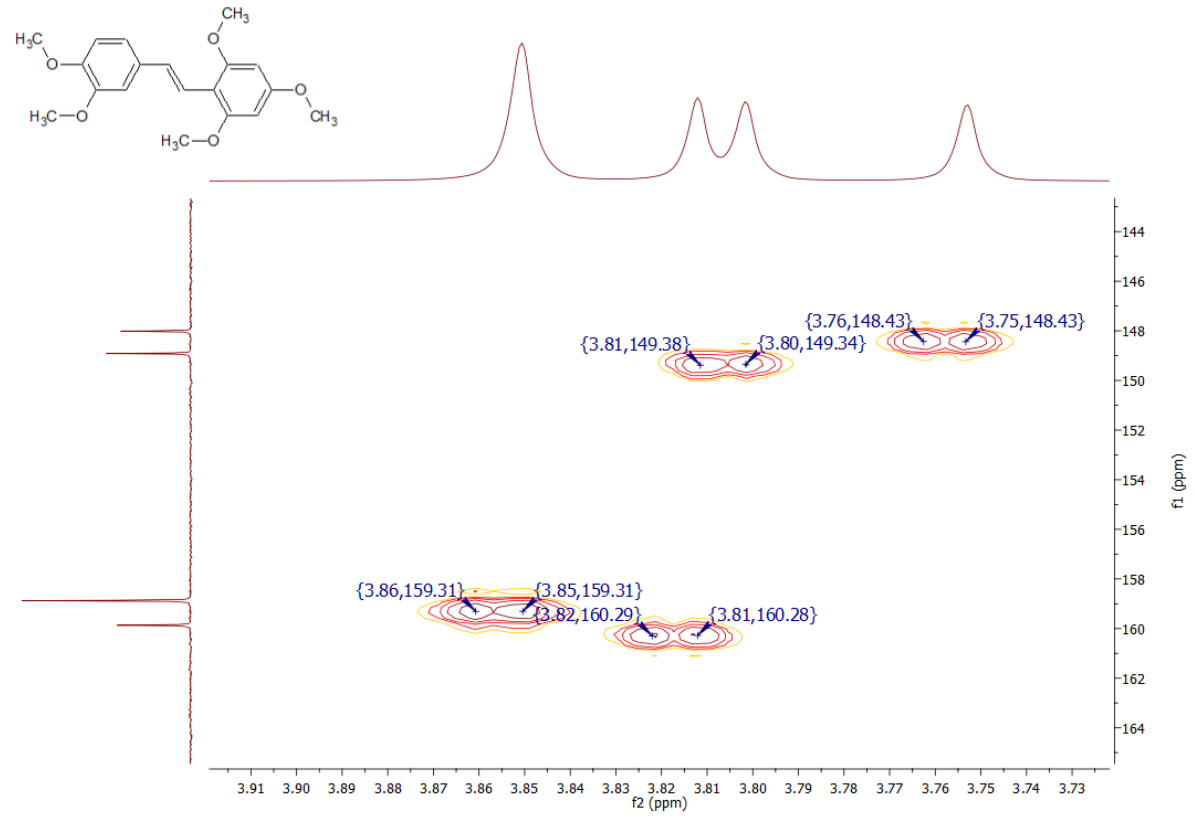

55.7
55.5
55.4
55.2
f1 (ppm)

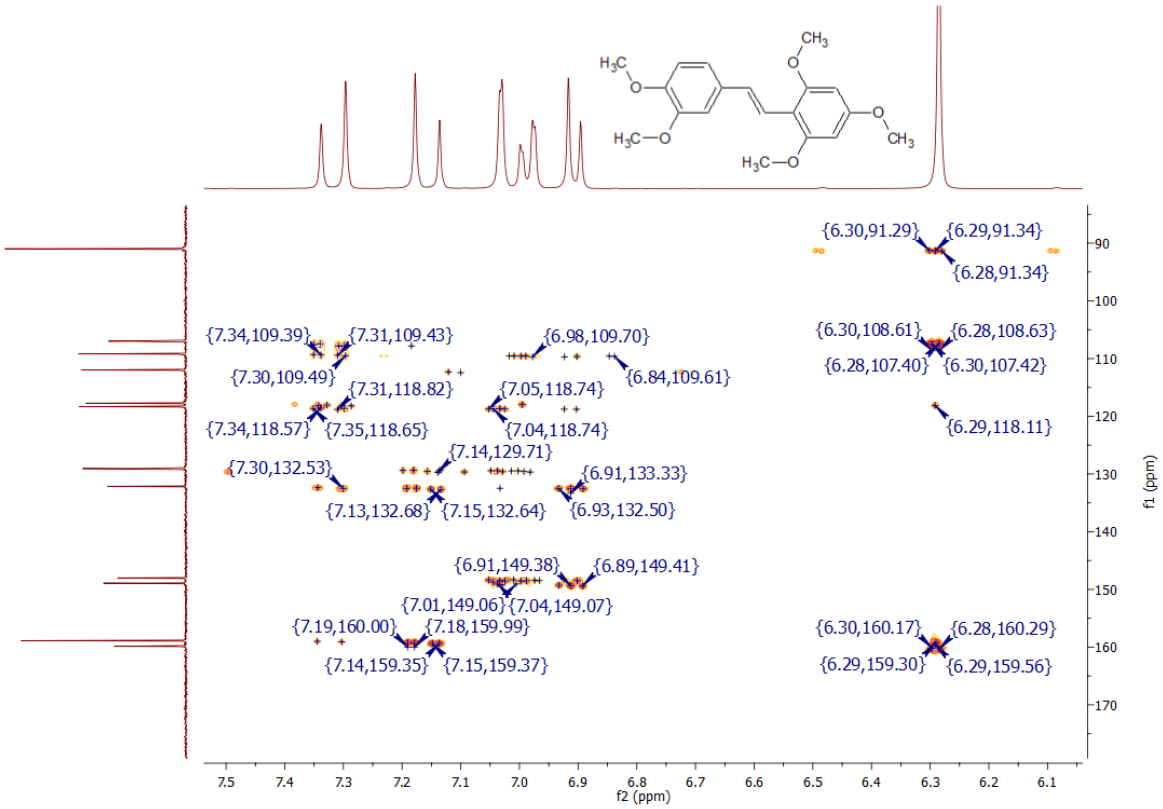
1H1H COSY


{7.18,6.29}
{7.34,7.19}
f2 (ppm)
f1 (ppm)


{7.18,6.29}
{7.04,6.92}
{6.98,6.92}
{7.34,6.98}
{7.30,6.98}
{6.98,6.90}
{7.34,7.04}
{7.30,7.04}
{6.92,7.04}
{6.90,7.04}
{7.34,7.00}
{6.98,7.04}
{7.30,7.14}
{7.34,7.19}
{7.30,7.18}
{7.34,7.18}
{6.29,7.14}
{6.29,7.18}
{7.04,7.34}
{6.98,7.34}
{7.04,7.30}
{6.98,7.30}
f2 (ppm)
f1 (ppm)

HMBC


{3.76,148.43}
{3.75,148.43}
{3.81,149.38}
{3.80,149.34}
{3.86,159.31}
{3.85,159.31}
{3.82,160.29}
{3.81,160.28}
f1 (ppm)
f2 (ppm)


{6.30,91.29}
{6.29,91.34}
{6.28,91.34}
{7.34,109.39}
{7.31,109.43}
{6.98,109.70}
{7.30,109.49}
{6.84,109.61}
{6.30,108.61}
{6.28,108.63}
{6.28,107.40}
{6.30,107.42}
{7.31,118.82}
{7.05,118.74}
{7.34,118.57}
{7.35,118.65}
{7.04,118.74}
{6.29,118.11}
{7.14,129.71}
{7.30,132.53}
{6.91,133.33}
{7.13,132.68}
{7.15,132.64}
{6.93,132.50}
{6.91,149.38}
{6.89,149.41}
{7.01,149.06}
{7.04,149.07}
{7.19,160.00}
{7.18,159.99}
{6.30,160.17}
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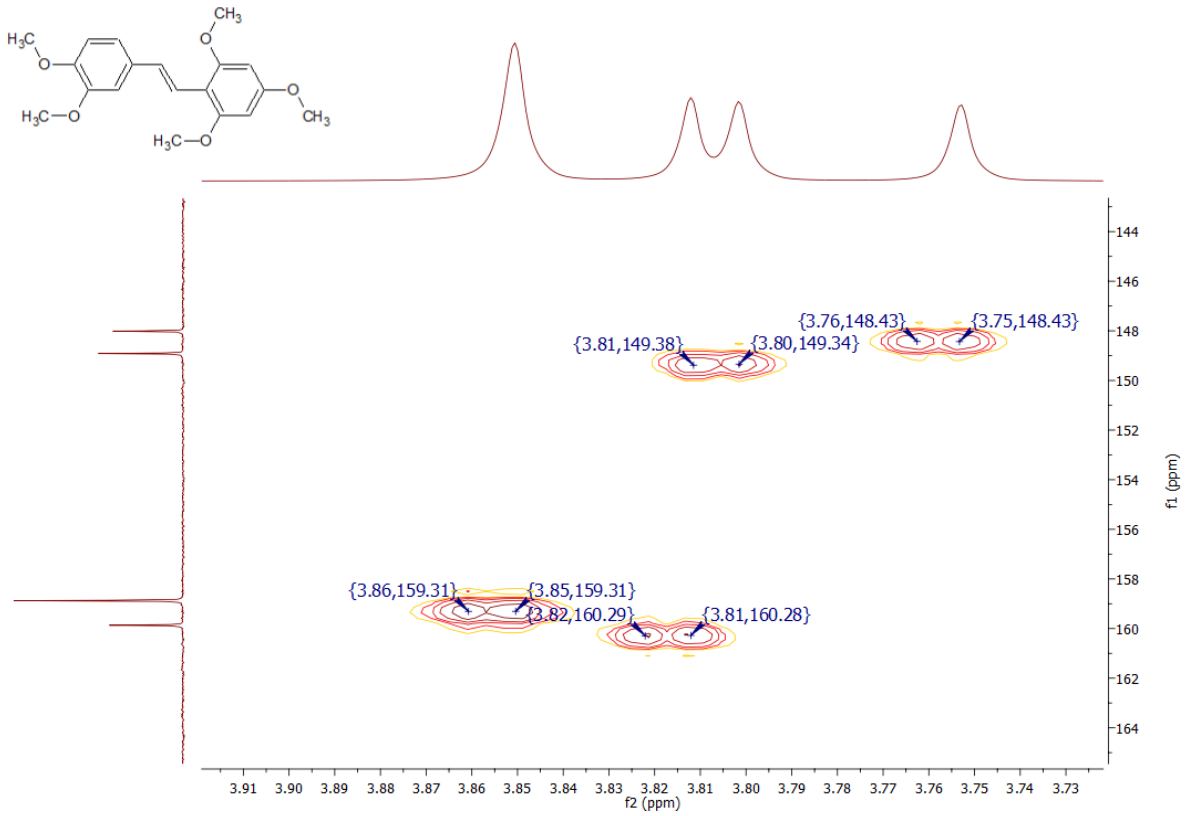
{7.14,159.35}
{7.15,159.37}
{6.29,159.30}
{6.29,159.56}
f1 (ppm)
f2 (ppm)



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