

# Supporting Information

## Flash-metathesis for the coupling of renewable (poly)hydroxyl $\beta$ -methylstyrenes from essential oils

Julien HITCE, Magali CRUTIZAT, Céline BOURDON, Aude VIVES, Xavier MARAT, Maria DALKO-CSIBA

L'OREAL Research & Innovation, 1 Avenue Eugène Schueller, Aulnay-sous-Bois, France

### Table of Contents

**General Experimental S2**

**Detailed experimental procedure S2**

**Composition of the essential oils S3**

**Characterization data of the new compounds S4**

**$^1\text{H}$  &  $^{13}\text{C}$ - NMR Spectra of products S7**

## General Experimental Section:

General: All commercially available chemicals and reagents were used without any further purification unless otherwise indicated. Notably the  $\beta$ -methylstyrenes were used as commercially available mixtures of (*Z*)- and (*E*)-isomers: isoeugenol was purchased from Acros-France (ref 122575000), acetyl isoeugenol was purchased from Sigma-Aldrich (ref W247006), anethole was purchased from Fluka-France (ref 10370), methyl isoeugenol was purchased from Sigma-Aldrich (ref W247618). Star anise and fennel essential oils were purchased from Sigma-Aldrich France (ref. W209619 and W248207, respectively).

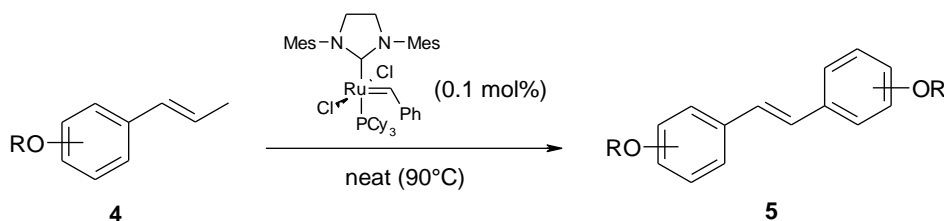
$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AVANCE I 400 Fourier transform spectrometer, operating at 400.13 MHz for  $^1\text{H}$  and at 100.62 MHz for  $^{13}\text{C}$ , using a 5 mm QNP probe operating at 300 K.

The spectra were recorded in  $\text{CDCl}_3$ ,  $\text{DMSO}-d_6$  or  $\text{acetone}-d_6$  as solvent. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), etc. and coupling constants (J) were given in Hz. Chemical shifts are reported in ppm relative to solvent residual peak as an internal standard. The peaks around delta values of  $^1\text{H}$  NMR (7.2), and  $^{13}\text{C}$  NMR (77.0) correspond to deuterated chloroform. The peaks around delta values of  $^1\text{H}$  NMR (2.5), and  $^{13}\text{C}$  NMR (40.0) correspond to deuterated DMSO. The peaks around delta values of  $^1\text{H}$  NMR (2.05), and  $^{13}\text{C}$  NMR (39.5; 206.3) correspond to deuterated acetone.

Gas chromatography (GC) analysis of essential oils was performed with a Agilent GC 6850 apparatus equipped with a DB1 MS column (20 m).

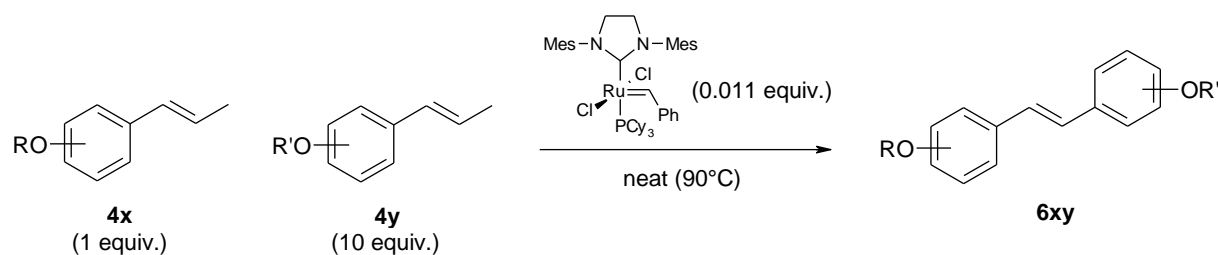
## Detailed experimental procedures:

### General procedure for the self cross-metathesis of $\beta$ -methylstyrenes



A mixture of neat styrene **4** and Grubbs II precatalyst (0.1 mol%) was heated in a round bottom flask at 90°C under an argon flow for 10-60 min (the reaction mixture usually became solid after 2-5 min). After the reaction mixture was cooled to room temperature, a  $^1\text{H}$  NMR spectrum of an aliquot was recorded in order to determine the conversion of **4** into stilbene **5**. The crude product was suspended in DCM (1 vol.) and cold MeOH was introduced (2 vol.). The mixture was stirred at 0°C for 1h, filtered-off and washed with 4 vol. of cold MeOH. The solid was dried under vacuum to afford stilbene **5** as a pure compound.

## General procedure for the hetero cross-metathesis of $\beta$ -methylstyrenes



A mixture of neat styrenes **4x** (1 equiv.) and **4y** (10 equiv.) together with Grubbs II pre-catalyst (0.011 equiv.) was heated in a round bottom flask at 90°C under an argon flow for 30 min (the reaction mixture usually became solid after 2-5 min). After the reaction mixture was cooled to room temperature, a  $^1\text{H}$  NMR spectrum of an aliquot was recorded in order to quantify the overall conversion of substrates **4x** and **4y** and to determine the selectivity of the transformation of **4x** (hetero cross-metathesis vs self cross-metathesis). Product **6xy** was isolated by column chromatography using heptane/acetone mixtures as an eluent.

### Preliminary experiments: ruling out catalyst irreversible deactivation

By analogy to the procedure reported by Grubbs *et al.* for the self cross-metathesis of eugenol,<sup>1</sup> a mixture of neat isoeugenol **4a** and 1 mol% pre-catalyst **A** (Grubbs II) was stirred at r.t. under vacuum. After 30min, the reaction mixture had solidified and conversion of **4a** to **5a** had stopped at 67 % (as determined by  $^1\text{H}$  NMR of an aliquot of the reaction mixture) suggesting catalyst deactivation.

In order to check if the catalyst was still active, fresh isoeugenol **4a** was added and the mixture was solubilized in toluene in order to run the reaction under conventional metathesis conditions. After stirring 1 h at rt, full conversion of isoeugenol was observed by  $^1\text{H}$  NMR, thus showing that at least part of the metathesis catalyst was still active.

## Composition of the essential oils (as determined by GC)

The relative purity of anethole **4c** within the essential oils was determined semi-quantitatively by GC using a flame ionization detector.

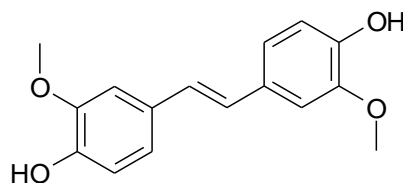
The results are indicated in the table below.

Essential oil	Commercial Reference	Relative purity ( <b>4c</b> )
Star anise	Sigma-Aldrich France W209619	88 %
Fennel	Sigma-Aldrich France W248207	73 %

<sup>1</sup> H. E. Blackwell, D. J. O'Leary, A. K. Chatterjee, R. A. Washenfelder, D. A. Bussmann and R. H. Grubbs, *J. Am. Chem. Soc.*, 2000, **122**, 58.

## Characterization data of prepared compounds

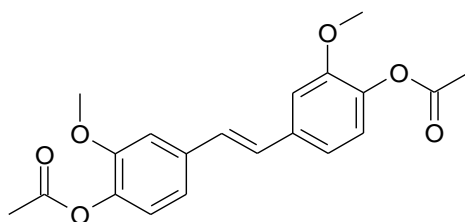
### 4,4'-Dihydroxy-3,3'-dimethoxystilbene – 5a



Reaction performed on 6.1 mmol isoeugenol.

Light pink solid (0.8 g, 92 %);  $^1\text{H NMR}$  (400 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  7.18 (d,  $J = 2.0$  Hz, 2H), 6.99 (s, 2H), 6.98 (dd,  $J = 2.0, 8.1$  Hz, 2H), 6.82 (d,  $J = 8.2$  Hz, 2H), 3.91 (s, 6H).  $^{13}\text{C NMR}$  (100 MHz,  $(\text{CD}_3)_2\text{CO}$ )  $\delta$  148.6, 147.2, 131.0, 127.1, 120.7, 115.9, 110.0, 59.3. Elemental analysis: Found C, 70.4; H, 5.9; O, 23.7. Calc. for  $\text{C}_{16}\text{H}_{16}\text{O}_4$ : C, 70.6; H, 5.9; O, 23.5%.

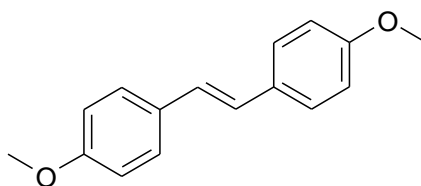
### 4,4'-Diacetoxy-3,3'-dimethoxystilbene – 5b



Reaction performed on 33.7 mmol isoeugenyl acetate.

White solid (5.54 g, 92 %);  $^1\text{H NMR}$  (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.36 (d,  $J = 1.3$  Hz, 2H), 7.27 (s, 2H), 7.17 (dd,  $J = 1.3, 8.2$  Hz, 2H), 7.08 (d,  $J = 8.2$  Hz, 2H), 3.85 (s, 6H), 2.26 (s, 6H).  $^{13}\text{C NMR}$  (100 MHz,  $\text{DMSO}$ )  $\delta$  169.0, 151.5, 139.3, 136.5, 128.6, 123.4, 119.5, 110.7, 56.2, 20.8. Elemental analysis: Found C, 67.5; H, 5.6; O, 26.8. Calc. for  $\text{C}_{20}\text{H}_{20}\text{O}_6$ : C, 67.4; H, 5.7; O, 26.9%.

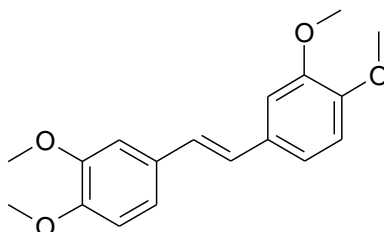
### 4,4'-Dimethoxystilbene – 5c



Reaction performed on 33.7 mmol anethole.

White solid (3.84 g, 95 %);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (m, 4H), 6.93 (s, 2H), 6.89 (m, 4H), 3.83 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.1, 130.6, 127.4, 126.3, 114.2, 55.3. Elemental analysis: Found C, 79.9; H, 6.7; O, 13.1. Calc. for  $\text{C}_{16}\text{H}_{16}\text{O}_2$ : C, 80.0; H, 6.7; O, 13.3%.

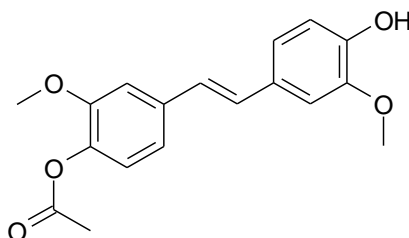
#### 3,3',4,4'-Tetramethoxystilbene – **5d**



Reaction performed on 33.7 mmol methyl isoeugenol.

Light yellow solid (4.27 g, 84 %);  $^1\text{H}$  NMR (400 MHz,  $\text{DMSO}-d_6$ )  $\delta$  7.20 (d,  $J = 1.8$  Hz, 2H), 7.07 (m, 4H), 6.94 (d,  $J = 8.3$  Hz, 2H), 3.82 (s, 6H), 3.77 (s, 6H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{DMSO}$ )  $\delta$  149.4, 148.9, 130.8, 126.8, 119.8, 112.4, 109.5, 56.0, 55.9. Elemental analysis: Found C, 71.8; H, 6.7; O, 21.2. Calc. for  $\text{C}_{18}\text{H}_{20}\text{O}_4$ : C, 72.0; H, 6.7; O, 21.3%.

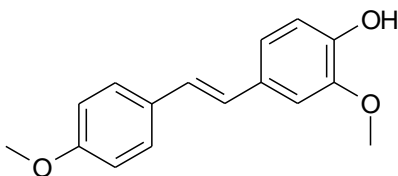
#### 4-Acetoxy-4'-hydroxy-3,3'-dimethoxystilbene – **6ab**



Reaction performed on 1.5 mmol isoeugenyl acetate.

Slightly pink solid (198 mg, 42 %);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.12 (s, 1H), 7.30 (d,  $J = 1.8$  Hz, 1H), 7.12 (m, 5H), 6.99 (dd,  $J = 1.8, 8.2$  Hz, 1H), 6.77 (d,  $J = 8.2$  Hz, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 2.25 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  168.6, 151.0, 147.8, 146.8, 138.3, 136.6, 129.0, 128.6, 124.7, 122.9, 120.2, 118.5, 115.6, 109.87, 109.85, 55.7, 55.6, 20.4. Elemental analysis: Found C, 68.7; H, 5.8; O, 25.4. Calc. for  $\text{C}_{18}\text{H}_{18}\text{O}_5$ : C, 68.8; H, 5.8; O, 25.5%.

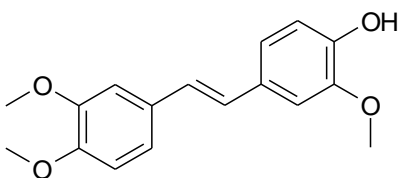
4-Hydroxy-3,4'-dimethoxystilbene – **6ac**



Reaction performed on 1.5 mmol anethole.

Light yellow solid (70 mg, 18 %);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 (m, 2H), 7.00 (m, 2H), 6.90 (m, 5H), 3.95 (s, 3H), 3.83 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  159.2, 146.9, 145.5, 130.6, 130.5, 127.6, 126.8, 126.3, 120.3, 114.7, 114.3, 108.3, 56.1, 55.5.

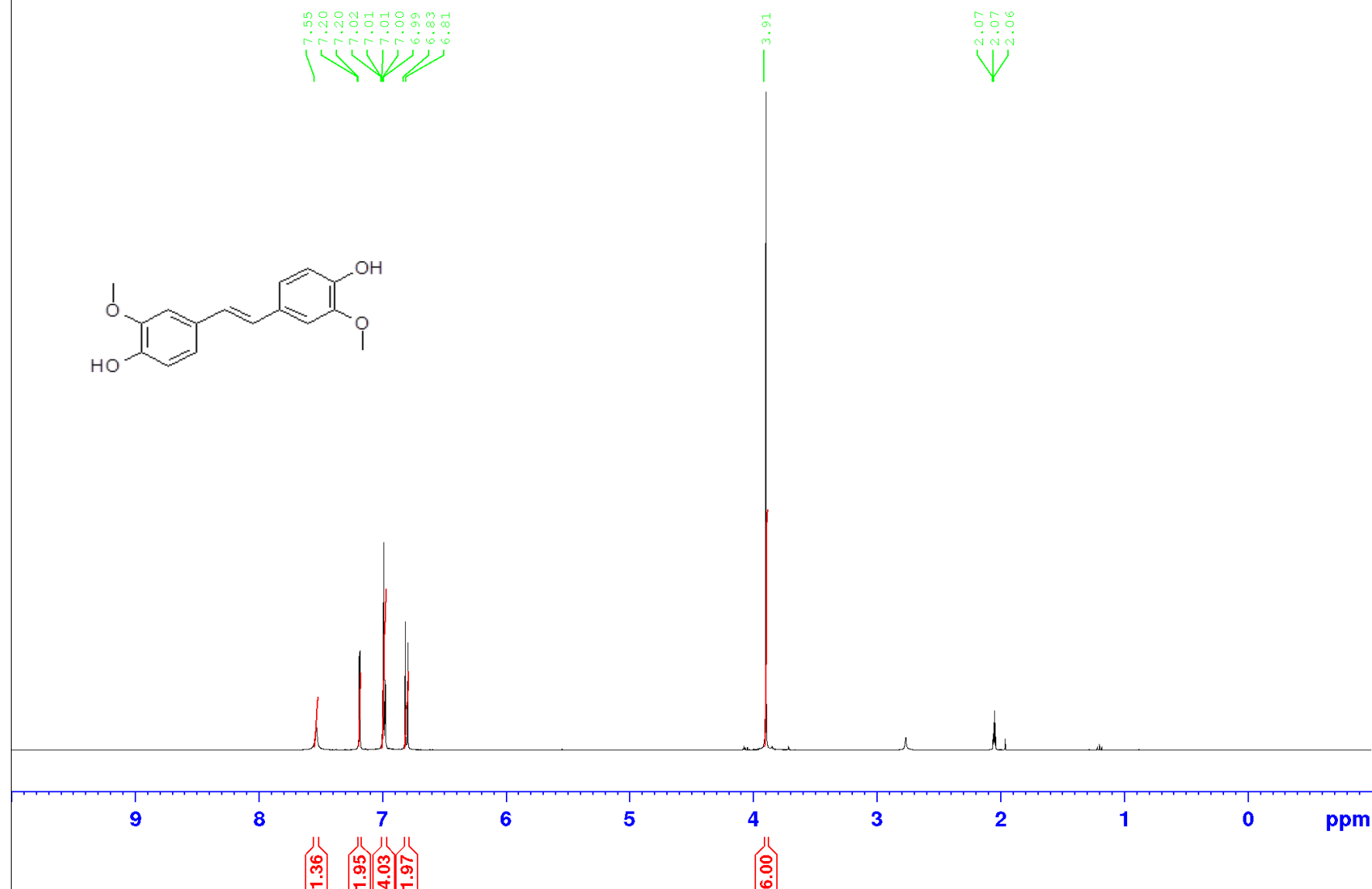
4-Hydroxy-3,3', 4'-trimethoxystilbene – **6ad**

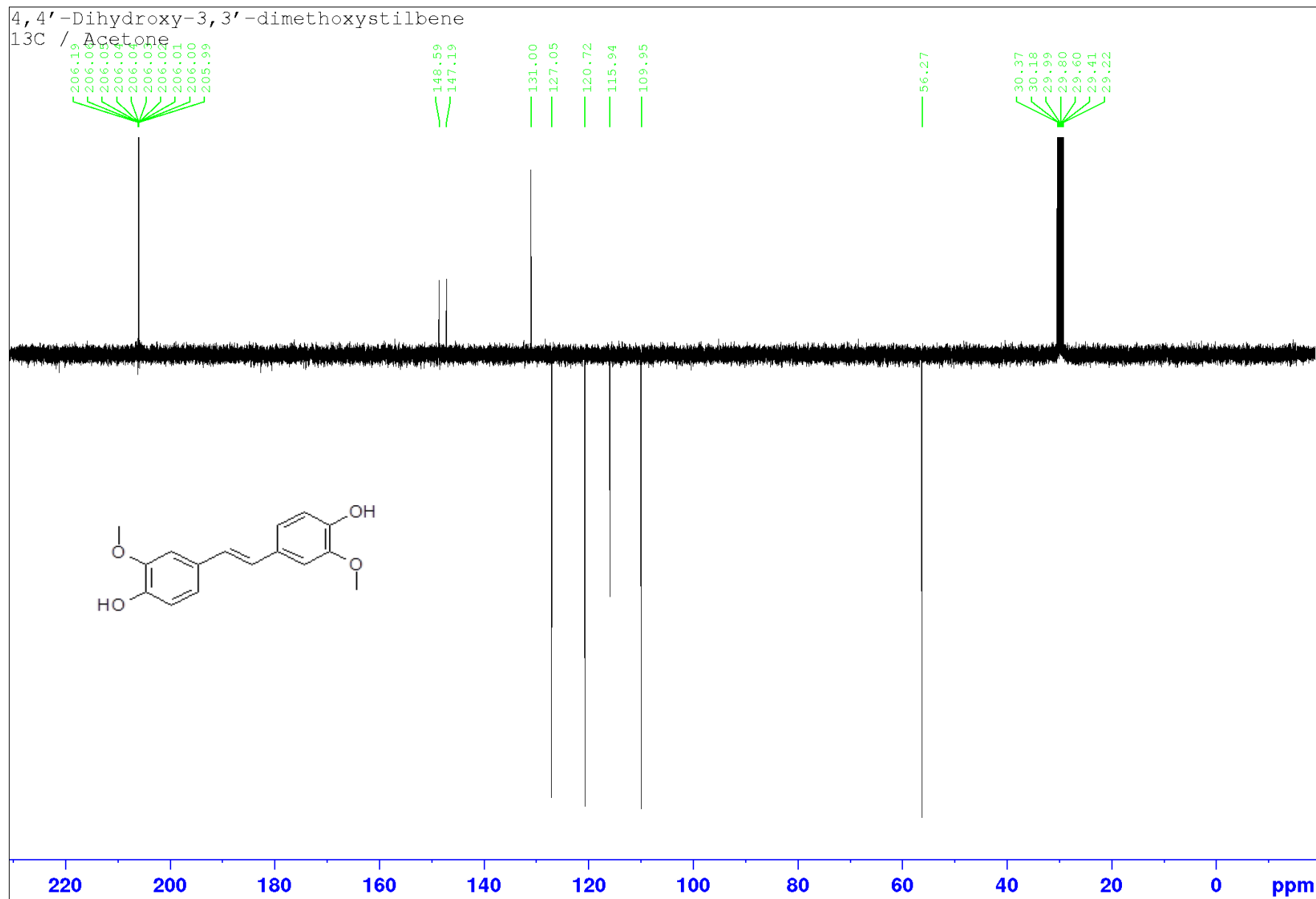


Reaction performed on 1.5 mmol methyl isoeugenol.

Slightly pink solid (214 mg, 50 %);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  9.03 (s, 1H), 7.17 (dd,  $J$  = 1.9, 8.2 Hz, 2H), 7.05 (m, 1H), 6.97 (d,  $J$  = 3.4 Hz, 2H), 6.94 (m, 2H), 6.75 (d,  $J$  = 8.2 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.76 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  149.0, 148.3, 147.8, 146.3, 130.6, 129.0, 126.7, 125.4, 119.7, 119.2, 115.6, 111.9, 109.6, 109.0, 55.6, 55.53, 55.46. Elemental analysis: Found C, 71.4; H, 6.3; O, 22.2. Calc. for  $\text{C}_{17}\text{H}_{18}\text{O}_4$ : C, 71.3; H, 6.3; O, 22.4%.

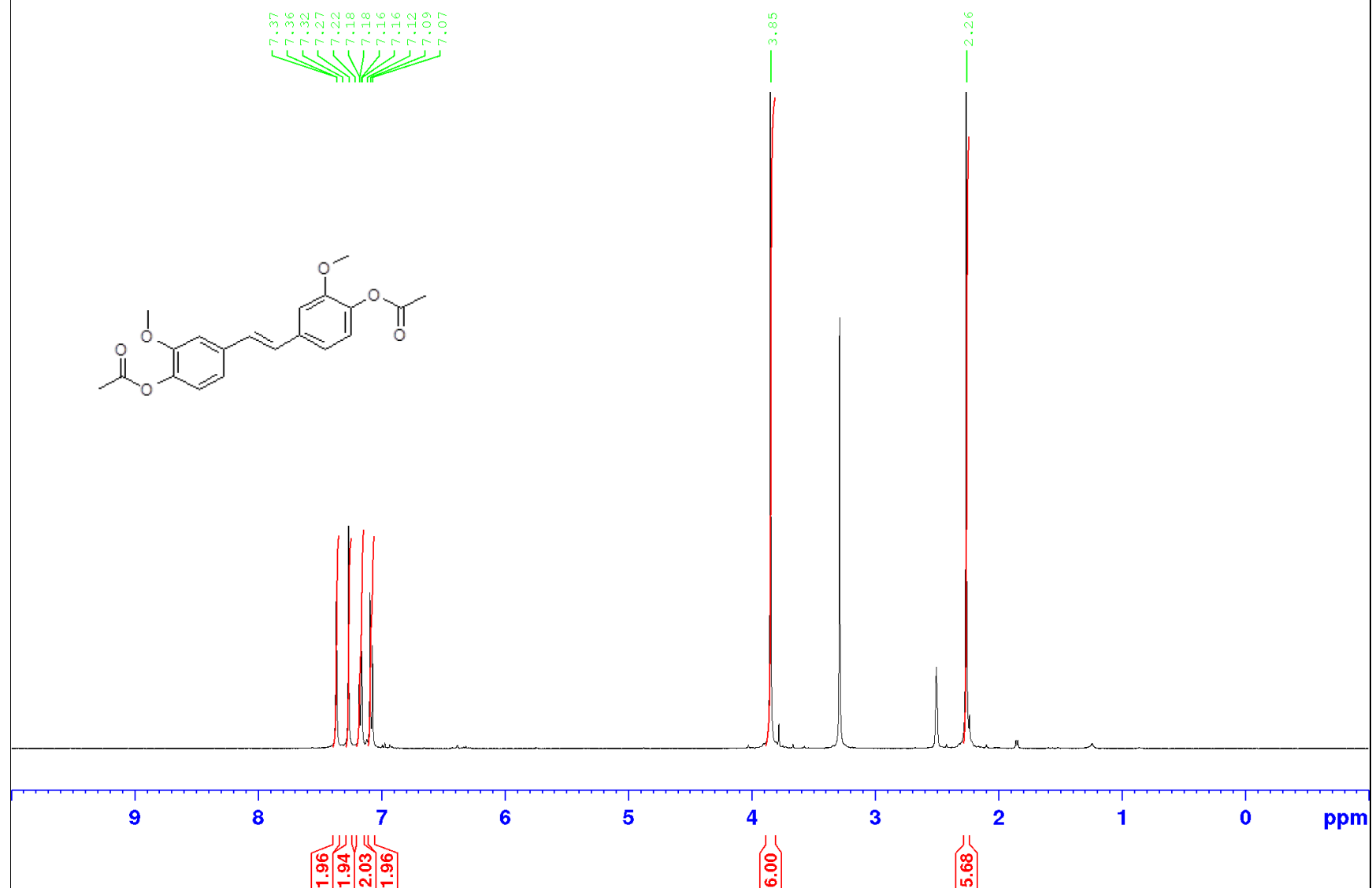
4,4'-Dihydroxy-3,3'-dimethoxystilbene  
1H / Acetone



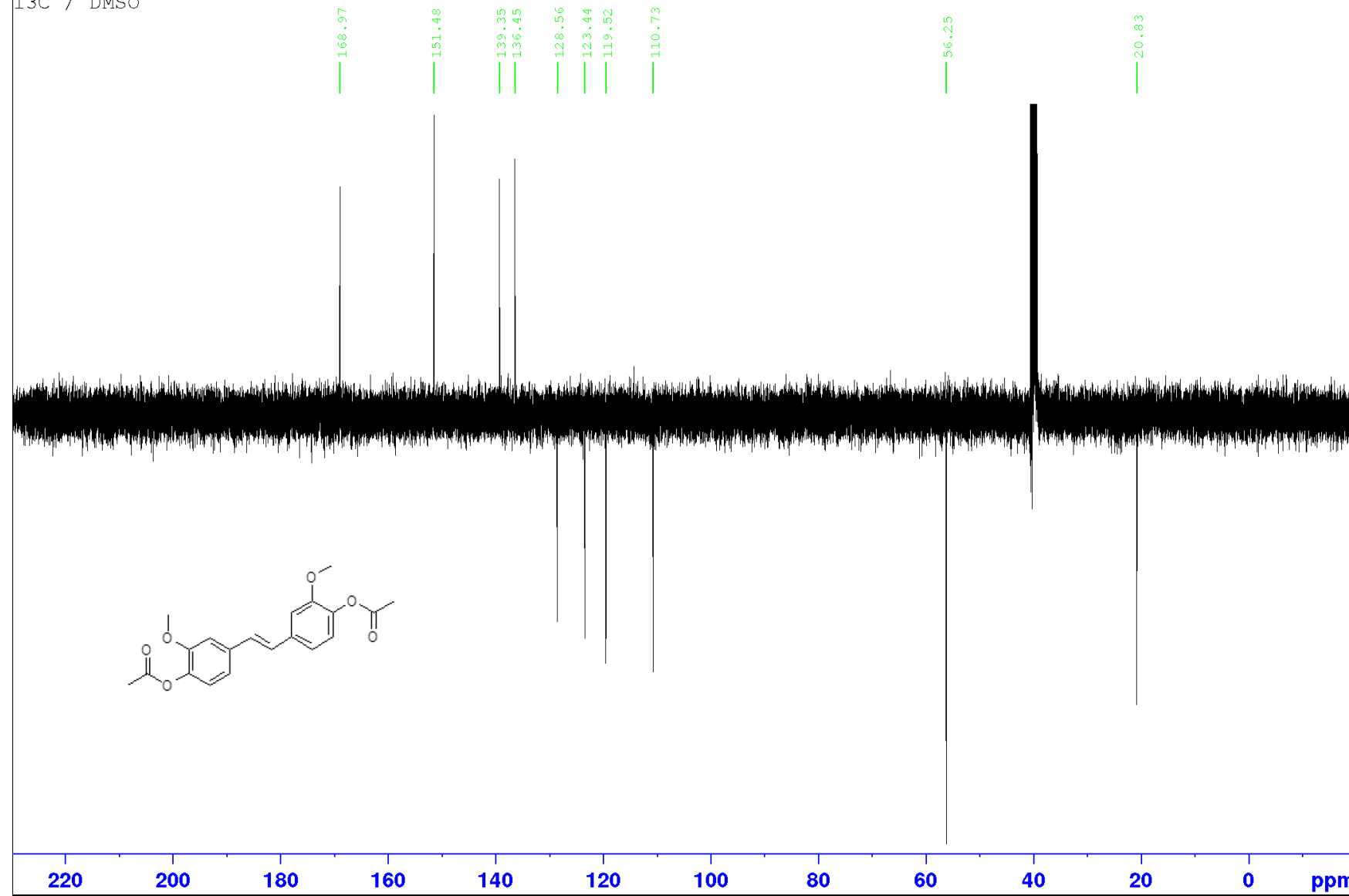




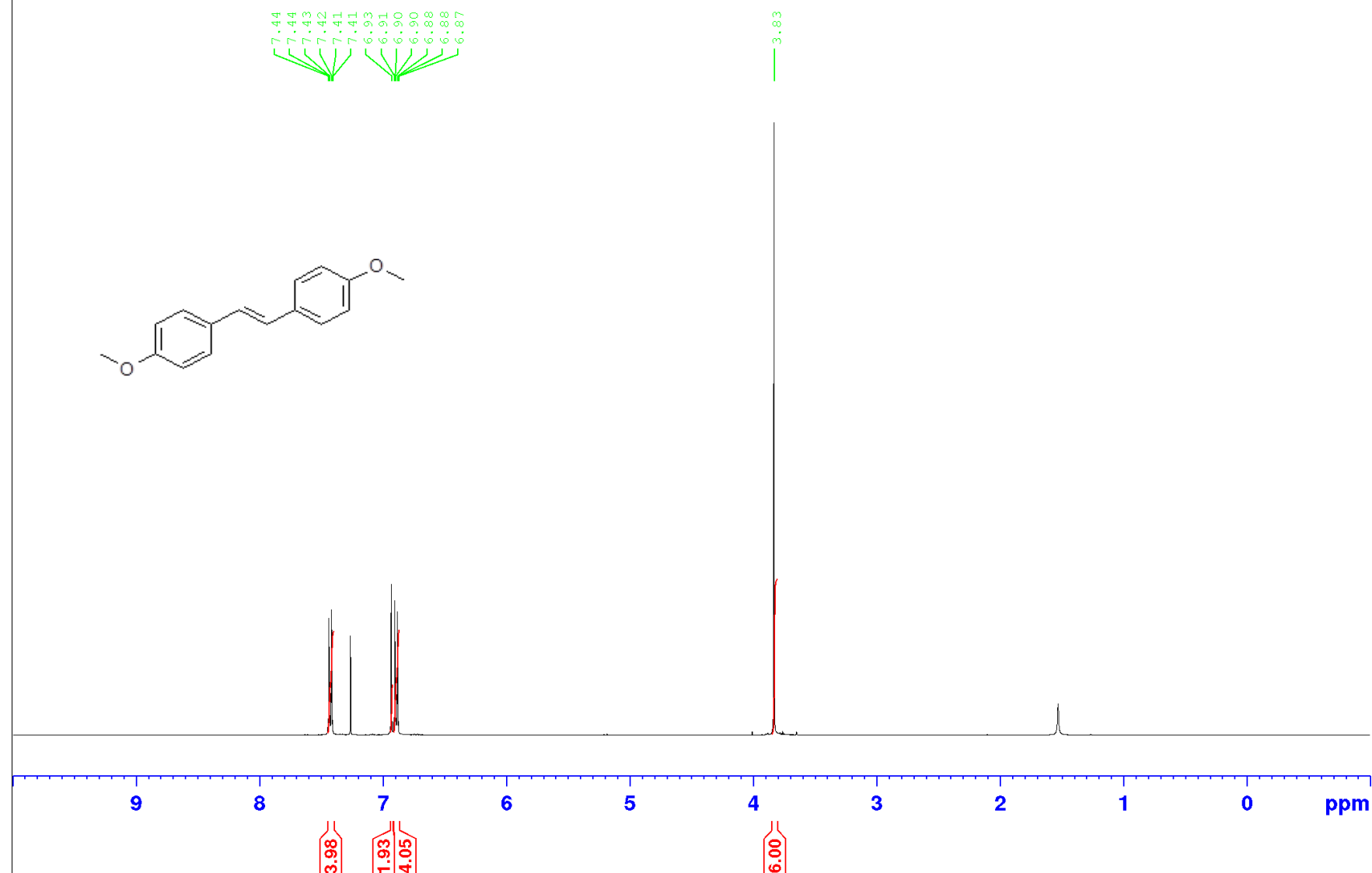
4,4'-Diacetoxy-3,3'-dimethoxystilbene  
1H / DMSO



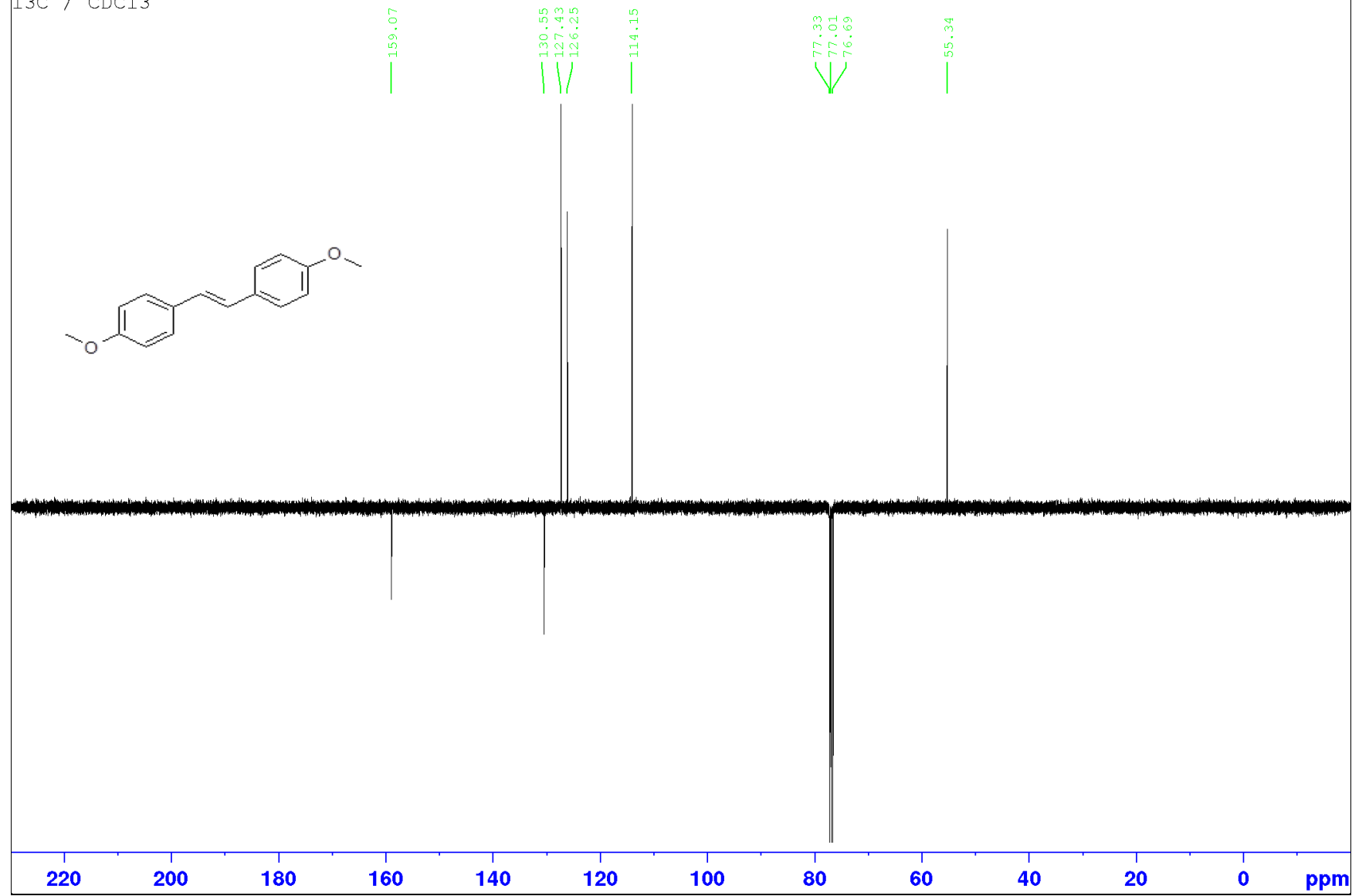
4,4'-Diacetoxy-3,3'-dimethoxystilbene  
13C / DMSO



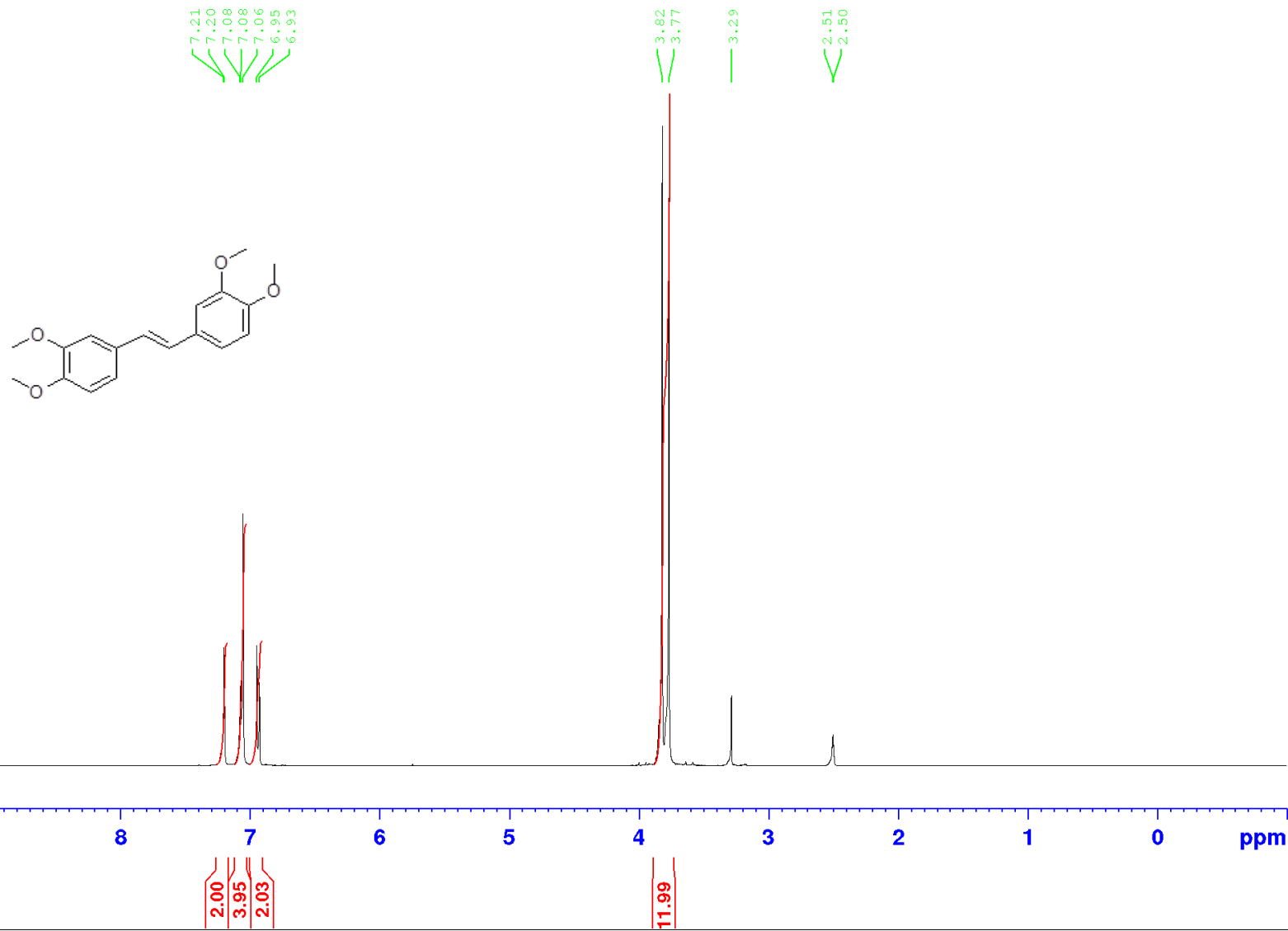
4,4'-Dimethoxystilbene  
1H / CDCl3



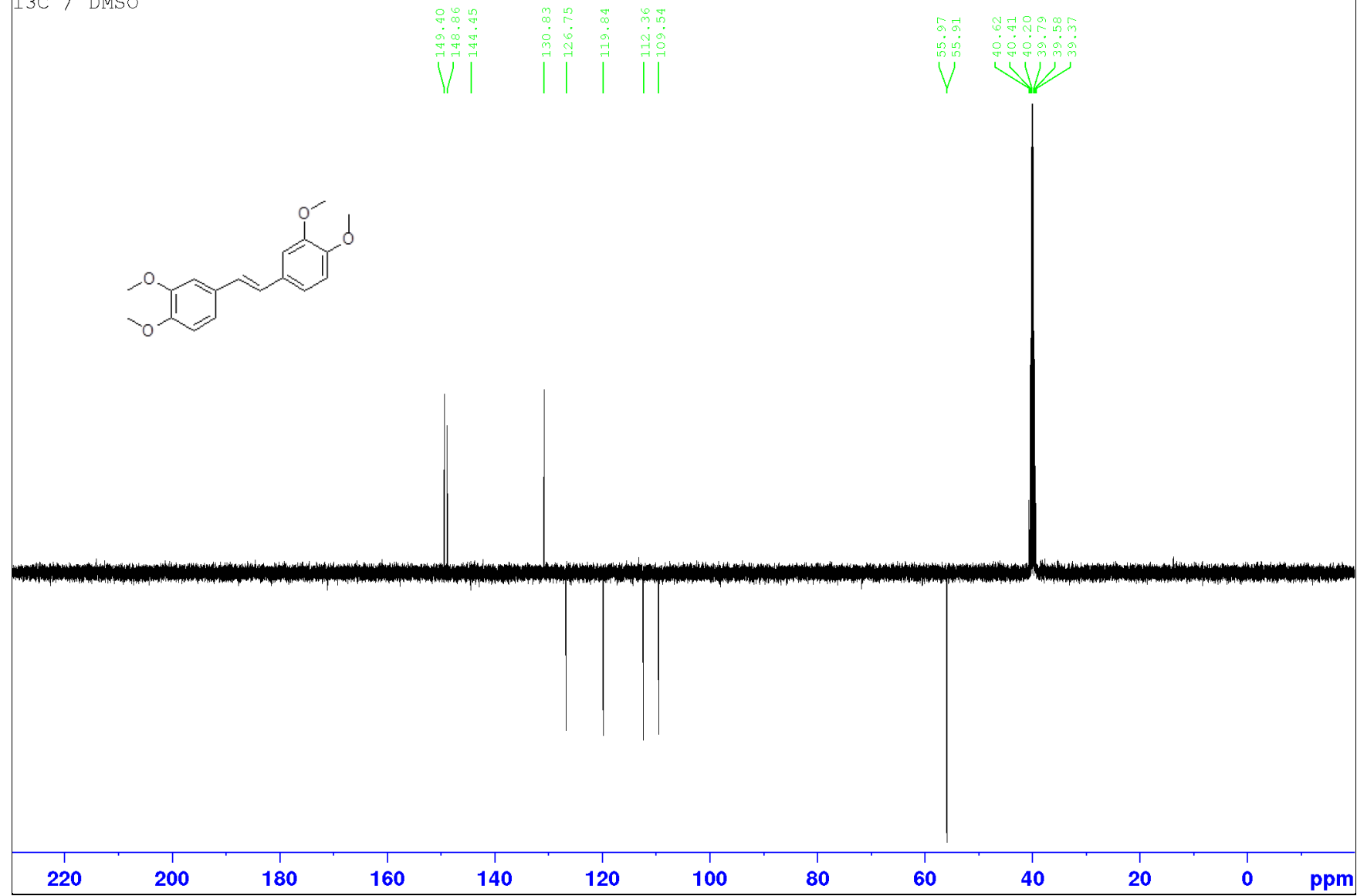
4,4'-Dimethoxystilbene  
13C / CDCl3



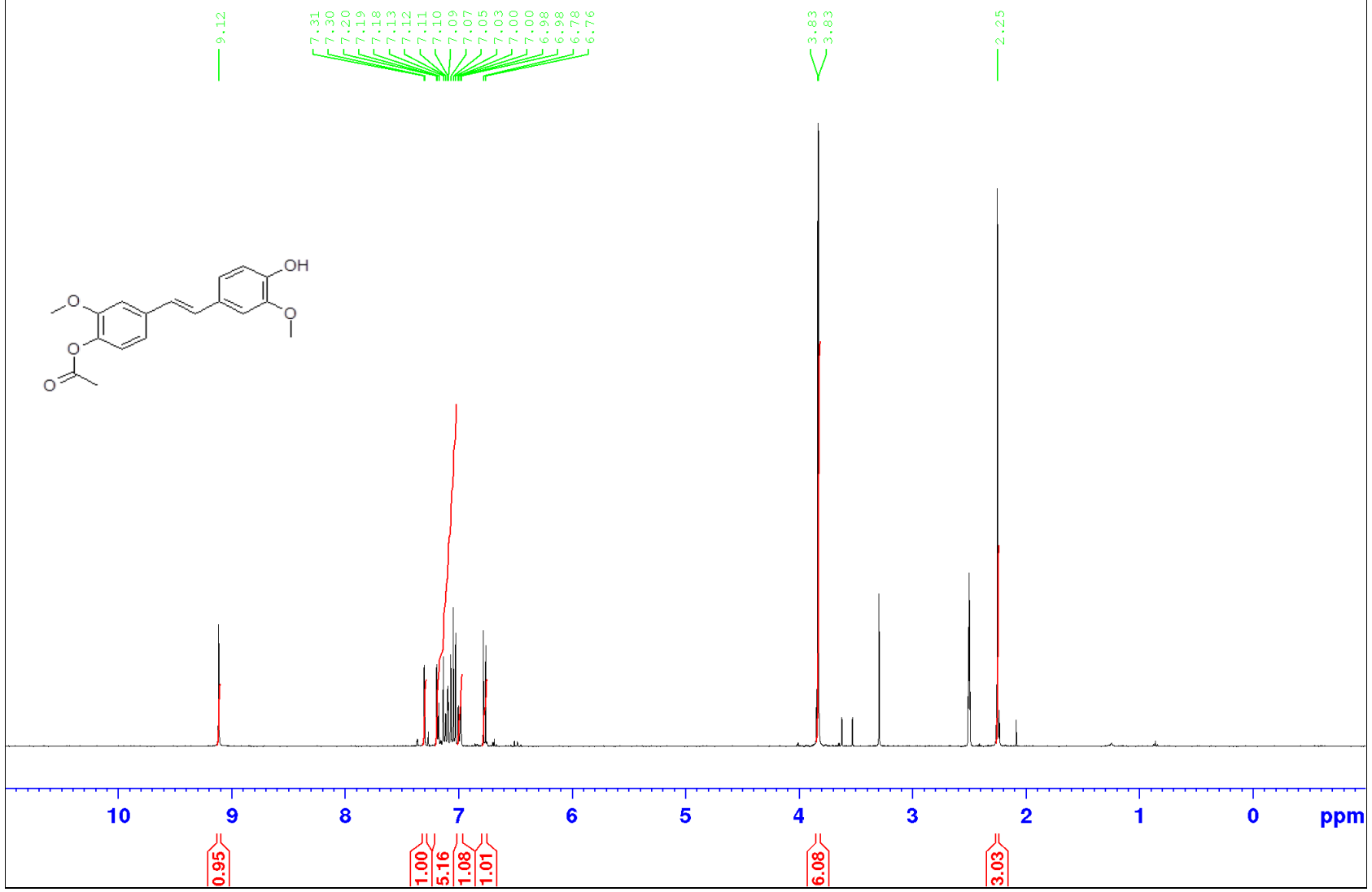
3,3',4,4'-Tetramethoxystilbene  
1H / DMSO



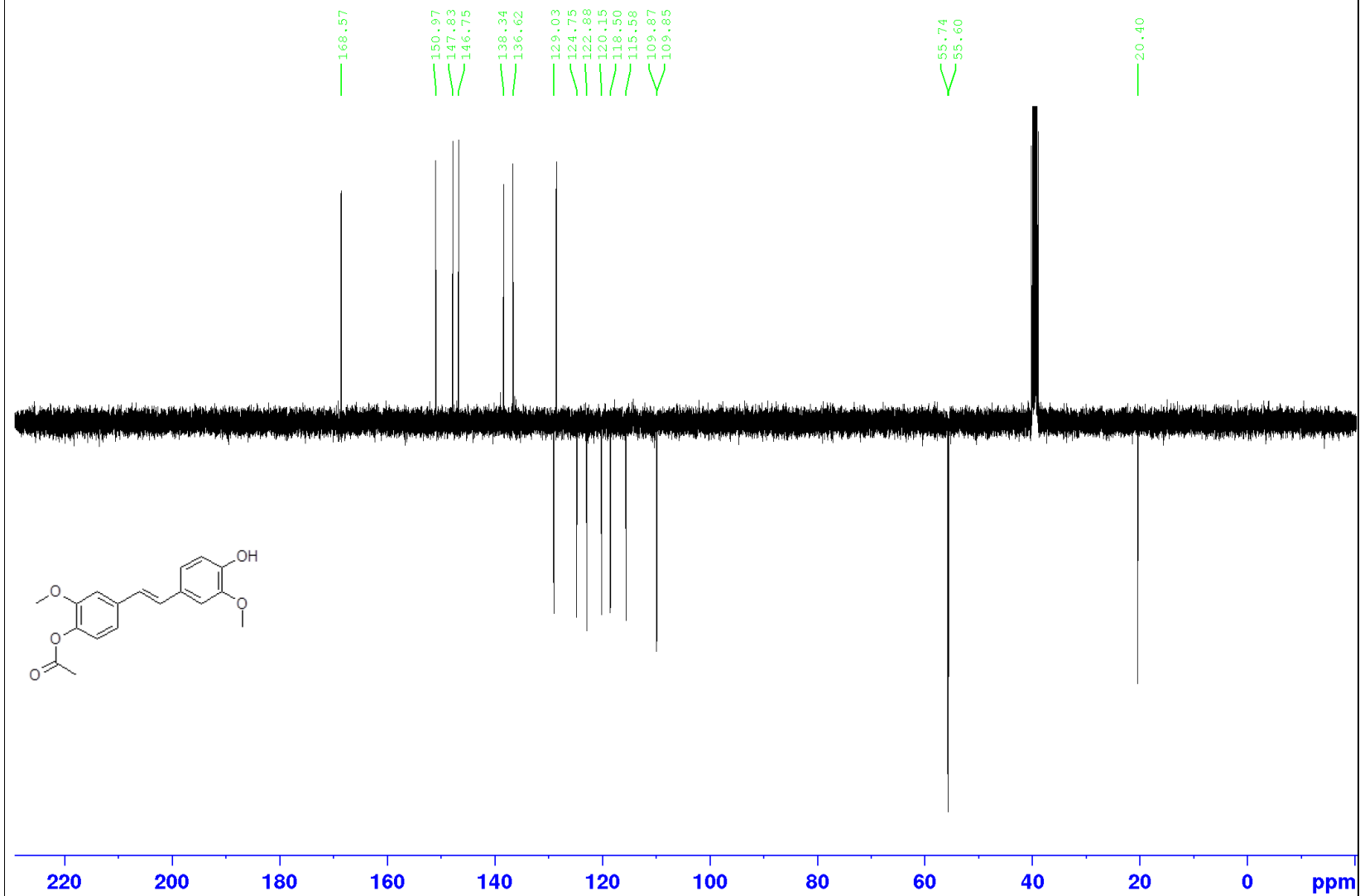
3,3',4,4'-Tetramethoxystilbene  
13C / DMSO



4-Acetoxy-4'-hydroxy-3,3'-dimethoxystilbene  
1H / DMSO

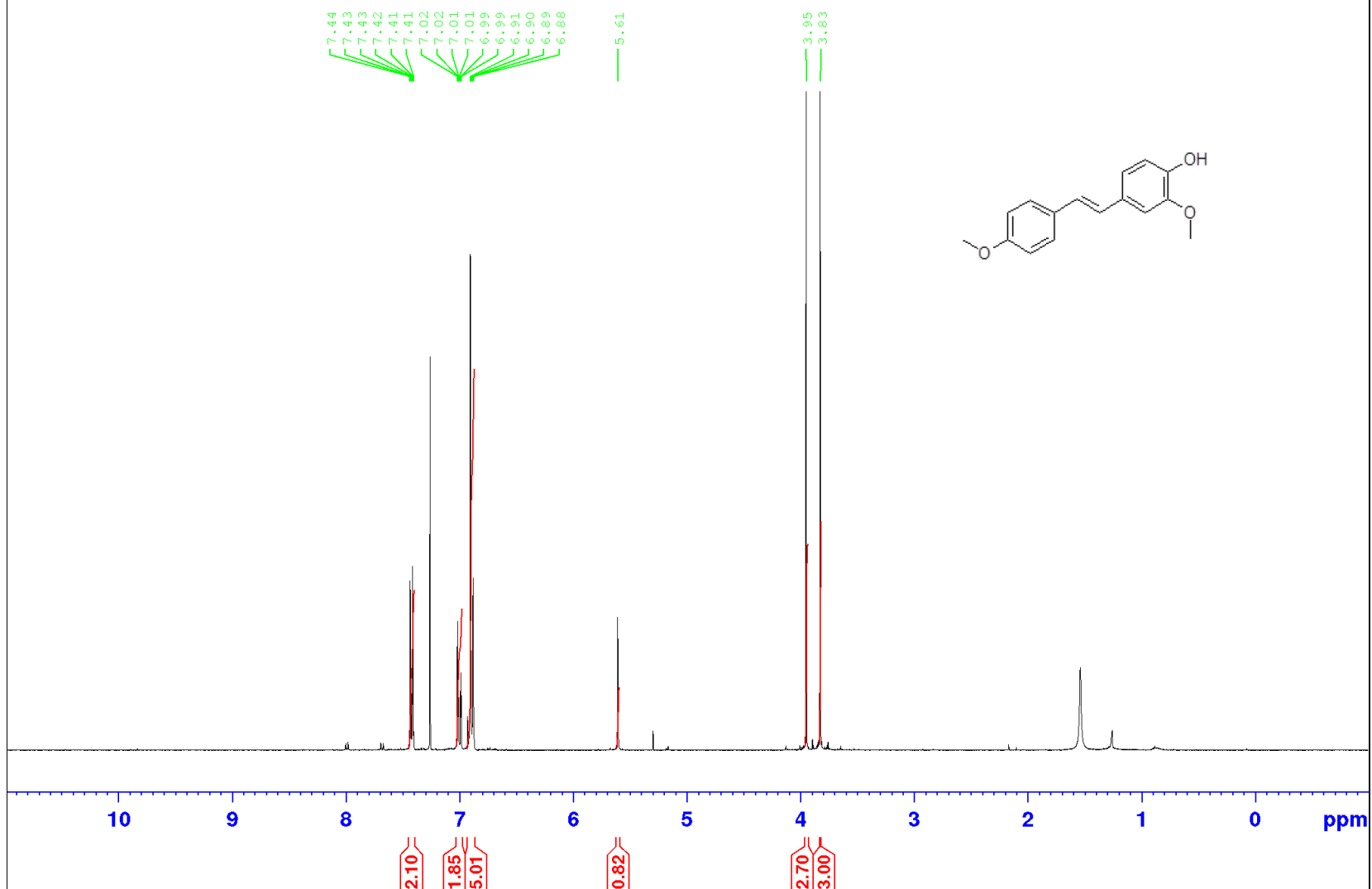


4-Acetoxy-4'-hydroxy-3,3'-dimethoxystilbene  
13C / DMSO

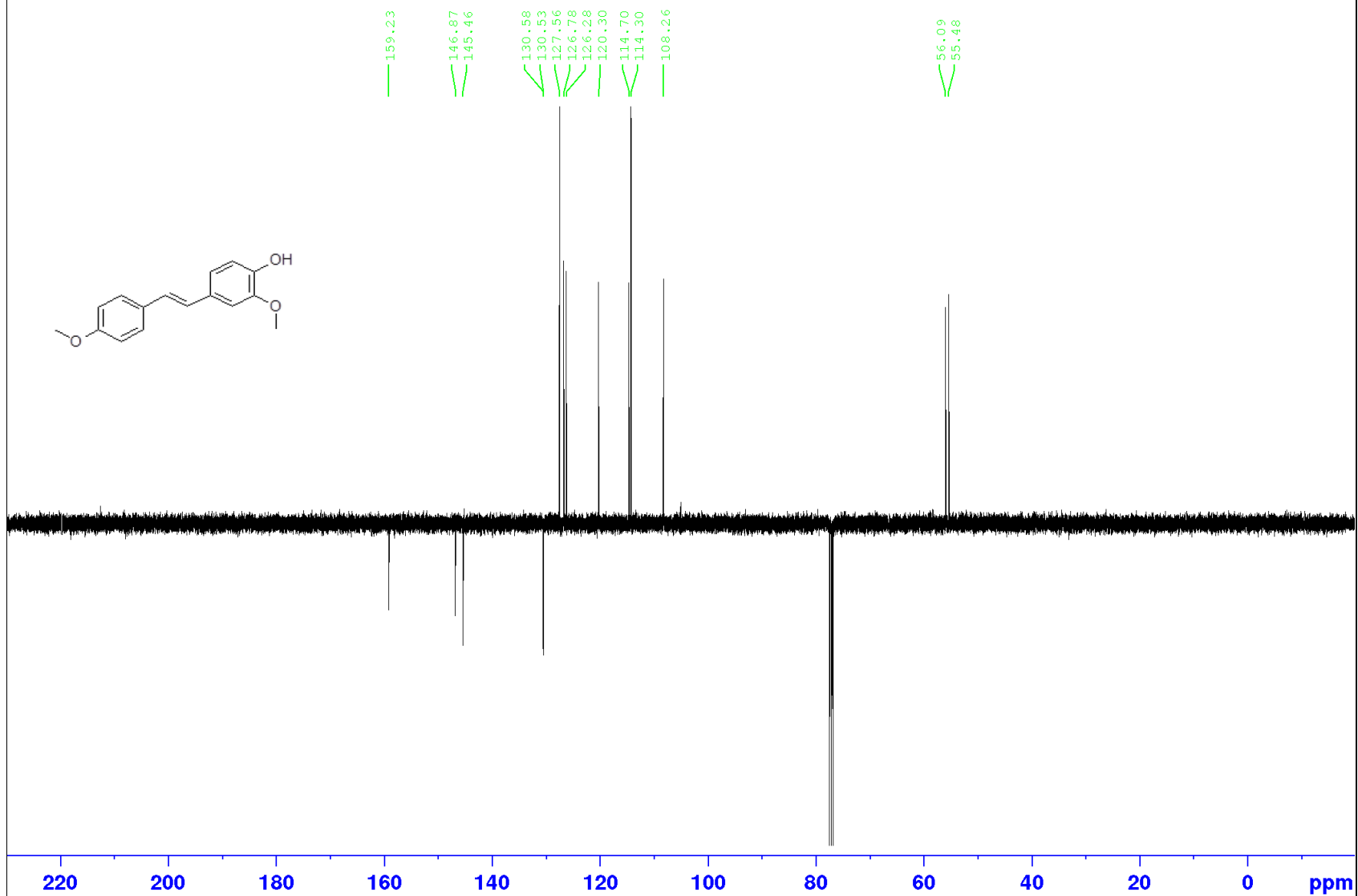




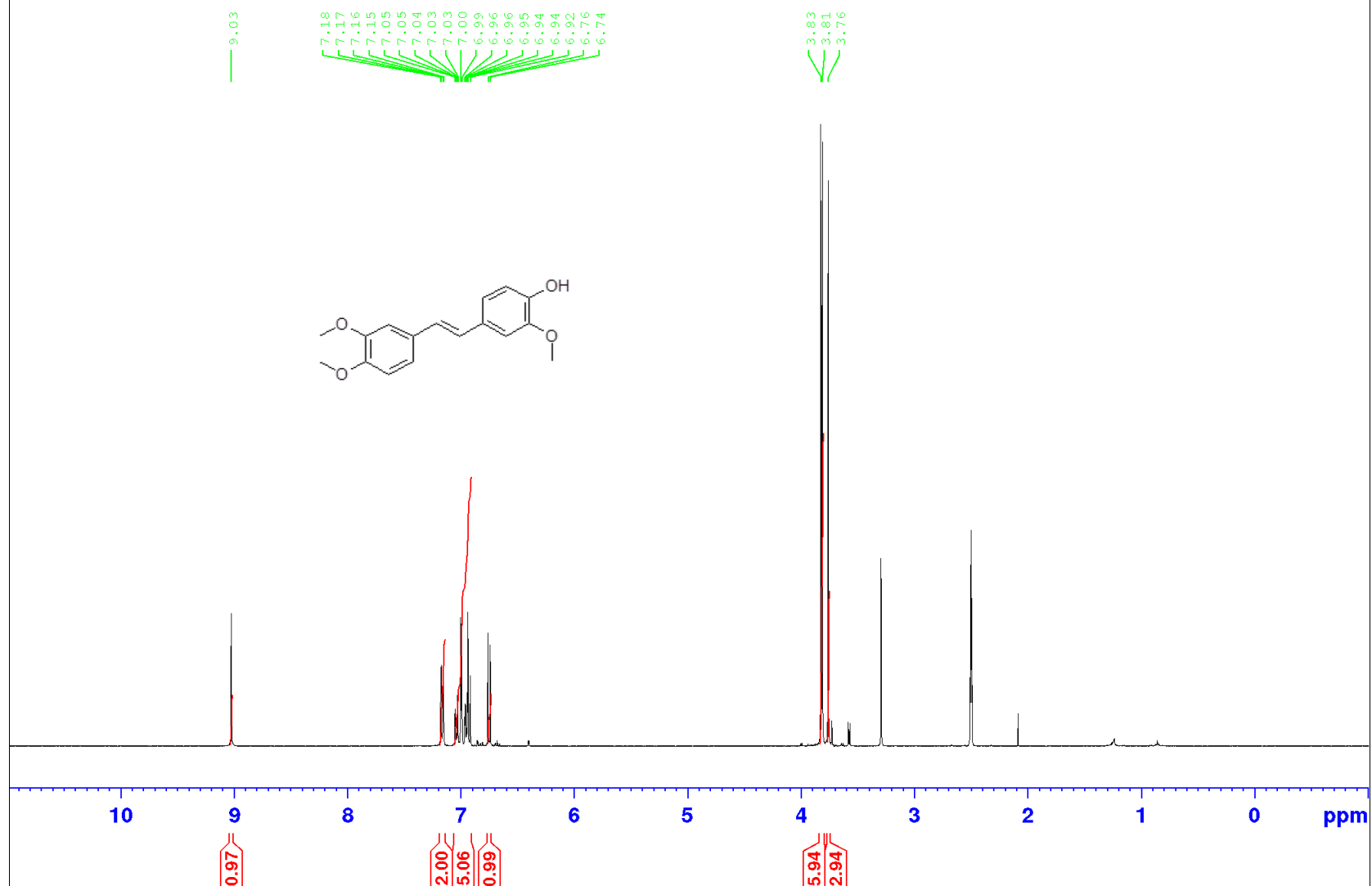
4-Hydroxy-3,4'-dimethoxystilbene  
1H / CDCl3



4-Hydroxy-3,4'-dimethoxystilbene  
13C / CDCl3



4-Hydroxy-3,3', 4'-trimethoxystilbene  
1H / DMSO



4-Hydroxy-3,3', 4'-trimethoxystilbene  
13C / DMSO

