Cobalt-catalyzed three-component assembling of aromatic oximes with substituted dienes and formaldehyde

*Priyambada Prusty and Masilamani Jeganmohan**

Department of Chemistry, Indian Institute of Technology Madras, Chennai 600036, Tamil Nadu, India

Email: mjeganmohan@iitm.ac.in

Electronic Supporting Information (ESI)

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Experimental Section

General Information. All reactions were carried out under the N_2 atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with nitrogen prior to use (three times). Dry solvents were used for the reaction. Column chromatographical purifications were performed using SiO_2 (100-200 mesh ASTM) from Avra Pvt. Ltd., India. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. $[CoCp^*COI_2]$[1] and Oximes[2-4] were prepared according to literature procedures. Commercially available dienes, metal salts, para formaldehyde and other chemicals were purchased from Sigma-Aldrich and Spectrochem. Pvt. Ltd., India. These chemicals were used without further purification.

General Procedure for the Sequential Three-Component C-H Functionalization.

Ketoxime **1** (50 mg) (1 equiv), HCHO (3 equiv), $CoCp^*COI_2$ (10 mol %), $AgSbF_6$ (20 mol %) and 2-mesitylenecarboxylic acid (50 mol %) were taken in a 15-mL pressure tube. Dry trifluoro ethanol (TFE) (2.0 mL) was added to the reaction mixture under N_2 medium. Then, dienes **2, 8 or 9** (2.0 equiv) was added followed by the addition of dry TFE (2.0 mL) and the reaction mixture was stirred under an N_2 atmosphere for five minutes. Then, a screw cap was used to cover the tube and the reaction mixture was allowed to stir at 60 °C for 20 h. Then, the reaction mixture was diluted with CH_2Cl_2, filtered through celite, and the filtrate was concentrated. The crude residue was purified by column chromatography silica-gel 120-200 mesh, EtOAc:Hexane gave the desired products **4, 6, 8, 9 and 11.**

Note: For the preparation of compounds **6** and **9**, AcOH (50 mol %) was used instead of 2-mesitylenecarboxylic acid (50 mol %).

Procedure for the Alkenylation followed by hydroxymethyl arylation of Ketoxime (1a) with isoprene (2) and Formaldehyde (3) by a Cobalt catalysis (1 mmol scale).

Ketoxime **1a** (149 mg, 1 mmol), HCHO (3 equiv), $CoCp^*COI_2$ (10 mol %, 0.1 mmol, 47.5 mg), $AgSbF_6$ (20 mol %) and Mes-COOH (50 mol %, 0.5 mmol, 82 mg) were taken in a 15-mL pressure tube. Dry trifluoro ethanol (TFE) (5.0 mL) was added to the reaction mixture. Then, diene **2** (2.0 equiv, 2 mmol) was added followed by the addition of dry TFE (5.0 mL) and the reaction mixture was stirred under N_2 atmosphere for five minutes. Then, a screw cap was used to cover the tube and the reaction mixture was allowed to stir at 60 °C for 20 h. Then, the reaction mixture was diluted with CH_2Cl_2, filtered through celite, and the filtrate

was concentrated. The crude residue was purified by column chromatography silica-gel 120-200 mesh, EtOAc:Hexane gave desired products **4a**, 160 mg in 65% yield as colourless liquid.

Preparation of Starting Materials 1 and 2.

Substituted Oximes **1b−n, 5a-h, 10a-d** were prepared by the known reported procedurse.[2-4] Remaining dienes are purchased from Sigma-Aldrich and Spectrochem. Pvt. Ltd., India.

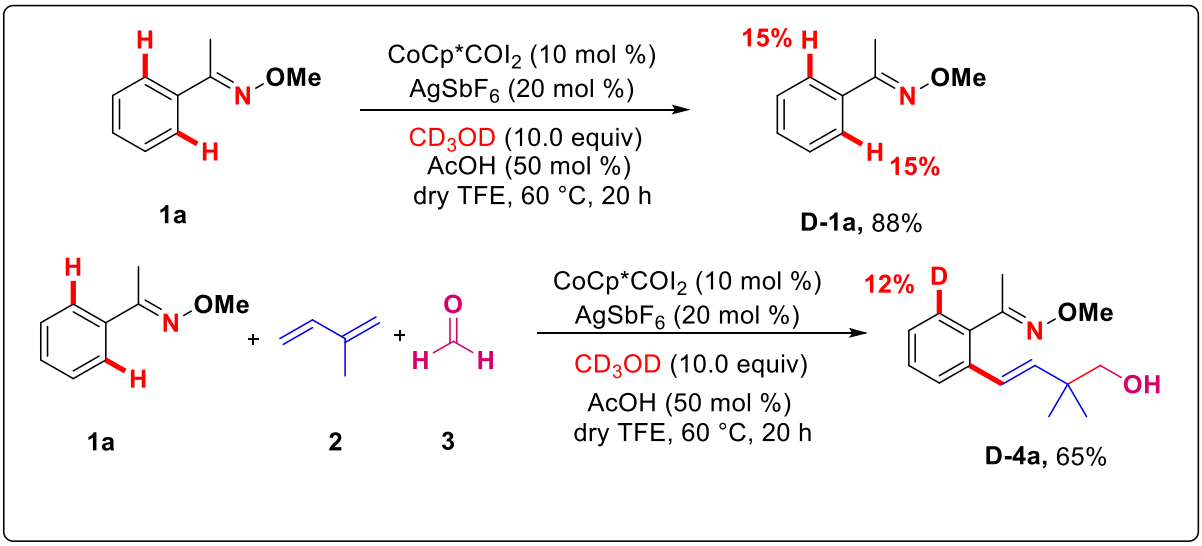
Mechanistic Investigation

Deuterium Labelling Studies for D-1a.

A 15 mL pressure tube with a septum containing Ketoxime **1a** (75 mg), $CoCp^*COI_2$ (10 mol %), $AgSbF_6$ (20 mol %), and AcOH (50 mol%), dry TFE (2.0 mL) were added to the reaction. Then, CD_3OD (10.0 equiv) was added and the reaction mixture was stirred under N_2 atmosphere for five minutes. Then, a screw cap was used to cover the tube and the reaction mixture was allowed to stir at 60 °C for 20 h. Then, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite, and the filtrate was concentrated. The crude residue was purified by column chromatography silica-gel 120-200 mesh, EtOAc:Hexane gave product **D-1a**. In the reaction, product **D-1a** was observed in 88% yield with 15% of deuterium incorporation at both the ortho carbons of oxime ether **1a**.

Preparation of Compounds D-4a.

Ketoxime **1a** (75 mg) (1.0 equiv), HCHO (3 equiv), $CoCp^*COI_2$ (10 mol %), $AgSbF_6$ (20 mol %), and AcOH (50 mol %), dry TFE (2.0 mL) were taken in a 15-mL pressure tube. CD_3OD (10.0 equiv) were added to the reaction mixture. Then, diene **2** (3.0 equiv) was added followed by the addition of dry TFE (2.0 mL) and the reaction mixture was stirred under N_2 atmosphere for five minutes. Then, a screw cap was used to cover the tube and the reaction mixture was allowed to stir at 60 °C for 20 h. Then, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite, and the filtrate was concentrated. The crude residue was purified by column chromatography silica-gel 120-200 mesh, EtOAc:Hexane gave product **D-4a** in 65%. In the reaction, 13% of deuterium incorporation was observed at the free ortho position of functionalised oxime ether. This result also clearly reveals that the C-H bond activation as a key intermediate in the reaction as well as it is the reversible process.



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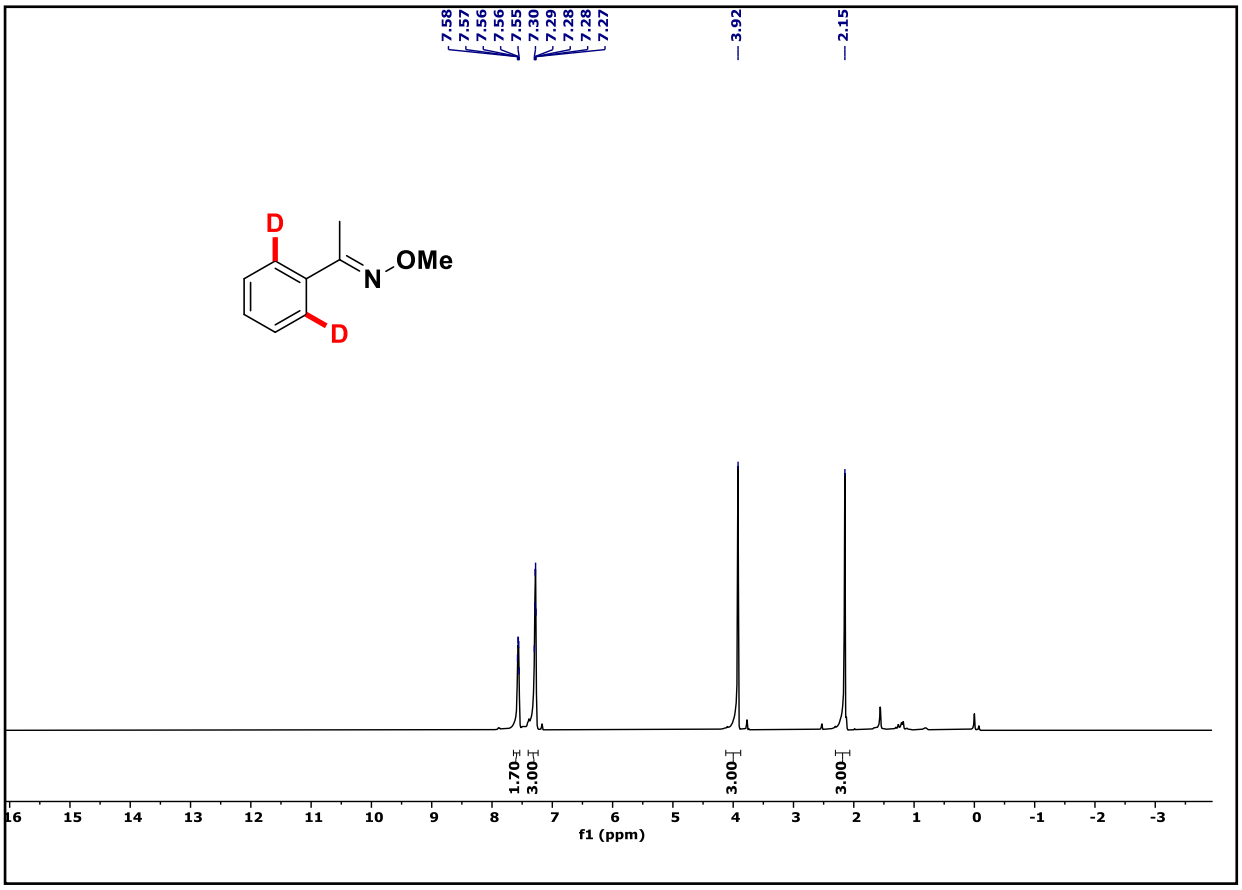
^{1}H Spectra of Compound **D-1a.**



^{1}H Spectra of Compound **D-4a.**

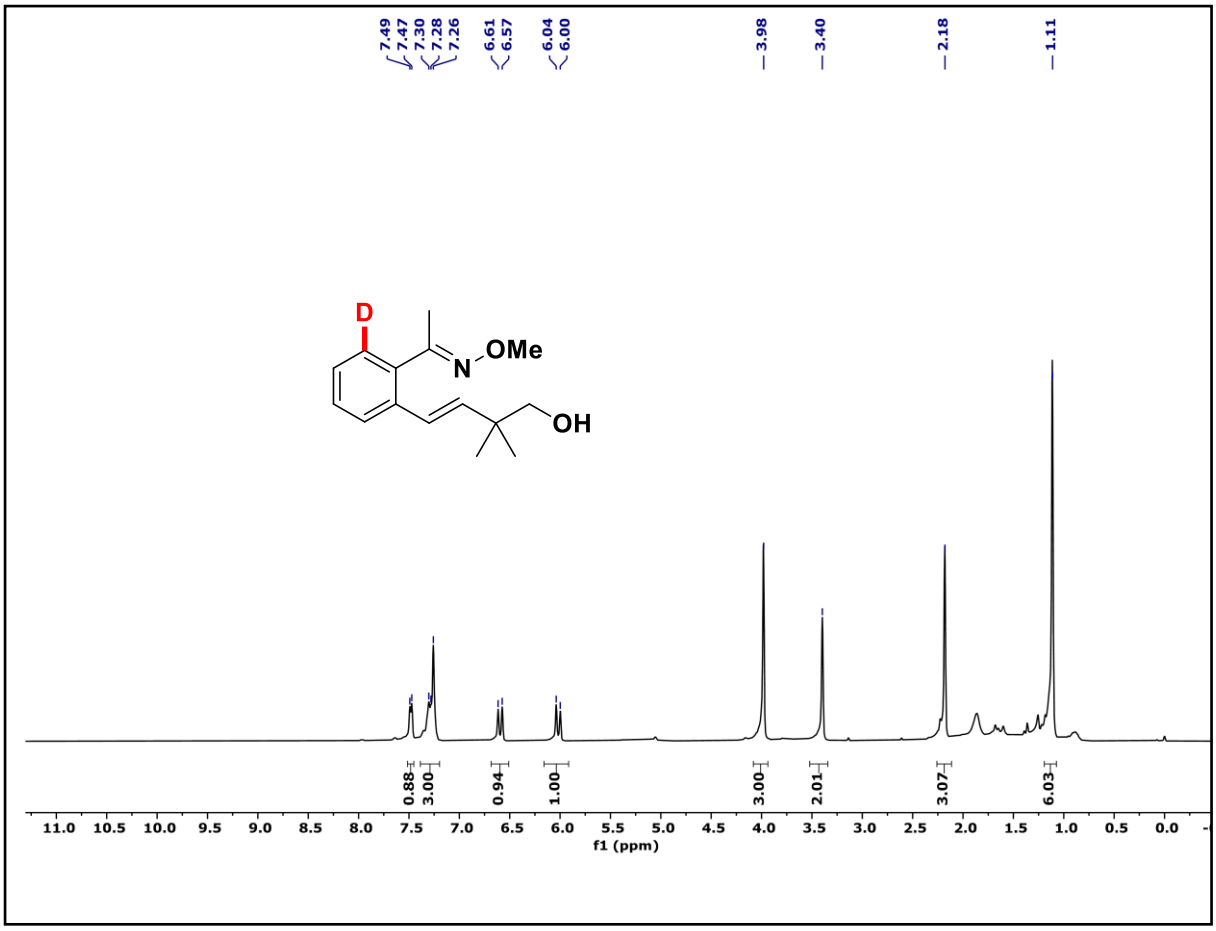


Table S1. Optimization Studies[a]

Sl. No	Solvent	Catalyst (10 mol %)/Additive (20 mol %)	Acid	Temperature	Yield (%)[b]
1	TFE	$[Co(Cp^*)(CH_3CN)_3)][SbF_6]_2$	AcOH	60 ˚C	25
2	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	AcOH	60 ˚C	40
3	TFE	$[Co(Cp^*)COI_2]$/ $AgBF_4$	AcOH	60 ˚C	25
4	TFE	$[Co(Cp^*)COI_2]$/ $AgNTf_2$	AcOH	60 ˚C	32
5	TFE	$[Co(Cp^*)COI_2]$/ AgOTf	AcOH	60 ˚C	18
6	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	PivOH	60 ˚C	20
3	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	HCO_2H	60 ˚C	trace
4	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Ad-COOH	60 ˚C	trace
5	**TFE**	**$[Co(Cp^*)COI_2]$/ $AgSbF_6$**	**Mes-COOH**	**60 ˚C**	**82**
6	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	PhCOOH	60 ˚C	40
	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	LiOAc	60 ˚C	trace
	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	NaOAc	60 ˚C	trace
9	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Na_2CO_3	60 ˚C	NR
10	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Na_2HPO_4	60 ˚C	NR
11	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	AgOAc	60 ˚C	NR
12	TFE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	$Cu(OAc)_2 \cdot H_2O$	60 ˚C	NR
13	1,4-Dioxane	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	AcOH	60 ˚C	31
14	1,4-Dioxane	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	NaOAc	60 ˚C	33
	1,4-Dioxane	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Mes-COOH	60 ˚C	35
16	DCE	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Mes-COOH	60 ˚C	NR
17	THF	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Mes-COOH	60 ˚C	38
18	MeOH	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Mes-COOH	60 ˚C	45
19	Toluene	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Mes-COOH	60 ˚C	30
20	IsoAmyl	$[Co(Cp^*)COI_2]$/ $AgSbF_6$	Mes-COOH	60 ˚C	25

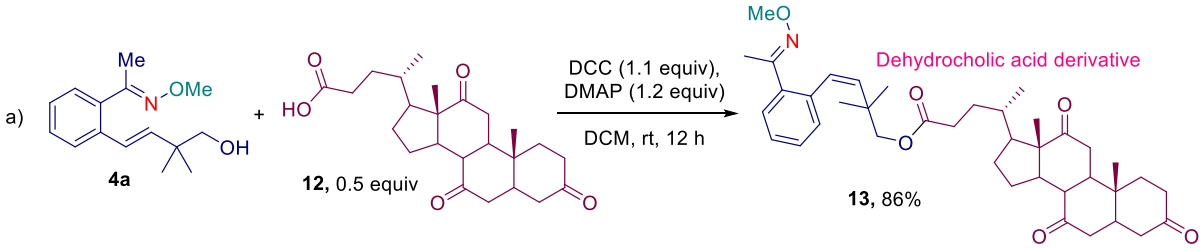
	alcohol				
21	CH_3CN	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	60 ˚C	42
22	DME	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	60 ˚C	40
23	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	80 ˚C	NR
24	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	100 ˚C	29
25	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	25 ˚C	52
26	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	60 ˚C[c]	50
27	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH	60 ˚C[d]	NR
28	TFE	$[RhCl_2Cp^*]_2$	AcOH (50 mol %)	60 ˚C	NR
29	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH (20 mol %)	60 ˚C	55
30	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH (1equiv)	60 ˚C	NR
31	TFE	$[Co(Cp^*)COI_2]/ AgSbF_6$	Mes-COOH (1.5equiv)	60 ˚C	30

[a] All reactions were carried out using substituted chalcone **1a** (50 mg), alkene **2a** (3.0 equiv), $[Cp^*Co(CO)I_2]$ (10 mol %), $AgSbF_6$ (20 mol %), Acid (50 mol %) in dry TFE under N_2 at 60 ˚C for 20 h. [b] Isolated yield. [c] (16 h) of reaction time. [d] (48 h) of reaction time.

Reference:

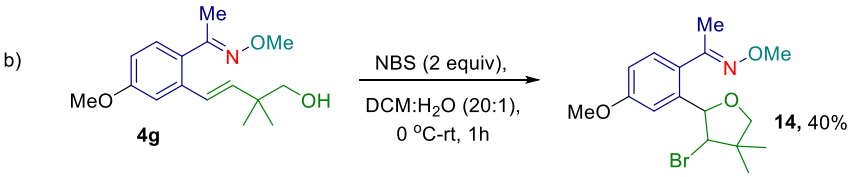
1. Sen, M.; Kalsi, D.; Sundararaju, B. Cobalt(III)-Catalyzed Dehydrative [4+2] Annulation of Oxime with Alkyne by C-H and N-OH Activation. *Chem. Eur. J.* **2015**, *21*, 15529.
2. Kornhaaß, C.; Ackermann, L. Cationic Ruthenium Catalysts for Alkyne Annulations with Oximes by C–H/N–O Functionalizations. *J. Org. Chem.* **2012**, *77*, 9190.
3. Aravindan, N.; Jeganmohan, M. A Short Total Synthesis of Benzo-phenanthridine Alkaloids *via* a Rhodium(III)-Catalyzed C−H Ring-Opening Reaction. *J. Org. Chem.* **2021**, *86*, 14826.
4. Vinayagam, V.; Mariappan, A.; Jana, M.; Jeganmohan, M. Rhodium(III)-Catalyzed Diastereoselective Ring-Opening of 7-Azabenzonorbornadienes with Aromatic Ketoximes: Synthesis of Benzophenanthridine Derivatives. *J. Org. Chem*. **2019**, *84*, 15590.

Synthesis for Compound 13.



A solution of **12** (0.5 equiv) and DMAP (1.2 equiv) in DCM (2.0 mL) was stirred at room temperature for 5 mins. Then the compound **4a** (50 mg, 1 equiv) in DCM (1 mL) was added to the reaction mixture and followed by the addition of DCC (1.1 equiv) was carried out. The resulting mixture was allowed to stir at room temperature for 12 h. Then the reaction was quenched with water and extracted twice with DCM (2 × 10 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. To get the pure compound **13**, the residue was purified by silica gel column chromatography with a gradient eluent of hexane/EtOAc.

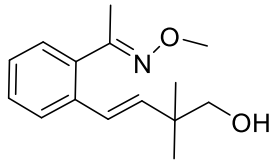
Synthesis for Compound 14.



A solution of *N*-bromosuccinimide (2.0 equiv) in DCM (1.0 mL) and H_2O (100 µL) was cooled to 0 °C. Then compound **4g** (50 mg, 1.0 equiv) in DCM (1.0 mL) was added dropwise and the resulting mixture was stirred for 15 minutes at 0 °C. The mixture was allowed to stir at room temperature for 1h. Then the mixture was extracted twice with DCM (2 × 50 mL). The combined organic phase was dried over Na_2SO_4 and the solvent was removed under reduced pressure. To get the pure compound **14**, the residue was purified by silica gel column chromatography with a gradient eluent of hexane/EtOAc.

Spectral Data of all Compounds:

(*E*)-1-(2-((*E*)-5-Hydroxy-4,4-dimethylpent-2-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (4a).



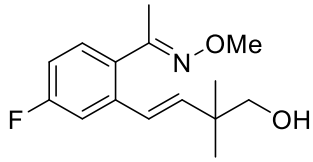
Colourless liquid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 67 mg of product was isolated and yield is 82%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.7 Hz, 1H), 7.22 – 7.16 (m, 3H), 6.53 (d, *J* = 16.2 Hz, 1H), 5.94 (dd, *J* = 16.2, 1.1 Hz, 1H), 3.91 (s, 3H), 3.33 (s, 2H), 2.10 (s, 3H), 1.04 (s, 6H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 156.5, 138.7, 136.1, 135.8, 128.6, 128.5, 127.6, 127.1, 126.5, 71.6, 61.8, 39.1, 23.9, 16.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}NO_2$ 248.1651; Found 248.1649.

(*E*)-1-(4-Fluoro-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (4b).

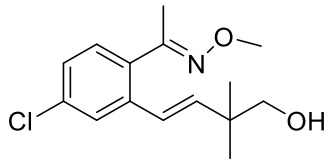


Colourless liquid; eluent (hexane, 12% ethyl acetate). The reaction scale is 50 mg, 56 mg of product was isolated and yield is 71%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 – 7.15 (m, 2H), 6.98 – 6.88 (m, 1H), 6.62 – 6.50 (m, 1H), 6.05 (d, J = 16.2 Hz, 1H), 3.97 (s, 3H), 3.40 (s, 2H), 2.16 (s, 3H), 1.11 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 157.2, 157.1, 141.0, 136.3, 133.7, 130.1, 127.5, 123.1, 122.5, 118.7, 117.1, 116.3, 109.3, 70.4, 38.1, 22.4, 21.8, 19.9.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{21}FNO_2$ 266.1556; Found 266.1548.

(*E*)-1-(4-Chloro-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)ethan-1-one*O*-methyl oxime (4c).



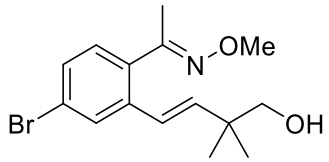
Colourless liquid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 61 mg of product was isolated and yield is 79%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.45 (s, 1H), 7.20 (t, *J* = 1.7 Hz, 2H), 6.54 (dd, *J* = 16.2, 1.9 Hz, 1H), 6.05 (dd, *J* = 16.2, 1.3 Hz, 1H), 3.97 (s, 3H), 3.40 (s, 2H), 2.15 (s, 3H), 1.11 (s, 6H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 155.6, 140.1, 138.0, 134.6, 134.2, 129.8, 127.0, 126.44, 126.41, 71.5, 61.8, 39.1, 23.8, 16.4.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{21}ClNO_2$ 282.1261; Found 282.1259.

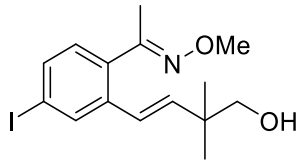
(*E*)-1-(4-Bromo-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (4d).



Colourless liquid; eluent (hexane, 15% ethyl acetate). The reaction scale is 50 mg, 42 mg of product was isolated and yield is 58%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.61 (d, J = 2.1 Hz, 1H), 7.36 (dd, J = 8.2, 2.1 Hz, 1H), 7.12 (d, J = 8.2 Hz, 1H), 6.53 (d, J = 16.2 Hz, 1H), 6.04 (d, J = 16.2 Hz, 1H), 3.97 (s, 3H), 3.41 (s, 2H), 2.14 (s, 3H), 1.11 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 155.6, 140.1, 138.2, 134.6, 130.05, 129.96, 129.4, 126.4, 122.8, 71.5, 61.9, 39.2, 23.8, 16.4.
HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{15}H_{20}BrNO_2$ 325.0677; Found 325.0707.

(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4-iodophenyl)ethan-1-one *O*-methyl oxime (4e).

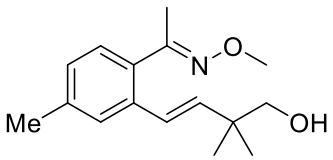


Colourless liquid; eluent (hexane, 18% ethyl acetate). The reaction scale is 50 mg, 51 mg of product was isolated and yield is 75%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 1.9 Hz, 1H), 7.62 – 7.52 (m, 1H), 6.98 (dd, J = 8.0, 2.1 Hz, 1H), 6.53 – 6.44 (m, 1H), 6.06 – 5.97 (m, 1H), 3.96 (s, 3H), 3.43 – 3.38 (m, 2H), 2.14 (s, 3H), 1.11 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 155.7, 140.0, 138.3, 135.9, 135.4, 135.3, 130.1, 126.3, 94.7, 71.5, 61.9, 39.2, 23.8, 16.3.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{21}NO_2I$ 374.0617; Found 374.0615.

(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4-methylphenyl)ethan-1-one *O*-methyl oxime (4f).



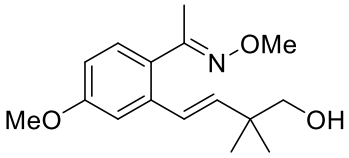
Colourless liquid; eluent (hexane, 22% ethyl acetate). The reaction scale is 50 mg, 50 mg of product was isolated and yield is 62%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (s, 1H), 7.16 (d, J = 7.8 Hz, 1H), 7.06 (d, J = 8.0 Hz, 1H), 6.59 (d, J = 16.1 Hz, 1H), 6.00 (d, J = 16.2 Hz, 1H), 3.97 (s, 3H), 3.39 (s, 2H), 2.35 (s, 3H), 2.16 (s, 3H), 1.11 (s, 6H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 156.5, 138.2, 135.9, 133.0, 129.0, 128.4, 127.9, 127.1, 125.9, 71.5, 61.7, 39.0, 23.8, 21.2, 16.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}NO_2$ 262.1807; Found 262.1797.

(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4-methoxyphenyl)ethan-1-one *O*-methyl oxime (4g).

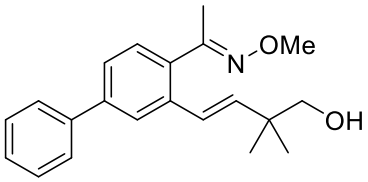


Colourless liquid; eluent (hexane, 25% ethyl acetate). The reaction scale is 50 mg, 61 mg of product was isolated and yield is 78%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.20 (d, J = 8.6 Hz, 1H), 6.98 (d, J = 2.7 Hz, 1H), 6.79 (dd, J = 8.5, 2.7 Hz, 1H), 6.60 (dd, J = 16.2, 1.4 Hz, 1H), 6.00 (d, J = 16.2 Hz, 1H), 3.96 (s, 3H), 3.82 (s, 3H), 3.39 (s, 2H), 2.15 (s, 3H), 1.11 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 159.7, 156.2, 138.7, 137.6, 129.8, 128.6, 127.9, 112.8, 111.7, 71.5, 61.7, 55.3, 39.0, 23.8, 16.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}NO_3$ 278.1756; Found 278.1752.

(*E*)-1-(3-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-[1,1'-biphenyl]-4-yl)ethan-1-one *O*-methyl oxime (4h).

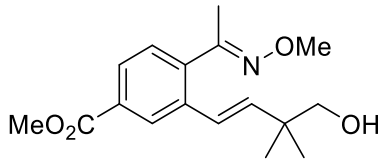


Colourless liquid; eluent (hexane, 68% ethyl acetate). The reaction scale is 50 mg, 36 mg of product was isolated and yield is 49%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68 (d, J = 1.9 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.50 – 7.43 (m, 3H), 7.37 (td, J = 8.4, 2.3 Hz, 2H), 6.68 (d, J = 16.3 Hz, 1H), 6.10 (d, J = 16.2 Hz, 1H), 4.01 (s, 3H), 3.44 (s, 2H), 2.23 (s, 3H), 1.15 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 155.3, 140.7, 139.6, 137.8, 135.5, 133.7, 128.0, 127.8, 126.9, 126.5, 126.2, 125.0, 124.4, 70.6, 60.8, 38.2, 22.9, 15.5.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}ON_2$ 279.1497; Found 279.1496.

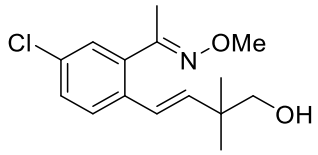
Methyl 3-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)-4-((*E*)-1-(methoxyimino)ethyl)benzoate (4i).



Colourless liquid; eluent (hexane, 28% ethyl acetate). The reaction scale is 50 mg, 35 mg of product was isolated and yield is 48%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (d, J = 1.8 Hz, 1H), 7.88 (dd, J = 8.1, 1.8 Hz, 1H), 7.33 (d, J = 7.9 Hz, 1H), 6.59 (d, J = 16.2 Hz, 1H), 6.14 (d, J = 16.2 Hz, 1H), 3.99 (s, 3H), 3.93 (s, 3H), 3.43 (s, 2H), 2.17 (s, 3H), 1.13 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 166.7, 155.8, 140.0, 136.5, 130.2, 128.7, 128.5, 127.9, 127.8, 126.7, 71.5, 61.9, 52.2, 39.2, 23.8, 20.0, 16.3.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{23}NNaO_4$ 328.1525; Found 328.1527.

(*E*)-1-(5-Chloro-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (4j).

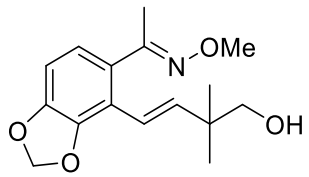


Colourless liquid; eluent (hexane, 15% ethyl acetate). The reaction scale is 50 mg, 35 mg of product was isolated and yield is 45%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 7.9, 0.9 Hz, 1H), 7.20 – 7.18 (m, 2H), 6.46 (d, J = 16.2 Hz, 1H), 5.95 (d, J = 16.2 Hz, 1H), 3.91 (s, 3H), 3.35 (s, 2H), 2.08 (s, 3H), 1.05 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 154.4, 138.4, 136.3, 133.7, 131.8, 127.7, 127.5, 126.9, 125.5, 70.6, 60.9, 38.1, 22.8, 15.4.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}N_4O$ 282.1261; Found 282.1255.

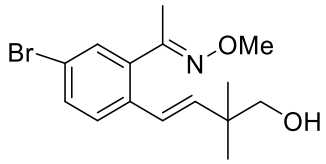
(*E*)-1-(6-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)benzo[d][1,3]dioxol-5-yl)ethan-1-one *O*-methyl oxime (4k).



Colourless liquid; eluent (hexane, 26% ethyl acetate). The reaction scale is 50 mg, 60 mg of product was isolated and yield is 80%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.78 (d, J = 8.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 6.40 – 6.32 (m, 2H), 6.00 (s, 2H), 3.96 (s, 3H), 3.39 (s, 2H), 2.13 (s, 3H), 1.11 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 156.3, 147.7, 145.3, 142.3, 130.5, 122.7, 121.8, 118.7, 106.6, 101.0, 71.5, 61.7, 39.4, 23.6, 16.9.
HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{22}NO_4$ 292.1549; Found 292.1550.

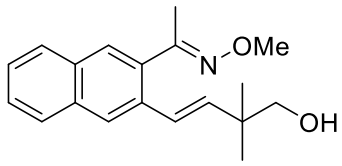
(*E*)-1-(5-Bromo-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (4l).



Brown liquid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 38 mg of product was isolated and yield is 52%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.33 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.3 Hz, 1H), 6.42 (d, J = 16.2 Hz, 1H), 5.96 (d, J = 16.3 Hz, 1H), 3.90 (d, J = 2.3 Hz, 3H), 3.32 (s, 2H), 2.07 (s, 3H), 1.03 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 155.4, 139.6, 137.5, 135.2, 131.6, 131.3, 128.1, 126.4, 120.7, 71.5, 62.0, 39.1, 23.8, 16.5.
HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}FN_3O$ 264.1660; Found 264.1668.

(*E*)-1-(3-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)naphthalen-2-yl)ethan-1-one *O*-methyl oxime (4m)



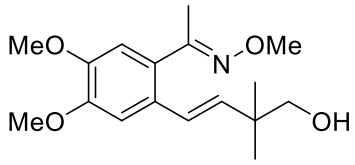
Colourless liquid; eluent (hexane, 28% ethyl acetate). The reaction scale is 50 mg, 51 mg of product was isolated and yield is 68%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (s, 1H), 7.74 – 7.65 (m, 3H), 7.36 (dt, J = 7.7, 3.7 Hz, 2H), 6.59 (d, J = 16.1 Hz, 1H), 6.06 (d, J = 16.1 Hz, 1H), 3.94 (s, 3H), 3.35 (s, 2H), 2.16 (s, 3H), 1.07 (s, 6H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 156.9, 139.1, 134.4, 134.1, 133.3, 132.2, 128.5, 127.9, 127.8, 127.5, 126.7, 126.0, 125.5, 71.6, 61.8, 39.1, 23.8, 16.8.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{24}NO_2$ 298.1807; Found 298.1800.

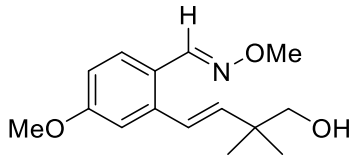
(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4,5-dimethoxyphenyl)ethan-1-one *O*-methyl oxime (4n).



Colourless liquid; eluent (hexane, 26% ethyl acetate). The reaction scale is 50 mg, 56 mg of product was isolated and yield is 76%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (s, 1H), 6.74 (s, 1H), 6.52 (d, J = 16.2 Hz, 1H), 5.91 (d, J = 16.2 Hz, 1H), 3.96 (s, 3H), 3.90 (s, 3H), 3.87 (s, 3H), 3.39 (s, 2H), 2.15 (s, 3H), 1.10 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 156.4, 149.3, 148.3, 136.9, 129.0, 128.7, 127.2, 111.5, 109.2, 71.6, 61.7, 56.0, 38.9, 29.6, 24.0, 16.8.
HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{26}NO_4$ 308.1862; Found 308.1862.

(*E*)-2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4-methoxybenzaldehyde *O*-methyl oxime (6a).



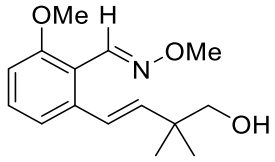
Colourless liquid; eluent (hexane, 14% ethyl acetate). The reaction scale is 50 mg, 51 mg of product was isolated and yield is 62%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.52 (d, J = 8.6 Hz, 1H), 6.91 (d, J = 2.7 Hz, 1H), 6.85 – 6.78 (m, 2H), 5.97 (d, J = 16.1 Hz, 1H), 3.96 (s, 3H), 3.84 (s, 3H), 3.44 (s, 2H), 1.14 (s, 6H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 160.6, 148.0, 140.5, 139.0, 129.9, 127.0, 121.9, 113.2, 112.1, 71.4, 61.8, 55.3, 39.2, 24.0.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}NO_3$ 264.1600; Found 264.1572.

(*E*)-2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-6-methoxybenzaldehyde *O*-methyl oxime (6b).

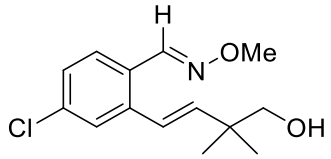


Colourless liquid; eluent (hexane, 17% ethyl acetate). The reaction scale is 50 mg, 55 mg of product was isolated and yield is 68%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (s, 1H), 7.26 (d, J = 6.3 Hz, 1H), 7.05 (d, J = 7.8 Hz, 1H), 6.98 (d, J = 16.3 Hz, 1H), 6.79 (d, J = 8.3 Hz, 1H), 5.89 (d, J = 16.2 Hz, 1H), 3.98 (s, 3H), 3.83 (s, 3H), 3.41 (s, 2H), 1.14 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 158.5, 146.1, 146.0, 139.0, 130.3, 130.2, 119.8, 119.7, 118.0, 71.4, 62.2, 61.6, 56.0, 55.5, 39.1.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{22}NO_3$ 264.1600; Found 264.1600.

(*E*)-4-Chloro-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)benzaldehyde *O*-methyl oxime (6c).



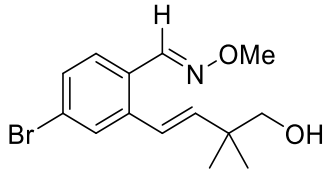
Colourless liquid; eluent (hexane, 12% ethyl acetate). The reaction scale is 50 mg, 52 mg of product was isolated and yield is 65%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.55 (d, J = 8.3 Hz, 1H), 7.39 (d, J = 2.1 Hz, 1H), 7.24 – 7.16 (m, 1H), 6.73 (d, J = 16.1 Hz, 1H), 6.02 (d, J = 16.1 Hz, 1H), 3.98 (s, 3H), 3.44 (s, 2H), 1.14 (s, 6H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 147.0, 141.9, 138.8, 135.5, 129.1, 127.5, 127.3, 127.0, 125.3, 71.4, 62.1, 39.3, 23.8.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}ClNO_2$ 268.1104; Found 268.1096.

(*E*)-4-Bromo-2-((*E*)-4-hydroxy-3,3-dimethylbut-1-en-1-yl)benzaldehyde *O*-methyl oxime (6d).



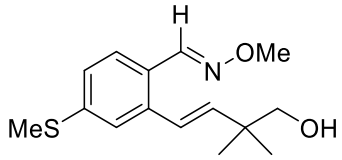
Colourless liquid; eluent (hexane, 15% ethyl acetate). The reaction scale is 50 mg, 35 mg of product was isolated and yield is 48%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.25 (s, 1H), 7.56 (d, J = 2.0 Hz, 1H), 7.48 (d, J = 8.3 Hz, 1H), 7.36 (dd, J = 8.4, 2.1 Hz, 1H), 6.73 (d, J = 16.1 Hz, 1H), 6.02 (d, J = 16.2 Hz, 1H), 3.98 (s, 3H), 3.45 (s, 2H), 1.14 (s, 6H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 147.0, 142.0, 139.1, 130.2, 130.0, 129.3, 128.0, 125.3, 123.9, 71.5, 62.1, 39.3, 23.9.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}Br\ NO_2$ 312.0599; Found 312.0630.

(*E*)-2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4-(methylthio)benzaldehyde *O*-methyl oxime (6e)

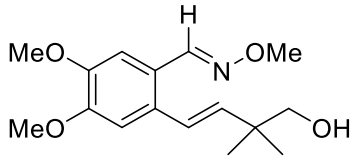


Colourless liquid; eluent (hexane, 22% ethyl acetate). The reaction scale is 50 mg, 48 mg of product was isolated and yield is 62%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.26 (s, 1H), 7.52 (d, J = 8.3 Hz, 1H), 7.25 (d, J = 2.0 Hz, 1H), 7.11 (dd, J = 8.3, 2.1 Hz, 1H), 6.78 (d, J = 16.1 Hz, 1H), 5.98 (d, J = 16.1 Hz, 1H), 3.97 (s, 3H), 3.45 (s, 2H), 2.51 (s, 3H), 1.14 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 147.8, 141.0, 137.8, 130.4, 128.5, 126.5, 125.9, 125.0, 124.8, 71.5, 62.0, 39.2, 24.0, 15.5.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{215}H_{22}NO_2S$ 280.1371; Found 280.1373.

(*E*)-2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4,5-dimethoxybenzaldehyde *O*-methyl oxime (6f).

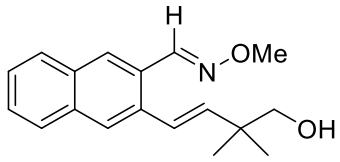


Colourless Solid; eluent (hexane, 28% ethyl acetate). The reaction scale is 50 mg, 34 mg of product was isolated and yield is 45%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.20 (s, 1H), 6.86 (s, 1H), 6.71 (d, J = 16.0 Hz, 1H), 5.92 (d, J = 16.1 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 3.91 (s, 3H), 3.44 (s, 2H), 1.14 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 150.4, 148.4, 147.1, 139.4, 130.8, 125.4, 121.7, 109.0, 109.0, 71.6, 61.9, 55.9, 55.9, 39.2, 24.0.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{16}H_{24}NO_4$ 294.1705; Found 294.1700.

(*E*)-3-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-2-naphthaldehyde *O*-methyl oxime (6g).

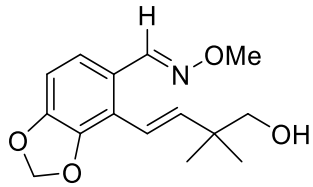


Colourless Solid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 32 mg of product was isolated and yield is 42%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.99 (s, 1H), 7.84 – 7.77 (m, 3H), 7.46 (ddd, J = 12.8, 7.9, 1.3 Hz, 2H), 6.97 (d, J = 16.0 Hz, 1H), 6.05 (d, J = 16.0 Hz, 1H), 4.03 (s, 3H), 3.48 (s, 2H), 1.19 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 149.1, 140.2, 135.0, 133.8, 132.2, 128.8, 128.1, 128.0, 127.7, 127.5, 127.2, 126.2, 126.1, 71.5, 62.0, 39.2, 24.1.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{22}N O_2$ 284.1651; Found 284.1642.

(*E*)-4-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)benzo[d][1,3]dioxole-5-carbaldehyde *O*-methyl oxime (6h).

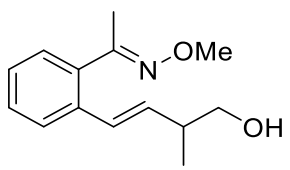


Colourless liquid; eluent (hexane, 25% ethyl acetate). The reaction scale is 50 mg, 46 mg of product was isolated and yield is 59%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.21 (s, 1H), 7.11 (d, J = 8.1 Hz, 1H), 6.69 (dd, J = 8.1, 1.1 Hz, 1H), 6.63 (dd, J = 16.5, 1.1 Hz, 1H), 6.31 (dd, J = 16.5, 0.8 Hz, 1H), 6.01 (s, 2H), 3.95 (s, 3H), 3.42 (s, 2H), 1.13 (s, 6H).
^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 148.5, 148.3, 145.4, 143.7, 123.6, 123.1, 120.8, 119.5, 107.0, 101.2, 71.4, 61.8, 39.5, 23.7.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}NO_4$ 278.1392; Found 278.1392.

(*E*)-1-(2-((*E*)-4-Hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (8aa).

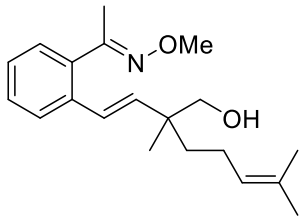


Colourless liquid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 51 mg of product was isolated and yield is 65%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J = 7.7 Hz, 1H), 7.27 – 7.20 (m, 1H), 7.19 – 7.13 (m, 2H), 6.56 (d, J = 15.9 Hz, 1H), 5.89 (dd, J = 15.9, 7.8 Hz, 1H), 3.90 (s, 3H), 3.53 – 3.37 (m, 2H), 2.50 – 2.38 (m, 1H), 2.10 (s, 3H), 1.02 (d, J = 6.8 Hz, 3H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 156.7, 135.8, 134.4, 129.4, 128.6, 128.5, 128.4, 127.2, 126.4, 67.2, 61.7, 40.1, 16.7, 16.3.
HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{20}NO_2$ 234.1494; Found 234.1484.

(*E*)-1-(2-((*E*)-3-(Hydroxymethyl)-3,7-dimethylocta-1,6-dien-1-yl)phenyl)ethan-1-one *O*-methyl oxime (8ab).

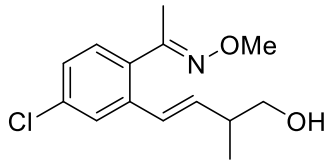


Colourless liquid; eluent (hexane, 14% ethyl acetate). The reaction scale is 50 mg, 58 mg of product was isolated and yield is 55%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.48 (dd, J = 7.6, 1.2 Hz, 1H), 7.33 – 7.23 (m, 3H), 6.59 (d, J = 16.3 Hz, 1H), 5.98 (d, J = 16.3 Hz, 1H), 5.15 – 5.08 (m, 1H), 3.98 (s, 3H), 3.48 – 3.38 (m, 2H), 2.19 (s, 3H), 1.98 (td, J = 12.6, 6.1 Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.44 (ddd, J = 17.3, 10.9, 5.7 Hz, 2H), 1.13 (s, 3H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 156.5, 137.7, 136.2, 135.8, 131.5, 128.7, 128.6, 128.4, 127.1, 126.5, 124.6, 70.5, 61.8, 42.3, 37.8, 25.6, 22.7, 20.3, 17.6, 16.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{30}NO_2$ 316.2277; Found 316.2277.

(*E*)-1-(4-Chloro-2-((*E*)-4-hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (8ca).



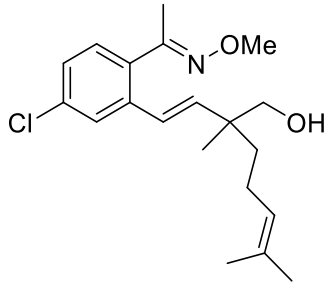
Colourless liquid; eluent (hexane, 18% ethyl acetate). The reaction scale is 50 mg, 41 mg of product was isolated and yield is 55%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (s, 1H), 7.20 (d, J = 5.3 Hz, 2H), 6.58 (d, J = 15.9 Hz, 1H), 6.00 (dd, J = 15.9, 7.8 Hz, 1H), 3.97 (s, 3H), 3.62 – 3.46 (m, 2H), 2.59 – 2.48 (m, 1H), 2.15 (s, 3H), 1.10 (d, J = 6.8 Hz, 3H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 155.7, 137.6, 135.8, 134.6, 134.2, 129.8, 128.3, 127.1, 126.3, 67.2, 61.9, 40.2, 16.6, 16.2.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{19}ClNO_2$ 268.1104; Found 268.1095.

(*E*)-1-(4-Chloro-2-((*E*)-3-(hydroxymethyl)-3,7-dimethylocta-1,6-dien-1-yl)phenyl)ethan-1-one *O*-methyl oxime (8cb).

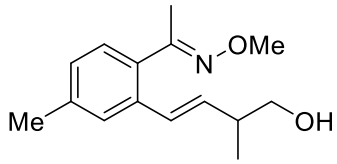


Colourless liquid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 32 mg of product was isolated and yield is 32%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.44 (d, J = 1.9 Hz, 1H), 7.26 – 7.18 (m, 2H), 6.53 (d, J = 16.2 Hz, 1H), 6.01 (d, J = 16.3 Hz, 1H), 5.11 (tt, J = 5.7, 1.6 Hz, 1H), 3.97 (s, 3H), 3.47 (s, 1H), 3.41 (d, J = 10.7 Hz, 1H), 2.15 (s, 3H), 1.97 (d, J = 15.4 Hz, 2H), 1.68 (s, 3H), 1.59 (s, 3H), 1.48 – 1.42 (m, 2H), 1.13 (s, 3H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 155.5, 139.1, 138.0, 134.6, 134.1, 131.6, 129.8, 127.5, 127.1, 126.5, 124.5, 70.4, 61.9, 42.4, 37.7, 25.7, 22.7, 20.2, 17.6, 16.5.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{29}ClNO_2$ 350.1887; Found 350.1855.

(*E*)-1-(4-Chloro-2-((*E*)-4-hydroxy-3-methylbut-1-en-1-yl)phenyl)ethan-1-one *O*-methyl oxime (8fa).



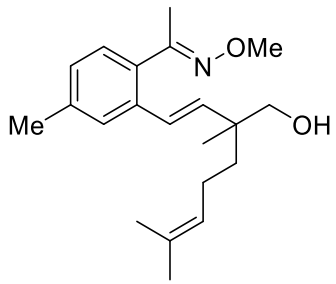
Colourless liquid; eluent (hexane, 22% ethyl acetate). The reaction scale is 50 mg, 38 mg of product was isolated and yield is 50%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (s, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.06 (d, J = 7.8 Hz, 1H), 6.62 (d, J = 15.9 Hz, 1H), 5.95 (dd, J = 15.8, 7.9 Hz, 1H), 3.96 (s, 3H), 3.56 (dd, J = 10.7, 5.5 Hz, 1H), 3.47 (dd, J = 10.6, 7.6 Hz, 1H), 2.51 (p, J = 7.0 Hz, 1H), 2.34 (s, 3H), 2.16 (s, 3H), 1.09 (d, J = 6.8 Hz, 3H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 156.7, 138.4, 135.6, 134.1, 133.0, 129.6, 128.4, 127.9, 127.0, 67.2, 61.6, 40.1, 21.1, 16.7, 16.3.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}NNaO_2$ 270.1470; Found 270.1501.

(*E*)-1-(2-((*E*)-3-(Hydroxymethyl)-3,7-dimethylocta-1,6-dien-1-yl)-4-methylphenyl)ethan-1-one *O*-methyl oxime (8fb).

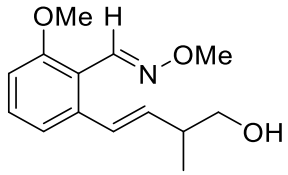


Colourless liquid; eluent (hexane, 18% ethyl acetate). The reaction scale is 50 mg, 64 mg of product was isolated and yield is 64%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (t, J = 9.8 Hz, 1H), 7.16 (t, J = 8.1 Hz, 1H), 7.06 (t, J = 7.3 Hz, 1H), 6.57 (t, J = 15.7 Hz, 1H), 5.98 (dd, J = 23.8, 16.3 Hz, 1H), 5.08 (dt, J = 21.4, 7.8 Hz, 1H), 4.17 (s, 1H), 3.96 (d, J = 2.5 Hz, 3H), 3.70 (d, J = 8.7 Hz, 1H), 3.44 (d, J = 23.9 Hz, 1H), 2.39 – 2.28 (m, 6H), 2.15 (d, J = 24.8 Hz, 3H), 1.67 (d, J = 15.7 Hz, 3H), 1.57 (d, J = 18.0 Hz, 3H), 1.19 (s, 3H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 156.5, 138.5, 137.3, 135.6, 129.0, 128.7, 128.5, 128.1, 127.1, 124.7, 124.2, 73.2, 70.6, 61.8, 40.3, 37.8, 25.7, 22.7, 21.2, 20.2, 17.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{32}NO_2$ 330.2433; Found 330.2428.

(*E*)-2-((*E*)-4-Hydroxy-3-methylbut-1-en-1-yl)-6-methoxybenzaldehyde *O*-methyl oxime (9ba).



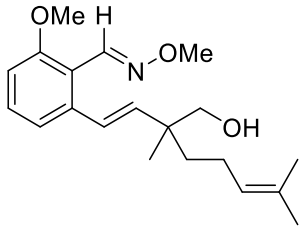
Colourless liquid; eluent (hexane, 22% ethyl acetate). The reaction scale is 50 mg, 42 mg of product was isolated and yield is 55%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 7.29 (d, J = 8.4 Hz, 1H), 7.12 – 6.96 (m, 2H), 6.80 (d, J = 8.4 Hz, 1H), 5.86 (dd, J = 16.0, 7.9 Hz, 1H), 3.97 (s, 3H), 3.83 (s, 3H), 3.62 (dd, J = 10.8, 4.7 Hz, 1H), 3.45 (t, J = 9.4 Hz, 1H), 2.57 (s, 1H), 1.11 (d, J = 6.9 Hz, 3H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 158.4, 146.1, 138.6, 134.5, 131.8, 130.2, 119.7, 117.8, 109.3, 67.2, 61.9, 55.7, 39.9, 16.1.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{20}NO_3$ 250.1443; Found 250.1435.

(*E*)-2-((*E*)-3-(Hydroxymethyl)-3,7-dimethylocta-1,6-dien-1-yl)-6-methoxybenzaldehyde *O*-methyl oxime (9bb).

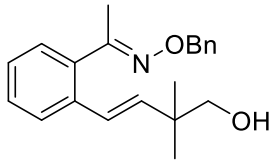


Colourless liquid; eluent (hexane, 22% ethyl acetate). The reaction scale is 50 mg, 48 mg of product was isolated and yield is 48%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 7.27 (d, J = 8.2 Hz, 1H), 7.04 (d, J = 7.7 Hz, 1H), 6.94 (d, J = 16.2 Hz, 1H), 6.80 (d, J = 8.3 Hz, 1H), 5.89 – 5.80 (m, 1H), 5.14 (d, J = 7.4 Hz, 1H), 3.97 (s, 3H), 3.83 (s, 3H), 3.49 (d, J = 10.8 Hz, 1H), 3.39 (d, J = 10.9 Hz, 1H), 2.10 – 1.94 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.44 (ddd, J = 18.1, 10.8, 6.2 Hz, 2H), 1.16 (s, 3H).
^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 158.4, 146.1, 139.1, 137.7, 131.4, 131.0, 130.3, 124.7, 119.8, 117.7, 109.2, 70.3, 61.8, 55.7, 42.4, 38.1, 25.7, 22.7, 20.5, 17.6.

HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{30}NO_3$ 332.2226; Found 332.2216.

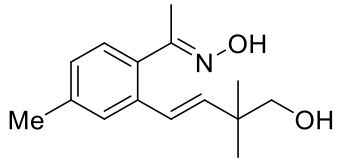
(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)ethan-1-one *O*-benzyl oxime (11a)



Colourless liquid; eluent (hexane, 18% ethyl acetate). The reaction scale is 50 mg, 46 mg of product was isolated and yield is 65%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47 (d, J = 7.7 Hz, 1H), 7.43 – 7.39 (m, 2H), 7.38 – 7.34 (m, 2H), 7.32 – 7.27 (m, 2H), 7.26 – 7.23 (m, 2H), 6.57 (d, J = 16.3 Hz, 1H), 6.02 (d, J = 16.2 Hz, 1H), 5.24 (s, 2H), 3.38 (s, 2H), 2.22 (s, 3H), 1.08 (s, 6H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 157.3, 138.9, 138.1, 136.1, 136.0, 128.7, 128.6, 128.3, 127.9, 127.7, 127.4, 127.1, 126.5, 76.0, 71.6, 39.0, 23.8, 17.1.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{21}H_{25}O_2NaN$ 346.1783; Found 346.1783.

(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)-4-methylphenyl)ethan-1-one oxime (11b)

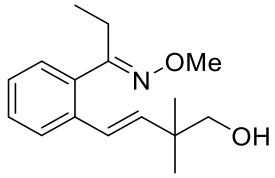


Colourless liquid; eluent (hexane, 28% ethyl acetate). The reaction scale is 50 mg, 50 mg of product was isolated and yield is 58%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, J = 7.7 Hz, 1H), 7.21 (d, J = 17.1 Hz, 1H), 6.77 (s, 1H), 6.50 (d, J = 16.2 Hz, 1H), 6.23 (s, 1H), 5.86 (d, J = 16.3 Hz, 1H), 3.32 (s, 2H), 2.27 (s, 3H), 2.18 (s, 3H), 1.03 (s, 6H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 157.1, 138.9, 136.5, 135.4, 128.8, 128.5, 128.2, 127.1, 126.8, 71.3, 39.0, 23.8, 21.1, 20.0, 16.1.
HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{21}NNaO_2$ 270.1470; Found 270.1482.

(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)propan-1-one *O*-methyl oxime (11c).



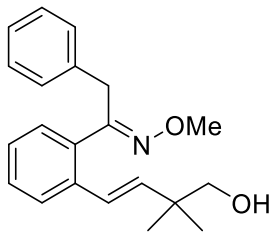
Colourless liquid; eluent (hexane, 18% ethyl acetate). The reaction scale is 50 mg, 58 mg of product was isolated and yield is 72%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 – 7.47 (m, 1H), 7.32 – 7.21 (m, 3H), 6.56 (d, J = 16.2 Hz, 1H), 6.04 (d, J = 16.2 Hz, 1H), 3.95 (s, 3H), 3.40 (s, 2H), 2.67 (d, J = 7.6 Hz, 2H), 1.11 (s, 6H), 1.00 (t, J = 7.6 Hz, 3H).

^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 161.6, 138.6, 136.4, 134.7, 128.7, 128.6, 127.3, 127.0, 126.2, 71.6, 61.7, 39.1, 23.8, 23.3, 10.1.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{23}NNaO_2$ 284.1626; Found 284.1584.

(*E*)-1-(2-((*E*)-4-Hydroxy-3,3-dimethylbut-1-en-1-yl)phenyl)-2-phenylethan-1-one *O*-methyl oxime (11d).



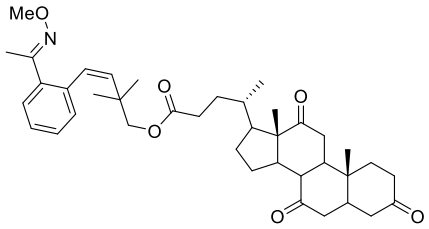
Colourless liquid; eluent (hexane, 16% ethyl acetate). The reaction scale is 50 mg, 34 mg of product was isolated and yield is 47%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (d, J = 7.8 Hz, 1H), 7.18 (s, 1H), 7.15 – 7.06 (m, 5H), 7.06 – 7.01 (m, 2H), 6.34 (d, J = 16.3 Hz, 1H), 5.87 (d, J = 16.3 Hz, 1H), 3.97 (s, 2H), 3.93 (s, 3H), 3.28 (s, 2H), 0.98 (s, 6H).

^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 157.8, 138.4, 136.6, 135.9, 134.6, 129.2, 128.8, 128.6, 128.4, 128.4, 128.3, 127.6, 126.9, 126.4, 126.3, 71.5, 61.8, 39.0, 36.3, 29.7, 23.8.

HRMS (ESI-TOF) m/z: $[M]^+$ Calcd for $C_{21}H_{25}NO_2$ 323.1885; Found 323.1925.

(*Z*)-4-(2-((*E*)-1-(methoxyimino)ethyl)phenyl)-2,2-dimethylbut-3-en-1-yl (4S)-4-((10R, 13S)-10,13-dimethyl-3,7,12-trioxohexadecahydro-*1H*-cyclopenta[a]phenanthren-17-yl)pentanoate (13).

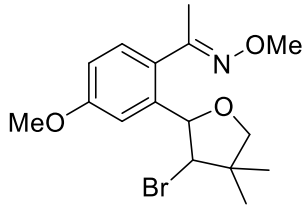


Yellow Solid; eluent (hexane, 12% ethyl acetate). The reaction scale is 50 mg, 183 mg of product was isolated and yield is 86%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J = 7.9 Hz, 1H), 7.28 (d, J = 23.0 Hz, 3H), 6.55 (d, J = 16.3 Hz, 1H), 6.09 (d, J = 16.3 Hz, 1H), 3.96 (d, J = 18.1 Hz, 5H), 2.89 (dt, J = 20.7, 10.8 Hz, 4H), 2.38 – 2.27 (m, 6H), 2.15 (s, 4H), 2.02 (d, J = 14.5 Hz, 5H), 1.81 (t, J = 9.1 Hz, 5H), 1.40 (s, 6H), 1.15 (s, 6H), 1.06 (d, J = 15.2 Hz, 5H), 0.84 (s, 3H).
^{13}C{1H} NMR (101 MHz, $CDCl_3$): δ 211.9, 209.1, 208.6, 174.0, 156.6, 154.0, 138.1, 135.9, 128.6, 128.4, 127.0, 126.3, 126.1, 71.9, 61.7, 56.7, 51.6, 48.8, 46.6, 45.3, 44.8, 42.6, 38.5, 37.1, 36.3, 35.8, 35.3, 35.1, 31.3, 30.3, 27.4, 25.0, 24.2, 21.7, 18.4, 16.6, 11.7.

HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{39}H_{54}NO_6$ 632.3951; Found 632.3935.

(*E*)-1-(2-(3-Bromo-4,4-dimethyltetrahydrofuran-2-yl)-4-methoxyphenyl)ethan-1-one *O*-methyl oxime (14).

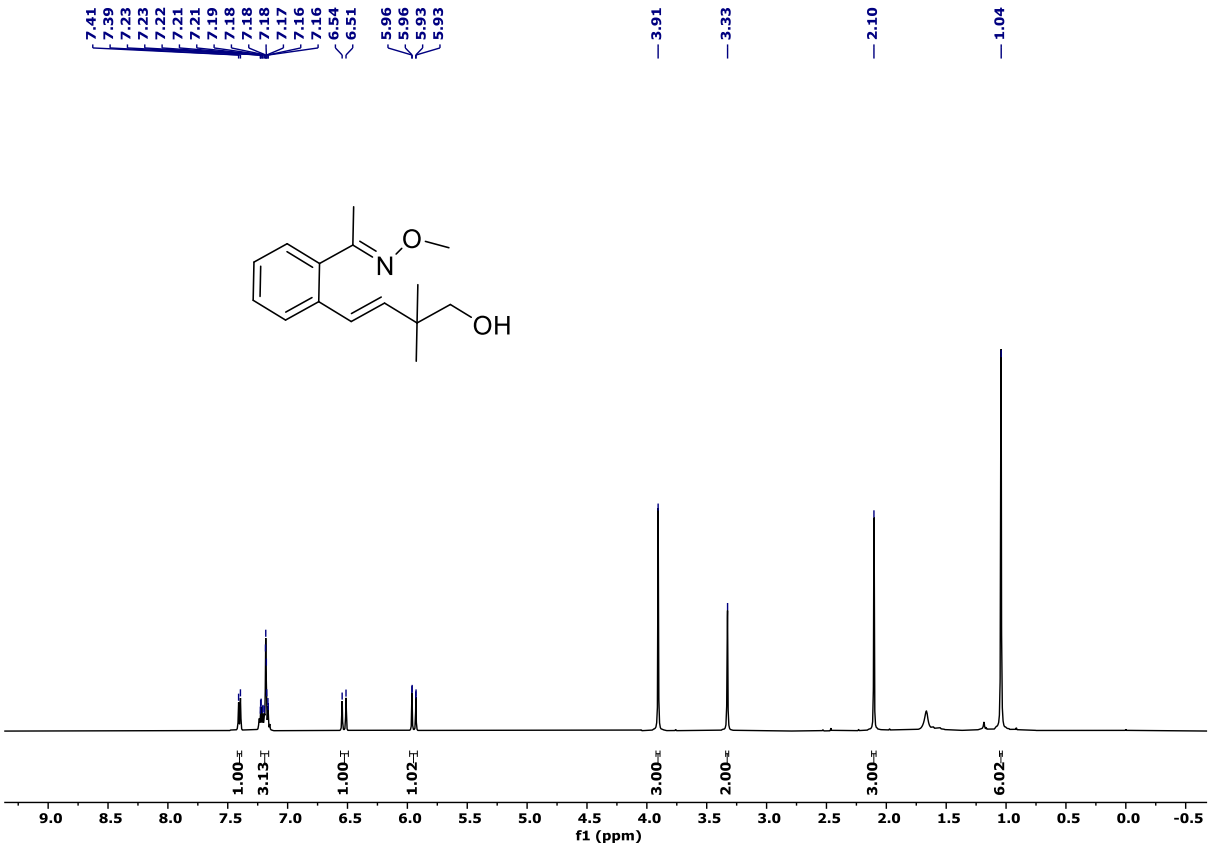


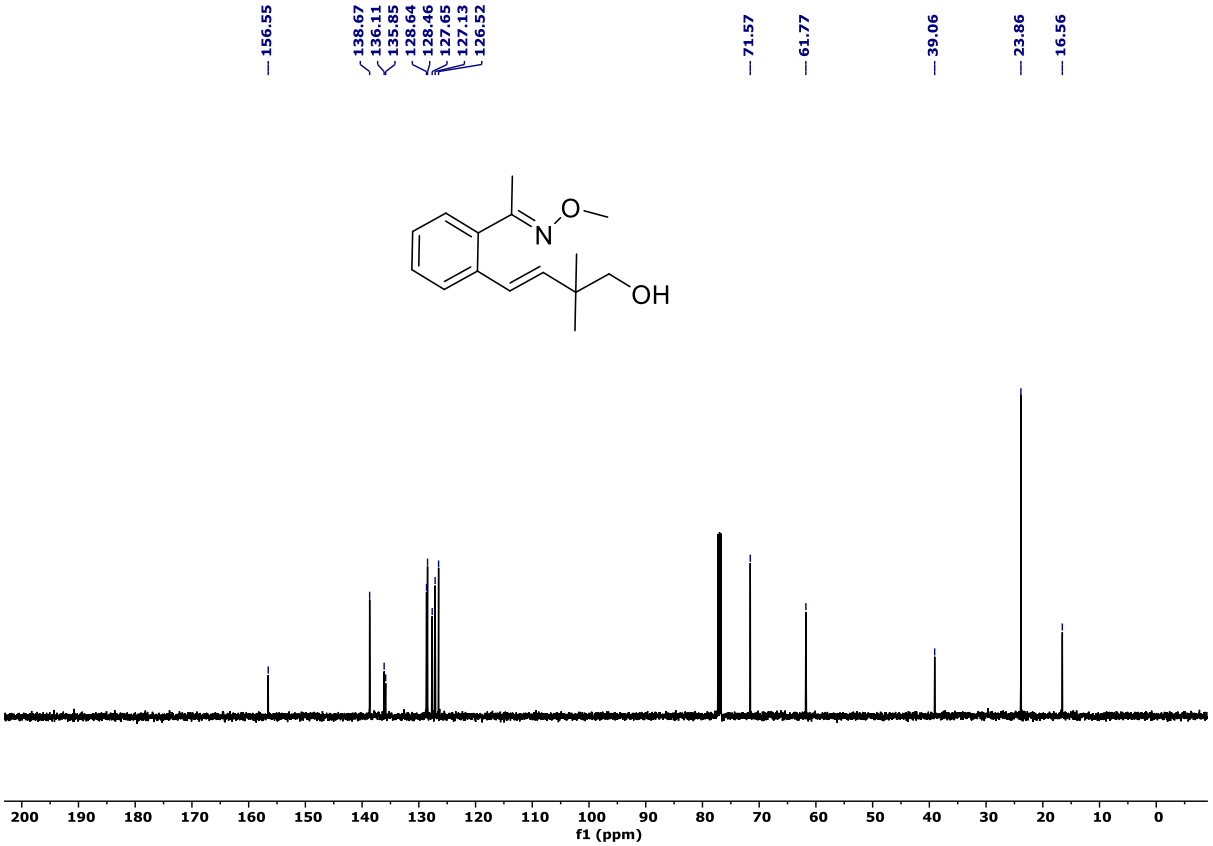
Colourless liquid; eluent (hexane, 4% ethyl acetate). The reaction scale is 50 mg, 25 mg of product was isolated and yield is 40%.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.13 (d, J = 8.4 Hz, 1H), 6.96 (d, J = 2.7 Hz, 1H), 6.85 (dd, J = 8.5, 2.7 Hz, 1H), 5.20 (d, J = 9.2 Hz, 1H), 4.10 (d, J = 9.5 Hz, 1H), 3.93 (s, 3H), 3.85 (d, J = 8.4 Hz, 1H), 3.82 (s, 3H), 3.79 (d, J = 7.2 Hz, 1H), 2.16 (s, 3H), 1.23 (s, 3H), 1.12 (s, 3H).
^{13}C{1H} NMR (126 MHz, $CDCl_3$): δ 159.4, 157.3, 139.0, 130.1, 129.8, 113.5, 113.3, 84.5, 78.4, 64.5, 61.6, 55.4, 42.7, 23.7, 23.4, 17.8.

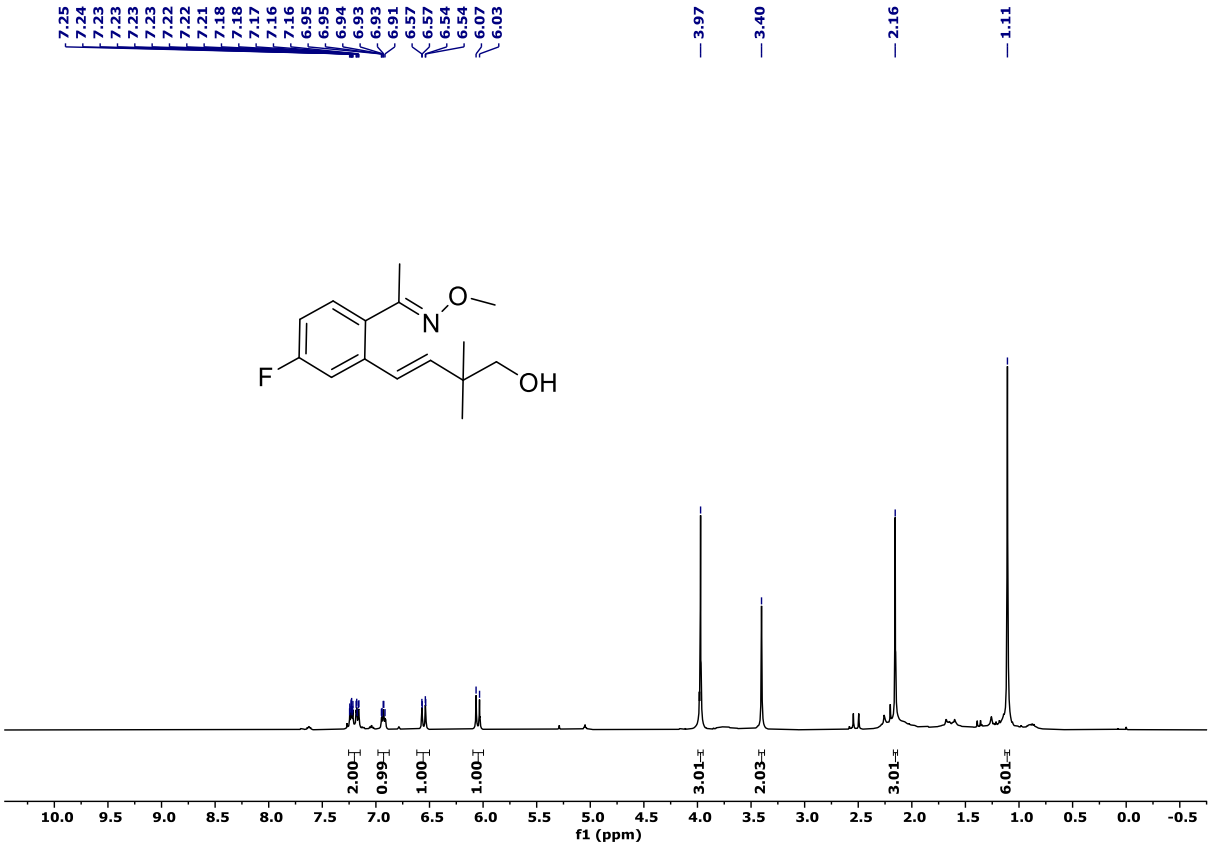
HRMS (ESI-TOF) m/z: $[M+H]^+$ Calcd for $C_{16}H_{23}BrNO_3$ 356.0861; Found 356.0858.

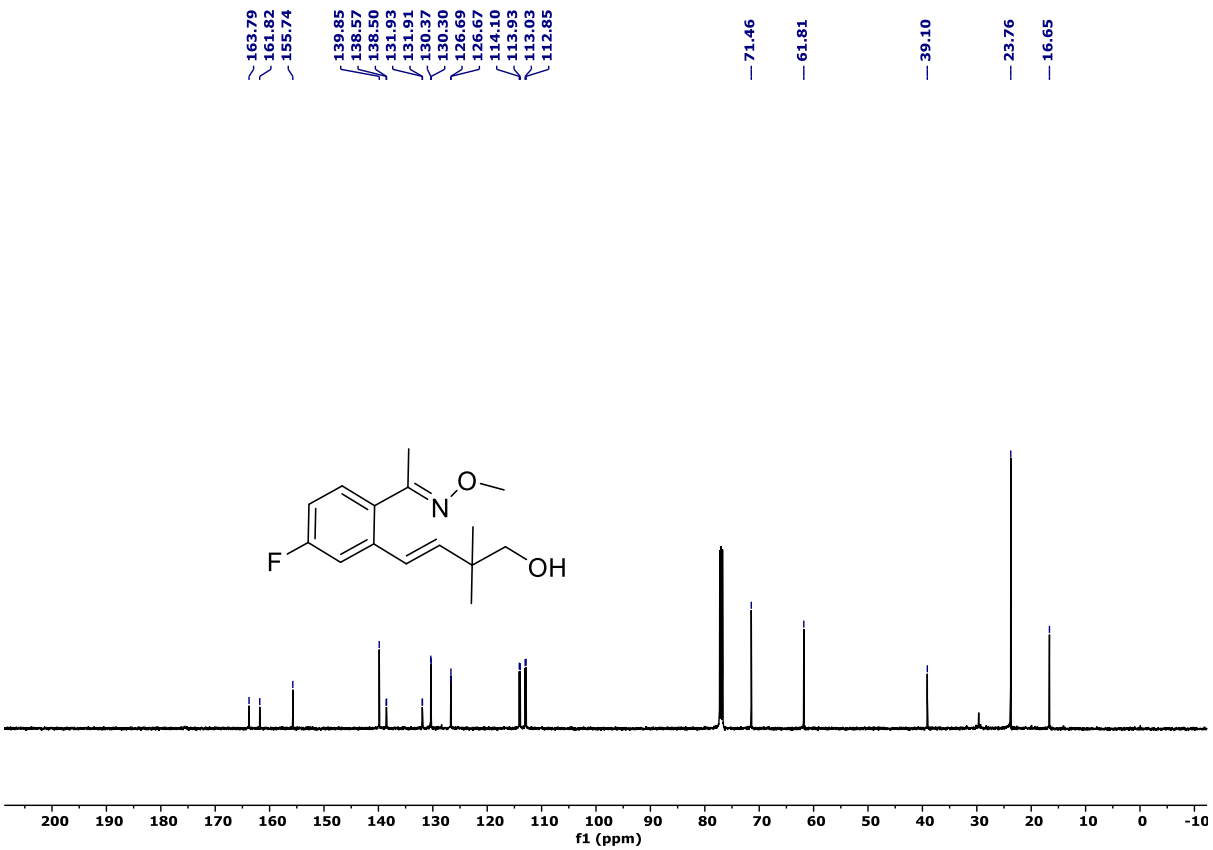
^{1}H and ^{13}C NMR Spectra of Compound **4a.** ($CDCl_3$ solvent was used, 500 NMR MHz)



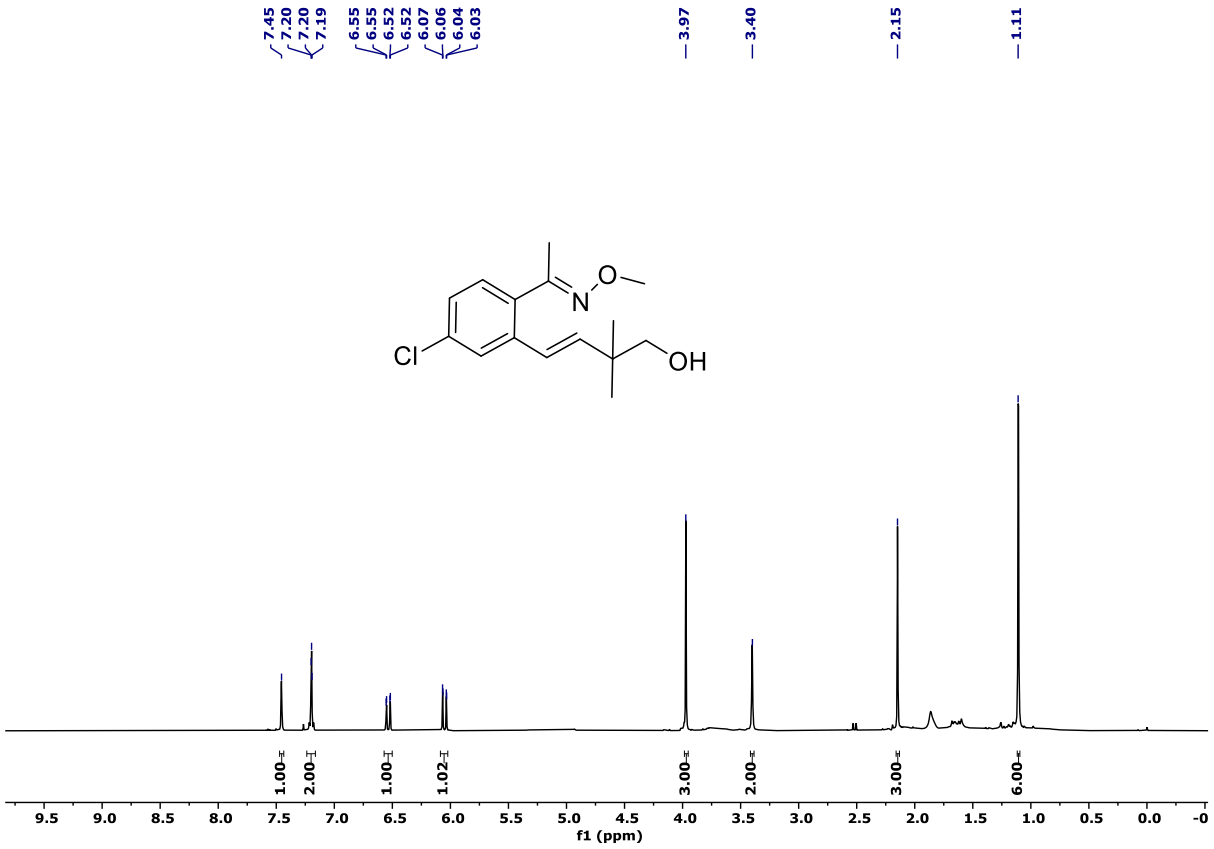


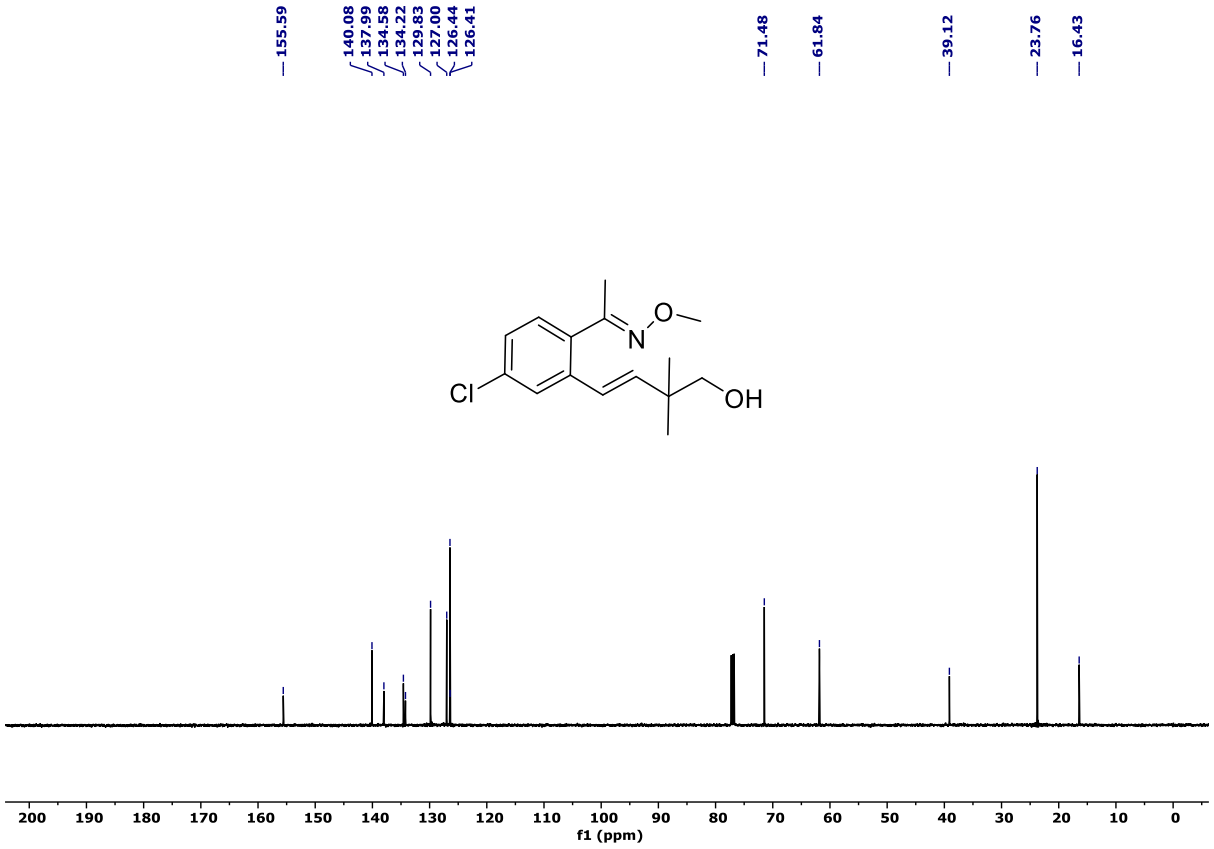
^{1}H and ^{13}C NMR Spectra of Compound **4b.** ($CDCl_3$ solvent was used, 500 NMR MHz)



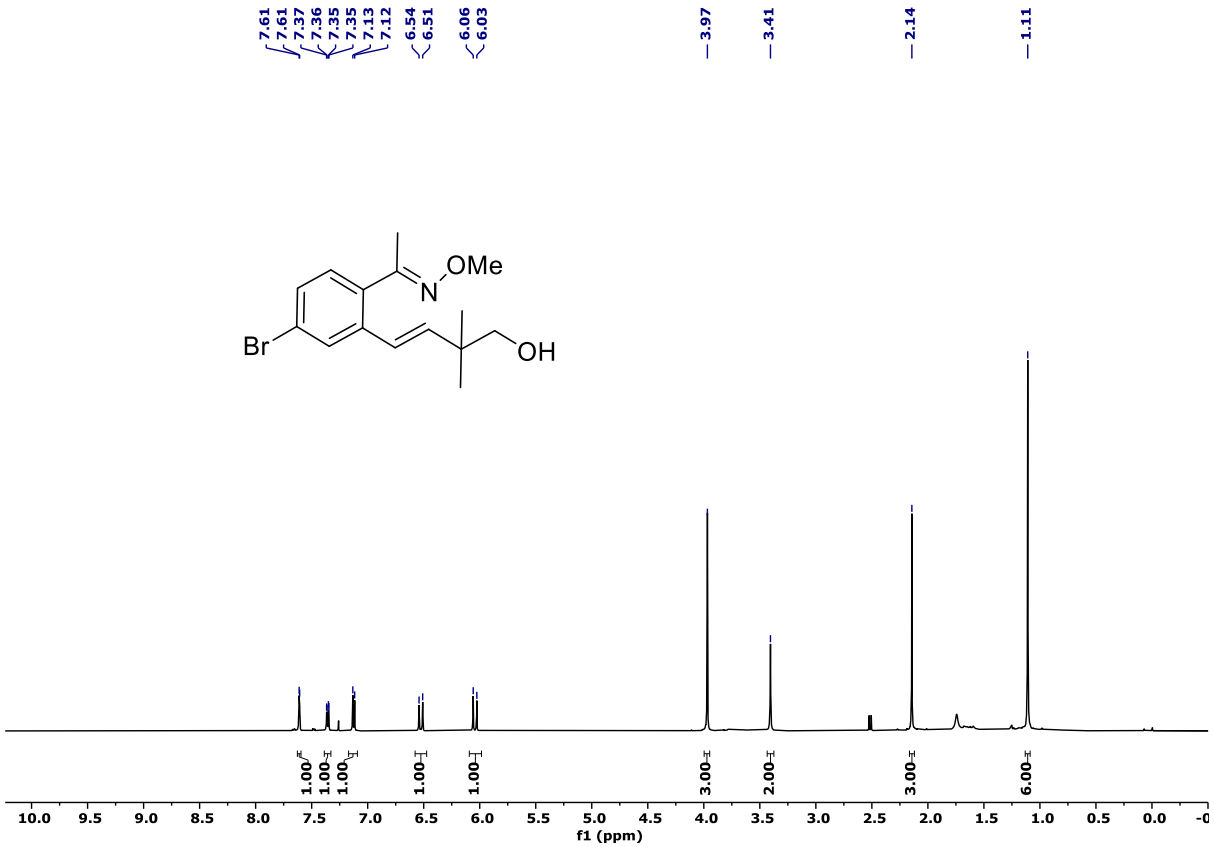


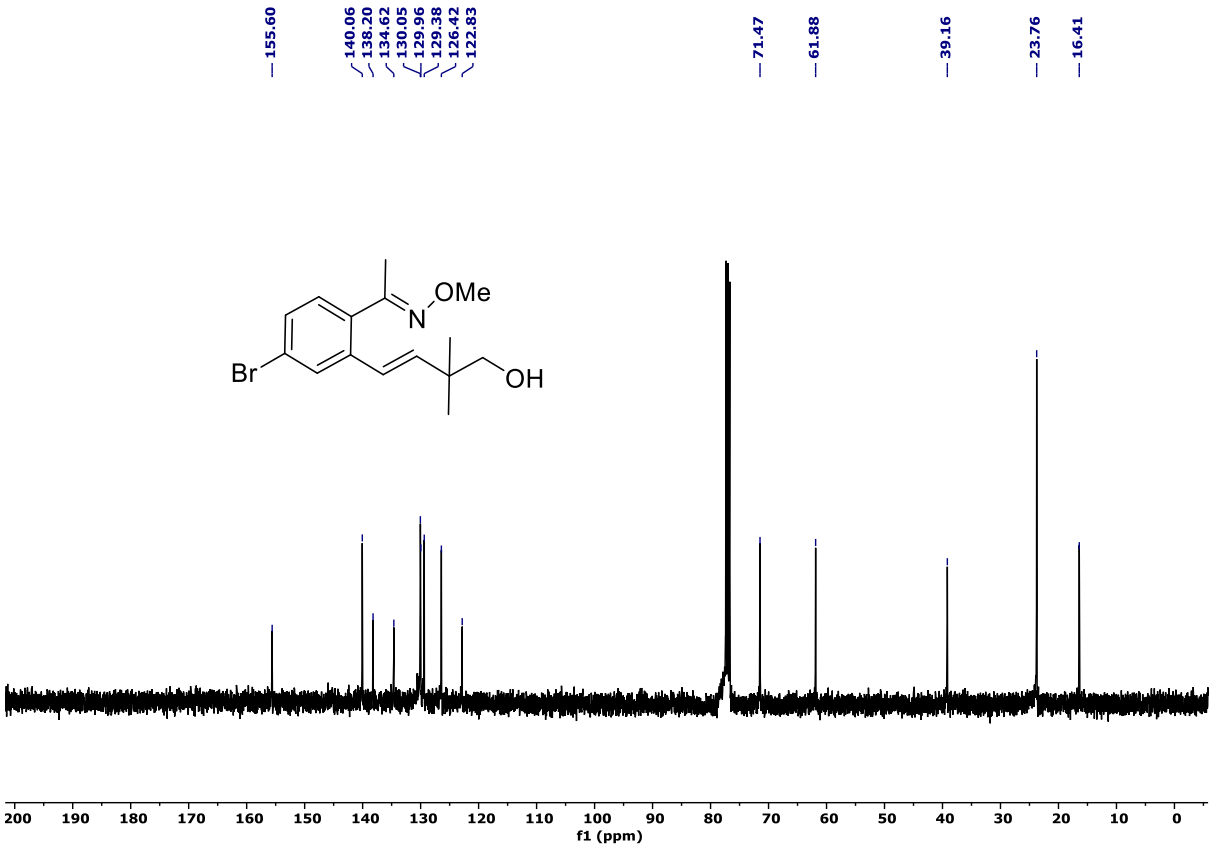
^{1}H and ^{13}C NMR Spectra of Compound **4c.** ($CDCl_3$ solvent was used, 400 NMR MHz)



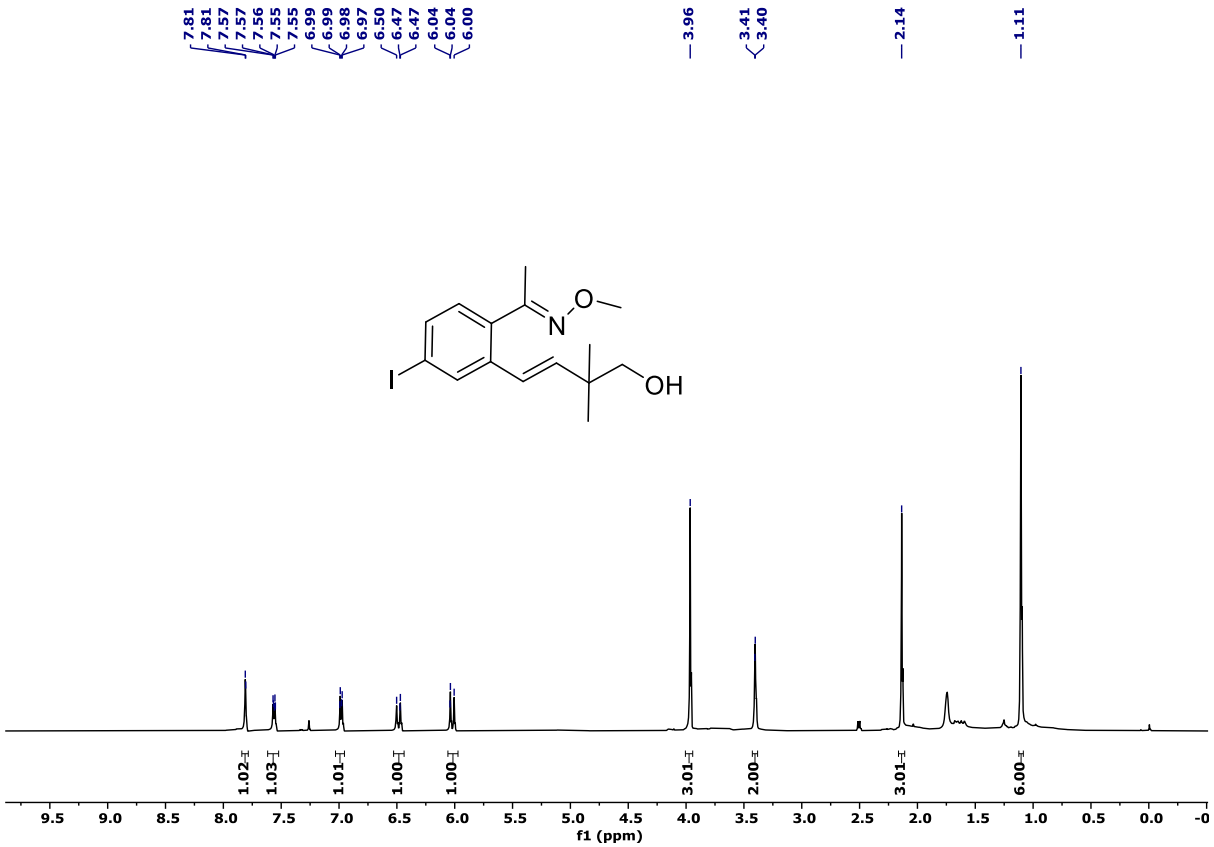


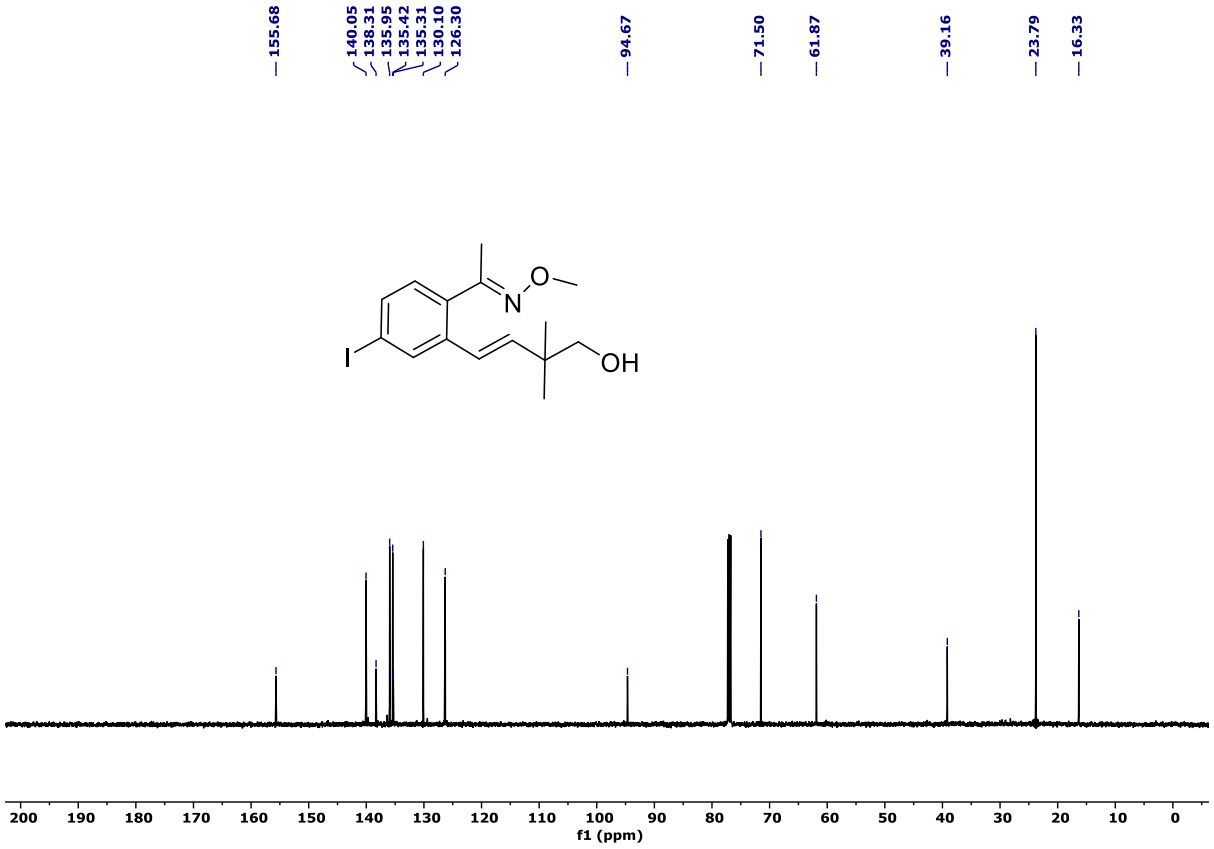
^{1}H and ^{13}C NMR Spectra of Compound **4d.** ($CDCl_3$ solvent was used, 500 NMR MHz)



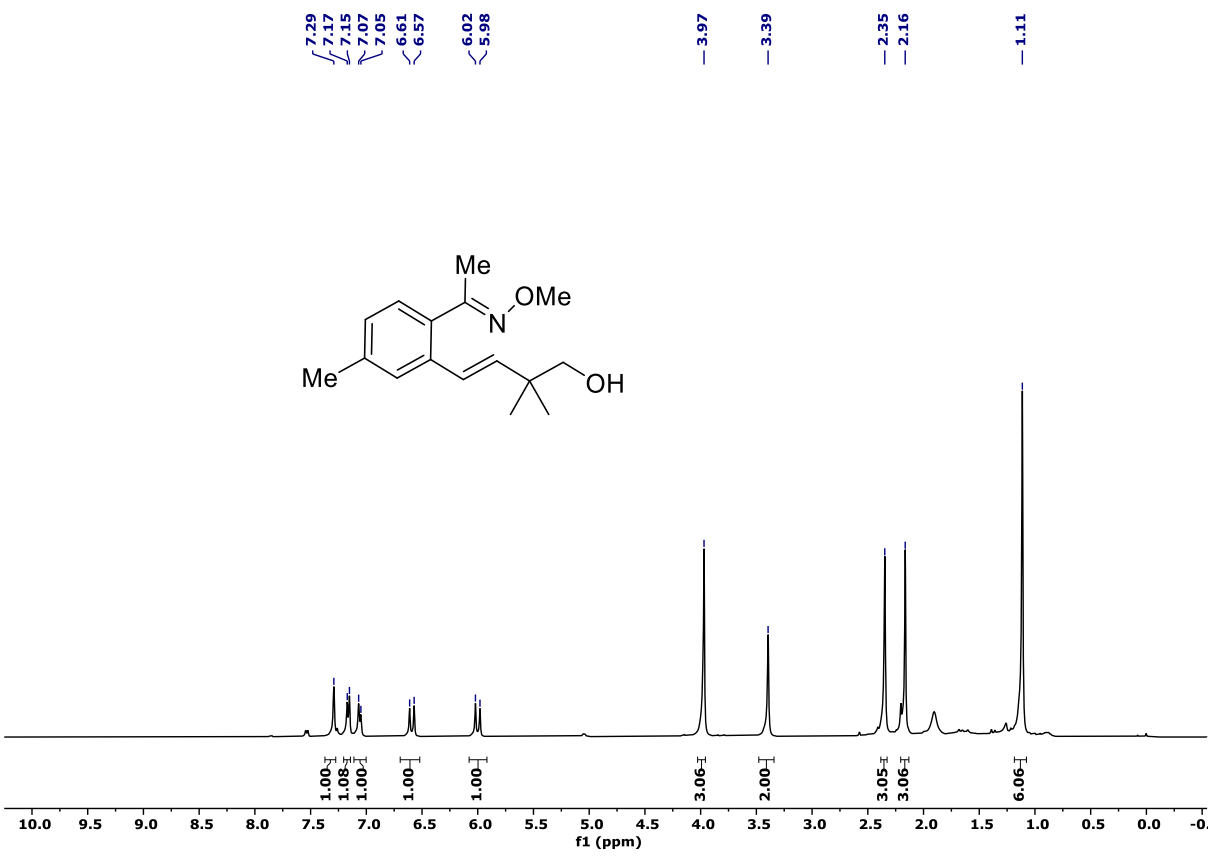


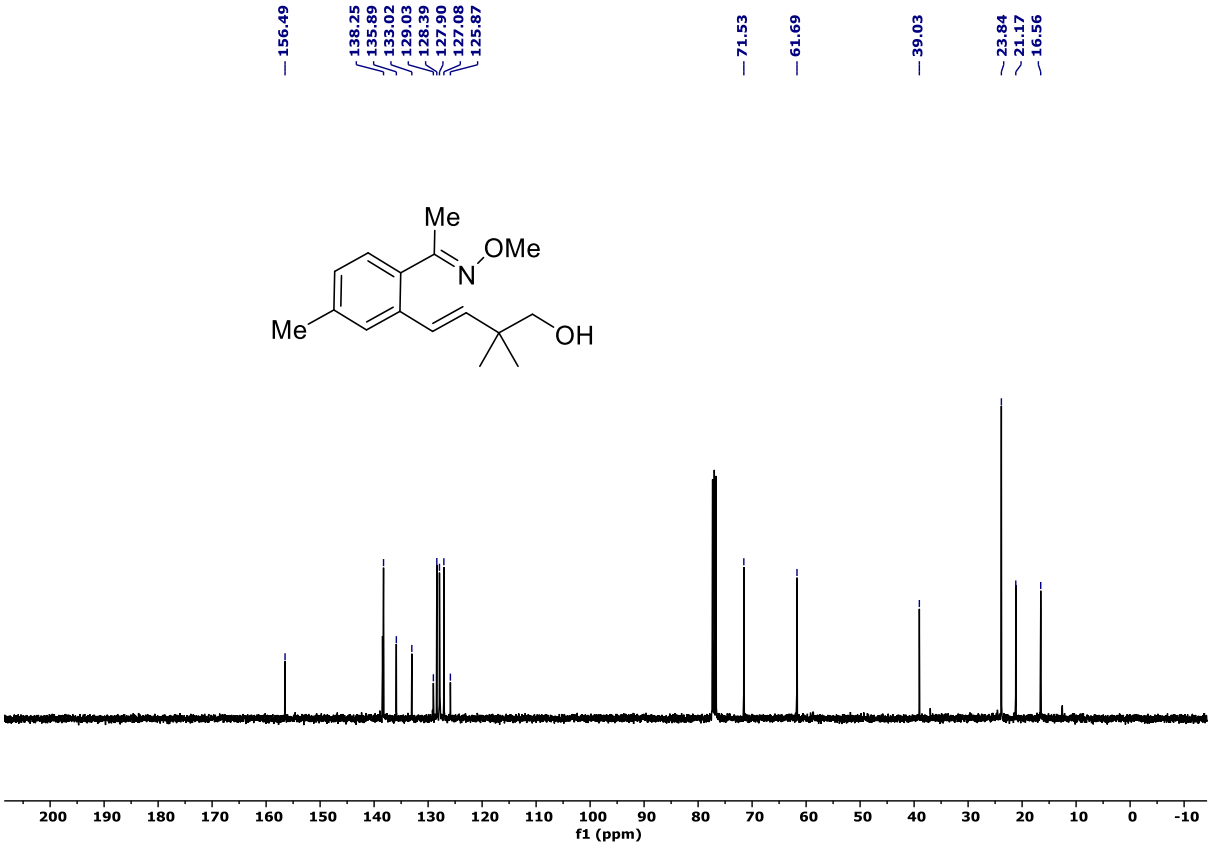
^{1}H and ^{13}C NMR Spectra of Compound **4e.** ($CDCl_3$ solvent was used, 500 NMR MHz)



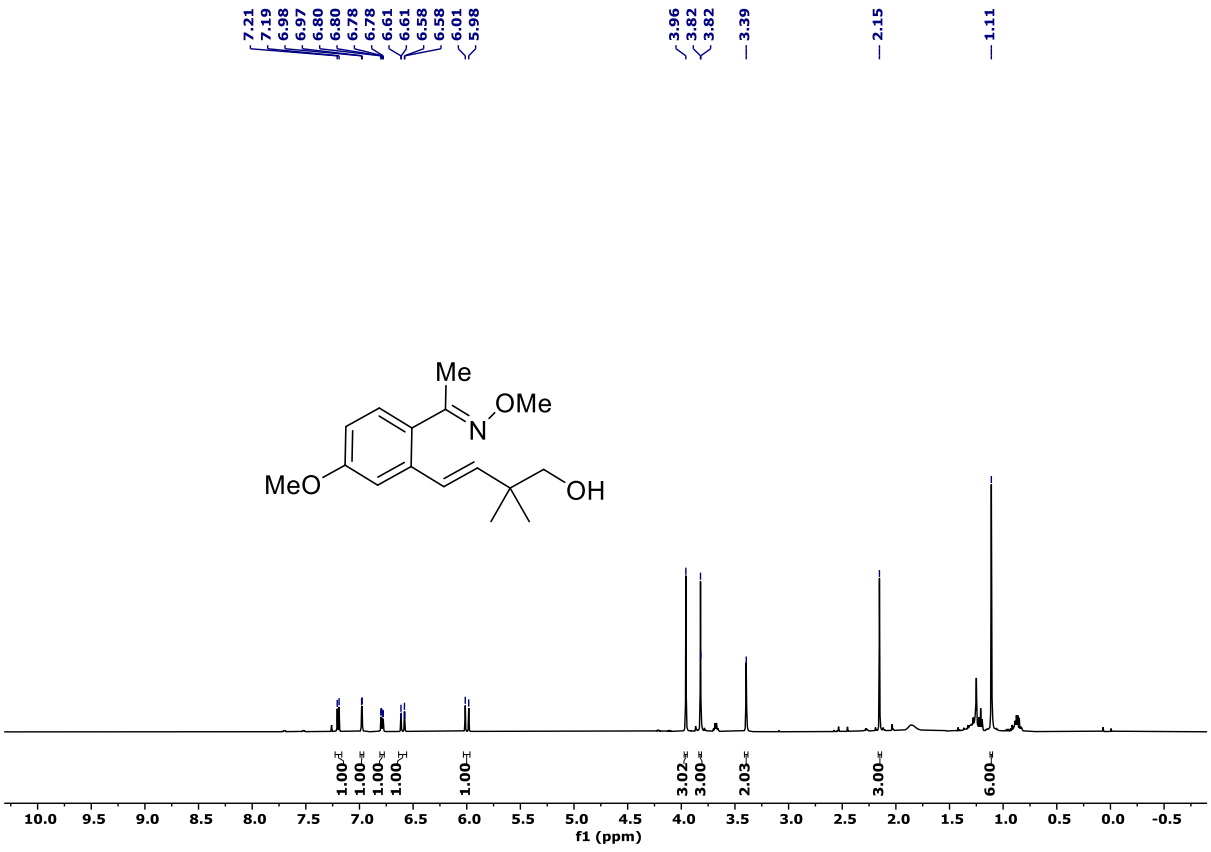


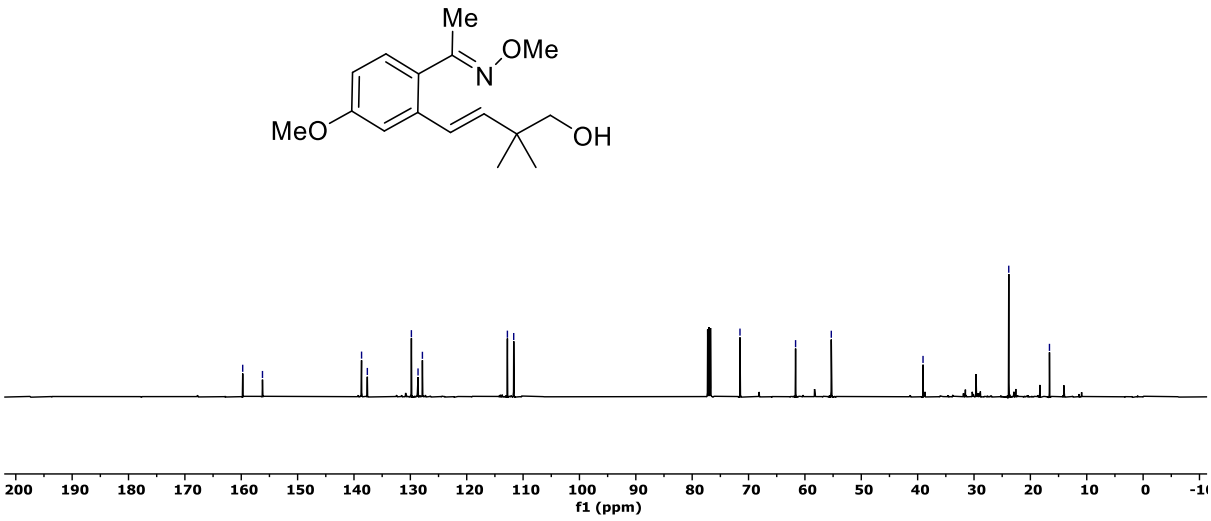
^{1}H and ^{13}C NMR Spectra of Compound **4f.** ($CDCl_3$ solvent was used, 400 NMR MHz)



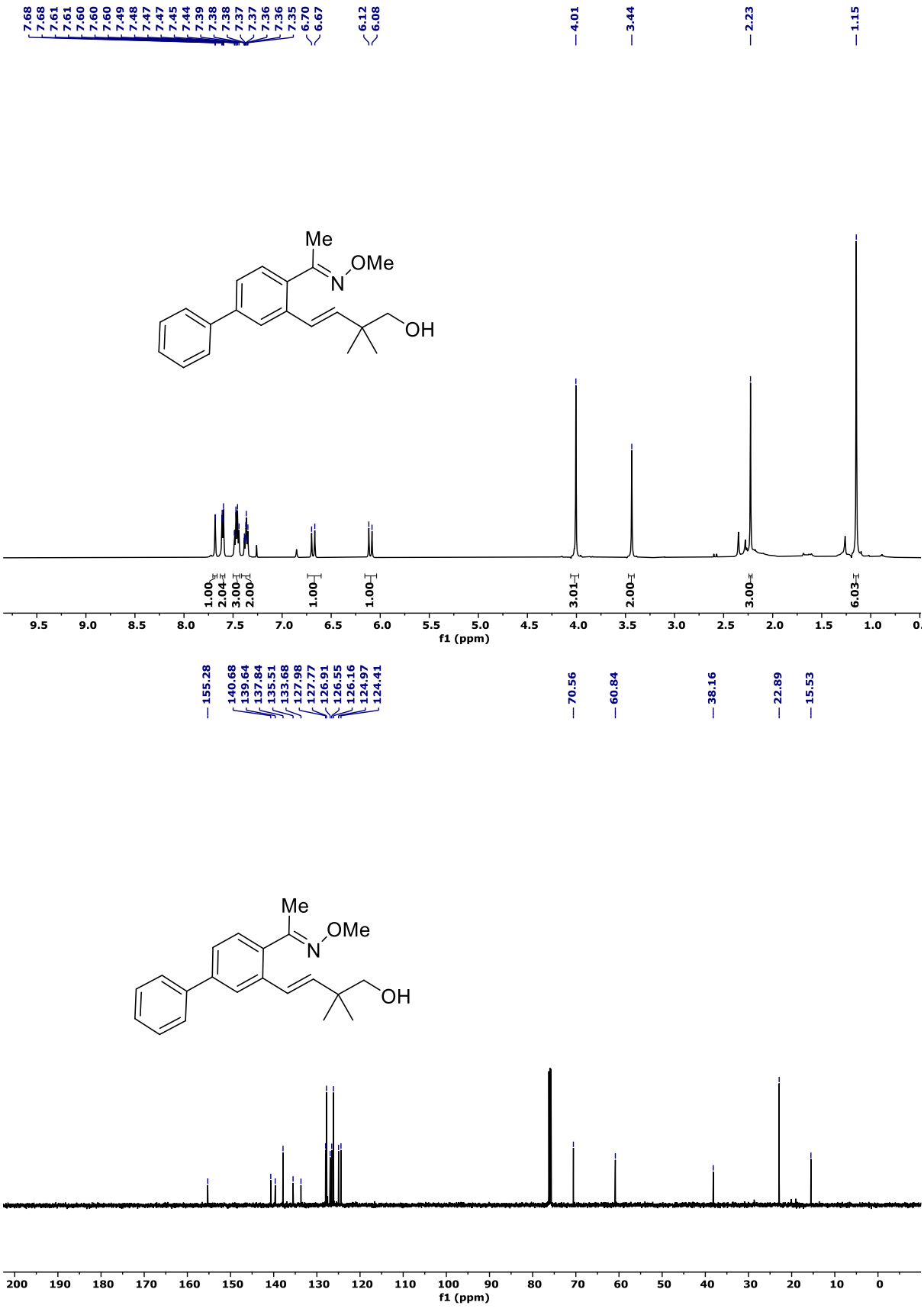


^{1}H and ^{13}C NMR Spectra of Compound **4g.** ($CDCl_3$ solvent was used, 500 NMR MHz)

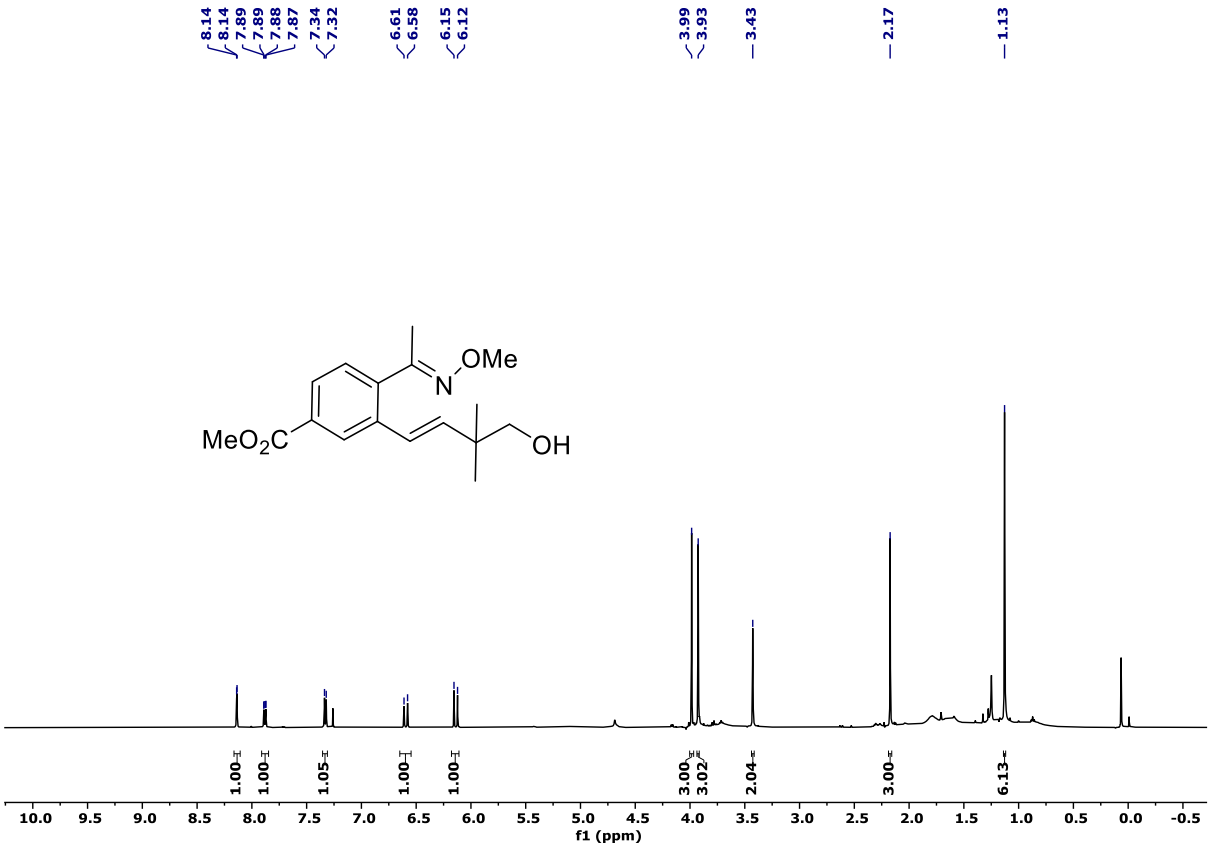


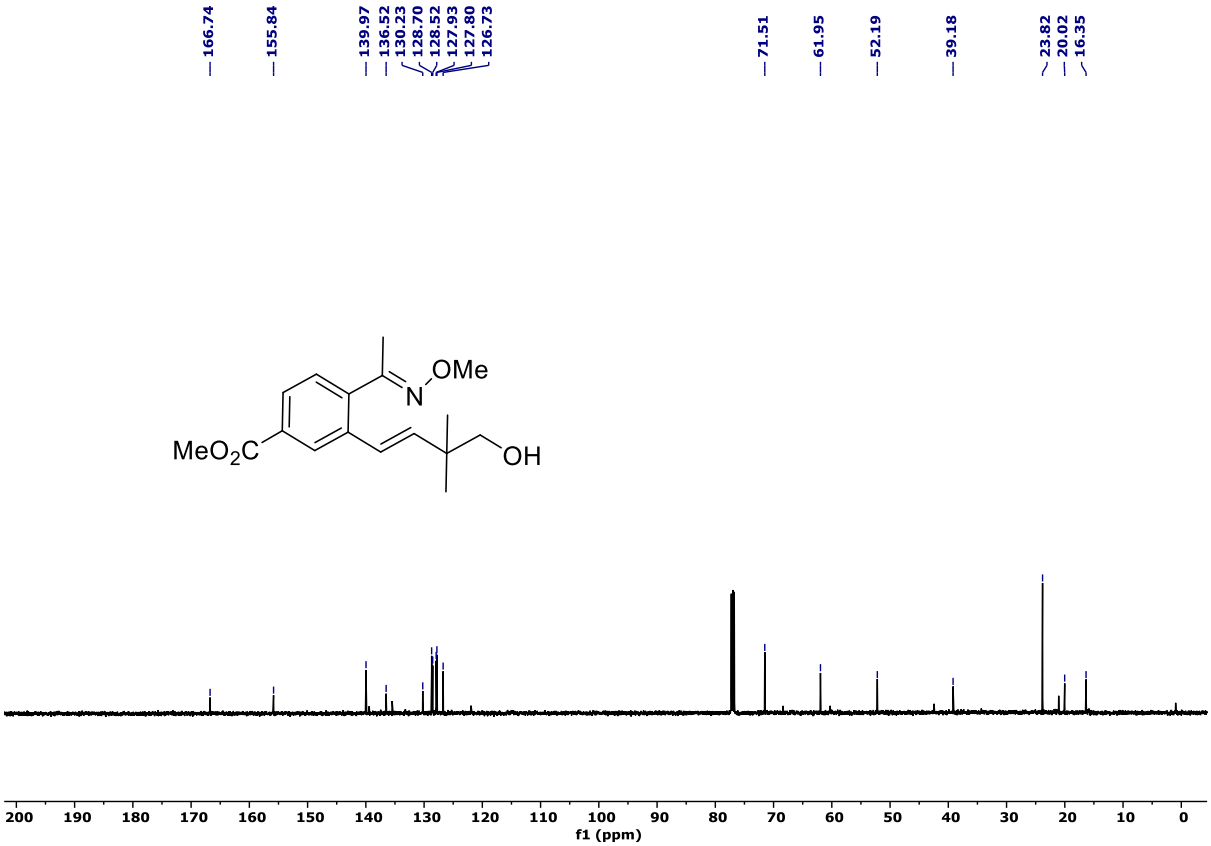


^{1}H and ^{13}C NMR Spectra of Compound **4h.** ($CDCl_3$ solvent was used, 500 NMR MHz)

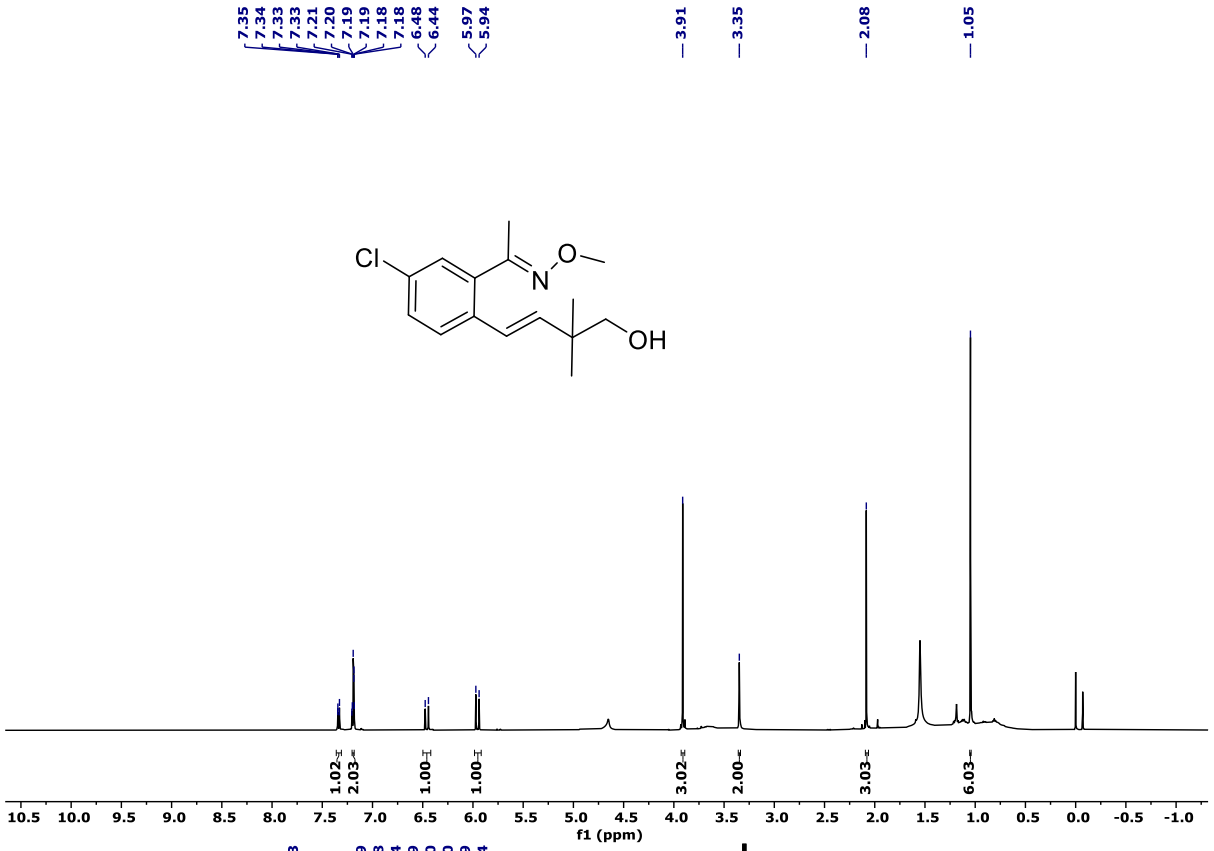


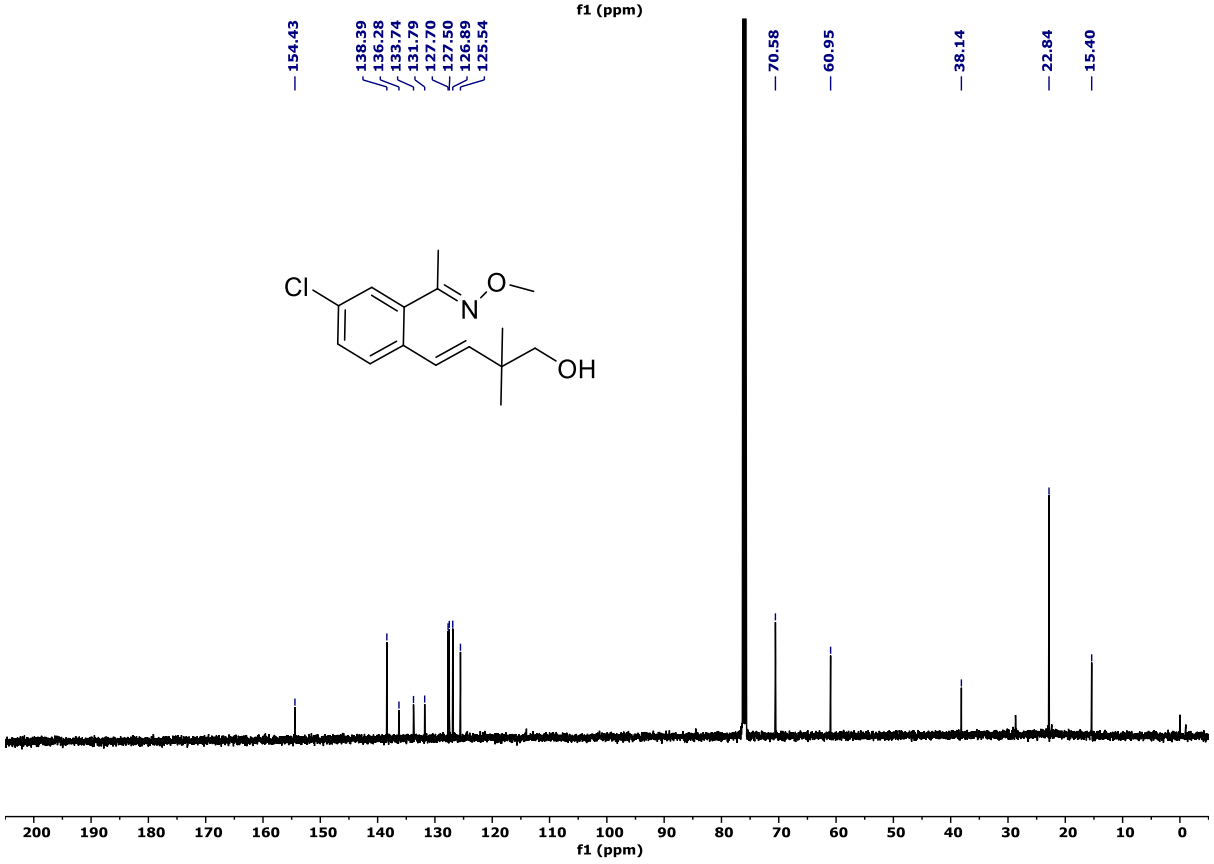
^{1}H and ^{13}C NMR Spectra of Compound **4i.** ($CDCl_3$ solvent was used, 500 NMR MHz)



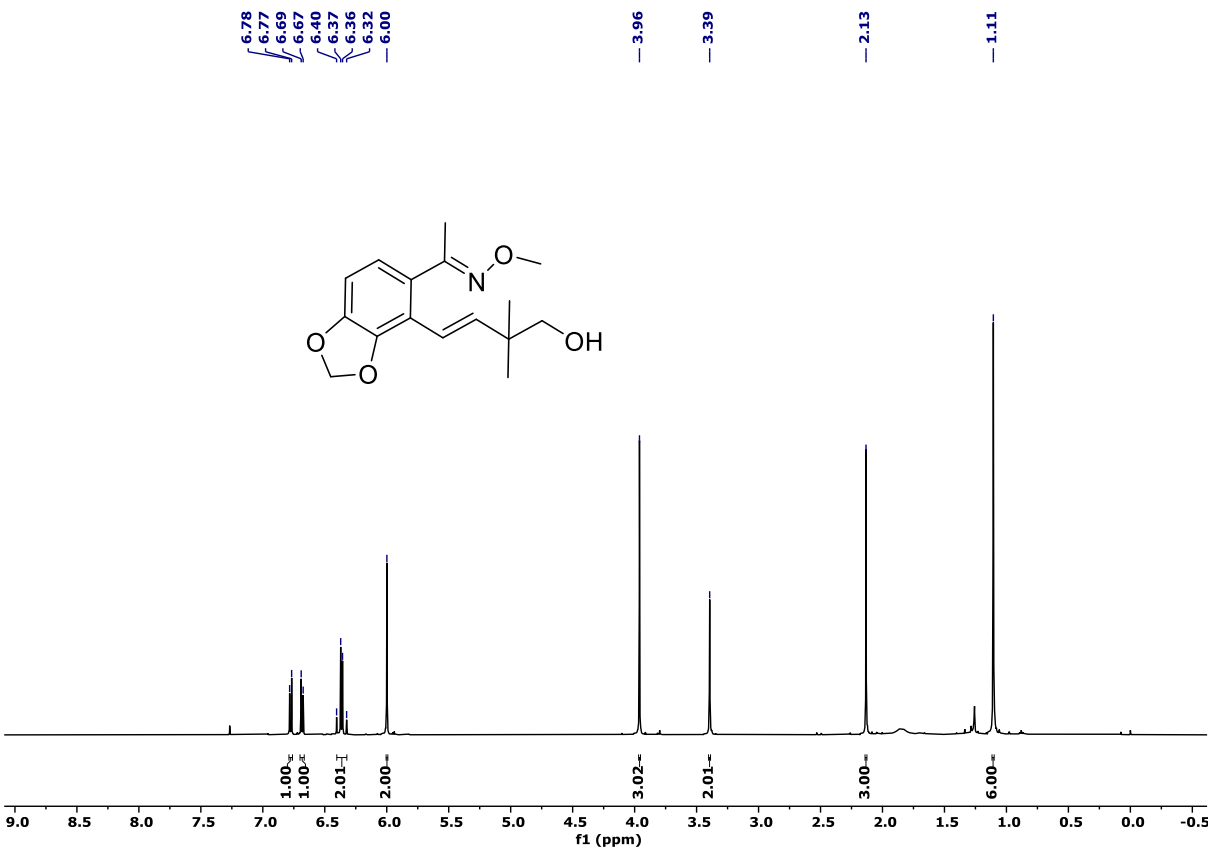


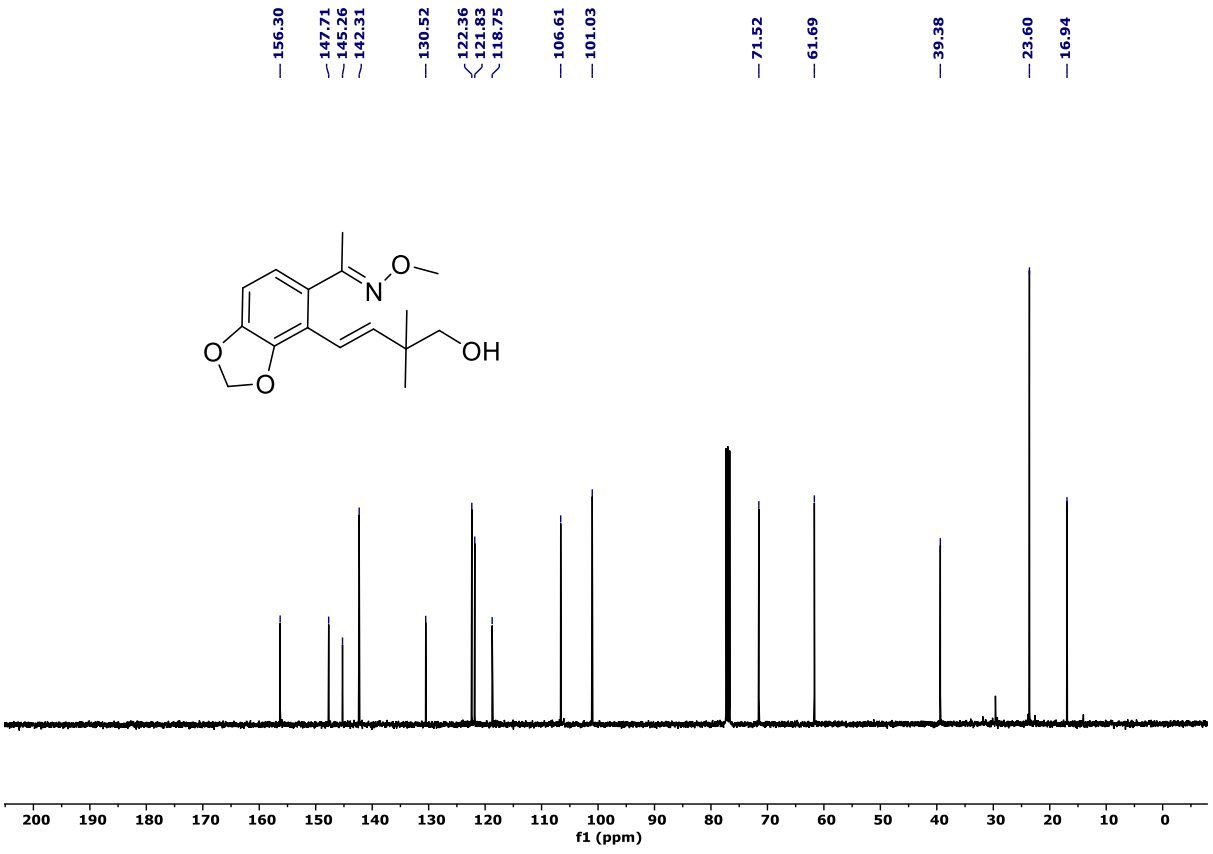
^{1}H and ^{13}C NMR Spectra of Compound **4j.** ($CDCl_3$ solvent was used, 500 NMR MHz)



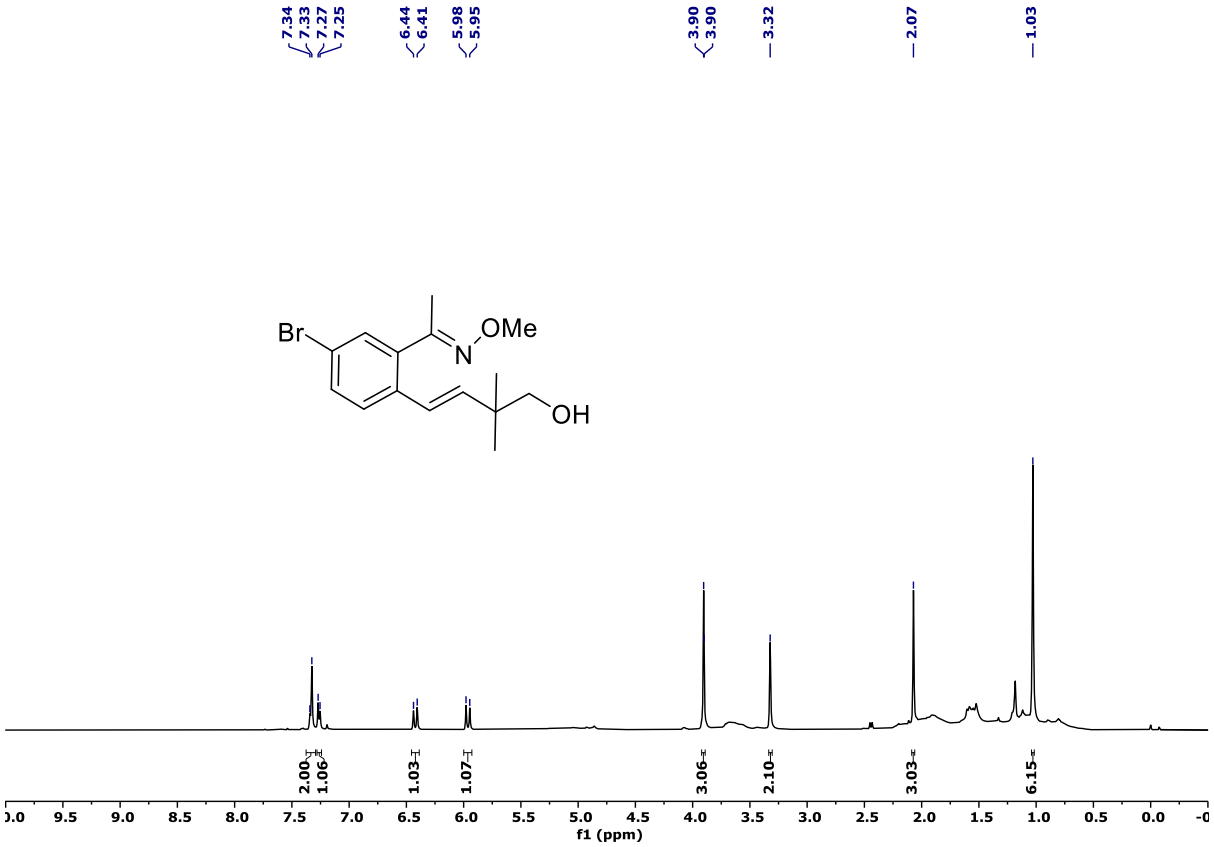


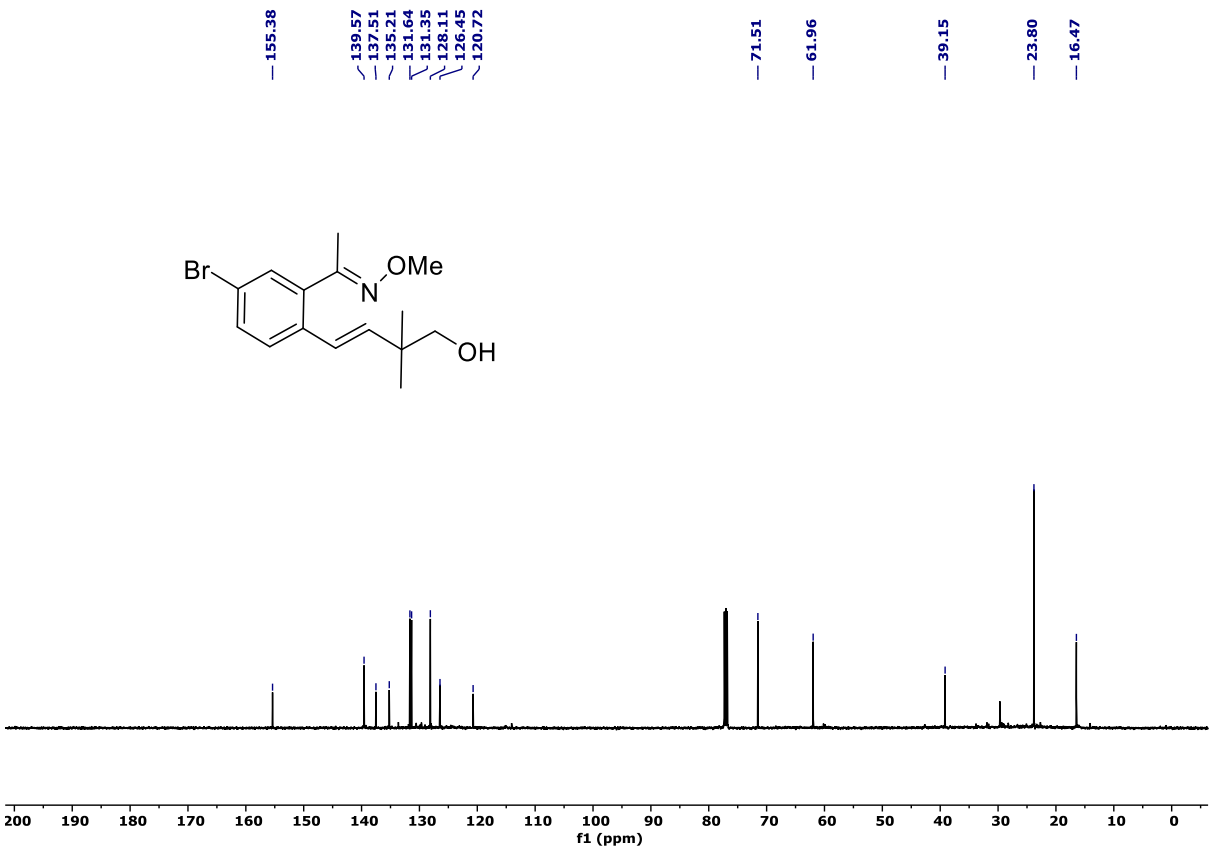
^{1}H and ^{13}C NMR Spectra of Compound **4k.** ($CDCl_3$ solvent was used, 500 NMR MHz)



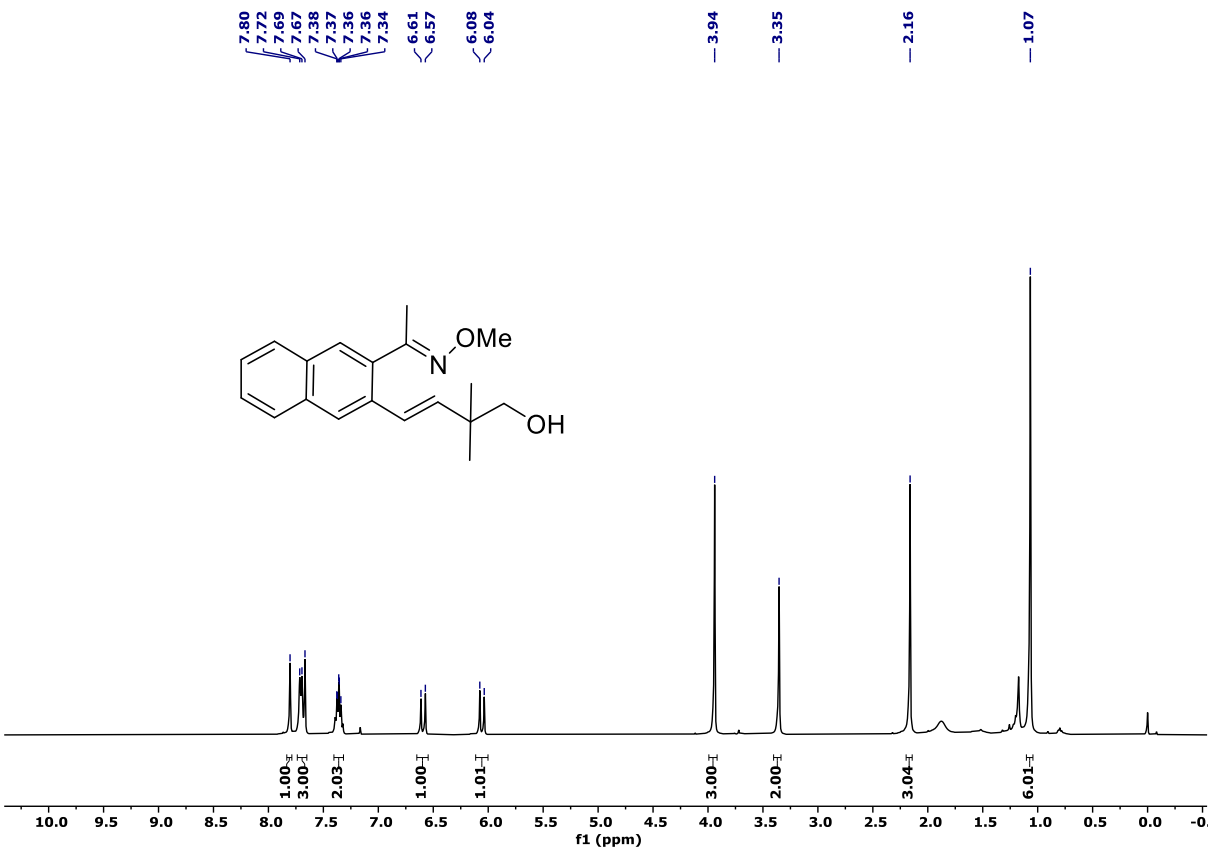


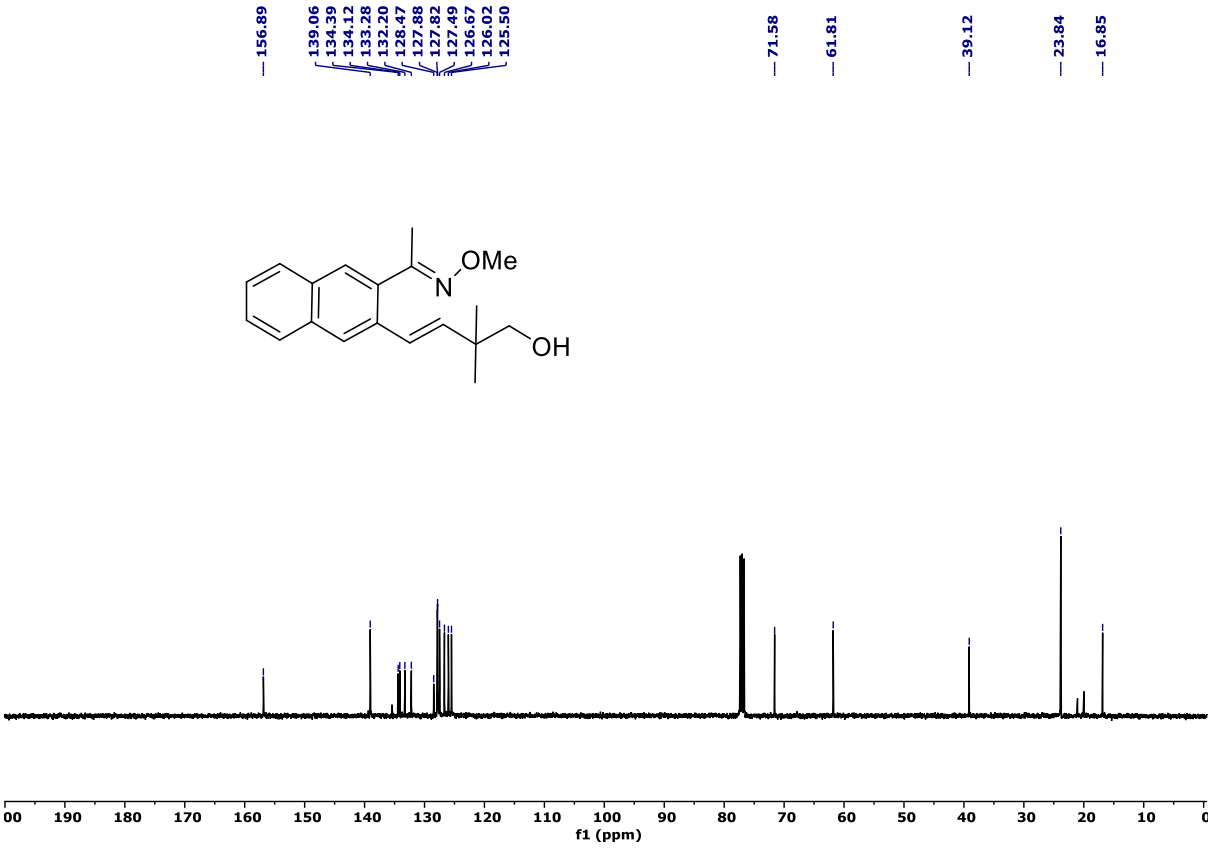
^{1}H and ^{13}C NMR Spectra of Compound **4l.** ($CDCl_3$ solvent was used, 500 NMR MHz)



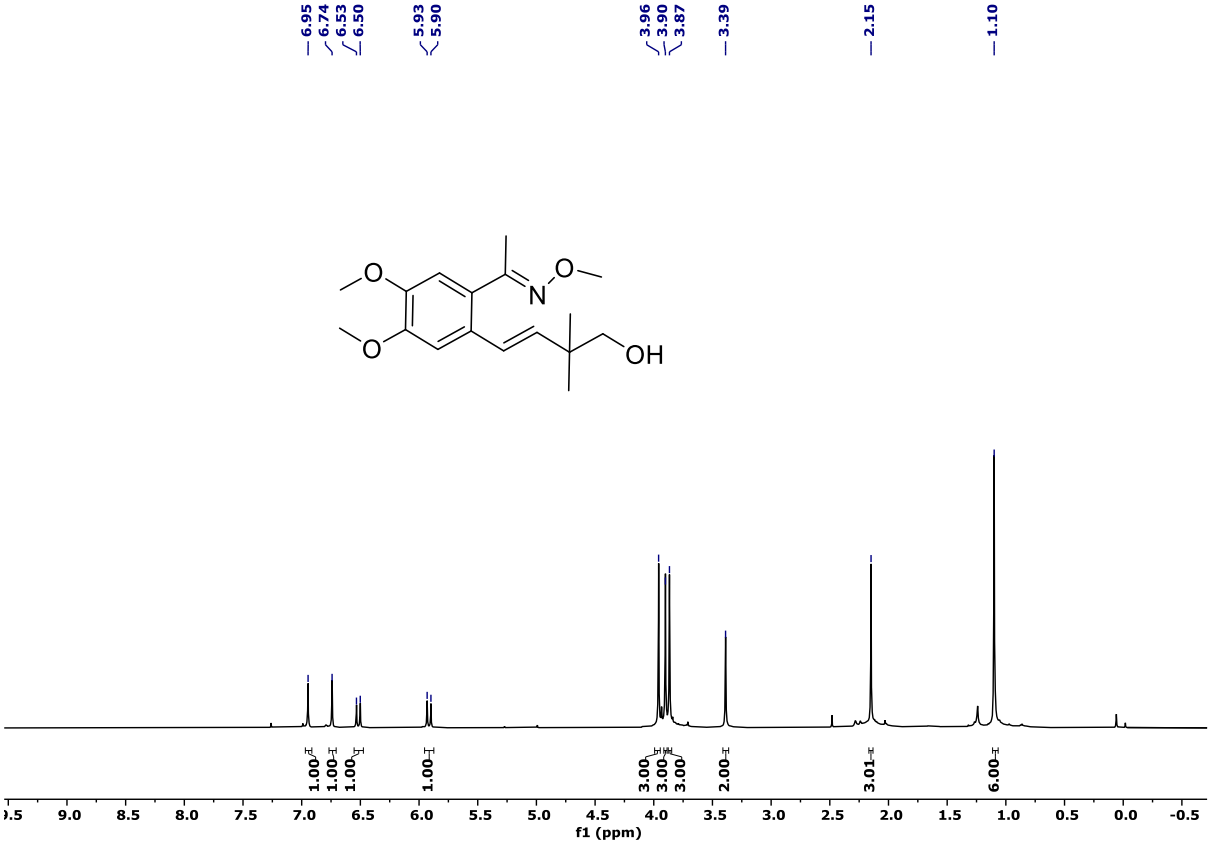


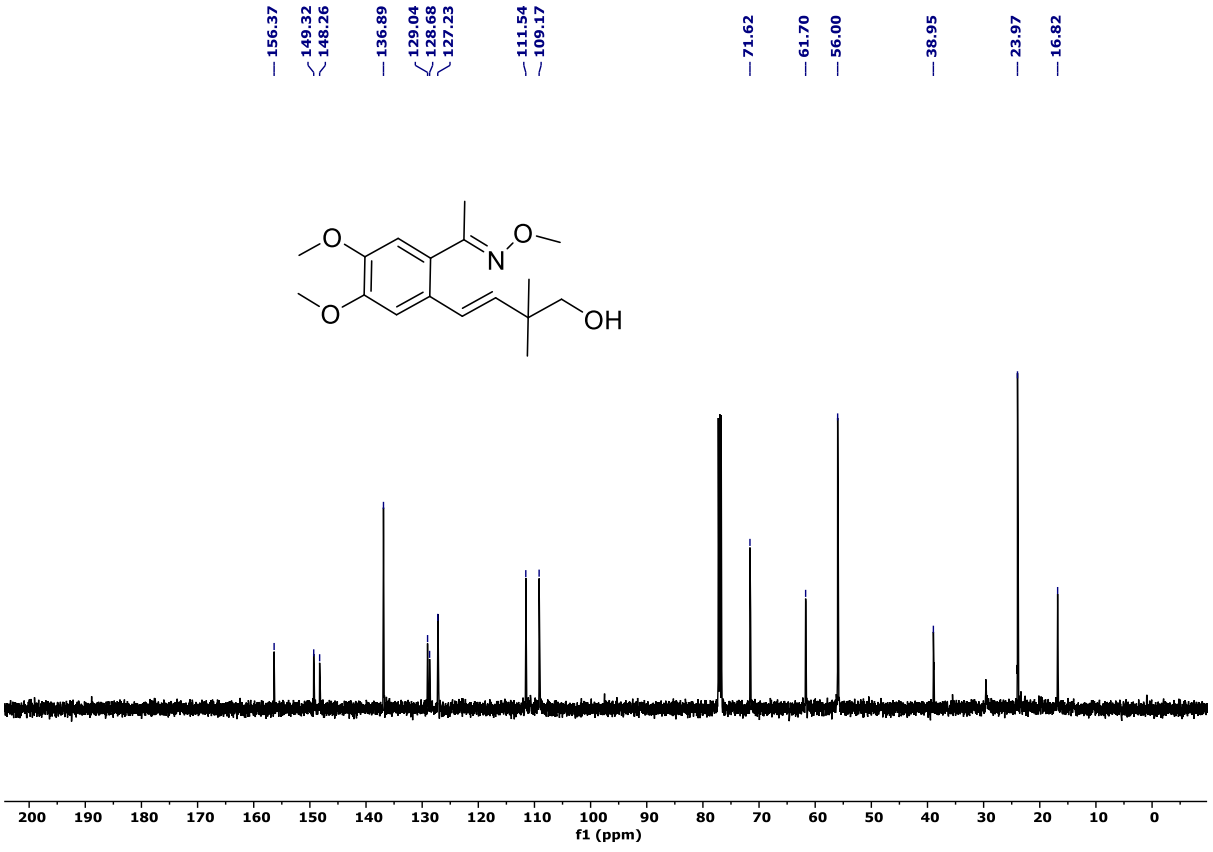
^{1}H and ^{13}C NMR Spectra of Compound **4m.** ($CDCl_3$ solvent was used, 400 NMR MHz)



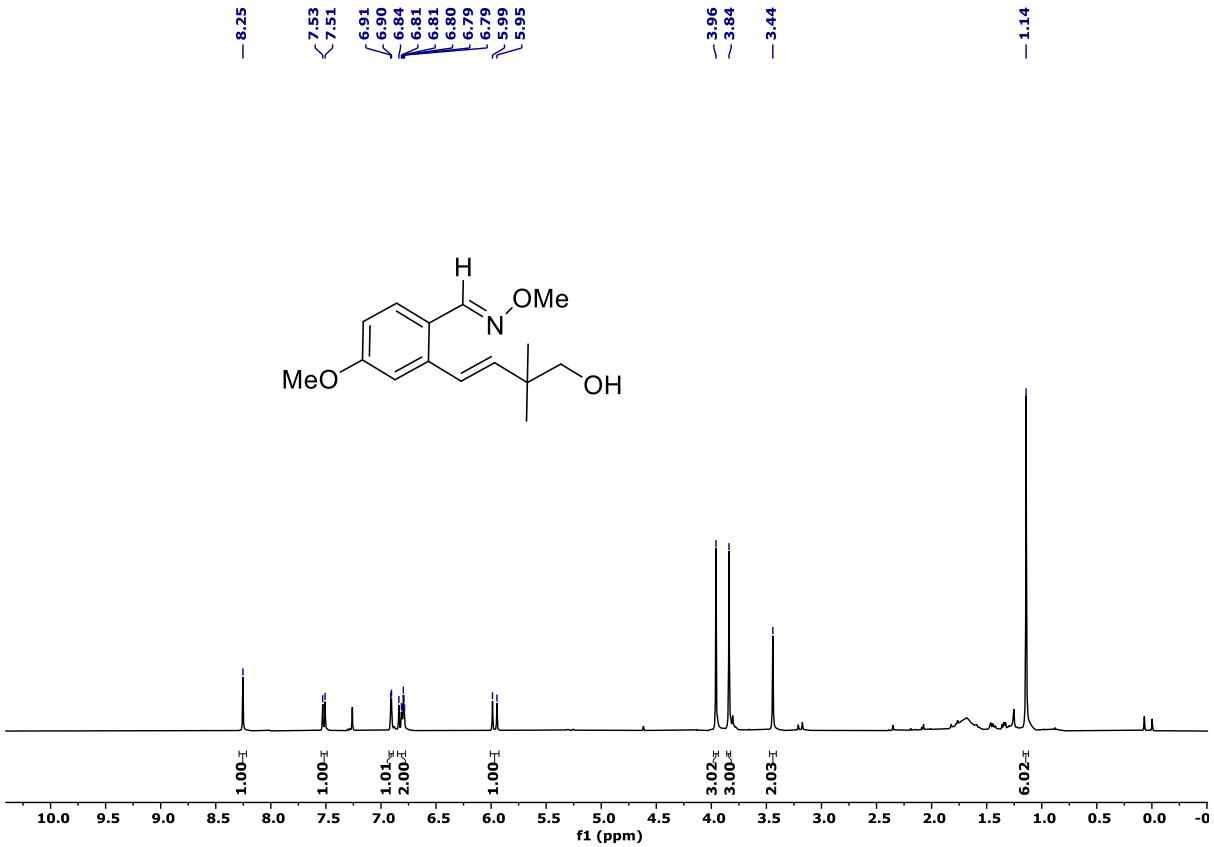


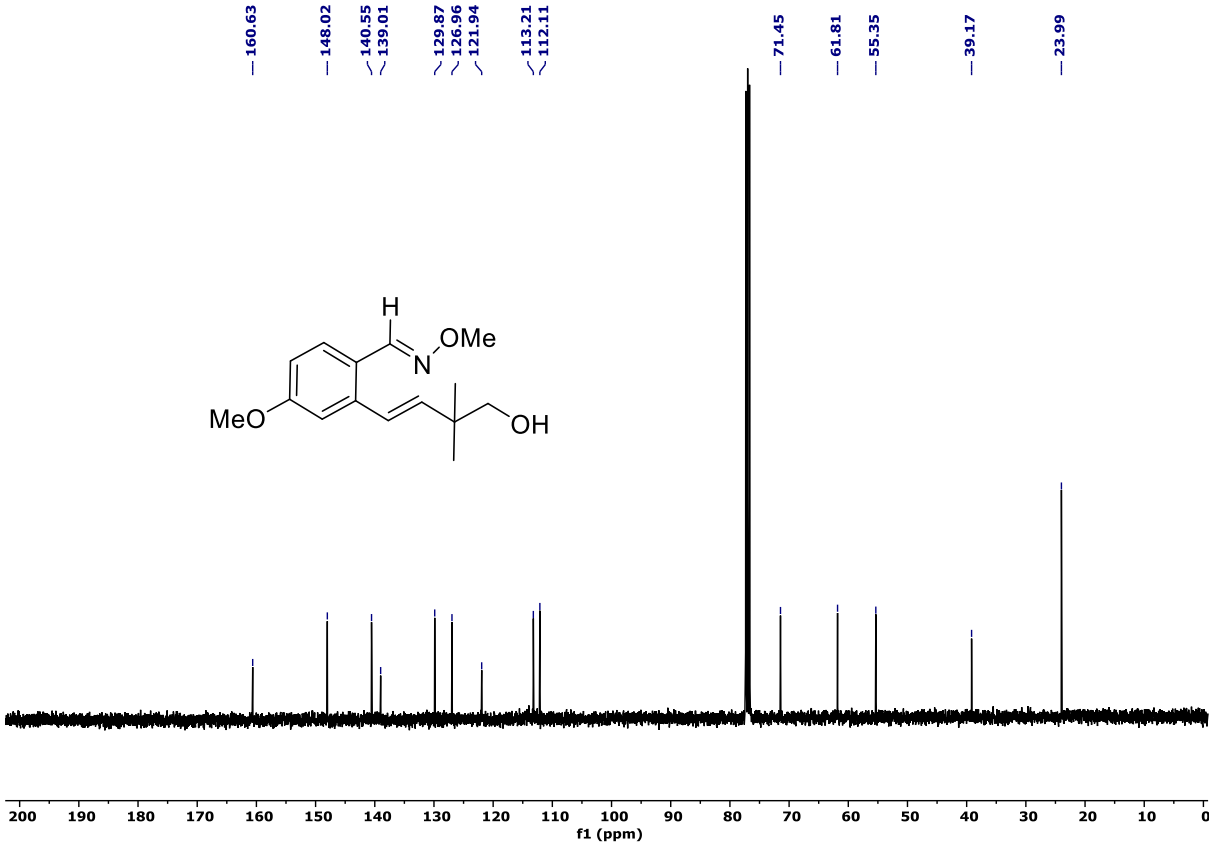
^{1}H and ^{13}C NMR Spectra of Compound **4n.** ($CDCl_3$ solvent was used, 500 NMR MHz)



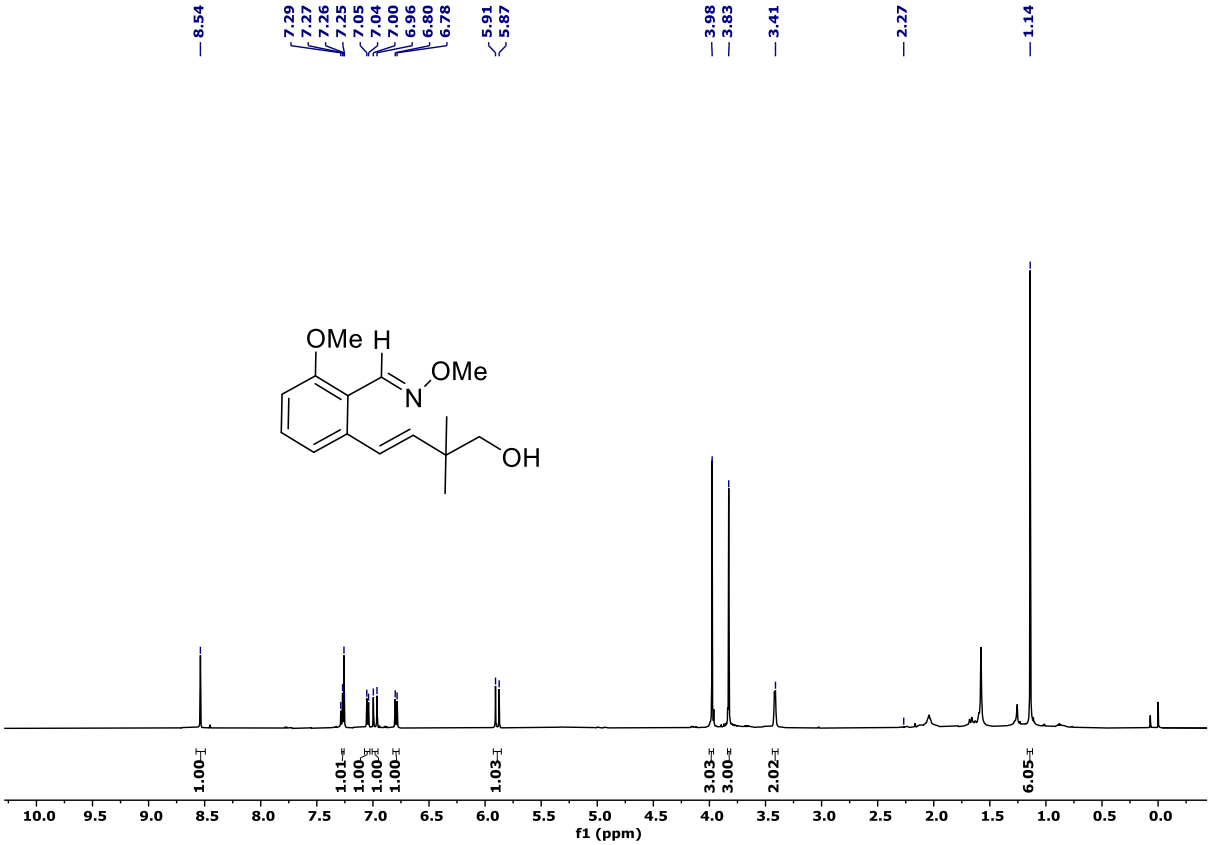


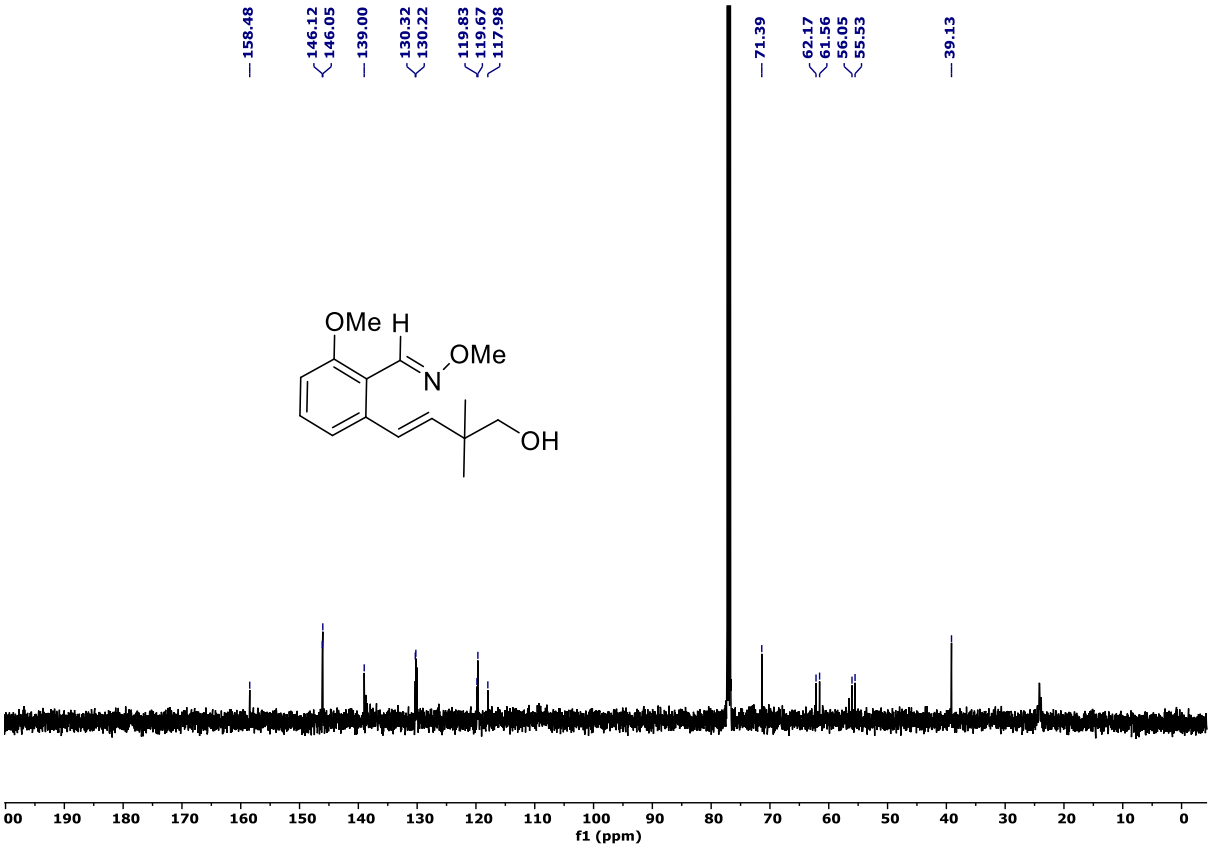
^{1}H and ^{13}C NMR Spectra of Compound **6a.** ($CDCl_3$ solvent was used, 400 NMR MHz)



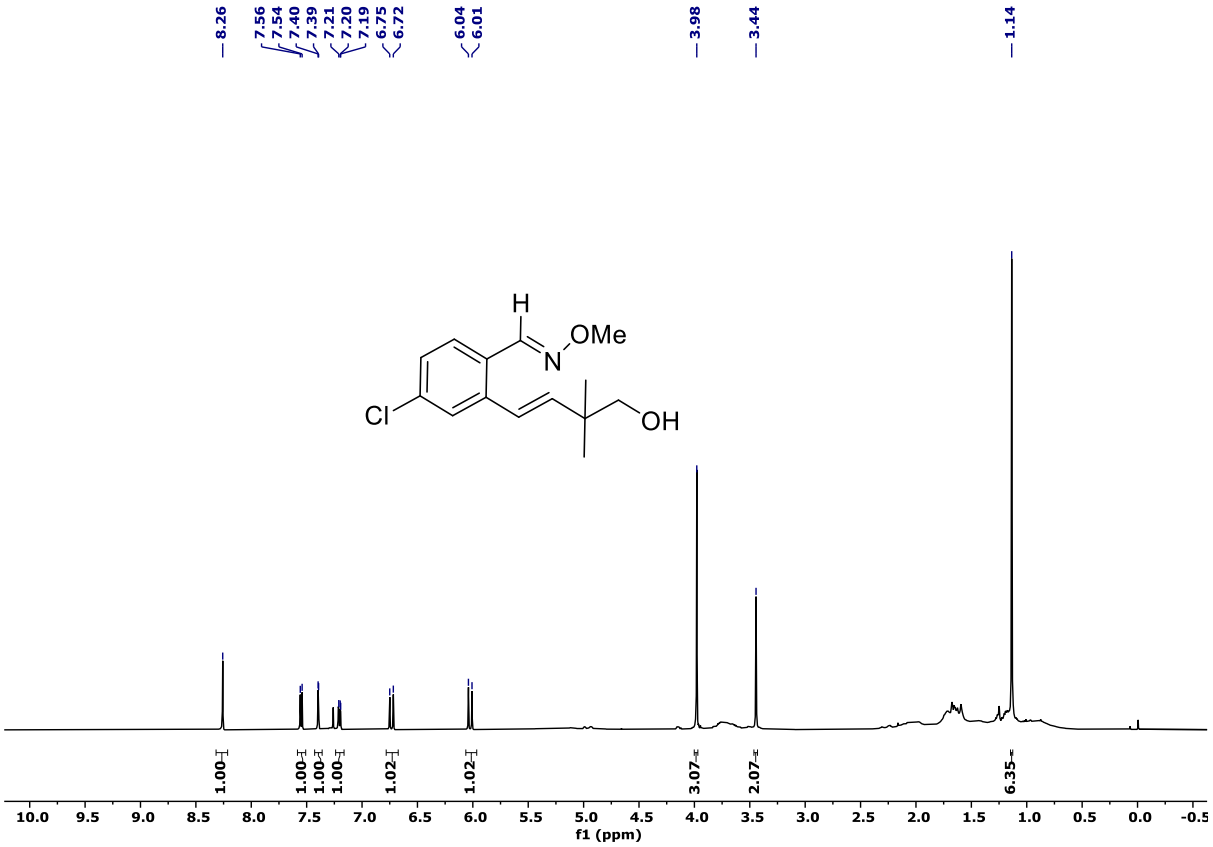


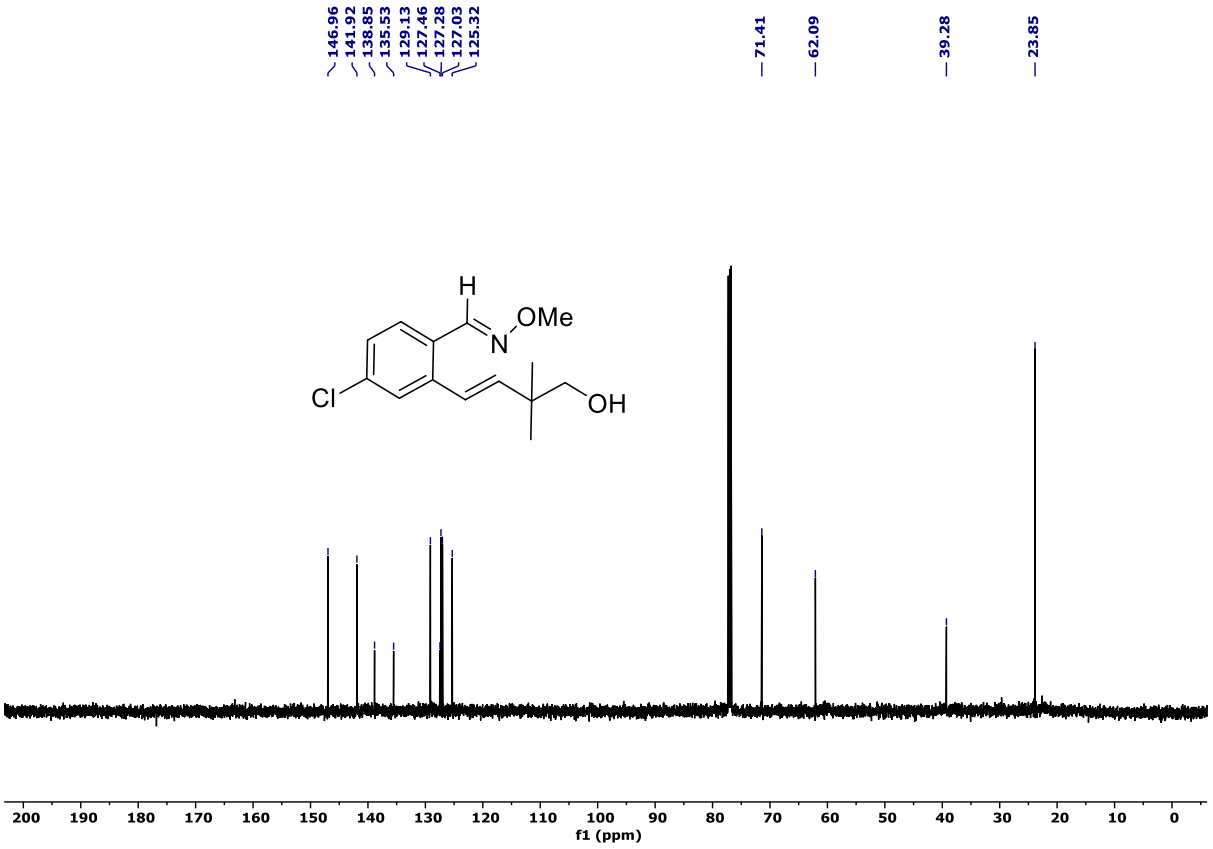
^{1}H and ^{13}C NMR Spectra of Compound **6b.** ($CDCl_3$ solvent was used, 500 NMR MHz)



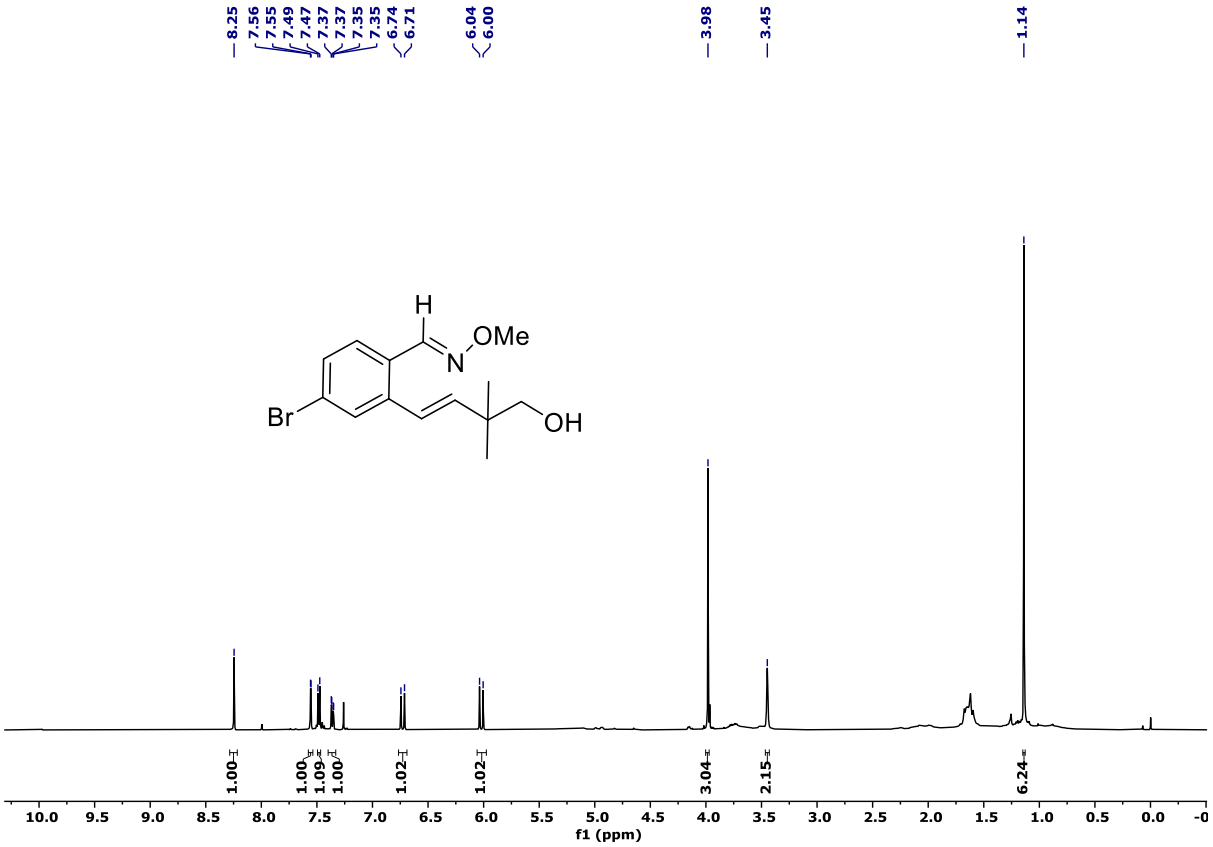


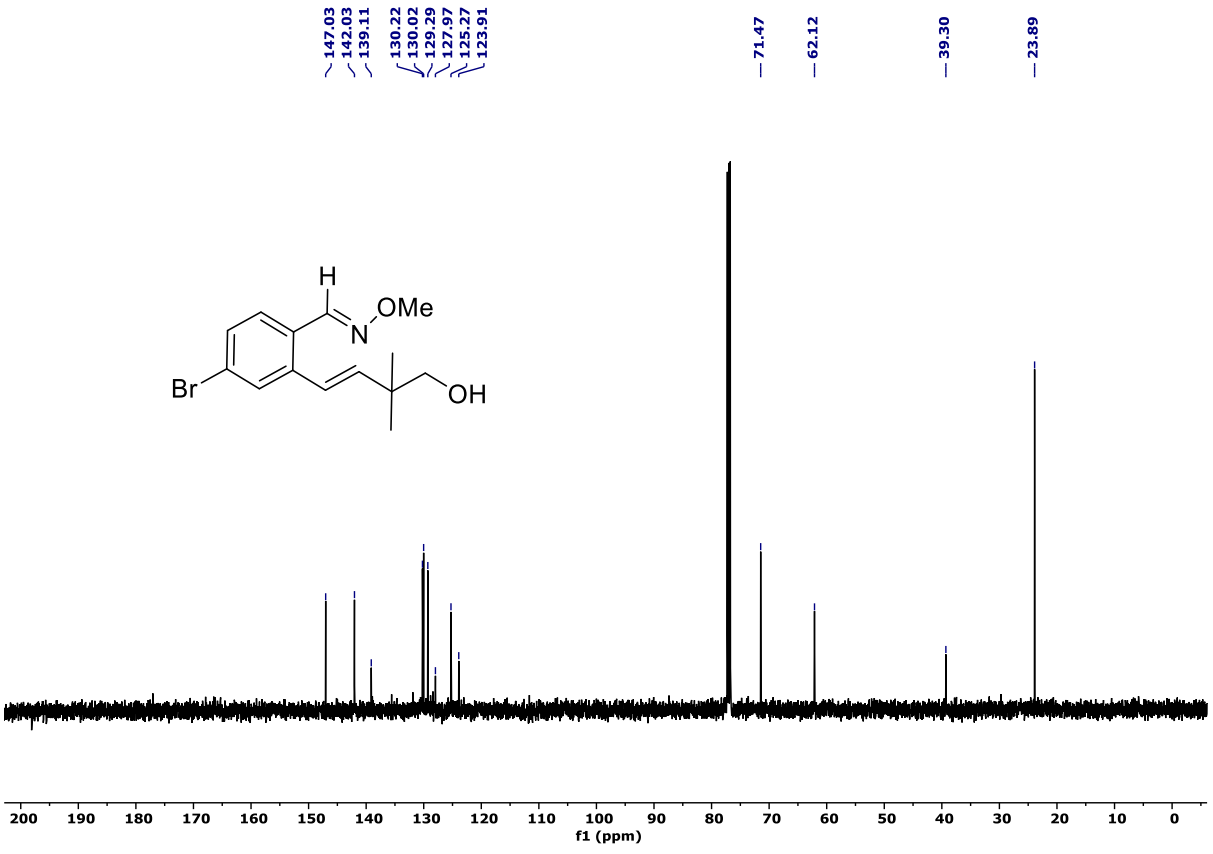
^{1}H and ^{13}C NMR Spectra of Compound **6c.** ($CDCl_3$ solvent was used, 500 NMR MHz)



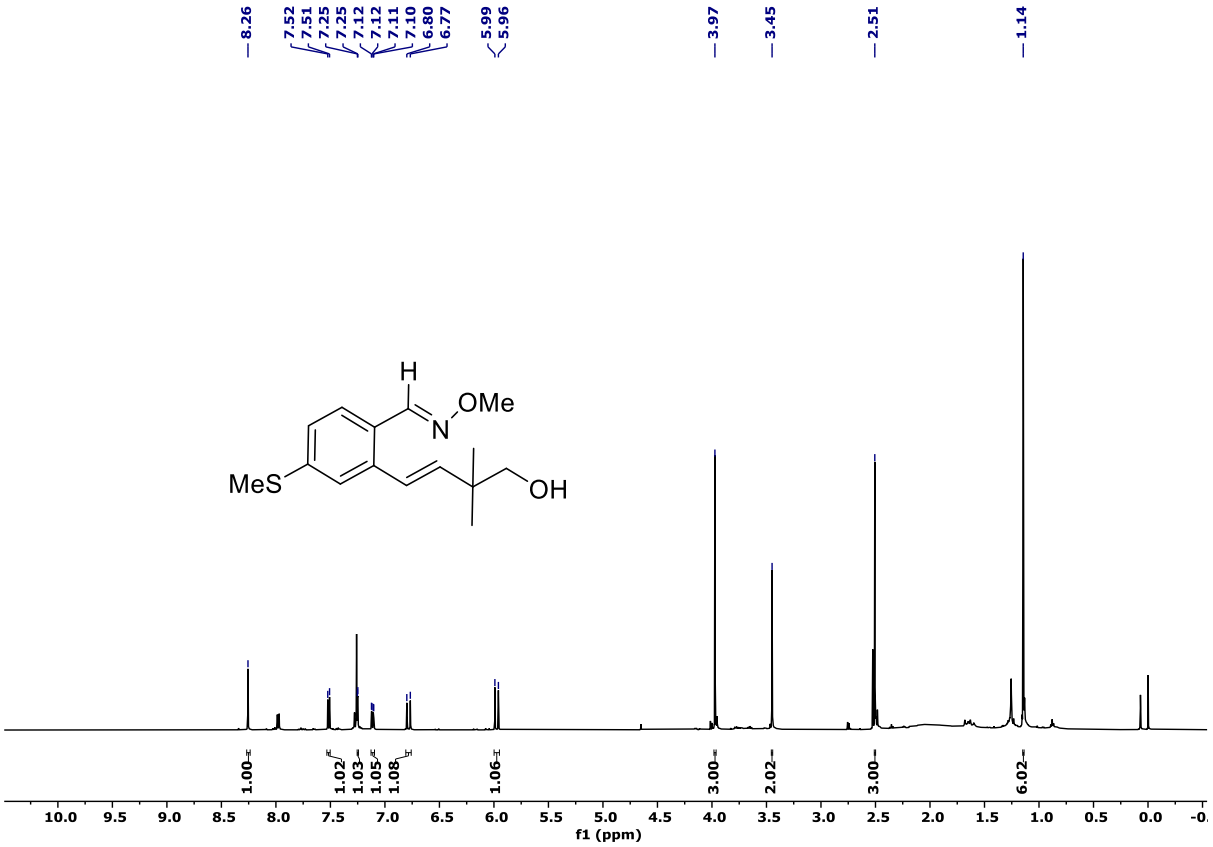


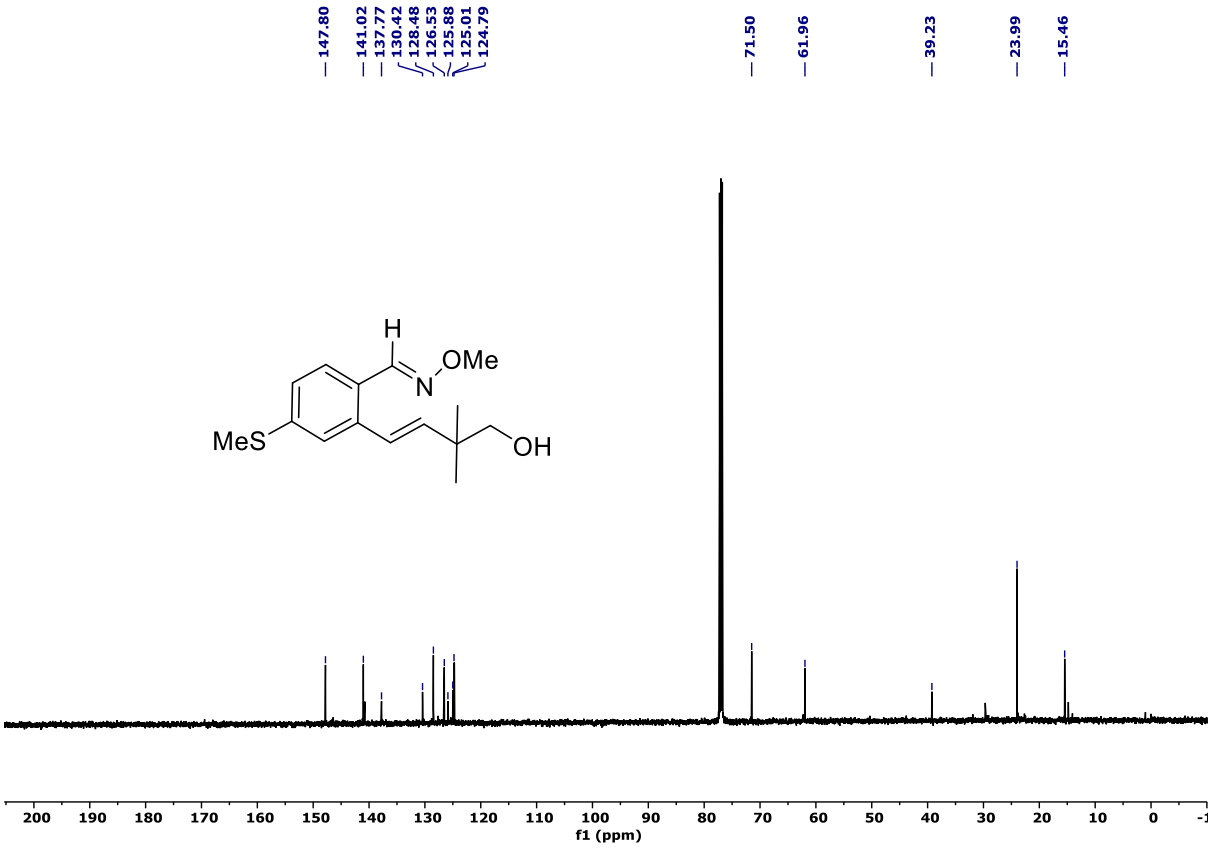
^{1}H and ^{13}C NMR Spectra of Compound **6d.** ($CDCl_3$ solvent was used, 500 NMR MHz)



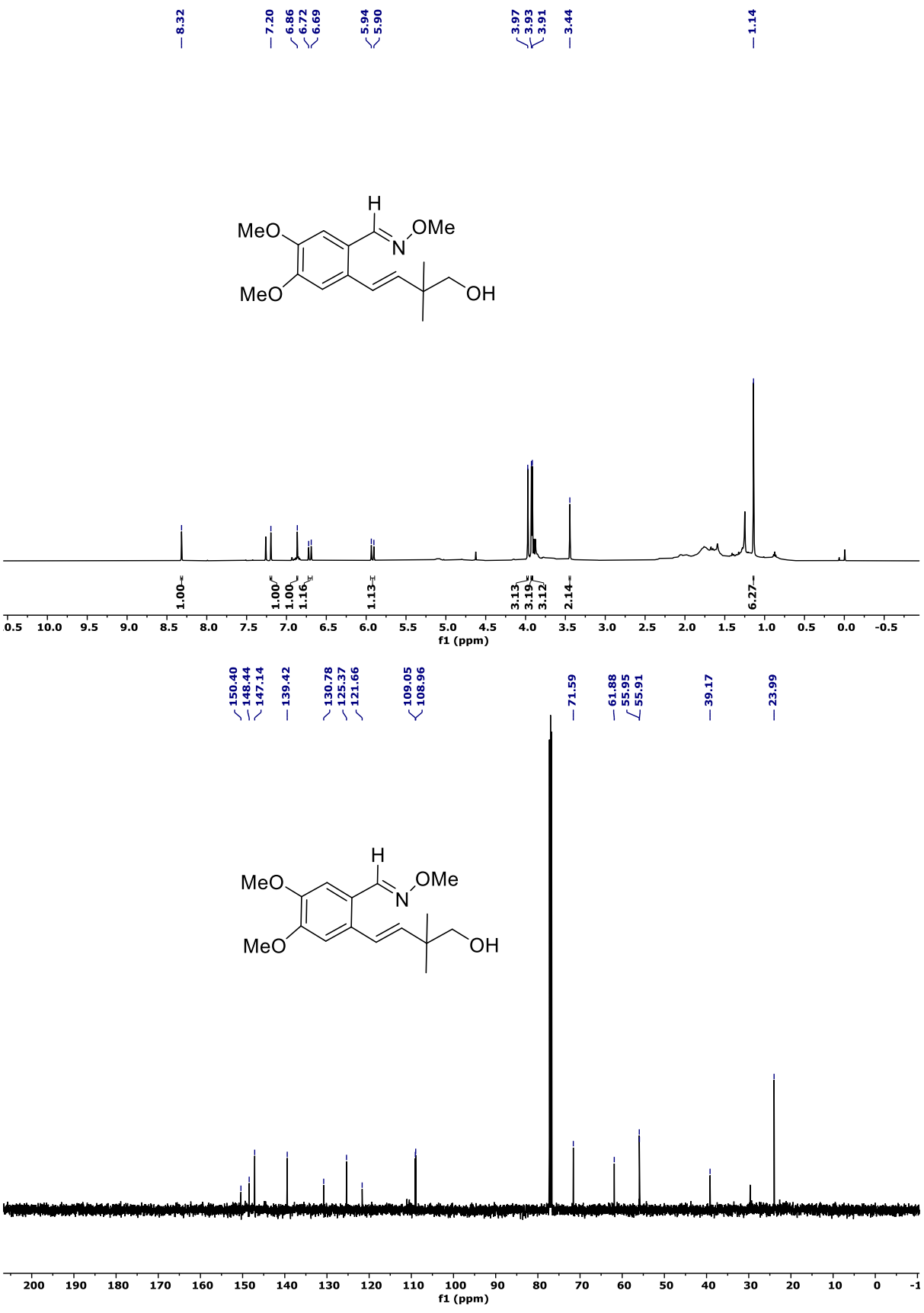


^{1}H and ^{13}C NMR Spectra of Compound **6e.** ($CDCl_3$ solvent was used, 500 NMR MHz)

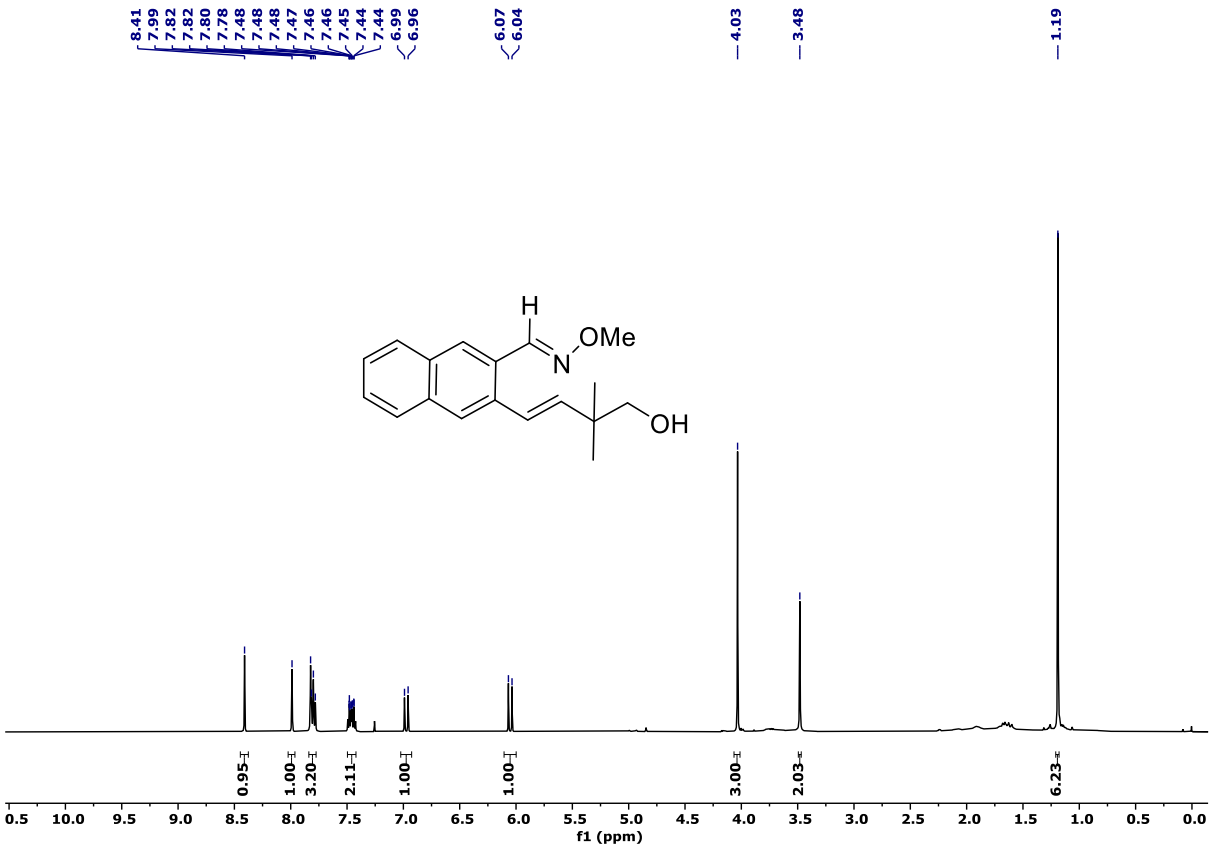


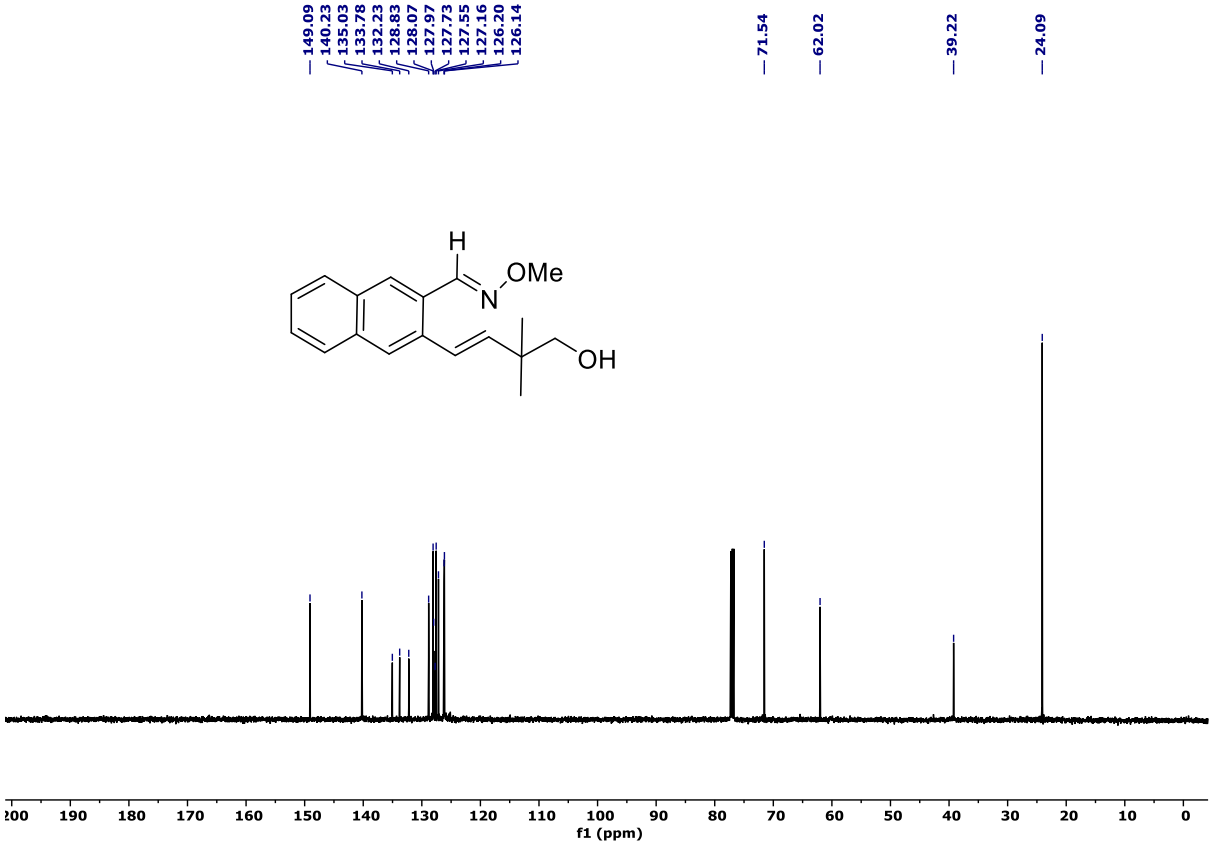


^{1}H and ^{13}C NMR Spectra of Compound **6f.** ($CDCl_3$ solvent was used, 500 NMR MHz)

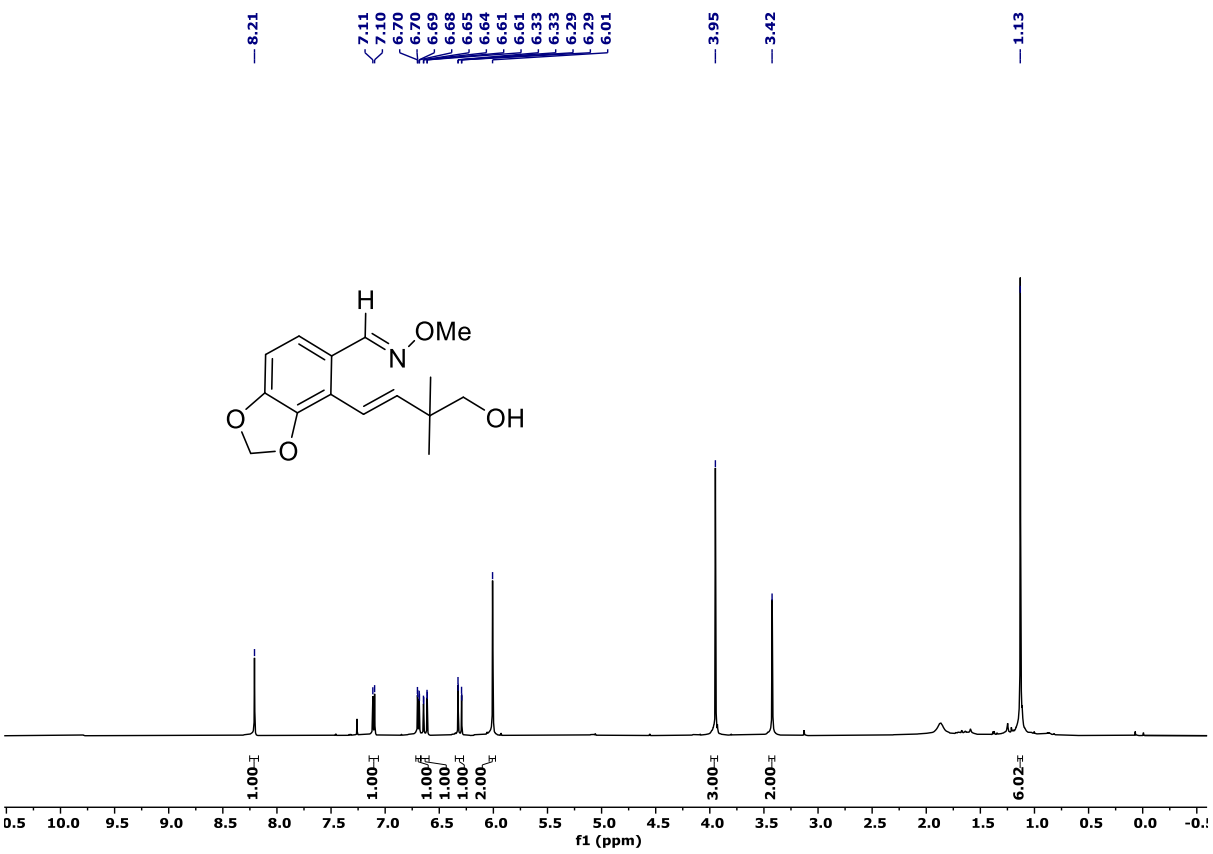


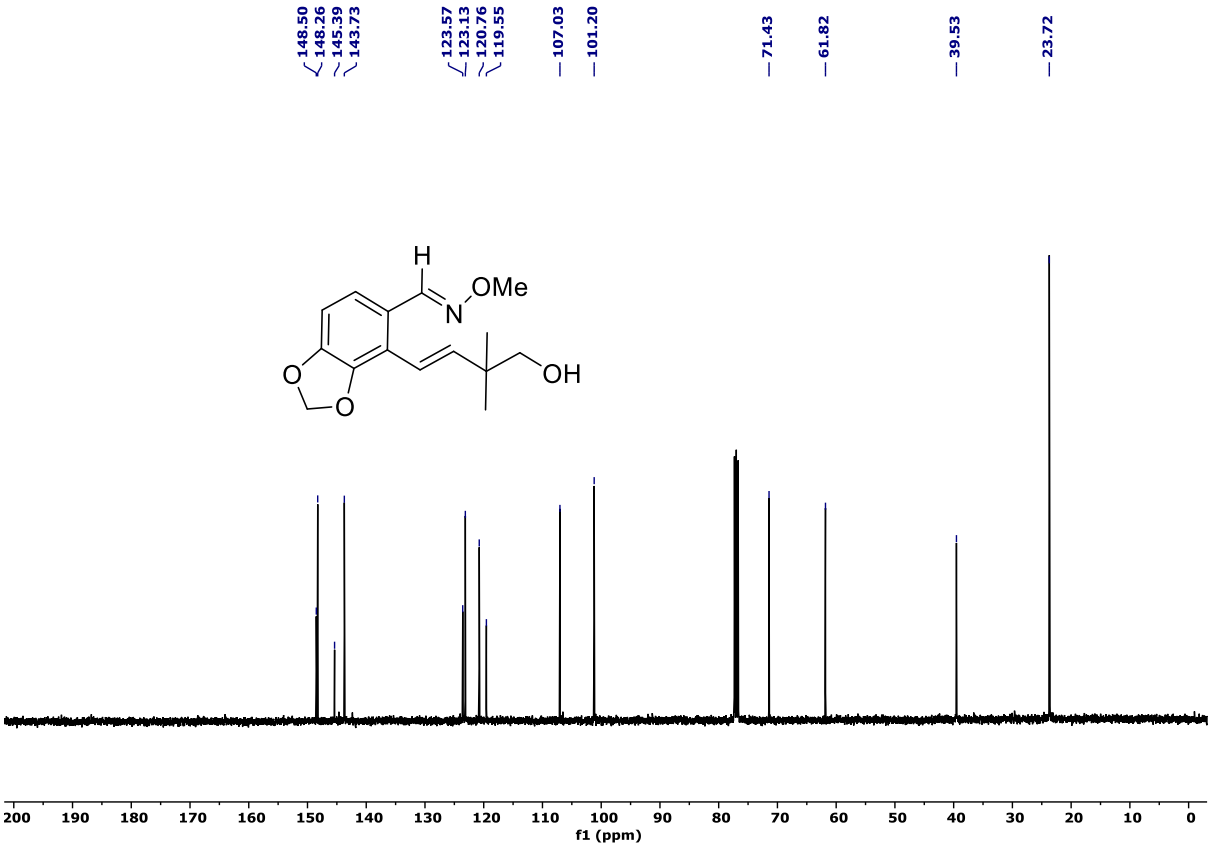
^{1}H and ^{13}C NMR Spectra of Compound **6g.** ($CDCl_3$ solvent was used, 500 NMR MHz)



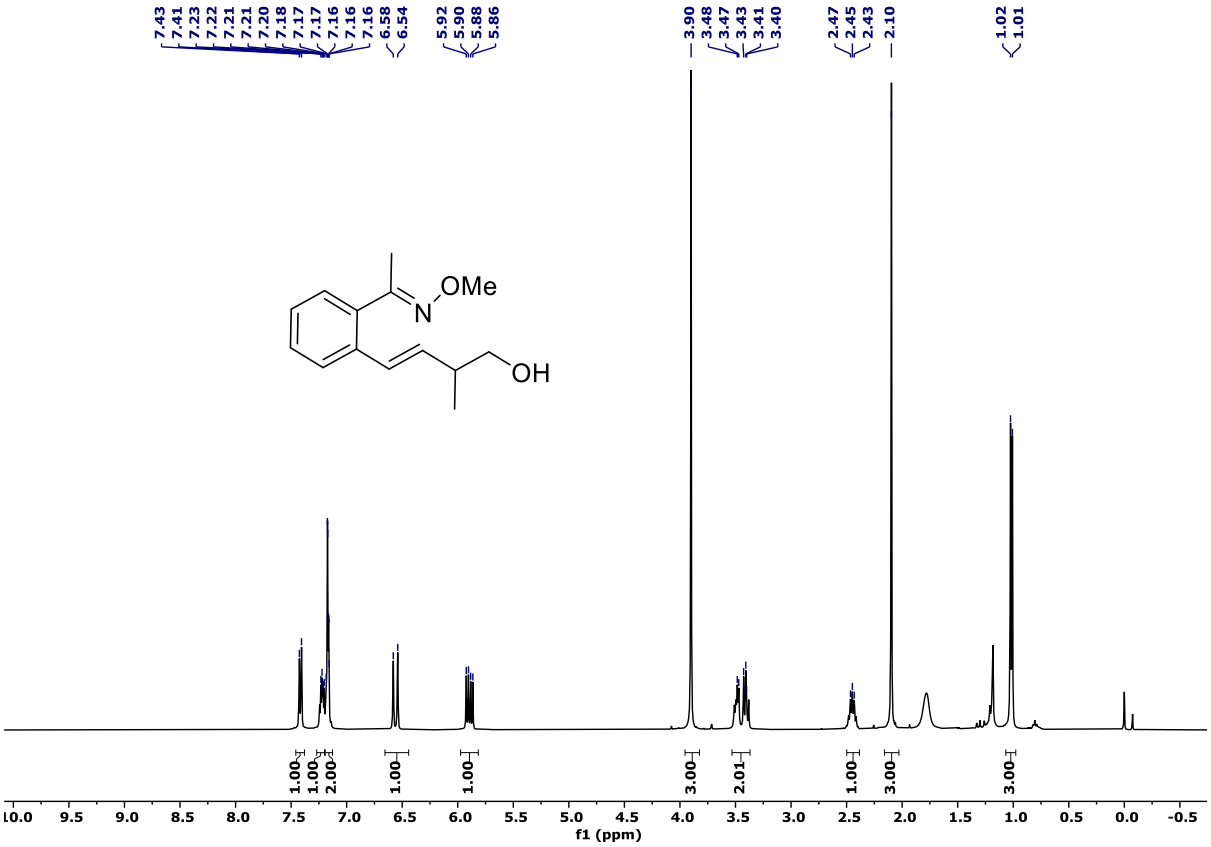


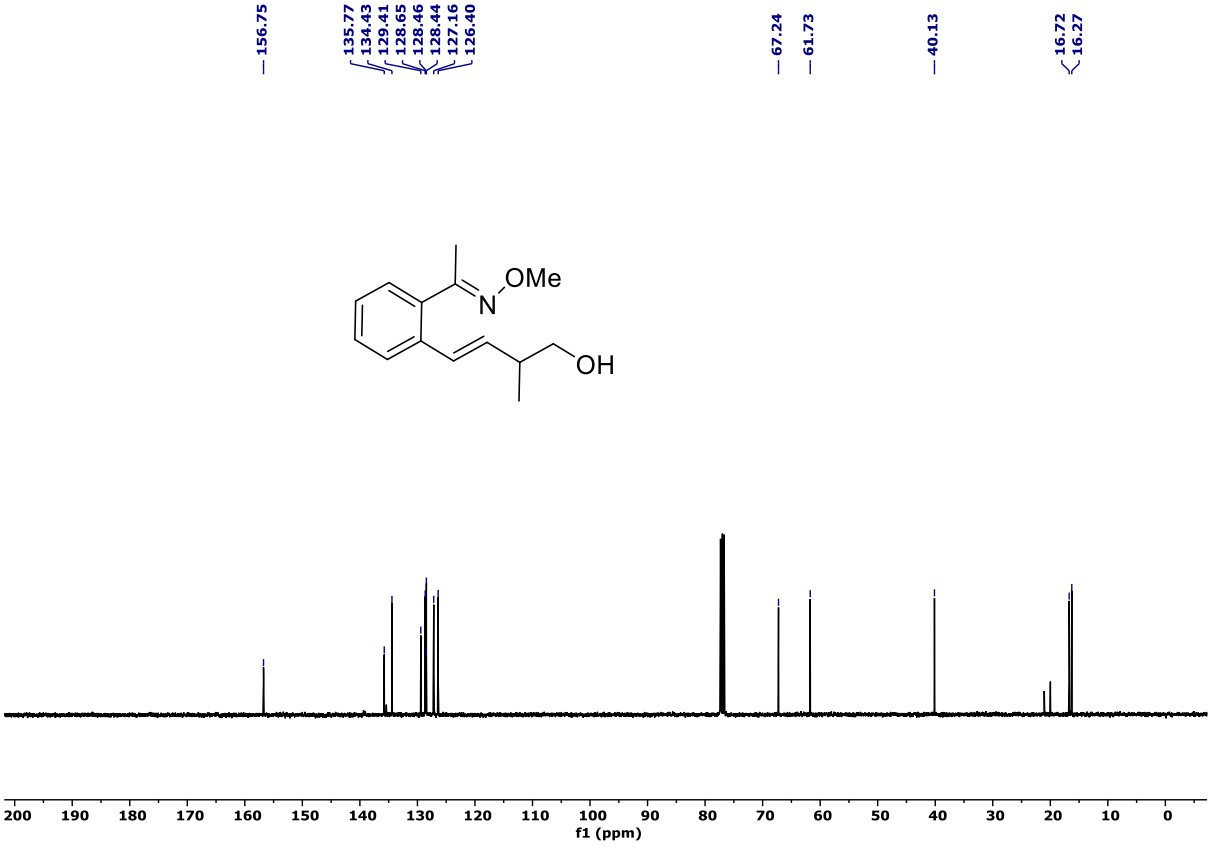
^{1}H and ^{13}C NMR Spectra of Compound **6h.** ($CDCl_3$ solvent was used, 500 NMR MHz)



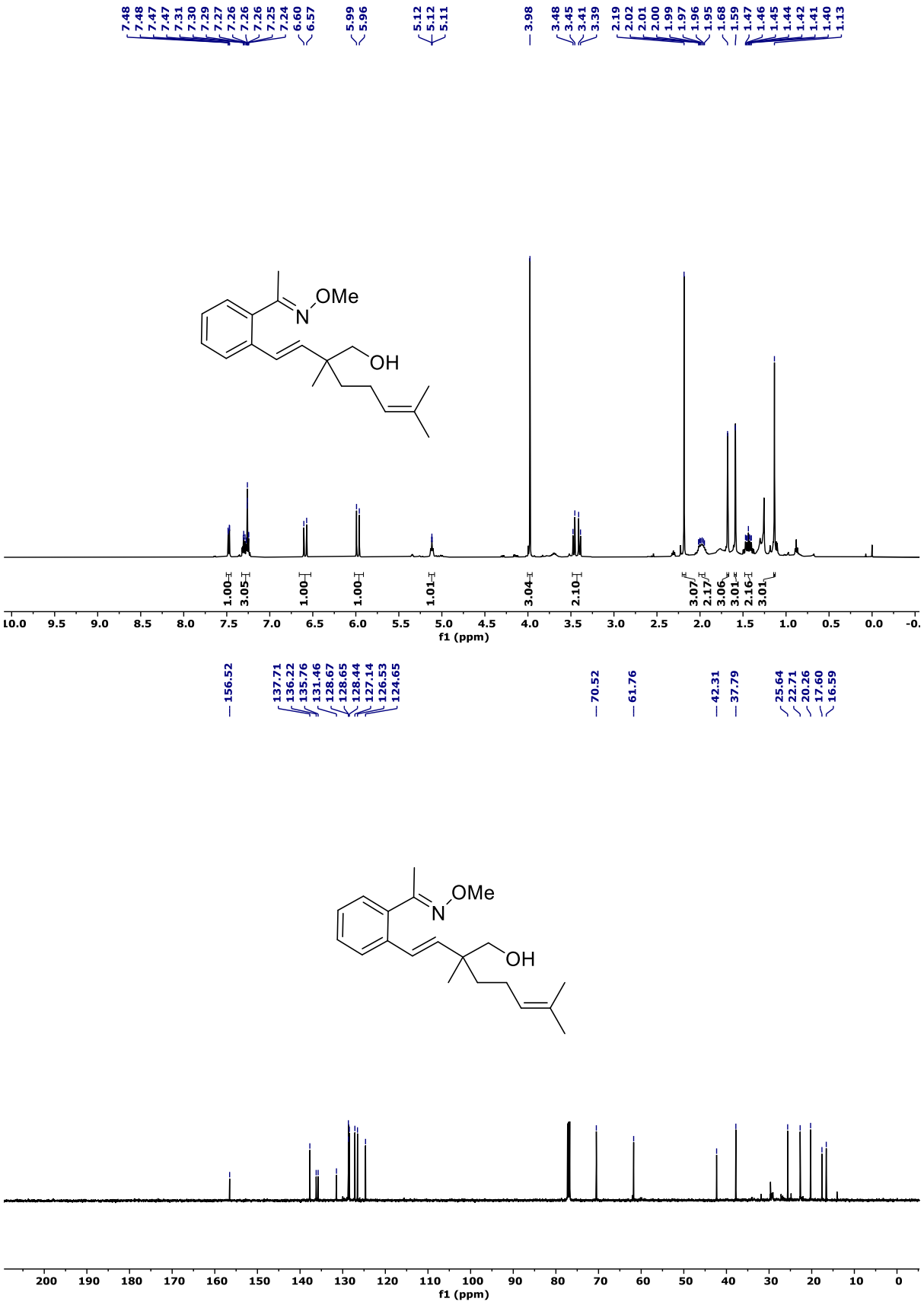


^{1}H and ^{13}C NMR Spectra of Compound **8aa.** ($CDCl_3$ solvent was used, 400 NMR MHz)

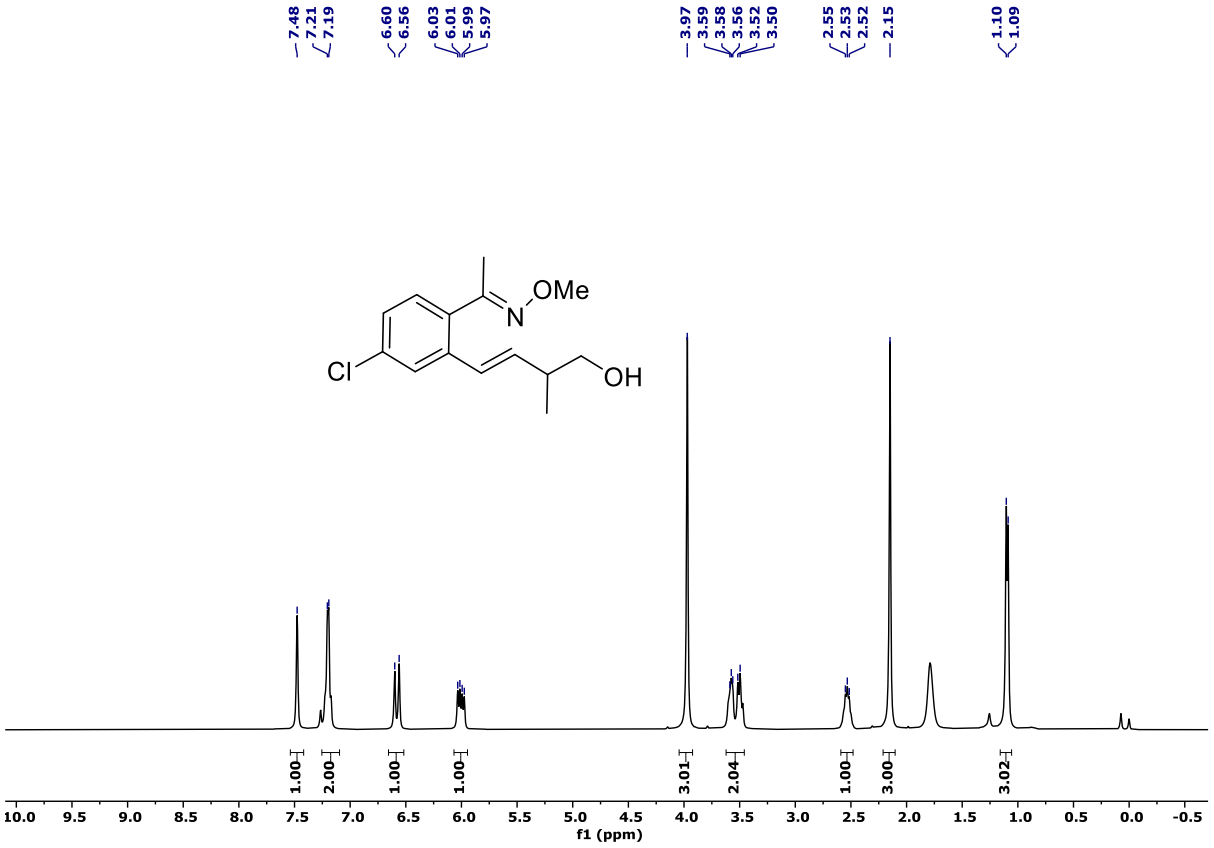


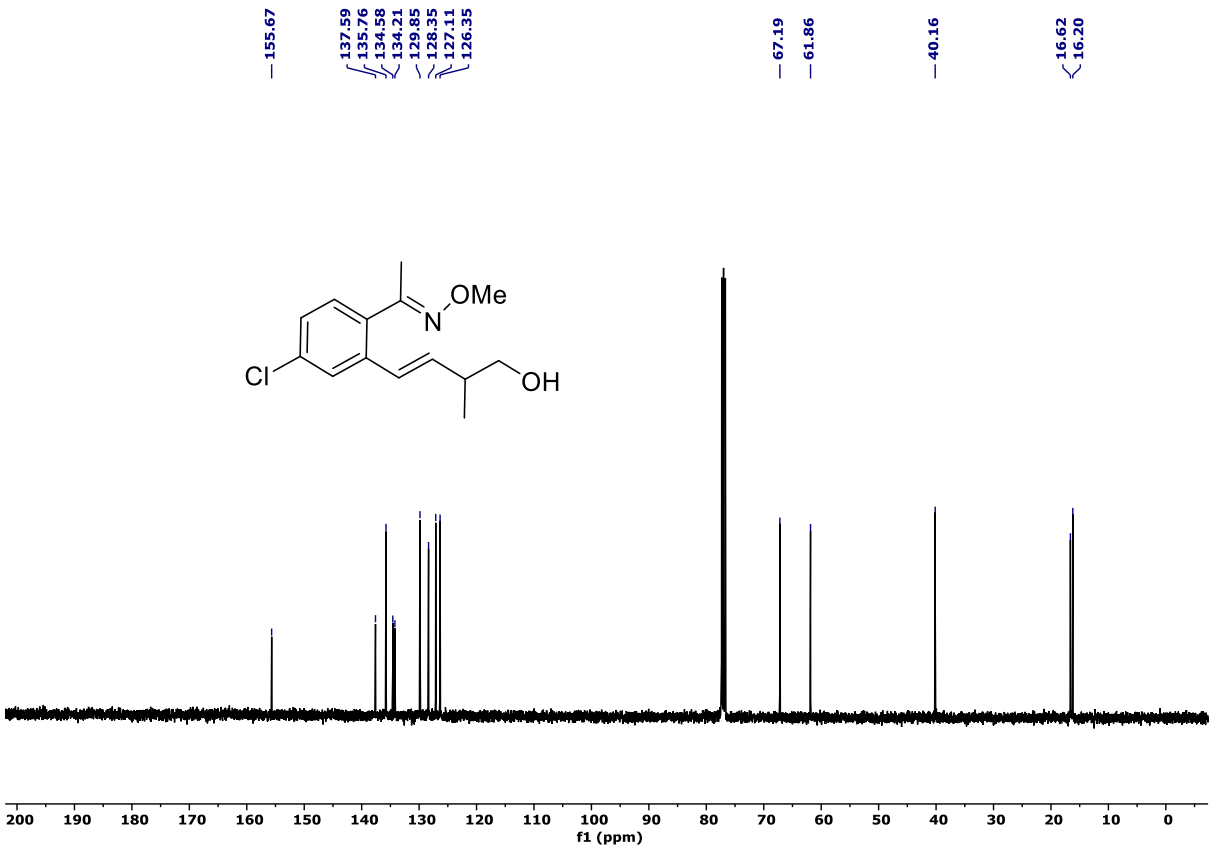


^{1}H and ^{13}C NMR Spectra of Compound **8ab.** ($CDCl_3$ solvent was used, 500 NMR MHz)

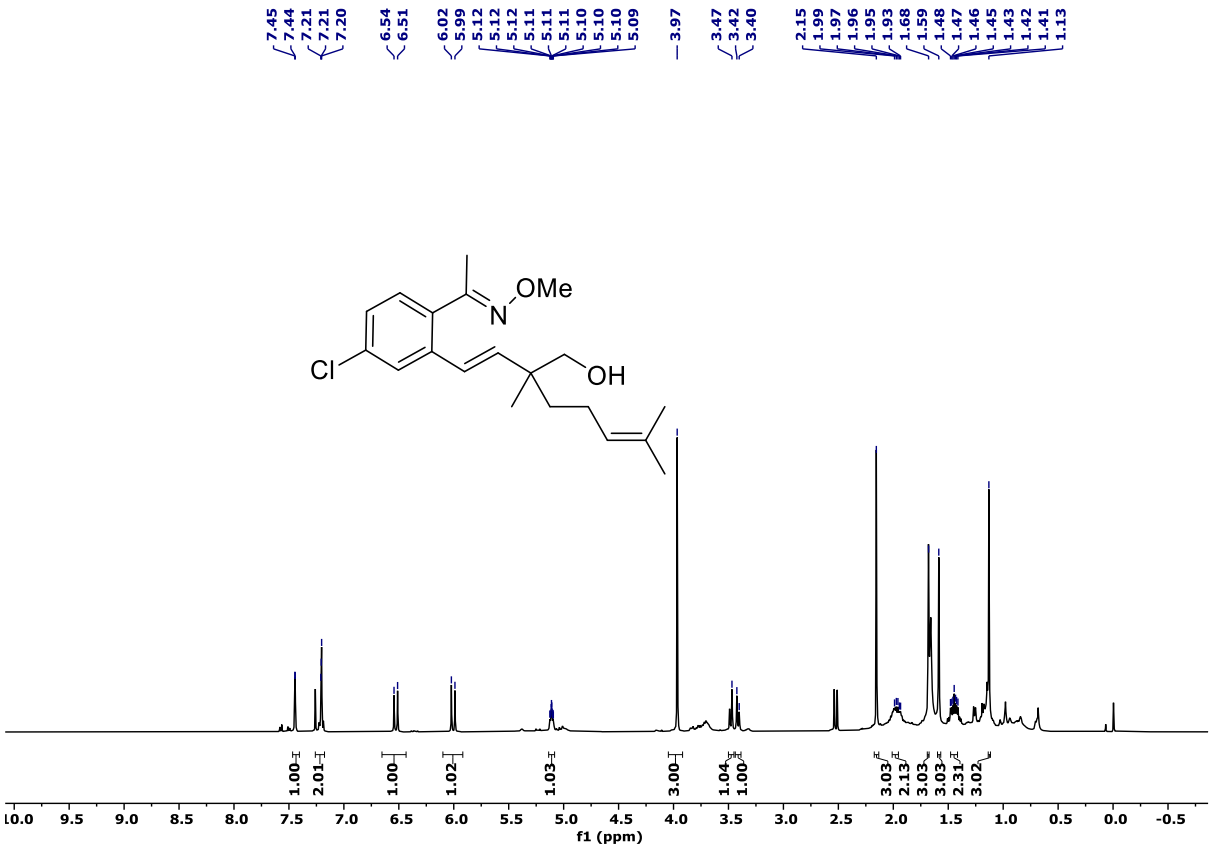


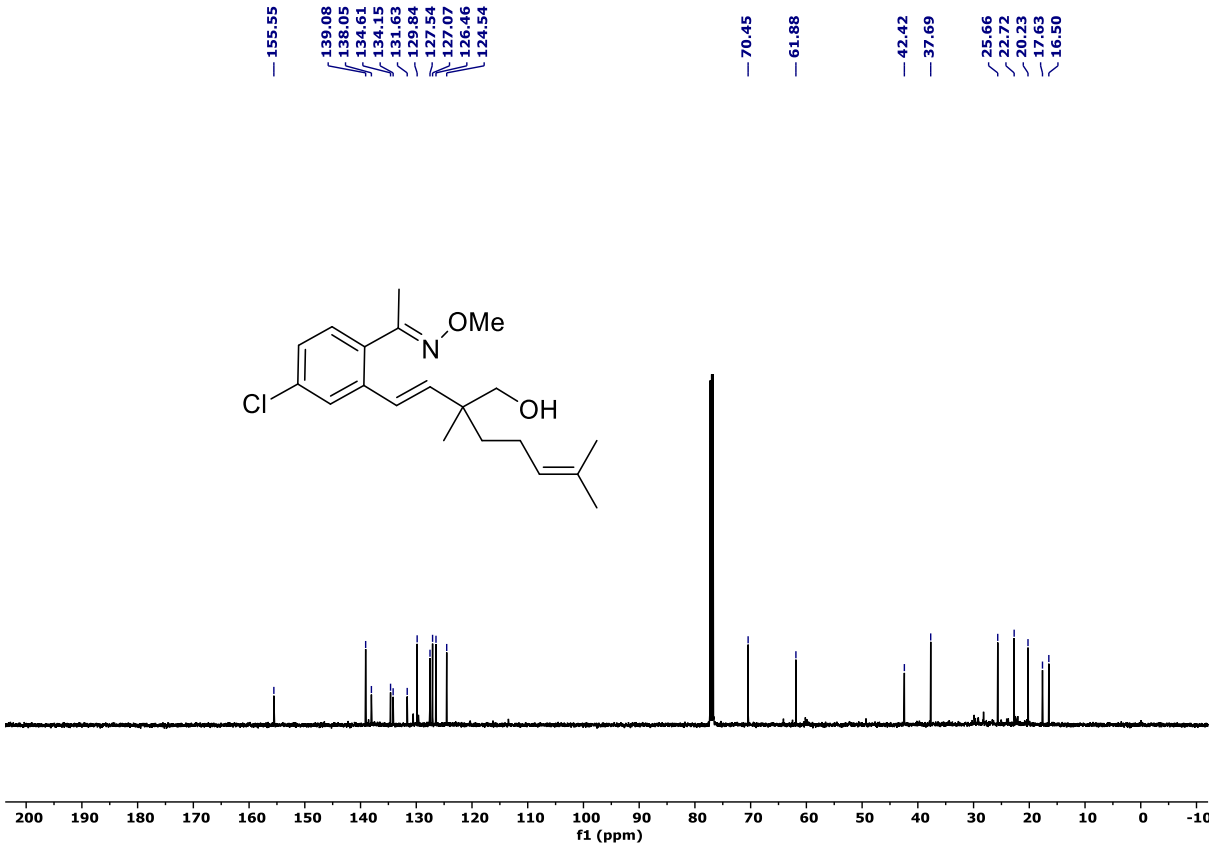
^{1}H and ^{13}C NMR Spectra of Compound **8ca.** ($CDCl_3$ solvent was used, 400 NMR MHz)



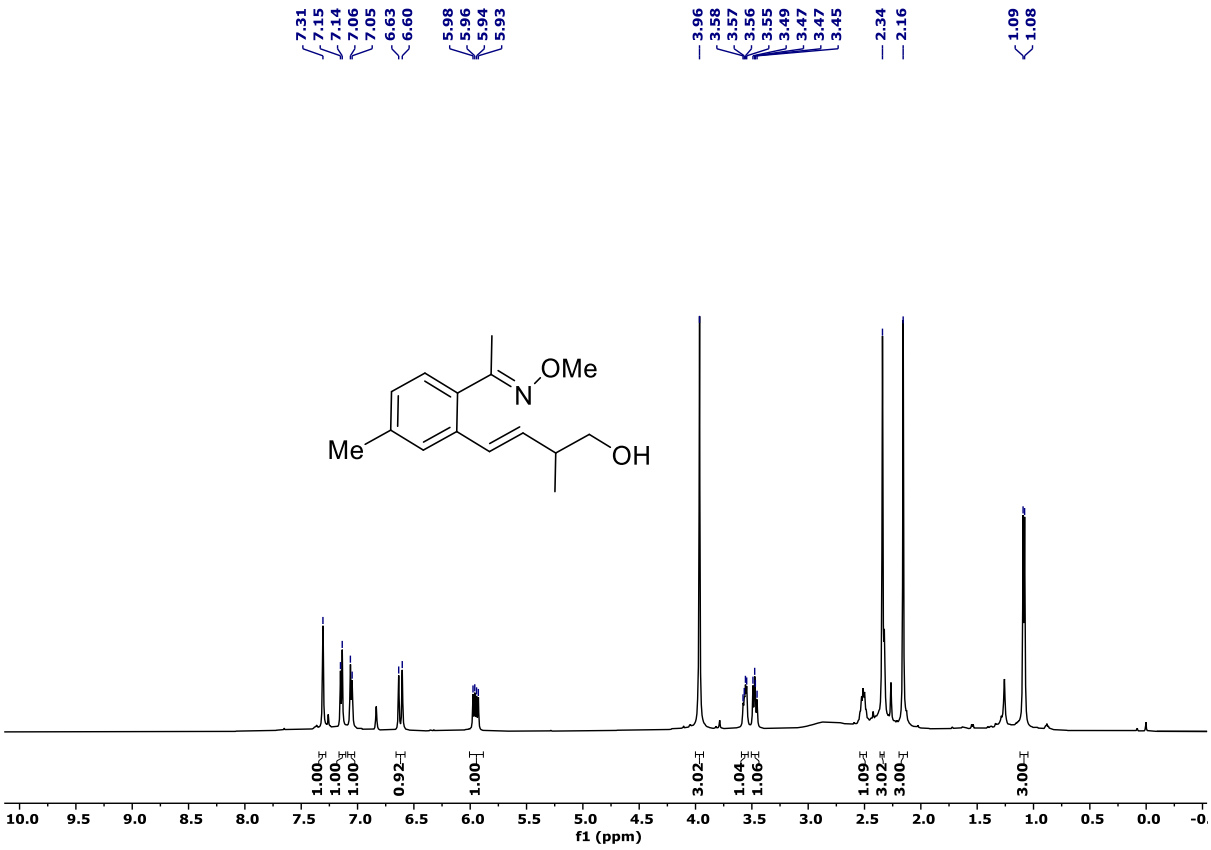


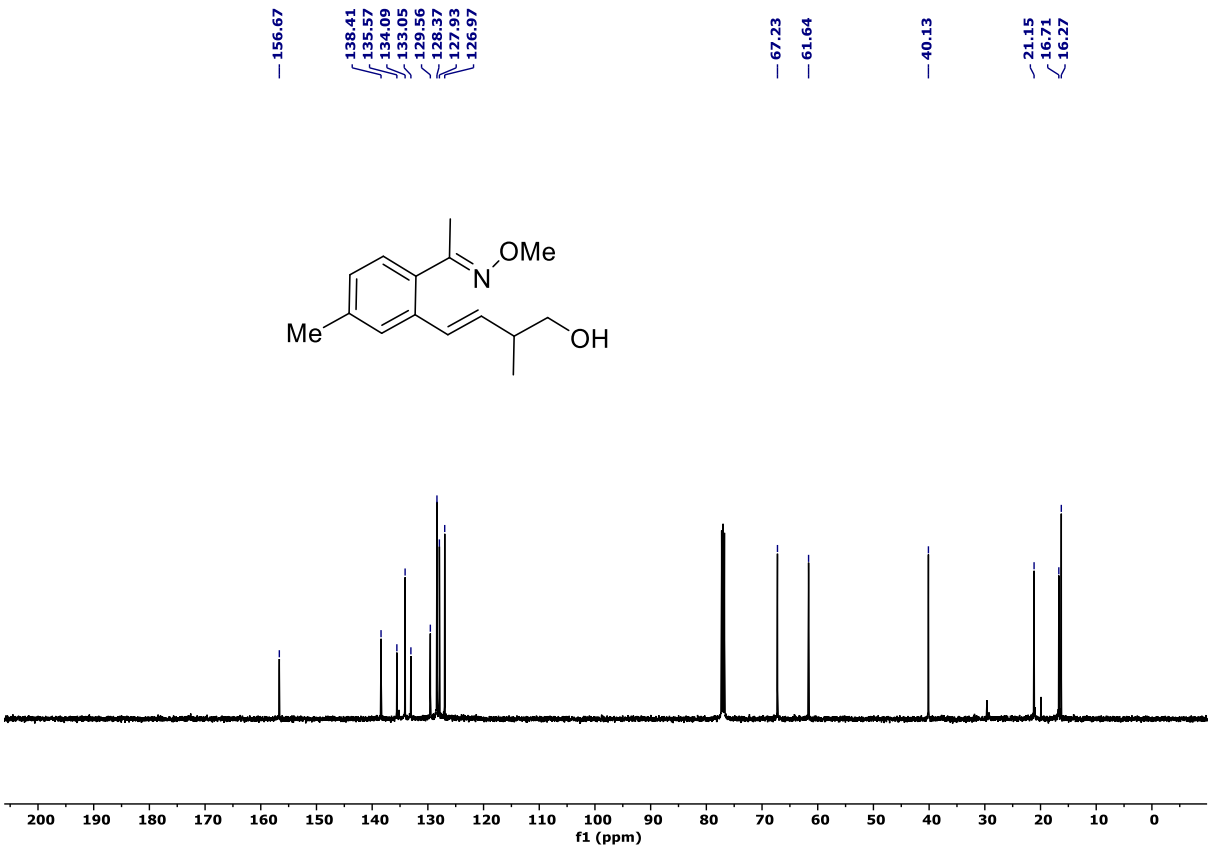
^{1}H and ^{13}C NMR Spectra of Compound **8cb.** ($CDCl_3$ solvent was used, 500 NMR MHz)



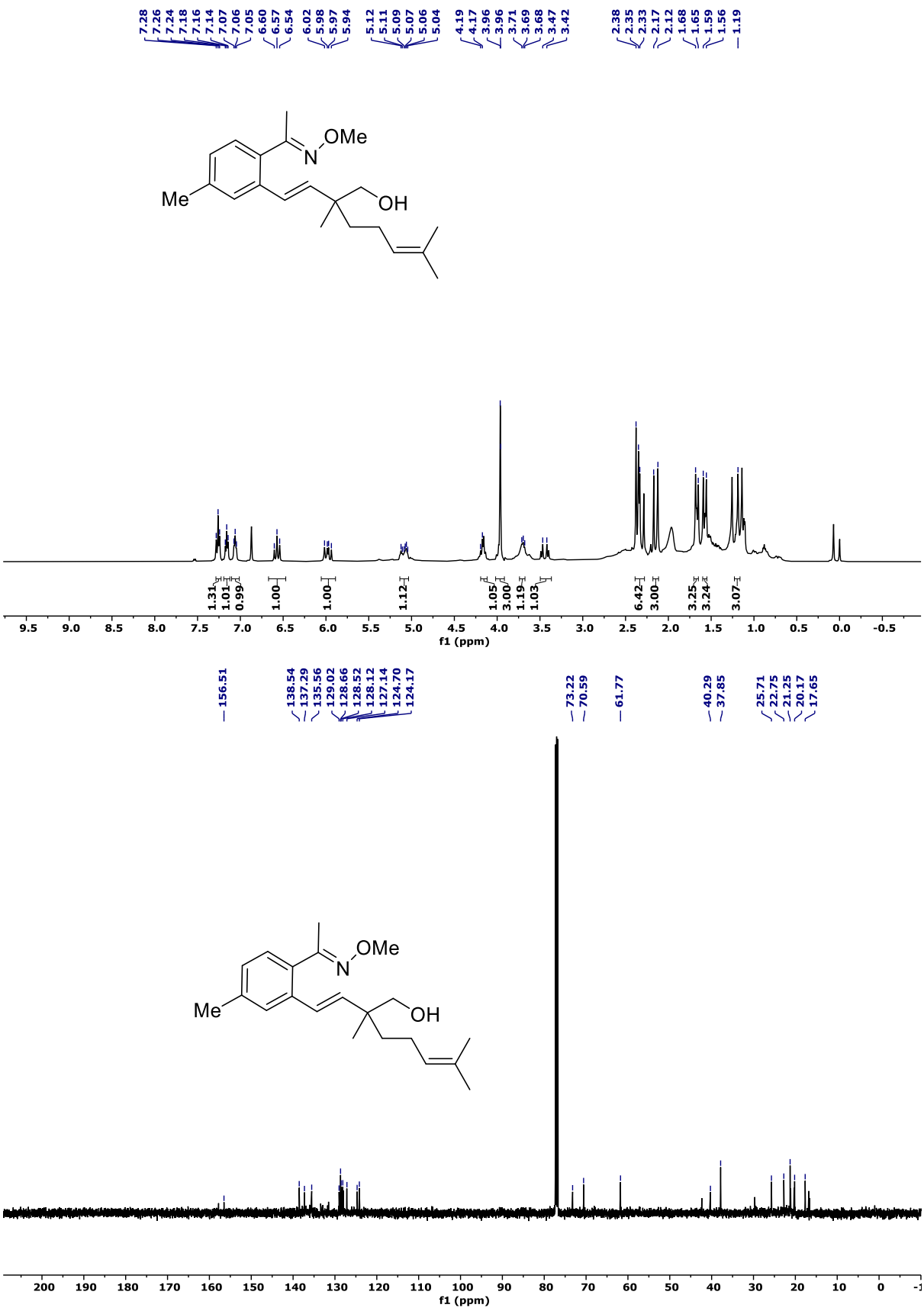


^{1}H and ^{13}C NMR Spectra of Compound **8fa.** ($CDCl_3$ solvent was used, 500 NMR MHz)

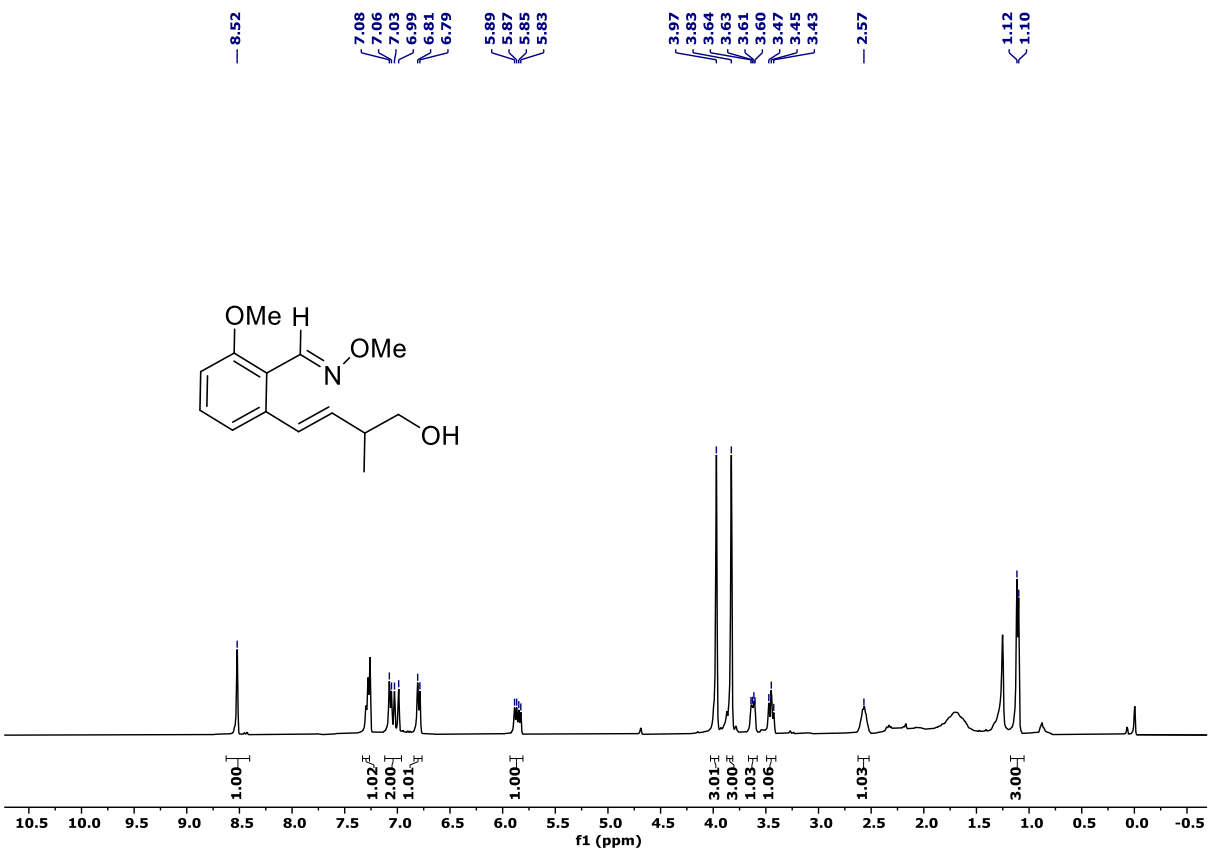


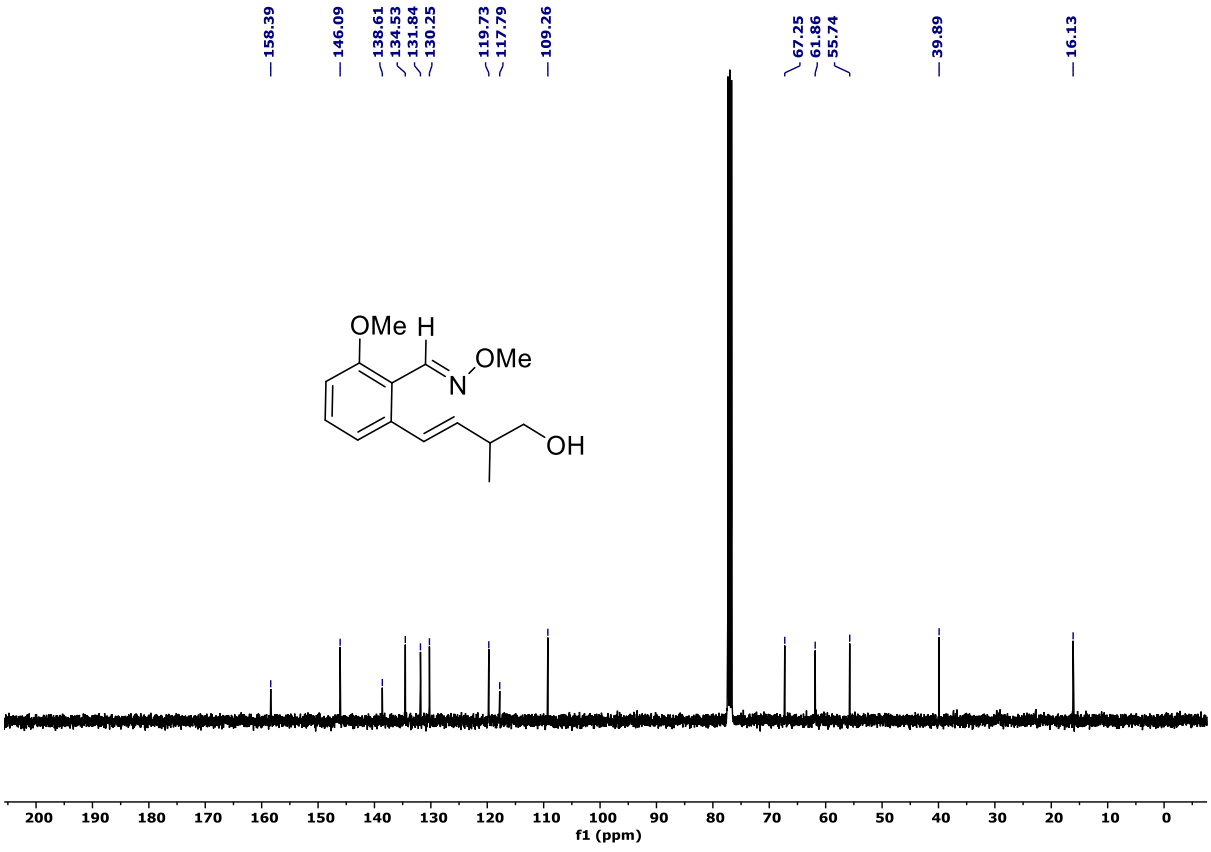


^{1}H and ^{13}C NMR Spectra of Compound **8fb.** ($CDCl_3$ solvent was used, 500 NMR MHz)

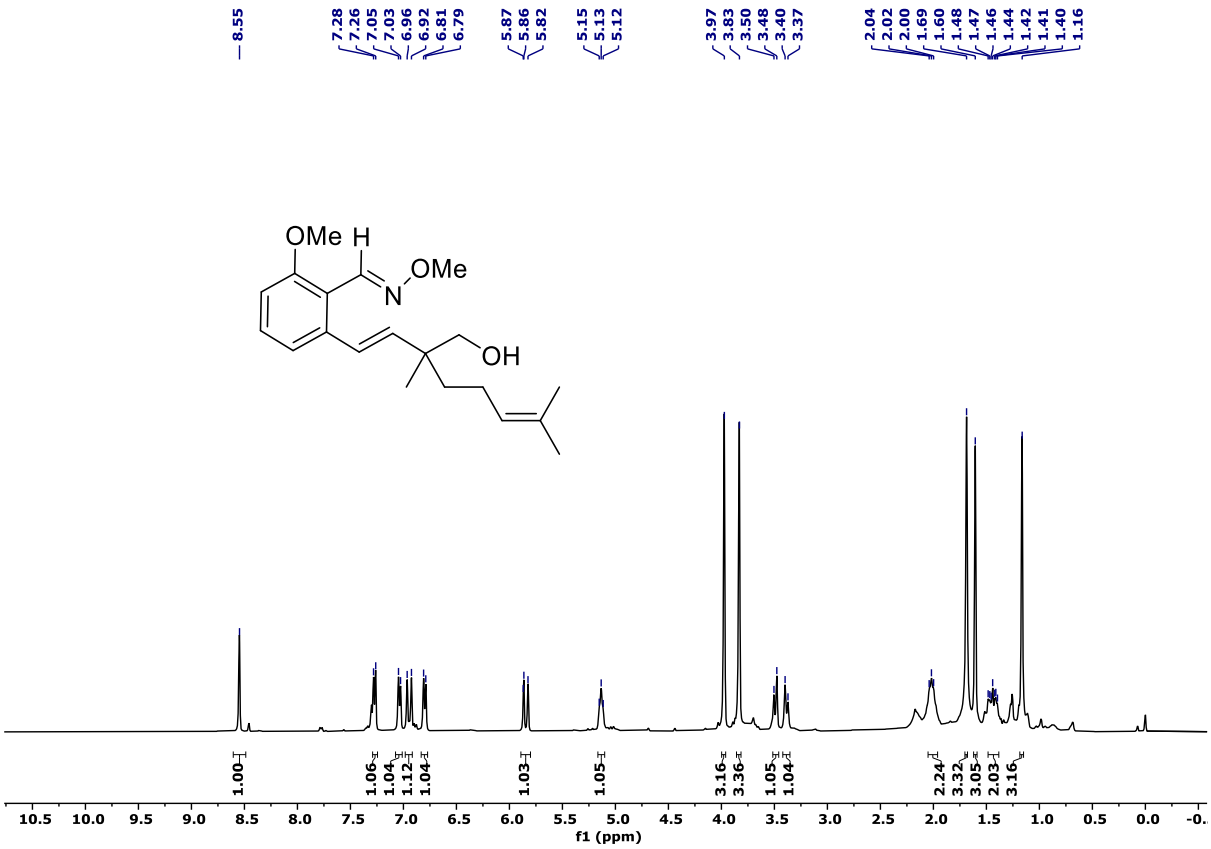


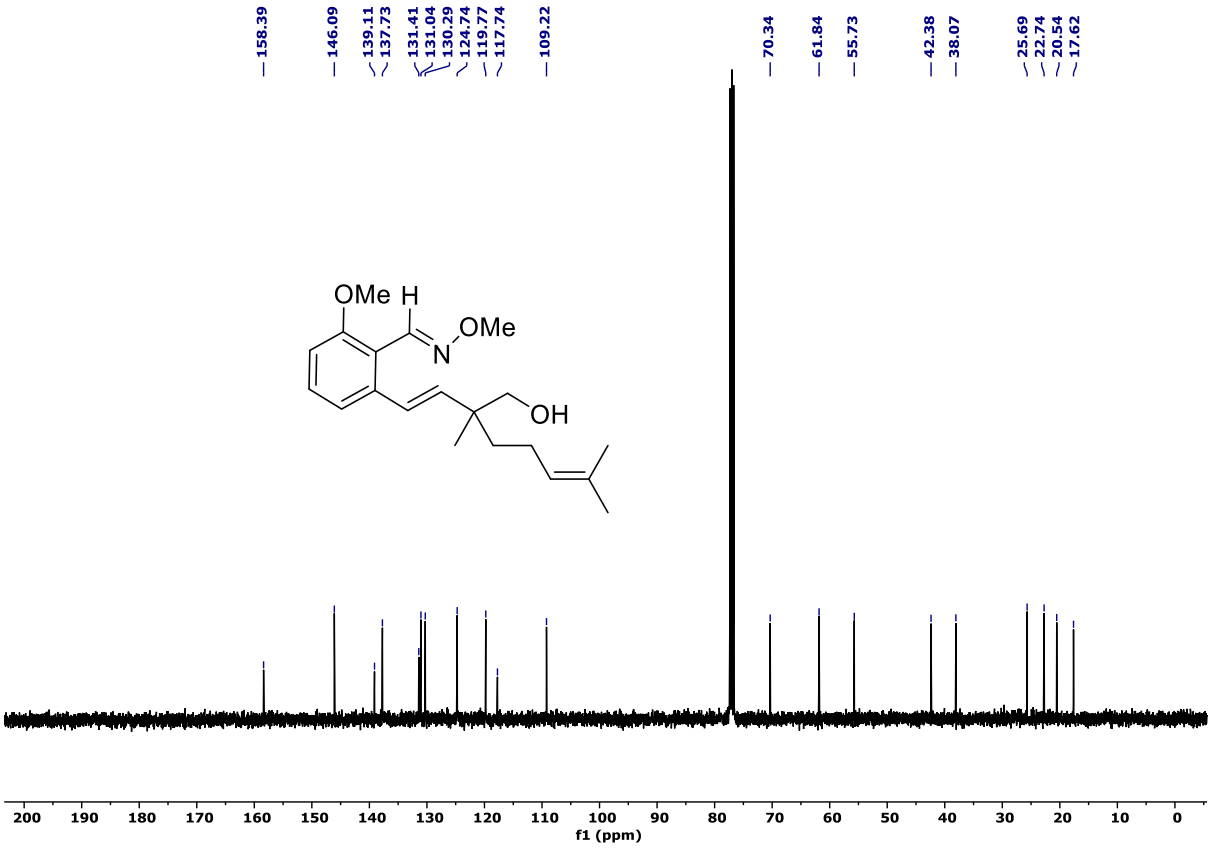
^{1}H and ^{13}C NMR Spectra of Compound **9ba.** ($CDCl_3$ solvent was used, 400 NMR MHz)



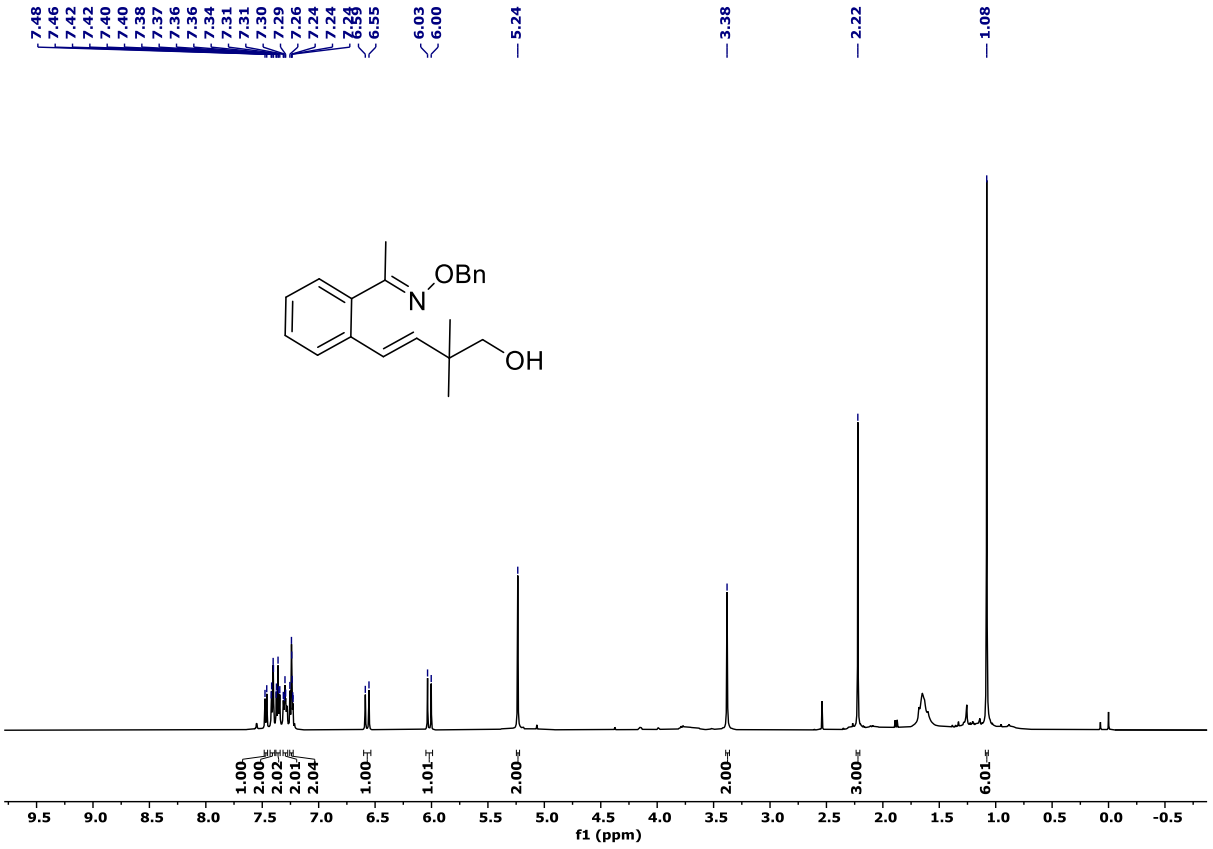


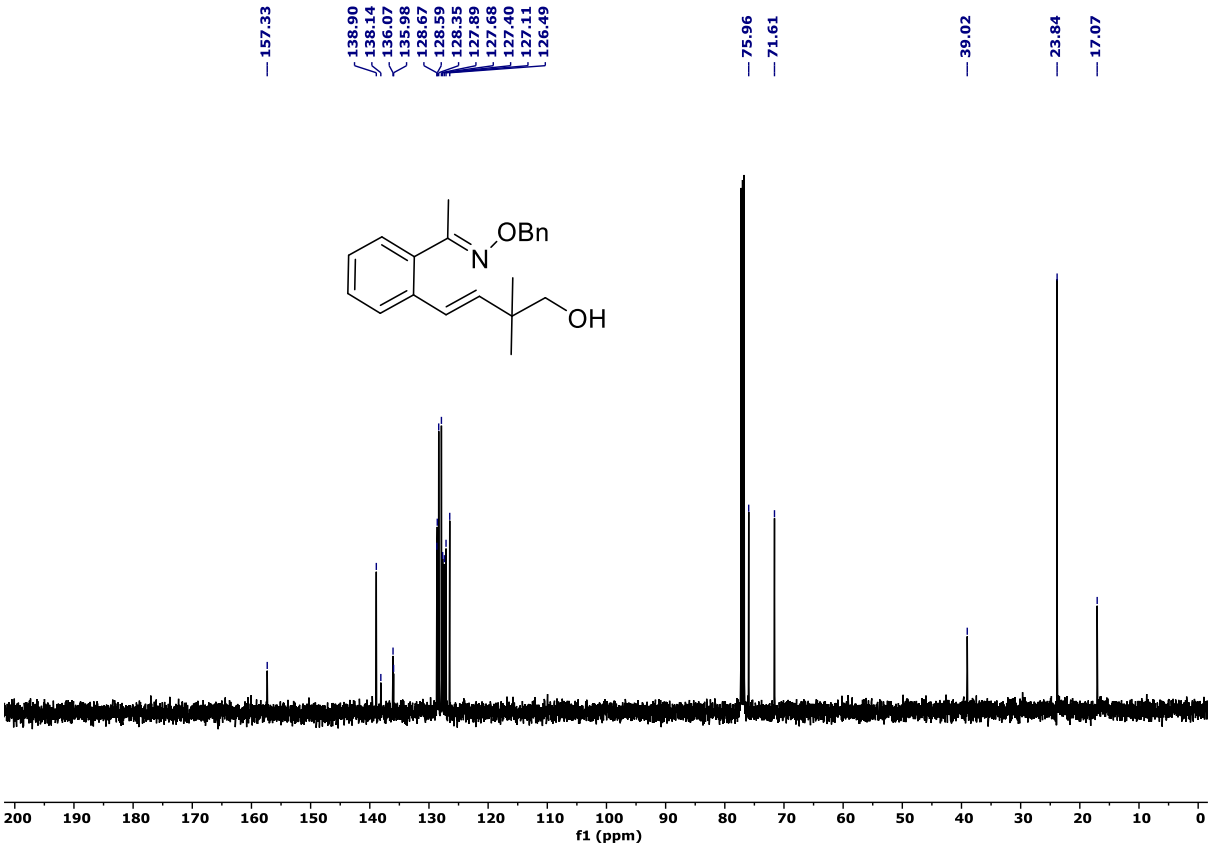
^{1}H and ^{13}C NMR Spectra of Compound **9bb.** ($CDCl_3$ solvent was used, 400 NMR MHz)



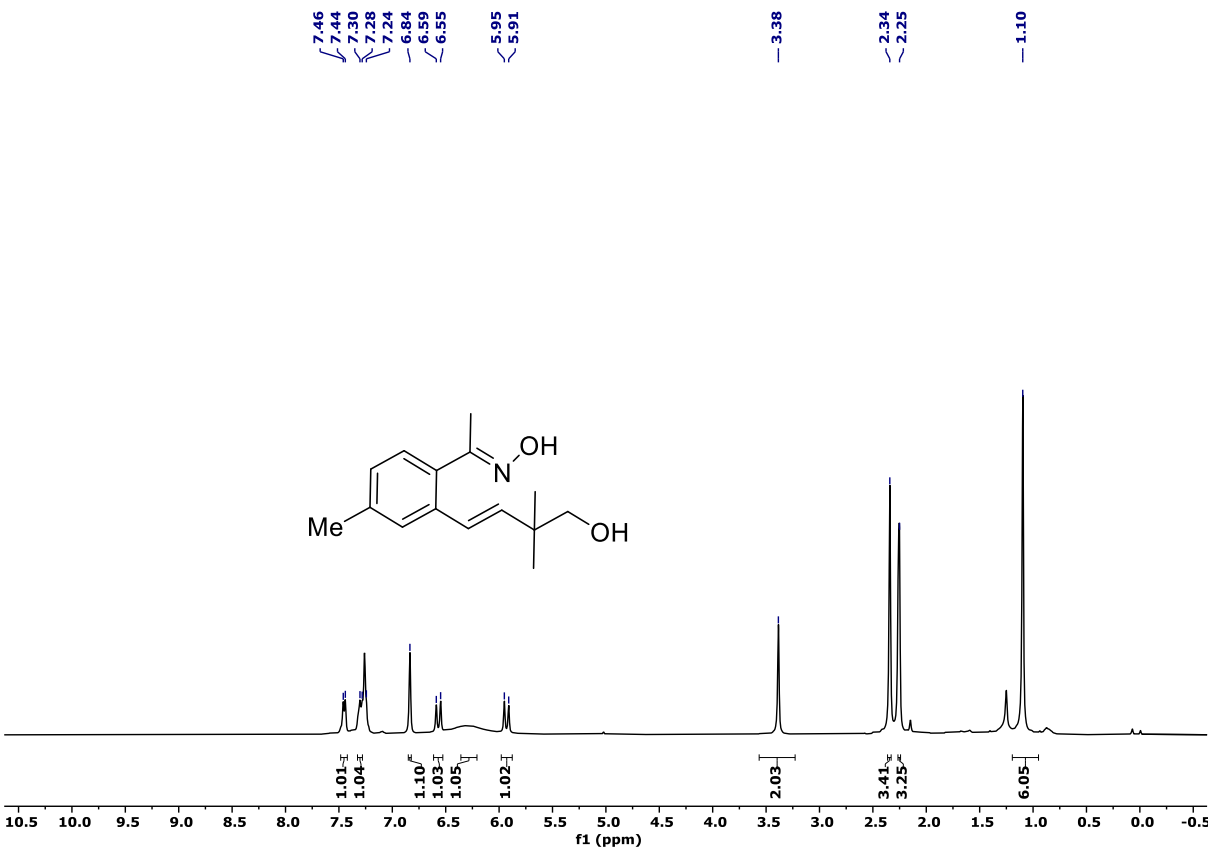


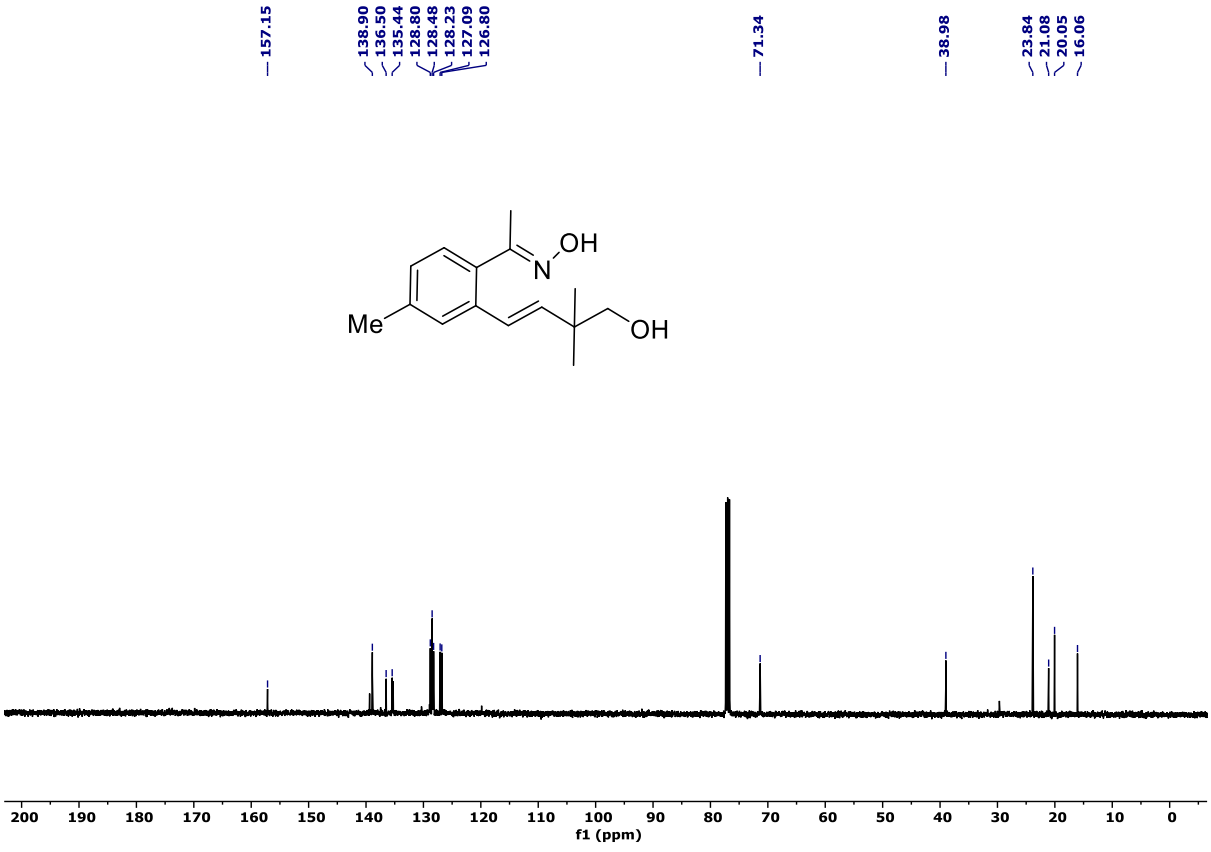
^{1}H and ^{13}C NMR Spectra of Compound **11a.** ($CDCl_3$ solvent was used, 500 NMR MHz)



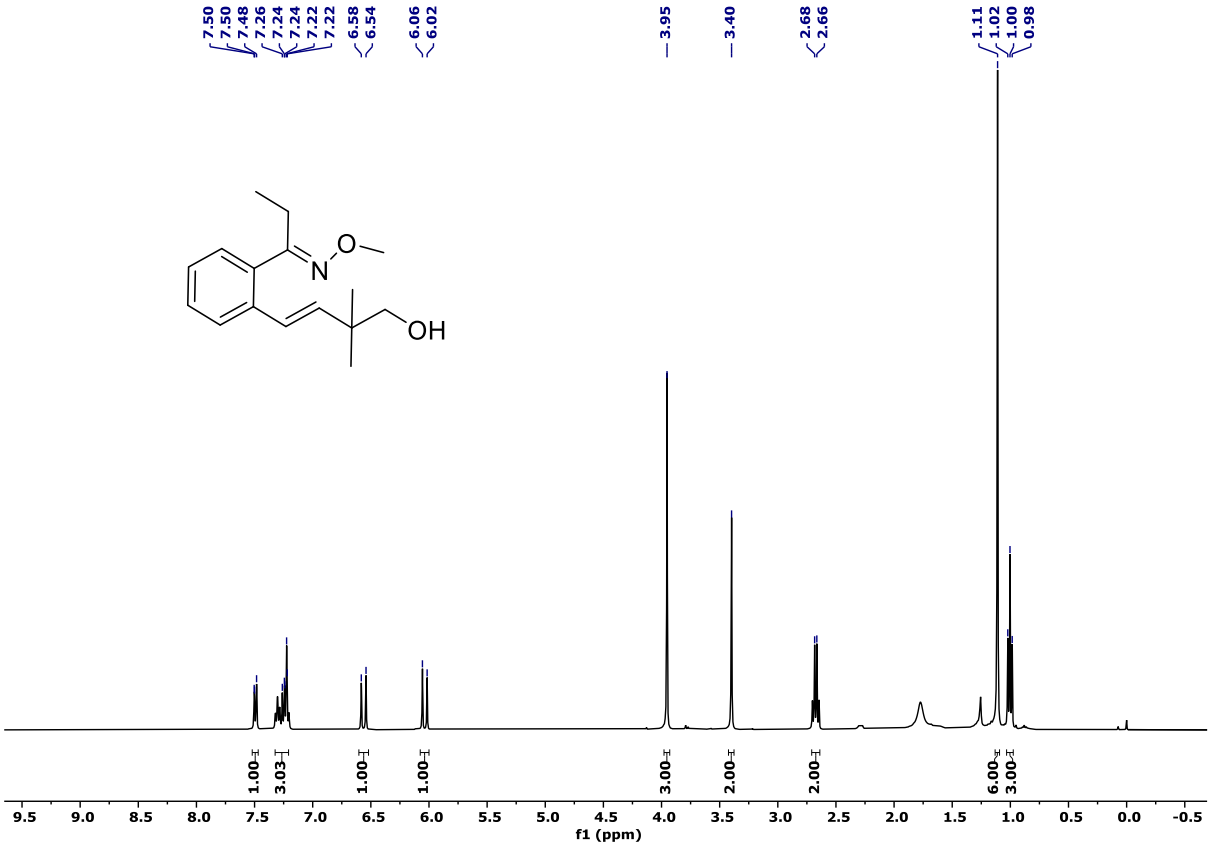


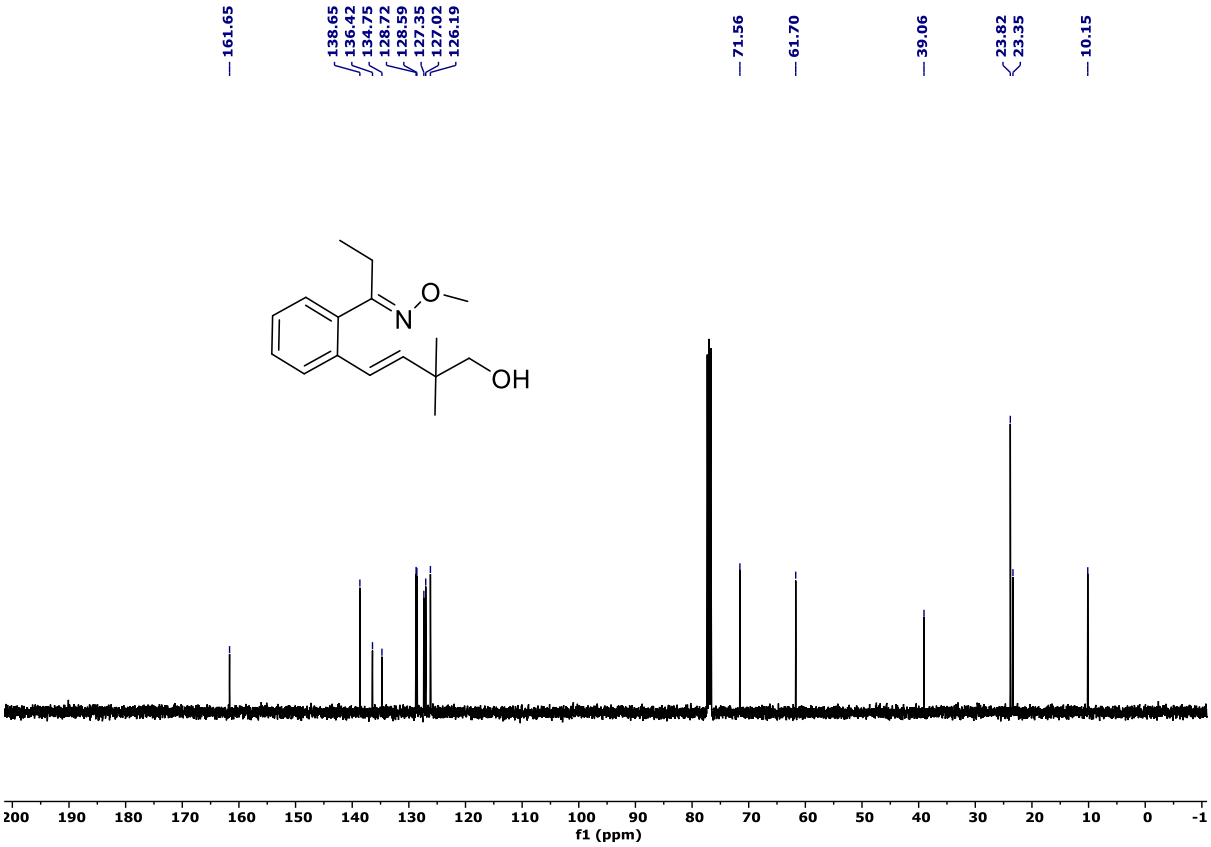
^{1}H and ^{13}C NMR Spectra of Compound **11b.** ($CDCl_3$ solvent was used, 400 NMR MHz)



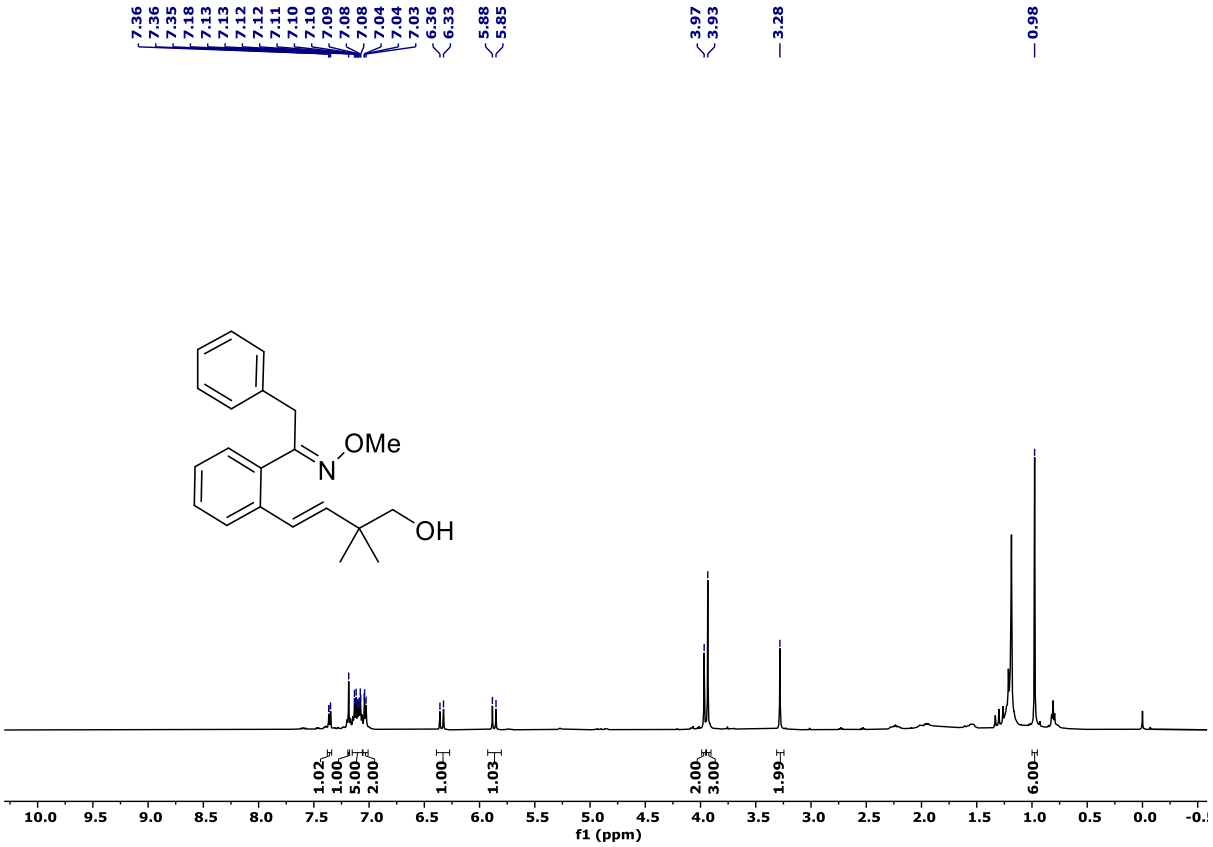


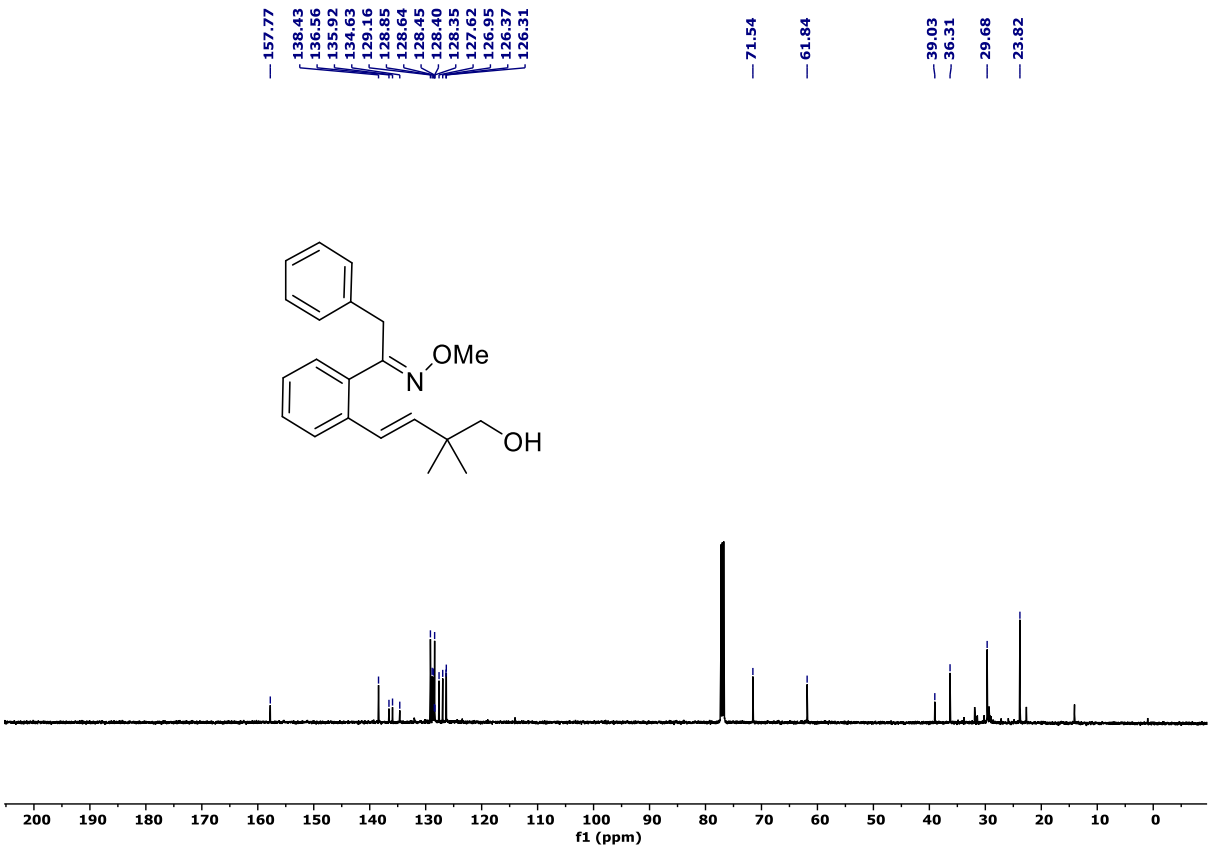
^{1}H and ^{13}C NMR Spectra of Compound **11c.** ($CDCl_3$ solvent was used, 400 NMR MHz)



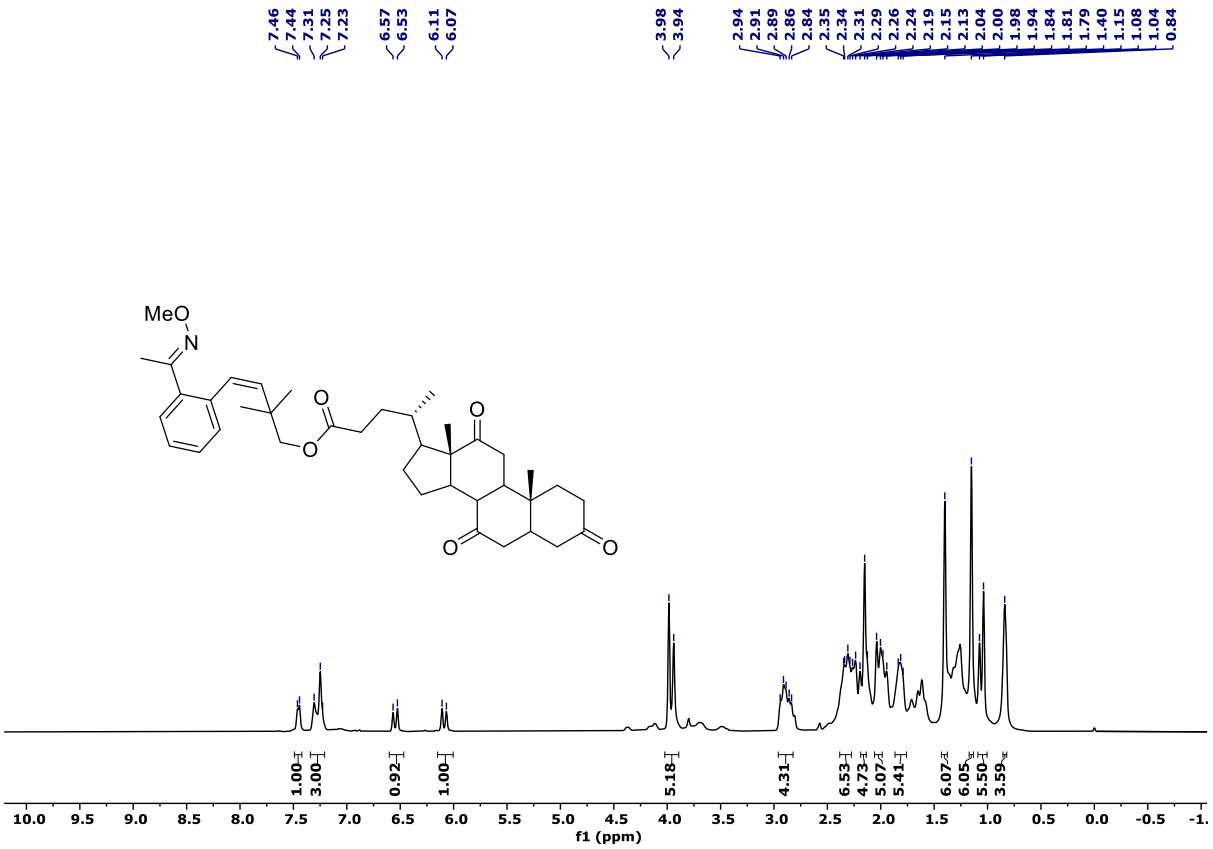


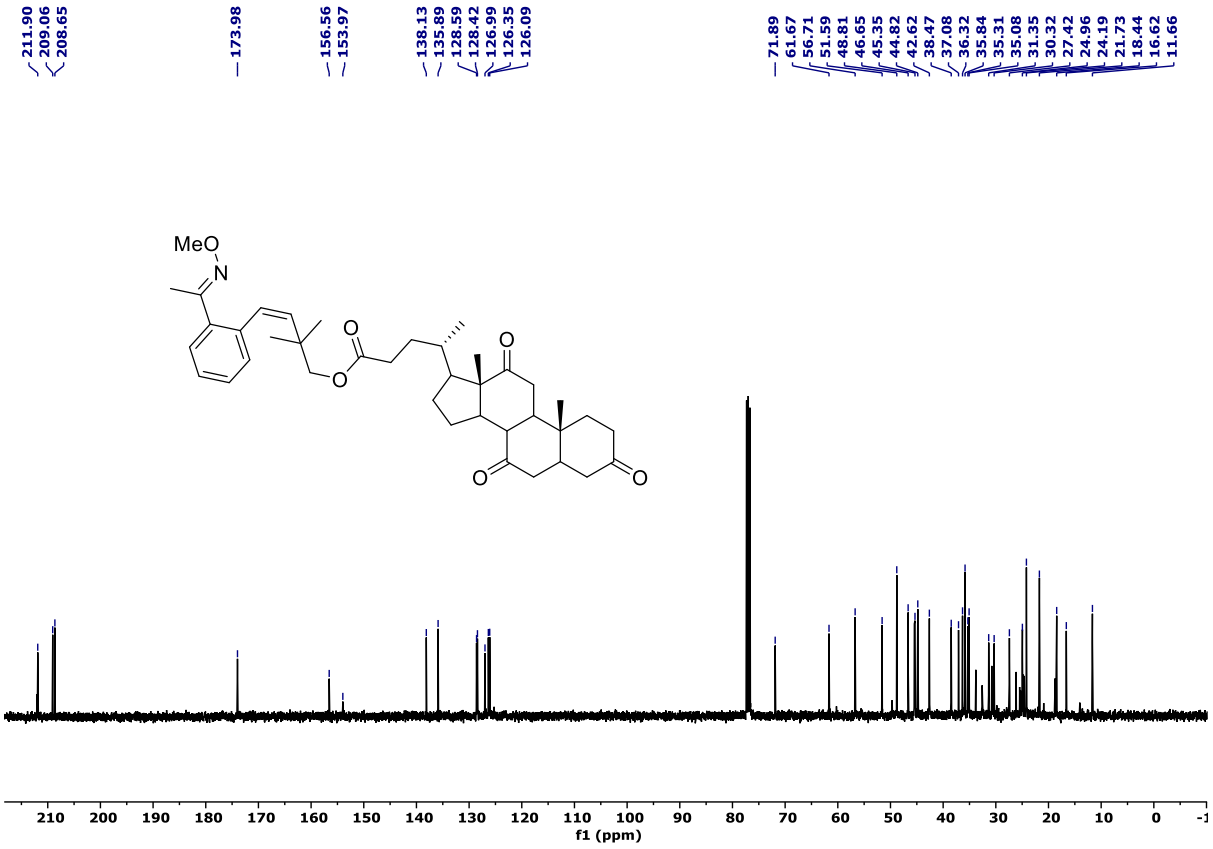
^{1}H and ^{13}C NMR Spectra of Compound **11d.** ($CDCl_3$ solvent was used, 500 NMR MHz)



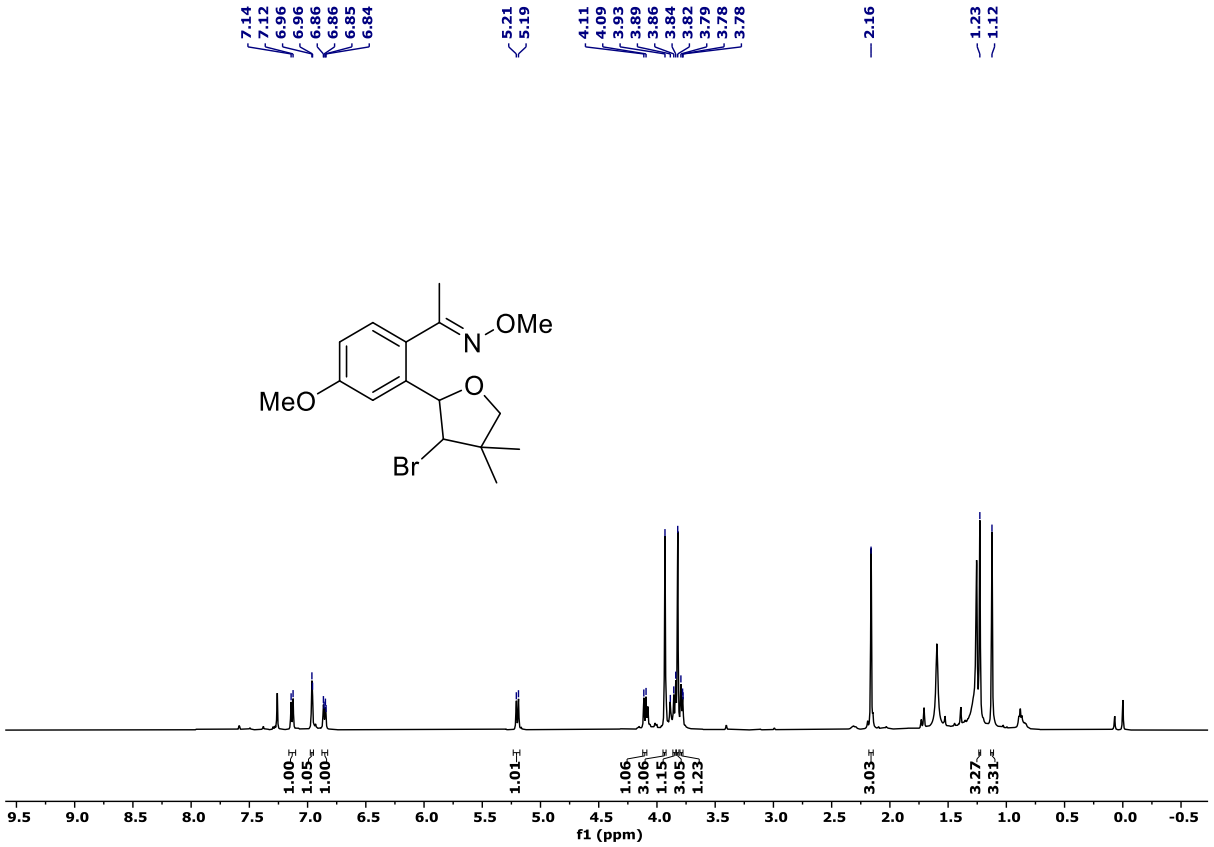


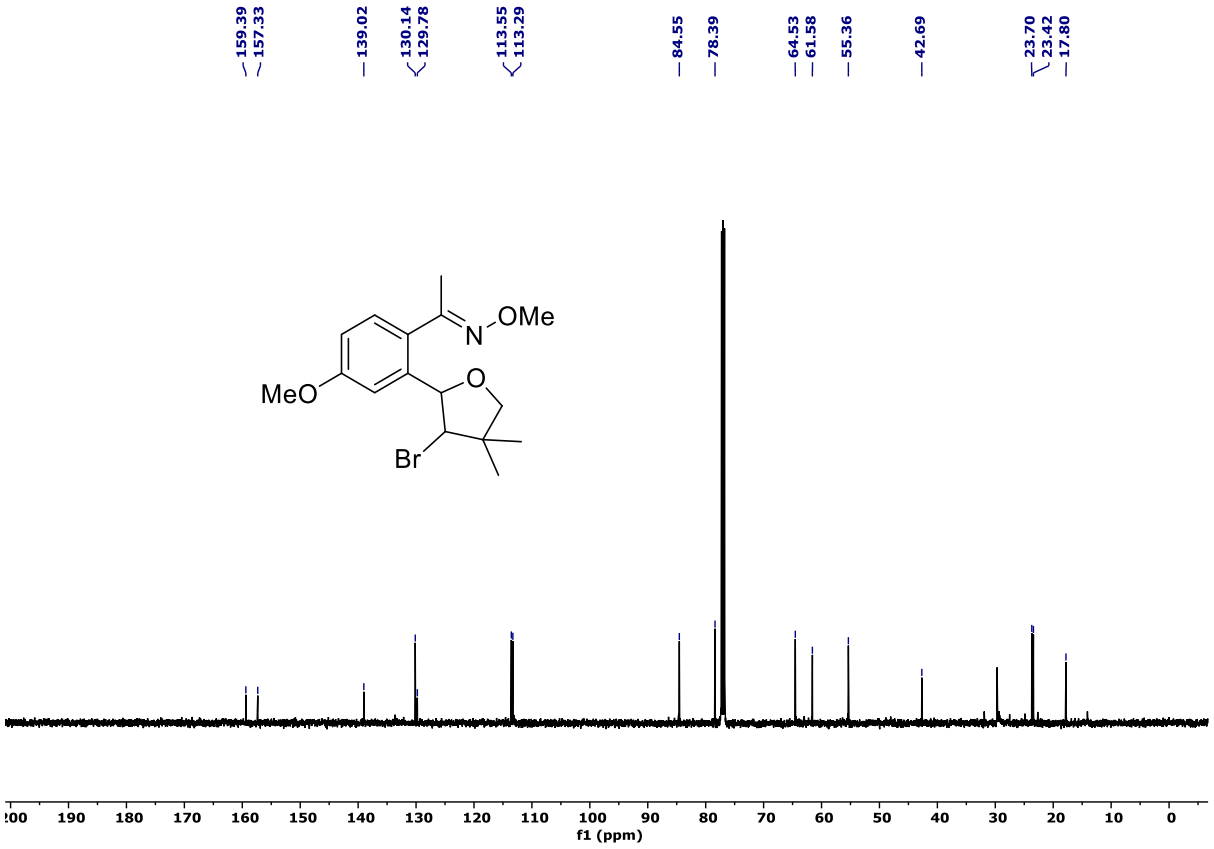
^{1}H and ^{13}C NMR Spectra of Compound **13.** ($CDCl_3$ solvent was used, 400 NMR MHz)





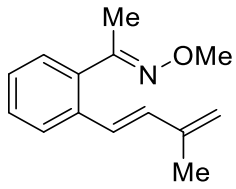
^{1}H and ^{13}C NMR Spectra of Compound **14.** ($CDCl_3$ solvent was used, 500 NMR MHz)





HRMS Data of Compound **15**.

(*E*)-1-(2-((*E*)-3-Methylbuta-1,3-dien-1-yl)phenyl)ethan-1-one *O*-methyl oxime (15).

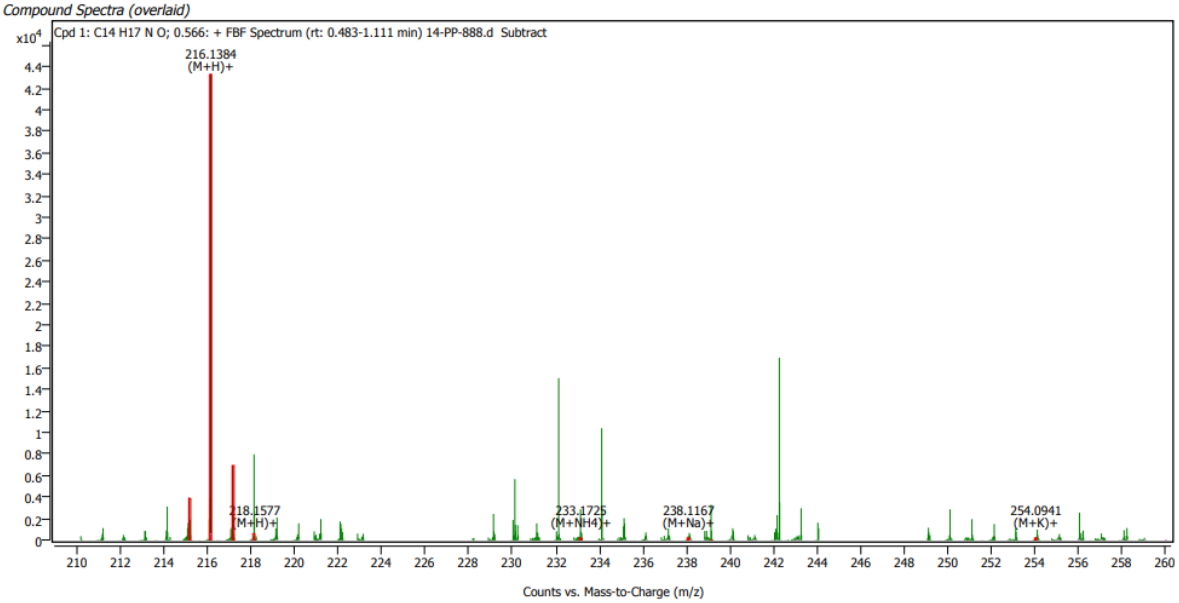


HRMS (ESI-TOF) m/z: $[M + H]^+$ Calcd for $C_{14}H_{18}NO$ 216.1388; Found 216.1384.

Compound Details

Cpd. 1: C14 H17 N O

Compound Spectra (overlaid)



Compound ID Table

Cpd	Formula	Mass (Tgt)	Calc. Mass	Mass	Species	Diff(Tgt.ppm)	mDa
1	C14 H17 N O	215.1310	215.1312	215.1345 216.1384 233.1725 238.1167 254.0941	M+ (M+H)+ (M+NH4)+ (M+Na)+ (M+K)+	0.99	0.21